Novel Applications of a 4-DMAP-derived Organic Electron Donor under Photoactivation

A thesis submitted to the University of Strathclyde in part fulfilment of regulations for the degree of Doctor of Philosophy in Chemistry

by

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This thesis is the result of the author's original research. It has been composed by the author and has not been previously submitted for examination that has led to the award of a degree.

Signed: Date:

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Contents

Abbreviations

°C	Degrees Celsius
A	Ampere
Ac	Acetyl
AIBN	Azo*bis*isobutyronitrile
APCI	Atmospheric pressure chemical ionisation
Aq.	Aqueous
Ar	Aryl
BMEA	Bismethoxyethylamine
bpy	2,2'-Bipyridine
Bu	Butyl
cat.	Catalyst
Cgr	Control gate electrode
CI	Chemical ionisation
Cm	Centimetre
CoB	Coenzyme B
COD	Cyclooctadiene
CoM	Coenzyme M
CP	Cyclopropane
Cy	Cyclohexyl
d	Doublet
DBB	di-*tert*-Butylbiphenyl
DBD	Doubly-bridged donor
DCE	1,2-Dichloroethane
DCM	Dichloromethene
de	Diastereomer excess
DEAD	Diethyl azodicarboxylate
DET	Double electron transfer
DiBAL-H	Diisobutylaluminium hydride
DMA	Dimethylacetamide
4-DMAP	4-Dimethylaminopyridine
DME	1,2-Dimethoxyethane

DMF	*N*,*N*-Dimethylformamide
DMSO	Dimethyl sulfoxide
DP	Diarylpropanes
$e^{\ominus}$	Electron
EI	Electron ionisation
eq.	Equivalent(s)
ESI	Electrospray ionisation
FAD	Flavin adenine dinucleotide
$FADH_2$	Reduced flavin adenine dinucleotide
g	Gram(s)
GC	Gas-phase chromatography
h	Hour
HMPA	Hexamethylphosphoramide
HOMO	Highest occupied molecular orbital
h*ν*	Irradiation
Hz	Hertz
IR	Infrared
J	Coupling constant
KHMDS	Potassium bis(trimethylsilyl)amide
LDA	Lithium diisopropylamide
LED	Light-emitting diode
Liq.	Liquid
LUMO	Lowest unoccupied molecular orbital
m	Meta
M	Molar (mole/litre)
m-CPBA	*meta*-Chloroperbenzoic acid
MCR	Methyl-coenzyme M reductase
mg	Milligram
min	Minute
mL	Millilitre
mol	Mole
mp	Melting point
Ms	Mesyl (methanesulfonyl)
MS	Mass spectrometry

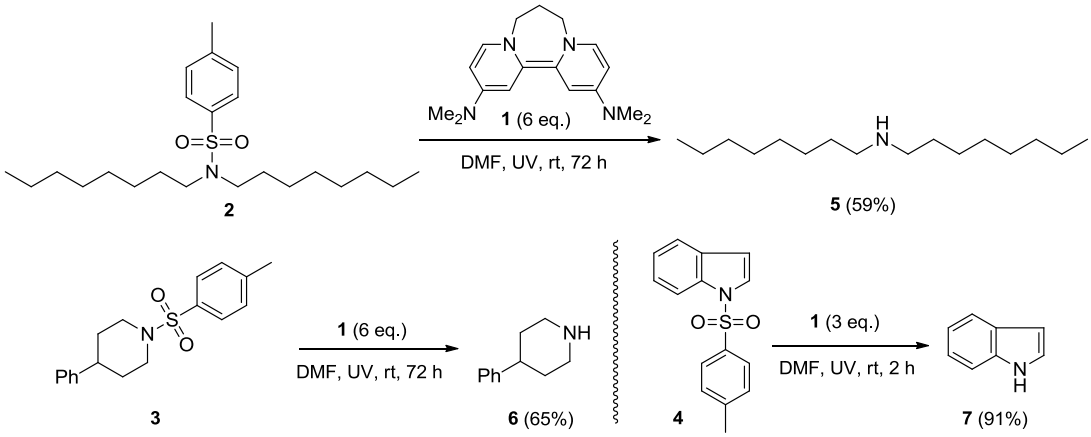
NAD	Nicotinamide adenine dinucleotide
NADH	Reduced nicotinamide adenine dinucleotide
NBS	*N*-Bromosuccinimide
nm	nanometer
NMP	*N*-Methyl-2-pyrrolidone
NMQ	*N*-Methylquinolinium
NMR	Nuclear magnetic resonance
n*O*e	Nuclear overhauser effect
o	*Ortho*
p	*Para*
PET	Photo-induced electron transfer
Ph	Phenyl
Piv	Pivaloyl
PMDTA	Pentamethyldiethylenetriamine
ppm	Parts per million
ppy	2-Phenylpyridine
Pr	Propyl
q	Quartet
rt	Room temperature
s	Singlet
sat.	Saturated
SCE	Saturated calomel electrode
SED	Super-electron donor
SET	Single electron transfer
SHE	Standard hydrogen electrode
S.M.	Starting material
t	Triplet
TDAE	1,1,2,2-Tetra(dimethylamino)ethene
OTf	Triflate (trifluoromethanesulfonate)
THF	Tetrahydrofuran
TLC	Thin layer chromatography
TMEDA	Tetramethylethylenediamine
TTF	Tetrathiafulvalene
UV	Ultra-violet

vs.	Versus
V	Volt
δ	Chemical shift

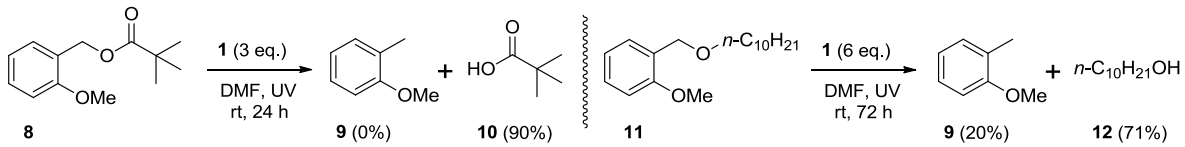
Abstract

4-DMAP-derived neutral organic super-electron-donor **1** has previously been successfully applied to a number of electron transfer reactions under thermal activation in the Murphy group. The research programme focuses on the photoactivation of the donor **1** and its novel applications in achieving more demanding electron-transfer reactions.

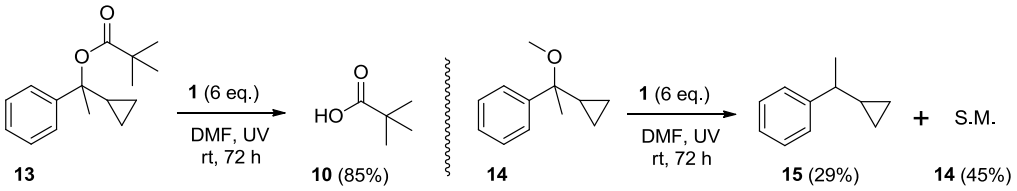
Chapter Two highlights the enhanced reducing power of the donor **1** under photoactivation. The reduction of the most challenging unactivated arenesulfonamides, where the nitrogen leaving group will be an unstabilised dialkylamide anion, *e.g.* **2** and **3**, had not been achieved under thermal activation of **1**. In contrast, photoactivated donor **1** has now provided the reduction of **2** and **3** in good yields, while activated sulfonamides *e.g.* **4** were reduced in excellent yields with lower loadings of **1** at room temperature compared with the thermal activation.



Chapter Three investigates metal-free reductive C-O bond fragmentations of benzylic esters and ethers with photoactivated donor **1**. Benzylic esters *e.g.* **8** were reduced to acids *e.g.* **10** via SET process and the complete absence of isolated toluenes *e.g.* **9** was attributed to trapping of benzyl radical intermediates with the radical-cation of **1**. Interestingly, benzylic ethers *e.g.* **11** provided reduced products **9** and **12** from either side of the ether moiety, and the generation of **9** indicated the presence of benzyl anion intermediates that were arising via a DET process.

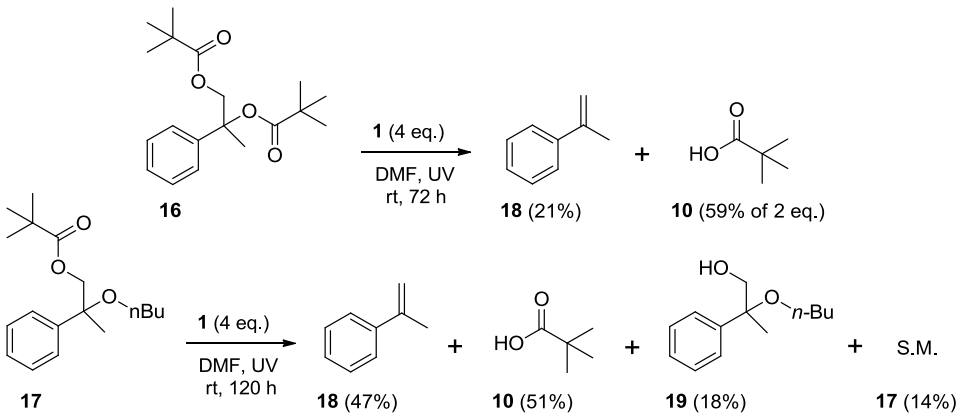


To test whether the benzylic radicals were mandatory intermediates in these cleavages, cyclopropyl substrates **13** and **14** were prepared and tested. Cyclopropyl ester **13** afforded acid product **10** only and this supported the trapping of radical intermediates formed via a SET process. On the other hand, cyclopropyl ether **14** afforded intact cyclopropane **15** that could not have arisen from a benzylic radical intermediate; rather the benzylic anion must be its precursor, supporting a DET process in reaction of **14**.



13 **10** (85%) **14** **15** (29%) **14** (45%)

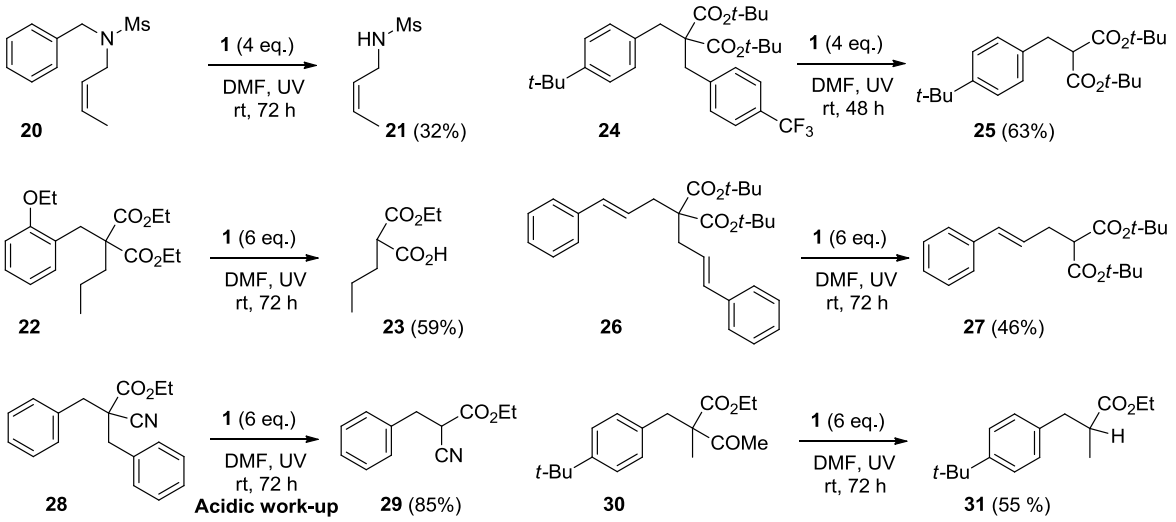
To probe further for benzylic anion intermediates, substrates **16** and **17**, containing not only a benzylic leaving group but also a potential leaving group (pivalate) in the adjacent β-position, have been designed and synthesised. Upon photoactivation, substrate **17** provided a considerably better yield of α-methylstyrene **18** compared with substrate **16** and supported a DET process in the ether cleavage seen in the challenging substrate **17**.



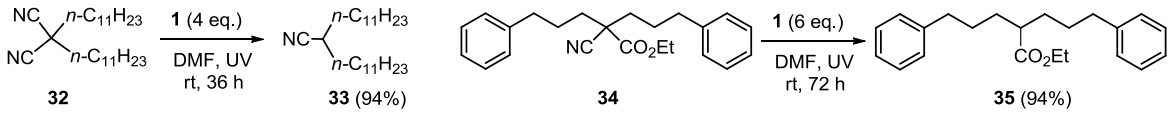
16 **18** (21%) **10** (59% of 2 eq.)

17 **18** (47%) **10** (51%) **19** (18%) **17** (14%)

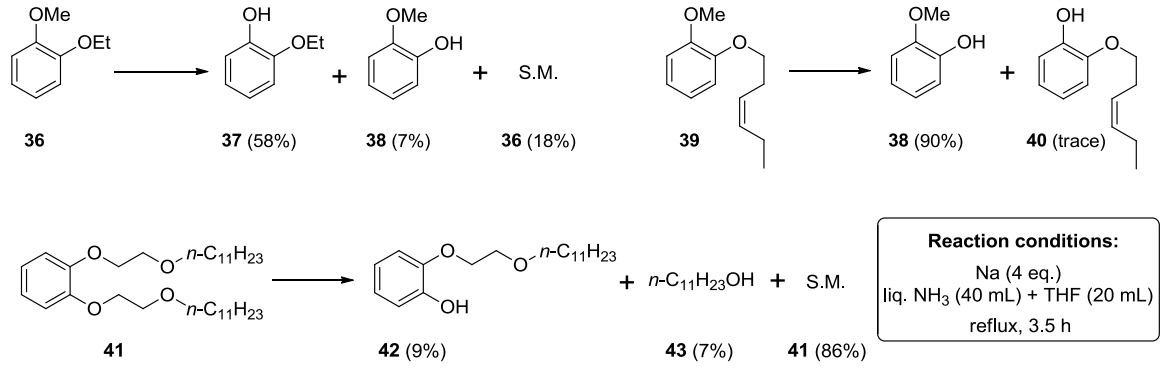
Chapter Four describes briefly the discovery of benzylic C-N bond cleavages *e.g.* **20** and provides a detailed account of challenging benzylic C-C σ-bond fragmentations under photoactivation of **1**. This chemistry is perfectly general as seen when it was extended to substrates including *e.g.* electron-rich **22**, electron-poor **24**, dicinnamyl **26** (for an example of homologous cleavage) and cyanoester **28**. All these reactions proceeded through a SET process as evident from the complete absence of toluene products. However, β-ketoester **30** provided fragmentation of the acyl group and this was further supported by Spartan calculations.



Chapter Five discusses the decyanation of malononitriles *e.g.* **32** and cyanoacetates *e.g.* **34** under photoactivation of the donor **1** and provided an alternative to the traditional methods involving metal reagents such as SmI_2 and carcinogenic solvents *e.g.* HMPA. Decyanation of malononitriles was faster than that of cyanoacetates and required lower loadings of **1**.



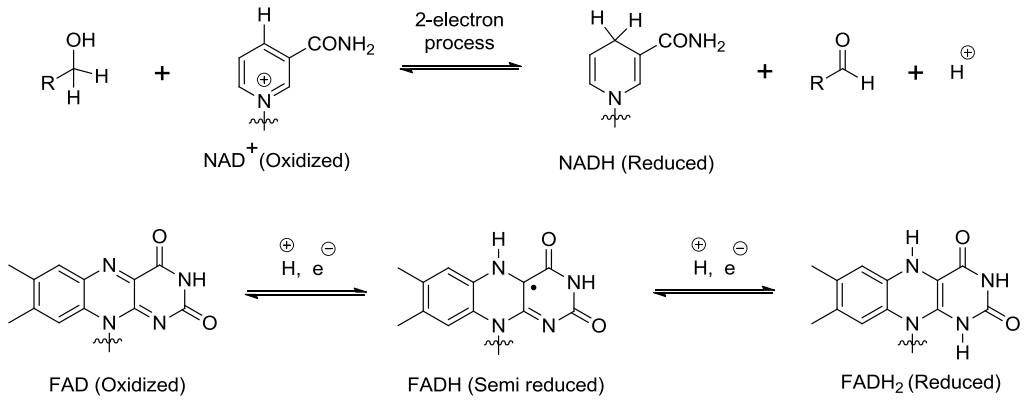
Chapter Six provides an insight into regioselective ArO-C bond cleavages of *ortho*-dialkoxybenzenes, under Birch conditions. The site of fragmentation, generally, depends upon the combined stability of the fragmented species. It was also found that the greater the stability of the charge on the alkyl group, the greater was its ease of formation.



Chapter Seven provides the detailed experimental procedures and data for the compounds discussed in the Chapters two to six.

1 Introduction to Reductive Electron-Transfer Reagents

Oxidation and reduction reactions are the backbone of biological processes. In metabolism, nicotinamide adenine dinucleotide NAD^+ (and NADH) and flavin adenine dinucleotide FAD (and $FADH_2$) are biologically very important coenzyme redox pairs.[1] NAD^+ is generally reduced by alcohols to NADH and this is a reversible process involving two electrons (Scheme 1.1). However, the important thing to notice here is the absence of metals in these redox reactions.



Scheme 1.1

In the laboratory, most reagents used in electron-transfer reactions are based on either metals or organometallic compounds.[2] Organic reducing agents are under-represented and so this provides a rich scope for discovery of new reactions and selectivity. This suggested a new avenue of research with purely organic reducing reagents, which are environmentally benign and, although equally powerful, or even less powerful, than classical metal-based reagents, can carry out difficult reductions under mild conditions. These reactions can be carried out in organic solvents using conventional glassware at room or elevated temperatures or, as in this work, under UV conditions. These neutral organic electron donors provide new selectivities and are pushing the boundaries of reactivity to improve various aspects of classical electron transfer reactions. This thesis will describe the observations of my study and the elegance of neutral organic electron donors as electron-transfer reagents in achieving very challenging transformations.

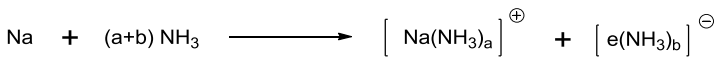
This chapter provides an introduction to electron-transfer reagents and also serves as background to the work performed during these research studies. Section 1.1 discusses electron-transfer reactions mediated by metals and metal complexes. These reagents include alkali metals, with particular focus on Birch reductions, transition metals and lanthanides. Section 1.2 summerises the sequential development of neutral organic super electron donors from the model tetrathiafulvalene (TTF) entity and their applications in electron-transfer reactions. Section 1.3 covers the theme of photo-induced electron transfer chemistry and describes enhanced reactivity of the excited neutral organic super electron donors. Finally, sections 1.4-1.7 deal with literature reports of various transformations setting the research in this thesis in context.

1.1 Electron-transfer reactions mediated by metals and metal complexes

Electron-transfer reactions are one of the major parts of organic chemistry. To a large extent, electron-transfer chemistry is dominated by metals and metal-based reagents. Therefore, this section highlights various metal-based electron-transfer reactions.

1.1.1 Alkali metals

Alkali metals (Li, Na, K) are the strongest reducing agents due to their very easy loss of electrons, and their oxidation potentials are the measure of their reactivity. Oxidation potentials of metals (which are the same as reduction potentials of their cations), generally, vary with solvent due to variation in solvation of the cation. The more negative the measured potential, the more powerful the reductant. Sodium in liquid ammonia produces solvated sodium cations along with deep-blue solvated electrons (Scheme 1.2).[3]



Scheme 1.2

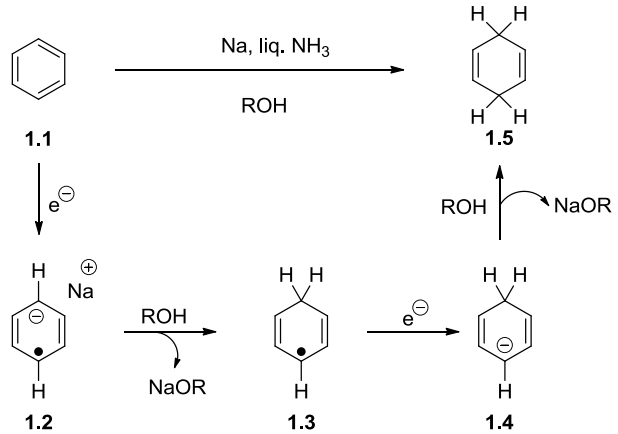
Standard redox potentials of these metals, E^o, in water are shown in Fig. 1.1[3] and illustrates the relative reducing power of these metals.

Half reaction	E^o (V)
$Li^{\oplus} + e^{\ominus} \rightarrow Li$	-3.045
$K^{\oplus} + e^{\ominus} \rightarrow K$	-2.925
$Na^{\oplus} + e^{\ominus} \rightarrow Na$	-2.714

Figure 1.1: Standard reduction potentials of alkali metal ($Li^{\oplus}$, $Na^{\oplus}$, $K^{\oplus}$) cations

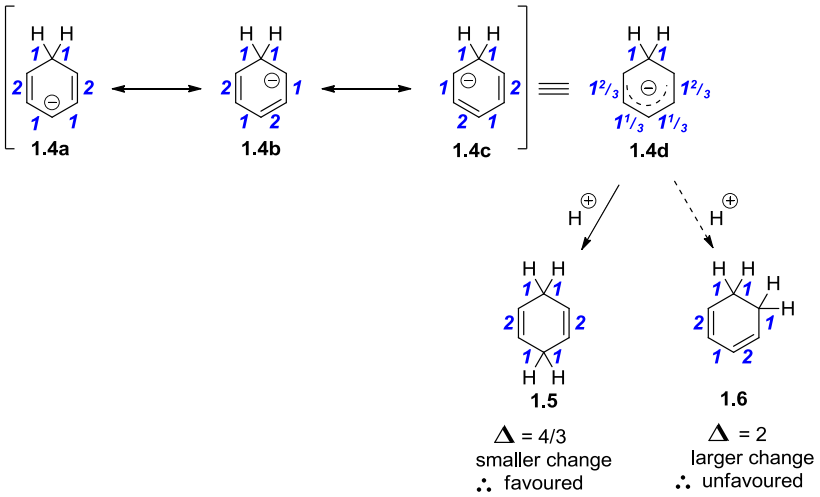
Birch reduction[4-6] is one of most well recognised reactions using alkali metals in liquid ammonia and this was discovered in 1940's by Arthur J. Birch. It is an elegant and simple method to access dihydro-counterparts from benzenes and benzene-derived compounds, although it suffers from poor selectivity due to high reducing power of these metals. During the reaction, the metal dissolved in liquid ammonia produces a blue coloured solution of solvated electrons. These solvated electrons are then transfered to the LUMO of the substrate to provide the radical-anion of the substrate.

Sodium in liquid ammonia is often used together with a proton source, such as an alcohol, in Birch reactions. As shown in Scheme 1.3,[7] after the metal, here Na, is dissolved in liquid ammonia, it produces solvated electrons and one of these is transferred to benzene **1.1** to form a radical-anion **1.2**. This is then protonated by the alcohol, such as ethanol or tertiary butanol, to form radical **1.3**. This radical **1.3** is further reduced to anion **1.4** upon accepting a second electron, which finally takes another proton from the alcohol to produce cyclohexadiene **1.5**, a 1,4-diene.



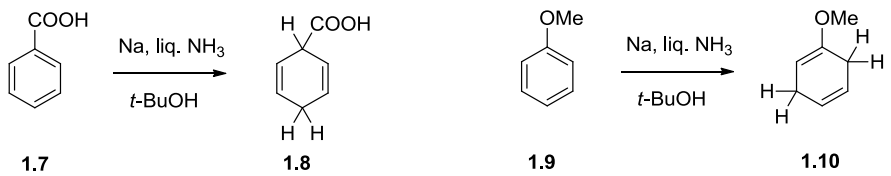
Scheme 1.3

It is quite surprising that 1,4-diene **1.5**, a thermodynamically less favoured product, is formed preferentially to a conjugated 1,3-diene **1.6**. This can be explained by the principle of least motion,[8] which proposes that the product will be formed via the pathway which involves least change of atomic position and electronic configuration. This is further explained in Scheme 1.4. In this method, each bond is assigned with a value (1 for a single bond and 2 for a double bond). Structure **1.4** can have three resonance-stabilised structures **1.4a**-**1.4c**. After assigning the bond values, the average bond values are shown in structure **1.4d**. Thus, upon protonation of **1.4d** to form 1,4-diene **1.5**, the smaller overall change in bond orders (Δ = 4/3) occurs while the change (Δ = 2) is higher for forming 1,3-diene **1.6**.



Scheme 1.4

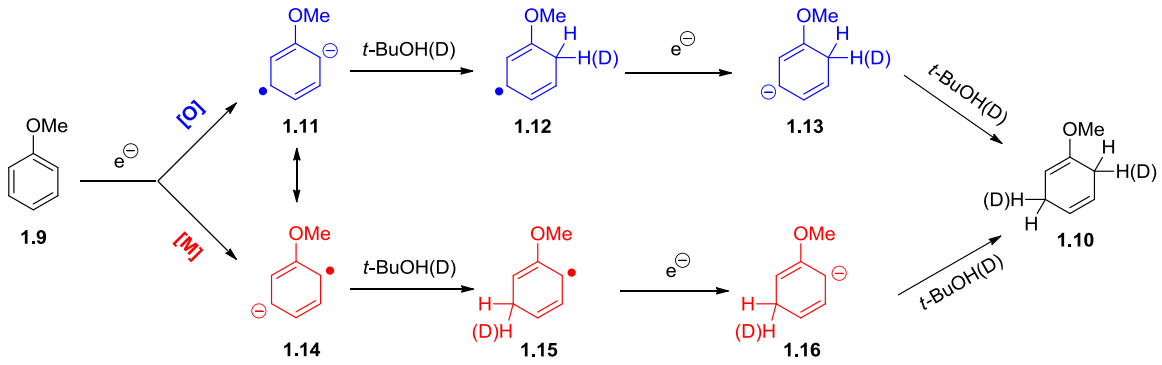
Birch reduction of electronically different benzenes provided regioselective products and this is illustrated in Scheme 1.5. Benzoic acid **1.7**, containing an electron-withdrawing group, provided 1,4-diene **1.8** via *ipso*, *para* reduction. But anisole **1.9**, containing an electron-donating group, provided 1,4-diene **1.10** via *ortho*, *meta* reduction. Again, the generation of these products can be explained by the principle of least motion,[8] which favours the formation of 1,4-dienes over conjugated dienes.



Scheme 1.5

The issue of selective reaction pathway, particularly in anisole **1.9**, was studied extensively and opened a debate on the order of protonation at *ortho*- and *meta*- positions. In **1.9**, the reaction can proceed through two different pathways labelled as [O] for first protonation at the *ortho*-position and [M] for first protonation at the *meta*-position, with both these pathways leading to the same product (Scheme 1.6).

In the path [O], initial electron-transfer occurs to form the radical-anion that can be represented as **1.11**, bearing the greatest anionic character *ortho* to the methoxy group. Protonation at this site leads to radical **1.12** that is further reduced to a carbanion *meta* to the methoxy group **1.13**. This carbanion can be protonated rapidly and provide **1.10** as a final product. Alternatively as shown in path [M], the initial electron-transfer can also lead to the same radical anion but represented as **1.14**, bearing the greatest anionic character *meta* to the methoxy group and can also lead to the same final product after following the subsequent steps shown.

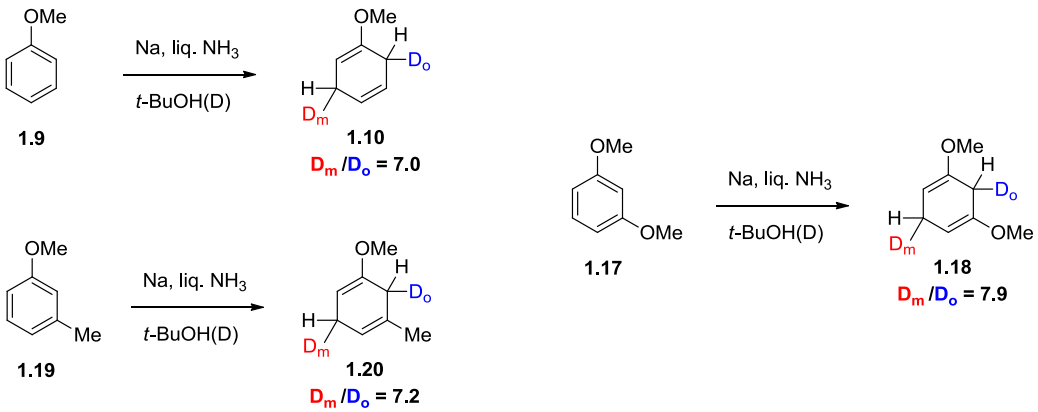


Scheme 1.6

Birch proposed, in his early paper,[9] that path [M] was more feasible, assuming the greatest electron density at the *meta*-position of the radical-anion **1.14**. Later,[10] Zimmerman suggested path [O] to be the reaction pathway to be followed based on his Hückel calculations on anisole. He revealed that the *ortho*-position to the methoxy group is the most electron-rich position in the radical-anion and supported the initial protonation at the *ortho*-position. Later,[11] Birch suggested protonation at both sites with a slight preference for the *ortho* site based on his *ab initio* calculations and argued that both mechanisms are operating. As this debate got more intense, Zimmerman attempted to solve this problem based on both practical and theoretical approaches.[12,13] He devised a

method based on the deuterium isotope effect and used partially deuterated *tert*-butyl alcohol (*ca*. 2% deuterated) as a protonating source.

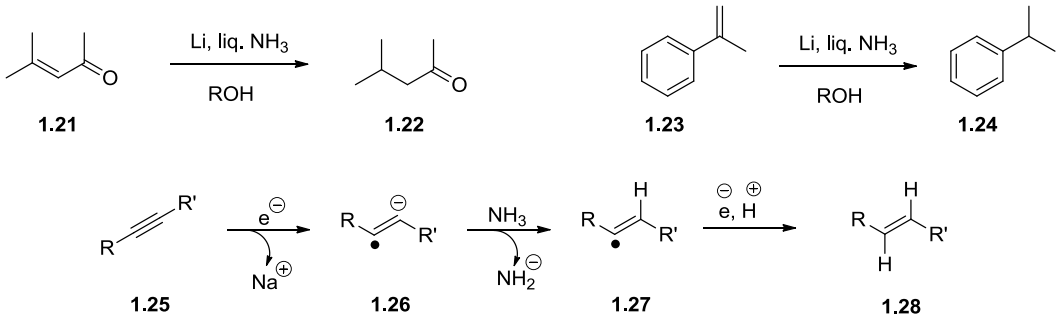
Since radical-anions are less basic than carbanions,[14] these radical-anions could act as a more selective base[15] in deuterium incorporation. Thus when running a competition reaction in the presence of partially deuterated *tert*-butyl alcohol, less deuterium should be incorporated into the more selective radical-anion, and conversely more deuteration would be expected at the site of the more reactive carbanion. Hence, if [O] is the reaction pathway to be followed, then protonation of the radical-anion **1.11** at the *ortho*-position to the methoxy group should lead to less deuterium incorporation than at the *meta*-position, where the anion **1.13** is protonated. However, if pathway [M] is followed, then the *meta*-position should have less deuterium incorporation than the *ortho*-position. This concept was applied to the reductions of anisole **1.9**, 1,3-dimethoxybenzene **1.17** and 3 methoxytoluene **1.19** (Scheme 1.7) with the finding that there was a strong preference (7:1) for the deuteration at the *meta*-position over the *ortho*-position. This supports the [O] pathway offered by Zimmerman. There was concern about the proton/deuterium exchange reaction, which could alter the ratio of deuterium incorporation at the *ortho*- and the *meta*- positions. However, the controled reactions that were carried out with the dienes under basic conditions, simulating the Birch conditions, did not provide any alterations.



Scheme 1.7

Ordinary olefins are usually inert under classical Birch reaction conditions due to their high energy LUMO. But, conjugated and phenyl-substituted alkenes are easily reduced due to the decrease in the energy of the LUMO by conjugation. However, isolated alkynes can be reduced to the corresponding *trans*-alkenes under these conditions. Product

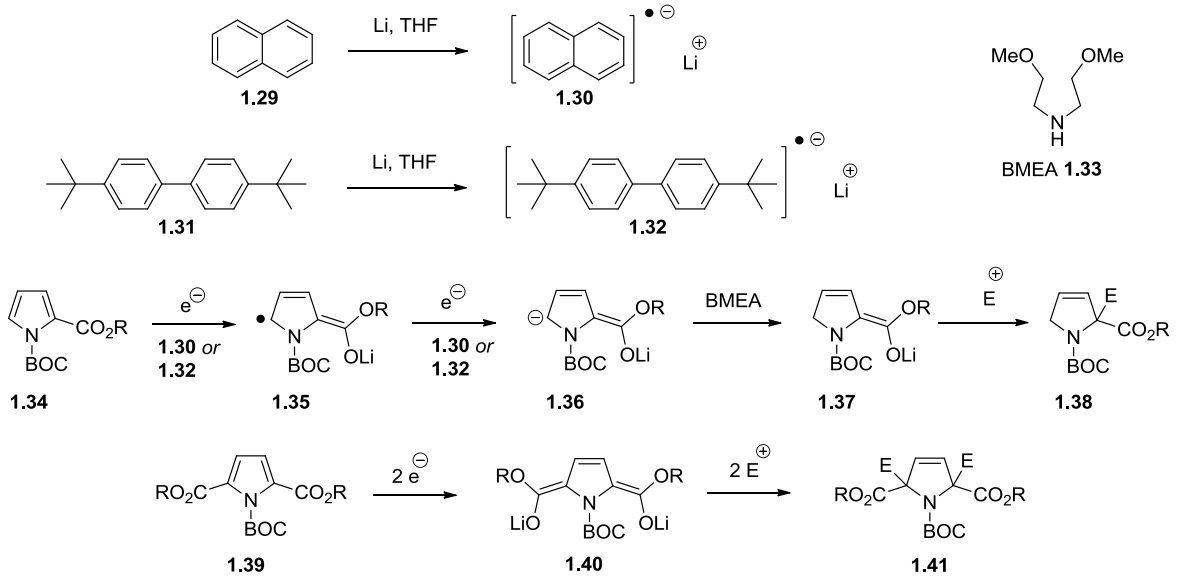
selectivity in reduction of alkynes arises from the electronic repulsion between the radical and anionic charge in radical-anion, which prefers to have an *E*-configuration (Scheme 1.8). No additional proton source is required as the vinyl anions are basic enough to deprotonate ammonia.[15,16]



Scheme 1.8

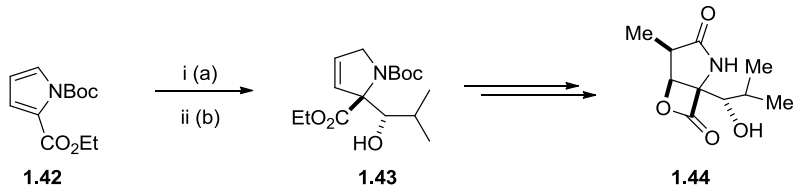
Although the Birch reaction is widely used in the reduction of arenes and derived compounds, it suffers from a number of disadvantages such as the difficulty in handling alkali metals and ammonia gas, cryogenic temperatures, special design of apparatus, poor selectivity and low tolerance of functional groups. Many research groups have attempted to improve the reaction by showing modifications to overcome the above limitations and these are briefly discussed in the following pages.

Recently, Donohoe *et al*. made an important contribution to Birch reductions by using lithium in THF *i.e*. ammonia-free conditions for the reduction of electron-deficient 2,5-disubstituted pyrroles (Scheme 1.9).[17-20] In these studies, they have used naphthalene **1.29** or 1,4'-di-*tert*-butylbiphenyl (DBB) **1.31** as electron carriers. In these reactions, lithium donates an electron to naphthalene **1.29** or DBB **1.31** and forms the corresponding radical-anion **1.30** or **1.32**, which could give away electrons to the electron-deficient protected pyrroles **1.34** or **1.39** generating anionic intermediates **1.36** and **1.40** respectively. These intermediates can be trapped by protonation with bismethoxyethylamine (BMEA) **1.33** and an equivalent of electrophile ($E^{\oplus}$) or, alternatively, two equivalents of electrophile ($E^{\oplus}$) to result in reduced products **1.38** and **1.41** respectively (Scheme 1.9).



Scheme 1.9

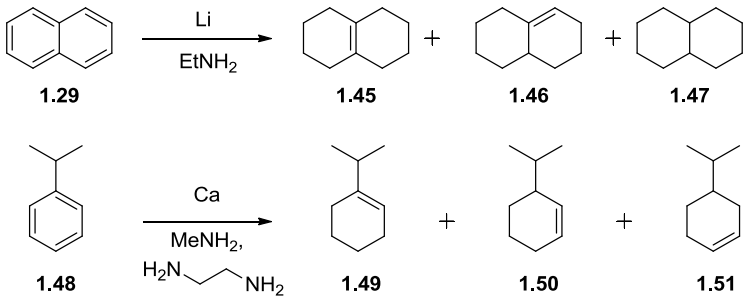
More recently, Donohoe and co-workers successfully applied the above ammonia-free Birch reaction conditions to the total synthesis of *clasto*-Lactacystin β-lactone **1.44** (Scheme 1.10).[20]



Reaction conditions: a) Li, DBB, BMEA, -78 ^{o}C; b) $MgBr_2$, Et_2O, *i*PrCHO

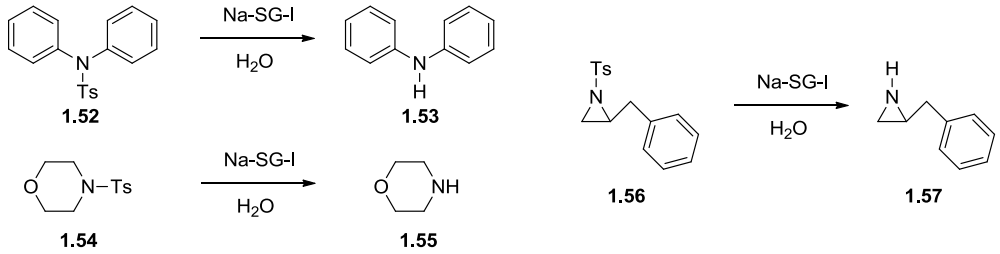
Scheme 1.10

Benkeser modified the Birch reaction by employing low molecular weight amines, such as ethylamine, in the place of liquid ammonia and using lithium and calcium as metals; this reaction is popularly known as Benkeser reaction.[21,22] As these alkylamines are liquids at ambient temperaures, it adds practical advantage to the reaction. Later, Benkeser replaced lithium with calcium, as the handling of calcium is easier than lithium or sodium. Benkeser conditions are significantly more reducing than Birch conditions, leading to *mono*-olefin products. When naphthalene is subjected to lithium in ethylamine, $\Delta^{9,10}$ and $\Delta^{1,9}$-octalin **1.45** and **1.46** were produced along with decalin **1.47**. These workers successfully applied their system to reduce **1.48** to the corresponding cyclic *mono*-alkenes **1.49-1.51** (Scheme 1.11).



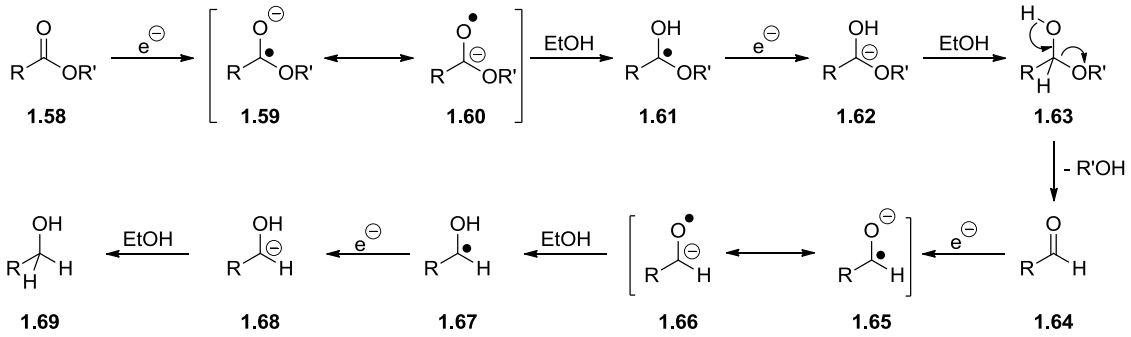
Scheme 1.11

Very recently Lefenfeld and co-workers developed solid alkali metal-based reductions by using non pyrophoric alkali metal-silica gel (M-SG) reagents.[23-25] These reagents can be prepared by thermal absorption (intercalation) of alkali metals into nanostructured silica. Liquid Na-K alloys are added to silica gel at different temperatures in three different stages providing three varieties of materials and these are denoted by M-SG-0 (at room temperature), M-SG-I (heated at 150 ^{o}C) and M-SG-II (heated at 400 ^{o}C). Through this method, about 40% of metal can be incorporated into these materials and the reducing power of the parent metals is almost retained. M-SG-0 materials are strongly reducing pyrophoric powders while M-SG-I materials are non-pyrophoric, free-flowing black powders with reactivity equivalent to neat alkali metals. M-SG-II materials have less reducing power compared with the other two varieties. These materials were successfully utilised in the reduction of sulfonamides (Scheme 1.12).[23-25]



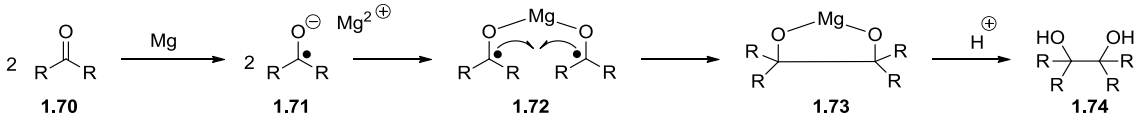
Scheme 1.12

Reduction of ester groups with alkali metals is a classical reaction and popularly known as the Bouveault-Blanc reduction,[16,26] although this is outdated due to the emergence of metal hydrides based on aluminium and boron. When ester compounds are submitted to sodium in protic solvents such as ethanol, they are readily reduced to alcohols. In this process, esters are reduced to aldehydes first and further reduction of intermediate aldehydes provides alcohols (Scheme 1.13).



Scheme 1.13

However, in aprotic solvents such as benzene or diethyl ether, no protons are readily available for radical-anion **1.59** to convert into radical intermediates such as **1.61** and leads to acyloin products.[27] However, starting with aldehydes or ketones under aprotic conditons, the concentration of ketyl radical-anions such as **1.71** steadily increases and eventually leads to coupling of these ketyl radicals and this is popularly known as pinacol coupling.[28] But, the success of this radical-coupling depends upon minimisation of the repulsion between the anionic charges. When divalent magnesium is used in these reactions, it binds to the anionic sites and helps the radicals to couple together and ultimately leads to diols (Scheme 1.14).

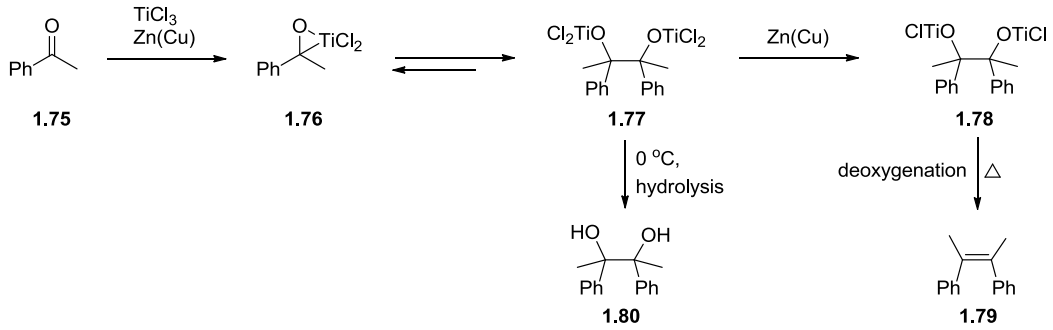


Scheme 1.14

1.1.2 Transition metals

Many transition metals such as Sc, Ti, V, Cr, Mn, Fe, Co, Ni, Cu and Zn are widely used in electron transfer reactions.[29] However, only reduction with Ti is shown here to relay the flavour of these reduction processes.

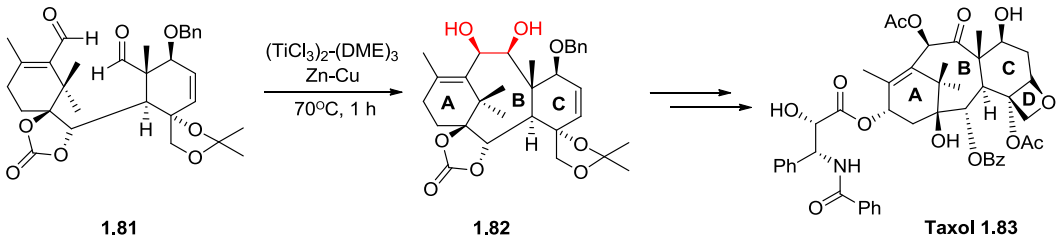
In the early 1970's, Mukaiyama,[30] Tyrlik[31] and McMurry[32] independently and almost simultaneously used low valent titanium species to couple carbonyl compounds in a similar fashion to pinacol coupling.[28] Later, this reaction was further developed by McMurry and became well known as the McMurry reaction.



Scheme 1.15

Several mechanisms have been discussed for this reaction.[33] Low-valent titanium species, which are generated by the reduction of $TiCl_3$ or $TiCl_4$ with $LiAlH_4$ or Zn/Cu, induce coupling of the carbonyls by single electron-transfer to the carbonyl groups, forming pinacolate **1.77**. Upon heating of the reaction mixture, deoxygenation occurs and results in alkene product **1.79**. However, the reaction can be stopped at intermediate **1.77** by lowering the temperature to 0 °C, and upon hydrolysis provides diol **1.80** as a product (Scheme 1.15).

The McMurry reaction was elegantly applied by a number of research groups in the total synthesis of various natural and non-natural products and it is worth mentioning Nicolaou's total synthesis of Taxol[34] in this context. The crucial cyclisation of **1.81** to form the ABC ring system in **1.82** was completed by using a highly optimised McMurry reaction as shown in Scheme 1.16.



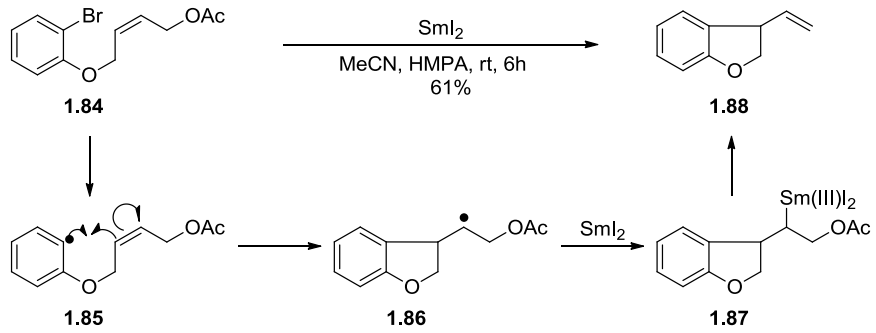
Scheme 1.16

1.1.3 Lanthanides

Lanthanides have been used in electron transfer chemistry for a long time but this field is greatly dominated by samarium reagents. Ever since Kagan developed the versatile coupling and reducing agent samarium diiodide in the late 1970's,[35,36] there has been

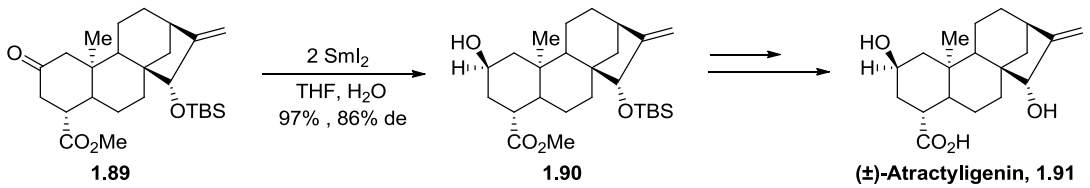
remarkable activity in finding new reactions in which this reagent can be used.[37] Several reviews have been published on the diverse reactivity of samarium(II) diiodide.[38-42] Samarium(II) iodide is typically prepared by reacting samarium metal with 1,2-diiodoethane under an inert atmosphere. The reducing power of samarium diiodide in THF is highly sensitive to the presence of co-solvents such as HMPA.[43,44] It has been shown that HMPA decreases the oxidation potential of SmI_2 from -1.33 to -2.05 V (*vs*. a $Ag/AgNO_3$ electrode in THF).[45]

Samarium(II) diiodide acts as a single-electron donor. There are a number of reports present in the literature, of which a few selected examples are described here. Radical cyclisation reactions are one of the important classes of reactions that are well studied with this reagent. Aryl halides such as **1.84** are readily reduced to aryl radical **1.85**, which then cyclises onto a suitably placed double bond generating cyclised radical **1.86**. This alkyl radical **1.86** couples with another SmI_2 molecule forming organosamarium(III) intermediate **1.87**, which may lead to other reactions (Scheme 1.17).[46]



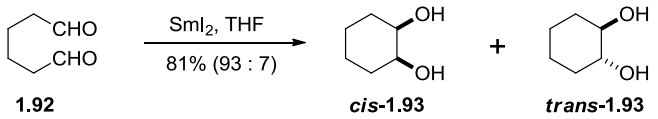
Scheme 1.17

Samarium(II) diiodide reduces carbonyl compounds to alcohols in the presence of a proton source such as water or an alcohol. Corey *et al.* successfully applied this reagent in the reduction of a ketone in the total synthesis of (±)-Atractyligenin **1.91** (Scheme 1.18).[47]



Scheme 1.18

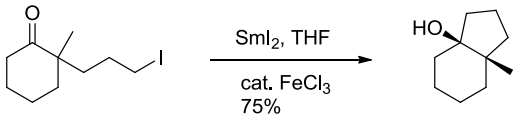
However, in aprotic solvents, as in Birch reactions (see Scheme 1.14), carbonyl groups undergo intramolecular pinacolic coupling reactions with this reagent. Hanessian *et al*. were the first to see this intramolecular pinacol coupling of dialdehydes *e.g.* **1.92** to vicinal diols *e.g.* **1.93** (Scheme 1.19).[48]



1.92 ***cis*-1.93** ***trans*-1.93**

Scheme 1.19

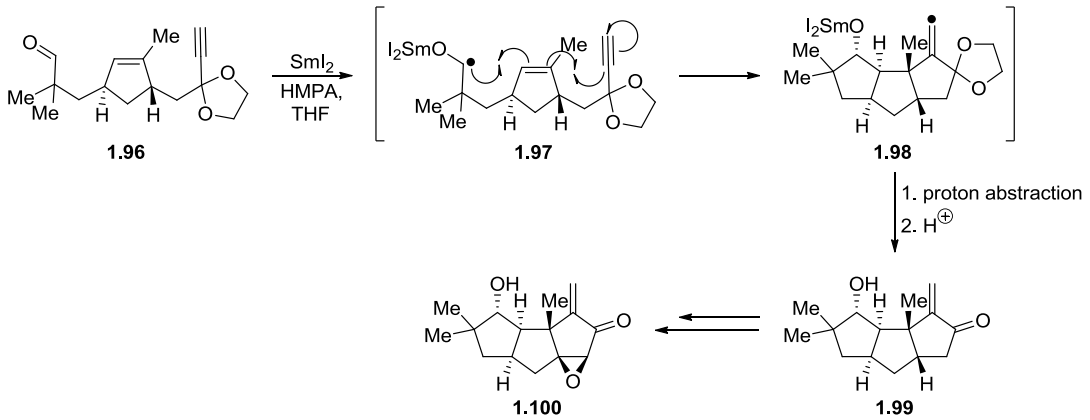
Molander *et al*. successfully applied samarium(II) diiodide in intramolecular Barbier reactions to construct bicyclic systems.[49] Before their discovery, there was no convenient method available to construct these bicyclic systems (Scheme 1.20).



1.94 **1.95**

Scheme 1.20

Curran *et al*. elegantly used samarium(II) diiodide in constructing complex moieties by exploring carbonyl reduction followed by tandem radical cyclisation processes. They successfully applied this strategy in the total synthesis of (±)-Hypnophilin **1.100** (Scheme 1.21).[50]

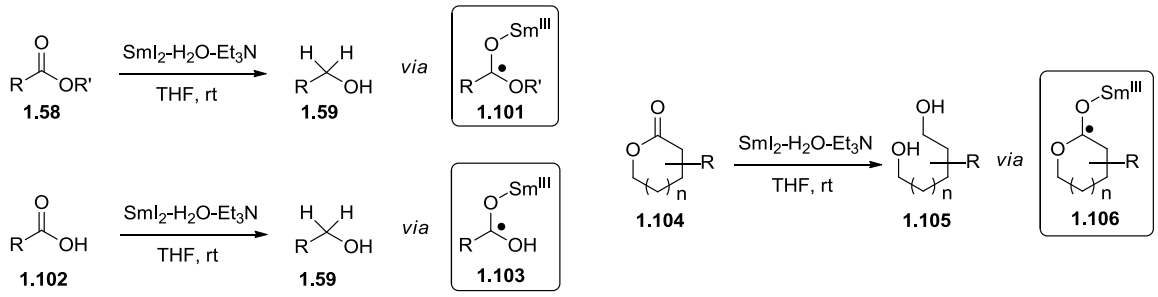


1.96 **1.97** **1.98** **1.99** **1.100**

Scheme 1.21

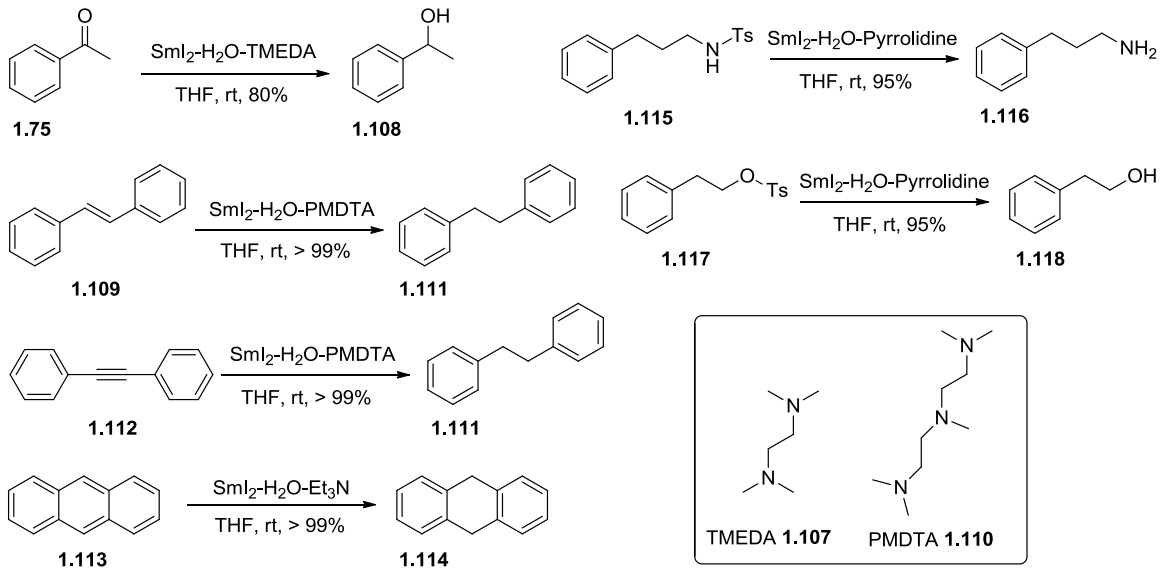
In recent times, Procter group has been actively involved in finding new applications for these samarium reagents. In a recent review,[51] these researchers highlighted the selective

reductive transformations using an SmI_2-water system. They have also utilised a SmI_2-water-amine system, first introduced by Hilmersson,[52] to achieve transformation of esters,[53] acids[54] and lactones[55] into their corresponding alcohols. These methodologies worked very well for all kinds of aryl, cyclic and acyclic substrates (Scheme 1.22).



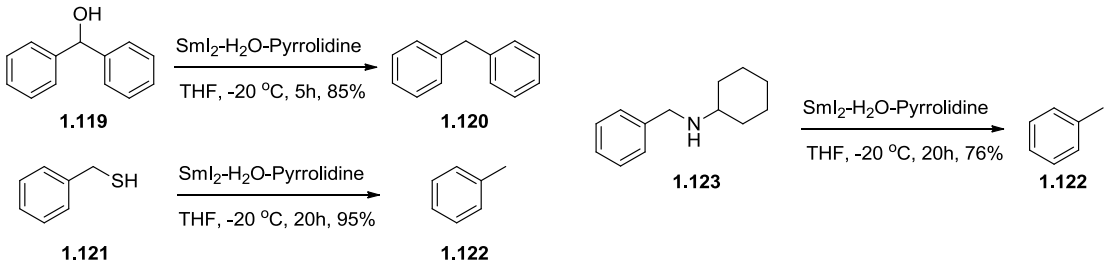
Scheme 1.22

Hilmersson and co-workers successfully applied SmI_2-H_2O-amine reaction conditions where the water and amine acted as co-solvents to achieve a number of instantaneous reductions of various functional groups such as ketones,[56,57] unsaturated hydrocarbons,[58,59] tosylamides[60] and tosyl esters[60] (Scheme 1.23).



Scheme 1.23

Recently, the Hilmersson group disclosed the reductive cleavage of benzyl-heteroatom bonds using the SmI_2-H_2O-amine system (Scheme 1.24).[61] Out of all these reductions, our interest lies in benzyl-heteroatom bond cleavages, and hence these reductions are discussed in detail in the later parts of this Introduction.



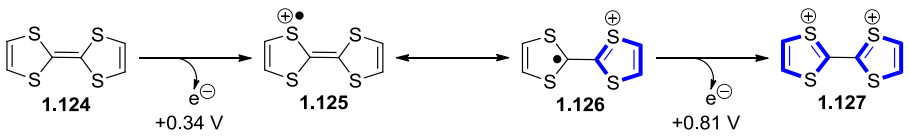
Scheme 1.24

1.2 Neutral organic electron donors

With the drawbacks associated with the classical metal or metal complex mediated electron-transfer processes, the use of alternative organic reagents has become increasingly popular. Neutral organic molecules that are capable of donating electrons to suitable substrates from their ground state or exicted states are clean and provide metal-free alternatives in electron-transfer processes.

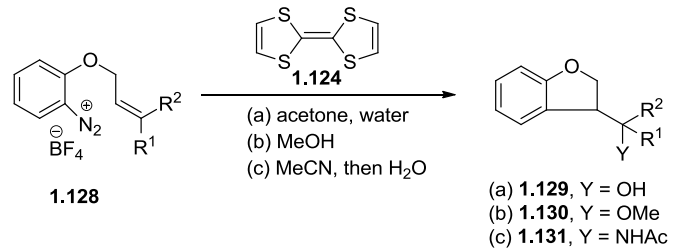
1.2.1 Early organic electron-transfer reagents

In the process of generating various organic electron transfer reagents, tetrathiafulvalene (TTF) **1.124** perhaps could be taken as a model system. TTF **1.124** is a neutral, air-stable organic compound containing four sulfur atoms that can donate electron density to the π-system, providing an electron-rich donor. TTF **1.124** was first synthesised by Wudl[62] in 1970 and, subsequently, semi-conducting properties of its salts, *e.g.* $[TTF^{\oplus}]Cl^{\ominus}$, were studied in 1972.[63] TTF **1.124** has been used extensively for its electron donor properties in materials chemistry, conducting polymers, photochemistry and also in the field of molecular switches.[64] However, its use as an electron donor in organic synthesis was limited before the work of Murphy and co-workers.[65] our laboratory used TTF **1.124** as an organic electron donor to achieve a number of electron transfer reactions under mild reaction conditions.[66] The driving force for electron transfer from TTF **1.124** is associated with the gain in aromatic stabilisation energy upon oxidation to radical cation **1.126** and dication **1.127** (aromatic rings are shown in blue in Scheme 1.25).



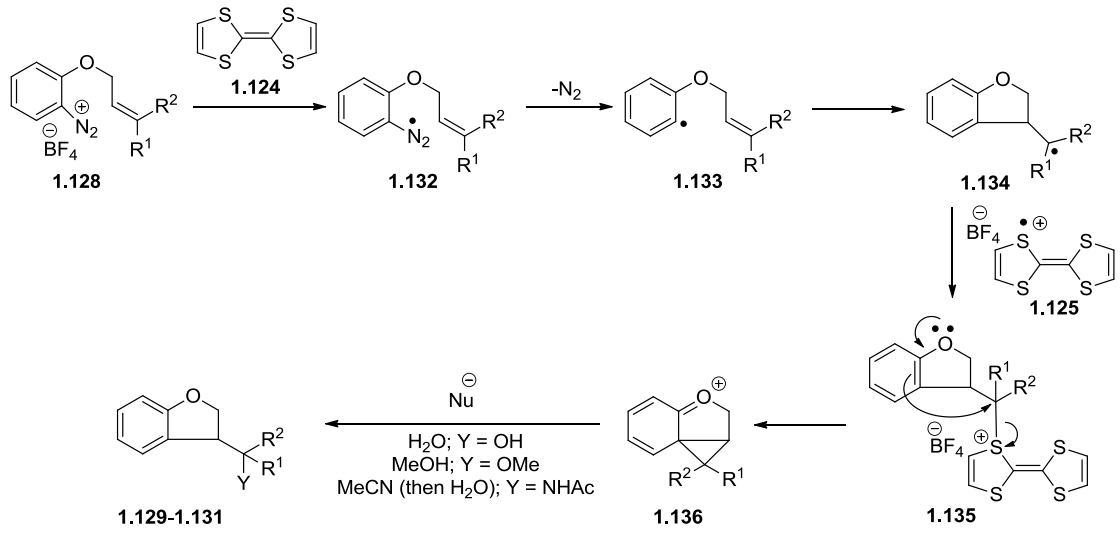
Scheme 1.25

TTF **1.124** has a first ionisation potential of +0.34 V *vs.* SCE and a second of +0.81 V *vs.* SCE in PhCN.[67] Initial electron transfer properties of TTF **1.124** with diazonium salts **1.128** are highlighted in a radical-polar crossover reaction[66] (Scheme 1.26).



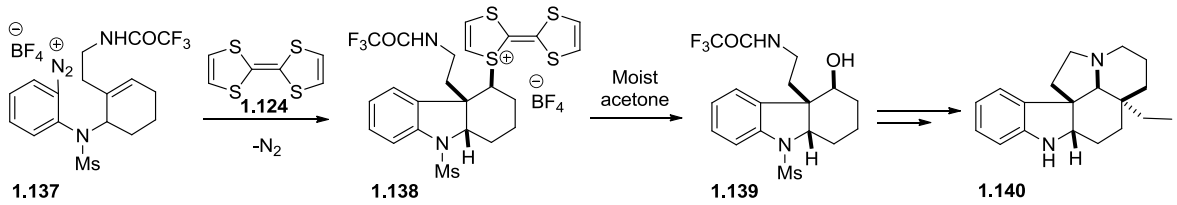
Scheme 1.26

Initially, an electron is transferred from the HOMO of TTF **1.124** to the LUMO of the arenediazonium salt **1.128** resulting in the unstable arenediazenyl radical **1.132**, which quickly gives **1.133** by loss of nitrogen gas. Aryl radical **1.133** cyclises rapidly onto the alkene and produces a more stable alkyl radical **1.134**. This alkyl radical **1.134** combines with TTF radical-cation **1.125**, which is produced by the loss of an electron from TTF **1.124**, to give polar intermediate **1.135**, defining crossover from radical species to polar species. Expulsion of the TTF **1.124** moiety from **1.135** gives rise to tricyclic intermediate **1.136**, which is then quenched with a number of nucleophiles to give various substituted dihydrobenzofuran products **1.129-1.131** (Scheme 1.27). Therefore the radical-polar crossover method successfully provided a synthetic route to functionalised dihydro-benzofurans.[68,69]



Scheme 1.27

The use of TTF **1.124** as an electron transfer agent has also been extended to the total synthesis of alkaloids such as (±)-aspidospermidine **1.140** (Scheme 1.28).[65,70] Electron transfer from TTF **1.124** to the diazonium salt **1.137** followed by cyclisation resulted in a [6,5]-fused ring system, leaving a cyclohexyl radical that reacts with TTF radical-cation **1.125** to form sulfonium salt **1.138**. Unimolecular solvolysis of **1.138** in moist acetone formed the corresponding alcohol **1.139**. This alcohol **1.139** was then converted to (±)-aspidospermidine **1.140** through a series of steps in stereoselective fashion. This demonstrates the usefulness of radical cyclisations in forming [6,5]-fused ring systems with *cis* geometry at the ring junction.



Scheme 1.28

Other powerful classes of sulfur-containing electron donors such as 2,2′-bis(1,3-dithiole) derivatives **1.141-1.143** (Fig. 1.2) have also been developed.[71,72]

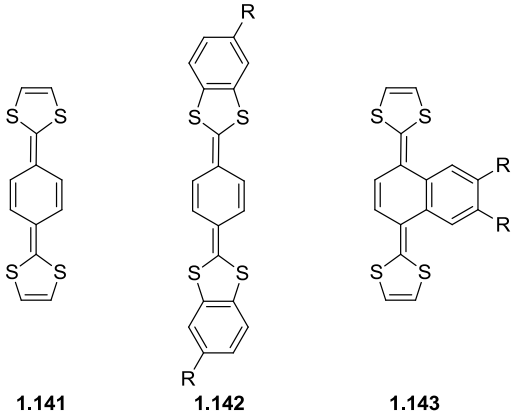
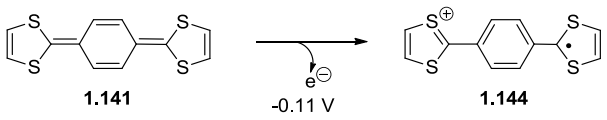


Figure 1.2: Other sulfur-containing electron donors

These donors utilise the aromatic stabilisation resulting from the formation of their radical cations (Scheme 1.29) and are promising organic electron donors reported to behave as "organic metals".[71] Donor **1.141** has the first oxidation potential of -0.11 V *vs*. SCE in MeCN,[71] which in comparison to the model TTF **1.124** (+0.28 V *vs*. SCE in MeCN),[71] demonstrates that **1.141** is a more powerful electron donor (Scheme 1.29). Unfortunately,

the synthesis of these donors is complicated and characterisation is not straightforward. So their use as organic electron donors is practically limited.



Scheme 1.29

Although diazonium salts were reduced by TTF **1.124**, attempts to reduce aryl or alkyl halides, known to be more difficult to reduce, were unsuccessful.[66] The reduction potential of bromobenzene is -2.43 V *vs.* SCE in DMF[73] while the more easily reduced iodobenzene has -1.91 V *vs.* SCE in DMF.[73] But, TTF **1.124** has a first oxidation potential of +0.37 V *vs.* SCE in DMF (Fig. 1.3)[74] which clearly illustrates that TTF **1.124** is not strong enough to reduce aryl halides and thereby invites the search for stronger electron donors.

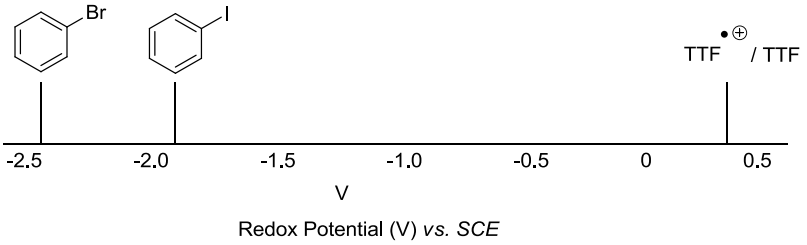
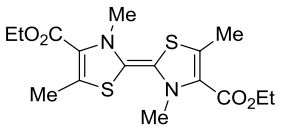


Figure 1.3: Reduction potentials of aryl halides *vs*. TTF **1.124**

The limitations of TTF **1.124** demonstrated the need for electron-rich atoms capable of pushing π-electron density into the neighbouring alkene. A variety of diazadithiafulvalenes such as **1.145** (Fig. 1.4)[75] were synthesised by replacing two sulfur atoms in TTF **1.124** with nitrogen. The first oxidation potential of **1.145** is -0.3 V *vs.* SCE in DMF.[76] The strong π-electron donating nature of nitrogen in comparison to sulfur makes **1.145** a more powerful electron donor than TTF **1.124**. However, diazadithiafulvalenes **1.145** undergo a side-reaction with arenediazonium salts forming undesired products.[77] In addition, while **1.145** is a more powerful electron donor than TTF **1.124**, it is not powerful enough to reduce aryl halides.[78]

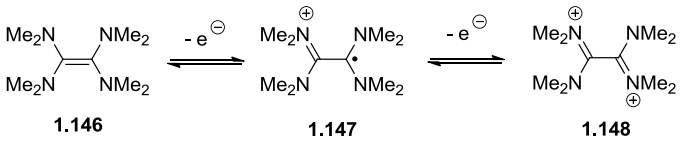


1.145

Figure 1.4: Diazadithiafulvalene-based electron donor **1.145**

However, the improved electron donating ability of **1.145** highlights the importance of using more electron-rich atoms with greater π-electron donating nature. Nitrogen is better at stabilising an adjacent carbocation compared with sulfur. Nitrogen-containing compounds would have better orbital overlap with adjacent carbon atoms due to similar size, thus leading to greater aromaticity in the oxidised forms of the analogous electron donors. All these observations were considered when developing more powerful electron donors.

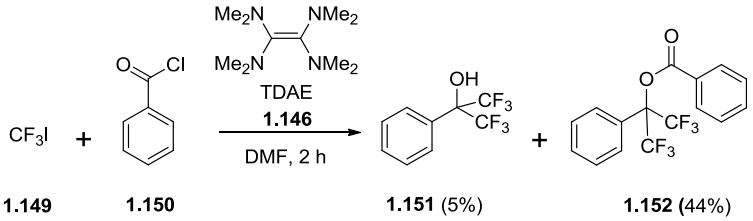
Médebielle and co-workers reported the use of TDAE [1,1,2,2-tetra-(dimethylamino)ethene] **1.146** as an electron donor for the reduction of electron-deficient halide compounds.[79,80] The oxidation potential of **1.146** is -0.78 V *vs.* SCE for the first ionisation and -0.61 V *vs.* SCE for the second in MeCN.[81] This demonstrates that TDAE **1.146** is much more powerful than TTF **1.124**. This highly reducing nature is due to the replacement of all four sulfur atoms with nitrogen, which has a greater π-electron donating nature (Scheme 1.30). However, TDAE **1.146** is not powerful enough to reduce unactivated aryl halides.[80]



1.146 **1.147** **1.148**

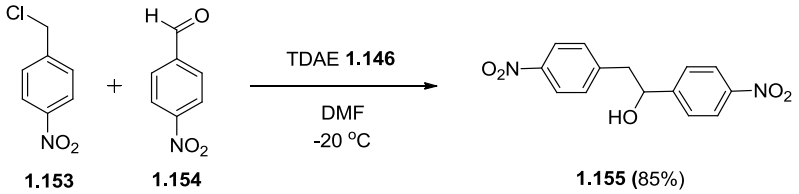
Scheme 1.30

The reaction between iodotrifluoromethane **1.149** and benzoyl chloride **1.150** in the presence of TDAE **1.146** gave rise to two products, **1.151** and **1.152**, indicating the presence of trifluoromethyl anion intermediates.[79] Alcohol **1.151** was obtained from double attack of trifluoromethyl anions on **1.150** followed by work-up, while ester **1.152** is due to esterification of **1.150** with the alkoxide corresponding to **1.151** (Scheme 1.31).



Scheme 1.31

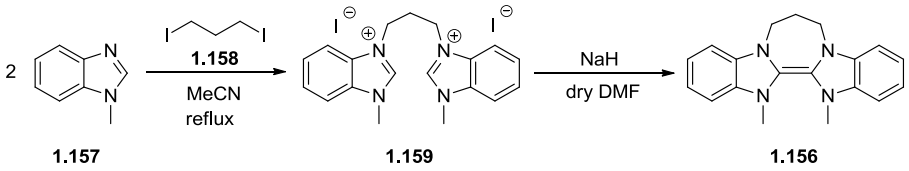
Furthermore, mild conditions were used to convert *p*-nitrobenzyl chloride **1.153** into its benzyl anion upon treating with TDAE **1.146**. Following addition of 4-nitrobenzaldehyde **1.154**, this resulted in alcohol **1.155** in good yield (Scheme 1.32).[80]



Scheme 1.32

1.2.2 Neutral organic super electron donors

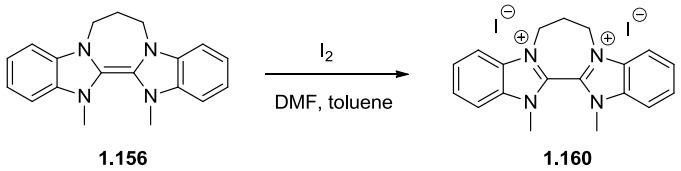
From previous discussions, it is clear that aromatic stabilisation and use of nitrogen in place of sulfur are essential for the development of powerful neutral organic electron donors. This concept was explored more broadly by the Murphy group. In 2005, Murphy *et al*. published the first ever neutral super organic electron donor **1.156**, based on the *N*-methylbenzimidazole moiety (Scheme 1.33).[78,82,83] The synthesis of the precursor salt **1.159** is straightforward and it was prepared by the alkylation of *N*-methylbenzimidazole **1.157** with 1,3-diiodopropane **1.158** under reflux conditions in acetonitrile for 72 h. Subsequent deprotonation of the salt **1.159** using strong base such as sodium hydride afforded donor **1.156** as a highly air-sensitive yellow solid.



Scheme 1.33

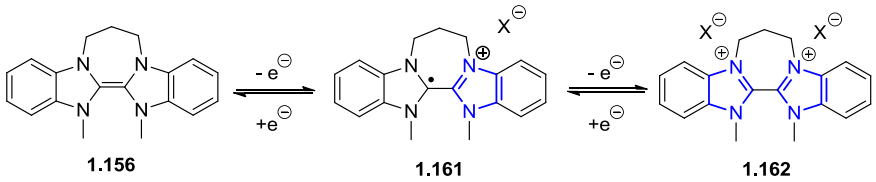
The formation of **1.156** was confirmed by NMR studies, with a characteristic peak at δ 123.1 ppm in ^{13}C NMR corresponding to the central alkene carbons. To further confirm donor formation, **1.156** was reacted with 1 equivalent of molecular iodine to give disalt

1.160. This disalt **1.160** was isolated and identified by ^{1}H and ^{13}C NMR, giving clear assurance of formation of donor **1.156** (Scheme 1.34).[78]



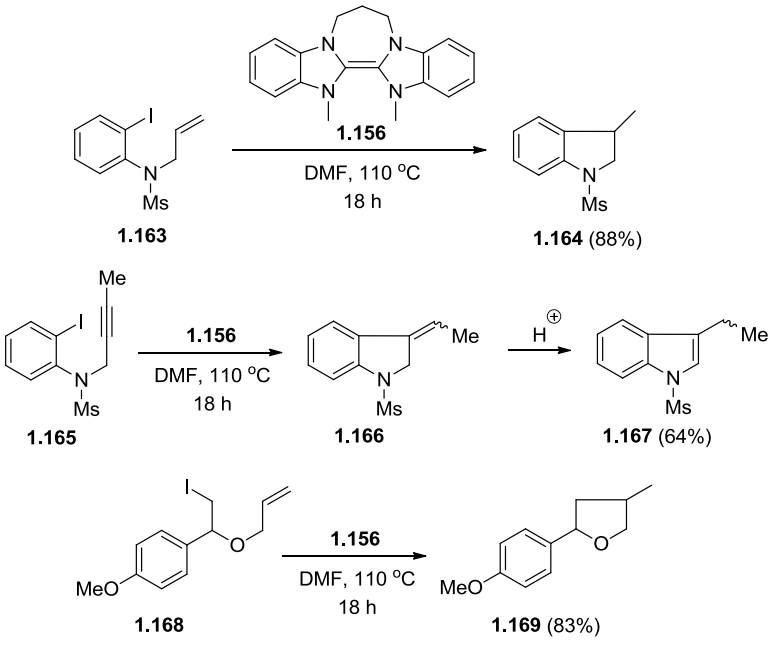
Scheme 1.34

The benzimidazole-derived donor **1.156** has four strong π-electron donating nitrogen atoms and can gain aromatic stabilisation (shown in blue) from radical-cation **1.161** and dication **1.162** upon oxidation (Scheme 1.35). The first oxidation potential of **1.156** is -0.82 V *vs.* SCE and the second oxidation potential is -0.75 V *vs.* SCE in DMF.[78]



Scheme 1.35

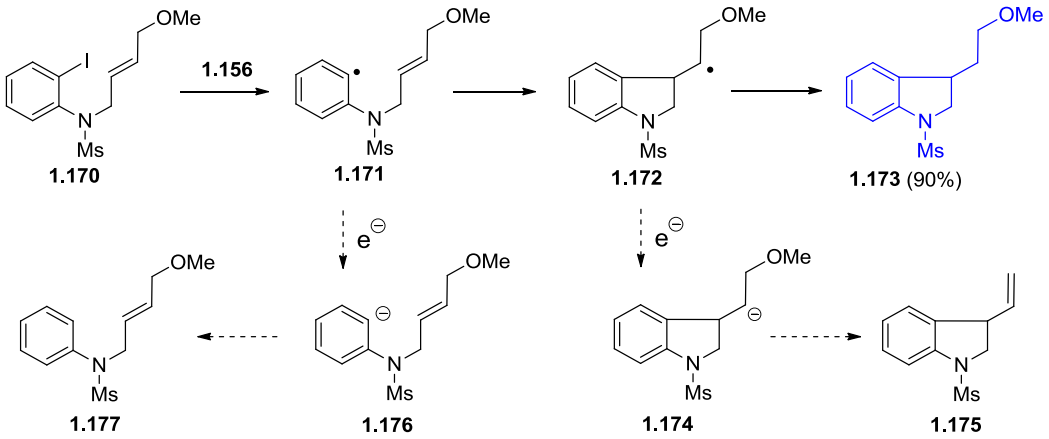
A wide variety of electron transfer reactions were carried out with aryl and alkyl iodides and all the substrates converted to desired products in good to excellent yields (Scheme 1.36).[78]



Scheme 1.36

Reduction of aryl iodide **1.163** gave the corresponding indoline **1.164** in excellent yield. Moreover, the reduction of alkyne-containing aryl iodide **1.165** gave exocyclic alkene **1.166**, which was then converted to indole derivative **1.167** upon treatment with acid. Additionally, an aliphatic iodide **1.168** was reduced to the corresponding cyclic product **1.169** via an alkyl radical intermediate (Scheme 1.36).[78]

Substrate **1.170** was designed to establish the reaction pathway, as well as the number of electrons that **1.156** could donate. There are two possibilities through which the reaction could lead to different products. The first one is the single electron transfer from donor **1.156** and that would only give rise to a single product **1.173**. Double electron transfer would lead to either **1.175** or **1.177** (Scheme 1.37).

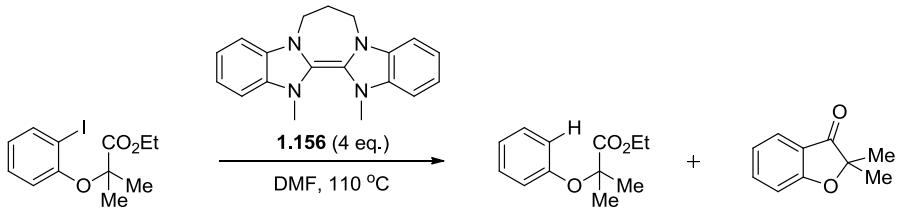


Scheme 1.37

Initial electron transfer from **1.156** to **1.170** gives aryl radical **1.171**. Cyclisation of this aryl radical **1.171** onto the alkene provides **1.172** and, followed by hydrogen abstraction, it affords **1.173** in excellent yield (90%). In principle, the donor can lose a second electron that could lead to anion intermediates **1.174** and **1.176**. Elimination of the methoxide ion from the anion **1.174** would generate alkene **1.175**.[78] The anion **1.176** could abstract a proton from the reaction to give **1.177**. However, no such alternative products were seen. This not only supports the radical pathway but also underpins the theory that only a single electron is donated by the donor **1.156** in this reaction.

To further support the radical pathway and the single electron donating nature of donor **1.156**, substrate **1.178** was designed. The aryl anion formed from the substrate **1.178** would readily attack the ester while an aryl radical could not. The donor **1.156**

successfully reduced **1.178** into **1.179** in good yield (83%), with no other product such as **1.180** being observed (Scheme 1.38).[78] This confirmed that no aryl anions had been formed in the course of reaction despite the promising first (-0.82 V) and second (-0.75 V) reduction potentials of donor **1.156**. This established the fact that the donor **1.156** acts only as a single electron donor to iodoarenes.

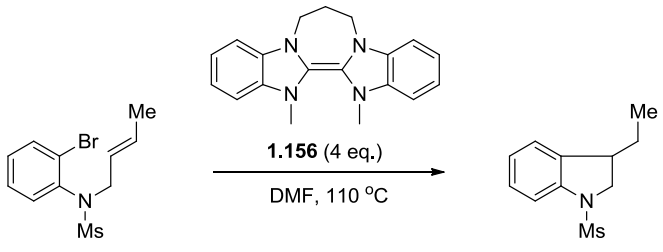


1.178 **1.179** (83%) **1.180** (0%)

Scheme 1.38

The source of the hydrogen atom to be abstracted by the radical intermediate **1.172** has yet to be determined although reactions carried out in deuterated DMF (d_7-DMF) suggested that the source was not the solvent, as the isolated product did not contain an isotopic label. The benzimidazole-based electron donor **1.156** is the first known neutral organic ground-state organic electron donor to successfully cleave aryl iodides and does so in excellent yield.

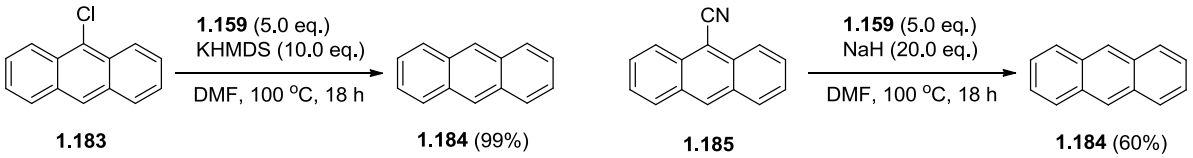
The scope of the reactivity of donor **1.156** was further investigated with substrates such as aryl bromides.[84] If successful, this would allow **1.156** to be a widely useful reagent for reduction of aryl halide compounds. Aryl bromide **1.181** was tested with donor **1.156** under different reaction conditions but provided only poor yields (20-30 %) of desired product **1.182** (Scheme 1.39). Hence the donor **1.156** is not powerful enough to reduce unactivated aryl bromides efficiently.



1.181 **1.182** (20-30%)

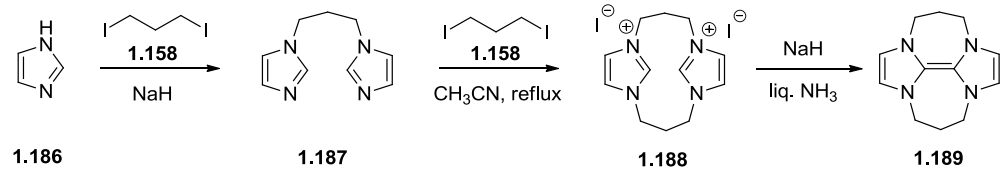
Scheme 1.39

Another set of reactions to probe the scope of the donor **1.156** was the reduction of anthracene derivatives. The reduction potential of 9-chloroanthracene **1.183** is -1.71 V *vs*. SCE in DMF.[85] The C-Cl bond in **1.183** was reductively cleaved to give an almost quantitative amount (99%) of anthracene **1.184**. In addition, the C-CN bond in 9-cyanoanthracene **1.185** was also successfully cleaved to provide a fair yield of anthracene **1.184** as reduced product (Scheme 1.40).[85] However, the reduction of anthracene itself into the corresponding dihydro compound was not successful.



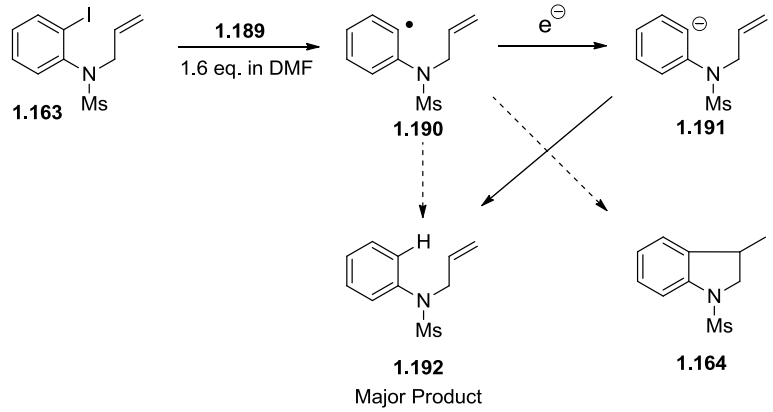
Scheme 1.40

In 2007, a more powerful neutral organic electron donor, named the "double-bridged donor" (DBD) **1.189** based on imidazole, was developed within the Murphy group.[86-88] This donor **1.189** was thought to be more powerful than **1.156** due to its greater gain in aromatisation energy upon oxidation. The donor **1.189** has first and second reduction potentials of -1.37 V vs. SCE and -1.18 V vs. SCE in MeCN, respectively.[86] This confirms that the DBD **1.189** was more powerful than donor **1.156**. The stable precursor salt **1.188** was synthesised using imidazole **1.186** and diiodopropane **1.158** in two steps under dilute reaction conditions. Synthesis of **1.187** is straightforward. However, the synthesis of **1.188** requires alkylation of one of the imidazole units followed by intramolecular alkylation onto the second imidazole unit. To prevent the formation of higher amounts of polymer, the starting materials are added regularly over 20 days followed by additional stirring for 4 days. The DBD **1.189** was then prepared from precursor salt **1.188** using a strong base such as NaH in liquid ammonia under air-free and moisture-free conditions (Scheme 1.41).



Scheme 1.41

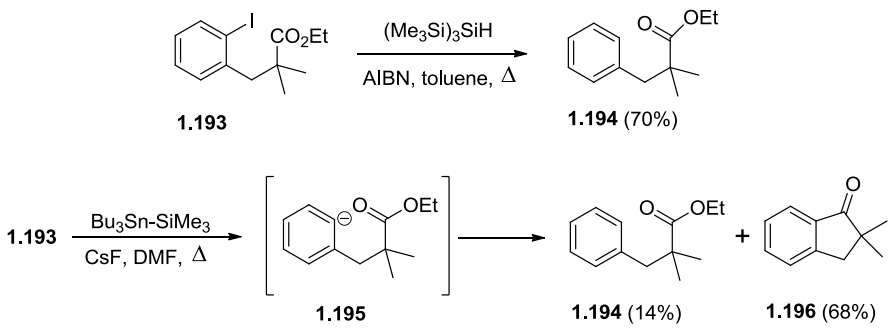
To compare the activities of donor **1.156** and DBD **1.189**, the same aryl halide substrates were tested. When the substrate **1.163** was treated with DBD **1.189**, surprisingly, **1.192** was formed as the major product while only a trace amount of **1.164** was observed (Scheme 1.42).



Scheme 1.42

This opens the possibility of two electron donation by DBD **1.189**. Since cyclisation of aryl radicals tends to occur at much faster rates ($k > 10^9\ s^{-1}$) than hydrogen abstraction,[89] formation of **1.164** should be the major product, if aryl radical **1.190** is the intermediate. But, formation of **1.192** as a major product indicates that aryl anion **1.191** is the intermediate, which is in turn formed very rapidly from **1.190** by accepting a second electron (Scheme 1.42).

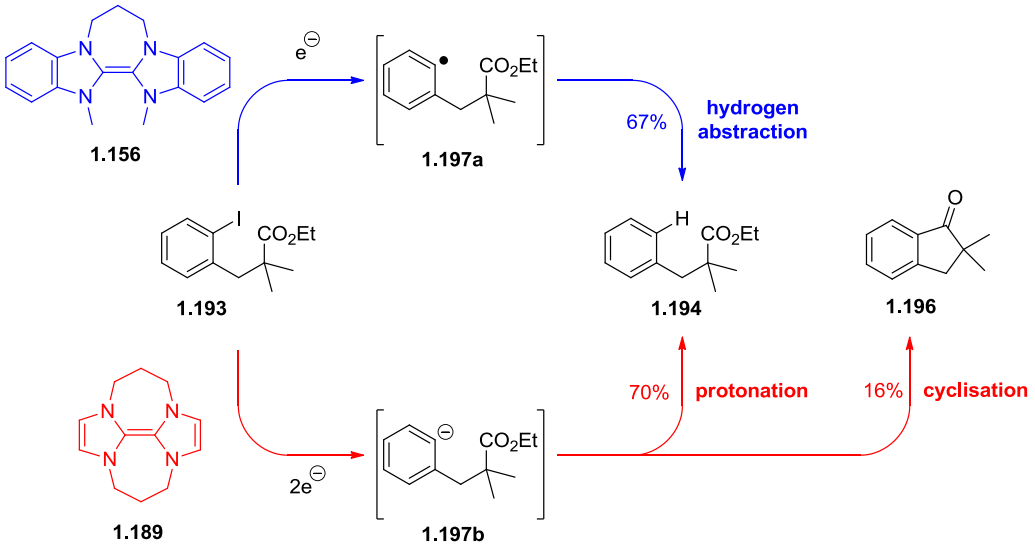
To further confirm whether the reactions with the donor **1.156** and DBD **1.189** proceeded through formation of an aryl radical or aryl anion intermediates, diagnostic test reactions were carried out as shown in Scheme 1.43.[86]



Scheme 1.43

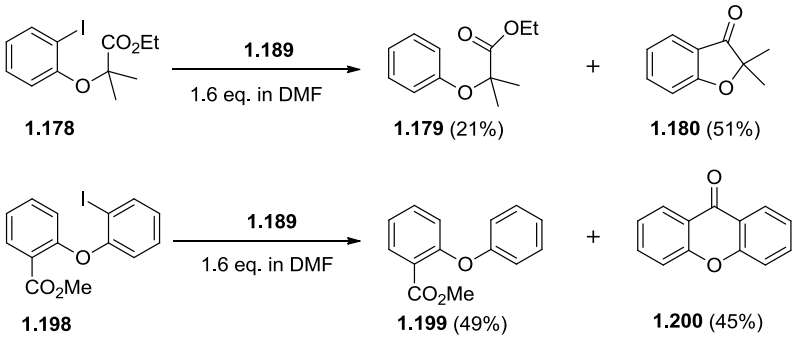
The first test reaction uses $(Me_3Si)_3SiH$ and AIBN, which are well known reagents used to generate purely radical species.[90] From this it can be deduced that the formation of uncyclised product **1.194** can occur through a purely radical mechanism. The second test reaction using trimethyl(tributylstannyl)silane[91,92] with caesium fluoride, as a source of fluoride ions, proceeds through formation of aryl anion **1.195** and leads to **1.196**, as the major product and is indicative of the aryl anion intermediate (Scheme 1.43).[86]

When the substrate **1.193** was tested with the donor **1.156**, it provided uncyclised product **1.194** as a single product (67%). This confirms that the reactions with the donor **1.156** proceed through aryl radical intermediate **1.197a** and therefore **1.156** is acting as a single electron donor. However, the same substrate **1.193**, under the same reaction conditions but with donor **1.189**, provided cyclised product **1.196** (16%) along with the uncyclised product **1.194** (70%). The formation of **1.196** can only happen through an aryl anion intermediate **1.197b** and therefore 16% yield of cyclised product reflects the minimum amount of aryl anion generated in the reaction (Scheme 1.44).



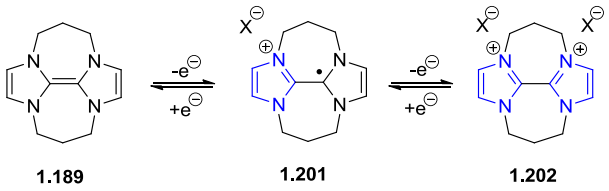
Scheme 1.44

To further confirm the existence of the aryl anion intermediate, substrates **1.178** and **1.198** were tested using the DBD **1.189** (Scheme 1.45).[86] The formation of the cyclised products **1.180** and **1.200** reinforced the generation of aryl anion intermediates via double electron transfer in these reactions. This was the first time that a neutral organic electron donor was capable of forming an aryl anion by two-electron transfer.



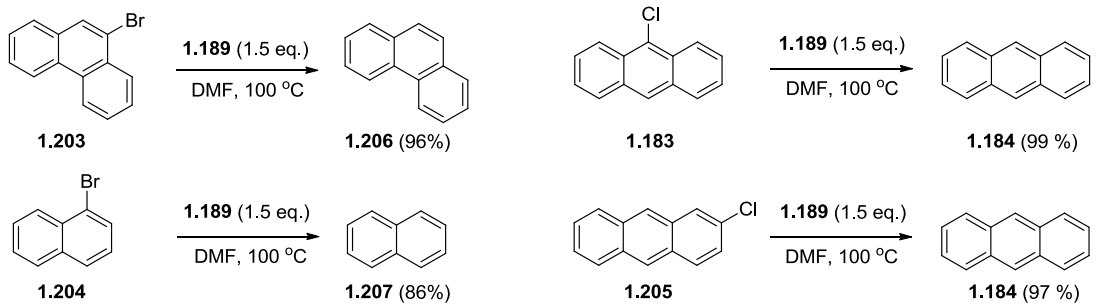
Scheme 1.45

From the experimental results, it was clear that DBD **1.189** was more powerful than the donor **1.156**. Several reasons justify why donor **1.189** is more powerful than **1.156**. Firstly, the imidazole rings in oxidised form **1.202** derived from **1.189** are not fused with other aromatics rings, as is the case with **1.162**, derived from the other donor **1.156**. Therefore, the formation imparts more aromatic stabilisation energy to the dication **1.202** (Scheme 1.46). Additionally, the presence of two aliphatic bridges on DBD **1.189** keeps the molecule planar after subsequent loss of electrons. The absence of these bridges on donor **1.156** results in the molecule becoming less planar after electron loss. Larger reorganisation energies are needed for donor **1.156**, due to the large changes in structure, and so it does not accommodate a positive charge as easily as **1.189**.[86]



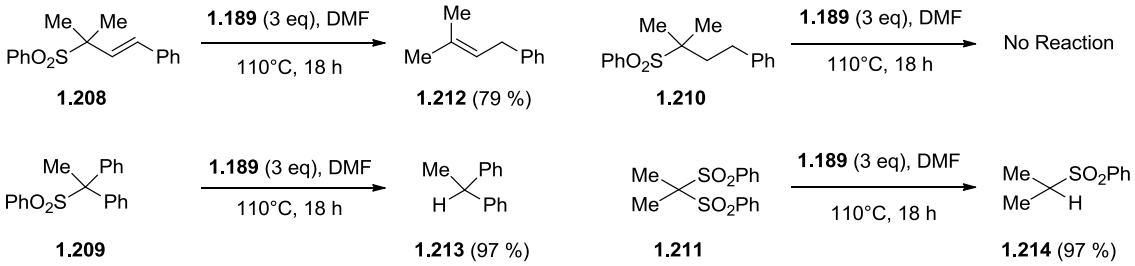
Scheme 1.46

The reducing power of DBD **1.189** was further explored by testing a variety of bromo and chloro aromatic substrates. The DBD **1.189** successfully reduced the compounds **1.203-1.205** and **1.183** in near quantitative yields (Scheme 1.47).[86] Previous attempts to reduce **1.204** with donor **1.156** had been unsuccessful. This shows again the greater reducing power of DBD **1.189** compared to the donor **1.156**.



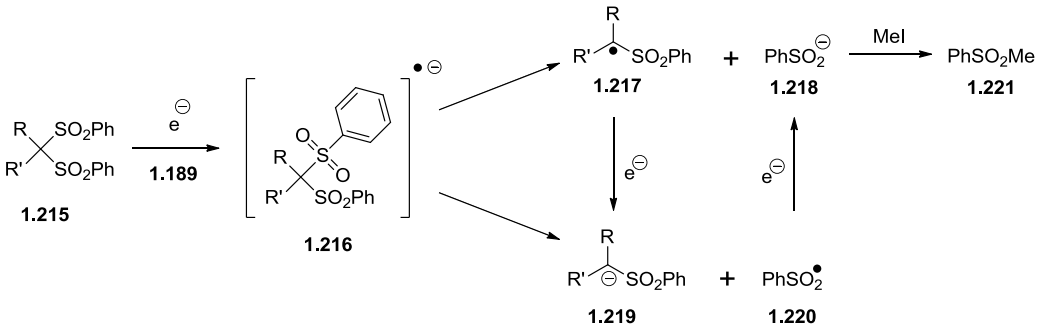
Scheme 1.47

Later, the DBD **1.189** was found to be very successful in reductively cleaving groups like sulfones and disulfones (Scheme 1.48).[84] Deprotection of these groups, generally, is carried out by highly reactive metal-containing reducing agents like alkali metals under Birch conditions or using SmI_2 with HMPA.[93] This was the first report of such cleavages using organic super electron donors. However, the sulfone substrates need to be further activated towards the cleavage. No reaction was observed with aryl alkyl sufone **1.210**. This is due to the high activation energy required to transfer an electron to the sulfone group in the unactivated sulfone compared with activated sulfones such as aryl allyl sulfone **1.208** and di-aryl sulfone **1.209**. The LUMOs of the activated sulfones have greater overlap with the σ*-orbital of their scissile C-S bonds, in comparison to the unactivated sulfone.[84] *gem*-Disulfones such as **1.211** were also sucessfully cleaved to monosulfones *e.g.* **1.214** in excellent yields.



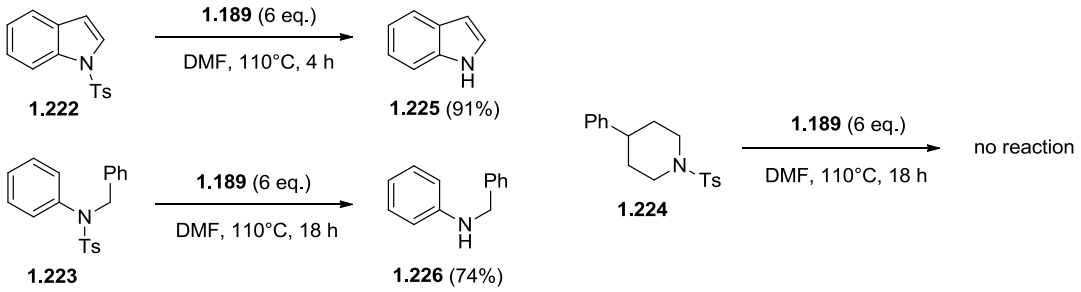
Scheme 1.48

In the proposed mechanism, a single electron transfer to the arenesulfonyl group affords radical-anion **1.216** that can undergo instantaneous scission of the C-S σ bond to form either [alkyl radical **1.217** + sulfinate anion **1.218]** or [sulfonyl radical **1.220** + carbanion **1.219]** (Scheme 1.49). Transfer of another electron results in a pair of anions **1.219** and **1.218**. The anion **1.219** can abstract a proton to provide monosulfone product. The presence of **1.218** was confirmed by the addition of MeI (excess) at the end of the reaction, which provided sulfone **1.221** in good yield (86%).[84]



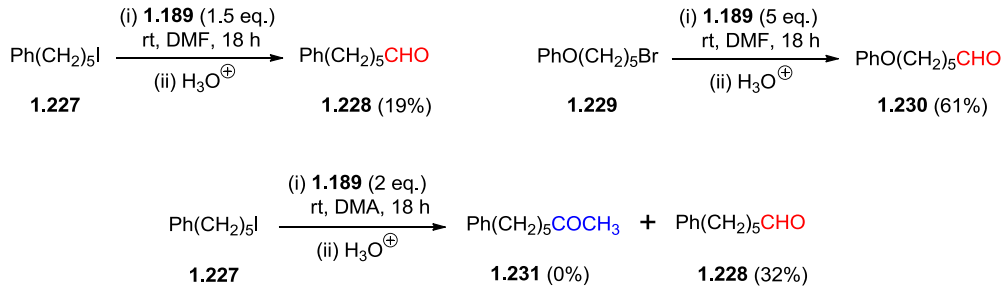
Scheme 1.49

The DBD **1.189** also successfully cleaved activated arenesulfonamides (Scheme 1.50).[84] The indolesulfonamide **1.222** gave an excellent yield of **1.225** (91%) and **1.223** gave a satisfactory yield of **1.226** (74%) over an extended reaction time of 18 h. However, **1.224** did not undergo reaction. Computational studies revealed that the inactivity of **1.224** is in analogy with sulfone cleavages and shows a high energy of activation for electron transfer. This energy is more than that needed for **1.222** and **1.223** due to instability of the resulting radical-anion.[84]



Scheme 1.50

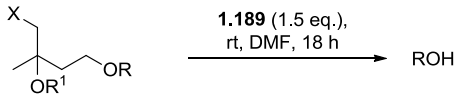
The DBD **1.189** was found to convert alkyl halides such as **1.227** and **1.229** to the corresponding aldehydes **1.228** and **1.230**, containing one carbon extra to their precursor halides (Scheme 1.51).[94]



Scheme 1.51

At first it was thought that the extra carbon atom in the product might be coming from either the solvent (DMF) or from the donor **1.189** itself. If DMF was a source of extra carbon, then the product might arise by the nucleophilic attack of the carbanion, generated from the precursor halide, onto the DMF. Thus, if DMF was replaced by DMA (dimethylacetamide), it should provide the corresponding ketone product instead of aldehyde. However, when the substrate **1.227** was submitted to the donor **1.189** using DMA as a solvent, none of the ketone **1.231** was observed but aldehyde **1.228** was isolated. This demonstrates that the extra carbon is most likely arising from donor **1.189** (Scheme 1.51).

In the reaction process, donor **1.189** was prepared *in situ* and subsequently reacted with these substrates. After neutral work-up, a trace of aldehyde was found in the ^{1}H-NMR spectrum of the crude product. Acid work-up, on the other hand, afforded higher amounts of aldehyde products suggesting that the aldehyde was in a protected state prior to work-up, and acidic work-up conditions were needed to release this product. To gain further insight into the reaction and its mechanism, alternative substrates were designed and tested. Substrates such as **1.232** were tested with DBD **1.189** and converted to alcohols **1.233** in good yield (Scheme 1.52).[94]

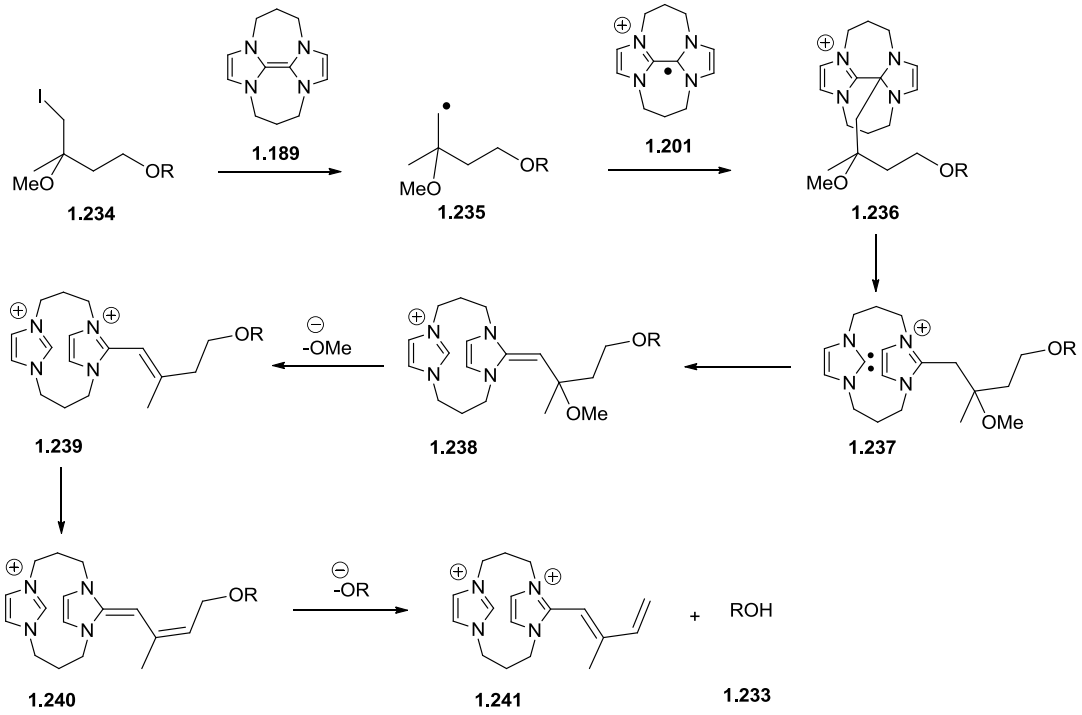


a) X = I, R = $(CH_2)_3$Ph, R^1 = Me, 70%
b) X = Br, R = $(CH_2)_3$Ph, R^1 = Me, 69%
c) X = I, R = $(CH_2)_4$Ph, R^1 = Me, 67%
d) X = I, R = $(CH_2)_3$OPh, R^1 = Me, 77%
e) X = I, R = $(CH_2)_3OC_6H_4$OMe-*p*, R^1 = Me, 63%
f) X = I, R = $(CH_2)_4O(CH_2)_3$Ph, R^1 = Me, 77%

Scheme 1.52

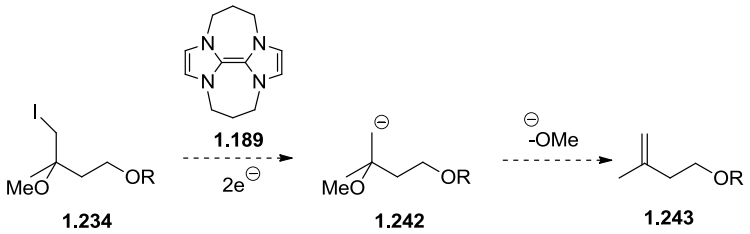
Mechanistic studies were performed on the reaction with methyl ether **1.234** and it is believed that, after the first electron transfer, **1.234** converts to alkyl radical **1.235**, which can be trapped by radical-cation **1.201** of the donor to form intermediate **1.236**. The stabilisation energy gained from aromatisation in forming the imidazole ring is the driving force for the generation of carbene intermediate **1.237**. Proton transfer in **1.237** would give enediamine **1.238**. This compound will expel methoxide to generate imidazolium dication **1.239**. This can be deprotonated in the basic medium to afford **1.240**, which is in

a good position to liberate the alkoxide ($RO^{\ominus}$), giving the corresponding alcohol **1.233** (Scheme 1.53).



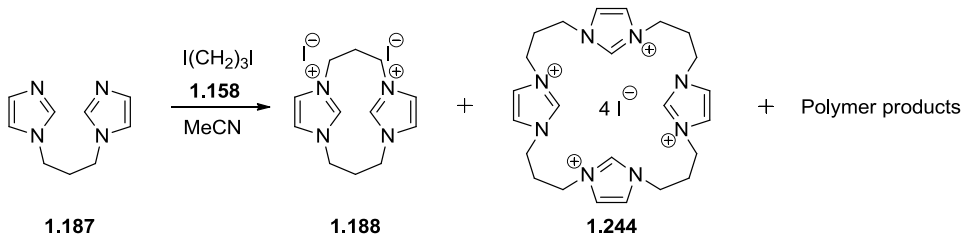
Scheme 1.53

There was an alternative possibility *i.e.* of donating two electrons into substrate **1.234** and this would lead to the formation of alkyl carbanion **1.242** instead of alkyl radical **1.235**. Formation of any such carbanion **1.242** would lead to the elimination of methoxide to afford alkene **1.243**.[95] The process to form **1.243** would likely occur in a concerted manner. But no sign of alkene **1.243** was found. This result strengthens the argument that the reaction in Scheme 1.53 proceeds through a radical mechanism and not through an anionic pathway (Scheme 1.54).



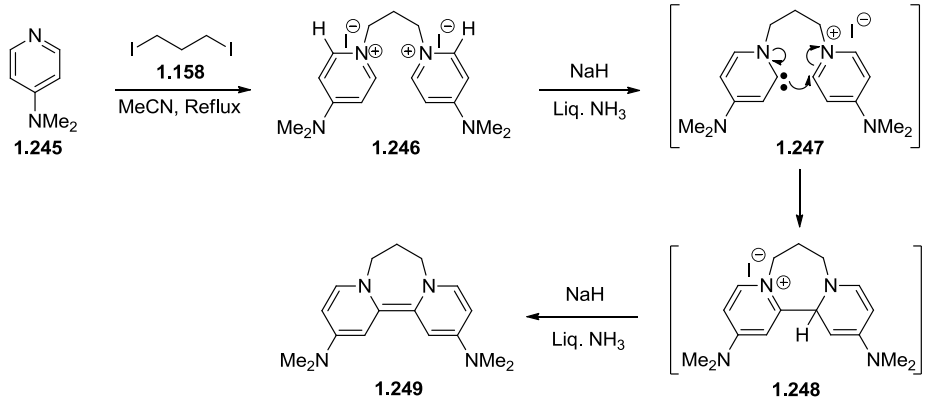
Scheme 1.54

Despite the high reducing power of DBD **1.189**, its synthesis uses **1.188** as precursor and preparation of this compound always suffers from unwanted side-reactions leading to macrocyclic products, principally **1.244** (Scheme 1.55).



Scheme 1.55

These unwanted reactions can be minimised by adding the starting materials under dilute conditions over a period of one month. However, this synthesis is further affected by a laborious work-up process. This triggered the search for more powerful and easily accessible donors. As a result, a new donor **1.249**, of similar reducing power to DBD **1.189** and having 4-dimethylaminopyridine as its core structure, was developed within the Murphy group.[96] Synthesis of the donor **1.249** is straightforward and it is prepared in two simple steps (Scheme 1.56).

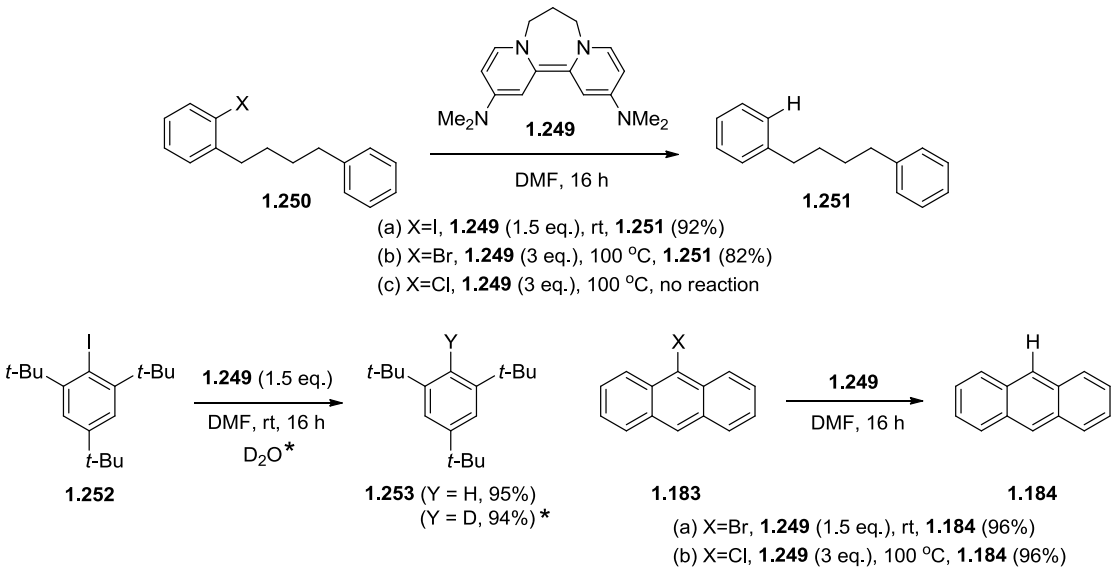


Scheme 1.56

Stable precursor salt **1.246** was easily synthesised from 4-dimethylaminopyridine **1.245** and 1,3-diiodopropane **1.158**. Deprotonation of **1.246** using a strong base like NaH in liq. NH_3 results in formation of a moisture- and air-sensitive donor **1.249** as a purple solid.

Cyclic voltammetry of donor **1.249** showed a single reversible two-electron peak at $E_{1/2}$ (DMF) = -1.13 V *vs.* Ag/AgCl/KCl (sat.) which translates to -1.24 V *vs.* SCE and hence

this donor is expected to be as strong as DBD **1.189**.[96] Cyclic voltammetry of DBD **1.189** showed the two electron transfer steps almost at identical potentials; donor **1.249** showed a clean, two-electron peak, indicating that loss of the second electron occurs at the same potential as the first electron.[96]

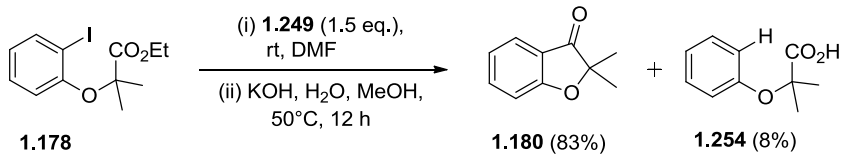


Scheme 1.57

The reactivity of donor **1.249** was explored by testing with a number of different substrates. The donor **1.249** was able to reduce aryl iodides and bromides to the corresponding products by two-electron donation. Unsurprisingly, aryl bromide **1.250b** reduction needed elevated temperatures and higher amounts of donor **1.249**, while aryl iodide **1.250a** reduction took place at room temperature. Aryl chloride **1.250c** reduction did not happen even under forceful conditions. Reduction of hindered iodide **1.252** went cleanly under mild reaction conditions to provide an excellent yield of **1.253** (Scheme 1.57). From the above results, it is likely that these reactions proceed though aryl anion intermediates. The regiospecific formation of the C-D bond, when D_2O was added to the reaction mixture, is consistent with an aryl anion intermediate.[96] Surprisingly, reduction of 9-bromoanthracene **1.183a** happened at room temperature using 1.5 eq. of donor **1.249**, while reduction of 9-chloroanthracene **1.183b** took place at 100 °C using 3 eq. of donor **1.249**. However, the reduction potential of anthracene (-2.19 V *vs.* SCE in CH_3CN)[97] is much less negative than that of benzene (-3.31 V *vs.* SCE in DME)[98] indicating that the LUMO of the former is lower in energy. The lower LUMO energy of anthracenes compared to benzenes allows initial electron transfer to occur under milder conditions and

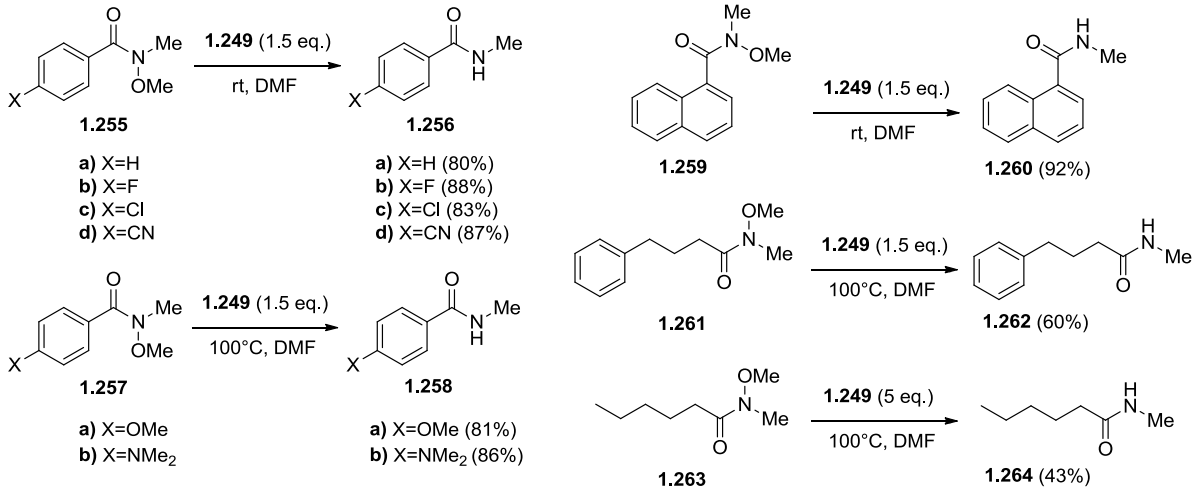
so elevated temperatures are only required for electron transfer to the σ* orbital of the C-X bond from the π* orbital.

To further confirm the formation of aryl carbanions from double electron transfer, substrate **1.178** was tested with donor **1.249**. As expected, the cyclised product **1.180** was formed as the major product and the reaction also gave the ester corresponding to acid product **1.254** in low yield (Scheme 1.58).[96] Ketone **1.180** was formed together with the ethyl ester of acid **1.254** as an inseparable mixture. The crude product was then hydrolysed to separate the products and gave an excellent yield (83%) of ketone **1.180** along with acid product **1.254** (8%). It has been previously discussed that aryl radicals cannot react with an ester group to give cyclised product but only an aryl anion can provide this. This establishes that two electrons are transferred to **1.178**.



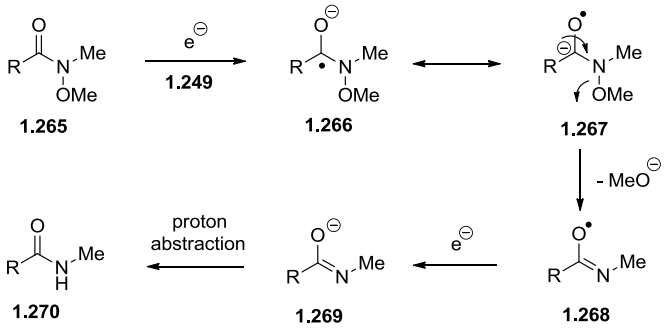
Scheme 1.58

The reactivity of donor **1.249** was further tested in the cleavage of N-O bonds of Weinreb amides (Scheme 1.59).[99] In Weinreb amides having an electron-withdrawing group on the arene **1.255a-d**, the N-O bond was easily cleaved at room temperature using 1.5 eq. of donor **1.249**. However, Weinreb amides **1.257a-b** containing electron-donating groups needed higher temperature to provide good yields. The reaction with naphthalene substrate **1.259** went smoothly and gave an excellent yield of **1.260** (92%). Substrates such as **1.261** with long alkyl chains separating aromatic and Weinreb amide groups provided a lower yield of product **1.262** at elevated temperature. The N-O bond cleavage was even more difficult in aliphatic Weinreb amides such as **1.263** and provided a moderate yield only by using more donor **1.249** (5 eq.) at elevated temperature. This led to the conclusion that the presence of the phenyl ring aids in the cleavage of the N-O bond in Weinreb amides, despite being separated from the amide group. The observed electronic effects were in agreement with the fact that it was relatively difficult to transfer electrons into a more electron-rich system such as **1.257a-b**.



Scheme 1.59

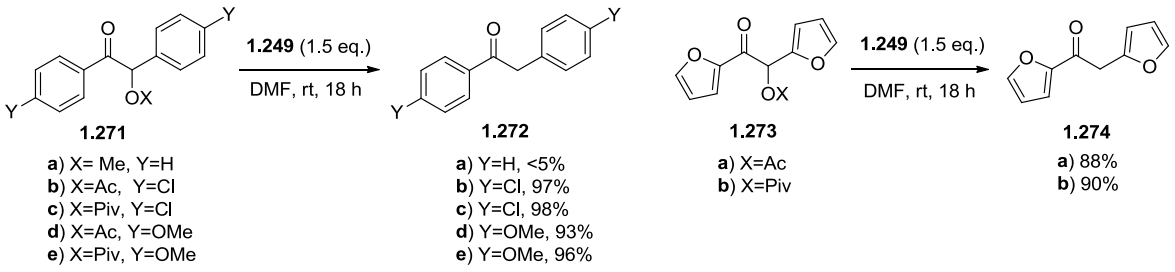
The proposed mechanism of the cleavage step in the Weinreb amide reaction is shown in Scheme 1.60.[99] Initial single electron transfer (SET) from the donor **1.249** to the LUMO of the Weinreb amide **1.265** generates ketyl radical anion **1.267**. The LUMO has essentially π* character and the electron needs to be transferred to the σ* of the N-O bond to assure cleavage. This ketyl radical anion **1.267** leads to the cleavage of the N-O bond and affords enolyl radical **1.268**. The resulting enolyl radical **1.268** takes another electron and forms enolate **1.269**, which abstracts a proton to generate amide **1.270**.



Scheme 1.60

The reactivity of donor **1.249** was further extended to cleave C-O σ-bonds in acyloin derivatives.[100] Methylated benzoin derivative **1.271a** gave very little reductive C-O bond cleavage. However, when the methoxy group was replaced by electron-withdrawing groups such as acetate or pivalate, benzoin derivatives **1.271b-e** gave excellent yields of deoxybenzoin derivatives **1.272b-e** at room temperature using 1.5 eq. of donor **1.249**. The same reaction was also successful on benzoin-related compounds derived from furans

1.273a-b (Scheme 1.61). From the above results, it is concluded that the electronic character of the O-X bond is very important for decreasing the energy of the LUMO of the acyloin system, thereby helping the reaction to proceed.



1.271
a) X= Me, Y=H
b) X=Ac, Y=Cl
c) X=Piv, Y=Cl
d) X=Ac, Y=OMe
e) X=Piv, Y=OMe

1.272
a) Y=H, <5%
b) Y=Cl, 97%
c) Y=Cl, 98%
d) Y=OMe, 93%
e) Y=OMe, 96%

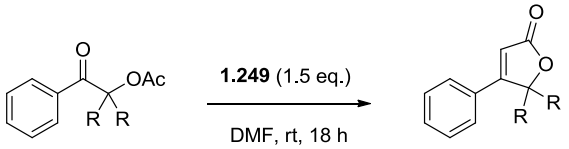
1.273
a) X=Ac
b) X=Piv

1.274
a) 88%
b) 90%

Scheme 1.61

The mechanism of the reaction is analogous to that of the Weinreb amide N-O bond cleavages, in this case with the expulsion of carboxylate anion from ketyl radical anion instead of methoxide anion in Weinreb amides. Hence, it is not discussed in detail in this case.

However, α-acetoxycarbonyl substrates **1.275**, upon reacting with the donor **1.249** under the same reaction conditions, provided unsaturated lactones **1.276**. This provides strong evidence for the basic nature of the donor **1.249** (Scheme 1.62).

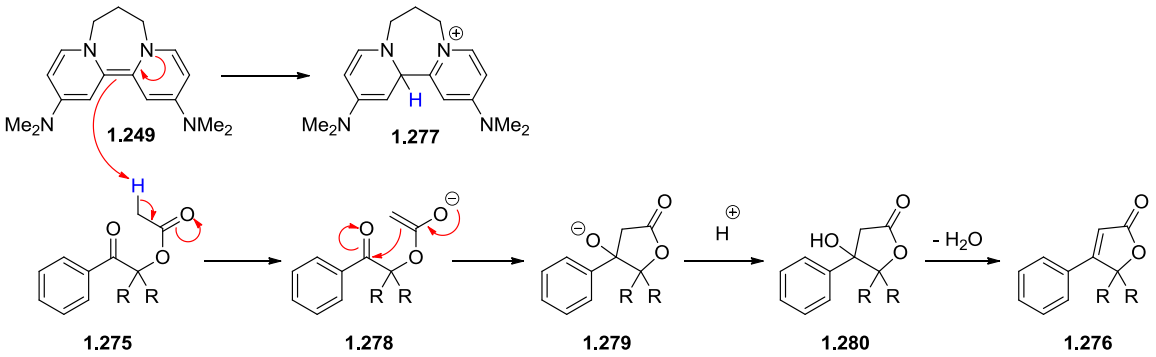


1.275
a) R = Me
b) R = $(CH_2)_5$

1.276
a) R = Me, 86%
b) R = $(CH_2)_5$, 85%

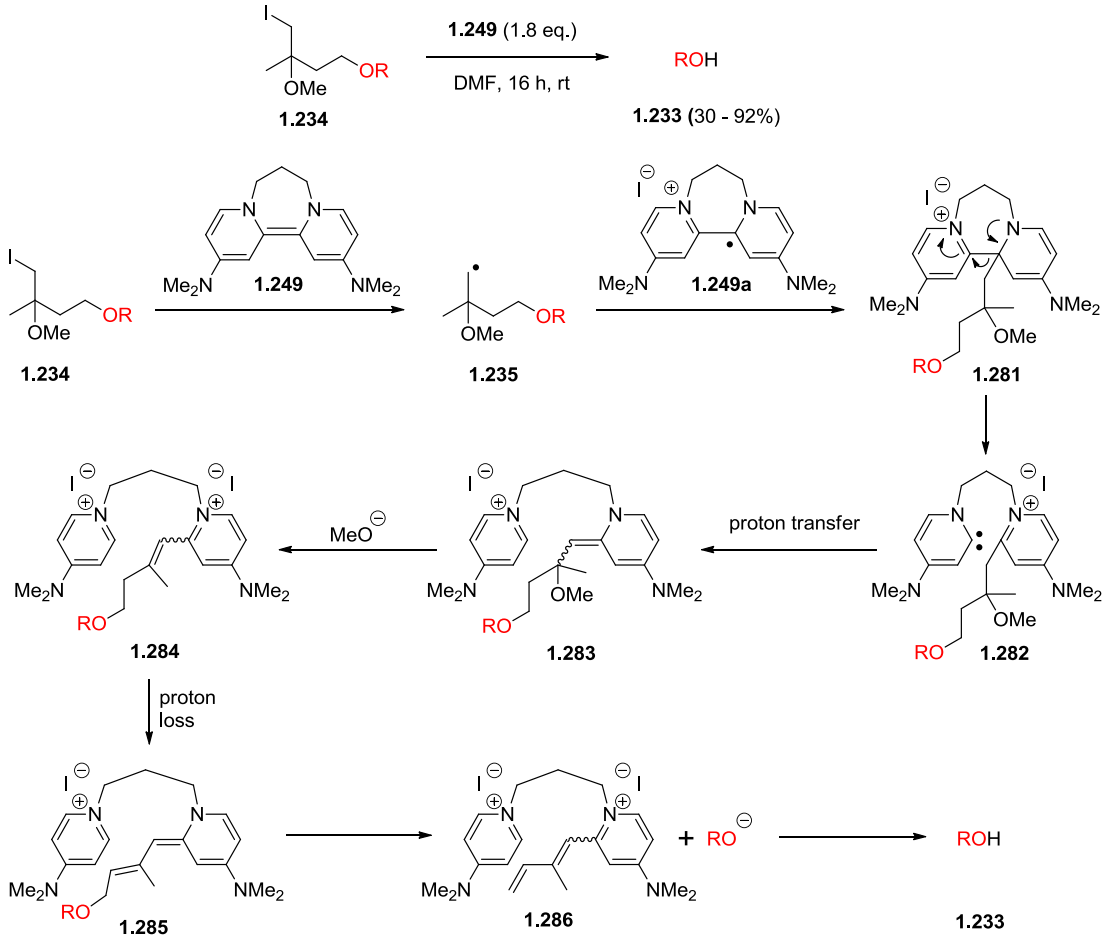
Scheme 1.62

The proposed mechanism for the above transformation is shown in Scheme 1.63. During the reaction, the donor **1.249** deprotonates the acidic acetoxy group to generate enolate anion **1.278** and this is driven by the gain in aromaticity in the pyridinium salt of the donor **1.277**. The enolate anion **1.278** attacks the benzoyl carbonyl group to afford hydroxylactone **1.280**, which undergoes easy dehydration to form butenolide **1.276**.



Scheme 1.63

Similar to the alkyl radical trapping experiments with the DBD **1.189** (see page 30), a number of substrates were prepared and submitted to the donor **1.249** to investigate similar reactivity.[101]



Scheme 1.64

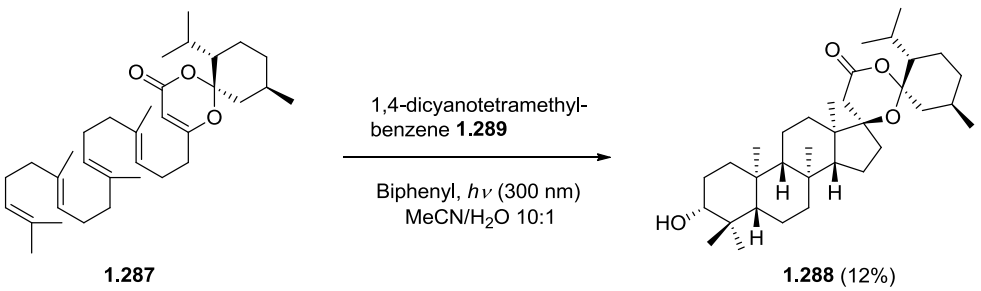
Analogous to the previous results seen with DBD **1.189**, alcohols were also isolated from these reactions, supporting the alkyl radical trapping with radical-cation of the donor

1.249. The possible mechanism for this radical trapping was shown in Scheme 1.64 and it was well described in page 31.

1.3 Photo-induced electron transfer (PET)

The discovery and development of new photochemical processes has gained a lot of attention in recent times for producing new reactivities which are not achieved using conventional methods and for delivering synthetic targets in just a few steps. Generally, these reactions are based on the high reactivity of the excited state species. However, the formation of radical species to initiate these reactions often needs the use of toxic (tributyltin hydride), potentially explosive (AIBN and peroxides) or pyrophoric (trialkylboranes) compounds.[102] So, there has been a lot of interest in further developing this class of reactions for environmentally-friendly organic synthesis. Thus, this section is dedicated to briefly report the advances in this class of reactions using UV and visible-light sources.

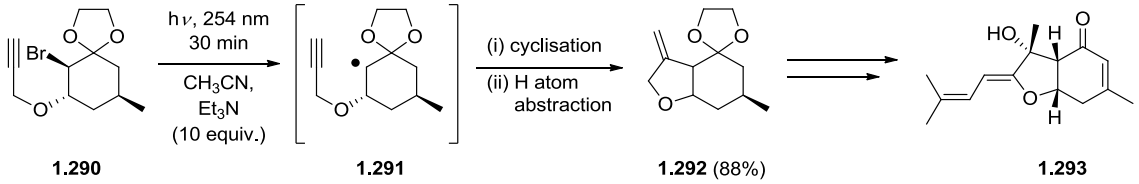
Some of the photochemical reactions are carried out using a photosensitiser, which absorbs UV light preferentially to the substrate and leads to the promotion of an electron from its HOMO to its LUMO. This promotion of an electron leaves a hole in the low lying orbital (this is capable of taking up an electron from the substrate and thereby oxidising it) and an electron in the higher energy orbital (that can be donated to the substrate thereby reducing it).[103] Demuth *et al.* used photoinduced cascade reactions for the total synthesis of steroid **1.288** by using 1,4-dicyanotetramethylbenzene **1.289** as a photosensitiser.[104] In the reaction, **1.289** is excited preferentially by UV light leading to the oxidation of substrate **1.287** to provide a radical-cation intermediate that undergoes further cascade reactions to provide final product **1.288** (Scheme 1.65).



1.287 **1.288** (12%)

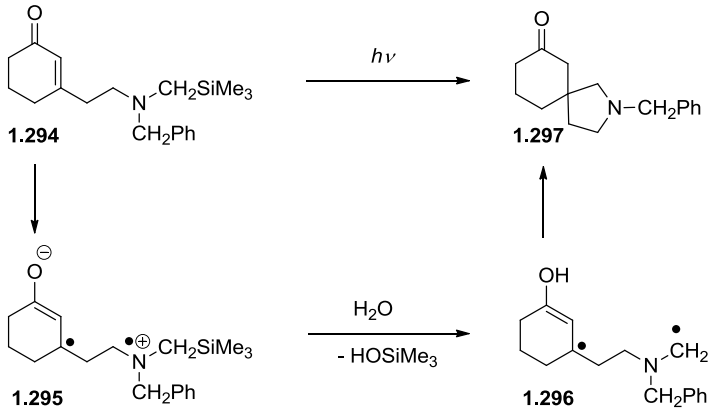
Scheme 1.65

Photo-induced electron transfer is also useful for generating radical species from alkyl halides in the presence of triethylamine. Cossy *et al*. successfully applied this concept in the total synthesis of (±)-bisabolangelone **1.293**.[105] This method does not require any photosensitiser, in contrast to the previous example. Substrate **1.290**, under photo-induced conditions, generates radical intermediate **1.291** that undergoes 5-*exo-dig* cyclisation onto the suitably placed alkyne to afforded heterocycle **1.292**, which upon further reactions provides (±)-bisabolangelone **1.293** (Scheme 1.66).



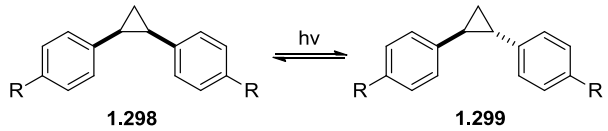
Scheme 1.66

Mariano *et al*. developed single electron transfer-promoted photocyclization reactions of trimethylsilyl substituted aminoalkyl α,β-unsaturated ketones.[106] Substrate **1.294** is excited by UV-light leading to intramolecular single electron transfer from the the amine moiety to the carbonyl group to give rise to zwitterionic intermediate **1.295**. This intermediate, upon desilylation, generates diradical **1.296** that undergoes radical coupling to afford spiro compound **1.297** (Scheme 1.67).



Scheme 1.67

The geometric isomerisation of 1,2-diarylcyclopropanes is another important aspect of photo-induced electron transfer processes and this has been widely investigated from the 1960s (Scheme 1.68). Hammond *et al.* were the first to see this kind of reactivity.[107]



Scheme 1.68

These workers observed that *cis*- and *trans*-1,2-diphenylcyclopropanes **1.298** and **1.299** can be interconverted by photosensitisation with the use of different UV-light absorbing sensitisers such as naphthalene-1,4-dicarbonitrile **1.300**, benzil **1.301** and chloranil **1.302** (Figure 1.5).

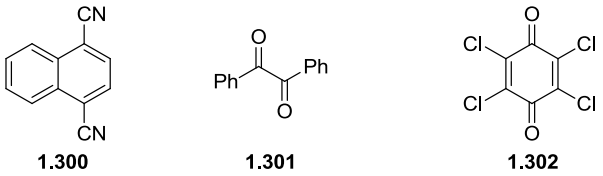
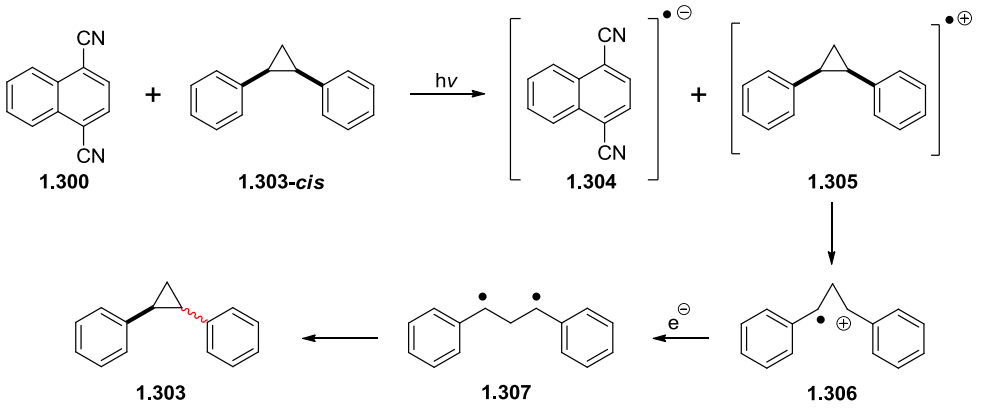


Figure 1.5 UV-light sensitisers

It was proposed that the excited molecule did not return directly to the ground state but via different intermediate stages[108] and the energy liberated was sufficient to break the weakest C-C bond of cyclopropane (usually, the bond having two aryl substituents) and lead to a triplet 1,3-biradical.[107,109] As the cyclopropane ring was broken, free rotation around the C-C bonds could be possible. The two radicals after some time could convert to singlet biradical and then combined once again to deliver geometric isomers of 1,2-diarylcyclopropane. After a certain period of irradiation, a photostationary state was attained and this would depend upon the sensitiser, solvent and irradiation method.[107,110-112] The *cis*/*trans* ratio of the isomers, formed after recombination, is determined by the ease with which the bi-radical is formed from the two isomers and the relative rates of ring-closure.[112,113]

Arnold and Wong were the first to propose a fully fledged mechanism (Scheme 1.69) for the geometric isomerisation of cyclopropanes.[114] They reported that isomerisation happens through radical-cation intermediates. The excitation of singlet state sensitiser **1.300** leads to the formation of the radical-anion of the sensitiser **1.304** and radical-cation of the cyclopropane **1.305** through single electron transfer. Reactive intermediate **1.305** undergoes cleavage at the weakest C-C bond of the cyclopropane *i.e.* the bond having two aryl substituents, and generates **1.306**. After back electron transfer, a 1,3-bi-radical **1.307**

and ground state sensitiser **1.300** are obtained. This bi-radical **1.307** cyclises rapidly to provide isomerised 1,2-diphenylcyclopropane **1.303**. The polarity of the solvent plays a key role in stabilising the radical-ions and the free energy change is important for the electron transfer.[114,115]



Scheme 1.69

1.3.1 UV-light mediated electron-transfer reactions using neutral organic electron donors

In recent times, the Murphy group at University of Strathclyde has focused on further activating the neutral organic electron donors to achieve more demanding electron transfer reactions. As discussed in the earlier sections of the introduction, reduction of sulfones, sulfonamides, bromo- and chloroaryl substrates had been carried out at elevated temperatures with non-metallic organic electron donor species. However, these methods have their own limitations such as decomposition of compounds and volatility of some products at elevated temperatures. So to enhance the scope of donors and to use them for a broad range of reductions, it would be ideal to carry out these reactions at room temperature. But, to perform these difficult reductions at room temperature, one should have even more powerful organic electron donors, which is an ongoing research in our lab. However, these reductions can potentially be performed at room temperature by activating the same donors using photo-induced electron transfer.[116]

Due to intense colour of these donors [DMAP-derived donor **1.249** (deep purple), DBD **1.189** (yellow), benzimidazole-derived donor **1.156** (yellow)], they are excellent candidates for photoexcitation. Garnier[117] has done UV absorption studies on the donor

1.249 and it showed maxima at 260, 345 and 520 nm (Figure 1.6), indicating that it might be susceptible to near-UV excitation.

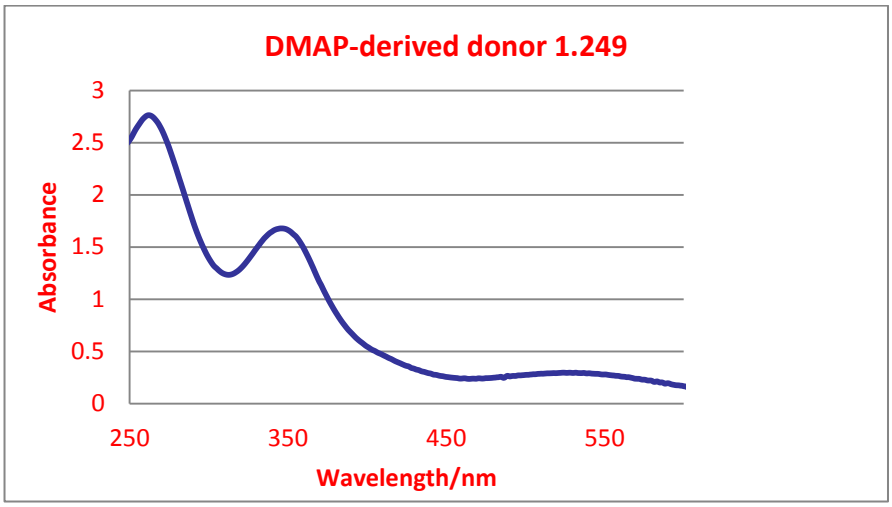
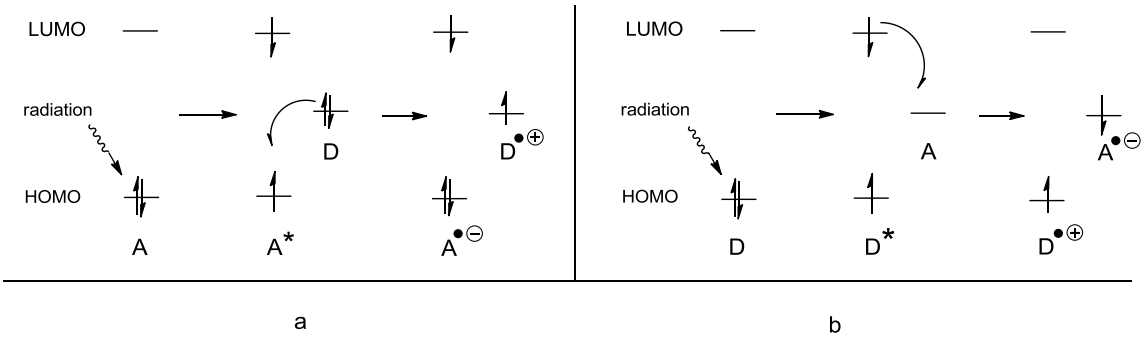


Figure 1.6 UV absorption spectrum of donor **1.249**[117]

There are two different possible activations in PET. Either activation of substrate/acceptor (A) or activation of donor (D) is possible (Scheme 1.70). In the activation of the acceptor, an electron is excited from the HOMO to the LUMO by the irradiation and a gap is left in the HOMO, which is at a low energy level compared with the LUMO level. So it is easy for the donor to give an electron into the gap in the HOMO (Scheme 1.70a). In the case of donor activation, an electron is excited from the HOMO to the LUMO of the donor. The electron in the LUMO is at higher energy and can be easily donated to the acceptor (Scheme 1.70b).

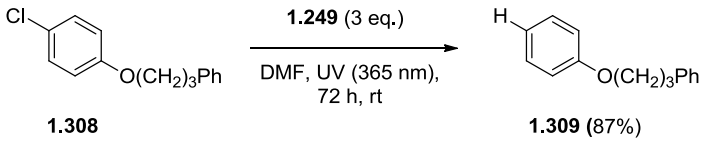


Scheme 1.70

Out of these two processes, activation of the donor is straightforward and requires a single UV source only to activate it, while different substrates need different UV sources for the same purpose.[117-121] A UV source having λ=365 nm, which is a near match to the

aborption peak at 345 nm of the donor **1.249**, has been selected for activating the donor **1.249.**

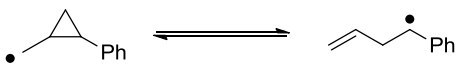
Earlier efforts to reduce more challenging substrates like chlorobenzenes had been unsuccessful using thermal activation of the donors. So, this is a good substrate to test the new reactivity of the donor **1.249** under photoactivation conditions. When substrate **1.308** in the presence of donor **1.249** was submitted to the UV source with emission at 365 nm, it afforded de-chlorinated product **1.309** in excellent yield (Scheme 1.71). On the other hand, a simultaneous reaction done under UV-blank reaction conditions (substrate was irradiated with the same UV source at the same time but without using the donor **1.249**) afforded no reductive cleavage. This reaction illustrates the enhanced reactivity of the donor under photo-induced conditions.[122]



1.308 **1.309** (87%)

Scheme 1.71

The enhanced reactivity of the photoexcited donor **1.249** encouraged our research group to further investigate whether the photoexcited donor **1.249** might be capable of transferring an electron to even more challenging benzene molecules. Newcomb[123] and Ingold[124] had used phenylcyclopropylcarbinyl radicals as probes for very fast ring-opening of cyclopropanes to phenylbutenyl radicals (Scheme 1.72). However, if cyclopropane ring opening is reversible, it will again generate the starting material. And so, the use of stereochemically pure compounds would provide better insight into these reactions.

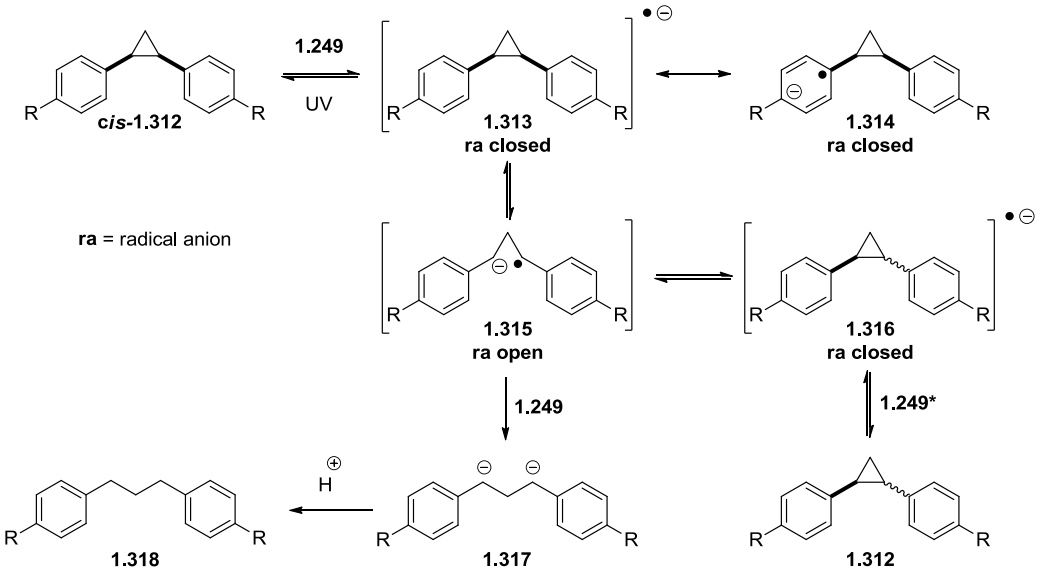


1.310 **1.311**

Scheme 1.72

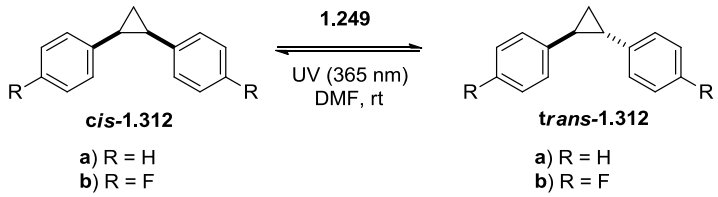
This led Cahard from the Murphy group to investigate electron transfer to stereochemically pure diphenylcyclopropanes under photoactivation conditions.[122] If the photoexcited donor **1.249** successfully transfered an electron to arene molecule ***cis*-1.312**, it would generate the radical-anion of the arene **1.313**. Similar to the Newcomb[123] and

Ingold[124] studies, the presence of a cyclopropane ring next to the radical site would lead to opening of the cyclopropane ring to form **1.315**. If the cyclopropane ring opening is reversible, it will generate again radical anion of the arene **1.316**. Since back electron transfer is possible in photochemical processes, the radical-anion may finally convert to starting arene compound **1.312**. So, if the reaction were carried out with stereochemically pure substrate like ***cis*-1.312**, then the re-formed cyclopropane **1.312** would have diminished stereochemical purity. Alternatively, if the ring opened radical-anion **1.315** takes another electron from the donor **1.249**, it would form dianion **1.317**, which, upon protonation would convert to diarylpropane **1.318** (Scheme 1.73).



Scheme 1.73

When stereochemically pure cyclopropane substrates (Scheme 1.74) were submitted to the UV source (λ=365 nm, carousel of 8 bulbs with 12 watts each), isomerisation was indeed observed and the results were shown in Table 1.1. UV-blank experiments performed along with the original reactions afforded an unchanged ratio of the starting materials.[122]

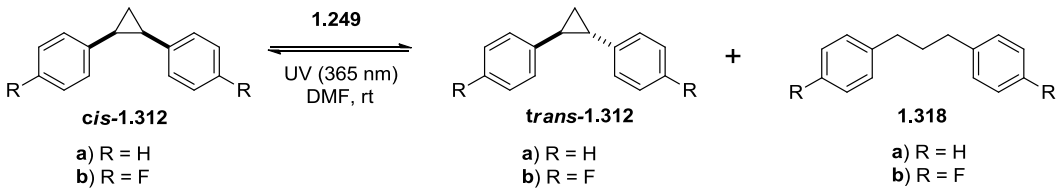


Scheme 1.74

Arene	CP *trans/cis* starting ratio	Donor **1.249** (equiv.)	Irradiation time (h)	isolated CP *trans/cis* ratio	isolated % yield
***cis*-1.312a**	2 : 98	3.0	24	19 : 81	79
***cis*-1.312b**	2 : 98	1.5	24	14 : 86	59
***trans*-1.312a**	99.5 : 0.5	3.0	24	95 : 5	88
***trans*-1.312b**	99 : 1	1.5	17	95 :5	35

Table 1.1 Outcomes of irradiation of arenes with donor **1.249** (CP = cyclopropane).

In efforts to increase the amount of isomerisation of cyclopropanes, the above reactions were repeated with an intense irradiation source (UVP Black-Ray focussed lamps, 365 nm, 2 x 100 watts) for an extended reaction time of 90h. These repeated experiments afforded a higher percentage of isomerisation along with minor amounts of 1,3-diphenylpropanes **1.318** (Scheme 1.75) and the results are shown in Table 1.2.



Scheme 1.75

Arene	CP *trans/cis* starting ratio	Donor **1.249** (equiv.)	Irradiation time (h)	CP *trans/cis* yield (%)	DP [yield (%)]
***cis*-1.312a**	2 : 98	2.0	90	46.8 : 19.6	**1.318a** (6.1)
***cis*-1.312b**	2 : 98	2.0	90	28.3 : 31.3	**1.318b** (2.8)
***trans*-1.312a**	99.5 : 0.5	2.0	90	54.2 : 7.0	**1.318a** (13.7)
***trans*-1.312b**	99 : 1	2.0	90	41.8 : 5.3	**1.318b** (5.6)

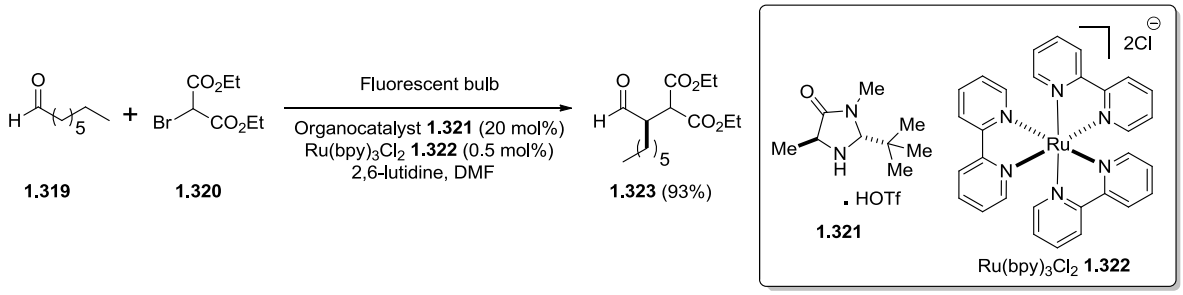
Table 1.2 Outcomes of irradiation of arenes with donor **1.249** (CP = cyclopropane, DP = diarylpropanes).

However, when chlorophenyl substrates were submitted for isomerisation under the identical photoactivated conditions, this afforded dechlorination as a competitive reaction and it provided further evidence of involvement of radical-anions.

1.3.2 Visible-light mediated electron-transfer

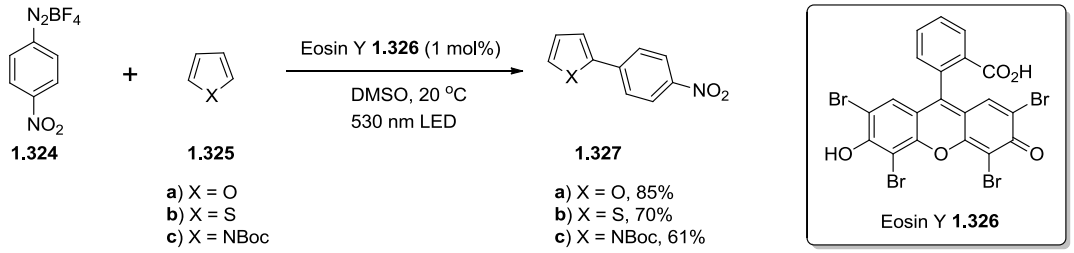
In recent times, the use of visible-light mediated photoredox catalysis to generate radical species has become popular[102] and this section aims to briefly provide a quick flavour of these reactions.

Photoredox catalysis and organocatalysis represent two powerful fields of molecule activation and they have widespread applications in chemistry. In 1980's, Kellogg *et al*. reported the reduction of activated halides, sulfonium salts and pyridinium salts by using alkyl-2,3-dihydrobenzothiazole under visible light conditions.[125] These workers found that the use of $Ru(bpy)_3Cl_2$ **1.322**, a photocatayst, greatly enhanced the reactivity. However, in 2008, MacMillan *et al*. merged these two catalysis fields and published ground-breaking asymmetric single-electron mediated organic tranformations as shown in Scheme 1.76 under visible light activation.[126] These workers used $Ru(bpy)_3Cl_2$ **1.322** as a photoredox catalyst and imidazolidinone **1.321** as a organocatalyst. They postulated that $Ru(bpy)_3^{2+}$ would be excited by a fluorescent bulb. This high energy $*Ru(bpy)_3^{2+}$ efficiently removes a single electron from an enamine intermediate and converts to $Ru(bpy)_3^{+}$, which rapidly reduces the alkyl halide **1.320** to an alkyl radical while returning to $Ru(bpy)_3^{2+}$.



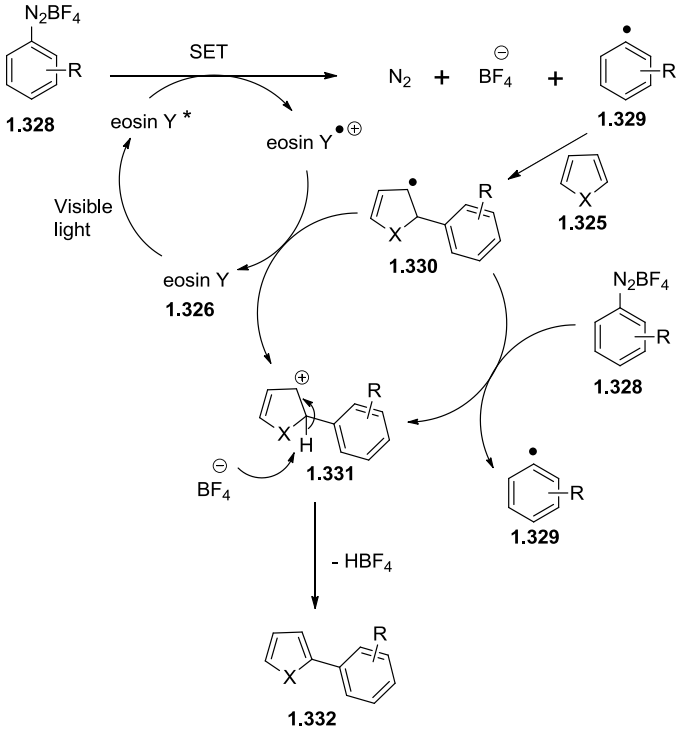
Scheme 1.76

Very recently, König *et al*. reported metal-free, visible light-mediated coupling reaction of heteroarenes with arenediazonium salts using eosin as a photoredox catalyst via a single electron transfer process (Scheme 1.77).[127] This method provides a valuable alternative to cross-coupling reactions and avoids use of transition metals, ligands, bases, or elevated temperatures.



Scheme 1.77

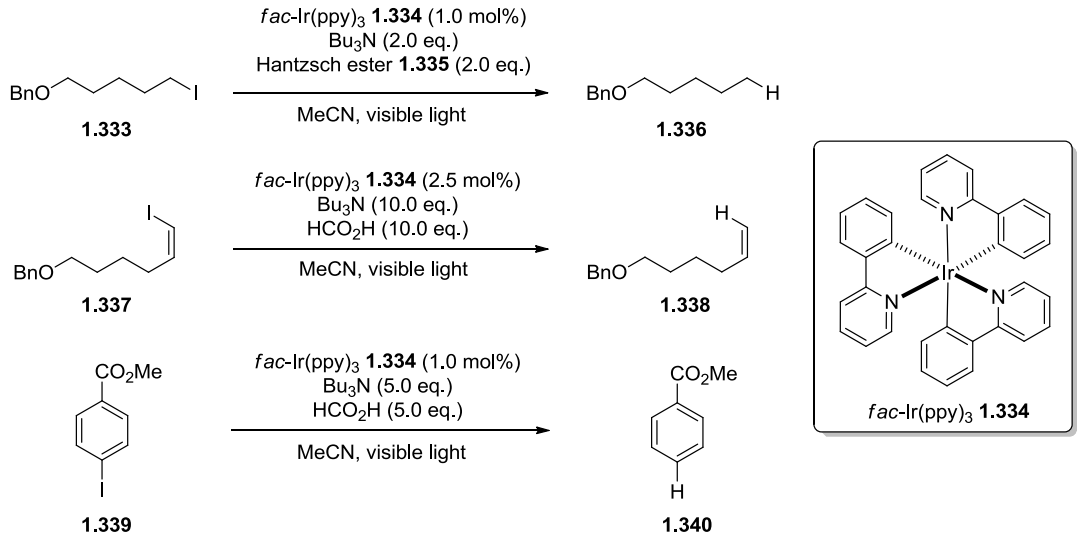
These workers proposed that aryl radical **1.329** is formed initially by single electron transfer (SET) from the excited eosin Y **1.326** to arenediazonium salt **1.328**. Addition of this aryl radical **1.329** to the heteroarene **1.325** generates new radical intermediate **1.330**, which is further transformed into carbocation intermediate **1.331** by either oxidation of the radical **1.330** by eosin Y radical-cation or oxidation of this radical intermediate **1.330** by another molecule of diazonium salt **1.328**. Finally the carbocation intermediate is deprotonated to afford the coupling product **1.332** (Scheme 1.78).



Scheme 1.78

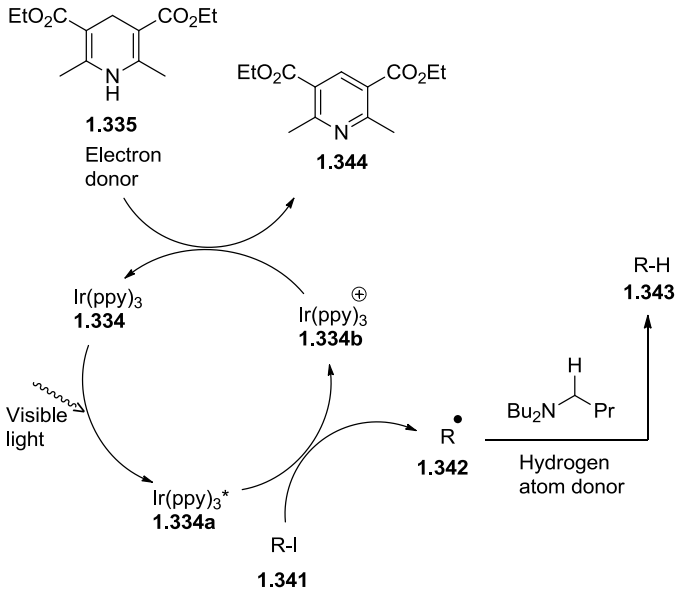
Even more recently, Stephenson *et al.* reported the generation of free radicals from unactivated alkyl, alkenyl and aryl iodides via visible-light mediated photoredox process.[102,128] The reaction protocol utilises *fac*-Ir(ppy)$_3$ as a photoredox catalyst and

formic acid/trialkylamine or Hantzsch ester **1.335**/trialkylamine combination as an effective electron donor/hydrogen atom donor (Scheme 1.79).[129]



Scheme 1.79

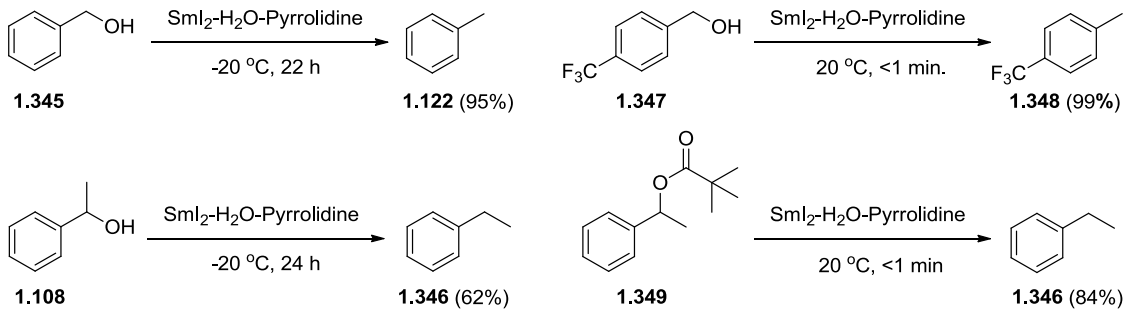
These workers proposed that visible-light excited Ir(ppy)$_3$ **1.334a** donates an electron to the carbon-iodine bond of **1.341** to afford alkyl radical **1.342** and Ir(ppy)$_3^{\oplus}$ **1.334b**, which is reduced back into its ground state **1.334** by electron donor **1.335**. Alkyl radical **1.342** abstracts hydrogen atom from trialkylamine to afford the reduced product **1.343** (Scheme 1.80).



Scheme 1.80

1.4 Benzylic C-O bond cleavages

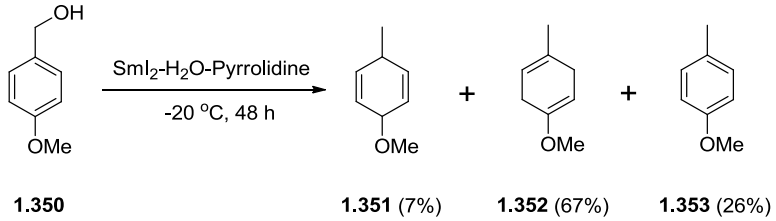
Recently, the Hilmersson group disclosed reductive cleavage of benzylic C-O bonds using an SmI_2-H_2O-amine system.[57] A series of substituted benzyl alcohols was efficiently reduced in good yields by using this system (Scheme 1.81).



Scheme 1.81

Benzyl alcohol **1.345** was reduced to toluene **1.122** in excellent yield (95%), while 1-phenylethanol **1.108** gave only 62% of product **1.346** under similar reaction conditions. Amazingly, the trifluoromethyl-substituted benzyl alcohol **1.347** and benzyl alcohol-derived ester **1.349** were reduced instantaneously to give the corresponding products **1.348** and **1.346** in good yields.

In contrast, *p*-methoxybenzyl alcohol **1.350** gave only 26% of the expected product **1.353** even after 48 h reaction time. It was found that the major products were cyclohexadiene derivatives **1.351** and **1.352**, which were characteristic of Birch reduction processes (Scheme 1.82).

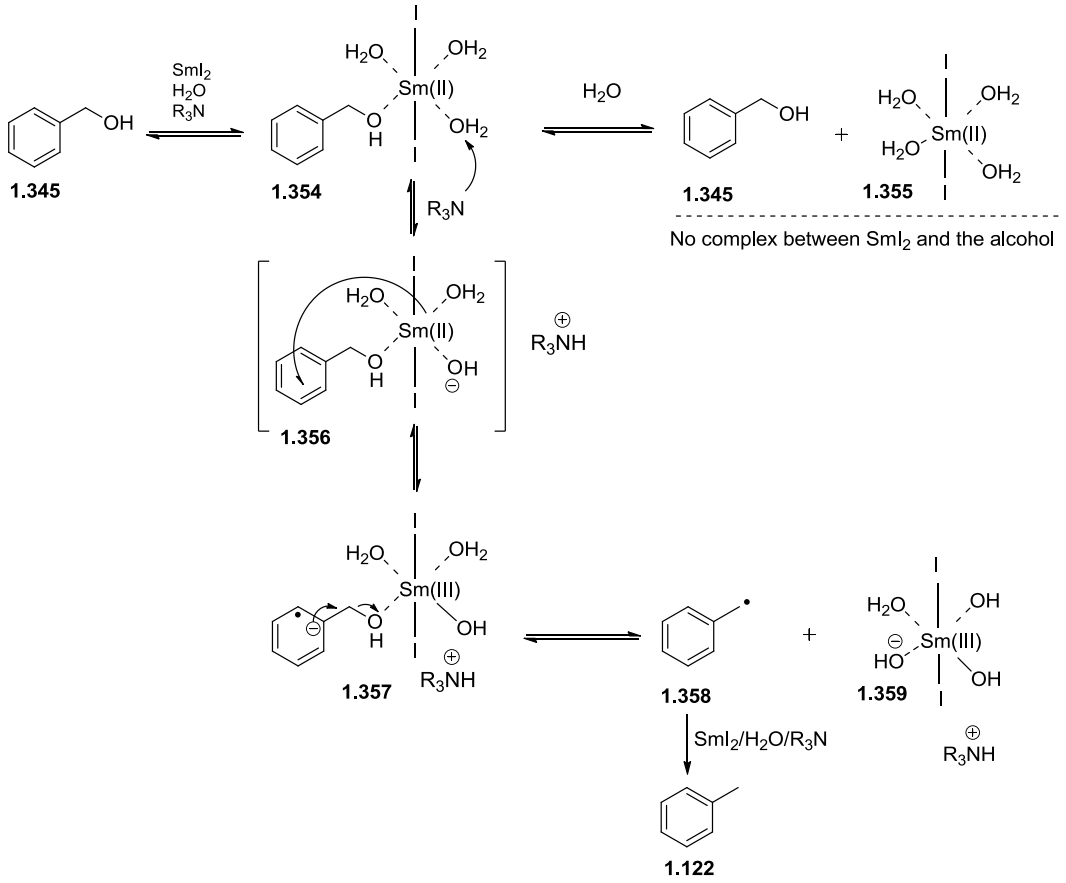


Scheme 1.82

From the above results, it was concluded that both steric bulk around the benzyl carbon and electronic factors were playing a significant role in the success of the reaction. From kinetic studies, it was noted that electron-withdrawing groups on the aromatic ring

enhanced the rate of the reaction while *p*-methoxy substrates had lower rates. It should be noted that *p*-methoxy substituents might destabilise the radical-anion formed in the reaction and thereby lower the overall rate of the reaction.

The proposed mechanism of these reductions is shown in Scheme 1.83.

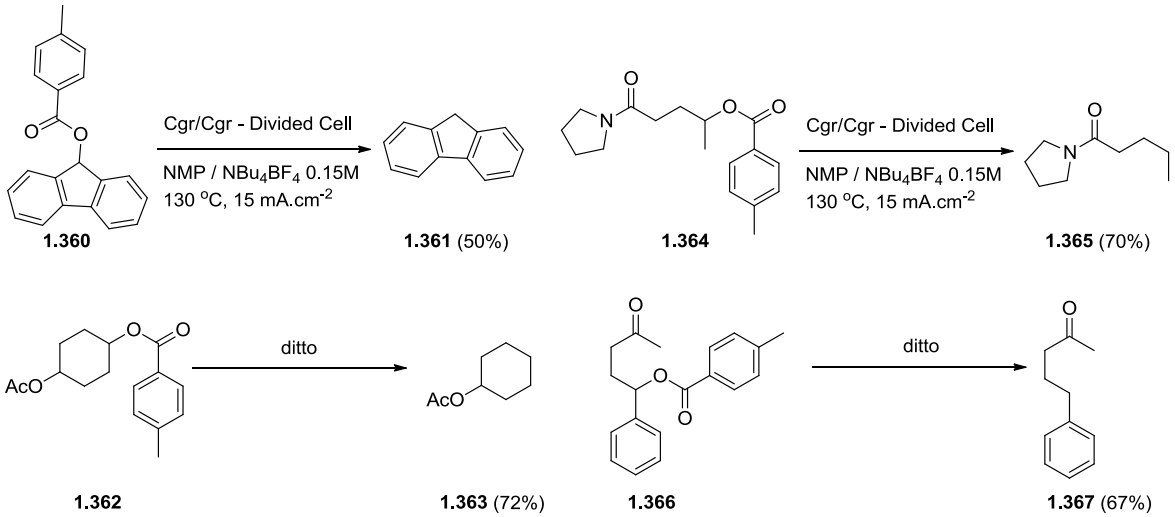


Scheme 1.83

With the use of three equivalents of water, the reduction rate was found to be high and greater amounts of water resulted in a lowered rate. As water coordinates strongly, compared with benzyl alcohol, to the metal ion, water can replace benzyl alcohol, leading to no complexation between metal and benzyl alcohol. Strong dependence on electronic factors indicates that the reaction goes through a radical anion intermediate. The role of the amine is to deprotonate the complex. Keeping all these points in mind, the following mechanism is suggested by these workers. Benzyl alcohol **1.345** and water are coordinated to samarium diiodide in forming complex **1.354**, and the amine will deprotonates this species to form complex intermediate **1.356**. The samarium transfers one electron to form radical anion complex **1.357**, which rearranges to form benzyl

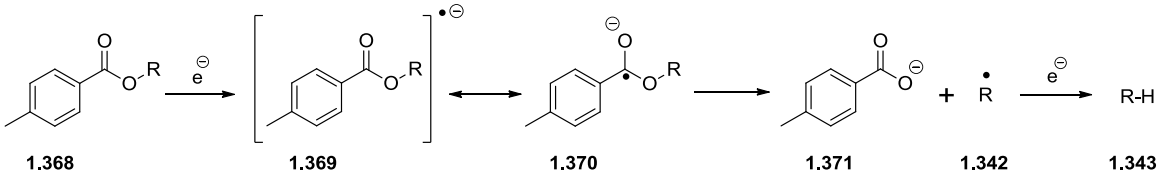
radical **1.358**. This benzyl radical **1.358** takes another electron and a proton to give toluene **1.122** as the reduced product.

Recently, Marko *et al.* developed a new concept of using toluates as versatile radical precursors,[130,131] using both electrochemical[132] and chemical[133] methods to reduce these toluates. When the reaction was conducted in a divided H-type cell in *N*-methyl-2-pyrrolidone (NMP) at 130 ^{o}C, using tetrabutylammonium tetrafluoroborate as the supporting electrolyte, they found that substrate **1.360** was reduced to **1.361** in 50% yield. The temperature of the reaction played a vital role and it was found that no reaction occurred at room temperature. When a wide range of substrates with different functional groups such as esters **1.362**, amides **1.364** and ketones **1.366** were tested, the toluate ester was selectively reduced (Scheme 1.84). The same reaction also worked well using SmI_2 in THF and HMPA under refluxing conditions.[133]



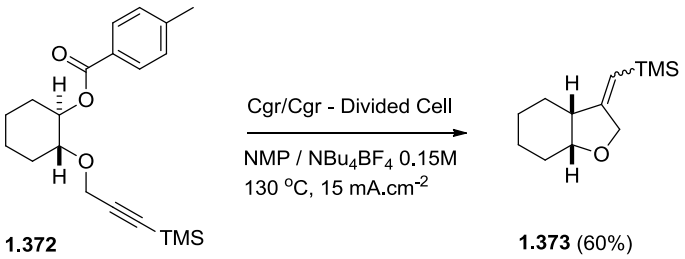
Scheme 1.84

The proposed mechanism of reduction of toluates under electrochemical conditions is shown in Scheme 1.85. The aromatic esters **1.368** are first reduced to radical anion **1.370**. This radical anion **1.370** decomposes to carboxylate **1.371** and radical **1.342**. The rate of decomposition depends on the stability of radical **1.342** formed in the reaction. The more stable the radical, the faster is the breakdown of radical anion **1.370**. The radical **1.342** can accept one electron and a proton to form the corresponding reduced product **1.343**.



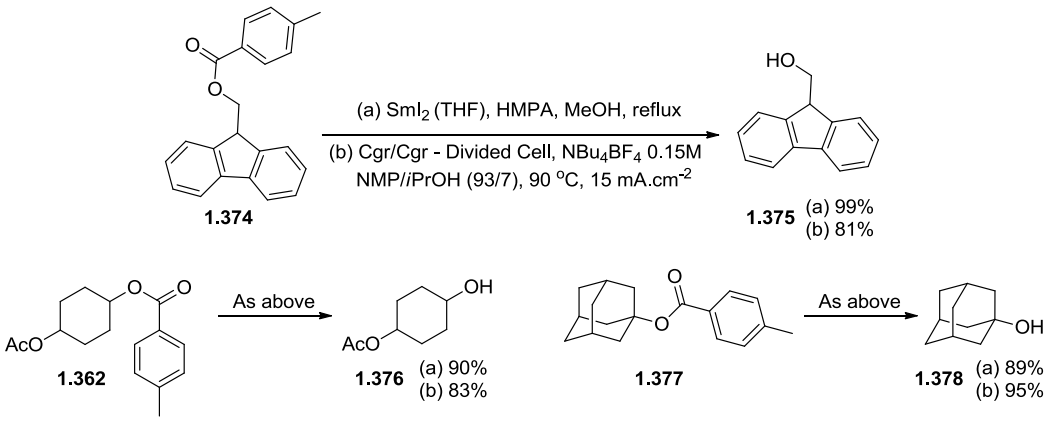
Scheme 1.85

To demonstrate the formation of the radical during the electrochemical process, a well designed substrate having a suitably positioned triple-bond **1.372** was tested under the same reaction conditions. As expected, tetrahydrofuran **1.373** was isolated in good yield following cyclisation of the intermediate radical (Scheme 1.86). As previously discussed, carbanions were not capable of undergoing cyclisation, which supported the formation of the radical intermediate.



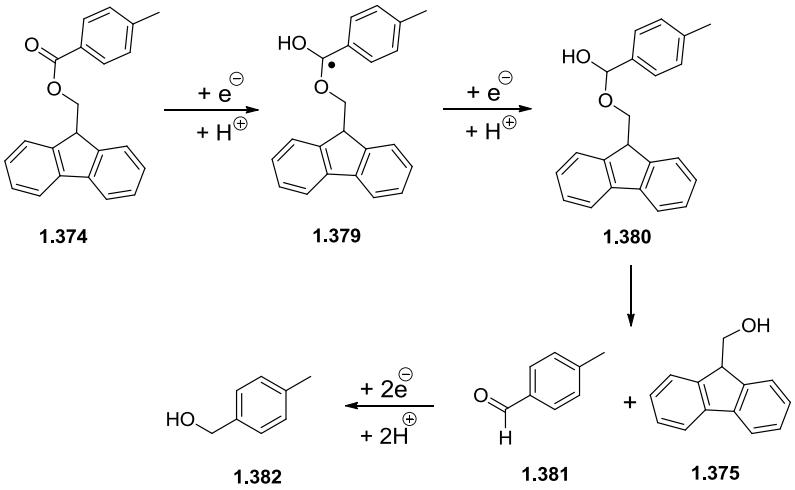
Scheme 1.86

Surprisingly, upon the addition of a protic source, such as an alcohol, to the previously used reduction conditions for toluates ($TolCO_2R$), alcohols (ROH) were formed as products instead of the deoxygenated counterparts.[131] This was a useful method to deprotect toluate esters chemoselectively in the presence of other sensitive protecting groups. Cyclic voltammetry studies revealed that addition of alcohol to the electrolytic reaction medium quenched the *in situ* generated radical anion and completely suppressed reversibility of the reduction process. A series of substrates was tested under the new reduction conditions (Scheme 1.87). It was observed that primary **1.374**, secondary **1.362** and tertiary toluate **1.377** were reduced to afford high yields of free alcohols with equal efficiency, indicating that toluate was the electro-active portion of the substrate during the reduction process.



Scheme 1.87

When substrate **1.374** was tested with a large excess of samarium diiodide, *p*-methylbenzyl alcohol **1.382** was isolated as by-product along with **1.375**.[130] This led to the proposal of the following mechanism (Scheme 1.88). *In situ* generated radical anion from **1.374** was rapidly protonated by the alcohol giving the radical **1.379**, which was then transformed into hemiacetal **1.380** by a second electron-transfer and proton abstraction. Hemiacetal **1.380** then spontaneously decomposed into alcohol **1.375** and aldehyde **1.381**. This aldehyde **1.381** was subsequently reduced to 4-methylbenzyl alcohol **1.382** through a double electron-transfer and proton abstraction sequence.

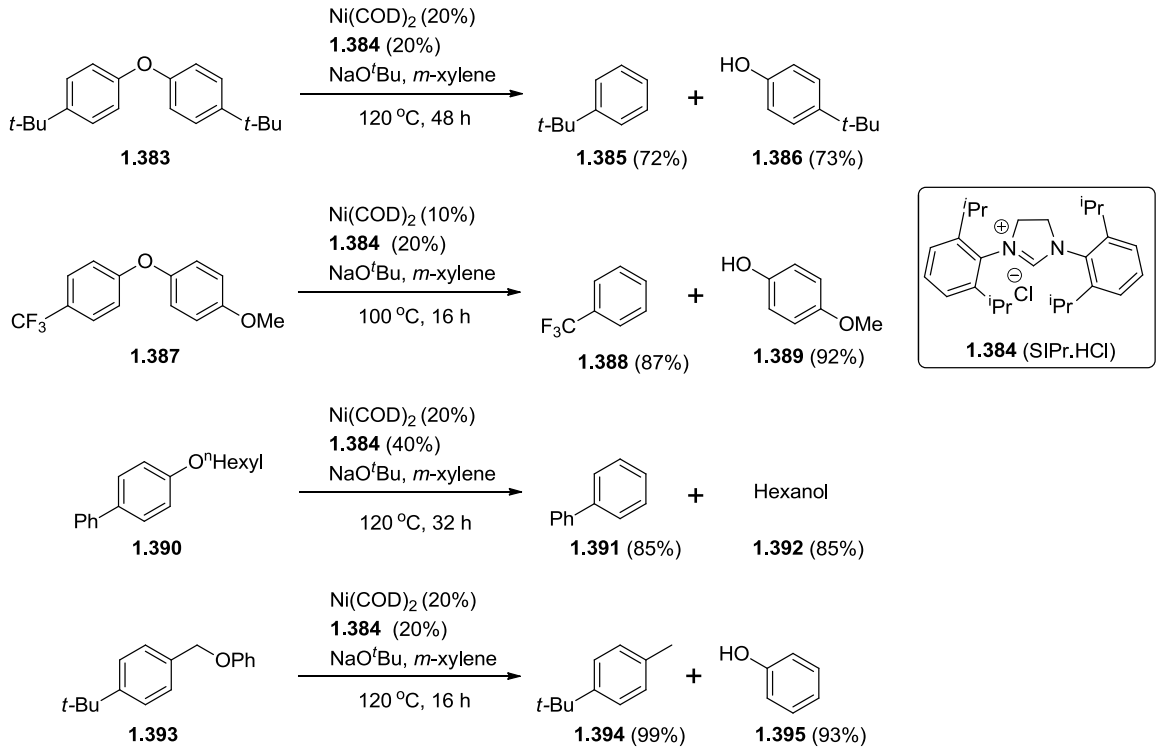


Scheme 1.88

Activation of aryl C-OR bonds is very challenging due to the relatively high bond strength and stability of these linkages. However, in light of diminishing fossil fuels, this type of selective hydrogenolysis is an important process for the degradation of oxygen-rich

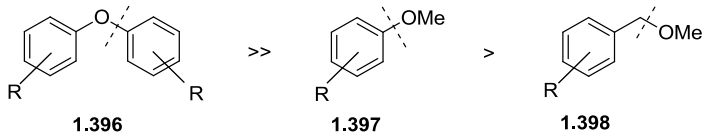
lignocellulosic plant biomass, such as lignin, and for providing renewable chemicals and fuels. There are a number of reports on degradation of lignin, where C-O bonds are cleaved either by reduction or oxidation using transition metal-based catalysts and, in fact, the selectivity can be tuned by the choice of transition metals.[134-138]

Sergeev and Hartwig recently reported that a nickel carbene catalyst could selectively provide hydrogenolysis of various diaryl e.g. **1.383** and **1.387**, aryl alkyl e.g. **1.390** and benzyl aryl ethers e.g. **1.393** (Scheme 1.89).[134] It was found that hydrogenolysis occurred faster in substrates containing electron-withdrawing groups such as **1.387** than substrates containing electron-donating groups such as **1.383**.



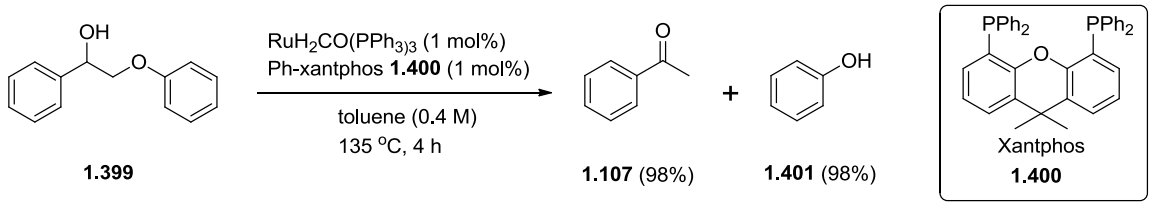
Scheme 1.89

These workers also performed competition reactions in which two substrates were taken at a time in a reaction flask and they found that hydrogenolysis of benzyl alkyl ethers, such as **1.398**, was much more difficult than diaryl and aryl alkyl ethers, such as **1.396** and **1.397**, respectively (Scheme 1.90).



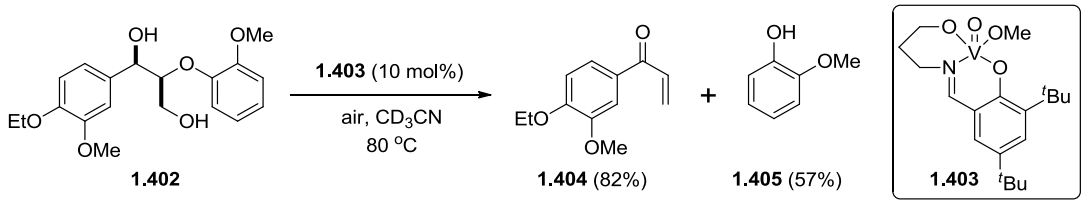
Scheme 1.90

Bergman and co-workers described tandem catalytic dehydrogenation and C-O bond cleavages.[137] This method required a catalyst that could perform both hydrogen shuttling and C-O bond cleavage in tandem fashion. They successfully applied the ruthenium xantphos catalyst to achieve depolymerisation of lignin-related polymers in high yields. A model reaction is represented in Scheme 1.91 using substrate **1.399**.



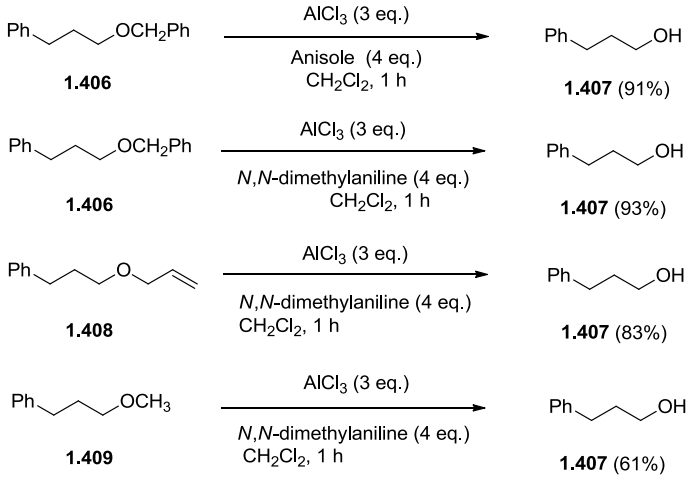
Scheme 1.91

Son and Toste recently reported C-O bond cleavages in lignin model compound **1.402** using vanadium catalyst **1.403** under aerobic oxidation conditions and provided alkene **1.404** and 2-methoxyphenol **1.405** as major products.[138] This strategy did not require any other reagents and provided water as the only by-product of reduction. (Scheme 1.92)



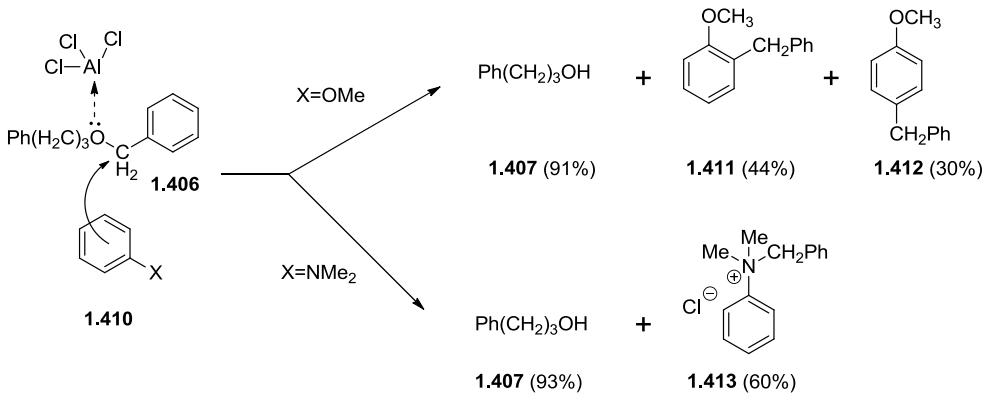
Scheme 1.92

A combination of Lewis acid and soft nucleophile such as $AlCl_3$-anisole or $AlCl_3$-*N*,*N*-dimethylaniline was used as a deprotecting agent and successfully cleaved benzyl ethers *e.g.* **1.406**, allyl ethers *e.g.* **1.408** and methyl ethers *e.g.* **1.409** and provided parent alcohol **1.407** in good yield (Scheme 1.93).[139] When triethylamine or pyridine was used as a soft nucleophile, no reaction was seen and this might be due to strong complex formation of the $AlCl_3$ and amine.



Scheme 1.93

During the reaction, $AlCl_3$ coordinates with the ether oxygen in **1.406** and soft nucleophile **1.410** attacks the soft benzyl carbon atom in **1.406**. In the case of anisole, Friedel-Crafts alkylation products **1.411** and **1.412** were produced in addition to the parent alcohol **1.407**. In contrast, *N*,*N*-dimethylaniline provided a salt **1.413** along with alcohol **1.407** (Scheme 1.94).

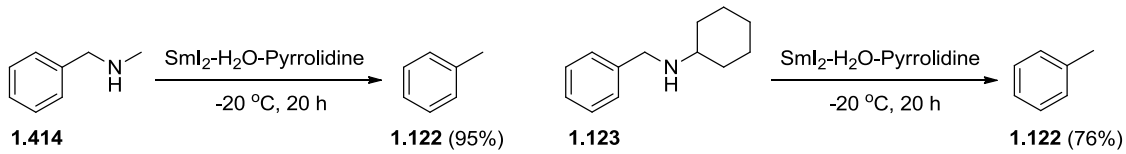


Scheme 1.94

In addition to the above Lewis acid and soft nucleophile systems, a number of reagents such as trimethylsilyl iodide (TMSI),[140] TMSCl/NaI,[141] $SiCl_4$/NaI,[142] TMSCl/Ac_2O/cat. H_2SO_4,[143] BF_3/EtSH,[144] $BF_3.OEt_2/Me_2S$,[145] $BF_3.OEt_2$/NaI[146] and DDQ[147] have been successfully applied as deprotecting agents for the cleavage of benzyl ethers.

1.5 Benzylic C-N bond cleavages

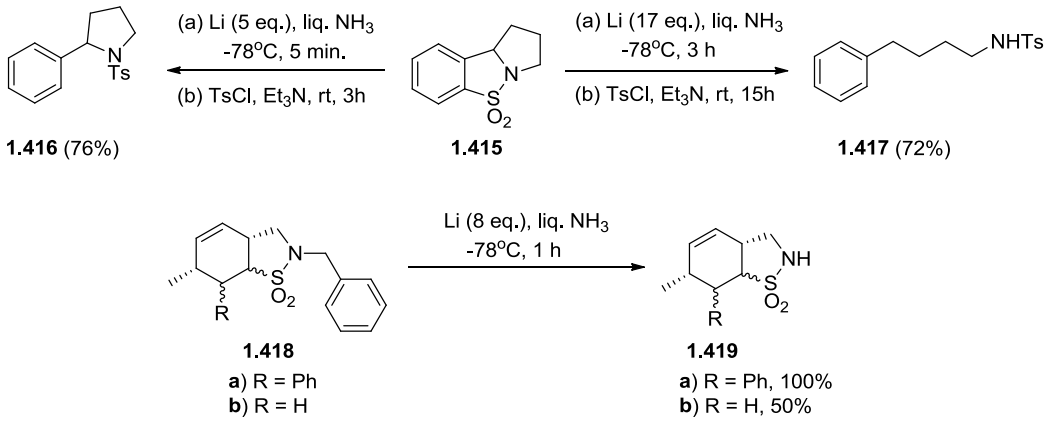
Hilmersson and co-workers extended the chemistry of the SmI_2-H_2O-pyrrolidine system to the reductive cleavage of benzylic C-N bonds.[71] Substrates **1.414** and **1.123** provided good yields of reduced product **1.122** similar to the benzylic C-O bond cleavages (Scheme 1.95). These workers had done kinetic studies and revealed that the rate of reduction of these amine substrates was lower than that of benzyl alcohol substrates.



1.414 **1.122** (95%) **1.123** **1.122** (76%)

Scheme 1.95

Evans *et al*. used Birch conditions for double reduction of sulfonamides, like **1.415**, to synthesize aryl substituted pyrrolidines **1.416**.[148,149] But, when a large excess of lithium (17 eq.) was used in the reaction, it afforded exclusive benzylic C-N bond cleavage product **1.417**. These workers reasoned that benzylic cleavage had occurred after the desired sulfonamide reduction. However, when they submitted *N*-benzyl compounds **1.418**, which did not have an α-arene ring to the sulfone moiety, they saw exclusive rapid debenzylation (benzylic C-N bond cleavage) reaction. The presence of a β-phenyl group to the sulfone moeity in **1.418a** helped the reaction to afford a better yield compared with **1.418b** and this might be due to the lowering of activation energy associate electron-transfer in **1.418a** (Scheme 1.96).



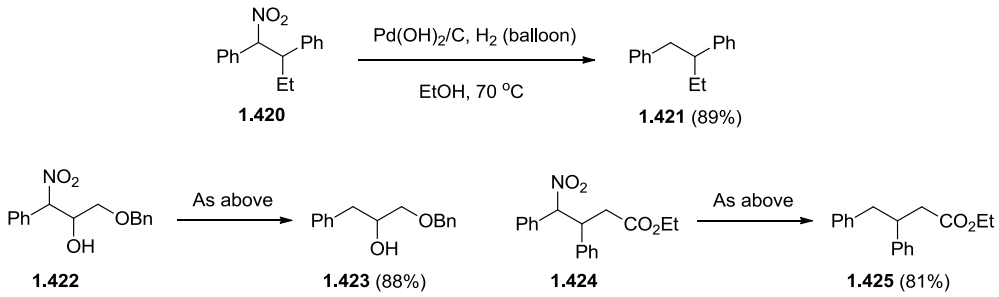
1.416 (76%) **1.415** **1.417** (72%)

1.418
a) R = Ph
b) R = H

1.419
a) R = Ph, 100%
b) R = H, 50%

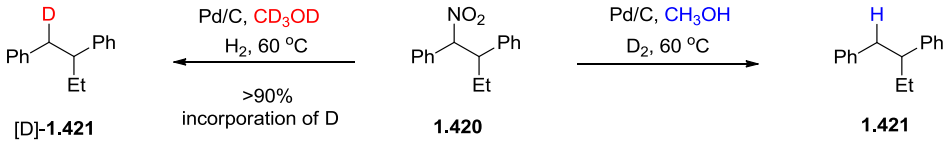
Scheme 1.96

Carreira and co-workers found that submitting benzylic nitroalkanes **1.420**, **1.422** and **1.424** to Pearlman's catalyst, $Pd(OH_2)/C$, in ethanol under hydrogen gas provided heterolytic reductive cleavage of the C-N bond and afforded parent alkanes in good yield.[150] The presence of electron-withdrawing and electron-donating groups in the substrates was well tolerated under the reaction conditions (Scheme 1.97).



Scheme 1.97

They also carried these reactions in CH_3OH and CD_3OD and claimed that the solvent was acting as a source of benzylic hydrogen atoms (Scheme 1.98).

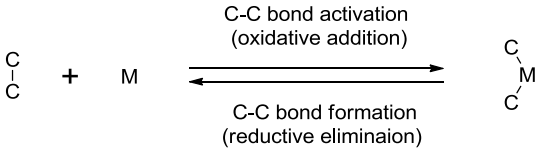


Scheme 1.98

1.6 Benzylic C-C bond cleavages

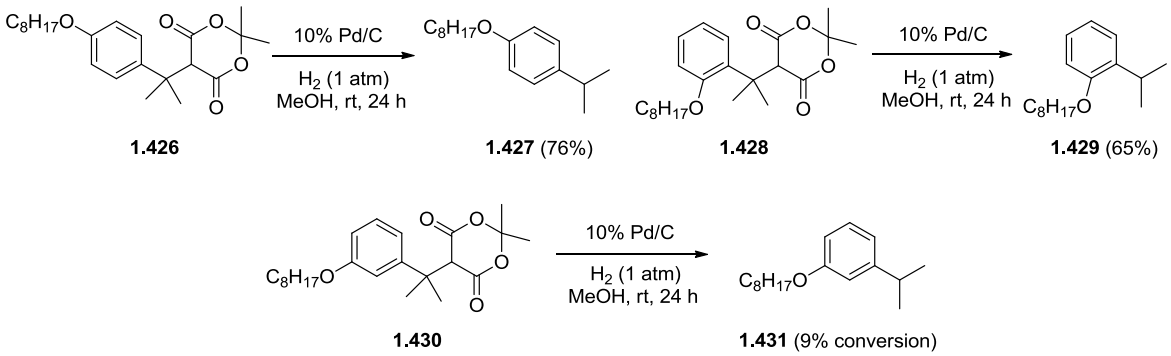
Activation of unstrained sp^3-hybridised carbon-carbon bonds has attracted many organic chemists due to its potential applications in organic synthesis. This topic remains unexplored due to the inherent challenges of such a strong and stable carbon-carbon bond.[151-154] Although hydrogenolysis of C-X bonds (X = N, O, S) is well known, the corresponding hydrogenolysis of carbon-carbon bonds under mild reaction conditions is unprecedented.[155] Successful C-C bond cleavages reported so far in the literature necessitate strained rings, such as cyclopropanes and cyclobutanes,[156,157] or high temperature and pressure.[158,159]

The C-C bond activation by metal (oxidative addition) can be considered as the reverse of the C-C bond formation (reductive elimination) and C-C bond activation is thermally less favourable as two weak carbon-metal bonds are formed at the expense of a relatively strong C-C bond (Scheme 1.99).[154]



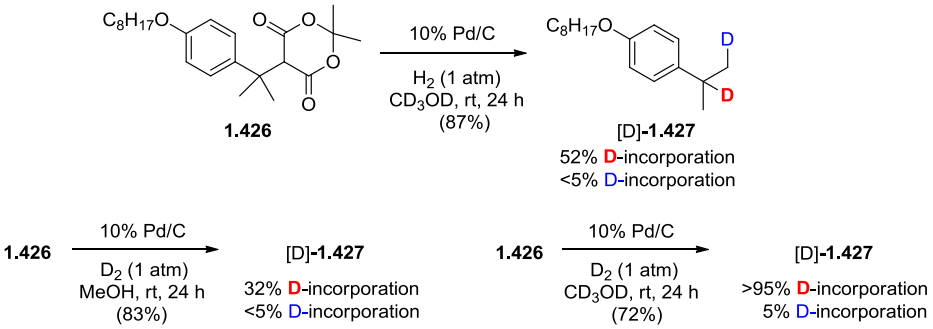
Scheme 1.99

Fillion and co-workers recently communicated the hydrogenolysis of unstrained sp^3-hybridised benzylic carbon-carbon σ bonds using Pd/C.[160] They reported that this C-C bond cleavage was highly dependent on electronic factors where *para*- and *ortho*-analogues **1.426** and **1.428** were readily cleaved compared to *meta*-substituted compound **1.430** (Scheme 1.100).



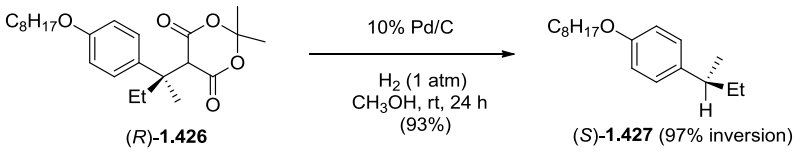
Scheme 1.100

These reactions were further investigated through labelling studies with the combination of D_2 gas and CD_3OD and deuterium incorporation was observed in all cases, as shown in Scheme 1.101.[160]



Scheme 1.101

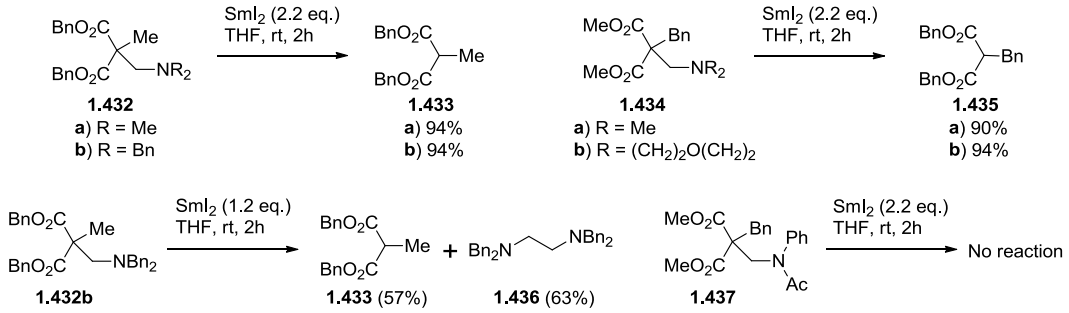
Further insight into the mechanism was gained by submitting enantioenriched substrate (*R*)-**1.426** to the above reaction conditions where product (*S*)-**1.427** was formed with nearly complete inversion. This strongly suggested that the C-C σ bond scission was following an S_N2 mechanism (Scheme 1.102). Therefore, these fragmentation reactions most likely don't involve electron transfer but involve palladium hydride or a "hydride equivalent" that attacks the susceptible C-C bond in *(R)*-1.426 as a nucleophile.[160]



(*R*)-**1.426** (*S*)-**1.427** (97% inversion)

Scheme 1.102

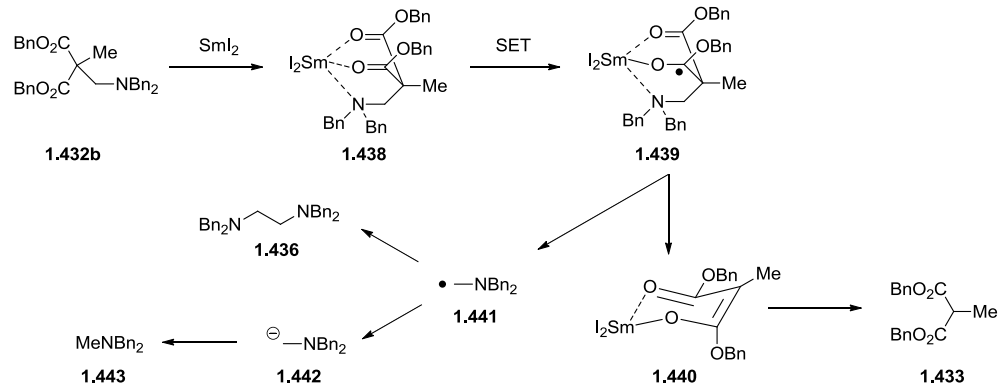
Recently, Zhai *et al.* reported samarium diiodide mediated C-C bond fragmentation in α-aminomethyl malonates.[161] They claimed that the presence of the amino group is necessary for the success of the reaction. Substrates **1.432** and **1.434** afforded excellent yields of fragmented products **1.433** and **1.435** respectively (Scheme 1.103).



Scheme 1.103

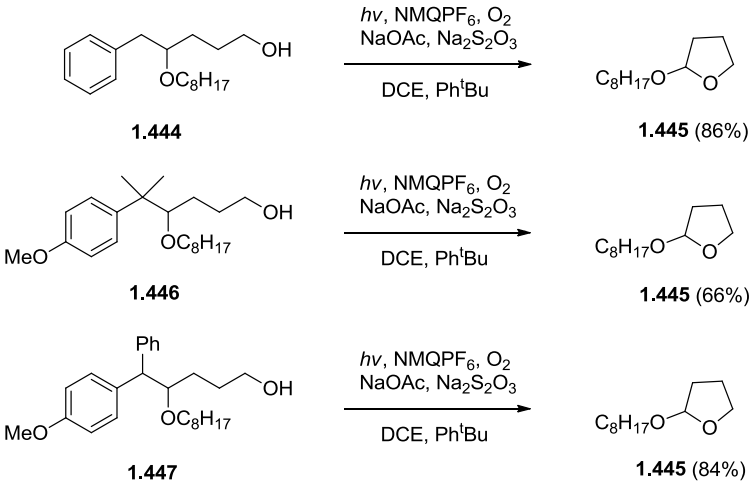
These workers proposed that samarium forms simultaneous coordination with the electron-rich nitrogen atom and two carbonyl oxygen atoms as shown in **1.438**. Subsequently, SET from samarium leads to ketyl radical-anion **1.439**, in which samarium(III) is coordinated with the nitrogen and the carbonyl oxygen of the other ester group. Fragmentation of **1.439** leads to samarium(III) enolate **1.440** and radical **1.441**. After aqueous work-up, **1.440** affords fragmented product **1.433**. On the other hand, the radical **1.441** can alternatively undergo homocoupling to provide **1.436** or undergo further reduction to anion **1.442** in the presence of excess SmI_2. This anion **1.442** converts to **1.443** during aqueous work-up (Scheme 1.104). Controlled reaction of **1.432b** with 1.2 eq.

of SmI_2 afforded **1.436**, supporting the generation of radical **1.441**. Unsuccessful reaction of **1.437** presumably resulted from failure of formation of tridentate coordination to samarium (Scheme 1.103).



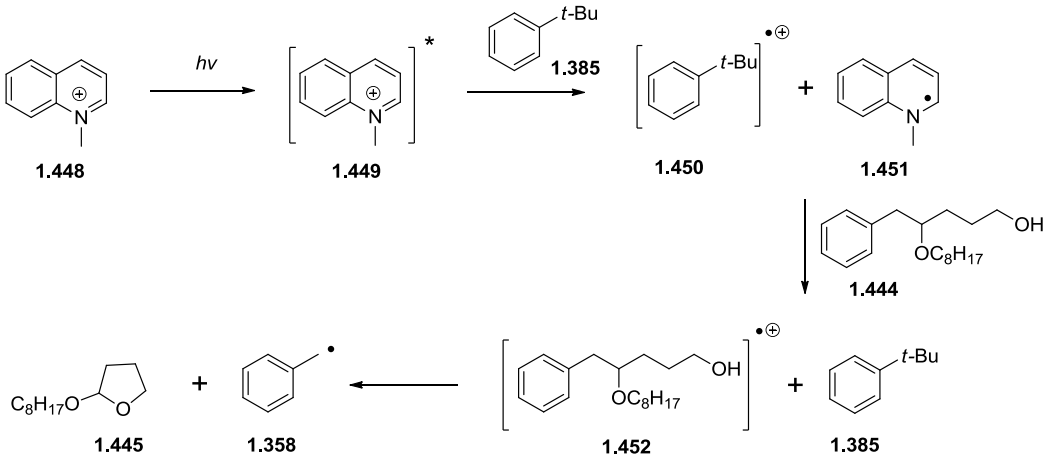
Scheme 1.104

Floreancig and co-workers have divulged the mesolytic carbon-carbon σ bond cleavages of homobenzylic ethers via photoinduced electron transfer.[162-164] Initiailly, substrate **1.444** did not produce any cyclised product using Arnold's conditions[165] *i.e.* *hv* and 1,4-dicyanobenzene as a photosensitizer. Later, Floreancig's group envisioned that increasing the lifetime of radical-cations would result in the desired reaction. Hence, *N*-methylquinolinium hexafluorophosphate ($NMQPF_6$), NaOAc (buffer), *tert*-butylbenzene (co-sensitizer) and aerobic conditions were used to test **1.444** and the reaction provided cyclised product **1.445** in good yield.[163] 4-Methoxy substrates **1.446** and **1.447**, in which radical stabilising groups were added at the benzylic position, gave good results under the same reaction conditions (Scheme 1.105).



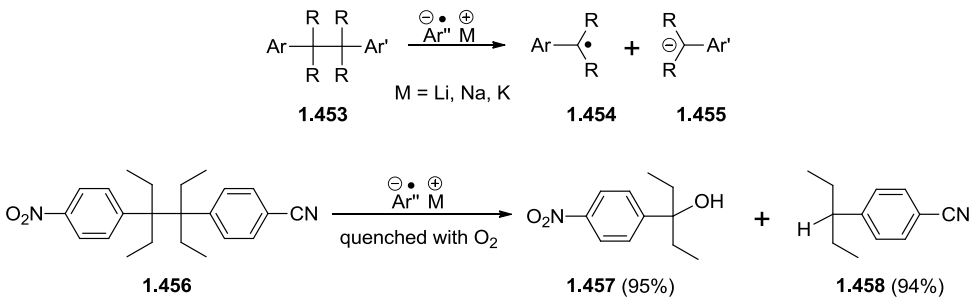
Scheme 1.105

N-Methylquinolinium hexafluorophosphate **1.448** and *tert*-butylbenzene **1.385** acted as photosensitizers and the substrate **1.444**, under photoactivation, converted to radical-cation **1.452** upon losing one electron to this system. Later, **1.452** provided benzylic radical **1.358** and cyclised product **1.445** through electron transfer initiated cyclisation (Scheme 1.106).



Scheme 1.106

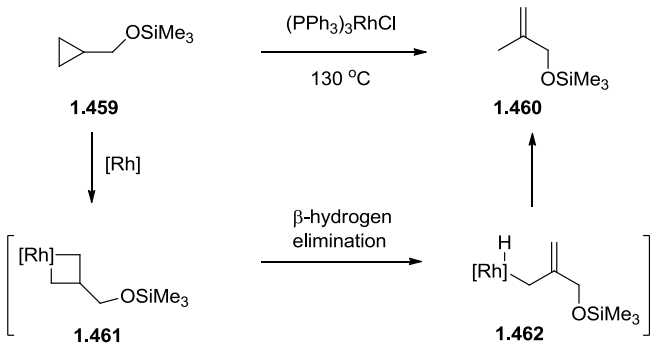
Reductive C-C cleavages where arenes play the role of electron acceptor are rarer, although Maslak in particular has studied the reductive mesolytic cleavage of crowded 1,1,2,2-tetraalkyl-1,2-diphenylethanes **1.453**.[166,167] For the cleavage to occur, sterically encumbered substrates must be used and to facilitate the reduction, an electron-withdrawing group was usually present on at least one of the arene rings. Low-valent metal complexes such as lithium 2,4,6-tri-*t*-butylnitrobenzenide or potasium or sodium salts of *N*,*N*-dimethylaminonaphthalenide are key to all of these fragmentation reactions.



Scheme 1.107

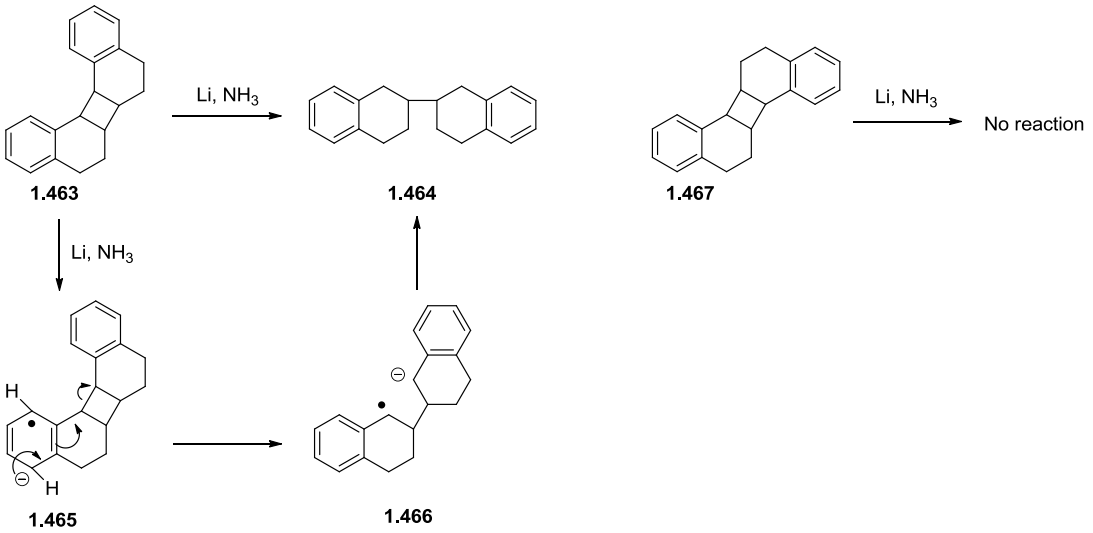
There are a number of reports of C-C bond cleavage of ring-strained compounds compared to unstrained molecules in literature and the driving force for these cleavages is

the relief of ring-strain. Recently, Bart and co-workers reported C-C bond cleavage of cyclopropane derivative **1.459** using a rhodium catalyst.[168] Initially, a non-sterically hindered carbon-carbon bond in cyclopropane **1.459** was cleaved by rhodium catalyst to give complex **1.460**. This complex **1.461** upon β-hydrogen elimination followed by reductive eleimination provided alkene **1.460** (Scheme 1.108).



Scheme 1.108

There are also a number of reports of alkali-metal induced carbon-carbon bond cleavages in strained molecules.[169-171] Eisenbraun and co-workers have seen that photodimer **1.463**, on subjecting to lithium/sodium in ether-ammonia, was selectively cleaved to hydrocarbon **1.464**. In contrast, photodimer **1.467**, an isomer of **1.463**, was totally inert under the same reaction conditions. This surprising difference in reactivity is envisaged to arise from a combination of ring-strain and stabilisation of anionic intermediate **1.466** by the adjacent phenyl ring (Scheme 1.109).[169]

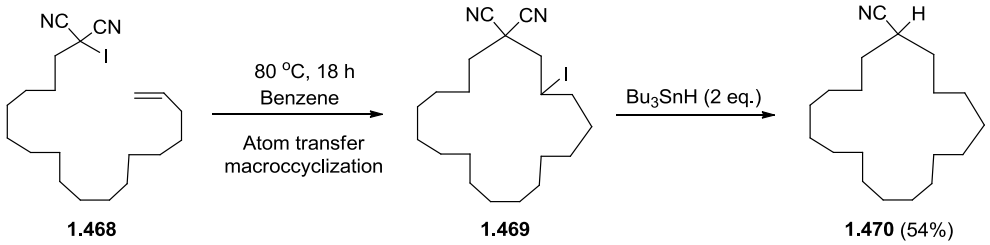


Scheme 1.109

1.7 Reductive decyanation of malononitriles

Decyanation of malononitriles (*gem*-dinitriles) to mono nitriles is an important transformation in view of the usefulness of the nitrile functionality in organic synthesis. Nitrile groups can be easily hydrolysed to carboxylic acids and reduced to amines. Alkyl nitriles are sufficiently acidic to form the α-carbanion and can be alkylated using a wide variety of electrophiles.

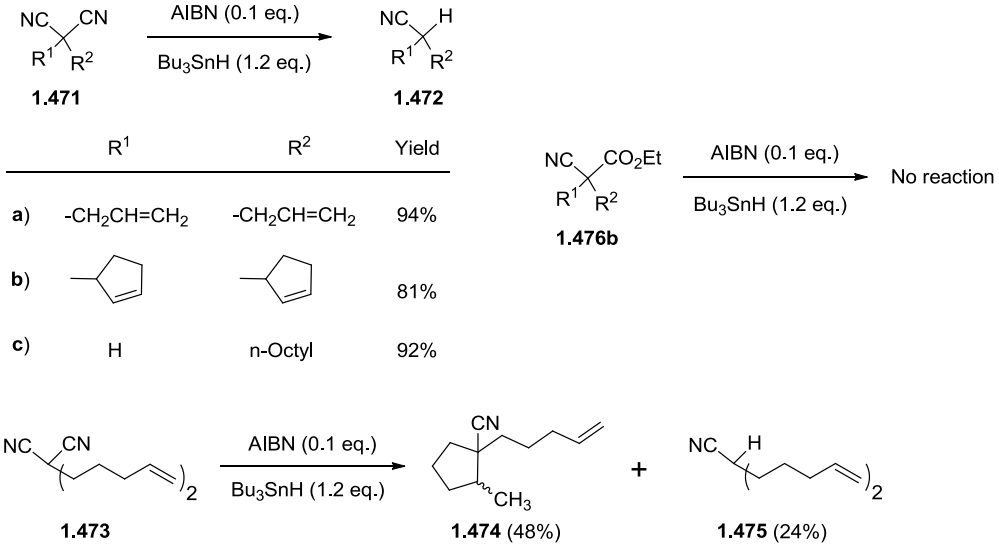
Curran and Seong accidently discovered decyanation during their investigations on atom-transfer radical cyclisations.[172] Heating of iodomalononitrile **1.468** in benzene at 80 ^{o}C provided a substantial amount of desired atom transfer macrocyclization product **1.469**. To facilitate the isolation of macrocyclic product, they treated the crude product **1.469** with 2 equivalents of Bu_3SnH to ensure complete deiodination. But, to their surprise, they saw product **1.470** arising from both deiodination and decyanation (Scheme 1.110).



1.468 **1.469** **1.470** (54%)

Scheme 1.110

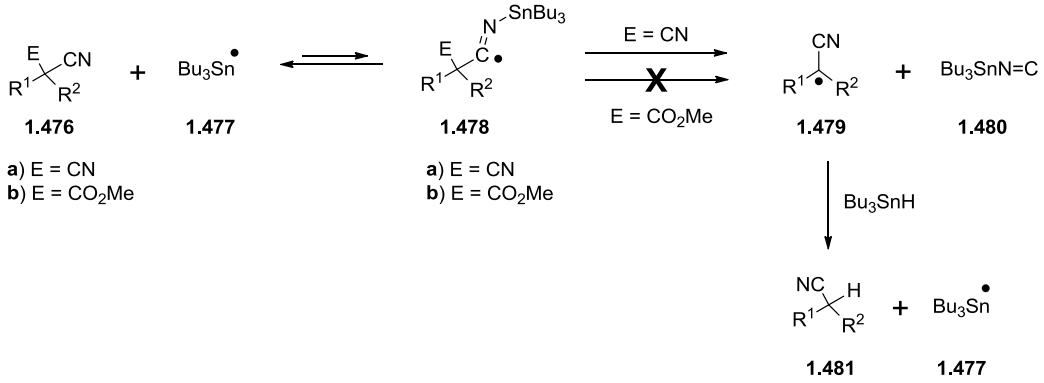
Later, they made a full study of these transformations, as shown in Scheme 1.111.[173]



Scheme 1.111

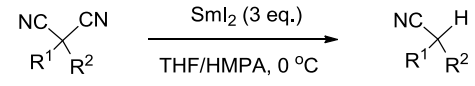
A series of malononitriles **1.471** was successfully reductively decyanated to **1.472** in excellent yields. Substrate **1.473** having suitably placed alkene groups provided cyclised product **1.474** in addition to the usual decyanated product **1.475** (Scheme 1.111). This suggested the presence of radical intermediates.

They proposed that trybutyltin radical adds (probably reversibly) to the nitrogen atom of the substrate **1.476a** and generates intermediate **1.478a**. Fragmentation of this intermediate **1.478a** must rapid enough to afford mono nitrile radical **1.479**, which is supported by the generation of cyclised product **1.474** in the reaction of **1.473**. Finally, a standard hydrogen transfer from tributyltin hydride to **1.479** completes the chain and provides the decyanated product **1.481**. However, cyanoacetates **1.476b** did not provide any reaction under the same conditions. They reasoned that the fragmentation of intermediate **1.478b** is not fast enough, compared to the reverse addition, to propagate a chain (Scheme 1.112).



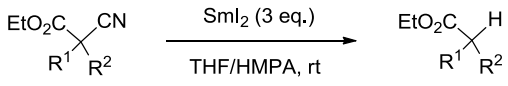
Scheme 1.112

In 1995, Kang and Hong reported similar reductive decyanation reactions of malononitriles mediated by samarium diiodide-THF-HMPA system.[174] They successfully decyanated malononitriles **1.482** at 0 ^{o}C and cyanoacetates **1.484** at room temperature. However, substrates **1.482c** and **1.484c** having suitably placed alkene groups provided no cyclised product but just the usual decyanated products **1.483c** and **1.485c** respectively. They did not discuss the mechanism in detail but the conversion of radical intermediates to anionic intermediates might be very fast in the presence of excess samarium diiodide so that they would not observe the type of cyclised products seen in Curran's work[173] (Scheme 1.113).



1.482 **1.483**

	R^1	R^2	Yield
a)	$-CH_2C_6H_5$	-H	85%
b)	$-CH_2C_6H_5$	$-CH_2C_6H_5$	97%
c)	$-(CH_2)_3CH=CH_2$	$-(CH_2)_3CH=CH_2$	53%



1.484 **1.485**

	R^1	R^2	Yield
a)	$-CH_2C_6H_5$	-H	54%
b)	$-CH_2C_6H_5$	$-CH_2C_6H_5$	87%
c)	$-(CH_2)_3CH=CH_2$	$-(CH_2)_3CH=CH_2$	87%

Scheme 1.113

1.8 Aims of this study

The topics discussed above in the Introduction of this thesis are used as a platform for the research studies discussed here in. The aim of this programme is to enhance the reactivity and to find the wider applications of the donor **1.249** at room temperature. This study targets the following points:

(i) Reductive cleavage of difficult unactivated arene sulfonamides,

(ii) Metal-free reductive cleavage of C-O bonds in benzylic esters and ethers,

(iii) Reductive cleavage of ArC-X (X = N, C) bonds via selective reduction of arenes,

(iv) Reductive decyanation of malononitriles and cyanoacetates, and

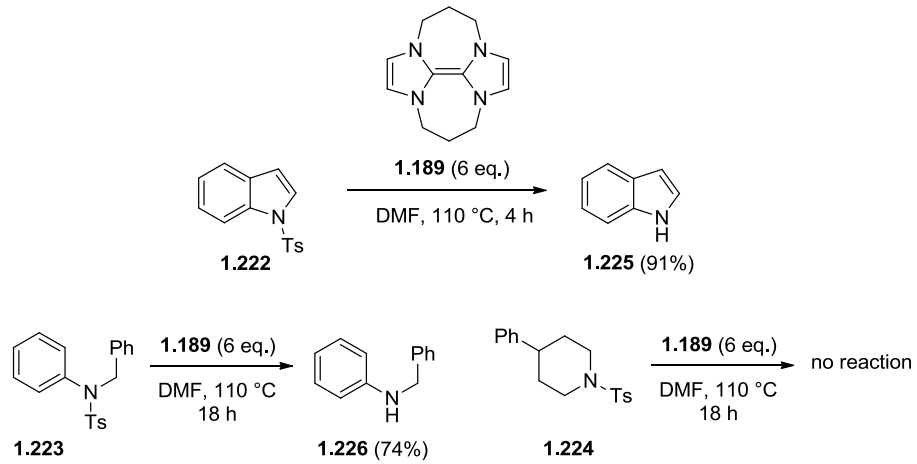
(v) Insight into Birch reductions: regioselective ArO-C bond fission of *ortho*-dialkoxybenzenes (a study not involving donor **1.249**).

2 Reductive Cleavage of Difficult Unactivated Arenesulfonamides

2.1 Introduction

Protection and deprotection of the amine functionality is very common in synthesizing nitrogen-containing, biologically active substances.[175] One of the most commonly used protecting groups for amines is the sulfonamide group.[176] At the end of their role, the protecting groups need to be removed and the traditional way of deprotecting sulfonamides is hydrolysis with strong acids such as HBr or $HClO_4$.[175] For reductive cleavage of sulfonamides, different methods use alkali metals (Li, Na, K), lithium naphthalenide, SmI_2, or $LiAlH_4$ in the presence of nickel compounds.[84,177]

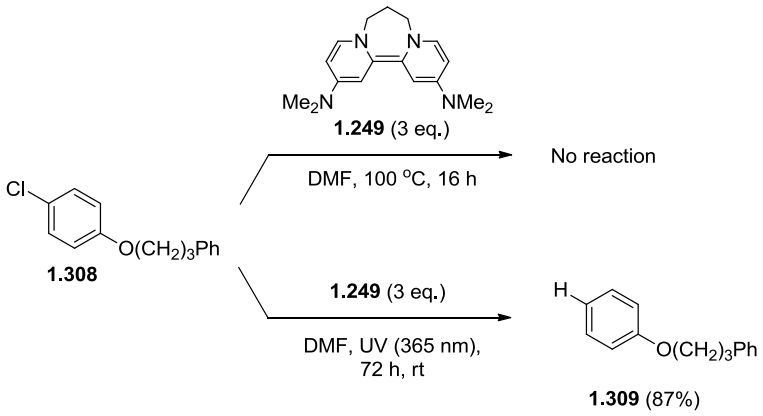
In 2007, Schoenebeck *et al*. reported the first reductive cleavage of various activated arenesulfonamides *e.g.* **1.222** and **1.223** using thermal activation of neutral organic electron donor **1.189**.[84] However, these reaction conditions failed in reductively cleaving unactivated arenesulfonamides *e.g.* **1.224** (Scheme 1.50) due to the high energy of activation associated with the initial electron transfer and the formation of a non-conjugated *N*-anion after cleavage.



Scheme 1.50

In 2008, after the successful launch of DBD **1.189**, the Murphy group developed another, easily preparable, and equally powerful neutral organic electron donor **1.249** derived from

the DMAP moiety.[96] As the reducing powers of both DBD **1.189** and DMAP-derived donor **1.249** are almost equal based on their cyclic voltammograms, the reductive cleavages of sulfonamides were never studied fully with the donor **1.249**. However, very recently, it has been established that the reactivity of these donors can be further enhanced by photoactivation and these donors are now capable of reducing aryl chlorides *e.g.* **1.308** to de-chlorinated compounds **1.309** with high yields, at room temperature (Scheme 2.1).[122]

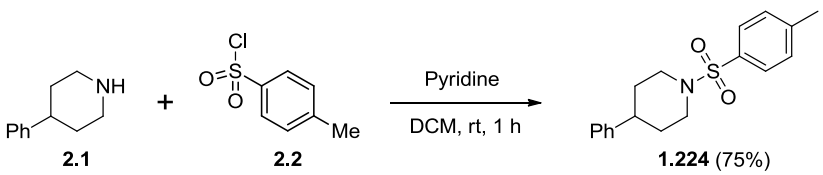


Scheme 2.1

The above enhanced reactivity of the photoexcited donor **1.249** encouraged us to undertake the investigation of reductive cleavages of unactivated arenesulfonamides, which had never worked with neutral organic super electron donors under thermal conditions.

2.2 UV-activated difficult reductions of arenesulfonamides

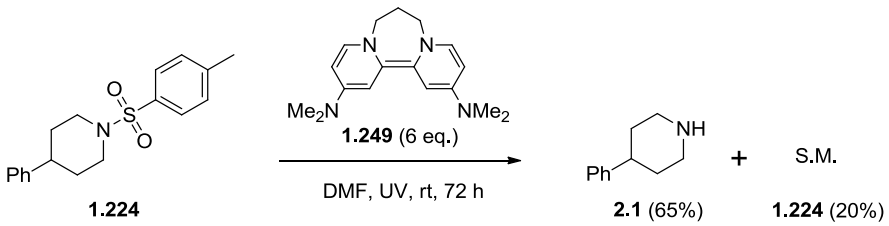
The starting point for this investigation was to re-submit the substrate **1.224**, which did not provide any reaction earlier with thermally activated donor **1.189**, to photoexcited donor **1.249**. The sulfonamide **1.224** was synthesised quite easily from 4-phenylpiperidine **2.1** and tosyl chloride **2.2** with pyridine in good yield (75%), as shown in Scheme 2.2.



Scheme 2.2

UV-absorption studies of the donor **1.249**[117] showed that it has maxima at 260, 345 and 520 nm. For that reason, a UV source (two focused Blak-ray B-100 series lamps with filters from UVP Ltd.) having λ=365 nm, which is a near match to the absorption peak at 345 nm of the donor **1.249**, and each of 100 watts power, were selected. During the reaction, these lamps were placed opposite to each other, around the reaction flask, at room temperature.

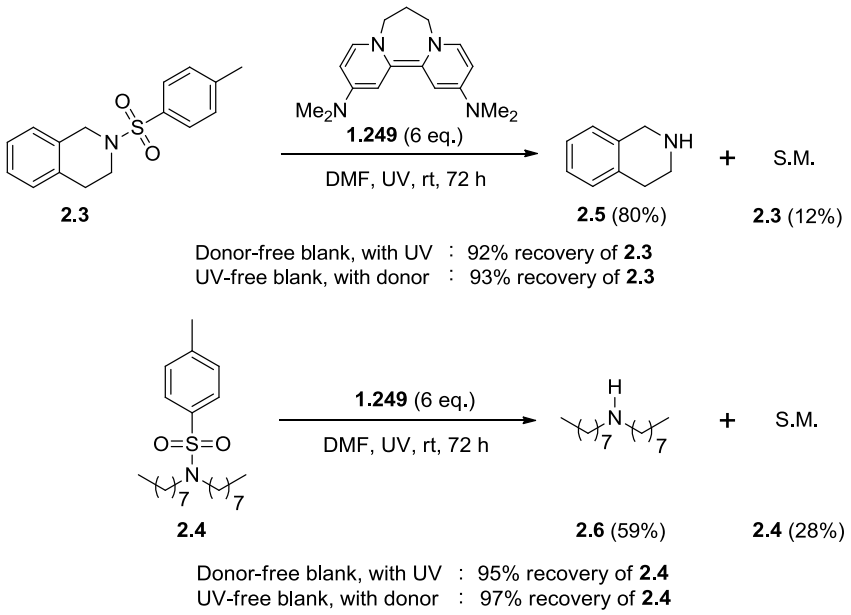
Substrate **1.224** was submitted to photoexcited donor **1.249** (6 eq.) for 72 h at room temperature. To our surprise, **1.224** was reduced under these conditions and provided reduced product **2.1** in good yield (65%) along with recovery of starting material **1.224** (20%). To confirm the fact that the reaction was only achieved with the help of UV irradiation of the donor **1.249**, blank reactions were performed. Both the donor-free, but UV-activated, blank reaction and the original reaction were carried out at the same time by placing the two flasks under the same UV source for the same amount of time. Another UV-free, but donor-activated, blank reaction was carried out at room temperature at the same time. As expected, both the blank reactions provided starting material **1.224** only (Scheme 2.3).



Donor-free blank, with UV : 95% recovery of **1.224**
UV-free blank, with donor : 96% recovery of **1.224**

Scheme 2.3

The success of the above reaction with **1.224** proved again that the reactivity of the donor **1.249** was enhanced under the photoactivation conditions. Later, two other unactivated arenesulfonamides **2.3** and **2.4** were prepared from amines **2.5** and **2.6** respectively by following the method applied for the synthesis of **1.224**. Later, these substrates **2.3** and **2.4** were submitted to the same reaction conditions *i.e*. photoactivation of the donor **1.249** (6 eq.) for 72 h at room temperature. Substrate **2.3** provided an excellent yield of reduced product **2.5**, while the other substrate **2.4** provided a good yield of reduced product **2.6**. The blank reactions, as discussed earlier, were performed also with **2.3** and **2.4** and resulted in recovery of starting material only (Scheme 2.4).



Scheme 2.4

The presence of the arene group in **2.3** might have helped the reaction by lowering the activation energy of the LUMO for the initial electron transfer from the donor **1.249**. A similar neighbouring effect of a phenyl group has been seen earlier by the Murphy group (see Scheme 1.59)[99] and in another case by the Evans group (see Scheme 1.96).[149]

Later, it was planned to test other sulfonamides including activated sulfonamides **2.7**-**2.9** and an N-H sulfonamide **2.10**. Activated sulfonamides had worked well earlier, but, by using higher amounts of the donor **1.189** (6 eq.) at elevated temperatures such as 110 ^{o}C. It is predicted that the enhanced reactivity of the photoexcited donor **1.249** would offer the reaction to carry out with lower amounts of the donor **1.249** (3 eq.) at room temperature. To test this, sulfonamides **2.7**-**2.10** were prepared from the corresponding amines and tosyl chloride **2.2** in good yields, by following the method described for the synthesis of **1.224** (Figure 2.1).

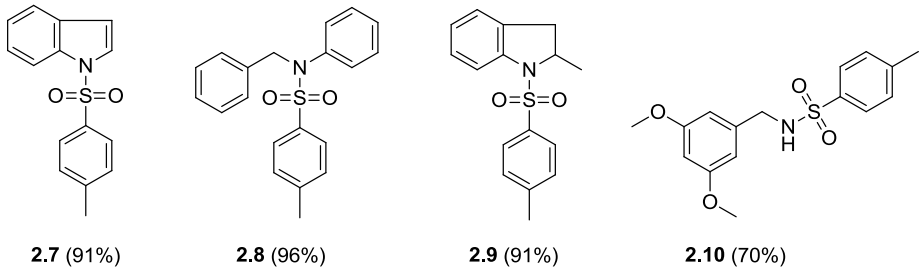
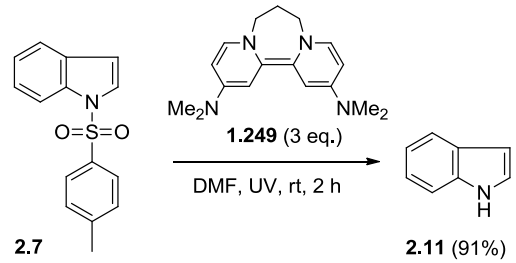


Figure 2.1: Series of other sulfonamides prepared to test with donor **1.249**

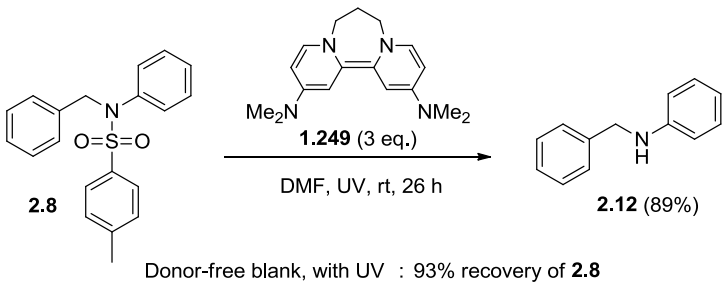
1-Tosyl-1H-indole **2.7** was tested with three equivalents of the donor **1.249** under photoactivation conditions at room temperature. The reaction was completed in 2 h and provided an excellent yield of indole **2.11** (91%). A donor-free UV-activated blank experiment that was performed simultaneously with the original reaction provided only 4% conversion of **2.7** into indole **2.11**, as seen from ^{1}H-NMR of the crude reaction mixture (calculated from the relative integration of the new peak at δ = 6.60 to the peak at δ = 6.66 of starting material). However, a UV-free donor-activated blank reaction performed parallel to the original reaction also provided 31% of the reduced product **2.11**.



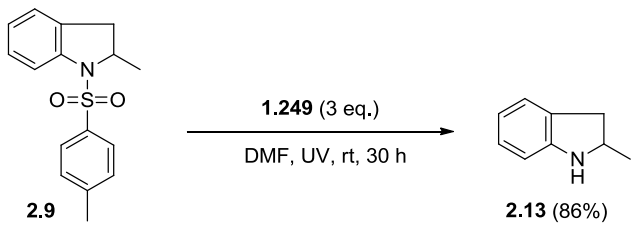
Donor-free blank, with UV : **2.11** (4%) from ^{1}H-NMR of crude product
UV-free blank, with donor : **2.11** (31%)

Scheme 2.5

Activated sulfonamide substrates **2.8** and **2.9** were tested with photoactivated donor (3 eq.) and, as expected, both the reactions provided excellent yields of reduced products (Scheme 2.6) under mild reaction conditions. The blank reactions resulted in starting materials only.



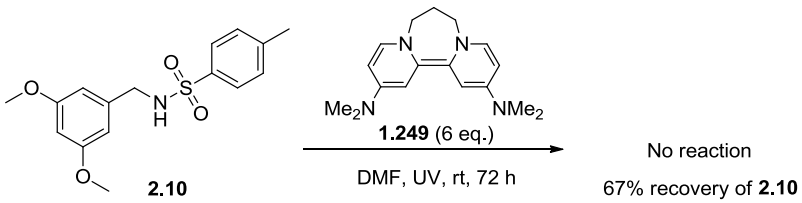
Donor-free blank, with UV : 93% recovery of **2.8**
UV-free blank, with donor : 95% recovery of **2.8**



Donor-free blank, with UV : 92% recovery of **2.9**
UV-free blank, with donor : 91% recovery of **2.9**

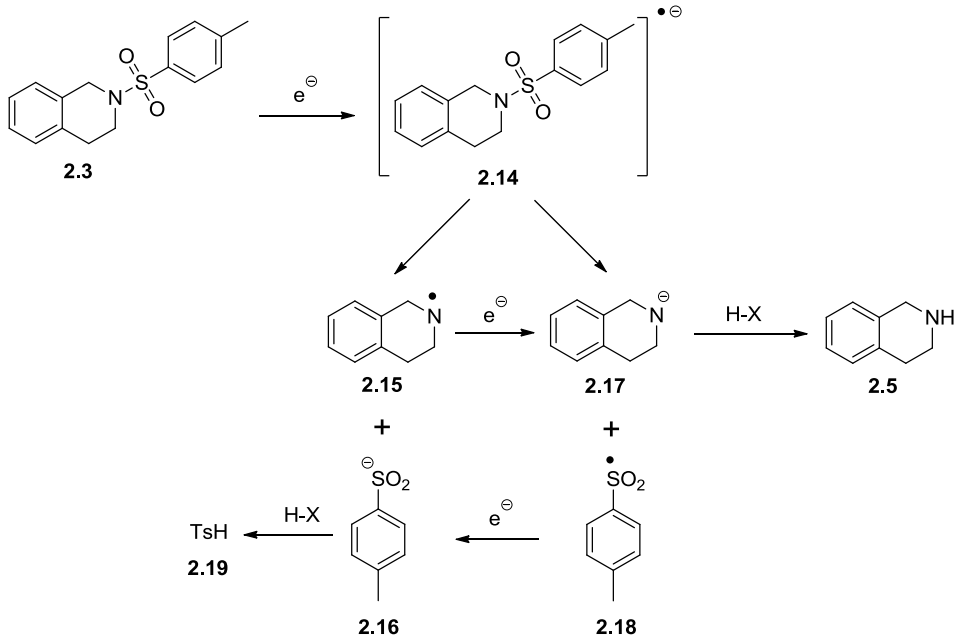
Scheme 2.6

Unfortunately, the reduction of unactivated, N-H sulfonamide **2.10** did not provide any expected product under the same reaction conditions that were used for **2.3** (Scheme 2.7). This reaction provided recovery of the starting material (67%) only. In this reaction, the donor **1.249** might have acted as a base and deprotonated the N-H group instead of effecting electron-transfer to the substrate **2.10**. A similar kind of basic bahaviour of the donor **1.114** has been seen in the case of reduction of acyloin esters.[100]



Scheme 2.7

The suggested mechanism for the reduction of the substrate **2.3** is shown in scheme 2.8, following the lines of the sulfone reduction.[84] An electron is transferred to the arenesulfonyl group, generating radical anion **2.14**. This radical anion **2.14** could undergo heterolytic cleavage of the N-S bond in two ways and forming either aminyl radical **2.15** and a sulfinate anion **2.16** or sulfonyl radical **2.18** and anion **2.17**. Transfer of another electron would result in a pair of anions **2.17** and **2.16**. The anion **2.17** could abstract a proton during the reaction to provide **2.5** (Scheme 2.8).



Scheme 2.8

2.3 Conclusion

In conclusion, difficult reductions of sulfonamides to the corresponding amines were successfully carried out by the photo-activation of the novel neutral organic electron donor **1.249** at room temperature. Previously, the same reductions had proved difficult by the thermal activation of the equally powerful DBD donor **1.189**. This confirmed that the photo-activation of the donors is a useful technique to improve the reducing power of the donors thereby helping in achieving more demanding reductions at room temperature. The blank reactions were carried out under the same reaction conditions along with the original reaction and they, in general, did not provide any success, confirming that the reaction is happening only due to the photo-activation of the donor **1.249**. The reductions of the activated sulfonamide substrates **2.7**-**2.9** were now carried out using lower loading (3 eq. compared to previous 6 eq.) of the donor **1.249** under photo-activated conditions than thermally activated conditions.[84] However, this method did not find success in reducing sulfonamides such as **2.10**, derived from primary amines, possibly due to deprotonation by the basic donor **1.249**.

3 Metal-Free Reductive Cleavage of C-O Bonds in Benzylic Esters and Ethers

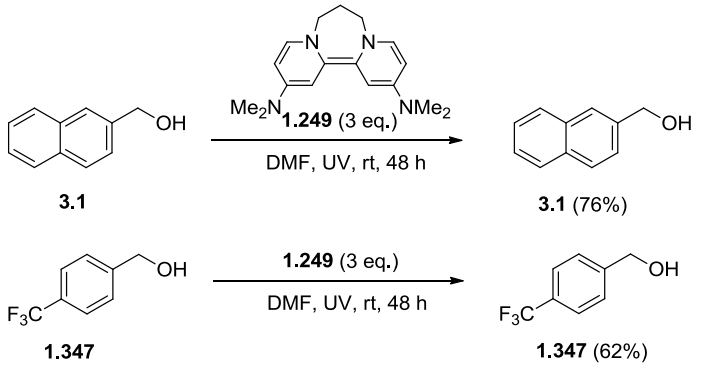
3.1 Introduction

Reductive deprotections of benzylic esters to carboxylic acids and benzylic ethers to alcohols are very widely used transformations (Scheme 3.1).[178,179] These transformations can be effected via hydrogenolysis (H_2 with catalyst)[180] and electron-transfer processes that include chemical, electrochemical and photochemical methods.[179] Very recently, a SmI_2-H_2O-amine system was elegantly applied by the Hilmersson group, for successful cleavage of benzyl-heteroatom bonds.[57]

Scheme 3.1

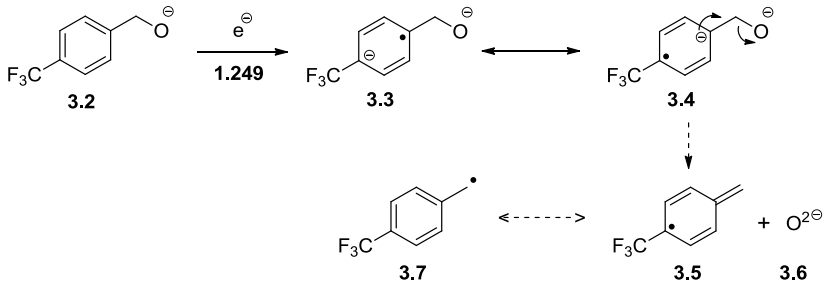
3.2 Early efforts to cleave benzylic C-O bonds

Inspired by the Hilmersson work on benzyl-heteroatom cleavages[61] mediated by the SmI_2-H_2O-amine system, we wondered if photoexcited super neutral organic donors could achieve similar benzylic C-O bond cleavages. The donor **1.249** is capable of giving electron(s) to the aryl system and if an electron is transferred to the σ* orbital of the benzylic C-O bond, then it is possible to have C-O bond cleavage. To test this, naphthalen-2-ylmethanol **3.1** was reacted with 3 equivalents of the donor **1.249** under UV conditions for 48 h at room temperature. Unfortunately, there was no reaction and starting material **3.1** (76%) only was recovered. The donor **1.249** might have acted as a base[100] and deprotonated the hydroxy proton instead of providing the desired benzylic C-O bond cleavage. To further support this, the same reaction conditions were applied to the substrate **1.347**. This reaction also provided only starting material (62%) perhaps due to the basic nature of donor **1.249** (Scheme 3.2).



Scheme 3.2

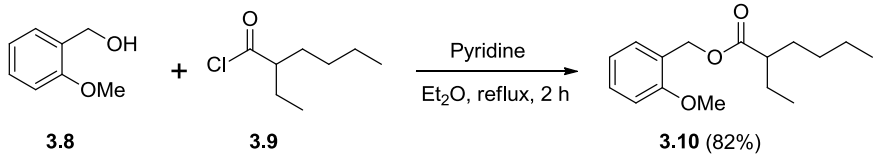
Donation of one electron from the donor **1.249** to the corresponding (4-(trifluoromethyl)phenyl)methanolate **3.2**, formed by the deprotonation of **1.347**, would lead to the liberation of **3.6** at the end of the reaction. As the liberation of **3.6** is not likely to happen, it is believed that this is the reason that no reaction was seen under these reaction conditions (Scheme 3.3).



Scheme 3.3

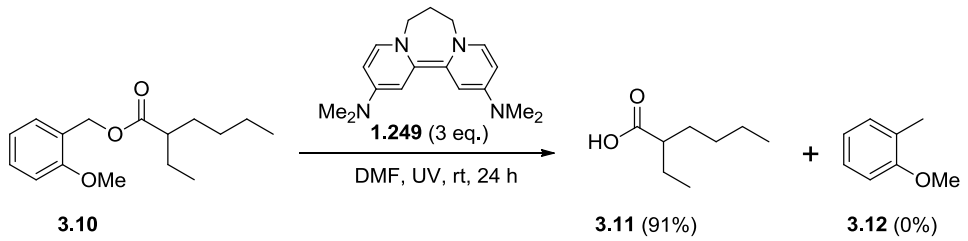
3.3 Benzylic C-O bond cleavages in esters

To escape from the basic nature of the donor **1.249**, it was proposed to test benzyl ester substrates under the same reaction conditions. It had also been seen previously that benzyl alcohol-derived esters were reduced more easily than benzyl alcohol itself in SmI_2-mediated reactions.[61] So this suggested that our organic electron donors could achieve benzyl-ester bond cleavages under mild reaction conditions. Substrate **3.10** was synthesised easily from 2-methoxybenzyl alcohol **3.8** and 2-ethylhexanoyl chloride **3.9** using pyridine under reflux conditions for 2 h (Scheme 3.4).



Scheme 3.4

Substrate **3.10** was then submitted to photoactivation with the donor **1.249** (3 eq.) for 16 h at room temperature, using the same UV source. Then, the reaction mixture was quenched with water and extracted with diethyl ether to provide recovery of starting material **3.10** (14%) from the organic phase. Acid work-up of the aqueous phase with 2N HCl, provided 2-ethylhexanoic acid **3.11** in good yield (69%). Upon increasing the reaction time to 24 h, the reaction went to completion and provided 2-ethylhexanoic acid **3.11** in excellent yield (91%) (Scheme 3.5). Donor-free blank reaction, carried out simultaneously with the orginal reaction for the same amount of time, provided recovery of the starting material **3.10** (87%).

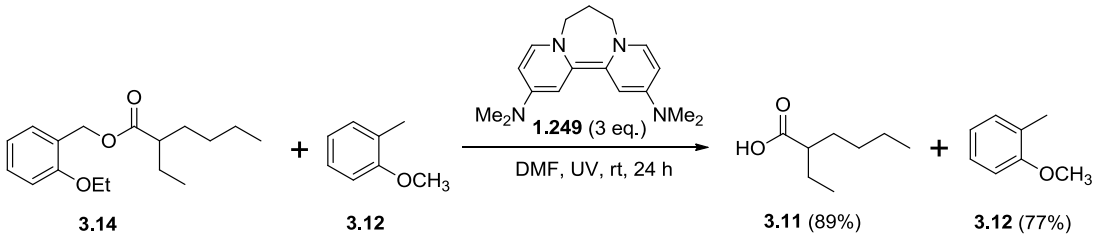


Scheme 3.5

Comparing the above benzyl ester **3.10** cleavage reaction with the results seen by Hilmersson and co-workers,[61] 2-methylanisole **3.12** should be obtained (see Scheme 1.81). But, in our case, the reaction with the substrate **3.10** did not provide any such product **3.12**. There are two possible explanations for this. The first one is that the reaction is proceeding through a benzyl radical intermediate via single electron transfer (SET) from the donor **1.249**. The corresponding benzylic radical may be trapped completely by the radical-cation of the donor **1.249** before it can receive a second electron (DET) to change into an anion *i.e.*, limiting this process to single electron transfer (SET). The second and less likely option is the loss of 2-methylanisole **3.12** during the work-up process or the solvent evaporation process, by using a rotary evaporator, due to volatility, despite the relatively high boiling point (170-172 ^{o}C).

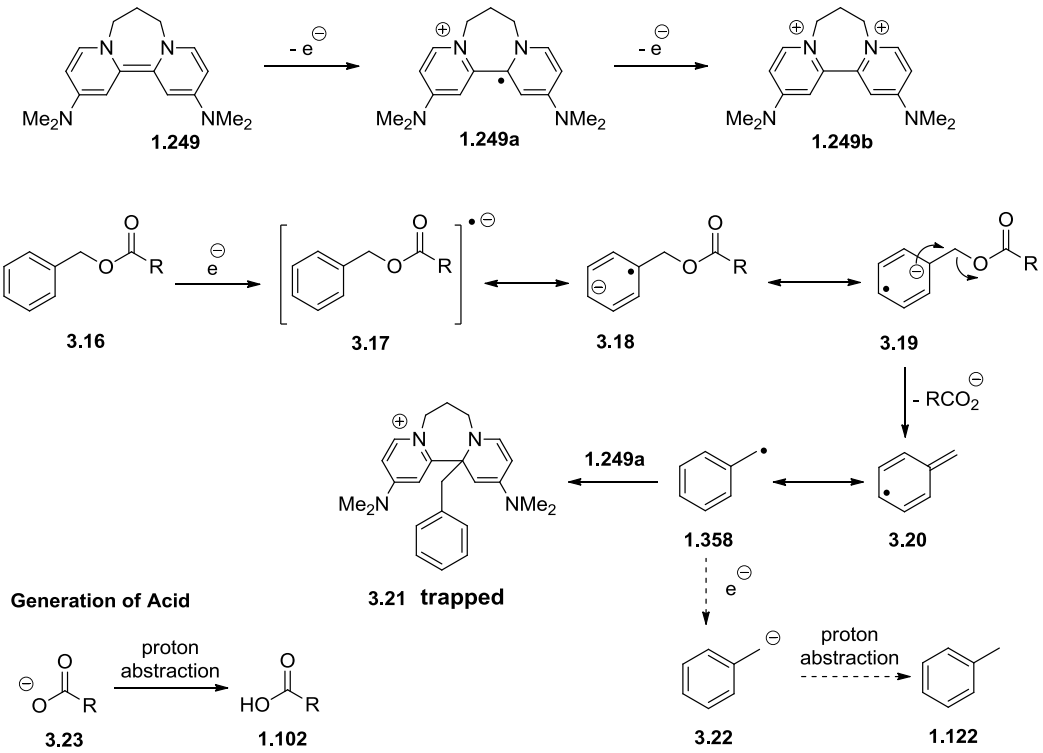
To test the second option, substrate **3.14** was prepared from (2-ethoxyphenyl)methanol **3.13** and 2-ethylhexanoyl chloride **3.9** by following the method described for the synthesis of **3.10**. A new reaction, in which 2-methylanisole **3.12** (48 mg, 0.4 mmol) was added as a dopant to the substrate **3.14** (111 mg, 0.4 mmol), was designed and the mixture was submitted to the same reaction conditions. The reaction provided an excellent yield of 2-

ethylhexanoic acid **3.11** (89%) along with a recovery of 2-methylanisole **3.12** (77%) and no other products were seen (Scheme 3.6). Every care was taken during the workup process, coupled with the boiling point of 1-ethoxy-2-methylbenzene **3.15** most likely being greater than that of 2-methylanisole **3.12**, and so there was very little chance of losing 1-ethoxy-2-methylbenzene **3.15** by evaporation prior to 2-methylanisole **3.12**. This eliminated the second option and supported the trapping of the intermediate 2-alkoxybenzyl radical by the radical-cation of the donor **1.249**; similar trapping was observed earlier with the donors **1.189**[94] and **1.249**.[101]



Scheme 3.6

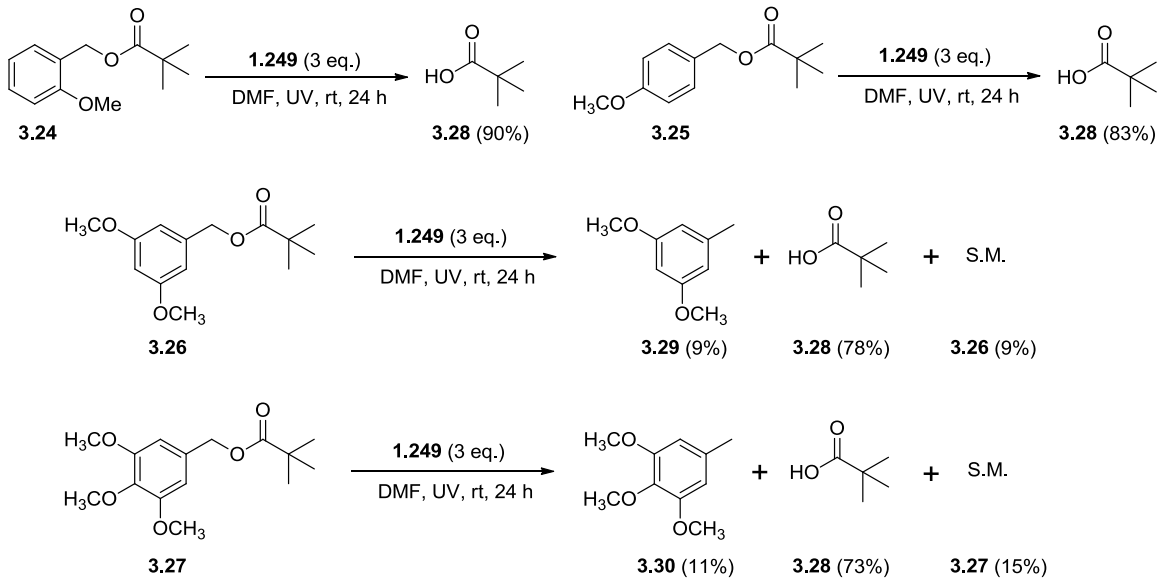
A plausible mechanism for the reduction of benzyl esters is shown in Scheme 3.7.



Scheme 3.7

The donor **1.249** forms radical-cation **1.249a** after loss of an electron. Single electron transfer (SET) from the donor **1.249** to the LUMO of the substrate **3.16** generates resonance-stabilised radical-anion **3.17**, as shown in Scheme 3.7. The radical-anion **3.19** expels carboxylate anion **3.23** to form radical **1.358** which is trapped by the radical-cation **1.249a** of the donor, leading to no isolated products from the neutral organic phase. The carboxylate anion **3.23** protonates on acid work-up and can be isolated as the corresponding acid **1.102**. If the radical **1.358** received a second electron via a double electron transfer (DET) process from the donor **1.249** or radical-cation of the donor **1.249a**, it could convert to the benzyl anion intermediate **3.22** and could provide the final reduced product **1.122** upon protonation from the reaction medium or acid work-up (Scheme 3.7).

A series of substrates **3.24**-**3.27** was prepared by following the method described for the synthesis of **3.10** and then submitted to the same reaction conditions. To our delight, all the reactions provided excellent yields of the corresponding acid **3.28** along with varying but very low yields of aryl alkanes (Scheme 3.8).



Donor-free, UV-active blank reactions provided only recovery of starting ester as follows: **3.24** (90%), **3.25** (88%), **3.26** (89%), **3.27** (91%). UV-free, donor-active blank reaction of ester **3.24** provided only recovery of starting ester (92%).

Scheme 3.8

Both the donor-free UV-active and UV-free donor-active blank reactions, carried out along with the original reactions under the same reaction conditions, provided only a recovery of the starting materials as shown in footnote to Scheme 3.8.

The substrates **3.24** and **3.25**, similar to esters **3.10** and **3.14**, underwent complete reaction and these substrates did not provide any of the possible toluene products. This indicated that these reactions were proceeding through radical intermediates via a SET process. After expulsion of carboxylate anion, the benzyl radical formed was trapped completely by the radical-cation of the donor **1.249a**.

However, due to increased electron density on the benzene ring in substrates **3.26** and **3.27**, the reaction did not go to completion in 24 h and starting materials **3.26** (9%) and **3.27** (15%) were recovered along with toluene products **3.29** (9%) and **3.30** (11%) respectively. These reduced products **3.29** and **3.30** could arise from the benzyl radical, if the relative rate of trapping of this radical intermediate is lower than hydrogen abstraction. Alternatively, the isolated toluene products could arise from benzyl anion intermedites, which are formed by further reduction of benzyl radical intermediates by seeking another electron from the donor.

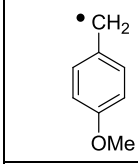
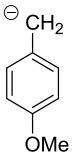
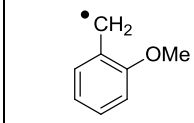
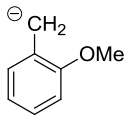
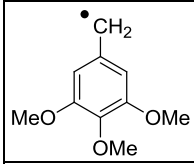
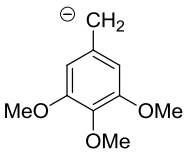
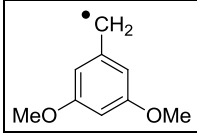
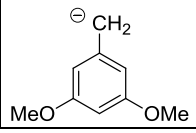
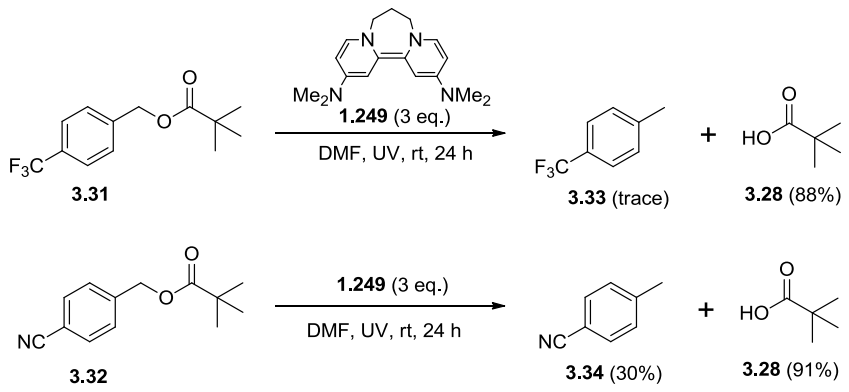
Radical	Energy (a.u.)	Anion	Energy (a.u.)	[Energy anion]-[Energy radical]
	-385.446384		-385.537680	-0.091296 a.u. (-239.697 kJ/mol)
	-385.446103		-385.540188	-0.094085 a.u. (-247.020 kJ/mol)
	-614.480972		-614.576721	-0.095749 a.u. (-251.388 kJ/mol)
	-499.969362		-500.069586	-0.100224 a.u. (-263.138 kJ/mol)

Table 3.1 Computation of the energy changes going from the respective benzyl radical to benzyl anion.

To check the second option, computational studies were undertaken using DFT calculations (B3LYP 6-31G*, modeled in a DMF solvent continuum). Computation of

the energy changes going from the respective benzyl radical to benzyl anion support this, at least qualitatively, showing that the reduction of the 4-methoxybenzyl radical to its anion is the least favourable, likely due to the +M mesomeric influence of the methoxy group. The 2-methoxy isomer is similar, but a little (7.3 kJ/mole) more favourable. For the 3,5-dimethoxy case, the transformation is 23.4 kJ/mole more favourable than for the 4-methoxy case, while the other 3,4,5-trimethoxybenzyl example is 11.7 kJ/mole more favourable than the 4-MeO case (Table 3.1).

Later, substrates **3.31** and **3.32**, containing electron-withdrawing groups, were submitted to the same reaction conditions, *i.e.* photoactivation of the donor **1.249** (3 eq.) for 24 h at room temperature, and provided excellent yields of the pivalic acid. Moreover, substrate **3.31** provided trace amounts (as seen from ^{1}H-NMR of the crude product) of toluene product **3.33**, while substrate **3.32** provided 4-methylbenzonitrile **3.34** (30%) (Scheme 3.9). The isolation of relatively large quantity of **3.34** might be due to strong electron-withdrawing nature of *p*-cyano group, which forces the reaction to follow DET process, and this was explaine below. This reflects a minimum for the amount of cyanobenzyl anion intermediate generated in the reaction through a DET process.

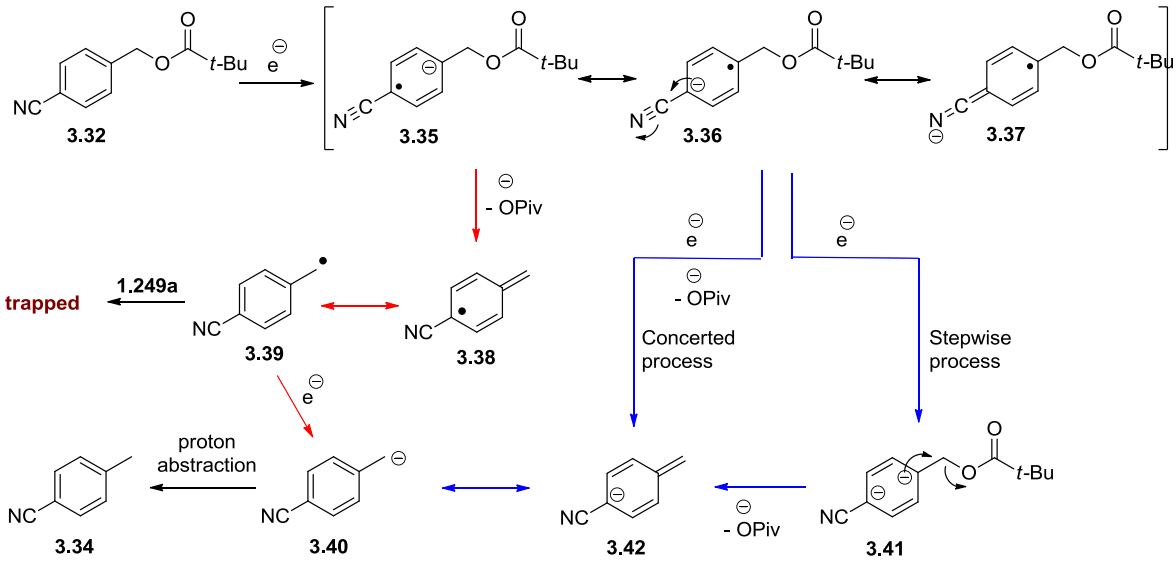


Donor-free, UV-active blank reactions provided only recovery of starting ester as follows: **3.31** (83%), **3.32** (91%).

Scheme 3.9

The generation of 4-methylbenzonitrile **3.34** can be explained in two pathways (red and blue routes), as shown in Scheme 3.10. The compound **3.32**, if it proceeds through a SET process, provides cynobenzyl radical **3.39** after expelling pivalate anion (route red). Similar to other ester substrates, the cyanobenzyl radical **3.39** can be trapped by the radical-cation of the donor **1.249a**. However, it is also possible for the electron-deficient cyanobenzyl radical intermediate **3.39** to obtain a second electron via DET process from

the donor **1.249** or radical-cation of the donor **1.249a** and to be further reduced to cyanobenzyl anion **3.40**, in competition with trapping by the radical-cation of the donor **1.249a**. In the other pathway (route blue), the presence of the *para*-cyano group stabilises the radical-anion **3.36** formed after the SET process and a lowered reactivity towards fragmentation of this radical anion permits a second electron transfer via a DET process from the donor **1.249** or radical-cation of the donor **1.249a**. Now, expulsion of pivalate anion can happen in a stepwise or concerted manner to afford cyanobenzyl anion **3.40**. The cyanobenzyl anion **3.40**, obtained from either of the pathways can abstract a proton, yielding 4-methylbenzonitrile **3.34** (30%). However, the lower yield of 4-methylbenzonitrile **3.34** seen here, compared with the high isolated yield of acid **3.28** (91%), is consistent with the reaction proceeding mostly (~70%) through a SET process and partly (~30%) via a DET process.

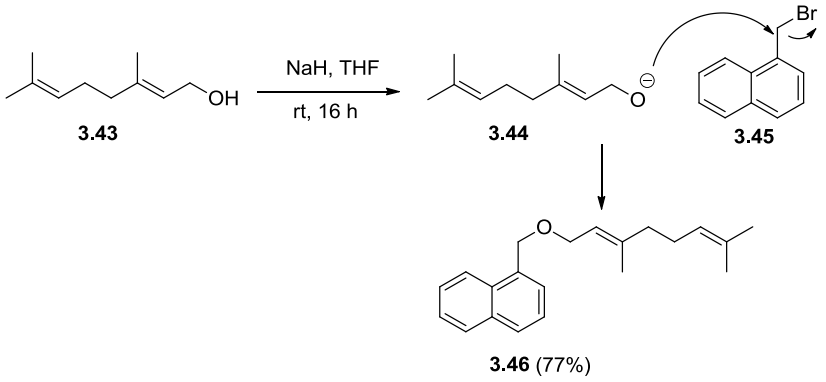


Scheme 3.10

3.4 Benzylic C-O bond cleavages in ethers

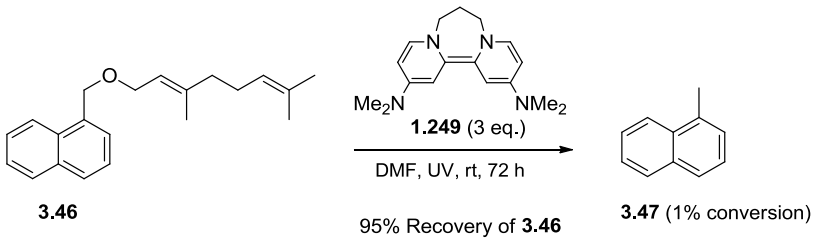
With the successful cleavage of the benzylic C-O bond in esters, it was proposed to extend these cleavage reactions to benzyl ether substrates, which were likely to be more difficult to cleave than benzyl esters, under photoactivation conditions. It was planned to test naphthalene-derived ethers such as **3.46**, which might provide products such as 1-methylnaphthalene **3.47** and geraniol **3.43**, upon successful reaction. Synthesis of the substrate **3.46** involved facile deprotonation of geraniol **3.43** using sodium hydride to

generate anion **3.44**, which was then reacted with 1-bromomethylnaphthalene **3.45** to provide **3.46** in good yield (Scheme 3.11).



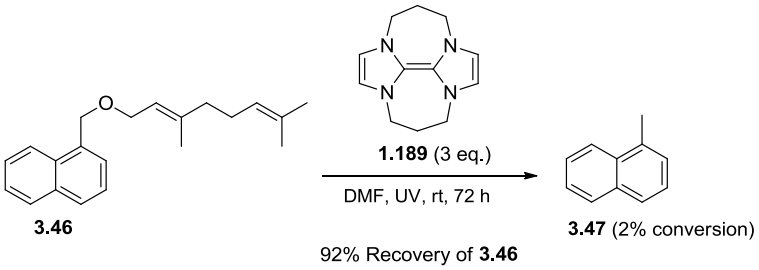
Scheme 3.11

The substrate **3.46** was tested with the donor **1.249** (3 eq.) under UV conditions for 72 h at room temperature. To our delight, a singlet peak was seen at δ = 2.74 in the ^{1}H-NMR spectrum of the crude reaction mixture and this is suspected to be due to the methyl group in the expected product, 1-methylnaphthalene **3.47**. Unfortunately, only 1% (calculated from the relative integration of the singlets at δ = 2.74 to δ = 4.98) conversion of starting material **3.46** to 1-methylnaphthalene **3.47** was observed (Scheme 3.12). No attempt was made to isolate products from the crude reaction mixture pending other substrates giving better yields of cleavage products.



Scheme 3.12

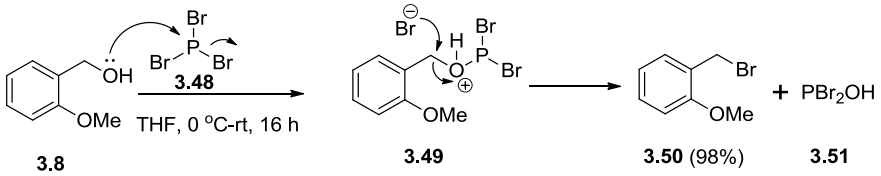
The same reaction was repeated with the alternative donor **1.189** to check if this species would provide a better yield. We were delighted to see the singlet peak at δ = 2.74 in the ^{1}H-NMR spectrum of crude reaction mixture but the reaction provided only 2% conversion of starting material **3.46** into **3.47** (Scheme 3.13). ^{1}H-NMR spectrum of the crude reaction mixture was compared with that of 1-methylnaphthalene **3.47**[181] and the peak at δ = 2.74 matched exactly. No attempt was made to isolate products from the crude reaction mixture pending other substrates giving better yields of cleavage products.



Scheme 3.13

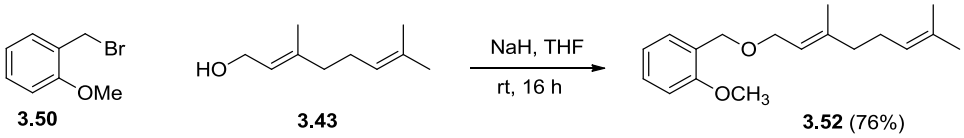
For a successful C-O bond cleavage reaction, the added electron in the arene ring, donated by the donor, should be transfered into the σ* orbital of C-O bond. We reasoned that in these naphthalene systems, the electron might not be easily transferred into σ* orbital of C-O bond because of extensive delocalisation in the naphthalene ring. An altenative possibility is that the naphthalene chromophore absorbs the UV light preferentially. However, UV absorption studies with the substrate **3.46** did not show any absorption at around 350 nm and this argument was discarded. From the above results, substrates based on benzene instead of naphthalene were tested in subsequent experiments.

1-(Bromomethyl)-2-methoxybenzene **3.50** was synthesised from (2-methoxyphenyl) methanol **3.8** by using phosphorus tribromide **3.48** (Scheme 3.14). A ^{1}H-NMR spectrum of the crude mixture indicated that the formed product was **3.50** and it was almost impurity-free. Purification of the crude product through column chromatography, however, led to its decomposition. Thereafter, it was decided to use compound **3.50** without further purification.



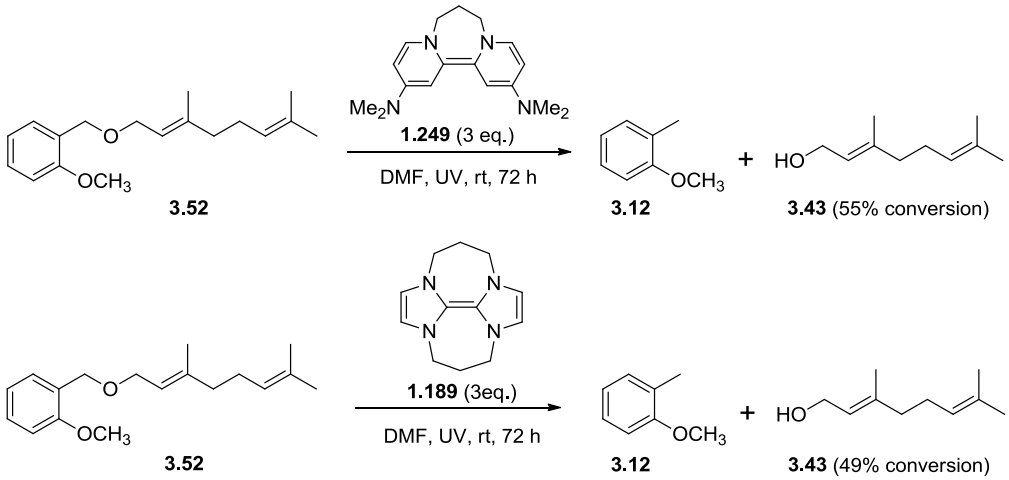
Scheme 3.14

Substrate **3.52** was synthesised from geraniol **3.43** and crude 1-(bromomethyl)-2-methoxy benzene **3.50** by using sodium hydride, in a similar way to the synthesis of **3.46** (see Scheme 3.11), in good yield (76%) (Scheme 3.15).



Scheme 3.15

Substrate **3.52** was tested under the same UV-activated reaction conditions with both the donors **1.249** and **1.189**. These reactions proceeded much more effectively than the previous reactions with naphthalene-derived substrates. From the ^{1}H-NMR spectrum of crude mixtures, it was observed that the reaction with the donor **1.249** gave a 55% conversion of starting material to geraniol **3.43** while the donor **1.189** gave only 49% conversion of starting material to geraniol **3.43** (Scheme 3.16) [the above yields were calculated by taking geraniol **3.43** as reference instead of **3.12** from the crude reaction mixture, since the boiling point of geraniol **3.43** (229 ^{o}C) is higher than that of 2-methylanisole **3.12** (170-172 ^{o}C) and there is little chance of losing **3.43** during the evaporation of solvent using a rotary evaporator]. No attempt was made to isolate the products from this reaction; this will be reported below after optimisation of suitable conditions.

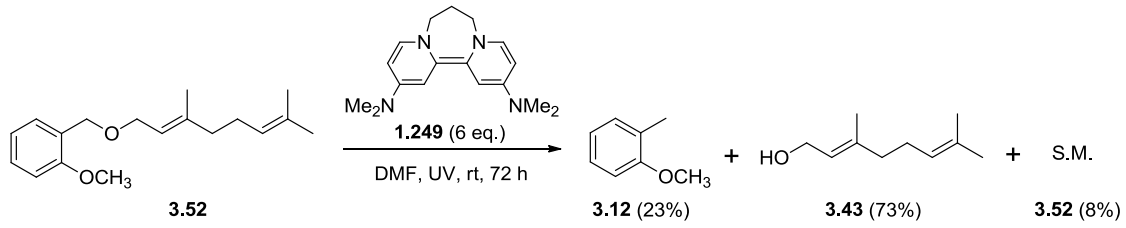


Scheme 3.16

From the above results, it was understood that the donor **1.249** was producing more effective outcomes than donor **1.189** in achieving C-O bond cleavage benzyl ethers under these conditions. Moreover, synthesis of the donor **1.249** is easier than the synthesis of DBD **1.189**. So, it was planned to use the donor **1.249** henceforth for these cleavages.

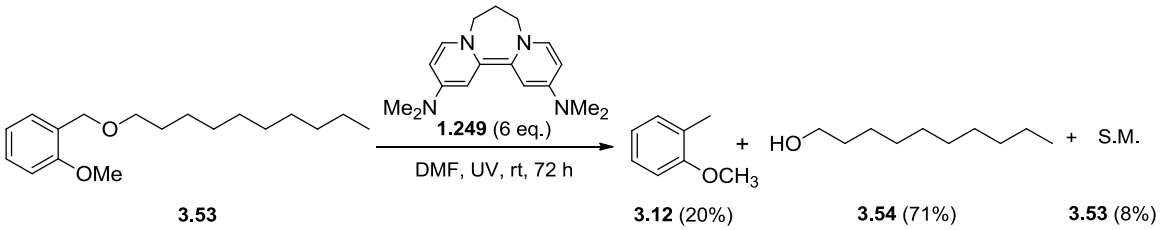
The next efforts were to optimise the reaction conditions to enhance the yield of the reaction. When the substrate **3.52** was reacted with six equivalents of donor **1.249** and by using the same UV source (365 nm, 2 bulbs each 100 watts) for 72 h at room temperature, it provided a good isolated yield of geraniol **3.43** (73%) and a lower yield of 2-methylanisole **3.12** (23%), along with recovery of starting material **3.52** (8%) (Scheme 3.17). Another minor product (3% relative to geraniol) was also noticed in the ^{1}H-NMR of

the crude reaction mixture. Close inspection of the peaks relating to this minor product suggested that it was an alcohol. It was thought that it might be (2-methoxyphenyl)methanol **3.8**, formed due to the O-C cleavage on the other side of the ether linkage. Comparison with the ^{1}H-NMR spectrum of **3.8**, showed an exact match. The experiments now need to be repeated on a larger scale to isolate and characterise this minor product. To confirm the fact that the reaction was only achieved with the help of UV irradiation of the donor **1.249**, a donor-free blank reaction was performed. Both the donor-free blank reaction and the original reaction were carried out at the same time by placing two flasks under the same UV source for the same amount of time. As expected, the blank reaction provided recovery of the starting material **3.52** (89%) only.



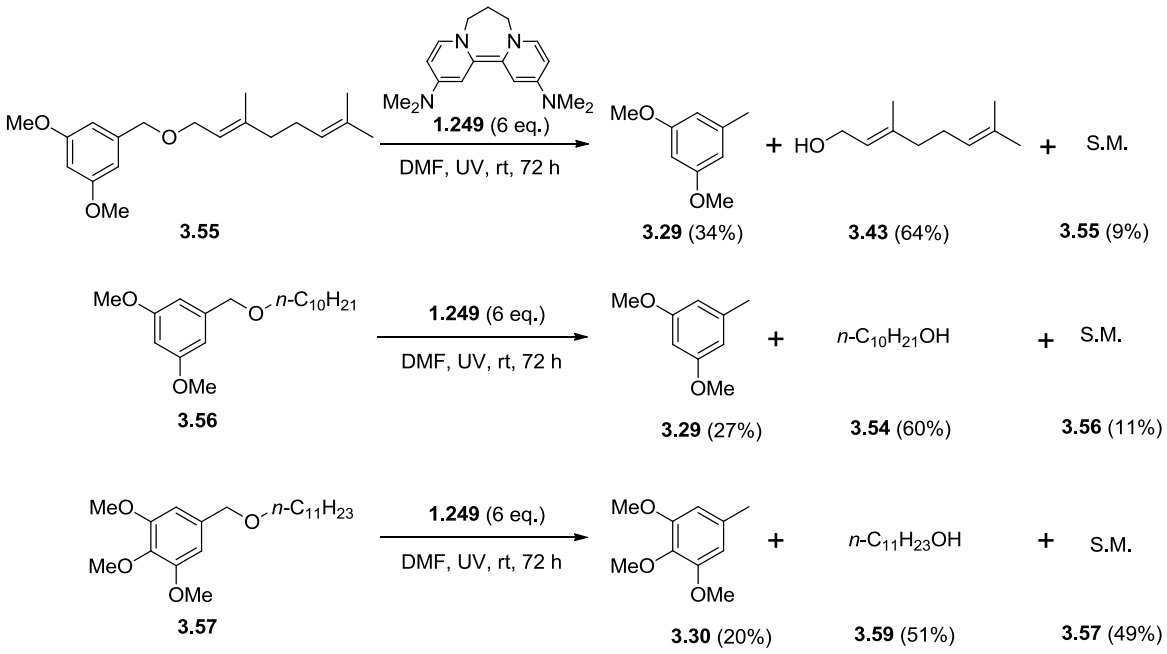
Scheme 3.17

To check the scope of the above reaction conditions for different substrates, substrate **3.53** was prepared from crude 1-(bromomethyl)-2-methoxybenzene **3.50** and 1-decanol **3.54** by using sodium hydride (see Scheme 3.11). The substrate **3.53**, on reacting with donor **1.249** under the same reaction conditions, provided a good isolated yield of 1-decanol **3.54** (71%) and a low yield of 2-methylanisole **3.12** (20%) along with recovery of starting material **3.53** (8%) (Scheme 3.18). No other minor product relating to the O-C bond cleavage was seen, unlike in the reaction with substrate **3.52**, in the ^{1}H-NMR spectrum of the crude reaction mixture. A blank reaction was carried out along with the original reaction with **3.53** and, as expected, it provided starting material **3.53** (91%) only.



Scheme 3.18

With the success of the above reactions, electron-rich substrates such as 3,5-dimethoxybenzyl ethers **3.55** and **3.56** and 3,4,5-trimethoxybenzyl ether **3.57** were prepared similarly to the previous substrates.



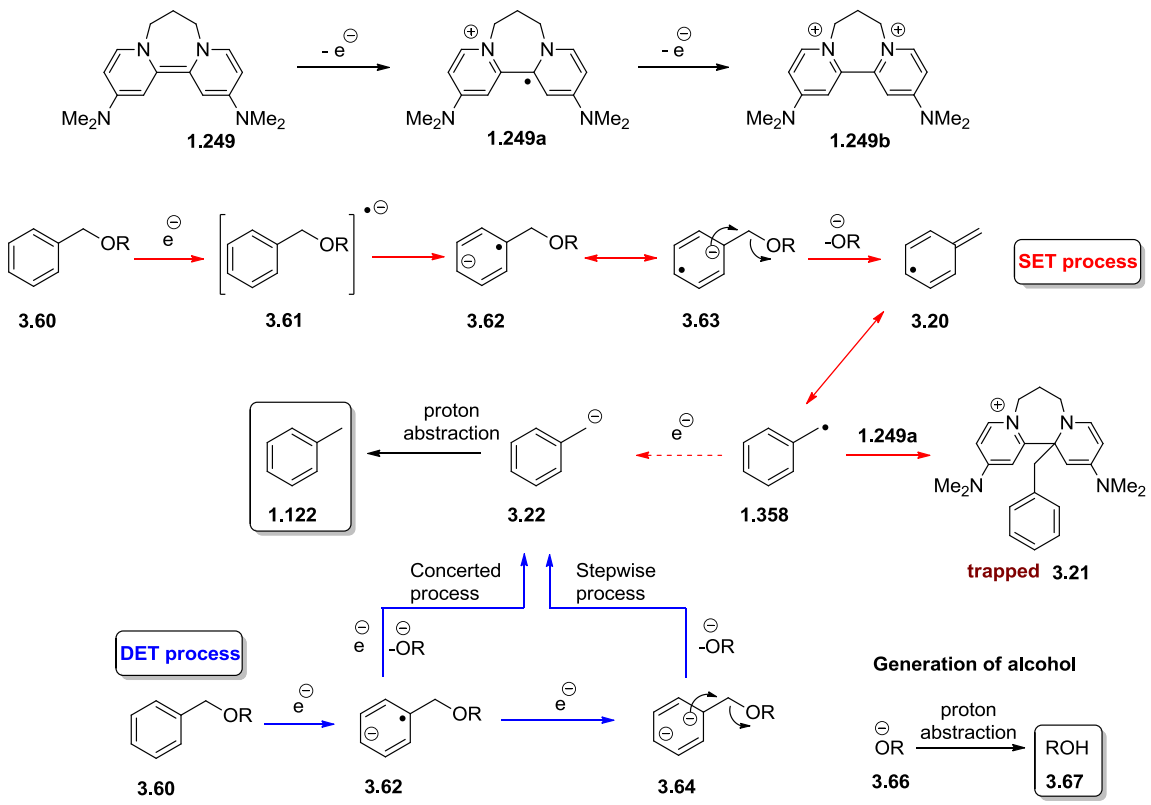
Donor-free, UV-active blank reactions provided only recovery of starting ether as follows: **3.55** (92%), **3.56** (89%), **3.57** (91%).

Scheme 3.19

The substrate **3.55** under the same reaction conditions provided a good isolated yield of geraniol **3.43** (64%) and a low yield of 3,5-dimethoxytoluene **3.29** (34%) along with a recovery of the starting material **3.55** (9%). Another minor product (3% relative to geraniol), arising from the alternative O-C bond cleavage on the other side of ether, was also observed in the ^{1}H-NMR of the crude reaction mixture (not shown in Scheme 3.19). With the previous experience, ^{1}H-NMR spectrum of the crude mixture was compared with that of (3,5-dimethoxyphenyl)methanol **3.58**. This exactly matched, but the experiment needs to be repeated on larger scale to isolate and characterise this product. Substrate **3.56**, under the same reaction conditions, provided a good isolated yield of 1-decanol **3.54** (60%) and a low yield of 3,5-dimethoxytoluene **3.29** (27%) along with a recovery of the starting material **3.56** (11%). On the other hand, substrate **3.57** afforded 1-undecanol **3.59** (51%), 3,4,5-trimethoxytoluene **3.30** (20%) along with recovery of the starting material **3.57** (49%). No other minor product relating to the alternative O-C bond cleavage was seen with the substrates **3.56** and **3.57** in the ^{1}H-NMR spectrum of the crude reaction mixture. This again suggested that the minor product (alternative O-C bond cleavage product) formed in the reaction with the substrate **3.55** was facilitated by the

presence of allylic alkene group. Donor-free blank reactions were carried out along with the original reactions and, as expected, they provided a recovery of starting materials only, as shown in footnote (Scheme 3.19).

Unlike C-O bond cleavages in benzyl esters, the reduced products from both sides of the ether moiety were obtained in benzyl ethers, although there was a mismatch in the yields of the two reduced products. This itself indicates that the C-O bond cleavages in benzyl ethers were different from those of benzyl esters. For ethers, these cleavages were going through a different intermediate, likely a benzyl anion, as seen to some degree in case of the substrate **3.32**, compared with benzyl esters, which were mostly occurring through benzyl radical intermediates. The discrepancy seen in the yields of the two reduced products for the ethers *i.e.* the alcohol and the methyl arene might be due to the trapping of the benzylic radical intermediate with the radical-cation of the donor **1.249a**. It was also found that the cleavage of C-O bond in benzyl ethers was more difficult compared with the corresponding cleavages in benzyl esters and needed higher loadings (6 eq.) of the donor **1.249** and longer reaction times (72 h) against lower loadings (3 eq.) of the donor **1.249** and lesser reaction times (24 h) in benzyl esters.



Scheme 3.20

Keeping all these points in mind, the following tentative mechanism is proposed for C-O bond cleavages in benzyl ethers (Scheme 3.20). Donor **1.249** is capable of donating two electrons. After the loss of a first electron it forms radical cation **1.249a** and subsequent loss of another electron leads to dication **1.249b**. Initial single electron transfer (SET) from the donor **1.249** to the LUMO of the substrate **3.60** generates π-radical anion **3.61** which can be resonance-stabilised, as shown in Scheme 3.20. At this point, two possibilities exist *i.e.* pathway **(a)** shown in red and pathway **(b)** shown in blue in Scheme 3.20, which are discussed below:

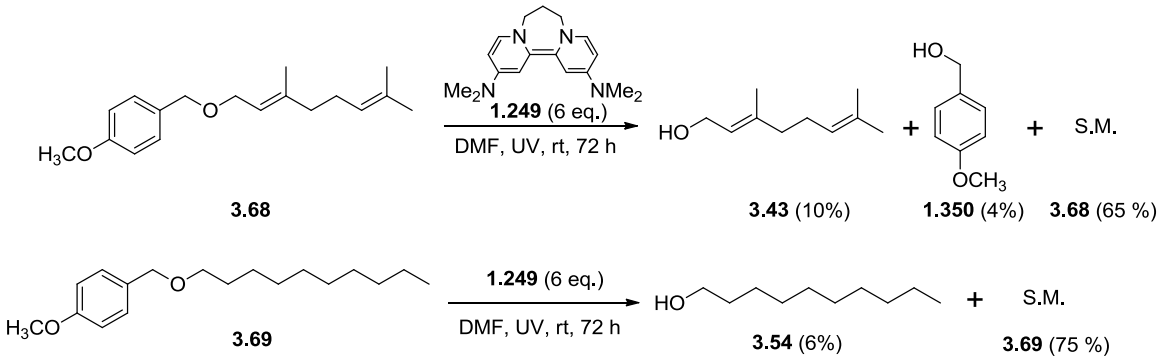
(a) The electron is transfered to the σ* orbital of the benzylic C-O bond to promote cleavage of the C-O bond, thereby expelling alkoxide **3.66**. This leads to the formation of radical **1.358**. This radical **1.358** can be trapped[94,101] by the radical-cation of the donor **1.249a** to form **3.21** or can receive one more electron to form benzyl anion **3.22**. This anion **3.22** upon proton abstraction provides reduced product (aryl alkane) **1.122**. But, may be the trapping of radical **1.358** with the radical-cation of the donor **1.249a** is more likely than absorption of one more electron by the radical **1.358** and so the isolated yield of aryl alkane is lower than that of corresponding alcohol **3.67**.

(b) This is the case of double electron transfer (DET). Elimination of an alkoxide is much more difficult compared with that of a carboxylate anion and this was seen in earlier reactions of various ether substrates. So, the radical-anion **3.62** *i.e.* radical-anion that is more reluctant to participate in liberation of the alkoxide after the SET process, can now receive a second electron via a DET process from the donor **1.249** or radical-cation of the donor **1.249a** to form di-anion **3.64**. This loses alkoxide **3.66** in a stepwise or concerted manner to provide benzyl anion **3.22**. However, it is unlikely that a discrete anti-aromatic arene dianion is formed prior to fragmentation, and so this suggests that in forming a benzylic anion, C-O cleavage is concerted with the transfer of the second electron. The liberated benzyl anion **3.22**, upon proton abstraction, provides the reduced product (methyl arenes) **1.122**.

Finally, the expelled alkoxide **3.66** takes one proton from the reaction medium, perhaps on work-up, to afford alcohol **3.67** (Scheme 3.20).

The low isolated yields of methyl arenes **1.122** compared with alcohols **3.67** indicated that the reaction was following both of the proposed mechanistic pathways. We believe that through pathway **(a)**, the aryl alkane **1.122** is not being formed due to the trapping of the intermediate radical **1.358**, as seen in benzyl ester cleavages, and the isolated aryl alkane is coming mostly through pathway **(b)**. But, the extent of the reaction following either pathway **(a)** or pathway **(b)** depends upon the electronic nature and position of substituents on the benzene ring, as well as the type of alkyl moiety on the ether.

The isolated yields of alcohols from the reactions with the substrates **3.52** and **3.53** are greater than those with substrates **3.55-3.57**. The substrates **3.55-3.57** contain additional methoxy groups compared with substrates **3.52** and **3.53**, which makes them even more electron-rich compounds. So the donation of electrons from the donor **1.249** to the substrates **3.55-3.57** is more difficult compared with that of the substrates **3.52** and **3.53** and results in lower yields of alcohols.



Donor-free, UV-active blank reactions provided only recovery of starting ether as follows: **3.8** (90%), **3.69** (93%).

Scheme 3.21

Substrates **3.68** and **3.69** derived from 4-methoxybenzyl alcohol **1.350** were also prepared similarly to the previous substrates. The substrate **3.68**, on reacting with donor **1.249** under the same reaction conditions, provided a very low yield of geraniol **3.43** (10%) and a recovery of more starting material **3.68** (65%), along with the isolation of 4-methoxybenzyl alcohol **1.350** (4%). None of the expected 4-methylanisole **3.70** was isolated from the reaction. This might be due to the complete trapping of the intermediate

radical by the radical-cation of the donor **1.249a**. The isolation of 4-methoxybenzyl alcohol **1.350** (4%) confirmed the cleavage of the allylic C-O bond in **3.68**; more of this cleavage is discussed later in this report (section **3.5** dealing with allylic C-O bond cleavages, page 92). When the substrate **3.69** was treated under the same reaction conditions, it provided a very low yield of 1-decanol **3.54** (6%) along with starting material **3.69** (75%) and no other products, such as 4-methylanisole **3.70** and 4-methoxybenzyl alcohol **1.350**, were noticed. Donor-free blank reactions, conducted along with the original reactions, provided recovery of the starting materials only, as shown in footnote (Scheme 3.21).

Very poor yields of fragmented products and re-isolation of starting materials in good yield from the reactions of 4-methoxy aryl substrates **3.68** and **3.69**, are reminiscent of Hilmersson's results for 4-methoxybenzyl substrates with SmI_2.[61] The poor reactivity might be due to difficulty in transferring an electron from the π* orbital of the aryl ring into the σ* orbital of C-O bond in **3.68** and **3.69**.

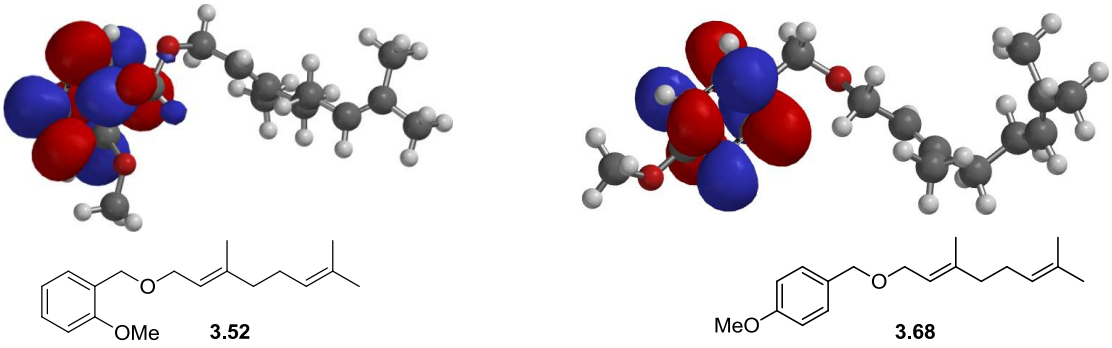
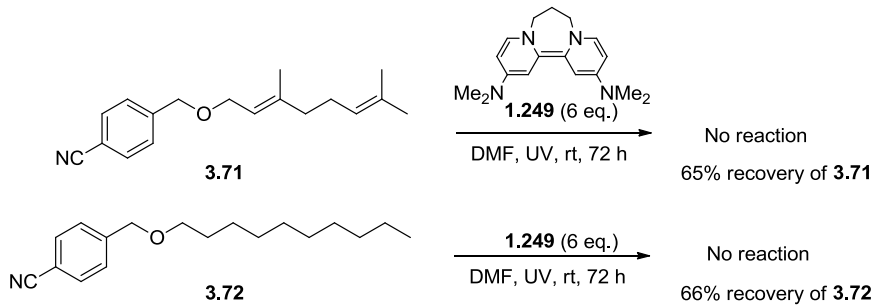


Figure 3.1 LUMO of the substrates **3.52** and **3.68**

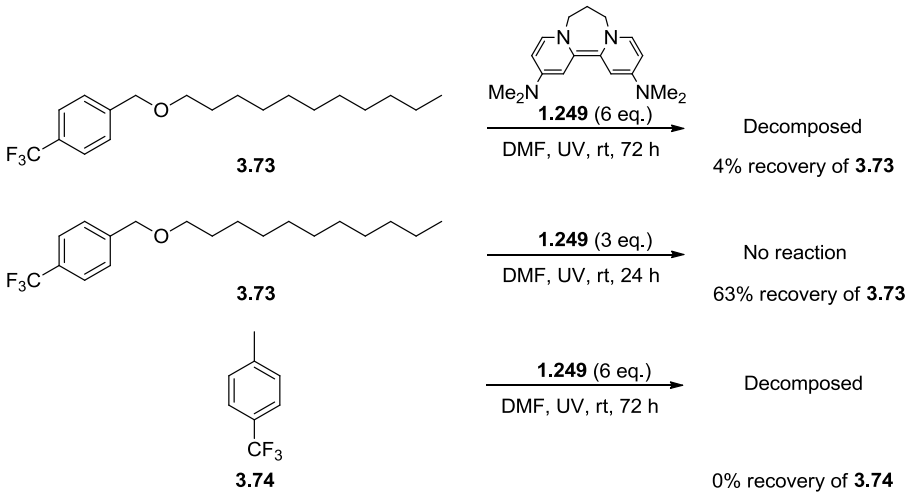
Spartan calculations predicted that the LUMO of the substrate **3.52** has a some electron density spreading over the benzylic C-O bond and facilitates easy transfer of an electron from the π* orbital of aryl ring into the σ* orbital of C-O bond and thereby allowing easy cleavage of the C-O bond. But, such electron density over the benzylic C-O bond is not noticed in the LUMO of the substrate **3.68** (Figure 3.1).

These reactions were extended to a set of substrates **3.71**-**3.73**, containing electron-withdrawing groups. Unfortunately, the *p*-cyano ether substrates **3.71** and **3.72** did not provide any fragmented products but provided recovery of the starting materials (Scheme 3.22).



Scheme 3.22

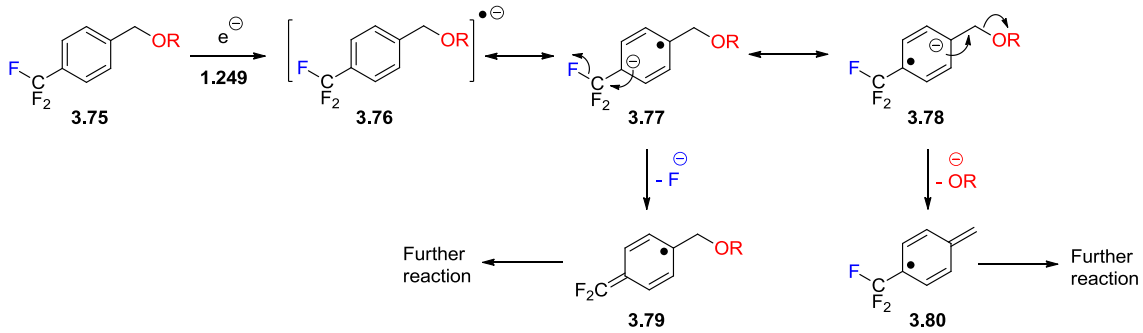
This result is entirely different than that observed in the *p*-cyano benzyl ester **3.32**, where complete reaction was obtained. Lluch, in a theoretical study of competitive homolytic/heterolytic aniomesolytic cleavages of C-O alkyl ether bonds,[182] reported that intramolecular electron migration into the σ* antibonding orbital of a C-O bond becomes more difficult with increasing electron-withdrawing power of substituents. In other words, there is compitition between the electron transfer into σ* orbital of the benzylic C-O bond and the electron-withdrawing character of the cyano-group. The fate of the reaction will depend on the collective effect of these two opposing forces. In the case of *p*-cyano ether substrates, the electron-withdrawing character of the cyano-group might be predominant and therefore resulted in no reaction. The ease with which a carboxylate anion can be liberated compared to a alkoxide ion may account for the facile reaction of the *p*-cyano ester.



Scheme 3.23

On the other side, the *p*-trifluoromethyl susbstrate **3.73** was almost completely decomposed, under identical reaction conditions *i.e.* photoactivation of the donor **1.249** (6

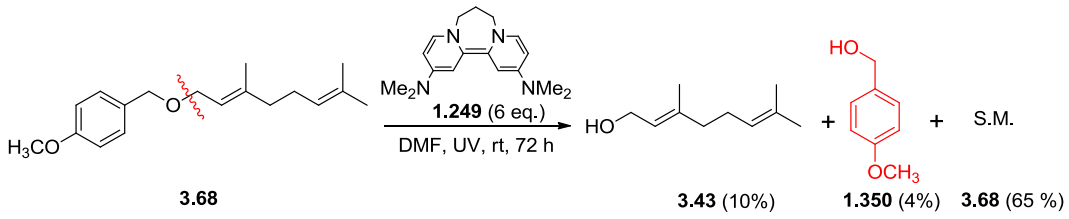
eq.) for 72 h. However, the same substrate **3.73**, under mild conditions, *i.e.* photoactivation of the donor **1.249** (3 eq.) for 24 h, afforded recovery of the starting material **3.73** in fair amounts (63%) (Scheme 3.23). In this case, in addition to the electron-withdrawing character of the trifluoromethyl group, competition may arise between the elimination of the two benzylic groups - alkoxide and fluoride, with fluoride loss predominating (Scheme 3.24).[183] *p*-Trifluoromethyltoluene **3.74**, upon photoactivation of the donor **1.249** (6 eq.) for 72 h, was completely decomposed, supporting the above argument that envisages loss of fluoride (Scheme 3.23).



Scheme 3.24

3.5 UV-activated allylic C-O bond cleavages

When the substrate **3.68** was submitted to the photoactivation of the donor **1.249**, it provided *p*-methoxybenzyl alcohol **1.350** in addition to the other expected products (Scheme 3.21).

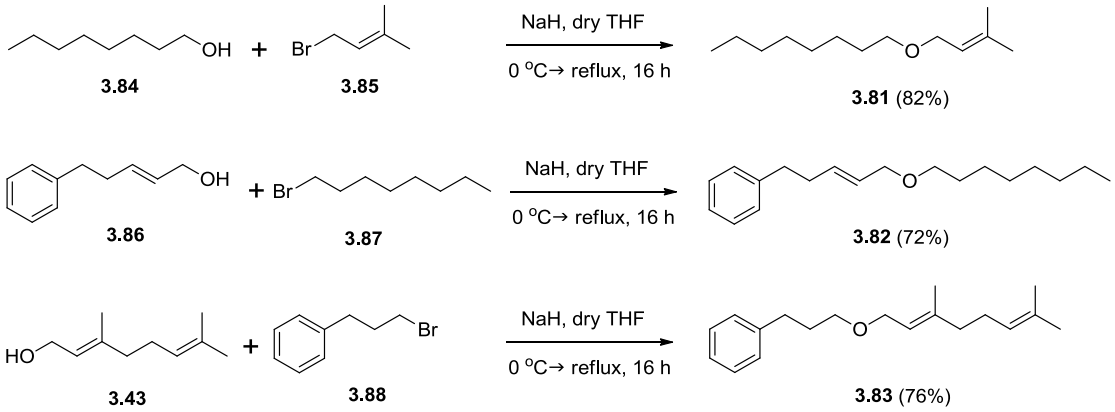


Scheme 3.21

The isolated *p*-methoxybenzyl alcohol **1.350** (4%) is believed to be formed by the cleavage of the allylic C-O bond. This could happen in two ways. In the first one, the presence of the allylic double-bond to the oxygen lowers the energy of the σ* orbital that incorporates the C-O unit. So direct electron transfer from the donor **1.249** into the π* orbital of allylic double-bond is easier than for non-allylic systems, which in turn can promote an electron into the σ* orbital of the C-O bond (*i.e.* other side of the ether) and

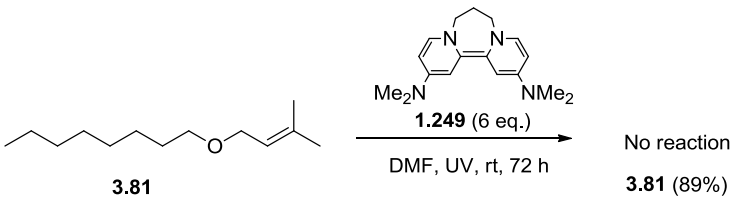
facilitate the breaking of this bond leading to 4-methoxybenzyl alcohol **1.350** as a minor product. In the second one, the donor **1.249** transfers an electron into the π* orbital of the aryl group and subsequently the electron is promoted into the π* orbital of the allylic double-bond and, thereafter, it follows the first option leading to 4-methoxybenzyl alcohol **1.350**. To look more deeply into these options, a set of substrates **3.81**-**3.83** was prepared.

1-[(3-Methylbut-2-en-1-yl)oxy]octane **3.81** was prepared in good yield (82%) by treating 1-octanol **3.84** and 3,3-dimethylallyl bromide **3.85** with sodium hydride. Similarly, substrates **3.81** and **3.83** were prepared in good yield by treating the corresponding alcohol and bromide precursors with sodium hydride (Scheme 3.25).



Scheme 3.25

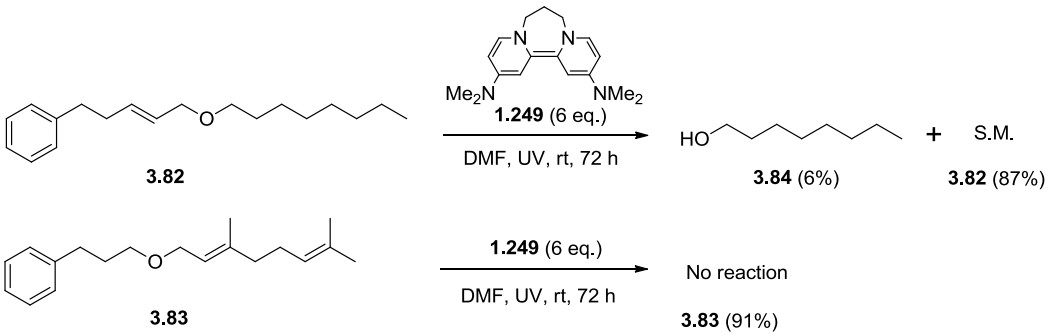
When the substrate **3.81** was submitted to the photoactivation of the donor **1.249** (6 eq.) for 72 h at room temperature, it did not provide any reaction and the starting material **3.81** was recovered (Scheme 3.26). This clearly indicated that the electron from the donor **1.249** could not be accepted directly by the π* orbital of the allyl system. Hence, the previously seen allylic C-O bond cleavage could have occurred with the help of an electron in the π* orbital of the aryl group which was transferred into the σ* orbital of the allylic C-O bond via the π* orbital of the allylic double-bond.



Scheme 3.26

After probing the concepts behind allylic C-O bond cleavages, we explored how far the electron in the aryl group can be transferred to the π* orbital of the allyl system. To test this, the substrates **3.82** and **3.83** were used as model substrates.

When substrate **3.82**, in which the allylic double-bond was close (separated by 2 x C atoms) to the aryl system, was submitted to the normal photoactivation conditions, it provided a notable reaction and 1-octanol **3.84** (6%) was isolated. In contrast, the substrate **3.83**, in which the allyl system was far away (separated by 4 x C and 1 x O atoms) from the aryl system, did not provide any reaction (Scheme 3.27). This further supports the role of the aryl system in allylic C-O bond cleavages and the close proximity of the allyllic system to the aryl system is required to achieve these cleavages. More detailed examination of this subject will be reported in future investigations by others.



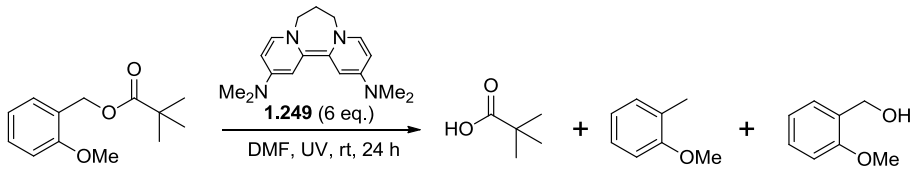
Scheme 3.27

3.6 Competition studies between SET and DET

Benzylic C-O bond cleavages in both esters and ethers went smoothly by using photoexcited donor **1.249** at room temperature. These two processes differ in the amount of donor used (use of 3 eq. of donor **1.249** for esters against 6 eq. of the donor **1.249** in ethers) and the length of the reaction times (24 h in esters against 72 h in ethers). However, the major difference between these two classes of reactions was the isolation of notable yields of toluene products in the case of ether substrates. The different results for benzylic ethers and benzylic esters caused us to reflect on whether fragmentation of benzylic ethers and benzylic esters occur through the same intermediates.

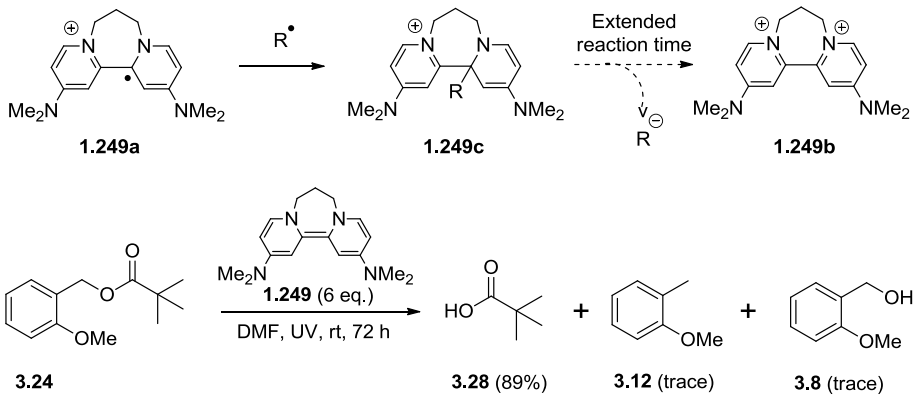
Benzylic C-O bond cleavage in esters required use of 3 eq. of the donor **1.249** and showed all the signs of fragmenting through their radical anions to form benzyl radical

intermediates; however we now wondered whether use of 6 eq. of the donor **1.249**, like in our procedure for ethers, could generate benzylic anions as intermediates. Therefore, substrate **3.24** was tested by using 6 eq. of the photoexcited donor **1.249** for 24 h and provided an excellent yield of pivalic acid **3.28** along with trace amounts of 2-methoxytoluene **3.12** and 2-methoxybenzyl alcohol **3.8** (Scheme 3.28). The trace amounts of **3.12** might be formed via a DET process, while generation of trace amounts of **3.8** could be possible by the nucleophilic nature of the donor.[100]



Scheme 3.28

The length of reaction time for C-O bond cleavage in esters was 24 h against 72 h in ethers. It was suggested earlier that the isolation of methyl arene products from ether substrates might arise from benzyl anion intermediates formed via a second electron transfer (DET process) before expelling the alkoxide. However, we now wondered whether it is possible for the trapped entity **1.249c** (benzyl radical intermediate trapped by the radical-cation of the donor **1.249a)** to slowly break down as benzyl anion and donor dication **1.249b** over the extended reaction times (72 h) in the ether substrates (Scheme 3.29). If this is the possible explanation for the generation of benzyl anions and thereby for the methyl arene products arising from ethers, then it should also generate similar toluene products in ester cleavages under the extended reaction time (72 h) conditions.



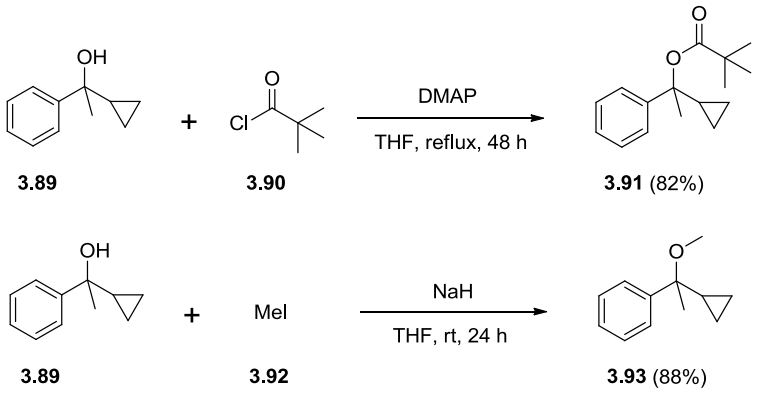
Scheme 3.29

However, when substrate **3.24** was treated with 6 eq. of the photoexcited donor **1.249** for 72 h, it gave a parallel result to earlier experiments and provided an excellent yield of pivalic acid **3.28** along with trace amounts of 2-methoxytoluene **3.12** and 2-methoxybenzyl alcohol **3.8** (Scheme 3.29).

The above experiments show that benzylic radicals are not reduced to their anions by the additional equivalents of donor **1.249** that were used in our ether cleavage protocol. These experiments also suggested that the formation of benzylic anions in ether substrates was at least partly arising from pathway **(b)** involving DET process (discussed in page 87) without intermediacy of benzyl radicals.

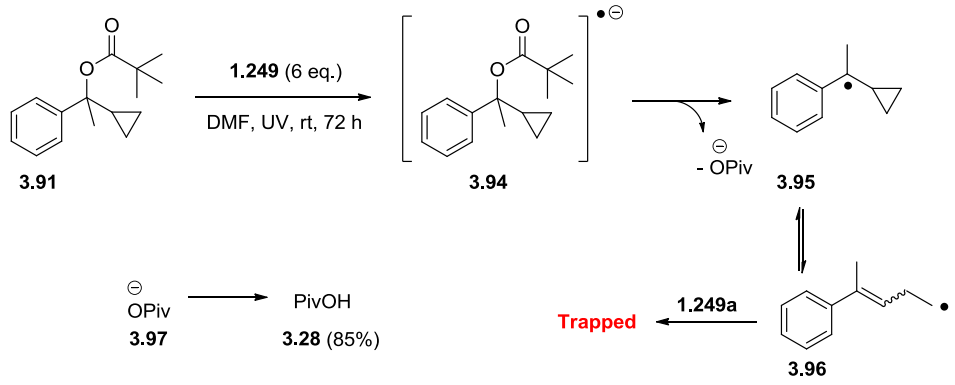
To further confirm that the reduction of benzyl esters is occurring through a SET process and that a DET process plays a role in the reduction of benzyl ethers, a sensitive method that would respond quickly to the presence of benzyl radical intermediates was required. Previous results[122] from our laboratory have shown that isomerisation of stereochemically defined cyclopropanes was achieved with the donor **1.249** (Scheme 1.40). However, this time, it was planned to explore cyclopropane substrates for their characteristic rapid ring opening of the cyclopropane in the presence of benzylcyclopropyl radicals.[123,124] On the other hand, any benzylic anions that are formed directly *i.e.* without passing through the benzylic radicals should leave the cyclopropanes untouched.

To probe this, cyclopropane ester **3.91** and ether **3.93** were designed and each was prepared in a single step from commercially available 1-cyclopropyl-1-phenylethanol **3.89** as shown in Scheme 3.30.



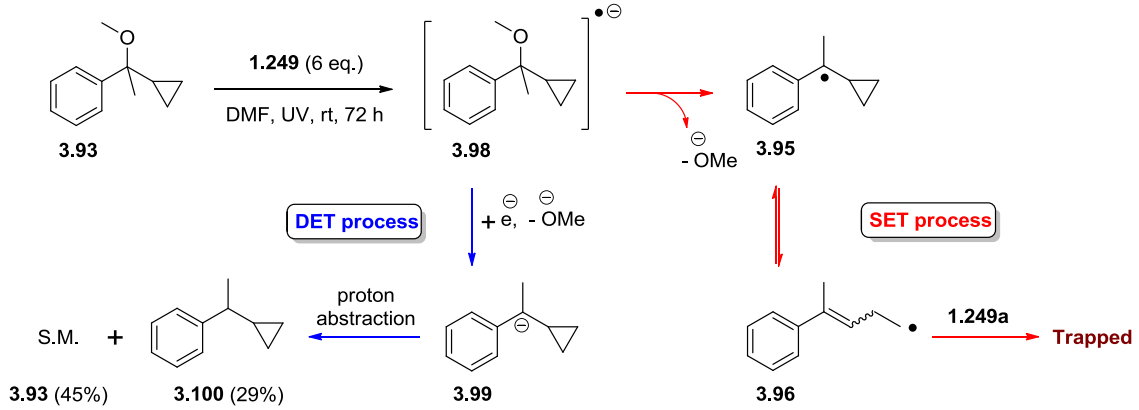
Scheme 3.30

It was expected that the ester substrate **3.91** would fragment to generate benzyl radical **3.95** and pivalate anion **3.97** upon a SET from the photoactivated donor **1.249**. This benzyl radical **3.95** should lead to a very rapid opening of the cyclopropane to generate new radical **3.96** and both of these radicals, **3.95** and **3.96**, should be trapped by the radical-cation of the donor **1.249a**. Indeed, treatment of the ester substrate **3.91** with the donor **1.249** under photoactivation conditions for 72 h, *i.e.* normal benzyl ether reduction conditions, provided an excellent yield of pivalic acid **3.28** only. This result clearly supported the proposal that the C-O bond cleavages in benzyl ester were proceeding via a SET process (Scheme 3.31).



Scheme 3.31

In contrast, when the corresponding ether substrate **3.93** was submitted to the same reaction conditions *i.e.* photoactivation of the donor **1.249** (6 eq.) for 72 h, reduced product **3.100** (29%) was isolated together with starting material **3.93** (45%) (Scheme 3.32).

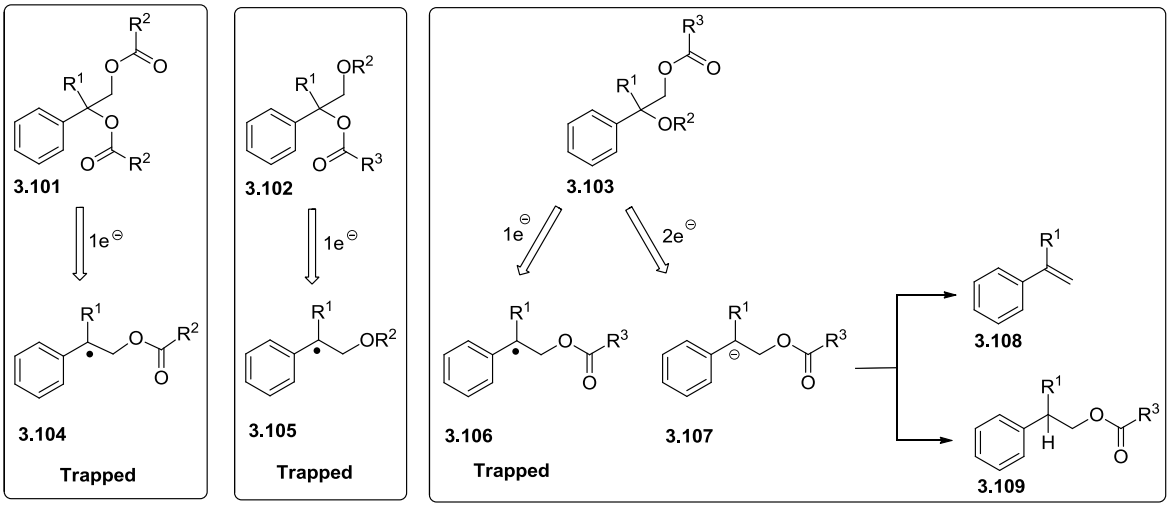


Scheme 3.32

If the reaction was proceeding through a SET process (shown in red arrows), similar to the ester reaction, it would generate intermediates **3.95** and **3.96** that were trapped by the radical-cation of the donor **1.249a**. However, if the reaction was proceeding through a DET process (shown in blue arrows), without passing through benzylic radical intermediates, it would fragment to generate benzyl anion **3.99** and methoxide anion. Finally, benzyl anion **3.99**, upon proton abstraction, affords intact cyclopropane **3.100** (Scheme 3.32).

The above experiments indicated that the fragmentation of benzylic C-O bond is faster in the ester substrate **3.91** compared with the ether substrate **3.93**. These experiments clearly show that benzylic radicals are exclusive intermediates formed via the SET process in the benzylic C-O bond cleavage of cyclopropane esters. The intact cyclopropane **3.100** cannot have arisen from a benzylic radical intermediate. Rather, the benzylic anion **3.99** must be its precursor, supporting a DET process in ether substrates.

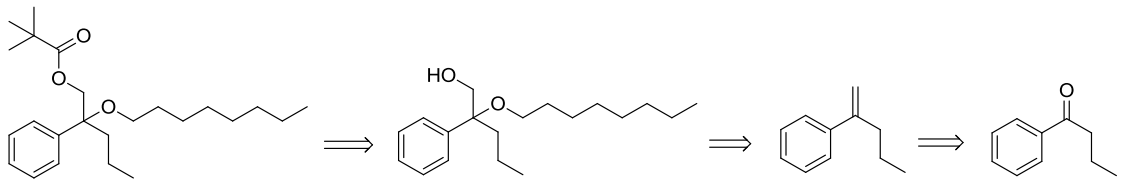
To further confirm that, in general, the reduction of benzyl esters is occurring through a SET process while the reduction of benzyl ethers follows both a SET process and a DET process, a series of substrates **3.101**-**3.103**, which can potentially demonstrate the above argument, was designed. These substrates contain not only a benzylic leaving group, but also a potential leaving group (carboxylate in **3.101** and **3.103** and alkoxide in **3.102**) in the adjacent β-position (Scheme 3.33).



Scheme 3.33

According to our assumption, substrates like **3.101** and **3.102**, after the SET process from the donor **1.249** and expulsion of carboxylate anion, should form benzyl radicals **3.104** and **3.105**, respectively. These radicals are expected to be trapped completely by the radical-cation of the donor **1.249a** and no other products should be isolated from the organic phase of the reaction. Similarly, if the substrate **3.103** follows a SET process, it will provide benzyl radical **3.96** after expulsion of alkoxide. This benzyl radical **3.106** is most likely to be trapped by the radical-cation of the donor. In contrast, if **3.103** follows a DET process, then it will provide benzyl anion **3.107** after expulsion of alkoxide and **3.107** cannot be trapped by the radical-cation of the donor **1.249a**. This anion **3.107** may undergo further reaction to form styrene derivative **3.108** by expelling the carboxylate anion or it can take a proton from the reaction to give the reduced product **3.109** (Scheme 3.33).

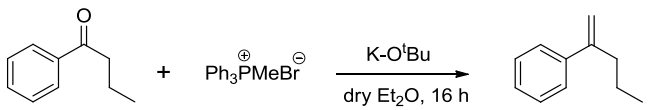
To start with, synthesis of the substrate **3.110** was attempted. The retrosynthetic route to **3.110** is shown below (Scheme 3.34).



3.110 **3.111** **3.112** **3.113**

Scheme 3.34

The compound **3.112** was synthesised quite easily from butyrophenone **3.113** and methyltriphenylphosphonium bromide **3.114** by using potassium *tert*-butoxide as a base via a Wittig reaction (Scheme 3.35).

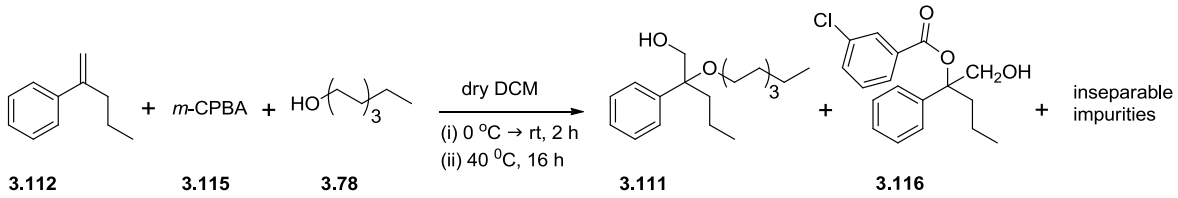


3.113 **3.114** **3.112** (62%)

Scheme 3.35

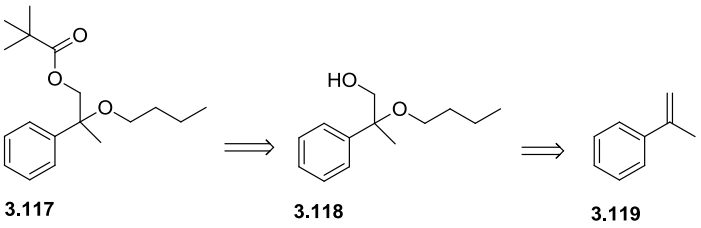
Synthesis of **3.111** was attempted from pent-1-en-2-ylbenzene **3.112** (1 eq.) and 1-octanol **3.78** (3 eq.) by using *m*-CPBA **3.115** (1.5 eq.) and by following the method described by Monk *et al.*[184] Unfortunately, the pure desired product **3.111** could not be isolated from

the crude reaction mixture. The compound **3.116** might be arising due to the ring-opening of the intermediate protonated epoxide by the 3-chlorobenzoate anion instead of by 1-octanol **3.105** (Scheme 3.36). To minimise this unwanted ring-opening of the epoxide, use of excess alcohol is desired. However, it was also mentioned that increase of steric crowding around the benzyl carbon led to lower yields of the desired products.[184]



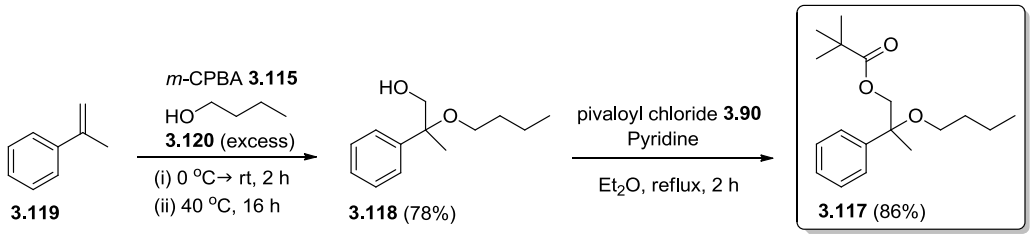
Scheme 3.36

To simplify the problem, the less complex compound **3.117**, whose retrosynthesis is shown in Scheme 3.37, was designed.



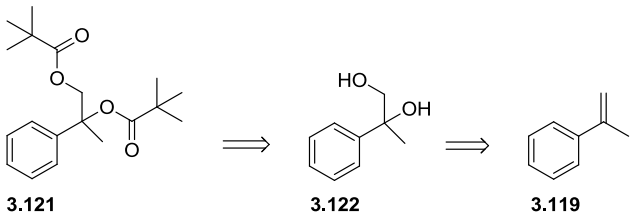
Scheme 3.37

The compound **3.118** was synthesised in good yield (78%) from the reaction of α-methylstyrene **3.119** with *m*-CPBA **3.115** and by using excess of *n*-butanol **3.120**. Subsequently, the target molecule **3.117** was synthesised in good yield (86%) by treating **3.118** with pivaloyl chloride **3.90** under reflux conditions using pyridine (Scheme 3.38).



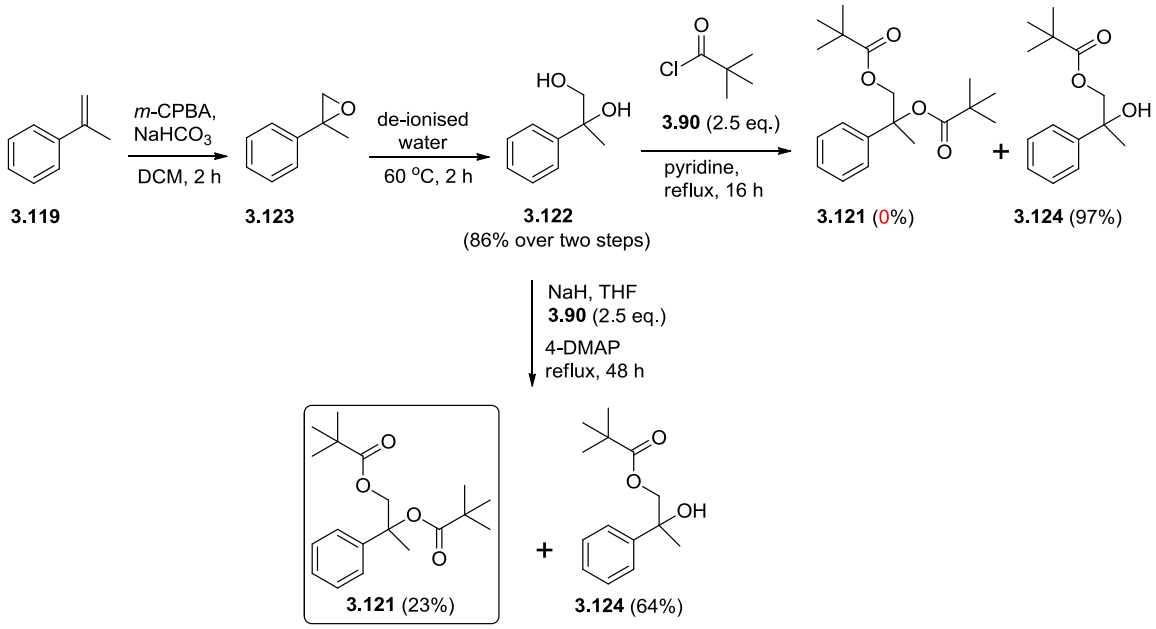
Scheme 3.38

Subsequently, it was planned to prepare di-ester substrate **3.121** whose retrosynthetic route is shown below in Scheme 3.39.



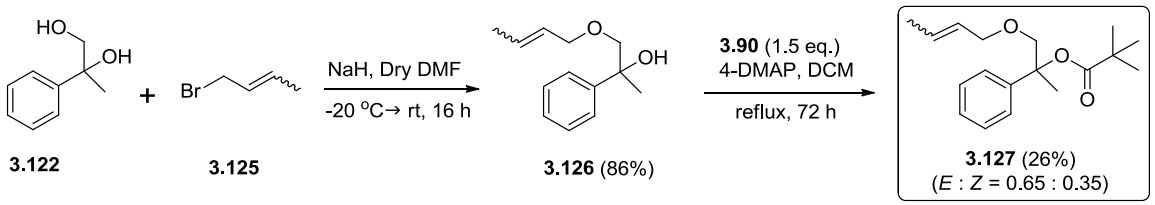
Scheme 3.39

The diol **3.122** was synthesised from α-methylstyrene **3.119** in good yield (86%) over two steps. In the first step, α-methylstyrene **3.119** was treated with *m*-CPBA **3.115** to provide epoxide **3.123**. This crude product **3.123** was then used without further purification in the next step using de-ionised water as a nucleophile and heating at 60 ^{o}C for 2 h and provided **3.122** in good yield (86% over two steps). The diol **3.122** was then treated with pivaloyl chloride **3.90** (2.5 eq.) and pyridine to obtain di-ester **3.121**. Unfortunately, none of the di-ester **3.121** was formed but mono-ester **3.124** was isolated in an excellent yield (97%). By this, it was understood that harsher conditions were required to reach di-ester **3.121**. The diol **3.122** was then treated with sodium hydride and DMAP instead of pyridine, and pivaloyl chloride **3.90** (2.5 eq.) was added to afford di-ester **3.121** in a useful yield (23%) and mono-ester **3.124** (64%) after 48 h reaction in THF at reflux conditions (Scheme 3.40). The low yield of the **3.121** was likely due to the steric effects around the quaternary carbon centre.



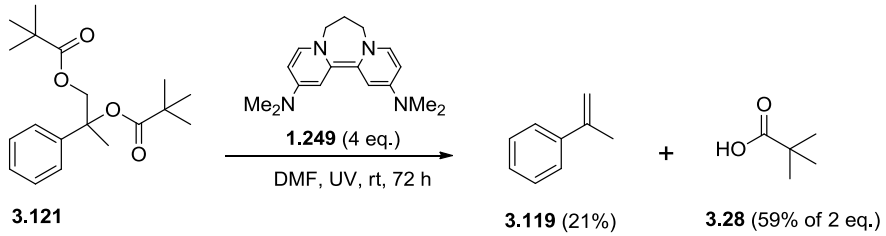
Scheme 3.40

Substrate **3.127** was then designed and synthesised in two steps as shown in Scheme 3.41. The diol **3.122** was treated with sodium hydride and 1-bromobut-2-ene **3.125** at low temperature to avoid double alkylation and provided the desired mono-alkylated product **3.126** (86%) in good yield. This product **3.126**, upon reaction with pivaloyl chloride **3.90** (1.5 eq.) and 4-DMAP under reflux conditions, provided the final desired product **3.127** as a mixture of isomers (*E* : *Z* = 0.65 : 0.35) in a useful but modest yield (26%) along with starting material **3.126** (62%). The low yield of the **3.127** was due to the steric effects around the quaternary carbon centre.



Scheme 3.41

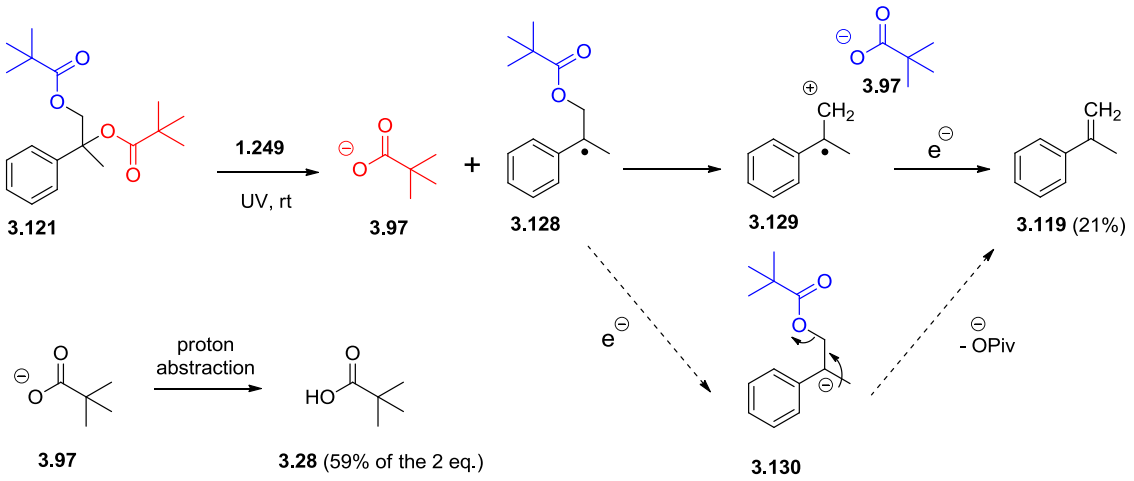
With the substrates **3.117**, **3.121** and **3.127** in hand, the main UV reactions were tested with the donor **1.249**. The di-ester substrate **3.121**, upon reaction with the donor **1.249** (4 eq.) for 72 h, provided α-methylstyrene **3.119** (21%) and the expected pivalic acid **3.28** (59% of the two equivalents) (Scheme 3.42).



Scheme 3.42

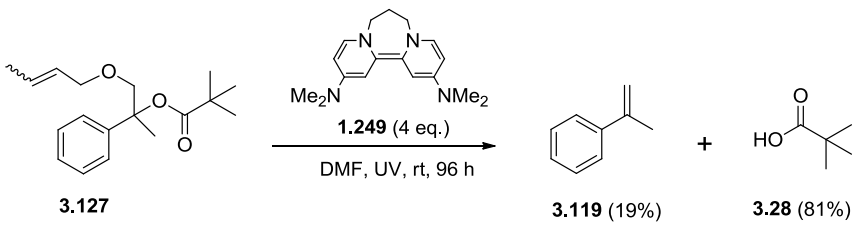
The generation of the α-methylstyrene **3.119** is explained in Scheme 3.43. The di-ester **3.121** forms benzyl radical **3.128** after a SET process followed by the expulsion of the pivalate group **3.97** (shown in red). If this radical **3.128** is trapped quickly by the radical-cation of the donor **1.249a**, as seen in earlier examples, then no arene derived product should be found. However, this radical **3.128** could undergo direct further fragmentation to a pivalate anion **3.97** (shown in blue) and the radical-cation of α-methylstyrene **3.129**, a well precedented reaction of β-acyloxyalkyl radicals.[185,186] The resulting styrene radical-cation **3.129** would receive another electron from the donor **1.249** or radical-cation of the

donor **1.249a** and forms α-methylstyrene **3.109** (21%). Transformation of benzyl radical **3.128** to benzyl anion **3.130** is an unlikely process, as similar attempts to convert benzyl radicals to benzyl anions did not work with substrate **3.24** (see Scheme 3.28 and discussion therein). The pivalate anion **3.97** takes a proton from the acidic work-up and provides pivalic acid **3.28** (59% of the two equivalents). The low yield of α-methylstyrene **3.119** indicates the competition between the trapping of the benzyl radical **3.128** and its evolution into the styrene radical-cation **3.129**.



Scheme 3.43

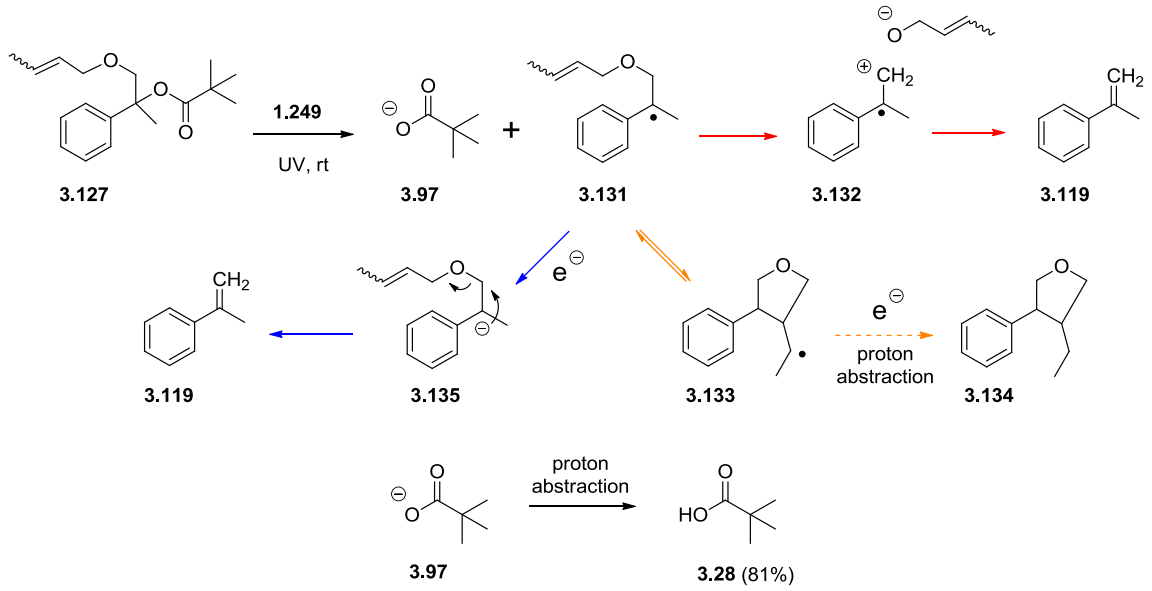
When the ester-ether substrate **3.127** was submitted to the donor **1.249** (4 eq.) under UV conditions for 96 h, it provided a low yield of α-methylstyrene **3.119** (19%) along with a good yield of pivalic acid **3.28** (81%) (Scheme 3.44).



Scheme 3.44

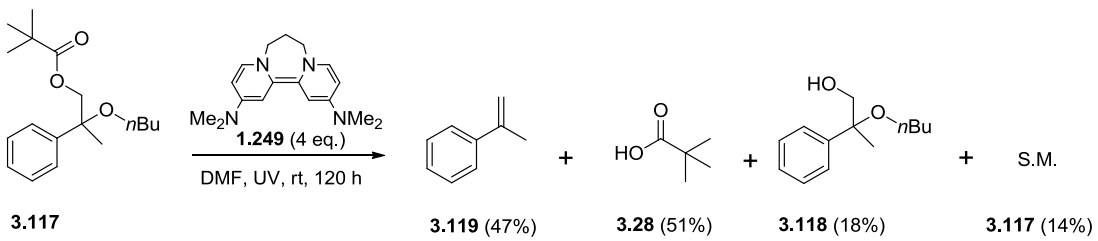
During the course of the reaction, the benzyl radical **3.131** will be formed easily by SET together with loss of pivalate anion **3.97** from the ester-ether substrate **3.127**. Similar to the above example, the formation of the α-methylstyrene **3.119** might occur by the loss of alkoxide from the β- position of the benzyl radical **3.131** as shown in **3.132**. However, there are no reports of this type of elimination of an alkoxide adjacent to a radical in the

literature. At the same time, the cyclisation of the benzyl radical onto the alkene is likely to be slow and possibly reversible and hence, no cyclised product **3.134** is isolated from the reaction. The formation of α-methylstyrene **3.119** may also arise from the benzyl anion intermediate **3.135**, which is in turn formed from benzyl radical **3.131** upon accepting another electron from the donor **1.249** or radical-cation of the donor **1.249a** (Scheme 3.45). The important thing here to note is the mismatch in the yields of the two reduced products **3.119** (19%) and **3.28** (81%) and again trapping of the formed benzyl radical **3.131** by the radical-cation of the donor is believed to be playing a major role.



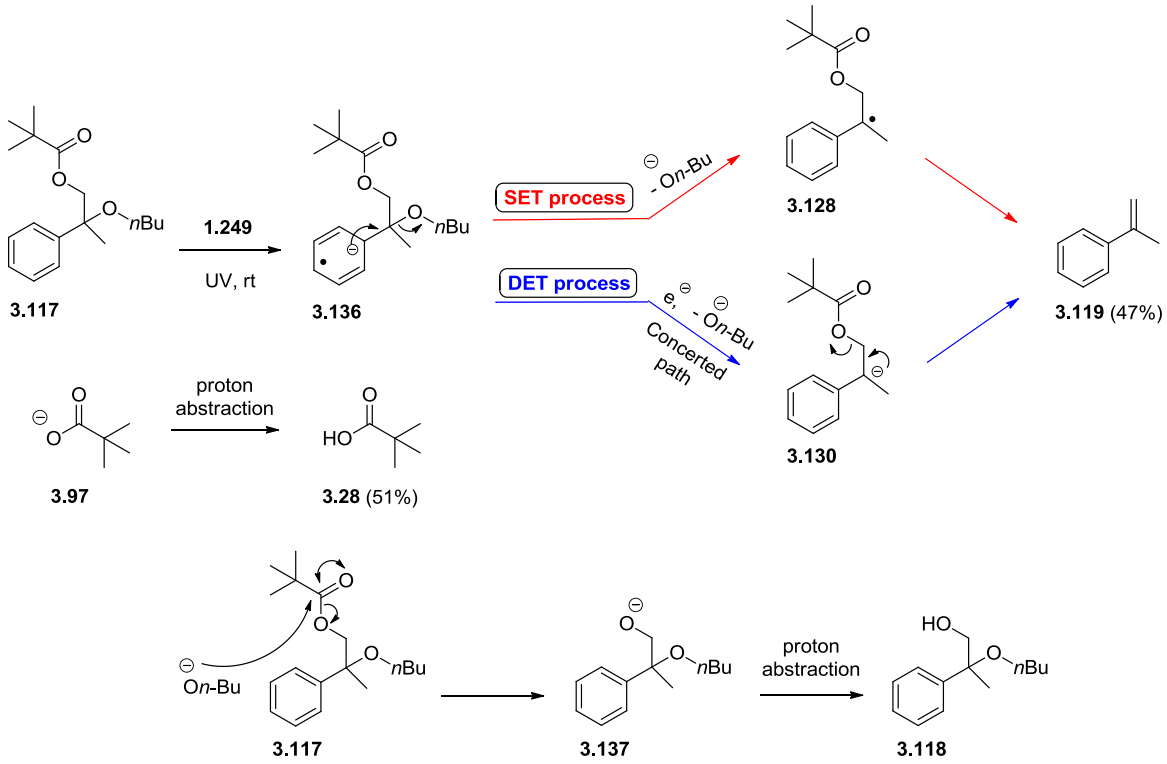
Scheme 3.45

Finally, ether-ester substrate **3.117** was submitted to the photoactivation using the donor **1.249** and it provided α-methylstyrene **3.119** (47%), pivalic acid **3.28** (51%) and alcohol **3.118** (18%). A longer reaction time (120 h) is required, as the expulsion of the butoxide anion is difficult compared to the expulsion of pivalate anion (Scheme 3.46).



Scheme 3.46

The substrate **3.117** takes an electron from the donor **1.249** and forms radical-anion **3.136** via an SET process and then partly converts into benzyl radical **3.128** after losing the butoxide anion. On the other hand, similar to previous ether substrates, the radical-anion **3.136** receives another electron and fragments in a concerted manner to provide benzyl anion **3.130** via a DET process. Both the benzylic species **3.128** and **3.130** could proceed to the α-methylstyrene **3.119** (47%) by following the schemes 3.43 and 3.45, respectively, and yielding **3.119** more than twice as efficiently as for the other two substrates **3.121** and **3.127** (Scheme 3.47). The *n*-butanol resulting from expulsion of *n*-butoxide was too volatile to isolate but, before workup, some of the butoxide deacylated the starting ester **3.117** to afford alcohol **3.118** (18%).



Scheme 3.47

3.7 Conclusion

A series of benzyl esters has been successfully reduced to the corresponding acid products in excellent yields, using photoactivated donor **1.249** (3 eq.) for 24 h at room temperature. More importantly, these reactions proceeded mostly through a SET process and did not provide any significant amounts of methyl arene products due to complete trapping of the radical intermediates with the radical-cation of the donor **1.249a**. However, *di*- and *tri*-

methoxyaryl derived electron-rich esters **3.26** and **3.27**, did not provide complete reaction under the same reaction conditions and, provided small amounts of methyl arene products **3.29** (9%) and **3.30** (11%) respectively. These reduced products **3.29** and **3.30** could arise from the benzyl radical, if the relative rate of trapping of this radical intermediate is lower than hydrogen abstraction. Alternatively, these methyl arene products could arise by further reduction of benzyl radical intermediates to benzyl anions and computational studies, at least qualitatively, support this argument, likely due to the – I (inductive) effect of the methoxy group. On the other hand, electron-deficient ester substrates were reduced to acid products in excellent yields, under the same reaction conditions. However, lowered reactivity towards fragmentation of the radical anion in **3.32** permitted a second electron transfer and provided *p*-cyanotoluene **3.34**. Blank reactions were carried out along with the original reactions under the same reaction conditions and resulted in the recovery of starting material only.

Later, benzylic C-O bond cleavages were successfully extended to a series of ether substrates. As expected, C-O cleavages in ethers needed higher amounts of the donor **1.249** (6 eq.) and extended reaction times (72 h). But, more importantly, these cleavages proceeded through both the SET and the DET processes and provided both the methyl arenes and alcohols in unequal yields. The discrepancy seen in the yields of the two reduced products might be due to the trapping of the benzylic radical intermediate with the radical-cation of the donor **1.249a**. Unlike benzyl esters, success of the C-O bond cleavage reaction in benzyl ethers depends highly on electronic factors. Particularly, *p*-methoxy-substituted compounds have limited success, reminiscent of Hilmersson's findings for reduction of *p*-methoxybenzyl substrates with SmI_2.[57] Surprisingly, no reaction was seen with substrates having electron-withdrawing groups on the arene ring due to predominating electron-withdrawing character of these groups on the benzene ring in competition with the electron transfer into σ* orbital of the benzylic C-O bond. Blank reactions were carried out along with the original reactions under the same reaction conditions and resulted in the recovery of starting material only.

The isolated 4-methoxybenzyl alcohol **1.350** (4%) in the reaction of **3.68** arises due to the cleavage of the allylic C-O bond. A series of compounds **3.81**- **3.83** was prepared and submitted to the photoactivation conditions and it was established that proximity of the

allylic system to the aryl system was required to achieve these allylic C-O bond cleavages.

Later, benzyl ester substrate **3.24** was treated with the donor **1.249** using the conditions that were used for ether substrates *i.e.* photoactivation of **1.249** (6 eq.) for 72 h and these experiments suggested that transformation of benzyl radical intermediates to benzyl anions could not happen with the use of additional equivalents of donor **1.249** for extended reaction times.

To further probe the presence of benzylic radical and benzylic anion intermediates, cyclopropyl ester **3.91** and ether **3.93** substrates were submitted to photoactivated donor **1.249**. These experiments clearly show that benzylic radicals were exclusive intermediates formed via a SET process in the cleavage of cyclopropyl esters. The intact cyclopropane **3.100**, formed in the reaction of cyclopropyl ethers, could not have arisen from a benzylic radical intermediate, but rather the benzylic anion **3.89** must be its precursor, supporting a DET process in cleavage of benzylic ether substrates. Later, a series of substrates, containing not only a benzylic leaving group, but also a potential leaving group in the adjacent β-position, were submitted to normal reaction conditions. All these experiments provided α-methylstyrene **3.119** along with acid product. However, benzyl ether ester substrate **3.117** provided α-methylstyrene **3.119** more than twice as efficiently as for other two substrates **3.121** and **3.127**, further supporting a DET process in ether substrates.

Finally, the benzylic C-O bond in both esters and ethers is cleaved by neutral organic electron donor **1.249**, upon photoactivation. The greater selectivity of this reagent versus traditional Birch conditions *i.e.* Na/NH_3(liq.) allows differences to be observed between the cleavages in benzylic esters, (SET), and benzylic ethers, where DET plays a role.

3.8 Future work

- The above discussed C-O bond cleavages in benzylic esters and ethers can be extended to substrates featuring a C-O fragmentation site (shown in red) away from the arene ring. A series of possible test substrates is shown in Fig. 3.2.

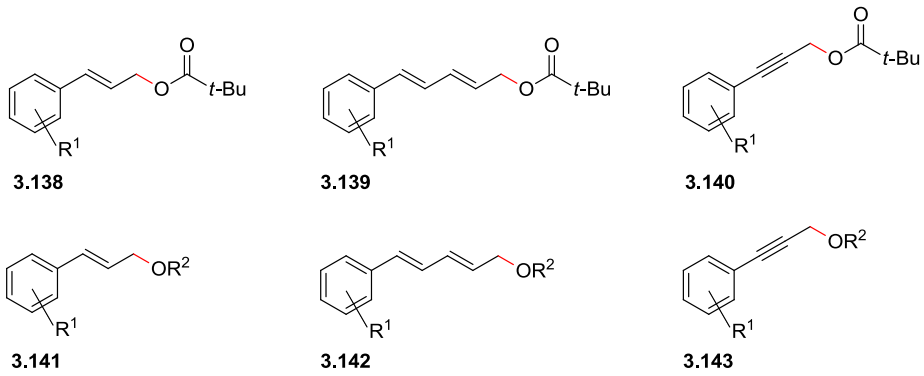
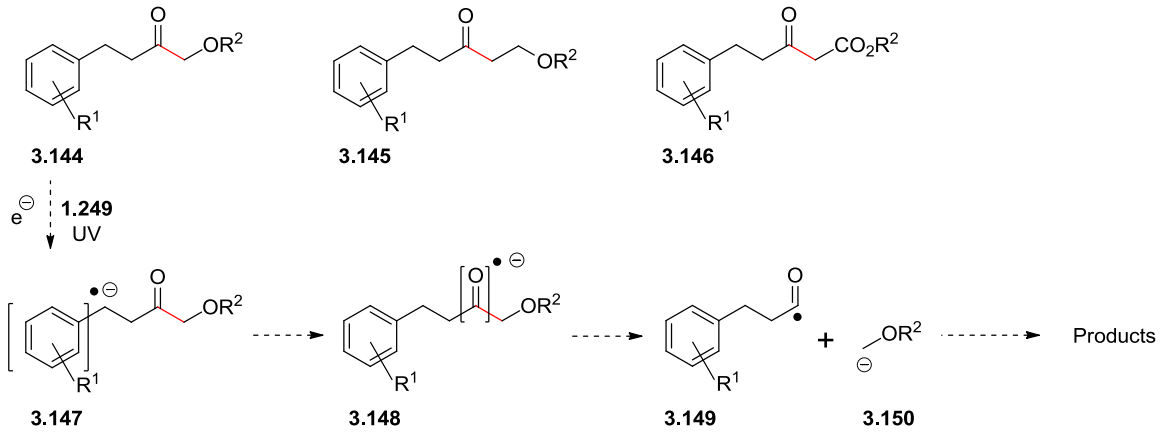


Figure 3.2: Test substrates for C-O bond cleavages in extended systems

- In allylic C-O bond cleavages, it was found that the added electron in the arene ring of a radical-anion was transferred intramolecularly to the nearby allylic system to afford C-O bond fragmentation. In reductive chemistry, carbonyl groups are generally key electron acceptors.[161] Therefore, it would be interesting to test substrates featuring a carbonyl group instead of the allylic system (Scheme 3.48).

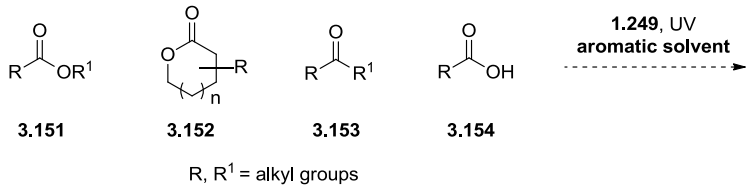


Scheme 3.48

- Do aromatic solvents help reduction reactions with organic electron-donors?

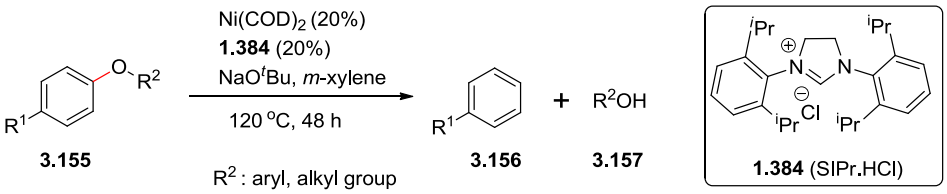
  In all our reductions, dry DMF was used as solvent. Most of these processes involve initial electron-transfer to arene rings. Allylic C-O bond cleavages showed potential

intramolecular electron-transfer. So, it would be interesting to test reduction by using aromatic solvents, which can create a pool of electrons in the solvent that can transfer intermolecularly to the reactive sites in the substrates to provide better reactions. If this works out, it would also be interesting to test reduction of alkyl esters **3.151**, lactones **3.152**, carbonyl compounds **3.153** and acids **3.154** under the same reaction conditions.



Scheme 3.49

- Very recently, Hartwig and co-workers reported the C-O bond cleavages in diaryl ethers or aryl alkyl ethers such as **3.155**, using a nickel carbene complex (Scheme 3.50).[134] Although not seen so far, it is expected that the highly reducing, photoactivated donor **1.249** may also be able to provide similar Ar-O cleavages via electron-transfer to the arene ring. Therefore, testing of these substrates under photoactivation of the donor **1.249** is left to future endeavours.



Scheme 3.50

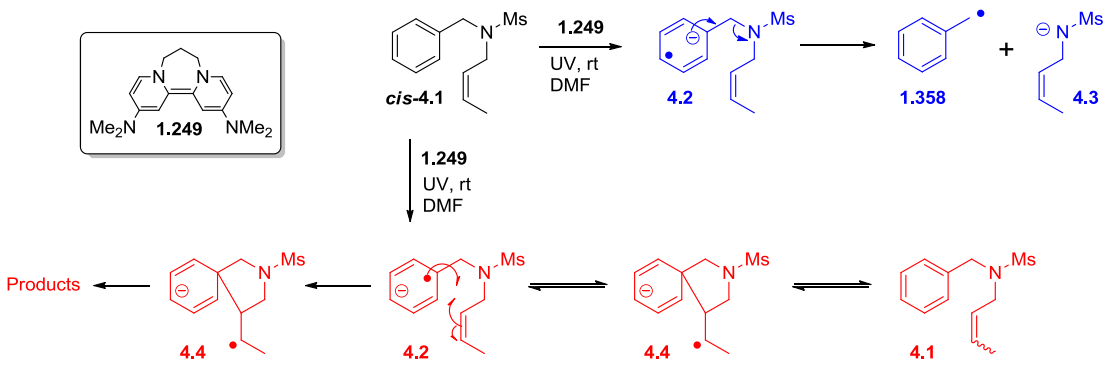
4 Reductive Cleavage of ArC-X (X = N, C) Bonds via Selective Reduction of Arenes

4.1 Introduction to benzylic C-N bond cleavages

N-Benzylation is popular as a robust protective transformation for amines in multistep syntheses, where *N*-debenzylation is an essential conversion for the deprotection at later stages of the synthetic route.[176] There are a number of reductive *N*-benzyl deprotections using metals and metal-based complexes, as discussed in the introduction of this thesis. However, some of these metal-based methods have their own limitations, for example, less selectivity towards easily reducible functional groups such as alkenes, alkynes and esters present within the substrates. To address these limitations, more selective and environmentally benign reducing agents are required. With the success of *O*-debenzylation of esters and ethers with neutral organic super-electron-donors, as discussed in Chapter 3 of this thesis, our attention was turned to *N*-debenzylations, which had never been attempted with non-metallic, organic reducing agents.

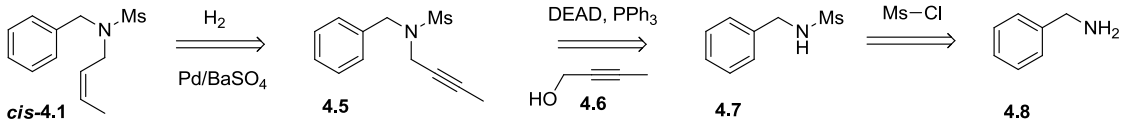
4.2 Benzylic C-N bond cleavages

To test the first ever benzylic C-N bond cleavages with organic electron donors, substrate ***cis*-4.1**was designed. In accordance with the previously seen *O*-debenzylation of esters and ethers, it was envisaged that photoexcited donor **1.249** would donate an electron to the arene ring to generate radical-anion of the substrate **4.2**. Therefore, the substrate ***cis*-4.1** affords an opportunity for the anionic nature of the arene radical-anion to be expressed via fragmentation of the benzylic C-N bond to a benzyl radical **1.358** and a sulfonamide anion **4.3** (shown in the blue path). The presence of the mesyl group on the nitrogen atom stabilises the anion intermediate **4.3**. Substrate ***cis*-4.1** also features a stereochemically defined (*Z*)-alkene group, as a potential indicator of radical reactivity of the arene radical-anion via radical cyclisation onto the appropriately placed alkene group. If this cyclisation were reversible, it would be signalled by the decrease in the stereochemical purity of (a) any starting material **4.1** recovered after the reaction (shown in the red path) or (b) product **4.3** (Scheme 4.1).



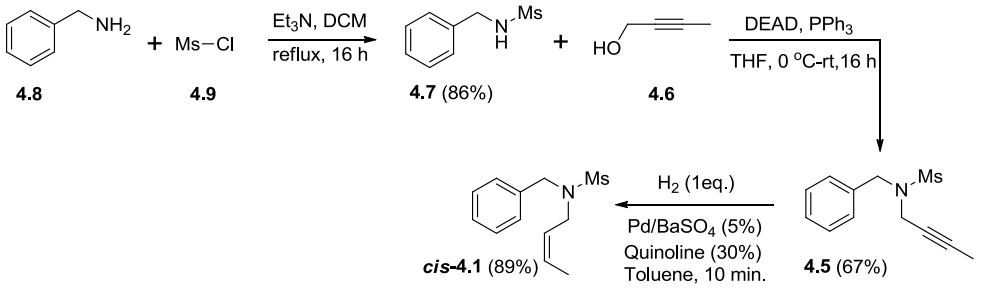
Scheme 4.1

The retrosynthetic route for this substrate ***cis*-4.1** is shown in Scheme 4.2.



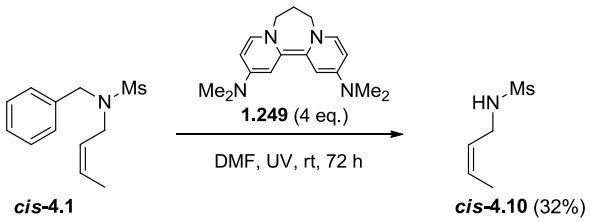
Scheme 4.2

N-Benzylmethanesulfonamide **4.7** was prepared in good yield (86%) by treating benzylamine **4.8** with mesyl chloride **4.9** and triethylamine in dichloromethane under reflux conditions. *N*-Benzyl-*N*-(but-2-yn-1-yl)methanesulfonamide **4.5** was then prepared in good yield (59%) through Mitsunobu reaction from *N*-benzylmethanesulfonamide **4.7** and 2-butyn-1-ol **4.6** using triphenylphosphine and diethyl azodicarboxylate (DEAD). The final desired *cis*-alkene ***cis*-4.1** was prepared in excellent yield (89%) by the partial reduction of **4.5** using hydrogen gas and Lindlar's catalyst ($Pd/BaSO_4$, 5 mol%). Quinoline (30%) acted as a catalyst poison and prevented further reduction into a saturated side-chain (Scheme 4.3).



Scheme 4.3

The reduction of the substrate ***cis*-4.1** was then performed in the presence of donor **1.249** (4 eq.) in DMF as solvent, while irradiating with 365 nm UV lamps (2 x 100 W each) for 72 h at room temperature. This wavelength is near to a maximum absorption for the donor **1.249**, but is not absorbed by simple arenes. To our delight, for the first time, benzylic C-N bond cleavage was successfully achieved with the donor **1.249** under photoactivation conditions. However, this reaction did not produce any other cyclised or isomerised products via radical cyclisation onto the appropriately placed alkene group. From the ^{1}H-NMR of the crude product, it was seen that the reaction went to completion but it provided (*Z*)-*N*-(but-2-en-1-yl)methanesulfonamide ***cis*-4.10** in low yield (32%) (Scheme 4.4). The remaining work to optimise these benzylic C-N bond cleavages was performed elsewhere in our laboratory.



Scheme 4.4

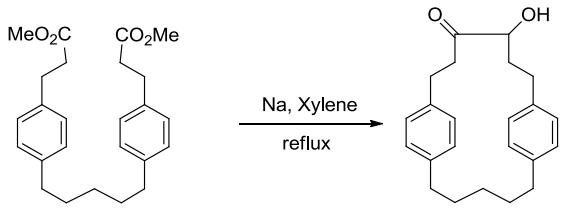
It has been found that an electron received from the photoactivated donor **1.249** is transferred intramolecularly from the π* orbital of the arene (LUMO) to the σ* orbital of the benzylic C-N bond, resulting in bond cleavage to provide the sulfonamide anion along with a benzylic radical. It is believed that the benzylic radical is trapped by the radical-cation of the donor **1.249a** and hence nothing is recovered from the organic phase. Acid work-up of the aqueous phase provided the sulfonamide **4.10** as the sole product.[187]

4.3 Introduction to benzylic C-C bond cleavages

Controlled cleavage of sp^{3}-hybridised carbon-carbon σ-bonds in unstrained systems is very challenging and important in the simplification of complex molecules for example in the break down of lignin.[188] In recent years, both oxidative and reductive approaches have provided intriguing innovations in C-C σ-bond cleavages and they have been well discussed in the introduction of this thesis. In reductive chemistry, carbonyl groups are generally key electron acceptors.[161] Reductive C-C cleavages where arenes play the role of electron acceptor are rarer, although Maslak in particular has studied the reductive

mesolytic cleavage of crowded 1,1,2,2-tetraalkyl-1,2-diphenylethanes.[166,167] However, the common thing in all the above-discussed fragmentation reactions is the requirement of low-valent metals and metal complexes as reagents. After successfully taking advantage of the extensive chromophores within the donor molecule **1.249** to make it even more powerful under photoactivation conditions for the cleavage of benzylic C-O and C-N bonds, it was now planned to test even more difficult and challenging benzylic C-C bond cleavages under the same reaction conditions.

As mentioned above, carbonyl groups are central to reductions by electron transfer. Electrochemical reduction potentials for ester groups are much less negative than for benzenes,[189] and therefore, esters might be expected to undergo preferential reduction by electron donor reagents in the presence of arenes. Indeed, acyloin reactions of such substrates as **4.11** proceed in high yield, through selective reduction of the ester group by sodium (Scheme 4.5).[190] The stability of arenes to the reducing conditions is even seen in the fact that xylene is the normal choice of solvent for these reactions.



4.11 **4.12**

Scheme 4.5

Our aim was now to exploit the strong reducing power of the photoactivated donor **1.249**. The fact that our organic electron donors are milder reducing reagents than the alkali metals ought to endow them with greater selectivity, and this was our focus for investigation. To start with, substrate **4.13**, containing both ester and arene groups, was designed. Computational studies (B3LYP 6-31G* modeled in DMF as a solvent continuum) carried out on the substrate **4.13** showed that the LUMO incorporates both the ester and aryl groups, while attempts to locate the SOMO of the corresponding radical anion led to spontaneous fragmentation to form an enolate anion **4.15** and a methoxyacyl radical **4.16** (Fig. 4.1) consistent with reduction of the substrate to ketyl radical-anion **4.14** (red pathway in Scheme 4.6). Thus selective reduction at a malonate ester group, similar to the above-discussed acyloin condensation, should afford this fragmentation.[190]

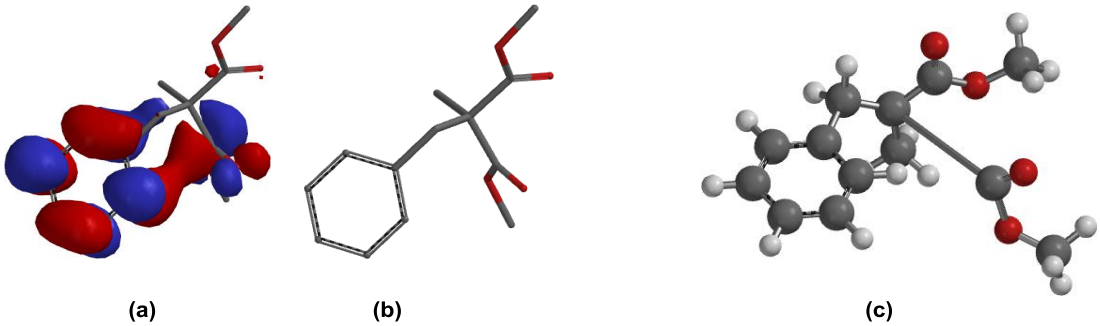
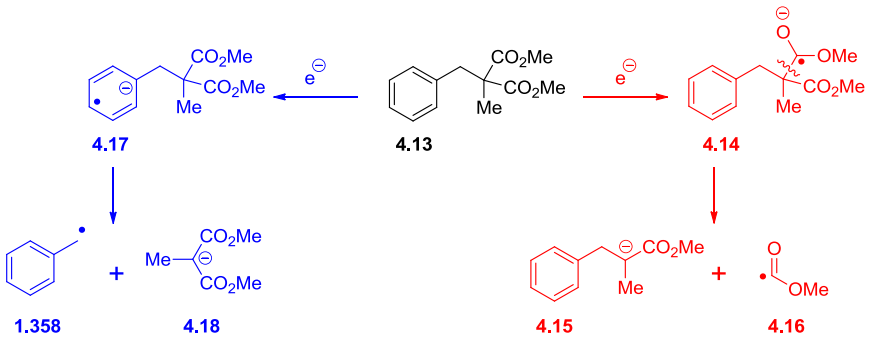


Figure 4.1: **(a)** Represents the LUMO of **4.13** and **(b)** represents the molecule alignment of the LUMO of **4.13** for a better understanding [hydrogen atoms are omitted for clarity in both **(a)** and **(b)**]. **(c)** Represents the SOMO of **4.13**.

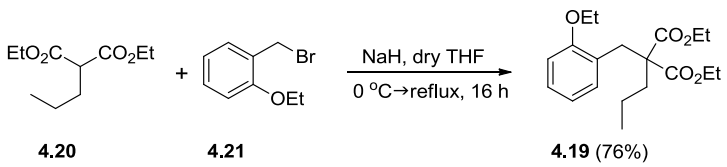
However, our initial impression of previously seen benzylic C-O and C-N cleavages suggested that a different outcome *i.e.* benzylic C-C bond cleavage might also result (blue pathway). These two possibilities are shown in Scheme 4.6.



Scheme 4.6

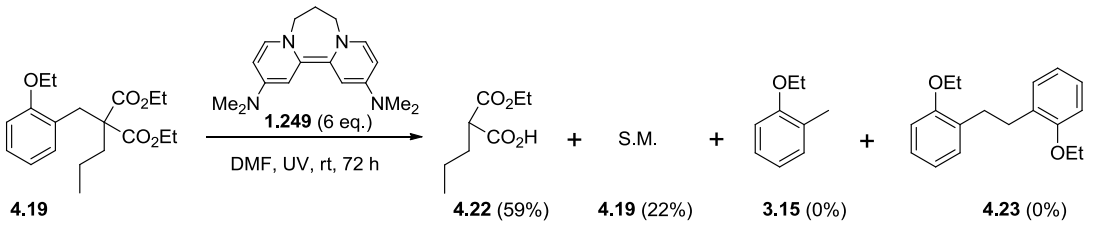
4.4 Benzylic C-C bond cleavage of malonates

Based on the above background understanding, substrate **4.19** containing both the arene and ester groups was selected and easily prepared in good yield (76%) by treating diethyl propylmalonate **4.20** and *o*-ethoxybenzyl bromide **4.21** with sodium hydride (Scheme 4.7).



Scheme 4.7

The reduction of the substrate **4.19** was then performed in the presence of donor **1.249** (6 equiv) in DMF as solvent, while irradiating with 365 nm UV lamps (2 x 100 W each) for 72 h at room temperature.



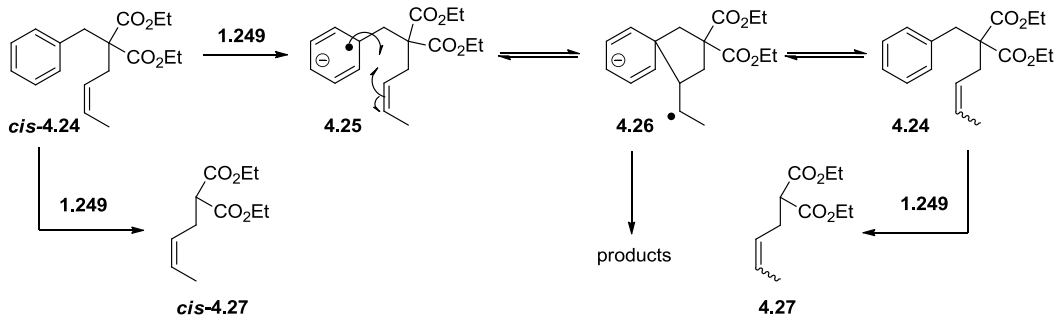
Scheme 4.8

At the end of the reaction, the reaction mixture was quenched with water and extracted with diethyl ether to separate the aqueous phase from the organic phase. After following the remaining usual work-up process with the organic phase, it provided recovery of starting material **4.19** (22%). Then, acidic work-up of the aqueous phase was carried out with dil. HCl (1N) and it provided 2-(ethoxycarbonyl)pentanoic acid **4.22** in good yield (59%) (Scheme 4.8). A notable point was that no methyl arene product **3.15** had been observed from the benzyl radical intermediate. In addition, no 1,2-diphenylethane **4.23**, which might arise on coupling of two benzyl radical intermediates, was observed. In fact, this outcome is completely consistent with the recent report on the rapid trapping of substrate-derived radical intermediates with the radical-cation of the donor **1.249a** to afford water-soluble products.[101] Another important thing to notice here was the conversion of the diester substrate to monoacid, monoester product **4.22**, the origin of which will be discussed later in this chapter.

However, the generation of **4.22** indicates that the reaction proceeds through selective cleavage of the benzylic C-C bond. This result is completely opposite to the computational results, which predicted the selective reduction at the malonate ester group in **4.13**. From the above reaction, unlike metals, organic electron donor **1.249** prefers to pump electrons into the arene system over the ester groups, completely overturning the reactivity of metal-based electon donors. This is a particularly notable piece of selectivity shown by organic electron donors and identified for the first time in our laboratory.

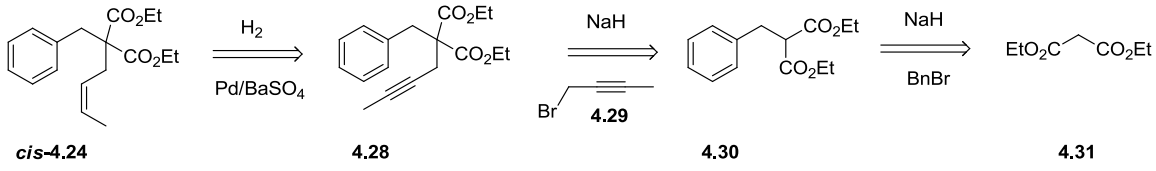
The above reaction suggested that photoexcited donor **1.249** donates an electron to the arene ring and generates the radical-anion of the substrate **4.19**; subsequently

fragmentation at the benzylic C-C bond supports the anionic nature of the arene radical-anion. However, as benzylic C-C bonds are expected to be stronger and more difficult to cleave than benzylic C-O or C-N bonds, it may provide an opportunity for the radical nature of the arene radical-anion to be expressed via radical cyclisation onto the potential trap in appropriate substrates. Therefore, it was planned to prepare substrate ***cis*-4.24** that features a stereochemically defined (*Z*)-alkene group together with malonate esters groups. If the substrate ***cis*-4.24** undergoes radical cyclisation onto alkene then it leads to **4.26** and provides further products. However, if this radical cyclisation is reversible, it would be signalled by the decrease in the stereochemical purity of the starting material ***cis*-4.24** recovered after the reaction. Similarly if fragmentation leads to isolation of butenyl diethyl malonate, the stereochemistry of its alkene can be examined. Loss of stereochemical purity could again signal reversible cyclisation prior to fragmentation (Scheme 4.9).



Scheme 4.9

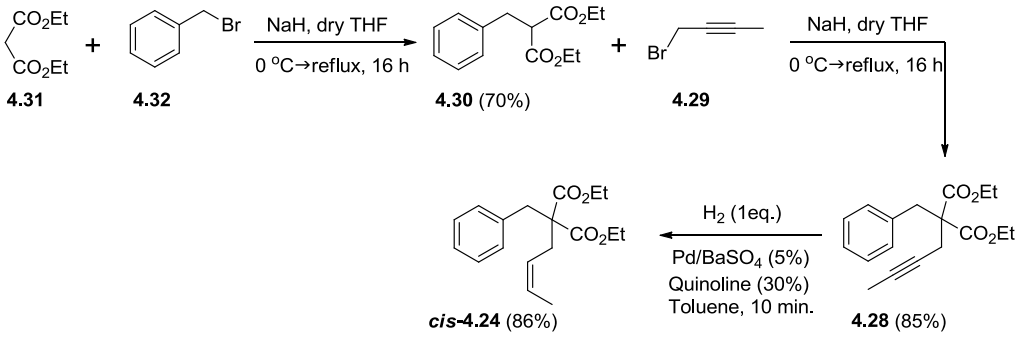
The retrosynthetic route for the substrate ***cis*-4.24** was shown in scheme 4.10.



Scheme 4.10

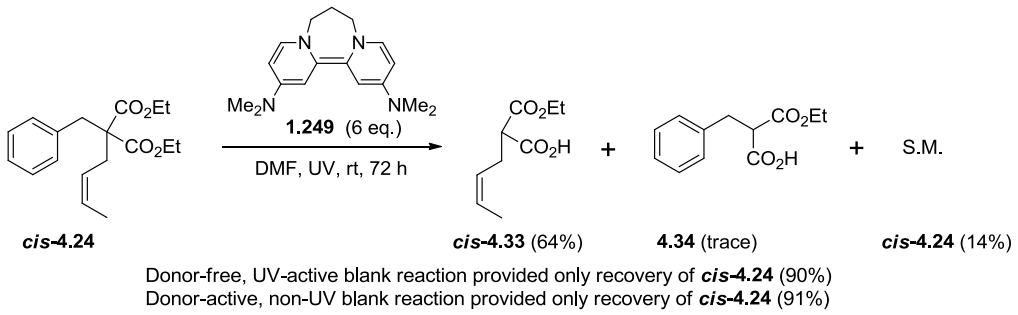
Diethyl 2-benzylmalonate **4.30** was prepared in good yield (70%) by treating diethyl malonate **4.31** and benzyl bromide **4.32** with sodium hydride. Later, diethyl 2-benzyl-2-(but-2-yn-1-yl)malonate **4.28** was prepared in good yield (85%) by deprotonating **4.30** with sodium hydride, followed by the addition of 1-bromobut-2-yne **4.29** into the reaction flask. The final desired alkene compound ***cis*-4.24** was prepared in good yield (86%) by the partial reduction of **4.28** using hydrogen gas and Lindlar's catalyst ($Pd/BaSO_4$, 5

mol%). Quinoline (30%) acted as a catalyst poison and prevented further reduction to the saturated side-chain (Scheme 4.11).



Scheme 4.11

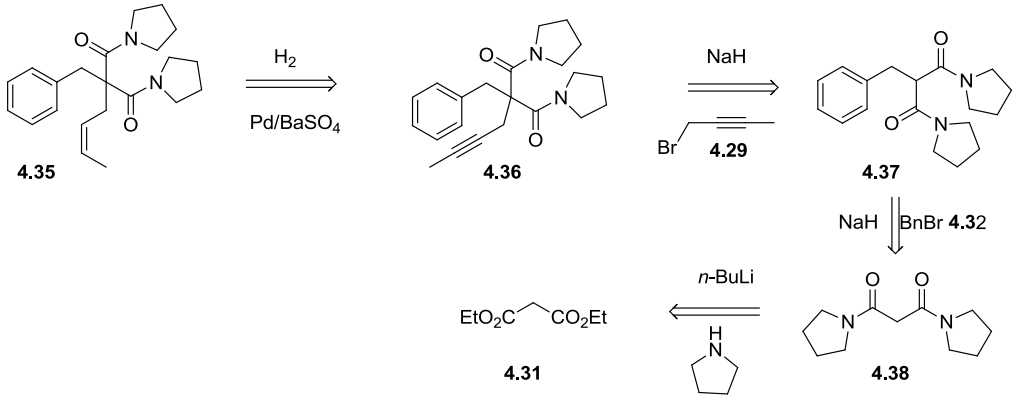
The substrate ***cis*-4.24** was then submitted to the photoactivation using the donor **1.249** (6eq.) for 72 h at room temperature. After following the work-up process that was described for the reaction of substrate **4.19**, it provided (*Z*)-2-(ethoxycarbonyl)hex-4-enoic acid ***cis*-4.33** (64%) as a major product along with a recovery of starting material ***cis*-4.24** (14%). This result is reminiscent of the previous result of substrate **4.19** and did not provide any cyclised product or an isomerised starting material **4.24**. Retention of stereochemical purity in both the starting material ***cis*-4.24** and product ***cis*-4.33** removed any speculation of radical cyclisation onto the alkene group in the radical-anion of substrate, **4.25**. A trace amount of 2-benzyl-3-ethoxy-3-oxopropanoic acid **4.34** was also noticed in the ^{1}H-NMR of the crude product (Scheme 4.12). The generation of **4.34** might be arising from the allylic C-C bond cleavage and similar types of allylic C-O bond cleavages were noticed and studied in detail in chapter 3. The important thing to notice here was again the conversion of one of the ester groups to acid in both the products **4.33** and **4.34**. No attempt was made to isolate reduced product from the other side of benzylic C-C bond cleavage, toluene, due to volatility. However, similar to previous reaction of **4.19**, it is most likely for the benzyl radical interemediate to be trapped by the radical-cation of the donor **1.249a**. Both the donor-free UV-active and donor-active non-UV blank reactions were carried out simultaneously with the original reaction for the same amount of time and provided recovery of the starting material ***cis*-4.24** only.



Scheme 4.12

After the successful demonstration of benzylic C-C bond cleavages in the above two examples, it was now planned to explore more of these cleavages. Before making a full study of these benzylic C-C bond cleavages, it is worth knowing the reasons behind the conversion of one of the ester groups to an acid. Initially, it was suspected that this could be happening through either base (donor **1.249** can also act as a base[100] and a higher concentration of the donor **1.249** was used in this reaction) mediated hydrolysis or acid mediated hydrolysis during the acidic work-up of the aqueous phase.

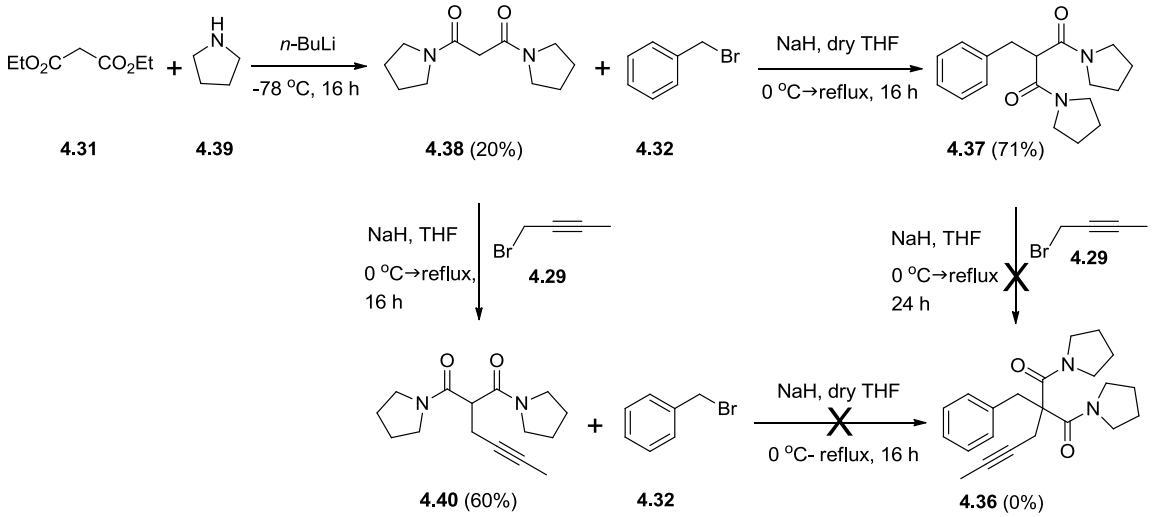
To avoid the hydrolysis issues, diamide **4.35** was designed for the test reaction. Amides are known to be relatively inert under hydrolysis conditions and the substrate **4.35**, if it gives the benzylic C-C bond cleavage reaction, should provide product without any alteration in amide groups. The retrosynthetic route for this diamide **4.35** is shown in Scheme 4.13.



Scheme 4.13

Pyrrolidine **4.39** was deprotonated by *n*-butyllithium and the resulting solution was transferred via cannula into a flask containing diethyl malonate **4.31** at -78 ^{o}C. The reaction was then continued for 16 h at room temperature and provided 1,3-di(pyrrolidin-

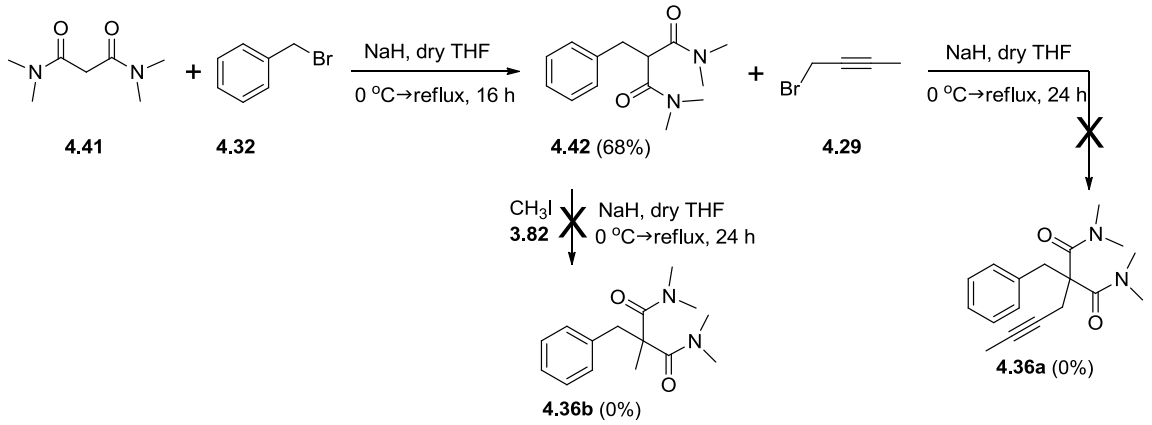
1-yl)propane-1,3-dione **4.38** in workable yield (20%). Compound **4.38** and benzyl bromide **4.32** were treated with sodium hydride to provide 2-benzyl-1,3-di(pyrrolidin-1-yl)propane-1,3-dione **4.37** in good yield (71%). The compound **4.37** and 1-bromobut-2-yne **4.29** were treated with sodium hydride at reflux conditions and provided recovery of the starting material **4.37** only (Scheme 4.14). This result may be due to steric effects around the quaternary carbon centre in the expected product.



Scheme 4.14

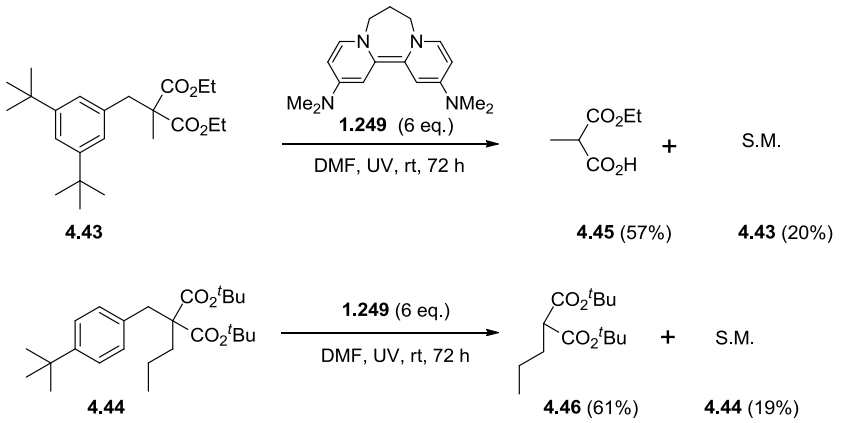
Later, it was planned to interchange the last two steps to see whether any reaction occurred. The compound **4.38** and 1-bromobut-2-yne **4.29** were treated with sodium hydride and provided compound **4.40** in good yield (60%). Now, compound **4.40** and benzyl bromide **4.32** were treated with sodium hydride and did not provide any desired product **4.36** (Scheme 4.14).

Later, it was decided to use a simple commercially available diamide such as N^1,N^1,N^3,N^3-tetramethylmalonamide **4.41**. Diamide **4.41** and benzyl bromide **4.32** were treated with sodium hydride and provided compound **4.42** in good yield (68%). Compound **4.42**, upon treating again with sodium hydride and 1-bromobut-2-yne **4.29** did not provide any desired product **4.36a**. Following this, compound **4.42** was treated with sodium hydride and simplest alkyl halide, iodomethane **3.82**. Steric effects again played a major role and it was noted that the reaction did not work to afford **4.36b** (Scheme 4.15).



Scheme 4.15

After unsuccessful trials to prepare diamide substrates, our focus again shifted towards synthesis of diester substrates. To test the generality of this cleavage reaction, further substrates were prepared with differing substitution patterns on the arene ring and varying esters groups. Diethyl malonate-derived substrate **4.43** and di-*t*-butyl malonate-derived substrated **4.44** were prepared by following the method used for the synthesis of **4.20**. The donor reactions with these substrates may provide more insight into these cleavages and may suggest whether benzylic C-C bond cleavage is dependent upon the transformation of one of the ester groups into an acid group. Both the substrates **4.43** and **4.44** were submitted to the photoactivation of the donor **1.249** and afforded benzylic C-C bond fragmentation in good yields in both cases. The substrate **4.43**, similar to previous substrates, afforded monoester, monoacid product **4.45** while di-*t*-butyl malonate substrate **4.44** afforded diester product **4.46** (Scheme 4.16).



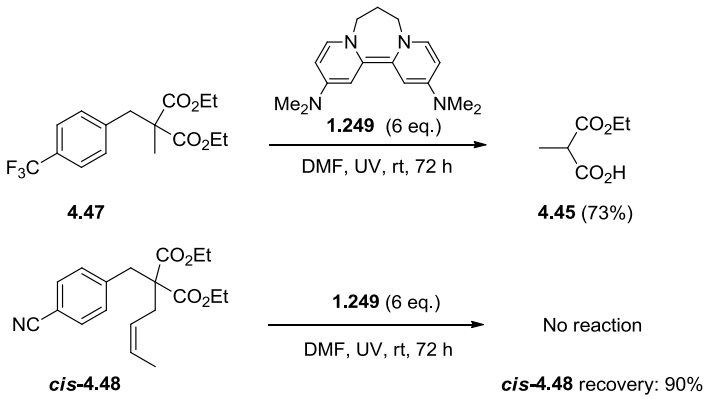
Scheme 4.16

The above experiment with **4.44** clearly shows that the benzylic C-C bond cleavages are not dependent upon the conversion of one of the ester groups into acid group. But, the

generation of diester product **4.46** from bulky di-*t*-butyl malonate substrate **4.44** suggested that the formation of an acid-ester product **4.45** from the substrate **4.43** might be due to alkaline hydrolysis issues on work-up, where *t*-butyl esters are less prone to hydrolysis compared with diethyl esters due to steric factors.

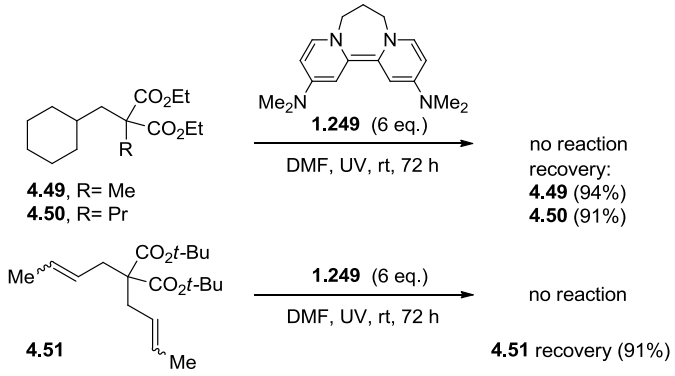
Electron-deficient substrates **4.47**, containing a *p*-trifluoromethyl substituent, and ***cis*-4.48,** containing a *p*-cyano substitent, were prepared by following the methods used for the synthesis of **4.19** and ***cis*-4.24** respectively. In benzyl C-O bond cleavages, it had previously been found that *p*-cyano substrates **3.72** and **3.72** did not provide any reaction probably because of the greater stability of the arene radical-anion. If it is the case again with *p*-cyano substrates in benzylic C-C bond cleavages, the presence of suitably placed (*Z*)-alkene may provide an opportunity for the radical nature of the arene radical-anion to be expressed via radical cyclisation onto the alkene group. If this radical cyclisation were reversible, it would be signalled by the decrease in the stereochemical purity of the starting material ***cis*-4.48** recovered after the reaction.

Substrates **4.47** and ***cis*-4.48** were then submitted to the usual photoreaction conditions *i.e.* photoactivation of donor **1.249** (6 eq.) for 72 h at room temperature. Substrate **4.47** underwent complete reaction and provided monoester monoacid product **4.45** in good yield (73%). Complete consumption of starting material **4.47** reflected the ready acceptance of electrons by electron deficient molecules compared with other substrates. On the other hand, *p*-cyano substrate ***cis*-4.48** did not provide any benzylic C-C bond cleavage. Excellent recovery of pure ***cis*-4.48** removed any speculation of radical cyclisation onto the alkene group (Scheme 4.17). In electron-deficient substrates like **4.47** and ***cis*-4.48**, there is competition between the electron transfer into σ* orbital of the benzylic C-C bond and the electron pulling character of electron-withdrawing group. The fate of the reaction will depend on the collective effect of these two opposing forces. In case of *p*-cyano substrate ***cis*-4.48**, the electron-withdrawing character of the cyano-group predominated, therefore resulting in no reaction.



Scheme 4.17

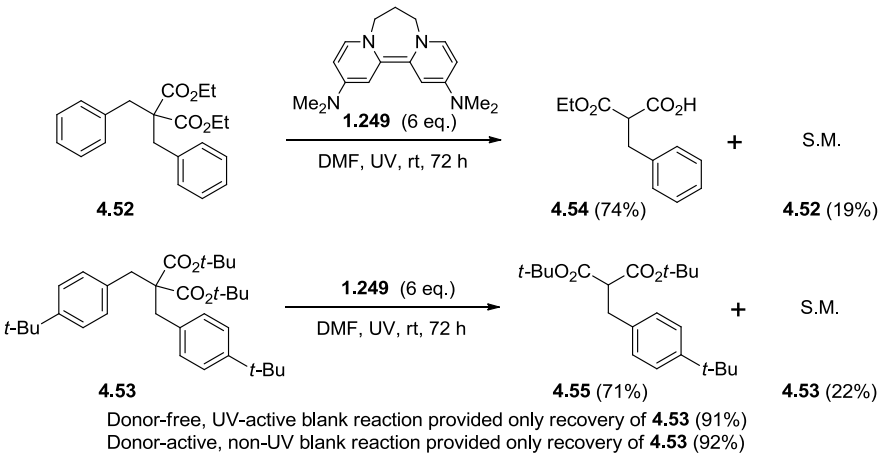
To investigate the necessity of an aryl system for the success of the reaction, it was planned to test non-arene compounds under the same reaction conditions. Diethyl cyclohexylmethyl alkyl malonates **4.49** and **4.50** were synthesised easily and submitted to the photoactivation of donor **1.249**. Both the substrates **4.49** and **4.50** did not provide any fragmentation reaction but afforded excellent recovery of starting materials in 94% and 91% yields respectively (Scheme 4.18).



Scheme 4.18

Dicrotyl malonate substrate **4.51** was prepared to test whether a simple allyl system could receive an electron from the photoactivated donor **1.249**. However, no fragmentation was detected, and the substrate **4.51** was reisolated on work-up (91%) (Scheme 4.18). These reactions emphasise the requirement of an aryl ring in the molecule for the successful C-C bond fragmentation and supports the affinity of the donor **1.249** for an aryl group over the malonate group, a characteristic feature that had never been observed with metals and metal complexes.

Later, it was planned to extend these reactions to dibenzyl malonate systems. Substrates **4.52** and **4.53** were prepared and subjected to the normal reaction conditions. Both the diaryl malonates **4.52** and **4.53** provided better yields of fragmented products compared to monoaryl malonates due to the lower activation energies of LUMO of diaryl systems (Scheme 4.19).

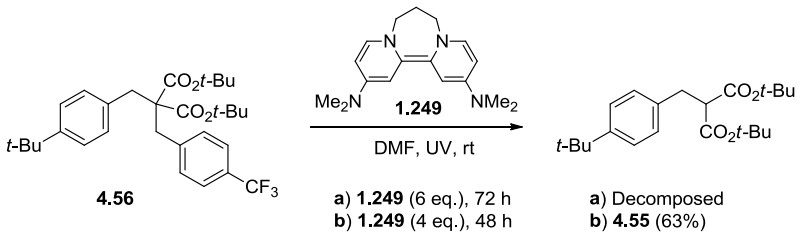


Scheme 4.19

Similar to previous observations, diethyl malonate substrate **4.52** provided monoester monoacid product **4.54** while di-*t*-butyl malonate substrate **4.53** afforded diester product **4.55**. Both the blank reactions that were carried out for the substrate **4.53** provided recovery of the starting material **4.53** only (Scheme 4.19).

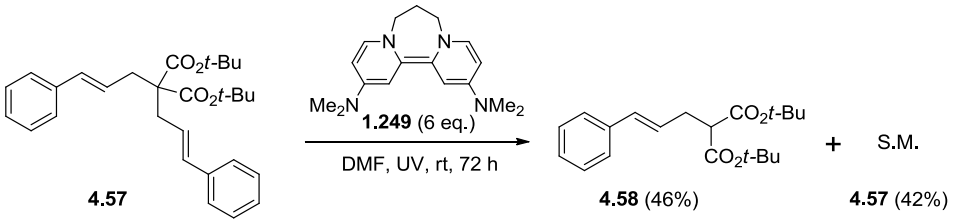
To test the selectivity of the donor **1.249** in transferring electrons selectively into one aryl ring over the other in a diaryl system, a mixed diaryl substrate **4.56**, containing *para*-trifluoromethyl and *para*-*t*-butyl groups on different aryl rings, was prepared. The substrate **4.56** gave decomposition when exposed to normal reaction conditions *i.e.* photoactivation of the donor **1.249** (6 eq.) for 72 h at room temperature. But, performing the same reaction with 4 equivalents of the donor **1.249** for 48 h at room temperature gave completely selective cleavage of the trifluoromethylbenzyl group, affording the *t*-butyl substituted aryl product **4.55** in 63% yield and no starting material was recovered (Scheme 4.20). Diester **4.55** is the expected fragmentation product, since the LUMO of the mixed substrate **4.56** is located on the relatively electron-poor trifluoromethylphenyl ring and donor **1.249** selectively pumped an electron into this aryl ring. The decomposition of trifluoromethyl containing substrate **4.56** may be due to competition between the elimination of two benzylic groups *i.e.* *para*-*t*-butylbenzyldiester and

fluoride, with fluoride loss predominating and these two possibilities were discussed in Scheme 3.24 of Chapter 3.



Scheme 4.20

Later, dicinnamyl substrate **4.57** was prepared and submitted to the normal reaction conditions to test whether an electron can be pumped from the more extensive styryl electrophore to the active site to provide a successful C-C bond fragmentation. To our delight, it provided a homologous cleavage reaction to give di-*t*-butyl cinnamylmalonate **4.58** (46 %) together with recovered substrate **4.57** (42 %). The lower yield of this reaction compared with other dibenzyl substrates may be attributed to high LUMO activation energy of the dicinnamyl substrate **4.57** (Scheme 4.21).



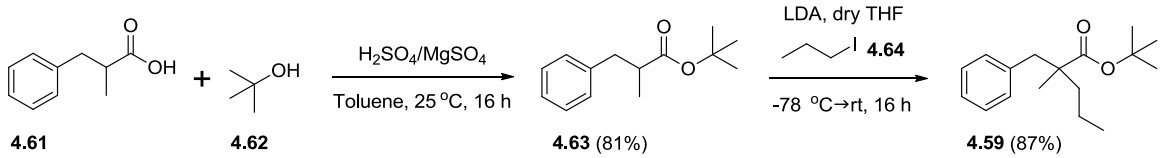
Scheme 4.21

4.5 Attempted benzylic C-C bond cleavage of monoester and sulfone

To test whether the electron-withdrawing ability of a malonate unit was needed, or whether a group that would provide lesser stabilization to the anionic product of a fragmentation would be sufficient, the mono-ester **4.59** and the sulfone **4.60** were prepared to submit to the same reaction conditions used for other substrates.

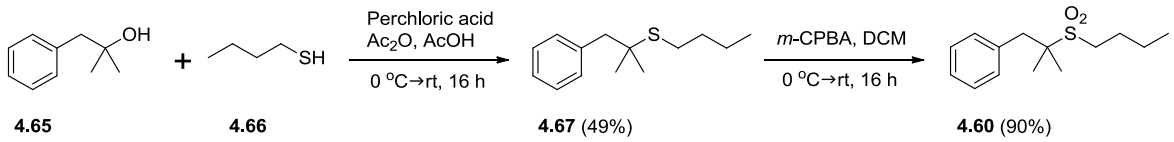
The desired mono-ester **4.59** was prepared in two steps; in the first step, *t*-butyl 2-methyl-3-phenylpropanoate **4.63** was prepared by following the method described by Wright *et al*.[191] To a vigorously stirred suspension of $MgSO_4$ in toluene, conc. H_2SO_4 was added at room temperature and the resulting mixture was stirred for 15 min. before adding 2-methyl-3-phenylpropanoic acid **4.61** and *t*-butanol **4.62**. Upon work-up, the reaction provided *t*-butyl 2-methyl-3-phenylpropanoate **4.63** in good yield (81%). Later,

compound **4.63** was treated with LDA and 1-iodopropane **4.64** to afford the desired mono-ester **4.59** in good yield (87%) (Scheme 4.22).



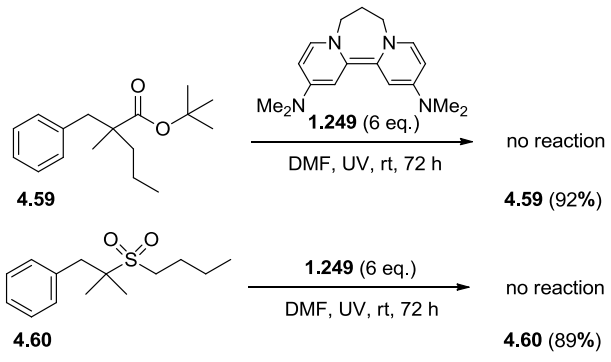
Scheme 4.22

Synthesis of desired sulfone **4.60** was done in two steps; in the first step, benzyldimethylcarbinyl butyl sulfide **4.67** was prepared by following the method described by Cain *et al.*[192] Into a flask containing acetic acid, perchloric acid and acetic anhydride were added at 0 °C and the stirring continued until the exothermic reaction ceased. Later, benzyldimethylcarbinol **4.65** and butanethiol **4.66** were added into the reaction flask and the resulting mixture continued stirring at room temperature for 16 h. Upon work-up, the reaction provided benzyldimethylcarbinyl butyl sulfide **4.67** in moderate yield (49%). Later, sulfide **4.67** was treated with *m*-CPBA to afford the desired sulfone **4.60** in excellent yield (90%) (Scheme 4.23).



Scheme 4.23

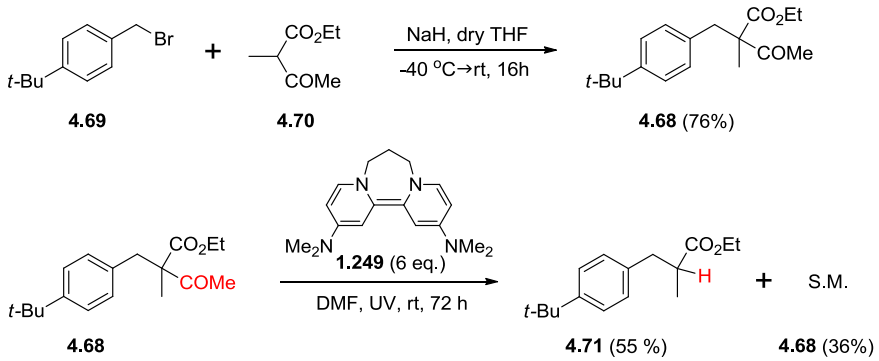
Both the mono-ester **4.59** and sulfone **4.60** were submitted to photoactivation of the donor **1.249** using the same conditions that had been used for other substrates. But, both of these reactions showed no desired fragmentation, and led solely to recovery of the unreacted starting materials **4.59** (92%) and **4.60** (89%) (Scheme 4.24). These reactions suggested that stabilisation from mono-ester and sulfone is not enough to provide successful reaction.



Scheme 4.24

4.6 C-C bond fragmentation of β-ketoester

Moving from malonate esters, it was now planned to extend these cleavages to other similar stabilising groups. Firstly, β-ketoester substrate **4.68** was planned and it was prepared easily by treating ethyl 2-methylacetoacetate **4.70** and 1-(bromomethyl)-4-(*t*-butyl)benzene **4.69** with sodium hydride. When this substrate **4.68** was submitted to the normal photoactivation conditions using the donor **1.249**, it provided a diferent outcome. β-ketoester substrate **4.68** did not show any benzylic C-C bond fragmentation, but the acyl group of the ketone was fragmented and afforded **4.71** in good yield (55%) along with reisolation of starting material **4.68** (36%) (Scheme 4.25).



Scheme 4.25

This fragmentation of the acyl group suggested that electron transfer to the ketone group of the β-ketoester had occurred preferentially, unlike the other substrates where electron transfered to arene group had prevailed. Spartan calculations (B3LYP 6-31G*, modeled in a DMF solvent continuum) revealed that most of the LUMO lies on the β-ketoester region of the molecule **4.68a** (Fig. 4.2) and supports the observed acyl fragmentation.

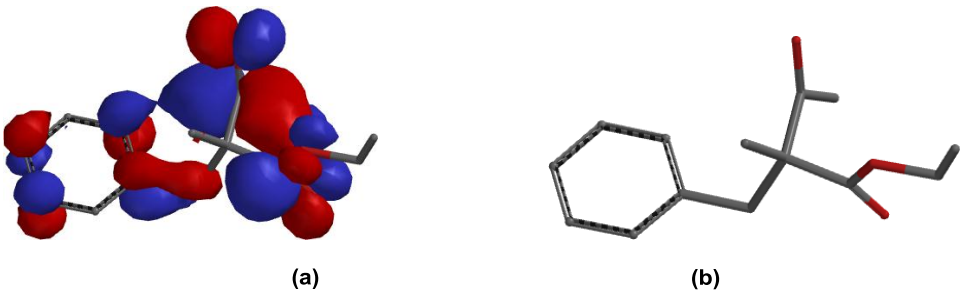
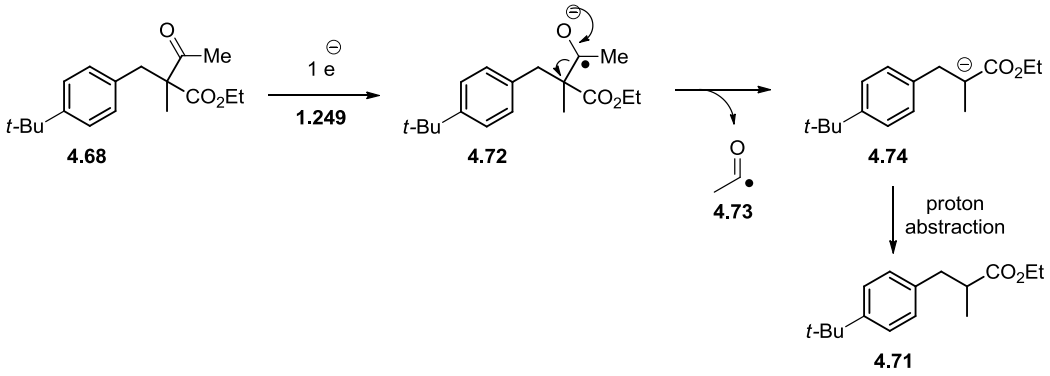


Figure 4.2: **(a)** Represents the LUMO of β-ketoester **4.68a** and **(b)** represents the molecule alignment of the LUMO of the same molecule, for a better understanding [hydrogen atoms are omitted for clarity in both **(a)** and **(b)**].

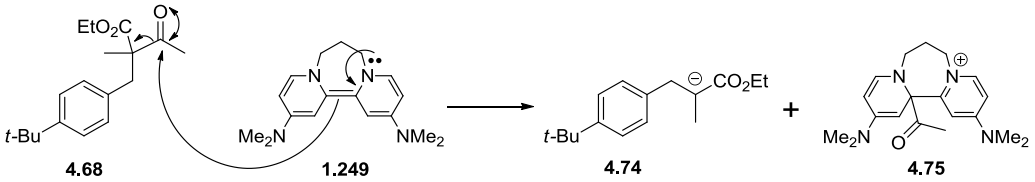
The proposed mechanism for this acyl cleavage is shown in Scheme 4.26.



Scheme 4.26

Donor **1.249** pumps an electron into the ketone group of β-ketoester substrate **4.68** and generates ketyl radical anion **4.72**. This ketyl radical-anion **4.72** undergoes acyl group fragmentation to afford anion **4.74** and acyl radical **4.73**. Anion **4.74**, upon work-up, abstracts a proton and provides final product **4.71**.

However, the nucleophilic attack of the donor **1.249** onto the carbonyl centre of ketone could also afford liberation of same anion **4.74**. This anion **4.74**, upon abstraction of proton, could provide the same final product **4.71** (Scheme 4.27).

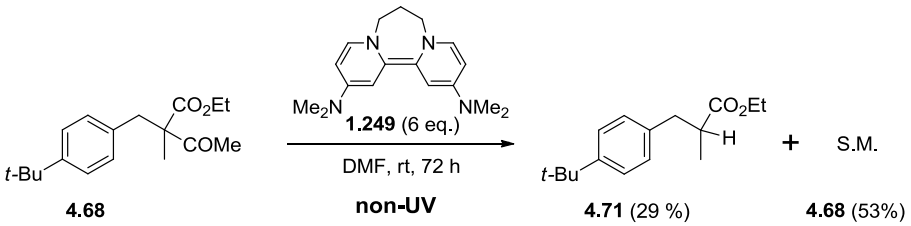


Scheme 4.27

Therefore, it is important to identify the correct process *i.e.* either electron transfer from the photoactivated donor **1.249** or nucleophilic attack of the donor **1.249** that result in the above fragamentation. So, the reaction was now repeated but under non-UV conditions. If this reaction provided no fragmentation, this would completely rule out the argument of fragmentation via nucleophilic effect of the donor **1.249** and would support fragamentation through electron transfer process.

β-ketoester substrate **4.68** has treated with the donor **1.249** under non-UV conditions and provided a comparatively lower yield (29%) of fragmentation product **4.71** than in the UV-activated reaction (55%) (Scheme 4.28). The non-UV reactions carried out earlier with malonate substrates **4.53** and ***cis*-4.24** showed no reaction and led to complete

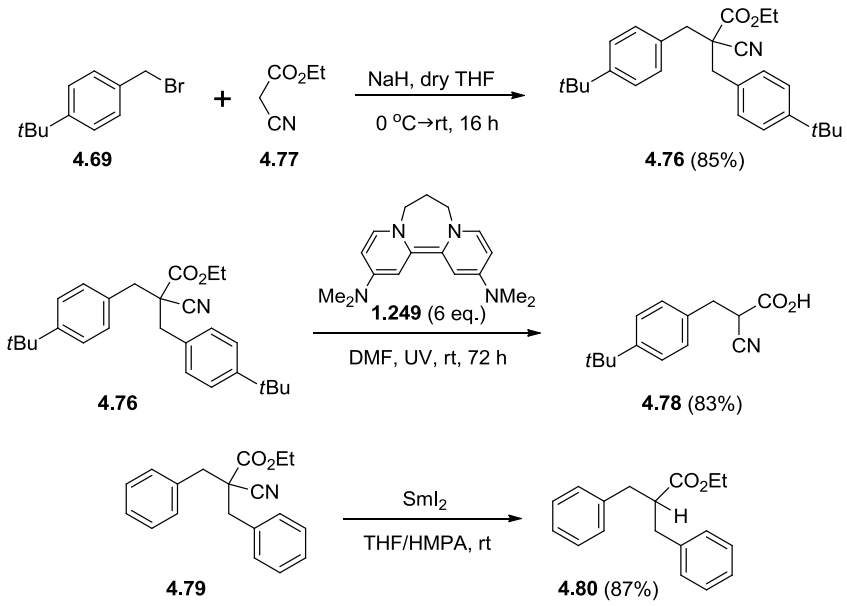
recovery of the starting materials. So, it may suggest that the observed fragmentation with the β-ketoester substrate **4.68**, under non-UV conditions, may arise by the nucleophilic attack of the donor **1.249** onto the ketone group in **4.68**. But, it should be kept in mind that both the malonate and β-ketoester substrates are quite different in their reactivities and so, it may be possible for the β-ketoester substrate **4.68** to undergo electron-transfer under non-UV conditions and determination of this is left to future endeavours. However, this experiment clearly supports the enhanced acyl fragmentation yields, under UV-active conditions, arising through an electron-transfer process.



Scheme 4.28

4.7 Benzylic C-C bond cleavage of cyanoacetates and malononitriles

Later, it was planned to test the cyanoester substrate **4.76** under the normal photoactivation conditions. Cyanoester **4.76** was prepared in a single step by treating ethyl 2-cyanoacetate **4.77** and 4-(*t*-butyl)benzyl bromide **4.69** with sodium hydride (Scheme 4.29).

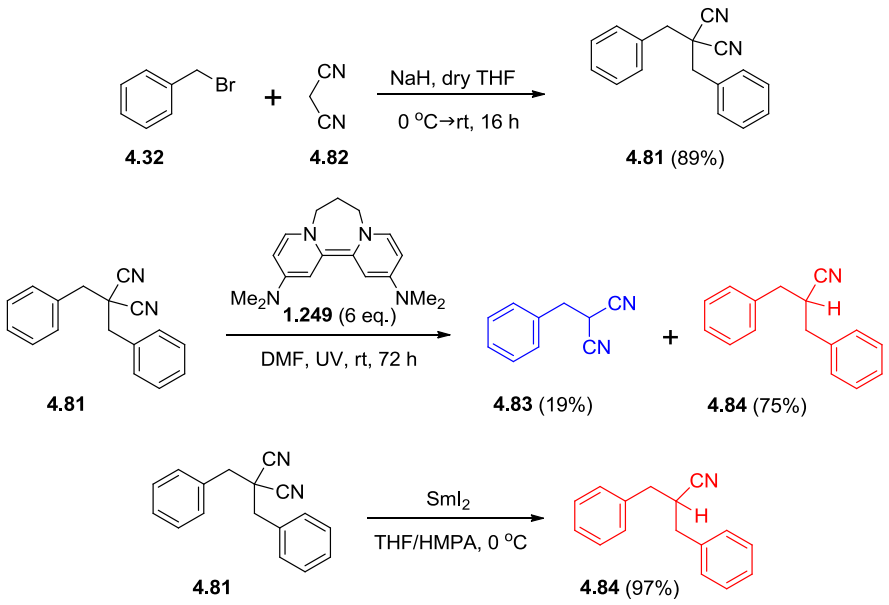


Scheme 4.29

When cyanoester **4.76** was subjected to photoactivation of the donor **1.249** (6 eq.) for 72 h at room temperature, it afforded the expected benzylic C-C bond cleavage and provided cyanoacid **4.78** in good yield (83%) (Scheme 4.29).

It was again seen that the ester group in **4.76** converted to a carboxylic acid group under the usual work-up conditions. However, when a similar cyanoester **4.79** had been treated with samarium diiodide, unlike organic electron donor **1.249**, it had afforded a decyanation reaction and had provided ester **4.80**.[174] These reactions showed that metal-based reducing agents (for *e.g.* SmI_2) and non-metal (organic electron donor **1.249**) reducing agents have completely different reactivities towards the identical substrates. The reaction of **4.76** with the donor **1.249** also emphasises the selectivity of the organic electron donors in transferring an electron into an arene group over a cyanoester group, which generally get reduced using metallic reagents.

Later, it was planned to test malononitrile (*gem*-dicyano) substrate **4.81** under the normal photoactivation conditions. Substrate **4.81** was prepared in a single step by treating malononitrile **4.82** and benzyl bromide **4.32** with sodium hydride.



Scheme 4.30

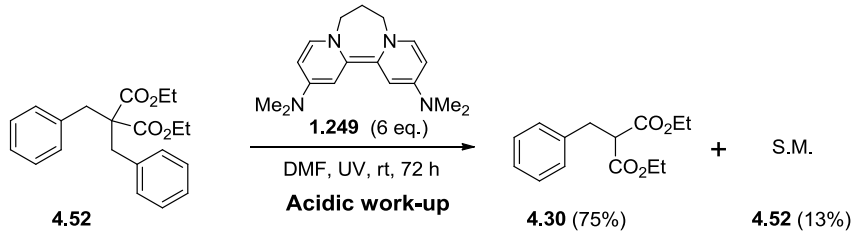
When *gem*-dicyano substrate **4.81** was subjected to photoactivation of the donor **1.249** (6 eq.) for 72 h at room temperature, in addition to the expected benzylic C-C bond cleavage, it also provided a decyanation reaction. The major product (75%) is 2-benzyl-3-

phenylpropanenitrile **4.84** arising from a decyanation reaction, while the minor product (19%) is 2-benzylmalononitrile **4.83** arising from the benzylic C-C bond cleavage. This unexpected decyanation was studied fully afterwards and will be discussed in the next chapter. However, the same substrate **4.81** had undergone complete and selective decyanation to afford **4.84**, upon treating with SmI_2[174] (Scheme 4.30). This is another example that identifies the different reactivities of metal-based reagents and organic electron donors.

4.8 Addressing the conversion of ester group to carboxylic acid

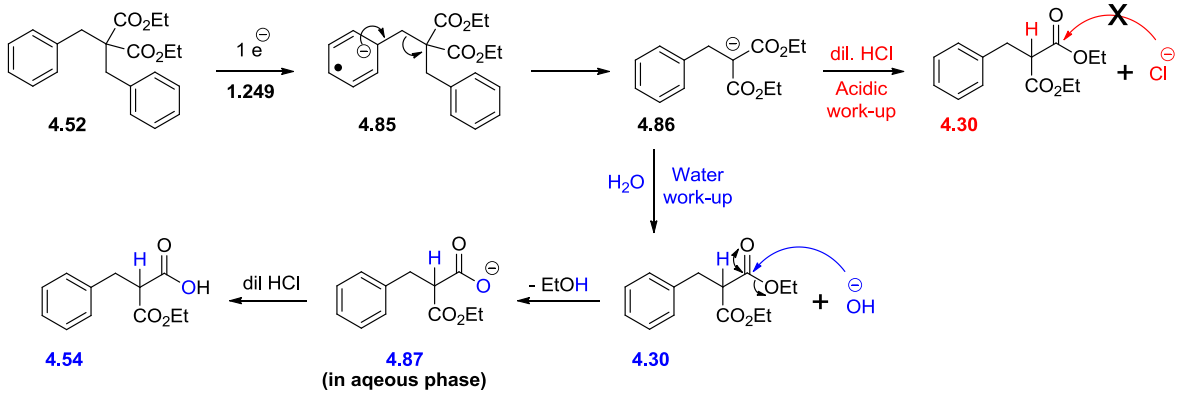
It was reported above that one of the ester groups in diethyl malonate substrates and the ester group in cyanoester substrates was converted to a carboxylic acid in the fragmented products. However, *t*-butyl ester groups in *t*-butyl malonate substrates and ester groups in unreacted diethyl malonate substrates were preserved without being converted into acid groups. The work-up process for all these reactions was the same and involved the quenching of the reaction mixture with water first, and then acid work-up of the aqueous phase with dil. HCl (1N). Initially, conversion of ester group to acid was ascribed to hydrolysis of fragmented products, which can occur during the course of the reaction or during the work-up process. To address this conversion of ester to acid, it was planned to change the work-up process a little, to involve direct quenching of the reaction mixture with dil. HCl (1N).

Substrate **4.52** was tested again using the same reaction conditions that were used earlier. At the end of the reaction, the reaction mixture was quenched with dil HCl (1N) and the remaining work-up process was followed as usual. The repeated reaction, under changed work-up conditions, provided diester product **4.30** in good yield and no conversion of one of the ester groups to acid was seen (Scheme 4.31).



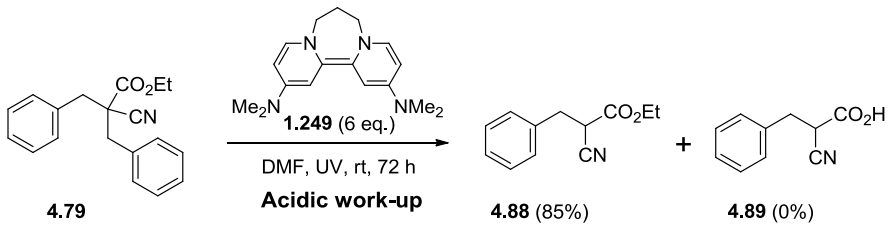
Scheme 4.31

From the above result, it is clear that the conversion of ester to acid is assisted by the water work-up of the reaction mixture and it can be easily explained as follows. Substrate **4.52** generates malonate anion intermediate **4.86** after the successful benzyl C-C bond cleavage. Upon water work-up, 1 mole of the anion **4.86** gets protontated and forms diester product **4.30** (shown in blue) along with 1 mole of hydroxide anion. As hydroxide anion is a strong nucleophile, it can attack one of the ester groups and converts it into carboxylic acid group. As 1 mole of hydroxide anion only generated in the previous step, it can only convert one of the ester groups, providing monoester monoacid product **4.54**. However, in case of *t*-butyl malonate substrates, due to steric factors, hydroxide anion cannot approach the carbonyl site of the *t*-butyl ester groups so easily and therefore no conversion of *t*-butyl ester to acid is seen. During acidic work-up of the reaction mixture with dil. HCl, 1 mole of malonate anion intermediate gets protonated to form diester **4.30** (shown in red) along with 1 mole of chloride anion. As chloride anion is a weak nucleophile and as the hydrolysis of these ester groups is slower in acidic conditions than their extraction into organic solvents, no hydrolysis is seen (Scheme 4.32).



Scheme 4.32

Subsequently, dibenzyl cyanoester substrate **4.79** was prepared easily by following the method used for the synthesis of the substrate **4.76** and submitted to normal photoactivtion of the donor **1.249**. After acidic work-up of the reaction mixture, it afforded cyanoester product **4.88** instead of cyanoacid product **4.89**, supporting the above discussion about the conversion of ester groups to acids under alkaline work-up conditions (Scheme 4.33).



Scheme 4.33

4.9 Conclusion

This chapter started with the aim of addressing benzylic C-N bond cleavages using photoactivated organic electron donor **1.249**. It has been found that donor **1.249** can successfully effect the benzylic C-N bond fragmentations at room temperature under photoactivation conditions. Later, it was planned to extend this chemistry to even more challenging benzylic sp^3-C-C σ-bond fragmentations. All the arene substrates derived from diethyl malonates, di-*t*-butyl malonates, cyanoesters and malononitrile groups afforded benzylic C-C fragmentations for the first time using photoactivation of the donor **1.249**. The novel feature of all these cleavages was that the donor **1.249** selectively transfered an electron into the arene ring in the presence of other active electron-accepting groups and showed a new type of selectivity, which had never been observed with metals and metal-complexes in reductive chemistry. On the other hand, the β-ketoester substrate provided acyl fragmentations, which was further supported by Spartan calculations.

It was found that the presence of an arene ring in the molecule was necessary for successful benzylic C-C bond cleavages and non-arene and allylic substrates did not show any fragmentations. These fragmentation reactions worked well for both electron-rich and electron-deficient systems. However, *p*-cyano substrates were special cases in which the electron-withdrawing character of the cyano-group inhibited the electron transfer into the σ* orbital of the benzylic C-C bond and resulted in no cleavage reaction. The cinnamyl substrate provided a homologous cleavage reaction. In a mixed diaryl substrate, an electron was transfered into the arene ring containing the relatively electron-poor substituent and afforded the corresponding benzylic C-C bond fragmentation. It was also found that stabilisation of the anionic intermediate following C-C fragmentation was a key for the success of the reaction and the less stabilised monoester and sulfone substrates did not provide any cleavage reaction. Cyanoester substrates exclusively produced

benzylic C-C bond fragmented products, whereas SmI_2 effected decyanation of the same substrates. This was another reaction that differentiates the reactivities of organic electron donors and metal-based reducing agents towards the same substrates. A malononitrile substrate provided both a benzylic C-C fragmentation and a decyanation reaction.

In all the diethyl malonate derived substrates, one of the ester groups was converted to carboxylic acid and provided monoester monoacid products after successful fragmentation. However, it was found that this conversion of diethyl ester to acid is not a prerequisite of successful fragmentation reactions. Repeated experiments, where the resulting reaction mixture was treated directly with dil. HCl instead of water, produced diester products. Therefore it was confirmed that the conversion of diethyl ester to acid was a result of aqueous non-acidic work-up and this explanation was fully discussed in this chapter.

4.10 Future work

- Photoactivated donor **1.249** mediated benzylic C-N bond cleavages have much potential and can be extended to a number of aryl systems shown in Fig. 4.3.

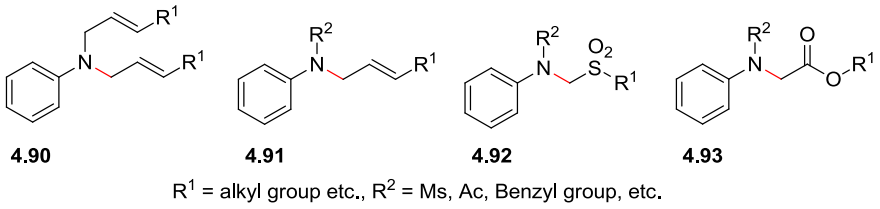
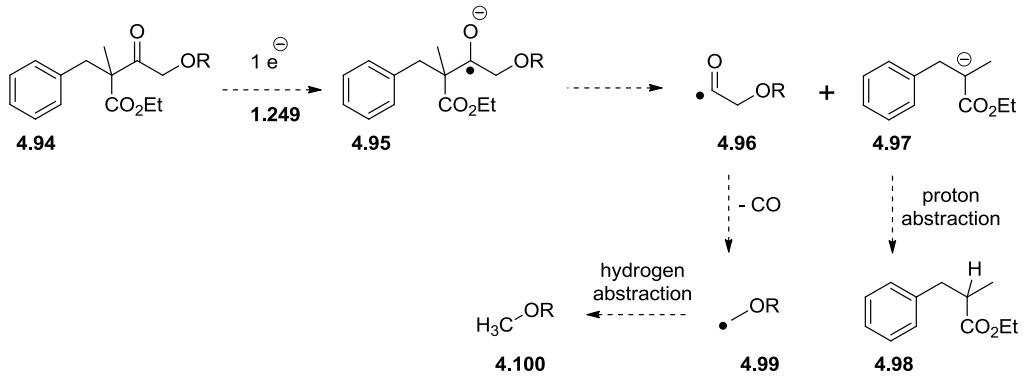


Figure 4.3: Test substrates for aryl N-C bond cleavages

- Further reactions of β-ketoester substrates need to be carried out to rule out the possibility of acyl fragmentation due to nucleophilic attack of donor **1.249** onto the carbonyl group. Therefore, substrate **4.94** is proposed and the expected reactivity under photoactivation of the donor **1.249** is shown in Scheme 4.34. Loss of CO from acyl radical **4.96** leads to alkoxyalkyl radical **4.99** and some latest evidence in our group suggests that alkyl radicals of this type may not be trapped by the radical-cation of the donor, **1.249a**.


O
OR
CO2Et
1 e
1.249
4.94
4.95
4.96
4.97
- CO
proton
abstraction
hydrogen
abstraction
H3C
4.100
4.99
4.98

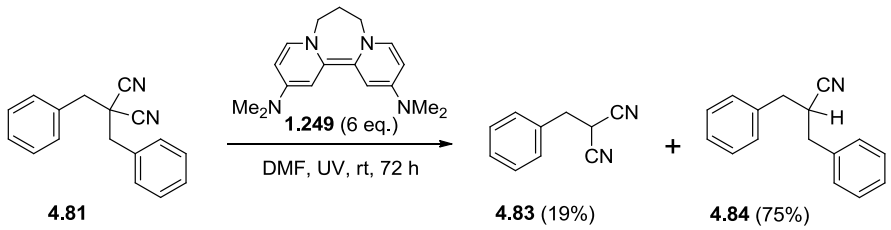
Scheme 4

5 Reductive Decyanation of Malononitriles and Cyanoacetates

5.1 Introduction

Malononitriles have useful applications in both ionic[193] and radical[172,194] reactions. But, they are much less popular intermediates in organic synthesis than their close cousins malonic esters, acetoacetates, sulfonyl esters and acetates. This is partly because of the greater difficulty in removing the extra functional group in malononitriles (a nitrile) than removal of a corresponding group (carboxyl or sulfonyl) in its relatives.[173] Therefore, the discovery of mild and general reductive routes for removal of a nitrile would encourage synthetic applications of malononitriles in organic chemistry. There have been reports of reductive decyanation of malononitriles using tributyltin hydride under reflux in benzene[173] and SmI_2/HMPA.[174] However, these methods required toxic metals and carcinogenic solvents, which have drastic effects on life and on the environment. So, there is a need for milder and more environmentally benign procedures to reduce malononitriles.

During our studies on benzylic C-C bond fragmentations, we accidentally found the decyanation of malononitrile substrate **4.81** to provide mono-nitrile **4.84** as the major product, under our usual reaction conditions *i.e.* photoactivation of the donor **1.249** for 72 h at room temperature.

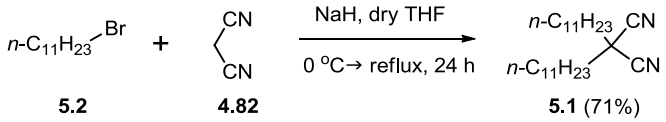


Scheme 5.1

At first, it was thought that the nucleophilic nature of the donor **1.249**[100] was playing a role in the decyanation of the substrate **4.81**. However, the reductive methods described for decyanation of malononitriles prompted us to study these reactions further with donors.

5.2 Decyanation of malononitriles

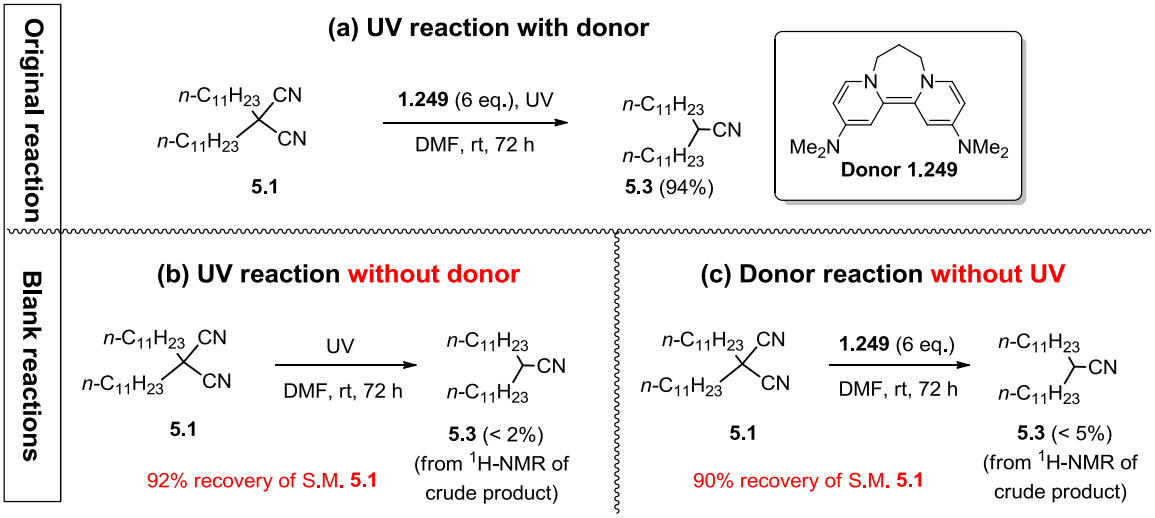
Decyanation of substrate **4.81** suggested a direct electron transfer from the donor **1.249** into the nitrile goups instead of into the arene ring. So, it was planned to test dialkyl malononitrile substrates rather than the usual aryl substrates to understand the decyanation process with donor **1.249**. Dialkyl malononitrile substrate **5.1** was prepared easily by treating malononitrile **4.82** and 1-bromoundecane **5.2** with sodium hydride (Scheme 5.2).



5.2 **4.82** **5.1** (71%)

Scheme 5.2

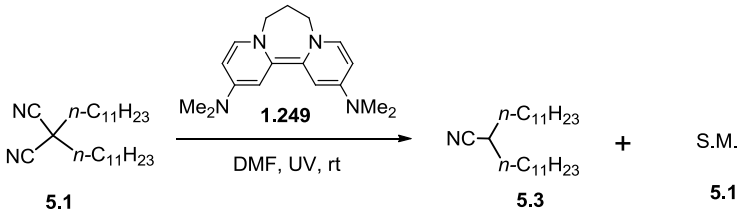
The first important thing to confirm is that the decyanation, if it occurs again with substrate **5.1**, is happening via an electron-transfer process. Secondly, it needs to be proved that both photoactivation of the substrate by itself and the basic nature of the donor **1.249** have no role in the success of the reaction. So, a set of three reactions were planned, which could answer the above questions; **(a)** an original reaction to be carried out using photoactivation of the donor **1.249**, **(b)** a blank reaction to be carried out under photoactivation conditions in the absence of the donor **1.249** and **(c)** a blank reaction to be performed using the donor **1.249** without photoactivation. The plan was to carry out all the three reactions simultaneously for the same amount of time.



Scheme 5.3

Both the original and blank reactions were done as per conditions mentioned in Scheme 5.3. To our delight, after following the normal water work-up of the reaction mixture, the original reaction provided mononitrile product **5.3** in excellent yield (94%) and starting material **5.1** was completely consumed. On the other hand, the blank reactions provided excellent recovery of starting material **5.1** [92% and 90% for **(b)** and **(c)** respectively] along with very poor conversion [<2% and <5% for **(b)** and **(c)** respectively] of starting material **5.1** to products (Scheme 5.3). No attempt was made to isolate products from the blank reactions. If photoactivation of the substrate has a role in the success of the reaction, blank reaction **(b)** should have provided a good yield of product **5.3**. Similarly, if the basic nature of the donor **1.249** plays an important role, blank reaction **(c)** should have given excellent yield of mononitrile product **5.3**. Therefore, the above reactions support the electron-transfer-mediated decyanation reaction with the donor **1.249** under photoactivation conditions. These reactions also confirm that cyano groups are the reactive sites and confirm that the decyanation reaction observed in dibenzylmalononitrile **4.81** was due to direct electron transfer into the cyano groups instead of into the arene ring.

Following these results, it was planned to optimise the reaction conditions to establish whether milder reaction conditions might also ensure a complete decyanation reaction. Substrate **5.1** was treated with donor **1.249** under various conditions and the results are shown in Scheme 5.4 and Table 5.1.



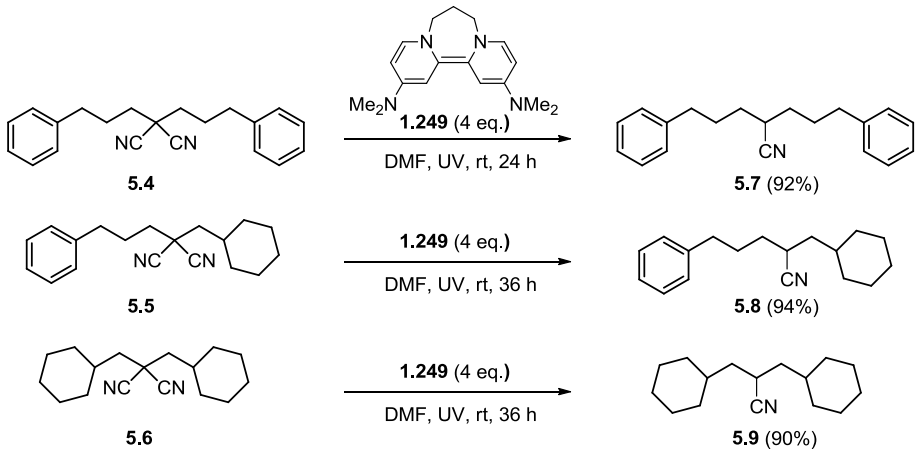
Scheme 5.4

Experiment	**1.249** (eq.)	Time (h)	Ratio of **5.3**/**5.1** in the crude product	Isolated yield of **5.3**
i	4	48	100/0	---
ii	4	24	89/11	---
iii	4	36	100/0	92%

Table 5.1: Optimisation of reaction conditions for decyanation of malononitriles

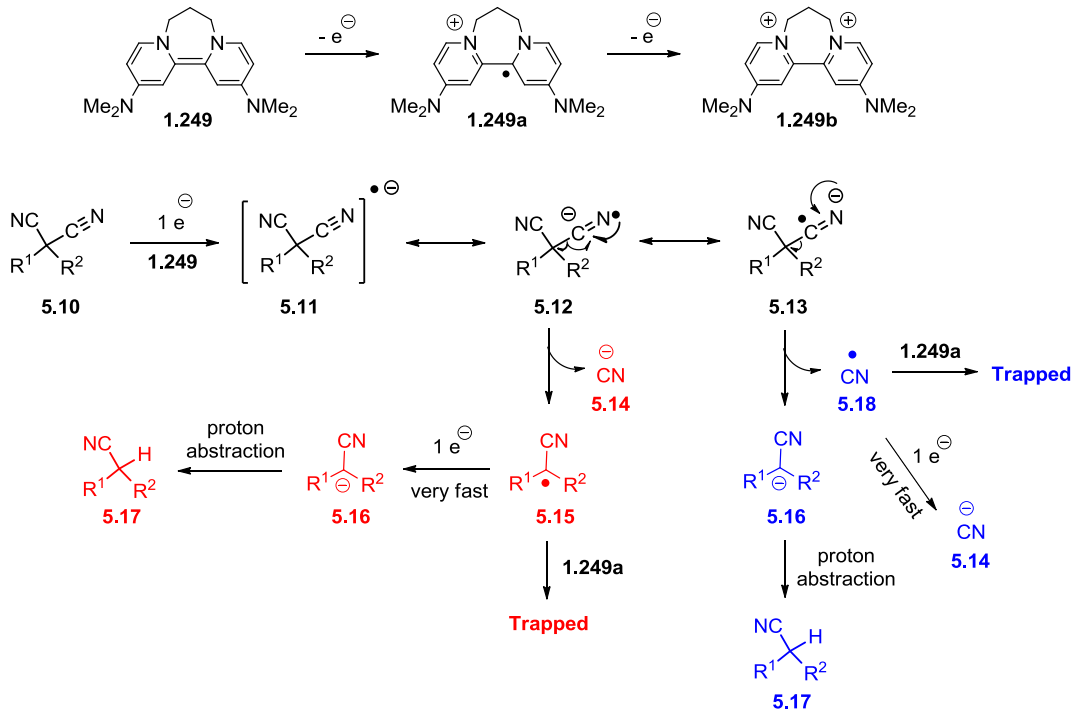
No attempt was made to purify the crude products from experiments **(i)** and **(ii)**. The crude product from experiment **(iii)** was purified and afforded an excellent yield (92%) of mononitrile product **5.3** (Table 5.1).

Later a series of substrates **5.4**-**5.6** was prepared and subjected to photoactivation of the donor **1.249**. All these reactions worked very well and provided mononitrile products in excellent yields as stated in Scheme 5.5. In all these reactions, starting materials were completely consumed.



Scheme 5.5

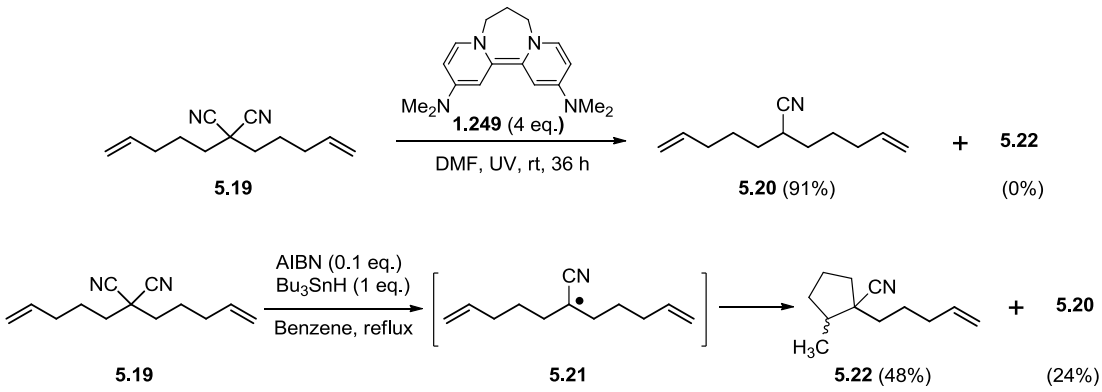
A plausible mechanism for the decyanation reaction is shown in Scheme 5.6.



Scheme 5.6

Donor **1.249** can donate an electron to malononitrile substrate **5.10** to form the radical anion of substrate **5.11** and the radical-cation of the donor, **1.249a**. Now, the radical-anion **5.11** can fragment in two ways *i.e.* at **5.12** to afford cyanide anion **5.14** and mononitrile alkyl radical **5.15** (red pathway) or at **5.13** to afford cyano radical **5.18** and mononitrile alkyl anion **5.16** (blue pathway). In the red pathway, the mononitrile alkyl radical **5.15**, similar to other cleavage reactions discussed in this thesis, can be trapped by the radical-cation of the donor **1.249a** or it can quickly take a second electron from **1.249** or **1.249a** and is converted to mononitrile alkyl anion **5.16**. On the other hand, if the reaction proceeds through the blue pathway, it provides mononitrile alkyl anion **5.16** directly and the formed cyano radical **5.18** may be trapped by **1.249a** or reduced further to cyanide anion **5.14**. Mononitrile alkyl anion **5.16** formed from either route (red or blue pathways), upon proton abstraction, provides mononitrile product **5.17** (Scheme 5.6).

Later, substrate **5.19** featuring suitably placed alkene groups was planned and prepared. Presence of mononitrile alkyl radical intermediate **5.15** can be expressed via radical cyclisation onto the alkene group.

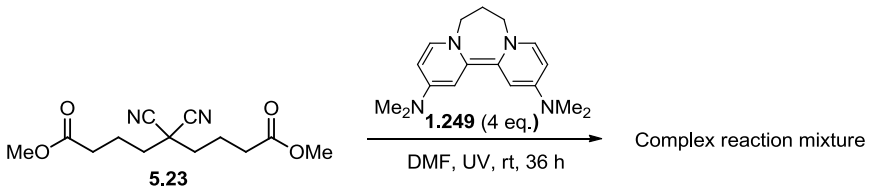


Scheme 5.7

Substrate **5.19** was then submitted to reaction with photoactivated of the donor **1.249** (4 eq.) for 36 h at room temperature and provided uncyclised mononitrile product **5.20** in excellent yield (91%). None of the cyclized product **5.22** was obtained. However, Curran *et al.*[173] observed both cyclised **5.22** (48%) and uncyclised **5.20** (24%) products with the same substrate **5.19** using tributyltin hydride (Scheme 5.7). They identified cyanoalkyl radicals such as **5.21** as intermediates. As no cyclized product **5.22** was obtained in our case, it is most likely that cyanoalkyl anions such as **5.16** are the possible intermediates. However this doesnot distinguish between the two fragmentation pathways as the

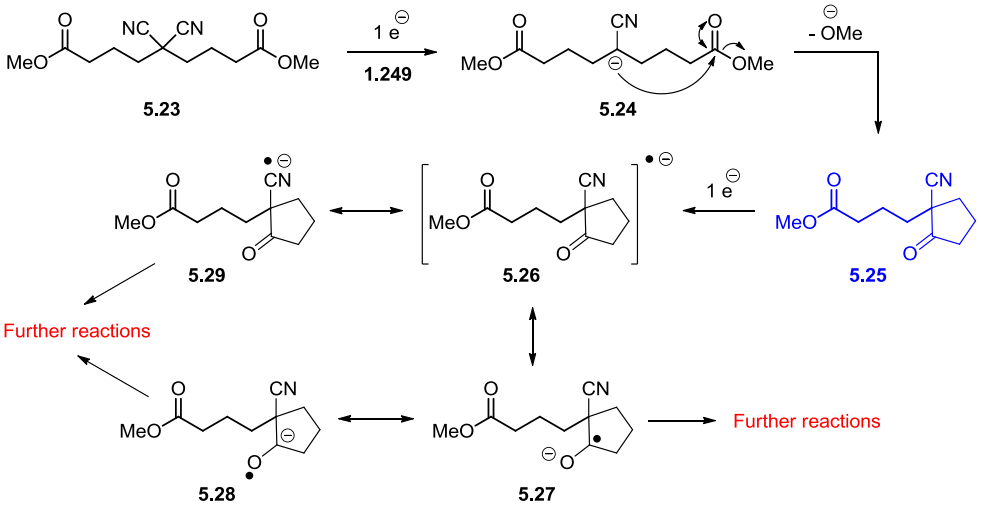
cyanoalkyl radicals such as **5.15** could receive a second electron from the donor **1.249** or **1.249a** faster than radical cyclisation onto alkene group or radical trapping by **1.249a**, converting them into cyanoalkyl anions such as **5.16**.

Later, substrate **5.23**, containing suitably placed ester group was planned and prepared to trap the cyanoalkyl anionic intermediates that were formed after fragmentaion. However, when the substrate **5.23** was submitted to reaction involving photoactivation of the donor **1.249** (4 eq.) for 36 h, all the stating material **5.23** was consumed and it provided a very complex outcome for the reaction (Scheme 5.8).



Scheme 5.8

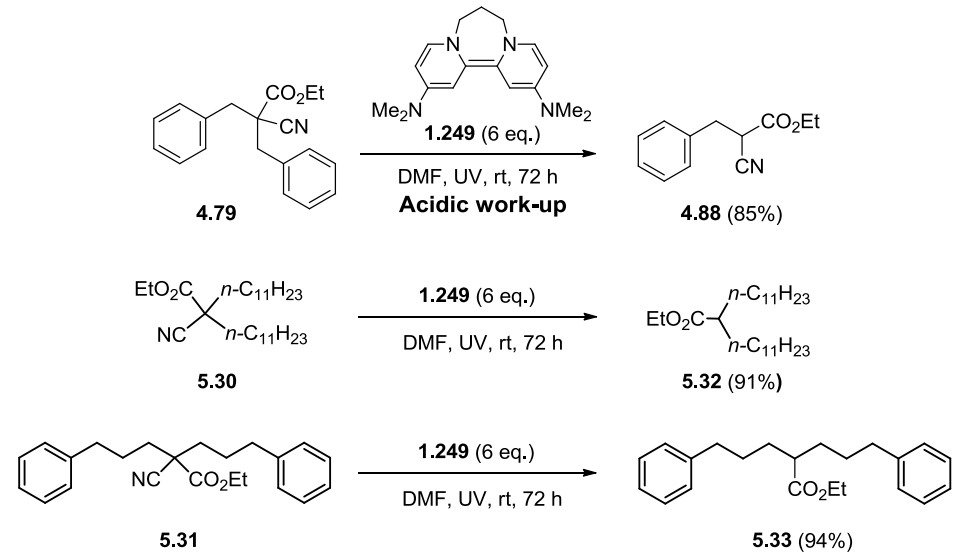
This result is not completely surprising and can be explained as below. Substrate **5.23** forms anionic intermediate **5.24** upon single-electron-transfer from the donor **1.249** followed by fragmentation. This anion **5.24** undergoes cyclisation onto an ester group and forms cylised, β-ketocyano product **5.25**. If this β-ketocyano product **5.25**, similar to a β-ketoester substrate in C-C bond fragmentations (chapter 4), receives another electron from the donor **1.249** or radical-cation of the donor **1.249a**, it forms radical-anion of **5.25**, which can undergo a number of other reactions and leads to a very complex outcome for the reaction.



Scheme 5.9

5.3 Decyanation of cyanoacetates

It was now planned to extend the above decyanation reactions to cyanoacetate ester substrates. Decyantion of cyanoacetates did not work with tributyltin hydride[173] but worked well using SmI_2.[174] However, dibenzyl cyanoester **4.79**, submitted earlier to photoactivated donor **1.249** (in benzylic C-C bond cleavages, chapter 4) had provided exclusive benzylic C-C bond fragmentation. So, to avoid possible benzylic C-C bond fragmentation, it was now planned to prepare dialkyl and extended arene substrates **5.30** and **5.31** respectively to test for decyanation reactions using the donor **1.249**.



Scheme 5.10

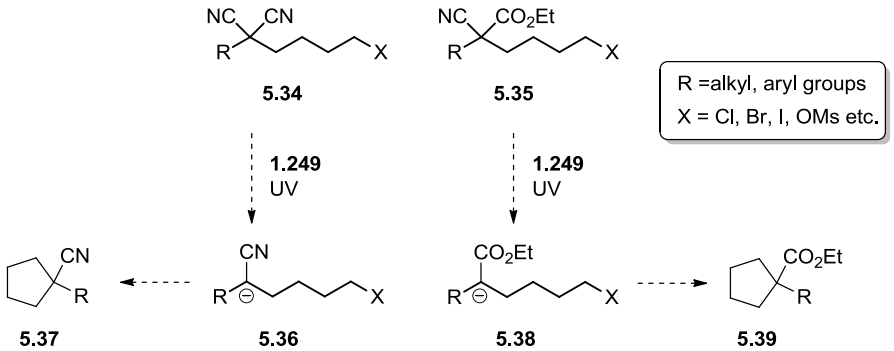
Substrates **5.30** and **5.31** were prepared and then submitted to photoactivation of the donor **1.249** (6 eq.) for 72 h at room temperature and provided excellent yields of decyanation products *i.e.* esters **5.32** (91%) and **5.33** (94%) respectively (Scheme 5.10). The mechanism that is proposed for the decyanation in cyanoacetates is similar to the malononitrile substrates. Decyanation of cyanoacetates is more difficult than for malononitriles as seen in the use of higher amounts of donor **1.249** (6 eq.) and in extended photoactivation times (72 h) for getting complete reaction. This might be due to less stabilisation of ester enolate intermediates arising from cyanoacetates compared with the cyanoalkyl anion arising from malononitrile substrates.[173]

5.4 Conclusion

Reductive decyanation of various malononitriles and cyanoacetates was successfully achieved with the photoactivated donor **1.249** at room temperature and provided an alternative to the traditional methods involving toxic metals and carcinogenic solvents. It was found that decyanation of malononitriles was faster than that of cyanoacetates and required lower loadings of the donor **1.249**. The reactive site for these reactions is found to be the malononitrile or cyanoacetate group and so, a wide range of substrates can be reduced in excellent yields using donor **1.249**. Reaction of malonate substrate **5.19** featuring suitably placed alkene did not provide any cyclised product **5.22** via radical cyclisation onto alkene and suggests rapid formation of anionic intermediates. However, substrate **5.23** designed to witness anionic cyclisation provided a very complex reaction, which can be understood as a result of further reactions of the cyclised intermediate, β-ketocyano product, **5.25**.

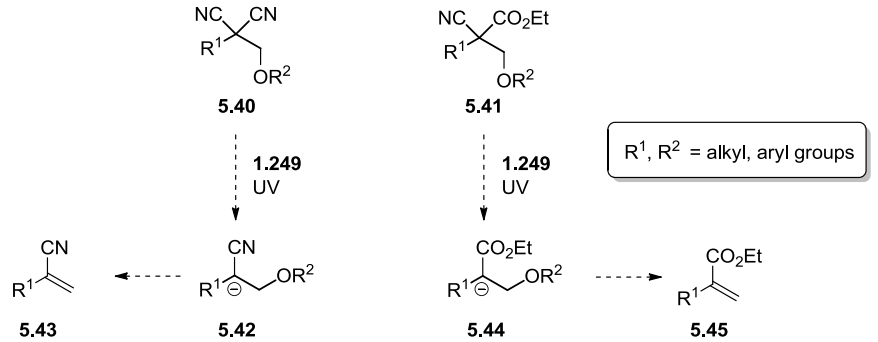
5.5 Future work

- It was found that trapping of the anionic intermediates from the reaction of malononitrile ester substrate **5.23** with the donor **1.249** led to a complex reaction due to the presence of a β-ketocyano group, a potential electron acceptor, in the cyclized product. Therefore, testing of substrates **5.34** and **5.35**, containing potential leaving groups (Cl, Br, I, OMs) instead of ester groups, may provide trapping of anionic intermediates (Scheme 5.11). However, the relative reactivity of the nitrile group and potential leaving groups to electron-transfer will need to be determined.



Scheme 5.11

- Similarly, the presence of anionic intermediates can be expressed via elimination of β−alkoxide groups in substrates **5.40** and **5.41** to generate valuable acrylonitriles **5.43** and α,β-unsaturated esters **5.45**, respectively (Scheme 5.12).



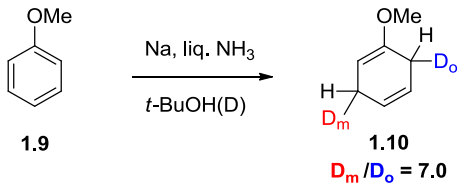
Scheme 5.12

- Very recently, Stephenson *et al*. reported the use of visible light for the generation of free radicals from unactivated alkyl, alkenyl and ary iodides using photoredox chemistry.[102] So it would be interesting to test our decyanation processes under activation by visible light or LED light sources. Indeed, all of our electron-transfer reactions using UV could also be tested with visible light or LED light.

6 Insight into Birch Reductions: Regioselective ArO-C Bond Fission of *ortho*-Dialkoxy-benzenes

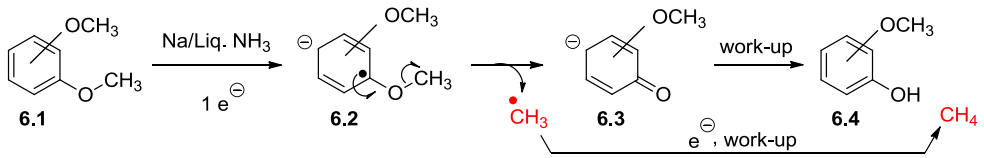
6.1 Introduction

Birch reduction[4-6] is one of the most well recognised reactions using alkali metals in liquid ammonia and was discovered in 1940's by Arthur J. Birch. It is an elegant and simple method to access dihydro-counterparts from benzenes and benzene-derived compounds. There had been debate over the decades about the detailed ordering of steps in the mechanism of this reduction. With Birch continuing to support *meta* protonation until the early 1990's, Zimmerman and Wang[12,13] devised an experiment using deuterated and non-deuterated alcohols that demonstrated the *ortho* protonation mechanism predominated in the reduction of anisole (Scheme 6.1). These studies were well discussed in the Introduction of this thesis.



Scheme 6.1

Very recently, Zimmerman published a mechanistic analysis of the Birch reductions, in which he briefly discussed the regioselectivity of O-C bond fission in dimethoxybenzenes.[195-197] He proposed that radical-anion **6.2** underwent O-C bond fission to liberate a methyl radical (shown in red) (Scheme 6.2).

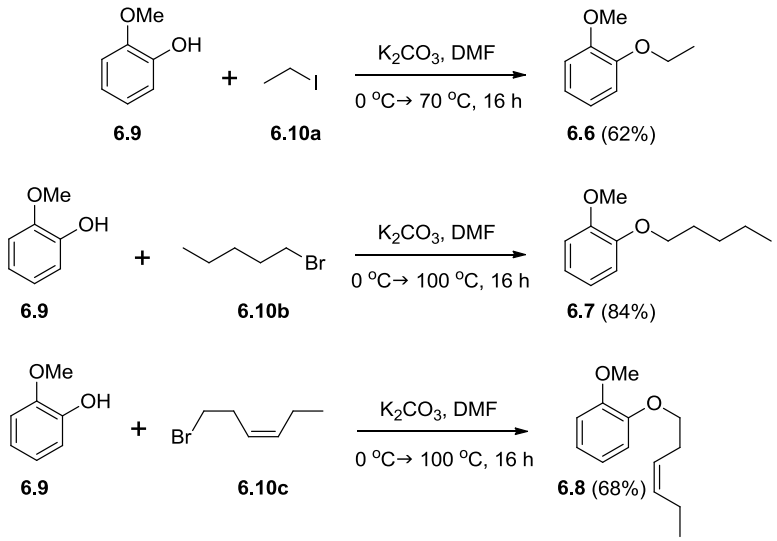


Scheme 6.2

Liberation of methyl radicals is not that common and it is interesting that the loss of methyl radical (shown red) happened in preference to methyl carbanion (methyl carbanion will be liberated, if anion of **6.2** participates in ArO-C fission). So, it was planned to investigate these ArO-C fragmentations more closely under Birch conditions.

6.2 Regioselective ArO-C bond fission of *ortho*-dialkoxybenzenes

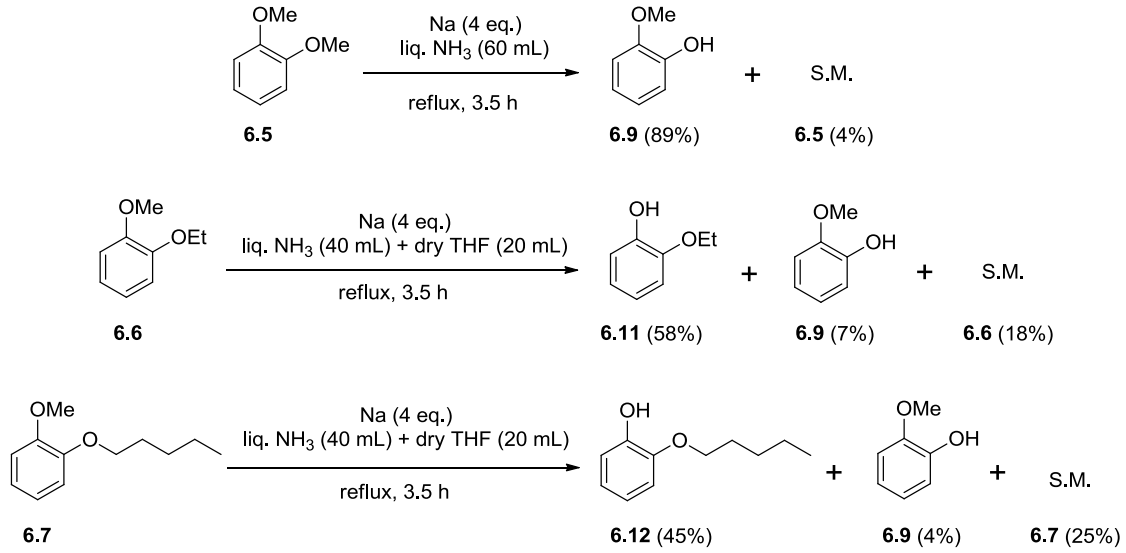
Both Birch[196] and Bunnett[197] found that the reactivity of ArO-C bond cleavages of three dimethoxybenzenes were in the order of *ortho* > *meta* >> *para*. So, *ortho*-dialkoxybenzene substrates were selected for our work to test these cleavages. A series of dialkoxybenzene substrates **6.6**-**6.8** was prepared easily in good yields by treating precursor alcohol **6.9** and alkyl halides **6.10a-c** with K_2CO_3 in DMF (Scheme 6.3).



Scheme 6.3

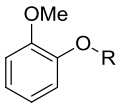
The dialkoxybenzenes **6.5**-**6.7** were then tested under Birch conditions by following the method described by Bunnett[197] (Scheme 6.4). Substrate **6.5** was completely soluble in liq. ammonia (60 mL), while substrates **6.6** and **6.7** were partly soluble in liq. ammonia. So, dry THF (20 mL) was added to the resulting reaction mixtures in liq. ammonia (40 mL) for substrates **6.6** and **6.7** to dissolve insoluble starting materials.[197] Addition of THF provided a clear solution in the case of **6.6** but, there was still some insoluble starting material left in the case of **6.7**. Later, freshly cut sodium (4 eq.) was added to all the reactions and the resulting reaction mixtures were left stirring at reflux conditions for 3.5 h. Following the general work-up process described by Bunnett,[197] substrate **6.5** provided

the ArO-Me cleavage product **6.9** (89%) in excellent yield along with recovery of the starting material **6.5** (4%). However, substrates **6.6** and **6.7** provided lower yields of cleavage products compared with **6.5** and also provided largely ArO-Me cleavages in preference to ArO-Et or ArO-*n*-C_5H_{11} cleavages respectively (Scheme 6.4).



Scheme 6.4

The ease of removal of methyl group in preference to ethyl and *n*-pentyl groups in **6.6** and **6.7** respectively is completely consistent with Birch's findings,[196] and perhaps due to the less destabilized anion in the case of methyl *vs*. ethyl/*n*-pentyl. He found that the more stabilised was the negative charge on the leaving alkyl group, the greater was its ease of formation. Birch's observations are shown in Fig. 6.1.



6.13

Ease of cleavage of R being in the order CH_2Ph, CH_2CO_2H > CH_3 > *n*-C_3H_7, *iso*-C_3H_7

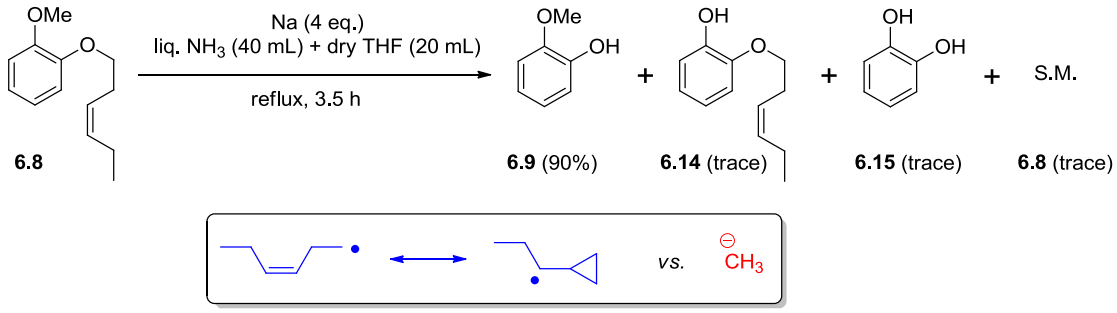
Figure 6.1 The relative ease of removal of alkyl groups from substrate **6.13**, as described by Birch.[196]

In substrates **6.6** and **6.7**, demethylation occurred as the major reaction and this suggests that a methyl anion is expelled instead of a methyl radical. If the substrate has to expel the methyl group as a methyl radical, it should provide demethylation as the minor product, as alkyl radicals are more stable than methyl radical, unless kinetic factors impede this (Fig. 6.2).

6.6, R = ethyl
6.7, R = *n*-pentyl

Figure 6.2 Relative stabilities of methyl and alkyl groups R as anions and radicals.

Susbtrate **6.8** was then submitted to the same Birch reaction conditions and provided dealkylation product **6.9** as a major product and only trace amounts of the demethylation product **6.14**, catechol **6.15** and starting material **6.8** were observed from the ^{1}H-NMR of the crude product. In this reaction, as described by Birch,[196] stability of the fragmented species played a major role. And, the observed reactivity might be a result of higher stability of alkyl radical (shown in blue) formed after ArO-C fragmentation over methyl anion (shown in red) (Scheme 6.5).

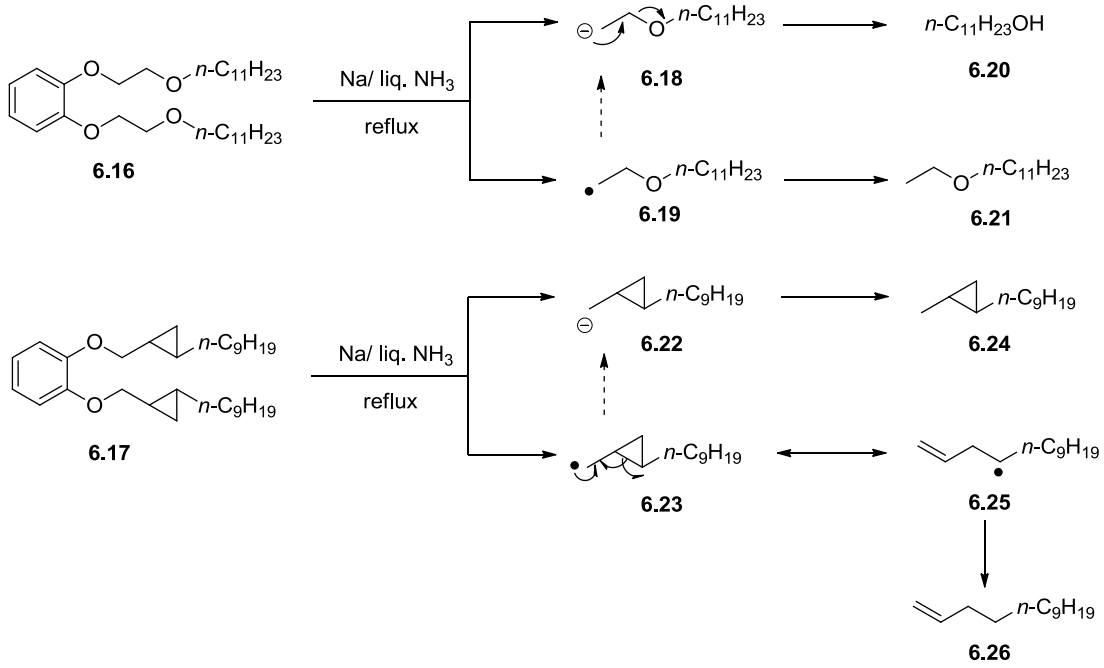


6.8 **6.9** (90%) **6.14** (trace) **6.15** (trace) **6.8** (trace)

Scheme 6.5

To further understand these ArO-C cleavages, substrates **6.16** and **6.17** were designed. The quick outline of expected reactivities of these substrates **6.16** and **6.17** under Birch conditions is discussed below (Scheme 6.6). If the substrate **6.16** undergoes ArO-C cleavage by providing alkyl anion **6.18**, then **6.18** would readily collapse into alkoxide anion that can provide alcohol **6.20** upon work-up. If the substrate **6.16** provides radical intermediate **6.19** after ArO-C cleavage, this radical could quickly take a hydrogen atom and would provide ether product **6.21**. Alternatively, rapid further reduction of **6.19** might afford **6.18**. Similarly, if the substrate **6.17** provides alkyl anion intermediate **6.22** after ArO-C cleavage, it would convert to cyclopropyl product **6.24**, upon work-up. If the substrate **6.17** provides radical intermediate **6.23** after ArO-C cleavage, this radical **6.23** would quickly open the cyclopropane ring and convert to the more stable radical

intermediate **6.25**, which finally would provide **6.26**. Alternatively, rapid further reduction of **6.23** might afford **6.22** (Scheme 6.6).



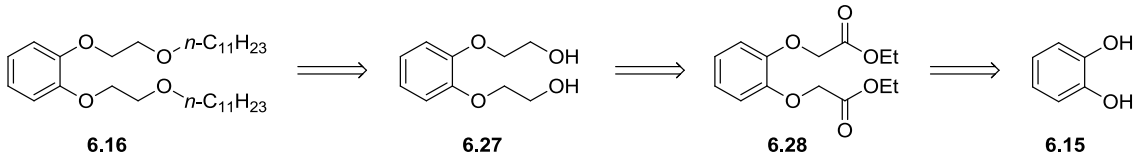
Scheme 6.6

To our best knowledge, there are no literature reports claiming the conversion of alkyl radicals such as **6.19** and **6.23** to the corresponding alkyl anions **6.18** and **6.22** respectively, under Birch conditions. However, the reduction potentials for the aliphatic redicals shown in Table 6.1[198] predict that conversion of alkyl radicals to alkyl anions could be possible under highly reducing Birch conditions.

Radical substrate	E / V *vs.* SCE
Methyl	-1.19
Primary alkyl radicals	-1.57 to -1.62
Dodec-1-yl	-2.12
Secondary alkyl radicals	-1.68 to -1.72
Benzyl	-1.43

Table 6.1: Reduction potentials for aliphatic radicals

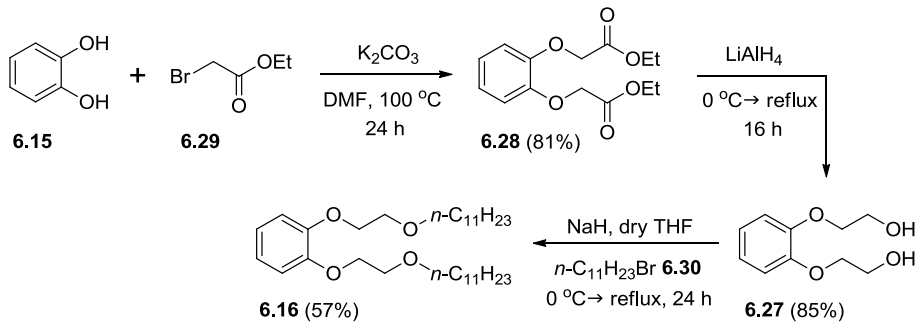
The retrosynthetic route for the substrate **6.16** is shown in Scheme 6.7.



6.16 **6.27** **6.28** **6.15**

Scheme 6.7

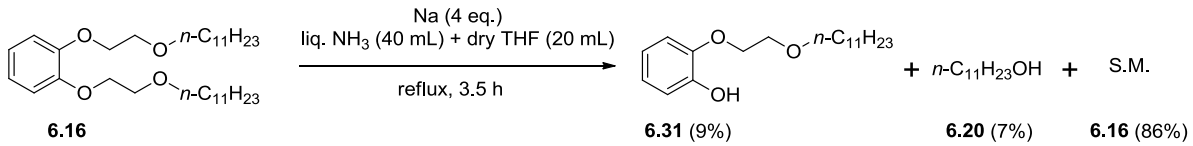
Synthesis of the desired product **6.16** was achieved in a series of steps as shown in Scheme 6.8. Diester **6.28** was prepared in good yield (81%) by treating catechol **6.15** and ethyl 2-bromoacetate **6.29** with K_2CO_3 at 100 ^oC in DMF for 24 h. Then, diester **6.28** was reduced by $LiAlH_4$ and afforded dialcohol **6.27** in good yield (85%). Finally, diol **6.27** and 1-bromoundecane **6.30** were treated with sodium hydride and afforded the desired product **6.16** in good yield (57%) (Scheme 6.8).



6.15 **6.29** **6.28** (81%) **6.16** (57%) **6.27** (85%)

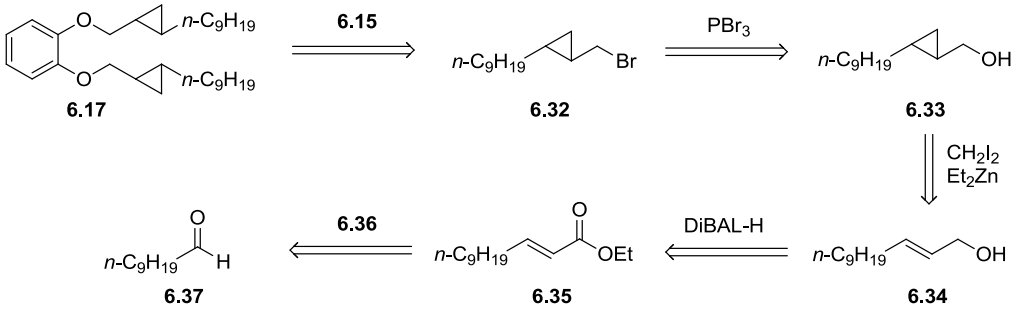
Scheme 6.8

Substrate **6.16** was then submitted to normal Birch conditions. Into a three-neck flask containing liq. NH_3 (40 mL) and equipped with dry ice condenser, substrate **6.16** in dry THF (20 mL) was added under argon gas. The substrate was mostly insoluble in the resulting mixture of liq. NH_3 and dry THF. Then, freshly cut sodium (4 eq.) was added into the flask and the resulting blue solution was refluxed for 3.5 h. After following the general work-up process described by Bunnett,[197] the reaction provided low yields of the expected undecan-1-ol **6.20** (7%) and phenolic product **6.31** (9%) along with the excellent recovery of the starting material **6.16** (86%) (Scheme 6.9). The low yields of ArO-C cleavage products may be partly due to very low solubility of the substrate **6.16**.[196] However, the generation of alcohol **6.20** supports presence of alkyl anion **6.18** after ArO-C cleavage.



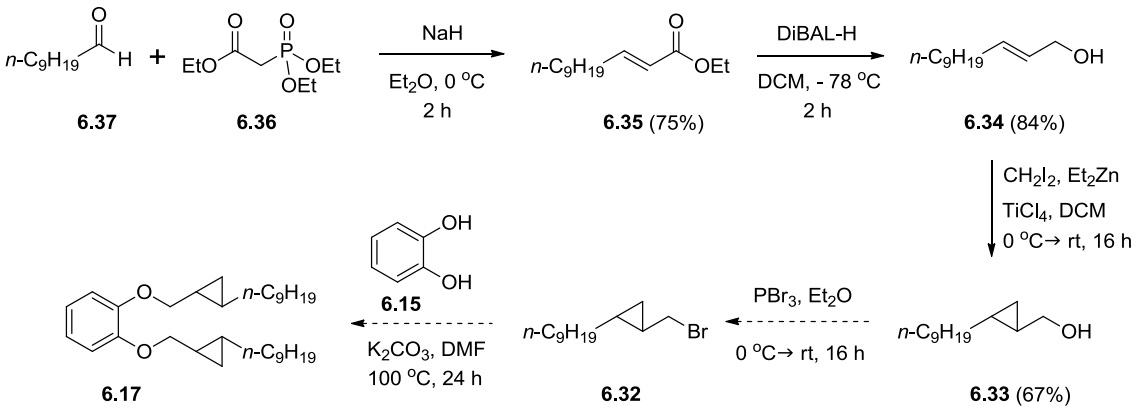
Scheme 6.9

Now, it was planned to prepare the cyclopropane-derived substrate **6.17** to check for the presence of alkyl radical intermediate **6.23** after ArO-C cleavage. The retrosynthetic route for the substrate **6.17** is shown in Scheme 6.10.



Scheme 6.10

The synthesis of allyl ester **6.35** was carried out by treating *n*-decanal **6.37** and triethyl phosphonoacetate **6.36** with sodium hydride using a Horner-Wadsworth-Emmons reaction.[199] Conjugate ester **6.35** was then treated with DiBAL-H and reduced to allylic alcohol **6.34**. Then, alcohol **6.34** was converted to cyclopropyl methyl alcohol **6.33** by following the method described by Charette *et al*.[200] Further steps that lead to the final desired compound **6.17** and its submission to Birch conditions still need to be performed (Scheme 6.11).



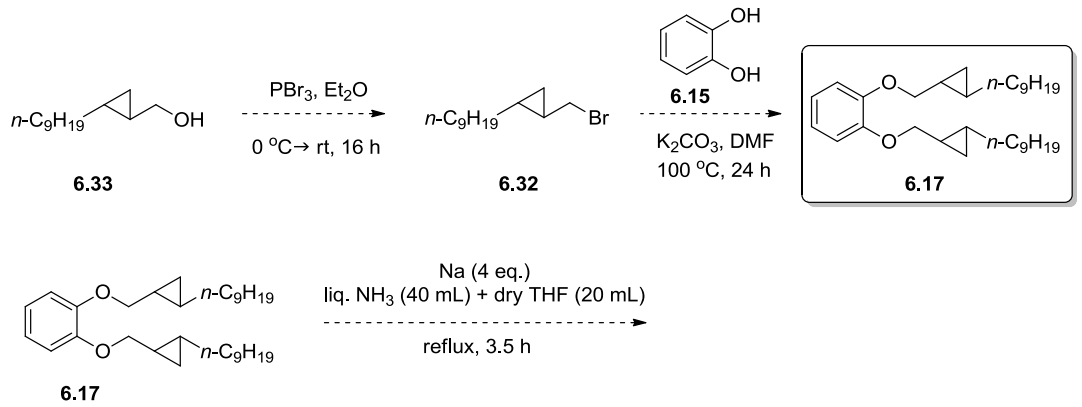
Scheme 6.11

6.3 Conclusion

A series of *ortho*-dialkoxybenzenes were prepared and submitted to Birch conditions by following the method described by Bunnett.[197] In all these reactions, it was found that ArO-C bonds were regioselectively fragmented at the ArO-Me site over the ArO-Alkyl site except in **6.8**. Selective cleavage at a particular site is generally dictated by the stability of the fragmented ions.[196] As the methyl anion is more stable than competitive alkyl anions that are generated in our examples, it supports the above seen preferential fragmentation at ArO-Me site. Therefore, it is unlikely that methyl radical is liberated over methyl anion in *ortho*-dimethoxybenzene, as described by Zimmerman.[195] However, in **6.8** the cleavage might have gone through alkyl radical intermediate that can be stabilized by the hexenyl double bond. Specially designed substrate **6.16** provided low yields of fragmented products but supported the presence of alkyl anion intermediates after ArO-C fragmentation. The low yields of the reaction may be partly due to very poor solubility of the substrate **6.16**. Another cyclopropyl-derived substrate **6.17** is planned to test for the identification of alkyl radicals, if formed after ArO-C cleavage. Synthesis of the important intermediate, cyclopropyl alcohol, **6.33** was completed and further steps are needed to finsh the synthesis of **6.17**.

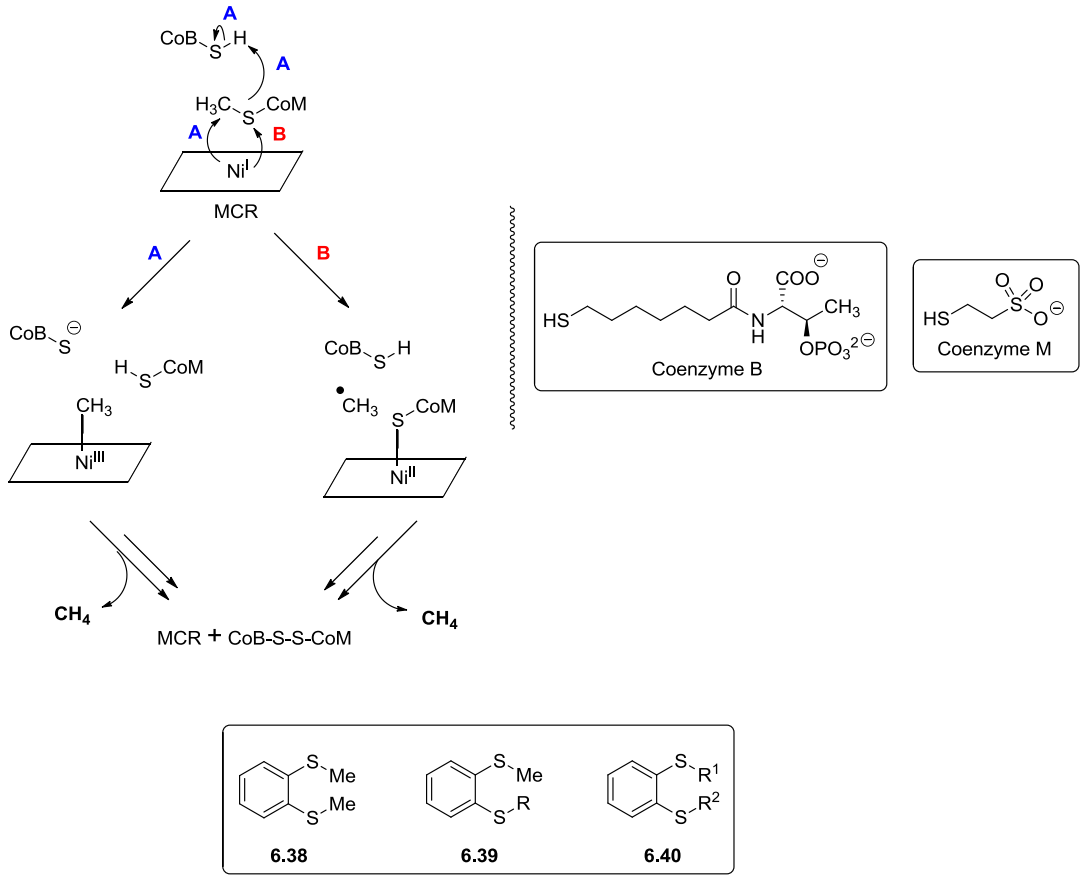
6.4 Future work

- The immediate future work will be the synthesis of substrate **6.37** and submitting it to Birch conditions to look for evidence of alkyl radicals formed after ArO-C fragmentation (Scheme 6.14).



Scheme 6.14

- Reductive cleavage of C-S bonds is synthetically important[201,202] and notably has major role in biology.[203] Methanogenesis in methanogenic archaeabacteria is catalyzed by nickel-containing methyl-coenzyme M reductase (MCR) and this process involves S-C bond cleavage. This nickel complex, containing a nickel(I) porphyrinoid cofactor, $Ni^{I}F_{430}$, catalyzes conversion of methyl-coenzyme M (CH_3-SCoM) and coenzyme B (CoB-SH) to methane and heterodisulfide (CoM-S-S-CoB) (Scheme 6.15). Recently, Siegbahn *et al.*[203] proposed that the cleavage does not involve intermediate organonickel species (path **A**), but instead arises simply from electron-transfer from Ni(I) to the S-CH_3 bond (path **B**). If so, then our organic electron donors might also be able to cleave this or related C-S bonds and provide supporting evidence for Siegbahn's proposal. So, it would be interesting to extend our cleavage studies to C-S bonds with alkylthioarenes **6.38**-**6.40** suggested as the very first substrates to test (Scheme 6.15).



Scheme 6.15

7 Experimental Details

7.1 General experimental information

All reagents were bought from commercial suppliers and used without further purification unless stated otherwise. All the reactions were performed in oven-dried or flame-dried apparatus and preparation of the substrates was carried out under argon atmosphere using dry solvents. Diethyl ether, tetrahydrofuran, dichloromethane and hexane were dried with a Pure-Solv 400 solvent purification system by Innovative Technology Inc., U.S.A. Organic extracts were, in general, dried over anhydrous sodium sulfate (Na_2SO_4). A Büchi rotary evaporator was used to concentrate the reaction mixtures. Thin layer chromatography (TLC) was performed using aluminium-backed sheets of silica gel and visualized under a UV lamp (254 nm). The plates were developed using vanillin or $KMnO_4$ solution. Column chromatography was performed to purify compounds by using silica gel 60 (200-400 mesh).

A glove box (Innovative Technology Inc., U.S.A.) was used for the work-up of the donor **1.249** preparation reaction. Solvents used in the glovebox were degassed under reduced pressure for at least 30 min, then purged with argon prior to being sealed and transferred to the glovebox port. The port was evacuated then purged with nitrogen at least ten times before transfer into the glovebox. To weigh out the super electron donor (SED) into the reaction flask, the same procedure as above was followed. All UV reactions were carried out by using two focused UV lamps with filters (λ = 365 nm, each 100 watts) bought from Ultra-Violet products (UVP) company. During the reaction, the two UV lamps were placed opposite to each other, around the reaction flask, at room temperature.

Proton (^1H) NMR spectra were recorded at 400.13, 400.03 and 500.16 MHz on Bruker AV3, AV400 and AV500 spectrometers, respectively. Carbon NMR (^{13}C) spectra were similarly recorded at 100.61, 100.59 and 125.75 MHz on Bruker AV3, AV400 and AV500 spectrometers, respectively. The NMR experiments were carried out in deuterochloroform ($CDCl_3$), d_6-dimethylsulfoxide (DMSO-d_6) and d_6-benzene (C_6D_6). The chemical shifts are quoted in parts per million (ppm) by taking tetramethylsilane as a

reference (δ = 0) but calibrated on the residual non-deuterated solvent signal. Signal multiplicities are abbreviated as: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad singlet; coupling constants (*J*) are given in Hertz (Hz).

Infra-Red spectra were recorded on (i) a Perkin Elmer Spectrum One FT IR Spectrometer either pressed as discs in KBr or as films applied on NaCl crystal plates or (ii) an ATR-IR spectrometer. Melting points were determined on a Gallenkamp Melting point apparatus. High resolution mass spectra were recorded at the EPSRC National Mass Spectrometry Service Centre, Swansea. The spectra were recorded using electron ionisation (EI), chemical ionization (CI), electrospray ionization (ESI), Gas-phase Chromatography (GC), or Atmospheric Pressure Chemical Ionisation (APCI) techniques, as stated for each compound.

7.2 General procedure for UV-activated reductions

Under an inert atmosphere, a solution of the donor **1.249** or DBD **1.189** in dry *N*,*N*-dimethylformamide (5 mL) was added to the flask containing the appropriate substrate in a glove-box. The sealed flask was then submitted to UV irradiation for a specified time, using two focused UV lamps (365 nm, each 100 watts). After application of the general work-up procedure, the crude product was adsorbed onto silica and purified by column chromatography, providing the corresponding reduced products in yields as stated.

7.2.1 General acid-base work-up procedure for the reduction of arenesulfonamides

The reaction mixture was quenched with 1N HCl (10 mL) and then extracted with diethyl ether (3 x 10 mL). The combined ether layers were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The filtered solution was concentrated to afford recovery of pure starting materials in yields as stated. The collected aqueous phase was then basified with 2N NaOH and extracted with diethy ether (3 x 10 mL). The combined ether layers were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The filtered solution was concentrated to afford the corresponding pure reduced products in yields as stated.

7.2.2 General water (alkaline) work-up procedure

The reaction was quenched with water (5 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic layers were then washed once again with water (10 mL), brine (10 mL) and dried over anhydrous sodium sulfate. The crude product was obtained after evaporation of solvent under reduced pressure using a rotary evaporator.

7.2.2.1 ***Acidic work-up of aqueous phase*****:** The resulting aqueous solution was treated with 1N HCl (15 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic layers were washed with brine (10 mL) and dried over anhydrous sodium sulfate. The crude product was obtained after evaporation of solvent under reduced pressure using a rotary evaporator.

7.2.3 General acidic work-up procedure

The reaction was quenched with 1N HCl (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic layers were then washed once again with water (10 mL), brine (10 mL) and dried over anhydrous sodium sulfate. The crude product was obtained after evaporation of solvent under reduced pressure using a rotary evaporator.

7.2.4 General procedures for blank experiments

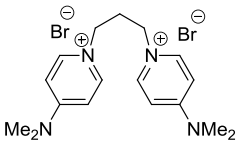
7.2.4.1 ***For donor-free UV-activated blank reaction*****:** Following the preparation protocol devised for UV-activated reductions, a donor-free sample was prepared. Both the donor-free blank reaction and the original reaction were carried out at the same time by placing two flasks under the same UV source for the same amount of time. After following the above discussed general work-up procedure, the crude product was adsorbed onto silica and purified by column chromatography, providing exclusively the starting material and the reduced product (where the reaction works) in yields as stated.

7.2.4.2 ***For UV-free donor-activated blank reaction*****:** Following the preparation protocol devised for UV-activated reactions, samples were prepared. Both the UV-free blank reaction and the original reaction under UV conditions were carried out for the same

amount of time. After following the above discussed general work-up procedure, the crude product was adsorbed onto silica and purified by column chromatography, providing exclusively the starting material and the reduced product (where the reaction works) in yields as stated.

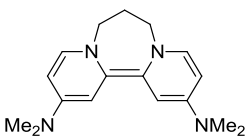
7.3 Preparation of donor 1.249

Synthesis of 1,3-*bis*(*N*',*N*'-dimethyl-4-aminopyridinium)propane dibromide[183]



A solution of 4-(dimethylamino)pyridine **1.245** (9.16 g, 75 mmol, 2.5 eq.) and 1,3-dibromopropane (6.06 g, 30 mmol, 1.0 eq.) in a flask containing acetonitrile (60 mL) was stirred at reflux for 16 h, under argon. Diethyl ether (10 mL) was added to the reaction flask and the product precipitated instantaneously, and was then filtered. To precipitate more of the solid, an additional amount of diethyl ether (20 mL) was added to the filtrate. After filtration, the solid was washed with diethyl ether (3 x 50 mL) and dried under vacuum to give 1,3-bis(*N*',*N*'-dimethyl-4-aminopyridinium)propane dibromide[183] (13 g, 97%) as a white solid m.p. 199-203 ^{o}C (lit.:[183] 199-203 ^{o}C); [Found: (ESI^{+}) $(M\text{-}Br)^{+}$ 365.1338. $C_{17}H_{26}BrN_4$ (M-Br) requires 365.1335]; ν_{max}(KBr)/cm^{-1} 3027, 2725, 2468, 1649, 1571, 1403; ^{1}H-NMR (400 MHz, DMSO-d_6) δ 2.36 (2H, quintet, J = 7.2 Hz, $CH_2CH_2CH_2$), 3.18 (12H, s, NCH_3), 4.28 (4H, t, J = 7.2 Hz, NCH_2), 7.04 (4H, d, J = 7.6 Hz, ArH), 8.34 (4H, d, J = 7.6 Hz, ArCH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 31.2 (CH_2), 39.8 (CH_3), 53.7 (CH_2), 107.8 (CH), 141.8 (CH), 155.8 (C); *m/z* (ESI^{+}) 367 [$(M\text{-}^{81}Br)^{+}$, 28%], 365 [$(M\text{-}^{79}Br)^{+}$, 28%], 285 (5), 143 (100).

Synthesis of *N*,*N*,*N'*,*N'*-tetramethyl-7,8-dihydro-*6H*-dipyrido[1,2-a;2',1'-c][1,4] diazepine-2,12-diamine 1.249[96]

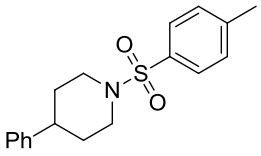


A mixture of 1,3-*bis*(*N'*,*N'*-dimethyl-4-aminopyridinium)propane dibromide (13.38 g, 30 mmol, 1.0 eq.) and pre-washed NaH (~95%, stored in glovebox, 4.55 g, 180 mmol, 6 eq.)

were taken in a Schlenk flask mounted with a dry ice condenser, and the atmosphere was made oxygen-free by flushing with argon. At this point, ammonia (75 mL) was condensed, left at reflux for 4 h and was subsequently allowed to evaporate overnight (14 h) under a steady argon flow. The flask was then transfered to an oxygen-free, moisture-free glove box. The solid was extracted with dry diethyl ether (300 mL) and the solvent was then removed by distillation and under vacuum (10-20 mbar) to give the pure *N*,*N*,*N'*,*N'*-tetramethyl-7,8-dihydro-6H-dipyrido-[1,2-a;2',1'-c][1,4]-diazepine-2,12-diamine **1.249** (7.61 g, 89%) as a purple-black, moisture-sensitive and highly oxygen-sensitive solid. ^{1}H-NMR (400 MHz, benzene-d_6) δ 1.00 (2H, quintet, J = 6.3 Hz, $CH_2CH_2CH_2$), 2.46 [12H, s, $N(CH_3)_2$], 3.03 (4H, t, J = 6.3 Hz, NCH_2), 4.91 (2H, dd, J = 7.5, 2.2 Hz, ArH), 5.14 (2H, d, J = 2.2 Hz, ArH), 5.64 (2H, d, J = 7.5 Hz, ArH); ^{13}C-NMR (100 MHz, benzene-d_6) δ 24.5 (CH_2), 40.8 (CH_3), 52.6 (CH_2), 95.8 (CH), 96.2 (CH), 116.0 (C), 138.7 (CH), 143.7 (C). The ^{1}H-NMR and ^{13}C-NMR spectral data are consistent with previously published data of **1.249**.[96]

7.4 Experimental for Chapter 2

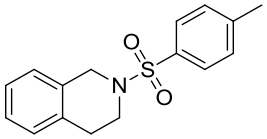
Synthesis of 4-phenyl-1-tosylpiperidine 1.224[84]



To a mixture of 4-phenylpiperidine **2.1** (0.483 g, 3 mmol) and pyridine (1 mL), *p*-toluenesulfonyl chloride **2.2** (0.686 g, 3.6 mmol) in dry dichloromethane (10 mL) was added slowly and stirred at room temperature for 1 h. The reaction mixture was then washed with aqueous 1N HCl (10 mL) and extracted with diethyl ether (2 x 10 mL). The combined organic phases were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The filtered solution was concentrated and was purified by column chromatography [5% ethyl acetate in petroleum ether] to yield 4-phenyl-1-tosylpiperidine **2.3**[84] (0.714 g, 75%) as a white powder m.p. 150-152 ^{o}C (lit.:[84] 151-152 ^{o}C); [Found: (CI corona^{+}) $(M+H)^{+}$ 316.1368. $C_{18}H_{22}NO_2S$ (M+H) requires 316.1366]; ν_{max}(ATR)/cm^{-1} 3025, 2943, 2922, 2840, 1595, 1493, 1450, 1341, 1164; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.83-1.91 (4H, m, $ArCH(CH_2)_2$), 2.33-2.43 (3H, m, ArC*H*,

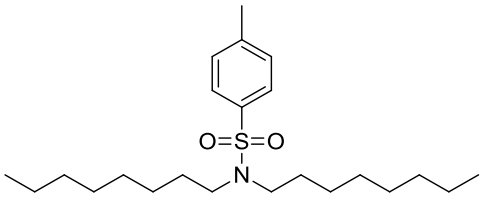
NC*H*$_2$), 2.46 (3H, s, ArC*H*$_3$), 3.93-3.97 (2H, m, NC*H*$_2$), 7.15 (2H, d, *J* = 7.2 Hz, ArH), 7.19-7.24 (1H, m, ArH), 7.28-7.36 (2H, m, ArH), 7.35 (2H, d, *J* = 8.0 Hz, ArH), 7.69 (2H, d, *J* = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.6 (CH_3), 32.6 (CH_2), 41.9 (CH), 46.9 (CH_2), 126.7 (CH), 126.8 (CH), 127.9 (CH), 128.7 (CH), 129.7 (CH), 133.3 (C), 143.6 (C), 145.0 (C); *m/z* (ESI^+) 316 [$(M+H)^+$, 100%], 247 (6).

Synthesis of 2-tosyl-1,2,3,4-tetrahydroisoquinoline 2.3[204]



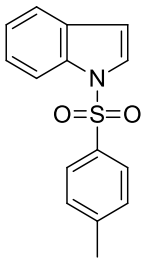
To a mixture of 1,2,3,4-tetrahydroisoquinoline **2.5** (0.2663 g, 2 mmol) and pyridine (0.5 mL), *p*-toluenesulfonyl chloride **2.2** (0.46 g, 2.4 mmol) in dry dichloromethane (5 mL) was added slowly and stirred at room temperature for 1 h. The reaction mixture was then washed with aqueous 1N HCl (10 mL) and extracted with diethyl ether (2 x 10 mL). The combined organic phases were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The filtered solution was concentrated and was purified by column chromatography [5% ethyl acetate in petroleum ether] to yield 2-tosyl-1,2,3,4-tetrahydroisoquinoline **2.3** (0.505 g, 88%) as a white solid m.p. 145-146 ^{o}C (lit.:[205] 147 ^{o}C); [Found: (ESI^+) $(M+H)^+$ 288.1052. $C_{16}H_{18}NO_2S$ (M+H) requires 288.1053]; ν_{max}(film)/cm^{-1} 3023, 2935, 2861, 1594, 1455, 1352, 1339, 1165, 1136; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.42 (3H, s, ArC*H*$_3$), 2.93 (2H, t, *J* = 5.6 Hz, ArC*H*$_2$CH$_2$N), 3.36 (2H, t, *J* = 5.6 Hz, ArCH$_2$C*H*$_2$N), 4.25 (2H, s, ArC*H*$_2$N), 7.01-7.03 (1H, m, ArH), 7.06-7.08 (1H, m, ArH), 7.12-7.14 (2H, m, ArH), 7.32 (2H, d, *J* = 7.6 Hz, ArH), 7.73 (2H, d, *J* = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.6 (CH_3), 29.0 (CH_2), 43.8 (CH_2), 47.7 (CH_2), 126.46 (CH), 126.49 (CH), 126.8 (CH), 127.9 (CH), 128.9 (CH), 129.8 (CH), 131.8 (C), 133.2 (C), 133.4 (C), 143.8 (C); *m/z* (ESI^+) 305 [$(M+NH_4)^+$, 7%], 288 [$(M+H)^+$, 100%].

Synthesis of 4-methyl-*N*,*N*-dioctylbenzenesulfonamide 2.4[206]



To a mixture of di-*N*-octylamine **2.6** (0.482 g, 2 mmol) and pyridine (0.5 mL), *p*-toluenesulfonyl chloride **2.2** (0.46 g, 2.4 mmol) in dry dichloromethane (5mL) was added slowly and stirred at room temperature for 1 h. The reaction mixture was then washed with aqueous 1N HCl (10 mL) and extracted with diethyl ether (2 x 10 mL). The combined organic phases were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The filtered solution was concentrated and was purified by column chromatography [4% ethyl acetate in petroleum ether] to yield 4-methyl-*N*,*N*-dioctylbenzenesulfonamide **2.4** as a colourless oil (0.556 g, 70%). [Found: (ESI^+) $(M+H)^+$ 396.2931. $C_{23}H_{42}NO_2S$ (M+H) requires 396.2931]; ν_{max}(film)/cm^{-1} 3029, 2927, 2856, 1599, 1466, 1376, 1341, 1159; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.88 (6H, t, J = 7.2 Hz, $CH_2CH_2CH_3$), 1.26-1.31 (20H, m, $NCH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$), 1.48-1.54 (4H, m, $NCH_2CH_2CH_2$), 2.42 (3H, s, $ArCH_3$), 3.09 (4H, t, J = 7.6 Hz, $NCH_2CH_2CH_2$), 7.28 (2H, d, J = 8.0 Hz, ArH), 7.68 (2H, d, J = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 21.5 (CH_3), 22.7 (CH_2), 26.8 (CH_2), 28.7 (CH_2), 29.26 (CH_2), 29.27 (CH_2), 31.8 (CH_2), 48.2 (CH_2), 127.19 (CH), 129.57 (CH), 137.3 (C), 140.9 (C); *m/z* (ESI^+) 808 [$(2M+NH_4)^+$, 100%], 396 [$(M+H)^+$, 85%].

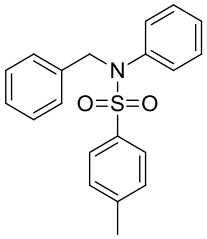
Synthesis of 1-tosyl-1H-indole 2.7[207]



To a mixture of indole **2.11** (0.234 g, 2 mmol) and pyridine (0.5 mL), *p*-toluenesulfonyl chloride **2.2** (0.46 g, 2.4 mmol) in dry dichloromethane (5mL) was added slowly and stirred at room temperature for 1 h. The reaction mixture was then washed with aqueous 1N HCl (10 mL) and extracted with diethyl ether (2 x 10 mL). The combined organic phases were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The filtered solution was concentrated and purified by column chromatography (10% diethyl ether in petroleum ether) to yield 1-tosyl-1H-indole **2.7** (0.522 g, 91%) as a white solid m.p. 82-84 ^oC (lit.:[207] 83-84 ^oC); **[**Found: (ESI^+) $(M+H)^+$ 272.0739. $C_{15}H_{14}NO_2S$ (M+H) requires 272.0740]; ν_{max}(KBr)/cm^{-1} 3116, 2919, 1596, 1446, 1369, 1260, 1168, 1128; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.32 (3H, s, CH_3), 6.66

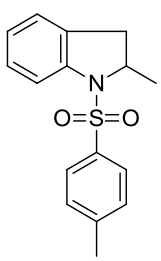
(1H, dd, *J* = 3.6, 0.8 Hz, ArH), 7.20-7.26 (3H, m, ArH), 7.29-7.33 (1H, m, ArH), 7.52-7.54 (1H, m, ArH), 7.57-7.58 (1H, m, ArH), 7.75-7.78 (2H, m, ArH), 7.99-8.02 (1H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.7 (CH_3), 109.1 (CH), 113.6 (CH), 121.4 (CH), 123.4 (CH), 124.7 (CH), 126.4 (CH), 126.9 (CH), 130.0 (CH), 130.9 (C), 134.9 (C), 135.4 (C), 145.0 (C); *m/z* (ESI^+) 289 [$(M+NH_4)^+$, 29%], 272 [$(M+H)^+$, 100%].

Synthesis of *N*-benzyl-4-methyl-*N*-phenylbenzenesulfonamide 2.8[208]



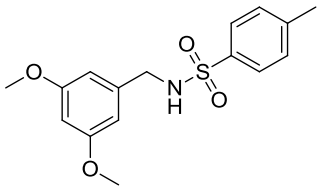
To a mixture of *N*-benzylaniline **2.12** (0.916 g, 5 mmol) and pyridine (2 mL), *p*-toluenesulfonyl chloride **2.2** (1.1439 g, 6 mmol) in dry dichloromethane (10 mL) was added slowly and stirred at room temperature for 90 min. The reaction mixture was then washed with aqueous 1N HCl (10 mL) and extracted with diethyl ether (2 x 10 mL). The combined organic phases were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The filtered solution was concentrated and purified by column chromatography [30% ethyl acetate in petroleum ether] to yield *N*-benzyl-4-methyl-*N*-phenylbenzenesulfonamide **2.8** (1.616 g, 96%) as a white solid m.p. 138-140 ^{o}C (lit.:[208] 139-140 ^{o}C); **[**Found: (ESI^+) $(M+H)^+$ 338.1204. $C_{20}H_{20}NO_2S$ (M+H) requires 338.1209]; ν_{max}(film)/cm^{-1} 3027, 2919, 1597, 1492, 1347, 1153, 1095; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.43 (3H, s, ArC*H*$_3$), 4.73 (2H, s, ArC*H*$_2$NAr), 6.97-7.0 (2H, m, ArH), 7.19-7.33 (8H, m, ArH), 7.27-7.29 (2H, m, ArH), 7.54-7.56 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.7 (CH_3), 54.8 (CH_2), 127.7 (CH), 127.9 (CH), 128.5 (CH), 128.6 (CH), 128.9 (CH), 129.0 (CH), 129.1 (CH), 129.6 (CH), 135.8 (C), 136.1 (C), 139.1 (C), 143.6 (C); *m/z* (ESI^+) 355 [$(M+NH_4)^+$, 55%], 338 [$(M+H)^+$, 100%], 183 (3).

Synthesis of 2-methyl-1-tosylindoline 2.9[209]



To a mixture of 2-methylindoline **2.13** (0.266 g, 2 mmol) and pyridine (0.5 mL), *p*-toluenesulfonyl chloride **2.2** (0.46 g, 2.4 mmol) in dry dichloromethane (5mL) was added slowly and stirred at room temperature for 1 h. The reaction mixture was then washed with aqueous 1N HCl (10 mL) and extracted with diethyl ether (2 x 10 mL). The combined organic phases were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The filtered solution was concentrated and was purified by column chromatography [10% diethyl ether in hexane] to yield 2-methyl-1-tosylindoline **2.9** (0.522 g, 91%) as a white solid m. p. 62-64 ^{o}C (lit.:[210] 63-64 ^{o}C); [Found: (ESI^{+}) $(M+H)^{+}$ 288.1054. $C_{16}H_{18}NO_2S$ (M+H) requires 288.1053]; ν_{max}(KBr)/cm^{-1} 3032, 2926, 2858, 1595, 1481, 1375, 1344, 1156; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.42 (3H, d, J = 6.8 Hz, NCHCH_3), 2.34 (3H, s, ArCH_3), 2.41-2.46 (1H, m, ArCH_2CH(CH_3)N), 2.89 (1H, dd, J = 16.0, 1.2 Hz, ArCH_2CH(CH_3)N), 4.31-4.38 (1H, m, NC*H*CH_3), 6.99-7.05 (2H, m, ArH), 7.15-7.22 (3H, m, ArH), 7.55 (2H, d, J = 8.4 Hz, ArH), 7.65 (1H, d, J = 8.0 Hz, ArH) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.6 (CH_3), 23.5 (CH_3), 36.3 (CH_2), 58.6 (CH), 117.2 (CH), 124.6 (CH), 125.3 (CH), 127.1 (CH), 127.8 (CH), 129.6 (CH), 131.7 (C), 135.5 (C), 141.2 (C), 143.8 (C); *m/z* (ESI^{+}) 305 [$(M+NH_4)^{+}$, 16%], 288 [$(M+H)^{+}$, 100%].

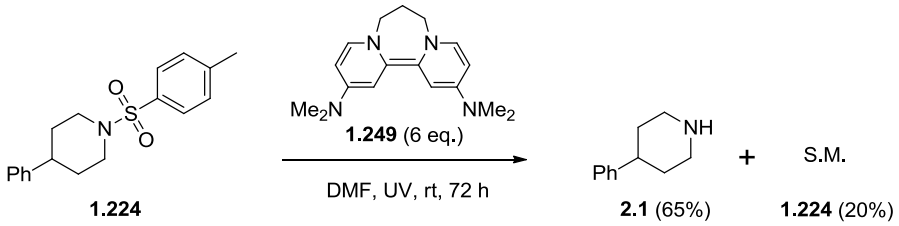
Synthesis of *N*-(3,5-dimethoxybenzyl)-4-methylbenzenesulfonamide 2.10



To a mixture of (3,5-dimethoxyphenyl)methanamine (0.334 g, 2 mmol) and pyridine (0.5 mL), *p*-toluenesulfonyl chloride **2.2** (0.46 g, 2.4 mmol) in dry dichloromethane (5 mL) was added slowly and stirred at room temperature for 1 h. The reaction mixture was then washed with aqueous 1N HCl (10 mL) and extracted with diethyl ether (2 x 10 mL). The combined organic phases were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The filtered solution was concentrated and was purified by column chromatography (5% ethyl acetate in petroleum ether) to yield *N-(3,5-dimethoxybenzyl)-4-methylbenzenesulfonamide* **2.10** (0.556 g, 70%) as a light brown solid m.p. 84-86 ^{o}C; [Found: (ESI^{+}) $(M+H)^{+}$ 322.1108. $C_{16}H_{20}NO_4S$ (M+H) requires 322.1108]; ν_{max}(film)/cm^{-1} 3291, 3064, 2927, 2843, 1610, 1468, 1317, 1151, 1090; ^{1}H-NMR (400

MHz, $CDCl_3$) δ 2.42 (3H, s, ArC*H*$_3$), 3.70 (6H, s, ArOC*H*$_3$), 4.05 (2H, d, *J* = 6.4 Hz, ArC*H*$_2$NH), 4.89 (1H, bs, ArCH$_2$N*H*), 6.31 (3H, s, Ar*H*), 7.29 (2H, d, *J* = 8.0 Hz, ArH), 7.75 (2H, d, *J* = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.6 (CH_3), 47.5 (CH_2), 55.4 (CH_3), 100.1 (CH), 105.7 (CH), 127.3 (CH), 129.8 (CH), 137.0 (C), 138.7 (C), 143.6 (C), 161.1 (C); *m/z* (ESI$^+$) 339 [$(M+NH_4)^+$, 66%], 322 [$(M+H)^+$, 100%], 151 (18).

UV-activated reduction of 4-phenyl-1-tosylpiperidine 1.224

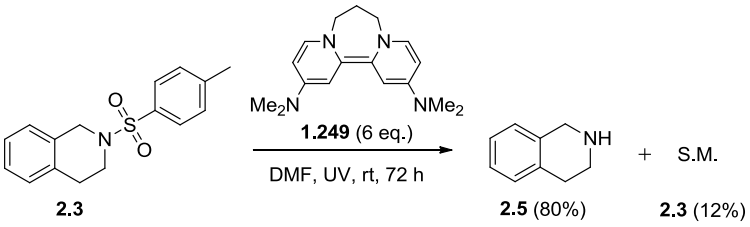


Donor-free blank, with UV : 95% recovery of **1.224**
UV-free blank, with donor : 96% recovery of **1.224**

The general procedure for electron transfer reactions under UV conditions was applied to 4-phenyl-1-tosylpiperidine **1.224** (94.0 mg, 0.3 mmol, 1 eq.) using the donor **1.249** (341 mg, 1.8 mmol, 6 eq.) for 72 h at room temperature. After following the general acid-base work-up procedure for the reduction of arenesulfonamides, pure starting material **1.224** (19 mg, 20%) and 4-phenylpiperidine **2.1**[211] (31 mg, 65%) were obtained as white solids. For **2.1**: m.p. 62-64 ^{o}C (lit.:[211] 62-64 ^{o}C); [Found: (CI corona$^+$) $(M+H)^+$ 162.1277. $C_{11}H_{16}N$ (M+H) requires 162.1277]; ν_{max}(ATR)/cm^{-1} 3293, 2931, 2917, 2848, 1644, 1543, 1451, 1413, 1370, 1247; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.60-1.71 (2H, m, ArCHC*H*$_2$), 1.79 (1H, bs, N*H*), 1.83-1.87 (2H, m, ArCHC*H*$_2$), 2.59-2.67 (1H, m, ArC*H*), 2.72-2.79 (2H, m, NHC*H*$_2$), 3.19-3.22 (2H, m, NHC*H*$_2$), 7.18-7.25 (3H, m, ArH), 7.29-7.33 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 34.7 (CH_2), 43.2 (CH), 47.3 (CH_2), 126.2 (CH), 126.9 (CH), 128.5 (CH), 146.9 (C). The spectral data were consistent with the literature data of the same compound.[211]

Donor-free blank and UV-free blank reactions were performed as per the general procedure and provided the starting material **1.224** (0.089 g, 95%) and (0.090 g, 96%), respectively.

UV-activated reduction of 2-tosyl-1,2,3,4-tetrahydroisoquinoline 2.3

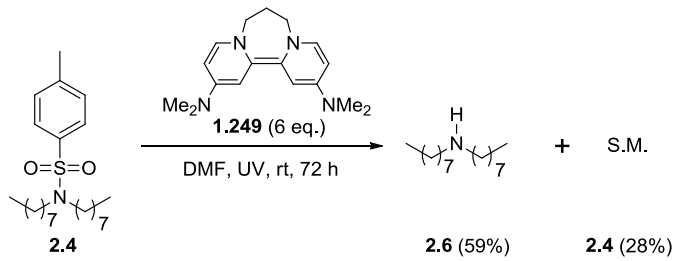


Donor-free blank, with UV : 92% recovery of **2.3**
UV-free blank, with donor : 93% recovery of **2.3**

The general procedure for electron transfer reactions under UV conditions was applied to 2-tosyl-1,2,3,4-tetrahydroisoquinoline **2.3** (86.2 mg, 0.3 mmol, 1 eq.) using the donor **1.249** (511 mg, 1.8 mmol, 6 eq.) for 72 h at room temperature. After following the general acid-base work-up procedure for the reduction of arenesulfonamides, pure starting material **2.3** (10.6 mg, 12%), as a white solid, and 1,2,3,4-tetrahydroisoquinoline **2.5**[212] (32.0 mg, 80%), as a yellow liquid, were obtained. For **2.5**: [Found: (EI^+) $(M\text{-}H)^+$ 132.0808. $C_9H_{10}N$ (M-H) requires 132.0808]; ν_{max}(film)/cm^{-1} 3290, 3019, 2923, 2834, 1668, 1581, 1495, 744; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.93 (1H, bs, NH), 2.81 (2H, t, J = 6.0 Hz, ArCH_2CH$_2$N), 3.15 (2H, t, J = 6.0 Hz, ArCH$_2$CH_2N), 4.03 (2H, s, ArCH_2N), 6.99-7.03 (1H, m, ArH), 7.08-7.14 (3H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 29.3 (CH_2), 44.0 (CH_2), 48.4 (CH_2), 125.8 (CH), 126.1 (CH), 126.3 (CH), 129.4 (CH), 134.9 (C), 136.1 (C). The spectral data were consistent with the literature data.[212]

Donor-free and UV-free blank reactions were performed as per the general procedure and provided the starting material **2.3** (0.0791 g, 92%) and (0.0803 g, 93%), respectively.

UV-activated reduction of 4-methyl-*N*,*N*-dioctylbenzenesulfonamide 2.4



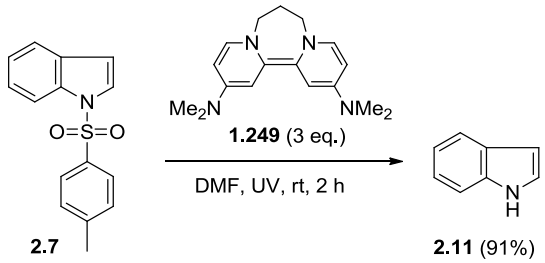
Donor-free blank, with UV ; 95% recovery of **2.4**
UV-free blank, with donor ; 97% recovery of **2.4**

The general procedure for electron transfer reactions under UV conditions was applied to 4-methyl-*N*,*N*-dioctylbenzenesulfonamide **2.4** (118.6 mg, 0.3 mmol, 1 eq.) using the

donor **1.249** (511 mg, 1.8 mmol, 6 eq.) for 72 h at room temperature. After following the general acid-base work-up procedure for the reduction of arenesulfonamides, pure starting material **2.4** (32.9 mg, 28%) and di-*N*-octylamine **2.6**[213] (42.8 mg, 59%) were obtained as colourless oils. For **2.6**: [Found: (ESI$^+$) $(M+H)^+$ 242.2841. $C_{16}H_{36}N$ (M+H) requires 242.2842]; ν_{max}(film)/cm^{-1} 3274, 3116, 2955, 2924, 2853, 1468, 720; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.87 (6H, t, J = 7.6 Hz, $N(CH_2)_7CH_3$), 1.04 (1H, bs, NH), 1.27-133 (20H, m, $N(CH_2)_2(CH_2)_5CH_3$), 1.44-1.49 (4H, m, $NCH_2CH_2(CH_2)_5CH_3$), 2.58 (4H, t, J = 7.2 Hz, $NCH_2(CH_2)_7CH_3$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 27.6 (CH_2), 29.4 (CH_2), 29.7 (CH_2), 30.4 (CH_2), 31.9 (CH_2), 50.3 (CH_2); *m/z* (ESI$^+$) 242 [$(M+H)^+$, 100%].

Donor-free and UV-free blank reactions were performed as per the general procedure and provided the starting material **2.4** (0.113 g, 95%) and (0.1152 g, 97%), respectively.

UV-activated reduction of 1-tosyl-1H-indole 2.7

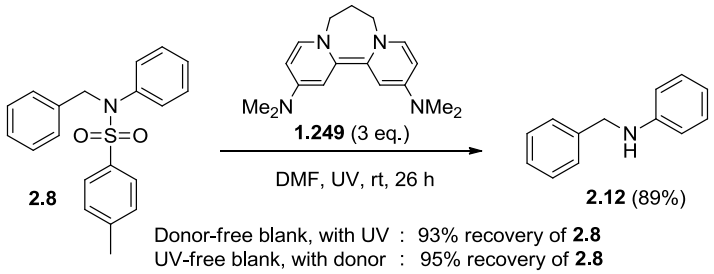


Donor-free blank, with UV : **2.11** (4%) from ^{1}H-NMR of crude product
UV-free blank, with donor : **2.11** (31%)

The general procedure for electron transfer reactions under UV conditions was applied to 1-tosyl-1H-indole **2.7** (81.3 mg, 0.3 mmol, 1 eq.) using the donor **1.249** (255 mg, 0.9 mmol, 3 eq.) for 2 h at room temperature. After following the general acid-base work-up procedure for the reduction of arenesulfonamides, only indole **2.11**[214] (31.8 mg, 91%) was obtained as a white solid m.p. 51-53 ^{o}C; (lit.:[214] 51-53 ^{o}C); ν_{max}(KBr) /cm^{-1} 3400, 3098, 3049, 1576, 1506, 1456, 1247, 745; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.59-6.60 (1H, m, ArH), 7.14-7.18 (1H, m, ArH), 7.22-7.27 (2H, m, ArH), 7.42 (1H, dd, J = 8.0, 0.4 Hz ArH), 7.92 (1H, d, J = 8.0 Hz, ArH), 8.11 (1H, bs, NH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 102.7 (CH), 111.1 (CH), 119.9 (CH), 120.9 (CH), 122.1 (CH), 124.2 (CH), 127.9 (C), 135.9 (C). The spectral data were consistent with the literature data.[214]

Donor-free and UV-free blank reactions were performed as per the general procedure and provided the product **2.11** in 4% conversion (from ^{1}H-NMR of the crude product) and (0.011 g, 31%), respectively.

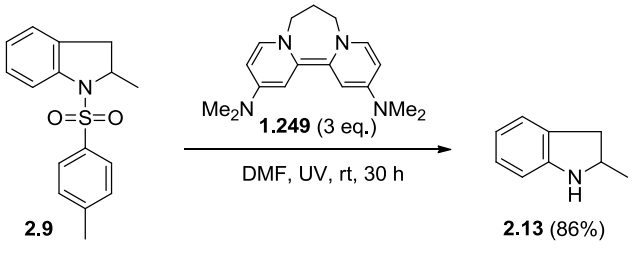
UV-activated reduction of *N*-benzyl-*N*-phenyl-4-methylbenzenesulfonamide 2.8



The general procedure for electron transfer reactions under UV conditions was applied to *N*-benzyl-*N*-phenyl-4-methylbenzenesulfonamide **2.8** (101 mg, 0.3 mmol, 1 eq.) using the donor **1.249** (255 mg, 0.9 mmol, 3 eq.) for 26 h at room temperature. After following the general acid-base work-up procedure for the reduction of arenesulfonamides, only *N*-benzylaniline **2.12**[215] (48 mg, 89%) was obtained as a white solid m.p. 34-35 ^{o}C (lit.:[215] 33-34 ^{o}C); **[**Found: (ESI$^+$) $(M+H)^+$ 184.1122. $C_{13}H_{14}N$ (M+H) requires 184.1121]; ν_{max}(KBr) /cm^{-1} 3417, 3022, 2924, 2846, 1603, 1512, 1329, 736; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.25 (1H, bs, NH), 4.35 (2H, s, ArC*H*$_2$N), 6.66-6.68 (2H, m, ArH), 6.72-6.76 (1H, m, ArH), 7.17-7.22 (2H, m, ArH), 7.28-7.31 (1H, m, ArH), 7.34-7.41 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 48.4 (CH_2), 113.0 (CH), 117.7 (CH), 127.3 (CH), 127.6 (CH), 128.7 (CH), 129.4 (CH), 139.3 (C), 148.2 (C); *m/z* (ESI$^+$) 184 [$(M+H)^+$, 100%].

Donor-free and UV-free blank reactions were performed as per the general procedure and provided the starting material **2.8** (0.0942 g, 93%) and (0.096 g, 95%), respectively.

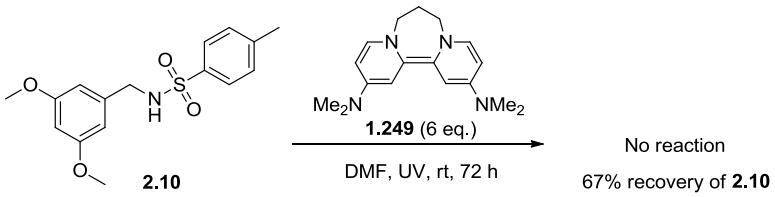
UV-activated reduction of 2-methyl-1-tosylindoline 2.9



The general procedure for electron transfer reactions under UV conditions was applied to 2-methyl-1-tosylindoline **2.9** (86.2 mg, 0.3 mmol, 1 eq.) using the donor **1.249** (255 mg, 0.9 mmol, 3 eq.) for 30 h at room temperature. After following the general acid-base work-up procedure for the reduction of arenesulfonamides, only 2-methylindoline **2.13**[216] (34.4 mg, 86%) was obtained as a colourless liquid; **[**Found: (EI^+) $(M)^+$ 133.0884. $C_9H_{11}N$ (M) requires 133.0886]; ν_{max}(film)/cm^{-1} 3369, 3029, 2961, 2844, 1610, 1484, 1248, 747; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.31 (3H, d, J = 6.4 Hz, ArNCHCH_3), 2.60-2.68 (1H, m, ArCH_2), 3.13-3.19 (1H, m, ArCH_2), 3.63 (1H, bs, NH), 3.97-4.03 (1H, m, ArNCHCH$_3$), 6.62 (1H, d, J = 8.0 Hz, ArH), 6.69-6.73 (1H, m, ArH), 7.01-7.05 (1H, m, ArH), 7.09 (1H, d, J = 7.2 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 22.4 (CH_3), 37.9 (CH_2), 55.3 (CH), 109.4 (CH), 118.7 (CH), 124.8 (CH), 127.4 (CH), 129.0 (C), 150.9 (C); *m/z* (EI^+) 133 [M^+, 38%], 118 (100), 91 (22), 77 (5), 65 (7), 51 (4).

Donor-free and UV-free blank reactions were performed as per the general procedure and provided the starting material **2.9** (0.0793 g, 92%) and (0.078 g, 91%), respectively.

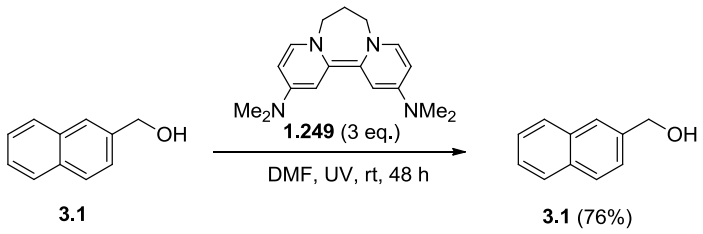
UV-activated reduction of *N*-(3,5-dimethoxybenzyl)-4-methylbenzenesulfonamide 2.10



The general procedure for the electron transfer reactions under UV conditions was applied to *N*-(3,5-dimethoxybenzyl)-4-methylbenzenesulfonamide **2.10** (96.3 mg, 0.3 mmol, 1 eq.) using the donor **1.249** (511 mg, 1.8 mmol, 6 eq.) for 72 h at room temperature. After following the general work-up, the crude material was purified by column chromatography (5% ethyl acetate in petroleum ether) and provided a recovery of starting material **2.10** (64.7 mg, 67%) only.

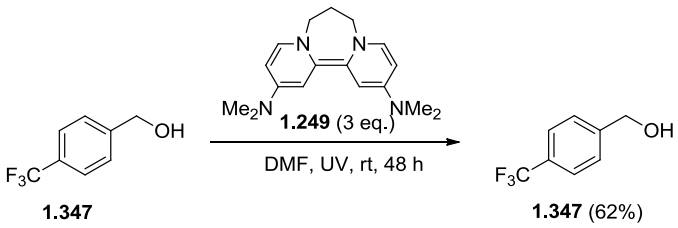
7.5 Experimental for Chapter 3

Attempted UV-activated reduction of naphthalen-2-ylmethanol 3.1



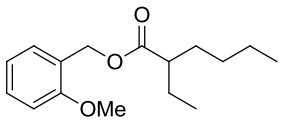
The general procedure for the electron transfer reactions under UV conditions was applied to naphthalen-2-ylmethanol **3.1** (31.6 mg, 0.2 mmol, 1 eq.) using the donor **1.249** (170.5 mg, 0.6 mmol, 3 eq.) for 48 h. After following the general work-up, the crude material was purified by column chromatography (20% ethyl acetate in petroleum ether) and provided a recovery of starting material **3.1**[217] (24 mg, 76%) only. ν_{max}(film)/cm^{-1} 3264, 3057, 2918, 2853, 1601; ^{1}H-NMR (400.13 MHz, $CDCl_3$) δ 2.00 (1H, bs, O*H*), 4.85 (2H, s, CH_2OH), 7.47-7.53 (3H, m, ArH), 7.81-7.96 (4H, m, ArH); ^{1}H-NMR and IR spectral data of S.M. **3.1** are consistent with literature data.[217]

Attempted UV-activated reduction of (4-(trifluoromethyl)phenyl)methanol 1.347



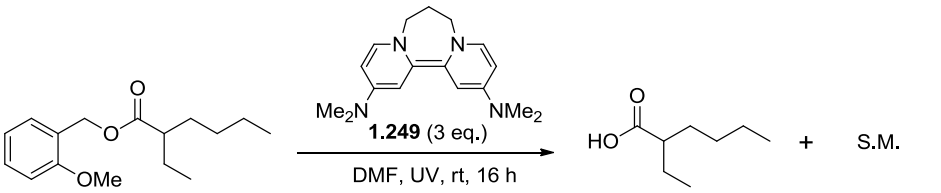
The general procedure for the electron transfer reactions under UV conditions was applied to (4-(trifluoromethyl)phenyl)methanol **1.347** (35.2 mg, 0.2 mmol, 1 eq.) using the donor **1.114** (170.5 mg, 0.6 mmol, 3 eq.) for 48 h. After following the general work-up, the crude material was purified by column chromatography (25% ethyl acetate in petroleum ether) and provided a recovery of starting material **1.347** (21.7 mg, 62%) only. ν_{max}(film)/cm^{-1} 3321, 2942, 1621,1419, 1321, 1107, 1015; ^{1}H-NMR (400.13 MHz, $CDCl_3$) δ 2.10 (1H, bs, O*H*), 4.77 (2H, s, CH_2OH), 7.48 (2H, d, *J* = 8.0 Hz, ArH), 7.62 (2H, d, *J* = 8.4 Hz, ArH); ^{1}H-NMR and IR spectral data of S.M. **1.347** were consistent with literature data.[218]

Synthesis of 2-methoxybenzyl 2-ethylhexanoate 3.10



2-Methoxybenzyl alcohol **3.8** (1.1053 g, 8 mmol) and pyridine (0.6328 g, 8 mmol) were dissolved in dry diethyl ether (10 mL) in a three-necked flask equipped with a condenser. 2-Ethylhexanoyl chloride **3.9** (1.3012 g, 8 mmol) was added slowly into the reaction flask, which was then refluxed for 2 h. After cooling the solution, water was added to dissolve pyridinium salts and the aqueous phase was discarded. The ether phase was washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to yield 2-methoxybenzyl 2-ethylhexanoate **3.10**[183] (1.7346 g, 82%) as a colourless liquid; [Found: (ESI$^+$) $(M+H)^+$ 265.1795. $C_{16}H_{25}O_3$ (M+H) requires 265.1798]; ν_{max}(film) /cm^{-1} 3042, 2960, 2936, 2874, 1732, 1605, 1495, 1464, 1248, 1031, 753; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.86-0.92 [6H, m, C*H*$_3$CH$_2$CH(CH$_2$)$_3$C*H*$_3$], 1.24-1.32 (4H, m, CHCH$_2$(C*H*$_2$)$_2$CH$_3$), 1.48-1.56 (2H, m, CHC*H*$_2$(CH$_2$)$_2$CH$_3$), 1.63-1.68 (2H, m, CHC*H*$_2$CH$_3$), 2.31-2.35 (1H, m, OC(O)C*H*), 3.84 (3H, s, ArOC*H*$_3$), 5.19 (2H, s, ArC*H*$_2$O), 6.90 (1H, d, *J* = 8.0 Hz, ArH), 6.96 (1H, dt, *J* = 7.5, 1.0 Hz, ArH), 7.29-7.35 (2H, m, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 11.9 (CH_3), 14.0 (CH_3), 22.7 (CH_2), 25.6 (CH_2), 29.7 (CH_2), 31.9 (CH_2), 47.5 (CH), 55.4 (CH_3), 61.5 (CH_2), 110.4 (CH), 120.4 (CH), 124.7 (C), 129.5 (CH), 129.7 (CH), 157.6 (C), 176.4 (C=O); *m/z* (ESI$^+$) 265 [$(M+H)^+$, 20%], 121 (100).

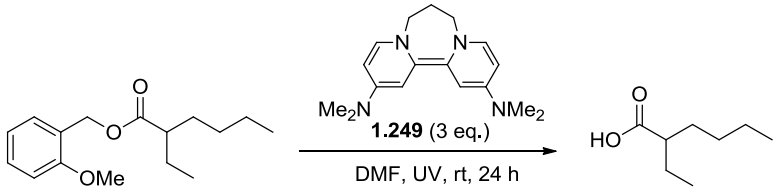
UV-activated reduction of 2-methoxybenzyl 2-ethylhexanoate 3.10 for 16 h



The general procedure for electron transfer reactions under UV conditions was applied to 2-methoxybenzyl 2-ethylhexanoate **3.10** (105.7 mg, 0.4 mmol, 1 eq.) using the donor **1.249** (341 mg, 1.2 mmol, 3 eq.) for 16 h. After following the general water work-up process, starting material **3.10** (15 mg, 14%) was obtained from the organic phase. Acidic work-up of the aqueous phase provided 2-ethylhexanoic acid **3.11** (39.6 mg, 69%) as a

yellow liquid; [Found: (ESI^+) $(M+NH_4)^+$ 162.1489. $C_8H_{20}NO_2$ $(M+NH_4)$ requires 162.1489]; ν_{max}(film) /cm^{-1} 3300-2500, 2963, 2935, 2876, 1706, 1460, 1289, 944; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.89-0.92 [3H, m, $CH(CH_2)_3CH_3$], 0.95 (3H, t, J = 7.5 Hz, $CHCH_2CH_3$), 1.29-1.35 (4H, m, $CHCH_2(CH_2)_2CH_3$), 1.48-1.69 (4H, m, $CH_2CHCH_2(CH_2)_2CH_3$), 2.27-2.32 (1H, m, HO_2CCH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 11.9 (CH_3), 14.0 (CH_3), 22.8 (CH_2), 25.3 (CH_2), 29.7 (CH_2), 31.6 (CH_2), 47.2 (CH), 183.1 (CO_2H); *m/z* (CI^+) 162 [$(M+NH_4)^+$, 100%], 127 (3), 87 (2), 52 (5).

UV-activated reduction of 2-methoxybenzyl 2-ethylhexanoate 3.10 for 24 h



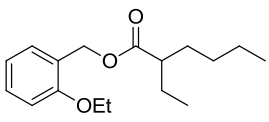
3.10 **3.11** (91%)

Donor-free blank reaction: 87% recovery of **3.10**

The general procedure for electron transfer reactions under UV conditions was applied to 2-methoxybenzyl 2-ethylhexanoate **3.10** (105.7 mg, 0.4 mmol, 1 eq.) using the donor **1.249** (341 mg, 1.2 mmol, 3 eq.) for 24 h. After following the general water work-up process, no product was obtained from the organic phase. Acidic work-up of the aqueous phase provided 2-ethylhexanoic acid **3.11**[219] (52.3 mg, 91%) as a yellow liquid; Spectral data of the product **3.11** were consistent with previous data of the same compound.

A donor-free blank reaction provided recovery of the starting material **3.10** (91 mg, 87%) only.

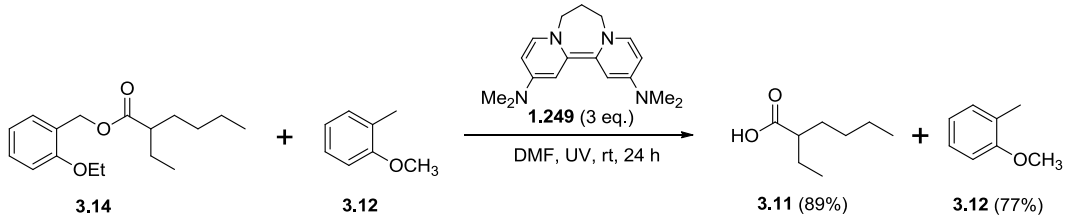
Synthesis of 2-ethoxybenzyl 2-ethylhexanoate 3.14[183]



2-Ethoxybenzyl alcohol **3.13** (0.7609 g, 5 mmol) and pyridine (0.3955 g, 5 mmol) were dissolved in dry diethyl ether (10 mL) in a three-necked flask equipped with a condenser. 2-Ethylhexanoyl chloride **3.9** (0.8133 g, 5 mmol) was added slowly into the reaction flask, which was then refluxed for 2 h. After cooling the solution, water was added to dissolve pyridinium salts and the aqueous phase was discarded. The ether phase was

washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to yield 2-ethoxybenzyl 2-ethylhexanoate **3.14** (1.2642 g, 91%) as a colourless liquid; [Found: (ESI^+) $(M+NH_4)^+$ 296.2221. $C_{17}H_{30}NO_3$ $(M+NH_4)$ requires 296.2220]; ν_{max}(film) /cm^{-1} 3043, 2961, 2875, 1732, 1605, 1496, 1247, 1170, 1048, 751; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.87-0.94 [6H, m, C*H*$_3$CH$_2$CH(CH$_2$)$_3$C*H*$_3$], 1.27-1.33 (4H, m, CHCH$_2$(C*H*$_2$)$_2$CH$_3$), 1.43 (3H, t, *J* = 6.8 Hz, ArOCH$_2$C*H*$_3$), 1.51-1.59 (2H, m, CHC*H*$_2$(CH$_2$)$_2$CH$_3$), 1.65-1.70 (2H, m, CH$_3$C*H*$_2$CH(CH$_2$)$_3$CH$_3$), 2.33-2.37 (1H, m, OC(O)C*H*), 4.08 (2H, q, *J* = 7.2 Hz, ArOC*H*$_2$CH$_3$), 5.21 (2H, s, ArC*H*$_2$O), 6.89 (1H, d, *J* = 8.4 Hz, ArH), 6.96 (1H, dt, *J* = 7.6, 0.8 Hz, ArH), 7.27-7.32 (1H, m, ArH), 7.35 (1H, dd, *J* = 7.6, 1.6 Hz, ArH) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 12.0 (CH_3), 14.0 (CH_3), 14.9 (CH_3), 22.8 (CH_2), 25.6 (CH_2), 29.7 (CH_2), 31.9 (CH_2), 47.5 (CH), 61.6 (CH_2), 63.7 (CH_2), 111.4 (CH), 120.3 (CH), 124.9 (C), 129.4 (CH), 129.6 (CH), 157.0 (C), 176.5 (C=O); *m/z* (ESI^+) 296 [$(M+NH_4)^+$, 4%], 205 (6), 165 (9), 135 (100).

UV-activated reduction of mixture of 2-ethoxybenzyl 2-ethylhexanoate 3.14 and 1-methoxy-2-methylbenzene 3.12, a specially designed reaction

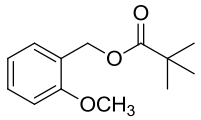


The general procedure for electron transfer reactions under UV conditions was applied to mixture of 2-ethoxybenzyl 2-ethylhexanoate **3.14** (111 mg, 0.4 mmol, 1 eq.) and 1-methoxy-2-methylbenzene **3.12** (0.048 g, 0.4 mmol) using the donor **1.249** (341 mg, 1.2 mmol, 3 eq.) for 24 h. After following the general water work-up process, the crude material from the organic phase was purified by column chromatography and provided 1-methoxy-2-methylbenzene **3.12**[220] (0.037 g, 77%) as a colourless oil. Acidic work-up of the aqueous phase provided 2-ethylhexanoic acid **3.11**[219] (51.2 mg, 89%) as a yellow liquid. Spectral data of **3.11** were consistent with previous data of the same compound and as reported earlier in this thesis.

For 1-methoxy-2-methylbenzene **3.12**: ν_{max}(film) /cm^{-1} 3022, 2950, 2835, 1602, 1497, 1288, 1245, 1123, 1034, 750; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.24 (3H, s, ArC*H*$_3$), 3.84

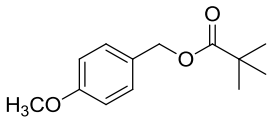
(3H, s, ArOC*H*$_3$), 6.83-6.89 (2H, m, ArH), 7.14-7.20 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 16.3 (CH_3), 55.4 (CH_3), 110.1 (CH), 120.4 (CH), 126.7 (C), 126.9 (CH), 130.7 (CH), 157.9 (C). Spectral data of **3.12** were consistent with the literature data of the same compound.[220]

Synthesis of 2-methoxybenzyl pivalate 3.24[183]



2-Methoxybenzyl alcohol **3.8** (0.6908 g, 5 mmol) and pyridine (0.3955 g, 5 mmol) were dissolved in diethyl ether (10 mL) in a three-necked flask equipped with a condenser. Trimethylacetyl chloride **3.80** (0.602 g, 5 mmol) was added slowly into the reaction flask, which was then refluxed for 2 h. After cooling the solution, water was added to dissolve pyridinium salts and the aqueous phase was discarded. The ether phase was washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to yield 2-methoxybenzyl pivalate **3.24** (0.941 g, 85%) as a colourless liquid; [Found: (ESI$^+$) $(M+H)^+$ 223.1325. $C_{13}H_{19}O_3$ (M+H) requires 223.1329]; ν_{max}(film) /cm^{-1} 2971, 2843, 1728, 1605, 1465, 1248, 1152, 1031, 753; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.25 [9H, s, C(C*H*$_3$)$_3$], 3.84 (3H, s, ArOC*H*$_3$), 5.17 (2H, s, ArC*H*$_2$O), 6.89 (1H, d, J = 8.0 Hz, ArH), 6.96 (1H, dt, J = 7.6, 0.8 Hz, ArH), 7.28-7.33 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.4 (CH_3), 39.0 (C), 55.5 (CH_3), 61.8 (CH_2), 110.5 (CH), 120.5 (CH), 125.0 (C), 128.8 (CH), 129.2 (CH), 157.4 (C), 178.5 (C=O); *m/z* (EI$^+$) 222 [M$^+$, 46%], 137 (27), 121 (100), 93 (10), 91 (60), 57 (16).

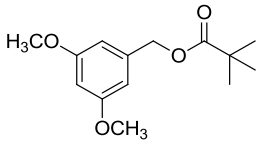
Synthesis of 4-methoxybenzyl pivalate 3.25[221]



(4-Methoxyphenyl)methanol **1.350** (0.828 g, 6 mmol) and pyridine (0.475 g, 6 mmol) were dissolved in dry diethyl ether (10 mL) in a three-necked flask equipped with a condenser. Trimethylacetyl chloride **3.80** (0.723 g, 6 mmol) was added slowly into the reaction flask, which was then refluxed for 2 h. After cooling the solution, water was

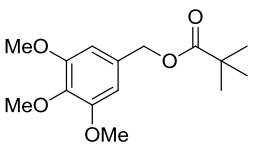
added to dissolve pyridinium salts and the aqueous phase was discarded. The ether phase was washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to yield 4-methoxybenzyl pivalate **3.25** (1.136 g, 85%) as a colourless liquid; [Found: (ESI^+) $(M+NH_4)^+$ 240.1595. $C_{13}H_{22}NO_3$ $(M+NH_4)$ requires 240.1594]; ν_{max}(film) /cm^{-1} 2972, 2838, 1728, 1615, 1516, 1480, 1249, 1149, 1035, 822; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.21 [9H, s, C(C*H*$_3$)$_3$], 3.82 (3H, s, ArOC*H*$_3$), 5.05 (2H, s, ArC*H*$_2$O), 6.89 (2H, d, J = 8.8 Hz, ArH), 7.28 (2H, d, J = 8.8 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.3 (CH_3), 38.9 (C), 55.4 (CH_3), 66.0 (CH_2), 114.0 (CH), 128.7 (C), 129.7 (CH), 159.6 (C), 178.6 (C=O); *m/z* (ESI^+) 240 [$(M+NH_4)^+$, 100%], 149 (20).

Synthesis of 3,5-dimethoxybenzyl pivalate 3.26[183]



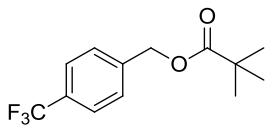
(3,5-Dimethoxyphenyl)methanol **3.58** (0.840 g, 5 mmol) and pyridine (0.3955 g, 5 mmol) were dissolved in dry diethyl ether (10 mL) in a three-necked flask equipped with a condenser. Trimethylacetyl chloride **3.80** (0.602 g, 5 mmol) was added slowly into the reaction flask, which was then refluxed for 2 h. After cooling the solution, water was added to dissolve pyridinium salts and the aqueous phase was discarded. The ether phase was washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (15% diethyl ether in petroleum ether) to yield 3,5-dimethoxybenzyl pivalate **3.26** (1.114 g, 88%) as a colourless liquid; [Found: (ESI^+) $(M+H)^+$ 253.1430. $C_{14}H_{21}O_4$ (M+H) requires 253.1434]; ν_{max}(film) /cm^{-1} 2961, 2841, 1729, 1599, 1463, 1154, 1069, 834; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.25 [9H, s, C(C*H*$_3$)$_3$], 3.80 (6H, s, ArOC*H*$_3$), 5.06 (2H, s, ArC*H*$_2$O), 6.40-6.41 (1H, m, ArH), 6.49 (2H, d, J = 2.4 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.3 (CH_3), 28.9 (C), 55.4 (CH_3), 65.9 (CH_2), 99.9 (CH), 105.4 (CH), 138.9 (C), 161.0 (C), 178.3 (C=O); *m/z* (ESI^+) 270 [$(M+NH_4)^+$, 18%], 253 [$(M+H)^+$, 100%], 217 (5), 151 (48).

Synthesis of 3,4,5-trimethoxybenzyl pivalate 3.27[222]



3,4,5-Trimethoxybenzyl alcohol (1.0901 g, 5.5 mmol) and pyridine (0.434 g, 5.5 mmol) were dissolved in dry diethyl ether (10 mL) in a three-necked flask equipped with a condenser. Trimethylacetyl chloride **3.80** (0.602 g, 5 mmol) was added slowly into the reaction flask, which was then refluxed for 2 h. After cooling the solution, water was added to dissolve pyridinium salts and the aqueous phase was discarded. The ether phase was washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (40% diethyl ether in petroleum ether) to yield 3,4,5-trimethoxybenzyl pivalate **3.27** (1.126 g, 80%) as a colourless liquid; [Found: (CI^+ corona) $(M+NH_4)^+$ 300.1807. $C_{15}H_{26}NO_5$ $(M+NH_4)$ requires 300.1805]; ν_{max}(film) /cm^{-1} 2960, 2939, 2839, 1724, 1591, 1508, 1458, 1236, 1143, 1122, 1006, 823; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.25 [9H, s, C(C*H*$_3$)$_3$], 3.85 (3H, s, ArOC*H*$_3$), 3.87 (6H, s, ArOC*H*$_3$), 5.06 (2H, s, ArC*H*$_2$O), 6.56 (2H, s, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.2 (CH_3), 38.8 (C), 56.1 (CH_3), 60.8 (CH_3), 66.1 (CH_2), 104.6 (CH), 132.2 (C), 137.6 (C), 153.3 (C), 178.3 (C=O); *m/z* (ESI^+) 582 $[(2M+NH_4)^+$, 10%], 300 $[(M+NH_4)^+$, 38%], 181 (100).

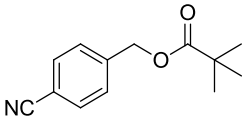
Synthesis of 4-(trifluoromethyl)benzyl pivalate 3.31[221]



4-(Trifluoromethyl)benzyl alcohol **1.347** (0.968 g, 5.5 mmol) and pyridine (0.434 g, 5.5 mmol) were dissolved in diethyl ether (10 mL) in a three-necked flask equipped with a condenser. Trimethylacetyl chloride **3.80** (0.602 g, 5 mmol) was added slowly into the reaction flask, which was then refluxed for 2 h. After cooling the solution, water was added to dissolve pyridinium salts and the aqueous phase was discarded. The ether phase was washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (20% diethyl ether in petroleum ether) to yield 4-(trifluoromethyl)benzyl pivalate **3.31** (0.966 g, 74%) as a colourless liquid; [Found: (CI^+ corona) $(M+NH_4)^+$ 278.1361. $C_{13}H_{19}F_3NO_2$ $(M+NH_4)$ requires 278.1362]; ν_{max}(film) /cm^{-1} 2974, 2908, 2875, 1732, 1622, 1481, 1323, 1280, 1122, 1064, 1018, 821; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.25 [9H, s, C(C*H*$_3$)$_3$], 5.17 (2H, s, ArC*H*$_2$O), 7.46 (2H, d, J = 8.0 Hz, ArH), 7.30 (2H, d, J = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.3 (CH_3), 38.9 (C), 65.2 (CH_2), 124.0 (q, J_{CF} = 271 Hz, CF_3), 125.6 (q,

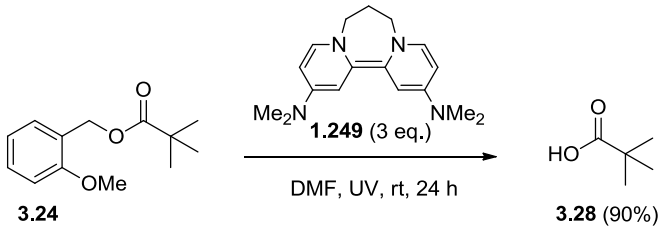
J_{CF} = 4 Hz, CH), 127.8 (CH), 130.2 (q, J_{CF} = 32 Hz, C), 140.6 (C), 178.2 (C=O); *m/z* (ESI^+) 278 [$(M+NH_4)^+$, 7%], 261 [$(M+H)^+$, 100%], 159 (69).

Synthesis of 4-cyanobenzyl pivalate 3.32[221]



4-(Hydroxymethyl)benzonitrile **2.91** (0.665 g, 5 mmol) and pyridine (0.395 g, 5 mmol) were dissolved in dry diethyl ether (10 mL) in a three-necked flask equipped with a condenser. Trimethylacetyl chloride **2.128** (0.602 g, 5 mmol) was added slowly into the reaction flask, which was then refluxed for 2 h. After cooling the solution, water was added to dissolve pyridinium salts and the aqueous phase was discarded. The ether phase was washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (15% diethyl ether in petroleum ether) to yield 4-cyanobenzyl pivalate **3.32** (0.878 g, 81%) as a colourless liquid; [Found: (ESI^+) $(M+NH_4)^+$ 235.1436. $C_{13}H_{19}N_2O_2$ $(M+NH_4)$ requires 235.1441]; ν_{max}(film) /cm^{-1} 2975, 2843, 2230, 1732, 1480, 1281, 1144, 1035, 819; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.25 [9H, s, $C(CH_3)_3$], 5.16 (2H, s, $ArCH_2O$), 7.45 (2H, d, J = 8.4 Hz,ArH), 7.65 (2H, d, J = 8.4 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.2 (CH_3), 38.9 (C), 65.0 (CH_2), 111.9 (CN), 118.7 (C), 128.0 (CH), 132.5 (CH), 141.9 (C), 178.1 (C=O); *m/z* (ESI^+) 235 [$(M+NH_4)^+$, 100%].

UV-activated reduction of 2-methoxybenzyl pivalate 3.24



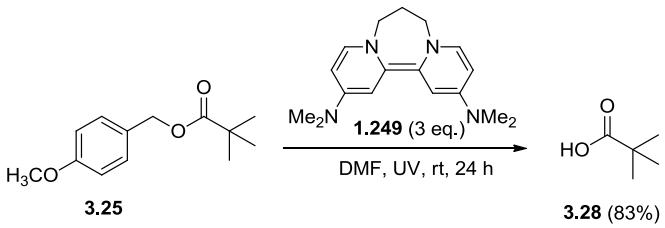
Donor-free blank, with UV : 90% recovery of **3.24**
UV-free blank, with donor : 92% recovery of **3.24**

The general procedure for electron transfer reactions under UV conditions was applied to 2-methoxybenzyl pivalate **3.24** (133.3 mg, 0.6 mmol, 1 eq.) using the donor **1.249** (511 mg, 1.8 mmol, 3 eq.) for 24 h. After following the general water work-up process, no product was obtained from the organic phase. Acidic work-up of the aqueous phase

provided pivalic acid **3.28**[223] (55 mg, 90%) as a white low melting crystalline solid m.p. 33-35 ^{o}C; (lit.[223]: 34 ^{o}C); [Found: (ESI^{+}) $(M)^{+}$ 102.0675. $C_5H_{10}O_2$ (M) requires 102.0675]; ν_{max}(film) /cm^{-1} 3400-2500, 2974, 1708, 1484, 1305, 939; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.24 (9H, s, $(CH_3)_3$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.1 (CH_3), 38.7 (C), 185.6 (CO_2H); *m/z* (EI^{+}) 102 [M^{+}, 7%], 87 (15), 59 (15), 57 (100), 45 (34), 41 (92), 39 (37).

Donor-free and UV-free blank reactions provided recovery of the starting material **3.24** (120.5 mg, 90%) and (122.4 mg, 92%), respectively.

UV-activated reduction of 4-methoxybenzyl pivalate 3.25

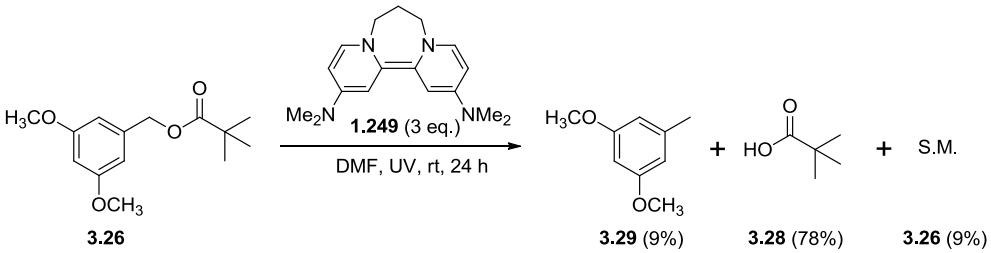


Donor-free blank reaction: 88% recovery of **3.25**

The general procedure for electron transfer reactions under UV conditions was applied to 4-methoxybenzyl pivalate **3.25** (88.8 mg, 0.4 mmol, 1 eq.) using the donor **1.249** (341 mg, 1.2 mmol, 3 eq.) for 24 h. After following the general water work-up process, no product was obtained from the organic phase. Acidic work-up of the aqueous phase provided pivalic acid **3.28**[223] (33.1 mg, 83%) as a white low melting crystalline solid. Spectral data of **3.28** were consistent with the previous data of the same compound and as previously reported in this thesis.

A donor-free blank reaction provided recovery of the starting material **3.25** (78 mg, 88%) only.

UV-activated reduction of 3,5-dimethoxybenzyl pivalate 3.26



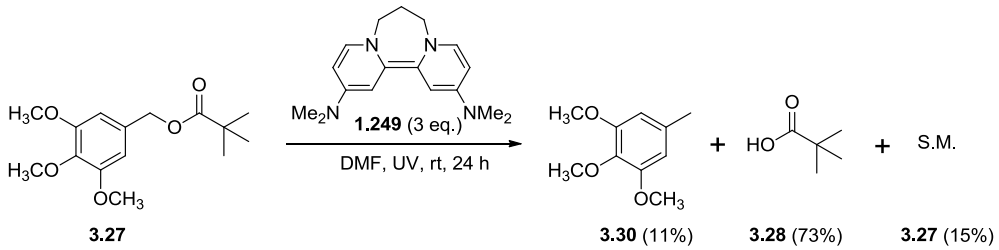
Donor-free blank reaction: 89% recovery of **3.26**

The general procedure for electron transfer reactions under UV conditions was applied to 3,5-dimethoxybenzyl pivalate **3.26** (100.9 mg, 0.4 mmol, 1 eq.) using the donor **1.249** (341 mg, 1.2 mmol, 3 eq.) for 24 h. After following the general water work-up process, the crude material from the organic phase was purified by column chromatography (5% diethyl ether in petroleum ether) and provided 1,3-dimethoxy-5-methylbenzene **3.29**[224] (56 mg, 9%) and starting material **3.26** (9 mg, 9%) as colourless oils. Acidic work-up of the aqueous phase provided pivalic acid **3.28**[223](31.9 mg, 78%) as a white low melting crystalline solid. Spectral data of **3.28** were consistent with the previous data of the same compound and as previously reported in this thesis.

For 1,3-dimethoxy-5-methylbenzene **3.29**: [Found: (ESI^+) $(M)^+$ 152.0833. $C_9H_{12}O_2$ (M) requires 152.0832]; ν_{max}(film) /cm^{-1} 2999, 2939, 2838, 1597, 1460, 1205, 1150, 1069, 828; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.31 (3H, s, ArCH_3), 3.78 (6H, s, ArOCH_3), 6.30 (1H, t, J = 2.0 Hz, ArH), 6.35 (2H, d, J = 2.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.9 (CH_3), 55.4 (CH_3), 97.7 (CH), 107.3 (CH), 140.4 (C), 160.9 (C); *m/z* (EI^+) 152 [M^+, 100%], 137 (10), 123 (48), 109 (17), 92 (9), 91 (21), 79(16), 51 (9).

A donor-free blank reaction provided recovery of the starting material **3.26** (89.3 mg, 89%) only.

UV-activated reduction of 3,4,5-trimethoxybenzyl pivalate 3.27



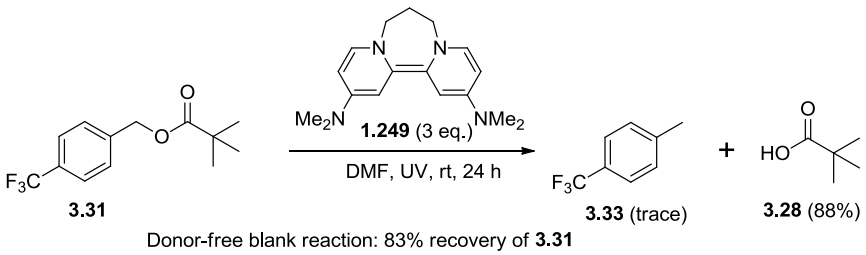
Donor-free blank reaction: 91% recovery of **3.27**

The general procedure for electron transfer reactions under UV conditions was applied to 3,4,5-trimethoxybenzyl pivalate **3.27** (113 mg, 0.4 mmol) using the donor **1.249** (341 mg, 1.2 mmol, 3 eq.) for 24 h. After following the general water work-up process, the crude material was purified by column chromatography and provided 1,2,3-trimethoxy-5-methylbenzene **3.30**[225] (8.1 mg, 11%) and starting material **3.27** (17.2 mg, 15%) from the organic phase and pivalic acid **3.28** (29.7 mg, 73%) from the acidic work-up of the aqueous phase. Spectral data of product **3.28** were consistent with previous data of the same compound.

For 1,2,3-trimethoxy-5-methylbenzene **3.30**[225]: ν_{max}(film) /cm^{-1} 2998, 2939, 2837, 1589, 1465, 1415, 1330, 1238, 1129, 1010, 778; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.33 (3H, s, ArC*H*$_3$), 3.83 (3H, s, ArOC*H*$_3$), 3.86 (6H, s, ArOC*H*$_3$), 6.40 (2H, s, ArH). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 22.0 (CH_3), 56.1 (CH_3), 61.0 (CH_3), 106.0 (CH), 133.7 (C), 135.8 (C), 153.1 (C); Spectral data of this compound were consistent with the literature data of the same compound.[225]

A donor-free blank reaction provided recovery of the starting material **3.27** (103.2 mg, 91%) only.

UV-activated reduction of 4-(trifluoromethyl)benzyl pivalate 3.31

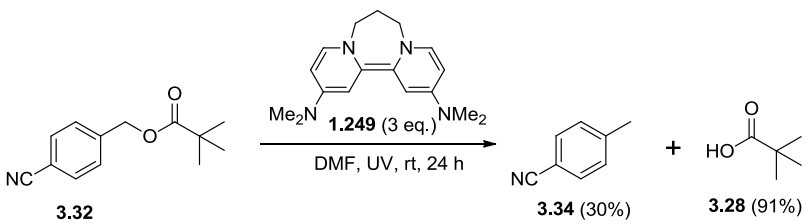


Donor-free blank reaction: 83% recovery of **3.31**

The general procedure for electron transfer reactions under UV conditions was applied to 4-(trifluoromethyl)benzyl pivalate **3.31** (104 mg, 0.4 mmol) using the donor **1.249** (341 mg, 1.2 mmol, 3 eq.) for 24 h. After following the general water work-up process, trace amount of 1-methyl-4-(trifluoromethyl)benzene **3.33** was seen in the ^{1}H-NMR of the crude product from the organic phase (singlet peak at δ = 2.44 representing ArC*H*$_3$). Acidic work-up of the aqueous phase provided pivalic acid **3.28** (36 mg, 88%). Spectral data of product **3.28** were consistent with previous data of the same compound.

A donor-free blank reaction provided recovery of the starting material **3.31** (86.7 mg, 83%) only.

UV-activated reduction of 4-cyanobenzyl pivalate 3.32

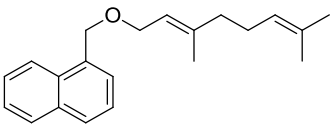


Donor-free blank reaction: 91% recovery of **3.32**

The general procedure for electron transfer reactions under UV conditions was applied to 4-cyanobenzyl pivalate **3.32** (86 mg, 0.4 mmol, 1 eq.) using the donor **1.249** (341 mg, 1.2 mmol, 3 eq.) for 24 h. After following the general water work-up process, the crude material from the organic phase was purified by column chromatography and provided 4-methylbenzonitrile **3.34**[226] (0.014 g, 30%) as a white low melting solid. Acidic work-up of the aqueous phase provided pivalic acid **3.28**[223] (37 mg, 91%) as a white low melting crystalline solid. For 4-methylbenzonitrile **3.34**: m.p. 25-26 ^{o}C; (lit.:[226] 26-27 ^{o}C); [Found: (ESI^{+}) $(M)^{+}$ 117.0574. C_8H_7N (M) requires 117.0573]; ν_{max}(film) /cm^{-1} 3038, 2925, 2229, 1605, 1509, 817; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.43 (3H, s, ArC*H*$_3$), 7.28 (2H, d, J = 8.0 Hz, ArH), 7.55 (2H, d, J = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 22.0 (CH_3), 109.4 (CN), 119.3 (C), 130.0 (CH), 132.2 (CH), 143.8 (C); *m/z* (CI^{+}) 135 [$(M+NH_4)^{+}$, 100%], 116 (5), 89 (3). Spectral data of **3.28** were consistent with previous data of the same compound.

A donor-free blank reaction provided recovery of the starting material **3.32** (78 mg, 91%).

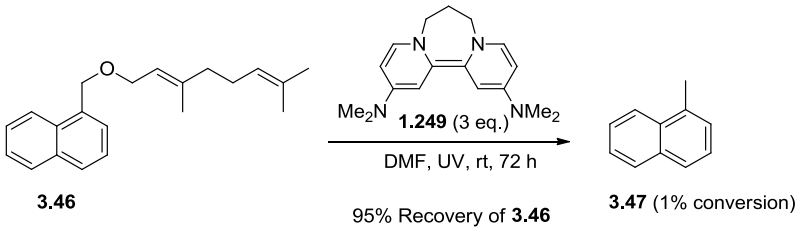
Synthesis of (*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)naphthalene 3.46



A solution of geraniol **3.43** (0.848 g, 5.5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of pre-washed sodium hydride (~95%, stored in glove box, 0.151 g, 6 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-bromomethylnaphthalene **3.45** (1.1 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% ethyl acetate in petroleum ether) to yield (*E*)-1-(((7-methylocta-2,6-dien-1-yl)oxy)methyl)naphthalene **3.46**[183] (1.137 g, 77%) as a yellow oil; [Found: (ESI^{+}) $(M+NH_4)^{+}$ 312.2317, $C_{21}H_{30}NO$ $(M+NH_4)$ requires 312.2322]; ν_{max}(film) /cm^{-1} 3047, 2915, 2855, 1444, 1068, 776; ^{1}H-NMR (400.13 MHz, $CDCl_3$) δ 1.63 [3H, s,

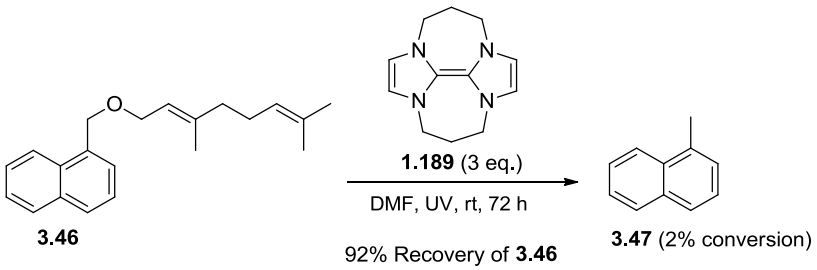
=C(CH_3)(CH_3)], 1.69 [3H, s, =C(CH_3)(CH_3)], 1.71 [3H, d, *J* = 0.8 Hz, OCH_2CH=C(CH_3)(CH_2)], 2.07-2.16 (4H, m, =C(CH_3)CH_2CH_2CH=), 4.14 [2H, d, *J* = 8.0 Hz, OCH_2CH=C(CH_3)(CH_2)], 4.98 (2H, s, ArCH_2OCH_2), 5.12-5.16 [1H, m, CH_2C*H*=C(CH_3)(CH_3)], 5.46-5.50 [1H, m, OCH_2C*H*=C(CH_3)(CH_2)], 7.43-7.58 (4H, m, ArH), 7.83 (1H, d, *J* = 8.0 Hz, ArH) 7.88 (1H, dd, *J* = 7.6, 1.6 Hz, ArH), 8.17 (1H, dd, *J* = 7.6 Hz, 1.2 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 16.6 (CH_3), 17.8 (CH_3), 25.8 (CH_3), 26.5 (CH_2), 29.7 (CH_2), 66.7 (CH_2), 70.4 (CH_2), 120.9 (CH), 124.1 (CH), 124.2 (CH), 125.2 (CH), 125.8 (CH), 126.2 (CH), 126.6 (CH), 128.3 (2 x CH), 131.7 (C), 131.9 (C), 133.8 (C), 134.1 (C), 140.6 (C); *m/z* (ESI$^+$) 312 [(M+NH_4)$^+$, 100%], 277 (5), 242 (6), 137 (6).

UV-activated reduction of *(E)*-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)naphthalene 3.46 using the donor 1.249



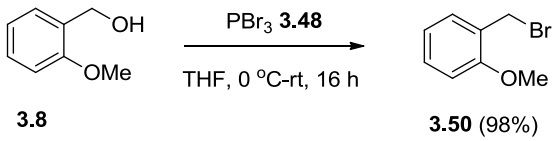
The general procedure for electron transfer reactions under UV conditions was applied to *(E)*-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)naphthalene **3.46** (88 mg, 0.3 mmol) using the donor **1.249** (255 mg, 0.9 mmol, 3 eq.) for 72 h. After following the general water work-up process, the solvent was evaporated under reduced pressure to provide crude product. ^{1}H-NMR spectrum of the crude reaction mixture was compared with that of 1-methylnaphthalene **3.47**[181] and the peak at δ = 2.74 (representing the methyl group) exactly matched and a 1% conversion of starting material **3.46** to **3.47** was recorded. The crude product was then purified by column chromatography (10% diethyl ether in petroleum ether) and provided starting material **3.46** (84 mg, 95%) only.

UV-activated reduction of *(E)*-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)naphthalene 3.46 using the DBD 1.189



The general procedure for electron transfer reactions under UV conditions was applied to *(E)*-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)naphthalene **3.46** (88 mg, 0.3 mmol) using the DBD **1.189** (194 mg, 0.9 mmol, 3 eq.). After following the general water work-up process, the solvent was evaporated under reduced pressure to provide crude product. The ^{1}H-NMR spectrum of the crude reaction mixture was compared with that of 1-methylnaphthalene **3.47**[181] and the peak at δ = 2.74 (representing methyl group) exactly matched and a 2% conversion of starting maerial **3.46** to **3.47** was recorded. The crude product was then purified by column chromatography (10% diethyl ether in petroleum ether) and provided starting material **3.46** (81.6 mg, 92%) only.

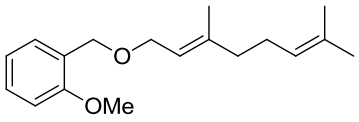
Synthesis of 1-(Bromomethyl)-2-methoxybenzene 3.50[227]



A solution of phosphorus tribromide **3.48** (2.7016 g, 10.0 mmol) was added slowly to the flask containing (2-methoxyphenyl) methanol **3.8** (3.4542 g, 25 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was heated to room temperature and further stirred for 16 h. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The resulting solution was concentrated under reduced pressure using rotary evaporator and provided 1-(bromomethyl)-2-methoxybenzene **3.50**[227] in good yield (4.937 g, 98%) as white solid m.p. 46-48 ^{o}C; (lit.:[227] 47-50 ^{o}C); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.91 (3H, s, OCH_3), 4.59 (2H, s, CH_2Br), 6.88-6.96 (2H, m,

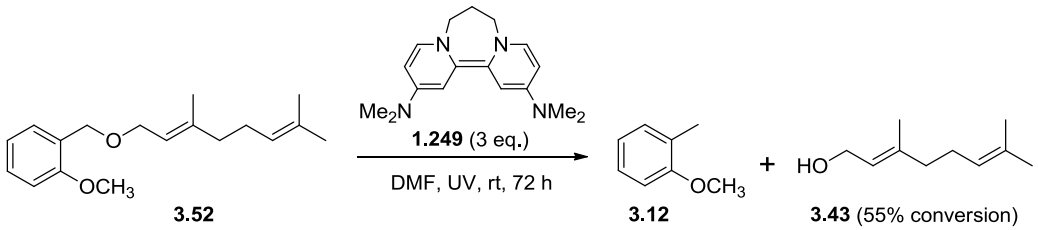
ArH), 7.28-7.38 (2H, m, ArH); A ^{1}H-NMR spectrum of the crude mixture indicated that the formed product **3.50** was almost impurity-free and the data were consistent with the literature data.[227]

Synthesis of (*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-2-methoxybenzene 3.52[183]



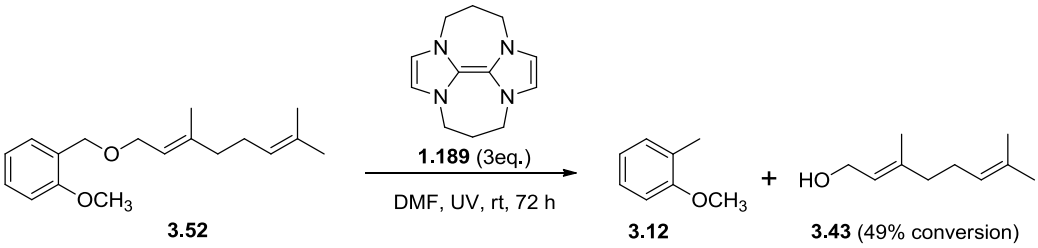
A solution of geraniol **3.43** (1.0797 g, 7.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of pre-washed sodium hydride (~95%, stored in glove box, 0.212 g, 8.4 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-(bromomethyl)-2-methoxybenzene **3.50** (1.4081 g, 7 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (6% ethyl acetate in petroleum ether) to yield (*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-2-methoxybenzene **3.52** (1.4616 g, 76%) as a colourless liquid; [Found: (ESI^{+}) $(M+NH_4)^{+}$ 292.2273. $C_{18}H_{30}NO_2$ $(M+NH_4)$ requires 292.2271]; ν_{max}(film) /cm^{-1} 3025, 2917, 2855, 1603, 1493, 1242, 1077, 753; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.63 [3H, s, =C(CH_3)(CH_3)], 1.68 [3H, s, =C(CH_3)(CH_3)], 1.70 [3H, d, J = 0.8 Hz, OCH_2CH=C(CH_3)(CH_2)], 2.05-2.16 (4H, m, =C(CH_3)CH_2CH_2CH=), 3.85 (3H, s, ArOCH_3), 4.10 [2H, d, J = 5.6 Hz, OCH_2CH=C(CH_3)(CH_2)], 4.57 (2H, s, ArC$H_2$$OCH_2$), 5.11-5.15 [1H, m, CH_2CH=C(CH_3)(CH_3)], 5.43-5.46 [1H, m, OCH_2CH=C(CH_3)(CH_2)], 6.80 (1H, d, J = 6.4 Hz, ArH), 6.95-6.98 (1H, m, ArH), 7.25-7.29 (1H, m, ArH), 7.14-7.39 (1H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 16.5 (CH_3), 17.7 (CH_3), 25.7 (CH_3), 26.5 (CH_2), 39.7 (CH_2), 55.3 (CH_3), 66.8 (CH_2), 67.0 (CH_2), 110.2 (CH), 120.5 (CH), 121.3 (CH), 124.2 (C), 127.1 (CH), 128.6 (CH), 129.1 (CH), 131.6 (C), 140.0 (C), 157.2 (C); *m/z* (ESI^{+}) 292 [$(M+NH_4)^{+}$, 100%], 257 (62), 153 (5), 137 (30).

Initial results: UV-activated reduction of (((*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-2-methoxybenzene 3.52 with the donor 1.249



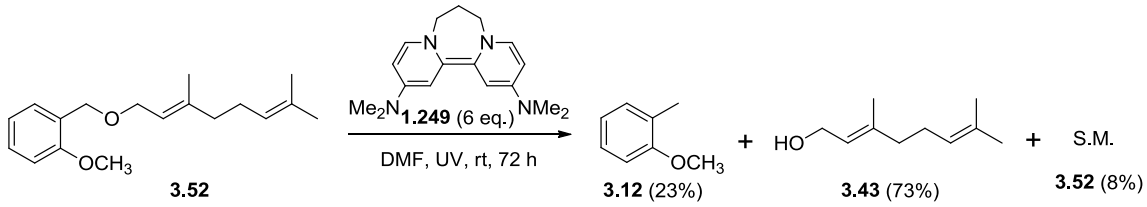
The general procedure for electron transfer reactions under UV conditions was applied to (*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-2-methoxybenzene **3.52** (82.3 mg, 0.3 mmol) using the donor **1.249** (255 mg, 0.9 mmol, 3 eq.) for 72 h. After following the general water work-up process, the crude material was obtained. From the ^{1}H-NMR spectrum of the crude product, it was observed that the reaction gave a 55% conversion of starting material **3.52** to geraniol **3.43** [calculated from the relative integration of the doublets at δ = 4.10 ($ArCH_2OCH_2$, in **3.52**) to δ = 4.16 ($HOCH_2$, **3.43**)]. No attempt was made to isolate the products from this reaction.

Initial results: UV-activated reduction of (((*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-2-methoxybenzene 3.52 with DBD 1.189



The general procedure for electron transfer reactions under UV conditions was applied to (*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-2-methoxybenzene **3.52** (82.3 mg, 0.3 mmol) using the donor **1.189** (194 mg, 0.9 mmol, 3 eq.) for 72 h. After following the general water work-up process, the crude material was obtained. From the ^{1}H-NMR spectrum of the crude product, it was observed that the reaction gave a 49% conversion of starting material **3.52** to geraniol **3.43** [calculated from the relative integration of the doublets at δ = 4.10 ($ArCH_2OCH_2$, in **3.52**) to δ = 4.16 ($HOCH_2$, **3.43**)]. No attempt was made to isolate the products from this reaction.

UV-activated reduction of (((*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-2-methoxybenzene 3.52



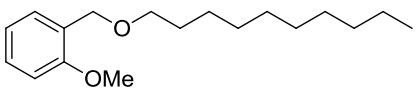
Donor-free UV-active blank reaction: 89% recovery of **3.52**

The general procedure for electron transfer reactions under UV conditions was applied to (*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-2-methoxybenzene **3.52** (109 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-up process, the crude material was purified by column chromatography (5% and then 30% diethyl ether in petroleum ether) and provided 1-methoxy-2-methylbenzene **3.12**[220] (11.2 mg, 23%), geraniol **3.43**[218] (40.6 mg, 73%) and starting material **3.52** (9 mg, 8%) as colourless oils. For geraniol **3.43**: [Found: (CI^+) (M^+) 154.1350. $C_{10}H_{18}O$ (M^+) requires 154.1352]; ν_{max}(film)/cm^{-1} 3337, 2966, 2917, 1668, 1441, 998; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.61 [3H, s, =C(C*H*$_3$)CH_2CH_2], 1.69 [6H, s, CH=C(C*H*$_3$)(*CH*$_3$)], 2.03-2.14 (4H, m, =C(CH_3)C*H*$_2$*CH*$_2$), 4.16 (2H, d, *J* = 5.2 Hz, HOC*H*$_2$), 5.09-5.12 [1H, m, CH_2C*H*=C(CH_3)(CH_3)], 5.45 (1H, m, HOCH_2C*H*=); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 16.4 (CH_3), 17.8 (CH_3), 25.8 (CH_3), 26.5 (CH_2), 39.7 (CH_2), 59.5 (CH_2), 123.5 (CH), 124.0 (CH), 131.8 (C), 139.8 (C); *m/z* (CI^+) 154 [M^+, 98%], 137 (100), 81 (32).

For 1-methoxy-2-methylbenzene **3.12**: [Found: (ESI^+) $(M)^+$ 122.0725. $C_8H_{10}O$ (M) requires, 122.0726]; ν_{max}(film) /cm^{-1} 3022, 2950, 2835, 1602, 1497, 1288, 1245, 1123, 1034, 750; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.24 (3H, s, ArC*H*$_3$), 3.84 (3H, s, ArOC*H*$_3$), 6.83-6.89 (2H, m, ArH), 7.14-7.20 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 16.3 (CH_3), 55.4 (CH_3), 110.1 (CH), 120.4 (CH), 126.7 (C), 126.9 (CH), 130.7 (CH), 157.9 (C); *m/z* (CI^+) 123 (16), 122 [M^+, 100%], 107 (8), 91 (7), 78 (3).

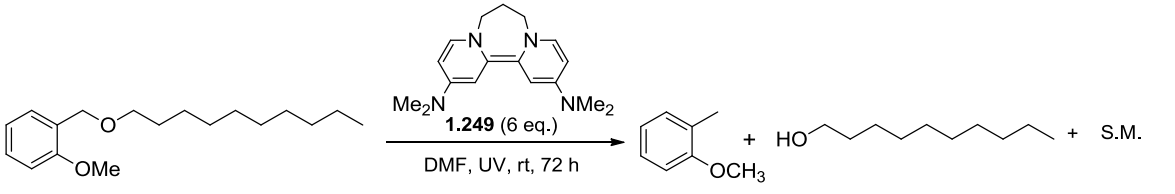
A donor-free blank reaction provided recovery of the starting material **3.52** (97 mg, 89%) only.

Synthesis of 1-((decyloxy)methyl)-2-methoxybenzene 3.53[228]



A solution of 1-decanol **3.54** (1.266 g, 8.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of pre-washed sodium hydride (~95%, stored in glove box, 0.242 g, 9.6 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-(bromomethyl)-2-methoxybenzene **3.50** (1.609 g, 8 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (6% ethyl acetate in petroleum ether) to yield 1-((decyloxy)methyl)-2-methoxybenzene **3.53** (1.8216 g, 82%) as a colourless liquid; [Found: (ESI^{+}) $(M+NH_4)^{+}$ 296.2585. $C_{18}H_{34}NO_2$ $(M+NH_4)$ requires 296.2584]; ν_{max}(film)/cm^{-1} 3023, 2926, 2854, 1604, 1494, 1243, 1098, 752; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.90-0.88 [3H, m, $O(CH_2)_9CH_3$], 1.27-1.39 (14H, m, $O(CH_2)_2(CH_2)_7CH_3$), 1.61-1.67 (2H, m, $OCH_2CH_2(CH_2)_7CH_3$) , 3.51 (2H, t, J = 5.2 Hz, $OCH_2(CH_2)_8CH_3$), 3.84 (3H, s, $ArOCH_3$), 4.55 (2H, s, $ArCH_2O$), 6.87 (1H, d, J = 6.8 Hz, ArH), 6.96 (1H, td, J = 6.4, 0.8 Hz, ArH), 7.24-7.28 (1H, m, ArH), 7.38 (1H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 26.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 29.8 (CH_2), 29.9 (CH_2), 32.0 (CH_2), 55.4 (CH_3), 67.6 (CH_2), 70.9 (CH_2), 110.3 (CH), 120.5 (CH), 127.3 (C), 128.5 (CH), 128.8 (CH), 157.1 (C); *m/z* (ESI^{+}) 296 [$(M+NH_4)^{+}$, 100%], 279 (4), 241 (6).

UV-activated reduction of 1-((decyloxy)methyl)-2-methoxybenzene 3.53



3.53 **3.12** (20%) **3.54** (71%) **3.53** (8%)

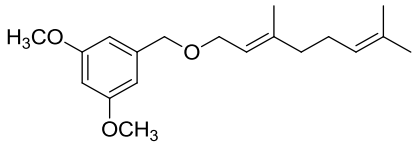
Donor-free blank reaction : 91% recovery of **3.53**

The general procedure for electron transfer reactions under UV conditions was applied to 1-((decyloxy)methyl)-2-methoxybenzene **3.53** (111 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.). After following the general water work-up process, the crude material was purified by column chromatography (5% and then 30% diethyl ether in petroleum ether) and provided 1-methoxy-2-methylbenzene **3.12** (9.6 mg, 20%), 1-decanol **3.54**[53] (45.1 mg, 71%) and starting material **3.53** (9 mg, 8%) as colourless oils. Spectral data of 1-methoxy-2-methylbenzene **3.12** were consistent with the previous data of the same compound, reported in this thesis.

For 1-decanol **3.54**: [Found: (ESI$^+$) $(M+NH_4)^+$ 176.2011. $C_{10}H_{26}NO$ $(M+NH_4)$ requires 176.2009]; ν_{max}(film) /cm^{-1} 3307, 2925, 2855, 1466, 1057, 721; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.88-0.90 [3H, m, $HO(CH_2)_9CH_3$], 1.25-1.38 (14H, m, $O(CH_2)_2(CH_2)_7CH_3$), 1.55-1.60 (2H, m, OCH_2CH_2), 3.46 (2H, t, J = 7.0 Hz, $OCH_2(CH_2)_8CH_3$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.9 (CH_2), 25.9 (CH_2), 29.4 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 29.8 (CH_2), 32.0 (CH_2), 32.9 (CH_2), 63.2 (CH_2); *m/z* (CI$^+$) 176 [$(M+NH_4)^+$, 98%], 111 (7), 96 (8), 83 (13), 71 (12), 58 (100).

A donor-free blank reaction provided recovery of the starting material **3.53** (101 mg, 91%) only.

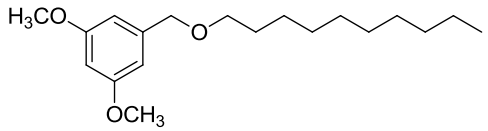
Synthesis of (*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-3,5-dimethoxybenze -ne 3.55[183]



A solution of geraniol **3.43** (0.617 g, 4.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of pre-washed sodium hydride (~95%, stored in glove box, 0.121 g, 4.8 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-(bromomethyl)-3,5-dimethoxybenzene (0.924 g, 4 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified

by column chromatography (8 % diethyl ether in petroleum ether) to yield (*E*)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-3,5-dimethoxybenzene **3.55** (0.896 g, 74%) as a colourless liquid; [Found: (ESI$^+$) $(M+H)^+$ 305.2114. $C_{19}H_{29}O_3$ (M+H) requires 305.2111]; ν_{max}(film) /cm^{-1} 3015, 2916, 2854, 1598, 1462, 1205, 1155, 1066, 831; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.61 [3H, s, =C(CH_3)(CH_3)], 1.66 [3H, s, =C(CH_3)(CH_3)], 1.69 [3H, d, J = 0.8 Hz, OCH_2CH=C(CH_3)(CH_2)], 2.04-2.14 (4H, m, =C(CH_3)CH_2CH_2CH=), 3.80 (6H, s, ArOCH_3), 4.03 [2H, d, J = 6.8 Hz, OCH_2CH=C(CH_3)(CH_2)], 4.46 (2H, s, ArCH_2OCH_2), 5.09-5.13 [1H, m, CH_2CH=C(CH_3)(CH_3)], 5.39-5.43 [1H, m, OCH_2CH=C(CH_3)(CH_2)], 6.39 (1H, t, J = 2.4 Hz, ArH), 6.53 (2H, d, J = 2.4 Hz, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 16.6 (CH_3), 17.7 (CH_3), 25.8 (CH_3), 26.5 (CH_2), 39.7 (CH_2), 55.3 (CH_3), 66.6 (CH_2), 71.9 (CH_2), 99.7 (CH), 105.5 (CH), 120.8 (CH), 124.1 (CH), 131.7 (C), 140.5 (C), 141.2 (C), 160.9 (C); *m/z* (ESI$^+$) 305 [$(M+H)^+$, 100%], 287 (16), 167 (5), 151 (14).

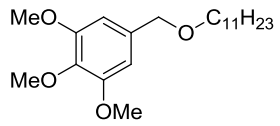
Synthesis of 1-((decyloxy)methyl)-3,5-dimethoxybenzene 3.56[183]



A solution of 1-decanol **3.54** (0.6331 g, 4 mmol) in dry tetrahydrofuran (2mL) was added slowly to the suspension of pre-washed sodium hydride (~95%, stored in glove box, 0.151 g, 6 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-(bromomethyl)-3,5-dimethoxybenzene (0.9247 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to yield 1-((decyloxy)methyl)-3,5-dimethoxybenzene **3.56** (0.967 g, 78%) as a colourless liquid; [Found: (ESI$^+$) $(M+H)^+$ 309.2419. $C_{19}H_{33}O_3$ (M+H) requires 309.2424]; ν_{max}(film) /cm^{-1} 3025, 2926, 2854, 1598, 1465, 1205, 1155, 1067, 832; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.87-0.90 [3H, m, O$(CH_2)_9$CH_3], 1.27-1.38 (14H, m, O$(CH_2)_2$(C$H_2)_7CH_3$), 1.58-1.65 (2H, m, O(CH)(CH_2)$(CH_2)_7CH_3$), 3.46 (2H, t, J = 6.8 Hz, O(CH_2)$(CH_2)_8CH_3$), 3.80 (6H,

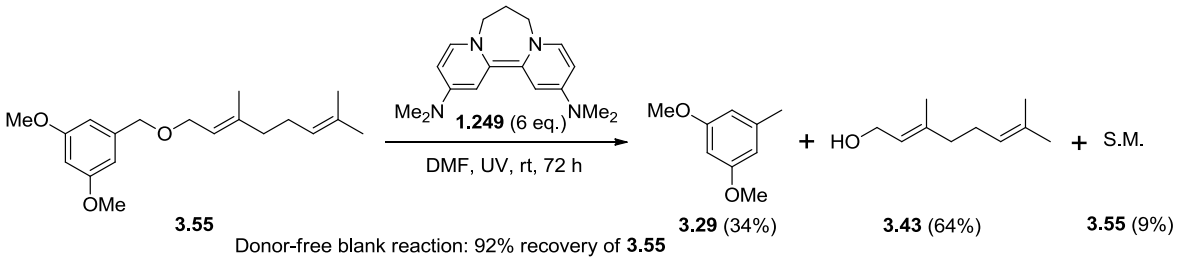
s, ArOC*H*$_3$), 4.46 (2H, s, ArC*H*$_2$O), 6.39 (1H, t, *J* = 2.4 Hz, ArH), 6.51 (2H, d, *J* = 2.4 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 26.4 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 29.8 (CH_2), 29.9 (CH_2), 32.0 (CH_2), 55.4 (CH_3), 70.6 (CH_2), 72.9 (CH_2), 99.6 (CH), 105.4 (CH), 141.3 (C), 161.0 (C); *m/z* (ESI$^+$) 309 [(M+H)$^+$, 100 %], 151 (13).

Synthesis of 1,2,3-trimethoxy-5-((undecyloxy)methyl)benzene 3.57[183]



A solution of 3,4,5-Trimethoxybenzyl alcohol (0.8721 g, 4.4 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.192 g, 4.8 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min. at room temperature and 1-bromoundecane (0.940 g, 4 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h at reflux conditions under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (15% ethyl acetate in hexane) to yield 1,2,3-trimethoxy-5-((undecyloxy)methyl)benzene **3.57** (1.0781 g, 77%) as a colourless liquid; [Found: (CI$^+$ corona) (M+NH_4)$^+$ 370.2952. $C_{21}H_{40}NO_4$ (M+NH_4) requires 370.2952]; ν_{max}(film) /cm^{-1} 2922, 2852, 1591, 1504, 1456, 1232, 1126, 1101, 1010, 823; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 [3H, t, *J* = 7.2 Hz, O(CH_2)$_{10}$C*H*$_3$], 1.23-1.39 (16H, m, O(CH_2)$_2$(C*H*$_2$)$_8$$CH_3$), 1.60-1.67 (2H, m, OC$H_2$C*H*$_2$($CH_2$)$_8$$CH_3$), 3.48 (2H, t, *J* = 6.8 Hz, OC*H*$_2$(CH_2)$_9$$CH_3$), 3.84 (3H, s, ArOC*H*$_3$), 3.87 (6H, s, ArOC*H*$_3$), 4.44 (2H, s, ArC*H*$_2$O), 6.58 (2H, s, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 26.3 (CH_2), 29.4 (CH_2), 29.6 (CH_2), 29.7 (3 x CH_2), 29.9 (CH_2), 32.0 (CH_2), 56.13 (CH_3), 60.9 (CH_3), 70.7 (CH_2), 73.1 (CH_2), 104.6 (CH), 134.5 (C), 137.4 (C), 153.3 (C); *m/z* (CI$^+$ corona) 370 [(M+NH_4)$^+$, 15%], 353 [(M+H)$^+$, 87%], 279 (9), 181 (100).

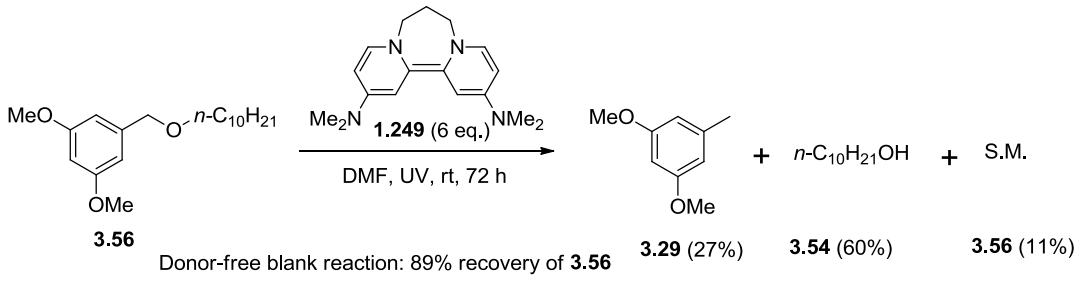
UV-activated reduction of *(E)*-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-3,5-dimethoxybenzene 3.55



The general procedure for electron transfer reactions under UV conditions was applied to *(E)*-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-3,5-dimethoxybenzene **3.55** (121 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-up process, the crude material was purified by column chromatography (5% and then 30% diethyl ether in petroleum ether) and provided 1,3-dimethoxy-5-methylbenzene **3.29**[224] (20.4 mg, 34%), geraniol **3.43** (39.2 mg, 64%) and starting material **3.55** (11 mg, 9%) as colourless oils. Spectral data of the products **3.29** and **3.43** were consistent with the previous data of the same compounds.

A donor-free blank reaction provided recovery of the starting material **3.55** (111 mg, 92%) only.

UV-activated reduction of 1-((decyloxy)methyl)-3,5-dimethoxybenzene 3.56

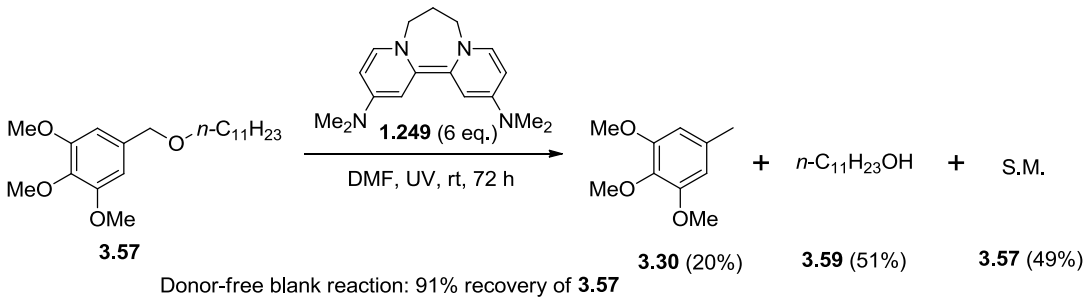


The general procedure for electron transfer reactions under UV conditions was applied to 1-((decyloxy)methyl)-3,5-dimethoxybenzene **3.56** (123 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-up process, the crude material was purified by column chromatography (5% and then 30% diethyl ether in petroleum ether) and provided 1,3-dimethoxy-5-methylbenzene **3.29** (16.5 mg, 27%), 1-decanol **3.54** (38.1 mg, 60%) and starting material **3.56** (13 mg, 11%) as

colourless oils. Spectral data of **3.29** and **3.54** were consistent with the previous data of the same compounds.

A donor-free blank reaction provided recovery of the starting material **3.56** (109 mg, 89%) only.

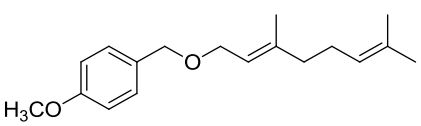
UV-activated reduction of 1,2,3-trimethoxy-5-((undecyloxy)methyl)benzene 3.57



The general procedure for electron transfer reactions under UV conditions was applied to 1,2,3-trimethoxy-5-((undecyloxy)methyl)benzene **3.57** (141 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-up process, the crude material was purified by column chromatography (5% and then 30% diethyl ether in petroleum ether) and provided 1,2,3-trimethoxy-5-methylbenzene **3.30** (20%), starting material **3.57** (49%) and undecan-1-ol **3.59**[229] (32 mg, 51%) from the organic phase. Spectral data of **3.30** were consistent with the previous data of the same compound. For undecan-1-ol **3.59**:[229] ν_{max}(film) /cm^{-1} 3329, 2922, 2852, 1463, 1055, 721; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.89 [3H, t, J = 8.5 Hz, $HO(CH_2)_{10}CH_3$], 1.27-1.39 (16H, m, $HO(CH_2)_2(CH_2)_8CH_3$), 1.54-1.61 (2H, m, $HOCH_2CH_2$), 3.65 (2H, t, J = 8.0 Hz, OCH_2CH_2); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 25.9 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (3 x CH_2), 32.1 (CH_2), 33.0 (CH_2), 63.2 (CH_2). Spectral data of **3.59** were consistent with the literature data of the same compound.[229]

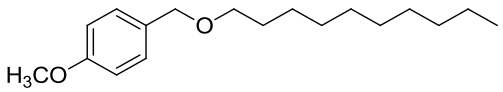
A donor-free blank reaction provided recovery of the starting material **3.56** (128.7 mg, 91%) only.

Synthesis of (E)-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-4-methoxybenzene 368[230]



A solution of geraniol **3.43** (0.617 g, 4.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of pre-washed sodium hydride (~95%, stored in glove box, 0.121 g, 4.8 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-(bromomethyl)-4-methoxybenzene (0.804 g, 4 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to yield *(E)*-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-4-methoxybenzene **3.68** (0.852 g, 78%) as a colourless liquid; [Found: (ESI$^+$) $(M+NH_4)^+$ 292.2267. $C_{18}H_{30}NO_2$ $(M+NH_4)$ requires 292.2271]; ν_{max}(film) /cm^{-1} 3026, 2914, 2854, 1613, 1513, 1442, 1248, 1069, 820; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.61 [3H, s, =C(CH_3)(CH_3)], 1.65 [3H, s, =C(CH_3)(CH_3)], 1.69 [3H, d, J = 1.0 Hz, OCH_2CH=C(CH_3)(CH_2)], 2.04-2.14 (4H, m, =C(CH_3)CH_2CH_2CH=), 3.81 (3H, s, ArOCH_3), 4.01 [2H, d, J = 5.6 Hz, OCH_2CH=C(CH_3)(CH_2)], 4.44 (2H, s, ArCH_2OCH_2), 5.10-5.13 [1H, m, CH_2CH=C(CH_3)(CH_3)], 5.39-5.42 [1H, m, OCH_2CH=C(CH_3)(CH_2)], 6.89 (2H, d, J = 5.6 Hz, ArH), 7.28 (2H, d, J = 5.6 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 16.6 (CH_3), 17.7 (CH_3), 25.8 (CH_3), 26.5 (CH_2), 39.7 (CH_2), 55.3 (CH_3), 66.4 (CH_2), 71.7 (CH_2), 113.9 (CH), 121.1 (CH), 124.1 (CH), 129.5 (CH), 130.8 (C), 131.7 (C), 140.3 (C), 159.3 (C); *m/z* (ESI$^+$) 292 [$(M+NH_4)^+$, 100%], 257 (15), 205 (10), 190 (26), 165 (54).

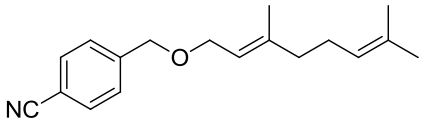
Synthesis of 1-((decyloxy)methyl)-4-methoxybenzene 3.69[228]



A solution of 1-decanol **3.54** (0.791 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of pre-washed sodium hydride (~95%, stored in glove box, 0.151 g, 6 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-(bromomethyl)-4-methoxybenzene (1.005 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL).

The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to yield 1-((decyloxy)methyl)-4-methoxybenzene (1.076 g, 77%) **3.69** as a colourless liquid; [Found: (ESI^+) $(M+NH_4)^+$ 296.2579. $C_{18}H_{34}NO_2$ $(M+NH_4)$ requires 296.2579]; ν_{max}(film)/cm^{-1} 3021, 2926, 2854, 1614, 1513, 1247, 1099, 1038, 820; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.87-0.90 [3H, m, $O(CH_2)_9CH_3$], 1.27-1.36 (14H, m, $O(CH_2)_2(CH_2)_7CH_3$), 1.57-1.62 (2H, m, $O(CH_2)(CH_2)(CH_2)_7CH_3$), 3.44 (2H, t, J = 6.4 Hz, $O(CH_2)(CH_2)_8CH_3$), 3.81 (3H, s, $ArOCH_3$), 4.44 (2H, s, $ArCH_2O$), 6.87-6.89 (2H, m, ArH), 7.26-7.28 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 26.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.71 (CH_2), 29.75 (CH_2), 29.9 (CH_2), 32.0 (CH_2), 55.4 (CH_3), 70.4 (CH_2), 72.6 (CH_2), 113.9 (CH), 129.3 (CH), 131.0 (C), 159.2 (C); *m/z* (ESI^+) 296 [$(M+NH_4)^+$, 97%], 279 (4), 138 (7), 121 (100).

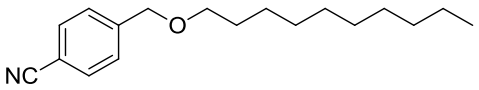
Synthesis of (*E*)-4-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)benzonitrile 3.71[183]



A solution of geraniol **3.43** (0.4627 g, 3.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of pre-washed sodium hydride (~95%, stored in glove box, 0.090 g, 3.6 mmol) in dry tetrahydrofuran (5 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 45 min at room temperature and 4-(bromomethyl)benzonitrile (0.588 g, 3 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (15% diethyl ether in petroleum ether) to yield (*E*)-4-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)benzonitrile **3.71** (0.5861 g, 73%) as a colourless liquid; [Found: (ESI^+) $(M+Na)^+$ 292.1666. $C_{18}H_{23}NONa$ (M+Na) requires 292.1672]; ν_{max}(film) /cm^{-1} 2962, 2919, 2857, 2229, 1610, 1445, 1079, 819; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.61 [3H, s, $=C(CH_3)(CH_3)$], 1.67 [3H, s, $=C(CH_3)(CH_3)$], 1.69 [3H, d, J = 0.8 Hz, $OCH_2CH=C(CH_3)(CH_2)$], 2.04-2.13 (4H, m, $=C(CH_3)CH_2CH_2CH=$), 4.07 [2H, d, J =

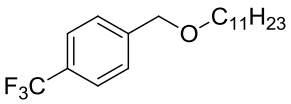
6.8 Hz, OC*H*$_2$CH=C(CH$_3$)(CH$_2$)], 4.55 (2H, s, ArC*H*$_2$OCH$_2$), 5.08-5.12 [1H, m, CH$_2$C*H*=C(CH$_3$)(CH$_3$)], 5.38-5.42 [1H, m, OCH$_2$C*H*=C(CH$_3$)(CH$_2$)], 7.46 (2H, d, *J* = 8.4 Hz, ArH), 7.64 (2H, d, *J* = 8.4 Hz, ArH); ^{13}C-NMR (100 MHz, CDCl$_3$) δ 16.6 (CH$_3$), 17.8 (CH$_3$), 25.8 (CH$_3$), 26.4 (CH$_2$), 39.7 (CH$_2$), 67.2 (CH$_2$), 70.9 (CH$_2$), 111.3 (CN), 119.0 (C), 120.4 (CH), 124.0 (CH), 128.0 (CH), 131.9 (C), 132.3 (CH), 141.2 (C), 144.4 (C); *m/z* (ESI$^+$) 292 [(M+Na)$^+$, 97%], 279 (20), 205 (6), 190 (46), 165 (100).

Synthesis of 4-((decyloxy)methyl)benzonitrile 3.72[231]



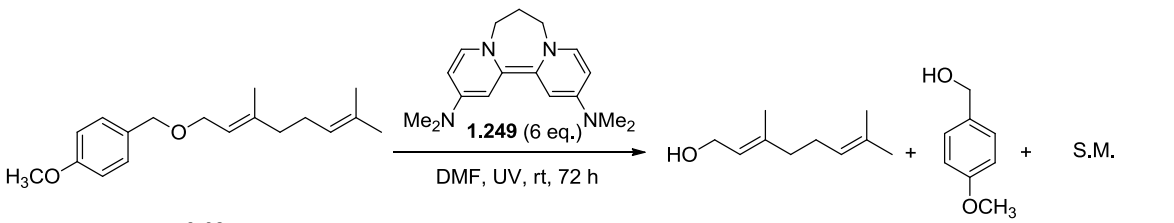
A solution of 1-decanol **3.54** (0.451 g, 2.85 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of pre-washed sodium hydride (~95%, stored in glove box, 0.082 g, 3.42 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 4-(bromomethyl)benzonitrile (0.560 g, 2.85 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in hexane) to yield 4-((decyloxy)methyl)benzonitrile **3.72** (0.596 g, 76%) as a colourless liquid; [Found: (ESI$^+$) (M+NH$_4$)$^+$ 291.2434. C$_{18}$H$_{31}$N$_2$O (M+NH$_4$) requires 291.2431]; ν_{max}(film) /cm^{-1} 2926, 2855, 2229, 1611, 1459, 1103, 818; ^{1}H-NMR (400 MHz, CDCl$_3$) δ 0.87-0.90 [3H, m, O(CH$_2$)$_9$C*H*$_3$], 1.27-1.39 (14H, m, O(CH$_2$)$_2$(C*H*$_2$)$_7$CH$_3$), 1.60-1.67 (2H, m, O(CH$_2$)(C*H*$_2$)(CH$_2$)$_7$CH$_3$), 3.50 (2H, t, *J* = 6.8 Hz, O(C*H*$_2$)(CH$_2$)$_8$CH$_3$), 4.55 (2H, s, ArC*H*$_2$O), 7.45 (2H, d, *J* = 8.4 Hz, ArH), 7.64 (2H, d, *J* = 8.4 Hz, ArH); ^{13}C-NMR (100 MHz, CDCl$_3$) δ 14.2 (CH$_3$), 22.8 (CH$_2$), 26.3 (CH$_2$), 29.4 (CH$_2$), 29.6 (CH$_2$), 29.7 (CH$_2$), 29.7 (CH$_2$), 29.8 (CH$_2$), 32.0 (CH$_2$), 71.3 (CH$_2$), 72.0 (CH$_2$), 111.3 (C), 119.0 (CN), 127.8 (CH), 132.3 (CH), 144.6 (C); *m/z* (ESI$^+$) 291 [(M+NH$_4$)$^+$, 56%], 245 (17), 190 (91), 165 (100), 135 (45).

Synthesis of 1-(trifluoromethyl)-4-((undecyloxy)methyl)benzene 3.73[183]



A solution of 4-(trifluoromethyl)benzyl alcohol **1.347** (0.7750 g, 4.4 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.192 g, 4.8 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min. at room temperature and 1-bromoundecane (0.940 g, 4 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in hexane) to yield 1-(trifluoromethyl)-4-((undecyloxy)methyl)benzene **3.73** (0.986 g, 75%) as a colourless liquid; [Found: (CI^+ corona) $(M+NH_4)^+$ 348.2509. $C_{19}H_{33}NOF_3$ $(M+NH_4)$ requires 348.2509]; ν_{max}(film) /cm^{-1} 2924, 2854, 1323, 1163, 1122, 1064, 1018, 821; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 [3H, t, J = 6.8 Hz, $O(CH_2)_{10}CH_3$], 1.27-1.39 (16H, m, $O(CH_2)_2(CH_2)_8CH_3$), 1.60-1.67 (2H, m, $OCH_2CH_2(CH_2)_8CH_3$), 3.49 (2H, t, J = 6.8 Hz, $OCH_2(CH_2)_9CH_3$), 4.56 (2H, s, $ArCH_2O$), 7.46 (2H, d, J = 8.0 Hz, ArH), 7.61 (2H, d, J = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 26.3 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (3 x CH_2), 29.9 (CH_2), 32.1 (CH_2), 71.1 (CH_2), 72.2 (CH_2), 124.4 (q, J_{CF} = 270 Hz, CF_3,), 125.4 (q, J_{CF} = 4 Hz, CH), 127.6 (CH), 129.8 (q, J_{CF} = 32 Hz, C), 143.1 (C); *m/z* (CI^+ corona) 661[$(2M+H)^+$, 12%], 331 [$(M+H)^+$, 7%], 171 (100).

UV-activated reduction of *(E)*-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-4-methoxybenzene 3.68

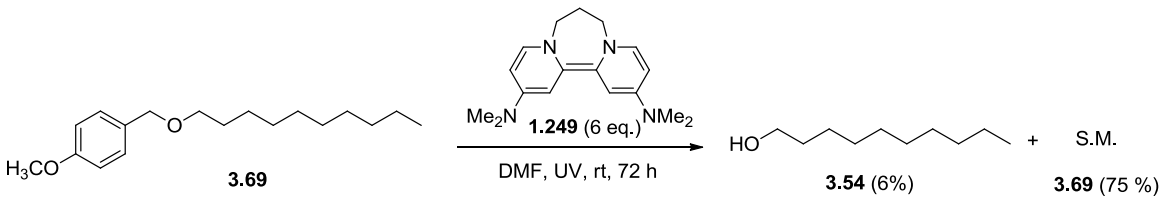


Donor-free blank reaction: 90% recovery of **3.68**

The general procedure for electron transfer reactions under UV conditions was applied to *(E)*-1-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)-4-methoxybenzene **3.68** (109 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-up process, the crude material was purified by column chromatography (5% and then 30% diethyl ether in petroleum ether) and provided geraniol **3.43** (5.8 mg, 10%) and starting material **3.68** (71 mg, 65%) as colourless oils and 4-methoxybenzyl alcohol **1.350**[232] (2.4 mg, 6%) as a white low melting solid m.p. 23-25 ^{o}C (lit.:[232] 23-25 ^{o}C); For 4-methoxybenzyl alcohol **1.350**:[232] ν_{max}(film) /cm^{-1} 3349, 3001, 2935, 2836, 1612, 1514, 1463, 1247, 1033, 817; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.54 (1H, t, J = 6.0 Hz, OH), 3.82 (3H, s, ArOCH_3), 4.63 (2H, d, J = 5.6 Hz, ArCH_2OH), 6.91 (2H, d, J = 8.8 Hz, ArH), 7.31 (2H, d, J = 8.8 Hz, ArH); ^{1}H-NMR and IR spectral data of **1.350** were consistent with the literature data.[232]

A donor-free blank reaction provided recovery of the starting material **3.68** (98 mg, 90%) only.

UV-activated reduction of 1-((decyloxy)methyl)-4-methoxybenzene 3.69

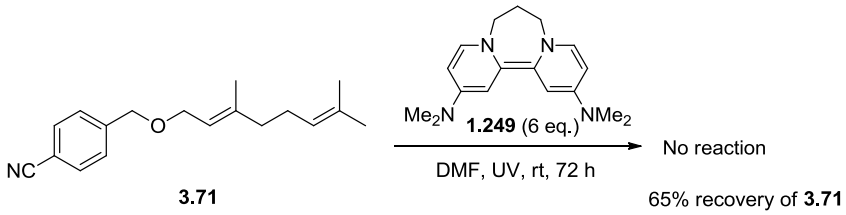


Donor-free blank reaction: 93% recovery of **3.69**

The general procedure for electron transfer reactions under UV conditions was applied to 1-((decyloxy)methyl)-4-methoxybenzene **3.69** (111.3 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-up process, the crude material was purified by column chromatography (5% and then 30% diethyl ether in petroleum ether) and provided 1-decanol **3.54** (3.6 mg, 6%) and starting material **3.69** (84 mg, 75%) as colourless oils. Spectral data of **3.54** were consistent with the previous data of the same compound.

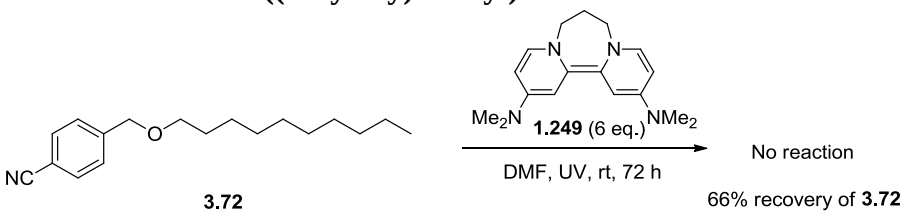
A donor-free blank reaction provided recovery of the starting material **3.69** (103 mg, 93%) only.

UV-activated reduction of *(E)*-4-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)benzonitrile 3.71



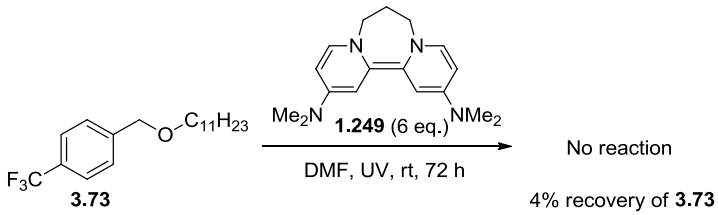
The general procedure for electron transfer reactions under UV conditions was applied to *(E)*-4-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)benzonitrile **3.71** (107 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.). After following the general water work-up process, the crude material was purified by column chromatography (15% diethyl ether in petroleum ether) and provided recovery of the starting material **3.71** (72 mg, 65%) as a colourless oil.

UV-activated reduction of 4-((decyloxy)methyl)benzonitrile 3.72



The general procedure for electron transfer reactions under UV conditions was applied to 4-((decyloxy)methyl)benzonitrile **3.72** (109.3 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, the crude material was purified by column chromatography (10% diethyl ether in petroleum ether) and provided recovery of the starting material **3.72** (71 mg, 66%) as a colourless oil.

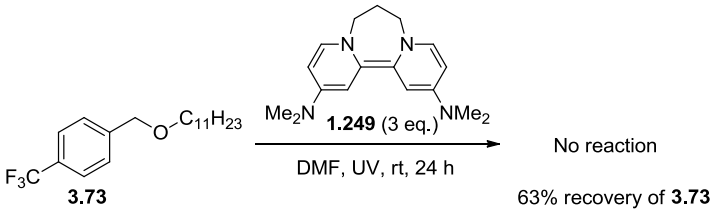
UV-activated reduction of 1-(trifluoromethyl)-4-((undecyloxy)methyl)benzene 3.73



The general procedure for electron transfer reactions under UV conditions was applied to 1-(trifluoromethyl)-4-((undecyloxy)methyl)benzene **3.73** (132 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-

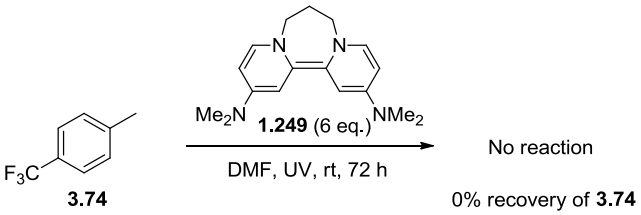
up process, the crude material was purified by column chromatography (10% diethyl ether in petroleum ether) and provided starting material **3.73** (5 mg, 4%) as a colourless oil.

UV-activated reduction of 1-(trifluoromethyl)-4-((undecyloxy)methyl)benzene 3.73



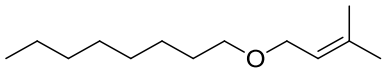
The general procedure for electron transfer reactions under UV conditions was applied to 1-(trifluoromethyl)-4-((undecyloxy)methyl)benzene **3.73** (132 mg, 0.4 mmol) using the donor **1.249** (341 mg, 1.2 mmol, 3 eq.) for 24 h. After following the general water work-up process, the crude material was purified by column chromatography (10% diethyl ether in petroleum ether) and provided starting material **3.73** (83 mg, 63%) as a colourless oil.

UV-activated reduction of *p*-trifluoromethyltoluene 3.74



The general procedure for electron transfer reactions under UV conditions was applied to *p*-trifluoromethyltoluene **3.74** (64 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-up process, none of the starting material **3.74** was recovered.

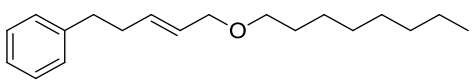
Synthesis of 1-((3-methylbut-2-en-1-yl)oxy)octane 3.81[233]



A solution of 1-octanol **3.84** (0.7808g, 6.0 mmol) in dry tetrahydrofuran (2mL) was added slowly to the suspension of sodium hydride (~60%, 0.264g, 6.6 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 3,3-dimethylallyl bromide **3.85** (0.9835g, 6.6 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with

water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to yield 1-((3-methylbut-2-en-1-yl)oxy)octane **3.81**[233] (0.976 g, 82%) as a colourless oil; [Found: (EI^+) $(M)^+$ 198.1983. $C_{13}H_{26}O$ (M) requires 198.1978]; ν_{max}(film) /cm^{-1} 2927, 2855, 1675, 1453, 1377, 1092; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 6.4 Hz, CH_3), 1.28-1.36 (10H, m, (CH_2)$_5$CH$_3$), 1.57-1.60 (2H, m, OCH$_2$CH_2), 1.68 (3H, s, =C(CH_3)), 1.75 (3H, d, J = 0.8 Hz, =C(CH_3)), 3.40 (2H, t, J = 6.8 Hz, CH$_2$CH_2O), 3.95 (2H, d, J = 6.8 Hz, CH$_2$OCH_2C=), 5.34-5.39 (1H, m, OCH$_2$CH=); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 18.1 (CH_3), 22.8 (CH_2), 25.9 (CH_3), 26.4 (CH_2), 29.4 (CH_2), 29.6 (CH_2), 29.9 (CH_2), 31.9 (CH_2), 67.3 (CH_2), 70.5 (CH_2), 121.6 (CH), 136.6 (C); *m/z* (EI^+) 183 (12), 86 (22), 71 (100), 69 (78), 41 (78). Spectral data of **3.81** are consistent with literature data.[233]

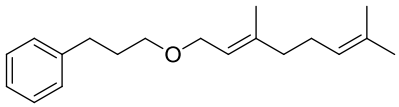
Synthesis of (*E*)-(5-(octyloxy)pent-3-en-1-yl)benzene 3.82



A solution of (*E*)-5-phenylpent-2-en-1-ol **3.86** (0.486g, 3.0 mmol) in dry tetrahydrofuran (2mL) was added slowly to the suspension of sodium hydride (~60%, 0.144g, 3.6 mmol) in dry tetrahydrofuran (5 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-bromooctane **3.87** (0.633g, 3.3 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to yield ***(E)-(5-(octyloxy)pent-3-en-1-yl)benzene*** **3.82** (0.591 g, 72%) as a colourless liquid; [Found: (ESI^+) $(M+NH_4)^+$ 292.2638. $C_{19}H_{34}NO$ ($M+NH_4$) requires 292.2635]; ν_{max}(film) /cm^{-1} 3027, 2927, 2854, 1686, 1454, 1363, 1108; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 6.8 Hz, CH_3), 1.20-1.33 (10H, m, (CH_2)$_5$CH$_3$), 1.55-1.61 (2H, m, OCH$_2$CH_2), 2.38 (2H, q, J = 7.2 Hz, PhCH$_2$CH_2), 2.70-2.74 (2H, m, PhCH_2), 3.38 (2H, t, J = 6.8 Hz, OCH_2), 3.91 (2H, d, J = 6.0 Hz, CH_2O), 5.58-5.65 (1H, m, CH=CHCH$_2$O), 5.71-5.78 (1H, m, CH=CHCH$_2$O),

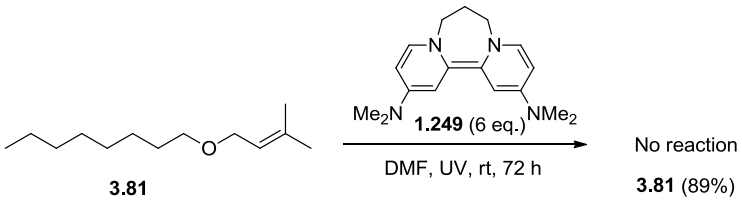
7.18-7.20 (3H, m, ArH), 7.27-7.30 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 26.4 (CH_2), 29.4 (CH_2), 29.6 (CH_2), 29.9 (CH_2), 31.9 (CH_2), 34.2 (CH_2), 35.7 (CH_2), 70.4 (CH_2), 71.6 (CH_2), 125.9 (CH), 127.4 (CH), 128.4 (CH), 128.5 (CH), 133.4 (CH), 141.9 (C); *m/z* (ESI$^+$) 292 [$(M+NH_4)^+$, 100%], 145 (28).

Synthesis of (*E*)-(3-((3,7-dimethylocta-2,6-dien-1-yl)oxy)propyl)benzene 3.83



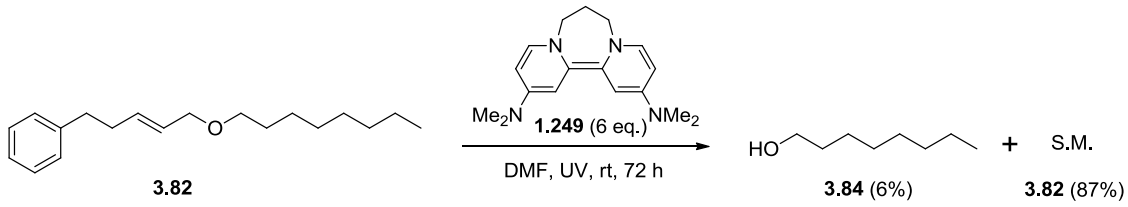
A solution of geraniol **3.43** (0.925g, 6.0 mmol) in dry tetrahydrofuran (2mL) was added slowly to the suspension of sodium hydride (~60%, 0.288 g, 7.2 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-bromo-3-phenyl propane **3.88** (1.314 g, 6.6 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% ethyl acetate in petroleum ether) to yield *(E)-(3-((3,7-dimethylocta-2,6-dien-1-yl)oxy)propyl)benzene* **3.83** (1.2386 g, 76%) as a colourless liquid; [Found: (ESI$^+$) $(M+NH_4)^+$ 290.2482. $C_{19}H_{32}NO$ $(M+NH_4)$ requires 290.2478]; ν_{max}(film) /cm^{-1} 3026, 2924, 2856, 1669, 1453, 1376, 1105; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.62 [3H, s, =C(CH_3)(C*H*$_3$)], 1.692 [3H, s, =C(C*H*$_3$)(CH_3)], 1.694 [3H, d, *J* = 0.8 Hz, OCH_2CH=C(C*H*$_3$)(CH_2)], 1.88-1.95 (2H, m, $CH_2CH_2CH_2O$), 2.05-2.13 (4H, m, =C(CH_3)C*H*$_2$C*H*$_2$CH=), 2.71 (2H, t, *J* = 7.2 Hz, PhC*H*$_2$), 3.44 (2H, t, *J* = 6.4 Hz, $PhCH_2CH_2CH_2O$), 3.99 (2H, d, *J* = 7.2 Hz, OC*H*$_2$CH=), 5.11-5.12 [1H, m, CH_2CH=C(CH_3)(CH_3)], 5.36-5.39 [1H, m, OCH_2CH=C(CH_3)(CH_2)], 7.19-7.21 (3H, m, ArH), 7.26-7.31 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 16.6 (CH_3), 17.8 (CH_3), 25.8 (CH_3), 26.5 (CH_2), 31.5 (CH_2), 32.6 (CH_2), 39.8 (CH_2), 67.4 (CH_2), 69.4 (CH_2), 121.2 (CH), 124.2 (CH), 125.9 (CH), 128.4 (CH), 128.6 (CH), 131.8 (C), 140.0 (C), 142.2 (C); *m/z* (ESI$^+$) 290 [$(M+NH_4)^+$, 100%], 242 (6), 137 (31).

UV-activated reduction of 1-((3-methylbut-2-en-1-yl)oxy)octane 3.81



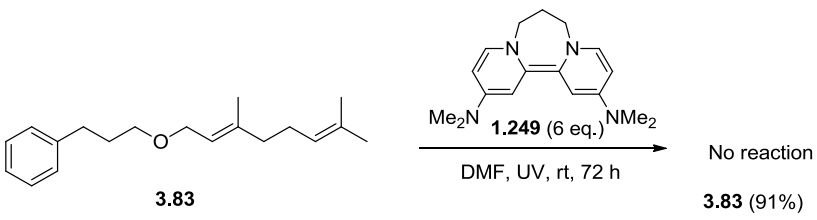
The general procedure for electron transfer reactions under UV conditions was applied to 1-((3-methylbut-2-en-1-yl)oxy)octane **3.81** (79.2 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-up process, the crude material was purified by column chromatography (5% diethyl ether in petroleum ether) and provided recovery of starting material **3.81** (70.47 mg, 89%) only.

UV-activated reduction of (*E*)-(5-(octyloxy)pent-3-en-1-yl)benzene 2.96



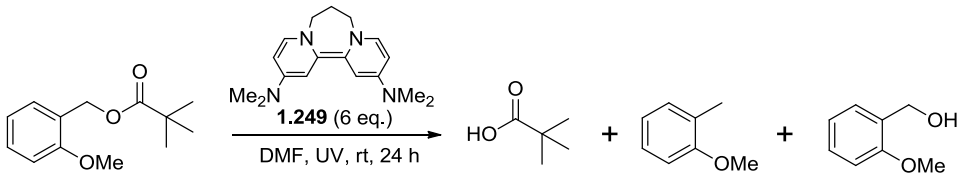
The general procedure for electron transfer reactions under UV conditions was applied to (*E*)-(5-(octyloxy)pent-3-en-1-yl)benzene **3.82** (109.3 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-up process, the crude material was purified by column chromatography (5% and then 30% diethyl ether in petroleum ether) and provided 1-octanol **3.84**[175] (3.2 mg, 6%) and starting material **3.82** (95 mg, 87%). For 1-octanol **3.84**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 [3H, t, J = 7.2 Hz, $HO(CH_2)_7CH_3$], 1.25-1.38 (10H, m, $O(CH_2)_2(CH_2)_5CH_3$), 1.54-1.61 (2H, m, OCH_2CH_2), 3.65 (2H, t, J = 6.8 Hz, $OCH_2(CH_2)_6CH_3$); The spectral data of the product **3.84** were consistent with the literature data.[175]

UV-activated reduction of (*E*)-(3-((3,7-dimethylocta-2,6-dien-1-yl)oxy)propyl) benzene 3.83



The general procedure for electron transfer reactions under UV conditions was applied to (*E*)-(3-((3,7-dimethylocta-2,6-dien-1-yl)oxy)propyl)benzene **3.83** (99 mg, 0.365 mmol) using the donor **1.249** (622 mg, 2.19 mmol, 6 eq.) for 72 h. After following the general water work-up process, the crude material was purified by column chromatography (5% diethyl ether in petroleum ether) and provided recovery of the starting material **3.83** (89.7 mg, 91%) only.

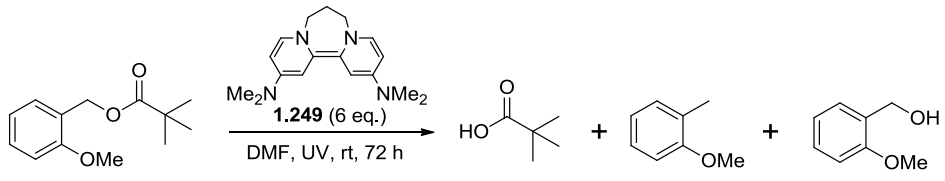
UV-activated reduction of 2-methoxybenzyl pivalate 3.24 using 1.249 (6 eq.) for 24 h



3.24 **3.28** (86%) **3.12** (trace) **3.8** (trace)

The general procedure for electron transfer reactions under UV conditions was applied to 2-methoxybenzyl pivalate **3.24** (89 mg, 0.4 mmol, 1 eq.) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 24 h. After following the general water work-up process, trace amounts (< 2%) of 2-methoxytoluene **3.12** and 2-methoxybenzyl alcohol **3.8** were detected in the ^{1}H-NMR of the crude product obtained from organic phase. Acidic work-up of the aqueous phase provided pivalic acid **3.28**[223] (35 mg, 86%). Spectral data of **3.28** were consistent with the previously mentioned data of the same compound.

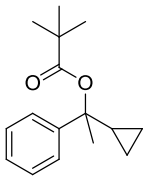
UV-activated reduction of 2-methoxybenzyl pivalate 3.24 using 1.249 (6 eq.) for 72 h



3.24 **3.28** (89%) **3.12** (trace) **3.8** (trace)

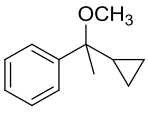
The general procedure for electron transfer reactions under UV conditions was applied to 2-methoxybenzyl pivalate **3.24** (89 mg, 0.4 mmol, 1 eq.) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general water work-up process, trace amounts (< 2%) of 2-methoxytoluene **3.12** and 2-methoxybenzyl alcohol **3.8** were detected in the ^{1}H-NMR of the crude product obtained from organic phase. Acidic work-up of the aqueous phase provided pivalic acid **3.28**[223] (36.2 mg, 89%). Spectral data of **3.28** were consistent with the previously mentioned data of the same compound.

Synthesis of 1-cyclopropyl-1-phenylethyl pivalate 3.91[183]



1-Cyclopropyl-1-phenylethanol **3.89** (0.811 g, 5 mmol) and 4-DMAP (0.916 g, 7.5mmol) were dissolved in dry THF (10 mL) in a three-necked flask equipped with a condenser. Trimethylacetyl chloride **3.90** (1.2057 g, 10 mmol) was added slowly into the reaction flask at 0 ^{o}C and then the reaction contents were refluxed for 48 h. After cooling the solution, water was added to quench the reaction and the mixture was extracted with diethyl ether (3 x 10 mL). The combined ether phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (2% diethyl ether in petroleum ether) and provided 1-cyclopropyl-1-phenylethyl pivalate **3.91** (0.281 g, 23%) as a colourless oil. [Found: (ESI^{+}) $(M+Na)^{+}$ 269.1515. $C_{16}H_{22}O_2Na$ (M+Na) requires 269.1512]; ν_{max}(film) /cm^{-1} 3088, 2974, 2870, 1730, 1477, 1284, 1147, 1095, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.49-0.62 (4H, m, CH_2CH_2), 1.21 (9H, s, C(CH_3)$_3$), 1.51-1.56 (1H, m, C*H*), 1.69 (3H, s, CCH_3), 7.23-7.26 (1H, m, ArH), 7.30-7.38 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 1.4 (CH_2), 2.8 (CH_2), 22.3 (CH), 24.3 (CH_3), 27.3 (3 x CH_3), 39.5 (C), 82.1 (C), 124.8 (2 x CH), 127.0 (CH), 128.2 (2 x CH), 145.3 (C), 176.6 (C=O); *m/z* (ESI^{+}) 515 [$(2M+Na)^{+}$, 28%], 269 [$(M+Na)^{+}$, 100%], 145 (34).

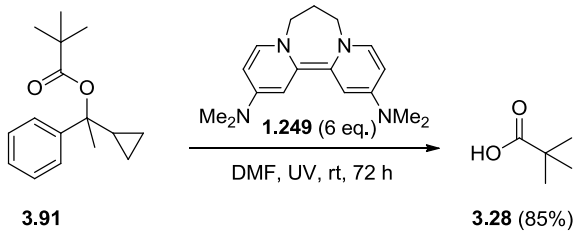
Synthesis of (1-cyclopropyl-1-methoxyethyl)benzene 3.93[234]



A solution of 1-cyclopropyl-1-phenylethanol **3.89** (0.811 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to a suspension of sodium hydride (~60%, 0.300 g, 7.5 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was then stirred for 45 min. at room temperature and then iodomethane **3.92** (1.0644 g, 7.5 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred for 24 h at room temperature under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with

water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (2% diethyl ether in petroleum ether) to yield (1-cyclopropyl-1-methoxyethyl)benzene **3.93**[234] (0.772 g, 88 %) as a colourless oil. [Found: (CI^+ corona) $(M\text{-}OCH_3)^+$ 145.1010. $C_{11}H_{13}$ $(M\text{-}OCH_3)$ requires 145.1012]; ν_{max}(film) /cm^{-1} 3086, 2978, 2823, 1446, 1228, 1087, 1068, 698; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.37-0.54 (4H, m, C*H*$_2$C*H*$_2$), 1.18-1.23 (1H, m, C*H*), 1.40 (3H, s, CCH_3), 3.15 (3H, s, OCH_3), 7.25-7.28 (1H, m, ArH), 7.35 (2H, t, J = 8.0 Hz, ArH), 7.45 (2H, d, J = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 1.1 (CH_2), 2.5 (CH_2), 21.4 (CH), 22.7 (CH_3), 50.6 (C), 78.7 (CH_3), 126.6 (2 x CH), 126.9 (CH), 128.1 (2 x CH), 145.1 (C); *m/z* (CI^+) 161 [$(M\text{-}CH_3)^+$, 8%], 145 [$(M\text{-}OCH_3)^+$, 100%].

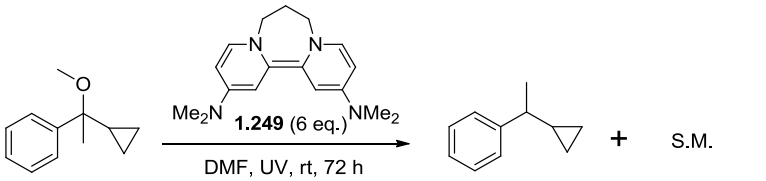
UV-activated reduction of 1-cyclopropyl-1-phenylethyl pivalate 3.91



3.91 **3.28** (85%)

The general procedure for electron transfer reactions under UV conditions was applied to 1-cyclopropyl-1-phenylethyl pivalate **3.91** (98.5 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, no product was obtained from the organic phase. Acidic work-up of the aqueous phase provided pivalic acid **1.249**[223] (34.7 mg, 85%) as a white low melting crystalline solid and spectral data of this product were consistent the previously mentioned data of the same compound.

UV-activated reduction of (1-cyclopropyl-1-methoxyethyl)benzene 3.93

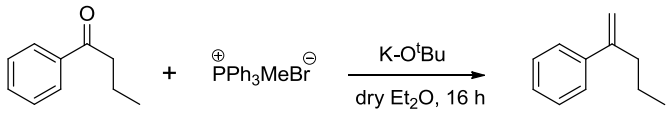


3.93 **3.100** (29%) **3.93** (45%)

The general procedure for electron transfer reactions under UV conditions was applied to (1-cyclopropyl-1-methoxyethyl)benzene **3.93** (70 mg, 0.4 mmol) using the donor **1.249** (682 mg, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, the

crude material was purified by column chromatography (1% diethyl ether in petroleum ether) and provided (1-cyclopropylethyl)benzene **3.100**[235] (16.6 mg, 29%) and starting material **3.93** (31.7 mg, 45%) as colourless oils. For (1-cyclopropylethyl)benzene **3.100**[235]: [Found: (CI corona$^+$) $(M+H)^+$ 147.1166. $C_{11}H_{15}$ (M+H) requires 147.1168]; ν_{max}(film) /cm^{-1} 3076, 2962, 2872, 1492, 1450, 1263, 1016, 908; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.14-0.25 (2H, m, C*H*$_2$), 0.40-0.47 (1H, m, C*H*$_2$), 0.54-0.59 (1H, m, C*H*$_2$), 0.92-0.99 (1H, m, C*H*), 1.35 (3H, d, J = 7.2 Hz, CHC*H*$_3$), 1.98-2.02 (1H, m, C*H*CH$_3$), 7.18-7.23 (1H, m, ArH), 7.26-7.35 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 4.4 (CH_2), 4.7 (CH_2), 18.7 (CH), 21.7 (CH_3), 44.7 (CH), 126.0 (CH), 127.1 (2 x CH), 128.4 (2 x CH), 147.5 (C); *m/z* (CI corona$^+$) 185 [$(M+K)^+$, 16%], 161 (61%), 147 [$(M+H)^+$, 100%], 105 (49).

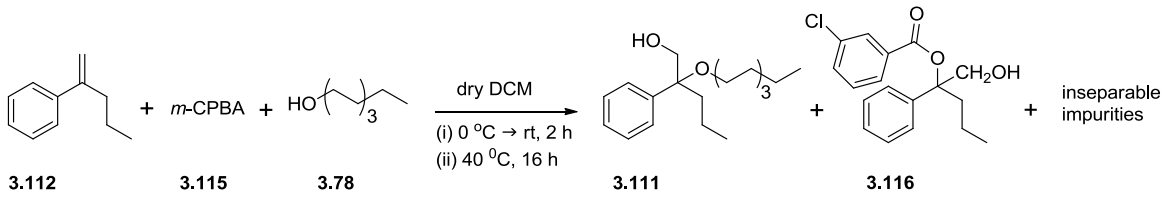
Synthesis of pent-1-en-2-ylbenzene 3.112[236]



3.113 **3.114** **3.112** (62%)

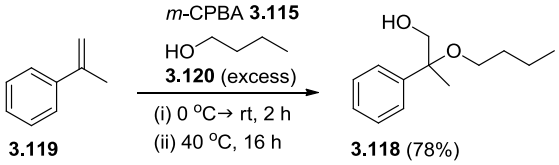
Methyltriphenylphosphonium bromide **3.114** (4.286 g, 12 mmol) and potassium *tert*-butoxide (1.3466 g, 12 mmol) were added to a flask containing diethyl ether (50 mL) under argon gas and stirred vigorously for 30 min. The reaction mixture turned into canary yellow colour and the colour of this solution was discharged into greyish white upon dropwise addition of butyrophenone **3.113** (1.4821 g, 10 mmol). The resulting reaction mixture was further stirred for 16 h and filtered through celite. The filtrate was then concentrated and purified using column chromatography (100% hexane) to provide pent-1-en-2-ylbenzene **3.112** (0.912 g, 62%) as a colourless oil. [Found: (EI$^+$) $(M)^+$ 146.1089. $C_{11}H_{14}$ (M) requires 146.1090]; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.93 (3H, t, J = 7.6 Hz, $CCH_2CH_2CH_3$), 1.45-1.52 (2H, m, $CCH_2CH_2CH_3$), 2.49 (2H, t, J = 7.6 Hz, $CCH_2CH_2CH_3$), 5.06 (1H, q, J = 1.6 Hz, C=C*H*$_2$), 5.28 (1H, d, J = 2.0 Hz, C=C*H*$_2$), 7.24-7.29 (1H, m, ArH), 7.31-7.35 (2H, m, ArH), 7.40-7.42 (2H, m, ArH); *m/z* (EI$^+$) 146 [$(M)^+$, 20%], 131 (23), 118 (100), 103 (22), 91 (32). The spectral data of the compound **3.112** were consistent with the literature data.[236]

Attempted synthesis of 2-(octyloxy)-2-phenylpentan-1-ol 3.111



Into a three-necked flask equipped with condenser, *m*-CPBA **3.115** (1.1855 g, 6.87 mmol) and dry DCM (10 mL) were added. Pent-1-en-2-ylbenzene **3.112** (0.670 g, 4.58 mmol) and 1-octanol **3.78** (1.789 g, 13.74 mmol) were added slowly at 0 ^{o}C and the flask was allowed to warm to room temperature. The reaction was further stirred for 16 h at 40 ^{0}C. Later, the reaction was quenched with 1N NaOH (20 ml) and then extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed again with water (10 mL), brine (10 mL) and dried over anhydrous sodium sulfate. The concentrated crude product was subjected to column chromatography (30% ethyl acetate in hexane) but did not provide any pure *2-(octyloxy)-2-phenylpentan-1-ol* **3.111**.

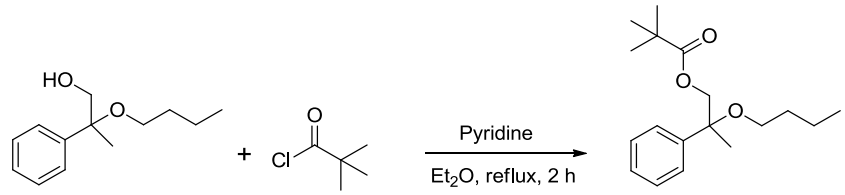
Synthesis of 2-butoxy-2-phenylpropan-1-ol 3.118[182]



Into a three-necked flask equipped with condenser, *m*-CPBA **3.115** (2.07 g, 12 mmol) was placed. α-Methylstyrene **3.119** (1.18 g, 10 mmol) and *n*-butanol **3.120** (30 mL) were added slowly at 0 ^{o}C and the flask was allowed to warm to room temperature in 2 h. The reaction was further stirred for 16 h at 40 ^{0}C. The reaction was then quenched with 1N NaOH (20 ml) and then extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed again with water (10 mL), brine (10 mL) and dried over anhydrous sodium sulfate. The concentrated crude product was purified by column chromatography (15 % EtOAc in hexane) to provide 2-butoxy-2-phenylpropan-1-ol **3.118** (1.618 g, 78%) as a colourless liquid; [Found: (ESI^{+}) $(M+H)^{+}$ 209.1536. $C_{13}H_{21}O_2$ (M+H) requires 209.1533]; ν_{max}(film)/cm^{-1} 3436, 3027, 2958, 2872, 1446, 1233, 1073, 700; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.92 [3H, t, J = 7.5 Hz, $O(CH_2)_3CH_3$], 1.36-1.41 (2H, m, $O(CH_2)_2CH_2CH_3$),

1.54-1.60 (2H, m, $OCH_2CH_2CH_2CH_3$), 1.63 (3H, s, $ArCCH_3$), 2.09-2.10 (1H, m, CH_2OH), 3.14-3.18 (1H, m, $OCH_2CH_2CH_2CH_3$), 3.30-3.34 (1H, m, $OCH_2CH_2CH_2CH_3$), 3.49 (1H, dd, J = 11.0, 8.5 Hz, CH_2OH), 3.65 (1H, dd, J = 11.0, 4.0 Hz, CH_2OH), 7.28-7.31 (1H, m, ArH), 7.35-7.41 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.1 (CH_3), 19.5 (CH_3), 20.0 (CH_2), 32.5 (CH_2), 62.4 (CH_2), 71.8 (CH_2), 79.2 (C), 126.5 (CH), 127.5 (CH), 128.4 (CH), 142.9 (C); *m/z* (ESI^+) 226 [$(M+NH_4)^+$, 51%], 209 [$(M+H)^+$, 76%], 152 (11), 135 (100).

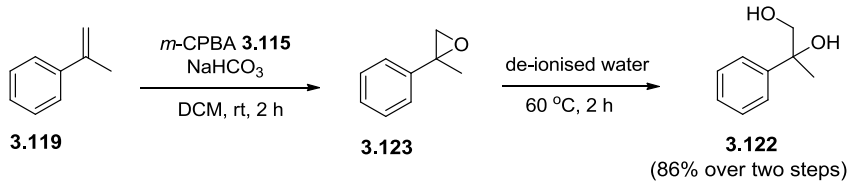
Synthesis of 2-butoxy-2-phenylpropyl pivalate 3.117[183]



3.118 **3.90** **3.117**(86%)

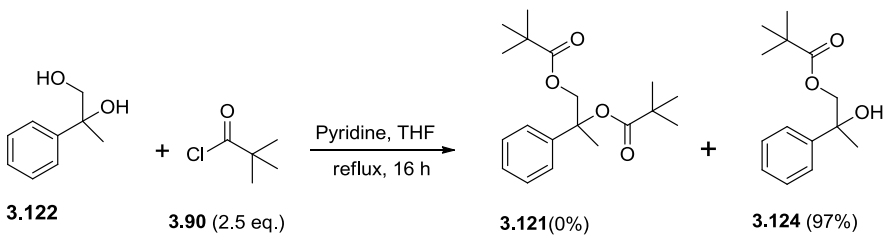
2-Butoxy-2-phenylpropan-1-ol **3.118** (0.6908 g, 5 mmol) and pyridine (0.4 mL, 5 mmol) were dissolved in dry diethyl ether (10 mL) in a three-necked flask equipped with a condenser. Trimethylacetyl chloride **3.90** (0.602 g, 5 mmol) was added slowly into the reaction flask, which was then refluxed for 2 h. After cooling the solution, water was added to dissolve pyridinium salts and the aqueous phase was discarded. The ether phase was washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to yield 2-butoxy-2-phenylpropyl pivalate **3.117** (1.251 g, 86%) as a colourless liquid; [Found: (ESI^+) $(M+Na)^+$ 315.1931. $C_{18}H_{28}O_3Na$ (M+Na) requires 315.1931]; ν_{max}(film) /cm^{-1} 3028, 2959, 2872, 1733, 1480, 1284, 1154, 1078, 763; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.90 [3H, t, J = 7.2 Hz, $O(CH_2)_3CH_3$], 1.14 (9H, s, $C(CH_3)_3$), 1.35-1.42 (2H, m, $O(CH_2)_2CH_2CH_3$), 1.51-1.58 (2H, m, $OCH_2CH_2CH_2CH_3$), 1.61 (3H, s, $ArCCH_3$), 3.15-3.20 (1H, m, $OCH_2CH_2CH_2CH_3$), 3.27-3.32 (1H, m, $OCH_2CH_2CH_2CH_3$), 4.19 (2H, s, $ArCCH_2OCO$), 7.25-7.29 (1H, m, ArH), 7.33-7.37 (2H, m, ArH), 7.40-7.43 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.1 (CH_3), 19.5 (CH_3), 21.7 (CH_2), 27.2 (CH_3), 32.5 (CH_2), 38.9 (C), 62.4 (CH_2), 70.5 (CH_2), 76.8 (C), 126.6 (CH), 127.4 (CH), 128.2 (CH), 142.7 (C), 178.1 (C=O); *m/z* (ESI^+) 315 [$(M+Na)^+$, 7%], 219 (100).

Synthesis of 2-phenylpropane-1,2-diol 3.122[148]



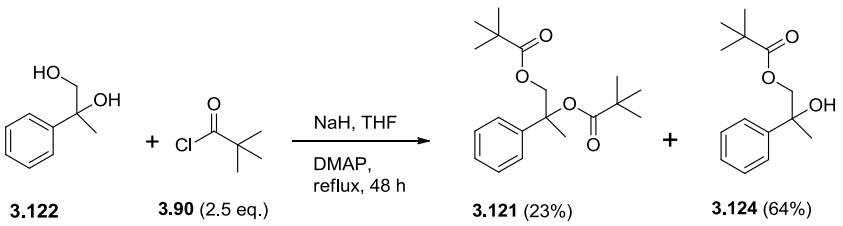
Into a three-necked flask containing DCM (10 mL), *m*-CPBA **3.115** (70%, 2.711 g, 11 mmol) and $NaHCO_3$ (0.924 g in 2 mL water, 11 mmol) were placed and α-methylstyrene **3.119** (1.18 g, 10 mmol) was added slowly at room temperature. The reaction was stirred for 2 h and washed with aqueous sodium sulfite (10 mL). The resulting solution was extracted with DCM (2 x 10 mL) and the combined organic phases were washed once again with $NaHCO_3$ (10 mL), brine (10 mL) and dried over anhydrous sodium sulfate. The concentrated crude product (2-methyl-2-phenyloxirane) **3.123** was used as such in next reaction. 2-Methyl-2-phenyloxirane **3.123** was added to de-ionised water (15 mL) in a flask equipped with a condenser. The resulting suspension was stirred for 2 h at 60 ^{0}C and after cooling, the reaction mixture was extracted with ethyl acetate (2 x 15 mL). The combined organic layers were washed with brine (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (50% ethyl acetate in petroleum ether) to provide 2-phenylpropane-1,2-diol **3.122**[148] (1.312 g, 86%) as a colourless viscous liquid which turned into a white solid on cooling; m. p. 43-45 ^{o}C; (lit.[237] : 44-45 ^{o}C); [Found: (EI^+) $(M)^+$ 152.0831. $C_9H_{12}O_2$ (M) requires 152.0832]; ν_{max}(film) /cm^{-1} 3362, 3022, 2945, 1600, 1380, 1048, 759; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.55 (3H, s, ArCC*H*$_3$], 1.73-1.76 (1H, m, O*H*) 2.54 (1H, s, O*H*), 3.63-3.68 (1H, m, C*H*$_2$OH), 3.80-3.84 (1H, m, C*H*$_2$OH), 7.27-2.31 (1H, m, ArH), 7.36-7.40 (2H, m, ArH), 7.46-7.47 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 26.2 (CH_3), 71.2 (CH_2), 74.9 (C), 125.2 (CH), 127.3 (CH), 128.6 (CH), 145.1 (C); *m/z* (EI^+) 152 [$(M)^+$, 64%], 121 (98), 43 (100).

Attempted synthesis of 2-phenylpropane-1,2-diyl bis(2,2-dimethylpropanoate) 3.121[183]



Into a three-necked flask equipped with a condenser, 2-phenylpropane-1,2-diol **3.122** (0.730 g, 4.8 mmol), pyridine (0.759 g, 9.6 mmol) and dry THF (10 mL) were added. Later, pivaloyl chloride **3.90** (1.273 g, 10.56 mmol) was added dropwise into the flask at 0 ^{o}C and then the reaction contents were refluxed for 16 h. The reaction was then quenched with water (10 mL) and extracted with diethyl ether (3 x 15 mL). The collected ether phases were washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (30% diethyl ether in petroleum ether) to yield 2-hydroxy-2-phenylpropyl pivalate **3.124**[183] (1.0968 g, 97%) as a colourless oil. None of the desired 2-phenylpropane-1,2-diyl bis(2,2-dimethylpropanoate) **3.121** was obtained. For 2-hydroxy-2-phenylpropyl pivalate **3.124**: [Found: (ESI^{+}) $(M+Na)^{+}$ 259.1307. $C_{14}H_{20}O_3Na$ (M+Na) requires 259.1305]; ν_{max}(film) /cm^{-1} 3480, 3029, 2976, 2874, 1714, 1480, 1285, 1157, 1031, 763; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.27 [9H, s, C(C*H*$_3$)$_3$], 1.58 (3H, s, ArCC*H*$_3$), 2.57 (1H, bs, ArCO*H*), 4.20 (1H, d, J = 11.2 Hz, ArCC*H*$_2$OC=O), 4.35 (1H, d, J = 11.2 Hz, ArCC*H*$_2$OC=O), 7.30 (1H, m, ArH), 7.34-7.38 (2H, m, ArH), 7.45-7.48 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 26.6 (CH_3), 27.2 (CH_3), 38.9 (C), 71.9 (CH_2), 74.0 (C), 125.1 (CH), 127.3 (CH), 128.3 (CH), 144.5 (C), 178.6 (C=O); *m/z* (ESI^{+}) 259 [$(M+Na)^{+}$, 28%], 219 (100).

Synthesis of 2-phenylpropane-1,2-diyl bis(2,2-dimethylpropanoate) 3.121[183]

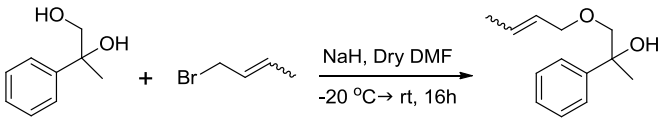


Sodium hydride (60%, 0.840 g, 21 mmol) and 4-DMAP (1.8814 g, 15.4 mmol) were added to a three-necked flask equipped with a condenser and dry THF (10 mL) was added. A solution of 2-phenylpropane-1,2-diol **3.122** (1.0652 g, 7 mmol) in dry THF (2 mL) was added dropwise into the flask at 0 ^{o}C under argon gas flow and stirred for 2 h at room temperature. Trimethylacetyl chloride **3.90** (1.8569 g, 15.4 mmol) was added dropwise into the reaction flask and the contents were then refluxed for 48 h. The reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 15 mL). The collected ether phases were washed again with water (10 mL), brine (10 mL) and dried over sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl

ether in petroleum ether) to yield 2-phenylpropane-1,2-diyl bis(2,2-dimethylpropanoate) **3.121** (0.512 g, 23%) and 2-hydroxy-2-phenylpropyl pivalate **3.124** (1.063 g, 64%) as colourless oils. For 2-phenylpropane-1,2-diyl bis(2,2-dimethylpropanoate) **3.121**: [Found: (ESI^+) $(M+NH_4)^+$ 338.2329. $C_{19}H_{32}NO_4$ $(M+NH_4)$ requires 338.2326]; ν_{max}(film) /cm^{-1} 2974, 2873, 1734, 1480, 1366, 1282, 1149; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.17 [9H, s, $C(CH_3)_3$], 1.24 [9H, s, $C(CH_3)_3$], 1.89 (3H, s, $ArCCH_3$), 4.29 (1H, d, J = 11.6 Hz, $ArCCH_2$), 4.42 (1H, d, J = 11.6 Hz, $ArCCH_2$), 7.26-7.31 (1H, m, ArH), 7.33-7.37 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.9 (CH_3), 27.2 $(CH_3)_3$, 38.9 (C), 39.4 (C), 69.9 (CH_2), 81.3 (C), 124.9 (CH), 127.7 (CH), 128.4 (CH), 141.6 (C), 176.6 (C=O), 177.8 (C=O); *m/z* (ESI^+) 338 [$(M+ NH_4)^+$, 100 %], 219 (40).

For 2-hydroxy-2-phenylpropyl pivalate **3.124**: Spectral data were consistent with previously mentioned data of the same compound.

Synthesis of 1-(but-2-en-1-yloxy)-2-phenylpropan-2-ol 3.126

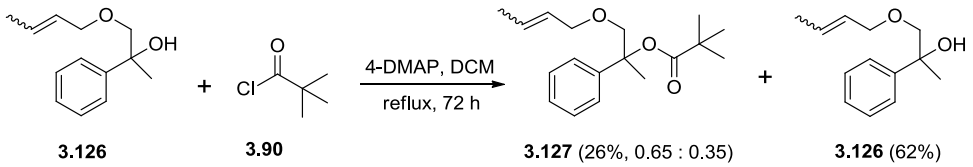


3.122 **3.125** **3.126** (86%)

A solution of 2-phenylpropane-1,2-diol **3.122** (1.2174 g, 8 mmol) in dry DMF (2mL) was added slowly to the suspension of sodium hydride (~60%, 0.352 g, 8.8 mmol) in dry DMF (5 mL) at -20 ^{o}C under argon gas. The resulting solution was stirred for 30 min at -20 ^{o}C and 1-bromobut-2-ene **3.125** (1.188 g, 8.8 mmol) in dry DMF (2 mL) was added dropwise. The reaction contents were then heated to room temperature and stirred for 16 h. Water (10 mL) was added to quench the reaction and the aqueous solution was extracted with diethyl ether (3 x 10 mL). The combined ether portions were washed again with water (10 mL), brine (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (20% diethyl ether in petroleum ether) to yield *1-(but-2-en-1-yloxy)-2-phenylpropan-2-ol* **3.126** (1.412 g, 86%) as a colourless liquid. [Found: (ESI^+) $(M+Na)^+$ 229.1200. $C_{13}H_{18}O_2Na$ (M+Na) requires 229.1199]; ν_{max}(film) /cm^{-1} 3459, 3026, 2975, 2858, 1603, 1447, 1369, 1099, 1067, 966; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.53 (3H, s, CCH_3), 1.71 (3H, d, J = 6.4 Hz, $=CCH_3$), 2.90 (1H, bs, O*H*), 3.50-3.62 (2H, m, CCH_2O), 3.95 (2H, dd, J = 6.4, 0.8 Hz, OCH_2), 5.50-5.57 (1H, m,

CH=C*H*CH_3), 5.64-5.72 (1H, m, C*H*=$CHCH_3$), 7.24-7.28 (1H, m, Ar*H*), 7.36 (2H, t, *J* = 8.0 Hz, Ar*H*), 7.48 (2H, d, *J* = 8.0 Hz, Ar*H*); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 17.8 (CH_3), 26.9 (CH_3), 72.3 (CH_2), 73.9 (C), 77.9 (CH_2), 125.1 (CH), 126.9 (CH), 127.5 (CH), 128.2 (CH), 129.8 (CH), 145.7 (C); *m/z* (ESI^+) 229 [$(M+ Na)^+$, 100 %], 206 [$(M)^+$, 28%], 171 (61), 135 (94).

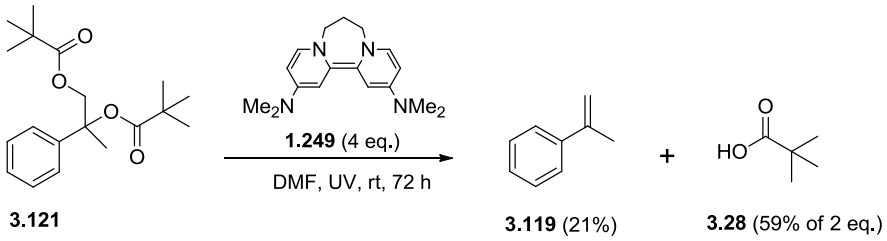
Synthesis of 1-(but-2-en-1-yloxy)-2-phenylpropan-2-yl pivalate 3.127



3.126 **3.90** **3.127** (26%, 0.65 : 0.35) **3.126** (62%)

1-(But-2-en-1-yloxy)-2-phenylpropan-2-ol **3.126** (0.722 g, 3.5 mmol) and 4-DMAP (0.641 g, 5.25 mmol) were dissolved in dry dichloromethane (10 mL) in a three-necked flask equipped with a condenser. Trimethylacetyl chloride **3.90** (0.633 g, 5.25 mmol) was added slowly into the reaction flask under argon flow, and the reaction mixture was then refluxed for 72 h. Water (5 mL) was added to quench reaction and the aqueous solution was extracted with diethyl ether (3 x 10 mL). The combined ether portions were washed again with water (10 mL), brine (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to yield *1-(but-2-en-1-yloxy)-2-phenylpropan-2-yl pivalate* **3.127** (0.269 g, 26%) as a mixture of isomers in (0.65 : 0.35) ratio along with recovery of the starting material **3.126** (0.444 g, 62%) and both as colourless oils. For major isomer of **3.127**: [Found: (ESI^+) $(M+H)^+$ 291.1957. $C_{18}H_{27}O_3$ (M+H) requires 291.1955]; ν_{max}(film) /cm^{-1} 3061, 2971, 2870, 1733, 1603, 1479, 1448, 1368, 1163, 1029; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.23 (9H, s, (CH_3)$_3$), 1.69-1.71 (3H, m, =CCH_3), 1.86 (3H, s, CCH_3), 3.66-3.75 (2H, m, CCH_2O), 3.90-3.95 (2H, m, OCH_2), 5.48-5.52 (1H, m, CH=C*H*CH_3), 5.63-5.65 (1H, m, C*H*=$CHCH_3$), 7.24-7.32 (1H, m, Ar*H*), 7.32-7.34 (4H, m, Ar*H*); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 17.8 (CH_3), 22.3 (CH_3), 27.3 (CH_3), 39.3 (C), 72.5 (CH_2), 76.7 (CH_2), 82.7 (C), 124.9 (CH), 127.3 (CH), 127.8 (CH), 128.3 (CH), 129.1 (CH), 143.1 (C), 176.9 (C=O); *m/z* (ESI^+) 313 (10), 291 [$(M+H)^+$, 5%], 189 (55), 171 (100), 145 (24), 135 (57).

UV-activated reduction of 2-phenylpropane-1,2-diyl bis(2,2-dimethylpropanoate) 3.121

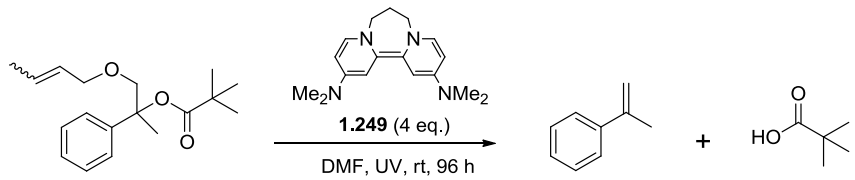


3.121 **3.119** (21%) **3.28** (59% of 2 eq.)

The general procedure for electron transfer reactions under UV conditions was applied to 2-phenylpropane-1,2-diyl bis(2,2-dimethylpropanoate) **3.121** (128 mg, 0.4 mmol) using the donor **1.249** (454 mg, 1.6 mmol, 4 eq.) for 72 h. After following the general water work-up process, the crude material was purified by column chromatography (2% diethyl ether in petroleum ether) and provided α-methylstyrene **3.119**[238] (9.8 mg, 21%) from the organic phase and pivalic acid **3.28** (48.1 mg, 59%) from the acidic work-up of the aqueous phase. For α-methylstyrene **3.119**: ν_{max}(film) /cm^{-1} 3084, 2973, 2945, 1629, 1442; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.18 (3H, dd, J = 1.2, 0.4 Hz CH_3), 5.09-5.11 (1H, m, =C*H*), 5.38 (1H, d, J = 1.6 Hz, =C*H*), 7.26-7.30 (1H, m, Ar*H*), 7.32-7.36 (2H, m, Ar*H*), 7.47-7.50 (2H, m, Ar*H*); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.9 (CH_3), 112.5 (CH_2), 125.6 (CH), 127.5 (CH), 128.3 (CH), 141.4 (C), 143.4 (C). Spectral data of **3.119** were consistent with the literature data.[238]

For pivalic acid **3.28**: spectral data were consistent with the previously mentioned data of the same compound.

UV-activated reduction of 1-(but-2-en-1-yloxy)-2-phenylpropan-2-yl pivalate 3.127

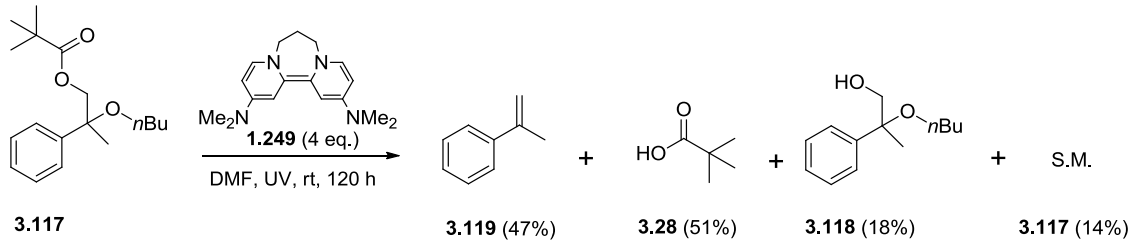


3.127 **3.119** (19%) **3.28** (81%)

The general procedure for electron transfer reactions under UV conditions was applied to 1-(but-2-en-1-yloxy)-2-phenylpropan-2-yl pivalate **3.127** (116 mg, 0.4 mmol) using the donor **1.249** (454 mg, 1.6 mmol, 4 eq.) for 96 h. After following the general work-up process, the crude material was purified by column chromatography (2% diethyl ether in

petroleum ether) and provided α-methylstyrene **3.119** (9.1 mg, 19%) from the organic phase and pivalic acid **3.28** (33.2 mg, 81%) from acidic work-up of the aqueous phase. Spectral data of products **3.119** and **3.28** were consistent with the previous data of the same compounds.

UV-activated reduction of 2-butoxy-2-phenylpropyl pivalate 3.117

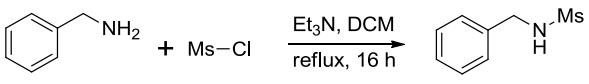


3.117 | **3.119** (47%) | **3.28** (51%) | **3.118** (18%) | **3.117** (14%)

The general procedure for electron transfer reactions under UV conditions was applied to 2-butoxy-2-phenylpropyl pivalate **3.117** (292 mg, 1 mmol) using the donor **1.249** (1.1369 g, 4 mmol, 4 eq.) for 120 h. After following the general work-up process, the crude material was purified by column chromatography (2% and then 20% diethyl ether in petroleum ether) and provided α-methylstyrene **3.119** (56 mg, 47%), 2-butoxy-2-phenylpropan-1-ol **3.118** (37 mg, 18%) and starting material **3.117** (41 mg, 14%) from the organic phase and pivalic acid **3.28** (52.6 mg, 51%) from acid work-up of the aqueous phase. The spectral data of the products **3.119**, **3.28**, **3.118** and **3.117** were consistent with the previous data of the same compounds.

7.6 Experimental for Chapter 4

Synthesis of *N*-benzylmethanesulfonamide 4.7[239]

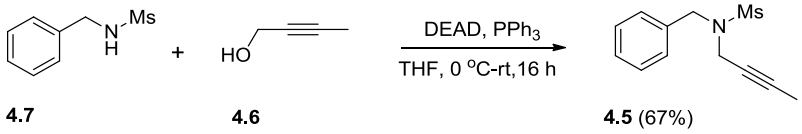


4.8 | **4.9** | **4.7** (86%)

Benzylamine **4.8** (1.0716 g, 10 mmol) and triethylamine (1.6 mL, 12 mmol) were added to a flask containing dry DCM (10 mL). Mesyl chloride **4.9** (1.3746 g, 12 mmol) was added dropwise into the reaction flask under argon flow and refluxed for 16 h. The reaction mixture was then quenched with water (5 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organic layers washed with brine solution (10 mL) and dried

over anhydrous sodium sulfate. The resulting solution was then concentrated using a rotary evaporator and purified by column chromatography (50% ethyl acetate in petroleum ether) to yield *N*-benzylmethanesulfonamide **4.7**[239] (1.5853g, 86%) as a white crystalline solid. m.p. 61-63 ^{o}C (lit.:[239] 63-64 ^{o}C); ν_{max}(solid) /cm^{-1} 3232, 3014, 1461, 1438, 1320, 1134, 1062, 769; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.89 (3H, s, CH_3), 4.34 (2H, d, J = 10.0 Hz, ArCH_2), 4.58 (1H, bs, NH), 7.31-7.41 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 41.3 (CH_3), 47.4 (CH_2), 128.0 (CH), 128.3 (CH), 129.1 (CH), 136.7 (C). Spectral data were consistent with the literature data.[239]

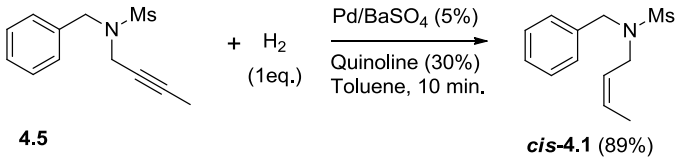
Synthesis of *N*-benzyl-*N*-(but-2-yn-1-yl)methanesulfonamide 4.5



4.7 **4.6** **4.5** (67%)

N-Benzylmethanesulfonamide **4.7** (1.4816 g, 8 mmol) and 2-butyn-1-ol **4.6** (0.616 g, 8.8 mmol) were added to a flask containing triphenylphosphine (2.7278 g, 10.4 mmol) in dry THF (10 mL) and cooled to 0 ^{o}C. DEAD (1.811 g, 10.4 mmol) was added dropwise into the reaction flask at 0 ^{o}C and stirred for 16 h at room temperature. The reaction was then quenched with water (10 mL) and extracted with ethyl acetate (3 x 15 mL). The combined organic layers washed with brine solution (10 mL) and dried over anhydrous sodium sulfate. The resulting solution was then concentrated using rotary evaporator and purified by column chromatography (20% ethyl acetate in petroleum ether) to yield *N-benzyl-N-(but-2-yn-1-yl)methanesulfonamide* **4.5** (1.274g, 67%) as a white solid m.p. 51-53 ^{o}C; [Found: (ESI^{+}) $(M+H)^{+}$ 238.0899. $C_{12}H_{16}NO_2S$ (M+H) requires, 238.0896]; ν_{max}(solid) /cm^{-1} 3027, 2926, 2218, 1448, 1367, 1326, 1142; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.89 (3H, t, J = 2.4 Hz, CCH_3), 3.01 (3H, s, CH_3), 3.88 (2H, q, J = 2.4 Hz, NCH_2) 4.43 (2H, s, ArCH_2), 7.32-7.41 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 3.6 (CH_3), 36.1 (CH_2), 38.4 (CH_3), 49.9 (CH_2), 72.4 (C), 82.5 (C), 128.2 (CH), 128.8 (2 x CH), 135.3 (C); *m/z* (ESI^{+}) 255 [$(M+NH_4)^{+}$, 65%], 238 [$(M+H)^{+}$, 100%], 143 (34).

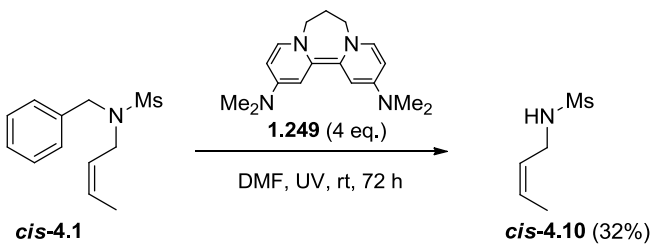
Synthesis of (*Z*)-*N*-benzyl-*N*-(but-2-en-1-yl)methanesulfonamide *cis*-4.1



4.5 ***cis*-4.1** (89%)

Lindlar's catalyst ($Pd/BaSO_4$, 0.318 g, 0.15 mmol) was added to a flask containing dry toluene (5 mL) and kept under argon gas. *N*-benzyl-*N*-(but-2-yn-1-yl)methanesulfonamide **4.5** (0.711 g, 3 mmol) was added into the reaction flask and stirred for 10 min before adding quinoline (0.114 g, 0.9 mmol). This flask was then taken to the hydrogenation setup and the inside atmosphere was removed by vacuum and filled with hydrogen. The consumption of the hydrogen gas was monitored on a graduated column and 69 mL of hydrogen gas was utilised for the reaction and the reaction was finished in just 10 min. The reaction mixture was then filtered through celite and washed with toluene (2 x 10 mL). The resulting solution was then concentrated using a rotary evaporator and purified by column chromatography (20 % ethyl acetate in petroleum ether) to yield *(Z)-N-benzyl-N-(but-2-en-1-yl)methanesulfonamide* ***cis*-4.1** (0.641 g, 89%) as a light yellow oil. [Found: (ESI^+) $(M+H)^+$ 240.1057. $C_{12}H_{18}NO_2S$ (M+H) requires 240.1053]; ν_{max}(film) /cm^{-1} 3027, 2926, 1496, 1455, 1321, 1144, 791; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.58 (3H, dd, J = 6.8, 0.8 Hz, =CHCH_3), 2.88 (3H, s, CH_3), 3.85 (2H, d, J = 6.8 Hz, NCH_2) 4.39 (2H, s, ArCH_2), 5.48 (1H, qq, J = 8.8, 2.0 Hz, NCH_2CH=C), 5.70-5.78 (1H, m, =C$H$$CH_3$), 7.29-7.37 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.0 (CH_3), 40.0 (CH_3), 42.8 (CH_2), 50.1 (CH_2), 123.9 (CH), 128.0 (CH), 128.5 (CH), 128.8 (CH), 129.7 (CH), 136.1 (C); *m/z* (ESI^+) 262 [(M+Na), 82%], 257 [$(M+NH_4)^+$, 30%], 240 [$(M+H)^+$, 100%], 200 (22), 186 (70).

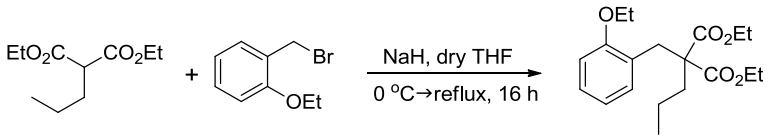
UV-activated reduction of (*Z*)-*N*-benzyl-*N*-(but-2-en-1-yl)methanesulfonamide *cis*-4.1



***cis*-4.1** ***cis*-4.10** (32%)

The general procedure for electron transfer reactions under UV conditions was applied to (*Z*)-*N*-benzyl-*N*-(but-2-en-1-yl)methanesulfonamide ***cis*-4.1** (0.0957 g, 0.4 mmol) using the donor **1.249** (0.454 g, 1.6 mmol, 4 eq.) for 72 h. After following the general work-up process, nothing was recovered from organic phase. Acidic work-up of the aqueous phase, and followed by column chromatography (20 % ethyl acetate in petroleum ether), provided *(Z)-N-(but-2-en-1-yl)methanesulfonamide* ***cis*-4.10** (0.0189 g, 32%) as a colourless oil. [Found: (EI^+) $(M-H)^+$ 148.0426. $C_5H_{10}NO_2S$ (M-H) requires 148.0427]; ν_{max}(film) /cm^{-1} 3281, 3024, 2935, 1433, 1409, 1305, 1139, 1056, 964, 754; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.71 (3H, d, J = 7.2 Hz, =CHCH_3), 2.98 (3H, s, SO_2CH_3), 3.82 (2H, t, J = 6.4 Hz, NCH_2) 4.25 (1H, bs, N*H*), 5.48 (1H, qq, J = 8.8, 2.0 Hz, NCH_2CH=CH), 5.68-5.76 (1H, m, =C*H*CH_3); *m/z* (EI^+) 149 [M, 3%], 134 (24), 107 (10), 70 (100), 53.8 (18).

Synthesis of diethyl 2-(2-ethoxybenzyl)-2-propylmalonate 4.19

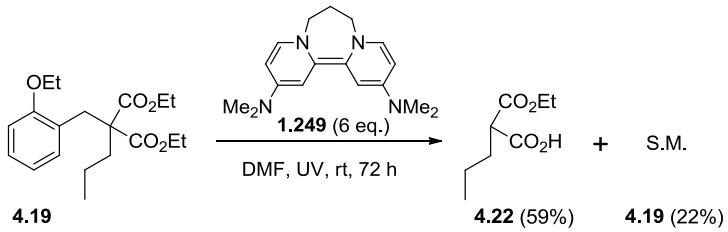


4.20 **4.21** **4.19** (76%)

A solution of diethyl propylmalonate **4.20** (1.2135 g, 6 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.288 g, 7.2 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at room temperature and then *o*-ethoxybenzyl bromide **4.21** (1.283 g, 6 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to afford *diethyl 2-(2-ethoxybenzyl)-2-propylmalonate* **4.19** (1.536 g, 76%) as a colourless oil. [Found: (ESI^+) $(M+H)^+$ 337.2007. $C_{19}H_{29}O_5$ (M+H) requires, 337.2010]; ν_{max}(film) /cm^{-1} 2975, 2939, 1729, 1453, 1243, 1211, 1125, 1037, 747; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (3H, t, J = 7.2 Hz, $CH_2CH_2CH_3$), 1.24 (6H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 1.32-1.38 (2H, m, $CH_2CH_2CH_3$), 1.41 (3H, t, J = 6.8 Hz, OCH_2CH_3), 1.69-1.73 (2H, m, $CH_2CH_2CH_3$), 3.32 (2H, s, $ArCH_2$), 4.01 (2H, q, J = 6.8 Hz, OCH_2CH_3), 4.13-4.22 (4H, m, $CO_2CH_2CH_3$),

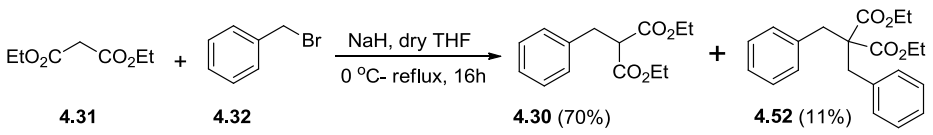
6.80-6.84 (2H, m, ArH), 7.01-7.03 (1H, m, ArH), 7.15-7.19 (1H, m, Ar*H*); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.1 (CH_3), 14.5 (CH_3), 14.7 (CH_3), 17.7 (CH_2), 31.5 (CH_2), 34.2 (CH_2), 59.1 (C), 60.9 (CH_2), 63.6 (CH_2), 111.2 (CH), 120.1 (CH), 125.2 (C), 128.1 (CH), 131.4 (CH), 157.7 (C), 171.8 (C=O); *m/z* (ESI^+) 359 (7), 337 [$(M+H)^+$, 100 %], 291 (14).

UV-activated reduction of diethyl 2-(2-ethoxybenzyl)-2-propylmalonate 4.19



The general procedure for electron transfer reactions under UV conditions was applied to diethyl 2-(2-ethoxybenzyl)-2-propylmalonate **4.19** (0.1344 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, the crude material was purified by column chromatography (5% diethyl ether in petroleum ether) and provided recovery of the starting material **4.19** (0.029 g, 22%) from the organic phase. Acidic work-up of the aqueous phase provided 2-(ethoxycarbonyl)pentanoic acid **4.22**[240] (0.041 g, 59%) as a colourless oil. For 2-(ethoxycarbonyl)pentanoic acid **4.22**: [Found: (ESI^-) $(M-H)^-$ 173.0824. $C_8H_{13}O_4$ (M-H) requires 173.0819]; ν_{max}(film) /cm^{-1} 3213, 2964, 2875, 1727, 1709, 1371, 1238, 1176, 1159; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (3H, t, *J* = 7.6 Hz, $CH_2CH_2CH_3$), 1.29 (3H, t, *J* = 7.2 Hz, $CO_2CH_2CH_3$), 1.40 (2H, sextet, *J* = 7.6 Hz, $CH_2CH_2CH_3$), 1.88-1.95 (2H, m, $CH_2CH_2CH_3$), 3.40 (1H, t, *J* = 7.2 Hz, $CHCO_2H$), 4.23 (2H, q, *J* = 7.2 Hz, $CO_2CH_2CH_3$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 13.7 (CH_3), 14.1 (CH_3), 20.6 (CH_2), 30.9 (CH_2), 51.6 (CH), 61.8 (CH_2), 169.6 (C=O), 175.3 (C=O); *m/z* (ESI^-) 347 [$(2M-H)^-$, 26%], 173 [$(M-H)^-$, 51%], 129 (100), 83 (7).

Synthesis of diethyl 2-benzylmalonate 4.30[241]



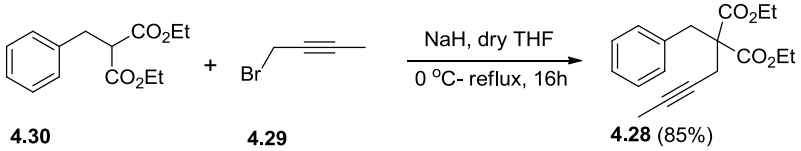
A suspension of sodium hydride (~60%, 0.440 g, 11.0 mmol) in dry tetrahydrofuran (10 mL) was added slowly via cannula into the flask containing solution of diethyl malonate

4.31 (1.6017 g, 10.0 mmol) in dry tetrahydrofuran (2 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 15 min at 0 ^{o}C and benzyl bromide **4.32** (1.7104 g, 10.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to yield diethyl 2-benzylmalonate **4.30**[241] (1.752 g, 70%) and diethyl 2,2-dibenzylmalonate **4.52**[242] (0.356 g, 11%) as colourless oils.

For diethyl 2-benzylmalonate **4.30**: [Found: (ESI^{+}) $(M+H)^{+}$ 251.1281. $C_{14}H_{19}O_4$ (M+H) requires 251.1278]; ν_{max}(film) /cm^{-1} 2986, 1727, 1453, 1369, 1224, 1146; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.22 (6H, t, J = 7.2 Hz, CH_3), 3.23 (2H, d, J = 8.0 Hz, ArCH_2), 3.65 (1H, t, J = 7.6 Hz, ArCH$_2$CH), 4.14-4.20 (4H, m, CO$_2$CH_2CH$_3$), 7.20-7.23 (3H, m, ArH), 7.26-7.30 (2H, m, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.1 (CH_3), 34.8 (CH_2), 53.9 (CH), 61.6 (CH_2), 126.8 (CH), 128.6 (CH), 128.9 (CH), 138.0 (C), 168.9 (C=O); *m/z* (ESI^{+}) 268 [$(M+NH_4)^{+}$, 68%], 251 [$(M+H)^{+}$, 100 %], 177 (8).

For diethyl 2,2-dibenzylmalonate **4.52**: [Found: (ESI^{+}) $(M+H)^{+}$ 341.1752 $C_{21}H_{25}O_4$ (M+H) requires 341.1747]; ν_{max}(film) /cm^{-1} 3030, 2980, 1724, 1494, 1244, 1174, 1085; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.17 (6H, t, J = 7.2 Hz, CH_3), 3.25 (4H, s, ArCH_2), 4.12 (4H, q, J = 7.2 Hz, CO$_2$CH_2CH$_3$), 7.18-7.31 (10H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.9 (CH_3), 39.3 (CH_2), 60.3 (C), 61.3 (CH_2), 127.0 (CH), 128.3 (CH), 130.3 (CH), 136.5 (C), 171.0 (C=O); *m/z* (ESI^{+}) 363 [$(M+Na)^{+}$, 6%], 341 [$(M+H)^{+}$, 100 %], 295 (21%), 249 (61%).

Synthesis of diethyl 2-benzyl-2-(but-2-yn-1-yl)malonate 4.28

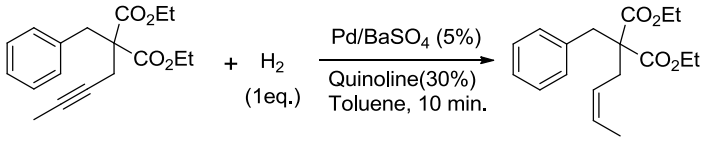


4.30 **4.29** **4.28** (85%)

A solution of diethyl 2-benzylmalonate **4.30** (1.4261 g, 5.7 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.342 g, 8.55

mmol) in dry tetrahydrofuran (10 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at room temperature and 1-bromobut-2-yne **4.29** (0.9103 g, 6.84 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to yield *diethyl 2-benzyl-2-(but-2-yn-1-yl)malonate* **4.28** (1.461 g, 85%) as a colourless oil. [Found: (ESI^{+}) $(M+H)^{+}$ 303.1595. $C_{18}H_{23}O_4$ (M+H) requires, 303.1591]; ν_{max}(film) /cm^{-1} 3027, 2980, 1733, 1442, 1278, 1198, 1179, 1095; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.26 (6H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 1.85 (3H, t, J = 2.4 Hz, CH_2CCCH_3), 2.63 (2H, q, J = 2.4 Hz, CH_2CCCH_3), 3.38 (2H, s, $ArCH_2$), 4.17-4.25 (4H, m, $CO_2CH_2CH_3$), 7.17-7.28 (5H, m, Ar*H*); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 3.7 (CH_3), 14.1 (CH_3), 22.6 (CH_2), 37.4 (CH_2), 58.5 (C), 61.6 (CH_2), 74.0 (C), 79.6 (C), 127.1 (CH), 128.4 (CH), 130.0 (CH), 136.0 (C), 170.1 (C=O); *m/z* (ESI^{+}) 341 [$(M+K)^{+}$, 10%], 303 [$(M+H)^{+}$, 100%], 269 (15), 251 (24).

Synthesis of (*Z*)-diethyl 2-benzyl-2-(but-2-en-1-yl)malonate *cis*-4.24

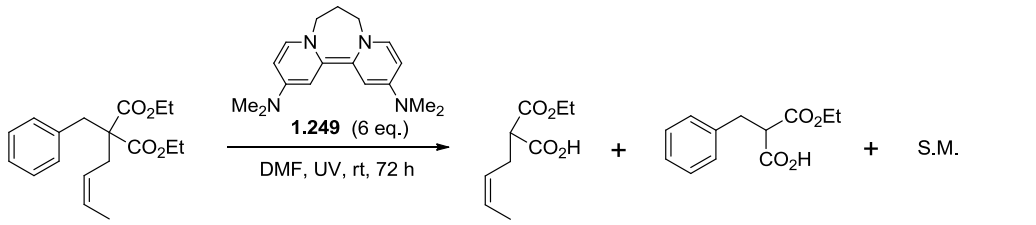


4.28 ***cis*-4.24** (86%)

Lindlar's catalyst ($Pd/BaSO_4$, 0.318 g, 5 mol%, 0.15 mmol) was added to a flask containing dry toluene (5 mL) and kept under argon gas. Diethyl 2-benzyl-2-(but-2-yn-1-yl)malonate **4.28** (0.906 g, 3 mmol) was added into the reaction flask and stirred for 10 min. before adding quinoline (0.114 g, 30 mol%, 0.9 mmol). This flask was then taken to the hydrogenation setup and the inside atmosphere was removed by vacuum and filled with hydrogen. The consumption of the hydrogen gas was monitored on a graduated column and 69 mL of hydrogen gas was utilised for the reaction and the reaction was finished in just 10 min. The reaction mixture was then filtered through celite and washed with toluene (2 x 10 mL). The resulting solution was then concentrated using a rotary evaporator and purified by column chromatography (10% diethyl ether in petroleum ether) to yield *(Z)-diethyl 2-benzyl-2-(but-2-en-1-yl)malonate* ***cis*-4.24** (0.7862 g, 86%) as

a light yellow oil. [Found: (ESI^+) $(M+H)^+$ 305.1749. $C_{18}H_{25}O_4$ (M+H) requires 305.1747]; ν_{max}(film) /cm^{-1} 3027, 2980, 1729, 1446, 1263, 1198, 1045; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.25 (6H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 1.60 (3H, dd, J = 6.8, 1.6 Hz, $CH_2CH{=}CHCH_3$), 2.56 (2H, dd, J = 7.2, 0.4 Hz, $CH_2CH{=}CHCH_3$), 3.25 (2H, s, $ArCH_2$), 4.20 (4H, q, J = 7.6 Hz, $CO_2CH_2CH_3$), 5.40 (1H, qq, J = 8.0, 1.6 Hz, $CH_2CH{=}CHCH_3$), 5.62-5.67 (1H, m, $CH_2CH{=}CHCH_3$), 7.08-7.10 (2H, m, Ar*H*), 7.19-7.28 (3H, m, Ar*H*); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 13.3 (CH_3), 14.2 (CH_3), 29.5 (CH_2), 38.1 (CH_2), 58.8 (C), 61.4 (CH_2), 124.0 (CH), 127.0 (CH), 127.8 (CH), 128.3 (CH), 130.1 (CH), 136.3 (C), 171.2 (C=O); *m/z* (ESI^+) 305 [$(M+H)^+$, 100%].

UV-activated reduction of (*Z*)-diethyl 2-benzyl-2-(but-2-en-1-yl)malonate *cis*-4.24



Donor-free, UV-active blank reaction provided only recovery of ***cis*-4.24** (90%)
Donor-active, non-UV blank reaction provided only recovery of ***cis*-4.24** (91%)

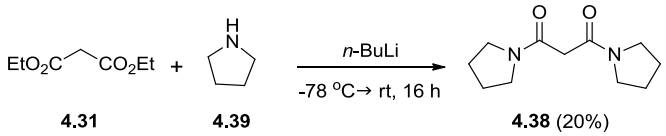
The general procedure for electron transfer reactions under UV conditions was applied to (*Z*)-diethyl 2-benzyl-2-(but-2-en-1-yl)malonate ***cis*-4.24** (0.1216 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, the crude material was purified by column chromatography (10% diethyl ether in petroleum ether) and provided recovery of the starting material ***cis*-4.24** (0.0176 g, 14%) from organic phase. Acidic work-up of the aqueous phase provided *(Z)-2-(ethoxycarbonyl)hex-4-enoic acid* ***cis*-4.33** (0.0476 g, 64%) as a colourless oil. A trace amount of 2-benzyl-3-ethoxy-3-oxopropanoic acid **4.34**[243] (trace amount) was also noticed in the ^{1}H-NMR of the crude product.

For (*Z*)-2-(ethoxycarbonyl)hex-4-enoic acid ***cis*-4.33**: [Found: (ESI^+) $(M+H)^+$ 187.0967. $C_9H_{15}O_4$ (M+H) requires 187.0965]; ν_{max}(film) /cm^{-1} 3521, 3176, 2986, 1711, 1373, 1228, 1159; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.30 (3H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 1.65 (3H, dt, J = 6.8, 0.8 Hz, $=CHCH_3$), 2.71 (2H, dd, J = 10.4, 7.6 Hz, $=CHCH_2CH$), 3.44 (1H, t, J = 7.6 Hz, $CHCO_2H$), 4.24 (2H, q, J = 7.2 Hz, $CO_2CH_2CH_3$), 5.35 (1H, qq, J = 7.6, 2.4 Hz, $CH_2CH{=}CHCH_3$), 5.57-5.65 (1H, m, $CH_2CH{=}CHCH_3$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ

12.9 (CH_3), 14.2 (CH_3), 26.6 (CH_2), 51.7 (CH), 61.9 (CH_2), 125.2 (CH), 127.7 (CH), 169.3 (C), 174.3 (C=O); *m/z* (CI^+) 204 [$(M+NH_4)^+$, 100%], 187 [$(M+H)^+$, 21%], 160 (26), 143 (13).

Donor-free, UV-active and donor-active, non-UV blank reactions were performed as per general procedure and provided the starting material ***cis*-4.24** (0.109 g, 90%) and (0.1108 g, 91%, respectively.

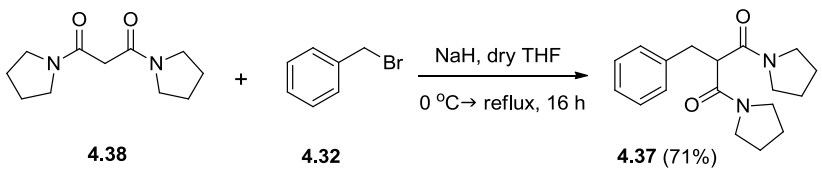
Synthesis of 1,3-di(pyrrolidin-1-yl)propane-1,3-dione 4.38[244]



4.31 **4.39** **4.38** (20%)

n-Butyllithium (2.3 M in hexane, 13 mL, 30 mmol) was added dropwise into a flask containing dry pyrrolidine **4.39** (2.1336 g, 30 mmol) in dry THF (20 mL) at -78 °C under argon gas. The reaction contents were stirred for 30 min. before transferring dropwise into another flask containing diethyl malonate **4.31** (1.6017 g, 10 mmol) in dry THF (10 mL) via cannula at -78 °C. The resulting reaction mixture was further stirred at room temperature for 16 h. The reaction was then quenched with water (10 mL) and concentrated. The crude solid was purified by recrystallization from diethyl ether to provide 1,3-di(pyrrolidin-1-yl)propane-1,3-dione **4.38** (0.412 g, 20%) **2.237**[244] as a white solid m.p. 108-110 °C (lit.:[244] 109-110 °C). [Found: (ESI^+) $(M+H)^+$ 211.1444. $C_{11}H_{19}O_2N_2$ (M+H) requires 211.1441]; ν_{max}(film) /cm^{-1} 2973, 2868, 1630, 1438, 1196; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.84-1.91 (4H, m, NCH_2CH_2), 1.93-2.00 (4H, m, NCH_2CH_2), 3.41 (2H, s, $COCH_2CO$), 3.49 (4H, t, J = 6.8 Hz, NCH_2CH_2), 3.59 (4H, t, J = 6.8 Hz, NCH_2CH_2); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 24.4 (CH_2), 26.0 (CH_2), 43.2 (CH_2), 45.9 (CH_2), 47.3 (CH_2), 165.4 (C=O); *m/z* (ESI^+) 443 [$(2M+Na)^+$, 58%], 233 (12), 211 [$(M+H)^+$, 100%].

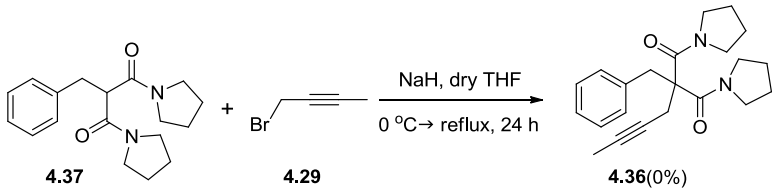
Synthesis of 2-benzyl-1,3-di(pyrrolidin-1-yl)propane-1,3-dione 4.37



4.38 **4.32** **4.37** (71%)

A solution of 1,3-di(pyrrolidin-1-yl)propane-1,3-dione **4.38** (0.451 g, 2.15 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.094 g, 2.365 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at 0 ^{o}C and benzyl bromide **4.32** (0.367 g, 2.15 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 16 h under argon gas. The reaction was then quenched with water (5 mL) and concentrated using rotary evaporator. The crude solid was purified by recrystallization from hexane to provide *2-benzyl-1,3-di(pyrrolidin-1-yl)propane-1,3-dione* **4.37** (0.461 g, 71%) as a white solid m.p. 116-118 ^{o}C; [Found: (ESI^{+}) $(M+H)^{+}$ 301.1911. $C_{18}H_{25}O_2N_2$ (M+H) requires, 301.1911]; ν_{max}(film) /cm^{-1} 3500, 3463, 2969, 2881, 1632, 1617, 1422; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68-1.87 (8H, m, NCH_2CH_2), 2.97-3.03 (2H, m, NCH_2CH_2), 3.19-3.25 (2H, m, NCH_2CH_2), 3.28 (2H, d, J = 7.2 Hz, $ArCH_2$), 3.42-3.52 (4H, m, NCH_2CH_2), 3.64 (1H, t, J = 7.6 Hz, COCHCO), 7.19-7.29 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 24.2 (CH_2), 26.2 (CH_2), 36.0 (CH_2), 46.1 (CH_2), 46.3 (CH_2), 53.3 (CH), 126.6 (CH), 128.5 (CH), 129.4 (CH), 139.5 (C), 167.6 (C=O); *m/z* (ESI^{+}) 623 [$(2M+Na)^{+}$, 29%], 323 [$(M+Na)^{+}$, 5%], 301 [$(M+H)^{+}$, 100%].

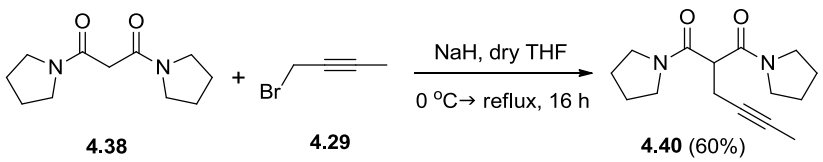
Attempted synthesis of 2-benzyl-2-(but-2-yn-1-yl)-1,3-di(pyrrolidin-1-yl)propane-1,3-dione 4.36



4.37 **4.29** **4.36**(0%)

A solution of 2-benzyl-1,3-di(pyrrolidin-1-yl)propane-1,3-dione **4.37** (0.600 g, 2.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.120 g, 3.0 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-bromobut-2-yne **4.29** (0.319 g, 2.4 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. The reaction was then quenched with water (5 mL) and concentrated using rotary evaporator. The crude solid was purified by recrystallization from hexane and provided recovery of the starting material **4.37** (0.485 g, 81%) only.

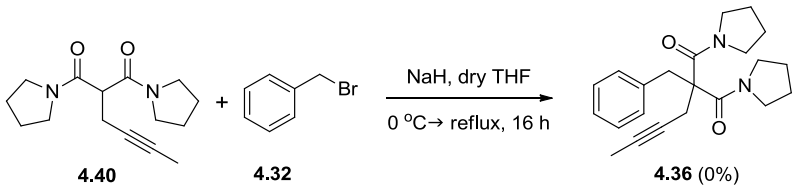
Synthesis of 2-(but-2-yn-1-yl)-1,3-di(pyrrolidin-1-yl)propane-1,3-dione 4.40



4.38 **4.29** **4.40** (60%)

A solution of 1,3-di(pyrrolidin-1-yl)propane-1,3-dione **4.38** (0.420 g, 2.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.088 g, 2.2 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at 0 ^{o}C and 1-bromobut-2-yne **4.29** (0.292 g, 2.2 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 16 h under argon gas. The reaction was then quenched with water (5 mL) and concentrated using rotary evaporator. The crude solid was purified by recrystallization from hexane to provide *2-(but-2-yn-1-yl)-1,3-di(pyrrolidin-1-yl)propane-1,3-dione* **4.40** (0.317 g, 60%) as a white solid m.p. 130-132 ^{o}C; [Found: (ESI^{+}) $(M+H)^{+}$ 263.1757. $C_{15}H_{23}O_2N_2$ (M+H) requires 263.1754]; ν_{max}(film) /cm^{-1} 2963, 2866, 1630, 1422, 1166; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.74 (3H, t, J = 2.8 Hz, C*H*$_3$), 1.83-2.01 (8H, m, NCH$_2$C*H*$_2$), 2.79-2.82 (2H, m, CH$_3$CCC*H*$_2$), 3.36-3.42 (2H, m, NC*H*$_2$CH$_2$), 3.53 (4H, t, J = 6.8 Hz, NC*H*$_2$CH$_2$), 3.63-3.69 (3H, m, NC*H*$_2$CH$_2$, COC*H*CO); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 3.7 (CH_3), 19.5 (CH_2), 24.4 (CH_2), 26.4 (CH_2), 46.4 (CH_2), 46.5 (CH_2), 50.3 (CH), 76.4 (C), 77.0 (C), 167.1 (C); *m/z* (ESI^{+}) 547 [$(2M+Na)^{+}$, 35%], 285 [$(M+Na)^{+}$, 7%], 263 [$(M+H)^{+}$, 100%].

Attempted synthesis of 2-benzyl-2-(but-2-yn-1-yl)-1,3-di(pyrrolidin-1-yl)propane-1,3-dione 4.36

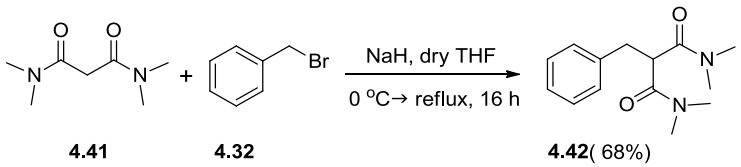


4.40 **4.32** **4.36** (0%)

A solution of 2-(but-2-yn-1-yl)-1,3-di(pyrrolidin-1-yl)propane-1,3-dione **4.40** (0.213 g, 0.81 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.048 g, 1.215 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 45 min at room temperature and benzyl bromide **4.32** (0.166 g, 0.972 mmol) in dry tetrahydrofuran (2 mL) was added slowly into

the reaction flask. The reaction mixture was further stirred at reflux conditions for 16 h under argon gas. The reaction was then quenched with water (5 mL) and concentrated using a rotary evaporator. The crude solid was purified by recrystallization from hexane and provided recovery of the starting material **4.40** (0.184 g, 86%) only.

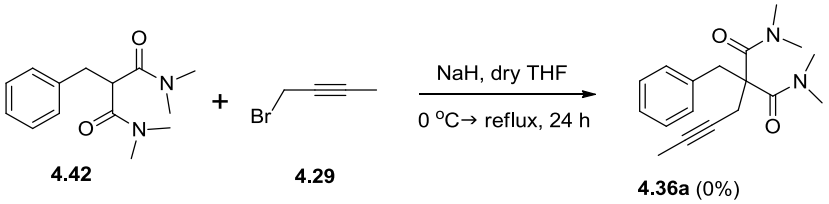
Synthesis of 2-benzyl-N^1,N^1,N^3,N^3-tetramethylmalonamide 4.42



4.41 **4.32** **4.42**(68%)

A solution of N^1,N^1,N^3,N^3-tetramethylmalonamide **4.41** (0.948 g, 6.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.240 g, 6.0 mmol) in dry tetrahydrofuran (5 mL) at 0 °C under argon gas. The resulting solution was stirred for 30 min at 0 °C and benzyl bromide **4.32** (1.026 g, 6.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 16 h under argon gas. The reaction was then quenched with water (5 mL) and concentrated. The crude solid was purified by recrystallization from diethyl ether to provide *2-benzyl-N^1,N^1,N^3,N^3-tetramethylmalonamide* **4.42** as a white solid (1.134 g, 76%). [Found: (ESI^+) $(M+H)^+$ 249.1597. $C_{14}H_{21}O_2N_2$ (M+H) requires 249.1598]; ν_{max}(film) /cm^{-1} 3027, 2926, 1634, 1491, 1394, 1263, 1133, 1036, 756; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.78 (6H, s, N(C*H*$_3$)$_2$), 2.94 (6H, s, N(*CH*$_3$)$_2$), 3.26 (2H, d, J = 7.2 Hz, ArC*H*$_2$), 3.91 (1H, t, J = 7.2 Hz, ArCH$_2$C*H*), 7.22-7.30 (5H, m, Ar*H*); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 36.07 (CH_3), 36.12 (CH_3), 36.9 (CH_2), 50.2 (CH), 126.7 (CH), 128.5 (CH), 129.3 (CH), 139.4 (C), 169.3 (C=O); *m/z* (ESI^+) 519 [$(2M+Na)^+$, 27%], 271 [$(M+Na)^+$, 21%], 249 [$(M+H)^+$, 100%], 204 (6).

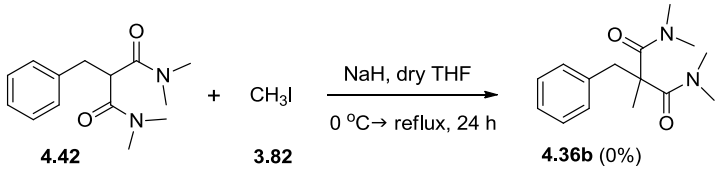
Attempted synthesis of 2-benzyl-2-(but-2-yn-1-yl)- N^1,N^1,N^3,N^3-tetramethylmalon amide 4.36a



4.42 **4.29** **4.36a** (0%)

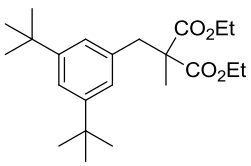
A solution of 2-benzyl-N^1,N^1,N^3,N^3-tetramethylmalonamide **4.42** (0.235 g, 0.95 mmol) in dry tetrahydrofuran (2 mL) was added slowly to a suspension of sodium hydride (~60%, 0.057 g, 1.425 mmol) in dry tetrahydrofuran (5 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-bromobut-2-yne **4.29** (0.151 g, 1.14 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. The reaction was then quenched with water (5 mL) and concentrated. The crude solid was purified by recrystallization from hexane and provided recovery of the starting material **4.42** (0.198 g, 84%) only.

Attempted synthesis of 2-benzyl- N^1,N^1,N^3,N^3,2-pentamethylmalonamide 4.36b



A solution of 2-benzyl-N^1,N^1,N^3,N^3-tetramethylmalonamide **4.42** (0.868 g, 3.5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.182 g, 4.55 mmol) in dry tetrahydrofuran (5 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 45 min at room temperature and iodomethane **3.82** (0.645 g, 4.55 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. The reaction was then quenched with water (5 mL) and concentrated. The crude solid was purified by recrystallization using hexane and provided recovery of the starting material **4.42** (0.691 g, 80%) only.

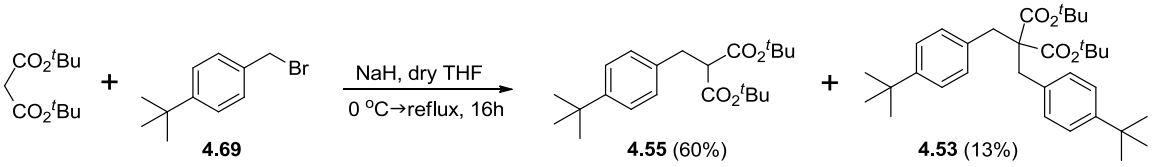
Synthesis of diethyl 2-(3,5-di-tert-butylbenzyl)-2-methylmalonate 4.43



A solution of diethyl methylmalonate (0.340 g, 1.95 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.094 g, 2.34 mmol) in dry tetrahydrofuran (5 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 30

min at room temperature and 1-(bromomethyl)-3,5-di-*tert*-butylbenzene (0.550 g, 1.95 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to afford *diethyl 2-(3,5-di-tert-butylbenzyl)-2-methylmalonate* **4.43** (0.617 g, 84%) as a colourless oil. [Found: (ESI^+) $(M+H)^+$ 377.2690. $C_{23}H_{37}O_4$ (M+H) requires, 377.2686]; ν_{max}(film) /cm^{-1} 2956, 2904, 1732, 1598, 1462, 1236, 1105; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27 (6H, t, J = 7.0 Hz, $CO_2CH_2CH_3$), 1.30 [18H, s, $C(CH_3)_3$], 1.33 (3H, s, CCH_3), 3.23 (2H, s, $ArCH_2$), 4.17-4.23 (4H, m, $CO_2CH_2CH_3$), 6.95 (2H, d, J = 2.0 Hz, ArH), 7.27 (1H, t, J = 2.0 Hz, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.2 (CH_3), 19.8 (CH_3), 31.6 (CH_3), 34.8 (C), 41.7 (CH_2), 55.1 (C), 61.3 (CH_2), 120.7 (CH), 124.5 (CH), 135.3 (C), 150.4 (C), 172.2 (C=O); *m/z* (ESI^+) 770 [$(2M+NH_4)^+$, 4%], 394 [$(M+NH_4)^+$, 86%], 377 [$(M+H)^+$, 100 %], 331 (9), 257 (10).

Synthesis of di-*tert*-butyl 2-(4-(*tert*-butyl)benzyl)malonate 4.55 and di-*tert*-butyl 2,2-*bis*(4-(*tert*-butyl)benzyl)malonate 4.53



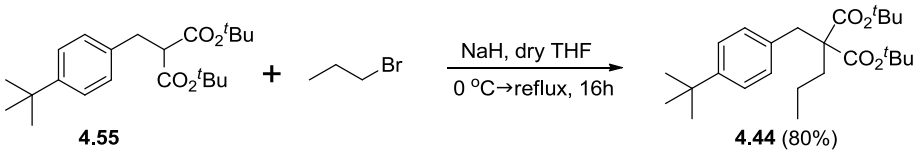
A solution of di-*tert*-butyl malonate (0.865 g, 4 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.176 g, 4.4 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at room temperature and 1-(bromomethyl)-4-(*tert*-butyl)benzene **4.69** (0.908 g, 4 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to afford *di-tert-butyl 2-*

(4-(tert-butyl)benzyl)malonate **4.55** (0.863 g, 60%) as a colourless oil and *di-tert-butyl 2,2-bis(4-(tert-butyl)benzyl)malonate* **4.53** (0.263 g, 13%) as a white crystalline solid m.p. 110-112 ^{o}C.

For di-*tert*-butyl 2-(4-(*tert*-butyl)benzyl)malonate **4.55**: [Found: (ESI^{+}) $(M+H)^{+}$ 363.2535. $C_{22}H_{35}O_4$ (M+H) requires 363.2530]; ν_{max}(film) /cm^{-1} 2986, 1726, 1458, 1367, 1247, 1134; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (9H, s, ArC(CH_3)$_3$), 1.41 (18H, s, 2 x OC(CH_3)$_3$), 3.10 (2H, d, J = 8.0 Hz, ArCH_2), 3.46 (1H, t, J = 8.0 Hz, ArCH$_2$*CH*), 7.14 (2H, d, J = 8.5 Hz, ArH), 7.29 (2H, d, J = 8.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 28.0 (6 x CH_3), 31.5 (3 x CH_3), 34.2 (CH_2), 34.5 (C), 55.6 (CH), 81.5 (2 x C), 125.3 (CH), 128.7 (CH), 135.4 (C), 149.4 (C), 168.5 (C=O); *m/z* (ESI^{+}) 742 [$(2M+NH_4)^{+}$, 7%], 380 [$(M+NH_4)^{+}$, 91 %], 363 [$(M+H)^{+}$, 15 %], 307 (42), 251 (100), 195 (35), 147 (7).

For di-*tert*-butyl 2,2-*bis*(4-(*tert*-butyl)benzyl)malonate **4.53**: [Found: (ESI^{+}) $(M+H)^{+}$ 509.3622. $C_{33}H_{49}O_4$ (M+H) requires 509.3625]; ν_{max}(film) /cm^{-1} 2980, 1724, 1453, 1365, 1236, 1138; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (18H, s, 2 x ArC(CH_3)$_3$), 1.38 (18H, s, 2 x OC(CH_3)$_3$), 3.16 (4H, s, ArCH_2), 7.17 (4H, d, J = 8.0 Hz, ArH), 7.27 (4H, d, J = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 28.0 (6 x CH_3), 31.5 (6 x CH_3), 34.5 (2 x CH_2), 38.6 (2 x C), 60.5 (C), 81.7 (2 x C), 125.1 (CH), 130.2 (CH), 134.1 (C), 149.5 (C), 170.6 (C=O); *m/z* (ESI^{+}) 1034 [$(2M+NH_4)^{+}$, 8%], 531 [$(M+Na)^{+}$, 34 %], 397 (100), 361 (39), 147 (17).

Synthesis of di-*tert*-butyl 2-(4-(tert-butyl)benzyl)-2-propylmalonate 4.44

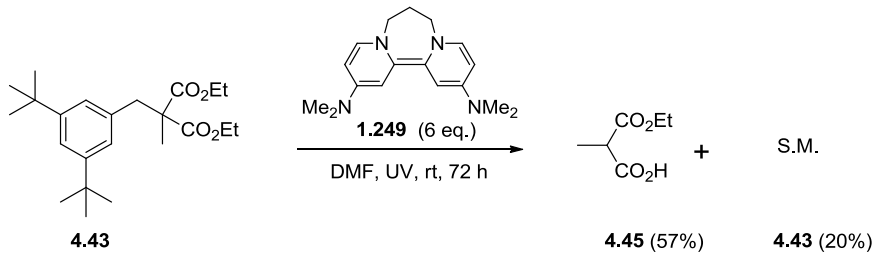


4.55 **4.44** (80%)

A solution of di-*tert*-butyl 2-(4-(*tert*-butyl)benzyl)malonate **4.55** (0.543 g, 1.5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.072 g, 1.8 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at room temperature and 1-propyl bromide (0.221 g, 1.8 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the

reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to afford *di-tert-butyl 2-(4-(tert-butyl)benzyl)-2-propylmalonate* **4.44** (0.482 g, 80%) as a white crystalline solid m.p. 80-82 ^{o}C. [Found: (ESI^{+}) $(M+H)^{+}$ 405.2998. $C_{25}H_{41}O_4$ (M+H) requires 405.2999]; ν_{max}(film) /cm^{-1} 2962, 1722, 1450, 1365, 1224, 1145; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (3H, t, J = 7.2 Hz, $CH_2CH_2CH_3$), 1.30 (9H, s, $ArC(CH_3)_3$), 1.31-1.36 (2H, m, $CH_2CH_2CH_3$), 1.46 (18H, s, 2 x $OC(CH_3)_3$), 1.67-1.71 (2H, m, $CH_2CH_2CH_3$), 3.14 (2H, s, $ArCH_2$), 7.07 (2H, d, J = 8.0 Hz, ArH), 7.26 (2H, d, J = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.6 (CH_3), 17.6 (CH_2), 28.1 (6 x CH_3), 31.5 (3 x CH_3), 34.2 (CH_2), 34.5 (C), 37.3 (CH_2), 59.6 (C), 81.2 (2 x C), 125.1 (CH), 129.9 (CH), 133.9 (C), 149.5 (C), 170.9 (C=O); *m/z* (ESI^{+}) 831 [$(2M+Na)^{+}$, 27%], 427 [$(M+Na)^{+}$, 28%], 405 [$(M+H)^{+}$, 36 %], 349 (23), 293 (100), 275 (32), 229 (15).

UV-activated reduction of diethyl 2-(3,5-di-tert-butylbenzyl)-2-methylmalonate 4.43

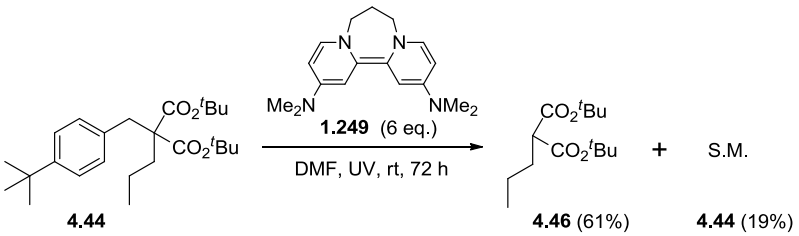


4.43 **4.45** (57%) **4.43** (20%)

The general procedure for electron transfer reactions under UV conditions was applied to diethyl 2-(3,5-di-*tert*-butylbenzyl)-2-methylmalonate **4.43** (0.1505 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.). After following the general work-up process, the crude material was purified by column chromatography (5% diethyl ether in petroleum ether) and provided recovery of the starting material **4.43** (0.0296 g, 20%) from the organic phase. Acidic work-up of the aqueous phase provided 3-ethoxy-2-methyl-3-oxopropanoic acid **4.45**[245] (0.033 g, 57%) as a colourless oil. For **4.45**: [Found: (CI^{+} corona) $(M+H)^{+}$ 147.0650. $C_6H_{11}O_4$ (M+H) requires 147.0652]; ν_{max}(film) /cm^{-1} 3242, 2981, 2945, 1727, 1709, 1460, 1178, 1083; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (3H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 1.46 (2H, d, J = 7.2 Hz, $CHCH_3$), 3.48 (1H, q, J = 7.2 Hz, $CHCO_2H$), 4.23 (2H, q, J = 7.2 Hz, $CO_2CH_2CH_3$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 13.7

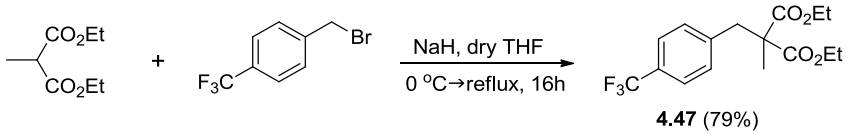
(CH_3), 14.1 (CH_3), 46.1 (CH), 61.9 (CH_2), 170.1 (C), 175.6 (C=O); *m/z* (CI^+ corona) 147 [$(M+H)^+$, 100%], 129 (37).

UV-activated reduction of di-*tert*-butyl 2-(4-(*tert*-butyl)benzyl)-2-propylmalonate 4.44



The general procedure for electron transfer reactions under UV conditions was applied to di-*tert*-butyl 2-(4-(*tert*-butyl)benzyl)-2-propylmalonate **4.44** (0.121 g, 0.3 mmol) using the donor **1.249** (0.511 g, 1.8 mmol, 6 eq.). After following the general work-up process, the crude material was purified by column chromatography (5% diethyl ether in petroleum ether)and provided *di-tert-butyl 2-propylmalonate* **4.46** (0.0476 g, 61%) along with recovery of the starting material **4.44** (0.023 g, 19%) from the organic phase. For **4.46**: [Found: (ESI^+) $(M+H)^+$ 259.1908. $C_{14}H_{27}O_4$ (M+H) requires 259.1904]; ν_{max}(film) /cm^{-1} 2976, 2875, 1726, 1367, 1246, 1134; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, t, J = 7.6 Hz, $CH_2CH_2CH_3$), 1.30-1.40 (2H, m, $CH_2CH_2CH_3$), 1.46 (18H, s, $CO_2C(CH_3)_3$), 1.76-1.81 (2H, m, $CH_2CH_2CH_3$), 3.13 (1H, t, J = 7.6 Hz, $CHCH_2CH_2CH_3$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.9 (CH_3), 20.6 (CH_2), 28.1 (6 x CH_3), 30.8 (CH_2), 53.9 (CH), 81.3 (C), 169.2 (C=O); *m/z* (ESI^+) 534 [$(2M+NH_4)^+$, 6%], 259 [$(M+H)^+$, 8%], 203 (44), 147 (100).

Synthesis of diethyl 2-methyl-2-(4-(trifluoromethyl)benzyl)malonate 4.47

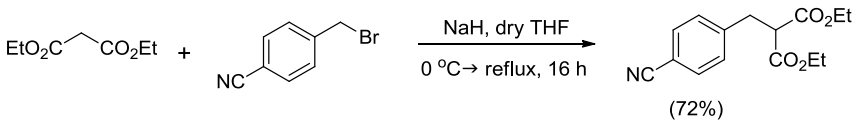


A solution of diethyl methylmalonate (0.348 g, 2 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.088 g, 2.2 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at room temperature and 1-(bromomethyl)-4-(trifluoromethyl)benzene (0.478 g, 2 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the

reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (20% diethyl ether in petroleum ether) to afford *diethyl 2-methyl-2-(4-(trifluoromethyl)benzyl)malonate* **4.47** (0.526 g, 79%) as a colourless oil. [Found: (ESI$^+$) $(M+H)^+$ 333.1313. $C_{16}H_{20}F_3O_4$ (M+H) requires 333.1308]; ν_{max}(film) /cm^{-1} 2981, 2939, 1728, 1618, 1323, 1109, 1066, 1018; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.26 (6H, t, J = 7.5 Hz, $CO_2CH_2CH_3$), 1.35 (3H, s, CCH_3), 3.28 (2H, s, ArCH_2), 4.20 (4H, qd, J = 7.0, 1.5 Hz, $CO_2CH_2CH_3$), 7.26 (2H, d, J = 8.5 Hz, ArH), 7.52 (2H, d, J = 8.5 Hz, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.1 (CH_3), 19.9 (CH_3), 41.0 (CH_2), 54.8 (C), 61.6 (CH_2), 124.3 (d, CF_3, $J_{C\text{-}F}$ = 271.25 Hz), 125.2 (CH), 129.4 (q, C-CF_3, $J_{C\text{-}F}$ = 31.25 Hz), 130.7 (CH), 140.7 (C), 171.7 (C=O); *m/z* (ESI$^+$) 350 [$(M+NH_4)^+$, 37%], 333 [$(M+H)^+$, 100 %], 287 (5), 213 (4).

Synthesis of (*Z*)-diethyl 2-(but-2-en-1-yl)-2-(4-cyanobenzyl)malonate *cis*-4.48

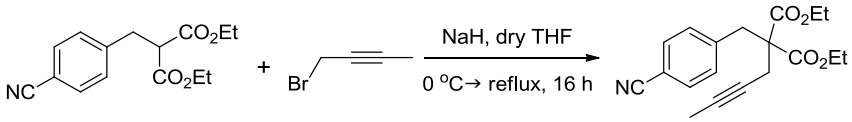
(a) Synthesis of diethyl 2-(4-cyanobenzyl)malonate[246]



A solution of diethyl malonate **4.31** (0.640 g, 4.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.176 g, 4.4 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 15 min at 0 ^{o}C and 4-(bromomethyl)benzonitrile (0.784 g, 4.0 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (15% ethyl acetate in petroleum ether) to yield diethyl 2-(4-cyanobenzyl)malonate[246] (0.794 g, 72%) as a colourless liquid. [Found: (ESI$^+$) $(M+H)^+$ 276.1233. $C_{15}H_{18}NO_4$ (M+H) requires 276.1230]; ν_{max}(film) /cm^{-1} 2980, 2939, 2231, 1727, 1394, 1272, 1147, 1034; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.22 (6H, t, J = 6.8 Hz,

CH_2CH_3), 3.27 (2H, d, J = 7.6 Hz, $ArCH_2$), 3.64 (1H, t, J = 7.6 Hz, $ArCH_2CH$), 4.13-4.22 (4H, m, $CO_2CH_2CH_3$), 7.40 (2H, d, J = 8.0 Hz, Ar*H*), 7.59 (2H, d, J = 8.0 Hz, Ar*H*); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.1 (CH_3), 34.7 (CH_2), 53.2 (CH), 61.9 (CH_2), 110.9 (C), 118.9 (C), 129.9 (CH), 132.4 (CH), 143.7 (C), 168.4 (C=O); *m/z* (ESI^+) 573 [$(2M+Na)^+$, 24%], 293 [$(M+ NH_4)^+$, 78%], 276 [$(M+H)^+$, 100%].

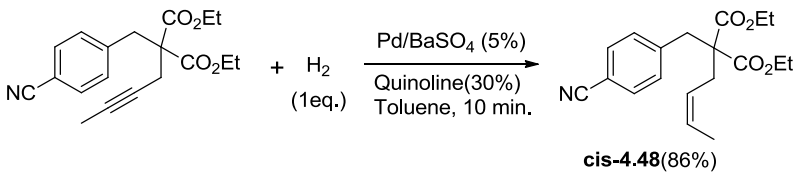
(b) Synthesis of diethyl 2-(but-2-yn-1-yl)-2-(4-cyanobenzyl)malonate



4.29 (69%)

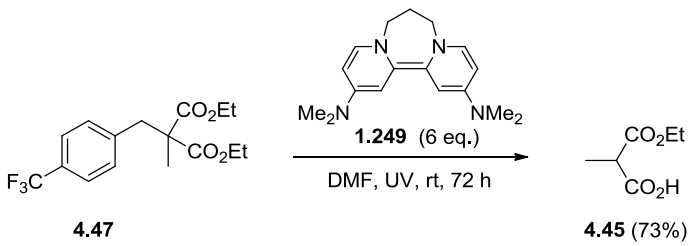
A solution of diethyl 2-(4-cyanobenzyl)malonate (0.413 g, 1.5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.090 g, 2.25 mmol) in dry tetrahydrofuran (5 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 45 min at room temperature and 1-bromobut-2-yne **4.29** (0.240 g, 1.8 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% ethyl acetate in petroleum ether) to yield *diethyl 2-(but-2-yn-1-yl)-2-(4-cyanobenzyl)malonate* (0.339 g, 69%) as a white solid. [Found: (ESI^+) $(M+H)^+$ 328.1548. $C_{19}H_{22}NO_4$ (M+H) requires 328.1543]; ν_{max}(film) /cm^{-1} 2986, 2934, 2223, 1750, 1446, 1280, 1181; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (6H, t, J = 6.8 Hz, CH_2CH_3), 1.85 (3H, t, J = 2.8 Hz, CCH_3), 2.60 (2H, q, J = 2.8 Hz, CH_2CCCH_3), 3.43 (2H, s, $ArCH_2$), 4.15-4.27 (4H, m, $CO_2CH_2CH_3$), 7.31 (2H, d, J = 8.0 Hz, Ar*H*), 7.57 (2H, d, J = 8.0 Hz, Ar*H*); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 3.7 (CH_3), 14.2 (CH_3), 22.8 (CH_2), 37.6 (CH_2), 58.3 (C), 61.9 (CH_2), 73.5 (C), 80.3 (C), 111.2 (C), 118.9 (C), 130.9 (CH), 132.2 (CH), 141.9 (C), 169.6 (C=O); *m/z* (ESI^+) 350 [$(M+Na)^+$, 14%], 328 [$(M+H)^+$, 100%], 300 (5).

(c) Synthesis of (*Z*)-diethyl 2-(but-2-en-1-yl)-2-(4-cyanobenzyl)malonate *cis*-4.48



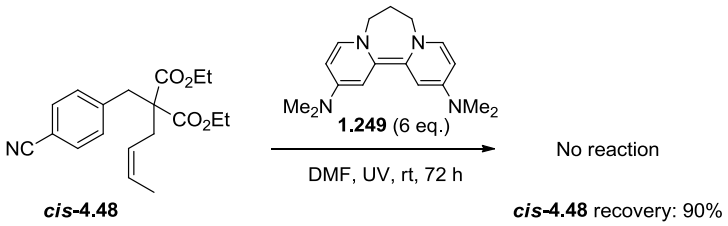
Lindlar's catalyst ($Pd/BaSO_4$, 0.0795 g, 0.0375 mmol) was added to a flask containing dry toluene (5 mL) and kept under argon gas. Diethyl 2-(but-2-yn-1-yl)-2-(4-cyanobenzyl)malonate (0.245 g, 0.75 mmol) was added into the reaction flask and stirred for 10 min. before adding quinoline (0.030 g, 0.225 mmol). This flask was then taken to the hydrogenation setup and the inside atmosphere was removed by vacuum and filled with hydrogen. The consumption of the hydrogen gas was monitored on a graduated column and 18 mL of hydrogen gas was utilised for the reaction and the reaction was finished in just 10 min. The reaction mixture was then filtered through celite and washed with toluene (2 x 10 mL). The resulting solution was then concentrated and purified by column chromatography (10% ethyl acetate in petroleum ether) to yield *(Z)-diethyl 2-(but-2-en-1-yl)-2-(4-cyanobenzyl)malonate* ***cis*-4.48** (0.212 g, 86%) as a white solid m.p. 88 - 90 ^{o}C; [Found: (ESI^+) $(M+H)^+$ 330.1691. $C_{19}H_{24}NO_4$ (M+H) requires 330.1700]; ν_{max}(film) /cm^{-1} 3010, 2989, 2227, 1729, 1606, 1446, 1328, 1198, 855; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (6H, t, J = 7.2 Hz, CH_2CH_3), 1.60 (3H, d, J = 6.8 Hz, $=CHCH_3$), 2.56 (2H, dd, J = 6.8, 0.8 Hz, $CH_2CH=CHCH_3$), 3.28 (2H, s, $ArCH_2$), 4.12-4.24 (4H, m, $CO_2CH_2CH_3$), 5.31-5.38 (1H, m, $CH_2CH=CH$), 5.63-5.72 (1H, m, $CH_2CH=CH$), 7.23 (2H, d, J = 8.4 Hz, Ar*H*), 7.55 (2H, d, J = 8.4 Hz, Ar*H*); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.3 (CH_3), 14.1 (CH_3), 29.9 (CH_2), 38.3 (CH_2), 58.7 (C), 61.7 (CH_2), 111.0 (C), 118.9 (C), 123.4 (CH), 128.4 (CH), 131.0 (CH), 132.1 (CH), 142.3 (C), 170.7 (C=O); *m/z* (ESI^+) 681 $[(2M+Na)^+$, 24%], 368 $[(M+K)^+$, 14%], 330 $[(M+H)^+$, 100%].

UV-activated reduction of diethyl 2-methyl-2-(4-(trifluoromethyl)benzyl)malonate 4.47



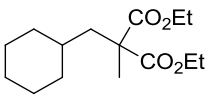
The general procedure for electron transfer reactions under UV conditions was applied to diethyl 2-methyl-2-(4-(trifluoromethyl)benzyl)malonate **4.47** (0.1328 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, no starting material was recovered from the organic phase. Acidic work-up of the aqueous phase provided 3-ethoxy-2-methyl-3-oxopropanoic acid **4.45**[245] (0.042 g, 73%) as a colourless oil. [Found: (CI^+ corona) $(M+H)^+$ 147.0650. $C_6H_{11}O_4$ (M+H) requires 147.0652]; ν_{max}(film) /cm^{-1} 3242, 2981, 2945, 1727, 1709, 1460, 1178, 1083; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.29 (3H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 1.46 (3H, d, J = 7.2 Hz, $CHCH_3$), 3.48 (1H, q, J = 7.2 Hz, $CHCO_2H$), 4.23 (2H, q, J = 7.2 Hz, $CO_2CH_2CH_3$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 13.7 (CH_3), 14.1 (CH_3), 46.1 (CH), 61.9 (CH_2), 170.1 (C), 175.6 (C); *m/z* (CI^+ corona) 147 [$(M+H)^+$, 100%], 129 (37).

UV-activated reduction of (*Z*)-diethyl 2-(but-2-en-1-yl)-2-(4-cyanobenzyl)malonate *cis*-4.48



The general procedure for electron transfer reactions under UV conditions was applied to (*Z*)-diethyl 2-(but-2-en-1-yl)-2-(4-cyanobenzyl)malonate ***cis*-4.48** (0.132 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, starting material ***cis*-4.48** (0.119 g, 90%) was recovered from organic phase. No product was obtained from acidic work-up of the aqueous phase.

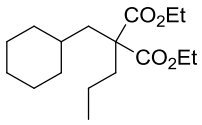
Synthesis of diethyl 2-(cyclohexylmethyl)-2-methylmalonate 4.49[247]



A solution of diethyl methylmalonate (0.870 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.240 g, 6 mmol) in dry tetrahydrofuran (5 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 30 min at room temperature and (bromomethyl)cyclohexane (0.885 g, 5 mmol) in dry

tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to afford diethyl 2-(cyclohexylmethyl)-2-methylmalonate **4.49** (1.106 g, 82%) as a colourless oil. [Found: (ESI^+) $(M+H)^+$ 271.1908. $C_{15}H_{27}O_4$ (M+H) requires 271.1904]; ν_{max}(film) /cm^{-1} 2981, 2922, 1728, 1448, 1371, 1251, 1226, 1105; ^1H NMR (400 MHz, $CDCl_3$) δ 0.90-1.01 (2H, m, C_6H_{11}), 1.10-1.39 (10H, m, $CO_2CH_2CH_3$, C_6H_{11}), 1.42 (3H, s, CCH_3), 1.58-1.68 (5H, m, C_6H_{11}), 1.83 (2H, d, J = 5.6 Hz, $CyCH_2$), 4.17 (4H, q, J = 7.2 Hz, OCH_2CH_3); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.1 (CH_3), 20.2 (CH_3), 26.3 (CH_2), 26.4 (CH_2), 33.9 (CH), 34.4 (CH_2), 42.4 (CH_2), 53.3 (C), 61.2 (CH_2), 172.9 (C=O); *m/z* (ESI^+) 563 [$(2M+Na)^+$, 5%], 293 [$(M+Na)^+$, 12%], 271 [$(M+H)^+$, 100 %], 197 (4%).

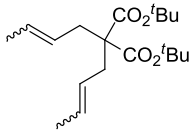
Synthesis of diethyl 2-(cyclohexylmethyl)-2-propylmalonate 4.50[248]



A solution of diethyl propylmalonate **4.20** (0.809 g, 4 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.192 g, 4.8 mmol) in dry tetrahydrofuran (5 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 30 min at room temperature and (bromomethyl)cyclohexane (0.708 g, 4 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to afford diethyl 2-(cyclohexylmethyl)-2-propylmalonate **4.50** (0.992 g, 82%) as a colourless oil. [Found: (ESI^+) $(M+H)^+$ 299.2214. $C_{17}H_{31}O_4$ (M+H) requires 299.2217]; ν_{max}(film) /cm^{-1} 2922, 1728, 1448, 1367, 1215, 1147; ^1H NMR (400 MHz, $CDCl_3$) δ 0.89-0.98 (5H, m, $CH_2CH_2CH_3$, C_6H_{11}), 1.08-1.30 (12H, m, $CO_2CH_2CH_3$, C_6H_{11}), 1.58-1.68 (5H, m,

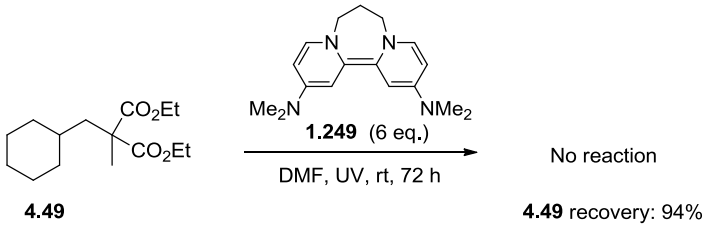
$CH_2CH_2CH_3$, C_6H_{11}), 1.84-1.90 (4H, m, $CH_2CH_2CH_3$, $CyCH_2$), 4.16 (4H, q, J = 7.2 Hz, OCH_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.1 (CH_3), 14.5 (CH_3), 17.7 (CH_2), 26.3 (CH_2), 26.4 (CH_2), 33.6 (CH), 34.4 (CH_2), 35.0 (CH_2), 39.5 (CH_2), 57.0 (C), 61.0 (CH_2), 172.4 (C=O); *m/z* (ESI$^+$) 619 [$(2M+Na)^+$, 6%], 299 [$(M+H)^+$, 100 %], 225 (10%).

Synthesis of di-*tert*-butyl 2,2-di(but-2-en-1-yl)malonate 4.51



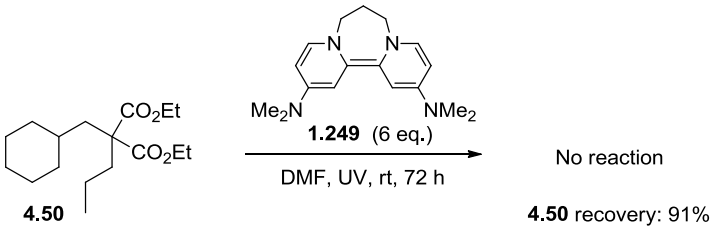
A solution of di-*tert*-butyl malonate (0.648 g, 3 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.264 g, 6.6 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at room temperature and crotyl bromide (1.048 g, 6.6 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to afford *di-tert-butyl 2,2-di(but-2-en-1-yl)malonate* **4.51** (0.839 g, 86%) as a colourless oil. [Found: (ESI$^+$) $(M+H)^+$ 325.2379. $C_{19}H_{33}O_4$ (M+H) requires 325.2373]; ν_{max}(film) /cm^{-1} 2976, 1724, 1660, 1438, 1367, 1246, 1147; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (18H, s, $C(CH_3)_3$), 1.64 (6H, d, J = 6.4 Hz, $=CHCH_3$), 2.47 (4H, d, J = 7.6 Hz, $=CHCH_2$), 5.21-5.31 (2H, m, CH_3CH=CH), 5.46-5.62 (2H, m, CH_3CH=CH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 18.1 (CH_3), 28.1 (CH_3), 35.4 (CH_2), 58.3 (C), 81.0 (C), 125.3 (CH), 129.3 (CH), 170.5 (C=O); *m/z* (ESI$^+$) 666 [$(2M+NH_4)^+$, 19%], 347 [$(M+Na)^+$, 27 %], 325 [$(M+H)^+$, 31 %], 269 (16), 213 (100), 177 (16).

UV-activated reduction of diethyl 2-(cyclohexylmethyl)-2-methylmalonate 4.49



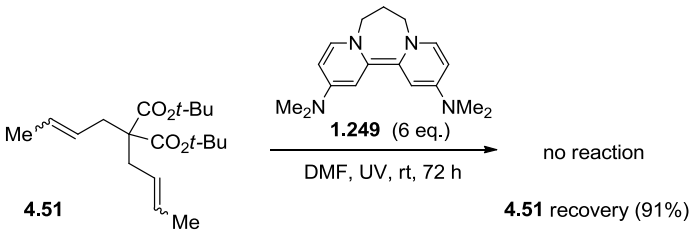
The general procedure for electron transfer reactions under UV conditions was applied to diethyl 2-(cyclohexylmethyl)-2-methylmalonate **4.49** (0.1081 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, only starting material **4.49** (0.1012 g, 94%) was recovered from the organic phase. No product was obtained from acidic work-up of the aqueous phase.

UV-activated reduction of diethyl 2-(cyclohexylmethyl)-2-propylmalonate 4.50



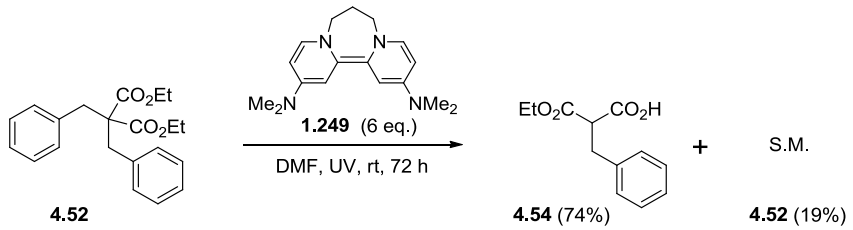
The general procedure for electron transfer reactions under UV conditions was applied to diethyl 2-(cyclohexylmethyl)-2-propylmalonate **4.50** (0.0894 g, 0.3 mmol) using the donor **1.249** (0.511 g, 1.8 mmol, 6 eq.) for 72 h. After following the general work-up process, only starting material **4.50** (0.081 g, 91%) was recovered from the organic phase. No product was obtained from acidic work-up of the aqueous phase.

UV-activated reduction of di-*tert*-butyl 2,2-di(but-2-en-1-yl)malonate 4.51



The general procedure for electron transfer reactions under UV conditions was applied to di-*tert*-butyl 2,2-di(but-2-en-1-yl)malonate **4.51** (0.1297 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, only starting material **4.51** (0.1177 g, 91%) was recovered from the reaction.

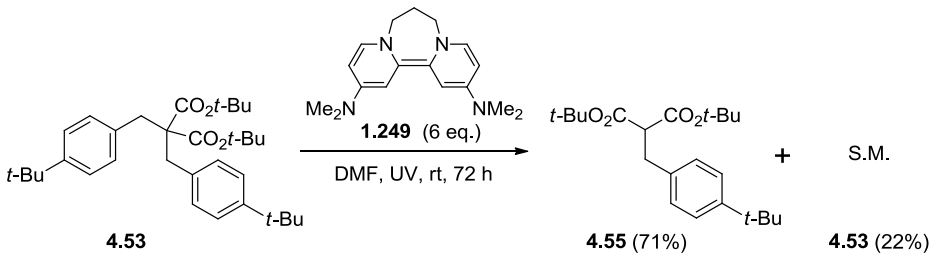
UV-activated reduction of diethyl 2,2-dibenzylmalonate 4.52



The general procedure for electron transfer reactions under UV conditions was applied to diethyl 2,2-dibenzylmalonate **4.52** (0.102 g, 0.3 mmol) using the donor **1.249** (0.511 g, 1.8 mmol, 6 eq.) for 72 h. After following the general work-up process, starting material **4.52** (0.020 g, 19%) was recovered from the organic phase. Acidic work-up of the aqueous phase provided 2-benzyl-3-ethoxy-3-oxopropanoic acid **4.54**[249] (0.049 g, 74%) as a colourless oil.

For 2-benzyl-3-ethoxy-3-oxopropanoic acid **4.54**: [Found: (CI^+ corona) $(M+H)^+$ 223.0966. $C_{12}H_{15}O_4$ (M+H) requires 223.0965]; ν_{max}(film) /cm^{-1} 3251, 2961, 2876, 1727, 1710, 1460, 1367, 1178, 1080; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22 (3H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 3.27 (2H, dd, J = 7.6, 1.6 Hz, $ArCH_2$), 3.71 (1H, t, J = 7.6 Hz, $ArCH_2CH$), 4.18 (4H, q, J = 7.2 Hz, $CO_2CH_2CH_3$), 7.21-7.32 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.1 (CH_3), 34.9 (CH_2), 53.6 (CH), 62.0 (CH_2), 127.0 (CH), 128.7 (CH), 128.9 (CH), 137.6 (C), 168.9 (C), 173.8 (C=O); *m/z* (CI^+ corona) 223 [$(M+H)^+$, 100%], 205 (62), 179 (13), 159 (7), 151 (21), 133 (42).

UV-activated reduction of di-*tert*-butyl 2,2-*bis*(4-(*tert*-butyl)benzyl)malonate 4.53



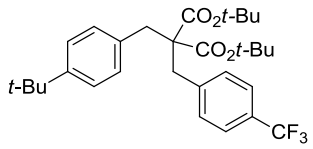
Donor-free, UV-active blank reaction provided only recovery of **4.53** (91%)
Donor-active, non-UV blank reaction provided only recovery of **4.53** (92%)

The general procedure for electron transfer reactions under UV conditions was applied to di-*tert*-butyl 2,2-*bis*(4-(*tert*-butyl)benzyl)malonate **4.53** (0.1017 g, 0.2 mmol) using the donor **1.249** (0.341 g, 1.2 mmol, 6 eq.) for 72 h. After following the general work-up

process, *di-tert-butyl 2-(4-(tert-butyl)benzyl)malonate* **4.55** (0.0514 g, 71%) was obtained along with recovery of the starting material **4.53** (0.022 g, 22%), from the organic phase. The spectral data of **4.55** were consistent with the previously mentioned data of the same compound.

Donor-free, UV-active and donor-active, non-UV blank reactions were performed as per general procedure and provided the starting material **4.53** (0.0926 g, 91%) and (0.0938 g, 92%), respectively.

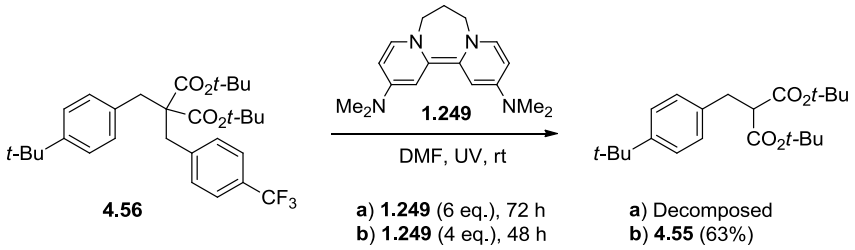
Synthesis of di-*tert*-butyl 2-(4-(*tert*-butyl)benzyl)-2-(4-(trifluoromethyl)benzyl)malonate 4.56



A solution of di-*tert*-butyl 2-(4-(*tert*-butyl)benzyl)malonate **4.55** (0.543 g, 1.5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.072 g, 1.8 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at room temperature and 4-(trifluoromethyl)benzyl bromide (0.358 g, 1.5 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to afford *di-tert-butyl 2-(4-(tert-butyl)benzyl)-2-(4-(trifluoromethyl)benzyl)malonate* **4.56** (0.686 g, 88%) as a white crystalline solid m.p. 87-89 ^{o}C. [Found: (ESI^{+}) $(M+H)^{+}$ 521.2860. $C_{30}H_{40}F_3O_4$ (M+H) requires 521.2873]; ν_{max}(film) /cm^{-1} 2964, 1724, 1616, 1427, 1323, 1157, 1103, 1066; ^{1}H NMR 400 MHz, $CDCl_3$) δ 1.31 (9H, s, ArC(C*H*$_3$)$_3$), 1.39 (18H, s, 2 x OC(C*H*$_3$)$_3$), 3.18 (2H, s, Ar*CH*$_2$), 3.20 (2H, s, Ar*CH*$_2$), 7.13 (2H, d, J = 8.4 Hz, ArH), 7.29 (2H, d, J = 8.4 Hz, ArH), 7.34 (2H, d, J = 8.4 Hz, ArH), 7.51 (2H, d, J = 8.0 Hz, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 28.0 (6 x CH_3), 31.5 (3 x CH_3), 34.5 (C), 39.0 (CH_2), 39.1 (CH_2), 60.3 (C), 82.1 (2 x C), 124.4 (q, CF_3, $J_{C\text{-}F}$ = 268.75 Hz), 125.0 (2 x CH), 125.2 (2 x CH), 128.8 (q, C-CF_3, $J_{C\text{-}F}$ =

32.5 Hz), 130.1 (2 x CH), 130.9 (2 x CH), 133.5 (C), 141.6 (C), 149.8 (C), 170.2 (C=O); *m/z* (ESI^+) 1058 [$(2M+NH_4)^+$, 12%], 521 [$(M+H)^+$, 13 %], 465 (23), 409 (100), 373 (12), 147 (5).

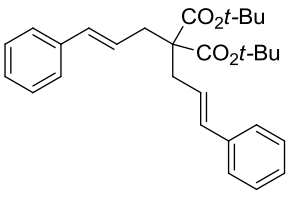
UV-activated reduction of di-*tert*-butyl 2-(4-(*tert*-butyl)benzyl)-2-(4-(trifluoromethyl) benzyl)malonate 4.56



(a) The general procedure for electron transfer reactions under UV conditions was applied to di-*tert*-butyl 2-(4-(*tert*-butyl)benzyl)-2-(4-(trifluoromethyl)benzyl)malonate **4.56** (0.208 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, nothing was obtained from the reaction.

(b) The general procedure for electron transfer reactions under UV conditions was applied to di-*tert*-butyl 2-(4-(*tert*-butyl)benzyl)-2-(4-(trifluoromethyl)benzyl)malonate **4.56** (0.208 g, 0.4 mmol) using the donor **1.249** (0.454 g, 1.6 mmol, 4 eq.) for 48 h. After following the general work-up process, *di-tert-butyl 2-(4-(tert-butyl)benzyl)malonate* **4.55** (0.0916 g, 63%) was obtained from the organic phase. The spectral data of **4.55** were consistent with the previously mentioned data of the same compound.

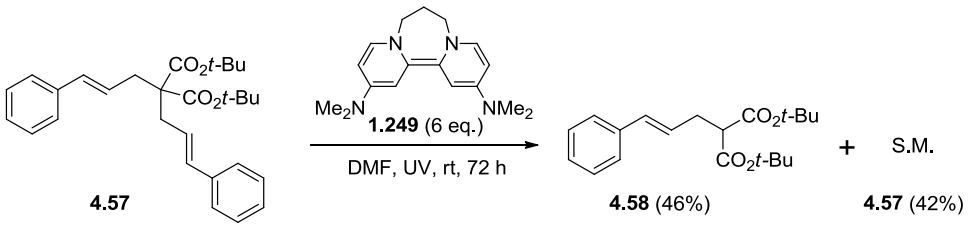
Synthesis of di-*tert*-butyl 2,2-dicinnamylmalonate 4.57



A solution of di-*tert*-butyl malonate (0.648 g, 3 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.264 g, 6.6 mmol) in dry tetrahydrofuran (5 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 30 min at room temperature and cinnamyl chloride (1.007 g, 6.6 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction

mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to afford *di-tert-butyl 2,2-dicinnamylmalonate* **4.57** (1.102 g, 82%) as a white solid m.p. 96-98 ^{o}C. [Found: (ESI^{+}) $(M+Na)^{+}$ 471.2502. $C_{29}H_{36}O_4Na$ (M+Na) requires 471.2506]; ν_{max}(film) /cm^{-1} 3001, 2972, 2933, 1724, 1693, 1448, 1365, 1143; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (18H, s, $C(CH_3)_3$), 2.76 (4H, dd, J = 7.6, 1.2 Hz, $=CHCH_2$), 6.11 (2H, dt, J = 15.6, 7.6 Hz, $ArCH=CH$), 6.47 (2H, d, J = 16 Hz, $ArCH=CH$), 7.20-7.25 (2H, m, ArH), 7.28-7.35 (8H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 28.1 (6 x CH_3), 36.6 (CH_2), 58.7 (C), 81.6 (C), 124.7 (CH), 126.3 (CH), 127.4 (CH), 128.6 (CH), 133.9 (CH), 137.4 (C), 170.2 (C=O); *m/z* (ESI^{+}) 914 [$(2M+NH_4)^{+}$, 7%], 471 [$(M+Na)^{+}$, 41%], 403 (49), 337 (97), 319 (100), 291 (41), 273 (17), 213 (7), 167 (7).

UV-activated reduction of di-*tert*-butyl 2,2-dicinnamylmalonate 4.57

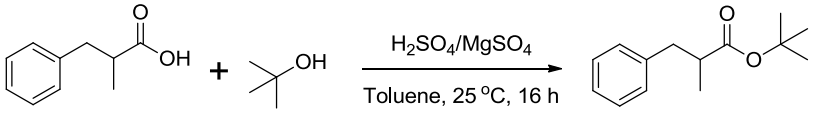


The general procedure for electron transfer reactions under UV conditions was applied to di-*tert*-butyl 2,2-dicinnamylmalonate **4.57** (0.179 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, the crude product was purified by column chromatography (5% diethyl ether in petroleum ether) and provided *di-tert-butyl 2-cinnamylmalonate* **4.58** (0.0612 g, 46%), as a colourless oil, along with starting material **4.57** (0.0753 g, 42%). For di-*tert*-butyl 2-cinnamylmalonate **4.58**: [Found: (ESI^{+}) $(M+NH_4)^{+}$ 350.2330. $C_{20}H_{32}NO_4$ ($M+NH_4$) requires 350.2326]; ν_{max}(film) /cm^{-1} 3006, 2967, 2933, 1724, 1681, 1448, 1369, 1143; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (18H, s, $C(CH_3)_3$), 2.72 (2H, td, J = 7.2, 1.2 Hz, $=CHCH_2$), 3.31 (1H, t, J = 7.2 Hz, CH_2CH), 6.11-6.21 (1H, m, $ArCH=CH$), 6.47 (2H, d, J = 16 Hz, $ArCH=CH$), 7.19-7.24 (1H, m, ArH), 7.28-7.35 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 28.1 (6 x CH_3), 32.3 (CH_2), 54.0 (CH), 81.7 (C), 126.3 (CH),126.4 (CH),

127.4 (CH), 128.6 (CH), 132.5 (CH), 137.4 (C), 168.5 (C=O); *m/z* (ESI^+) 687 [$(2M+Na)^+$, 8%], 350 [$(M+NH_4)^+$, 37%], 221 (100).

Synthesis of *tert*-butyl 2-benzyl-2-methylpentanoate 4.59

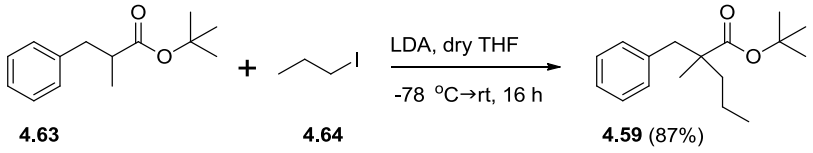
(a) Synthesis of *tert*-butyl 2-methyl-3-phenylpropanoate 4.63[250]



4.61 **4.62** **4.63** (81%)

Synthesis of *tert*-butyl 2-methyl-3-phenylpropanoate followed the method described by Wright *et al*.[191] To a vigorously stirred suspension of $MgSO_4$ (4.81 g, 40 mmol) in toluene (30 mL), conc. H_2SO_4 (0.55 mL, 10 mmol) was added at room temperature and the resulting mixture was stirred for another 15 min. 2-Methyl-3-phenylpropanoic acid **4.61** (1.642 g, 10 mmol) and *t*-butanol **4.62** (3.706 g, 50 mmol) were added into the reaction flask and stirred for 16 h at 25 °C. Then, the reaction was then quenched with sat. $NaHCO_3$ (30 mL) and extracted with diethyl ether (3 x 20 mL). The combined ether layers were washed again with water (10 mL) and brine (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to yield *tert*-butyl 2-methyl-3-phenylpropanoate **4.63** (1.786 g, 81%) as a colourless oil. [Found: (ESI^+) $(M+H)^+$ 221.1538. $C_{14}H_{21}O_2$ (M+H) requires 221.1536]; ν_{max}(film) /cm^{-1} 2976, 2933, 1724, 1454, 1365, 1145; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (3H, d, J = 6.4 Hz, CHCH_3), 1.38 (9H, s, OC(CH_3)$_3$), 2.59-2.68 (2H, m, ArCH_2CH, ArCH_2CH), 2.94-3.01 (1H, m, 1H-ArCH_2CH), 7.18-7.22 (3H, m, ArH), 7.26-7.30 (2H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 17.1 (CH_3), 28.1 (3 x CH_3), 39.9 (CH_2), 42.4 (CH), 80.1 (C), 126.3 (CH), 128.3 (CH), 129.2 (CH), 139.8 (C), 175.6 (C=O); *m/z* (ESI^+) 445 (41), 344 (43), 238 [$(M+NH_4)^+$, 53%], 180 (29), 165 (100).

(b) Synthesis of *tert*-butyl 2-benzyl-2-methylpentanoate 4.59

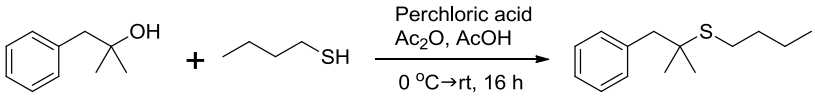


4.63 **4.64** **4.59** (87%)

To a solution of *tert*-butyl 2-methyl-3-phenylpropanoate **4.63** (0.881 g, 4 mmol) in dry THF (10 mL), LDA (1.5 M in THF, 3.2 mL, 4.8 mmol) was added dropwise at -78 ^{o}C and the resulting solution was stirred for 45 min at -78 ^{o}C. 1-Iodopropane **4.64** (0.815 g, 4.8 mmol) in dry THF (2 mL) was added slowly into the reaction flask and the resulting solution was warmed to room temperature over 16 h. Then, the reaction was quenched with water (20 mL) and extracted with diethyl ether (3 x 20 mL). The combined ether layers were washed again with water (10 mL) and brine (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (3% diethyl ether in petroleum ether) to yield *tert-butyl 2-benzyl-2-methylpentanoate* **4.59** (0.914 g, 87%) as light yellow oil. [Found: (ESI^{+}) $(M+NH_4)^{+}$ 280.2275. $C_{17}H_{30}NO_2$ $(M+NH_4)$ requires 280.2271]; ν_{max}(film) /cm^{-1} 2960, 2933, 1720, 1454, 1365, 1230, 1139; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (3H, t, J = 7.2 Hz, CH_2CH_3), 1.04 (3H, s, CCH_3), 1.23-1.41 (3H, m, $CH_2CH_2CH_3$), 1.44 (9H, s, $OC(CH_3)_3$), 1.60-1.72 (1H, m, $CH_2CH_2CH_3$), 2.67 (1H, d, J = 13.2 Hz, $ArCH_2$), 3.01(1H, d, J = 13.2 Hz, $ArCH_2$), 7.15-7.28 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.8 (CH_3), 18.1 (CH_3), 21.1 (CH_2), 28.2 (3 x CH_3), 42.2 (CH_2), 45.4 (CH_2), 47.7 (C), 80.2 (C), 126.4 (CH), 128.0 (CH), 130.5 (CH), 138.3 (C), 176.3 (C=O); *m/z* (ESI^{+}) 280 [$(M+NH_4)^{+}$, 18%], 207 (63), 161 (100).

Synthesis of benzyldimethylcarbinylbutyl sulfone 4.60

(a) Synthesis of benzyldimethylcarbinyl butyl sulfide 4.67

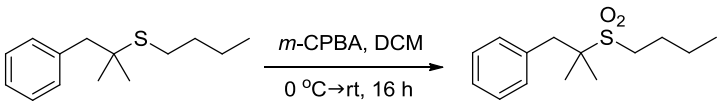


4.65 **4.66** **4.67** (49%)

Synthesis of benzyldimethylcarbinyl butyl sulfide **4.67** followed the method described by Cain *et al.*[192] Into a flask containing acetic acid (40 mL), perchloric acid (1.4064 g, 14 mmol) followed by acetic anhydride (2.24 g, 22 mmol) were added at 0 ^{o}C and the stirring continued until the exothermic reaction ceased. Benzyldimethylcarbinol **4.65** (3.0042 g, 20 mmol) and butanethiol **4.66** (2.1645 g, 24 mmol) were added into the reaction flask and the resulting mixture continued stirring at room temperature for 16 h. Then, the reaction contents were poured into brine solution (20 mL) and extracted with petroleum ether (3 x 20 mL). The combined ether layers were washed with sat. $NaHCO_3$ (20 mL)

and water (20 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% DCM in petroleum ether) to yield *benzyldimethylcarbinyl butyl sulfide* **4.67** (2.157 g, 49%) as a colourless oil. [Found: (CI^+ corona) $(M+H)^+$ 223.1517. $C_{14}H_{23}S$ (M+H) requires 223.1515]; ν_{max}(film) /cm^{-1} 2956, 1494, 1454, 1381, 1363, 1124, 1029; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (3H, t, J = 7.2 Hz, CH_2CH_3), 1.28 (6H, s, $C(CH_3)_2$), 1.43 (2H, sextet, J = 7.2 Hz, $SCH_2CH_2CH_2CH_3$), 1.57 (2H, quintet, J = 6.8 Hz, $SCH_2CH_2CH_2CH_3$), 2.53 (2H, t, J = 7.6 Hz, $SCH_2CH_2CH_2CH_3$), 2.87 (2H, s, $ArCH_2$), 7.20-7.32 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.9 (CH_3), 22.5 (CH_2), 27.8 (CH_2), 28.4 (2 x CH_3), 31.9 (CH_2), 45.5 (C), 49.1 (CH_2), 126.5 (CH), 127.9 (CH), 130.8 (CH), 137.9 (C); *m/z* (CI^+ corona) 355 (19), 239 (12%), 223 [$(M+H)^+$, 100 %], 133 (93).

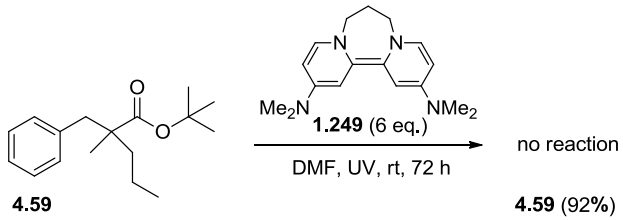
(b) Synthesis of benzyldimethylcarbinylbutyl sulfone 4.60



4.67 **4.60** (90%)

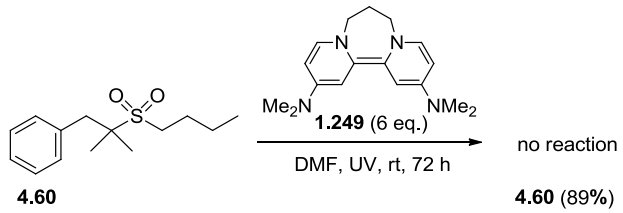
To a flask containing benzyldimethylcarbinyl butyl sulfide **4.67** (0.889 g, 4 mmol) in DCM (10 mL), *m*-CPBA (77%, 4.141 g, 24 mmol) in DCM (10 mL) was added slowly at 0 °C and the reaction continued for 16 h at room temperature. Then, the reaction was quenched with water and extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with sat. $NaHCO_3$ (20 mL) and brine (20 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% ethyl acetate in petroleum ether) to yield *benzyldimethylcarbinylbutyl sulfone* **4.60** (0.9177 g, 90%) as a white crystalline solid m.p. 40-44 °C. [Found: (ESI^+) $(M+NH_4)^+$ 272.1684. $C_{14}H_{26}NO_2S$ $(M+NH_4)$ requires 272.1679]; ν_{max}(film) /cm^{-1} 2956, 1494, 1454, 1381, 1363, 1222, 1124, 1029; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.98 (3H, t, J = 7.6 Hz, CH_2CH_3), 1.33 (6H, s, $C(CH_3)_2$), 1.50 (2H, sextet, J = 7.2 Hz, $SCH_2CH_2CH_2CH_3$), 1.88-1.96 (2H, m, $SCH_2CH_2CH_2CH_3$), 2.89-2.93 (2H, m, $SCH_2CH_2CH_2CH_3$), 3.09 (2H, s, $ArCH_2$), 7.20-7.22 (2H, m, ArH), 7.28-7.36 (3H, m, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 13.8 (CH_3), 20.4 (2 x CH_3), 22.2 (CH_2), 22.6 (CH_2), 40.4 (CH_2), 46.1 (CH_2), 62.9 (C), 127.3 (CH), 128.4 (CH), 131.1 (CH), 135.2 (C); *m/z* (ESI^+) 526 [$(2M+NH_4)^+$, 3%], 272 [$(M+NH_4)^+$, 100%], 255 [$(M+H)^+$, 13%], 133 (6).

UV-activated reduction of *tert*-butyl 2-benzyl-2-methylpentanoate 4.59



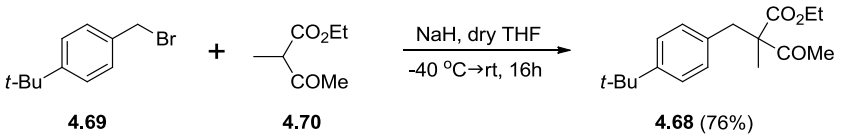
The general procedure for electron transfer reactions under UV conditions was applied to *tert*-butyl 2-benzyl-2-methylpentanoate **4.59** (0.1049 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, only starting material **4.59** (0.097 g, 92%) was recovered from the reaction.

UV-activated reduction of benzyldimethylcarbinylbutyl sulfone 4.60



The general procedure for electron transfer reactions under UV conditions was applied to benzyldimethylcarbinylbutyl sulfone **4.60** (0.1017 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, only starting material **4.60** (0.0909 g, 89%) was recovered from the reaction.

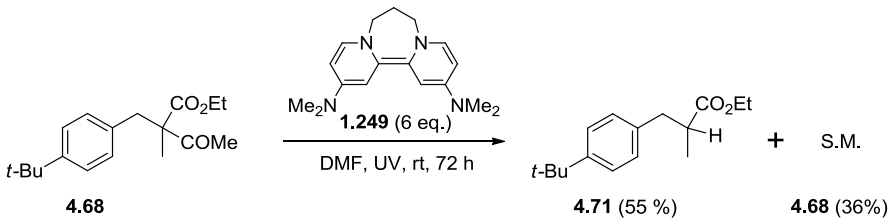
Synthesis of ethyl 2-(4-(*tert*-butyl)benzyl)-2-methyl-3-oxobutanoate 4.68



A solution of ethyl 2-methylacetoacetate **4.70** (0.432 g, 3 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.132 g, 3.3 mmol) in dry tetrahydrofuran (5 mL) at -40 ^{o}C under argon gas. The resulting solution was stirred for 30 min at -40 ^{o}C and 1-(bromomethyl)-4-(*tert*-butyl)benzene **4.69** (0.681 g, 3 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further stirred at room temperature for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x

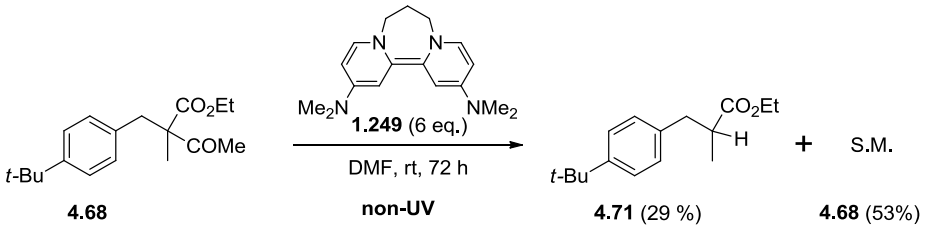
10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to afford *ethyl 2-(4-(tert-butyl)benzyl)-2-methyl-3-oxobutanoate* **4.68** (0.660 g, 76%) as a colourless oil. [Found: (ESI$^+$) $(M+H)^+$ 291.1960. $C_{18}H_{27}O_3$ (M+H) requires 291.1955]; ν_{max}(film) /cm^{-1} 2962, 1739, 1710, 1462, 1355, 1269, 1180, 1093; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (3H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 1.30 (12H, s, ArC(CH_3)$_3$, CCH_3), 2.18 (3H, s, COCH_3), 3.03 (1H, d, J = 14.0 Hz, ArCH_2), 3.25 (1H, d, J = 14.0 Hz, ArCH_2), 4.15-4.24 (2H, m, $CO_2CH_2CH_3$), 7.02 (2H, d, J = 8.4 Hz, ArH), 7.27 (2H, d, J = 8.4 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.1 (CH_3), 19.2 (CH_3), 26.6 (CH_3), 31.5 (3 x CH_3), 34.5 (C), 40.1 (CH_2), 61.0 (C), 61.4 (CH_2), 125.2 (CH), 129.9 (CH), 133.4 (C), 149.7 (C), 172.6 (CO_2Et), 205.5 (C=O); *m/z* (ESI$^+$) 291 [$(M+H)^+$, 100%], 273 (16), 245 (3), 147 (11).

UV-activated reduction of ethyl 2-(4-(*tert*-butyl)benzyl)-2-methyl-3-oxobutanoate 4.68



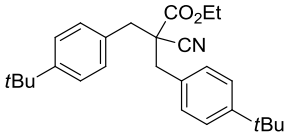
The general procedure for electron transfer reactions under UV conditions was applied to ethyl 2-(4-(*tert*-butyl)benzyl)-2-methyl-3-oxobutanoate **4.68** (0.1161 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.). After following the general work-up process, *ethyl 3-(4-(tert-butyl)phenyl)-2-methylpropanoate* **4.71** (0.0548 g, 55%) was obtained as a colourless oil along with starting material **4.68** (0.04138 g, 36%) from the organic phase. [Found: (ESI$^+$) $(M+H)^+$ 249.1853. $C_{16}H_{25}O_2$ (M+H) requires 249.1849]; ν_{max}(film) /cm^{-1} 2964, 2872, 1732, 1512, 1462, 1365, 1159, 813; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (3H, d, J = 6.8 Hz, CHCH_3), 1.19 (3H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 1.31 (9H, s, ArC(CH_3)$_3$), 2.61-2.76 (2H, m, CHCH$_3$, ArCH_2), 2.99 (1H, dd, J = 12.8, 6.4 Hz, ArCH_2), 4.10 (2H, q, J = 7.2 Hz, $CO_2CH_2CH_3$), 7.10 (2H, d, J = 8.4 Hz, ArH), 7.30 (2H, d, J = 8.4 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.3 (CH_3), 16.9 (CH_3), 31.5 (3 x CH_3), 34.5 (C), 39.4 (CH_2), 41.6 (CH), 60.4 (CH_2), 125.3 (CH), 128.8 (CH), 136.4 (C), 149.2 (C), 176.4 (C=O); *m/z* (ESI$^+$) 266 [$(M+NH_4)^+$, 77%], 249 [$(M+H)^+$, 100%], 193 (35), 147 (58).

Reduction of ethyl 2-(4-(*tert*-butyl)benzyl)-2-methyl-3-oxobutanoate 4.68, under non-UV conditions



The general procedure for electron transfer reactions under non-UV (donor-active, UV-free blank reaction) conditions was applied to ethyl 2-(4-(*tert*-butyl)benzyl)-2-methyl-3-oxobutanoate **4.68** (0.1161 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.). After following the general work-up process, *ethyl 3-(4-(tert-butyl)phenyl)-2-methylpropanoate* **4.71** (0.0289 g, 29%), as a colourless oil, was obtained along with starting material **4.68** (0.0607 g, 53%) from the organic phase.

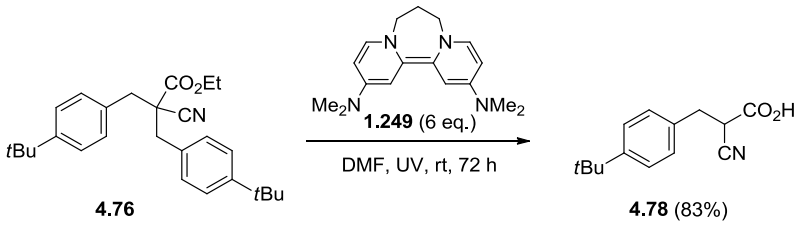
Synthesis of ethyl 2-(4-(*tert*-butyl)benzyl)-3-(4-(*tert*-butyl)phenyl)-2-cyanopropanoate 4.76



A solution of ethyl 2-cyanoacetate **4.77** (0.226 g, 2 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.176 g, 4.4 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at room temperature and 4-(*tert*-butyl)benzyl bromide **4.69** (0.908 g, 4 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (15% diethyl ether in petroleum ether) to afford *ethyl 2-(4-(tert-butyl)benzyl)-3-(4-(tert-butyl)phenyl)-2-cyanopropanoate* **4.76** (0.690 g, 85%) as a white crystalline solid m.p. 98-100 ^{o}C. [Found: (ESI^{+}) $(M+NH_4)^{+}$ 423.3008. $C_{27}H_{39}N_2O_2$ $(M+NH_4)$ requires 423.3006]; ν_{max}(film) /cm^{-1} 2958, 2902, 2249, 1728, 1462, 1361, 1213, 1045; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (3H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 1.31 (18H, s,

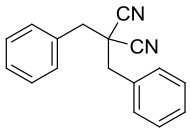
2 x ArC(CH_3)$_3$), 3.10 (2H, d, *J* = 13.6 Hz, ArCH_2), 3.28 (2H, d, *J* = 13.2 Hz, ArCH_2), 4.01 (2H, q, *J* = 6.8 Hz, $CO_2CH_2CH_3$), 7.24 (4H, d, *J* = 8.0 Hz, ArH), 7.34 (4H, d, *J* = 8.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.9 (CH_3), 31.4 (6 x CH_3), 34.6 (C), 43.0 (CH_2), 53.3 (C), 62.5 (CH_2), 119.1 (C), 125.6 (CH), 129.8 (CH), 131.2 (C), 150.8 (C), 168.4 (C=O); *m/z* (ESI$^+$) 828 [(2M+NH_4)$^+$, 8%], 423 [(M+NH_4)$^+$, 100 %], 406 [(M+H)$^+$, 3 %], 350 (3).

UV-activated reduction of ethyl 2-(4-(*tert*-butyl)benzyl)-3-(4-(*tert*-butyl)phenyl)-2-cyanopropanoate 4.76



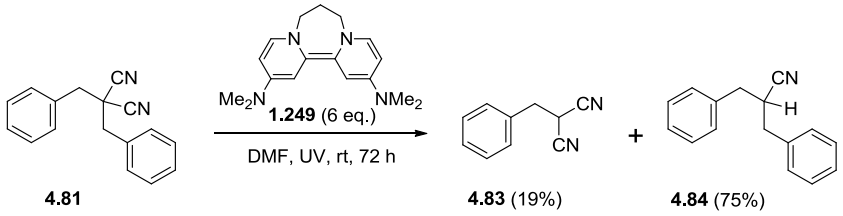
The general procedure for electron transfer reactions under UV conditions was applied to ethyl 2-(4-(*tert*-butyl)benzyl)-3-(4-(*tert*-butyl)phenyl)-2-cyanopropanoate **4.76** (0.162 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.). After following the general work-up process, no starting material was recovered from the organic phase. Acid work-up of the aqueous phase provided *3-(4-(tert-butyl)phenyl)-2-cyanopropanoic acid* **4.78** (0.0765 g, 83%) as a white solid m.p. 108-110 ^{o}C. [Found: (CI$^+$ corona) (M+H)$^+$ 232.1333. $C_{14}H_{18}NO_2$ (M+H) requires 232.1332]; ν_{max}(film) /cm^{-1} 3282, 2954, 2864, 2254, 1728, 1516, 1415, 1298, 1109; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (9H, s, C(CH_3)$_3$), 3.21 (1H, dd, *J* = 14.0, 8.8 Hz, ArCH_2), 3.30 (1H, dd, *J* = 14.0, 5.6 Hz, ArCH_2), 3.80 (1H, dd, *J* = 8.4, 5.6 Hz, $CHCO_2H$), 7.24 (2H, d, *J* = 8.4 Hz, ArH), 7.39 (2H, d, *J* = 8.4 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 31.4 (CH_3), 34.7 (C), 35.3 (CH_2), 39.9 (CH), 115.6 (C), 126.1 (CH), 128.8 (CH), 131.9 (C), 151.1 (C), 170.7 (C=O); *m/z* (CI$^+$ corona) 463 [(2M+H)$^+$, 6%], 249 [(M+NH_4)$^+$, 7%], 232 [(M+H)$^+$, 100%], 179 (8), 163 (49).

Synthesis of 2,2-dibenzylmalononitrile 4.81[251]



A solution of malononitrile **4.82** (0.396 g, 6 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.528 g, 13.2 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min. at room temperature and benzylbromide **4.32** (2.257 g, 13.2 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (20% diethyl ether in petroleum ether) to afford 2,2-dibenzylmalononitrile **4.81** (1.316 g, 89%) as a white solid m.p. 128-130 ^{o}C; (lit.:[251] 128-130 ^{o}C); [Found: (CI^{+} corona) (M+H)$^{+}$ 247.1234. $C_{17}H_{15}N_2$ (M+H) requires 247.1230]; ν_{max}(film) /cm^{-1} 3032, 2933, 2247, 1496, 1442, 1269, 1089; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.26 (4H, s, Ar*CH*$_2$), 7.40-7.46 (10H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 41.3 (C), 43.6 (CH_2), 115.1 (C), 129.0 (CH), 129.1 (CH), 130.4 (CH), 132.1 (C); *m/z* (CI^{+} corona) 247 [(M+H)$^{+}$, 100 %], 222 (10%).

UV-activated reduction of 2,2-dibenzylmalononitrile 4.81



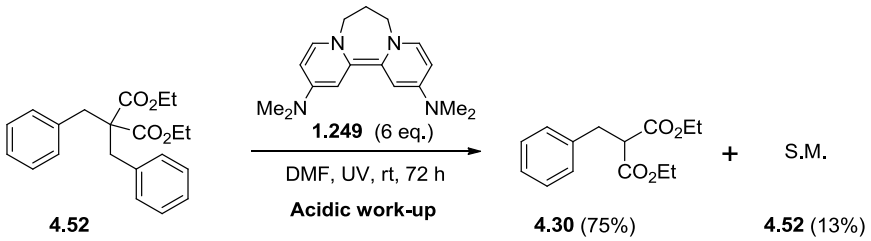
The general procedure for electron transfer reactions under UV conditions was applied to 2,2-dibenzylmalononitrile **4.81** (0.098 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.). After following the general work-up process, the crude product was purified by column chromatography (10% diethyl ether in petroleum ether) and afforded 2-benzyl-3-phenylpropanenitrile **4.84**[252] (0.066 g, 75%), as a white solid m.p. 88-90 ^{o}C (lit.:[252] 92-92.5 ^{o}C), and 2-benzylmalononitrile **4.83**[253] (0.0119 g, 19%), as a white solid m.p. 84-86 ^{o}C (lit.:[253] 88 ^{o}C), from the organic phase.

For 2-benzyl-3-phenylpropanenitrile **4.84**: [Found: (CI^{+} corona) (M+H)$^{+}$ 222.1281. $C_{16}H_{16}N$ (M+H) requires 222.1277]; ν_{max}(film) /cm^{-1} 3026, 2933, 2241, 1604, 1492, 1454,

1080, 1026; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.94 (4H, d, J = 7.0 Hz, ArCH_2), 3.05 (1H, quintet, J = 7.0 Hz, C*H*CN), 7.25-7.31 (6H, m, ArH), 7.34-7.38 (4H, m, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 36.0 (CH), 38.1 (CH_2), 121.4 (C), 127.5 (CH), 128.9 (CH), 129.2 (CH), 136.9 (C); *m/z* (CI^+ corona) 443 [$(2M+H)^+$, 100%], 304 (15), 222 [$(M+H)^+$, 77 %].

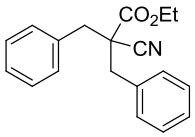
For 2-benzylmalononitrile **4.83**: [Found: (CI^+ corona) $(M+H)^+$ 157.0758. $C_{10}H_9N_2$ (M+H) requires 157.0760]; ν_{max}(film) /cm^{-1} 3030, 2951, 2358, 2272, 1496, 1446, 1073; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.30 (2H, d, J = 6.8 Hz, ArCH_2), 3.92 (1H, t, J = 6.8 Hz, *CH*CN), 7.32-7.45 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.1 (CH), 36.9 (CH_2), 112.3 (C), 128.9 (CH), 129.3 (CH), 129.4 (CH), 133.1 (C); *m/z* (CI^+ corona) 157 [$(M+H)^+$, 100%].

UV-activated reduction of diethyl 2,2-dibenzylmalonate 4.52



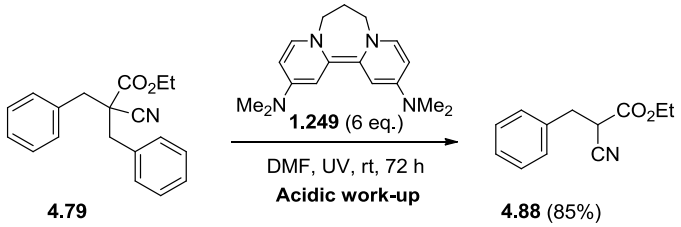
The general procedure for electron transfer reactions under UV conditions was applied to diethyl 2,2-dibenzylmalonate **4.52** (0.102 g, 0.3 mmol) using the donor **1.249** (0.511 g, 1.8 mmol, 6 eq.). At the end of reaction, the reaction mixture was quenched with dil. HCl (2N, 10 mL) and then extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in petroleum ether) to yield diethyl 2-benzylmalonate **4.30**[254] (0.0565 g, 75%) and recovery of the starting material **4.52** (0.0134 g, 13%), as colourless oils. For diethyl 2-benzylmalonate **4.30**: [Found: (ESI^+) $(M+H)^+$ 251.1281. $C_{14}H_{19}O_4$ (M+H) requires 251.1278]; ν_{max}(film) /cm^{-1} 2986, 1727, 1453, 1369, 1224, 1146; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.22 (6H, t, J = 7.2 Hz, CH_3), 3.23 (2H, d, J = 8.0 Hz, ArCH_2), 3.65 (1H, t, J = 7.6 Hz, $ArCH_2CH$), 4.14-4.20 (4H, m, $CO_2CH_2CH_3$), 7.20-7.30 (5H, m, Ar*H*); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.1 (CH_3), 34.8 (CH_2), 54.0 (CH), 61.6 (CH_2), 126.8 (CH), 128.6 (CH), 129.0 (CH), 138.0 (C), 169.0 (C=O); *m/z* (ESI^+) 268 [$(M+NH_4)^+$, 68%], 251 [$(M+H)^+$, 100 %], 177 (8).

Synthesis of ethyl 2-benzyl-2-cyano-3-phenylpropanoate 4.79[255]



A solution of ethyl 2-cyanoacetate **4.77** (0.565 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.440 g, 11 mmol) in dry tetrahydrofuran (5 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min. at room temperature and benzyl bromide **4.32** (1.7103 g, 10 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The resulting reaction mixture was further refluxed for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 10 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (15% diethyl ether in petroleum ether) to afford ethyl 2-benzyl-2-cyano-3-phenylpropanoate **4.79**[255] (0.998 g, 68%) as a white solid m.p. 40-42 ^{o}C (lit.[255] 40-42 ^{o}C). ν_{max}(film) /cm^{-1} 2987, 2902, 2357, 1734, 1455, 1226, 1207, 1045; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (3H, t, J = 7.2 Hz, $CO_2CH_2CH_3$), 3.12 (2H, d, J = 13.6 Hz, ArCH_2), 3.33 (2H, d, J = 13.2 Hz, ArCH_2), 4.02 (2H, q, J = 6.8 Hz, $CO_2CH_2CH_3$), 7.25-7.38 (10H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.8 (CH_3), 43.5 (CH_2), 53.3 (C), 62.7 (CH_2), 118.7 (C), 128.0 (CH), 128.7 (CH), 130.2 (CH), 134.2 (C), 168.3 (C=O). The spectral data of **4.79** were consistent with the literature data[255] of the same compound.

UV-activated reduction of ethyl 2-benzyl-2-cyano-3-phenylpropanoate 4.79

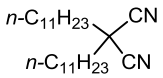


The general procedure for electron transfer reactions under UV conditions was applied to ethyl 2-benzyl-2-cyano-3-phenylpropanoate **4.79** (0.1174 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.). At the end of reaction, the reaction mixture was quenched with dil. HCl (2N, 10 mL) and then extracted with diethyl ether (3 x 10 mL).

The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (20% diethyl ether in hexane) to yield ethyl 2-cyano-3-phenylpropanoate[256] (0.069 g, 85%) as a colourless oil. ν_{max}(film) /cm^{-1} 2986, 2924, 2361, 1739, 1498, 1453, 1265, 1206, 1039; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (3H, t, J = 7.2 Hz, CHCH_3), 3.20 (1H, dd, J = 14.0, 8.0 Hz, ArCH_2), 3.29 (1H, dd, J = 14.0, 5.6 Hz, ArCH_2), 3.72 (1H, dd, J = 8.4, 5.6 Hz, ArCH$_2$CH), 4.25 (2H, q, J = 7.2 Hz, $CO_2CH_2CH_3$), 7.27-7.38 (5H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.1 (CH_3), 35.9 (CH_2), 39.8 (CH), 63.1 (CH_2), 116.3 (C), 127.9 (CH), 129.0 (CH), 129.2 (CH), 135.4 (C), 165.7 (C=O). The spectral data of the product **4.88** were consistent with the literature data[256] of the same compound.

7.7 Experimental for Chapter 5

Synthesis of 2,2-diundecylmalononitrile 5.1

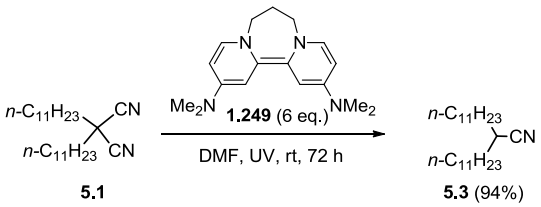


A solution of malononitrile **4.82** (0.396 g, 6 mmol) in dry tetrahydrofuran (2 mL) was added slowly to suspension of sodium hydride (~60%, 0.600 g, 15 mmol) in dry tetrahydrofuran (10 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 15 min at room temperature and 1-bromoundecane **5.2** (3.104 g, 13.2 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. At this point, the reaction was quenched with water (15 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (2% diethyl ether in petroleum ether) to yield *2,2-diundecylmalononitrile* **5.1** (1.598 g, 71%) as a white crystalline solid m.p. 40-42 ^{o}C. [Found: (CI corona$^+$) $(M+H)^+$ 375.3732. $C_{25}H_{47}N_2$ (M+H) requires 375.3734]; ν_{max}(film)/cm^{-1} 2958, 2914, 2846, 2247, 1469, 1379, 719; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 [6H, t, J = 6.8 Hz, $(CH_2)_{10}CH_3$], 1.28-1.41 (32H, m, $CCH_2CH_2(CH_2)_8CH_3$), 1.63-1.71 (4H, m, $CCH_2CH_2(CH_2)_8CH_3$), 1.89-1.94 (4H, m, $CCH_2(CH_2)_9CH_3$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 25.7 (CH_2), 29.0 (CH_2), 29.3 (CH_2), 29.4 (CH_2),

29.5 (CH_2), 29.7 (2 x CH_2), 29.8 (C), 32.0 (CH_2), 38.0 (CH_2), 116.0 (C); *m/z* (CI corona$^+$) 375 [$(M+H)^+$, 100%], 350 [$((M-CN)+H)^+$, 26%], 327 (41).

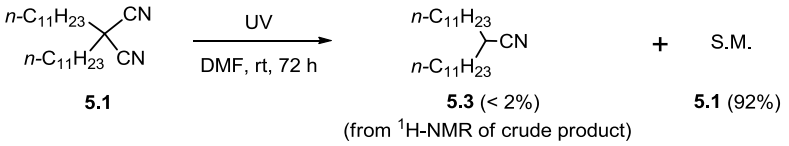
UV-activated reduction of 2,2-diundecylmalononitrile 5.1

(a) UV reaction with donor 1.249



The general procedure for electron transfer reactions under UV conditions was applied to 2,2-diundecylmalononitrile **5.1** (0.149 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, column chromatography (2% diethyl ether in petroleum ether), provided *2-undecyltridecanenitrile* **5.3** (0.131 g, 94%) as a white crystalline solid m.p. 28-30 ^oC. [Found: (CI corona$^+$) $(M+H)^+$ 350.3778. $C_{24}H_{48}N$ (M+H) requires 350.3781]; ν_{max}(film)/cm^{-1} 2986, 2922, 2852, 2241, 1465, 1377, 721; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 [6H, t, J = 6.8 Hz, $CH(CH_2)_{10}CH_3$], 1.27-1.37 (32H, m, $CHCH_2CH_2(CH_2)_8CH_3$), 1.39-1.66 (8H, m, $CHCH_2CH_2(CH_2)_8CH_3$), 2.47-2.53 (1H, m, C*H*CN); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.3 (CH_3), 22.8 (CH_2), 27.3 (CH_2), 29.3 (CH_2), 29.48 (CH_2), 29.52 (CH_2), 29.7 (CH_2), 29.8 (2 x CH_2), 31.8 (CH), 32.1 (CH_2), 32.4 (CH_2), 122.7 (C); *m/z* ((CI corona$^+$) 350 $[(M+H)^+$, 86%], 327 (100), 220 (24), 155 (16).

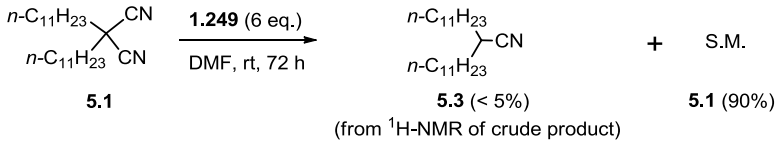
(b) UV reaction without donor 1.249



The general procedure for UV-activated, donor-free blank reaction was applied to 2,2-diundecylmalononitrile **5.1** (0.149 g, 0.4 mmol) with out using donor **1.249**, for 72 h. After following the general work-up process, crude product was obtained. From the ^{1}H-NMR of the crude product, it was noticed that only <2% of the starting material **5.1** was converted to product **5.3**. No attempt was made to isolate this product, but column

chromatography (2% diethyl ether in petroleum ether) of the crude product provided an excellent recovery of starting material **5.1** (92%).

(c) Donor reaction without UV



The general procedure for donor-activated, UV-free blank reactions was applied to 2,2-diundecylmalononitrile **5.1** (0.149 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, crude product was obtained. From the ^{1}H-NMR of the crude product, it was noticed that only <5% of the starting material **5.1** was converted to product **5.3**. No attempt was made to isolate this product, but column chromatography (2% diethyl ether in petroleum ether) of the crude product provided an excellent recovery of starting material **5.1** (90%).

Optimisation of reaction conditions for UV-activated reduction of 5.1

(i) Using 4 equivalents of 1.249 for 48 h

The general procedure for electron transfer reactions under UV conditions was applied to 2,2-diundecylmalononitrile **5.1** (0.149 g, 0.4 mmol) using the donor **1.249** (0.454 g, 1.6 mmol, 4 eq.) for 48 h. After following the general work-up process, crude product was obtained. From the ^{1}H-NMR of the crude product, it was observed that the starting material **5.1** was completely consumed and provided exclusively decyanated product **5.3**. No attempt was made to isolate this product **5.3**.

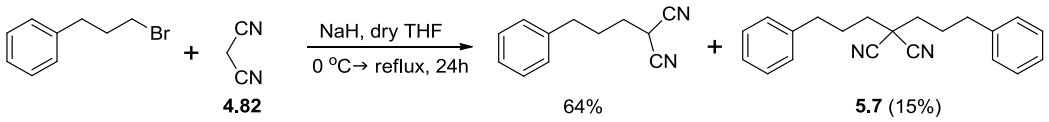
(ii) Using 4 equivalents of 1.249 for 24 h

The general procedure for electron transfer reactions under UV conditions was applied to 2,2-diundecylmalononitrile **5.1** (0.149 g, 0.4 mmol) using the donor **1.249** (0.454 g, 1.6 mmol, 4 eq.) for 24 h. After following the general work-up process, crude product was obtained. From the ^{1}H-NMR of the crude product, it was observed that the starting material **5.1** was not completely consumed. The ratio of decyanated product **5.3** to starting material **5.1** in the crude product was found to be 89:11.

(iii) Using 4 equivalents of 1.249 for 36 h

The general procedure for electron transfer reactions under UV conditions was applied to 2,2-diundecylmalononitrile **5.1** (0.149 g, 0.4 mmol) using the donor **1.249** (0.454 g, 1.6 mmol, 4 eq.) for 36 h. After following the general work-up process, crude product was obtained. From the ^{1}H-NMR of the crude product, it was observed that the starting material **5.1** was completely consumed. Column chromatography (2% diethyl ether in petroleum ether) of the crude product provided exclusively decyanated product **5.3** (92%). Spectral data of the product **5.3** were consistent with the previous data of the same compound.

Synthesis of 2-(3-phenylpropyl)malononitrile[257] and 2-(3-phenylpropyl)malononitrile 5.4



4.82 64% **5.7** (15%)

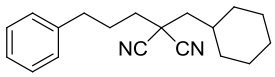
A solution of malanonitrile **4.82** (1.3212 g, 20 mmol) in dry tetrahydrofuran (2 mL) was added slowly to suspension of sodium hydride (~60%, 0.600 g, 15 mmol) in dry tetrahydrofuran (10 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 15 min at room temperature and (3-bromopropyl)benzene (2.986 g, 15 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. At this point, the reaction was quenched with water (15 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in hexane) to yield 2-(3-phenylpropyl)malononitrile (1.753 g, 64%) as a colourless oil and *2,2-bis(3-phenylpropyl)malononitrile* **5.4** (0.680 g, 15%) as a white crystalline solid m.p. 78-80 ^{o}C.

For 2-(3-phenylpropyl)malononitrile: [Found: (CI corona^{+}) $(M+H)^{+}$ 185.1071. $C_{12}H_{13}N_2$ (M+H) requires 185.1073]; ν_{max}(film)/cm^{-1} 3026, 2922, 2866, 2240, 1602, 1496, 1454, 698; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.95-2.01 (2H, m, $CHCH_2CH_2CH_2Ar$), 2.02-2.07 (2H, m, $CHCH_2CH_2CH_2Ar$), 2.75 (2H, t, J = 7.0 Hz, $ArCH_2$), 3.67 (1H, t, J = 7.0 Hz,

C*H*$(CN)_2$), 7.19 (2H, d, *J* = 7.0 Hz, ArH), 7.25 (1H, t, *J* = 7.0 Hz, ArH), 7.33 (2H, t, *J* = 7.0 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 22.6 (CH), 28.1 (CH_2), 30.2 (CH_2), 34.5 (CH_2), 112.6 (C), 126.7 (CH), 128.4 (CH), 128.8 (CH), 140.0 (C); *m/z* (CI corona$^+$) 185 [$(M+H)^+$, 100%], 141 (4).

For 2,2-bis(3-phenylpropyl)malononitrile **5.4**: [Found: (CI corona$^+$) $(M+H)^+$ 303.1853. $C_{21}H_{23}N_2$ (M+H) requires 303.1856]; ν_{max}(film)/cm^{-1} 3026, 2926, 2860, 2245, 1600, 1496, 1452, 702; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.88-1.91 (4H, m, $CCH_2CH_2CH_2Ar$), 1.97-2.03 (4H, m, $CCH_2CH_2CH_2Ar$), 2.72 (4H, t, *J* = 7.0 Hz, $ArCH_2$), 7.17 (4H, d, *J* = 7.0 Hz, ArH), 7.23 (2H, t, *J* = 7.5 Hz, ArH), 7.31 (4H, t, *J* = 7.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.1 (CH_2), 34.9 (CH_2), 37.2 (CH_2), 37.7 (C), 115.7 (C), 126.6 (CH), 128.5 (CH), 128.8 (CH), 140.2 (C); *m/z* (CI corona$^+$) 303 [$(M+H)^+$, 100%], 191 (4).

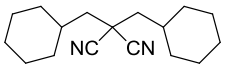
Synthesis of 2-(cyclohexylmethyl)-2-(3-phenylpropyl)malononitrile 5.5



A solution of 2-(3-phenylpropyl)malononitrile (0.460 g, 2.5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to suspension of sodium hydride (~60%, 0.120 g, 3 mmol) in dry tetrahydrofuran (10 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 15 min at room temperature and (bromomethyl)cyclohexane (0.531 g, 3 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. At this point, the reaction was quenched with water (15 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in hexane) to yield *2-(cyclohexylmethyl)-2-(3-phenylpropyl)malononitrile* **5.5** (0.562 g, 80%) as a white solid m.p. 36-38 ^{o}C. [Found: (CI corona$^+$) $(M+H)^+$ 281.2013. $C_{19}H_{25}N_2$ (M+H) requires 281.2012]; ν_{max}(film)/cm^{-1} 3062, 3028, 2933, 2856, 2245, 1602, 1494, 1448, 1028, 727; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.01-1.36 (5H, m, Cy), 1.56-1.79 (6H, m, Cy), 1.89-1.96 (4H, m, CCH_2Cy, $ArCH_2CH_2CH_2C$), 1.99-2.08 (2H, m, $ArCH_2CH_2CH_2C$), 2.74 (2H, t, *J* = 7.2 Hz, $ArCH_2$), 7.19-7.25 (3H, m, ArH), 7.32 (2H, t, *J* = 7.6 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.9 (2 x CH_2), 26.0 (CH_2), 27.0 (CH_2), 33.5 (2 x CH_2), 34.9 (CH), 35.7 (CH_2), 35.9 (C),

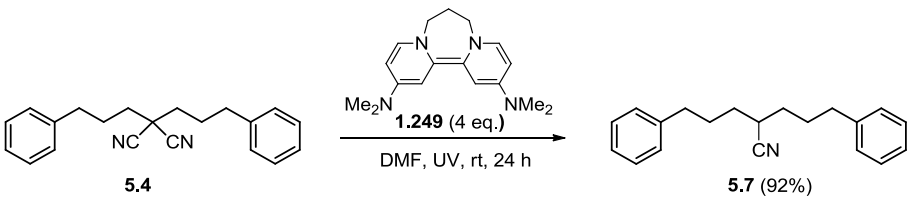
38.7 (CH_2), 44.8 (CH_2), 116.1 (C), 126.6 (CH), 128.5 (CH), 128.8 (CH), 140.3 (C); *m/z* (CI corona$^+$) 281 [$(M+H)^+$, 100%], 256 [$((M-CN)+H)^+$, 6%], 203 (7).

Synthesis of 2,2-bis(cyclohexylmethyl)malononitrile 5.6[258]



A solution of malaononitrile **4.82** (0.330 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to suspension of sodium hydride (~60%, 0.440 g, 11 mmol) in dry tetrahydrofuran (10 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 15 min at room temperature and (bromomethyl)cyclohexane (1.77 g, 10 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. At this point, the reaction was quenched with water (15 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in petroleum ether) to yield 2,2-bis(cyclohexylmethyl)malononitrile **5.6** (0.880 g, 68%) as a white solid m.p. 88-90 ^oC (lit.:[258] 90-92 ^oC). [Found: (CI corona$^+$) $(M+H)^+$ 259.2166. $C_{17}H_{27}N_2$ (M+H) requires 259.2169]; ν_{max}(film)/cm^{-1} 2918, 2848, 2242, 1446, 842; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.04-1.23 (6H, m, Cy), 1.27-1.39 (4H, m, Cy), 1.66-1.82 (12H, m, Cy), 1.92-1.96 (4H, m, CyCH_2C); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.98 (CH_2), 26.01 (CH_2), 33.6 (CH_2), 34.2 (C), 35.6 (CH), 46.2 (CH_2), 116.6 (C); *m/z* (CI corona$^+$) 517 [$(2M+H)^+$, 32%], 492 (13), 467 (16), 303 (29), 259 [$(M+H)^+$, 100%], 234 (69).

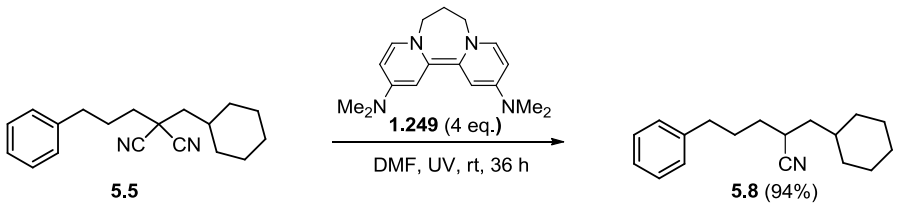
UV-activated reduction of 2,2-bis(3-phenylpropyl)malononitrile 5.4



The general procedure for electron transfer reactions under UV conditions was applied to 2,2-bis(3-phenylpropyl)malononitrile **5.4** (0.121 g, 0.4 mmol) using the donor **1.249** (0.454 g, 1.6 mmol, 4 eq.) for 24 h. After following the general work-up process, column chromatography (2% ethyl acetate in hexane) provided *5-phenyl-2-(3-*

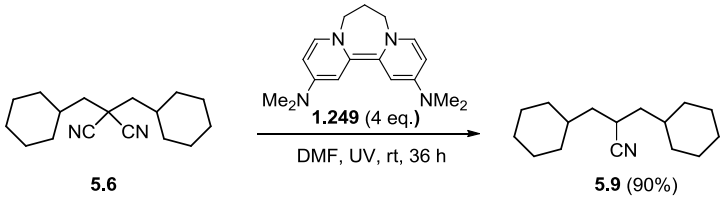
phenylpropyl)pentanenitrile **5.7** (0.1025 g, 92%) as a colourless oil. [Found: (CI corona$^+$) $(M+H)^+$ 278.1905. $C_{20}H_{24}N$ (M+H) requires 278.1903]; ν_{max}(film)/cm^{-1} 3026, 2941, 2860, 2235, 1602, 1494, 1452, 696; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.54-1.68 (6H, m, $CCH_2CH_2CH_2Ar$, $CCH_2CH_2CH_2Ar$), 1.83-1.94 (2H, m, $CCH_2CH_2CH_2Ar$), 2.49-2.56 (1H, m, C*H*CN), 2.65 (4H, t, *J* = 7.6 Hz, $ArCH_2$), 7.16-7.23 (6H, m, ArH), 7.30 (4H, t, *J* = 7.6 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 28.9 (CH_2), 31.6 (CH), 31.8 (CH_2), 35.4 (CH_2), 122.2 (C), 126.2 (CH), 128.5 (CH), 128.6 (CH), 141.4 (C); *m/z* (CI corona$^+$) 278 [$(M+H)^+$, 100%], 249 (15), 203 (13), 95 (16).

UV-activated reduction of 2-(cyclohexylmethyl)-2-(3-phenylpropyl)malononitrile 5.5



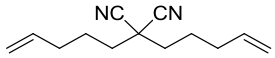
The general procedure for electron transfer reactions under UV conditions was applied to 2-(cyclohexylmethyl)-2-(3-phenylpropyl)malononitrile **5.5** (0.112 g, 0.4 mmol) using the donor **1.249** (0.454 g, 1.6 mmol, 4 eq.) for 36 h. After following the general work-up process, column chromatography (2% diethyl ether in hexane) provided *2-(cyclohexylmethyl)-5-phenylpentanenitrile* **5.8** (0.096 g, 94%) as a white solid m.p. 46-48 ^{o}C. [Found: (CI corona$^+$) $(M+H)^+$ 256.2060. $C_{18}H_{26}N$ (M+H) requires 256.2060]; ν_{max}(film)/cm^{-1} 3026, 2920, 2850, 2235, 1602, 1496, 1448, 698; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.82-0.95 (2H, m, Cy), 1.12-1.35 (4H, m, Cy), 1.44-1.90 (11H, m, Cy, $CHCH_2Cy$, $ArCH_2CH_2CH_2CH$), 2.58-2.65 (1H, m, C*H*CN), 2.68 (2H, t, *J* = 7.2 Hz, $ArCH_2$), 7.18-7.22 (3H, m, ArH), 7.30 (2H, t, *J* = 7.6 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 26.0 (CH_2), 26.1 (CH_2), 26.5 (CH_2), 28.9 (CH_2), 29.0 (CH_2), 32.3 (CH), 32.5 (CH_2), 33.7 (CH_2), 35.4 (CH_2), 35.5 (CH_2), 40.0 (CH), 122.5 (C), 126.1 (CH), 128.5 (CH), 128.6 (CH), 141.5 (C); *m/z* (CI corona$^+$) 256 [$(M+H)^+$, 100%], 249 (8), 95 (9).

UV-activated reduction of 2,2-bis(cyclohexylmethyl)malononitrile 5.6



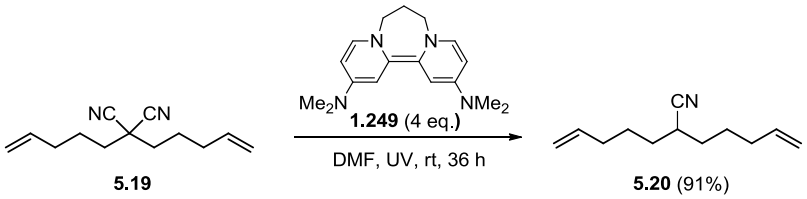
The general procedure for electron transfer reactions under UV conditions was applied to 2,2-bis(cyclohexylmethyl)malononitrile **5.6** (0.103 g, 0.4 mmol) using the donor **1.249** (0.454 g, 1.6 mmol, 4 eq.) for 36 h. After following the general work-up process, column chromatography (2% diethyl ether in hexane) provided *3-cyclohexyl-2-(cyclohexylmethyl)propanenitrile* **5.9** (0.0836 g, 90%) as a white solid m.p. 30-32 ^{o}C. [Found: (CI corona^{+}) $(M+H)^{+}$ 234.2212. $C_{16}H_{28}N$ (M+H) requires 234.2216]; ν_{max}(film)/cm^{-1} 2920, 2846, 2235, 1450, 842; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.82-0.99 (4H, m, Cy), 1.11-1.35 (8H, m, Cy), 1.44-1.58 (4H, m, Cy), 1.65-1.80 (10H, m, Cy, CyC*H*$_2$CH), 2.65-2.71 (1H, m, C*H*CN); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 26.1 (CH_2), 26.2 (CH_2), 26.4 (CH), 26.5 (CH_2), 32.5 (CH_2), 33.7 (CH_2), 35.5 (CH), 40.5 (CH_2), 122.9 (C); *m/z* (CI corona^{+}) 251 [$(M+NH_4)^{+}$, 10%], 234 [$(M+H)^{+}$, 100%], 195 (7).

Synthesis of 2,2-di(pent-4-en-1-yl)malononitrile 5.19[173]



A solution of malononitrile **4.82** (0.330 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to suspension of sodium hydride (~60%, 0.440 g, 11 mmol) in dry tetrahydrofuran (10 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 15 min at room temperature and 5-bromopent-1-ene (1.6392 g, 11 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. At this point, the reaction was quenched with water (15 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in hexane) to yield 2,2-di(pent-4-en-1-yl)malononitrile **5.19** (0.726 g, 72%) as a colourless oil. [Found: (CI corona^{+}) $(M+H)^{+}$ 203.1542. $C_{13}H_{19}N_2$ (M+H) requires 203.1543]; ν_{max}(film)/cm^{-1} 3080, 2933, 2866, 2241, 1641, 1460, 914; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.75-1.83 (4H, m, =CHCH$_2$C*H*$_2$CH$_2$), 1.91-1.96 (4H, m, CC*H*$_2$CH$_2$CH$_2$), 2.16-2.21 (4H, m, =CHC*H*$_2$CH$_2$CH$_2$), 5.04-5.11 (4H, m, C*H*$_2$=CHCH$_2$), 5.73-5.83 (2H, m, CH$_2$=C*H*CH$_2$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 24.7 (CH_2), 32.7 (CH_2), 37.2 (CH_2), 37.7 (C), 115.7 (C), 116.4 (CH_2), 136.7 (CH); *m/z* (CI corona^{+}) 203 [$(M+H)^{+}$, 100%], 178 (16).

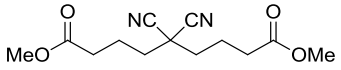
UV-activated reduction of 2,2-di(pent-4-en-1-yl)malononitrile 5.19



5.19 **5.20** (91%)

The general procedure for electron transfer reactions under UV conditions was applied to 2,2-bis(cyclohexylmethyl)malononitrile **5.19** (0.101 g, 0.5 mmol) using the donor **1.249** (0.568 g, 2.0 mmol, 4 eq.) for 36 h. After following the general work-up process, column chromatography (2% diethyl ether in hexane) provided 2-(pent-4-en-1-yl)hept-6-enenitrile **5.20** (0.0806 g, 91%) as a colourless oil. [Found: (CI corona$^+$) $(M+H)^+$ 178.1587. $C_{12}H_{20}N$ (M+H) requires 178.1590]; ν_{max}(film)/cm^{-1} 3078, 2931, 2862, 2237, 1641, 1460, 910; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.53-1.69 (8H, m, =CHCH$_2$C*H$_2$*CH$_2$, =CHCH$_2$CH$_2$C*H$_2$*), 2.08-2.13 (4H, m, =CHC*H$_2$*CH$_2$CH$_2$), 2.50-2.57 (1H, m, C*H*CN), 4.98-5.07 (4H, m, C*H$_2$*=CHCH$_2$), 5.74-5.84 (2H, m, CH$_2$=C*H*CH$_2$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 26.4 (CH_2), 31.5 (CH), 31.7 (CH_2), 33.2 (CH_2), 115.4 (CH_2), 122.3 (C), 137.8 (CH); *m/z* (CI corona$^+$) 195 [$(M+NH_4)^+$, 11%], 178 [$(M+H)^+$, 100%], 117 (14).

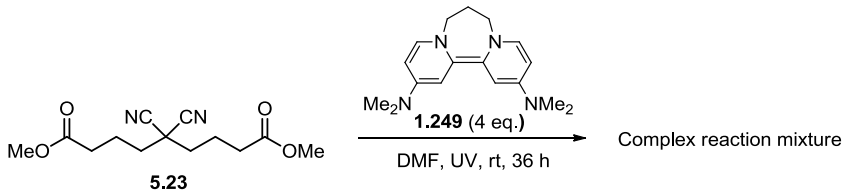
Synthesis of dimethyl 5,5-dicyanononanedioate 5.23



A solution of malononitrile **4.82** (0.330 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to suspension of sodium hydride (~60%, 0.440 g, 11 mmol) in dry tetrahydrofuran (10 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 15 min at room temperature and methyl 4-bromobutanoate (1.9914 g, 11 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. At this point, the reaction was quenched with water (15 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (25% ethyl acetate in hexane) to yield *dimethyl 5,5-dicyanononanedioate* **5.23** (0.935 g, 70%) as a colourless oil. [Found: (ESI$^+$) $(M+NH_4)^+$ 284.1609. $C_{13}H_{22}N_3O_4$ $(M+NH_4)$ requires 284.1605]; ν_{max}(film)/cm^{-1} 2954, 2360, 2328,

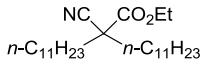
1730, 1436, 1259, 1170; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.97-2.06 (8H, m, $CH_2CH_2CO_2CH_3$), 2.47 (4H, t, J = 6.0 Hz, CCH_2), 3.71 (6H, s, CO_2CH_3); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 20.8 (CH_2), 32.6 (CH_2), 36.6 (CH_2), 37.2 (C), 51.9 (CH_3), 115.2 (C), 172.5 (C=O); *m/z* (ESI$^+$) 284 [$(M+NH_4)^+$, 100%], 267 [$(M+H)^+$, 4%], 199 (4).

UV-activated reduction of dimethyl 5,5-dicyanononanedioate 5.23



The general procedure for electron transfer reactions under UV conditions was applied to dimethyl 5,5-dicyanononanedioate **5.23** (0.106 g, 0.4 mmol) using the donor **1.249** (0.454 g, 1.6 mmol, 4 eq.) for 36 h. After following the general work-up process, crude product was obtained. ^{1}H-NMR of the crude product and TLC showed that the reaction led to very complex mixture of products. No attempt was made to isolate these products.

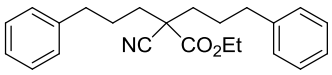
Synthesis of ethyl 2-cyano-2-undecyltridecanoate 5.30



A solution of ethyl 2-cyanoacetate **4.77** (0.452 g, 4 mmol) in dry tetrahydrofuran (2 mL) was added slowly to suspension of sodium hydride (~60%, 0.352 g, 8.8 mmol) in dry tetrahydrofuran (10 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 15 min at room temperature and 1-bromoundecane **5.2** (2.069 g, 8.8 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. At this point, the reaction was quenched with water (15 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in hexane) to yield *ethyl 2-cyano-2-undecyltridecanoate* **5.30** (0.896 g, 53%) as a colourless oil. [Found: (ESI$^+$) $(M+NH_4)^+$ 439.4255. $C_{27}H_{55}N_2O_2$ $(M+NH_4)$ requires 439.4258]; ν_{max}(film)/cm^{-1} 2953, 2922, 2852, 2237, 1741, 1463, 1377, 1217, 1022, 721; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.89 [6H, t, J =

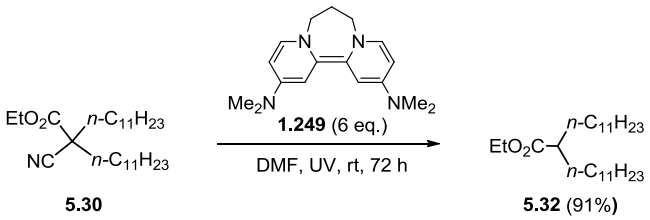
7.5 Hz, $(CH_2)_{10}CH_3$], 1.26-1.35 (37H, m, $CH_3(CH_2)_9$, $(CH_2)_8CH_3$, $CO_2CH_2CH_3$), 1.54-1.58 (2H, m, $CH_2(CH_2)_8CH_3$), 1.74-1.79 (2H, m, $CCH_2(CH_2)_9CH_3$), 1.86-1.92 (2H, m, $CCH_2(CH_2)_9CH_3$), 4.27 (2H, q, J = 7.5 Hz, $CO_2CH_2CH_3$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.25 (CH_3), 14.28 (CH_3), 22.8 (CH_2), 25.4 (CH_2), 29.4 (2 x CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.7 (2 x CH_2), 32.1 (CH_2), 37.7 (CH_2), 50.2 (C), 62.6 (CH_2), 119.7 (C), 169.5 (C=O); *m/z* (ESI$^+$) 860 [$(2M+NH_4)^+$, 7%], 439 [$(M+NH_4)^+$, 100%], 351 (16), 268 (28).

Synthesis of ethyl 2-cyano-5-phenyl-2-(3-phenylpropyl)pentanoate 5.31



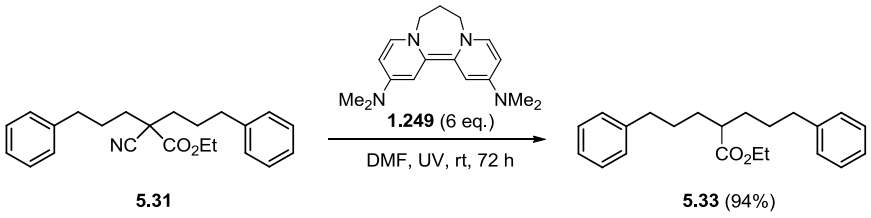
A solution of ethyl 2-cyanoacetate **4.77** (0.565 g, 5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to suspension of sodium hydride (~60%, 0.440 g, 11 mmol) in dry tetrahydrofuran (10 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 15 min. at room temperature and (3-bromopropyl)benzene (2.1898 g, 11 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. At this point, the reaction was quenched with water (15 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in hexane) to yield *ethyl 2-cyano-5-phenyl-2-(3-phenylpropyl)pentanoate* **5.31** (1.220 g, 70%) as a colourless oil. [Found: (ESI$^+$) $(M+NH_4)^+$ 367.2384. $C_{23}H_{31}N_2O_2$ $(M+NH_4)$ requires 367.2380]; ν_{max}(film)/cm^{-1} 3026, 2935, 2864, 2240, 1737, 1452, 1219, 1182, 1095, 1018, 698; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.29 [3H, t, J = 7.5 Hz, $CO_2CH_2CH_3$], 1.59-1.68 (2H, m, $CCH_2CH_2CH_2Ar$), 1.77-1.82 (2H, m, $CCH_2CH_2CH_2Ar$), 1.87-1.95 (4H, m, $CCH_2CH_2CH_2Ar$, $CCH_2CH_2CH_2Ar$), 2.65 (4H, t, J = 7.0 Hz, $ArCH_2$), 4.24 (2H, q, J = 7.0 Hz, $CO_2CH_2CH_3$), 7.16 (4H, d, J = 7.0 Hz, ArH), 7.20 (2H, t, J = 7.5 Hz, ArH), 7.29 (4H, t, J = 7.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 27.0 (CH_2), 35.3 (CH_2), 36.9 (CH_2), 49.8 (C), 62.7 (CH_2), 119.3 (C), 126.2 (CH), 128.4 (CH), 128.6 (CH), 141.0 (C), 169.1 (C=O); *m/z* (ESI$^+$) 367[$(M+NH_4)^+$, 100%].

UV-activated reduction of ethyl 2-cyano-2-undecyltridecanoate 5.30



The general procedure for electron transfer reactions under UV conditions was applied to ethyl 2-cyano-2-undecyltridecanoate **5.30** (0.126 g, 0.3 mmol) using the donor **1.249** (0.511 g, 1.8 mmol, 6 eq.) for 72 h. After following the general work-up process, column chromatography (2% diethyl ether in petroleum ether) provided *ethyl 2-undecyltridecanoate* **5.32** (0.108 g, 91%) as a colourless oil. [Found: (CI corona^{+}) $(M+H)^{+}$ 397.4041. $C_{26}H_{53}O_2$ (M+H) requires 397.4040]; ν_{max}(film)/cm^{-1} 2922, 2852, 1734, 1463, 1377, 1155, 1033, 721; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.89 [6H, t, J = 7.0 Hz, $(CH_2)_{10}CH_3$], 1.24-1.34 (37H, m, $CH_3(CH_2)_9$, $(CH_2)_8CH_3$, $CO_2CH_2CH_3$), 1.41-1.46 (2H, m, $CH_2(CH_2)_8CH_3$), 1.54-1.62 (4H, m, $CH(CH_2)_2$, 1.28-2.34 (1H, m, $CHCO_2Et$), 4.14 (2H, q, J = 7.0 Hz, $CO_2CH_2CH_3$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 14.5 (CH_3), 22.8 (CH_2), 27.6 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.7 (2 x CH_2), 29.8 (2 x CH_2), 32.1 (CH_2), 32.7 (CH_2), 45.9 (CH), 60.1 (CH_2), 176.8 (C=O); *m/z* (CI corona^{+}) 397 [$(M+H)^{+}$, 100%], 327 (16), 243 (23), 229 (31), 201 (32), 155 (23).

UV-activated reduction of ethyl 2-cyano-5-phenyl-2-(3-phenylpropyl)pentanoate 5.31

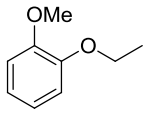


The general procedure for electron transfer reactions under UV conditions was applied to ethyl 2-cyano-5-phenyl-2-(3-phenylpropyl)pentanoate **5.31** (0.1396 g, 0.4 mmol) using the donor **1.249** (0.682 g, 2.4 mmol, 6 eq.) for 72 h. After following the general work-up process, column chromatography (5% diethyl ether in hexane) provided *ethyl 5-phenyl-2-(3-phenylpropyl)pentanoate* **5.33** (0.122 g, 94%) as a colourless oil. [Found: (ESI^{+}) $(M+H)^{+}$ 325.2169. $C_{22}H_{29}O_2$ (M+H) requires 325.2162]; ν_{max}(film)/cm^{-1} 3024, 2937, 2858, 1728, 1494, 1452, 1184, 1149, 1028, 696; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.24 [3H, t, J =

7.2 Hz, $CO_2CH_2CH_3$], 1.46-1.53 (2H, m, $CCH_2CH_2CH_2Ar$), 1.56-1.69 (6H, m, $CCH_2CH_2CH_2Ar$, $CCH_2CH_2CH_2Ar$), 2.35-2.40 (1H, m, $CHCO_2Et$), 2.60 (4H, t, J = 7.2 Hz, $ArCH_2$), 4.13 (2H, q, J = 7.2 Hz, $CO_2CH_2CH_3$), 7.15-7.20 (6H, m, ArH), 7.26-7.30 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.5 (CH_3), 29.3 (CH_2), 32.2 (CH_2), 35.9 (CH_2), 45.6 (CH), 60.2 (CH_2), 125.9 (CH), 128.4 (CH), 128.5 (CH), 142.3 (C), 176.4 (C=O); *m/z* (ESI^+) 342 [$(M+NH_4)^+$, 100%], 325 [$(M+H)^+$, 47%], 251 (3), 173 (5).

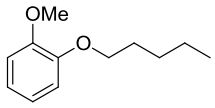
7.8 Experimental for Chapter 6

Synthesis of 1-ethoxy-2-methoxybenzene 6.6[259]



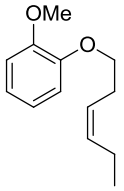
A solution of 2-methoxyphenol **6.9** (0.620 g, 5 mmol) in DMF (2 mL) was added slowly to the solution of K_2CO_3 (1.0365 g, 7.5 mmol) in DMF (10 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 15 min at room temperature and iodoethane **6.10** (0.935 g, 6 mmol) in DMF (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at 70 ^oC for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in hexane) to yield 1-ethoxy-2-methoxybenzene **6.6** (0.474 g, 62%) as a colourless oil. [Found: (EI^+) $(M)^+$ 152.0831. $C_9H_{12}O_2$ (M) requires 152.0832]; ν_{max}(film)/cm^{-1} 3062, 2980, 2833, 1591, 1502, 1247, 1124, 1028, 736; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.48 (3H, t, J = 7.2 Hz, OCH_2CH_3), 3.89 (3H, s, OCH_3), 4.11 (2H, q, J = 7.2 Hz, OCH_2CH_3), 6.88-6.94 (4H, m, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 15.0 (CH_3), 56.0 (CH_3), 64.4 (CH_2), 111.8 (CH), 113.0 (CH), 120.9 (2 x CH), 148.5 (C), 149.5 (C); *m/z* (EI^+) 152 [M^+, 38%], 124(39), 109 (61), 95 (52), 81 (100), 51 (40).

Synthesis of 1-methoxy-2-(pentyloxy)benzene 6.7[260]



A solution of 2-methoxyphenol **6.9** (1.2414 g, 10 mmol) in DMF (2 mL) was added slowly to the solution of K_2CO_3 (2.073 g, 15 mmol) in DMF (10 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 15 min at room temperature and 1-bromopentane (1.6615 g, 11 mmol) in DMF (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at 100 ^oC for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in hexane) to yield 1-methoxy-2-(pentyloxy)benzene 6.7 (1.636 g, 84%) as a light yellow oil. [Found: (ESI^+) $(M+NH_4)^+$ 212.1647. $C_{12}H_{22}NO_2$ $(M+NH_4)$ requires 212.1645]; ν_{max}(film)/cm^{-1} 3062, 2954, 2933, 1591, 1502, 1454, 1249, 1224, 1122, 1028, 736; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, t, J = 7.2 Hz, $O(CH_2)_4CH_3$), 1.35-1.49 (4H, m, $O(CH_2)_2(CH_2)_2CH_3$), 1.86 (2H, quintet, J = 7.2 Hz, OCH_2CH_2), 3.88 (3H, s, OCH_3), 4.02 (2H, t, J = 7.2 Hz, OCH_2CH_2), 6.88-6.93 (4H, m, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.1 (CH_3), 22.6 (CH_2), 28.3 (CH_2), 29.1 (CH_2), 56.1 (CH_3), 69.1 (CH_2), 112.0 (CH), 113.3 (CH), 120.9 (CH), 121.0 (CH), 148.8 (C), 149.6 (C); *m/z* (ESI^+) 212 [$(M+NH_4)^+$, 100%], 195 [$(M+H)^+$, 75%], 141 (24).

Synthesis of (*Z*)-1-(hex-3-en-1-yloxy)-2-methoxybenzene 6.8



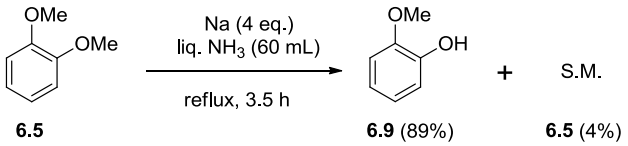
A solution of 2-methoxyphenol **6.9** (0.620 g, 5 mmol) in DMF (2 mL) was added slowly to the solution of K_2CO_3 (1.0365 g, 7.5 mmol) in DMF (10 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 15 min at room temperature and (*Z*)-1-bromohex-3-ene (0.972 g, 6 mmol) in DMF (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at 100 ^oC for 16 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 15 mL).

The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in hexane) to yield *(Z)-1-(hex-3-en-1-yloxy)-2-methoxybenzene* **6.8** (0.704 g, 68%) as a colourless oil. [Found: (ESI^+) $(M+NH_4)^+$ 224.1646. $C_{13}H_{22}NO_2$ $(M+NH_4)$ requires 224.1645]; ν_{max}(film)/cm^{-1} 3005, 2960, 1591, 1502, 1454, 1249, 1224, 1122, 1026, 736; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.99 (3H, t, J = 7.6 Hz, =CHCH$_2$C*H$_3$*), 2.07-2.14 (2H, m, =CHC*H$_2$*CH$_3$), 2.58-2.64 (2H, m, OCH$_2$C*H$_2$*), 3.88 (3H, s, OC*H$_3$*), 4.02 (2H, t, J = 7.6 Hz, OC*H$_2$*CH$_2$), 5.40-5.47 (1H, m, OCH$_2$CH$_2$CH=C*H*), 5.51-5.58 (1H, m, OCH$_2$CH$_2$C*H*=CH), 6.88-6.93 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.4 (CH_3), 20.8 (CH_2), 27.5 (CH_2), 56.1 (CH_3), 68.5 (CH_2), 112.0 (CH), 113.2 (CH), 121.0 (CH), 121.1 (CH), 123.8 (CH), 134.7 (CH), 148.5 (C), 149.6 (C); *m/z* (ESI^+) 224 [$(M+NH_4)^+$, 100%], 207 [$(M+H)^+$, 32%], 199 (12), 149 (14).

Standard Procedure for cleavage of ArO-C bond in 1,2-dialkoxybenzenes under Birch conditions[197]

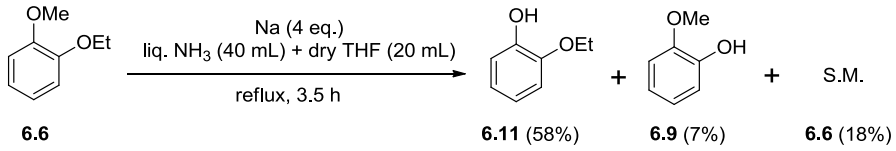
A three-necked flask was fitted with a dry ice condenser (cold finger) and connected to an ammonia cylinder. The inside atmosphere in the flask was replaced with argon gas and approximately 60 mL of ammonia was condensed into the flask. Then, 1,2-dialkoxybenzene substrate was added into the flask under argon gas (For reactions in which dry THF was used as a co-solvent: approximately 40 mL ammonia was condensed into the flask and the substrate dissolved in 20 mL of dry THF was added into the reaction flask). Then, freshly cut sodium (4 eq.) was added into the flask and the resulting blue solution was refluxed for 3.5 h. At this point, the reaction mixture was quenched with sodium benzoate (about 1 g) and a colour change from blue to orange signalled completion of this addition. Then, the excess base was neutralized with ammonium chloride (about 1 g) and a colour change from orange to colourless signalled the completion of this addition. Then, the reaction set-up was left over night for evaporation of ammonia. The reaction mixture was then quenched with sat. sodium bicarbonate solution (10 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography to provide products in yields as stated.

Cleavage of ArO-C bond in 1,2-dimethoxybenzene 6.5 using Birch conditions



The standard procedure for cleavage of ArO-C bond under Birch conditions was applied to 1,2-dimethoxybenzene **6.5** (0.276 g, 2 mmol) using sodium (0.184 g, 8 mmol). After following the general work-up process, column chromatography (5% and then 15% diethyl ether in hexane) provided starting material **6.5** (0.011 g, 4%) and 2-methoxyphenol **6.9**[261] (0.221 g, 89%) as colourless oils. ν_{max}(film)/cm^{-1} 3504, 2953, 1595, 1498, 1442, 1359, 1255, 1205, 1107, 1020, 738; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.90 (3H, s, OC*H*$_3$), 5.61 (1H, bs, O*H*), 6.83-6.95 (4H, m, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 56.0 (CH_3), 110.9 (CH), 114.7 (CH), 120.3 (CH), 121.6 (CH), 145.8 (C), 146.7 (C). Spectral data of **6.9** were consistent with the literature data of the same compound.[261]

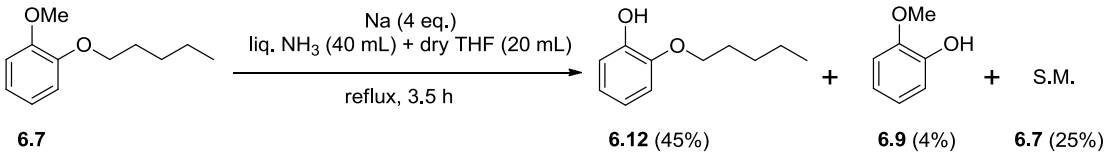
Cleavage of ArO-C bond in 1-ethoxy-2-methoxybenzene 6.6 using Birch conditions



The standard procedure for cleavage of ArO-C bond under Birch conditions was applied to 1-ethoxy-2-methoxybenzene **6.6** (0.152 g, 1 mmol) using sodium (0.092 g, 4 mmol). After following the general work-up process, column chromatography (5% and then 10% diethyl ether in hexane) provided 2-ethoxyphenol **6.11**[262] (0.080 g, 58%) and 2-methoxyphenol **6.9**[261] (0.0084 g, 7%) along with recovery of starting material **6.6** (0.0278 g, 18%), as colourless oils. For 2-ethoxyphenol **6.11**: ν_{max}(film)/cm^{-1} 3535, 3054, 2984, 1596, 1442, 1040, 925, 743; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.46 (3H, t, J = 7.2 Hz, OCH_2CH_3), 4.13 (2H, q, J = 7.2 Hz, OCH_2CH_3), 5.68 (1H, bs, O*H*), 6.81-6.90 (3H, m, ArH), 6.93-6.96 (1H, m, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 15.0 (CH_3), 64.6 (CH_2), 111.8 (CH), 114.6 (CH), 120.2 (CH), 121.5 (CH), 146.0 (2 x C). Spectral data of **6.11** were consistent with the literature data of the same compound.[262]

Spectral data of **6.9** were consistent with the previously mentioned data of the same compound.

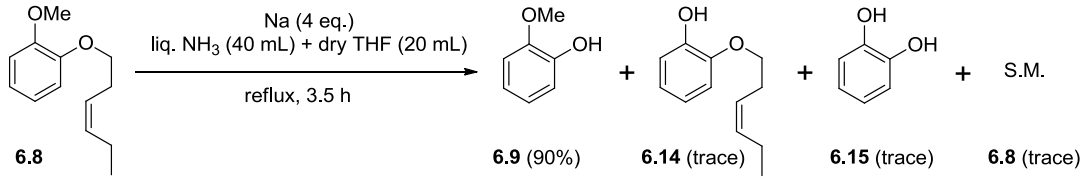
Cleavage of ArO-C bond in 1-methoxy-2-(pentyloxy)benzene 6.7 using Birch conditions



The standard procedure for cleavage of ArO-C bond under Birch conditions was applied to 1-methoxy-2-(pentyloxy)benzene **6.7** (0.388 g, 2 mmol) using sodium (0.184 g, 8 mmol). After following the general work-up process, column chromatography (5% and then 10% diethyl ether in hexane) provided 2-(pentyloxy)phenol **6.12**[263] (0.161 g, 45%) and 2-methoxyphenol **6.9**[261] (0.009 g, 4%) along with recovery of starting material **6.7** (0.098 g, 25%), as colourless oils. For 2-(pentyloxy)phenol **6.12**: ν_{max}(film)/cm^{-1} 3541, 3448, 2954, 2931, 2860, 1597, 1498, 1467, 1255, 1220, 1105, 1033, 738; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.96 (3H, t, J = 7.0 Hz, $O(CH_2)_4CH_3$), 1.37-1.49 (4H, m, $O(CH_2)_2(CH_2)_2CH_3$), 1.84 (2H, quintet, J = 7.0 Hz, OCH_2CH_2), 4.05 (2H, t, J = 6.5 Hz, OCH_2CH_2), 5.67 (1H, bs, O*H*), 6.82-6.89 (3H, m, ArH), 6.93-6.96 (1H, m, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.1 (CH_3), 22.6 (CH_2), 28.3 (CH_2), 29.1 (CH_2), 69.0 (CH_2), 111.8 (CH), 114.6 (CH), 120.2 (CH), 121.4 (CH), 146.0 (C), 146.1 (C). Spectral data of **6.11** were consistent with the literature data of the same compound.[263]

Spectral data of **6.9** were consistent with the previously mentioned data of the same compound.

Cleavage of ArO-C bond in (*Z*)-1-(hex-3-en-1-yloxy)-2-methoxybenzene 6.8 using Birch conditions

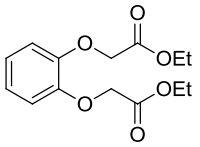


The standard procedure for cleavage of ArO-C bond under Birch conditions was applied to (*Z*)-1-(hex-3-en-1-yloxy)-2-methoxybenzene **6.8** (0.206 g, 1 mmol) using sodium (0.092 g, 4 mmol). After following the general work-up process, column chromatography (15% diethyl ether in hexane) provided 2-methoxyphenol **6.9**[261] (0.112 g, 90%)

exclusively and only trace amounts of demethylation product **6.14**, catechol **6.15** and starting material **6.8** were observed from the ^{1}H-NMR of crude product. Spectral data of **6.9** were consistent with the previously mentioned data of the same compound.

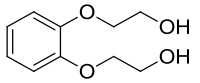
Synthesis of 1,2-bis(2-(undecyloxy)ethoxy)benzene 6.16

(a) Synthesis of diethyl 2,2'-(1,2-phenylenebis(oxy))diacetate 6.28[264]



A solution of catechol **6.15** (2.2022 g, 20 mmol) in DMF (5 mL) was added slowly to a solution of K_2CO_3 (8.2926 g, 60 mmol) in DMF (30 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 30 min at room temperature and ethyl 2-bromoacetate **6.29** (7.3484 g, 44 mmol) in DMF (5 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at 100 ^{o}C for 24 h under argon gas. At this point, the reaction was quenched with water (10 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (40% ethyl acetate in petroleum ether) to yield diethyl 2,2'-(1,2-phenylenebis(oxy))diacetate **6.28** (4.586 g, 81%) as a colourless oil. [Found: (ESI^{+}) $(M+H)^{+}$ 283.1181. $C_{14}H_{19}O_6$ (M+H) requires 283.1176]; ν_{max}(film)/cm^{-1} 2981, 2933, 1753, 1595, 1498, 1269, 1178, 1064, 1024, 742; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.29 (6H, t, J = 7.2 Hz, OCH_2CH_3), 4.26 (4H, q, J = 7.2 Hz, OCH_2CH_3), 4.72 (4H, s, $ArOCH_2$), 6.89-6.97 (4H, m, ArH); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 14.2 (CH_3), 61.3 (CH_2), 66.9 (CH_2), 115.8 (CH), 122.7 (CH), 148.3 (C), 169.1 (C=O); *m/z* (ESI^{+}) 305 [$(M+Na)^{+}$, 100%], 283 [$(M+H)^{+}$, 54%].

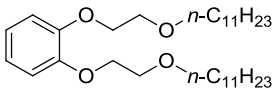
(b) Synthesis of 2,2'-(1,2-phenylenebis(oxy))diethanol 6.27[265]



A solution of diethyl 2,2'-(1,2-phenylenebis(oxy))diacetate **6.28** (2.258g, 8 mmol) in dry tetrahydrofuran (5 mL) was added slowly to the suspension of $LiAlH_4$ (0.607 g, 16 mmol) in dry tetrahydrofuran (20 mL) at 0 ^{o}C under argon gas. The resulting solution was further

stirred at reflux conditions for 16 h under argon gas. At this point, the excess of $LiAlH_4$ was quenched slowly with methanol (about 2 mL) and 10% aqueous hydrochloric acid (10 mL) was added to the resulting solution that was then extracted with ethyl acetate (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (60% ethyl acetate in petroleum ether) to yield 2,2'-(1,2-phenylenebis(oxy))diethanol **6.27** (1.342 g, 85%) as a white solid m.p. 80-82 ^{o}C (lit.:[266] 82-84 ^{o}C). [Found: (CI^+ corona) $(M+H)^+$ 199.0965. $C_{10}H_{15}O_4$ (M+H) requires 199.0965]; ν_{max}(film)/cm^{-1} 3491, 3387, 2956, 2926, 1593, 1504, 1450, 1317, 1253, 1215, 1124, 1037, 731; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.80 (2H, bs, O*H*), 3.93 (4H, t, *J* = 4.4 Hz, C*H*$_2$OH), 4.13 (4H, t, *J* = 4.4 Hz, ArOC*H*$_2$), 6.86-6.97 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 61.3 (CH_2), 71.8 (CH_2), 115.5 (CH), 122.4 (CH), 149.1 (C); *m/z* (CI^+ corona) 397 [$(2M+H)^+$, 95%], 199 [$(M+H)^+$, 100%].

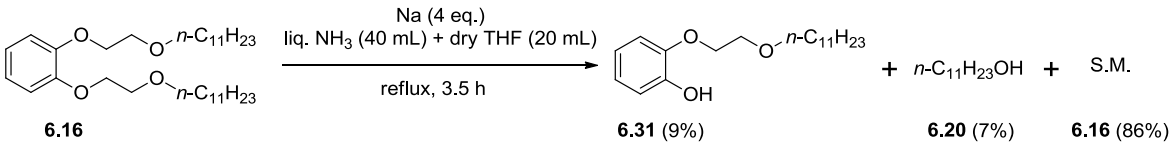
(c) Synthesis of 1,2-bis(2-(undecyloxy)ethoxy)benzene 6.16



A solution of 2,2'-(1,2-phenylenebis(oxy))diethanol **6.27** (0.693 g, 3.5 mmol) in dry tetrahydrofuran (2 mL) was added slowly to the suspension of sodium hydride (~60%, 0.350 g, 8.75 mmol) in dry tetrahydrofuran (10 mL) at 0 ^{o}C under argon gas. The resulting solution was stirred for 15 min. at room temperature and 1-bromoundecane **6.30** (1.8111 g, 7.7 mmol) in dry tetrahydrofuran (2 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at reflux conditions for 24 h under argon gas. At this point, the reaction was quenched with water (15 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (5% diethyl ether in hexane) to yield *1,2-bis(2-(undecyloxy)ethoxy)benzene* **6.16** (1.012 g, 57%) as a white solid m.p. 26-28 ^{o}C, along with recovery of starting material **6.27** (0.139 g, 20%). For **6.16**: [Found: (ESI^+) $(M+NH_4)^+$ 524.4670. $C_{32}H_{62}NO_4$ ($M+NH_4$) requires 524.4673]; ν_{max}(ATR)/cm^{-1} 2953, 2920, 1593, 1500, 1454, 1255, 1122, 1047, 738; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 (6H, t, *J* = 7.2 Hz, C*H*$_3$), 1.27-1.37 (32H, m, O$(CH_2)_2$(C*H*$_2$)$_8$CH$_3$), 1.60 (4H, quintet, *J* = 6.8 Hz, OCH$_2$C*H*$_2$$(CH_2)_8CH_3$), 3.54 (4H, t, *J* = 6.8 Hz, OC*H*$_2$$(CH_2)_9CH_3$), 3.79 (4H, t, *J* = 5.6

Hz, $ArOCH_2CH_2$), 4.17 (4H, t, J = 5.2 Hz, $ArOCH_2CH_2$), 6.90-6.96 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.3 (CH_3), 22.8 (CH_2), 26.3 (CH_2), 29.5 (CH_2), 29.7 (CH_2), 29.8 (3 x CH_2), 29.9 (CH_2), 32.1 (CH_2), 69.1 (CH_2), 69.4 (CH_2), 71.9 (CH_2), 115.4 (CH), 121.8 (CH), 149.3 (C); *m/z* (ESI^+) 1030 [$(2M+NH_4)^+$, 42%], 524 [$(M+NH_4)^+$, 100%], 507 [$(M+H)^+$, 6%].

Cleavage of ArO-C bond in 1,2-bis(2-(undecyloxy)ethoxy)benzene 6.16 using Birch conditions



6.16 **6.31** (9%) **6.20** (7%) **6.16** (86%)

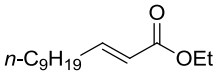
The standard procedure for cleavage of ArO-C bond under Birch conditions was applied to 1,2-bis(2-(undecyloxy)ethoxy)benzene **6.16** (0.253 g, 0.5 mmol) using sodium (0.046 g, 2 mmol). After following the general work-up process, column chromatography (5% and then 15% diethyl ether in hexane) provided *2-(2-(undecyloxy)ethoxy)phenol* **6.31** (0.014 g, 9%), as a light yellow oil, and undecan-1-ol **6.20**[229] (0.006 g, 7%), as a colourless oil, along with recovery of starting material **6.16** (0.218 g, 86%).

For 2-(2-(undecyloxy)ethoxy)phenol **6.31**: [Found: (ESI^+) $(M+H)^+$ 309.2430. $C_{19}H_{33}O_3$ (M+H) requires 309.2424]; ν_{max}(film)/cm^{-1} 3373, 2922, 2852, 1595, 1496, 1456, 1373, 1261, 1222, 1109, 1035, 740; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 7.2 Hz, CH_3), 1.27-1.39 (16H, m, $O(CH_2)_2(CH_2)_8CH_3$), 1.65 (2H, quintet, J = 6.8 Hz, $OCH_2CH_2(CH_2)_8CH_3$), 3.55 (2H, t, J = 6.8 Hz, $OCH_2(CH_2)_9CH_3$), 3.73 (2H, t, J = 4.8 Hz, $ArOCH_2CH_2$), 4.16 (2H, t, J = 4.8 Hz, $ArOCH_2CH_2$),6.74 (1H, bs, ArO*H*), 6.79-6.83 (1H, m, ArH), 6.94-6.97 (3H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.3 (CH_3), 22.8 (CH_2), 26.2 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.7 (2 x CH_2), 29.8 (2 x CH_2), 32.1 (CH_2), 69.3 (CH_2), 71.1 (CH_2), 71.9 (CH_2), 115.8 (CH), 116.8 (CH), 120.1 (CH), 123.6 (CH), 146.2 (C), 148.1 (C); *m/z* (ESI^+) 639 [$(2M+Na)^+$, 9%], 326 [$(M+NH_4)^+$, 100%], 309 [$(M+H)^+$, 31%].

For undecan-1-ol **6.20**: ν_{max}(film)/cm^{-1} 3363, 2922, 2852, 1465, 1056, 721; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 6.5 Hz, CH_3), 1.27-1.39 (16H, m, $HO(CH_2)_2(CH_2)_8CH_3$), 1.57 (2H, quintet, J = 6.5 Hz, $HOCH_2CH_2$), 3.65 (2H, t, J = 6.5 Hz, $HOCH_2$); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.3 (CH_3), 22.8 (CH_2), 25.9 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (3

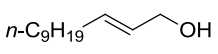
x CH_2), 32.1 (CH_2), 33.0 (CH_2), 63.3 (CH_2). Spectral data of **6.20** were consistent with the literature data of the same compound.[229]

Synthesis of (*E*)-ethyl dodec-2-enoate 6.35[267]



A solution of ethyl 2-(diethoxyphosphoryl)acetate **6.36** (9.8643 g, 44 mmol) in dry diethyl ether (5 mL) was added slowly to suspension of sodium hydride (~60%, 1.76 g, 44 mmol) in dry diethyl ether (20 mL) at 0 ^oC under argon gas. The resulting solution was stirred for 15 min at 0 ^oC and decanal **6.37** (6.248 g, 40 mmol) in dry diethyl ether (5 mL) was added slowly into the reaction flask. The reaction mixture was further stirred at 0 ^oC for 2 h and then the quenched with water (15 mL) and extracted with diethyl ether (3 x 20 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (10% diethyl ether in hexane) to yield (*E*)-ethyl dodec-2-enoate **6.35** (6.832 g, 75%) as a colourless oil. [Found: (CI^+ corona) $(M+H)^+$ 227.2007. $C_{14}H_{27}O_2$ (M+H) requires 227.2006]; ν_{max}(film)/cm^{-1} 2954, 2924, 2854, 1720, 1654, 1463, 1367, 1263, 1178, 1043, 979; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 6.4 Hz, CH_3), 1.27-1.31 (15H, m, $CO_2CH_2CH_3$, $(CH_2)_6CH_3$), 1.42-1.58 (2H, m, $=CHCH_2CH_2$), 2.19 (2H, dq, J = 7.6, 1.6 Hz, $=CHCH_2$), 4.19 (2H, q, J = 7.2 Hz, $CO_2CH_2CH_3$), 5.82 (1H, dt, J = 15.6, 1.6 Hz, CH=CHCH_2), 6.97 (1H, dt, J = 16.0, 6.8 Hz, CH=CHCH_2); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 14.4 (CH_3), 22.8 (CH_2), 28.2 (CH_2), 29.3 (CH_2), 29.4 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 32.0 (CH_2), 32.3 (CH_2), 60.2 (CH_2), 121.4 (CH), 149.6 (CH), 166.9 (C=O); *m/z* (CI^+ corona) 227 [$(M+H)^+$, 100%].

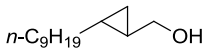
Synthesis of (*E*)-dodec-2-en-1-ol 6.34[268]



A solution of (*E*)-ethyl dodec-2-enoate **6.35** (5.6548 g, 25 mmol) in dry DCM (30 mL) was added to a flask and DiBAL-H (1 M in hexane, 55 mL, 55 mmol) was added dropwise into the reaction flask at - 78 ^oC under argon gas. The resulting solution was stirred for 2 h at - 78 ^oC and then quenched slowly with water (10 mL). The resulting solution was extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous

sodium sulfate. The concentrated solution was purified by column chromatography (20% ethyl acetate in hexane) to yield (*E*)-dodec-2-en-1-ol **6.34** (3.860 g, 84%) as a colourless oil. [Found: (CI^+ corona) $(M+NH_4)^+$ 202.2168. $C_{12}H_{28}NO$ $(M+NH_4)$ requires 202.2165]; ν_{max}(film)/cm^{-1} 3319, 2954, 2922, 2852, 1463, 1089, 1001, 968, 721; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 0.89 (3H, t, J = 7.0 Hz, C*H*$_3$), 1.26-1.40 (14H, m, (C*H*$_2$)$_7$CH$_3$), 2.03-2.07 (2H, m, =CHC*H*$_2$), 4.09 (2H, d, J = 6.0 Hz, HOC*H*$_2$CH=), 5.61-5.74 (2H, m, C*H*=C*H*); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2 (CH_3), 22.8 (CH_2), 29.29 (CH_2), 29.33 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.7 (CH_2), 32.1 (CH_2), 34.4 (CH_2), 64.0 (CH_2), 129.0 (CH), 133.8 (CH); *m/z* (CI^+ corona) 202 [$(M+NH_4)^+$, 100%], 184 [$(M)^+$, 92%], 167 (40), 111 (66), 97 (44).

Synthesis of (2-nonylcyclopropyl)methanol 6.33



Synthesis of the desired cyclopropane followed the method described by Charette *et al.*[269] To a solution of diiodomethane (6.9635 g, 26 mmol) in dry DCM (15 mL), diethyl zinc (1M in hexane, 13 mL, 13 mmol) was added dropwise at 0 ^oC. The resulting solution was stirred at 0 ^oC for 15 min and a white precipitate was formed. The reaction mixture was then cooled to - 78 ^oC and (*E*)-dodec-2-en-1-ol **6.34** (2.396 g, 13 mmol) in dry DCM (5 mL) was added. The resulting solution was then stirred for 15 min at - 20 ^oC and $TiCl_4$ (1M in DCM, 2 mL, 1.95 mmol) was added. After 3 h stirring at - 20 ^oC, the reaction mixture was quenched with sat. ammonium chloride and extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed once again with water (10 mL), brine solution (10 mL) and dried over anhydrous sodium sulfate. The concentrated solution was purified by column chromatography (20% ethyl acetate in hexane) to yield *(2-nonylcyclopropyl)methanol* **6.33** (1.724 g, 67%) as a colourless oil. [Found: (CI^+ corona) $(M+H)^+$ 199.2054. $C_{13}H_{27}O$ (M+H) requires 199.2056]; ν_{max}(film)/cm^{-1} 3329, 2997, 2920, 2852, 1463, 1028, 1010, 721; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.29-0.39 (2H, m, *CP*-C*H*$_2$), 0.56-0.64 (1H, m, *CP*-C*H*), 0.80-0.90 (4H, m, *CP*-C*H*, C*H*$_3$), 1.20-1.40 (16H, m, (C*H*$_2$)$_8$CH$_3$), 3.40-3.49 (2H, m, HOC*H*$_2$); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 10.1 (CH), 14.3 (CH_3), 17.4 (CH_2), 21.4 (CH), 22.8 (CH_2), 29.5 (CH_2), 29.6 (CH_2), 29.8 (2 x CH_2), 29.8 (CH_2), 32.1 (CH_2), 33.7 (CH_2), 67.4 (CH_2); *m/z* (CI^+ corona) 397 [$(2M+H)^+$, 15%], 379 (31), 361 (40), 199 [$(M+H)^+$, 26%], 181 (37), 125 (73), 111 (100).

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