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Part of this thesis has previously been published:

“Amidine Dications: Isolation and [Fe]-Hydrogenase-Related Hydrogenation” Corr, M. J.; Gibson, K. F.; Kennedy, A. R.; Murphy, J. A. *J. Am. Chem. Soc.* **2009**, *131*, 9174-9175.

“Amidine Dications as Superelectrophiles” Corr, M. J.; Gibson, K. F.; Kennedy, A. R.; Roydhouse, M. D.; Zhou, S. Z.; Murphy, J. A. *J. Am. Chem. Soc.* **2009**, *131*, 17980-17985.

ACKNOWLEDGEMENTS

First and foremost, I would like to thank Prof. John A. Murphy. His excellent guidance and advice, as well as his constant encouragement, has been of invaluable benefit throughout the entire project.

I would also like to thank Dr. Sheng-Ze Zhou and Dr. Mark Roydhouse for their advice and assistance throughout the project. I would also like to thank Prof. Jonathan Percy for his comments and advice as my internal examiner.

My thanks also to Dr. John Parkinson and Craig Irving for their help with NMR experiments, Pat Keating for help with GC-MS analysis, Dr. Tell Tuttle for computational analysis, Dr. Alan R. Kennedy for X-ray crystal structure analysis and Gavin Bain for assistance with the HPLC and hydrogenation experiments.

Thanks to everyone in the Murphy group, particularly Neil Findlay, for their encouragement, advice and assistance during the project and for making the laboratory an enjoyable place to work.

I would like to thank the EPSRC and WestCHEM for funding and the EPSRC National Mass Spectrometry service for mass spectrometry analyses.

Finally, a special thanks to my friends, family and Kirstyn for their love and support throughout my studies.

ABBREVIATIONS

AAS	atomic absorption spectroscopy
Ac	acetyl
Ala	alanine
allyl	allylic
Ar	aryl
atm	atmosphere(s)
B	base
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
Bn	benzyl
Boc	<i>tert</i> -butoxycarbonyl
Bu	butyl
Bz	benzoyl
c	cyclo
°C	degree(s) centigrade
cal	calorie(s)
cat	catalyst
cf.	<i>confere</i>
CH≡H₄MPT⁺	<i>N</i> ⁵ , <i>N</i> ¹⁰ -methenyltetrahydromethanopterin
CH₂=H₄MPT	<i>N</i> ⁵ , <i>N</i> ¹⁰ -methylenetetrahydromethanopterin
cm	centimetre(s)
conc.	concentrated
cond	conditions
Cys	cysteine
d	doublet
<i>d</i>	deuterium
Da	Dalton(s)
DABCO	1,4-diazabicyclo[2.2.2]octane
dba	dibenzylideneacetone
DCC	1,3-dicyclohexycarbodiimide
DCE	dichloroethane
DCM	dichloromethane
dec.	decomposition
dm	decimetre(s)
DMAP	<i>N,N</i> -dimethylaminopyridine
DMF	dimethylformamide
DMSO	dimethyl sulfoxide

ABBREVIATION

DPPF	diphenylphosphinoferrrocene
DTT	dithiothreitol
E	energy
<i>E.</i>	<i>Escherichia</i>
e^-	electron
EA	ethyl acetate
Ed	editor(s)
EDTA	ethylenediaminetetraacetic acid
ee	enantiomeric excess
<i>e.g.</i>	<i>exempli gratia</i>
EI	electron impact
EPR	electron paramagnetic resonance
equiv or eq	equivalent(s)
ESI	electrospray ionisation
e.s.r.	electron spin resonance
Et	ethyl
<i>et al.</i>	<i>et alii</i>
EXAFS	extended X-ray absorption fine structure
FeGP	iron guanosine monophosphate co-factor in H ₂ -forming methylenetetrahydromethanopterin dehydrogenase
g	gram(s)
G	Gibbs free energy
GC	gas chromatography
GC-MS	gas chromatography-mass spectrometry
h	hour(s)
H₀	Hammett acidity value
H₄MPT	5,6,7,8-tetrahydromethanopterin
HCl	hydrochloric acid
Hex	hexyl
His	histidine
Hmd	H ₂ -forming methylenetetrahydromethanopterin dehydrogenase
HOESY	heteronuclear Overhauser effect spectroscopy
HOMO	highest occupied molecular orbital
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	Hertz

ABBREVIATION

<i>i</i>	iso (branched chain)
ICP-MS	inductively coupled plasma mass spectrometry
<i>i.e.</i>	<i>id est</i>
inc.	including
Inc	incorporated
IR	infrared
JMOD	J modulation experiment
k	rate constant
K	degree(s) Kelvin
K₂₂₂	Kryptofix-222
KHMDS	potassium hexamethyldisilazide
kJ	kilojoules
l	litre(s) or liquid (as evident from the context)
LA	Lewis acid
LC-MS	liquid chromatography-mass spectrometry
LDA	lithium diisopropylamide
lit.	literature
LRMS	low resolution mass spectrometry
LUMO	lowest unoccupied molecular orbital
M	metal or molar or molecular ion (as evident from the context)
<i>M.</i>	Methanobacterium or Methanococcus or Methanogenic (as evident from the context)
m	multiplet (for ¹ H NMR spectra) or gradient (as evident from the context)
<i>m</i>	<i>meta</i>
Me	methyl
mg	milligram(s)
MHz	megahertz
min	minute(s)
ml	millilitre(s)
mol	mole(s)
mmol	millimole(s)
mp	melting point
MPT⁺	<i>N</i> ⁵ , <i>N</i> ¹⁰ -methenyltetrahydromethanopterin model substrate
Ms	methanesulfonyl

ABBREVIATIONS

MS	mass spectrometry
MW	microwave
<i>m/z</i>	ratio of mass to charge
<i>n</i>	normal (straight chain)
n	number of moles
N	normal
N.D.	not determined
nm	nanometres
NMIM	<i>N</i> -methylimidazole
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
Nuc	nucleophile
<i>o</i>	<i>ortho</i>
OEA	one-electron acceptor
ORTEP	Oak Ridge thermal ellipsoid plot
P	Page
<i>p</i>	<i>para</i>
Pd/C	palladium on activated carbon
PE	petroleum ether
<i>pH</i>	potential hydrogen
Ph	phenyl
Ph-MPT⁺	<i>N</i> ⁵ , <i>N</i> ¹⁰ -methenyltetrahydromethanopterin model substrate
<i>pK_a</i>	acid dissociation constant
ppm	parts per million
PPY	pyrrolidinopyridine
Pr	propyl
psi	pounds per square inch pressure
Py	pyridine
q	quartet (for ¹ H NMR spectra)
R	alkyl residue, unless otherwise specified
<i>R</i>	<i>rectus</i>
rds	rate-determining step
rec	recovered/recovery
rel	relative
r.t.	room temperature
RT	retention time

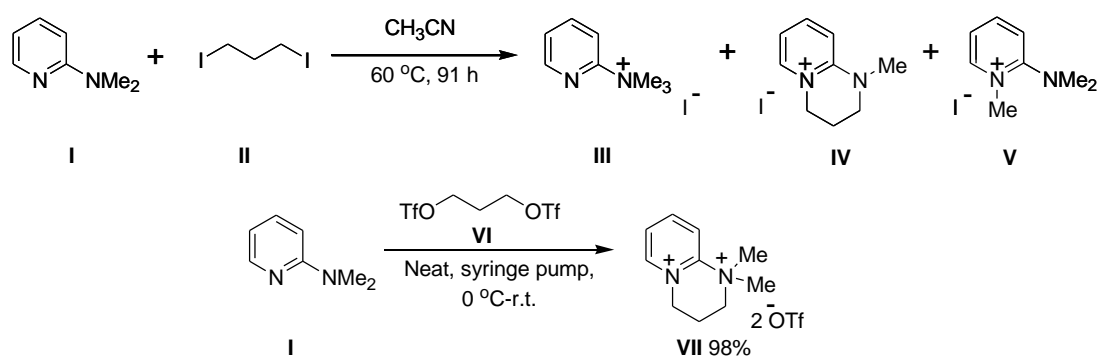
ABBREVIATIONS

s	singlet (for ^1H NMR spectra) or second or selectivity factor (as evident from the context)
S	<i>sinister</i>
Sat.	saturated
SED	super electron donor
SM	starting material
<i>t</i> or <i>tert</i>	tertiary
t	triplet (for ^1H NMR spectra) or time (as evident from the context)
$t_{1/2}$	half-life
T or Temp	temperature
TBME	<i>tert</i> -butyl methyl ether
TBS	<i>tert</i> -butyldimethylsilyl
TEA	triethylamine
THF	tetrahydrofuran
Tf	trifluoromethanesulfonyl
TFA	trifluoroacetic acid
TLC	thin layer chromatography
TMS	trimethylsilyl
Tol	tolyl or toluene (as evident from the context)
Ts	<i>para</i> -toluenesulfonyl
TXRF	total reflection X-ray fluorescence
U	unit of enzyme activity or unknown ligand (as evident from the context)
UV	ultraviolet
V	volts
Vol	volume
X	residue linked through a heteroatom, often halogen
Y	any residue, usually specified in text
3c-2e	3-centre, 2-electron
δ	chemical shift
τ	Torr

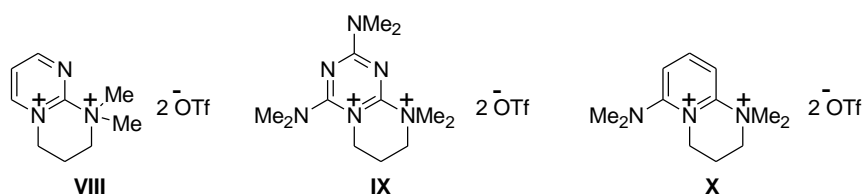
ABSTRACT

This thesis details the research conducted on the synthesis and reactivity of superelectrophilic di- and polycation salts based on 2-DMAP **I**.

The reaction of 2-DMAP **I** and 1,3-diiodopropane **II** proceeded unexpectedly to give products **III-V**, thought to occur via a dicationic intermediate. Investigation of the reaction conditions allowed for the successful synthesis of 2-DMAP disalt **VII** from 2-DMAP **I** and ditriflate **VI**.

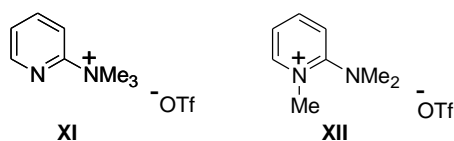


This represents the first time such a dication species has been synthesised and isolated. Based on the 2-DMAP unit, a variety of superelectrophile disalts have been synthesised (**VIII-X**) and characterised.

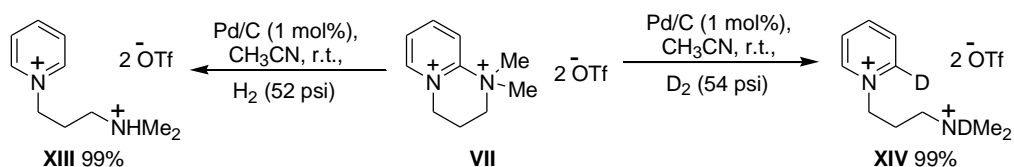


2-DMAP disalt **VII** showed enhanced reactivity over its monocationic counterparts **XI** and **XII** in the methylation of triphenylphosphine. In the 1:1 competition reaction with dimethyl sulfate in the methylation of triethylamine, 2-DMAP disalt **VII** and 2-dimethylaminopyrimidine disalt **VIII** showed greater reactivity than dimethyl sulfate, with disalt **VIII** being over 2.5 times more reactive.

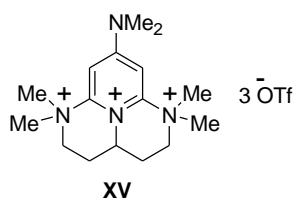
ABSTRACT



The reactivity of 2-DMAP disalt **VII** towards hydrogenation was also examined. It was found that in the presence of palladium on activated carbon (1 mol%), disalt **VII** underwent regiospecific hydrogenation (or deuteration) in the 2-position to give pyridinium disalt **XIII** (or **XIV** in the case of deuteration). In this case, 2-DMAP disalt **VII** showed similar reactivity to the substrate $\text{CH}\equiv\text{H}_4\text{MPT}^+$ in the [Fe]-hydrogenase enzyme. This significantly enhanced reactivity over monocationic salts provides support for the proposal that superelectrophilic activation of $\text{CH}\equiv\text{H}_4\text{MPT}^+$ in the enzyme active-site may contribute to the observed reaction of $\text{CH}\equiv\text{H}_4\text{MPT}^+$ with hydrogen gas.

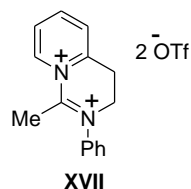
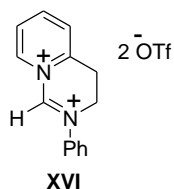


Superelectrophile trisalt **XV** was also synthesised. This trisalt showed slightly decreased reactivity compared to dimethyl sulfate in the methylation of triethylamine. The high reactivity of the tricationic species was tempered by the dimethylamino group in the 4-position, which served to decrease the reactivity by delocalising the positive charge on the pyridinium ring nitrogen.



ABSTRACT

Amidine disalts **XVI** and **XVII** based on amides have also been synthesised. Isolation of these superelectrophiles provides some evidence that such species may exist as intermediates in a variety of synthetic reactions cited in this work. Disalt **XVI** was shown to be an effective reagent for the formylation of anisole under mild conditions.



The synthesis and isolation of these superelectrophile disalts based on the 2-DMAP unit shows that highly reactive superelectrophiles can be obtained using standard laboratory conditions, which considerably widens the scope for synthesis and investigation of such species.