Reactions of a super-electron donor with diarylcyclopropanes and epoxides

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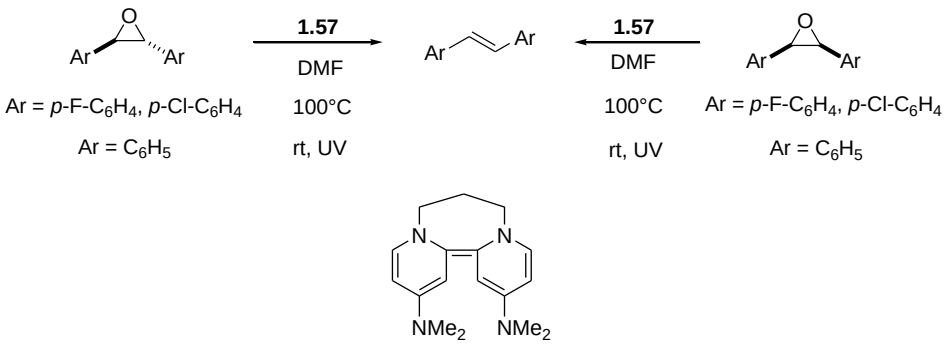
Abbreviations

°C	Degree Celsius
4-DMAP	4-dimethylaminopyridine
CIDNP	Chemically Induced Dynamic Nuclear Polarisation
cm	Centimetre
d	Doublet
DMF	Dimethylformamide
DMSO	Dimethylsulfoxide
e^-	Electron
EI	Electron ionisation
eq.	Equivalent
ESI	Electrospray ionisation
Exp.	Experience
g	Gram
GC	Gas chromatography
h	Hour
h*ν*	Irradiation
Hz	Hertz
IR	Infrared
J	Coupling constant
kcal	Kilocalorie
LUMO	Lowest Unoccupied Molecular Orbital
m	Molecular mass
*m*CPBA	*meta*-chloroperbenzoic acid
Me	Methyl
min	Minute
mL	Millilitre
mol	Mole
mp	Melting point
Ms	Mesyl
MS	Mass spectrometry

nm	Nanometre
NMR	Nuclear Magnetic Resonance
Ph	Phenyl
ppm	Parts per million
q	Quintet
rt	Room temperature
RT	Retention time
s	Singlet
sat.	Saturated
SCE	Saturated Calomel Electrode
SED	Super-electron donor
SET	Single-electron transfer
SHE	Standard Hydrogen Electrode
t	Triplet
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
UV	Ultraviolet
V	Volt
z	Charge
δ	Chemical shift

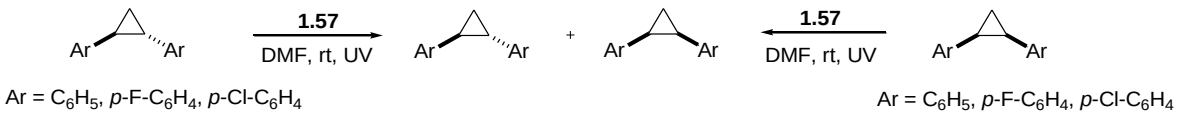
Abstract

The selective deoxygenation of both *cis*- and *trans*-isomers of 2,3-*bis*(4-fluorophenyl)oxirane, 2,3-*bis*(4-chlorophenyl)oxirane and 2,3-diphenyloxirane was achieved by the DMAP-derived electron donor **1.57** (Scheme 1). In each case, only the *trans*-alkene product was isolated. The reaction conditions depend on the energy level of the LUMO of the molecule. The higher the LUMO is, the harsher the conditions are. The use of UV-light was necessary to achieve reductive cleavage of the unsubstituted 2,3-diphenyloxiranes. In the case of 2,3-*bis*(4-chlorophenyl)oxirane, partial reductive cleavage of the aryl C-Cl bond was also observed. Dichloro- and monochlorostilbenes were isolated. However no monochlorinated oxirane was observed.



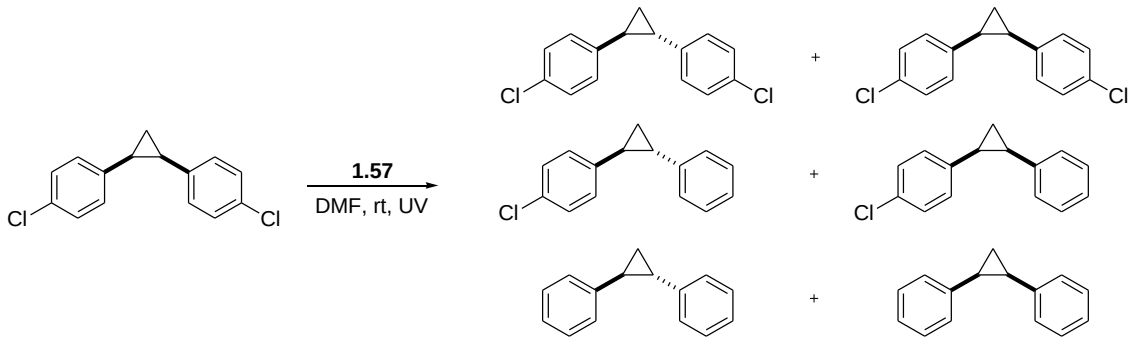
Scheme 1 – Reactivity of epoxides with electron donor **1.57**.

The geometric isomerisation of diarylcyclopropanes was also achieved by DMAP-derived electron donor **1.57**. Both geometric isomers of 1,2-*bis*(4-fluorophenyl)cyclopropane and 1,2-diphenylcyclopropane were isomerised when submitted to **1.57** (Scheme 2). However, no complete isomerisation was observed. These reactions required activation by UV-light. However, it has been proved that the isomerisation was not seen in the absence of donor **1.57**, even if UV activation was used.



Scheme 2 – Reactivity of 1,2-*bis*(4-fluorophenyl)cyclopropane and 1,2-diphenylcyclopropane with **1.57**.

A different reactivity was observed when submitting both geometric isomers of 1,2-*bis*(4-chlorophenyl)cyclopropane to the electron donor **1.57** (Scheme 3). Whereas in this case isomerisation of 1,2-*bis*(4-chlorophenyl)cyclopropane was mainly due to UV-light, the electron donor **1.57** was responsible for the cleavage of aryl C-Cl bonds giving rise to a complex mixture of both geometric isomers of di-, mono- and non-chlorinated diarylcyclopropanes.



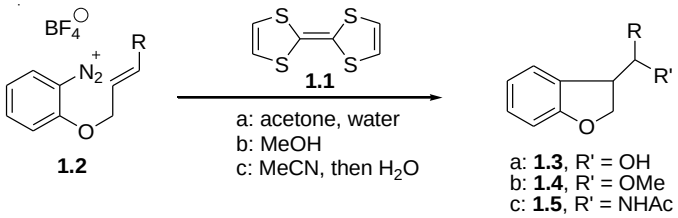
Scheme 3 – Reactivity of of 1,2-*bis*(4-chlorophenyl)cyclopropane with electron donor **1.57**.

Chapter 1 - General introduction

1.1 Neutral organic super-electron donors

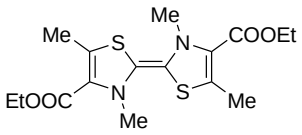
The development of neutral organic super-electron donors[7,8,11,13,15,19,22] affords a new way to carry out reductions under very mild neutral conditions. These reductions can be performed in conventional glassware, with organic solvents and at low or high temperatures. These electron donors are also more tolerant towards other functional groups. All this shows the advantages of neutral organic electron donor over the pre-existing methods. These methods are very diverse. Metal-based chemistry (metals in low oxidation states[1] or reduction by lithium naphthalenide[2]), electrochemical reduction at a cathode,[3] photochemically-assisted electron transfer[4] and, finally, reduction by solvated electrons[5] or related radical-anions of organic molecules[6] were used.

The first neutral organic electron donor developed by our group was tetrathiafulvalene (TTF, **1.1**).[7] This electron donor has a first ionisation potential of +0.56 V *vs.* SHE and a second of +1.03 V *vs.* SHE.[8] TTF reacts with diazonium salts, **1.2**, in a radical-polar crossover reaction which leads to the formation of alcohols, **1.3**, ethers, **1.4**, or amides, **1.5** (Scheme 4).



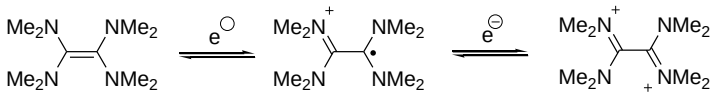
Scheme 4

Attempts to reduce aryl or alkyl halides, known to be more difficult to reduce,[9] were unsuccessful.[7] Even more powerful agents such as diazadithiafulvalene derivatives, as **1.6** (first ionisation at -0.06 V *vs.* SHE),[10] are not strong enough to reduce this kind of molecule.[11] Moreover these derivatives undergo side-reactions with arenediazonium salts.[12]



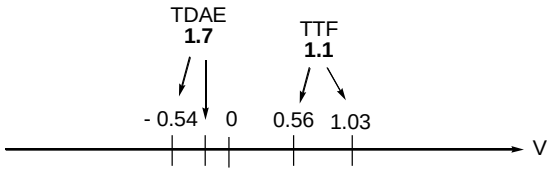
1.6

Médebielle and co-workers reported the use of TDAE **1.7** [1,1,2,2-tetra-(dimethylamino)ethene] as an electron donor to reduce very electron-deficient organic halides (Scheme 5).[13] The reduction potential is -0.54 V *vs.* SHE for the first ionisation and -0.37 V *vs.* SHE for the second.[14] Therefore the potential reduction of this new electron donor has been improved compared to the previous ones (Scheme 6). The more negative the reduction potential becomes, the more powerful is the reducing agent. However, TDAE cannot reduce unactivated aryl and alkyl halides.[11]



1.7 **1.8** **1.9**

Scheme 5

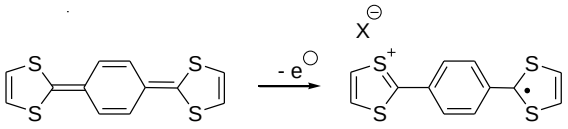


0 V *vs.* SCE = + 0.241 V *vs.* SHE

Scheme 6 – Reduction potential scale

Molecules **1.6** and **1.7** show that the presence of nitrogen on the electron donor is helpful for the electron donation as the formed cation is stabilised by the nitrogen (Scheme 5).

Other powerful sulfur-containing organic electron donors, such as **1.10**, have also been developed.[15] The reduction potential is more negative (-0.11 V *vs.* SHE) than TTF **1.1**.[16] The driving force for the loss of an electron is the aromatisation of the molecule (Scheme 7). The released energy is really important as two rings out of three can be represented as aromatic after the first electron donation, as shown in radical-cation **1.11**.

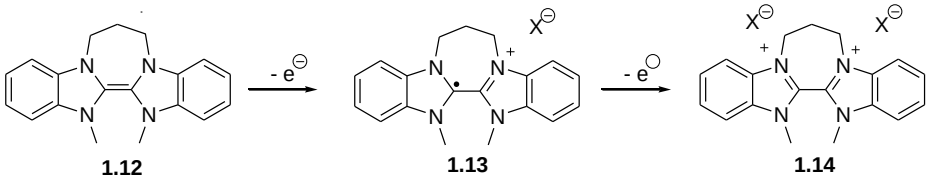


1.10 **1.11**

Scheme 7

As the synthesis of such compounds is not easy, they could not be used as routine reagents. But it highlights that electron donation is easier when the driving force is the aromatic stabilisation energy.

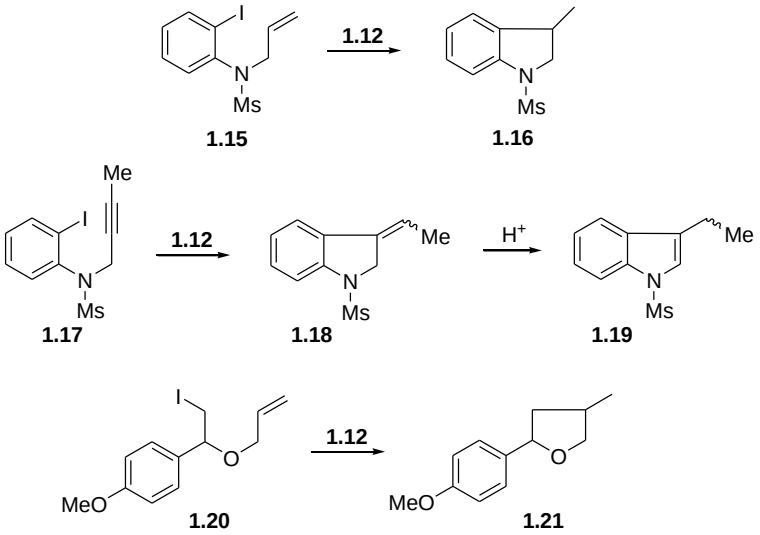
From these two observations, a new neutral ground-state electron donor **1.12** was developed.[11] This electron donor is able to give two electrons, giving rise to the dication **1.14**, stabilised by aromatic conjugation and the presence of nitrogen atoms (Scheme 8). These two factors afford a more powerful electron donor with a first reduction potential at -0.82 V *vs.* SCE and the second at -0.75 V *vs.* SCE.[17]



1.12 **1.13** **1.14**

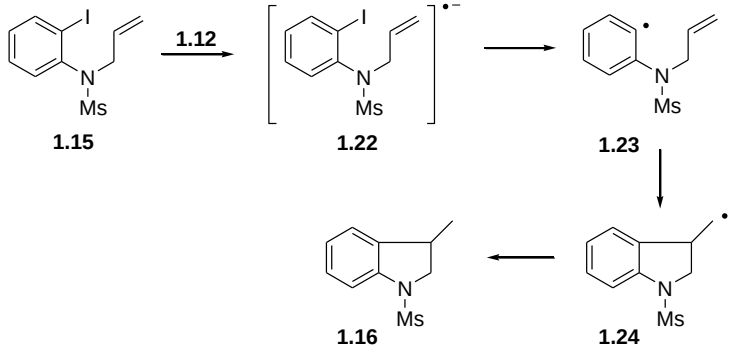
Scheme 8

Donor **1.12** is now powerful enough to reduce unactivated aryl iodide **1.15** and affords the corresponding indoline **1.16** in excellent yields.[11] Along the same lines, aliphatic iodide **1.20** gave the cyclised product **1.21** after reaction with **1.12**. Moreover alkyne-containing aryl iodide **1.17** was reduced to the exocyclic alkene, **1.18**, which afforded the indole **1.19** after treatment with acid (Scheme 9).



Scheme 9

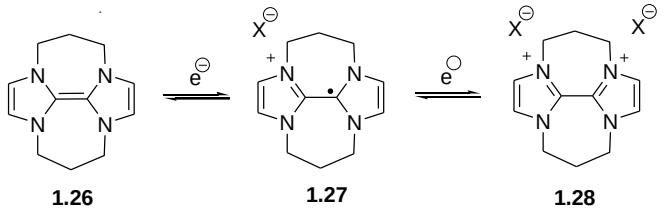
A mechanism has been proposed for such a reduction (Scheme 10).[11] The first electron transfer to the substrate leads to the aryl radical **1.23**. Savéant *et al.* have shown that the electron transfer and the C-X bond breaking can occur at the same time or at sequential times depending on the activation driving-force of the donor.[18] The aryl radical **1.23**, after cyclisation and hydrogen transfer, affords the indoline **1.16**. It has been proved by the use of specific reactions that the reaction doesn't go through an aryl anion intermediate but only through radicals.[11,19] However, in principle, the reduction of the aryl radical to an aryl anion should be able to proceed since the reduction potential of the donor **1.12**, $E_{1/2}$ = -0.82 V *vs.* SCE,[11] is more negative than the standard potential for the reduction of the aryl radical, E^0 = +0.05 V *vs.* SCE.[19]



Scheme 10

A more powerful reducing agent was then developed in order to check that aryl radicals can be reduced to aryl anions.[19] This electron donor **1.26** is based on two imidazole units. As for

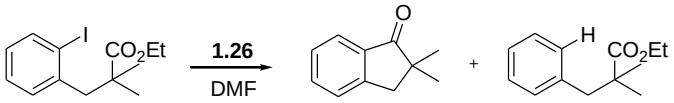
1.12, **1.26** gives two electrons leading to the dication **1.28** (Scheme 11). The donor **1.26** has reduction potentials of $E_{1/2}$ = -1.18 V and -1.37 V *vs.* SCE.[19] An advantage of these reagents is that after reducing a substrate, the by-products (here **1.27** and **1.28**) can be simply separated from the organic product by aqueous extraction.



1.26 **1.27** **1.28**

Scheme 11

The reaction of this donor with an aryl iodide **1.29** afforded the reduced product **1.31** and the indanone **1.30** (Scheme 12). The latter proves that the reaction goes through an aryl anion since only aryl anions and not aryl radicals are likely to attack esters.[19] Therefore the imidazole-based donor **1.26** is powerful enough to reduce aryl radicals. This is the first neutral organic reagent, called super-electron donor (SED), which is able to achieve this kind of transformation.

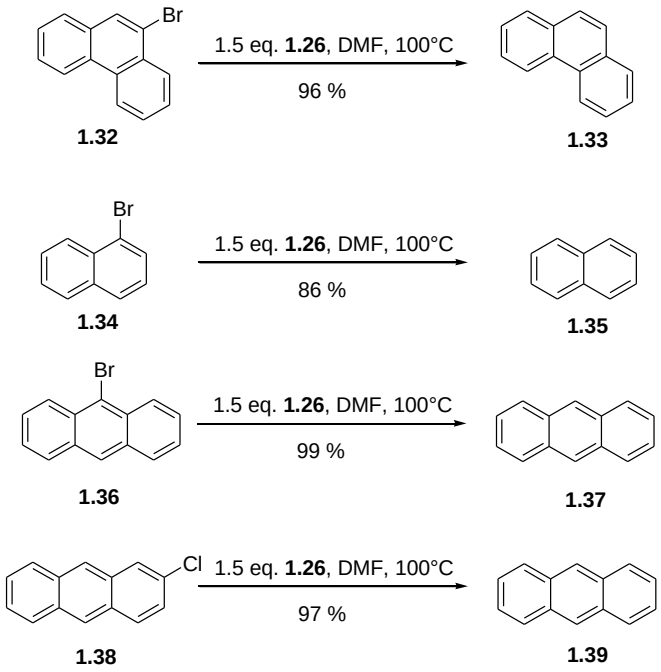


1.29 **1.30** **1.31**

Scheme 12

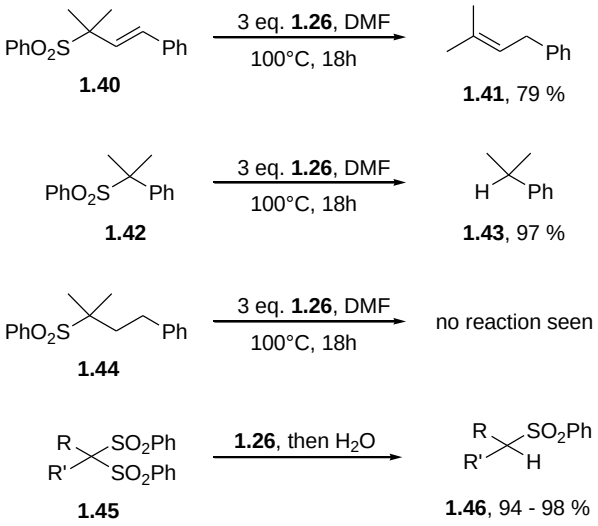
The reactivity difference between the donors **1.12** and **1.26** has been discussed.[19] In both cases, the second electron is harder to donate, -0.75 V *vs.* SCE for **1.12** and -1.18 V *vs.* SCE for **1.26**. The dications **1.14** and **1.28** are less stable than the monocations **1.13** and **1.27** since more charge repulsions are present. However, the ring containing the radical in **1.13** and **1.27** is almost aromatic (Scheme 11). Therefore the energy gained by aromatisation of this ring would be greater than the charge repulsion of the dication. Moreover the maintenance of planarity during the loss of electrons in **1.26** by the double bridge between the imidazoles may be a factor assisting its ability to act as a very strong second electron donor. A flat structure would be able to interact closely with the π-system of the acceptor and assist the process with stabilisation through the formation of a complex.

Donor **1.26** shows an unprecedented reactivity for a neutral ground-state organic super-electron donor. It is able to reduce naphthalene halides or anthracene halides (Scheme 13). This different behaviour between **1.12** and **1.26** shows a well-defined delineation between their reductive capabilities with aryl halides.

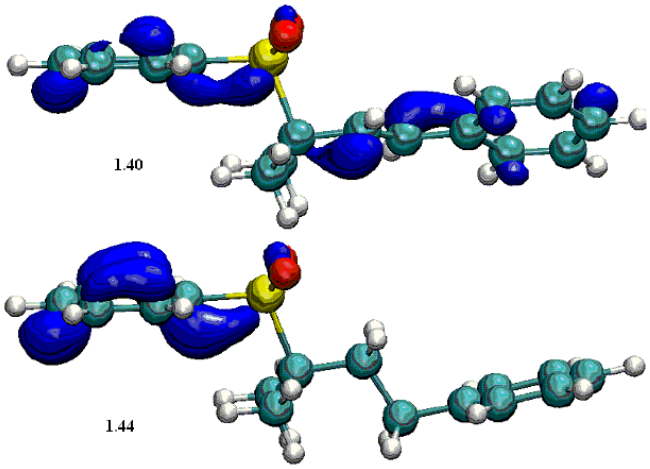


Scheme 13

Later, **1.26** was reported as the first neutral organic super-electron donor to achieve reductive cleavage of sulfones (Scheme 14).[20] However the sulfone moiety needs to be activated for the reaction to proceed. No reaction was observed with aryl alkylsulfone **1.44**. The activation energy required for the electron transfer was shown to be higher than for aryl allylsulfones **1.40** and aryl benzylsulfones **1.42**.[20] There is almost no overlap between the LUMO of **1.44**, which is on the phenylsulfonyl group ring, and the σ*-orbital of the breakable C-S bond compared to **1.40** and **1.42** (Scheme 15).[21] This explains the lack of cleavage for the radical-anion derived from aryl alkylsulfone **1.44** and the spontaneous dissociation of the radical-anions derived from **1.40** and **1.42**. Donor **1.26** is also able to cleave *gem*-disulfones **1.45**, known to be more activated than monosulfones (Scheme 14).[20]

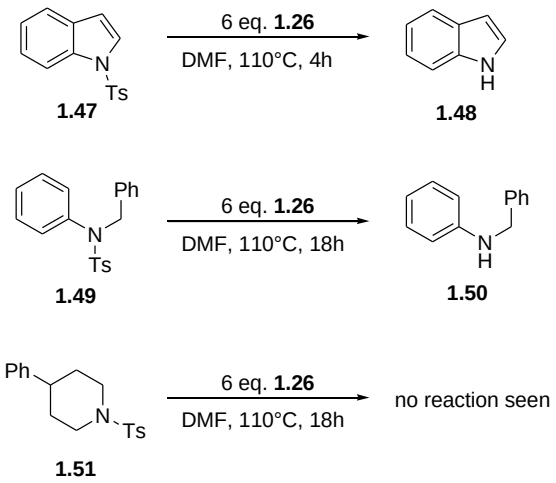


Scheme 14



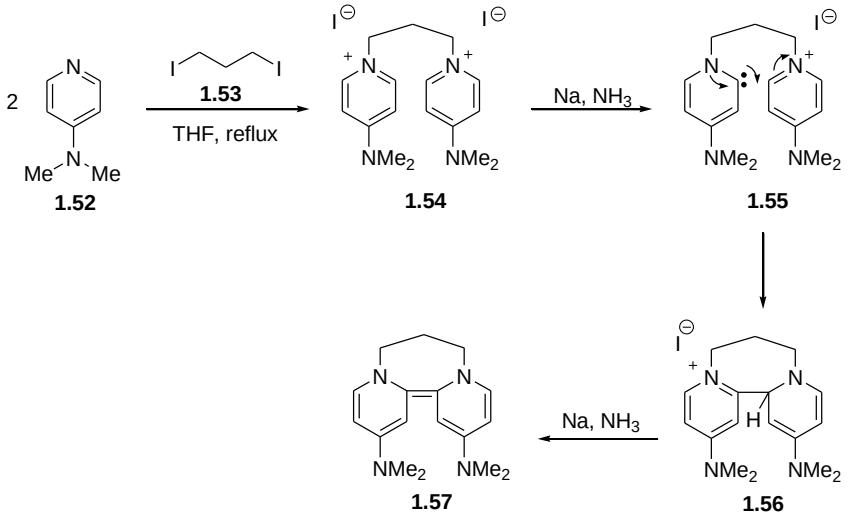
Scheme 15 – LUMO orbital of aryl allylsulfones **1.40** and aryl alkylsulfones **1.44**.[21]

The electron donor **1.26** also cleaved activated sulfonamides (Scheme 16).[20] Computational studies showed that the reasons for **1.26**'s inactivity towards unactivated sulfonamides **1.51** are the same as for the sulfones.[20] Alkyl sulfonamides **1.51** have a large activation energy associated with the electron transfer. This energy is bigger than for **1.47** and **1.49** due to the instability of the resulting radical-anion.



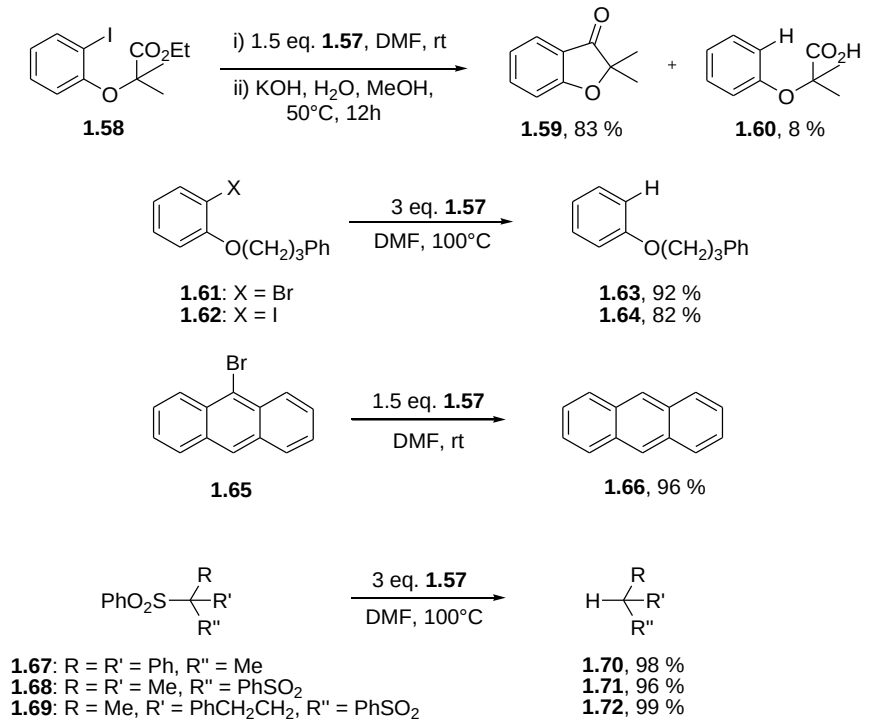
Scheme 16

The search for more powerful neutral organic super-electron donors led to the development of **1.57,** based on 4-dimethylaminopyridine.[22] Each of the four nitrogen atoms adds electron density to the π-system. Cyclic voltammetry showed that **1.57** is as powerful as **1.26**. Whereas **1.26** showed two electron transfer steps at almost identical potentials, **1.57** has a clean and single two-electron peak.[20,22] This means that the two electrons are released at almost the same potential (30 mV difference).[23] Donor **1.57** is very easily made from 4-DMAP **1.52** and 1,3-diiodopropane **1.53** in a two-step reaction (Scheme 17). It is therefore the most conveniently prepared super-electron donor so far. As with the other reactive donors, **1.57** is sensitive to air and has to be stored under oxygen-free and moisture-free atmosphere.



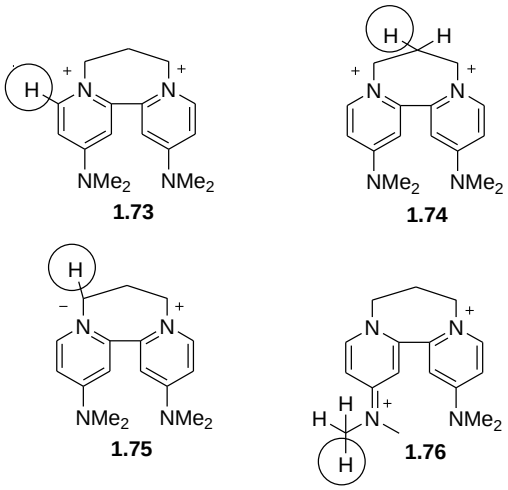
Scheme 17 – DMAP-derived donor **1.57** synthesis.

As a super-electron donor,[22] **1.57** leads to the formation of aryl anions. Indeed the formation of the cyclic ketone **1.59** from aryl iodide **1.58** is typical from the aryl anion.[17] Donor **1.57** has the same reactivity as **1.26** as it is able to reduce aryl bromides and iodides **1.61** and **1.62**, bromoanthracene **1.65** and all kinds of activated sulfones **1.67** – **1.69** (Scheme 18).[22]



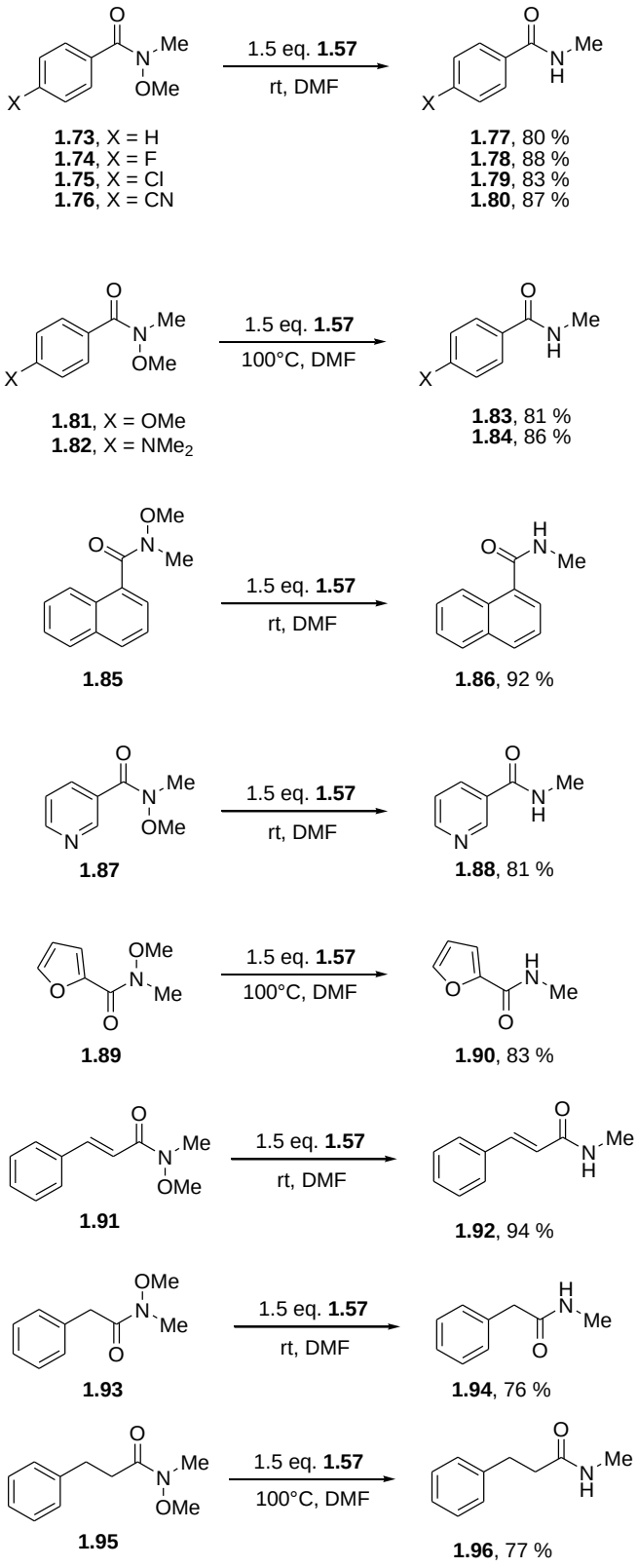
Scheme 18

Deuterium-labelling studies showed that aryl anions are quenched by proton abstraction from the pyridinium α-CH proton **1.73** (Scheme 19).[24] Almost no protons were abstracted from the trimethylene bridge **1.74** and **1.75** or the *N*-alkyl position of the pyridine ring **1.76**.



Scheme 19

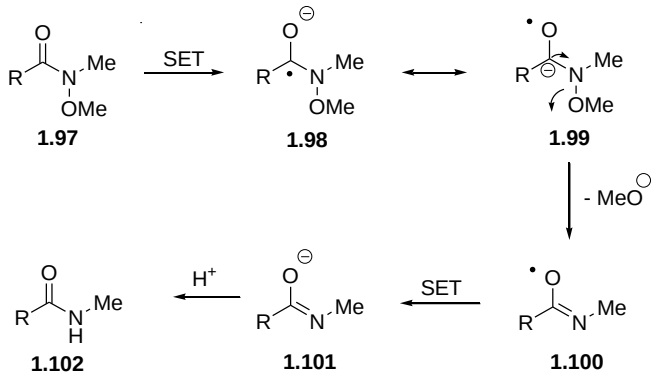
The scope of reductive cleavages by **1.57** has recently been extended. The N-O bond from Weinreb amides can be efficiently reduced by **1.57**.[25] A library of Weinreb amides has been prepared (Scheme 207). The reactivity of these amides depends on their structure. Monoaromatic systems with or without electron-withdrawing groups in the *para* position **1.73-1.76** and polycyclic aromatic systems **1.85** undergo smooth cleavage in very high yields, at room temperature using 1.5 equivalents of **1.57**. However, the cleavage of electron-rich aromatic Weinreb amides **1.81** and **1.82** needed an increase in temperature. Regarding heteroaromatic substrates **1.87** and **1.89**, high temperature is needed if they are electron-rich such as furan **1.89**. If the amide is not conjugated to any π-system but separated by an alkyl chain such as **1.95**, the reaction will be more difficult as the alkyl chain length increases. The π-system is needed to help the reaction as the LUMO of the substrate is associated with the phenyl ring and not with the Weinreb amide group.[25] Moreover the energy level of the LUMO decreases when the phenyl ring is conjugated with the Weinreb amide. The cleavage of the N-O bond is therefore easier.



Scheme 20

A mechanism for this reaction was also proposed (Scheme 21).[25] Donor **1.57** gives an electron to the LUMO of the substrate which is on the π-system of the molecule by a single-electron

transfer (SET). As the LUMO of the substrate has principally π* character, the electron requires to be transferred to the σ* of the N-O bond giving rise to the cleavage of that bond. The formed enolyl radical **1.100** can then receive another electron from **1.57** by another SET. The arising enolate **1.101** abstracts a proton from the radical-cation or the dication of **1.57** as seen above to give the reduced product **1.102**.



Scheme 21

The extension of the scope of reductive cleavages of **1.57** is still under investigation. This report presents two of these investigations featuring more challenging cleavages carried out by **1.57**: (i) the reductive cleavage of epoxides and (ii) the isomerisation of cyclopropanes.

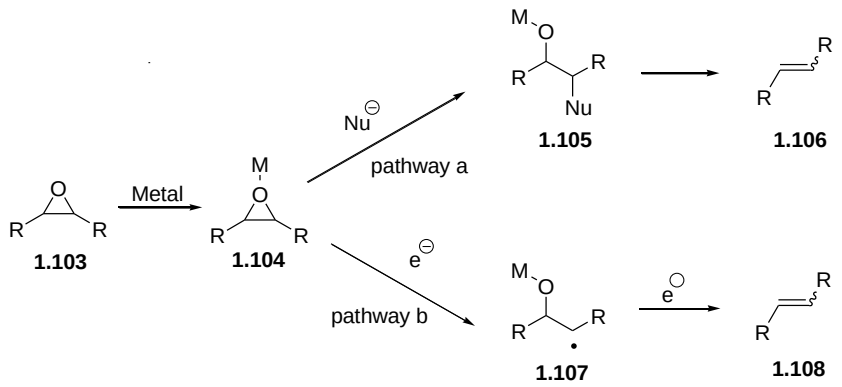
1.2 Deoxygenation of epoxides

The epoxide is an important functional group in organic chemistry and especially in synthesis. Its deoxygenation leading to alkenes can be carried out with retention or inversion of configuration.[26] Epoxides can therefore be used as a protective group when their deoxygenation leads to retention of the configuration of the alkene or as an isomerisation tool when inversion of the configuration of the alkene takes place during the deoxygenation. All these characteristics have important applications, in particular in total syntheses of natural products.

Many methods have been developed since the 1970s.[26] Elements such as tungsten, selenium, silicon, ruthenium, phosphorus and alkali metals such as lithium and sodium were used.[26] Nowadays the deoxygenation of epoxides is still under investigation with cheaper and easier-

to-handle metals to give rise to better rates and controlled stereochemistry and selectivity. More general reagents which can effect reductive cleavage of several functional groups such as epoxides, amine *N*-oxides or sulfoxides are also under examination.[27]

The reductive cleavage of epoxides can be divided into two categories. For all reactions, the epoxide first needs to be activated by a Lewis acid or by a metal with strong affinity for oxygen. The first category involves a nucleophilic attack on the activated epoxide followed by a reductive elimination (pathway a, Scheme 22). The other pathway is a single-electron transfer (SET) to the metal complex (pathway b, Scheme 22).

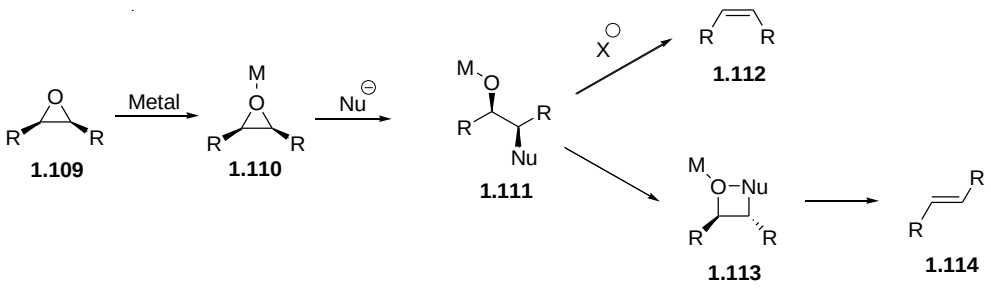


Scheme 22 – Deoxygenation of epoxides

Many methods exist to carry out reductive deoxygenation of epoxides.[26] Here are presented the most recent of each category.

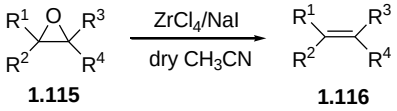
1.2.1 S_N2-elimination pathway

The oxygen is first bonded by the metal. The 3-membered ring is then opened by a nucleophilic attack. This is possible since the carbons of the epoxide ring are more electrophilic as the oxygen is activated by the metal. The alkene is obtained by elimination of the metal oxide and the nucleophile. Depending on the reaction conditions, retention or inversion of configuration is obtained (Scheme 23).[28]

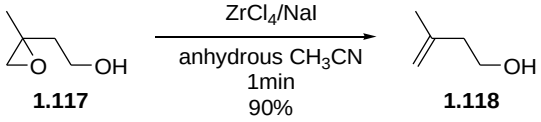


Scheme 23 – Mechanism for the retention or inversion of configuration for the epoxides' deoxygenation.

Firouzabadi and Iranpoor have recently reported deoxygenation of epoxides with $ZrCl_4$/NaI.[29]

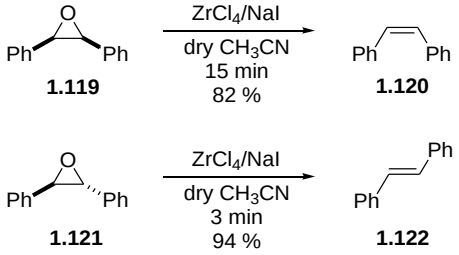


Compared to the previous methods,[28] $ZrCl_4$/NaI is safe, cheap and highly efficient. Indeed all yields have been improved over previous methods. This is nowadays a very important factor when looking for new reagents. Moreover the deoxygenation was much quicker. The reaction was achieved within minutes whereas the other methods such as $[Co(salen)_2]/Na(Hg)$[30] or $LReO_3/PPh_3$[31] required hours. A wide range of substrates can be deoxygenated by this method. Epoxides carrying alkyl, aryl, ether, carbonyl and ester have been converted into alkenes in very high yields. The deoxygenation is also regioselective as epoxides with hydroxyl groups in *α*- or *β*-position of the oxirane ring such as **1.117** have been reduced without cleaving the hydroxyl group (Scheme 24).



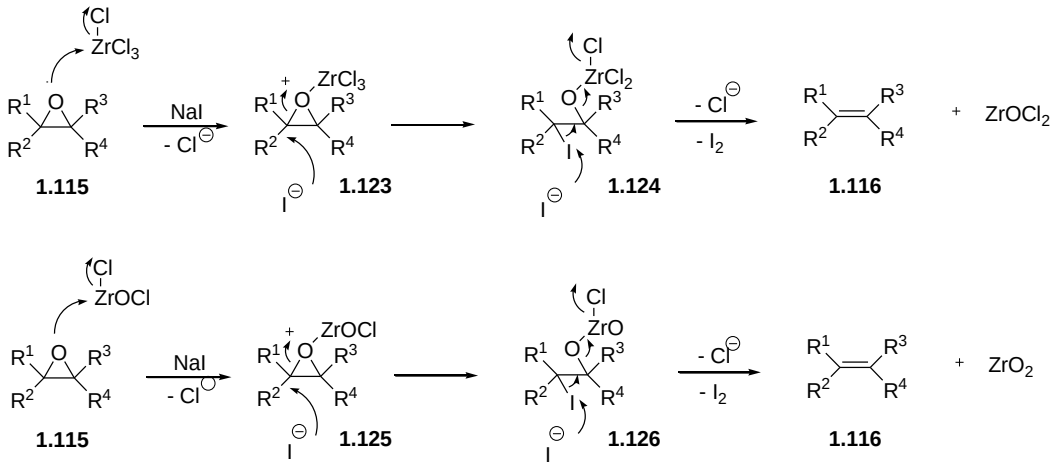
Scheme 24

The stereospecificity of this method has also been studied with *cis*- and *trans*-stilbene oxiranes **1.119** and **1.121** (Scheme 25). In each case, the corresponding alkene was recovered in very good yields. However the *cis*-stilbene oxirane needed more time to react than its isomer.



Scheme 25

A mechanism has been proposed (Scheme 23).[29] The epoxide is first activated by binding to zirconium. The nucleophilic attack by iodide is then easier and is followed by elimination of iodine and zirconium oxide to afford the alkene. The stereochemistry is retained as the elimination is anti-periplanar.

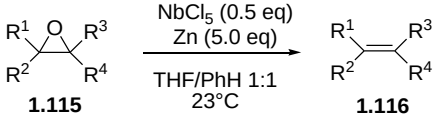


Scheme 26 – Proposed mechanism for the deoxygenation of epoxides by $ZrCl_4/NaI$[29]

1.2.2 Deoxygenation via a single electron transfer (SET)

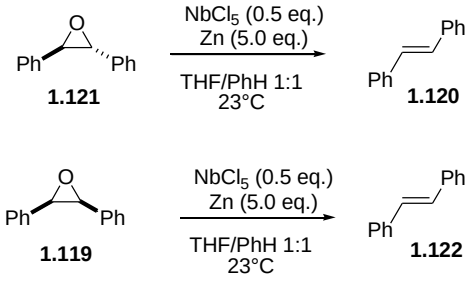
After activation of the epoxide by chelation of the oxygen to a Lewis acid or an oxophilic metal, the oxirane ring is opened by a SET reaction.

The most recent method has been developed by Oh and Knabe this year.[27] The reagent is a low-valent niobium complex prepared from $NbCl_5$ and Zn.



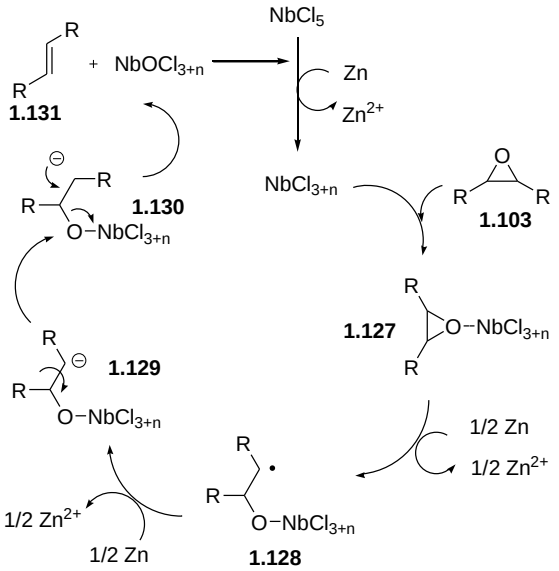
The niobium complex acts as a complexing agent to lower the potential energy of the C-O σ^* orbital. Niobium has indeed a very strong affinity for oxygen.[32] This complexation promotes a SET reaction by zinc metal. The use of zinc rather than other metals is essential for the promotion of the deoxygenation.[27,33] The deoxygenation of aryl epoxides and *α,β*-epoxy carbonyl compounds was quickly and easily achieved in very good yields. However substrates without an adjacent radical-stabilising group led to lower yields and side-reactions.

The deoxygenation of *cis*- and *trans*-stilbene oxiranes, **1.119** and **1.121**, has shown that this method is stereoselective. Both isomers only gave rise to the *trans*-stilbene (Scheme 27).



Scheme 27

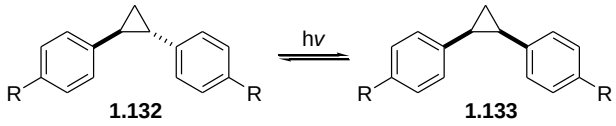
The mechanism is thought to go through an electron transfer (Scheme 28).[27] Zinc metal reduces first $NbCl_5$ to a low-valent niobium complex. The niobium species complexes then to the epoxide. It is believed that Nb(III) and Nb(V) are both involved in the complexation with the oxygen of the substrate. Zinc metal gives then an electron to the complex **1.127** by a SET process. This electron transfer induces the opening of the epoxide and affords a β-nioboxy radical **1.128**. A further SET forms the anionic species **1.129**, which collapses to give the *trans*-alkene **1.131** after a single bond rotation. The niobium species can then be recycled by reduction with zinc metal.



Scheme 28 – Proposed mechanism for the deoxygenation of epoxides by $NbCl_5/Zn$[27]

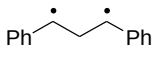
1.3 Isomerisation of 1,2-diarylcyclopropanes under irradiation

The geometric isomerisation of 1,2-diarylcyclopropanes under irradiation has been widely studied, especially in the 1960s. It has led to the development of concepts such as triplet sensitization.[33]

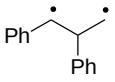


Hammond *et al.* were the first to report this reactivity.[34] Photosensitized interconversion of *cis*- and *trans*-1,2-diphenylcyclopropane was observed for different light-absorbing sensitisers (see p.26). They proposed a mechanism for the interconversion. The energy transfer occurs by a non-vertical process.[35] They proposed this concept a year before reporting the interconversion of diphenylcyclopropanes to explain the photosensitised isomerisation of stilbenes. This means that the excited molecule does not go back directly to the ground-state but via different intermediate excited states. This energy is sufficient to break the weakest carbon-carbon bond of the cyclopropane, the one substituted by the two phenyl rings. The opened intermediate is a triplet 1,3-biradical **1.134**.[34,36] It does not seem to form bonds to the sensitiser. If it were to bind to it, the biradical would cyclise rather than re-form the 1,2-diphenylcyclopropane by elimination reactions.[37]

As the cyclopropane ring is now opened, rotation of the C-C bonds substituted with the phenyl rings can easily happen.[38] The two radicals react with each other to reform the 1,2-diphenylcyclopropane. After a certain time of irradiation, a photostationary state is attained.[39] This photostationary state mainly depends on the sensitiser, the solvent and the irradiation.[40] The *cis*/*trans* ratio attained is determined by the ease with which the biradical is formed from the two isomers and by the relative rate of ring-closure of the biradical to both isomers.[40,41]

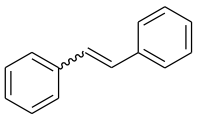


1.134

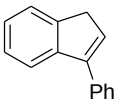


1.135

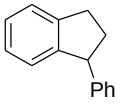
A year later, Griffin *et al.*[42] confirmed the nature of the 1,3-biradical intermediate **1.134**. Two possible biradicals can be formed from the opening of the cyclopropane: a symmetric 1,3-diphenyl biradical **1.134** or an asymmetric 1,2-diphenyl biradical **1.135**. As no 1,2-diphenylpropene and 1,2-diphenylpropane were observed, the 1,2-diphenyl biradical **1.135** was excluded. They also reported side-reactions to the isomerisation. The first one is a 1,2-hydrogen migration of the 1,3-biradical giving rise to both 1,3-diphenylprop-1-ene isomers **1.136**. Cyclisation of the 1,3-biradical **1.134** on one of the phenyl rings followed by rearomatisation could also happen leading to the 3-phenyl-1*H*-indane **1.138**. 3-Phenyl-1*H*-indene **1.137**, derived from the 3-phenyl-1*H*-indane **1.138**, was also isolated. These side-reactions can be avoided by limiting the exposure to irradiation.



1.136



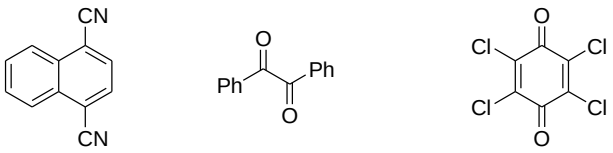
1.137



1.138

Several years after, the photosensitised interconversion of 1,2-diphenylcyclopropane was still under investigation. Hayes *et al.* carried out electronic studies to predict the percentage of diradical character of the open forms of cyclopropanes.[43] They showed that the probability for a cyclopropane to open to the biradical **1.134** is about 80%. Quantum mechanical studies of the cleavage of the carbon-carbon bond of the cyclopropane have also been carried out.[44] These studies pointed out information about the C-C-C bond angle and the barriers to internal rotation of the 1,3-biradical **1.134**.

At the same time, Sigal *et al.*[45] showed the relative instability of *cis*-1,2-diphenylcyclopropane compared to the *trans*. The conjugation between the cyclopropane ring and the phenyl rings is weaker than for the *trans* compound. This explains why more *trans* is almost always observed in the photostationary state. They stipulated as well that the energy is absorbed by a π-π* transition. Indeed the presence of phenyl groups permits the existence of relatively low-lying benzene-like π-π* states.[46] Last but not least, they also proved that the isomerisation is not self-sensitised. Another molecule is needed to give enough energy to the substrate to isomerise. Therefore, the 1,2-diphenylcyclopropane cannot undergo isomerisation on its own when irradiated. These molecules, called sensitisers, are usually aromatic compounds with electron-withdrawing groups. Some of the main sensitisers used are 1,4-cyanonaphthaldehyde **1.139**, benzil **1.140** or chloranil **1.141** (Scheme 29).

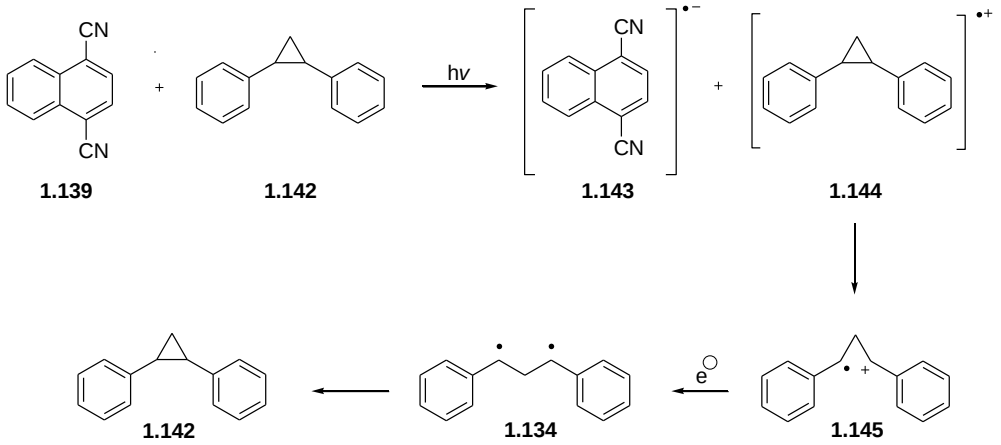


1.139 **1.140** **1.141**

Scheme 29 – Main sensitisers used for the isomerisation of diarylcyclopropanes

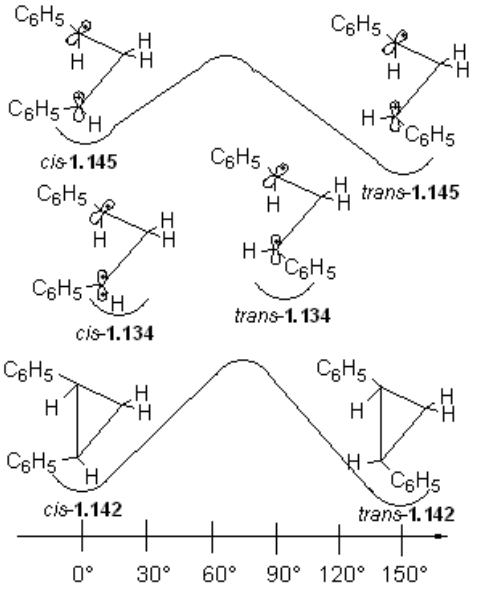
Almost a decade later, Arnold and Wong[47] were the first to propose a full mechanism for the geometric isomerisation, based on CIDNP studies. They were the first to report a radical-cation as an intermediate (Scheme 30). The excitation of a singlet state sensitiser leads to the formation of a singlet geminate radical-ion pair **1.143** and **1.144** by electron transfer: a radical-anion of the sensitiser and a radical-cation of the cyclopropane. At this point, the cyclopropane is still closed since the electron has been taken from the phenyl ring. In CIDNP, the benzylic carbon appears in emission whereas the other carbons appear in absorption. These results showing a polarisation pattern on the benzylic carbon have led to the acceptance of a radical-cation species.[47,48] A hyperfine interaction and a spin-orbit coupling allow the radical-cation to open. This bond fragmentation can occur with 100 % quantum efficiency.[49] The radical-ion pair changes its multiplicity by an intersystem crossing and becomes a triplet. After a back electron-transfer from this radical-ion pair, a triplet 1,3-biradical **1.134** and the ground-state sensitiser are obtained. The energy of the *trans* triplet biradical is unusually low and is equal to ~ 53 kcal.mol^{-1} relative to the ground-state.[50] The biradical then closes rapidly back to the 1,2-diphenylcyclopropane. The polarity of solvents is very important for the

relative stability of radical-ions and the free energy change for the electron transfer.[51] Polarity helps the dissociation of the radical ion pair.[52]



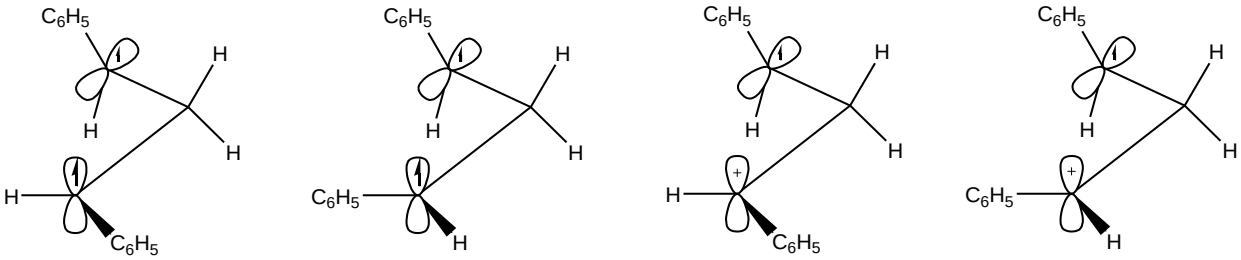
Scheme 30 – Proposed mechanism for the isomerisation of cyclopropanes via a radical-cation[52]

Later on, Roth and Schilling[53,54] proposed a structure for the two intermediates: the radical-cation **1.145** and the 1,3-biradical **1.134**. They highlighted the importance of a singlet state sensitiser for the back electron transfer as no isomerisation takes place from a triplet state sensitiser.[55] The 1,3-biradical **1.134** is formed by triplet recombination and is energetically accessible. The triplet recombination corresponds to a back electron transfer in triplet ion pairs. The triplet biradical **1.134** allows the geometric isomerisation to take place whereas the radical cation **1.145** is conformationally stable.[55] This is why no isomerisation is observed from a triplet state sensitiser as only the radical-cation **1.145** is generated. The reactivity difference between these intermediates is mainly due to their energy surfaces (Scheme 31).[55] For each substrate, two minima with geometry corresponding to each isomer of the 1,2-diarylcyclopropane appear. The radical-cation surface has minima separated by a barrier sufficiently high to prevent interconversion. On the other hand, the biradical surface has minima which allow conversion between the two isomers with comparable ease.



Scheme 31 – Energy surfaces of the intermediates[55]

The two isomers of the 1,3-biradical **1.134** are represented below (Scheme 32).[53] Isomers of the radical-cation **1.145** have the same type of structure as the 1,3-biradical.



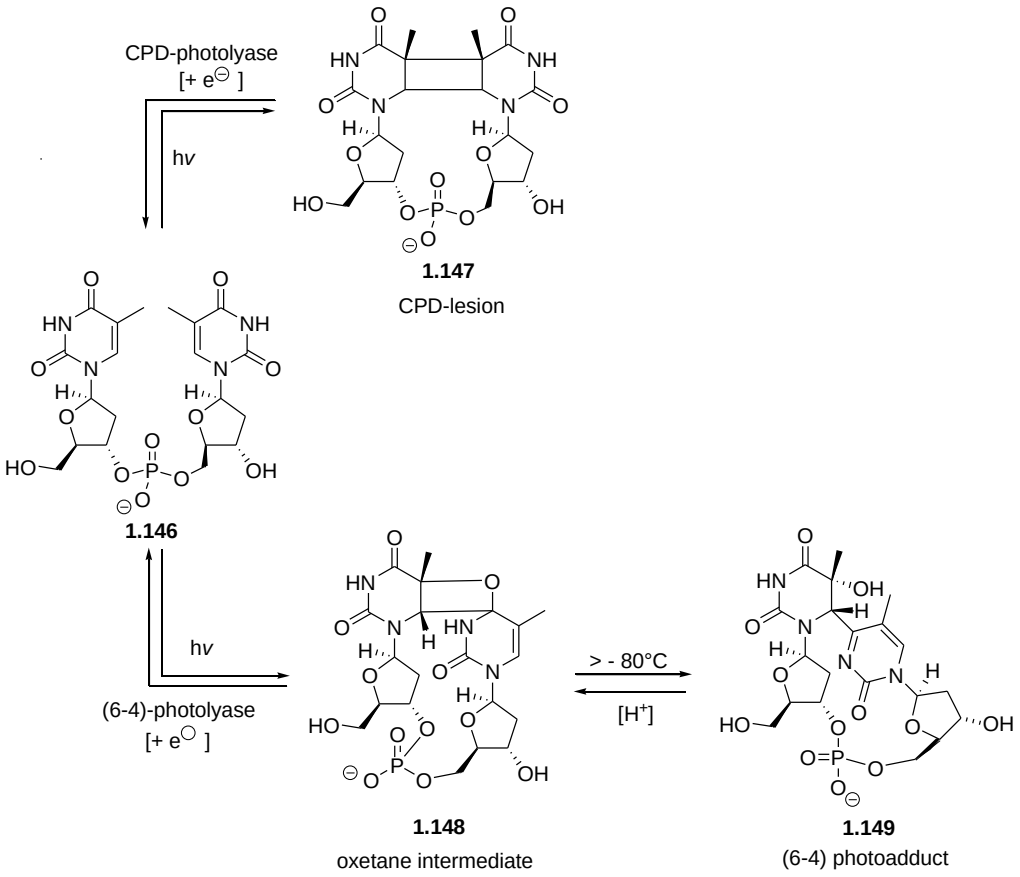
Scheme 32 – Intermediate structures[53]

More recent studies agree with a dissociative return electron transfer for the interconversion leading to the formation of a radical-cation.[56]

Since then, all investigations mainly focus on methods to push the isomerisation of 1,2-diphenylcyclopropane to one side of the equilibrium, especially from the *cis*-isomer. Mizuno *et al.*[57] were the first to report additives to do so. The use of metal salts such as $Mg(ClO_4)_2$, $LiClO_4$ and $LiBF_4$ pushes the equilibrium towards the *cis*-isomer. Since then, other additives have been developed to increase the isomerisation yield such as zeolites,[58] host-guest complexes and cyclodextrin.[59]

1.4 Motivation for this project

Exposure of cells to UV-light (λ = 200 – 300 nm) leads to the formation of modifications in DNA.[60,61] These lesions are known to be mutagenic, carcinogenic and lethal.[62,63] The formation of cyclobutanes **1.147** and (6-4) photoadducts **1.149** by reaction of two neighbouring pyrimidine bases **1.146** are the main lesion caused by irradiation (Scheme 33).[60,61,63] These dimers cause structural distortion of the corresponding DNA region. These alterations block the replication and transcription of DNA and lead to cell death.



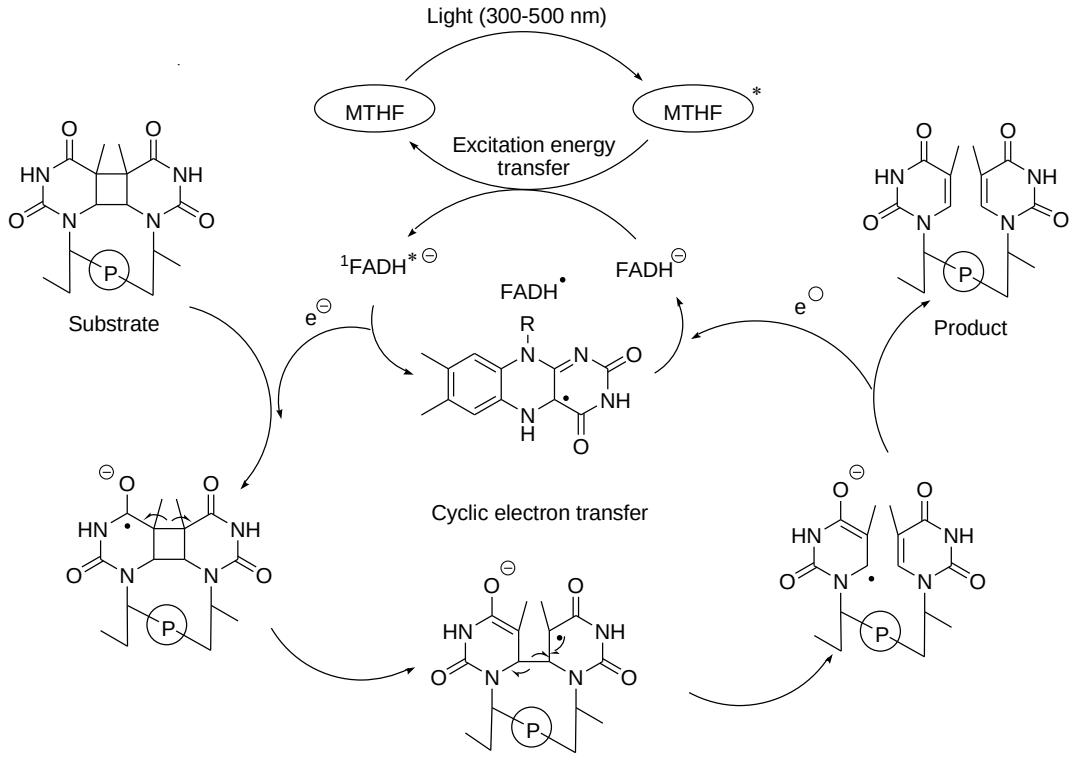
Scheme 33 – DNA lesions caused by UV irradiation[63]

The formation of cyclobutane-pyrimidine dimers (CPD lesions) is a well-known event.[60] Under irradiation of the double-stranded DNA, two neighbouring pyrimidine bases undergo a photochemically allowed [2π + 2π] cycloaddition of their C_5-C_6 double bonds (Scheme 33). This leads to the formation of the *cis-syn* cyclobutane pyridimine dimer **1.147**.

The formation of (6-4) photoadducts has also been studied.[63,64] Two adjacent pyrimidines in the double-stranded DNA undergo a [2+2] cycloaddition (Paterno-Büchi) of the C_4 carbonyl of the 3' thymine to the 5-6 double-bond of the 5' thymine. This generates an oxetane **1.148** which rearranges to the "open form" (6-4) photoadduct **1.149** by a proton shift and a C-O bond scission (Scheme 33).

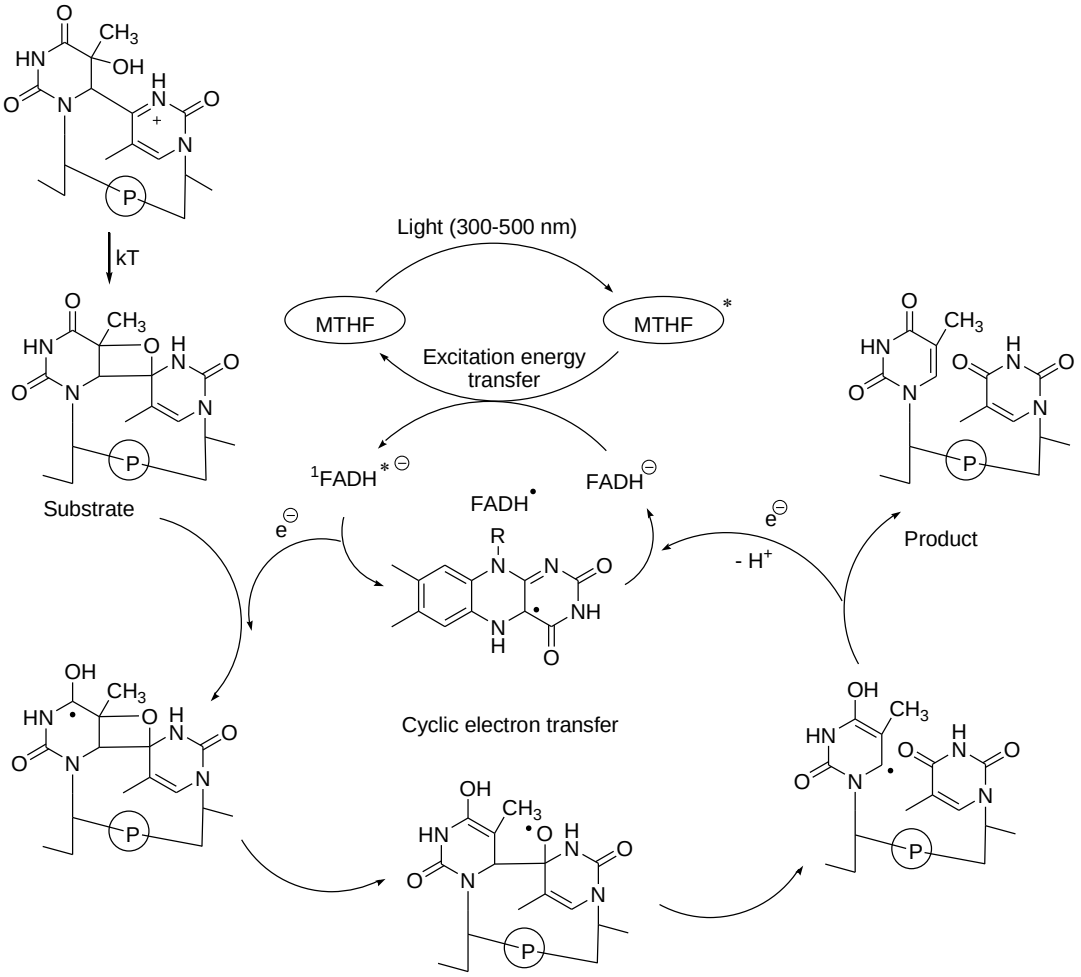
These lesions can be biologically repaired by excision repair or by photoreactivation under irradiation (λ = 300 – 500 nm).[60] Excision repair requires several enzymes and is less easy to study. However, the photoreactivation relies on only one enzyme, DNA photolyase. It is a flavin-dependent DNA-repair enzyme which cleaves both lesions back into the monomers.[65]

For cyclobutane-pyrimidine dimers, the cleavage of the dimer occurs in a concerted light-dependent single-electron transfer.[60,64] The photolyases recognise defect sites on DNA. Photolyases contain a reduced and deprotonated flavin, $FADH^-$. Under excitation by light, another part of the photolyases, MTHF, is first excited. The excitation energy is transferred to $FADH^-$. $FADH^-$ donates an electron to the dimer which cleaves spontaneously into its monomer and its monomer radical-anion (Scheme 34).



Scheme 34 – Proposed mechanism for the repair of CPD lesions[64]

In contrast, (6-4) lesions are exclusively repaired by (6-4) photolyases.[64] These photolyases act in the same way as the other photolyases except that the 3' residue may be protonated by a histidine upon binding (Scheme 35).



Scheme 35 – Mechanism of (6-4) lesions repair[64]

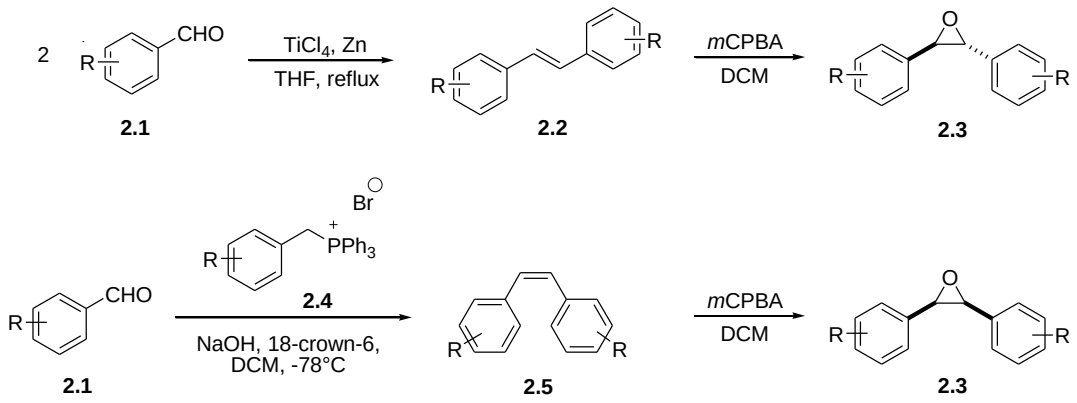
As the depletion of the ozone layer and skin cancers are becoming a worldwide concern,[62,65] repair of DNA lesions caused by UV irradiation are attracting significant research efforts in recent years. With this in mind, the cleavage of small-member ring by the recent electron donors developed in our group, DMAP-derived donor **1.57**, has been investigated. The aims of the current project are to study the reactivity of (i) epoxides and (ii) cyclopropanes with the electron donor **1.57**.

Chapter 2 - Reactivity of the donor towards activated epoxides

In this chapter the reactivity of the DMAP-derived electron donor **1.57** towards diarylepoxides is studied. Several substrates were synthesised in order to simulate different levels of reactivity arising from different levels of LUMO energy.

2.1 Development of the reaction through electron poor epoxides

The *trans*-substrates **2.3** were made by a McMurry reaction followed by an epoxidation with *m*CPBA (Scheme 6). The *cis*-substrates **2.6** were prepared by a Wittig reaction[66] between the phosphonium salt **2.4** and the aldehyde **2.1** and then an epoxidation with *m*CPBA.

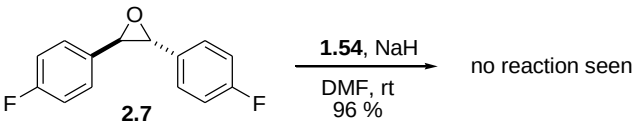


Scheme 36 – Preparation of the substrates

The donor **1.57** can be obtained by two methods. In the *in situ* method, the donor is made from its salt **1.54** and sodium hydride under argon, and then transferred by cannula to the substrate. In the "isolated" method, the donor **1.57** is isolated once formed by extraction into organic solvent and evaporation and then stored. It has to be kept in an oxygen- and moisture-free atmosphere as it would decompose when exposed to air (see section 1.1).

Trans-2,3-*bis*(4-fluorophenyl)oxirane **2.7** was first submitted to the electron donor **1.57** under the standard conditions used for the majority of reactions with DMAP-derived donor, the *in situ* method.[23] The reaction was stirred overnight at room temperature. However, these

conditions were not sufficient to cleave the epoxide. Only starting material was recovered (Scheme 37).



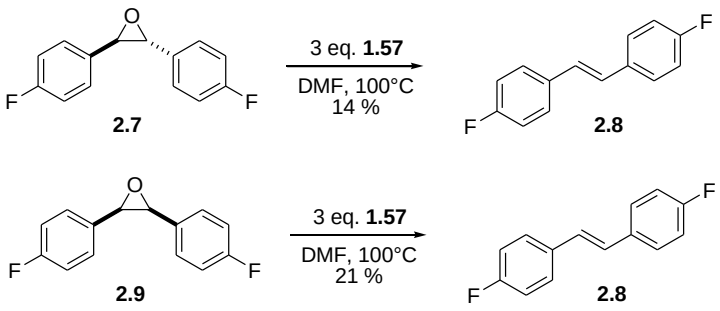
Scheme 37

Other conditions were explored as reported below. For each reaction, the solvent was DMF.

Exp.	Temperature	Donor or its precursor	Method	Results (from the NMR of the crude reaction mixture)
1	rt	1.5 eq. **1.54**	*In situ*	Only starting material
2	100°C	1.5 eq. **1.54**	*In situ*	34:66 :: **2.7**:**2.8**
3	100°C	3 eq. **1.54**	*In situ*	45:55 :: **2.7**:**2.8**
4	100°C	1.5 eq. **1.57**	Isolated	45:55 :: **2.7**:**2.8**
5	100°C	3 eq. **1.57**	Isolated	8:92 :: **2.7**:**2.8**

Complete cleavage of the epoxide was obtained by using 3 equivalents of isolated donor **1.57** at 100°C. The *in situ* method is then less efficient as the reaction mixture was too dilute and the quantity of added donor was hard to control.

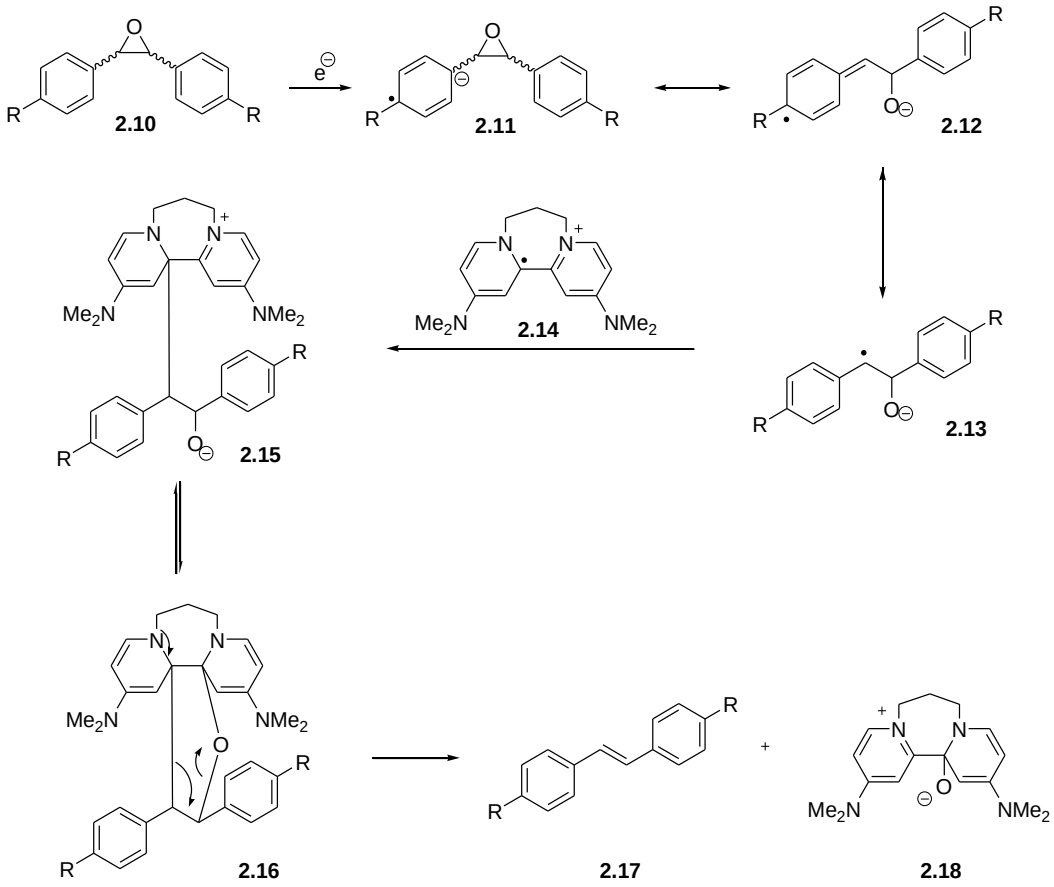
Now that optimised conditions were found, the *cis*- and *trans*-isomers of 2,3-*bis*(4-fluorophenyl)oxirane **2.7** and **2.9** were submitted to the electron donor **1.57** (Scheme 38).



Scheme 38 – Deoxygenation of 2,3-*bis*(4-fluorophenyl)oxiranes with **1.57**.

The *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8** was isolated in each case, starting from either the *cis*- or the *trans*-epoxide, in very low yields, respectively 21 % and 14 %. Only traces of *(Z)*-1,2-*bis*(4-fluorophenyl)ethene were observed by NMR for both experiments.

A mechanism can be proposed (Scheme 39). First of all, a common intermediate such as **2.13** could be envisaged as each isomer gives rise to the same product. Moreover the opening of the epoxide allows rotation of the σ bonds and the formation of the more stable *E*-isomer of the alkene. The *trans*-isomer seems more stable as the two phenyl rings are opposite to each other on each side of the double-bond.



Scheme 39 – Proposed mechanism for the deoxygenation of epoxides.

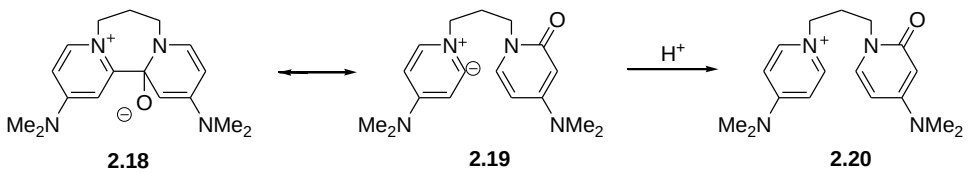
The electron donor gives an electron to the LUMO of the stilbene oxirane. The anion from the formed radical-anion **2.11** opens the epoxide by breaking of the C-O bond. However opening of the ring by cleavage of the C-C bond is also possible and has previously been reported in reactions of benzyl radicals.[67] The molecule is now free to rotate around the σ bonds to afford the more stable product. The radicals of alkoxide **2.13** and of the radical-cation **2.14** can react

together to form the adduct product **2.15**. **2.15** is in equilibrium with **2.16**, formed by nucleophilic attack of the alkoxide onto the pyridinium ring. The presence of this adduct proves that the reaction goes through radicals and not anions. After rearrangement, the adduct is broken into two molecules: the *trans*-stilbene **2.17** and pyridinium-pyridone salt **2.18**.

Whereas the conversion was almost complete from the NMR of the crude reaction mixture, the isolated yields of the reaction were very low. This cannot be due to the volatility of the substrates as they are solids. Different extraction solvents were tried (ether, ethyl acetate, toluene) without success. Furthermore the reaction was also carried out in other solvents such as toluene or ether. This resulted in lower conversion of the oxirane into alkene, as shown below.

Solvent	Results (from the NMR of the crude reaction mixture)
DMF	3:97 :: **2.7**:**2.8**
Toluene	61:39 :: **2.7**:**2.8**
Ether	60:40 :: **2.7**:**2.8**

Another explanation for these low isolated yields is the formation of an adduct between the substrate and the electron donor **1.57** such as **2.16** (Scheme 39). This is even more plausible as adducts with this kind of electron donor have previously been observed.[68] A mass spectrum from the aqueous layer showed mainly the DMAP-derived radical-cation **2.14** (peak at *m/z* = 285). The peak corresponding to the donor adduct after the cleavage, pyridinium-pyridone salt **2.20**, was also observed (peak at *m/z* = 301). The formation of the pyridinium-pyridone salt **2.20** can be explained by protonation of the carbene **2.19**.

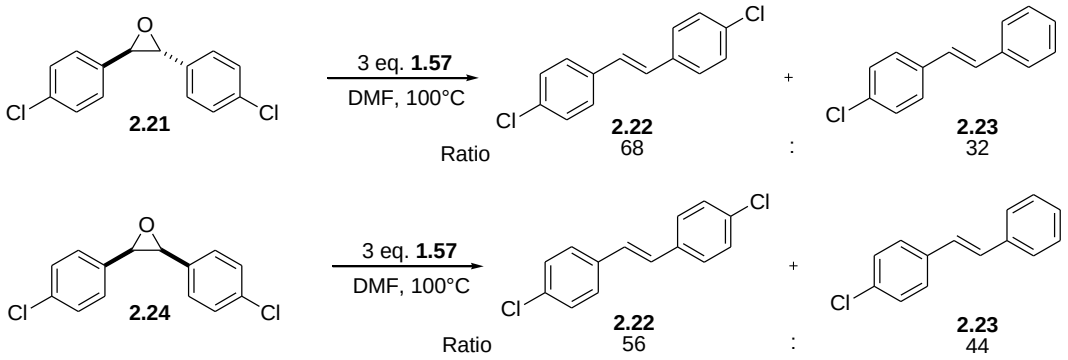


This also explains why more than one equivalent of donor **1.57** was needed. **1.57** is a two-electron donor.[23] The transfer of two electrons should be enough to effect the reaction.

However the substrate is bonded to the donor and later recovered in the aqueous layer as it is a cationic species. This could explain why a low yield of product was recovered.

2.2 Novel reactivity

Both isomers of 2,3-*bis*(4-chlorophenyl)oxirane **2.21** and **2.24** were separately submitted to the electron donor **1.57** under the same conditions as 2,3-*bis*(4-fluorophenyl)oxiranes (Scheme 40).



Scheme 40 – Deoxygenation of 2,3-*bis*(4-chlorophenyl)oxiranes with **1.57**.

In both cases, a mixture of dichlorinated and monochlorinated *trans*-stilbene **2.22** and **2.23** was obtained. This mixture was isolated but **2.22** and **2.23** were not separable. The ratios between these two compounds were determined by NMR and the composition confirmed by GC-MS. The *trans*-2,3-*bis*(4-chlorophenyl)oxirane **2.21** after reaction with **1.57** gave a mixture with a ratio of 68:32 of *trans*-dichlorinated stilbene **2.22** and *trans*-monochlorinated stilbene **2.23**. In the same way, a mixture with a ratio of 56:44 of *trans*-dichlorinated stilbene **2.22** and *trans*-monochlorinated stilbene **2.23** was recovered from the *cis*-2,3-*bis*(4-chlorophenyl)oxirane **2.24**.

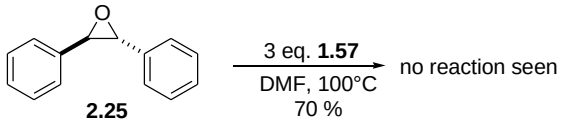
The 2,3-*bis*(4-chlorophenyl)oxiranes reacted in the same way as the 2,3-*bis*(4-fluorophenyl)oxiranes. The *trans*-1,2-*bis*(4-chlorophenyl)ethene **2.22** was obtained from both the *cis*- and *trans*-oxiranes **2.21** and **2.24**. The recovered masses of these reactions were also very low. Mass spectra of the aqueous layers showed evidence of an adduct between the electron donor **1.57** and the substrate (see section 2.1). The formation of this adduct can help to explain the low yield of the reaction.

The monochlorinated stilbene **2.23** was also observed in quite large amounts. Garnier has shown that aryl C-I and C-Br bonds can be reduced using the DMAP-derived electron donor **1.57**,[23,24] C-Cl bonds being more difficult to reduce. The conditions used here are strong enough to observe some C-Cl bond cleavage. However, from section 2.1, the electron donor **1.57** is too weak to reduce aryl C-F bonds.

Only the monochlorinated alkene **2.23** was isolated and no monochlorinated oxirane was observed. This suggests that the deoxygenation is faster than the aryl C-Cl bond reduction. However the more concentrated the reaction mixture, the more monochlorinated compound was formed. When the concentration of the reaction mixture was doubled, the monochlorinated compound was the main isolated product in a ratio of 55:45 (from the NMR of the crude reaction mixture). It seems then that the cleavage of the epoxide is easier to carry out and hence is faster. Very concentrated reaction mixtures (and so harsher conditions) would indeed be needed to obtain more C-Cl reduction.

2.3 Substrates with higher energy LUMO's

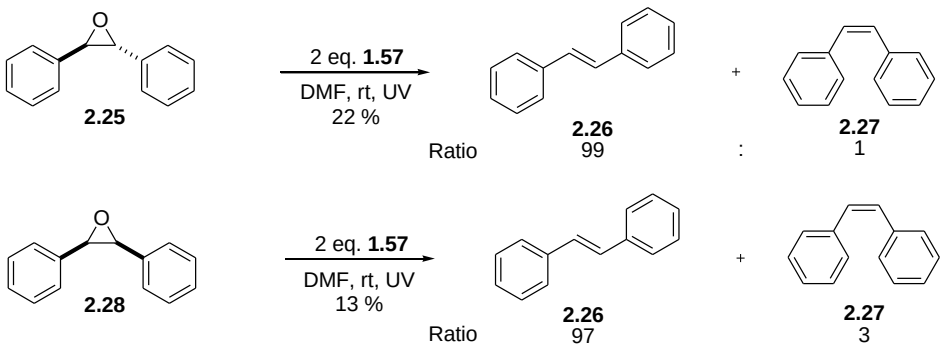
In order to push further the reactivity of the DMAP-derived donor **1.57**, substrates with higher LUMO energy were studied. These substrates were the *cis*- and *trans*-2,3-diphenyloxirane, respectively **2.25** and **2.28**. The absence of an electron-withdrawing group on the phenyl rings raises the level of the LUMO of the molecule, 3.39 eV for the *trans*-2,3-diphenyloxirane and 3.71 eV for *cis*-2,3-diphenyloxirane.[69]



Scheme 41

The *trans*-2,3-diphenyloxirane **2.25** was first submitted to the donor **1.57** under the same conditions as for the 2,3-*bis*(4-fluorophenyl)oxiranes and 2,3-*bis*(4-chlorophenyl)oxiranes (Scheme 41). Only starting material was recovered. It has previously been shown in our group that the DMAP-derived donor **1.57** is more powerful under UV light (350 nm).[23] Both

isomers of 1,2-diphenyloxirane were submitted separately to the electron donor **1.57** under UV-light (Scheme 42).



Scheme 42 – Deoxygenation of 2,3-diphenyloxiranes with **1.57**.

The *trans*-2,3-diphenyloxirane **2.25** afforded a mixture composed of 99:1 *trans*-stilbene **2.26** and *cis*-stilbene **2.27** in 22 % yield and the *cis*-1,2-diphenyloxirane **2.28** gave rise to a mixture ratio of 97:3 of *trans*-stilbene **2.26** and *cis*-stilbene **2.27** in 13 % yield.

The results are concordant with that observed with the 2,3-*bis*(4-fluorophenyl)oxiranes (see section 2.1). Both *trans*- and *cis*-oxiranes give rise to the *trans* reduced product **2.26**. The difference is that more powerful conditions were needed. This is due to the higher energy level of the LUMO of the stilbene oxirane. The UV-light excites the donor and brings it more energy. This allows the electron to "jump" to a higher LUMO.

The observed *cis*-stilbene **2.27** does not come from the direct cleavage of the epoxide following excitation by UV-light. A solution of each 2,3-diphenyloxirane in DMF under irradiation without donor **1.57** showed no isomerisation. This means that the *trans*-epoxide **2.25** is not isomerised to the *cis*-epoxide **2.28** and then reduced to the corresponding stilbene **2.27**. However, isomerisation was observed under UV-light from solutions of each isomer of stilbene **2.26** and **2.27** in DMF without donor **1.57**. The photo-interconversion of stilbene is a well-known fact and is reported in the literature.[70] The *cis*-stilbene **2.27** comes therefore from the isomerisation of the reduced product, the *trans*-stilbene **2.26**.

In order to prove that the observed reactivity requires the presence of electron donor **1.57** and is not due to the UV-light, blank experiments were carried out. Each isomer of 2,3-diphenyloxirane was exposed to the same conditions as above but without donor and at the

same time as the donor reaction (see p.53). In each case, only starting material was recovered. This definitively proves that the deoxygenation of the epoxides is only due to the electron donor **1.57**. However, care must be taken not to over-expose the reaction mixture to UV-light as a photostationary state could be attained.[42] As seen above, the separation of the two isomers of the stilbene **2.26** and **2.27** is difficult (Scheme 42).

2.4 Conclusions

A new reactivity of the DMAP-derived donor **1.57** has been developed. This involves a harder reductive cleavage than achieved so far. Epoxides are cleaved to afford the corresponding *trans*-alkene.

Both *cis*- and *trans*-isomers of activated epoxides were cleaved to afford only the more stable stilbene derivative, the *trans*-alkene. The reaction conditions depend on the energy of the LUMO of the substrate. Whereas compounds with low LUMO energy are cleaved by heating, those with higher LUMO energy need to be carried out under UV-light for greatest activation of the electron donor.

The yields of these reactions were quite low. The formation of an adduct between the electron donor and the substrate is a possible explanation. Evidences of this cation adduct were found in the aqueous layer after work-up of the reaction.

A new reactivity has also been highlighted. The electron donor **1.57** can reduce aryl C-Cl bonds. However the conditions used were not strong enough to give a complete reduction.

DMAP-derived electron donor **1.57** can be compared with the new reagents which are developed for reductive cleavage as seen for the deoxygenation of epoxides (see section 1.2). It can also cleave N-O bond from Weinreb amides.[25]

2.5 Future work

Several aspects of this reaction can still be studied.

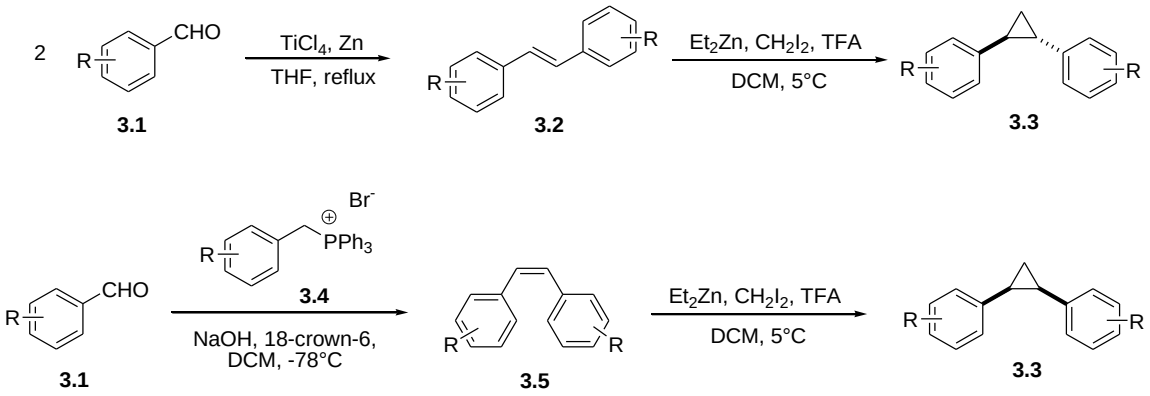
First of all, the range of substrates can be extended. The deoxygenation of other oxygenated small rings could be studied. Oxetanes could be an interesting starting point as their cleavage will have great impacts in biology. Oxetanes are known to be formed by two adjacent pyrimidines in DNA under UV irradiation. These oxetanes then lead to cell death as the resulting structural distortion prevents the replication and transcription of DNA (see section 1.4). The cleavage of oxetanes affords a repaired DNA.

Another point which can be further developed is the reduction of aryl C-Cl bonds. So far, only partial aryl C-Cl bond cleavage has been observed. However, the use of UV-light gives rise to a more powerful electron donor (see section 2.3). Under these conditions, the electron donor could then be able to achieve a complete reduction of aryl C-Cl bonds.

Chapter 3 - Reactivity of the donor towards diarylcyclopropanes

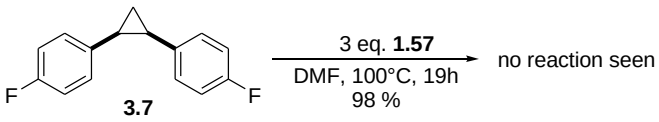
In this chapter, the reactivity of diarylcyclopropanes towards the electron donor **1.57** is studied. As for the epoxides, the substrates studied have different LUMO energy levels illustrating a diverse range of reactivity.

3.1 Preparation of diarylcyclopropanes and development of the reaction



Scheme 43 – Preparation of substrates for the isomerisation of diarylcyclopropanes.

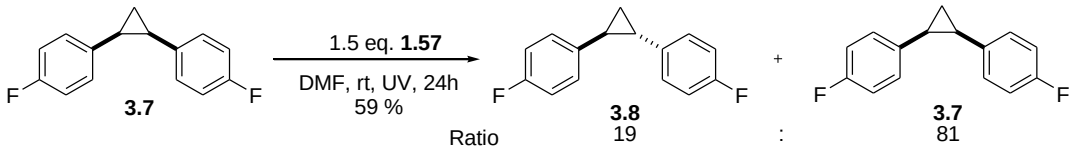
Each substrate, **3.3** and **3.6**, was prepared from its alkene by the stereoselective Simmons-Smith reaction (Scheme 43). *Trans*-alkenes **3.2** were obtained by a McMurry reaction from the aldehyde **3.1**. The *cis*-alkenes **3.5** were prepared by a Wittig reaction between the aldehyde **3.1** and the phosphonium salt **3.4**.[66]



Scheme 44

The reaction was first carried out under the same conditions as used for the electron-poor epoxides (see section 2.1 and 2.2). The *cis*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7** was submitted to the donor **1.57** and heated overnight (Scheme 44). As expected, only starting

material was recovered. *Cis*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7** was then submitted to the electron donor under harsher conditions, irradiation with UV-light (Scheme 45). A ratio of 81:19 of starting material, *cis*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7**, and isomerised product, *trans*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.8**, in a modest 59 % yield was isolated after submitting **3.7** to the electron donor **1.57** under UV-light (350 nm). The same reaction was carried out with 3 equivalents donor and exposed 28h to UV-light. No further isomerisation was observed.

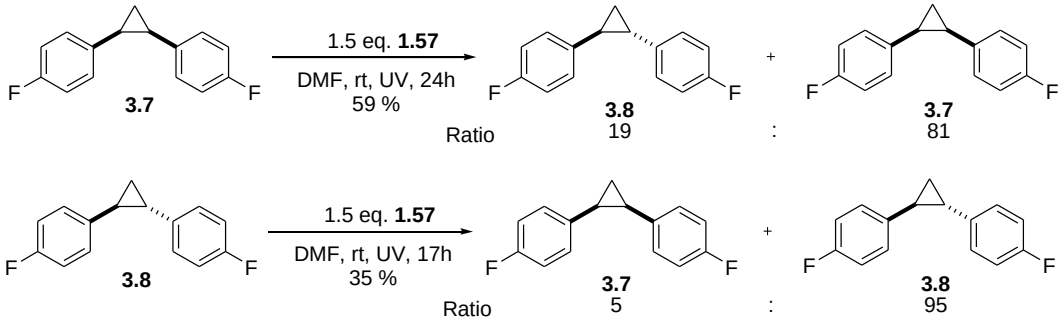


Scheme 42

To explain this limited reactivity, some possibilities can be quickly eliminated. First of all, the reaction glassware (Pyrex volumetric flasks) doesn't absorb the light emitted by the lamp (F8T5BLB, Higuchi Inc, US).[23] Also, the solvent, DMF, does not absorb above 300 nm and the lamp emits between 315 nm and 400 nm.[76] Two explanations can now be proposed. The first is that the reactivity of the donor has been pushed as far as possible. A more powerful electron donor is then needed to carry out total isomerisation. The other one is that a photostationary state has been achieved. This hypothesis seems more likely since such equilibria have already been reported and depend on the solvent and the irradiation.[71]

A blank experiment was run in the same way as for the 2,3-diphenyloxiranes and at the same time (see section 2.3). No isomerisation was observed in these experiments. The observed reactivity implicates the electron donor **1.57** and is not due to UV-light alone.

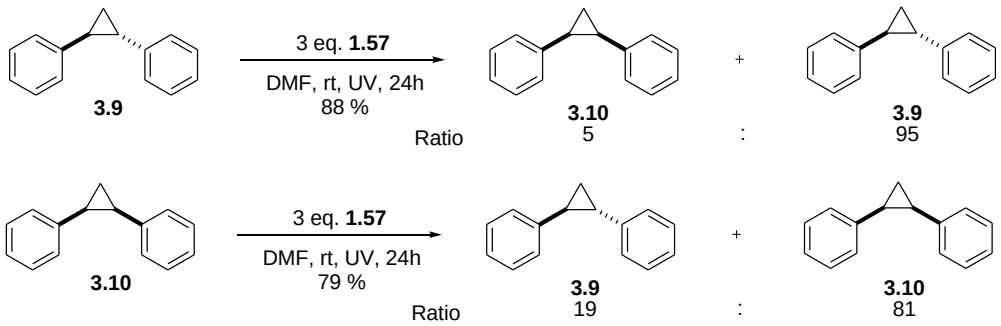
3.2 Isomerisation of cyclopropanes



Scheme 46 – Isomerisation of 1,2-*bis*(4-fluorophenyl)cyclopropanes with **1.57**.

Both isomers of the 1,2-*bis*(4-fluorophenyl)cyclopropane **3.7** and **3.8** were separately submitted to the electron donor **1.57** under UV-light (Scheme 46). The isolated mixture when starting from the *trans*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.8** was composed of isomerised product, **3.7**, and starting material, **3.8**, in a ratio of 5:95 respectively and an overall 35 % yield. More interconversion was obtained with the *cis*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7** as the isolated mixture was composed of isomerised product **3.8** and starting material **3.7** 19:81 in 59 % yield. As the two isomers were inseparable, the ratio was determined by NMR after purification of the crude reaction mixture and the composition of the mixture by GC-MS.

Blank experiments were run for each experiment at the same time as the reaction but without electron donor **1.57** (see p.53). No isomerisation occurred for **3.7** and **3.8**. This indicates that the isomerisation involves the electron donor **1.57**.

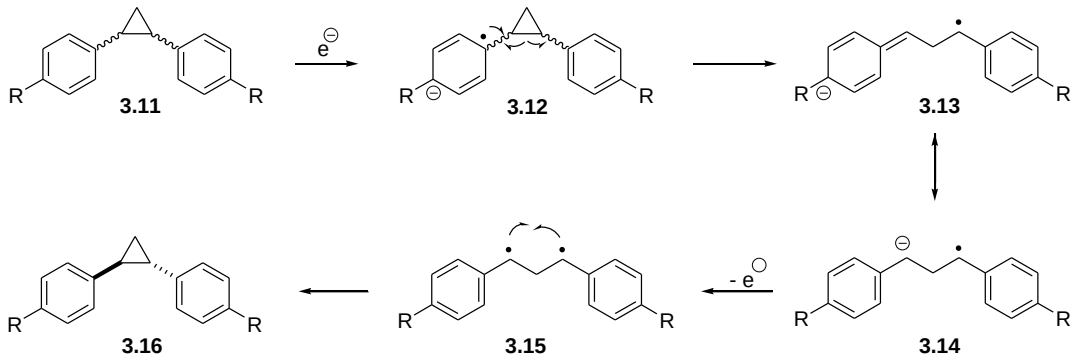


Scheme 47 – Isomerisation of 1,2-diphenylcyclopropanes with **1.57**.

The same reactivity was observed with 1,2-diphenylcyclopropane. The electron donor **1.57** isomerised both isomers of 1,2-diphenylcyclopropane **3.9** and **3.10** (Scheme 47). The mixture

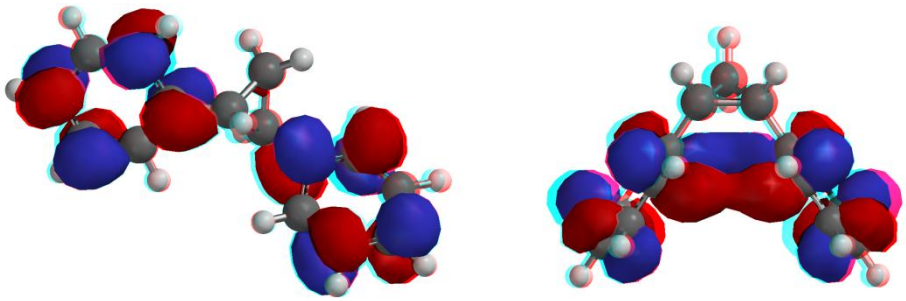
isolated after reaction of the *trans*-1,2-diphenylcyclopropane **3.9** with the electron donor **1.57** was composed of isomerised product **3.10** and starting material **3.9** 5:95 in 88 % yield. The reaction of *cis*-1,2-diphenylcyclopropane **3.10** gave rise to a mixture composed of isomerised product **3.9** and starting material **3.10** 19:81 in 79 % yield. No isomerisation was seen in blank experiments.

The mechanism of the interconversion of cyclopropanes with **1.57** is still under investigation. However some mechanisms can be proposed based on these results. The first possibility is that the reaction goes through a ring-opened intermediate (Scheme 48).



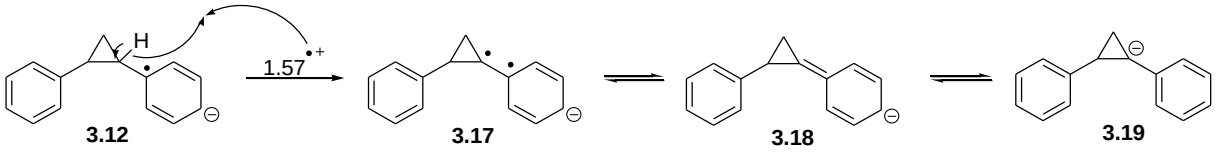
Scheme 48 – Ring-opening mechanism.

Assuming that **1.57** donates an electron to the LUMO of **3.11** (Scheme 49), this would lead to radical-anion **3.12**. This kind of species has not been discussed a lot in the literature but has been proved to exist.[72] A likely way forward would be for this molecule to suffer C-C cleavage in the cyclopropane to afford **3.13**. The radical-anion **3.13** is stabilised by the adjacent phenyl ring. As the cyclopropane is now opened, the σ bonds are free to rotate and will minimise the hindrance of the molecule: the two phenyl rings will adopt a *trans* geometry. After this rearrangement, the electron donor **1.57** takes an electron back from **3.14**. The two radicals then react with each other to form the more stable cyclopropane **3.16**. However, recent computational chemistry studies show no opening of the radical-anion cyclopropane **3.12**.[73]



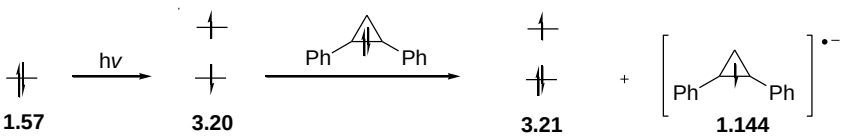
Scheme 49 – LUMO orbital of *trans*-1,2-diphenylcyclopropane on the left and *cis*-1,2-diphenylcyclopropane on the right[69]

Two other mechanisms seem then likely to explain the isomerisation. First of all, the reaction could also go through a hydrogen abstraction. The electron donor **1.57** is excited by irradiation and gives an electron to the cyclopropane. Hydrogen from the cyclopropyl ring of the radical-anion **3.12** can be abstracted by the radical-cation donor (Scheme 50). This biradical anion **3.17** seems to be planar.[74] Abstraction of a hydrogen from the reaction mixture leads then to either isomer.



Scheme 50 – Isomerisation via hydrogen abstraction.

On the other hand, the interconversion of the cyclopropanes could also be explained by the transfer of an electron from the cyclopropyl ring to the excited singlet donor **3.20** (Scheme 51). This transfer affords a radical-cation **1.144** which is well described in the literature as an intermediate in the isomerisation of cyclopropanes (see section 1.3). Subsequently the radical-cation **1.144** receives an electron to afford **3.11**.

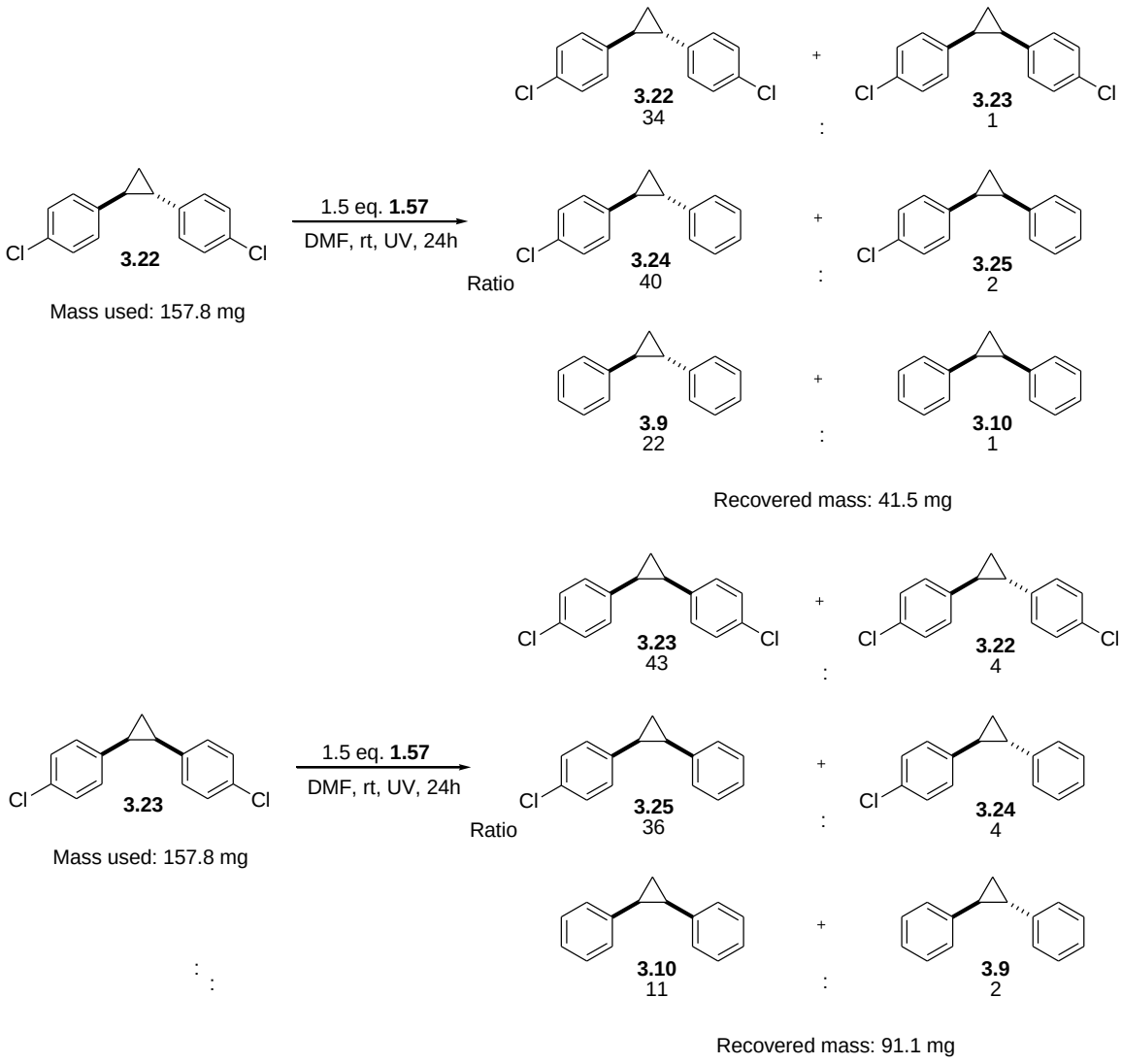


Scheme 51 – Isomerisation via electron transfer from the cyclopropane to the donor **1.57**.

For all substrates, no side-reactions of the types reported in the literature,[75] were observed. GC-MS spectra confirmed that only both isomers of the 1,2-diarylcyclopropane derivatives were recovered. This confirms that a 1,3-diphenyl biradical is formed and not a 1,2-diphenyl

biradical corresponding to the breakage of the other C-C bond of the cyclopropane. Moreover this agrees with the triplet intermediate as isomerisation was observed.[41,46]

3.3 Cleavage of aryl C-Cl bonds



Scheme 52 – Reactivity of 1,2-*bis*(4-chlorophenyl)cyclopropanes with **1.57**.

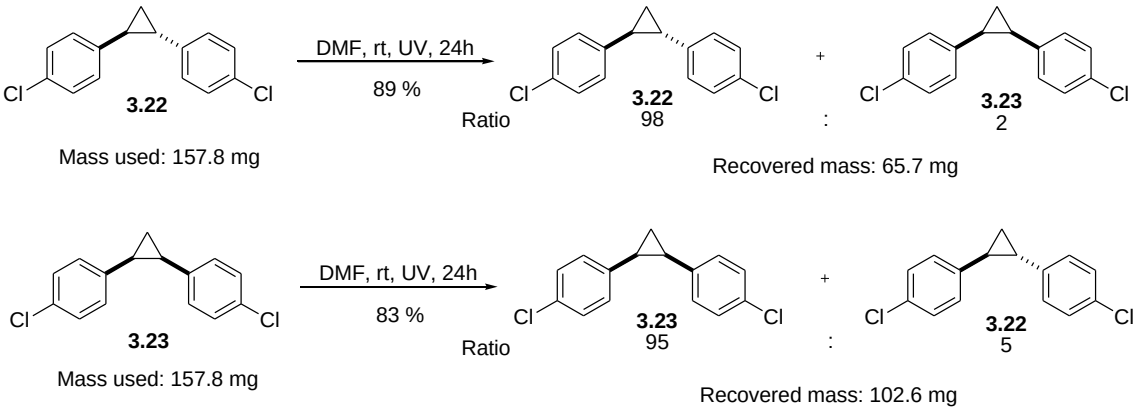
A complicated mixture was obtained when reacting the 1,2-*bis*(4-chlorophenyl)cyclopropane **3.22** and **3.23** with the electron donor **1.57** (Scheme 52). The ratio of each mixture, determined by NMR, is reported below. The composition of the mixture was determined by GC-MS.

Starting material / Products	*Trans*-1,2-*bis*(4-chloro--phenyl)cyclopropane **3.22**	*Cis*-1,2-*bis*(4-chloro--phenyl)cyclopropane **3.23**
Trans-dichlorinated **3.22**	34	4
Cis-dichlorinated **3.23**	1	43
Trans-monochlorinated **3.24**	40	4
Cis-monochlorinated **3.25**	2	36
Trans-stilbene **3.9**	22	2
Cis-stilbene **3.19**	1	11

Some isomerisation was observed but the main reaction seems to be the reduction of aryl C-Cl bonds. Only less than 5 % isomerisation products were isolated whereas an average of 50 % reduced product was observed. This indicates a competition between reduction of the aryl C-Cl bond and the geometric isomerisation. This reactivity of the electron donor has already been seen in the study of the epoxides (see section 2.2). However both aryl C-Cl bonds are reduced here. The electron donor is now powerful enough to cleave aryl C-Cl bonds.

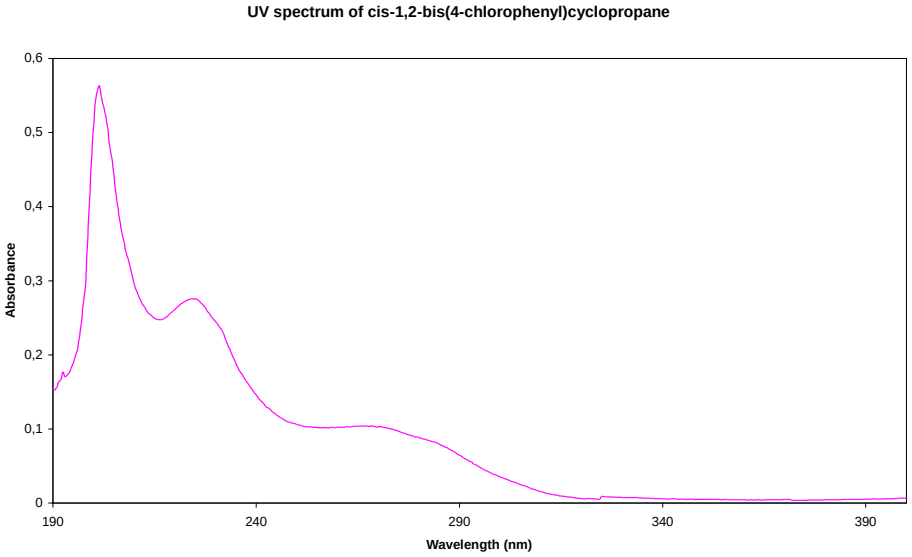
As for 1,2-*bis*(4-fluorophenyl)cyclopropane and 1,2-diphenylcyclopropane (see section 3.2), more isomerisation was obtained when starting from the *cis*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.23**. This suggests that the isomerisation of the 1,2-*bis*(4-chlorophenyl)cyclopropane **3.22** and **3.23** goes through the same mechanism as for 1,2-*bis*(4-fluorophenyl)cyclopropane and 1,2-diphenylcyclopropane (see section 3.2).

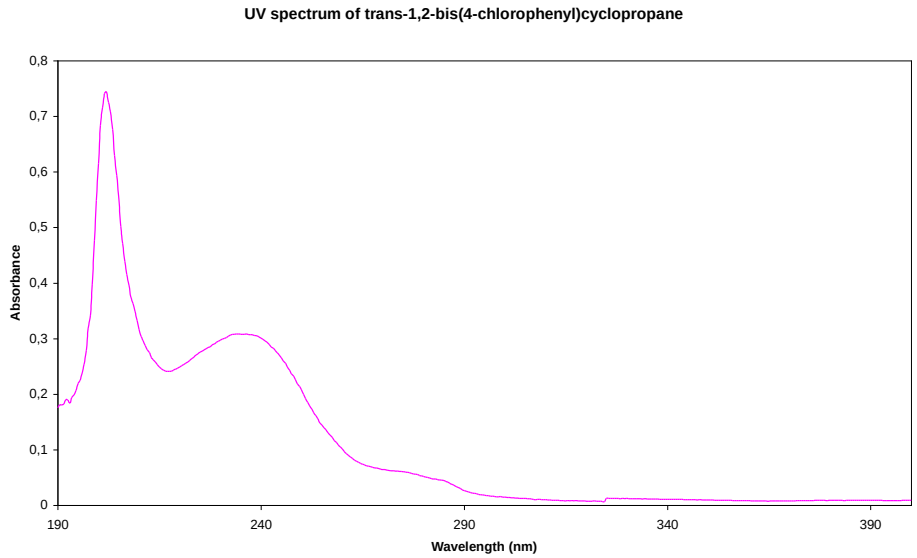
As for all reactions under UV-light, blank experiments were carried out. However in this case, it appeared that some isomerisation did take place even if the electron donor was not present in the reaction mixture. The reaction mixture isolated from the reaction of *cis*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.23** afforded a ratio of 95:5 starting material **3.23** and isomerised product **3.22**. Also, a ratio of 98:2 starting material : reduced product was isolated from *trans*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.22** (Scheme 53).

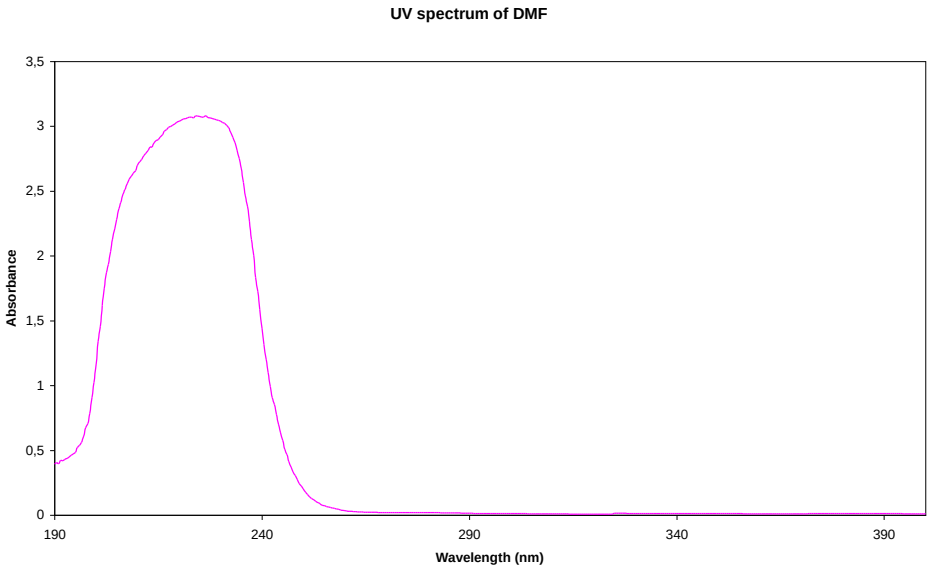


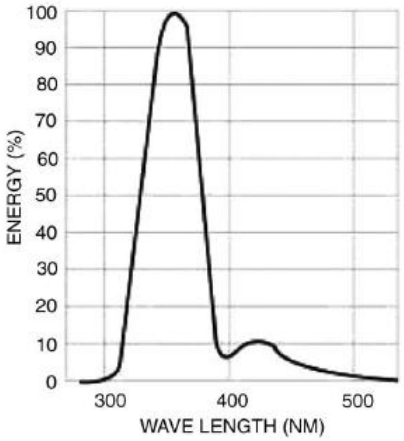
Scheme 53 – Blank experiments for 1,2-*bis*(4-chlorophenyl)cyclopropanes.

These results pose a question: is the isomerisation also due to UV-light or only due to the action of the electron donor **1.57**? The UV spectrum of the *cis*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.23** shows some absorption up to 340 nm (Scheme 54). However the *trans*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.22** does not absorb between 315 nm and 400 nm where the lamp emits. This can explain why more *cis* compound **3.23** was isomerised in the blank experiments as it is excited by the irradiation. The order of isomerisation observed in the blank experiments was more or less the same as observed during the donor reaction. This suggests that the isomerisation taking place with the electron donor is mainly due to UV-light and not to the electron donor **1.57**.









Scheme 54 – UV spectra of *cis*- and *trans*-isomer of the 1,2-*bis*(4-chlorophenyl)cyclopropane **3.23** and **3.22**, DMF and the emission spectrum[76] of the UV lamp used.

No dechlorination was observed in these blank experiments. This means that the irradiation is not responsible for the reduction of these bonds. This reduction is the result of the action of the electron donor **1.57**.

3.4 Conclusions

Novel uses of DMAP-derived electron donor **1.57** have been highlighted here.

This electron donor allows the isomerisation of 1,2-*bis*(4-fluorophenyl)cyclopropanes and 1,2-diphenylcyclopropanes. Harsher conditions (UV-light) are needed than was used for 2,3-diarylepoxides as the cyclopropanes are harder to reduce. It has been proved that this reactivity is only due to the activated donor and not to UV-light alone.

Several mechanisms have been proposed to explain this geometric interconversion. The reaction could go through a ring-opening mechanism and a 1,3-biradical. A hydrogen abstraction could also be the starting point of the isomerisation. Finally isomerisation could take place after electron transfer from the substrate to the DMAP-derived electron donor **1.57**.

A different reactivity was observed with the 1,2-*bis*(4-chlorophenyl)cyclopropanes. The reduction of aryl C-Cl bonds seems in this case the first reaction to occur as almost no isomerisation was seen. Blank experiments have revealed that the electron donor **1.57** reduces the C-Cl bonds whereas irradiation was mainly responsible for the isomerisation. Following previous reduction of aryl C-I and C-Br bonds, the electron donor **1.57** is now able to reduce aryl C-Cl bonds under photochemical activation.

3.5 Future work

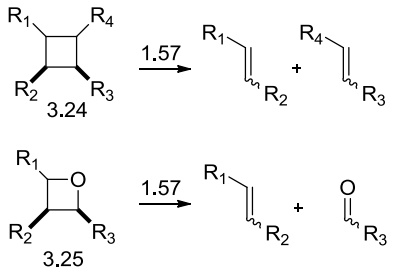
The range of substrates can be extended. Other small-member rings such as cyclobutanes can be studied (see section 1.4).

Further investigations about the competition between isomerisation of 1,2-*bis*(4-chlorophenyl)cyclopropane and aryl C-Cl reduction can be carried out. Some questions have been raised and could be interesting to study.

The mechanism of the isomerisation of the diarylcyclopropanes could also be investigated. Few possibilities have been proposed but the definitive mechanism is still unknown.

The reactivity of the DMAP-derived donor **1.57** seems to have been pushed as far as possible. The reaction of isomerisation can then be studied with more powerful electron donors. This might give rise to a complete isomerisation.

A large range of applications of the DMAP-derived donor **1.57** has now been developed. The DMAP-derived donor **1.57** has been proved to reduce N-O bonds from Weinreb amides[25] and now to reduce C-O bonds from diarylepoxides. Moreover the reduction of diarylcyclopropanes leads to isomerisation of the substrate. To widen the uses of this electron donor, its reactivity towards oxetanes **3.25** or cyclobutadienes **3.24** could now be studied as a new departure for the DMAP-derived donor **1.57**.



Scheme 55 – Possible new departure for the DMAP-derived donor **1.57**.

Chapter 4 - Experimental section

Proton NMR (^{1}H) spectra were recorded either at 400.13 MHz on a Bruker DPX 400 spectrometer or at 500.13 MHz on a Bruker AV500 spectrometer. Carbon NMR (^{13}C) spectra were recorded at 100.61 MHz, using a J-mod pulse program for resolving the carbon assignments on a Bruker DPX 400 spectrometer. The chemical shifts are quoted in parts per million (ppm) and referenced to tetramethylsilane but calibrated on the solvent residual signal. The coupling constants are given in Hertz (Hz).

The high resolution mass spectra were recorded at the EPSRC National Mass Spectrometry Service Centre, Swansea, on a JLZX 102, VGZAB-E or a VG micromass instrument. The GC-MS spectra were recorded at the Strathclyde University Mass Spectrometry Service on a ThermoFinnigan PolarisQ Ion Trap Spectrometer (EI). The samples were heated 20°C/mn from 40°C to 320°C with a flow of 1 mL/min of helium. The mass spectra of the aqueous layers were recorded on a ThermoFinnigan LCQ DUO mass spectrometer (ESI) at the Strathclyde University Mass Spectrometry Service.

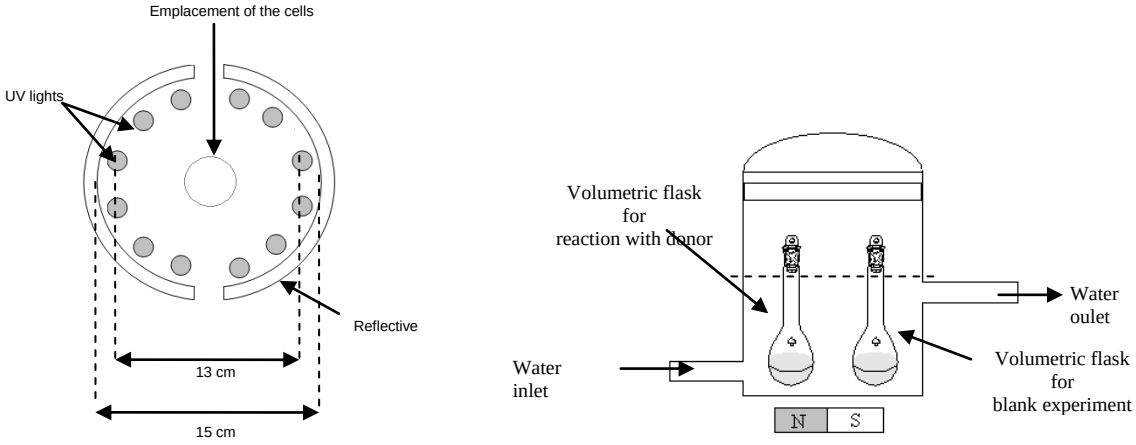
Column chromatography was performed using silica gel 60 (200-400 mesh). Melting points were measuring using a Gallenkamp meting point apparatus. IR spectra were recorded on a Perkin Elmer Spectrum One FT-IR spectrometer, either pressed as disks in a potassium bromide matrix (KBr), or as films applied on NaCl plates.

"Concentrated under reduced pressure" refers to the evaporation on rotavap instrumentation, using a diaphragm pump vacuum with final pressure typically between 1-10 mbar and temperature of 20-30°C.

All reagents were obtained from commercial suppliers and used without further purification. Tetrahydrofuran, dichloromethane, diethyl ether, hexane and toluene were dried with a Pure-Solv 400 solvent purification system from Innovative Technology Inc., U.S.A.

To prevent unwanted side-reactions in procedures where liquid ammonia was used as a solvent, the gas was filtered systematically on an alumina column prior to condensation.[23]

Experiments conducted using UV irradiation were performed using a home-made vertical UV concentric reactor using twelve 8W UV bulbs (F8T5BLB, Higuchi Inc, US) and consisting of two half-circle units, forming once closed a concentric circle of bulbs with a diameter of 13 cm and enclosed by a reflective surface surrounding the unit (15 cm in diameter) but leaving open the top and the bottom of the apparatus, for a total of 26 cm in height (Scheme 56). Centred in the reactor, reaction vessels were Pyrex volumetric flasks immersed within a larger Pyrex vessel.



Scheme 56 - UV apparatus

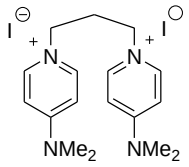
UV spectra were recorded on a Hελios β spectrometer from Spectratronic. Lamps were of tungsten and deuterium types, with a switch at 325 nm. Scans were performed from 190 nm to 800 nm with a data interval of 0.5 nm. Recording speed was automatically set-up by a smart-mode ("quantitative" settings). Bandwidth was 2.0 nm.

This project was started by another student in our research group, Sylvain Cutulic. Where experiments were conducted by him, these are acknowledged below, but the experiments are included to give a complete account.

Further information on the computational study for the isomerisation of cyclopropanes can be found in Appendices.

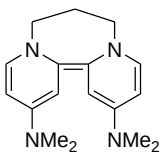
4.1 DMAP-derived donor synthesis

Preparation of 1,3-bis-(*N'*,*N'*-dimethyl-4-aminopyridinium)propane diiodide **1.54**[23]



A solution of 4-DMAP (13.75 g, 112.5 mmol, 2.5 eq.) and 1,3-diiodopropane (13.35 g, 45 mmol, 1 eq.) in acetonitrile (150 mL) was stirred at reflux overnight under argon. After cooling, the solid that had appeared was filtered. The solid was washed with acetonitrile (3 x 50 mL) and with diethyl ether (3 x 50 mL) and dried under vacuum to afford 1,3-bis(*N'*,*N'*-dimethyl-4-aminopyridinium)propane diiodide **1.54** (23.8 g, 98 %) as a white solid; mp: 280-285°C; [Found: (ESI^+) $(M\text{-}I)^+$ 413.1194. $C_{17}H_{26}I_2N_4$ requires M-I, 413.1197]; ^{1}H-NMR (500 MHz, DMSO-d_6) δ 2.33 (2H, q, J = 7.2 Hz, CH_2), 3.19 (12H, s, CH_3), 4.22 (4H, t, J = 7.2 Hz, NCH_2), 7.03 (4H, d, J = 8 Hz, ArH), 8.25 (4H, d, J = 8 Hz, ArH); ^{13}C-NMR (100 MHz, DMSO-d_6) δ 31.0 (CH_2), 39.8 (CH_3), 53.6 (CH_2), 107.8 (CH), 141.8 (CH), 155.8 (C).

Preparation of *N*,*N*,*N'*,*N'*-tetramethyl-7,8-dihydro-6H-dipyrido[1,2-a;2',1'-c][1,4]diazepine-2,12-diamine **1.57**[23]



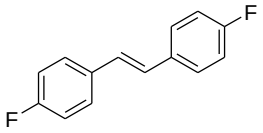
A mixture of 1,3-bis(*N'*,*N'*-dimethyl-4-aminopyridinium)propane diiodide **1.54** (10.8 g, 20 mmol, 1 eq.) and Na (60 % dispersed in mineral oil, 8 g, 200 mmol, 10 eq.) was placed under argon in a flask mounted with a dry-ice condenser. The mixture was washed with hexane and dried under vacuum before being put back under argon. While stirring, ammonia (100 mL) was condensed, left at reflux for 3 h and was then allowed to evaporate overnight. Once the flask was at room temperature, still under argon, it was transferred to an oxygen-free, moisture-free glovebox. The solid was then extracted with diethyl ether. The solvent was

removed by distillation and under vacuum (10-20 mbar) to afford the pure *N*,*N*,*N'*,*N'*-tetramethyl-7,8-dihydro-6H-dipyrido[1,2-a;2',1'-c][1,4]diazepine-2,12-diamine **1.57** (5.1 g, 90 %) as a purple-black, moisture sensitive and highly oxygen-sensitive solid; ^{1}H-NMR (500 MHz, benzene-d_6) δ 1.00 (2H, q, J = 6.3 Hz, CH_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 Hz and J = 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).

4.2 Experimental section for the epoxide study

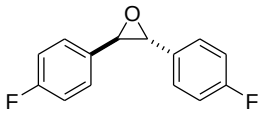
4.2.1. Preparations of reagents and substrates

Preparation of *(E)*-1,2-bis(4-fluorophenyl)ethene **2.8**[77]



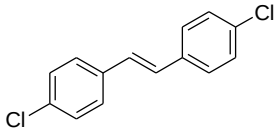
Under cooling, $TiCl_4$ (5 mL, 45 mmol, 3 eq.) was added dropwise to a solution of 4-fluorobenzaldehyde (1.66 mL, 15 mmol, 1 eq.) and zinc powder (5.88 g, 90 mmol, 6 eq.) in dry THF (75 mL). The mixture was stirred overnight at reflux under an inert atmosphere. After cooling, the reaction was quenched with sat. $NaHCO_3$ (250 mL). The mixture was extracted with dichloromethane (3 x 50 mL). The combined organic phases were then washed with sat. $NaHCO_3$ (2 x 50 mL) and brine (50 mL). The resulting organic phase was finally dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8** (1.51 g, 94 %) as a white solid; [Found: (EI^+) $[M]^+$ 216.0742, $C_{14}H_{10}F_2$ requires M, 216.0745]; mp: 143-146°C (lit.[78] 148-151°C); ν_{max}(KBr)/cm^{-1}: 529, 835, 1234, 1506, 1593, 3049; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.99 (2H, s, CH), 7.06 (4H, d, J = 8.8 Hz, ArH), 7.47 (4H, d, J = 8.8 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 115.7 (CH, d, $J_{C\text{-}F}$ = 21.6 Hz), 137.3 (CH), 127.9 (CH, d, $J_{C\text{-}F}$ = 8 Hz), 133.4 (C), 162.4 (C, $J_{C\text{-}F}$ = 245.8 Hz).

Preparation of *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7**[77]



*m*CPBA (1.81 g, 10.5 mmol, 1.5 eq.) was added to a solution of *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8** (1.51 g, 6.99 mmol, 1 eq.) in dichloromethane (50 mL). The mixture was stirred at rt for 24h. The reaction was quenched with sat. $Na_2S_2O_3$ (250 mL). The aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined organic phases were washed with sat. $Na_2S_2O_3$ (2 x 50 mL) and brine (50 mL). The resulting organic phase was finally dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether – diethyl ether 9:1) to afford *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7** (1.35 g, 84 %) as a white powder; [Found: (CI^+) $(M-H)^+$ 231.0616‡. $C_{14}H_{10}F_2O$ requires M-H, 231.0616]; mp: 79-80°C (lit.[77] 82-83°C); ν_{max}(KBr)/cm^{-1}: 574, 844, 1238, 1514, 1611, 1906, 2973; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.82 (2H, s, CH), 7.09 (4H, tt, J = 8.8 Hz, ArH), 7.33 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 62.2 (CH), 115.6 (CH, $J_{C\text{-}F}$ = 22 Hz), 127.2 (CH, $J_{C\text{-}F}$ = 8.1 Hz), 132.7 (C), 162.8 (C, $J_{C\text{-}F}$ = 245.4 Hz); *m/z* (CI^+) 232 [M^+, 5 %], 124 (12), 108 (29), 96 (18), 72 (20), 58 (36), 52 (100), 44 (60).

Preparation of *(E)*-1,2-*bis*(4-chlorophenyl)ethene **2.22**[79]

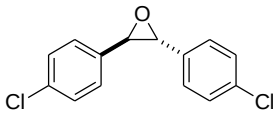


Under cooling, $TiCl_4$ (5 mL, 45 mmol, 3 eq.) was added dropwise to a solution of 4-chlorobenzaldehyde (2.11 g, 15 mmol, 1 eq.) and zinc powder (5.88 g, 90 mmol, 6 eq.) in dry THF (75 mL). The mixture was stirred overnight at reflux under an inert atmosphere. After cooling, the reaction was quenched with sat. $NaHCO_3$ (250 mL). The mixture was extracted with dichloromethane (3 x 50 mL). The combined organic phases were then washed with sat. $NaHCO_3$ (2 x 50 mL) and brine (50 mL). The resulting organic phase was finally dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then

‡ The accurate mass measurement has been done on the $[M-H]^+$ ion because the M^+ ion was not isotopically pure as it will also contain the ^{13}C isotope of the $[M-H]^+$ ion.

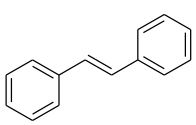
adsorbed onto silica and purified by column chromatography (petroleum ether) to afford *(E)*-1,2-*bis*(4-chlorophenyl)ethene **2.22** (1.58 g, 84 %) as a white solid; [Found: (EI^+) M^+ 248.0153. $C_{14}H_{10}Cl_2$ requires M, 248.0154]; mp: 171-174°C (lit.[80] 175-176°C); ν_{max}(film)/ cm^{-1}: 740, 1265, 3054; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.03 (2H, s, CH), 7.33 (4H, d, J = 10.5 Hz, ArH), 7.43 (4H, d, J = 10.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 127.7 (CH), 128.0 (CH), 128.9 (CH), 133.5 (C), 135.5 (C); *m/z* (EI^+) 252 [M(^{37}Cl)$^+$, 3 %], 250 [M(^{35}Cl, ^{37}Cl)$^+$, 19], 248 [M(^{35}Cl)$^+$, 25], 178 (100), 88 (32), 75 (21), 50 (33).

Preparation of *(2R*,3R*)*-2,3-*bis*(4-chlorophenyl)oxirane **2.21**[81]



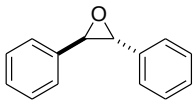
*m*CPBA (1.64 g, 9.51 mmol, 1.5 eq.) was added to a solution of *(E)*-1,2-*bis*(4-chlorophenyl)ethene **2.22** (1.58 g, 6.34 mmol, 1 eq.) in dichloromethane (50 mL). The mixture was stirred at rt one day. The reaction was quenched with sat. $Na_2S_2O_3$ (250 mL). The aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined organic phases were washed with sat. $Na_2S_2O_3$ (2 x 50 mL) and brine (50 mL). The resulting organic phase was finally dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether – diethyl ether 95:5) to afford *(2R*,3R*)*-2,3-*bis*(4-chlorophenyl)oxirane **2.21** (1.59 g, 95 %) as a white powder; [Found: (CI^+) M^+ 264.0102. $C_{14}H_{10}Cl_2O$ requires M, 264.0103]; mp: 122-123°C (lit.[80] 123-124°C); ν_{max}(film)/cm^{-1}: 740, 1265, 2988, 3054; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.81 (2H, s, CH), 7.28 (4H, d, J = 8.4 Hz, ArH), 7.37 (4H, d, J = 8.4 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 62.2 (CH), 126.8 (CH), 128.8 (CH), 134.3 (C), 135.3 (C); *m/z* (CI^+) 286 [$(M+NH_4)^+$, ^{37}Cl, 5 %], 284 [$(M+NH_4)^+$, ^{35}Cl, ^{37}Cl, 53], 282 [$(M+NH_4)^+$, ^{35}Cl, 34], 268 [M(^{37}Cl)$^+$, 4], 266 [M(^{35}Cl, ^{37}Cl)$^+$, 11], 264 [M(^{35}Cl)$^+$, 12], 252 (10), 250 (60), 248 (100), 178 (15), 139 (16), 52 (57).

Preparation of *(E)*-1,2-diphenylethene **2.26**[82]



Under cooling, $TiCl_4$ (5 mL, 45 mmol, 3 eq.) was added dropwise to a solution of benzaldehyde (1.52 mL, 15 mmol, 1 eq.) and zinc powder (5.88 g, 90 mmol, 6 eq.) in dry THF (75 mL). The mixture was stirred overnight at reflux under an inert atmosphere. After cooling, the reaction was quenched with sat. $NaHCO_3$ (250 mL). The mixture was extracted with dichloromethane (3 x 50 mL). The combined organic phases were then washed with sat. $NaHCO_3$ (2 x 50 mL) and brine (50 mL). The resulting organic phase was finally dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford *(E)*-1,2-diphenylethene **2.26** (865.1 mg, 63 %) as a white solid; [Found: (EI^+) M^+ 180.0936. $C_{14}H_{12}$ requires M, 180.0934]; mp: 122-123°C (lit.[83] 124°C); ν_{max}(film)/cm^{-1}: 692, 764, 963, 1452, 3021; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.13 (2H, s, CH), 7.27 (2H, d, J = 7.2 Hz, ArH), 7.37 (4H, t, J = 7.2 Hz, ArH), 7.53 (4H, d, J = 7.2 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 126.5 (CH), 127.6 (CH), 128.6 (CH), 128.7 (CH), 137.3 (C); *m/z* (EI^+) 180 [M^+, 75 %], 179 (70), 178 (52), 165 (34), 102 (30), 63 (40), 51 (69), 37 (100).

Preparation of *(2R*,3R*)*-2,3-diphenyloxirane **2.25**[82]

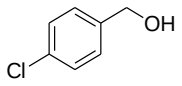


*m*CPBA (1.15 g, 6.66 mmol, 1.5 eq.) was added to a solution of *(E)*-1,2-diphenylethene **2.26** (800 mg, 4.44 mmol, 1 eq.) in dichloromethane (30 mL). The mixture was stirred at rt overnight. The reaction was quenched with sat. $Na_2S_2O_3$ (250 mL). The aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined organic phases were washed with sat. $Na_2S_2O_3$ (2 x 50 mL) and brine (50 mL). The resulting organic phase was finally dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether – diethyl ether 9:1) to afford *(2S*,3R*)*-2,3-diphenyloxirane **2.25** (468.2 mg, 54 %) as a white solid; [Found: (EI^+) M^+ 196.0882. $C_{14}H_{12}O$ requires M, 196.0883]; mp: 61-62°C (lit.[84] 68-69°C); ν_{max}(film)/cm^{-1}: 508, 697, 747, 1452, 2988, 3034; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.88 (2H, s, CH), 7.37 (10H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 62.8 (CH), 125.5 (CH), 128.3

(CH), 128.6 (CH), 137.1 (C); *m/z* (EI^+) 196 [M^+, 13 %], 195 (16), 178 (12), 167 (40), 152 (10), 105 (33), 89 (100), 77 (70), 63 (51), 51 (60), 39 (38).

Preparation of (4-chlorophenyl)methanol **4.1**

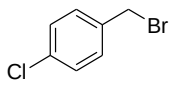
This reaction has been carried out by S.P.Y. Cutulic.[66]



Lithium aluminium hydride (5.69 g, 150 mmol, 1 eq.) was added in small portions to a solution of 4-chlorobenzaldehyde (21.08 g, 150 mmol, 1 eq.) in anhydrous THF (250 mL) at 0°C. The resulting suspension was then warmed to room temperature and stirred at room temperature overnight. Diethyl ether (200 mL) was added to the reaction mixture and the reaction was successively quenched with water (5.5 mL), aqueous sodium hydroxide solution 15 % (5.5 mL) and water (16.5 mL). Anhydrous magnesium sulfate was then added to the resulting suspension and the solid was filtered off. The filtrate was then concentrated under reduced pressure. The residue was then taken in ethyl acetate (200 mL) and successively washed with water (3 x 150 mL) and brine (3 x 150 mL). The combined organic layers were eventually dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulting off-white solid was adsorbed onto silica and purified by column chromatography to afford (4-chlorophenyl)methanol **4.1** as a pure white solid (20.73 g, 97 %); mp. 70-72°C; ν_{max} (film)/cm^{-1} 3262, 2955, 2924, 1597, 1492, 1451, 1405, 1265, 1086, 1013; [Found: (EI^+) M^+ 142.0179, C_7H_7ClO requires M, 142.0180]; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.24 (1H, t, J = 4.7 Hz, OH), 4.62 (2H, d, J = 4.7 Hz, CH_2), 7.27 (2H, d, J = 8.5 Hz, Ar-H), 7.32 (2H, d, J = 8.5 Hz, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 64.4 (CH_2), 128.3 (CH), 128.7 (CH), 133.3 (C), 139.2 (C).

Preparation of (1-bromomethyl)-4-chlorobenzene **4.2**

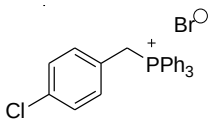
This reaction has been carried out by S.P.Y. Cutulic.[66]



Phosphorus tribromide (5.74 mL, 60 mmol, 0.5 eq.) was added dropwise to a solution of (4-chlorophenyl)methanol **4.1** (17.04 g, 120 mmol, 1 eq.) in anhydrous diethyl ether (120 mL) at 0°C under argon. The resulting solution was then warmed to room temperature and stirred at room temperature overnight. The resulting orange solution was then quenched with water (10 mL) and washed with water (3 x 100 mL) and brine (3 x 100 mL). The resulting organic layer was eventually dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was then adsorbed onto silica and purified by column chromatography (petroleum ether - ethyl acetate 95:5) to afford (1-bromomethyl)-4-chlorobenzene **4.2** as a white powder (23.2 g, 94 %); mp. 48-50°C; ν_{max} (film)/cm^{-1} 3031, 2969, 1596, 1492, 1407, 1225, 1201, 1093, 1015, 831, 599; [Found: $[M]^+$ (EI^+) 203.9333, C_7H_6BrCl requires $[M]^+$, 203.9336]; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.46 (2H, s, CH_2), 7.33 (4H, m, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 32.4 (CH_2), 129.0 (CH), 130.4 (CH), 134.3 (C), 136.3 (C).

Preparation of (4-chlorobenzyl)triphenylphosphonium bromide **4.3**

This reaction has been carried out by S.P.Y. Cutulic.[66]

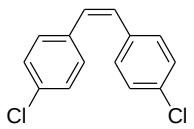


Triphenylphosphine (20.6 g, 78 mmol, 1.05 eq.) was added to a solution of (1-bromomethyl)-4-chlorobenzene **4.2** (15.41 g, 75 mmol, 1 eq.) in toluene (75 mL). The resulting solution was then heated to 100°C overnight. The resulting white solid was filtered off and successively washed with toluene (2 x 100 mL) and diethyl ether (3 x 100 mL). The resulting solid was dried under reduced pressure to afford (4-chlorobenzyl)triphenylphosphonium bromide **4.3** as a fine electrostatic white powder (34.7 g, 99 %); mp. 278-280°C; ν_{max} (film)/cm^{-1} 3071, 3043, 3005, 2988, 2866, 2847, 2773, 1587, 1483, 1436, 1111, 1088, 1011, 996; [Found: $[M\text{-}Br]^+$ (ES^+) 387.1060, $C_{25}H_{21}BrClP$ requires $[M\text{-}Br]^+$, 387.1064]; ^{1}H-NMR (400 MHz, DMSO) δ 5.25 (2H, d, J = 15.8 Hz, CH_2), 7.00 (2H, dd, J = 8.5 Hz, 2.5 Hz, Ar-H), 7.31 (2H, dd, J = 8.5 Hz and J = 0.7 Hz, Ar-H), 7.69-7.78 (12H, m, Ar-H), 7.89-7.93 (3H, m, Ar-H); ^{13}C-NMR (100 MHz, d^6-DMSO) δ 27.5 (d, $J_{C\text{-}P}$ = 46.6 Hz, CH_2), 117.6 (d, $J_{C\text{-}P}$ = 85.2 Hz, C), 127.04 (d, $J_{C\text{-}P}$ = 8.4 Hz, C), 128.3 (d, $J_{C\text{-}P}$ = 3.0 Hz, CH), 130.1 (d, $J_{C\text{-}P}$ = 12.4 Hz, CH), 132.5 (d, $J_{C\text{-}P}$ =

5.5 Hz, CH), 133.2 (d, J_{C-P} = 4.4 Hz, C), 134.0 (d, J_{C-P} = 10.2 Hz, CH), 135.1 (d, J_{C-P} = 3.0 Hz, CH).

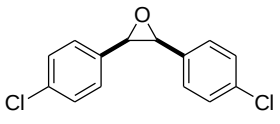
Preparation of *(Z)*-1,2-*bis*(4-chlorophenyl)ethene **4.4**

This reaction has been carried out by S.P.Y. Cutulic.[66]



Sodium hydroxide (4.32 g, 108 mmol, 2.4 eq.) was added as a freshly ground white powder to a solution of 4-chlorobenzaldehyde (6.32 g, 45 mmol, 1 eq.), (4-chlorobenzyl)triphenylphosphonium bromide **4.3** (25.2 g, 54 mmol, 1.2 eq.) and 18-crown-6 (1.2 g, 4.5 mmol, 0.1 eq.) in anhydrous dichloromethane (120 mL) under argon at -78°C. The reaction mixture was then stirred at -78°C under argon and slowly brought to room temperature and stirred under argon overnight. The reaction mixture was then extracted with a sat. NH_4Cl (3 x 100 mL) and brine (3 x 100 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford *(Z)*-1,2-*bis*(4-chlorophenyl)ethene **4.4** as a colourless oil that slowly crystallised into white needles (9.74 g, 87 %); mp. 44-46°C; ν_{max} (KBr)/cm^{-1} 3415, 3021, 2923, 1486, 1083, 1012, 877, 821, 736; [Found: $[M]^+$ (EI^+) 248.0154, $C_{14}H_{10}Cl_2$ requires $[M]^+$, 248.0154]; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.63 (2H, s, CH), 7.15 (4H, d, J = 6.5 Hz, Ar-H), 7.21 (4H, d, J = 6.5 Hz, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 128.5 (CH), 129.6 (CH), 130.1 (CH), 133.0 (C), 135.2 (C).

Preparation of *(2R*,3S*)*-2,3-*bis*(4-chlorophenyl)oxirane **2.24**[81]

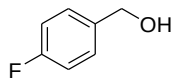


*m*CPBA (1.56 g, 9.03 mmol, 1.5 eq.) was added to a solution of *(Z)*-1,2-*bis*(4-chlorophenyl)ethene **4.4** (1.5 g, 6.02 mmol, 1 eq.) in dichloromethane (50 mL). The mixture was stirred at rt overnight. The reaction was quenched with sat. $Na_2S_2O_3$ (250 mL). The

aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined organic phases were washed with sat. $Na_2S_2O_3$ (2 x 50 mL) and brine (50 mL). The resulting organic phase was finally dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether – diethyl ether 9:1) to afford *(2R*,3S*)*-2,3-*bis*(4-chlorophenyl)oxirane **2.24** (1.51 g, 95 %) as a yellow oil; ν_{max}(film)/cm^{-1}: 1014, 1090, 1492, 2924; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.32 (2H, s, CH), 7.09 (4H, d, J = 8.8 Hz, ArH), 7.18 (4H, d, J = 8.8 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 59.1 (CH), 128.1 (CH), 128.2 (CH), 132.5 (C), 133.6 (C).

Preparation of (4-fluorophenyl)methanol **4.5**

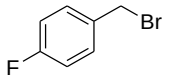
This reaction has been carried out by S.P.Y. Cutulic.[66]



Lithium aluminium hydride (5.69 g, 150 mmol, 1 eq.) was added in small portions to a solution of 4-fluorobenzaldehyde (18.62 g, 150 mmol, 1 eq.) in anhydrous THF (250 mL) at 0°C. The resulting suspension was then warmed to room temperature and stirred at room temperature overnight. Diethyl ether (200 mL) was added to the reaction mixture and the reaction was successively quenched with water (5.5 mL), aqueous sodium hydroxide solution 15 % (5.5 mL) and water (16.5 mL). Anhydrous magnesium sulfate was then added to the resulting suspension and the solid was filtered off. The filtrate was then concentrated under reduced pressure. The residue was taken in ethyl acetate (200 mL) and successively washed with water (3 x 150 mL) and brine (3 x 150 mL). The combined organic layers were eventually dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The resulting off-white solid was adsorbed onto silica and purified by column chromatography to afford (4-fluorophenyl)methanol **4.5** as a colourless oil (18.16 g, 96 %); ν_{max} (film)/cm^{-1} 3325, 2933, 2879, 1604, 1510, 1461, 1418, 1222, 1156, 1096, 1012, 823; [Found: (EI$^+$) $[M]^+$ 126.0485, C_7H_7FO requires M, 126.0483]; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 1H, OH), 4.60 (s, 2H, CH_2), 7.01-7.06-7.06 (m, 2H, Ar-H), 7.28-7.32 (m, 2H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 64.5 (CH_2), 115.3 (d, J_{C-F} = 21.4 Hz, CH), 128.7 (d, J_{C-F} = 8.0 Hz, CH), 136.6 (d, J_{C-F} = 3.2 Hz, CH), 162.3 (d, J_{C-F} = 244.2 Hz, C).

Preparation of (1-bromomethyl)-4-fluorobenzene **4.6**

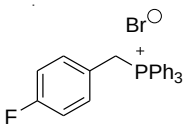
This reaction has been carried out by S.P.Y. Cutulic.[66]



Phosphorus tribromide (3.59 mL, 37.5 mmol, 0.5 eq.) was added dropwise to a solution of (4-fluorophenyl)methanol **4.5** (9.45 g, 75 mmol, 1 eq.) in diethyl ether (100 mL) at 0°C. The resulting mixture was then brought to room temperature and stirred at room temperature under argon overnight. The resulting solution was quenched with water (20 mL) and the organic phase was washed with water (3 x 100 mL) and brine (3 x 100 mL). The resulting organic extract was then dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was adsorbed onto silica and purified by column chromatography (petroleum ether - ethyl acetate 9:1) to afford (1-bromomethyl)-4-fluorobenzene **4.6** as a colourless oil (13.14 g, 94 %); ν_{max} (film)/cm^{-1} 3072, 3044, 2971, 1607, 1510, 1442, 1415, 1294, 1230, 1201, 1157, 1088, 1015, 848, 834; [Found: (EI$^+$) [M]$^+$ 187.9637, C_7H_7BrF requires M, 187.9639]; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.49 (s, 2H, CH_2), 7.02-7.07 (m, 2H, Ar-H), 7.37-7.40 (m, 2H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 32.7 (CH_2), 115.8 (d, J_{C-F} = 23 Hz, CH), 130.9 (d, J_{C-F} = 9 Hz, CH), 133.8 (d, J_{C-F} = 3 Hz, C), 162.6 (d, J_{C-F} = 247 Hz, C).

Preparation of 4-(fluorobenzyl)triphenylphosphonium bromide **4.7**

This reaction has been carried out by S.P.Y. Cutulic.[66]

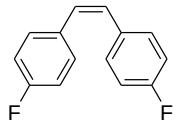


A solution of (1-bromomethyl)-4-fluorobenzene **4.6** (11.3 g, 60 mmol, 1 eq.) and triphenylphosphine (16.5 g, 63 mmol, 1.05 eq.) in toluene (50 mL) was heated to 100°C under argon overnight. The resulting suspension was cooled to room temperature and the white solid was filtered off and washed with toluene (50 mL) and diethyl ether (3 x 100 mL). The resulting solid was then dried under reduced pressure to afford 4-(fluorobenzyl)triphenylphosphonium bromide **4.7** as an electrostatic fine white powder (25.45 g, 94 %); mp. 280-282°C; ν_{max} (film)/cm^{-1} 3005, 2988, 2872, 2843, 2775, 1596, 1499,

1435, 1215, 1157, 1112, 856; [Found: (ES^+) $[M-Br]^+$ 371.1355, $C_{25}H_{21}BrFP$ requires $[M-Br]^+$, 371.1359]; ^{1}H-NMR (400 MHz, d^6-DMSO) δ 5.22-5.26 (2H, d, J_{H-P} = 15.4 Hz, CH_2), 7.00-7.11 (4H, m, Ar-H), 7.67-7.77 (12H, m, Ar-H), 7.89-7.92 (3H, m, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 27.8 (d, J_{C-P} = 46.9 Hz, CH), 116.3 (d, J_{C-F} = 21.8 Hz, CH), 118.1 (d, J_{C-P} = 84.8 Hz, C), 124.6 (dd, J_{C-P} = 8.3 Hz, J_{C-F} = 2.8 Hz, C), 130.6 (d, J_{C-P} = 12.9 Hz, CH), 133.3 (m, CH), 134.5 (d, J_{C-P} = 9.8 Hz, CH), 135.6 (CH), 162.4 (dd, J_{C-F} = 244.0 Hz, J_{C-P} = 4.2 Hz, C).

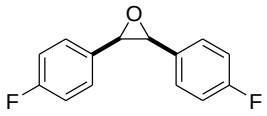
Preparation of *(Z)*-1,2-*bis*(4-fluorophenyl)ethane **4.8**

This reaction has been carried out by S.P.Y. Cutulic.[66]



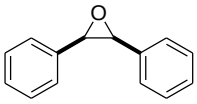
Sodium hydroxide (4.32 g, 108 mmol, 2.4 eq.) was added as a freshly ground white powder to a solution of 4-fluorobenzaldehyde (5.58 g, 45 mmol, 1 eq.), 4-(fluorobenzyl)triphenylphosphonium bromide **4.7** (24.37 g, 54 mmol, 1.2 eq.) and 18-crown-6 (1.19 g, 4.5 mmol, 0.1 eq.) in anhydrous dichloromethane (120 mL) at -78°C. The resulting solution was then stirred at -78°C for 3 h, warmed to room temperature and stirred at room temperature overnight. The resulting solution was then washed with an aqueous ammonium chloride solution (3 x 100 mL) and brine (3 x 100 mL). The resulting organic layer was then dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography on silica gel (petroleum ether) to afford *(Z)*-1,2-*bis*(4-fluorophenyl)ethene **4.8** as a colourless liquid that slowly crystallised into white needles (8.46 g, 87 %); mp. 104-106°C; ν_{max} (film)/cm^{-1} 3068, 3051, 1595, 1507, 1421, 1219, 1203, 840, 829; [Found: $(EI)^+$ $[M]^+$ 216.0743, $C_{14}H_{10}F_2$ requires $[M]^+$, 216.0743]; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.53 (2H, s, CH), 6.91-6.98 (m, 4H, Ar-H), 7.17-7.24 (m, 4H, Ar-H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 115.2 (d, J_{C-F} = 21.3 Hz, CH), 129.1 (CH), 130.5 (d, J_{C-F} = 8.2 Hz, CH), 133.0 (d, J_{C-F} = 3.7 Hz, C), 161.9 (d, J_{C-F} = 245.7 Hz, C).

Preparation of *(2R*,3S*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9**[85]



*m*CPBA (1.80 g, 10.41 mmol, 1.5 eq.) was added to a solution of *(Z)*-1,2-*bis*(4-fluorophenyl)ethene **4.8** (1.5 g, 6.94 mmol, 1 eq.) in dichloromethane (50 mL). The mixture was stirred at rt overnight. The reaction was quenched with sat. $Na_2S_2O_3$ (250 mL). The aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined organic phases were washed with sat. $Na_2S_2O_3$ (2 x 50 mL) and brine (50 mL). The resulting organic phase was finally dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether – diethyl ether 9:1) to afford *(2R*,3S*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9** (1.29 g, 80 %) as a yellow liquid; [Found: (EI^+) M^+ 232.0694. $C_{14}H_{10}F_2O$ requires M, 232.0694]; ν_{max}(film)/cm^{-1}: 559, 784, 1223, 1512, 2982, 3073; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 4.32 (2H, s, CH), 6.89 (4H, d, J = 8.8 Hz, ArH), 7.12 (4H, d, J = 8.8 Hz, ArH) ; ^{13}C-NMR (100 MHz, $CDCl_3$) δ 59.1 (CH), 114.9 (CH, d, $J_{C\text{-}F}$ = 15.9 Hz), 128.5 (CH, d, $J_{C\text{-}F}$ = 6.5 Hz), 130.0 (C), 162.2 (C, d, $J_{C\text{-}F}$ = 196.2 Hz); *m/z* (EI^+) 232 [M^+, 30 %], 203 (100), 201 (27), 183 (32), 123 (49), 108 (72), 107 (73), 94 (35).

Preparation of *(2R*,3S*)*-2,3-diphenyloxirane **2.28**[82]

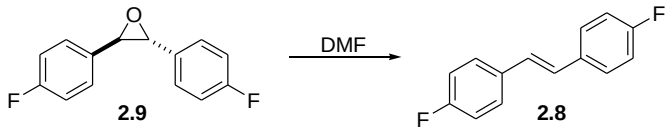


*m*CPBA (1.81 g, 10.5 mmol, 1.5 eq.) was added to a solution of *cis*-stilbene (1.25 mL, 7.0 mmol, 1 eq.) in dichloromethane (50 mL). The mixture was stirred at rt overnight. The reaction was quenched with sat. $Na_2S_2O_3$ (250 mL). The aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined organic phases were washed with sat. $Na_2S_2O_3$ (2 x 50 mL) and brine (50 mL). The resulting organic phase was finally dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether – diethyl ether 9:1) to afford *(2R*,3S*)*-2,3-diphenyloxirane **2.28** (1.59 g, 96 %) as a colourless liquid; [Found: (CI^+)

$(M+NH_4)^+$ 214.1224. $C_{14}H_{12}O$ requires $M+NH_4$, 214.1226]; ν_{max}(film)/cm^{-1}: 697, 897, 1497, 2977, 3031; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.37 (2H, s, CH), 7.18 (10H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 59.8 (CH), 126.9 (CH), 127.5 (CH), 127.8 (CH), 134.4 (C); *m/z* (CI^+) 214 [$(M+NH_4)^+$, 87 %], 197 [$(M+H)^+$, 35], 180 (44), 108 (52), 98 (62), 94 (81), 84 (79), 72 (100), 70 (66).

4.2.2. Epoxide cleavages and product characterisations

Cleavage of *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9**



First attempt: rt, in situ method, 1.5 eq. of donor salt

DMAP-derived salt **1.54** (810.4 mg, 1.5 mmol, 1.5 eq.) and NaH (0.6 g, 15 mmol, 15 eq.) were washed with hexane (3 x 15 mL). 15 mL dry DMF was added (purple solution) and the mixture was stirred 4h30 at rt. After centrifuged, the mixture was transferred via canula to *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9** (232 mg, 1 mmol, 1 eq.). The mixture was stirred overnight at rt. The mixture was extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford the starting material, *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9** (220.4 mg, 95 %).

Second attempt: 100°C, in situ method, 1.5 eq. of donor salt

DMAP-derived salt **1.54** (810.4 mg, 1.5 mmol, 1.5 eq.) and NaH (0.6 g, 15 mmol, 15 eq.) were washed with hexane (3 x 15 mL). 15 mL dry DMF was added (purple solution) and the mixture was stirred 4h30 at rt. After centrifuged, the mixture was transferred via canula to *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9** (232 mg, 1 mmol, 1 eq.). The mixture was stirred 3 days at 100°C. The mixture was extracted with ethyl acetate (3 x 25 mL). The

combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford a mixture between the cleaved product, *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8**, and the starting material, *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9**, 2:1 169.4 mg.

Third attempt: 100°C, in situ method, 3 eq. of donor salt

DMAP-derived salt **1.54** (810.4 mg, 1.5 mmol, 3 eq.) and NaH (0.6 g, 15 mmol, 15 eq.) were washed with hexane (3 x 15 mL). 15 mL dry DMF was added (purple solution) and the mixture was stirred 4h30 at rt. After centrifuged, the mixture was transferred via canula to *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9** (116 mg, 0.5 mmol, 1 eq.). The mixture was stirred overnight at 100°C. The mixture was extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford a mixture between the cleaved product, *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8**, and the starting material, *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9**, 1:4 63.7 mg.

Fourth attempt: 100°C, isolated donor, 1.5 eq. of donor

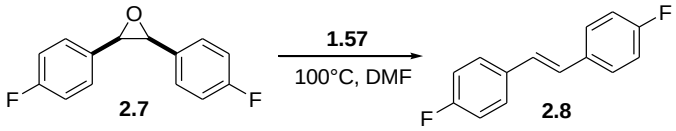
In an inert atmosphere, isolated DMAP-derived donor **1.57** (255.6 mg, 0.9 mmol, 1.5 eq.) in dry DMF (5 mL) was added to *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9** (139.2 mg, 0.6 mmol, 1 eq.). The mixture was stirred overnight at 100°C. The mixture was extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford a mixture between the cleaved product, *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8**, and the starting material, *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9**, 55:45, 88.6 mg.

Fifth attempt: 100°C, isolated donor, 3 eq. of donor

In an inert atmosphere, isolated DMAP-derived donor **1.57** (853.2 mg, 3 mmol, 3 eq.) in dry DMF (15 mL) was added to *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.9** (232.3 mg, 1

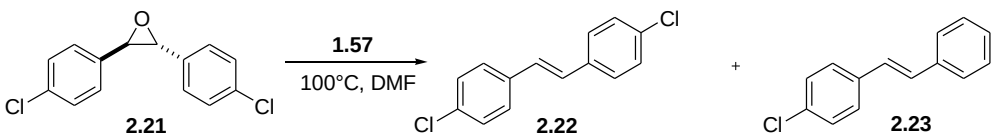
mmol, 1 eq.). The mixture was stirred 19h at 100°C. The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (hexane - diethyl ether 95:5) to afford *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8** (31 mg, 14 %); [Found: (EI^+) M^+ 216.0745. $C_{14}H_{10}F_2$ requires M, 216.0745]; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.99 (2H, s, CH), 7.06 (4H, d, J = 8.8 Hz, ArH), 7.47 (4H, d, J = 8.8 Hz, ArH).

Cleavage of *(2R*,3S*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7**



In an inert atmosphere, isolated DMAP-derived donor **1.57** (512.0 mg, 1.8 mmol, 3 eq.) in dry DMF (10 mL) was added to *(2R*,3S*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7** (139.4 mg, 0.6 mmol, 1 eq.). The mixture was stirred 22h at 100°C. The reaction was quenched with brine (5 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (hexane) to afford *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8** (13.4 mg, 21 %); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.99 (2H, s, CH), 7.06 (4H, d, J = 8.8 Hz, ArH), 7.47 (4H, d, J = 8.8 Hz, ArH).

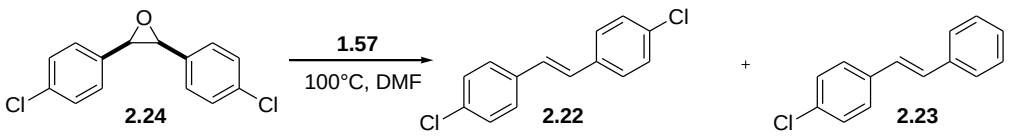
Cleavage of *(2R*,3R*)*-2,3-*bis*(4-chlorophenyl)oxirane **2.21**



In an inert atmosphere, isolated DMAP-derived donor **1.57** (853.2 mg, 3 mmol, 3 eq.) in dry DMF (15 mL) was added to *(2R*,3R*)*-2,3-*bis*(4-chlorophenyl)oxirane **2.21** (265.2 mg, 1 mmol, 1 eq.). The mixture was stirred 16h at 100°C. The reaction was quenched with brine

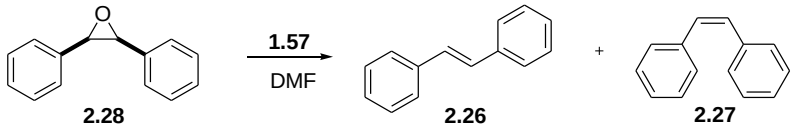
(15 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (hexane - diethyl ether 95:5) to afford a mixture of *(E)*-1,2-*bis*(4-chlorophenyl)ethene **2.22** and *(E)*-1-(4-chlorostyryl)benzene **2.23** 68 : 32 (48.6 mg); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.03 (2H, **2.22**, s, CH), 7.08 (2H, **2.23**, d, J = 2.8 Hz, CH), 7.29 (4H, **2.23**, d, J = 8 Hz, ArH), 7.33 (4H, **2.22**, d, J = 10.5 Hz, ArH), 7.39 (4H, **2.23**, d, J = 7.4 Hz, ArH), 7.43 (4H, **2.22**, d, J = 10.5 Hz, ArH), 7.52 (1H, **2.23**, d, J = 7.4 Hz, ArH).

Cleavage of *(2R*,3S*)*-2,3-*bis*(4-chlorophenyl)oxirane **2.24**



In an inert atmosphere, isolated DMAP-derived donor **1.57** (512.0 mg, 1.8 mmol, 3 eq.) in dry DMF (10 mL) was added to *(2R*,3S*)*-2,3-*bis*(4-chlorophenyl)oxirane **2.24** (159.1 mg, 0.6 mmol, 1 eq.). The mixture was stirred 16h at 100°C. The reaction was quenched with brine (5 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (hexane) to afford a mixture of *(E)*-1,2-*bis*(4-chlorophenyl)ethene **2.22** and *(E)*-1-(4-chlorostyryl)benzene **2.23** 56 : 44 (24.3 mg); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.03 (2H, **2.22**, s, CH), 7.08 (2H, **2.23**, d, J = 2.8 Hz, CH), 7.29 (4H, **2.23**, d, J = 8 Hz, ArH), 7.33 (4H, **2.22**, d, J = 10.5 Hz, ArH), 7.39 (4H, **2.23**, d, J = 7.4 Hz, ArH), 7.43 (4H, **2.22**, d, J = 10.5 Hz, ArH), 7.52 (1H, **2.23**, d, J = 7.4 Hz, ArH).

Cleavage of *(2R*,3S*)*-2,3-diphenyloxirane **2.28**



First attempt: 100 °C, 3 eq. donor

In an inert atmosphere, isolated DMAP-derived donor **1.57** (255.6 mg, 0.9 mmol, 3 eq.) in dry DMF (5 mL) as added to *(2R*,3S*)*-2,3-diphenyloxirane **2.28** (58.9 mg, 0.3 mmol, 1 eq.). The mixture was stirred 19h at 100°C. The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (hexane - diethyl ether 95:5) to afford the starting material *(2R*,3R*)*-2,3-diphenyloxirane **2.28** (41.1 mg, 91 %); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.37 (2H, s, CH), 7.18 (10H, m, ArH).

Second attempt: rt, UV light, 1.5 eq. donor

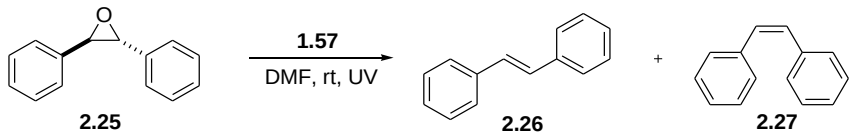
In an inert atmosphere, isolated DMAP-derived donor **1.57** (568.8 mg, 2 mmol, 2 eq.) in dry DMF (15 mL) was added to *(2R*,3S*)*-2,3-diphenyloxirane **2.28** (196.3 mg, 1 mmol, 1 eq.). The mixture was stirred 40h at rt under UV light. The reaction was quenched with brine (15 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (hexane - diethyl ether 95:5) to afford a mixture of *(E)*-1,2-diphenylethene **2.26** and *(Z)*-1,2-diphenylethene **2.27** 99 : 1 (23.9 mg, 13 %); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.63 (2H, **2.27**, s, CH), 7.15 (2H, **2.26**, s, CH), 7.29 (2H, d, J = 7.2 Hz, ArH), 7.39 (4H, d, J = 7.2 Hz, ArH), 7.55 (4H, d, J = 7.2 Hz, ArH).

Blank experiment of the second attempt

In an inert atmosphere, a solution of degassed DMF (15 mL) was added to *(2R*,3S*)*-2,3-diphenyloxirane **2.28** (196.3 mg, 1 mmol, 1 eq.). The reaction mixture was stirred under UV-light at rt under cooling at the same time as the reaction with the donor. The reaction was quenched with brine (15 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under

reduced pressure. The crude product was then adsorbed onto silica and purified by column chromatography (hexane - diethyl ether 9:1) to afford the starting material *(2R*,3S*)*-2,3-diphenyloxirane **2.28** (116.7 mg, 90 %); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.37 (2H, s, CH), 7.18 (10H, m, ArH).

Cleavage of *(2R*,3R*)*-2,3-diphenyloxirane **2.25**



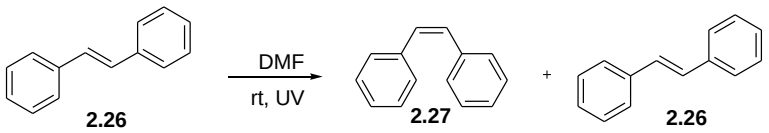
In an inert atmosphere, isolated DMAP-derived donor **1.57** (426.6 mg, 1.5 mmol, 1.5 eq.) in dry DMF (15 mL) was added to *(2R*,3R*)*-2,3-diphenyloxirane **2.25** (196.3 mg, 1 mmol, 1 eq.). The mixture was stirred 55h at rt under UV light. The reaction was quenched with brine (15 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (hexane) to afford a mixture of *(E)*-1,2-diphenylethene **2.26** and *(Z)*-1,2-diphenylethene **2.27** 97 : 3 (39.4 mg, 22 %); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.63 (2H, **2.27**, s, CH), 7.15 (2H, **2.26**, s, CH), 7.27 (2H, t, *J* = 7.2 Hz, ArH), 7.40 (4H, t, *J* = 7.2 Hz, ArH), 7.56 (4H, d, *J* = 7.2 Hz, ArH).

Blank experiment

In an inert atmosphere, a solution of degassed DMF (15 mL) was added to *(2R*,3S*)*-2,3-diphenyloxirane **2.25** (196.3 mg, 1 mmol, 1 eq.). The reaction mixture was stirred under UV-light at rt under cooling at the same time as the reaction with the donor. The reaction was quenched with brine (15 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was then adsorbed onto silica and purified by column chromatography (hexane - diethyl ether 9:1) to afford the starting material *(2R*,3S*)*-2,3-diphenyloxirane **2.25** (180.6 mg, 92 %); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.99 (2H, s, CH), 7.06 (4H, d, *J* = 8.8 Hz, ArH), 7.47 (4H, d, *J* = 8.8 Hz, ArH).

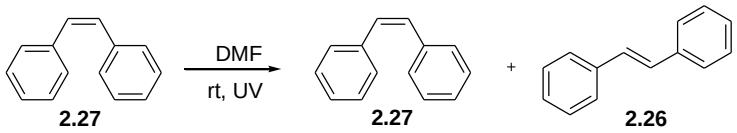
Isomerisation of stilbene

*Isomerisation of (Z)-1,2-diphenylethene **2.26***



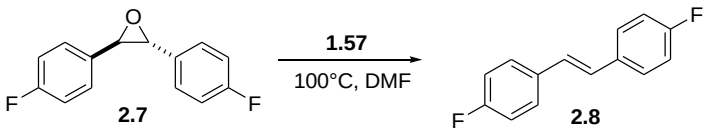
In an inert atmosphere, a solution of degassed DMF (5 mL) was added to *(E)*-1,2-diphenylethene **2.26** (54 mg, 0.3 mmol, 1 eq.). The reaction mixture was stirred under UV-light at rt under cooling 5 days. The reaction was quenched with brine (15 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford a mixture of *(E)*-1,2-diphenylethene **2.26** and *(Z)*-1,2-diphenylethene **2.27** 48:52 (54 mg); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 6.62 (2H, **2.27**, s, CH), 7.05-7.40 (20H, **2.27** + **2.28**, m), 7.53 (2H, **2.26**, d, J = 7.2 Hz, ArH).

*Isomerisation of (Z)-1,2-diphenylethene **2.27***



In an inert atmosphere, a solution of degassed DMF (5 mL) was added to *(Z)*-1,2-diphenylethene **2.27** (54 mg, 0.3 mmol, 1 eq.). The reaction mixture was stirred under UV-light at rt under cooling 5 days. The reaction was quenched with brine (15 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford a mixture of *(E)*-1,2-diphenylethene **2.26** and *(Z)*-1,2-diphenylethene **2.27** 42:58 (54 mg); ^{1}H- NMR (400 MHz, $CDCl_3$) δ 6.62 (2H, **2.27**, s, CH), 7.05-7.40 (20H, **2.27** + **2.28**, m), 7.53 (2H, **2.26**, d, J = 7.2 Hz, ArH).

Low yield investigations



Reaction solvent = toluene

In an inert atmosphere, isolated DMAP-derived donor **1.57** (170.4 mg, 0.6 mmol, 2 eq.) in dry toluene (5 mL) was added to *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7** (69.8 mg, 0.3 mmol, 1 eq.). The mixture was stirred 21h at 100°C. The reaction was quenched with brine (15 mL). The mixture was extracted with toluene (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford a mixture (68.0 mg) of *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8** and *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7** 39:61.

Reaction solvent = ether

In an inert atmosphere, isolated DMAP-derived donor **1.57** (170.4 mg, 0.6 mmol, 2 eq.) in dry ether (5 mL) was added to *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7** (69.8 mg, 0.3 mmol, 1 eq.). The mixture was stirred 15h at 100°C. The reaction was quenched with brine (15 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford a mixture (22.1 mg) of *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8**, *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7** 40:60.

Extraction solvent = toluene

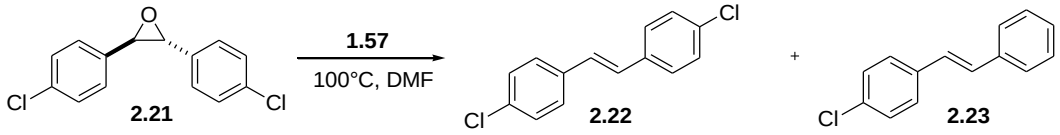
In an inert atmosphere, isolated DMAP-derived donor **1.57** (170.4 mg, 0.6 mmol, 2 eq.) in dry toluene (5 mL) was added to *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7** (69.8 mg, 0.3 mmol, 1 eq.). The mixture was stirred 21h at 100°C. The reaction was quenched with brine (15 mL). The mixture was extracted with toluene (3 x 25 mL). The combined organic phases

were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford a mixture (68.0 mg) of *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8** and *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7** 39:61.

Extraction solvent = ethyl acetate

In an inert atmosphere, isolated DMAP-derived donor **1.57** (255.6 mg, 0.9 mmol, 1.5 eq.) in dry DMF (5 mL) as added to *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7** (139.2 mg, 0.6 mmol, 1 eq.). The mixture was stirred 19h at 100°C. The mixture was extracted with ethyl acetate (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford a mixture (88.6 mg) of *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8** and *(2R*,3R*)*-2,3-*bis*(4-fluorophenyl)oxirane **2.7** 55:45.

<u>Concentration effect for the *(2R*,3R*)*-2,3-*bis*(4-chlorophenyl)oxirane **2.21**</u>

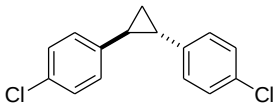


In an inert atmosphere, isolated DMAP-derived donor **1.57** (511.2 mg, 1.8 mmol, 3 eq.) in dry DMF (5 mL) was added to *(2R*,3R*)*-2,3-*bis*(4-chlorophenyl)oxirane **2.21** (159.6 mg, 0.6 mmol, 1 eq.). The mixture was stirred 16h at 100°C. The reaction was quenched with brine (15 mL). The mixture was extracted with diethyl ether (3 x 25 mL). The combined organic phases were washed with water (2 x 25 mL) and brine (25 mL). The resulting organic phase was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford a mixture of *(E)*-1,2-*bis*(4-chlorophenyl)ethene **2.22** and *(E)*-1-(4-chlorostyryl)benzene **2.23** (39.7 mg); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.03 (2H, s, CH), 7.07 (2.40H, d, *J* = 2.8 Hz, CH), 7.28-7.53 (18.5H, m, ArH).

4.3 Experimental section for the cyclopropane study

4.3.1. Preparation of reagents and substrates

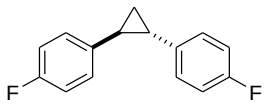
Preparation of *(1S*,2S*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.22**[86]



A solution of TFA (1.85 mL, 24.08 mmol, 4 eq.) in 6 mL dry dichloromethane was added at 5°C *very slowly* to a solution of diethyl zinc (24 mL, 24.08 mmol, 6 eq.) in 13 mL dry DCM and the mixture was stirred at 5°C for 30 min. A solid was formed on the side of the flask. A solution of diiodomethane (2 mL, 24.08 mmol, 6 eq.) in 6 mL dry DCM was added to the previous mixture at 5°C. The resulting mixture was stirred 40 min at 5°C. A solution of *(E)*-1,2-*bis*(4-chlorophenyl)ethene **2.20** (1.5 g, 6.02 mmol, 1 eq.) in 6 mL dry DCM was then added to the mixture at 5°C. The resulting mixture was stirred 19h at rt. The reaction was quenched with sat. NH_4Cl (50 mL). The aqueous layer was extracted with DCM (3 x 100 mL). The combined organic layers were washed with sat. $NaHCO_3$ (2 x 50 mL), water (50 mL) and eventually brine (2 x 50 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The same reaction conditions were applied again to the crude product. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford a mixture of *(1S*,2S*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.22** and *(E)*-1,2-*bis*(4-chlorophenyl)ethene **2.20** (1.34 g) as a white solid. This mixture was dissolved in DCM (10 mL). *m*CPBA (180 mg) was added to the mixture which was stirred overnight at rt. The reaction was quenched with sat. $Na_2S_2O_3$ (100 mL). The aqueous layer was extracted with DCM (2 x 50 mL). The combined organic layers were washed with sat. $Na_2S_2O_3$ (2 x 50 mL) and brine (50 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford *(1S*,2S*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.22** (1.15 g, 73 %) as a white solid; [Found: (EI^+) M^+ 262.0310. $C_{15}H_{12}Cl_2$ requires M, 262.0310]; mp: 78-80°C (lit.[87] 83°C); ν_{max}(film)/cm^{-1}: 513, 819, 1013, 1093, 1494, 2924, 3027; ^{1}H-NMR (400 MHz, $CDCl_3$)

δ 1.43 (2H, t, J = 7.2 Hz, CH_2), 2.11 (2H, t, J = 7.2 Hz, CH), 7.07 (4H, d, J = 8.4 Hz, ArH), 7.27 (4H, d, J = 8.4 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 18.1 (CH_2), 27.4 (CH), 127.1 (CH), 128.5 (CH), 131.5 (C), 140.6 (C). *m/z* (EI^+) 266 [M^+, ^{37}Cl, 9 %], 264 [M^+, ^{35}Cl, ^{37}Cl, 49], 262 [M^+, ^{35}Cl, 70], 229 (38), 227 (100), 194 (29), 192 (41), 149 (29), 125 (39), 115 (48).

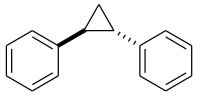
Preparation of *(1S*,2S*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.8**[88]



A solution of TFA (2.15 mL, 27.78 mmol, 4 eq.) in 7 mL dry dichloromethane was added at 5°C *very slowly* to a solution of diethyl zinc (28 mL, 27.78 mmol, 4 eq.) in 15 mL dry DCM and the mixture was stirred at 5°C 35 min – formation of a solid on the side of the flask. A solution of diiodomethane (2.2 mL, 27.78 mmol, 4 eq.) in 7 mL dry DCM was added to the previous mixture at 5°C. The resulting mixture was stirred 35 min at 5°C. A solution of *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8** (1.5 g, 6.95 mmol, 1 eq.) in 7 mL dry DCM was then added to the mixture at 5°C. The resulting mixture was stirred at rt overnight. The reaction was quenched with sat. NH_4Cl (50 mL). The aqueous layer was extracted with DCM (3 x 50 mL). The combined organic layers were washed with sat. $NaHCO_3$ (2 x 50 mL), water (50 mL) and brine (2 x 50 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The same conditions were applied again to the crude product. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford a mixture of *(1S*,2S*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.8** and *(E)*-1,2-*bis*(4-fluorophenyl)ethene **2.8** (1.35 g) as a white solid. This mixture was dissolved in DCM (30 mL). *m*CPBA (100 mg) were added to the mixture which was stirred overnight at rt. The reaction was quenched with sat. $Na_2S_2O_3$ (100 mL). The aqueous layer was extracted with DCM (2 x 100 mL). The combined organic layers were washed with sat. $Na_2S_2O_3$ (2 x 50 mL) and brine (50 mL). The resulting organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford *(1S*,2S*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.8** (1.21 g, 76 %) as a white solid; [Found: (EI^+) $(M-H)^+$

229.0826.[§] $C_{15}H_{12}F_2$ requires M-H, 229.0823]; mp: 67-68°C (lit.[88] 67-68°C); ν_{max}(film)/cm^{-1}: 743, 1229, 1510, 2925, 3008, 3046; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.38 (2H, t, J = 7.2 Hz, CH_2), 2.10 (2H, t, J = 7.2 Hz, CH), 6.99 (4H, d, J = 8.8 Hz, ArH), 7.11 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 17.8 (CH_2), 26.9 (CH), 115.2 (CH, J_{C-F} = 20.9 Hz), 127.2 (CH, J_{C-F} = 8.0 Hz), 137.87 (C), 161.3 (C, J_{C-F} = 242.0 Hz); *m/z* (EI$^+$) 230 [(M+H)$^+$, 100 %], 215 (22), 133 (59), 121 (20), 109 (31).

Preparation of *(1S*,2S*)*-1,2-diphenylcyclopropane **3.9**[89]

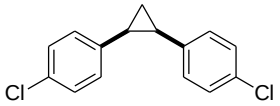


A solution of TFA (0.77 mL, 10 mmol, 2 eq.) in 5 mL dry dichloromethane was added at 5°C *very slowly* to a solution of diethyl zinc (10 mL, 10 mmol, 2 eq.) in 10 mL dry DCM and the mixture was stirred 1h at 5°C – formation of a solid on the side of the flask. A solution of diiodomethane (0.8 mL, 10 mmol, 2 eq.) in 5 mL dry DCM was added to the previous mixture at 5°C. The resulting mixture was stirred 20 min at 5°C. A solution of *(E)*-1,2-diphenylethene **2.24** (901.2 mg, 5 mmol, 1 eq.) in 5 mL dry DCM was then added to the mixture at 5°C. The resulting mixture was stirred 2h at rt. The reaction was quenched with sat. NH_4Cl (45 mL). The aqueous layer was extracted with DCM (3 x 100 mL). The combined organic layers were washed with sat. $NaHCO_3$ (2 x 50 mL), water (50 mL) and brine (2 x 50 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The same conditions were applied again to the crude product but with 4 eq. of each reagent. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford a mixture of *(1S*,2S*)*-1,2-diphenylcyclopropane **3.9** and *(E)*-1,2-diphenylethene **2.24** (640 mg, 3.3 mmol, 66%) as a yellow oil. This product was dissolved in DCM (10 mL). *m*CPBA (345 mg) was added to the mixture which was stirred overnight at rt. The reaction was quenched with sat. $Na_2S_2O_3$ (100 mL). The aqueous layer was extracted with DCM (2 x 50 mL). The combined organic layers were washed with sat. $Na_2S_2O_3$ (2 x 50 mL) and brine (50 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford *(1S*,2S*)*-1,2-

[§] The accurate mass measurement has been done on the [M-H]$^+$ ion because the M$^+$ ion was not isotopically pure as it will also contain the ^{13}C isotope of the [M-H]$^+$ ion.

diphenylcyclopropane **3.9** (398.1 mg, 41 %) as a colourless oil; [Found: (EI^+) $(M-H)^+$ 193.1011.** $C_{15}H_{14}$ requires M-H, 193.1012]; ν_{max}(film)/cm^{-1}: 696, 1499, 1603, 3029; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.47 (2H, t, J = 7.5 Hz, CH_2), 2.19 (2H, t, J = 7.5 Hz, CH), 7.19 (6H, m, ArH), 7.31 (4H, t, J = 7.5 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 18.2 (CH_2), 28.0 (CH), 125.7 (CH), 125.8 (CH), 128.4 (CH), 142.5 (C); *m/z* (EI^+) 194 [M^+, 100 %], 179 (32), 165 (8), 115 (34), 103 (10), 91 (14).

Preparation of *(1S*,2R*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.23**[86]

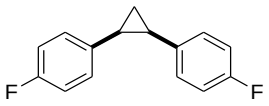


A solution of TFA (2.8 mL, 36.12 mmol, 6 eq.) in 6 mL dry dichloromethane was added at 5°C *very slowly* to a solution of diethyl zinc (36 mL, 36.12 mmol, 6 eq.) in 13 mL dry DCM and the mixture was stirred 30 mn at 5°Cs – formation of a solid on the side of the flask. A solution of diiodomethane (2.9 mL, 36.12 mmol, 6 eq.) in 6 mL dry DCM was added to the previous mixture at 5°C. The resulting mixture was stirred 40 min at 5°C. A solution of *(Z)*-1,2-*bis*(4-chlorophenyl)ethene **4.4** (1.5 g, 6.02 mmol, 1 eq.) in 6 mL dry DCM was then added to the previous mixture at 5°C. The resulting mixture was stirred 2h30 at rt. The reaction was quenched with sat. NH_4Cl (50 mL). The aqueous layer was extracted DCM (3 x 100 mL). The combined organic layers were washed with sat. $NaHCO_3$ (2 x 50 mL), water (50 mL) and brine (2 x 50 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was submitted again following the same procedure and using 4 eq. of diethyl zinc, TFA and diiodomethane. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford *(1S*,2R*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.23** (873 mg, 55 %) as a white solid; [Found: (EI^+) M^+ 262.0310. $C_{15}H_{12}Cl_2$ requires M, 262.0311]; mp: 47-49°C (lit.[80] 50-52°C); ν_{max}(film)/cm^{-1}: 836, 1012, 1089, 1492, 2924, 3019; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.31 (1H, t, J = 6 Hz, CH_2), 1.49 (1H, m, CH_2), 2.45 (2H, dd, J = 8.4 Hz, 6.4 Hz, CH), 6.85 (4H, d, J = 8.4 Hz, ArH), 7.08 (4H, d, J = 8.4 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 11.5 (CH_2), 23.7 (CH), 127.9 (CH), 130.2 (CH), 131.6 (C), 136.5 (C); *m/z* (EI^+) 266 [$M(^{37}Cl)^+$, 6 %], 264

** The accurate mass measurement has been done on the $[M-H]^+$ ion because the M^+ ion was not isotopically pure as it will also contain the ^{13}C isotope of the $[M-H]^+$ ion.

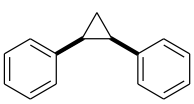
[M(^{35}Cl, ^{37}Cl)$^+$, 36], 262 [M(^{35}Cl)$^+$, 52], 229 [(M-Cl)$^+$, ^{37}Cl, 32], 227 [(M-Cl)$^+$, ^{35}Cl, 100], 192 (63), 165 (22), 148 (43), 124 (29), 115 (84), 94 (29), 88 (42), 74 (16), 62 (18).

Preparation of *(1S*,2R*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7**[88]



A solution of TFA (2.15 mL, 27.75 mmol, 4 eq.) in 7 mL dry dichloromethane was added at 5°C *very slowly* to a solution of diethyl zinc (28 mL, 27.75 mmol, 4 eq.) in 15 mL dry DCM and the mixture was stirred at 5°C 1h – formation of a solid on the side of the flask. A solution of diiodomethane (2.25 mL, 27.75 mmol, 4 eq.) in 7 mL dry DCM was added to the previous mixture at 5°C. The resulting mixture was stirred 40 min at 5°C. A solution of *(Z)*-1,2-*bis*(4-fluorophenyl)ethene **4.8** (1.5 g, 6.93 mmol, 1 eq.) in 7 mL dry DCM was then added to the previous mixture at 5°C. The resulting mixture was stirred 18h at rt. The reaction was quenched with sat. NH_4Cl (50 mL). The aqueous layer was extracted with DCM (3 x 100 mL). The combined organic layers were washed with sat. $NaHCO_3$ (2 x 50 mL), water (50 mL) and brine (2 x 50 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford *(1S*,2R*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7** (1.34 g, 84 %) as a colourless liquid; [Found: (EI$^+$) M$^+$ 230.0901. $C_{15}H_{12}F_2$ requires M, 230.0902]; ν_{max}(film)/cm^{-1}: 838, 1158, 1222, 1512, 1604, 3009; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.29 (1H, t, J = 6 Hz, CH_2), 1.47 (1H, m, CH_2), 2.44 (2H, dd, J = 8.7 Hz, 6 Hz, CH), 6.80 (4H, t, J = 9 Hz, ArH), 6.88 (4H, m, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 11.4 (CH_2), 23.3 (CH), 114.6 (CH, d, $J_{C\text{-}F}$ = 21.6 Hz), 130.3 (CH, d, $J_{C\text{-}F}$ = 7.8 Hz), 133.7 (C), 161.1 (C, d, $J_{C\text{-}F}$ = 242.6 Hz); *m/z* (EI$^+$) 230 [M$^+$, 100 %], 215 (32), 133 (86), 121 (30), 109 (49), 101 (19), 82 (22).

Preparation of *(1S*,2R*)*-1,2-diphenylcyclopropane **3.10**[89]



A solution of TFA (2.15 mL, 28 mmol, 4 eq.) in 7 mL dry dichloromethane was added at 5°C *very slowly* to a solution of diethyl zinc (28 mL, 28 mmol, 4 eq.) in 15 mL dry DCM and the mixture was stirred at 5°C 30 min – formation of a solid on the side of the flask. A solution of diiodomethane (2.25 mL, 28 mmol, 4 eq.) in 7 mL dry DCM was added to the previous mixture at 5°C. The resulting mixture was stirred 40 min at 5°C. A solution of *cis*-stilbene (1.25 g, 7 mmol, 1 eq.) in 7 mL dry DCM was then added to the mixture at 5°C. The resulting mixture was stirred 18h at rt. The reaction was quenched with sat. NH_4Cl (50 mL). The aqueous layer was extracted with DCM (3 x 100 mL). The combined organic layers were washed with sat. $NaHCO_3$ (2 x 50mL), water (50 mL) and brine (2 x 50 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The same conditions were applied again on the crude product. The residue was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford *(1S*,2R*)*-1,2-diphenylcyclopropane **3.10** (980.1 mg, 72 %) as a colourless liquid; [Found: (EI^+) M^+ 194.1084. $C_{15}H_{14}$ requires M, 194.1090]; ν_{max}(film)/cm^{-1}: 696, 776, 1458, 1603, 2925, 3027; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.40 (1H, t, J = 6.4 Hz, CH_2), 1.50 (1H, m, CH_2), 2.51 (2H, dd, J = 8.4 Hz, 6.4 Hz, CH), 6.97 (4H, m, ArH), 7.05 (2H, d, J = 7.2 Hz, ArH), 7.12 (4H, d, J = 7.2 Hz, ArH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 11.4 (CH_2), 24.3 (CH), 125.6 (CH), 127.6 (CH), 129.0 (CH), 138.4 (C); *m/z* (EI^+) 194 [M^+, 100 %], 179 (38), 165 (17), 115 (72), 91 (30), 76 (15), 64 (14).

4.3.2. General procedure for the isomerisation of cyclopropane substrates

General procedure for isomerisation reactions

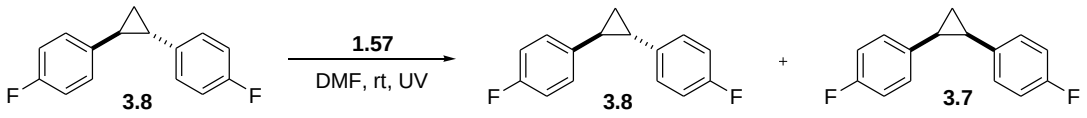
In an inert atmosphere, a solution of isolated donor **1.57** in degassed DMF (10 mL) was added to the appropriate substrate (0.6 mmol, 1 eq.). The reaction mixture was stirred under UV-light at rt under cooling. The reaction was quenched with water (5 mL). The reaction mixture was added to brine (100 mL) and extracted with diethyl ether (100 mL and 2 x 50 mL). The combined organic layers were then washed with water (3 x 50 mL) and brine (3 x 50 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford a mixture of compounds as reported. The ratio between the two isomers is determined by NMR.

General procedure for blank experiments:

In an inert atmosphere, a solution of degassed DMF (10 mL) was added to the appropriate substrate (0.6 mmol, 1 eq.). The reaction mixture was stirred under UV-light at rt under cooling at the same time as the reaction with the donor. The reaction was quenched with water (5 mL). The reaction mixture was added to brine (100 mL) and extracted with diethyl ether (100 mL and 2 x 50 mL). The combined organic layers were then washed with water (3 x 50 mL) and brine (3 x 50 mL). The resulting organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was then adsorbed onto silica and purified by column chromatography (petroleum ether) to afford the starting material.

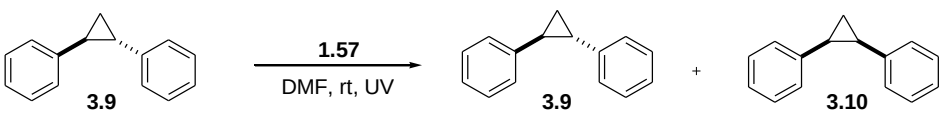
4.3.3. Isomerisation reactions and product characterisations

Isomerisation of *(1S*,2S*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.8**



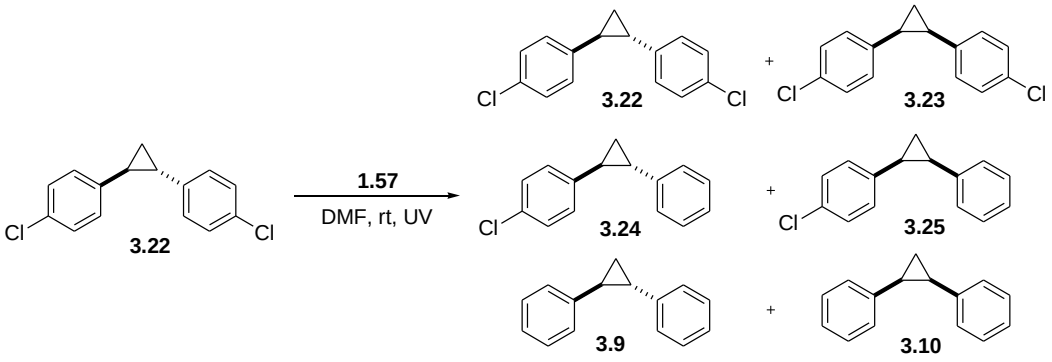
Application of the general procedure for isomerisation reactions to substrate **3.8** with 1.5 eq. (256 mg, 0.9 mmol) donor **1.57** for 17h provided a mixture (49.2 mg, 0.21 mmol, 35 %) of *(1S*,2R*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7** and *(1S*,2S*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.8**, respectively 5 : 95. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.38 (2H, t, J = 7.2 Hz, CH_2), 2.10 (2H, t, J = 7.2 Hz, CH), 6.99 (4H, tt, J = 8.8 Hz, ArH), 7.10 (4H, tt, J = 8.8 Hz); GC-MS: **3.7** (RT = 11.58 min, *m/z* = 230), **3.8** (RT = 12.10 min, *m/z* = 230). Blank experiment provided recovery of the starting material *(1S*,2S*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.8** (100.1 mg, 72 %).

Isomerisation of *(1S*,2S*)*-1,2-diphenylcyclopropane **3.9**



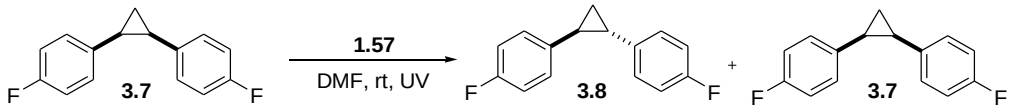
Application of the general procedure to substrate **3.9** with 3 eq. (512 mg, 1.8 mmol) donor **1.57** for 24h provided a mixture (103.0 mg, 0.53 mmol, 88 %) of *(1S*,2R*)*-1,2-diphenylcyclopropane **3.10** and *(1S*,2S*)*-1,2-diphenylcyclopropane **3.9**, respectively 5 : 95. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.54 (2H, t, J = 7.5 Hz, CH_2), 2.27 (2H, t, J = 7.5 Hz, CH), 7.23 (4H, d, J = 7.5 Hz, ArH), 7.27 (2H, t, J = 7.5 Hz, ArH), 7.39 (4H, t, J = 7.5 Hz, ArH); GC-MS: **3.10** (RT = 11.52 min, *m/z* = 194), **3.9** (RT = 12.09 min, *m/z* = 194). Blank experiment provided recovery of the starting material *(1S*,2S*)*-1,2-diphenylcyclopropane **3.9** (94.4 mg, 82 %).

Isomerisation of *(1S*,2S*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.22**



Application of the general procedure to substrate **3.22** with 1.5 eq. (256 mg, 0.9 mmol) donor **1.57** for 11h provided a mixture (41.5 mg) of 22 % *(1S*,2S*)*-1,2-diphenylcyclopropane **3.9**, 40 % *(1S*,2S*)*-1-(2-(4-chlorophenyl)cyclopropyl)benzene **3.24**, 34 % *(1S*,2S*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.22**, 1 % *(1S*,2R*)*-1,2-diphenylcyclopropane **3.10**, 2 % *(1S*,2R*)*--1-(2-(4-chlorophenyl)cyclopropyl)benzene **3.25**, 1 % *(1S*,2R*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.23**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.46 (6H, m, CH_2), 2.21 (6H, m, CH), 7.08 (6H, tt, J = 4.8 Hz, ArH), 7.20 (6H, m, ArH), 7.31 (9H, m, ArH); GC-MS: **3.10** (RT = 11.52 min, *m/z* = 194), **3.9** (RT = 12.09 min, *m/z* = 194), **3.25** (RT = 12.70 min, *m/z* = 228), **3.24** (RT = 13.25 min, *m/z* = 228), **3.23** (RT = 13.79 min, *m/z* = 262), **3.22** (RT = 14.37 min, *m/z* = 262). Blank experiment provided the recovery of the starting material *(1S*,2S*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.22** and its isomer *(1S*,2R*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.23**, respectively 98.4 : 1.6 (65.7 mg, 83 %).

Isomerisation of *(1S*,2R*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7**



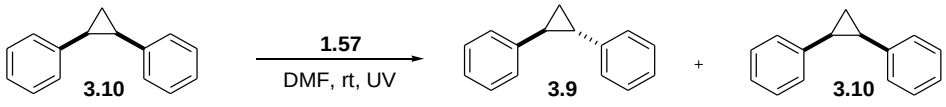
Reaction with 1.5 eq. donor

Application of the general procedure to substrate **3.7** with 1.5 eq. (256 mg, 0.9 mmol) donor **1.57** for 24h provided a mixture (80.9 mg, 0.35 mmol, 59 %) of *(1S*,2R*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7** and *(1S*,2S*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.8**, respectively 86 : 14. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.29 (1H, **3.7**, q, J = 6 Hz, CH_2), 1.38 (2H, **3.8**, t, J = 7.5 Hz, CH_2), 1.47 (1H, **3.7**, m, CH_2), 2.10 (2H, **3.8**, t, J = 7.5 Hz, CH), 2.44 (2H, **3.7**, dd, J = 8.7 Hz, J = 6 Hz, CH), 6.80 (4H, **3.7**, t, J = 8.5 Hz, ArH), 6.88 (4H, **3.7**, m, ArH), 6.99 (4H, **3.8**, t, J = 9 Hz, ArH), 7.11 (4H, **3.8**, m, ArH). Blank experiment provided the recovery of the starting material *(1S*,2R*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7** (127.8 mg, 92 %).

Reaction with 3 eq. donor

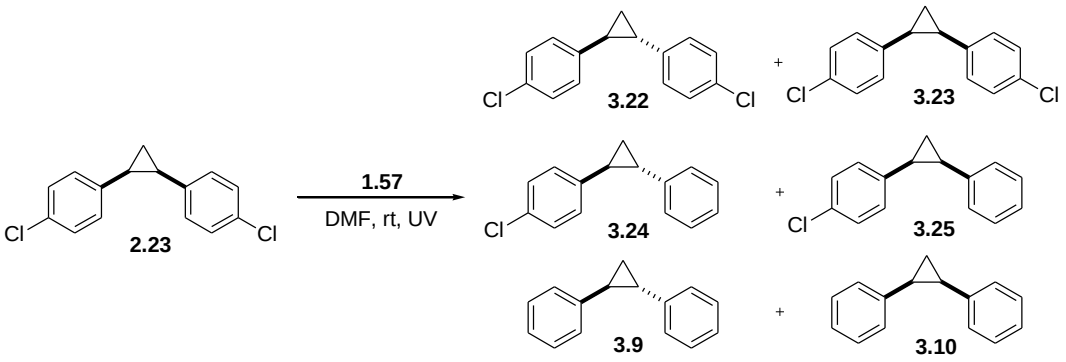
Application of the general procedure to substrate **3.7** with 3 eq. (512 mg, 1.8 mmol) donor **1.57** for 28h provided a mixture (136.7 mg) of *(1S*,2R*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.7** and *(1S*,2S*)*-1,2-*bis*(4-fluorophenyl)cyclopropane **3.8**, respectively 85 : 15. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 1.29 (1H, **3.7**, q, J = 6 Hz, CH_2), 1.38 (2H, **3.8**, t, J = 7.5 Hz, CH_2), 1.47 (1H, **3.7**, m, CH_2), 2.10 (2H, **3.8**, t, J = 7.5 Hz, CH), 2.44 (2H, **3.7**, dd, J = 8.7 Hz, J = 6 Hz, CH), 6.80 (4H, **3.7**, t, J = 8.5 Hz, ArH), 6.88 (4H, **3.8**, m, ArH), 6.99 (4H, **3.8**, t, J = 9 Hz, ArH), 7.11 (4H, **3.8**, m, ArH); GC-MS **3.7** (RT = 11.58 min, *m/z* = 230), **3.8** (RT = 12.10 min, *m/z* = 230).

Isomerisation of *(1S*,2R*)*-1,2-diphenylcyclopropane **3.10**



Application of the general procedure to substrate **3.10** with 3 eq. (512 mg, 1.8 mmol) donor **1.57** for 24h provided a mixture (92.2 mg, 0.47 mmol, 79 %) of *(1S*,2S*)*-1,2-diphenylcyclopropane **3.9** and *(1S*,2R*)*-1,2-diphenylcyclopropane **3.10**, respectively 19 : 81. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.40 (1H, q, J = 6.4 Hz, CH_2), 1.49 (1H, m, CH_2), 2.20 (0.5H, t, J = 7.2 Hz, CH), 2.52 (2H, dd, J = 8.4 Hz and J = 6.4 Hz, CH), 6.97 (4H, m, ArH), 7.05 (2H, tt, J = 7.2 Hz, ArH), 7.12 (4H, tt, J = 7.2 Hz, ArH), 7.16-7.22 (6H, m, ArH), 7.31 (4H, t, J = 7.5 Hz, ArH); GC-MS: **3.10** (RT = 11.52 min, *m/z* = 194), **3.9** (RT = 12.09 min, *m/z* = 194). Blank experiment provided the recovery of the starting material *(1S*,2R*)*-1,2-diphenylcyclopropane **3.10** (100.3 mg, 86 %).

Isomerisation of *(1S*,2R*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.23**



Application of the general procedure to substrate **3.23** with 1.5 eq. (256 mg, 0.9 mmol) donor **1.57** for 24h provided a mixture (91.1 mg) of 11 % *(1S*,2R*)*-diphenylcyclopropane **3.10**, 36 % *(1S*,2R*)*--1-(2-(4-chlorophenyl)cyclopropyl)benzene **3.25**, 43 % *(1S*,2R*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.23**, 2 % *(1S*,2S*)*-diphenylcyclopropane **3.9**, 4 % *(1S*,2S*)*--1-(2-(4-chlorophenyl)cyclopropyl)benzene **3.24** and 4 % *(1S*,2S*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.22**. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.36 (3H, **3.10**, **3.25**, **3.23**, m, CH_2), 1.47 (3H, **3.10**, **3.23**, **3.25**, m, CH_2), 2.15 (6H, **3.9**, **3.22**, **3.24**, m, CH), 2.48 (12H, m, CH), 6.87 (8H, tt, J = 6.4 Hz, ArH), 6.96 (4H, m, ArH), 7.06-7.14 (15H, m, ArH); GC-MS: **3.10** (RT = 11.52 min, *m/z* = 194), **3.9** (RT = 12.09 min, *m/z* = 194), **3.25** (RT = 12.69 min, *m/z* = 228), **3.24** (RT = 13.26 min, *m/z* = 228), **3.23** (RT = 13.78 min, *m/z* = 262), **3.22** (RT = 14.40 min, *m/z* = 262). Blank experiment provided the recovery of the starting material *(1S*,2R*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.23** and its isomer *(1S*,2S*)*-1,2-*bis*(4-chlorophenyl)cyclopropane **3.22** 95 : 5 (102.6 mg, 88 %).

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