The photo-Friedel-Crafts acylation of Naphthoquinone in Alternative "Green" Media

and

The Photochemical Generation of Novel Biaryl Trifluoro Phthalonitriles, their Condensation to Phthalocyanines and Evaluation as Singlet Oxygen Sensitisers

by

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A thesis presented for the degree of Doctor of Philosophy (PhD)

at

Dublin City University

Under the supervision of;

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Dedicated to Mam and Dad

Declaration

I hereby certify that this material, which I now submit for assessment on the programme of study leading to the award of Ph.D. is entirely my own work, that I have exercised reasonable care to ensure that the work is original, and does not to the best of my knowledge breach any law of copyright, and has not been taken from the work of others save and to the extent that such work has been cited and acknowledged within the text of my work.

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Brian Murphy

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There is indeed great satisfaction in acquiring skill, in learning to thoroughly understand the qualities of the materials at hand and in learning to use the instruments we have – in the first place, our hands! - in an effective and controlled way.

- M. C. Escher

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List of abbreviations

4FPN	4-fluorophthalonitrile
^{13}C-NMR	carbon nuclear magnetic resonance
^{1}H-NMR	proton nuclear magnetic resonance
AIBN	azobisisobutyronitrile
BET	back electron transfer
C_2D_6CO	deuterated acetone
$CDCl_3$	deuterated chloroform
CO_2	carbon dioxide
conc.	concentrated
DBN	1,8-diazabicyclonon-5-ene
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
dd	doublet of a doublet
ddd	doublet of a doublet of a doublet
dq	doublet of a quartet
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DMAE	dimethylaminoethanol
DMF	dimethylformamide
DMSO-d_6	deuterated dimethyl sulphoxide
equiv.	equivalents
et al.	and others
g	gram
g/mol	gram per mole
H_2O	distilled water
H_2SO_4	sulfuric acid
Harom.	aromatic proton
Holef.	olefinic proton
hr	hour(s)
hυ	light
i-butyl	iso butyl group
IC	internal conversion
ISC	intersystem crossing

IUPAC	Internal Union of Pure and Applied Chemistry
J	coupling constant
K_2CO_3	potassium carbonate
m	multiplet
$MgSO_4$	magnesium sulphate
min	minute(s)
ml	millilitre(s)
mmol	millimole(s)
mol	mole(s)
MPc	metallo phthalocyanine
NaCl	sodium chloride
nm	nanometres
NMR	nuclear magnetic resonance
^oC	degrees Celsius
Pc	phthalocyanine
PDT	photodynamic therapy
PET	photoinduced electron transfer
Ph	phenyl
ppm	parts per million
s	singlet
t	triplet
t-butyl	tertiary butyl group
TFA	trifluoroacetic acid
TFPN	tetrafluorophthalonitrile
THF	tetrahydrofuran
TLC	thin layer chromatography
UV	ultraviolet
Δ	heat
μg/ml	microgram per millilitre
π	pi
σ	sigma

List of ionic liquid abbreviations

Cations

EMIM	1-Ethyl-3-methylimidazolium
C4MIM	1-Butyl-3-methylimidazolium
C_6MIM	1-Hexyl-3-methylimidazolium
C_8MIM	1-Octyl-3-methylimidazolium
C_2DMIM	1-Ethyl-2,3-dimethylimidazolium
BMPyrr	1-Butyl-1-methyl-pyrrolidinium

Anions

OTf	Triflate
NTf_2	Bistriflimide
BF_4	Tetrafluoroborate
PF_6	Hexafluorophosphate

Abstract

The aim of this research was to investigate the photo-Friedel-Crafts acylation of napthoquinone with a variety of aldehydes using a Rayonet reactor. The long-term aim of this project was to apply this research to the synthesis of biologically active natural products such as alkannin and shikonin.

As a 100% atom efficient, solar reaction, the photo-Friedel-Crafts acylation of naphthoquinone is understood to be a very environmentally friendly reaction. With this in mind, it was undertaken to improve the "green" nature of this reaction by replacing harmful traditional solvents such as benzene with more benign alternatives. Ionic liquids were chosen for this purpose, due to their low vapour pressure, recyclability, low flammability and customisable solubilising and catalytic properties, as well as the fact that they have been shown to stabilise reactions with radical intermediates. The reaction was also performed in microemulsions.

As an extension of previous work done in DCU by Pratt *et al.* it was undertaken photochemically generate a series of biaryl trifluorophthalonitriles, and optimise the reaction conditions necessary for their synthesis. Once these novel phthalonitriles had been generated a method for condensing them to phthalocyanines was developed. The novel phthalocyanines generated using this method were then assessed as catalysts for photooxygenation reactions. It was hoped that the introduction of peripheral aryl groups would increase the solubility of the phthalocyanines as well as reducing aggregation.

1.0 Photochemistry

1.1 Introduction

Light is such a common part of everyday life that it is easy to forget that it is a form of energy, and as such is capable of acting as the driving force of a chemical reaction. The science of photochemistry is concerned with harnessing this energy to drive chemical reactions. Probably the most fundamental photochemical reaction is photosynthesis, which uses light energy to convert carbon dioxide and water into sugars, making this process essential to life. Recently there has been considerable interest in "solar cells". These are devices which are capable of converting sunlight directly into electrical energy. They are of major concern from an environmental standpoint as they have the potential to produce limitless amounts of energy with no harmful by-products.

One of the fundamental laws of chemistry, known as the Grotthus-Draper law, states that only light which is absorbed can result in a photochemical effect.[1] This is often referred to as the first law of photochemistry. The second law of photochemistry, known as the Stark-Einstein law, states that for each photon of light absorbed by a chemical system, only one molecule is activated for photochemical reaction. This principal is also commonly known as the photoequivalence law.

Absorption of a photon of light by a molecule typically results in the promotion of an electron to a higher energy orbital. An example of an orbital energy diagram is shown in Figure 1.1.1. In its ground state (S_0) all the lowest energy (bonding) orbitals are filled. Upon absorption of a photon of light by a molecule, an electron is promoted to a higher energy (anti-bonding) orbital. If the two unpaired electrons

have opposite spin directions, this is known as a singlet state (S_1). If the unpaired elections have the same spin direction, this is known as a triplet state (T_1).

In the case of molecules containing heteroatoms, the highest energy electrons in the ground state (S_0) may belong to non-bonding orbitals (n). In this case, photochemical excitation may result in a (n, π*) or (n, σ*) transition.

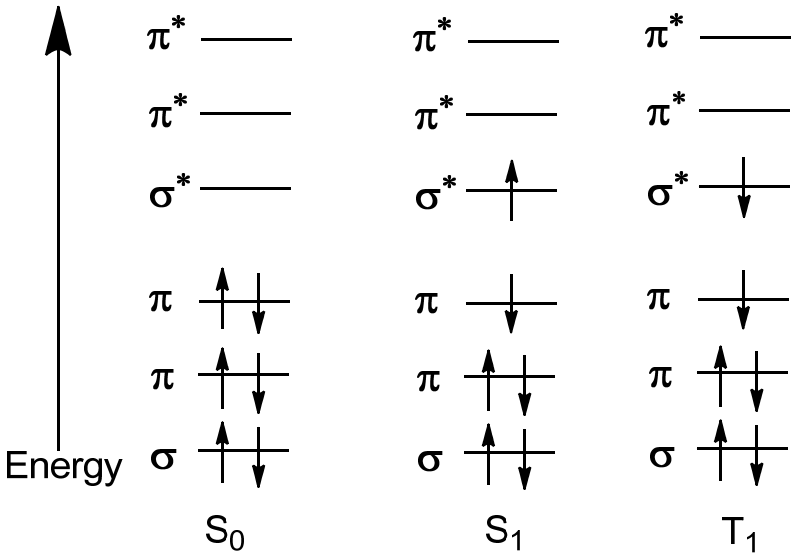


Figure 1.1.1: Orbital energy level diagram.

If a photochemically excited molecule is not involved in a reaction it must decay to the ground state via one of several pathways; the most important of these can be summarised in a Jablonski diagram (Figure 1.1.2).

Transmissions which result in the emission of radiation are known as radiative transmissions. In cases where there is no change in spin state (e.g. $S_1 \rightarrow S_0$) this process is known as fluorescence (iv). When a change in spin states is observed (e.g. $T_1 \rightarrow S_0$) this process is known as phosphorescence (v).

Photochemically excited molecules may also undergo transmissions which do not result in an emission of radiation: these are known as non-radiative transmissions.

Transmissions of this type which do not include a change in spin state are known as internal conversions (ii); when a change in spin state does occur, the process is known as intersystem conversion (iii). This includes the transmission from S_1 to T_1, and from T_1 to S_0.

Photochemical reactions generally occur via the S_1 or T_1 state, however, a reaction must compete with decay to the ground state, either radiative or non-radiative.[2]

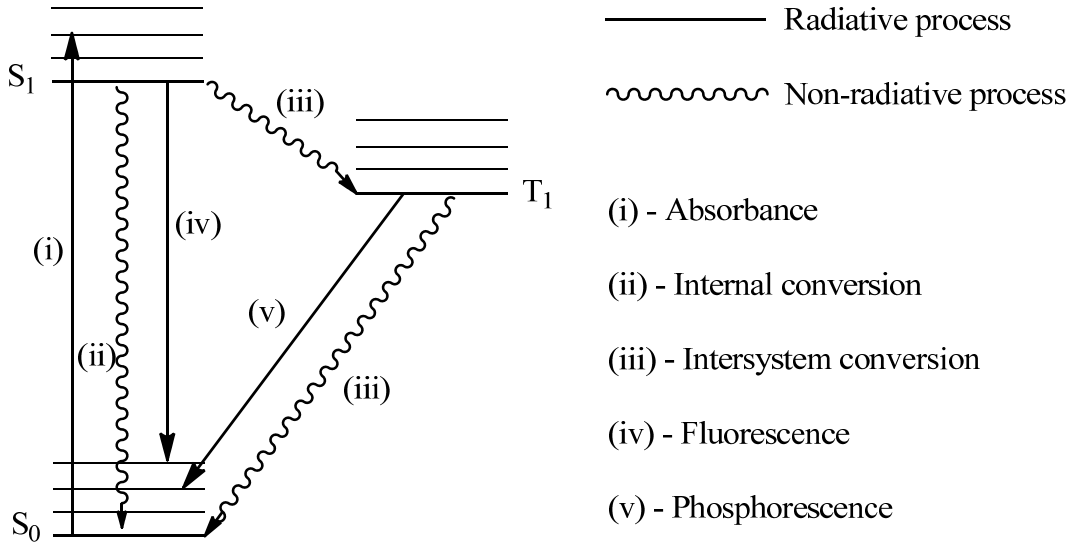
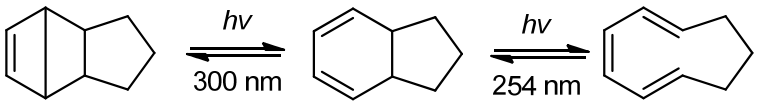


Figure 1.1.2: Jablonski diagram of photochemical processes.

From the viewpoint of a synthetic chemist light has many advantages as an energy source compared to traditional thermal methods. Light is much easier to control than thermal energy. The broad spectrum of light allows for "tuning" of reactions by selecting specific wavelengths for an individual reaction. The last point is best exemplified in reactions where different wavelengths can drive a reaction down different pathways. An interesting example of this kind of reaction has been observed with the irradiation of bicyclo[4.3.0]nona-2,4-diene **1** (Figure 1.1.3).[3]



(1)

Figure 1.1.3: An example of a wavelength dependant reaction.

1.2 Classes of photochemical reaction

1.2.1 Isomerisation of alkenes

One of the simplest and most basic photochemical reactions is the cis-trans isomerisation of an alkene, as seen in Figure 1.2.1.

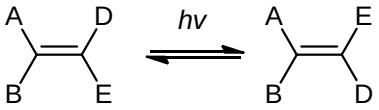


Figure 1.2.1: *Cis-trans* isomerisation of an alkene.

In its simplest form it involves a 180° rotation around a double bond. This reaction can be generated thermally, catalytically or photochemically. The mechanism of this reaction proceeds via the (π,π*) excited state. When a π band electron is promoted to an antibonding orbital the double bond is lost in the photoexcited state thus allowing for free rotation to the lowest energy configuration for the compound via a 90° twist. From this state rapid radiationless decay can lead to either geometric isomer to give a photostationary state consisting of a mixture of both isomers. The relative composition of the photostationary state is dependent on the irradiation wavelength and the absorption spectrum of each isomer. The mechanism of this process is shown in Figure 1.2.2.

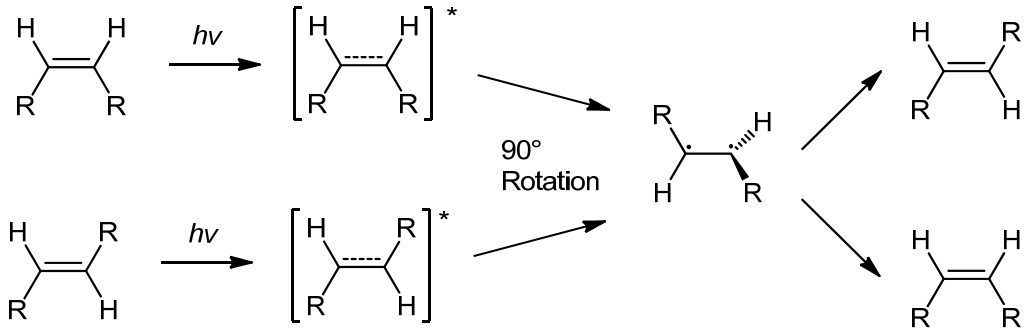


Figure 1.2.2: Mechanism of *cis-trans* isomerisation of alkenes.

The wavelength sensitive nature of *cis-trans* isomerisations has been a major factor in the synthesis of previtamin D **3** (Figure 1.2.3). Typically, previtamin D is synthesised by photochemical ring opening of the B rings of ergosterol **2a** and 7-dehydrocholesterol **2b**. This is followed by thermal rearrangement to give vitamin D **4**. Unfortunately, previtamin D derivatives can absorb in the same spectral region as the starting materials, which can lead to undesirable side products, such as **5**. These side products can be minimised by careful selection of the wavelength to give a photostationary state in which previtamin D is the major component.[4]

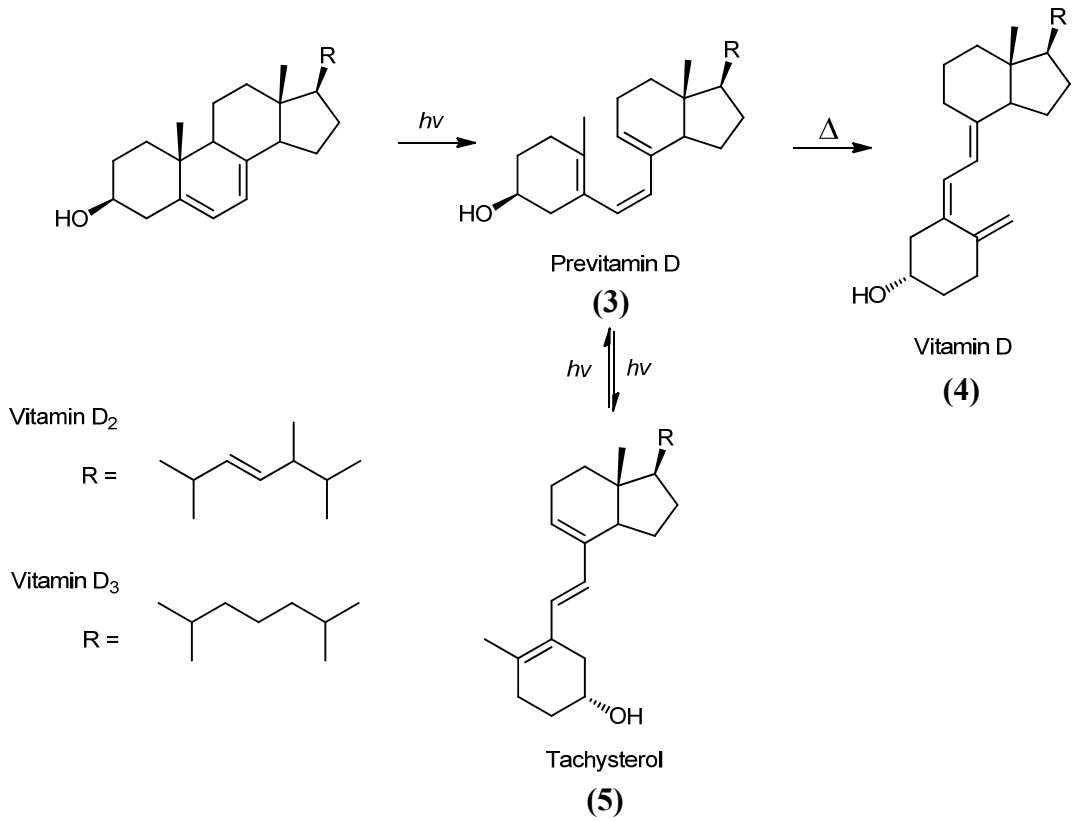


Figure 1.2.3: Various possible reaction pathways in the synthesis of previtamin D **3**.

Table 1.2.1: Effects of varying wavelengths on previtamin D **3** yield.

Wavelength (nm)	Photostationary State Composition (%)	
	Previtamin D **3**	Tachysterol **5**
248	26	71
254	20	75
302	53	26
308	36	3
(248 + 337)	80	2
(248 + 353)	80	11

1.2.2 Cycloaddition reactions

1.2.2.1 [2+2] Cycloaddition

1.2.2.1.1 Cyclobutane synthesis

The synthesis of cyclobutanes by [2+2] photocycloaddition of alkenes is one of the most commonly applied photoreactions in organic synthesis.[5] The reaction may occur with a wide variety of unsaturated substrates.

Frontier molecular orbital theory has been used to explain this class of reaction. Take the dimerisation of ethene (Figure 1.2.4) as an example; in the ground state the highest occupied molecular orbital (HOMO) is the π-bonding orbital, while the lowest unoccupied molecular orbital (LUMO) is the π-antibonding orbital. In order for a reaction to be viable, there must be a correlation between the orbitals of the HOMO of one ethene molecule and the LUMO of another. This is known as suprafacial addition. It can be seen that, in the case of [2+2] cycloadditions, in the ground state there is no overlap. This would indicate that the reaction is thermally unfavourable.

However, upon irradiation with light an electron is promoted to the higher energy orbital to generate an excited HOMO. It can be seen that this new HOMO* overlaps sufficiently with the LUMO of a ground state molecule, indicating that the reaction is favourable.

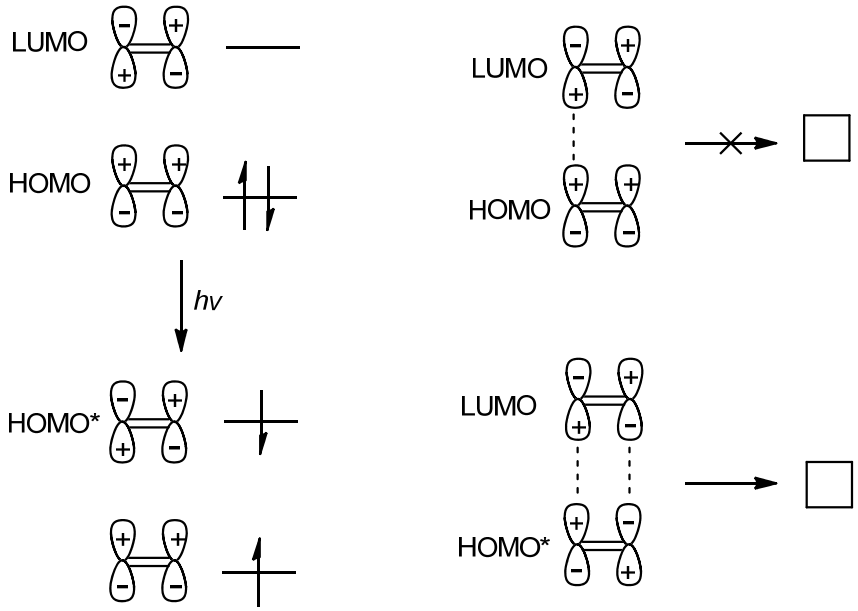


Figure 1.2.4: Frontier orbitals of a suprafacial [2+2] cycloaddition reaction.

There are however exceptions to this rule. One well know example is the thermal [2+2] cycloaddition of ketenes to alkenes.[6] In this case, due to low steric hindrance the orbitals are capable of aligning antarafacially (Figure 1.2.6).

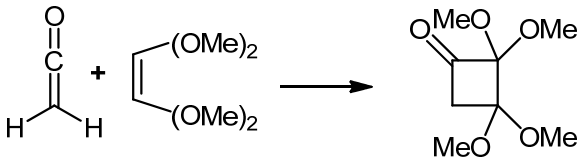


Figure 1.2.5: Thermal [2+2] cycloaddition of a ketene to an alkene.[7]

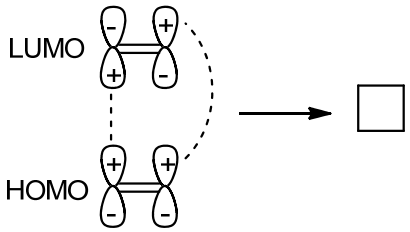


Figure 1.2.6: Antarafacial cycloaddition.

This mechanism is still not completely understood. A common belief is that excimers or exciplexes involving the singlet or triplet state could be

photointermediates on the path to cyclobutanes. This theory has arisen from the occasional detection of excimer/exiplex fluorescence; however this is not necessarily conclusive evidence of the mechanism. It is currently thought that single electron transfer is responsible for sensitised photodimerisations as shown in Figure 1.2.7. The drawback to this theory is the inefficiency due to the need for charge separation and the great complexity of the dimerisation processes.

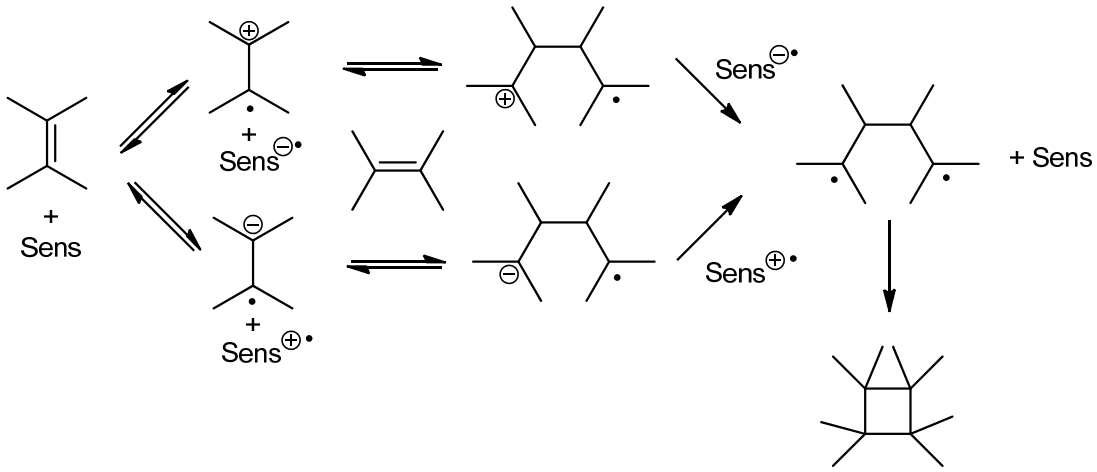


Figure 1.2.7: Alternative mechanism of [2+2] photocycloaddition.

[2+2] Photocycloadditions have been instrumental in the synthesis of numerous natural products. One such example is the attempted synthesis of the natural hatching agent of the potato cyst nematode, solanoeclepin A **8** (Figure 1.2.8) .[8] A sensitised intramolecular [2+2] photocycloaddition has been used to gain access to the cyclobutane containing tricyclic core structure **7**. In one photochemical step **7** was obtained with the required relative configuration. Reductive opening of the lactone leads to the methyl and hydroxyl groups in the correct stereochemical arrangement.

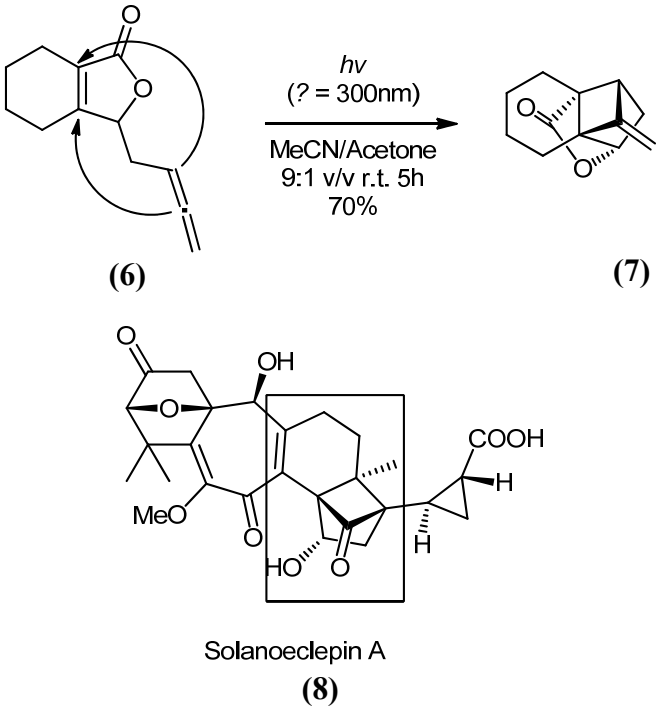
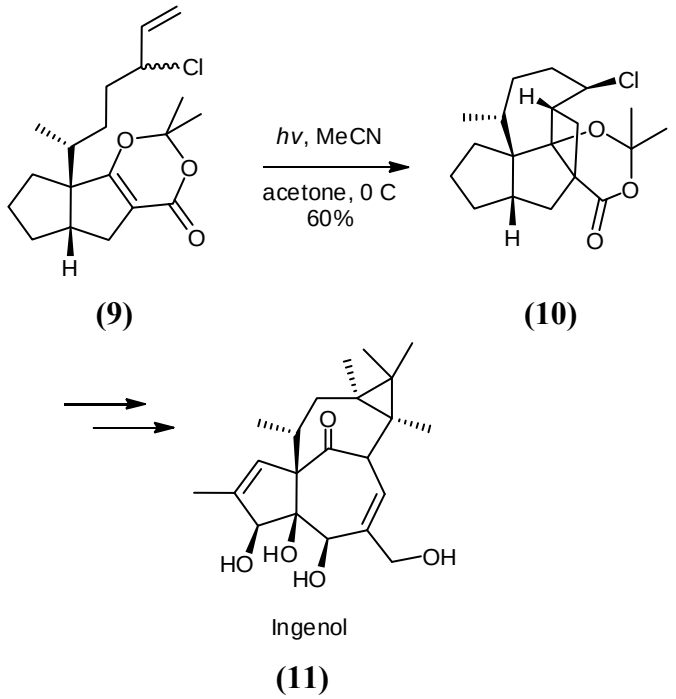


Figure 1.2.8: Synthesis of Solanoeclepin A **8**.

Likewise, a similar approach was taken in the synthesis of the highly bioactive natural product ingenol **11** (Figure 1.2.9).[9] Due to a longer tether, and in contrast to the previously mentioned synthesis, only the straight adduct **10** was formed. It should be noted that this strategy is particularly efficient for building the *trans*-fused [4.4.1] bicyclic undecane core structure.

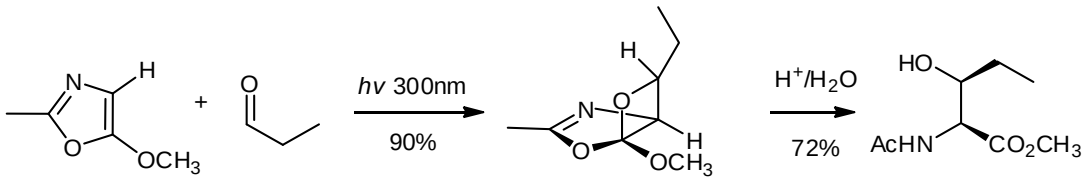


(9) **(10)** **(11)**

Figure 1.2.9: Synthesis of Ingenol **11**.

1.2.2.1.2 Heterocycle formation

The photocycloaddition between a ketone and an alkene (the Paternò-Büchi reaction[10]) is an important photochemical [2+2] reaction which has received significant interest. The oxetane product of this reaction can be an important intermediate for synthetic purposes. A simple example of this can be seen in the reaction of an alkoxyoxazole **12** with propionaldehyde (Figure 1.2.10). The product of this reaction **13** can then be converted to the erythro-α-amino-β-hydroxy acid derivative **14**.



(12) **(13)** **(14)**

Figure 1.2.10: Synthesis of a erythro-α-amino-β-hydroxy acid derivative of an alkoxyoxazole.

The Paternò-Büchi reaction can also be performed with thiocarbonyl compounds. Thiobenzophenone **15** and other aromatic thiones react readily with electron-rich alkenes upon long-wavelength irradiation to give thietanes and/or 1,4-dithianes. The reaction with 1-phenylpropene shows the regioselective but non-stereoselective nature of the process (Figure 1.2.11).[11]

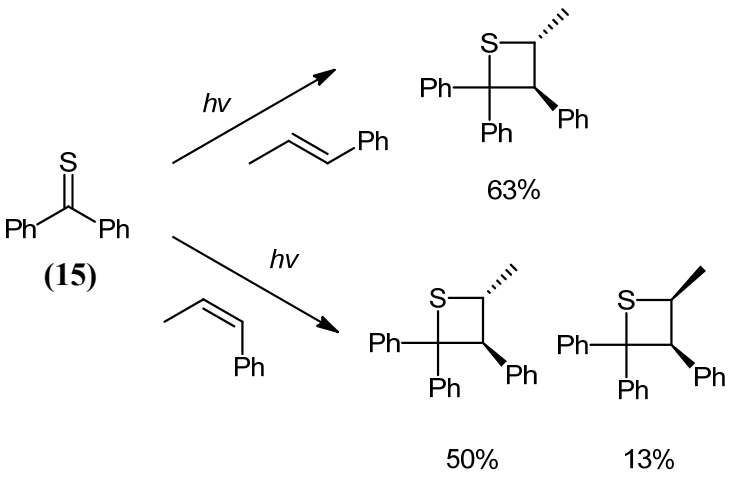


Figure 1.2.11: Paternò-Büchi reaction involving thiobenzophenone.

Likewise, the reaction of **15** with ethyl vinyl ether **16** demonstrates the formation of dithane product as well as the regioselective preference of the reaction (Figure 1.2.12).[12] The divergence of pathways between thietane and 1,4-dithiane arises because the intermediate biradical can be trapped by a molecule of ground-state thioketone.

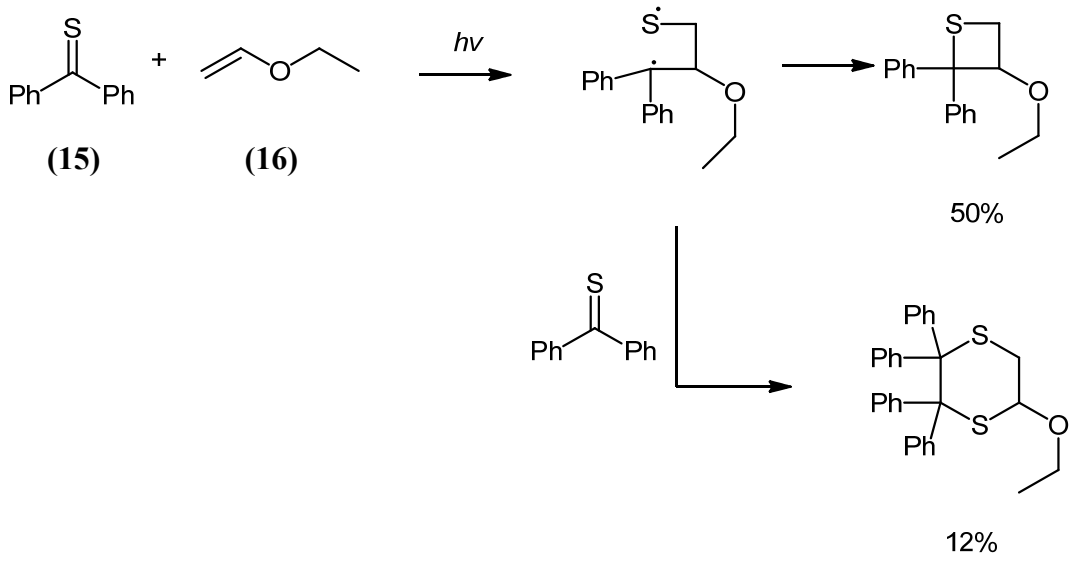


Figure 1.2.12: Asymmetric Paternò-Büchi reaction involving thiobenzophenone.

In the case of thioamides or thioimides, the thiethanes which are initially formed are not always stable. As a result of this they are frequently used as intermediates in the synthesis of nitrogen-containing heterocycles. An example of this can be seen in the irradiation of a thiosuccinimide **17** to induce a intramolecular thio-analogous Paterno-Buchi reaction (Figure 1.2.13).[13] Subsequent transformations were performed to yield the spirocyclic pyrrolicidine derivative **18**.

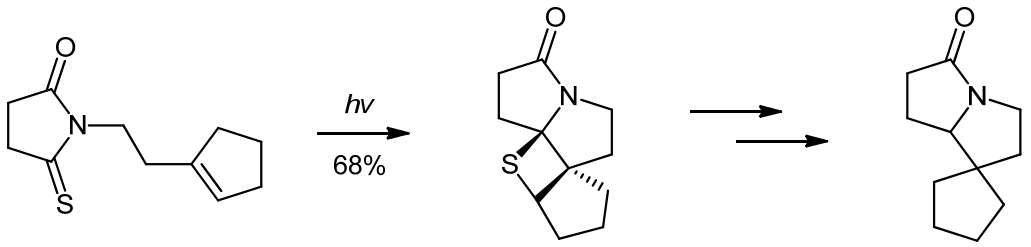
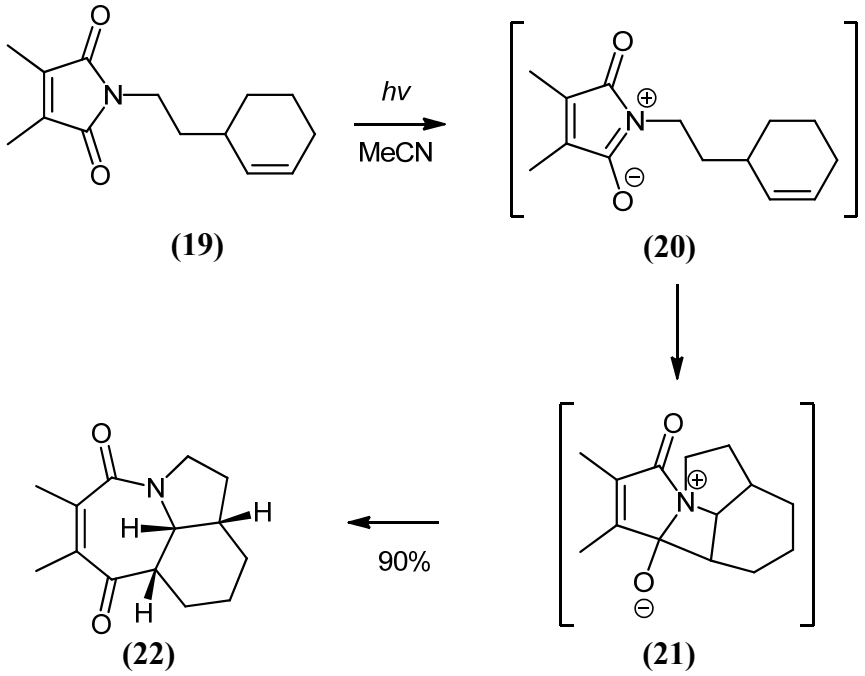


Figure 1.2.13: Intramolecular thio-Paternò-Büchi reaction.

An intramolecular [2+2] photocycloaddition has been shown to occur between a maleimide moiety **19** and an alkene (Figure 1.2.14).[14] Due to ring strain and steric hindrance, the reaction proceeds by a direct [2+2] cycloaddition onto the excited

amide structure **20**. This zwitterionic tricyclic intermediate **21** undergoes spontaneous fragmentation to yield the final product **22**.



(19) **(20)** **(21)** **(22)**

1.2.14: Intramolecular [2+2] photocycloaddition of maleimide and an alkene.

1.2.2.2 [4+2] Cycloadditions

[4+2] Cycloadditions are commonly observed in the ground state between dienes and dienophiles as the Diels-Alder reaction.[15] The reaction proceeds rapidly in the ground state but is unfavourable in the excited state. This is explained by means of orbital symmetry according to the Woodward-Hoffmann rules for concerted reactions.[16] As a result of this direct photochemical [4+2] photocycloadditions are rare; however there are examples of photochemical *cis-trans* isomerisations being used to generate highly strained intermediates. These intermediates are capable of undergoing [4+2] cycloadditions which would be unfavourable in the ground state due to increased stability of the starting materials. This has been demonstrated intermolecularly with the thermal addition of various dienes to *trans*-2-cyclooctene-

1-one **24** which is photochemically generated *in situ* from *cis*-2-cyclooctene-1-one **23** (Figure 1.2.15).[17]

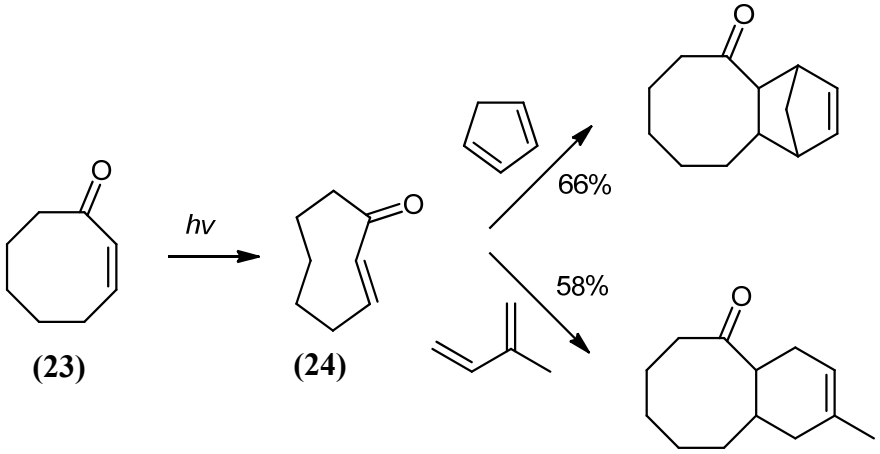


Figure 1.2.15: [4+2] Photocycloaddition reactions of *trans*-2-cyclooctene-1-one **24**.

An intramolecular example of this class of reaction has been demonstrated in the synthesis of the tricyclic compound **25** (Figure 1.2.16).[18]

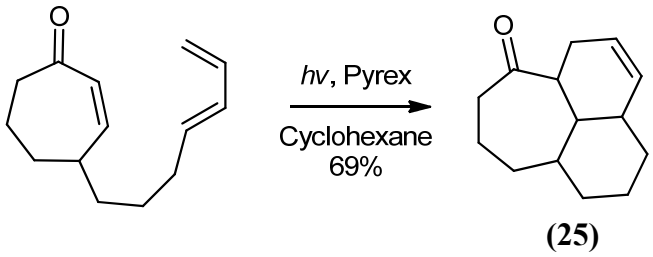
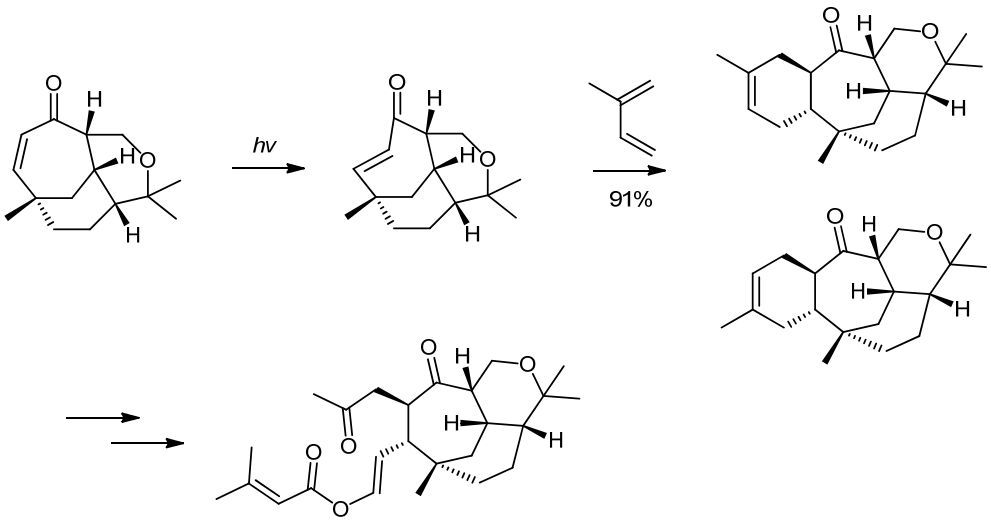


Figure 1.2.16: Intramolecular [4+2] photochemical reaction.

This synthetic strategy has been used as a key step in the synthesis of (±)-5-epi-10-epi-Vibsanin E **26** (Figure 1.2.17).[19]



(26)

Figure 1.2.17: Synthesis of (±)-5-epi-10-epi-Vibsanin E **26**.

1.2.2.3 [4+4] Cycloaddition

[4+4] Cycloadditions are rare in the ground state and usually require promotion to an excited state to proceed. Some simple examples of this are the intermolecular[20] or intramolecular[21] additions of two pyridone moieties (Figure 1.2.18).

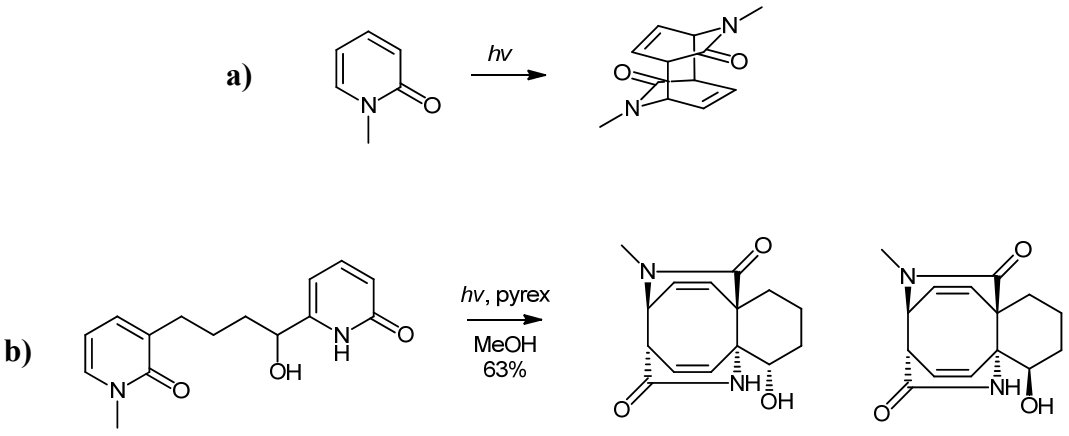


Figure 1.2.18: a) Inter- and **b)** intramolecular [4+4] reactions of pyridone.

This class of reaction provides an excellent route to the synthesis of cyclooctanes and their tricyclic derivatives. An example of this can be seen in the synthesis described in Figure 1.2.19. The product of this reaction **27** is a potential precursor in the synthesis of various members of the fusicoccin family of diterpenoid fungal

products[22] with particular interest in compounds with structures similar to that of traversianal.[23]

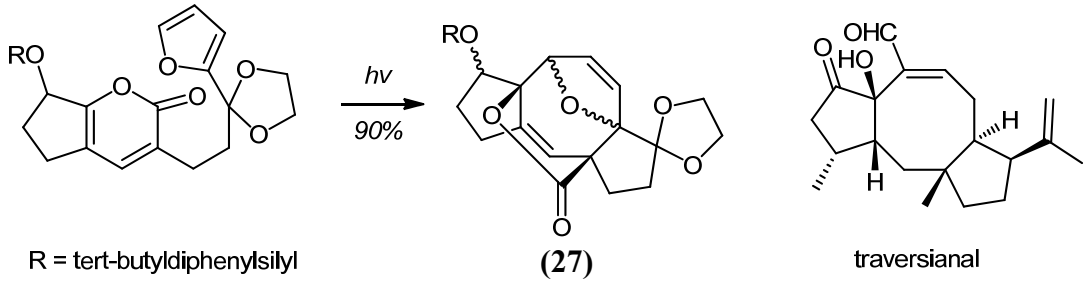


Figure 1.2.19: Synthesis of potential traversianal precursor.

1.2.3 Photooxygenation

Photooxygenation is defined as the incorporation of molecular oxygen into a molecular entity.[24]

The ground state electronic configuration of oxygen consists of two unpaired electrons in degenerate orbitals, according to Hund's rule of maximum multiplicity. Thus, the ground state of oxygen is the triplet state. Due to the presence of unpaired electrons in the ground state we can expect oxygen to exhibit radical characteristics and to react readily with radicals which may be produced in photochemical processes. Type I photooxygenations involve the reaction of photochemically formed radicals with triplet oxygen. As such, the presence of oxygen can greatly inhibit and/or modify photoprocesses. As a result of this, solvents for use in photochemical reactions are often purged of oxygen using inert gasses such as nitrogen or argon, or by freeze-pump-thaw cycles.

Oxygen may also exist in the much more reactive singlet form. The most common method of production of singlet oxygen is dye-sensitised photoexcitation, (Figure 1.2.20). This involves excitation of a suitable dye by the relevant wavelength. Dyes

commonly used as sensitisers include methylene blue, rose bengal and various porphyrins. Excitation of the sensitiser is followed by intersystem crossing (ISC) to the triplet state. The excitation energy of singlet oxygen is lower than the excited state energy of many organic triplets, thus energy transfer occurs. In most cases, the energy difference is small enough to make the process fast, yet large enough to make it irreversible.[25]

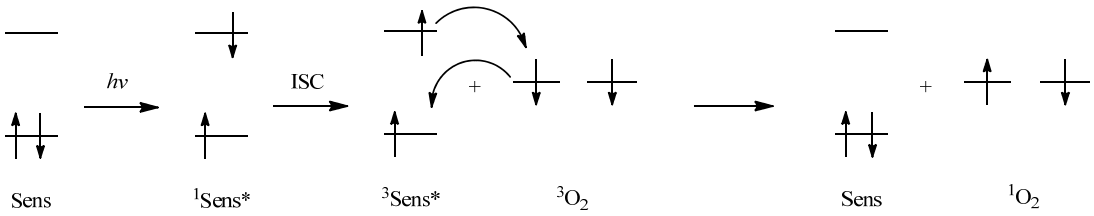


Figure 1.2.20: Sensitised generation of singlet oxygen.

Type II photooxygenations involve the reaction of photochemically produced singlet molecular oxygen with unsaturated compounds to give rise to oxygen containing molecular entities. The three main classes of photooxygenations involving singlet oxygen are; ene-reactions (Schenck-ene reaction), [2+2]-cycloadditions and [4+2]-cycloadditions.

1.2.3.1 Schenck-ene reaction

The Schenck-ene reaction involves the reaction of singlet oxygen with an alkene that possesses an allylic hydrogen to yield an allylic hydroperoxide (Figure 1.2.21). Despite considerable investigation, the mechanism of this reaction is not completely understood. Various intermediates such as biradicals, zwitterions or perepoxides have been suggested.[26] A simple example of this type of reaction can be seen in the photooxygenation of citronellol **28** (Figure 1.2.22).[27] In this case the initially generated hydroperoxide is reduced to the alcohol by sodium sulfite.

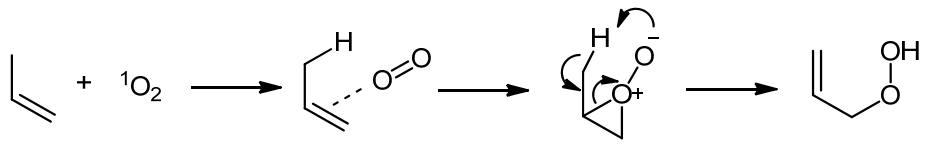


Figure 1.2.21: The Schenck-ene reaction.

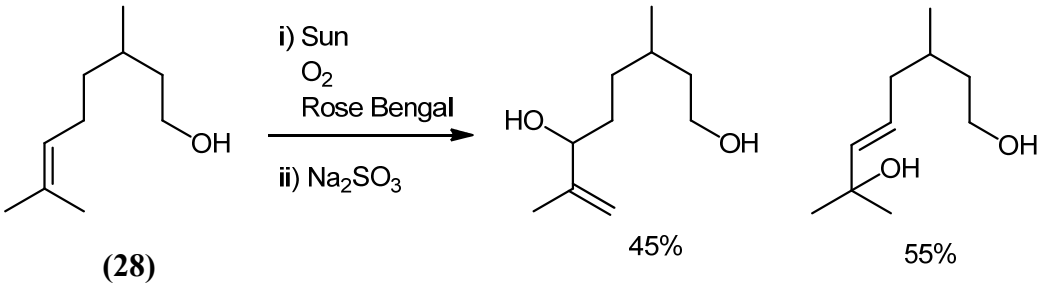


Figure 1.2.22: Photooxygenation of citronellol **28**.

The Schenck-ene reaction has also been recently applied to the synthesis of **29** which possesses antimalarial activity (Figure 1.2.23).[28]

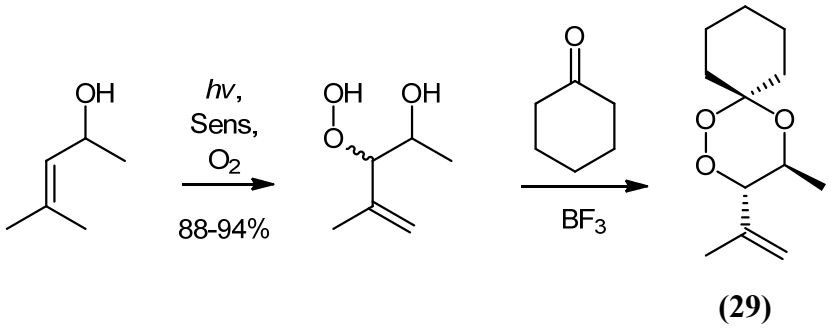


Figure 1.2.23: Synthesis of a novel antimalarial **29**.

1.2.3.2 [2+2] Photooxygenation

In the absence of an allylic hydrogen, electron-rich alkenes are known to undergo sensitised photooxygenation to give dioxetanes (Figure 1.2.24). Like the Schenk-ene reaction, the precise mechanism of this reaction is not fully understood, however it is believed to proceed via a zwitterionic peroxide. Dioxetanes are thermally unstable and usually decompose to yield two vicinal carbonyl compounds.

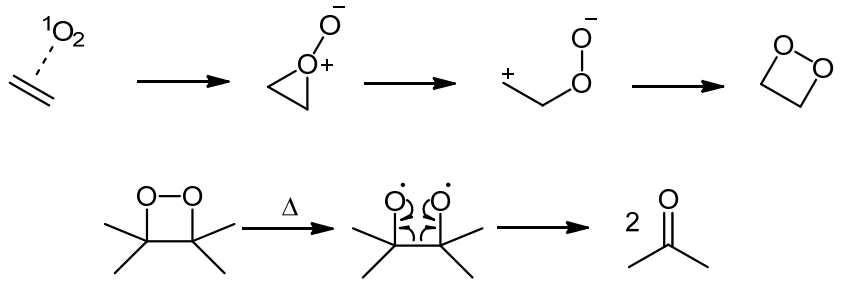


Figure 1.2.24: [2+2] Photooxygenation and follow-up reaction.

A similar reaction has been observed for thioketones (Figure 1.2.25). In this case singlet oxygen adds to the ground state thione to give an unstable thiadioxetane which decomposes to form a ketone. In some cases a sulfine product is also observed.[29] In this class of reaction the singlet oxygen can be generated by dye-sensitisation or by sensitisation of the thioketone.

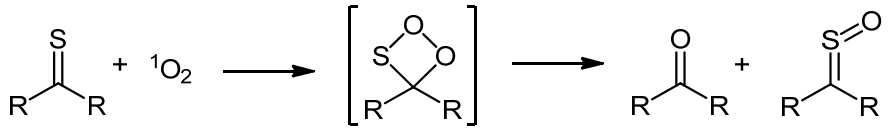


Figure 1.2.25: [2+2] Photooxygenation of a thioketone.

1.2.3.3 [4+2] Photooxygenation

Singlet oxygen is capable of behaving as a powerful dienophile and participating in Diels-Alder additions to produce cyclic peroxides. A simple example of this is shown in Figure 1.2.26. The reaction is known to proceed with a wide variety of substrates such as cyclic and acyclic dienes and select aromatic compounds.[30]

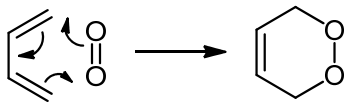
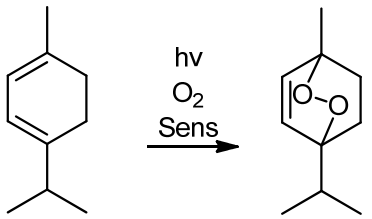


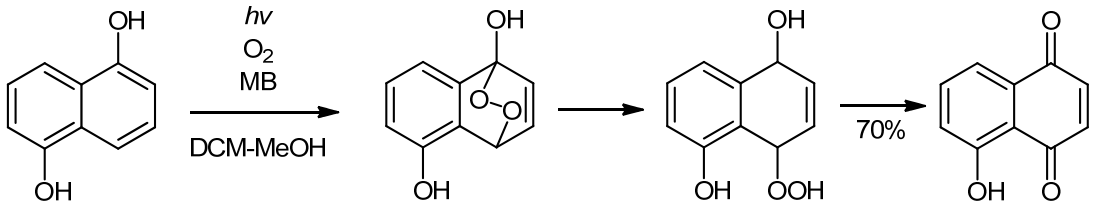
Figure 1.2.26: [4+2] Photooxygenation.

Some notable photooxygenations of this type include the synthesis of ascaridol **31** from α-terpinene **30** (Figure 1.2.27) and the synthesis of juglone **33** from 1,5-dihydroxynaphthalene **32**[31] (Figure 1.2.28).



(30) **(31)**

Figure 1.2.27: Synthesis of ascaridol **31**.



(32) **(33)**

Figure 1.2.28: Synthesis of juglone **33**.

1.2.4 Radical photochemistry of carbonyl compounds

A radical is defined as an atom or molecule possessing an unpaired electron. This unpaired electron tends to make the atom or molecule highly reactive, although there are some examples of stable radicals. A radical species may be neutral, or may hold a positive or negative charge. With regards to photochemistry one of the most common methods of radical generation is by homolytic cleavage of covalent bonds. The simplest example of this is in the generation of halogen radicals (Figure 1.2.29).

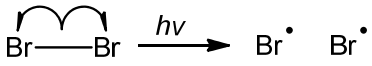


Figure 1.2.29: Photochemical homolytic cleavage of halogens.

If the radicals are generated in the presence of an alkane they can then initiate a halogenation chain reaction by the pathway shown in Figure 1.2.30. This process will continue until two radicals meet, resulting in termination

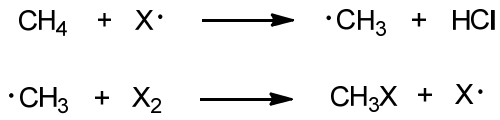


Figure 1.2.30: Radical chain reaction.

Another example of this class of photochemical reaction can be seen in the free radical bromination of cyclohexane (Figure 1.2.31).[32]

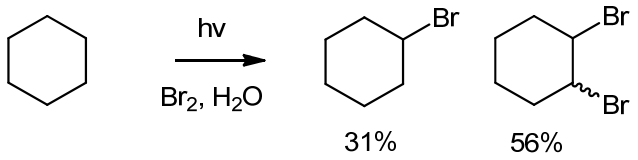


Figure 1.2.31: Free radical bromination of cyclohexane.

The photochemically generated radicals can also be used as initiators for the synthesis of polymers. A common photoinitiator is azoisobutylnitrile (AIBN) **34**. An example of AIBN initiated polymerisation is shown in Figure 1.2.32.

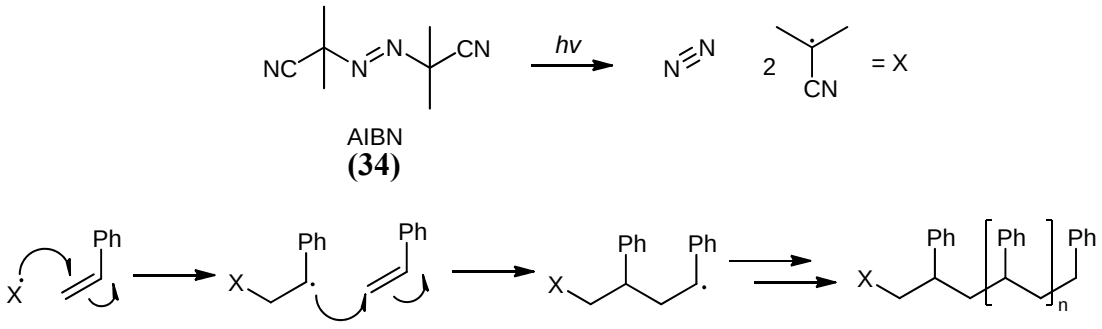


Figure 1.2.32: Free radical polymerisation of styrene initiated by azoisobutylnitrile.

Carbonyl compounds are known to react photochemically via radical intermediates. With regards to the photochemistry of carbonyl compounds, aldehydes and ketones tend to generate a greater interest due to their higher reactivity when compared to carboxylic acids. Aldehydes and ketones tend to absorb light in the region of 280 – 300nm, whereas carboxylic acids usually absorb light in the region of 200 – 220nm. Intersystem crossing from (n, π*) singlet to triplet state is fast since they are close in energy. Thus, the photochemical reactions of aliphatic ketones may involve singlet or triplet (or both) excited states. In conjugated systems such as aryl ketones and enones the (n, π*) and (π, π*) excited singlet states are lower in energy and hence absorptions are at longer wavelengths compared to their aliphatic counterparts. Furthermore, the rate coefficients for intersystem crossing are increased appreciably by conjugation and the quantum yield of this process for aryl aldehydes and ketones and for enones is unity or very close to it. In practice therefore we are only concerned with the triplet (n, π*) and (π, π*) states of such carbonyl compounds as these states have comparable energy. (n, π*) Triplet carbonyl chromophores have

chemical and physical characteristics of a diradical and in particular have appreciable similarities to alkoxy radicals with respect to α-cleavage, hydrogen abstraction abilities and attack on carbon-carbon multiple bonds.

1.2.4.1 α-Cleavage

A photochemically excited carbonyl may undergo α-cleavage, known as the Norrish type I reaction, to form acyl and aliphatic radicals. From here there are various reaction pathways available (Figure 1.2.33).

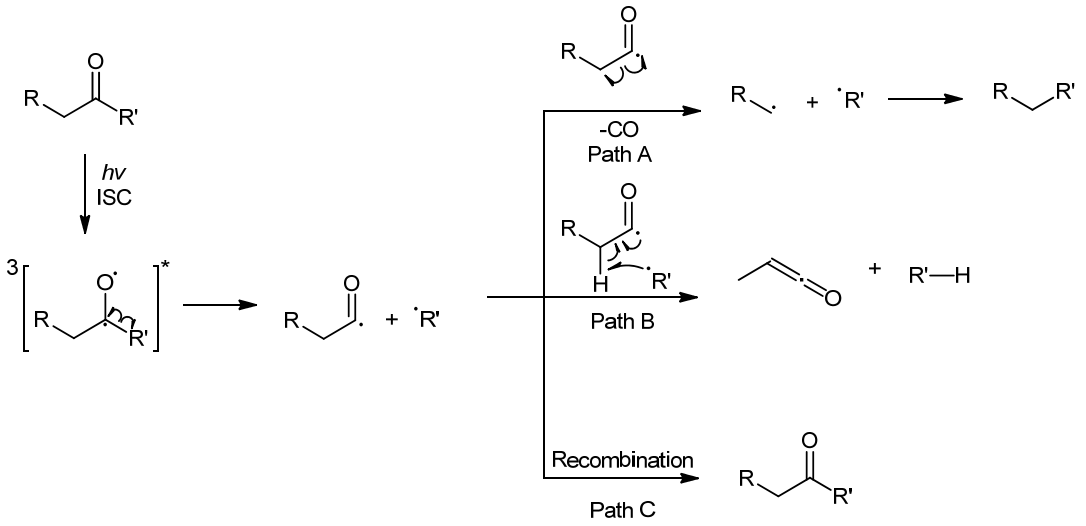


Figure 1.2.33: Norrish type I cleavage and follow up reactions.

The acyl radical may fragment to loose carbon monoxide and form a new aliphatic radical which may recombine to form a new alkane (Path A). This decarbonylation reaction has been utilised in the synthesis of (±)-Herbertenolide **35** (Figure 1.2.34).[33]

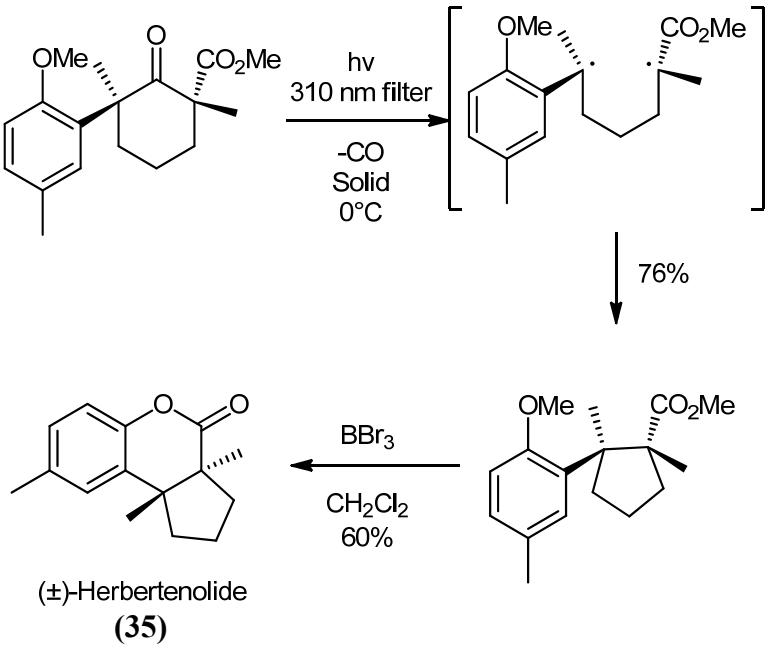


Figure 1.2.34: Synthesis of (±)-Herbertenolide **35** via decarbonylation.

In the case of acyl radicals with an α-hydrogen, hydrogen abstraction may occur to yield a ketene (Path B), however these tend to be unstable and prone to follow-up reactions. This method has been utilised as a key step in the synthesis of the sesterterpenoid nitiol **36** (Figure 1.2.35).[34]

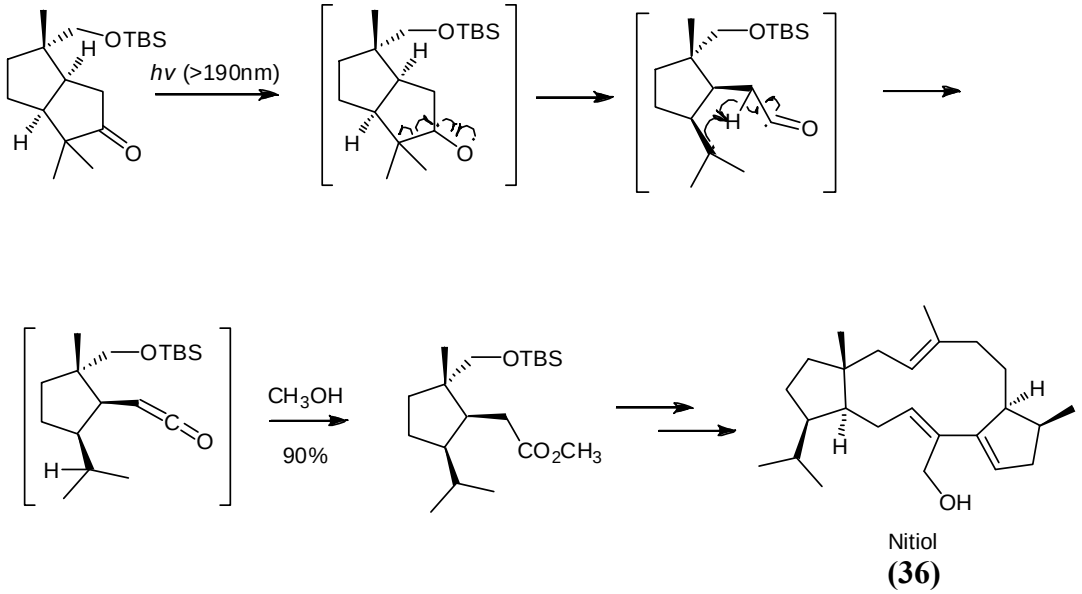


Figure 1.2.35: Synthesis of nitiol **36** via ketene formation.

Finally, the two radicals may recombine to reform the original carbonyl compound (Path C).

1.2.4.2 γ-Hydrogen abstraction

Upon photochemical excitation carbonyl compounds containing a γ-hydrogen are capable of undergoing a characteristic 1,5-hydrogen shift to yield a 1,4-biradical. This can result in the well-known Norrish type II cleavage yielding either an alkene and enol; or a Yang-cyclisation[35] may occur to form a cyclobutanol. The mechanism of both of these pathways is shown in Figure 1.2.36.

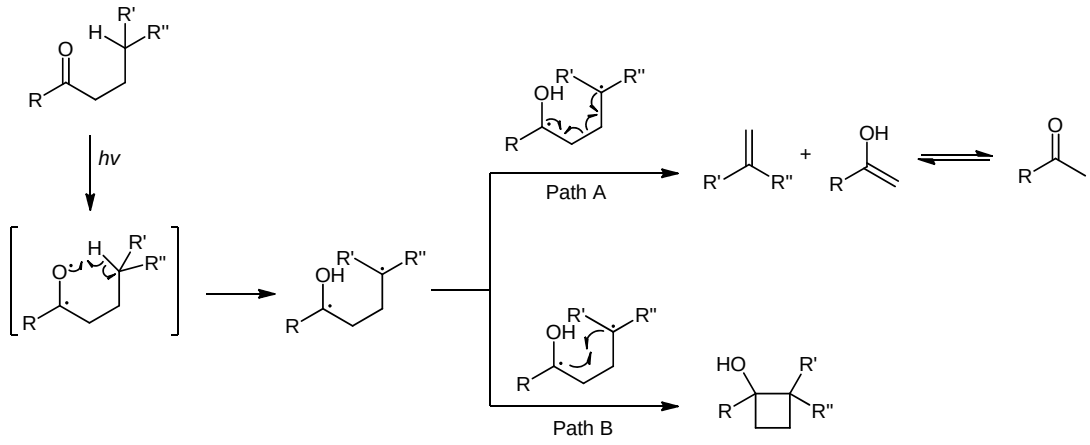


Figure 1.2.36: Possible reaction routes following γ-hydrogen abstraction.

An example of the application of the Norrish type II reaction is the synthesis of the enantiomerically pure unnatural amino acid azetidine-2-carboxylic acid **37** (Figure 1.2.37).[36]

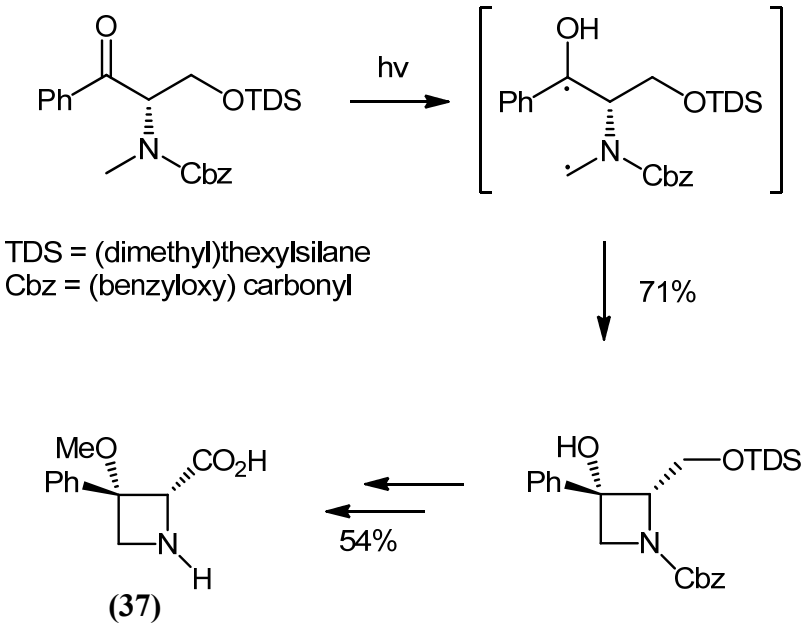


Figure 1.2.37: Synthesis of azetidine-2-carboxylic acid **37**.

1.2.5 Photoinduced electron transfer reactions

It has been shown that molecules in a photoexcited state are capable of facilitating the transfer of electrons. In order for electron transfer to be viable the energy of the highest molecular orbital (HOMO) of the reductant must be higher in energy compared to the lowest unoccupied molecular orbital (LUMO) of the oxidant. With photochemical excitation an electron is promoted from the HOMO to the LUMO to generate two molecular orbitals, each occupied by one electron (SOMO). In this configuration electron transfer becomes feasible by the process shown in Figure 1.2.38.

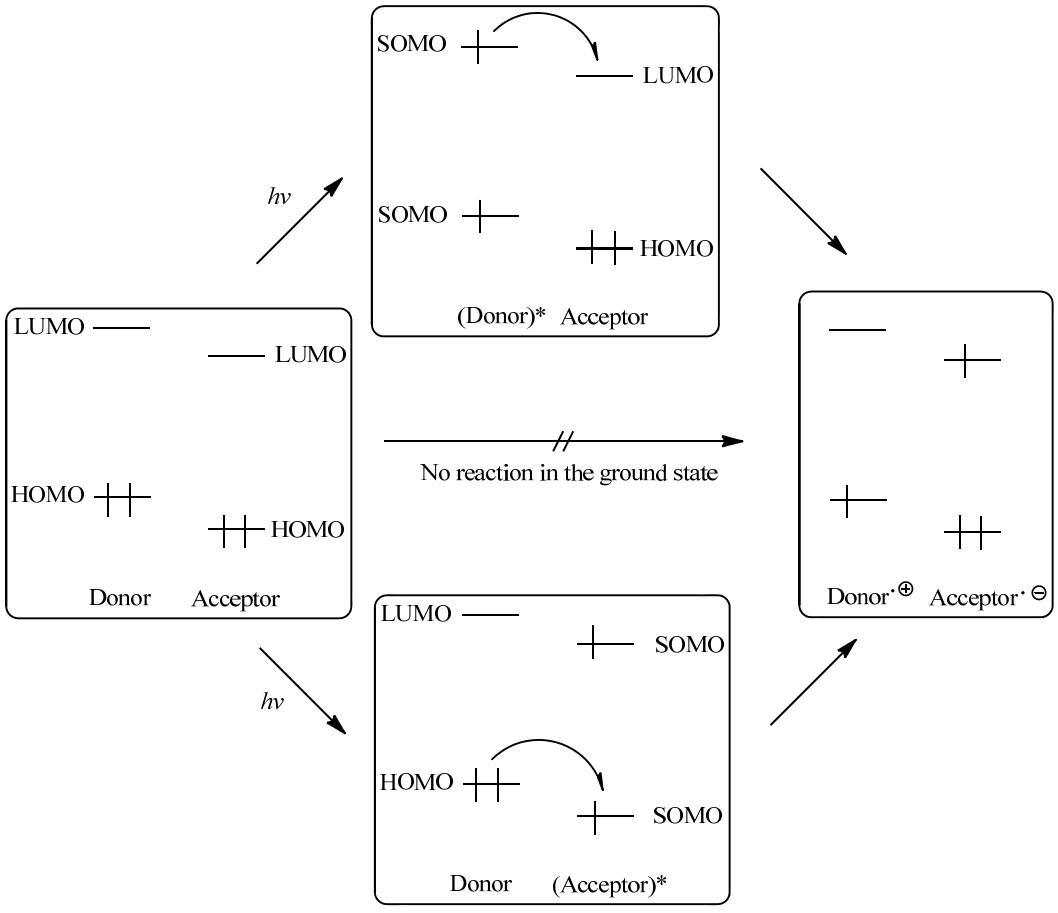


Figure 1.2.38: Electron transfer via photoexcitation.

Based on this mechanism the first step in a photoinduced electron transfer (PET) reaction involves absorption of light by a suitable molecule (AH in Figure 1.2.39) and its subsequent electron transfer to generate a radical ion pair. This is often followed by proton exchange to generate neutral radicals.

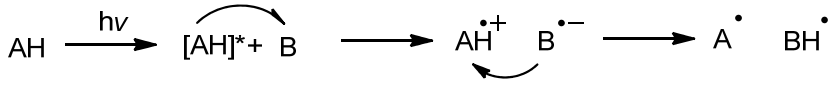


Figure 1.2.39: Photoinduced electron transfer.

1.2.5.1 Unsensitised PET

In the case of a PET reaction where the initial step involves absorption of light by one of the reactants, this is known as an unsensitised reaction. A simple example of this class of reaction is the photoreduction of ethyl phenylglyoxylate **38** (Figure 1.2.40).[37] Following photochemical excitation, the ethyl phenylglyoxylate biradical **39** is capable of undergoing single electron transfer (SET) with a suitable donor molecule to form a radical ion pair **40**. Following proton exchange the neutral molecules are then capable of forming either the addition product **41** or the ethyl phenylglyoxylate dimer **42**. This reaction has also been demonstrated to occur intramolecularly.

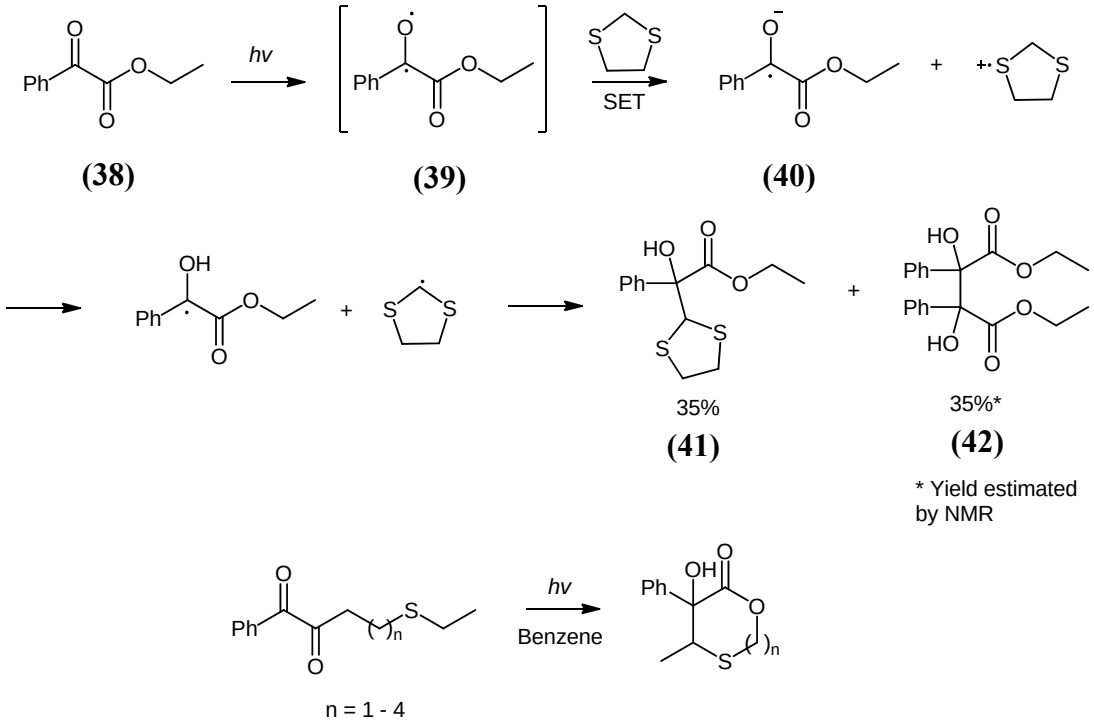


Figure 1.2.40: Inter- and intramolecular PET reaction of ethyl phenylglyoxylate **38**.

Another class of compounds which have been investigated with respect to SET photochemistry are the phthalimides.[38] Examples of inter- and intra-molecular SET reactions of phthalimide are shown in Figures 1.2.41 and 1.2.42.

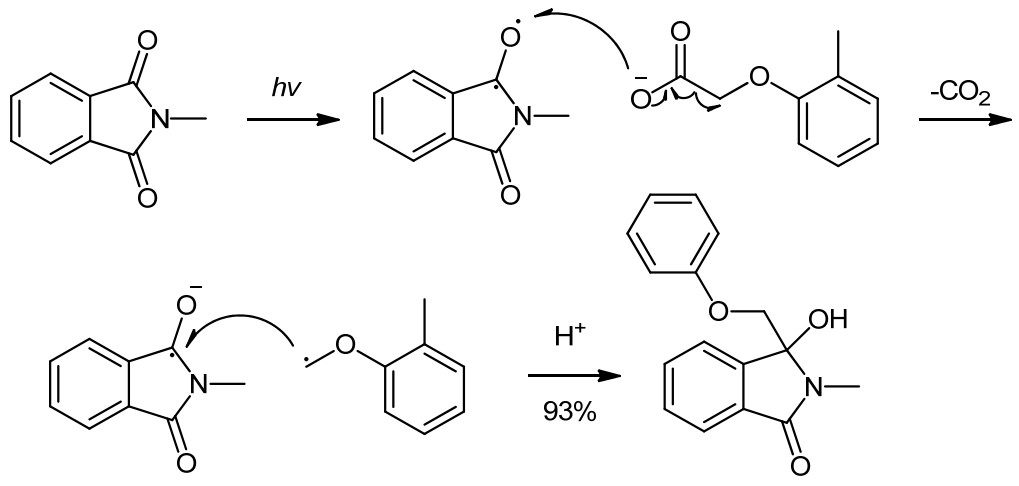


Figure 1.2.41: SET addition of phthalimide to 2-(o-tolyloxy)acetic acid.

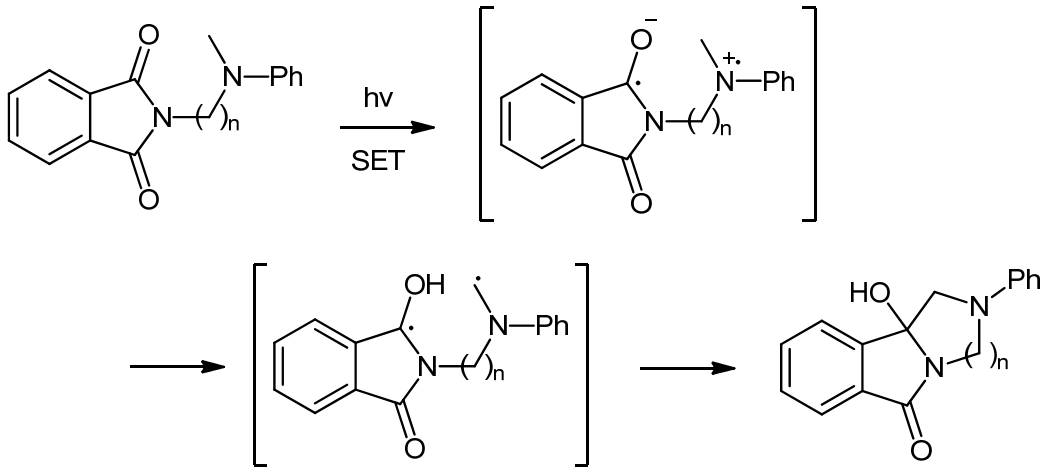


Figure 1.2.42: Intra-molecular SET reactions of phthalimides.

A major application of this type of chemistry is the usage of silicon as an electron donor and leaving group.[39] In these reactions the phthalimide moiety is excited by either direct light absorption or by sensitisation. Intramolecular SET leads to a radical ion pair **43**. The corresponding neutral radical **44** is generated by protonation of the aminoketyl radical anion of the phthalimide followed by the reaction with a nucleophile (often methanol or water), enabling desilylation. An example of this type of reaction is shown in Figure 1.2.43.

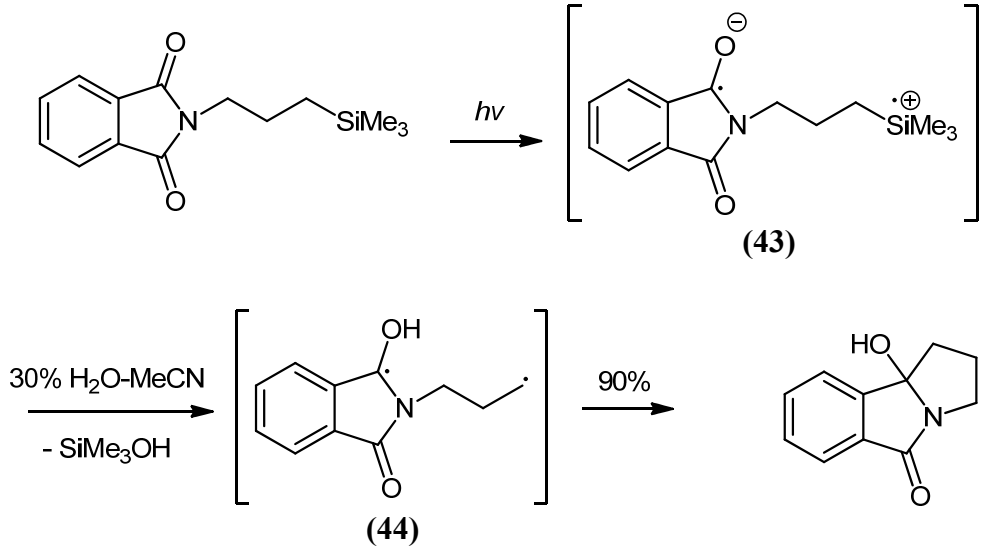


Figure 1.2.43: An example of an intramolecular SET reaction with silicon.

This strategy has been used to synthesise products resembling biologically active cyclopeptides such as cyclosporine **45** by the method shown in Figure 1.2.44.[40]

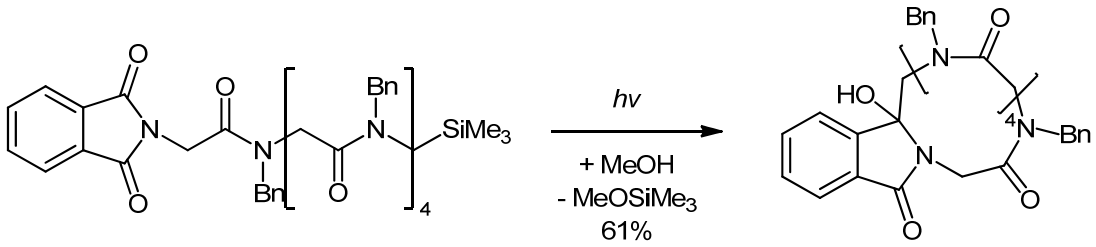
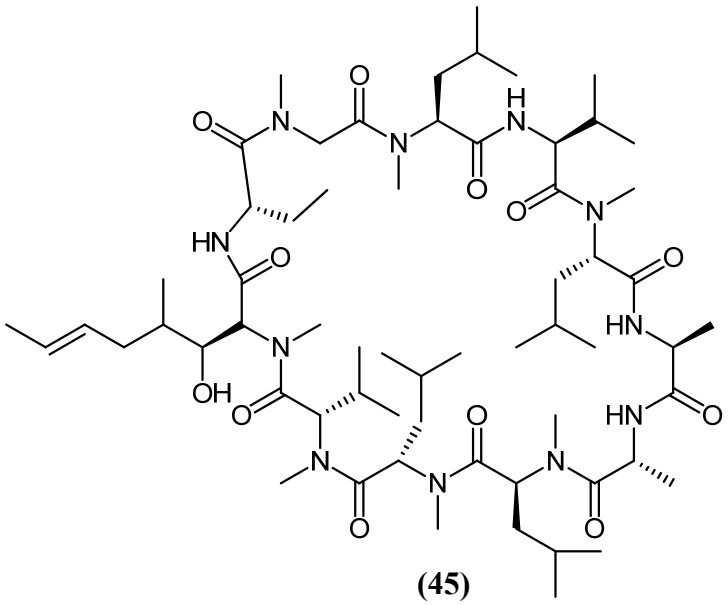


Figure 1.2.44: PET synthesis of a phthalimide-cyclosporine derivative.



(45)

Figure 1.2.45: Cyclosporine **45**.

The photoinduced PET radical addition of amines, in particular tertiary amines, to double bonds has been frequently studied.[41] An acceptor molecule is photochemically excited and a single electron is transferred from the amine to the acceptor molecule, leading to a radical ion pair. After proton exchange, neutral radicals are obtained, among them α-amino alkyl radicals. Various radical reactions are then possible. A simple example of this is the addition of a tertiary amine to stilbene (Figure 1.2.46).[42]

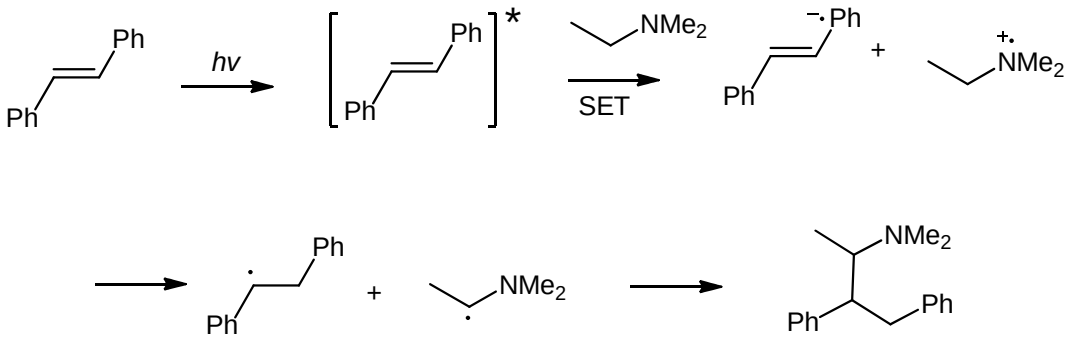


Figure 1.2.46: Addition of a tertiary amine to stilbene.

Fullerenes have been the subject of much investigation with respect to their ability as electron acceptors. The fullerene C_{60}, for example, is capable of reversibly accepting up to six electrons[43]. PET has been applied to the functionalisation of these compounds. A simple example of this is the addition of triethylamine to the C_{60} fullerene (Figure 1.2.47).[44]

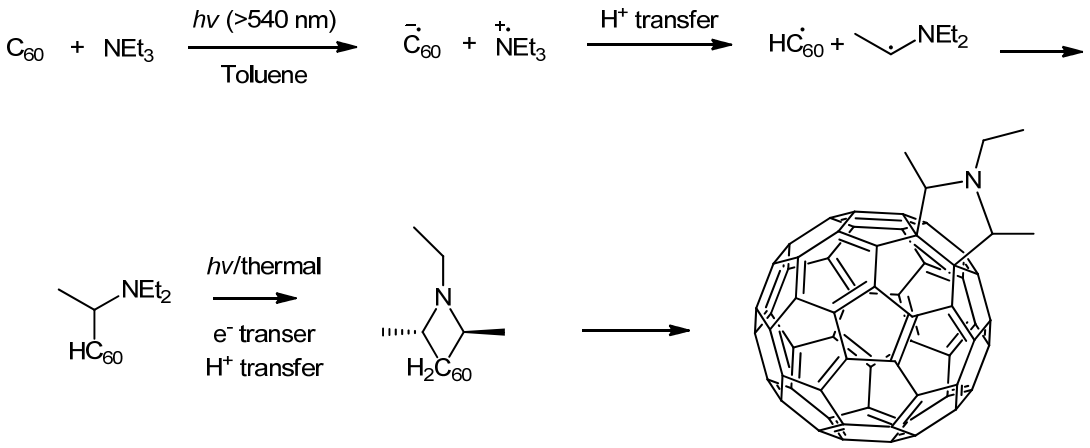


Figure 1.2.47: Addition of triethylamine to fullerene C_{60}.

This synthetic strategy has recently been applied to the addition of the alkaloid scandine to fullerene C_{60}.

1.2.5.2 Sensitised PET reactions.

In all previous examples the photochemically excited species participated directly in the reaction and formed part of the final product. This is not always the case; many

PET reactions are sensitiser driven. In photochemically sensitised reactions, light absorption not of the substrate but of the sensitiser leads to a chemical transformation. A photochemical excited sensitiser may abstract or donate an electron to a substrate. The radical ion of the substrate then proceeds to take part in the reaction. Often the sensitiser is consumed and thus is required in stoichiometric or higher amounts; however there is currently much investigation into the development of catalytic sensitisers. In this case, the sensitiser is regenerated and thus is required in much smaller amounts and in some cases can be recovered after a reaction.

Recently this type of catalysed PET reaction has been applied to the addition of tertiary amines to electron deficient alkenes.[45] Particular interest has been paid to the addition of *N*-methylpyrrolidine **47** to menthyloxyfuranone **49** with the aim towards the synthesis of the pyrrolizidine alkaloids (-)-isoretronecanol and (+)-laburnin (Figure 1.2.48). In this reaction the aromatic ketone sensitiser **46** is photochemically excited (step a) and abstracts an electron from the amine. This is followed by hydrogen transfer (step b) to generate the neutral radical pair. The α-aminoalkyl radical **48** is now nucleophilic and easily adds to the electron deficient alkene moiety of **49** (step c). The newly generated oxoallyl radical **50** is then capable of abstracting a hydrogen atom from a molecule of **47** to generate the final product **51** and a new molecule of **48** (step d). Alternately, **50** can abstract a hydrogen atom from the sensitiser radical to regenerate the neutral sensitiser (step e).

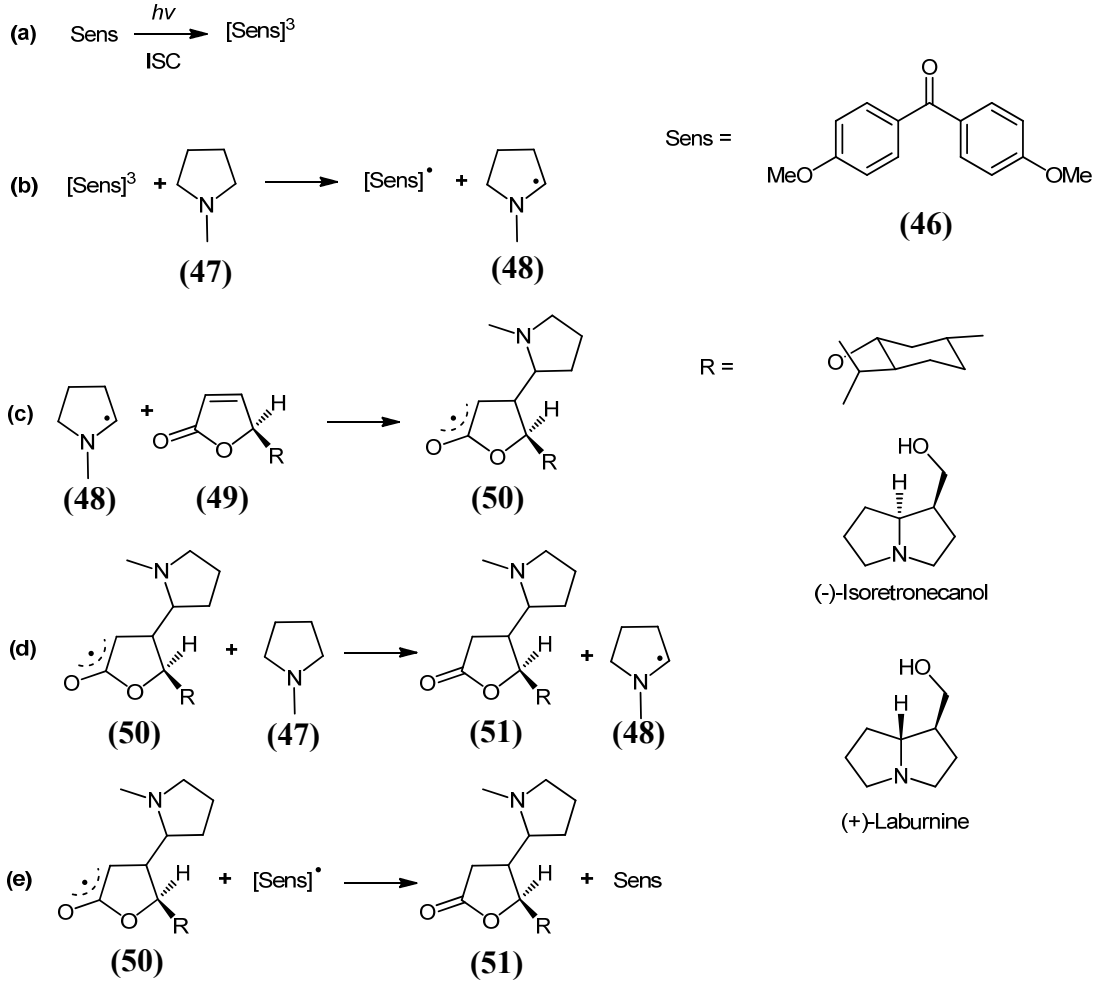


Figure 1.2.48: Sensitised PET synthesis of pyrrolizidine alkaloid precursors.

PET has also been used to initiate [4+2] cycloadditions which would be otherwise unfavourable in the ground state. A recent example of this can be seen in the sensitised addition of arylimines to *N*-vinylpyrrolidinone **52** and *N*-vinylcarbazole (Figure 1.2.49).[46] The sensitiser used in this case is 2,4,6-triphenylpyrylium tetrafluoroborate **58** (TBT). This sensitiser has found extensive use in the field of synthetic photochemistry due to the fact that it absorbs well in the visible region, is easily accessible, highly soluble in organic solvents and a good oxidising agent in its excited state.[47]

Following photochemical excitation (step a), **58** abstracts an electron from the double bond of **52** to generate a radical cation **53** (step b). This radical cation then

proceeds to add to the imine **54** (step c). This is followed by cyclisation to generate the bicyclic intermediate **56** (step d). A rearomatisation step takes place in order to generate the final product **57**, which was obtained in yields of up to 91% (step e). This step includes the regeneration of the sensitiser by e^- transfer.

Tetrahydroquinoline derivatives like the ones generated by this method have long been an area of intense interest for organic chemists due to the presence of these scaffolds within the framework of numerous biologically active natural products and pharmaceutical agents.

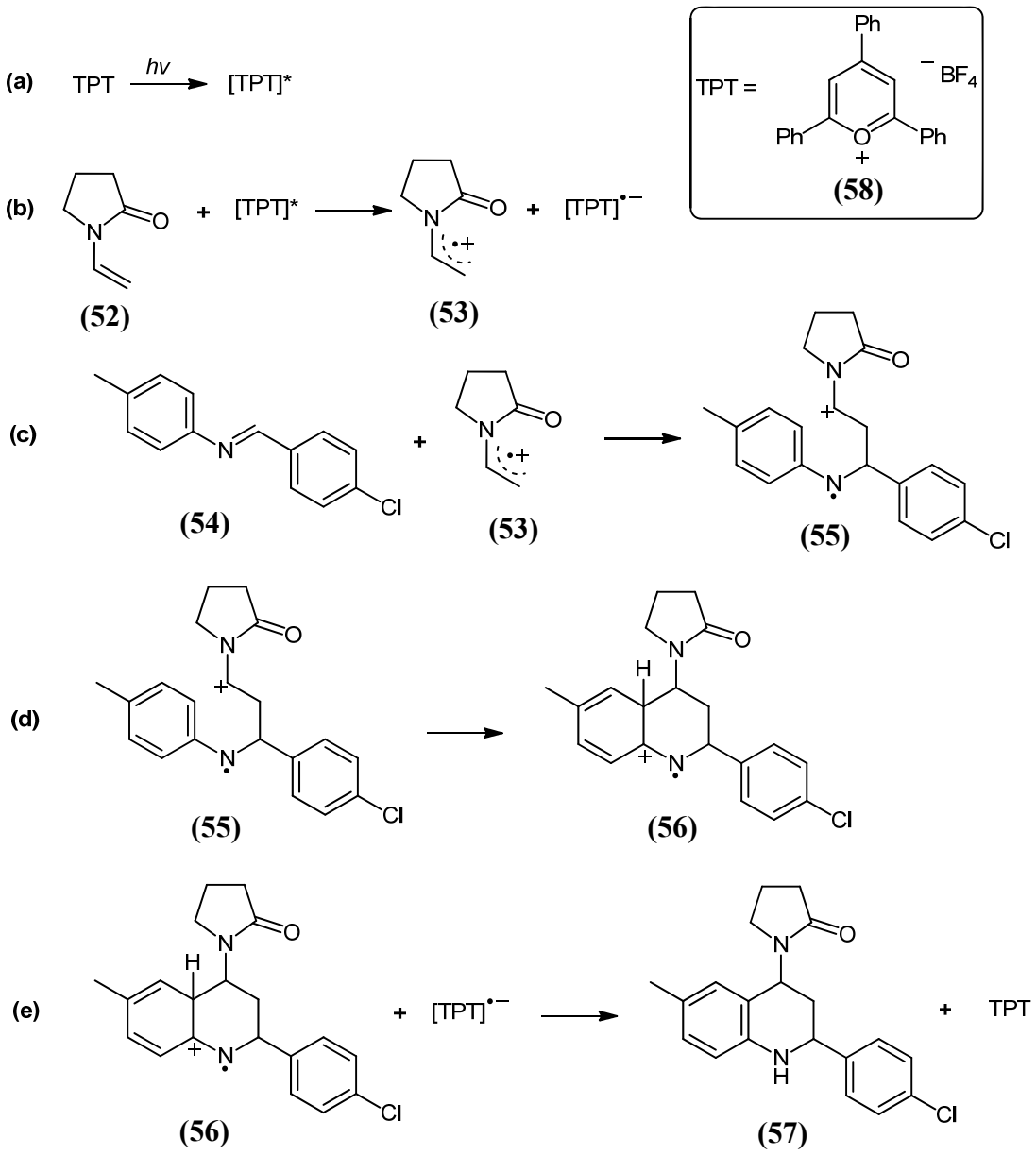


Figure 1.2.49: Sensitised PET synthesis of tetrahydroquinoline derivative **57**.

There is currently considerable interest in using semiconductors as photosensitisers.[48] Materials such as TiO_2 are being investigated for their applications in water treatment.[49] Upon irradiation with light an electron can be transferred from the valence band to the conductor band of a semiconductor particle to generate a free electron (e^-) and a hole (h^+). The wavelength of light required is dependent on the band gap of the semiconductor.

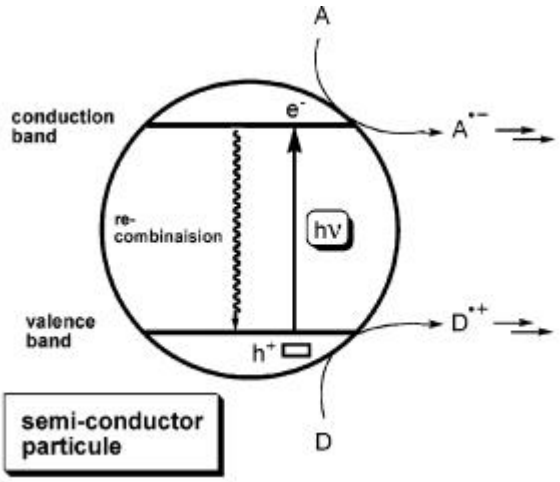


Figure 1.2.50: Semiconductor radical ion generation.

Inorganic semiconductors have found use as sensitisers in organic synthesis (Figure 1.2.50). An example of this can be seen in the TiO_2 sensitised reaction between 4-methoxybenzyl(trimethyl)silane **59** and maleic anhydride **62** (Figure 1.2.51).[50] In this reaction TiO_2 is irradiated to form an electron (e^-) and hole (h^+) pair (step a). An electron is abstracted from **59** (step b) to yield **60**, which then fragments to yield the neutral radical **61** (step c). At the same time **62** absorbs an electron to generate the radical ion **63** (step d). A molecule of **61** then proceeds to react with the alkene functionality of **62** to yield the radical intermediate **64** (step e). This is followed by electron transfer from the alkene radical ion **66** generated in step d to **64**, and hydrogen transfer from water to yield the final neutral product **65** (step f).

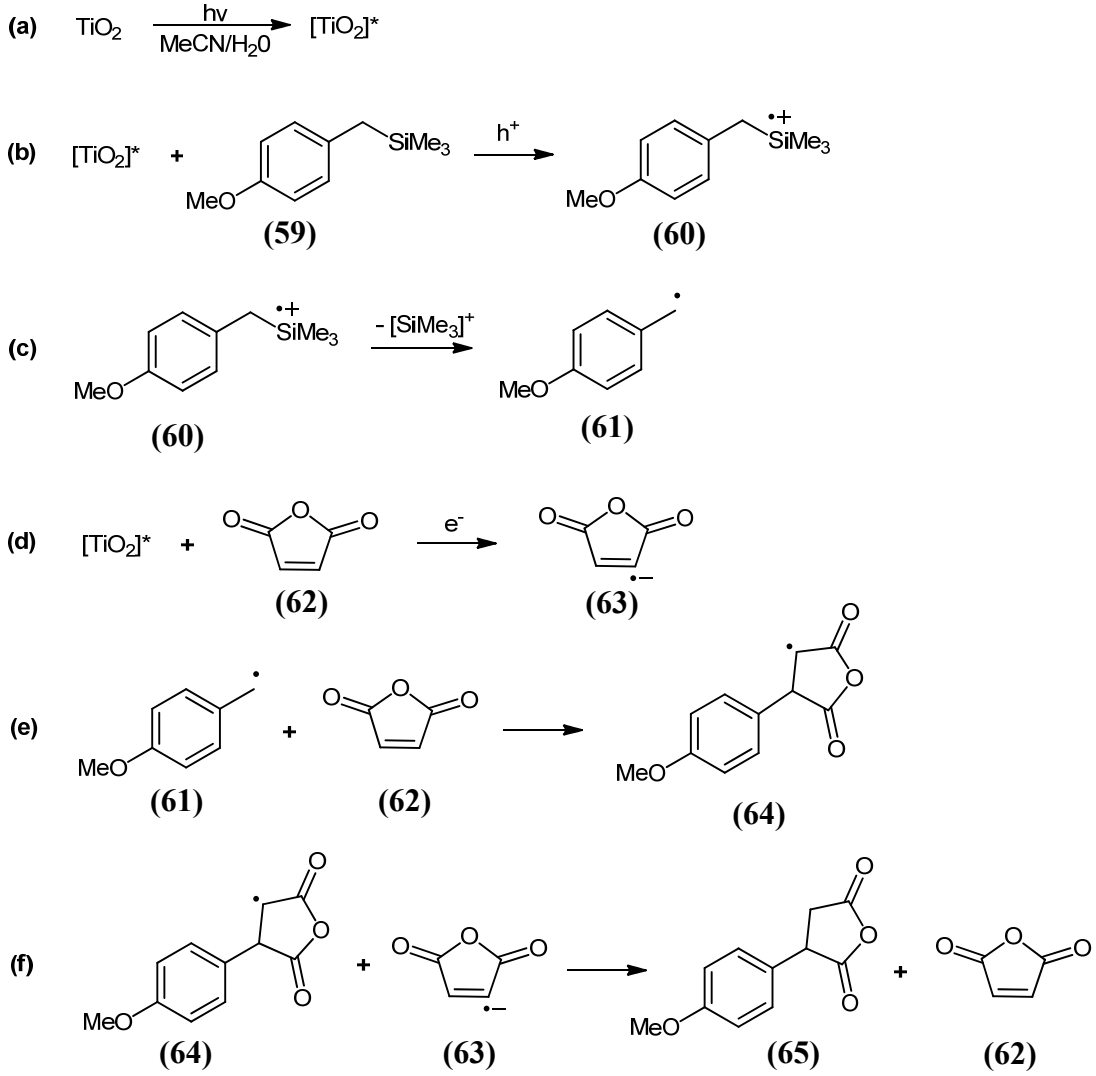


Figure 1.2.51: Semiconductor sensitised PET synthesis.

A similar approach was applied to the photochemical synthesis of unsaturated α-amino esters from imines and olefins using silica-supported cadmium sulphide as a sensitizer (Figure 1.2.52).[51] An electron from photochemically excited cadmium sulphate is transferred to **66**, followed by proton exchange to generate the neutral radical **67**. At the same time, the photochemically excited cadmium sulphate extracts an electron from **68** to yield the neutral radical **69** and a proton. The two neutral radicals **67** and **69** combine to form the final product **70**.

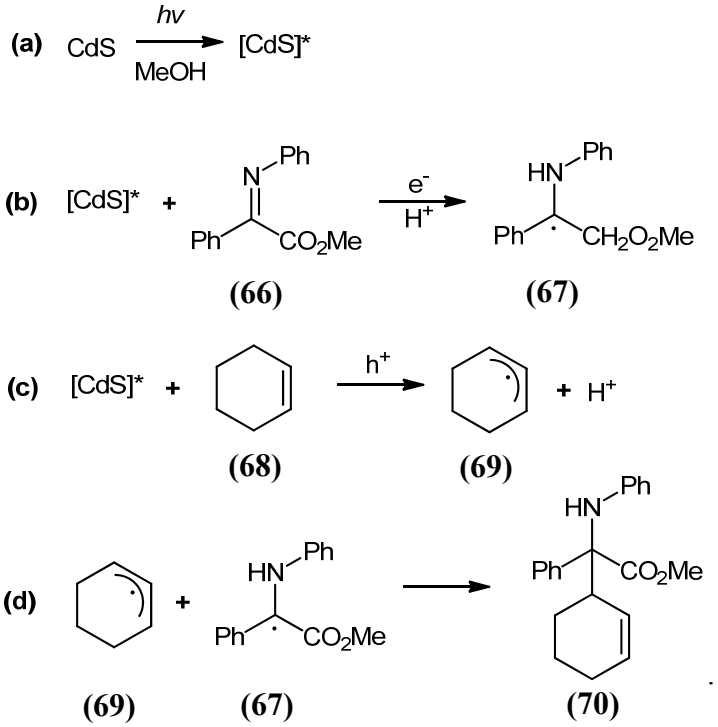


Figure 1.2.52: Semiconductor sensitised PET synthesis of unsaturated α-amino esters.

1.2.6 Photochemistry of aromatic compounds

Compared to other chromophores, photochemical interest in aromatic compounds has only developed relatively recently. Indeed, benzene was considered an ideal solvent for photochemistry as late as the 1950's due to its UV stability. This changed in 1957 with the publication of the photoisomerisation of benzene to fulvene.[52] The irradiation products of benzene are shown in Figure 1.2.53. Quantum yields for the formation of benzvalene and fulvene from benzene are of the order of 0.01 to 0.03. Dilution with alkanes increases the photoisomerisation efficiency. (Maximum concentrations of each isomer of *ca*. 300 to 500 mg/L can be obtained from neat benzene.[53]) Benzene can only be converted to Dewar benzene by irritation with light in the 200 nm region, whereas irradiation with 254 nm light yields only benzvalene and fulvene. The UV spectrum of benzene has three maxima centred at 254, 203 and

180 nm, corresponding to the transition from the S_0 state to the S_1, S_2 and S_3 states respectively.

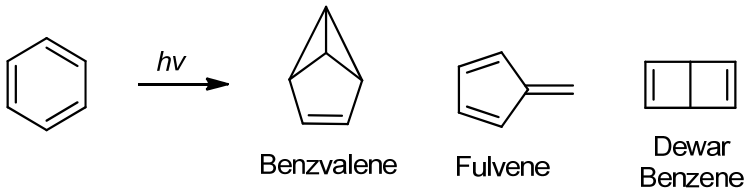


Figure 1.2.53: Irradiation products of benzene.

Thermal reactions of aromatic compounds are almost entirely limited to substitution processes. The retention of aromaticity is a major factor or driving force. The photoexcitation of the benzene ring can lead to a rich variety of reactions, frequently yielding nonaromatic products. The energy of excitation promotes the formation of unstable and highly strained compounds which are inaccessible from arenes by conventional thermal routes. Photochemical aromatic reactions are typically classified as ring isomerisations, photoadditions, photosubstitutions, cyclisation reactions, photodimerisations and lateral nuclear rearrangements. It should be noted that this section will only be dealing with reactions involving a photochemically generated aromatic excited state, and not reactions involving the reaction of aromatics with other photochemically generated excited species.

1.2.6.1 Aromatic photosubstitution

Amongst the various classifications of aromatic photochemical reactions one of the most important is photochemical aromatic substitution. The substitution of ground state aromatic compounds is one of the best known and most extensively studied classes of organic reactions, having wide scope and enormous synthetic potential. Electrophilic substitution is particularly common in the ground state, due to the electron rich nature of aromatic compounds. This is not the case however for the

excited state; nucleophilic substitution is far more common. This can be explained by the nature of the excited state of aromatic compounds. An electron has been promoted from the HOMO to the LUMO. On one hand this makes the molecule somewhat more electrophilic as it can accept an electron into its half-filled HOMO from a good electron donor. The radical anion generated can undergo further reactions leading to substitution, or it can react with a nucleophile. On the other hand, the electron in the half-filled LUMO can be taken up by a good electron acceptor and the resulting radical anion can combine with a nucleophile. Both of these processes are detailed in Figure 1.2.54.

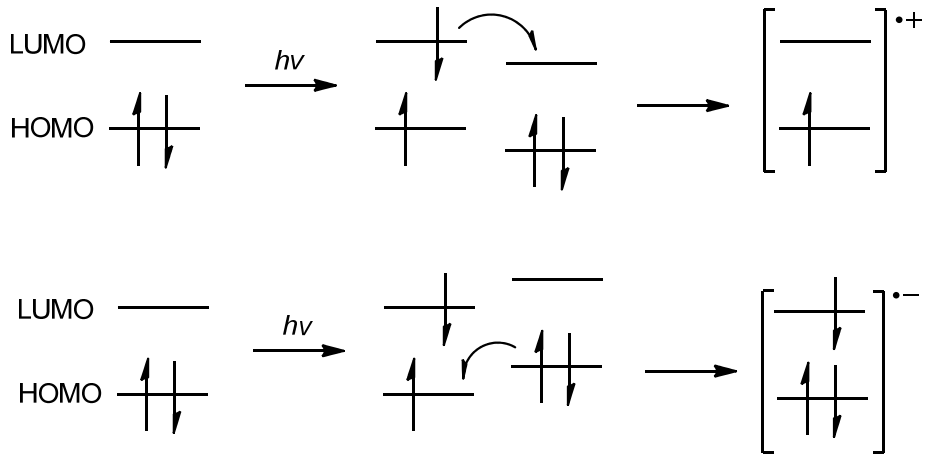


Figure 1.2.54: Orbital diagram of an aromatic system as an electron donor or acceptor.

There are numerous examples of photoinduced nucleophilic aromatic substitutions involving both anionic and neutral nucleophiles. These reactions tend to give high conversions and yields, however they have been poorly utilised for synthetic purposes. An interesting aspect to aromatic photosubstitution is that the substitution positions for substituents is generally the reverse of that observed for ground state aromatic compounds; thus, electron withdrawing groups activate the *meta* positions towards nucleophilic substitution, whereas electron donating groups activate the

ortho and *para* positions. One of the first published examples of nucleophilic aromatic substitution is the addition of cyanide to various aromatics (Figure 1.2.55).[54]

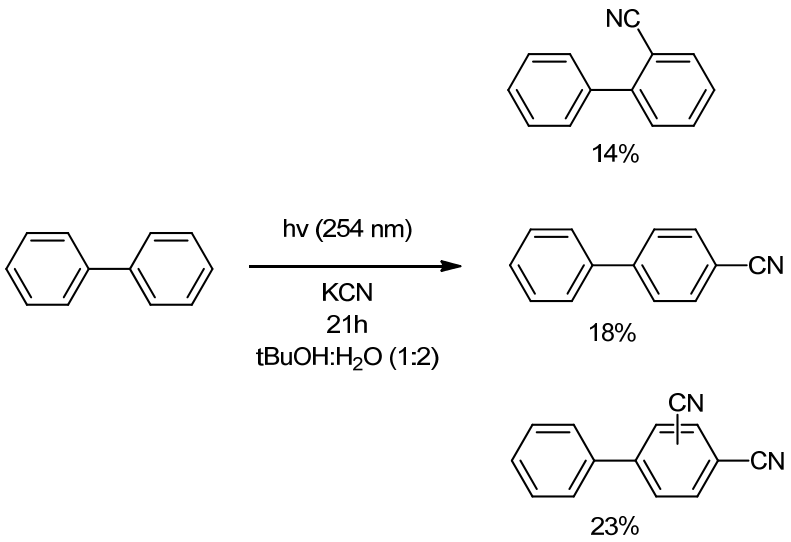


Figure 1.2.55: Photosubstitution of biphenyl with cyanide.

Two classes of compounds known to undergo photochemical aromatic substitution are haloaromatics[55] and anisole[56] **71**.

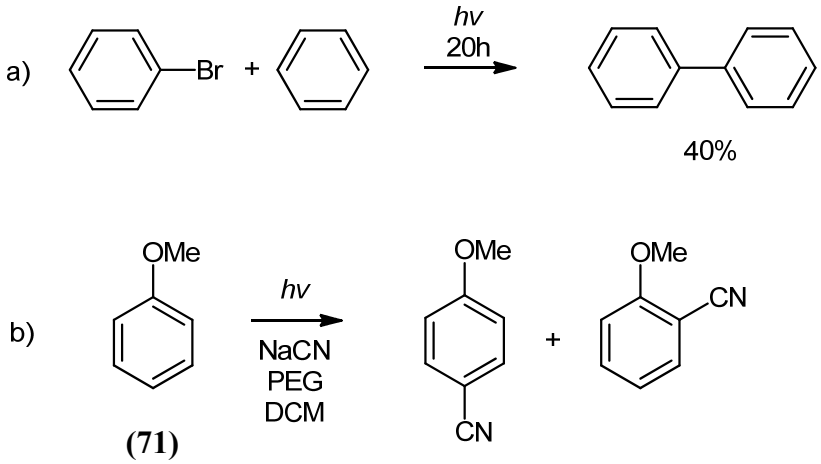


Figure 1.2.56: Examples of photosubstitutions of a) haloaromatics and b) methoxybenzenes.

The photochemistry of these two classes of compounds has been applied to the synthesis of biaryl phthalonitriles (Figure 1.2.57).[57] Whether the reaction proceeds via direct excitation (Path a) or PET (Path b) is determined by the donor-acceptor abilities of the reactants.

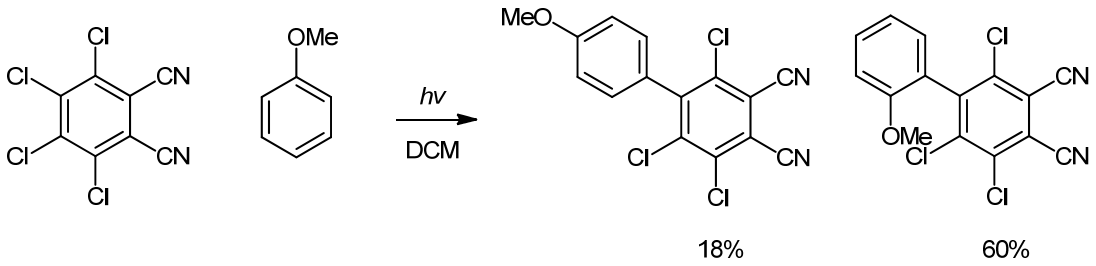


Figure 1.2.57: Synthesis of novel biphenyl phthalonitriles.

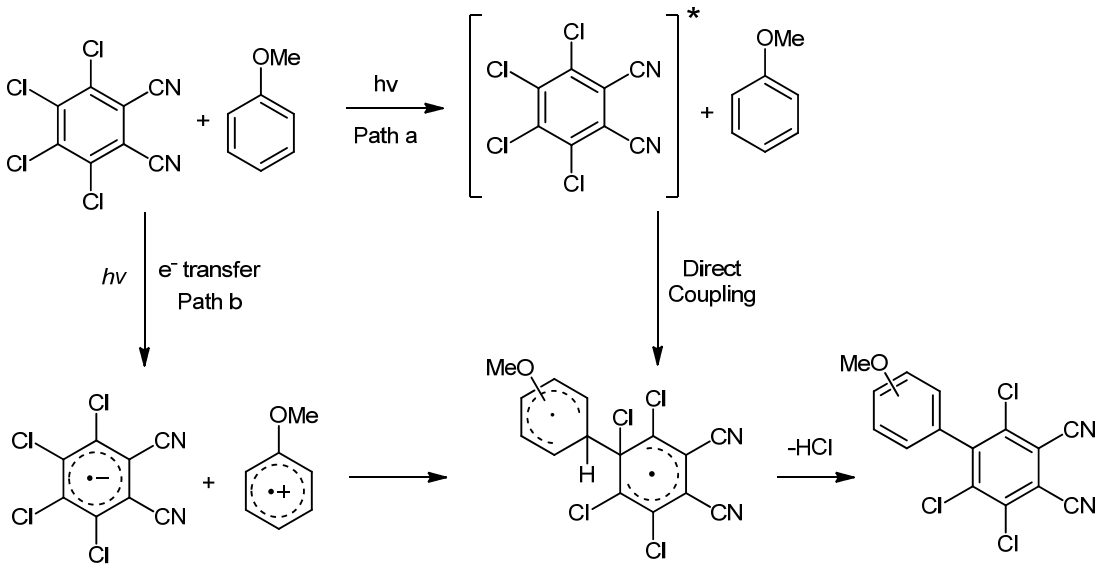


Figure 1.2.58: Possible mechanisms of novel biphenyl phthalonitrile synthesis.

1.2.7 The photo-Friedel-Crafts reaction

The photo-Friedel-Crafts reaction involves the irradiation of quinone compounds to yield products similar to those obtained from a classical Friedel-Crafts acylation.[58] Unfortunately, the classical method often suffers from the use of acid chlorides and equimolar amounts of harmful Lewis acids (usually $AlCl_3$), the formation of undesired by-products (especially volatile hydrochloric acid) and certain restrictions on functionalities in the starting materials.[59] The photochemical alternative also represents a significant advantage in terms of "green" chemistry. The reaction is 100% atom efficient and viable using sunlight as a light source.

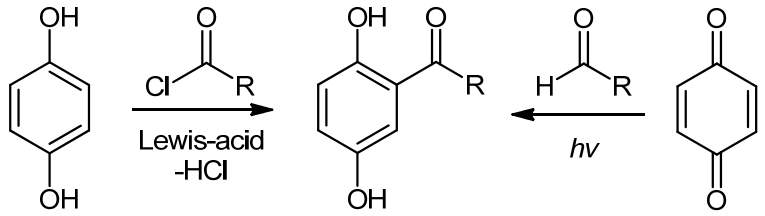


Figure 1.2.59: Photo-Friedel-Crafts acylation vs. Classical Friedel-Crafts acylation.

The prevalence of quinone and hydroquinone moieties in bioactive natural products makes this a fruitful area of study.[60] Products of the photo-Friedel-Crafts acylation reaction have been used as starting materials in the synthesis of the benzodiazepine skeleton (Figure 1.2.60).[61]

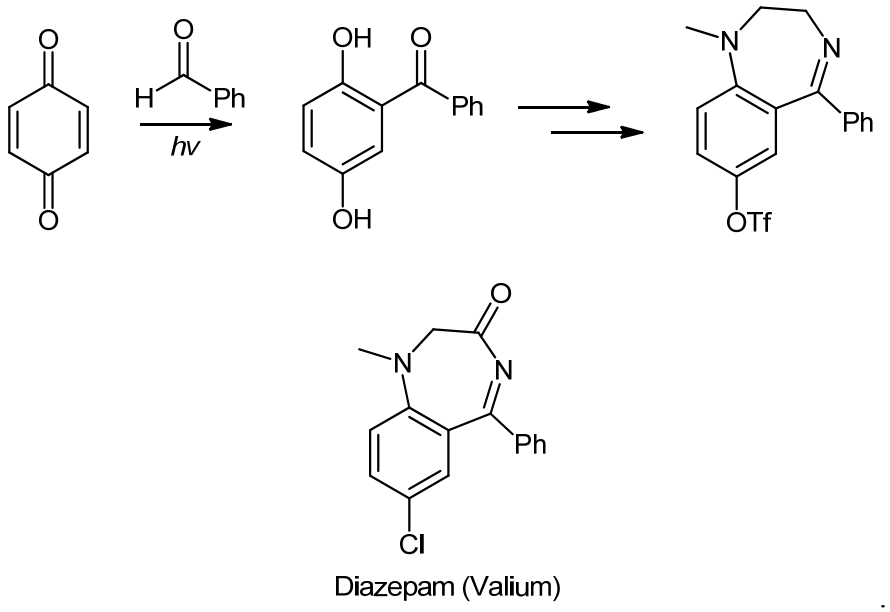
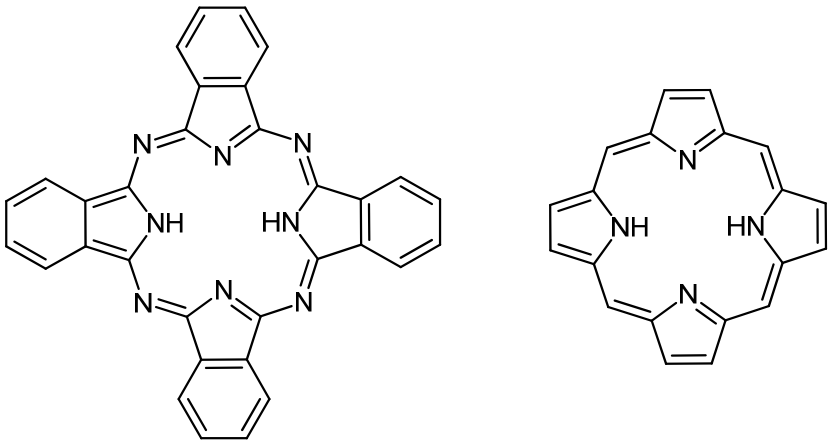


Figure 1.2.60: Use of photo-Friedel-Crafts products in the generation of the benzodiazepine skeleton.

1.3 Phthalocyanines

Phthalocyanine (Pc) was first observed as an unidentified by-product in the conversion of phthalimide to ortho-cyanobenzamide in 1907. Potential applications as a dye led to significant interest in the blue-green material. A combination of techniques (such as elemental analysis, ebullioscopic molecular mass determination and oxidative degradation) allowed Reginald P. Linstead of the Imperial College London to correctly elucidate the structure of the by-product as **72** (Figure 1.3.1) His results were later confirmed by X-ray diffraction.



(72) **(73)**

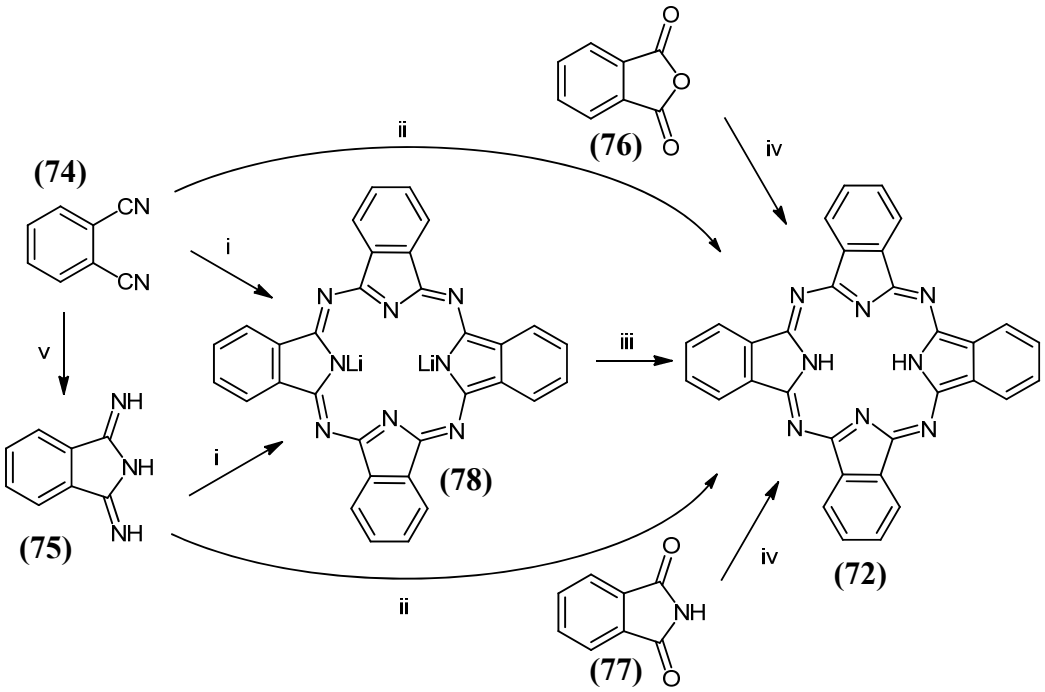
Figure 1.3.1: General structure of metal-free phthalocyanine **72** and porphine **73**.

Phthalocyanines are planar symmetric macrocycles composed of four iminoisoindole units with a central cavity capable of complexing metal ions. Due to their planar nature and the conjugated array of 18 π-electrons, Pcs exhibit aromatic characteristics as described by Huckel's theory of aromaticity. This accounts for some of the otherwise unexpected properties of Pcs, such as high stability and low solvency in polar media.

It has been noted that phthalocyanines bear a strong resemblance to the naturally occurring class of compounds, porphyrins **73** (Figure 1.3.1). The main differences between these two classes of compounds are the four benzo-subunits and the nitrogen atoms at each of the four *meso* positions. Unlike phthalocyanines, many important natural products are based on porphyrins; for example the porphyrin heme is an important part of the oxygen transport system in mammals, while chlorophyll plays a vital role in converting light to energy in plants. Despite this, the improved stability, spectroscopic properties and synthetic flexibility make phthalocyanines an important industrial class of compounds.

1.3.1 Synthesis of unsubstituted Pcs

Pcs can be synthesised from several distinct starting materials, many of which are interconvertible.[62] A summary of the most common methods of Pc synthesis are shown in Figure 1.3.2. It should be noted that most Pc precursors are *ortho* substituted benzenes, with the most commonly used being phthalonitrile **74**.



i) Lithium, reflux;pentanol
ii) Heat; 1,8-diazabicyclonon-5-ene (DBN); pentanol or dimethylaminoethanol (DMAE) and pentanol
iii) Acid
iv) heat in a high boiling point solvent with urea
v) Sodium metal; ammonium; methanol

Figure 1.3.2: Synthesis of Pcs.

One of the most common methods of synthesising metal free Pc is thermally. Phthalonitrile **74** is heated to over 200 °C in the presence of a suitable reducing agent such as hydroquinone.[63] This can be done in a high boiling point solvent, or in the absence of a solvent. Another method of preparing phthalocyanines from phthalonitriles involves refluxing in a long chain alcohol such as pentanol in the presence of lithium.[64] This generates the dilithium Pc **78**, which can be converted to the metal free Pc **72** by treating with acid.

Alternatively, metal free Pcs can also be synthesised from **74** with yields of up to 90% by heating in a basic solvent such as 2-*N*,*N*-dimethylaminoethanol (DMAE) while bubbling with ammonia.[65] Likewise, strong organic bases such as 1,8-diazabicycloundec-7-ene (DBU) have been used with phthalonitriles in alcohol to form metal free Pcs.[66] Alternatively, **74** may be readily converted to diiminoisoindoline **75** by bubbling with ammonia[67] which can then be condensed to a Pc under relatively mild conditions.[67-68]

Alternatively, Pcs can also be synthesised from phthalic anhydride **76** or phthalimide **77** by heating in the presence of urea and a catalyst (ammonium molybdate).[69]

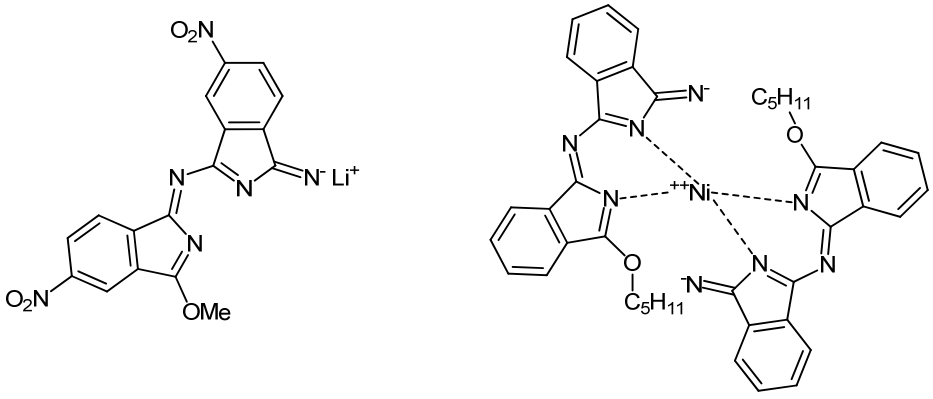
Metal free Pcs can be converted to the metalated form by heating in a high boiling point solvent with the appropriate metal salt. Metallated Pcs can also be prepared directly from phthalonitrile by heating phthalonitrile in the presence of the appropriate metal salt.[64]

Typically, metals inserted into a Pc are in the +1 (alkali metals) or +2 oxidation state, however complexes containing metals in the +3 or +4 state are not uncommon.[70] In the case of metals which typically have an oxidation state of +1 the central nitrogen atoms ligate two ions. However, space in the central cavity is insufficient to accommodate both metal ions, and hence they protrude above and below the plane of the Pc. This disrupts the intermolecular (π-π stacking) forces required for aggregation, and as a result, Pcs containing alkali metals tend to have enhanced solubility in organic solvents.[71] In a similar manner, metals ions with an oxidation state above +2 usually coordinate axial ligands above or below the plane of the Pc which can also improve solubility.

1.3.2 Mechanism of Pc formation

Like many other common reactions, the exact mechanism of Pc formation is not completely understood. This is in part due to the fact that Pcs can be synthesised from several different classes of starting materials via many different reaction pathways. These pathways may have common intermediates, without necessarily having a common mechanism. Determination of the mechanism of Pc formation is further complicated by the harsh conditions required to synthesise them. Despite this, the isolation of some key intermediates has given significant evidence for the mechanism of Pc formation.

One important intermediate which has been isolated is **79**, (Figure 1.3.3). This has been obtained by the reaction of 4-nitrophthalonitrlie with lithium alkoxide.[72] This has been shown to be similar to **80** which is known to be a key intermediate in the preparation of nickel(II)Pc from di-imino-isoindoline.[73]



(79) **(80)**

Figure 1.3.3: Intermediates isolated from Pc synthesis.

From here, the reaction can proceed in one of two ways as shown in Figure 1.3.4.

1) Two units of **79** may condense to form the macrocycle frame of a Pc **81**. This tends to be the favoured pathway in the presence of a +2 metal due to metal templation.

2) Addition of further phthalonitrile units leads to a trimeric and tetrameric **82** species, which continues to cyclise to a Pc. This method is more common in the absence of a metal or in the presence of a +1 metal.

Finally, a two-electron reduction of the macrocycle occurs to give the 18π-electron aromatic system. This is achieved by loss of an aldehyde after oxidation of the alkoxide. This oxidation step generates H^+ which is mopped up by lithium alkoxide.

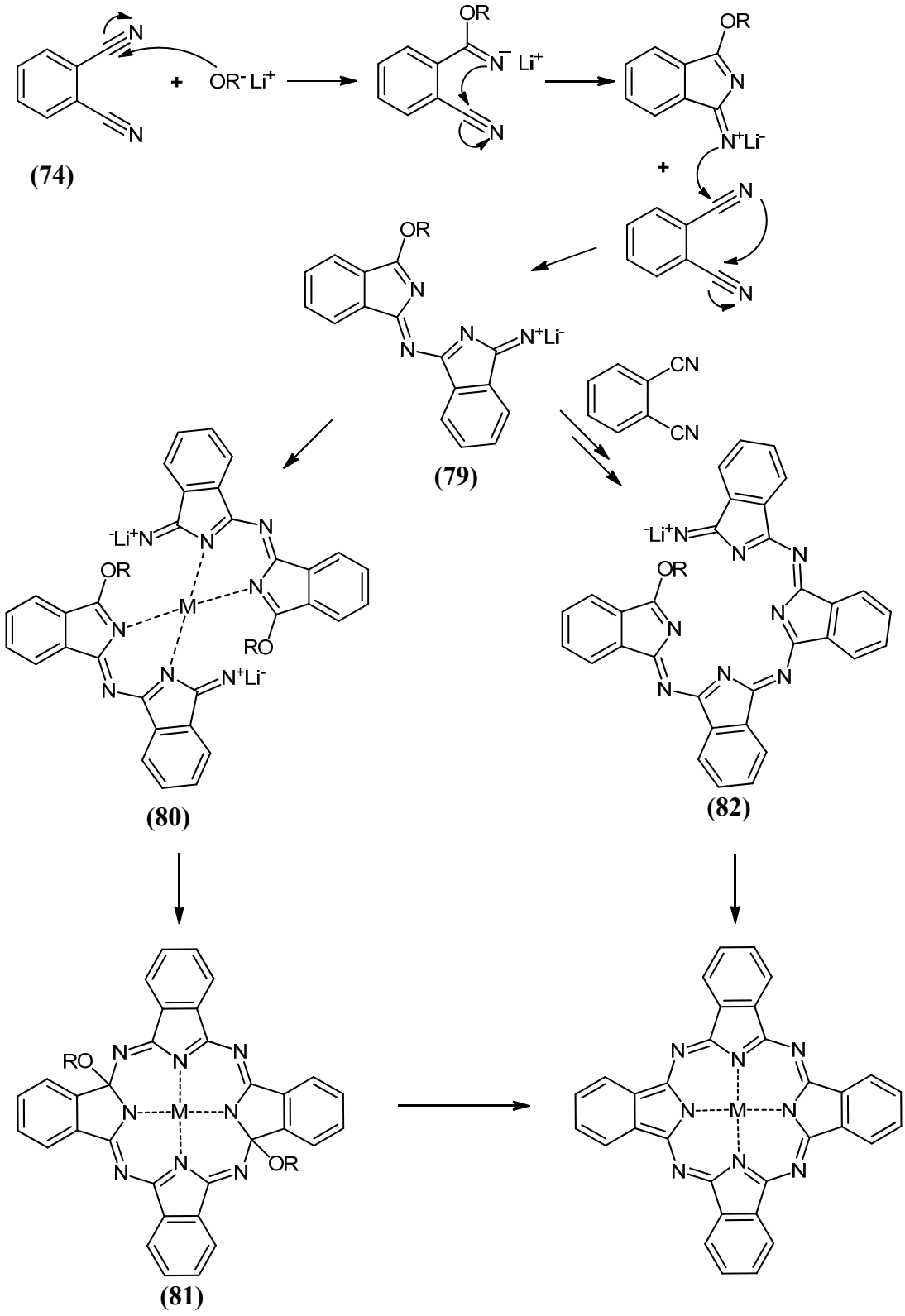


Figure 1.3.4: Proposed mechanism of Pc formation.

1.3.3 Symmetric peripherally substituted Pcs

There are two main strategies for introducing peripheral substituents into a Pc. The first is direct electrophilic substitution onto the Pc. Unfortunately, this suffers from the drawback that substitution is not selective, leading to multiple substitutions. This can result in up to sixteen different compounds with the formula $Pc(X)_n$ (n = 1-16). An example of this type of substitution is shown in Figure 1.3.5. Electrophilic substitution methods such as these are sometimes used to create pigments for the dye industry where the degree of substitution is not important, and hence separation and purity can be neglected.

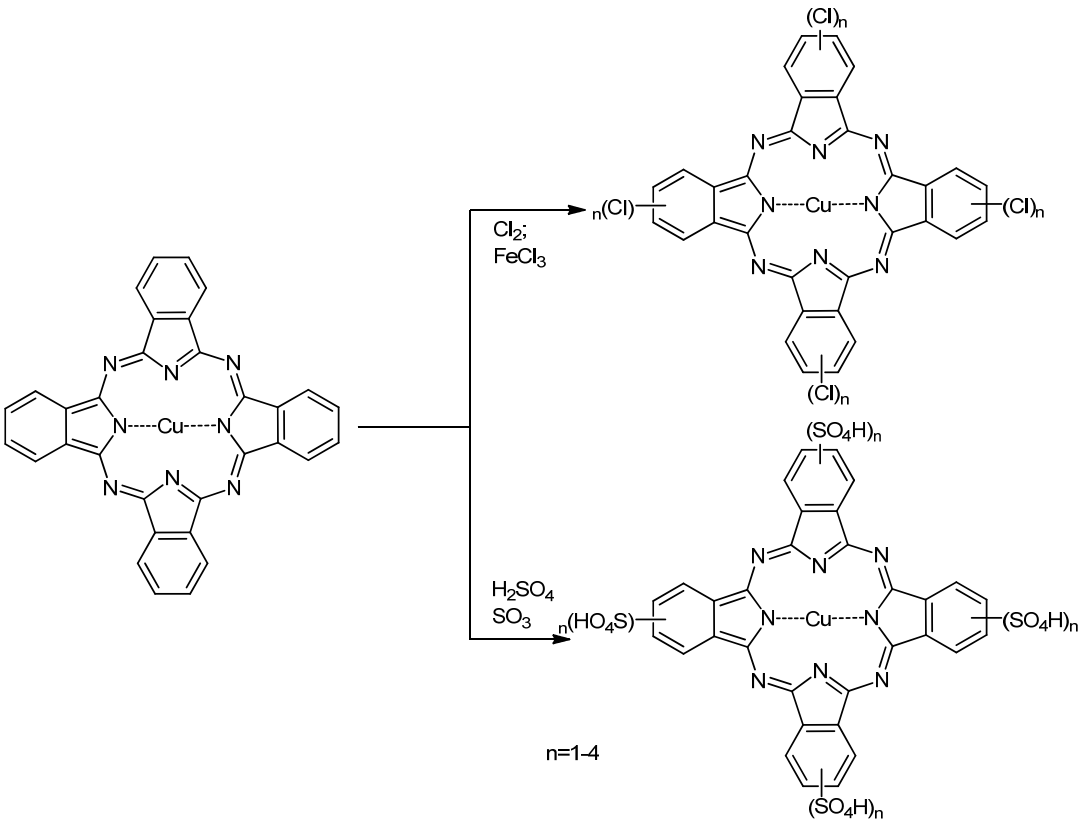


Figure 1.3.5: Partial substitution of Pcs.

A much more practical approach to the generation of peripherally substituted Pcs is modification of the parent phthalonitrile. The advantage of this is that a Pc with a

specific composition of $PcR_{4X}M$ (where X is the substituent(s) on the phthalonitrile precursor) can be generated. This method has become much more popular with the advent of commerically available substituted phthalonitriles which contain versatile functional groups. Of particular interest are phthalonitriles equipped with groups such as halogens and/or nitro groups (Figure 1.3.6), as they are capable of undergoing reactions such as nucleophilic aromatic substitution or couplings (Figure 1.3.7).

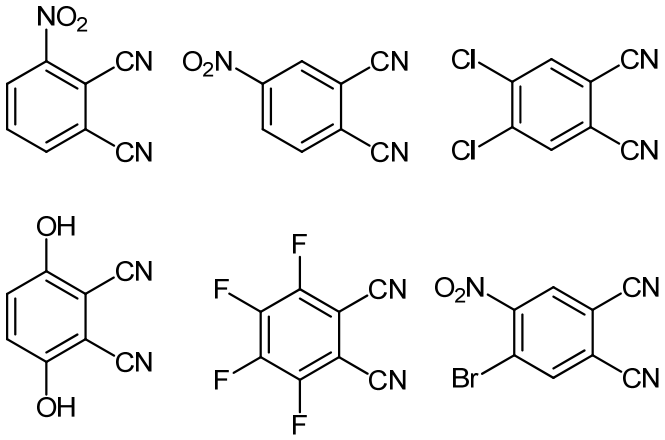


Figure 1.3.6: Some commerically available substituted phthalonitriles.

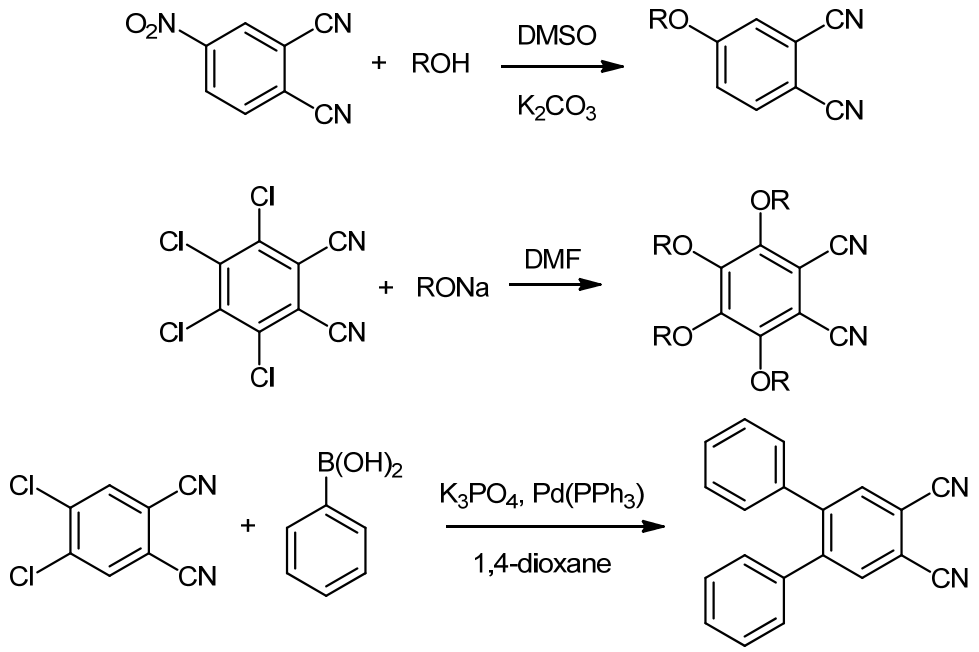


Figure 1.3.7: Examples of phthalonitrile substitution reactions.[74]

1.3.3.1 Positional isomers

An unfortunate drawback to using substituted starting materials is that, in the case of asymmetric starting materials, a statistical mixture of positional isomers is obtained. An example of this can be seen in the condensation of 4-*t*-butylphthalonitrile **83** (Figure 1.3.8).[75]

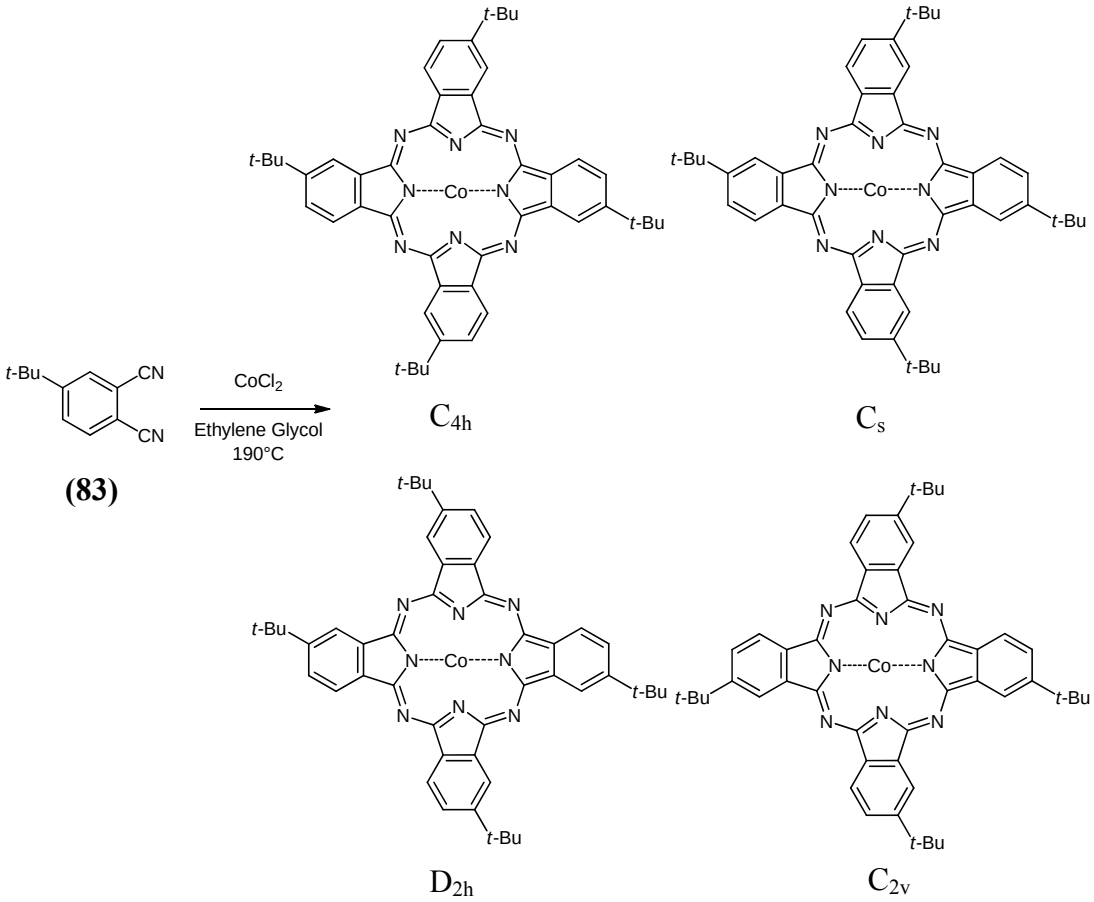


Figure 1.3.8: Potential substitution patterns of asymmetrical phthalonitriles.

Approaches to prepare single isomers from asymmetrically substituted phthalonitriles have been developed. One such approach involves the introduction of bulky groups in the 3-position of the phthalonitrile which allows for the production of only a single isomer, due to steric effects.[74a] An example of this is the synthesis of **84** (Figure 1.3.9). The product was obtained as a single isomer with a yield of 40%.

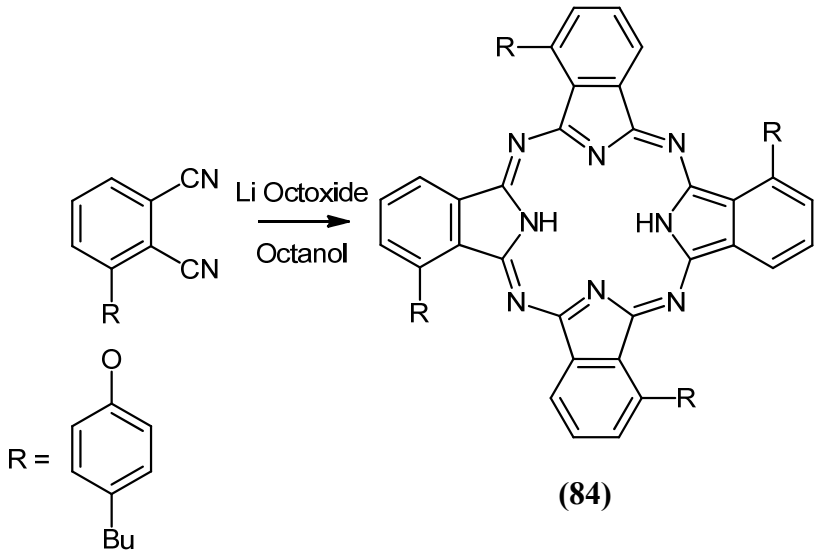


Figure 1.3.9: Synthesis of asymmetric α-substituted Pc.

A novel approach for the preparation of a single Pc isomer is achieved by the condensation of bisphthalonitriles. By linking two phthalonitriles by an appropriate bridge, they are effectively locked in conformation. This allows for the preparation of the D_{2h} isomer in yields of up to 21%.[76] An example of this can be seen in Figure 1.3.10.

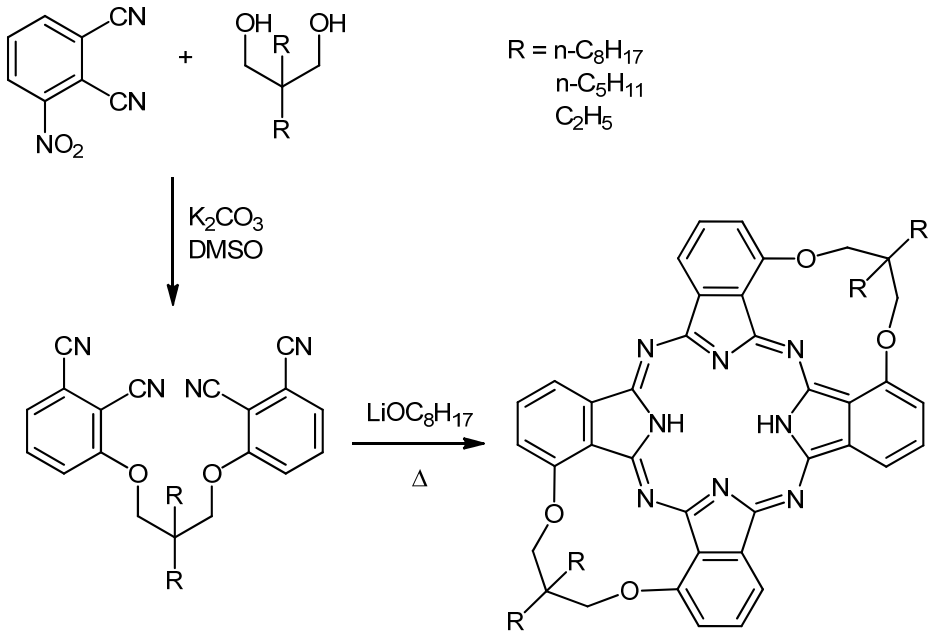


Figure 1.3.10: Condensation of bisphthalonitrile to Pc.

1.3.3.2 Symmetrically substituted Pcs

One advantage of using symmetric phthalonitrile starting materials is that it eliminates the possibility of products with various positional isomers. One important example of this is the synthesis of alkynyl phthalonitriles and their condensation to Pcs.[77]

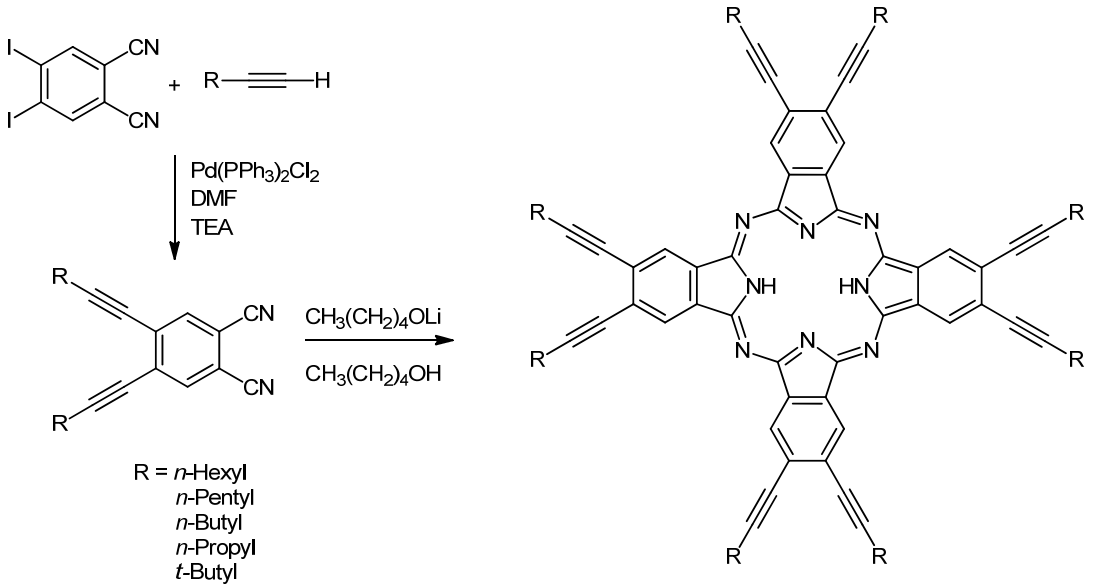


Figure 1.3.11: Synthesis of β-substituted Pc from symmetric phthalonitrile starting material.

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Thesis Proposal

Part 1

There is considerable interest in acylated quinones and hydroquinones and their derivatives, due to their similarity to various natural products and other biologically active compounds. With this in mind, it was proposed to examine the photo-Friedel-Crafts acylation reaction as a method of generating acylated hydroquinones, which maybe be subsequently oxidised to the corresponding quinone.

It was proposed to generate an extensive series of acylated hydroquinones by reacting naphthoquinone with a variety of aldehydes including aromatic, unsaturated, linear and branched aldehydes.

While the photo-Friedel-Crafts acylation of napthoquinone is conventionally carried out in either benzene or acetonitrile, in recent times there has been a push to avoid using toxic solvents such as these. In response to this trend, it was attempted to evaluate the reaction using alternative, environmentally friendly, "green" solvents.

Room temperature ionic liquids (RTILs) were chosen as one alternative to traditional toxic solvent systems. RTILs are commonly defined as ionic salts with a melting point below 100 °C. Their negligible vapour pressure and recyclable nature, and powerful solubilising ability make them a promising "green" alternative to other solvent systems. RTILs have been used as solvents in other photochemical reactions to great success.[78] Their transparency above 300 nm and ability to stabilise radicals makes them a suitable solvent for photochemical reactions.

A second approach is the evaluation of microemulsions (MEs). MEs consist of two immiscible liquids (often water and an organic solvent) combined in the presence of

a surfactant. A long chain alcohol may also be included as a co-surfactant. MEs are transparent and macroscopically homogeneous, and have much in common with micellar solutions. These properties make MEs a suitable alternative solvent for photochemical reactions. It was thus undertaken to investigate the efficiency of the photo-Friedel-Crafts acylation of naphthoquinone in MEs.

Part 2

Based on previously published work by Pratt *et al*. it was proposed to investigate the potential products available via the photo-aryl substitution of tetrafluorophthalonitrile (TFPN). It was undertaken to optimise this reaction under various parameters such as concentration and stoichiometry. It was also proposed to generate and characterise a library of substituted phthalonitriles.

This series of phthalonitriles was of considerable interest for a number of reasons. It was proposed that the extension of conjugation caused by the introduction of an aromatic ring to the phthalonitrile would have an impact on the spectral properties of the final molecule.

Any novel phthalonitriles generated would also make excellent precursors for conversion to phthalocyanines. These phthalocyanines would potentially have enhanced stability, due to the replacement of the chemically labile hydrogen atoms with fluorine. As well as this, the introduction of peripheral aromatic groups should result in enhanced solubility in organic solvents and a reduction in aggregation. All of these factors would make these phthalocyanines excellent catalysts for photooxygenation.

2.0 The photo-Friedel-Crafts acylation of naphthoquinone in benzene

2.1. Introduction

Acylated naphthoquinones and their derivatives represent an important class of natural products, with applications in various areas.[60a] 2-Dodecanoyl-3-hydroxy-1,4-naphthoquinone (DHN), for example, shows antibiotic properties, whereas acequinocyl is commercially used as a miticide.[79] The enantiomeric naphthoquinones alkannin and shikonin are natural products extracted from the roots of many plants in the *boraginaceae* family. They have been used as natural dyes or wound healing drugs for centuries.[80] These and other acylated quinones can serve as useful key intermediates for pharmaceutically active compounds. Acylated quinone compounds can usually be easily accessed by oxidation of the corresponding hydroquinone.

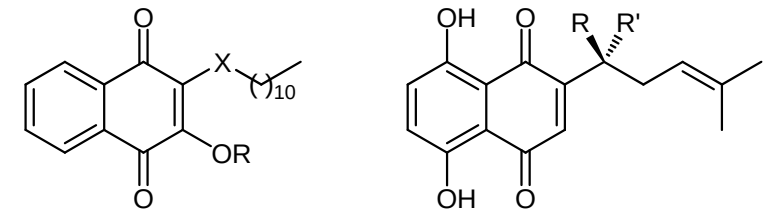


Figure 2.1.1: Some examples of quinone based natural products.

Acylated hydroquinones can be prepared by several traditional synthetic methods, such as Friedel-Crafts acylation[81], Thiele-Winter reaction[82], Hauser-Kraus annulations[83] and Fries or photo-Fries[84] rearrangement. Unfortunately, these methods suffer from harsh reaction conditions, formation of unwanted by-products or starting material limitations.

The photo-Friedel-Crafts reaction represents an alternative green pathway to the synthesis of these compounds; a) it is a 100% atom efficient reaction and b) is viable in sunlight, c) requires little post reaction work up, making it an ideal example of a "green" reaction.[85] An outline of the mechanism of this reaction is shown in Figure 2.1.2.

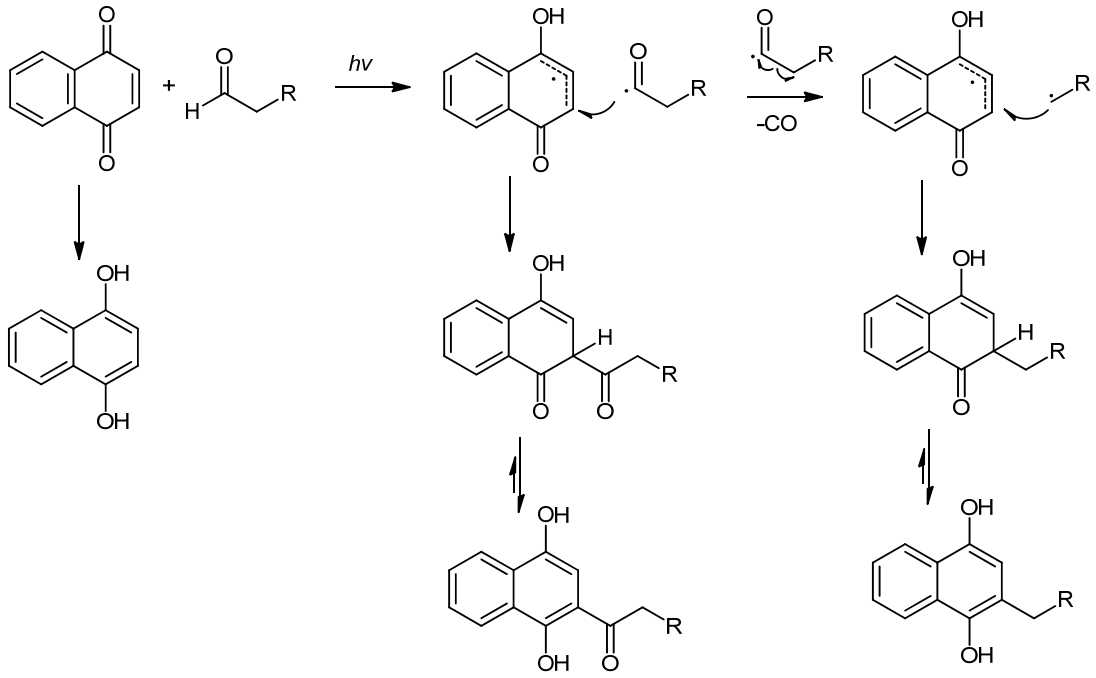


Figure 2.1.2: Mechanistic scheme for the photo-Friedel-Crafts acylation of naphthoquinone.

Up to now, the most popular photosynthetic experimental procedure for these compounds involves extended irradiation using a medium-pressure mercury lamp.[86] Unfortunately, this method suffers from several drawbacks. A medium-pressure mercury lamp emits light at several wavelengths (Figure 2.1.3), while the absorbance spectrum of 1,4-naphthoquinone is between approximately 300 and 375 nm (Figure 2.1.4), meaning the only valuable emissions of the mercury lamp are at 334 and 365 nm, with all other emissions essentially being wasted energy. It should also be noted that most acylated hydroquinones absorb between 350 and 450 nm, thus quenching

the effect of the 365 nm emission as the reaction progresses, and giving rise to potential side reactions.

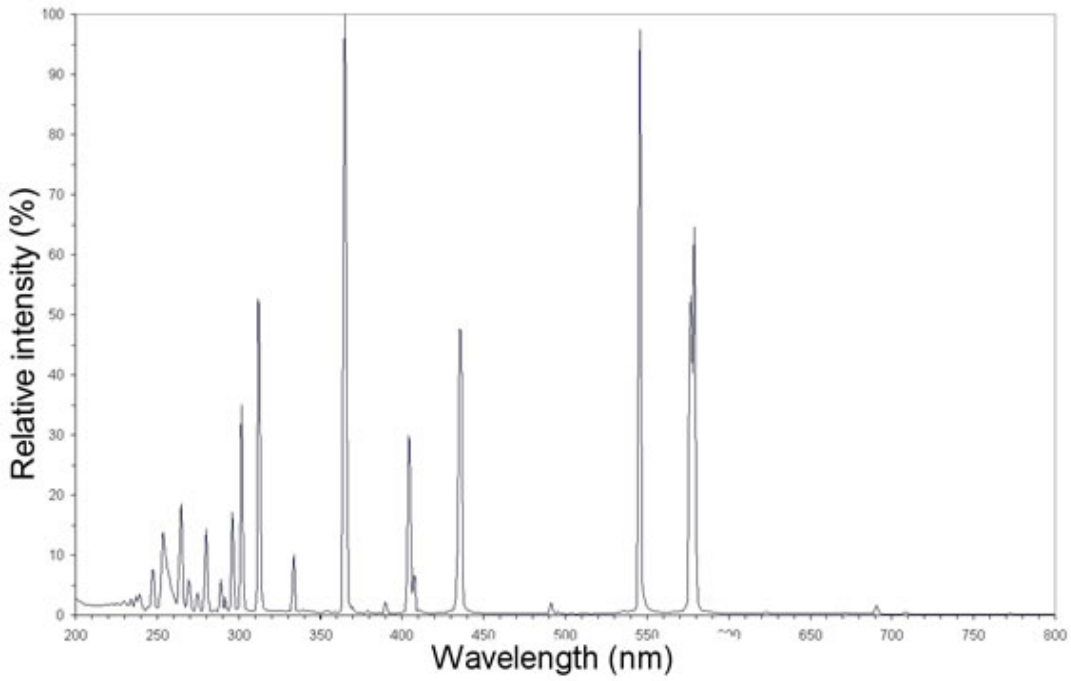


Figure 2.1.3: Emission spectrum of a medium-pressure Hg lamp.

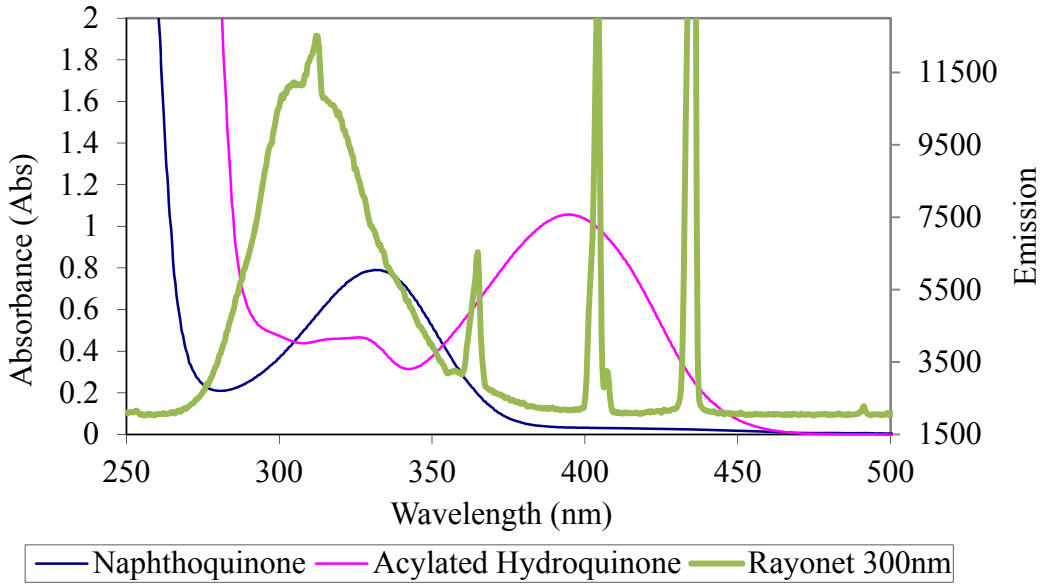


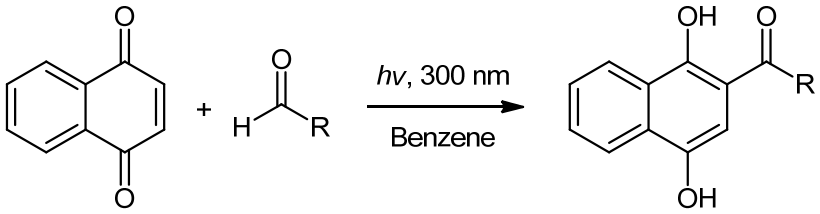
Fig 2.1.4: Emission spectrum of 300 nm Rayonet lamps versus absorption of naphthoquinone and a typical acylated hydroquinone.

With the aim of optimising the photo-Friedel-Crafts acylation reaction, naphthoquinone was irradiated in the presence of various aldehydes using the Rayonet Photochemical Reactor (RPR-200; Southern New England Ultraviolet Company) equipped with RPR-3000 Å lamps as a light source. These lamps have a λ_{max} of 300 ± 25 nm. It can be seen in Figure 2.1.4 that the emission of the 300 nm lamps overlaps very well with the absorption spectrum of naphthoquinone. It can also be seen that the lamps emissions have minimum overlap with the acylated product.

Benzene is an ideal solvent for these reactions as it is transparent above 280 nm and both starting materials are readily soluble in it. It is also important to note that the acylated hydroquinone products of these reactions are usually only sparingly soluble in benzene. This can be advantageous as it can often lead to products precipitating if the reaction is carried out at high concentrations, thus removing the product from the reaction mixture and eliminating the chance for follow-up reactions and improving the quantum efficiency of the reaction. Unfortunately benzene is a known carcinogen.

2.2 Results and discussion

Using parameters (concentration, stoichiometry etc.) previously optimised by a member of the research group (Michael Ryan), a series of reactions between naphthoquinone and various aldehydes were carried out. The general scheme of the reaction is shown in Figure 2.1.5. A wide selection of aldehydes was chosen in order to test the tolerance of the reaction to varying substrates. Examples included unsaturated, aromatic linear and branched aliphatic aldehydes.



1.6 mmol (78) 8 mmol (79a-x) (80a-x)

Figure 2.1.5: Photo-Friedel-Crafts acylation of naphthoquinone in benzene.

Table 2.1.1: Results of photo-Friedel-Crafts acylation of naphthoquinone.

Entry	Aldehyde	R	Yield (%)
a	Acetaldehyde	CH_3	75
b	Propionaldehyde	C_2H_5	73
c	Butyraldehyde	C_3H_7	58
d	Valeraldehyde	C_4H_9	80
e	Hexanal	C_5H_{11}	77
f	Heptanal	C_6H_{13}	75
g	Octanal	C_7H_{15}	68
h	Nonanal	C_8H_{17}	69
i	Undecanal	$C_{10}H_{21}$	61
j	Lauraldehyde	$C_{11}H_{23}$	69
k	Cyclohexanecarbaldehyde	C_6H_{11}	34
l	Isobutyraldehyde	$CH(CH_3)_2$	35
m	2-methylpentanal	$CH(CH_3)(C_3H_7)$	44
n	2-Methylbutanal	$CH(CH_3)(C_2H_5)$	83
o	3-methylbutanal	$CH_2CH(CH_3)_2$	48
p	Pivaldehyde	$C(CH_3)_3$	-
q	Acrolein	$CH=CH_2$	-
r	Crotonaldehyde	$CH=CHCH_3$	50
s	Hexa-2,4-dienal	$CH=CHCH=CHCH_3$	-
t	Benzaldehyde	Ph	71
u	Phenylacetaldehyde	CH_2Ph	59
v	Hydrocinnamaldehyde	$(C_2H_4)Ph$	43
w	Terephthaldehyde	Ph-*p*-COH	25
x	Cinnamaldehyde	CH=CHPh	-

The results obtained show that the reaction is viable for most classes of compounds with some exceptions. Yields for linear aliphatic aldehydes were generally good (up to 80%), with a general trend of longer aldehydes giving lower yields. This could possibly be explained by the nature of the isolation procedure. In the case of shorter chain aldehydes (C2-C5) the product can be isolated by evaporating the remaining aldehyde starting material under low pressure or, failing this, by recrystallising the product in cold benzene. As the longer chain aldehydes tend to have higher boiling points, it becomes impractical to evaporate the aldehyde. This results in the final product being dissolved in any remaining aldehyde starting material. In these cases the final product must be isolated by column chromatography.

In the case of branched aldehydes there are typically moderate to good yields, with the notable exception in the case of the reaction with pivaldehyde. This can be explained by a radical rearrangement of the aldehyde with the loss of carbon monoxide. In order for this alternative pathway to be viable there must be a tertiary carbon in the α-position of the aldehyde in order to stabilise the resulting radical product.

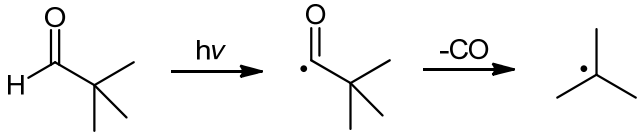


Figure 2.1.6: Decarbonylation of pivaldehyde.

It can be seen that the reaction has a high selectivity with regards to α-β unsaturated aldehydes, as summarised in Figure 2.1.7. The reaction with crotonaldehyde proceeds readily, however, the reaction ceases with the removal of the terminal methyl group, as in the case of acrolein, and with extension of conjugation, as in the

case of hexa-2,4-dienal or the addition of a phenyl group, as in the case of cinnamaldehyde. This is unfortunate as these products are of considerable interest due to the potential absorption properties caused by their extended conjugation, as well as their similarity to other bioactive compounds[87]. Figure 2.1.8 shows that the extension of conjugation caused by the presence of the double bond in crotonaldehyde induces a 25 nm bathochromic shift compared to the similar unsaturated compound.

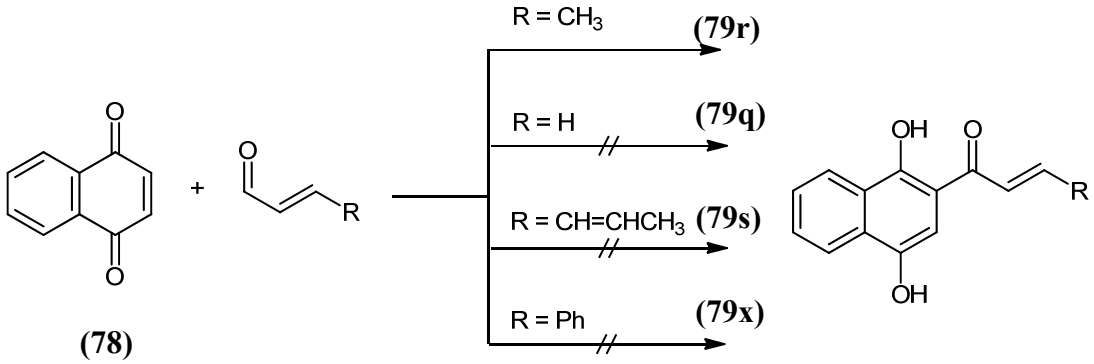


Figure 2.1.7: Summary of reactions between naphthoquinone and unsaturated aldehydes.

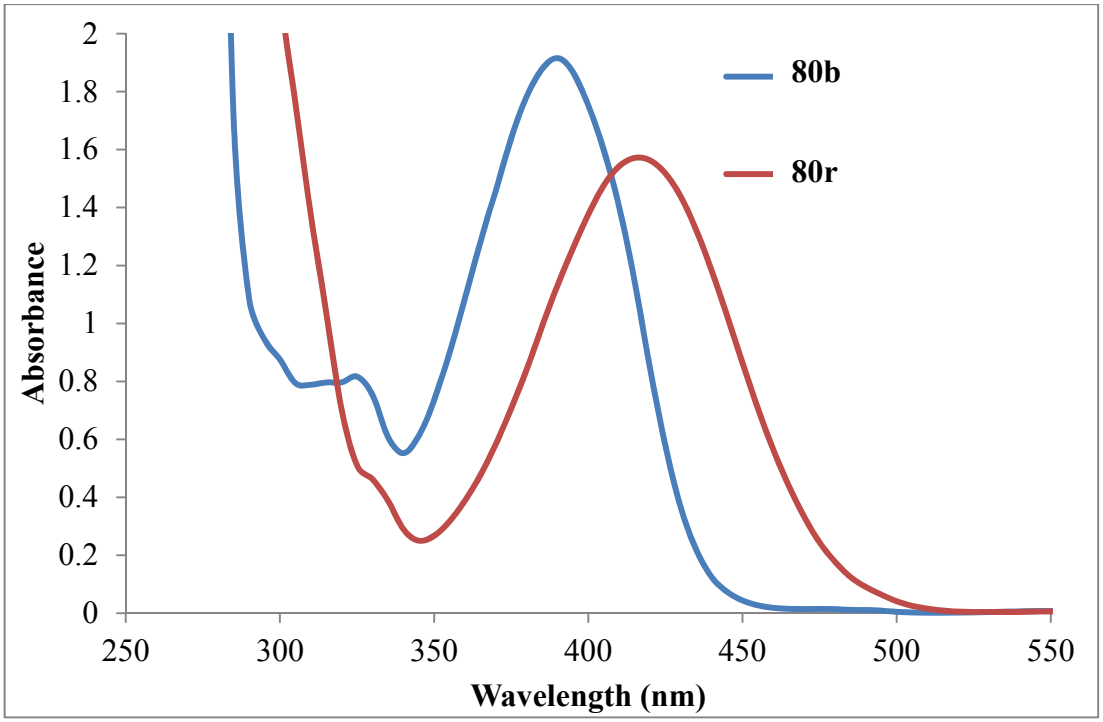


Figure 2.1.8: Comparison of absorbance spectra of **80b** and **80r**.

Aromatic aldehydes gave reasonably good yields. The most interesting of these was the product obtained from the reaction with terphthaldehyde. It is interesting to note that the final product of this reaction retains an aldehyde functional group, allowing for potential further reaction.

Having investigated the photo-Friedel-Crafts acylation of naphthoquinone in traditional solvents, it was undertaken to see if it was possible to improve the "green" nature of the reaction even further by replacing harmful benzene and acetonitrile with more environmentally friendly alternatives. Ionic liquids and microemulsions were chosen for this purpose.

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3.0 The photo-Friedel-crafts acylation of naphthoquinone in alternative "green" media

3.1 The photo-Friedel-crafts acylation of naphthoquinone in ionic liquids

3.1.1 Introduction

The term "ionic liquid" can be applied to any ionic salt which can be melted without decomposition[88]. With conventional salts the temperature at which this occurs is usually excessively high, for example, sodium chloride becomes a liquid at approximately 800 °C. Recently there have been many developments in the area of room temperature ionic liquids (RTILs).[89] These are salts with a melting point typically below 100 °C.

RTILs are typically composed of bulky organic cations, such as alkyl imidazoles and pyridinium salts, and a variety of anions. The anions range from halogens (which tend to have higher melting points) to inorganic species such as tetrafluoroborate (BF_4^-) and hexafluorophosphate (PF_6^-), or organics such as triflate (OTf^-) and bistriflimide (Tf_2N^-). Varying any one of these components can have a dramatic effect on the properties of the RTIL such as melting point, viscosity or solubility. For example, most RTILs with triflate as the anion are water soluble whereas if triflate is replaced with bistriflimide the RTIL is usually immiscible with water. Varying the cation can also affect the properties of the RTIL. For example, in the case of alkylimidazolium based RTILs, extension of the R group usually lead to an increase in viscosity of the RTIL. Figure 3.1.1 summarises the most commonly used cations and anions.

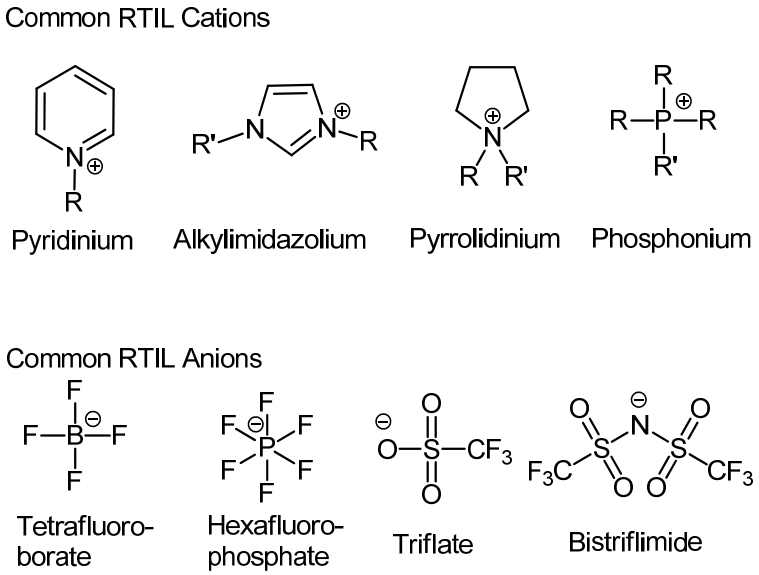

Figure 3.1.1: Common ions used in RTILs.

Due to their very low vapour pressure, recyclability, low flammability and customisable solubilising and catalytic properties, ionic liquids are currently emerging as new solvents, with particular applications in the area of "green" chemistry.[90] They have also been shown to stabilise radicals and radical ions in solution more efficiently than many conventional organic solvents.[91] This, coupled with their low to absent light absorption above 300 nm makes them potentially ideal solvents for photochemical reactions.[78b, 92] With this in mind we investigated their potential as a solvent for the photo-Friedel-Crafts acylation of naphthoquinone to replace the traditional hazardous solvents benzene and acetonitrile.

3.1.2 Results and discussion

3.1.2.1 Synthesis of RTILs

Due to the expense of many of the RTILs, we prepared many of them in house. In the case of RTILs consisting of imidazolium, pyrrolidinium and pyridinium cations the first step was addition of a bromoalkane to the tertiary nitrogen to form the

bromide salt. The two liquid components were mixed in the absence of solvent to give the solid salt which was crushed and washed with acetone to remove any unreacted starting material.

The final RTIL was then formed by ion exchange between the bromide salt of the cation and the sodium salt of the desired anion. When a tetrafluoroborate or hexafluorophosphate anion was desired, the two components were dissolved in acetonitrile and allowed to stir overnight at room temperature. A white precipitate of sodium bromide was observed. This was removed by filtration and the solution was thoroughly evaporated to give the final RTIL, usually in very high yield.

In the case of a RTIL with a bistriflimide anion, the two salts were dissolved in water and again allowed to stir overnight to form two layers. The lower water layer was removed and the RTIL was washed continuously with water to remove any remaining sodium bromide.

These methods were effective for RTILs with imidazolium, pyrrolidinium and pyridinium cations. A summary of the RTILs used and the reaction scheme of their synthesis is shown in Figure 3.1.2

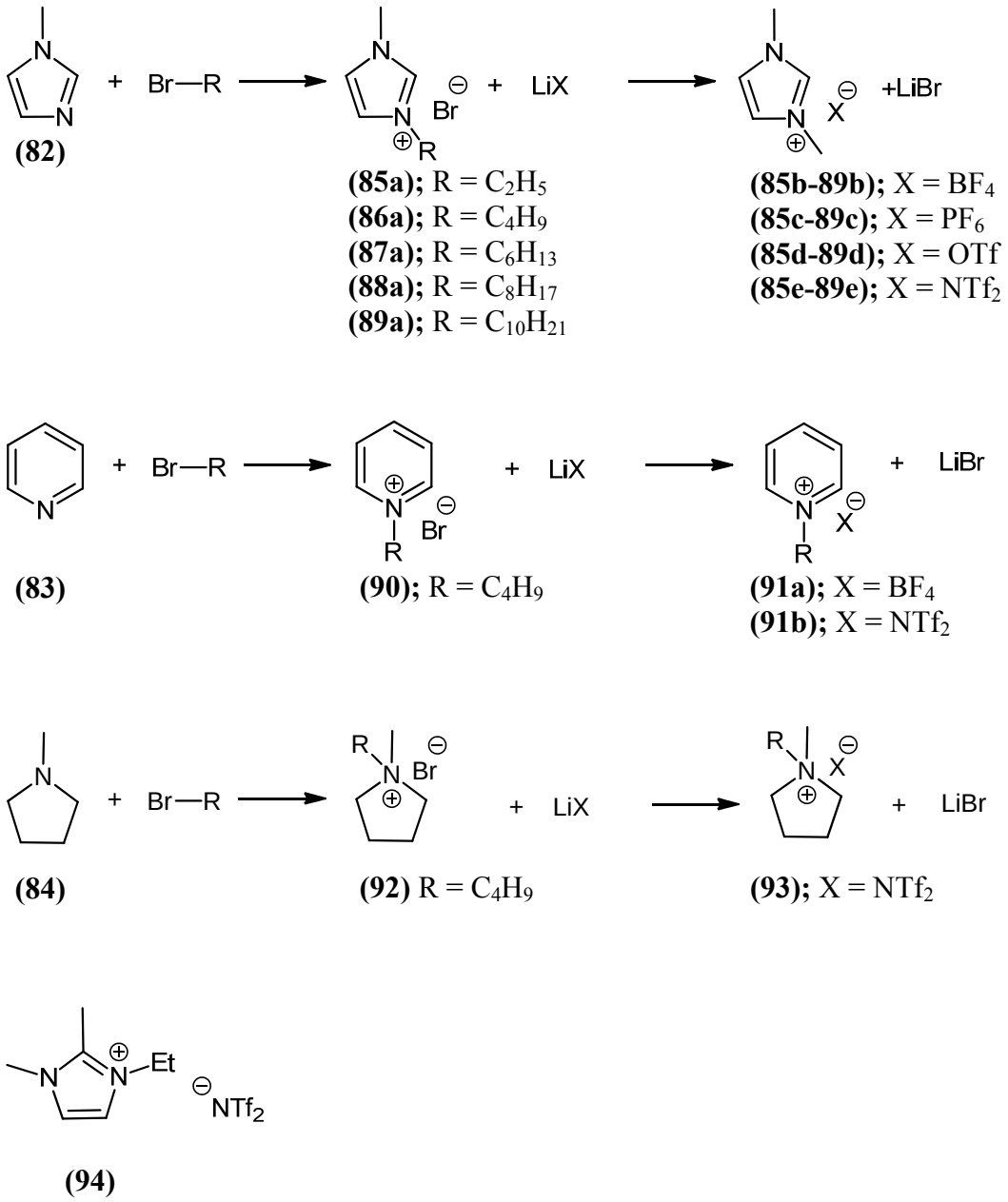

Figure 3.1.2: A summary of RTILs.

3.1.2.2 Screening of ionic liquids

In order to test the viability of the various ionic liquids a model reaction was carried out in a series of ionic liquids with varying cations and anions. The model reaction chosen was the photo-Friedel-Crafts acylation of naphthoquinone with butanal. This

reaction was chosen due to its previously observed relatively high yield, and simplicity of workup.

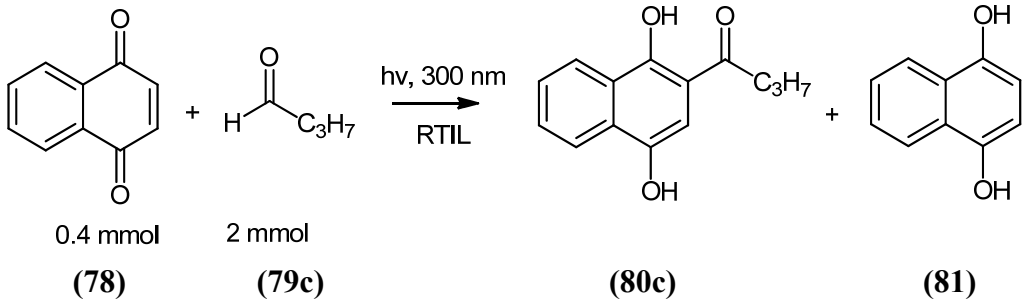

Figure 3.1.3: Model reaction for the photo-Friedel-Crafts reaction in RTILs.

Control reactions were carried out in benzene and acetonitrile. This was done in order to observe the effect of varying cations and anions of the RTIL, with a particular focus on the effect of alkyl chain length of cations. The scale and irradiation time of all reactions were kept constant in order to obtain comparable results.

Initially, an investigation was made into the efficiency of the extraction process. Naphthoquinone and an acylated product obtained from a previous reaction [1-(1,4-dihydroxynaphthalen-2-yl)butan-1-one] were dissolved in separate 5 ml volumes of ethyl methylimidazole bistriflimide ([EMIM][NTf_2]). The solutions were then extracted with five 5 ml portions of diethyl ether and the mass of extracted product was obtained. The results obtained showed the extraction process was 74% and 80% for naphthoquinone and the acylated product respectively. This indicated that both product and starting material could be extracted from a RTIL with reasonable efficiency, and without showing preference to either substance.

In the case of the RTIL reactions, workup consisted of extracting the RTIL with diethyl ether which was then dried over $MgSO_4$, filtered and evaporated. The

benzene and acetonitrile reactions simply required evaporation of the solvent. The crude mixture was analysed by ^{1}H NMR and conversion was obtained by integration of characteristic peaks.

The RTILs investigated were composed of imidazole, pyridine and pyrrolidine cations. The results obtained are summarised in table 3.1.1.

Table 3.1.1: Results of photo-Friedel-Crafts acylation in RTILs.

Solvent	% composition		
	78	**81**	**80c**
[EMIM][OTf]	11	0	89
[EMIM][NTf_2]	13	4	83
[EMIM][BF_4]	55	0	45
[EMIM][PF_6]	-	-	-
[C_4MIM][NTf_2]	23	53	25
[C_6MIM][PF_6]	39	45	16
[C_8MIM][PF_6]	39	49	12
[C_2DMIM][NTf_2]	53	9	38
[BMPyrr][NTf_2]	11	7	82
[Butylpyridinium][NTf_2]	24	22	54
Benzene	49	7	44
Acetonitrile	31	8	62

*For an explanation of ionic liquid names, see list of abbreviations.

From these results of the model photo-Friedel-Crafts acylation reaction it can be seen that there is a wide variability in the conversion ratios for different RTILs. In comparison to control reactions, some of the RTILs were observed to have greater selectivity between the photoreduction and photo-Friedel-Crafts reaction pathways. The most impressive of these were [EMIM][OTf], [EMIM][NTF_2] and [BMPyrr][NTF_2]. It can be seen that imidazole RTILs with longer alkyl chains tend

to negatively affect conversion to product with the $[C_8MIM][PF_6]$ giving only 12% conversion to the photo-Friedel-Crafts product and 45% of the photoreduction product.

RTILs composed of the $[PF_6]^-$ tended to perform poorly, with $[EMIM][PF_6]$ completely decomposing the reaction mixture. It has been suggested that this was because the $[PF_6]^-$ anion was capable of generating hydrogen fluoride (HF) when heated.[93] The presence of such a strong acid may decompose either starting materials or products.

Interestingly, the reaction in $[EMIM][BF_4]$ gave a relative product yield comparable to that of benzene, but without the formation of unwanted hydroquinone.

While it has been shown that certain RTILs are capable of giving higher conversion to the acylated product, it should be noted that this does not necessarily translate to higher isolated yields. The process of extracting the RTIL is difficult and inefficient, especially when compared with the simple task of evaporating and washing a reaction in benzene or acetonitrile. This fact is strongly reflected in the isolated yields of reactions in benzene (41%) and acetonitrile (57%) compared to the isolated yield of a reaction in [EMIM][OTf] (10%), especially considering the higher conversion obtained in the RTIL.

3.1.2.3: Evaluation of RTILs as a suitable solvent for the photo-Friedel-Crafts acylation of naphthoquinone

Once a range of RTILs had been screened for their viability as a photochemical solvent, further investigation was carried out using two of the top performing candidates. The photo-Friedel-Crafts acylation of naphthoquinone using aldehydes of varying chain lengths in both [EMIM][OTf] and $[EMIM][NTf_2]$ was performed.

The composition of the final reaction mixture was then determined by ^{1}H-NMR to give an indication of the efficiency of the RTIL for each aldehyde, the results of which are listed below in Tables 3.1.2 and 3.1.3.

Table 3.1.2: Results of the photo-Friedel-Crafts acylation of naphthoquinone with various aldehydes in [EMIM][OTf].

	[EMIM][OTf]			
Entry	**Aldehyde**	**78**	**81**	**80a-j,r,t**
a	Acetaldehyde	32	3	65
b	Propionaldehyde	24	0	76
c	Butyraldehyde	11	0	89
d	Valeraldehyde	26	0	74
e	Hexanal	10	10	80
f	Heptanal	31	0	69
g	Octanal	20	19	61
h	Nonanal	35	6	60
i	Undecanal	62	8	31
j	Lauraldehyde	62	11	27
r	Benzaldehyde	58	0	42
t	Crotonaldehyde	40	12	48

Table 3.1.3: Results of the photo-Friedel-Crafts acylation of naphthoquinone with various aldehydes in [EMIM][NTf_2].

	[EMIM][NTf2]			
Entry	**Aldehyde**	**79**	**81**	**80a-j,r,t**
a	Acetaldehyde	29	0	71
b	Propionaldehyde	25	0	75
c	Butyraldehyde	13	4	83
d	Valeraldehyde	36	13	51
e	Hexanal	24	8	64
f	Heptanal	40	14	46
g	Octanal	21	11	68
h	Nonanal	63	11	26
i	Undecanal	59	11	30
j	Lauraldehyde	51	15	34
r	Benzaldehyde	41	11	48
t	Crotonaldehyde	46	11	43

These reactions show a general tendency for conversion to decrease with higher chain length aldehydes; a trend that was not observed in traditional solvents. This is probably due to the relatively non-polar long chain aldehydes having poor solubility in the strongly polar RTILs, which leads to an increase in hydrogen abstraction from the RTIL. This was particularly noticeable in reactions with C_9 and longer aldehydes, in which a separate layer was formed. Despite this, relatively high conversions were obtained for C_2 to C_8 aldehydes, with conversion dropping off significantly for the immiscible aldehydes. There was also a general tendency for a higher selectivity for photoreduction with longer chain aldehydes.

It is difficult to say whether the differences observed in RTILs compared to conventional solvents is due purely to solubility. It is also possible that the unique

ordered nature of ionic liquids is affecting the outcome of a reaction. It has been argued that the solvent properties of ionic liquids may not be well accounted for by conventional macroscopic parameters like polarity, dielectric constant and viscosity which have been extensively used to classify molecular solvents, and thus there may be some unknown "ionic liquid effect" at work.[94]

The mechanism of the photo-Friedel-Crafts acylation of quinones has been studied extensively. It has been found that the reaction proceeds via both an *in-cage* and *out-of-cage* mechanism with the predominating route being determined by the specific conditions of the reaction i.e. temperature, solvent and aldehyde/quinone.[95] The higher viscosity of RTILs may result in a trapping of the quinone/aldehyde radical pair, thus favouring the *in-cage* mechanism (figure 3.1.4). Mechanisms similar to this have been seen in other photochemical reactions in ionic liquids.[78d]

This may also account for high levels of photoreduction of naphthoquinone in reactions with a longer chain aldehyde. It has been observed that molecules in a triplet excited state are capable of hydrogen abstraction from a RTIL.[78e, 96] In reactions where an aldehyde is poorly available due to low solubility, hydrogen abstraction may be the predominating pathway.

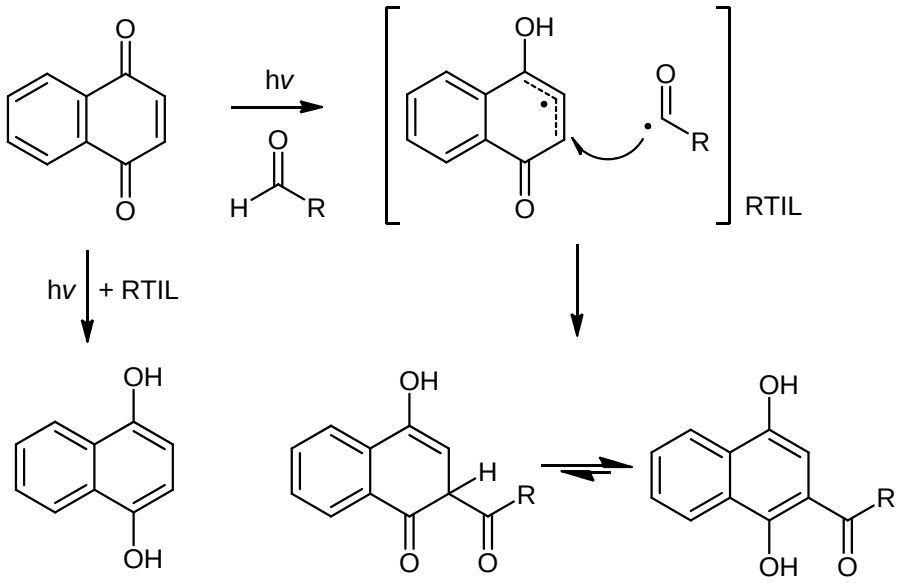

Figure 3.1.4: Mechanism of acylation in RTILs.

Investigations were also made into the re-use of the RTILs. After each reaction an attempt was made to recycle the RTIL. After extraction with diethyl ether the solvent was shown to be pure by ^{1}H NMR, however, the RTIL usually remained coloured. This was unacceptable, as it would affect light transmission and would hence have a negative effect on subsequent reactions. In an attempt to solve this problem the RTIL was diluted with methanol and allowed to stir overnight with activated carbon. This was then filtered through a short pad of Celite to remove the activated carbon. Excess methanol was then removed *in vacuo*. Shown below is the UV-Vis spectrum of a fresh, clean RTIL compared to the same RTIL untreated after a reaction and again after it has been cleaned. Figure 3.1.5 shows that the used RTIL has a strong absorption at the wavelength needed for the reaction compared to the clean RTIL. After the washing procedure there is still some evidence of possible impurities, but absorption in the reaction region is significantly reduced. Despite this, RTILs were frequently re-used several times with negligible loss of efficiency.

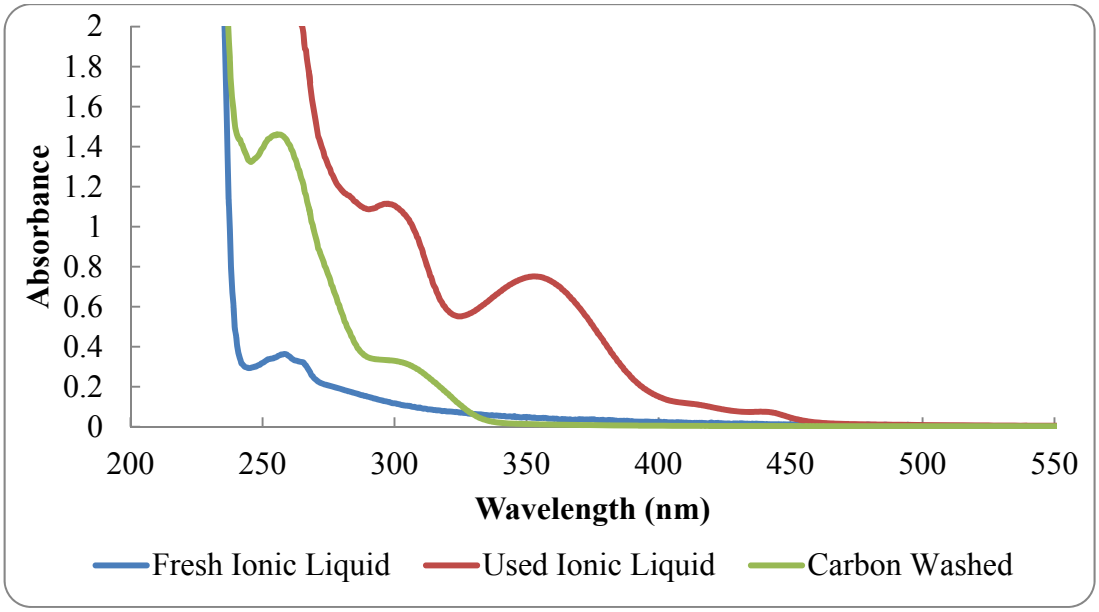

Figure 3.1.5: Typical UV-Vis spectra of fresh and recycled RTILs.

In conclusion, it has been shown that the photo-Friedel-Crafts acylation of naphthoquinone can proceed with high conversion in RTILs. They do show potential as a "green" replacement for traditional, toxic solvents such as benzene and acetonitrile. Despite this, there are still several drawbacks which I believe prevent them for being a practical alternative at present, and these are listed below.

1) The high conversion of the reaction in RTILs is offset by the low isolated yield, which is likely a result of the difficult, inefficient work-up procedure. The difficult work-up procedure also has an impact on the environmentally friendly nature of RTILs as a solvent.

2) A major factor in the "greenness" of RTILs is their ability to be recycled, however the viscous nature of most RTILs can make them difficult to work with and can result in loss during the intricate work-up. This leads to an overall loss of the solvent and limits the amount of recycling a single batch of solvent is capable of undergoing before the overall loss is significant. As well

as this, the need for an extraction solvent during work-up reduces the "greenness" of RTILs even further.

3) It should also be noted that while RTILs are being investigated as an alternative to the toxic solvents benzene and acetonitrile, the toxicity of many RTILs is unknown and is currently the subject of several investigations.

4) It is also important to remember that most RTILs must be generated by a multi step synthesis, which often involves the generation of harmful halogen side products. This has a significant impact on the green nature of RTILs as solvents.

3.2 The photo-Friedel-Crafts acylation of naphthoquinone in microemulsions

3.2.1 Introduction

Microemulsions are an emerging class of reaction media for organic synthesis.[97] They consist of two immiscible liquid phases, usually water, an organic solvent, and surfactants. Unlike traditional emulsions, microemulsions are thermodynamically stable. Physically, microemulsions are transparent and macroscopically homogenous but microscopically heterogeneous, with separate phases typically being in the nanometre size range. This leads to massive surface interactions between organic and aqueous phases. The structure is highly dynamic. Each interface disintegrates and reforms in the time scale of milliseconds.

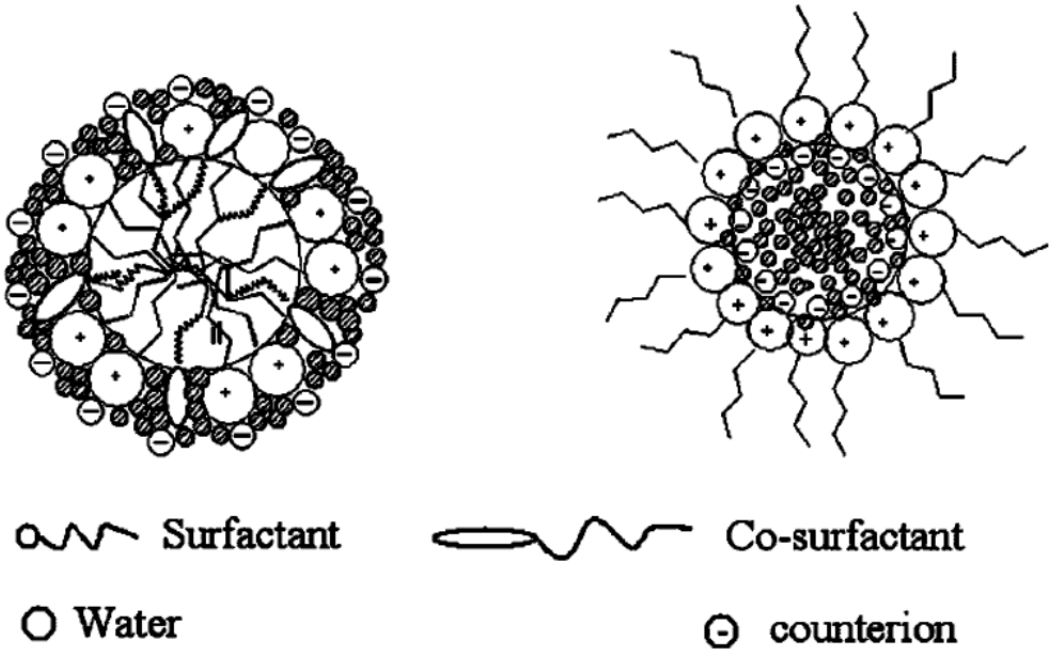

Figure 3.2.1: Microemulsion with a positively charged surfactant.[98]

One of the most obvious advantages of using a microemulsion is its ability to overcome reactant incompatibility. Because of their biphasic nature microemulsions

are capable of acting as both an aqueous and organic solvent allowing them to accommodate both hydrophobic and hydrophilic substrates. The extremely high surface interaction of the two phases ensures the compounds availability to each other. This gives microemulsions strong potential in areas such as alkaline hydrolysis of lipophilic esters, oxidative cleavage of olefins with permanganate-periodate, addition of hydrogen sulfite to both aldehydes and terminal olefins, preparation of alkyl sulfonates by treatment of an alkyl chloride by sodium sulfite or by addition of sodium hydrogen sulfite to an epoxide, among many others.[99]

As well as the ability to overcome reagent incompatibility, the ability of microemulsions to compartmentalise and concentrate reactants can also lead to considerable rate enhancement compared to single-phase systems.

All these factors, coupled with their good transparency and relative "green" nature as a solvent makes microemulsions a potential replacement for benzene and similar hazardous solvents used in photochemistry.

The main advantage of using microemulsions as a solvent for this class of reaction is it allows access to water soluble aldehydes such as formaldehyde or glutaraldehyde (figure 3.2.2). The products of reactions using compounds such as these retain an aldehyde functionality, and hence are capable of reacting with another naphthoquinone molecule to yield some potentially interesting products.

Reactions with these aldehydes would be impractical in conventional organic solvents such as benzene due to their immiscibility in organic solvents. It was thought that microemulsions may present a solution to this problem.

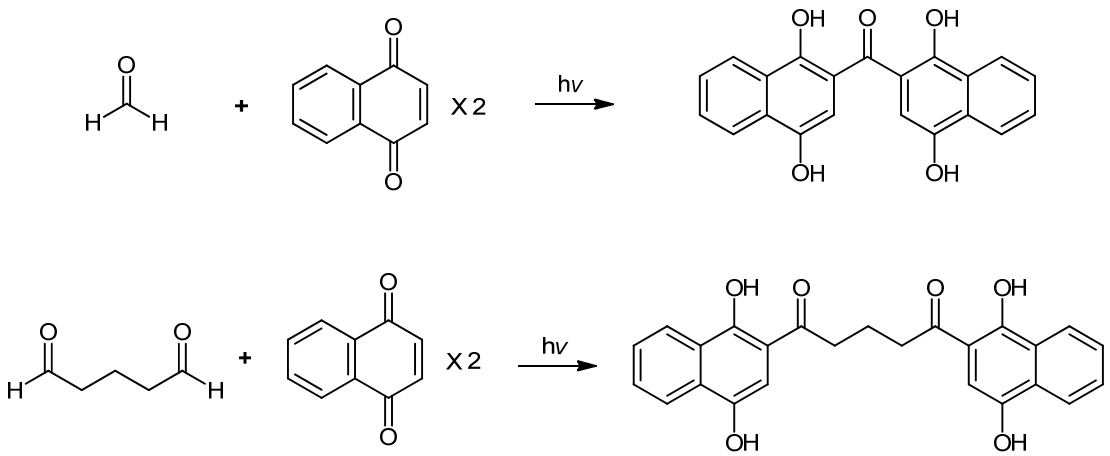

Figure 3.2.2: Reaction of naphthoquinone with bisfunctionalised aldehydes.

3.2.2 Results and discussion

It was undertaken to investigate the viability of a water/ethyl acetate microemulsion as a solvent for the photo-Friedel-Crafts acylation of naphthqoquinone. Initially a model reaction between naphthoquinone and butyraldehyde was carried out in neat ethyl acetate to determine if it was a suitable organic solvent for the reaction. With a yield of 50%, the results were comparable with a similar reaction carried out in benzene (54%). Following this success of ethyl acetate as a photochemical solvent, further investigations were then carried out using microemulsions.

According to an optimised formula determined by another member of the research group (Emma Coyle), a 100 g batch microemulsion was prepared by mixing sodium dodecyl sulphate (7.5 g, 7.5% w/w) and t-amyl alcohol (7.5 g, 7.5% w/w) with ethyl acetate (70 g, 70% w/w). Water (15 g, 15%w/w) was then added slowly (with stirring) to give a clear solution.

A series of photo-Friedel-Crafts reactions between naphthoquinone and aldehydes were carried out in the microemulsion (Figure 3.2.3).

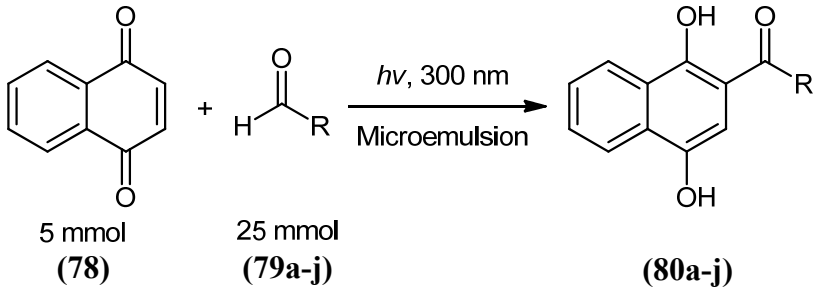

Figure 3.2.3: Reaction scheme for the photo-Friedel-Crafts reaction in a microemulsion.

The reactions were irradiated for at least 16 hours overnight in a Rayonet Photochemical Reactor (RPR-200; Southern New England Ultraviolet Company) equipped with RPR-3000 Å lamps. Reactions were monitored by thin layer chromatography and were judged to be complete when naphthoquinone was no longer observed. Reaction work-up involved the addition of a saturated sodium chloride solution, which caused the microemulsion to separate into two separate phases. The organic layer (ethyl acetate) was washed repeatedly with a dilute sodium chloride solution in order to remove any remaining sodium dodecyl sulphate (SDS). The organic layer was then washed twice with brine and dried over $MgSO_4$. For the short chain aldehydes the optimum purification procedure involved washing the crude mixture with cold benzene to remove any remaining aldehyde: if necessary, this was followed by an ether was to remove any remaining SDS.

Attempts were made to eliminate the need for washing with benzene by recrystallisation with various solvents such as toluene and ethyl acetate/hexane mixtures, however these proved to be unsuccessful.

This purification procedure was not suitable for reactions involving longer chain aldehydes, as all components of the crude mixture are soluble in benzene. In these cases, residual unreacted aldehyde was removed by washing with cold hexane. Any

SDS impurity was again removed by washing with diethyl ether. All yields are listed in Table 3.2.1.

Table 3.2.1: Yields obtained for photo-Friedel-Crafts acylation of naphthoquinone in ME.

Entry	Aldehyde	R	Yield (%)
a	Acetaldehye	CH_3	-
b	Propionaldehyde	C_2H_5	28
c	Butyraldehyde	C_3H_7	42
d	Valeraldehyde	C_4H_9	32
e	Hexanal	C_5H_{11}	30
f	Heptanal	C_6H_{13}	31
g	Octanal	C_7H_{15}	23
h	Undecanal	$C_{10}H_{19}$	25
i	Lauraldehyde	$C_{11}H_{23}$	36

The yields obtained were relatively low (28-42%), especially compared to similar reactions in benzene (58-80%) and some RTILs (27-89% in [EMIM][NTf_2]). Although the yields are relatively low, TLC monitoring suggests much higher conversions. This indicates that a significant portion of the product is lost during work up. It is likely that the addition of brine does not completely separate the microemulsion into two layers, and that the aqueous layer still retains some surfactant and ethyl acetate, and hence is still capable of solubilising a portion of the product.

Once it had been determined that microemulsions were a valid (if inefficient) solvent for the photo-Friedel-Crafts acylation of naphthoquinone, the reaction was carried out using the two water soluble aldehydes, formaldehyde and acetaldehyde.

Unfortunately, 1H-NMR of the crude products of the reaction failed to show the expected characteristic peaks of the acylated product.

Due to the low toxicity of their components, microemulsions do show some potential as a "green" alternative to traditional solvents in organic chemistry. Unfortunately, for the photo-Friedel-Crafts reaction, the low yields and difficult, inefficient, workup procedure (with benzene) make it an impractical option for this class of reaction. The only noteworthy point is that the final isolated products of the photo-Friedel-Crafts reactions carried out in microemulsions are of high purity, usually only requiring a wash with cold benzene or hexane, depending on the chain length of the aldehyde used.

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4.0 Synthesis of novel biaryl trifluoro phthalonitriles

4.1 Introduction

Phthalonitriles represent an important class of precursor in the synthesis of phthalocyanines (Pcs). The maximum absorption (λ_{max}) of a Pc is particularly sensitive to both the metal centre and peripheral substitution of the macrocycle. It has been noted that Pcs equipped with substituents which extend conjugation tend to show significant red shifts in the q-band region of the UV-Vis spectrum. With this in mind there has been considerable interest in the synthesis of peripherally substituted phthalonitriles, particularly those equipped with unsaturated moieties.

An important aspect of Pcs is their potential as photosensitisers for the generation of singlet oxygen. This gives rise to applications in areas such as photo-oxygenations in organic synthesis, waste water treatment, photo-oxygenations and photodynamic therapy (PDT). The creation of red-shifted Pcs is particularly important to the field of PDT, as the transmission of light through human tissue is highest above 650 nm[100].

Another significant driving force in the design of new Pcs is the reduction of aggregation. Pc applications such as non-linear optics, photochemical sensitisation or photodynamic therapy can be inhibited by molecular aggregation via π–π stacking interactions. This can affect the absorption properties of the Pc as well as resulting in a shortening of their triplet excited state lifetimes which causes inefficient energy transfer. A common solution to this is the introduction of bulky peripheral groups to sterically inhibit “stacking”.

Another common problem with the application of Pcs in photo-oxygenations (including PDT applications) is that they can be photobleached by the singlet oxygen

that they generate. With this in mind, it would be ideal to design a Pc with increased stability to oxidation. One possible approach to achieve this goal is to replace the ring C-H bonds in the Pc ring with thermodynamically stronger C-F bonds.

4.1.1 Target compound

With these parameters in mind, it was proposed to prepare a new class of Pc with the following properties: 1) reduced aggregation, 2) red shifted Q-band, 3) incorporation of fluorine into the macrocycle ring. The proposed Pc structure that fits these criteria is shown in Figure 4.1.1. The presence of the electron rich aryl rings has two effects – it will extend the conjugation of the Pc ring, causing a red shift in the Q-band of the UV-Vis absorption spectrum, and by placing methoxy groups in the *ortho* positions of the phenyl rings this should inhibit aggregation.

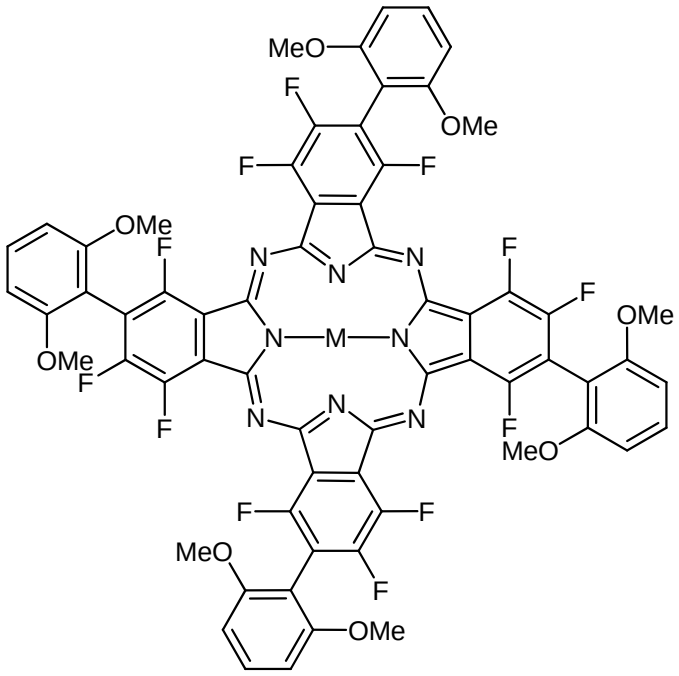


Figure 4.1.1: Target compound.

There are two main strategies for introducing peripheral substituents into a Pc. The first is direct substitution onto the Pc. Unfortunately, this suffers from the drawback

that substitution cannot be selectively controlled. To prepare the target Pc it will be necessary to introduce the desired aryl substituent into a fluorinated phthalonitrile. The biaryl trifluoro phthalonitrile required to prepare the target Pc is shown in Figure 4.1.2.

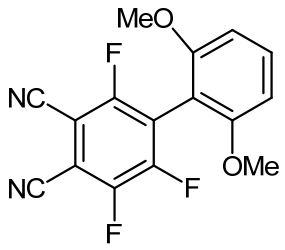


Figure 4.1.2: Target biaryl trifluoro phthalonitrile

4.1.2 Conventional synthetic methods for the preparation of aryl substituted phthalonitriles

A typical approach to the synthesis of biaryl phthalonitriles is using Suzuki coupling methods (Figure 4.1.3).[74c] This involves the palladium-catalysed cross coupling between organoboronic acids and halides. Aryl substituted phthalonitriles have been prepared using this method with yields of up to 79%. The disadvantages of this method include being limited to boronic acid starting materials as well as the requirement of one equivalent of base to activate the organopalladium halide intermediate complex. This has the disadvantages of excluding some potential staring materials and reducing the overall atom efficiency of the reaction.

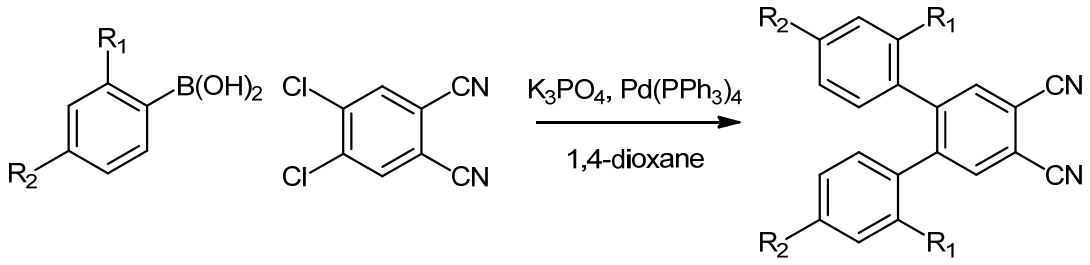


Figure 4.1.3: Generation of biaryl phthalonitriles by Suzuki coupling methods.

Another method which has been used for the generation of aryl substituted phthalonitriles is the Stille coupling reaction (Figure 4.1.4).[101] This involves the palladium-catalysed cross coupling of organostannanes with organic halides.[102] As well as suffering from many of the disadvantages of the Suzuki method, the primary drawback of this method is the generation of highly toxic organic tin by-products which can often be difficult to remove, which makes the process particularly unfavourable for the generation of pharmaceutical agents.

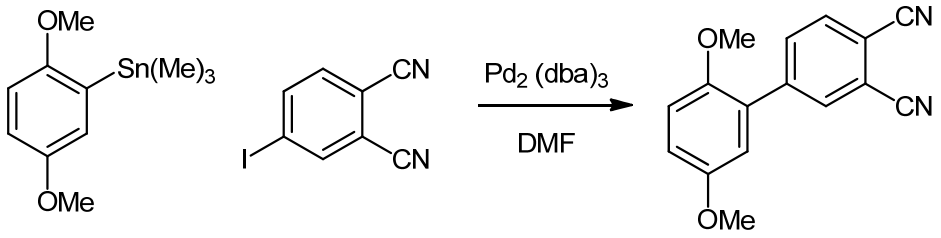


Figure 4.1.4: Generation of biaryl phthalonitriles by Stille coupling methods.

4.1.3 Photochemical method

A report by Pratt *et al*. demonstrates that irradiation of mixtures of halogenated phthalonitriles and both aliphatic[103] and aromatic ethers[57] with a medium-pressure mercury lamp can give the target aryl substituted phthalonitrile with conversions of up to 78%.[57] It has been suggested that this reaction proceeds via an electron transfer mechanism, similar to the photosubstitution of 1,2,4,5-tetracyanobenzene in toluene.[104] Ultimately, this method allows for a simple, one-pot photochemical synthesis of biaryl halogenated phthalonitriles by the method shown in Figure 4.1.5.

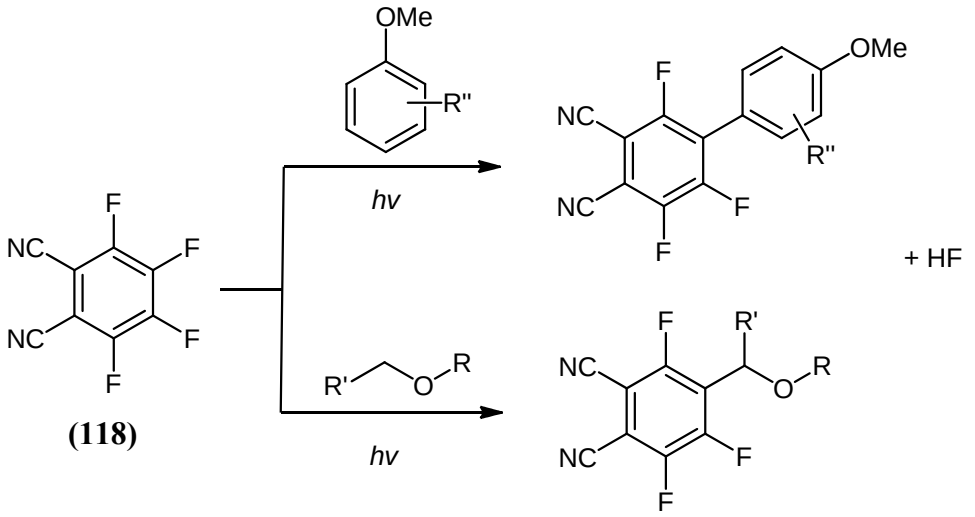


Figure 4.1.5: Reaction of TFPN **118** with aromatic and aliphatic ethers.

The photochemical coupling method developed by *Pratt et al*. has several advantages compared to traditional coupling methods. The reaction does not require a catalyst, and has excellent overall atom efficiency. Furthermore, substitution occurs in a controlled manner: that is only a single aryl substituted should be introduced into the tetrafluorophthalonitrile (TFPN) **118**, leaving the remaining positions of the phthalonitrile with fluorine substituents, giving the target phthalonitrile.

The method described by Pratt *et al*. uses a medium-pressure mercury lamp as a light source. Previous work has noted that due to its broad emission spectrum, this can be an inefficient light source and this can result in poor reaction rates or undesirable follow up reactions. With this in mind it was undertaken to recreate, and hopefully improve the efficiency of this reaction using a Rayonet photochemical reactor as a light source. The wavelength of light used was selected based on the absorption spectrum of the chromophore of the reaction, **118**. It should also be noted that due to the different geometry of the two reactors, the scale and concentration of the reaction may require adjustment.

Another aspect of this reaction which requires further examination is the substitution pattern with respect to both the phthalonitrile and ether starting materials. With respect to the phthalonitrile ring, there are two sites available for substitution in the 3- and 4- positions relative to the nitrile groups, as shown in Figure 4.1.6. It is understood that electron withdrawing groups (EWGs) such as nitriles activate a benzene ring in the *meta* position; however the 1,2-substitution pattern of the nitriles means all four available sites are activated equally. Steric hindrance from the nitrile groups would suggest that the 4- or 5- positions would be favoured for substitution; however this does not eliminate the possibility of substitution in the 3- or 6- positions. It is important to determine which position is favoured for substitution, and to what degree. With this in mind there are still two pairs of equivalent sites available for substitution which gives rise to the possibility of multiple substitutions. It is important to note if single or double substitutions are observed, and if so in what ratio.

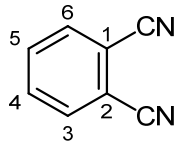


Figure 4.1.6: Substitution sites available on phthalonitrile.

The potential substitution pattern of the aromatic ethers is also an important consideration. It is known that electron donating groups (EDGs) activate aromatic rings in the *ortho* and *para* positions. In the case of anisole this leaves a maximum of three sites available for reaction, while di- and tri-methoxy benzenes give rise to more complex potential substitution patterns. Similar to the investigation of the substitution patterns of the phthalonitrile, it is important to observe which position is favoured, and if multiple additions are occurring.

4.1.4 Further applications

While previous work by Pratt *et al*. primarily deals with additions with methoxybenzenes there are also several other classes of compounds with sufficiently similar properties which should be capable of participating in the reaction. The scope of this type of reaction could be greatly expanded by investigating the viability of other classes of compounds, including extended aromatics such as methoxy-naphthalenes and biphenyls. Phthalonitriles synthesised from these compounds could potentially have very interesting properties, due to their extended conjugation.

As well as extended aromatics, another interesting class of compounds for this reaction include benzene equipped with other EDGs, such as thio-ethers and aniline derivatives. The varying electron donating strength of these groups may have an effect on the rate of reaction. Furthermore, these different groups may also have an effect on the overall properties of the resulting phthalonitrile and its Pc derivative. For example, the product of a reaction between TFPN and aniline is of particular interest. The presence of the amine group in the resulting product will have a pH 'tuneable' solubility for both the phthalonitrile and the resulting Pc after condensation. As well as this, an amino group provides an excellent reactive handle for further functionalisation.

4.1.5 Phthalonitrile properties

While phthalonitriles are primarily used as a precursor to Pcs, it should be noted that they can possess interesting photophysical properties themselves. The extension of conjugation created by the formation of the biaryl system should have a dramatic effect on the spectral properties of the new phthalonitrile derivatives. All these factors would suggest that, as well as being precursors to a novel class of Pc, these

phthalonitriles may have interesting properties themselves, with absorbance and fluorescence being of particular note.

4.2 Synthesis and characterisation of aryl trifluoro phthalonitriles

4.2.1 Photochemical Optimisation

Based on the absorption spectrum of TFPN (**118**), a Rayonet reactor equipped with sixteen 300 nm lamps was selected as the light source. The emission spectrum of the Rayonet overlaps satisfactorily with the absorption spectrum of **118** (Figure 4.2.1). This has many advantages over a mercury lamp as a light source, which was previously used by Pratt *et al.* to prepare similar compounds. The narrower emission spectrum of the Rayonet lamps should increase the overall efficiency of the reaction, as well as reducing the opportunity for side reactions.

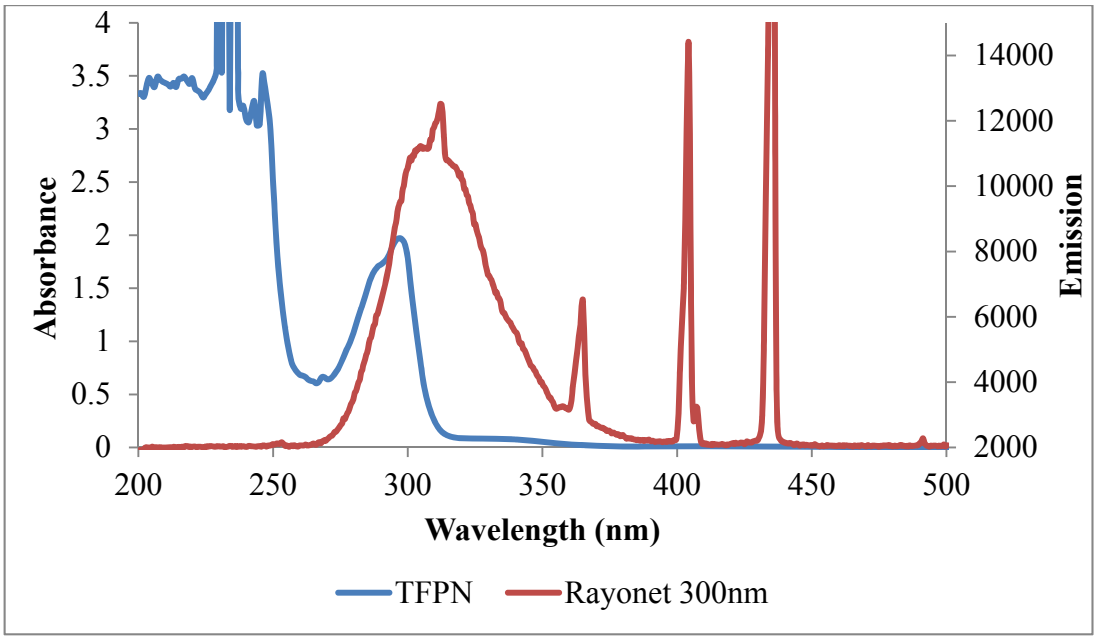
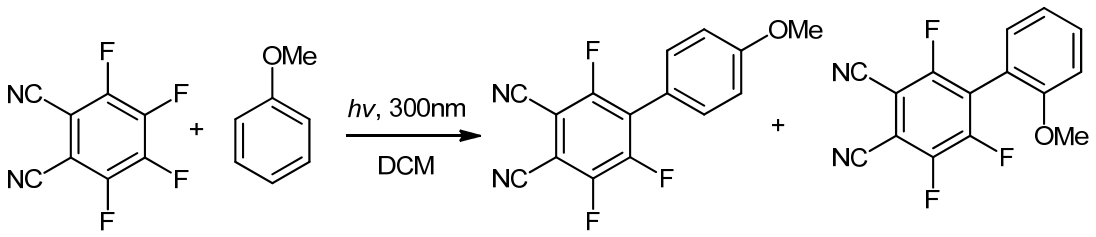


Figure 4.2.1: Absorption spectrum of **118** *vs.* the emission spectrum of a Rayonet equipped with 300 nm lamps.

The first study undertaken was to determine the optimum concentration for the reaction. A model reaction using anisole **119** and **118** at a 5 mmol concentration (1:1

stoichiometry) with an irradiation time of 16 hours was chosen for reaction optimisation (Figure 4.2.2). It should be noted that two possible isomers can be formed as shown in Figure 4.2.2.



(118) **(119)** **(120a)** **(120b)**

Figure 4.2.2: Reaction of anisole with tetrafluorophthalonitrile.

Integration of the ^{19}F NMR of the crude product should determine both percentage conversion and isomer distribution, however it was necessary to validate this hypothesis.

4.2.2 Isomer Distribution of 120

After the first reaction the crude ^{19}F NMR of the reaction mixture (Figure 4.2.3) showed the presence of two isomers. It was apparent that substitution of anisole to **118** occurred in both the *para* (**120a**) and *ortho* (**120b**) positions with respect to the methoxy group of anisole. It was also found that substitution into **118** occurred only at the 4 position. To assign the spectra of both isomers the isolated crude product from the reaction was purified by column chromatography to give **120a** and **120b**. Both the ^{1}H and ^{19}F NMR spectra of each isomer are shown in figure 4.2.4 to figure 4.2.7. The ^{19}F spectra corresponds with 4 substitution since a triplet is observed for F_3 (F_3 split by F_5 and F_6) and two doublet of doublets are observed for both F_5 and F_6. It was found that the *para* substituted product **120a** was the dominant product and was identified based on the presence of two doublets in the aromatic region of

the ^{1}H NMR. Product **120b** was also confirmed by ^{1}H NMR with the presence of two triplets and two doublets in the aromatic region.

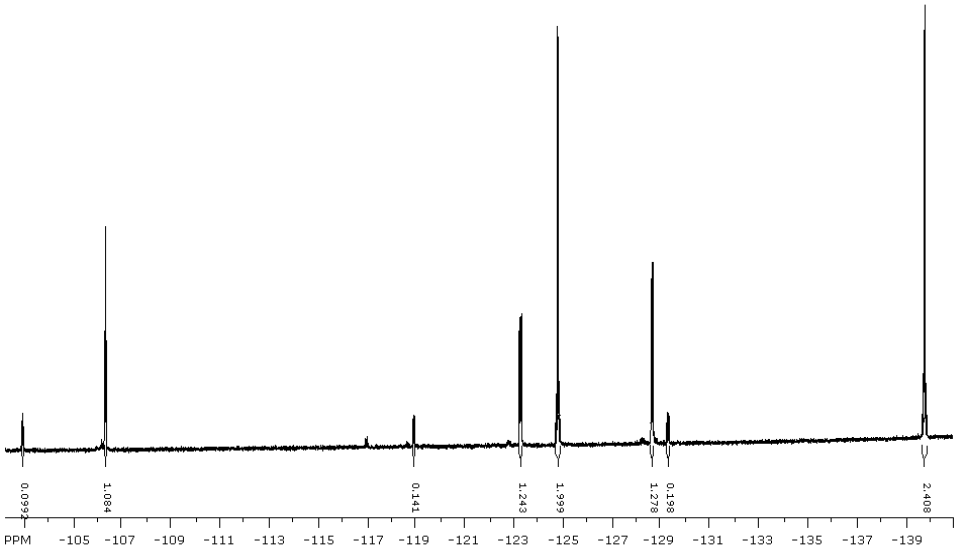


Figure 4.2.3: Crude ^{19}F spectrum of reaction between **118** and anisole **119**.

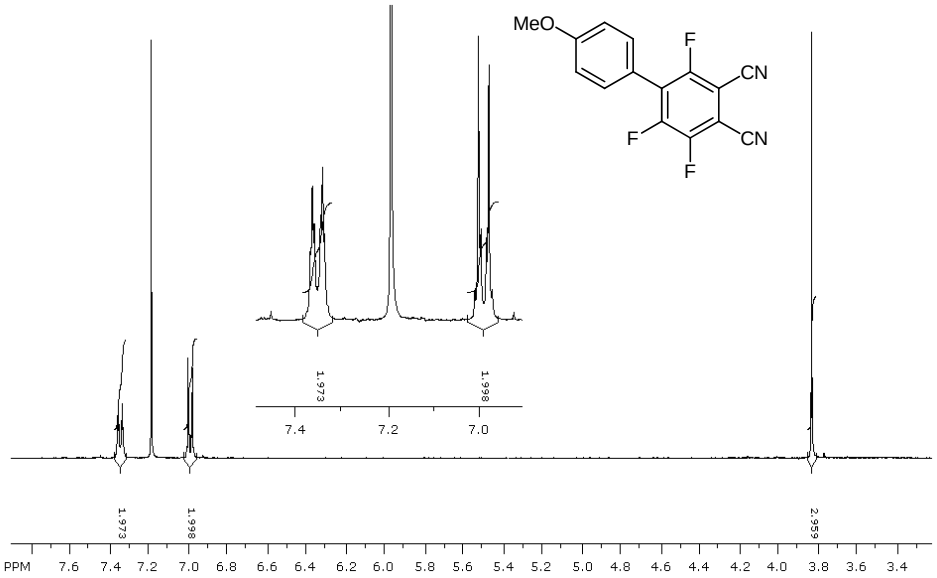


Figure 4.2.4: ^{1}H spectrum of purified *para* anisole product **120a**.

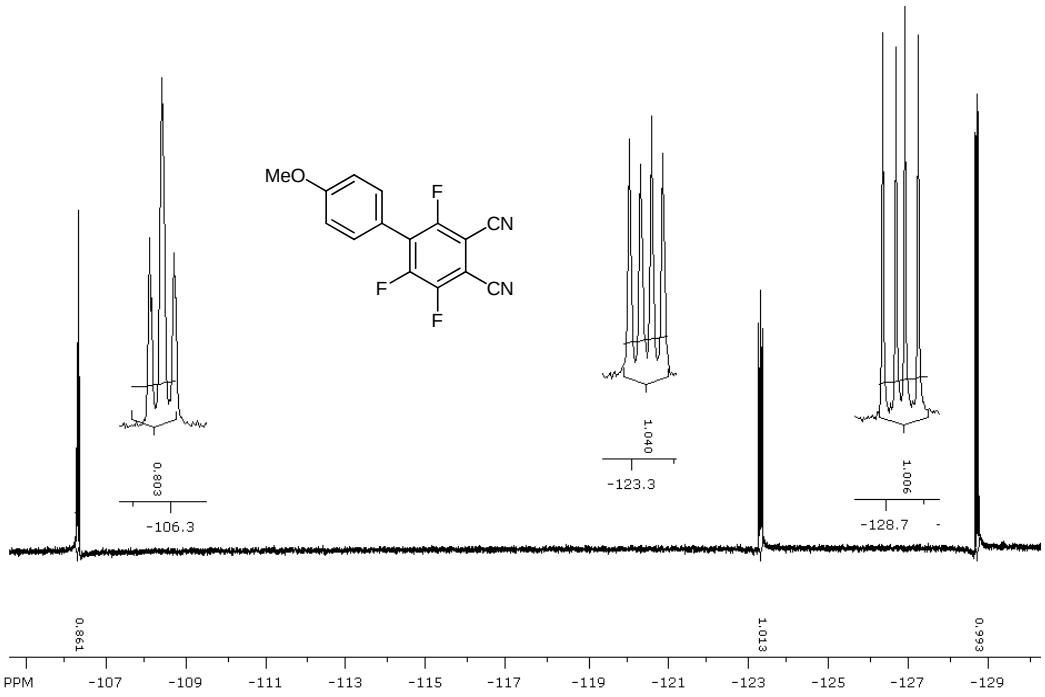


Figure 4.2.5: ^{19}F spectrum of purified *para* anisole product **120a**.

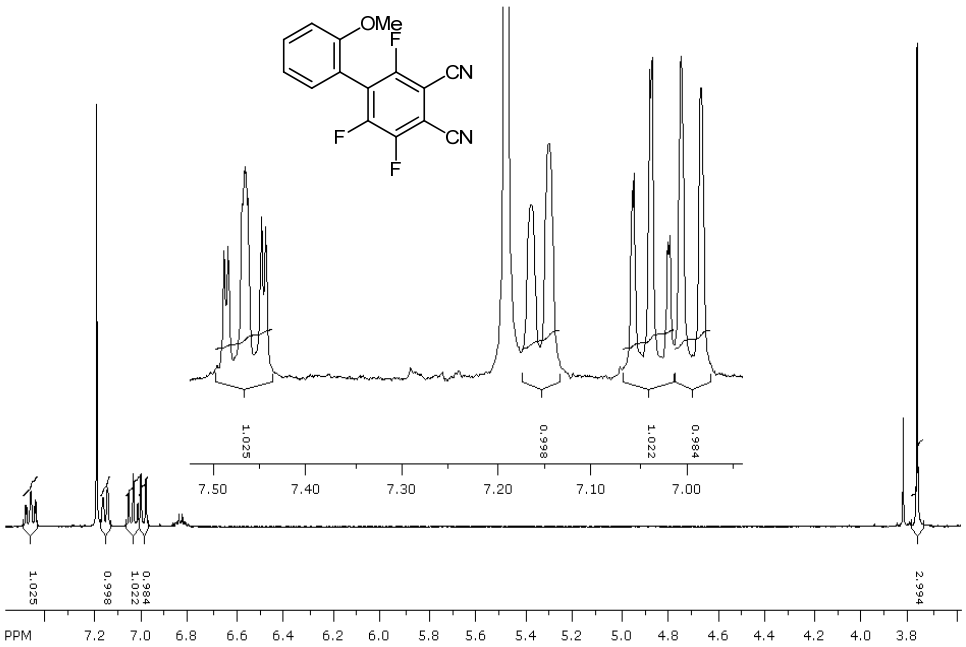


Figure 4.2.6: ^{1}H spectrum of purified *ortho* anisole product **120b**.

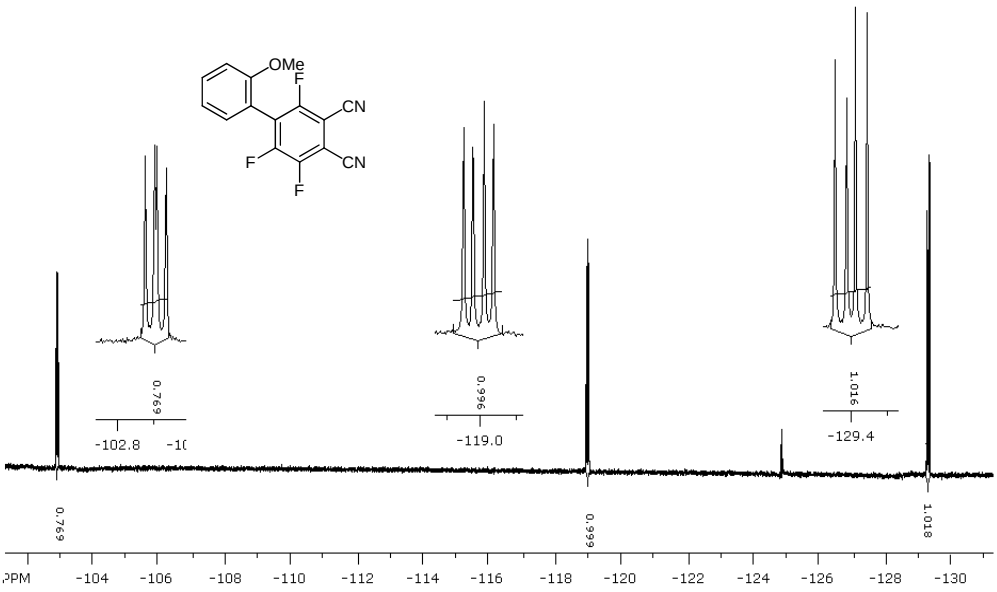


Figure 4.2.7: ^{19}F spectrum of purified *ortho* anisole product **120b**.

Now that accurate identification of the two isomers had been achieved it was now possible to analyse the ^{19}F NMR of the crude product and determine if the integration ratios of the respective fluorine peaks of each isomer can accurately determine the isomer distribution. Comparison of the combined integration values of the characteristic peaks of the products **120a** and **120b** gives a value of 9:1 (**120a**:**120b)**, which corresponds with the isolated yields.

Since integration can be used for the determination of per cent conversion it was realised that a parallel reactor could be used with the single Rayonet reactor. By using a parallel reactor it would be possible to speed the optimisation process up. We built a holder system for six 20 ml tubes that could be placed into the centre of the Rayonet reactor. Reactions were carried out at room temperature and it was found that the reaction mixtures did not significantly heat under irradiation (One of the advantages of the Rayonet RPM 200 is that heating with the fan on is at a minimum). A series of experiments were then undertaken, using the 'parallel' Rayonet reactor to

determine the optimum concentration for the conversion of **118** to **120a/b**; the results are shown in figure 4.2.8.

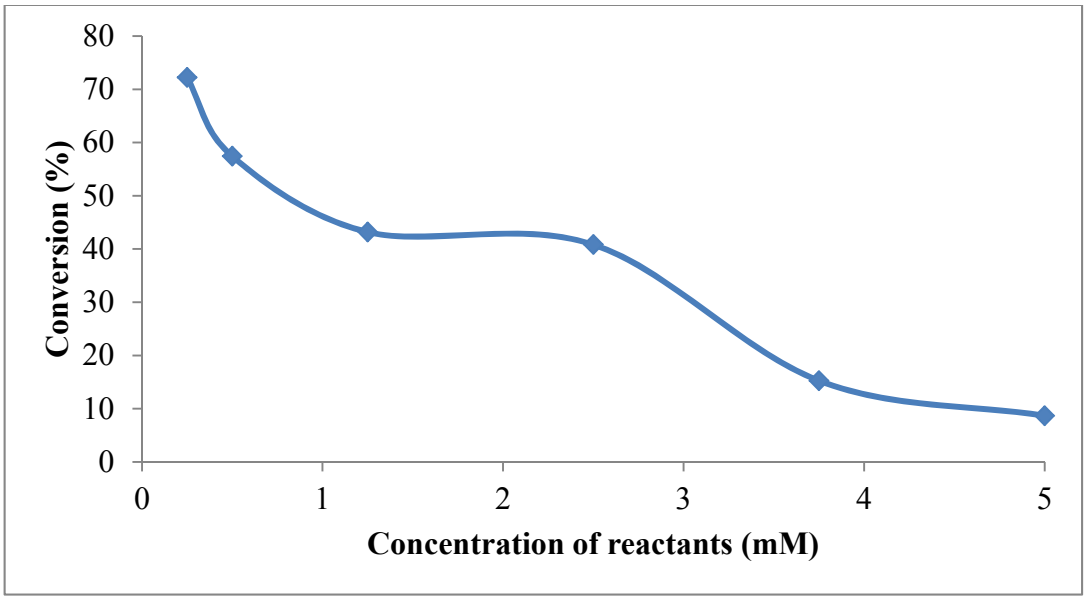


Figure 4.2.8: Conversion of **118** to **120a/b** at varying concentrations.

The result of this study showed a tendency for increased conversion at lower concentrations. The optimum conversion was observed at 2.5 mmol. A reaction was also undertaken at a concentration of 2.5 mmol with extended irradiation (72 hours) however, no improvement in conversion was found. It is likely that the poor conversions of **118** to **120a/b** at higher concentration are due to the absorption spectrum overlap of **120a/b** with that of **118**, (Figure 4.2.9). Once a sufficient concentration of the product is generated, light transmission drops to a level which inhibits the reaction. The fact that high conversions can only be obtained at low concentrations may pose some difficulty in the generation of large quantities of product. It should also be noted that addition to **118** only occurred in the 4-position of **118** and only single arylation of **118** was observed in all reactions.

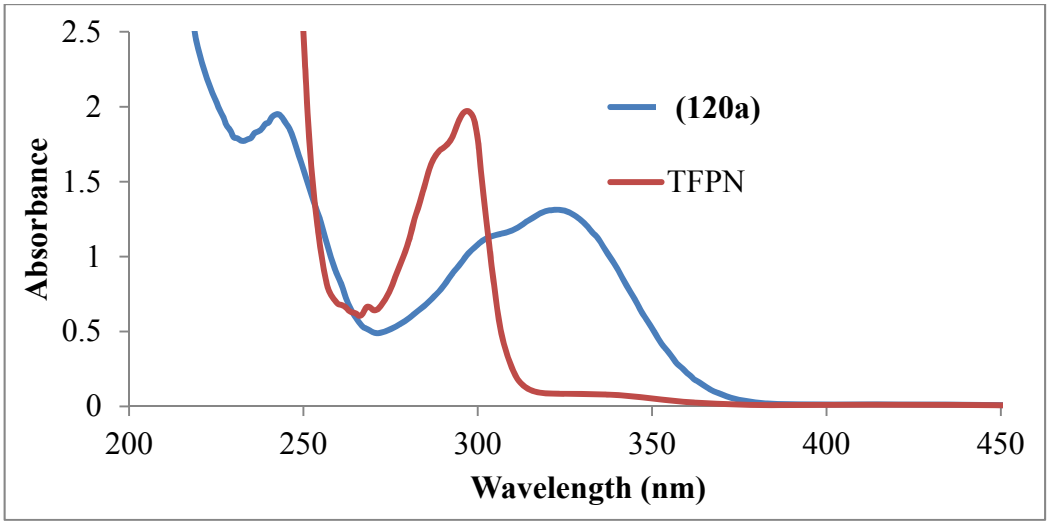


Figure 4.2.9: Absorption spectrum of **118** and **120a**.

A second study was then undertaken to determine to optimum stoichiometry for the reaction. These reactions were run at a concentration of 2.5 mmol using the 'parallel' Rayonet reactor and the results are shown in figure 4.2.10. It was found that two equivalents of anisole to **118** gave the optimum conversion.

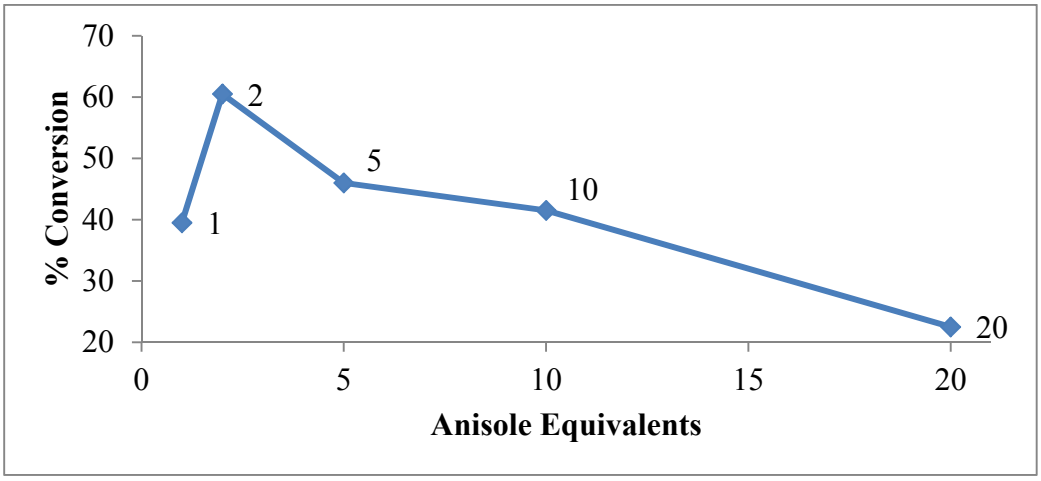


Figure 4.2.10: Conversion of **118** with varying equivalents of anisole **119**.

Based on the above work it was found that:

1) the optimum conditions for the conversion of **118** to **120a/b** was at a concentration of 2.5mmol with a stoichiometric ratio of 2:1(**119**:**118**) with 16 hours irradiation. The per cent conversion for these conditions ranged from 60-70%.
2) Anisole adds either para or ortho with respect to the methoxy group.
3) It should be noted that **118** could not be completely converted to **120a/b**, even under extended irradiation times (72hrs).
4) Substitution in the 3-position of **118** was not observed, this can be explained on the basis of steric hindrance between anisole protons with the nitrile group in the 2 position. [105]
5) we did not observe any dehalogenation at the 4 position of **118**. This product was reported by Pratt *et al*. however, it was not observed in any reactions undertaken in this work.
6) no double addition of anisole to **118** was observed.

Since no double addition of anisole to **118** was observed in any of the reactions undertaken this would suggest that the aryl ring of the phthalonitrile must be strongly electron deficient in order for the reaction to proceed which is in agreement with the proposed mechanism (Figure 4.2.11).

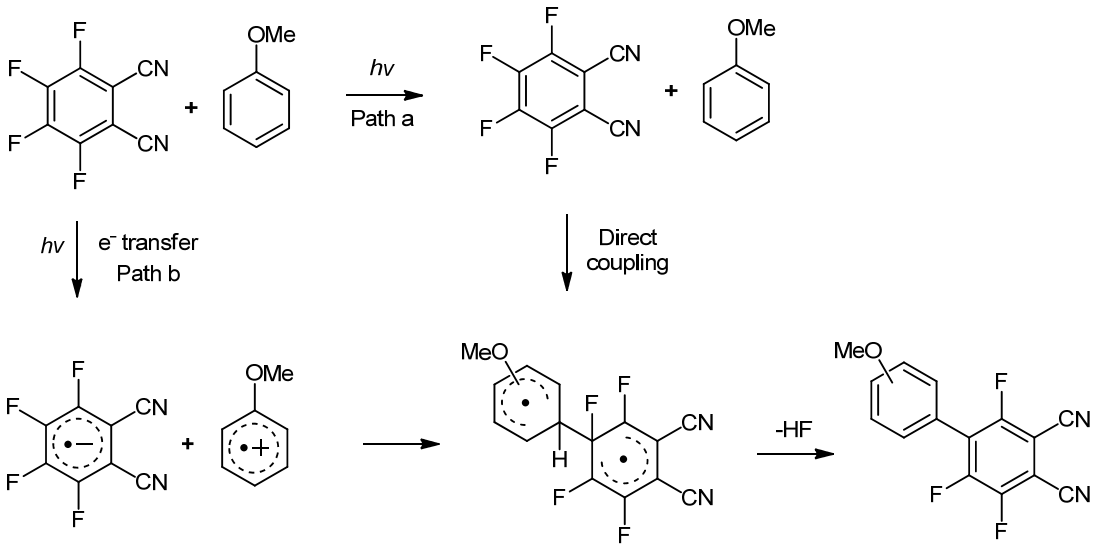
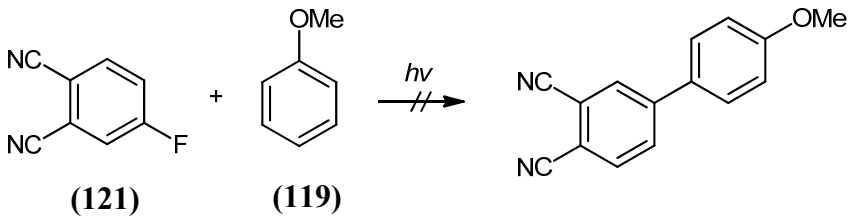


Figure 4.2.11: Proposed mechanism for photochemical aryl coupling with **118** and anisole.

The introduction of a single aryl group reduces the electron accepting capacity of the aryl phthalonitrile, relative to **118**, thereby inhibiting further substitution. To further demonstrate this point a reaction between 4-fluorophthalonitrile (**121)** and anisole was undertaken using the optimum reaction conditions (Figure 4.2.12). No reaction was observed, demonstrating that **121** is not a strong enough electron acceptor for the reaction to proceed.



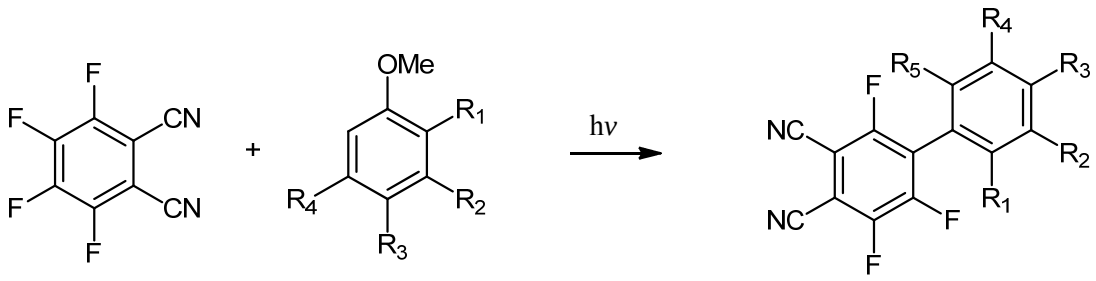
(121) **(119)**

Figure 4.2.12: Attempted reaction of 4FPN **121** with anisole **119**.

4.2.3 Reaction Versatility

In an effort to investigate the versatility of the reaction, and expand the number of potential products, a series of exploratory reactions was carried out with other aromatic and aliphatic ethers. The first series of reactions was the photo aryl

coupling of di and tri methoxy benzenes **122-125** with **118** (Figure 4.2.13). All reactions attempted were carried out using the 'parallel' Rayonet set-up which also allowed concentration studies for each transformation to be carried out simultaneously. All percentage conversions for these reactions were determined using ^{19}F NMR integration ratios of the 3 position fluorine in the product to the 3,6 F of **118**. The results of these reactions are outlined in Table 4.2.1.



(118)

(122); R_1=OMe, R_2=R_3=R_4=H
(123); R_2=OMe, R_1=R_3=R_4=H
(124); R_3=OMe, R_1=R_2=R_4=H
(125); R_2=R_4=OMe, R_1=R_3 =H

(126); R_1=R_2=OMe, R_3=R_4=R_5=H
(127); R_1= R_3=OMe, R_2=R_4=R_5=H
(128); R_1=R_4=OMe, R_2=R_3=R_5=H
(129); R_1=R_3=R_5=OMe, R_2=R_4=H

Figure 4.2.13: Reaction of **118** with aryl ethers.

Table 4.2.1: Results of the reaction of TFPN **118** with aryl ethers.

Entry	Aryl ethers	Product	Max Conversion (%)	Concentration* (µM)	Previously published Max Conversion (%)
119	Anisole	**120a/b**	72	0.25	40
122	1,2-Dimethoxybenzene	**126**	76	0.25	-
123	1,3-Dimethoxybenzene	**127**	72	0.25	55
124	1,4-Dimethoxybenzene	**128**	42	0.25	36
125	1,3,5- Trimethoxybenzene	**129**	74	0.25	-

* Concentration of TFPN **118** at which the maximum conversion was obtained.

It can be seen that three of the aromatic ethers selected, 1,2-dimethoxybenzene, 1,3-dimethoxybenzene and 1,3,5-trimethoxybenzene, proceeded with good conversions of up to 76%. The best conversions for all reactions were again at a concentration of 2.5 mmol. It should also be noted that both 1,2 and 1,3-dimethoxy benzene can form a mixture of isomers (Figure 4.2.14).

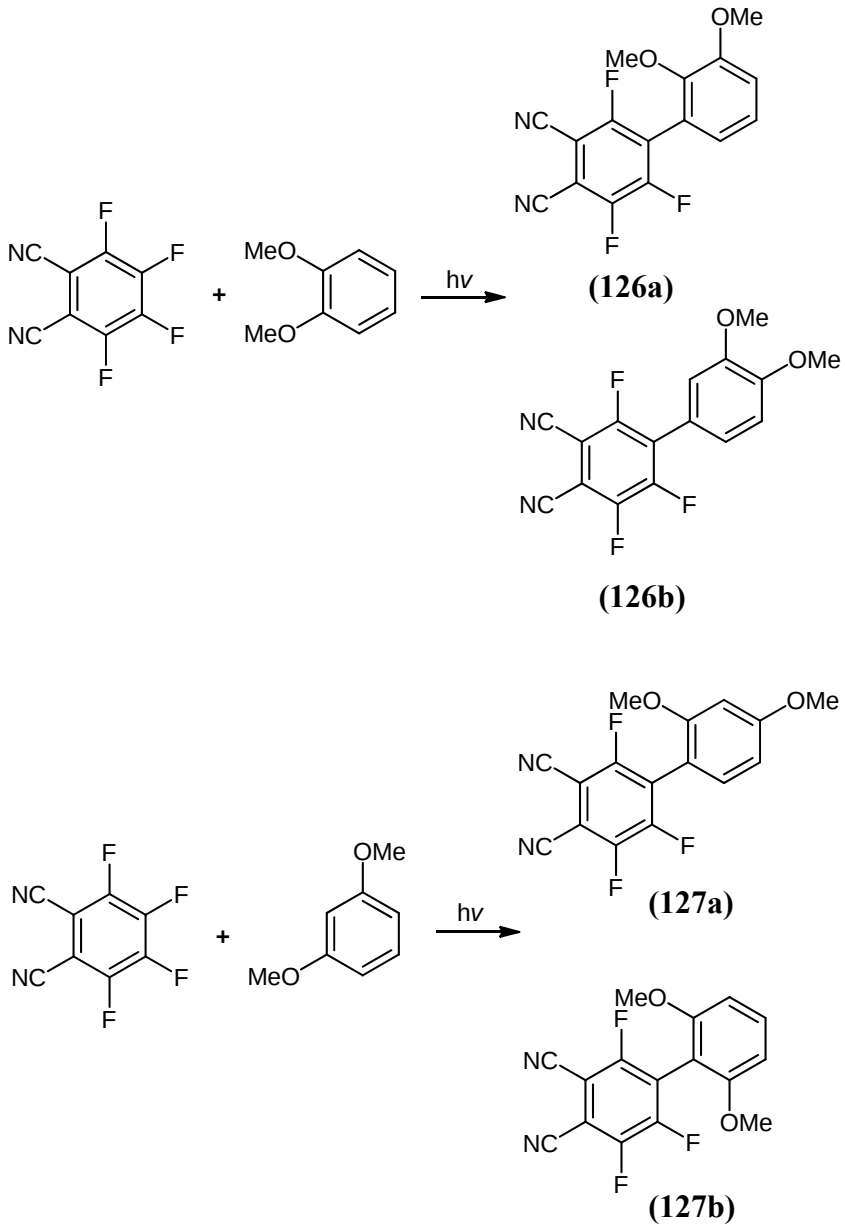


Figure 4.2.14: Possible products of the addition of **122** or **123** to **118**.

The ^{19}F NMR for both of these reactions is shown in figures 4.2.15 and 4.2.16. Two isomers are indeed present, however the second isomer formed in the case of 1,3-dimethoxybenzene is produced in smaller quantities compared to 1,2-dimethoxybenzene. We believe that in the case of **127**, that steric hindrance caused by the two methoxy groups maybe favouring the formation of **127a** over **127b**.

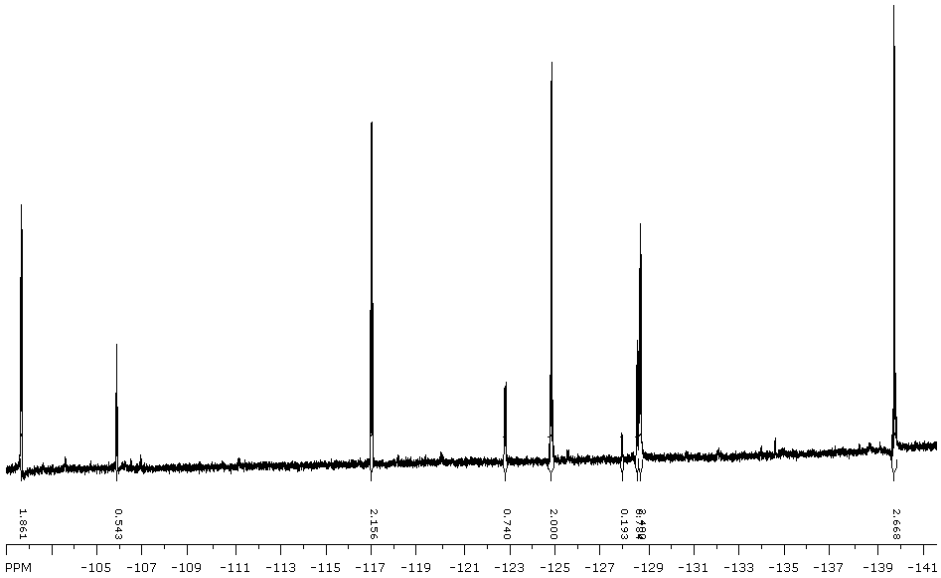


Figure 4.2.15: Crude ^{19}F NMR of the reaction between **118** and **122**.

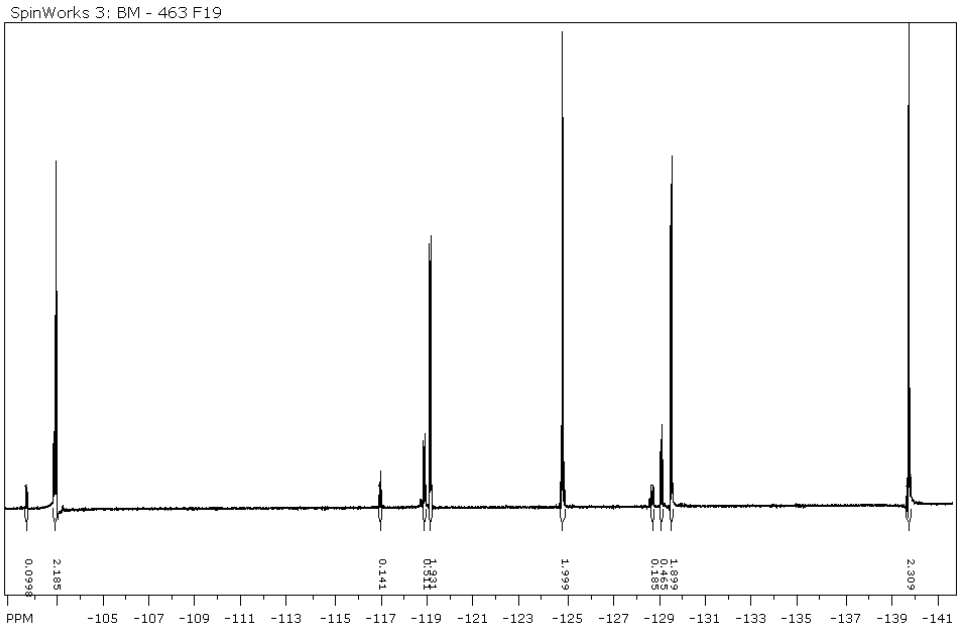


Figure 4.2.16: Crude ^{19}F NMR of the reaction between **118** and **123**.

The reactions with 1,4-dimethoxybenzene and 1,3,6-trimethoxybenzene should only yield a single isomer. The crude ^{19}F NMR spectra for these reactions are shown in Figures 4.2.17 and 4.2.18.

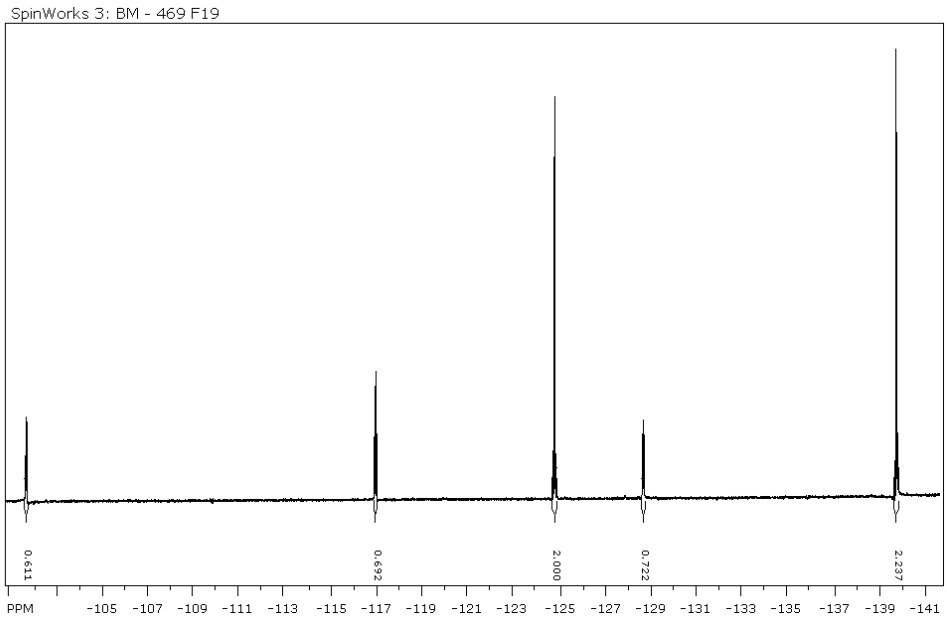


Figure 4.2.17: Crude ^{19}F NMR of the reaction between **118** and **124**.

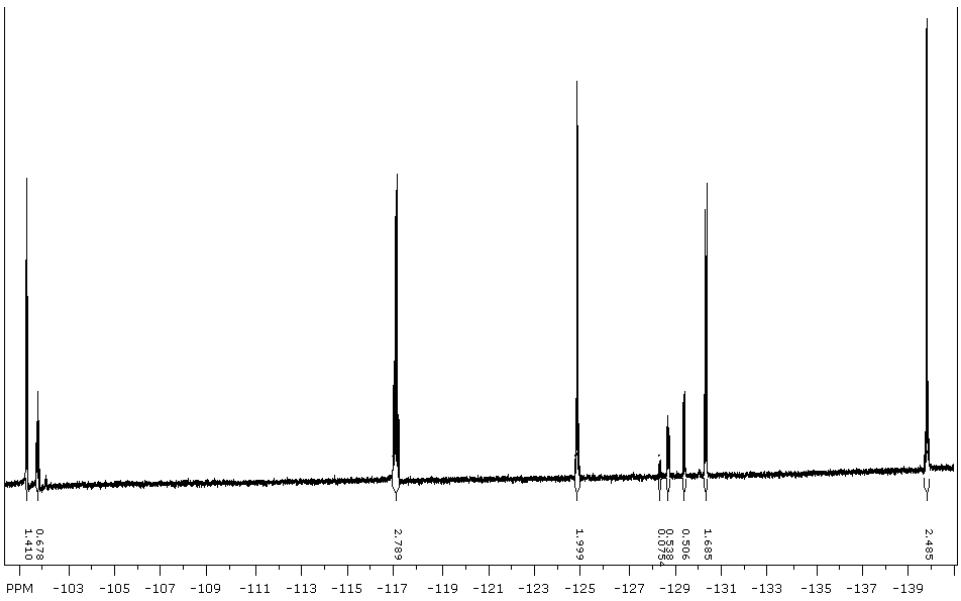


Figure 4.2.18: Crude ^{19}F NMR of the reaction between **118** and **125**.

The reaction of 1,4-dimethoxy benzene does indeed give a single product however the reaction with 1,3,5-trimethoxy benzene shows the production of some impurities. The conversions for both reactions are 42 and 74% respectively. These reactions and by products will be discussed in further detail in section 4.2.4 scale-up section.

Two more aryl ethers were screened for reactivity (Figure 4.2.19) with **118** however, despite previously published work,[106] no conversion was observed for the reaction between TFPN **118** and 1-methoxynaphthalene **114** and 2-methoxybiphenyl **146**.

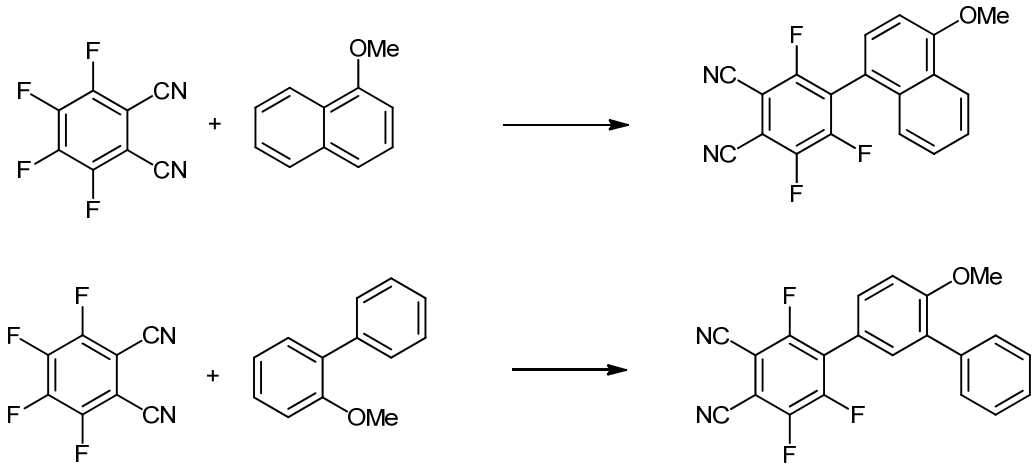
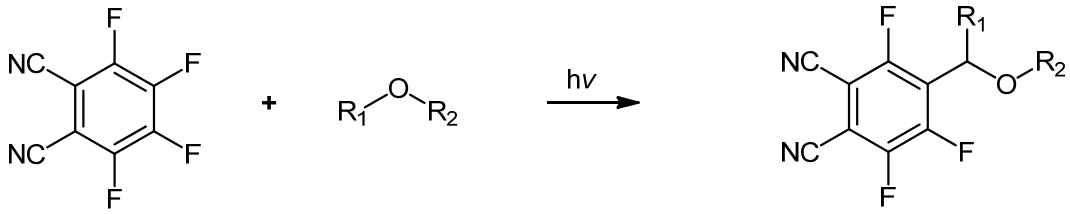


Figure 4.2.19: Reaction of **118** with extended aromatic ethers.

Another series of experiments were carried out which involved the reaction of **118** with aliphatic ethers (Figure 4.2.20). Four ethers were selected and were reacted with **118** at six different concentrations; the results are shown in Table 4.2.2.



(130); $R_1=R_2=C_2H_5$
(131); $R1=-(CH_2)_4-=R_2$
(132); $R_1=-CH_2O(CH_2)_2-=R_2$
(133); $R_1=CH_3$
$R_2=C(CH_3)_3$

(134); $R_1=CH_3$
$R_2=C_2H_5$
(135); $R1= -(CH_2)_3-R_2$
(136); $R_1=-O-CH_2-CH_2-=R_2$
(137); $R_1=H$
$R_2=C(CH_3)_3$

Figure 4.2.20: Reaction of **118** with aliphatic ethers.

Table 4.2.2: Results of the reaction of **118** with aliphatic ethers.

Entry	Aliphatic ethers	Product	Max Conversion (%)	Concentration* (mM)	Previously published Max Conversion (%)
130	Diethylether	**134**	10	2.5	-
131	Tetrahydrofuran	**135**	-	-	-
132	Dioxolane	**136**	10	10	-
133	t-Butylmethyl ether	**137**	10	2.5	-

* Concentration of **118** and alkyl ethers at which the maximum conversion was obtained

Results obtained from the reactions between **118** and aliphatic ethers were unimpressive. Three of the alkyl ethers gave observable product based on ^{19}F NMR. A crude ^{19}F NMR for the reaction of t-butylmethyl ether is shown in Figure 4.2.21. The percentage conversion yield for this transformation was 10% based on integration ratios at a reaction concentration of 2.5mmol. Interestingly, dioxolane gave the highest conversion of product at a concentration of 10mmol, which is the highest concentration observed in the series studied, however the conversion was only 10%.

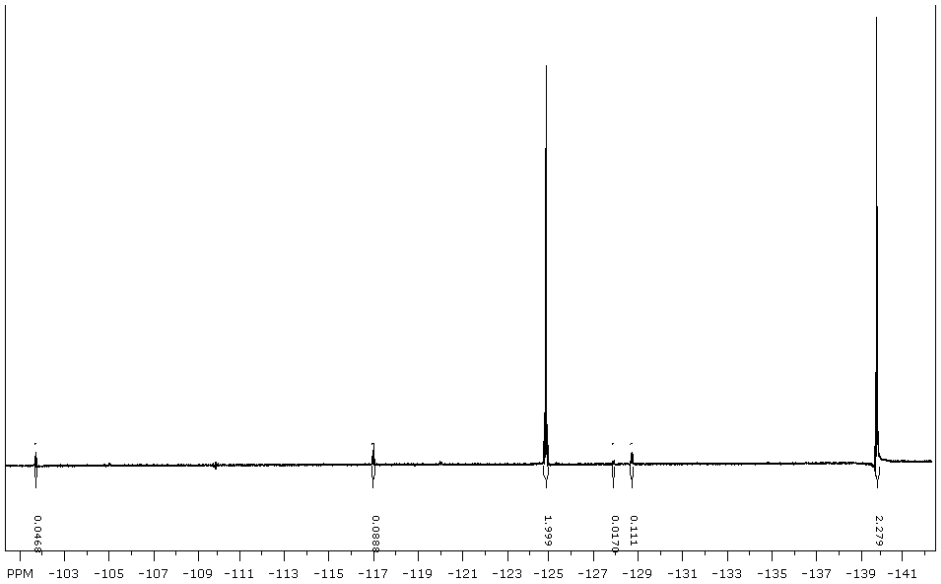
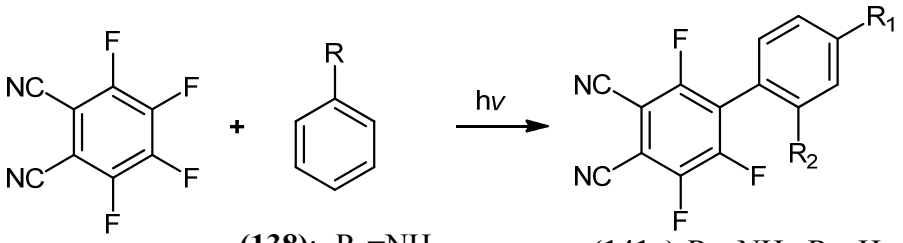


Figure 4.2.21: Crude ^{19}F NMR of the reaction of **118** with t-butylmethyl ether **133**.

The final series of exploratory experiments undertaken involved the reaction of **118** with alternative electron donating groups as outline in Figure 4.2.22 .



(138); $R_1=NH_2$
(139); $R1=N(CH_3)_2$
(140); $R_1=SCH_3$

(141a);$R_1=NH_2$, $R_2=H$
(141b);$R_1=H$, $R_2=NH_2$
(142); $R_1=N(CH_3)_2$, $R_2=H$
(133); $R_1=SCH_3$, $R_2=H$

Figure 4.2.22: Reaction of **118** with EWG equipped benzenes

Table 4.2.3: Results of the reaction of **118** with benzene equipped with alternative electron donating groups.

Entry	Other	Product	Max Conversion (%)	Concentration* (µM)	Previously published Max Conversion (%)
138	Aniline	**141a/b**	84	10	-
139	*N*,*N*-dimethylaniline	**142**	0	-	-
140	Thioanisole	**143**	39	0.25	-

* Concentration of **118** at which the maximum conversion was obtained.

Some interesting results (Table 4.2.23) were obtained from these reactions. It can be seen that thioanisole **140** reacted poorly compared to anisole **119**, even at low concentrations. One possible explanation for this is the weaker electron donating effect of the thioether compared to a methoxy group. The reaction of **118** with N,N-dimethylaniline yielded no observable product, however the reaction of **118** with aniline did proceed with 84% conversion based on ^{19}F NMR (Figure 4.2.23) at a 10 mM concentration. It was observed during the course of the reaction with aniline that a precipitate formed which was identified as the quaternary salt of aniline. It should also be noted that it would appear that only a single isomer was formed with aniline unlike the case with anisole where two isomers were prepared.

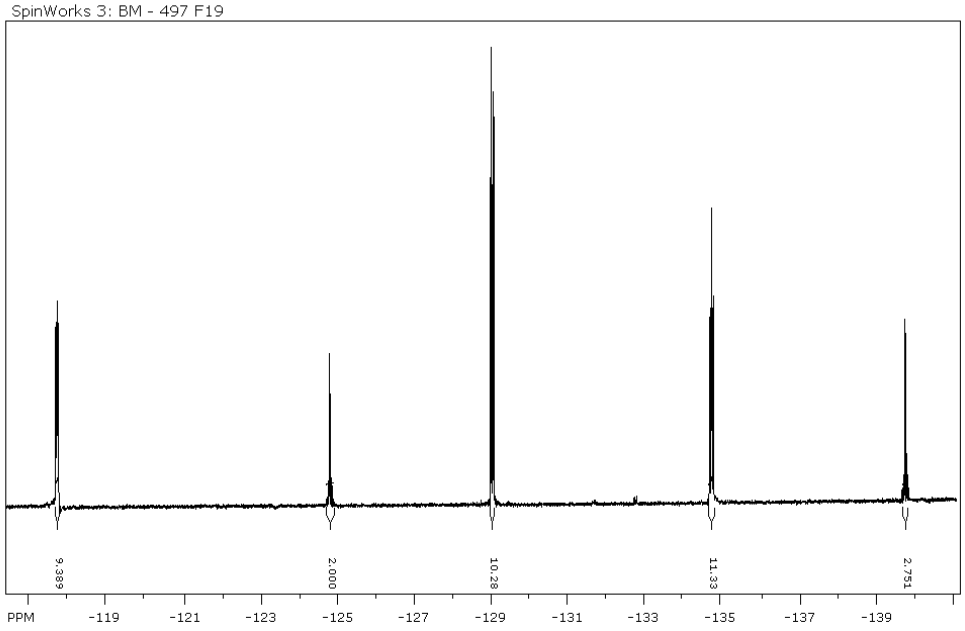


Figure 4.2.23: Crude ^{19}F NMR of the reaction of **118** with aniline **138**.

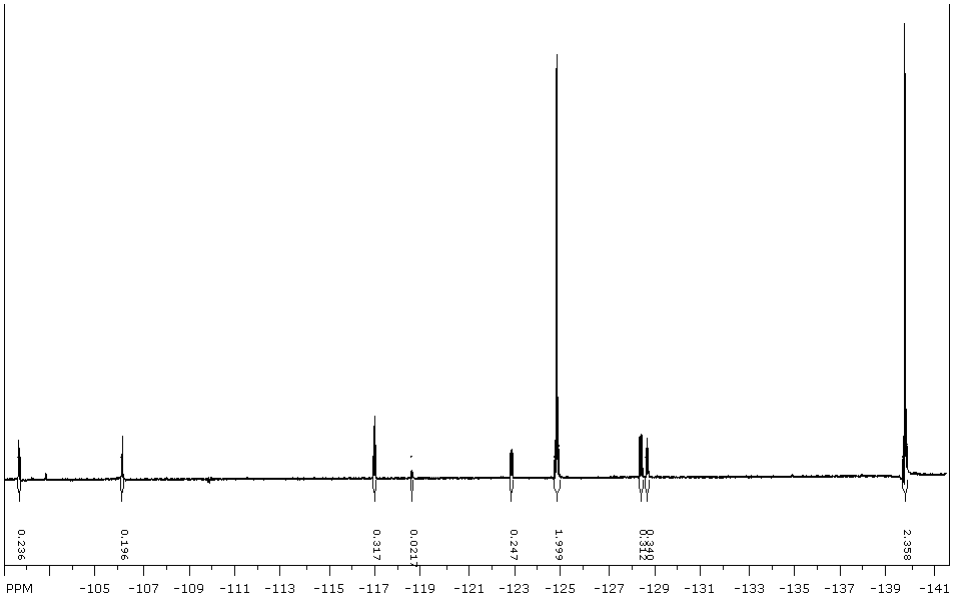


Figure 4.2.24: Crude ^{19}F NMR of the reaction of **118** with thioanisole **140**.

The above work has demonstrated both the scope and limitations of the photo-aryl coupling with **118**. Perhaps the greatest limitation is the low concentrations that are required for good conversions to product. It was decided to focus our attention on the

scale-up for compounds **120a**, **127a** and **129** since these compounds are not only prepared in respectable conversions but they were our initial targets for the preparation of a new series of fluorinated phthalocyanines.

4.2.4 Reaction Scale-up for the preparation of 120a, 127a and 129

A large scale synthesis was devised using the previously optimised conditions. This involved the irradiation of a dichloromethane (DCM) solution in a Rayonet reactor containing 1 mmol TFPN **118** (~200mg scale) and 2 mmol aromatic ether in the largest photochemical vessel available, a 350 ml Pyrex flask. Initially, the reactions were purified by column chromatography; however this method was found to be laborious and time consuming as well as environmentally unfriendly from the point of view of solvent consumption. With the relatively low temperature of sublimation of **118** in mind, a new procedure was devised. This involved the drying of the crude sample and the removal of any unreacted **118** by sublimation at ~50 °C, 0.5-0.02 Bar. The product(s) of the reaction were then isolated by further sublimation at 150–200 °C. This new procedure proved to be considerably more efficient in terms of time, labour and solvent, as well as allowing unreacted starting material to be recovered. Unfortunately, this procedure was unable to separate individual product isomers (in the case of **120** and **127**) but it did make it easier to purify the sample by column chromatography. In the case of **129**, sublimation gave pure product.

The isolated yield for **120a** was 39%, 50% for **127a** and 47% for **129**. (The other isomers **120b** and **127b** were actually isolated in yields of less than 5% along with some trace by-products). It should be noted that these yields only give 100-164mg of product based on the optimised reaction conditions and they could not be increased using the available Rayonet reactor.

Shown below are the crude ^{19}F spectrum and purified ^{1}H and ^{19}F spectra of the reaction between **118** and 1,3-trimethoxybenzene to give **127a/b** (Figures 4.2.25-4.2.27).

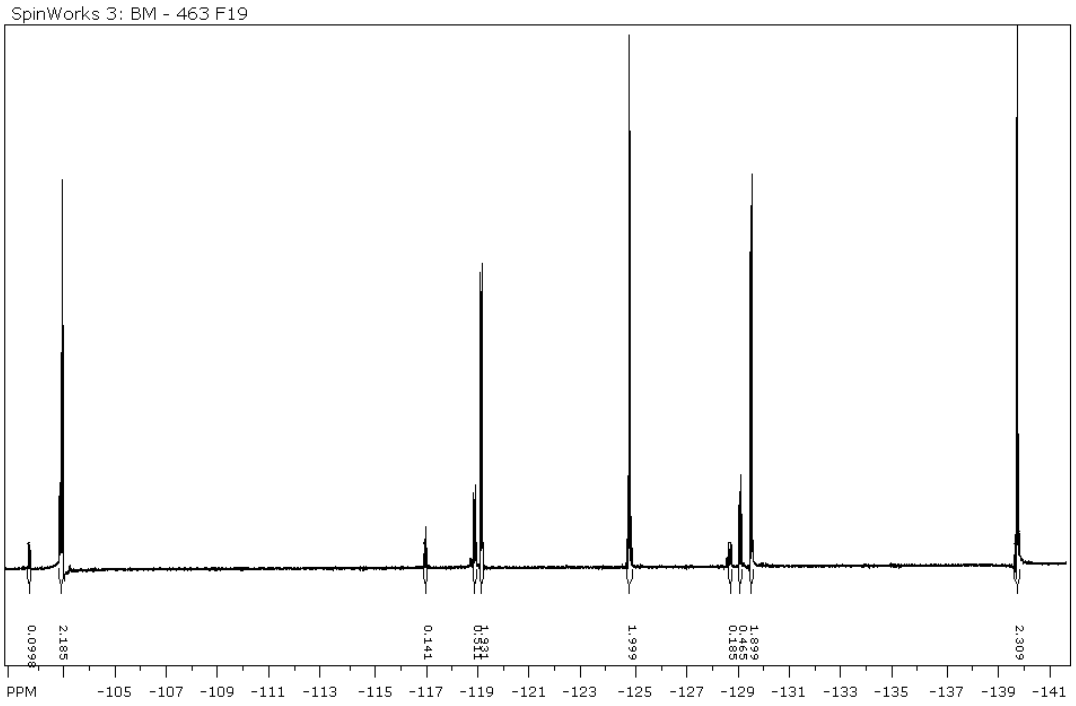


Figure 4.2.25: Crude ^{19}F spectrum of reaction between **118** and **123**.

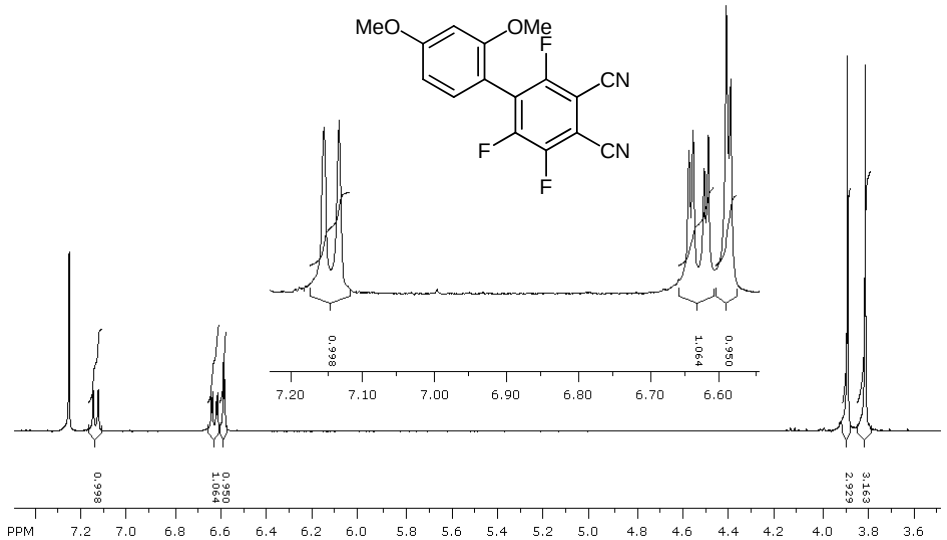


Figure 4.2.26: Purified ^{1}H spectrum of **127a**

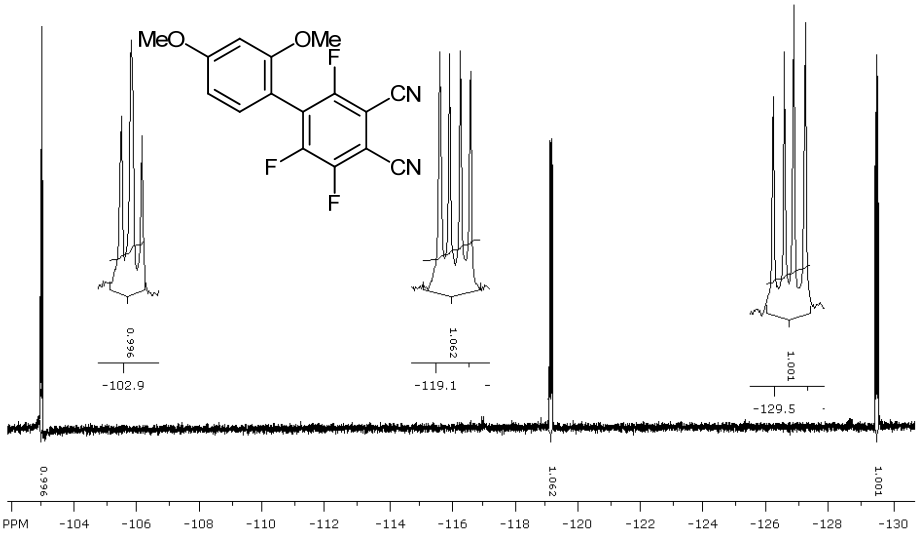


Figure 4.2.27: Purified ^{19}F spectrum of **127a**.

While the major product **127a** was successfully isolated other minor products were also visible in the crude ^{19}F spectrum. One of these was successfully isolated in trace amounts during purification. The ^{1}H and ^{19}F NMR spectra are shown in Figures 4.2.28 and 4.2.29 along with a proposed structure for the by-product. This compound would be an excellent precursor for the preparation of a binuclear phthalocyanine, unfortunately it is only made in trace quantities.

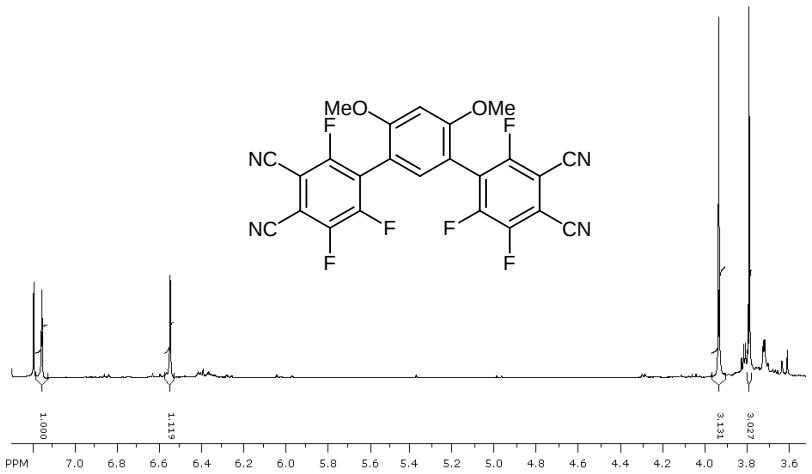


Figure 4.2.28: ^{1}H NMR spectrum of a possible side product of the reaction between **118** and **123**.

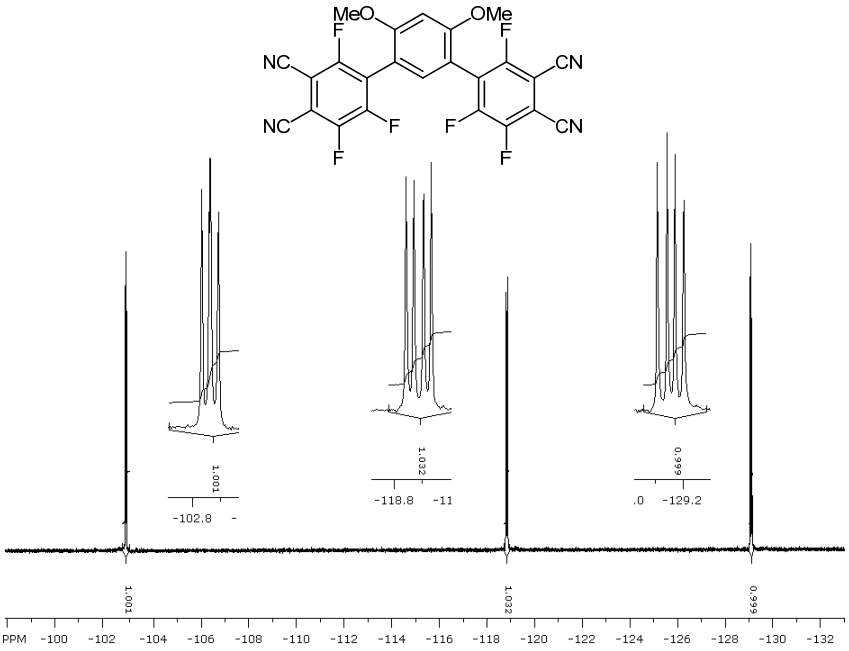


Figure 4.2.29: ^{19}F NMR spectrum of a possible side product of the reaction between **118** and **123**

The reaction between **118** and 1,3,5-trimethoxybenzene was also of particular interest with respect to trace by-products.. Shown below are the crude ^{19}F and purified ^{1}H and ^{19}F spectra of this reaction (Figures 4.2.30, 4.2.31and 4.2.32).

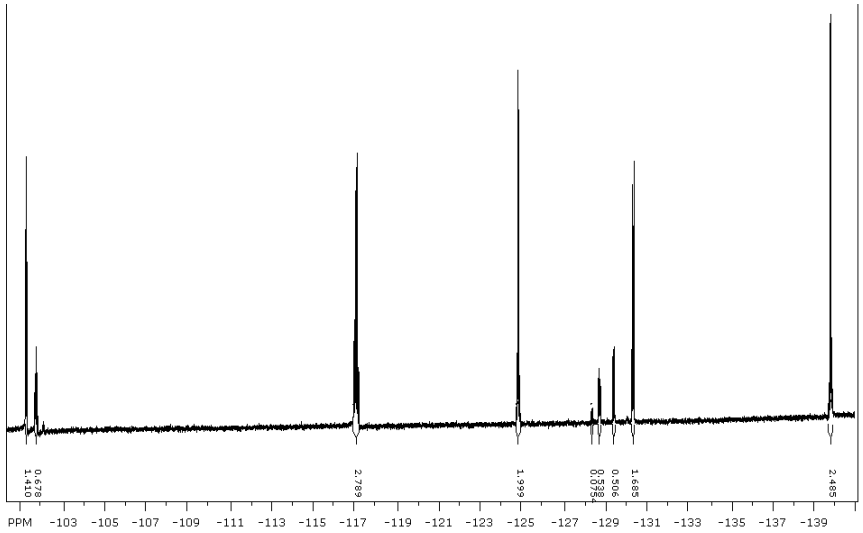


Figure 4.2.30: Crude ^{19}F NMR of the reaction between **118** and **125**.

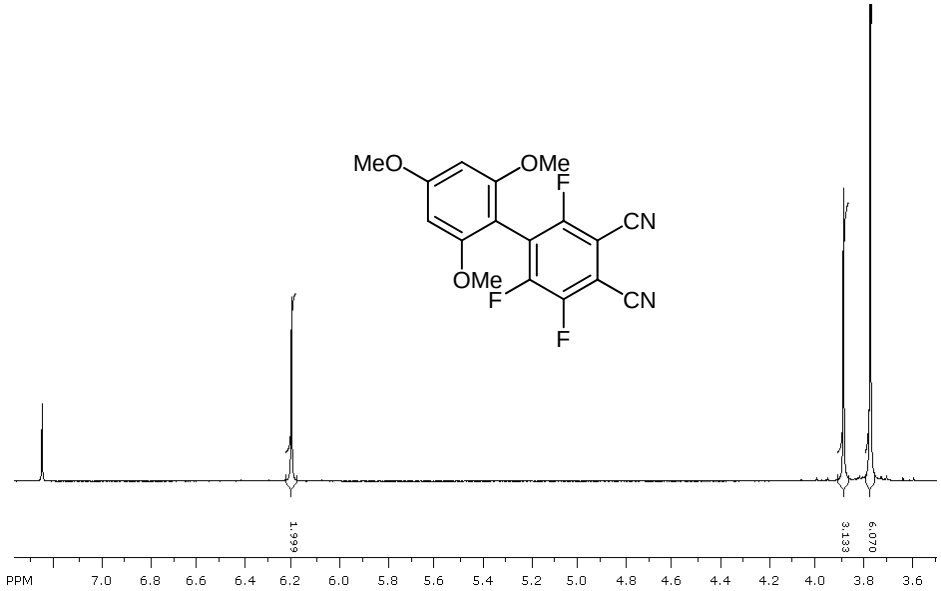


Figure 4.2.31: Purified ^{1}H NMR of **129**.

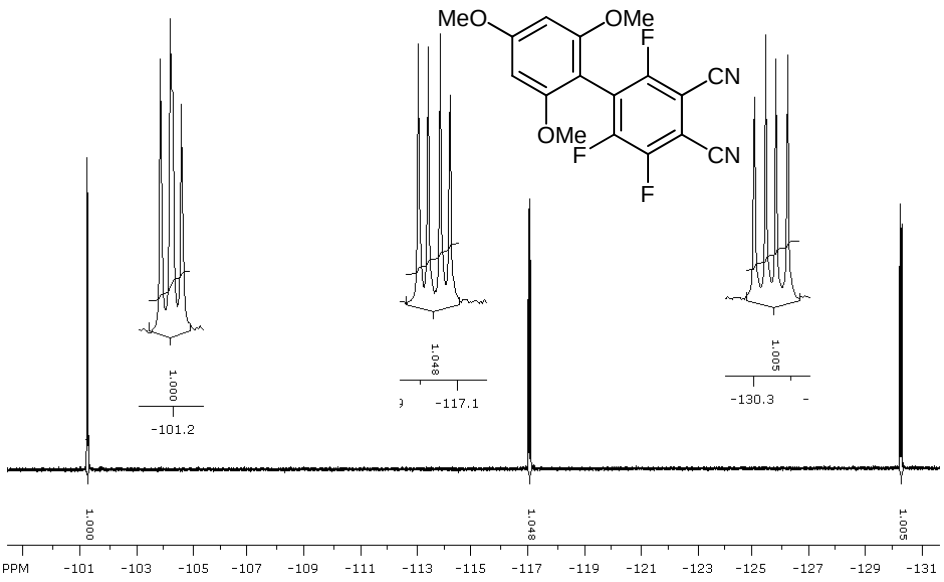


Figure 4.2.32: Purified ^{19}F NMR of **129**.

Again, while the target product was isolated in 47% yield, the crude ^{19}F NMR and ^{1}H NMR shows other minor products. This is particularly interesting as the symmetry of 1,3,5-trimethoxybenzene would suggest that only one product (**129**) should be formed. The double addition of 1,3,5-trimethoxybenzene to **118** was not observed (isolated) , furthermore double addition of **118** to 1,3,5-trimethoxybenzene was also not observed (isolated) (Figure 4.2.33).

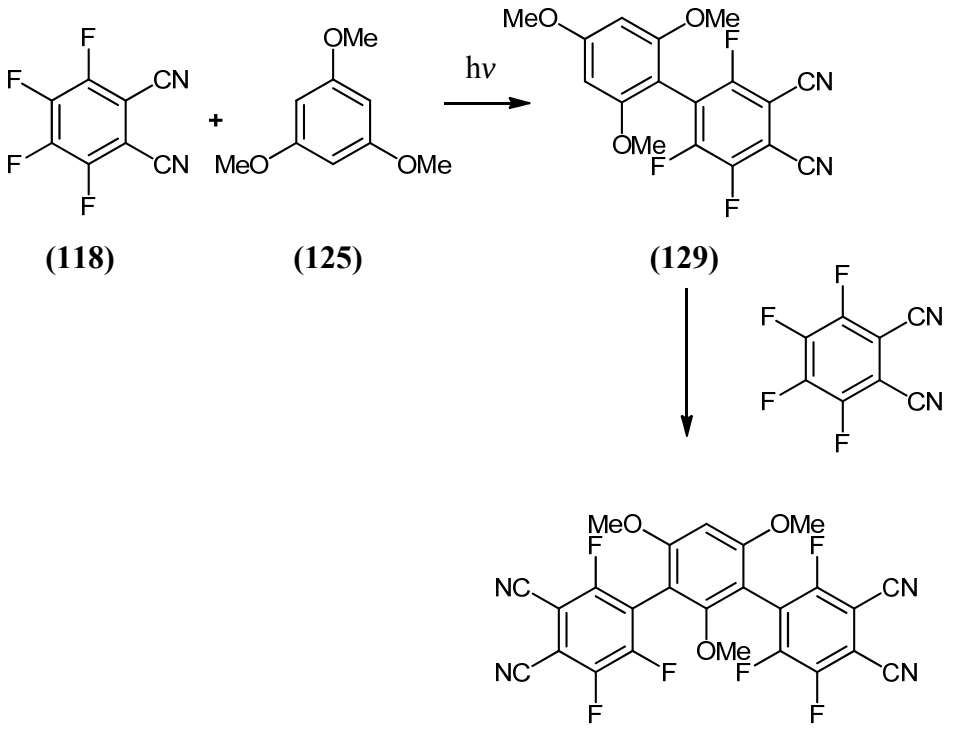


Figure 4.2.33: Double addition of **118** to **125**.

However, during purification one by-product was isolated. The ^{1}H spectrum and suggested structure of this product are shown in Figure 4.2.34. No peaks were observed in the ^{19}F spectrum for this compound.

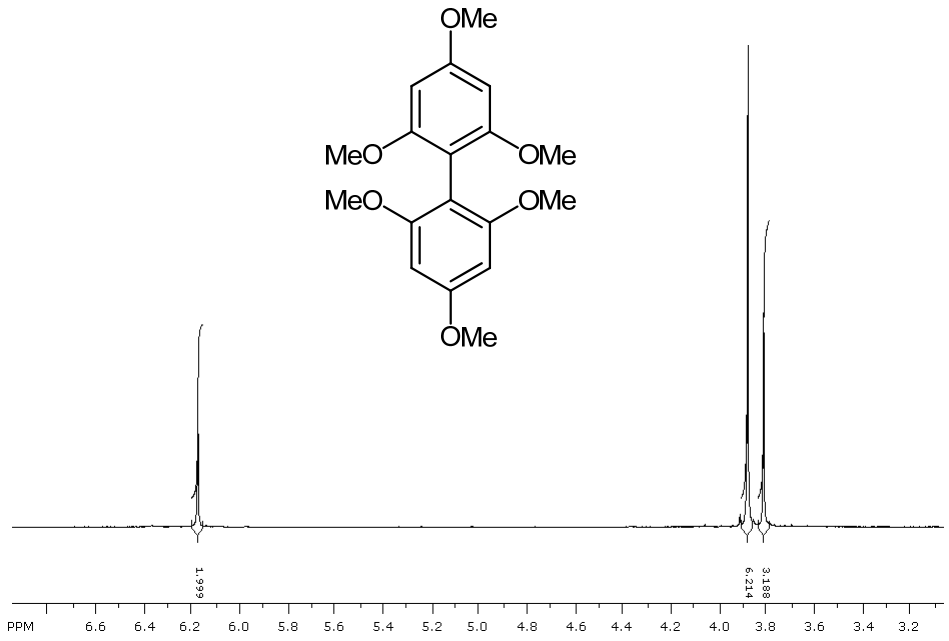


Figure 4.2.34: ^{1}H spectrum and proposed structure of isolated product.

4.2.5 Physiochemical properties of 210a, 127a and 129.

4.2.5.1 UV-Vis and fluorescence spectroscopy

UV-Vis spectroscopic analysis of the substituted phthalonitriles shows a significant red shift in the λ_{max} of **120a** (~34 nm) compared to **118** (Figure 4.2.35). Furthermore, this red shift is increased by an additional 45 nm in the case of **127** and **129**.

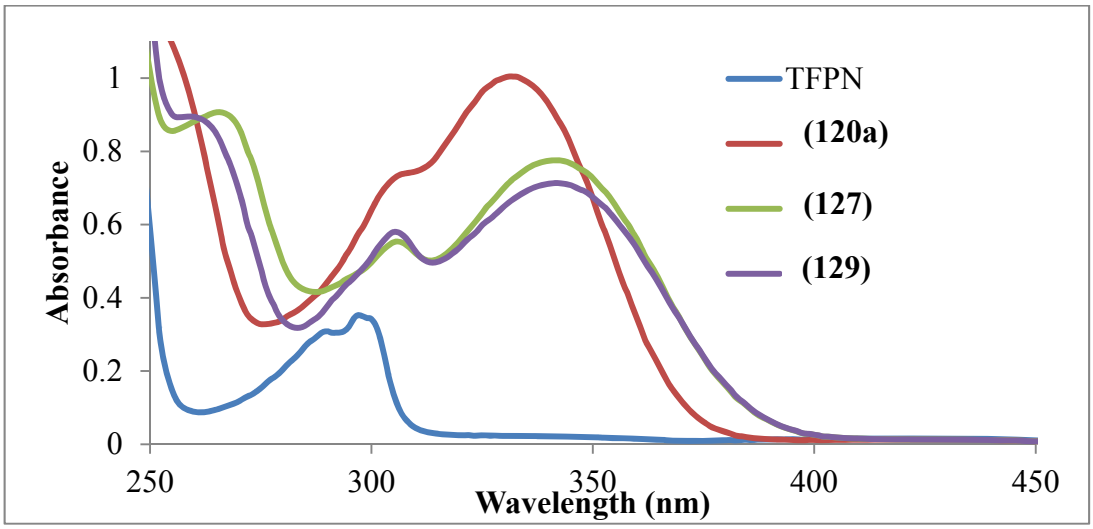


Figure 4.2.35: UV-Vis spectrum of **118** vs. biaryl phthalonitriles.

Analysis of the new phthalonitriles uncovered some interesting spectral properties, particularly phosphorescence as shown in Figure 4.2.36.

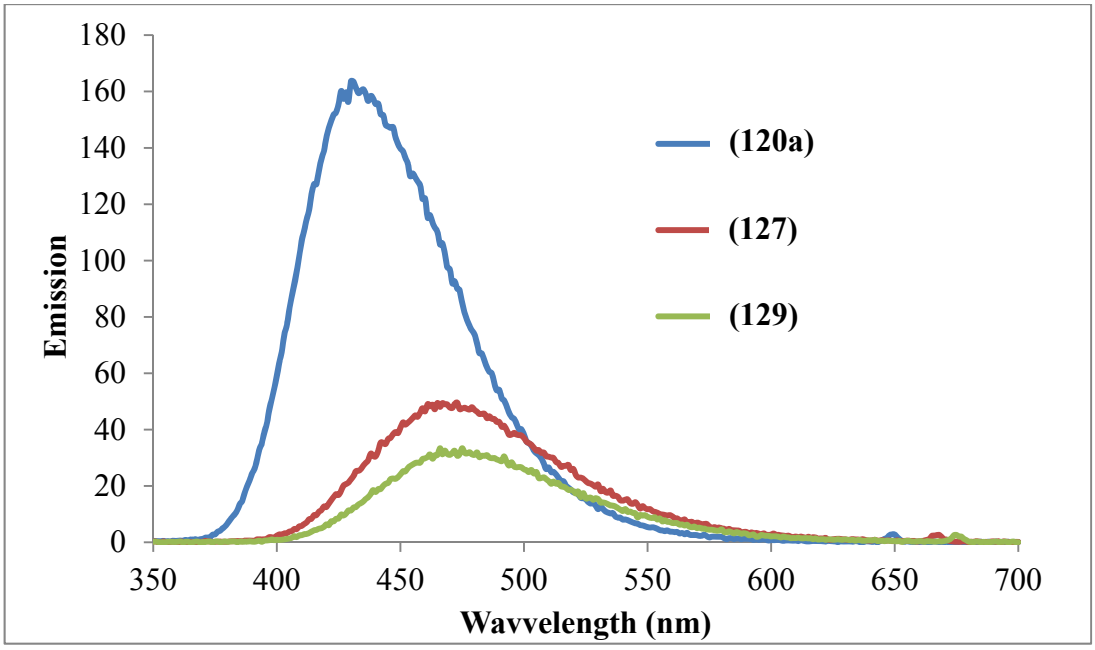


Figure 4.2.36: Fluorescence spectrum of biaryl phthalonitriles **120a, 127** and **129**.

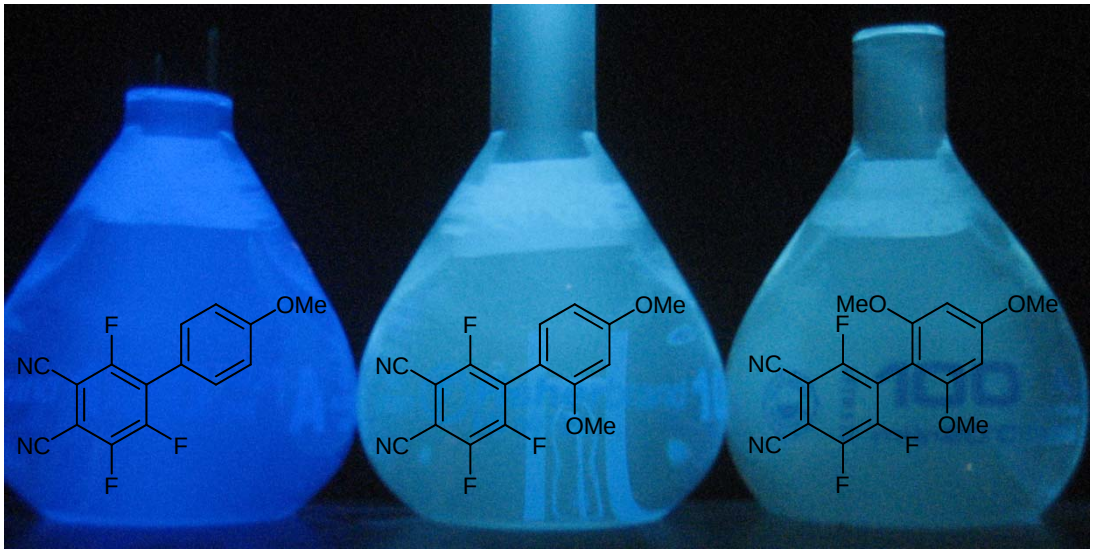


Figure 4.2.37: Phosphorescence of biaryl phthalonitriles at 365 nm.

It can be seen that these compounds, particularly the anisole derivative **120a**, show strong phosphorescence in the visible region. This, coupled with their small size, moderate polarity and stability makes them ideal candidates as cell imaging agents. The major drawback to these compounds in this area of application is their poor water solubility; however attempts are currently being made to overcome this

problem, such as sulfonation and the use of previously mentioned aniline salt derivatives.

The excited state lifetime for **120a** was measured in various solvents, which were performed by Thibault Tabarin of Tia Keyes's research group. The results are shown in Table 4.2.4.

Table 4.2.4: Excited state lifetimes of **120a** in various solvents.

Solvent	Methanol	Dichloromethane	Acetonitrile
Time (ns)	1.54	4.24	5.16

The shorter excited state life time suggests there is quenching occurring in polar solvents, possibly due to hydrogen bonding with the fluorines or the nitrile groups.

4.3 References

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5.0 Condensation of novel biaryl phthalonitriles to phthalocyanines and their subsequent evaluation as singlet oxygen photocatalysts

5.1 Introduction

It was proposed to design and optimise a procedure to condense the fluorinated biaryl phthalonitriles **120a**, **127a** and **129** to their respective Pcs. The Pcs generated by this method would be of considerable interest for the following reasons:

1) The replacement of C-H aromatic bonds with C-F bonds would result in enhanced stability for the proposed Pc.
2) The presence of aromatic groups in the peripheral positions should result in an extension of conjugation which is known to cause a red-shift in the UV-Vis spectrum of the Pc.
3) The inclusion of aromatic groups should increase the overall organic characteristics of the Pc, and hence result in increased solubility.
4) The bulky aromatic group should also be able to orientate itself orthogonally to the plane of the Pc. This would be expected to disrupt aggregation, also increasing the solubility of the Pc.

5.2 Synthesis of new Pcs from 120a, 127a and 129

The condensation of **118** to hexadecafluorinated phthalocyanine is typically carried out in a melt at temperatures above 180^{o}C; the more traditional method of condensation of **118** in a high boiling alcohol solvent is not reported in the literature.

For the condensation of **120a**, **127a**, and **129** to their respective Pcs it would be desirable to use an alcohol method since the temperature is far lower than the melt methodology. A further advantage of a low temperature synthesis is that it may allow

for the preparation of a single isomer instead of a statistical mixture of isomers which are typically observed for unsymmetrical substituted phthalonitriles. In the case of asymmetric phthalonitriles, resonance effects may lead to the preferential activation of one nitrile group over the other which may lead to the preferential synthesis of one isomer over another.

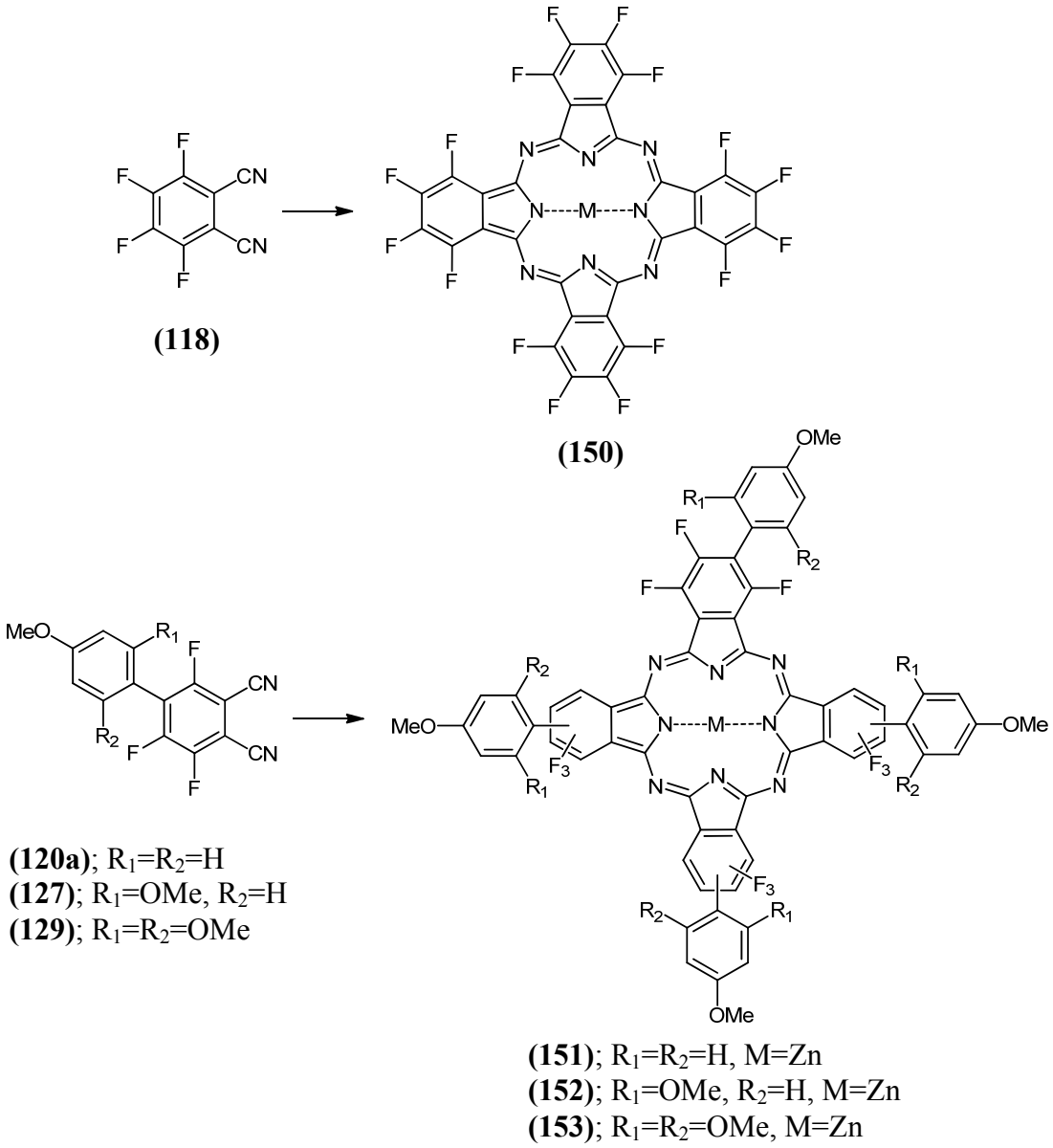


Figure 5.2.1: Synthetic scheme for the new Pcs.

5.2.1 Lithium alkoxide method

Due to the difficulty in synthesising large quantities of the aryl phthalonitriles **120a**, **127a** and **129**, all initial attempts to develop a condensation method were carried out using **118**. It was also initially decided to design a low temperature synthesis based on more recent reports in the literature. [107108]

Initial attempts were made to condense **118** using the lithium alkoxide method, using both n-pentanol and n-octanol as the alcohol. The general procedure was to allow lithium pellets to stir in a small volume (5–10 ml) of the appropriate alcohol at 60 °C, until a homogenous solution was obtained. The solution was allowed to cool to room temperature and **118** was added and stirring continued for 4-6 hours at 60 °C. Unfortunately, these methods failed to provide the characteristic green colour of a successful reaction, even when augmented with the organic base dimethylaminoethanol (DMAE).

As it is well known that this condensation method works for other phthalonitriles, it is reasonable to assume that the presence of fluorine atoms on the phthalonitrile ring impacts the electron density of the ring sufficiently to disrupt the reaction. Another possible explanation is that the condensation failed due to a competing nucleophilic displacement reaction of the alkoxide nucleophile with the fluorinated phthalonitrile (Figure 5.2.2).[109]

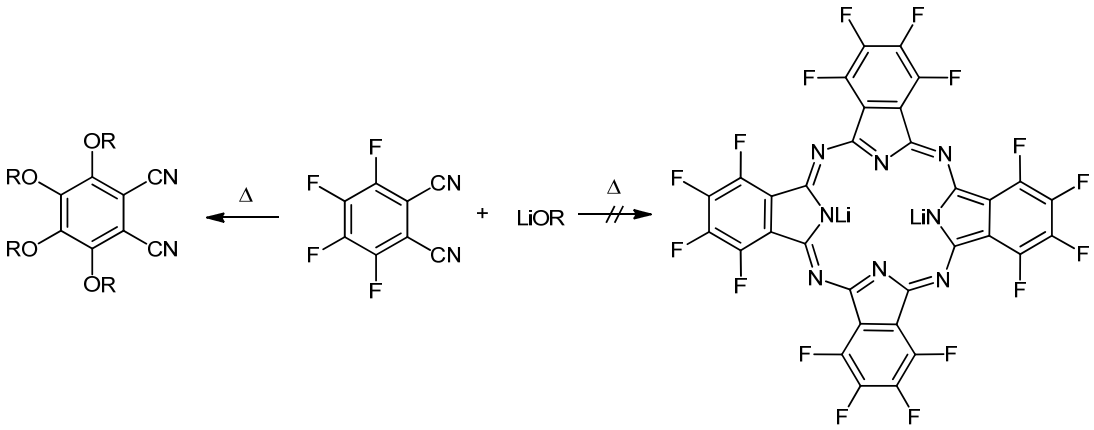


Figure 5.2.2: Reactions of **118** with lithium alkoxide.

5.2.2 High temperature fusion

As an alternative to the lithium alkoxide method, a high temperature fusion method was attempted. Two approaches were made, 1) using chloronaphthalene as a solvent with a metal template 2) as a phthalonitrile melt in the absence of a solvent with metal template.

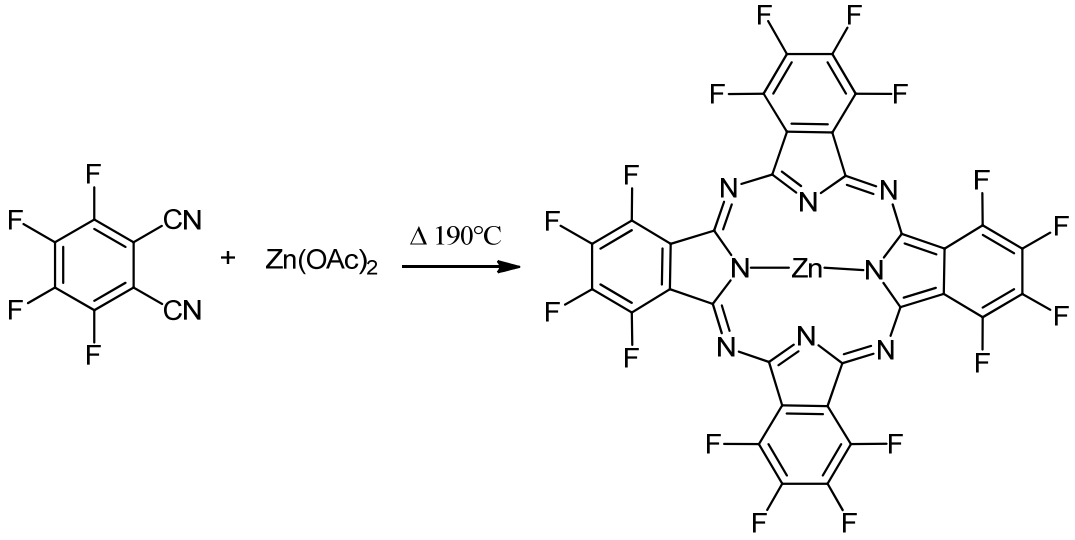


Figure 5.2.3: High temperature fusion of **118** to a Pc **150**.

The first reaction was carried out using chloronaphthalene as a solvent. One mmol of **118** and half a molar equivalent of zinc acetate was added to 5 ml of the solvent.

This was then heated to 190 °C under an inert atmosphere for 2-3 hours. Typically, the clear/cloudy white solution changed to the characteristic dark green colour of Pc almost immediately. After the reaction had concluded (3 h) it was allowed to return to room temperature. Hexane was added to precipitate the Pc. The crude product was isolated by filtration. The phthalonitrile starting material was removed by sublimation, while the metal salt was removed by washing with warm water.

The second approach attempted for the preparation of **150** from **118** was done in the absence of a solvent. A mixture of 1 mmol of **118** and half a molar equivalent of zinc acetate was prepared using a small pestle and mortar. This was then heated to 190 °C under an inert atmosphere for 2–3 hours. It was observed that a homogenous melt was formed. Again, the characteristic green colour of a Pc was observed. Once the melt had been allowed to cool, it was crushed and unreacted starting materials were removed by washing with warm water followed by sublimation.

It was found that both methods proceeded with reasonable to good yields (35% in 1-chloronaphthalene, 46% in the absence of a solvent) however, the poor solubility of zinc acetate in chloronaphthalene and increased complexity of the isolation of the product discouraged the use of chloronaphthalene as a solvent. All reactions were monitored by UV-Vis and IR spectroscopy. Figures 5.2.4 and 5.2.5 show that the nitrile stretch of the phthalonitrile starting material (2245 cm^{-1}) is no longer present in the Pc product. The UV-vis spectrum also confirms the presence of **150**, however due to the poor solubility of **150** a poorly resolved UV-vis spectrum is obtained

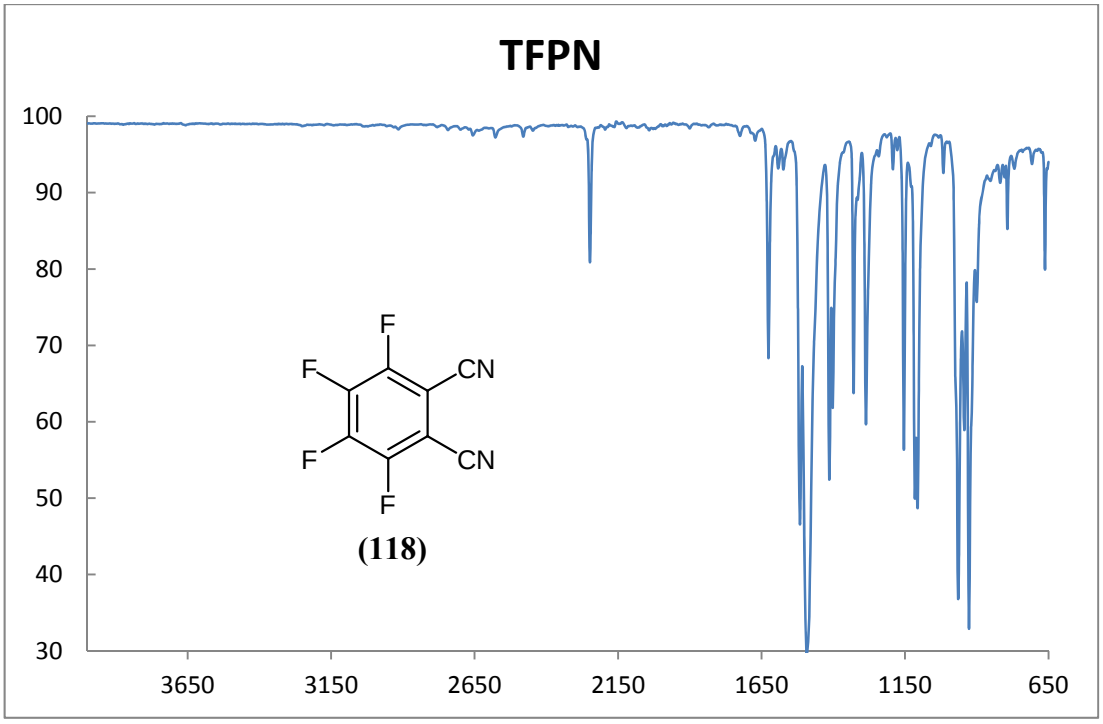


Figure 5.2.4: Infra-red spectrum of **118**.

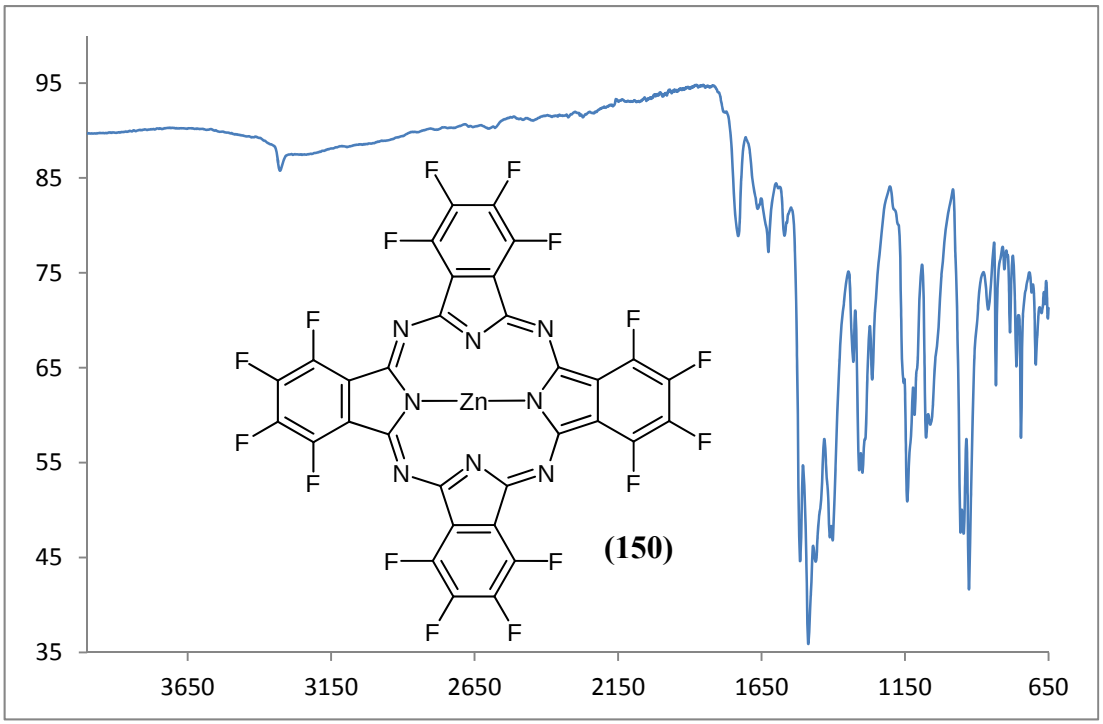
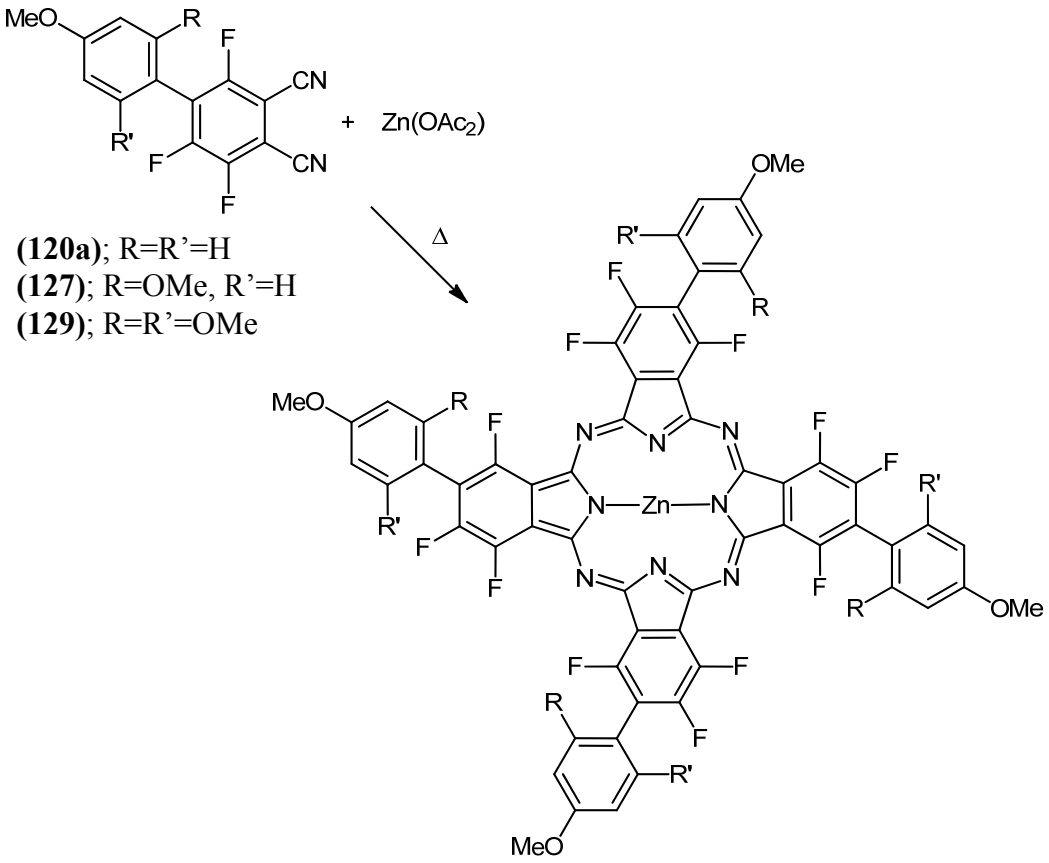


Figure 5.2.5: Infra-red spectrum of Pc **150**.

One important aspect of this method that should be kept in mind is the low temperature of sublimation of **118** (Sublimation of **118** has been reported at 75 °C,[110] but has been observed at temperatures as low as 50 °C). It was frequently observed that during reactions, crystals of **118** would condense near the cooler top of the reaction vessels. This effectively removed them from the reaction, and may lead to a lowering in the overall yield. In an attempt to overcome this, reactions were heated to the reaction temperature of 190 °C as quickly as possible.

The effects of the low temperature of sublimation were not all negative. It also allowed unreacted starting material to be easily separated from the product and recovered using a simple sublimation apparatus. By heating a finely powdered crude sample to 75 °C under vacuum it was possible to remove the TFPN starting material.

Once an effective condensation procedure for fluorinated phthalonitriles had been established, it was applied to the previously synthesised biaryl phthalonitriles to generate a series of tetra-aryl substituted Pcs with moderate to good yields (46% – 67%). The scheme for these reactions is shown in Figure 5.2.6. The high temperature melt method was found to be effective and despite their relatively higher melting/boiling points the previously used sublimation purification method was still effective, albeit at higher temperatures (~175–200 °C).



(120a); R=R'=H
(127); R=OMe, R'=H
(129); R=R'=OMe

(151); R=R'=H, M=Zn
(152); R=OMe, R'=H, M=Zn
(153); R=R'=OMe, M=Zn

Figure 5.2.6: Reaction scheme for the synthesis of novel Pcs.

5.3 Characterisation of novel Pcs 151-153

Once the desired Pcs had been synthesised and purified, they were characterised using a combination of ^{1}H and ^{19}F NMR spectroscopy, FTIR, UV-Vis spectroscopy and mass spectrometry (MS). Unfortunately, NMR spectroscopy was of limited use due to the presence of positional isomers.

5.3.1 UV-Vis studies of the new Pcs

From UV-Vis spectroscopic analysis, it was observed that introduction of an aromatic substituent induces a bathochromic shift of 24 nm compared to **150** (672 nm), regardless of the number of methoxy groups substituted on the aromatic ring (Figure 5.3.1). Taking into account the effect of the fluorine substituents, this gives a

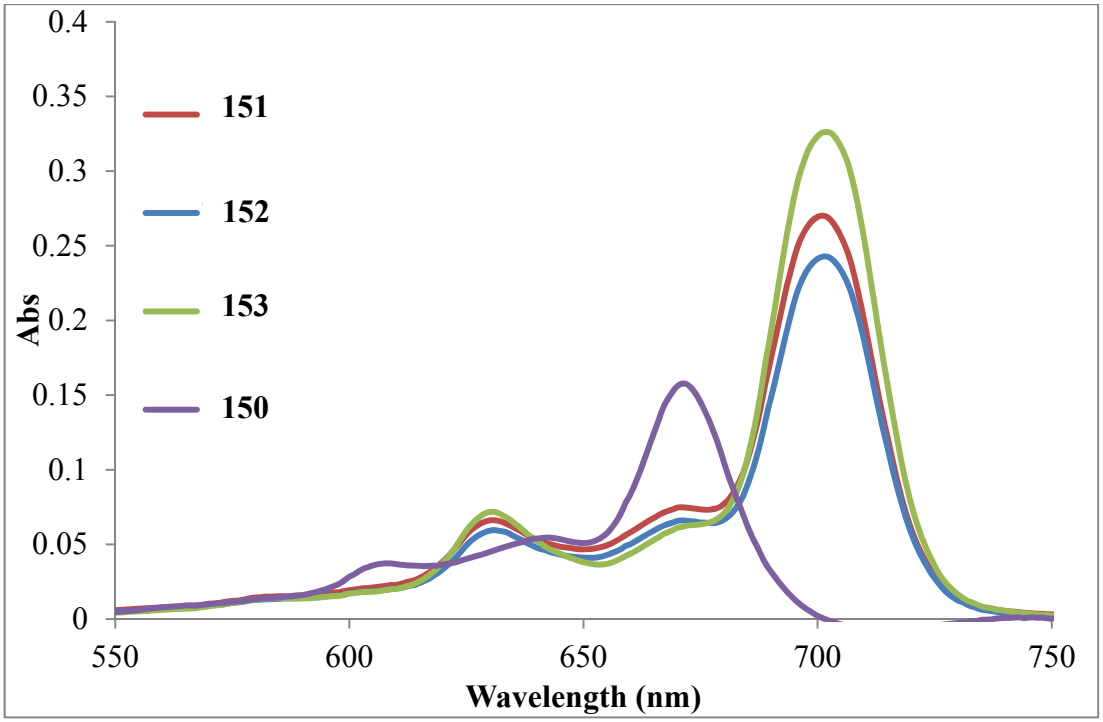


Figure 5.3.1: UV-Vis spectra of new Pcs.

total red-shift of 30 nm compared to ZnPc (665 nm).[111]. The fact that the three aryl-substituted Pcs have the same λ_{max} would suggest that only the extension of conjugation by the aromatic groups is responsible for the absorption properties of the Pcs, and that the number of methoxy groups present has little or no direct effect on the UV-Vis spectra.

Table 5.3.1: Selected UV-Vis data for the new Pcs

Compound No.	λ_{max} (nm)	Log ε (M^{-1} cm^{-1})
150	671	5.78
151	702	6.03
152	702	5.99
153	701	6.12

5.3.2 Mass spectrometric studies of the new Pcs

The molecular mass of the new Pcs **152** and **153** was confirmed using MALDI-mass spectrometry. The best results were obtained using a sinapinic acid matrix. Figure 5.3.2 shows the mass spectrum of **153** with an observed MW of 1458.27 (Calculated molecular weight = 1458.5). The observed mass for all **152** was 1338.2 amu (see table 5.3.2).

Table 5.3.2: MS data for **152** and **153**.

Compound No.	M/z (predicted)	M/z (observed)
152	1338.4	1338.2
153	1458.5	1458.3

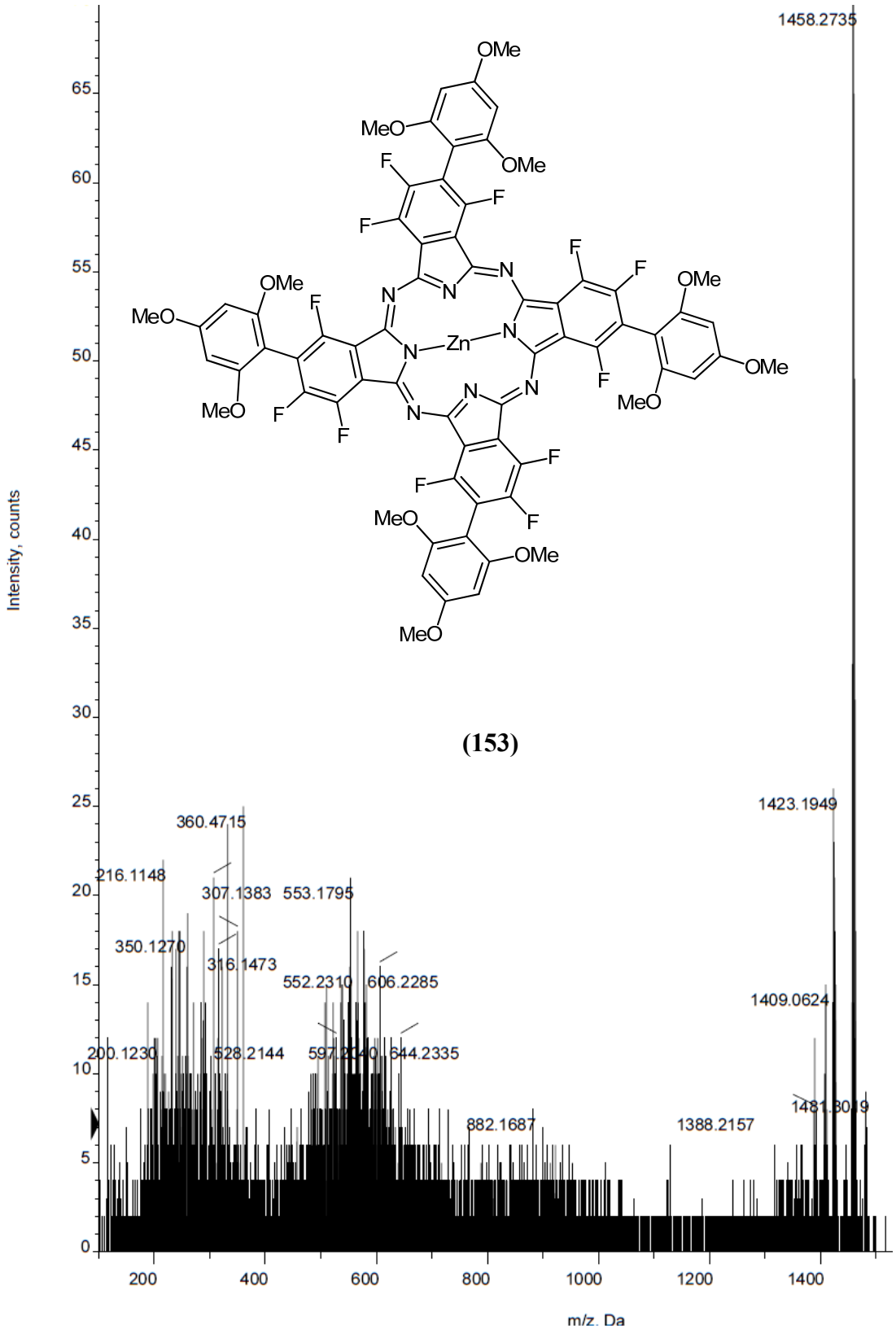


Figure 5.3.2: MALDI-MS of new Pc **153**.

5.3.3 Aggregation studies of novel Pcs

Aggregation of Pcs can result in a variety of spectral effects, with the most noticeable being a hypsochromic shift in the Q band,[62] and this effect can be used to determine the relative aggregation of a Pc at a given concentration. Probably the most obvious spectral effect of aggregation is the emergence of a secondary absorbance band, blue shifted relative to the Q-band, which increases relative to aggregation. This provides a valuable tool for the approximate determination of the degree of aggregation. In order to assess the aggregation potential of the new Pcs **151-153**, a series of UV-Vis spectra at varying concentrations in THF were obtained for each compound.

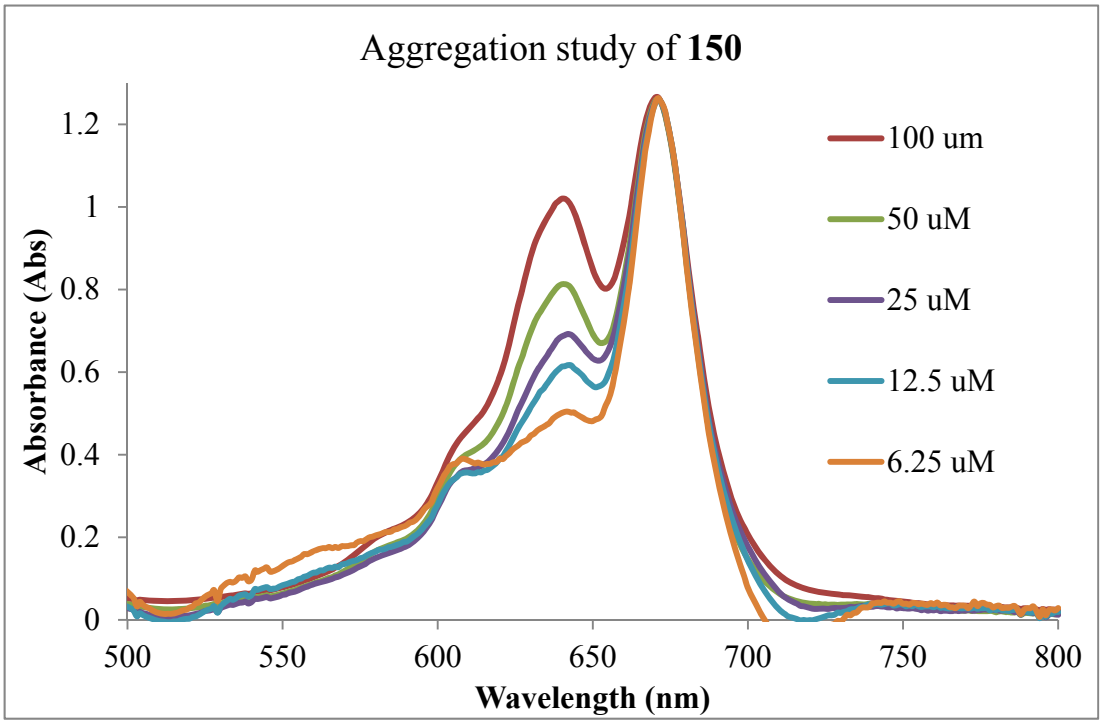


Figure 5.3.3: Aggregation study of Pc **150**.

As seen in Figure 5.3.3, the series of normalised spectra of **150** are a good example of the concentration dependant emergence of two individual species of Pc.

Absorption maxima are observed at 673 nm and 643 nm. It is reasonable to assume that absorbance at 643 nm is due to the dimer, while 673 nm is the monomer. The spectra obtained (which have been scaled up and normalised for clarity) clearly show that the relative intensity of the dimeric species decreases as the concentration is lowered.

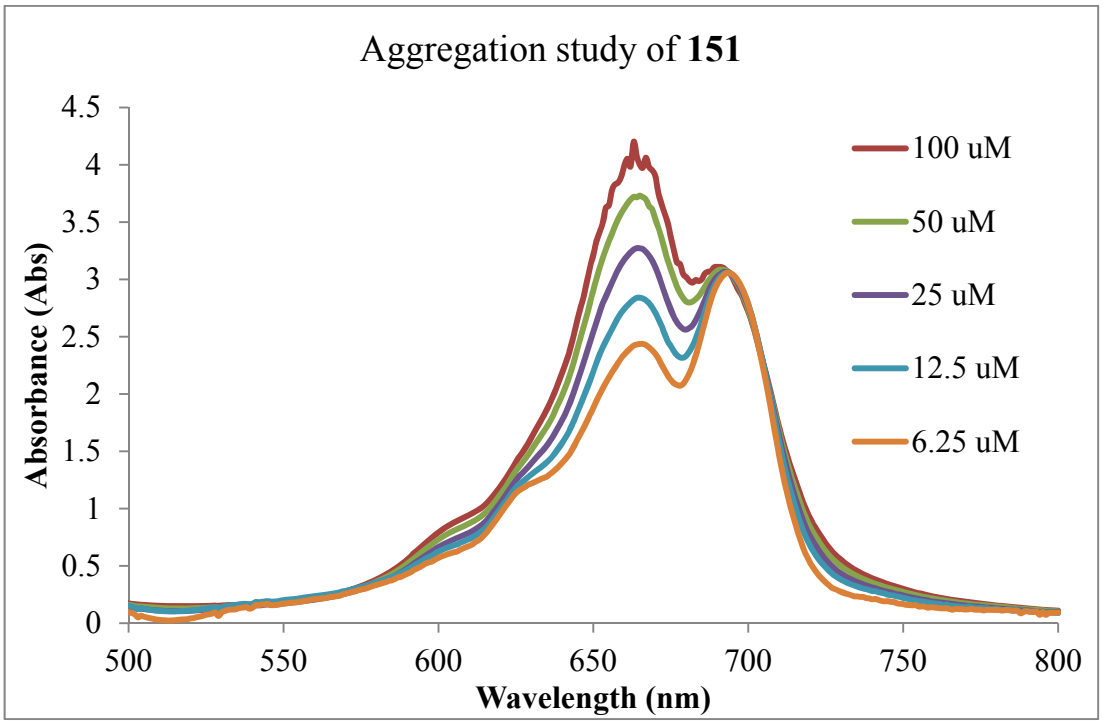


Figure 5.3.4: Aggregation study of Pc **151**.

In an interesting development, the UV-Vis spectra of the Pc equipped with *p*-anisole **151** (Figure 5.3.4) shows a greater portion of dimer (667 nm) relative to monomer (696 nm) at similar concentrations compared to **150**. In fact, the spectra shown in Figure 5.3.5 would suggest that the dimer is the major component at concentrations greater than 25 μM. A reasonable explanation of this is that the peripheral aryl rings are capable of orientating with the plane of the Pc, which results in an increased capacity for π-π stacking.

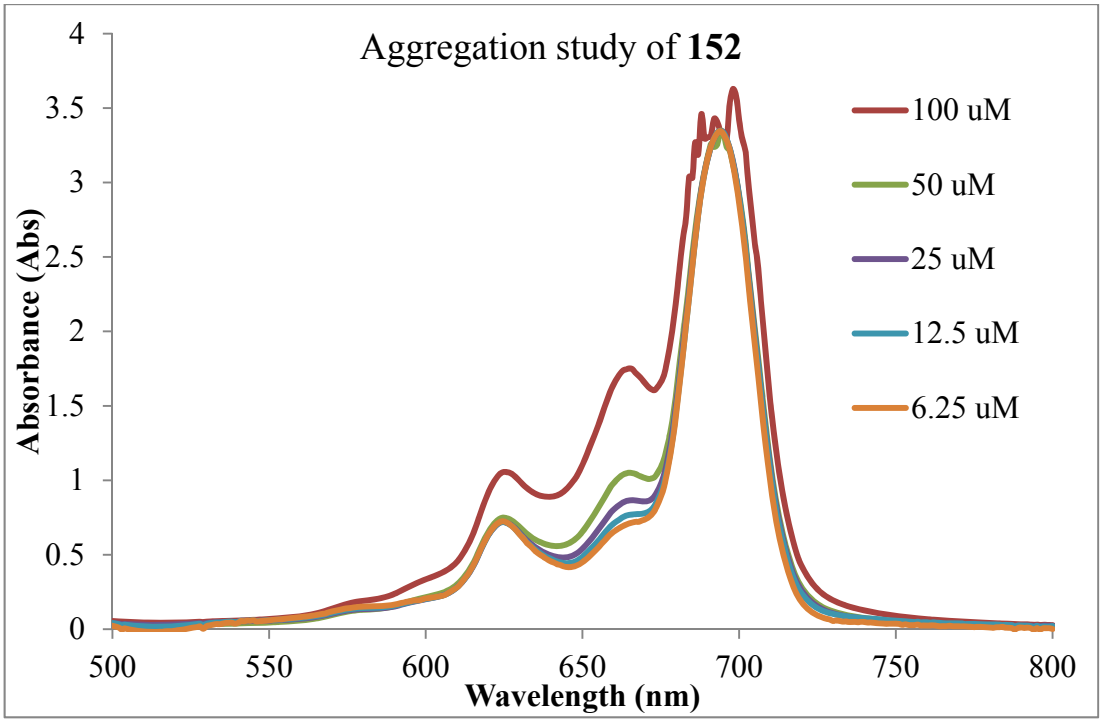


Figure 5.3.5: Aggregation study of new Pc **152**.

In the case of the Pc possessing 2,4-dimethoxybenzene substituents **152**, Figure 5.3.5 shows that there is a significant reduction in aggregation. Indeed, at concentrations lower than 25 μM, the spectral evidence of the dimer (667 nm) has practically disappeared, with the monomer (696 nm) remaining. This would suggest that a methoxy group in the *ortho* position (relative to the Pc) of the peripheral aryl ring has a very significant impact on the aggregation properties of the Pc, just as predicted from our initial design.

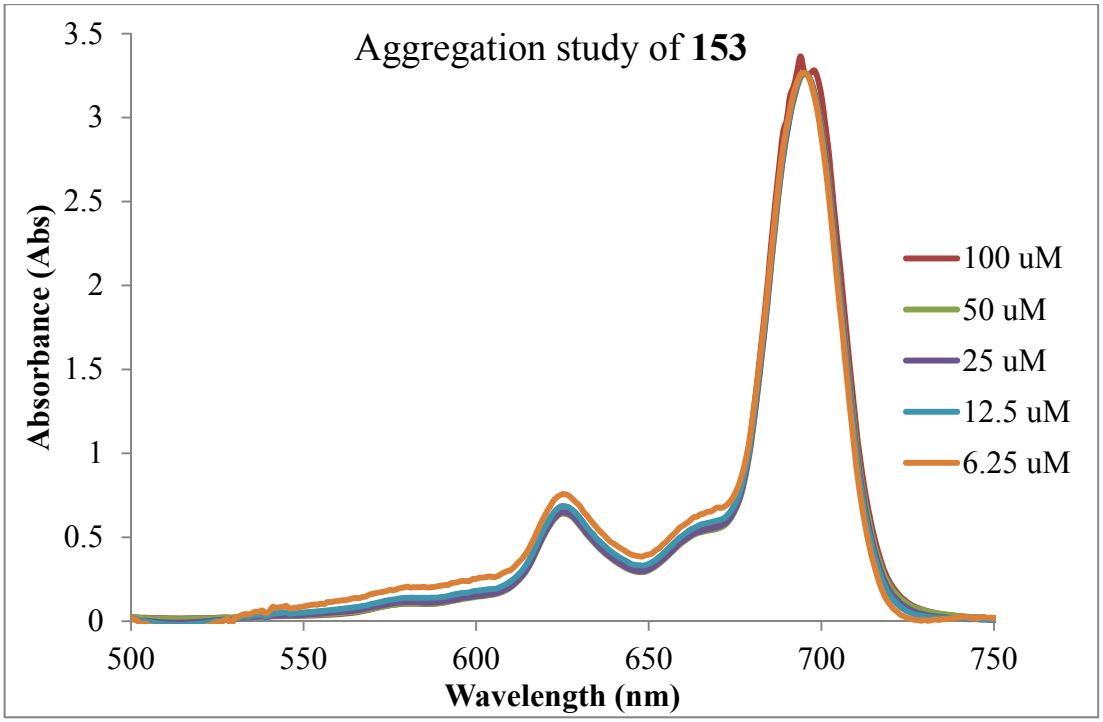


Figure 5.3.6: Aggregation study of novel Pc **153**.

The effect of a methoxy group in the *ortho* position of the peripheral aryl ring is very clearly demonstrated in the UV-Vis spectra of the **153** (Figure 5.3.6). In this case it was not possible to find the concentration at which dimerisation occurs! A reasonable explanation for this is that steric effects from the *ortho* methoxy groups twist the peripheral aryl rings into an orthogonal orientation relative to the plane of the Pc. This steric effect significantly interferes with the Pcs ability to stack. By comparing the spectra of this compound to those of **152**, it is apparent that the position of the methoxy groups in the *ortho* position inhibits aggregation in solution. 3-D models for both **151** and **153** are shown in figures 5.3.7 and 5.3.8. These models confirm the position of the methoxy groups in **153** are indeed above and below the plane of the Pc.

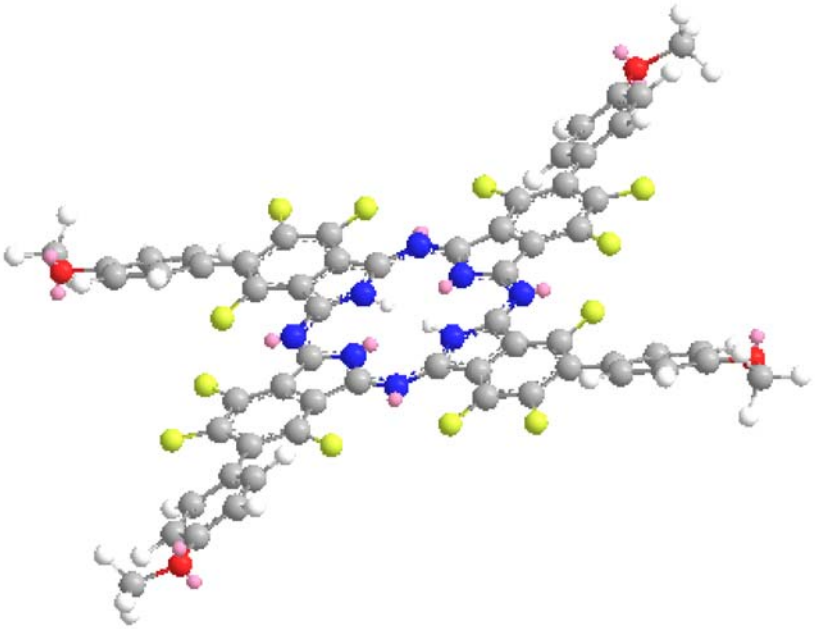


Figure 5.3.7: 3D Model of Pc **151**.

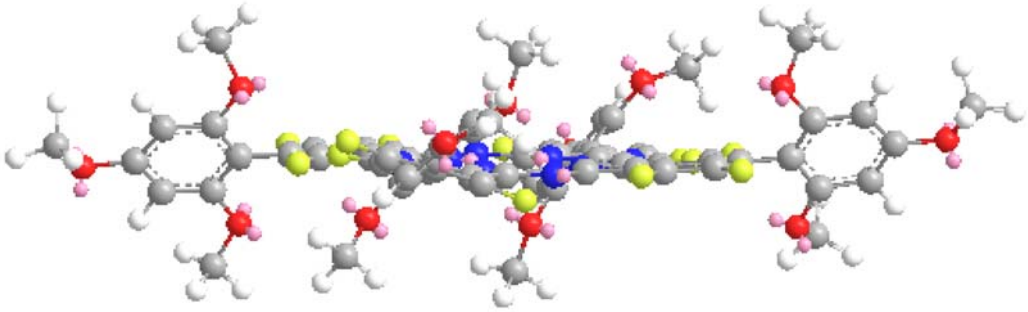


Figure 5.3.8: 3D Model of Pc **153**.

5.3.4 Solubility studies of new Pcs

The new Pcs had some unexpected solubility properties; both **152** and **153** are alcohol soluble, which is very rare for most neutral substituted Pcs. We believe this unique solubility property is a combination of reduced aggregation caused by the *ortho* methoxy groups of the aryl substituents and further stabilisation afforded by the hydrogen bonding between solvent and the fluorine substituents of the Pc macrocycle. It was now important to determine if an aqueous solution of the Pcs

could be generated. This would be an important factor for the biological applications of these Pcs, especially in photodynamic therapy (PDT) and imaging.

It had been previously observed during workup that none of the Pcs were directly soluble in water. In an attempt to generate an aqueous solution of the Pcs, an appropriate amount of each sample was dissolved in 0.5 ml of methanol which was then volumetrically made up to 50 ml with water in order to give a 25 μM solution in 1% MeOH/H_2O. These solutions were then analysed by UV-Vis spectroscopy. The spectra obtained are shown in Figure 5.3.9

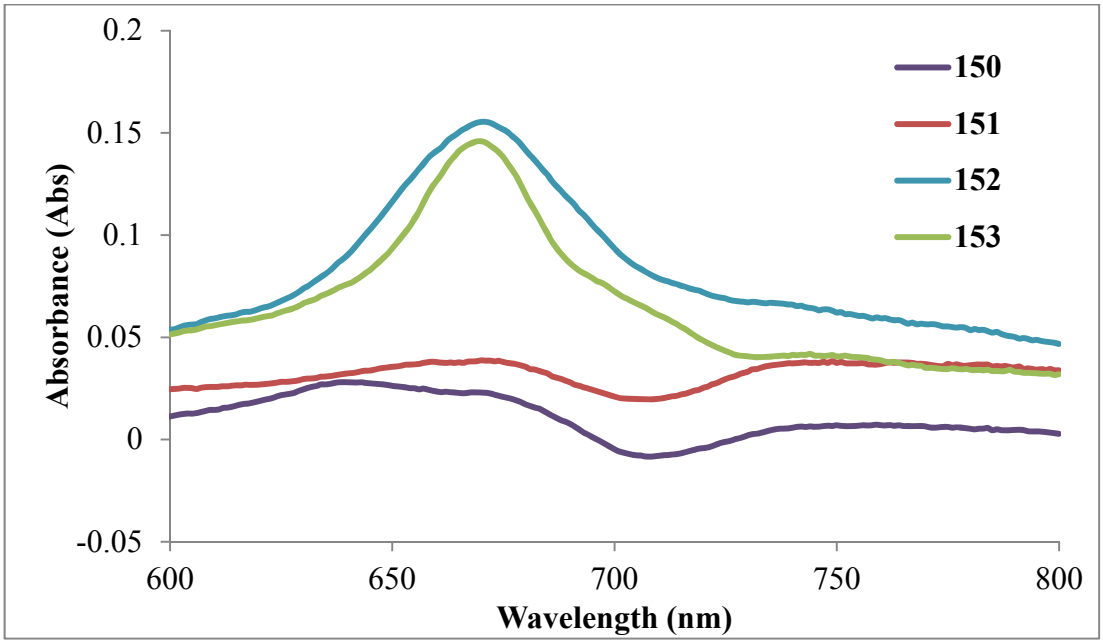


Figure 5.3.9: UV-Vis spectra of Pcs in 1% MeOH/H_2O.

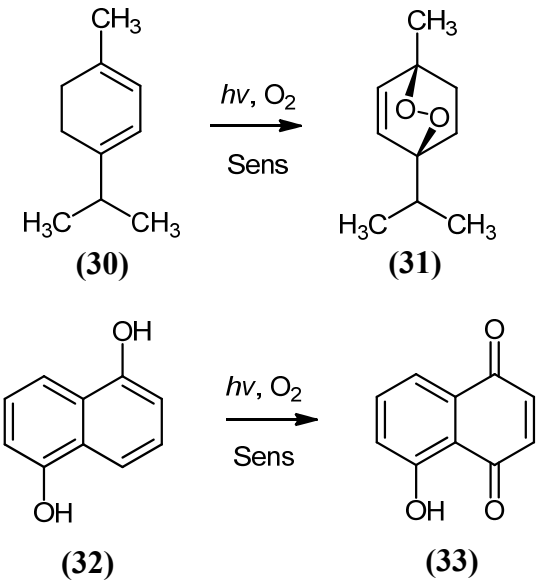
From the spectra shown, it can be seen that in the case of Pcs **150** and **151**, very little of the compound remained in solution, while in the case of Pcs **152** and **153** it can be seen that there is absorbance at the wavelength associated with the aggregated form of the Pcs (667 nm). This would suggest that small amounts of these Pcs are capable of dissolving in the methanol/water solution.

The fact that the level of absorbance observed is lower than in other solvents, coupled with the fact that precipitation was observed would suggest that the solution is at saturation at 25 μM.

5.4 Evaluation of novel Pcs as singlet oxygen photocatalysts

5.4.1 Reaction choice

The photosensitisation capability of the new phthalocyanines was measured using the photooxygenation of β-citronellol as a model reaction.[112] This reaction was chosen from other possible photooxygenations, such as the conversion of α-terpinene **30** to ascaridole **31**,[113] or the conversion of 1,5-dihydroxynaphthalene **32** to juglone **33**.[114] The photooxygenation of β-citronellol was chosen as a model reaction due to its simplicity, ease of work up and convenient analysis as well as the suitability of the solvent system – methanol, a green solvent which the new Pcs are soluble in.



(30) **(31)** **(32)** **(33)**

Figure 5.4.1: Common singlet oxygen reactions.

Although the photooxygenation of α-terpinene to ascaridole may appear to be the preferable reaction due to the single product formed, previous work has shown that the volatile nature of the product can make determination of conversion difficult, as product may be lost during evaporation steps.

The photooxygenation of β-citronellol is the favourable reaction in this respect. Although there are two possible products for the oxidation of β-citronellol with

singlet oxygen, they both have low volatility, and are easily identifiable by distinct characteristic peaks in ^{1}H-NMR (Figure 5.4.2). This allows for simple, rapid determination of conversion. It is also appropriate to use this reaction as a benchmark, as there are other literature examples using a similar technique. This allows for a broader range of comparison with other sensitisers.[107b, 112]

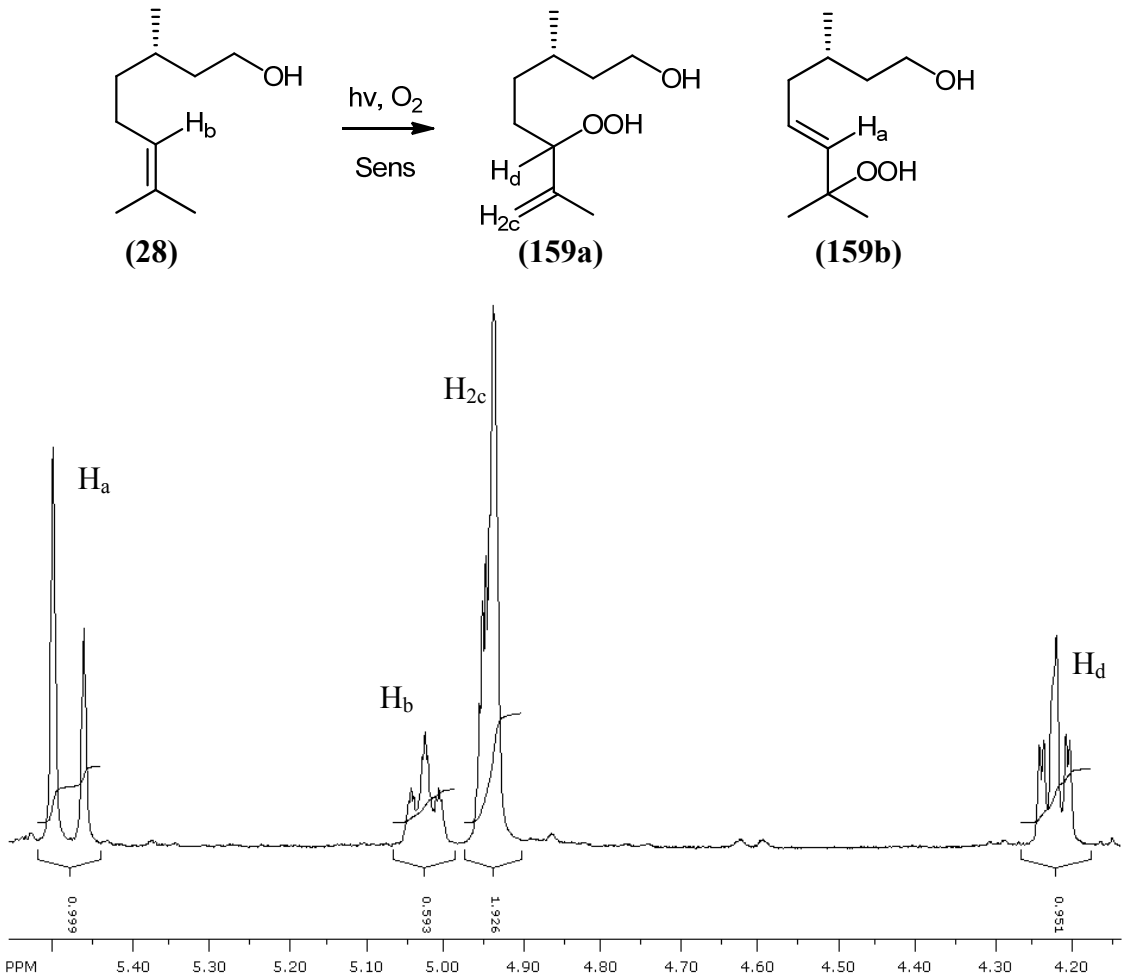


Figure 5.4.2: The photooxygenation of β-citronellol.

5.4.2 Results

Phthalocyanines **150-153**, methylene blue and Rose Bengal were all evaluated in this study. The standard procedure used for all sensitisers involved the irradiation of a solution of β-citronellol (1 mmol) and the sensitiser (1 μmol) in 50ml methanol using

a halogen lamp. Samples were taken at 3 hour intervals for a total of 6 hours and the total conversion to both isomers was measured by ^{1}H-NMR. It should be first noted that based on the data obtained, none of the sensitisers in this study showed any selectivity to either potential isomer **159a** or **159b**.

The results obtained are shown in Figure 5.4.3.

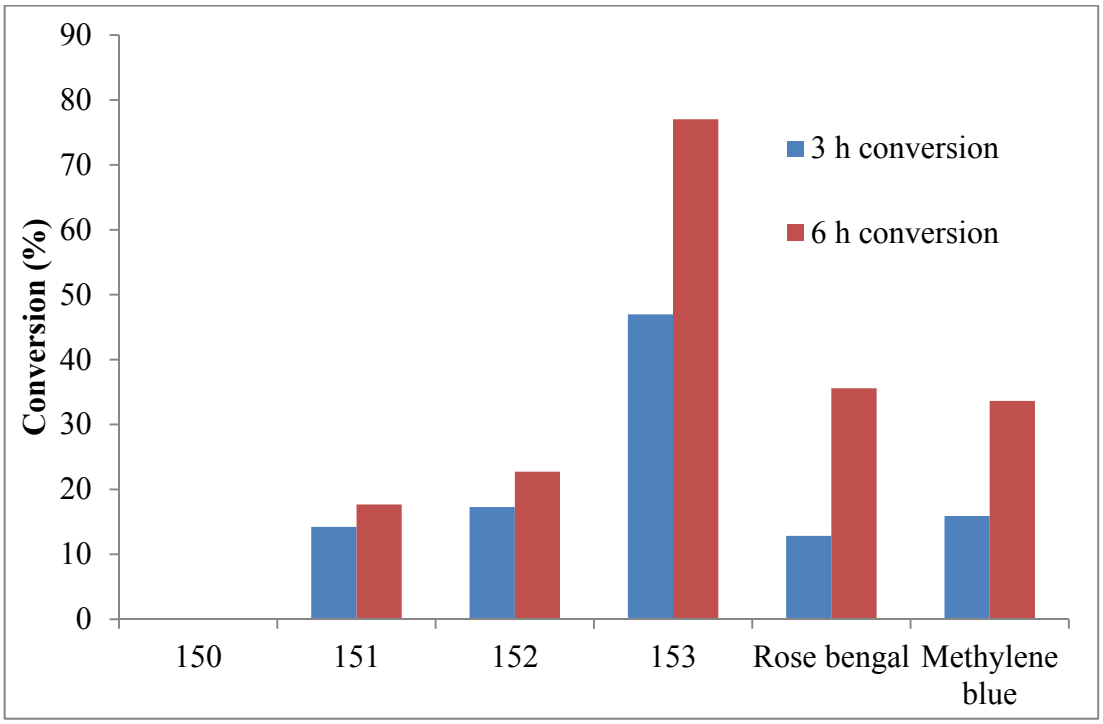


Figure 5.4.3: Evaluation of photosensitiser by conversion of β-citronellol.

Several conclusions can be drawn from these results:

1) It can be seen that when Pc **150** was used as a sensitiser, no conversion was observed. It is possible that this is due to aggregation, and hence quenching of the sensitiser, due to poor solubility. This is a common problem for most Pcs, especially in methanol.

2) With regards to the Pcs **151** and **152**, it can be seen that although the initial conversion was favourable compared to the conventional sensitisers

methylene blue and rose bengal, it appears that the rate of reaction dropped off considerably as the reaction progressed, with final conversions being between 18% and 13% less than that of rose bengal. One possible explanation for this is that the sensitisers are being decomposed as the reaction progressed. This is supported by the change of colour of the solution from green to yellow as the reaction progressed.

3) The most promising result was obtained when **153** was used as a sensitiser. Conversions after 3 hours for this sensitiser were in excess of that obtained after 6 hours using the conventional sensitisers methylene blue and rose bengal.

The difference in reactivity between **150** and **153** correlates with the difference in aggregation between the Pcs. The least aggregated Pc, **153**, gives the best results of all the phthalocyanines studied. Furthermore, **153** significantly outperforms the conventional sensitisers methylene blue and rose bengal which was not expected.

5.5 References

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6.0 Conclusions

6.1 Chapter 2 – The photo-Friedel-Crafts acylation of naphthoquinone in benzene

The photo-Friedel-Crafts acylation of napthoquinone was carried out with a wide range of aliphatic, unsaturated and aromatic aldehydes. It was observed that the reaction generally proceeded well for aliphatic aldehydes with a general tendency for slightly lower conversions for longer chain lengths. Similar trends were observed for reactions involving aromatic aldehydes. It was proposed that the lower yields of these compounds were due to loss during purification.

The reaction was also observed to have a poor tolerance for unsaturated aldehydes, with the exception of crotonaldehyde which proceeded well, with all other unsaturated compounds yielding none of the desired product.

6.2 Chapter 3.1 – The photo-Friedel-Crafts acylation of naphthoquinone in room temperature ionic liquids

A series of ionic liquids were synthesised. A model acylation was carried out in a range of RTILs with varying cations and anions. Conversion was monitored by ^{1}H NMR. Results varied with some conversions being higher than those in traditional solvents and some being significantly lower. The following trends were observed:

- Cations with longer length alkyl chains tended to give poorer conversions.
- Phosphorous containing anions tended to give very poor conversions.

Two of the best performing RTILs were then selected for further investigation with a wider library of aldehydes. A series of acylations with various aldehydes were

performed in the RTILs [EMIM][OTf] and [EMIM][NTf_2] with conversion being monitored by ^1H NMR. Yields were generally good; however a sharp drop in conversion was noticed for longer chain aldehydes (greater than C_9 or C_{10}) due to solubility issues.

While conversions were generally high, this did not necessarily translate to higher isolated yields. The isolation and purification procedure for reactions in RTILs was much less efficient than corresponding reactions in traditional solvents.

This coupled with the high expense and unknown toxicity of RTILs makes them an unsuitable "green" replacement for traditional photochemical solvents at this time.

6.3 Chapter 3.2 – The photo-Friedel-Crafts acylation of naphthoquinone in microemulsions

A series of acylation reactions using various aldehydes was carried out in an oil/water microemulsion. Conversions for these reactions were good, based on NMR and TLC evidence; however isolated yields tended to be very poor. This was likely due to the cumbersome isolation procedure, which involved multiple washings and extractions.

Despite the low toxicity of their components low yields and complex work-up procedures make microemulsions poor "green" alternatives to convention photochemical solvents.

6.4 Chapter 4 - Synthesis of novel biaryl trifluoro phthalonitriles

Based on previous work by Pratt *et al.* a photochemical method of generating biaryl phthalonitriles by reaction **118** with aromatic ethers was recreated and optimised. It

was found that the key parameter for obtaining high conversions was concentration; i.e. highest conversions were obtained at low concentrations. It was suggested that this was due to quenching by the product as the reaction proceeded.

One exception to this rule was the reaction between **118** and aniline **138**. It was found that the highest conversion for this reaction occurred at higher concentrations. Unfortunately, a final product for this reaction could not be isolated.

In addition to the reaction between **118** and aniline **138**, the series of reactions was expanded to include previously untried aromatic ethers, aliphatic ethers and aromatics equipped with other EDGs. These attempts produced mixed results. In the case of reactions between TFPN and aliphatic ethers, conversions were typically low, with the highest conversion being obtained from the reaction with THF **131** (33%). As for the reactions between TFPN **118** and aromatics equipped with other EDGs, thioanisole **140** gave an optimum conversion of 39%, while no reaction occurred between **118** and dimethylaniline **139**.

6.5 Chapter 5 - Condensation of novel biaryl phthalonitriles to phthalocyanines and their subsequent evaluation as singlet oxygen photocatalysts

Three of the biaryl phthalonitriles (**120a, 127 and 129**) were selected for condensation to Pcs. Attempts to develop a low temperature condensation method were unsuccessful, however it was found that a high temperature melt was capable of successfully condensing all the phthalonitriles to Pcs. The novel Pcs were found to have bathochromic shifts of 24 nm compared to the fluorinated Pc.

The presence of the periphery aryl rings also had a significant impact on the aggregation properties of the Pcs. It was found that the Pc equipped with *p*-methoxybenzene **151** was subject to a greater degree of stacking compared to the

hexadecafluorinated Pc, while the Pc equipped with 2,4,6-trimethoxybenzene **153** was subject to significantly less aggregation.

It was also noted that the new Pcs had interesting properties; they showed good solubility in polar solvents such as methanol. This is unusual for Pcs which tend to have poor solubility in polar media. It was particularly interesting to note that although it was not directly soluble in water, **153** could be dissolved in a minimum amount of methanol, and further diluted with relatively large quantities of water without precipitating.

The new Pcs were also evaluated as singlet oxygen sensitisers. This was done by using them as photocatalysts in a model reaction; the photooxygenation of β-citronellol. It was found that Pcs **151** and **152** outperformed traditional photooxygenation catalysts (rose bengal and methylene blue) initially, however the conversion rate dropped off significantly after 3 hours. It was thought that this was due to photobleaching, which could be inferred from a change in colour of the reaction solution.

It was particularly interesting to note that Pc **153** significantly outperformed traditional photooxygenation catalysts. The conversion for **153** after 3 hours exceeded the conversion for either traditional catalysts after 6 hours.

Pc **150** was unsuccessful as a photocatalyst; no conversion was observed.

7.0 Future work

7.1 Chapter 2 – The photo-Friedel-Crafts acylation of naphthoquinone in benzene

All of the acylated hydroquinones synthesised have the potential to be oxidised back to their respective quinones. As previously mentioned, these quinones have some resemblance to natural products. With this in mind, it may be worth subjecting them to biological screening.

Also of interest is the product of the photo-acylation of naphthoquinone with terphthaldehyde. As previously mentioned, this compound has the potential for further reaction with naphthoquinone. With oxidation and subsequent further reaction there is the (theoretical) potential to produce a very interesting product.

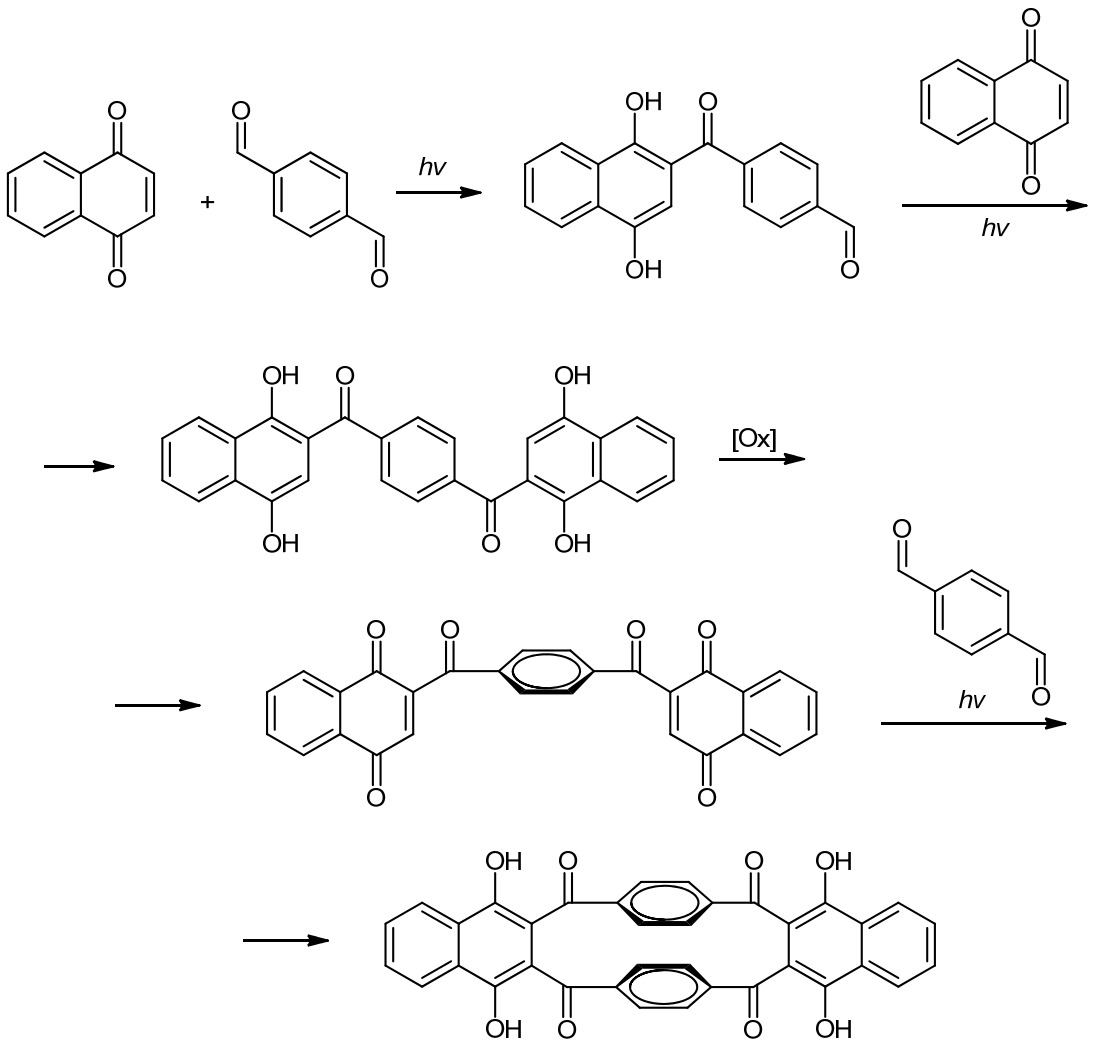


Figure 7.1.1: Potential product from the reaction between naphthoquinone and terphthaldehyde.

7.2 Chapter 3 – The photo-Friedel-Crafts acylation of naphthoquinone in room temperature ionic liquids

As RTILs belong to a relatively new branch of chemistry, there are new developments in the subject all the time. One fruitful avenue of research in this subject is computer modelling. It is becoming more and more apparent that RTILs are often more complex than initially though; for example molecular modelling has predicted that the components of RTILs may be ordering themselves to produce hydrophobic and hydrophilic regions. Research in this area may help to explain

"ionic liquid effect". With further insight it may be possible to design an ionic liquid which is optimised to the photo-Friedel-Crafts acylation of naphthoquinone.

7.4 Chapter 4 - Synthesis of novel biaryl trifluoro phthalonitriles

Much work remains to be done with the synthesis of novel biaryl trifluoro phthalonitriles. While a wide library of potential products was generated, only a few were selected for further study. Further research with some of the less successful reactions may yield interesting results.

Of particular interest is the product of the reaction between TFPN and aniline. It is unfortunate that this compound could not be isolated as it has significant potential. The polar nature of the amino functionality suggests it could be converted to a water soluble salt. This could be of great use in biological systems, especially if it were somehow possible to condense the phthalonitrile to a Pc with the amino groups intact.

As well as this, the thioanisole substituted derivative may be of interest. It has been observed that the increased electron donating ability of sulphur compared to oxygen can result in a larger red shift in Pcs.[115] With this in mind, it would be of considerable interest to isolate and examine a thioanisole substituted phthalonitrile, as well as any Pc generated from it.

8.0 Experimental

8.1 Experimental Note

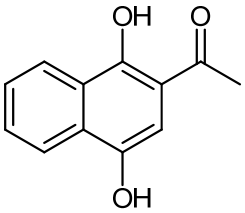
All chemicals were purchased from Sigma-Aldrich and used as received. Commercial grade reagents were used without further purification. When necessary, all solvents were purified and dried prior to use. Riedel-Haën silica gel was used for thin layer and column chromatography. Melting points were determined using a Griffin melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR with ATR. UV-Vis spectra were recorded on a Hewlett Packard 8452 A diode array UV-Vis spectrophotometer. ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded in deuterated solvents on a Bruker Avance 400 NMR. The 1H, 19F and 13C NMR chemical shifts are reported in ppm (parts per million). Tetramethylsilane (TMS) or the residual solvent peaks have been used as an internal reference. All coupling constants (J) are in Hertz. The abbreviations for the peak multiplicities are as follows: s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), quin (quintet), sex (sextet), sept (septet) and m (multiplet).

8.2 Chapter 2: The Photo-Friedel-Crafts acylation of naphthoquinone in benzene

General procedure for the photo-Friedel-Crafts addition of aldehydes to naphthoquinone (GP-1)

Naphthoquinone (1.6 mmol) and aldehyde (8 mmol) were dissolved in 50 ml of benzene which had been degassed by bubbling with nitrogen for 15 mins. This was

placed in a Pyrex vessel equipped with a cold finger. The solution was irradiated overnight. In the case of some short chain aldehydes precipitation was observed. In these cases, the solution was filtered and washed with cold benzene. Otherwise the solution (or filtrate) was evaporated down and stored in a fridge overnight to aid precipitation. Any solid obtained was washed with cold benzene and filtered. If precipitation was not observed the product was isolated by column chromatography.

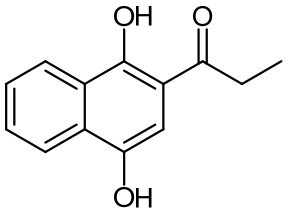


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)ethanone 80a. Acetaldehyde (447 µl, 352 mg, 8 mmol) was added to a solution of naphthoquinone (253 mg, 1.6 mmol) in 50 ml degassed benzene in a 50 ml Schlenk flask. The flask was equipped with a cold finger and irradiated using a Rayonet Photochemical reactor (RPR-200; Southern New England Ultraviolet Company) equipped with RPR-3000 Å lamps (λmax = 300 ±25 nm). The benzene was removed *in vacuo*. The remaining product was washed with a small quantity of cold benzene to yield a yellow solid (243 mg, 75%).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.6 (1H; s; OH); 8.44 (1H; d, J = 8.2 Hz; Naph-H); 8.1 (1H; d, J = 8.3Hz; Naph-H); 7.67 (1H; t, J = 7.7 Hz; Naph-H); 7.57 (1H; t, J = 7.6 Hz; Naph-H); 6.98 (1H; s; Naph-H); 2.62 (3H; s; CO-CH_3).

Melting Point: 198-202 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**): (log ε)** 390 (5.18)



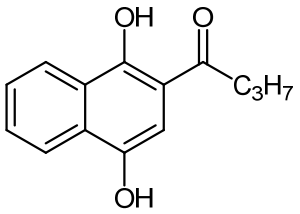
Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)propan-1-one 80b.

The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), propanal (573 µl, 465 mg, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow/orange solid (253 mg, 75%).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.7 (1H; s; OH); 8.46 (1H; d, J = 9 Hz; Naph-H); 8.1 (1H; d, J = 8.3Hz; Naph-H); 7.68 (1H; t, J = 7.7 Hz; Naph-H); 7.58 (1H; t, J = 7.6 Hz; Naph-H); 7.03 (1H; s; Naph-H); 3.03 (2H; q, J = 7.4 Hz; CO-CH_2); 1.28 (3H; t, J = 7.4; CH_3).

Melting Point: 169-171 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**): (log ε)** 390 (5.28)



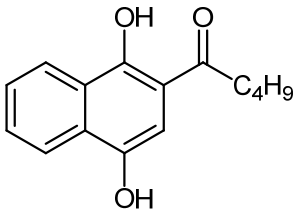
Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)butan-1-one 80c. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), butyraldehyde (721 µl, 577 mg, 8 mmol). The product was isolated by

washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (215 mg, 56%).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.78 (1H; s; OH); 8.46 (1H; d, J = 8.2 Hz; Naph-H); 8.1 (1H; d, J = 8.3 Hz; Naph-H); 7.68 (1H; t, J = 7.6 Hz; Naph-H); 7.58 (1H; t, J = 7.6 Hz; Naph-H); 7.03 (1H; s; Naph-H); 2.96 (2H; t, J = 7.3 Hz; $CO-CH_2$); 1.82 (2H; sex, J = 7.4; $COCH_2-CH_2$); 1.05 (3H; t, J = 7.4; $CO(CH_2)_2-CH_2$).

Melting Point: 135-140 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**): (log ε)** 390 (5.1)

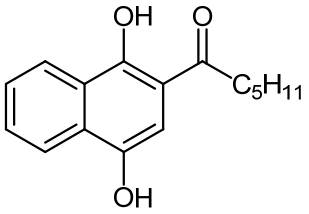


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)pentan-1-one 80d. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), valeraldehyde (851 µl, 689 mg, 8 mmol). The product was isolated by washing with a small amount (10 - 15 ml) of ice cold benzene to give the title product as a yellow solid (313 mg, 81%).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.78 (1H; s; OH); 8.46 (1H; d, J = 8.3 Hz; Naph-H); 8.1 (1H; d, J = 8.3 Hz; Naph-H); 7.67 (1H; t, J = 7.6 Hz; Naph-H); 7.57 (1H; t, J = 7.7 Hz; Naph-H); 7.02 (1H; s; Naph-H); 2.97 (2H; t, J = 7.4 Hz; $CO-CH_2$); 1.76 (2H; quin, J = 7.7; $COCH_2-CH_2$); 1.45 (2H; sex, J = 7.6 Hz; $CO(CH_2)_2-CH_2$); 0.98 (3H; t, J = 7.3 Hz; CH_3).

Melting Point: 134-141 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**): (log ε)** 390 (5.26).

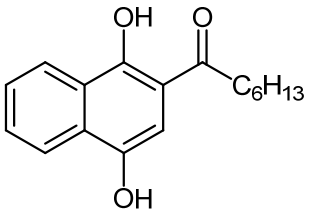


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)hexan-1-one 80e. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), hexanal (984 µl, 801 mg, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (318 mg, 75%).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.78 (1H; s; OH); 8.46 (1H; d, J = 8.3 Hz; Naph-H); 8.1 (1H; d, J = 8.2 Hz; Naph-H); 7.68 (1H; t, J = 7.6 Hz; Naph-H); 7.58 (1H; t, J = 7.7 Hz; Naph-H); 7.02 (1H; s; Naph-H); 2.97 (2H; t, J = 7.4 Hz; CO-CH_2); 1.79 (2H; quin, J = 7.45 Hz; $COCH_2$-CH_2); 1.1-1.7 (4H; m, aliphatic); 0.93 (3H; t, J = 6.9 Hz; CH_3).

Melting Point: 157-159 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**): (log ε)** 390 (5.04)



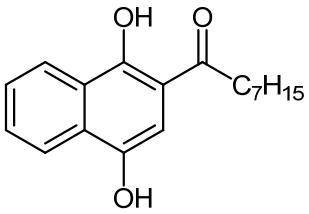
Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)heptan-1-one 80f. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), heptanal (1.128 ml, 0.914 g, 8 mmol). The product was isolated by washing

with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (326 mg, 75%).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.78 (1H; s; OH); 8.46 (1H; d, J = 8.3 Hz; Naph-H); 8.1 (1H; d, J = 8.2 Hz; Naph-H); 7.68 (1H; t, J = 7.6 Hz; Naph-H); 7.58 (1H; t, J = 7.7 Hz; Naph-H); 7.02 (1H; s; Naph-H); 2.96 (2H; t, J = 7.5 Hz; $CO-CH_2$); 1.78 (2H; quin, J = 7.4 Hz; $COCH_2-CH_2$); 1.24-1.45 (6H; m, aliphatic); 0.89 (3H; t, J = 7.0Hz; CH_3).

Melting Point: 135-136 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**): (log ε)** 390 (4.66)

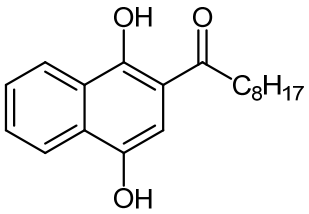


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)octan-1-one 80g. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), octanal (1.265 ml, 1.026 g, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (312 mg, 69%).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.78 (1H; s; OH); 8.46 (1H; d, J = 8.3 Hz; Naph-H); 8.1 (1H; d, J = 8.2 Hz; Naph-H); 7.68 (1H; t, J = 7.6 Hz; Naph-H); 7.58 (1H; t, J = 7.7 Hz; Naph-H); 7.02 (1H; s; Naph-H); 2.96 (2H; t, J = 7.5 Hz; $CO-CH_2$); 1.78 (2H; quin, J = 7.4 Hz; $COCH_2-CH_2$); 1.24-1.45 (8H; m, aliphatic); 0.89 (3H; t, J = 6.96 Hz; CH_3).

Melting Point: 130-134 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**): (log ε)** 390 (5.16)

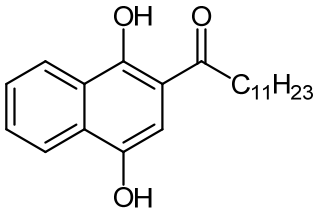


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)nonan-1-one 80h. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), nonanal (1.376 ml, 1.138 g, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (332 mg, 69%).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.78 (1H; s; OH); 8.46 (1H; d, J = 8.3 Hz; Naph-H); 8.1 (1H; d, J = 8.2 Hz; Naph-H); 7.68 (1H; t, J = 7.6 Hz; Naph-H); 7.58 (1H; t, J = 7.6 Hz; Naph-H); 7.02 (1H; s; Naph-H); 2.97 (2H; t, J = 7.5 Hz; CO-CH_2); 1.78 (2H; quin, J = 7.4 Hz; $COCH_2$-CH_2); 1.19-1.45 (10H; m, aliphatic); 0.89 (3H; t, J = 7.0 Hz; CH_3).

Melting Point: 124-129 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**): (log ε)** 390 (4.89)



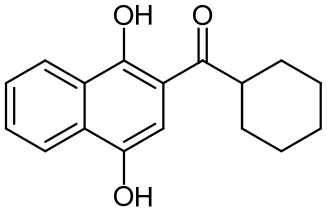
Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)dodecan-1-one 80j. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6

mmol), dodecanal (1.641 ml, 1.362 g, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (378 mg, 69%).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.78 (1H; s; OH); 8.46 (1H; d, J = 8.4 Hz; Naph-H); 8.1 (1H; d, J = 8.3 Hz; Naph-H); 7.68 (1H; t, J = 7.6 Hz; Naph-H); 7.58 (1H; t, J = 7.6 Hz; Naph-H); 7.03 (1H; s; Naph-H); 2.97 (2H; t, J = 7.5 Hz; CO-CH_2); 1.78 (2H; quin, J = 7.4 Hz; $COCH_2$-CH_2); 1.2-1.46 (14H; m, aliphatic); 0.88 (3H; t, J = 6.9 Hz; CH_3).

Melting Point: 130-133 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**): (log ε)** 390 (5.03)

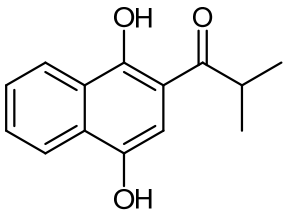


Synthesis of cyclohexyl(1,4-dihydroxynaphthalen-2-yl)methanone 80k. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), cyclohexanecarbaldehyde (969 µl, 897 mg, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (147 mg, 34 %).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 14 (1H; s; OH); 8.46 (1H; d, J = 8.4 Hz; Naph-H); 8.1 (1H; d, J = 8.3 Hz; Naph-H); 7.67 (1H; t, J = 7.6 Hz; Naph-H); 7.57 (1H; t, J = 7.6 Hz; Naph-H); 7.04 (1H; s; Naph-H); 3.21 (1H; t,t; J = 11.5 Hz, 3 Hz; CO-CH); 1.84-1.98 (4H; m; COCH-$(CH_2)_2$); 1.5-1.63 (2H; m; $COCH(CH_2$-$CH_2)_2$-CH_2); 1.22-1.46 (4H; m; $COCH(CH_2)_2$-$(CH_2)_2$).

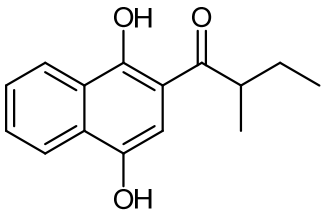
Melting Point: 136-138 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**) (log ε)** 390 (5.2)



Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)-2-methylpropan-1-one 80l. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), isobutyraldehyde (730 µl, 577 mg, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (129 mg, 35 %).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.83 (1H; s; OH); 8.35 (1H; d, J = 8.3 Hz; Naph-H); 8.02 (1H; d, J = 8.3 Hz; Naph-H); 7.56 (1H; t, J = 7.6 Hz; Naph-H); 7.46 (1H; t, J = 7.6 Hz; Naph-H); 6.9 (1H; s; Naph-H); 3.36 (1H; sep; J = 6.8 Hz; CO-CH); 1.14 (6H; d; J = 6.8 Hz CH-$(CH_3)_2$)

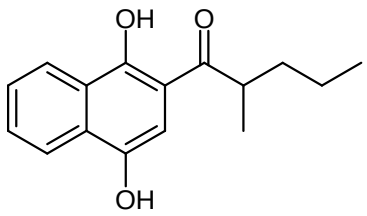


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)-2-methylbutan-1-one 80n. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), 2-methylbutanal (871 µl, 688 mg, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (324 mg, 83 %).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.95 (1H; s; OH); 8.36 (1H; d, J = 8.3 Hz; Naph-H); 8.03 (1H; d, J = 8.3 Hz; Naph-H); 7.56 (1H; t, J = 7.5 Hz; Naph-H); 7.46 (1H; t, J = 7.6 Hz; Naph-H); 6.94 (1H; s; Naph-H); 3.19 (1H; sex; J = 6.8 Hz; CO-CH); 1.8-1.7, 1.45-1.35(1H, 1H; m,m; COCH-CH_2); 1.11 (3H; d; COCH-CH_3), 0.81 (3H; t; J = 7.4 Hz; $COCHCH_2$-CH_3).

Melting Point: 155-157 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**) (log ε)** 391 (4.6)

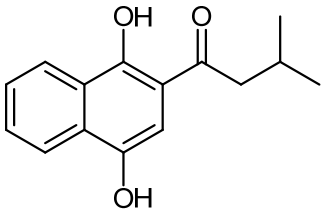


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)-2-methylpentan-1-one 80m. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), 2-methylpentanal (992 µl, 801 mg, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (182 mg, 44 %).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 14.06 (1H; s; OH); 8.47 (1H; d, J = 8.2 Hz; Naph-H); 8.1 (1H; d, J = 8.3 Hz; Naph-H); 7.68 (1H; t, J = 7.6 Hz; Naph-H); 7.58 (1H; t, J = 7.7 Hz; Naph-H); 7.05 (1H; s; Naph-H); 3.44 (1H; sex; J = 6.8 Hz; CO-CH); 1.9-1.78, (1H; m; COCH-CH_2); 1.41-1.31 (2H; m; $COCHCH_2$-CH_2), 1.25 (3H; d; J = 6.8 Hz; COCH-CH_3), 0.92 (3H; t; J = 7.3 Hz; $COCHCH_2CH_2$-CH_3).

Melting Point: 156-160 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**) (log ε)** 391 (4.58)

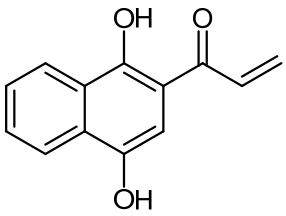


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)-3-methylbutan-1-one 80o. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), 3-methylbutanal (858 µl, 689 mg, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (185 mg, 48 %).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.89 (1H; s; OH); 8.47 (1H; d, J = 8.3 Hz; Naph-H); 8.1 (1H; d, J = 8.3 Hz; Naph-H); 7.69 (1H; t, J = 7.5 Hz; Naph-H); 7.58 (1H; t, J = 7.6 Hz; Naph-H); 7.02 (1H; s; Naph-H); 2.84 (2H; d; J = 6.9 Hz; $CO-CH_2$); 2.34 (1H; sep; J = 6.9 Hz; COCH-CH); 1.04 (6H; d; J = 6.9 Hz; $COCH_2CH-(CH_3)_2$).

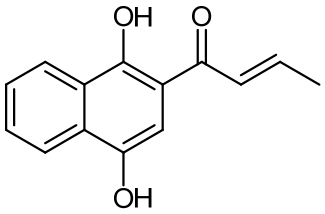
Melting Point: 156-158 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**) (log ε)** 391 (4.61)



Attempted synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)prop-2-en-1-one 80q. The synthesis attempted following that of **GP-1** using the following reagents:

naphthoquinone (253 mg, 1.6 mmol), acrolein (535µl, 449 mg, 8 mmol). No product was observed.

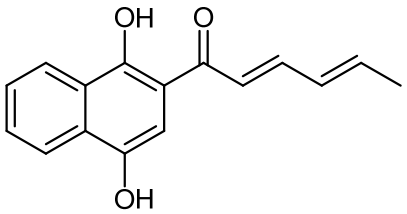


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)but-2-en-1-one 80r. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), crotonaldehyde (663µl, 561 mg, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a bright red solid (183 mg, 50 %).

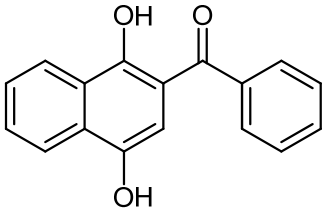
^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 14.09 (1H; s; OH); 8.27 (1H; d, J = 8.3 Hz; Naph-H); 8.05 (1H; d, J = 8.2 Hz; Naph-H); 7.5 (1H; t, J = 7.5 Hz; Naph-H); 7.39 (1H; t, J = 7.6 Hz; Naph-H); 7.08 (1H; dq, J = 8.1 Hz; CO-CH=CH); 7.0 (1H; s; Naph-H); 6.93 (1H; d; J = 15.1 Hz; CO-CH); 1.92 (3H; d; J = 6.8 Hz; COCH=CH-CH_3).

Melting Point: 160-162 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**) (log ε)** 415 (5.2)



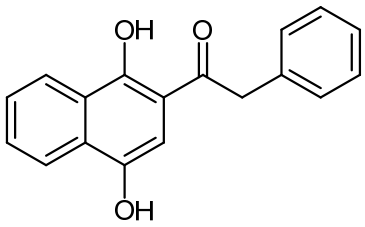
Attempted synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)hexa-2,4-dien-1-one 80s. The synthesis was attempted following that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), hexa-2,4-dienal (897µl, 769 mg, 8 mmol). No product was observed.



Synthesis of (1,4-dihydroxynaphthalen-2-yl)(phenyl)methanone 80t. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), benzaldehyde (815µl, 849 mg, 8 mmol). The product was isolated by column chromatography (mobile phase Hexane:Ethyl acetate 4:1) to give the title product as a yellow-orange solid (300 mg, 71 %).

Melting Point: 120-128 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**) (log ε)** 336 (5.19)

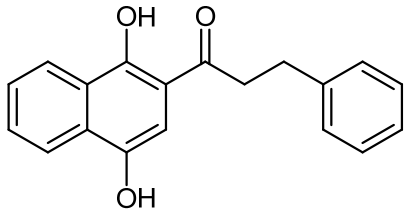


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)-2-phenylethanone 80u. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), 2-phenylacetaldehyde (957µl, 961 mg, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (263 mg, 59 %).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.64 (1H; s; OH); 8.46 (1H; d, J = 8.3 Hz; Naph-H); 8.1 (1H; d, J = 8.3 Hz; Naph-H); 7.69 (1H; t, J = 7.5 Hz; Naph-H); 7.58 (1H; t, J = 7.7 Hz; Naph-H); 7.3-7.39 (5H; m; Ar-H); 7.07 (1H; s; Naph-H); 4.3 (2H; s; CO-CH_2).

Melting Point: 169-172 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**) (log ε)** 394 (5.0)

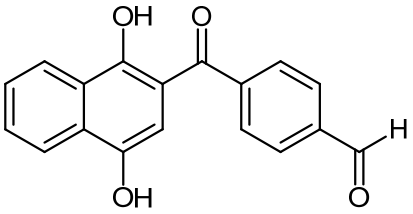


Synthesis of 1-(1,4-dihydroxynaphthalen-2-yl)-3-phenylpropan-1-one 80v. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), hydrocinnamaldehyde (1.073 ml, 1.053 g, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a yellow solid (202 mg, 43 %).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.67 (1H; s; OH); 8.46 (1H; d, J = 8.1 Hz; Naph-H); 8.1 (1H; d, J = 8.3 Hz; Naph-H); 7.68 (1H; t, J = 7.6 Hz; Naph-H); 7.58 (1H; t, J = 7.7 Hz; Naph-H); 7.35-7.2 (5H; m; Ar-H); 6.97 (1H; s; Naph-H); 3.32 (2H; t, J = 7.1 Hz; CO-CH_2); 3.11 (2H; t, J = 7.1 Hz; $COCH_2$-CH_2).

Melting Point: 140-143 °C

UV/Vis λ_{max} (nm) (in DCM 1 x 10^{-4}M**) (log ε)** 390 (5.22)



Synthesis of 4-(1,4-dihydroxy-2-naphthoyl)benzaldehyde 80w. The synthesis followed that of **GP-1** using the following reagents: naphthoquinone (253 mg, 1.6 mmol), hydrocinnamaldehyde (1.073 ml, 1.053 g, 8 mmol). The product was isolated by washing with a small amount (10-15 ml) of ice cold benzene to give the title product as a red solid (119 mg, 25 %).

^{1}H-NMR; (400 MHz, $CDCl_3$) δ (ppm): 13.15 (1H; s; OH); 9.93 (1H; s; CHO); 8.25 (1H; d, J = 8.3 Hz; Naph-H); 7.98 (1H; d, J = 8.2 Hz; Naph-H); 7.84 (2H; d, J = 8.1 Hz; Ar-H); 7.67 (2H; d, J = 8.1 Hz; Ar-H); 7.47 (1H; t, J = 7.7 Hz; Naph-H); 7.37 (1H; t, J = 7.5 Hz; Naph-H); 6.63 (1H; s; Naph-H).

Melting Point: >250 °C

8.3 Chapter 3: The photo-Friedel-crafts acylation of naphthoquinone in alternative "green" media

8.3.1 Synthesis of ionic liquids – synthesis of halide salts

General procedure for the synthesis of halide salts (GP-2)

The appropriate bromoalkane was added to either *N*-methylimidazole, pyridine, or *N*-methylpyrrolidine and allowed to stir overnight at room temperature. The solid formed was crushed and washed with cold acetone to yield the product.

Synthesis of Ethylmethylimidazoliom Bromide ($[EMIM]^+$ $[Br]^-$) 85a. Bromoethane (163 g, 112 ml, 1.5 mol) was added to 1-methylimidazole (83 g, 81 ml, 1mol) and allowed to stir overnight at 65 ^oC. A white solid was formed. This was crushed and washed with cold acetone to yield the title product (185 g, 97%).

Synthesis of Butylmethylimidazolium Bromide ($[C_4MIM]^+$ $[Br]^-$) 86a. The synthesis followed that of **GP-2** using the following reagents: 1-methylimidazole (8.21 g, 8 ml, 0.1 mol), 1-bromobutane (20.6 g, 16.1 ml, 0.15 mol). The product was isolated by washing with a small amount of ice cold acetone to give the title product as a white solid (20 g, 91%).

Synthesis of Hexylmethylimidazolium Bromide ($[C_6MIM]^+$ $[Br]^-$) 87a. The synthesis followed that of **GP-2** using the following reagents: 1-methylimidazole (8.21 g, 8 ml, 0.1 mol), 1-bromohexane (25 g, 21.3 ml, 0.15 mol). The product was isolated by washing with a small amount of cold acetone to give the title product as a white solid (23 g, 92%).

Synthesis of Octylmethylimidazolium Bromide ($[C_8MIM]^+$ $[Br]^-$) 88a. The synthesis followed that of **GP-2** using the following reagents: 1-methylimidazole (8.21 g, 8 ml, 0.1 mol), 1-bromooctane (29 g, 26 ml, 0.15 mol). The product was isolated by washing with a small amount of cold acetone to give the title product as a white solid (25 g, 91%).

Synthesis of Decylmethylimidazolium Bromide ($[C_{10}MIM]^+$ $[Br]^-$) 89a. The synthesis followed that of **GP-2** using the following reagents: 1-methylimidazole (8.21 g, 8 ml, 0.1 mol), 1-bromodecane (33 g, 31 ml, 0.15 mol). The product was isolated by washing with a small amount of cold acetone to give the title product as a white solid (28 g, 92%).

Synthesis of 1-Butylpyridinium Bromide 90. The synthesis followed that of **GP-2** using the following reagents: pyridine (57 g, 59 ml, 0.725 mol), 1-bromobutane (119 g, 93 ml, 0.87 mol). Washing with a small amount of cold acetone afforded the title product as a white solid (178 g, 94%).

8.3.2 Synthesis of ionic liquids by ion exchange

General procedure for the synthesis of ionic liquids by ion exchange (GP-3)

The sodium salt of the desired anion was added to a stirring solution of the appropriate cation-bromide salt in acetonitrile and allowed to stir overnight at room temperature. The solution was then filtered to remove the white precipitate of sodium bromide, followed by removal of the solvent *in vacuo* to give the desired product.

Synthesis of ionic liquids containing a bistriflimide $[NTf_2]^-$ anion. (GP-4)

A solution of sodium bistriflimide in 50 ml water was added to a solution of the appropriate cation-bromide salt in 50 ml water and allowed to stir overnight at room temperature. This resulted in the formation of two layers. The aqueous layer is removed by decanting, and the organic layer is washed repeatedly with water to remove any remaining bromide salt. The ionic liquid was then dried under high vacuum.

Synthesis of Ethylmethylimidazoliom Tetrafluoroborate ($[EMIM]^+$ $[BF_4]^-$) 85b. Sodium tetrafluoroborate (6 g, 55 mmol) was added to a stirring solution of $[EMIM]^+[Br]^-$ (10 g, 52 mmol) in acetonitrile (50 ml) and allowed to stir overnight at room temperature. A white precipitate of sodium bromide was observed. The solution was filtered to remove the precipitate and the solvent was removed *in vacuo* to give the title product as a clear liquid (8.5g, 82%).

Ethylmethylimidazoliom Hexafluorophosphate ($[EMIM]^+$ $[PF_6]^-$) 85c. The synthesis followed that of **GP-3** using the following reagents: $[EMIM]^+[Br]^-$ (10 g, 52 mmol), sodium hexafluorophosphate (9.2 g, 55 mmol). The product was isolated as a very pale yellow clear liquid (11 g, 84%).

Synthesis of Ethylmethylimidazoliom Bistriflimide ($[EMIM]^+$ $[NTf_2]^-$) 85e. A solution of sodium bistriflimide (15.1 g, 52.5 mmol) in water (50 ml) was added to a stirring solution of $[EMIM]^+[Br]^-$ (9.55 g, 50 mmol) in water (50 ml) and allowed to stir overnight at room temperature. Two layers were formed. The aqueous layer was decanted and the organic layer was washed repeatedly with water to remove any lithium bromide salt. The title product was isolated as a clear liquid (15 g, 77%).

Synthesis of Butylmethylimidazolium Bistriflimide ($[C_4MIM]^+$ $[NTf_2]^-$) 86e. The synthesis followed that of **GP-4** using the following reagents: $[C_4MIM]^+[Br]^-$ (11 g,

50 mmol), sodium bistriflimide (15.1 g, 52.5 mmol). The product was isolated as a clear liquid (15.5 g, 70%).

Synthesis of Hexylmethylimidazolium Bistriflimide ($[C_6MIM]^+$ $[NTf_2]^-$) 87e. The synthesis followed that of **GP-4** using the following reagents: $[C_6MIM]^+[Br]^-$ (12.4 g, 50 mmol), sodium bistriflimide (15.1 g, 52.5 mmol). The product was isolated as a clear liquid (17.9 g, 76%).

Synthesis of Octylmethylimidazolium Bistriflimide ($[C_8MIM]^+$ $[NTf_2]^-$) 88e. The synthesis followed that of **GP-4** using the following reagents: $[C_8MIM]^+[Br]^-$ (13.8 g, 50 mmol), sodium bistriflimide (15.1 g, 52.5 mmol). The product was isolated as a clear liquid (18 g, 72%).

Synthesis of Decylmethylimidazolium Bistriflimide ($[C_{10}MIM]^+$ $[NTf_2]^-$) 89e. The synthesis followed that of **GP-4** using the following reagents: $[C_{10}MIM]^+[Br]^-$ (15.2 g, 50 mmol), sodium bistriflimide (15.1 g, 52.5 mmol). The product was isolated as a clear liquid (18.3 g, 69%).

Synthesis of 1-Butylpyridinium Tetrafluoroborate 91a. Sodium tetrafluoroborate (10 g, 91 mmol) was added to a stirring solution of 1-butylpyridinium bromide (19.5 g, 90 mmol) in acetonitrile (50 ml) and allowed to stir overnight at room temperature. A white precipitate of sodium bromide was observed. The solution was filtered to remove the precipitate and the solvent was removed *in vacuo* to give the title product as a clear liquid (18.7g, 93%).

Synthesis of 1-Butylpyridinium Bistriflimide 91b. The synthesis followed that of **GP-4** using the following reagents: 1-butylpyridinium bromide (6.5 g, 30 mmol),

sodium bistriflimide (8.9 g, 31 mmol). The product was isolated as a clear liquid (10 g, 80%).

8.3.3 Photochemical reactions in ionic liquids

General procedure for the photo-Friedel-Crafts acylation of naphthoquinone in ionic liquids (GP-5)

Sublimed naphthoquinone was dissolved in 5 ml of the appropriate ionic liquid by mild heating and vigorous stirring. The appropriate aldehyde was added and the solution was irradiated for 16 hours using a Rayonet photochemical reactor equipped with eight 300 nm lamps. The solution was then extracted using five 10 ml portions of diethyl ether. The organic layers were combined and dried over $MgSO_4$ and evaporated.

The crude product was analysed by ^1H NMR and the conversion was determined by integration of characteristic peaks. If desired, the final product was then isolated by column chromatography.

8.3.3.1 Screening of Ionic liquids as potential photochemical solvents

Synthesis of 80c in $[EMIM]^+$ $[OTf]^-$ 85d. Sublimed naphthoquinone (63mg 0.4mmol) was dissolved in 5 ml of the named ionic liquid by mild heating and vigorous stirring. Butyraldehyde (144 mg, 180 µl, 2 mmol) was added and the solution was irradiated for 16 hours using a Rayonet photochemical reactor equipped with eight 300 nm lamps. The solution was then extracted using five 10 ml portions of diethyl ether. The organic layers were combined and dried over $MgSO_4$ and evaporated.

The crude product was analysed by ^{1}H NMR and the conversion to the named product **85d** was determined by integration of characteristic peaks (91%). The crude product was purified by column chromatography (Mobile phase Ethyl acetate:Hexane 1:4) to give the title product as a brown-yellow solid (9.2 mg, 10%).

Synthesis of 80c in $[EMIM]^{+}$ $[NTf_2]^{-}$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), butyraldehyde (144 mg, 180 µl, 2 mmol).

The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80c** was determined by integration of characteristic peaks (81%). The crude product was purified by column chromatography (Mobile phase Ethyl acetate:Hexane 1:4) to give the title product as a brown-yellow solid (37 mg, 40%).

Synthesis of 80c in $[EMIM]^{+}$ $[BF_4]^{-}$ 85b. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68mg, 0.4 mmol), butyraldehyde (144 mg, 180 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80c** was determined by integration of characteristic peaks (42%). The final product was not isolated.

Synthesis of 80c in $[C_4MIM]^{+}$ $[NTf_2]^{-}$ 86e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68mg, 0.4 mmol), butyraldehyde (144 mg, 180 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80c** was determined by integration of characteristic peaks (25%). The final product was not isolated.

Synthesis of 80c in $[C_6MIM]^{+}$ $[PF_6]^{-}$ 87c. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68mg, 0.4 mmol), butyraldehyde

(144 mg, 180 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80c** was determined by integration of characteristic peaks (13%). The final product was not isolated.

Synthesis of 80c in $[C_8MIM]^+$ $[PF_6]^-$ 88c. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68mg, 0.4 mmol), butyraldehyde (144 mg, 180 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80c** was determined by integration of characteristic peaks (10%). The final product was not isolated.

Synthesis of 80c in 1-Butylpyridinium Bistriflimide 91b. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68mg, 0.4 mmol), butyraldehyde (144 mg, 180 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80c** was determined by integration of characteristic peaks (75%). The final product was not isolated.

Synthesis of 80c in 1-Butyl-1-methylpyrrolidinium Bistriflimide 93. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68mg, 0.4 mmol), butyraldehyde (144 mg, 180 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80c** was determined by integration of characteristic peaks (83%). The final product was not isolated.

8.3.3.2 The photo-Friedel-Crafts acylation of naphthoquinone in ionic liquids

Synthesis of 80b in $[EMIM]^+$ $[OTf]^-$ 85d. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), propanal (116 mg, 143 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to

the named product **80b** was determined by integration of characteristic peaks (45%). The final product was not isolated.

Synthesis of 80f in [EMIM]$^+$ [OTf]$^-$ 85d. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), heptanal (228 mg, 282 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80f** was determined by integration of characteristic peaks (70%). The final product was not isolated.

Synthesis of 80g in [EMIM]$^+$ [OTf]$^-$ 85d. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), octanal (256 mg, 310 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80g** was determined by integration of characteristic peaks (50%). The final product was not isolated.

Synthesis of 80h in [EMIM]$^+$ [OTf]$^-$ 85d. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), nonanal (285 mg, 344 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80h** was determined by integration of characteristic peaks (56%). The final product was not isolated.

Synthesis of 80i in [EMIM]$^+$ [OTf]$^-$ 85d. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), undecanal (341 mg, 410 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80i** was determined by integration of characteristic peaks (32%). The final product was not isolated.

Synthesis of 80t in [EMIM]$^+$ [OTf]$^-$ 85d. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), benzaldehyde (212 mg, 204 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80t** was determined by integration of characteristic peaks (50%). The final product was not isolated.

Synthesis of 80r in [EMIM]$^+$ [OTf]$^-$ 85d. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), crotonaldehyde (140 mg, 166 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80r** was determined by integration of characteristic peaks (52%). The final product was not isolated.

Synthesis of 80a in [EMIM]$^+$ [NTf$_2$]$^-$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), acetaldehyde (88 mg, 112 µl, 2mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80a** was determined by integration of characteristic peaks (70%). The final product was not isolated.

Synthesis of 80b in [EMIM]$^+$ [NTf$_2$]$^-$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), propanal (116 mg, 143 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80b** was determined by integration of characteristic peaks (74%). The final product was not isolated.

Synthesis of 80d in [EMIM]$^+$ [NTf$_2$]$^-$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), valeraldehyde (172 mg, 212 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the

conversion to the named product **80d** was determined by integration of characteristic peaks (48%). The final product was not isolated.

Synthesis of 80e in $[EMIM]^+$ $[NTf_2]^-$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), hexanal (200 mg, 247 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80e** was determined by integration of characteristic peaks (66%). The final product was not isolated.

Synthesis of 80f in $[EMIM]^+$ $[NTf_2]^-$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), heptanal (228 mg, 282 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80f** was determined by integration of characteristic peaks (47%). The final product was not isolated.

Synthesis of 80g in $[EMIM]^+$ $[NTf_2]^-$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), octanal (256 mg, 310 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80g** was determined by integration of characteristic peaks (70%). The final product was not isolated.

Synthesis of 80h in $[EMIM]^+$ $[NTf_2]^-$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), nonanal (285 mg, 344 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80h** was determined by integration of characteristic peaks (23%). The final product was not isolated.

Synthesis of 80i in $[EMIM]^+$ $[NTf_2]^-$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), undecanal (341 mg, 410 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80i** was determined by integration of characteristic peaks (51%). The final product was not isolated.

Synthesis of 80j in $[EMIM]^+$ $[NTf_2]^-$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), dodecanal (369 mg, 410 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80j** was determined by integration of characteristic peaks (41%). The final product was not isolated.

Synthesis of 80t in $[EMIM]^+$ $[NTf_2]^-$ 85e. The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), benzaldehyde (212 mg, 204 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80t** was determined by integration of characteristic peaks (52%). The final product was not isolated.

Synthesis of 80r in $[EMIM]^+$ $[NTf_2]^-$ 85e The synthesis followed that of **GP-5** using the following reagents: naphthoquinone (68 mg, 0.4 mmol), crotonaldehyde (140 mg, 166 µl, 2 mmol). The crude product was analysed by ^{1}H-NMR and the conversion to the named product **80r** was determined by integration of characteristic peaks (43%). The final product was not isolated.

8.3.4 Photochemical reactions in microemulsions

Formulation of microemulsion (ME)

The micro emulsion was prepared batch-wise by dissolving the surfactants Sodium Dodecyl Sulphate (7.5 g, 7.5%w/w) and t-amyl alcohol (7.5 g, 7.5%w/w) in Ethyl Acetate (70 g, 78 ml 70% w/w). This was stirred vigorously for 10-15 min. Water (15 ml, 15% w/w) was then added with further stirring to produce a clear solution.

General procedure for the photo-Friedel-Crafts acylation of naphthoquinone in ME (GP-6)

The appropriate aldehyde (25 mmol) was added to a solution of naphthoquinone (791 mg, 5 mmol) in 50 ml ME in a 50 ml Schlenk flask. The flask was equipped with a cold finger and irradiated using a Rayonet Photochemical reactor (RPR-200; Southern New England Ultraviolet Company) equipped with RPR-3000 Å lamps (λmax = 300 ±25 nm). The reaction was allowed to proceed overnight and was allowed to continue until TLC monitoring no longer showed the presence of naphthoquinone starting material.

Brine was added to the solution to break the emulsion. The aqueous layer was discarded. The organic layer was then washed repeatedly with a dilute sodium chloride solution to remove any sodium dodecyl sulphate (SDS). The organic layer was then washed once more with brine and dried over $MgSO_4$. Solvent was removed *in vacuo.* The crude product was then analysed by ^{1}H-NMR. The crude mixture was then washed with diethyl ether to separate the desired product from any remaining SDS. The solution was then filtered and dried *in vacuo* to isolate the final product.

Attempted synthesis of 80a in ME. The synthesis followed that of **GP-6** using the following reagents: naphthoquinone (791 mg, 5mmol), acetaldehyde (1.4 ml, 1.1 g, 25 mmol). No product was observed.

Synthesis of 80b in ME. The synthesis followed that of **GP-6** using the following reagents: naphthoquinone (791 mg, 5mmol), propanal (1.79 ml, 1.45 g, 25 mmol). The title product **80b** was isolated a brown solid (462mg, 42%).

Synthesis of 80c in ME. The synthesis followed that of **GP-6** using the following reagents: naphthoquinone (791 mg, 5 mmol), butyraldehyde (2.25 ml, 1.8 g, 25 mmol). The title product **80c** was isolated as a brown solid (320 mg, 28%).

Synthesis of 80d in ME. The synthesis followed that of **GP-6** using the following reagents: naphthoquinone (791 mg, 5 mmol), valeraldehyde (2.66 ml, 2.15 g, 25 mmol). The title product **80d** was isolated as a brown solid (389 mg, 32%).

Synthesis of 80e in ME. The synthesis followed that of **GP-6** using the following reagents: naphthoquinone (791 mg, 5 mmol), hexanal (3.08 ml, 2.5 g, 25 mmol). The title product **80e** was isolated as a brown solid (388 mg, 30%).

Synthesis of 80f in ME. The synthesis followed that of **GP-6** using the following reagents: naphthoquinone (791 mg, 5 mmol), heptanal (3.52 ml, 2.85 g, 25 mmol). The title product **80f** was isolated as a brown solid (426 mg, 31%).

Synthesis of 80g in ME. The synthesis followed that of **GP-6** using the following reagents: naphthoquinone (791 mg, 5 mmol), octanal (3.91 ml, 3.21 g, 25 mmol). The title product **80g** was isolated as a brown solid (326 mg, 23%).

Synthesis of 80i in ME. The synthesis followed that of **GP-6** using the following reagents: naphthoquinone (791 mg, 5 mmol), undecanal (4.71 ml, 3.91 g, 25 mmol). The title product **80i** was isolated as a brown solid (387 mg, 25%).

Synthesis of 80j in ME. The synthesis followed that of **GP-6** using the following reagents: naphthoquinone (791 mg, 5 mmol), lauraldehyde (5.55 ml, 4.61 g, 25 mmol). The title product **80j** was isolated as a brown solid (615 mg, 36%).

8.4 Chapter 4: Synthesis of novel biaryl trifluoro phthalonitriles

8.4.1 Optimisation experiments

All optimisation reactions were carried out using a parallel reactor set-up. This was achieved by suspending multiple 20 ml test tubes in the reactor using a custom wire frame.

Percentage conversion achieved by integrating characteristic peaks in the ^{19}F NMR spectrum of the crude reaction mixture. Conversion then determined by analysing the integration ratio of the 3 fluorine in the product(s) with the 3,6 fluorines of **118** in the ^{19}F NMR spectrum.

Stoichiometry optimisation

100 mg TFPN (0.5 mmol) was dissolved in 100 ml DCM. This was divided into five 20 ml portions and placed in test tubes. Varying amounts of anisole (0.1 mmol, 0.2 mmol 0.5 mmol 1 mmol and 2 mmol) were added to each portion. All five samples were irradiated for 16 hours overnight in a Rayonet reactor. The samples were then evaporated to dryness and analysed by NMR. Conversion was measured by integration of characteristic peaks in the ^{19}F NMR spectrum.

Concentration optimisation

General procedure the determination of optimal concentration experiment (GP-7)

A 60 ml DCM solution containing 3 mmol TFPN and the appropriate ether was made. A series of serial dilutions was made on this solution to obtain six samples with TFPN concentrations of 2.5, 5, 10, 20, 37.5 and 50 mmol/L. These solutions were then irradiated overnight (16 h) in a Rayonet. Solvent was then removed by rotary evaporation and the samples were analysed by NMR. Conversion was measured by integration of characteristic peaks in the ^{19}F NMR spectrum.

Determination of the optimum concentration for the synthesis of 120a/b

A 60 ml DCM solution containing TFPN **118** (3 mmol, 600 mg) and anisole **119** (3 mmol, 324 mg, 326 µl) was made. A series of serial dilutions was made on this solution to obtain six samples with TFPN concentrations of 2.5, 5, 10, 20, 37.5 and 50 mmol/L. These solutions were then irradiated overnight (16 h) in a Rayonet reactor. Solvent was then removed by rotary evaporation and the samples were analysed by NMR. Conversion was measured by integration of characteristic peaks in the ^{19}F NMR spectrum. The results are as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50
Conversion (%)	72	57	43	41	15	9

Determination of the optimum concentration for the synthesis of 126

The procedure followed that of **GP-7** using the following reagents: TFPN **118** (3 mmol, 600 mg) and 1,2-dimethoxybenzene **122** (3 mmol, 415 mg, 382 µl). The results obtained were as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50
Conversion (%)	76	53	20	9	6	2

Determination of the optimum concentration for the synthesis of 127

The procedure followed that of **GP-7** using the following reagents: TFPN **118** (3 mmol, 600 mg) and 1,3-dimethoxybenzene **123** (3 mmol, 415 mg, 395 µl). The results obtained were as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50
Conversion (%)	72	68	45	22	15	9

Determination of the optimum concentration for the synthesis of 128

The procedure followed that of **GP-7** using the following reagents; TFPN **118** (3 mmol, 600 mg) and 1,4-dimethoxybenzene **124** (3 mmol, 415 mg). The results obtained were as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50
Conversion (%)	42	36	22	11	3	14

Determination of the optimum concentration for the synthesis of 129

The procedure followed that of **GP-7** using the following reagents: TFPN (3 mmol, 600 mg)and 1,3,5-trimethoxybenzene **125** (3 mmol, 415 mg). The results obtained were as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50
Conversion (%)	74	61	39	18	12	6

Determination of the optimum concentration for the synthesis of 141a/b

The procedure followed that of **GP-7** with the exception of an additional sample with a concentration of 100mmol/L being included. TFPN **118** (5 mmol, 1g), and aniline **138** (3 mmol, 466 mg, 456 µl) were dissolved in 50 ml DCM, and diluted to obtain the required concentration which were irradiated as usual. The results obtained were as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50	100
Conversion (%)	0	0	0	15	20	35	84

Determination of the optimum concentration for the synthesis of 142

The procedure followed that of **GP-7** using the following reagents: TFPN **118** (3 mmol, 600 mg) and *N*,*N*-dimethylaniline **139** (3 mmol, 364 mg 380 µl). No conversion was observed by ^{19}F NMR.

Determination of the optimum concentration for the synthesis of 143

The procedure followed that of **GP-7** using the following reagents: TFPN **118** (3 mmol, 600 mg) and thioanisole **143** (3 mmol, 373 mg 355 µl). The results obtained were as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50
Conversion (%)	39	34	22	6	6	4

Determination of the optimum concentration for the synthesis of 145

The procedure followed that of **GP-7** using the following reagents: TFPN **118** (3 mmol, 600 mg) and 1-methoxynaphthalene **144** (3 mmol, 475 mg). No conversion was observed by ^{19}F NMR.

Determination of the optimum concentration for the synthesis of 147

The procedure followed that of **GP-7** using the following reagents: TFPN (3 mmol, 600 mg) and 2-mehoxybiphenyl **146** (3 mmol, 553 mg, 540 µl). No conversion was observed by ^{19}F NMR.

Determination of the optimum concentration for the synthesis of 134

The procedure followed that of **GP-7** using the following reagents: TFPN **118** (3 mmol, 600 mg) and diethyl ether **130** (3 mmol, 222 mg 311 µl). The results obtained were as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50
Conversion (%)	10	0	0	0	0	0

Determination of the optimum concentration for the synthesis of 135

The procedure followed that of **GP-7** using the following reagents: TFPN **118** (3 mmol, 600 mg) and THF **131** (3 mmol, 216 mg 243 µl). The results obtained were as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50
Conversion (%)	33	33	33	19	7	9

Determination of the optimum concentration for the synthesis of 136

The procedure followed that of **GP-7** using the following reagents: TFPN **118** (3 mmol, 600 mg) and dioxolane **132** (3 mmol, 222 mg 212 µl). The results obtained were as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50
Conversion (%)	4	6	10	8	8	0

Determination of the optimum concentration for the synthesis of 137

The procedure followed that of **GP-7** using the following reagents: TFPN **118** (3 mmol, 600 mg) and t-butylmethyl ether **133** (3 mmol, 264 mg 357 µl). The results obtained were as follows:

Concentration (mmol/L)	2.5	5	10	25	37.5	50
Conversion (%)	10	8	5	0	0	0

8.4.2 Synthetic experiments

General procedure for the synthesis of biaryl phthalonitriles (GP-8):

TFPN (1 mmol, 200 mg) and the selected ether (2 mmol) were dissolved in 350 ml DCM. This was placed in a Pyrex vessel equipped with a cold finger. The solution was irradiated for 16 h overnight. Solvent was removed by rotary evaporation. In the case of reactions using liquid ethers, the crude product mixture was recrystalised from ethyl acetate and hexane. Unreacted TFPN was then removed by sublimation at 50 °C under vacuum and recovered. The product was then isolated by sublimation at 150-215 °C under vacuum. In the case of reactions with a single product, no further purification was necessary; if multiple isomeric products were present, these were separated by column chromatography.

Synthesis of 120a/b

Anisole **119** (2 mmol, 216 mg, 217 ml) was added to a solution of TFPN **118** (1 mmol, 200mg) in 350 ml DCM. This was placed in a Pyrex vessel equipped with a cold finger. The solution was irradiated for 16 h overnight. Solvent was removed by rotary evaporation. The crude product mixture was recrystalised from ethyl acetate and hexane. Unreacted TFPN was then removed by sublimation at 50 °C under vacuum. The product mixture was then isolated by sublimation at 150 °C under vacuum. (0.112 g, 3.9 mmol, 39%) The major *para* product **120a** was separated from the minor *ortho* product **120b** by column chromatography (Mobile phase ethyl acetate: hexane 1:6).

120a

^{1}H-NMR: (400 MHz, $CDCl_3$): δ (ppm) = 7.42 (td; ^{3}J = 8.8 Hz; ^{4}J = 1.7 Hz; 2H CH_{arom}), 7.06 (td; ^{3}J = 8.9 Hz; ^{4}J =3 Hz; 2H; CH_{arom}), 3.89 (s; 3H; OCH_3).

^{19}F-NMR: (376 MHz, $CDCL_3/C_6F_6$): δ (ppm) = -131.8 (dd; ^{3}J = 21.8 Hz; ^{4}J = 12.5 Hz; 1F; CF_{arom}), -126.4 (dd; ^{3}J = 22.1 Hz; ^{5}J = 9.9 Hz; 1F; CF_{arom}), -109.2 (t; J = 12 Hz; 1F; CF_{arom}).

^{13}C-NMR: (100 MHz, $CDCl_3$): δ (ppm) = 55.6 (1C; OCH_3), 114.8 (2C; C_{arom}), 131.6 (2C; C_{Arom}), 161.7 (1C; Cq).

UV/Vis λ_{max} (nm) (in DCM 0.1mM)**: (log ε)** 332 (4.0); 308 (3.87)

IR (cm^{-1})(Neat): 3000-2824, 2245

120b

^{1}H-NMR: (400 MHz, $CDCl_3$): δ (ppm) = 7.54 (td; ^{3}J = 8 Hz; ^{4}J = 1.7 Hz; 1H CH_{arom}), 7.22 (d; J = 7.6 Hz; 1H; CH_{arom}), 7.11 (td; ^{3}J = 7.52 Hz; ^{4}J = 0.8 Hz; 1H CH_{arom}), 7.06 (d; J = 8.4 Hz; 1H; CH_{arom}), 3.83 (s; 3H; OCH_3).

^{19}F-NMR: (376 MHz, $CDCL_3/C_6F_6$): δ (ppm) = -132.4 (dd; ^{3}J = 21.8 Hz; ^{4}J = 12.3 Hz; 1F; CF_{arom}), -124 (dd; ^{3}J = 22 Hz; ^{5}J = 11 Hz; 1F; CF_{arom}), -105.9 (t; J = 14.6 Hz; 1F; CF_{arom}).

Synthesis of 127

The procedure followed that of **GP-8** using the following reagents: TFPN **118** (1 mmol, 200 mg) and 1,3-dimethoxybenzene **123** (2 mmol, 276 mg 262 µl). The final product was obtained as a white solid (0.16 g, 5 mmol, 50%)

^{1}H-NMR: (400 MHz, $CDCl_3$): δ (ppm) = 7.14 (d; *J* = 8.4 Hz; 1H CH_{arom}), 6.63 (dd; ^{3}J = 8.5 Hz; ^{4}J = 2.3 Hz; 1H; CH_{arom}), 6.59 (d; *J* = 2.24 Hz; 1H CH_{arom}), 3.88 (s; 3H; OCH_3), 3.8 (s; 3H; OCH_3).

^{19}F-NMR: (376 MHz, $CDCl_3/C_6F_6$): δ (ppm) = -105.9 (t; *J* = 12 Hz; 1F; CF_{arom}), -122.2 (dd; ^{3}J = 22.3 Hz; ^{5}J = 10.7 Hz; 1F; CF_{arom}), -132.5 (dd; ^{3}J = 22.4 Hz; ^{4}J = 12 Hz; 1F; CF_{arom}).

^{13}C-NMR: (100 MHz, $CDCl_3$): δ (ppm) = 55.7 (1C; OCH_3), 55.9 (2C; C_{arom}), 99.1 (1C; C_{Arom}), 105.5 (1C; Cq), 131.9 (1C; CH_{arom}), 131.9 (1c; CH_{arom}), 158.2 (1C; Cq), 163.4 (1C; Cq).

UV/Vis λ_{max} (nm) (in DCM 0.1mM**): (log ε)** 341 (3.89); 306 (3.74)

IR (cm^{-1})(Neat): 3013-2823, 2244

Synthesis of 129

The procedure followed that of **GP-8** using the following reagents: TFPN **118** (1 mmol, 200 mg) and 1,3,5-trimethoxybenzene **129** (2 mmol, 276 mg 262 µl). The final product was obtained as a very pale yellow solid. (0.164 g, 4.7 mmol, 47%)

^{1}H-NMR: (400 MHz, $CDCl_3$): δ (ppm) = 6.2 (s; 2H; CH_{arom}), 3.88 (s; 6H; OCH_3 X 2), 3.77 (s; 3H; OCH_3).

^{19}F-NMR: (376 MHz, $CDCL_3/C_6F_6$): δ (ppm) = -106.9 (t; *J* = 12 Hz; 1F; CF_{arom}), -122.3 (dd; ^{3}J = 22.7 Hz; ^{5}J = 10.2 Hz; 1F; CF_{arom}), -132.7 (q; ^{3}J = 22.5 Hz; ^{4}J = 11.8 Hz; 1F; CF_{arom}).

^{13}C-NMR: (100 MHz, $CDCl_3$): δ (ppm) = 55.7 (1C; OCH_3), 56 (2C; OCH_3 X 2), 90.8 (2C; C_{Arom}), 158.8 (1C; Cq), 131.9 (1C; CH_{arom}), 164.2 (1C; CH_{arom}).

UV/Vis λ_{max} (nm) (in DCM 0.1mM**): (log ε)** 342 (3.85); 305 (3.76)

IR (cm^{-1})(Neat): 3062-2832, 2245

8.5 Chapter 5: Condensation of novel biaryl phthalonitriles to phthalocyanines and their subsequent evaluation as singlet oxygen photocatalysts.

8.5.1 Synthesis of novel Pcs

General procedure for the synthesis of phthalocyanines (GP-9)

An intimate mixture of phthalonitrile (1 mmol) and zinc acetate (0.5 mmol) was made by grinding in a small pestle and mortar. This mixture was then placed in a 5 ml RBF equipped with a septum seal and flushed with nitrogen gas. The flask was then immersed in an oil bath at 190 °C for 5h. A strong green colour was observed at this stage. Once the reaction was complete, the crude mixture was crushed and washed thoroughly with warm water to remove any remaining metal salt. This was followed by sublimation at 200 °C to remove any remaining unreacted phthalonitrile. The purified product was analysed by ^{1}H and ^{19}F NMR, UV-Vis spectroscopy and MALDI mass spectrometry.

Synthesis of 150

An intimate mixture of TFPN **118** (1 mmol, 200 mg) and zinc acetate dihydrate (1 mmol, 220 mg) was made in a small pestle and mortar. This mixture was then placed in a 5 ml RBF equipped with a septum seal and flushed with nitrogen gas. The flask

was then immersed in an oil bath at 190 °C for 5h. A strong green colour was observed at this stage. Once the reaction was complete, the crude mixture was crushed and washed thoroughly with warm water to remove any remaining metal salt, followed by sublimation at 200 °C to remove any remaining unreacted phthalonitrile. The final product **150** was obtained as a dark green powder which was analysed by ^{1}H and ^{19}F NMR, UV-Vis spectroscopy and MALDI mass spectrometry (100 mg, 46%).

UV/Vis λ_{max} (nm) (in DCM 2.5 X 10^{-7}M**) : (log ε)** 671 (5.78)

Synthesis of 151

The procedure followed that of **GP-9** using the following reagents: **120a** (1 mmol, 288 mg) and zinc acetate dihydrate (1 mmol, 220 mg). The product was obtained as a dark green powder (204 mg, 67%).

^{1}H-NMR: (400 MHz, $CDCl_3$): δ (ppm); 7.42 (d; *J* = 7.64 Hz; 2H; CH_{arom}), 7.06 (d; *J* = 7.8 Hz; 2H; CH_{arom}), 3.88 (s; 3H; OCH_3).

UV/Vis λ_{max} (nm) (in DCM 2.5 X 10^{-7}M**) : (log ε)** 701 (6.03)

Synthesis of 152

The procedure followed that of **GP-9** using the following reagents: **127** (1 mmol, 318 mg) and zinc acetate dihydrate (1 mmol, 220 mg). The product was obtained as a dark green powder (195 mg, 58%).

^{1}H-NMR: (400 MHz, $CDCl_3$): δ (ppm); 7.15 (d; *J* = 8.4 Hz; 1H CH_{arom}), 6.63 (dd; ^3J = 8.5 Hz; ^4J = 2.2 Hz; 1H; CH_{arom}), 5.59 (d; *J* = 2 Hz; 1H CH_{arom}), 3.88 (s; 3H; OCH_3), 3.82 (s; 3H; OCH_3).

UV/Vis λ_{max} (nm) (in DCM 2.5 X 10^{-7}M**) : (log ε)** 702 (5.99)

Maldi MS (Sinapinic acid matrix): *m/z* = 1338.2; Required for $C_{64}H_{36}F_{12}N_8O_8Zn$ = 1338.4.

Synthesis of 153

The procedure followed that of **GP-9** using the following reagents: **129** (1 mmol, 348 mg) and zinc acetate dihydrate (1 mmol, 220 mg). The product was obtained as a dark green powder (264 mg, 46%).

^{1}H-NMR: (400 MHz, $CDCl_3$): δ (ppm) = 5.21 (s; 2H; CH_{arom}), 2.88 (s; 3H; OCH_3), 2.77 (s; 6H; OCH_3 X 2).

UV/Vis λ_{max} (nm) (in DCM 2.5 X 10^{-7}M**) : (log ε)** 702 (6.12)

Maldi MS (Sinapinic acid matrix): *m/z* = 1458.3; Required for $C_{68}H_{44}F_{12}N_8O_{12}Zn$ = 1458.5.

8.5.2 Evaluation as photosensitisers

General procedure for the determination of photosensitisation ability (GP-10)

The appropriate sensitiser (1 μmol) was dissolved in methanol (50 ml). This occasionally required sonication and mild heating. The solution was then placed in a schenk flask equipped with a cold finger and air bubbling apparatus. β-Citronellol (1 mmol, 156 mg, 183 μl) was added to the solution. Air bubbling was initiated and a

sample was taken once a homogenous solution was obtained. This sample was stored in a dark box prior to analysis. Following this, irradiation with a halogen lamp at a fixed distance was initiated. Samples were then taken after 3 and 6 hours irradiation. These samples were also stored in a dark box when not in use.

Once the reaction had concluded, the samples were dried under vacuum, and analysed by ^{1}H NMR. Conversions were obtained by integration of characteristic peaks at 5.09 ppm for the starting material **28**, 4.95 ppm and 4.24 ppm for **159a** and 5.55 ppm for **159b**.

Evaluation of 150 as a photooxygenation sensitiser

The experiment was carried out according to the general procedure **GP-10** with the following weights; **150** (2.16 mg) was dissolved volumetrically in 25 ml of methanol. 10 ml of this solution was used in the irradiation experiment.

Samples were taken at 0 h, 3 h and 6 h intervals. No conversion was observed by ^{1}H NMR.

Evaluation of 151 as a photooxygenation sensitiser

The experiment was carried out according to **GP-10** with the following weights; 151 (3.05 mg) was dissolved volumetrically in 25 ml of methanol. 10 ml of this solution was used in the irradiation experiment.

Samples were taken at 0 h, 3 h and 6 h intervals. The following conversions were observed by ^{1}H NMR.

	Starting material	Products		
	28	**159a**	**159b**	Total
0h	100	0	0	0
3h	86	5	9	14
6h	82	9	9	18

Evaluation of 152 as a photooxygenation sensitiser

The experiment was carried out according to **GP-10** with the following weights; **152** (3.35 mg) was dissolved volumetrically in 25 ml of methanol. 10 ml of this solution was used in the irradiation experiment.

Samples were taken at 0 h, 3 h and 6 h intervals. The following conversions were observed by ^{1}H NMR.

	Starting material	Products		
	28	**159a**	**159b**	Total
0h	100	0	0	0
3h	83	5	13	17
6h	77	12	10	23

Evaluation of 153 as a photooxygenation sensitiser

The experiment was carried out according to **GP-10** with the following weights; **153** (3.65 mg) was dissolved volumetrically in 25 ml of methanol. 10 ml of this solution was used in the irradiation experiment.

Samples were taken at 0 h, 3 h and 6 h intervals. The following conversions were observed by ^{1}H NMR.

	Starting material	Products		
	28	**159a**	**159b**	Total
0h	100	0	0	0
3h	53	22	25	47
6h	23	39	38	77

Evaluation of rose bengal as a photooxygenation sensitiser

The experiment was carried out according to **GP-10** with the following weights; Rose bengal (2.54 mg) was dissolved volumetrically in 25 ml of methanol. 10 ml of this solution was used in the irradiation experiment.

Samples were taken at 0 h, 3 h and 6 h intervals. The following conversions were observed by ^{1}H NMR.

	Starting material	Products		
	28	**159a**	**159b**	Total
0h	100	0	0	0
3h	87	2	11	13
6h	64	14	22	36

Evaluation of methylene blue as a photooxygenation sensitiser

The experiment was carried out according to the general procedure **GP-10** with the following weights; Methylene blue (1.6 mg) was dissolved volumetrically in 25 ml of methanol. 5 ml of this solution was used in the irradiation experiment.

Samples were taken at 0 h, 3 h and 6 h intervals. The following conversions were observed by ^{1}H NMR.

	Starting material	Products		
	28	**159a**	**159b**	Total
0h	100	0	0	0
3h	84	4	12	16
6h	66	11	22	34

9.0 References

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