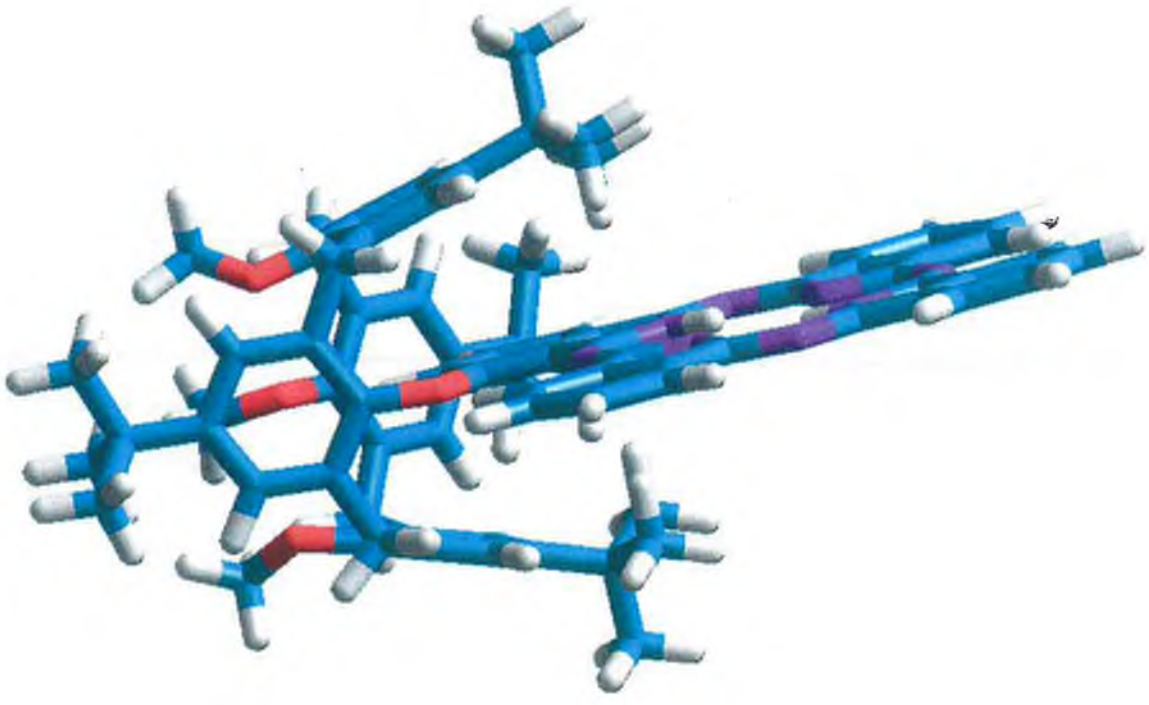
Thesis for the degree of Doctor Of Philosophy

Synthesis of Architecturally Novel Calix[4]arene Phthalocyanines.



By Shane O' Malley B.Sc.

Dublin City University
School of chemical Sciences

DCU

June 2005

Supervised by Kieran Nolan

Authors Declaration

I hereby certify that this material, which I now submit for assessment on the programme of study leading to the award of Doctor of Philosophy by research and thesis, is entirely my own work and has not been taken from work of others, save and to the extent that such work has been cited within the text of my work.

Signed: S e omalley.

Shane O' Malley

Student I.D. No.: 96501651

Date: 10/02/06

ACKNOWLEDGEMENTS

I would first of all like to thank Kieran for allowing me the opportunity to do this research project. I greatly appreciate his immense support, guidance, enthusiasm, advice and friendship over the last number of years. Special thanks must go out to all the chemistry technical staff. Especially Mick and Maurice for there assistance using the instrumentation. I must also thank my fellow postgraduates in SB04.

ABBREVIATIONS

Δ	Heat
CH_2Cl_2	Methylene Chloride
DBN	1,5-Diazabicyclo[4.3.0]non-5-ene
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DIBAL	Di-Isobutyl Aluminum Hydride
DMAE	2-*N,N*-Dimethylaminoethanol
DMF	*N,N*-Dimethylformamide
EtOH	Ethanol
ESI	Electrospray Ionisation
FAB	Fast Atom Bombardment
FD	Field Desorption
FT-IR	Fourier Transform Infrared
HMDS	Hexamethyldisilazane
^{1}H NMR	Hydrogen Nuclear Magnetic Resonance
HPLC	High Performance Liquid Chromatography
IR	Infrared
K_2CO_3	Potassium Carbonate
MALDI	Matrix Assisted Laser Desorption Ionization
MALDI-ToF	Matrix Assisted Laser Desorption Ionization Time of Flight
M	Molarity

MeOH	Methanol
MeI	Methyl Iodide
MM+	Molecular Mechanics
mmol	Milli Moles
MP	Melting Point
NaH	Sodium Hydride
NH_3	Ammonia
NLO	Nonlinear Optics
nm	nanometer
Pc	Phthalocyanine
Pc^{2-}	Phthalocyanine Anion
PcH_2	Metal-Free Phthalocyanine
PDT	Photodynamic Therapy
PPM	Parts Per Million
rpm	Rotations Per Minute
RT	Room Temperature
TFA	Trifluoro Acetic Acid
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
UV-Vis	Ultra Violet

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ABSTRACT :SYNTHESIS OF ARCHITECTURALLY NOVEL CALIX[4]ARENE PHTHALOCYANINES

One of the major problems associated with phthalocyanines is their strong tendency to aggregate in both solution and the solid state. As a consequence, their application as sensors, optical filters and as photosensitisers in polar media can be limited. It is the target of this work to prepare a new series of phthalocyanines which possess an isolated core, by isolating the core aggregation between phthalocyanine rings will be eliminated.

The strategy employed involved the preparation of a 3 and 4 calix[4]arene substituted phthalonitrile. This was achieved in three steps and interestingly we were able to prepare a partial cone derivative for the 3-calix[4]arene phthalonitrile where the phthalonitrile is within the upper rim of the calix[4]arene. Such an arrangement places two of the t-butyl groups of the calix[4]arene above and below the phthalonitrile ring. Furthermore, this conformation was found to be stable at temperatures in excess of 120°C. On the other-hand the 4-calix[4]arene phthalonitrile gave both a partial cone and cone conformation.

We found that the 4-calix[4]arene phthalonitrile could be readily self-condensed to the tertacalix[4]arenephthalocyanine in good yields, on the other hand the 3-calix[4]arene phthalonitrile only yielded traces of the phthalocyanine on self-condensation, and this is due to steric congestion. The 3-calix[4]arene phthalonitrile was then cross-condensed with phthalonitrile to give the unsymmetrical monocalix[4]arenephthalocyanine, with the phthalocyanine perched into the upper rim of the calix[4]arene.

All calix[4]arene phthalocyanines were studied for aggregational behaviour in both polar solution and the solid state. It was found that the tetracalix[4]arene phthalocyanine does not show any aggregation either in the solid state or solution. The unsymmetrical'perched' phthalocyanine does not aggregate in polar solution but forms dimers in the solid state.

Also reported within the thesis are the synthesis of a series of new novel calix[4]arene bridged binuclear phthalocyanines. Their synthesis and properties are discussed.

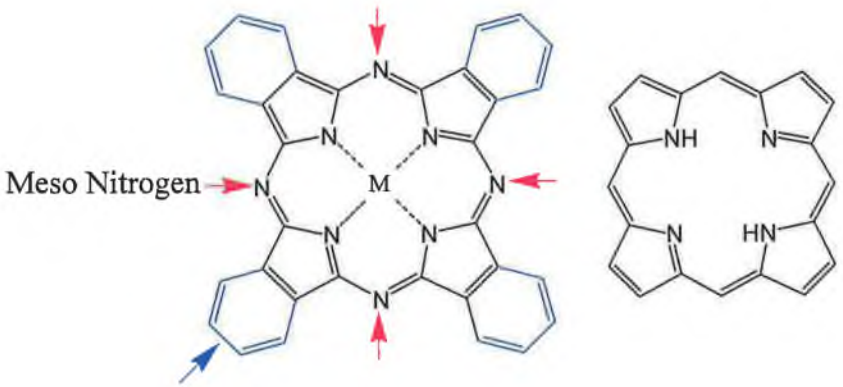
1. Synthesis and Characterization of Phthalocyanines

Literature Review

1.1 Introduction

Braun and Tcherniac first discovered phthalocyanines as a coloured impurity in the attempted conversion of phthalimides to ortho-cyanobenzamide in 1907[1]. In the 1930's Reginald P. Linstead, a lecturer at Imperial College London, developed most of the synthetic strategies that are still used today for the synthesis of these macrocycles[1]. A combination of techniques (elemental analysis, ebullioscopic molecular mass and oxidative degradation) was used by Linstead to deduce the planar structure of phthalocyanines. However, definitive proof came in the late 1920's when Robertson elucidated the structure by X-ray diffraction[1].

Phthalocyanines, like their closely related porphyrins, are both part of the tetra-pyrrolic family; the main structural variations between these compounds can be seen in Figure 1. Phthalocyanines unlike porphyrins contain nitrogen in all *meso*-positions and they also contain an extended π conjugation as a result of the peripheral benzene units.



(1) M = H_2
(2) M = Cu
(3)

Figure 1: *General structure of metal-free phthalocyanine* **(1)**, *copper phthalocyanine* **(2)** *and porphine* **(3)**

Huckel's theory of aromaticity predicts that both macrocycles show aromatic behaviour since they both contain a planar conjugated 18 π electron array. Porphyrins, unlike phthalocyanines, exist in nature and play a significant role in the cycle of life. Heme is involved in the cellular transport of oxygen in the respiratory system of humans and animals, while chlorophyll plays a vital role in converting light into energy in plant cells. Porphyrins are used extensively in nature because of their characteristic chemical, physical and spectral properties in conjunction with their structural diversity. These properties also allow for their use in a wide range of potential applications. Phthalocyanines are sometimes referred to as

the "unsophisticated relative"[2]. However, the simple structural differences mentioned above lead to a change in their properties, for instance they possess improved stability, enhanced spectroscopic features and synthetic flexibility, which allow phthalocyanines to be more versatile than porphyrins in certain applications.

The unintentional discovery of phthalocyanines probably symbolised the most important chromophoric system developed in the 20th century. This chromophoric system has been used in a wide variety of applications. Phthalocyanine's intense blue/green colour makes them perfect for use as industrial colorants. They have been used in this way since the late 1930s because of their colouring properties and their immense stability towards light, weathering and insolubility in a wide variety of solvents. Metalated phthalocyanines, for example copper phthalocyanine **(2)**, tend to be used because they give a more defined shade. Copper phthalocyanine **(2)** is the most widely used in the colorant industry to date[3].

Their use as potential catalysts has also been extensively investigated and they are the only tetra-pyrolic system used industrially for this specific reason. In the last number of years phthalocyanines have also been used in a number of high-tech industrial applications such as ink jet printing[4] and photocopying devices[5]. Phthalocyanines are now finding application as chemical sensors[6], liquid crystals[7], Langmir-Blodgett films[7], nonlinear optics (NLO)[8], optical data storage[9] and medical therapies (for example photosensitizers in photodynamic therapy)[10]. The ability of phthalocyanines to be applied in an extensive range of fields is largely due to their extraordinary stability, aromaticity, electronic spectra and synthetic flexibility.

1.2 Phthalocyanine Synthesis

Since their discovery in the early 20th century, phthalocyanines have been synthesised from a range of precursors using various methods. This has lead to the synthesis of many diversely substituted phthalocyanines and also several phthalocyanine analogs. Over the years phthalocyanine synthesis has been reviewed in a number of different monographic publications, one of the first was by Moser and Thomas[11]. In 1989 a handbook on the synthesis, properties, and applications of phthalocyanines appeared in the literature[12]. More recently McKeown[1] revisited this subject and in 2002 The Porphyrin Handbook Volume 15 was published[13].

1.2.1 Phthalocyanine Precursors

There are numerous precursors used for the synthesis of phthalocyanines. The principal starting materials are the aromatic *ortho*-dicarboxylic acid derivatives; phthalic acid **(4)**, phthalic anhydride **(5)**, phthalimides **(6)**, *o*-cyanobenzene **(7)**, phthalonitrile **(8)**, and diiminoisoindolines **(9)** (Figure 2). All of these precursors have a distinguishing feature; *ortho*-substituted carboxylic acids or related functionalities are a key requirement.

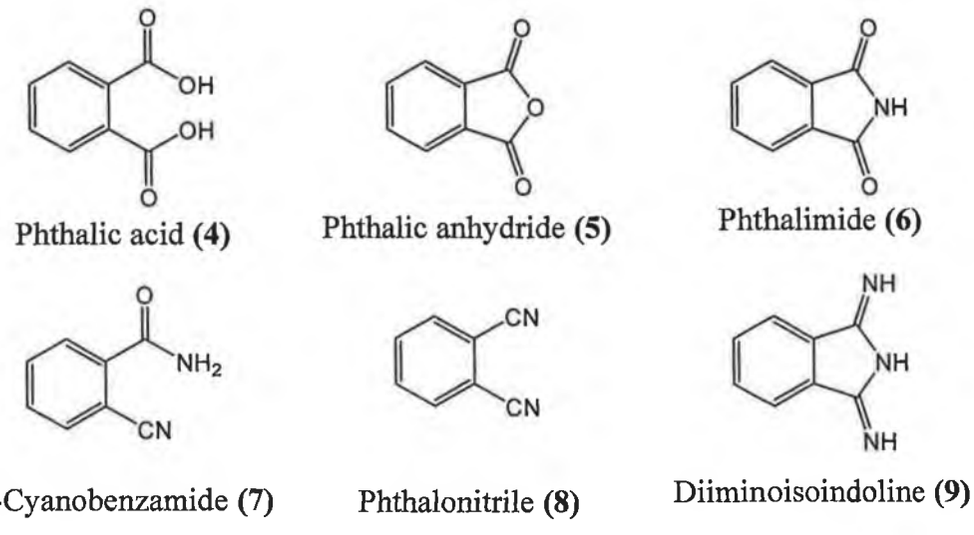


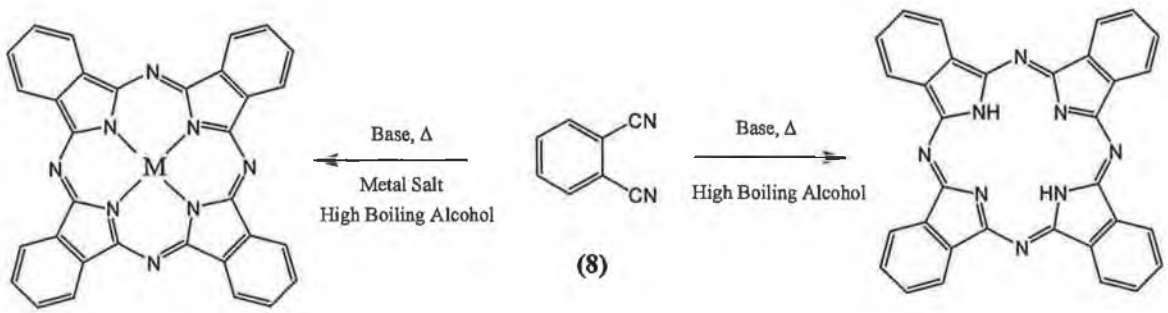
Figure 2: *Phthalocyanine precursors*

Certain *ortho*-halogenated benzene ring structures can also be used as starting materials. *o*-halobenzonitrile and *o*-dihalobenzenes can be heated with cuprous cyanide to form phthalonitrile (Rosenmund-von Braun reaction), which then condenses to form phthalocyanine. It should be noted that most of these starting materials are interlinked and

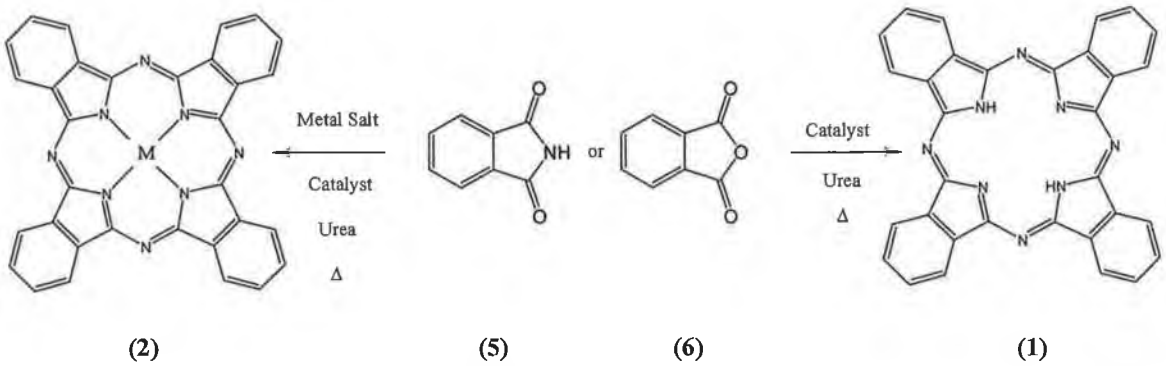
one precursor can be an intermediate for another in the condensation process. However substitution of the benzene ring on all the phthalocyanine precursors is quite easy and leads to a wide diverse range of phthalocyanines[14].

1.2.2 Phthalocyanine Condensation

There are numerous ways to prepare phthalocyanines in either its metal-free or metallated form. Typically, phthalonitrile **(8)** is heated in a appropriate high boiling solvent in the presence of base or metal depending on whether metal-free or metallated phthalocyanine is required see Scheme 1. Alternatively, phthalocyanines can be prepared from either phthalic anhydride or phthalimide in the presence of a nitrogen source (urea) or a catalyst (ammonium molybdate) see Scheme 2. These precursors however give more unpredictable results and impurities are more prevalent. The use of high temperatures, catalyst and a nitrogen source also limits the type of functionalities, which can be placed in the precursors. Despite these drawbacks phthalic anhydride is widely used in the industrial synthesis of phthalocyanines simply because it is cheap[14].



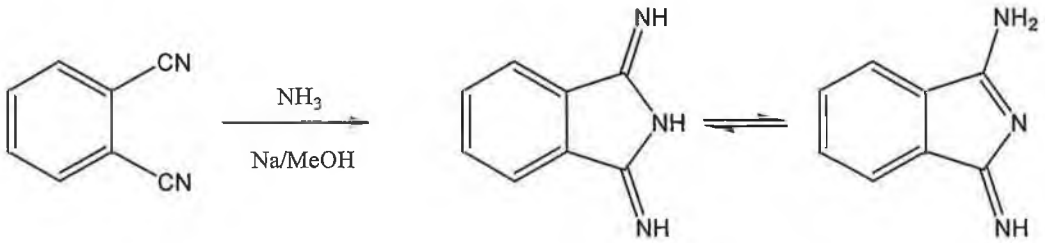
Scheme 1: *Metal-free and metallated phthalocyanine from phthalonitrile* **(8)** *and base*[14].



(2) (5) (6) (1)

Scheme 2: *Metal-free and metallated phthalocyanine from phthalimids* **(8)** *or phthalic anhydride using a catalyst, a urea nitrogen source and high temperatures*[14].

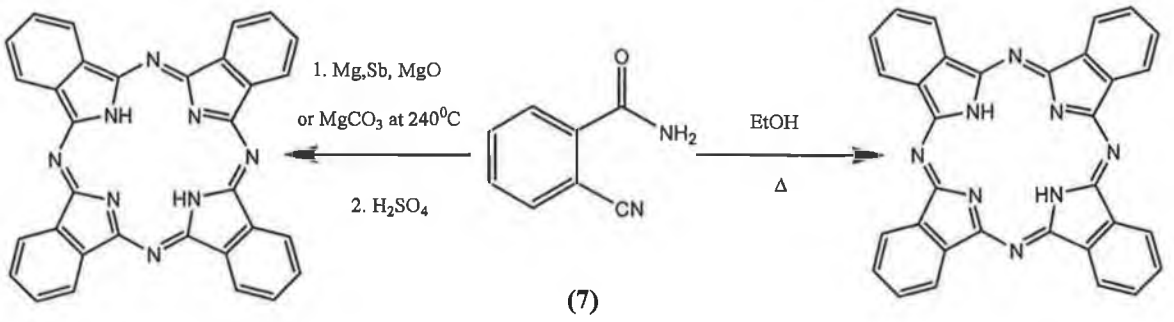
Over 70 metals have been placed in the central core of the phthalocyanine and this is achieved by carrying out the condensation in the presence of a metal salt. Alternatively, metallated phthalocyanines can be prepared from metal-free phthalocyanine, but this is a less common approach because it can be difficult to force the reaction to completion. Metal-free phthalocyanines can be prepared by different methods one such method uses 1,3-diiminoisoindoline **(9)**, which is simply synthesised by bubbling ammonia through a solution of phthalonitrile **(8)** (Scheme 3). The 1,3-diiminoisoindoline can then be condensed to PcH_2 by heating to reflux in dimethylaminoethanol[2].



(8) **(9)**

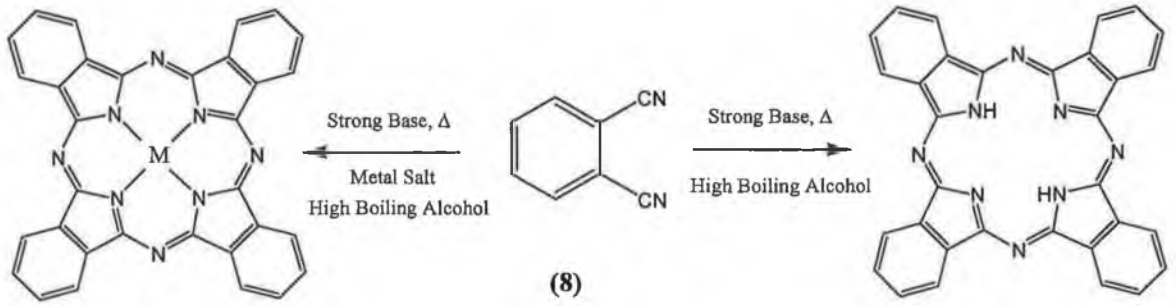
Scheme 3: *Synthesis of 1,3-diiminoisoindoline* **(9)** *from phthalonitrile* **(8)**[3].

The first ever metal-free phthalocyanine **(1)** was synthesised by heating *o*-cyanobenzene **(7)** in refluxing ethanol but PcH_2 was obtained in low yields[15]. When this starting material was condensed under the same conditions in the presence of Mg^{2+} (a labile metal) the yields where increased to ~ 40%[16] (Scheme 4). The magnesium could then be removed from the phthalocyanine by treatment with acid.



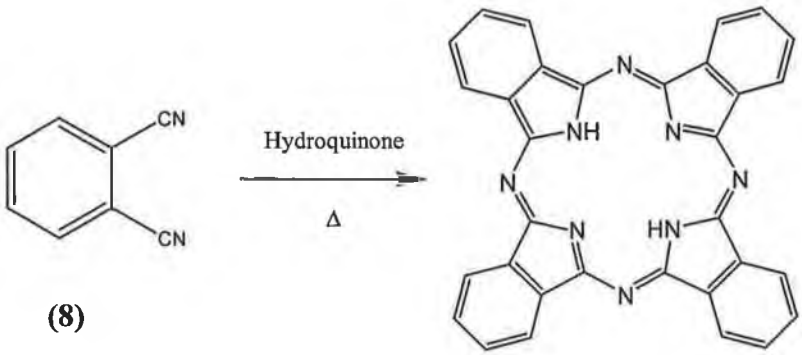
Scheme 4: *Two methods for the synthesis of metal-free phthalocyanine from o-cyanobenzamide*(**7**)[17].

Metal-free phthalocyanine **(1)** can also be synthesised by heating **(8)** in the presence of a base and solvent (Scheme 1). When **(8)** is heated in the presence of gaseous ammonia (base) and 2-*N,N*-dimethylaminoethanol (DMAE) (basic solvent), **(1)** is synthesised in a 90 % yield[18]. The use of gaseous ammonia as a base leads to the formation of a 1,3-diiminoisoindoline **(9)** intermediate. Further heating of **(9)** in DMAE leads also to the formation of the desired phthalocyanine product. Strong organic bases[19,20] such as DBU and DBN have also been used with phthalonitriles in alcohol to form metal free phthalocyanines. Metallated phthalocyanines can also be synthesised with the addition of a metal salt under the above conditions (Scheme 5).



Scheme 5: *Metal-free and metallated phthalocyanine from* **(8)** *using a strong Base.*

Phthalonitriles can also be used in conjunction with a suitable organic reducing agent to form a metal-free phthalocyanine (Scheme 6)[17]. Organic reducing agents such as hydroquinone and 1,2,3,6-tetrahydropyridine[21] are used. There are also many examples of substituted phthalocyanines, which have been synthesised in this way. Diiminoisoindoline **(9)** when heated in the presence of a hydrogen donor can also form metal-free phthalocyanine **(1)**. Some hydrogen donors that may be used are succinonitrile or tetralin.[18]

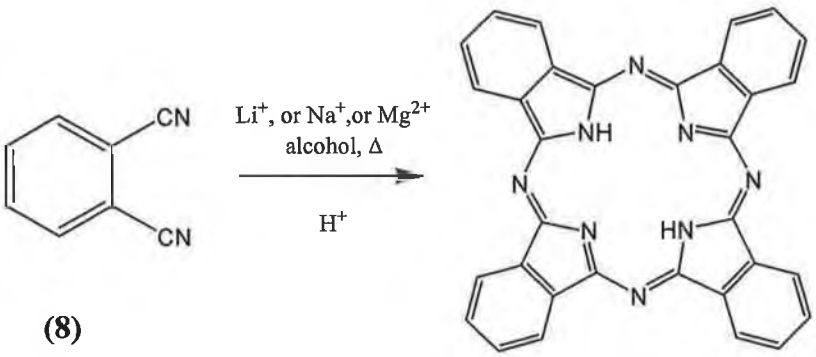


(8)

Scheme 6: *Synthesis of metal-free phthalocyanine from phthalonitrile and an organic reducing agent such as hydroquinone*[17].

Perhaps the most commonly used route for the preparation of PcH_2 uses a metal-templated cyclotetramerization, however the metal used can be removed to form the metal free phthalocyanine by simple addition of an acid (Scheme 7). The use of this method is limited to metal ions such as Li^+, Na^+, K^+, Mg^{2+}, Be^{2+}, Ag^{2+}, Cd^{2+}, Hg^{2+}, Pb^{2+}, and Sb^{2+}. Linstead devised a method that employs the use of Li^+, Na^+ and Mg^{2+} in pentan-1-ol to form an alkoxide and the subsequent addition of phthalonitrile and heat[2]. When the reaction was completed the metal was removed either by an acidic or aqueous workup.

If a look is taken at all the methods above they have one thing in common, high temperatures and harsh conditions. These kinds of conditions are not suitable for phthalonitriles containing sensitive substitutents so attempts have been made over the years to reduce temperatures for phthalocyanine synthesis. This reduction in temperature should also increase yields and reduce impurities. Leznoff *et al.* showed that the use of octan-1-olate in octan-1-ol could be used to prepare a variety of phthalocyanines at RT after several days, while its counter part pentan-1-olate in pentanol failed to do so[22]. Improvement in yields and purity of reaction mixtures can be achieved by the use of milder base such as hexamethyldisilazane (HMDS)[23]. Nevertheless the old methods seem to prevail as they are cheap and speedily accomplished.



(8)

Scheme 7: *Metal-free phthalocyanine by acidified removal of a labile metal ion*[2].

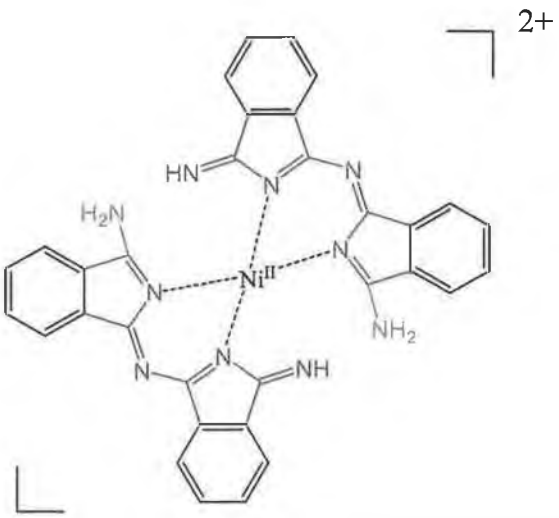
1.2.3 General Mechanism For Phthalocyanine Formation

A century of synthetic work has been carried out on phthalocyanines; however, there are very few papers dealing with the mechanism of phthalocyanine formation. This area is fraught with problems because the condensation process is highly exothermic and takes place under harsh conditions. Therefore conventional methods cannot be used to clarify the mechanism. Another problem is that phthalocyanines can be made from a range of starting materials via many different reaction pathways, even though these pathways have common intermediates, it does not mean that they form through a common mechanism. Intermediates have mainly been isolated from reactions that involve alcohols as the solvent. This section pays particular attention to the proposed mechanism (Scheme 8)[2] for Linstead's method, which uses phthalonitrile, pentanol and a labile metal such as lithium; however, other starting materials are mentioned to back up some of the mechanistic information.

A Russian scientist Borodkin[24] provided the first part of the condensation puzzle; he isolated the protonated iminoisoindoline anions **(10)** and **(11)**. The former is thought to be formed in methanol/ethanol while **(11)** is mainly formed in longer chain alcohols[25]. The second part of the puzzle involved the isolation of a half Pc intermediate **(12)**. This was not isolated starting from phthalonitrile, instead a reaction with lithium methoxide and 4-nitrophthalonitrile gave the desired intermediate **(13)**[26]. This dimer intermediate **(14)** was prepared under similar conditions to those used in Pc condensation [27] (Figure 3). This compound readily forms Pc when heated in refluxing 1-butanol and 1-pentanol.

From here the condensation mechanism may go in two directions; the first is that two dimers condense to form a Pc, this is thought to happen when a metal with a 2+ charge chelates two

dimers **(15)**; the second is that a trimeric species may be formed **(16)** which goes on to form a tetrameric intermediate **(17)** which cyclizes into a Pc. This tends to take place when there is no +2 metal present or in the presence of a 1+ metal.



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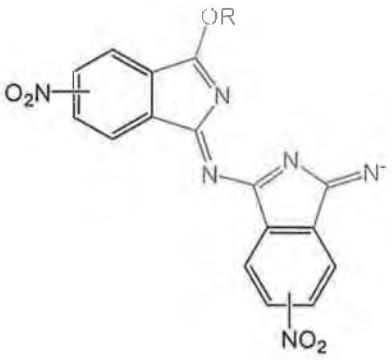
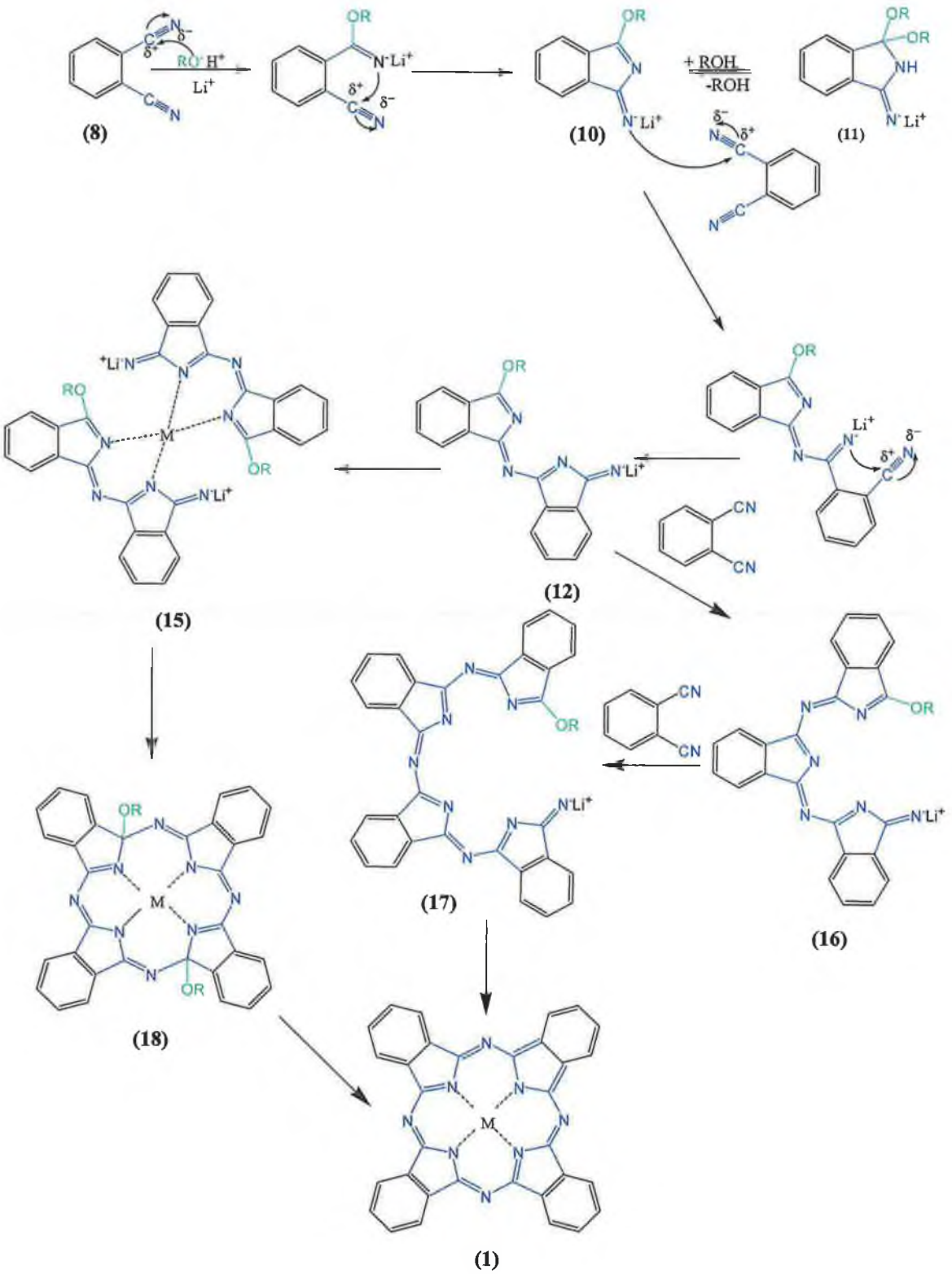


(14)

Figure 3: *Intermediates found in certain phthalocyanine synthesis*[25-26].

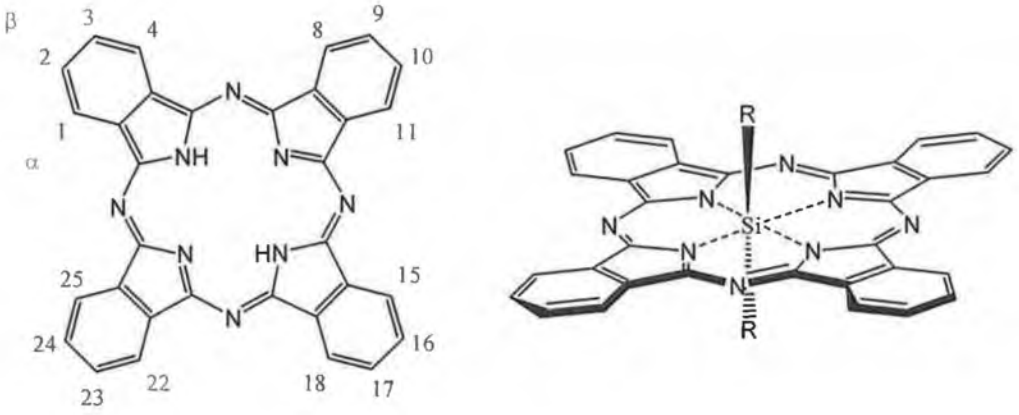
Finally, cyclization occurs with a two-electron reduction of the macrocycle leaving an 18 π electron aromatic system in the final step. This step takes place via **(18)** which has readily been isolated from a solvothermal synthesis in methanol. A single crystal XRD study was used to characterise this intermediate[28]. Aromatisation of **(2)** happens by the loss of an aldehyde, after oxidation of the alkoxide (Scheme 8). This oxidation step generates H^+ that is mopped up by another mole of lithium alkoxide. Therefore two moles of alkoxide are required per one mole of Pc made under these conditions. As can be seen above there is a huge amount of evidence for this type of proposed mechanism, yet definitive studies remain to be accomplished.



Scheme 8: *A proposed mechanism for phthalocyanine formation*[2].

1.3 Substituted Phthalocyanines

The introduction of substitutents into the phthalocyanine macrocycle can significantly influence its electronic, chemical and physical properties. It is well known that one of the main disadvantages of unsubstituted Pcs is their insolubility. The aromatic core of this macrocycle is very hydrophobic and their planarity allows them to stack (aggregate), which prevents them from solublizing[14]. This aggregation is reduced by the introduction of substituents and leads to Pcs that are more soluble. Substituents can also effect the position of the Q band in the UV-Vis spectrum of Pcs, this will be dealt with in the UV section. This means that phthalocyanines can be fine tuned for particular applications by the introduction of an appropriate functional group. Pcs can be substituted in two regions. The first is on the peripheral benzo sub-units of the Pc ring, while the second is known as axial substitution, this occurs at the metal centre of the Pc ring and can only occur with certain metals (Figure 4).



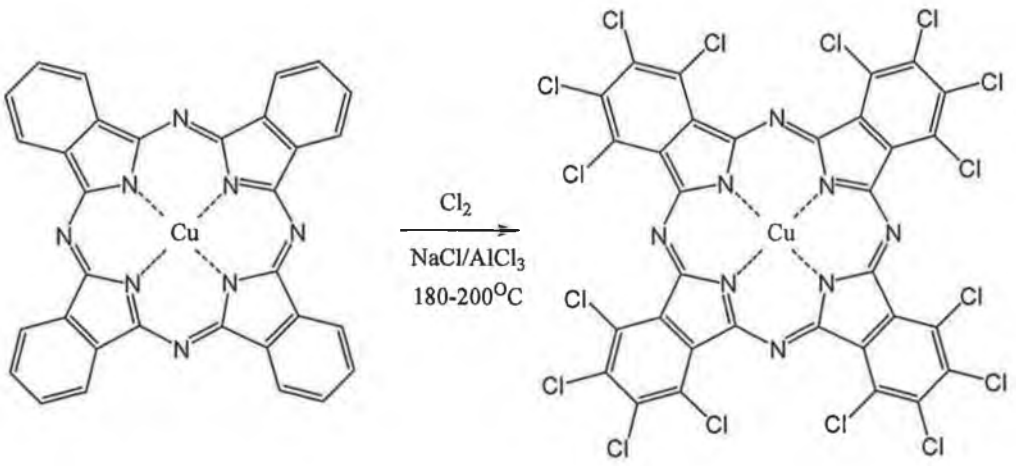
(a) **(b)**

Figure 4: *All the possible substitution positions on a phthalocyanine ring* ***(a)*** *positions in which peripheral substitution can take place and* ***(b)*** *where axial substitution can take place.*

1.3.1 Benzo-Substitution of the Phthalocyanine ring

There are two key types of peripheral substitution methods used, the first is mainly used in the colourant industry and it involves direct substitution on to the phthalocyanine ring. An example is chlorination of a copper phthalocyanine **(2)** using heat, chlorine gas, aluminium and sodium chloride in a melt (Scheme 9). The problems encountered with this reaction are, 1) complicated isomeric mixtures, and 2) varying degrees of substitution (Figure 4 **(a)**).

Isolation and purification of these mixtures would be extremely difficult. This conversely does not affect its use in the colourant industry because purity is not a priority.



(2) **(19)**

Scheme 9: *Chlorination of a copper phthalocyanine*[3].

High tech industries on the other hand do depend on knowing the specific structure of the phthalocyanine. This can be achieved by using a method, involving the condensation of a substituted precursor. The advantages of this method are; 1) a specific structure $PcR_{4x}M$ (where x = number of substitutents contained on the phthalonitrile precursor) is obtained only and 2) purification is made much simpler by the elimination of varying degrees of substitution. Problems encountered in this method are; 1) the required substituted phthalonitrile must be obtainable, 2) substituent must be stable under the conditions used in the preparation of the Pc and 3) formation of positional isomers when the phthalonitrile is unsymmetrically substituted[14].

The first problems mentioned above are simply solved by the use of a number of commercially available substituted phthalonitriles, which contain versatile functional groups that can be modified to form the desired substituted phthalonitrile. Only in the last two decades have these substituted phthalonitriles become available (Figure 5)[14]. These phthalonitriles possess reactive functional groups such as halogens and nitro groups, which can undergo nucleophilic aromatic substitutions, couplings etc.

The harsh Pc condensation conditions influence what substitutents can be introduced into the phthalonitrile starting material, since they may interfere with or decompose during the condensation process. Groups such as hydroxy and esters are good examples. In the last few years Pcs containing hydroxy groups have come under investigation because of their possible use as PDT agents for cancer therapy. A single isomer tetra-hydroxy Pc **(28)** was synthesised from a benzyl protected phthalocyanine **(27)** by a simple cleavage of the benzyl groups using TFA[29]. (Scheme 10).

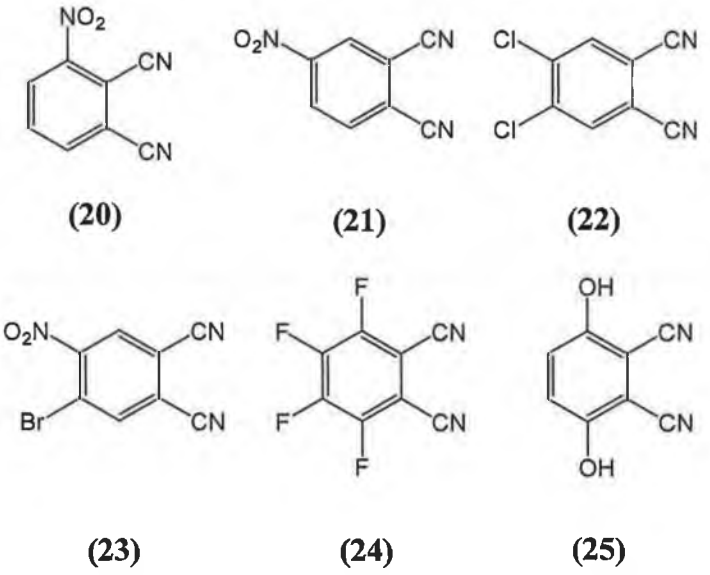
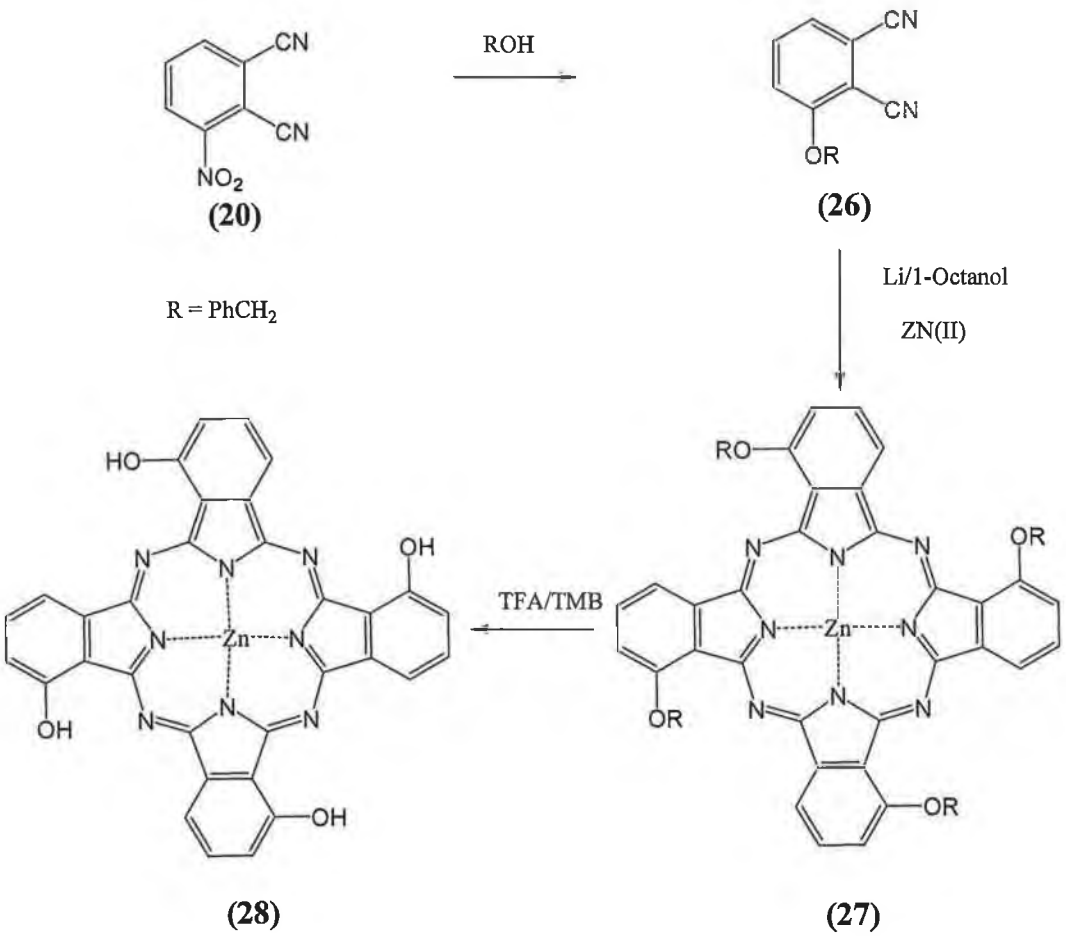


Figure 5: *Some commercially available substituted phthalonitriles*[14].



Scheme 10: *Synthesis of a single isomer tetra-hydroxy Pc in the α-position*[29].

1.3.1.1 Symmetrically Substituted Phthalocyanines

1.3.1.1.1 Symmetrically Substituted Phthalocyanine Containing Positional Isomers

Condensation of unsymmetrically substituted phthalonitriles leads to the formation of positional isomers. Four positional isomers tend to be formed having D_{2h}, C_{4h}, C_{2v} and C_s symmetry. These isomers are generally produced in a 1:1:2:4 ratio respectively. The most common examples are the tetra-substituted Pcs that are substituted either in the α {1(4),8(11),15(18),22(25) tetra-substituted} or β {2(3),9(10),16(17),23(24) tetra-substituted} position (Figure 6)[14]. In the last decade separation of these positional isomers has been achieved by HPLC and MPLC. The first ever separation of all four positional isomers was carried out on a 1(4),8(11),15(18),22(25)-tetrakis[((2-ethylhexyl)oxy)-phthalocyaninato]nickel(II) using a commercially available nitrophenyl column[30]. In later attempts Michael Hanack *et al.* also used specially designed silica HPLC phases to achieve complete separation of all four isomers[31,32].

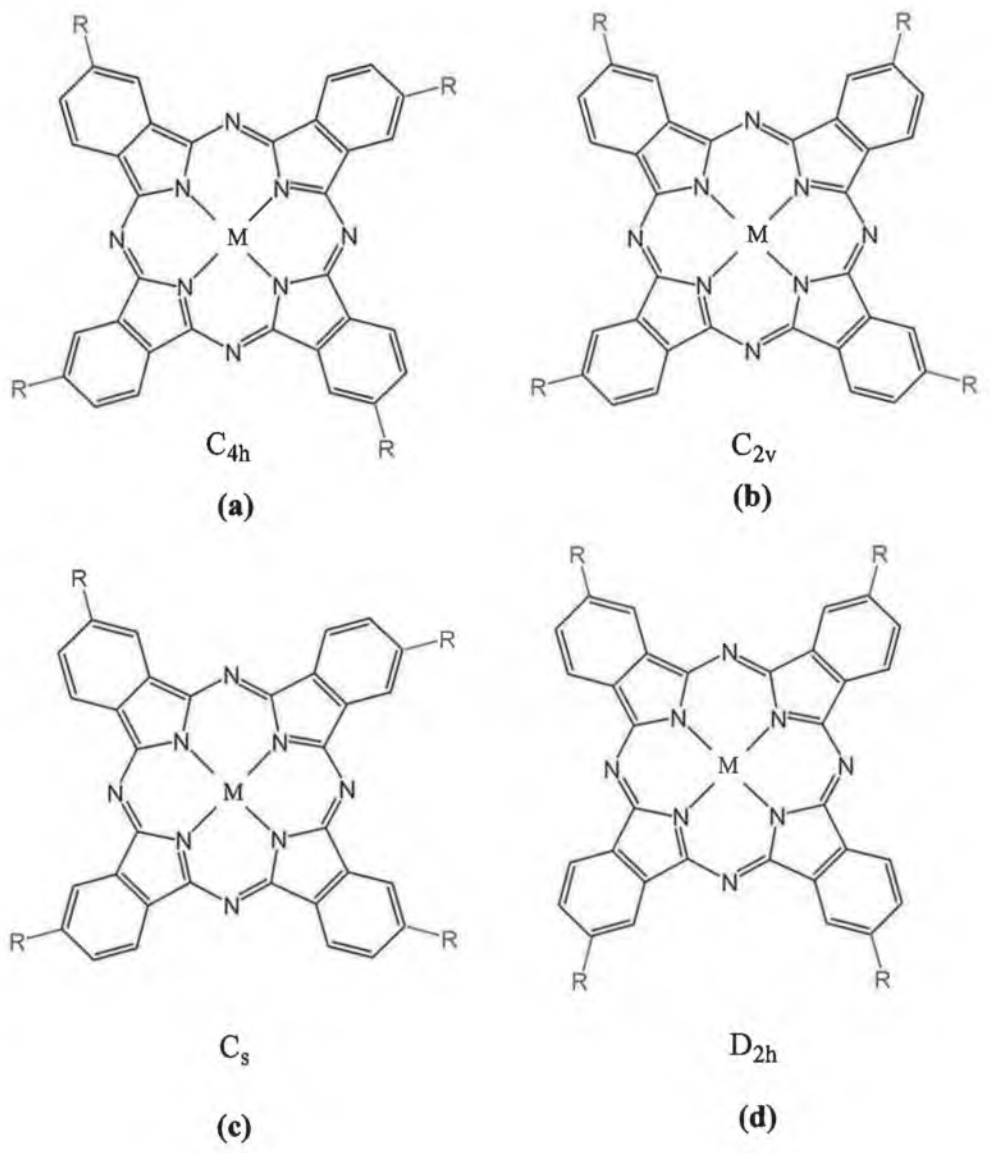


Figure 6: *Four positional isomers*[14].

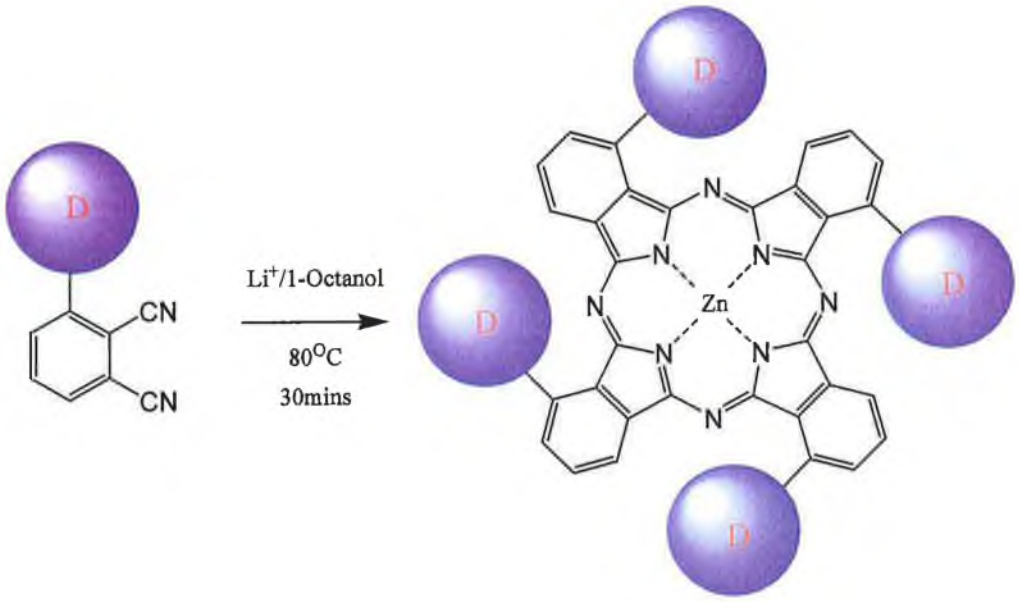
1.3.1.1.2 Symmetrical Substituted Phthalocyanines Containing Single Isomers

Single isomers have been gaining a lot of attention because they can be investigated for interesting NLO affects. There are a wide variety of single isomers, which can be produced. Single isomer systems for tetra substituted Pcs are quite simple to make in the α-poisition by the use of bulky substitutents. An interesting example of this is a α substituted dendritic Pc system shown in (Scheme 11) where the dendritic groups play a vital role in sterically orientating the starting material in a certain way to form only the wheel C_{4h} isomer[33]. Figure 7 shows all the possible orientations of the starting material before condensation and from this it can be deduced that the other conformations D_{2h}, C_{2v} and C_s are too sterically hindered

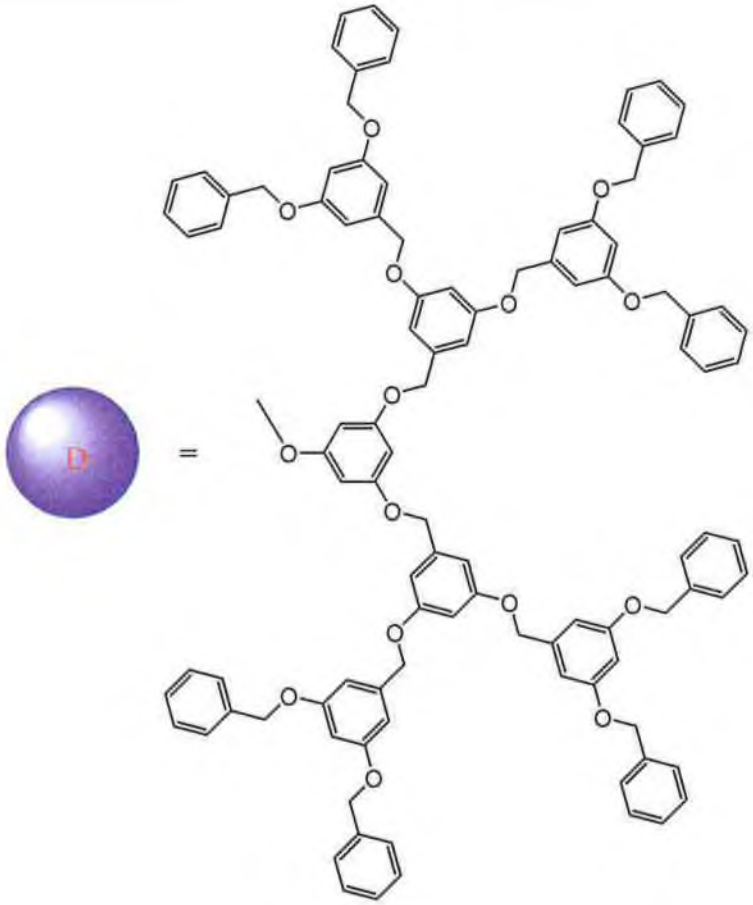
to be formed. However, when the substitutent is placed in the β-position the steric constraint does not effect the condensation and the usual percentage of positional isomers are formed. Gaspard and Maillard[34] however produced a pure isomer of 2,9,17,24-tetra-tert-butylphthalocyanine zinc(II), using metallic zinc as the condensing agent. Leznoff[35] also attempted to make a single isomer in the β position by first treating substituted phthalonitriles with Lawsson's reagent, this treatment allows condensation to occur at low temperatures, however, it does not allow the formation of a single isomer (Scheme 12).

Another unsymmetrically substituted 3,4-bis(3,3-dimethyl-1-butynyl)phthalonitrile **(37)** can be condensed to form a single isomer 1,2,8,9,15,16,22,23-octakis(3,3-dimethyl-1-butynyl)phthalocyanine **(38)** in a 35% yield[36] (Scheme 13).

A novel approach to preparing a D_{2h} isomer is shown in Scheme 14. This approach involves the condensation of an unsymmetrical substituted bisphthalonitrile **(39)** linked by a five atom bridge. The bridge effectively "constrains" the two phthalonitriles on self-condensation, to give the D_{2h} isomer of **(40)** in a yield of up to 20%[37].



(29) **(30)**



Scheme 11: *Single isomer synthesis of a α-positioned dendritic phthalocyanine*[33].

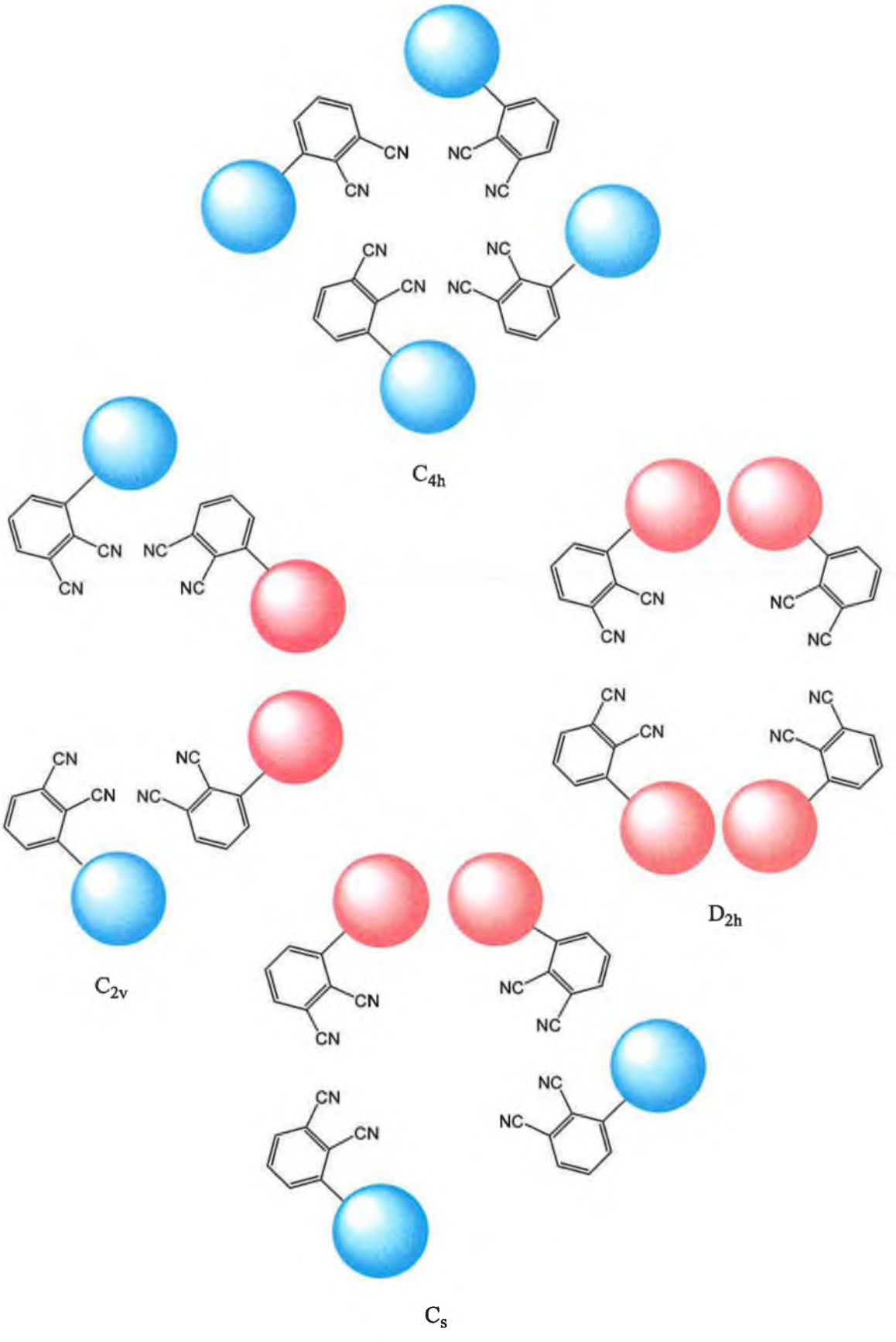
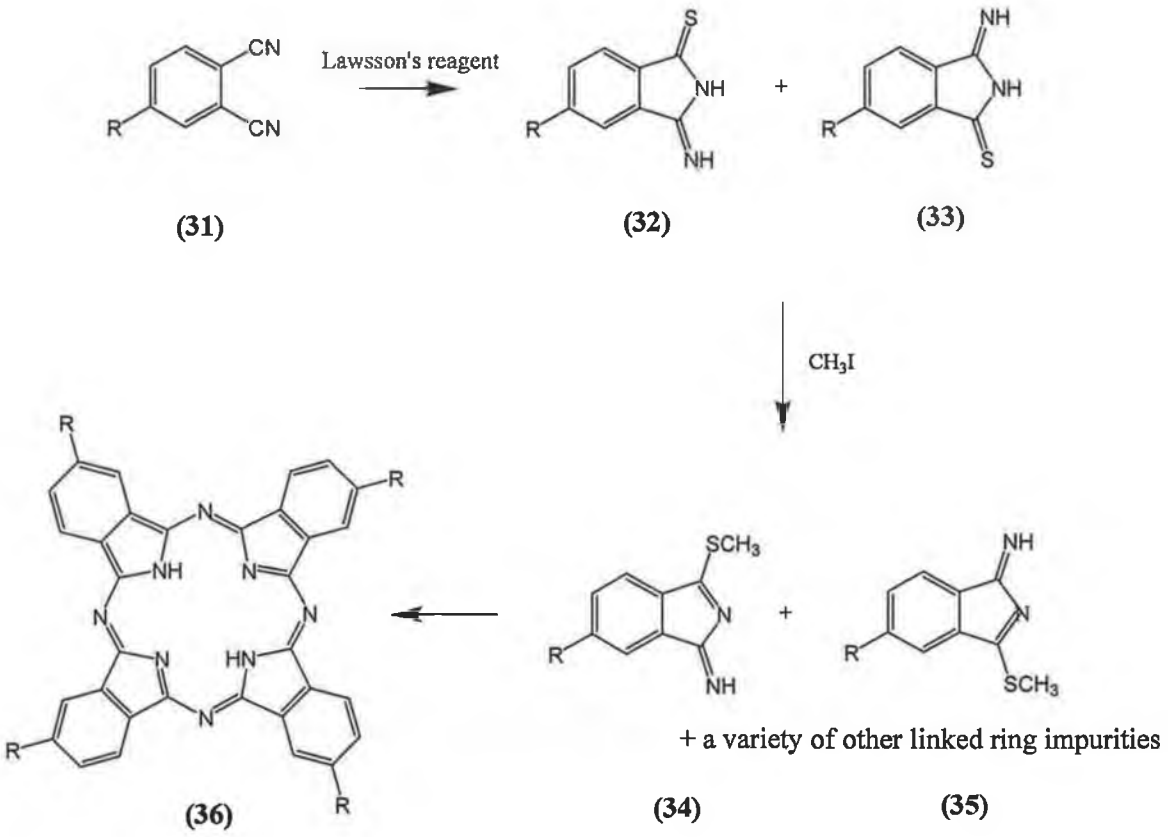


Figure 7: *Possible orientation of the phthalonitrile before condensation showing that the C_{4h} isomer can only be synthesised (red shows unfavourable steric interaction).*

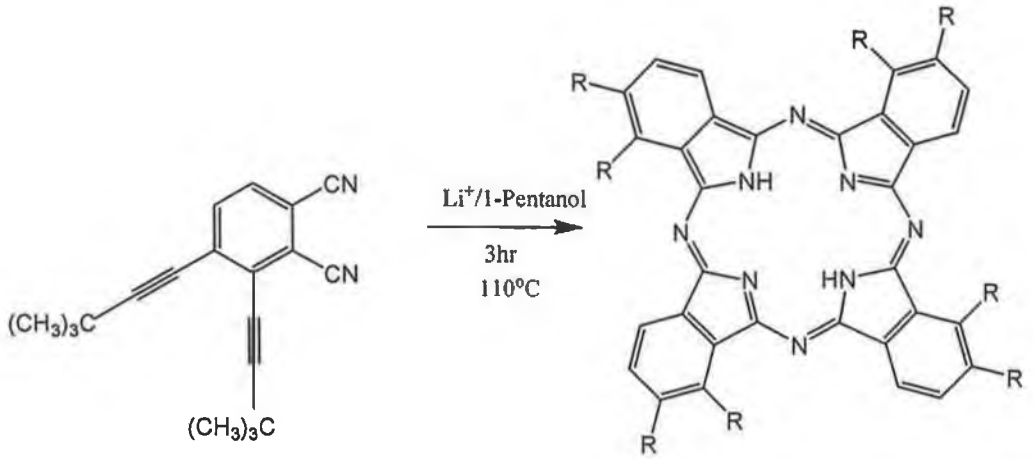


(31) (32) (33)

(36) (34) (35)

Where R = $OCH_2C(CH_3)_3$

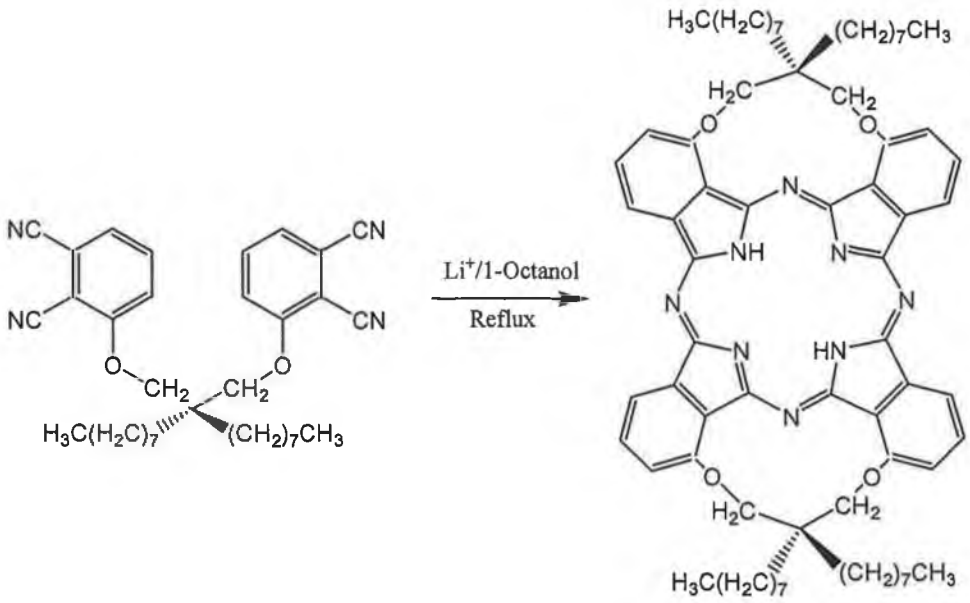
Scheme 12: *Attempted synthesis of a pure single isomer 2,9,16,23-tetrasubstituted phthalocyanine*[35].



where R = $-C\equiv C-C(CH_3)_3$

(37) (38)

Scheme 13: *A synthetic procedure for the synthesis of a single isomer system*[36].

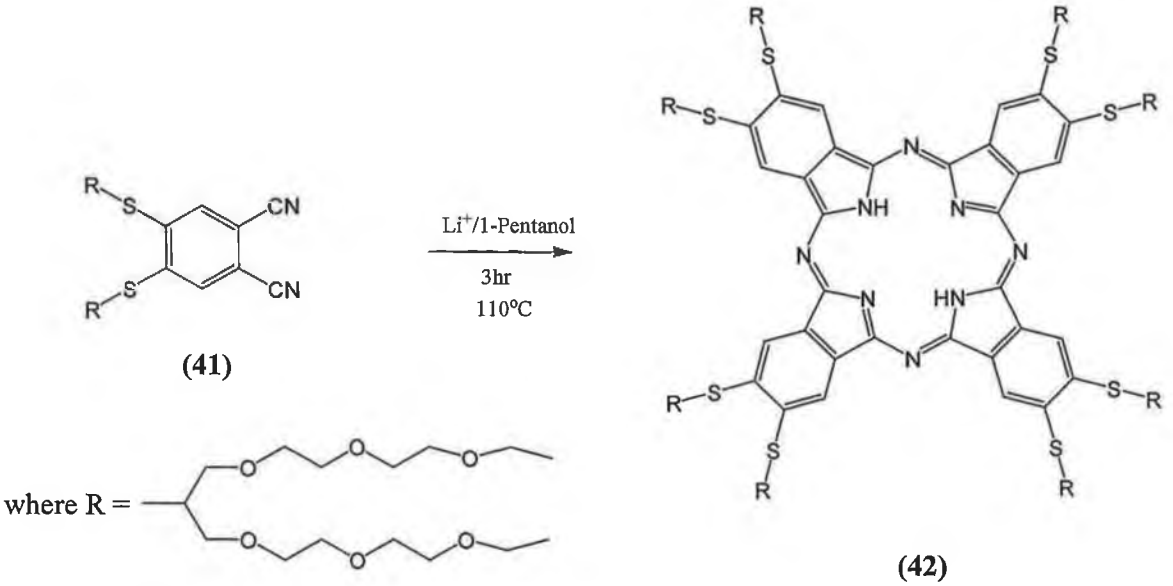


(39) **(40)**

Scheme 14: *A synthetic route for the synthesis of the bridged D_{2h} isomer*[37].

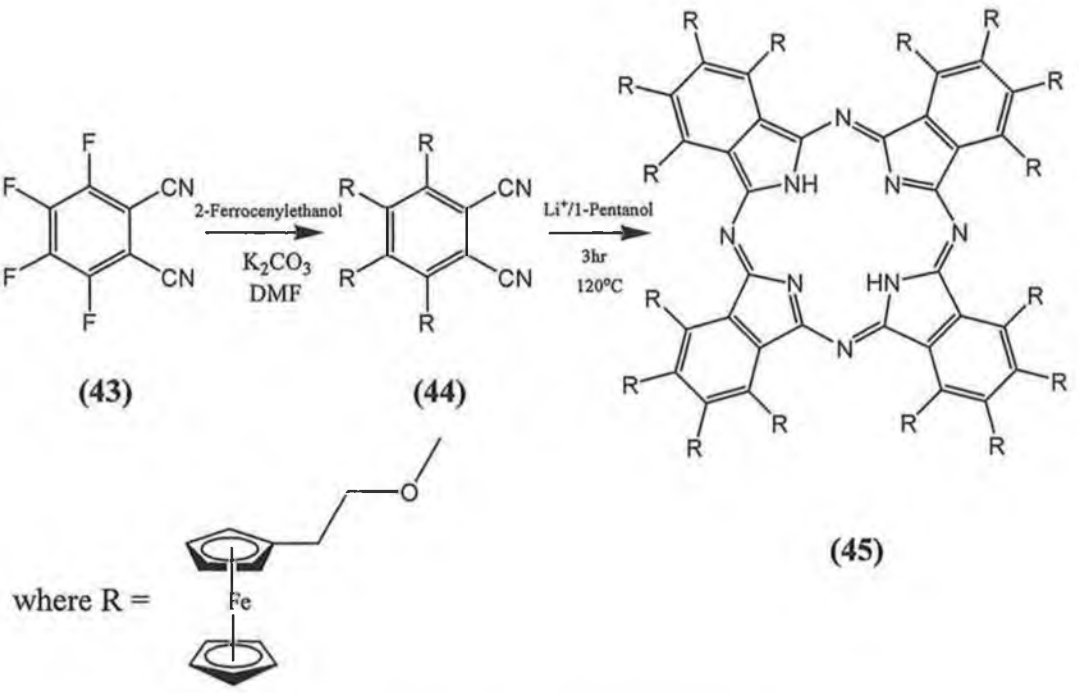
1.3.1.1.3 Symmetrically Substituted Phthalocyanines From Disubstituted Phthalonitriles

Perhaps the simplest method used to prepare single isomer Pcs is through condensing symmetrically substituted phthalonitriles. An octasubstituted single isomer Pc **(42)** [38] can be made from a disubstituted phthalonitrile **(41)** as shown in Scheme 15 or a single isomer hexadecasubstituted Pc **(45)** [39] can be synthesised from a tetra-substituted phthalonitrile **(44)** shown in Scheme 16.



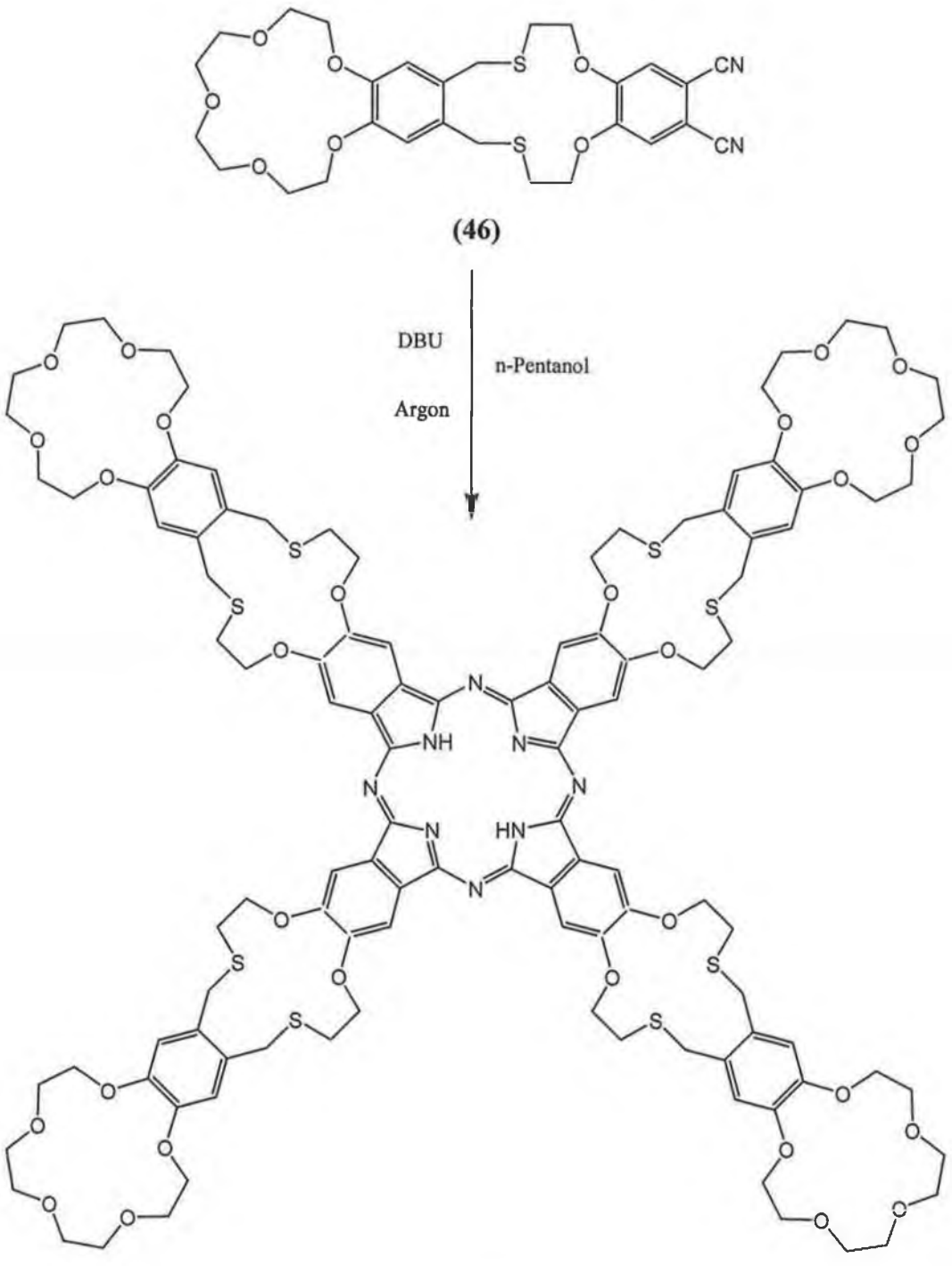
(41) **(42)**

Scheme 15: *Synthesis of an octasubstituted single isomer Pc*[38].



Scheme 16: *Synthesis of a hexadecasubstituted Pc*[39]

Phthalonitriles that are symmetrically substituted in both α-positions condense to form single isomers[40-41]. An interesting example of a bis β substituted Pc is **(47)**. This Pc is prepared from a phthalonitrile conaining a novel dilooped dioxodithia crown ether macrocycle **(46)** seen in Scheme 17 [42].



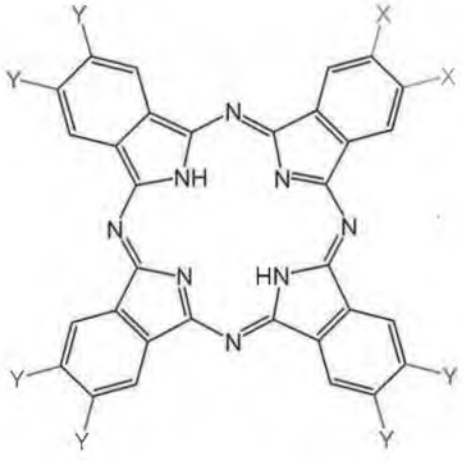
(46)

(47)

Scheme 17: *Synthesis of a symmetrically substituted crown phthalocyanine*[42].

1.3.1.2 Synthesis of Unsymmetrical Substituted Phthalocyanines

The high symmetry of the molecules mentioned in the last section can limit their applications. In this section we deal with phthalocyanines, which contain an unsymmetrical substitution pattern around the phthalocyanine. Unsymmetrical substitution of the Pc ring causes electronic perturbation, which can have a significant effect on the physical and electrochemical properties of the resulting phthalocyanine, and as a result of this, these unsymmetrical substituted Pcs (Figure 8) are useful in a wide variety of applications[43]. For example positioning of electron-donating and electron-withdrawing groups on different parts of the Pc macrocycle causes interesting NLO effects[44]. Some of the most well ordered films produced for Langmuir-Blodgett films[45] use amphiphilic Pcs that contain a combination of hydrophilic and hydrophobic groups. These unsymmetrical substituted Pcs can also show liquid crystal behaviour[46].



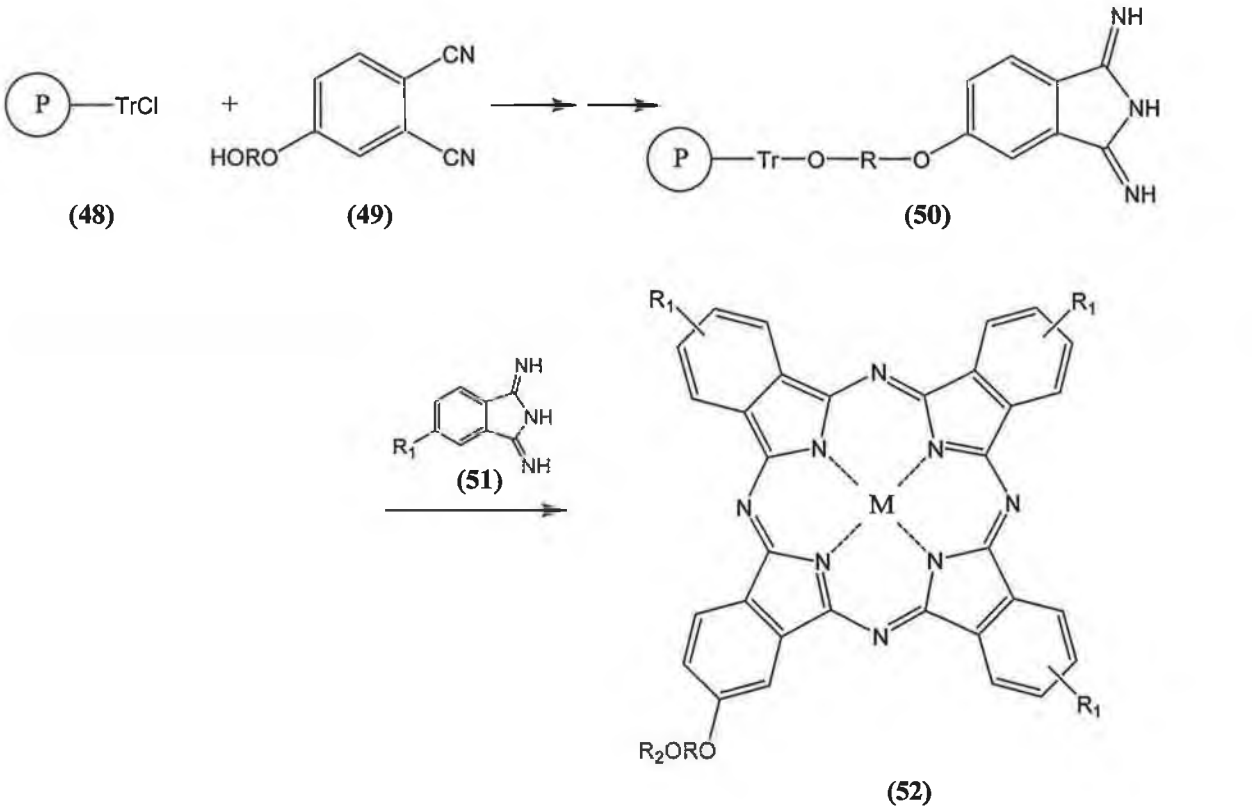
Where X and Y are not equal

Figure 8: *Unsymmetrically substituted phthalocyanine.*

The synthesis of unsymmetrical substituted Pcs is fraught with complications. There are three principle methods, which can be used to prepare unsymmetrical Phthalocyanine. These are polymer support synthesis, ring enlargement of subphthalocyanines and mixed condensation (using varying stoichiometries of two different phthalonitriles). These three methods are outlined below.

1.3.1.2.1 Polymer Support Synthesis

Heterogeneous polymer supported synthesis was one of the first methods employed in the synthesis of pure unsymmetrical substituted A_3B phthalocyanines. Leznoff and co-workers were the innovators in this approach and in Scheme 18 [47] is shown an example of their work. The polymer support used in this example is a tritylated 2% crosslinked divinylbenzene polystyrene **(48)** which is treated with 4-(6-hydroxyhex-1-yloxy)phthalonitrile **(49)** and subsequently converted to the diiminoisoindoline **(50)**.

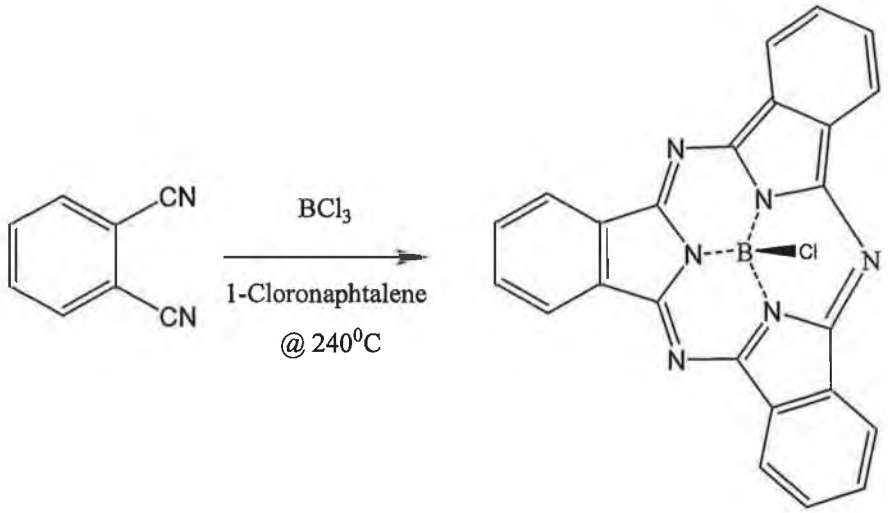


Scheme 18: *A polymer support method towards an unsymmetrical phthalocyanine*[47].

This polymer bound diiminoisoindoline was then cross-condensed with a second soluble diiminoisoindoline which is in large excess to form a polymer bound Pc **(51)**. Purification simply involves washing the polymer to remove the undesired symmetrically substituted $Pc(R_2)_4M$ by product. The desired product **(52)** is obtained by a simple acid cleavage of the Pc from the polymer. Dieter Wöhrle *et al.*[48] have recently used new supports such as modified silica gels. However, the application of the polymer support method is limited by certain factors; 1) polymer loading capacity 2) low yields limit their usefulness in large-scale chemistry and 3) phthalonitriles must contain an appropriate functionalised handle, such as a hydroxy group, that can bind to the polymer.

1.3.1.2.2 Ring Enlargement of Subphthalocyanines

Ossko and Meller synthesised subphthalocyanines for the first time in 1972 (Scheme 19). Subphthalocyanines contain three N-fused diiminoisoindoline sub-units, which encircle a boron core. The 14 π electron aromatic structure surprisingly is not planar, it is a cone shaped trigonal structure which has a curved molecular surface.

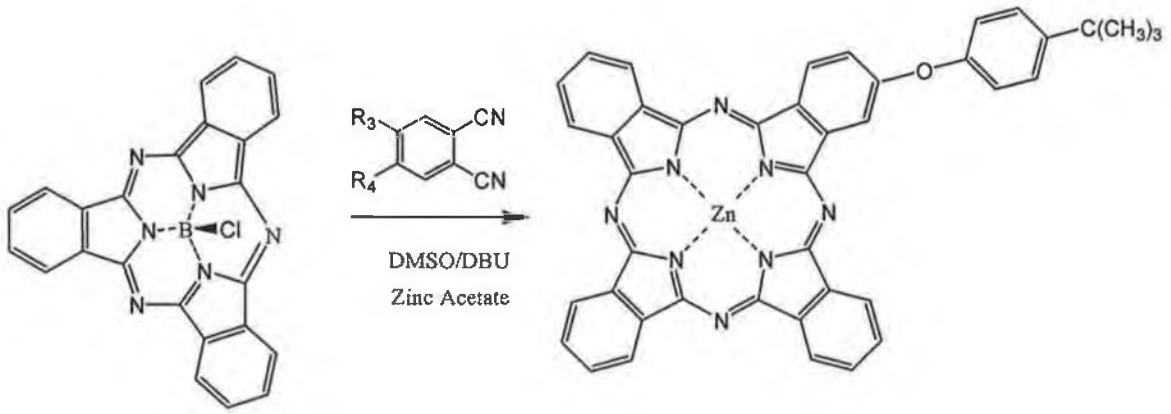


(53) **(54)**

Scheme 19: *Synthetic strategy for the synthesis of the first subphthalocyanine.*

Subphthalocyanines have lately enjoyed a revival as precursors in the synthesis of unsymmetrical substituted A_3B Pcs via ring expansion. Kobayashi *et al.*[49] was the first to use this type of ring enlargement reaction, which was supposed to revolutionise asymmetric phthalocyanine synthesis. A mono-functional Pc **(56)** was synthesised from subphthalocyanine **(55a)** and a substituted phthalonitrile **(55b)** or alternatively 1,3 diiminoisoindoline in the presence of distilled DMSO-1-chloronaphthalene (2:1), DBU and zinc(II)acetate at 130°C (Scheme 20) to give 2-mono(tert-butylphenoxy)phthalocyanato zinc(II) was synthesised in a 35% yield[50] .

Even though this method shows huge potential for the synthesis of A_3B Pcs it has its drawbacks. The first being the formation of other statistically substituted phthalocyanines, this is caused by the catalysed ring opening of the subphthalocyanine and cleavage into different fragments that lead to additional condensations to give undesired phthalocyanine by-products. Yields are low because of this. Also, recent work has shown that as well as the formation of di and tri substituted Pcs, chlorinated unsubstituted Pcs are also formed. These by-products have proven difficult to separate.



(55) **(56)**

Scheme 20: *Ring expansion of subphthalocyanines to form an unsymmetrically substituted phthalocyanine*[50].

1.3.1.2.3 Mixed Condensation

This is probably the most widely used condensation strategy for the synthesis of unsymmetrical substituted phthalocyanines. It involves the homogeneous cross condensation of two different phthalonitriles/diiminoisoindoline A and B, which when condensed produces a possible mixture of 6 compounds (Figure 9)[14]. Stoichiometry however can be used to maximize the production of a certain unsymmetrical substituted Pc over the others. However these mixtures must be separated and its their separation which has historically limited the use of this approach. Recently it has been demonstrated that unsymmetrical phthalocyanines can be efficiently separated by size exclusion chromatography[51].

Unsymmetrical substituted A_3B phthalocyanines are usually synthesised using a stoichiometry of 3:1 (A:B). A mixture of A_4(33%), A_3B(44%) and other products(23%) are produced when both A and B have the same reactivity (Figure 9). An unsymmetrical substituted zinc tri(tert-butyl)-4-nitrophthalocyanine **(58)** was synthesised using this stoichometric ratio (Scheme 21). The clever positioning of the reactive NO_2 group in this phthalocyanine allows for easy derivatisation to different unsymmetrically substituted phthalocyanines[52]. Using higher ratios such as 9:1 will raise the amount of A_4 formed and reduce the amount of A_3B formed, however it will limit the other unwanted cross-condensation products(A_2B_2, A_1B_3, B_4), which may hinder separation.

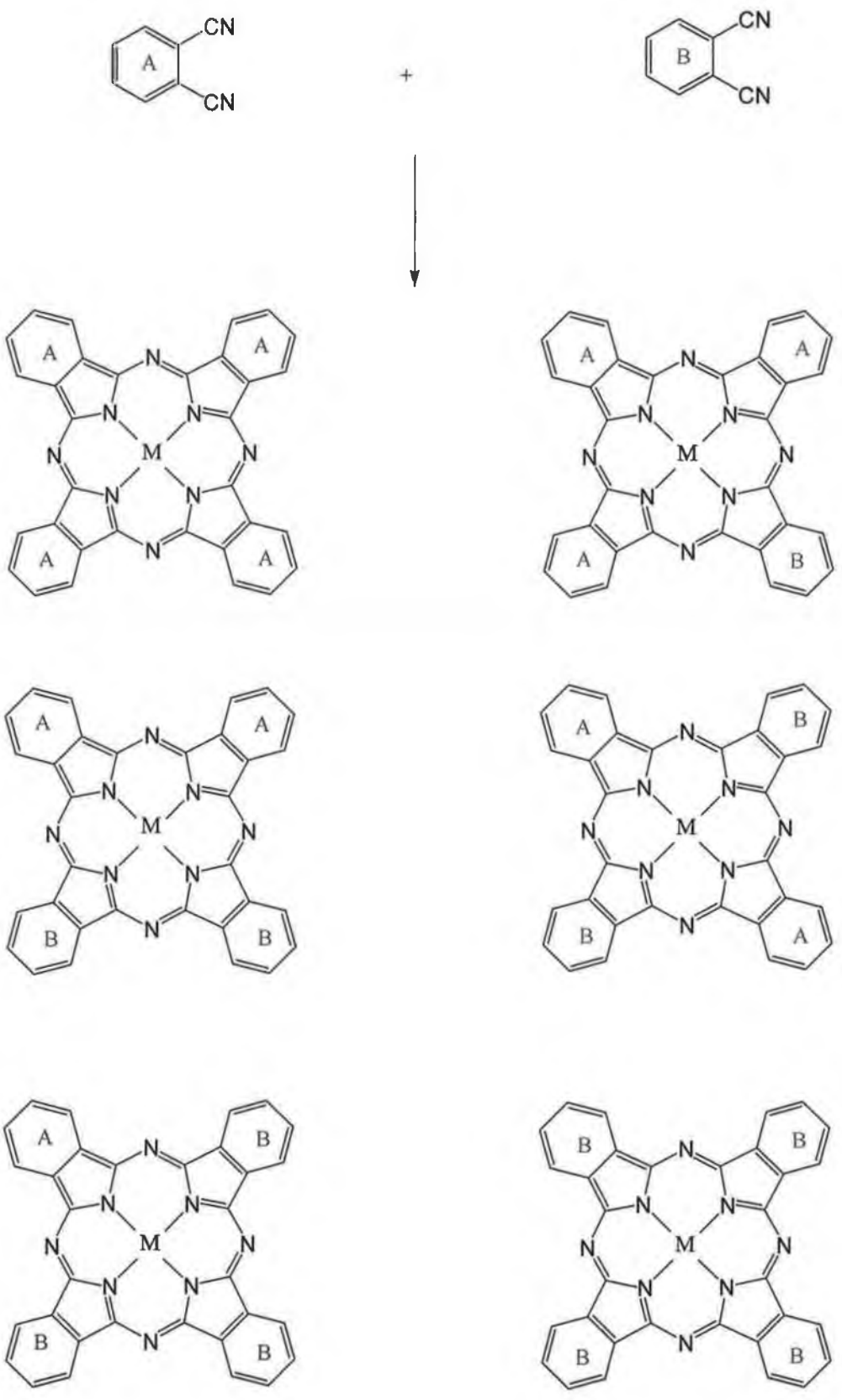
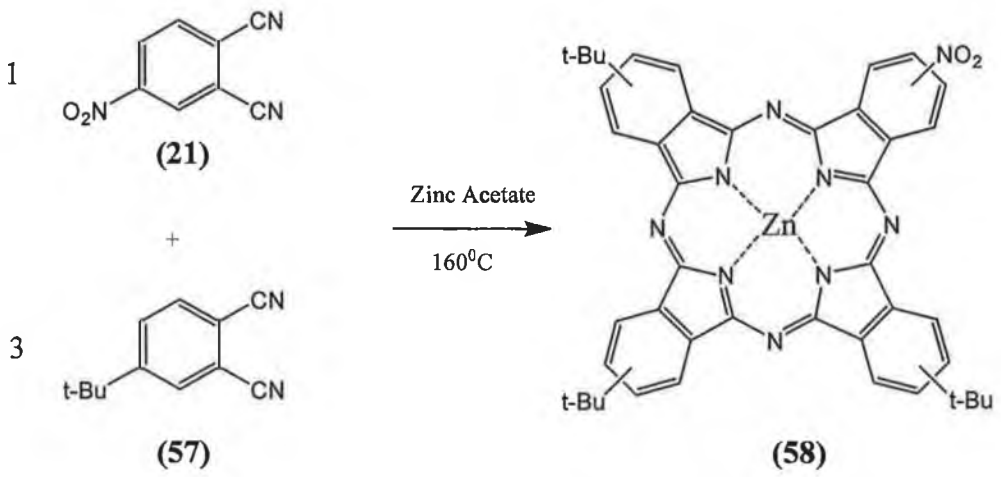
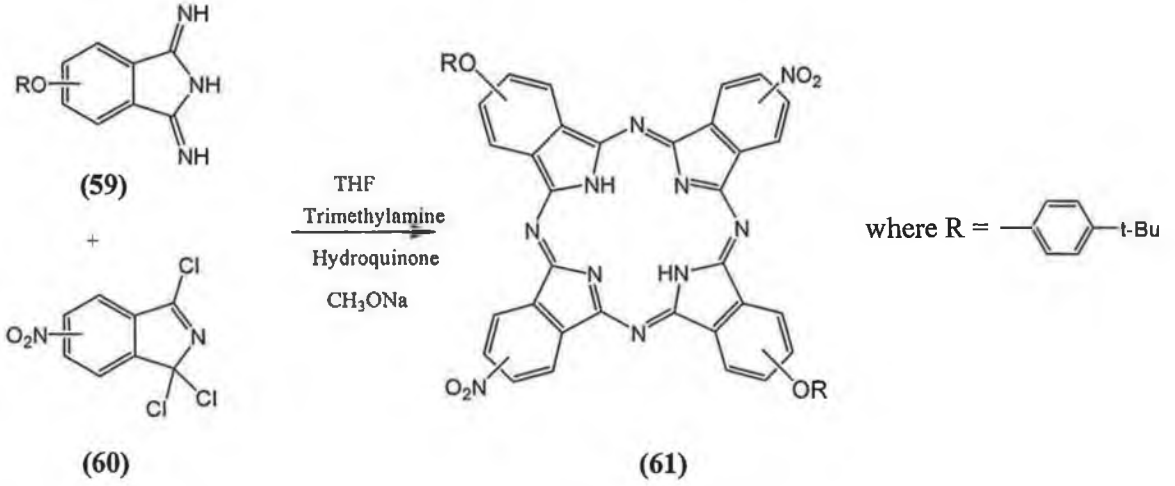


Figure 9: *The six possible substituted phthalocyanines formed from the condensation of two differently substituted symmetrical phthalonitriles A and B*[14].



Scheme 21: *Synthesis of zinc tri(tert-butyl)-4-nitrophthalocyanine using a mixed condensation ratio of 3:1*[52].

Other lower symmetry phthalocyanines such as the opposite (ABAB) D_{2h} phthalocyanine have also been synthesised by a cross condensation. An opposite 4,4"-bis(4-tert-butylphenoxy)-4',4'"-dinitrophthalocyanine **(61)** was formed selectively by the condensation of 1,3-diminoisoindoline derivative **(59)** and a 1,3,3-trichloroisoindoline **(60)** in a ratio of 1:1 in the presence of a base and a reducing agent (Scheme 22)[53]. Yields of up to 50% where obtained for this reaction. However this selective synthesis has been repeated[54] and yields have been found to be lower and the product seems to be slightly contaminated with the A_3B isomer. Despite these problems this reaction shows an enrichment of the ABAB isomer.



Scheme 22: *Synthesis of an oppositely substituted 4,4"-bis(4-tert-butylphenoxy)-4',4'"-dinitrophthalocyanine*[53].

1.3.1.2.4 Binuclear Phthalocyanine Synthesis

Over the past two decades unsymmetrical substituted binuclear phthalocyanines have attracted a lot of attention because of their exceptional spectroscopic, electrocatalytic and photocatalytic properties. Their porphyrin counter parts have been fairly effective in the four-electron reduction of oxygen to water[55]. However these compounds tend to lose catalytic activity with time, this is where phthalocyanines step in since phthalocyanines tend to be more stable towards oxygen and light. Metallated binuclear phthalocyanines have been synthesised using a wide variety of bridges covalently linked by -1[56],0[57],1[58],2[59],3[60],4[61],5[62] and 6[63] atoms. Binuclear phthalocyanines can be arranged either as linear or co-facially (stacked by π-aggregation) depending on the flexibility and geometry of the bridges.

Binuclear Pcs are synthesised in much the same way as unsymmetrical substituted phthalocyanines, with the use of an appropriate bisphthalonitrile and an excess of partner phthalonitrile (1:9). Leznoff has been the principal researcher in this area over the last two decades. His group has synthesised a wide variety of binuclear phthalocyanines with different bridges. Saturated alkyl chains have widely been used to link two phthalocyanines together. However, if a face-to-face co-facial arrangement is desired then ridged spacers that constrain the system into this form are used. Some examples are naphthalene[64], anthracene[64], ferrocene[65] and catechol[66] (Figure 10). Conjugated spacers are also used because they utilize the electronic and photonic-based partnership between the phthalocyanine units via conjugation. Alkene, alkyne and oligoethyne bridges have been used to exploit this effect (Figure 10). As with mononuclear phthalocyanines, single isomers of binuclears can be difficult to make however when symmetrical substituted partner phthalonitriles are used the problem of positional isomers can be averted[67].

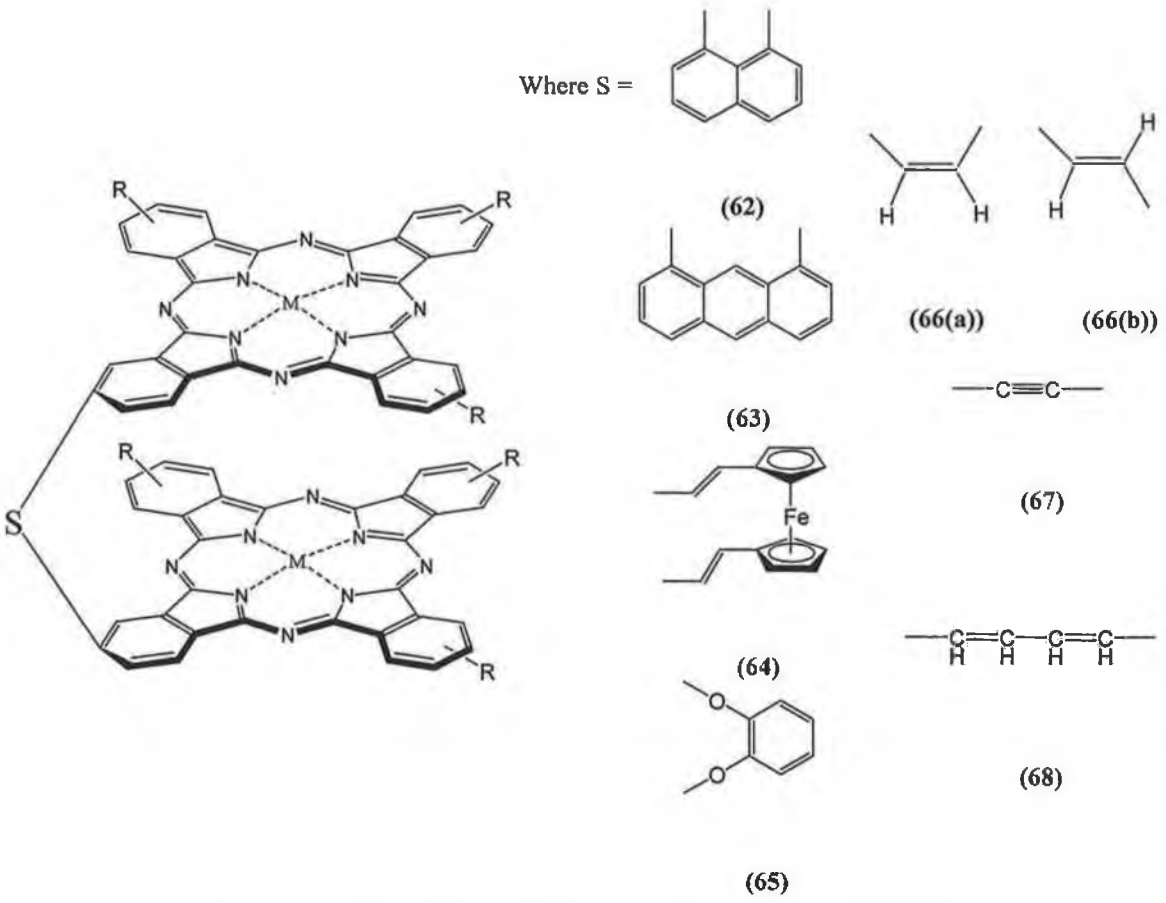
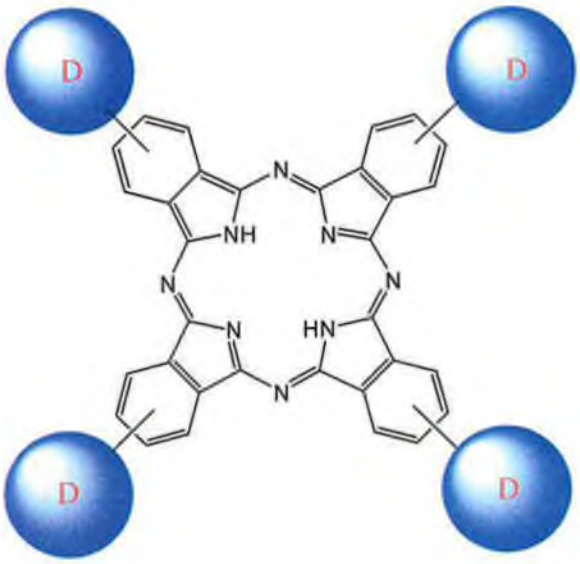


Figure 10: *A variety of bridged binuclear phthalocyanines.*

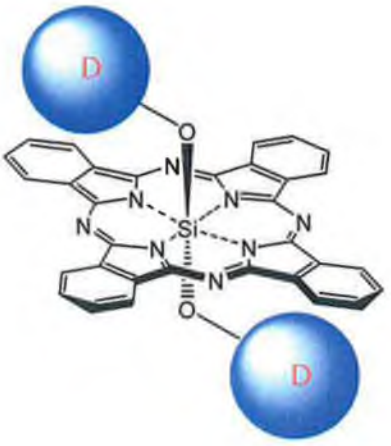
1.3.2 Axial Substituted Phthalocyanines

Substitution can also be achieved by the axial co-ordination of ligands to specific metallated phthalocyanines. This type of substitution reduces aggregation, which in turn makes these Pcs more soluble. The attachment of these ligands leads to some interesting optical and optoelectronic properties however axial ligation is limited to metals that have an oxidation state of +3(Al, Ga, In) or +4(Si, Ge, Sn). It should be noted that metals in the +3 oxidation bond one ligand while metals in the +4 oxidation state bond two[1].

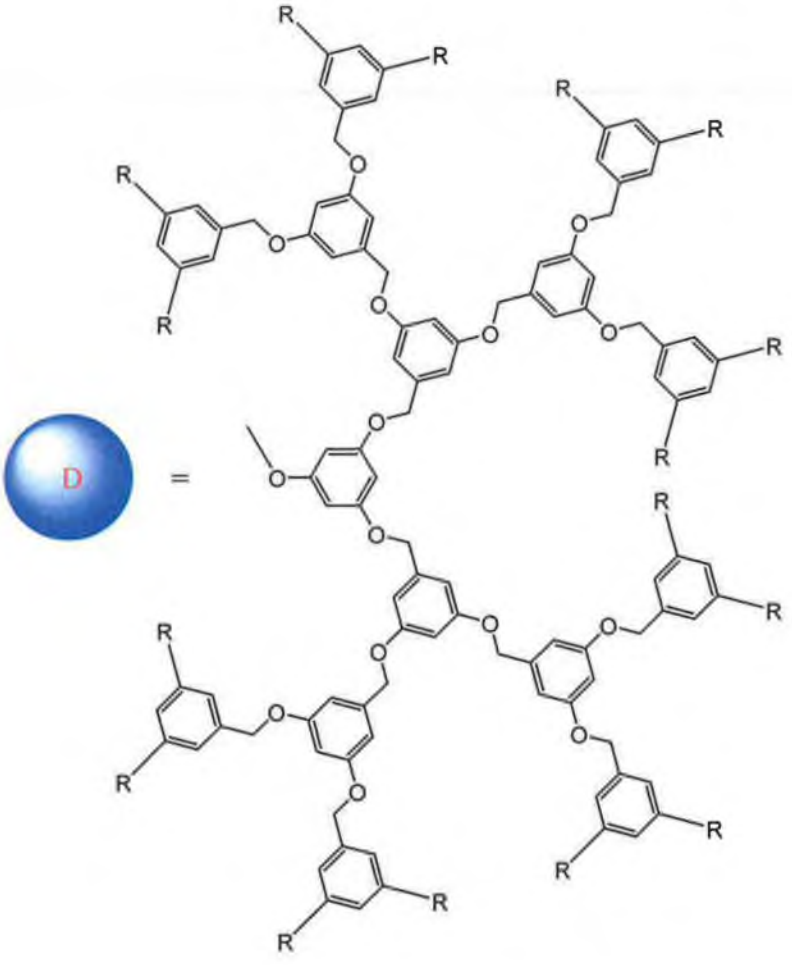
Silicon is the most widely used metal for this type of application. The starting material (Cl_2SiPc) is made by simply condensing phthalonitriles/diiminoisoindoline with silicon tetrachloride. This can then be converted into $(HO)_2SiPc$ quite simply by a hydrolysis reaction using sodium hydroxide. Cl_2SiPc and $(HO)_2SiPc$ are the main starting materials and have been widely derivatised using alkyl halides etc[1]. McKeown *et al.*[68] has lately placed huge dendritic ligands on this metal centre **(70)** to see its effect on aggregation compared with the peripheral dendritic substituted phthalocyanine **(69)** see Figure 11[69]. In the last number of years substitution of the silicon metal with two different ligands has been attempted with some success. First a chlorodimethyloctylsilane or L_1 is reacted with a dihydroxyphthalocyaninatosilicon at 60°C in pyridine to form **(71)**. **(71)** is then taken and reacted with the second ligand (L_2), which is a dendrimer, in refluxing toluene to form **(72)** (Scheme 23)[70].



(69)

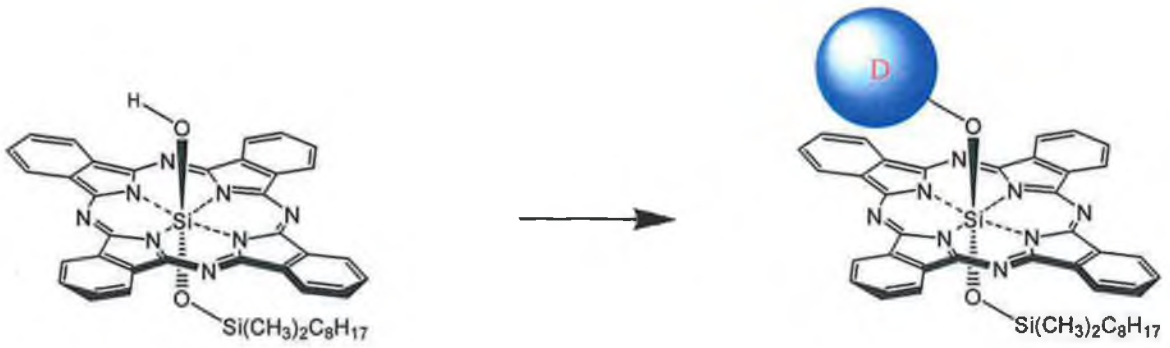


(70)

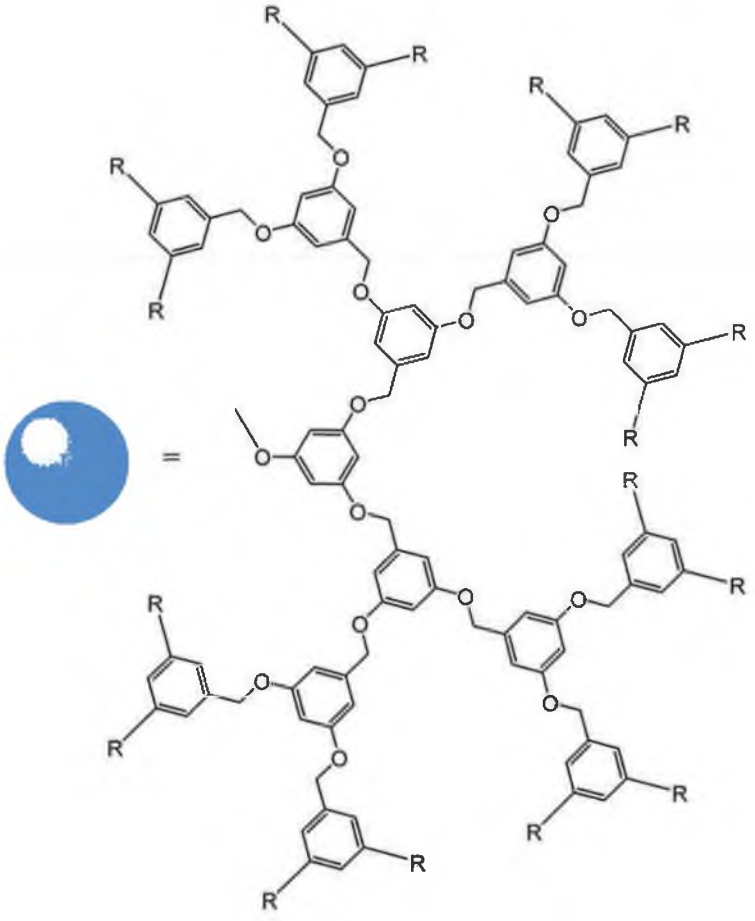


Where R = $O(CH_2CH_2O)_3CH_3$

Figure 11: *Example of McKeown's dendritic phthalocyanines in the peripheral and axial positions*[68-69].



(71) **(72)**



Where R = $CO_2CH_2CH_3$

Scheme 23: *Synthesis of a novel phthalocyanine dendrimer capable of forming spherical micelles*[70].

1.4 Characterisation and Purification of Phthalocyanines

Phthalocyanines, as we know, were first discovered in the 20th century at a time when technology was not advanced enough to elucidate its complicated structure. Colour was their main method for identification and characterization. This all changed in the late 1930's when new technologies such as X-ray diffraction were used by Robertson to characterize these compounds. In this section we investigate some of the technologies, which are used today to characterize and purify phthalocyanines.

1.4.1 Purification

Phthalocyanines are well known for their stability and this property has been exploited in their purification. An example of this is sublimation, which is a technique that involves the use of temperatures up to 600°C in *vacuo*. The use of concentrated acid for their reprecipitation also exploits this key property. It is well known that these techniques are more suitable to unsubstituted derivatives since a variety of substituted phthalocyanines may decompose under high temperatures or face hydrolysis under acidic conditions[2].

Substituted derivatives however can show partial solubility in organic solvents and this is exploited for their purification by a variety of conventional organic techniques such as recrystalisation from organic solvents and silica gel column chromatography. However aggregation can effect clean separation. Lately size exclusion chromatography has been applied in the separation of phthalocyanines. This technique has become vital in the separation of products prepared from cross-condensations otherwise unsymmetrical phthalocyanines could not be efficiently obtained in pure form[2].

1.4.2 Characterisation

1.4.2.1 UV-Vis Spectroscopy

Phthalocyanines contain a large extended π-conjugation that is responsible for its strong absorption maxima at 670-700 nm and at ~350 nm with extinction coefficients of ~10^5. The absorption at 670-700 nm is called the Q-band and is assigned the a_{1u}-e_g transition, while the absorption at ~350 nm is known as the B-band and is assigned to the a_{2u}-e_g transition. There are also weak vibrational over-tones found at ~600 nm. The Q-band is responsible for the intense blue or green colour of the phthalocyanines. The shape of this Q-band however is highly dependent on the symmetry of the phthalocyanine. Metalled phthalocyanines belong to the D_{4h} point group and as a result only one peak is observed in the Q-band region because the e_g orbitals are degenerate. However PcH_2 belongs to the D_{2h} symmetry point group and this causes the e_g orbitals to become non-degenerate. This splits the Q-band into two peaks see Figure 12 (a) and (b). This split is a simple way of checking to see if a Pc contains a metal or not. This Q-band splitting is lost when H_2Pc is treated with strong base such as tetrabutyl ammonium hydroxide to form the Pc^{2-} anion, which belongs to the D_{4h} point group[1]. In the dye industry metalled derivatives tend to be chosen over metal-free because they give a more definite shade[14].

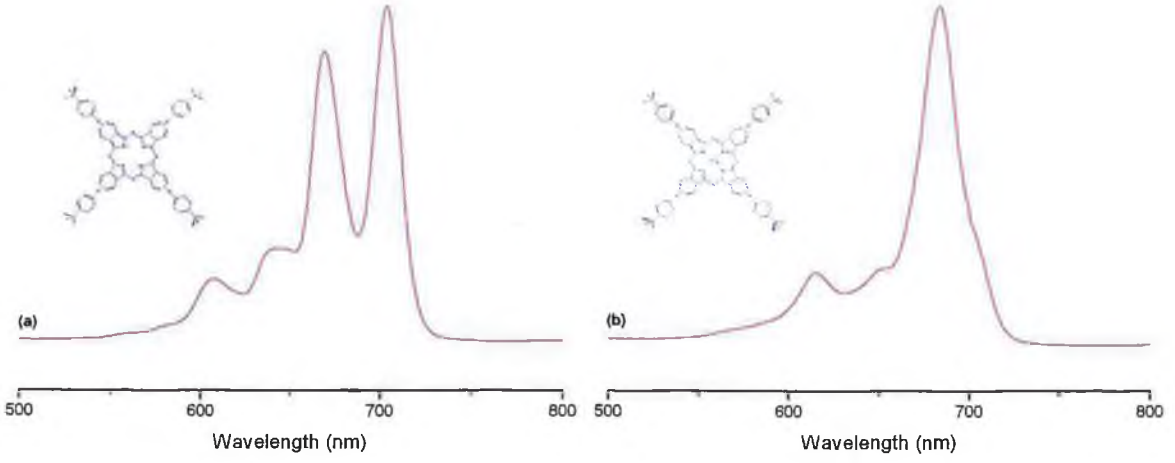


Figure 12: An example *UV-Vis spectrum of a (a) metal-free Pc and (b) metallated Pc from 550nm to 750nm*[71].

The λmax of the Q-band can be effected in a variety of ways and in theory we can fine-tune this absorption band. There are a number of ways in which this can be achieved; the first method involves changing the metal ion in an unsubstituted phthalocyanine core to see its effect. Across the first row of transition metals it was noted that FePc is the least bathochromic while the vanadyl derivative shows the largest bathachromic shift however, there was no pattern found across this row. Going down the d-block transition metals from Ni-Pd-Pt a pronounced hypsochromic shift of the absorption band was noted[72].

The second method which can be used to fine-tune the Q-band is the placing of sustitutents in the α and β positions. It has been noted that sustituents placed in the α-position give a larger bathochromic shift than those in the β-position[73]. When an alkoxy group is placed in the α-position there is a large shift resulting from the electron donating ability of this group which changes the electronic configuration of the phthalocyanine ring. Tetra-3-nitro phthalocyanine is an exception to this rule because it has a hypsochromic shift when compared to the β-positioned nitro group. This may be explained by steric constraints forcing the nitro group out of planarity[72]. Subsitution in the β-position usually has very little effect on the position of the Q-band, however when the subsitiutents extend the conjugation (e.g. benzoannulation) of the phthalocyanine the Q-band has a bathochromic shift[74].

Solution phase aggregation has an effect on the shape and positioning of the Q-band. This well known phenomena occurs between two phthalocyanine rings (or more), which leads to coupling between their electronic states. This coupling is often refereed to as exiton coupling[1]. Phthalocyanine cofacial aggregates are categorized by a substantial broadening of the Q-band in addition to a blue-shift of the Q-band. To highlight this effect a concentration study is outlined in Figure 13.

These phthalocyanine aggregates also quench the strong Pc fluorescence, which exists in the non-aggregated state. This type of aggregation is referred to as intermolecular aggregation. Certain types of phthalocyanines (binuclear clam-shell) however show aggregation even at concentrations of 1×10^{-7} M. This intramolecular aggregation only occurs when the rings lie on top of each other and like intermolecular aggregation leads to exiton coupling between both rings. Clamshell phthalocyanine Q-bands are generally always blue shifted and broaden when compared with their mononuclear counter parts.

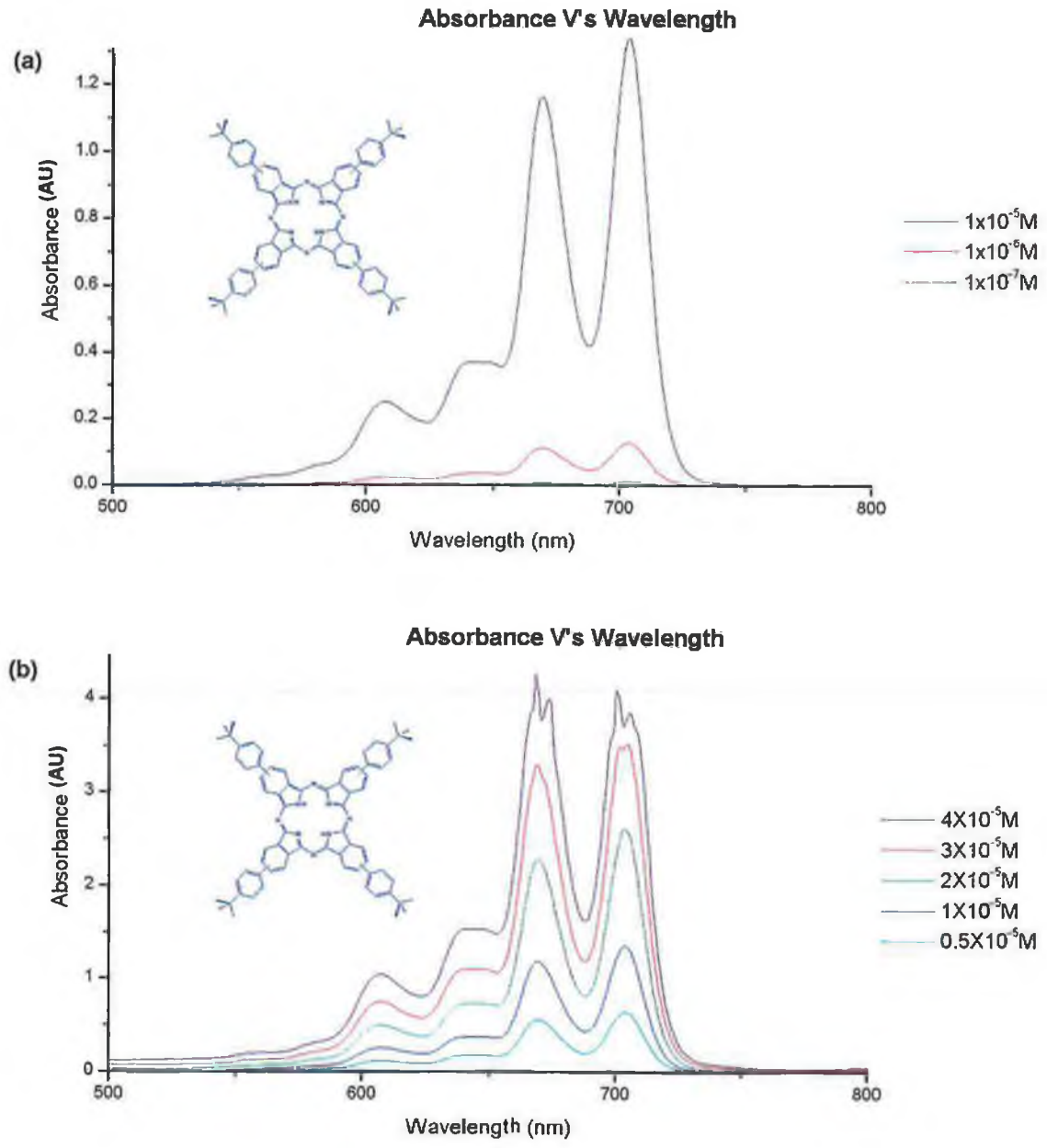


Figure 13: *Examples of concentration studies*[75].

1.4.2.2 Mass Spectrometry

Mass spectrometry is a widely used method for the molecular weight identification of phthalocyanines and related analogues. Some techniques that have been used are FD[76], FAB[77], MALDI[78] and MALDI-TOF[79]. Probably the most reliable technique for analysing phthalocyanines is MALDI-TOF-MS because it is simple, fast and inexpensive. A matrix, which complicates the spectrum, does not have to be used with low molecular weight phthalocyanines[80]. This makes interpretation simpler.

1.4.2.3 ^{1}H NMR

In the early days ^{1}H NMR analysis of soluble phthalocyanines was limited by the presence of positional isomers and use of lower field instruments that do not allow the collection of data on dilute samples. Resolved spectra of phthalocyanines were hard to obtain as a result of their strong tendency to aggregate in solution, which causes peak broadening[2]. However with the advent of single isomer phthalocyanine systems and Fourier Transform, ^{1}H NMR has become a very beneficial technique.

There are two regions of interest, 1) the aromatic protons on the benzo substitutents and 2) the internal protons in metal-free phthalocyanines. The benzo-substituted hydrogens for an unsubstituted ZnPc are usually found in the 8-10 ppm range. They are generally found in two clusters one for the 3,6 protons and one for the 4,5 protons (Figure 14). The 3,6 protons are found furthest down field because of the anisotropic effect in the phthalocyanine ring. A five-loop model shown in Figure 15 gave the best calculations for the ring current effect of the Pc and this model demonstrates that the 3,6 protons of the benzo rings are more deshielded than the 4,5 protons which is also experimentally observed[81]. The internal protons however are strongly shielded by the ring and are found further upfield than a typical N-H absorption. Values for the internal protons typically range from –2 to –6 ppm.

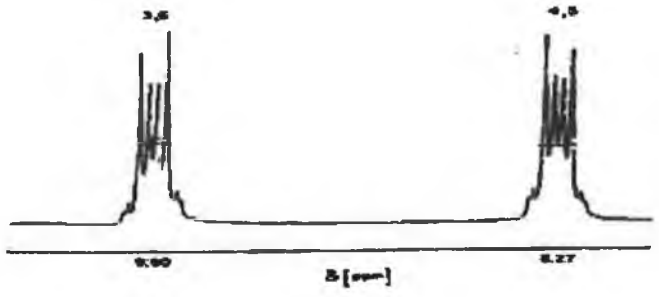


Figure 14: *Aromatic protons in unsubstituted phthalocyanine*[81].

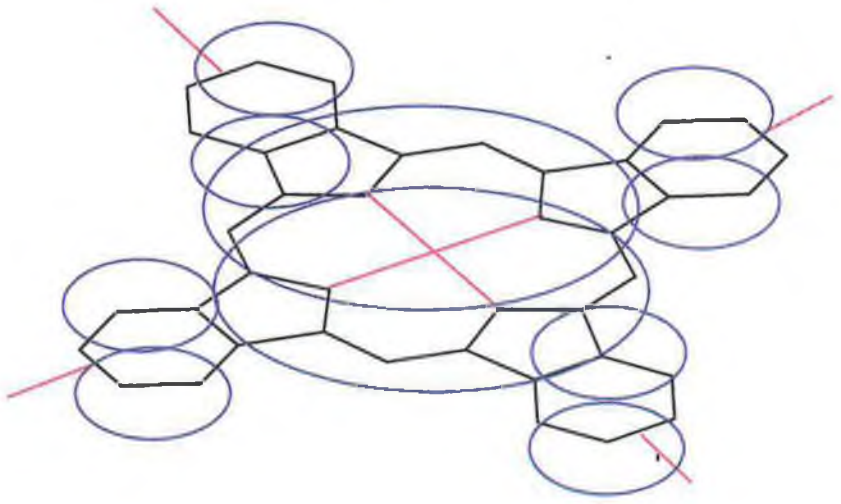


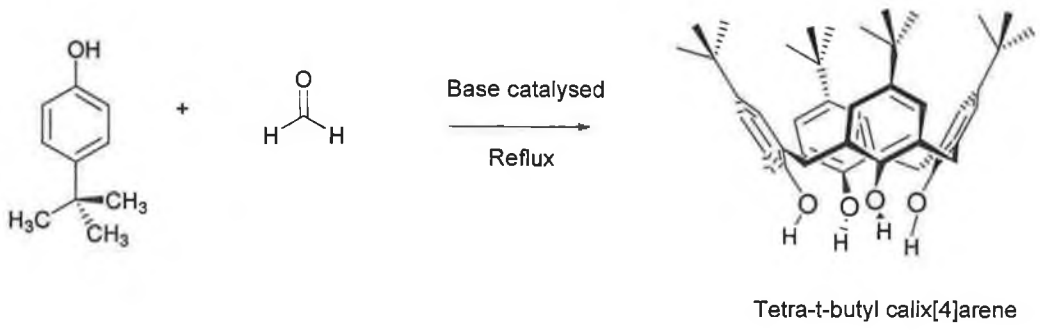
Figure 15: *The five loop model to describe the ainsotropic effect of the phthalocyanine*[81].

The aggregation phenomena in Pc chemistry has a substantial effect on the above chemical shifts of both the internal and benzo-substituted protons. This means that temperature, concentration and solvent will have an effect on both the resolution and chemical shift of the protons in the Pc. Leznoff and co-workers[81] used a single isomer octaalkynylphthalocyanine to demonstrate these effects. They found that the internal proton over a concentration range of 10^{-2} to10^{-5} in benzene-d_6 was shifted downfield by 2 ppm. This demonstrates that chemical shift changes with the degree of aggregation of the phthalocyanine. It also demonstrates that the aromaticity of one Pc core generally causes an upfield shift on its aggregated partner. Temperature however effects the aromatic 3,6 protons which move downfield from 9.30 ppm @ 27°C to 9.53 ppm @ 137°C (concentration 10^{-3}). This was also observed for the internal protons which had a more substantial shift downfield from -1.35 ppm to +0.30 ppm @ 157°C. Solvents have also been seen to affect the chemical shifts of phthalocyanine protons when they compared this phthalocyanine in benzene and nitrobenzene.

1.5 Calix[4]arenes

The calixarenes are a class of cyclooligomers formed via a phenol-formaldehyde condensation (Scheme 23(a)). The calixarenes were first isolated by Zinke in the 1940's (quite often referred to as Zinke compounds) and a cyclic oligomer structrue was proposed. Conforth's group in the 1950's found that the cyclic compounds prepared from the base

condensation of t-butylphenol and formaldehyde by Zinke were actually mixtures of macrocycles.



Scheme 23(a). *Preparation of calix[4]arene.*

It wasn't until the 1970's that these mixtures were properly separated and structurally characterised. This pioneering work was carried out by Gutsche's group and he was able to isolate and identify three components in the reaction mixtures which he identified to be bowl shaped cyclic oligomers containg four (calix[4]arene), six (calix[6]arene) and eight (calix[8]arene) phenol units. Gutshe used the term calixarene, which comes from the Greek word calixcrater used to describe bowl like vases, to describe these rigid bowl shaped macrocycles.

The calix[4]arene possesses a defined upper and lower rim and a central aromatic annulus (Figure 15(a)). The hydrogen bonding on the lower rim locks the calix[4]arene into a cone conformation. Upon removal of the hydrogen bonds it is possible for the phenoxy groups of the calix[4]arene to rotate through the annulus of the calixarene into the upper rim, forming new conformations referred to as partial cone, 1,3-alternate and 1,2-alternate (see Figure 21). It should be noted that the t-butyl groups of the calix[4]arene are too bulky to pass through the annulus of the ring.

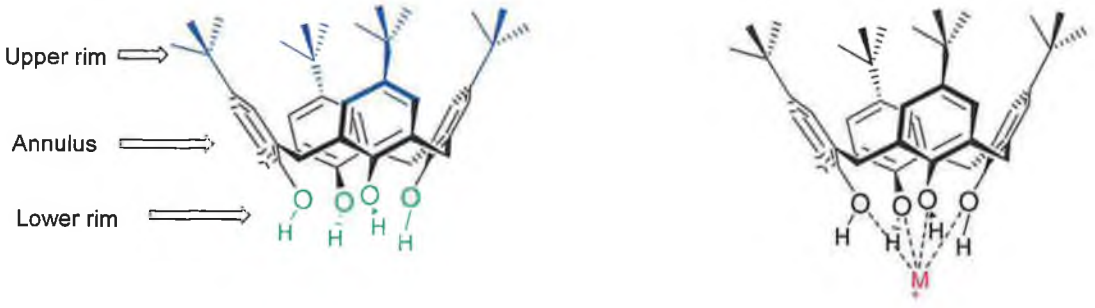
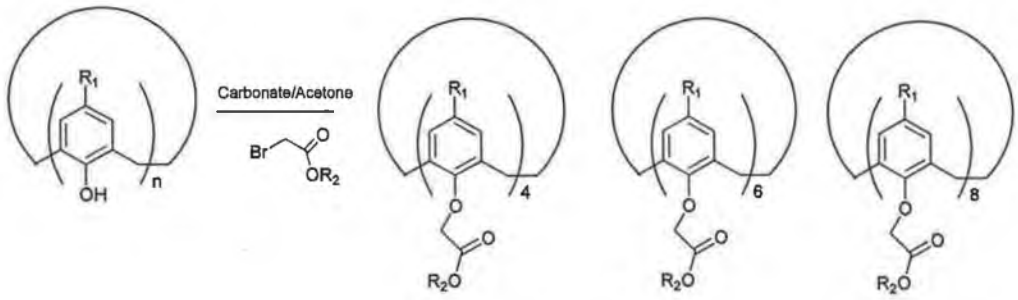


Figure 15(a). *Calix[4]arene and metal coordination on the lower rim.*

Calix[4]arene is now typically prepared from the base catalysed condensation of t-butylphenol with formaldehyde, these methods yield the calix[4]arene in good yields in the absence of the larger calix[6]arene and calix[8]arene.

The rigid conformation enables the calixarenes to act as host molecules as a result of their preformed cavities. By functionally modifying either the upper and/or lower rims it is possible to prepare various hosts with differing selectivity's for various ions and small molecules.

Substitution onto the lower rim of calix[4]arene can be readily accomplished using base conditions in the presence of an alkylating agent (Scheme 23(b)). Most products prepared from these methods remain in the cone conformation, furthermore if subtituents larger than ethyl are introduced onto the lower rim of calix[4]arene it has been found that rotation through the calix[4]arene annulus is prevented thus conformation interconversion cannot occur after substitution.

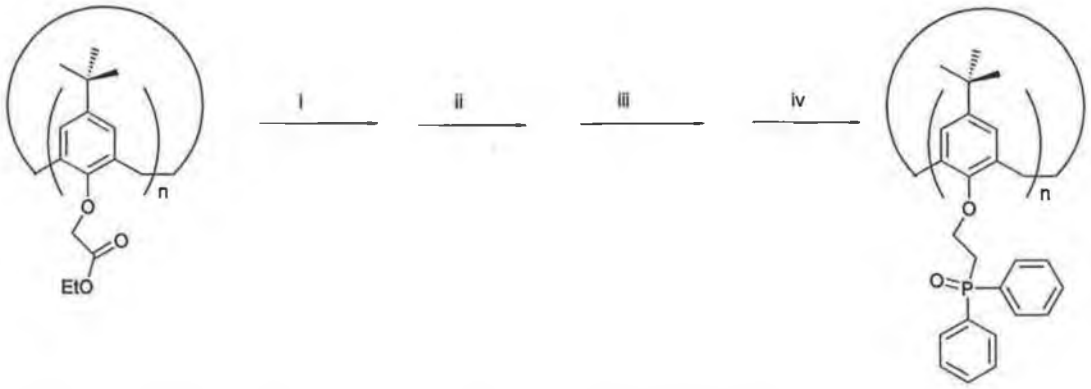


a. R1 = t-butyl
b. R1 = t-butyl, R2 = ethyl
c. R1 = t-butyl, R2 = methyl

Scheme 23(b). *Preparation of ester derivatives of calixarenes.*

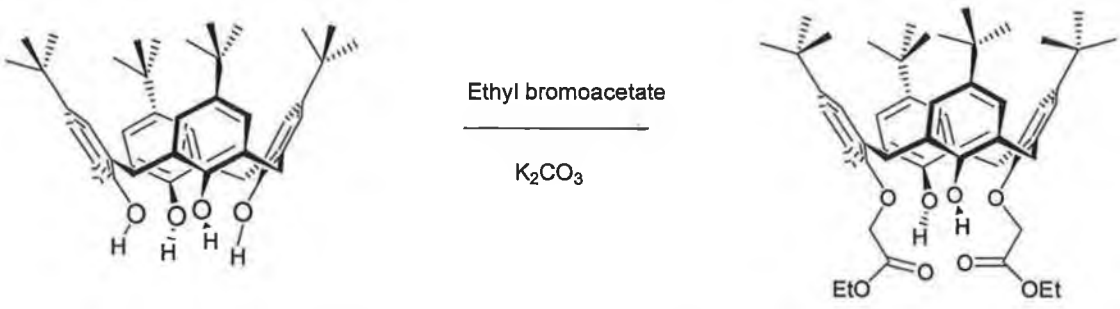
Post modification of substituted calix[4]arenes can be readily accomplished as outlined in Scheme 23(c). In this case the tetraethyl ester calix[4]arene is converted into the tetraphosphineoxide in four steps, demonstrating the synthetic versatility of these compounds.

Methods for the preparation of unsymmetrical 1,3-distal substituted-tetra-t-



Scheme 23(c). *Preparation of phosphine oxide calix[4]arene. i) DIBAL, ii) TsCl, iii) diphenylphosphine chloride/Li iv) peroxide.*

butylcalix[4]arenes (Scheme 23(d)) were developed which typically involved using both a weak carbonate base (potassium or caesium) and stoichiometric control of the alkylating agent. These reactions led to 1,3-distal substituted calix[4]arenes, in the absence of 1,2-substituted isomers. These new methods allow for the preparation of novel low symmetry calix[4]arenes since a different, second functionality, can be introduced into the remaining 4,5-positions of the lower rim.



Scheme 23(d). *Preparation of 1,3-distal substituted calix[4]arene.*

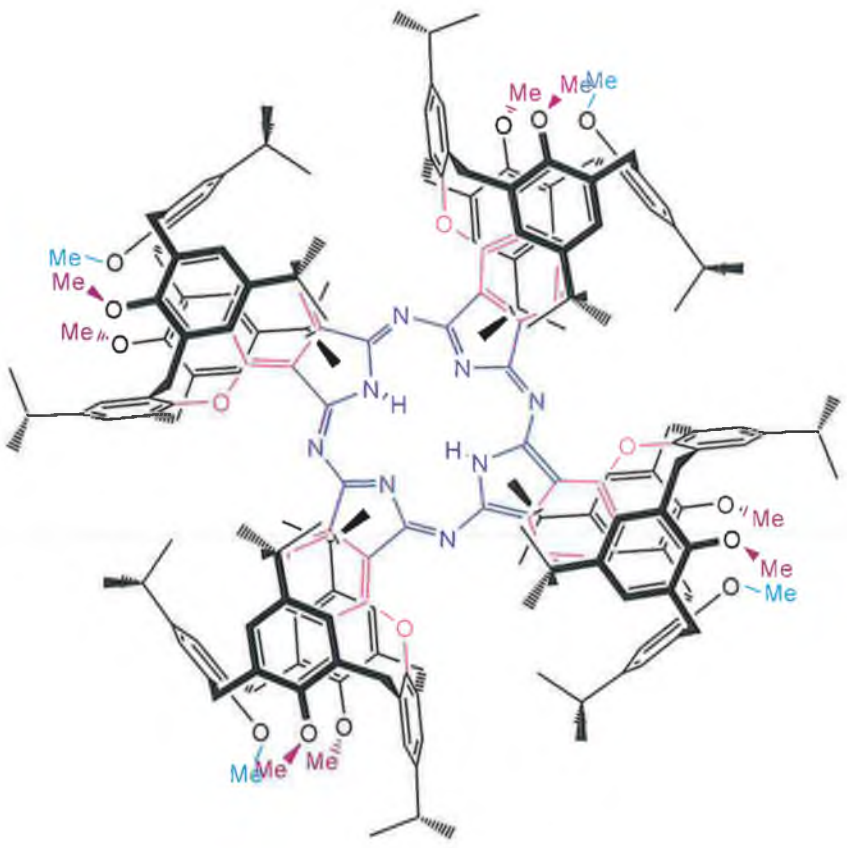
1.6 Thesis Proposal

This project synthetically entails the amalgamation of two different macrocyclic molecules. In essence we are introducing a calix[4]arene into a phthalocyanine in order to prevent aggregation.

How can we eliminate aggregation? The answer to that lies in the steric isolation of the phthalocyanine core. Steric isolation has been manipulated to some extent by the use of bulky substitutents such as dendrimers. Dendrimers are polymers in which the atoms are arranged in many branches and sub-branches along a central backbone of carbon atoms. From McKeown's[82] and McGrath's[83] work it has been found that peripherally substituted dendritic phthalocyanines if not coupled with electrostatic repulsion are only adequate at preventing aggregation. This even applies to the new third generation dendritic substitutents. Aggregation studies on these phthalocyanines were carried out in solution (CH_2Cl_2, ethanol) where the concentration of phthalocyanine was kept constant and the percentage ethanol of the solution increased form 0 % to 90 %. It was found that peripherally substituted dendritic phthalocyanines aggregate at about 30 % EtOH and fall out of solution at 50 % EtOH. However when these substitutents are placed in the axial position aggregation is virtually completely prevented. The major drawback is that axial substitutents can only be placed on a small number of metals in the centre of the phthalocyanine, which limits their applications.

Why choose calix[4]arenes? calix[4]arenes, like dendritic substitutents are sizable (large molecular weight), the one major difference is that calix[4]arenes are ridged in structure while the dendritic substitutents are flexible and under certain solvent conditions may fold into a small volume. Another possible advantage of introducing a calix[4]arene into a phthalocyanine which caught our eye comes from the ability of preparing calix[4]arenes in the partial cone conformation.[84-85] We believe that we can manipulate this chemistry and actually place the t-butyl groups of the calix[4]arene above and below the plane of the phthalocyanine! (Figure 16).In essence we would be creating a picket-fenced phthalocyanine, such a structure should show minimal aggregational behaviour. We are interested in preparing such phthalocyanines from both 3 and 4-calixarylsubstituted phthalonitriles. Of

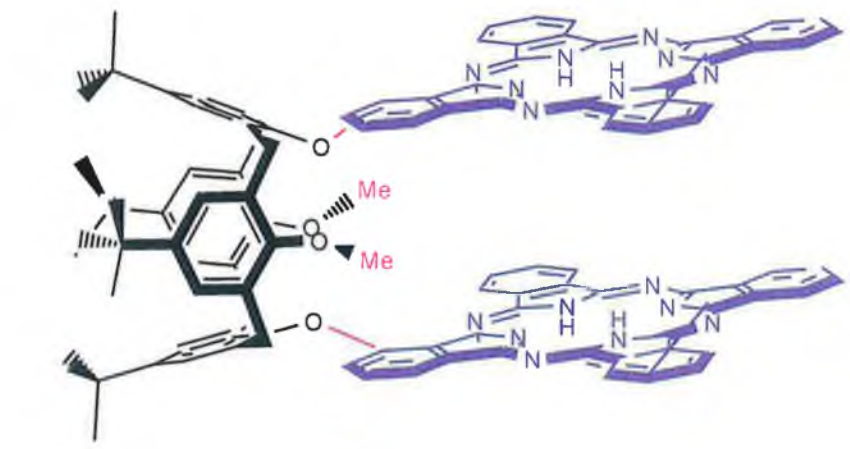
particular interest is the 3-substituted phthalonitrile since this should yield a single isomer phthalocyanine on condensation.



(73)

Figure 16: *Target tetra-substituted calix[4]arene phthalocyanine.*

In our exploration of the marriage of calix[4]arenes and phthalocyanines we were also interested in applying calix[4]arenes as bridges for the creation of a series of binuclear phthalocyanines. We believe that the calixarene bridge can incorporate significant solubility into the system thus eliminating the need for the use of partner phthalonitriles containing bulky solubilising groups. We also believe that the phthalocyanine rings will lie in a co-facial arrangement on the lower rim of the calix[4]arene, creating an ionophoric pocket. We are interested in synthesising both a short **(74)** and a long **(75)** chain binuclear phthalocyanine in order to compare bridge length and flexibility (Figure 17). This calixarene bridge due to its steric bulk has potential to be the first ever solublizing bridge.

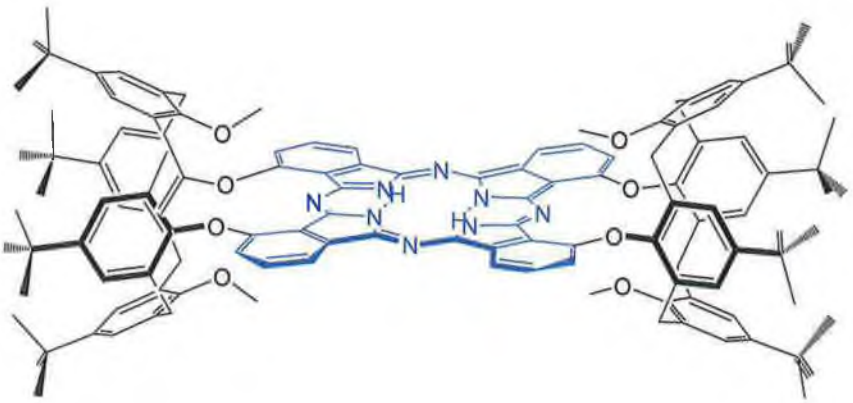


(74)

(75)

Figure 17: *Target short and long chain binuclear.*

From molecular modelling we have found that the starting material required to prepare the short chain binuclear phthalocyanine **(74)** had the correct potential geometry to form a constrained phthalocyanine **(76)** (Figure 18). This would lead to the formation of a single D_{2h} isomer and from model studies we believe that **(76)** may also exist as a non-aggregated system.



(76)

Figure 18: *Target constrained calix[4]arene phthalocyanine.*

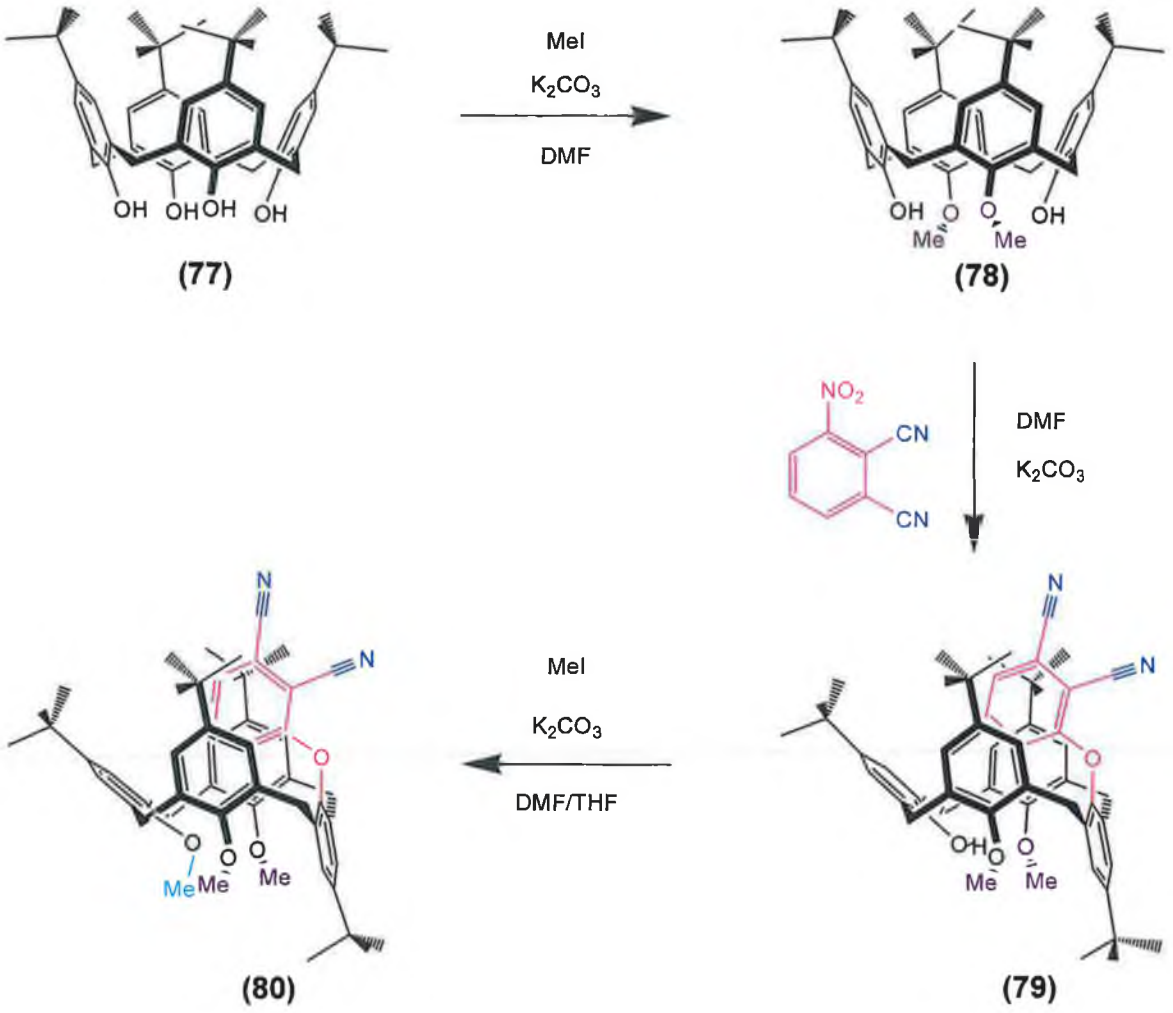
2. Synthesis of Self Filled Partial Cone 5,11,17,23-tetra-t-butyl-26,27,28-trimethoxy-25-(-3-[-1,2-dicyanobenzene])calix[4]arene

2.1 Introduction

In Scheme 24 a synthetic route is outlined for the synthesis of a self filled partial cone 5,11,17,23-tetra-t-butyl-26,27,28-trimethoxy-25-(-3-[-1,2-dicyanobenzene])calix[4]arene **(80)**. This compound **(80)** is the required starting material for the synthesis of "picket fence" type phthalocyanines, which are described in chapter 3. A prerequisite for the synthesis of this precursor is the protection of all four hydroxys on the calix[4]arene starting material since they will interfere with the condensation of **(80)** to the respective phthalocyanine. The protection and selective substitution was accomplished in three stages, the first of which involved the partial etherification of the p-tert-butylphenolcalix[4]arene **(77)** to form the distal~1,3dimethoxycalix[4]arene **(78)**.This could be treated with 3-nitrophthalonitrile under weak base conditions to form **(79).** The final hydroxyl was then protected by the use of an etherification reaction to form **(80).**

2.2 Synthesis of Phthalonitrile Calix[4]arene

The first stage of this synthesis involves a partial etherification of the lower rim of p-tert-butylphenolcalix[4]arene **(77)** to form a distal~1,3dimethoxycalix[4]arene **(78)** using K_2CO_3, methyl iodide and DMF as solvent at 70°C for 4 days. Etherification reactions using alkyl halides are very common in calix[4]arene chemistry and they can be manipulated to form fully or partially substituted calix[4]arenes. A variety of factors affect this, including solvent, base strength and Stoichiometry. Fully substituted derivatives are usually synthesised by the use of strong bases such as NaH in the presence of an aprotic solvent such as DMF and a large excess of alkyl halide[86]. Partial substituted calix[4]arenes such as **(78)**, are generally synthesised by the use of a weak base such as M_2CO_3 (where M = K^+, Na^+ etc.) which generally prevents the reaction from going beyond the distal 1,3 substitution[86].



Scheme 24: *The synthesis of an self filled partial cone phthalonitrile Calix[4]arene.*

The initial preparation of 1,3-dimethoxycalix[4]arene involved the treatment of calix[4]arene with methyl iodide and K_2CO_3 in a 1:4:4 stiochometric ratio for 48 hrs. The isolated product was recrystallised from ethanol, but by TLC analysis we found trace contaminant impurities specifically the trimethoxy derivative. By TLC the target product and the impurity had similar retention times making purification by column chromatography extremely difficult. A set of time studies were carried out with the above reaction to determine whether the by-product could be eliminated to make for a more facile purification. The first reaction was carried for 2 hrs and we found by TLC that the reaction was complete, however the trimethoxy impurity was still present. Reactions were run for 10 minutes, 20 minutes and 1 hr, we found that the yields for these reactions were equivalent, but trace trimethoxy impurities still remained. We proceeded to purify the reaction mixtures by column chromatography on silica using a 90:10 hexane: ethyl acetate mobile phase. Yields of around

33 % were achieved for **(78)** after chromatography. Column chromatography still had to be utilised for final purification however we could now use shorter reaction times (1 hr was chosen).

^{1}H NMR spectroscopy is one of the most powerful tools in the identification of calix[4]arenes. To get an idea of some of the main features found in the calixarene we will first look at the starting material p-tert-butylcalix[4]arene **(77)**, the spectrum is shown in Figure 19. The aromatic protons are found at 7 ppm, the tert-butyl protons at 1.2 ppm, and the hydroxyl protons are singlets at 10.3 ppm, while the protons from the methylene bridging protons are a pair of doublets at 3.48 and 4.24 ppm respectively. The high symmetry of **(77)** is the reason for the simple spectrum. Distal~1,3 dimethoxycalix[4]arene **(78)** is partially substituted on the lower rim, which lowers the symmetry making the ^{1}H NMR spectrum slightly more complicated (Figure 20). In this case there are two aromatic protons at 6.8 and 7.1 ppm, two tert-butyl protons at 0.9 and 1.3 ppm, a singlet for the hydroxyl protons at 7.3 ppm and a singlet for the methoxy protons at 3.95 ppm. The methylene bridging protons are also a pair of doublets at 3.32 and 4.27 ppm respectively, which confirms the presence of **(78)**. Both NMRs where obtained using deuterated chloroform.

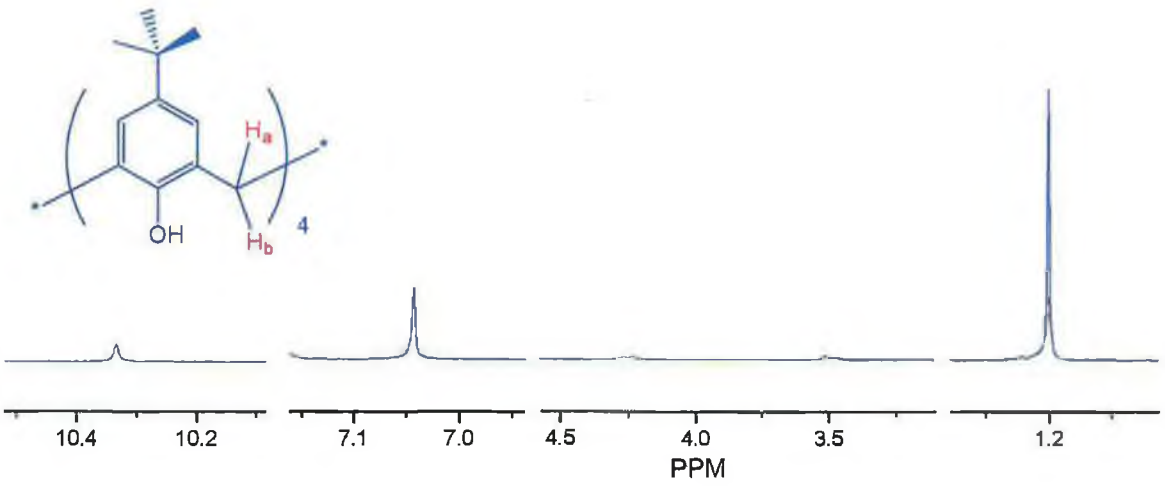


Figure 19: *^{1}H NMR Spectrum of (77)*

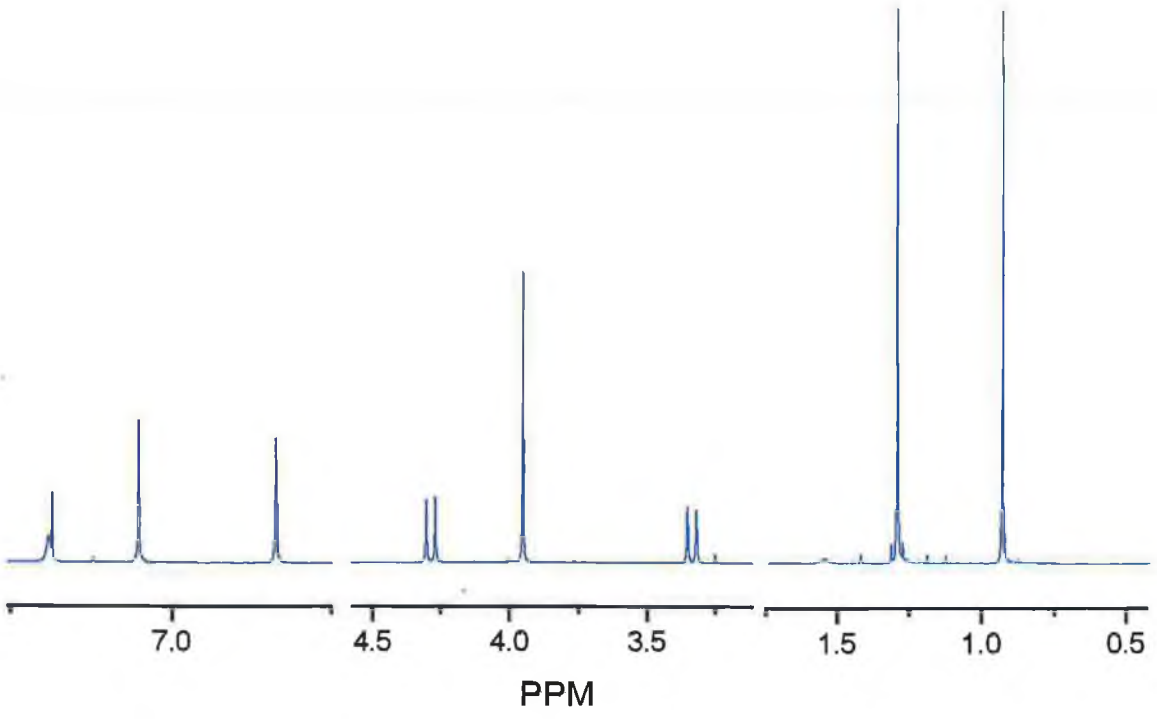


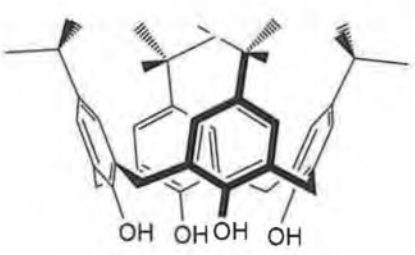
Figure 20: *^{1}H NMR Spectrum of (78)*

Conformational flexibility of calix[4]arenes in solution have been widely studied over the years. Calix[4]arenes have four conformations that are shown in Figure 21. X-ray crystallography is the surest way to assign conformation, however ^{1}H NMR has been used as a good alternative because for each conformer displayed there is a characteristic splitting pattern in the methylene region of the spectrum, which is outlined in Table 1[86(a)]. From this we can say that both the starting material **(77)** and our partially etherified calix[4]arene **(78)** (in solution) are in the cone conformation since the methylene bridging protons are found as

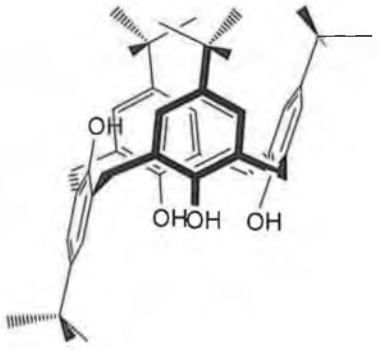
a pair of doublets at 3.33 and 4.28 ppm. In the literature it has been well postulated that partially etherified calixarenes are often less conformationally flexible than their fully etherified counter parts. This is a result of the synergistic interplay of intramolecular hydrogen bonding and steric factors[86].

Conformation	H^1 NMR
Cone	One pair of doublets
Partial Cone	Two pairs of doublets (ratio1:1) or one pair of
	doublets and one singlet (ratio 1:1)
1,3 Alternate	One singlet
1,2 Alternate	One singlet and two doublets (ratio1:1)

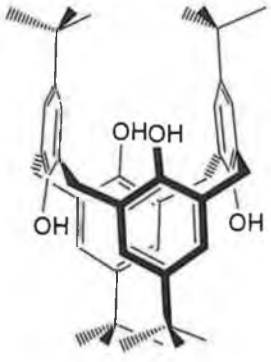
Table 1: *^1H NMR patterns for the CH_2 bridging protons of a calix[4]arene in all four conformations[86(a)].*



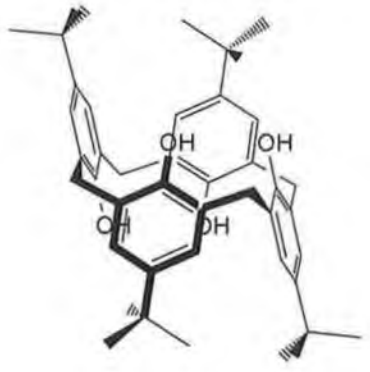
(77a)



(77b)



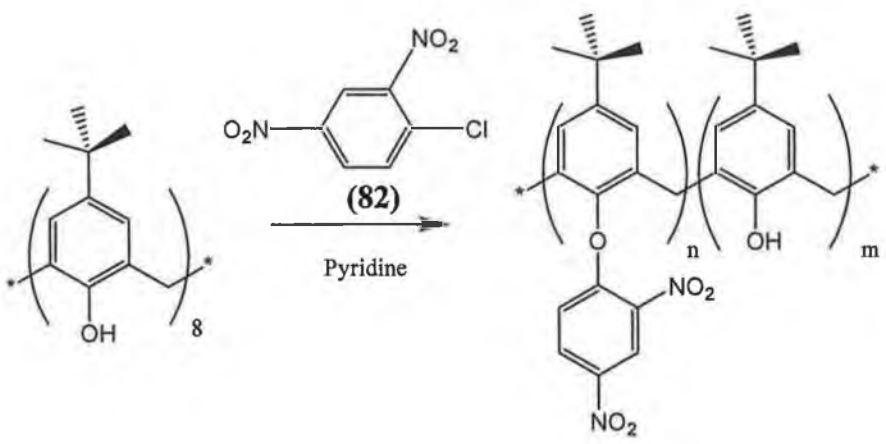
(77c)



(77d)

Figure 21: *Conformations of the calix[4]arene **(77a)** cone, **(77b)** partial cone, **(77c)** 1,3 alternate and **(77d)** 1,2 alternate.*

The preparation of **(79)** involves a S_NAr displacement between the distal 1,3-dimethoxy calixarene **(78)** and 3-nitrophthalonitrile using K_2CO_3 in DMF under vacuum[37]. This type of direct substitution of an aromatic system was first attempted by Gutsche[87] in 1979 for calix[8]arene system using 2,4-dinitrophenyl **(82)** Scheme 25, however it was not until 2001[88] that such a reaction was attempted for calix[4]arene systems. Our first attempts were aimed at the synthesis of the distal~substituted phthalonitrile derivative **(85)** in Scheme 26 where large excess of base and 3-nitrophthalonitrile **(20)** where added over days under vacuum. The separation of these reaction mixtures proved difficult while a negible amount of the distal bisphthalonitrile product **(85)** was found. It was however noted that a small amount of the



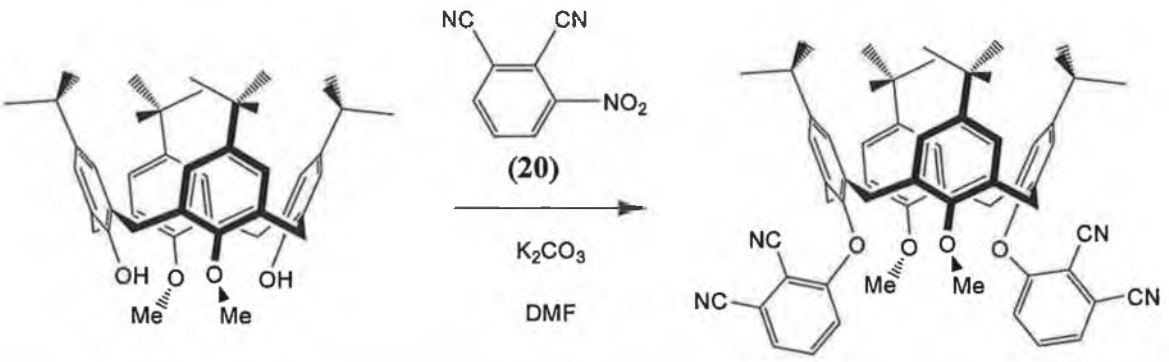
(81)

(83a) = (n=6, m=2)
(83b) = (n=1, m=7)
(83c) = (n=2, m=6)

Scheme 25: *Synthesis of the first partially substituted phenoxy linked aromatic* [87]

mono~substituted phthalonitrile **(79)** product was present even after 10 days. This led to the design of a pathway, for the synthesis of the mono~substituted **(79)** product. We found that by controlling the stiochiometry of the 3-nitrophthalonitrile **(20)** and **(78)** in a ratio of 1:4 we could increase the yield of **(79)** from 10 % to 37 % and eliminate the bis-substitution product **(85)**. The separation of these reaction mixtures proved difficult while a negible amount of the distal bis~phthalonitrile product **(85)** was found.

Purification of **(79)** was achieved on silica gel by using a hexane: ethyl acetate 80:20 mobile phase. The first spot to elute from this column was our target compound **(79)**. Final purification of **(79)** could be achieved by washing with a small amount of DMF to attain high purity. Yields of 37 % were achieved for **(79)** after chromatography.



(84) **(85)**

Scheme 26: *Synthesis of the distal~substituted phthalonitrile calix[4]arene derivative (85).*

Electrospray ionisation generally gives you protonated , sodiated or potassiated calix[4]arene molecular ion peaks. Because calix[4]arenes process ionophoric properties, where they encapsulate ions such as sodium and potassium they usually give very intense peaks[Error! Bookmark not defined.] In our case **(79)** gave us two peaks one at 825 m/z and the second at 841 m/z, which corresponds to the sodiated and potassiated derivatives of **(79)**. The peaks however where not very intense and they tended to fluctuate in intensity, this may be due to **(79)** being in the desired partial cone conformation a conformation, which lowers the ionophoric properties of the calixarene[89].

The ^{1}H NMR of compound **(79)** was carried out in deuterated nitrobenzene (d_5). The alkyl region of the ^{1}H NMR shows that the t-butyl groups give three different peaks at 1 ppm, 1.4 ppm and 1.5 ppm, which is to be expected because there are three different types of t-butyl groups (Figure 22). The methylene bridging protons appear as two pairs of doublets, the first pair is at 3.4 and 4.2 ppm, while the second pair are found at 3.9 and 4.0 ppm respectively (Figure 22). This splitting pattern indicates the presence of a partial cone conformation see Table 1[86(a)].

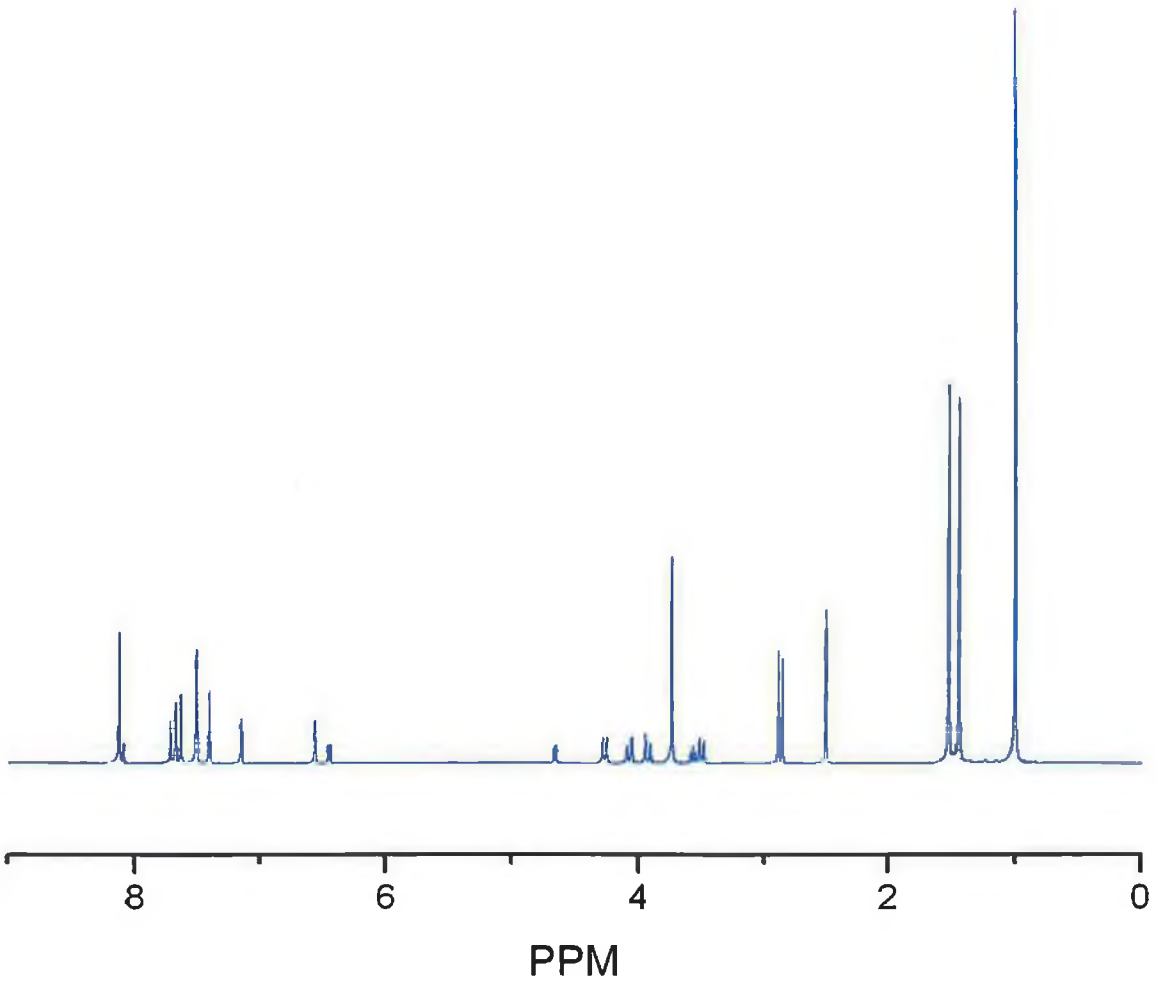
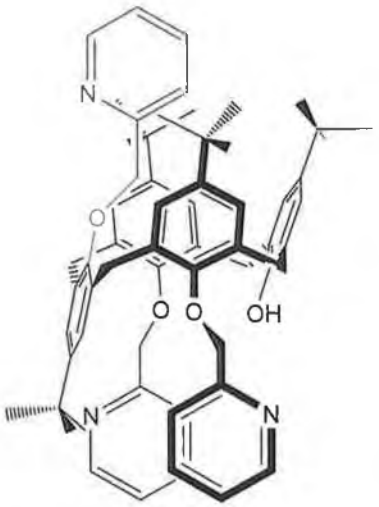


Figure 22: *^{1}H NMR Spectrum of (79)*

The aromatic region of this spectrum proved interesting for a couple of reasons. Firstly the aromatic protons of the calix[4]arene found at 6.57 ppm, 7.14 ppm, 7.4 ppm, and 7.62 ppm indicate a loss of symmetry because each of the calix[4]arene rings are different (Figure 22). But perhaps most interesting is that the phthalonitrile protons are not found in the aromatic region. If we first look at the H_4 and H_5 protons on the phthalonitrile substituent we see a dramatic shift of these protons upfield to 4.6 and 3.5 ppm respectively. These protons would usually be typically found in the aromatic region (7 – 8.5 ppm), such an upfield shift could only be caused by an anisotropic effect on the phthalonitrile protons, indicating that the phthalonitrile substituent lies within the aromatic annulus of the calixarene. The last phthalonitrile proton H_6 at 6.4 ppm is not significantly shifted; therefore we believe it is not inside the calixarene ring system or is just outside.

Pappalardo *et al.* synthesised a partial cone tri[(2-pyridylmethyl)oxy]-28-hydroxy-calix[4]arene **(86)** (Figure 23), where the aromatic protons are sitting in or around the calix[4]arene aromatic annulus. The upfield shifts for these protons are less compared to ours since the aromatic ring of **(86)** is not buried into the cavity since the spacer prevents this[84].

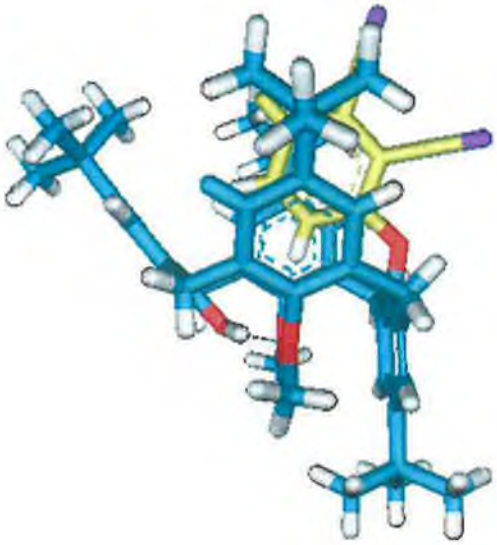


(86)

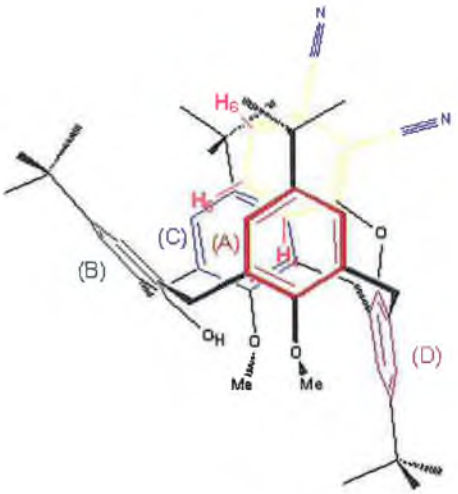
Figure 23: *Pappalardo's partial cone tri[(2-pyridylmethyl)oxy]-28-hydroxy-calix[4]arene (86)*[84].

Crystals of **(79)** were grown from ethyl acetate and hexane and an x-ray structure obtained, the results are shown in Figure 24. The x-ray structure confirms that **(79)** does exist in a partial cone conformation, with the phthalonitrile lying within the aromatic annulus of the calixarene. A pi-pi stacking arrangement between the A and D rings of the calixarene and phthalonitrile is evident. There also appears to be a T-bond between the H_5 of phthalonitrile and the B ring of the calixarene, and a H-bond between the remaining calixarene hydroxyl group attached to the B ring and the adjacent methoxy groups attached to the A ring. This hydrogen bond tilts the phthalonitrile aromatic ring over to the A ring. We believe that all four interactions are stabilizing this novel inclusion complex.(The x-ray structure of **79** is further described in Chapter 7)

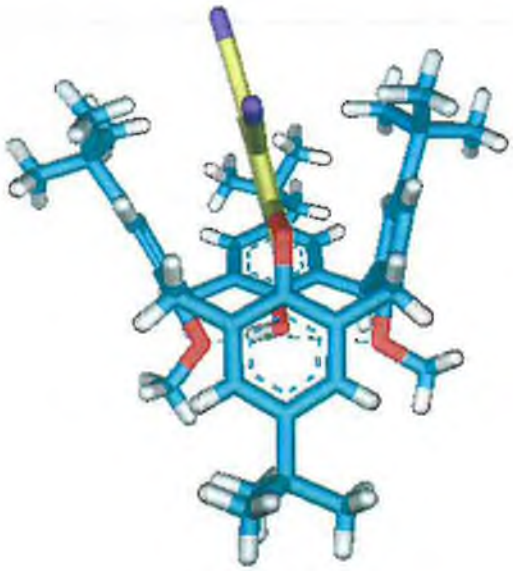
(79a)



(79c)



(79b)



(79d)

Figure 24: *(a) ORTEP representation of the crystal structure of* ***(79a)*** [90] *(b) side view of* ***(79b)*** *(c) labelled drawing of* ***(79c)*** *(d) front view of* ***(79d)***

Temperature variable ^{1}H NMR studies were carried out on **(79)** in deuterated nitrobenzene and revealed that the inclusion conformation is stable up to temperatures of 125°C! The only significant change observed in the spectrum was a slight upfield shift of the H_5 triplet (see Figure 25), we believe this is due to the B ring of the calixarene tilting away at higher temperatures. Upon cooling of the sample the triplet reverts to its original chemical shift at 3.5 ppm. When Pappolardo's compound **(86)** was analysed by temperature variable ^{1}H NMR a significant down field shift is noted for the aromatic protons, as they are "pushed-out" of the cavity[84]. The stability of our inclusion complex compared to **(86)** comes down to a lack of flexibility, as our compound does not contain a methylene spacer.

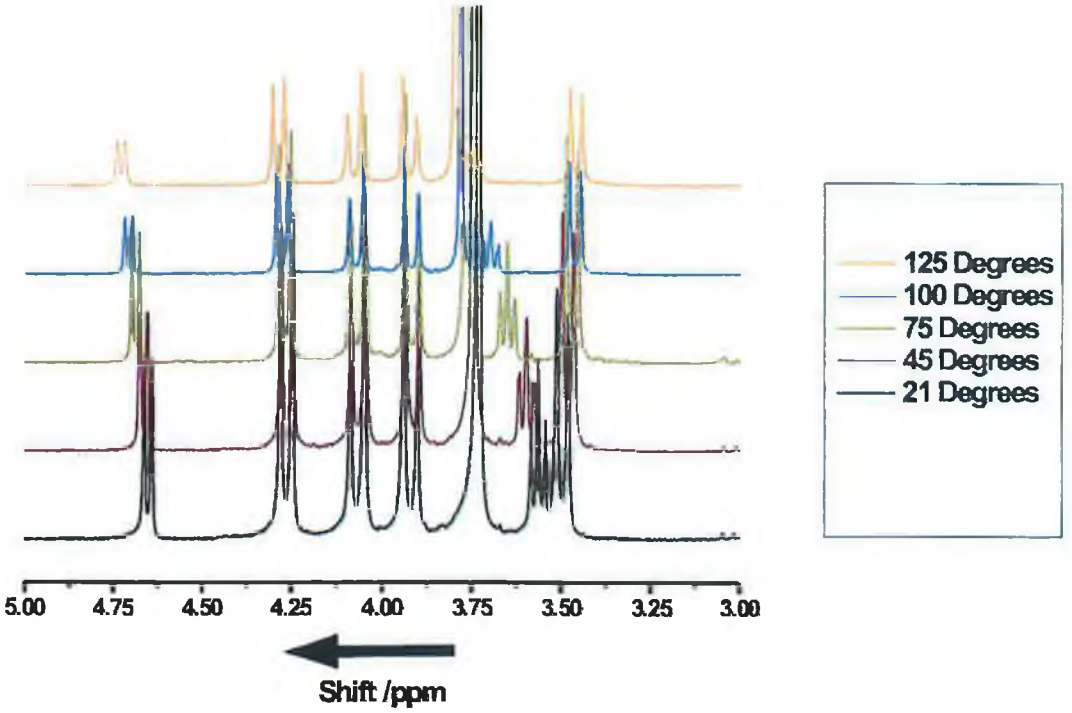


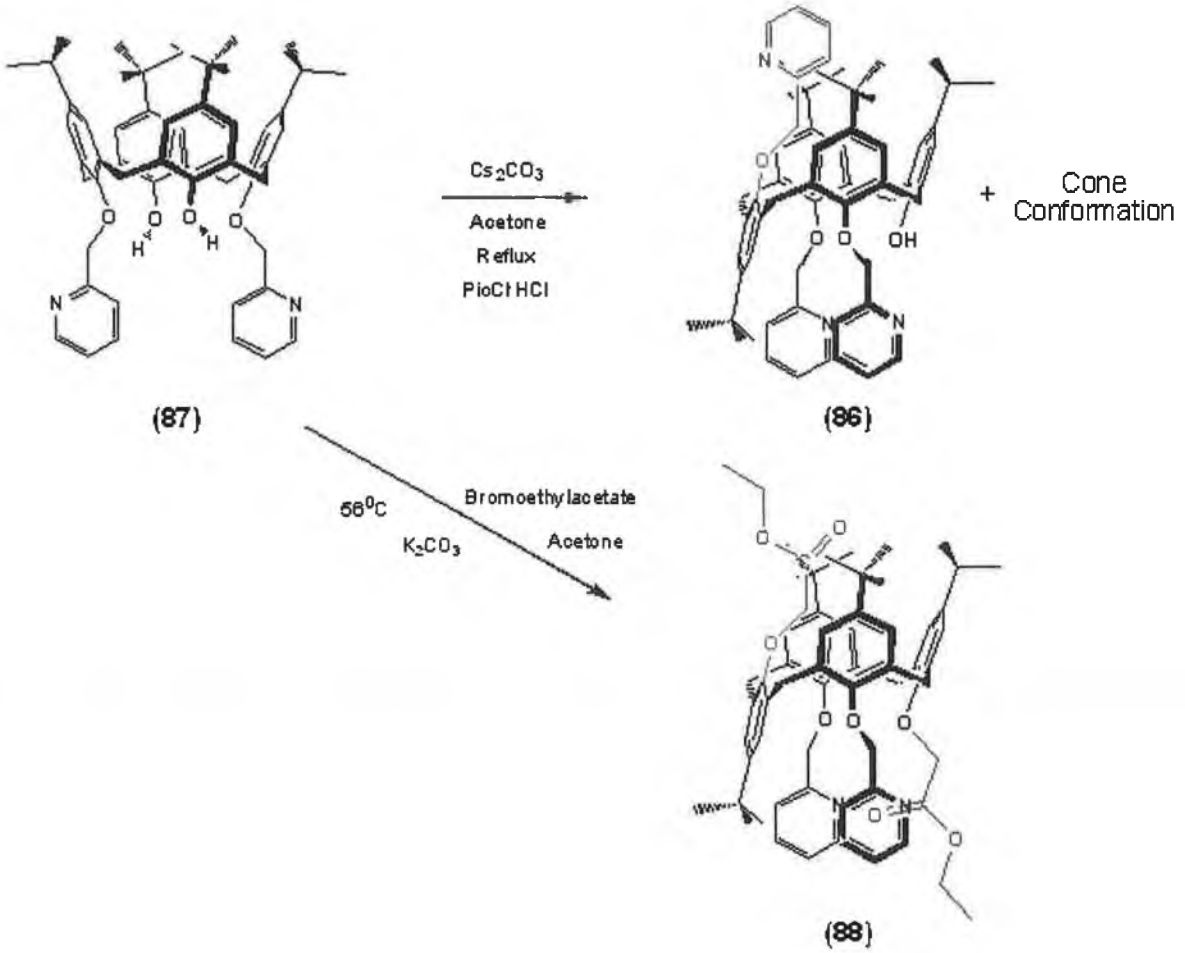
Figure 25: *Temperature ^{1}H NMR of* ***(79)*** *in deuterated nitrobenzene*

2.3 *Mechanism of Formation of Self Filled Partial Cone 5,11,17,23-tetra-t-butyl-27-hydroxy-26,28-dimethoxy-25-(-3-[-1,2-dicyanobenzene])calix[4]arene (79).*

Conformational mobility of calix[4]arenes has been mentioned above and generally in the formation of mono and di~substituted calix[4]arenes such as **(78)**, the cone conformation is the most prevalent and stable form in solution and solid phases due to the presence of hydrogen bonding. However in the stepwise reaction of a distal~calix[4]arene to form tri or tetra~ substituted calix[4]arenes the ArOH moieties have the ability for assuming either the up or down position since the lower rim hydrogen bonding is lost. In the literature there is a whole plethora of examples of this conformational change to all the possible conformations using different bases[91].

There are a variety of examples in the literature, which can be used to give the partial cone conformation using carbonate bases, however the products formed are not always conformationally pure. In the conversion of **(87)** into a partial cone tri~sustituted calix[4]arene **(86)** using a one equivalence of 2-(chloromethyl)pyridine hydrochloride and Cs_2CO_3 a 34 % yield of the partial cone conformation was formed. This also contained 11 % of the cone conformation determined by ^1H NMR analysis of the product mixture[92]. The reaction to form a partial cone tetra-substituted **(88)** from **(87)** was achieved using K_2CO_3 in a 98 % yield of which only the partial cone was obtained in a 100 % yield which was estimated by HPLC [91]. Scheme 27 shows the reaction conditions and it should also be noted that these reactions are carried out at around 70°C.

In the case of the preparation of **(79)**, we used K_2CO_3 base in DMF at room temperature, which yielded the partial cone inclusion complex. Mechanistically how is the partial cone synthesised in favour of the cone? The first key point is that substitution onto the lower rim of **(78)** by 3-nitrophthalonitrile is *not possible* due to steric interaction between the nitrile group, ortho to the nitro leaving group, and the two methyl substituents on the lower rim of **(78).** This steric hindrance allows for substitution to occur solely on the upper rim. The next question to be answered: Does the substitution event take place within the annulus of the calixarene or outside the annulus on the upper rim? For substitution to take place within the annulus of the calixarene first the aromatic substrate must be able to fit into the upper rim of the calixarene and second there must be enough space to allow for a tetrahedral intermediate to form.



Scheme 27: *Synthetic strategies towards the partial cone*[92,92].

Endo encapsulation of aromatic solvents have been widely studied since the late 70's when the first X-ray structure t-Butylphenolcalix[4]arene: Toluene (1:1) clathrate was found[93]. Figure 26 shows a side view and top view of a minimized CPK space filled model of an encapsulated toluene: distal 1,3 dimethoxycalix[4]arene **(78)**. This model demonstrates that toluene fits quite neatly into **(78)**. Also, it has been found that large aromatic ammonium cations such as those seen in Figure 27(a) can be used to effectively stabilize the cone conformation of a p-sulfonatocalix[4]arene in solution by forming an inclusion complex. It was found by ^{1}H NMR that the hydrogens para to the ammonium group and the ammonium CH_3 are shifted upfield indicating that they lie within the aromatic calixarene core. In the case of the di and tri cationic systems only small up-field shifts where noted so in these cases the cations were perched on top of the calixarene[94].

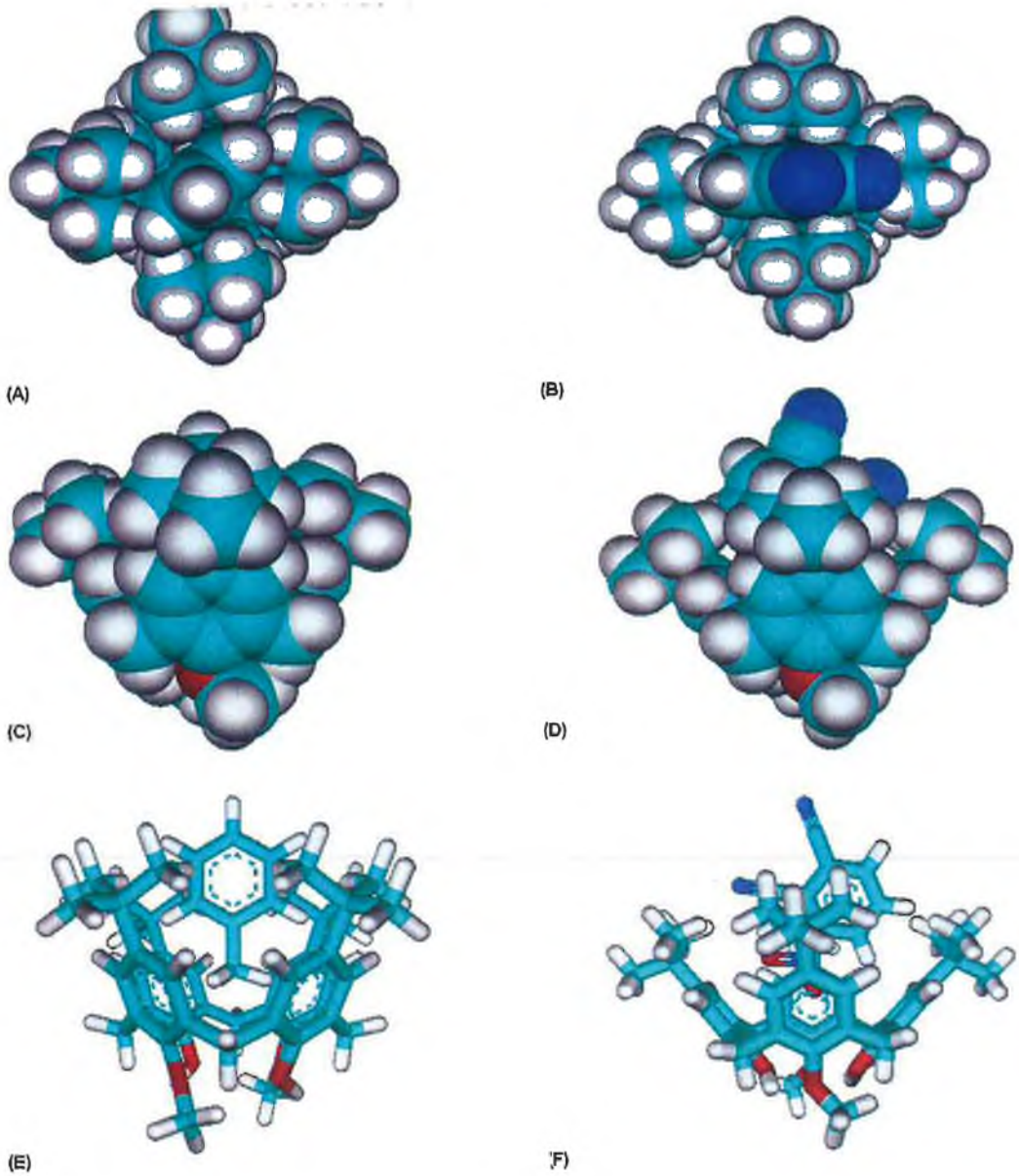


Figure 26: *(A) Spacefill of a p-t-butylphenoxycalix[4]arene toluene inclusion complex top view (B) Spacefill of a p-t-butylphenoxycalix[4]arene 3-nitrophthalonitrile inclusion complex top view (C) Spacefill of a p-t-butylphenoxycalix[4]arene toluene inclusion complex side view and (D) Spacefill of a p-t-butylphenoxycalix[4]arene 3-nitrophthalonitrile inclusion complex side view (E) Stick representation of a p-t-butylphenoxycalix[4]arene toluene inclusion complex side view (F) Stick representation of a a p-t-butylphenoxycalix[4]arene 3-nitrophthalonitrile inclusion complex side view.*

We believe that these results can aid us in understanding what is occurring in our system. If we take a look at Figure 26 you will find a side view and top view of a minimized CPK space filled model of an encapsulated 3-nitrophthalonitrile **(20)** into a distal 1,3 dimethoxycalix[4]arene **(78)**. This shows that the 3-nitrophthalonitrile **(20)** emulates the di and tri cationic systems rather than toluene and tell us that it is more than likely perched at the top of **(78)**.

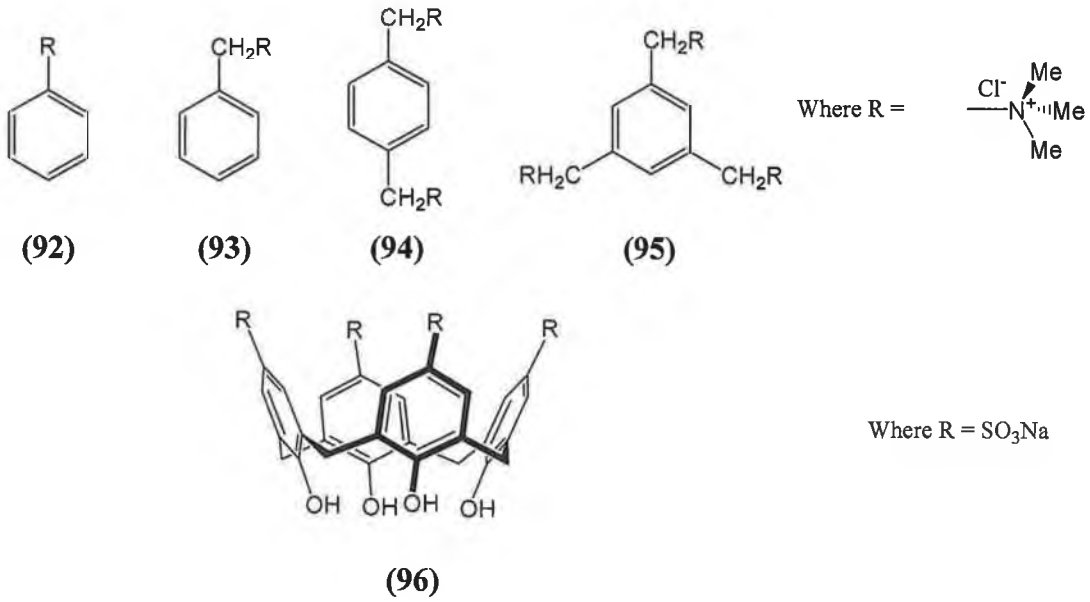


Figure 27(a): *Aromatic ammonium guest which can be encapsulated in to a p-sulfontated calix[4]arene.*

We believe that the use of a weak base such as K_2CO_3 will only generate the monophenoxide anion intermediate. In the literature it has been postulated by MM2 calculations that the monophenoxide anion of the distal 1,3 [(2-pyridylmethyl)oxy]-26,28-dihydroxy-calix[4]arene can exist in the cone or partial cone conformation and the two conformations are isoenergetic and approach the flattened cone conformation[91]. We believe that our compound can also achieve this conformation as the reaction progresses. The approach to the flattened cone (Figure 27(b)) would bring the phenoxide anion closer for nucleophilic attack on the encapsulated 3-nitrophthalonitrile driving the reaction. This may also explain the observed angle in the x-ray crystal structure of **(79)** of the tilted aromatic ring which lies at an angle of 138° from the plane of the bridging carbons of the calixarene.

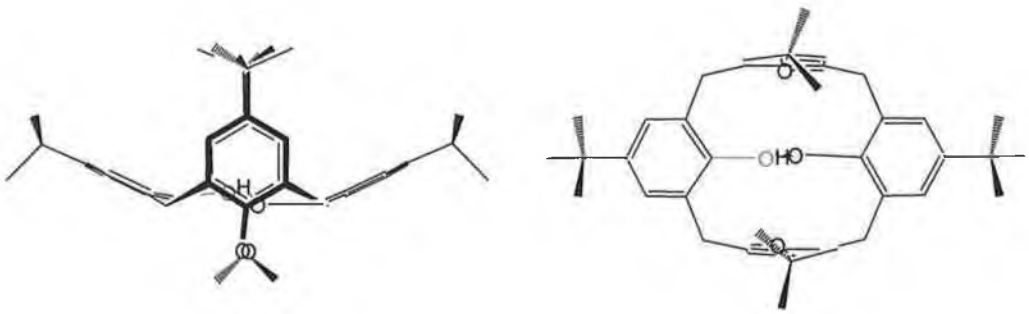


Figure 27(b): *Representation of the flattened cone conformation.*

Other work has demonstrated that bulky benzyltrimethylammonium groups can also be encapsulated into the upper rim of sulphonated calix[4]arenes, with the tetrahedral cation existing within the annulus of the calix[4]arene. Thus bulky tetrahedral species can fit into the calix[4]arene annulus, implying that it may indeed be possible for a tetrahedral intermediate to form within the upper annulus of the calix[4]arene see Figure 27(c). We believe the following process may be occurring: 1) first the perched encapsulation of the 3-nitrophthalonitrile on the upper rim of the calixarene. 2) the deprotanation of the lower rim hydroxy group of the calixarene which leads to the flattened cone, 3) followed by a quick displacement of the NO_2 group (Scheme 28).

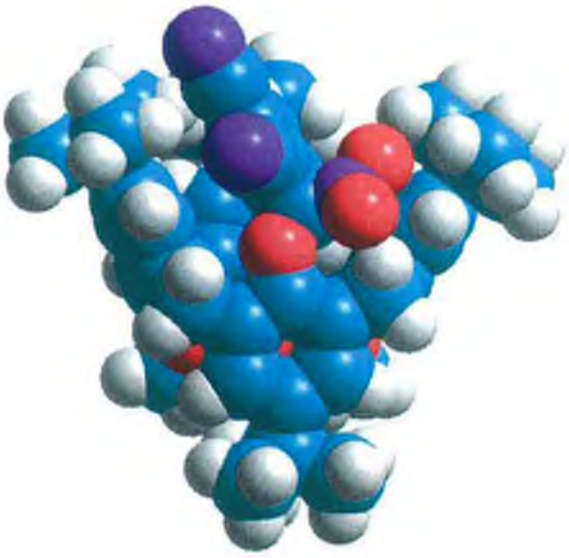
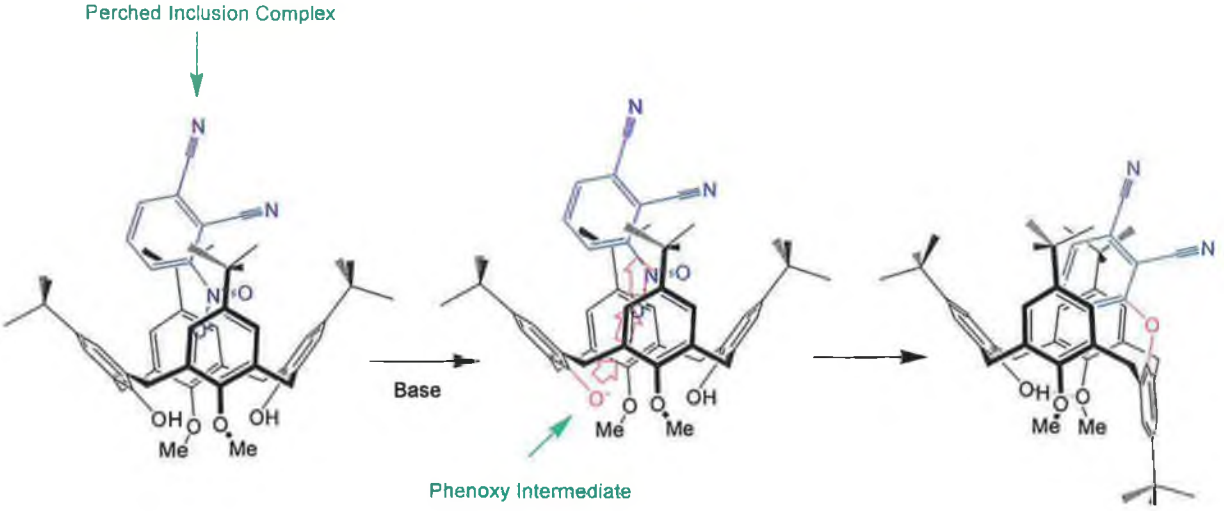


Figure 27(c): *Tetrahedral intermediate calculated using MM+.*



(89) **(90)** **(91)**

Scheme 28: *Mechanistic representation of partial cone formation.*

An alternative mechanism to explain the observed outcome involves the phenoxide ion completely rotating through the annulus of the calix[4]arene and attacking 3-nitrophthalonitrile on the outside of the upper rim. The final step would involve the phthalonitrile to tilt back into the upper rim to give the observed conformation. ^{1}H NMR of a mixture of 3-nitrophthalonitrile **(20)** and **(78)** in DMSO-d_6 were attempted however no real significant changes were observed.

Both mechanisms described are feasible, however further detailed mechanistic work will have to be carried out to elucidate a better understanding of the mechanism for this reaction.

2.4 *Preparation of Self Filled Partial Cone 5,11,17,23-tetra-t-butyl-26,27,28-trimethoxy-25-(-3-[-1,2-dicyanobenzene])calix[4]arene*

The final stage in the synthesis of the phthalonitrile calix[4]arene **(80)** is a methylation reaction using MeI and K_2CO_3. In this reaction we had to control the temperature to prevent self-condensation of **(79)** from occurring in the presence of base, therefore we proceeded to carry this reaction out at 60^0C under nitrogen.

To prepare **(80)** we initially treated **(79)** with methyl iodide and K_2CO_3 base (1:2:2 stoichiometric ratio) at 60°C. However only starting material was recovered after this attempt. A second reaction was set-up where the amount of methyl iodide and base was increased to a stiochometric ratio of 1:4:4 , again only starting material was recovered. We realised that the volatility of methyl iodide was the problem (boiling point of 41°C to 43°C), so we chose to use a large excess of methyl iodide to calixarene (1:400) and the stiochometric ratio of calixarene :base was held at 1:4. A comparison study was carried out to determine the difference between a dropwise addition of methyl iodide over one hour compared to a total addition at the beginning of the reaction. Both reactions yielded the same results with yields in the range of only 20 %. We believed the low yields may be a result of using weak base, removal of the last proton in a calix[4]arene is quite difficult since it is highly stabilised by intramolecular hydrogen bonding as confirmed by the x-ray structure. To improve yields it was found that NaH and 300 % molar excess of MeI could be used to give **(80)** in a yield of 90 %[95].

Purification of **(80)** was achieved on silica gel by using a hexane: ethyl acetate 80:20 mobile phase. The first spot to elute from this column was the target compound **(80)** and the second spot was our starting material **(79)**.

The ^{1}H NMR of **(80)** (Figure 28) did not differ significantly from **(79)** (Figure 20). Two different types of Me groups are found at 3.7 and 3.6 ppm in a 2:1 ratio. The ^{1}H NMR of **(80)** again reveals an upfield shift for the H_4 and H_5 protons of the phthalonitrile indicating that the phthalonitrile is still within the calixarene annulus. The crystal structure of **(80)** grown from ethyl acetate and hexane is shown in Figure 29 and confirms that the phthalonitrile has

remained within the calixarene annulus. A single temperature ^{1}H NMR study in nitrobenzene-d_5 at 125°C revealed that the conformation of **(80)** is again stable. This indicates that there is no free rotation of the methoxy groups through the annulus of the calix[4]arene because the phthalonitrile group is blocking the inner annulus and secondly this result indicates that the original H-bond in **(79)** does not appear to be significant in the stabilisation of **(79)**. However, the removal of the hydrogen bond removes the tilt of the phthalonitrile ring in **(79)** see Figure 29. However the removal of this tilt does not lead to a significant change in symmetry since there is very little difference in the ^{1}H NMR of **(80)** compared to **(79)**. (also see Chapter 7)

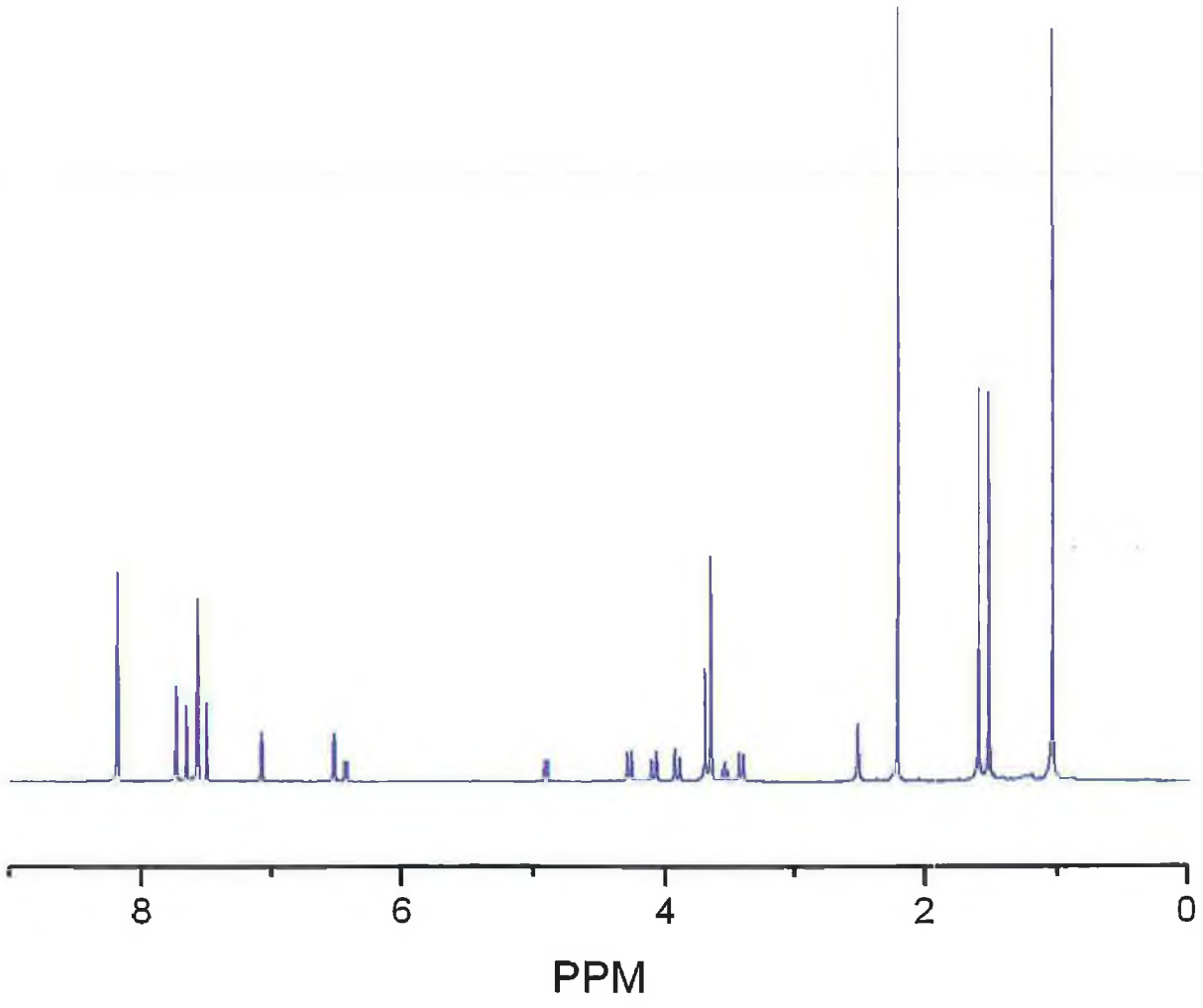


Figure 28: *^{1}H NMR of (80)*

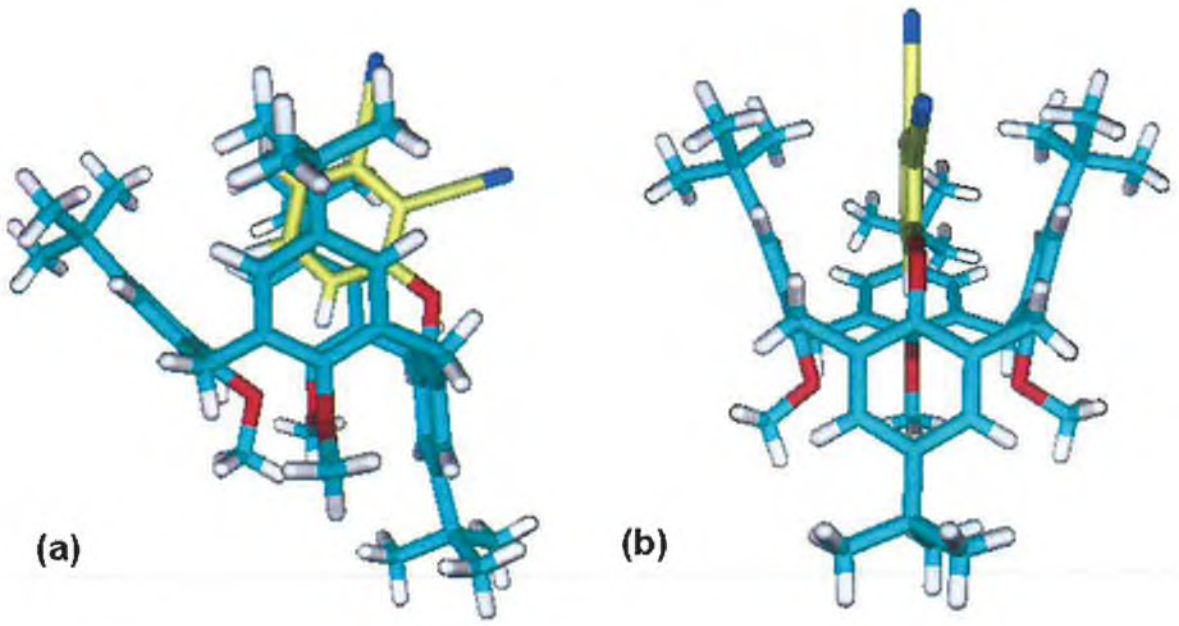


Figure 29: *(a) Side view of* ***(80)****'s crystal structure (b) Front view of* ***(80)****'s crystal structure*

2.5 Experimental

Column chromatography was carried out on all of the compounds using Riedel de Haen silica gel 60. Thin layer chromatography (TLC) was carried out on a Riedel de Haen silica 60F254 plates using specified solvents. All solvents used were HPLC grade.

A variety of techniques were under taken to elucidate the structure of these compounds. All NMR experiments where carried out on a Bruker AM 400 spectrometer and this means our ^{1}H NMR spectra were measured at 400 MHz while the ^{13}C NMR are measured at 100 MHz. Mass spectra were analysed on a Esquire-Bruker/Hewlett Packard LC-MS 1100 series, equipped with an electrospray ion source. IR spectra where recorded on a Perkin Elmer 2000 FT-IR spectrometer. Melting points are carried out on a Bibby Stuart Scientific melting point SMP1. Crystal structures where run an a Bruker-Axis Smart Apex CCD three-circle diffractometer.

2.5.1 5,11,17,23-Tetra-tert-butyl-25,27-Dihydroxy-26,28-Dimethoxycalix[4]arene (78).

K_2CO_3 (4.25 g, 30 mmol), **(77a)** (2.00 g, 3.09 mmol) and Methyl iodide (0.75 ml, 12.35 mmol) were heated to 70°C for one hour in anhydrous DMF (25 ml). The reaction mixture was then poured on to ice water (100 ml), this layer was then extracted with ethyl acetate (3 x 30 ml). The organic extracts were combined, then washed with a saturated saltwater solution, dried over Mg_2SO_4, filtered and evaporated to yield a cream powder. The crude product was recrystallised from ethanol and further purified by column chromatography (using 90:10 hexane: ethyl acetate) a white powder was obtained (0.95 g, 1.36 mmol, 44 % yield).

Product was characterised by **^{1}H NMR:** ($CDCl_3$) δ (ppm); 0.94, (s, 18 H, t-Bu); 1.30, (s, 18 H, t-Bu); 3.33, (d, 4 H, J=12 Hz, Ar-CH_2-Ar); 3.95, (s, 3 H, CH_3); 4.28, (d, 4 H, J=13 Hz, Ar-CH_2-Ar); 6.77, (s, 4 H, Ar H); 7.07, (s, 4 H, Ar H); 7.27, (s, 2 H, OH).
ESI m/z: 699 ($M + Na^+$) $C_{46}O_4H_{60}$

2.5.2 Self filled partial cone 5,11,17,23-tetra-t-butyl-27-hydroxy-26,28-dimethoxy-25-(-3-[-1,2-dicyanobenzene])calix[4]arene (79).

K_2CO_3 (0.82 g, 5.92 mmol), **(78)** (1.00 g, 1.48 mmol) and 3-nitrophthalonitrile (1.02 g, 5.92 mmol) were stirred under vacuum in anhydrous DMF (15 mls) for one day at RT. The reaction mixture was then poured on to ice water (50 ml), filtered and the solid was washed with hot water (2 x 25 mls). The crude brown solid was purified by column chromatography using 80:20hexane: ethyl acetate, a white solid was obtained (0.45 g, 0.55 mmol, 37 % yield).

Product was characterised by **^{1}H NMR** (Nitrobenzene d_5) δ (ppm); 0.99, (s, 18 H, t- Bu); 1.44, (s, 9 H, t-Bu); 1.51, (s, 9 H, t-Bu); 3.49, (d, 2 H, J= 12.8 Hz, Ar-CH_2-Ar); 3.56, (t, 1 H, J= 8.0 Hz, Ar-H); 3.73 (s, 6 H, O-CH_3); 3.92, (d, 2 H, J= 15.2 Hz, Ar-CH_2-Ar); 4.06, (d, 2 H, J= 15.2 Hz, Ar-CH_2-Ar); 4.26, (d, 2 H, J= 12.8 Hz, Ar-CH_2-Ar); 4.65, (d, 1 H, J= 8.0 Hz, Ar-H); 6.45, (d, 1 H, J= 8.0 Hz, Ar-H); 6.58, (s, 2 H, Ar-H); 7.14, (s, 2 H, Ar-H); 7.4, (s, 2 H, Ar-H); 7.62, (s, 2 H, Ar-H); 7.71, (s, 1 H, OH).

ESI m/z: 825 ($M + Na^+$), 841 ($M + K^+$) $C_{54}H_{62}O_4N_2$

IR: (KBr [cm^{-1}]): 3342 cm^{-1} ν(O-H), 2960 cm^{-1} ν(Bu_t), 2224 cm^{-1} ν(CN).

MP: 256 – 258°C

Crystal Structure: See attached cd.

Elemental Analysis: C= 80.66 % H = 8.08 % N = 3.2 5 % (Theoretical $C_{54}H_{62}O_4N_2$ C= 80.76 % H = 7.78 % N = 3.49 %)

2.5.3 Self filled partial cone 5,11,17,23-tetra-t-butyl-26,27,28-trimethoxy-25-(-3-[-1,2-dicyanobenzene])calix[4]arene (80).

K_2CO_3 (0.5 g, 3.62 mmol), and **(79)** (0.5 g, 0.62 mmol) in DMF/THF (15 cm^3 50:50 mix) were heated to 60°C under nitrogen. Methyl iodide (10 mls, 0.16 mmol) was added dropwise over one hour and the mixture was allowed heat for a further 24 hrs. On day two K_2CO_3 (0.5 g, 3.62 mmol) and methyl iodide (10 mls, 0.16 mmol) were added and this was repeated again on day 3. 24 hrs later the methyl iodide was distilled off and the reaction mixture was then dissolved in chloroform and washed with a saturated saltwater solution, dried over Mg_2SO_4, filtered and evaporated to yield a cream powder. The crude product was purified by column chromatography using 90:10 hexane: ethyl acetate a white powder was obtained (0.11 g, 21.62 % yield).

Product was characterised by **^{1}H NMR** (Nitrobenzene d_5) δ (ppm): 0.98, (s, 18 H, t-Bu); 1.45, (s, 9 H, t-Bu); 1.53, (s, 9 H, t-Bu); 3.35, (d, 2 H, J=12.4 Hz, Ar-CH_2-Ar); 3.47, (t, 1 H, J= 8.8 Hz, Ar-H); 3.58, (s, 6 H, O-CH_3); 3.63, (s, 3 H, O-CH_3); 3.84, (d, 2 H, J= 14.8H z, Ar-CH_2-Ar); 4.02, (d, 2 H, J= 14.8 Hz, Ar-CH_2-Ar); 4.21, (d, 2 H, J= 12.4 Hz, Ar-CH_2-Ar); 4.84, (d, 1 H, J= 8.8 Hz, Ar-H); 6.36, (d, 1 H, J= 8.8 Hz, Ar-H); 6.45, (s, 2 H, Ar-H); 7.01, (s, 2 H, Ar-H); 7.43, (s, 2 H, Ar-H); 7.59, (s, 2 H, Ar-H)

ESI: m/z 839 ($M + Na^+$), 855 ($M + K^+$) $C_{55}H_{64}O_4N_2$

IR: (KBr [cm^{-1}]): 2962 cm^{-1} ν(Bu_t), 2225 cm^{-1} ν(CN).

MP: 278 – 280°C

Crystal Structure: See attached cd.

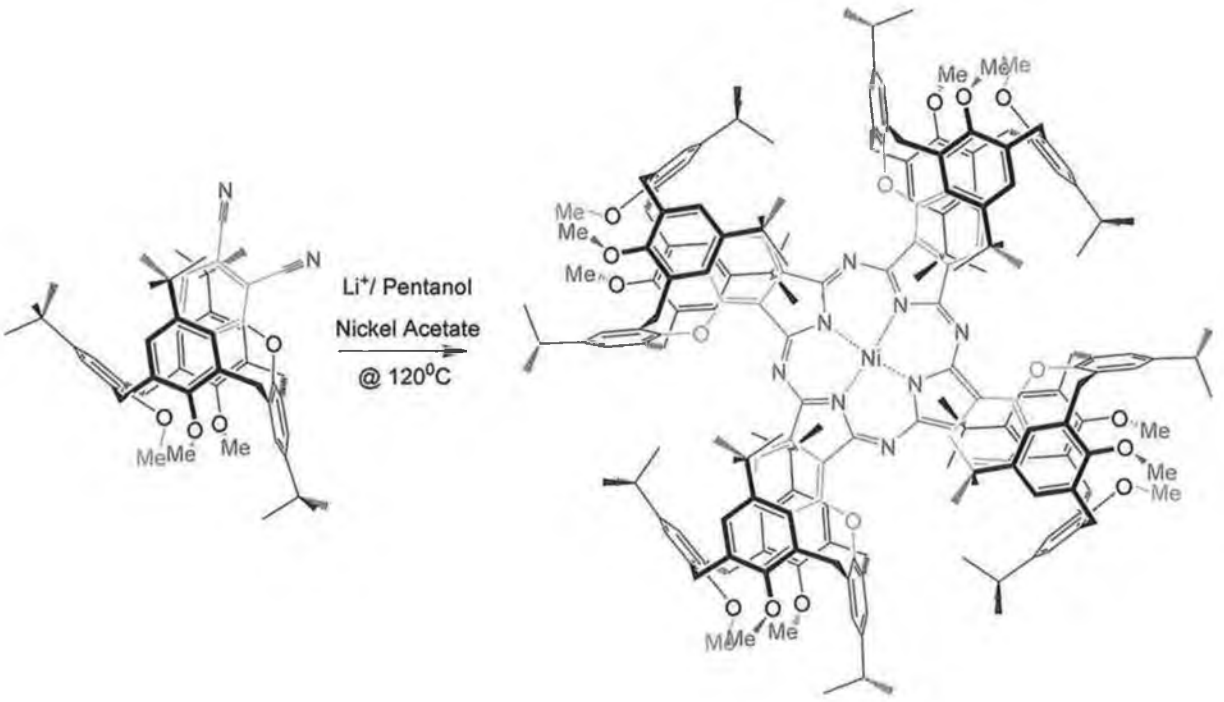
3. 1-(-27-[Partial Cone 5,11,17,23-Tetra-tert-butyl-25,26,28-trimethoxy Calix[4]arene]) Phthalocyaine

3.1 Tetra-t-butylCalix[4]arene Phthalocyanine in the α-Position

Given the difficulty arising from the methylation of the final hydroxyl group of **79** we attempted to self-condense **(79)** using Li/pentanol conditions at 110-120°C. It is known that hydroxyl groups can interfere in the condensation process if present in the phthalonitrile precursors. However we believed that the free hydroxy in **(79)** is highly sterically hindered and as such may not interfere in the condensation of **(79)**. On the self-condensation of **(79)** a brown product formed after one hour with no further colour change. TLC ($CHCl_3$ as eluent) indicated the absence of any phthalocyanine product. The reaction was repeated again, this time it was stopped after 30 minutes, again no pigment was obtained as determined by TLC.

After developing an efficient preparation of **(80)** (NaH method) we proceeded to self-condense **(80)** under Li/pentanol conditions at 110-120°C. After 24 hrs the mixture remained a brown colour, indicating that no phthalocyanine had formed. We believe that this maybe due to steric hindrance. It had been previously reported that sterically constrained Pcs could be prepared using Ni templation[96]. This method was then attempted using Li/pentanol in the presence of nickel acetate. After 1 hour of reaction time the mixture had turned to a dark brown colour and TLC indicated the absence of any phthalocyanine product. The reaction was attempted again at a higher concentration of **(80)**, again the reaction mixture turned dark brown after an hour of reaction time with no evidence of phthalocyanine formation by TLC.

Another repeat of the reaction at higher concentration was performed, this time the reaction was monitored by UV-Vis. The UV-Vis analysis of the reaction mixture gave a weak peak at 720nm (Figure 30), which may correspond to phthalocyanine formation even though no colour change was noted. This reaction mixture was treated with water and the brown precipitate was collected. A MALDI MS was obtained on this product and evidence of the Ni phthalocyanine was indicated by a cluster at 3349 which corresponds to a M+23(Na). It would appear that the presence of the calixarene is causing a large steric effect between the phthalonitrile partners preventing efficient cyclisation from occurring.



(80) (73)

Scheme 29: *Synthesis of the tetra-t-butylcalix[4]arene nickelphthalocyanine in the 3-position.*

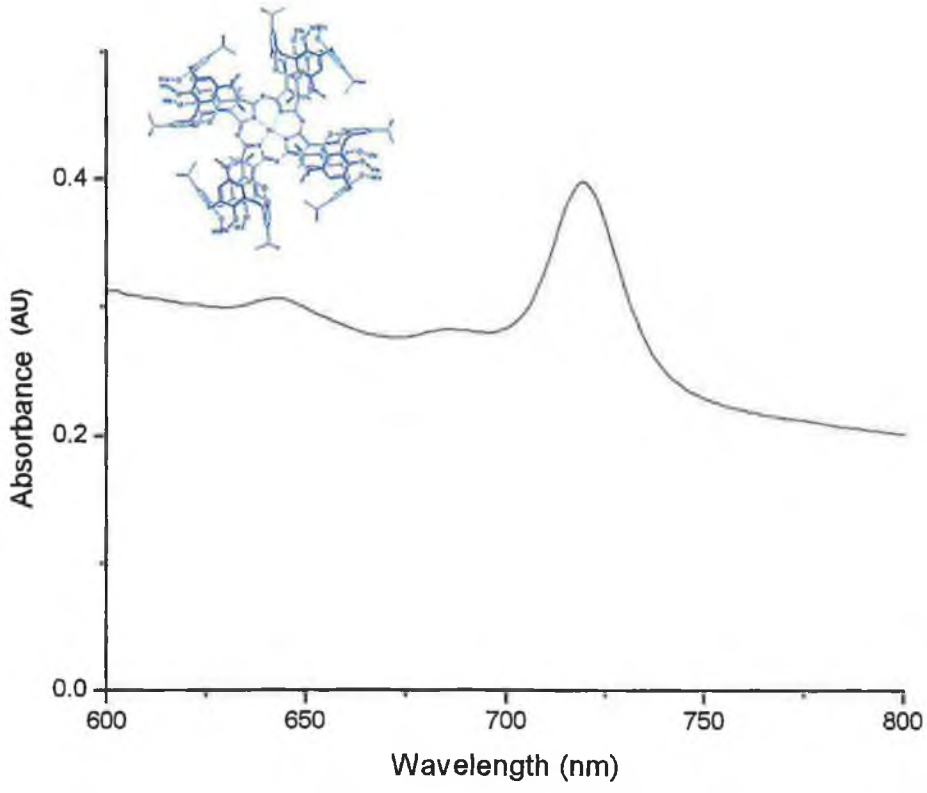


Figure 30: *UV-Vis spectrum of* ***(73).***

This steric hindrance is more pronounced when a CPK diagram is looked at (Figure 31). In this diagram you can see that on one side base initiated attack of the nitrile is blocked by the tert-butyl group and on the other side the oxygen hinders the formation of the dimer intermediate Figure 31.

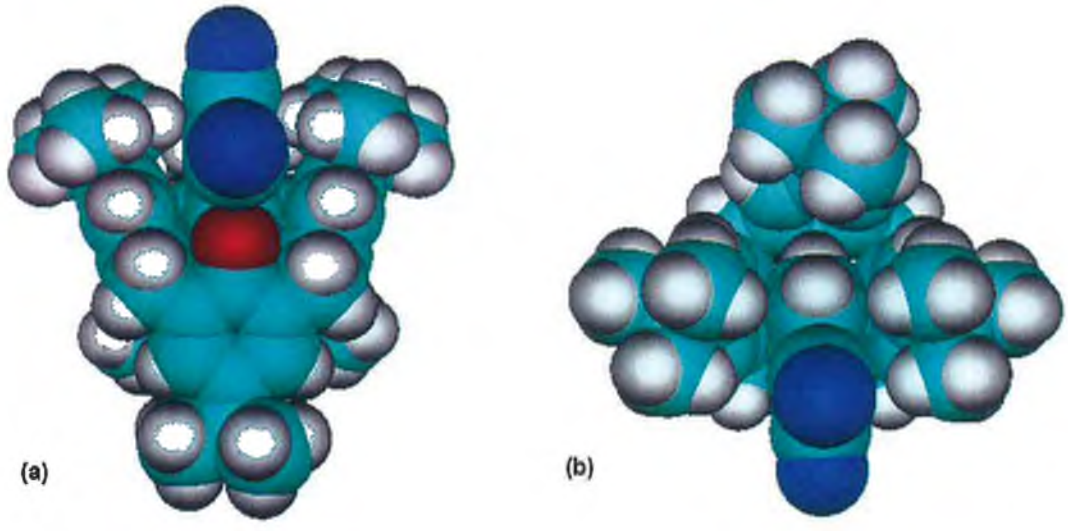
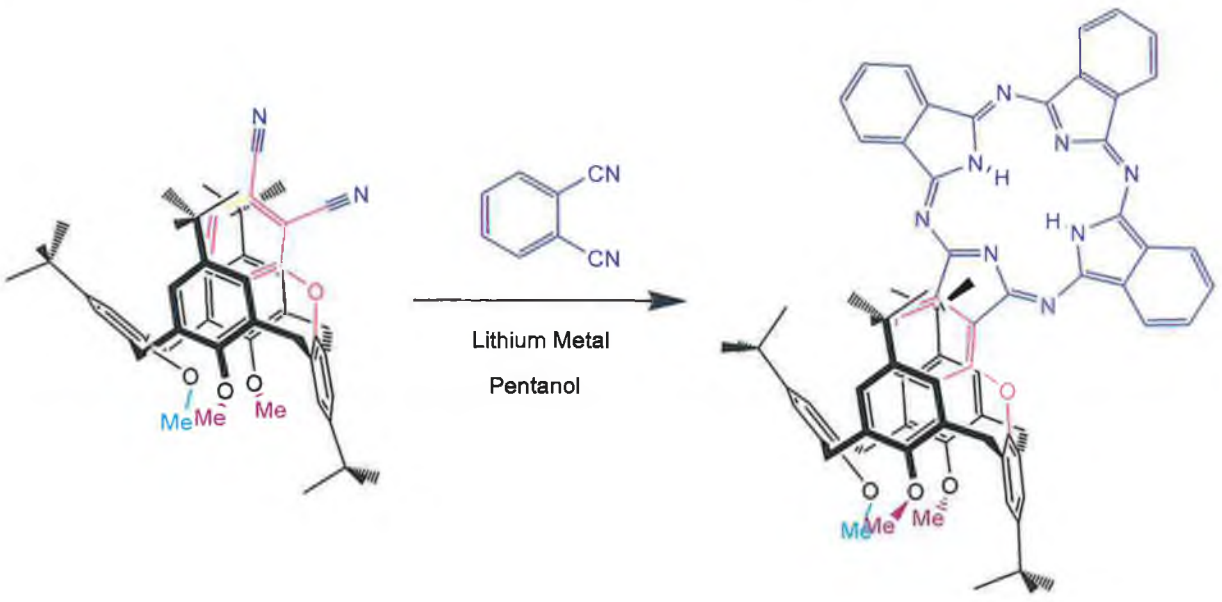


Figure 31: *CPK spacefill model of* ***(80)*** *(a) top view (b) front view.*

3.2 Synthesis of Unsymmetrical Phthalocyanine

Phthalocyanine **(97)** was synthesised via a cross condensation of **(80)** with **(8)** under Li/pentanol conditions at 110-120°C for 24 hrs see Scheme 30. Cross condensation between different phthalonitriles will normally lead to a mixture of phthalocyanines. However by using a stiochometric ratio of the partner: calixarene (9:1) led to the formation of only two phthalocyanines **(97)** and the unsubstituted phthalocyanine derivative **(1)**.



(80) **(97)**

Scheme 30: *Synthesis of unsymmetrical (97).*

This crude reaction mixture could easily be separated on a silica gel column using chloroform as the eluent since the unsubstituted phthalocyanine derivative is insoluble in all organic solvents. On the column only a single blue band was isolated. This was then re-columned on silica and then further purified by size exclusion chromatography using SX-3 bio-beads. The bio-bead column used THF as the eluent and it was noted that there was only a single band present. Yields of around 20.5 % were achieved for **(97)** after chromatography.

MALDI-TOF mass-spectrometry is a widely used technique in the molecular weight determination identification of phthalocyanines. In high molecular weight Pcs such as **(97)** neat samples can be used[97]. The presence of a single cluster at 1202 m/z corresponds to **(97)**. It was also noted that the sodiated and potassiated molecular ions where found at 1225 m/z and 1241 m/z respectively see Figure 32. However no other calixarene-substituted phthalocyanines were observed by MALDI-TOF.

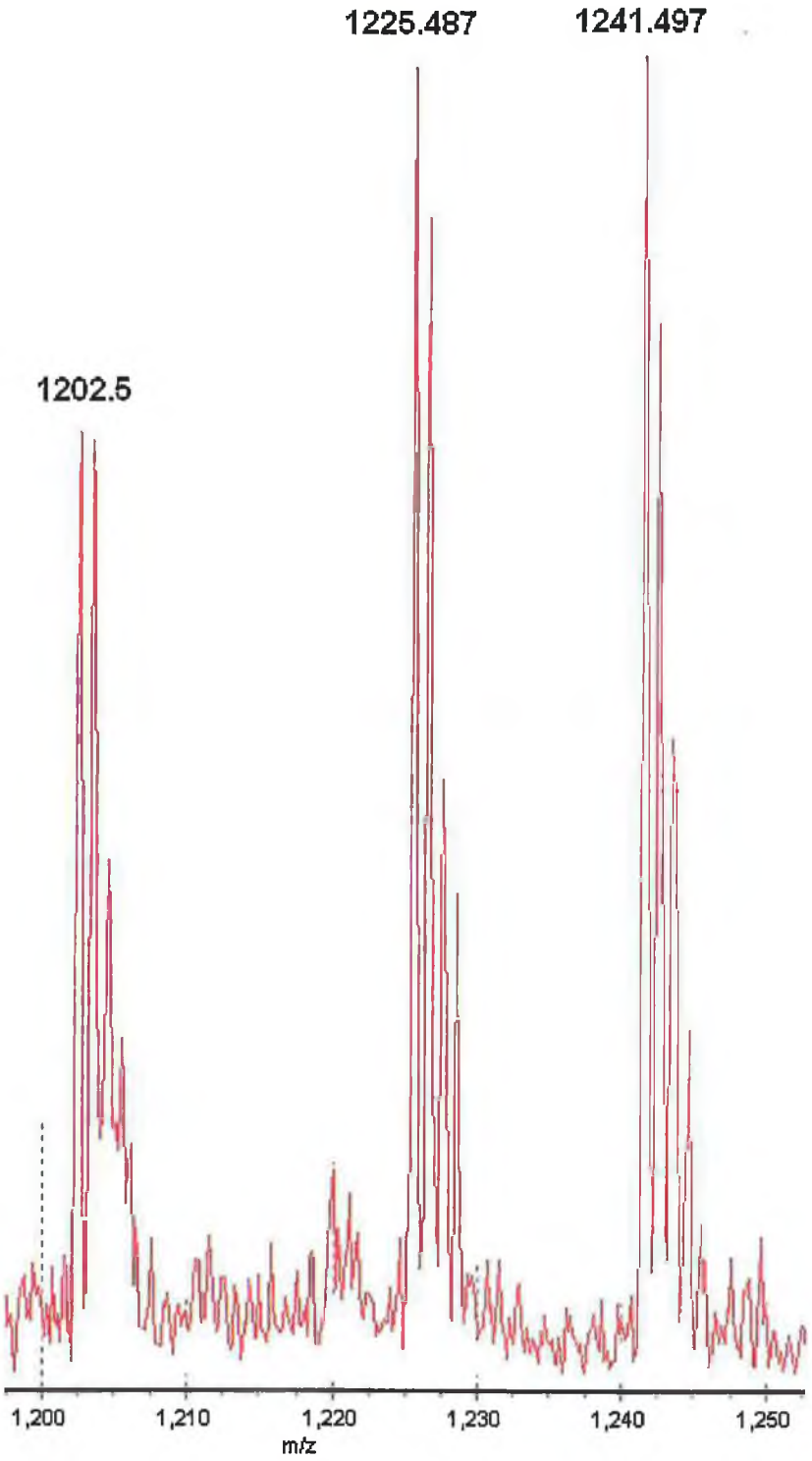


Figure 32: *MALDI-TOF spectrum of (97).*

^{1}H NMR was used on this compound in an attempt to verify the positioning of the phthalocyanine in relation to the calixarene basket. The ^{1}H NMR of **(97)** in toluene-d_8 (Figure 33) suggests that the peripheral benzo ring containing the calixarene still exists as an inclusion complex. There is a doublet present at 5.5 ppm and a triplet at 4.55 ppm. Interestingly, the t-butyl groups show up as three peaks. The peak at 0.5 ppm can be assigned to the two symmetrical t-butyls of the calixarene, which lie above and below the phthalocyanine ring, these peaks are slightly upfield shifted as a result of the anisotropic effect of the phthalocyanine ring. The conformation of the calixarene has slightly changed, the AB spectrum of the bridging protons has gone back toward an AX system indicating that all rings of the calixarene are now parallel and the calixarene exists as a true partial cone.

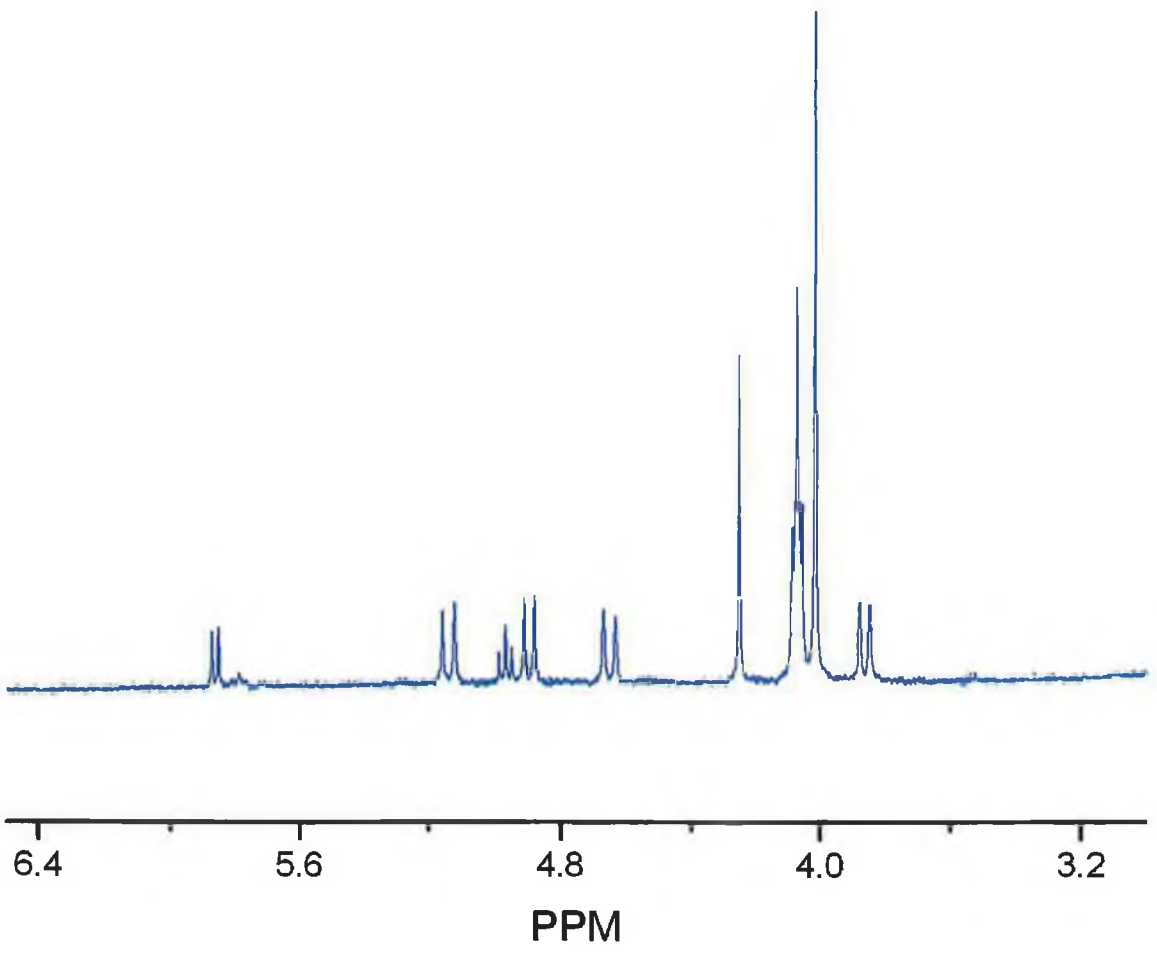
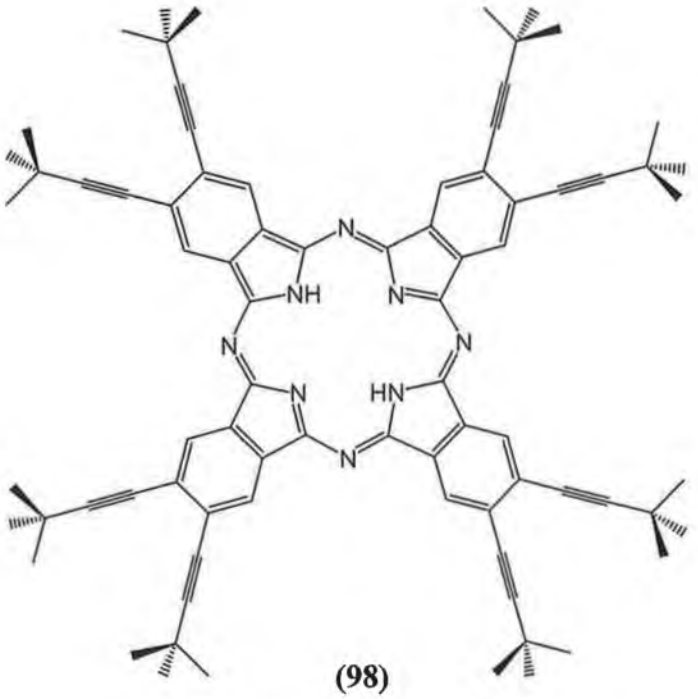


Figure 33: *^{1}H NMR of (97) in toluene-d_8*

^{1}H NMR can also be used to identify the presence or absence of π-π stacking by measuring the chemical shift of the phthalocyanine internal protons. These internal protons usually

appear at around –1 to –6 ppm in the presence of π-π stacking. In the case of **(97)** the internal protons were observed at –0.3 and –0.28 ppm when run in nitrobenzene-d_5 and toluene-d_6 respectively at a concentration of 2 x 10^{-4} M. When these values are compared to the literature it appears that the single calixarene substituent has a similar shift to an octa-t-butylethynyl system **(98)** shown in Figure 34 at the same concentration[98]. When Leznoff and co-workers investigated this system they found that the bulky nature of these t-butylethynyl moieties out performed the linear alkyl derivatives, this implies that the steric bulk of the eight groups in this phthalocyanine plays a vital role in reducing aggregation. In our system the partial cone calix[4]arene substituent is bulky but this is not the reason for the reduced π-π stacking . Our effect is owing to the conformational orientation of the calix[4]arene which leads to two of the upper rim t-butyl groups protruding out either side of the phthalocyanine in a picket fenced type arrangement see Figure 35. These two t-butyl groups prevent the phthalocyanines from lying flat on top of each other preventing stacking from occurring.



(98)

Figure 34: *Octa-t-butylethynyl phthalocyanine (98)*

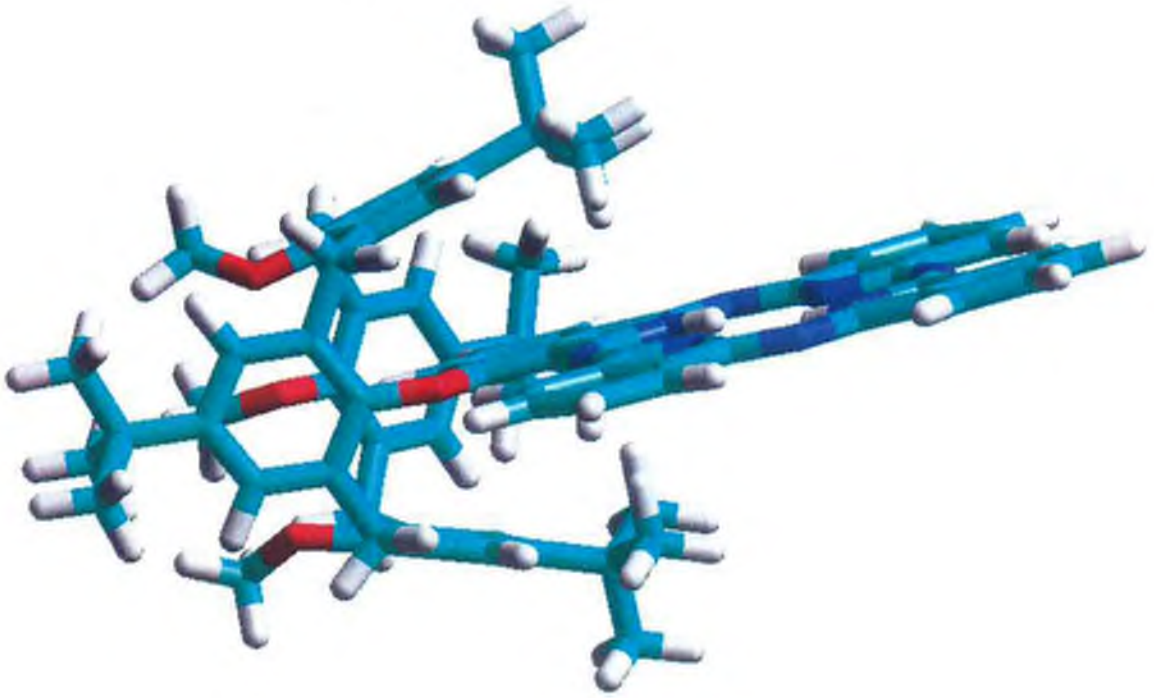


Figure 35: *Side view of unsymmetrical phthalocyanine (97).*

The UV-Vis spectrum of **(97)** shows the outer Q-band red-shifted to 707 nm, which is expected for a single alkoxy substituent in the 1-position of the phthalocyanine in HPLC grade chloroform (Figure 36). Previously our ^{1}H NMR samples where run in aromatic solvents, which help to break up π-π stacking at the central core of the phthalocyanine moiety. In order to reduce this effect of solvent interference a sample was tested in deuterated chloroform. This had a very interesting effect; the deuterated chloroform decomposed the sample over time from a green solution to a colourless liquid. When this compound was then dissolved in both bench grade chloroform and even freshly distilled chloroform no decomposition was found. Deuterated chloroform is well known to contain hydrochloric acid and phosgene, which could be possibly decomposing the phthalocyanine calix[4]arene over time. When a UV-Vis spectrum of **(97)** in $CDCl_3$ was taken at 5-minute intervals a loss in Q-band intensity was noted over time (Figure 37). This study also showed an increase in an infrared band at 1190 nm. Triethylamine was added in an attempt to reverse the decomposition of the Q-band, upon addition decomposition stopped. This study indicates that decomposition of **(97)** begins with the protonation of one of the *meso*-nitrogens of the phthalocyanine ring.

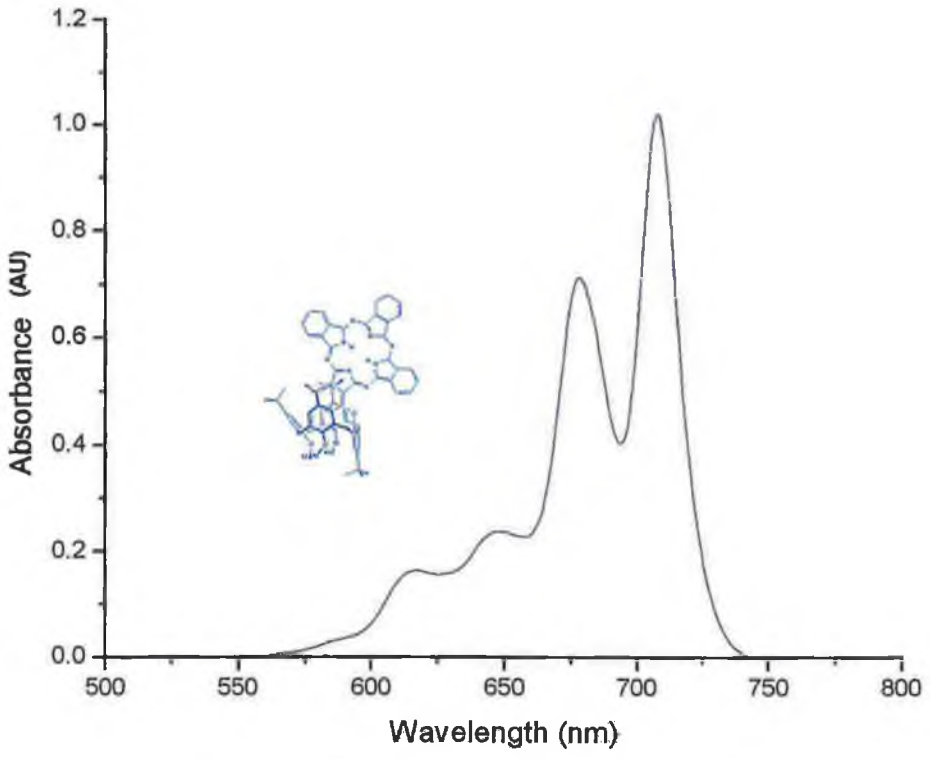


Figure 36: *Unsymmetrical phthalocyanine (97) in chloroform.*

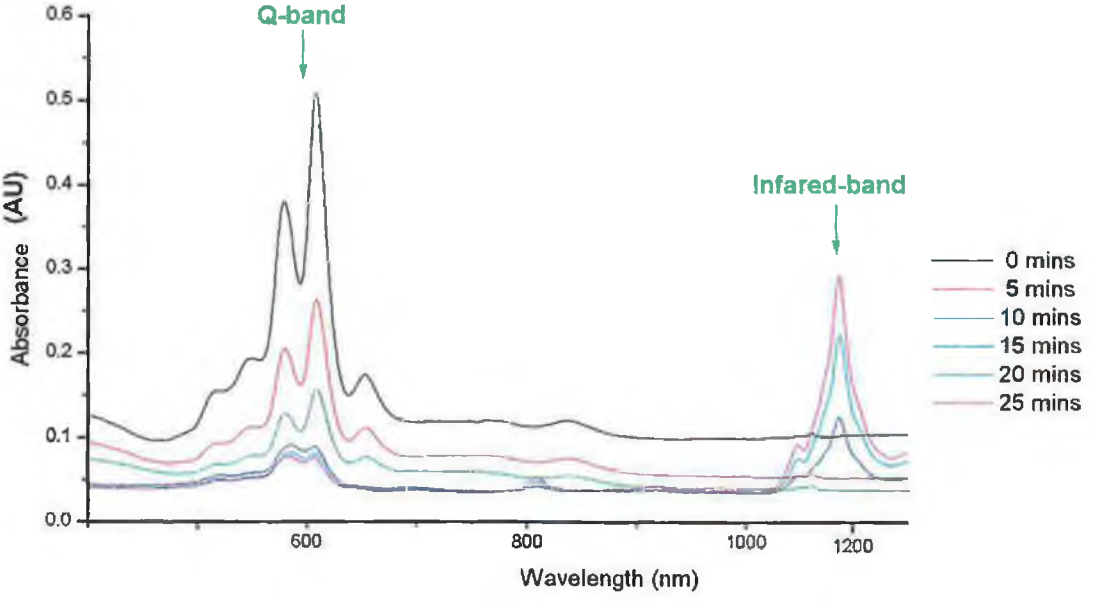


Figure 37: *Decomposition of (97)'s Q-band over time in deuterated chloroform.*

3.3 UV-Vis Aggregational Studies

Aggregation is synonymous with phthalocyanines, however compound **(97)** looks promising as a non-aggregated system since the internal protons where found to be at -0.3 ppm. This was similar to those internal protons of octa-t-butylethynyl phthalocyanine **(98)**, which is recognized as a very good non-aggregated system. In order to investigate the aggregational properties of **(97)** we compared **(97)** with **(98)** using two different UV-Vis experiments in an attempt to compare aggregational behaviour.

The first of these UV-Vis experiments is a concentration study, which can be seen in Figure 38 and 39 for **(98)** and **(97)** respectively. The concentrations used were 1 X 10^{-04} M, 5 X 10^{-05} M, 1 X 10^{-05} M, 5 X 10^{-06} M, 1 X 10^{-06} M, 5 X 10^{-07} M and 1 X 10^{-07} M. Aggregation is generally noted by a blue shift in the Q-band or changes in shape of the Q-band peak. In both traces we notice very little changes in the Q-band shape even at high concentration, which is consistent with a non-aggregated phthalocyanine species.

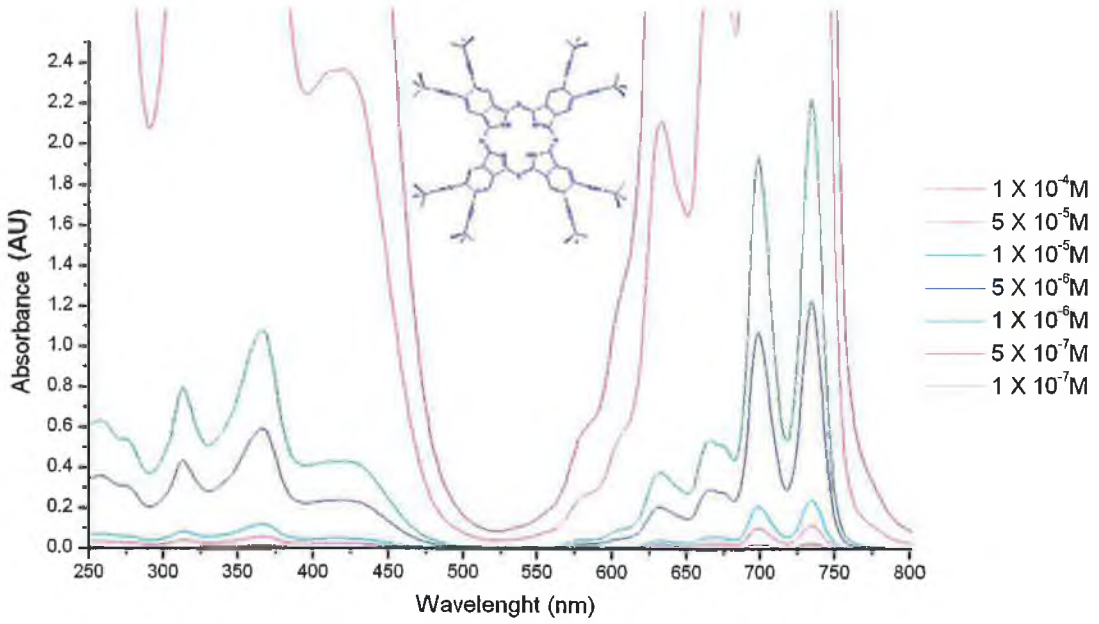


Figure 38: *Concentration study of octa-t-butylethynyl phthalocyanine (98).*

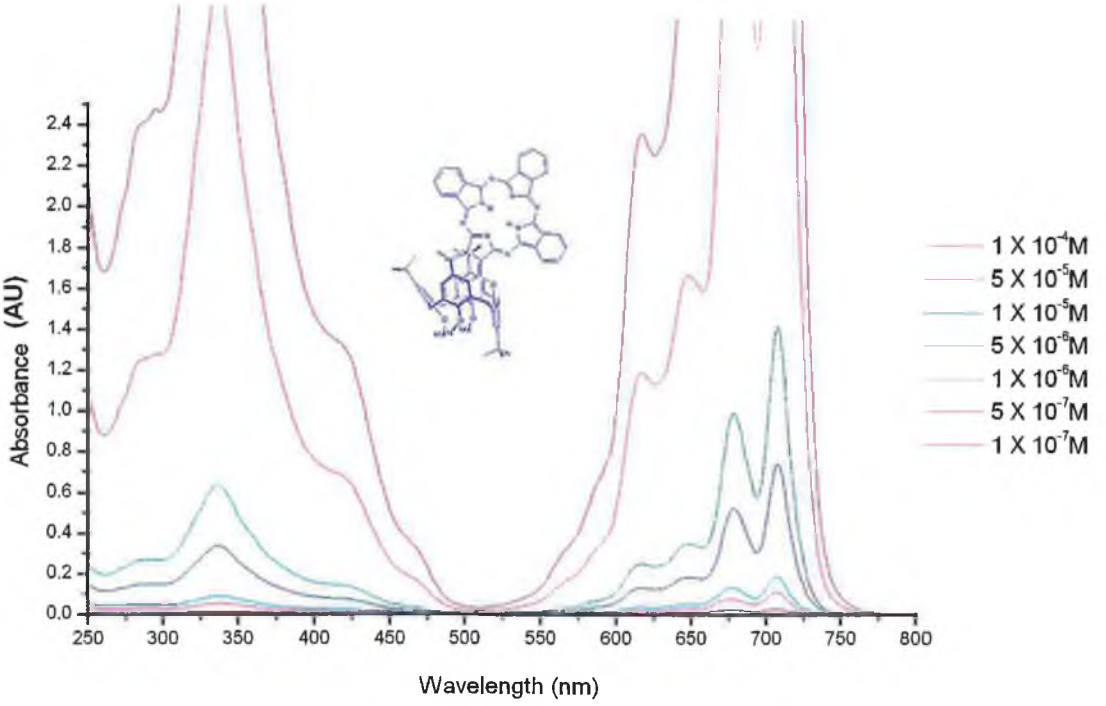


Figure 39: *Concentration study on unsymmetrical phthalocyanine* ***(97).***

A second UV-Vis study was undertaken involving a gradual change in polarity of the solvent with greater additions of ethanol. McKeown[82] and McGrath[83] where the first pioneers of this technique for dendritic phthalocyanines. In this experiment we kept the phthalocyanine concentration at 1 X 10^{-5} M, while increasing the percentage volume of ethanol. The additional ethanol should force the phthalocyanines together to aggregate because of its polar nature. As in the concentration study we should notice two things that would indicate the presence of aggregation: 1) blue shift of the Q-band and/or 2) a change in shape of the Q-band. From Figure 40 it can be seen that Leznoff's octa-t-butylethynyl phthalocyanine **(98)** starts to aggregate in a 10 % ethanol solution. When increasing amounts of ethanol were added to the octa-t-butylethynyl phthalocyanine more dramatic changes of the Q-band occurred until a dimeric species was reached. This emulates what McGrath found for his peripherally substituted dendritic phthalocyanines. He found the smallest dendrimer started to aggregate in a 10 % ethanol solution. However by increasing the size of the dendron (third generation) the onset of aggregation was shifted to higher ethanol content. McGrath also noticed for peripheral substituted third generation dendritic phthalocyanines that precipitation occurred at ~50 % ethanol[83]. However in the case of the octa-t-butylethynyl phthalocyanine no precipitation was noted even at 90 % ethanol solution, although slight aggregation was noticed to occur at 10 % ethanol.

Our unsymmetrical phthalocyanine behaves rather differently see Figure 41. For **(97)** we noticed no dramatic shift or change in the shape of the Q-band indicating that there is very little aggregation present. This result indicates that our unsymmetrical phthalocyanine aggregates less in polar solvents. It also verifies the important contribution the partial cone conformation makes in blocking phthalocyanine aggregation.

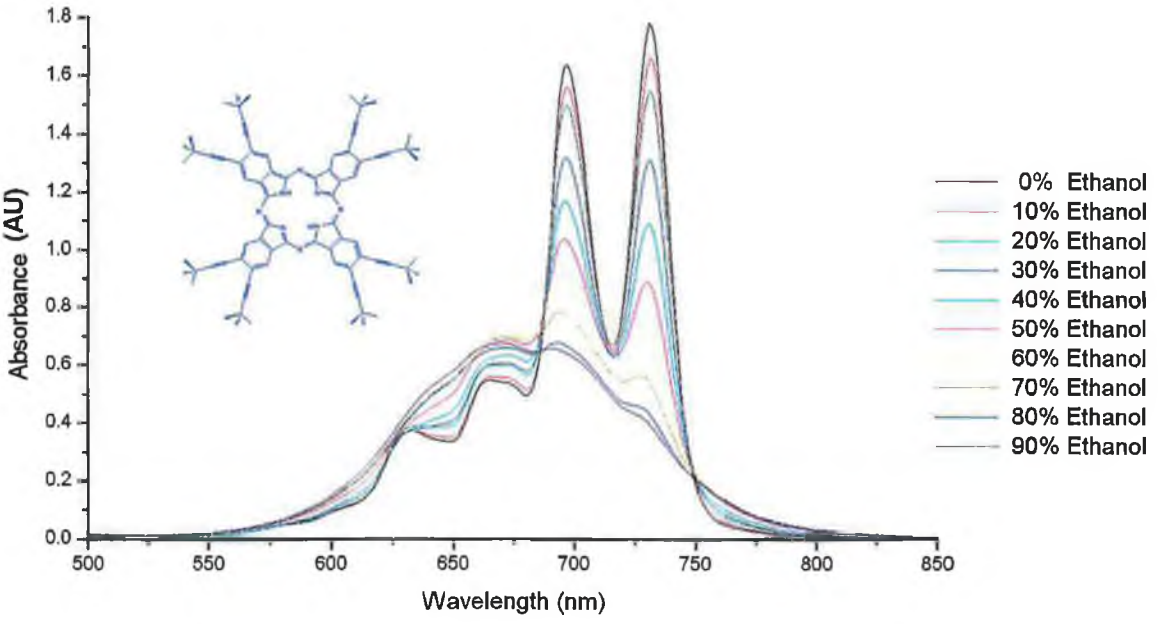


Figure 40: *Ethanol UV-Vis study on octa-t-butylethynyl phthalocyanine **(98)**.*

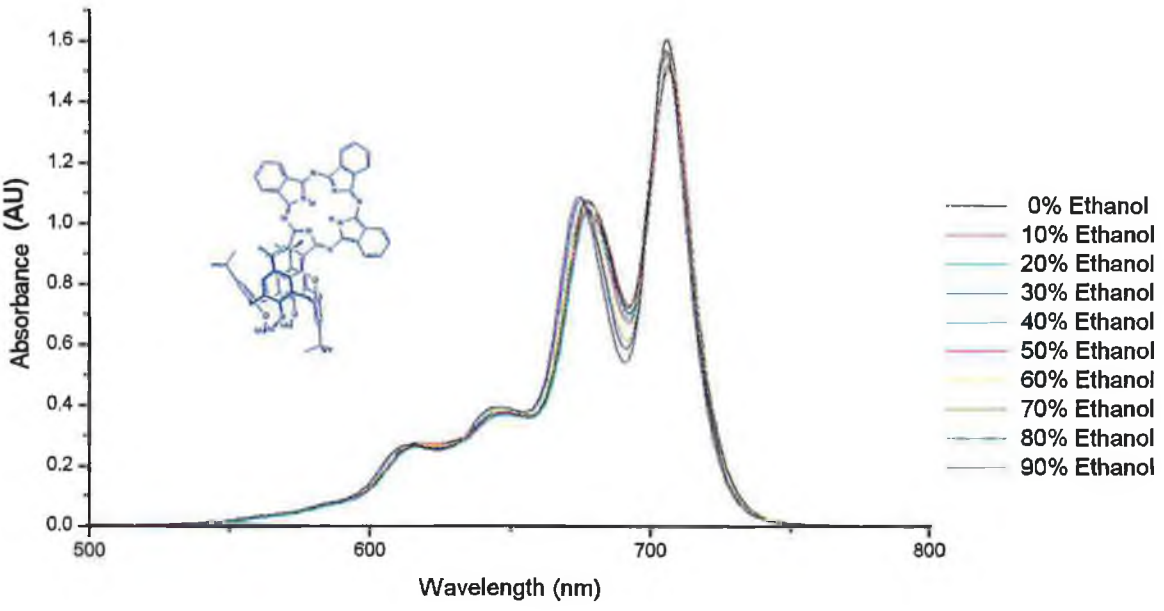


Figure 41: *Ethanol UV-Vis study on unsymmetrical phthalocyanine **(97)**.*

However if we want to know if **(97)** is totally deaggregated, then we must look at its UV-Vis absorption in the solid state. If we have a non-aggregated system we should see the equivalent UV-Vis spectrum in the solid state (Figure 42) as we do in solution (Figure 36) of **(97)**. As you can see from the results they are totally different indicating there is aggregation present in the solid state. This indicates that we probablely have dimer formation because the partial cone picket fence calix[4]arene substitutent will only allow for this kind of aggregation and secondly the shape of the Q-band indicates dimer formation[99].

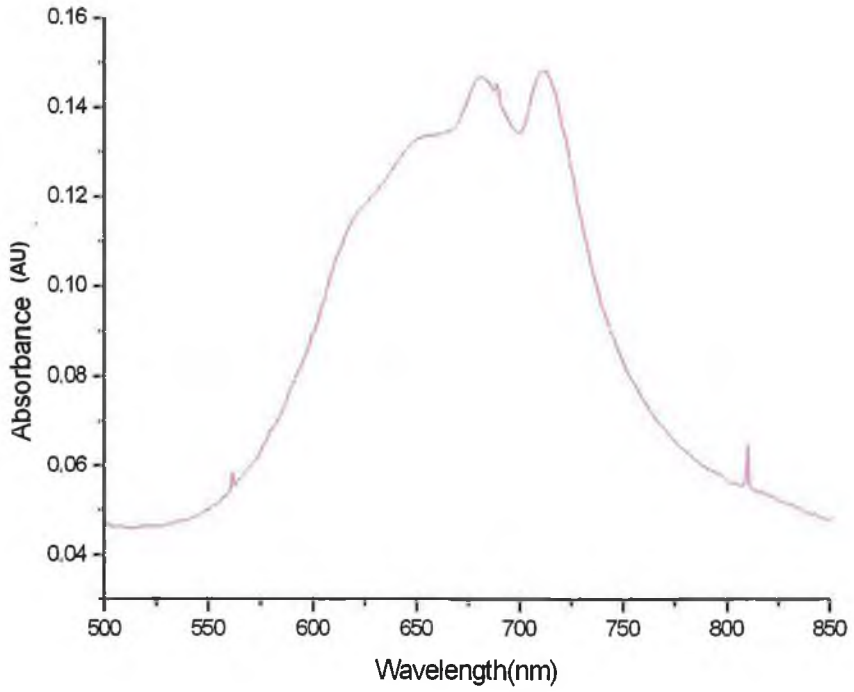


Figure 42: *Solid state UV-Vis of* ***(102)***.

3.4 Experimental

Column chromatography was carried out on all of the compounds using Riedel de Haen silica gel 60. Thin layer chromatography (TLC) was carried out on a Riedel de Haen silica 60F254 plates using specified solvents. Size exclusion chromatography was carried out using SX-3 bio-beads with THF as mobile phase. All solvents used where of HPLC grade.

A variety of techniques were under taken to elucidate the structure of these compounds. All NMR experiments where carried out on a Bruker AM 400 spectrometer our ^{1}H NMR spectra were measured at 400 MHz. Mass spectra were analysed on a Ettan MALDI-TOF Pro from Amersham BioSciences. A Perkin Elmer Lambda 900 UV/Vis/NIR spectrometer was used to obtain the λ max of these compounds.

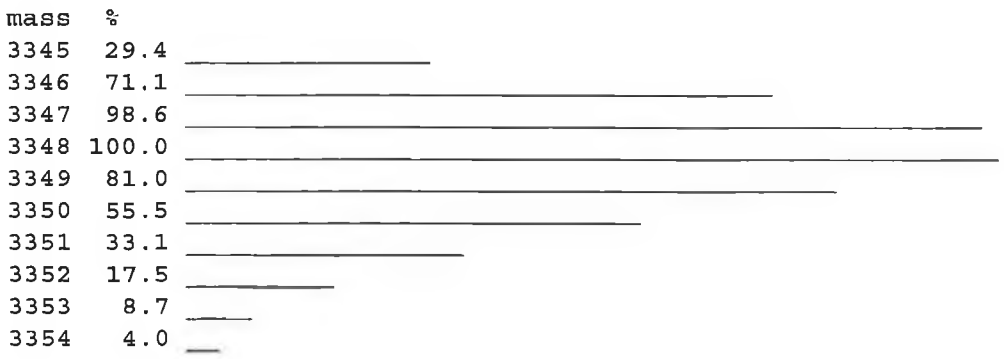
3.4.1 1,8(11),15(18),22(25)-tetra(-27-[Partial Cone 5,11,17,23-Tetra-tert-butyl-25,26,28-trimethoxy Calix[4]arene]) Phthalocyanate Nickel (II) (73)

Lithium (0.03 g, 4.28 mmol) was added to 1 ml of pentanol in a 10 ml round bottom flask and heated to 50°C to form the lithium alkoxide for 30 minutes. To this reaction flask **(80)** (0.1 g, 0.122 mmol), nickel acetate (0.2 g, 0.806 mmol) was added to the reaction mixture and this was then heated up to 110°C for 24hr. The reaction mixture was then poured on to ice water (20 mls), this layer was then extracted with ethyl acetate (3 x 10 mls) in a separation funnel. The organic extracts were combined, then washed with a saturated saltwater solution, dried over $MgSO_4$, filtered and evaporated to yield a brown mixture. This crude mixture was not separated.

Product was characterised by **UV-Vis:** (Chloroform) 720 nm

MALD-TOF m/z: 3349.59 ($M + Na^+$) http://www.chem.shef.ac.uk/WebElements.cgi$isot

Calculated for formula: $C_{220}H_{256}O_{16}N_8Ni_1Na_1$



3.4.2 1-(-27-[Partial Cone 5,11,17,23-Tetra-tert-butyl-25,26,28-trimethoxy Calix[4]arene]) Phthalocyane (97)

Lithium (0.03 g, 4.28 mmol) was added to 1 ml of pentanol in a 10 ml round bottom flask and heated to 50°C to form the lithium alkoxide for 30 minutes. To this reaction flask monophthalonitrile-trimethoxycalix[4]arene **(80)** (0.1 g, 0.122 mmol) and 1,2-dicyanobenzene (0.125 g, 0.976 mmol) where added to the reaction mixture and this was then heated up to 110°C. The reaction mixture was then poured on to ice water (20 mls), this layer was then extracted with ethyl acetate (3 x 10 mls) in a separation funnel. The organic extracts were combined, then washed with a saturated saltwater solution, dried over $MgSO_4$, filtered and evaporated to yield a green mixture. The crude product was purified by column chromatography using chloroform as the eluant to give a blue/green powder. This was then repeated on a second silica column followed by a size exclusion column column containing biobeads (SX-3) with THF as mobile phase. A blue green powder was obtained in a (0.03 g, 0.025 mmol, 20.5 % yield).

Product was characterised by **^{1}H NMR** (toluene-d_8) were run for 10,000 scans at a concentration of 1 X 10^{-04} M.

MALD-TOF m/z: 1202 (M^+), 1225 ($M + Na^+$) and 1241 ($M + K^+$) $C_{79}H_{78}O_4N_8$

UV-Vis: (Chloroform) 677 nm and 707 nm.

3.4.3 UV-Vis Concentration Study

A 10 ml stock solution (1 X 10^{-04} M) of phthalocyanine was made up using dichloromethane and a serial dilution was used to prepare the following concentrations 5 X 10^{-05} M, 1 X 10^{-05} M, 5 X 10^{-06} M, 1 X 10^{-06} M, 5 X 10^{-07} M and 1 X 10^{-07} M.

3.4.4 UV-Vis Ethanol Study

A 20 ml stock solution (1 X 10^{-04} M) of phthalocyanine was made in a volumetric flask using dichloromethane as the solvent. Then ten 10 ml solutions where prepared keeping the concentration constant, however varying the ethanol content from 0 to 90 % see Table 2.

3.4.5 Solid State UV-Vis

In order to take a solid state UV-Vis of **(97)** we first had to spin coat a sample on to a microscope slide. This involed three steps:

1. **(97)** was dissolved in chloroform at a high concentration (10^{-2} M)
2. 4 drops of the solution were placed on a microscope slide.
3. The microscope slide was then placed on a spinner and was spun at 2000 rpm for a few seconds.

The microscope slide was removed to dry for 24 hr, in order to leave a solid film of **(97)** on its surface. The slide was placed in the UV-VIS in an upright position and the spectrum taken.

% Ethanol	Stock Solution (mls)	Dichloromethane (mls)	Ethanol (mls)
0	1	9	0
10	1	8	1
20	1	7	2
30	1	6	3
40	1	5	4
50	1	4	5
60	1	3	6
70	1	2	7
80	1	1	8
90	1	0	9

Table 2: *Solutions make up for ethanol UV-Vis study.*

4. Synthesis of Calix[4]arene Phthalocyanines from a β-Substituted Phthalonitrile Calix[4]arene

4.1 Introduction

The synthetic route for the synthesis of **(99)** is the same as that used for the preparation of **(80)**. The motivations for preparing **(73)** was to form a single isomer tetra-substituted calix[4]arene phthalocyanine and to determine if four calix[4]arene substitutents could isolate the phthalocyanine core (due to the orientation of the t-butyl groups on the calix[4]arene). Since this did not work we then directed our attention towards the preparation of the 4-positioned phthalonitrile calix[4]arene **(100)**, which may under go self condensation, as it should be less sterically hindered than its α-positioned counter part **(80)**. Molecular models were generated using MM+ calculations, assuming the conformation of the 4-positioned phthalonitrile calixarene would be the same as the 3-positioned. A CPK model is shown in Figure 43, the CH spacer in the aromatic ring between the oxygen and the nitrile group allows for enough space for the alkoxide to initiate the condensation. This condensation also gives the possibility of the formation of one isomer as the t-butyl group of the calix[4]arene hinders attack from one side of the phthalonitrile see Figure 43(b). In Scheme 31 a synthetic route is outlined for the synthesis of a self filled partial cone 5,11,17,23-tetra-t-butyl-26,27,28-trimethoxy-25-(-4-[-1,2-phthalonitrile])calix[4]arene **(100)**. The self-condensation of **(100)** can also be seen in Scheme 31

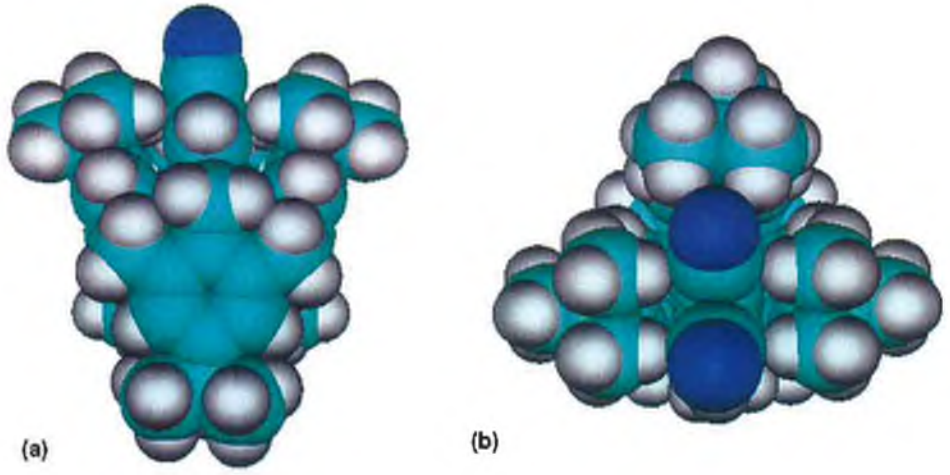
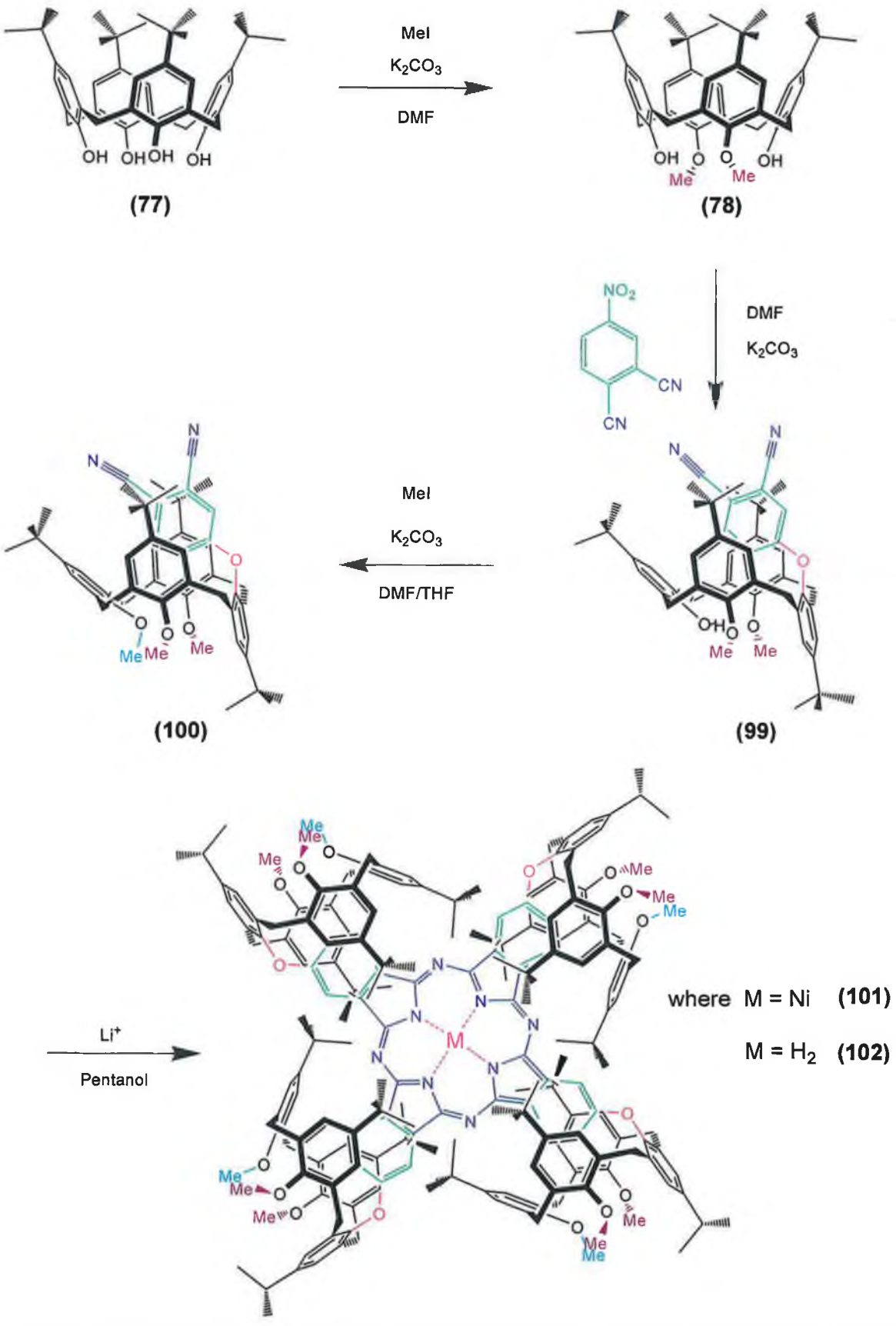


Figure 43: *CPK space fill model of* ***(100)*** *(a) front view (b) top view*



Scheme 31: *Synthetic pathway to the formation of the β-positioned phthalonitrile (100) followed by the self-condensation to form the tetra-substituted-calix[4]arene phthalocyanine (101).*

4.2 Synthesis of 5,11,17,23-tetra-t-butyl-27-hydroxy-26,28-dimethoxy-25-(-4-[-1,2-dicyanobenzene])calix[4]arene (100).

The first stage in the synthesis of **(77)** involves the protection of two of the hydroxy groups to form the distal~1,3 dimethoxy calix[4]arene **(78)** as described in Chapter 2. The second stage involves an S_NAr displacement between the distal~1,3-dimethoxy calix[4]arene **(78)** and 4-nitrophthalonitrile **(21)** using K_2CO_3 base under vacuum. This reaction is a direct copy of the conditions used with 3-nitrophthalonitrile **(20)** described in Chapter 1.

Purification of the crude reaction mixture was achieved on a silica gel column using a hexane: ethyl acetate mobile phase. The first spot to elute was our target compound **(99)**. A methanol wash was then used to remove the yellow tinge that remained on the compound. Yields of around 37 % where achieved after washing.

The presence of **(99)** was verified by electro-spray mass spectrometry giving two peaks at 825 and 841 m/z for the sodiated and potassiated molecular ions respectively. The ^1H NMR spectra of **(99)** at RT were not fully resolved. We believe that this could be due to: 1) the partial cone inclusion complex is present however the phthalonitrile is slightly pushed out of the core allowing for free rotation of the other methoxy groups through the annulus, 2) there are different fixed conformations present. A high temperature ^1H NMR was run on **(99)** in deuterated nitrobenzene, however, this did not simplify the spectrum (Figure 44). We believe that this indicates that the compound **(99)** must be present in a couple of fixed conformations.

In an attempt to elucidate the structure of **(99)** our attention was turned to x-ray crystallography. Crystals of this compound were grown from ethyl acetate and hexane and an x-ray structure obtained, the results are shown in Figure 45. From Figure 45 we can see the x-ray structure confirms that **(99)** exists in two conformations in the solid state: (a) the partial cone conformation and (b) the cone conformation. (see Chapter 7 for a detailed analysis of both conformations) This may explain why the ^1H NMR does not resolve at high temperature, since these conformations may not be interchangeable.

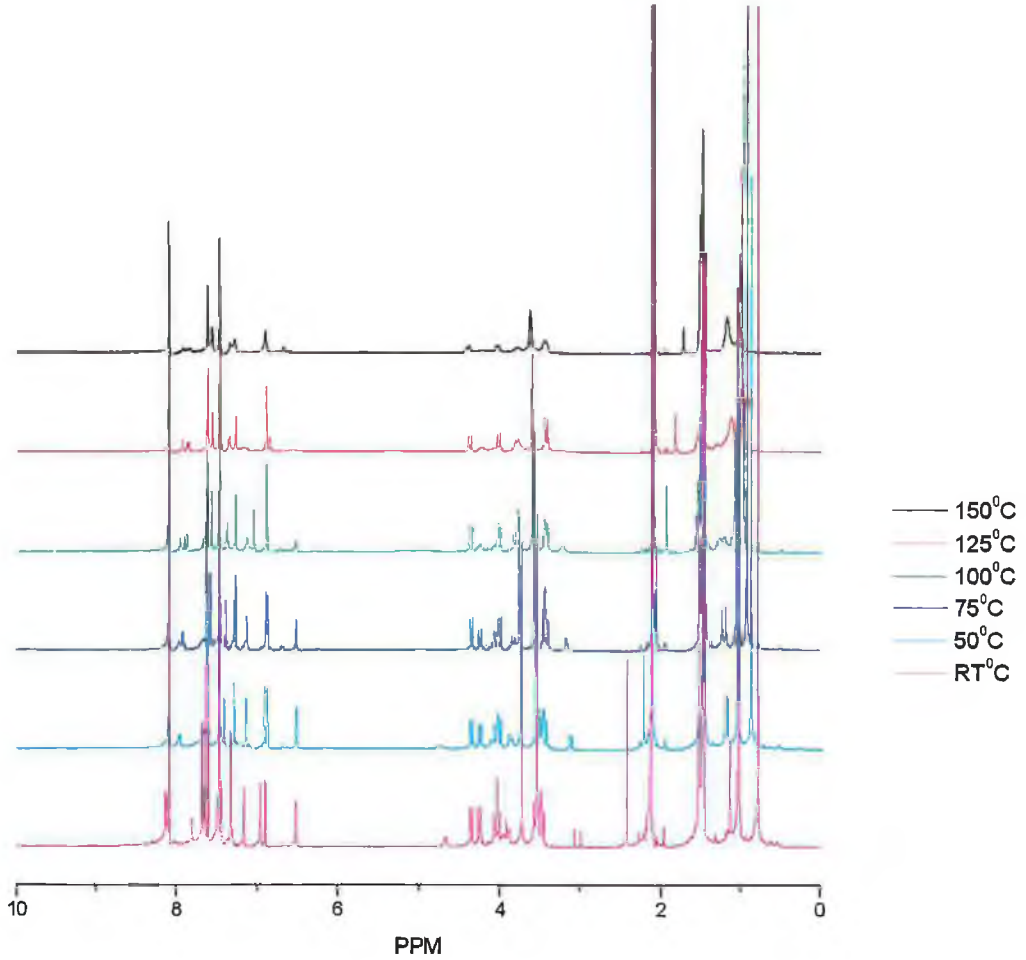


Figure 44: *High temperature ^{1}H NMR experiment on* ***(99)***.

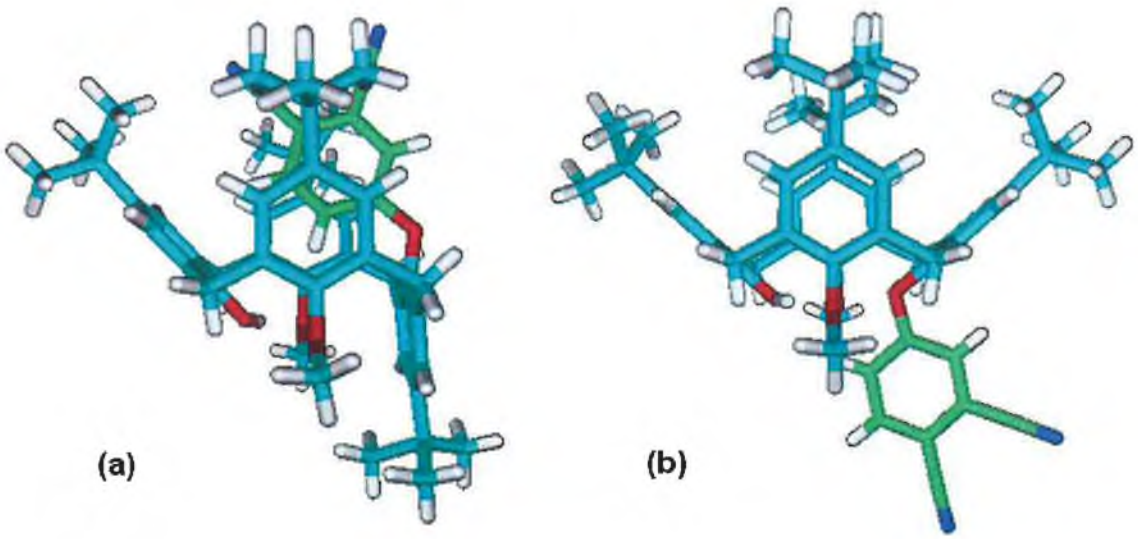


Figure 45: *(a) Partial cone of* ***(99)*** *and (b) Cone of* ***(99)*****.**

4.3 Mechanism of Formation of the Cone and Self Filled Partial Cone of 5,11,17,23-tetra-t-butyl-27-hydroxy-26,28-dimethoxy-25-(-4-[-1,2-dicyanobenzene])calix[4]arene (99).

Why mechanistically do we obtain two conformations for **(99)** (the self-filled partial cone and the cone) while we only obtain a single conformation for **(79)**? The answer to this question could be in the positioning of the NO_2 group on the phthalonitrile. For 3-nitrophthalonitrile **(20)** the nitro group is very sterically hindered on the lower rim due to the two methyl substituents on the calixarene therefore nucleophilic displacement at the lower rim is more difficult and as a result we believe that encapsulation occurs first followed by displacement. On the other hand 4-nitrophthalonitrile **(21)** is less sterically hindered by the methyl groups on the lower rim therefore lower rim nucleophilic attack (Figure 46) competes with inclusion (Figure 47) and this leads to the formation of two conformations.

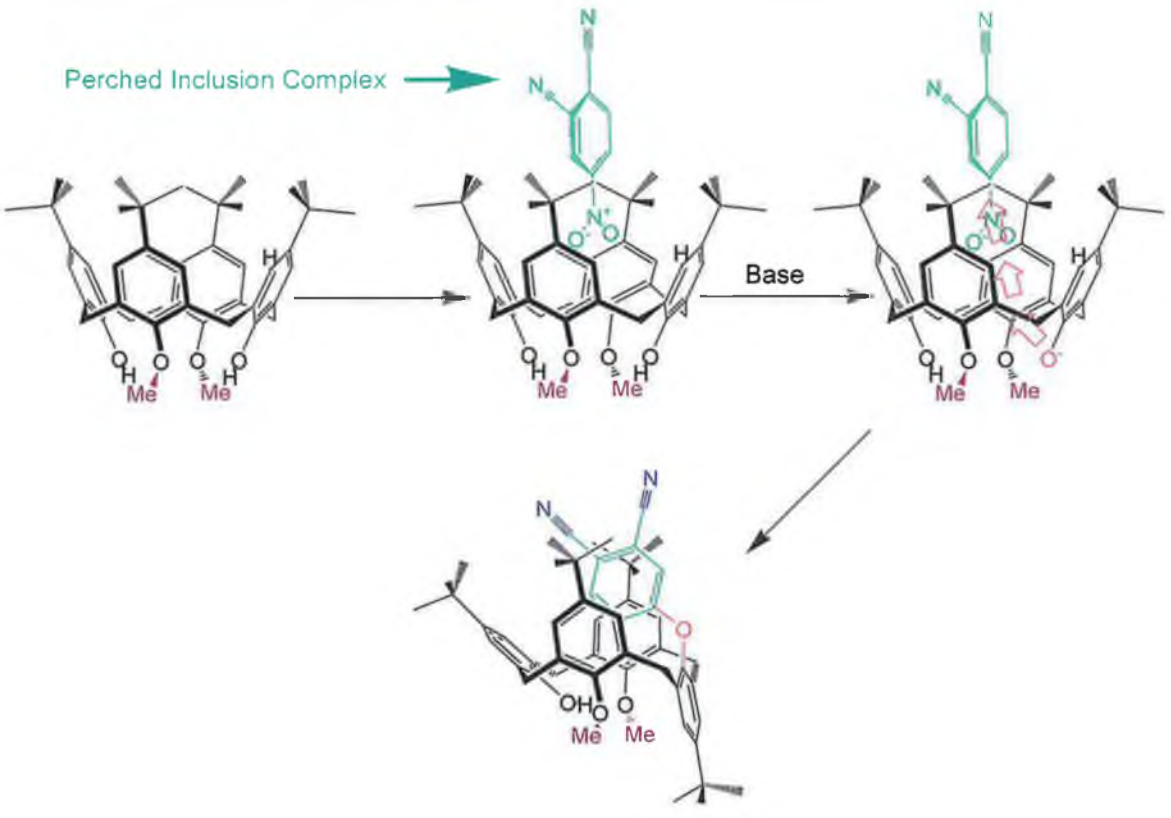


Figure 46: *Mechanism for the synthesis of cone conformation of* ***(99)****.*

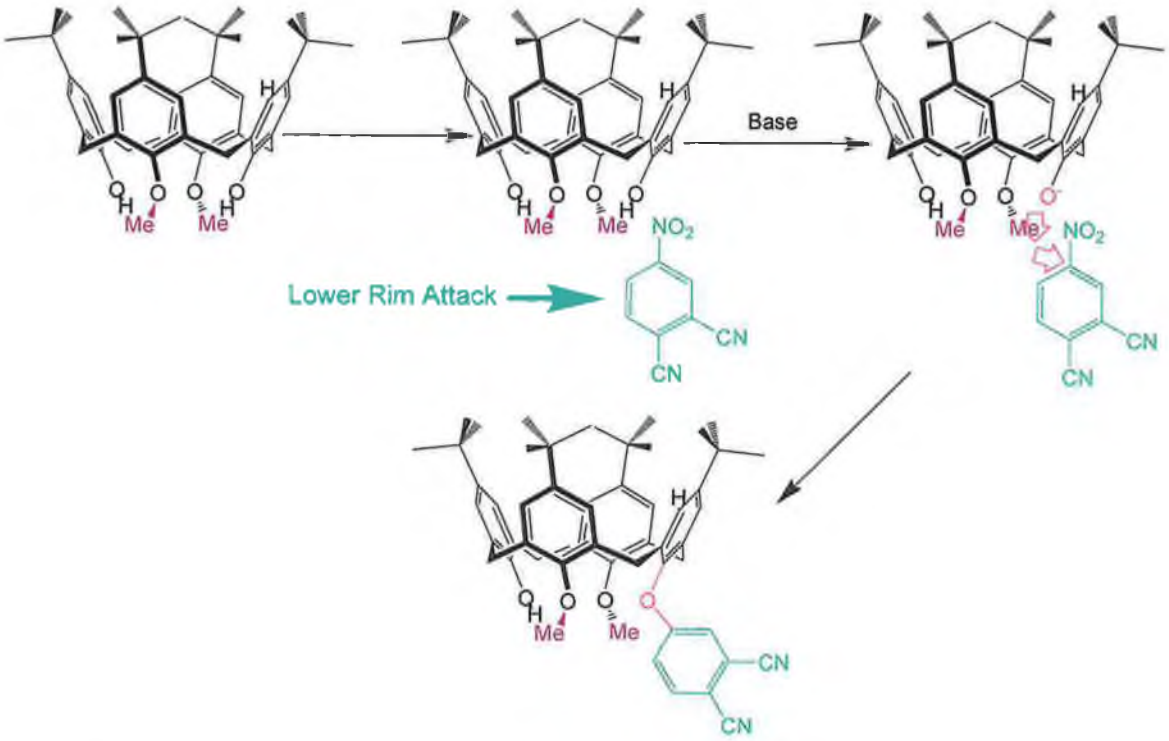


Figure 47: *Mechanism for the synthesis of the partial cone conformation of* ***(99)****.*

4.4 Preparation of the Cone and Self Filled Partial Cone of 5,11,17,23-tetra-t-butyl-26,27,28-trimethoxy-25-(-4-[-1,2-dicyanobenzene])calix[4]arene

The final stage in the synthesis of the required phthalonitrile **(100)** is a simple methylation reaction using MeI and K_2CO_3. In this synthetic step like for its 3-positioned counter part, the temperature had to be controlled to prevent the self-condensation of **(100)** from occurring in the presence of base, this was achieved by carrying out the reaction at 60°C under nitrogen. As this reaction tends to be sluggish a large excess of base and methyl iodide were used. The use of excess alkyating reagent would not interfere with the purification as it can be removed by simple heating under a nitrogen stream since methyl iodide boils at 41-43°C.

Purification of the crude reaction mixture was achieved on a silica gel column using a hexane: ethyl acetate mobile phase. The first band to elute was our target compound **(100)**. Yields of 21 % where achieved after chromatography.

The ^1H NMR spectra of **(100)** at RT where not fully resolved, indicating that there is conformational flexibility at RT (Figure 48). Again a electrospray mass spectrum was obtained for **(100)** and peaks were found at 839 m/z ($M + Na^+$) and 855 m/z ($M + K^+$) verifying the presence of **(100)**. At this stage it was decided not to run high temperature ^1H NMR experiments, as we believed that more than one conformation was present.

Crystals of this compound where then grown using hexane/ ethyl acetate, in an attempt to elucidate the structure of **(100)**. The x-ray crystal structure of **(100)** revealed that a single conformation was present see Figure 49.(see Chapter 7) This result suggests that only one conformation was present, however, (high temperature) ^1H NMR studies demonstrate that **(100)** exists in more than one conformation in solution.

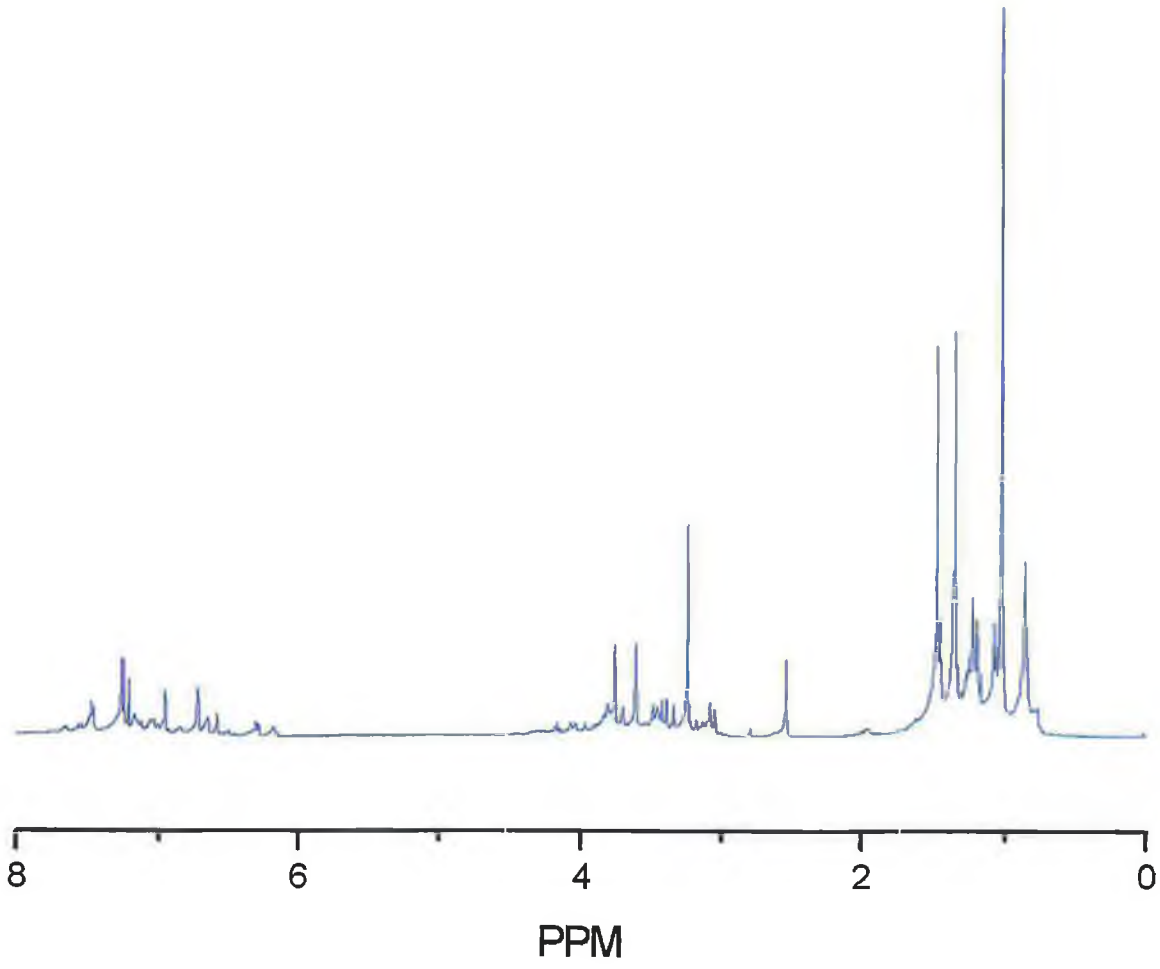


Figure 48: *Room temperature*^{1}*H NMR of* ***(100).***

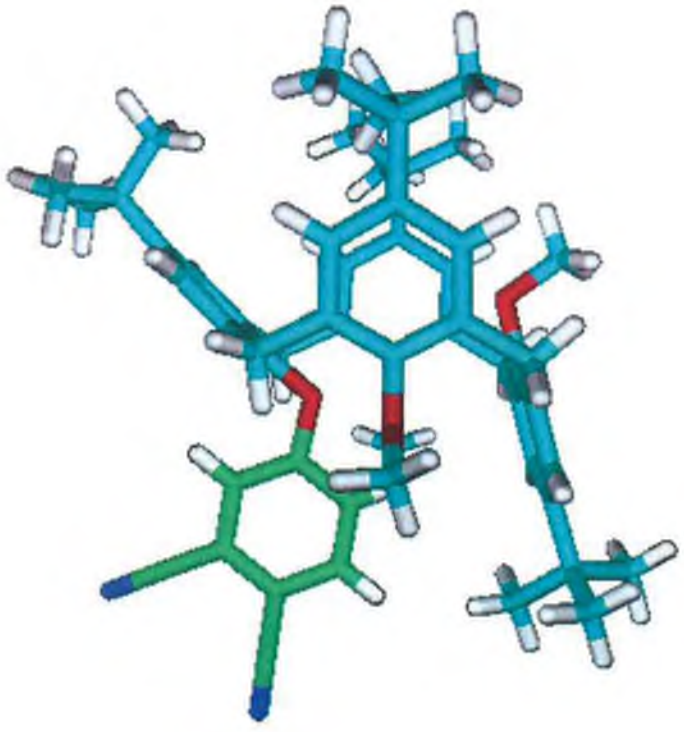


Figure 49: *X-ray crystal obtained for* ***(100).***

4.5 Tetra-t-butylcalix[4]arene phthalocyanine

4.5.1 Nickel Tetra-t-butylcalix[4]arene phthalocyanine (101)

This self-condensation was first attempted in Li/ pentanol at 110-120^{0}C in the presence of nickel (II) acetate. Ni templation was once again utilized because it had been previously reported that sterically constrained Pcs could be prepared using it. As anticipated our reaction mixture turned green.

The crude reaction mixture was placed on a silica gel column with chloroform as the eluent. From the column only a single green/blue band was isolated. This was then further purified by size exclusion chromatography using SX-3 bio-beads. THF was used as the eluent and only a single band was present in both cases. Yields of 10 % where achieved for the Nickel derivative.

This compound was first identified by MALD-TOF showing a cluster at 3326.98 m/z (see experimental). It was impressive to see that this was a pure cluster. Phthalocyanine **(101)** gave a single peak at 684 nm in the UV-Vis spectrum (Figure 50). However ^{1}HNMR analysis of **(101)** revealed a complicated spectrum indicating the presence of positional isomers. Thus, our initial hope of preparing a single isomer, based on molecular modelling (page 86), was inaccurate.

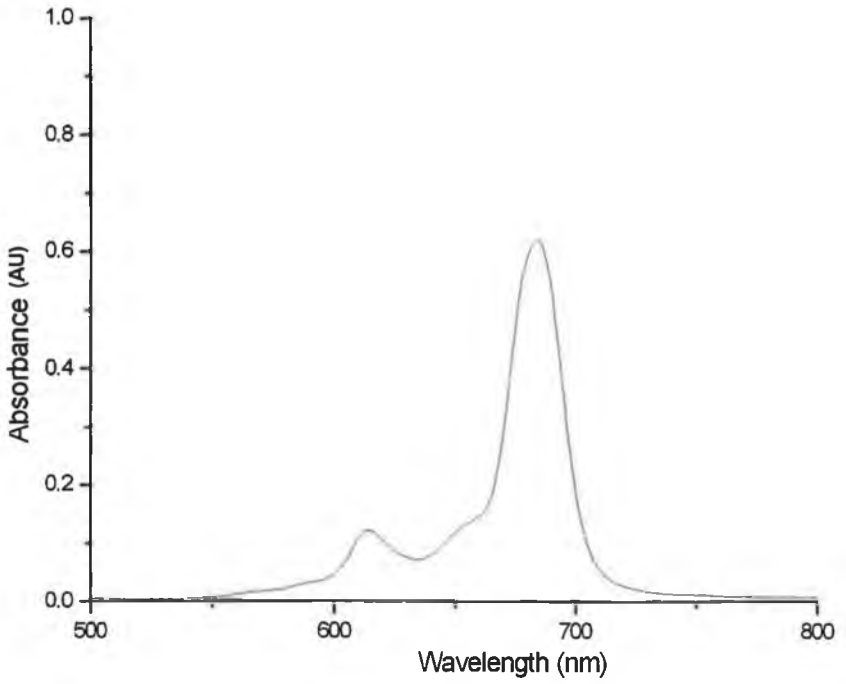


Figure 50: *UV-Vis of (101) in dichloromethane*

4.5.2 Metal-Free Tetra-t-butylcalix[4]arene phthalocyanine (102)

In an attempt to ascertain if Ni-templation had any effect on the condensation of **(100)** we attempted to prepare the metal-free phthalocyanine. This self-condensation was also carried out using Li/ pentanol at 110-120°C to give us a green hue, suggesting that this reaction proceeds with or without the presence of metal templation.

The crude reaction mixture was placed on a silica gel column with chloroform as the eluent. From the column only a single green/blue band was isolated. This band was further purified by size exclusion chromatography using SX-3 bio-beads, with THF as the eluent to give **(102)** in a 4 % yield. However this yield is half of what was obtained for the Ni templation reaction, demonstrating the effect metal templation has on this condensation reaction.

This compound was first identified by MALD-TOF mass spectrometry with a peak at 3273 m/z. It was impressive to see that this was a pure cluster. Compound **(102)** gave two peaks at 677 nm and 710 nm in the UV-Vis spectrum indicating metal-free phthalocyanine (Figure 51).

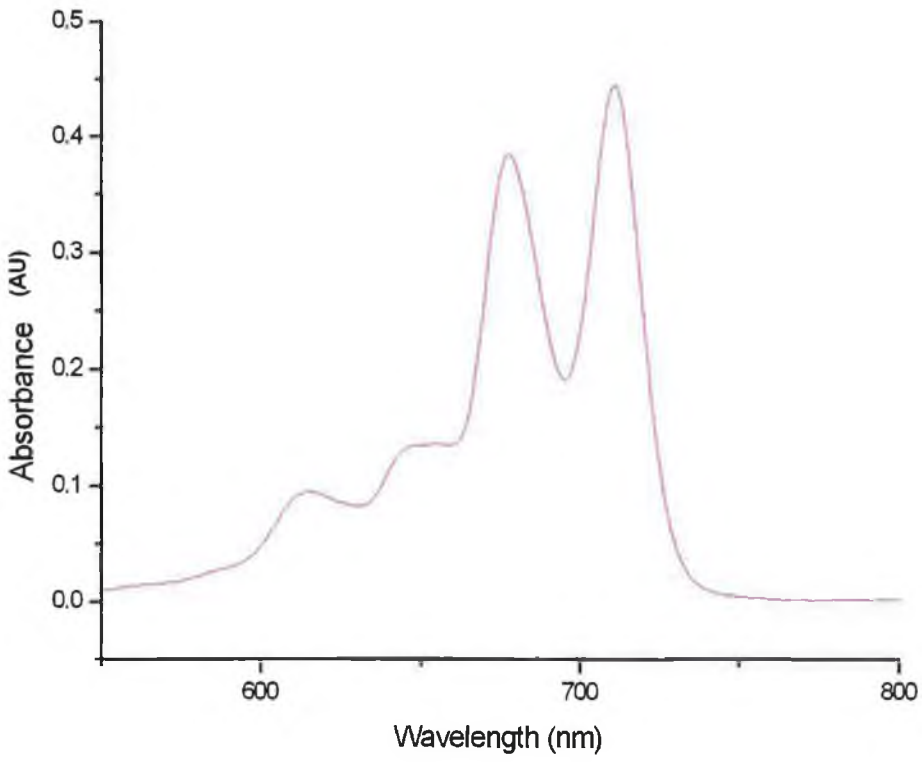


Figure 51: *UV-Vis of (102) in chloroform.*

Again ^{1}H NMR spectroscopy was not very informative since the tetra calix[4]arene phthalocyanine **(102)** is a mixture of positional isomers, leading to a very complicated spectrum. The reason for the sheer amount of isomers is due to: 1) the different conformational isomers of the stating material **(100)** as can be seen from the X-ray structures in Figure 45 and 49 and 2) 2) when unsymmetrical phthalonitriles condense such as **(100)** they form four positional isomers. Therefore each conformation of **(100)**, when condensed, will contain four positional isomers (if they individually self-condense), however this will not be the only case, they will also cross condense with other conformations of **(100)** leading to a huge variety of positional and conformational isomers.

^{1}H NMR spectroscopy can be used to identify the presence or absence of π-π stacking by measuring the shift of the internal protons. In the previous Chapter 3 the internal protons of **(97)** were shifted downfield from -2 to –4 ppm to -0.3 ppm in nitro-benzene (d_6) at 1 X 10^{-4} M. This substantial shift is in the presence of only one calixarene moiety in the "picket fence arrangement". What will the result be in the case of **(102)**, where four calixarene moieties are present? [However it should be noted that all calix[4]arene are not in the partial cone isomer.] When the ^{1}H NMR of **(102)** was analysed the internal protons are not seen in the +1 to –4 ppm region of the spectrum see Figure 52. Above 1 ppm the spectrum cannot be interpreted

because the t-butyl region of the calixarene moiety (16 t-butyl groups) obscures the region. We believe that the internal protons of **(102)** are under the t-butyl peaks of the calix[4]arene substitutents, that is they are some where between 1-2 ppm! We believe this to be a first for phthalocyanine chemistry where the internal protons are above 1 ppm, which is strong evidence that **(102)** does not aggregate in solution.

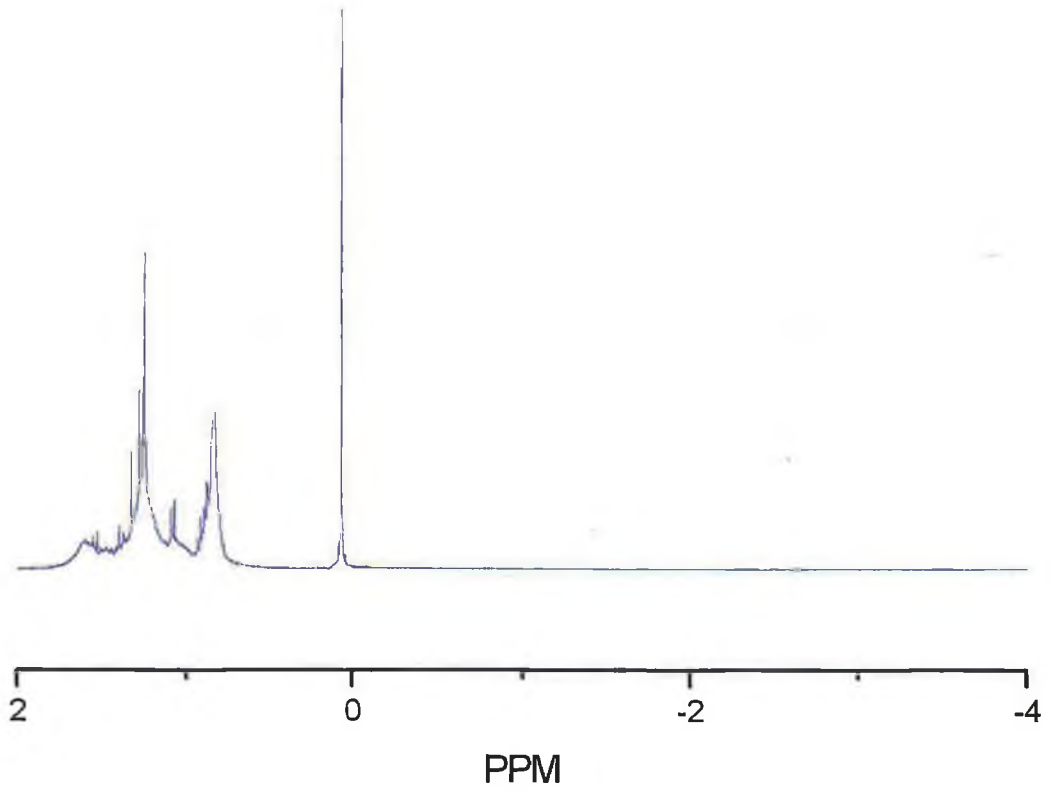


Figure 52: *^{1}H NMR of **(102)** from +1 to –4 ppm.*

4.5.3 Molecular Models of these Tetra-t-butylcalix[4]arene substituted phthalocyanine

CPK molecular models of the tetra-substituted cone and partial cone calix[4]arene phthalocyanine (Figure 53 and 54 respectively) were minimized in order to ascertain if the calixarene in the cone would emulate the ability of the partial cone to reduce π-π stacking. The four calixarenes, which are in a picket fence arrangement leads to a totally non-aggregated phthalocyanine in the absence of axial substitution. From Figure 53 (c) it can be seen that the 4 sets of t-butyl groups that lie above and below the plane of the phthalocyanine, totally isolating the phthalocyanine core. However, the cone conformation does not place 4

sets of t-butyl groups above and below the phthalocyanine plane. Does this hinder its ability to prevent π-π stacking? If we take a look at Figure 54 (c) again the Calix[4]arene lies centred on the phthalocyanine ring and this forms a "wall" around the phthalocyanine plane above and below inhibiting π-π stacking. Therefore we believe that this conformation should also yield a totally non-aggregated system. However in the condensation we will not obtain pure conformational forms of these compounds, we will obtain mixed conformations. This should not affect our results, as all conformations will isolate the phthalocyanine core.

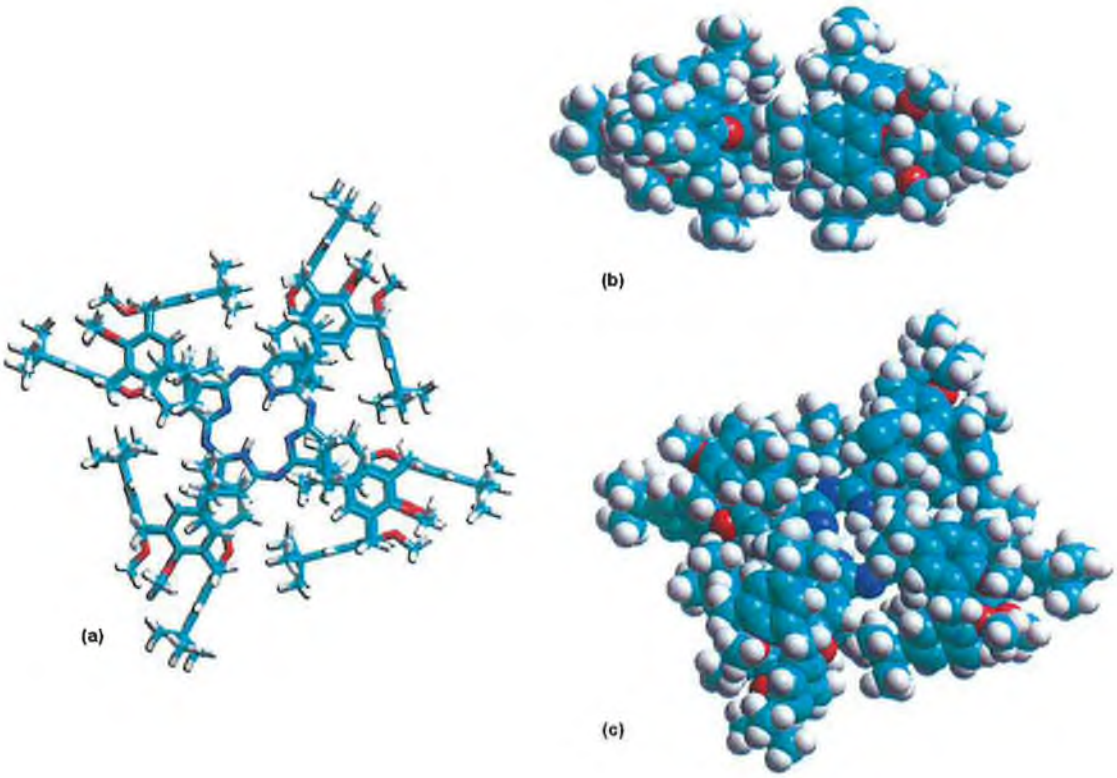


Figure 53: *Molecular model of* ***(102)*** *using only the X-ray crystal of the partial cone* ***(99)*** *as a starting point (Figure 45(a)). Where (a) tube representation from above, (b) CPK representation from the side and (c) CPK representation from the above.*

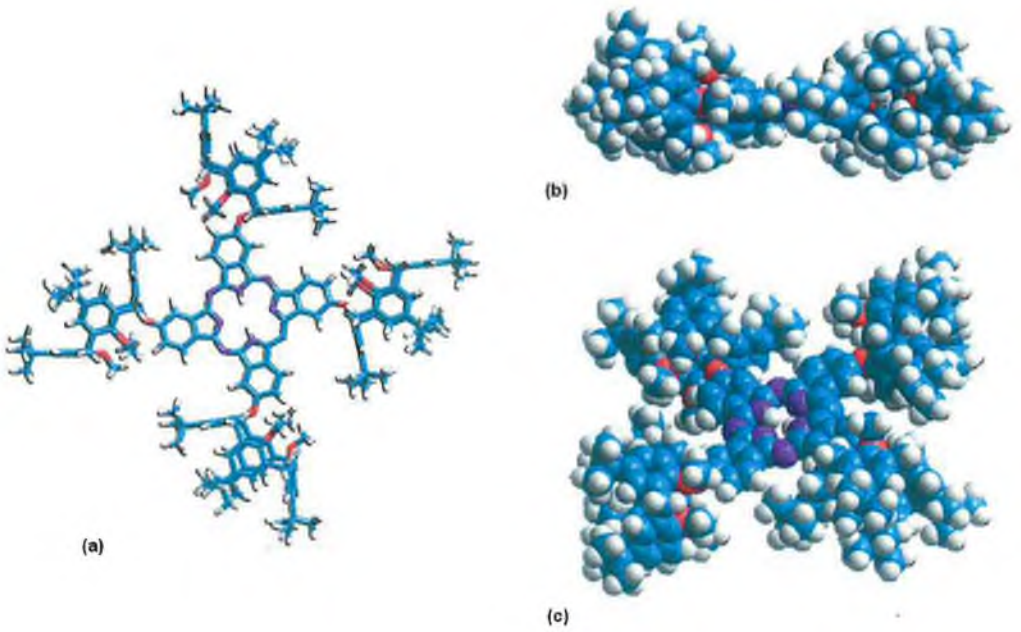


Figure 54: *Molecular model of* ***(102)*** *using only the x-ray crystal of the cone* ***(99)*** *as a starting point (Figure 45(b)). Where (a) tube representation from above, (b) CPK representation from the side and (c) CPK representation from the above.*

4.5.4 UV-Vis Aggregational Studies

The metal-free compound **(102)** demonstrates exceptional non-aggregation as the internal protons appear to be above the +1 to –4 ppm. This even outperforms the unsymmetrical **(97)** and **(98)** described in Chapter 3. As described in Chapter 3 there are two different UV-Vis studies that can be carried out to ascertain the aggregational behaviour of both **(101)** and **(102)**.

The first of these UV-Vis experiments is a concentration study for **(101)**, which is shown in Figure 54. The concentrations used were 1 X 10^{-04} M, 5 X 10^{-05} M, 1 X 10^{-05} M, 5 X 10^{-06} M, 1 X 10^{-06} M, 5 X 10^{-07} M and 1 X 10^{-07} M. Aggregation is generally noted by a blue shift in the Q-band or changes in shape of the Q-band peak. In this trace we notice very little change in the Q-band shape even at high concentration, which is consistent with a non-aggregated phthalocyanines species.

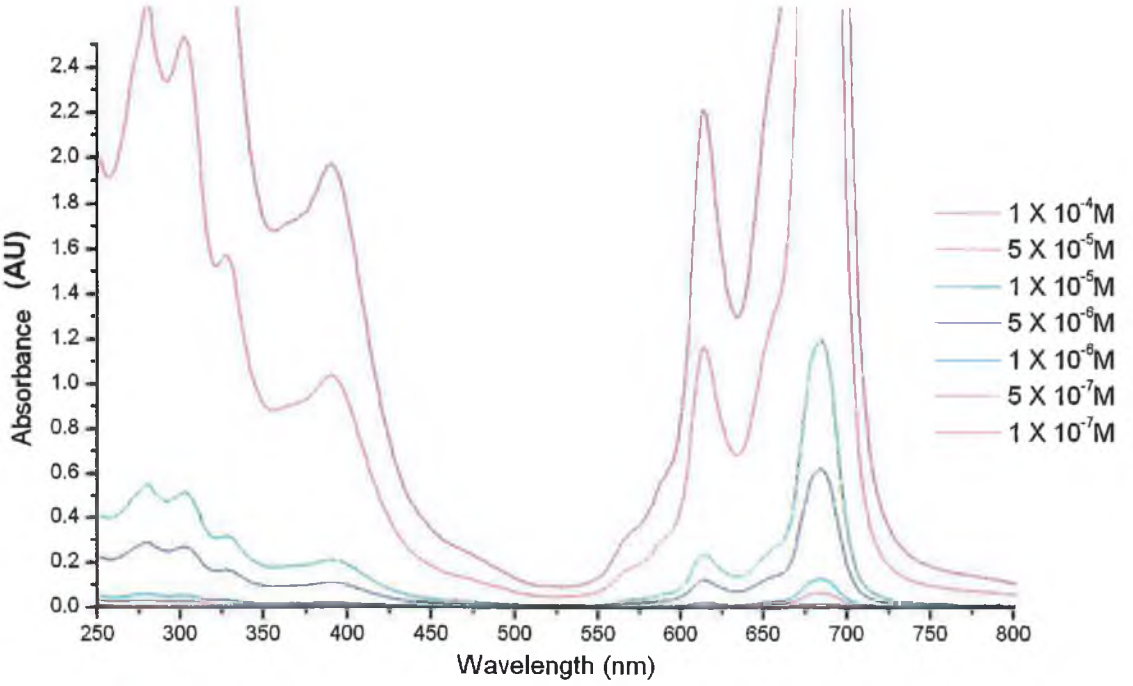


Figure 54: UV-Vis *concentration study on nickel tetracalix[4]arene phthalocyanine* ***(101).***

A second UV-Vis study was then carried out on **(101)** which keeps the concentration of the phthalocyanine at 1 X 10^{-05} M, while increasing the percentage volume of ethanol (Figure 55). The additional ethanol should force the phthalocyanines together to aggregate because of its polar nature. As in the concentration study we should notice two things that would indicate the presence of aggregation: 1) blue shift of the Q-band or/and 2) a change in shape of the Q-band. On the addition of the ethanol there was no observable change, this was unlike the unsymmetrical **(97)** which had a slight change indicating dimer formation. This indicates that **(101)** exists as a non-aggregated species in polar solution even though the "picket fence" arrangement is not completely present in all the calix[4]arene substitutents. This suggests that this short attachment with the bulky calix[4]arene substitutent is enough to prevent aggregation, confirming our molecular modelling studies.

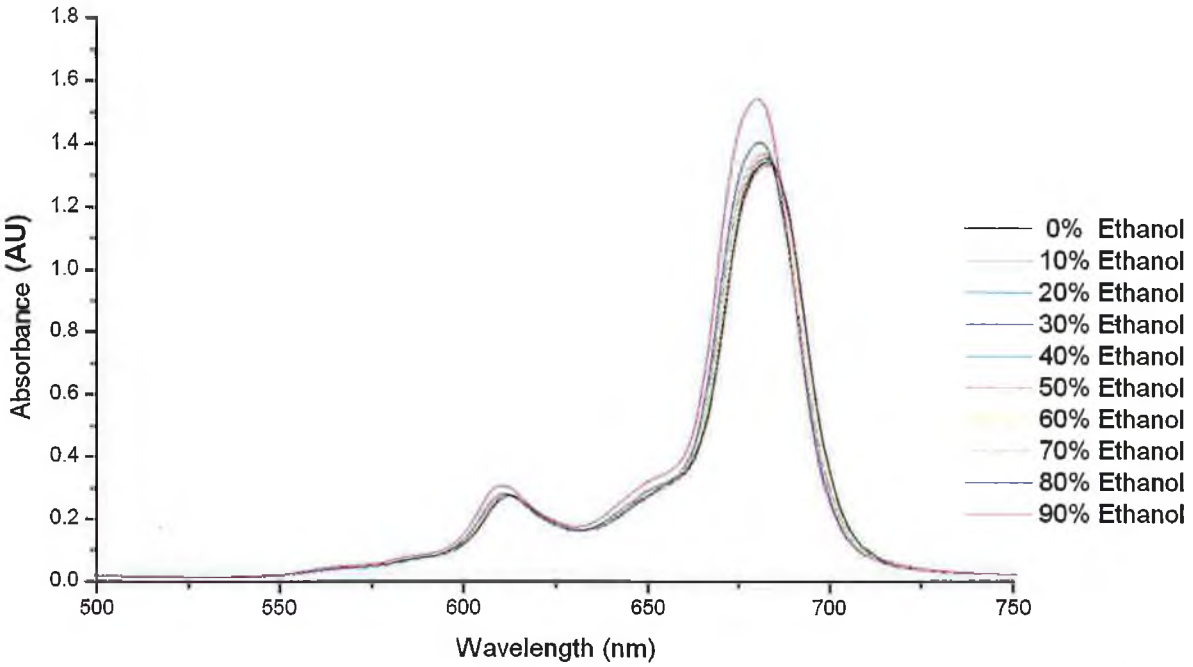


Figure 55: *Ethanol UV-Vis study on nickel tetracalix[4]arene phthalocyanine* ***(101).***

In order to fully prove that this was a completely non-aggregated system we again decided to obtain a solid state UV-Vis. However, unlike **(97)**, the UV-Vis spectrum of both the solid (Figure 56) and solution (Figure 51) states of **(101)** where identical indicating that we had indeed synthesised a totally non-aggregated phthalocyanine.

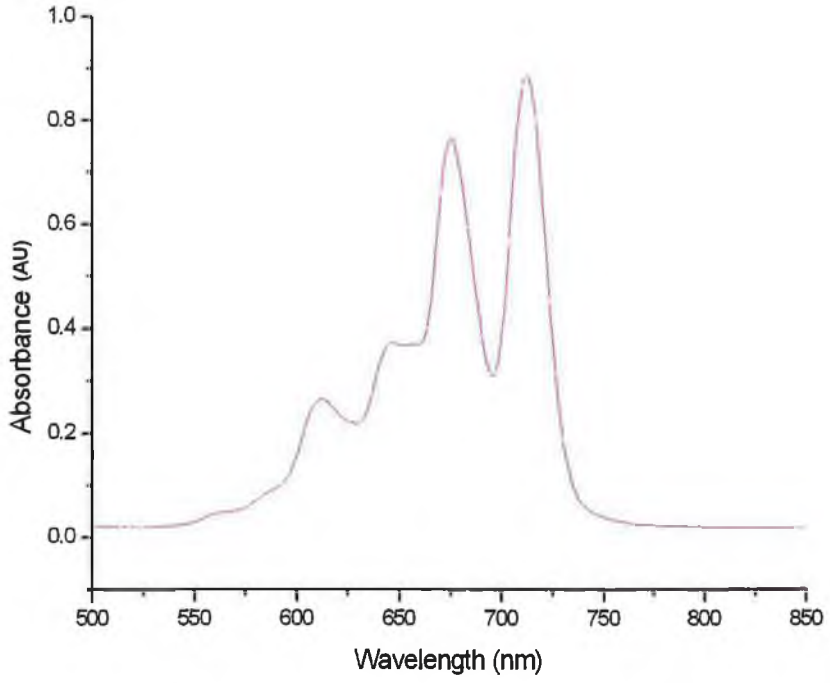


Figure 56: *Solid State UV-Vis of* ***(102).***

4.6 Experimental

Column chromatography was carried out on all of the compounds using Riedel de Haen silica gel 60. Thin layer chromatography (TLC) was carried out on Riedel de Haen silica 60F254 plates using specified solvents. Size exclusion chromatography was carried out using SX-3 bio-beads with THF as mobile phase. All solvents used where of HPLC grade.

A variety of techniques where under taken to elucidate the structure of these compounds. All NMR experiments where carried out on a Bruker AM 400 spectrometer and this means our ^{1}H NMR spectra were measured at 400 MHz. Mass spectra were analysed on two different instruments 1) a Esquire-Bruker/Hewlett Packard LC-MS 1100 series, equipped with an electrospray ion source for the phthalonitrile starting materials **(99)** and **(100)** and 2) a Ettan MALDI-TOF Pro from Amersham BioSciences for the phthalocyanine dyes **(101)** and **(102)**. IR spectra were recorded on a Perkin Elmer 2000 FT-IR spectrometer. A Perkin Elmer Lambda 900 UV/Vis/NIR spectrometer was used to obtain the UV-Vis spectra of all compounds. Melting points are carried out on a Bibby Stuart Scientific melting point SMP1. Crystal structures where run an a Bruker-Axis Smart Apex CCD three-circle diffractometer.

4.6.1 5,11,17,23-tetra-t-butyl-27-hydroxy-26,28-trimethoxy-25-(-4-[-1,2-phthalonitrile])calix[4]arene (99)

K_2CO_3 (0.82 g, 5.92 mmol), **(78)** (1.00g, 1.48mmol) and 4-nitrophthalonitrile (1.02 g, 5.92 mmol) were stirred under vacuum in anhydrous DMF (15 cm^3) for one day. The reaction mixture was then poured on to ice water (50 mls), filtered and the solid was washed with hot water (2x25 ml). The crude brown solid was purified by column chromatography using 80:20hexane: ethyl acetate, a white solid was obtained (0.45 g, 38 % yield).

Product was characterised by **^{1}H NMR:** ($CDCl_3$) Spectrum was unresolved

ESI m/z: 825 ($M + Na^+$), 841 ($M + K^+$) $C_{54}H_{62}O_4N_2$

IR: (KBr [cm^{-1}]): 3306 cm^{-1} ν(O-H), 2962 cm^{-1} ν(Bu_t), 2229 cm^{-1} ν(CN).

MP: 210 – 210°C

Crystal Structure: See attached cd.

Elemental Analysis: C= 80.47 % H = 7.75 % N = 3.41 % (Theoretical $C_{55}H_{64}O_4N_2$ C= 80.76 % H = 7.78 % N = 3.49 %)

4.6.2 5,11,17,23-tetra-t-butyl-26,27,28-trimethoxy-25-(-4-[-1,2-phthalonitrile])calix[4]arene (100)

K_2CO_3 (0.5 g, 3.62 mmol) and **(99)** (0.5 g, 0.62 mmol) in DMF/THF (15 cm^3 50:50 mix) were heated to 60°C under nitrogen. Methyl iodide (10 mls, 0.16 mmol) was added drop wise over one hour and the mixture was allowed heat for a further 24 hrs. On day two K_2CO_3 (0.5 g, 3.62 mmol) and methyl iodide (10 mls, 0.16 mmol) were added and this was repeated again on day 3. After 24 hrs the methyl iodide was distilled off and the reaction mixture was then dissolved in chloroform and washed with a saturated saltwater solution, dried over $MgSO_4$, filtered and evaporated to yield a cream powder. The crude product was purified by column chromatography using 90:10 hexane: ethyl acetate a white powder was obtained (0.11 g, 21.62 % yield).

Product was characterised by ^{1}**H NMR:** ($CDCl_3$) Spectrum was unresolved

ESI: m/z 839 ($M + Na^+$), 855 ($M + K^+$) $C_{55}H_{64}O_4N_2$

IR: (KBr [cm^{-1}]): 2956 cm^{-1} ν (Bu_t), 2228 cm^{-1} ν (CN)

MP: 290 – 294°C

Crystal Structure: See attached cd.

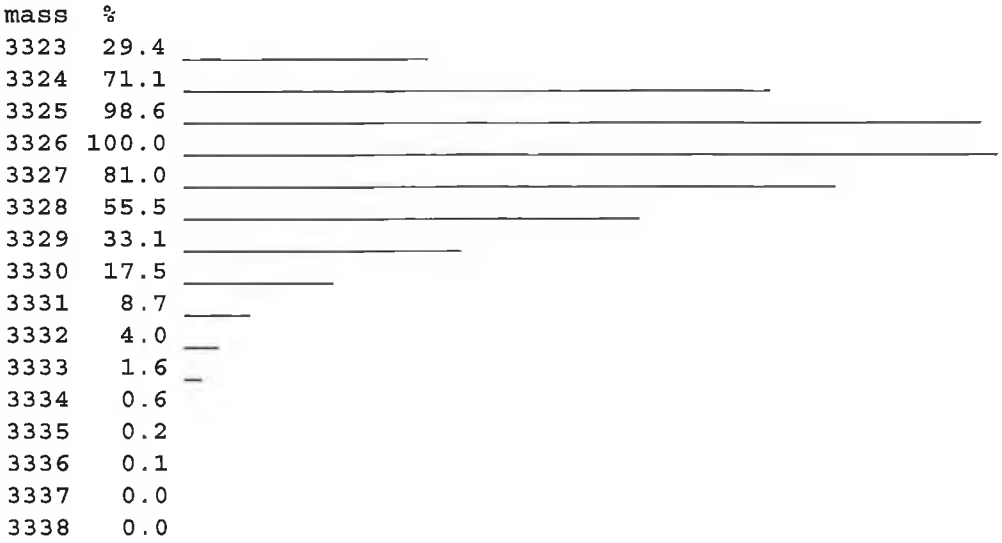
4.6.3 Nickel tetra(5,11,17,23-tetra-tert-butyl -25,26,28- trimethoxy) calix[4]arenephthalocyanine in the 4-position (101)

Lithium (0.03 g, 4.28 mmol) was added to 1 ml of pentanol in a 10 ml round bottom flask and heated to 50°C to form the lithium alkoxide for 30 minutes. To this reaction flask **(100)** (0.1 g, 0.122 mmol) and nickel acetate (0.2 g, 0.806 mmol) were added to the reaction mixture and this was then heated up to 110°C for 24 hr. The reaction mixture was then poured on to ice water (20 mls), this layer was then extracted with ethyl acetate (3 x 10 ml) in a separatory funnel. The organic extracts were combined, then washed with a saturated saltwater solution, dried over $MgSO_4$, filtered and evaporated to yield a green mixture. The crude product was purified by column chromatography using chloroform as the eluant to give a green compound. This was then repeated on silica again and then run on a size exclusion column containing bio-beads (SX-3) using THF as a mobile phase. A green product was obtained in a (0.041 g, 0.011 mmol, 10 % yield).

MALD-TOF m/z: 3327.11 (M=1) http://www.chem.shef.ac.uk/WebElements.cgi$isot

UV-Vis (Methylene Chloride)**:** 684 nm.

Calculated for formula: $C_{220}H_{257}O_{16}N_8Ni_1$



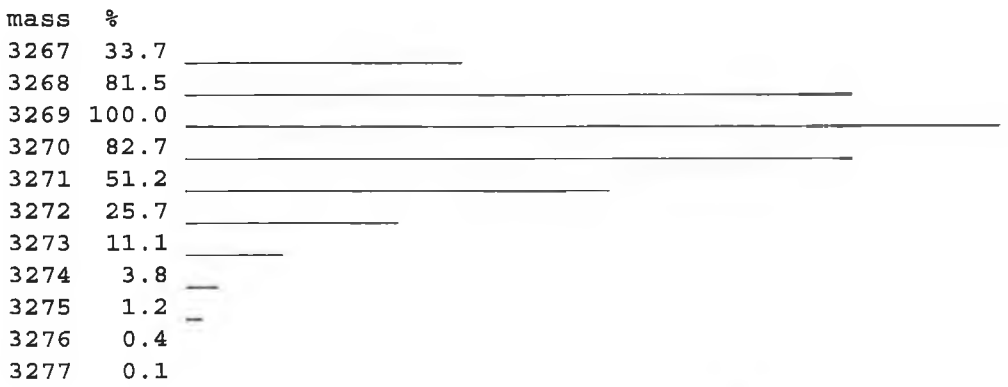
4.6.4 Metal-free tetra(5,11,17,23-tetra-tert-butyl -25,26,28- trimethoxy) calix[4]arenephthalocyanine in the 4-position (102)

Lithium (0.03 g, 4.28 mmol) was added to 1 ml of pentanol in a 10 ml round bottom flask and heated to 50°C to form the lithium alkoxide for 30 minutes. To this reaction flask **(100)** (0.1 g, 0.122 mmol) was added and the reaction mixture was then heated to 110°C for 24hr. The reaction mixture was then poured on to ice water (20 mls), this layer was then extracted with ethyl acetate (3 x 10 ml) in a separatory funnel. The organic extracts were combined, then washed with a saturated saltwater solution, dried over $MgSO_4$, filtered and evaporated to yield a green mixture. The crude product was purified by column chromatography using chloroform as the eluant to give a blue/green powder. This was further purified on a second silica column followed by a size exclusion column containing bio-beads (SX-3) using THF as a mobile phase. A blue green powder was obtained (0.017 g, 0.0052 mmol, 4% yield).

Product was characterised by **MALD-TOF m/z:** 3273.855

UV-Vis (Methylene Chloride)**:** 677 and 710 nm.

Calculated for Formula: $C_{220}H_{259}O_{16}N_8$



4.6.5 Molecular Modelling

All molecular modelling was carried out using a Dell Inspiron 1150 Intel (R), Celeron(R) CPU 2.4 GHz, 512 MB of RAM using HyperChem software version 7.51. In order to model the partial cone conformation of **(102)** (seen in Figure 52) three steps where under taken. The first step involved using the crystal structure of **(99a)** (Figure 44) as a starting point. This was placed into HyperChem software and minimized using a molecular mechanics force field called MM+ calculations. To this structure a methyl group was then added and minimized again using the same force field. Step two involves minimizing unsubstituted phthalocyanine to use as the centre piece of **(102)**. The third and final step involves piecing together the molecule before it is minimized to give our structure, which is presented in Figure 52. This was achieved by placing the minimized unsubstituted phthalocyanine and lining up **(99a)** in the correct plane and position, which could then be joined together and minimized. A molecular model of **(102)** in the cone conformation (Figure 53) was manipulated using the same procedure with **(99b)** as a starting point.

4.6.6 UV-Vis Concentration Study

A 10ml stock solution (1×10^{-04} M) of phthalocyanine was made up using dichloromethane and a serial dilution was used to make-up the following concentrations 5×10^{-05} M, 1×10^{-05} M, 5×10^{-06} M, 1×10^{-06} M, 5×10^{-07} M and 1×10^{-07} M.

4.6.7 UV-Vis Ethanol Study

A 20 ml stock solution (1 X 10^{-04} M) of phthalocyanine was made in a volumetric flask using dichloromethane as the solvent. Then ten 10 ml solutions where made up keeping the concentration constant, however varying the ethanol content from 0 to 90 %. Table 2 (Chapter 3) shows how these solutions were prepared.

4.6.8 Solid State UV-Vis

In order to take a solid state UV-Vis of **(102)** we first had to spin coat a sample on to a microscope slide. This involed three steps:

1. **(102)** dissolved in chloroform at a high concentration (10^{-2} M)
2. 4 drops of the solution were placed on a microscope slide.
3. The microscope slide was then placed on a spinner and was spun at 2000 rpm for a few seconds.

The microscope slide was removed to dry for 24 hrs, in order to leave a solid film of **(102)** on its surface. The slide was placed in the UV-VIS in an upright position and the spectrum taken.

5. Synthesis of Constrained Calix[4]arene Phthalocyanine

5.1 Introduction

Bisphthalonitriles such as **(85)** have traditionally been used as precursors for the synthesis of binuclear and polynuclear phthalocyanines. In this Chapter we attempt the synthesis of the binuclear **(74)** and also a constrained phthalocyanine **(76)**. The reason for attempting the synthesis of the constrained came from molecular models which indicated that the geometric positioning of the phthalonitrile substitutents on the calix[4]arene were correctly positioned for a self-condensation to take place. This would lead to the formation of a single D_{2h} isomer and from molecular modelling it would appear that this phthalocyanine has the potential to be a deaggregated system. The short chain binuclear has a wide range of potential uses in both sensing and catalysis etc. Synthetic routes are outlined in Scheme 32.

5.2 Synthesis of the Bisphthalonitrile Calix[4]arene (85)

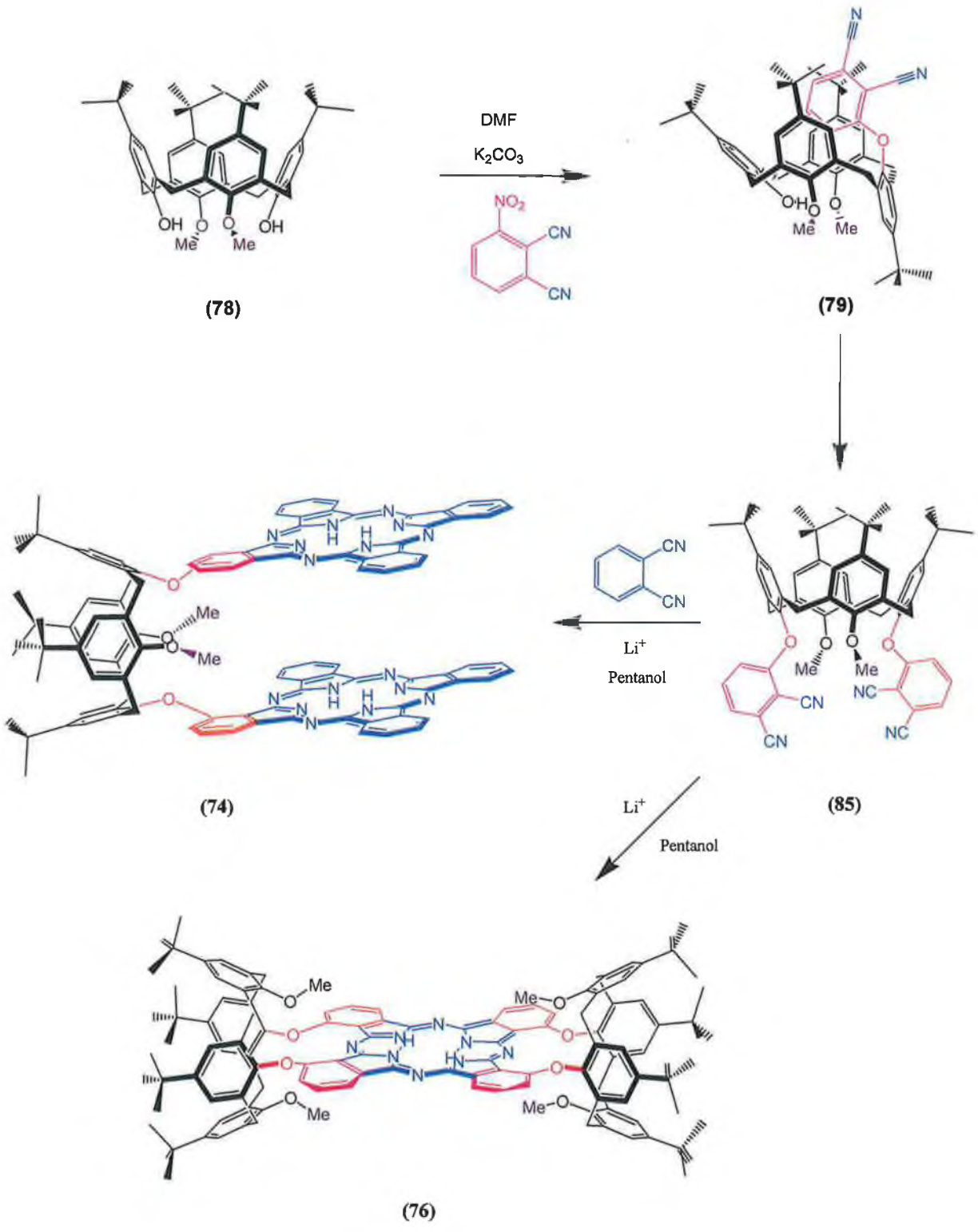
The first stage in the synthesis of **(77)** involves the protection of two of the hydroxy groups to form the distal~1,3 dimethoxy Calix[4]arene **(78)** as described in Chapter 1. The dimethoxycalix[4]arene was treated with 3-nitrophthalonitrile and base in a 1:4:4 stiochometric ratio. The reaction was allowed to proceed at room temperature for 10 days. In an attempt to drive the reaction to completion, additional aliquots of base and 3-nitrophthalonitrile (1:1:1 stiochometric amounts to the calixarene starting material) were added to the reaction mixture each day. By the end of ten days the reaction mixture was worked up and we found a total of eight products by TLC. The reaction mixture was separated by silica gel column chromatography using hexane:ethyl acetate (9:1), of the fractions obtained the target bisphthalonitrile could not be found, however the monophthalonitrile derivative was isolated (note that this chemistry was chronol;ogically carried out before Chapter 2). The above reaction conditions were repeated twice and the results were the same in each case, thus the target bisphthalonitrile could not be obtained using this method.

We employed an alternative stepwise strategy to prepare the bisphthalonitrile. This strategy involved the preparation and isolation of the monophthalonitrile first, followed by a second reaction on the monophthalonitrile derivative. It was found that the optimum conditions for the preparation of the monophthalonitrile derivative used the same stoichiometric ratio (Chapter 2) as for the initial attempts to prepare the bisphthalonitrile. However, it was found that only 24 hr reaction times were needed to give the same yield of the monophthalonitrile

and only three spots were present by TLC. Separation could be readily achieved by silica gel column chromatography using hexane :ethyl acetate (9:1) as eluent.

The bisphthalonitrile Calix[4]arene **(85)** was then prepared from **(79)** by a second S_NAr displacement using 3-nitrophthalonitrile and K_2CO_3 . We initially encountered a solubility problem, **(79)** wasn't overly soluble in DMF, we were able to solve this problem by employing THF as a co-solvent. All reagents were added in a DMF/THF solvent mix under vacuum over a 5 day period with extra aliquots of **(20)** and base being added each day. After 5 days of reaction time TLC analysis revealed 6 spots by TLC, it would appear that this reaction produces fewer by-products than the earlier attempts at preparing **(85)** from the distal-1,3-dimethoxycalix[4]arene.

Purification of the crude reaction mixture was achieved on a silica gel column first using a 70:30 hexane: ethyl acetate mobile phase. The first spot to elute was the mono substituted starting material **(79)**. The second spot to elute off the column was **(85)** but this was still contaminated. A second column was needed using hexane: ethyl acetate (80:20). Yields of around 23 % where achieved, for **(85)**.



Scheme 32: *Synthetic strategy for the synthesis of* ***(76)*** *and short chain binuclear* ***(74).***

Compound **(85)** was identified using electrospray mass spectrometry where peaks at 951 and 967 m/z indicated the formation of sodiated and potassiated derivatives of **(85)**. ^{1}H NMR analysis of **(85)** shown in Figure 57 shows a cone conformation at room temperature, indicated by the presence of doublets at 3.05 ppm and 4.02 ppm. The positioning of the phthalonitrile peaks as a multiplet between 7.30 ppm and 7.50 ppm indicates that the inclusion complex has disappeared. Crystals of this compound were grown using hexane: ethyl acetate. The x-ray structure of **(85)** confirmed the presence of the cone conformation in the solid state (Figure 58), which supports the ^{1}H NMR analysis.

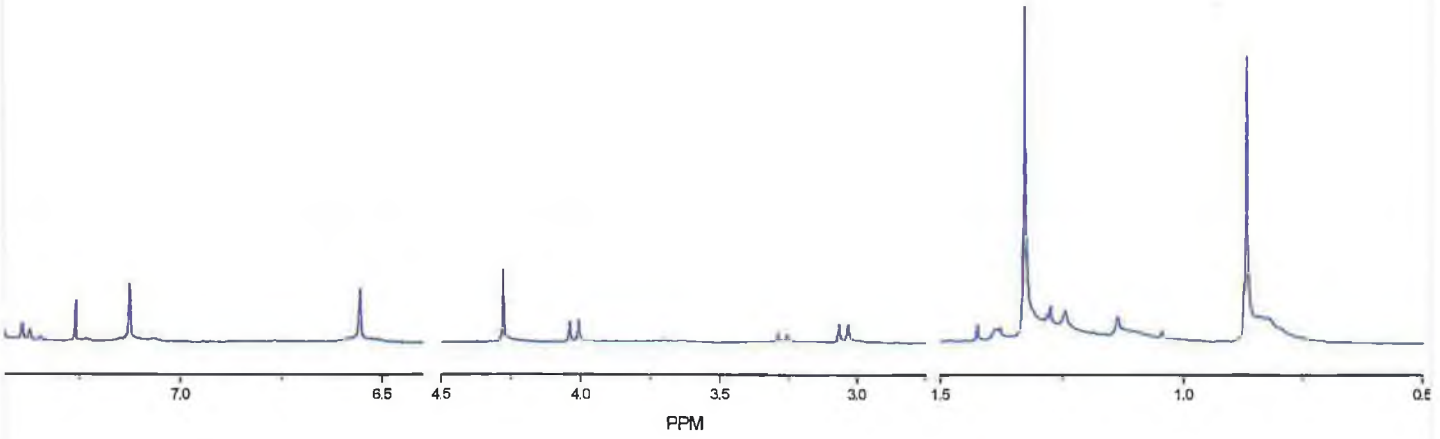


Figure 57: *^{1}HNMR of (85).*

The formation of the cone conformation bisphthalonitrile **(85)** is fascinating as we start with the self-filled partial cone **(79)**! In order for this conformation to be synthesised the reaction must proceed via a similar mechanism as outlined in Chapter 2 for the preparation of **(79)**. We can conclude this based on the following: In the reaction of **(80)** with methyl iodide no inversion to the cone occurred, we believe this is because methyl iodide is a small/strong alkylating agent which is not sterically hindered for reaction to occur on the lower rim. However, 3-nitrophthalonitrile is sterically hindered for reaction on the lower rim, which may allow time for the phenoxide to rotate through the calixarene annulus. If the phenoxide rotates through the annulus the T-bond stabilisation of the inclusion complex is lost and we believe that the phthalonitrile substituent positioned on the upper rim is forced out of the annulus. As this process is occurring it is possible for the reactant, 3-nitrophthalonitrile, to sit into the annulus via the upper rim, to give a preferred reactive set-up. It should also be noted that if the S_NAr displacement of the 3-nitrophthalonitrile reactant was to take place on the

lower rim, it would be sterically hindered by the methyl substituents and furthermore it is not sterically possible for the phthalonitrile substituent (if it did substitute onto the lower rim) to rotate through the annulus to give the observed cone conformation. The final step involves the inversion of the methoxy substituents to give the cone conformation, the methoxy groups should be free to rotate through the calixarene annulus and when this occurs the final cone conformation is stabilised via coordination with potassium cation. (Electro spray mass spectral results indicate the potassium adduct of **(85)** forms)

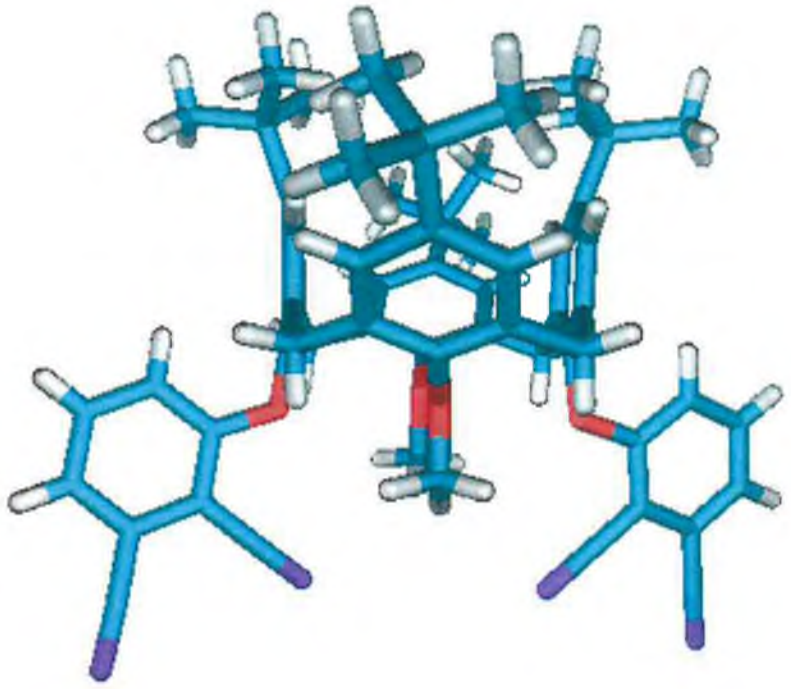


Figure 58: *Crystal structure of (85).*

5.3 Self-Condensation to form the Constrained Phthalocyanine Calix[4]arene (76)

In the preceding section 5.2 we have seen how the starting material **(85)** was synthesised. The self-condensation **(76)** was attempted using bisphthalonitrile **(85)** in the presence of Li/ pentanol at 110°C for 24hr. After 24 hrs the mixture remained a brown colour, indicating that no phthalocyanine was formed. We believe that the failure of this reaction may be due to thermal instability. It is possible that the Pc is forming and decomposing rapidly at high temperature. This idea is supported by results found from the metallation reactions of **(98)** and **(101)**. These reactions were carried out at 110°C in pentanol and it was found that the

starting metal-free phthalocyanine completely decomposed within a few minutes, demonstrating the instability of these novel calixarene phthalocyanines.

5.4 Preparation of the Cofacial Binuclear Phthalocyanine Calix[4]arene (74)

We decided to cross condense **(85)** with **(20)** to prepare the binuclear phthalocyanine **(74)**. Phthalonitrile **(20)** was selected since the resulting by-product, unsubstituted phthalocyanine is highly insoluble and can be easily separated from the target **(74)**. This phthalonitrile also eliminates the problem of positional isomers. The cross condensation of **(74)** with phthalonitrile was carried out in the presence of Li/ pentanol at 110°C for 24hr. In this type of synthetic strategy, the chance of bi-product is increased by the close proximity of the phthalonitrile moieties on the calixarene allowing them to self-condense. Therefore a 8-fold excess of partner phthalonitrile was used.

Separation of **(74)** was carried out first on silica gel chromatography using chloroform as eluant. All bands were collected and rechromatographed a second time on a silica gel column using chloroform as eluant. All phthalocyanine fractions were collected and the solvent removed under reduced pressure. A quantity of the phthalocyanine mixture was then dissolved up in a minimum amount of THF and applied to a size exclusion column (Bio-Beads SX-3). The mixture was separated into two bands, the first band was the 'target binuclear Pc'. The binuclear band was eluted through the size exclusion column a second time, only a single band was observed.

The UV-Vis of the pure sample indicated the formation of a phthalocyanine by giving a sharp absorbance at 671 and 705 nm (Figure 59). However it did not give us the characteristic broad blue shifted Q-band absorption, which would be expected of a co-facial binuclear phthalocyanine (see Chapter 6). The shape and absorption indicated the formation of a mononuclear metal-free phthalocyanine.

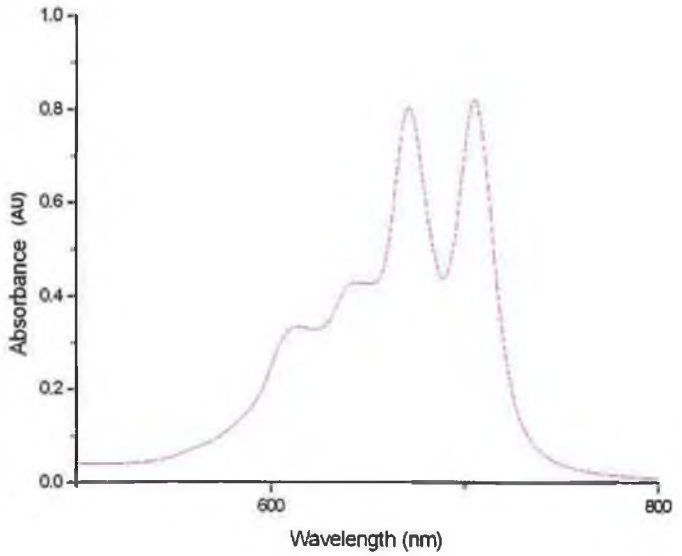


Figure 59: *UV-Vis of pure sample in THF.*

A MALDI-TOF mass spectrum and FTIR spectrum were obtained for the isolated phthalocyanine product. A single cluster is present at 1334 m/z (Figure 60) and a stron nitrile stretch is observed in the FTIR (Figure 62). Two proposed structures to explain the observed data are outlined Figure 61.

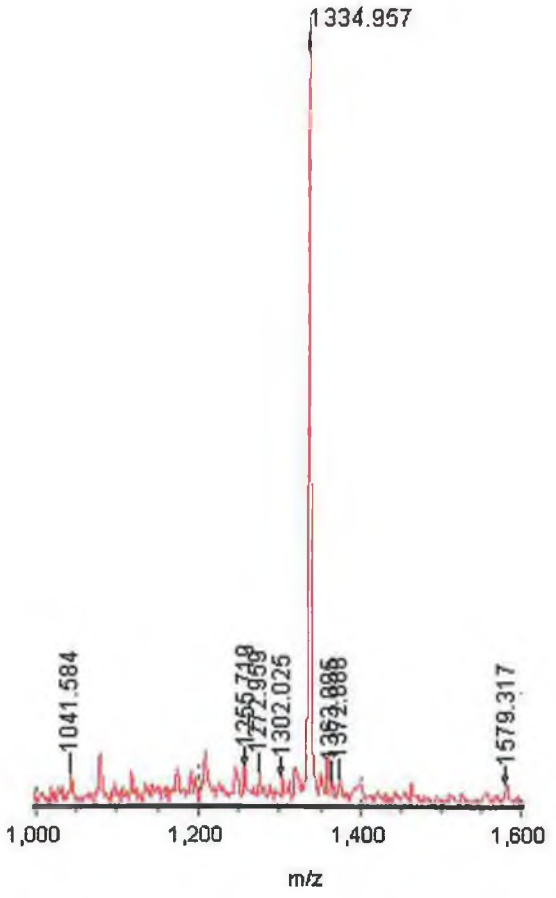
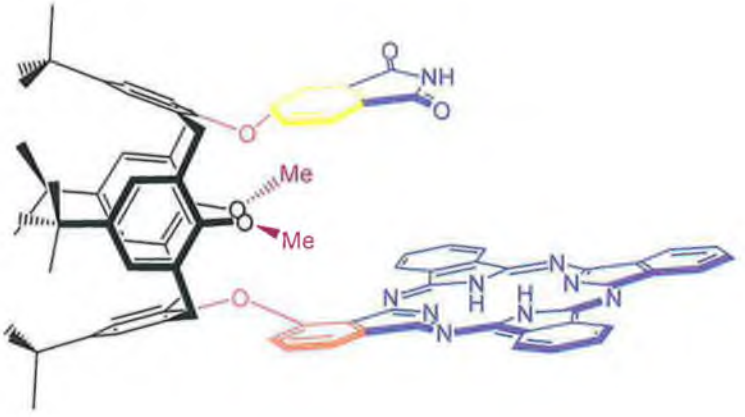


Figure 60: *MALDI-TOF of pure sample*

(103)

OR



(104)

Figure 61: *Proposed structures from the Mass Spectrum.*

The problem left is how to distinguish between these two structures and correctly identify the product? Shown in Figure 61 are two potential structures which match the parent ion cluster found by MALDI-TOF MS. When we take an IR of our pure sample (Figure 62) we can identify a C=O stretch at 1737 cm^{-1}, we also observe a rather intense peak at 2230cm^{-1} which corresponds to a nitrile group absorption. We believe that structure **(103)** corresponds to what is observed in the IR spectrum since it possesses a nitrile absorption. (to aid in this assignment we also compared the IR spectrum of the isolated product with phthalic anhydride **(105)** phthalimide **(106)** and 3-hydroxyphthalic anhydride **(107),** their IR spectra are in the appendix). However, the calculated mass spectrum of **(103)** (see experimental) does not correspond to the mass spectral data obtained, but it does fit **(104)** (M+1). Reliable assignment cannot be made with the conflicting spectral data.

It would appear that there is too much steric constraint in **(85)** to effectively form a binuclear phthalocyanine, only one of the phthalonitrile groups of **(85)** participates in the condensation reaction, and the remaining phthalonitrile is partially hydrolysed/left unreacted. There have been previous reports of similar phenomena, one such report involves the mixed condensation of a 1,1'-bis(4-phthalonitrile)ferrocene with 4-neopentoxy phthalonitrile. This reaction yielded only a trace quantity of the binuclear phthalocyanine, the main product was a mononuclear phthalocyanine with a phthalonitrile substitutent left unreacted. A second report involves the cross condensation of a catechol bisphthalonitrile which yielded again a mononuclear species with a single phthalonitrile left unreacted. This product was again condensed to give a mixed binuclear phthalocyanine. Unfortunately we only obtained small quantities of material and a second attempt to convert the phthalimide group to Pc was not attempted, but it may be possible to achieve this in the future

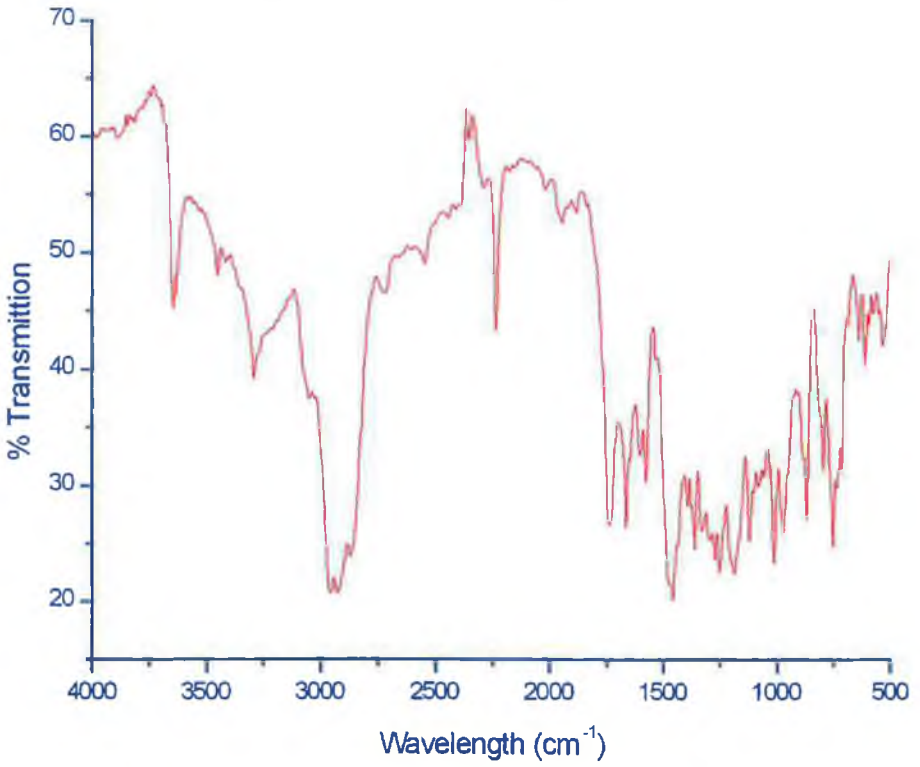


Figure 62: *IR of pure sample*

5.5 Experimental

Column chromatography was carried out on all of the compounds using Riedel de Haen silica gel 60. Thin layer chromatography (TLC) was carried out using Riedel de Haen silica 60F254 plates using specified solvents. Gel permeation chromatography was carried out using SX-3 bio beads with THF as mobile phase. All solvents used were of HPLC grade.

A variety of techniques where under taken to elucidate the structure of these compounds. All NMR experiments where carried out on a Bruker AM 400 spectrometer. Mass spectra were analysed on two different instruments 1) a Esquire-Bruker/Hewlett Packard LC-MS 1100 series, equipped with an electrospray ion source for the phthalonitrile starting marterials **(85)** and 2) a Ettan MALDI-TOF Pro from Amersham BioSciences was used for the phthalocyanine dyes **(104)**. IR spectra where recorded on a Perkin Elmer 2000 FT-IR spectrometer. A Perkin Elmer Lambda 900 UV/Vis/NIR spectrometer was used to obtain the UV-Vis spectra. Melting points are carried out on a Bibby Stuart Scientific melting point SMP1. Crystal structures where run an a Bruker-Axis Smart Apex CCD three-circle diffractometer.

5.5.1 5,11,17,23-tetra-t-butyl-25,27-dimethoxy-26,28-(-3-[-1,2-phthalonitrile])calix[4]arene (85)

K_2CO_3 (0.66 g, 4.76 mmol), **(79)** (1.00 g, 1.19 mmol) and 3-nitrophthalonitrile (0.82 g, 4.76 mmol) were stirred under vacuum in anhydrous DMF/THF (15 cm^3/5 cm^3) for ten days. On day three and every subsequent day K_2CO_3 (0.17 g, 1.19 mmol) and 3-nitrophthalonitrile (0.21 g, 1.19 mmol) were added. After ten days the reaction mixture was then poured on to ice water (50 mls), filtered and the solid was washed with hot water (2x25 ml). The crude brown solid was purified by column chromatography using 70:30 hexane: ethyl acetate and then recolumned using 80:20 hexane: ethyl acetate. A yellow solid was obtained (0.24 g, 0.26 mmol, 23 % yield).

Product was characterised by **^{1}H NMR** ($CDCl_3$)δ (ppm); 0.87, (s, 18 H, t-Bu); 1.33, (s, 18 H, t-Bu); 3.05, (d, 4 H, J=12.8 Hz, Ar-CH_2-Ar); 4.02, (d, 4 H, J=12.8 Hz, Ar-CH_2-Ar); 4.28, (s, 3H, CH_3); 6.56, (s, 4 H, Ar H); 7.13, (s, 4 H, Ar H); 7..4, (s, 6 H, ArH).
ESI m/z : 951 ($M + Na^+$), 967 ($M + K^+$) $C_{62}H_{64}O_4N_4$

IR(KBr [cm^{-1}]): 2960 cm^{-1} $\nu(Bu_t)$, 2229 cm^{-1} ν(CN).

MP: Decomposed into a brown solid at 290°C

Crystal Structure: See attached cd.

5.5.2 Metal-free tetra(5,11,17,23-Tetra-tert-butyl -25,26,28- trimethoxy) calix[4]arenephthalocyanine (76)

Lithium (0.03 g, 4.28 mmol) was added to 1 ml of pentanol in a 10 ml round bottom flask and heated to 50°C for 30 minutes to form the lithium alkoxide. To this reaction flask **(85)** (0.1 g, 0.107 mmol) was added and the reaction mixture was then heated to 110°C for 24 hr. The reaction mixture was then poured on to ice water (20 mls), this layer was then extracted with ethyl acetate (3 x 10 mls) in a separatory funnel. The organic extracts were combined, then washed with a saturated saltwater solution, dried over $MgSO_4$, filtered and evaporated to yield a brown solid. Then a UV-Vis spectrum of this crude product was taken. No phthalocyanine was present in the crude product.

5.5.3 1-(-27-[Cone 5,11,17,23-Tetra-tert-butyl-25-phthalimide-26,28-dimethoxy Calix[4]arene]) Phthalocyane (104)

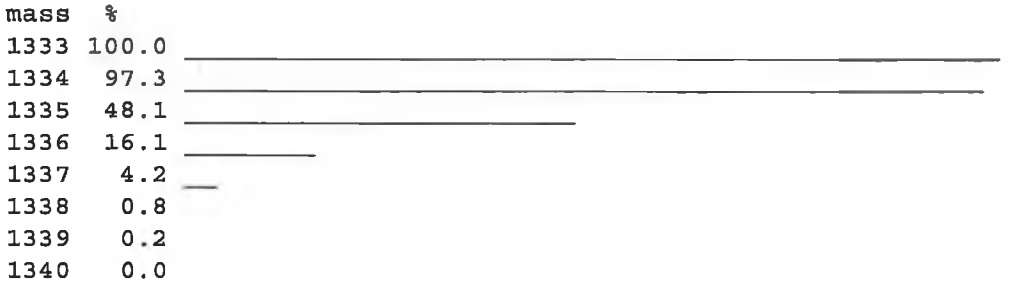
Lithium (0.03 g, 4.28 mmol) was added to 1 ml of pentanol in a 10 ml round bottom flask and heated to 50°C to form the lithium alkoxide for 30 minutes. To this reaction flask **(85)** (0.1 g, 0.107 mmol) and **(8)** (0.12 g, 0.963 mmol) was added and the reaction mixture was then heated to 110°C. The reaction mixture turned green after 1 hr and was then poured on to ice water (20 mls) 24hr later, this layer was then extracted with ethyl acetate (3 x 10 ml) in a separatory funnel. The organic extracts were combined, then washed with a saturated saltwater solution, dried over $MgSO_4$, filtered and evaporated to yield a green solid. This was then separated on silica gel column using chloroform as eluant. The collected green fractions were evaporated to dryness. Final purification involved dissolving the green product in a minimum of THF (~1ml) which was then applied to size exclusion column (bio-beads SX-3) using THF as eluant to give (0.012 g, 0.009 mmol, 8 % yield).

IR(KBr [cm^{-1}]): 3293 cm-1 ν(), 2924 cm^{-1} $\nu(Bu_t)$, 2234 cm^{-1} ν(CN), 1737 ν(C=O), 1666 ν(), 1602 ν(), 1577 ν().

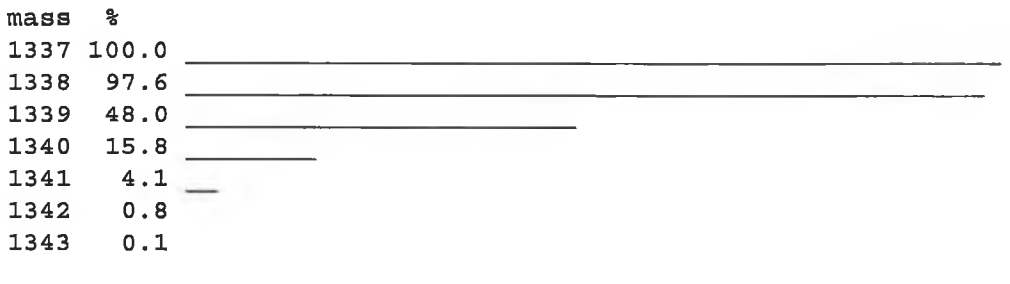
Product was characterised by **ESI m/z :** 1334 m/z (see below)

UV-Vis (THF): 671 and 705 nm

Calculated for **(104)**Formula: $C_{86}H_{79}O_6N_9$



Calculated for **(103)** Formula: $C_{86}H_{78}O_4N_{10}Na_1$



6. The Synthesis of a Spacer Linked Calix[4]arene Cofacial Binuclear Phthalocyanine

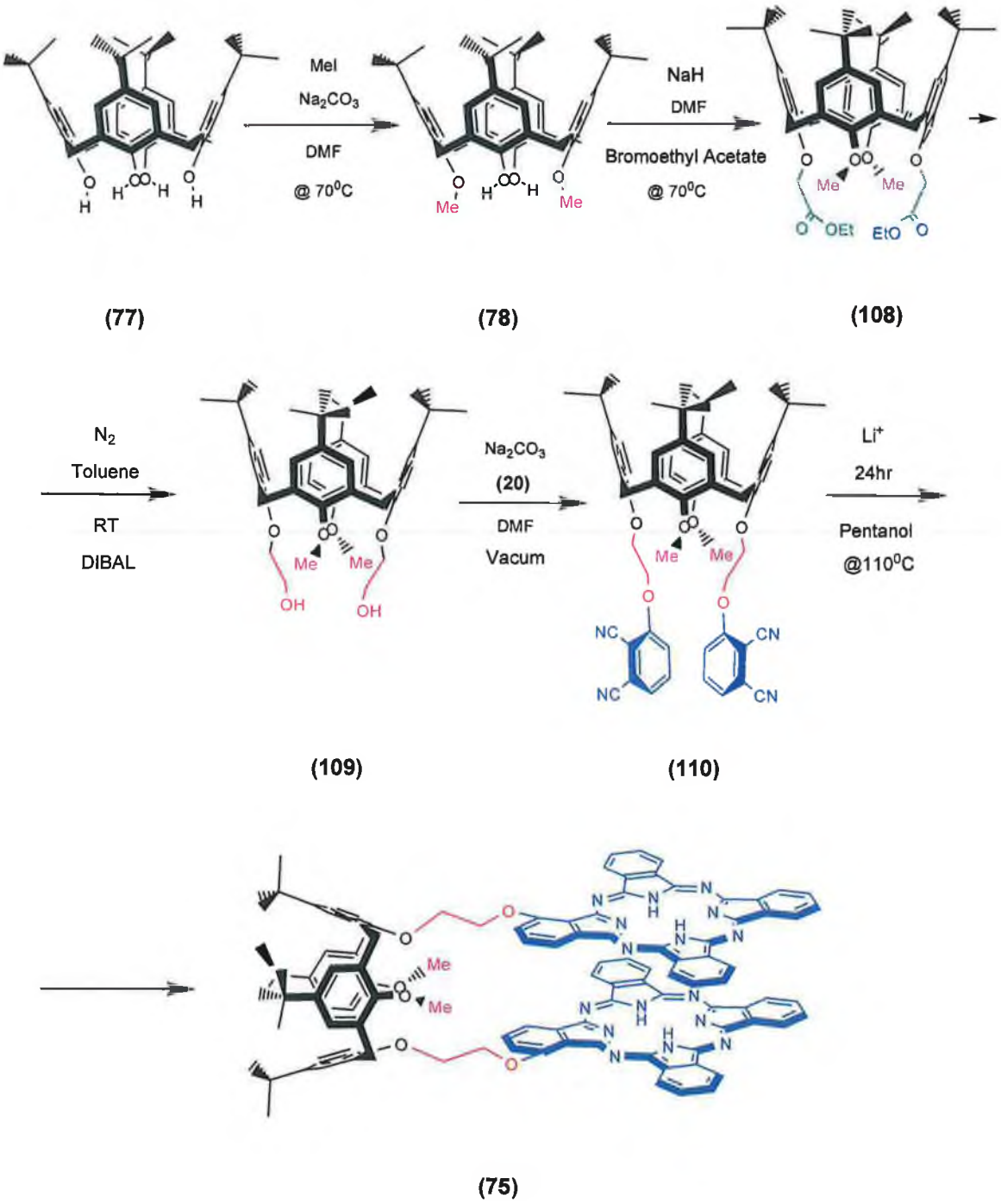
6.1 Introduction

Scheme 1 outlines a synthetic pathway for the preparation of a co-facial binuclear phthalocyanine calix[4]arene **(75)**. In this synthetic strategy we again must first start with **(78)** allowing us to introduce the spacer in a distal arrangement. The preparation of the spacer requires two steps; first an ester is placed on **(108)** and it is then subsequently reduced to the bisalcohol **(109)**[100]. The resulting bisalcohol is then utilized to prepare the bisphthalonitrile. The phthalonitrile calix[4]arene **(110)** which is formed from this reaction is subsequently cross condensed with phthalonitrile to form the co-facial binuclear phthalocyanine **(75)**. This reaction sequence is 5 stages long which lead to all the reactions being repeated a number of times to build up material for the final product.

6.2 Long Chain Spacer Synthesis

6.2.1 Synthesis of 5,11,17,23-tetra-tert-butyl-25,27-diethoxycarbonylmethyleneoxy-26,28-dimethoxycalix[4]arene

The first stage in the spacer formation involves the esterification of the lower rim of **(78)** using NaH, ethyl bromo acetate in DMF at 70°C for 2-days[101]. Extra additions of base and ethyl bromo acetate where added on the second day (Scheme 33). This esterification reaction, like the etherification reaction, is influenced by a variety of factors including solvent, base strength and stoichiometry. In our attempt to fully substitute **(78)** with ester groups a strong base such as NaH was used with a large excess of alkylating agent in order to give optimum yields. Also the use of a strong base should lead to the formation of the cone conformation, which in the end is desired as we want two co-facially arranged phthalocyanines, as described in Chapter 2. If a weaker base such as K_2CO_3 was to be used there is the possibility that a mixture of conformations could be formed. This reaction was first worked up using a 2 N HCL wash. However when the reaction mixtures were analysed by HPLC[102], we found that a mixture of products had been formed including the target diester calix[4]arene, but what was perhaps most interesting is that the methyl groups had been cleaved off. This acid cleavage is under further investigation as a synthetic method for the synthesis of the diester. A similar cleavage with tetra methoxy calix[4]arene under treatment with K_2CO_3 (using an acid work-up), the product of this reaction was the dimethoxy calix[4]arene[103]. To prevent this cleavage from happening we simply removed the acid from the work-up.



Scheme 33: *Synthetic pathway for the formation of the cofacial-binulear phthalocyanine calix[4]arene (75).*

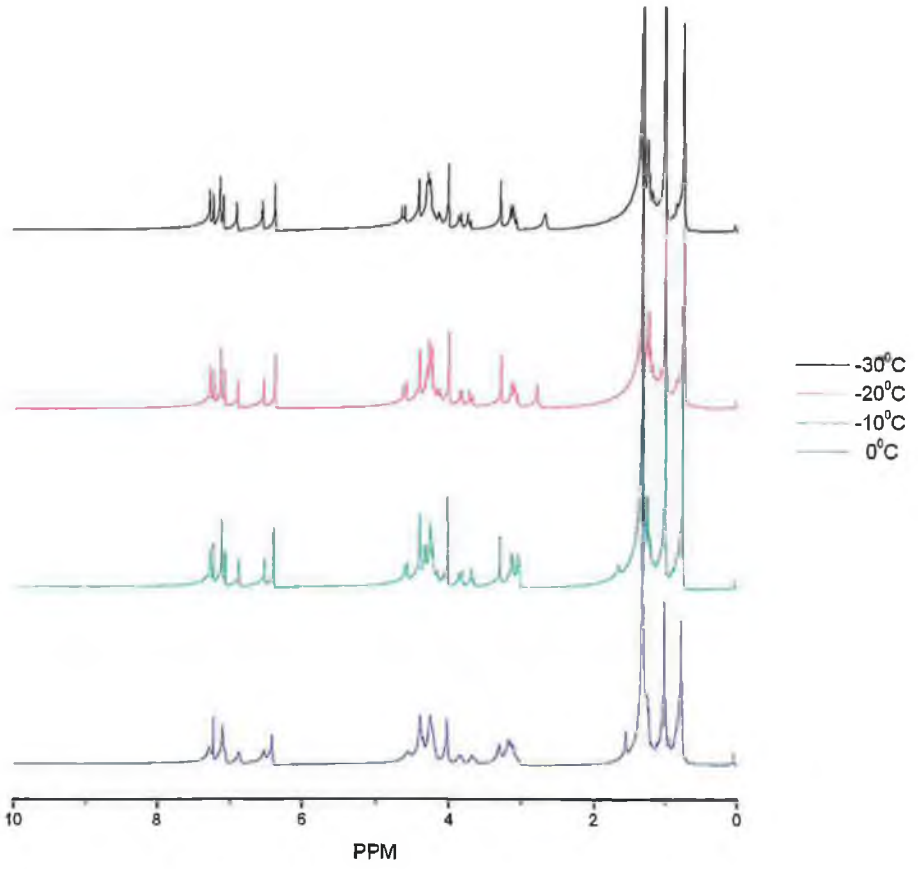


Figure 63: *Low temperature ^{1}H NMR study on* ***(108).***

Purification of this compound was two fold. First the crude was boiled in methanol to remove the excess esterification agent plus inorganic salts and this white mixture was subsequently purified by silica gel chromatography using a 90:10 hexane: ethyl acetate eluent. The first band, which eluted from this column, was our product. Yields of 50 % were achieved for **(108)** after chromatography.

The characterization and conformational identification of **(108)** by ^{1}H NMR at RT was impossible! Only a poorly resolved spectrum was obtained. NMR is the paramount way of determining conformational impurity. From previous work we found that mass spectrometry can identify our compound **(108)** as we obtain a peak at 871 m/z (This peak corresponds to the sodiated peak of **(108)** which is to be expected because NaH were used as bases.), however this does not give a full idea of conformational purity. In an attempt to solve our problem we first doped our ^{1}H NMR at RT with sodium salts (sodium iodide) to see if we could organize **(108)** by means of co-ordination, this had no real effect. There are many

reports in the literature that calixarenes containing methyl or ethyl groups on the lower rim in the absence of hydrogen bonding rotate in and out of the annulus freely at RT[86]. This leads to the unresolved peaks at RT so high and low temperature ^{1}H NMR studies were under taken to see if the spectrum of **(108)** could be resolved. Szydzik *et al.*[104] had previously resolved the ^{1}H NMR of **(108)** using DMSO however we could not get **(108)** to dissolve in DMSO so different solvents were used . Low temperature studies in $CDCl_3$ did not resolve the spectrum into two conformations (Figure 63) as Szydzik *et al.*[104] had indicated in his paper. In a bid to resolve this ^{1}H NMR we turned our attention to high temperature studies in deuterated nitrobenzene (Figure 64). (Due to the explosive nature of this compound we required a C49 explosives form from the gardaí this took 4 months to obtain.) You can see as we go up in temperature there is an immense change in the spectrum with temperature and a full resolved spectrum was observed at 150°C. At this temperature **(108)** is in the cone conformation since there is a pair of doublets for the methylene protons at 3.49 ppm and 4.47 ppm. The ester groups are present because the methylene protons of the ester group appear as a singlet at 4.53 ppm and the ethyl group of the ester as a triplet and a quartet at 1.35 ppm and 4.34 ppm respectively (Figure 65).

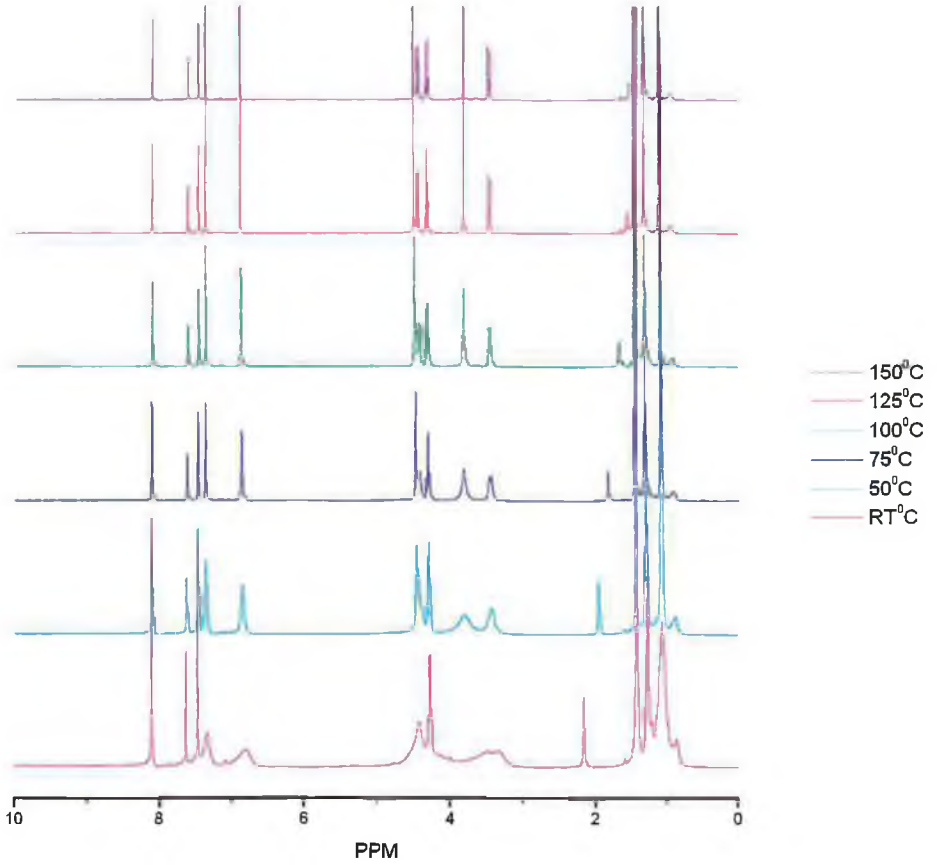


Figure 64: *High temperature ^{1}H NMR study on* ***(108)***.

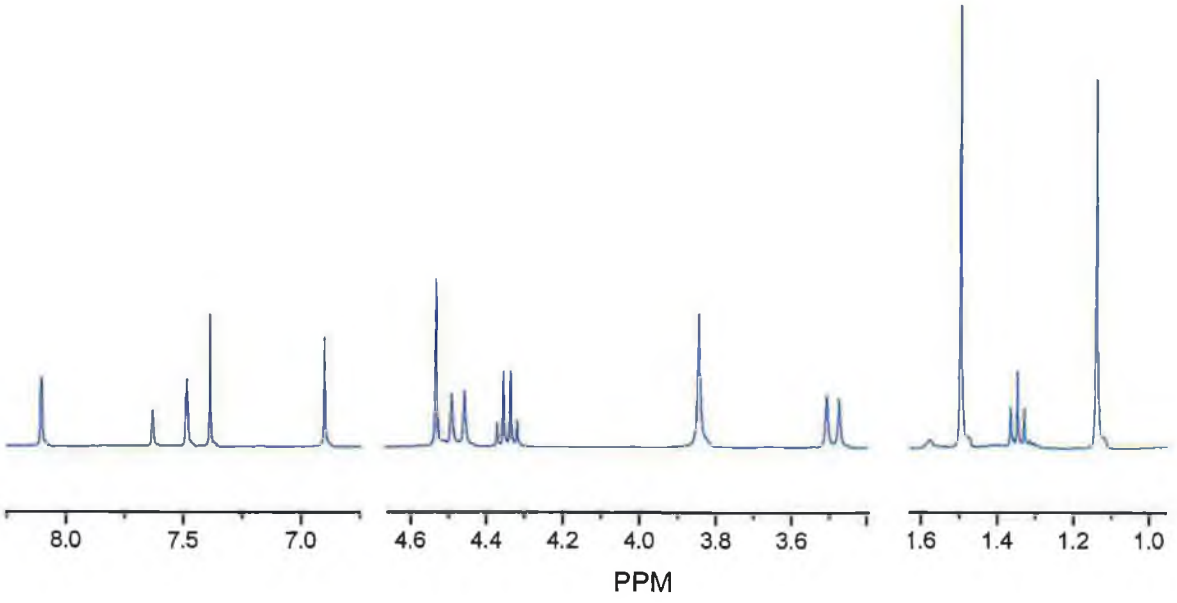


Figure 65: *^{1}H NMR spectrum of* ***(108)*** *@ 150 °C.*

6.2.2 Synthesis of 5,11,17,2 3-Tetra-tert-butyl-25,27-dihydroxyethyleneoxy-26,28-Dimethoxycalix[4]arene (109)

This ester was converted to the alcohol using $LiAlH_4$ in THF for 24 hr under N_2, after purification it was realised full conversion had not taken place. We optimised the conditions and found DIBAL to be quite effective at giving complete reduction, the conditions were DIBAL, toluene for 24 hr under N_2[105].

We found the most efficient way to purify this mixture was to use a short silica column with a 80:20 hexane: ethyl acetatemobile phase. Approximately 200 ml of mobile phase was run through the column to remove organic soluble impurities. The eluent was then changed to methanol, which removes our compound in its pure form. Yields of 70 % were achieved for **(109)** after chromatography.

The ^{1}H NMR spectrum of this compound at RT was again poorly resolved since the methoxy groups can rotate through the annulus. So for identification an electrospray mass spec was run. A peak was found at 787 m/z, which again corresponds to the sodiated peak for **(109)**.

Once identification had been achieved high temperature studies where initiated for **(109)**. Figure 66 again shows how effective high temperature is at resolving the spectrum of the calix[4]arene scaffold. The Calix[4]arene scaffold is in the cone conformation at 150°C which is confirmed by the presence of a pair of doublets at 3.55 and 4.40 ppm. The t-butyl groups are found at 1.31 and 1.33 ppm and the aromatic peaks are found at 7.17 and 7.19 ppm, these two peaks are coalescing due to the similarities in the different pendant groups attached to the scaffold (Figure 67) . These pendant groups however are not very resolved this is more than likely due to the ability of the dihydroxyethyleneoxy groups being able to hydrogen bond either to each other or to the methoxy oxygen's on the lower rim. As a result the lower rim substituents may exist in more than one 'conformation' causing poor resolution of the ethyl and methyl protons.

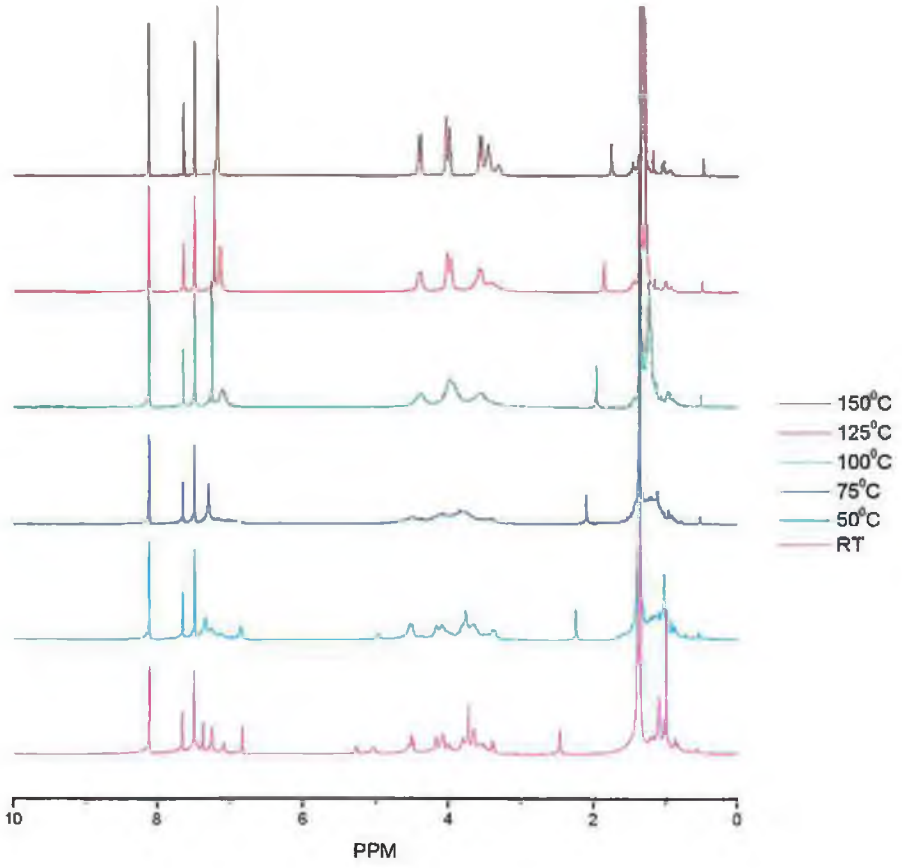


Figure 66: *High temperature ^{1}H NMR study on (109).*

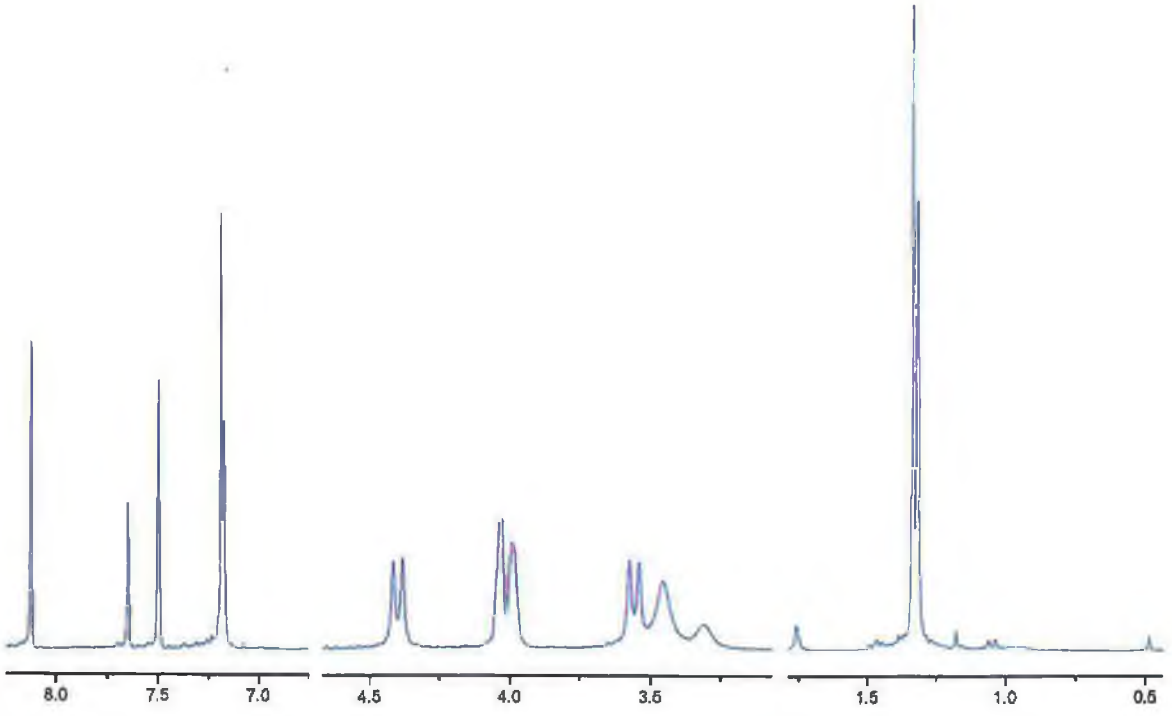


Figure 67: *^{1}H NMR spectrum of (109) @ 150℃.*

6.3 *Phthalonitrile Synthesis*

The preparation of **(110)** is done under similar conditions to the phthalonitrile **(79)** described in Chapter 2 and **(99)** found in Chapter 4[37]. The alcohol **(109)** is stirred in the presence of K_2CO_3 and 3-nitrophthalonitrile in a solution of DMF under vacuum for five days. It was noted that the reaction is slightly quicker than that used to prepare **(85)**. This is due to the flexibility of the long chain ethyl groups.

Purification of **(110)** involved a silica gel column using a 80:20 hexane: ethyl acetate eluent. The first band off the column was our desired compound **(110)**. Yields of around 25 % where achieved for **(110)** after chromatography.

Again ^{1}H NMR analysis of **(110)** at room temperature lead to an unresolved spectrum for the same reasons as stated earlier, the methoxy groups are highly flexible and rotate through the annulus of the calix[4]arene. Electro-spray mass spectrometry was the first identification technique used and it gave us peaks at 1039 and 1055 m/z, which correspond to the sodiated and potassiated derivatives of **(110)**. High temperature studies of **(110)** (Figure 68) in nitrobenzene (d_5) again showed that a spectrum could be resolved at 150°C. In this spectrum the doublet for the methylene proton can be seen at 3.55 ppm and 4.47 ppm respectively (Figure 69). This suggests that **(110)** is still in the cone conformation. The spacer methylene groups (of the ethyl substituents) can be seen at 4.39 ppm and 4.73 ppm however these are not fully resolved. The phthalonitrile hydrogen can be seen as a triplet at 7.73 ppm and a doublet at 7.4 ppm, however the other doublet cannot be seen as it lies under one of the solvent peaks. It is worth mentioning that when this sample was heated up to 195°C the spectrum split the methylene spacer groups into triplets Figure 70.

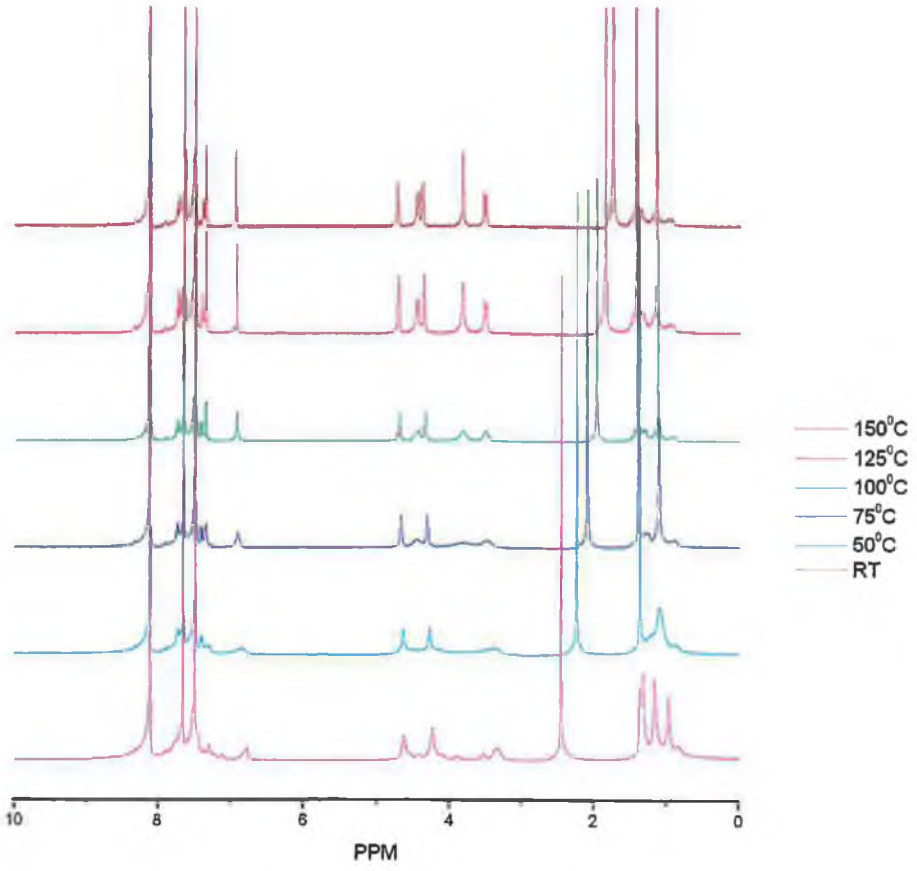


Figure 68: *High temperature ^{1}H NMR study on* ***(110)***.

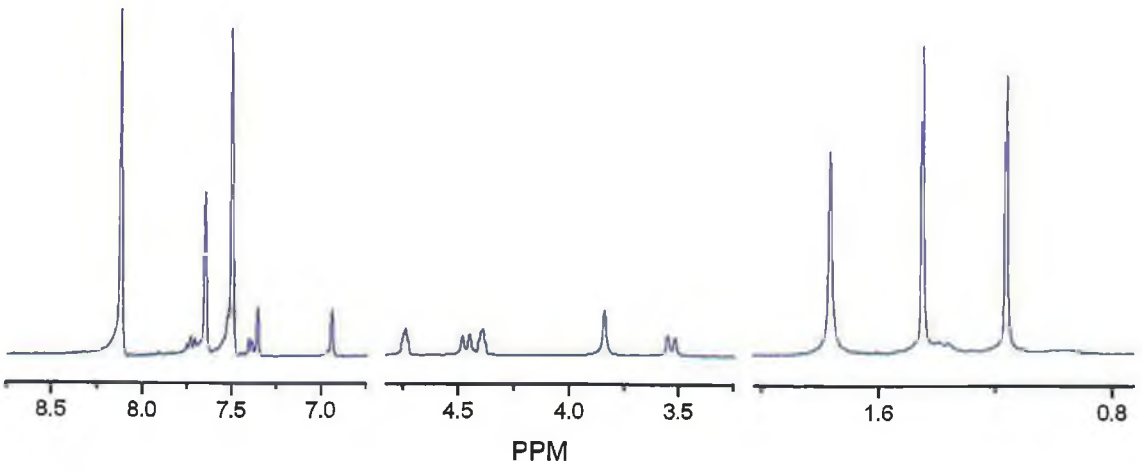


Figure 69: *^{1}H NMR spectrum of* ***(110)*** *@ 150℃.*

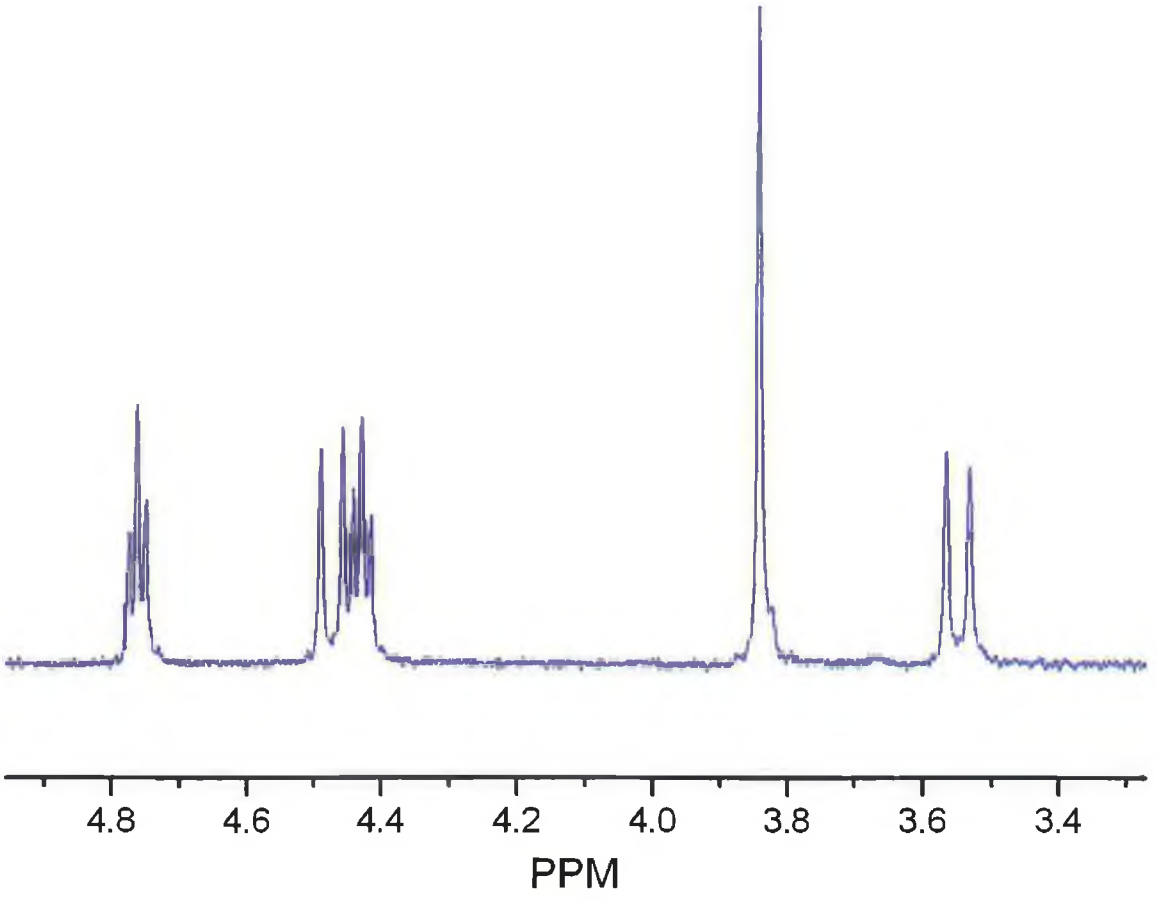


Figure 70: *^{1}H NMR spectrum of **(110)** @ 195 °C from 3.3 ppm to 4.9 ppm.*

6.4 Long Chain Binuclear Phthalocyanine Calix[4]arene

6.4.1 Synthesis of Unsubstituted Binuclear (75(a))

The cross condensation of **(110)** with phthalonitrile partner to prepare a binuclear phthalocyanine was carried out in the presence of Li/ pentanol at 110°C for 24 hr. In this type of synthetic strategy, the chance of bi-product is increased by the close proximity of the phthalonitriles moieties on the calixarene. Therefore these reactions are typically carried out using an 8-fold excess of partner phthalonitrile. Again unsubstituted phthalonitrile was chosen as in the synthesis of **(97)** in Chapter 3 because the by-product unsubstituted phthalocyanine is not soluble in organic solvent, which makes separation less complicated and secondly we will obtain a single isomer.

Separation of this compound was carried out first on silica gel using chloroform as eluent, followed by THF. All bands were collected and chromatographed for a second time on a silica gel column using THF as eluent. All phthalocyanine fractions were collected and the solvent removed under reduced pressure. A quantity of the phthalocyanine mixture was then

dissolved up in a minimum amount of THF and applied to a size exclusion column (Bio-Beads SX-3). The mixture was separated into two bands, the first band was the target **(75(a))**. This band was collected and eluted a second time through the size exclusion column, only a single band was observed. The fraction collected from the size exclusion column was further purified by another silica gel column using THF as eluent, the collected Pc was then reprecipitated from THF/Methanol (yield = 8 %).

The presence of **(75(a))** was confirmed by MALDI with a cluster peak at 1788 m/z. The UV-Vis of the binuclear Pc gave a characteristic broad blue shifted Q-band absorption at 690 nm. From the literature the shape of the Q-band indicates that the phthalocyanine moieties are co-facial see Figure 71.

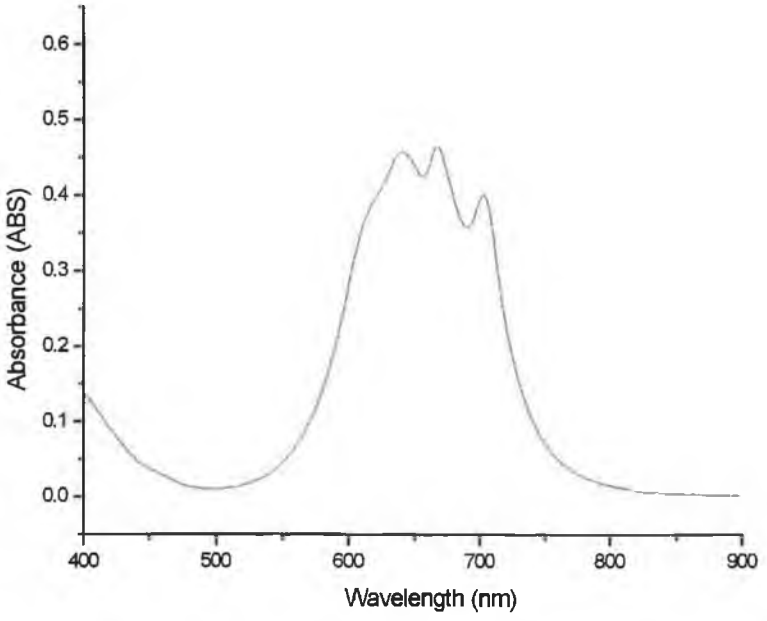
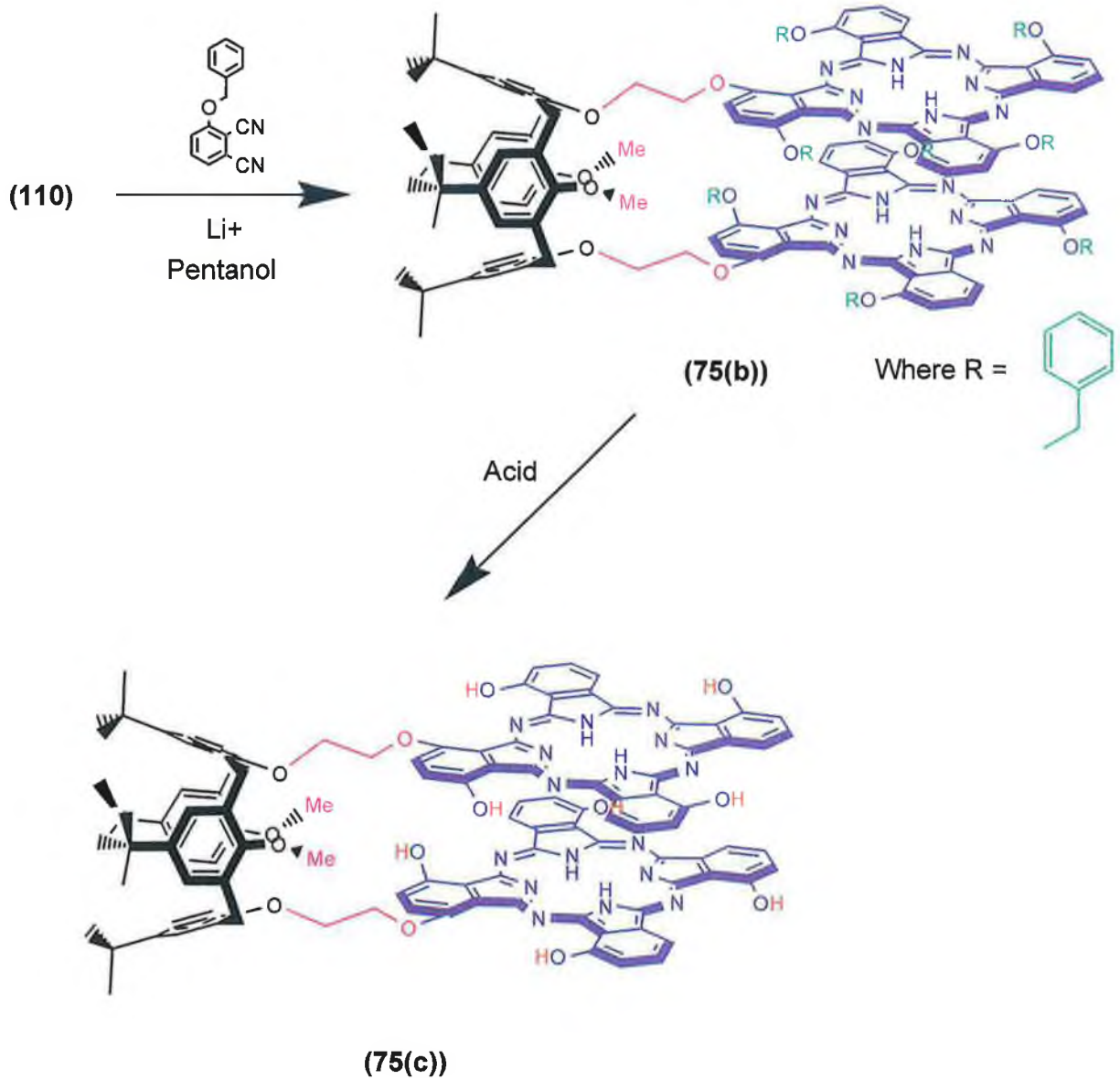


Figure 71: *UV-Vis of (75).*

6.4.3 Synthesis of Substituted Binuclear (75(b))

The same experimental procedure that was used successfully for the unsubstituted binuclear phthalocyanine was used to prepare **(75 (b))**. The partner phthalonitrile that was chosen was 3-benzyloxyphthalonitrile which was prepared by a nucleophilic displacement reaction between benzyl alcohol and 3-nitrophthalonitrile. The first attempt at preparing the partner phthalonitrile was at elevated temperatures of 70°C, unfortunately phthalocyanine condensation occurred. The same reaction conditions described in Chapter 2 were then applied and the target product was obtained in a 60 % yield. The motivation behind choosing

this partner was simple. The benzyl substitutent can be cleaved by acid to form give a hydroxyl group which will also allow us to prepare a hydroxy substituted binuclear phthalocyanine. (see Scheme 35.)



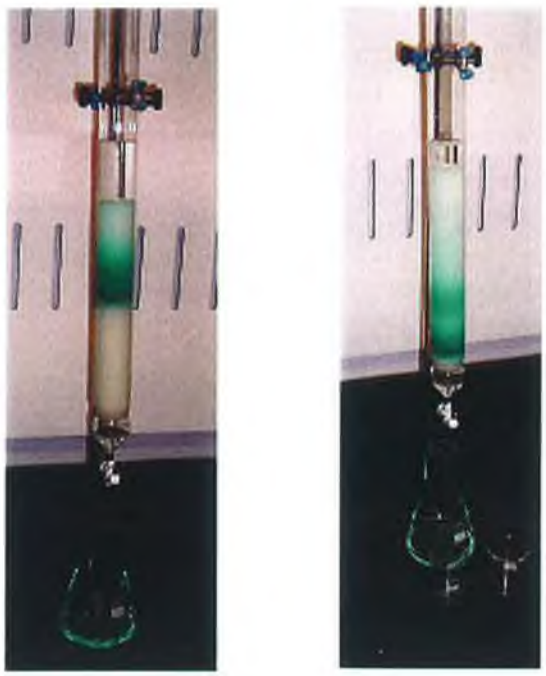
Scheme 34: *Synthetic route for the synthesis of substituted binuclear* **(75(b)) and (75(c))**

Both the bisphthalonitrile **(110)** and the partner 3-benzyloxyphthalonitrile were reacted under the same conditions used to prepare **(75(a))**. The crude product was purified by silica gel chromatography using chloroform as eluant. In the case of this reaction, unlike with **(75(a)),** the by-product phthalocyanine tetrabenzyloxyphthalocyanine is highly soluble in organic solvents. As a result purification of this reaction mixture was far more troublesome than with **(75(a))**. A first column was run on the reaction crude using chloroform as eluant. The fractions that were collected in the first three hours of running the column were solely the by product as determined by both TLC and UV-VIS analysis. The later fractions off the column,

obtained after hour four of running the column, contained a mixture of both the binuclear Pc **(75(b))** and the by-product phthalocyanine. We confirmed this by UV-VIS spectroscopy, there was a slight change in the UV-VIS spectrum with a broad peak beginning to show up under the Q-band of the tetrabenzyloxyphthalocyanine by-product. All fractions from this point on were collected until no further soluble fractions remained on the column (column was run for 8 hours). A second silica gel column was run on the fractions collected in the last hours from the above column. Chloroform again was used as eluant, this column was used to remove baseline impurities. The collected fractions from this column were combined and chromatographed again until all baseline impurities were removed.

Of the material collected from this exhaustive chromatographic procedure 10 mg was taken up in 5 ml of THF and applied to a size exclusion column (SX-3 polystyrene). Two bands eluted from the column, the first contained the binuclear Pc, the second was the mononuclear Pc. The photographs in Figure 72 illustrate the superb separation of the two phthalocyanines using size exclusion chromatography. It should be noted that typically we can not apply more than 15mg of the phthalocyanine mixture through the column in a single run, thus to purify this mixture requires multiple runs, a typical run requires slightly over 1.5 hours to complete.

The binuclear Pc **(75(b))** obtained from the size exclusion column was then flushed through another silica column with THF as eluant, and the collected Pc was reprecipitated from THF/methanol. The collected precipitate was analysed by MALDI-TOF MS, unfortunately no parent ion cluster was observed for the target phthalocyanine. A sample of this phthalocyanine was further purified by another silica gel column and again reprecipitated and analysed by MALDI-TOF, unfortunately no parent ion was observed. Although the UV-VIS spectrum, solubility properties and size exclusion separation is typical of a binuclear phthalocyanine, we cannot conclusively characterise this product and work was discontinued on this compound.



START **END**

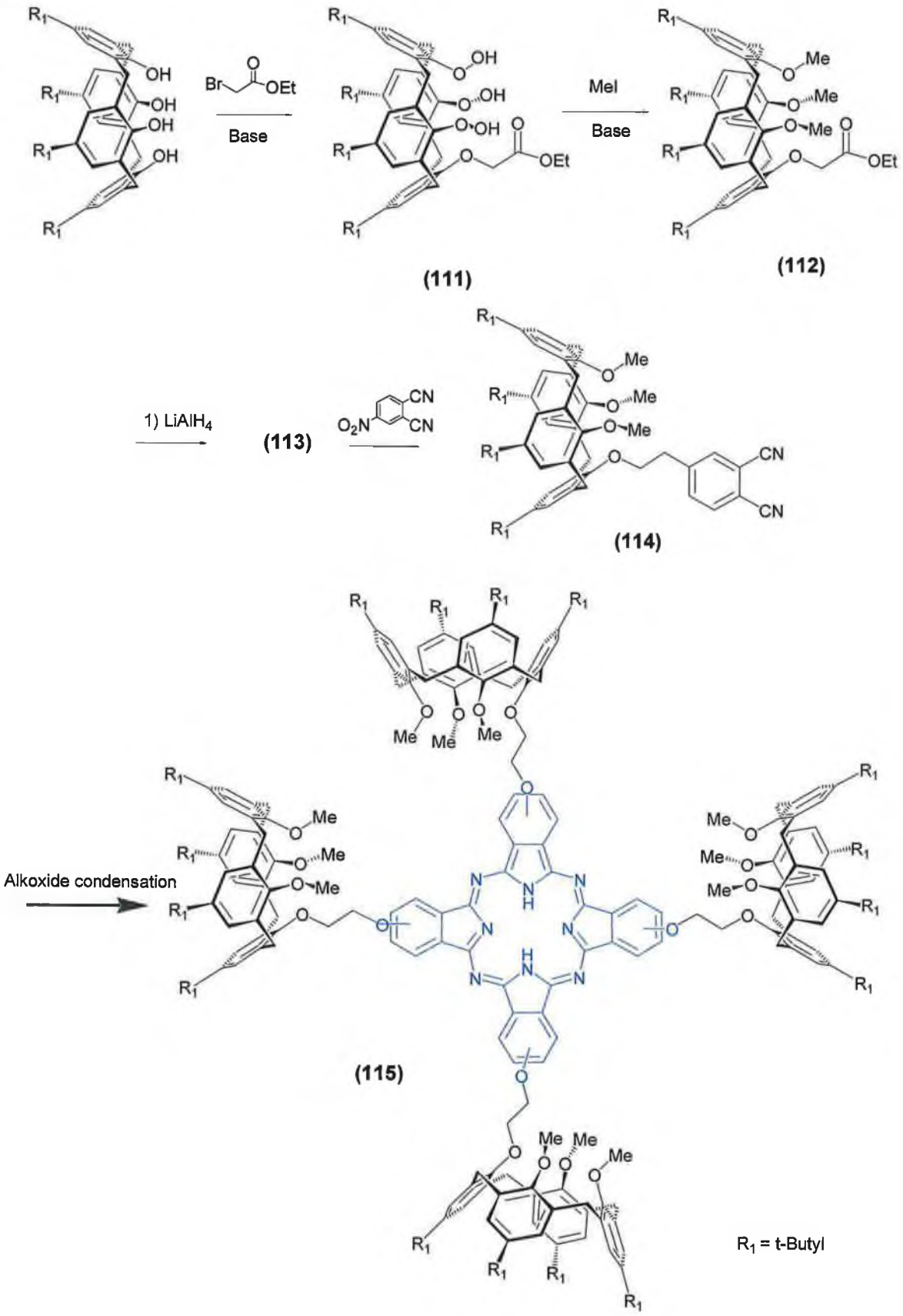
Figure 72: *Separation of* ***75(b)*** *on SX-3 bio-beads (THF). Front running bacd is the binuclear* ***75(b)*** *followed by tetrabenzyloxyphthalocyanine.*

6.5 *Attempted Preparation of a Long Spacer Tetracalix[4]arene Phthalocyanine*

Parallel to the long spacer binuclear phthalocyanine project we decided to prepare a long-spacer tetracalix[4]arene phthalocyanine, we were interested in determining if spacing the calixarene away from the phthalocyanine ring would have any significant effect on performance compared to our other tetracalixarene phthalocyanines described earlier. Outlined in Scheme 35 is a proposed route to our target phthalocyanine **(115)**.

To prepare **(115)** we must first synthesise the monoester from tetra-t-butylcalix[4]arene. Earlier work in our group[Error! Bookmark not defined.] had focussed on the preparation of the 1,3-distaldiestercalix[4]arene, however this work was fraught with the presence of many impurities in particular the monoestercalix[4]arene. We decided to reproduce this work except focussing on optimising the yield of the monoester over the distal 1,3-diester product utilising stoichiometric control (we found that a ratio of 1:4 of ethyl bromo acetate worked best). The yields of this reaction were extremely poor at only 5 % and involved exhaustive column chromatography to separate from the reaction mixture. In order to obtain a gram of starting material we had to do 10 reactions, in an attempt to reduce the time invovled the reaction was scaled up. This made the mono ester tougher to obtain and lower yielding.

After 'optimising' the yields for **(111)** we then proceeded to methylate the remaining hydroxy groups on the calixarene. This reaction was carried out using excess alkylating agent, MeI, and K_2CO_3 in DMF. Surprisingly this alkylation step generated a mixture of starting material, monomethyl and dimethyl derivatives of **(111)** along with trace amounts of **(112)**. Various conditions (varying bases [various carbonate bases], very large excesses of alkylating agent, solvents (DMSO, acetonitrile and acetone) were employed to try and eliminate the unwanted by-products, but unfortunately none of the modifications worked. Attempts at developing separation techniques were limited in their success, since we always found trace contamination of **(112)** by TLC. As a result of this problem we discontinued this project.



Scheme 35: *Proposed synthetic route to* ***(115)***.

6.6 Experimental

Column chromatography was carried out on all of the compounds using Riedel de Haen silica gel 60. Size exclusion chromatography was carried out on SX-3 Bio-bead column. Thin layer chromatography (TLC) was carried out on a Riedel de Haen silica 60F254 plates using specified solvents. Gel permeation chromatography was carried out using SX-3 bio-beads with THF as mobile phase. All solvents used where of HPLC grade.

A variety of techniques where under taken to elucidate the structure of these compounds. All NMR experiments where carried out on a Bruker AM 400 spectrometer and this means our ^{1}H NMR spectra were measured at 400 MHz. Mass spectra were analysed on two different machines 1) a Esquire-Bruker/Hewlett Packard LC-MS 1100 series, equipped with an electrospray ion source for the phthalonitrile starting materials **(108)** to **(110)** and 2) a Ettan MALDI-ToF Pro from Amersham BioSciences was used for the phthalocyanine dyes **(75)**. A Perkin Elmer Lambda 900 UV/Vis/NIR spectrometer was used to obtain the λ max of these compounds.

6.6.1 5,11,17,23-Tetra-tert-butyl-25, 27-Diethoxycarbonylmethyleneoxy-26, 28-Dimethoxycalix[4]arene (108)

To a stirred solution of **(78)** (1.45 g, 2.14 mmol) in DMF(30 mls), 60 % oil dispersion NaH (0.31 g, 0.54 mmol) was added gradually over 30 minutes under a nitrogen atmosphere and left to stir for an hour. Ethylbromoacetate (1.2 mls, 10.8 mmol) was added and reaction mixture was heated to 70°C overnight. The next day the reaction mixture was cooled to room temperature, another NaH (0.15 g, 0.27 mmol) as added and allowed to stir under nitrogen for an hour. The reaction mixture was then poured on to ice water (100 mls), this layer was then extracted with ethyl acetate (3 x 30 ml). The organic extracts were combined, then washed with a saturated saltwater solution, dried over $MgSO_4$, filtered and evaporated to yield a yellow/orange powder. The crude product was recrystallised from methanol and further purified by column chromatography using 90:10 hexane: ethyl acetate a white powder was obtained (0.95 g, 1.12 mmol, 50 % yield).

Product was characterised by **^{1}H NMR** ($CDCl_3$) δ (ppm) @ 150°C; 1.16, (s, 18 H, t-Bu); 1.37, (t, 6 H, J=7.2 Hz, $OCH_2\mathbf{CH_3}$); 1.52, (s, 18 H, t-Bu); 3.5, (d, 4 H, J=13 Hz, Ar-CH_2-Ar); 3.85, (s, 3 H, CH_3); 4.36, (q, 4 H, J=7.2 Hz, $O\mathbf{CH_2}CH_3$) 4.48, (d, 4 H, J=13 Hz, Ar-CH_2-Ar); 4.54, (s, 4 H, OCH_2CO_2Et); 6.92, (s, 4 H, Ar H); s 7.40, (s, 4 H, Ar H).

ESI m/z 871 ($M + Na^+$) $C_{54}H_{72}O_8$

IR (KBr [cm^{-1}]): 3500 cm^{-1} ν(O-H), 3000 cm^{-1} ν(Bu_t)

6.6.2 5,11,17,23-Tetra-tert-butyl-25,27-dihydroxyethyleneoxy-26,28-Dimethoxycalix[4]arene (109)

A 300 % molar excess of DIBAL (1.5 M solution in toluene) was added to a solution of the **(108)** (ca. 5 %) in dry toluene under nitrogen. The reaction mixture was stirred at room temperature for 24 hr. Excess reducing agent was destroyed by drop wise addition of methanol until hydrogen evolution had ceased. The precipitated inorganic salts where broken up by the addition of methanol/water and were subsequently removed by filtration through a celite. The inorganic residue was washed with hot chloroform, and the organic layer separated and washed with brine; each brine wash is further backwashed with chloroform. The combined organic extracts were dried over $MgSO_4$, and concentrated at reduced pressure to yield the crude calixarene alcohol.

Product was characterised by **^{1}H NMR** ($CDCl_3$) δ (ppm) @ 150°C; 1.33, (m, 36 H, t-Bu); 3.32, (broad s, 2 H, OH); 3.46, (broad s, 6 H, OCH_3); 3.56, (d, 4 H, J=13 Hz, Ar-CH_2-Ar); 4.00, (broad s, 4 H, CH_2 spacer); 4.04, (m, 4 H, CH_2 spacer) 4.41, (d, 4 H, J=13 Hz, Ar-CH_2-Ar); 7.18, (m, 8 H, Ar H).

ESI m/z: 787 ($M + Na^+$) $C_{50}H_{68}O_6$

IR (KBr [cm^{-1}]): 3500 cm^{-1} ν(O-H), 3000 cm^{-1} ν(Bu_t)

6.6.3 5,11,17,23-Tetra-tert-butyl-25,27-diethyleneoxyphthalonitrile-26,28-Dimethoxycalix[4]arene (110)

(109) (1.05 g, 1.37 mmol), K_2CO_3 (0.76 g, 5.5 mmol) and 3-nitrophthalonitrile (0.95 g, 5.5 mmol) were stirred under vacuum in anhydrous DMF (15 cm^3) for five day. Each day K_2CO_3 (0.19 g, 1.37 mmol) and 3-nitrophthalonitrile (0.23 g, 1.37 mmol) were added to force the reaction on to completion. On day six the reaction mixture was then poured on to ice water (50 mls), filtered and the solid was washed with hot water (2 x 25 ml). The crude brown solid was purified by column chromatography using 70:30 hexane: ethyl acetate, a light green solid was obtained (0.34 g, 0.34 mmol, 24.8 % yield).

Product was characterised by **^{1}H NMR:** ($CDCl_3$) δ (ppm) @ 195°C; 1.7, (m, 18 H, t-Bu); 1.9, (m, 18 H, t-Bu); 3.55, (d, 4 H, J=13.0 Hz, Ar-CH_2-Ar); 3.84, (s, 6 H, 2Me); 4.43, (t, 4 H, J=

5.0 Hz, CH_2 spacer); 4.47, (d, 4 H, J=13.0 Hz, Ar-CH_2-Ar); 4.76, (t, 4 H, J= 5.0 Hz, CH_2 spacer); 6.67, (s, 4 H, Ar H); 7.36, (s, 4H, Ar H); 7.40, (d, 2 H, J=7.6 Hz, ArH); 7.72, (t, 2 H, J=7.6 Hz, ArH).

ESI m/z: 1039 ($M + Na^+$), 1055 ($M + K^+$) $C_{66}H_{72}O_6N_4$

IR: (KBr [cm^{-1}]): 3500 cm^{-1} ν(O-H), 3000 cm^{-1} $\nu(Bu_t)$

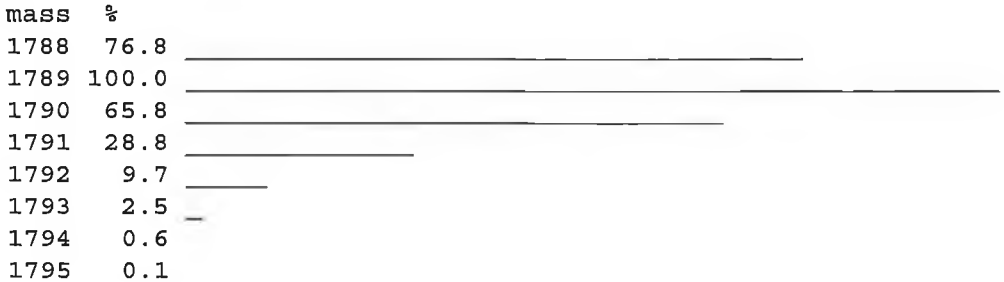
6.6.4 5,11,17,23-Tetra-tert-butyl-26,28-dimethoxycalix[4]arene(diethyleneoxy) Binuclear Phthalocyanine (75(a))

lithium (0.03 g, 4.28 mmol) was added to 3 ml of pentanol in a 10 ml round bottom flask and heated to 60°C to form the lithium alkoxide for 30 minutes under nitrogen. To this reaction flask **(110)** (0.1 g, 0.122 mmol) and phthalonitrile (0.14 g, 1.10 mmol) were added to the reaction mixture and this was then heated up to 110°C under nitrogen for 24 hr. The reaction mixture was cooled to room temperature and poured into 1 N HCL. A blue precipitate was formed and collected by centrifuge and was further washed first with water and then methanol. Chromatography was carried out on a silica gel column using chloroform as eluant, followed by THF. Then a second column was carried out on all bands using a THF as the mobile phase. 0.03 g of the phthalocyanine crude was then dissolved and applied to a size exclusion column (Bio-Beads SX-3) using THF as mobile phase. The Binuclear band was then rerun on the bio-bead column. This Binuclear was then columned again on a silica gel column using THF as eluant. A blue compound was obtained (0.017 g, 0.01 mmol, 8 % yield)

Product was characterised by **MALD-TOF m/z:** 1790.28 (M+1) (see calculated)

UV-Vis (Chloroform)**:** Broad absorption at around 690 nm.

Calculated for formula: $C_{114}H_{100}O_6N_{16}$

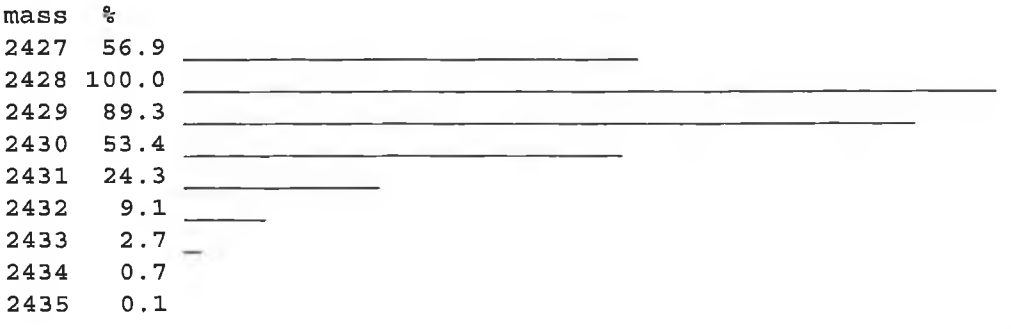


6.6.5 5,11,17,23-Tetra-tert-butyl-26,28-dimethoxycalix[4]arene(diethyleneoxy) Binuclear hexabenzyloxyphthalocyanine (75(b))

Lithium (0.03 g, 4.28 mmol) was added to 3 ml of pentanol in a 10 ml round bottom flask and heated to 60°C to form the lithium alkoxide for 30 minutes under nitrogen. To this reaction flask **(110)** (0.1 g, 0.122 mmol) and 3-benzyloxy phthalonitrile (0.26 g, 1.10 mmol) were added to the reaction mixture and this was then heated up to 110°C under nitrogen for 24 hr. The reaction mixture was cooled to room temperature and poured into 1 N HCL. A green precipitate was formed and collected by centrifuge and was further washed first with water and then methanol. Chromatography was carried out on a silica gel column using chloroform as eluant, followed by THF. Then a second column was carried out on all bands using a THF as the mobile phase. 0.03 g of the phthalocyanine crude was then dissolved and applied to a size exclusion column (Bio-Beads SX-3) using THF as mobile phase. The Binuclear band was then rerun on the bio-bead column. This Binuclear was then columned again on a silica gel column using THF as eluant. A green compound was obtained in a (0.015 g, 0.01 mmol, 8 % yield)

MALDI gave no identifiable peaks for $C_{159}H_{139}O_{12}N_{16}$

Calculated for formula: $C_{156}H_{139}O_{12}N_{16}$



6.6.6 5,11,17,23-Tetra-tert-butyl-26 –(ethoxycarbonylmethyleneoxy)-25, 27, 28-(trihydroxy) calix[4]arene (115)

(77a) (2.00 g, 2.95 mmol), Na_2CO_3 (0.1 g, 0.94 mmol) and Bromoethyl Acetate (0.1 ml, 0.94 mmol) were heated to 70°C for 24 hr in anhydrous DMF (20 ml). The reaction mixture was then poured on to ice water (100 ml), this layer was then extracted with ethyl acetate (3 x 30 ml). The organic extracts were combined, then washed with a saturated saltwater solution, dried over $MgSO_4$, filtered and evaporated to yield a cream powder. The crude product was

recrystallised from ethanol and further purified by column chromatography (using 90:10 hexane: ethyl acetate) and was then rerun on another silica gel column using the same eluent, a white powder was obtained (0.08 g, 0.14 mmol, 5 % yield).

Product was characterised by **^{1}H NMR** ($CDCl_3$) δ (ppm) @ 150°C; 1.22, (m, 36 H, t-Bu); 1.40, (t, 3 H, J=7.2 Hz, CH_3); 3.45, (d, 4 H, J=13.0 Hz, Ar-CH_2-Ar); 4.32, (d, 2 H, J=13.0 Hz, Ar-CH_2-Ar); 4.41, (q, 2 H, J=7.2 Hz, C(O)CH_2); 4.50, (d, 2 H, J=13.0 Hz, Ar-CH_2-Ar); 4.90, (s, 2 H, OCH_2); 7.00, (s, 2 H, J=2.4 Hz, Ar H); 7.06, (s, 4 H, J=1.7 Hz, Ar H); 7.11, (s, 2 H, Ar H); 9.28, (s, 2 H, OH); 10.25, (s, 1 H, OH).
ESI m/z: 757.4 ($M + Na^+$)

7. Crystal Structure Analysis

Compound **(79)** exists in a partial cone conformation with the phthalonitrile tilted into the calix[4]arene annulus. The bond angle between C34-O3-C29 is 121.89° with the phthalonitrile substituent tilted in toward the calix[4]arene annulus. A hydrogen bond exists between the lower rim hydroxyl group H10 and the O4 (3.478 Å) and O2 (1.79 Å) oxygens of lower rim. The unsubstituted ring of the calix[4]arene is tilted at an angle of 137.46° from the plane of the bridging carbons of the calix[4]arene. The two planes of the rings containing the methoxy substituents lie at an angle of 40.64° to each other and plane A created by the ring (C43-C48) lies at an angle of 102.5° to the plane of the bridging carbons. Plane B, created by the ring (C12-C17), lies at an angle of 117.84° from the plane of the bridging carbons of the calix[4]arene. The phthalonitrile substituent lies at an angle of 102.39° from the plane of the bridging methylene groups of the calix[4]arene. The methyl substitutents on the lower rim protrude outward from the lower rim at an angle of 112.82° (C53-O4-C48) and at 113.41° (C22-O2-C17).

The phthalonitrile proton (H39) is 3.441 Å from the C3 carbon of the tilted unsubstituted ring of the calix[4]arene. The H38 proton of the phthalonitrile substituent is 3.63 Å from the C3 carbon and 2.82 Å from the C6 carbon of the unsubstituted phenol ring. The C36 of the phthalonitrile substituent is 4.059 Å away from C14 (t-butyl carbon) and is 4.52 Å away from the C45 carbon of the other ring. The N2 of the phthalonitrile is 6.076 Å from C49

(central t-butyl carbon) and 5.052 Å from C18.

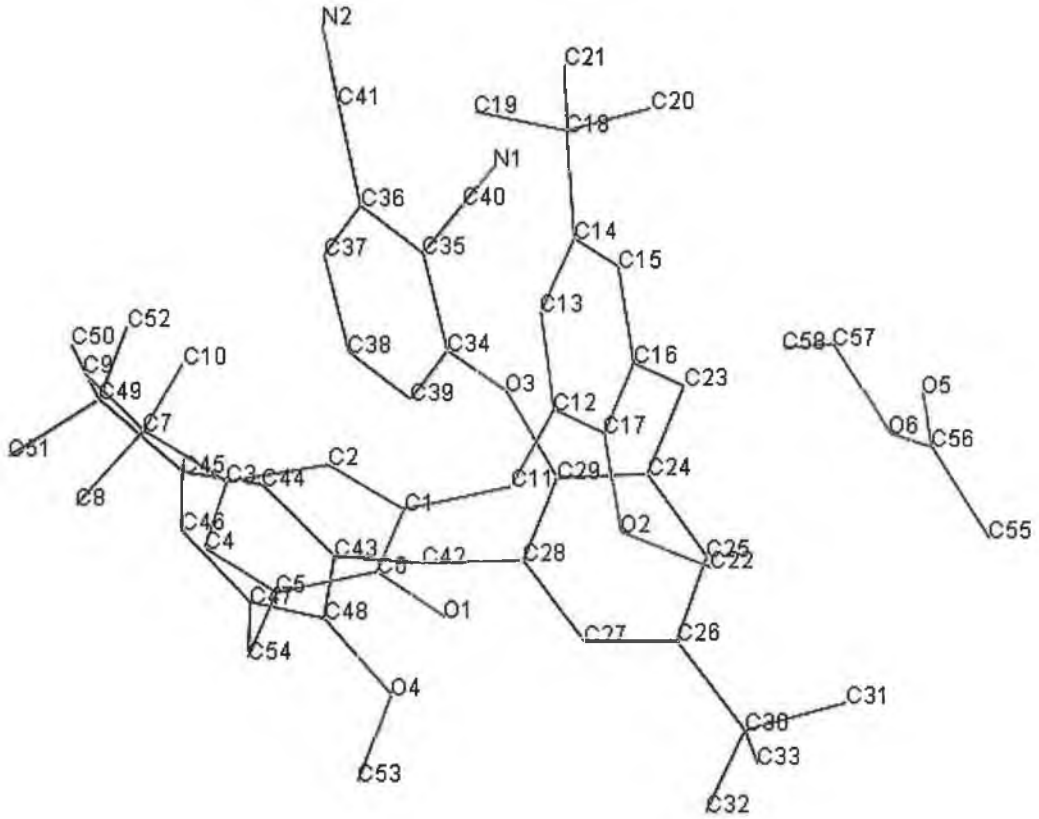


Figure 73: *Labled diagram of (79).*

Compound **(80)** also exists in the partial cone conformation with the phthalonitrile tilted into the calix[4]arene annulus with a bond angle of (C7-O1-C2) 121.37° which is not much unchanged from **(79)**. The hydrogen bond present in **(79)** is now removed, however the tilt angle of ring (C32-C37) to the plane of the bridging carbons of the calix[4]arene is 138.66° which is only a slight change of 1.2° from **(79)** indicating that the hydrogen bonding that is present in **(79)** is not important for the stabilisation of the inclusion complex of both **(79)** and **(80)**. The two planes created by the rings C20-C25 and C44-C49 intersect at an angle of 34.31° which is smaller than the angle created by the same rings in **(79)**. The angle created by the plane from ring (C20-C25) and the plane of the bridging methylene groups is 104.59° and the angle between the plane created from ring (C44-C49) and the bridging methylene groups of the calix[4]arene is 109.31° . A significant change is seen with the plane of ring (C1-C6) of **(79)** and the same plane in **(80)**. The methoxy groups adjacent to the phthalonitrile substituted ring of **(80)** are pointing out of the lower rim at angles of 113.24° (C50-O4-C45) and 112.01° (C26-O2-C21) unchanged from **(79)**. The methyl group opposite to the

phthalonitrile substituted ring is at an angle of 116.04° (C38-O3-C33) pointing outward from the lower rim. The phthalonitrile substituent lies at an angle of 90.43° from the plane of the bridging methylene groups of the calix[4]arene which is a smaller tilt than that observed for **(79)**.

The phthalonitrile proton H11 is a distance of 3.050Å to C36 and 2.734Å from C33 which is an insignificant change from **(79)**. The same Nitrogen as analysed above is 5.249Å from C27 and 5.543Å from C51.

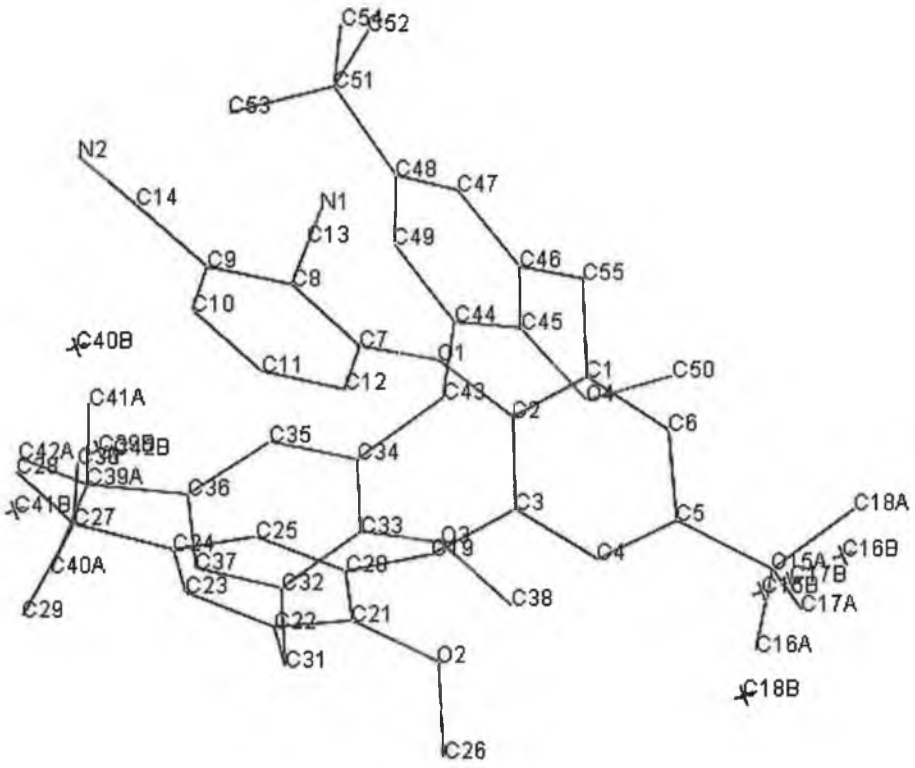


Figure 74. *Labelled structure of (80).*

For the partial cone conformation of **(99)** the phthalonitrile substituent is tilted into the upper rim of the calix[4]arene at an angle of 122.39° (C61-O5-C55). The angle made between the planes created from rings C74-C79 and C97-C102 is 37.47° which is very similar to the same angle found for **(79)**. The angle of the plane created from the ring C74-C79 and the plane of the bridging carbons of the calix[4]arene is 119° and the plane between ring (C74-C79) is 97.90° ,again very similar to the angles found in **(79)**. The angle of the ring containing the hydroxyl group (C86-C91) and the plane of the bridging carbons of calix[4]arene is 138.14°

which is again very similar to the angle made by the same ring in **(79).** Interestingly, unlike in **(79)** only a single H-bond exists between the proton of the unsubstituted phenol on the lower rim and the neighbouring oxygens (H7 and O8 distance 1.853 Å). The distance between H7 and the other neighbouring oxygen (O6) is 3.696 Å. The phthalonitrile substituent lies at an angle of 77.69° from the plane of the bridging methylene groups of the calix[4]arene which is a larger tilt than that observed for **(79)**. The methyl substituents on the lower rim point outward at angles of 114.14° (C103-O8-C98) and 111.07° (C80-O6-C75).

The H65 proton of phthalonitrile is 3.139 Å from C90 and 2.856 Å from C87. The N68 of the phthalonitrile substituent is 4.88 Å from C104 (central carbon of t-butyl) and 5.306 Å from C81 (central carbon of t-butyl) and intersects the plane of the ring C97-C102 at an angle of 17.12° and intersects the plane of ring C74-C79 at an angle of 20.52° .

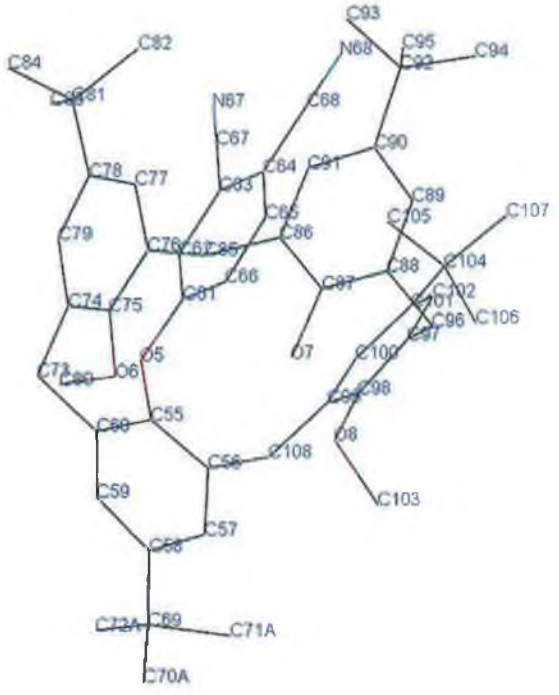


Figure 75. *Labelled structure for (99) in the partial cone conformation.*

For the cone conformation of **(99)** a single H-bond exists between H3 of the unsubstituted hydroxy group and O4 (1.978 Å). The other adjacent oxygen O2 is 3.78 Å away from H3. The phthalonitrile is bound at an angle of 116.57° facing out of the lower rim of the calix[4]arene, which is very similar for the phthalonitrile substituent of **(100)**. The C1-C6 ring that is bound to the phthalonitrile substituent is tilted back at an angle of 139.50° from the plane of the bridging methylene groups of the calix[4]arene. The opposite ring C32-C37 is also tilted outward and makes an angle with the plane of the bridging methylene groups at

136.50° . The C43-C48 ring is tilted outward at an angle of 102.78° and ring C20-C25 ring is tilted slightly inward at an angle of 82.63° from the plane of the bridging methylene groups.

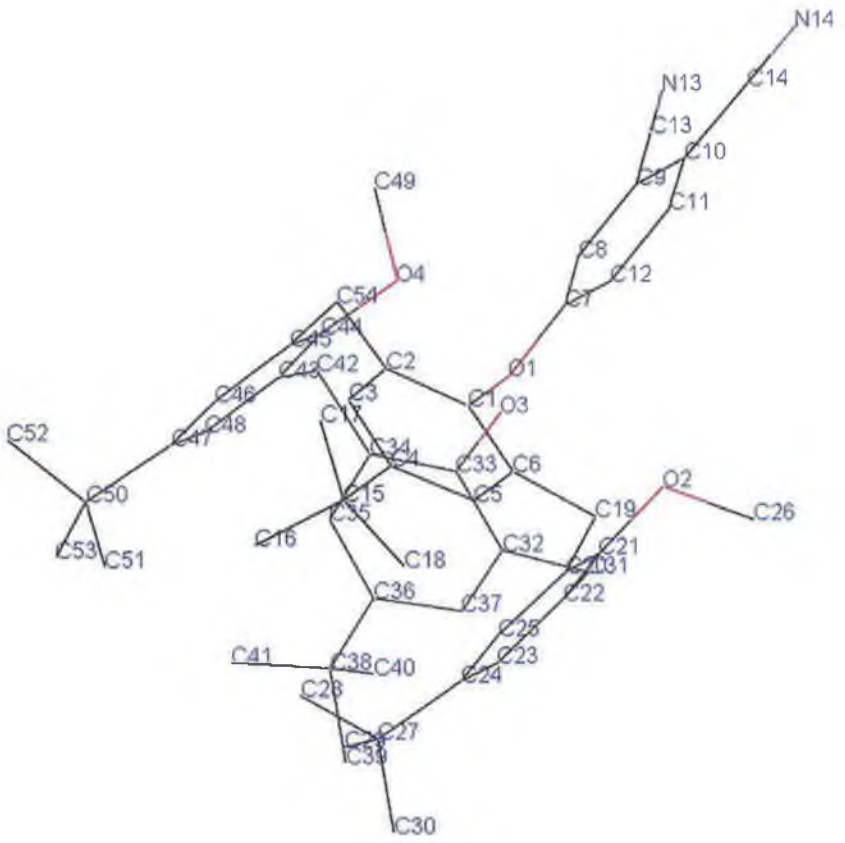


Figure 76. *Labelled structure for the cone conformation of* ***(99)***.

For compound **(100)** the x-ray structure again shows a partial cone conformation, however, the phthalonitrile is on the lower rim of the calix[4]arene, and it is the methoxy substituent of the ring C32-C37 that lies in the upper rim. The C38 carbon (the methyl substituent in the upper rim) does not lie within the calix[4]arene annulus unlike the phthalonitrile in the partial cone conformations; instead it lies facing out of the upper rim at an angle of 113.74° .

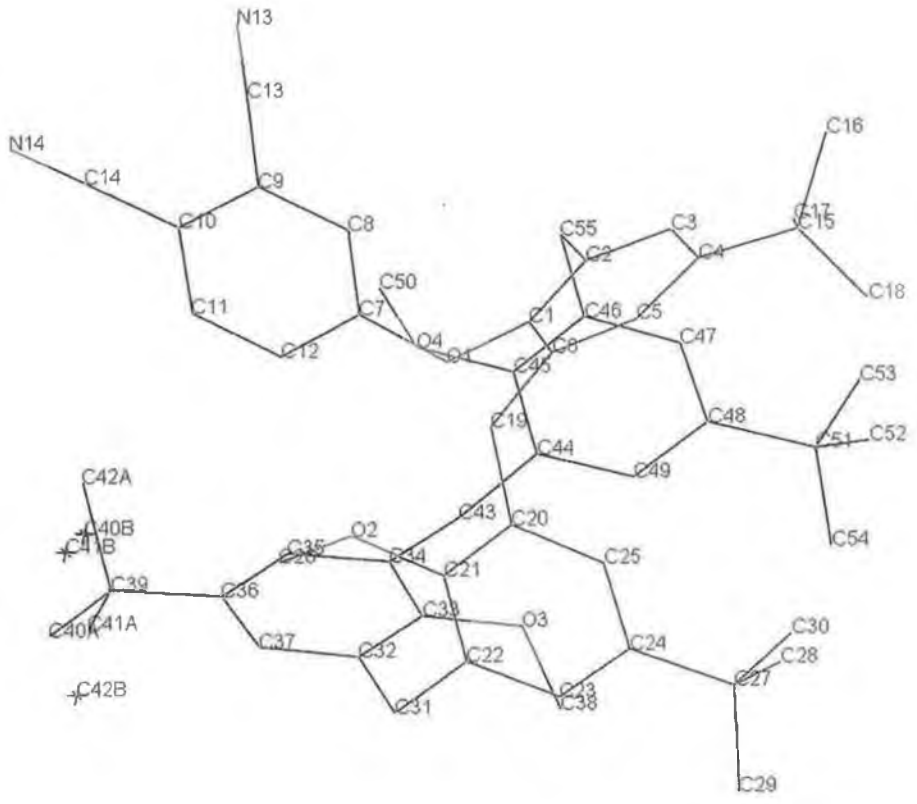


Figure 77. *Labelled structure of* ***(100)***.

The phthalonitrile sitting on the lower rim is tilted at 118.41° with the nitriles facing out of the lower rim. The phenol group of the calix[4]arene (C1-C6) that is bound to the phthalonitrile substituent lies at an angle of 39.39° with the plane of the bridging carbons of the calix[4]arene. Ring (C32-C37), opposite to the substituted ring of the calix[4]arene, is at an angle of 110.66° with the plane of the bridging carbons of the calix[4]arene. The planes made from the C20-C25 ring and the C44-C49 rings intersect at an angle of 14.95° (close to parallel). The C20-C25 ring also intersects the plane of the bridging carbons at an angle of 82.46. Ring C44-C49 makes an angle of 82.72° with the plane of the bridging carbons of the calix[4]arene. The O4 methyl group (C50-O4-C45) is at an angle of 97.93° facing out of the lower rim and the O2 (C26-O2-C21) methyl group is at an angle of 115.08° facing out of the lower rim. O4 to O1 is 2.938 Å and O2 to O1 is 2.969 Å.

8. Conclusion

In this work we set out to accomplish the preparation of new calix[4]arene phthalocyanines. We have achieved most of our principle goals.

Our first aim of the project involved the selective synthesis of a deaggregated phthalocyanine by manipulating the partial cone conformation of calixarene. We achieved this goal by preparing **(79)** using room temperature weak base reaction conditions, the resulting product indeed exists as a partial cone conformation with part of the aryl substituent being placed within the calixarene annulus. The ^{1}H NMR of both **(79)** and **(80)** show how the inclusion of the phthalonitrile in the calix[4]arene cavity shields the aromatic protons and shifts them up-field from ~7 ppm to ~4 ppm. While our temperature ^{1}H NMR studies indicate the stability of this inclusion complex, as there is no major change even at 175^{0}C.

As was anticipated, this conformation has the potential to reduce aggregation because of its structure, which has a t-butyl group both above and below the plane of the phthalonitrile. However, when attempts where made to self condense **(80)** the steric hindrance of the calix[4]arene led only to the formation of inconsequential amounts of **(73)**. We then decided to carry out a cross condensation of **(80)** with the less sterically hindered phthalonitrile **(8)**, this led to the formation of **(97)** in a 20% yield. ^{1}H NMR confirms that the partial cone conformation is maintained after the condensation, further demonstrating the stability of this novel conformation.

Aggregational studies were carried out on **(97)** using UV-VIS. Results indicate that this compound does not aggregate in polar solvents such as ethanol, demonstrating that **(97)** should have excellent photophysical properties in polar solvents, making it an excellent candidate for use in PDT, non-linear optics and optical filtering. Conversely the solid state UV-Vis indicates that **(97)** is not fully deaggregated and from this work we can ascertain that dimers are being formed in the solid state on comparison to literature results.

However the preparation of a totally deaggregated tetra-substituted calix[4]arene phthalocyanine **(101)** and **(102)** was achieved from the self-condensation of **(100)**. Unlike **(80)** , **(100)** is less sterically hindered since the calixarene substituent is positioned further from the nitrile groups and as a result self-condensation occurred. We also found that metal templation affects this condensation giving a much higher yield (10%) for **(101)** while the metal-free **(102)** was prepared in a 4% yield. UV-Vis aggregational studies of **(101)** suggested that aggregates are not formed in polar solvents. This illustrates that the partial

cone conformation is not the only factor that can be used to reduce aggregation. Again **(101)** like **(97)** will give excellent photophysical properties in polar solvents which in turn will make it an excellent candidate for use in PDT, non-linear optics and optical filtering. Solid state UV-Vis studies of **(102)** revealed that the tetra-substituted calix[4]arene phthalocyanine is a fully deaggregated phthalocyanine.

We also set out to prepare a novel constrained phthalocyanine and a series of binuclear phthalocyanines, both systems were to be prepared from their respective bisphthalonitriles.

The first bisphthalonitrile we targeted was **(85)** since molecular modelling results indicated an excellent arrangement for constrained self-condensation to form **(76).** However, experimentally this was not the case. We found that **(85)** would not self-condense to give the desired target **(76)**. Furthermore the conversion of **(85)** to the binuclear phthalocyanine **(74)** yielded an interesting mononuclear phthalocyanine possessing a phthalimide handle. We hope in the future to develop appropriate conditions to convert the phthalimide to a second phthalocyanine leading to a 'mixed' binuclear phthalocyanine.

We also prepared the bisphthalonitrile **(110)** in four steps, **(110)** was successfully converted to the binuclear phthalocyanine by cross condensing **(110)** with phthalonitrile. The resulting unsubstituted binuclear phthalocyanine was highly soluble in organic solvents which is quite novel in itself since binuclear phthalocyanines prepared to date typically require bulky substituents in all of the periphey benzo groups of the phthalocyanines to obtain solubility. The successful cross condensation of **(110)** also demonstrates that by spacing the phthalonitriles away from the calixarene allows for efficient condensation to occur, unlike the case with **(85)**.

Future work with all of the compounds described herein will involve further performance evaluation with respect to ionophoric properties, gas sensing, photosensitisers and oxidation catalysis. Also I recommend further work concerning the S_{Naryl} reactions described in Chapter 2 and Chapter 4. Is it possible to place other aromatic systems within the calix[4]arene annulus? If it is possible this may allow for the application of the stable partial cone inclusion complexes to 'isolate' other dyes (eg borondipyrromethenes from aryl aldehydes) and even macrocyclic systems.

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