SYNTHESIS AND FUNCTIONALIZATION OF NOVEL MESO-SUBSTITUTED TETRABENZOTRIAZAPORPHYRINS

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This thesis is submitted in partial fulfilment of the requirements of the degree of Doctor of Philosophy at the University of East Anglia, Norwich.

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Preface

The research described in this thesis is, to the best of my knowledge, original and my own work, except where due reference has been made.

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Norwich, September 2014

Abstract

Phthalocyanine derivatives have seen many important developments since their discovery in 1907 by Braun and Tcherniac. These interesting materials are one of the most significant classes of macroheterocyclic organic materials owing to their remarkable electrical and physical properties which can be tuned by suitable derivatization of their rigid inner core. A brief summary of the syntheses, properties and applications of these complexes is clarified in Chapter 1.

The work described in this thesis concerns the synthesis of phthalocyanine (Pc)/tetrabenzoporphyrin (TBP) hybrids – intermediates between the widely studied Pc and TBP parents. Such hybrids have received a very little attention, mainly because they have previously proved difficult to synthesise. Among the series of the phthalocyanine/tetrabenzoporphyrin hybrids, tetrabenzotriazaporphyrins (TBTAPs) are the most widely studied and they are the focus of this thesis. They have a single *meso*-carbon linkage which can offer an additional site for the attachment of various functional groups, thus would provide a wide range of functionalized TBTAP derivatives.

The syntheses of the phthalonitriles have been achieved successfully through the investigation of different strategies. Phthalonitriles have been constructed by the nickel or palladium catalysed Kumada cross-coupling reaction using 1,2-dichlorobenzene as precursor, followed by electrophilic bromination and Rosenmund von Braun cyanation reaction in the last step. An alternative route towards the formation of the phthalonitriles was used in order to synthesise alternative target phthalonitriles in good yield; the method employed Kumada cross-coupling reaction using 4,5-dibromoveratrole as precursor followed by a sequence of synthetic steps and finally cyanation reaction following the procedure described by Hanack and Drechsler. A series of *meso*-phenyl substituted tetrabenzotriazaporphyrins (TBTAPs) bearing different functional groups has been prepared successfully *via* the investigation of various approaches. The traditional synthetic methods and their new modified versions *via* Grignard reagents have been developed as well as the modern technique *via* aminoisoindoline that was discovered recently by our group. Most importantly, synthesis of functionalised TBTAPs has been achieved.

Expansion of the π-conjugated system of TBTAPs has been attempted as first experimental examinations in this field through several chemical and photochemical cyclisation methods, but the desired products were not isolated. Finally, transformations of the functionalised *meso*-phenyl TBTAP macrocycles through the palladium-catalysed Suzuki and copper-free Sonogashira cross-coupling reactions have been accomplished successfully resulting in the formation of a new series of materials. The new strategies combine to open up the potential for many new hybrid structures.

To My Parents and Family

Acknowledgements

First of all I would like to give thanks to the almighty God for giving me life, wisdom and strength to come this far with my education. I would also like to express my sincere gratitude to my supervisor, Prof. Andrew N. Cammidge for giving me this opportunity to work under him and for all his support. Without his encouragement, help, and confidence in me, this project would not have been possible. I am grateful to him for the advice, patience and attentiveness that he has given me and the impact he has had on my life.

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Lastly, I would like to give a special thanks to my parents and family for continuous encouragement and financial support during my studies at UEA.

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Publications

Improved syntheses of meso-aryl tetrabenzotriazaporphyrins (TBTAPs), Alharbi, N.; Díaz-Moscoso, A.; Tizzard, G. J.; Coles, S. J.; Cook, M. J.; Cammidge, A. N. *Tetrahedron* **2014**, *70*, 7370-7379.

Oral presentations

Synthesis and Characterisation of Octa-substituted TetraBenzoTriaza Porphyrins, *School of Organic Chemistry*, 17th January 2013, UEA, Norwich.

Poster presentations

Synthesis and Modification of TetraBenzoTriAzaPorphyrins (TBTAPs), *Eighth International Conference on Porphyrins and Phthalocyanines (ICPP-8)*, 22nd- 27th June 2014. Istanbul, Turkey.

Abbreviations

Å	Angström
Ac	acetyl
acac	acetylacetonate
aq.	aqueous
Ar	aryl
Bp	boiling point
br	broad
Bu	butyl
t-Bu	tertiary butyl
CI	chemical ionisation
Col_h	columnar hexagonal
Col_r	columnar rectangular
conc.	Concentrated
°C	Celsius
d	doublet
dd	doublet of doublets
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DCM	dichloromethane

Dec.	decomposed
DMAE	dimethylaminoethanol
DME	1,2-dimethoxyethane
DMF	N, N-dimethylformamide
DMSO	Dimethylsulfoxide
dppe	1,3-bis(diphenylphosphino)ethane
dppf	1,1′-bis(diphenylphosphino)ferrocene
dppp	1,2-bis(diphenylphosphino)propane
δ	chemical shift in ppm
e	electron
eq.	equivalent
Et	ethyl
ether	diethylether
eV	electron volt(s)
Fig.	Figure
h	hour(s)
HOMO	Highest occupied molecular orbital
HRMS	high resolution mass spectrometry
Hz	Hertz
I	isotropic liquid
IR	infrared

IUPAC	International union of pure and applied chemistry
J	coupling constant in NMR spectroscopy
Jg^{-1}	Joules per gram
LB	Langmuir-Blodgett
LC	liquid crystal
LCD	liquid crystal display
LHMDS	Lithium hexamethyldisilazide
LiH	Lithium hydride
Lit.	literature
LUMO	Lowest unoccupied molecular orbital
λ	lambda (wavelength)
m-	meta
m	multiplet
M	metal or molarity of solution
MALDI	matrix assisted laser desorption ionisation
max.	maximum
Me	methyl
MHz	megahertz
min	minute(s)
mol	mole
mmol	millimole

mmHg	millimetres of mercury
Mp	melting point
MS	mass spectrometry
Mw	Microwave
NBS	N-bromosuccinimide
NMR	Nuclear magnetic resonance
nm	nanometres
nr	no result
o-	ortho
OLED	organic light emitting diode
p-	para
PE	petroleum ether
Pc	phthalocyanine
PDT	photodynamic therapy
Ph	phenyl
ppm	parts per million
q	quartet
R	alkyl group
R_f	retention factor
RT or rt	room temperature
s	singlet

t	triplet
temp.	temperature
Tf	trifluoromethylsulphonyl
TMS	tetramethylsilane
TOF	time of flight
Tol	toluene
Ts	p-toluenesulphonyl
THF	Tetrahydrofuran
TLC	thin layer chromatography
UV-Vis	Ultraviolet-Visible
W	watt(s)
X	halide or heteroatom

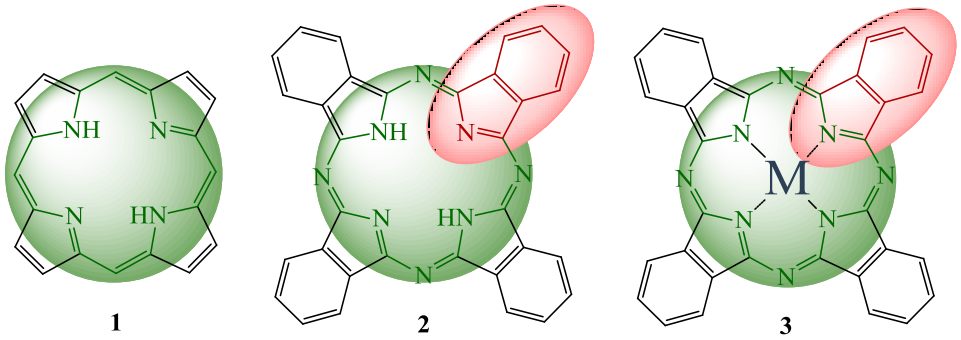
Contents

CHAPTER 1

Introduction to Phthalocyanines and Tetrabenzo(aza)porphyrin Hybrids

1.1 Introduction to Phthalocyanines

Phthalocyanines (Pcs, **2**) are one of the most important and interesting classes of macroheterocyclic organic materials due to their high chemical and thermal stability, electronic absorption due to aromaticity, synthetic flexibility and ability to adapt to a broad variety of applications. The name *Phthalocyanine* originates from the Greek words for *Phthalo* (meaning rock oil) and for *Cyanine* (meaning dark blue). This term was first used by R. P. Linstead to describe a set of organic dyes, whose colours range from reddish blue to yellowish green.[1-6] Phthalocyanines **2** and their metal analogues metallophthalocyanines (MPcs, **3**; Figures 1.1), are planar structures containing a central aromatic core of 18-π electrons. They are man-made macrocyclic molecules which are structurally similar to the naturally occurring prophyrins **1**, such as haemoglobin, vitamin B_{12} and chlorophyll. In the Pc system, the four methine groups in porphyrin ring are replaced by four imine groups. Pcs consist of four isoindole units joined together by four nitrogen atoms known as *aza*-bridges. In other words, each of the pyrrole unit is fused to a benzenoid ring. According to the similarity between these two structures, phthalocyanines have also been termed as *tetrabenzotetraazaporphyrins*. The central cavity of phthalocyanine can accommodate two hydrogen atoms (i.e. metal-free Pcs) or more interestingly various metal ions (i.e. metallated Pcs) due to the complementary size of the Pc core.[7-9]



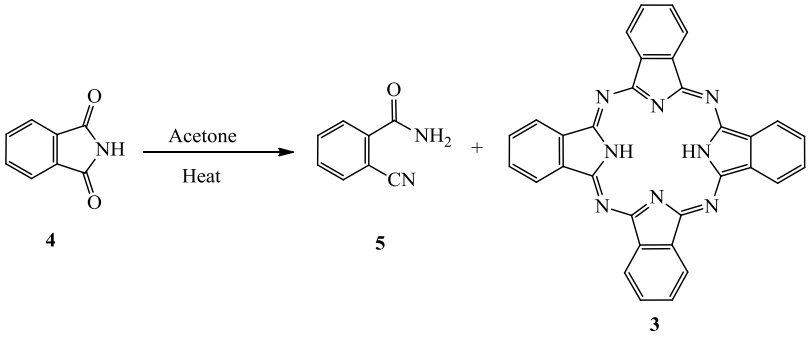
1 **2** **3**

Figure 1.1: Molecular structures of metal free porphyrin **1**, phthalocyanine **2** and metallophthalocyanine **3**.

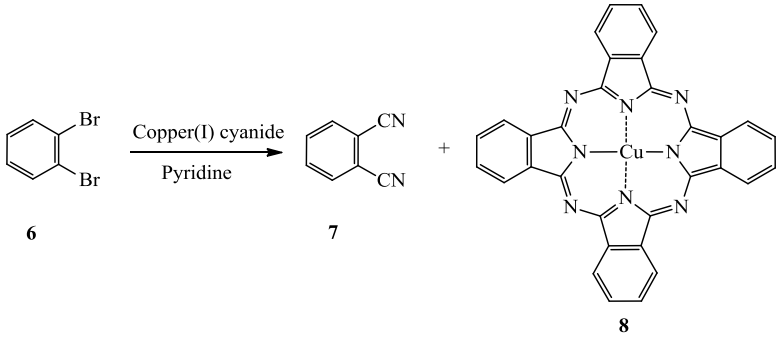
1.2 Discovery and History of Phthalocyanines

Phthalocyanines were firstly observed by Braun and Tcherniac in 1907 as a dark insoluble by-product during the industrial preparation of *o*-cyanobenzamide **5** from phthalimide **4** in acetone (Scheme 1.1).[10] Unfortunately, no further attention was given

to that discovery at that time. Later, in 1927, de Diesbach and Von der Weid obtained a blue material during the cyanation of *o*-dibromobenzene **6** with copper (I) cyanide in refluxing pyridine (Scheme 1.2).[11]

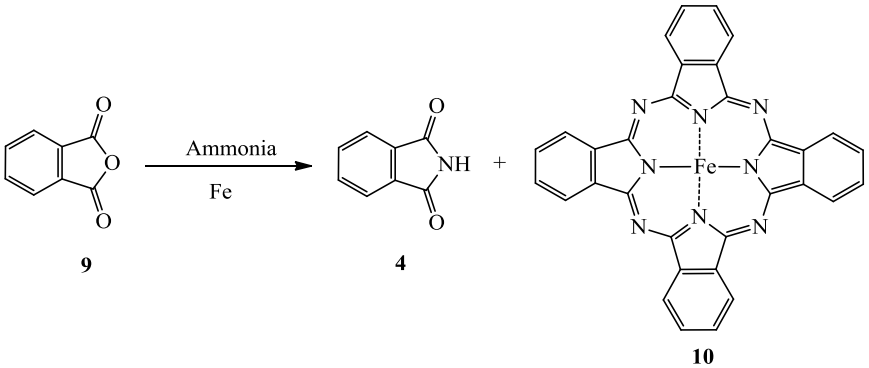


Scheme 1.1: Attempted preparation of *o*-cyanobenzamide by Braun and Tcherniac.



Scheme 1.2: Cyanation of *o*-dibromobenzene by de Diesbach and Von der Weid.

In 1928, another accidental preparation of a blue green product was discovered by chemists at the Grangemouth factory of Scottish Dyes Ltd (later known as Imperial Chemical Industries; ICI) during the preparation of phthalimide **4** from phthalic anhydride **9** and ammonia (Scheme 1.3). The isolated blue green material was examined and identified later as iron phthalocyanine **10**. The metal ion was obtained from the iron vessel used in the synthesis procedure.[12]



Scheme 1.3: Accidental preparation of iron phthalocyanine.

In subsequent years, these compounds were studied in depth by Sir Reginald Patrick Linstead.[1] Using a variety of analytical techniques, he was able to clarify the molecular structure of phthalocyanine as well as procedures for preparing a wide range of metal-free and metallophthalocyanines.[2-5,12] Later on, the molecular structure Linstead proposed was confirmed by Robertson using X-ray crystallography.[13-15]

1.3 Applications of Phthalocyanines

In recent years, phthalocyanines have received an enormous interest. They are mostly used as dyes and pigments which can be applied to various substrates (textiles, leather, paints, polymers, papers *etc.*).[8] Pcs are also found to be useful in a wide variety of high-technology industrial applications due to their high degree of aromaticity, characteristic intense blue-green colour, high thermal, chemical and photochemical stabilities, low solubility in organic and aqueous solutions, excellent fastness to light, synthetic flexibility, significant absorption in the visible region and large absorption coefficients.[16-20] These unique properties of phthalocyanines are not easy to obtain in other colorants. For example, the naturally occurring dyes chlorophyll and haemoglobin are extremely sensitive to light and easy to destroy by heat.[20] Examples of the potential applications for phthalocyanines include homogenous and heterogenous catalysts in chemical reactions,[7] nonlinear optical materials,[21] Langmuir-Blodgett (LB) films,[22] liquid crystals,[23] low dimensional metals,[24] electrochromic substances,[25] photoelectrochemical cells,[26] photosensitizers,[27] gas sensors,[28] optical data storage (computer recordable DVDs),[29] electrophotographic applications,[30] and as NIR electrochromic materials.[31] Pcs derivatives work as photodynamic reagents for cancer therapy and other medical applications (e. g. Zn and AlPcs).[32]

1.4 Properties of Phthalocyanines

Phthalocyanines are planar macrocyclic aromatic compounds possessing conjugated 18-π electrons which can be delocalized over alternating carbon and nitrogen atoms. The π conjugated system is responsible for the intense blue-green colour and the unique chemical and physical properties of phthalocyanines. The chemical and physical properties of Pcs can be affected significantly by modifying the structure of the molecule, such as changes in solubility, colour, structural shape and liquid

crystalline behaviour.[33] Structural variation of the Pc macrocycles can be achieved by either inserting different elemental ions in the central cavity or introducing variety of substituents onto the ring system of Pcs.[7,34] Those impacts are discussed in further detail below.

1.4.1 Effects of the central metal ions

Phthalocyanine possesses a central cavity which is able to accommodate either two hydrogen atoms (i.e. metal-free phthalocyanine H_2Pc) or various metal ions (i.e. metallophthalocyanine MPc). More than 70 different elements could be hosted into the central phthalocyanine cavity by coordination with the isoindolic nitrogens inside the phthalocyanice ring. The metal-free macrocycle usually presents as a dianion (Pc^{2-}) and acts as a ligand to the metallic cation to introduce metallated phthalocyanines which can be further amended by the coordination of axial ligands on the metal depending on its oxidation state.[7]

Small alkali metals that have an oxidation state of +1, such as lithium and sodium, form 2:1 metal: phthalocyanine complexes. Both metal ions cannot fit in the central cavity and prefer to lie above and below the plane of the Pc ring. In this case, the planar form is distorted to a concave form, and thus the solubility in polar organic solvents is increased. Metallophthalocyanines can often be easily converted to the metal-free phthalocyanines by treatment by dilute acid.[35,36]

Transition metals such as copper, cobalt and iron in +2 oxidation state normally yield 1:1 stable metal: phthalocyanine complexes. Central metals in this case are accommodated in the central cavity of Pcs and form square planar complexes without any significant distortion of the Pc macrocycles. However, the large metals such as lead cannot be accommodated completely in the central cavity of Pc and hence sit out of the plane of the ring and form distorted rings (i.e. non-planar complexes).[35,37]

Metals that exist in an oxidation state larger than +2 (i.e. 3+, 4+) such as rhodium and tin, usually form complexes with axial ligands which also will increase the solubility in organic solvents, whereas, trivalent lanthanide ions such as the rare earth are too big to accommodate in the central cavity of the Pc macrocycle. They prefer to form dimers, wherein the metal ion is located between two distorted phthalocyanine rings (i.e. sandwich bis-phthalocyanines).[35,38]

1.4.2 Effects of the attached substituents

A large variety of substituents can be presented at the 16 available positions on the fused benzene rings of phthalocyanine (Figure 1.2).[13] The chemical and physical properties of the Pcs are greatly influenced by a number of factors which include nature of substituents, presence or absence of central metal ion, number and position of substituents (either *α*- non-peripheral substitution or *β*- peripheral substitution) attached to the Pc macrocycle.[8,39,40] For example, attachment of aliphatic chains with reasonable length will improve the solubility of Pcs in common organic solvents, whereas sulfonyl-, carboxy- or amino- substituents are effective for solubility in aqueous media.[7,46-54] The most common substituents are alkyl (C_xH_{2x+1}), alkoxy (OC_xH_{2x+1}) and alkoxymethyl ($CH_2OC_xH_{2x+1}$) chains.

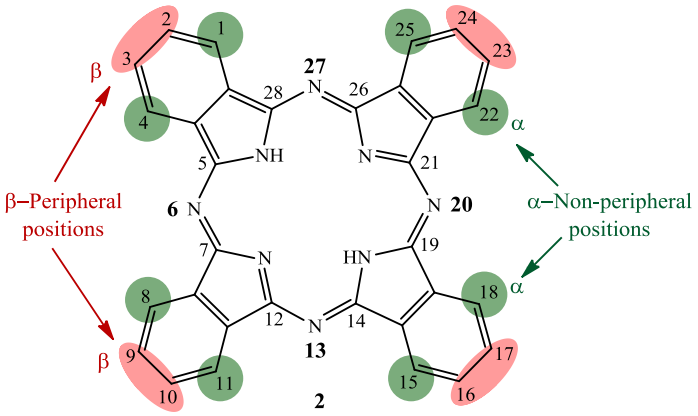


Figure 1.2: Numbering of the atoms on phthalocyanine macrocycle.

Condensation of mono-, di- or tetra-substituted phthalonitriles produces the corresponding symmetrical tetra-, octa- or 16-substituted Pcs. Monosubstituted phthalonitriles at position 3 or 4 form tetrasubstituted Pcs, typically as a mixture of four positional isomers with C_{4h}, D_{2h}, C_{2v}, and C_s symmetries (Figure 1.3),[8,41-43] whereas symmetrical 3,6- and 4,5-disubstituted phthalonitriles give octasubstituted Pcs as a single isomer (Figure 1.4). Introduction of the substituents at {(2, 3), (9, 10), (16, 17) and (23, 24)} positions is termed as a *peripheral* (*β*) substitution while the substituents at {(1, 4), (8, 11), (15, 18) and (22, 25)} positions of the benzene rings is called a *non-peripheral* (*α*) substitution (Figure 1.4).[7]

Non-peripherally octasubstituted Pc is more difficult to synthesise and normally produces lower yields due to the steric hindrance between the attached substituents

compared with the peripheral one. However, *np*-Pc is more soluble in common organic solvents and gives less aggregation than the *p*-Pc.[44,45]

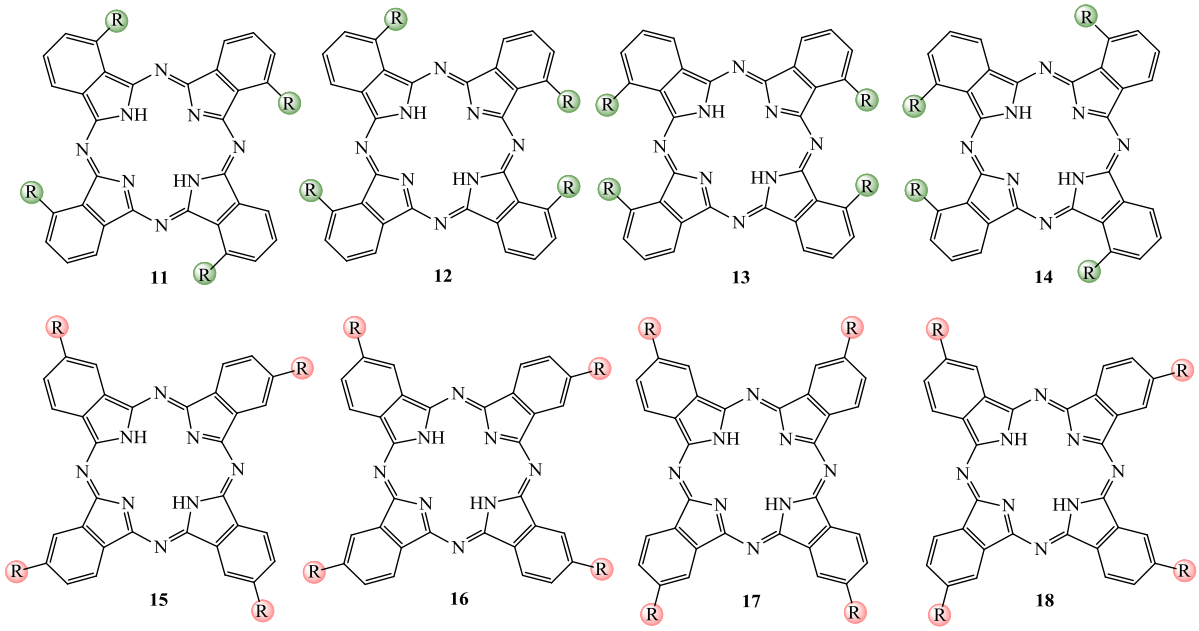


Figure 1.3: The structural isomers of tetrasubstituted metal-free phthalocyanines.

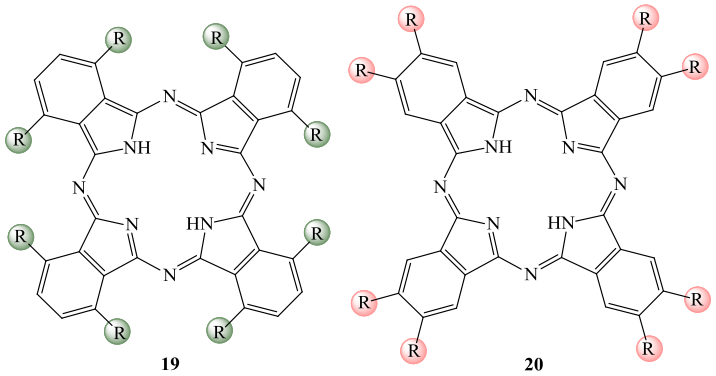


Figure 1.4: Non-peripheral and peripheral octasubstituted metal-free phthalocyanines.

Condensation of two different types of mono- or di-substituted phthalonitriles will produce six different Pcs in the product mixture as illustrated in Figure 1.5 and Figure 1.6. However, controlling the ratio of the two phthalonitrile precursors will increase the yield of the desired unsymmetrical Pc.[7]

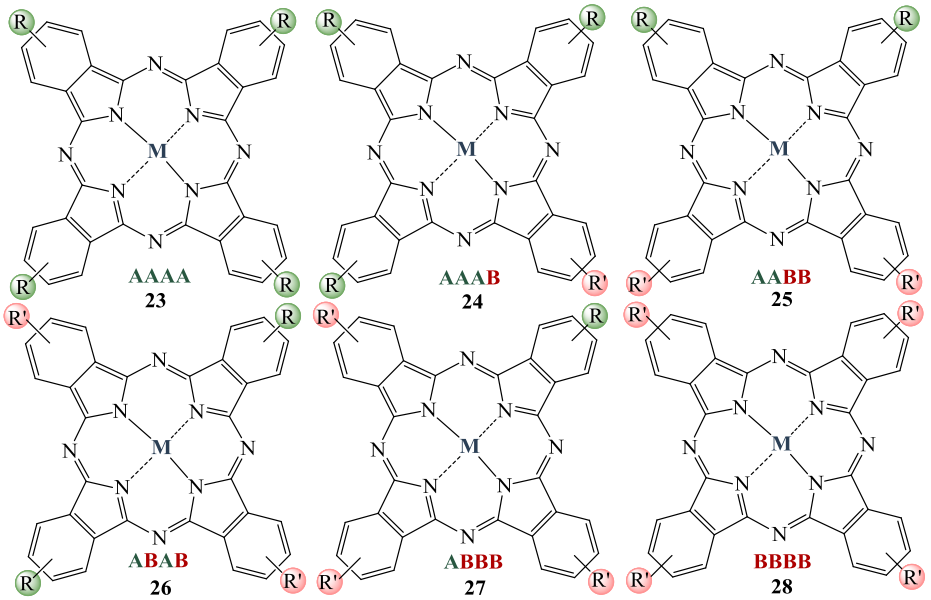


Figure 1.5: Tetra-substituted Pcs.

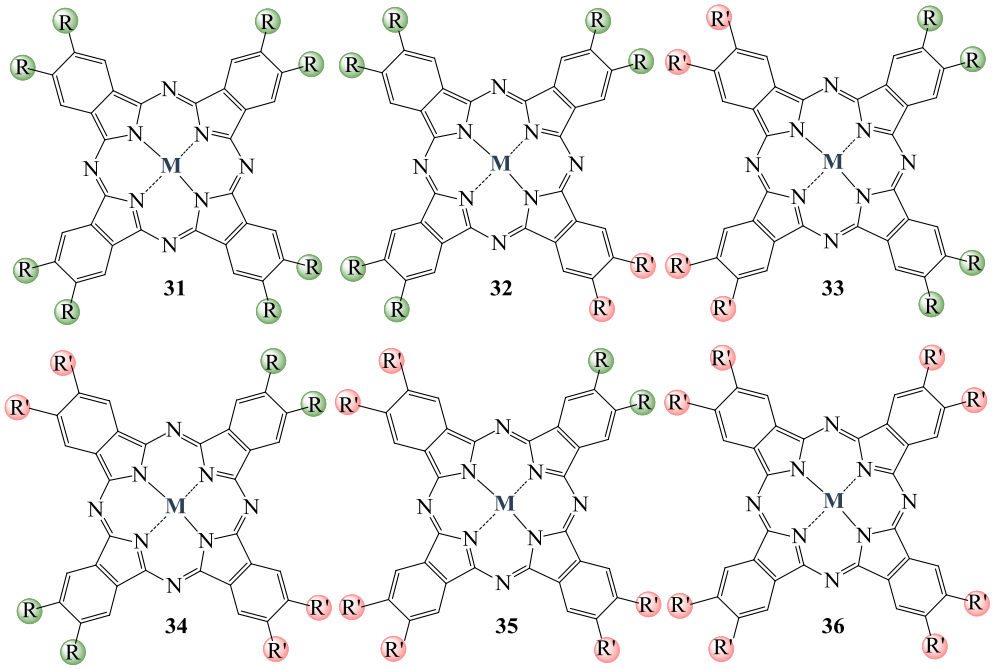


Figure 1.6: Octa-substituted Pcs.

1.5 Absorption Spectra of Phthalocyanines

Phthalocyanines have characteristic ultraviolet-visible (UV-Vis) spectra with a strong absorption band in the red end of the visible region called the *Q-band*, at approximately 670-720 nm, which is responsible for the intense colour of the phthalocyanine, and a weaker absorption in the blue region of the UV-Vis spectrum

called the *B*- or the *Soret band*, at about 320-370 nm.[7] The Q-band as well as the B-band are assigned to the $\pi \rightarrow \pi^*$ electronic transitions from the HOMO (highest occupied molecular orbital) to the LUMO (lowest unoccupied molecular orbital) of the Pc ring. The origins of these $\pi \rightarrow \pi^*$ transitions can be understood by Gouterman's four-orbital linear combination of atomic orbital model (LCAO), presented in Figure 1.7.[23,55-61] The Q-band absorption is due to transitions from the HOMO, (a_{1u} symmetry (π)), to the LUMO (e_g symmetry (π^*)) whereas the transition from a_{2u} and b_{2u} to e_g results in the *B*-band absorption. It was observed that the Soret band splits into two components, B_1 and B_2, which occur at about the same energy and form the broad band seen in the spectra.[7]

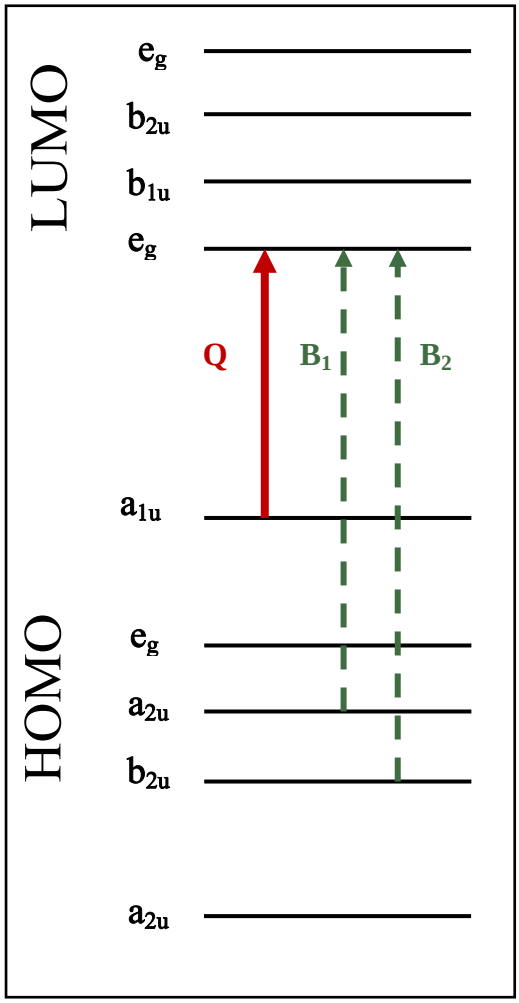


Figure 1.7: Electronic transitions in phthalocyanines.

Figure 1.8 illustrates a typical absorption spectrum of metal-free and metallated phthalocyanine. In the case of metal-free phthalocyanine (H_2Pc), the *Q* band splits into two peaks due to the presence of the two protons in the cavity which reduce the

symmetry to D_{2h} and consequently loss of degeneracy of the LUMO orbital to produce Q_y and Q_x, at lower and higher energy, respectively. The absorption spectrum of metallated phthalocyanine (MPc) is visibly different to that of H_2Pc. The Q-band exhibits as a sharp single peak as a result of the presence of a single ion in the central core of the phthalocyanine. In this case, the degeneracy of the LUMO is maintained due to their high symmetry (D_{4h}).[7,62,63]

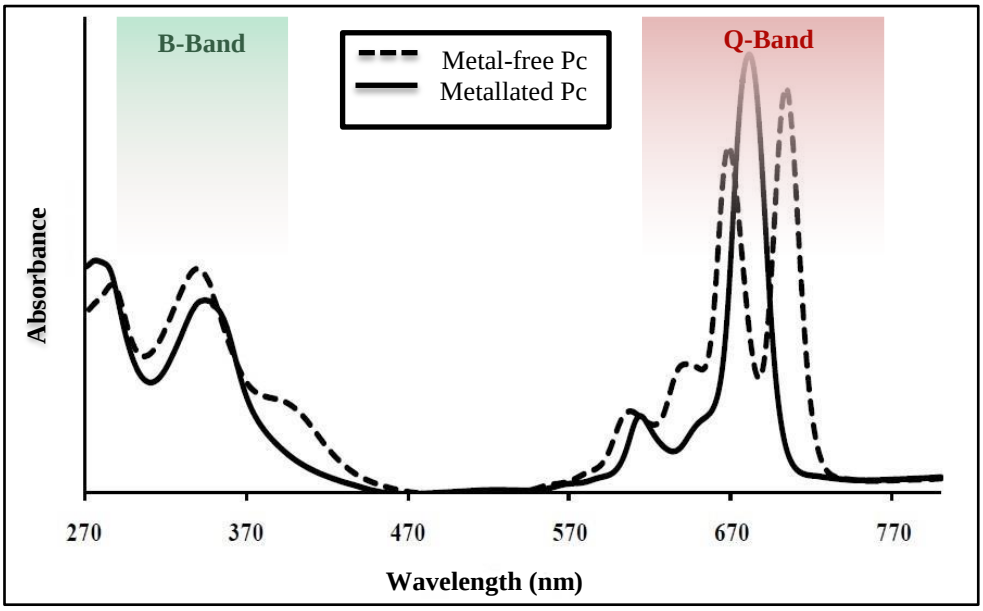


Figure 1.8: Typical UV-Vis absorption spectra of metallated (solid line) and metal-free (dashed line) phthalocyanines, showing the *Q* and *B* absorption bands.

Further absorption bands (N, L and C) can be observed, between the *Q* and *B* at higher energy (210 – 280 nm). These bands are typically not used in the analysis of phthalocyanines and are not discussed anymore.[56,64-66] The electronic absorption spectra of Pcs can be modified depending on the type, number and position of attached substituents, central coordinating atoms in the Pc ring, type of solvent used and the aggregation of the molecules.[49,67-73]

The introduction of a metal ion inside the Pc cavity can result in an excitation transfer between the metal's atomic orbitals and the phthalocyanine ligand and consequently the *Q* band undergoes a slight blue shift. The *Q* band can shift to the red region in the case of occupation the metal ion outside the central core of Pc, such as PbPc. Substitution on the benzene ring results a shift (*bathochromic* or *hypsochromic* shift depending on the type of functional group substituted) of the Q-band compared to unsubstituted Pc. Non-peripheral substitutions demonstrate a larger shift than peripheral substitutions, as shown

in Figure 1.9. [7,19,67,72,74] Electron donating substituents at the α-position generate a red shift of the Q-band due to reduction in the HOMO-LUMO energy gap, whereas substituents at the β-position shift to a blue region.[72] In contrast, the effect of electron-withdrawing groups results an absolutely the opposite effect in regard to the $\alpha-$ and $\beta-$ positions. In addition, the aromatic solvents and extension of the π-system exhibit a bathochromic shift of the intense Q absorption band into the near infrared NIR region.[73-76]

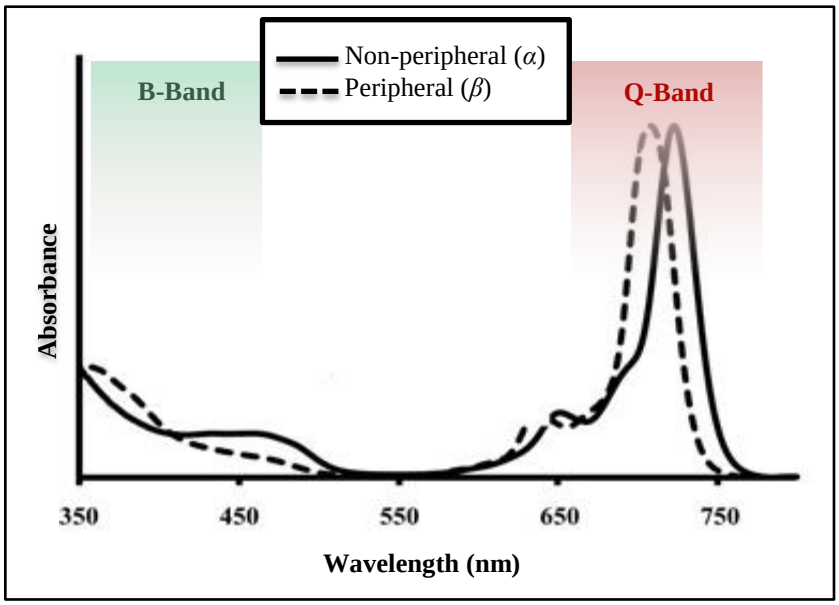


Figure 1.9: Absorption spectra of peripheral (β) (dashed line) and non-peripheral (α) (solid line) substituted metallated phthalocyanines**.**

1.6 Solubilisation of Phthalocyanines

The solubility of unsubstituted phthalocyanines is generally very low in most organic solvents due to intramolecular interactions within their π-system.[77,78] They are also hard to dissolve in high-boiling aromatic solvents such as quinoline or α-bromo or α-chloronaphthalene even at concentrations around 10^{-5} M.[79] Sulfuric acid at concentrations greater than 8 M was found to be the most effective solvent for these materials. Furthermore, this solvent acts to protonate the phthalocyanines and thus alters their basic properties. As a result of the insolubility, their applications are very limited.

Their solubility can dramatically increase by the introduction of substituents into the Pc ring either on the peripheral (β) or non-peripheral (α) positions. Consequently, these substituents reduce the intermolecular attractions due to increasing the distance

between the stacked molecules.[7,42,78,80-84] Tetra- and octa-substituted phthalocyanines are the most commonly studied.[7,80] Generally, the solubility of octa-substituted phthalocyanines is significantly lower than for the tetra-substituted analogues due to the fact that the tetra-substituted phthalocyanines are formed as a mixture of isomers and thus give rise to a lower degree of order in the solid state, compared with the octa-substituted phthalocyanines.[47,48,78,86] Moreover, the solubility of peripherally tetra or octa-substituted phthalocyanines is higher than the non-peripherally substituted compounds.[85]

The insolubility of phthalocyanines has been thoroughly investigated an extensive work carried out in order to add substituents to the phthalocyanine macrocycle and this has led to enhanced solubility. Improving the solubility of phthalocyanines in common organic solvents was not only the reason for these explorations but also to improve their potential usefulness in numerous possible applications.[87] Synthesis of functionalised phthalocyanines was achieved using a wide range of substituents such as aliphatic chains and higher order aromatics, acids, amines, thiols and halides and these are discussed in detail further on the chapter.

1.7 Liquid Crystal Properties of Phthalocyanines

It is known that matter exists in three common forms; solid, liquid and gas. The atoms or molecules in crystals exist in a highly ordered arrangement while no such order presents in liquids. The sort of phase that takes place between isotropic liquid and crystalline solid and shares some of the their properties is termed as *liquid crystalline* phase, *mesophase* or *mesomorphic* phase and the materials are called *liquid crystals*, *mesomorphs* or *mesomorphic* substances (Figure 1.10).[88-90]

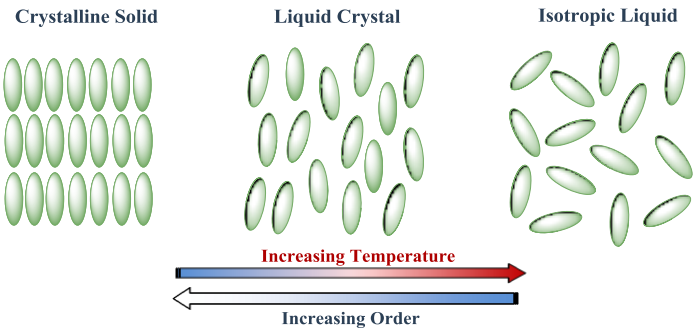


Figure 1.10: Liquid crystal phase.

Liquid crystalline phases can be formed *via* two different ways. For example, they can be obtained by heating or cooling the materials and these are called *thermotropic* liquid crystals, whereas the liquid crystals that obtained by dissolving the materials in controlled amount of solvents, are named *lyotropic* liquid crystals. Depending on the molecular shapes, the thermotropic liquid crystals are classified as a *calamitic* (rod-like) and *discotic* (disc-like) liquid crystals. Phthalocyanines typically belong to thermotropic, discotic liquid crystalline phases. Liquid-crystalline behaviour of phthalocyanines was first reported by Simon and co-workers in 1982.[91] These phthalocyanines possess eight long alkyloxymethyl chains at the peripheral positions (Figure 1.11). Later on, Pcs with octaalkyl and octaalkyloxy chains were also found to exhibit discotic mesomorphism.[23,92-95] After several studies, researchers found that the peripherally substituted octa- alkoxymethyl, alkoxy and alkyl phthalocyanines led to formation of columnar hexagonal mesophases.[23,92,96-100] Non-peripherally substituted phthalocyanines have also been found to exhibit discotic liquid-crystalline behaviours.[44,67,101-105]

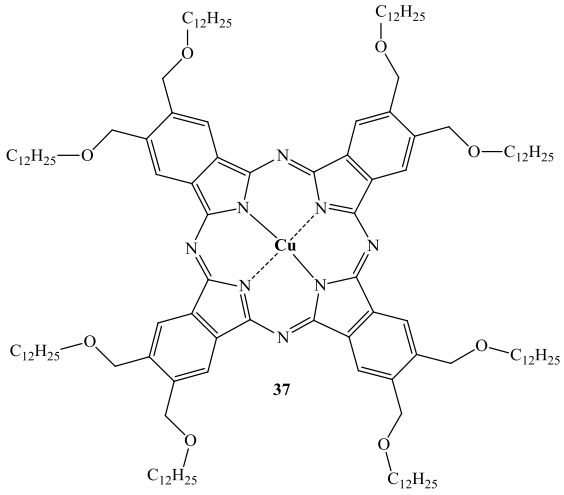


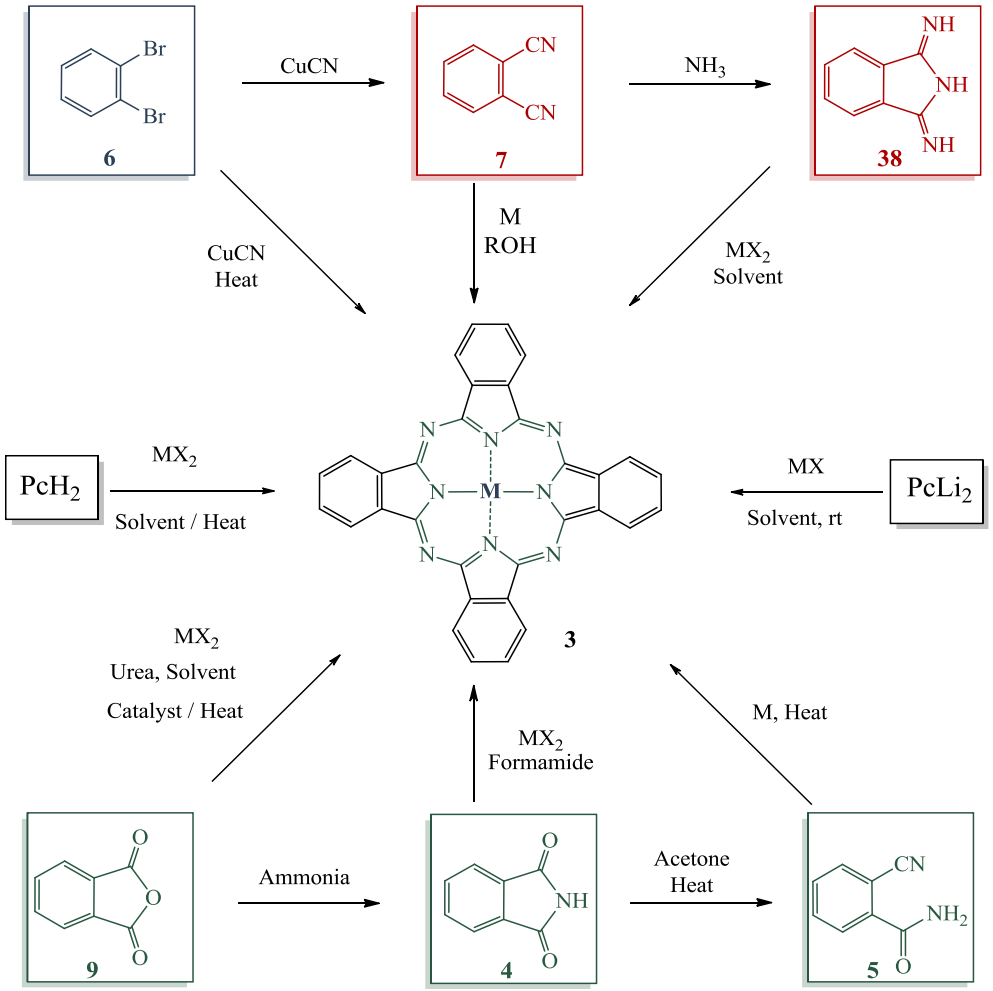
Figure 1.11: First liquid-crystalline phthalocyanine.

1.8 Synthesis of Phthalocyanines and its Phthalonitrile Precursors

1.8.1 General synthetic methods for the preparation of phthalocyanines

Various synthetic routes can be used to prepare Pcs and the method chosen is affected by several factors. For example, the type of phthalocyanine to be prepared (metal free or metallated, symmetrical or unsymmetrical), the nature of the functional groups attached (alkyl, alkoxyalkyl), and the kind of the metal ions inserted into the Pc macrocycle (metal salts, oxides, halides). Reaction conditions (solvents, temperatures,

catalysts and bases) can also influence the synthetic pathways to Pcs. Generally, Pcs can be prepared from the cyclotetramerisation of aromatic *ortho*-dicarboxylic acid derivatives, such as phthalonitrile (**7**), phthalic anhydride (**9**), phthalimide (**4**), *o*-cyanobenzamide (**5**), and diiminoisoindoline (**38**) in presence of metal salts for metallated Pcs and in the absence of the metal salts for the free-metal Pcs (Scheme 1.4).[7,8,78,107-110]



Scheme 1.4: Basic synthetic routes for preparing phthalocyanines.

Phthalonitrile **7** (1,2-dicyanobenzene) is the most commonly used precursor for preparing substituted phthalocyanines. Generally, this compound readily produces pure phthalocyanine complexes in good yields with nearly all the metals of the periodic table (except silver and mercury).[79] Most syntheses involve simply heating the phthalonitrile in a high boiling solvent such as quinoline, nitrobenzene, chlorobenzene or 1-chloro-naphthalene in the presence of a metal ion or metal salt.[80,111] Organic bases such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[112], 1,5-

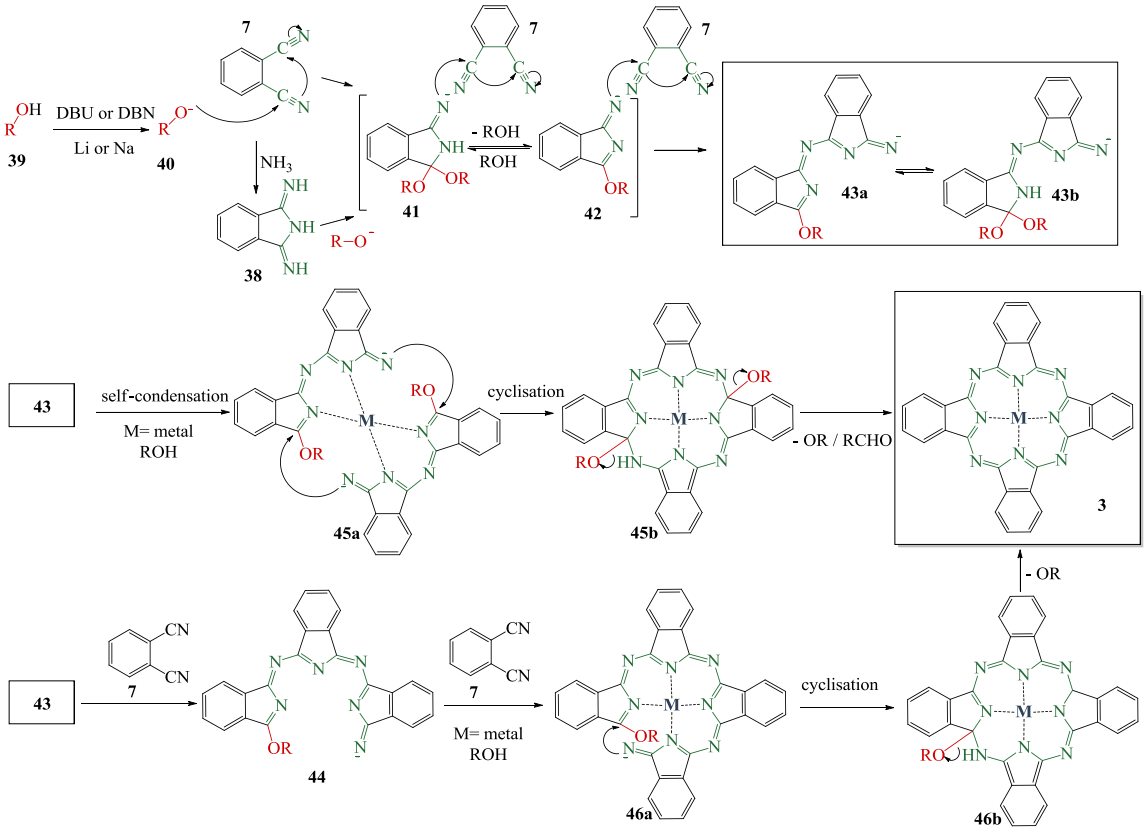
diazabicyclo[4.3.0]non-5-ene (DBN)[113], piperidine or cyclohexylamine can be used for the cyclotetramerisation of phthalonitriles in alcoholic solutions (e.g. pentanol, octanol), with the metal ion as template for the synthesis of metallophthalocyanines.[78] In addition, the refluxing solution of phthalonitrile with lithium, sodium or potassium alkoxide in an alcoholic solvent such as pentanol forms an alkali metal Pc.[7]

Alternatively, the reaction of phthalonitrile with ammonia forms the diiminoisoindoline which is then cyclised in the presence of metal salt and dimethylaminoethanol (DMAE) as solvent to form the metallophthalocyanine. Demetallation of MPcs using dilute aqueous acid forms the metal free phthalocyanine which can be turned into MPcs by refluxing in the presence of metal salts.[7,114,115] This alternative pathway is used to avoid the formation of by-products which are commonly produced with other strong bases. Recently, substituted Pcs can be prepared in a high yield in a very short period of time *via* microwave irradiation in the presence of suitable solvent.[116-120]

1.8.2 Mechanism of phthalocyanine formation

There are generally different suggested mechanisms for the phthalocyanine formation depending on the starting materials and the reaction promoters.[121,122] However, the mechanism is still not fully understood.[123-126] Scheme 1.5 describes the proposed mechanism for the formation of metallophthalocyanine in the presence of an alcohol from a phthalonitrile and diiminoisoindoline precursors.[124,127,128] Alcohol is assumed to be firstly deprotonated by some basic promoters such as DBU or DBN leading to strong nucleophillic alkoxide species **40**. An alkoxide ion attacks the nitrile or imide linkage in case of phthalonitrile and diiminoisoindoline, respectively. This obtains the monomeric alkoxyiminoisoindolenine intermediates[125] **41** and **42** which are suggested to react with further phthalonitrile molecule to form the dimeric intermediates[129] **43a,b**. Subsequently, the dimeric intermediates **43a,b** can react with another phthalonitrile molecule to produce the trimeric indolenine intermediate **44** which reacts with further phthalonitrile molecule to form **46a**. An alternative proposed mechanism involves the self-condensation of two half phthalocyanine units to form the tetrameric intermediate[130] **45a.** Cyclisation of intermediates **45** and **46** occur in the last step, to give a stable 18-π electron aromatic system. The cyclisation involves the nucleophilic attack on the aryl ether by the imide group (**45a**,**46a**) followed by the loss of an aldehyde and a hydride (**45b**,**46b**), leading to the formation of the

phthalocyanine molecule **3**.[125] The same mechanism is also proposed for the reactions, which involve the use of Li or Na.



Scheme 1.5: Mechanism of phthalocyanine formation.

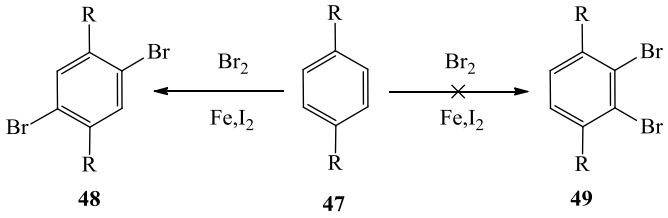
1.8.3 Synthesis of phthalonitriles

Phthalonitriles (1,2-dicyanobenzenes) are commonly favoured as phthalocyanine precursors and generally used in the laboratory scale syntheses, since they can be easily prepared *via* various synthetic routes. Phthalonitriles in particular can lead to mild, clean reaction process in high yields of pure phthalocyanine complexes, whereas the other precursors such as phthalimide and other phthalic acid derivatives lead to very unreliable yields. The most useful pathways for the synthesis of phthalonitriles have been reviewed[7,111,131] and are described below.

1.8.3.1 Synthesis of "non-peripherally" substituted phthalonitriles

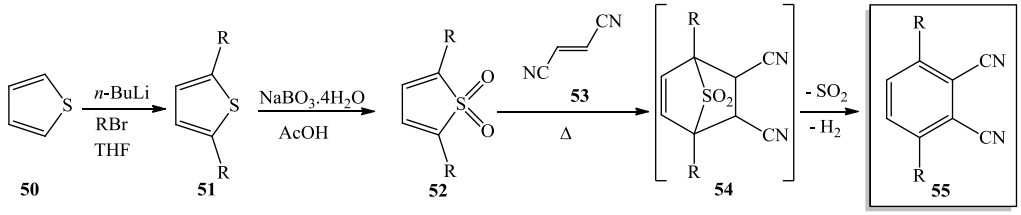
3,6-Dialkylsubstituted phthalonitriles **22** are synthesised *via* one of the three different methods shown in the schemes (Schemes 1.7, 1.8 and 1.9). All these routes have been developed at UEA by Cook and co-workers.[132] Direct electrophilic aromatic substitution onto 1,4-disubstituted benzene **47** cannot be used in the case of

preparation of 3,6-disubstituted phthalonitriles, due to the fact that the bromination of 1,4-disubstituted benzene derivatives favour the 2,5-positions **48** rather than the required 2,3-positions **49** (Scheme 1.6).



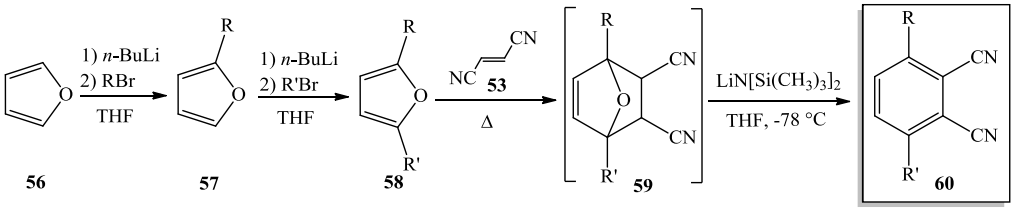
Scheme 1.6: Bromination of 1,4-disubstituted benzene **47**.

The Diels-Alder [4+2] cycloaddition reaction has been successfully used as a key step for the synthesis of 3,6-disubstituted phthalonitriles.[132,133] Fumaronitrile **53** is the most common dienophile used in synthesis of 3,6-dialkylphthalonitrile. The diene is 2,5-dialkylthiophene-1,1-dioxide **52** which can be prepared *via* dialkylation of thiophene **50** using *n*-butyllithium and an alkylating agent (e.g. RBr) in one step.[134] Oxidation of the dialkylated thiophene **51** was then achieved in order to obtain the corresponding sulphone **52**. Cycloaddition using fumaronitrile **53** was followed by *in situ* extrusion of sulfur dioxide and subsequent dehydrogenation to form the desired 3,6-dialkylphthalonitrile **55** (Scheme 1.7).[132,133,135]



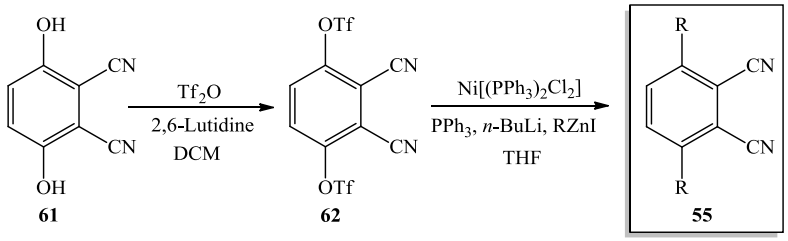
Scheme 1.7: Synthesis of 3,6-dialkyl phthalonitrile **55** *via* thiophene.

Furan **56** has similarly been used to synthesise 3,6-dialkylphthalonitriles **55** (Scheme 1.8).[132] The alkylation in this case was achieved through two steps and thus allows introduction of the second alkyl source into the molecule. The dialkylated product **58** then undergoes Diels-Alder reaction with fumaronitrile **53** giving the intermediate **59** which then dehydrates with the hindered base lithium bis(trimethylsilyl)amide to yield the desired 3,6-dialkylphthalonitriles **60**. This synthetic route is mainly used to prepare unsymmetrical 3,6-disubstituted phthalonitriles.[132] Moreover, other functional groups such as phenyl, alkenes, alkoxycarbonyls, *bis-ortho* esters , alkoxymethyls have been introduced onto the benzene ring using this procedure.[136]



Scheme 1.8: Synthesis of unsymmetrical substituted phthalonitrile **60** *via* furan.

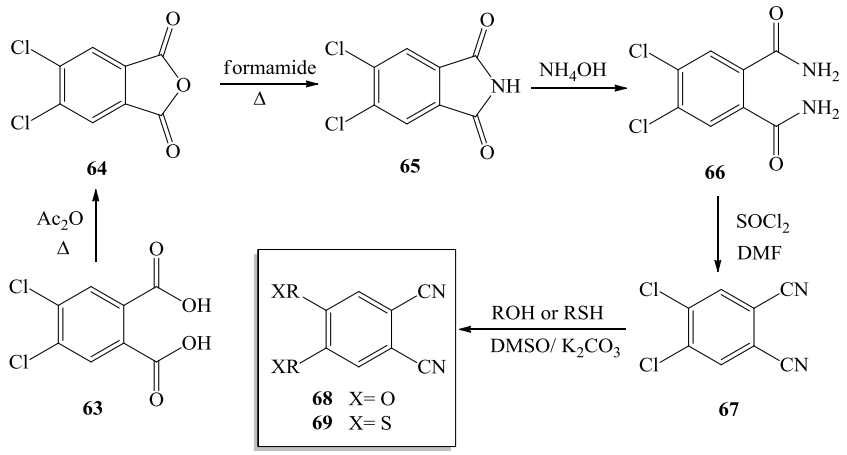
A recent procedure used for the synthesis of 3,6-dialkyl phthalonitrile **55** has been developed by Cammidge and Cook.[137] This route uses a Negishi[138] cross-coupling reaction between 3,6-phthalonitrile-bistriflate **62**, which is easily prepared from the commercially available 2,3-dicyanohydroquinone **61**, and an alkylzinc halide (Scheme 1.9) to yield the desired 3,6-dialkyl phthalonitrile **55**.[138-141]



Scheme 1.9: The Negishi cross-coupling route.

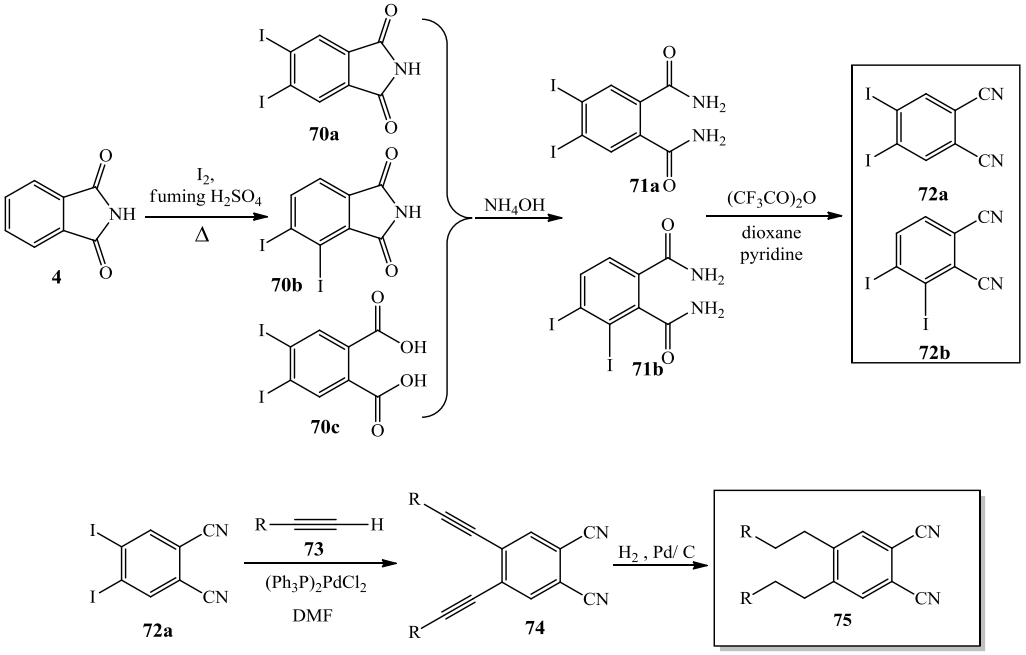
1.8.3.2 Synthesis of peripherally substituted phthalonitriles

A number of different methods are available for the synthesis of 4,5-dialkylphthalonitriles and have been reported in the literature.[114,137,142-145] For example, phthalic acid derivatives have been used as starting materials to prepare a number of 4,5-disubstituted phthalonitriles.[114] Wöhrle's method involves the conversion of 4,5-dichlorophthalic acid **63** into the corresponding dichlorophthalic anhydride **64** and the formation of dichlorophthalimide **65**. Formamide is used as a solvent and a source of ammonia during the formation of the phthalimide **65**. Addition of ammonia solution results in the formation of dichlorophthalamide **66** which is dehydrated using thionyl chloride and DMF to yield 4,5-dichorophthalonitrile **67** as shown in Scheme 1.10.[114] This compound **67** can react with a number of alcohols or thiols in a nucleophilic displacement reaction to give the desired 4,5-disubstituted phthalonitriles **68** and **69**.



Scheme 1.10: Synthesis of 4,5-disubstituted phthalonitriles *via* Wöhrle's method.

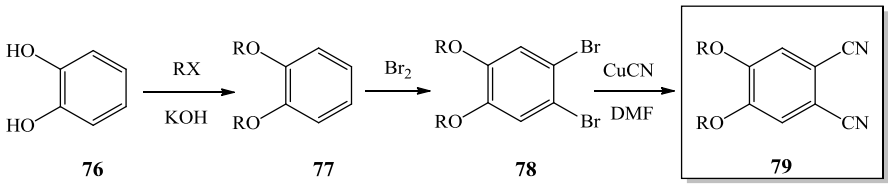
A similar method, developed by Leznoff and co-workers in 1996, has also been used to prepare 4,5-disubstituted phthalonitriles (Scheme 1.11).[143] The reaction starts with iodination of phthalimide **4** with formation of **70 (a,b,c)**. Ammonolysis was then followed to give **71(a+b)** which has been treated with trifluoroacetic anhydride in dry dioxane/ pyridine in order to obtain a mixture of diiodophthalonitriles **72(a+b)**. 4,5-diiodophthalonitrile **72a** has been used as starting material for the preparation of 4,5-disubstituted phthalonitriles. The introduction of the alkynyl substituents can be achieved by the Sonogashira cross-coupling reactions between alkynes **73** and 4,5-diiodophthalonitrile **72a** to give **74**. Reduction of this compound **74** leads to formation of the target 4,5-dialkylphthalonitriles **75**.



Scheme 1.11: Synthesis of 4,5-dialkylphthalonitriles **75** *via* Leznoff's route.

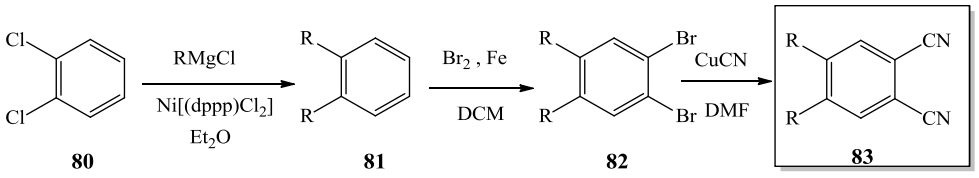
4,5-Dihalogenated phthalonitriles considered as good substrates for transition metal catalysed cross-coupling reactions. 4,5-Disubstituted phthalonitriles have also prepared from the halogenated starting materials *via* palladium catalysed Heck,[143] Stille,[146] and Suzuki[147] cross-coupling reactions.

4,5-Alkoxysubstituted phthalonitriles can be prepared by alkylation and Rosenmund-von Braun reactions. [95,142,148] For example, 4,5-dialkoxyphthalonitrile can be prepared by simple alkylation of commercially available catechol **76** followed by the bromination reaction to form 1,2-dibromo-4,5-dialkoxybenzene **78**. Finally, cyanation of dibromide **78** can be achieved using CuCN to give the corresponding 4,5-dialkoxy phthalonitrile **79** (Scheme 1.12).



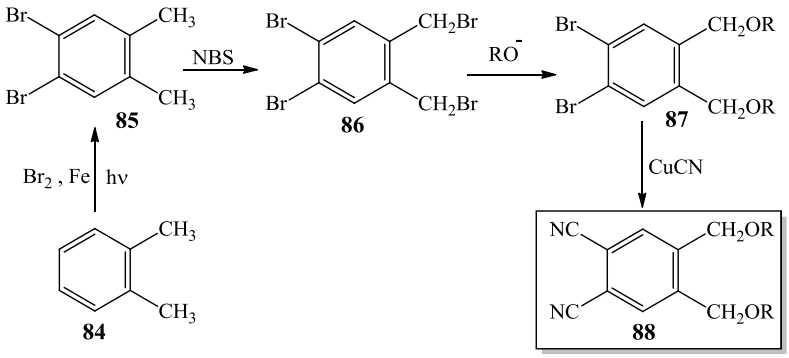
Scheme 1.12: Synthesis of 4,5-dialkoxyphthalonitrile **79**.

An alternative route to the Rosenmund-von Braun cyanation for the preparation of 4,5-dialkylphthalonitrile[149] starts with Kumada-coupling[150] between 1,2-dichlorobenzene **80** and the Grignard reagent to give **81,** followed by bromination and finally cyanation to yield the target 4,5-dialkylphthalonitrile **83** (Scheme 1.13).[149]



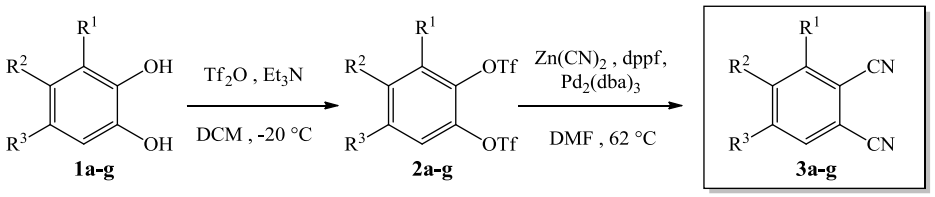
Scheme 1.13: Synthesis of 4,5-dialkylphthalonitrile **83** *via* Kumada-coupling.

Preparation of 4,5-dialkoxymethylphthalonitrile precursors have also been widely studied.[151-154] Bromination of *o*-xylene **84** led to formation of 4,5-dibromo-o-xylene **85** which is followed by free radical bromination of the side chains using NBS to form **86**. The nucleophilic substitution of the bromide by alkoxy groups for the side chains, is then achieved to give **87** which then undergoes the Rosenmund-von Braun reaction to form the target 4,5-bis(alkoxymethyl)phthalonitrile **88** (Scheme 1.14).



Scheme 1.14: Synthesis of 4,5-bis(alkoxymethyl)phthalonitrile **88**.

The Rosenmund-von Braun reaction has been used for preparation a wide range of 4,5-disubstituted phthalonitrile derivatives, but disadvantages result in the development of other synthetic strategies. An alternative route was developed by Hanack *et al.* in which the triflated catechols were converted into their corresponding nitriles.[144] Cyanation of triflates was achieved using tris(dibenzylideneacetone) dipalladium as a source of palladium (0) and DPPF as ligand. The reaction was carried out in DMF and zinc cyanide was added portionwise to the reaction mixture over a prolonged period (Scheme 1.15). The use of zinc cyanide as source of cyanide minimizes the concentration of free cyanide (a poison for the catalyst). No product was obtained when the zinc cyanide was added in one portion. These reaction conditions have been successfully adapted for the formation of phthalonitriles from dihalides with good yields of the products.[144,155,156] Overall, the palladium-catalysed cyanations of aryl triflates or halides are highly valuable strategies for synthesis of phthalonitriles.



	R^1	R^2	R^3
1a, 2a, 3a	H	CH_3	H
1b, 2b, 3b	CH_3	H	H
1c, 2c, 3c	H	CO_2Et	H
1d, 2d, 3d	$(CH_2)_4CO_2Me$	H	H
1e, 2e, 3e	H	$CH_2CH(NHBoc)CO_2Me$	H
1f, 2f, 3f	H	$C_2H_4CO_2Et$	$C_2H_4CO_2Et$
1g, 2g, 3g	H	-CH=CH-CH=CH-	-CH=CH-CH=CH-

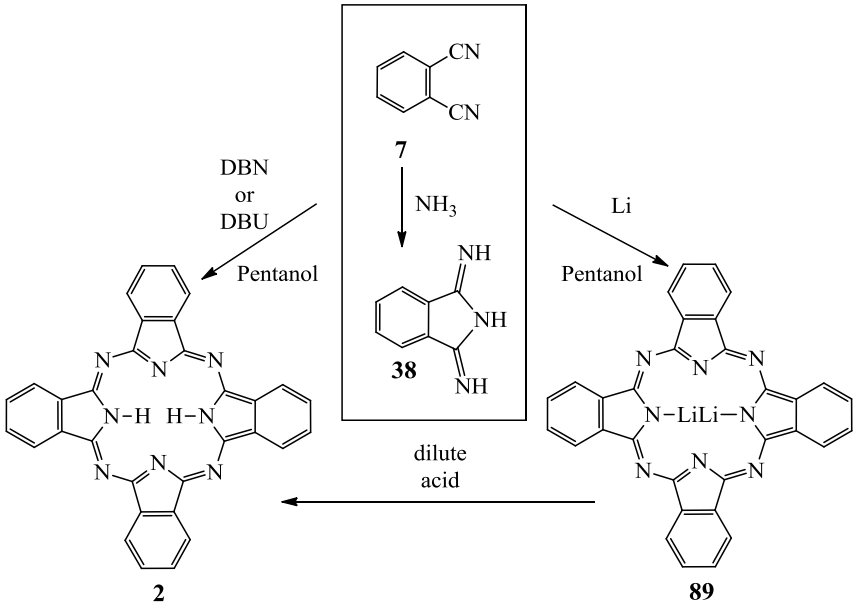
Scheme 1.15: Synthetic route using the Hanack reaction.

We have thus addressed most of the potential approaches of the preparation of peripherally and non-peripherally substituted phthalonitrile precursors which can result in formation of the corresponding phthalocyanines which are discussed in next section.

1.8.4 Synthesis of phthalocyanines

1.8.4.1 Synthesis of unsubstituted metal-free phthalocyanines (PcH_2)

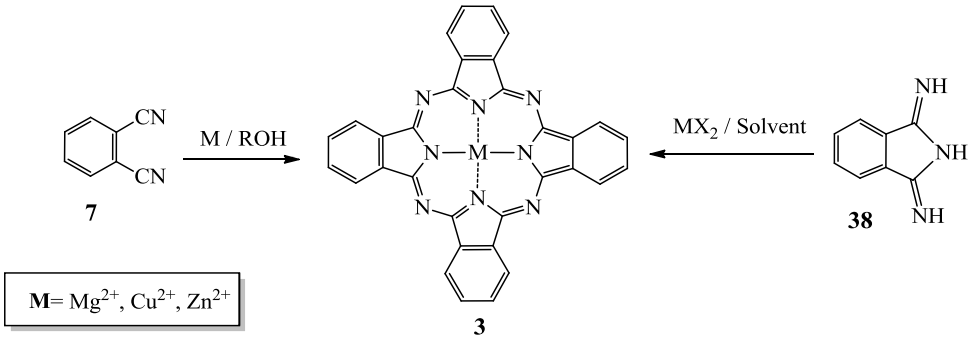
Metal-free phthalocyanine is obtained by cyclotetramerisation of phthalonitrile. A typical synthetic method involves the treatment of phthalonitrile **7** with ammonia and sodium metal in methanol under the mild conditions to form 1,3-diiminoisoindoline **38** which is then condensed in a reducing solvent such as dimethylaminoethanol (DMAE), to form PcH_2 **2**. Non-nucleophilic hindered bases such as 1,8-diazabicyclo[4.3.0] non-5-ene (DBN) and 1,8-diazabicyclo [5.4.0] undec-7-ene (DBU) can also be used for the preparation of metal-free Pcs from phthalonitriles in either a melt or in pentanol solution. Alternatively, PcH_2 can also be prepared by refluxing phthalonitrile and lithium metal in pentanol to form $PcLi_2$ **58**, which is then treated with dilute acid, to produce PcH_2 **2** (Scheme 1.16).[114]



Scheme 1.16: Synthesis of unsubstituted demetallated phthalocyanine.

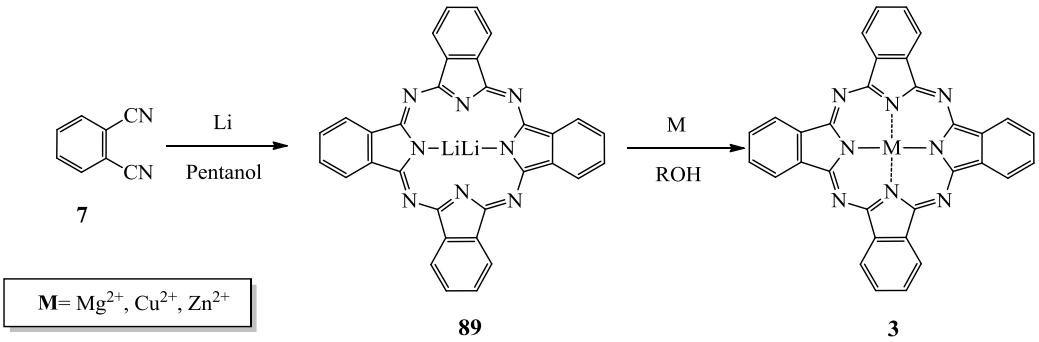
1.8.4.2 Synthesis of unsubstituted metallated phthalocyanines (MPc)

Unsubstituted metallated phthalocyanines can be prepared from the cyclotetramerisation of phthalonitrile or diiminoisoindoline in the presence of the metal salts (MX_n) (Scheme 1.17).[7]



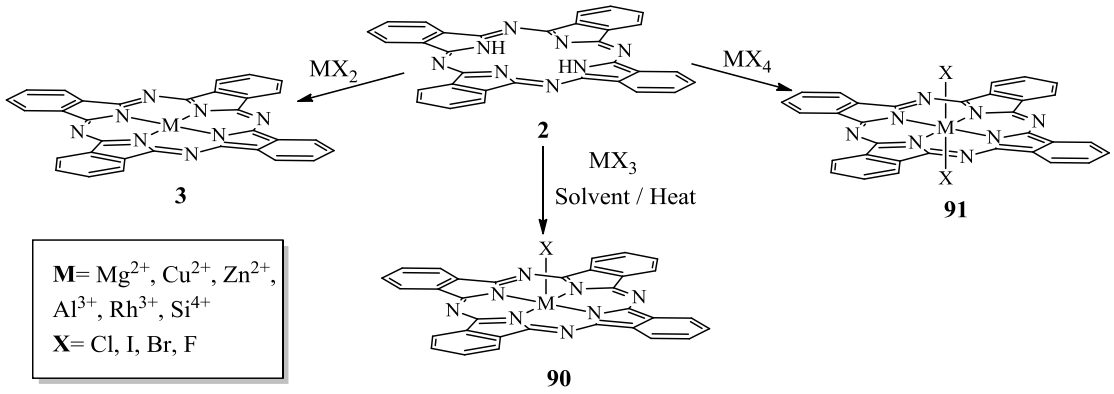
Scheme 1.17: Synthesis of unsubstituted metallated phthalocyanine.

Alternatively, MPcs can also be prepared by treating phthalonitrile with lithium metal to form Li_2Pc which can be undergone the metal-ion-exchange reaction to form MPcs (Scheme 1.19).[7]



Scheme 1.19: Formation of MPcs using metal-ion-exchange reaction.

It also could be prepared by the reaction of PcH_2 with a suitable metal salt (MX_2, MX_3, MX_4) in a high boiling point solvent such as quinoline or 1-chloronaphthalene to ensure complete metallation (Scheme 1.18).[7]



Scheme 1.18: Synthesis of MPcs.

Many ions (e.g. Fe^{2+}, Si^{4+}, Mg^{2+}, Al^{3+}) can be accommodated into the phthalocyanine core, however, the most common metals inserted in Pc core are of a +2 oxidation state. PcM complexes with central metals in a +3 or +4 oxidation state are able to link one or two axial ligands. These complexes exhibit improved solubility in common organic solvents and reduce the intermolecular interaction.[7]

1.8.4.3 Synthesis of substituted phthalocyanines

The solubility of unsubstituted MPc and H_2Pc is low in common organic solvents. Enhancement of solubility in common organic solvents can be achieved by introducing substituents onto the four benzo rings of the Pc core at the peripheral sites (2,9,16,23 or 2,3,9,10,16,17,23,24) or non-peripheral positions (1,8,15,22 or 1,4,8,11,15,18,22,25) (Figure1.12).[7]

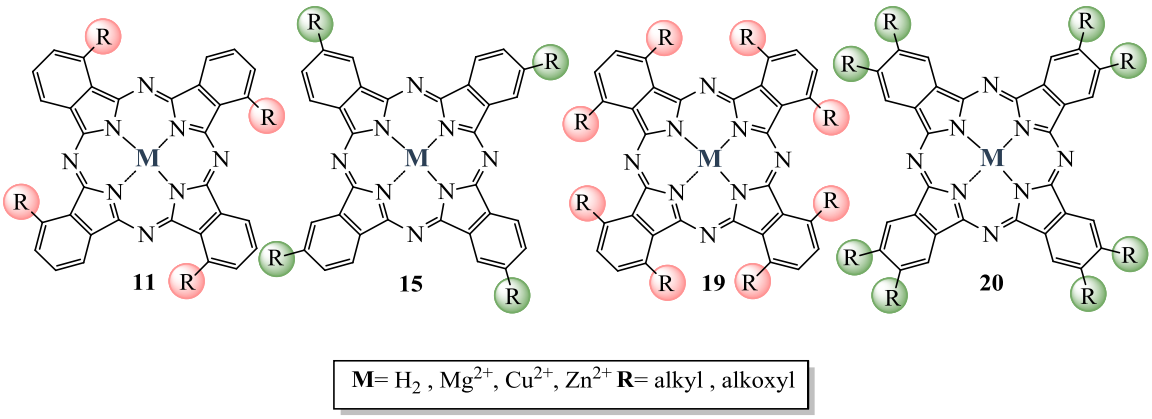


Figure 1.12: The structures of peripheral 2,9,16,23-tetra-substituted Pc **15**; 2,3,9,10,16,17,23,24-octa-substituted Pc **20** and non-peripheral 1,8,15,22-tetra-substituted Pc **11**; 1,4,8,11,15,18,22,25-octa-substituted Pc **19**.

Substituents on the four benzo rings can be divided into two different classes; symmetrical and unsymmetrical substituted Pcs (Figure 1.13). These are discussed in sections 1.8.4.3.2 and 1.8.4.3.3 in more details.

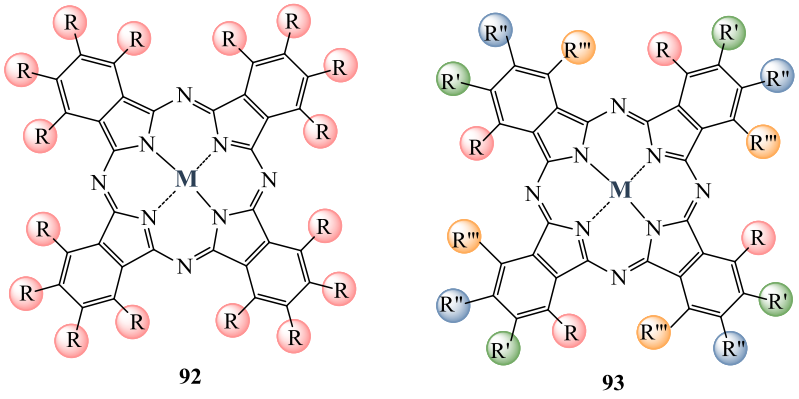
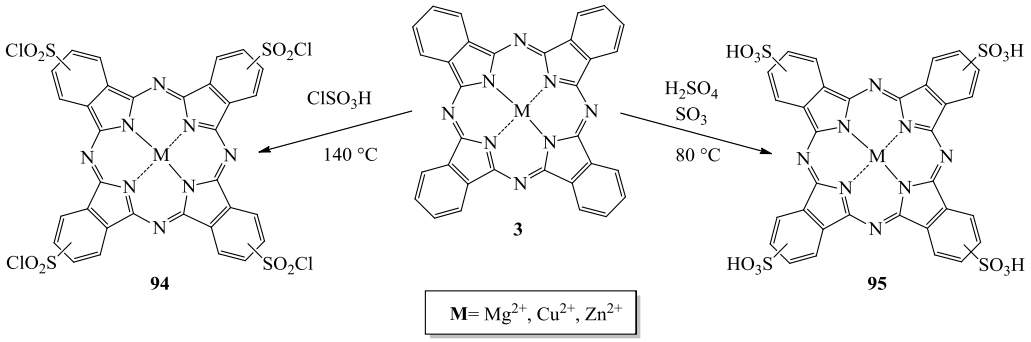


Figure 1.13: Examples of the structures of symmetrical **92** and unsymmetrical **93** substituted Pcs.

1.8.4.3.1 Direct incorporation of substituents on the preformed unsubstituted phthalocyanines

Substituted Pcs can be prepared by the direct electrophilic aromatic substitutions of the preformed Pcs, such as the preparations of halogenated and sulfonated Pc derivatives. These procedures usually give a mixture of substituted Pcs which are really difficult to separate. These mixtures are commonly used as colour pigments in the dye industry. Examples of these reactions are shown in Scheme 1.19.[7,108]

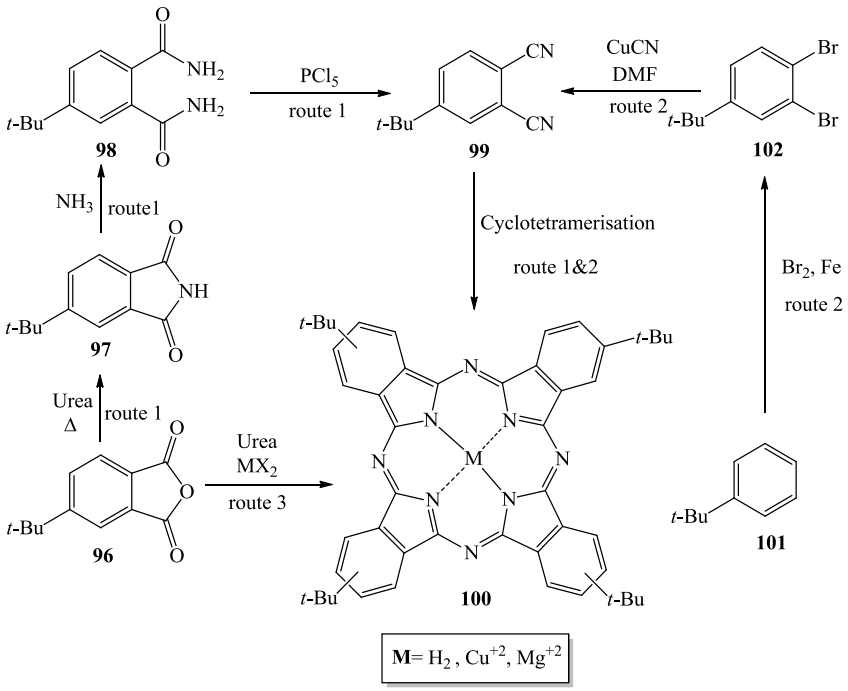


Scheme 1.19: Examples of the electrophilic aromatic substitutions of the Pcs.

1.8.4.3.2 Synthesis of symmetrical substituted phthalocyanines

1.8.4.3.2.1 Tetra-substituted Pcs

Due to the failure of chemists to produce a single pure substituted Pc using the direct electrophilic substitutions, they started to discover other synthetic strategies to obtain pure substituted Pcs. They widely studied tetra-*tertiary*-butyl Pc, which is a good example to prepare the symmetrical tetra-substituted Pcs because their high solubility in common organic solvents due to the four bulky substituents in benzo rings. In 1971, tetra-*tertiary*-butyl Pc was first prepared by Mikhalenko *et al.*[157] as shown in Scheme 1.20 (route 1). The synthesis of this Pc started from 4-*t*-butylphthalic anhydride **96**, and after three steps gave the tetra (*t*-butyl) Pc **100**. It also was prepared by Kovshev *et al.*[158] in 1976 starting from bromination of *t*-butylbenzene **101** to give **102** which was treated with CuCN in DMF to form **99**. Cyclotetramerisation of **99** gave the target Pc **100** (Scheme 1.20, route 2). Alternatively, tetra-*t*-butylphthalocyanines can also be achieved in one step *via* cyclotetramerisation of 4-*t*-butylphthalic anhydride **96** with metal salts and urea (Metz *et al.*, 1984)[159] (Scheme 1.20, route 3).[7]

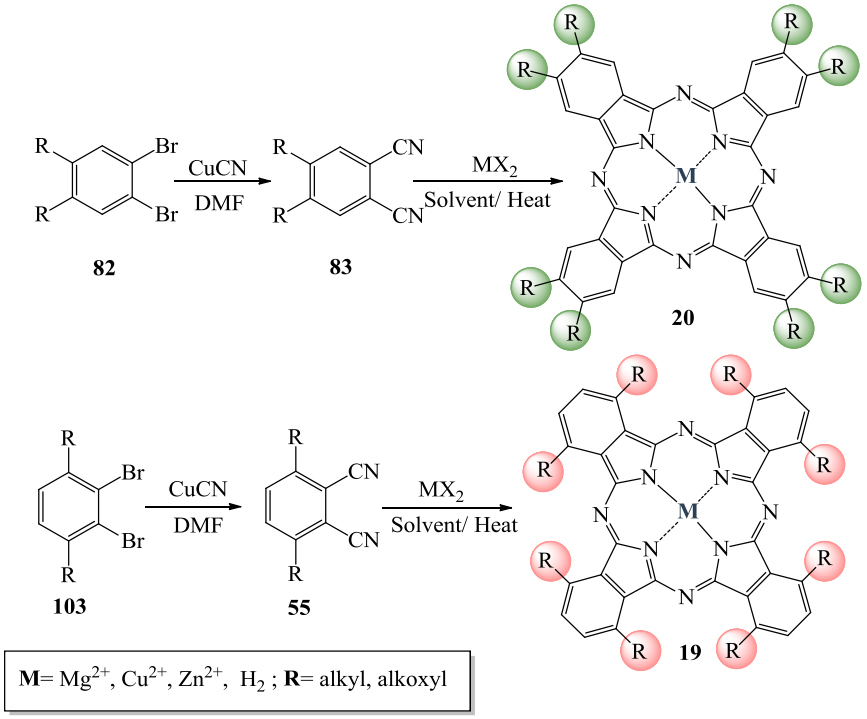


Scheme 1.20: Synthesis of tetra-*tertiary*-butyl Pc.

Typically, a mixture of four isomers is generated in this reaction which are extremely difficult to separate. In 1996, Hanack's group[41] demonstrated that the separation of these isomers can be accomplished using a high performance liquid chromatography (HPLC).[7]

1.8.4.3.2.2 Octa-substituted Pcs

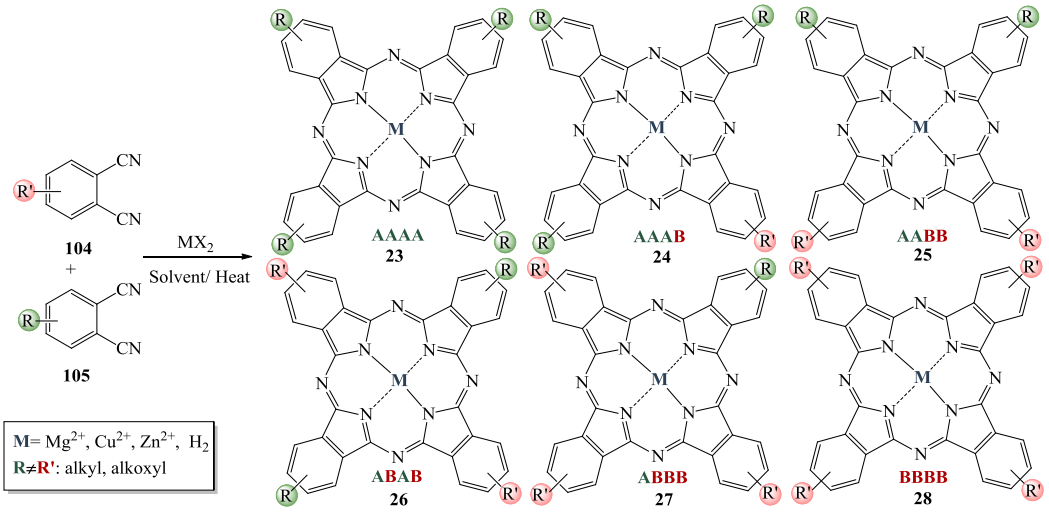
Octa-substituted Pcs are typically prepared from 4,5-disubstituted phthalonitriles **83** or 3,6-disubstituted phthalonitriles **55** precursors. Once reasonable amounts of phthalonitrile precursors had been formed, which have been described in section 1.8.3, the peripherally **20** and non-peripherally **19** substituted phthalocyanine derivatives can be produced (Scheme 1.21).[7,160]



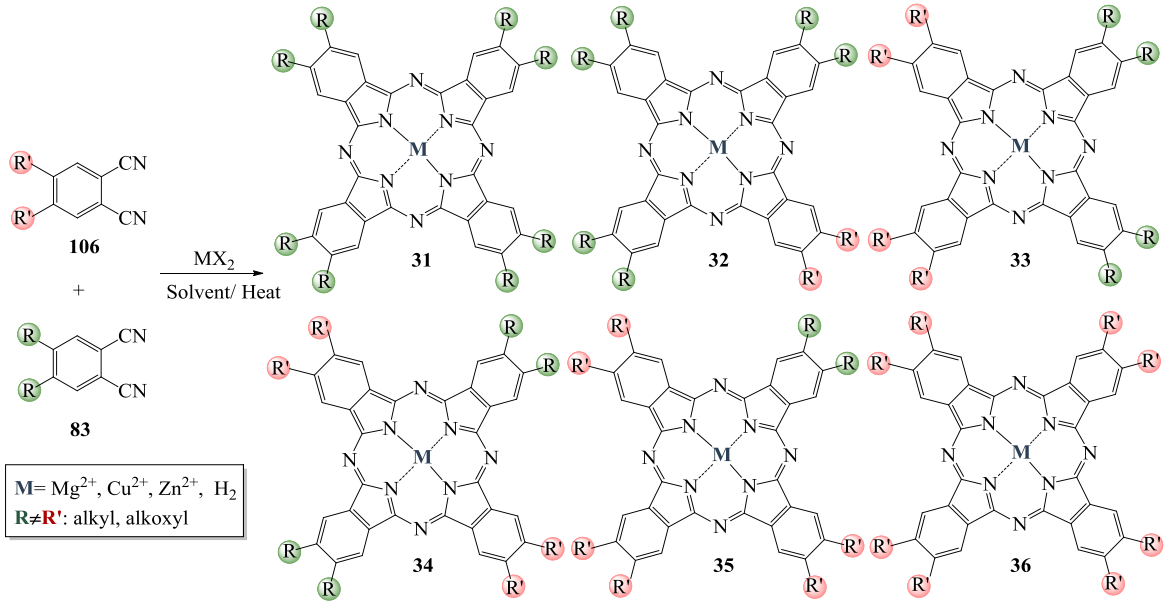
Scheme 1.21: Typical synthesis of symmetrical octa-substituted MPcs

1.8.4.3.3 Synthesis of unsymmetrical substituted phthalocyanines

Unsymmetrical substituted Pcs can be typically prepared by the cross-condensation of two different phthalonitriles or diiminoisoindolines using an appropriate ratio.[148] Typically, condensation of two differently precursors forms six different Pcs in the product mixture and this leads to difficulties in the separation and purification. A mixture of compounds that have a combination of very different functional groups can improve the separation. Increasing the yield of a particular unsymmetrical Pc can be achieved by controlling the ratio of the two phthalonitrile precursors. The synthetic pathways that are used to form unsymmetrical tetra-substituted and octa-substituted Pcs are shown in Scheme 1.22 and Scheme 1.23, respectively.[7]



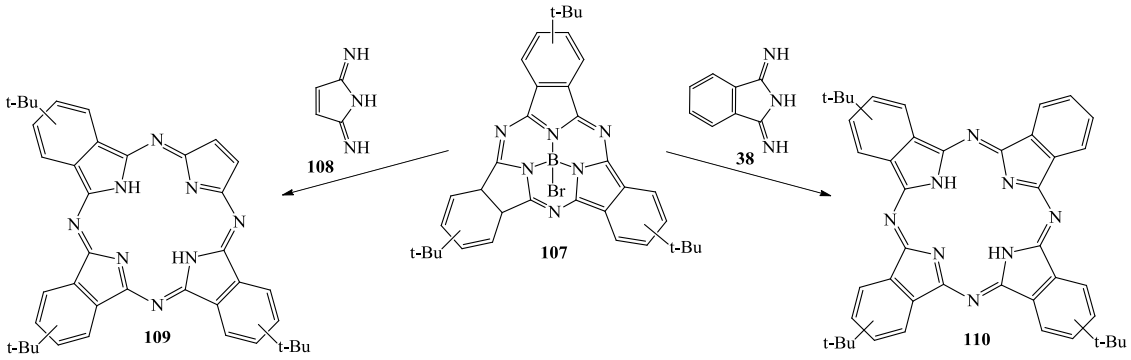
Scheme 1.22: Synthesis of tetra-substituted Pcs from the cross-condensation of two different mono-substituted phthalonitriles.



Scheme 1.23: Synthesis of octa-substituted Pcs from the cross-condensation of two different di-substituted phthalonitriles.

A new synthetic route for the preparation of unsymmetrical substituted Pcs was reported by Kobayashi[161] and co-workers in 1990. They found that the subphthalocyanine undergoes ring expansion reaction when treated with 1,3-diiminoisoindolines or their analogues, producing the metal-free or metallated

unsymmetrical substituted Pcs. Examples of this new route are illustrated below (Scheme 1.24).[161]



Scheme 1.24: Subphthalocyanine ring expansion method for the preparation of the unsymmetrical substituted Pcs.

1.8.4.3.4 Synthesis of benzannulated phthalocyanines: expansion of the π-system

Benzannulated phthalocyanines are analogs of phthalocyanines which possess an additional four benzo groups fused to the peripheral benzo groups of the Pc macrocycles, such as 2,3-naphthalocyanine (Nc) **111**, **112** (Figure 1.14).[16,162-166]

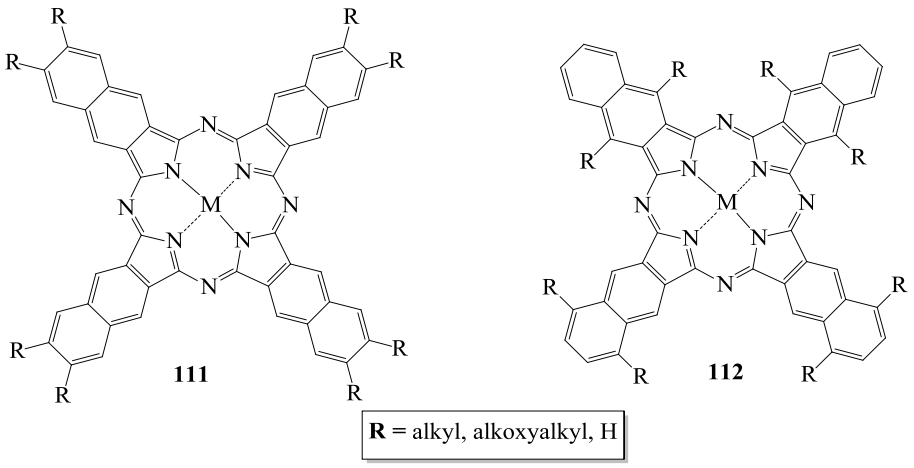
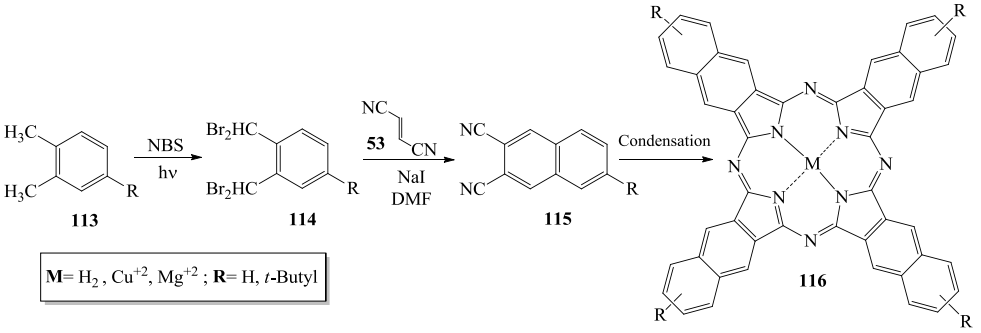


Figure 1.14: Examples of benzannulated phthalocyanines.

Synthetic approaches to phthalocyanines with an extended system of π-electron conjugation are carried out under similar conditions to those of general phthalocyanine synthesis. An example of this strategy is illustrated in Scheme 1.25. The preparation involves the bromination of substituted 3,4-dimethylbenzene **113** to form 1,2-bis(dibromomethy1)benzene **114** which then treaded with fumaronitrile **53**

and sodium iodide undergoing an elimination-Diels-Alder reaction to give the substituted 2,3-dicyanonaphthalene precursor **115**. The cyclotetramerisation of this precursor **115** results in the formation of the target 2,3-naphthalocyanine **116**.[165,166] The unique physical and chemical properties of these complexes are generally because of their extended π-electron conjugated systems. For instance, their Q-bands in the electronic absorption spectra are shifted to red region (bathochromic shift) by approximately 90 and 170 nm, depending on central metal atom, as compared to the corresponding phthalocyanines.[75,167]



Scheme 1.25: Preparation of tetra-substituted naphthalocyanine.

Extension of the molecular π-system can also be achieved *via* replacement of the benzene rings of phthalocyanines by triphenylene and perylene units. The resulting materials (triphenylenophthalocyanines **117** and perylenophthalocyanines **118**; Figure 1.15) exhibit a bathochromic shift to the long wavelength in the UV-Vis spectrum owing to improved π-conjugated system in the molecules in comparison with the phthalocyanines **119** synthesised by Simon *et al.*[169] and phthalocyanine **3** itself. These molecules show discotic liquid crystalline behaviors due to their large and flat aromatic cores. The first heavily substituted triphenylenophthalocyanines were reported at UEA by Cammidge *et al.* in 2002, whereas the first perylenophthalocyanines were synthesised in 2006 by the same group.[76,168,170]

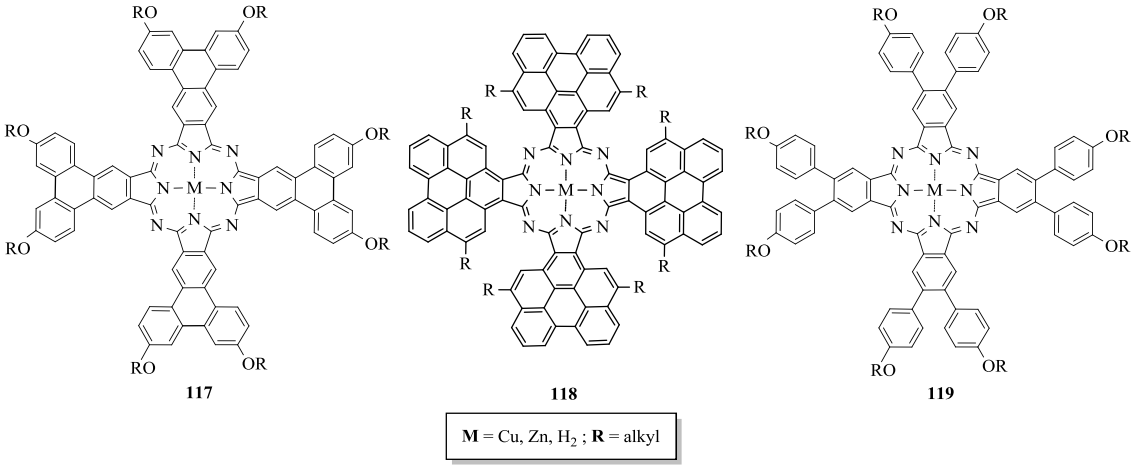
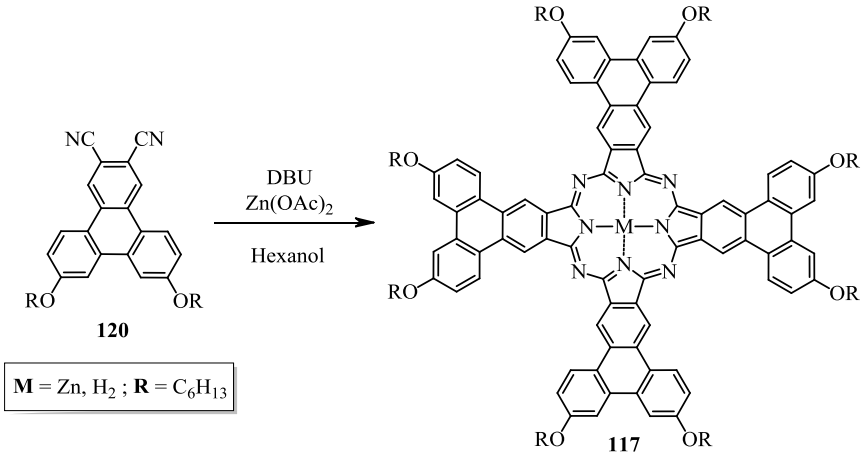


Figure 1.15: π-Extended Pcs prepared by Cammidge and Pcs synthesised by Simon.

Preparation of these materials from their phthalonitrile precursors was achieved using procedures showed below. Once the phthalonitrile precursors were prepared successfully, the corresponding benzannulated phthalocyanines can be accomplished by heating dinitriles with metal salts and bases in refluxing alcohol. An example of the preparation of triphenylenophthalocyanine is illustrated in Scheme 1.26.[76]



Scheme 1.26: Synthesis of triphenylenophthalocyanine.

1.9 Introduction to Tetrabenzo(aza)porphyrin Hybrids

Porphyrin – phthalocyanine hybrids known as *Tetrabenzo(aza)porphyrins* are a set of compounds that are structurally related to the phthalocyanine **2** and porphyrin **1** macrocycles. They are rarely studied compared to the corresponding phthalocyanines which are well studied and known for over 70 metals and metalloids. Phthalocyanine can undergo two different classes of structural amendments. Modifications of the 18 π-electrons central core themselves by replacement of one, two or three of the four aza-nitrogen bridges by methine (CH) bridges leads to the formation of different types of hybrid macrocycles: tetrabenzotriazaporphyrin (**TBTAP**), *cis*- and *trans*-tetrabenzodiazaporphyrin (**TBDAP**), tetrabenzomonoazaporphyrin (**TBMAP**) and tetrabenzoporphyrin (**TBP**), which are shown in Figure 1.16. Further modifications can be obtained when the additional heterocyclic rings are fused to the benzene rings of the phthalocyanine macrocycles resulting in formation of novel phthalocyanine analogues which were explained above in section 1.8.4.3.4.[16]

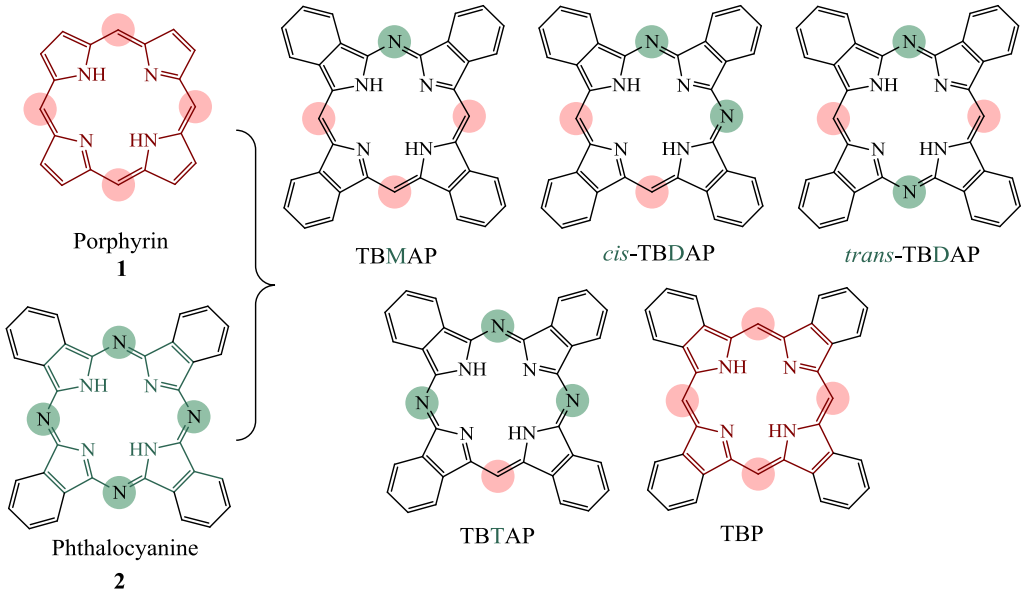


Figure 1.16: Phthalocyanine/ porphyrin analogues.

The nomenclature that is used to describe the tetrabenzo(aza)porphyrin macrocycles refers to the phthalocyanine and porphine numbering systems.[172] The numbering of the atoms on a tetrabenzo(aza)porphyrin is illustrated in Figure 1.17. Therefore, the substituents on the benzenoid rings of the tetrabenzo(aza)porphyrin system were

numbered similarly to those of the phthalocyanine system **3**, whereas the locations of the imino nitrogen atoms were termed based on those of fused tetrapyrroles. The letters *b*, *g*, *l* and *q* refer to the positions of the fused benzene rings on the pyrrole in the porphyrin ring, lettering beginning with "*a*" for the side (1,2), "*b*" for (2,3) and lettering every side around the periphery of the porphyrin inner ring. The first letter of the alphabet was given to the side where the fusion happens.[171,172]

Similar to the phthalocyanines, tetrabenzo(aza)porphyrin hybrids possess sixteen possible sites of substituents on the macrocycle. Accommodation of substituents on the benzene rings at 2, 3, 9, 10, 16, 17, 23, 24 positions, are termed as the *peripheral* (*p*) sites, whereas those at positions 1, 4, 8, 11, 15, 18, 22, 25, called the *non-peripheral* (*np*) sites (Figure 1.17).

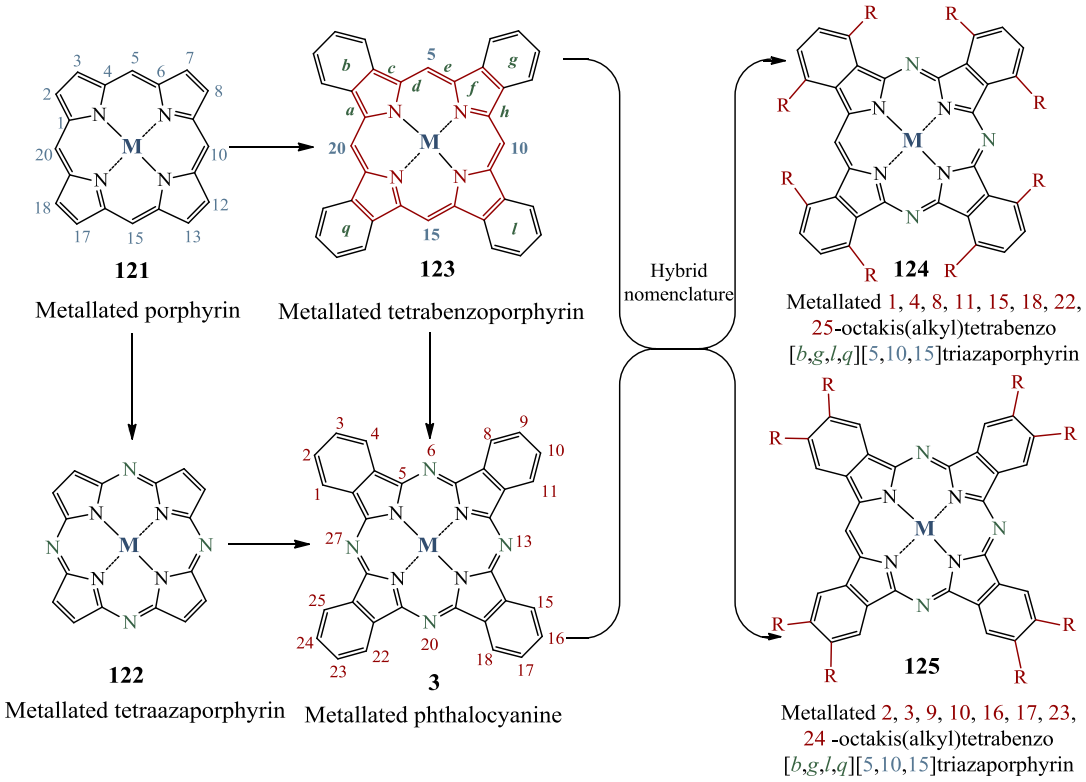
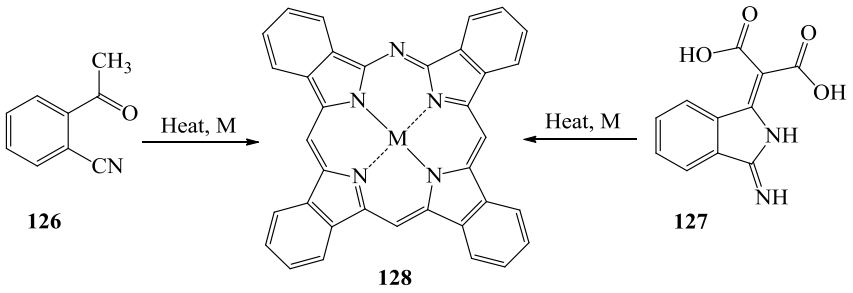


Figure 1.17: Combined nomenclature system for the peripheral and non-peripheral metallated tetrabenzo(aza)porphyrin macrocycles.

1.10 Discovery and Synthesis of Tetrabenzo(aza)porphyrins

These hybrid structures were discovered accidentally in 1934 when Lowe and Linstead studied the possibility of synthesis of *N*-alkylphthalocyanines from the reaction between methylmagnesium iodide and phthalonitrile. In their early

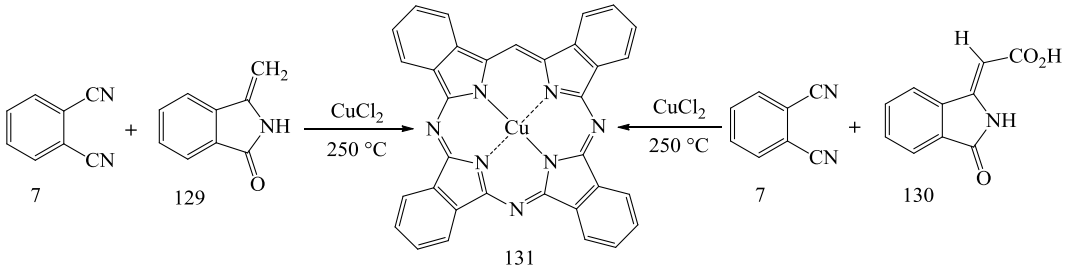
experiments, the resulting materials consisted of a phthalocyanine and a poor yield of side-product. A similar reaction was examined, using benzylmagnesium chloride and phthalonitrile, and yielded a phthalocyanine only. According to those results, they concluded that alkylphthalocyanines could not be prepared using that route. They were not be able either to further investigate the side-product that formed by the reaction between methylmagnesium iodide and phthalonitrile due to the poor yield.[5,173] In 1936, Fischer *et al*. reported the preparation of the first macrocyclic molecules that were structurally related to phthalocyanines, these molecules consisting of four pyrrole rings linked together by methine groups and nitrogen atoms.[174,175] Soon afterwards, in 1937, Helberger[176] announced the synthesis of similar macrocyclic molecules containing a benzene ring fused to each of the four pyrrole rings. He was able to prepare the copper derivatives of tetrabenzomonoazaporphyrin TBMAP and tetrabenzodiazaporphyrin TBDAP in 10 and 20% yields, respectively. CuTBMAP was obtained by heating an *o*-halogenoacetophenone with cuprous cyanide, whereas the CuTBDAP prepared by reacting phthalonitrile with cuprous cyanide and in this case, the *o*-cyanoacetophenone **126** was proposed as a key intermediate.[176] Later, Helberger and von Rebay declared similar results using of this preformed intermediate.[177] Linstead *et al*. reported that the preparation of these pigments could also be achieved using malonate derivative **127** which is considered as another useful intermediate in this synthesis (Scheme 1.27).[178]



Scheme 1.27: Synthesis of MTBMAP *via o*-cyanoacetophenone and malonate derivative intermediates.

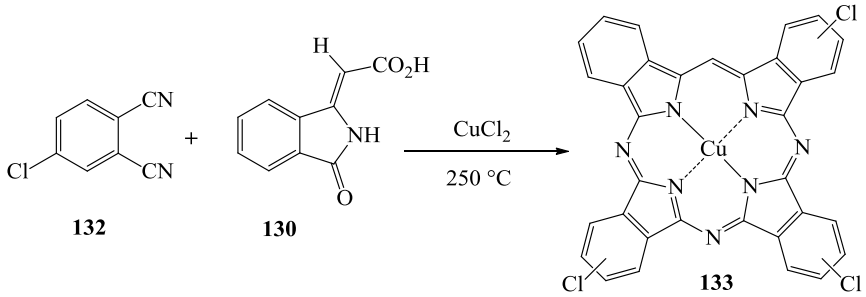
A year later, a better yield of the copper derivative was obtained by Dent.[179] The reaction was achieved by condensation of an equimolar amount of phthalonitrile **7** and either 3-methylenephthalimidine **129** or its carboxylic derivative phthalimidine acetic acid **130** at 250 °C, in the presence of a copper salt. It readily gave a 30% yield of a new pigment greener than, but otherwise similar in properties to, the corresponding

CuPc. This pigment was identified as CuTBTAP **131** (Scheme 1.28). Dent was unable to prepare the other hybrid molecules with more than one methine group (e.g. CuTBDAPs or CuTBMAP) under the same reaction conditions.



Scheme 1.28: Synthesis of CuTBTAP by condensation of phthalonitrile and either methylenephthalimidine **129** or phthalimidine acetic acid **130**.

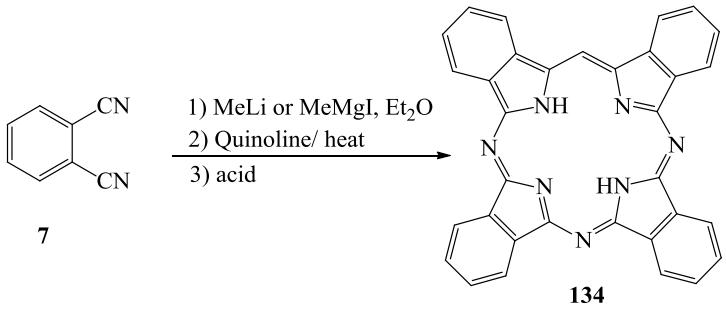
Moreover, the reaction stoichiometry was examined for example; using 3 moles of phthalonitrile with 1 mole of phthalimidine acetic acid and 1 mole of cuprous chloride gave a reasonably good yield (70-80%) of the CuTBTAP with a small impurity of copper phthalocyanine, whereas no green pigment was obtained when using a 1:3 ratio of phthalonitrile to phthalimidine acetic acid. In addition, varying precursors were investigated such as using 4-chlorophthalonitrile as precursor and condensed with phthalimidine acetic acid in the presence of cuprous chloride under the same previous conditions formed a Cl_3-CuTBTAP which containing three phthalonitrile units and one methylenephthalimidine unit (Scheme 1.29).[179]



Scheme 1.29: Synthesis of Cl_3-CuTBTAP using 4-chlorophthalonitrile as precursor.

In view of these developments, Linstead and co-workers re-examined the reaction between phthalonitrile and organometallic reagents in the hope of obtaining and fully characterising the previously formed green side-product. The synthesis of this unknown green product was found to be somewhat complicated; however, a successful synthetic method was generated after several experimental attempts.[2-5,173] The synthetic technique was found to consist of two main steps. The first step was the

initial reaction between phthalonitrile and either methyllithium or methylmagnesium iodide as an organometallic source in a low-boiling ethereal solvent at room temperature that leads to formation of a coloured intermediate. It was observed at this step that if the reaction was followed by an acid work-up the product could be decomposed and it was difficult to isolate any pigment. The following step was the removal of the solvent and heating the mixture at a high temperature in a high-boiling solvent, such as quinoline, *α*-naphthyl methyl ether or cyclohexanol that gives rise to a green product known as MgTBTAP. Quenching the resulting materials by means of an acid following the final step led to remove the magnesium from the central cavity of TBTAP and thus allowed other elemental ions, such as lithium, nickel, copper, iron, or zinc to be accommodated. A metal-free TBTAP was isolated in a 40% yield as a green crystalline form (Scheme 1.30). The identity of the product as metal-free TBTAP has been confirmed by spectral analysis, quantitative oxidations and X-ray diffraction.[173]

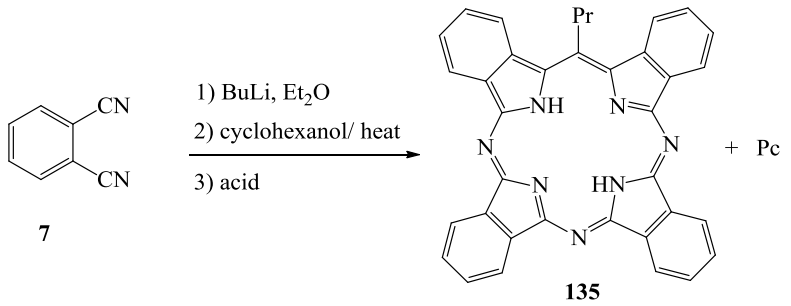


7 **134**

Scheme 1.30: Synthetic route for preparing metal-free TBTAP.

According to the demonstration introduced by Gilman *et al.* which explained the reactivities of organolithium and organomagnesium compounds toward the certain aromatic nitriles.[180] They found that certain aromatic nitriles are more readily attacked by methyllithium than by methylmagnesium iodide. Linstead was also able to prepare 15% yield of the TBTAP derivative from the reaction between the phthalonitrile and an equimolar amount of methyllithium using the two-steps procedure described above. Formation of lower nitrogen-containing compounds (i.e. tetrabenzodiazaporphyrin TBDAP) can be obtained, when methyllithium was used instead of methylmagnesium iodide, along with TBTAP and an amount of phthalocyanine. However, using *n*-butyllithium in an attempt to introduce a propyl group at the *meso*-position resulted in formation of a mixture of TBTAP and Pc (Scheme 1.31). Unfortunately, pure TBTAP could not be isolated from the phthalocyanine side-product.[181] This agreed with the

earlier results achieved from the use of other bulky Grignard reagents. In other words, the tendency of organometallic compounds to obtain pigments containing methine (CH) bridges is greatest when methyl organometallic derivatives are used.[173] However, due to these unsuccessful attempts, the introduction of substituents at the *meso*-position was not examined until much later.

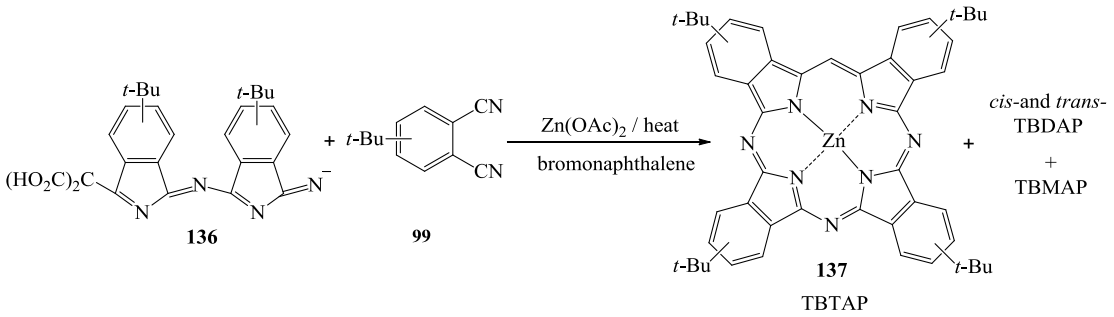


7 **135**

Scheme 1.31: Linstead's attempt to introduce a propyl group at the *meso*-position of TBTAP.

Furthermore, Linstead found that when treating the phthalonitrile with a slight excess of methylmagnesium iodide, the yield of phthalocyanine decreased while the yield of TBTAP increased. The same results were achieved when the methyllithium employed in place of MeMgI. When using a large excess of MeMgI, pigments containing more methine (CH) bridges were obtained (i.e. TBDAP).[173] Tetrabenzmonoazaporphin (TBMAP) can also be conveniently obtained in 17% yield, when excess of methylmagnesium iodide (2.5 moles) reacted with phthalonitrile at high temperature.[178]

The investigation of these hybrid materials and their properties was extremely challenging due to the low yield and poor solubility in common organic solvents. In order to study the properties of these hybrids, Luk'yanets and co-workers have investigated the preparation of these materials in order to obtain them in reasonable yield and high solubility in a wide range of organic solvents.[182] A *tert*-butyl group was introduced on the periphery of the hybrid macrocycle using a *t*-Bu-substituted dimeric isoindolic unit, which is the product from the condensation of potassium 4-*t*-butylphthalimide with malonic acid. The reaction of isolated intermediate **136** with phthalonitrile **99** in the presence of zinc acetate in bromonaphthalene as solvent at 280 °C gave rise to a mixture of the *tert*-butyl-substituted mono-, di-, and triaza analogues of zinc tetrabenzoporphyrin (Scheme 1.32).[182]

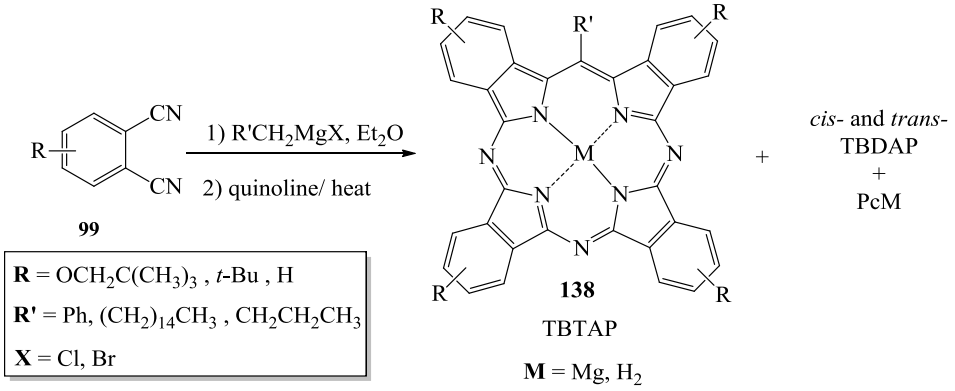


Scheme 1.32: Synthesis of zinc tetrabenzo(aza)porphyrin analogues by Luk'yanets.

For several decades, the tetrabenzo(aza)porphyrin analogues were prepared using the general cyclisation approaches with only minor modification. For example, Hoffman and co-workers subsequently reported the synthesis of NiTBTAP and CuTBTAP by means of Linstead's strategies.[183] Magnesium and cadmium derivatives were also generated from a mixture of phthalimidine acetic acid with either phthalonitrile or *o*-dicyanobenzamide.[184,185] More recently, Antunes and Nyokong have also used Linstead's procedures to prepare the metal-free tetrabenzotriazaporphyrin and then converted to the corresponding dihydroxyphosphorus derivative.[186]

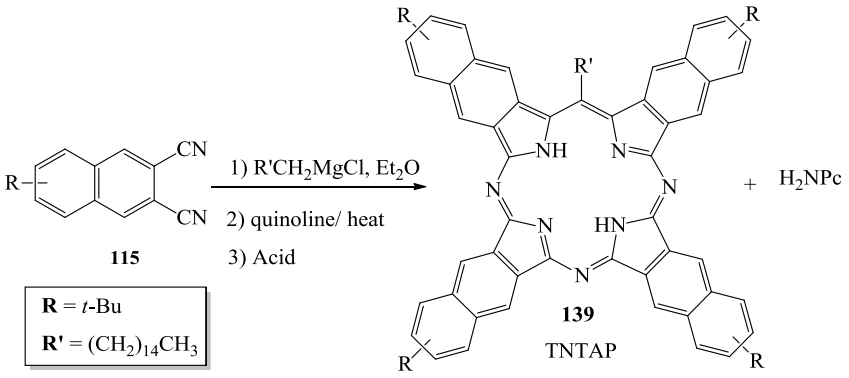
Deeper investigations of the synthesis of tetrabenzo(aza)porphyrins started to appear in the 1980's. A number of mixed cyclisations using substituted precursors were reported to give a variety of substituted hybrid derivatives.[185,187-189] Unsuccessful attempts to prepare these hybrid derivatives by combination of substituents in the *meso*-position led to a low interest in investigating these hybrids by several research groups at that time. However, a few years after the original reports, Leznoff and McKeown reinvestigated and described the preparation of a variety of *meso*-substituted TBTAPs from sterically hindered phthalonitriles with different Grignard reagents (Scheme 1.33).[190] The resulting materials consisted of a mixture of TBTAP, phthalocyanine and sometimes traces of TBDAP (*cis*- and *trans*- isomers). Introduction of long alkyl chains or bulky Grignard reagents led to improved possibility for separating this mixture and hence a pure *meso*-substituted TBTAP was isolated by means of chromatographic methods. It was observed that the synthesis of peripherally substituted TBTAPs using this route should give materials possessing high solubility and less aggregation similarly to the well-documented *neo*-pentoxyphthalocyanine[47] and tetra-*tert*-butylphthalocyanine[157]. This clarified the initial problem that Linstead[173] and co-workers were faced when they tried to separate

the *meso*-substituted TBTAP from the phthalocyanine derivative, but it was impossible at that time due to the high aggregation.[190]



Scheme 1.33: Preparation of TBTAPs reported by Leznoff and McKeown.

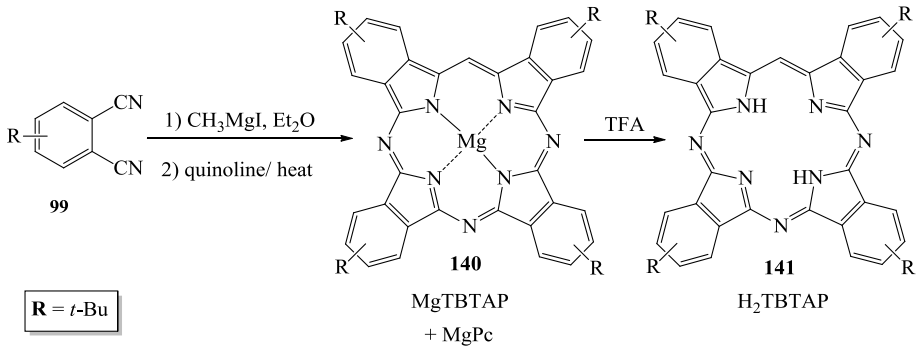
The introduction of an aromatic substituent at the *meso*-position was successfully accomplished in both unsubstituted and *t*-butyl-substituted tetrabenzotriazaporphryrins using the commercially available benzylmagnesium chloride with 4-*tert*-butylphthalonitrile or phthalonitrile.[190] Leznoff and McKeown have also successfully prepared *meso*-substituted tetranaphthotriazaporphyrin derivative using a *tert*-butylnaphthalonitrile with a Grignard reagent (Scheme 1.34).[190]



Scheme 1.34: Preparation of TNTAP reported by Leznoff and McKeown.

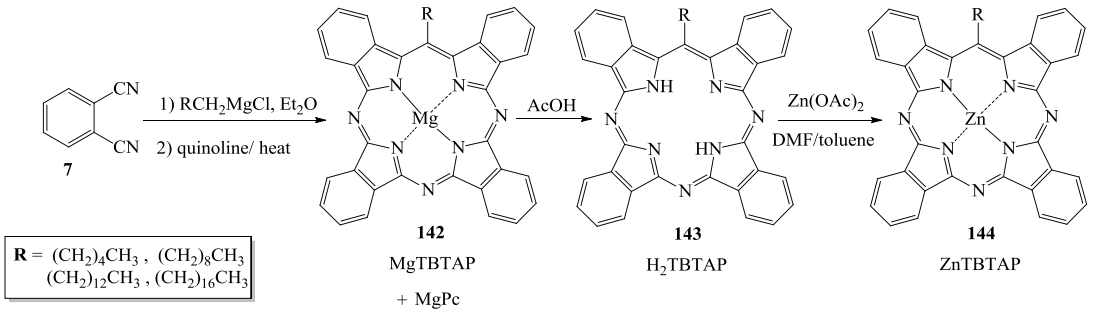
Recently, Ivanova and co-workers have prepared *t*-butyl-substituted tetrabenzotriazaporphryrins by treating *t*-butylphthalonitrile with methylmagnesium iodide.[191] The resulting materials (MgTBTAP and MgPc) were separated by means of

chromatography before elimination of the metal by the reaction with trifluoroacetic acid to yield a free-metal TBTAP (Scheme 1.35).[191]



Scheme 1.35: Preparation of TBTAP reported by Ivanova.

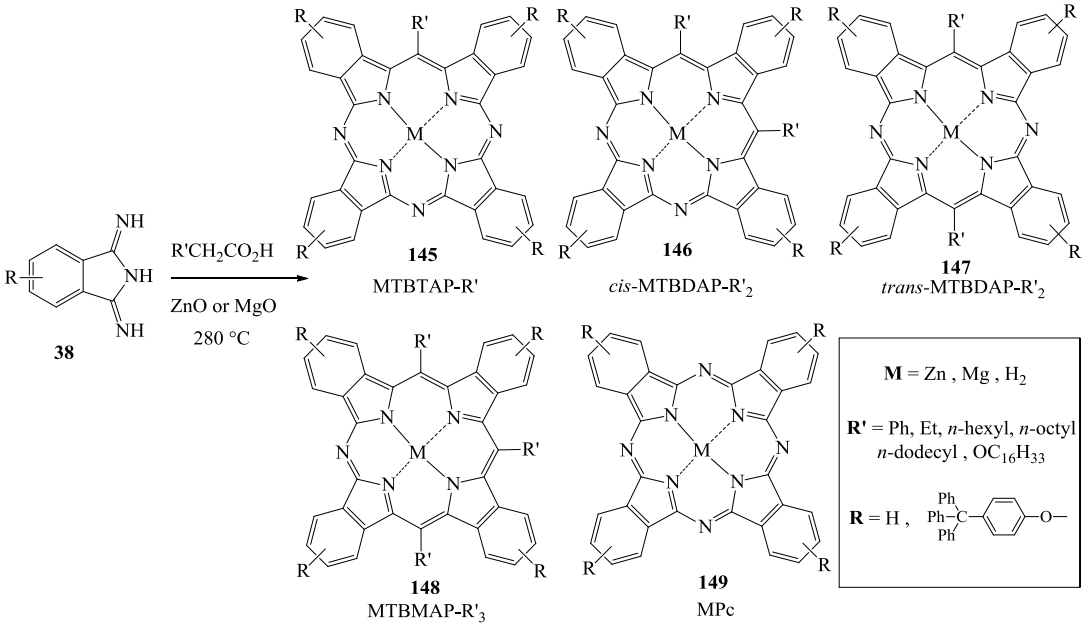
Tse and co-workers have also used Linstead's method to prepare a wide range of metal-free and metallated TBTAPs substituted at the *meso*-position.[192] The reaction involves the treatment of phthalonitriles with a variety of alkylmagnesium halides of different lengths of alkyl chains and led to the formation of magnesium TBTAP derivatives with MgPc as a side-product (Scheme 1.36). They can be separated by chromatography using coordinating solvents such as pyridine and THF. Demetallation of MgTBTAP results in the formation of metal-free TBTAPs which are treated with anhydrous zinc acetate in order to form ZnTBTAP derivatives.[192]



Scheme 1.36: Preparation of *meso*-substituted TBTAP derivatives.

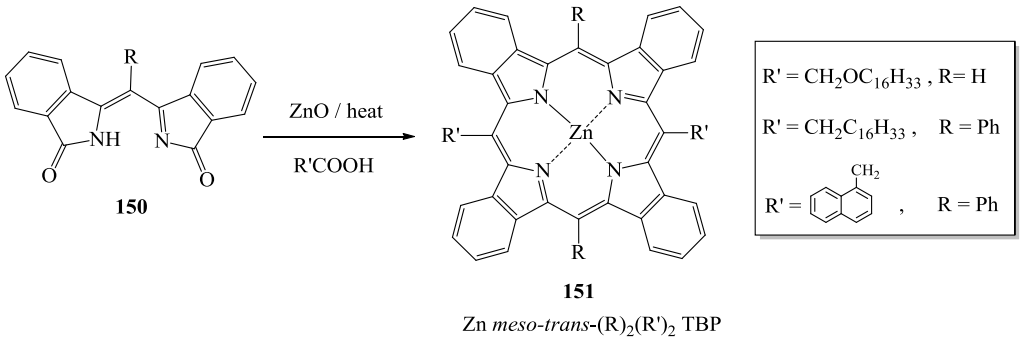
More recently, Galanin and co-workers described the preparation of a series of magnesium and zinc complexes of *meso*-substituted tetrabenzo(aza)porphyrins. The reactions involve the refluxing of 1,3-diiminoisoindolines or its derivatives with variety of carboxylic acids at 280-300 °C with ZnO or MgO as template agent to give a mixture of magnesium or zinc complexes.[193-201] In these investigation, they

observed that the resulting materials formed based on the ratios of the reactants used in these reactions where an excess of the carboxylic acids result in the formation of complexes with more methine bridges, whereas the more nitrogen bridges can be formed when decreasing the ratio of carboxylic acids to diiminoisoindolines.[193] Galanin's route is generally faster than the other previous methods where a mixture of hybrid complexes including TBTAP, TBDAP and TBMAP are formed in an hour or sometimes less than one hour. [193-201] An example of this synthetic route is shown in Scheme 1.37.



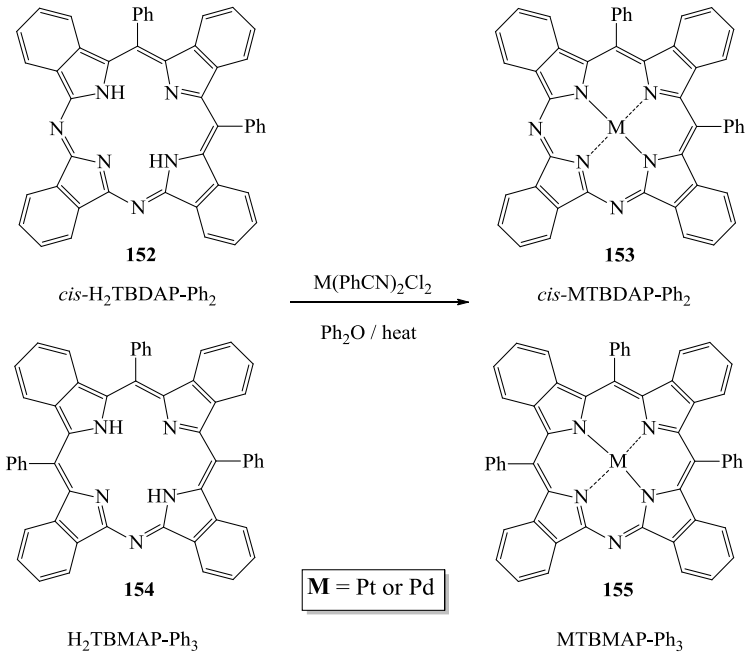
Scheme 1.37: *Meso*-substituted tetrabenzo(aza)porphyrin analogues reported by Galanin.

A selective method for the preparation of *meso-trans*-(alkoxy)$_2$TBP, *meso-trans*-(alkyl)$_2$TBP and *meso-trans*-(aryl)$_2$(alkoxy)$_2$TBP complexes was also described by Galanin and co-workers.[196,199,202,203] Heating the dimeric intermediate **150** with acids in the presence of zinc oxide at 300 °C for 30 minutes gave zinc complexes of *meso-trans*-(alkoxy)$_2$TBP **151**.[199,202] Similarly, the zinc complexes of *meso-trans*-(aryl)$_2$(alkoxy)$_2$ tetrabenzoporphyrins can be prepared.[196,203] An example of *meso-trans*-substituted TBP obtained by this route is shown in Scheme 1.38.



Scheme 1.38: Selective method for the preparation of *meso-trans*-substituted TBP.

Borisov *et al*. followed the synthetic strategies described by Galanin to prepare ZnTBTAP-Ph_3 and *cis*-ZnTBDAP-Ph_2 which then undergoes demetallation to afford the metal-free complexes. Inserting platinum(II) and palladium(II) metals into the central cavity of the macrocycles results in formation of the Pd and Pt *cis*-TBDAP-Ph_2 **153** and TBMAP-Ph_3 **155** complexes (Scheme 1.39) which are suitable for application in optical oxygen-sensing materials.[204]

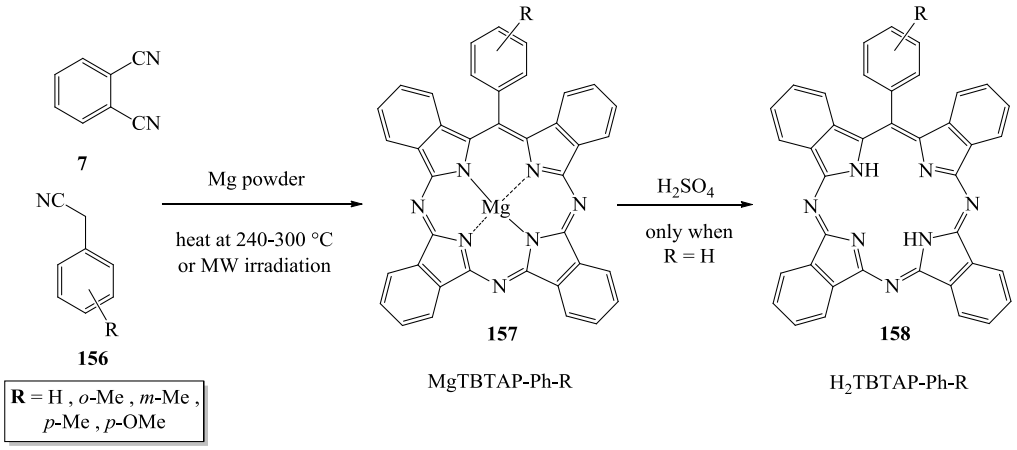


Scheme 1.39: Inserting Pt and Pd into the central cavity of *meso*-substituted TBDAP and TBMAP.

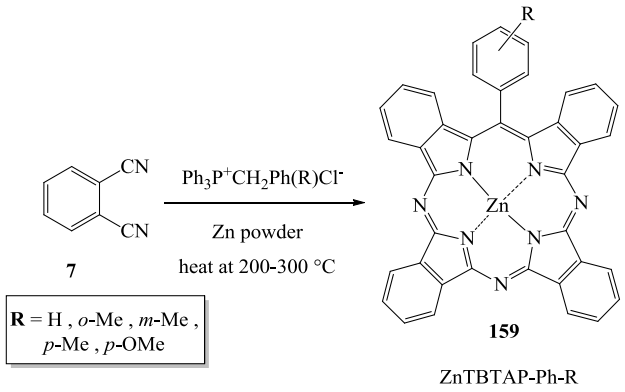
A series of single *meso*-substituted tetrabenzotriazaporphyrins, obtained as magnesium derivatives, was reported by Tomilova *et al*. in 2011.[205] They investigated two different methods to prepare these complexes. The first approach involved simply

heating phthalonitriles with arylacetonitriles, which possess substituents on the benzene ring, in the presence of magnesium powder and led to 9% yields of aryltetrabenzotriazaporphyrin complexes. TBTAP complexes can also be prepared by microwave irradiation of the starting materials. This procedure gives a higher yield in short period of time unlike the fusion technique (Scheme 1.40).[205]

A new synthetic route for the synthesis of zinc TBTAP complexes has been achieved by heating a mixture of phthalonitrile and quaternary salts of triphenylphosphonium gradually from 200 to 300 °C in the presence of zinc powder as a template agent. The resulting materials were filtered to remove the zinc phthalocyanine from the reaction mixture. Purification of the product by column chromatography gave the desired zinc TBTAP complex in a reasonable yield (Scheme 1.41).[206]



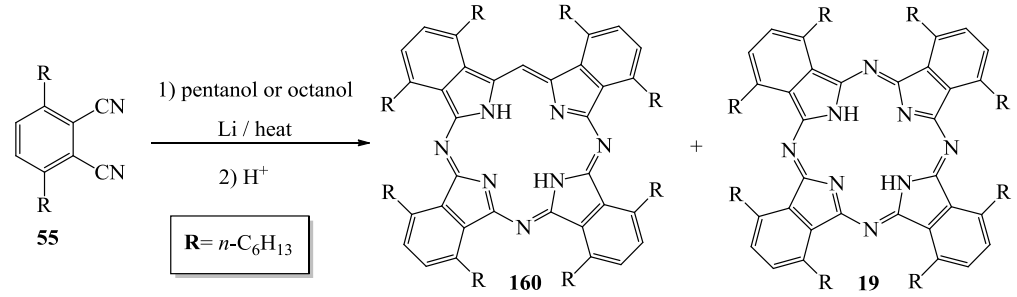
Scheme 1.40: Tomilova's synthetic routes.



Scheme 1.41: Synthesis of zinc TBTAP complexes.

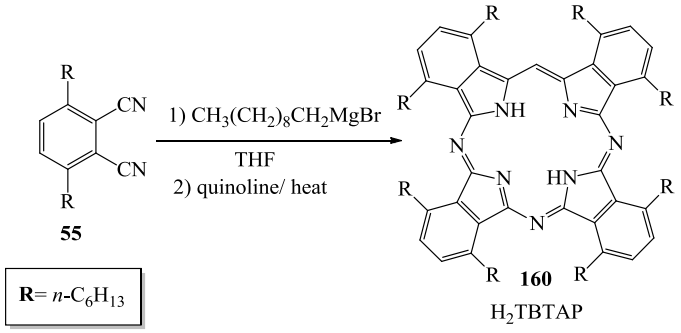
In 2005, accidental preparation of a dark green product was discovered by Cammidge, Cook and co-workers at UEA during the preparation of non-peripherally substituted octaalkyl-phthalocyanine using 3,6- dialkylphthalonitrile as precursor in the presence of an excess of freshly cut lithium metal and pentanol as solvent. The

cyclotetramerisation of this precursor results in the formation of substituted octaalkyl-phthalocyanine along with a by-product later identified as substituted octaalkyl-tetrabenzotriazaporphyrin (*np*-alkyl)$_8$TBTAP (Scheme 1.42).[207] The synthesis of a peripherally substituted tetrabenzotriazaporphyrin using 4-*t*-butylphthalonitrile or 4,5-dihexylphthalonitrile as precursors proved to give unsuccessful results under the same conditions. Moreover, they investigated the source of the *meso*-carbon using ^{13}C labelling experiments. The final result of these experiments indicated that the solvent used in the reaction is responsible for the introduction of methine group at *meso*-position.[207]



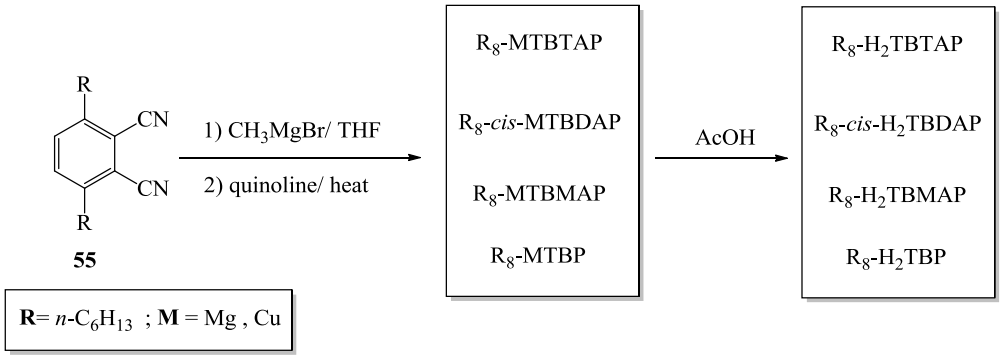
Scheme 1.42: Accidental preparation of non-peripherally substituted octaalkyl-tetrabenzotriazaporphyrin.

Leznoff's procedure was also used by Cammidge-Cook groups to introduce bulky substituents at the *meso*-position of TBTAP macrocycles. Cyclisation of 3,6-dihexylphthalonitrile with Grignard reagent (decylmagnesium bromide) using Leznoff's conditions formed only non-peripherally octahexyl-H$_2$TBTAP (Scheme 1.43).[207] To understand this reaction, Cammidge and co-workers studied the factors that control the efficiency of the formation of the non-peripherally substituted octaalkyl tetrabenzotriazaporphyrins.[208]



Scheme 1.43: Preparation of metal-free *np*-octahexylTBTAP unsubstituted at the *meso*-position.

Novel derivatives of the metal-free as well as magnesium and copper derivatives of tetrabenzo(aza)porphyrin hybrids were successfully prepared using the controlled synthetic strategies which were described by Cammidge and Cook *et al.*in 2011.[208] Their controlled method modified Linstead's procedure and can be summarized in two main steps. Treatment of a solution of 3,6-dialkylphthalonitriles in ether or THF with different amounts of the Grignard reagent followed by exchange the solvent to quinoline and heating the mixture at high temperature in order to obtain the tetrabenzo(aza)porphyrin magnesium derivatives. The obtained analogues can undergo a demetallation reaction to give metal-free derivatives followed by the insertion of copper in the central cavity of macrocyclic complexes (Scheme 1.44).[173,208] Consequently, they studied these hybrids using a series of stoichiometric ratios in order to clarify the effects of changing the ratios of starting materials on the formation of resulting green materials. These investigations are outlined in Table1.1. Starting with 1:4 equivalents of MeMgBr to phthalonitrile, the reaction failed to obtain any hybrid molecule, whereas changing the equivalents of starting materials (MeMgBr: phthalonitrile) to a 1:1 ratio gave a mixture of green coloured products (later identified as TBTAP and TBDAP). Significant amounts of TBTAP, TBDAP and TBMAP were observed when the equivalents of starting materials (MeMgBr: phthalonitrile) increased to a 2:1 ratio with traces of Pc and TBP. Changing the ratios (1:1, 2:1, 3:1, 4:1, 5:1) of starting materials (MeMgBr:phthalonitrile) were also examined and proved to give a full range of tetrabenzo(aza)porphyrin derivatives (i.e. TBTAB, *cis*- and *trans*-TBDAP, TBMAP, TBP, Pc). As a result of these investigations, increasing the number of equivalents of MeMgBr further led to reduce the formation of phthalocyanine-like hybrids, whereas the formation of benzoporphyrin-like macrocyclic products was increased. Generally, this controlled procedure provides a particularly convenient synthesis of these hybrid molecules.[208]



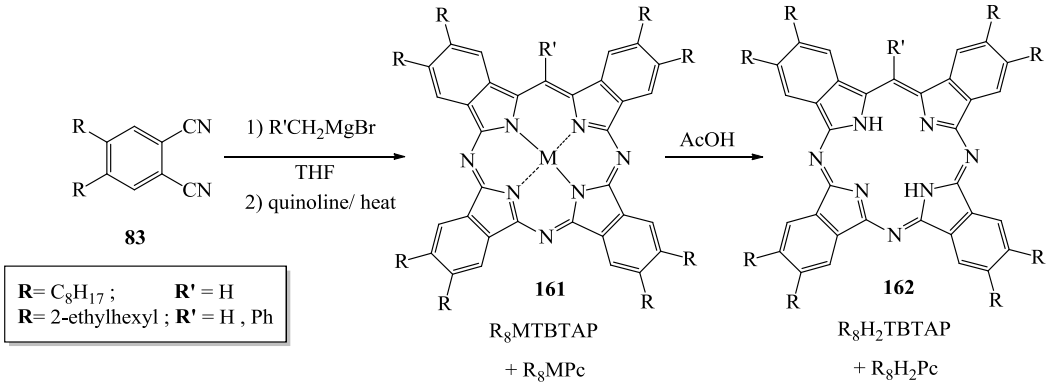
Scheme 1.44: Preparation of metal-free and metallated *np*-octahexyl hybrids.

Phthalonitrile	Grignard reagents	R_8-H_2TBTAP	R_8-*cis*- and *trans*-H_2TBDAP*	R_8-H_2TBMAP	R_8-H_2TBP	R_8-H_2Pc
4	**1**	**-**	**-**	**-**	**-**	**-**
1	**1**	**24%**	**14%**	**trace**	**-**	**trace**
1	**2**	**27%**	**9%**	**3%**	**trace**	**trace**
1	**3**	**18%**	**8%**	**4%**	**1%**	**-**
1	**4**	**trace**	**trace**	**trace**	**12%**	**-**
1	**5**	**-**	**-**	**-**	**1%**	**-**

* A mixture of *cis* and *trans* isomers was observed.

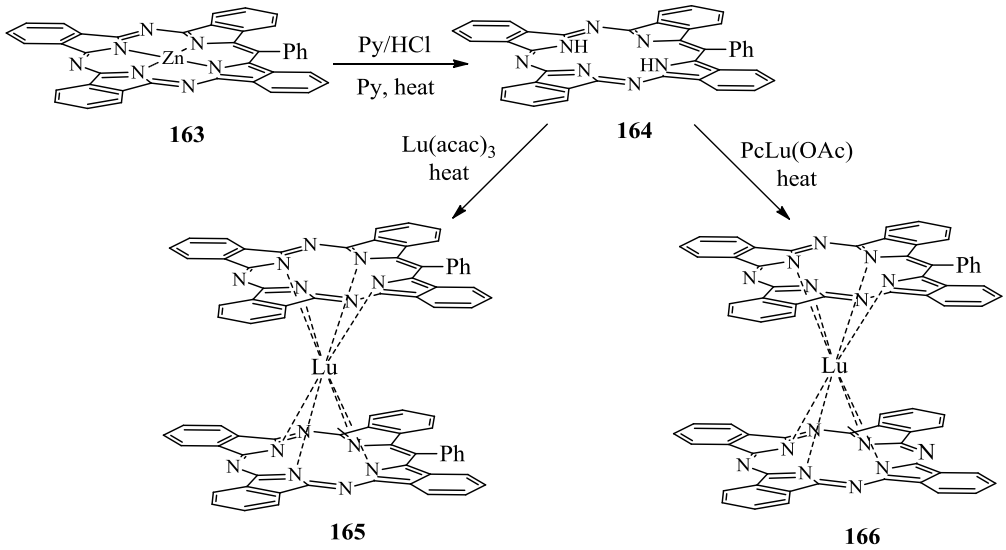
Table 1.1: Yields obtained by the reaction between 3,6-dihexylphthalonitrile and varying equivalents of MeMgBr followed by the demetallation reaction.

The reactions between 4,5-dialkylphthalonitrile and 2 equivalents of Grignard reagent MeMgBr were also investigated by Cammidge-Cook groups. The results of these investigations are mostly in line with the outcomes of Leznoff and McKeown when employing 4-*t*-butylphthalonitrile as a precursor. In other words, the resulting product mixtures contained only TBTAP and Pc (Scheme 1.45). It was also observed that the introduction of phenyl group or a long chain alkyl group at the *meso*-position of the TBTAP can be achieved when the 4,5-dialkylphthalonitrile **83** was treated with a benzyl or long chain alkyl Grignard reagent, whereas using the 3,6-dialkylphthalonitrile **55** can only form the TBTAP unsubstituted at the *meso*-position TBTAP-CH.[190,208]



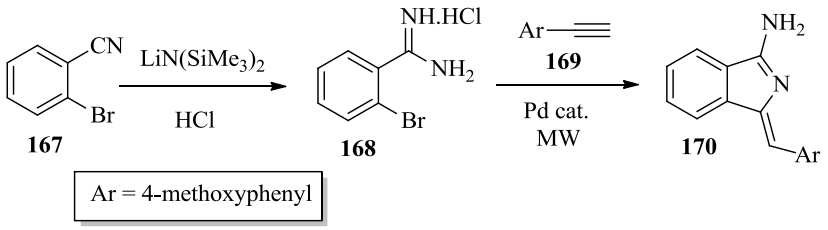
Scheme 1.45: Preparation of metal-free and metallated peripherally octaalkylTBTAP and Pc.

Recently, Pushkarev *et al*. reported the preparation of the first lutetium bis-(tetrabenzotriazaporphyrin) sandwich complex (homoleptic $(Ph\text{-}TBTAP)_2Lu$) and heteroleptic (tetrabenzotriazaporphyrinato) (phthalocyaninato) lutetium derivative ((Ph-TBTAP)LuPc).[209] Demetallation of preformed zinc *meso*-phenyl TBTAP results in formation of a free-metal molecule which undergo complexation with lutetium(III) acetylacetonate to give a homoleptic complex. Direct interaction of free metal *meso*-phenyl TBTAP with preformed lutetium mono phthalocyanine leads to formation of a heteroleptic dyad (Scheme 1.46).[209,210]



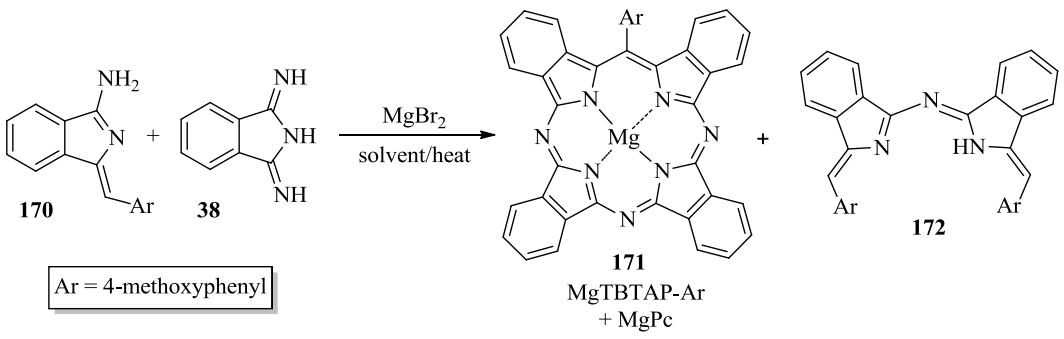
Scheme 1.46: First sandwich-type TBTAP complexes.

In recent years, a considerable attention has been focused on the preparation of TBTAPs using more precise methods. Cammidge's group invented a modern approach for the preparation of substituted *meso*-phenyl TBTAP as a single product of hybrid macrocycles.[211] This method proved to give a significant yield of TBTAP and avoided the formation of further hybrid complexes. The synthetic strategy involves the preparation of the aminoisoindoline or its derivatives by applying the procedure demonstrated by Hellal *et al*.[212] Treatment of a tetrahydrofuran solution of 4-bromobenzonitrile **167** with a solution of lithium bis(trimethylsilyl)amide (LiHMDS) in THF followed by quenching with isopropanol/HCl led to formation of 2-bromobenzimidamide hydrochloride **168** in good yield.[213] The resulting material underwent a copper-free Sonogashira coupling and cyclisation under microwave irradiation to afford the target molecule **170** (Scheme 1.47).[212]

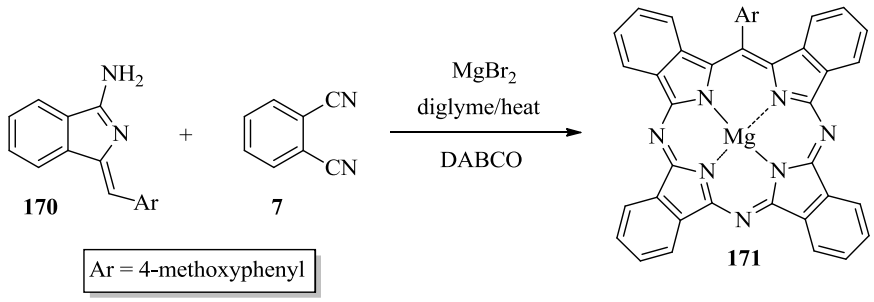


Scheme 1.47: Synthesis of aminoisoindoline derivatives.

Once a reasonable amount of aminoisoindoline precursors has been prepared, the functionalized *meso*-phenyl TBTAP can be obtained in good yield.[211] The first attempts to synthesise this molecule began with heating a solution of diiminoisoindoline **38** and aminoisoindoline **170** in high boiling organic solvents (starting with quinoline, DMEA, DMF, and finally diglyme) in the presence of magnesium bromide as a template agent (Scheme 1.48). The reaction mixture was found to contain the desired *meso*-phenyl TBTAP along with Pc and further unknown material which was identified later as a self-condensation product of aminoisoindoline **172**. Due to unsatisfactory outcomes and side-product formation, the reaction was studied carefully in order to obtain the target compound in a good yield and decreasing the formation of Pcs and other side-products. Modification of this reaction started with using phthalonitrile instead of the more reactive diiminoisoindoline **38** (which can be the reason for the formation of unwanted Pc). Further modifications included using the additional amounts of phthalonitrile **7**, controlling the addition of aminoisoindoline **170** to the reaction mixture and adding DABCO to the reaction mixture (which can help to release the unreacted aminoisoindoline **170** from its complex with the MgTBTAP molecule and then complete the consumption of the phthalonitrile **7**). All these modifications enhanced the synthesis of these hybrid macrocycles and hence improved the yields of the *meso*-phenyl TBTAP **171** formation (Scheme 1.49).[211]



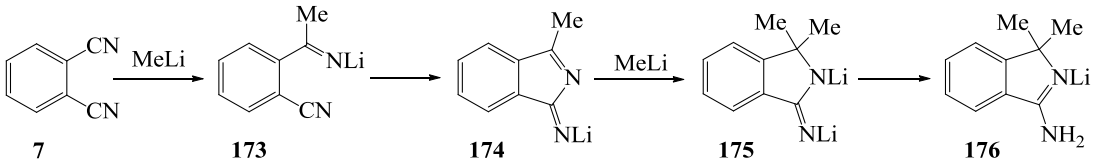
Scheme 1.48: Formation of TBTAP along with Pc and dimeric side product **172**.



Scheme 1.49: Synthesis of functionalized *meso*-phenyl TBTAP *via* intermediate **170**.

1.11 Mechanism of Tetrabenzo(aza)porphyrins Formation

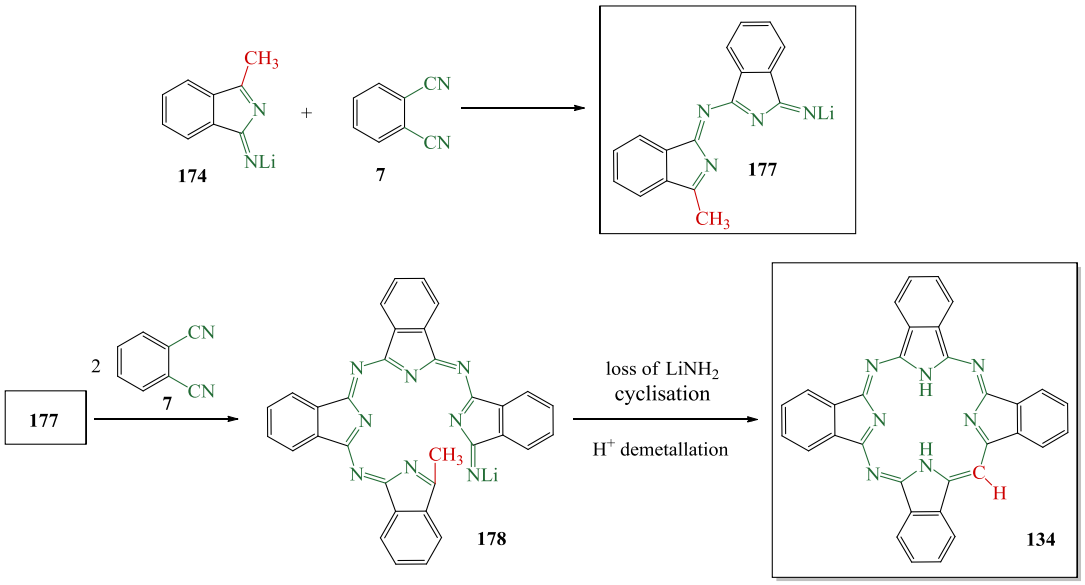
The proposed mechanism of preparation of these hybrid complexes was described by Linstead and co-workers. In particular, understanding of the mechanism for the formation of metal-free tetrabenzotriazaporphyrin was provided by the study of the effect of an excess amount of methylmagnesium iodide or methyllithium (2 equivalents) on phthalonitrile. Heating the starting materials together at 200 °C in the presence of cyclohexanol as a solvent resulted in formation of a free base, 3-amino-1,1-dimethylisoindole **176**, after it went through a series of intermediates as illustrated in Scheme 1.50.[173]



Scheme 1.50: Isolated intermediates in TBTAP formation.

Indeed, when the tetrabenzotriazaporphyrin was prepared from equimolecular quantities of phthalonitrile and methyl magnesium iodide or methyllithium, an excess of the nitrile was observed at the end of the first condensation which could be responsible for the formation of nitrogen bridges in the triaza-complexes. However, intermediates **174** and **175** could be responsible for the introduction of the methine group at the *meso*-position. Intermediate **174** can react with a further molecule of phthalonitrile **7** to produce a dimeric compound **177** which after further addition of two phthalonitrile **7** molecules gives a tetrameric complex **178**. Cyclisation of this tetrameric intermediate (tetra-isoindolic molecule) affords the tetrabenzotriazaporphyrin molecule **134**. The final step involves the elimination of either lithium amide or methylamine (dependent on the organometallic used in the

reaction) which can only occur in the second step of the reaction when the high boiling point solvent was applied (Scheme 1.51). The general mechanism for the hybrid macrocycle formation remains unclear due to the lack of adequate studies covering this area since the investigations described by Linstead and co-workers.[173]



Scheme 1.51: Proposed mechanism of TBTAP formation.

1.12 Properties and Applications of Tetrabenzo(aza)porphyrins

Tetrabenzo(aza)porphyrins are remarkable macrocyclic molecules because of their unique physical and chemical properties which are similar to those in the parent phthalocyanine structures. Tetrabenzo(aza)porphyrin derivatives have been successfully applied in many fields of science and technology. They are demonstrated to be useful photosensitisers in photo-oxidation,[214] as gas sensors[215-219] and as fluorescent dyes.[220-222]

1.12.1 Optical Properties

One of the most obvious differences between the tetrabenzo(aza)porphyrins and its parent phthalocyanines is in the observed colour. The tetrabenzo(aza)porphyrins have a bright green colour whereas the Pcs have an intense blue-green colour. The absorption spectra of tetrabenzo(aza)porphyrins are comparable to those of phthalocyanines with absorption in the *Q*- and *B*-band regions (figure 1.18). The origins of the *Q*- and *B*-bands can be understood by Gouterman's four-orbital model.[58] This model clarifies the electronic transitions of tetrapyrrole macrocycles. The *Q*- and

B-band absorptions are assigned to the $\pi \rightarrow \pi^*$ electronic transitions from the HOMO (highest occupied molecular orbital (a_{2u})), the second highest energy occupied orbital, (a_{1u}), to the LUMO (lowest unoccupied molecular orbital (e_g)) which is not the case for phthalocyanines where the HOMO (a_{1u}) is higher energy than the (a_{2u}) (figure 1.19). Thus the absorptions from these transitions in porphyrins show a hypsochromic shift relative to the absorptions resulting from the corresponding Pcs. The tetrabenzo(aza)porphyrin molecular structure can be distorted due to losing the symmetry since one of the nitrogen atom is replaced by a carbon atom and this can lead to interesting spectral changes in Pc/TBP hybrids compared to Pcs.[223]

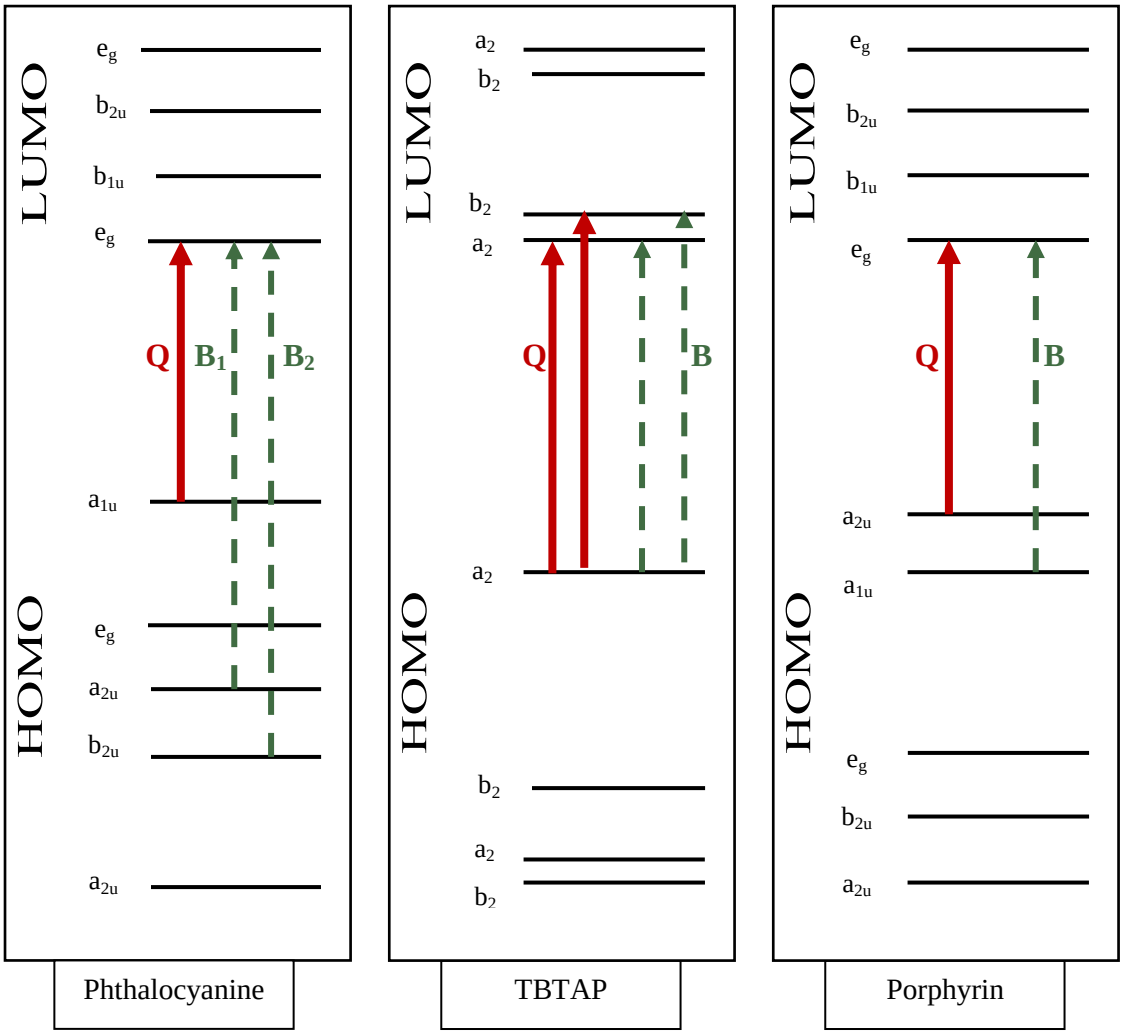


Figure 1.18: The origin of the UV-Vis spectra of phthalocyanine, porphyrin and TBTAP.

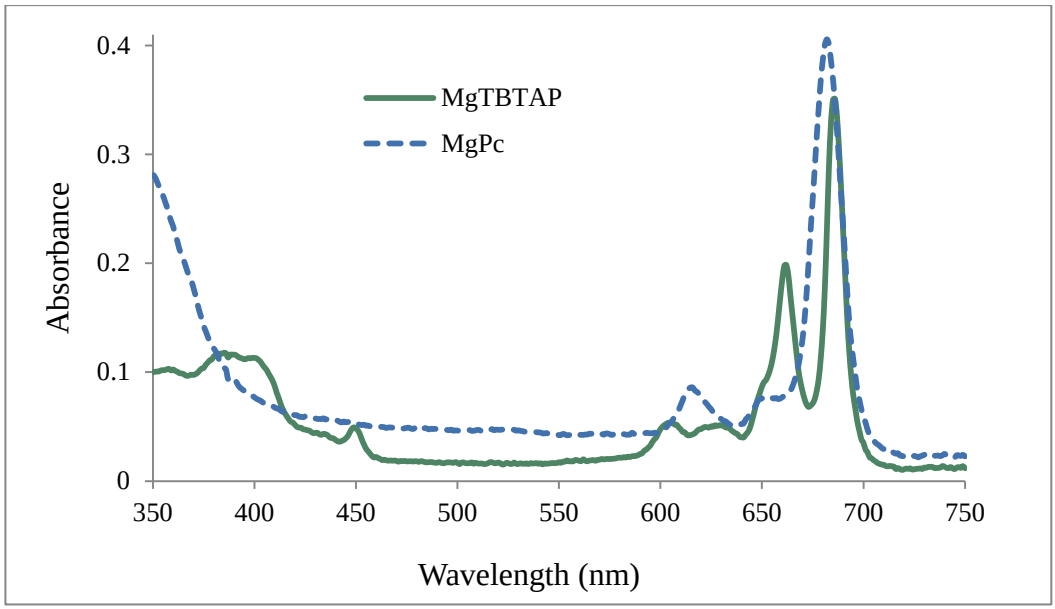


Figure 1.19: UV-Vis spectra of MgPc and its analogue MgTBTAP.

It was observed by Linstead *et al.* that along the series of Pc, TBTAP, TBDAP's, TBMAP, TBP the Q-band is shifted to shorter wavelengths and the *B*-band increases in intensity.[178] The explanation of the spectral features of tetrabenzo(aza)porphyrins employing the LCAO-MO method was reported by Solov'ev and co-workers.[224] The exceedingly comprehensive examinations were made by Kobayashi and Konami employing the Pariser-Parr-Pople (PPP) approximation to calculate the energy levels of molecular orbitals (MO) of the tetrabenzo(aza)porphyrins.[73] Calculations predict that the Q-band exhibits a shift to the blue region along the hybrid series Pc, TBTAP, TBMAP, TBP with the exception of the TBDAP isomers which are different from each other. These predictions were coordinated with Linstead's investigations.[73,178]

Further MO calculations have been achieved by Kobayashi and co-workers using the ZINDO (Zerner's Intermediate Neglect of Differential Overlap) program which give additional analytical information and thus can offer an advanced understanding of the electronic absorption spectra of tetrabenzo(aza)porphyrins.[225]

A large selection of UV-Vis spectroscopy data of metal-free and metallated substituted or unsubstituted tetrabenzo(aza)porphyrins in different kinds of solvents was described in detail in a review published in 2003.[226] Consequently, when the *aza* bridges replaced by methine groups, the Q-band corresponding to the lowest energy π-π^* absorption exhibits a hypsochromic shift towards a shorter wavelength and lower intensity as well as increasing the intensity of the *B*-band in the case of metallated

tetrabenzo(aza)porphyrins with the exception of the *trans*-TBDAP compounds. However, the Q-band in the metal-free tetrabenzo(aza)porphyrins shows a split into two peaks. It was observed that the Q-bands also exhibit a shift to the red region (bathochromic shift) with an increase in the ratio between the *Q*- and *B*-band intensities in tetrabenzo(aza)porphyrins which contain an the extension of the molecule's π-system (e.g TNTAP, Figure 1.20).[225]

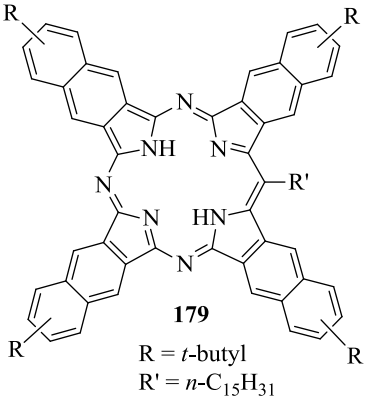
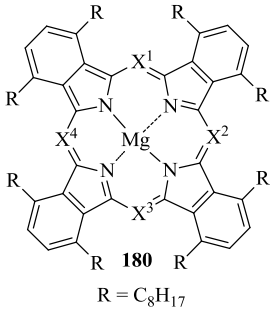


Figure 1.20: Tetranaphthotriazaporphyrin TNTAP.

The UV-Vis absorption spectra of non-peripherally substituted magnesium $(n\text{-}C_8H_{17})_8$ hybrid derivatives (Figure 1.21) reported by Cammidge, Cook and co-workers is illustrated in Figure 1.22. The Q-band shows the following series of shifts: (MgPc) λ_{max} 700 nm, (MgTBTAP) 694 nm, (*cis*-MgTBDAP) 662 nm, (MgTBMAP) 659 nm, (MgTBP) 641 nm. Depending on the central metal atoms attached, the Q-bands can undergo a red or blue shift, such as inserting the copper metal in the central cavity of tetrabenzo(aza)porphyrin derivatives led to a hypsochromic shift whereas a red shift occurred when the lead metal was attached to the central core.[208] More detailed information for the UV-Vis spectroscopy data of tetrabenzo(aza)porphyrins are presented in The Porphyrin Handbook.[223]



X^1, X^2, X^3, X^4, = CH (TBP)
X^1, X^2 , X^3 = CH ; X^4 = N (TBMAP)
X^1, X^2 = CH ; X^3 , X^4 = N (*cis*-TBDAP)
X^1, X^2 , X^3 = N ; X^4 = CH (TBTAP)
X^1, X^2, X^3, X^4, = N (Pc)

Figure 1.21: Non-peripherally substituted magnesium hybrid derivatives.

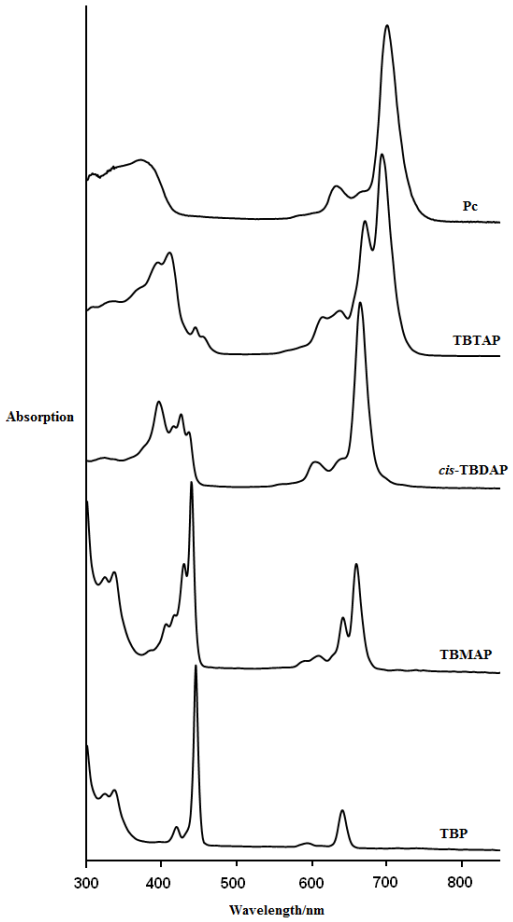
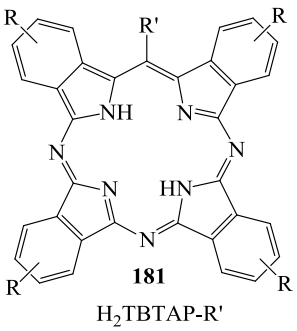


Figure 1.22: UV-Vis spectra of non-peripherally substituted magnesium tetrabenzo(aza)porphyrin derivatives in THF.

1.12.2 Mesophase behaviour

Tetrabenzo(aza)porphyrin derivatives were expected to exhibit mesophase behaviour due to the similarity of these novel compounds with the corresponding phthalocyanine. McKeown and Leznoff in 1992 reported the thermotropic mesomorphism of TBTAP derivatives (Figure 1.23).[227]



181

H_2TBTAP-R'

R = $OCH_2C(CH_3)_3$; **R'** = $(CH_2)_{14}CH_3$

Figure 1.23: Tetrabenzotriazaporphyrin TBTAP.

Meso-substituted *neo*pentoxy-tetrabenzotriazaporphyrin exhibits liquid crystalline behaviour at 130 °C. Transformation of the phase from solid to mesophase happened in broad temperature ranges (100-125 °C). It was observed that peripherally tetra-substituted TBTAP obtained by Leznoff *et al*. was a mixture of isomers due to the absence of a sharp transition from the solid phase to the mesophase. Stability of this TBTAP towards the thermal decomposition was high which made this molecule able to be heated in a naked flame without any changes in the colour or stability of the compound. Cooling TBTAP to room temperature results in formation of the solid sample in mainly homeotropic texture with the presence of focal-conic fan texture areas when viewed under a polarising optical microscopy (POM). The compounds were investigated by a combination of differential scanning calorimetry (DSC) and X-ray diffraction analysis and those analytical methods indicate that the mesophase of the TBTAP had a lamellar structure similar to the molecular arrangement found in the Smectic A phase of nematic (rod-like) compounds.[105] McKeown continued the examination of the thermotropic mesophase behaviour of this TBTAP. It was observed from optical, DSC and X-ray studies that the mesophase formed did not have the lamellar structure as initially believed, but was a disordered hexagonal columnar structure.[228] A new series of columnar liquid crystals was investigated by Cammidge and Cook *et al*. in 2011. They studied the mesophase behaviour of *np*-octahexyl substituted TBTAP, TBDAP, TBMAP and TBP compounds using POM and DSC.[208] The thermotropic mesophase behaviours of the Pc/TBP analogues are similarly to those observed in parent phthalocyanine which was found to display a columnar hexagonal mesophase (Col_h), and in some cases a columnar rectangular phase (Col_r) (Figure 1.24).[101,105, 208,223,228]

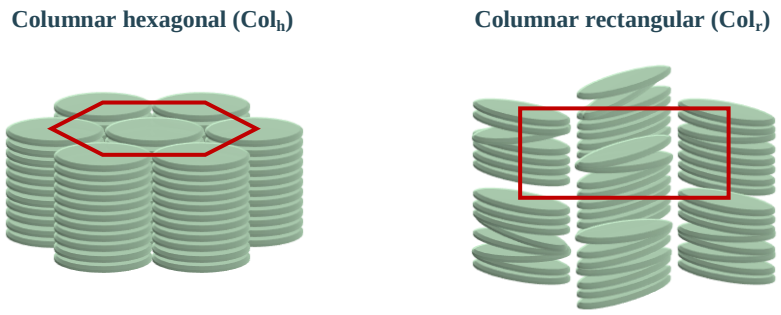


Figure 1.24: Most common mesophases observed in phthalocyanine derivatives.

1.12.3 Langmuir-Blodgett Films

The Langmuir-Blodgett[229] technique offers the possibility of constructing thin films of organic molecules, such as porphyrins[230], phthalocyanines[231-233] and their hybrid macrocycles by transferring molecular monolayers at an air-water interface onto a substrate, one monolayer at a time.[233] The optical and electrochemical properties of Pcs and porphyrins make them particularly valuable when assembled into well-organised LB films, for applications in areas such as molecular electronics[234], optical devices[235] and chemical gas sensors.[236] The similarity between the tetrabenzo(aza)porphyrin hybrids and their parent phthalocyanine molecules make them suitable materials for the LB technique. However, there are limited studies investigating the impact of applying tetrabenzo(aza)porphyrin derivatives in the LB film. In 1994, Leznoff and co-workers studied a LB film of TBTAP **182** with stearic acid.[237] In their examinations, they found that the TBTAP **182** molecules change their orientation from a fundamentally vertical arrangement on the water surface, when assembled as a monolayer, to an approximately horizontal orientation on the water when long chain hydrocarbon species such as stearic acid was added. The reason behind this change in orientation when the more stearic acid is added is probably because of the reduction of the interactions among the *tert*-butyl groups of the TBTAP and the interaction of stearic acid with the long chain of the TBTAP, thus the TBTAP molecules tend to lie horizontally on the water surface. Switching from vertical to horizontal orientations leads to a wide range of optical and chemical properties. Comparable studies on (*t*-Bu)$_4$-CuTBTAP molecules were achieved by Valkova and co-workers.[238-240] Cammidge and Cook *et al*. reported the synthesis of lead tetrabenzo(aza)porphyrin hybrids which are considered as suitable materials used for the preparation of spin coated films.[208,223,241]

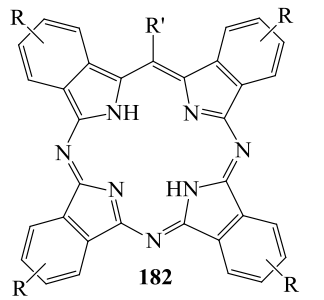


Figure 1.25: Tetrabenzotriazaporphyrin TBTAP reported by Leznoff.

1.13 Aims of the Present Project

1.13.1 Synthesis of metallated substituted and unsubstituted TBTAP derivatives

Despite their properties and potential use in a wide range of applications, like parent porphyrin and phthalocyanine, tetrabenzo(aza)porphyrin hybrids did not receive much attention since their discovery by Linstead and co-workers.[173] However, the synthesis of these analogues has advanced significantly over recent years through contributions from the UEA group and others. These synthetic advances allow much more tetrabenzo(aza)porphyrin derivatives to be made. The present research is, in particular, aimed to investigate the synthesis and characterisation of novel tetrabenzotriazaporphyrins TBTAPs designed for use in a wide range of applications such as Langmuir-Blodgett (LB) films, liquid crystals, photoelectrochemical cells, photosensitizers, and optical data storage (DVDs). Moreover, this research has been focused on the improvement of the reaction conditions. The peripherally octa-substituted tetrabenzotriazaporphyrins and their magnesium derivatives (Figure 1.26) have been prepared following the conventional procedure provided by Linstead and co-workers[173] who described the synthesis of TBTAP derivatives *via* two main steps and this method is described in more details in the experimental section.

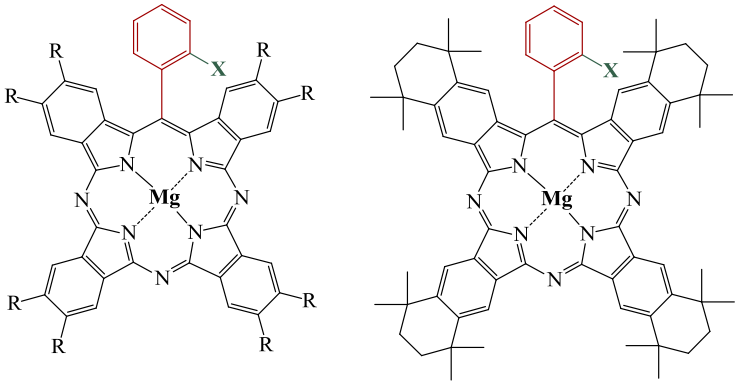


Figure 1.26: Peripherally octa-substituted tetrabenzotriazaporphyrin magnesium derivatives.

The present project also aimed to synthesise the first series of functionalised *meso*-phenyl TBTAPs (Figure 1.27) by reaction between phthalonitrile and the isomeric

series of 2-, 3- and 4-bromobenzylmagnesium bromides which can be key precursors in synthesis of a new sequence of TBTAP derivatives bearing a variety of active groups. This may lead to the discovery of a wide range of desirable properties TBTAPs in fields in which the porphyrins and phthalocyanines have already found applications.

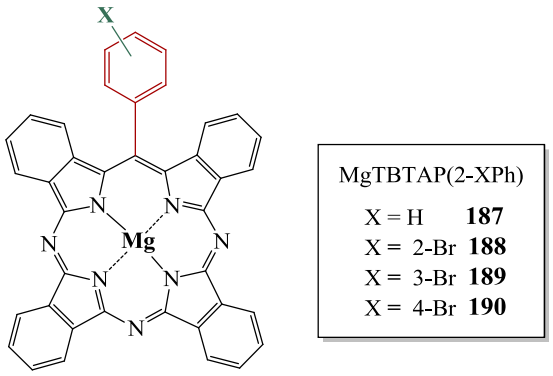


Figure 1.27: Unsubstituted tetrabenzotriazaporphyrin magnesium derivatives.

Furthermore, a new straightforward and controlled technique for preparing unsubstituted tetrabenzotriazaporphyrins magnesium derivatives was performed following a new controllable technique. This method was recently discovered by UEA group providing the TBTAP derivatives in a much better yield compared with TBTAPs prepared by previous route as well as avoiding the formation of other hybrids and by-products. [211] The target functionalised *meso*-phenyl tetrabenzotriazaporphyrins magnesium derivatives are illustrated in Figure 1.28.

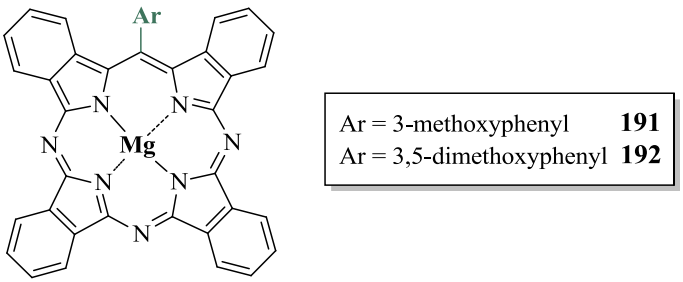


Figure 1.28: *Meso*-substituted tetrabenzotriazaporphyrins derivatives.

1.13.2 Synthetic transformations of functionalized *meso*-phenyl TBTAPs

The aim of this research work was also to provide a new series of the synthetic transformations of functionalized *meso*-phenyl TBTAP derivatives with different chemical and physical properties which could find application in new devices. The

formation of a new carbon-carbon bond can be performed *via* several synthetic routes. In our proposal, we have been employed the Suzuki and Sonogashira cross-coupling reactions with some modifications of the original reaction conditions (Figure 1.29).

Suzuki	Sonogashira
Ar = 2-Ph **194** Ar = 3-Ph **195** Ar = 4-Ph **196**	**Ar** = 2-ethynylbenzene **197** **Ar** = 3-ethynylbenzene **198** **Ar** = 4-ethynylbenzene **199**

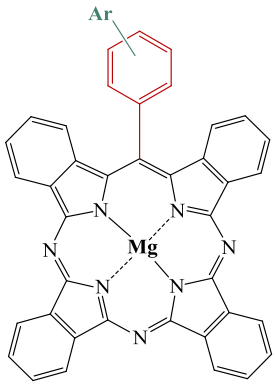


Figure 1.29: Transformations of functionalized *meso*-phenyl TBTAP derivatives.

1.13.3 Intramolecular coupling of TBTAP: expansion of the π-system

Extension of the planar phthalocyanine core has been reported in the literature e.g. naphthalocyanines[162,163] phenanthrene[242] or anthracene[164] based phthalocyanines. It was observed that the extension of the molecule's π-system of phthalocyanines leads to a longer wavelength electronic absorption (red shifted spectra). Extended π-electron conjugation in porphyrins is also reported in the literature.[243-249] This expansion can be achieved by either increasing the number of rings or intramolecular oxidative coupling. The resulting chromophores show strong absorptions in the red region compared to those of normal 18 π porphyrins. Because of the similarity between Pcs, porphyrins and TBTAPs, it is possible that tetrabenzotriazaporphyrins could also undergo an extension of the π-conjugated system and give rise to interesting materials. Thus, in these systems the optical absorption maxima (Q-band) will shift bathochromically relative to its non-extended TBTAPs. Therefore, the aim of the research was to study the preparation of a new class of π-conjugated tetrabenzotriazaporphyrins (Figure 1.30).

R = 2-ethylhexyl
X= H **183**
X= Br **184**
R= H
X= H **187**
X= Br **188**

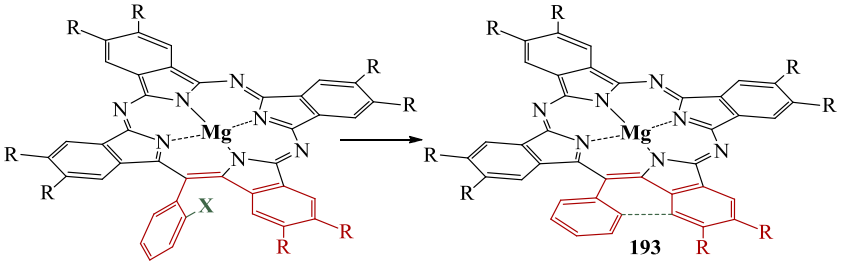


Figure 1.30: Extension of the π-conjugated tetrabenzotriazaporphyrins.

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CHAPTER 2

Synthesis and Functionalization of Tetrabenzotriazaporphyrin derivatives

2.1 Introduction

Despite various optical, electronic and chemical properties,[1] capacity to be soluble in common organic solvents, ability to be synthesised, potential use in Langmuir-Blodgett films,[2] and ability for functionalisations and modifications, tetrabenzo(aza)porphyrin hybrids have not received a great attention since their discovery by Linstead and co-workers[3] compared to the parent phthalocyanines which have been studied widely during the past few years.

Tetrabenzotriazaporphyrin derivatives (**TBTAPs**), in particular, are the most studied hybrid molecules in the last few years. TBTAPs are a system which represents the most limited structural modification to the parent phthalocyanine within a sequence of the hybrid molecules. They have a single *meso*-carbon linkage which can offer an additional site for the attachment of various functional groups, thus would provide a wide range of functionalised TBTAP derivatives. TBTAP molecules are also considered as good materials for applications in optical devices, molecular electronic applications and chemical gas sensors.[4-6]

In this chapter, we describe the synthesis of a set of TBTAP complexes, with their precursors, using different synthetic strategies and modifications of these routes to make those methods suitable for the preparation of our target molecules.

2.2 Synthesis of Peripherally Octa-alkyl Substituted Tetrabenzotriaza porphyrin Magnesium and its Precursor

Preparation of magnesium peripherally octa-substituted tetrabenzotriazaporphyrin derivatives were achieved through the formation of phthalonitrile units which can be obtained *via* several synthetic methods. The targeted molecules are illustrated in Figure 2.1 below.

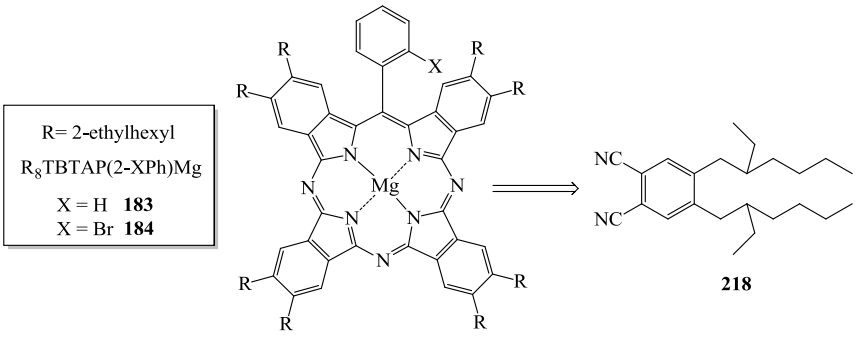


Figure 2.1: Target tetrabenzotriazaporphyrins and required precursor.

Before we describe the synthetic design of our target phthalonitrile **218** we discuss the potential methods which could be used to synthesise such phthalonitriles in next section.

2.2.1 Possible synthetic pathways for preparing 4,5-dialkylsubstituted phthalonitriles

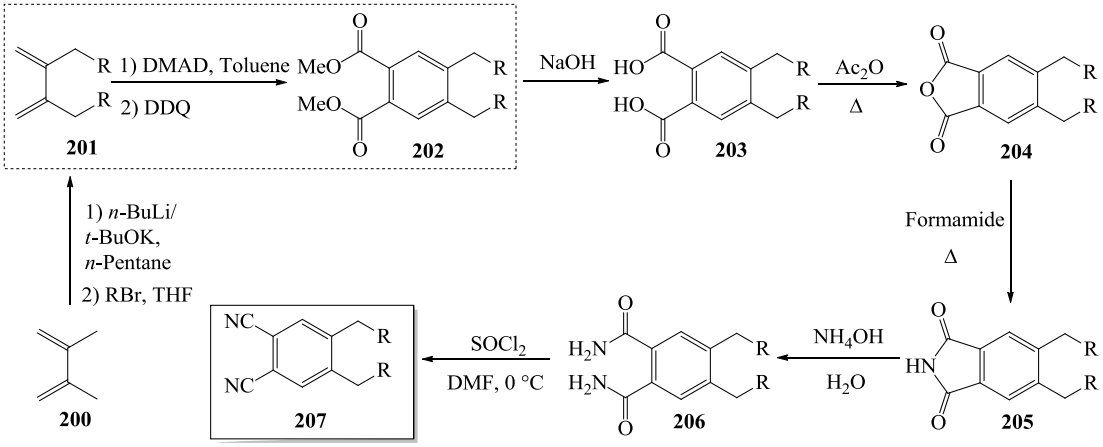
There are several synthetic routes reported in the literature and can be used to prepare the 4,5-dialkylsubstituted phthalonitriles. Most reactions have previously been attempted in our laboratory and all have limitations. Some of these methods proved to give unsatisfactory outcomes (poor yield, facing purification problems, recovering the starting materials or obtaining several products alongside the desired product). However, we are discussed the some of the available protocols for the preparation of targeted phthalonitrile below.

2.2.1.1 Synthesis of 4,5-dialkylphthalonitriles *via* Diels-Alder reaction

The Diels-Alder [4+2] cycloaddition is a well-known method for preparing 4,5-disubstituted phthalonitriles (Scheme 2.1). The general sequence of this method involves a double deprotonation of 2,3-dimethyl-1,3-butadiene **200** using Lochmann's base system (*n*-BuLi/potassium *tert*-butoxide in *n*-pentane), followed by the alkylation with *n*-bromopentane to give 2,3- disubstituted-1,3-butadiene **201**.[8] Product **201** can be prepared using an alternative route which begins with treatment of 2,3-bis(trimethylstannyl)-1,3-butadiene with two equivalents of methyllithium followed by quenching with an electrophile. However, this approach was not preferred because several steps are required to prepare the starting material (2,3-bis(trimethylstannyl)-1,3-butadiene) from 2,3-dichloro-1,3-butadiene which is not commercially available.[9]

The next step involves the synthesis of dimethyl 4,5-dialkylphthalate **202** which was achieved following the procedure reported by Farooq,[10] and developed later by Cammidge, Cook and co-workers.[11] Cycloaddition [4+2] reaction between compound **201** and dimethylacetylenedicarboxylate (DMAD) in the presence of DDQ as oxidizing agent gave dimethyl 4,5-dialkylphthalate **202**. Demethylation of **202** using an aqueous solution of sodium hydroxide gave 4,5-dialkylphthalic acid **203**. The latter was treated with acetic anhydride to give 4,5-dialkylphthalic anhydride **204** which, after heating with formamide, produced 4,5-dialkylphthalimide **205**.[12] Heating phthalimide under reflux with an aqueous solution of ammonia gave the diamide **206**

which finally underwent a dehydration reaction using thionyl chloride to afford the desired 4,5-dialkylphthalonitrile **207**. Scheme 2.1 shows the synthetic route towards the formation of 4,5-dialkylsubstituted phthalonitriles.



Scheme 2.1: Synthesis of phthalonitrile **207** *via* Diels-Alder cycloaddition.

2.2.1.2 Synthesis of 4,5-dialkylphthalonitriles *via* cross-coupling reaction

In the literature, novel metal catalysed cross-coupling reactions can be employed to prepare alkylated phthalonitriles, such as Suzuki-Miyaura,[21] Negishi,[20] Sonogashira[26] and Kumada[31] cross-coupling reactions. These are considered as extremely powerful and widely used strategies for generating C–C, and C–heteroatom bonds.[12-24] 4,5-Dihalogenated phthalonitrile **67,** 1,2-dichlorobenzene **80** and the 4,5-dibromoveratrole **196** (Figure 2.2) are the most dominant substrates for transition metal catalysed cross-coupling reactions methods leading to the formation of alkylated phthalonitriles. Some of known cross-coupling reactions are discussed below.

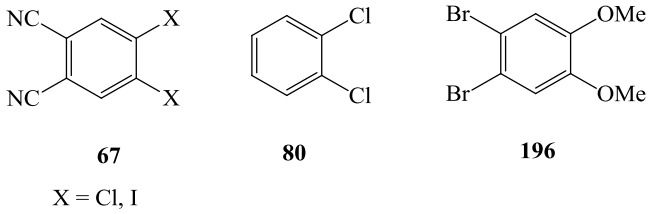
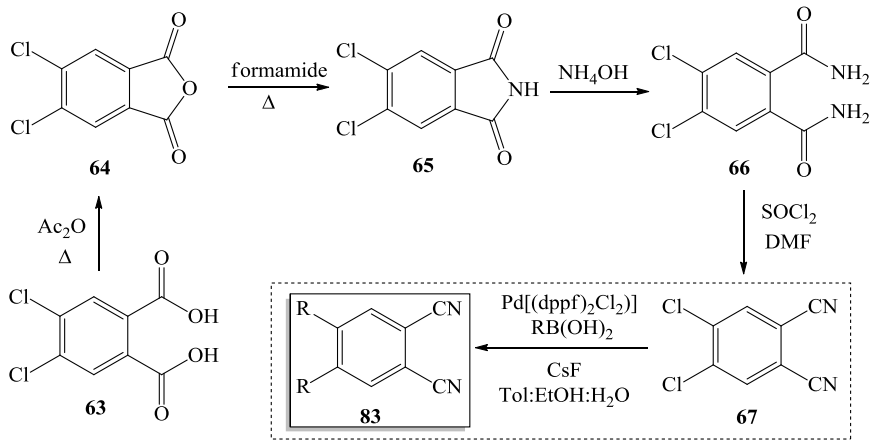


Figure 2.2: Possible substrates used for the synthesis of 4,5-dialkylsubstituted phthalonitriles.

2.2.1.2.1 Cross-coupling reaction using 4,5-dihalogenated phthalonitrile as precursors

a) Synthesis of 4,5-dialkylphthalonitriles *via* Suzuki-Miyaura cross-coupling

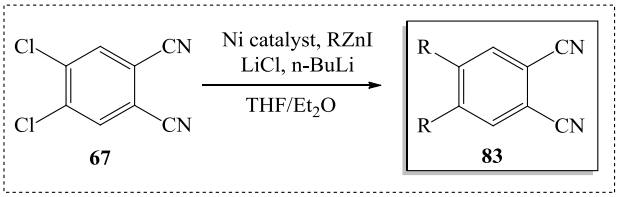
Suzuki-Miyaura cross-coupling reaction[21] is one of the most reliable and convenient reactions for carbon-carbon bond formation. This type of coupling uses organoboron reagents as one coupling partner and organic halides or related electrophiles as the other. Several advantages, such as high efficiency of the reaction, high stability of the organoboron compounds towards air, moisture and thermal treatment, high functional group compatibility, and yielding non-toxic side-products, make Suzuki-Miyaura cross-coupling reaction one of the most broadly used of all the available cross-coupling reactions. The general method for Suzuki cross-coupling involving treatment of aryl chlorides with arylboronic acids in the presence of a $Pd[(dppf)_2Cl_2)]$ catalyst system, with CsF as the base (Scheme 2.2). A vast number of coupled macrocycles have been prepared using this approach.



Scheme 2.2: Synthesis of 4,5-dialkylphthalonitrile **83** *via* Suzuki-Miyaura coupling.

b) Synthesis of 4,5-dialkylphthalonitriles *via* Negishi cross-coupling

Negishi nickel or palladium-catalysed cross-coupling reactions of aryl halides/triflates with organozinc reagents represents a powerful and straightforward method for forming carbon-carbon bonds. 4,5-Dialkylphthalonitrile can be prepared in a single step through Negishi coupling using 4,5-dichlorophthalonitrile[12] as precursor.[13,20]

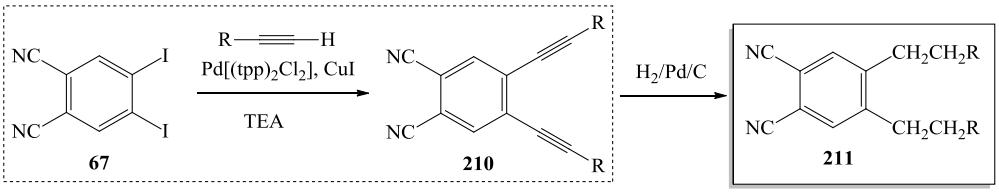


Scheme 2.3: Synthesis of 4,5-dialkylphthalonitrile **83** *via* Negishi coupling.

4,5-Dichlorophthalonitrile underwent the Negishi-coupling[20] with previously prepared or commercially obtained alkylzinc iodide reagent to form the 4,5-dialkylphthalonitrile (Scheme 2.3). The purification of this compound proved to be very difficult due to the similar mobilities of 4,5-dialkylphthalonitrile and 4-alkyl-5-chlorophthalonitrile which can be obtained in the reaction mixture in some cases.

c) Synthesis of 4,5-dialkylphthalonitriles *via* Sonogashira cross-coupling

Another synthetic route for the preparation of 4,5-dialkylphthalonitriles was reported by Leznoff and co-workers by means of a Sonogashira cross-coupling reaction.[13,26] An excess of the terminal alkyne reacts with 4,5-diiodophthalonitrile in triethylamine (TEA) at 110 °C using $Pd(PPh_3)_2Cl_2$ and CuI as catalysts to give the 4,5-dialkynylphthalonitriles.[26,27] Hydrogenation of 4,5-dialkynylphthalonitrile **210** can offer a better alternative way for the preparation of **211** in contrast with other multistep preparations of 4,5-dialkylphthalonitrile which require low-yield reactions using copper cyanide (Scheme 2.4).[28-30]

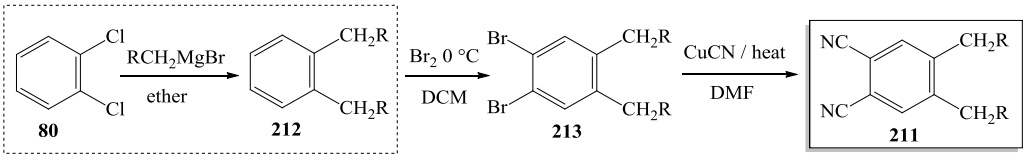


Scheme 2.4: Synthesis of 4,5-dialkylphthalonitrile *via* Sonogashira coupling.

2.2.1.2.2 Cross-coupling reaction using 1,2-dichlorobenzene as precursor

a) Synthesis of 4,5-dialkylphthalonitriles *via* Kumada cross-coupling

Kumada cross-coupling[31] can also be used to prepare 4,5-dialkylphthalonitrile following the procedure used by Hanack[29] where the dichlorobenzene was treated with a freshly prepared alkylmagnesium bromide and Ni catalyst to give dialkylbenzene which underwent bromination and then cyanation to form the targeted phthalonitrile (Scheme 2.5).[32] This route has proved to be difficult to apply, but still can be utilised in some cases. Several dialkylsubstituted phthalonitriles were prepared from their precursors (brominated dialkylbenzene) through Kumada cross-coupling reactions.

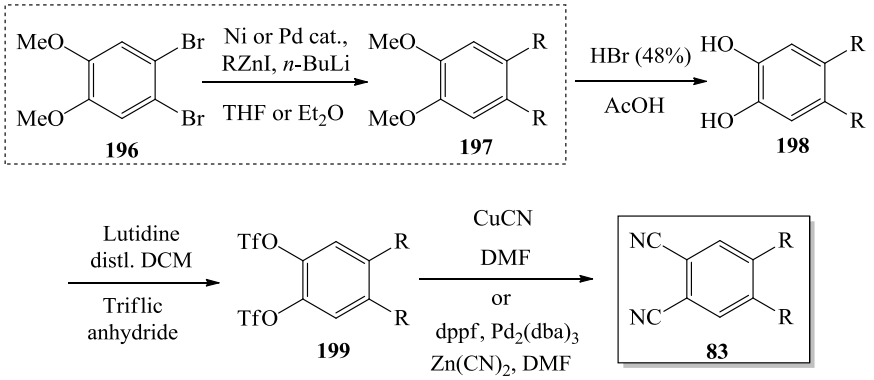


Scheme 2.5: Synthesis of 4,5-dialkylphthalonitrile *via* Kumada coupling.

2.2.1.2.3 Cross-coupling reaction using 4,5-dibromoveratrole as precursor

a) Synthesis of 4,5-dialkylphthalonitriles *via* Negishi cross-coupling

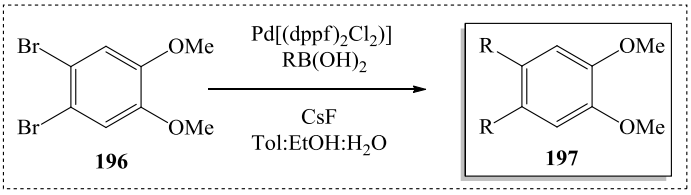
4,5-Dialkylphthalonitriles can be synthesised following the Negishi cross-coupling reaction[20] utilising 4,5-dibromoveratrole as precursor.[20] Treatment of 4,5-dibromoveratrole and alkylzinc iodide reagent with palladium or nickel catalyst leads to the formation of 4,5-dialkylveratrole. Several synthetic steps were applied in order to obtain the target phthalonitrile as shown in Scheme 2.6.



Scheme 2.6: Negishi cross-coupling of 4,5-dibromoveratrole.

b) Synthesis of 4,5-dialkylphthalonitriles *via* Suzuki-Miyaura cross-coupling

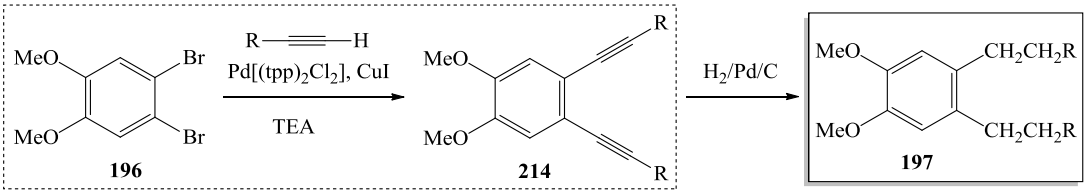
Suzuki cross-coupling reaction[21] conditions are used to convert **196** into the corresponding dialkylated phthalonitrile **197** in the presence of palladium catalyst and cesium fluoride as a base (Scheme 2.7). This reaction was followed by several steps as illustrated in Scheme 2.6 above to form the target phthalonitrile **83**.



Scheme 2.7: Suzuki-Miyaura cross-coupling of 4,5-dibromoveratrole.

c) Synthesis of 4,5-dialkylphthalonitriles *via* Sonogashira cross-coupling

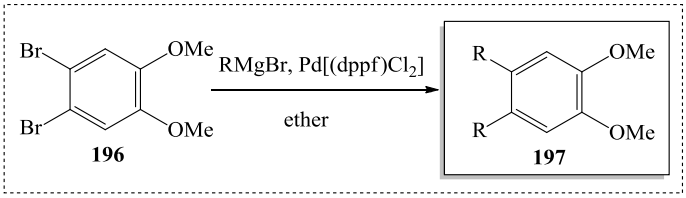
Sonogashira cross-coupling[26] reaction can also be used as an alternative method for the preparation of 4,5-dialkylphthalonitriles. Treatment of 4,5-dibromoveratrole with alkyne in the presence of Pd catalyst and copper (I) iodide in TEA can obtain the desired **214** which can undergo a hydrogenation reaction to obtain 4,5-dialkylveratrole (Scheme 2.8). The use of a number of synthetic steps as depicted in Scheme 2.6 leads to the formation of required 4,5-dialkylphthalonitrile.



Scheme 2.8: Sonogashira cross-coupling of 4,5-dibromoveratrole.

d) Synthesis of 4,5-dialkylphthalonitriles *via* Kumada cross-coupling

Synthesis of 4,5-dialkylphthalonitriles can also be achieved from its precursors (4,5-dibromoveratroles) *via* Kumada cross-coupling reactions[31] (Scheme 2.9), followed by several synthetic steps and finally cyanation to afford the desired phthalonitriles (Scheme 2.6). Kumada cross-coupling reactions offer a successful and straightforward way for preparing several examples of dialkylated veratroles in reasonable yields.

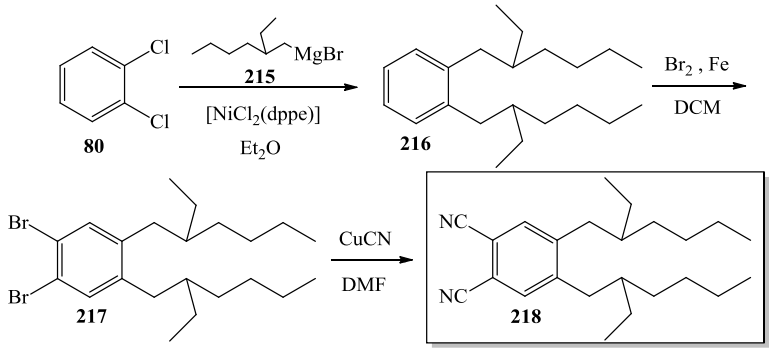


Scheme 2.9: Kumada cross-coupling of 4,5-dibromoveratrole.

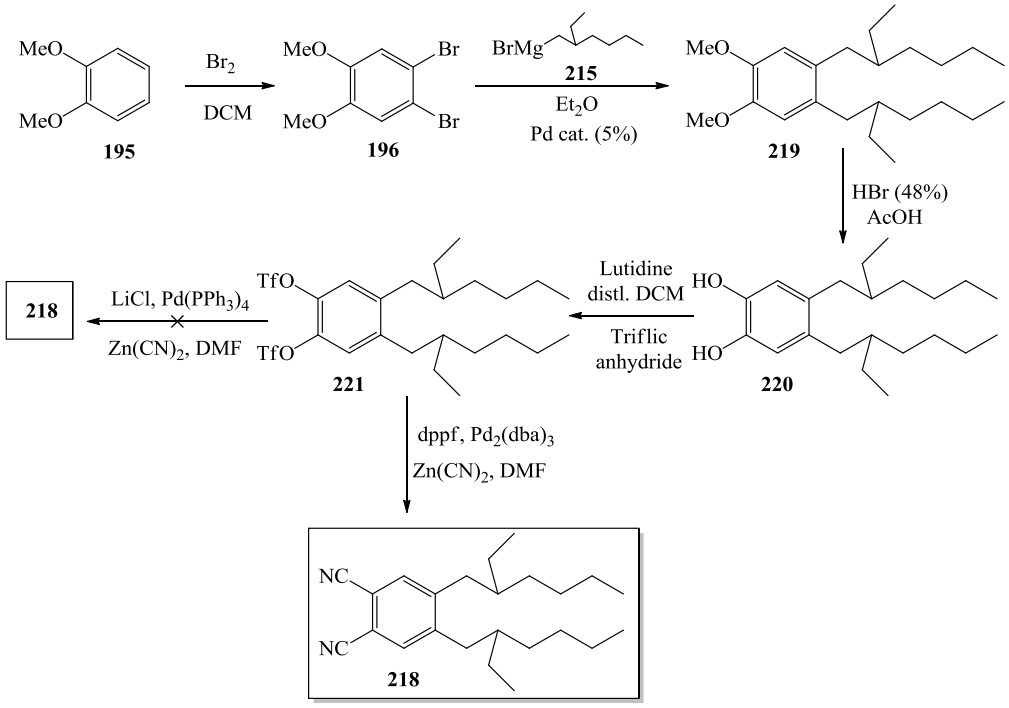
After this review of the possible ways for synthesising phthalonitriles, we discuss the chosen methods for preparing our target phthalonitriles in the following sections.

2.2.2 Synthetic design of targeted phthalonitrile 218

The first challenge was the synthesis of 4,5-bis(2-ethylhexyl)phthalonitrile **218**. These precursors were chosen because the branched (chiral) chains, introduced using racemic 2-ethylhexyl bromide, confer excellent solubility on phthalocyanine macrocycles[61] and this behaviour was also observed in TBTAPs. Several potential synthetic routes could be used to prepare phthalonitrile **218**. Two of these designed strategies have been chosen to synthesise the required phthalonitrile **218** as depicted in Schemes 2.10 and 2.11, respectively. Preliminary investigation was carried out and gave promising results but conditions were thoroughly studied during the course of this work. This set of reactions and modifications to the scheme below are discussed in the next section.



Scheme 2.10: First synthetic route towards phthalonitrile **218** using 1,2-dichlorobenzene as precursor.



Scheme 2.11: An alternative synthetic route towards phthalonitrile **218** using 4,5-dibromoveratrole as precursor.

2.2.3 Synthesis of 4,5-bis(2-ethylhexyl)phthalonitrile *via* Kumada cross-coupling reaction using 1,2-dichlorobenzene as precursor

The initial attempt to synthesise the target phthalonitrile **218** was through Kumada cross-coupling[31] reaction using 1,2-dichlorobenzene as precursor, followed by electrophilic bromination and Rosenmund von Braun cyanation reaction[17] in the last step (Scheme 2.10). Following the procedure described by Hanack for preparing analogous compounds,[29] 1,2-dichlorobenzene **80** was stirred with a nickel catalyst

([1,2-bis(diphenylphosphino)ethane]dichloronickel(II)). A freshly prepared solution of (2-ethylhexyl)magnesium bromide **215** in diethyl ether was added dropwise to the previous mixture at room temperature and left under reflux overnight. A series of colour changes during the addition of Grignard reagent at room temperature was detected. After work-up of the reaction, 1,2-bis(2-ethylhexyl)benzene **216** was isolated as a liquid in 90% yield. Characterisation by ^{1}H NMR spectroscopy confirmed the identity of the product obtained. There was a singlet at 7.10 ppm in the aromatic region of the spectrum integrating for four protons. A multiplet at 2.54 ppm integrated for four protons was assigned to the benzylic protons. The rest of the aliphatic protons also appeared in the ^{1}H NMR spectrum as expected.

The next step in the preparation of phthalonitrile **218** was the bromination of **216**. A similar reaction was also employed by Hanack[29] and required keeping the bromination reaction at 0 °C for a period of 44 hours which was not convenient for us as we had no means of keeping the temperature at 0 °C for that length of time. In our case, the bromination was achieved using the method described by Ashton and co-workers.[33] Iodine and iron powder was added to a solution of 1,2-bis(2-ethylhexyl)benzene **216** in DCM which was then treated with a bromine at 0 °C over two hours. The mixture was then left to stir overnight. The reaction was worked-up and washed several times with an aqueous solution of sodium metabisulfite and sodium bicarbonate. The product was isolated by column chromatography using PE as eluent giving the desired product as a liquid in 83% yield. Analysis by ^{1}H NMR spectroscopy indicated the presence of the required product **217**. In some cases, the reaction gave a mono-brominated compound which was separated from the desired di-brominated product during the column chromatography.

The final step involved the cyanation of 1,2-dibromo-4,5-bis(2-ethylhexyl)benzene **217** to form the target 4,5-bis(2-ethylhexyl)phthalonitrile **218**. The reaction followed the extremely common procedure for preparing phthalonitriles known as the Rosenmund von Braun cyanation reaction.[17] At the first attempt, a mixture of di-brominated compound **217** and copper cyanide in dry DMF was heated under reflux overnight resulting in the formation of a trace amount of the desired product with a side-product identified as the corresponding copper phthalocyanine. Formation of the copper phthalocyanine was only observed when the reaction was left at a high temperature for a long time in the presence of copper ions. Indeed, these conditions were considered as traditional reaction conditions for preparing metallated

phthalocyanine. Due to this problematic synthesis, in the following attempt, care was taken not to heat the reaction for any longer time than necessary as well as avoiding heating at high temperature, as the unwanted copper phthalocyanine could probably form under such conditions. In this case the reaction was allowed to reflux at 150 °C under an argon atmosphere for 16 h. After cooling, the reaction crude was stirred with an aqueous solution of ammonia for 24 h in order to remove the excess of copper cyanide. Purification using column chromatography was accomplished in order to obtain a pure product **218** as a bright yellow oil in 7% yield. Analysis by ^{1}H NMR spectroscopy was used to characterise compound **218**. The ^{1}H NMR spectrum showed a singlet at 7.49 ppm assigned to the two aromatic protons and a multiplet at 2.57 ppm integrating for four protons represented the four benzylic protons. The rest of the aliphatic protons were also presented in the ^{1}H NMR spectrum. Product **218** was also analysed by ^{13}C NMR spectroscopy which indicated twelve signals corresponding to the twelve different carbon environments of compound **218**.

Synthesis of phthalonitrile **218** using the technique described above in Scheme 2.10 gave unsatisfactory results due to the problematic synthesis in bromination and cyanation steps. In the bromination step, the formation of mono-brominated product led to difficulties to isolate the required product from the side-products even after several attempts to separate them. In addition, in the cyanation step, the purification of the product was more difficult to achieve due to the formation of copper phthalocyanine in some cases. Indeed, if phthalonitrile **218** was successfully prepared without any side-product, it was still difficult to remove the excess of copper cyanide and we needed to wash the compound several times by an aqueous solution of ammonia. It also was observed that the cyanation reaction gave a really low yield. As a result of all problematic synthesis and purification, an alternative synthetic route has been employed in order to synthesise the target phthalonitrile **218** in a better yield. Detailed descriptions of this alternative method will be discussed below in next section.

2.2.4 Synthesis of 4,5-bis(2-ethylhexyl)phthalonitrile *via* Kumada cross-coupling reaction using 4,5-dibromoveratrole as precursor

An alternative route was attempted through Kumada cross-coupling reaction,[31] followed by a sequence of synthetic steps and finally cyanation reaction in order to synthesise the target 4,5-bis(2-ethylhexyl) phthalonitrile **218** (Scheme 2.11). This

route begins with bromination of the commercially available veratrole **195** to give di-brominated veratrole in a yield of 100%.[94] Analysis by ^{1}H NMR spectroscopy proved the presence of all the expected signals. The aromatic proton peaks were observed at 7.06 ppm as a singlet integrating for two protons. The chemical shift of the aromatic peak was found further downfield than that of compound **195**. This was due to the de-shielding effects of the bromine atoms. The CH_3 protons next to the oxygen atoms were present at 3.85 ppm.

The next step was the Kumada cross-coupling reaction[31] which has been subjected to several amendments by our group. 4,5-Dibromoveratrole was stirred with tris(dibenzylideneacetone)dipalladium at room temperature under an inert atmosphere. A freshly prepared solution of (2-ethylhexyl) magnesium bromide was added dropwise at room temperature and then the mixture heated to reflux overnight. The reaction mixture was worked-up and purified by column chromatography over silica gel (hexane/EtOAc, 5:1) to give 1,2-bis(2-ethylhexyl)-4,5-dimethoxybenzene **219** as an oil in 71% yield. ^{1}H NMR spectroscopy was used to characterise this compound and to confirm its identity. A singlet at 6.61 ppm assigned to the two aromatic protons and a multiplet at 2.41 ppm integrating for four protons represented the four benzylic protons. The CH_3 protons next to the oxygen atoms were observed at 3.85 ppm and all the rest of the aliphatic protons were present in the ^{1}H NMR spectrum as expected.

The next step in the preparation of phthalonitrile **218**, involving the demethylation of **219**, used the procedure described by Piatelli *et al*.[54] Conversion of methoxy groups to hydroxyl groups was achieved using a 1:1 mixture of hydrobromic acid and glacial acetic acid. The mixture was left to reflux overnight. Initial analysis of this mixture by TLC indicated the formation of a trace of desired product but unfortunately, the starting material was still present in the reaction mixture. However, when the reaction was left to reflux for a long period of time (72 h), the product **220** was formed in a high yield 99% and no starting material was recovered at the end of the reaction. Characterisation by ^{1}H NMR spectroscopy confirmed the identity of the product obtained.

Aryl triflates can be conveniently prepared from phenol derivatives in reasonable yields. In this reaction, the phenol was treated with trifluoromethanesulfonic anhydride (triflic anhydride) in the presence of a base such as pyridine, lutidine or triethylamine at low temperature.[34] Investigation of this reaction by our group led to the conclusion that the yield of the reaction was very low when the reaction was

carried out in the presence of pyridine as base, whereas employing lutidine instead of pyridine gave satisfactory results.[25] In our case, compound **220** and lutidine were dissolved in dry DCM and then cooled down to -78 °C. Initial addition of the triflic anhydride was performed and the mixture left to warm to room temperature overnight. This led to formation of triflated product in a quite low yield. However, improved yield was obtained when the addition of the triflic anhydride was done over an hour under an inert atmosphere and then left to warm to room temperature and stirred overnight. The resulting reaction mixture was worked-up and purification by column chromatography afforded the product in 66% yield. Lutidine has been considered as useful material in this reaction in two ways, as a co-solvent to dissolve the starting material **220** and to neutralise the triflic acid which can be formed in the reaction mixture. It also prevented any further attack on compound **221** due to its lower nucleophilicity compared with pyridine which can be subjected to a nucleophilic substitution.[34,35] Analysis of compound **221** by ^{1}H NMR spectroscopy displayed a single peak at 7.17 ppm, corresponding to the two aromatic protons and a multiplet at 2.53 ppm integrating for four protons represented the four benzylic protons. All aliphatic protons were shown in the ^{1}H NMR spectrum as expected.

The next step involved the conversion of the ditriflate **221** into required phthalonitrile **218** (Scheme 2.11) which proved to be more challenging than expected. Several reaction methods was reported in the literature.[37-39] Nevertheless, the initial synthesis of phthalonitrile **218** followed the procedure descried by Kobuta and Rice.[40] In this reaction, $Pd(PPh_3)_4$ was employed as catalyst and zinc cyanide as cyanide source in the presence of dry DMF at 120 °C. Unfortunately, the reaction failed to form the required phthalonitrile under such conditions and no starting material was recovered.

An alternative method was employed, involving the cyanation of 4,5-bis(2-ethylhexyl)-1,2-phenylene bis(trifluoromethanesulfonate) to give 4,5-bis(2-ethylhexyl)phthalonitrile **218** using the procedure described by Hanack and Drechsler. This also proved to be more challenging than expected.[19] In their investigations, the triflated catechols were converted into their corresponding nitriles using tris(dibenzylideneacetone) dipalladium as source of palladium (0) and DPPF as ligand in the presence of anhydrous DMF as solvent. Zinc cyanide was added portionwise to the reaction mixture over a prolonged period of time (2 h). DPPF was used in this reaction to stabilise the intermediate cationic species and also to protect the palladium from forming the tetracyano palladium complex with excess cyanide. The reason

behind adding the $Zn(CN)_2$ portionwise over a period of time was to keep the concentration of free cyanide to a minimum.[19] It was observed that when the nickel catalyst was used in this reaction, no useful results were obtained.[41]

Several attempts were made by our group in order to find the appropriate reaction conditions. For example, changing the number of portions (5, 16, 17, 18, 21), using dry and wet DMF, applying different temperatures (40, 50, 60, 63, 65, 70 °C) and changing the reaction time (5, 6, 22, 24 h). After all these attempts to optimise the reaction and improve the yield, our group found that the best result was obtained when the $Zn(CN)_2$ was added in 16 portions and the reaction heated at 63 °C for 22 h after the addition of $Zn(CN)_2$. This reaction is an exothermic reaction and leads to a rise in the temperature inside the flask. Due to this behaviour, this reaction should be monitored carefully. It also was observed that when the oil bath is employed as heating source, the results were quite good as well as the ability of controlling the reaction temperature became accessible whereas using the DrySyn® heating plates led to a failure of stabilisation of the reaction temperature and the formation of decomposed materials.[25]

After all these modifications by our group we were able to use this procedure confidently to target molecule **218** in reasonable yield. Several attempts have been made in order to optimise the reaction towards synthesis our target phthalonitrile (Table 2.1). The initial attempts followed the modified Hanack's procedure.[25] Zinc cyanide was added portionwise (16 portions) over 2 h at 62 °C to a mixture of aryl triflate (large scale) and palladium catalyst in dry DMF. No product was obtained and only starting materials recovered. However, using a small scale (0.50g) of aryl triflate gave a good yield (59%). It was observed that the yield obtained was influenced by the quantities of starting materials used in the reaction. A small portion of aryl triflate (0.50-2.00 g) therefore was used in order to synthesise the desired phthalonitrile. Improvement in phthalonitrile yield has been detected when the reaction temperature rose up to 90 °C with a decrease in the number of zinc cyanide portions added. Best result was obtained as illustrated in line 5 (Table 2.1). In addition, efficient results were obtained when the DMF was divided into two parts, one used to dissolve the catalyst and ligand, while the other to dissolve the starting material completely in the solvent. The usage of wet DMF did not improve the result further.[42]

After the formation of the product was successfully completed, the work-up and purification afforded the clean product as a yellow liquid. For the purification, the

crude was washed several times by hexane and filtered through a filtration paper to remove the brown sticky materials which included the rest of catalyst and ligand used in the reaction. The rest of clear yellow solution was evaporated to remove the solvent and then applied to a silica gel column using hexane:ethyl acetate (30:1) to remove any impurities from the product. The product obtained from this reaction was analysed by ^{1}H NMR spectroscopy to confirm its identity. A singlet at 7.52 ppm represented the two aromatic protons and a multiplet at 2.59 ppm integrated for four protons indicated to the four benzylic protons. All the aliphatic protons appeared in the ^{1}H NMR spectrum as expected. ^{13}C NMR spectroscopy displayed twelve different carbon environments which confirmed the success of the formation of product **218**.

SM (221) quantity (g)	$Zn(CN)_2$	Solvent	Temp (°C)	Time after addition	Results
8.00 g	16 portions	dry DMF	60-64	24 h	SM
1.00 g	16 portions	dry DMF	60-64	24 h	SM
0.50 g	16 portions	dry DMF	60-62	24 h	59 % product
0.50 g	2 portions	dry DMF	85-87	24 h	72 % product
1.00 g	2 portions	dry DMF	70-75	24 h	82 % product
2.00 g	1 portion	dry DMF	88-90	24 h	74 % product

Table 2.1: Summary of attempted conditions for cyanation of **221**.

Synthesis of phthalonitriles **218** proved to be challenging, it also does have some drawbacks which severely hindered this investigation. Their syntheses were unpredictable and purifications tedious to achieve. Because of these observations, we decided to investigate the synthesis of another phthalonitrile, **222**, which proved to be easy to synthesise, has high symmetry yet is heavily branched, conferring solubility and preventing aggregation.

2.3 Synthesis of Alternative Peripherally Substituted Tetrabenzotriaza porphyrins and its Precursors

Synthesis of an alternative tetrabenzotriazaporphyrin was investigated through the formation of phthalonitrile **222**. The target molecules (TBTAPs and its precursor) are represented in Figure 2.4 below.

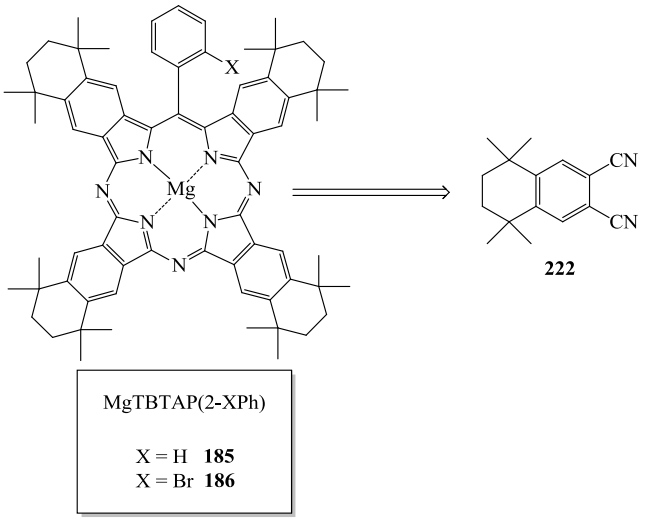
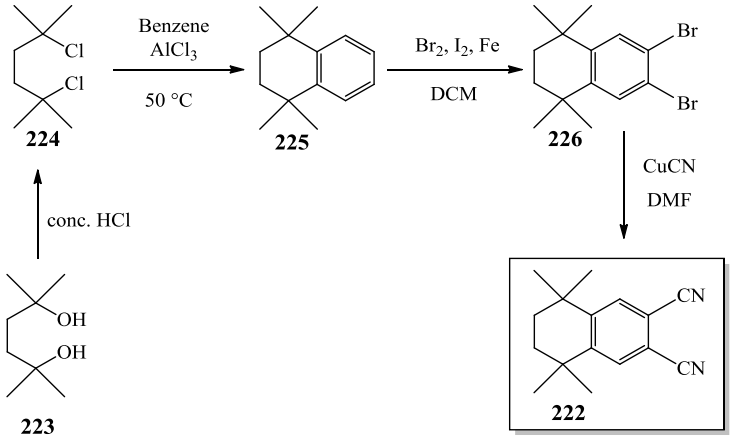


Figure 2.4: Tetrabenzotriazaporphyrin target molecules and required precursor.

2.3.1 Synthetic design of the required phthalonitrile 222

The second challenge targeted the synthesis of alicyclic alkyl substituted phthalonitrile **222**.[43] The synthetic route followed the methods shown in Scheme 2.12.

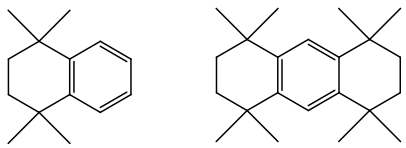


Scheme 2.12: Synthetic routes towards 4,5-disubstituted phthalonitrile **222**.

2.3.2 Synthesis of 6,7-dicyano-1,1,4,4-tetramethyltetralin

This route started with the conversion of diol **223** into dichloride **224**.[44-46] A solution of concentrated hydrochloric acid saturated with hydrogen chloride gas was added to diol **223** cooled in an ice bath then left to stir at room temperature overnight. The crude was then washed several times with water and extracted with DCM. Concentration of the resulting material gave the product in 74% yield. Characterisation by ^{1}H NMR spectroscopy confirmed the identity of the product obtained.

Second step was achieved using Bruson's procedure *via* Friedel-Crafts reaction.[46] The reaction was involved the condensation of 2,5-dichloro-2,5-dimethylhexane with benzene in the presence of anhydrous aluminium chloride, and gave a liquid mono- and a crystalline di-cycloalkylation product, **225** and **227**, respectively (Figure 2.5).[46] It was observed that when the reaction was carried out at room temperature, the yield was a little low, therefore we decided to increase the reaction temperature to 50° C and we noticed that the yield improved significantly and the formation of by-product decreased. After cooling, the resulting material was worked-up using DCM and then washed by methanol to remove the side-product **227** which was easy to crystallise as white crystals from MeOH, leaving behind the desired compound **225** dissolved in the solvent. The product was washed several times by MeOH to ensure that all the side-products were removed from the target molecule. Product **225** was obtained as a colourless liquid in 94% yield. Analysis of the crude by TLC showed two spots corresponding to compounds **225** and **227**. After purification, TLC of product **225** showed only one spot and subsequently analysed by ^{1}H NMR spectroscopy, showing all the signals corresponding to the desired compound **225**.



225 **227**

Figure 2.5: Possible products from the condensation of 2,5-dichloro-2,5-dimethylhexane with benzene.

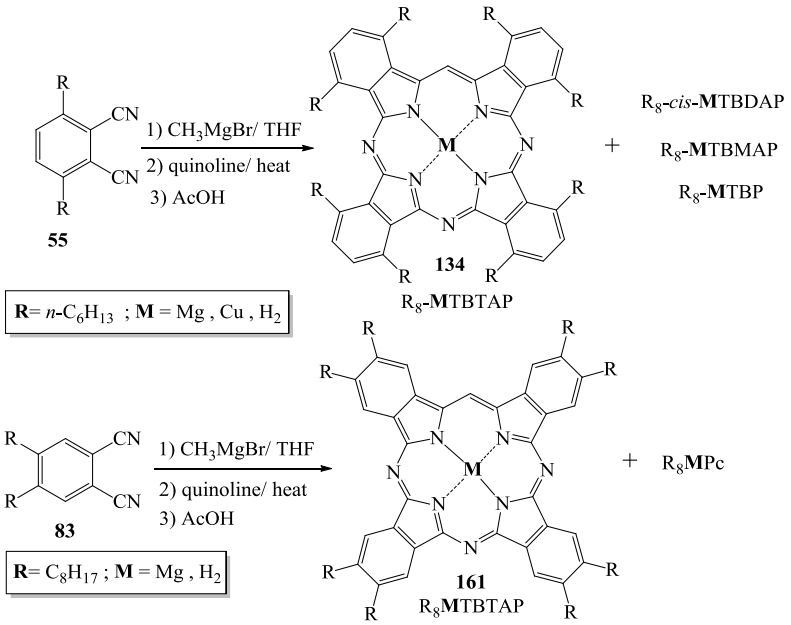
The next step involved the bromination of 1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene **225** using Ashton's procedure.[33] A mixture of compound **225** with iodine and iron powder was dissolved in DCM and then treated with a bromine at 0 °C over 30 min. The mixture was then left to stir at room temperature overnight. After working-up and washing several times by an aqueous solution of sodium metabisulfite and sodium bicarbonate to remove the excess bromine, the product was purified using column chromatography with PE:DCM (3:2) as eluent yielding the desired product in 86% yield. The mono-brominated side product can be separated easily from product **226** by column chromatography. Product **226** was characterised by ^{1}H NMR spectroscopy which displayed all the signals corresponding to the desired compound **226**. At 7.50 ppm, two aromatic protons were represented by a singlet. It was found that the signals of two aromatic protons were further downfield as a result of the de-shielding effects of the bromine atoms. The rest of the aliphatic protons were presented in the ^{1}H NMR spectrum as expected.

Introduction of dinitrile groups in last step was achieved following the Rosenmund von Braun cyanation reaction.[17] A solution of di-brominated compound **226** in dry DMF was heated under reflux with copper cyanide. After 3 hours, the reaction was checked by TLC in order to see if the reaction was complete. Unfortunately, the TLC showed two spots; one was the starting material and the other was the product. The reaction mixture was therefore left to reflux overnight in order to push the reaction towards the formation of the desired product. Analysis of the crude mixture by TLC showed the product along with a blue spot identified as the corresponding copper phthalocyanine. The formation of unwanted phthalocyanine could be due to the prolonged refluxing in presence of obtained phthalonitrile and copper metal (these considered as the appropriate conditions for synthesis of CuPc). However, CuPc can be separated from the product by column chromatography. In the next attempt, the reaction was allowed to reflux at 150 °C under an argon atmosphere for 16 h to avoid the formation of unwanted blue materials. After cooling, the mixture was stirred with an aqueous solution of ammonia at room temperature for 24 h under a stream of air in order to remove excess copper cyanides. Purification by column chromatography using PE:DCM (3:2) gave the desired product as a yellow solid in 27% yield. ^{1}H NMR spectroscopy showed the aromatic proton signal at 7.71 ppm as a singlet integrating for two protons. The CH_2 proton signals were found at 1.72 ppm as a singlet integrating for four protons. Moreover, the CH_3 aliphatic proton signals were

obtained at 1.30 ppm as a singlet integrating for twelve protons. Synthesis of TBTAP using 6,7-dicyano-1,1,4,4-tetramethyltetralin as precursor is discussed in the next section.

2.4 General Synthesis of Peripherally Substituted Tetrabenzotriaza porphyrins

Synthesis of metal-free and metallated tetrabenzo(aza)porphyrin derivatives can be achieved following Linstead's procedure[3] which was modified and developed later by Cammidge, Cook and co-workers.[4] They established a controlled manner for accessing the full range of hybrid molecules (TBTAP, TBDAP, TBMAP and TBP) from reactions of 3,6-dialkylphthalonitrile with Grignard reagent MeMgBr. In addition, their results included a clarification of difference in the chemistry and reactivity of 3,6- and 4,5-dialkylphthalonitriles towards Grignard reagents. This synthetic route consisted of two main steps; the treatment of a solution of 3,6-dialkylphthalonitriles in ether or THF with different amounts of the Grignard reagent followed by exchange the solvent to quinoline and heating under reflux in order to obtain the target tetrabenzo(aza)porphyrin magnesium derivatives. Metal-free tetrabenzo(aza)porphyrins can be achieved by treating the metallated products with acids to obtain metal-free derivatives. The latter can be reacted with any metals like copper or zinc in order to insert those metals inside the central core of hybrid molecules which thus can offer new green materials possessing various chemical and physical properties (Scheme 2.13).[3,4] This reaction underwent a series of colour changes during the reaction progress. In first step, the colour was changed from a colourless solution to a deep blue/mauve mixture and this could be due to the formation of an oligomer intermediate. When the THF was removed under a stream of argon and the dry quinoline added, the reaction mixture changed to an intense red/mauve colour. A clear green colour was obtained after heating the mixture for 2-3 hours.[25]



Scheme 2.13: Synthetic route for preparing metallated and metal-free tetrabenzo(aza)porphyrin derivatives.

A series of stoichiometric ratios have been investigated deeply by our group in order to understand the effects of altering the ratios of reactants on the formation of products. 3,6-Dialkylphthalonitrile was used as a main precursor in this investigation which was treated with different amounts of MeMgBr. A full range of tetrabenzo(aza)porphyrin derivatives have been distinguished including TBTAB, *cis*-TBDAP (methine groups adjacent) and *trans*-TBDAP (methine groups apart), TBMAP, TBP and Pc depending on the amounts of MeMgBr used in the reaction. Best results for preparing TBTAP, TBDAP and TBMAP have been obtained when 2:1 equivalents of MeMgBr to phthalonitrile were employed. However, when 4,5-dialkylphthalonitrile was reacted with 2 equivalents of Grignard reagent MeMgBr, only TBTAP and Pc can be detected (Scheme 2.13).[3-6] These results were consistent with Leznoff and McKeown[7] outcomes where they attempted to prepare *meso*-substituted TBTAPs using 4-substituted phthalonitriles and various Grignard reagents. The reaction mixture in their investigations contained TBTAPs with phthalocyanine and trace amounts of the TBDAPs, however, no TBMAPs and TBPs were obtained.[7] More information about this investigation is discussed in chapter one.

In addition, it has been observed that when a large quantity of Grignard reagent was used in the reaction, the formation of the more porphyrin-like materials were identified whereas using a small quantity of MeMgBr led to the formation of less

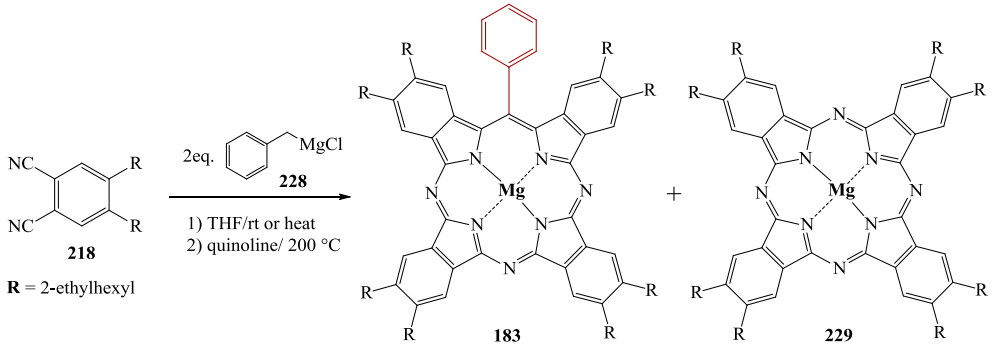
porphyrin-like materials. It was also noticed that the formation of tetrabenzo(aza)porphyrin derivatives can be affected by the quinoline used in the reaction whether it was added freshly after distillation or after a period of time. Best results have been obtained when both solvents (THF and quinoline) added to the reaction are freshly after distillations and de-gassed. This technique helped to avoid the oxygen which can negatively impact on the reaction yields. Moreover, heating using an oil bath was preferred rather than the ordinary DrySyn® heating plates because it reduces the fluctuation of temperature during the reaction. Both solvents (THF and quinoline) played as key roles in this reaction, where several experimental attempts were conducted to ascertain the significance of their presence in the reaction. These experiments resulted in the importance of the presence of THF in the first step for the formation and stability of the oligomer intermediate and the necessity of quinoline (high boiling point solvent) in the final step to close the ring. It was detected that the best results were obtained when removing THF firstly with leaving a small amount of this solvent in the reaction mixture and finally adding the quinoline to the mixture and heating the reaction at high temperature (approx. 220 °C).[25]

In the light of previous results we decided to use 4,5-dialkylphthalonitrile as precursor and investigate its chemistry and reactivity towards various Grignard reagents. Novel tetrabenzotriazaporphyrin derivatives and their precursors have been synthesised through traditional synthetic procedures[3,4] and their modified version[47] as well as a new route discovered by our group[48] that could find application in organic electronic devices on the basis of their interesting properties.

2.4.1 Synthesis of [2,3,9,10,15,16,23,24-octakis(2-ethylhexyl)-27-phenyl-tetrabenzo[*b,g,l,q*] [5,10,15]triazaporphinato] magnesium

The conditions used for the cyclisation of phthalonitrile to produce the peripherally substituted TBTAP were based on the methodology investigated by Leznoff and McKeown[7] (their procedure is similar to that discovered by Linstead[3] but they use exclusively Grignard reagents for the prompting the cyclisation and quinoline as the cyclisation reaction medium) and modified later by Cammidge, Cook and co-workers.[4] Cammidge's investigations proved that when 2:1 equivalents of Grignard reagents to phthalonitriles were utilised in the reaction, a reasonable amount of TBTAP was obtained compared with other hybrid complexes.[4,25] A number of experimental attempts were performed following the established procedure[4] in order

to synthesise *meso*-phenyl TBTAP, but ended with no results in some cases. There is no doubt that the introduction of an aromatic substituent at the *meso*-position of TBTAP macrocycles is much more complicated than preparing TBTAPs bearing only a methine group at the *meso*-site, especially if the aromatic substituent possesses a variety of functional groups. Indeed, it was a challenge to find the best reaction conditions for preparing the targeted macrocycles. Diverse conditions were applied in order to obtain the required TBTAPs. Table 2.2 shows the summary of the attempted conditions and their outcomes.



Scheme 2.14: Preparation of *meso*-phenyl TBTAP **183**.

Solvent I	Status	Temp. °C	Time	Solvent II	Status	Temp. °C	Time	Results
THF	freshly distilled	rt	30 min	quinoline	freshly distilled	200	3 h	nr
THF	freshly distilled	80	30 min	quinoline	freshly distilled	200	2 h 3 h 6 h 24h	nr nr nr 28% TBTAP, Pc
THF	freshly distilled	80	30 min	quinoline	freshly distilled	200	≥ 48 h	TBDAP, Pc trace TBTAP
THF	freshly distilled	80	30 min	quinoline	distilled (3 days, kept with molecular sieves under Ar)	200	24 h	19% TBTAP, Pc
Ether	freshly distilled	rt	30 min	quinoline	freshly distilled	200	24 h	nr
THF	freshly distilled	80	30 min	diglyme	freshly distilled	200	24 h	nr

Table 2.2: Summary of attempted conditions for preparing TBTAPs.

From all these attempted experiments we gained an understanding of which conditions are favoured to produce TBTAP **183**. The conclusions we reached are; the THF should be distilled freshly before use in the reaction and the mixture must be heated gradually (i.e. rt →80 °C) in order to form the required oligomer intermediate. No product was obtained when the THF was stirred with phthalonitrile and Grignard reagent at room temperature. Moreover, using ether instead of THF gave no TBTAP product. In the second step, the quinoline must also be distilled freshly in order to obtain good results. However, when the quinoline is used after 3 days from the distillation process and kept dry using molecular sieves under Ar, the product was obtained but in a lower yield than the one produced when fresh quinoline was used. Exchanging the quinoline by diglyme gave no positive result even after prolonged refluxing. The reaction time played a key role in this reaction as well, where we noticed that when the reaction in the second step was refluxed for 2 h, no product was obtained. Thus the reaction was left to reflux for more time and closely checked for the changes in the mixture colour. After 24 h stirring in refluxing quinoline, we noticed the formation of green materials containing a combination of TBTAP, Pc and sometimes a trace amount of TBDAP.

Overall, preparation of TBTAP **183** was achieved taking into account all above-mentioned modifications (Scheme 2.14). The reaction begins with treatment of a solution of phthalonitrile **218** in freshly distilled THF with two equivalents of benzylmagnesium chloride **228**. The reaction temperature should be raised from rt to 80 °C gradually and the mixture was kept heating for approximately 30 min. After the removal of THF and cooling for 20 min, distilled quinoline was added in a single portion. The mixture was then left to heat at 200 °C for 24 h. During this period of time, the reaction mixture underwent a series of colour changes (honey→dark brown→olive→green). The reaction mixture was cooled to rt and passed through a silica gel plug, initially eluting with MeOH in order to remove the remaining quinoline and other polar side-products, then the residue was flushed out with THF and a dark green fraction was collected. After the removal of solvent under reduced pressure, the resulting green materials were analysed by MALDI-TOF mass spectrometry which showed a cluster of peaks around (*m/z* 1509) corresponding to the required compound **183** and the other around (*m/z* 1435) assigning to the side-product which was identified as magnesium peripherally substituted phthalocyanine (Figure2.6).

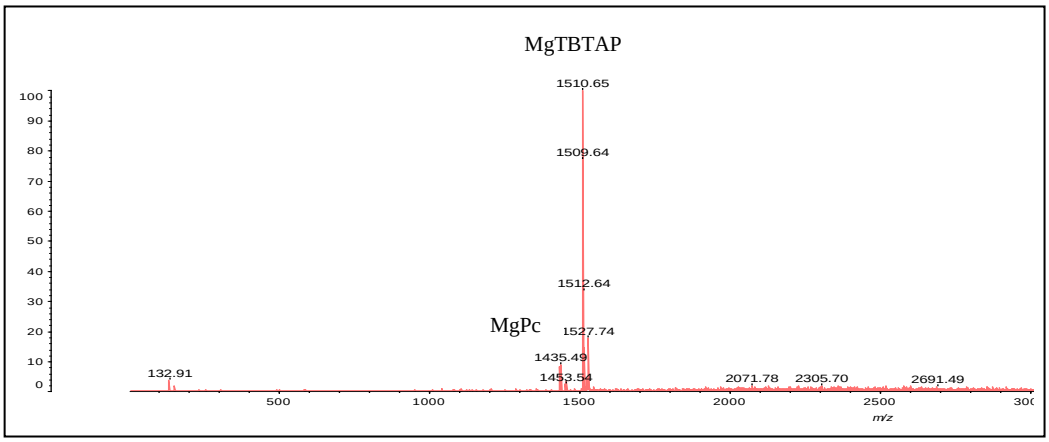


Figure 2.6: MALDI-TOF- MS of crude reaction mixture of TBTAP **183**.

The presence of eight alkyl chains was expected to improve solubility of TBTAPs in common solvents and was expected to be advantageous for purification purposes and characterisation by NMR spectroscopy. However, peripherally octa-substituted tetrabenzotriazaporphyrins showed increased aggregation which made the purification and characterisation of TBTAPs difficult compared with non-peripherally substitueted TBTAPs. In addition, ^{1}H NMR spectra can be complicated and broadened as a result of the formation of diastereomeric mixtures.

Chromatography was then performed to separate product **183** from the by-product using a mixture of PE:dry THF (15:1). Two fractions were isolated, a green fraction (MgTBTAP) and a blue fraction (MgPc). The green material was purified by further column chromatography using DCM:PE (1:15) followed by recrystallisation of the product using PE:dry THF (10:1) to afford a pure product in 28% yield. Several attempts have been employed to find the most appropriate eluent for the separation of the resulting green materials and also for the recrystallisation of the product.

Characterisation of TBTAP **183** was attempted by normal methods. Thus the compound gave exact molecular ion peak in the MALDI-TOF mass spectrum. TBTAP **183** also provided split Q-bands at 685 nm and 659 nm in the UV-Vis spectrum. A number of common NMR solvents such as chloroform-d, tetrachloroethane-d_2 and benzene-d_6 were used but gave complicated spectra, presumably due to aggregation. A successful NMR spectrum was obtained when deuteriated THF was used as NMR solvent. ^{1}H NMR spectroscopy indicated eight aromatic protons located on the non-peripheral positions of the tetrabenzotriazaporphyrin macrocycle in the 6.90-9.40 ppm range. The aromatic protons arising from the phenyl group at *meso*-position were found around 7.90-8.20 ppm range.

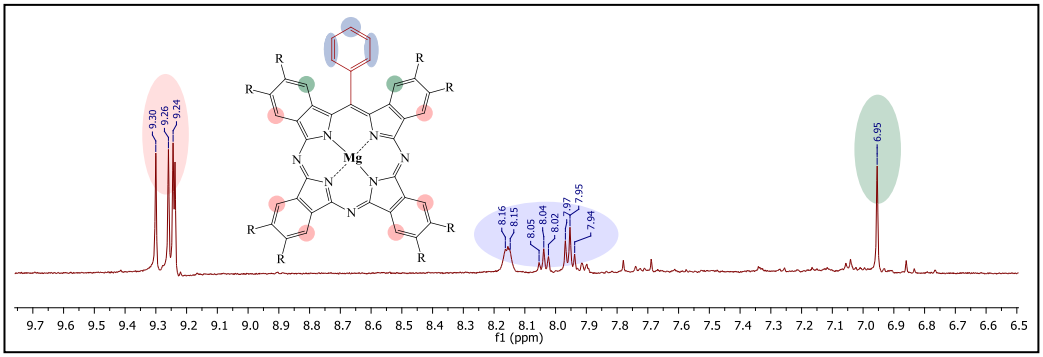
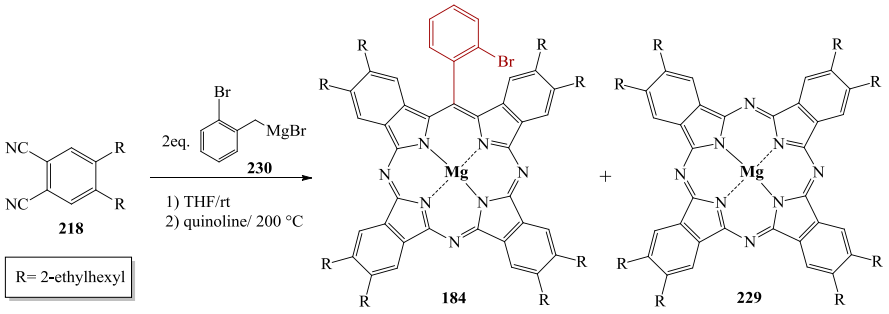


Figure 2.7: The ^{1}H NMR spectrum of TBTAP showing the aromatic protons.

2.4.2 Synthesis of [2,3,9,10,15,16,23,24-octakis(2-ethylhexyl)-27-(2-bromo phenyl)-tetrabenzo [*b,g,l,q*][5,10,15]triazaporphinato] magnesium

Synthesis of TBTAP **184** was achieved in a same manner as TBTAP **183** (Scheme 2.15). The Hanack transition metal-catalysed cyanation of aryl triflates was again used as the key step to generate the corresponding phthalonitrile **218** (Scheme 2.11). The synthesis of tetrabenzotriazaporphyrin **184** started with the cyclisation of the phthalonitrile with Grignard reagent taking into account all modifications mentioned earlier in preparation of TBTAP **183**. Two steps were employed in order to obtain the target TBTAP. In the first step, phthalonitrile **218** was dissolved in distilled THF and then followed by the addition of two equivalents of 2-bromobenzylmagnesium bromide **230**. The reaction mixture was allowed to heat at 80 °C for 30 min in order to generate the oligomer intermediate followed by exchange the solvent to quinoline and heating at 200 °C for 24 h to obtain sufficient amounts of the product for purification and characterisation. Purification of **184** by column chromatographies followed the same purifications described above for TBTAP **183**. The desired tetrabenzotriazaporphyrin magnesium was obtained in 16% yield.[47]



Scheme 2.15: Preparation of TBTAP **184**.

Characterisation of the TBTAP **184** was not straightforward, as encountered in the case of **183**. A correct molecular ion peak in the MALDI-TOF mass spectrum was obtained and the UV-Vis spectrum gave two Q-bands at 684 nm and 662 nm, respectively. The ^{1}H NMR spectrum showed the same problems as the TBTAP **183**. However, a clear ^{1}H NMR spectrum was obtained after several attempts (Figure 2.8). The aromatic protons corresponding to eight protons on the non-peripheral sites of the tetrabenzotriazaporphyrin molecule presented at 6.99, 9.25, 9.32 ppm. A set of peaks in 7.90-8.30 ppm range were observed. These were assigned as the aromatic protons of phenyl group at *meso*-position. ^{1}H NMR spectrum of TBTAP **184** gave broad signals which could be caused by some degree of aggregation of the products in THF. ^{1}H NMR spectroscopy is particularly informative, displaying distinct signals for the protons labelled in green colour (at 6.99 ppm) that lie in the shielding ring current of the *meso*-phenyl substituent.

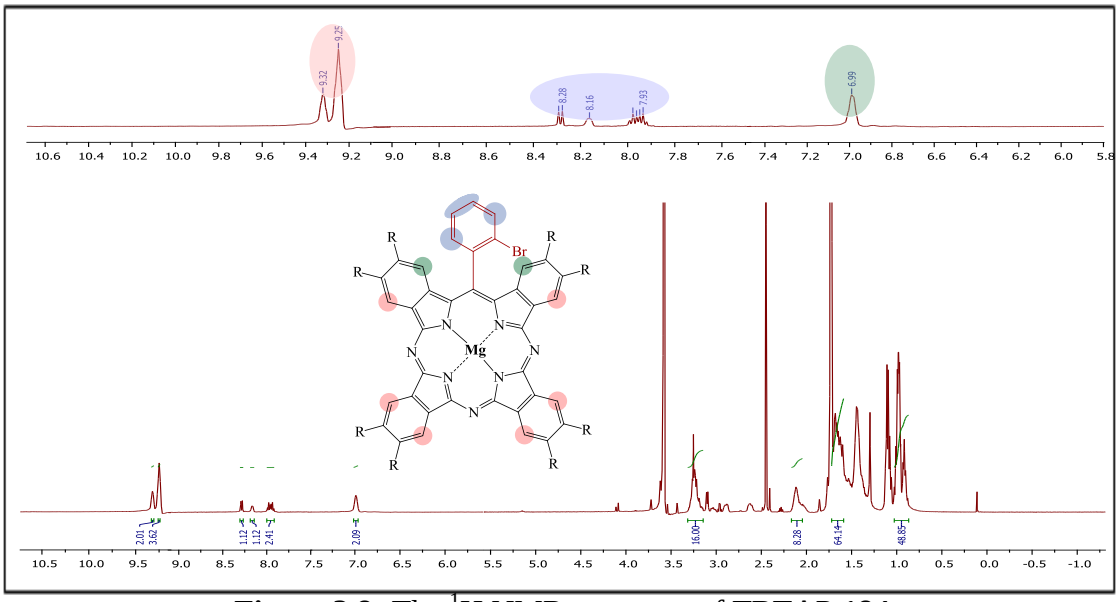
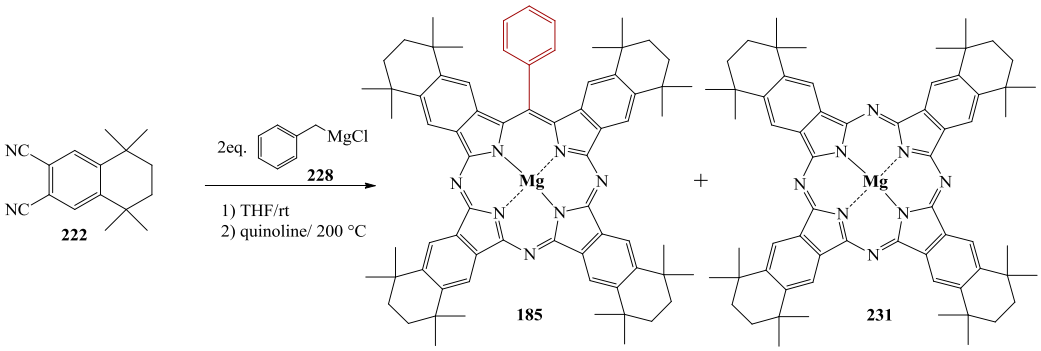


Figure 2.8: The ^{1}H NMR spectrum of TBTAP **184**.

2.4.3 Synthesis of [2,3,9,10,15,16,23,24-tetrakis(1,1,4,4-tetramethyl-6,7-tetralino)-27-phenyl-tetrabenzo[*b*,*g*,*l*,*q*][5,10,15]triazaporphinato] magnesium

Synthesis of TBTAP **185** was achieved under the same conditions described previously in section 2.4.1. The synthetic procedure for preparation TBTAP **185** started by reaction of phthalonitrile **222** with two equivalents of benzylmagnesium chloride **228** in freshly distilled THF followed by exchange of the solvent to quinoline and heating the mixture at 200 °C for 24 h. This led to generation of the target tetrabenzotriazaporphyrin magnesium **185** (Scheme 2.16). TBTAP **185** showed the

same difficulties faced during the purification and characterisation as the case in TBTAPs **183** and **184**. The highest yield obtained (8%) was consistent with the relatively low yields that were obtained from all other tetrabenzotriazaporphyrin macrocycles even after several careful attempts to synthesise the product. [47]



Scheme 2.16: Synthetic route towards TBTAP **185**.

The green product isolated from the reaction mixture exhibits a clear ^{1}H NMR spectrum after several attempts as illustrated in figure 2.9. The highly de-shielded signals at 9.53, 9.50, 9.48 ppm are present in the spectrum as well as a shielded signal at 7.24 ppm. Those signals arise from the eight aromatic protons presented on the non-peripheral locations of the tetrabenzotriazaporphyrin. Signals between 8.20-7.90 ppm originate from the five aromatic protons of the phenyl group located in *meso*-position. Furthermore, the Q-band absorptions at 662 nm and 687 nm were observed in its UV-Vis spectrum. The expected molecular ion (*m/z* 1052) was observed in the MALDI-TOF mass spectrum. All analytical data were consistent with the structure of the product.

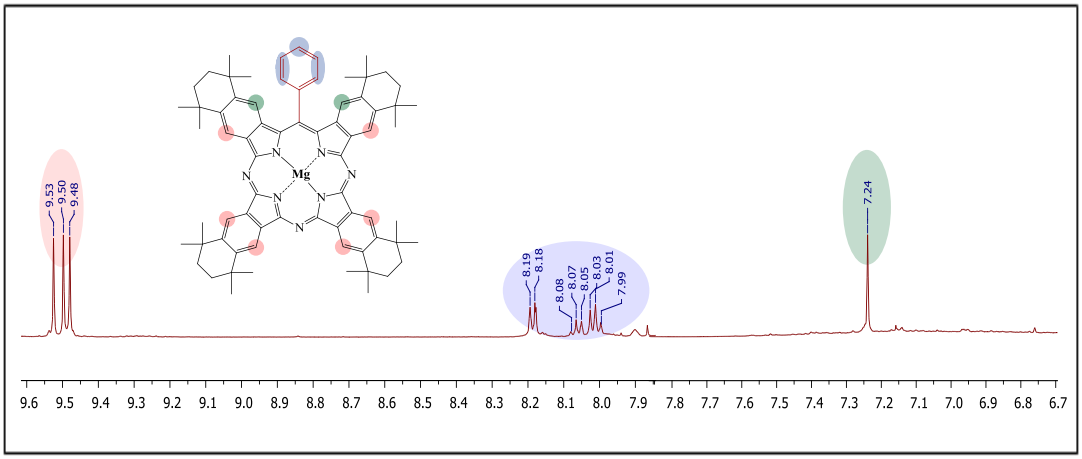
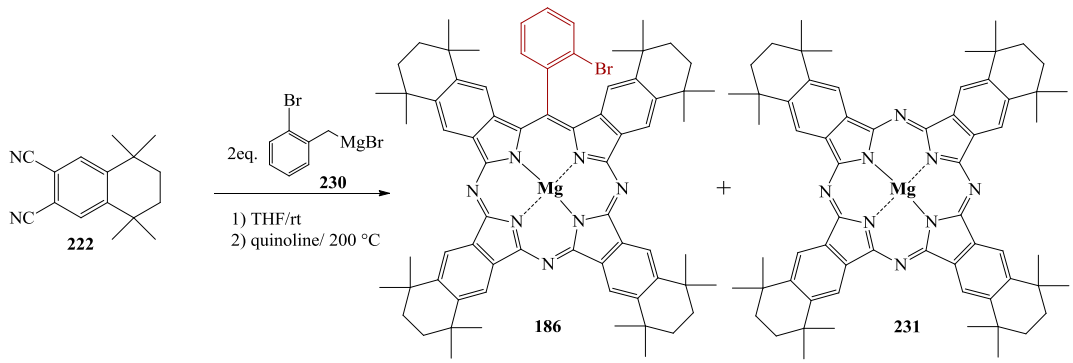


Figure 2.9: The ^{1}H NMR spectrum of TBTAP **185**.

2.4.4 Synthesis of [2,3,9,10,15,16,23,24-tetrakis(1,1,4,4-tetramethyl-6,7-tetralino)-27-(2-bromophenyl)-tetrabenzo[*b*,*g*,*l*,*q*][5,10,15]triazaporphinato] magnesium

The synthesis of tetrabenzotriazaporphyrin **186** from phthalonitrile **222** followed the same route as for previously prepared TBTAPs (Scheme 2.17). The first step involved the reaction between phthalonitrile and two equivalents of 2-bromobenzylmagnesium bromide **230** in distilled THF at 80 °C and led to the formation of a coloured intermediate. The following step included the removal of the THF and heating the mixture at 200 °C for 24 h in dry quinoline and gave rise to forming a green material identified as TBTAP **186**. Purification and characterisation of TBTAP **186** was also difficult to achieve. The yields were very low with the best achievable one being 12%.[47]



Scheme 2.17: Preparation of TBTAP **186**.

This reaction between phthalonitrile **222** and 2-bromobenzyl magnesium bromide received specific attention due to the formation of a remarkable side-product in 8% yield. ^{1}H NMR and X-Ray diffraction analysis proved the identification of the product as a phthalimidine **232** (Figure 2.10). Phthalimidine **232** is a direct analogue of Dent's original precursor used to synthesise TBTAP derivatives which is discussed in detail in chapter one. However, in our case its origin is likely to be through hydrolysis of the initial addition product formed between phthalonitrile **222** and 2-bromobenzyl magnesium bromide **230**.[47] The discovery of this new material led us to consider preparing TBTAPs using alternative methodology.

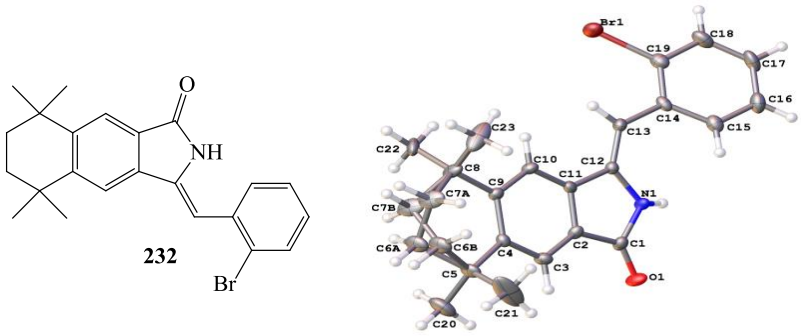


Figure 2.10: Phthalimidine isolated from the reaction between phthalonitrile and the Grignard reagent (with the structure obtained by X-Ray crystallography analysis).

The required TBTAP **186** gave the required peak in the MALDI spectrum at (*m/z* 1132) and provided a UV-Vis spectrum similar to TBTAP **185** with absorption at 665nm and 689 nm. ^{1}H NMR spectroscopy had to be performed in deuteriated tetrahydrofuran-d_8 as the compound did not give a good spectrum in common NMR solvents. The spectrum showed that the compound was pure and gave all signals corresponding to the aromatic protons introduced on the non-peripheral sites of the tetrabenzotriazaporphyrin **186**. Aromatic protons that belong to the phenyl group attached at *meso*-position of TBTAP **186** also appeared in the spectrum in the range of 7.90 to 8.40 ppm (Figure 2.11).

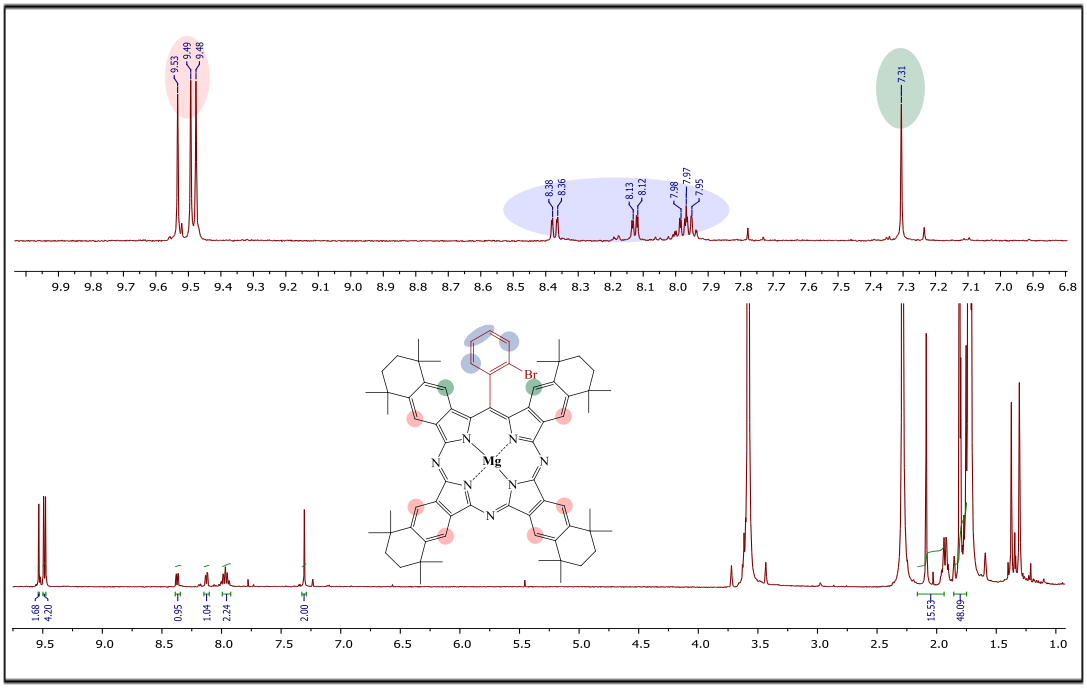
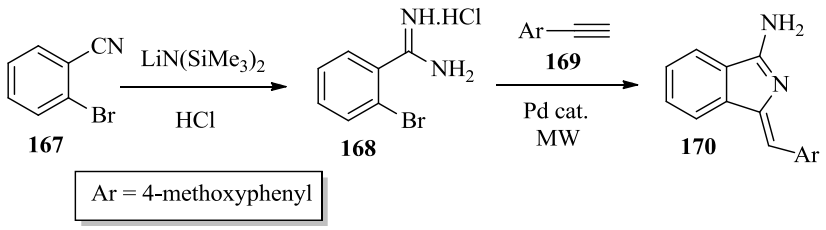


Figure 2.11: The ^{1}H NMR spectrum of TBTAP **186**.

2.5 A Modern Synthetic Route towards the Formation of Unsubstituted Magnesium Tetrabenzotriazaporphyrins

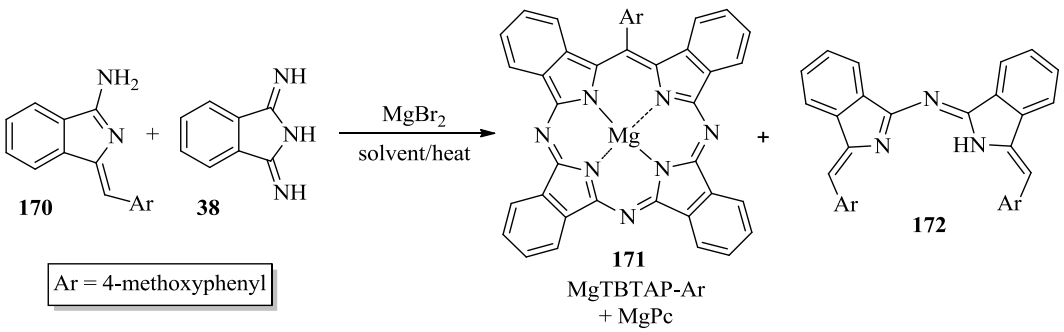
Different synthetic routes towards the formation of substituted *meso*-phenyl tetrabenzotriazaporphyrin have previously been attempted in our laboratory. However, the most reliably successful method for preparing TBTAPs as a single product of hybrid macrocycles was discovered by our group recently.[48] The investigated strategy started with the preparation of the aminoisoindoline or its derivatives by employing the procedure established by Hellal *et al*.[49] A solution of 4-bromobenzonitrile **167** in THF was treated with a solution of lithium bis(trimethylsilyl)amide (LiHMDS) in THF which then hydrolysed using a mixture of isopropanol/HCl in order to obtain the HCl salt of the bromoamidine **168** in good yield.[50] The intermediate **168** was then treated with 4-methoxyphenylacetylene using palladium catalysis under microwave irradiation resulting in the formation of the required compound **170** in reasonable yield. This reaction involved a copper-free Sonogashira cross-coupling (also known as Sonogashira[26]-Heck[57]-Cassar[56] coupling) and cycloisomerization technique as depicted in Scheme 2.18.[49]



Scheme 2.18: Synthesis of aminoisoindoline **170**.

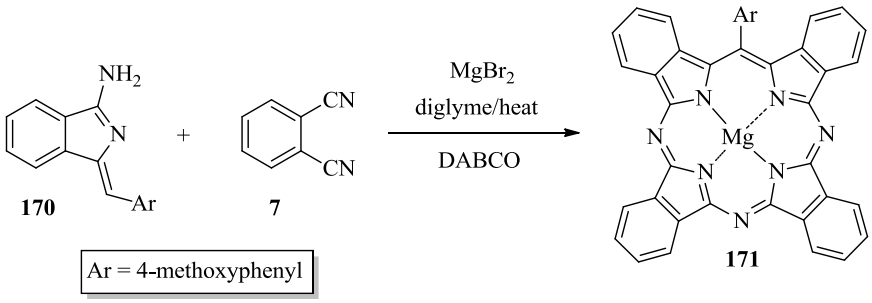
After a successful preparation of aminoisoindoline was achieved, our attention was directed into the available macrocyclization partners that can be used in this reaction. In the preliminary attempt the commercially available diiminoisoindoline **38** was selected as complementary macrocyclization partner. The reactions between **38** and aminoisoindoline **170** at high temperature in the presence of magnesium salt as a template (Scheme 2.19), were achieved in high boiling organic solvents (beginning with quinoline, DMEA, DMF, and ending with diglyme). Although the formation of the required product has been successfully performed, the results were not generally satisfactory due to the low yield obtained as well as the formation of unwanted side-products. It was easy to identify one of the side-products as a magnesium phthalocyanine (MgPc) as this product can form smoothly if appropriate conditions

are available (a high temperature, the presence of a template agent such as magnesium bromide and a high-boiling organic solvent as diglyme). A further coloured side-product has been isolated from the reaction mixture which was identified later as a self-condensation product of aminoisoindoline **170**. It also was noticed that when the dimeric intermediate **172** was re-subjected to the reaction conditions in the presence of excess amount of diiminoisoindoline, no TBTAP molecule was formed.[48]



Scheme 2.19: Formation of MgTBTAP along with Pc and dimeric intermediate **172**.

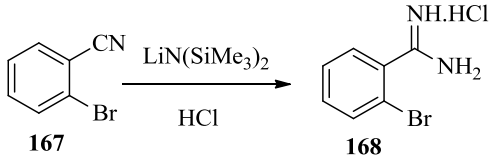
An additional modification was accomplished in order to improve the formed yield and obtain a more reliable and versatile route for preparing of *meso*-substituted TBTAPs. This modification included employing phthalonitrile **7** instead of the more reactive diiminoisoindoline **38** in order to decrease the formation of unwanted MgPc. Practically, a solution of phthalonitrile in dry diglyme was heated under reflux at 220 °C for 5 min followed by slow addition of a mixture of aminoisoindoline **170** and phthalonitrile **7** over 1 h. After a period of time (approximately 30 min), an additional amount of phthalonitrile **7** was added alongside DABCO (Scheme 2.20). The latter was added to the reaction mixture in order to release the unreacted aminoisoindoline **170** from its complex with the MgTBTAP product which then completed consuming the phthalonitrile **7** in order to obtain the required MgTBTAP in an improved yield.[48]



Scheme 2.20: A modern synthetic route towards *meso*-substituted TBTAP.[48]

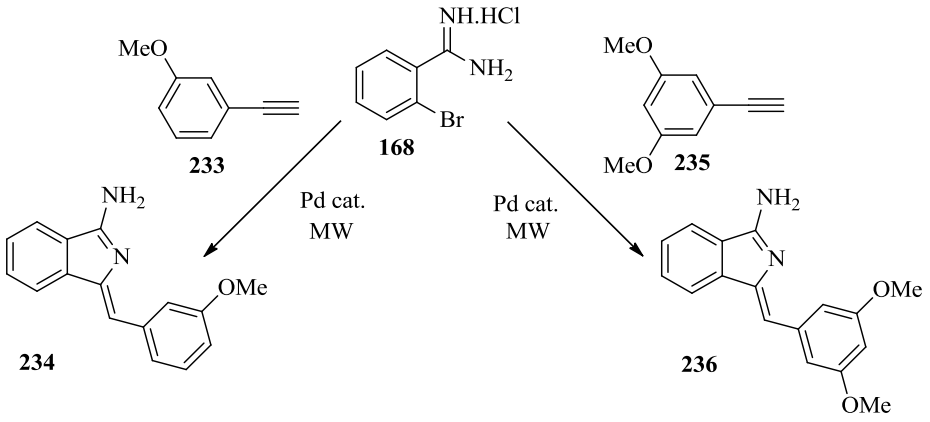
2.5.1 Synthesis of unsubstituted *meso*-(3-methoxyphenyl)TBTAP Mg and *meso*-(3,5-dimethoxyphenyl)TBTAP Mg *via* aminoisoindoline intermediates

Several *meso*-substituted TBTAP derivatives can be prepared following the procedure described above. This approach started with the synthesis of intermediate **168** from the commercially available 4-bromobenzonitrile **167**. A solution of nitrile **167** in THF was treated with a solution of lithium bis(trimethylsilyl)amide (LiHMDS) in THF followed by quenching with isopropanolic HCl to form amidine **168** in excellent yield (80%) (Scheme 2.21).[50]



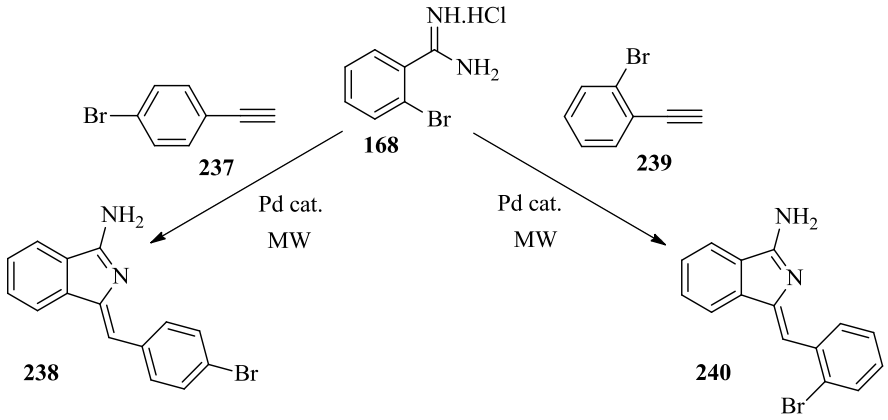
Scheme 2.21: Conversion of nitrile **167** to amidine **168**.

Once the synthesis of the amidine **168** was achieved successfully, we decided to embark on the preparation of a series of aminoisoindoline derivatives. Following the procedure reported by Hellal *et al*., a solution of substituted arylacetylenes and DBU in dry DMF was added to a mixture of amidines **168**, BINAP and $PdCl_2(MeCN)_2$.[49] The mixture was then irradiated in a microwave reactor at 120 °C for 1 h. After work-up and purification, the required products **234** and **236** were isolated in moderate yields of 41% and 25%, respectively (Scheme 2.22). Both products afforded satisfactory characterisation data by usual methods.[47] Generally, this tandem reaction involving a copper-free Sonogashira cross-coupling and cycloisomerization offers an efficient and stereoselective access to a vast number of the *Z*-isomers of aminoisoindoline derivatives.[49,62]



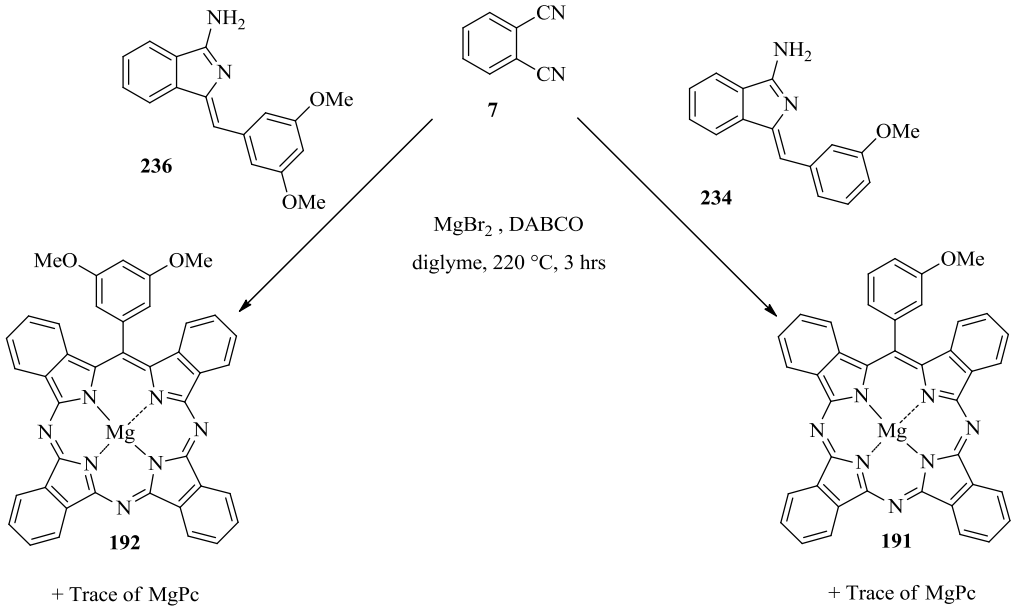
Scheme 2.22: Preparing substituted aminoisoindoline derivatives.

However, synthesis of brominated aminoisoindoline derivatives (Scheme 2.23) was much more complicated. The products obtained could not be isolated during the chromatographic separation due to the formation of several side products which were impossible to separate. Using different solvent systems did not improve the separation. Consequently, synthesis of *meso*-(bromophenyl)TBTAP could not be obtained through aminoisoindoline derivatives. This result was not surprising because we recognised that the presence of the extra bromoaryl unit could lead to many unwanted reactions.



Scheme 2.23: Synthetic route towards brominated aminoisoindoline derivatives.

Since a successful synthesis of aminoisoindoline derivatives has been achieved in a reasonable yield, the focus of the research moved onto the preparation of the target *meso*-substituted TBTAP derivatives. The cyclisation of phthalonitrile **7** and aminoisoindoline derivatives around a metal template (magnesium) was carried out following the process described by Cammidge and coworkers.[47,48] A suspension of phthalonitrile and $MgBr_2$ in dry diglyme was heated at 220 °C for 10 min under an argon atmosphere, in a preheated mantle. A further amount of phthalonitrile was added to a solution of aminoisoindoline in diglyme and sonicated for 5 min. The latter mixture was added slowly to the warm mixture during a period of time (approx. 1h) using a syringe pump. After finishing the addition, the reaction was left to reflux for 30 min. The final addition contained a solution of DABCO and an additional amount of phthalonitrile in diglyme over 1 h and then the reaction mixture was left to heat at 220 °C for 30 min (Scheme 2.24). When the reaction was left for more than 4 h, a drastic decrease in the overall yield of the TBTAP products can be observed.



Scheme 2.24: Preparation of *meso*-phenyl TBTAP derivatives.

Purification was carried out using a mixture of DCM:Et_3N:THF (10:1:4) as eluent leading to the isolation of a green material and a trace of blue product. The green fraction was purified further by column chromatography using PE:THF:MeOH (10:3:1) as eluent on a silica-gel column. Alternatively, size-exclusion chromatography over Bio-beads SX-3 using THF eluent could also be employed to give analytically pure material. Analysis of the blue fraction by UV-Vis spectroscopy and MALDI-TOF MS (Figure 2.12) proved the identification of the product as MgPcs, whereas the green product proved to be the required *meso*-phenyl MgTBTAPs. Both products **191** and **192** were isolated successfully in 20% and 8% yields, respectively.

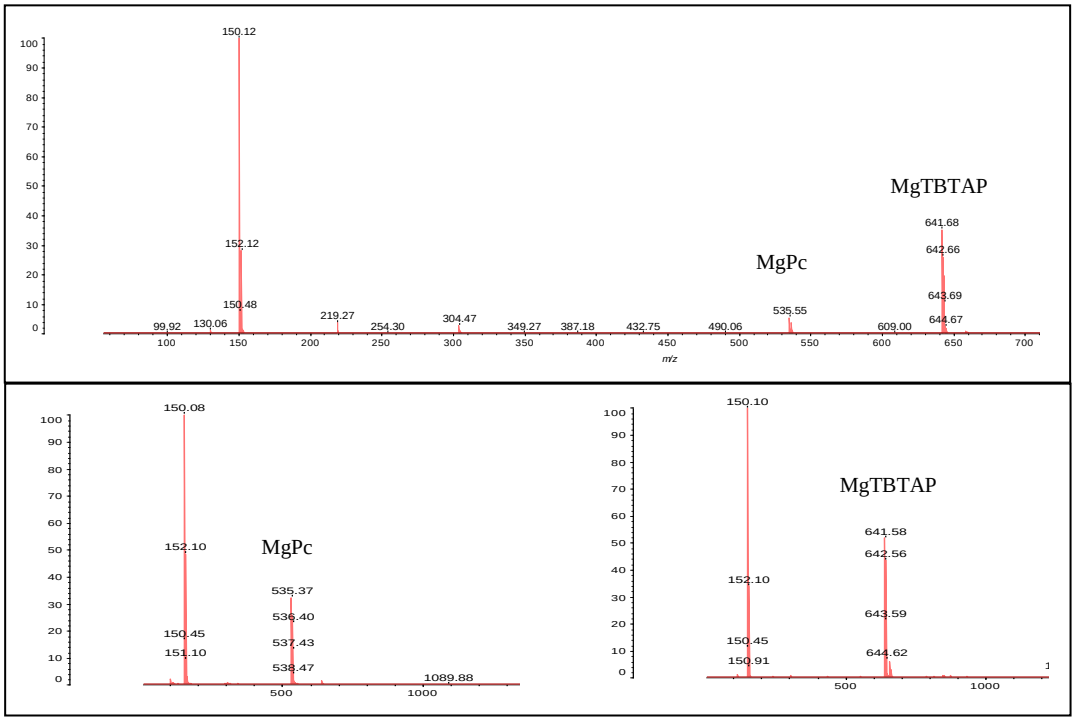


Figure 2.12: MALDI-TOF MS spectra of crude mixture (on the top) and the isolated (3-methoxyphenyl)TBTAP and magnesium phthalocyanine (on the bottom).

Several attempts were made to recrystallise the compound from different organic solvents. The best results were obtained when the products recystallised from acetone/EtOH (1:1) resulting in the formation of green crystals with purple reflex. Both crystalline materials were submitted for X-Ray crystallographic analysis. However, *meso*-(3-methoxyphenyl)TBTAP **191** failed to provide a suitable crystal for X-Ray diffraction analysis, whereas *meso*-(3,5-dimethoxyphenyl)TBTAP **192** gave a single crystal suitable for X-Ray diffraction analysis and its structure was unambiguously confirmed as shown in figure 2.13. It crystallises with a bound molecule of water and an acetone solvent molecule.

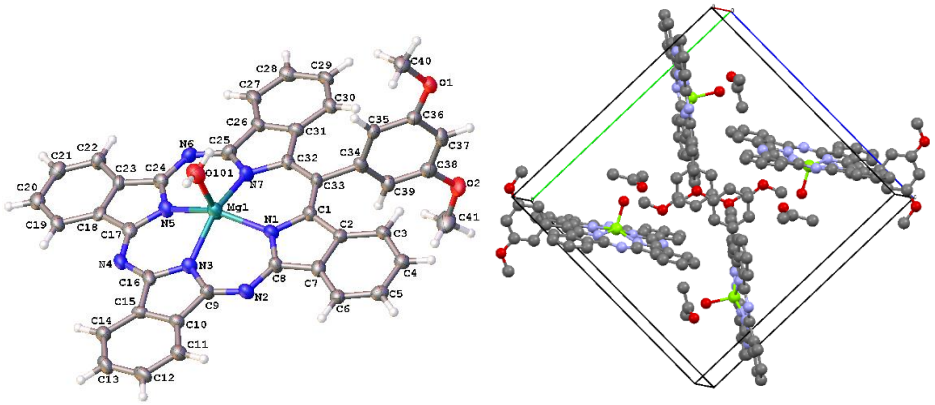


Figure 2.13: X-Ray structure for *meso*-(3,5-dimethoxyphenyl)TBTAP **192**.

Both products **191** and **192** were analysed by UV-Vis spectroscopy that showed the distinctive split Q-bands at 647 and 670 nm. The ^{13}C NMR spectra as well as the correct molecular ion peak in the MALDI-TOF mass spectra were achieved successfully. ^{1}H NMR spectra perfectly corresponded to the expected spectra for both products **191** and **192**. The ^{1}H NMR spectrum of *meso*-(3-methoxyphenyl)TBTAP **191** depicted in figure 2.14.

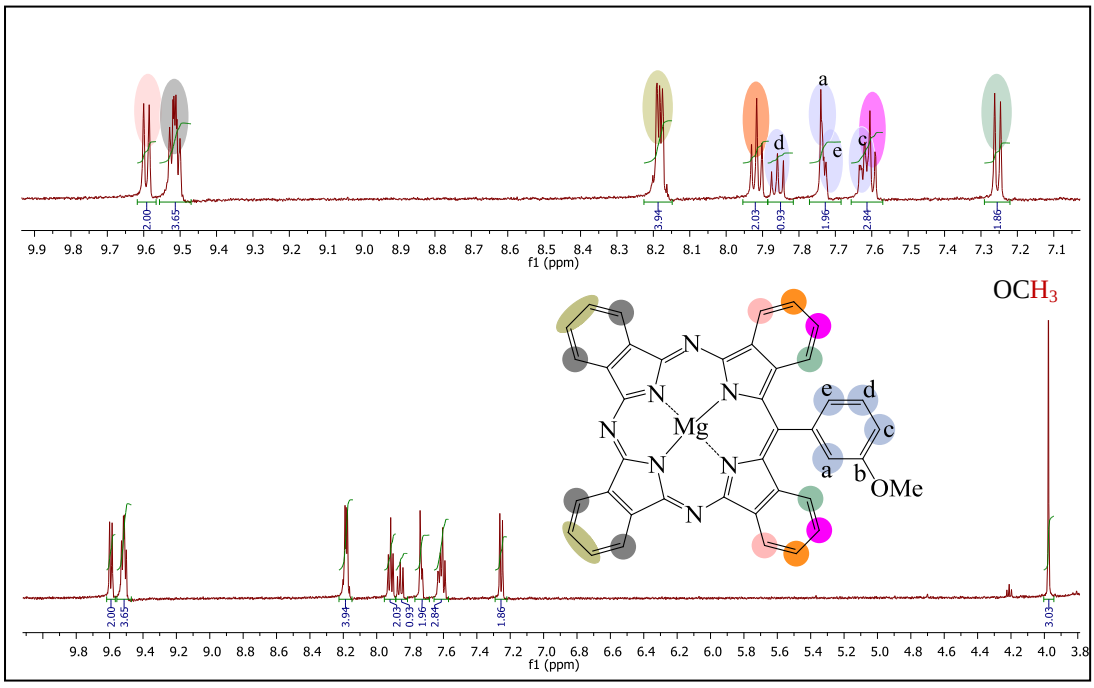
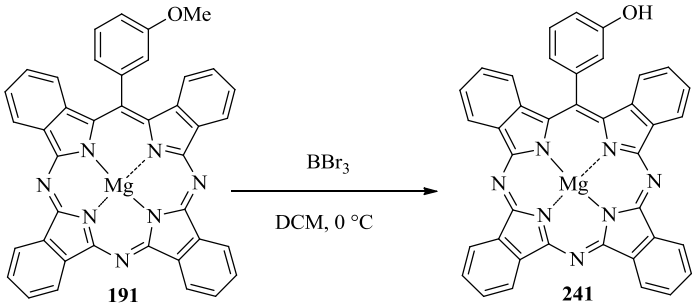


Figure 2.14: ^{1}H NMR spectrum of *meso*-(3-methoxyphenyl)TBTAP **191**.

2.5.2 Conversion of the methoxy groups of TBTAP derivatives into phenolic groups

With a successful formation of the *meso*-aryl TBTAP derivatives we were ready to embark on the successive conversion of the methoxy groups into phenolic groups (Scheme 2.25). Hydroxyl groups are very reactive to many reagents and can be used to synthesise new attractive hybrid materials.



Scheme 2.25: Demethylation of **191**.

Several reactions are available for such a hydrolysis. A number of methods have been reported for the cleavage of highly stable aryl methyl ethers employing strong acids or bases such as aluminum chloride,[51] cerium chloride,[52] and alkaline thiolate.[53] Another reaction follows the procedure described by Piatelli *et al.*[54] in which the methoxy substrate is stirred in a refluxing mixture of hydrobromic acid and glacial acetic acid. All these conditions were considered too harsh to be applied in this case due to the presence of metal ion in central core which can be easily exchanged to another metal ion or even removed from the central core. To avoid this issue we decided to use magnesium iodide as demethylating agent following the known procedure.[55] A successful conversion of *meso*-(4-methoxyphenyl)TBTAP into *meso*-(4-hydroxyphenyl)TBTAP has been achieved.[48] A solution of magnesium *meso*-(4-methoxyphenyl)TBTAP and MgI_2 in toluene was stirred at 170 °C for 19 h. However, the attempted demethylation of *meso*-(3-methoxyphenyl)TBTAP under the same reaction conditions led to unsatisfactory results even after leaving the reaction under reflux for more than 3 days. The starting material was always observed by TLC alongside the required product and the reaction could not be completed under these conditions. Moreover, we noticed in some cases, the product was decomposed during the work-up and no sign of any product has been observed when analysed by MALDI-TOF mass spectrometry (Table 2.3). Due to this issue we decided to proceed with using a common demethylation technique. This procedure included the conversion of

aryl methyl ether to the corresponding phenol using boron tribromide as demethylating agents.[55] Several conditions were attempted and the best results are illustrated as entry 14 (Table 2.3), confirmed by MALDI-TOF mass spectrometry of some experimental attempts as depicted in Figure 2.15. High temperature and acidic conditions should be avoided as acidic conditions are ideal for the formation of metal-free TBTAP by demetallation reaction of the corresponding magnesium TBTAP. The possible presence of HBr in reaction mixture during the removal of the solvent or transferring the sample might be the reason behind the formation of metal-free TBTAP in some experiments. BBr_3 is highly moisture sensitive and decomposes in air with evolution of HBr.

Entry	Agent	SM	Solvent	Temp (°C)	Time	Results
1	MgI_2 (5 eq.)	**191**	Tol	170	24 h	SM + trace prod.
2	excess				48 h	SM + trace prod.
3	excess				72 h	SM + trace prod.
4	excess				6days	prod. decomposed after workup +trace SM
5	MgI_2 (5 eq.)	**191**	no solvent	80	3 h	SM
6	MgI_2 (5 eq.)	**191**	dry (3:1) THF:ether	80	24 h	SM
7	excess				48 h	SM + trace prod.
8	MgI_2 (5 eq.)	**191**	dryDME	150	24 h	SM + trace prod.
9	BBr_3 (1 eq.)	**191**	dry DCM	rt	2 h	SM + trace prod. + (3-OH) PhTBTAP H_2
10	added once				3 h	prod. + (3-OH) PhTBTAP H_2
11	BBr_3 (2 eq.) added once	**191**	dry DCM	0 → rt	4 h	SM + prod.
				0 → rt	24 h	SM + prod.
12	excess			0 → rt	24 h	SM + prod.
13	BBr_3 (5 eq.) slow addition	**191**	dry DCM	0 → rt	24 h	prod. (39%)
14	BBr_3 (20 eq.) slow addition	**191**	dry DCM	0 → rt	2 h	prod. (50%)
15	BBr_3 (20 eq.) slow addition	**192**	dry DCM	0 → rt	2 h	several products + prod. (hard to isolate)

Table 2.3: Attempted conditions for synthesis of **241** and **242**.

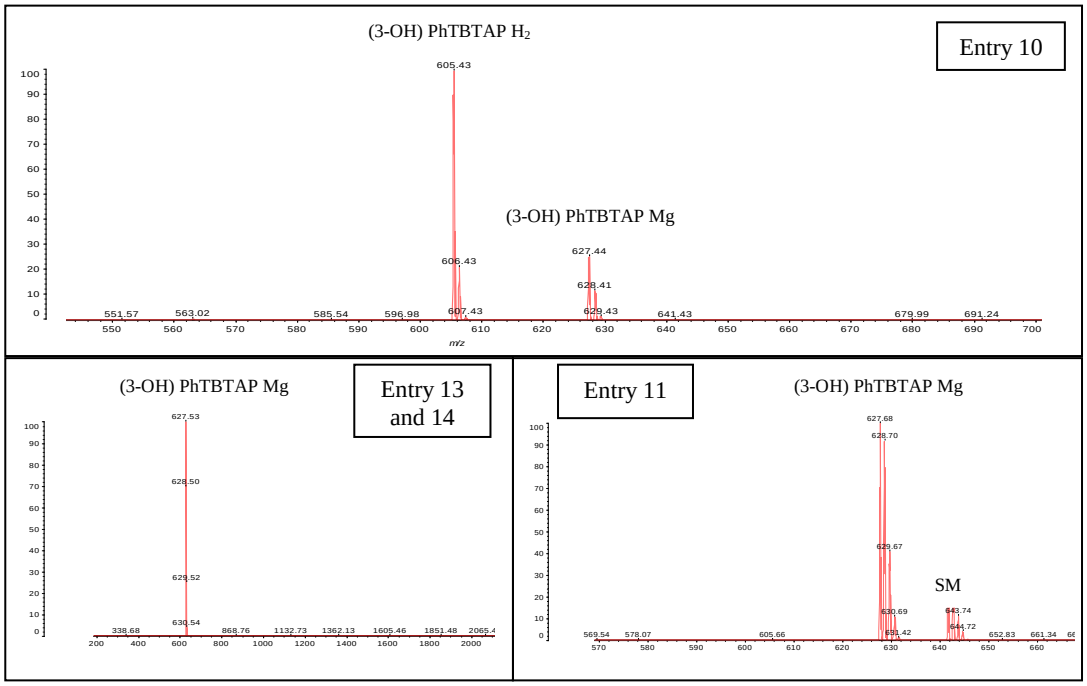


Figure 2.15: MALDI-TOF MS spectra of some attempted synthesis of **241**.

A solution of BBr_3 (1 M in DCM) was added slowly over 1 h to a solution of TBTAP **191** in cooled DCM. After finishing the addition, the reaction mixture was left to warm to room temperature and stirred for further 1 h. The reaction was repeated more carefully several times in order to obtain sufficient amounts of the product for purification and characterisation. After work-up and purification, the highest yield obtained for the formation of *meso*-(3-hydroxyphenyl)TBTAP **241** was 50%.

The product was analysed by UV-Vis spectroscopy, MALDI-TOF spectrometry, ^{1}H NMR (shown in figure 2.16) and ^{13}C NMR spectroscopy. Using *meso*-(3-hydroxyphenyl)TBTAP as precursor to form new materials proved to be challenging and required more investigations which are very complicated due to the difficulties faced in the synthesis and purification of starting materials as well as low yields obtained, consequently, we decided to focus on preparation of other functionalised complexes which would be more reliable to use in various organic syntheses.

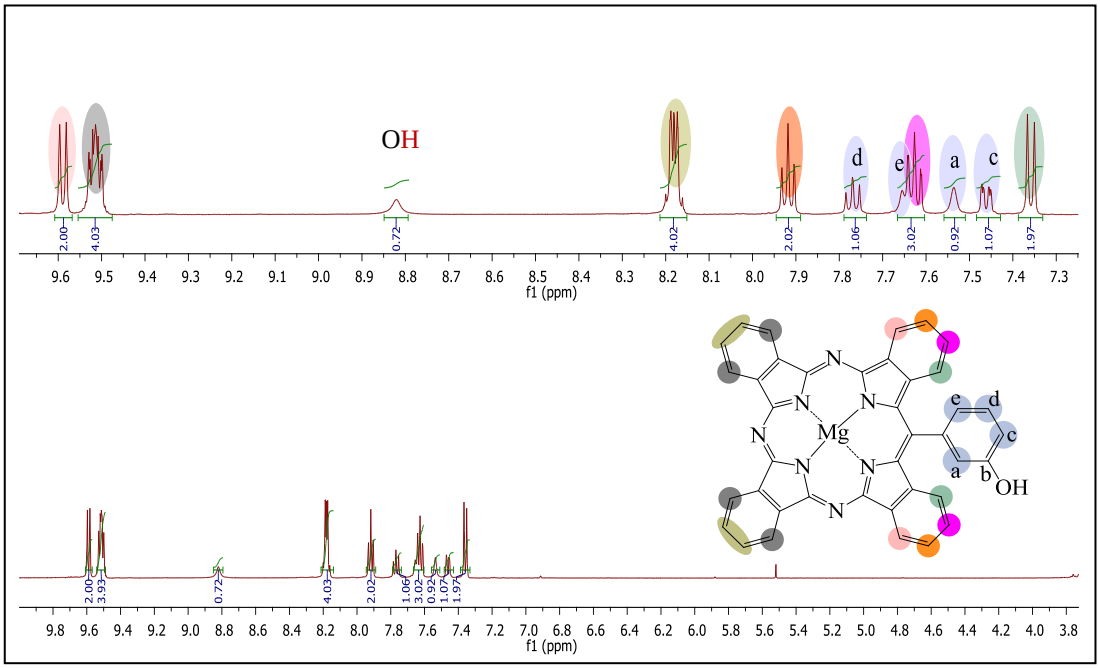


Figure 2.16: ^{1}H NMR for *meso*-(3-hydroxyphenyl)TBTAP **241**.

Preparation of (3,5-dihydroxyphenyl)TBTAP **242** was attempted by demethylation of the corresponding (3,5-dimethoxyphenyl)TBTAP **192** with boron tribromide in dry dichloromethane (Figure 2.17).[55] However, the reaction failed to give the desired product as a main product under the same optimised conditions previously used to prepare compound **241**. Several products were obtained which were impossible to separate even after a number of chromatographic attempts. Figure 2.18 shows the MALDI-TOF MS spectrum of the crude mixture from the demethylation reaction of **192**. Due to difficult separation and lack of a sufficient amount of the starting material, the synthesis of *meso*-(3,5-dihydroxyphenyl)TBTAP has not been investigated further.

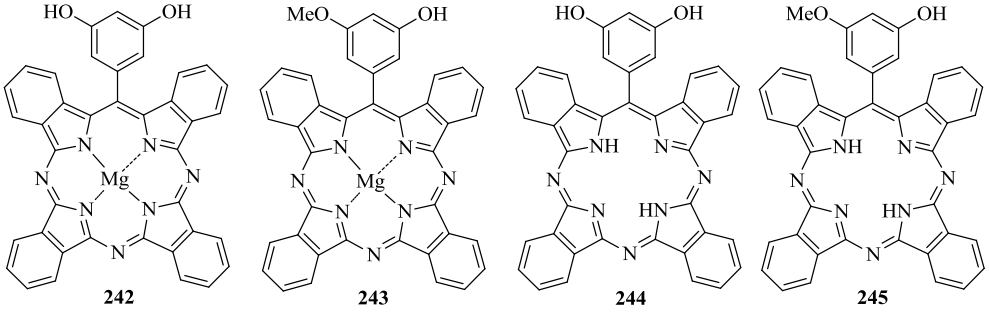


Figure 2.17: Products obtained in demethylation reaction of **192**.

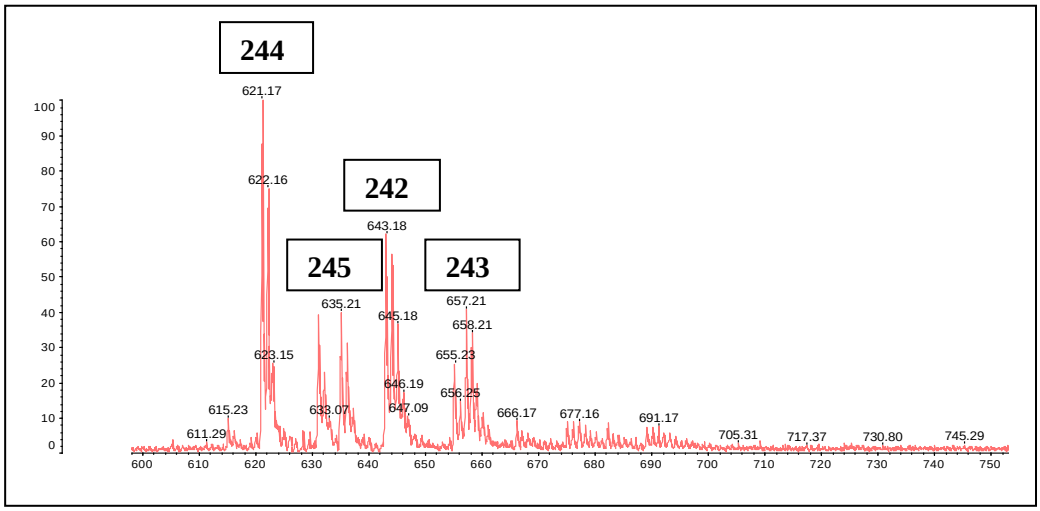
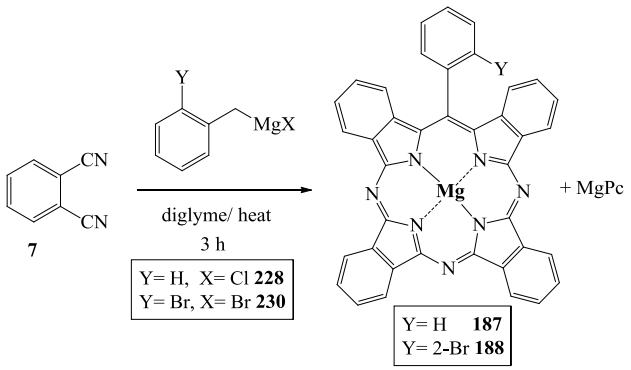


Figure 2.18: MALDI-TOF MS spectrum of crude mixture.

2.6 Direct Synthesis of Unsubstituted *meso*-(bromophenyl) Magnesium Tetrabenzotriazaporphyrins *via* Grignard reagents

Formation of the tetrabenzotriazaporphyrin derivatives proved to be typically difficult. Moreover, the synthesis of aminoisoindoline derivatives failed to give the brominated products which could be used to prepare functionalised *meso*-phenyl TBTAPs. The latter materials can be key precursors in synthesis of a number of new TBTAPs derivatives bearing a variety of reactive functional groups ready for further elaboration. We therefore decided to reinvestigate the procedure originally reported by Linstead *et al.*[3] to synthesise unsubstituted *meso*-phenyl TBTAP *via* the reaction between phthalonitrile and Grignard reagents (Scheme 2.26), but in this case we simplified the reaction using the unsubstituted phthalonitriles as precursors. The reaction was attempted more carefully several times in order to optimise the reaction towards the formation of functionalised *meso*-aryl TBTAPs. A summary of the conditions attempted and conclusions drawn are shown in Table 2.4 below.



Scheme 2.26: Formation of TBTAP **187**[96] *via* Grignard reagents.

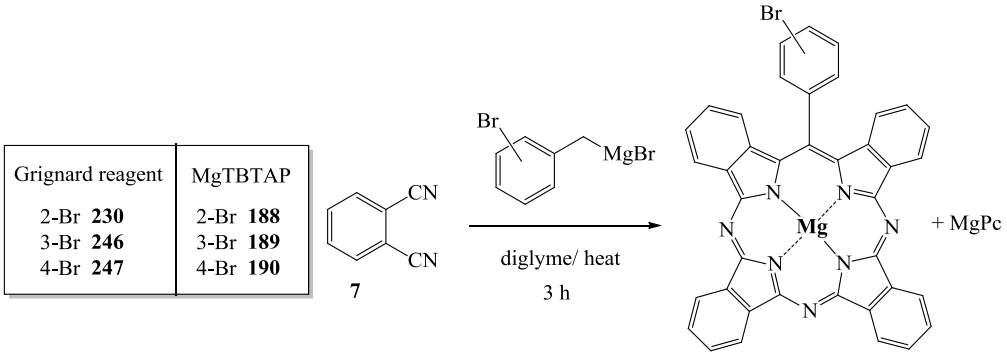
Solvent I	Reactants	Temp. °C	Time	Solvent II	Reactants	Temp. °C	Time	Results
distilled THF	1eq.**7** + 2eq. **228** (added once)	80	30 min	dry diglyme	-	200	3 h	only Pc
-	-	-	-	dry diglyme	1eq. **7** + 1eq. **228** (added once)	220	3 h	(5%) TBTAP + Pc
-	-	-	-	dry diglyme	1eq. **7** + 1eq. **230** (added once)	220	3 h	trace TBTAP + Pc
-	-	-	-	dry diglyme	2eq. **7** + 1eq. **230** $PhCH_2MgCl$ (added once)	220	3 h	trace TBTAP + Pc
-	-	-	-	dry diglyme	3eq. **7** + 1eq. **230** (added once)	220	3 h	(18%) TBTAP + Pc
-	-	-	-	dry diglyme	3eq. **7** + 1eq. **230** (added slowly over 1 h)	220	3 h	(56%)TBTAP + trace Pc

Table 2.4: Some attempted conditions for preparing **187** and **188**.

Initial experimental attempts followed modified versions of the procedure reported by Linstead and co-workers,[3] involving the treatment of a solution of phthalonitrile **7** (1 equiv.) in THF with benzylmagnesium chloride **228** (2 equiv.) and leaving the mixture to heat (80 °C) for 30 min. After removal of THF and adding distilled diglyme (instead of quinoline) the reaction mixture was left under reflux (200 °C) for 3 h. Unfortunately, the reaction failed to produce the required TBTAP and gave only the magnesium Pc as main product. We therefore decided to improve the procedure further by ignoring the first step and using the diglyme as a sole solvent in a single step. The temperature was also increased to 220 °C using a mantle as a source of heating. A series of stoichiometric ratios were undertaken starting with 1:1 equivalents (2-BrPh-CH_2-MgBr/phthalonitrile) and increased to a 1:3 (2-BrPh-CH_2-MgBr/ phthalonitrile). Moreover, in some experiential attempts, the Grignard reagent was added at once whereas in other trials it was added dropwise during 1 h. It has

been found that the best results were obtained when the ratio of 1:3 (2-BrPh-CH_2-MgBr/phthalonitrile) was used with a slow addition of 2-substituted Grignard reagent to a warm solution of phthalonitrile in diglyme. We also noticed that the formation of dimeric macrocycles or other side-products was avoided under these reaction conditions. The highest yield obtained was 56%, corresponding to *meso*-(2-bromophenyl) TBTAP as illustrated in the last line of table 2.3. These examinations made on the unsubstituted TBTAP provided a useful and straightforward technique for accessing further functionalised *meso*- phenyl TBTAPs.

A series of functionalised *meso*-phenyl TBTAPs were prepared by the reaction between phthalonitrile **7** and the isomeric series of 2-, 3- and 4-bromobenzylmagnesium bromides. The latter was prepared using a typical Grignard reagent synthetic procedure.[63] A solution of the isomeric series of 2-, 3- and 4-bromobenzylmagnesium bromides was added dropwise to a warm solution of phthalonitrile **7** in diglyme over 1 h. The mixture was left to heat at 220 °C for further 2 h (Scheme 2.27). After purification by column chromatography, the products were isolated in a satisfactory yield.[47]



Scheme 2.27: Synthetic method towards functionalised *meso*-phenyl TBTAPs.

Recrystallisation of the products from acetone/ethanol gave green crystals suitable for X-Ray diffraction analysis. However, a successful X-Ray crystal structure was obtained only for *meso*-2-bromophenyl MgTBTAP isomer **188** (Figure 2.19). The molecule crystallises with a bound molecule of ethanol (disordered). The isomeric products afforded the expected ^{1}H NMR spectra, ^{13}C NMR, MALDI-TOF mass spectra, UV-Vis spectra and high-resolution mass spectra. ^{1}H NMR spectrum of product **188** is illustrated in Figure 2.20.

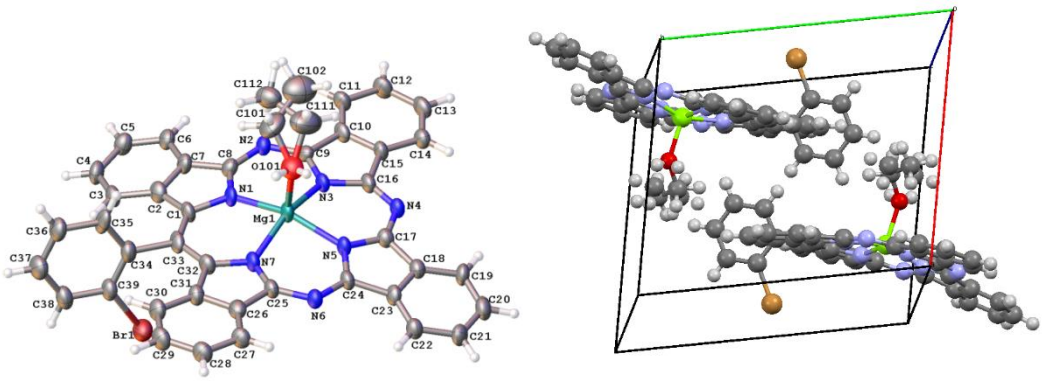


Figure 2.19: X-Ray structure for **188**.

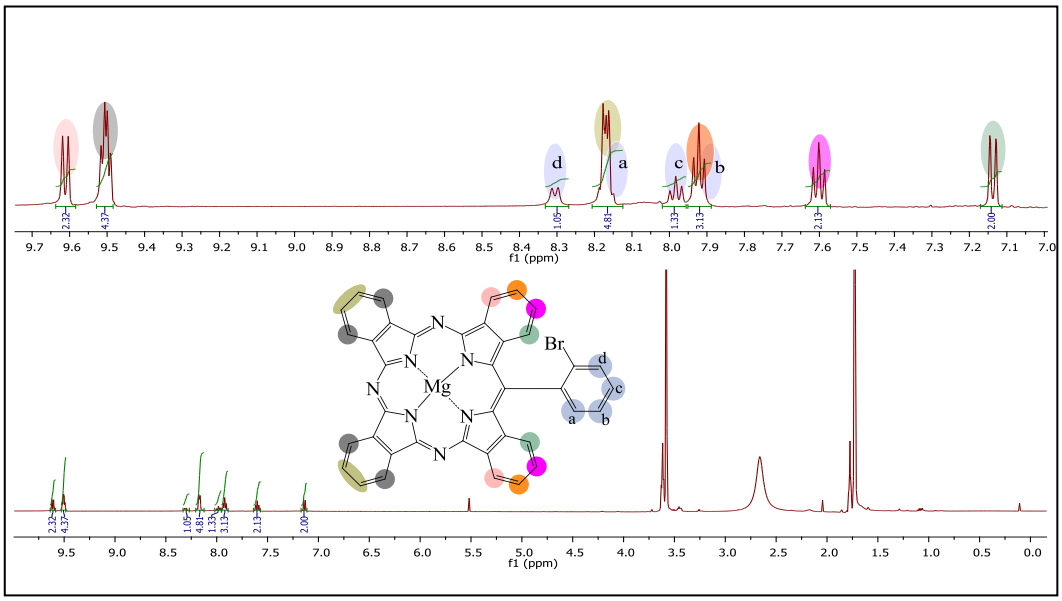
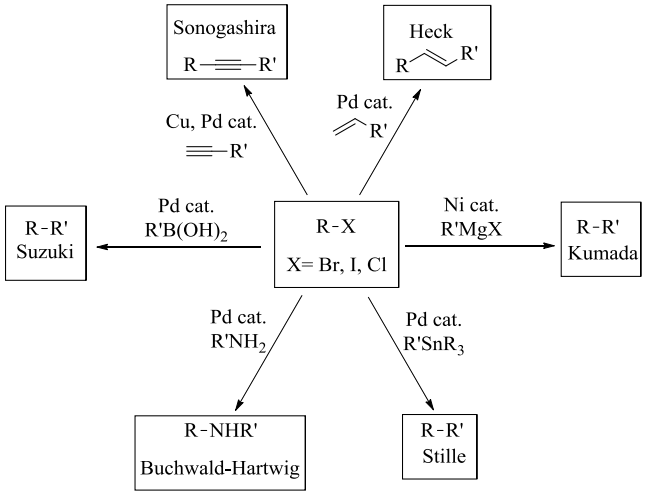


Figure 2.20: ^{1}H NMR spectrum of **188**.

2.7 Transformations of Functionalised *meso*-phenyl Magnesium Tetrabenzotriazaporphyrins

The investigations and developments of palladium-catalysed cross-coupling reactions of small organic molecules have received a great deal of attention in the literature, whereas the cross-coupling reactions of large conjugated complexes such as TBTAPs have been studied rarely or even non-existent. We decided therefore to synthesise a new series of coupled complexes through the palladium-catalysed cross-coupling reactions. Several transition metal catalysed cross-coupling reactions such as Kumada,[31] Negishi,[20] Heck,[13] Stille,[14] Suzuki[21] and copper-free Sonogashira cross-couplings can be used to form new carbon-carbon and carbon-heteroatom bonds (Scheme 28).[26,56,57]

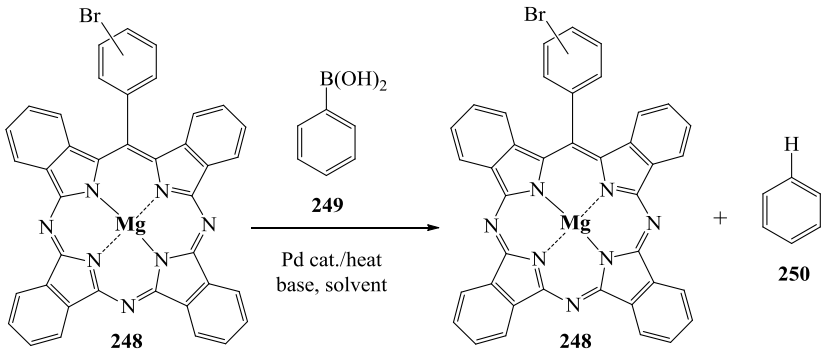


Scheme 2.28: Potential methods towards C−C bond formation *via* cross-coupling reactions.

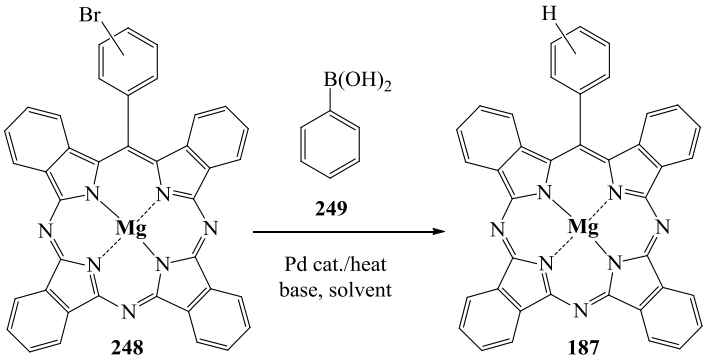
After the successful preparation of the isomeric *meso*-(2-, 3-, 4-bromo)phenyl TBTAP complexes, it became possible to functionalise these macrocycles *via* cross-coupling reactions to obtain a new series of materials that enable exploitation of their other properties and expand the scope of their applications into novel fields of photophysical, optoelectronic and semi-conducting properties.

Among the most commonly cross-couplings employed in organic synthesis, Suzuki and copper-free Sonogashira cross-couplings have been chosen for our purpose in order to synthesise new carbon–carbon bonds. The first cross-coupling reaction used was the Suzuki coupling using a palladium catalyst that led to the formation of the required product in a single step after several attempts. In this reaction, we used a bromo-aryl-TBTAP as the first coupling partner and a number of organoboronic acid reagents as the other. The coupling was attempted initially employing the normal Suzuki conditions but surprisingly, no product was obtained even after prolonged refluxing. Several more careful attempts and a number of various conditions gave no product and most of the starting material was recovered. It seems that the reactions proceed to obtain the deboronation product instead of the required coupling products (Scheme 2.29). In addition, dehalogenation of aryl halides also be occurred after prolonged refluxing, resulting in formation of unwanted dehalogenated product as a main product, the reason for this can be attributed to the steric hindrance which prevents the formation of any coupled product especially in *meso*-(*o*-bromoaryl) TBTAP (Scheme 2.30). The use of *meso*-(*p*-bromoaryl) TBTAP did however not show any advancement on the reaction outcome. Attempted conditions and results are

summarized in Table 2.5. In some reactions, the formation of the required products was observed alongside the starting material and *meso*-phenyl TBTAP, however, those products were not isolated during the purification process and only starting material and debrominated TBTAP were isolated.



Scheme 2.29: Recovered starting material.



Scheme 2.30: Formation of unwanted debrominated product **187**.

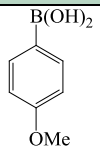
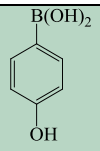
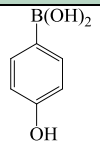
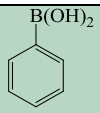
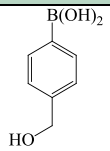
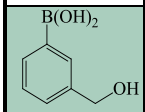
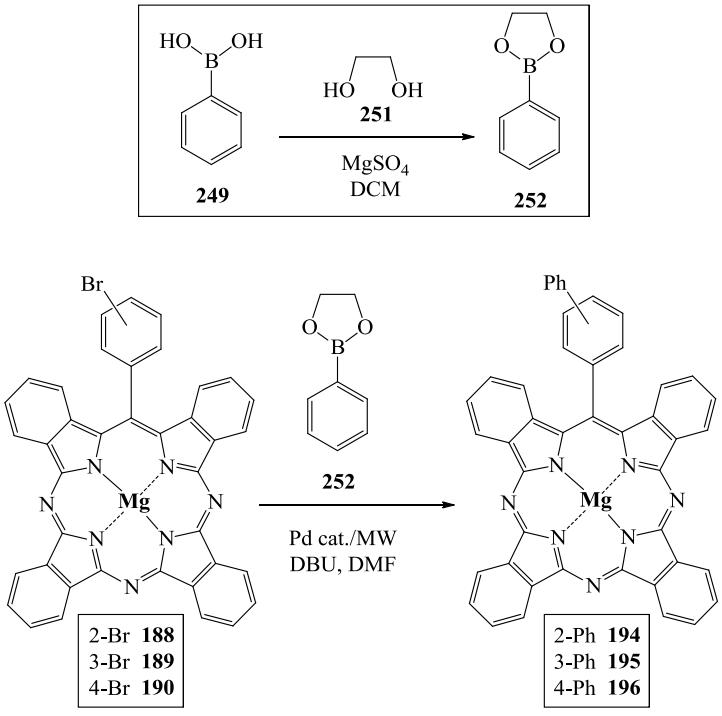
Boronic acid	SM	Catalyst	Base	Solvent	Temp. (°C)	Time	Results
	*meso*-(*o*-bromo aryl) TBTAP	$PdCl_2$(dppf)	CsF	dry DME	100-121	4 h	(BrPh)TBTAP (SM)
excess		excess	excess			24 h	Ph-TBTAP
	*meso*-(*o*-bromo aryl) TBTAP	$PdCl_2$(dppf)	CsF	dry DME	100-121	24 h	SM + Ph-TBTAP
	*meso*-(*o*-bromo aryl) TBTAP	$PdCl_2$(dppf)	CsF	dry DME	100-121	48 h	SM + Ph-TBTAP
	*meso*-(*o*-bromo aryl) TBTAP	$PdCl_2$(dppf)	CsF	dry DME	100-121	24 h 48 h 3dys 7days	SM SM SM SM
	*meso*-(*p*-bromo aryl) TBTAP	$PdCl_2$(dppf)	CsF	dry DME	100-105	14 h	SM + Ph-TBTAP
excess excess - excess		- - - excess	excess excess - excess			4 h 24 h 3days 4 h	SM + Ph-TBTAP SM + Ph-TBTAP SM + Ph-TBTAP Ph-TBTAP
	*meso*-(*p*-bromo aryl) TBTAP	$PdCl_2$(dppf)	CsF	dry DME	100-105	24 h	SM + Ph-TBTAP

Table 2.5: Attempted conditions for Suzuki cross-coupling reaction.

As a result of all these disappointments, we decided to investigate another synthetic procedure towards the formation of coupled product through using a boronic ester as a second coupling partner instead of the boronic acid. The Suzuki cross-coupling reaction employed used a palladium catalyst and DBU as a base in presence of dry DMF. A microwave reactor was used as a source of heating which also proved to be useful in speeding up the reaction and giving efficient results. Moreover, employing $PdCl_2$(dppf) catalyst and DBU as base was found to be appropriate for microwave-assisted Suzuki cross-coupling reactions.[59] The advantage of employing the boronic

ester is in the low amount of water (and proton sources) associated with ester compared with the boronic acid. In this experimental attempt, we avoided any source of protons which can impact adversely on the formation of desired compound. Synthesis of boronic ester **252** followed the procedure reported by Sigman and co-workers that involved the reaction between phenyl boronic acid **249** and ethylene glycol **251** in the presence of magnesium sulphate and dry DCM as solvent (Scheme 2.31).[58] The boronic ester was kept dry under Ar and use directly in next step. Finally, the Suzuki coupling reaction was achieved taking into account all the necessary precautions to avoid moisture. A mixture of *meso*-(2-, 3-, and 4-bromoaryl) TBTAPs and $PdCl_2$(dppf) catalyst was placed in a microwave vial which was then evacuated and backfilled with argon (3 times). A solution of DBU and phenyl boronic esters **252** in dry DMF was added to the previous mixtures and left to stir at room temperature for 5 min under Ar (Scheme 2.31). The reaction mixtures were irradiated in a microwave reactor at 120 °C for 1 h. After cooling to room temperature, DCM was added and the mixtures sonicated for 5 min. The crude mixtures were purified by column chromatography to give the desired products. Recrystallisation from acetone/EtOH (1:1) gave the products as crystalline materials albeit in low yields.



Scheme 2.31: Synthesis of *meso*-(2-, 3-, 4-biphenyl) TBTAPs.

Isolation of the isomeric series *meso*-(2-, 3-, 4-biphenyl) TBTAP derivatives **194-196** was accomplished successfully as well as their characterisation using several spectroscopic methods (^{1}H NMR, UV-Vis and MALDI-TOF spectrometry). All analytical data were consistent with the structure of the products. The ^{1}H NMR spectrum of *meso*-(2-biphenyl) TBTAP **194** is shown in Figure 2.21.

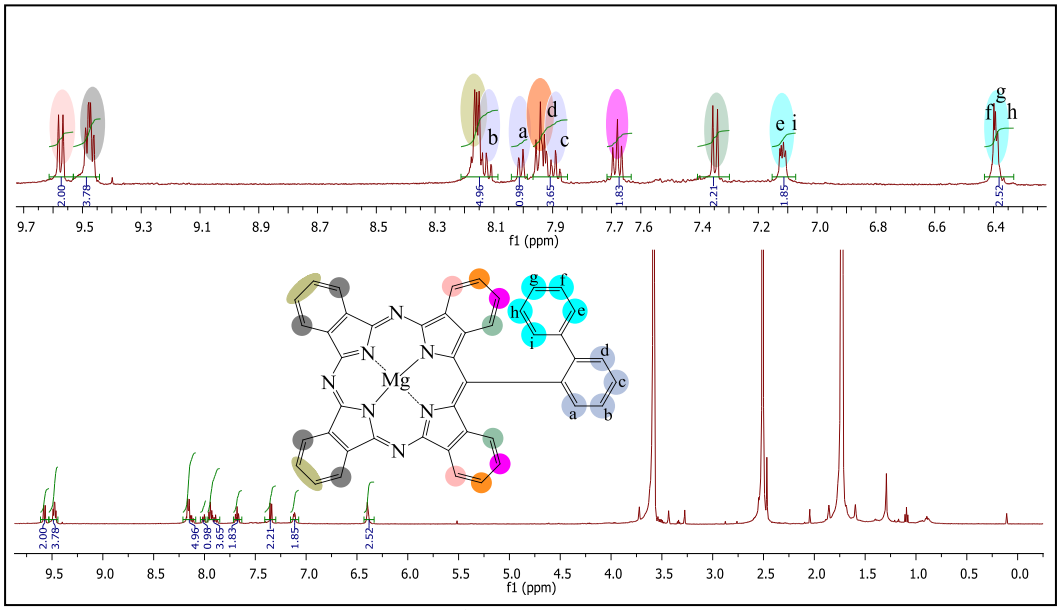
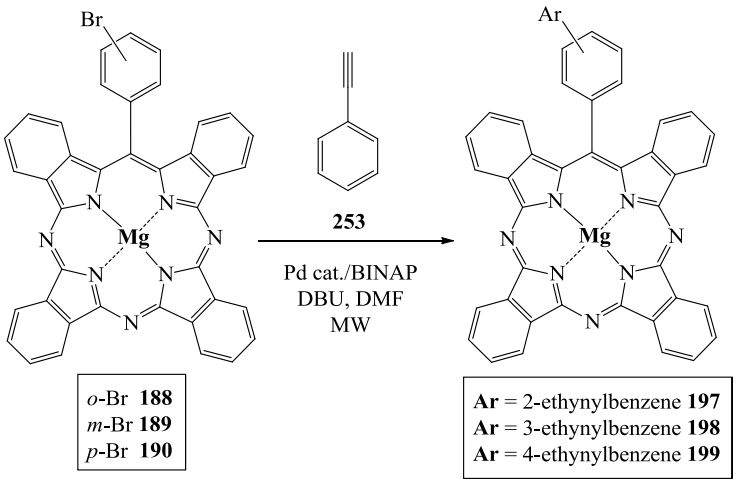


Figure 2.21: ^{1}H NMR spectrum of **194**.

Another transformation of functionalised *meso*-phenyl tetrabenzotriazaporphyrin complexes has been achieved *via* copper-free Sonogashira cross-coupling reaction.[26,49,56,57] In a typical Sonogashira cross-coupling reaction,[26] aryl halides are treated with terminal acetylenes, catalysed by a palladium catalyst in the presence of a copper metal as co-catalyst and a base to produce diaryl-subsitituted acetylenes. Using copper ions in this reaction can cause a problem in the formation of desired products due to the formation of the unwanted copper TBTAP as contaminant or dominant product, making purification and characterisation by NMR spectroscopy difficult. Therefore, we decided to employ a copper-free Sonogashira cross-coupling reaction using a palladium catalyst, BINAP as ligand and DBU as a base in presence of dry DMF (Scheme 2.32).[49,60] The combination of $PdCl_2(MeCN)_2$ and BINAP has proved to be reactive enough for the copper-free cross-coupling of *meso*-(bromoaryl) TBTAP derivatives. A microwave reactor was used as a source of heating instead of the normal heating to accelerate heating rates of the reaction and obtain the product in reasonable yields. The Sonogashira reaction involves the treatment of a mixture of

meso-(bromophenyl)TBTAPs, BINAP and $PdCl_2(MeCN)_2$ with a solution of phenylacetylenes **253** and DBU in dry DMF. The reaction mixture was irradiated in a microwave reactor at 120 °C for 1 h. Purification of the resulting materials by column chromatography gave the desired products.



Scheme 2.32: Synthesis of *meso*-(2-, 3-, 4-biphenyl) TBTAPs.

A successful single crystal of product **197** has been obtained after recrystallisation from acetone and ethanol. Figure 2.22 shows the X-Ray structure of *meso*-((2-phenylethynyl)phenyl)TBTAP **197** (it crystallises with a bound molecule of ethanol). Characterisation of the products by ^{1}H NMR, UV-Vis and MALDI-TOF spectrometries was consistent with the structure of the products. The ^{1}H NMR spectrum of product **197** is presented in Figure 2.23.

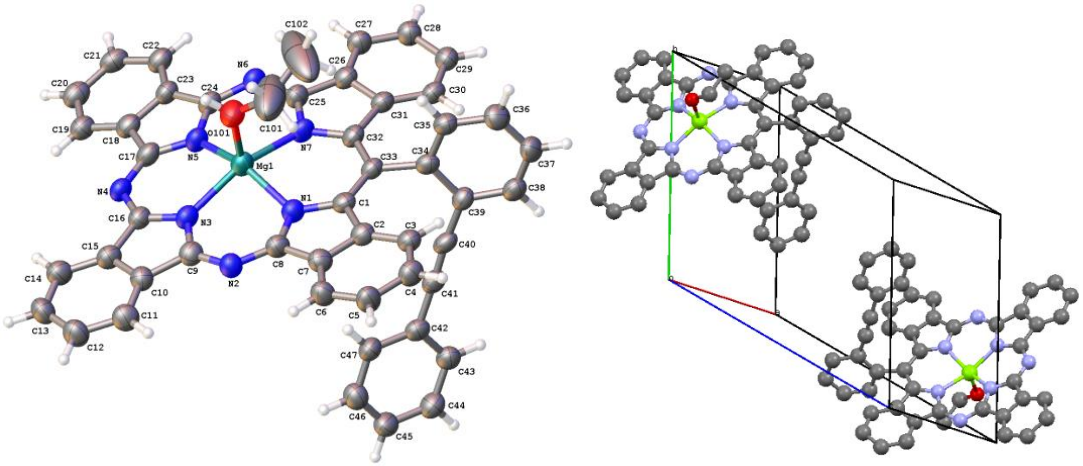


Figure 2.22: X-Ray structure of **197**.

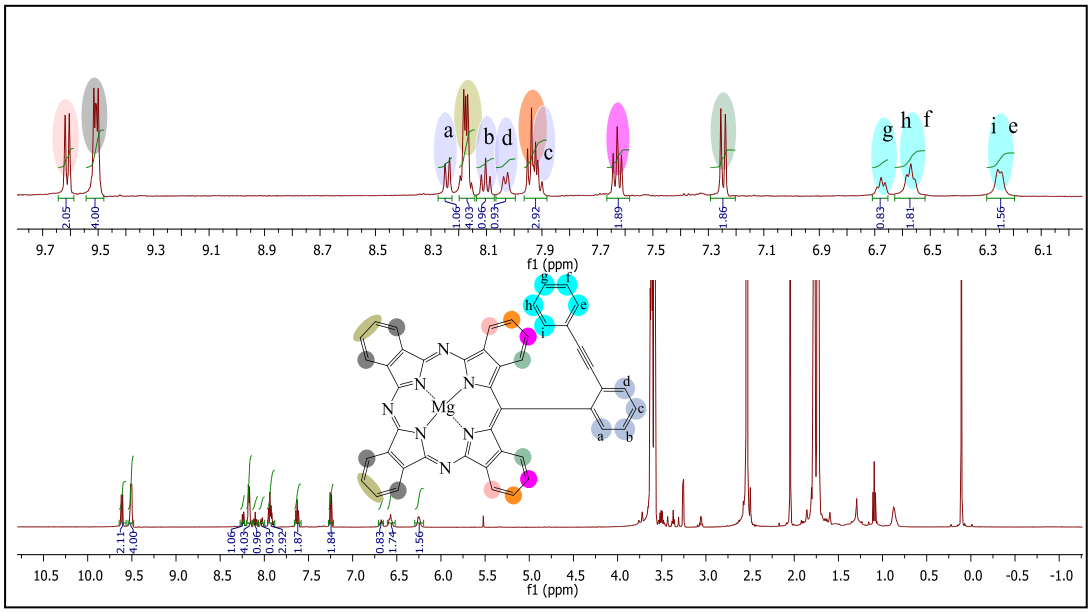


Figure 2.23: ^{1}H NMR spectrum of product **197**.

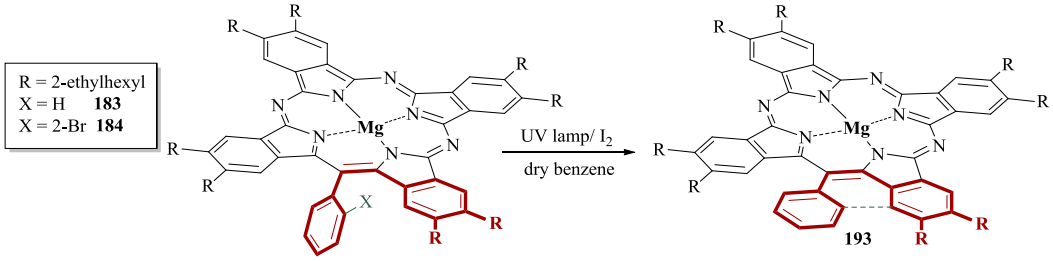
2.8 Expansion of the π-Conjugated System of Tetrabenzotriaza porphyrin Macrocycles

The strategy of π-extension has received a great deal of attention in the fields of porphyrin and phthalocyanine chemistry. Expansion of the π-system of porphyrin, and related macrocycles such as phthalocyanine and porphyrazine, offers attractive synthetic materials due to their unique combination of photophysical and optoelectronic properties.[64-68] Indeed, π-extension of porphyrin or phthalocyanine chromophores usually gives rise to a significant bathochromic shift in absorption spectra that make them attractive in various areas,[69,70] such as dye-sensititized solar cells (DSSCs)[71], photodynamic therapy (PDT)[72] and organic light-emitting diodes (OLEDs).[73]

Tetrabenzotriazaporphyrin macrocycles, which are structurally related to the porphyrin and phthalocyanine, are also expected to exhibit a red-shift in their UV-Vis spectra and thus can offer the new attractive materials. These π-extended complexes can introduce more remarkable photophysical properties relative to those of regular TBTAPs. To date, the investigation in this new field has not received attention, and there are no reports in the literature covering this area. This is easily explained by the lack of convenient methods previously available for synthesis of appropriate precursors. We demonstrate in this work the first attempted examinations towards synthesis of π-extended tetrabenzotriazaporphyrin macrocycles. A number of

chemical and photochemical cyclisation methods have been used in order to attempt synthesis of these extended complexes.

2.8.1 Intramolecular annulation of TBTAP *via* photochemical cyclisation



Scheme 2.33: Photochemical cyclisation of TBTAP.

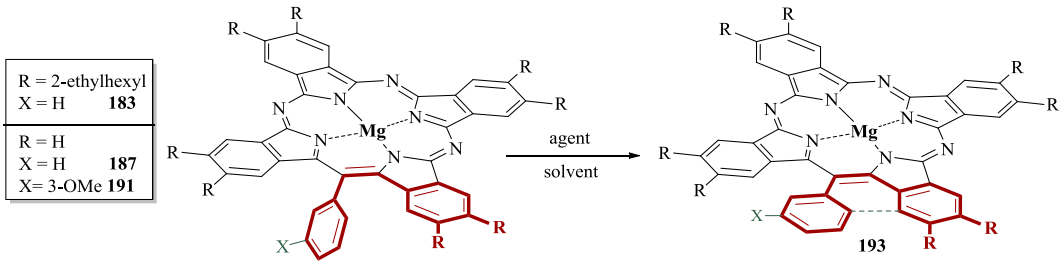
Several examples for the formation of carbon-carbon bonds *via* oxidative photocyclisations have been reported and reviewed in the literature.[74-77] In the light of these convenient and efficient routes, we decided to attempt the synthesis of our target molecule through the oxidative photocyclisation reaction. This reaction involved the irradiation of a dilute benzene solution (degassed) of *meso*-phenyl TBTAP containing an equimolar amount of iodine (Scheme 2.33). The mixture was checked with regular TLC analysis (Table 2.5) but unfortunately, there was no evidence that the reaction was successful and the starting material remained evident on the TLC plate. After 22 h, the reaction was resulted in decomposed starting material. No improvement has been obtained when the reaction was applied using *meso*-bomophenyl TBTAP as precursor. The failure of this reaction towards the formation of required molecule **193** focussed our attention on alternative strategies (chemical cyclisation methods) which will be discussed in next section.

Reaction Time	1 h	2 h	4 h	5 h	11 h	16 h	22 h
Results	SM	SM	SM	SM	SM	SM	nr (decomposed)

Table 2.5: Increasing the reaction times and their corresponding results.

2.8.2 Intramolecular annulation of TBTAP *via* chemical cyclisation

2.8.2.1 Formation of C-C bond *via* intramolecular Scholl reaction



Scheme 2.34: Attempted synthesis of cyclised product **193** *via* Scholl cyclisation.

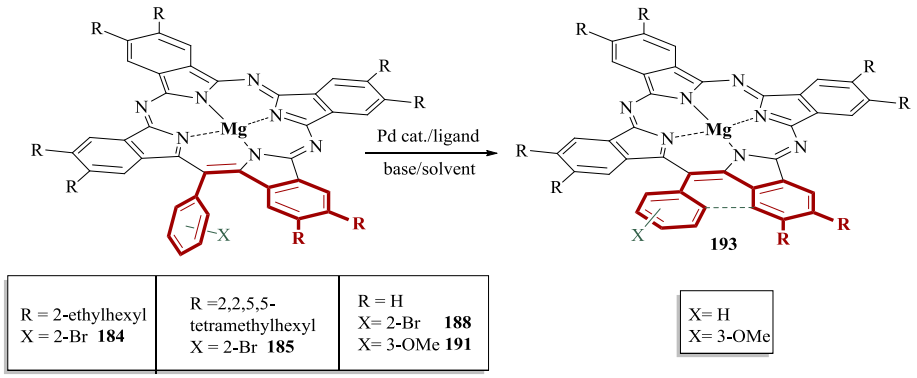
Iron (III) chloride (which is commercially available and inexpensive) can be used in oxidative carbon-carbon couplings of arenes and associated unsaturated compounds. Several examples have been reported in the literature for the synthesis of cyclised molecules using $FeCl_3$ as oxidising agent.[78-82]

The cyclisation of *meso*-phenyl TBTAP was investigated initially through reaction with iron chloride (Scheme 2.34). Various conditions were employed in order to obtain the fused product **193** (Table 2. 6). Nevertheless, the reaction failed to produce the cyclised molecules **193** in all cases, even after the addition of nitromethane to improve the solubility of the reagent. In one experiment, aluminium(III) chloride was used as alternative oxidising agent but the reaction gave no useful result. Further methods towards the formation of the fused product will be described in next section.

SM	Agent	Solvent	Temp. (°C)	Time	Results
TBTAP **183**	$FeCl_3$	dry DCM	rt	2 h	nr
TBTAP **183**	$FeCl_3$	Tol	110	24 h	nr
TBTAP **191**	$FeCl_3/CH_3NO_2$	dry DCM	0	30 min	SM
				1 h	SM
				24 h	SM
				48 h	nr
TBTAP **191**	$FeCl_3/CH_3NO_2$	dry DCM	rt	5 min	SM
				30 min	SM
				2 h	SM
				24 h	nr
TBTAP **187**	$FeCl_3/CH_3NO_2$	dry DCM	rt	3 h	SM
				6 h	SM
				24 h	SM
	excess			48 h	nr
TBTAP **191**	$AlCl_3$/DDQ	dry DCM:THF	0	2 h	SM
				24 h	SM
				≥ 72 h	nr

Table 2.6: Conditions used for attempted synthesis of fused product **193**.

2.8.2.2 Formation of C-C bond *via* intramolecular Heck-type cyclisation



Scheme 2.35: Attempted synthesis of π-extended TBTAPs *via* Heck-type cyclisation.

With the successful synthesis of the TBTAPs we were now ready to investigate the synthesis of the π-extended TBTAP. This synthesis was attempted through the intramolecular palladium-catalysed oxidative cyclisation methods which also known as Heck cyclisation.[83,84] Several conditions have been reported in the literature for the intramolecular Heck cyclisation of small molecules.[85-93] In general, Heck-type coupling reactions require an aryl halide with an alkene and a stoichiometric amount of base and palladium catalyst.

This reactions involve a C-H activation (occurs on adjacent aromatic rings tethered together with a sequence of carbon atom linkers) or elimination of C-X and therefore C-C bond formation. The cyclisation to afford the six-membered ring product was attempted using various TBTAP derivatives (Scheme 3.35). Consequently, several experiments were conducted employing different catalysts, bases and ligands. Unfortunately, no cyclized product was observed under these conditions. Table 2.7 displays the summary of the attempted conditions and their results. The use of directing functional groups (i.e. methoxy group) attached in *m*-position of *meso*-phenyl ring did not help to obtain the required product.

Entry	SM	Catalyst	Ligand	Base	Solvent	Temp. (°C)	Time	Results
1	TBTAP **184**	$Pd(OH)_2$ in C	-	KOAc	dry DMF	145	24 h	SM
2		excess		excess			48 h	SM
3		excess		excess			≥ 72 h	nr
4	TBTAP **184**	$Pd(OAc)_2$	PhDave-Phos*	K_2CO_3	dry DMA	135	24 h	nr
5	TBTAP **184**	$Pd(OAc)_2$	PhDave-Phos*	K_2CO_3	dry DMF	154	≥ 72 h	SM
6	TBTAP **184**	$Pd(OAc)_2$/LiCl	*n*-Bu_4NBr	K_2CO_3	dry DMF	110	18 h	SM
7							72 h	nr
8	TBTAP **185**	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	dry DMF	80-85	48 h	nr
9	TBTAP **191**	$Pd(OAc)_2$	PCy_3	K_2CO_3	dry DMF	100-120	3 h	SM
10							16 h	nr
11	TBTAP **188**	$PdCl_2(PPh_3)_2$	-	DBU	dry DMF	150-153	48 h	nr
12	TBTAP **188**	$PdCl_2(MeCN)_2$	BINAP	DBU	dry DMF	120 in MW	5 min	SM
13							30min	SM
14							1 h	trace of prod.
15							≥ 2 h	decomposed

*** 2-(diphenylphosphino)-2'-(*N, N*-dimethylamino)biphenyl**

Table 2.7: Attempted conditions for intramolecular Heck cyclisation.

After several experimental attempts we found the most appropriate conditions for the formation of cyclised product as illustrated in table 2.6; entry 14. The reaction was carried out using $PdCl_2(MeCN)_2$ catalyst, BINAP as ligand and DBU as a base that were placed in a microwave vial. A solution of starting materials in anhydrous DMF was added to the previous mixture which then evacuated and backfilled with argon several times. The reaction mixture was irradiated in a microwave reactor at 120 °C for 5 min and then 30 min. Unfortunately, only the starting material was recovered and when the reaction was left under irradiation for 1 h, a trace amount of the product was possibly obtained (based on MALDI-MS analysis). Leaving the reaction for more than 1 h (i.e. ≥ 2 h) resulted in decomposed starting material. Performing the reaction for second time again hinted at formation of a trace amount of the required product. Unfortunately, the formation of required product **193** was not improved further under

these conditions. Analysis of the crude reaction mixtures by MALDI-TOF mass spectrometry shows a cluster of expected peaks around (*m/z* 609.72) that corresponding to the required compound **193** (Figure 2.24). Purification of **193** by column chromatography was repeated more carefully several times in order to isolate the desired product, but unfortunately its isolation could not be achieved.

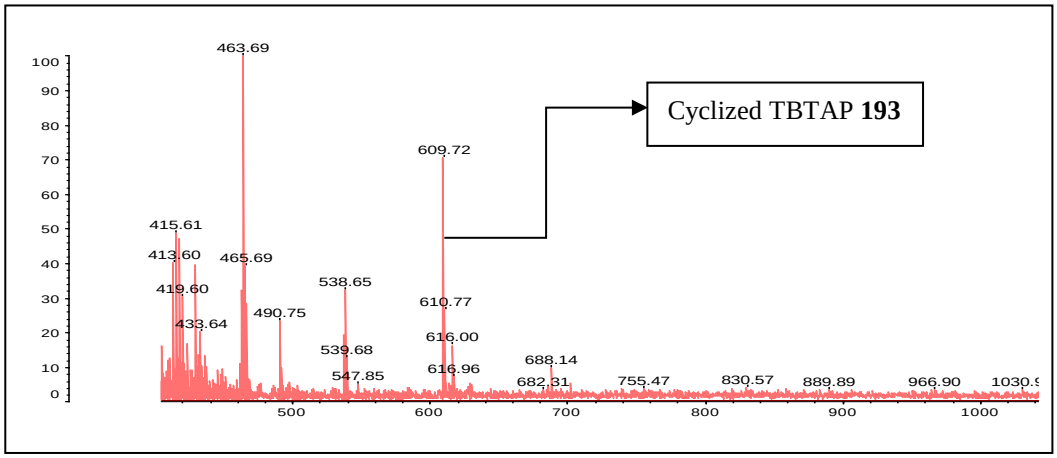


Figure 2.24: MALDI-TOF MS spectrum of crude mixture.

2.9 Conclusion

The syntheses of the phthalonitriles have been achieved successfully through the investigation of different strategies. Phthalonitriles have been constructed by the nickel or palladium catalysed Kumada cross-coupling reaction using 1,2-dichlorobenzene as precursor, followed by electrophilic bromination and Rosenmund von Braun cyanation reaction in the last step. An alternative route towards the formation of the phthalonitriles was used in order to synthesise alternative target phthalonitriles in good yield; the method employed Kumada cross-coupling reaction using 4,5-dibromoveratrole as precursor followed by a sequence of synthetic steps and finally cyanation reaction following the procedure described by Hanack and Drechsler.

A series of *meso*-phenyl substituted tetrabenzotriazaporphyrins (TBTAPs) bearing different functional groups has been prepared successfully *via* the investigation of various approaches. The traditional synthetic methods and their new modified versions *via* Grignard reagents have been developed as well as the modern technique *via* aminoisoindoline that was discovered recently by our group. Most importantly, synthesis of functionalised TBTAPs has been achieved.

Expansion of the π-conjugated system of TBTAPs has been attempted as first experimental examinations in this field through several chemical and photochemical cyclisation methods, but the desired products were not isolated. Finally, transformations of the functionalised *meso*-phenyl TBTAP macrocycles through the palladium-catalysed Suzuki and copper-free Sonogashira cross-coupling reactions have been accomplished successfully resulting in the formation of a new series of materials. The new strategies combine to open up the potential for many new hybrid structures.

2.10 References

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CHAPTER 3

Experimental

3.1 General Methods

Reagents and solvents were obtained from commercial sources and used without further purification unless otherwise stated. Phthalonitrile was recrystallised from hot xylene. THF, diethyl ether and DMA were freshly distilled from sodium and benzophenone. Dichloromethane and quinoline were distilled from calcium hydride and barium oxide, respectively. Reactions and distillation were carried out under an inert atmosphere (argon or nitrogen gas). Argon was used in particularly air-sensitive reactions. Temperature of -78 °C was accomplished by use of a mixture of acetone and dry ice. Brine is a saturated aqueous solution of sodium chloride. Organic layers were dried using anhydrous magnesium sulphate. Evaporation of solvent was performed using a Buchi rotary evaporator at reduced pressure. All glassware was dried before use.

^{1}H NMR spectra were recorded either at 400 MHz on an Ultrashield Plus^{TM} 400 spectrometer or 500 MHz on a Bruker Ascend^{TM} 500 spectrometer in 5 mm diameter tubes. Signals are quoted in ppm as δ downfield from tetramethylsilane (δ= 0.00) and coupling constants *J* given in Hertz. Spectra of TBTAPs are of recrystallised samples from EtOH/acetone or MeOH/THF and display coordinated solvents in agreement with X-ray crystal structures. ^{13}C-NMR spectra were recorded at 100.5 MHz or 125.7 MHz on the same spectrometers. NMR spectra were performed in solution using deuterated chloroform or tetrahydrofuran at room temperature unless otherwise stated.

Ultraviolet-Visible absorption spectra were recorded on an Hitachi U-3000 recording spectrophotometer in solvent as stated. MALDI-TOF mass spectra were carried out using a Shimadzu Biotech Axima instrument with a TA1586Ade plate. High resolution mass spectra (HRMS) were obtained *via* the ESPRC UK National Mass Spectrometry Service Centre at Swansea. X-Ray crystallography data was obtained through the UK National Crystallography Service at Southampton.

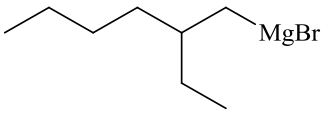
Thin layer chromatography (TLC) was performed using aluminum sheets coated with Alugram® Sil G/UV254 (Macherey-Nagel), and the compounds were visualised by viewing under short-wavelength UV-light at 254 nm or 366 nm and by charring with 0.1% ninhydrin in EtOH when required. Column chromatography was carried out

using silica gel Davisil® LC60A 40-63 micron (Grace GmbH & Co) under regular conditions (at ambient temperature and atmospheric pressure or occasionally at moderate pressure). Solvent ratios are given as v : v. Melting points were taken on a Reichart Thermovar microscope with a thermopar based temperature control.

3.2 Synthesis of Substituted Phthalonitrile (218)

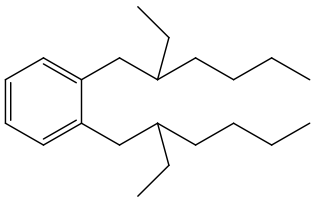
3.2.1 Through Kumada cross-coupling reaction using 1,2-dichlorobenzene as precursor

3.2.1.1 (2-Ethylhexyl) magnesium bromide (215)[1]



According to the general method for preparing Grignard reagents, magnesium turnings (6.50 g, 0.27 mol) were covered by distilled Et_2O (20 mL) under an inert atmosphere and left to stir for 10 min. A single crystal of iodine was added alongside 2-ethylhexyl bromide (36.28 mL, 0.2 mol) in Et_2O (25 mL) in a dropwise manner *via* an addition funnel. After the addition was completed, the reaction mixture was allowed to reflux for 2 h. The Grignard reagent was used immediately for the next step after cooling.

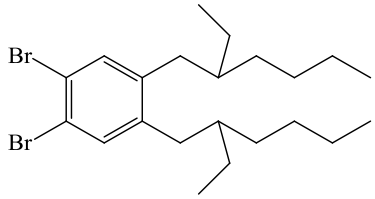
3.2.1.2 1,2-Bis(2-ethylhexyl)benzene (216)[2]



Following the procedure described by Hanack,[2,3] 1,2-dichlorobenzene (5.0 g, 0.034 mol) was stirred together with [1,2-bis(diphenylphosphino)ethane]dichloronickel(II) (0.90 g, 1.70 mmol) for 10 min under an inert atmosphere. (2-Ethylhexyl) magnesium bromide **215** was added to the mixture at room temperature *via* syringe. Then, the reaction mixture was heated to reflux and stirred overnight. After cooling the reaction mixture to 0 °C, 1 M HCl was added dropwise. The organic layer was washed with water, brine, extracted with petroleum ether (3×150 mL) and dried over $MgSO_4$. The solvent was removed *in vacuo* to leave a honey oil which was purified by column

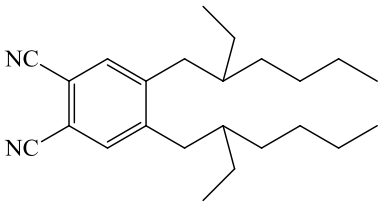
chromatography (eluting with petroleum ether) to give the pure *title compound* (9.21 g, 90%) as a colourless oil. ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 7.10 (s, 4H), 2.58 – 2.50 (m, 4H), 1.60 – 1.52 (m, 2H), 1.33 – 1.28 (m, 16H), 0.90 – 0.87 (m, 12H).

3.2.1.3 1,2-dibromo-4,5-Bis(2-ethylhexyl)benzene (217) [2,4]



Bromination was achieved using the method described by Ashton and co-workers.[2] 1,2-Bis(2-ethylhexyl)benzene (8.04 g, 26.6 mmol) was dissolved in DCM (40 mL). Iron powder (0.18 g, 3.19 mmol) and iodine (0.068 g, 0.27 mmol) were added to the mixture and cooled to 0 °C. Bromine (2.74 mL, 53.1 mmol) was added dropwise *via* an addition funnel to the stirring mixture over 2 h. After complete addition, the reaction mixture was allowed to warm up to room temperature and stirred for 24 h. The resulting orange mixture was washed in portions with an aqueous solution of sodium metabisulfite and sodium bicarbonate to remove the excess bromine. Water and brine were added and the mixture extracted with DCM (3×150 mL). The organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to give honey oil. The product was purified by column chromatography over silica gel using PE (100%) as eluent to give *the title compound* as a colourless oil (10.17 g, 83%). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm) = 7.19 (s, 2H), 2.58 – 2.50 (m, 4H), 1.61 – 1.53 (m, 2H), 1.35 – 1.26 (m, 16H), 0.92 – 0.81 (m, 12H).

3.2.1.4 4,5-Bis(2-ethylhexyl) phthalonitrile (218)[6]

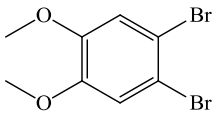


Following the procedure described by Rosenmund von Braun, a mixture of 1,2-dibromo-4,5-bis(2-ethylhexyl)benzene **217** (5.85 g, 12.7 mmol) and CuCN (5.69 g, 63.53 mmol) was refluxed in dry DMF (100 mL) at 150 °C under an argon

atmosphere for 16 h. The reaction mixture was cooled to room temperature and poured into an aqueous solution of ammonia (200 mL), and left to stir at room temperature for 24 h under a stream of air. The resulting material was extracted with hexane (3 x 100 mL), washed with H_2O (3 x 100 mL), saturated solution of $NaHCO_3$, dried over $MgSO_4$ and filtered. The filtrate was removed under reduced pressure to give the crude product. The crude material was purified by column chromatography (silica: PE/DCM, 3:2) to yield the product as a bright yellow oil (30.0 mg, 2%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) = 7.52 (s, 2H), 2.67 – 2.51 (m, 4H), 1.60 – 1.47 (m, 2H), 1.32 – 1.17 (m, 16H), 0.90 – 0.83 (m, 12H).^{13}C NMR (125.7 MHz, $CDCl_3$-d, 298 K): δ (ppm) = 147.26, 135.03, 115.99, 112.64, 40.58, 37.26, 32.48, 28.89, 25.66, 23.06, 14.15, 10.88.

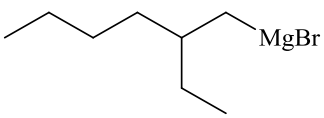
3.2.2 Through Kumada cross-coupling reaction using 4,5-dibromoveratrole as precursor

3.2.2.1 4,5-Dibromoveratrole (196)[5]



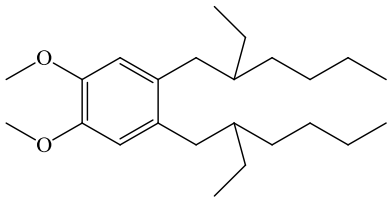
Following the procedure reported in the literature, [5,7] a solution of veratrole (40.0 g, 0.29 mol) in DCM (400 mL) was cooled to 0 °C. Bromine (32.8 mL, 0.64 mol) was added dropwise *via* an addition funnel to the stirring mixture over 2 h. After complete addition, the reaction mixture was allowed to warm to room temperature and left to stir for a further 1 h. The resulting material was washed with an aqueous solution of sodium metabisulfite to remove the excess bromine. Water and brine were added and the mixture extracted with DCM (3×150 mL). The combined organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to give a white powder. The crude solid was recrystallised from isopropanol to give large, clear, needle-type crystals (85.89 g, 100%). ^{1}H NMR (500 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 7.06 (s, 2H), 3.85 (s, 6H).

3.2.2.2 (2-ethylhexyl) magnesium bromide (215)[1]



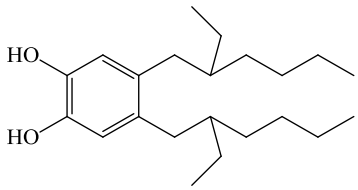
Following the same procedure described above in section 3.2.1.1, magnesium turnings (3.26 g, 0.14 mol) were stirred in distilled Et_2O (20 mL) under an inert atmosphere for 10 min. A single crystal of iodine was added together with 2-ethylhexyl bromide (18.32 mL, 0.1 mol) in Et_2O (25 mL) in a dropwise manner *via* addition funnel. After the addition was completed, the reaction mixture was allowed to reflux for 2 h. The Grignard reagent was used immediately for the next step after cooling.

3.2.2.3 4,5-bis(2-ethylhexyl)veratrole (219)[5]



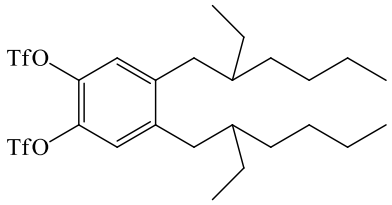
According to the established procedure,[5,8] 4,5-dibromoveratrole **196** (5.0 g, 0.02 mol) was stirred together with [1,1'- bis(diphenylphosphino)ferrocene]palladium(II) dichloride (0.69 g, 0.85 mol) under an inert atmosphere. (2-Ethylhexyl) magnesium bromide **215** was added at room temperature *via* syringe and left to stir for 30 min. The mixture was then allowed to reflux overnight. The reaction was poured into ice/water, filtered and extracted with Et_2O (3×150 mL). The organics were washed with 1.00 M HCl, water, brine, dried ($MgSO_4$), filtered and the solvent removed under reduced pressure. The crude brown oil was purified by column chromatography over silica gel (hexane/EtOAc , 5:1) to give *the title compound* as a light honey oil (10.30 g, 71 %). ^{1}H NMR (500 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 6.61 (s, 2H), 3.85 (s, 6H), 2.52 – 2.38 (m, 4H), 1.55 – 1.48 (m, 2H), 1.38 – 1.17 (m, 16H), 0.94 – 0.81 (m, 12H).

3.2.2.4 4,5-bis(2-ethylhexyl)-1,2-dihydroxybenzene (220)[5]



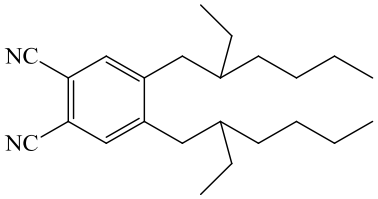
According to the procedure described in the literature,[5,9,10] a mixture of 48% hydrobromic acid and glacial acetic acid (200.0 mL, 1:1) was added to 4,5-bis(2-ethylhexyl)-1,2-dimethoxybenzene (9.87 g, 0.03 mol) and stirred to obtain an emulsion. The light orange emulsion was heated under reflux for 72 h under normal atmosphere. After cooling the mixture to room temperature, the crude was washed with water (3x100 mL), brine and extracted with DCM. The organic material was dried over $MgSO_4$ and the solvent removed under reduced pressure to give the product as a reddish oil (9.0 g, 99 %). ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm) = 6.61 (s, 2H), 5.19 (br s, 2H), 2.48 – 2.29 (m, 4H), 1.52 – 1.41 (m, 2H), 1.34 – 1.12 (m, 16H), 0.91 – 0.87 (m, 12H).

3.2.2.5 4,5-Bis(2-ethylhexyl)-1,2-bis(trifluoromethanesulfonyloxy)benzene (221)[5]



Following the procedure described in the literature,[5,11] a solution of 4,5-bis(2-ethylhexyl)-1,2-dihydroxybenzene (7.85 g, 0.024 mol) and lutidine (8.15 mL, 7.54 g, 0.07 mol) in distilled DCM was cooled to -78 °C. Trifluoromethanesulfonic anhydride (19.74 mL, 33.10 g, 0.12 mol) was added dropwise *via* syringe under an inert atmosphere. The mixture was left to warm to room temperature and stirred overnight. The organic mixture was washed with water (3x100 mL), brine, extracted with DCM, dried over $MgSO_4$ and filtered. The solvent was removed under reduced pressure and chromatographed through a short silica gel column. The column was eluted using petroleum ether and DCM (3:2) and a single fluorescent band was collected. The *title compound* was isolated as a yellow oil (9.26 g, 66 %). ^{1}H NMR (400 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 7.17 (s, 2H), 2.61 – 2.45 (m, 4H), 1.60 – 1.47 (m, 2H), 1.40 – 1.12 (m, 16H), 0.92 – 0.81 (m, 12H).

3.2.2.6 4,5-Bis(2-ethylhexyl)phthalonitrile (218)[5]



According to the procedure described by Hanack and Drechsler.[5,12] A solution of 4,5-bis(2-ethylhexyl)-1,2-bis(trifluoromethanesulfonyloxy)benzene **221** (1.0 g, 1.67 mmol) in anhydrous DMF (2.50 mL) was added to a solution of tris(dibenzylideneacetone)dipalladium (61.17 mg, 0.067 mmol, 4.0 mol%) and 1,1`-bis(diphenylphosphino)ferrocene (148.13 mg, 0.27 mmol, 16.0 mol%) in anhydrous DMF (2.50 mL) under argon atmosphere *via* syringe at room temperature. The reaction mixture was allowed to heat gradually until the temperature stabilised at 73 °C. Once the required temperature was obtained, zinc cyanide (235.31 mg, 2.0 mmol, 1.2 equiv) was added in two equal portions over a period of two hours whilst maintaining the temperature at 70-75 °C. When the addition was completed the reaction mixture was left stirring and heating at 70-75 °C for a further 24 h. The resulting crude product mixture was washed several times with hexane and the excess cyanide and spent catalyst filtered off. The rest of clear yellow solution was washed with brine, water and extracted with hexane. The organic material was dried over $MgSO_4$, filtered and the solvent evaporated under reduced pressure to give an orange oil. The oil was purified by column chromatography over silica gel (hexane/EtOAc, 30:1) to give the product as a bright yellow oil (484.8 mg, 82 %). ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 7.52 (s, 2H), 2.66 – 2.52 (m, 4H), 1.61 – 1.50 (m, 2H), 1.37 – 1.13 (m, 16H), 0.96 – 0.79 (m, 12H).^{13}C NMR (125.7 MHz, $CDCl_3$-d, 298 K): δ (ppm) = 147.26, 135.03, 115.99, 112.64, 40.58, 37.26, 32.48, 28.89, 25.66, 23.06, 14.15, 10.88.

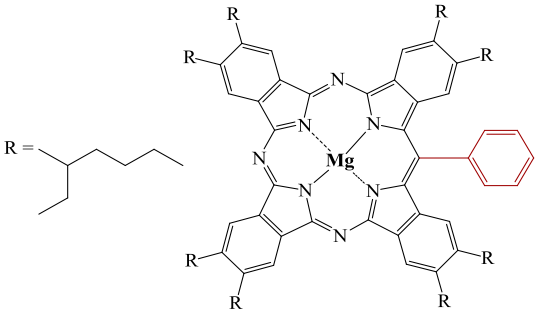
3.3 Synthesis of Substituted Tetrabenzotriazaporphyrins (183 and 184)

3.3.1 General synthetic procedure for the synthesis of substituted *meso*-aryl TBTAPs *via* the Grignard reagent route using quinoline as solvent

According to procedures modified by Cammidge, Cook and co-workers,[5,13] substituted phthalonitrile was dissolved in dry THF and stirred at room temperature, under an argon atmosphere. A solution of arylmagnesium halide was added dropwise *via* a syringe and the mixture was heated under reflux for 30 min. The reaction

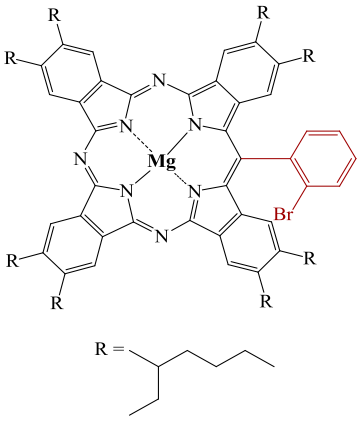
underwent a colour change from a yellow solution, to a dark brown colour. A stream of argon was passed through the reaction flask for 20 min to remove the THF. After removal of the solvent, distilled/degassed quinoline was added to the hot vessel *via* syringe, and the reaction mixture was heated at 200 °C for 24 h under argon. During this time the colour of the reaction mixture changed gradually from dark brown to green. Then, the majority of the quinoline was removed under a stream of argon. The crude product was cooled to room temperature and MeOH was added to the mixture. After sonication, the resulting suspension was purified by filtration through silica gel. MeOH was initially used to remove the remaining quinoline and other polar by-products, then the product was flushed out with THF and a dark green fraction was collected. The solvent was removed under reduced pressure and the resulting green material further purified by column chromatography eluting with PE/THF (15:1) to obtain a green (TBTAP) and then a blue fraction (Pc). Finally, the green material was subjected to a second chromatographic separation using DCM/PE (1:15).

3.3.1.1 [2,3,9,10,15,16,23,24-Octakis(2-ethylhexyl)-27-phenyl-tetrabenzo[*b,g,l,q*][5,10,15]triazaporphinato] magnesium (II) (183)[13]

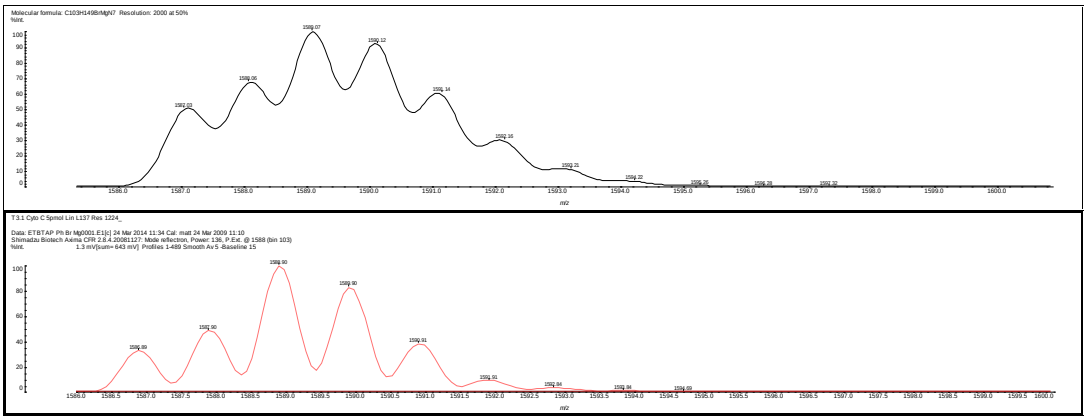


Synthesised using the general procedure described above from 4,5-bis(2-ethylhexyl) phthalonitrile (200.0 mg, 0.567 mmol, 1 equiv) and benzylmagnesium chloride (1.14 mL, 1.0 M in Et_2O, 1.13 mmol, 2 equiv) in dry THF (3.0 mL) first then in distilled/degassed quinoline (3.0 mL). The final material was recrystallised from PE:dry THF (10:1) yielding the *title compound* as a green solid (60.0 mg, 28%); mp >300 °C; UV-Vis (THF) λ_{max}/nm (ε) 685 (4.32×10^3), 659 (3.38×10^3), 606 (7.91×10^2), 433 (1.58×10^2), 383 (2.45×10^3). ^{1}H NMR (500 MHz, THF-d_8, 298 K) δ (ppm) = 9.30 (s, 2H), 9.25 (s, 4H), 8.19 – 8.12 (m, 2H), 8.04 (t, *J* = 7.6 Hz, 1H), 7.95 (t, *J* = 7.6 Hz, 2H), 6.95 (s, 2H), 3.25 – 3.24 (m, 16H), 2.12 (m, 8H), 1.72 – 1.59 (m, 64H), 1.03 – 0.87 (m, 48H). MS (MALDI-TOF) *m/z* 1509 $[M]^+$ (100%).

3.3.1.2 [2,3,9,10,15,16,23,24-Octakis(2-ethylhexyl)-27-(2-bromophenyl)-tetra benzo[*b*,*g*,*l*,*q*][5,10,15]triazaporphinato] magnesium (II) (184)

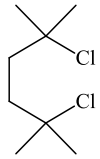


Synthesised uses the general procedure described above from 4,5-bis(2-ethylhexyl) phthalonitrile (200.0 mg, 0.567 mmol, 1 equiv) and 2-bromobenzylmagnesium bromide (4.54 mL, 0.25 M in Et_2O, 1.13 mmol, 2 equiv) in dry THF (3.0 mL) first then in distilled/degassed quinoline (3.0 mL). The final material was recrystallised from acetone/EtOH (1:1) yielding the *title compound* as a green solid (35.0 mg, 16%); mp >300 °C; UV-Vis (THF) λ_{max}/nm (ε) 685 (3.57×10^3), 662 (2.62×10^3), 606 (7.14×10^2), 450 (4.76×10^2), 390 (1.67×10^3). ^{1}H NMR (500 MHz, THF-d_8, 298 K) δ (ppm) = 9.32 (s, 2H), 9.25 (s, 4H), 8.28 (d, *J* = 8.0 Hz, 1H), 8.16 (br s, 1H), 7.99 – 7.92 (m, 2H), 6.99 (s, 2H), 3.25 – 3.24 (m, 16H), 2.12 (m, 8H), 1.72 – 1.59 (m, 64H), 1.03 – 0.87 (m, 48H). MS (MALDI-TOF) *m/z* 1589 $[M]^+$ (100%) (isotopic pattern matches theoretical prediction).



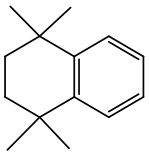
3.4 Synthesis of Substituted Phthalonitrile (222)

3.4.1 2,5-Dichloro-2,5-dimethylhexane (224) [14]



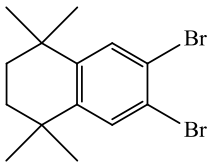
Following a known procedure reported in literature,[14-16] a solution of 2,5-dimethylhexane-2,5-diol (5.0 g, 34.24 mmol) in concentrated hydrochloric acid (50 ml) was stirred at 0 °C for 30 min. The mixture was left to warm to room temperature and completed stirring overnight. The light pink solid was filtered off and washed thoroughly with water. The solid was then dissolved in DCM, washed again by water and extracted with DCM (3x50 mL). The organic extracts were dried ($MgSO_4$) and the solvent removed under reduced pressure to afford the product as a white solid which was recrystallised in methanol to give compound **224** as white crystals (4.66 g, 74%). ^{1}H NMR (500 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 1.95 (s, 4H), 1.60 (s, 12H).

3.4.2 1,1,4,4-Tetramethyl-1,2,3,4-tetrahydronaphthalene (225)[16]



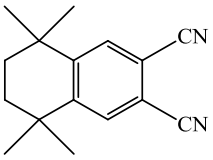
Following Bruson's procedure *via* Friedel-Crafts reaction,[16,17] a solution of 2,5-dichloro-2,5-dimethylhexane **224** (1.0 g, 5.46 mmol) in benzene (50 mL, 0.56 mol) was stirred for 10 min at 50 °C. Anhydrous aluminum trichloride (0.29 g, 2.18 mmol) was added in small portions over 30 min. The thick suspension was then stirred at 50 °C for 24 h. The resulting material was cooled to room temperature, poured into dilute hydrochloric acid and extracted with DCM (3x50 mL). The organics were washed with water, diluted sodium carbonate solution, dried (Na_2SO_4), filtered and the solvent removed under reduced pressure. The resulting material was washed several times by methanol to remove the side-products. The solvent was removed under reduced pressure to give the product as a colourless liquid (0.96 g, 94%). ^{1}H NMR (400 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 7.31 (dd, *J* = 5.9, 3.5 Hz, 2H), 7.13 (dd, *J* = 6.0, 3.4 Hz, 2H), 1.70 (s, 4H), 1.29 (s, 12H).

3.4.3 6,7-dibromo-1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene (226) [2]



Bromination of **225** was achieved using the method described by Ashton and co-workers.[2,4] 1,1,4,4-Tetramethyl-1,2,3,4-tetrahydronaphthalene **225** (0.96 g, 5.11 mmol) was dissolved in DCM (15 mL). Iron powder (34.0 mg, 0.61 mmol) and iodine (12.95 mg, 0.051 mmol) were added to the mixture and cooled to 0 °C. Bromine (0.53 mL, 10.19 mmol) was added dropwise *via* syringe to the stirring mixture over 30 min. After complete addition, the reaction mixture was allowed to warm up to room temperature and stirred for 24 h. The resulting mixture was washed with an aqueous solution of sodium metabisulfite and sodium bicarbonate to remove the excess bromine. Water and brine were added and the mixture extracted with DCM (3×50 mL). The organic extracts were dried over $MgSO_4$, filtered and the solvent removed under reduced pressure to give brownish solid. The product was purified by column chromatography over silica gel using PE/DCM (3:2) as eluents to give *the title compound* as a yellow solid (1.52 g, 86%). ^{1}H NMR (500 MHz, $CDCl_3$, 298 K) δ (ppm) = 7.50 (s, 2H), 1.65 (s, 4H), 1.25 (s, 12H).

3.4.4 6,7-Dicyano-1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene (222) [6]

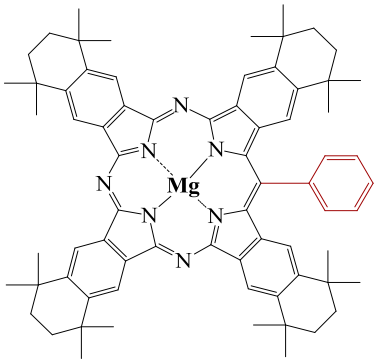


Following the procedure described by Rosenmund von Braun,[6,17] a mixture of 6,7-dibromo-1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene **226** (1.52 g, 4.39 mmol) and CuCN (1.97 g, 21.99 mmol) was refluxed in dry DMF (15 mL) under an argon atmosphere for 16 h. The reaction mixture was cooled to room temperature and poured into an aqueous solution of ammonia (50 mL), and left to stir at room temperature for 24 h under a stream of air. The resulting material was extracted with Et_2O (3 x 50 mL), washed with H_2O (3 x 50 mL) and saturated solution of $NaHCO_3$, dried over $MgSO_4$ and filtered. The filtrate was evaporated under reduced pressure to give the crude product. The crude material was purified by column chromatography

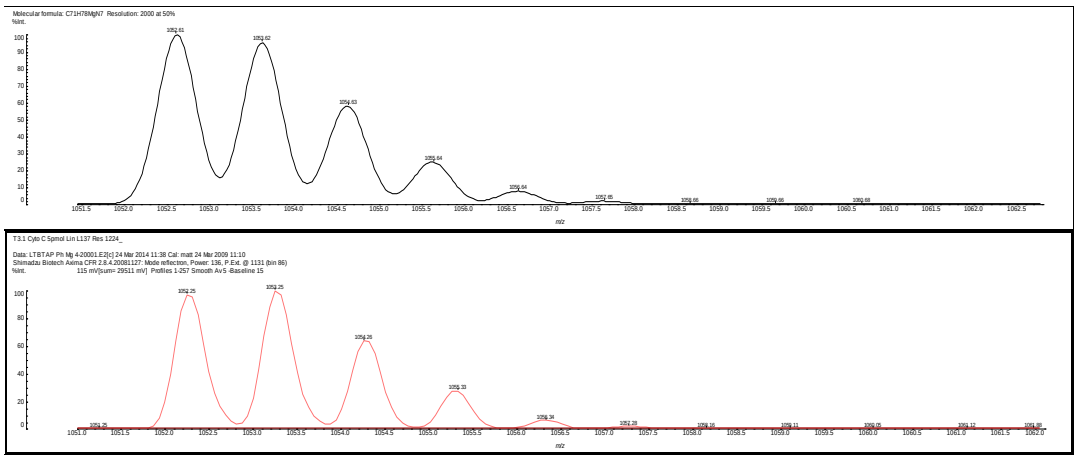
(silica: PE/ Et_2O, 7:1) to yield the product as a yellow solid (0.28 mg, 27%). ^{1}H NMR (400 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 7.71 (s, 2H), 1.72 (s, 4H), 1.30 (s, 12H).

3.5 Synthesis of Substituted Tetrabenzotriazaporphyrins (185 and 186)

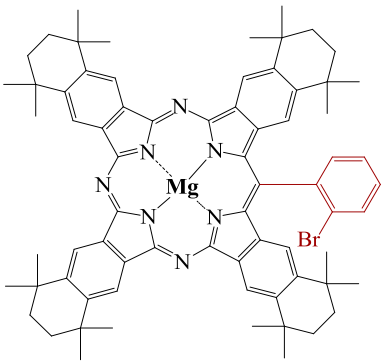
3.5.1 [2,3,9,10,15,16,23,24-tetrakis(1,1,4,4-tetramethyl-6,7-tetralino)-27-phenyl-tetrabenzo[*b*,*g*,*l*,*q*][5,10,15]triazaporphinato] magnesium (II) (185)



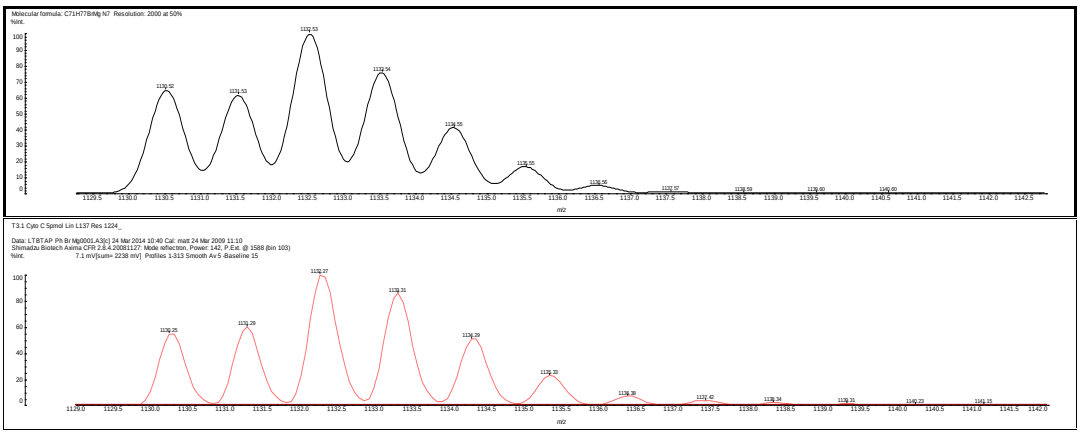
Following the general method previously described in section 3.3.1, the 6,7-dicyano-1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene **222** (200.0 mg, 0.840 mmol, 1 equiv) and benzylmagnesium chloride (1.68 mL, 1.68 mmol, 2 equiv, 1.0 M in Et_2O) were used to obtain the target compound. The final material was recrystallised from THF/EtOH (1:1) provided the *title compound* as a green solid (18.0 mg, 8%); mp >300 °C; UV-Vis (THF) λ_{max}/nm (ε) 688 (1.38×10^3), 662 (7.94×10^2), 605 (2.65×10^2), 451 (2.12×10^2), 383 (5.82×10^2). ^{1}H NMR (500 MHz, THF-d_8, 298 K) δ (ppm) = 9.53 (s, 2H), 9.50 (s, 2H), 9.48 (s, 2H), 8.19 (d, *J* = 8.1 Hz, 2H), 8.07 (t, *J* = 7.5 Hz, 1H), 8.01 (t, *J* = 7.2 Hz, 2H), 7.24 (s, 2H), 2.29 (s, 16H), 1.35 (s, 48H). MS (MALDI-TOF) *m/z* 1052 $[M]^+$ (100%) (isotopic pattern matches theoretical prediction).



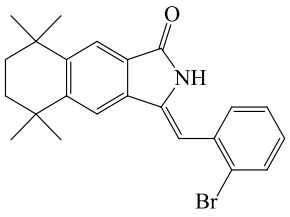
3.5.2 [2,3,9,10,15,16,23,24-tetrakis(1,1,4,4-tetramethyl-6,7-tetralino)-27-(2-bromophenyl)-tetrabenzo[*b*,*g*,*l*,*q*][5,10,15]triazaporphinato] magnesium (II) (186)



Prepared following the general procedure described in section 3.3.1 using 6,7-dicyano-1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene **222** (200.0 mg, 0.840 mmol, 1 equiv) and 2-bromobenzylmagnesium bromide (6.72 mL, 1.68 mmol, 2 equiv, 0.25 M in Et_2O). The final material was recrystallised from THF/EtOH (1:1) gave the *title compound* as a green solid (28.0 mg, 12%); mp >300 °C; UV-Vis (acetone) λ_{max}/nm (ε) 689 (3.29×10^4), 665 (2.34×10^4), 607 (4.75×10^3), 431 (4.75×10^3), 383 (1.22×10^4). ^{1}H NMR (500 MHz, THF-d_8, 298 K) δ (ppm) = 9.53 (s, 2H), 9.49 (s, 2H), 9.48 (s, 2H), 8.37 (dd, J = 7.9, 1.4 Hz, 1H), 8.13 (dd, J = 7.0, 2.0 Hz, 1H), 7.98 – 7.93 (m, 2H), 7.31 (s, 2H), 2.09 (s, 16H), 1.80 (s, 48H). MS (MALDI-TOF) *m/z* 1132 $[M]^+$ (100%) (isotopic pattern matches theoretical prediction).



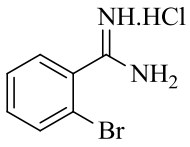
3.5.3 (*Z*)-3-(2-Bromobenzylidene)-5,5,8,8-tetramethyl-2,3,5,6,7,8-hexahydro-1*H*-benzo[*f*]isoindol-1-one (232)



The previous reaction was gave a side-product (in one experimental reaction) which recrystallised from THF/MeOH (1:4) to give (*Z*)-3-(2-bromobenzylidene)-5,5,8,8-tetramethyl-2,3,5,6,7,8-hexahydro-1*H*-benzo[*f*]isoindol-1-one as pale yellow crystals (28.0 mg, 8%); mp = 191 °C; UV-Vis (DCM) λ_{max}/nm (ε) 418 (1.23×10^2), 336 (2.46×10^3), 301 (1.97×10^3). ^{1}H NMR (400 MHz, THF-d_8, 298 K) δ (ppm) = 7.90 (s, 1H), 7.77 (s, 1H), 7.64 (dd, *J* = 8.0, 1.3 Hz, 2H), 7.39 (td, *J* = 7.4, 1.0 Hz, 1H), 7.15 (td, J = 7.6, 1.6 Hz, 1H), 6.58 (s, 1H), 1.73 (br s, 4H), 1.39 (s, 6H), 1.35 (s, 6H). ^{13}C NMR (125.7 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 169.15, 150.83, 148.00, 135.50, 134.99, 134.78, 133.65, 129.74, 129.10, 128.08, 126.68, 124.53, 122.10, 118.35, 103.83, 35.44, 35.23, 34.96, 34.82, 32.19, 30.50, 29.86. MS (MALDI-TOF) *m/z* 410 $[M]^+$ (100%).

3.6 Synthesis of Aminoisoindolines

3.6.1 Synthesis of 2-bromobenzimidamide hydrochloride (168)[18]

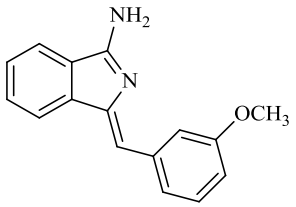


Following the method reported in literature,[18] a solution of 2-bromobenzonitrile (3.7 g, 20.33 mmol) in dry THF (3.0 mL) was added to a solution of 1 M $LiN(SiMe_3)_2$ in anhydrous THF (22.0 mL) and the reaction mixture was stirred at room temperature for 4 h. A 5 N HCl in isopropanol (15 mL) was added to the cooled mixture. The crude reaction mixture was left to stir at room temperature overnight. The precipitated product was filtered, washed with diethyl ether and finally recrystallised from Et_2O and MeOH to yield **168** (2.77 g, 69%) as colourless crystals. ^{1}H NMR (500 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 7.86 – 7.76 (m, 1H), 7.66 – 7.49 (m, 3H).

3.6.2 General synthetic procedure for the synthesis of aminoisoindolines

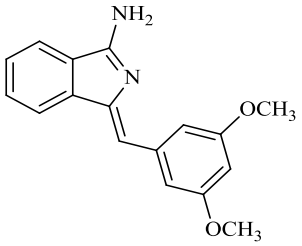
Following the reported procedure[19] a mixture of amidine, BINAP (0.055 equiv) and $PdCl_2(MeCN)_2$ (0.05 equiv) was sealed in a microwave vessel with a magnetic bar and then purged and refilled with N_2 three times. Then, a solution of substituted arylacetylene (1.2 equiv) and DBU (2.5 equiv) in dry DMF (12 ml) was added. The mixture was stirred under N_2 for 5 min to give a clear yellow solution with a white solid. Finally, the mixture was irradiated in a microwave reactor at 120 °C for 1 h. After cooling, 50 mL of EtOAc was added and the mixture washed with a saturated solution of $NaHCO_3$ (75 ml) three times. The organic layer was dried ($MgSO_4$), filtered and concentrated. The residue was finally purified by column chromatography using EtOAc → EtOAc /EtOH/H_2O (90:5:3) → EtOAc /EtOH/H_2O (45:5:3).

3.6.2.1 (*Z*)-1-(3-methoxybenzylidene)-1*H*-isoindol-3-amine (234)



Following the general procedure described above, a solution of 3-ethynylanisole (0.67 g, 5.09 mmol) and DBU (1.62 g, 10.64 mmol) in dry DMF (12 ml) was added to a mixture of amidine **168** (1.00 g, 4.25 mmol) , BINAP (0.13 g, 0.21 mmol) and $PdCl_2(MeCN)_2$ (0.06 g, 0.21 mmol). The reaction mixture was irradiated in a microwave reactor at 120 °C for 1 h. After purification, the yellow solid was recrystallised from a DCM/Petroleum ether (1:1) to yield the *title compound* as yellow needles (440.0 mg, 41%); mp = 183 – 184 °C; UV-Vis (DCM) λ_{max}/nm (ε) 367 (2.93×10^3), 292 (9.01×10^2). ^{1}H NMR (500 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 7.83 (br s, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.30 (t, *J* = 7.9 Hz, 1H), 6.82 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.73 (s, 1H), 5.74 – 5.35 (br s, 2H, NH2), 3.88 (s, 3H). ^{13}C NMR (125.7 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 165.04, 159.85, 159.84, 159.80, 138.10, 131.11, 129.47, 129.36, 127.40, 126.85, 123.40, 119.97, 119.02, 115.58, 113.64, 55.45. MS (MALDI-TOF) *m/z* 251 $[M]^+$ (100%). HRMS (ESI) ($C_{16}H_{14}N_2O$) $[M+H]^+$: calcd: 251.1179; found: 251. 1180.

3.6.2.2 (*Z*)-1-(3,5-dimethoxybenzylidene)-1*H*-isoindol-3-amine (236)



Following the general procedure described above, a solution of 1-ethynyl-3,5-dimethoxybenzene (0.83 g, 5.12 mmol) and DBU (1.62 g, 10.63 mmol) in dry DMF (12 ml) was added to a mixture of amidine **168** (1.00 g, 4.25 mmol) , BINAP (0.13 g, 0.21 mmol) and $PdCl_2(MeCN)_2$ (0.06 g, 0.21 mmol). The reaction mixture was irradiated in a microwave reactor at 120 °C for 1 h. After purification, the yellow solid was recrystallised from a DCM/Petroleum ether (1:1) to yield the *title compound* as yellow needles (300.0 mg, 25%); mp = 167 – 168 °C; UV-Vis (DCM) λ_{max}/nm (ε) 367 (1.18×10^3), 290 (3.36×10^2). ^{1}H NMR (500 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 77.79 (d, *J* = 7.5 Hz, 1H), 7.51 – 7.47 (m, 2H), 7.40 (t, *J* = 7.4 Hz, 1H), 7.30 (d, *J* = 2.0 Hz, 2H), 6.70 (s, 1H), 6.42 (t, *J* = 2.3 Hz, 1H), 3.87 (s, 6H). ^{13}C NMR (125.7 MHz, $CDCl_3$-d, 298 K) δ (ppm) = 164.76, 160.91, 159.76, 154.32, 153.83, 152.80, 138.20, 131.11, 129.80, 128.82, 127.64, 127.30, 120.05, 119.39, 108.49, 100.66, 55.61. MS (MALDI-TOF) *m/z* 281 $[M]^+$ (100%). HRMS (ESI) ($C_{17}H_{16}N_2O_2$) $[M+H]^+$: calcd: 281.1285; found: 281.1287.

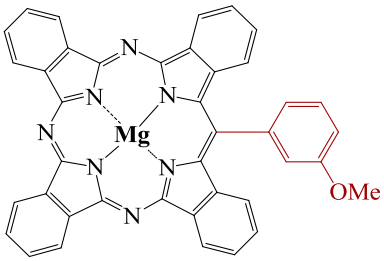
3.7 Synthesis of Unsubstituted Tetrabenzotriazaporphyrins

3.7.1 General synthetic procedure for the preparation of substituted *meso*-aryl TBTAPs *via* aminoisoindoline intermediate (191 and 192)

The reaction was carried out following the process described by Cammidge and coworkers.[20,21] A suspension of phthalonitrile (3 equiv) and $MgBr_2$ (1.5 equiv) in dry diglyme (0.5 ml) was heated at 220 °C for 10 min under an argon atmosphere, in a preheated mantle. A solution of aminoisoindoline (1 equiv) and phthalonitrile (1 equiv) in dry diglyme (1 ml) was added dropwise over 1 h using a syringe pump. After finishing the first addition, the reaction mixture was left to reflux at 220 °C for 30 min. Finally, a solution of phthalonitrile (1 equiv) and DABCO (1.5 equiv) in dry diglyme (0.5 ml) was added dropwise over 1 h. The reaction mixture was then refluxed at 220 °C under argon for further 30 min. A stream of argon was passed through the reaction vessel in order to remove the solvent. The reaction mixture was

cooled to room temperature and a mixture of DCM/MeOH (50 ml, 1:1) was added and the mixture sonicated. After the removal of solvent under reduced pressure, the resulting material was purified by two consecutive flash chromatographies. Firstly, the crude was loaded on silica-gel column and eluted with DCM/Et_3N/THF (10:1:4) in order to remove the yellow-brown impurities and obtain a green fraction. Finally, the green fraction was then subjected to a second column chromatography using PE/THF/MeOH (10:3:1) as elute to obtain the pure green product. Alternatively, analytically pure material could be obtained by size-exclusion chromatography over Bio-beads SX-3 using THF eluent.

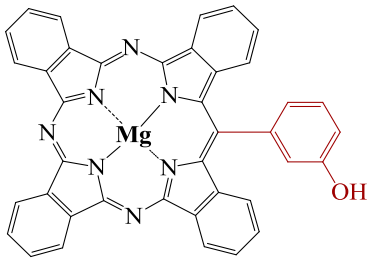
3.7.1.1 [20-(3-Methoxyphenyl)-tetrabenzo[b,g,q,l]-5,10,15-triazaporphyrinato] magnesium (II) (191)



Synthesised following the general procedure described above, a solution of phthalonitrile (154.0 mg, 1.20 mmol) and $MgBr_2$ (110.0 mg, 0.60 mmol) in dry diglyme (0.5 ml) was heated at 220 °C for 10 min under argon. A solution of aminoisoindoline **234** (100.0 mg, 0.40 mmol) and phthalonitrile (51.0 mg, 0.40 mmol) in dry diglyme (1.0 ml) was added dropwise over 1 h using a syringe pump. After finishing the first addition, the reaction mixture was left to reflux at 220 °C for 30 min. Finally, a solution of phthalonitrile (51.0 mg, 0.40 mmol) and DABCO (67.0 mg, 0.60 mmol) in dry diglyme (0.5 ml) was added dropwise over 1 h. The reaction mixture was then refluxed at 220 °C under argon for further 30 min. The final material was recrystallised from acetone/EtOH (1:1) gave the *title compound* as green crystals with purple reflex (50.0 mg, 20%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 670 (7.35×10^3), 647 (4.41×10^3), 592 (1.03×10^2), 442 (1.03×10^2), 397 (2.50×10^2). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.59 (d, *J* = 7.5 Hz, 2H), 9.53 – 9.50 (m, 4H), 8.23 – 8.15 (m, 4H), 7.92 (t, *J* = 7.1 Hz, 2H), 7.88 – 7.84 (m, 1H), 7.77 – 7.68 (m, 2H), 7.63 – 7.59 (m, 3H), 7.25 (d, *J* = 8.0 Hz, 2H), 3.98 (s, 3H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 169.56, 161.75, 156.84, 153.81, 152.87, 145.09, 143.05, 141.13, 141.00, 140.90, 140.20, 134.79, 134.51, 133.67, 132.79, 130.86,

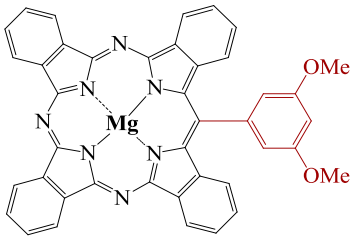
130.09, 129.80, 128.24, 127.39, 126.63, 125.81, 125.69, 123.86, 123.76, 123.64, 123.58, 122.46, 118.90, 115.86, 108.56, 98.90, 56.04. MS (MALDI-TOF) *m/z* 642 $[M]^+$ (100%). HRMS (ESI) ($C_{40}H_{23}MgN_7O$) $[M+H]^+$: calcd: 642.1887; found: 642.1885.

3.7.1.2 [20-(3-Hydroxyphenyl)-tetrabenzo[b,g,q,l]-5,10,15-triazaporphyrinato] magnesium (II) (241)



Synthesised following the general procedure,[22] a solution of TBTAP **191** (40 mg, 0.062 mmol) in distilled DCM (5 mL) was stirred at 0 °C for 5 min under an argon atmosphere. A solution of BBr_3 (1.25 mL, 1.25 mmol, 20 equiv, 1 M in DCM) was added dropwise over 1 h using a syringe pump. After finishing the addition, the reaction mixture was left to warm to room temperature and stirred for further 1 h. MeOH (5 ml) was added and the mixture sonicated for 5 min. The solvents were removed under reduced pressure and the crude was purified by column chromatography using DCM/Et_3N/THF (20:1:3) as eluent. The final material was recrystallised from acetone and EtOH gave the *title compound* as green crystals with purple reflex (19.40 mg, 50%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 670 (4.14×10^3), 646 (2.26×10^3), 592 (5.65×10^2), 444 (1.88×10^2), 428 (3.77×10^2), 383 (1.32×10^3). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.59 (d, *J* = 7.5 Hz, 2H), 9.53 – 9.50 (m, 4H), 8.82 (br s, 1H, OH), 8.21 – 8.15 (m, 4H), 7.92 (t, *J* = 7.0 Hz, 2H), 7.79 – 7.74 (m, 1H), 7.66 – 7.61 (m, 3H), 7.54 (s, 1H), 7.46 (ddd, *J* = 8.4, 2.4, 0.9 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 117.56, 114.60, 114.56, 114.52, 110.65, 102.69, 100.94, 98.95, 98.85, 98.72, 97.98, 94.30, 88.57, 87.84, 87.54, 86.00, 85.14, 84.76, 83.87, 81.96, 81.64, 81.41, 81.29, 78.53, 74.85. MS (MALDI-TOF) *m/z* 628 $[M]^+$ (100%). HRMS (ESI) ($C_{39}H_{21}MgN_7O$) $[M+H]^+$: calcd: 627.1653; found: 627.1654.

3.7.1.3 [20-(3,5-Dimethoxyphenyl)-tetrabenzo[b,g,q,l]-5,10,15-triazaporphyrinato] magnesium (II) (192)



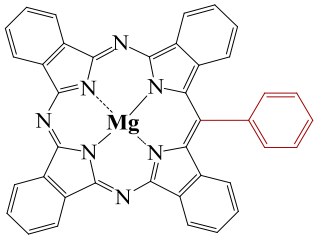
Synthesised following the general procedure described above, a solution of phthalonitrile (210.0 mg, 1.64 mmol) and $MgBr_2$ (148.0 mg, 0.80 mmol) in dry diglyme (0.5 ml) was heated at 220 °C for 10 min under argon. A solution of aminoisoindoline **236** (150.0 mg, 0.54 mmol) and phthalonitrile (69.0 mg, 0.54 mmol) in dry diglyme (1.0 ml) was added dropwise over 1 h using a syringe pump. After finishing the first addition, the reaction mixture was left to reflux at 220 °C for 30 min. Finally, a solution of phthalonitrile (69.0 mg, 0.54 mmol) and DABCO (90.10 mg, 0.80 mmol) in dry diglyme (0.5 ml) was added dropwise over 1 h. The reaction mixture was then refluxed at 220 °C under argon for further 30 min. The final material was recrystallised from acetone/EtOH (1:1) gave the *title compound* as green crystals with purple reflex (30.0 mg, 8%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 670 (6.45×10^3), 647 (4.23×10^3), 594 (1.21×10^3), 443 (1.41×10^3), 395 (2.82×10^3). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.59 (d, *J* = 7.5 Hz, 2H), 9.53 – 9.50 (m, 4H), 8.20 – 8.15 (m, 4H), 7.93 (t, *J* = 7.6 Hz, 2H), 7.65 (t, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 2.3 Hz, 2H), 7.18 (t, *J* = 2.3 Hz, 1H), 3.95 (s, 6H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 162.77, 156.73, 153.72, 152.83, 145.37, 142.92, 142.14, 141.16, 140.93, 140.21, 130.07, 129.78, 128.35, 127.41, 126.68, 125.97, 123.85, 123.65, 123.54, 111.75, 102.25, 56.14. MS (MALDI-TOF) *m/z* 672 $[M]^+$ (100%). HRMS (ESI) ($C_{41}H_{25}MgN_7O_2$) $[M+H]^+$: calcd: 671.1915; found: 671.1923.

3.7.2 General synthetic procedure for the preparation of substituted *meso*-aryl TBTAPs *via* the Grignard reagent route using diglyme as solvent (187-190)[21]

A suspension of phthalonitrile in dry diglyme was refluxed at 220 °C for 10 min under an argon atmosphere, in a preheated mantle. A solution of bromobenzylmagnesium bromide was added dropwise *via* a syringe over 1 h. The reaction mixture was heated at 220 °C under argon for 2 h. A stream of argon was passed through the reaction

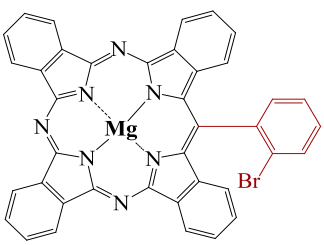
vessel in order to remove the solvent. After the reaction mixture cooled to room temperature, a mixture of DCM/MeOH (50 ml, 1:1) was added to the reaction mixture which was dissolved using an ultrasonic bath. After the removal of solvent under reduced pressure, the crude material was loaded on a silica-gel column and eluted with DCM/Et_3N/THF (10:1:4) in order to initially remove the yellow-brown impurities and the isolate green/blue fractions, which subjected to a second column chromatographic separation using PE:THF/MeOH (10:3:1) as elute to obtain the pure green product.

3.7.2.1 [27-phenyl-tetrabenzo[*b,g,q,l*][5,10,15]triazaporphyrinato] magnesium (II) (187)[23]



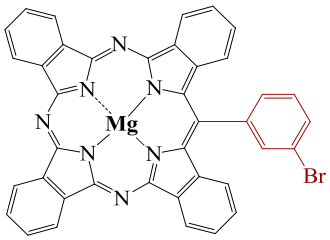
Prepared following the general procedure described above, a suspension of phthalonitrile (254.0 mg, 1.98 mmol, 3 equiv) in dry diglyme (1.0 ml) and a solution of benzylmagnesium chloride (0.663 mL, 0.663 mmol, 1 equiv, 1.0 M in Et_2O) were heated at 220 °C under argon for 3 h. After purification, the resulting green material was recrystallised from acetone/EtOH (1:1) gave the *title compound* as green crystals with a purple reflex (20 mg, 5%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 670 (1.58×10^2), 647 (1.01×10^2), 593 (2.39×10^1), 443 (2.57×10^1), 397 (6.06×10^1). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.59 (d, *J* = 7.5 Hz, 2H), 9.55 – 9.48 (m, 4H), 8.21 – 8.14 (m, 6H), 8.06 (t, *J* = 7.7 Hz, 1H), 7.96 (t, *J* = 7.6 Hz, 2H), 7.91 (t, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H). MS (MALDI-TOF) *m/z* 612 $[M]^+$ (100%).

3.7.2.2 [20-(2-Bromophenyl)-tetrabenzo[*b,g,q,l*][5,10,15]triazaporphyrinato] magnesium (II) (188)



Prepared follows the general procedure, a suspension of phthalonitrile (280.0 mg, 2.19 mmol, 3 equiv) in dry diglyme (1.0 ml) and a solution of 2-bromobenzylmagnesium bromide (2.92 mL, 0.729 mmol, 1 equiv, 0.25 M in Et_2O) were heated at 220 °C under argon for 3 h. After purification, the resulting green material was recrystallised from acetone/EtOH (1:1) gave the *title compound* as green crystals with a purple reflex (280 mg, 56%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 671 (2.12×10^3), 650 (1.11×10^3), 594 (2.33×10^2), 443 (1.55×10^2), 396 (5.96×10^3). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.61 (d, *J* = 7.5 Hz, 2H), 9.53 – 9.48 (m, 4H), 8.31 (d, *J* = 8.3 Hz, 1H), 8.18 – 8.16(m, 5H), 7.98 (t, *J* = 7.9 Hz, 1H), 7.92 (t, *J* = 7.2 Hz, 3H), 7.60 (t, *J* = 7.5 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 177.06, 156.67, 153.74, 152.68, 144.36, 142.51, 141.26, 141.03, 140.79, 140.31, 135.27, 134.70, 132.18, 130.15, 129.87, 129.64, 128.59, 127.60, 125.14, 124.71, 123.93, 123.83, 123.74, 108.57, 108.28, 107.83, 102.09, 98.92. MS (MALDI-TOF) *m/z* 692 $[M]^+$ (100%). HRMS (ESI) ($C_{39}H_{20}BrMgN_7$) $[M+H]^+$: calcd: 689.0808; found: 689.0807.

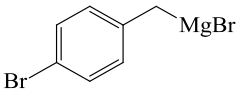
3.7.2.3 [20-(3-Bromophenyl)-tetrabenzo[*b,g,q,l*][5,10,15]triazaporphyrinato] magnesium (II) (189)



Phthalonitrile (280.0 mg, 2.19 mmol, 3 equiv) was dissolved in dry diglyme (1.0 ml) and a solution of 3-bromobenzylmagnesium bromide (2.92 mL, 0.729 mmol, 1 equiv, 0.25 M in Et_2O) was added dropwise to the previous solution. The mixture was heated at 220 °C under argon for 3 h. The crude was purified by column chromatography as described in general procedure. Recrystallisation from acetone/EtOH (1:1) yielded the *title compound* as green crystals with purple reflex (120 mg, 24%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 671 (3.29×10^3), 648 (1.91×10^3), 593 (4.15×10^2), 442 (2.90×10^2), 396 (1.09×10^3). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.61 (d, *J* = 7.6 Hz, 2H), 9.53 – 9.47 (m, 4H), 8.37 (s, 1H), 8.25 (d, *J* = 8.3 Hz, 1H), 8.19 – 8.15 (m, 5H), 7.94 – 7.87 (m, 3H), 7.62 (t, *J* = 7.5 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 176.28, 166.35, 160.34, 157.98,

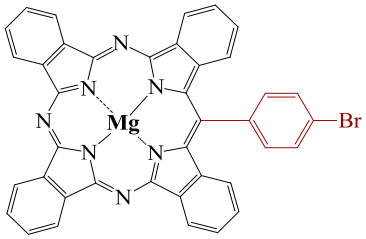
155.83, 154.80, 153.38, 152.27, 151.68, 150.48, 147.92, 146.41, 146.35, 145.95, 144.27, 143.15, 141.08, 140.88, 140.63, 140.14, 139.55, 139.40, 138.13, 133.19, 133.07, 130.15, 129.84, 128.32, 127.38, 125.16, 123.83, 123.80, 123.59. MS (MALDI-TOF) *m/z* 692 $[M]^+$ (100%). HRMS (ESI) ($C_{39}H_{20}BrMgN_7$) $[M+H]^+$: calcd: 689.0817; found: 689.0808.

3.7.2.4 4-bromobenzylmagnesium bromide solution (247)[24]



Prepared using a typical Grignard reagent synthetic procedure,[1,24] a suspension of magnesium turnings (0.56 gm, 23.25 mmol) in Et_2O (7.0 mL) was stirred for 10 min under an inert atmosphere. A single crystal of iodine was added to the preivous mixture. A solution of 4-bromobenzyl bromide (5.82 gm, 23.26 mol) in Et_2O (5.0 mL) was added dropwise *via* addition funnel. After the addition of 4-bromobenzyl bromide was completed, the mixture was heated under reflux for 2 h. The Grignard reagent was cooled and used immediately for the preparation of TBTAP in next step.

3.7.2.5 [20-(4-Bromophenyl)-tetrabenzo[*b,g,q,l*][5,10,15]triazaporphyrinato] magnesium (II) (190)



A mixture of phthalonitrile (4.41 gm, 34.45 mmol, 1.35 equiv) in dry diglyme (6.0 ml) and a 4-bromobenzylmagnesium bromide (11.98 mL, 25.52 mmol, 1 equiv, 2.13 M in Et_2O) was heated at 220 °C under argon for 3 h, as described previously in general method. Recrystallisation from acetone/EtOH (1:1) yielded the *title compound* as green crystals with purple reflex (400.0 mg, 2%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 671 (1.75×10^3), 648 (1.00×10^3), 594 (2.50×10^2), 443 (2.14×10^2), 394 (6.79×10^2). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.60 (d, *J* = 7.5 Hz, 2H), 9.52 – 9.48 (m, 4H), 8.19 – 8.13 (m, 6H), 8.10 (d, *J* = 7.8 Hz, 2H), 7.91 (t, *J* = 7.2 Hz, 2H), 7.63 (t, *J* = 7.5 Hz, 2H), 7.17 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 157.87, 154.69, 153.61, 143.25, 143.17, 141.06, 140.86, 140.68,

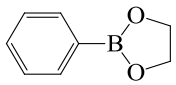
140.13, 135.23, 133.26, 130.13, 129.81, 128.28, 127.36, 125.22, 124.15, 123.82, 123.76, 123.57, 121.81, 108.56. MS (MALDI-TOF) *m/z* 692 $[M]^+$ (100%). HRMS (ESI) ($C_{39}H_{20}BrMgN_7$) $[M+H]^+$: calcd: 690.0888; found: 690.0887.

3.8 Transformations of Functionalised *meso*-phenyl Tetrabenzotriaza porphyrins

3.8.1 General synthetic procedure for the synthesis of *meso*-biphenyl tetrabenzotriazaporphyrins *via* palladium-catalysed Suzuki cross-coupling reactions (194-196)

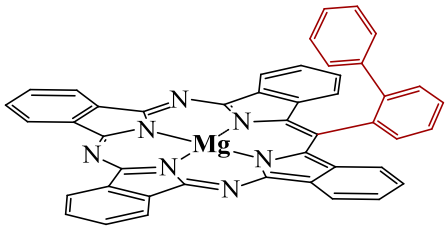
A mixture of bromophenyl TBTAP (1.0 equiv), $PdCl_2$(dppf) (0.1 equiv) was sealed in a microwave vessel with a magnetic bar and then evacuated and backfilled with argon three times. A solution of 2-phenyl-[1,3,2]-dioxaborolane (10.0 equiv) and DBU (2.5 equiv) in dry DMF (1.0 mL) was added and stirred under argon for 5 min. The mixture was then irradiated in a microwave reactor at 120 °C for 1 h. After cooling to room temperature, 10 mL of DCM was added and the mixture sonicated for 5 min. After the removal of the solvent under reduced pressure, the resulting material was purified by column chromatography over silica gel to give the desired product.

3.8.1.1 2-Phenyl-[1,3,2]-dioxaborolane (252) [25]

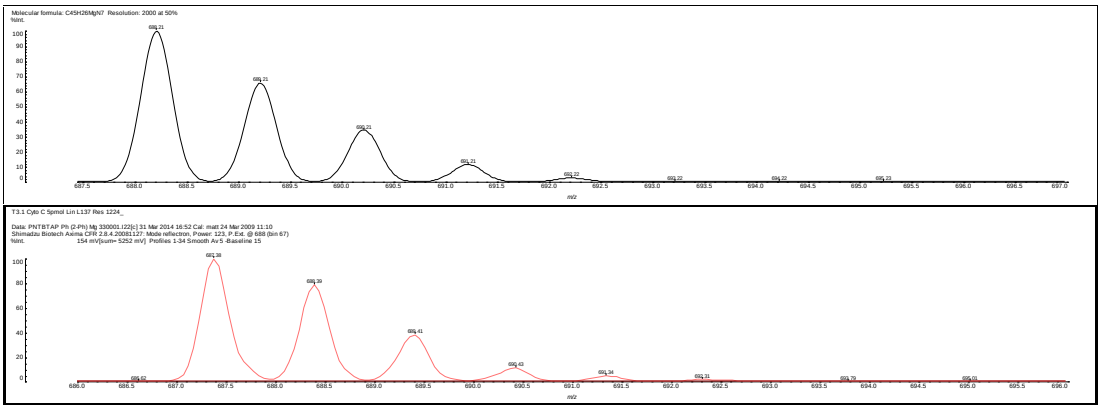


Prepared following the procedure reported by Sigman and co-workers,[25] a solution of phenyl boronic acid (2.00 g, 16.4 mmol, 1.00 equiv), ethylene glycol (1.12 g, 18.0 mmol, 1.10 equiv) and magnesium sulfate (1.97 g, 16.4 mmol, 1.00 equiv) in dry DCM (20.0 mL) was stirred at room temperature overnight under an inert atmosphere. The reaction mixture was filtered, washed with dichloromethane, and concentrated under reduced pressure to yield a colorless oil (2.33 g, 96%). ^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ (ppm) = 7.86 – 7.79 (m, 2H), 7.52 – 7.45 (m, 1H), 7.43 – 7.35 (m, 2H), 4.38 (s, 4H). ^{13}C NMR (125.7 MHz, $CDCl_3$, 298 K) δ (ppm) = 134.85, 131.51, 127.87, 66.06.

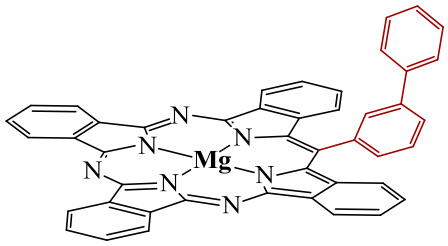
3.8.1.2 [20-{2-(1,1'-biphenyl)}-tetrabenzo[*b,g,q,l*][5,10,15]triaza porphyrinato] magnesium (194)



Prepared following the procedure described above, a mixture of 2-bromophenyl MgTBTAP **188** (30.0 mg, 0.043 mmol, 1.00 equiv) and $PdCl_2$(dppf) (4.0 mg, 4.90 µmol, 0.1 equiv) was sealed in a microwave vessel. A solution of 2-phenyl-[1,3,2]-dioxaborolane (64.0 mg, 0.43 mmol, 10.0 equiv) and DBU (16.50 mg, 0.11 mmol, 2.5 equiv) in dry DMF (1.0 mL) was added, stirred and then irradiated in a microwave reactor at 120 °C for 1 h. Purification by chromatography on silica gel using DCM → DCM/Et_3N (20:1) → DCM/Et_3N/THF (10:1:2) → DCM/THF (1:1) gave the oily green material. The green material was subjected to a size-exclusion chromatography over Bio-beads SX-3 using THF eluent to obtain a pure material. Recrystallisation from acetone/EtOH (1:1) yielded the *title compound* as green crystals with a purple reflex (2.70 mg, 9%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 672 (1.48×10^4), 649 (8.59×10^3), 593 (1.72×10^3), 446 (1.37×10^3), 397 (4.47×10^3). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.58 (d, *J* = 7.5 Hz, 2H), 9.51 – 9.45 (m, 4H), 8.19 – 8.13 (m, 4H), 8.12 (d, *J* = 9.1 Hz, 1H), 8.01 (d, *J* = 7.3 Hz, 1H), 7.97 – 7.91 (m, 3H), 7.89 (t, *J* = 7.5 Hz, 1H), 7.68 (t, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.12 (dd, *J* = 6.7, 3.1 Hz, 2H), 6.42 – 6.37 (m, 3H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 156.59, 153.49, 152.38, 145.16, 143.30, 142.75, 142.15, 141.19, 141.17, 140.94, 140.23, 134.10, 132.25, 130.43, 130.06, 129.75, 129.61, 129.18, 128.41, 127.87, 127.43, 127.09, 125.83, 125.46, 123.86, 123.74, 123.58. MS (MALDI-TOF) *m/z* 688 $[M]^+$ (100%) (isotopic pattern matches theoretical prediction).

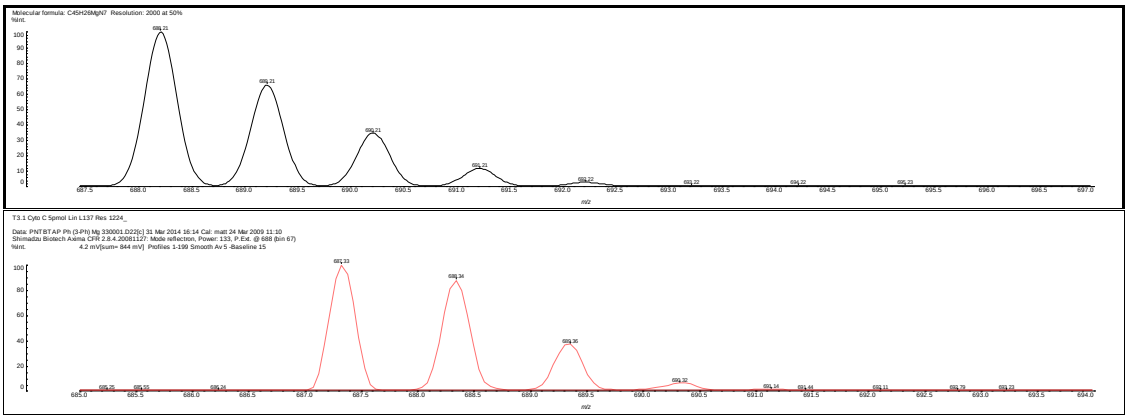


3.8.1.3 [20-{3-(1,1'-biphenyl)}-tetrabenzo[*b,g,q,l*][5,10,15]triaza porphyrinato] magnesium (195)

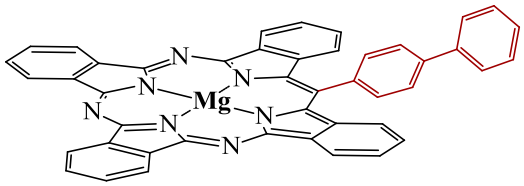


Prepared following the procedure described above, a mixture of 3-bromophenyl TBTAP **189** (38.0 mg, 0.055 mmol, 1.00 equiv) and $PdCl_2$(dppf) (5.0 mg, 6.13 µmol, 0.1 equiv) was sealed in a microwave vessel. A solution of 2-phenyl-[1,3,2]-dioxaborolane (81.4 mg, 0.55 mmol, 10.0 equiv) and DBU (21.0 mg, 0.14 mmol, 2.5 equiv) in dry DMF (1.0 mL) was added, stirred and then irradiated in a microwave reactor at 120 °C for 1 h. Purification by chromatography on silica gel using DCM → DCM/Et_3N (20:1) → DCM/Et_3N/THF (10:1:2) → DCM/THF (1:1) gave the oily green material. The green material was subjected to a size-exclusion chromatography over Bio-beads SX-3 using THF eluent to obtain a pure material. Recrystallisation from acetone/EtOH (1:1) obtained the *title compound* as green crystals with a purple reflex (2.10 mg, 6%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 670 (4.13×10^3), 647 (2.48×10^3), 593 (8.26×10^2), 444 (4.13×10^2), 396 (1.24×10^3). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.60 (d, *J* = 7.5 Hz, 2H), 9.53 – 9.50 (m, 4H), 8.50 (s, 1H), 8.36 (d, *J* = 7.9 Hz, 1H), 8.22 – 8.16 (m, 4H), 8.13 (d, *J* = 7.6 Hz, 1H), 8.05 (t, *J* = 7.5 Hz, 1H), 7.90 (dd, *J* = 14.7, 7.6 Hz, 4H), 7.58 (t, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.8 Hz, 2H), 7.33 (t, *J* = 7.4 Hz, 1H), 7.27 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (125.7 MHz,

THF-d_8, 298 K): δ (ppm) = 156.59, 153.49, 152.38, 145.16, 143.30, 142.75, 142.15, 141.19, 141.17, 140.94, 140.23, 134.10, 132.25, 130.43, 130.06, 129.75, 129.61, 129.18, 128.41, 127.87, 127.43, 127.09, 125.83, 125.46, 123.86, 123.74, 123.58. MS (MALDI-TOF) *m/z* 688 $[M]^+$ (100%) (isotopic pattern matches theoretical prediction).

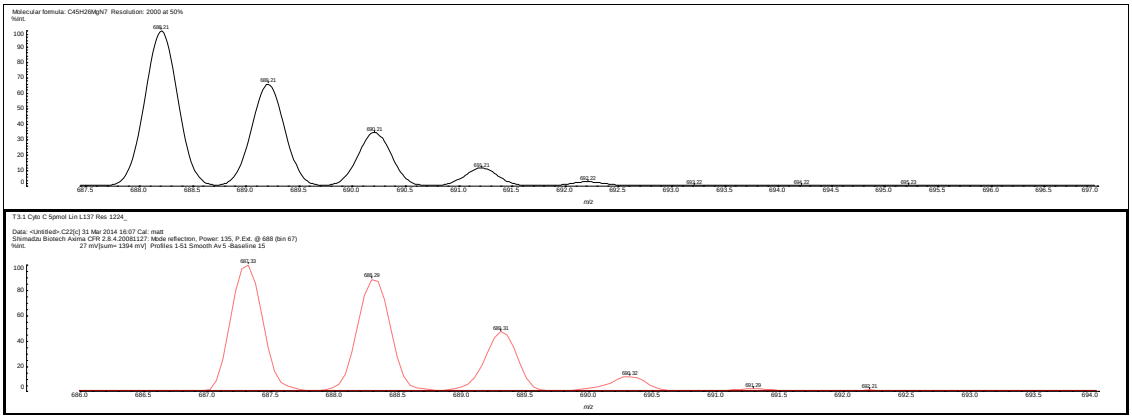


3.8.1.3 [20-{4-(1,1'-biphenyl)}-tetrabenzo[*b,g,q,l*][5,10,15]triaza porphyrinato] magnesium (196)



Prepared following the procedure described above, a mixture of 4-bromophenyl TBTAP **190** (21.8 mg, 0.032 mmol, 1.00 equiv) and $PdCl_2$(dppf) (3.0 mg, 3.68 µmol, 0.1 equiv) was sealed in a microwave vessel. A solution of 2-phenyl-[1,3,2]-dioxaborolane (46.0 mg, 0.31 mmol, 10.0 equiv) and DBU (12.01 mg, 0.079 mmol, 2.5 equiv) in dry DMF (1.0 mL) was added, stirred and then irradiated in a microwave reactor at 120 °C for 1 h. Purification by chromatography on silica gel using DCM → DCM/Et_3N (20:1) → DCM/Et_3N/THF (10:1:2) → DCM/THF (1:1) gave the oily green material. The green material was subjected to a size-exclusion chromatography over Bio-beads SX-3 using THF eluent to obtain a pure material. Recrystallisation from acetone/EtOH (1:1) gave the *title compound* as green crystals with a purple reflex (1.10 mg, 5%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 670 (2.27×10^4), 647 (1.24×10^4), 592 (4.12×10^3), 446 (2.06×10^3), 396 (6.19×10^3). ^{1}H NMR (500 MHz,

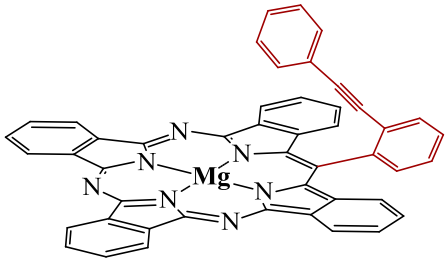
THF-d_8, 298 K): δ (ppm) = 9.60 (d, *J* = 8.3 Hz, 2H), 9.53 – 9.50 (m, 4H), 8.32 (d, *J* = 6.7 Hz, 2H), 8.25 (d, *J* = 7.9 Hz, 2H), 8.21 – 8.13 (m, 6H), 7.91 (t, *J* = 7.3 Hz, 2H), 7.66 (t, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 2H), 7.52 (t, *J* = 6.9 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 156.59, 153.49, 152.38, 145.16, 143.30, 142.75, 142.15, 141.19, 141.17, 140.94, 140.23, 134.10, 132.25, 130.43, 130.06, 129.75, 129.61, 129.18, 128.41, 127.87, 127.43, 127.09, 125.83, 125.46, 123.86, 123.74, 123.58. MS (MALDI-TOF) *m/z* 688 $[M]^+$ (100%) (isotopic pattern matches theoretical prediction).



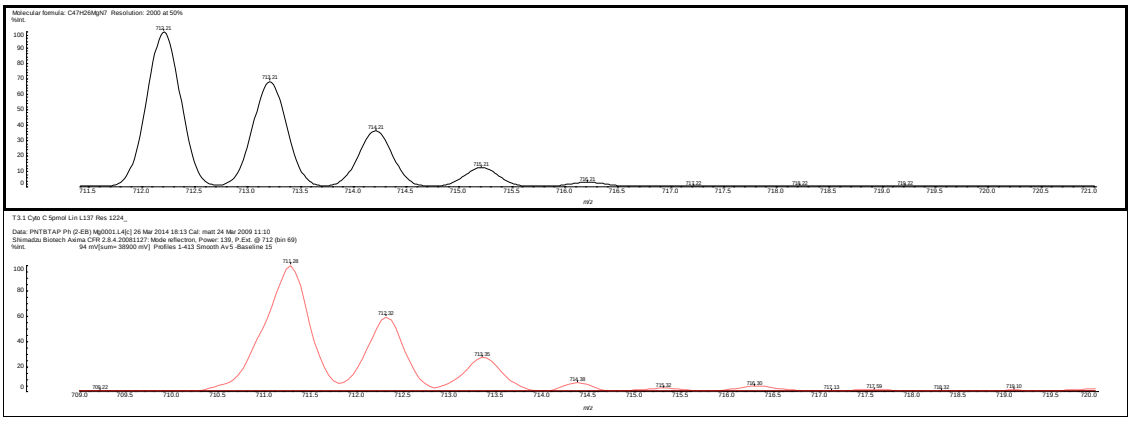
3.8.2 General synthetic procedure for the synthesis of *meso*-phenylethynyl-phenyl tetrabenzotriazaporphyrins *via* palladium-catalysed copper-free Sonogashira cross-coupling reactions (197-199)

A mixture of bromophenyl TBTAP (1.0 eq), BINAP (0.06 equiv) and $PdCl_2(MeCN)_2$ (0.07 equiv) was sealed in a microwave vessel with a magnetic bar and then evacuated and backfilled with argon thrice. A solution of phenylacetylene (1.6 equiv) and DBU (2.5 equiv) in dry DMF (1.0 mL) was added and stirred under argon for 5 min. The mixture was then irradiated in a microwave reactor at 120 °C for 1 h. After cooling to room temperature, 10 mL of DCM was added and the mixture sonicated. After the removal of the solvent under reduced pressure, the resulting material was purified by column chromatography over silica gel to give the desired product.

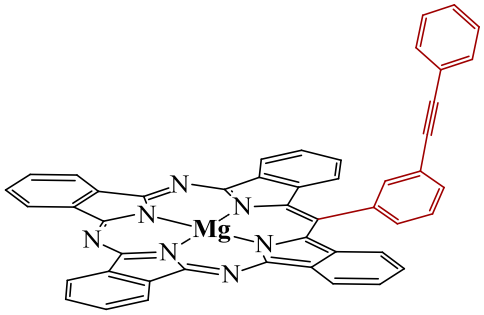
3.8.2.1 [20-{2-(phenylethynyl-phenyl)}-tetrabenzo[*b,g,q,l*][5,10,15]triaza porphyrinato] magnesium (197)



Prepared following the procedure described above, a mixture of 2-bromophenyl TBTAP **188** (40.0 mg, 0.058 mmol, 1.00 equiv), BINAP (2.16 mg, 3.47 µmol, 0.06 equiv) and $PdCl_2(MeCN)_2$ (1.05 mg, 4.05 µmol, 0.07 equiv) was sealed in a microwave vessel. A solution of phenylacetylene (9.46 mg, 0.093 mmol, 1.6 equiv) and DBU (22.0 mg, 0.145 mmol, 2.5 equiv) in dry DMF (1.0 mL) was added, stirred and then irradiated in a microwave reactor at 120 °C for 1 h. Purification by chromatography on silica gel using DCM → DCM/Et_3N (20:1) → DCM/Et_3N/THF (10:1:2) → DCM/THF (1:1) gave the oily green material which recrystallised from acetone/EtOH (1:1) yielded the *title compound* as green crystals with a purple reflex (30 mg, 73%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 670 (2.28×10^4), 648 (1.35×10^4), 592 (2.61×10^3), 444 (1.66×10^3), 395 (7.13×10^3). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.61 (d, *J* = 7.5 Hz, 2H), 9.52 – 9.50 (m, 4H), 8.24 (d, *J* = 8.0 Hz, 1H), 8.20 – 8.14 (m, 4H), 8.10 (t, *J* = 7.9 Hz, 1H), 8.03 (d, *J* = 7.2 Hz, 1H), 7.96 – 7.88 (m, 3H), 7.63 (t, *J* = 7.5 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.67 (d, *J* = 7.1 Hz, 1H), 6.57 (t, *J* = 7.1 Hz, 2H), 6.25 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 145.86, 145.74, 143.23, 143.20, 143.05, 142.75, 141.33, 141.20, 141.08, 141.01, 140.96, 140.27, 139.45, 134.45, 134.43, 134.13, 133.52, 131.73, 130.41, 130.21, 130.04, 129.76, 128.61, 128.52, 128.45, 127.48, 125.22, 125.14, 124.01, 123.87, 123.83, 123.68, 123.66, 123.66. MS (MALDI-TOF) *m/z* 712 $[M]^+$ (100%) (isotopic pattern matches theoretical prediction).

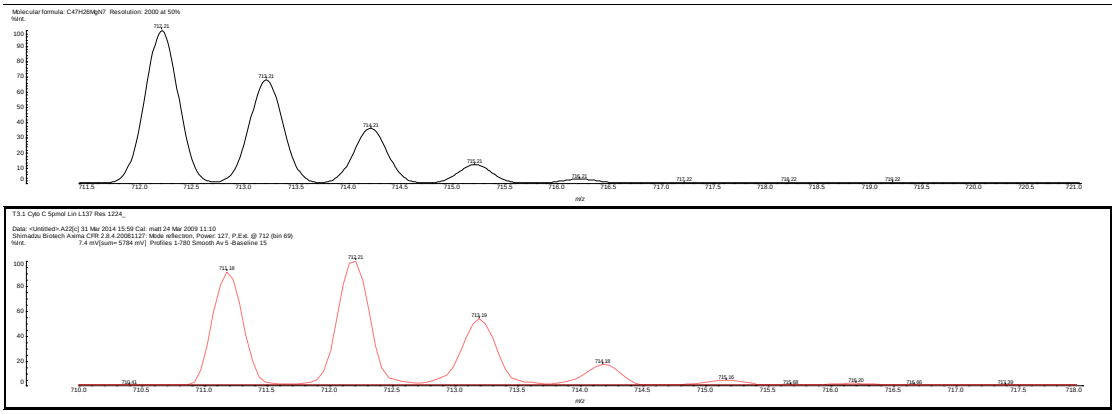


3.8.2.2 [20-{3-(phenylethynyl-phenyl)}-tetrabenzo[*b,g,q,l*][5,10,15]triaza porphyrinato] magnesium (198)

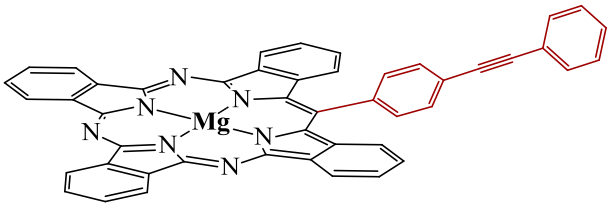


Prepared following the procedure described above, a mixture of 3-bromophenyl TBTAP **189** (80.0 mg, 0.12 mmol, 1.00 equiv), BINAP (4.33 mg, 6.95 µmol, 0.06 equiv) and $PdCl_2(MeCN)_2$ (2.10 mg, 8.10 µmol, 0.07 equiv) was sealed in a microwave vessel. A solution of phenylacetylene (18.92 mg, 0.185 mmol, 1.6 equiv) and DBU (44.10 mg, 0.289 mmol, 2.5 equiv) in dry DMF (1.0 mL) was added, stirred and then irradiated in a microwave reactor at 120 °C for 1 h. Purification by chromatography on silica gel using DCM → DCM/Et_3N (20:1) → DCM/Et_3N/THF (10:1:2) → DCM/THF (1:1) obtained the oily green material which recrystallised from acetone/EtOH (1:1) gave the *title compound* as green crystals with a purple reflex (11.6 mg, 25%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 670 (1.62×10^4), 647 (8.84×10^3), 593 (1.83×10^3), 443 (9.15×10^2), 393 (4.88×10^3). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.61 (d, *J* = 7.5 Hz, 2H), 9.52 – 9.50 (m, 4H), 8.37 (s, 1H), 8.24 (d, *J* = 8.0 Hz, 1H), 8.22 – 8.15 (m, 5H), 8.01 (t, *J* = 7.7 Hz, 1H), 7.93 (t, *J* = 7.1 Hz, 2H), 7.63 (t, *J* = 7.0 Hz, 2H), 7.54 (dd, *J* = 7.2, 2.3 Hz, 2H), 7.36 – 7.29 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 148.51, 147.76, 147.29, 146.20, 144.85, 144.42, 143.19, 141.77, 141.58, 141.30,

141.19, 140.97, 140.96, 140.94, 140.44, 140.23, 139.67, 137.98, 137.95, 137.22, 133.30, 133.06, 132.55, 130.22, 130.15, 130.07, 129.85, 129.48, 129.43, 129.40, 128.36, 128.26, 127.93, 127.43, 126.90, 125.70, 125.53, 125.42, 124.24, 123.91, 123.76, 123.67, 123.65. MS (MALDI-TOF) *m/z* 712 $[M]^+$ (100%) (isotopic pattern matches theoretical prediction).

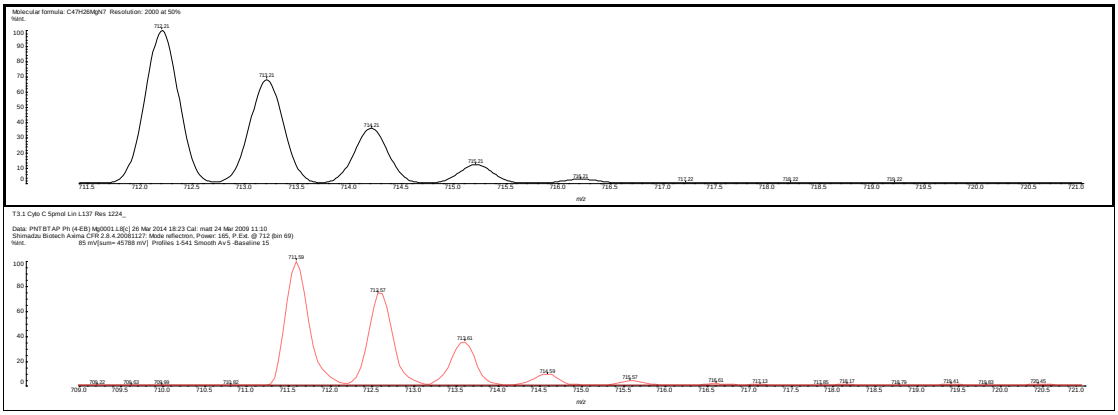


3.8.2.3 [20-{4-(phenylethynyl-phenyl)}-tetrabenzo[*b,g,q,l*][5,10,15]triaza porphyrinato] magnesium (199)



Prepared following the procedure described above, a mixture of 4-bromophenyl TBTAP **190** (45.50 mg, 0.066 mmol, 1.00 equiv), BINAP (2.46 mg, 3.95 µmol, 0.06 equiv) and $PdCl_2(MeCN)_2$ (1.19 mg, 4.61 µmol, 0.07 equiv) was sealed in a microwave vessel. A solution of phenylacetylene (10.75 mg, 0.105 mmol, 1.6 equiv) and DBU (25.04 mg, 0.165 mmol, 2.5 equiv) in dry DMF (1.0 mL) was added, stirred and then irradiated in a microwave reactor at 120 °C for 1 h. Purification by chromatography on silica gel using DCM → DCM/Et_3N (20:1) → DCM/Et_3N/THF (10:1:2) → DCM/THF (1:1) gave the oily green material which recrystallised from acetone/EtOH (1:1) obtained the *title compound* as green crystals with a purple reflex (18.9 mg, 23%); mp > 300 °C; UV-Vis (THF) λ_{max}/nm (ε) 669 (3.42×10^3), 646 (1.71×10^3), 592 (2.14×10^2), 444 (1.06×10^2), 394 (8.33×10^2). ^{1}H NMR (500 MHz, THF-d_8, 298 K): δ (ppm) = 9.61 (d, *J* = 7.5 Hz, 2H), 9.52 – 9.50 (m, 4H), 8.23 – 8.17

(m, 6H), 8.15 (d, *J* = 8.2 Hz, 2H), 7.93 (t, *J* = 7.2 Hz, 2H), 7.75 (dd, *J* = 8.0, 1.4 Hz, 2H), 7.65 (t, *J* = 7.5 Hz, 2H), 7.52 – 7.44 (m, 3H), 7.24 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (125.7 MHz, THF-d_8, 298 K): δ (ppm) = 148.51, 147.76, 147.29, 146.20, 144.85, 144.42, 143.19, 141.77, 141.58, 141.30, 141.19, 140.97, 140.96, 140.94, 140.44, 140.23, 139.67, 137.98, 137.95, 137.22, 133.30, 133.06, 132.55, 130.22, 130.15, 130.07, 129.85, 129.48, 129.43, 129.40, 128.36, 128.26, 127.93, 127.43, 126.90, 125.70, 125.53, 125.42, 124.24, 123.91, 123.76, 123.67, 123.65. MS (MALDI-TOF) *m/z* 712 $[M]^+$ (100%) (isotopic pattern matches theoretical prediction).



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