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Teaching old dogs new tricks:

Transition metal-catalysed reactions for the generation of rigid cubane and designer porphyrin scaffolds.

Submitted by

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B.A. (Mod.) Medicinal Chemistry

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A thesis submitted to the University of Dublin, Trinity College for the degree of

Doctor of Philosophy

University of Dublin, Trinity College *December 2014*

Declaration

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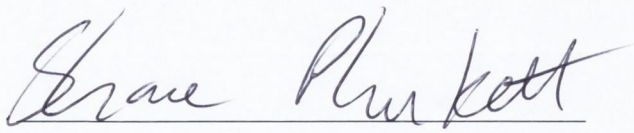

Shane Plunkett

Summary

The aim of this work was to use Pd-catalysis in the pursuit of novel, synthetically interesting, structural scaffolds based around either the rigid cubane framework or the optically active porphyrinoid core. In both cases, focus was on the application of the most modern chemical techniques to historically under-exploited or synthetically inaccessible organic scaffolds.

A series of chemically distinct, activated cubane scaffolds was synthesised through optimisation of the metal-halogen exchange reactions of iodinated cubane derivatives. This included the first ever examples of both borylated cubanes and a cubane-phosphorous adduct. Additionally, Zn, Sn, Si, S and various C-based systems were also attached in a high-yielding, one-pot reaction. A comprehensive programme investigating the reactivity of these cubane nucleophiles towards Suzuki-Miyaura, Negishi and Stille cross-coupling methodologies, never previously applied to cubane scaffolds, was then undertaken. While standard cross-coupling conditions allowed for recovery of the cubane system, by moving to more activated conditions; either through use of additives or highly active catalyst systems; transmetallation of the cubane systems led to complete decomposition of the cubane scaffold being observed. This process appears to be a new decomposition pattern for the cubane system, distinct from those reported previously.

Routes to effect the marriage of the two distinct scaffold systems under investigation – cubane and porphyrins were next attempted. An organolithium approach failed to give any cubane appended porphyrins. Condensation methodologies presented some success with oxidation-resistant cubane-porphodimethene compounds detected. Application of Sonogashira cross-coupling techniques to alkynylcubanes provided the first access to cubane-appended porphyrin systems. As an area of cubane chemistry not previously explored, an initial optimisation of the Sonogashira cross-coupling reactions of alkynylcubanes with simple aryl electrophiles was first performed. Pursuant to the success

of this investigation both a Ni(II) and free-base porphyrin-alkynylcubane adduct were successfully synthesised as well as a bis(alkynylcubane) system. These compounds represent the first examples of rigid, aliphatic linkers attached to the porphyrin core.

The search for novel linkers for use in porphyrinoid scaffolds led to investigation of the allenyl functional group as a synthon in porphyrin chemistry. A library of halogenated porphyrin systems in various metallation states was first synthesised followed by investigation of the general applicability of Suzuki-Miyaura cross-coupling chemistry developed previously within the Senge group. While this proved effective for a small group of allenylporphyrins it failed when applied to a broader range of substituted porphyrins. Application of sequential Sonogashira reactions with aminoalkyne precursors followed by Pd-catalysed rearrangements was found to be a much more robust method towards allenylporphyrins with a large library of diversely-substituted porphyrins generated. The utility of the installed allenyl group towards cycloaddition chemistry was then probed using both directly linked allenylporphyrins and those bearing a phenyl "spacer".

Finally, the synthesis of heteroatom-linked porphyrin systems for targeted applications was initiated. Sulfur-appended porphyrins displayed unprecedented reactivity, undergoing a unique S_NAr reaction to provide *S*-linked bisporphyrins, the first examples of this class of system. The synthesis of a library of these bisporphyrins and investigation of the S_NAr reactivity of their monomeric precursors with various organic electrophiles and nucleophiles was performed in collaboration with Dr. Aoife Ryan. Additionally, the tailored synthesis of 5,10-substituted donor-acceptor porphyrins was pursued to provide novel dyes for organic solar cell devices. Rearranging the dipole of the classical 5,15-systems in this manner has previously been shown to have a pronounced effect on the electronic properties of the porphyrin so modification of the state-of-the-art aminoporphyrin dyes was successfully performed with the products currently undergoing testing for their applicability in DSSCs.

Publications

S. Plunkett, K. J. Flanagan, B. Twamley, M. O. Senge. "Highly Strained Tertiary sp^3 Scaffolds: Synthesis of Functionalized Cubanes and Exploration of Their Reactivity under Pd(II) Catalysis" *Organometallics* **2015**, *34*, 1408-1414

A. A. Ryan, S. Plunkett, A. Casey, T. McCabe, M. O. Senge. "From thioether substituted porphyrins to sulfur linked porphyrin dimers: an unusual S_NAr *via* thiolate displacement?" *Chem. Commun.* **2014**, *50*, 353-355.

S. Plunkett, K. Dahms, M. O. Senge. "Synthesis and Reactivity of Allenylporphyrins" *Eur. J. Org. Chem.* **2013**, 1566-1579.

S. Plunkett, M. O. Senge. "Synthesis of Unsymmetrically meso-Substituted Porphyrins", *ECS Trans.* **2011**, *35*, 147-157.

Conference Abstracts

A. A. Ryan, S. Plunkett, A. Casey, M. O. Senge. "From thioether substituted porphyrins to sulfur linked porphyrin dimers: an unusual S_NAr *via* thiolate displacement?" *RSC Photochemistry Early Career Researchers Meeting*, University of Ulster, Belfast, Northern Ireland 15th - 16th May **2013**.

S. Plunkett, K. Dahms, M. O. Senge. "The Synthesis of Allenylporphyrins." *RSC Photochemistry Early Career Researchers Meeting*, University of Ulster, Belfast, Northern Ireland 15th - 16th May **2013**.

S. Plunkett, K. Dahms, M. O. Senge. "The Synthesis of Allenylporphyrins." *3rd Bilateral Sino-Ireland Symposium on Frontiers in Synthetic Chemistry,* TBSI, Trinity College Dublin, Ireland 23rd - 24th July **2012**.

M. M. Ebrahim, M. A. Bakar, S. Plunkett, M. O. Senge. "Synthesis of Nonplanar Porphyrins and Arrays" *Seventh International Conference of Porphyrins and Phthalocyanines (ICPP-7).* Jeju Island, South Korea 1st - 6th July **2012**.

S. Plunkett, K. Dahms, M. O. Senge. "The Synthesis of Allenylporphyrins." *Seventh International Conference of Porphyrins and Phthalocyanines (ICPP-7),* Jeju Island, South Korea 1st - 6th July **2012**.

S. Plunkett, K. Dahms, M. O. Senge. "The Synthesis of Allenylporphyrins." *Centre of Synthesis and Chemical Biology Meeting 2011* University College Dublin, Ireland. 9th December **2011**.

M. O. Senge, S. Plunkett, L. Rogers, C. Moylan. "The Synthesis of ABCD-type Porphyrins" *Porphyrins and Porphyrias (Tetrapyrrole Discussion Group meeting) 2011* Cardiff, Wales 10th - 14th April **2011**.

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Table of Contents

Abbreviations

acac	acetylacetonate
AIBN	2,2'-azobis(2-methylpropionitrile)
APCI	atmospheric-pressure chemical ionisation
Ar	aryl
9-BBN	9-borabicyclo[3.3.1]nonane
BINAP	2,2'-bis(diphenylphosphino)-1,1'-binaphthyl
BMPA	bis(*N*-methylpiperazinyl)aluminium hydride
br	broad
Bu	butyl
calcd.	calculated
cod	cyclooctadiene
COSY	correlation spectroscopy
Cy	cyclohexyl
d	doublet
dba	dibenzylideneacetone
DCTB	*trans*-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malonitrile
dd	doublet of doublets
DEA	diethylamine
DDQ	2,3-dichloro-5,6-dicyanobenzoquinone
DMF	*N,N*'-dimethylformamide
DMSO	dimethyl sulfoxide
dpePhos	bis-[2-(diphenylphosphino)phenyl]ether
DPM	dipyrromethane
dppe	1,2-bis(diphenylphosphino)ethane
dppf	1,1'-bis(diphenylphosphino)ferrocene
dppp	1,2-bis(diphenylphosphino)propane
DSSC	dye-sensitised solar cell
Elem. Anal.	elemental analysis
eq.	equivalents
EI	electron impact
ESI	electrospray ionisation
Et	ethyl
EWG	electron withdrawing groups

FGI	functional group interconversion
GC	gas chromatography
HMBC	heteronuclear multiple-bond correlation spectroscopy
HRMS	high resolution mass spectrometry
HSQC	heteronuclear single quantum coherence
HWE	Horner-Wadsworth-Emmons
IBDA	iodobenzene diacetate
*i*Hept	2-methylhexyl
IR	infrared
*i*Pr	isopropyl
*i*Pent	2-methylbutyl
LRMS	low resolution mass spectrometry
m	multiplet
m	*meta*
mCPBA	3-chloroperoxybenzoic acid
M.p.	melting point
MALDI	matrix assisted laser desorption ionisation
Me	methyl
m/z	mass-to-charge ratio
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
n/d	not determined
NHC	*N*-heterocycliccarbene
NLA	non-linear absorption
NLO	non-linear optics
NMP	*N*-methyl-2-pyrrolidinone
NMR	nuclear magnetic resonance
(nor)	2,5-norbornadiene
NP	nanoparticle
o	*ortho*
OAc	acetate
OEP	2,3,7,8,12,17,18-octaethylporphyrin
OTf	triflate
p	*para*
2PA	two-photon absorption

PCC	pyridinium chlorochromate
PDT	photodynamic therapy
PEPPSI	pyridine-enhanced precatalyst preparation stabilization and initiation
Ph	phenyl
ppm	parts per million
PTSA	*para*-toluenesulfonic acid
q	quartet in ^{1}H NMR; quaternary in ^{13}C NMR
R_f	retention factor
RSA	reverse saturable absorption
r.t.	room temperature
s	singlet
SA	saturable absorption
SAM	self-assembled monolayers
S.M.	starting material
S_N2	bimolecular nucleophilic substitution
S_NAr	nucleophilic aromatic substitution
t	triplet
TBAF	tetra-*n*-butylammonium fluoride
TBDMS	*tert*-butyldimethylsilane
TEA	triethylamine
TFA	trifluoroacetic acid
THF	tetrahydrofuran
TIPS	triisopropylsilane
TLC	thin layer chromatography
TM	transition metal
TMP	tetramethylpiperidide
TMS	trimethylsilane
TOF	time of flight
TPP	5,10,15,20-tetraphenylporphyrin
UV	ultraviolet
vis	visible
v/v	volume to volume
w/w	weight to weight
Xantphos	4,5-bis(diphenylphosphino)-9,9'-dimethylxanthene

Chapter 1:

Introduction

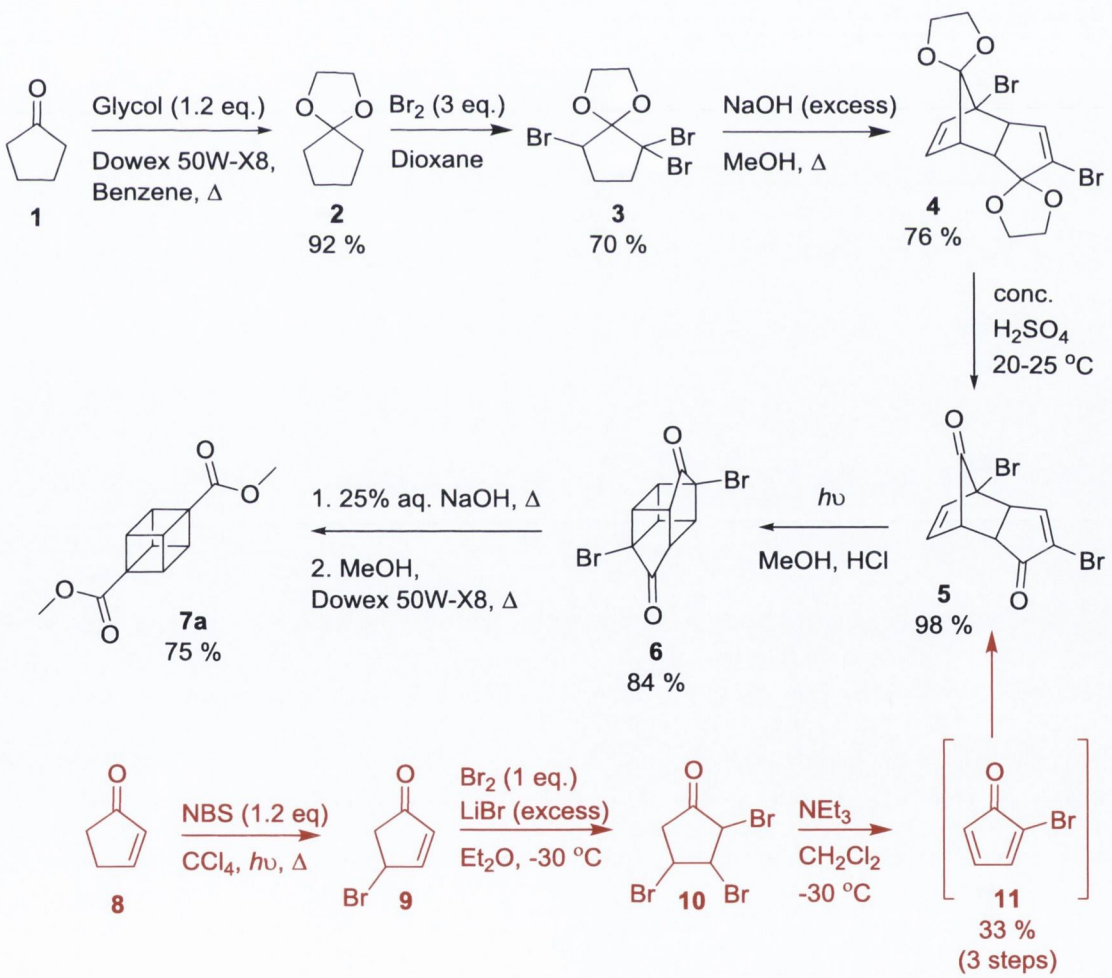
1.1 Cubane – a rigid synthetic scaffold

1.1.1 History of the cubane system

The concept of a rigid hydrocarbon cube fascinated chemists for much of the early half of the 20th century. While dismissed by some to be so sterically strained as to be synthetically impossible, this structural archetype, one of the three platonic hydrocarbons, was finally achieved by Eaton *et al.* in 1964.[1,2] The strength of Eaton's original synthesis is proven by the fact that, of all the subsequent syntheses, all bar two contain as their key step a double Favorskii rearrangement to facilitate the contraction of the *bis*homocubane system to the highly strained cubane scaffold. The major drawback of Eaton's seminal work was the bromination of cyclopent-2-en-1-one in the first step; a synthesis many subsequent chemists found challenging (red-coloured route in Scheme 1.1). A key modification of the initial synthesis was published by Chapman *et al.*[3] and utilises the ethylene ketal of cyclopentanone **1** as starting material. Bromination of this material proceeds much more readily and reliably, leading to radically improved overall yield and ease of handling of intermediates. Another, more modern modification of the synthetic route by Tsanaktsidis and co-workers in 1997[4] further improves on both of the classical syntheses by removing some of the more expensive and corrosive reagents and improving the crystallisation procedures for the key intermediates. This synthesis has reduced the overall process to five steps and can be performed in the laboratory on multi-gram amounts. Additionally, a pilot technical scale synthesis has been reported by the same group.[5,6]

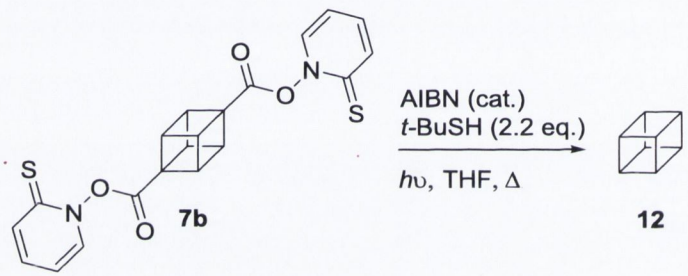
Details of the Tsanaktsidis approach are shown in Scheme 1.1. Bromination of **2** yields the tribromo-derivative **3** which undergoes hydro-debromination and highly *endo*-selective [4π+2π] Diels–Alder dimerisation when exposed to excess NaOH in boiling methanol to yield the *bis*ethylene ketal **4** in approximately 60 % yield from **2**. Concentrated sulfuric acid facilitates the conversion of **4** into the diketone **5**. Irradiation of **5** at room temperature in methanol containing concentrated HCl with a 450 W Hanovia medium-pressure mercury

lamp through Pyrex represents the other key step which has remained unchanged since the first cubane synthesis. Significant optimisation of solvent, temperature and substrate choice has been performed for this [2π+2π] ene-enone photocyclisation. In this case, the product is the caged dione **6** as a mixture of hemiketals and ketals. Conversion to the diketone with hot (acidic) water, followed by the double Favorskii reaction *via* treatment with refluxing aqueous NaOH for 4 hours, furnishes the diacid as a tan solid. Purification of the diacid is reportedly best achieved by esterification to the methyl ester and sublimation to give crystalline dimethyl cubane-1,4-dicarboxylate **7a**. Yields for this latter half of the synthesis (**5** → **7**) are reported as 42-47 %, a significant improvement on the *ca.* 20 % reported by both Eaton and Chapman. Overall, the reported yield for the entire process is ~25 %.[4]



Scheme 1.1: Best reported method (black) and Eaton's original synthesis (red) for the synthesis of dimethyl cubane-1,4-dicarboxylate **7a**.

Compound **7a** represents the most common and convenient entry point into most cubane syntheses. The free hydrocarbon **12** was classically synthesised by the decarboxylation of the *tert*-butyl perester of **7** at 150 °C in diisopropylbenzene.[2] A more convenient approach was published in 1995[7] (Scheme 1.2) and involves the much milder, Barton decarboxylation of **7b**. This radical-induced reaction can be employed to selectively remove any number of carboxylic groups from the cubane scaffold, making it a useful tool in synthetic manipulations. Nevertheless, **12** remains practically useless from a synthetic viewpoint but its synthesis did allow for many of the physical properties of cubane to be accurately measured and described.



Scheme 1.2: Barton decarboxylation of **7b** to yield unsubstituted cubane **12**.

1.1.2 Properties of the cubane system

Due to its exceptional structure, symmetry and pronounced strain, cubane has been a hallmark in organic chemistry since its discovery. Extensive studies have been reported on its properties, some of which are detailed in Table 1.1.[8,9] Cubane holds the position of being the highest density hydrocarbon known and its incredibly high strain energy has led to significant interest in the fields of high energy fuels and explosives.[10,11]

The geometry of the cubane system obviously necessitates a departure from classical sp^3 hybridisation. To accommodate the ring strain, the C-C bonds are forced to adopt more p-character while the exocyclic carbon orbital used for the C-H bond (and by extension any external C-R bond) compensates by become more s-rich. By calculating the ^{13}C-^{1}H coupling constant of 150.5 Hz, Della *et al.* have estimated the s-character of the C-H bonds in cubane as 30.1 %.[12] This compares with a value of around 26 % in adamantane and more closely

approximates as an sp^2 hybridised system (33 % s) than an sp^3 (25 % s). The hydrogen atoms of cubane are thus more acidic than those of conventional saturated hydrocarbons. The kinetic acidity of cubane is approximately 63,000 times greater than that of cyclohexane.[13] While still too low to be of direct synthetic use, this nature of the bonding in cubane has been exploited in the synthesis of diverse building blocks.

Table 1.1: Select physical properties of **12**.

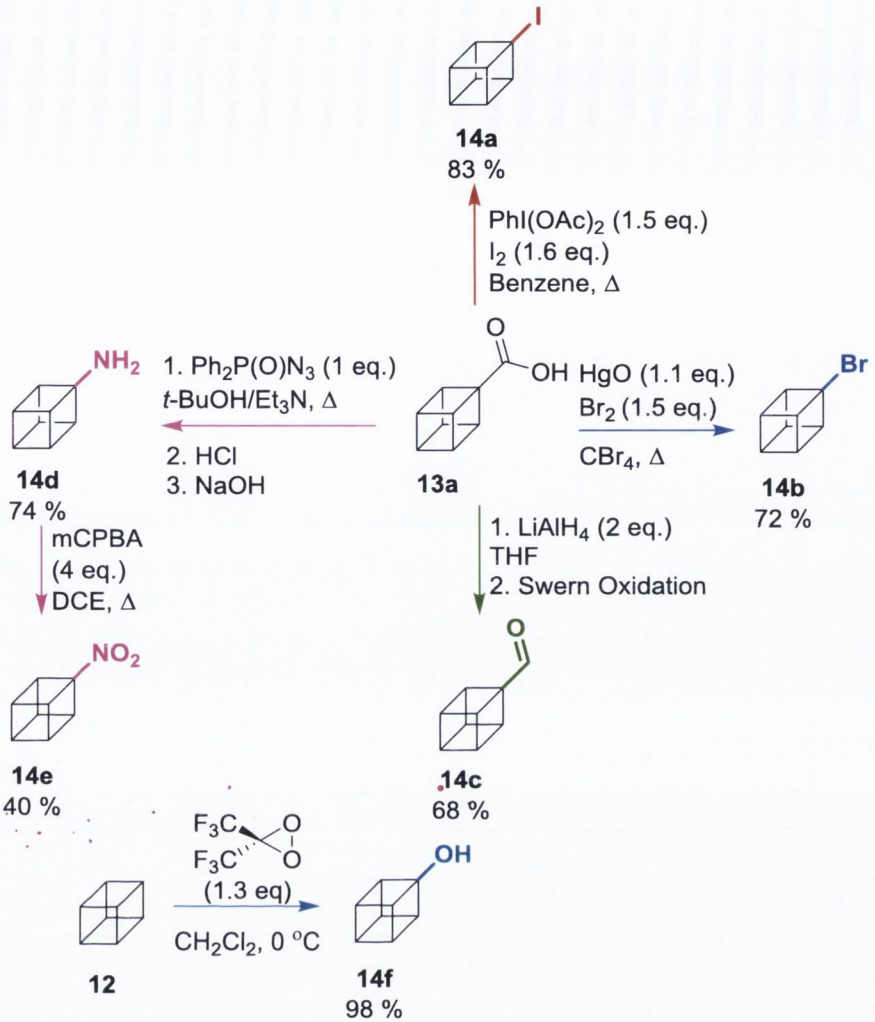
C-C distance	1.5727±0.0019 Å	***Melting Point***	130-131 °C
C-H distance	1.118±0.008 Å	***Density***	1.1 g cm^{-3}
Colour	Transparent	***Vapour Pressure***	1.1 mm (25 °C)
Toxicity	Nontoxic	***Solubility***	≈18 wt % (hexane)
Stability	Inert to light, water, air	***Heat of Formation***	+144 kcal mol^{-1}
Decomposition	>220 °C	***Strain energy***	+166 kcal mol^{-1}

The search for novel small molecule scaffolds and linking units in organic (and particularly medicinal) chemistry is an ever ongoing challenge.[14] One of the key requirements for any scaffold system is that the substituents must be arranged in a specific orientation which is precisely known and invariable under target conditions. As such, the majority of such units incorporate conjugating groups such as arenes, aromatic heterocycles, alkenes and alkynes due to the rigidity these enforce on molecules.[15,16] Comparatively little attention has been paid to saturated hydrocarbons, in spite of the many advantages these groups lend in terms of solubility and toxicity.[17] Primarily, this is due to the inherent flexibility of classic sp^3 systems. On account of its nature, cubane obviously serves as an excellent bridge in this respect – a perfectly rigid, saturated hydrocarbon, with up to eight distinct locations for substitution. Considering the geometry of cubane, it is noteworthy that the distance across the cube (the body diagonal) is 2.72 Å, which is almost equivalent to the distance across a benzene ring, *i. e.*, 2.79 Å.[18,19] This implies that, given robust substitution procedures, cubane could conceivably be used as a (nontoxic) isostere of benzene. Akin to a more rigid adamantane,[20,21] cubane should also serve as a highly efficient electronic

isolator – preventing bound groups from communicating to each other and potentially opening a unique avenue in scaffold and electron transfer chemistry.

1.1.3 Substitution on the cubane scaffold

From a synthetic viewpoint, one of the most positive aspects to emerge from the plethora of studies on the substitution on cubane is that, in spite of its strain, it remains a robust and versatile building block, tolerant of a wide range of conditions. The most direct way to effect substitution on the cubane scaffold is simply to utilise functional group manipulations on the two carboxylic groups present in **7**, the most common entry point into the cubane system. The carboxylic groups on **7** behave exactly as expected for aliphatic acids so a wide range of FGI is possible to quickly yield 1,4-disubstituted systems. For less symmetric systems, selective decarboxylation as described previously can be utilised for monosubstituted systems. Additionally, selective differentiation of the two ester groups using controlled amounts of NaOH[7] or introduction of specific groups through alteration of the initial cubane synthesis readily leads to systems with different functional groups at the 1 and 4 positions.[22] The range of possible functional groups that has been added in this manner is significant,[9] key synthetic examples include; bromo **14b**,[23] aldehyde **14c**,[24] amino/nitro **14d/e**,[25] hydroxy **14f**[26] and, perhaps most importantly, iodo **14a**[27] groups. A summary of the ways to prepare these systems is shown in Scheme 1.3.

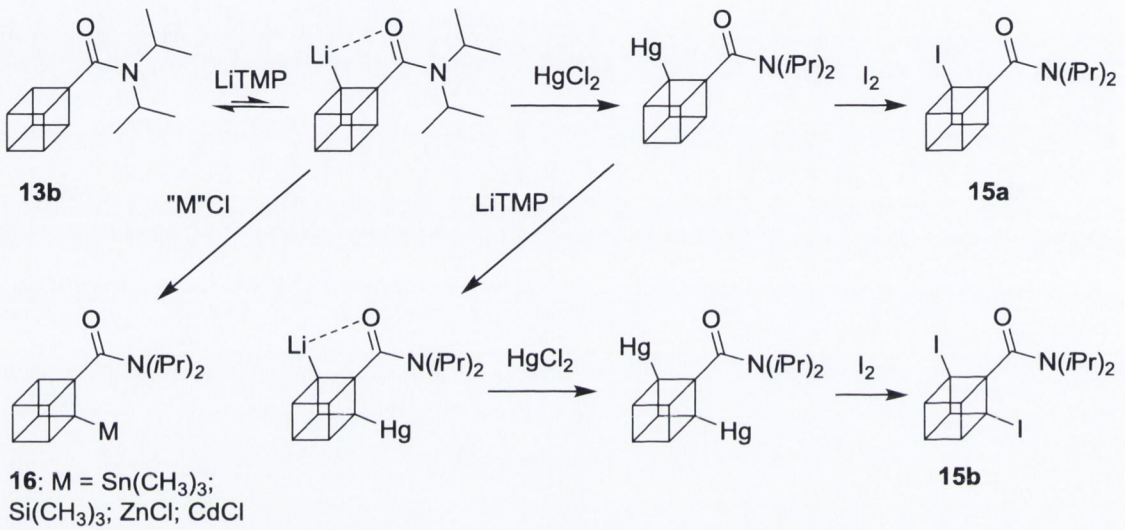


Scheme 1.3: Select FGI on the cubane scaffold.

1.1.3.1 *ortho*-Lithiation on the cubane framework

While manipulation of the carboxylic groups in this manner allows for quick functionalisation of the exterior of the cubane skeleton it fails to provide for higher order substituents nor ones not available through classical carboxylic chemistry. To this end, the Eaton group, in 1985,[28] published a key study where they showed that amide activation can be used to lithiate the position neighbouring a diisopropylamide in an appropriately functionalised cubane **13b** (Scheme 1.4). This exploits the acidity and orientation of the C-H bond in a manner analogous to that used in aromatic chemistry for *ortho*-lithiation. While the equilibrium concentration of this *ortho*-lithiated cubane is very low (~3 %) a further discovery found that, in the presence of mercury salts, the initially formed C-Li bond is

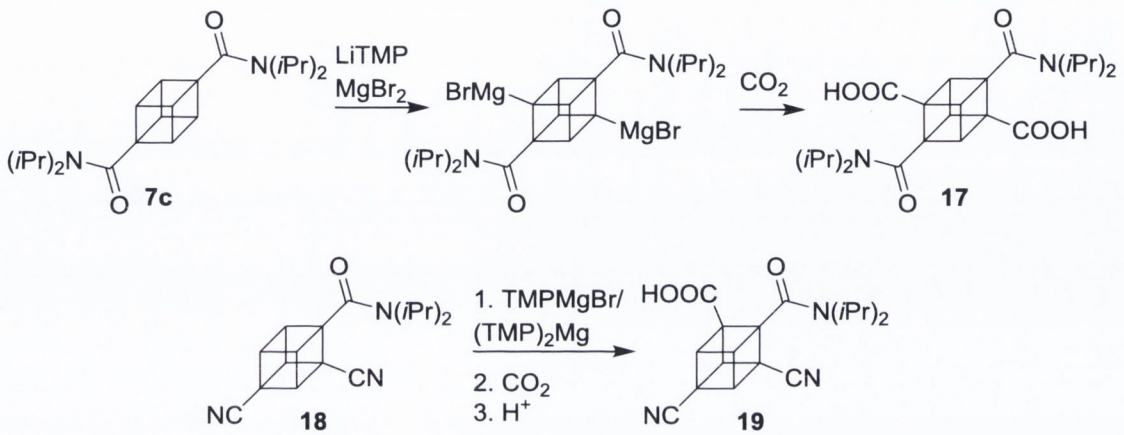
rapidly converted to a C-Hg bond. In this manner, the nature of the equilibrium can be altered so as to continuously replace, in a quantitative manner, a highly polar and reactive bond with one which is practically covalent and relatively inert.[28] Transmetallated systems formed in this manner undergo ready halogenation to yield highly useful compounds **15a**/**b** or metals such as zinc, silicon and tin **16** can be employed instead of mercury to give highly substituted systems of great synthetic utility.[29,30]



Scheme 1.4: Metallation and transmetallation of the cubane scaffold *via* amide activation.

Subsequent to Eaton's seminal work on *ortho*-lithiation and transmetallation, Bashir-Hashemi introduced transmetallation with magnesium salts, facilitating access to the mono- and *bis*-Grignard reagents of cubane[31] and eliminating the need for toxic mercury salts. The reaction proceeds in an analogous manner *via* stepwise lithiation/bromomagnesiation (Scheme 1.5); however, the increased polarity of the C-Mg bond with relation to the C-Hg bond causes the second metallation to occur at the most remote position from the first and further metallation does not occur. Quenching with CO_2 is the most common reported use of these Grignard reagents and yields of 90-95 % can be obtained for **17**.[31] Additionally, this methodology allowed access for the first time to phenylcubanes through use of a significant excess of bromobenzene as electrophile.[32] Expanding on this work, Eaton developed a new system that has shown useful synthetic utility both within and without the

realm of cubane chemistry.[33] By reacting 2,2,6,6-tetramethylpiperidine (TMPH) with one equivalent of ethylmagnesium bromide, the Hauser base,[34] tetramethylpiperidide magnesium bromide (TMPMgBr), is formed. These reagents can be used directly for *ortho*-magnesiation, eliminating the lithiation step entirely. Using CO_2 as electrophile produces **19** as a single isomer in upwards of 90 % yield.[35]



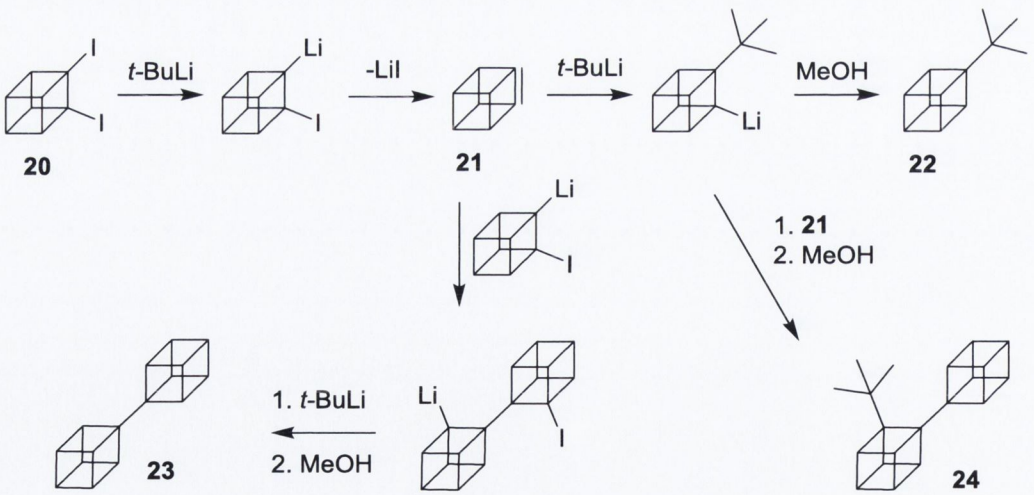
Scheme 1.5: Generation and use of cubyl Grignard reagents.

ortho-Transmetallation of the cubane skeleton is thus a powerful tool for the synthesis of an array of functionalised scaffolds. The primary advantage is the ability to start from a 1,4-disubstituted cubane and selectively functionalise the neighbouring C-H bonds. There are, however, major drawbacks. The first is the need for toxic mercury salts in the majority of instances. Secondly, the lithiating agents can often be quite unstable and are required in significant excess. The requirement of the diisopropylamide directing group is another issue. Due to its necessary stability towards the harsh conditions employed, it is also resistant to standard synthetic transformations of carboxylic groups. While successful routes around this problem have been described these all rely on severe reduction conditions which limit the groups which can be installed.[36-38] Finally, the reaction times for some of the reactions can be quite long – quantitative metallation/transmetallation from Li to Hg takes about 30 minutes while the Li-Zn process takes several hours and Li-Si is only achieved after several days.[29]

1.1.3.2 Metal-halogen exchange on the cubane framework

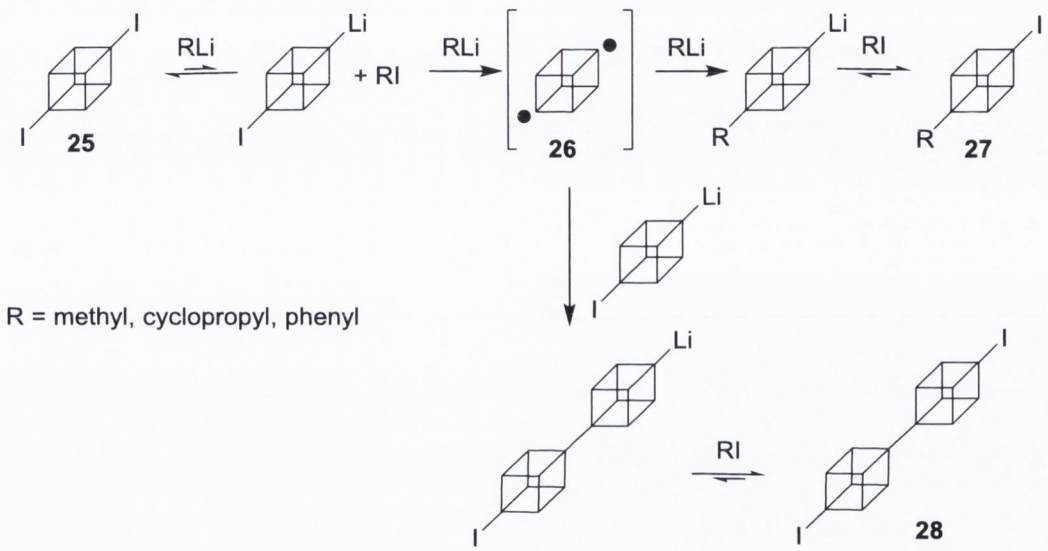
While useful, the drawbacks of the *ortho*-metallation limit its synthetic utility. A more useful approach - on paper at least - is direct metal-for-halogen exchange using halogenated cubanes. The ready availability of iodinated cubanes makes this an attractive route, but for various reasons this remains an area of cubane chemistry that has not been exploited.

The primary reason for this is some of the more unusual reactions that occur when disubstituted iodinated cubane derivatives are exposed to standard lithiating agents. The initial work on this reaction was performed by Eaton *et al.* in 1988[39] and a summary of their results is shown in Scheme 1.6. Treatment of 1,2-diiodocubane **20** with *t*-BuLi followed by quenching with alcohol gave as its primary product *tert*-butylcubane **22** but with the dicubyl species **23** and **24** also present. Further investigations proved that the only intermediate that possibly gives rise to these products is 1,2-dehydrocubane or cubene **21** – the most heavily pyramidalised olefin known. On treatment with *t*-BuLi, **20** is initially converted to 2-lithioiodocubane which loses lithium iodide to form **21**, which, due to its high reactivity, is consumed almost immediately.[8,39] The synthetic usefulness of **21** is thus impaired by this tendency to immediately react with the alkyllithium reagent present in excess.



Scheme 1.6: Generation and reactivity of cubene.

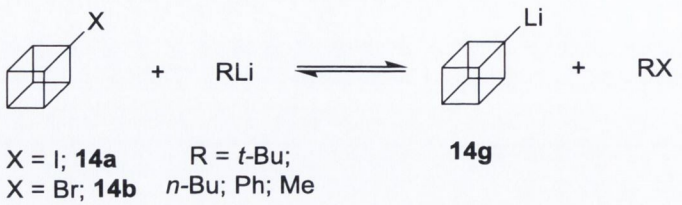
A more useful starting material for exploiting this unusual reactivity is 1,4-diodocubane **25**, itself available *via* iodinative decarboxylation of **7**. In this instance the intermediate is not cubene but rather 1,4-dehydrocubane (or cubane-1,4-diyl) **26**, which readily reacts to give an array of substituted cubanes.[40] Careful selection of the organolithium reagent can lead to a range of aryl and alkyl substituted cubanes **27**[41] as well as oligomeric cubane species **28**[42] (Scheme 1.7) with retention of one of the cubane iodides. The reaction is nevertheless again constrained by the lithiating agent employed.



Scheme 1.7: Reaction of 1,4-diiodocubane with organolithium reagents.

These lithiation reactions all rely on the relative tendency of halogenated cubane to undergo metal-halogen exchange as their first step. The mono-halogenated species provide a better avenue for exploiting this tendency – particularly because they react in a much more classical manner (Scheme 1.8). Iodocubane **14a** undergoes ready metal-halogen exchange with *tert*- or *n*-butyl lithium with none (*tert*-butyl) or little (*n*-butyl) coupled product observed. Bromocubane **14b** does not undergo any appreciable metal-halogen exchange or coupling with *n*-butyl lithium at 0 °C.[40] The equilibrium between cubyllithium plus iodobenzene and iodocubane plus phenyllithium, lies strongly toward the latter.[42] This is due to the increased acidity and s-character in the aryl system. In the case of methyllithium the equilibrium again favours methyllithium and iodocubane, as expected due to the relative

stability of primary alkyllithium reagents over tertiary as a result of inductive and associative effects.[41] Although the exact pK_a value for cubane is unknown, this reactivity would suggest that the pK_a of cubane must be greater than 43 and is most likely to be >50.[13,43]

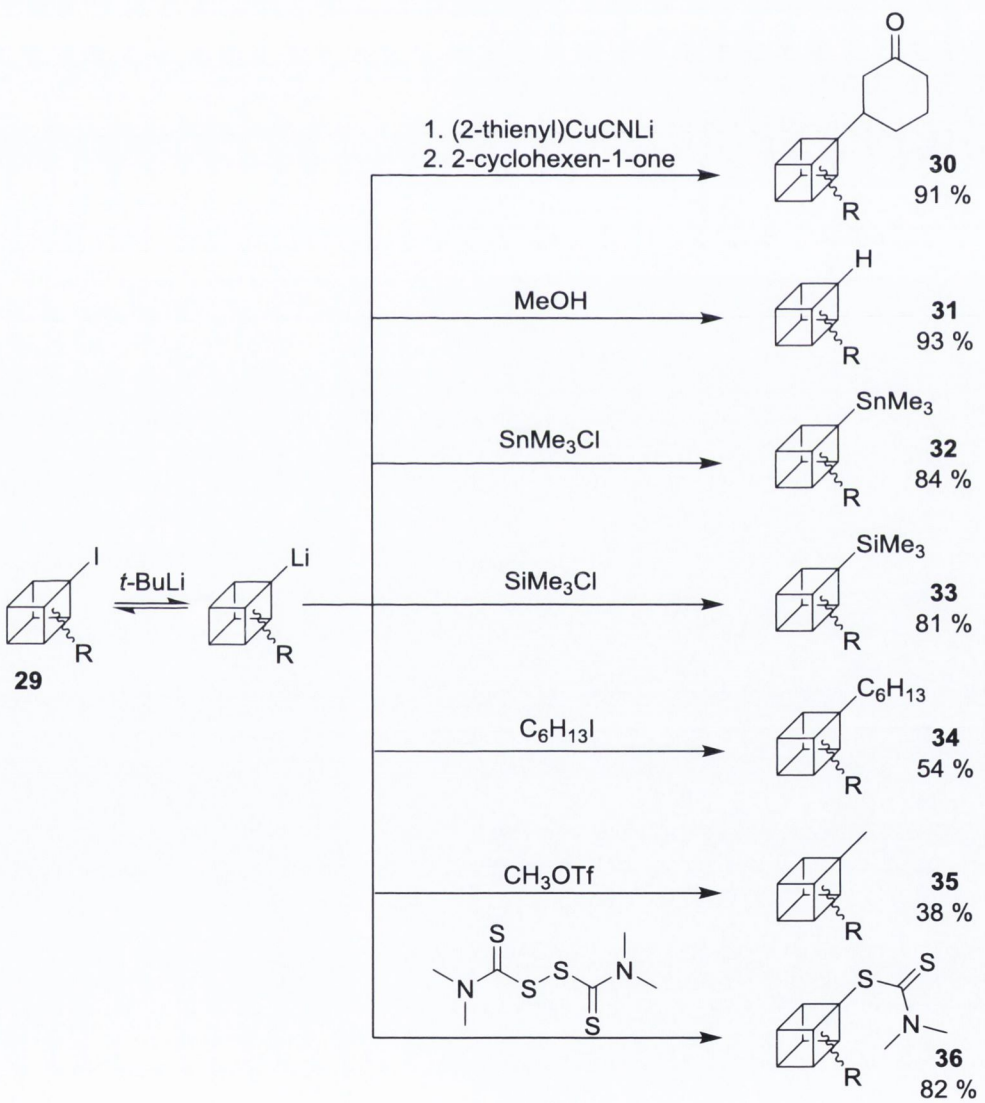


Scheme 1.8: Equilibrium between iodocubane and cubyllithium with various organolithium reagents.

In a practical sense, this means that when performing reactions for lithiation it is necessary to add at least two (often 3-4) equivalents of the alkyllithium reagent to force the equilibrium towards the cubyllithium system. This, however, can cause problems since the electrophile that is subsequently added must also be in significant excess. Additionally, the polarity of R-E (where R is the alkyl component of the organolithium reagent and E is the electrophile added) and cubane-E can be quite similar and therefore can present difficulties during isolation. Controlled addition of just two equivalents of *tert*-butyllithium presents the best solution as the initially generated *tert*-butyliodide undergoes preferential loss of HI with the second equivalent of *tert*-butyllithium to form 2-methylprop-1-ene, 2-methylpropane and lithium iodide. However, this also necessarily limits the possible functional groups that can be added as being stable to *tert*-butyllithium. Probably due to these potential problems, generation of the cubyl anion in this manner has never been commonly employed in the field of cubane chemistry. Scheme 1.9 illustrates the limited range of electrophiles that have been successfully added to the cube after the lithiation of iodocubane.[42,44-46]

As can be seen only seven distinct systems have been prepared *via* this methodology and the scope of electrophiles that have been successfully added to the cubane framework has been quite limited. Simple alkyl substitution (**31**, **34**, **35**) proceeds once the equilibrium between coupling and metal-halogen exchange with the alkyl halide favours the former.[42,44]

Transmetallation has been performed with silicon **32** and tin **33** on fluorinated cubanes,[44] while generation of a cubyl cuprate allows for Michael addition to a conjugated enone **30**. The most synthetically useful example of this branch of cubane chemistry is probably addition of a thioether substituent **36**, which upon harsh reduction conditions furnishes a mixture of the free thiol and disulfide.[44] This sparcity of synthetically useful products provides an avenue for expanding the 'synthetic toolkit' of cubane chemistry while potentially opening many new and interesting classes of substituted cubanes.



Scheme 1.9: Compounds generated *via* metal-halogen exchange of iodo-cubanes.

1.1.4 Palladium-catalysed cross-coupling reactions.

One significant series of synthetic modifications which have never been applied to the cubane scaffold is that of transition metal-catalysed cross-couplings. This is most likely due to the lack of appropriately substituted cubane precursors and also because, from a chronological perspective, major interest in the two areas has not coincided.

Following the publication of Heck's seminal paper in 1972,[47] where he demonstrated that aryl, benzyl and styryl halides can react with terminal alkenes under mild conditions in the presence of palladium salts, the field of transition metal-catalysed C-C bond formation simply exploded and has become a staple set of reactions for any synthetic chemist.[48] In addition to the Heck reaction numerous other named reactions have been published. The most notable of these include: Kumada coupling[49] (1972) between an organohalide and an organomagnesium reagent; Sonogashira reaction[50] (1975) between an organohalide and an alkyne; Negishi reaction[51] (1977) between an organohalide and an organozinc compound; Stille reaction[52] (1978) between an organohalide and an organostannane reagent; Suzuki-Miyaura reaction[53] (1979) between an organohalide and an organoboron compound; Hiyama reaction[54] (1988) between an organohalide and an organosilicon compound; Buchwald-Hartwig amination[55,56] (1994) between an organohalide and an amine. While each reaction is distinct in terms of the coupling partners involved, they all, with the exception of the Heck/Sonogashira reaction, share a general catalytic cycle (Figure 1.1).[57]

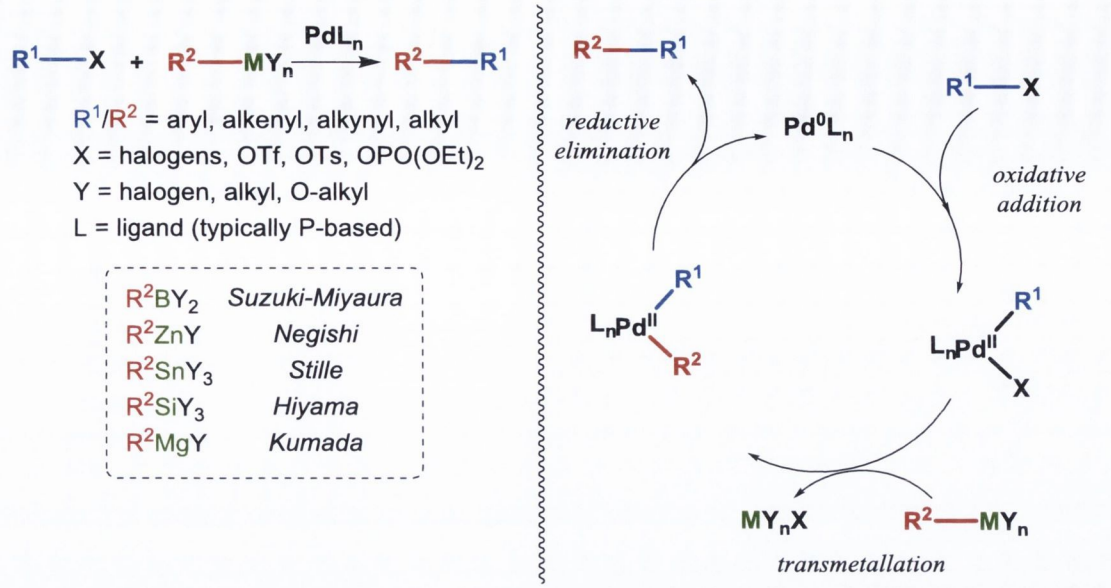


Figure 1.1: General catalytic cycle for Pd(0)/Pd(II)-catalysed cross-coupling reactions.

Countless variations of these reactions have been subsequently reported and the procedures have all evolved into highly efficient and often extremely mild methods for bond construction.[58-61] While this work will focus solely on the use of Pd(0)/Pd(II)-catalysis, other transition metals (notably Ni[62] and Fe[63]) have found common use in modern synthesis. The emergence of cross-coupling reactions as such a powerful tool over the past forty years is due both to the diversity of organometallic precursors now applicable in the reactions as well as the broad functional group tolerance supported by the most common reagents and conditions.[64,65] The importance of this field was recognised in 2010 with the awarding of the Nobel Prize in Chemistry to three of its earliest pioneers, Richard Heck, Ei-ichi Negishi and Akira Suzuki *"for palladium-catalysed cross-couplings in organic synthesis"*.[48]

The key parts of the catalytic cycles are theorised to involve the sequence of three key steps: (1) oxidative addition of an electrophilic carbon-heteroatom bond (halogen, triflate, tosylate or phosphonate) onto the low valent transition metal; (2) transmetallation or displacement of a heteroatom leaving group by the nucleophilic component and (3) reductive elimination of the coupled product. The oxidative addition is typically the rate limiting step

of the cross-coupling cycle.[66] Modern protocols exist for the effective addition of alkenyl, alkynyl, aryl, benzyl, allyl and alkyl halides.[57] Aryl and alkenyl halides possessing electron withdrawing groups are more reactive than those possessing electron donating groups due to the increased electrophilic nature of the C-X bond. Naturally, the reverse order holds true for the transmetallation step (*i. e.* increased nucleophilicity is favoured). Typically, the order of reactivity of the electrophilic partner has been established as: I ≫ Br > OTf ≫ Cl.[67,68] In terms of both oxidative addition and transmetallation, a marked difference is seen with relation to sp, sp^2 and sp^3 systems. While the first two tend to proceed effectively, the lack of a π-system in alkyl substituents severely limits their general applicability to this field of chemistry and has meant comparatively few efficient protocols exist for their couplings.[64]

1.1.5 Alkyl substituents in Pd-catalysed reactions

Historically, the use of sp^3 hybridised coupling partners (both electrophilic and nucleophilic) has suffered from significant obstacles, meaning this field has expanded at a slower rate than comparative sp and sp^2 systems. The major issues involved with using alkyl partners in the Pd(0)/Pd(II) catalytic cycle are: (1) the relatively slow oxidative addition or transmetallation of alkyl reagents (2) the rapid decomposition of Pd-alkyl complexes *via* reductive elimination or proto-demetallation and (3) the relative instability of alkyl organometallic reagents towards air/water requiring them to be generated *in situ* and often used in a 3-4 fold excess.

Successful addition of the alkyl partner to the palladium centre is the first major obstacle that needs to be overcome. Here, two avenues are available. The alkyl group can be introduced as either the electrophilic (R-X) or nucleophilic (R-M) component. Due to their inherent electron-rich nature the latter procedure is more often employed but both procedures are frequently used. Oxidative addition of sp and sp^2 halides tends to be a concerted mechanism whereas with sp^3 systems, the lack of a π-system means that the mechanism of addition more closely resembles nucleophilic substitution (S_N2) by the palladium

complex.[69] This, by its very nature, slows down the oxidative addition process (already rate-limiting) and limits the tolerance of the organic halide to unhindered (typically primary) systems. In terms of transmetallation, the process is more favourable but still not without its complications. In general, methods to overcome the limitations of transmetallation are specific to the individual metals involved and will be discussed in more detail later on.

While successful addition of the sp^3 system to the Pd centre is itself challenging – another problem immediately arises in the tendency of alkyl-Pd systems to undergo relatively fast decomposition. The major decomposition pathway is seen in those systems that possess hydrogen atoms adjacent to the metallated C centre – so called β-hydride elimination to give an alkene.[70,71] Additionally, this abstracted hydrogen can then be transferred to another organometallic species in a process known as protodemetallation (Figure 1.2).[72,73] This elimination pathway is in constant competition with reductive elimination and successful cross-couplings are characterised by having a more rapid reductive rather than β-hydride elimination process.[74]

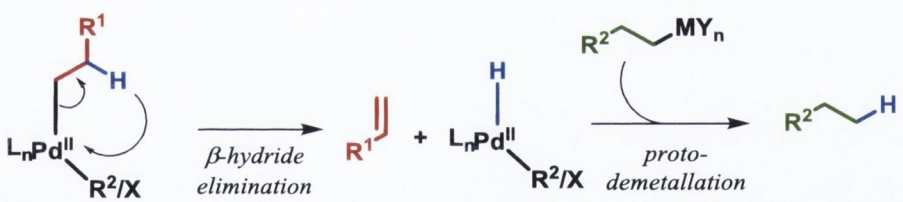


Figure 1.2: Mechanism of β-hydride elimination and protodemetallation

The most commonly used solution to overcome this problem is to use bulky, bidentate phosphine ligands, *e. g.*, *bis*(diphenylphosphino)ferrocene (dppf).[75] This bidentate ligand (and all others containing a similarly large 'bite angle') is presumed to favour reductive elimination by forcing the two coupling partners to adopt a *cis*-orientation on the square planar Pd^{II} complex (Figure 1.3). If the two substituents bind in a *trans*-orientation the complex must rearrange them to being *cis* for successful reductive elimination to occur.[71] By eliminating this process, the lifetime of the alkyl-Pd complex is dramatically shortened – thus reducing the timeframe for β-hydride elimination to occur. The large bite angle (∠P-

Pd-P = 99.07°) also favours reductive elimination by distorting the bond angle between the two coupling partners – forcing them closer together and dramatically increasing the rate of reductive elimination.[75]

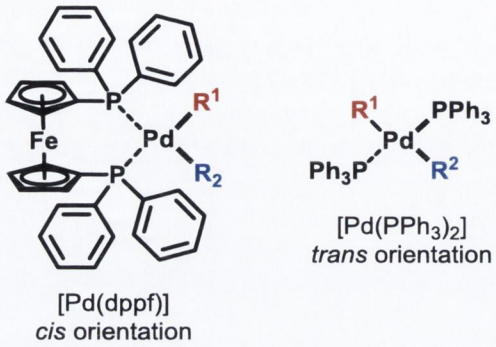


Figure 1.3: Palladium complexes in *cis* and *trans* orientations.

These issues in combination have made it necessary to identify oftentimes complex mixtures of ligands, metals, conditions and additives to effectively promote cross-coupling reactions of alkyl substituents. Unfortunately, one major breakthrough remains to be made – namely efficient protocols for the coupling of tertiary sp^3 systems. While for most primary and even secondary alkyl reagents, an effective coupling system can probably be found, the same is not true for tertiary systems.[76] The increased steric hindrance present in tertiary systems raises the energy barrier for addition to the Pd centre and isomerisation of the metalloalkane species often becomes more facile with increased substitution. As a result, successful examples of palladium-catalysed tertiary C(sp^3) couplings are exceedingly rare.[65]

For every named reaction there are a plethora of possible modifications and improvements that can be made. As a result only the two reactions which have historically proved most tolerant and versatile in their use of sp^3 coupling partners (the Suzuki-Miyaura and Negishi reactions) will be discussed in detail here. Frequently, however, the conditions which prove effective for one reaction are transferrable to the others.

1.1.5.1 The *B*-alkyl Suzuki-Miyaura reaction

The *B*-alkyl Suzuki-Miyaura reaction is probably the most widely used cross-coupling methodology for sp^3 systems.[64] This is due, at least in part, to the ready availability and thermal stability of alkyl boronates; the relative nontoxicity of the boron side products (particularly in relation to the organostannanes in the Stille reaction which they have largely supplanted); the mild reaction conditions often employed; its broad reaction group tolerance and the lack of sensitivity to water, which can often be used as a beneficial additive. The major factors which affect the rate of this reaction are the nature of the boron substituents, the catalyst and the base and solvent employed. All three areas have been extensively studied and will be discussed in turn.

Typically, Suzuki-Miyaura reactions are best performed with unhindered, electron-rich organoboranes and electron-deficient organohalides. As such, alkyl-boron compounds are the most commonly used way to install alkane functionality. Alkyl-substituted boronates and boranes are easily synthesised by two major routes – generation of an alkyllithium or alkylmagnesium reagent followed by quenching with an appropriate boron source[77-79] or hydroboration of an alkene.[80-82] Figure 1.4 shows some of the more common boron substituents employed as Suzuki partners.

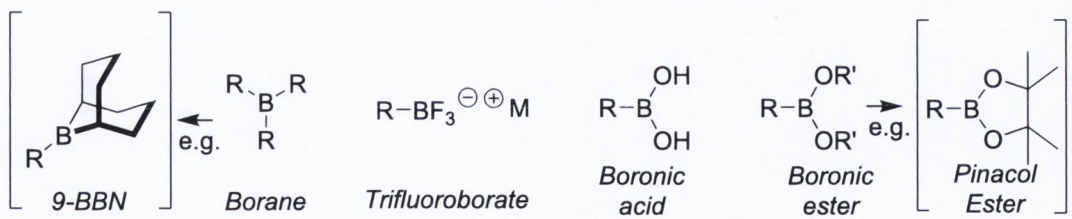
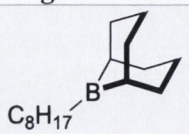
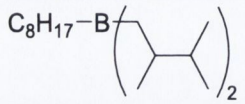
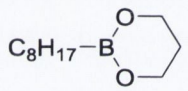
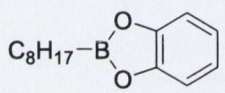
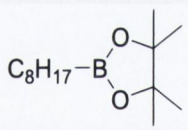


Figure 1.4: Typical organoboron reagents used.

In terms of stability, boronic acids and esters as well as the trifluoroborates are typically air and water stable and as such can be handled with ease. 9-BBN derivatives and other boranes tend to be air sensitive, however, and as such are typically generated and used *in situ*.[83] The boron substituent can have a profound impact on the rate and success of a coupling reaction. Extensive studies by Suzuki and co-workers[84,85] on the reaction between

iodobenzene and various alkyl boranes show that typically electron-rich B-(alkyl)$_3$ substituents outperform boronic acids or esters. These results are summarised in Table 1.2.

Table 1.2: Cross-coupling of iodobenzene with organoboron compounds.[84,85]

Entry	Organoboron	Base (eq.)	Solvent	Yield (%)[a]
1		NaOH (3)	THF/H_2O	99
2		NaOH (3)	THF/H_2O	82
3	C_8H_{17}-B-(cyclohexyl)$_2$	NaOH (3)	THF/H_2O	93
4	B(C_8H_{17})$_3$	NaOH (3)	THF/H_2O	98
5	B(sec-butyl)$_3$	KOH (3)	THF/H_2O	40
6	B(cyclopentyl)$_3$	KOH (3)	THF/H_2O	65
7	B(cyclohexyl)$_3$	KOH (3)	THF/H_2O	55
8		KOH (3) Tl_2CO_3 (1.5) TlOH (3)	THF/H_2O THF Benzene/THF	75 60 93[b]
9		KOH (3) TlOEt (3) Tl_2CO_3 (1.5) TlOH (3)	THF/H_2O THF/H_2O THF Benzene/THF	trace 41 93 84
10		TlOH (3) Tl_2CO_3 (1.5	THF/H_2O THF	34 trace
11	C_8H_{17}-B(OH)$_2$	TlOH (3)	THF/H_2O	trace

Reaction Conditions: Reactions were performed at 50 °C with $PdCl_2$(dppf) catalyst (3 mol %), organoboron compound (1.1 eq.) and iodobenzene (1 eq.). [a] Yields (GC) were based on iodobenzene. [b] $PdCl_2$(dppe) (3 mol %) was used as catalyst.

The catalyst $PdCl_2$(dppf) and other bidentate ligand complexes find routine use in the *B*-alkyl Suzuki-Miyaura reaction, as previously described. For unoptimised reactions, up to 10 mol % of the catalyst system may be required, but in more optimum procedures loadings as low as 1-3 mol % can suffice. More recent studies have identified other electron-rich and often quite sterically hindered ligands which possess high activity for sp^3 couplings.[68] These have enabled couplings of alkylboranes with aryl chlorides, reactions previously assumed impossible.[86,87] One particularly noteworthy class of modern catalyst systems have been developed around the *N*-heterocyclic carbene (NHC) class of ligands. These ligands present

an alternative to phosphine systems and have attracted much attention in recent years.[60,88] Their pronounced σ-donor ability, minimal backbonding and steric bulk greatly facilitates oxidative addition and allows stabilisation of both high and low oxidation state metals.[89,90] As a result, they have achieved very promising results (yields >99 % with 1 mol % catalyst loadings) not only as Suzuki-Miyaura cross-coupling ligands; but also in applications in Heck, Negishi and Sonogashira couplings.[91] The Pd-PEPPSI series (Figure 1.5) is an air and moisture stable, commercially available and highly active illustrative member of this class of catalyst system.[92-94]

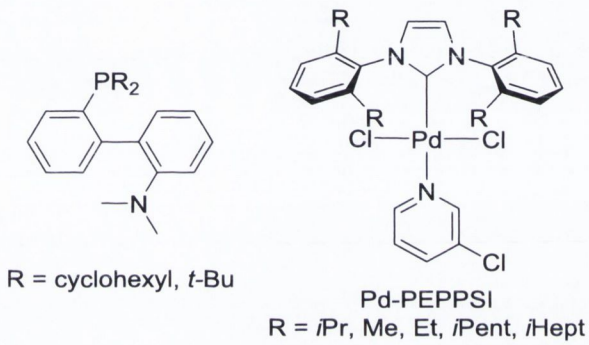


Figure 1.5: Examples of highly active ligands/catalysts used in sp^3 couplings.

The final key component in a Suzuki-Miyaura system is the base and solvent. More so than any other coupling methodology, the base plays a pivotal role in Suzuki-Miyaura couplings. Soderquist and co-workers have shown that the base is involved in at least five distinct steps in the catalytic cycle of alkylboranes, most notably the transmetallation process.[95] Suzuki's original report detailing the reactivity of alkyl substituents identified thallium(I) bases as the most effective at promoting transmetallation and thus coupling of sp^3 systems.[74] Similar studies have shown that strong bases such as NaOH, KOH and NaOMe are also effective once the reaction is run in aqueous media (typically THF/H_2O mixtures). Use of weaker bases such as K_2CO_3 and K_3PO_4 by contrast appear to work best in anhydrous polar solvents such as DMF (Table 1.3).[74,84,85] More recent investigations by Falck *et al.* have shown that replacing the highly toxic Tl bases with Ag(I) salts allowed for the effective coupling of *n*-butylboronic acid to a wide range of electrophiles.[96]

Table 1.3: Base and solvent investigation into reaction of *B*-octyl-9-BBN with iodobenzene.[74,84,85]

Entry	Catalyst	Base (eq.)	Solvent	Temp (°C)	Yield (%)
1	$PdCl_2(dppf)$	NaOH (3)	THF/H_2O (5:1)	65	99
2	$PdCl_2(dppf)$	TlOH (1.5)	THF/H_2O (5:1)	20	79
3	$PdCl_2(dppf)$	NaOMe (1.5)	THF	65	98
4	$PdCl_2(dppf)$	NaOMe (1.5)	THF/MeOH (5:1)	65	18
5	$PdCl_2(dppf)$	K_2CO_3 (2)	DMF	50	98
6	$PdCl_2(dppf)$	K_3PO_4 (2)	DMF	50	94
7	$Pd(PPh_3)_4$	NaOH (3)	THF/H_2O (5:1)	65	84
8	$Pd(PPh_3)_4$	NaOH (3)	$Benzene/H_2O$	80	97

Reaction Conditions: All reactions were performed with 3 mol % catalyst for 16 hours.

1.1.5.2 Alkylzinc reagents in the Negishi reaction

The Negishi reaction is the other most commonly utilised methodology to effect cross-couplings of sp^3 systems.[65] In general, organozinc reagents possess low reactivity towards classical addition reactions due to the highly covalent nature of the C-Zn bond. This low reactivity provides an excellent platform to selectively incorporate organozinc reagents into organic scaffolds. The presence of an empty, low-lying p-orbital on the zinc means that alkylzinc reagents display an excellent ability to undergo transmetallation – making them an ideal tool for $C(sp^3)$ couplings.

The major contrast to the Suzuki-Miyaura reaction is that organozinc reagents tend to be less stable than their organoboron counterparts and need to be kept scrupulously dry and often in an inert atmosphere. Nevertheless, numerous protocols for their synthesis and effective storage have been developed. The most popular of these is the use of highly active zinc metal, so called Rieke zinc (Zn^*), to insert zinc into an alkyl-halogen bond.[97-100] Rieke zinc can be generated *in situ* by reduction of zinc chloride with lithium naphthalenide in THF.[101] Addition of the alkyl halide then gives a solution of alkylzinc(II) halide which can be used directly in coupling reactions. One attractive alternative route, based on the known chemistry of cubane, is the transmetallation of alkyllithium reagents in the presence of zinc(II) halides, again giving a solution of alkylzinc(II) halide for *in situ* reaction.[102]

In terms of catalyst choice, the development of the field has been broadly similar to that described for Suzuki-Miyaura couplings previously. Hayashi *et al.* in 1984 provided the first analysis of catalyst systems applicable for the coupling of alkylzinc(II) halides with aryl halides and found $PdCl_2$(dppf) to be the most efficient catalyst.[75] Subsequently, bulky, electron-rich, phosphine ligands have historically been the most utilised. NHC-derived catalysts (*e. g.*, Pd-PEPPSI) have also experienced significant use in recent studies.[65,92,103]

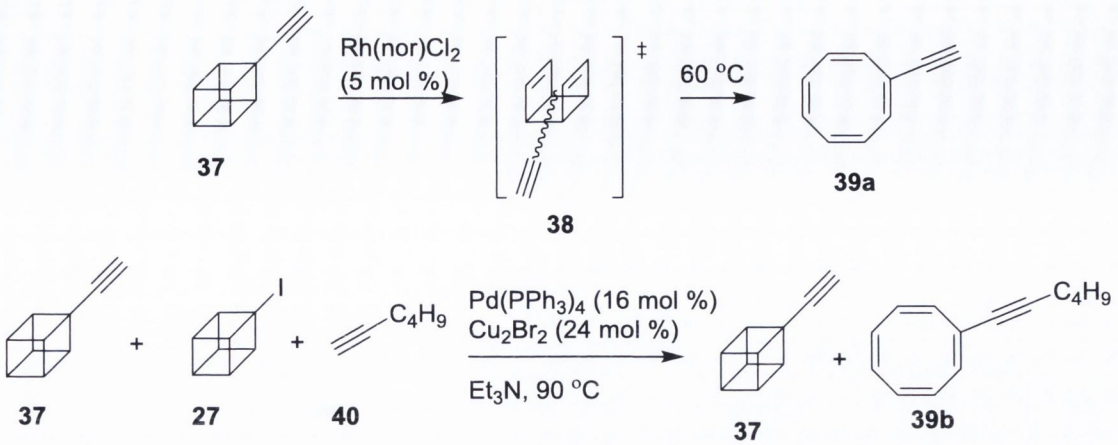
Additives play a crucial role in the success of a C(sp^3) Negishi reaction. With the generation of most alkylzinc complexes in THF and their sensitivity to water, solvent choice is limited. The benefits of adding polar aprotic solvents such as *N*-methyl-2-pyrrolidinone (NMP) or dimethyl sulfoxide (DMSO) have been widely reported.[103-105] The necessity for lithium salts (e. g., LiCl/Br) in the Negishi reaction has been investigated by a number of groups. Knochel and co-workers found that LiCl accelerated the formation of organozinc reagents that were prepared by a Br/Mg exchange method.[106] Studies by Oshima and co-workers suggested that LiCl enhanced the reactivity of organozinc halides toward transmetallation.[107] Depending on the method used to generate the organozinc halide, lithium salts can often be present in solution. Nevertheless, it has become quite common practice to add lithium halides to Negishi couplings in order to ensure a sufficient excess.[108]

1.1.6 Cubane as potential coupling partner

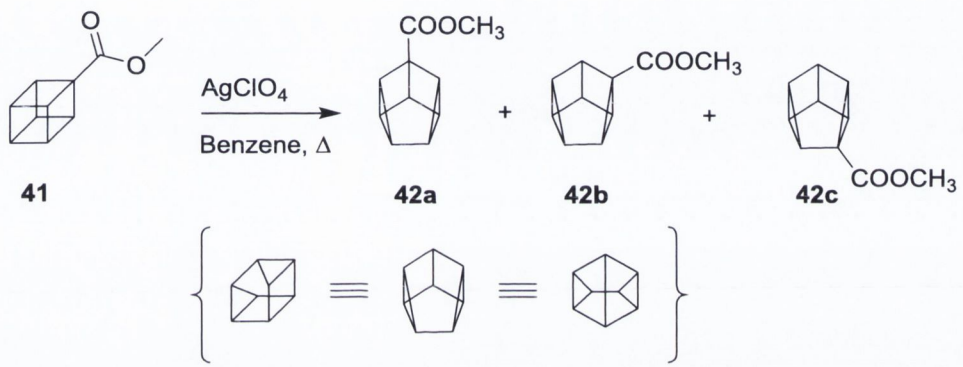
While tertiary alkanes are characteristically difficult as coupling partners certain properties of cubane lead to the assumption that it may prove an exception to this rule. Primarily, these focus on the nature of the bonding in cubane. First of all, the fact that the external bonds in cubane possess such a significant degree of s-character, implies that they could behave more like readily reactive alkenyl or aryl coupling partners rather than standard alkyl systems.[12] The major reason tertiary alkyl systems react so poorly under standard coupling methodologies is their tendency to undergo isomerisation *in lieu* of cross-coupling.[76] Tied to this is their increased tendency to undergo β-hydride elimination. It is

not an unreasonable assumption to expect that cubane will avoid these issues. Conversion of the cubane framework to cubene, while documented,[39] is an energetically disfavoured pathway due to the high ring strain of the pyramidalised olefin, and thus can be reasonably expected not to occur. However, some transition metal mediated isomerisation reactions of cubanes have been recorded and need to be considered (*vide infra*). Steric constraints are the final major hurdle towards successful tertiary sp^3 couplings. Again, the rigid orientation of cubane may prove to be a significant benefit here. Compared with the C-C-C bond angle in a *tert*-butyl group or adamantane (~109°), the 90° angle in cubane causes the adjacent carbon atoms to be somewhat 'tied back' from the reactive centre, theoretically decreasing the overall steric demand which has limited the successful couplings of tertiary alkanes.

Two distinct isomerisation reactions of cubane in the presence of transition metal salts have been reported. These are depicted in Schemes 1.10 and 1.11. The rhodium-induced rearrangement of cubane was first discovered in 1970[109] and the precise mechanism has been subsequently established.[45,110] Scheme 1.10 illustrates a particularly useful example of this chemistry starting from an alkynylcubane **37**. Rh(I) initially invades the cubane skeleton where it promotes oxidative addition and rapid ring opening to a *syn*-tricyclooctadiene **38**. These systems are thermally unstable and rearrange, on heating, to cyclooctatetraene **39a**.[45] In one instance a mixture of palladium and copper in refluxing triethylamine was shown to induce the same rearrangement with iodocubane **27** and terminal alkynes. High loadings of the metals (16 mol % Pd and 24 mol % Cu) were required and in stability studies the reaction was found not to proceed without both metals and the terminal acetylene present.[111] Interestingly, when the reaction was performed in the presence of **37**, **27** was entirely converted to **39b** with **37** remaining completely unchanged. This indicates some metal intermediate in the Sonogashira coupling of **27** is facilitating rearrangement to the cyclooctatetraene structure.



Scheme 1.10: Rh(I) and Pd/Cu induced rearrangement of cubanes.



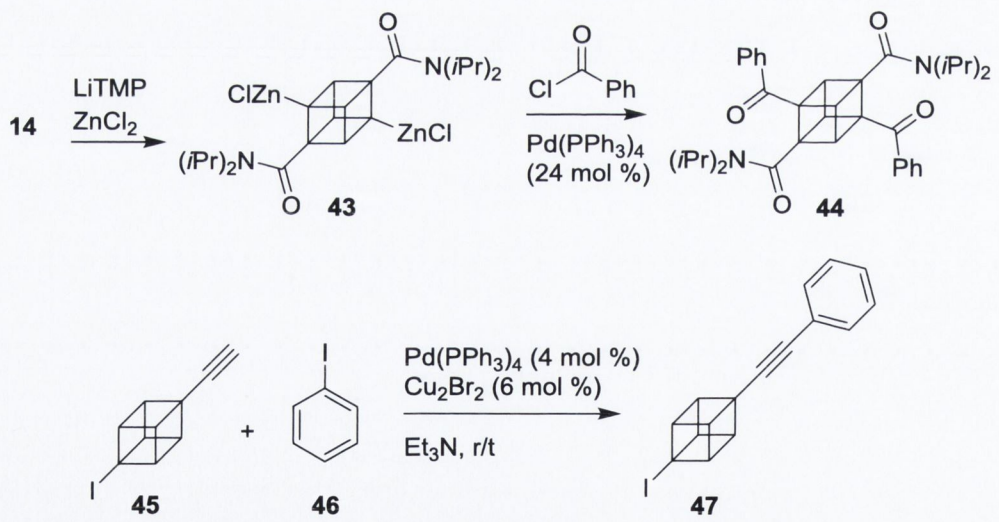
Scheme 1.11: Ag^+ induced rearrangement of cubane to cuneane.

The other transition metal induced rearrangement of cubanes was reported in 1970[112] and follows from similar reactions observed in homocubyl and *bis*homocubyl systems.[113,114] This rearrangement is promoted by silver(I) ions and leads to isomerisation of the cubane skeleton to the less sterically strained cuneane (pentacyclo[3.3.0.$0^{2,4}$.$0^{3,7}$.$0^{6,8}$]octane) framework **42** (Scheme 1.11). The mechanism is presumed to operate through oxidative addition of the metal ion into a C-C bond, followed by carbonium ion formation and rearrangement.[115] Reductive elimination of the metal gives the isomerised, wedge-shaped, system. All other reported synthetic avenues to cuneane utilise Ag(I) salts (typically perchlorate or perbromate) to catalyse the transformation.[116-118] In the original paper the authors claim that "*the catalytic activity of palladium(II) for the isomerization of cubane to cuneane is similar to that of silver(I)*".[112] This claim has been repeated with $PdCl_2$ mentioned as a possible Pd(II) source.[118] However, no experimental

conditions or investigation has been published on the activity of Pd(II) to effect this transformation.

1.1.7 Previous examples of cubane as coupling partner

To date, there has been no study on the general applicability of cubane as a reactant in transition metal-catalysed cross-coupling reactions. While this may appear unusual, one explanation is that the expansion of cross-coupling techniques to incorporate sp^3 systems (late 1980s onwards) coincided almost directly with the decline of interest in the synthetic transformations of cubane (~early 1990s). As a result there seems to be a significant absence in the synthetic chemistry of cubane. Just two examples of palladium-catalysed cross-coupling reactions of cubane have been reported (Scheme 1.12). The first is a Negishi-style condensation of a zinc-cubane system **43** (synthesised as described previously) with benzoyl chloride[29] and the second a Sonogashira cross-coupling of an alkynylcubane **45**.[111] Neither paper, however, contains any optimisation nor has any investigation into the limits of the reaction and neither reaction has been followed up in any way.



Scheme 1.12: Previous examples of cross-coupling reactions involving cubane.

1.2 Porphyrins as molecular scaffolds

1.2.1 Porphyrins – structure and nomenclature

Porphyrins (Figure 1.6) are macrocyclic compounds containing a tetrapyrrole ring with 22 π-electrons, 18 of which take part in the aromatic system. The other four π-electrons possess more double bond character. Although every carbon is sp^2 hybridised the symmetry of the molecule illustrates that there are three distinct carbon atoms present, namely the α- and β-carbons of the pyrrole subunits and the methine bridged meso carbons. As aromatic compounds, porphyrins undergo many of the characteristic electrophilic and nucleophilic substitution reactions including halogenation, nitration and acylation.[119] These reactions may occur either at the β- or meso-carbons and the reactivity of these two sites can be fine-tuned by various modifications to the macrocyclic core.[120]

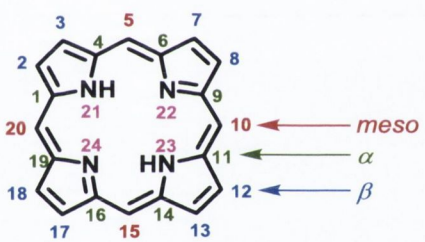
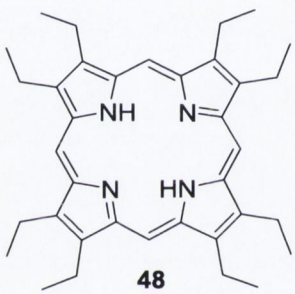


Figure 1.6: Porphyrin structure and the IUPAC numbering system with α, β and meso positions indicated.[121]

Due to their impressive optical and photophysical properties,[122-124] chemical stability,[119,125] conformational flexibility[126-128] and biological relevance;[120,129,130] porphyrins have long been studied as molecular scaffolds. Applications for the tetrapyrrole macrocycle have been found in areas as diverse as optics,[131-133] light harvesting,[134-138] surface chemistry[139-141] and cancer therapy.[142-146] Continuous research into the properties of porphyrinoid systems means they are among the most studied classes of organic compounds. The search for further applications for this robust scaffold, however, requires equally focused research into their synthetic availability. As such, the development of novel synthetic avenues to substituted porphyrin scaffolds remains an ongoing challenge.

1.2.2 Synthetic strategies towards substituted porphyrins

Traditionally the most widely used porphyrins for synthetic transformations have been β-substituted proto- and etioporphyrins or 2,3,7,8,12,13,17,18-octaethylporphyrin (OEP) **48** but interest in these has waned in recent years due to their reasonably complicated synthetic availability. Nowadays, more accessible meso-substituted porphyrins such as 5,10,15,20-tetraphenylporphyrin (TPP) **49** have become the workhorses of porphyrin chemistry. Whilst meso-substituted porphyrins do not exist in nature the relative ease of functionalising this position in the laboratory has led to their continued use as scaffold in a wide variety of applications.



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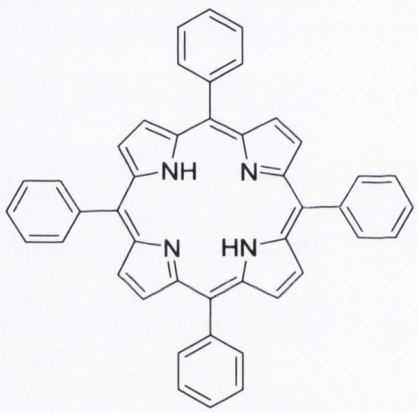

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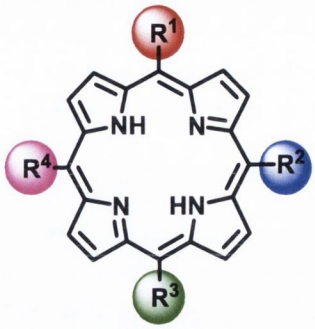
For the synthesis of such meso-substituted porphyrins a wide range of synthetic avenues are available. Generally speaking, the target compounds are members of the A_x- and ABCD-type series (Figure 1.7), colloquially termed the porphyrin alphabet soup.[119] Ideally, unsymmetrical systems with both meso-alkyl and aryl residues are required.[147-149] For fully symmetric systems a variety of condensation reactions can be performed, most notably Rothemund[150,151] and Lindsey[152-154] condensations whereby tetrasubstituted A_4 porphyrins can be synthesised *via* the acid-catalysed reaction of pyrrole with various aldehydes. For the synthesis of less symmetrical A_2 and A_2B_2 scaffolds, condensations involving MacDonald [2+2] condensations[155] using dipyrryl subunits (for 5,15-systems)[156-159] or [3+1]

condensations using tripyrryl analogues (for 5,10-systems)[160-162] have found widespread use.



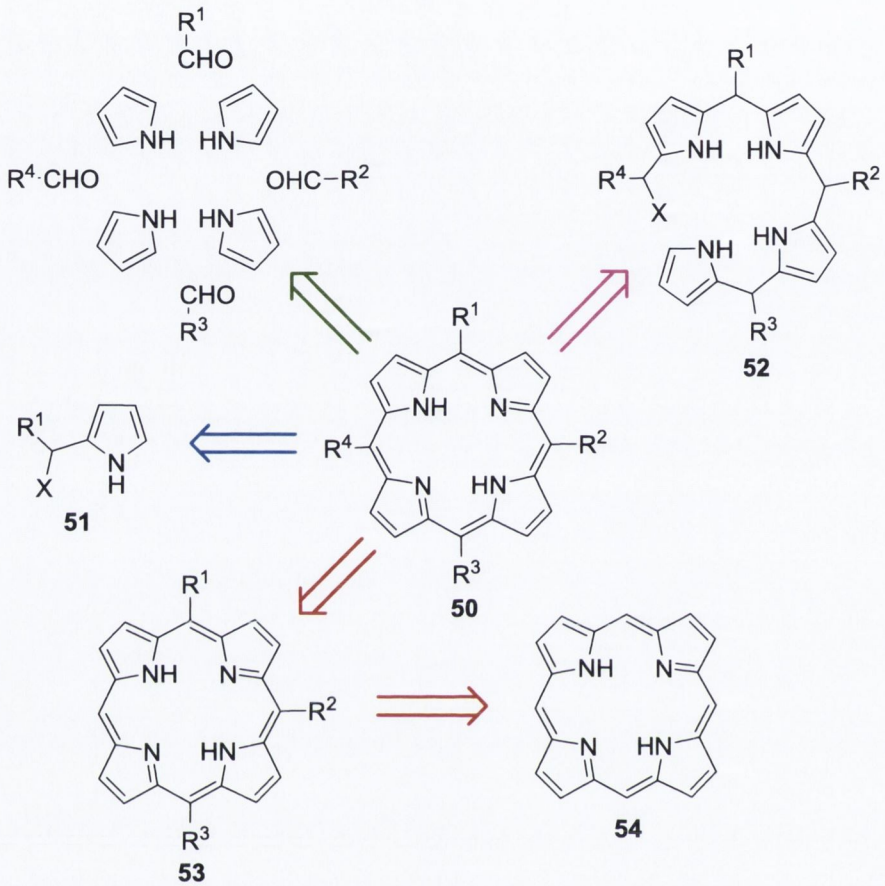
$R^1 = R^2 = R^3 = R^4$ A_4
$R^1 = R^2 = R^3 \neq R^4 = H$ A_3
$R^1 = R^2 \neq R^3 = R^4 = H$ $5,10\text{-}A_2$
$R^1 = R^2 \neq R^3 = R^4$ $5,10\text{-}A_2B_2$
$R^1 = R^3 \neq R^2 = R^4 = H$ $5,15\text{-}A_2$
$R^1 = R^3 \neq R^2 = R^4$ $5,15\text{-}A_2B_2$
$R^1 \neq R^2 = R^3 = R^4 = H$ A
$R^1 \neq R^2 \neq R^3 \neq R^4$ $ABCD$

Figure 1.7: meso-Substituted porphyrin classes according to ABCD-nomenclature.

Modern applications, however, tend to require the availability of more unsymmetric porphyrins. Thus, the primary goal for much of the recent past in this field has been to develop high yielding, reliable routes to unsymmetric, tetrasubstituted porphyrins, so-called ABCD-systems.[119] In practice there are three modern synthetic routes to make meso-substituted ABCD-type porphyrins **50**, namely: (1) mixed condensation, (2) total synthesis and (3) functionalisation of preformed systems (Scheme 1.13).

While on paper the direct mixed condensation reaction appears the most straightforward this is by far the least synthetically useful when a specific unsymmetric porphyrin is targeted. This is because this method tends to give a mix of all possible isomers which require lengthy chromatography to separate, if possible at all.[163] Whilst kinetic control can give desired isomers in high yield in some circumstances, this is not a generally applicable method for ABCD-type porphyrin synthesis, particularly where acid labile functional groups are desired. Use of sterically hindered groups also presents a problem as the formation of porphodimethenes can become quantitative under certain conditions.[164,165] The use of reactive pyrrole systems such as **51** improves selectivity but fails to overcome the main problems of this approach.[166] This is not to write off the utility of condensation reactions wholesale, however, as major improvements have been made. As mentioned previously, Lindsey's group in particular have developed several condensation methods

involving dipyrromethane derivatives, (2+2 additions), and tripyrromethane derivatives, (3+1 additions), which allow for the large scale preparation of 5,15-A_2-, 5,10-A_2- and A_2B_2-type porphyrins.[167]



Scheme 1.13: Retrosynthetic analysis for the synthesis of ABCD-type porphyrins.

The most obvious alternative route is a direct total synthesis. The synthesis of a bilane precursor **52** from the desired pyrrole and aldehyde subunits allows precise positioning of all four meso substituents. This can then be cyclised and oxidised to the desired porphyrin.[168,169] This is a powerful method but, as it is a total synthesis, suffers from the amount of synthetic steps and manipulations required.[170] Furthermore, acid induced scrambling of the final product presents a major problem – although newer methods for selected residues have helped overcome this.[171]

The Senge group has focused extensively on the third possibility, namely the stepwise introduction of desired functionalities to preformed systems. The challenge in making

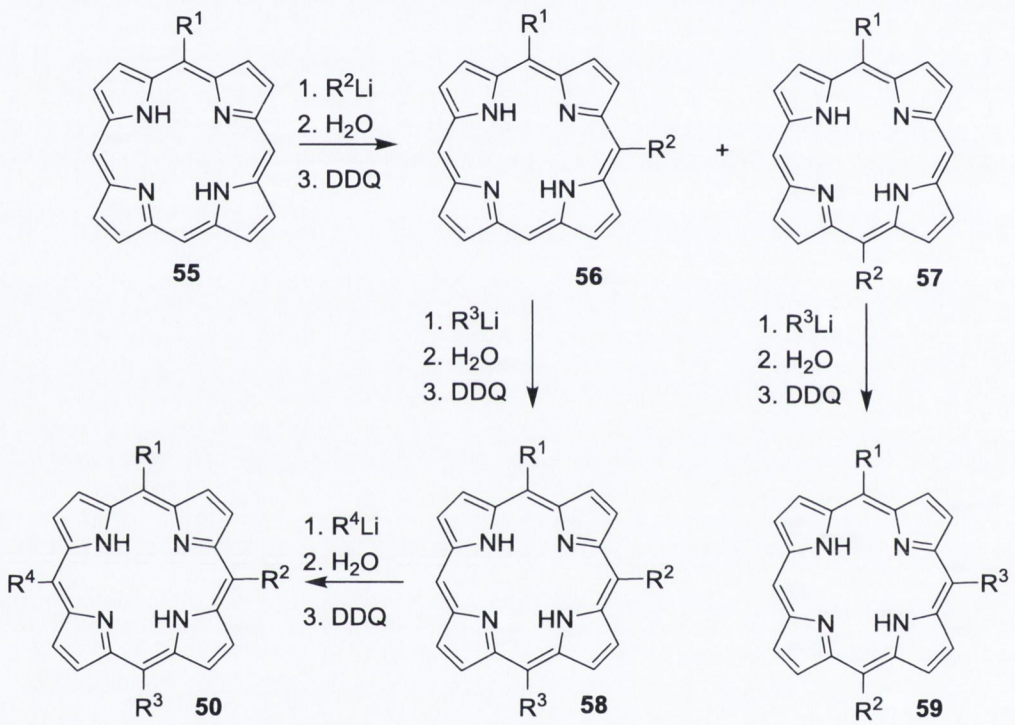
ABCD-type porphyrins is to use the whole repertoire of available porphyrin scaffolds and possible functionalisation reactions to develop the most efficient route to any unsymmetrical target.[172] Theoretically all ABCD-type porphyrins are accessible through consecutive functionalisation of porphine **54** with organolithium reagents but oftentimes this is far from the most practical route, *i. e.* if an A_2BC-type porphyrin is required it is probably much more sensible to start with a 5,15-A_2-type porphyrin from a [2+2] condensation rather than **54**. Overall, the synthetic strategies employed in this regard fall into three main categories: (1) monosubstitution using organolithium reagents; (2) disubstitution using R^1Li and R^2X in a one pot reaction and (3) the use of transition metal-catalysed C-C coupling reactions.

1.2.2.1 Monosubstitution using organolithium reagents

This procedure was discovered through work on highly substituted porphyrins already bearing eight β residues (e.g. OEP) and gave access to dodecasubstituted ABCD-type porphyrins.[173,174] Progress in this area then implied that the β-unsubstituted porphyrins may be similarly accessible.[175] The reaction **54** → **50** is reasonably straightforward but it does rely heavily on the availability of appropriate starting materials. Ultimately, what is required for this route to be fully complete is the synthetic availability of **54**. Historically this has been a significant issue as porphine suffers dramatically from low solubility. However, recent advances in porphine synthesis have overcome this problem to a large degree and the preparation and functionalisation of **54**, while still tricky, is at least now possible.[176]

This method relies on the reactivity of the porphyrin meso position towards strong nucleophiles.[175] In a straightforward addition/oxidation procedure virtually any alkyl or aryl residue can be installed onto a preformed porphyrin scaffold in what has become a powerful modification technique. It involves the formation of RLi reagents which can be reacted with either metallo- or free-base porphyrins. In general, Ni(II) porphyrin complexes provide best yields when installing alkyl residues while free-bases are preferential when aryl residues are desired. The major drawback, apart from the availability of certain organolithium reagents,

is that when working with sterically hindered alkyllithium reagents (*e. g.*, *t*-BuLi) multiple alkylation or β-alkylation products can be observed.[174,177,178] Also, the use with highly ruffled systems is not recommended due to the formation of porphodimethene products.[173,179,180] Scheme 1.14 shows the synthetic route to ABCD-type porphyrins, starting with an A-type porphyrin. By varying this chosen starting material or stopping at any point along the sequence almost any combination of meso substituent pattern is accessible *via* this route.

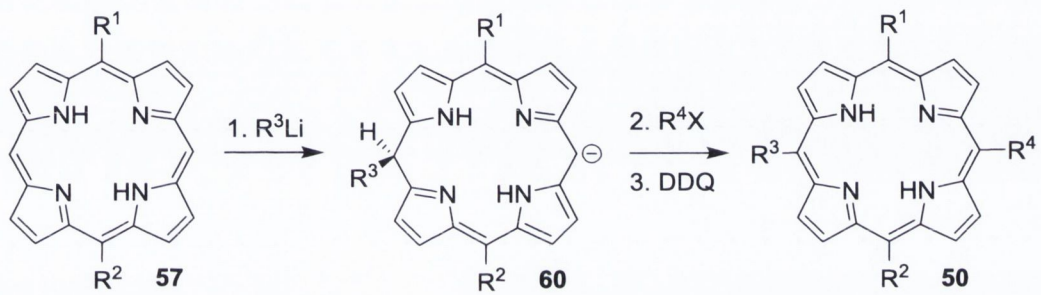


Scheme 1.14: Stepwise synthesis of ABCD-type porphyrins with organolithium reagents.

1.2.2.2 Disubstitution using R^1Li and R^2X

This method follows closely from above and works on the fact that the porphyrin "anion" **60** generated upon addition of a strong nucleophile may be trapped by an *in situ* electrophile. Instead of protonolysis of the intermediate anion to a porphodimethene, an organic electrophile is added which gives a disubstituted product where one residue has come from the organolithium reagent and the other from the organic electrophile. This route was initially only applicable to Ni(II) porphyrins but has since been optimised for free-base

systems. The main products of this procedure (24-28 %) tend to be monosubstituted products **58**, formed by substitution with R^n from the organolithium reagent only. However, the desired compounds **50** are also formed as minor products (18-21 %). The strength of this method lies in its ability to convert an AB-type porphyrin into an ABCD-type porphyrin in one step. Even with the low to moderate yields the method can still be favourable in some circumstances over other synthetic alternatives available, *i. e.* mixed condensations or multistep syntheses.[181,182]



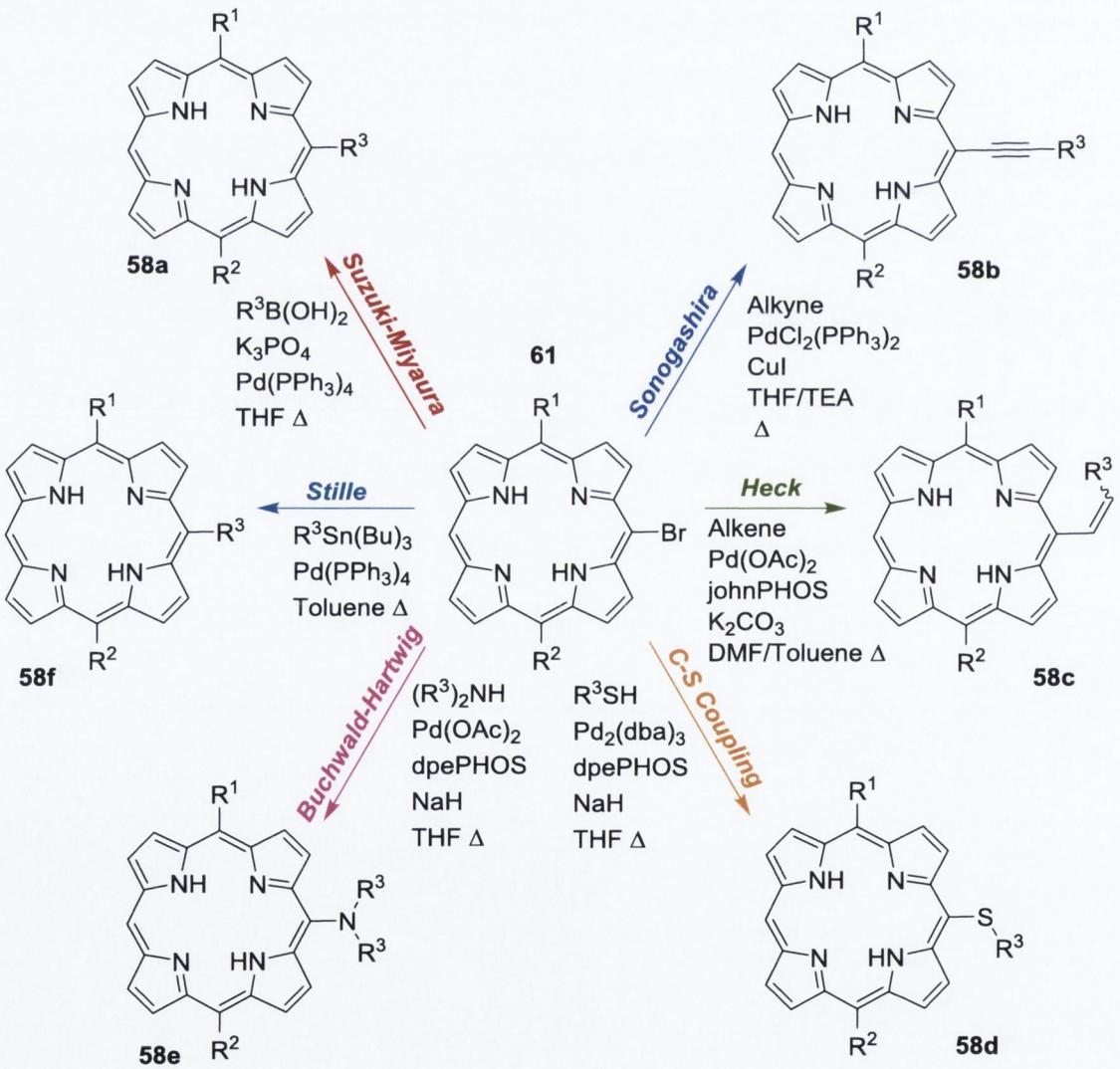
Scheme 1.15: Disubstitution using R^3Li/R^4X.

1.2.2.3 Transition metal-catalysed C-C coupling reactions

The use of transition metal catalysis is perhaps the most widely investigated method for the functionalisation of porphyrins and was the first generally applicable method for the modification of the meso positions. All of the classic TM cross-coupling methodologies have been used to some extent but, unsurprisingly, palladium-catalysed cross-coupling reactions tend to be the most utilised. All of the benchmark Pd-catalysed reactions including Stille, Heck, Sonogashira and Suzuki-Miyaura have been applied to the tetrapyrrole macrocycle with significant success in most cases.[183-187]

These reactions all require initial halogenation (bromination or iodination) of the porphyrin. Electrophilic addition of bromine to a porphyrin with one free meso position is a facile reaction with near quantitative yields available.[185,188] Selective bromination of porphyrins with more than one free meso is slightly more difficult and involves some tedious chromatography but careful control of the amount of NBS used tends to give high yielding

targeted substitutions.[189] The range of possible additions to these bromoporphyrins is vast and many interesting and useful functional groups can be installed that are not possible with any other method (*i. e.* labile groups).[183] This means that while TM-catalysed reactions are very powerful at installing simple alkyl and aryl residues (usually very high yielding) they can also be used to install specific functional groups which allow for further synthetic manipulations around the tetrapyrrole core. Select examples of these are illustrated in Scheme 1.16.[190-195] The scope of this type of reaction is limited only by the availability of starting materials. Thus, the search for new functional groups and methods to install them remains an ever ongoing challenge in porphyrin chemistry.



Scheme 1.16: Selected Pd-catalysed transformations on bromoporphyrins.

1.2.3 Future avenues for porphyrin functionalisation

Whilst transition metal-catalysed transformations on porphyrins have been extensively studied over the last few decades there are still certain areas where viable methodologies are lacking. One of these is in the installation of highly reactive functional groups, particularly those which may be reactive towards future synthetic modifications. This is an area of research in which the Senge group has been intimately involved for a number of years. The goal here is to find novel functional groups that, when installed on the porphyrin periphery, can be further functionalised to deliver novel molecular scaffolds. Recent and ongoing research has included studies into the introduction of carbazole,[196] ferrocenyl,[197] anthracenyl,[198,199] triptycenyl,[200,201] stannyl[190] and allenyl[202] groups *via* Pd-catalysed transformations. Additionally, work on the properties of such functionalised scaffolds has shown that they can undergo diverse further functionalisation (*e. g.*, *via* cycloaddition chemistry[203,204]) – giving access to highly substituted designer scaffolds. This all serves to indicate that, while heavily researched already, palladium catalysis has a lot left to offer as a method of porphyrin modification.

One key area of interest is the field of Pd-catalysed C-heteroatom bond formation. While Buchwald-Hartwig aminations[195] and carbon-sulfur bond formations[194] have been successfully applied to porphyrins, the relatively recent discoveries of these reactions means that their application to porphyrin scaffolds is much more limited than more classical TM-catalysed C-C bond formations. Due to the numerous applications already found for such heteroatom-substituted porphyrins,[134,205] the development of more robust methodologies for their synthesis and modification is a crucial challenge.

1.3 Objectives – marrying the two scaffolds

The primary objectives of the two parts of this work are broadly similar – namely the utilisation of the most modern synthetic techniques towards the synthesis of diverse chemical scaffolds.

For the first part of the research the major objective is straightforward. Transition metal-catalysed cross-coupling reactions have never been rigorously applied to the cubane framework. Thus, the aim here is to update the available chemistry of cubane by performing a thorough investigation into the Pd-catalysed cross-coupling reactions that this unique scaffold will participate in. In order to accomplish this, however, appropriate cubane synthons must first be prepared. Here, attention turns towards more classical chemical transformations in order to synthesise an array of appropriately substituted cubane systems. While halogenated cubanes are readily available; progress in the field of metallocubanes has been somewhat slower.[8] Consequently, an initial aim of this part of the work is to investigate methods to generate appropriately substituted precursors – primarily through comprehensive application of metal-halogen exchange chemistry, another topic historically overlooked in the field.

With relation to the second half of the work, the overarching objective is somewhat more fluid. Introduction of new functional groups and the design of tailored porphyrin scaffolds remains a constant challenge in synthetic porphyrin chemistry.[119] To this end the objectives here are again to use Pd-catalysed chemistry to introduce specific groups of synthetic interest onto porphyrin scaffolds and investigate their utility towards further synthetic modifications. Additionally, porphyrin scaffolds for specific, tailored, applications will be created using the best available techniques. Ideally, all of this work will involve applying modern chemical techniques to access completely new classes of porphyrins or those that have historically been neglected in one way or another.

1.3.1 Cubane and porphyrins

The marriage of these two distinct scaffold systems is a major goal of the project and will be highly dependant upon the success of the cubane functionalisations. The highly strained cubane system offers many possible rewards as a novel porphyrin substituent. Primarily, it is a sterically demanding system, which means it will almost definitely impart a high degree of nonplanarity to the porphyrin scaffold.[126] In this regard it can be seen as somewhat similar to a *tert*-butyl group. However, unlike the *tert*-butyl group, cubane is highly crystalline[7] so a tetracubylporphyrin could be expected to overcome some of the difficulties of crystallisation observed with 5,10,15,20-tetrakis(*tert*-butyl)porphyrin.[148] The benefits of attaching cubane to the porphyrin periphery extend far beyond this, however.

The search for novel linkers and spacers in porphyrin chemistry is constant.[119,187] Alkane based linkers, however, have received very little attention, due primarily to their flexibility.[206,207] Cubane, as a virtually inflexible carbon skeleton, overcomes this problem, theoretically allowing it to be used as an isolator in bridged porphyrin systems for electron transfer studies. Recently, significant study has been performed on the synthesis and properties of porphyrin dimers and arrays. However, these systems are almost invariably linked by electronically conjugating groups.[200,208,209] Due to the lack of applicable subunits; rigid, small molecule, aliphatically-linked *bis*porphyrins are a class of systems which have never been investigated in porphyrin chemistry.[186] These have a wide array of potential applications in light harvesting, nonlinear optics and even photodynamic therapy. With effective protocols for the quick introduction of cubane scaffolds *via* palladium catalysis, access to this previously unexplored class of tetrapyrrole systems becomes immediately accessible. Failing that, more classical methodologies (*e. g.*, condensations, organolithium chemistry) may also prove fruitful.

Chapter 2:

Synthesis of functionalised cubane systems

2.1 Background

The utility of cubane as a reactant in Pd-catalysed chemistry is conditional upon the availability of readily functionalised cubane derivatives. Broadly speaking, these fall into two classes – halogenated cubanes and metallocubanes. Significant research into the synthesis and reactivity of the cubane scaffold has been performed.[8] Methods to halogenated cubanes are now well established but there is a lack of generally applicable methods towards metallocubanes with many elements (*e. g.*, boron, phosphorous) having never been attached to the cubane system. Halogenated cubanes offer a quick entry point into this field of chemistry for two reasons. Firstly, they can serve as coupling partners in their own right – however imperfectly. Perhaps more importantly, appropriately halogenated cubanes allow for potentially easy access to a range of metallocubanes *via* metal-halogen exchange and subsequent functionalisation.[65]

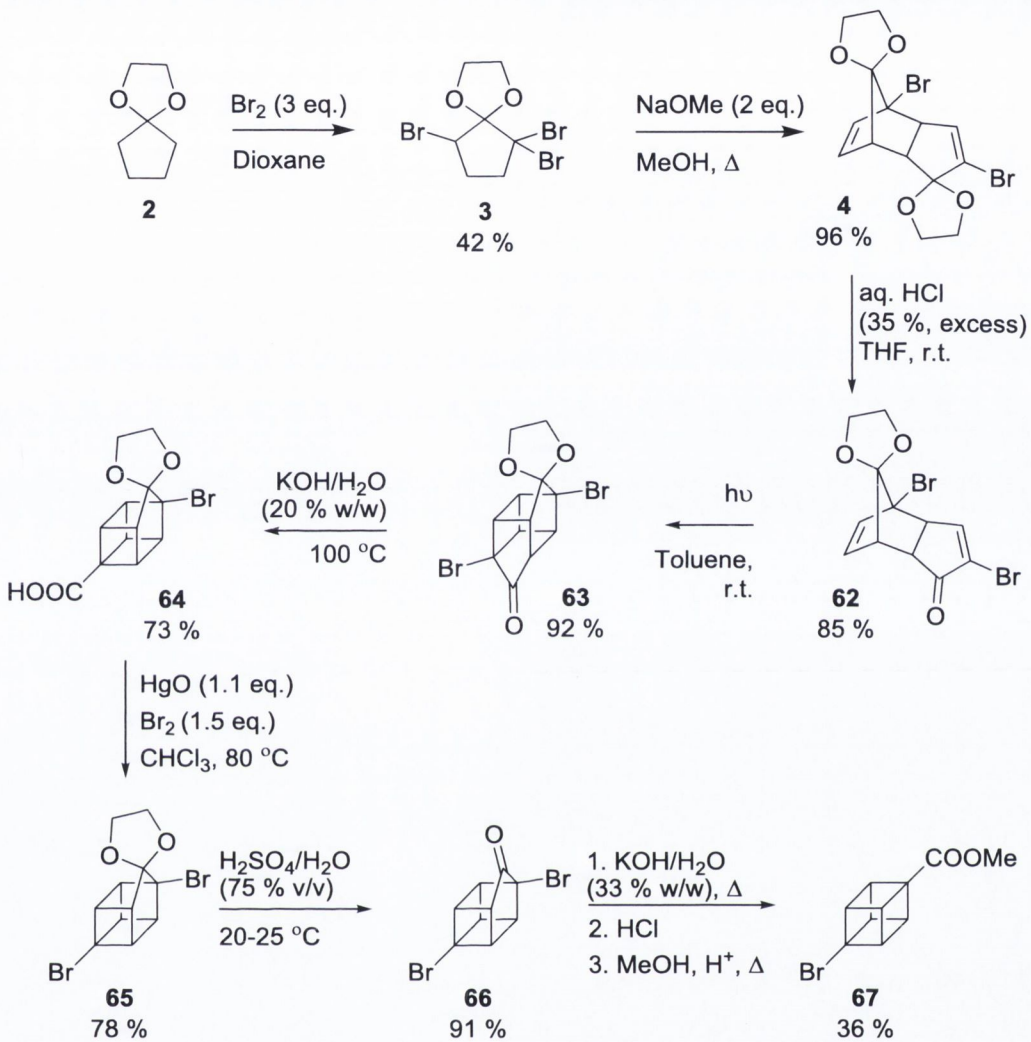
2.2 Synthesis of halogenated cubane systems

In terms of halogenated cubanes there are two halogens – bromine and iodine –that find widespread use in the chemistry in question.[76,88] Methods towards introducing both of these substituents have been among the most historically well developed within the field of cubane chemistry.[9] Given their synthetic accessibility, transformations of the carboxylic acids present from the standard cubane synthesis present the most popular access point to installing halide functionality. The goal, however, is to obtain systems with just one halogen atom present due to the problems associated with using dihalogenated species.[40] Depending on the route, this can be done either through selective introduction of the halogen or removal of any excess halogen atom(s) from a multiply substituted system.

2.2.1 Synthesis of bromocubanes

Introduction of bromine onto the cubane scaffold was first achieved by Klunder and Zwanenburg in 1972,[22] using Chapman's modification[3] to the original cubane synthesis

(Scheme 2.1). To date, this remains one of the most rational ways to introduce bromine onto the cubane scaffold and as such was the procedure followed for this work.



Scheme 2.1: Synthetic route to bromocubane **67**.

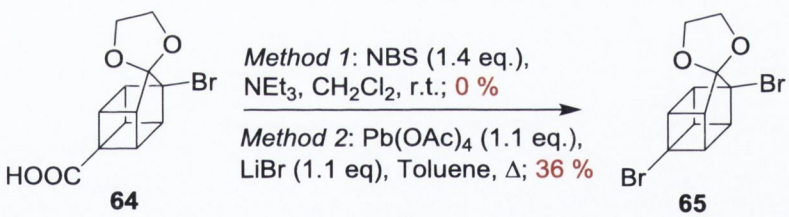
The main strength of this route is that, by using Chapman's sequential Favorskii rearrangements, a single cubane carboxylic acid is revealed midway through the synthesis (**63** → **64**). The earlier part of the synthesis (bromination and dimerisation; **2** → **4**) is the same as that discussed in the introduction. The bromination step in particular is highly sensitive to temperature, light and water and, as such, great care had to be taken to ensure formation of **3**. Additionally, the reaction releases large quantities of HBr gas which must be continuously removed so as not to inhibit product formation. The key modification introduced by Chapman is the mono-deprotection of diketal **4** to yield **62**. The asymmetry

between the two ketal groups of **4** facilitates this selective conversion. By performing the deprotection in dilute acid (HCl in THF) only one ketone group is produced. The ketone which is drawn into conjugation with the alkene is considerably preferred over the bridgehead ketone, which requires a much more concentrated acid (75 % H_2SO_4, **65** → **66**) to facilitate its deprotection.

With the monodeprotected product **62** the [2π+2π] ene-enone photocyclisation to furnish **63** is best performed in nonpolar solvents as the ketone polarises one of the alkenes to facilitate the reaction. Treatment of the caged product with concentrated base allows the first Favorskii reaction to yield **64**. Lack of significant ring strain at this juncture allows relatively high yields (73 %) to be obtained. Performing a modified Hunsdiecker reaction[210,211] with this carboxylate introduces the required bromide, which actually increases the yield for the remaining three steps (**65** → **67**, deprotection, Favorskii and esterification). Reported yields for these latter steps are in the region of 45 %, but the average obtained here was ~25 %. The Favorskii reactions are particularly sensitive to base concentration. Slight deviations were found to lead to dramatic differences (typically reductions) in yield. Compound **67** was, however, obtained in a reasonable overall yield and displayed the required functionality for future investigations.

The major flaw in the synthesis lies in the introduction of the bromine atom. From a synthetic viewpoint, the mercury salts utilised to effect the transformation are, at the end of the reaction, insoluble in the reaction medium and, as such, can be easily removed by filtration and disposed of. They nevertheless pose a significant environmental and health hazard so other avenues to introduce the desired functionality were investigated. Classically, halo-decarboxylations such as this required the presence of highly toxic, reactive metals.[212] Numerous modern avenues have been published which use more 'green' methodologies. Invariably, however, these require α,β-unsaturated systems.[213,214] Such is the advance in the field that conjugated acids readily undergo halo-decarboxylation in the presence of mild

reagents such as triethylamine and *N*-bromosuccinimide.[215] Unfortunately, the lack of an alkene meant that these methodologies proved unsuccessful when attempted on **64**. Returning to the more classic methodologies, three other metals are known to facilitate the halo-decarboxylation process, namely, silver, lead and thallium. The toxicity of thallium meant it was discounted as offering no additional benefits over Hg. Generation of silver(I) carboxylates is reported as a challenging process as the silver salts thus formed must be isolated and are sensitive to both air and moisture.[212] As such, mercury, in spite of its toxicity, is preferred due to increased yields and ease of handling of intermediates. Lead salts were thus seen as offering the best alternative.[216] While still not an environmentally 'friendly' metal, the hazard is reduced when compared with mercury salts. Unfortunately, the reaction of **64** with bromine in the presence of $Pb(OAc)_4$ and LiBr, proved less successful than the analogous Hg-facilitated process (of four trials only two gave product). Additionally, when successful, the yield of the reaction was just 36 %, a significant reduction on the 78 % average obtained with HgO.



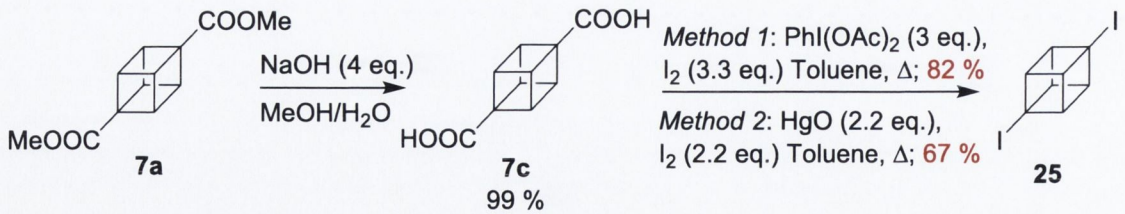
Scheme 2.2: Investigations into Hunsdiecker reaction of **64**.

2.2.2 Synthesis of iodocubanes

With the bromine-substituted system **67** thus available, attention turned to the synthesis of iodinated cubanes. A significant body of work exists on the synthesis of iodinated cubanes so the focus here was on tailoring the synthetic route to give the best yield of a monoiodinated cubane derivative. Introduction of iodine in an analogous way to that pursued for bromine proved unsuccessful. While iodine could be introduced in reasonable yields, either the iodine atom proved unstable towards the harsh conditions required for the

deketalisation and Favorskii rearrangement or its presence inhibited these reactions. In either case no appreciable yield of the iodinated version of **67** was obtained.

Iodocubane **14a** was seen as the most straightforward way to access the iodinated scaffold and is generally the most popular avenue reported.[5,45,46] The synthesis of **14a** starts from 1,4-dicarboxycubane **7** (the synthesis of which was detailed in Chapter 1), which undergoes a Moriarty rearrangement in the presence of iodobenzene diacetate (IBDA) and iodine to yield 1,4-diiodocubane **25** (Scheme 2.3).[27] The hypervalent iodine reagent provides for a powerful iodinative-decarboxylation process by eliminating the need for a toxic metal salt.[217,218] The yields obtained for this double iodination are quite high (82 % from pure **7c**) but the reaction suffers somewhat from the relatively high cost of reagents.[i] Additionally, the reported yield is only obtained when starting from an analytically pure sample of **7c**, not a particularly easy endeavour. Diacid **7c** was found to be a very difficult compound to obtain in high purity due to its poor solubility. The standard reported method of purification is *via* sublimation of the diester **7a**,[4] but this proved an ineffective way of purification. Numerous crystallisations of both **7a** and the diacid **7c** proved similarly fruitless. The most effective way to purify the system was found to be through the iodinated product **25**, which, due to its high solubility and crystallinity, could be easily purified by column chromatography on silica gel or recrystallisation from hexanes. While solving the purification issue, the need for a greater excess of IBDA increases the cost of the process.



Scheme 2.3: Synthetic routes to 1,4-diiodocubane **25**.

[i]IBDA retails (Fisher Scientific) at €1.50 per gram with 5g required to effect the transformation of 1g of **7c**.

As a result, other avenues towards **25** were investigated. Of these, reaction with red mercuric oxide and iodine proved most effective. The yield here is slightly lower (67 % from pure **7c**) but the reagents employed proved more economical.[i] Starting from crude **7c**, yields were roughly comparable for the two routes (typically 40-50 %). For the second route, yields suffer due to the competitive process of dimerisation when elemental iodine is used in the Hg-facilitated Hunsdiecker reaction.[211] This could be minimised, however, by carefully controlling the amount of iodine present with dimerisation preferred with 0.5 equivalents or less of iodine per acid group. The obvious drawback of the second route is the toxicity of the mercury salts. Proper storage and disposal can alleviate this problem, and when dealing with a bulk process such as this, it was found that the safe removal of large quantities of Hg waste proved more cost effective than the IBDA required in the green alternative. Nevertheless, both routes were used throughout the work – typically HgO for large scale, unpurified work and IBDA for work involving analytically pure starting materials on a smaller scale.

Due to the issues discussed previously with relation to the reactivity of **25** with organolithium reagents it may appear an unusual starting point for any synthesis.[40] The reason this avenue was initially pursued was because the synthesis outlined in Scheme 2.4 represents the most reported avenue to monoiodinated cubane **14a**. This synthesis was reported by Eaton *et al.* in 1994[45] and has gained widespread subsequent use.[5,46] The synthesis involves treating **25** with four equivalents of a Grignard reagent (EtMgBr) and cooling to -78 °C whereby the solution becomes cloudy. In this manner, a mono-Grignard reagent could be obtained. Addition of a further four equivalents of *n*-butyllithium produces a bright yellow colour, indicating transmetallation of Mg to Li; which, upon quenching with methanol, is reported as resulting in the selective removal of just one iodine atom in 91 % yield. However, in practice, this reaction was found to be entirely unreliable and subject to

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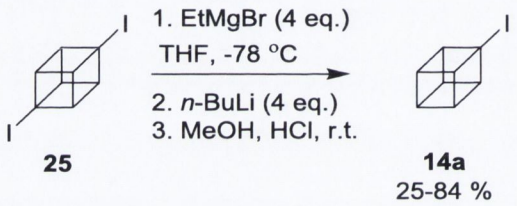
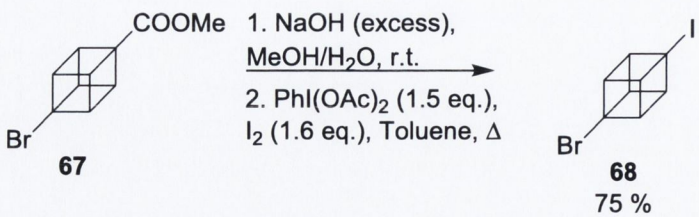
[i] HgO retails at € 0.30 per gram with 2.5 g required for the conversion of 1 g of **7c**.

a high degree of variation. Yields ranged from 25-84 % and reactions performed in parallel using identical conditions gave drastically deviant yields. The other significant product obtained was unreacted **25**, which, due to very similar retention factors, made purification tedious. This, coupled with the need for significant excesses of reagents, made the cost of this (unreliable) reaction prohibitive. Additionally, the removal of one of the iodine atoms results in a mass loss of roughly one third and prohibits any further modifications to the cubane scaffold. As a result, while significant amounts of **14a** were synthesised and utilised, other avenues towards monoiodinated cubane were investigated.



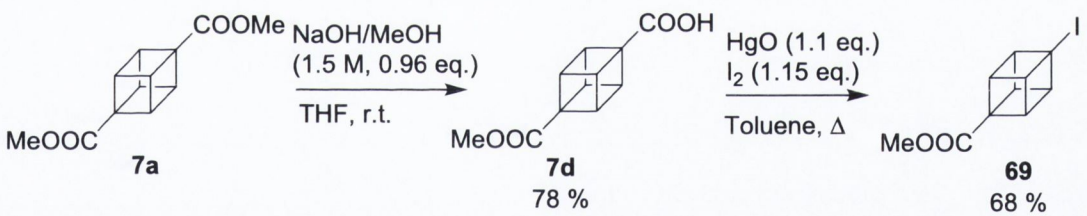
Scheme 2.4: Synthesis of iodocubane **14a**.

Reduction of the ester group of **67** followed by iodinative decarboxylation provides ready access to the 1,4-dihalogenated species **68** in 75 % yield (Scheme 2.5). While this material offers significant potential in terms of comparing the reactivities of the two halogen groups, the pathway is not a viable one on a large scale due to the lengthy synthesis involved for **67**. Additionally, as a probe for the reactivity of iodinated cubanes in metal-halogen exchange reactions the presence of an additional labile group could serve as a significant hindrance.



Scheme 2.5: Synthesis of 1-bromo-4-iodocubane **68**.

Attention thus returned to **7a** and methods to selectively introduce just one iodine atom onto the scaffold. Of the various routes devised and investigated, that depicted in Scheme 2.4 was ultimately chosen as the most efficient. Treatment of **7a** with 0.96 equivalents of methanolic NaOH in anhydrous THF[30] allows for initial desymmetrisation of the two carboxylic groups (Scheme 2.6). This process works primarily due to the insolubility of the carboxylate formed from hydrolysis of the first ester group, which precipitates slightly out of the THF solution – minimising hydrolysis of the second group. Addition of just under one equivalent of methanolic NaOH was found to be the most efficient protocol (78 % yield of **7d**) as even a slight excess of the base or the presence of additional water molecules led to hydrolysis of both esters over time. Iodinative-decarboxylation of **7d** provided the iodocubane ester **69** in 68 % yield. Either HgO or IBDA can be used to effect this process and the choice as to which to employ remains the same as that discussed previously. Compound **69** again presents an attractive point to purify the cubane scaffold and, in bulk syntheses, crude material was typically purified by column chromatography at this stage.



Scheme 2.6: Synthesis of methyl 4-iodocubane-1-carboxylate **69**.

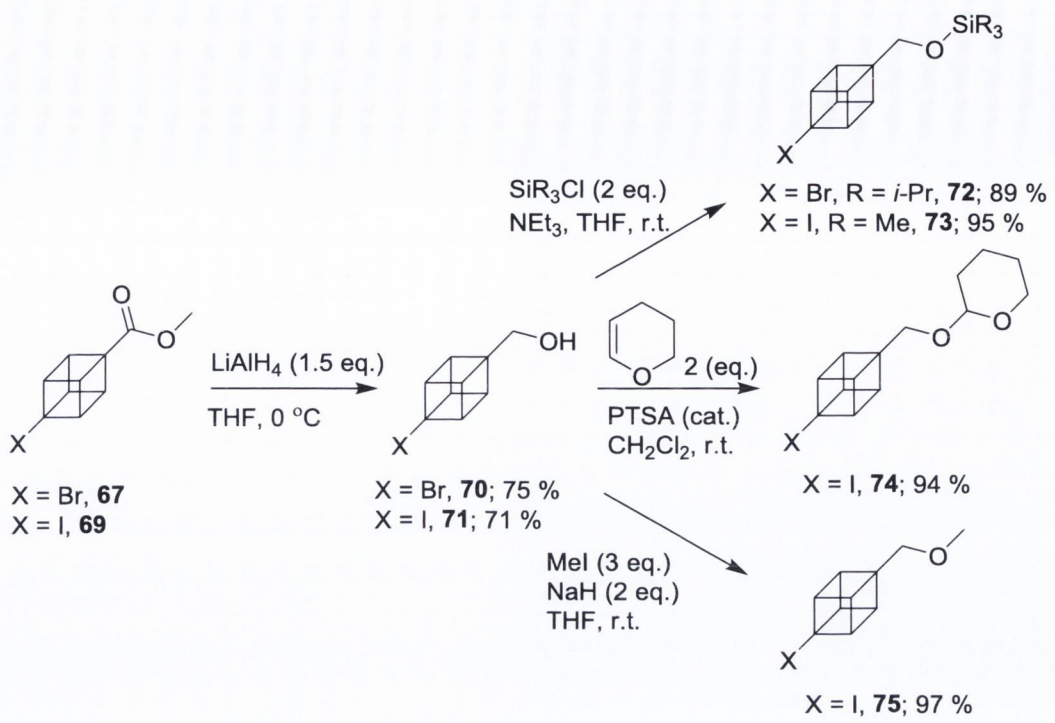
2.3 Synthesis of (hydroxymethyl)cubane derivatives

Compounds **67** and **69** both represent target compounds with relation to the initial goal of mono-halogenated cubane systems. However, both contain a problem in the form of the carboxylic group present. Ultimately, these compounds were intended as probes for the metal-halogen exchange reaction and, as such, the presence of additional reactive groups had to be avoided. Several methods to further functionalise these derivatives were considered. Barton decarboxylation[7] was discounted as this would limit the further utility of the scaffold

by completely removing a versatile functional group. FGI retaining the carboxylic oxidation state but remaining unreactive to lithiation (*e. g.*, amide) was also rejected due to the problems associated with reducing such groups to a more reactive form for subsequent modifications. Ultimately, the process employed was reduction to an alcohol followed by protection of the hydroxyl group to remove the reactive hydrogen atom. In this manner, it was anticipated that the most optimum trial compounds could be obtained in a minimum number of steps and with minimal mass loss. Additionally, the protected alcohol can theoretically be reoxidised back to the carbonyl oxidation state, allowing for easy further functionalisation of the scaffold.

Several methods for the reduction of cubane esters are reported. Here, $LiAlH_4$ was found to be the reducing agent of choice due to its low cost and high reactivity with both the brominated **70** and iodinated **71** (hydroxymethyl)cubanes achieved in moderate yields (Scheme 2.7; 75 % and 71 % respectively). Care must be taken with both derivatives that the temperature not exceed 0-10 °C, as higher temperatures led to significant reductive-dehalogenation of the cubane scaffold.[219,220] Poor solubility of the (hydroxymethyl)cubanes **70** and **71** posed a major issue and inhibited purification of the intermediates.

Removal of the hydroxyl functionality *via* protecting group chemistry then becomes the final step as this hydrogen atom is acidic enough to interfere with lithiation reactions. The selection of an appropriate protecting group is important as, for this work, the protecting group must fulfil three major challenges – (1) must be easy to install in near quantitative yield; (2) must be stable to the reaction conditions involved, in this case organolithium chemistry; and (3) the product must be soluble in standard solvents and easy to handle.[221,222] Additionally, it would be preferable if the introduced protecting group simplified spectroscopic analysis of the material and was easy to remove (deprotect) at the end of the synthesis. To this end four different protecting groups were installed onto **67** and **69** (Scheme 2.7).



Scheme 2.7: Reduction and protection of cubane esters **67** and **69**.

Silyl protecting groups were the first considered due to their ease of introduction and removal.[222] Both TIPS and TMS groups were introduced to yield **72** and **73** in high yields. However, these groups proved too labile on silica gel to allow for column chromatography. Additionally, a minor amount of deprotection was seen upon reaction with *t*-BuLi. Pyran was seen as an excellent protecting group to install due to its stability towards organolithium reagents and its tolerance of standard chromatography techniques.[222] While introduction of the group is facile, the product **74** is a semi-solid at room temperature making it difficult to weigh accurately. A further hindrance involved the presence of the chiral centre and four prochiral centres, which resulted in a complex ^{1}H NMR spectra of **74**, exacerbated by the fact that the signals of the protecting group overlap with the cubane resonances. Protection as a methyl ether **75** was ultimately chosen as the optimum route. While not technically a true protecting group due to the difficulty associated with its removal, this was seen as a very simple group to introduce to serve the above criteria. Addition yields were near quantitative and the methyl group presents a distinctive singlet in the ^{1}H NMR spectra – providing a handle for spectroscopic analysis. Furthermore, the compound is stable to all reaction

conditions and is highly crystalline. As a result, it was used predominantly in all further functionalisations. It is assumed that all of the subsequent chemistry performed with **75** (*vide infra*) could be easily reproduced with **74** – a compound which will undergo clean deprotection allowing for further functionalisation of the scaffold. Successful functionalisation reactions with **74** indicate that it is an equally viable candidate for this chemistry but the difficulties encountered prevented a more complete investigation of its utility.

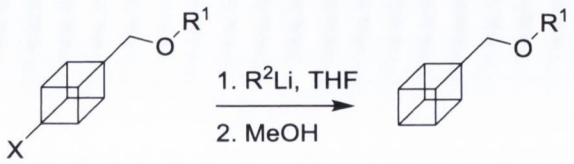
2.4 Metal-halogen exchange reactions

2.4.1 Probing reactivity – Br versus I

With appropriately functionalised bromo- **72** and iodocubanes **75** synthesised, the first step was to delineate the optimum reaction conditions and substrate which facilitate metal for halogen exchange. Reactions were performed at a constant concentration in THF using halogenated cubanes and an organolithium reagent. The reactions were allowed to generate for a specific time at varying temperatures (Table 2.1) before being quenched with MeOH and extracted from a dilute HCl solution. Any lithiated material should therefore be quenched to give the de-halogenated products **76a/b**. By comparing the ratio of unreacted starting material to **76** the optimum set of reactants, time and temperature could be delineated. A brief summary of the results of this study is shown in Table 2.1.

Iodinated cubanes clearly undergo metal-halogen exchange much easier than brominated analogues. Using **72** as the substrate no protonolysis was witnessed with *t*-BuLi at -78 °C and less than 20 % protonolysis was observed when the reaction was performed at higher temperatures. Unreacted **72** was obtained as the major product in all trials. By comparison, **75** underwent ready metal-halogen exchange with both *t*-BuLi and *n*-BuLi. Generation with two equivalents of *t*-BuLi at -78 °C for one hour was found to be the optimum conditions whereby all of the starting material had been consumed. As a result the conditions listed in Entry 3 were used in all subsequent reactions.

Table 2.1: Optimisation of metal-halogen exchange conditions.



X = Br, R^1 = TIPS, **72**
X = I, R^1 = Me, **75**

R^1 = TIPS, **76a**
R^1 = Me, **76b**

Entry	Cubane	R^2Li (eq.)	Time (min)	Temp (°C)	Result
1	**72**	*t*-BuLi (2)	60	-78	Unreacted **72**
2	**72**	*t*-BuLi (4)	60	0	<20 % **76a**[a]
3	**75**	*t*-BuLi (2)	60	-78	91 % **76b**
4	**75**	*t*-BuLi (2)	30	-78	85 % **76b**
5	**75**	*n*-BuLi (2)	60	-78	83 % **76b**
6	**75**	*t*-BuLi (1.5)	60	-78	74 % **76b**

Reaction conditions: All reactions were performed at a cubane concentration of 0.16 M in THF under argon. Isolated yields are given except where stated. [a] Estimated from ^{1}H NMR spectroscopic analysis.

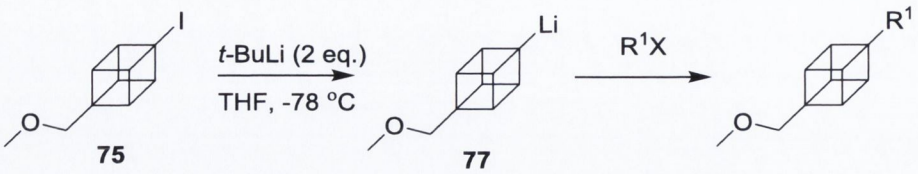
2.4.2 Exploiting the scaffold – C-C bond forming reactions

Having optimised a set of reaction conditions, attention turned to probing the utility of this methodology towards C-C bond forming reactions. As discussed previously, this area of cubane chemistry has received little attention. A range of carbon based electrophiles were thus added to a lithiated cubane 77, prepared from **75**. The results of this study are contained within Table 2.2.

Addition of simple alkyl halides led to hexyl- **78a**, tetradecyl- **78b** and 4-bromobutyl- **78c** substituted cubanes in high yields. The nature of the leaving group on the alkyl halide appears to play only a minor role with both iodoalkanes and bromoalkanes undergoing near quantitative displacement with 77. Iodomethane however, failed to give any product **78d**. The recovered material was simply the starting material **75**. Due to the visible generation of an alkyllithium this is presumably formed from a second metal-halogen transfer reaction with the iodomethane, rather than being unreacted starting material. This can be explained by the increased stability of the primary methyllithium over 77. Attempts to formylate the scaffold by introducing DMF into the reaction vessel proved largely unsuccessful. Some trace amounts of the aldehyde product **78e** were observed by ^{1}H NMR spectroscopic analysis

but the primary product was de-iodinated starting material **76b** together with some unreacted **75**. Attempts to isolate **78e** or increase the yield to significant levels failed.

Table 2.2: Reactivity of lithiocubane **77** with various carbon based electrophiles.



#	Electrophile R^1X (eq.)	Time (h)[a]	Product (R^1=)	Result
1	1-Iodohexane (2)	0.5	-C_6H_{13} **78a**	98 % yield
2	1-Bromotetradecane (2)	0.5	-$C_{14}H_{29}$ **78b**	94 % yield
3	1,4-Dibromobutane (3)	0.5	-C_4H_8Br **78c**	96 % yield
4	Iodomethane (5)	0.5	-CH_3 **78d**	Recovered **75**
5	*N,N*-Dimethylformamide (5)	4	-CHO **78e**	<10 % yield[b]
6	Propargyl tosylate (2)	1	-$CH_2C{\equiv}CH$ **78f**	Quantitative **76b**
7	3-Bromo-1-TMS-1-propyne (2)	1	-$CH_2C{\equiv}CTMS$ **78g**	Complex mixture
8	3-Iodo-1-propene (2)	1	-$CH_2C{=}CH_2$ **78h**	Recovered **75**
9	1-Bromo-2,4-dinitrobenzene (5)	2	-$C_6H_3(NO_2)_2$ **78i**	Complex mixture
10	4-Bromobenzyl bromide (5)	2	-$CH_2C_6H_4Br$ **78j**	Complex mixture

Reaction conditions: All reactions were performed at a cubane concentration of 0.16 M in THF under argon. Reactions were warmed to r.t. after addition of R^1X. Isolated yields are given except where stated. [a] Indicates time between addition of R^1X and quenching with dilute HCl. [b] Estimated from ^1H NMR spectroscopic analysis.

The success of simple alkyl substitution led to efforts to introduce more synthetically useful carbon fragments. Addition of propargyl tosylate (in an effort to generate propargyl substituted cubane **78f**) simply led to **76b**. This was explained by the presence of the acidic alkyne proton, which presumably quenched **77**. Using a protected substrate, 3-bromo-1-TMS-1-propyne, gave a complex mixture of products which could not be separated. Cubane products present in the mix included **76b** and the target **78g** but there also appeared to be some brominated cubane, presumably formed by exchange with the propargyl bromide. The ability of propargyl groups to stabilise negative charges by resonance is well documented[223] so the failure to cleanly generate target products *via* this methodology can be expected.

Addition of a halogenated alkene again gave **76b** indicating that the alkene hydrogens are also acidic enough to quench **77**.

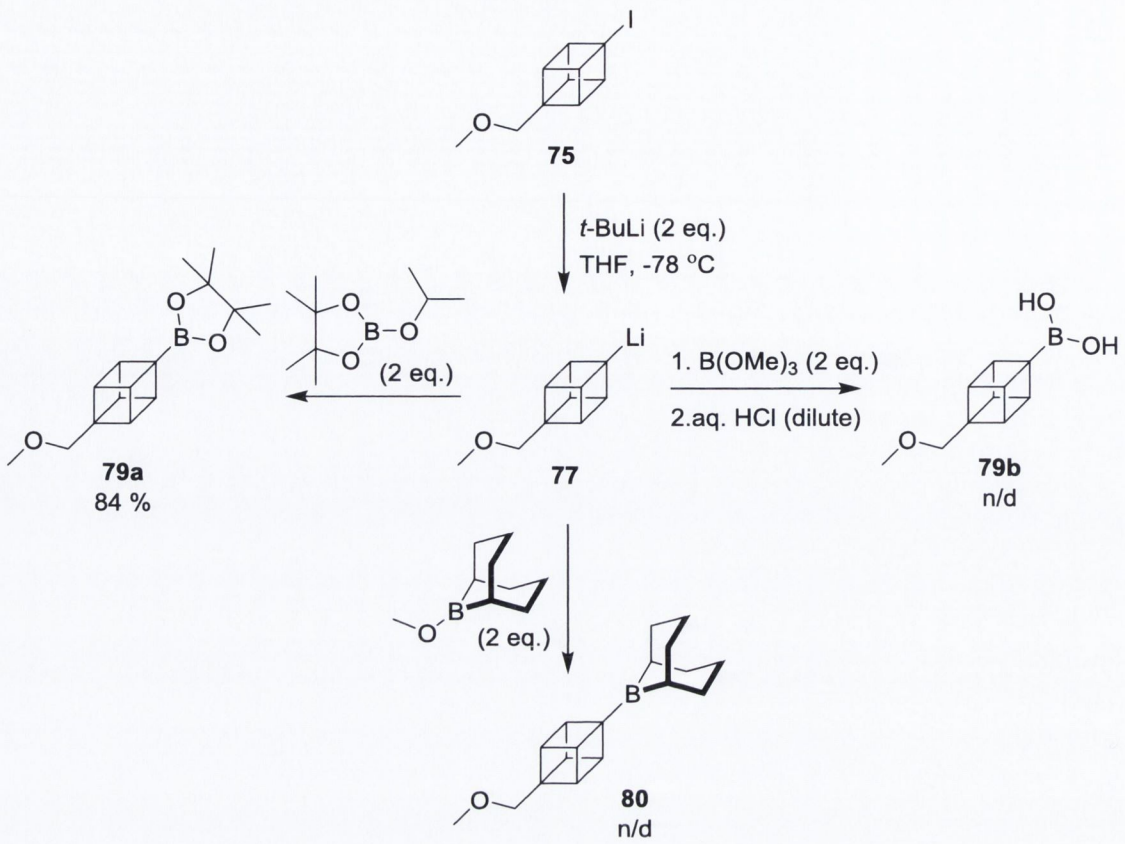
The failure to successfully add groups with multiple bonds indicated introduction of aromatic systems to be unlikely. Two such systems were nevertheless trialled, given the increased s-character of the cubane-lithium bond. Addition to 1-bromo-2,4-dinitrobenzene could presumably occur through an addition/elimination (S_NAr) mechanism facilitated by the two strongly EWG groups. The major products, however, were **76b** and brominated **77**, arising from protonolysis of any **77** remaining at the end of the reaction and the stability of the aryllithium favouring metal-halogen exchange, respectively. Addition of 4-bromobenzyl bromide proved similarly fruitless and gave an identical mix of cubane products. No aromatic substituted cubanes **78i** or **78j** were detected after either reaction.

2.4.3 Towards Pd-catalysis – generation of reactive cubane precursors

The overarching aim of this section of work was to synthesise appropriately substituted cubane scaffolds for use in various Pd-catalysed reactions. Three specific classes of cubane systems were targeted – (1) borylated cubanes (boranes and boronates) for use in the Suzuki-Miyaura cross-coupling reaction; (2) cubylzinc(II) halides for use in the Negishi reaction and (3) stannylcubanes for Stille couplings. Both zinc and tin have been successfully introduced onto the cubane framework previously *via ortho*-lithiation[29] whereas cubane-boron complexes represent a completely new structural archetype in cubane chemistry.

2.4.3.1 Introduction of boron to cubane scaffold

A wide range of alkylboron complexes have found utility in the *B*-alkyl Suzuki-Miyaura reaction, as discussed previously.[64] In order to fully probe the reactivity of cubane precursors, representatives from three distinct classes of organoboron compounds were synthesised as per Scheme 2.8. All three reactions proceeded readily, although some difficulties in isolation and purification were encountered.



Scheme 2.8: Generation of cubane-boron compounds **79a**, **79b** and **80**.

The synthesis of the cubaneboronic acid pinacol ester **79a** was the first attempted. Here, **77** was quenched with a 2-isopropoxyborolane species with isopropoxide acting as leaving group. On work-up this gave a sample of **79a** in a high degree of purity. Attempts to completely purify this material *via* standard chromatography on silica gel failed with only trace amounts of **79a** being recovered. Ester **79a** thus degraded on silica, presumably due to its acidic nature, so aluminium oxide (Al_2O_3, Alox) was used to effect the purification. Using neutral, Brockmann Grade III, Al_2O_3 as the stationary phase **79a** was obtained in 84 % yield. This represents the first synthetic example of a cubane-boron complex and proves the utility of metal-halogen exchange on the cubane scaffold as a synthetic tool to quickly introduce novel substituents.

Synthesis of the other boronate species, **79b**, proceeded *via* a two-step process. After standard generation, lithiocubane **77** was treated with trimethylborate with one methoxide ion acting as leaving group. The methyl boronic ester thus formed was then hydrolysed to

the free boronic acid **79b** by a simple acid wash with aqueous dilute HCl. Boronic acid **79b** was obtained as an off-white solid and gave ^{1}H and ^{13}C NMR spectra consistent with a high degree of purity. Attempts to purify the material by column chromatography either with silica or aluminium oxide produced no material, presumably due to the high polarity of the acid groups. Recrystallisation of the bulk material from hexanes provided a significant amount of an off-white solid which could not be unambiguously identified,[i] with some de-iodinated material **76b** present in the mother liquor. As a result, and due to the two step nature of its synthesis, **79b** was not pursued in follow up studies.

The final organoboron compound targeted was the cubane-BBN derivative **80**. This was obtained as per **79a** and **79b** by treatment of **77** with *B*-methoxy-9-BBN at -78 °C. Formation of the target material was observed *via* TLC analysis and ^{1}H NMR spectroscopic analysis. However, like analogous alkyl boranes,[64,79] **80** is susceptible to air and heat so efforts to purify the material proved unsuccessful. The absence of any significant de-iodinated material **76b** on work-up, however, indicated that the reaction proceeds at a rate similar to that of **79a** *i. e.,* near quantitative. As a result, generation and use of **80** *in situ* provided a reasonable avenue to utilising it as a coupling partner.

2.4.3.2 Generation of cubylzinc(II) halides

Methods to insert zinc into alkyl-halogen bonds have been well studied.[65] Of these, the most popular method is the generation and use of highly active Rieke zinc (Zn^{*}), which inserts into polarised bonds in an oxidative manner. This was therefore seen as a reasonable first effort in the synthesis of cubylzinc(II) halides. The advantage of using Zn^{*} is its high functional group tolerance – allowing for the use of cubane ester **69** rather than **75**. Rieke zinc is generated by first dissolving finely cut lithium and naphthalene in THF before adding

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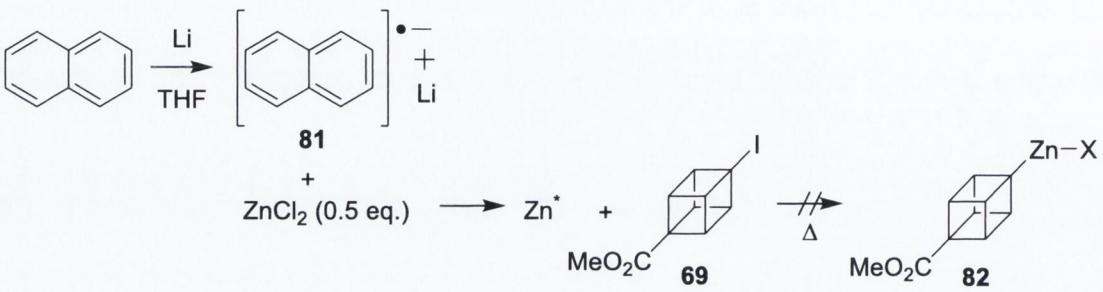
[i] Strangely, this solid would no longer dissolve in chlorinated solvents and ^{1}H NMR analysis using various deuterated solvents indicated a complete lack of any recognisable organic peaks. No plausible explanation can be found for this behaviour as from weight considerations alone the quantity of **79b** present before the recrystallisation must be present in the solid.

a solution of anhydrous $ZnCl_2$ in THF over 90 minutes.[100,101] The lithium naphthalenide **81** formed in the first step is able to quickly reduce the metal halide to very fine, highly active, particles. However, addition of **69** to the Zn^* generated in this manner failed to produce any oxidative insertion, with **69** recovered completely unchanged (Scheme 2.9).

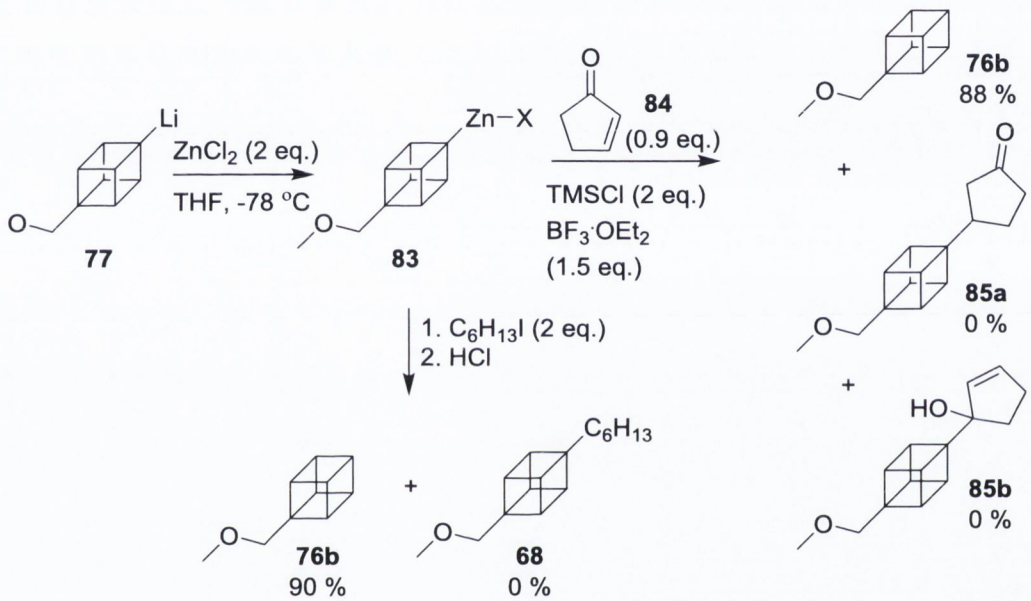


Scheme 2.9: Generation of Rieke zinc and attempted insertion into **69**.

Efforts to improve the generation of Zn^* also failed to effect the transformation to cubylzinc(II) halide **82**. This is possibly due either to errors in the generation of Zn^* or the inability of the tertiary alkyl halide to participate in an oxidative addition process. With relation to the generation process, difficulties were observed in the dissolution of the lithium wire in THF. Masses involved here were low (typically 50-100 mg) so cutting the lithium wire fine enough to interact with the naphthalene proved challenging. As a result, a significant amount of unreacted lithium was observed in many instances, likely accounting for the lack of any generation of **82**. However, in light of further observations regarding oxidative addition processes of cubane halides (see Chapter 3), it seems more likely that oxidative insertion procedures are simply ineffective with the tertiary halide.

The failure of the standard methodologies led to consideration of less common procedures to install a zinc functionality. Given the previous success with boron and other electrophiles, transmetallation from lithium to zinc[102] was investigated. Here, freshly recrystallised, anhydrous, zinc(II) chloride was added to a solution of 77 in THF (Scheme 2.10). The morphology of the reaction mixture changed immediately from distinct white precipitate to off-white cloudy – theorised to be due to the higher solubility of alkylzinc

complex **83** with relation to the alkyllithium reagent **77**. The Zn-X bond present in **83** is most likely to be Zn-Cl arising from the initial metal salt. The presence of LiI in solution (from the metal-halogen exchange process) may lead to some halogen transfer so a certain degree of Zn-I can be expected. The nature of the Zn-X bond plays no significant role in the Negishi coupling of alkylzinc compounds with alkyl-Zn-Cl, alkyl-Zn-Br and alkyl-Zn-I all displaying similar reactivities.[65] $ZnCl_2$ was chosen as the metal salt due to its ready availability but anhydrous $ZnBr_2$ or ZnI_2 would be expected to be equally effective.



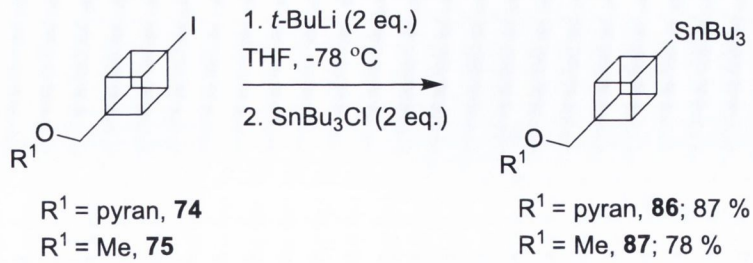
Scheme 2.10: Generation of **83** *via* transmetallation and attempts to prove its existence.

The reactive metal present in **83** meant that its direct isolation and characterisation was impossible. Efforts were therefore undertaken to prove that the transmetallation of **77** → **83** had indeed occurred. Simple protonolysis of the reaction mixture provided quantitative formation of **76b**. However, this could have as easily arisen from **77** as **83**. Addition to a cyclic enone **84** presented a good proof due to the reported 1,4-addition of tertiary alkylzinc(II) halides to α,β-unsaturated ketones, even in the absence of a copper catalyst.[224] The softer nature of zinc species **83** was expected to facilitate Michael addition yielding **85a** over direct attack at the ketone to give **85b** if **77** were still present. Unfortunately the only product observed was **76b**. This could be due either to the low reactivity of alkylzinc

compounds in the absence of appropriate catalysts in addition reactions or the steric bulk of the cubane. Addition of iodohexane was therefore expected to provide reasonable 'proof of the negative'. If **77** was still present in solution, the product of the reaction should be **78a** as shown previously. Zinc(II) halide **83**, however, is not expected to react with simple alkyl halides and the product should instead be **76b**. The latter proved to be the case, with **76b** obtained in near quantitative yield from the reaction and no indication of any formation of **78a**. While not a direct proof of the formation of **83**, this nevertheless proved that all of the lithiocubane was consumed prior to electrophile addition and, assuming conditions were indeed anhydrous, the only logical product is therefore **83**.

2.4.3.4 Synthesis of stannylated cubanes

Although largely supplanted in recent years by their less toxic analogues, the role of alkyl-tin complexes in the Stille cross-coupling reaction has long been one of the more robust methods of introducing alkyl substituents *via* Pd-catalysis.[59,65] While cubane complexes of tin have been reported previously,[29,44] these involve the more toxic trimethyltin residue. Introduction of the less environmentally toxic tri-*n*-butyltin residue through its chloride adduct provided ready access to stannylated cubanes **86** and **87** in high yields (Scheme 2.11). Both compounds are highly soluble and easily purified by column chromatography on silica gel. The use of **74** in this reaction proves the utility of more standard protecting groups in this branch of cubane chemistry. Both **86** and **87** were stable in aerobic environments but some degradation at room temperature over prolonged times was observed. As a result they were either formed *in situ* for use in coupling reactions or stored at 0-4 °C before use.



R^1 = pyran, **74**
R^1 = Me, **75**

R^1 = pyran, **86**; 87 %
R^1 = Me, **87**; 78 %

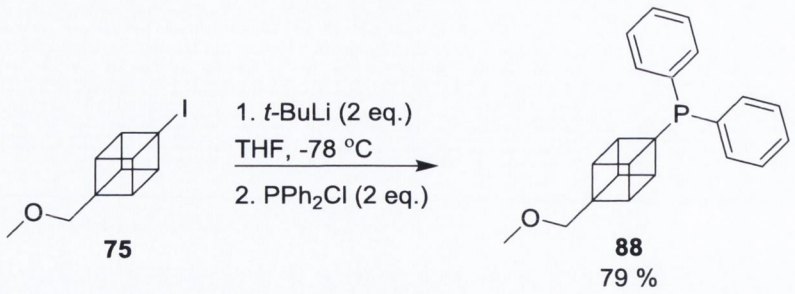
Scheme 2.11: Synthesis of stannylated cubanes **86** and **87**.

2.4.4 Expanding the scaffold – introduction of 2nd row elements

While the synthesis of reactants designed for Pd-catalysed reactions was the primary goal of this section, having developed procedures to quickly functionalise the cubane scaffold, it was decided to further investigate how generally applicable this chemistry is at synthesising diverse, novel scaffolds. To this end, focus shifted towards 2nd row elements which had either never been attached to the cubane system previously (phosphorous) or whose properties had not been fully investigated (silicon). Additionally, it was hoped to improve upon the known synthesis of thiocubanes through application of more robust electrophiles.

2.4.4.1 Phosphorous and cubane – a novel marriage

Together with boron, phosphorous stands out as being one of the few light, reactive, non-metals in having never been previously attached to the cubane scaffold. Due to the wealth of interesting chemistry organophosphorous compounds possess, phosphanylcubane **88** was chosen as a trial compound both to probe the reactivity of the cubane scaffold towards P insertion as well as creating a compound which may have many possible uses in the field of catalysis. Treatment of lithiated cubane **77** with chlorodiphenylphosphine (Scheme 2.12) produced the target compound **88** in 79 % yield. The reaction time here was extended from the standard one hour, as quenching at this point produced large quantities of **76b**. Stirring at room temperature overnight was sufficient to allow complete conversion of the lithiated cubane to **88**. Compound **88** decomposed on silica gel so direct transfer of the crude reaction product to an Al_2O_3 (Brockmann Grade III) column was required to effect its purification.

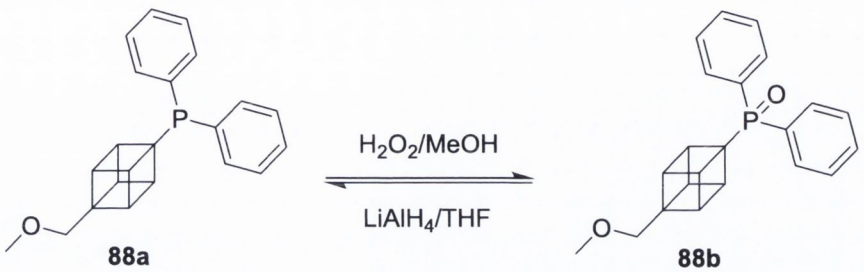


75 **88**
79 %

Scheme 2.12: Synthesis of phosphanylcubane system **88**.

All such phosphine(III) species possess a tendency to oxidise to phosphine(V) oxides. Some phosphines are particularly prone to this and the process occurs with ambient O_2 while others (such as PPh_3) are resistant to such oxidation. The electron density residing on the P centre and the steric bulk surrounding it are key determinants in whether oxidation is preferred.[225-228] A single compound was produced from the reaction of **75** depicted in Scheme 2.12 but initial analysis as to whether the true structure is the phosphine **88a** or phosphine oxide **88b** was not entirely conclusive. Reaction of **88** (Scheme 2.13) with either hydrogen peroxide (to force oxidation) or $LiAlH_4$ (to facilitate reduction) led to no change in the morphology or spectral characteristics of the compound. Whichever oxidation state is formed, therefore, possesses such stability as to prevent conversion to the other form. The sample of **88** obtained produces a ^{31}P NMR resonance at δ=25.70 ppm and the ^{31}P-^{13}C coupling constants of 67 Hz with the alkyl carbon and 100 Hz with the aryl. This data is equally indicative of both classic phosphine systems and phosphine oxide as there is significant overlap in these regions between the two oxidation states.[225] The HRMS (ESI) spectrum, however, indicates a parent ion peak for the phosphine oxide **88b** but none for **88a**. While providing evidence for the presence of **88b** this could potentially simply be a result of oxidation of **88a** to **88b** in the mass spectrometer. IR spectroscopy presents the most compelling argument. Phosphine oxides display a strong P=O stretch in the IR spectrum at approximately 1100 cm^{-1}. While with **88** this region is partially obscured by the C-O stretches, comparison with other systems (*e. g.*, **75**) indicates a complete lack of P=O vibrations. The standard P-C deformation bands are seen at 1320 and 1436 cm^{-1}. The

assignment of the correct structure of **88** was only achieved through acquisition of an X-ray crystal structure (Figure 2.1). of the product which unambiguously showed the presence of a phosphine oxide bond, thus indicating that **88b** is the correct structure of the product.



Scheme 2.13: Attempts to alter the P oxidation state.

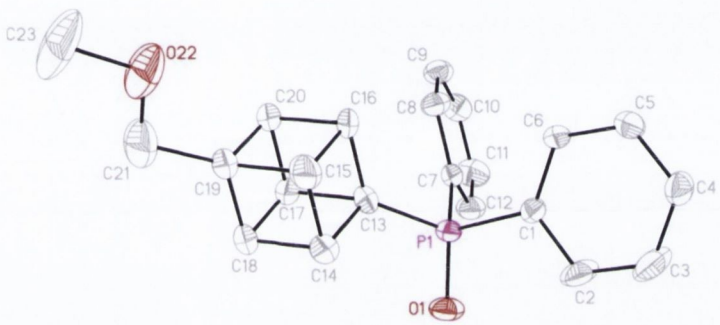


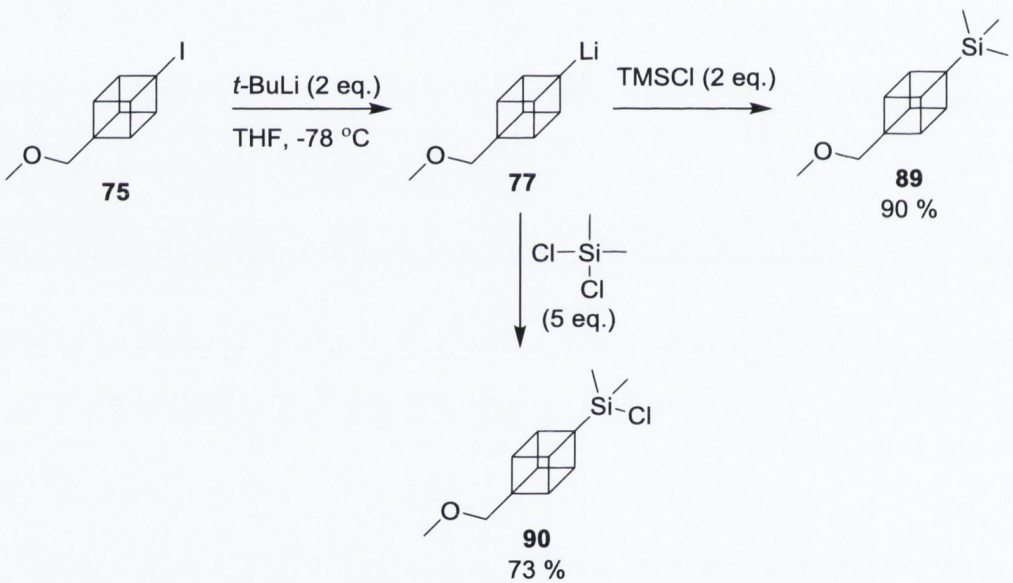
Figure 2.1: Molecular structure of **88b** (thermal displacement 50%, major component (68%) shown). Hydrogens omitted for clarity.

The potential uses of **88b** as a ligand in catalytic reactions are numerous[65,230] but further studies to investigate the binding affinity of **88b** to metal centres and its utility to effect cross-coupling reactions are required. Similarly, the synthesis of other cubane-phosphorous complexes such as the trialkylphosphine and phosphonate systems will be investigated.

2.4.4.2 Silylcubanes – unexplored potential protecting groups

Similar to stannylated cubanes, and as discussed in Chapter 1, silicon has been successfully introduced onto the cubane scaffold previously.[29,44] However, the most common use of silyl functionality in modern synthetic chemistry, namely in protecting group chemistry, has thus far been neglected. Two silylated cubanes were prepared. Quenching of lithiocubane with trimethylsilylchloride gave the TMS-appended cubane **89** in high yield,

while addition of an increased excess of dimethyldichlorosilane gave the chlorosilylcubane **90** (Scheme 2.14). Five equivalents of the dichlorosilane were added in an effort to minimise the formation of any dimeric species. The reactive Si-Cl bond present in **90** presented issues with relation to purification. No aqueous work-up was possible and the acidity of silica gel inhibited its use. Purification by vacuum distillation failed to yield any product. Column chromatography on Al_2O_3 proved successful with the compound obtained as a colourless oil in 73 % yield. As an analogue to TBDMS, the use of **90** as a protecting group offers significant potential. However, preliminary studies failed to achieve protection of simple alcohols and time constraints prevented a more thorough investigation. As a result, research into the applicability of **90** as a novel protecting group is ongoing.



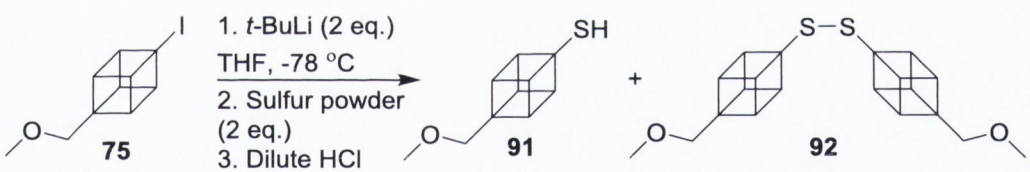
Scheme 2.14: Synthesis of silylated cubanes **89** and **90**.

2.4.4.3 Thiocubanes – odourless method modification

As discussed in Chapter 1, the synthesis of thiocubane is one of the few synthetically interesting examples of metal-halogen exchange reported on the cubane scaffold.[46] In this case, complex methodology involving reaction with tetramethylthiuram disulfide (thiram) followed by deprotection with $LiAlH_4$ at reflux was used to furnish cubane thiol, introducing sulfur onto the cubane periphery. Issues with this synthesis involve the odour of the sulfur

source and the harsh conditions required for its deprotection. As a conclusion to the work on lithiated cubanes a milder, general method for the introduction of sulfur onto the cubane core was investigated. A secondary goal, conditional upon the success of a more robust method, was to investigate the utility of thiocubanes towards TM-catalysed heteroatom coupling reactions.[231]

The most direct way to effect the transformation from Li to S is to add solid sulfur powder to an organolithium reagent.[232] The sulfur powder is reduced by the organolithium to create an organothiolate, which upon aqueous work-up produces the organic thiol. Reaction of **77** with elemental sulfur resulted in the formation of a complex mixture of products. The major cubane products, which co-eluted during purification, were identified as an approximately equivalent mixture of free thiol **91** and disulfide **92** (Scheme 2.15). This inseparable mixture of products presumably arose from the thiolate generated during the reaction so strategies to avoid this intermediate were considered.



Scheme 2.15: Reaction of lithiated cubane with elemental sulfur.

Following on from the work which will be described in Chapter 6, thiol precursor **93** was identified as a potential synthon for the introduction of a masked thiol group. Unlike other thiol derivatives, **93** is odourless and undergoes ready base deprotection.[i] Successful introduction of **93** to the cubane scaffold first required activation of the sulfur through addition of a good leaving group. Conversion to a sulfenylchloride **94** *via* chlorination with an appropriate chloride source was chosen as the most promising route (Scheme 2.16). The best yields obtained from the reaction of **77** with **94** indicate a need for further optimisation.

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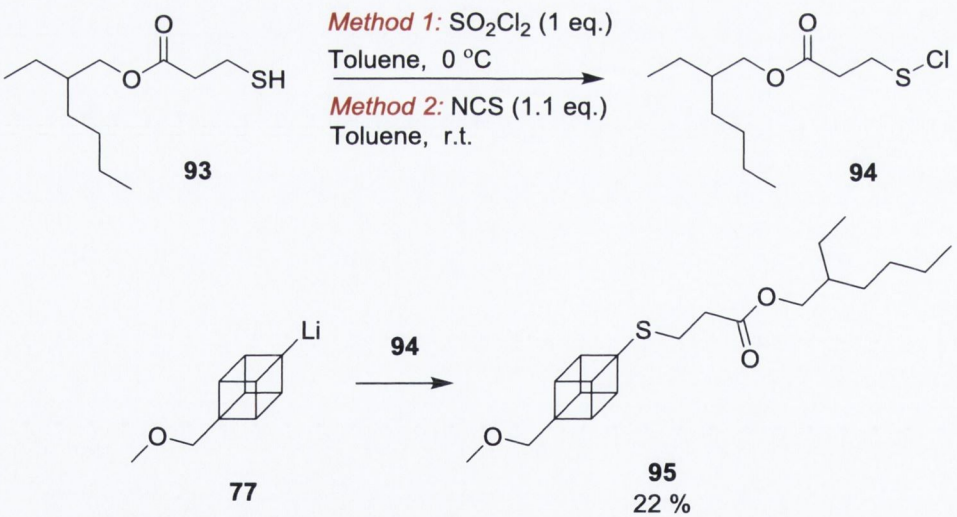
[i] The properties of **93** and its utility in synthetic chemistry will be discussed in detail in Chapter 6.

The difficulties are connected with the generation of **94**. Upon work-up of most reactions, the primary sulfur-containing product was identified as the disulfide version of **93**. Considering **93** is resistant to dimerisation, the quantitative formation of a disulfide dimer presumably arises from the immediate reaction of **93** with generated **94**. The active sulfenylchloride species must then be being consumed as quickly as it is generated, inhibiting any possible formation of **95**. The dimerisation process occurs at the same rate regardless of the chlorinating source (sulfuryl chloride or NCS) used. The maximum yield was obtained when a solution of **93** was added over two hours to a solution of NCS in toluene before addition of **77**. While this gave a yield of 22 %, a significant amount of disulfide was still present. The successful generation of **95** nevertheless represents an alternative (milder) method for sulfur insertion through use of sulfenylchlorides to that previously published. However, further optimisation of the reaction must be performed before it can be considered synthetically useful.



Scheme 2.16: Generation of sulfenyl chloride **94** and synthesis of **95**.

2.5 Conclusions and future work

In summary, the investigation of metal-halogen exchange on the cubane scaffold resulted in the successful synthesis of a large library of diversely functionalised cubane scaffolds. Methods to prepare mono-halogenated species were investigated and optimised. The retention of functionality at the 4-position of iodocubane presents an alternative to the standard use of iodinated cubanes by enabling further functionalisation of the cubane scaffold following modification of the cubane-iodide bond. The optimisation of procedures for the metal-halogen exchange reaction on iodinated cubanes facilitated the high yield synthesis of activated cubane nucleophiles (including the first examples of borylated cubanes) for use in Pd-catalysed reactions. The applicability of these metallocubanes towards said chemistry will be discussed in the following chapter. Introduction of phosphorous to the cubane scaffold represents the second novel structural archetype attainable *via* this route. Future investigations will focus on the generation of a library of cubane-phosphorous complexes and investigations into their utility as novel ligands in transition metal-catalysed reactions are planned. Further work is also required on improving the synthesis of thiolated cubanes and examining the utility of silylated cubanes in protecting group chemistry.

Chapter 3: Pd-catalysed cross-coupling reactions of cubanes

3.1 Background

Pd-catalysed cross-coupling reactions have become a staple in modern synthetic chemistry but have never been applied in a rigorous sense to the cubane scaffold. While numerous avenues towards the cross-couplings of sp^2 and sp systems exist, the development of the field of sp^3 cross-couplings has proceeded at a much slower pace.[64,65] The objectives of this chapter are to investigate the ability of functionalised cubane systems to participate in palladium-catalysed reactions and to delineate the appropriate conditions that allow for successful coupling of the cubane scaffold to other organic residues. This study will focus on those reactions which have, historically, been most utilised for alkyl couplings. Initially, the investigation will focus on halogenated (bromo- and iodo-) cubanes and their reactivity under Suzuki-Miyaura cross-coupling conditions. While electron-rich alkyl halides are not the most optimum coupling partners, this is nevertheless an avenue that needs exploration due to the ready availability of cubyl halides. Focus will then turn to the reactivity of the active cubane nucleophiles synthesised in Chapter 2. The applicability of borylated cubanes in the Suzuki-Miyaura cross-coupling, cubylzinc(II) halides in the Negishi reaction and stannylated cubanes under Stille coupling conditions will be examined. Both traditional avenues towards cross-couplings (*i. e.*, Pd-phosphine catalyst systems) but also more modern, highly active catalysts (*e. g.*, N-heterocyclic carbene [NHC] class of ligands) will be examined.

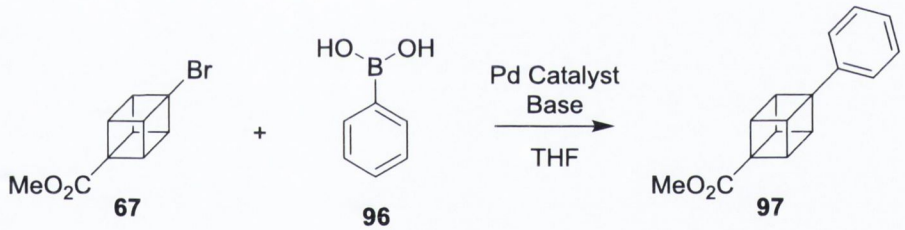
3.2 Halogenated cubanes as Suzuki-Miyaura partners

3.2.1 Bromocubane couplings

Testing of halogenated cubanes as Suzuki-Miyaura partners began with methyl 4-bromocubane-1-carboxylate **67**. While most research in the area of aliphatic Suzuki reactions utilises alkyl boronates it was decided to use a small amount of **67** in a simple cross-coupling reaction with phenylboronic acid **96**. A variety of conditions were trialled to investigate whether any reaction to give a phenyl substituted cubane **97** could be observed

and then optimised. Details of the various conditions used in this preliminary screen are shown in Table 3.1. A range of simple Pd(II) and Pd(0) catalysts were used in conjunction with various bases. The only products observed in all cases were homocoupled biphenyl and unreacted starting material **67**. This result correlates with the generally poor reactivity of alkyl bromides under Suzuki conditions.[64] While the C-Br bond was expected to be more activated towards cross-coupling reactions than similar aliphatic bromides due to its increased s-charatcer,[2,12] this proved to not be the case and connects with some of the other observations made about the low reactivity of the C-Br bond in cubane discussed in Chapter 2. In general, the Suzuki reaction tends to proceed best with electron-rich boranes and electron-poor iodides. Compound **67**, as an electron-rich bromide was therefore never expected to be the most viable coupling partner in this regard.

Table 3.1: Trial couplings of **67** as bromide partner in Suzuki-Miyaura cross-coupling.



Entry	Catalyst (mol %)	Base (eq.)	Temp (°C)	Time (h)	Yield (%)
1	$Pd(PPh_3)_4$ (10)	K_2CO_3 (5)	65	16	0
2	$PdCl_2$(dppf) (10)	K_2CO_3 (5)	65	16	0
3	$PdCl_2$(dppf) (10)	Cs_2CO_3 (5)	65	16	0
4	$PdCl_2$(dppf) (10)	K_3PO_4 (8)	65	16	0
5	$PdCl_2$(dppf) (10)	K_2CO_3 (8)/Ag_2O (7)	65	16	0
6	$PdCl_2$(dppf) (10)	25M (aq.) NaOH (10)	65	16	0

Reaction conditions: All reactions were performed at 20 mM cubane concentration using 3 equivalents of **96** under argon.

3.2.2 Iodocubane couplings

The absence of any coupled product observed from the reactions of **67** resulted in attention turning to a more reactive halide, namely iodocubanes. The initial trial material for these investigations was 1-bromo-4-iodocubane **68**, obtained *via* iodinative decarboxylation of **67**. Several trial reactions were performed on test scales with this material and **96** under a

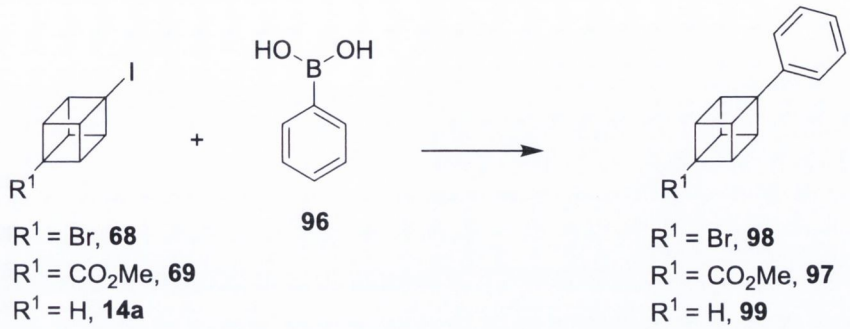
variety of conditions (Table 3.2, Entries 1-7). While no reaction went to completion, the results of this study were positive as in almost all cases the presence of coupled material was confirmed by EI mass spectrometry. Unfortunately, this material proved impossible to separate *via* standard column chromatography as the desired product **98**, starting material **68** and homocoupled biphenyl, have almost identical retention factors in *n*-hexane. As a result, accurate yields indicating how much coupled material was being formed were not obtained. Due to lack of sufficient material, it proved impossible at the time to scale up the reaction and thus obtain accurate conclusions as to the extent of the coupling reactions.

In order to probe this reaction further focus moved to two, more readily available, iodocubanes, methyl 4-iodocubane-1-carboxylate **69** (Table 3.2, Entries 8-12) and iodocubane **14a** (Table 3.2, Entries 13-15). These were subjected to a similar range of reactions as **68**; again using phenyl boronic acid **96** as the nucleophilic partner. With the starting materials available on a larger scale and with very distinct substitution patterns and R_f values, the products could be isolated much easier. In these cases coupled products were only identified in trace amounts;[i] insufficient for characterisation; with the major products in all cases being unreacted starting material and biphenyl. Standard methods of facilitating the coupling of alkyl halides; including the use of electron-rich, bulky ligands (*e. g.*, dppf - various entries) or the addition of Ag(I) salts (entries 2, 8, 13-15); proved ineffective at increasing yields to detectable levels. However, if any trend can be observed, it is that use of $PdCl_2$(dppf) or Ag_2O appears more likely to lead to trace product detection. The nature of the base employed seems to play a minimal role in the observed outcomes. Raising or lowering the temperature (entries 5 and 12), changing the solvent to DMF (entry 12), altering

[i] It remains an open question as to whether these coupled product were truly present. The only evidence for their formation was EI mass spectrometry from crude reaction mixtures. The column used in the EI mass spectrometer is permanently contaminated so full mass spectra were not attained. It is possible that the detected parent ion peaks of **97-99** thus arose from the column contaminants rather than the product mixtures. No other mass spectrometer gave any indication of formation of **97**, **98** or **99**. Analytically pure samples of the majority of the other cubane derivatives synthesised also failed to be detected on any of these machines, indicating a difficulty in the ionisation or separation of cubane fragments on the available MS equipment.

the catalyst loading (entry 6 vs 7) or increasing the reaction time (various entries) all proved similarly ineffective.

Table 3.2: Suzuki-Miyaura couplings of iodocubanes with **96**.



R^1 = Br, **68**
R^1 = CO_2Me, **69**
R^1 = H, **14a**

R^1 = Br, **98**
R^1 = CO_2Me, **97**
R^1 = H, **99**

Entry	S.M.	Catalyst (mol %)	Base (eq.)	Solvent	Time (h)	Temp (°C)	Result[a]
1	**68**	$PdCl_2(dppf)$ (10)	K_2CO_3 (8)	THF	72	65	Trace **98**
2	**68**	$PdCl_2(dppf)$ (10)	K_3PO_4 (8)/ Ag_2O (7)	THF	72	65	Trace **98**
3	**68**	$Pd(PPh_3)_4$ (10)	K_3PO_4 (8)	THF	16	65	**98** not detected
4	**68**	$PdCl_2(PPh_3)_2$ (10)	K_3PO_4 (8)	THF	16	65	Trace **98**
5	**68**	$PdCl_2(dppf)$ (10)	K_3PO_4 (8)	THF	16	r.t.	**98** not detected
6	**68**	$PdCl_2(dppf)$ (10)	Cs_2CO_3 (4)	THF	16	65	Trace **98**
7	**68**	$PdCl_2(dppf)$ (5)	Cs_2CO_3 (4)	THF	16	65	**98** not detected
8	**69**	$PdCl_2(dppf)$ (10)	K_3PO_4 (8)/ Ag_2O (7)	THF	16	65	Trace **97**
9	**69**	$Pd(PPh_3)_4$ (10)	K_3PO_4 (8)	THF	48	65	**97** not detected
10	**69**	$PdCl_2(PPh_3)_2$ (10)	K_3PO_4 (8)	THF	72	65	**97** not detected
11	**69**	$PdCl_2(dppf)$ (10)	K_3PO_4 (8)	THF	72	65	Trace **97**
12	**69**	$PdCl_2(dppf)$ (10)	K_2CO_3 (8)	DMF	72	120	Trace **97**
13	**14a**	$PdCl_2(PPh_3)_2$ (10)	K_3PO_4 (8)/ Ag_2O (7)	THF	72	65	Trace **99**
14	**14a**	$Pd(PPh_3)_4$ (10)	K_3PO_4 (8)/ Ag_2O (7)	THF	72	65	Trace **99**
15	**14a**	$PdCl_2(dppf)$ (10)	K_3PO_4 (8)/ Ag_2O (7)	THF	72	65	Trace **99**

Reaction conditions: All reactions were performed at 20 mM cubane concentration using 3 equivalents of **96** under argon. [a] Coupled products detected by EI MS

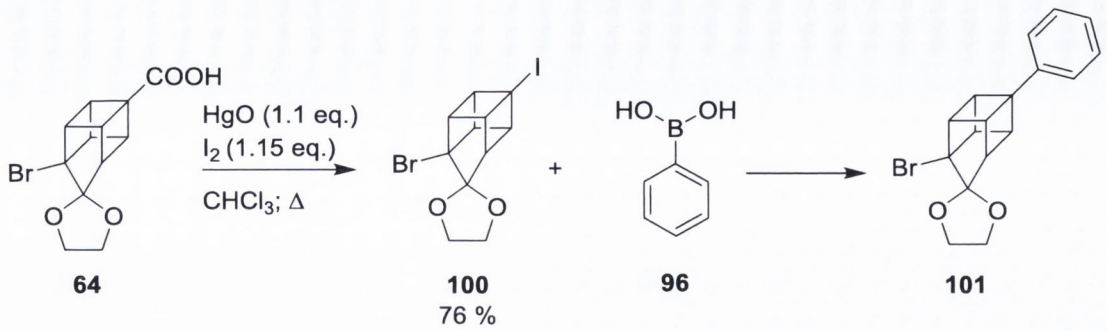
The results of these latter reactions imply that the coupled product indicated in the reaction products of **68** were in fact only present in trace amounts. An explanation for the inability to observe more than trace couplings is that the oxidative addition of cubane iodides

to Pd centres is, as reported for other alkyl halides,[76] a particularly slow process. Conversely, competitive homo-coupling of **96** (particularly considering the active conditions employed) is a fast process, with no unreacted **96** present in any reaction flask on work-up. As a result, this removal of free boronic acid **96** may be occurring at too fast a rate for any significant cross-coupling to occur. Reactions involving addition of **96** in multiple portions led to no noticeable change in reaction products.

Before entirely abandoning iodinated cubanes as viable Suzuki-Miyaura cross-coupling partners one last set of reactions was attempted. In this case, a key intermediate **64** in the synthesis of bromocubanes was iodinated, which allowed **100** to be obtained in high yield and before the particularly low yielding steps in the cubane synthesis. This material offered positive benefits both in terms of a much easier synthesis while still providing a fully formed cubane "edge" around the iodide, as well as allowing investigation as to whether the slightly reduced strain on the opposite face of the cubane framework would affect the reaction in any way. The coupling conditions employed are detailed in Table 3.3. Given identical conditions to those which resulted in trace product formation in Table 3.2, in no case was any coupled product **101** identified, indicating that the trace products identified previously required a fully formed cubane scaffold.

Considering the range of conditions employed and the lack of any significant coupling it does not appear as if halogenated cubanes are effective cross-coupling partners. This failure of any iodinated cubane derivatives to undergo any meaningful Suzuki coupling chemistry was not entirely unexpected. Again, the halide partner here is electron-rich, an unwanted trait in Suzuki-Miyaura chemistry. Furthermore, continuing research into the mechanism of oxidative addition of alkyl halides onto the Pd(II) metal centre indicates an S_N2-type mechanism where the palladium adds through the antibonding orbital of the C-X bond.[69] From a steric viewpoint this is impossible with the cubane system, thus negating any of the positive effects the cubane scaffold may be expected to impart in the reaction.

Table 3.3: Trial couplings of intermediate **100** with **96**.



64 **100** 76 % **96** **101**

#	Catalyst (mol %)	Base (eq.)	Solvent	Time (h)	Temp (°C)	Yield (%)
1	$Pd(PPh_3)_4$ (10)	K_3PO_4 (8)/ Ag_2O (7)	THF	16	65	0
2	$PdCl_2(PPh_3)_2$ (10)	K_3PO_4 (8)/ Ag_2O (7)	THF	16	65	0
3	$PdCl_2$(dppf) (10)	K_3PO_4 (8)/ Ag_2O (7)	THF	16	65	0
4	$PdCl_2$(dppf) (10)	K_3PO_4 (8)/ Ag_2O (7)	DMF	16	120	0
5	$PdCl_2(PPh_3)_2$ (10)	K_3PO_4 (8)	THF	48	65	0
6	$PdCl_2$(dppf) (10)	K_2CO_3 (8)	THF	48	65	0
7	$PdCl_2$(dppf) (10)	Cs_2CO_3 (4)	THF	48	65	0
8	$PdCl_2$(dppf) (10)	20M NaOH (8)	THF	48	65	0

Reaction conditions: All reactions were performed at 20 mM cubane concentration using 3 equivalents of **96** under argon.

3.3 Borylated cubanes in the Suzuki-Miyaura reaction

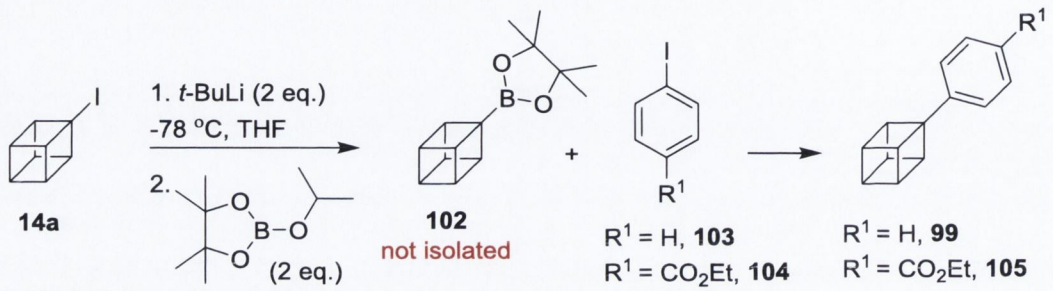
Introducing alkyl substituents *via* Suzuki-Miyaura cross-coupling reactions proceeds more readily with borylated alkanes acting as the nucleophilic component in the catalytic cycle. As a result, the classes of borylated cubanes synthesised *via* methodologies described in Chapter 2 were investigated to probe their reactivity towards this class of palladium-catalysed reactions.

3.3.1 Cubylboronic esters as coupling partners

The first of these borylated systems to be studied were the class of cubane boronic acid pinacol esters. In Chapter 2 the detailed synthesis of **79a** (a hydroxymethyl substituted cubane boryl ester) was described. However, this portion of the work was performed prior to the synthesis of **79a** and used **14a** as the iodinated cubane precursor (Table 3.4). The borylation reaction of **14a** proceeds exactly as described for **79a**, however, complete purification of **102**, proved more complicated than for the disubstituted system (presumably

due to enhanced stability and altered solubility profile afforded by the hydroxymethyl group). As a result, **102** was not isolated but instead typically generated and used *in situ*.[i] Table 3.4 outlines the various reaction conditions employed to effect the cross-coupling of **102** with two aryl iodides.

Table 3.4: Suzuki-Miyaura couplings of cubane boronic acid pinacol ester.



#	ArI	Catalyst (mol %)	Base (eq.)	Ag_2O (5 eq.)	Temp (°C)	Result
1	**103**	$PdCl_2(PPh_3)_2$ (10)	K_3PO_4 (8)	Yes	65	**102** recovered
2	**103**	$Pd(PPh_3)_4$ (10)	K_3PO_4 (8)	Yes	65	**102** recovered
3	**103**	$PdCl_2$(dppf) (10)	K_3PO_4 (8)	Yes	65	No cubane product
4	**103**	$PdCl_2$(dppf) (10)	10M NaOH (8)	Yes	65	No cubane product
5	**103**	$PdCl_2$(dppf) (10)	K_3PO_4 (8)	No	65	No cubane product
6	**103**	$PdCl_2$(dppe) (10)	K_3PO_4 (8)	Yes	65	No cubane product
7	**103**	$Pd_2(dba)_3$ (10)/ $AsPh_3$ (40)	K_3PO_4 (8)	Yes	65	No cubane product
8	**104**	$PdCl_2(PPh_3)_2$ (10)	K_3PO_4 (8)	Yes	65	No cubane product
9	**104**	$PdCl_2$(dppf) (10)	K_3PO_4 (8)	No	65	No cubane product
10	**104**	$PdCl_2$(dppf) (10)	Cs_2CO_3 (4)	No	65	No cubane product
11	**104**	$PdCl_2$(dppf) (10)	K_3PO_4 (8)	No	120[a]	No cubane product
12	**104**	$PdCl_2$(dppf) (10)	K_3PO_4 (8)	No	20	**102** recovered
13	**104**[b]	$PdCl_2$(dppf) (10)	Cs_2CO_3 (4)	No	65	No cubane product
14	**104**[b]	$PdCl_2$(dppf) (10)	K_3PO_4 (8)	No	120[a]	No cubane product

Reaction conditions: **102** was generated *in situ* from the reaction of **14a** with *t*-BuLi in THF at -78 °C. Catalyst, base and aryl iodide were added after generation and heated. All coupling reactions were performed at 20 mM cubane concentration for 16 hours in THF under argon using 1.2 equivalents of aryl iodide unless otherwise stated. [a] THF was removed *in vacuo* after generation of **102** and DMF added. [b] 0.33 equivalents of **104** added.

The Suzuki-Miyaura couplings of **102** present some interesting results. Two distinct results were observed – either recovery of the majority of the generated **102** or the complete

[i] In several cases **102** was isolated and gave spectra of reasonable purity. Use of this material gave identical results to cases where **102** was generated and used *in situ*.

absence of any cubane product after work-up. For the reaction between **102** and iodobenzene **103**, recovery of **102** was observed when either $Pd(PPh_3)_4$ or $PdCl_2(PPh_3)_2$ (Entries 1-2) were used as the catalyst. Use of a more active catalyst (Entries 3-7) resulted in the absence of any cubane product. This happened irrespective of the base used (Entry 3 *vs.* 4) or the presence of Ag_2O (Entry 3 *vs.* 5). Initially, this was postulated to be due to the volatility of phenylcubane **99**. As a result, the electron deficient (*i. e.*, more reactive) halide **104** was employed as the aryl halide partner. Using this halide resulted in consumption of **102** in the presence of $PdCl_2(PPh_3)_2$ (Entry 8). Altering the aryl halide failed to help identify the nature of the product, however, with no cubane product being identified in any of the heated reactions. The absence of Ag_2O similarly failed to improve product identification. Performing the reaction at room temperature (Entry 12) resulted in recovery of **102** indicating some element of thermal activity in the reaction. Elevating the temperature beyond 65 °C by utilising DMF as solvent failed to improve the result (Entry 11). Classically, an excess of alkyl boronate is preferred in such cross-coupling reactions. Utilising a three-fold excess of **102**, however, resulted again in the disappearance of the cubane scaffold (Entries 13 and 14). This last result cannot be explained solely by the volatility of **99** or **105**.

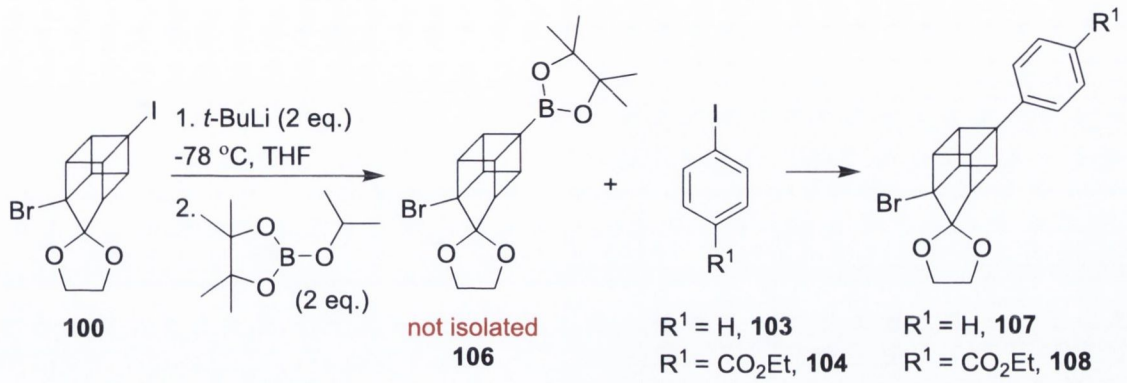
There are two explanations that can account for the entirety of these results. Firstly, that, with electron-rich, bulky ligands and at elevated temperatures, some palladium species is facilitating the decomposition of the cubane scaffold. No indication of any of the reported decomposition pathways of cubane (cyclooctatetraenes,[111] cuneanes[112] or cubenes[39]) was detected by ^{1}H NMR spectroscopic analysis after any reaction. From ^{1}H NMR analysis of unpurified reaction mixtures immediately following the removal of the solvent, only aryl halide signals could be identified, with no other identifiable organic signals present. The presence of the aryl halide in all crude mixtures supports the hypothesis that this decomposition is occurring somewhere between transmetallation of the alkylboronic ester and reductive elimination of the coupled product. The other possibility is that the products

99 and **105** are being formed but are unstable under the reaction conditions or that homo-coupling of **102** is also occurring and producing a volatile product. The only way identified to probe whether this theory is true is to perform GC-MS analysis on the reaction mixture at various time points. The majority of the cubane products successfully synthesised display poor detection on the mass spectrometers available unless they are available in a high degree of purity. As a result, no confidence could be placed in the absence of target compounds in the MS spectra as this could simply be due to the unreliability of the measurement rather than the absence of target compounds.

In an effort to test the validity of the first explanation, attention returned to cubane intermediate **100**. Here, the theory was, that if the Pd centre is facilitating a hitherto unknown decomposition pathway of the cubane scaffold, then utilising a homo-cubane scaffold should limit this pathway. The boryl component, however, is attached to the fully formed cubane 'edge' of the intermediate so successful coupling would support some of the assumptions made about the applicability of the tertiary cubane system towards Pd-catalysis. Under most conditions, *in situ* reaction of the borylated material **106** with either **103** or **104** led to the recovery of **106**. In one case (Table 3.5, Entry 7) it seemed that coupling had occurred with **108** obtained in approximately 40 % crude yield. Figure 3.1 shows the ^{1}H NMR spectra that led to this conclusion. Comparing the product spectra (**108** blue) with the starting material (**106** red) the absence of the boryl ester signal at approximately δ = 1.5 ppm and the shifts of the aliphatic signals at δ = 2-5 ppm clearly indicate alteration of the homocubane scaffold. Similarly, there are two distinct aromatic doublets present in the spectrum of **108**. These doublets are indicative of a disubstituted phenyl ring and are different from those present in both the starting material **104** and homocoupled aryl system **110**. Efforts to purify the product further and repeat the result using identical conditions failed and no explanation for what specifically led to this unique result could be provided. The failure of conditions which produced an effect in Table 3.4 to yield any change in **106** indicate that the process occurring

above does require a fully formed, highly strained, cubane scaffold, supporting the theory that a new decomposition pathway is being observed.

Table 3.5: Suzuki-Miyaura couplings of borylated intermediate **106**.



Entry	ArI	Catalyst (mol %)	Base (eq.)	Ag_2O (5 eq.)	Result
1	**103**	$Pd(PPh_3)_4$ (10)	K_3PO_4 (8)	No	**106** recovered
2	**103**	$PdCl_2(PPh_3)_2$ (10)	K_3PO_4 (8)	No	**106** recovered
3	**103**	$PdCl_2$(dppf) (10)	K_3PO_4 (8)	Yes	**106** recovered
4	**104**	$PdCl_2(PPh_3)_2$ (10)	K_3PO_4 (8)	Yes	**106** recovered
5	**104**	$Pd(PPh_3)_4$ (10)	K_3PO_4 (8)	Yes	**106** recovered
6	**104**	$PdCl_2$(dppf) (10)	K_3PO_4 (8)	Yes	**106** recovered
7	**104**	$PdCl_2$(dppf) (10)	K_3PO_4 (8)	Yes	~40% **108** (obtained once)

Reaction conditions: **106** was generated *in situ* from the reaction of **100** with *t*-BuLi in THF at -78 °C. Catalyst, base and aryl iodide were added after generation and heated. All coupling reactions were performed at 20 mM cubane concentration for 16 hours in THF under argon using 2 equivalents of aryl iodide.

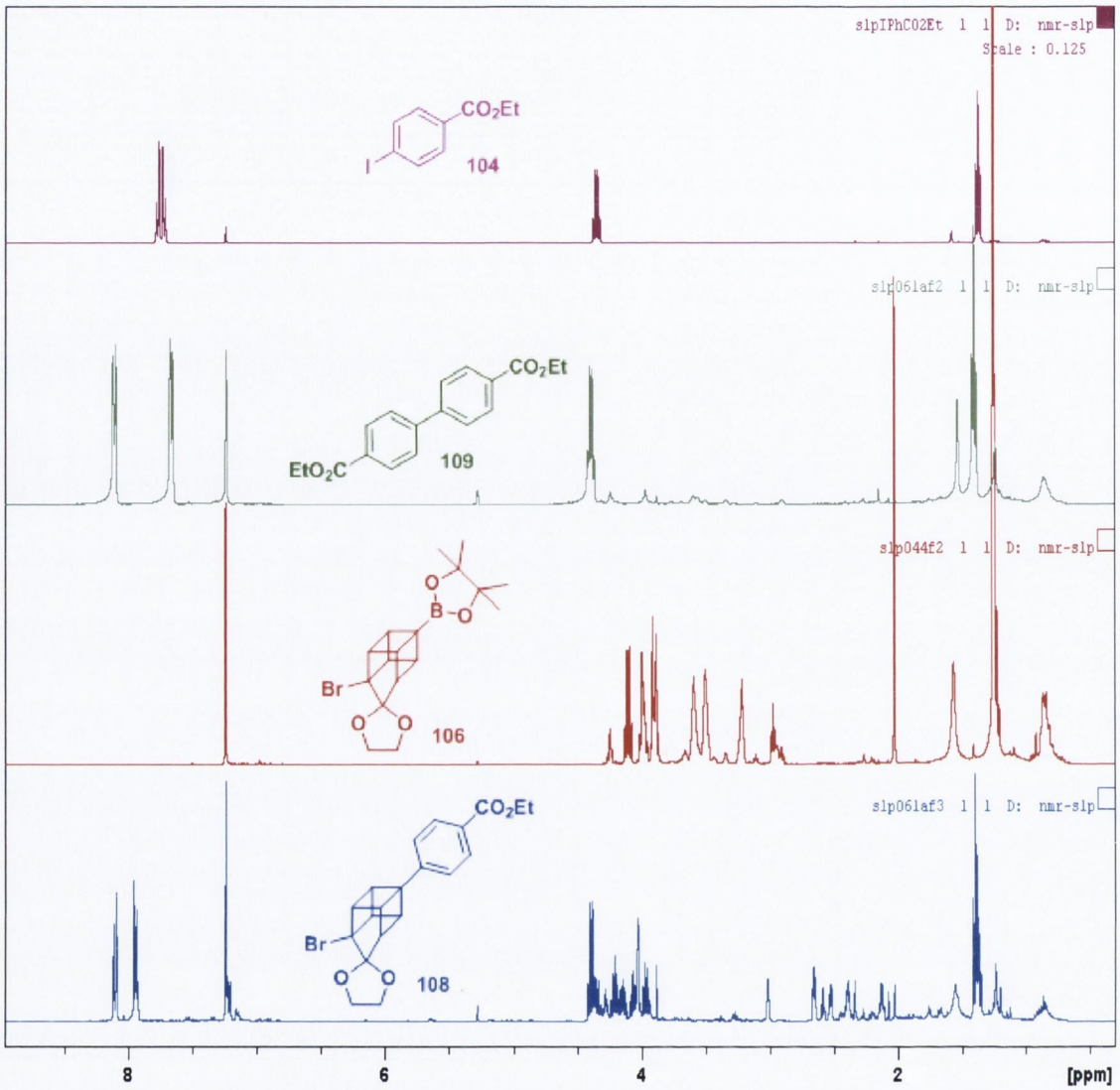
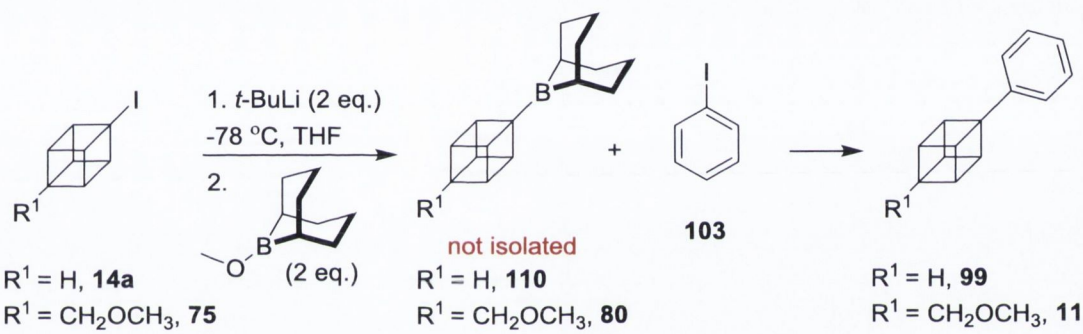


Figure 3.1: ^{1}H NMR spectra ($CDCl_3$) showing the relevant regions of **108** and its precursors.

3.3.2 Cubane-BBN derivatives as coupling partners

The failure of the boronic esters to produce any clear reaction led to the pursuit of more active substituents, namely cubane-BBN derivatives. The synthesis of hydroxymethyl derivative **80** was detailed in Chapter 2. In a manner akin to that described in Section 3.3.1 iodocubane **14a** was also used as a precursor for these reactions. In both cases the instability of alkyl-BBN derivatives required the active nucleophiles to be generated and used *in situ*. The results of the couplings of cubane-BBN derivatives **80** and **110** with iodobenzene are detailed in Table 3.6.

Table 3.6: Cross-coupling reactions of cubane-BBN derivatives **80** and **110**.



#	S.M.	Catalyst (mol %)	Base (eq.)	Solvent	Temp (°C)	Result
1	**110**[a]	$PdCl_2(dppf)$ (10)	K_3PO_4 (8)	THF	65	No cubane
2	**110**[a]	$Pd(PPh_3)_4$ (10)	K_3PO_4 (8)	THF	65	No cubane
3	**110**	$PdCl_2(dppf)$ (10)	NaOH (3)	THF:H_2O (5:1)	65	No cubane
4	**110**	$PdCl_2(dppf)$ (10)	NaOH (3)/ Ag_2O (3)	THF:H_2O (5:1)	65	No cubane
5	**110**	$PdCl_2(dppf)$ (10)	K_2CO_3 (8)/ Ag_2O (3)	DMF[b]	50	No cubane
6	**80**	$PdCl_2(dppf)$ (10)	NaOH (4)	THF:H_2O (5:2)	65	No cubane
7	**80**	$PdCl_2(dppf)$ (10)	NaOH (4)	THF:H_2O (5:2)	r.t.	No cubane
8	**80**	$PdCl_2(PPh_3)_2$ (10)	NaOH (4)	THF:H_2O (5:2)	65	No cubane
9	**80**	$Pd(PPh_3)_4$ (5)	NaOH (4)	THF:H_2O (5:2)	65	No cubane
10	**80**	$PdCl_2(dppf)$ (5)	K_2CO_3 (8)	DMF[b]	50	No cubane
11	**80**	$PdCl_2(dppf)$ (5)	K_2CO_3 (8)	DMF[b]	r.t.	No cubane

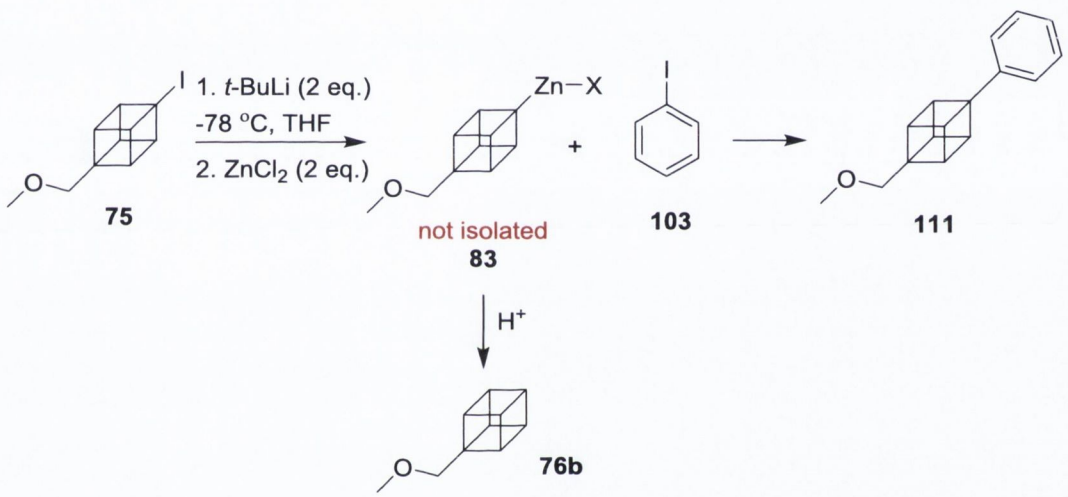
Reaction conditions: Nucleophiles were generated *in situ* from the reaction of iodocubanes with *t*-BuLi in THF at -78 °C. Catalyst, base and **103** were added after generation and heated. All coupling reactions were performed at 80 mM cubane concentration for 16 hours under argon using 0.9 equivalents of **103** unless stated. [a] 0.5 equivalents **103** added. [b] THF removed after generation and replaced with DMF.

In all cases, using cubane-BBN derivatives in the presence of palladium catalysts led to decomposition of the cubane scaffold. Upon work-up, no identifiable organic signals, with the exception of unreacted iodobenzene **103**, could be detected in the ^{1}H NMR spectra. This occurred independently of the Pd source used or the presence of silver(I) oxide. Using hydroxide bases in aqueous solvents or inorganic bases in THF or DMF similarly had no effect on the reaction outcome, with decomposition observed in every case. Additionally, regardless of the temperature of the reaction (room temperature up to 65 °C) or catalyst loading (5 *vs.* 10 mol %), decomposition occurred. The failure to recover any of the starting material from any reaction meant that, unlike the previous work with the boronic esters, thermal or aerobic decomposition of **110** or **80** could not be eliminated as the reason for the absence of any cubane material upon work-up. Several details from later studies (*vide infra*) support the hypothesis that, in an identical manner to that discussed previously, the palladium species, through an unknown pathway, is facilitating decomposition of the cubane scaffold. Unlike in the boronic ester case, however, the higher reactivity of the BBN derivatives towards transmetallation means that this process occurs more favourably and under milder conditions with BBN-appended cubanes. No new information regarding the mechanism of this decomposition could be gleaned from this study, however.

3.4 Negishi reactions of cubylzinc(II) halides

The Negishi cross-coupling of alkylzinc(II) halides with aryl or alkenyl halides has emerged as one of the most powerful methodologies to effect the cross-coupling of sp^3 systems.[65,233] As such, cubylzinc(II) halide **83** was an ideal candidate to probe the utility of the cubane scaffold under Negishi cross-coupling conditions. The results of stability studies on **83** and the initial studies into the Negishi coupling of **83** with iodobenzene **103** are detailed in Table 3.7.

Table 3.7: Negishi cross-couplings and stability studies of **83**.



Entry	Catalyst (10 mol %)	I-Ph (eq.)	NMP (% v/v)	LiCl (eq.)	Temp (°C)	Time (h)	Observation
1	N/A	0	0	0	r.t.	1	Quantitative **76b**
2	N/A	0	0	0	r.t.	18	Quantitative **76b**
3	N/A	0	0	0	65	18	Quantitative **76b**
4	N/A	1	33	4	65	18	Quantitative **76b**
5	$PdCl_2$(dppf)	2	0	0	65	16	Quantitative **76b**
6	$Pd(PPh_3)_4$	2	0	0	65	16	Quantitative **76b**
7	$PdCl_2$(dppf)	2	0	2	65	16	Quantitative **76b**
8	$PdCl_2$(dppf)	1	0	0	65	16	Quantitative **76b**
9	$PdCl_2$(dppf)	1	33	4	65	16	No cubane
10	$PdCl_2$(dppf)	0	33	4	65	16	No cubane
11	$PdCl_2$(dppf)	1	33	4	r.t.	16	Quantitative **76b**
12	$PdCl_2$(dppf)	1	33	4	40	16	Some **76b**
13	$Pd_2(dba)_3/P(Cy)_3$	1	33	4	65	16	No cubane

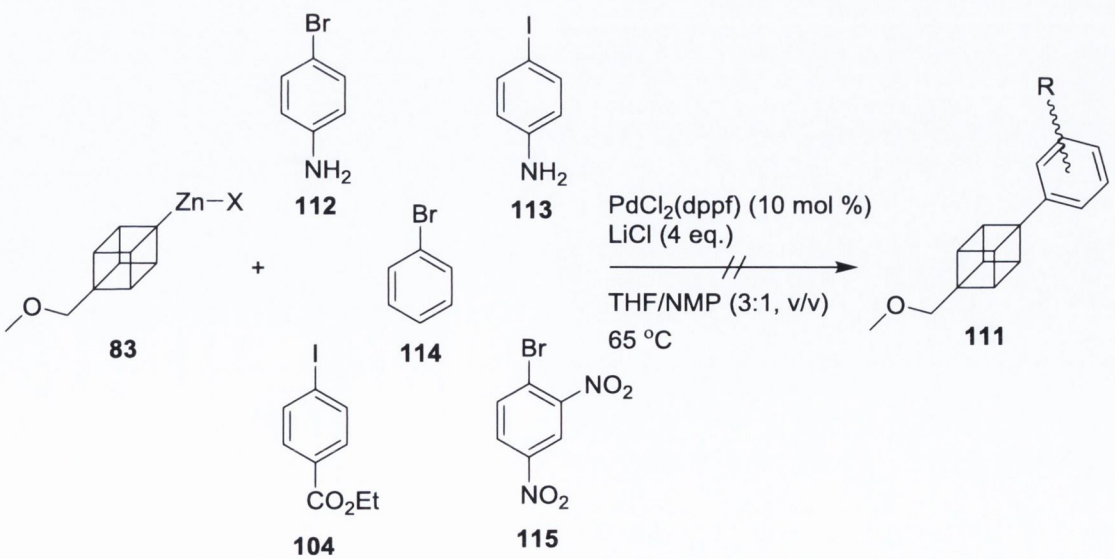
Reaction conditions: **83** was generated *in situ* from the reaction of **75** with *t*-BuLi in THF at -78 °C. Catalyst, salt and **103** were added after generation and heated. Reactions were quenched with dilute HCl. All reactions were performed at 85 mM cubane concentration under argon.

The initial four studies (Entries 1-4) were performed in order to assess the stability of **83** under the reaction conditions by omitting various reagents. Entries 1 and 2 indicate the stability of the cubane scaffold at room temperature in THF. Entry 3 shows that if **83** is heated overnight in THF, in the absence of any other materials, the de-iodinated product **76b** is obtained after work up and Entry 4 indicates that the same process occurs in the presence of all reagents with the exception of the palladium catalyst. When this protonolysis is occurring – *i. e.*, during the course of the reaction or upon work-up – was not examined as it was deemed unimportant with relation to this study. The iodinated starting material **75** was found to be entirely stable to all conditions employed in Table 3.7.

The process of the Negishi cross-coupling reaction appears remarkably similar to that observed in the Suzuki-Miyaura cross-couplings – *i. e.*, under appropriate conditions the cubane scaffold decomposes with no detectable organic residues remaining. Entries 5-8 in Table 3.7 detail the initial coupling methodologies employed. Here, **83** was heated in the presence of various palladium catalysts in THF overnight and in all cases a quantitative amount of the de-iodinated material **76b** was obtained on work-up. However, upon increasing the polarity of the solvent mix by adding 33 % (v/v) *N*-methylpyrrolidone (NMP), complete decomposition of the cubane system was observed (Entry 9). This reaction occurred independent of the presence of **103** (Entry 10) indicating that the decomposition is occurring prior to cross-coupling. The reaction also seems to require elevated temperatures with quantitative **76b** obtained after performing the reaction at room temperature (Entry 11) and heating to 40 °C (Entry 12) resulted in some **76b** but the ratio with **103** indicates a significant degree of decomposition. The nature of the palladium species seems to play little role in determining the outcome as both $PdCl_2$(dppf) (Entry 9) and $Pd_2(dba)_3$/P(cyclohexyl)$_3$ (Entry 13) resulted in disappearance of cubane. However, the requirement for some form of palladium species to be present is clear – definitively proving that the process is indeed a Pd-catalysed one.

From Table 3.7 the conditions that lead to the decomposition of the cubane system can be delineated – namely, heating in the presence of palladium in a highly polar NMP/THF system. Absence of any of these three conditions allows for the retrieval of de-iodinated cubane from the reaction mixture. This result therefore outlines (based on the working hypothesis) the conditions required to produce transmetallation of the cubane system. This must *per se* be the first step towards any successful coupling so, while the results themselves are not positive in the sense that no coupled product was observed, a significant level of insight into the reaction mechanism was nevertheless obtained.

The outstanding question from Table 3.7 is that if transmetallation to the Pd centre is occurring, then can a more suitable halide coupling partner produce effective cross-coupling? To this end, the reaction conditions which were shown to lead to decomposition (presumably initially *via* transmetallation) were applied for the coupling of **83** with various aromatic halides as the electrophilic coupling partner (Scheme 3.1). Both electron withdrawing and donating effects were investigated with this series of electrophiles as well as the nature of the halogen present. In all cases, no cubane product was obtained at the end of the reaction. This lends further proof towards the theory that the palladium-catalysed route in question is indeed independent of the standard cross-coupling catalytic cycle.



Scheme 3.1: Attempted Negishi reactions of **83** with various aryl halides.

As a whole, this section of work on the Negishi reaction possesses clear parallels to the earlier work on the Suzuki-Miyaura couplings and helps answer some of the outstanding questions from that section. In both cases, a decomposition process of activated cubane systems is occurring in the presence of palladium salts. Similarly both reactions require highly reactive conditions to effect this process – indicating an energy barrier akin to that existing in transmetallation. Indeed the conditions which, when employed, lead to decomposition, are identical to those reported as being most effective for the transmetallation and subsequent cross-coupling of alkyl substituents. The revised working hypothesis at this point is that, after transmetallation but prior to reductive coupling, the palladium centre is catalysing a sigma-sigma bond migration in an effort to relieve the ring strain of the cubane scaffold. In a departure from such systems which have been previously reported,[39,111,112] this rearranged intermediate must then be undergoing further decomposition, possibly due to the high temperatures required, leading to volatile organic fragments or long chain alkanes and ethers unidentifiable by spectroscopic analysis. The stability of the unactivated, iodinated, cubane scaffold to all of the above conditions has been established and no such decomposition process was observed in the trial couplings of halogenated cubanes previously. The present process must therefore require highly nucleophilic cubane systems.

3.5 Cubane and the Stille reaction

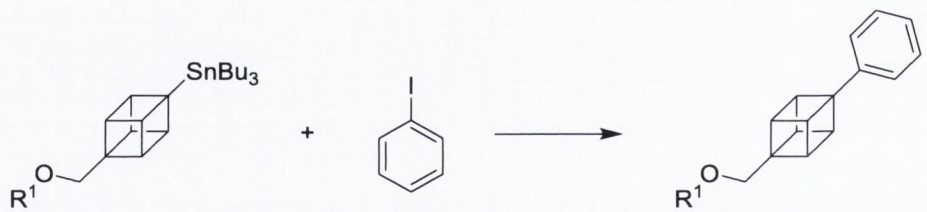
The Stille reaction between an organotin residue and appropriate halide was historically the most powerful cross-coupling methodology for the installation of sp^3 systems.[52,71] The high environmental toxicity of the tin by-products coupled with recent advances in the Negishi and Suzuki-Miyaura reactions have meant that, in more modern times, the pre-eminence of Stille methodologies for alkyl couplings has waned significantly.[234] Nevertheless, the reaction represents a reliable back-up option for efficient alkyl cross-couplings when more popular avenues have failed or are inapplicable. As a result,

Stille methodologies were the third and final cross-coupling conditions investigated as a route to the effective cross-coupling of cubane systems.

The studies into the effectiveness of Stille cross-coupling conditions were less detailed than those performed previously, in part due to the comparative lack of significant reported modifications and also because the observed initial results were broadly similar to those obtained with the other two methodologies. The results of this investigation are presented in Table 3.8. One significant advantage the Stille reaction has over the others discussed is the stability of the stannylated cubane component. Two such organotin compounds were investigated, **86** and **87**, and, unlike the borylated cubanes and cubylzinc(II) halides, these compounds are stable for short periods on silica gel and towards light, heat and air. This eliminates these means of decomposition as plausible avenues, allowing for a more conclusive analysis of results.

The results detailed in Table 3.8 illustrate an identical pattern of reactivity to that observed previously. Decomposition of the cubane scaffold occurs through use of a bidentate ligand on the Pd complex while heating in a highly polar solvent (Entries 4, 7 and 8). Otherwise, the stannylcubane can be recovered quantitatively from the reaction. The presence of CuI as an activator[235,236] plays a minimal role in comparison to the other conditions. Further optimisation efforts of the reaction were not performed but the results strongly support the working hypothesis stated previously. The stability of both **86** and **87** indicate that transmetallation of the cubane scaffold must be occurring. Highly activated conditions are required to promote transmetallation of the stannylated cubane scaffold, which may also be required to facilitate the decomposition reaction from the Pd-complex. Therefore, while not providing further information regarding the exact mechanism of this decomposition, the close agreement of results indicates that the pathway is largely independent of the specific methodologies employed but rather a general trait of the active Pd-cubane complex.

Table 3.8: Attempted Stille couplings of **86** and **87** with **103**.



R^1 = pyran, **86**
R^1 = Me, **87**

103

R^1 = pyran, **116**
R^1 = Me, **111**

Entry	S.M.	Catalyst (10 mol %)	Solvent	Salt (eq.)	Temp (°C)	Observation
1	**86**	$Pd(PPh_3)_4$	DMF	LiCl (4)	50	**86** recovered
2	**86**	$Pd(PPh_3)_4$	DMF	CuI (0.3)	50	**86** recovered
3	**86**	$PdCl_2$(dppf)	THF	LiCl (4)	65	**86** recovered
4	**86**	$PdCl_2$(dppf)	THF/NMP (3:1)	LiCl (4)	65	No cubane
5	**87**	$PdCl_2$(dppf)	THF	LiCl (4)	65	**87** recovered
6	**87**	$PdCl_2$(dppf)	THF/NMP (3:1)	LiCl (4)	65	No cubane
7	**87**	$PdCl_2$(dppf)	THF/NMP (3:1)	CuI (0.3)	65	No cubane
8	**87**	$PdCl_2$(dppf)	THF/NMP (3:1)	CuI (0.3)	r.t.	**87** recovered

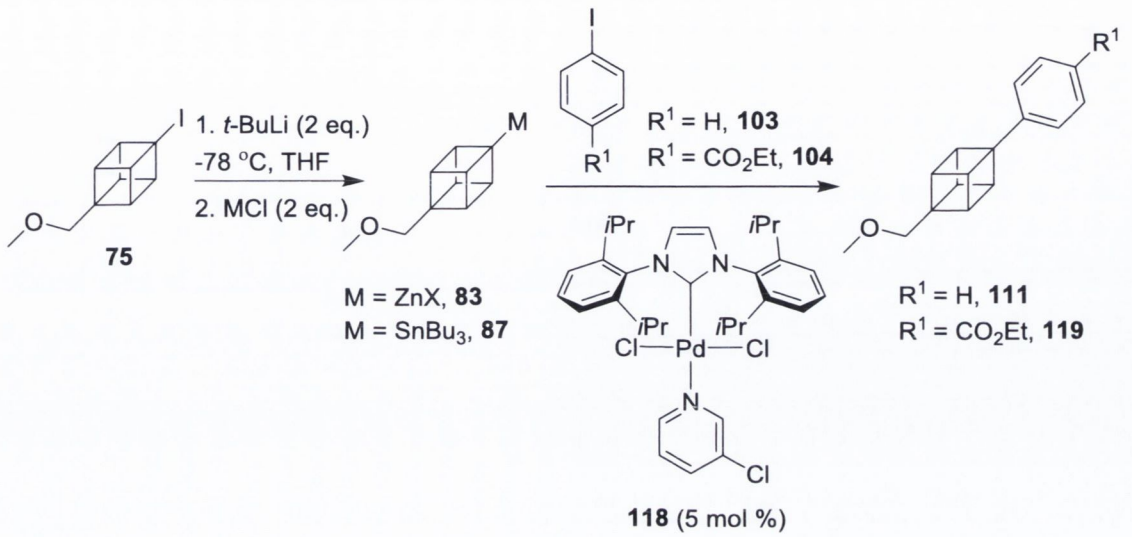
Reaction conditions: All reactions were performed at 85 mM cubane concentration under argon for 16 hours using 1 eq. **103**.

3.6 Utilisation of highly active catalyst systems

All of the work discussed thus far has focused on the use of standard palladium-phosphine catalyst systems. As noted previously, several new, highly active catalyst systems have emerged in recent years to challenge these standard catalytic systems. One class which has received significant attention due to its general applicability in a range of coupling protocols and generally excellent yields is the *N*-heterocyclic carbene class of Pd ligands.[60,89-91] Of these, the PEPPSI (**p**yridine-**e**nhanced **p**recatalyst **p**reparation **s**tabilization and **i**nitiation) series of catalysts stands out as being particularly noteworthy, due to their air and moisture stability, ease of synthesis (most are commercially available) and the typically very low catalyst loadings required (generally 1-2 mol %).[92-94,237] In a final attempt to effect the palladium-catalysed cross-coupling of cubane scaffolds, a member of this class of catalyst system (Pd-PEPPSI-*i*Pr **118**) was utilised in each of the three coupling methodologies discussed. The goal here was to attempt to obtain transmetallation at milder conditions to further probe the catalytic process. Table 3.9 outlines the results of this catalyst

under Negishi and Stille coupling conditions, whilst Table 3.10 illustrates the same for the Suzuki-Miyaura protocol.

Table 3.9: Use of Pd-PEPPSI-*i*Pr as catalyst in Negishi and Stille couplings.



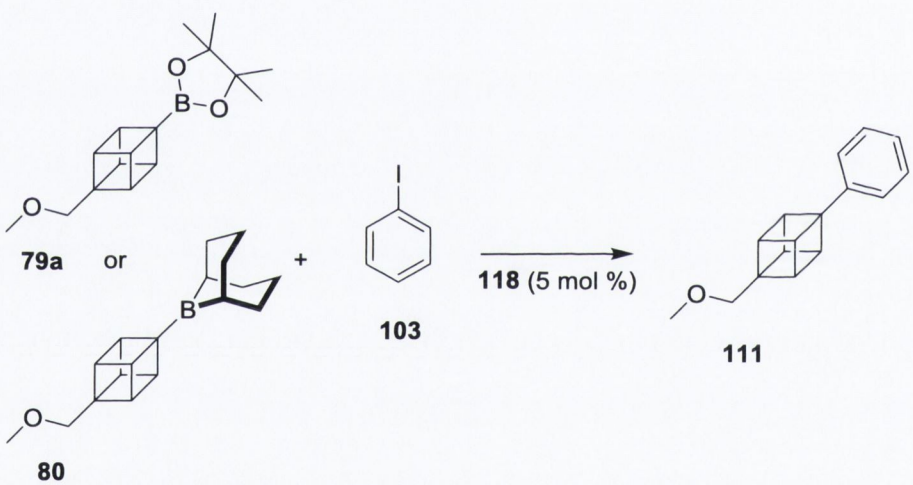
Entry	Cubane ("M")	Ar-I (eq.)	NMP (% v/v)	LiCl (eq.)	Temp (°C)	Time (h)	Observation
1	**83** (ZnX)	**104**	33	4	65	18	No cubane
2	**83** (ZnX)	**104**	0	4	65	18	No cubane
3	**83** (ZnX)	**104**	33	4	r.t.	18	No cubane
4	**83** (ZnX)	**104**	0	0	r.t.	18	No cubane
5	**83** (ZnX)	**103**	0	0	-55	3	No cubane
6	**83** (ZnX)	**103**[a]	0	0	-55	3	Trace **76b**
7	**87** ($SnBu_3$)	**104**	33	4	r.t.	18	No cubane
8	**87** ($SnBu_3$)	**104**	0	4	r.t.	18	No cubane

Reaction conditions: Metallocubanes were generated *in situ* from the reaction of **75** with *t*-BuLi in THF at -78 °C. Catalyst, salt and Ar-I were added after generation and heated. All coupling reactions were performed at 80 mM cubane concentration under argon using 5 mol % **118** and 1 eq. of Ar-I unless stated. [a] 0.33 equivalents **103** added.

Both tables present distinct reactivities with relation to the previous work. In all cases the PEPPSI catalyst was much more efficient at initiating transmetallation of the activated cubane nucleophiles than standard Pd-phosphine complexes. The product was still not a recognisable cubane system, however, and no organic residues, with the exception of the aryl halide, could be identified in any reaction flask. This led to the conclusion that, in all cases with **118** as catalyst, the cubane system underwent the same decomposition as was witnessed with the highly activated coupling conditions with Pd-phosphine complexes

discussed previously. This decomposition pathway and product(s) are still unidentifiable. Cyclooctatetraene can be confidently ruled out due to the absence of any alkene signals in the ^{1}H NMR spectra. Cuneane remains a possibility, but the complete absence of any spectral indication of its presence deems it unlikely. The lack of any discernible CH_3-O-CH_2 fragment in the ^{1}H NMR spectra provides compelling evidence that the products of the catalysis reactions are volatile alkanes and ethers which are too labile for characterisation. Removing the THF solvent in as mild a manner as possible failed to allow recovery of said fragments. Short of isolating the Pd-cubane complex, no further method of examining the mechanism could thus be conceived.

Table 3.10: Suzuki-Miyaura cross-couplings using Pd-PEPPSI-*i*Pr as catalyst.



Entry	Cubane	Base (eq.)	T (°C)	Time (h)	Result
1	**80**	1M NaOH/H_2O (4)	r.t.	18	No cubane
2	**80**	1M NaOH/H_2O (4)	r.t.	18	No cubane
3	**79a**	1M NaOH/H_2O (4)	r.t.	18	No cubane
4	**80**	1M NaOH/MeOH (4)	r.t.	18	No cubane
5	**80**	K_3PO_4 (10)	r.t.	18	No cubane
6	**80**	2M NaOH/MeOH (8)	-55	3	No cubane
7	**79a**	2M NaOH/MeOH (8)	-55	3	Trace **79a**
8	**80**[a]	2M NaOH/MeOH (8)	-55	3	Trace **80**
9	**79a**[a]	2M NaOH/MeOH (8)	-55	3	Trace **79a**

Reaction conditions: **79a** and **80** was generated *in situ* from the reaction of **75** with *t*-BuLi in THF at -78 °C. Catalyst, base and **103** were added after generation and heated. All coupling reactions were performed at 90 mM cubane concentration under argon using 5 mol % **118** and 1 equivalent of Ar-I unless stated. [a] 0.33 equivalents **103** added.

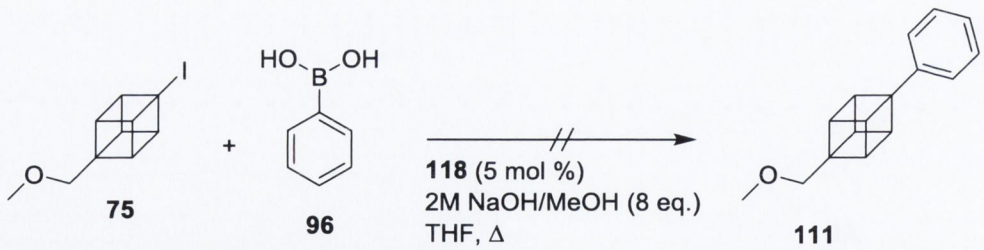
Certain key differences indicating the higher activity of the NHC-catalyst system with relation to the classical systems employed previously were nevertheless observed. Whilst with the standard Pd-phosphine catalysts there appeared to be a significant thermal effect with transmetallation/decomposition typically requiring elevated temperatures; the PdPEPPSI-catalysed transformation is temperature independent as both Negishi and Suzuki-Miyaura conditions led to decomposition at room temperature as well as when the reaction was performed at -55 °C for just three hours (Table 3.9, Entries 3-6; Table 3.10 Entries 1-6). Similarly, transmetallation and decomposition of the stannylcubane complex proceeded at room temperature (Table 3.9, Entry 8). The nature of the additives is also less crucial when utilising **118**. The presence of NMP in the Negishi or Stille reaction, which was previously a key component required for the catalytic decomposition, was unnecessary when using **118** as the catalyst system (Table 3.9, Entries 2, 5 and 8). The pronounced effect regarding the nature of the boron component in the Suzuki-Miyaura appears to be practically non-existent when using **118**. Only when performing the reaction at -55 °C for a short time period was any deviation between the reactivity of **79a** and **80** observed. Here, when using the pinacol ester (Table 3.10, Entry 7) trace starting material was recovered. This contrasts with the complete disappearance of BBN derivative **80** under identical conditions (Table 3.10, Entry 6).

To further probe the decomposition process three reactions with a significant excess (3 equivalents) of the cubane nucleophile were performed (Table 3.9, Entry 6 and Table 3.10, Entries 8 and 9). In all three cases, while some cubane was still present on work-up the ratio of cubane/aromatic material was so low as to indicate a significant level of decomposition occurred.

The decomposition of the cubane systems at -55 °C severely limits further analysis of the process. With the conditions discussed in the previous sections it was theorised that a thermal component may be involved in the decomposition pathway – indicating that if

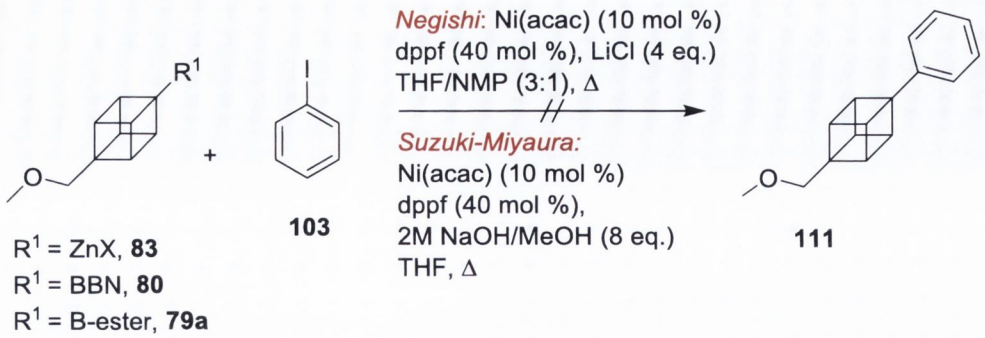
transmetallation could be achieved at lower temperatures reductive elimination and therefore cross-coupling may become competitive. The observed decomposition at low temperatures proves this assumption false, however. While proving that transmetallation can be achieved at much milder conditions it now also appears likely that the decomposition of the Pd-cubane complex is a favourable one both thermodynamically and kinetically and no avenues for trapping or observing this complex appear viable.

Before discarding the possibility of achieving the overall goal, four final reactions were performed. These involved reaction of iodocubane **75** with phenyl boronic acid **96** in the presence of **118** (Scheme 3.2) and the use of a simple nickel catalyst in the Negishi and Suzuki-Miyaura reactions (Scheme 3.3). Reaction of **75** and **96** gave unreacted cubane starting material, indicating that even with the highly active NHC catalyst the coupling of the tertiary halide remains impractical. In the presence of $Ni(acac)_2$ and dppf in THF heated to reflux overnight, the Negishi reaction of **83** gave de-iodinated cubane **76b** while the Suzuki-Miyaura couplings produced unreacted **79a** and **80**. Expansion of the investigations to more fully incorporate Ni-catalysis were not feasible given time constraints. However, the failure of the Ni catalyst used here to effect any noticeable change in the cubane materials under conditions effective for its Pd precursor imply that it is unlikely nickel will be any more effective than Pd as a catalytic centre.



75 96 111

Scheme 3.2: Attempted cross-coupling reaction of **75** using Pd-PEPPSI*i*Pr as catalyst.



Scheme 3.3: Cross-coupling reactions using nickel(II) catalysts.

3.7 Conclusions and future work

The failure to achieve any cross-coupling reaction with any of the various Pd-catalysed processes proved a significant disappointment. It does not seem likely that any palladium-catalysed cross-couplings of cubane scaffolds are viable synthetic pathways. While compelling evidence for the transmetallation of cubane nucleophiles was obtained in all cases, the exact nature of the decomposition products of this complex could not be determined. Ideally, the nature of this Pd-cubane intermediate would be determined, however, no facile way to achieve this could be envisaged and further investigations were deemed beyond the scope of the present synthetic study. Future work analysing the transition metal-catalysed cross-couplings of cubane will focus initially on the nickel or copper-catalysed processes of both halocubanes and the activated cubane nucleophiles previously discussed.[238-240] These catalytic systems have also been shown to effect the coupling of tertiary Grignard reagents in a Kumada-type cross-coupling.[241-243] In particular, the altered nature of the Cu catalytic cycles (or Cu-promoted processes) with relation to standard Pd-catalysed processes may be a benefit by modifying the standard transition metal intermediates.[244]

Ultimately, the goal of this work was to apply modern methodologies to a classical system – providing convenient access to a diverse scaffold system. Palladium-catalysed chemistry was thus the sole focus due to its synthetic utility, robustness and the fact that the two synthetic areas (cubane chemistry and sp^3 cross-couplings) had never been combined.

Another equally viable area of modern synthetic chemistry is the field of radical chemistry.[245-247] At the height of research into the cubane system the field of radical chemistry was in its infancy and often limited to harsh reagents and specific systems. From a more modern perspective, radical chemistry now offers mild, high yielding and chemoselective methodologies, allowing for the synthesis of diverse chemical systems *via* photocatalysis.[247,248] Application of some of these methodologies (*e. g.*, Burkhard König's recent work with the room temperature generation and coupling of alkyl radicals with aryl systems[249]) may ultimately facilitate the overarching goal of bringing cubane chemistry into the 21st century.

Chapter 4:

Cubane and

porphyrins

4.1 Background

Combining the two unique scaffolds of cubane and porphyrins under investigation in this work represents a key goal of the study. The unique structural characteristics of the cubane scaffold merged with the impressive optical and photophysical properties of the porphyrin framework offer a distinctive avenue in both fields. While porphyrins decorated with alkyl substituents are classical systems (*e. g.*, OEP), never before has a rigid alkane spacer been utilised in tetrapyrrole chemistry. By harnessing the rigidity and chemical stability of the cubane skeleton it was envisaged that electronically isolated, yet structurally defined porphyrin systems could be synthesised and their properties delineated. Initially, the marriage of these two scaffolds was to be accomplished *via* direct palladium-catalysed cross-coupling reactions. The failure of the chemistry discussed in Chapter 3 meant that alternate avenues, both direct and indirect, were pursued to achieve this combination. Three protocols were thus investigated; condensation chemistry, organolithium nucleophilic addition to the porphyrin macrocycle and Sonogashira reactions of alkynylcubanes. The results of each of these methodologies will be discussed in turn.

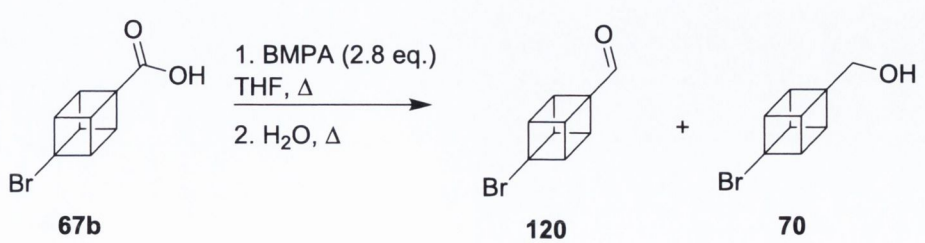
4.2 Condensation reactions of formylcubanes

Condensation techniques represent one of the most synthetically useful ways of introducing novel substituents at the meso position of the porphyrin core. Rothemund,[150,151] Lindsey[152-154] and MacDonald[155] condensations all allow for the ready synthesis of variously substituted porphyrins *via* the acid-catalysed reaction of pyrrole, or pyrrolic subunits, with aldehydes. This chemistry proceeds based on the nucleophilic reactivity of pyrroles at the 2-position, which combine with electrophilic carbon centres such as the carbonyl groups in aldehydes. The primary drawback of using condensation methodologies are the low yields often observed.[250] Condensation techniques such as this are effectively polymerisation reactions which occur as a combination of a series of reversible and irreversible steps. Target product formation only occurs when intermediates containing four

pyrrole subunits cyclise to form a porphyrinogen, allowing for subsequent oxidation to the porphyrin system. As a result, significant unwanted materials consisting of linear, polypyrromethane oligomers severely reduce the overall yield.[251] Additionally, acid-catalysed 'scrambling' of the tetrapyrrolic intermediates can cause major issues, particularly when less symmetrical systems are targeted, as this method tends to give a mixture of all possible isomers which require lengthy chromatography to separate, if possible at all.[163] Use of sterically hindered groups also presents a problem as the formation of oxidation-resistant porphodimethenes can become quantitative under certain conditions.[164,165]

4.2.1 Synthesis of formylated cubanes

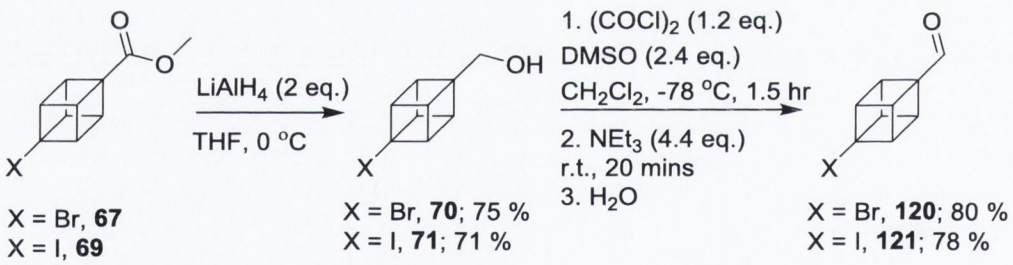
The first requirement for an investigation into any condensation reaction is the availability of significant amounts of appropriate aldehyde precursors. The most expedient way to synthesise large quantities of a formylated cubane derivative was thus considered. Reduction of 4-bromocubane-1-carboxylic acid **67b** directly to the aldehyde through use of *bis*(*N*-methylpiperazinyl)aluminium hydride (BMPA),[252,253] a reagent specifically tailored for the acid → aldehyde reduction, was initially attempted. As a reducing agent, BMPA proved unselective, with significant reduction to the alcohol oxidation state **70** occurring, as well as an overall loss of mass due to decomposition of the cubane scaffold (Scheme 4.1).[219] Low temperature reduction (-78 °C) of **67** with more standard reducing agents (*e. g.*, $LiAlH_4$, or $NaBH_4$) gave a similar mixture of aldehyde product **120** and hydroxyl product **70**, albeit with less decomposition of the cubane scaffold as seen with BMPA.



67b **120** **70**

Scheme 4.1: Attempted acid → aldehyde reduction on cubane system.

The relative ease with which acid **67b** was reduced to the alcohol **70** led to the synthesis of formylcubanes **120** and **121** through a two-step reduction/oxidation process starting from halogenated cubane esters **67** and **69**. The optimised reduction process was that described in Chapter 2 ($LiAlH_4$ at 0 °C for three hours). Several methods for the oxidation of (hydroxymethyl)cubanes are reported in the literature, with many giving high yields.[45,219,254-256] Use of the inexpensive, inorganic oxidant, pyridinium chlorochromate (PCC)[256] allowed for synthesis of **120** in 71 % yield. The significant amount of chromium waste, however, limited its application on a large scale. In spite of its odour, Swern conditions[257] were best employed for large scale syntheses,[24] and allowed for the synthesis of **120** and **121** in 80 and 78 % yield, respectively (Scheme 4.2). The retention of the halide functionality in both formylated cubanes was intended to provide an avenue for further manipulations of the cubane scaffold through the chemistry discussed in Chapter 2. In this manner, the complete exploitation of the cubane scaffold as a porphyrin substituent was envisaged.

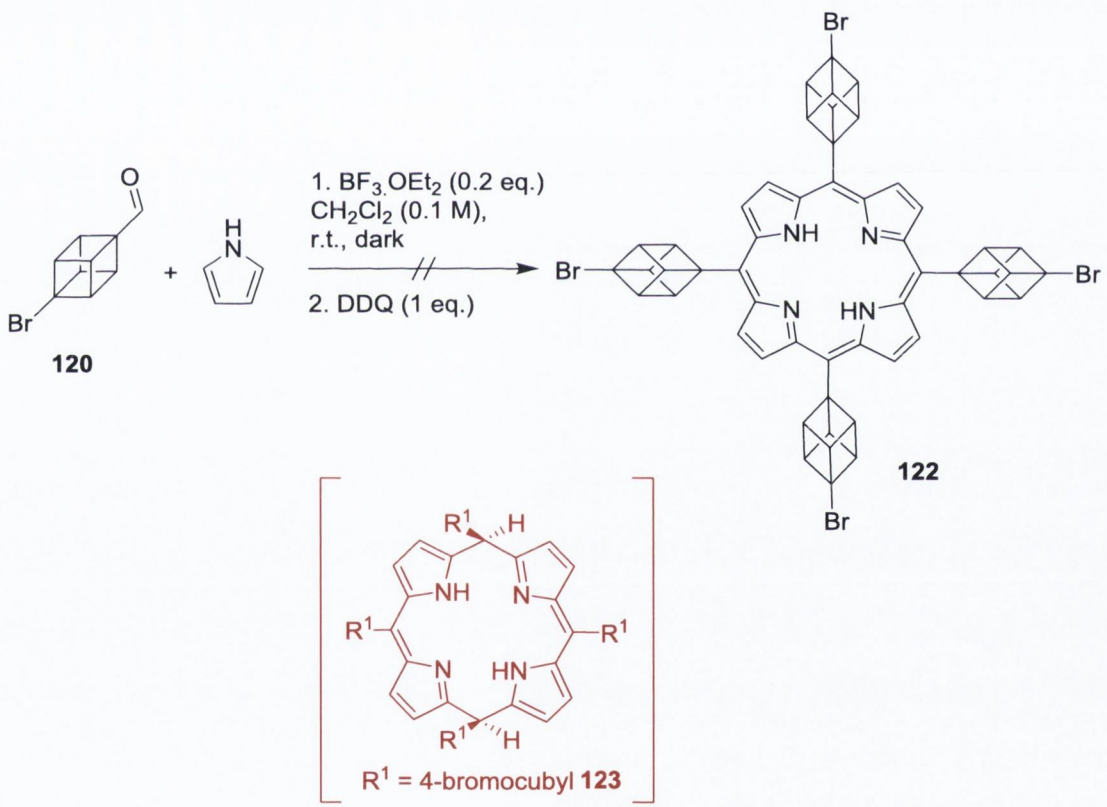


Scheme 4.2: Optimised reduction/oxidation route to formylated cubanes.

4.2.2 Trial condensation reactions

Typically, condensations involving aliphatic aldehydes are more challenging and lower yielding than aromatic condensations.[251] This is due, in part, to the reduced electrophilic nature of aliphatic aldehydes and their greater tendency to undergo scrambling, but more importantly to the increased distortion experienced in alkyl-substituted porphyrins which can inhibit tetrapyrrole formation while also leading to their rather unique photophysical properties.[126] This problem is further exacerbated when sterically hindered

aldehydes are utilised in conjunction with pyrrole to generate porphyrins, hindered by both the aforementioned distortions as well as the steric demand around the reactive carbonyl centre.[258] Using the *tert*-butyl group as a synthetic analogue for cubane; the early attempts to synthesise 5,10,15,20-tetrakis(*tert*-butyl)porphyrin proved highly problematic. While the yield of the current optimised synthesis is reasonably high at 15 %,[148] isolation and purification of this compound, due to its significant non-planarity, still proves challenging.[258] The conditions of this optimised synthesis (stirring overnight in the dark with boron triflouride etherate as the acid catalyst) were employed in the first attempt to generate a cubane-substituted porphyrin **122** (Scheme 4.3).



Scheme 4.3: Attempted synthesis of 5,10,15,20-tetracubylporphyrin **122** with probable porphodimethene product (red) **123**.

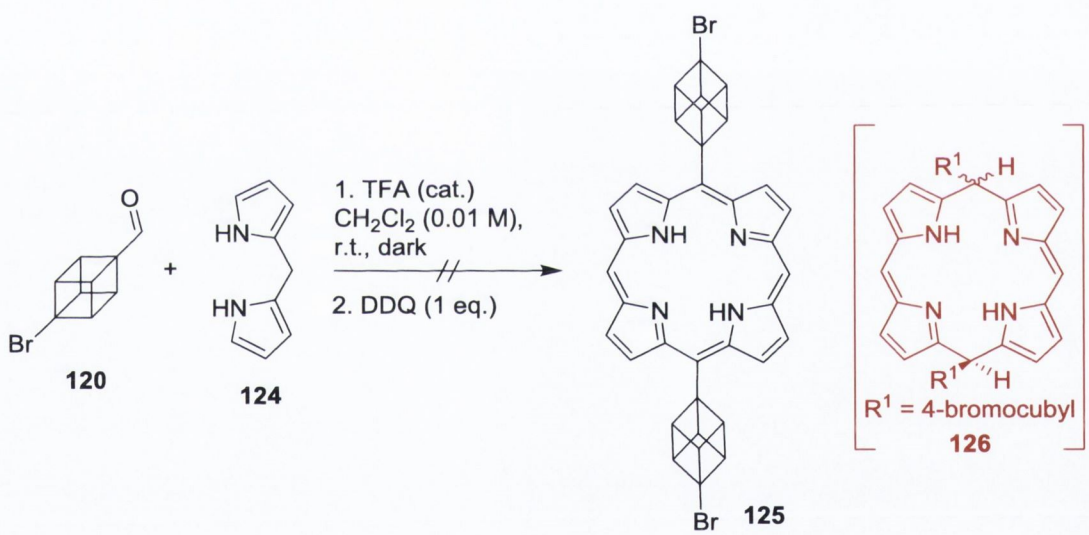
While aldehyde **120** was completely consumed during the course of the reaction, no porphyrin product could be observed amongst the reaction products. UV-vis spectroscopy indicated the presence of a porphodimethene product (a semi-reduced porphyrin

intermediate lacking some double bonds on the methine bridges, *e. g.*, **123**). Such porphodimethene compounds can be highly resistant to oxidation due to the steric demand of the substituents on the macrocycle and are often stabilised by positive *syn*-interactions of the groups in the 5- and 15-positions.[173,259] This tendency can become even more pronounced when sterically demanding groups, *e. g.*, adamantane, are bound to the meso positions.[260] This material could not be purified for characterisation so its exact structure could not be unambiguously determined. The main issue was the scale required to guarantee usable quantities of porphyrin. Here, 7 mmol of **120** were used but this, ideally, would need to be increased at least tenfold to allow for complete characterisation of intermediates formed.

Due to the failure to synthesise the tetrasubstituted porphyrin **122**, attention turned towards the 5,15-disubstituted system **125** (Scheme 4.4). The reduced substitution was expected to make this porphyrin more synthetically accessible by reducing the distortion present in the tetrasubstituted system, thereby making oxidation to the porphyrin product **125** more energetically favourable than the porphodimethene **126**. Additionally, [2+2] condensations between an aldehyde and dipyrromethane (DPM, **124**)[156] to make a 5,15-disubstituted porphyrin tend to be higher yielding than condensations to generate tetrasubstituted systems and, as such, can be performed on a much smaller scale.[155,159] Reported examples of similar syntheses show that 5,15-di(*tert*-butyl)porphyrin has been successfully synthesised just once in 4.8 % yield, a drastic reduction on the yields of 30-40 % seen with less hindered aliphatic aldehydes.[261]

The reaction depicted in Scheme 4.4 was performed twice on a 10 mmol scale but, again, no tetrapyrrole product could be obtained in large enough quantities for characterisation. The various isolated products in both cases were orange, red or pink, indicating some degree of tetrapyrrole formation. UV-vis analyses indicated some porphyrin products present but these could not be isolated. Metallation of the porphyrin core is a

commonly used synthetic method to improve separation and identification of tetrapyrrolic products. This was attempted using nickel(II) acetylacetonate with the crude reaction products here, but isolation and characterisation of the products was not improved. Again, scale presents the major issue with a significantly increased amount of reagents required to provide a conclusive assessment of what is occurring. Based on the spectroscopic information available, the most probable structure of the tetrapyrrolic material obtained as the major product is porphodimethene **126**. The fact that some tetrapyrrolic products are being formed is a promising sign and indicates that it should be possible to obtain cubyl porphyrins (albeit in low yields) in this manner. However, lack of sufficient cubyl starting material inhibited a more exhaustive analysis of this route at the present time.



Scheme 4.4: Attempted [2+2] condensation of **120** with probable product **126**.

4.3 Aromatic substitution reactions *via* organolithium chemistry

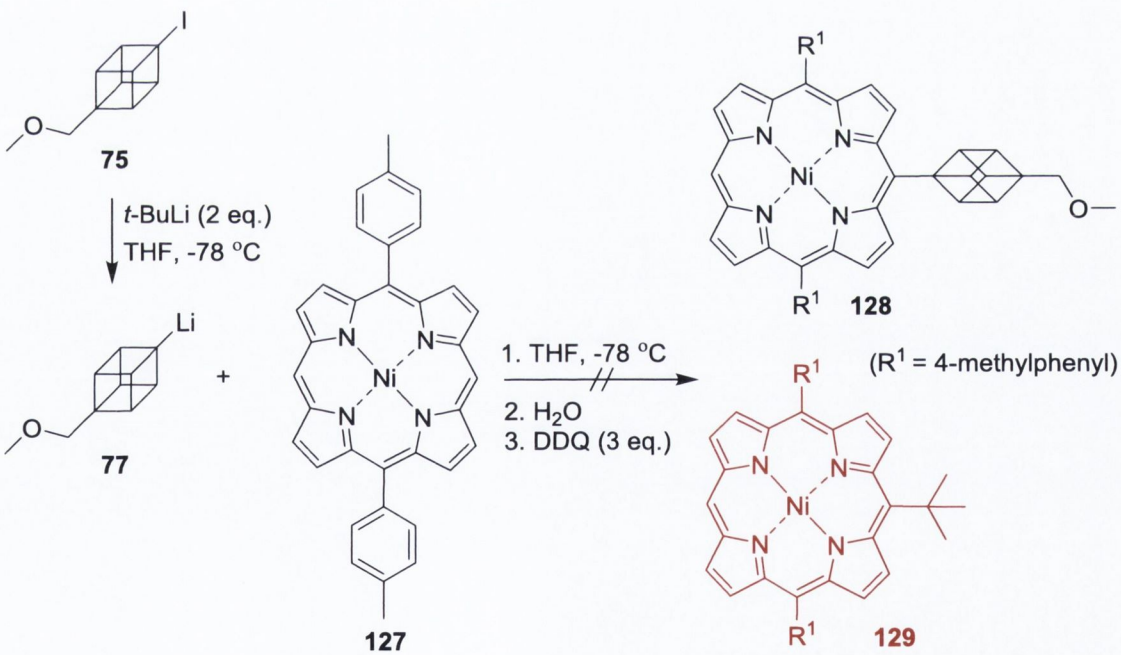
An organolithium approach is a powerful one, commonly used to effect the introduction of individual substituents, particularly alkyl groups, to the porphyrin macrocycle.[119,173] The primary advantage, here, with relation to condensation methodologies is the use of a preformed porphyrin scaffold. Thus, the low-yielding condensation reaction is avoided, allowing for a more efficient introduction of groups that possess a high synthetic cost. This straightforward addition/oxidation approach relies on the

reactivity of the porphyrin meso position towards strong nucleophiles and allows for the introduction of virtually any alkyl or aryl residue.[173,174,177,262] Typically, free-base porphyrins work better when installing aryl residues while Ni(II) complexes are preferential when introduction of alkyl residues is desired. The major drawback involves the formation of RLi reagents which must be kept scrupulously anhydrous and used in significant excess (often 6-10 equivalents).[175] With specific attention to the present work, other complications include multiple alkylation or β-alkylation products when working with sterically hindered alkyllithium reagents,[174,177,178] and the formation of porphodimethene products when highly distorted systems are targeted.[173,179,180] Using the *tert*-butyl group as an analogue again, its use in organolithium chemistry of this type has been somewhat limited, with less hindered alkanes (*e. g.*, *n*-hexyl or *n*-butyl) typically preferred when mixed alkyl/aryl systems are desired. One example of the successful addition of a *tert*-butyl group to the meso position in this manner has been reported.[177] Here, the product was obtained in 53 % yield when using a Ni(II) porphyrin with the presence of several chromophoric side products noted (most likely β-alkylation products). Reaction with a free-base porphyrin gave a complex mixture of side products and no formation of the target. While this proves that sterically demanding substituents may be installed *via* this route, the reaction is nevertheless quite demanding.

One significant advantage of employing this route is that it follows from the organolithium reactions of cubane described in Chapter 2. Thus, all optimisation of starting materials and generation conditions had been performed previously. Iodinated cubane **75** was lithiated with *t*-BuLi at -78 °C before dropwise addition to a solution of Ni(II) porphyrin **127** in THF under argon at -78 °C (Scheme 4.5). With five equivalents of **77**, no formation of target **128** was observed with the final compounds upon quenching being unreacted **127**, de-iodinated cubane **76b** and some unidentifiable coloured materials.[i] Increasing the

[i] Presumably porphyrin decomposition products. There was no indication that these chromophoric materials contained cubane-appended porphyrins and, as such, their isolation was not effected.

quantity of **77** employed to ten equivalents resulted in a significant increase of these side products as well as providing *tert*-butyl substituted porphyrin **129** in *ca.* 10 % yield. This was due to the significantly increased amount of organolithium required initially, resulting in some unreacted *t*-BuLi being present when the solutions of **77** and **127** were combined. Reactions were repeated to ensure consistency but no indication of **128** was observed in any trial.[i] The lack of any trace **128** product formation from any trial indicates that this is not a viable route towards cubane-substituted porphyrins. Trial reactions were also performed with NiOEP, the material employed in the discovery of this methodology.[262] In this case the products were simply unreacted porphyrin starting material and de-iodinated cubane **76b**. The most plausible explanation for the failure of **77** to participate in this chemistry is a steric argument – the added bulk and density of the cubane skeleton with relation to the *tert*-butyl group is enough to inhibit reaction of the former.



Scheme 4.5: Attempted substitution reaction of **127** with generated cubyllithium **77**.

[i] From personal experience and experiences of others within the Senge group, reactions with generated organolithium reagents (rather than those commercially available) such as this can often be challenging regardless of the substituent, with the reaction appearing extremely sensitive to the manner of organolithium generation. For example, aryllithium reagents that appeared to have generated perfectly can often lead to no reaction products.

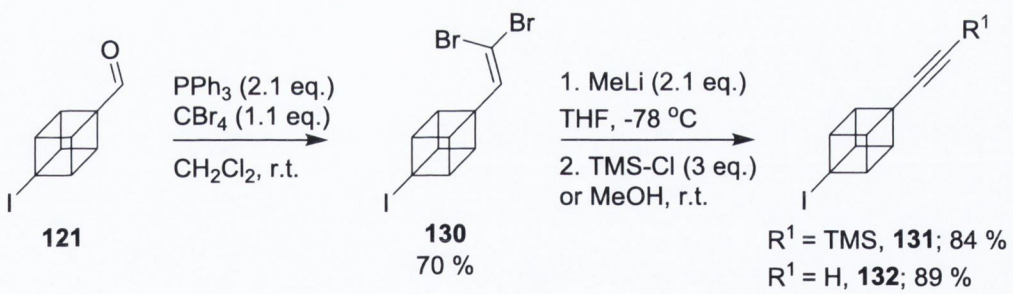
4.4 Alkynylcubanes as Sonogashira cross-coupling partners

This failure of direct substitution methods necessitated a revised synthetic route to cubanylporphyrins. Having exhausted the straightforward, classical routes, the only simple option remaining was transition metal-catalysed chemistry. Initially, this was the planned route but the failure of cubane to participate in direct palladium-catalysed reactions prevented its application. One avenue previously unexamined, however, was the introduction of a reactive linker/spacer on the cubane scaffold which would facilitate subsequent Pd-catalysis. Such methodologies have often been used in porphyrin chemistry (see Chapter 5) to overcome some of the electronic or steric influences of the porphyrin macrocycle when working with reactive functional groups.

The selected spacer needed to be small, easily installed through classical routes and chemically robust, as well as accommodating the structural benefits of attaching the cubane scaffold (*i. e.*, inflexibility and electronic isolation). Alkyne linkers and Sonogashira cross-couplings stood out in this respect as best fulfilling these criteria.[50,230,263] Attachment of an alkyne maintains the rigidity of the overall system – a key goal. Similarly, while the sp-hybridised alkynyl carbons are electronically conjugated, the sp^3 cubane skeleton will still inhibit any electronic communication between systems attached to the cubane skeleton. The major drawback is that addition of an alkyne spacer will inevitably reduce the structural impact the cubane moiety will have on the porphyrin macrocycle. Methodologies towards the synthesis of alkynylcubanes have been reported[45,111] but little work has been performed on their Sonogashira reactivity so this also resonates with the initial goal of updating cubane chemistry with modern techniques – albeit not at a site directly on the cubane scaffold. By performing the coupling chemistry at a distal site, the problems encountered with the activated cubanes previously were expected to be avoided as were significant steric interactions with the porphyrin core.

4.4.1 Synthesis of alkynylcubanes

The synthesis of alkynylcubanes was first documented by Eaton and co-workers in 1991[111] and further elaborated three years later.[45] While many synthetic avenues were investigated, the optimum synthesis for terminal cubylacetylenes is presented in Scheme 4.6. Here, formylated cubane **121** was initially subjected to the modified Wittig reaction[264,265] of Corey and Fuchs[266] using triphenylphosphine and carbon tetrabromide to provide dibromoalkene **130** in 70 % yield. Treatment with methyl lithium (to avoid metal-halogen exchange) furnished the lithium acetylide which, upon quenching with TMS-Cl, gave the TMS protected alkyne **131** in 84 % yield. Quenching with methanol instead produced the free acetylene **132** in 89 % yield. Both **131** and **132** were stable to standard work-up and chromatographic procedures but **132** had to be purified and refrigerated immediately to prevent polymerisation and decomposition of the free acetylene group.[i] The TMS-alkyne **131** is stable to both air and light so its purification and storage were more straightforward. This compound underwent near quantitative deprotection to **132** on treatment with KOH in methanol, providing another (safer) avenue to the terminal acetylene moiety.



Scheme 4.6: Synthesis of cubane monoacetylenes **131** and **132**.

Concomitantly, the synthesis of 1,4-diethynylcubanes **136** and **137** was also pursued (Scheme 4.7). Pending the successful application of Sonogashira methodologies to **132**, **137**

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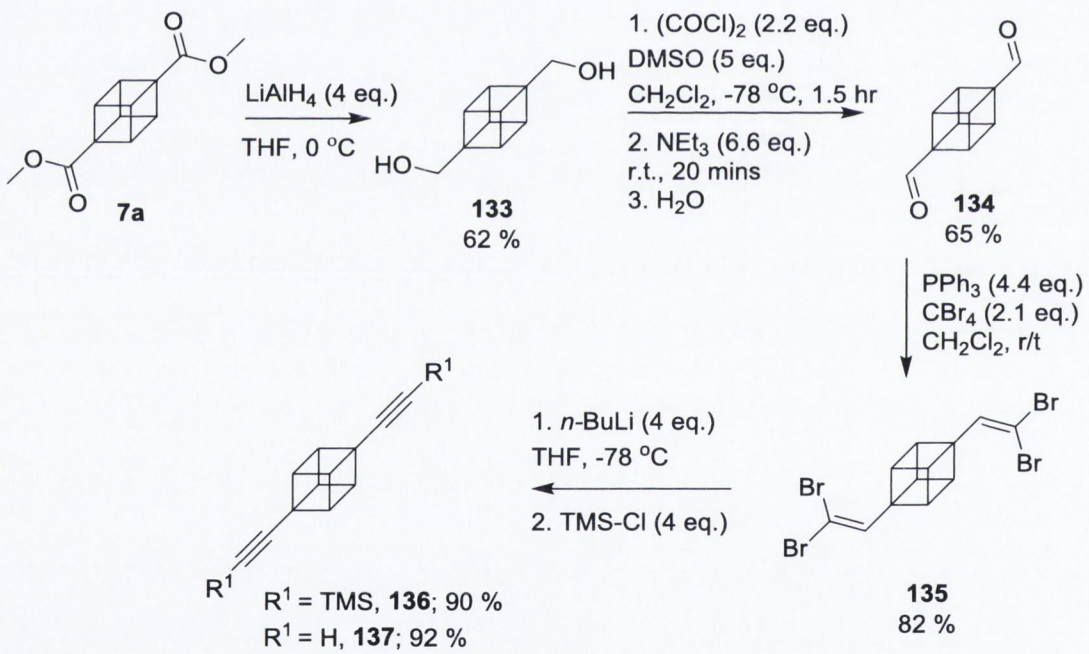
[i] Compound **132** is a potentially high-energy material as the original authors cite one instance where an old, crude sample of **132** exploded with force on contact with a spatula. No such difficulties were observed during the present work but great care was nevertheless taken when handling all alkynylcubanes.

was seen as an ideal system to fulfil the goal of utilising cubane as an isolator in bridged porphyrin systems with the cubane moiety orienting substituents in a precise, regiochemically defined manner. The synthesis of **136** and **137** proceeded exactly as described above; starting from the diester **7a** through reduction (→ **133**) and oxidation (→ **134)** followed by conversion to dialkene **135** and lithiation and trapping to provide protected *bis*alkyne **136** or terminal *bis*acetylene **137**. The lack of a halogen allowed the use of *n*-BuLi in the alkyne conversion, enabling higher yields than those obtained with MeLi previously. The insolubility of diol **133** in standard organic solvents presented the only complication. Here, the high polarity of the two hydroxyl groups required the addition of DMSO during the Swern oxidation process to solubilise **133**. Otherwise, both the protected *bis*alkyne **136** and terminal *bis*alkyne **137** were accessed without difficulty in high yields.[i]



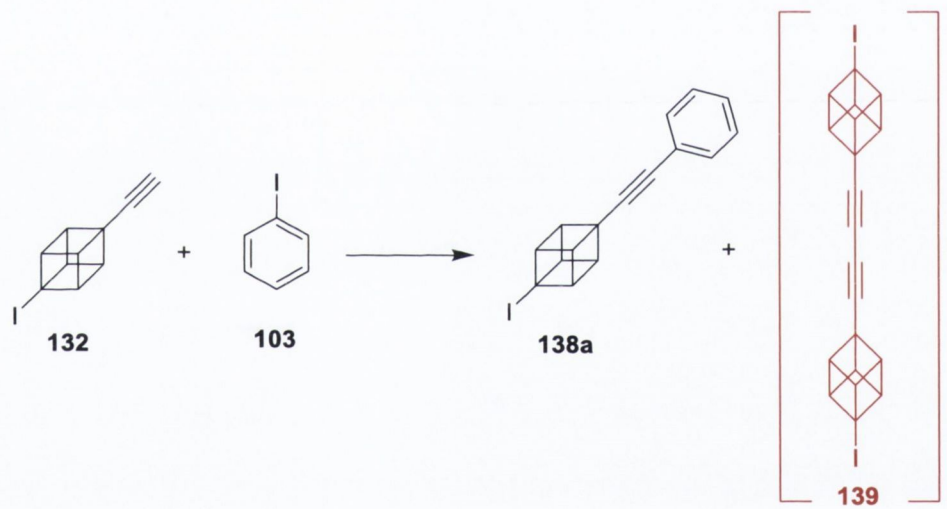
Scheme 4.7: Synthesis of diethynylcubanes **136** and **137**.

[i] Both **136** and **137** displayed complete stability on work-up but storage at 0 °C was required for **137** as per the monoalkyne **132**.

4.4.2 Preliminary reactivity studies

The Sonogashira cross-coupling of an alkynylcubane with iodobenzene, as discussed in Chapter 1, represents one of the two reported Pd-catalysed cross-coupling reactions involving the cubane scaffold.[111] Repeating the reported reaction conditions proved impossible, however, as the copper source employed, Cu_2Br_2, is an unusual one not commercially available. The lack of any reaction optimisation within this paper or any reference to the reaction in subsequent publications meant an initial investigation into the optimum conditions for the cross-coupling of **132** was required. The results of this optimisation of the reaction between **132** and iodobenzene **103** are detailed in Table 4.1.

Table 4.1 Optimisation of Sonogashira reaction between **132** and **103**.



Entry	Pd Catalyst (mol %)	Co-catalyst (mol %)	Base/ Solvent	Temp (°C)	Yield (%)
1	$Pd(PPh_3)_2Cl_2$ (10)	CuI (30)	TEA	r.t.	75
2	$Pd(PPh_3)_2Cl_2$ (10)	CuI (30)	TEA	80	44
3	$Pd(PPh_3)_2Cl_2$ (10)	CuI (30)	DEA	r.t.	51
4	$Pd(PPh_3)_2Cl_2$ (10)	CuI (30)	Piperidine	r.t.	74
5	$Pd(PPh_3)_2Cl_2$ (10)	CuI (30)	THF/TEA (5:1)	r.t.	56
6	$Pd(PPh_3)_4$ (10)	CuI (30)	TEA	r.t.	98
7	$Pd(dppf)Cl_2$ (10)	CuI (30)	TEA	r.t.	56
8	$Pd_2(dba)_3$ (15)/$AsPh_3$ (60)	N/A	TEA	r.t.	53

Reaction conditions: All reactions were performed at 0.1 M cubane concentration using 3 equivalents of **103** under argon for 16 hours. Yields are isolated yields after column chromatography (silica gel).

Table 4.1 shows that **132** represents a viable Sonogashira cross-coupling partner with successful coupling to form **138a** observed in all cases. The first reaction employed standard Sonogashira cross-coupling conditions [$Pd(PPh_3)_2Cl_2$, CuI in neat NEt_3, Entry 1] and gave a yield of 75 %. This was therefore used as the starting point for further optimisation. In terms of temperature the reaction progresses best at room temperature as heating the reaction to 80 °C (Entry 1 *vs.* Entry 2) led to a reduction of 30 % in the isolated yield. This reduction was caused by the presence of significant quantities of Glaser-coupled alkynylcubane **139**, presumably facilitated by the elevated temperature.[267] The nature of the base/solvent employed plays the most significant role in this cross-coupling.[263,268] Replacing triethylamine with the less hindered base diethylamine (Entry 3) led to a significant reduction in yield while use of the heterocyclic base piperidine (Entry 4) produced an almost identical yield. Use of THF as solvent in conjunction with TEA similarly reduced the yield (Entry 5). As such, neat triethylamine was chosen as the optimum solvent and base. Finally, a small catalyst screen was performed. Surprisingly, the addition of a Pd(0) catalyst in the form of $Pd(PPh_3)_4$ provided the best yield of 98 % (Entry 6) with the more hindered catalyst $Pd(dppf)Cl_2$ providing a yield of just 56 % (Entry 7). Given that the active Pd catalyst system in both $Pd(PPh_3)_4$ and $Pd(PPh_3)_2Cl_2$ is identical, the significantly improved yield with the Pd(0) precatalyst cannot be fully explained but the results were corroborated by repeat reactions. The most plausible explanation is that the presence of additional PPh_3 ligands in solution increases the catalyst turnover rate through ligand exchange and thus the reaction rate, [263] thereby inhibiting competitive processes such as Glaser coupling.[i] One final test to examine a copper-free Sonogashira reaction (effectively a Heck coupling) was performed (Entry 8).[230,269] While the yield of 53 % appears low, the room temperature cross-coupling in the absence of a significant level of Cu(I) was considered a success, given some of the

[i] No attempts to prove this theory using $Pd(PPh_3)_2Cl_2$ and excess PPh_3 were performed however, given the yield achieved with the $Pd(PPh_3)_4$ system.

sensitivities to copper encountered subsequently (*vide infra*). Ideally, a further screen of the catalyst loadings required would be performed as 10 mol % is relatively high by modern synthetic standards. Time constraints prevented this, however, and it remains a topic for further investigation.

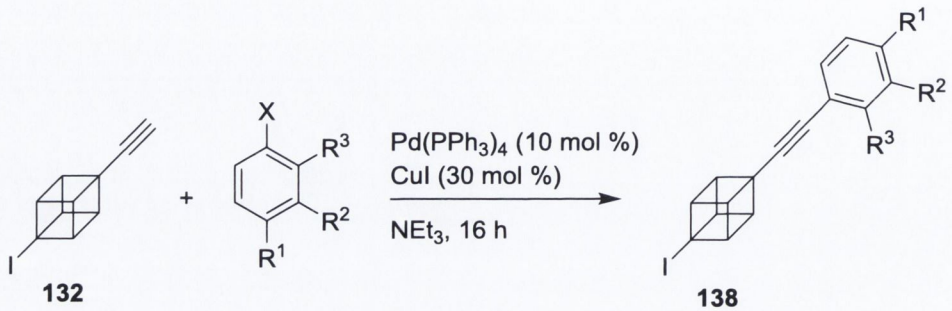
4.4.3 Probing the electronic tolerance

The investigations in Table 4.1 all utilised the highly reactive coupling partner iodobenzene. While indicating that **132** can participate in Sonogashira cross-coupling reactions, these results provide no information towards the electronic tolerance acceptable within the aryl halide component. Given the unique electronic nature of porphyrins, it was thus decided to further probe the reaction conditions using a small library of electron withdrawing and electron donating aryl halides. Results of this investigation are presented in Table 4.2. In this manner, it was hoped that, while probing the electronic tolerance of the reaction, introduction of groups with potential for subsequent reactivity would also be achieved. As such, only aryl halides possessing functional groups conducive to further functionalisation reactions were assayed.

The results in Table 4.2 indicate that the Sonogashira reaction of **132** is tolerant of electronic changes in the aryl substituent. As expected,[270] the presence of electron withdrawing groups on aryl iodides in the *para*- (-CO_2Et, Entry 1) or *ortho*- (-Br or -CHO, Entries 3&5) positions allow for the most efficient cross-couplings with yields in the region of 90 % obtained. Introducing an electron releasing group in the *para*- (-NH_2, Entry 2) or *meta*- (-OH, Entry 4) positions results in a slightly diminished yield of 75-80 %, which may, in part, be due to the reduced solubility of products **138c/e**. In each of the cases, products **138b-f** were isolated as solids by column chromatography (silica gel) and each possesses a functional group allowing for further expansion of the scaffold potential. Overall, regardless of electronic effects, aromatic iodides are thus robust Sonogashira cross-coupling partners

with **132** with the conditions optimised previously being generally applicable across a series of aromatic systems.

Table 4.2: Reaction of **132** with various aryl halides to probe electronic tolerance of the Sonogashira cross-coupling reaction.



132 **138**

Entry	X	R^1	R^2	R^3	Temp (°C)	Product	Yield (%)
1	I	CO_2Et	H	H	r.t.	**138b**	90
2	I	NH_2	H	H	r.t.	**138c**	76
3	I	H	H	Br	r.t.	**138d**	90
4	I	H	OH	H	r.t.	**138e**	79
5	I	H	H	CHO	r.t.	**138f**	88
6	Br	H	H	H	r.t.	**138a**	0
7	Br	H	H	H	65	**138a**	68
8	Br	NO_2	H	NO_2	65	**138g**	51
9	Br	CN	H	H	65	**138h**	64
10	Br	SH	H	H	65	**138i**	n/d
11	Br	CH_2Br	H	H	65	**138j**	n/d

Reaction conditions: All reactions were performed at 0.1 M cubane concentration using 3 equivalents of aryl halide, $Pd(PPh_3)_4$ (10 mol %) and CuI (30 mol %) under argon for 16 hours. Where applicable, yields are isolated yields after column chromatography (silica gel).

The success observed with aryl iodides led to investigation of their less reactive, but more readily available, brominated counterparts. While the coupling of **132** with iodobenzene was effected at room temperature, the application of identical methodologies to the coupling of **132** with bromobenzene produced no coupled product (Entry 6). Successful coupling to provide **138a** was only achieved when the reaction vessel was heated to 65 °C overnight (Entry 7). While the yield here of 68 % was significantly lower than that observed with iodobenzene, due to contamination with homodimer **139** caused by the elevated temperature, the result nevertheless proved that reasonable yields of cross-coupled products could be achieved with simple aryl bromides. It must also be noted that, typically,

Sonogashira reactions are performed with a slight excess of the alkyne partner.[230,263] Here, because **132** was the component under investigation, an excess of aryl halide was employed in all cases. While this had no effect with the aryl iodide couplings, better results might be obtained with aryl bromides if a slight excess of **132** was employed.

Subsequent expansion of this methodology to incorporate electronically activated and deactivated aromatic bromides provided similar results to those observed with the aryl iodides, albeit in lower yields. Electron withdrawing groups are once again preferred with 2,4-dinitrophenyl- (Entry 8) and 4-cyanophenyl- (Entry 9) successfully introduced in 51 and 64 % yields, respectively. While lower than their iodo analogues, these yields are still reasonable and the compounds **138g/h** both provide for further functionalisation avenues on the aryl system. The results with electron-rich aryl bromides were less successful. Addition of 4-bromobenzenethiol (Entry 10) gave several distinct products which were inseparable by standard chromatography. These were identified by mass spectrometry as various disulfide linked compounds. While successful coupling with **132** to give target compound **138i** was observed, the contamination with homo- and hetero-disulfide dimers made analysis of the degree of cross-coupling impossible. Similarly, addition of 4-bromobenzyl bromide (Entry 11) gave a complex mixture of products, presumably due to the two potential halide reaction sites. While this was not observed in the coupling of 1-bromo-2-iodobenzene (Entry 3), the reduced reactivity of the aryl bromide towards cross-coupling, together with the increased temperature, allowed the benzyl bromide to compete in the coupling reaction. Entry 3 presents the most compelling evidence for the divergent reactivity of the two halogen species. Only the brominated product **138d** was obtained with no indication of any cross-coupling through the aromatic bromide observed at room temperature.

The strengths and electronic limitations of the Sonogashira cross-coupling reaction of **132** were thus identified and both aromatic iodides and bromides were found to be viable coupling partners under appropriate conditions. Similarly, all of the novel products **138b-h**

formed possess reactive groups which will allow for further synthetic manipulation, potentially providing access to more highly substituted scaffold systems.

4.4.4 Sonogashira cross-couplings with porphyrin systems

Pursuant to the success of the cross-couplings with electronically altered aromatic systems attention returned to the initial goal of cubane-porphyrin constructs. The results in the previous section indicated electron deficient iodides as the most reactive cross-coupling partners. Porphyrins fulfil the initial electronic requirement but, in general, meso-brominated porphyrins are more readily available than their iodinated counterparts.[185] Studies discussed in Chapter 5 will also show little difference in the reactivity of meso iodinated and brominated porphyrin systems towards similar cross-coupling reactions. As such, meso brominated porphyrins **147b** and **154b** were utilised in the coupling reactions with **132** (Table 4.3).[i]

Two bromoporphyrins were used in this study, a Ni(II) complex **147b** and free-base **154b**. While the insight into the reactivity of **132** obtained in the previous section proved useful, the distinct reactivity of the porphyrin complexes necessitated a revisiting and slight modification of the optimised conditions. While three equivalents of aryl halides per equivalent of **132** was utilised previously, these ratios proved unworkable from a porphyrin perspective. Primarily, an excess of the alkynyl partner is required due to the reduced reactivity of porphyrinoid systems with respect to standard cross-coupling methodologies on account of their unique electronic properties.[193] Additionally, the weights of the reactants involved are quite divergent. Applying a 3:1 porphyrin to cubane ratio with an appropriate weight of **132** would require an impractically high amount of porphyrin. Reversing the ratio, however, and therefore resembling more typical porphyrin alkynylations,[271-273] makes the weights of the two species required much more practical. As such, a small optimisation of

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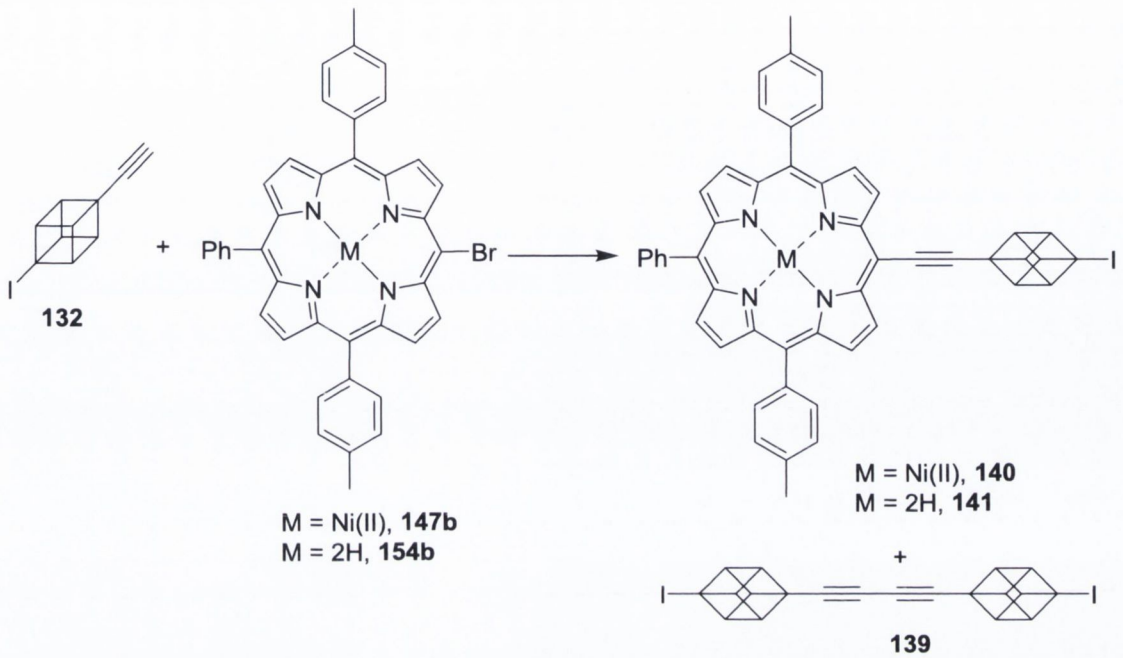
[i] The synthesis of these brominated porphyrins will be discussed in detail in Chapter 5.

the reactivity of **132** with **147b** and **154b** was initiated with the results displayed in Table 4.3.

Table 4.3: Sonogashira cross-coupling reactions of **132** with bromoporphyrins.



Entry	132 (eq.)	Por.	Catalyst System (mol %)	Temp (°C)	Solvent	Yield (%)
1	3	**147b**	$Pd(PPh_3)_4$ (10)/CuI (30)	60	TEA	n/d[b]
2	5	**147b**	$Pd(PPh_3)_4$ (10)/CuI (30)	80	TEA	n/d[b]
3	2.5[a]	**147b**	$Pd(PPh_3)_4$ (10)/CuI (30)	80	TEA	n/d[b]
4	5	**154b**	$Pd_2(dba)_3$ (15)/$AsPh_3$ (100)	65	TEA	0
5	2.5	**154b**	$Pd_2(dba)_3$ (15)/$AsPh_3$ (200)	65	THF:TEA (3:1)	73
6	2.5	**147b**	$Pd_2(dba)_3$ (15)/$AsPh_3$ (200)	65	THF:TEA (3:1)	63

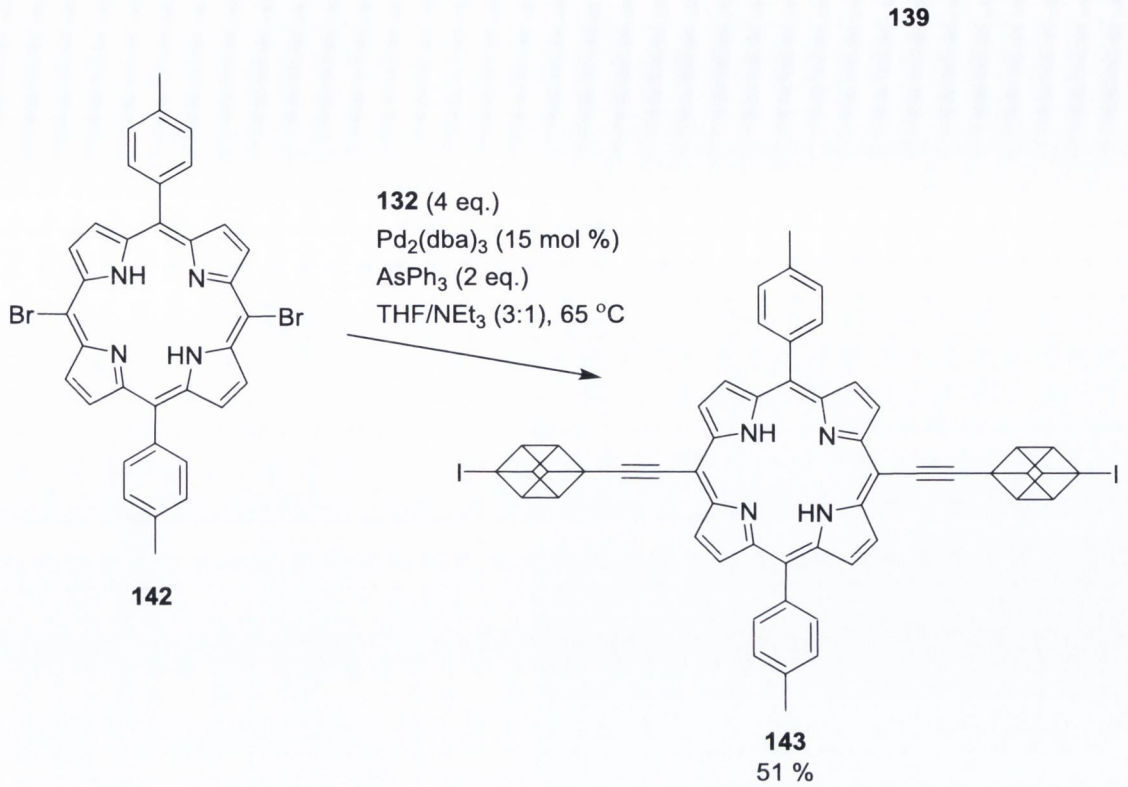
Reaction conditions: All reactions were performed at 30 mM porphyrin concentration under argon for 16 hours. Where applicable, yields are isolated yields after column chromatography (silica gel). [a] Alkynylcubane **132** was added in two portions over 3 hours. [b] Product isolation was impeded by Glaser-coupled dimer **132**.

Application of the optimised catalytic conditions using three equivalents of **132** and Ni(II) bromoporphyrin **147b** allowed for detection of target compound **140**, along with a significant amount of unreacted **147b**. Successful isolation of **140** from the product mixture proved impossible due to contamination of all porphyrin-containing fractions with homocoupled cubane dimer **139**. Attempts to maximise product formation *via* increasing the amount of **132** (Entry 2) proved unsuccessful due to concomitantly increased levels of **139**. The third attempt (Entry 3) focused on minimising this by-product by reducing the

equivalents of **132** and adding it in two portions to the reaction flask. While the quantity of **140** appeared to increase, it remained inseparable. The dimerisation process to **139** must be a Glaser process, which requires both O_2 and Cu.[267,274] All of the reactions were performed in a standard inert atmosphere using solvents thoroughly degassed with argon so the presence of Cu became the only controllable factor.

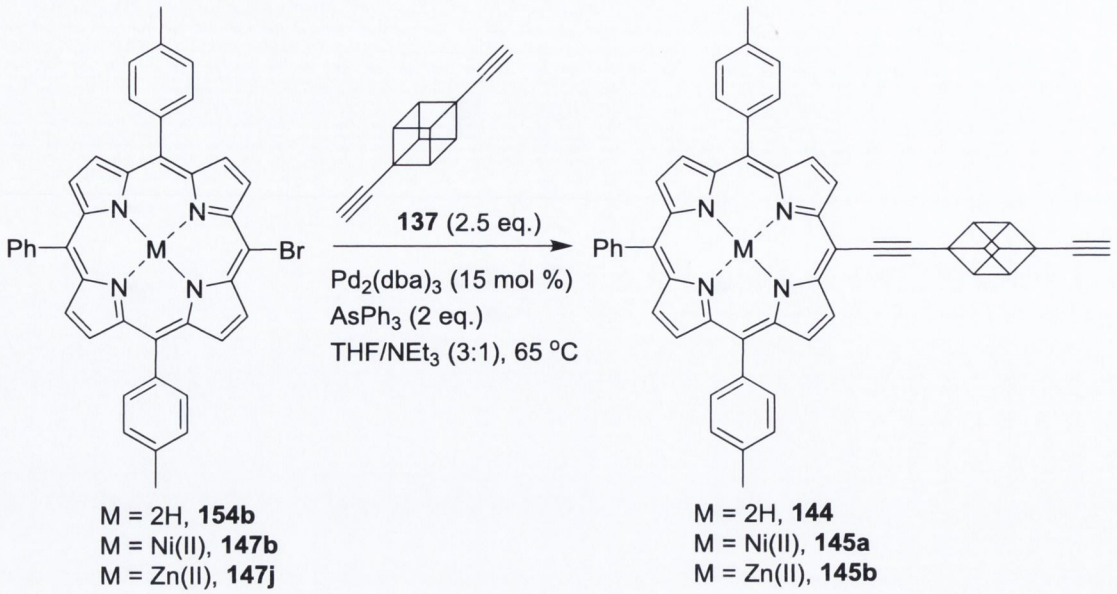
Copper-free Sonogashira coupling methodologies (*i. e.* Heck couplings) have long been employed in porphyrin chemistry, particularly with free-base porphyrins.[269] These conditions were shown to be effective for the coupling of simple aryl systems previously (Table 4.1). Application of **154b** also required removal of Cu as, like other small, divalent, transition metals, copper can easily insert into the porphyrin core, particularly at elevated temperatures.[275] Altering the retention factor of the cubanylporphyrin product was also anticipated to improve its isolation from the reaction mixture. While the first effort (Entry 4) produced no coupled products, altering the solvent system through the addition of THF (Entry 5) to improve solubility of porphyrinoid systems allowed for the clean formation of **141** in 73 % yield. In this case, no cubane dimer **139** was observed among the products, indicating the need for Cu(I) salts for its synthesis. Application of identical methodologies to **147b** allowed for the synthesis and isolation of Ni(II) complex **140** in 63 % yield.

Formation of **140** and **141** represent the first examples of cubane-porphyrin adducts and fulfil one of the primary goals of this research. The retention of iodo functionality on the cubane scaffold also presents a synthetic handle for further functionalisations and manipulations as per Chapter 2. Application of identical methodologies to a di-brominated porphyrin **142** enabled the synthesis of dicubyl system **143** in 51 % yield (Scheme 4.8). **143** expands the potential of the scaffold system by allowing for extension in two directions around a central porphyrin core.



Scheme 4.8: Synthesis of dicubyl porphyrin **143** *via* Sonogashira cross-coupling.

The initial proposal, however, was to use cubane as an electronic isolator in bridged systems so attention returned to the *bis*alkynyl system **137** and its introduction in porphyrin systems. The addition of **137** to bromoporphyrins can proceed *via* one of two routes – monoaddition providing a terminal alkyne for subsequent reactions or a one-pot dimerisation to give the symmetrical alkynylcubane-linked *bis*porphyrin. The requirement of an excess of alkynylcubane in the optimised process made the former process a more viable one. Additionally, while a one-pot dimerisation may be synthetically desirable, this process is necessarily limited to the synthesis of symmetrical dimers. Ultimately, the effect of the cubane isolator in an unsymmetric porphyrin dimer is the major goal with the former process being seen as more conducive in this respect. Three separate attempts towards the addition of **137** to various bromoporphyrins were attempted and are shown in Scheme 4.9.



Scheme 4.9: Introduction of *bis*alkynylcubane **137** to the porphyrin periphery.

Application of **137** towards cross-coupling reactions with bromoporphyrins proved much less successful than previous Sonogashira reactions. The first attempt utilised free-base porphyrin **154b** as coupling partner. The contents of the reaction flask were filtered through silica at the end of the reaction, but the isolated products consisted only of trace amounts of starting materials. A large amount of dark material at the top of the silica plug, which was initially assumed to be the Pd catalyst, was theorised to therefore contain the bulk of the porphyrin material. Insolubility of alkynylporphyrins (particularly dimeric species)[208] on silica gel has been observed previously so the reaction was repeated with **147b** as Ni(II) porphyrins typically display enhanced solubility on silica gel with respect to their free-base counterparts.[276] Unfortunately, the same isolated product mixture was observed, even after thoroughly extracting the silica gel plug with various solvents. Compound **147j** was thus employed as the coordinative properties of Zn(II) porphyrins often allow for isolation of otherwise insoluble porphyrins.[208] Here, *in lieu* of silica gel, the reaction product **145b** was isolated by vacuum filtration from the reaction vessel. In this manner, a significant amount of dark purple solid was obtained, which proved insoluble at room temperature in all available solvents. No characterisation of **145b** could thus be

performed but isolation of all materials contained in filtrates indicated that the majority of the porphyrinoid mass present at the beginning of the reaction was contained within the solid sample. The reaction product was thus subjected to another Sonogashira reaction with **147b**, as the most rational explanation for the dramatic insolubility of **144-145** is the presence of the terminal acetylene. This reaction was performed in DMF at reflux for three days but the entire quantity of **147b** was recovered from the reaction. This implies that either **145b** was never present, or its solubility is so low as to prevent reactivity even at 120 °C in a highly polar solvent. A sample of the recovered solid from this last reaction was dissolved in neat trifluoroacetic acid. Zn(II) porphyrins undergo ready deprotection in acidic media, thus, if a Zn(II) porphyrin was present it should be deprotected, furnishing a porphyrin dication, readily observable by UV-vis spectroscopy.[277] No alteration of the purple solid occurred however – strongly indicating that the product was no longer a porphyrinoid species.[i] Further investigations into this reaction were not performed due to time constraints.

[i] The reaction products in this case were therefore completely unassignable. The porphyrin appears to be undergoing some sort of decomposition. This is surprising, given the generally mild nature of Sonogashira cross-couplings and their successful application to cubane-porphyrin scaffolds previously. The reactivity of **137** must therefore be at fault and an investigation into the seemingly unique reactivity of this doubly activated scaffold will be the subject of further studies.

4.5 Conclusions and future work

Three distinct routes towards the construction of cubane-porphyrin systems were investigated. Of these, direct functionalisation of preformed porphyrin scaffolds *via* nucleophilic substitution with lithiocubane has been shown to be ineffective. Some promising results were observed with condensation methodologies incorporating cubane aldehydes. A more exhaustive study of this reaction proved impossible at this time and will thus be the subject of future investigations. Introduction of an alkyne group onto the cubane scaffold and subsequent Sonogashira cross-coupling proved an efficient way to effect the marriage of these two systems. This work also served to update the available chemical reactivity of the cubane system through successful application of modern cross-coupling techniques with simple aryl halides, both electron-rich and electron-deficient. In this manner, a small library of aryl-cubane systems possessing groups for further functionalisations were synthesised. The synthesis of both free-base and Ni(II) porphyrin-cubane adducts was also realised for the first time. These involved both mono- and dicubyl systems. The iodocubane residues in these systems will be the subject of future work through the metal-halogen exchange chemistry described in Chapter 2 – providing access to highly substituted, electronically isolated porphyrinoid systems. Introduction of a *bis*alkynylcubane to the porphyrin macrocycle under these methodologies could not be achieved, however, and the products of the reaction with free-base, Ni(II) and Zn(II) porphyrins were unidentifiable. Further investigation both into the isolated products of these reactions and further modifications of the reaction conditions will be performed. Particularly, the reactivity of this *bis*alkynylcubane system with simple aryl systems will be performed to delineate its reactivity with the subsequent application to porphyrin systems anticipated.

Chapter 5:

Synthesis and reactivity of allenylporphyrins

5.1 Background

The synthesis and functionalisation of porphyrins with novel and synthetically useful functional groups is an ongoing challenge for synthetic porphyrin chemists.[119] Tetrapyrroles play pivotal and diverse roles in nature and there is a continuing desire to exploit their properties for applications in medicine, catalysis and nanomaterials. As a result, functional group interconversion and synthetic transformations spanning the field of porphyrin chemistry are constantly being explored and improved.[278] One niche in the area of synthetic transformations that has received little to no attention with porphyrins,[202] however, is the use of 1,2-propadiene or allene, presumably due to its high reactivity and associated difficulties in synthesis and isolation.

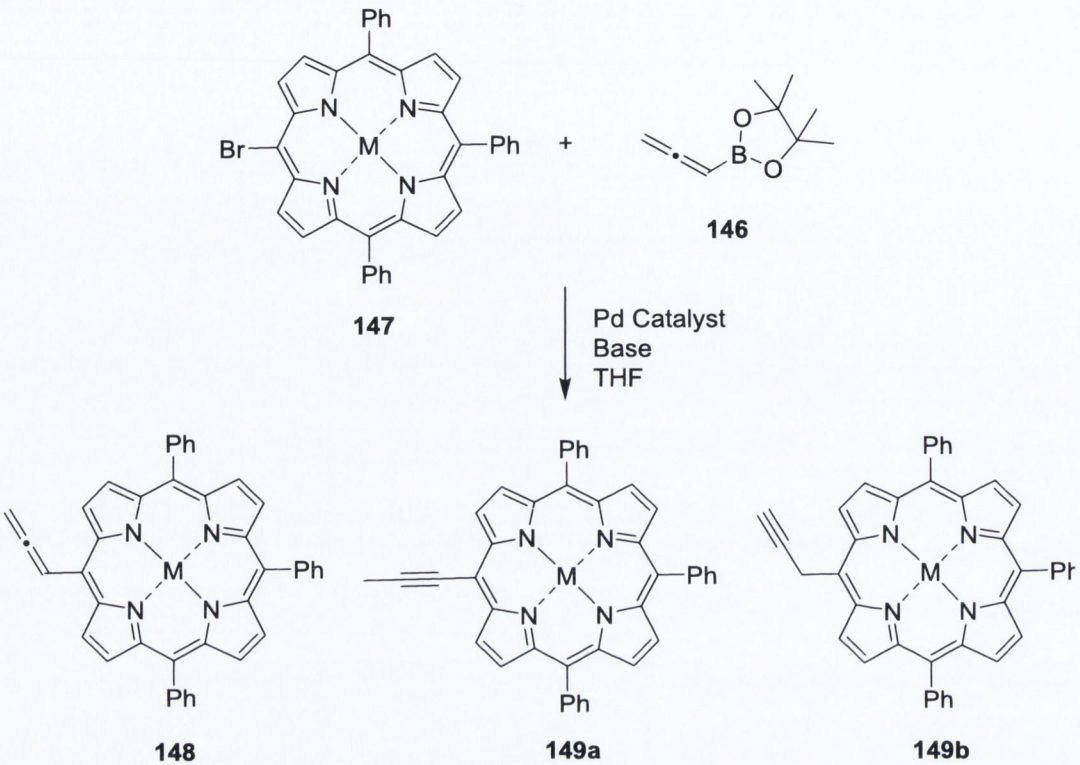
Allenes represent a highly versatile functional group that can be utilised as a building block in a variety of synthetic transformations. With the emergence of efficient protocols for their preparation, allenes have allowed chemists to access a variety of structurally interesting products that possess biological, chiral and optical activity.[279] While cumulenic porphyrin dimers linked by two carbons have been explored for their impressive optical properties, these dimers are quinoidal in nature and arise from modification of an internal alkyne, which results in exceptionally perturbed electronic absorption spectra.[280] Thus, the Senge group undertook a synthetic program aimed at the utilisation and subsequent transformation of terminal cumulative double bonds in porphyrinoid systems.[202] Allenes were seen as a synthetically interesting and useful functional group to introduce, as the orthogonal double bonds were anticipated to provide a facile route towards further functionalisations as well as creating structurally interesting compounds possessing both the interesting physiochemical, biological and catalytic properties of porphyrins[281] and the optical properties of allenic systems observed previously.[282,283] Research thus focused on initially installing a free allene onto the porphyrin core to be followed by investigations of reactivity.

5.2 Previous work towards allenylporphyrins

The commercially available allenylboronic acid pinacol ester (**146**) was then seen as a novel avenue to introduce allenyl functionality. Previously, **146** had been used mainly to take advantage of the allene in three- and four-component reactions[284] and in Ru(II)-catalysis to generate alkenylboronates.[285] Although **146** had never previously been used in a Suzuki-Miyaura cross-coupling reaction,[84] Pd-catalysed cross-coupling between **146** and triphenylbromoporphyrin **147** was a convenient way both to test the utility of **147** in such coupling reactions while providing entry to allenylporphyrin **148**. Results of this optimisation are summarised in Table 5.1. Few conditions were found to lead to allenylporphyrin **148** with isomeric products, 1-propynylporphyrin **149a**, or 2-propynylporphyrin **149b**, available depending on conditions employed. The conditions required for allenylporphyrin synthesis were realised as Ni(II) bromoporphyrins, 10 equivalents of **146,** 15 mol % $PdCl_2$(dppe) and 10 equivalents of K_2CO_3 heated to 80 °C for 18 hours in THF (Entry 10). This resulted in a maximum yield of 50 % for the target allenylporphyrin **148a**.

The major drawback of this optimisation work, aside from the poor yield, was that it exclusively used triphenylporphyrins **147a/i** as the halogenated cross-coupling partners. Having successfully achieved the first synthesis of an allenylporphyrin (**148a**) the graduation of the researcher involved meant the project concluded briefly. Attention returned with the present work, where it was decided to initially probe the versatility of the above reaction in installing allenyl functional groups by generating a library of allenylporphyrins, bearing diverse substituents, both aryl and alkyl. It was then proposed to test the reactivity of the allenic double bonds towards further functionalisation reactions, thereby proving its utility as a synthon in the generation of diverse porphyrin scaffolds.

Table 5.1: Previous optimisation work towards the Suzuki-Miyaura cross-coupling of bromoporphyrins **147** with **146**.[202]



Entry	M	Pd Catalyst (mol %)	Base (eq.)	Time (h)	Temp (°C)	Yield (%) 148	149a	149b
1	Ni(II)	$Pd(PPh_3)_4$ (15)	Cs_2CO_3 (2)	18	80	2	-	-
2	Ni(II)	$Pd(PPh_3)_4$ (15)	K_3PO_4 (2)	18	67	-	25	-
3	Ni(II)	$Pd(PPh_3)_4$ (15)	K_3PO_4 (20)	18	80	9	14	-
4	Ni(II)	$PdCl_2(PPh_3)_2$/ $AsPh_3$ (25)	Cs_2CO_3 (2)	18	80	8	-	-
5	Ni(II)	$PdCl_2(PPh_3)_2$/ $AsPh_3$ (15)	Cs_2CO_3(2)	5	80	10	-	-
6	Ni(II)	$Pd_2(dba)_3$/ $AsPh_3$ (15)	Cs_2CO_3 (2)	18	80	10	-	-
7	Ni(II)	$PdCl_2$(dppp) (15)	Cs_2CO_3 (2)	18	80	37	9	-
8	Ni(II)	$PdCl_2$(dppe) (15)	Cs_2CO_3 (2)	18	80	41	-	-
9	Ni(II)	$PdCl_2$(dppe) (15)	Cs_2CO_3 (10)	18	80	-	61	-
10	Ni(II)	$PdCl_2$(dppe) (15)	K_2CO_3 (10)	18	80	50	-	-
11	Zn (II)	$PdCl_2$(dppe) (15)	K_2CO_3(10)	18	80	-	-	46

Reaction conditions: All reactions were performed at 10 mM porphyrin concentration using 10 equivalents of **146** under argon. Yields are isolated yields after column chromatography (silica gel).

5.3 Synthesis of halogenated porphyrins

The first goal of the present work was to test the general applicability of the previously optimised work to a library of halogenated porphyrins. Based on their known reactivity, a mid-sized library of bromoporphyrins was initially targeted. Additionally, the synthesis of a smaller library of iodinated porphyrins was also executed in order to delineate the differences in reactivity between the two systems.[i] While Ni(II) porphyrins were found to perform best in the optimised reactions, selected examples encompassing other, synthetically useful, metalloporphyrins were also targeted.

5.3.1 Ni(II) bromoporphyrin library synthesis

The synthesis of the initial library of Ni(II) bromoporphyrins is shown in Scheme 5.1. Depending on the final structure planned, various modifications to the overall synthesis were employed. The first step, however, was universal and involved a simple MacDonald [2+2] condensation[155,159] between DPM (**124**, synthesised *via* the Lindsey method[156]) and an appropriate aldehyde. In all cases these condensation reactions proceeded readily to provide 5,15-disubstituted porphyrins **150** in high yields. This condensation step is the easiest point to introduce significant variability into the porphyrin library so various aromatic and aliphatic aldehydes were employed in order to fully cover the spectrum of electronic and steric effects. 5,15-Porphyrins such as these are the most common entry points in most modern porphyrin syntheses as they are available in reasonable yields from cheap starting materials and provide two free meso positions, which can be selectively functionalised to design an array of porphyrin scaffolds.[119]

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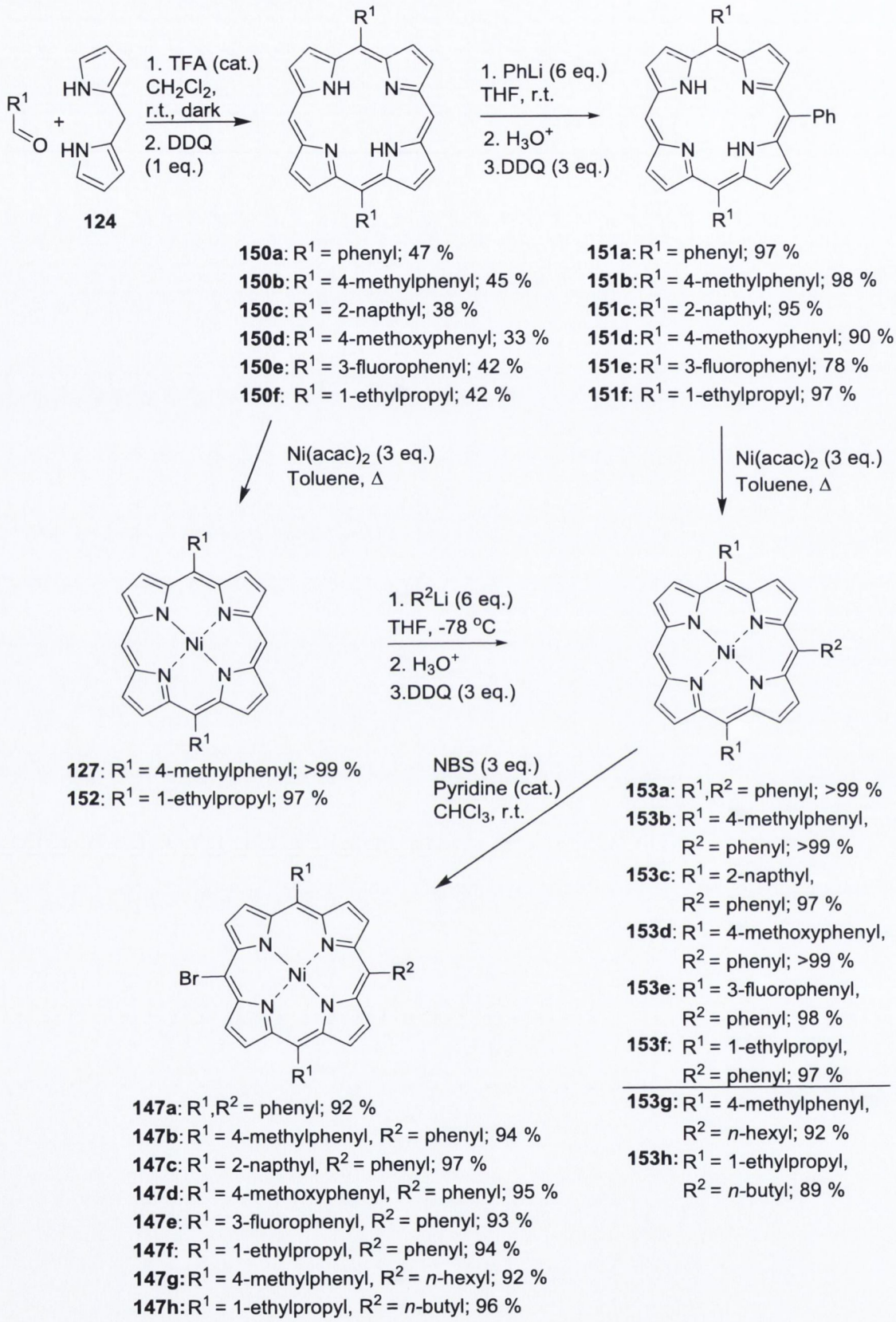
[i] The halogenated porphyrins synthesised here also found applications in Chapter 4 and Chapter 6.



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150a: R^1 = phenyl; 47 %
150b: R^1 = 4-methylphenyl; 45 %
150c: R^1 = 2-napthyl; 38 %
150d: R^1 = 4-methoxyphenyl; 33 %
150e: R^1 = 3-fluorophenyl; 42 %
150f: R^1 = 1-ethylpropyl; 42 %

151a: R^1 = phenyl; 97 %
151b: R^1 = 4-methylphenyl; 98 %
151c: R^1 = 2-napthyl; 95 %
151d: R^1 = 4-methoxyphenyl; 90 %
151e: R^1 = 3-fluorophenyl; 78 %
151f: R^1 = 1-ethylpropyl; 97 %

127: R^1 = 4-methylphenyl; >99 %
152: R^1 = 1-ethylpropyl; 97 %

153a: R^1,R^2 = phenyl; >99 %
153b: R^1 = 4-methylphenyl, R^2 = phenyl; >99 %
153c: R^1 = 2-napthyl, R^2 = phenyl; 97 %
153d: R^1 = 4-methoxyphenyl, R^2 = phenyl; >99 %
153e: R^1 = 3-fluorophenyl, R^2 = phenyl; 98 %
153f: R^1 = 1-ethylpropyl, R^2 = phenyl; 97 %
153g: R^1 = 4-methylphenyl, R^2 = *n*-hexyl; 92 %
153h: R^1 = 1-ethylpropyl, R^2 = *n*-butyl; 89 %

147a: R^1,R^2 = phenyl; 92 %
147b: R^1 = 4-methylphenyl, R^2 = phenyl; 94 %
147c: R^1 = 2-napthyl, R^2 = phenyl; 97 %
147d: R^1 = 4-methoxyphenyl, R^2 = phenyl; 95 %
147e: R^1 = 3-fluorophenyl, R^2 = phenyl; 93 %
147f: R^1 = 1-ethylpropyl, R^2 = phenyl; 94 %
147g: R^1 = 4-methylphenyl, R^2 = *n*-hexyl; 92 %
147h: R^1 = 1-ethylpropyl, R^2 = *n*-butyl; 96 %

Scheme 5.1: Synthesis of library of Ni(II) bromoporphyrins.

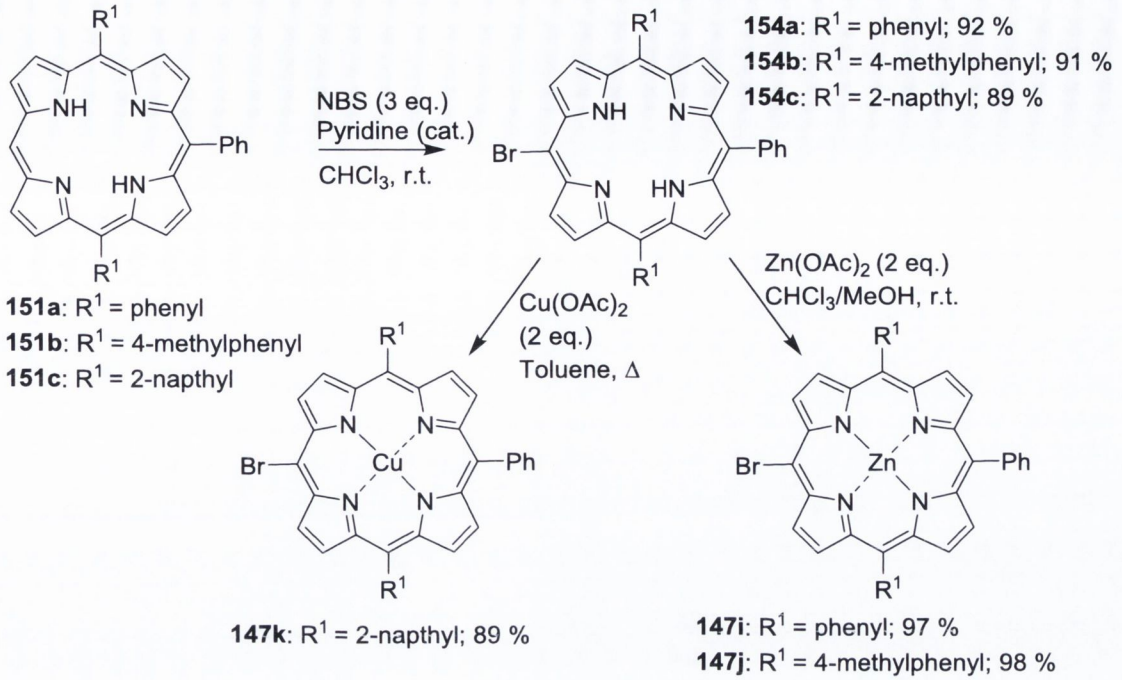
The next two steps utilised organolithium addition/oxidation chemistry[173] discussed previously and insertion of Ni(II) into the porphyrin core. This involved the nucleophilic addition of an aryl or alkyl organolithium reagent to one of the free meso positions followed by quenching of the generated anion with acid and subsequent oxidation to the substituted porphyrin product. Commercially available organolithiums were utilised in all cases to avoid issues regarding generation discussed in Chapter 4. For the addition of aromatic lithiating agents the reaction works best with free-base porphyrins so this step was performed first to give **151a-f** in near quantitative yields. System **151e** presents the only exception. Approximately 10-15 % of a biphenyl-appended porphyrin was observed, with its presence confirmed by HRMS analyses. The only explanation for this compound (not witnessed with any other system) is that, because of the strongly electron withdrawing nature of the porphyrin macrocycle, halides on the porphyrin periphery can act as leaving groups in an addition/elimination mechanism with strong nucleophiles (*e. g.*, PhLi). Here, in spite of its traditional status as a poor leaving group and its *meta*-position, a certain amount of fluorine displacement was observed. This has been observed previously with pentafluorophenyl porphyrins[286] but no similar examples with mono-fluorinated systems have been reported. Metallation of the series of phenyl-appended porphyrins **151a-f** with nickel(II) acetylacetonate furnished trisubstituted Ni(II) porphyrins **153a-f** in near quantitative yield.

In terms of the addition of alkyl substituents in this manner, best results are observed with nickel(II) porphyrins so the desired target functionality thus dictated the synthetic route followed. Free-base porphyrins **150b/f** were initially metallated to provide **127** and **152**. Reaction with either *n*-hexyllithium (to provide **153g**) or *n*-butyllithium (yielding **153h**) proceeded smoothly with high yields of two further trisubstituted Ni(II) porphyrins obtained. Yields of alkyl addition were slightly lower than those obtained with PhLi. This is accounted for by the higher reactivity of alkyllithiums which led to a small degree of decomposition of the porphyrin scaffold. With trisubstituted nickel(II) porphyrins **153a-h** in hand, bromination

with *N*-bromosuccinimide (NBS) to give **147a-h** became straightforward as there is only one reactive meso position remaining.[185] The synthesis of tetrasubstituted systems **147** was thus targeted, both because it gives maximum variation of chemically diverse mix substituents (aryl/aryl, aryl/alkyl, alkyl/alkyl) but also because adding an extra synthetic step makes the entire process higher yielding than a monobromination process from **150**. Typically, because each step in Scheme 5.1 is near quantitative and one porphyrin product was generally observed, the bulk synthesis for **150** → **147** could be accomplished without purification of intermediates, with just a final chromatographic purification of **147** required.

5.3.2 Synthesis of other metalloporphyrins

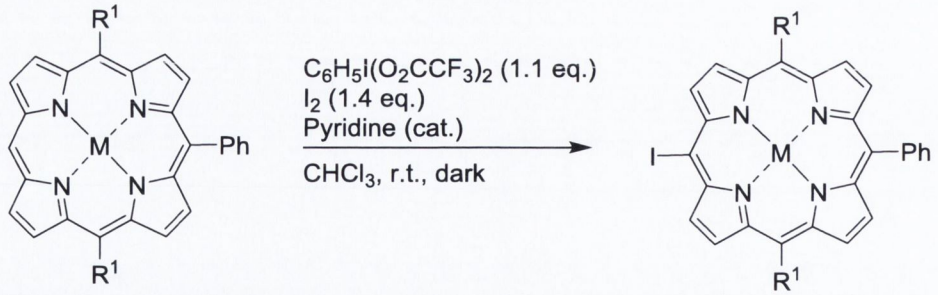
Having synthesised the library of Ni(II) bromoporphyrins, attention turned to the synthesis of a smaller library consisting of other, synthetically useful, metalloporphyrins; namely the free-base, Zn(II) and Cu(II) systems. Here, trisubstituted porphyrins **151a-c** were initially brominated with three equivalents of NBS (Scheme 5.2) to provide free-base bromoporphyrins **154a-c** in excellent yield. Metallation with zinc(II) actetate in chloroform and methanol at room temperature resulted in quantitative formation of Zn(II) bromoporphyrins **147i/j** while addition of copper(II) acetate in toluene and heating at reflux furnished the Cu(II) adduct **147k**.



Scheme 5.2: Synthesis of free-base, Zn(II) and Cu(II) bromoporphyrins.

5.3.3 Synthesis of iodoporphyrins

The final haloporphyrin library synthesised was a small collection of iodinated porphyrins (Scheme 5.3). While not as commonly utilised as their brominated counterparts, due to their more challenging synthesis, iodinated porphyrins have been shown to participate in cross-coupling reactions.[287] The increased reactivity of standard aryl iodides towards coupling chemistry meant that iodoporphyrins could potentially provide easier access to the allenylporphyrin motif. Iodination of trisubstituted porphyrins was achieved following the procedure of Boyle and co-workers[185,287] using [*bis*(trifluoroacetoxy)]iodobenzene and iodine in the presence of a catalytic amount of pyridine in chloroform. While analogous brominations using NBS typically require 2-3 hours, complete iodination of these porphyrins required a reaction time of up to 48 hours. Ni(II) iodoporphyrins **155a/b** were obtained in near quantitative yield while free-base system **155c** was produced in a slightly reduced yield of 83 %.



153a: R^1 = phenyl, M = Ni(II)
153c: R^1 = 2-naphthyl, M = Ni(II)
151b: R^1 = 4-methylphenyl, M = 2H

155a: R^1 = phenyl, M = Ni(II); 93 %
155b: R^1 = 2-naphthyl, M = Ni(II); 95 %
155c: R^1 = 4-methylphenyl, M = 2H; 83 %

Scheme 5.3: Synthesis of iodoporphyrins **155a-c**.

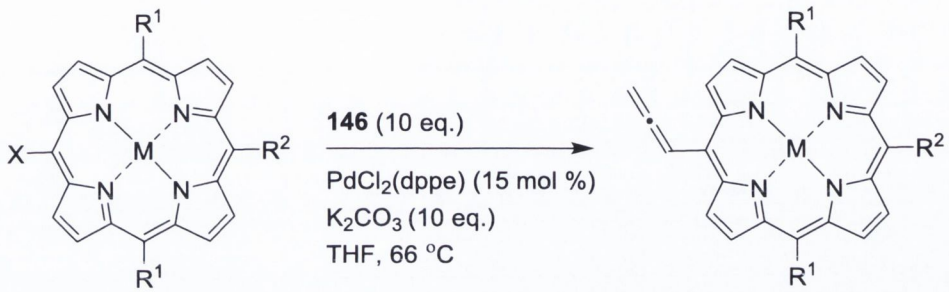
5.4 Allenylporphyrin synthesis

5.4.1 Suzuki-Miyaura cross-coupling reactions

The first phase of the investigation into the synthesis and reactivity of allenylporphyrins involved transforming the library of haloporphyrins using the Suzuki-Miyaura methodology developed previously.[202] Since this work successfully utilised Ni(II) triphenyl system **147a**, aromatically substituted Ni(II) porphyrins were the favoured initial starting point to test the general applicability of the synthetic methodology. The optimised conditions were employed using **147b** as a substrate (Table 5.2). A small degree of conversion was observed after 24 hours but most of the starting material had not been consumed. The reaction time was thus extended, and it was observed that after 72 hours all of the starting material had been converted, either into allenylporphyrin **148b**, or into debrominated starting material **153b** as well as into trace amounts of propynylporphyrins **149**. It was initially assumed that, within the Suzuki cycle, protodemetallation to give debrominated starting material and transmetallation leading to allenylporphyrins were competitive, but later tests with **147c** showed that after 36 hours the major products in the reaction flask were allenylporphyrin **148c** and unreacted starting material **147c**. The yield of **148c** attained after 36 hours could be increased with longer reaction time, but at this stage protodemetallation does begin to occur. Separation of the target allenylporphyrins **148** from debrominated porphyrins **153** proved much easier than separation of **148** from **147**, so the

time scale was extended to 72 hours for all subsequent syntheses. The main drawback of modifying the procedure in this manner is that no starting material can be recovered from the reaction, as after 72 hours, all of the C-Br bonds have been cleaved.

Table 5.2: Results of Suzuki-Miyaura cross-coupling reactions between **146** and haloporphyrins.



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Starting Material	M(II)	X	R^1	R^2	Product	Yield (%)
147a	Ni(II)	Br	Phenyl	Phenyl	**148a**	88
147b	Ni(II)	Br	4-Methylphenyl	Phenyl	**148b**	78
147c	Ni(II)	Br	2-Naphthyl	Phenyl	**148c**	91
147d	Ni(II)	Br	4-Methoxyphenyl	Phenyl	**148d**	Trace
147e	Ni(II)	Br	3-Fluorophenyl	Phenyl	**148e**	64
147f	Ni(II)	Br	1-Ethylpropyl	Phenyl	**148f**	Trace
147g	Ni(II)	Br	4-Methylphenyl	*n*-Hexyl	**148g**	8%
147h	Ni(II)	Br	1-Ethylpropyl	*n*-Butyl	**148h**	N/A
154b	2H	Br	4-Methylphenyl	Phenyl	**148i**	N/A
155a	Ni(II)	I	Phenyl	Phenyl	**148a**	42
155b	Ni(II)	I	2-Naphthyl	Phenyl	**148c**	73
155c	2H	I	4-Methylphenyl	Phenyl	**148i**	N/A

Reaction conditions: All reactions were performed at 10 mM porphyrin concentration under argon for 72 hours. Where applicable, yields are isolated yields after column chromatography (silica gel).

Table 5.2 illustrates the results of the Suzuki-Miyaura cross-coupling reactions using the Ni(II) bromoporphyrin library, free-base bromoporphyrin **154b** and the iodinated porphyrins **155a-c**. The first noteworthy result is that, when successful, yields were all greater than the 50 % achieved previously with the synthesis of **148a** after 16 hours. From the aromatic residues tested, however, this procedure appears limited in scope. Whilst high yields were achieved when using standard aromatic residues (**148a-c**), electronic alterations led to significantly reduced yields (**148d** and **148e**). In addition to expanding the allenic

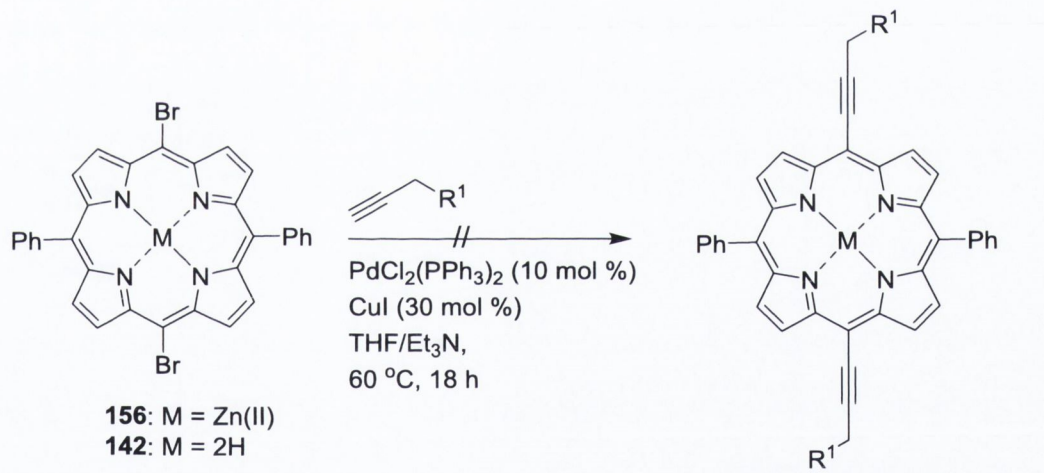
library using purely aromatic substituents, incorporation of alkyl substituents onto the porphyrin periphery was also attempted so as to further probe the versatility of the reaction conditions and yield more structurally interesting porphyrins. However, none of the porphyrins bearing alkyl substituents **148f-h** yielded an allenylporphyrin in sufficient amount to be characterised. Most likely, this is due to the known reduced reactivity of alkyl-substituted porphyrins towards standard transformations.[148] In terms of general trends in reactivity, as the number of aliphatic substituents increases, the yield of **148** decreases sharply. Porphyrins bearing just one aliphatic substituent could be converted to **148** in very low yields (**148g**), but those containing two or three alkyl groups only gave trace amounts, or no allenic product at all (**148f/h**).

Akin to the situation noted previously regarding Zn(II) porphyrins, conversion of free-base bromoporphyrin **154b** could not be effected *via* this methodology, with no cross-coupled products identifiable from the reaction mixture. Although aromatic iodides are expected to be significantly more activated than analogous bromides towards metal-catalysed cross-couplings with boronic esters, investigation of the reactivity of Ni(II) iodoporphyrins **155a/b** indicated this to not be true with respect to the porphyrinoid systems here. In this situation, the yields that were obtained are both lower than those involving bromoporphyrins **147a** and **147c**. Furthermore, the free-base iodoporphyrin **155c** was as unreactive under these conditions as the free-base bromoporphyrin tested previously.

5.4.2 Synthesis and rearrangements of propargylporphyrins

Although the Suzuki-Miyaura cross-coupling reactions proved successful for specific functional groups, the scope of the reaction is quite narrow, and therefore attention turned to other applicable methods to introduce allenyl functionality. One of the most commonly employed syntheses for terminal allenes begins with propargyl electrophiles that contain a terminal leaving group.[288,289] Sonogashira cross-coupling is employed to introduce the desired propargyl residues into the precursor molecule.[50] Pd-catalysed or thermal

rearrangement and loss of the leaving group at the propargyl substituent then affords the terminal allene. Dibromoporphyrins **142** and **156** were dissolved in THF and treated with triethylamine, $PdCl_2(PPh_3)_2$, copper(I) iodide and the respective propargyl compound and heated at reflux under an argon atmosphere (Scheme 5.4); analogous to the Sonogashira procedures discussed previously.[272,273] However, dipropargylporphyrins **157a-d** could not be isolated, and only the starting material and an insoluble polymer were obtained. Increasing the equivalents of CuI and triethylamine or decreasing the amount of porphyrin did not provide the desired products. An explanation for this behaviour is that the propargyl compounds necessarily carry good leaving groups and may react with themselves under the conditions employed. It is also possible that the desired porphyrins are formed, but undergo another reaction with either the propargyl compound or the starting dibromoporphyrin.



156: M = Zn(II)
142: M = 2H

157a: M = Zn(II), R^1 = Br
157b: M = Zn(II), R^1 = tosyl
157c: M = 2H, R^1 = Br
157d: M = 2H, R^1 = tosyl

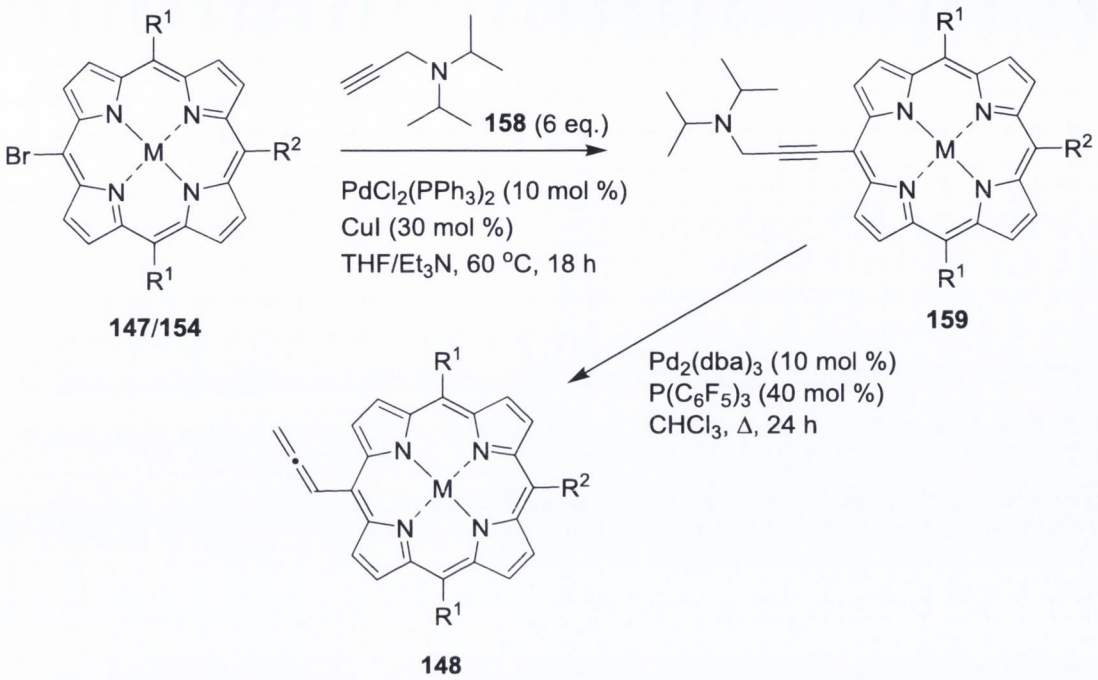
Scheme 5.4: Attempted Sonogashira cross-coupling reactions with dibromoporphyrins.

Less reactive propargyl groups that could be successfully coupled to the porphyrin core, yet still retain reactivity to undergo the desired rearrangement to give allenylporphyrins, were thus considered. One of the more recent advances in this area is work by Nakamura *et al.* that utilised propargylamines followed by a Pd-catalysed hydrogen transfer reaction.[290,291] The first step of this synthesis involved a Sonogashira reaction,

using *N,N*-diisopropylprop-2-yn-1-amine (**158**) as the alkyne partner. The resultant propargyl-appended porphyrin **159** was then dissolved in a minimum amount of chloroform and the solution heated to reflux in the presence of $Pd_2(dba)_3$ as the precatalyst and $P(C_6F_5)_3$ as the ligand source. This methodology was applied to a number of monobromoporphyrins with results shown in Table 5.3.

The results of this study show this method to be more robust and tolerant of a wider degree of variation around the porphyrin core than the Suzuki-Miyaura methodology employed previously and allowed for the facile introduction of a terminal allene group *via* a straightforward two-step process. The solubility of the amino-propargylporphyrins **159** posed one of the few issues with this synthesis. These porphyrins proved difficult to purify as, when eluting with chlorinated solvents on silica, they effectively had a retention factor of zero. Moreover, when using ethyl acetate, the target porphyrins co-eluted with the unreacted propargylamines. This contaminant proved not to effect the final transformation, however. Filtration through silica using dichloromethane as the eluent thus served to remove any undesired porphyrin by-products. Changing the eluent to ethyl acetate yielded the crude target porphyrin in a high enough degree of purity to be subjected to the Pd-catalysed rearrangement. The resultant allenylporphyrin could then be purified by standard methods. As a result, porphyrins of type **159** were not isolated and characterised and the yields displayed in Table 5.3 are for the two steps of the process.

Table 5.3: Results of the synthesis of allenylporphyrins **148** through Sonogashira cross-couplings followed by Pd-catalysed hydrogen transfer.



Starting Material	M(II)	R^1	R^2	Product	Yield (%)
147a	Ni(II)	Phenyl	Phenyl	**148a**	79
147b	Ni(II)	4-Methylphenyl	Phenyl	**148b**	84
147c	Ni(II)	2-Naphthyl	Phenyl	**148c**	82
147d	Ni(II)	4-Methoxyphenyl	Phenyl	**148d**	68
147e	Ni(II)	3-Fluorophenyl	Phenyl	**148e**	73
147f	Ni(II)	1-Ethylpropyl	Phenyl	**148f**	45
147g	Ni(II)	4-Methylphenyl	*n*-Hexyl	**148g**	53
147h	Ni(II)	1-Ethylpropyl	*n*-Butyl	**148h**	44
147i	Zn(II)	Phenyl	Phenyl	**148j**	N/A
147k	Cu(II)	2-Naphthyl	Phenyl	**148k**	47
154a	2H	2-Naphthyl	Phenyl	**148l**	N/A
154c	2H	Phenyl	Phenyl	**148m**	N/A

Reaction conditions: Sonogashira reactions were performed at 10 mM and rearrangement reactions at 35 mM porphyrin concentration under argon. Intermediates **159** were isolated by filtration through silica gel and used without further purification. Where applicable, yields are isolated yields for the two steps after column chromatography (silica gel).

The standard aromatic residues which enabled successful coupling using the Suzuki-Miyaura conditions (**147a-c**) proved to be similarly reactive under these Sonogashira/hydrogen transfer conditions. Residues with groups such as 4-methoxyphenyl (**147d**) and 3-fluorophenyl (**147e**), which previously showed diminished reactivity with relation to the more standard aromatic residues, exhibited comparable reactivity under these

conditions. The synthesis of allenylporphyrins that contain aliphatic residues, which could not be synthesised *via* the Suzuki methodology, was achieved in moderate yields (**148f-h**). This allowed for the generation of range of structurally diverse Ni(II) allenylporphyrins **148a-h**. Although lower than the yields obtained for the aromatically-substituted porphyrins, 50 % conversion of porphyrins containing aliphatic residues is indicative of the lowered reactivity of this class of porphyrins. The ability to introduce aliphatic substituents provides the ability to fine-tune the periphery of the porphyrin and could lead to many novel porphyrins incorporating the known nonplanar properties of alkylporphyrins with the impressive optical properties of allenes.

In terms of the metallation state of the porphyrin, the Suzuki-Miyaura conditions could only be employed with nickel(II) porphyrins. Cu(II) was successfully incorporated into an allenylporphyrin (**148k**) under these rearrangement conditions, starting from the appropriately metallated bromoporphyrin **147k**. By starting from bromoporphyrins **147j** or **154a/c**, successful synthesis of a Zn(II) allenylporphyrin **148j** or free-base allenylporphyrins **148l/m** could not be achieved, as the reactions yielded a complex mixture of polymeric material. Zn(II) allenylporphyrin **148j** could be identified in trace amounts from this material but could not be isolated. Theoretically a free-base allenylporphyrin could be obtained *via* demetallation of the appropriate Ni(II) porphyrin, and subsequent metallation could give access to the Zn(II) allenylporphyrin. However, considering the harsh conditions (conc. H_2SO_4 or a strong Lewis acid such as BBr_3) involved in removing nickel(II) from the porphyrin core, the chemically labile allene group was not expected to survive a demetallation attempt, and, as such, it was not attempted.

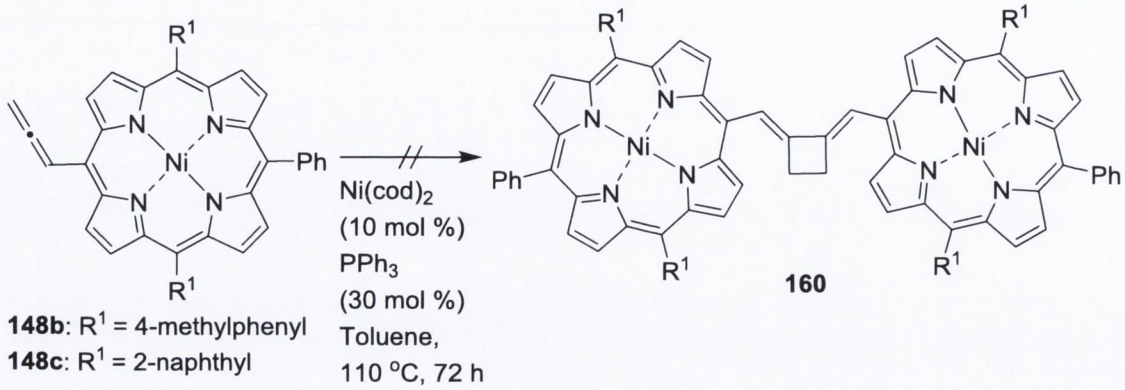
5.5 Spectroscopic analysis of allenylporphyrins

The presence of the allenyl functional group was unambiguously assigned by various spectroscopic methods. Using the values obtained for **148b** as a model, certain general trends in spectroscopic data become evident. First, in the ^{1}H NMR spectra ($CDCl_3$) the three allenic protons resonate as a distinct doublet at δ = 5.28 ppm representing the two terminal protons and a triplet at δ = 8.26 ppm for the internal hydrogen atom. These signals possess a significant $^{4}J_{H\text{-}H}$ coupling constant of 6.9 Hz. In terms of the ^{13}C NMR spectra, the terminal carbon appears at δ = 76.0 ppm, the porphyrin-adjacent carbon at δ = 92.5 ppm and the highly deshielded internal carbon atom at δ = 215.9 ppm. The analysis of all of these signals was confirmed by H-H, C-H and long range C-H coupling experiments. In the IR spectrum the fingerprint region for the allenic bond appears as a series of sharp signals at approximately 2900 cm^{-1} as well as a strong absorption at 1939 cm^{-1}. Any other allenic absorption signals are largely obscured by the many porphyrinoid signals below 1900 cm^{-1}. These spectroscopic traits are shared across the library of allenylporphyrins synthesised and allowed for a quick and easy determination of the presence of the allenyl group.

5.6 Reactivity of allenylporphyrins

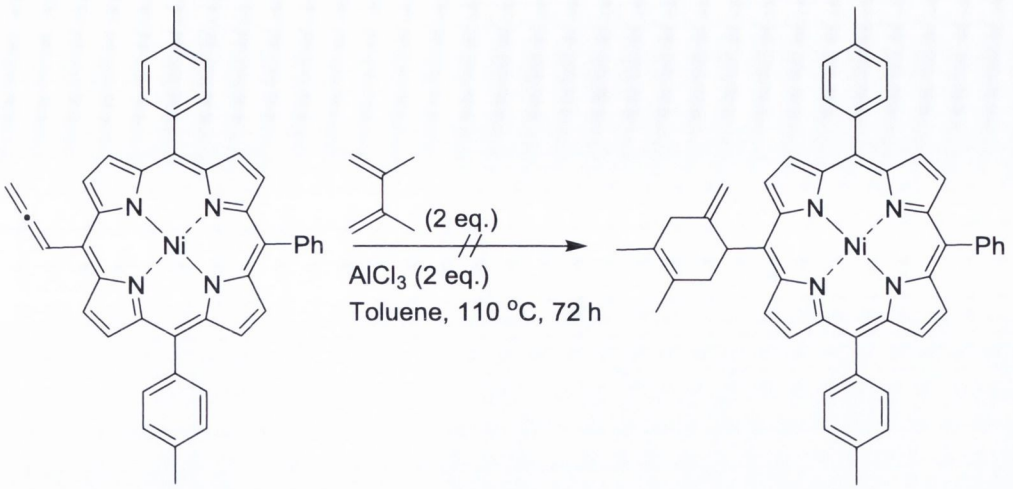
With the library of allenylporphyrins synthesised, some exploratory reactions of the allenyl group were attempted, focusing initially on straightforward cyclisation reactions.[288,292-294] Allenes can self dimerise upon heating to give cyclobutane derivatives, which are usually obtained as a complex mixture of isomers.[295] Recent work by Saito *et al.* into the use of Ni(II) catalysts that promote regioselective dimerisation of terminal allenes bonded to electron withdrawing groups[296] drew interest, both as a simple method of testing the reactivity of the installed group as well providing access to cyclobutane-linked porphyrin dimer **160**. Scheme 5.5 illustrates the reaction conditions employed. Regardless of which porphyrin residue (**148b** or **148c**) was used, the best outcome after heating at reflux for three days was a crude HRMS spectrum showing trace product formation. Presumably, the steric

hindrance invoked by the porphyrin core, coupled with its electronic impact, makes orientating both porphyrins too demanding for this cyclisation to occur.



Scheme 5.5: Attempted dimerisation of allenylporphyrins **148b** and **148c**.

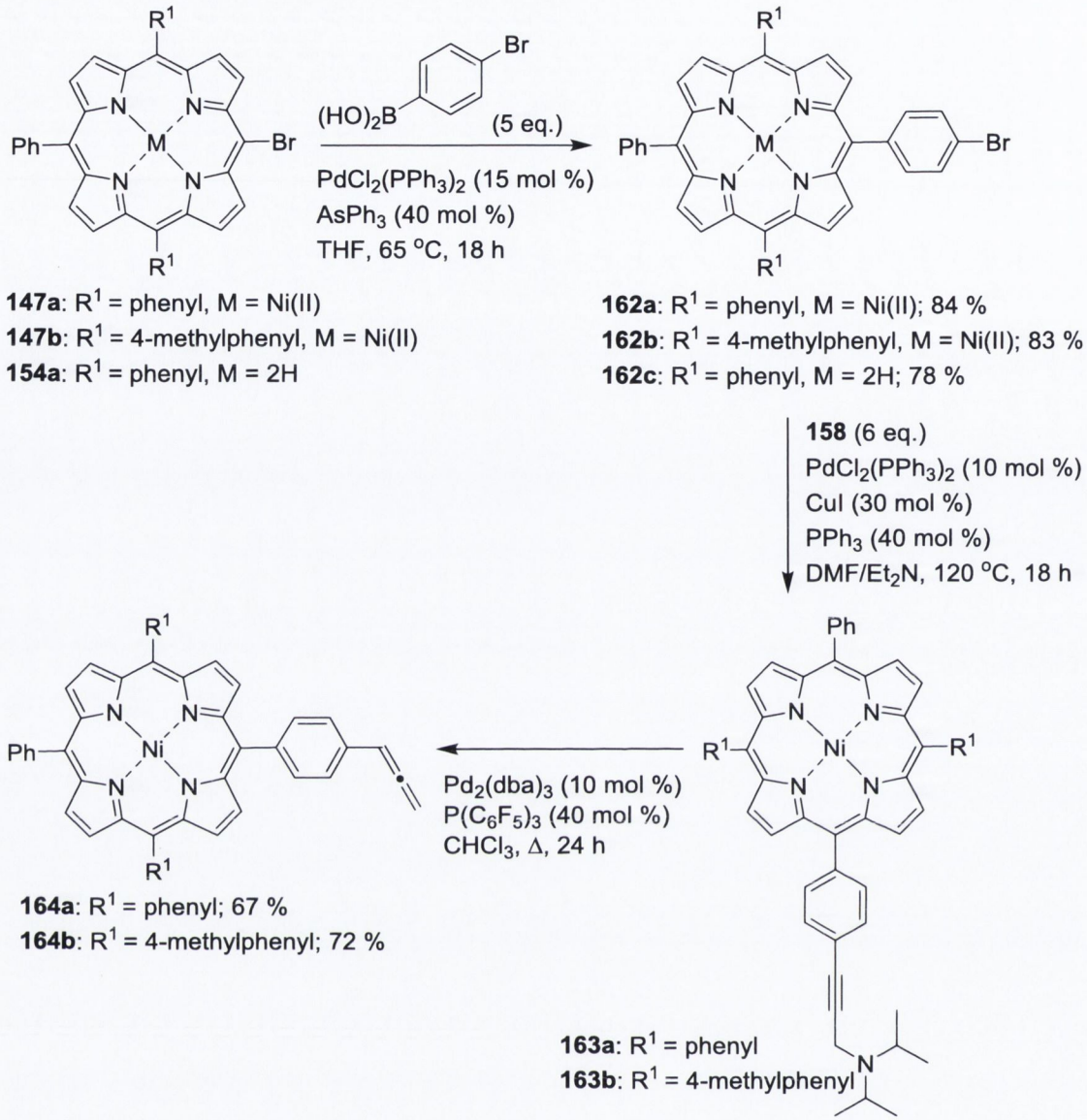
Perhaps the most straightforward cyclisation reaction that allenes can undergo is the classic Diels-Alder reaction.[297,298] Here, one of the double bonds of the allenyl unit acts as the dienophile and reacts with an appropriate diene. Tailoring the electronics of the group attached to the terminal allene dictates which of the two double bonds is more amenable to act as the dienophile. Scheme 5.6 depicts the Diels-Alder attempt using **148b** as the allenylporphyrin together with 2,3-dimethyl-1,3-butadiene. Ultimately, no conversion to **161** was observed after heating at reflux for 72 hours, with **148b** being completely recovered from the reaction mixture. Again, the steric encumbrance by the porphyrin core seems the most likely reason for the failure of **148b** to undergo any noticeable reaction. The problem is doubly compounded by the electronic withdrawing effect of the porphyrin, which is expected to activate the first, and therefore most sterically shielded, of the double bonds.



Scheme 5.6: Attempted Diels-Alder reaction on **148b**.

5.6.1 Introduction of phenyl "spacer"

Because steric constraints appeared to be the primary reason for the failure of the directly linked allenylporphyrins to display any further reactivity, installation of a phenyl 'spacer' between the porphyrin core and the allene group was considered. Theoretically a straightforward undertaking, this proved more challenging than initially expected. The first step of this synthesis involved taking the bromoporphyrin **147a** and performing a Suzuki-Miyaura cross-coupling reaction with 4-bromophenylboronic acid (Scheme 5.6). The target reaction proceeded readily, in spite of the complications presented by the multiple aromatic bromides, with porphyrin **162a** obtained in 84 % yield. Compound **162a** was then subjected to the standard Sonogashira coupling conditions employed previously, which were successful for all other Ni(II) bromoporphyrins, but in this case failed to produce any propargylporphyrin **163a**. This was an unusual result as the aromatic bromide in **162a** is expected to be more activated towards coupling reactions than the porphyrinoid bromide in **147a**. The lowered reactivity of **162a** under these conditions may also help explain the high yield of the monobromophenyl product from the Suzuki reaction *in lieu* of any higher order derivatives.

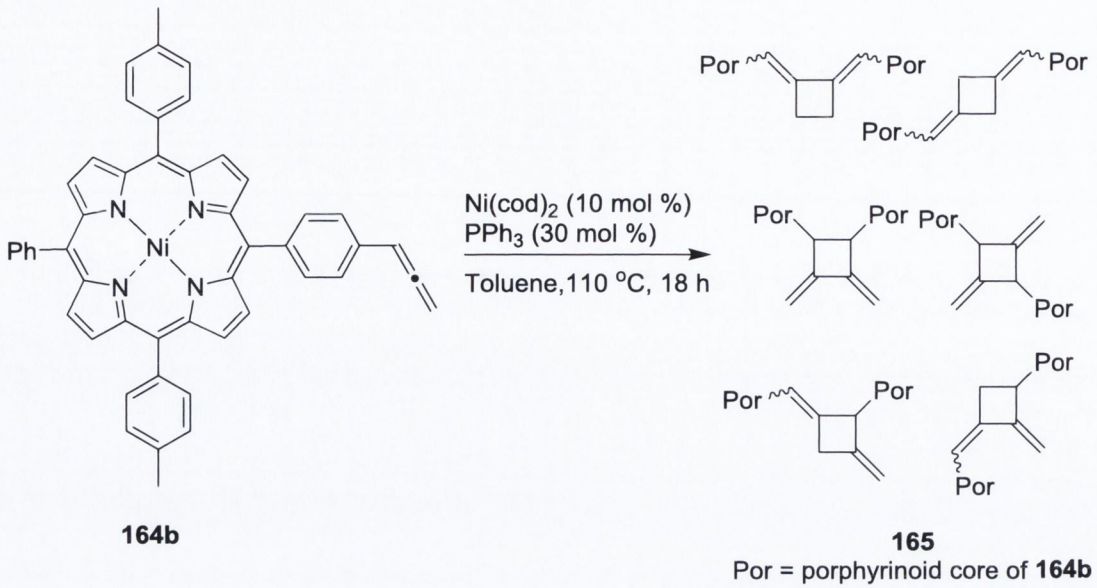


Scheme 5.7: Installation of phenyl "spacer" and subsequent allene formation.

Initially, the lack of reactivity of **162a** towards standard Sonogashira couplings was theorised to be a product of the known insolubility of [5,10,15,20-tetraphenylporphyrinato]nickel(II) (NiTPP), which is an intermediate in the catalytic coupling cycle of **162a**. However, neither installing different residues such as 4-methylphenyl in **162b**, nor changing the metallation of the porphyrin as in **162c** and utilising copper free conditions, resulted in any increase in the reactivity. Consequently, more forcing Sonogashira conditions were attempted. The catalyst turnover rate was increased by changing the base to the less sterically hindered diethylamine, more ligand was added in the

form of triphenylphosphine and the reaction temperature was increased by heating to reflux in DMF. When compounds **162a** and **162b** were subjected to the cross-coupling reaction under these conditions, products **163a** and **163b** were formed in near quantitative yield after 24 hours. The standard allene forming reaction on propargylporphyrins **163a/b** proceeded readily to give allenylporphyrins **164a** and **164b** in reasonable yield (Scheme 5.6). Free-base (bromophenyl)porphyrin **162c** failed to participate in the Sonogashira reaction as Cu(I) free conditions proved ineffective at facilitating cross-coupling.

Having achieved the synthesis of phenyl "spaced" allenylporphyrins **164a/b**, probing the reactivity of the installed allenyl group continued. The first reaction attempted was the head to head dimerisation described previously (*cf.* Scheme 5.5). While the directly linked allenylporphyrins **148b** and **148c** exhibited only minimal activity, the reactions with both **164a** and **164b** proceeded readily with complete consumption of starting material after 18 hours heating at reflux. However, this reaction displayed none of the expected selectivity with regards to which of the allenic bonds underwent reaction.[296] A complex mixture of poorly soluble dimers **165**, which could not be separated by column chromatography, was the result of this synthesis (Scheme 5.8). UV analysis showed negligible changes with respect to the spectrum of the starting material, which was expected considering the lack of conjugation between the distal allenic bond and the porphyrinoid system. HRMS (MALDI) indicated the presence of the target compound but NMR spectroscopic analysis proved unsatisfactory in analysing the cyclobutane region because of significant broadening of the NMR signals.



164b

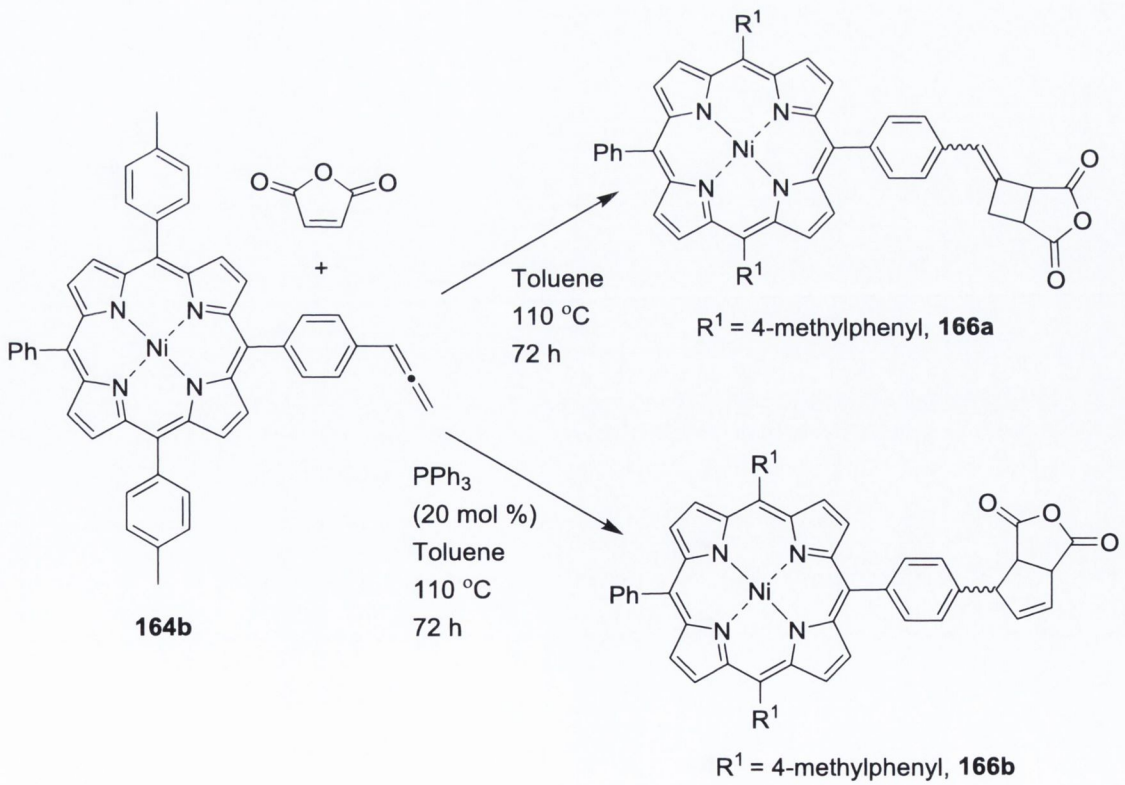
165
Por = porphyrinoid core of **164b**

Scheme 5.8: Ni(II) promoted dimerisation of **164b** with the possible isomerisation patterns of cycloadduct **165**, which could not be isolated or resolved.

The next reaction performed was a Diels-Alder reaction using 1,3-cyclohexadiene as the diene and **164b** as the dienophile. Even after heating for three days in toluene at reflux, no consumption of starting materials was observed. Examples in the literature report that Rh(I) salts can help promote Diels-Alder reactions of allenes.[294,299,300] Therefore, $Cl_2Rh_2(cod)_2$ was added to effect the desired reaction. After 18 hours, **164b** was entirely consumed but the Diels-Alder product was obtained in only trace amounts. Here, the [2+2] dimerisation reaction described in Scheme 5.8 proved to be the dominant reaction. Rh(I) salts are also known to promote [2+2] additions of allenes, nevertheless, the [4+2] product was expected to be more favoured than the disallowed [2+2] addition.

This apparent preference for [2+2] cycloadditions led to the attempt of a more straightforward reaction using the strongly electron-deficient maleic anhydride. Here, in the absence of any additives, the [2+2] addition between **164b** and maleic anhydride was effected after heating at reflux in toluene for three days (Scheme 5.9). The resultant porphyrin exhibited extremely poor solubility and could not be purified by column chromatography. Both TLC and HRMS analyses indicated the complete consumption of **164b** and formation of a [2+2] cycloadduct **166a**. Similarly, the IR spectrum of the product

showed the expected carbonyl stretching band at 1623.9 cm^{-1} with a shoulder appearing at 1768.7 cm^{-1} as well as a broad peak at 3256.4 cm^{-1}. Again, the regiochemistry of the addition could not be determined as a clear ^1H NMR spectra could not be obtained. Recent research by Lu and co-workers on the use of PPh_3 to effect the [3+2] addition of allenes[301,302] was envisaged as a final trial method to manufacture diverse ring systems from the allenylporphyrin system (Scheme 5.9). This reaction took three days to reach completion, and TLC as well as HRMS analysis indicated complete consumption of starting material **164b** and formation of a cycloadduct. Again, solubility became a major issue as the product was impossible to purify cleanly by column chromatography or recrystallisation. ^1H NMR analysis therefore proved impossible meaning the method and regioselectivity of the addition remained elusive. As a result, it was not possible to determine whether the desired [3+2] cycloaddition to form **166b** or the previously realised [2+2] cycloaddition yielding **166a** had occurred.



Scheme 5.9: Attempted [2+2] and [3+2] cycloaddition reactions between **164b** and maleic anhydride.

5.7 Conclusions and future work

The primary goal of this work was to establish the viable methodologies towards the installation of the chemically distinct and versatile allenyl functional group onto the porphyrin macrocycle. The synthesis of allenylporphyrins was thus investigated with two high yielding methods allowing for their successful preparation discovered. Of these, Suzuki-Miyaura cross-coupling conditions were found to be limited to the synthesis of nickel(II) porphyrins containing simple aromatic groups. Introduction of propargyl groups *via* Sonogashira chemistry followed by Pd-catalysed rearrangements proved to be a more robust method for the synthesis of a wider range of allenylporphyrins in high yield. Studies on the reactivity of this installed allenyl functional group showed that when directly attached to the porphyrin, steric or electronic effects prevent modification of the allenyl bonds. Introduction of a phenyl "spacer" between the porphyrin macrocycle and the installed functional group overcame this problem. Preliminary reactivity studies on these bridged systems have been promising but solubility issues involving the isolation and characterisation of the cycloaddition products thus formed were encountered. Future synthetic work will therefore focus on a more in-depth analysis of the reactivity of the allenylporphyrins in an effort to yield novel porphyrins bearing interesting structural, electronic and optical properties, further proving the synthetic utility of this porphyrin functional group. Further investigations will also focus on the applicability of these methods to beta functionalised porphyrins as well as physicochemical studies on the properties of the allenylporphyrin systems.

Chapter 6:

Tailored synthesis of heteroatom substituted porphyrins

6.1 Sulfur-appended porphyrins – unusual product formation[i]

6.1.1 Background – mercapto-porphyrins

Owing to their biological and medical importance,[303] the synthesis of organosulfur compounds has been the focus of thorough investigations.[304-306] Porphyrins bearing thiol and thioether substituents have a diverse range of optical applications due to their ability to form self-assembled monolayers (SAMs) on gold surfaces[205,307-309] and this attribute formed the basis for the present interest in mercapto-porphyrins. The initial work on thioporphyrins utilised a phenyl spacer between the porphyrin core and the sulfur atom. While simplifying syntheses, this effectively eliminates much of the electronic interaction of the porphyrin and thiol groups. Synthesis of porphyrins directly substituted with mercapto functionality at the meso position were first achieved *via* condensation methodologies[310,311] but more recent applications of Pd-catalysed chemistry provided access to a wide range of arylsulfanyl and alkysulfanyl porphyrins in moderate yields.[194] Nucleophilic displacement reactions have also been reported.[312,313] Isolation of the free thiol directly substituted onto the porphyrin has never been reported. In terms of other Group VI elements, hydroxyporphyrin complexes are the only ones reported and have been investigated in detail because of their significance in the natural heme degradation pathways and the keto-enol tautomerism of oxophlorins.[314] These complexes are typically generated *via* oxidative methodologies,[315] although Pd-catalysed routes have been reported.[192] The primary goal of the present work is therefore to investigate synthetic avenues for the introduction of sulfur containing groups to the porphyrin scaffold that may be successfully cleaved or deprotected to the free thiol.

One important development in the field of organosulfur chemistry is nucleophilic aromatic substitution (S_NAr) reactions with the thiolate anion.[316,317] Typically, thiolate S_NAr

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[i] The work detailed in this section (6.1) was all performed in close collaboration with Dr. Aoife A. Ryan, postdoctoral research fellow within the Senge research group. All Ni(II) porphyrins were synthesised by the author while Dr. Ryan performed the work on free-base and Zn(II) porphyrins.

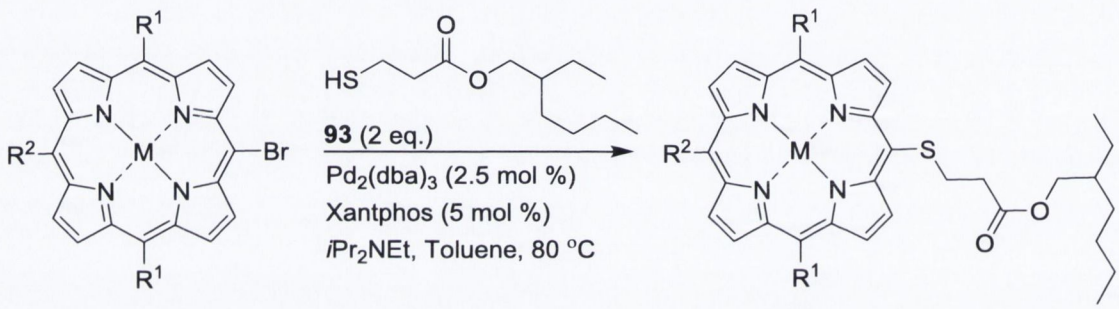
only occurs with activated aryls with leaving groups such as halides or tosylates, requiring a very strong base, elevated temperature and/or the use of metal catalysts.[318-321] Additionally, it is often hindered via competing oxidation reactions to form disulfide bonds.[322] A secondary goal of the present research was to probe the reactivity of generated porphyrin thiolates towards such S_NAr reactions.

6.1.2 Introduction of masked thiol group

The first stage of this work involved selection of appropriate thiol surrogates. The choice of mercaptan introduced was based on three major criteria – (1) stability and properties of the thiol precursor, (2) its ease of introduction and, (3) the ability to undergo quantitative deprotection to give the free thiol. Thiol 2-ethylhexyl-3-mercaptopropanoate **93** was found to fulfil all three conditions.[323-325] As a heavy thiol, **93** is practically odourless and resistant to simple oxidation to the disulfide. Additionally, it is stable to acidic conditions, Pd-catalysed cross-couplings and chromatographic purification but is reported to undergo clean, quantitative deprotection with mild base hydrolysis through a *β*-elimination process (see Scheme 6.1 for mechanism). The introduction of a masked thiol functionality to the porphyrin periphery was achieved through application of a versatile Pd-catalysed C-S bond forming reaction developed by Itoh and Mase.[324,325] Reaction of a small library of bromoporphyrins with **93** (Table 6.1) produced *S*-appended porphyrins, so-called protected thiols, in yields of 63-85 %; higher yields and at lower catalyst loadings than those reported *via* analogous methodologies.[194] The ligand employed played a key role in facilitating these improved yields. The original screen of phosphine ligands showed that the bidentate 4,5-*bis*(diphenylphosphino)-9,9-dimethylxanthene (Xantphos) ligand[326] gave optimum yields and selectivity for aryl-sulfur bond forming reactions[324] and this investigation proves it can be extended with minimal loss in yields to porphyrin chemistry. The reaction described proved tolerant of a range of both free-base and metalloporphyrins, although a slight reduction in yield was noted with Ni(II) porphyrin complexes. Both alkyl

and aryl residues were successfully incorporated as were meso free porphyrins **168 b/e/f**, obtained *via* mono-bromoporphyrins **167a-c**. Given the reported stability of the introduced thiol, these porphyrins provide avenues for further exploitation of the porphyrin scaffold through subsequent functionalisation reactions. These protected thiols also have the potential to be used in Au–NP formulation or as a photosensitiser delivery system in PDT,[327] but the primary goal here was for their use in deprotection reactions to yield free thiol porphyrins.

Table 6.1: Synthesis of porphyrin-thiol surrogates *via* Pd-catalysis.



168

Entry	S.M.	M	R^1	R^2	Product	Yield (%)
1	**154b**	2H	4-Methylphenyl	Phenyl	**168a**	70
2	**167a**	2H	Phenyl	H	**168b**	68
3	**147i**	Zn(II)	Phenyl	Phenyl	**168c**	76
4	**147j**	Zn(II)	4-Methylphenyl	Phenyl	**168d**	85
5	**167b**	Zn(II)	Phenyl	H	**168e**	76
6	**167c**	Ni(II)	4-Methylphenyl	H	**168f**	72
7	**147b**	Ni(II)	4-Methylphenyl	Phenyl	**168g**	63
8	**147a**	Ni(II)	Phenyl	Phenyl	**168h**	68
9	**147h**	Ni(II)	1-Ethylpropyl	*n*-Butyl	**168i**	65

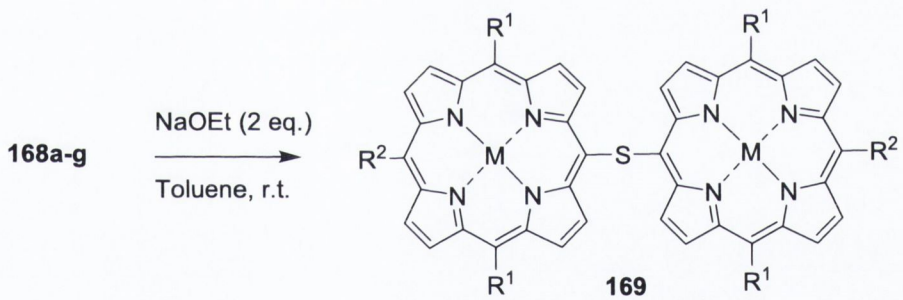
Reaction conditions: Reactions were performed at 15 mM porphyrin concentration under argon for 16 hours. All yields are isolated yields after column chromatography (silica gel). Entries 1-5 were performed by Dr. Aoife Ryan

6.1.3 Deprotection reactions – unique reactivity discovered

All protected thiols were subjected to base-mediated deprotection in an effort to obtain a free thiol group directly attached to the porphyrin macrocycle. However, deprotection through *β*-elimination of the thioether chain of masked compounds **168a–g**, gave unusual results, with the *S*-linked *bis*porphyrins **169a–g** isolated as the major products (Table 6.2). In a remarkable S_NAr, sulfur-linked, symmetrical, porphyrin dimers were generated *via*

simple deprotection of the thioether-appended porphyrins. Thus, the initial goal of a free thiol group directly attached to the porphyrin macrocycle *via* base deprotection was not realised, as *bis*porphyrin products were observed predominantly. Such sulfur linked *bis*porphyrins have not previously been reported and are easily produced, in contrast to other heteroatom linked porphyrin arrays which generally require many synthetic steps.[192] As such, these dimers offer potential as new scaffold systems in porphyrin research. Although presently in the midst of a partial renaissance, substitution reactions on porphyrins are limited, and typically require highly specific activated systems or reactive nucleophiles and high temperatures.[175,313,328-330] This room temperature *in situ* S_NAr of an apparently unactivated porphyrin in such fashion represents the first reaction of this type to be documented.

Table 6.2: Synthesis of *S*-linked *bis*porphyrins *via* base-mediated deprotections.



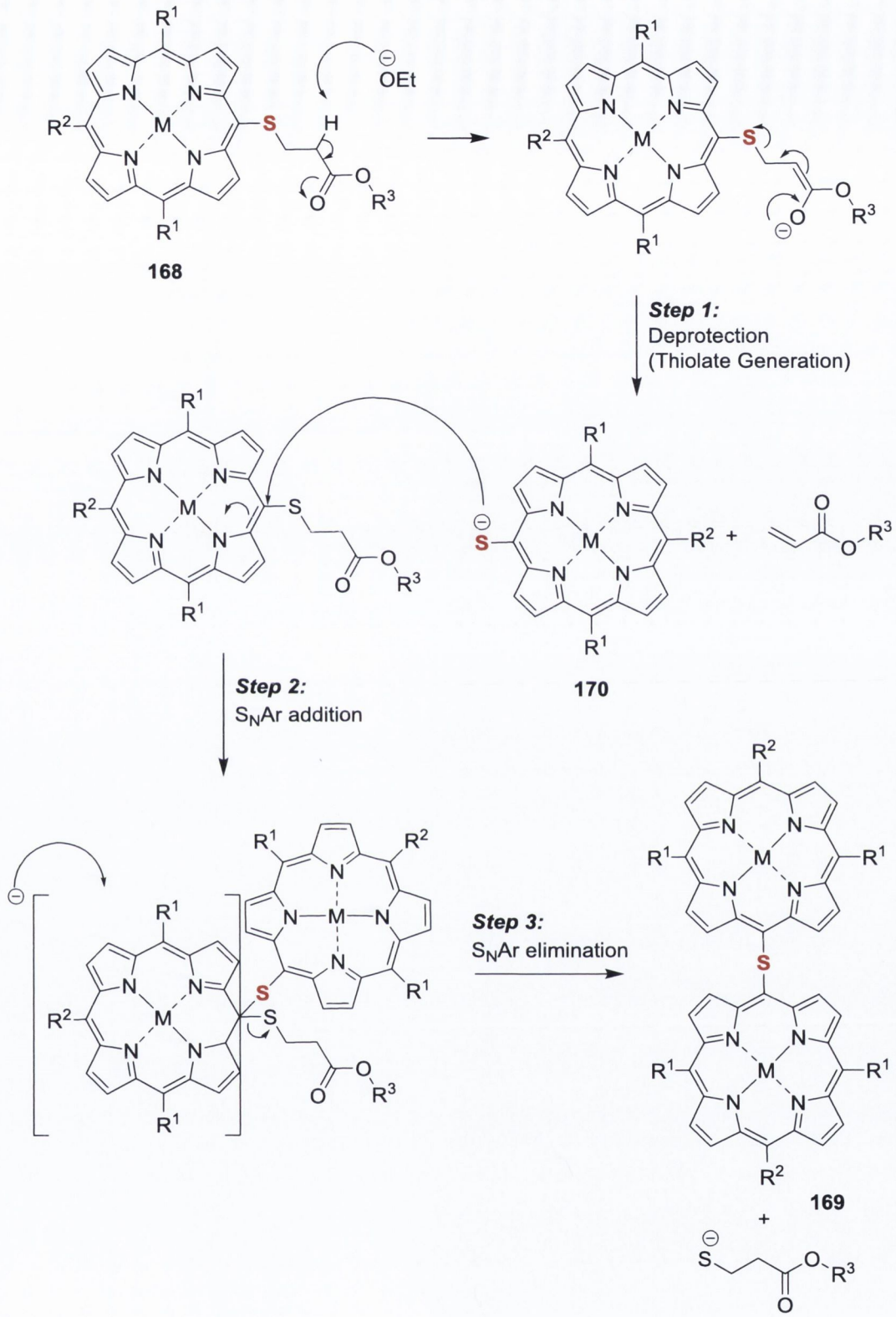
Entry	Thiol Surrogate	M	R^1	R^2	Dimer	Yield (%)[a]
1	**168a**	2H	4-Methylphenyl	Phenyl	**169a**	n/d[b]
2	**168b**	2H	Phenyl	H	**169b**	n/d[b]
3	**168c**	Zn(II)	Phenyl	Phenyl	**169c**	56
4	**168d**	Zn(II)	4-Methylphenyl	Phenyl	**169d**	63
5	**168e**	Zn(II)	Phenyl	H	**169e**	55
6	**168f**	Ni(II)	4-Methylphenyl	H	**169f**	72
7	**168g**	Ni(II)	4-Methylphenyl	Phenyl	**169g**	68

Reaction conditions: Reactions were performed at 4 mM porphyrin concentration under argon for 4 hours. [a] Isolated yields for dimeric species after column chromatography (silica gel). [b] Yields not determined due to inseparable mixtures of *S*-linked and disulfide linked *bis*porphyrins. Entries 1-5 were performed by Dr. Aoife Ryan.

The dimerisation reaction proceeded readily in all cases, with yields only being reduced slightly by the competing formation of free thiol and/or disulfide. These compounds

were easily purified *via* extraction into dichloromethane, with the free thiol and/or disulfide side products generally only solubilising in more polar solvents such as ethyl acetate. These side products were confirmed *via* HRMS analysis and UV-vis absorption spectra (Figure 6.1) but acceptable NMR spectra were not achieved. Zn(II) and Ni(II) dimers **169c-g** were isolated in good to excellent yields of 55–72 % with higher yields observed for the Ni(II) species, presumably due to increased nucleophilicity of the Ni(II) thiolate (*vide infra*). Free-base *bis*porphyrins **168a** and **169b** were more difficult to purify, with the *S*-linked dimers in most cases co-eluting with the disulfide derivative.

These *S*-linked dimers were generated *via* S_NAr by one porphyrin thiolate at the meso position of another substituted porphyrin, with the isooctyl-3-mercaptopropanoate group acting as leaving group and the porphyrin thiolate behaving as nucleophile (see Scheme 6.1 for proposed mechanism). The proposed mechanism is that β-elimination initially gives porphyrin thiolate **170**.The strength of this nucleophile is such that it reacts immediately with any remaining starting material **168** still present, forming the *bis*porphyrin anion *via* S_NAr. Elimination of the sulfanyl chain provides rearomatisation to the *S*-linked dimer **169**. Any remaining thiolate either precipitates out of solution or is oxidised to the disulfide-linked dimer upon work-up. Attempts to hinder thiolate S_NAr generation of **169** through the use of the more non-polar solvent *n*-hexane, in which the free thiolate **170** was likely to be insoluble and precipitate out of solution, were unsuccessful, with only starting materials **168** isolated.



Scheme 6.1: Proposed mechanism for the formation of *S*-linked *bis*porphyrins **169** through thiolate intermediate **170**.

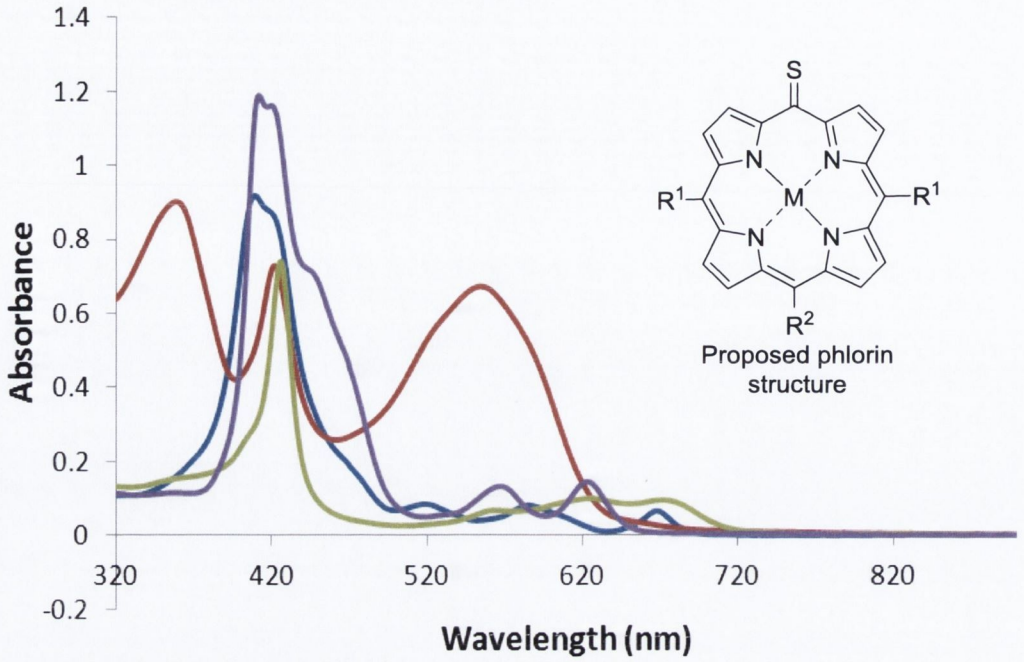


Figure 6.1: UV-vis absorption spectra of **169b** (purple), **169c** (blue) and respective phlorin side products with proposed structure (**169b**-red and **169c**-green) in CH_2Cl_2.[231]

The UV-vis absorption profiles of **169b** and **169c** are shown in Figure 6.1. The *S*-linked *bis*porphyrins **169b** and **169c** display broad Soret band absorption with respect to their thiol surrogates **168b** and **168c**. Additionally, the absorption profiles of side products of **169b** and **169c** from the reaction are shown in red and green respectively. These are presumed to be phlorin species as the profile shown is similar to those in the literature.[174] They were most likely generated *via* tautomerisation to the thione form of the free thiol (phlorin).[310] The X-ray structural analysis of **169c** definitively proves the thioether structure (Figure 6.2). The compound crystallised as the axial methanol adduct and exhibits a skewed co-facial structure.[i] The least-squares-planes of the two 24-atom macrocycles form an

[i] *Crystal data:* $C_{79}H_{52}N_8O_2SZn_2 \cdot 0.5CH_3OH$, $M = 1326.12$, triclinic, space group *P*-1, $a = 12.2362(6)$, $b = 15.0184(7)$, $c = 17.9322(9)$ Å, $\alpha = 99.999(2)°$, $\beta = 103.404(1)°$, $\gamma = 93.376(1)°$, $V = 3140.0(3)$ Å^3, $Z = 2$, T = 104 K, μ (MoK$_\alpha$) = 0.856 cm^{-1}, 26768 reflections measured, 10863 unique reflections measured ($R_{int} = 0.025$), 875 parameters, 8742 reflections with $I > 2.0\sigma(I)$, refinement against $|F^2|$, $R1(I > 2.0\ \sigma\ (I)) = 0.0855$, $wR2$ (all data) = 0.2226, $S = 1.05$, $\rho_{max} = 5.99$. The structure shows disorder of one axial methanol and one phenyl residue, both of which were refined with 50 % occupancy. A methanol of solvation was refined with 50 % occupancy. The residual electron density is located close to the S atom (0.8 Å). The supplementary crystallographic data for this compound is contained within the file CCDC 951823, available online from The Cambridge Crystallographic Data Centre.

angle of 58.4(1)° indicating an almost cofacial orientation of the two porphyrin systems. Such a skewed, yet unaggregated macrocycle orientation in *bis*porphyrins is rare and has only been observed in C-OH, NH and CH=CH linked systems.[192,331,332] These cofacial *S*-linked porphyrin scaffolds may have applications in the fields of photocatalysis or electron transfer studies.

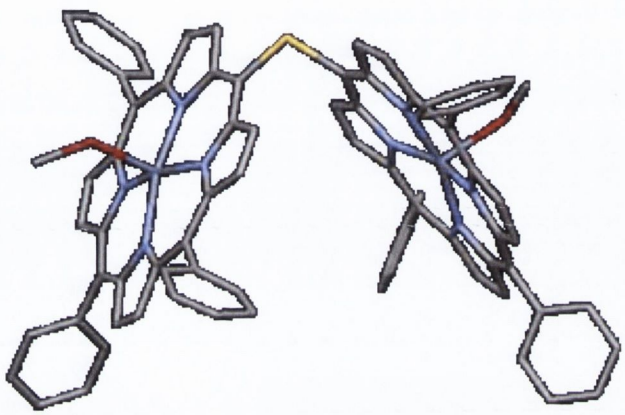
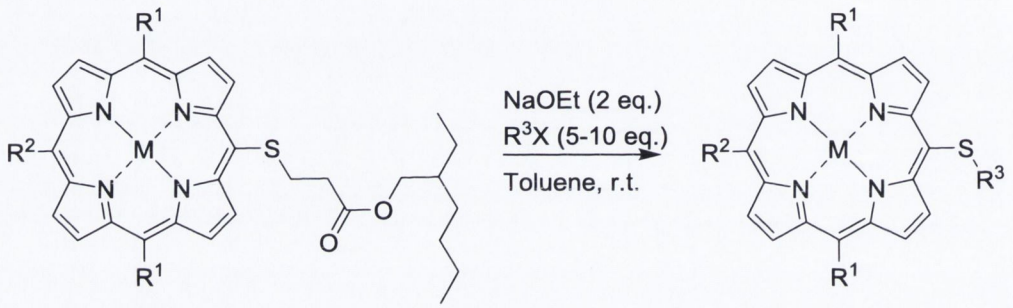


Figure 6.2: View of the molecular structure of **169c** in the crystal. Hydrogen atoms and disordered positions have been omitted for clarity. Selected bond lengths and angles: C5-S1 = 1.826(6) Å, C25-S1 = 1.856(7) Å, C5-S1-C25 = 104.8(3)°.[231]

6.1.4 Reactivity studies of porphyrin thiolates and thioethers

To further elucidate both the strength of the porphyrin thiolate as a nucleophile and the susceptibility of the isooctyl-3-mercaptopropanoate to act as a leaving group, displacement reactions both with the generated porphyrin thiolate and the thiol surrogates were executed with similar aryl and aliphatic halides (Tables 6.3 and 6.4).

Table 6.3: Displacement reactions of porphyrin thiolates with organic electrophiles.



168 **171**

#	S.M.	R^1	R^2	M	R^3	X	Target	Yield (%)
1	**168d**	4-Methylphenyl	Phenyl	Zn(II)	Methyl	I	**171a**	71
2	**168i**	1-Ethylpropyl	*n*-Butyl	Ni(II)	Methyl	I	**171b**	95
3	**168g**	4-Methylphenyl	Phenyl	Ni(II)	Hexyl	Br	**171c**	95
4	**168d**	4-Methylphenyl	Phenyl	Zn(II)	Hexyl	I	**171d**	<5[a]
5	**168d**	4-Methylphenyl	Phenyl	Zn(II)	Hexyl	Br	**171d**	<5[a]
6	**168g**	4-Methylphenyl	Phenyl	Ni(II)	Phenyl	I	**171e**	n/d[a]
7	**168d**	4-Methylphenyl	Phenyl	Zn(II)	Phenyl	Br	**171f**	n/d[a]
8	**168g**	4-Methylphenyl	Phenyl	Ni(II)	*p*-$C_6H_4NO_2$	Br	**171g**	n/d[a]
9	**168d**	4-Methylphenyl	Phenyl	Zn(II)	*p*-C_6H_4CHO	F	**171h**	n/d[a]

Reaction conditions: Reactions were performed at 10 mM porphyrin concentration under argon for 2 hours. Where applicable, yields are isolated yields after column chromatography (silica gel). [a] Predominant products were *S*-linked and disulfide linked *bis*porphyrins. Entries involving Zn(II) porphyrins were performed by Dr. Aoife Ryan.

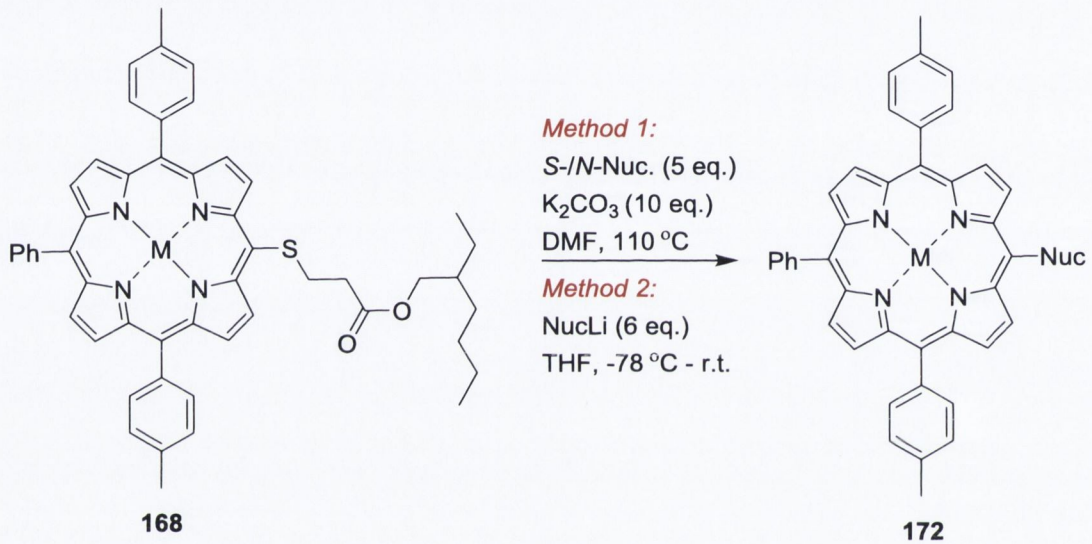
The first reactions screened were deprotections in the presence of aliphatic electrophiles. When Zn(II) and Ni(II) porphyrins **168d** and **168i**, were deprotected in the presence of iodomethane, the thiolate generated immediately reacted with the electrophile and methylthio- products **171a** and **171b** were formed in 71 and 95 % yields respectively, with no dimer formation (Table 6.3, Entries 1 and 2). In the presence of other electrophiles, however, an increasingly marked difference in reactivity of Ni(II) and Zn(II) porphyrins was

observed. For Ni(II) porphyrin **168g**, the reaction with 1-bromohexane was slower than with iodomethane (Entry 3). Ten equivalents of the brominated electrophile were required for the desired product **171c** to be obtained in near quantitative yield of 95 %. For Zn(II) compound **168d** and either bromo- or iodohexane (Entries 4 and 5), the thiohexyl substituted product **171d** was only obtained in trace yield, indicating that the Zn(II) thiolate is not as strong a nucleophile as its Ni(II) counterpart. For the aromatic displacements with aryl halides (Table 6.3 Entries 6-9); both activated and unactivated towards S_NAr chemistry; no target formation was observed. In the case of both Ni(II) and Zn(II) systems the dominant products were the *S*-linked *bis*porphyrins. While the porphyrin thiolates may be strong enough nucleophiles to successfully displace these groups, the reactions by their nature must be performed in the presence of an additional leaving group, *i. e.* porphyrin thioethers **168**. This indicates that while Ni(II) porphyrin thiolates are significantly more powerful than their Zn(II) analogues, the porphyrin thioether is a better leaving group than simple aryl halides.

Attention then turned to probing the ability of the thioether-appended porphyrins to participate in S_NAr reactions with other organic nucleophiles. Employing a variety of nucleophiles, the displacement of the thioether was investigated (Table 6.4) using free-base **168a**, Zn(II) **168d** and Ni(II) **168g** species. For *N*-based nucleophiles, only *S*-linked dimers were observed, indicating that these bases were effective at promoting β-elimination and that the nucleophilic strength of the porphyrin thiolate is greater than these amine bases (Table 6.4, Entries 1-3). In terms of other thiolate displacements the reaction between free-base **168a** and 4-bromobenzenethiol proved more successful than for Ni(II) complex **168g**. The free-base complex **172d** was obtained in 48 % yield while Ni(II) product **172e** could not be isolated from the reaction mixture. In this case a number of products were formed which could not be separated and identified. While showing that the thioether chain can be displaced using soft nucleophiles this result also correlates with the pronounced strength of the Ni(II) thiolate. When employing C-based nucleophiles some success was observed, with

butylated products **172f** and **173g** observed in approximately 10 % yield but with concomitant degradation of the porphyrin macrocycle due to the elevated temperatures required. Addition of PhLi to a solution of **168g** allowed for the starting material to be completely recovered, indicating this to be an insufficiently strong nucleophile to displace the thioether chain.

Table 6.4: Displacement reactions on thioether-porphyrins **168** with various organic nucleophiles.



168 **172**

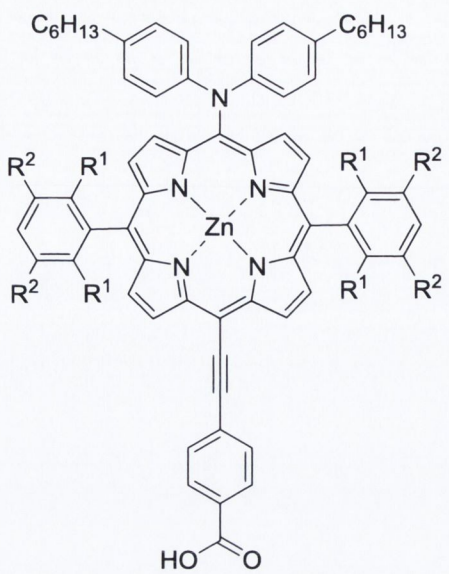
Entry	S.M.	M	Nuc.	Target	Result
1	**168d**	Zn(II)	Diisopropylamine[a]	**172a**	*S*-linked dimer **169d**
2	**168d**	Zn(II)	Piperidine[a]	**172b**	*S*-linked dimer **169d**
3	**168g**	Ni(II)	Piperidine[a]	**172c**	*S*-linked dimer **169g**
4	**168a**	2H	4-Bromobenzenethiol[a]	**172d**	48 % yield
5	**168g**	Ni(II)	4-Bromobenzenethiol[a]	**172e**	~30 % yield[c]
6	**168a**	2H	*n*-BuLi[b]	**172f**	<10 % yield[d]
7	**168g**	Ni(II)	*n*-BuLi[b]	**172g**	<10 % yield[d]
8	**168g**	Ni(II)	PhLi[b]	**172h**	Unreacted starting material

Reaction conditions: Reactions were performed at 10 mM porphyrin concentration under argon. Where applicable yields are isolated yields after column chromatography (silica gel). [a] Method 1. [b] Method 2. [c] Multiple products formed. Target could not be isolated from product mixture. [d] Predominant product was unreacted starting material. Entries involving free-base or Zn(II) porphyrins were performed by Dr. Aoife Ryan.

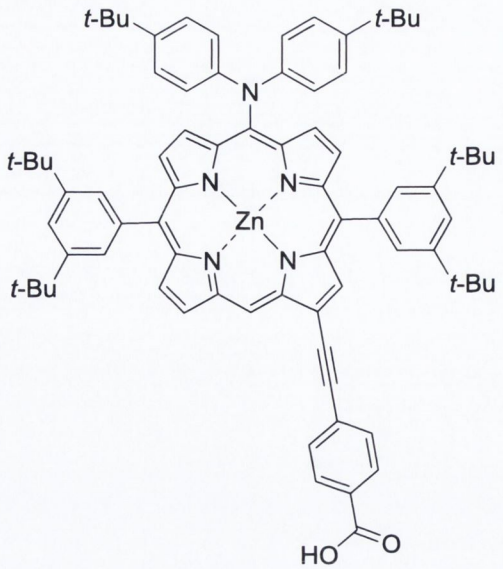
6.2 Rearranged aminoporphyrins – classic systems for a new purpose

6.2.1 Background – solar cells and porphyrin dipoles

Grätzel and O'Regan first published the concept of dye-sensitised solar cells (DSSCs) using a TiO_2 support in 1991.[333] Research throughout the 1990s and early 2000s found that ruthenium based complexes provided the best efficiency[334] with maximum power-conversion efficiency plateauing around 10 % for almost a decade with the peak efficiency recorded as 11.5 %.[335-337] Recent research by Grätzel and co-workers into cheaper and more environmentally friendly, organic dyes represented a major breakthrough in the field when they published a series of porphyrins that had efficiency rates of up to 12.3 % (YD2 **173** and YD2-o-C8 **174**), the greatest ever seen in such systems and trumping the previous standard, and presumed ceiling, for Ru dyes.[137,338] The optimum systems to emerge from this work involved "push-pull" porphyrins where electrons are transferred through the porphyrinoid core from a *N*-based electron donor to an electron sink, typically possessing carboxylic functionality. Follow up research using the same core aminoporphyrin scaffold allowed for increased efficiency to 13 %[134] through modification of the acceptor system to enable broader absorption in the visible spectrum. This series of highly efficient porphyrin dyes and practically all of the countless variations that have since been published are 5,15-substituted donor-acceptor scaffolds where the dipole of the porphyrin runs along a meso-meso axis. While these systems are typically the most accessible, the current field is severely limited as almost no research has been performed with systems containing an altered dipole moment. Ishida *et al.* have published a series of papers on an altered dipole system where the push-pull axis runs along a meso-beta axis (ZnEP1 **175**).[339,340] These systems exhibited decreased efficiency with relation to their 5,15-substituted analogues but clearly showed, however, that altering the dipole moment of these porphyrins can alter their solar energy conversion potential.



R^1 = H, R^2 = *t*-Butyl; YD2 **173**
R^1 = OC_8H_{17}, R^2 = H; YD2-o-C8 **174**



ZnEP1 **175**

The purpose of the present research was to determine the effect of a more significant alteration of the dipole of the porphyrinoid system on the efficiency of the dye in a DSSC through use of a completely modified porphyrin scaffold. The Senge group was instrumental in pioneering the use of 5,10-substituted porphyrins[122,341] and has adapted many high yielding reactions to synthesise this previously inaccessible class.[119,172] Previous work has shown that the modification of the dipole to run along the β-β axis by adopting a 5,10-substitution pattern significantly improves many of the electronic properties of the porphyrin, in particular their non-linear absorption (NLA) responses.[342-344] A series of 5,10-A_2B_2 porphyrins were found to possess effective nonlinear absorption coefficients (β_{eff}, derived from low input energy open Z-scan data) in the range of 4.8–18.1 cm W^{-1}; several orders of magnitude higher than those observed for their 5,15-A_2B_2 counterparts.[345] In addition, the 5,10-substituted systems displayed a unique reverse saturable absorption (RSA) to saturable absorption (SA) switch in the nanosecond regime, a highly desirable trait in the field of nonlinear optics (NLO) and one completely absent from their 5,15-analogues. 5,10-A_2B_2 compounds have thus already been shown to exhibit distinct photophysical properties. The goal of the present work was to utilise this trait of 5,10-porphyrins by modifying the

existing state of the art aminoporphyrin dyes **173** and **174** to adopt a 5,10-orientation of the donor and acceptor systems.

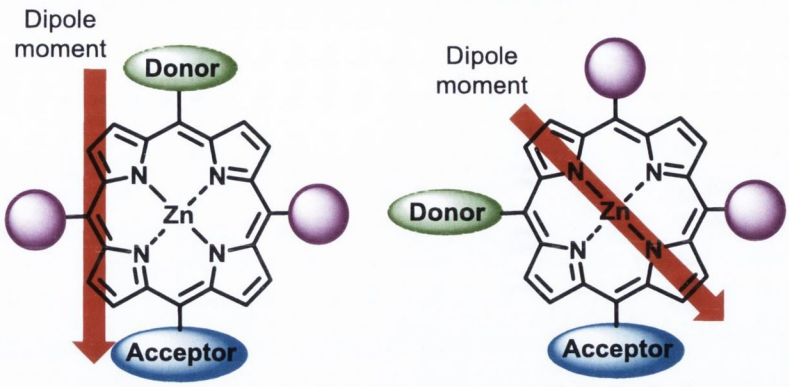
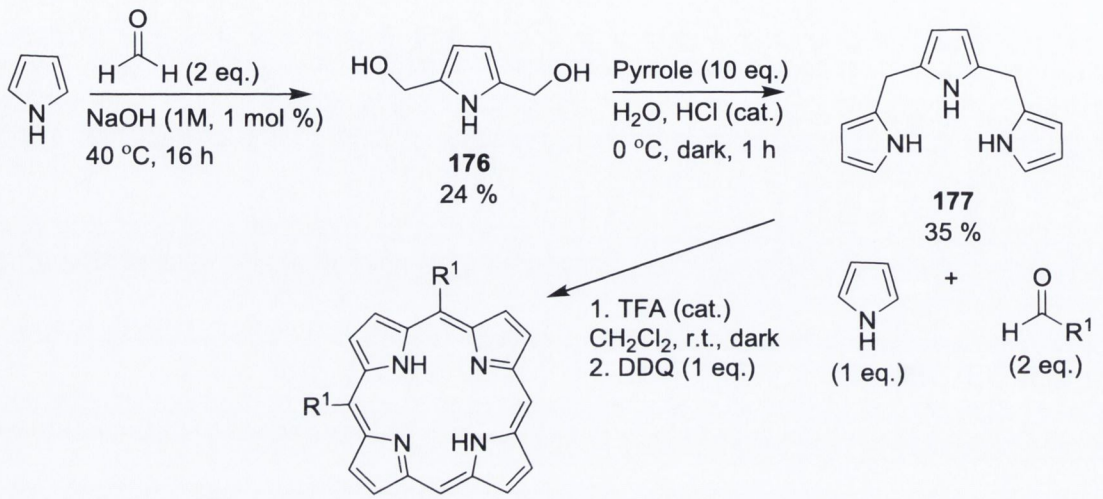


Figure 6.3: Dipole moments in 5,15- and 5,10-A_2BC donor-acceptor porphyrin scaffolds.

6.2.2 Condensation chemistry with tripyrrane

Akin to their 5,15-counterparts there are many available synthetic routes towards 5,10-substituted porphyrins.[119] While a total synthesis of a specific target from bilane precursors[169,346] or through mixed condensations are among the more favoured routes, a more modular approach was deemed most effective here, as it provides for easier modification of substituents and rapid generation of a library of dyes. While historically more demanding than 5,15-systems the synthesis of 5,10-porphyrins has been simplified through recent advances in the synthesis of appropriate tripyrryl precursors.[160-162] In a two-step process, pyrrole was initially reacted with an excess of formaldehyde to yield *bis*(hydroxymethyl)pyrrole **176** (Scheme 6.2). This was then reacted with an excess of pyrrole to yield tripyrrane **177**. Modification of the purification method for this compound through use of a cold recrystallisation from hexane enabled it to be synthesised in bulk and stored, similar to dipyrromethane **124**. Compound **177** was a key building block as condensation with an appropriate aldehyde and pyrrole provides access to any 5,10-disubstituted porphyrin. The issues with condensation methodologies discussed previously were amplified here, due to the addition of an extra distinct component required for tetrapyrrole formation. As such, yields for 5,10-condensations were typically in the 5-10 %

range rather than the 30-50 % obtained with 5,15-condensations from **124**.[341] Significant formation of both the 5- and 5,15-substituted porphyrins through acid scrambling[162] was also observed in all condensation reactions and often impaired purification.

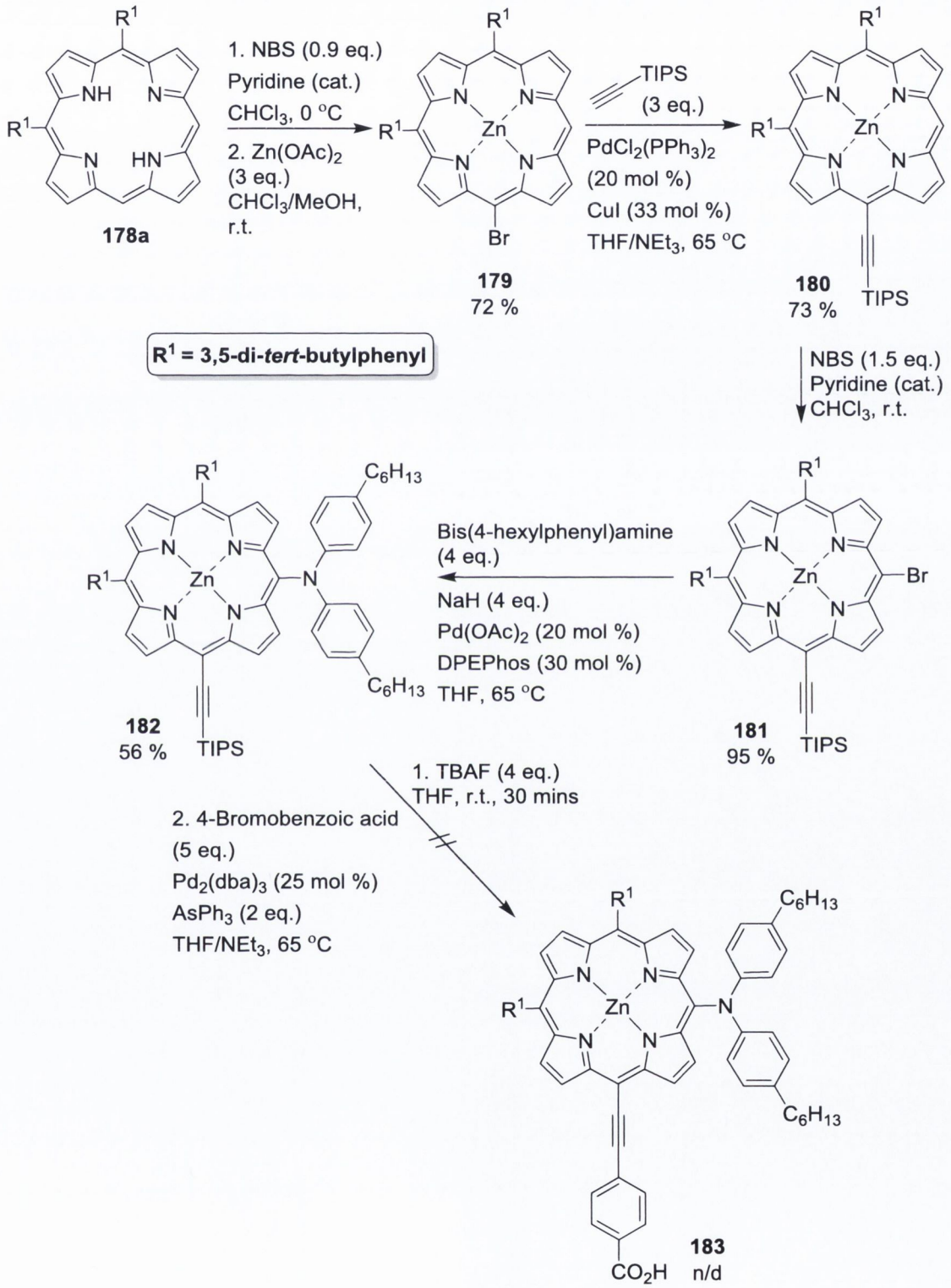


Scheme 6.2: Synthesis of tripyrrane **177** and condensation reactions to form 5,10-disubstituted porphyrins.

6.2.3 Functionalisation reactions

With the 5,10-orientation thus defined in starting porphyrins **178a** and **178b**, investigations focused on the optimum sequence to install the donor (diarylamine) and acceptor (conjugated carboxylic acid) groups onto the preformed scaffold as well as the required metallation of the system. Initially, the sequence followed was that reported in the original Grätzel porphyrin synthesis.[137,338] This synthesis was started with **178a** and details are shown in Scheme 6.3. Although this *tert*-butyl system has been shown to be less effective than the octyloxy-substituted porphyrin,[137] the known solubility of (3,5-di-*tert*-butylphenyl)porphyrins and their ease of characterisation[347-349] made this a preferential starting point for optimisation of the various steps on the 5,10-scaffolds before moving to the more active system. Here, sequential, selective, brominations followed by Pd-catalysed reactions were employed to install the desired functionality in a controlled, step-wise manner. The strengths of this approach are its modularity. At any stage a modified donor or

acceptor group can be installed – allowing for rapid generation and comparison of diverse electronic effects.



Scheme 6.3: Attempted synthesis of 5,10-*bis*(3,5-di-*tert*-butylphenyl)porphyrin system **183**.

The first Pd-catalysed reaction employed was a Sonogashira cross-coupling. This necessitated Zn(II) addition to form **179** be performed first to facilitate easier purification of product **180** by eliminating the possibility of copper insertion into the porphyrin macrocycle. Installation of the complete acceptor system at this stage was deemed infeasible as the carboxylic functionality would create issues regarding purification and functional group tolerance in the latter half of the synthesis. As such TIPS-acetylene was introduced in 73 % yield. Compound **180** could be handled and purified with ease and the TIPS group could be selectively removed to yield the free acetylene later in the synthesis. Subsequent bromination to yield **181** allowed the *bis*(4-hexylphenyl)amine moiety to be installed to give **182** in reasonable yield of 56 %. This was the first problematic step of the synthesis. The secondary amine was not commercially available and was synthesised as a yellow oil which defied crystallisation. The lack of a solid sample made accurately weighing and utilising this amine difficult. Additionally, a significant amount of debrominated material **180** was obtained from the Buchwald-Hartwig reaction – a complication not reported previously. While usable quantities of **182** were nevertheless achieved, attempted deprotection of the TIPS-acetylene and a second Sonogashira reaction to give target acid **183** failed, resulting solely in an unidentifiable porphyrin mixture. The issues encountered in this synthesis ultimately led to a re-evaluation of the target route for the other 5,10-scaffold.

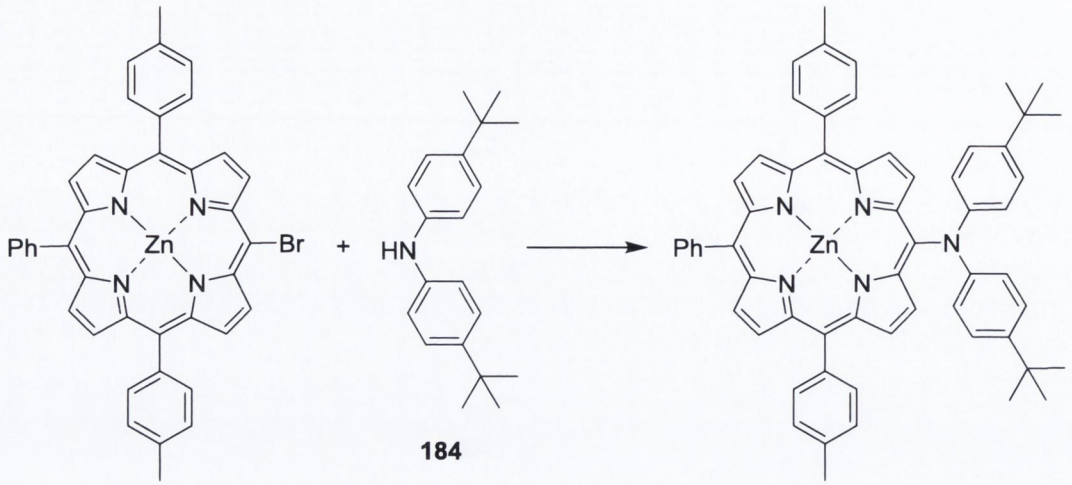
6.2.4 Synthetic optimisations

Before continuing the synthesis of the 5,10-scaffolds it was decided to investigate whether the problems encountered with the Buchwald-Hartwig amination could be overcome. To this end, a simple Zn(II) bromoporphyrin **147j** was subjected to numerous trial reactions with commercially available *bis*(4-*tert*-butylphenyl)amine **184** (Table 6.5). The nature of the substituent on the aryl group of the amine appears to play only minimal role in the efficiency of the original DSSC dyes.[135,136,334,350] Phenyl rings substituted with large alkyl groups were preferred as they limit charge recombination – as a result the *tert*-

butylphenyl amine was seen as a convenient analogue to the more optimum hexyl-substituted derivative. The purpose of the project is ultimately to delineate the effect of altering the dipole rather than the initial synthesis of an optimal dye. As such, the synthetic advantages of employing **184** outweighed the correspondingly reduced DSSC efficiency predicted in the final compound.

Buchwald-Hartwig amination reactions on porphyrins were first reported by Zhang and co-workers in 2003[195] and, with only minor alterations, their optimised procedures have been utilised in all subsequently reported procedures. Table 6.5 details the application of the most common alterations to this reaction that have been reported for other aminoporphyrin systems.[134,137,338-340] The initial reactions were performed to identify the optimum base and precatalyst combination when using the most commonly reported ligand, *bis*[2-(diphenylphosphino)phenyl]ether (DPEPhos). Using NaH as base the reaction provided higher yields in THF when $Pd(OAc)_2$ was employed as the precatalyst. However, toluene was a more effective solvent when using $Pd_2(dba)_3$ (Entries 1-4). In all cases a significant amount of debrominated starting material was observed. Potassium *tert*-butoxide proved a comparatively efficient base, with higher yields achieved with $Pd(OAc)_2$ in either solvent (Entries 5-8). In all of these cases a significant amount of debrominated material was present as well as target **185**. By way of contrast, Cs_2CO_3 proved an entirely ineffective base, with the sole product in all cases being debrominated starting material.

Table 6.5: Optimisation of Buchwald-Hartwig amination of **147j**.



147j **184** **185**

Entry	Pd Source (20 mol %)	Ligand (30 mol %)	Base (eq.)	Solvent	Temp. (°C)	Conversion (%)[a]
1	$Pd(OAc)_2$	DPEPhos	NaH (4)	THF	65	40
2	$Pd_2(dba)_3$	DPEPhos	NaH (4)	THF	65	<10
3	$Pd(OAc)_2$	DPEPhos	NaH (4)	Toluene	110	30
4	$Pd_2(dba)_3$	DPEPhos	NaH (4)	Toluene	110	66
5	$Pd(OAc)_2$	DPEPhos	KO*t*Bu (4)	THF	65	35
6	$Pd_2(dba)_3$	DPEPhos	KO*t*Bu (4)	THF	65	20
7	$Pd(OAc)_2$	DPEPhos	KO*t*Bu (4)	Toluene	110	55
8	$Pd_2(dba)_3$	DPEPhos	KO*t*Bu (4)	Toluene	110	30
9	$Pd(OAc)_2$	DPEPhos	Cs_2CO_3 (4)	Toluene	110	0
10	$Pd(OAc)_2$	DPEPhos	Cs_2CO_3 (4)	THF	65	0
11	$Pd_2(dba)_3$	DPEPhos	Cs_2CO_3 (4)	Toluene	110	0
12	$Pd(OAc)_2$	DPEPhos	NaH (4)[b]	THF	65	70
13	$Pd(OAc)_2$	DPEPhos	KO*t*Bu (4)[b]	THF	65	65
14	$Pd(OAc)_2$	DPEPhos	NaH (20)[b]	THF	65	80
15	$Pd(OAc)_2$	DPEPhos	KO*t*Bu (20)[b]	THF	65	75
16	$Pd(OAc)_2$	BINAP	NaH (20)[b]	THF	65	90
17	$Pd(OAc)_2$	BINAP	Cs_2CO_3 (10)[b]	THF	65	95
18	$PdCl_2(dppf)$	N/A	NaH (20)[b]	THF	65	60

Reaction Conditions: All reactions were performed at a 7 mM porphyrin concentration with 4 eq. of **184** under argon for 16 hours. [a] Conversion is estimated based on ^{1}H NMR spectroscopic analysis. Value is given relative to debrominated starting material. [b] Base and **184** were heated to the target temperature for 30 minutes prior to the addition of other reagents.

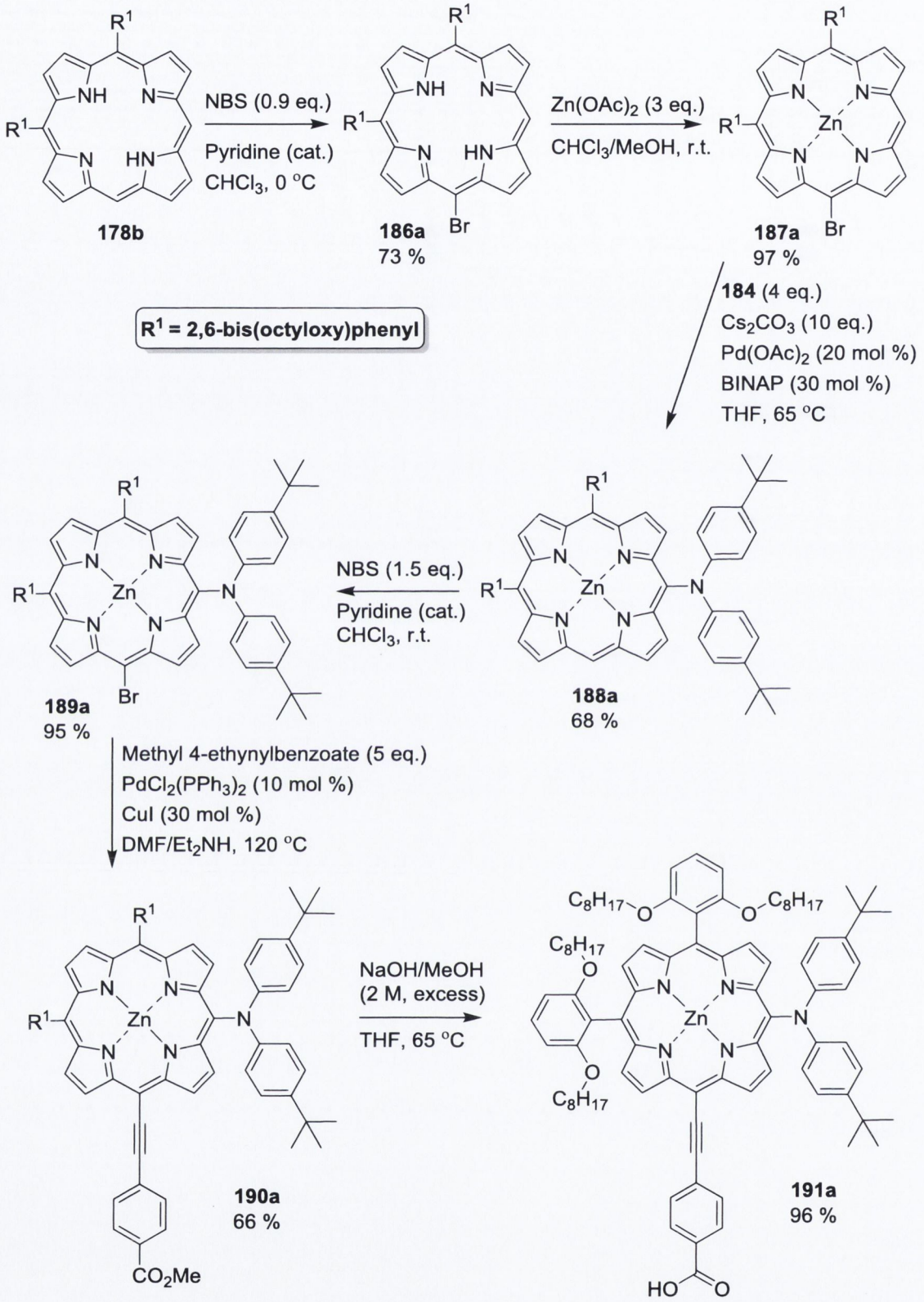
Alteration of the physical process of the reaction gave the first significant improvement in target formation. By allowing the base and amine to react together for 30 minutes before adding the remaining reagents, relative yields of 70 and 65 % for **185** were obtained for the reactions with NaH and KO*t*Bu, respectively (Entries 12 and 13). Increasing the amount of

base to 20 equivalents saw another 10 % increase in the relative yield of **185**. Entry 14 thus illustrates roughly 80 % conversion to **185**. Application of 2,2'-*bis*(diphenylphosphino)-1,1'-binaphthyl (BINAP) saw a further increase to 90 % conversion (Entry 16) while $PdCl_2$(dppf) led to a significant reduction (Entry 18). When using BINAP as ligand a further increase in conversion was observed when Cs_2CO_3 was employed as ligand (Entry 17). This corresponds with other reported procedures[339,340] but was surprising considering the inability of Cs_2CO_3 to effect the transformation when using DPEPhos. No explanation of this altered reactivity has been reported and none could be established here. As such, conditions detailed in Entry 16 were employed in all future Buchwald-Hartwig aminations.

6.2.5 Improved synthetic route

Having optimised the low-yielding steps from Scheme 6.2 the synthesis of the desired 5,10-A_2BC systems was restarted. Details of the improved route are shown in Scheme 6.3. Here, **178b** was utilised as the initial 5,10-scaffold as its synthesis proved slightly easier than **178a** and would ultimately give a more promising DSSC candidate.

The early part of the synthesis proceeds exactly as described previously. 5,10-disubstituted porphyrin **178b** was selectively brominated to give **186a** in 73 % yield before quantitative metal insertion to form **187a**. Introduction of the donor group **184** *via* the optimised Buchwald-Hartwig amination conditions then produced **188a** in 68 % yield. Another bromination reaction to give **189a** was followed by the introduction of the acceptor group in one step to give **190a** in 66 % yield, which was readily deprotected to the target carboxylic acid **191a**. The order of addition of the donor and acceptor groups was chosen based on the increased stability and functional group tolerance of the tertiary amine over the carboxylic ester. One attempt was made to introduce the groups in the opposite order but a significant amount of amide formation was observed during the amination reaction and as such that pathway was not pursued.

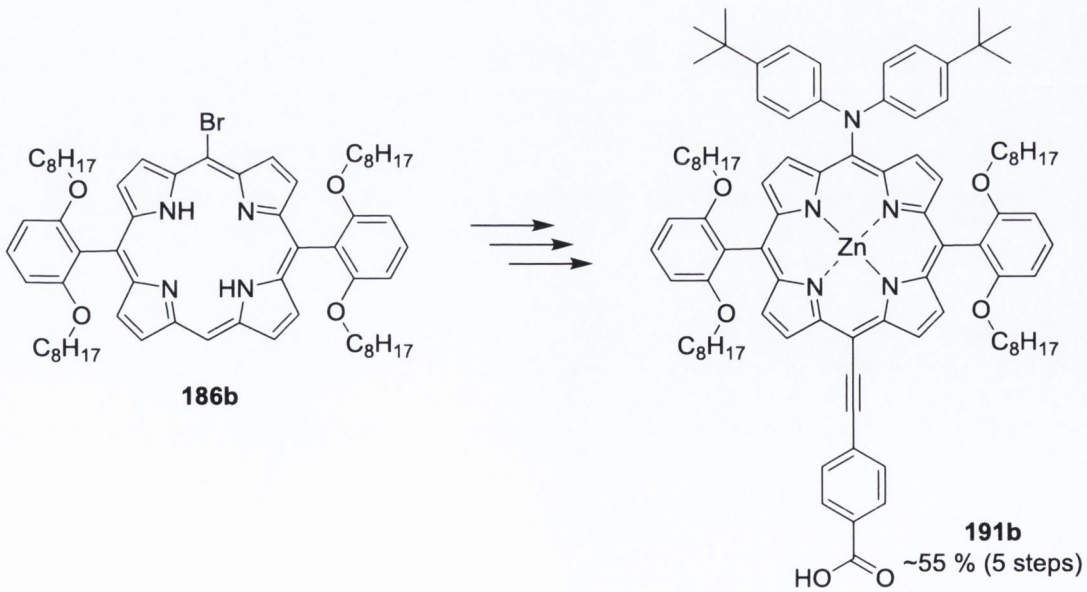


Scheme 6.3: Revised synthetic route to 5,10-donor-acceptor porphyrin **191a**.

The route described in Scheme 6.3 provides one key advantage over that outlined in Scheme 6.2, namely the introduction of the acceptor group in one step. Analysis of the

Sonogashira cross-coupling conditions found that rather than the troublesome two-step process employed earlier, installation of the acceptor system through use of an alkynylphenyl ester allowed for purification of intermediate **190a** before deprotection to the acid **191a**. By removing the silyl-deprotection step and introducing the acceptor group as the ester both the yield and purification of this late stage compound were improved. The one step introduction for both the donor and acceptor groups allows for complex groups to be synthesised separately, rather than built on the porphyrin core – allowing for a more rational and high-yielding synthesis of diverse electronic systems.

Considering the purpose of this work was to draw comparisons between the relative efficiencies of 5,10- and 5,15-porphyrin dyes in DSSCs the 5,15-analogue of **191a** was synthesised for comparison. This was accomplished through an identical route as Scheme 6.3 using 5,15- rather than 5,10-scaffolds. Thus, starting from 5,15-bromoporphyrin **186b**, analogues of each of the intermediates **187-190** (denoted as **187b**, **188b**, *etc.*) were synthesised before deprotection to the other target compound **191b** (Scheme 6.4). Both dyes **191a** and **191b** were thus synthesised in high overall yields and their relative potentials as DSSC dyes are currently under investigation.



Scheme 6.4: Synthesis of 5,15-A_2BC comparison dye **191b** (synthetic intermediates as per Scheme 6.3).

6.3 Conclusions and future work

The first half of this chapter detailed the synthesis of a library of thioether-appended porphyrins *via* Pd-catalysed cross-coupling reactions and their subsequent reactivity. While the synthesis of free thiol porphyrins was the primary goal, an unprecedented thiolate S_NAr instead occurred, generating the first example of sulfur-linked porphyrin dimers. This room temperature substitution reaction is practically unique in porphyrin chemistry and is even more unusual considering the displaced group, isooctyl-3-mercaptopropanoate, is not traditionally considered a good leaving group. Mechanistic insight was achieved *via* displacement chemistry, with studies investigating the nucleophilic ability of the thiolate porphyrin with more standard organic electrophiles as well as the propensity to displace the mercapto group with other nucleophiles. The dimerisation process appears to proceed *via* an addition/elimination mechanism, proven by the displacement reactions with alkyl halides. Additionally, both hard and soft nucleophiles can displace the thioether chain, although further work is required to improve yields and selectivity here. Work is currently ongoing into the exploitation of this unusual reactivity and in applying it to other heteroaromatic compounds (*e. g.*, pyridines). Structural analysis also indicates that these skewed, cofacially orientated *bis*porphyrins may have many potential applications including photocatalysis and electron transfer, which will be the subject of future studies.

The second half of the chapter involved structural modifications of aminoporphyrins with specific applications in solar energy conversion. The synthesis of 5,10-orientated donor-acceptor porphyrin dyes was achieved through a combination of classical porphyrin chemistry and modern Pd-catalysed techniques. Concurrently, the synthesis of the 5,15-analogue was completed. The strength of the route is highlighted by its modularity; at any stage different donor or acceptor groups can be installed, allowing for the rapid generation of a substantial library of systems to probe the optimal light harvesting arrangement. Both of these donor-acceptor scaffolds are currently under investigation (fluorescence emission,

cyclic voltammetry, Z-scan, FTIR, 2PA *etc.*) for their potential in DSSCs. Comparison of these two systems will give a clear indication of how the alteration of the dipole in a porphyrin system affects its ability to harness solar energy. Future work will then focus on the synthesis of libraries of 5,10-orientated porphyrin scaffolds. The 1st library of dyes will involve alteration of the alkyl groups on the donor substituent and aromatic residues in an effort to decrease aggregation and eliminate charge recombination. Investigation of the effect other heteroatoms (*e. g.*, sulfur) have on the properties of the dye will also be performed. The 2nd generation library will then take the best lead compound and modify it to improve absorption across the visible spectrum and in low light conditions. This will entail the introduction of other light harvesting components such as aromatic heterocycles in key areas (particularly as acceptor components) around the tetrapyrrole scaffold.

Chapter 7:

Experimental

7.1 General methods, instrumentation and considerations

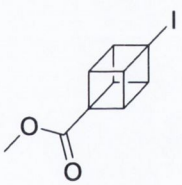
All commercial chemicals used were supplied by Sigma Aldrich, Frontier Scientific, Inc. and Tokyo Chemical Industry and used without further purification unless otherwise stated. Anhydrous CH_2Cl_2 was obtained *via* drying with phosphorus pentoxide followed by distillation; anhydrous THF was obtained by drying over sodium/benzophenone, followed by distillation. Silica gel 60 (Merck, 230-400 mesh) or aluminium oxide (neutral, activated with 6.5 % H_2O, Brockmann Grade III) were used for flash column chromatography. Analytical thin layer chromatography was carried out with silica gel 60 (fluorescence indicator F_{254}; Merck) or aluminium oxide 60 (neutral, F_{254}; Merck) plates and stained with vanillin or *p*-anisaldehyde solutions where necessary. Melting points are uncorrected and were measured with a Stuart SP-10 melting point apparatus. NMR spectra were recorded using Bruker DPX 400 (400.13 MHz for ^{1}H NMR and 100.61 MHz for ^{13}C NMR), Bruker AV 600 (600.13 MHz for ^{1}H NMR and 150.90 MHz for ^{13}C NMR), Bruker AV 400 (400.13 MHz for ^{1}H NMR, 128.41 MHz for ^{11}B NMR, 376.59 MHz for ^{19}F NMR, 162.02 MHz for ^{31}P NMR and 149.24 MHz for ^{119}Sn NMR) or Agilent MR400 (400.13 MHz for ^{1}H NMR and 100.61 MHz for ^{13}C NMR) instruments. Chemical shifts are given in ppm and referenced either to the deuterium peak in the NMR solvent or TMS used as an internal standard. The assignment of the signals was confirmed by 2D spectra (COSY, HMBC, HSQC) except for those compounds with low solubility. In NMR assignments *o*/*m*/*p* are defined with relation to either the cubane or porphyrin systems. MALDI Tof spectra were acquired using a Waters MALDI Q-Tof Premier in positive or negative mode with DCTB (trans-2-[3-(4-*tert*-butylphenyl)-2-methyl-2-propenylidene]malononitrile) as the MALDI matrix. ESI mass spectra were acquired in positive and negative modes as required, using a Micromass time of flight mass spectrometer (TOF), interfaced to a Waters 2690 HPLC or a Bruker micrOTOF-Q III spectrometer interfaced to a Dionex UltiMate 3000 LC. APCI experiments were carried out on a Bruker micrOTOF-Q III spectrometer interfaced to a Dionex UltiMate

3000 LC or direct insertion probe in positive or negative modes. EI mass spectra were acquired using a GCT Premier Micromass time of flight mass spectrometer (TOF) in positive mode at 70eV. IR spectra were recorded on a Perkin-Elmer Spectrum 100 FT-IR spectrometer. UV-vis absorption measurements were performed with a Shimadzu MultiSpec-1501. CHN analyses were performed on an Exeter Analytical CE 440 elemental analyser fitted with a Varian 55B SpectraAA atomic absorption spectrometer and are reported when detected within a 0.5 % error margin.

7.2 Synthesis of halogenated cubane precursors

Dimethyl cubanyl-1,4-dicarboxylate **7a** and its precursors (**2** → **6**) were synthesised as per Tsanaktsidis' method.[4] Iodocubane **14a**[45] and 1,4-diiodocubane **25**[42] were synthesised by Eaton's procedures from appropriate precursors. Methyl 1-bromocubanyl-4-carboxylate **67** and its precursors (**62** → **66**) were synthesised as described by Klunder and Zwanenburg.[22] 1-Bromo-4-iodocubane **68** and iodinated intermediate **100** were synthesised *via* Moriarty's process.[27] All compounds and intermediates had analytical data consistent with literature values.

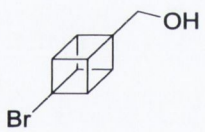
Methyl 4-iodocubanyl-1-carboxylate (69)[5]



A solution of NaOH (1.75 g, 43.6 mmol) dissolved in methanol (28 mL) was added dropwise to a solution of **7a** (10 g, 45.2 mmol) in THF (340 mL) at room temperature. The mixture was stirred for 16 h and then evaporated to dryness. The resultant solid was dissolved in water (400 mL) and extracted with $CHCl_3$ (3 × 200 mL) to remove unreacted **7a**. The aqueous solution was then acidified to pH 1 with concentrated HCl and extracted with $CHCl_3$ (3 × 200 mL), dried with $MgSO_4$ and evaporated to provide 4-(methoxycarbonyl)cubane

carboxylic acid **7c** (7.3 g) which was used directly without further purification. Crude **7c** (7.0 g, 34 mmol) and red mercuric oxide (8.1 g, 88 mmol) were dissolved in toluene (600 mL) and purged with argon for ten minutes. The mixture was heated to reflux with shielding from light before addition of iodine (9.6 g, 39 mmol) in small portions. The reaction mixture was heated at reflux for 16 h before Büchner filtration to remove solid mercury salts. The orange/red solution was then washed with a saturated aqueous solution of $Na_2S_2O_3$ (3 × 500 mL), then water (1 × 500 mL) and brine (1 × 500 mL). The organic layer was dried over $MgSO_4$, evaporated to dryness and purified by column chromatography (silica gel) using *n*-hexane:EtOAc (6:1, v/v) as eluent. The product eluted as 2nd fraction as a white solid after removal of solvents (6.9 g, 24 mmol, 53 % over 2 steps). The isolated product had analytical data consistent with the literature. M.p.: 181-183 °C (Lit. M.p.: 182-183 °C); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.71 (s, 3H, OC*H*$_3$), 4.31-4.33 (m, 3H, cubanyl-C*H*), 4.38-4.41 ppm (m, 3H, cubanyl-C*H*).[5]

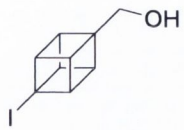
1-Bromo-4-(hydroxymethyl)cubane (70)[351]



$LiAlH_4$ (0.57 g, 15 mmol) was added to anhydrous THF (100 mL) in a dry three-necked RBF which had been purged with argon and the mixture was cooled to 0 °C. Methyl 4-bromocubanyl-1-carboxylate **67** (2.40 g, 10 mmol) was dissolved in THF (50 mL) and added dropwise over 30 minutes to the $LiAlH_4$ suspension. The reaction mixture was allowed to stir at 0 °C for 3 h before being quenched with ice (5 mL) and NaOH (1 M, 5 mL). EtOAc (100 mL) was added to solubilise the organic products and the mixture filtered through a pad of celite. The solid residue was thoroughly washed with EtOAc (500 mL) to ensure complete dissolution of the product. Removal of the solvents and recrystallisation (*n*-hexane) gave the title compound as a white solid (1.6 g, 7.5 mmol, 75 %). The isolated product had analytical data consistent with the literature.[220] M.p.: 122-124 °C (Lit. M.p.:

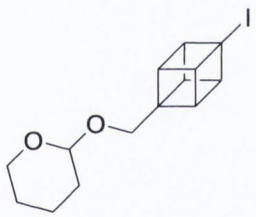
124.6-126.6 °C),[351] ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.79 (s, 2H, CC*H*$_2$O), 4.00-4.02 (m, 3H, cubanyl-C*H*), 4.16-4.19 ppm (m, 3H, cubanyl-C*H*).

1-Iodo-4-(hydroxymethyl)cubane (71)[352]



Synthesised as per the procedure for the synthesis of **70** from **69** (8.2 g, 28 mmol) and $LiAlH_4$ (1.6 g, 42 mmol). The product was isolated as a white solid (5.2 g, 20 mmol, 71 %) with analytical data consistent with the literature. M.p.: 110-112 °C (Lit. M.p.: 109-111 °C); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.76 (s, 2H, CC*H*$_2$O), 4.02-4.04 (m, 3H, cubanyl-C*H*), 4.18-4.20 ppm (m, 3H, cubanyl-C*H*).[352]

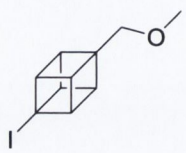
2-[(4-Iodocuban-1-yl)methoxy]tetrahydro-2H-pyran (74)



1-Iodo-4-(hydroxymethyl)cubane **71** (1.4 g, 5.4 mmol) was dissolved in CH_2Cl_2 (30 mL) at room temperature. 4-Toluenesulfonic acid (95 mg, 0.5 mmol) and 3,4-dihydro-*2H*-pyran (1.0 mL, 10.8 mmol) were added. The reaction mixture was stirred at room temperature until TLC analyses showed complete consumption of the starting material. Purification by column chromatography (silica gel, *n*-hexane:EtOAc, 7:1, v/v) and removal of solvents followed by recrystallisation (CH_3OH) gave the title compound as white crystals (1.75 g, 5.1 mmol, 94 %). M.p.: 52-53 °C; R_f = 0.43 (*n*-hexane:EtOAc, 7:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.47-1.59 (m, 4H, pyran-C*H*$_2$), 1.65-1.68 (m, 1H, pyran-C*H*$_2$), 1.76-1.81 (m, 1H, pyran-C*H*$_2$), 3.44-3.49 (m, 1H, OC*H*$_2$CH$_2$), 3.55-3.58 (d, $^2J_{H\text{-}H}$ = 11.5 Hz, 1H, CC*H*$_2$O), 3.79-3.83 (m, 1H, OC*H*$_2$CH$_2$), 3.82-3.84 (d, $^2J_{H\text{-}H}$ = 11.5 Hz, 1H,

CC*H*$_2$O), 4.00-4.02 (m, 3H, cubanyl-C*H*), 4.18-4.21 (m, 3H, cubanyl-C*H*), 4.53-4.55 ppm (t, $^3J_{H\text{-}H}$ = 4.1 Hz, 1H, OC*H*O); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 19.6 (pyran-*C*H$_2$), 25.4 (pyran-*C*H$_2$), 30.6 (pyran-*C*H$_2$), 39.2 (q, *C*I), 48.5 (cubanyl-*C*H), 54.9 (cubanyl-*C*H), 57.7 (q, *C*CH$_2$), 62.3 (O*C*H$_2$CH$_2$), 67.7 (CC*H*$_2$O) and 99.1 ppm (O*C*HO).[i]

1-Iodo-4-(methoxymethyl)cubane (75)



1-Iodo-4-hydroxymethylcubane **71** (3.5 g, 13.4 mmol) was dissolved in THF (100 mL) at room temperature. Sodium hydride (60 % dispersion in mineral oil, 1.12 g, 26.8 mmol) was added and the solution was stirred for 30 mins before the addition of iodomethane (2.5 mL, 40.2 mmol). The reaction mixture was stirred at room temperature until TLC analyses showed complete consumption of the starting material. Purification by column chromatography (silica gel, *n*-hexane:EtOAc, 7:1, v/v) and removal of solvents followed by recrystallisation (CH_3OH) gave the title compound as a white solid (3.56 g, 13 mmol, 97 %). R_f = 0.38 (*n*-hexane:EtOAc, 7:1, v/v); M.p.: 59-61 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.34 (s, 3H, OC*H*$_3$), 3.52 (s, 2H, CC*H*$_2$O), 4.02-4.04 (m, 3H, cubanyl-C*H*), 4.20-4.22 ppm (m, 3H, cubanyl-C*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 38.9 (q, CI), 48.5 (cubanyl-*C*H), 54.9 (cubanyl-*C*H), 57.8 (q), 59.2 (O*C*H$_3$) and 72.9 ppm (O*C*H$_2$); IR (neat): $\tilde{\nu}$ = 3360, 3136, 2979, 2822, 1453, 1389, 1299, 1195, 1097, 1029 and 698 cm^{-1}; HRMS (EI) *m/z* calcd. for $C_{10}H_{11}IO$ $[M]^+$: 273.9855, found 273.9861; Elem. Anal. calcd. for $C_{10}H_{11}IO$ 43.82 % C, 4.05 % H found 43.62 % C, 3.79 % H.

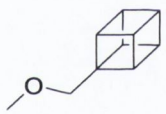
[i] Compound **74** was not detected *via* HRMS. Multiple attempts were made but these compounds were unable to be characterised with the machines available.

7.3 Cubane substitutions *via* metal-halogen exchange reactions

General Procedure 1 (Lithiation of halogenated cubanes):

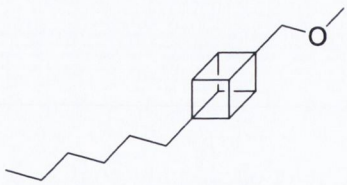
The relevant iodinated cubane (0.80 mmol) was dissolved in anhydrous THF (5 mL) in an oven-dried Schlenk flask, under argon, and cooled to -78 °C. *tert*-Butyl lithium (1.60 mmol) was added dropwise over 10 minutes and the organolithium reagent was allowed to generate at -78 °C for 1 hour. Lithiocubane species **77** was then quenched with the appropriate electrophile (1.60 mmol) and left to warm to room temperature over 1 hour. The reaction was quenched by pouring into dilute HCl (100 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were washed with brine (1 × 100 mL), dried over $MgSO_4$. The solvents were removed *in vacuo* and the product was purified by column chromatography (silica gel).

(Methoxymethyl)cubane (76b)



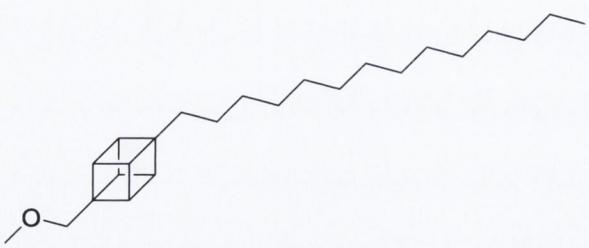
Following General Procedure 1 with **75** (220 mg, 0.80 mmol) and *t*-BuLi (1.0 mL of 1.6 M solution in hexanes, 1.60 mmol) using methanol (2 mL, excess) as the electrophile. Purification by column chromatography (silica; *n*-hexane:EtOAc, 9:1, v/v) and removal of solvents gave the title compound as a pale yellow oil (108 mg, 0.73 mmol, 91 %). $R_f = 0.28$ (*n*-hexane:EtOAc, 6:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.36 (s, 3H, OC*H*$_3$), 3.50 (s, 2H, CC*H*$_2$O), 3.88-3.92 (m, 6H, cubanyl-C*H*), 3.99-4.02 ppm (m, 1H, cubanyl-C*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 44.6 (cubanyl-*C*H), 47.5 (cubanyl-*C*H), 48.4 (cubanyl-*C*H), 57.1 (q), 59.1 (O*C*H$_3$) and 73.6 ppm (O*C*H$_2$); IR (neat): $\bar{\nu}$ = 2975, 2925, 1726, 1456, 1367, 1150, 1101 and 776 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{10}H_{13}O$ $[M+H]^+$: 149.0961, found 149.0993.

1-Hexyl-4-(methoxymethyl)cubane (78a)



Following General Procedure 1 with **75** (220 mg, 0.80 mmol) and *t*-BuLi (1.0 mL of 1.6 M solution in hexanes, 1.60 mmol) using 1-bromohexane (0.22 mL, 1.60 mmol) as the electrophile. Purification by column chromatography (silica; *n*-hexane:EtOAc, 9:1, v/v) and removal of solvents gave the title compound as a colourless oil (182 mg, 0.78 mmol, 98 %). R_f = 0.62 (*n*-hexane:EtOAc, 10:1, v/v); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 0.91 (t, $^3J_{H-H}$ = 6.9 Hz, 3H, CH_2CH_3), 1.27-1.33 (m, 8H, hexyl-CH_2), 1.57-1.59 (m, 2H, hexyl-CCH_2), 3.40 (s, 3H, OCH_3), 3.55 (s, 2H, CH_2O), 3.63-3.64 (m, 3H, cubanyl-CH), 3.72-3.74 ppm (m, 3H, cubanyl-CH); ^{13}C NMR (150 MHz, $CDCl_3$, 25 °C): δ = 13.9 (CH_3), 22.5 (CH_2), 23.8(CH_2), 29.4(CH_2), 31.8 (CH_2), 32.9 (CH_2), 43.9 (cubanyl-CH), 45.3 (cubanyl-CH), 47.4 (q, *C*-hexyl), 57.7 (q, CCH_2O), 59.0 (OCH_3) and 73.7 ppm (OCH_2); IR (neat): $\bar{\nu}$ = 2958, 2922, 2853, 1725, 1456, 1387, 1115, 1101, 950, 928, 839 and 724 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{16}H_{24}O$ $[M]^+$: 232.1822, found 232.1818.

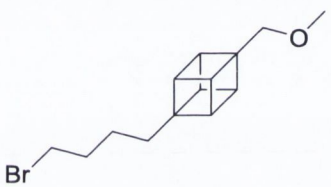
1-(Methoxymethyl)-4-tetradecylcubane (78b)



Following General Procedure 1 with **75** (220 mg, 0.80 mmol) and *t*-BuLi (1.0 mL of 1.6 M solution in hexanes, 1.60 mmol) using 1-bromotetradecane (0.47 mL, 1.60 mmol) as the electrophile. Purification by column chromatography (silica; *n*-hexane:EtOAc, 15:1, v/v) and removal of solvents gave the title compound as a low-melting, waxy, white solid (259 mg, 0.75 mmol, 94 %). M.p.: 32-34 °C; R_f = 0.58 (*n*-hexane:EtOAc, 10:1, v/v); ^{1}H NMR

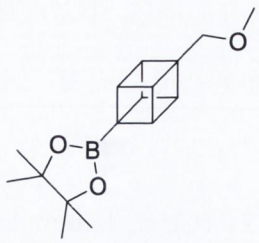
(400 MHz, $CDCl_3$, 25 °C): δ = 0.86 (t, $^3J_{H\text{-}H}$ = 6.3 Hz, 3H, CH_2CH_3), 1.24 (m, 24H, alkyl-CH_2), 1.53-1.54 (m, 2H, alkyl-CCH_2), 3.36 (s, 3H, OCH_3), 3.51 (s, 2H, CCH_2O), 3.59-3.60 (m, 3H, cubanyl-CH), 3.68-3.69 ppm (app. m, 3H, cubanyl-CH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.1 (CH_3), 22.7 (CH_2), 24.0 (CH_2), 29.3 (CH_2), 29.6 (multiple-CH_2), 29.7 (multiple-CH_2), 31.9 (CH_2), 33.0 (CH_2), 44.0 (cubanyl-CH), 45.4 (cubanyl-CH), 47.5 (q, C-alkyl), 57.8 (q, CCH_2O), 59.2 (OCH_3) and 73.8 ppm (OCH_2); IR (neat): $\bar{\nu}$ = 2957, 2915, 2897, 1470, 1384, 1323, 1120, 1103, 932, 838 and 720 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{24}H_{41}O$ $[M+H]^+$: 345.3152, found 345.3162.

1-(4-Bromobutyl)-4-(methoxymethyl)cubane (78c)



Following General Procedure 1 with **75** (220 mg, 0.80 mmol) and *t*-BuLi (1.0 mL of 1.6 M solution in hexanes, 1.60 mmol) using 1,4-dibromobutane (0.45 mL, 2.40 mmol) as the electrophile. Purification by column chromatography (silica; *n*-hexane:EtOAc, 9:1, v/v) and removal of solvents gave the title compound as a colourless oil (195 mg, 0.69 mmol, 86 %). R_f = 0.38 (*n*-hexane:EtOAc, 10:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.39-1.42 (m, 2H, CCH_2CH_2), 1.58 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 2H, CCH_2CH_2), 1.82-1.89 (m, 2H, CH_2CH_2Br), 3.36 (s, 3H, OCH_3), 3.40 (t, $^3J_{H\text{-}H}$ = 6.8 Hz, 2H, CH_2Br), 3.51 (s, 2H, CH_2O), 3.60-3.62 (m, 3H, cubanyl-CH), 3.69-3.72 ppm (m, 3H, cubanyl-CH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 22.8 (CCH_2CH_2), 32.1 (CCH_2CH_2), 33.0 (CH_2CH_2Br), 33.9 (CH_2Br), 44.0 (cubanyl-CH), 45.4 (cubanyl-CH), 48.5 (q, CCH_2CH_2), 57.9 (q, CCH_2O), 59.2 (OCH_3) and 73.7 ppm (OCH_2); IR (neat): $\bar{\nu}$ = 2965, 2927, 2831, 1726, 1453, 1387, 1117, 1099, 950, 927, 839 and 733 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{14}H_{20}BrO$ $[M+H]^+$: 283.0692, found 283.0699.

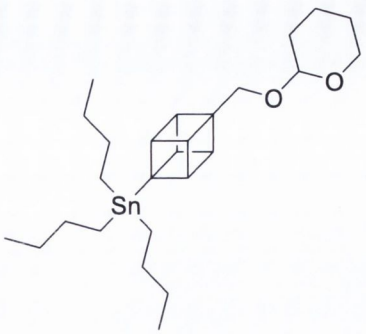
2-(4-(Methoxymethyl)cuban-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (79a)



Following General Procedure 1 with **75** (220 mg, 0.80 mmol) and *t*-BuLi (1.0 mL of 1.6 M solution in hexanes, 1.60 mmol) using 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.33 mL, 1.60 mmol) as the electrophile. Purification by column chromatography (Al_2O_3; *n*-hexane:EtOAc, 5:1, v/v) and removal of solvents gave the title compound as a viscous semi-solid (184 mg, 0.67 mmol, 84 %).[i] ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.29 (s, 12H, CC*H*$_3$) 3.40 (s, 3H, OC*H*$_3$), 3.55 (s, 2H, CC*H*$_2$O), 3.97 ppm (app. s, 6H, cubanyl-C*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 24.8 (4 × *C*H$_3$), 44.5 (cubanyl-*C*H), 47.9 (cubanyl-*C*H), 56.7 (q, *C*CH$_2$O), 59.2 (O*C*H$_3$), 60.4 (q, *C*B), 73.6 (O*C*H$_2$) and 83.0 ppm (q, O*C*(CH$_3$)$_2$); ^{11}B NMR (128 MHz, $CDCl_3$, 25 °C): 22.53 ppm; IR (neat): $\bar{\nu}$ = 3205, 2977, 2261, 1727, 1450, 1371, 1148, 1098, 851 and 710 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{16}H_{24}BO_3$ $[M+H]^+$: 275.1816, found 275.1758.

[i] Compound **79a** degraded on silica gel TLC plates and Al_2O_3 plates could not be stained to allow for product visualisation. As such, an accurate retention factor could not be obtained.

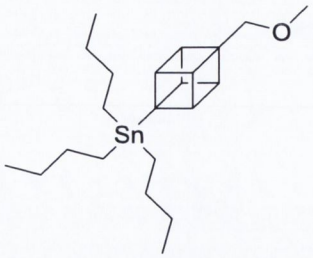
Tri-*n*-butyl[4-(((tetrahydro-*2H*-pyran-2-yl)oxy)methyl)cuban-1-yl]stannane (86)



Following General Procedure 1 with **74** (500 mg, 1.45 mmol) and *t*-BuLi (1.70 mL of 1.7 M solution in hexanes, 2.90 mmol) using tri-*n*-butyltin chloride (0.90 mL, 2.90 mmol) as electrophile. The product was purified *via* column chromatography (silica; *n*-hexane:EtOAc, 7:1, v/v) to yield the target compound as a yellow oil (640 mg, 1.26 mmol, 87 %). R_f = 0.85 (*n*-hexane:EtOAc, 7:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.82-0.92 (m, 15H, SnC*H*$_2$CH$_2$CH$_2$C*H*$_3$), 1.26-1.31 (m, 6H, SnCH$_2$C*H*$_2$CH$_2$), 1.31-1.40 (m, 4H, pyran-C*H*$_2$), 1.46-1.51 (m, 6H, C*H*$_2$CH$_3$), 1.66-1.72 (m, 1H, pyran-C*H*$_2$), 1.79-1.83 (m, 1H, pyran-C*H*$_2$), 3.45-3.49 (m, 1H, OC*H*$_2$CH$_2$), 3.57-3.60 (d, $^2J_{H\text{-}H}$ = 11.5 Hz, 1H, CC*H*$_2$O), 3.79-3.82 (d, $^2J_{H\text{-}H}$ = 11.5 Hz, 1H, CC*H*$_2$O), 3.82-3.86 (m, 1H, OC*H*$_2$CH$_2$), 3.88-3.91 (m, 3H, cubanyl-C*H*), 4.01-4.03 (m, 3H, cubanyl-C*H*), 4.57-4.59 ppm (m, 1H, OC*H*O); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 8.6 (Sn*C*H$_2$), 13.7 (CH$_2$*C*H$_3$), 19.6 (pyran-*C*H$_2$), 25.5 (pyran-*C*H$_2$), 26.6, 27.2 (SnCH$_2$*C*H$_2$CH$_2$), 29.3 (*C*H$_2$CH$_3$), 30.7 (pyran-*C*H$_2$), 44.6 (q, *C*Sn), 49.0 (cubanyl-*C*H), 50.0 (cubanyl-*C*H), 56.3 (q, *C*CH$_2$), 62.2 (O*C*H$_2$CH$_2$), 68.2 (CC*H*$_2$O) and 98.8 ppm (O*C*HO).[i]

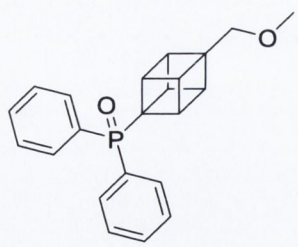
[i] Neither **86** nor **87** were detected *via* HRMS. Multiple attempts were made but these compounds were unable to be characterised with the machines available.

Tri-*n*-butyl(4-(methoxymethyl)cuban-1-yl)stannane (87)



Following General Procedure 1 with **75** (220 mg, 0.80 mmol) and *t*-BuLi (1.0 mL of 1.60 M solution in hexanes, 1.60 mmol) using tri-*n*-butyltin chloride (0.48 mL, 1.60 mmol) as the electrophile. Purification by column chromatography (silica; *n*-hexane:EtOAc, 19:1, v/v) and removal of solvents gave the title compound as a yellow oil (272 mg, 0.62 mmol, 78 %). R_f = 0.57 (*n*-hexane:EtOAc, 10:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.82-0.88 (m, 15H, Sn$CH_2CH_2CH_2CH_3$), 1.22-1.31 (m, 6H, $CH_2CH_2CH_2$), 1.47-1.51 (m, 6H, CH_2CH_3), 3.36 (s, 3H, OCH_3), 3.51 (s, 2H, CCH_2O), 3.90-3.92 (m, 3H, cubanyl-C*H*), 4.02-4.04 ppm (m, 3H, cubanyl-C*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 8.6 ($SnCH_2$), 13.7 (CH_2CH_3), 27.2 (CH_2CH_3), 29.3 ($CH_2CH_2CH_2$), 44.6 (q, Sn*C*), 49.0 (cubanyl-*C*H), 50.0 (cubanyl-*C*H), 56.4 (q, CCH_2), 59.1 (OCH_3) and 73.5 ppm (OCH_2); ^{119}Sn NMR (149 MHz, $CDCl_3$, 25 °C): -7.5 ppm; IR (neat): $\bar{\nu}$ = 2957, 2922, 2871, 2853, 1584, 1484, 1376, 1198, 1103, 947, 877, 841 and 668 cm^{-1}.

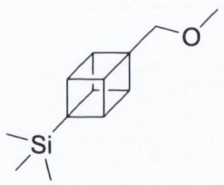
(4-(Methoxymethyl)cuban-1-yl)diphenylphosphine oxide (88b)



Following General Procedure 1 with **75** (220 mg, 0.80 mmol) and *t*-BuLi (1.0 mL of 1.6 M solution in hexanes, 1.60 mmol) using chlorodiphenylphosphine (0.29 mL, 1.60 mmol) as the electrophile. Purification by column chromatography (Al_2O_3; *n*-hexane:EtOAc, 8:1, v/v) and removal of solvents gave the title compound as an off-white

solid (210 mg, 0.63 mmol, 79 %). M.p.: 114-116 °C;[i] ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 3.38 (s, 3H, OC*H*$_3$), 3.54 (s, 2H, CC*H*$_2$O), 3.99-4.01 (m, 3H, cubanyl-C*H*), 4.24-4.27 (m, 3H, cubanyl-C*H*), 7.47-7.50 (m, 4H, Ph-*m*-C*H*), 7.54-7.56 (m, 2H, Ph-*p*-C*H*), 7.63-7.66 ppm (m, 4H, Ph-*o*-C*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 44.8 (d, $^3J_{P\text{-}C}$ = 5.5 Hz, cubanyl-*C*H), 46.6 (d, $^2J_{P\text{-}C}$ = 8.1 Hz, cubanyl-*C*H), 53.0 (d, $^1J_{P\text{-}C}$ = 67 Hz, q, *C*P), 57.4 (d, $^4J_{P\text{-}C}$ = 4.3 Hz, q, *C*CH$_2$O), 59.2 (O*C*H$_3$), 72.7 (d, $^5J_{P\text{-}C}$ = 2.3 Hz, O*C*H$_2$), 128.6 (d, $^3J_{P\text{-}C}$ = 11.7 Hz, Ph-*m*-*C*H), 130.9 (d, $^2J_{P\text{-}C}$ = 9.5 Hz, Ph-*o*-*C*H), 131.6 (d, $^1J_{P\text{-}C}$ = 100 Hz, q, Ph) and 131.7 ppm (d, $^4J_{P\text{-}C}$ = 2.7 Hz, Ph-*p*-*C*H); ^{31}P NMR (162 MHz, $CDCl_3$, 25 °C): δ = 25.70 ppm; IR (neat): $\bar{\nu}$ = 3355, 3136, 2972, 1640, 1436 (P-C deformation band), 1320, 1173, 1099, 1073, 924 and 696 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{22}H_{22}O_2P$ [M+OH]$^+$: 349.1352, found 349.1365.

(4-(Methoxymethyl)cuban-1-yl)trimethylsilane (89)

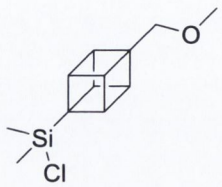


Following General Procedure 1 with **75** (220 mg, 0.80 mmol) and *t*-BuLi (1.0 mL of 1.6 M solution in hexanes, 1.60 mmol) using chlorotrimethylsilane (0.20 mL, 1.60 mmol) as the electrophile. Purification by column chromatography (silica; *n*-hexane:EtOAc, 8:1, v/v) and removal of solvents gave the title compound as a colourless oil (159 mg, 0.72 mmol, 90 %). R_f = 0.55 (*n*-hexane:EtOAc, 6:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = -0.77 (s, 9H, SiC*H*$_3$), 3.36 (s, 3H, OC*H*$_3$), 3.51 (s, 2H, CC*H*$_2$O), 3.73-3.76 (m, 3H, cubanyl-C*H*), 3.87-3.89 ppm (m, 3H, cubanyl-C*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = -4.9 (Si*C*H$_3$), 43.4 (cubanyl-*C*H), 47.8 (cubanyl-*C*H), 48.4 (q, *C*Si), 57.5 (q, *C*CH$_2$O), 59.1 (O*C*H$_3$) and 73.6 ppm (O*C*H$_2$); IR (neat): $\bar{\nu}$ = 2954, 2925, 2854, 1727, 1455, 1386, 1247, 1104, 832, 932,

[i] Compound **88** degraded on silica gel TLC plates and Al_2O_3 plates could not be stained to allow for product visualisation. As such, accurate retention factor could not be obtained.

834 and 742 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{13}H_{21}OSi$ $[M+H]^+$: 221.1356, found 221.1344.

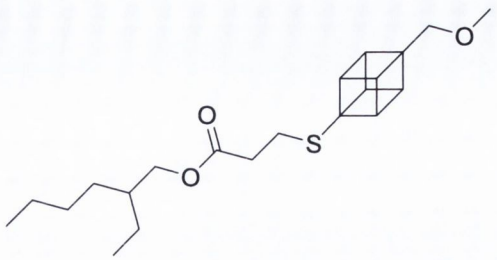
Chloro(4-(methoxymethyl)cuban-1-yl)dimethylsilane (90)



Following General Procedure 1 with **75** (220 mg, 0.80 mmol) and *t*-BuLi (1.0 mL of 1.6 M solution in hexanes, 1.60 mmol) using dichlorodimethylsilane (0.50 mL, 4.00 mmol) as the electrophile. Purification by column chromatography (Al_2O_3; *n*-hexane:EtOAc, 8:1, v/v) and removal of solvents gave the title compound as a colourless oil (140 mg, 0.58 mmol, 73 %). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.01 (s, 6H, SiC*H*$_3$), 3.36 (s, 3H, OC*H*$_3$), 3.51 (s, 2H, CC*H*$_2$O), 3.77-3.82 (m, 3H, cubanyl-C*H*), 3.87-3.90 ppm (m, 3H, cubanyl-C*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = -3.0 (Si*C*H$_3$), 43.5 (cubanyl-*C*H), 47.8 (cubanyl-*C*H), 49.4 (q, *C*Si), 57.2 (q, *C*CH$_2$O), 59.1 (O*C*H$_3$) and 73.5 ppm (O*C*H$_2$); IR (neat): $\bar{\nu}$ = 2959, 2821, 1729, 1451, 1386, 1256, 1083, 1028, 841, 789 and 666 cm^{-1}.[i]

[i] Compound **90** was not detected *via* HRMS. Multiple attempts were made but the compounds could not be characterised with the machines available. The compound also degraded on silica gel so an accurate R_f could not be measured.

(2-Ethylhexyl 3-((4-(methoxymethyl)cuban-1-yl)thio)propanoate (95)



Lithiated cubane **77** was prepared *via* General Procedure 1 with **75** (280 mg, 1.00 mmol) and *t*-BuLi (1.25 mL of 1.6 M soln. in hexanes, 2.00 mmol). In a separate flask freshly recrystallised *N*-chlorosuccinimide (130 mg, 1.00 mmol) was dissolved in anhydrous toluene (1 mL) under argon and shielded from light. 2-Ethylhexyl 3-mercaptopropanoate **93** (0.2 mL, 0.90 mmol) was dissolved in anhydrous toluene (1 mL) and added to the NCS solution over 30 minutes and left to stir at room temperature for another 30 minutes. The sulfenyl chloride **94** solution was then added dropwise to the lithiated cubane **77** at -78 °C and left to warm to room temperature over one hour. Purification by column chromatography (silica; *n*-hexane:EtOAc, 8:1, v/v) and removal of solvents gave the title compound as a colourless oil (72 mg, 0.20 mmol, 22 %). R_f = 0.31 (*n*-hexane:EtOAc, 6:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ= 0.90-0.94 (m, 6H, alkyl-C*H*$_3$), 1.28-1.40 (m, 9H, alkyl-C*H*$_2$/C*H*), 2.62 (t, $^3J_{H\text{-}H}$ = 7.5 Hz, 2H, SCH$_2$C*H*$_2$), 2.84 (t, $^3J_{H\text{-}H}$ = 7.5 Hz, 2H, SC*H*$_2$), 3.40 (s, 3H, OC*H*$_3$), 3.57 (s, 2H, CC*H*$_2$O), 3.87-3.89 (m, 3H, cubanyl-C*H*), 3.92-3.93 ppm (m, 3H, cubanyl-C*H*), 4.03-4.05 ppm (m, 2H, OC*H*$_2$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 11.0 (alkyl-*C*H$_3$), 14.1 (alkyl-*C*H$_3$), 23.0 (alkyl-*C*H$_2$), 23.8 (alkyl-*C*H$_2$), 24.6 (S*C*H$_2$), 28.9 (alkyl-*C*H$_2$), 30.4 (alkyl-*C*H$_2$), 35.5 (SCH$_2$*C*H$_2$), 38.7 (alkyl-*C*H), 44.7 (cubanyl-*C*H), 48.9 (cubanyl-*C*H), 58.0 (q, *C*CH$_2$O), 59.3 (O*C*H$_3$), 60.8 (q, S*C*), 67.2 (CO$_2$*C*H$_2$), 73.2 (O*C*H$_2$) and 172.1 ppm (q, *C*=O); IR (neat): $\bar{\nu}$ = 2960, 2927, 2859, 1734 (C=O), 1461, 1388, 1348, 1201, 1132, 1101 and 840 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{21}H_{33}O_3S$ $[M+H]^+$: 365.2145, found 365.2141.

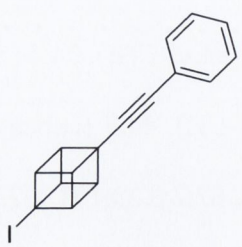
7.4 Synthesis of alkynylcubanes

Formylated precursors 4-bromocubanyl-1-carbaldehyde **120**[219], 4-iodocubanyl-1-carbaldehyde **121**[45] and cubanyl-1,4-dicarbaldehyde **134**[45] were synthesised using modified Swern conditions as described by Eaton *et al.*[45] Alkynylcubanes 1-ethynyl-4-iodocubane **132** and 1,4-diethynylcubane **137** were synthesised from their formylated precursors *via* Eaton's methodology.[45] The Glaser coupled product **139** had analytical data consistent with that described by Eaton *et al.*[45]

General Procedure 2 (Sonogashira cross-coupling of alkynylcubanes with aryl halides):

1-Ethynyl-4-iodocubane **132** (75 mg, 0.30 mmol), $Pd(PPh_3)_4$ (35 mg, 30 μmol) and copper(I) iodide (17 mg, 90 μmol) were placed in an oven-dried Schlenk flask and heated under vacuum. The flask was purged with argon and anhydrous triethylamine (3 mL) was added by syringe. The solution was subjected to three freeze-pump-thaw cycles before releasing to argon. Aryl halide (0.90 mmol) was added and the reaction left to stir for 16 h. The reaction mixture was then diluted with CH_2Cl_2 (10 mL) before removal of solvents *in vacuo*. The crude products were purified directly by column chromatography (silica gel). Arylalkynyl substituted cubanes typically eluted as the third fraction after Glaser homo-coupled cubane **139** and unreacted aryl halide, respectively.

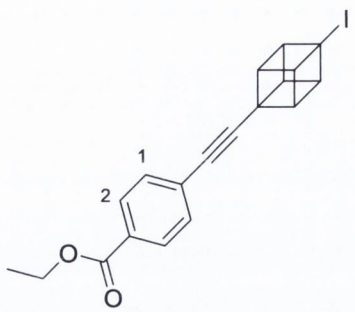
1-Iodo-4-(phenylethynyl)cubane (138a)[111]



Synthesised *via* General Procedure 2 from **132** (75 mg, 0.30 mmol), $Pd(PPh_3)_4$ (35 mg, 30 μmol), CuI (17 mg, 90 μmol) and iodobenzene (0.10 mL, 0.90 mmol) at room temperature for 16 h. Purification by column chromatography (silica, *n*-hexane) and removal of solvents

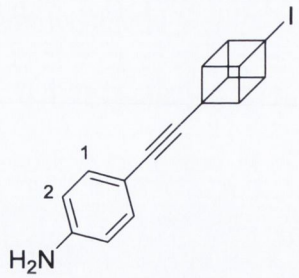
gave the title compound as a white solid (98 mg, 0.29 mmol, 98 %). Analytical data was consistent with the literature. M.p.: 137-139 °C (Lit. M.p.: 138-139 °C).[111]

Ethyl 4-((4-iodocuban-1-yl)ethynyl)benzoate (138b)



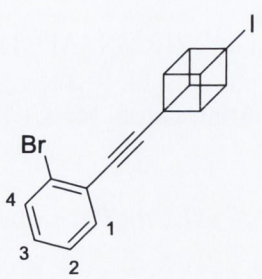
Synthesised *via* General Procedure 2 from **132** (75 mg, 0.30 mmol), $Pd(PPh_3)_4$ (35 mg, 30 µmol), CuI (17 mg, 90 µmol) and ethyl 4-iodobenzoate (0.15 mL, 0.90 mmol) in NEt_3 (3 mL). The reaction mixture was stirred at room temperature for 16 h. Purification by column chromatography (silica; *n*-hexane:CH_2Cl_2, 5:1, v/v) and removal of solvents gave the title compound as a white solid (108 mg, 0.27 mmol, 90 %). M.p.: 128-129 °C; R_f = 0.16 (*n*-hexane:CH_2Cl_2, 5:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.37 (t, $^3J_{H\text{-}H}$ = 7.1 Hz, 3H, C*H*$_3$), 4.28-4.32 (m, 6H, cubanyl-C*H*), 4.36 (q, $^3J_{H\text{-}H}$ = 7.1 Hz, 2H, C*H*$_2$), 7.42 (d, $^3J_{H\text{-}H}$ = 8.1 Hz, 2H, aryl-C(1)*H*), 7.95 ppm (d, $^3J_{H\text{-}H}$ = 8.1 Hz, 2H, aryl-C(2)*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.9 (*C*H$_3$), 36.0 (q, *C*I), 46.3 (q, cubane), 52.2 (cubanyl-*C*H), 54.5 (cubanyl-*C*H), 60.7 (*C*H$_2$), 89.7 (q, alkyne), 90.6 (q, alkyne), 127.5 (q, aryl), 129.0 (aryl-*C(2)*H), 129.1 (q, aryl-*C*CO$_2$Et), 130.7 (aryl- *C(1)*H) and 165.6 ppm (q, *C*=O); IR (neat): $\bar{\nu}$ = 3004, 2970, 2207 (C≡C stretch), 1710 (C=O stretch), 1601, 1403, 1365, 1264 (C-O stretch), 1169, 1092, 1025 and 765 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{19}H_{16}IO_2$ $[M+H]^+$: 403.0189, found 403.0173; Elem. Anal. calcd. for $C_{19}H_{15}IO_2$ 56.74 % C, 3.76 % H found 57.18 % C, 3.83 % H.

4-((4-Iodocuban-1-yl)ethynyl)aniline (138c)



Synthesised *via* General Procedure 2 from **132** (75 mg, 0.30 mmol), $Pd(PPh_3)_4$ (35 mg, 30 µmol), CuI (17 mg, 90 µmol) and 4-iodoaniline (197 mg, 0.90 mmol) in NEt_3 (3 mL). The reaction mixture was stirred at room temperature for 16 h. Purification by column chromatography (silica; *n*-hexane:CH_2Cl_2, 1:1, v/v) and removal of solvents gave the title compound as a pale yellow solid (79 mg, 0.23 mmol, 76 %). M.p.: decomposing without melting above 160 °C; R_f = 0.18 (*n*-hexane:CH_2Cl_2, 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 4.30 (app. s, 6H, cubanyl-C*H*), 7.17 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 2H, aryl- C(2)*H*), 7.23 ppm (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 2H, aryl- C(1)*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 37.2 (q, *C*I), 47.3 (q, cubane), 52.7 (cubanyl-*C*H), 54.9 (cubanyl-*C*H), 85.7 (q, alkyne), 91.2 (q, alkyne), 112.8 (q, aryl), 114.7 (aryl-*C(2)*H), 132.7 (aryl-*C(1)*H) and 146.4 ppm (q, *C*NH_2); IR (neat): $\bar{\nu}$ = 3481, 3385 (N-H stretch), 2994, 2212 (C≡C stretch), 1611 (N-H bend), 1513, 1285, 1198, 1023 and 823 (N-H wag) cm^{-1}; HRMS (ESI+) *m/z* calcd. for $C_{16}H_{13}IN$ $[M+H]^+$: 346.0087, found 346.0088.

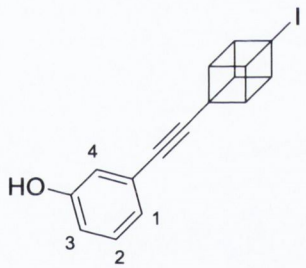
1-((2-Bromophenyl)ethynyl)-4-iodocubane (138d)



Synthesised *via* General Procedure 2 from **132** (75 mg, 0.30 mmol), $Pd(PPh_3)_4$ (35 mg, 30 µmol), CuI (17 mg, 90 µmol) and 2-bromoiodobenzene (0.12 mL, 0.90 mmol) in NEt_3 (3

mL). The reaction mixture was stirred at room temperature for 16 h. Purification by column chromatography (silica; petroleum ether:CH_2Cl_2, 15:1, v/v) and removal of solvents gave the title compound as a white solid (110 mg, 0.27 mmol, 90 %). M.p.: 116-118 °C; R_f = 0.52 (*n*-hexane:CH_2Cl_2, 10:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 4.29-4.36 (m, 6H, cubanyl-C*H*), 7.11-7.15 (m, 1H, aryl-C(3)*H*), 7.22-7.24 (m, 1H, aryl-C(2)*H*), 7.41-7.43 (m, 1H, aryl-C(1)*H*), 7.56-7.58 ppm (m, 1H, aryl-C(4)*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 36.6 (q, *C*I), 46.9 (q, cubane), 52.7 (cubanyl-*C*H), 55.0 (cubanyl-*C*H), 89.3 (q, alkyne), 92.6 (q, alkyne), 125.2 (q, aryl), 125.5 (q, aryl), 127.0 (aryl-*C(2)*H), 129.1 (aryl- *C(3)*H), 132.4 (aryl-*C(4)*H) and 133.1 ppm (aryl-*C(1)*H); IR (neat): $\bar{\nu}$ = 2990, 2922, 2852, 2212 (C≡C stretch), 1466, 1428, 1195, 1025, 834 and 749 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{16}H_{11}BrI$ $[M+H]^+$: 408.9083, found 408.9097.

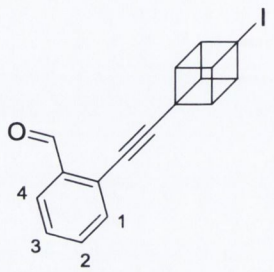
3-((4-Iodocuban-1-yl)ethynyl)phenol (138e)



Synthesised *via* General Procedure 2 from **132** (75 mg, 0.30 mmol), $Pd(PPh_3)_4$ (35 mg, 30 µmol), CuI (17 mg, 90 µmol) and 3-iodophenol (198 mg, 0.90 mmol) in NEt_3 (3 mL). The reaction mixture was stirred at room temperature for 16 h. Purification by column chromatography (silica; petroleum ether:CH_2Cl_2, 1:1, v/v) and removal of solvents gave the title compound as a white solid (82 mg, 0.24 mmol, 79 %). M.p.: 142-144 °C; R_f = 0.43 (CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 4.30 (app. s, 6H, cubanyl-C*H*), 4.85 (s, 1H, O*H*), 6.76-6.79 (m, 1H, aryl-C(3)*H*), 6.86 (s, 1H, aryl-C(4)*H*), 6.96-6.98 (m, 1H, aryl-C(1)*H*), 7.15-7.18 ppm (m, 1H, aryl-C(2)*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 36.8 (q, *C*I), 46.9 (q, cubane), 52.6 (cubanyl-*C*H), 54.9 (cubanyl-*C*H), 88.1 (q, alkyne), 90.3 (q,

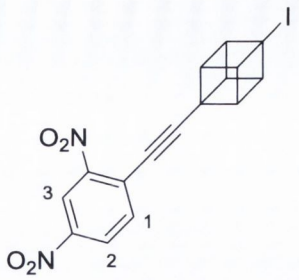
alkyne), 115.5 (aryl- *C(3)*H), 118.0 (aryl-*C(4)*H), 124.1 (aryl-*C(1)*H), 124.6 (q, aryl), 129.6 (aryl-*C(2)*H) and 155.3 ppm (q, *C*OH); IR (neat): $\bar{\nu}$ = 3219 (O-H stretch), 2922, 2212 (C≡C stretch), 1705, 1602, 1583, 1438, 1218, 1156, 1077, 1028 (C-O stretch), 797 and 686 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{16}H_{12}IO$ $[M+H]^+$: 346.9927, found 346.9937.

2-((4-Iodocuban-1-yl)ethynyl)benzaldehyde (138f)



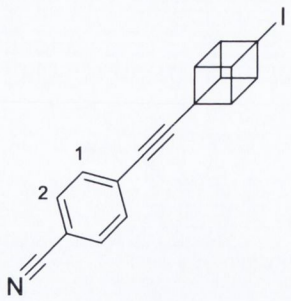
Synthesised *via* General Procedure 2 from **132** (75 mg, 0.30 mmol), $Pd(PPh_3)_4$ (35 mg, 30 µmol), CuI (17 mg, 90 µmol) and 2-iodobenzaldehyde (208 mg, 0.90 mmol) in NEt_3 (3 mL). The reaction mixture was stirred at room temperature for 16 h. Purification by column chromatography (silica; petroleum ether:CH_2Cl_2, 4:1, v/v) and removal of solvents gave the title compound as a white solid (95 mg, 0.27 mmol, 88 %). M.p.: 129-130 °C; R_f = 0.19 (*n*-hexane:CH_2Cl_2, 5:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 4.35-4.39 (m, 6H, cubanyl-C*H*), 7.42-7.46 (m, 1H, aryl-C(3)*H*), 7.52-7.59 (m, 2H, aryl-C(1/2)*H*), 7.92-7.94 (m, 1H, aryl- C(4)*H*), 10.52 ppm (s, 1H, C*H*O); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 36.3 (q, *C*I), 46.7 (q, cubane), 52.6 (cubanyl-*C*H), 54.9 (cubanyl-*C*H), 86.4 (q, alkyne), 95.2 (q, alkyne), 127.2 (aryl-*C(2)*H), 128.4 (aryl-*C(3)*H), 133.0 (aryl-*C(4)*H), 133.8 (aryl-*C(1)*H), 135.6 (q, aryl) and 192.0 ppm (q, *C*HO); IR (neat): $\bar{\nu}$ = 2924, 2853, 2211 (C≡C stretch), 1688 (C=O stretch), 1592, 1467, 1265, 1195, 1024 and 749 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{17}H_{12}IO$ $[M+H]^+$: 358.9927, found 358.9926.

1-((2,4-Dinitrophenyl)ethynyl)-4-iodocubane (138g)



Synthesised *via* General Procedure 2 from **132** (75 mg, 0.30 mmol), $Pd(PPh_3)_4$ (35 mg, 30 µmol), CuI (17 mg, 90 µmol) and 1-bromo-2,4-dinitrobenzene (222 mg, 0.90 mmol) in NEt_3 (3 mL). The reaction mixture was stirred at 65 °C for 16 h. Purification by column chromatography (silica; *n*-hexane:CH_2Cl_2, 5:2, v/v) and removal of solvents gave the title compound as a yellow solid (64 mg, 0.15 mmol, 51 %). M.p.: 155-157 °C; R_f = 0.24 (*n*-hexane:CH_2Cl_2, 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 4.36-4.39 (m, 3H, cubanyl-C*H*), 4.43-4.46 (m, 3H, cubanyl-C*H*), 7.78 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 1H, aryl-C(1)*H*), 8.42 (dd, $^3J_{H\text{-}H}$ = 8.6 Hz, $^5J_{H\text{-}H}$ = 2.3 Hz, 1H, aryl-C(2)*H*), 8.91 ppm (d, $^5J_{H\text{-}H}$ = 2.3 Hz, 1H, aryl-C(3)*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 35.4 (q, *C*I), 46.6 (q, cubane), 52.6 (cubanyl-*C*H), 55.0 (cubanyl-*C*H), 85.1 (q, alkyne), 102.9 (q, alkyne), 110.0 (q, aryl), 120.3 (aryl-*C(2)*H), 125.0 (q, *C*NO_2) 126.8 (aryl-*C(3)*H), 135.5 (aryl-*C(1)*H) and 146.1 ppm (q, *C*NO_2); IR (neat): $\bar{\nu}$ = 2923, 2853, 2202 (C≡C stretch), 1709, 1603, 1517 (N-O asymmetric stretch), 1337 (N-O symmetric stretch), 1178, 1027, 914, 830 and 739 cm^{-1}; HRMS (APCI+) *m/z* calcd. for $C_{16}H_{10}IN_2O_4$ $[M+H]^+$: 420.9679, found 420.9687.

4-((4-Iodocuban-1-yl)ethynyl)benzonitrile (328h)



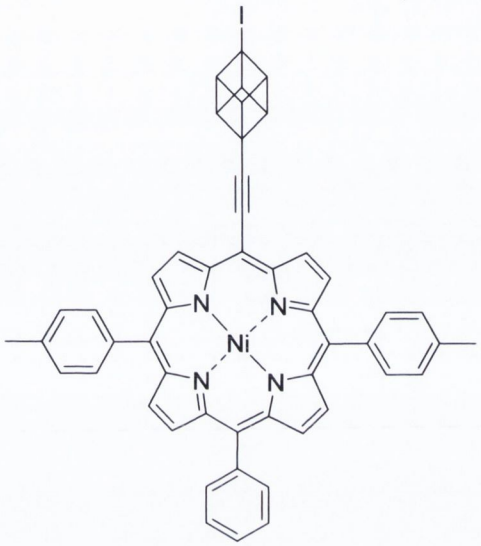
Synthesised *via* General Procedure 2 from **132** (75 mg, 0.30 mmol), $Pd(PPh_3)_4$ (35 mg, 30 µmol), CuI (17 mg, 90 µmol) and 4-bromobenzonitrile (164 mg, 0.90 mmol) in NEt_3 (3 mL). The reaction mixture was stirred at 65 °C for 16 h. Purification by column chromatography (silica; *n*-hexane:CH_2Cl_2, 3:1, v/v) and removal of solvents gave the title compound as a yellow solid (68 mg, 0.15 mmol, 64 %). M.p.: 151-154 °C (decomp.); R_f = 0.17 (*n*-hexane:CH_2Cl_2, 5:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 4.23-4.28 (m, 6H, cubanyl-C*H*), 7.39 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, 2H, aryl-C(2)*H*), 7.51 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, 2H, aryl-C(1)*H*); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 36.1 (q, *C*I), 46.6 (q, cubane), 52.5 (cubanyl-*C*H), 54.9 (cubanyl-*C*H), 89.3 (q, alkyne), 92.6 (q, alkyne), 111.2 (q, *C*CN), 118.5 (q, *C*N), 128.4 (q, aryl), 131.8 (aryl- *C(2)*H), 132.0 ppm (aryl-*C(1)*H); IR (neat): $\tilde{\nu}$ = 2923, 2853, 2210 (br, C≡N/C≡C stretch), 1600, 1499, 1275, 1195, 1171, 1027 and 834 cm^{-1}; HRMS (APCI-) *m/z* calcd. for $C_{17}H_9IN$ $[M+H]^+$: 353.9785, found 353.9796; Elem. Anal. calcd. for $C_{17}H_{10}IN$ 57.49 % C, 2.84 % H, 3.94 % N found 57.90 % C, 3.35 % H, 3.39 % N.

General Procedure 3 (Sonogashira cross-coupling of alkynylcubanes with porphyrins):

1-Ethynyl-4-iodocubane **132** (70 mg, 280 µmol), bromoporphyrin (112 µmol), $Pd_2(dba)_3$ (10 mg, 10 µmol) and triphenylarsine (75 mg, 224 µmol) were placed in an oven-dried Schlenk flask and heated under vacuum. The flask was purged with argon and anhydrous THF (3 mL) and triethylamine (1 mL) were added by syringe. The solution was subjected to three freeze-pump-thaw cycles before releasing to argon. The reaction mixture was heated to 65 °C for 16 h and then diluted with CH_2Cl_2 (10 mL) before removal of

solvents *in vacuo*. Crude products were purified directly by column chromatography (silica gel). Alkynylcubane substituted porphyrins typically eluted as the second porphyrin containing fraction after any unreacted bromoporphyrin.

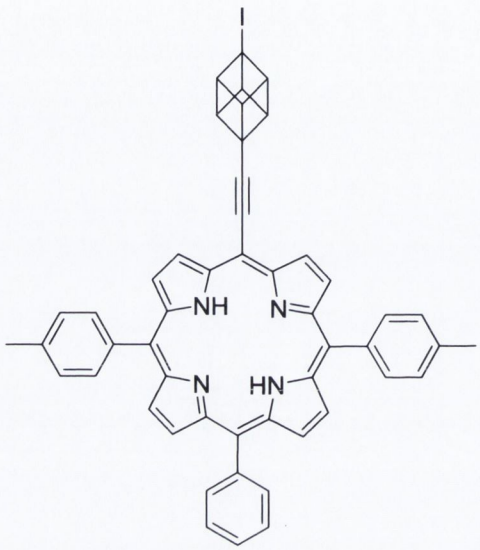
[5-((4-Iodocuban-1-yl)ethynyl)-10,20-*bis*(4-methylphenyl)-15-phenylporphyrinato]nickel(II) (140)



Synthesised *via* General Procedure 3 from **132** (70 mg, 280 µmol), bromoporphyrin **147b** (79 mg, 112 µmol), $Pd_2(dba)_3$ (17 mg, 17 µmol) and $AsPh_3$ (75 mg, 224 µmol) in THF (3 mL) and triethylamine (1 mL). The reaction mixture was stirred at 65 °C for 16 h. Purification by column chromatography (silica; *n*-hexane:CH_2Cl_2, 4:1, v/v) and removal of solvents followed by recrystallisation ($CHCl_3$/CH_3OH) gave the title compound as a purple solid (62 mg, 71 µmol, 63 %). M.p.: >300 °C; R_f = 0.53 (*n*-hexane:CH_2Cl_2, 2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.64 (s, 6H, tolyl-C*H*$_3$), 4.49 (m, 3H, cubanyl-C*H*), 4.63-4.64 (m, 3H, cubanyl-C*H*), 7.47 (d, $^3J_{H\text{-}H}$ = 7.9 Hz, 4H, tolyl-*o*-C*H*), 7.64-7.66 (m, 3H, Ph-*o*/*p*-C*H*), 7.86 (d, $^3J_{H\text{-}H}$ = 7.8 Hz, 4H, tolyl-*m*-C*H*), 7.95-7.99 (m, 2H, Ph-*m*-C*H*), 8.65-8.66 (m, 4H, H_β), 8.78 (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β), 9.41 ppm (d, $^3J_{H\text{-}H}$ = 4.7 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.5, 36.8, 47.8, 53.2, 55.2, 91.2, 95.4, 99.2, 119.7, 120.0, 126.7, 126.8, 127.5, 127.6, 127.7, 131.3, 131.9, 132.0, 132.1, 132.8, 133.5, 133.6, 133.7, 137.4, 137.5, 137.6, 137.9, 140.7, 142.4, 142.5, 142.7, 143.2 and 144.5 ppm; UV/Vis

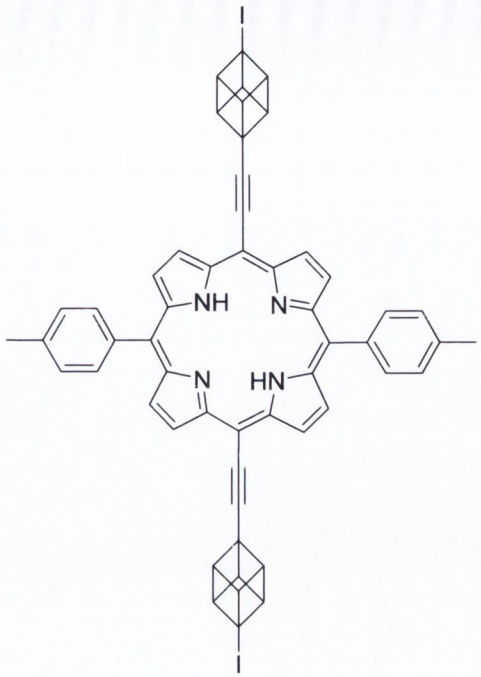
(CH_2Cl_2): λ_{max} (log ε) = 430 (5.28), 544 (4.11), 580 nm (3.91); HRMS (MALDI) *m/z* calcd. for $C_{50}H_{33}N_4INi$ $[M]^+$: 874.1103, found 874.1128.

5-((4-Iodocuban-1-yl)ethynyl)-10,20-*bis*(4-methylphenyl)-15-phenylporphyrin (141)



Synthesised *via* General Procedure 3 from **132** (70 mg, 280 µmol), bromoporphyrin **154b** (72 mg, 112 µmol), $Pd_2(dba)_3$ (17 mg, 17 µmol) and $AsPh_3$ (75 mg, 224 µmol) in THF (3 mL) and triethylamine (1 mL). The reaction mixture was stirred at 65 °C for 16 h. Purification by column chromatography (silica; *n*-hexane:CH_2Cl_2, 3:1, v/v), removal of solvents and recrystallisation ($CHCl_3$/CH_3OH) gave the title compound as a purple solid (67 mg, 82 µmol, 73 %). M.p.: >300 °C; R_f = 0.30 (*n*-hexane:CH_2Cl_2, 2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = -2.41 (s, 2H, N*H*), 2.70 (s, 6H, tolyl-CH_3), 4.52-4.55 (m, 3H, cubanyl-C*H*), 4.71-4.73 (m, 3H, cubanyl-C*H*), 7.55 (d, $^3J_{H\text{-}H}$ = 7.9 Hz, 4H, tolyl-*o*-C*H*), 7.69-7.75 (m, 3H, Ph-*o*/*p*-C*H*), 8.06 (d, $^3J_{H\text{-}H}$ = 7.9 Hz, 4H, tolyl-*m*-C*H*), 8.14-8.16 (m, 2H, Ph-*m*-C*H*), 8.72 (d, $^3J_{H\text{-}H}$ = 4.7 Hz, 2H, H_β), 8.76 (d, $^3J_{H\text{-}H}$ = 4.7 Hz, 2H, H_β), 8.88 (d, $^3J_{H\text{-}H}$ = 4.7 Hz, 2H, H_β), 9.57 ppm (d, $^3J_{H\text{-}H}$ = 4.7 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.5, 36.9, 48.0, 53.3, 55.2, 93.0, 95.1, 99.6, 121.0, 121.5, 126.6, 126.8, 127.5, 127.7, 129.8, 130.6, 130.7, 130.8, 130.9, 131.0, 131.1, 131.3, 131.8, 134.3, 134.4, 137.5, 138.7 and 142.0 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 432 (5.61), 532 (3.95), 572 (4.35), 610 (3.40), 666 nm (3.89); HRMS (MALDI) *m/z* calcd. for $C_{50}H_{35}IN_4$ $[M]^+$: 818.1906, found 818.1907.

5,15-*Bis*((4-iodocuban-1-yl)ethynyl)-10,20-*bis*(4-methylphenyl)porphyrin (143)



Synthesised *via* a modified General Procedure 3 from **132** (100 mg, 400 µmol), bromoporphyrin **142** (65 mg. 100 µmol), $Pd_2(dba)_3$ (17 mg, 17 µmol) and $AsPh_3$ (75 mg, 224 µmol) in THF (3 mL) and triethylamine (1 mL). The reaction mixture was stirred at 65 °C for 16 h. Purification by column chromatography (silica; *n*-hexane:CH_2Cl_2, 3:1, v/v) and removal of solvents followed by recrystallisation ($CHCl_3$/MeOH) gave the title compound as a purple solid (51 mg, 51 µmol, 51 %). M.p.: >300 °C; R_f = 0.15 (*n*-hexane:CH_2Cl_2, 2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = -2.11 (s, 2H, N*H*), 2.71 (s, 6H, tolyl-CH_3), 4.52-4.53 (m, 6H, cubanyl-C*H*), 4.71 (m, 6H, cubanyl-C*H*), 7.56 (d, $^3J_{H\text{-}H}$ = 7.6 Hz, 4H, tolyl-*o*-C*H*), 8.03 (d, $^3J_{H\text{-}H}$ = 7.6 Hz, 4H, tolyl-*m*-C*H*), 8.79 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 4H, H_β), 8.49 ppm (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 4H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.5, 36.8, 47.9, 53.2, 55.2, 92.9, 95.7, 101.1, 121.7, 127.6, 134.4, 137.6, 138.4 and 144.4 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 438 (5.26), 550 (3.51), 592 (4.42), 626 (3.29), 686 nm (4.04); HRMS (MALDI) *m/z* calcd. for $C_{54}H_{36}I_2N_4$ $[M]^+$: 994.1030, found 994.1061.

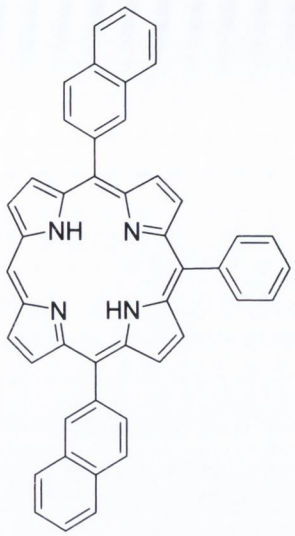
7.5 Synthesis of halogenated porphyrins

Dipyrromethane **124** was synthesised according to the Lindsey method.[156] 5,15-Disubstituted porphyrins **150a**,[353] **150b**,[159] **150c**,[354] **150d**,[159] **150e**,[355] and **150f**[356] were synthesised *via* standard condensation reactions. 5,10,15-Triphenylporphyrin **151a** and its nickel(II) complex **153a**,[177] 5,15-*bis*(4-methylphenyl)-10-phenylporphyrin **150b**[357] and Ni(II) complex **127**[358] were prepared using standard methodologies. Bromoporphyrins **142**,[359] **147a**,[360] **147i**,[361] **147j**,[362] **154a**,[360] **154b**[362] and **167c**[363] were obtained through bromination of appropriate precursors. All known porphyrins had analytical data consistent with those reported in the literature.

General Procedure 4 (Reaction of porphyrins with phenyllithium):

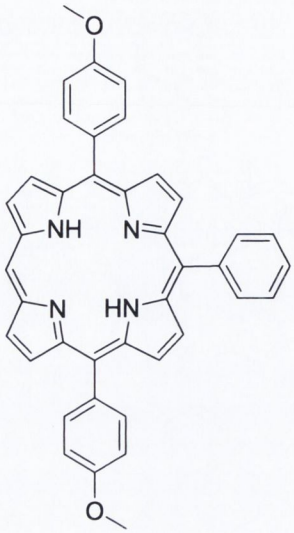
The free-base porphyrin (1 eq.) was dissolved in anhydrous THF in an oven-dried Schlenk flask and degassed under high vacuum. The reaction vessel was then purged with argon before the dropwise addition of PhLi (6 eq.) over 10 minutes. The solution was stirred at room temperature for two h and then quenched by adding a solution of water in THF (1:4, v/v). 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 3 eq.) was added in CH_2Cl_2 (10 mL) and the solution left to oxidise for 30 minutes. The solvents were removed *in vacuo* and the crude product was then filtered through silica gel using CH_2Cl_2 as eluent. Removal of the solvents followed by recrystallisation from $CHCl_3/CH_3OH$ provided the target porphyrins.

5,15-*Bis*(2-naphthyl)-10-phenylporphyrin (151c):



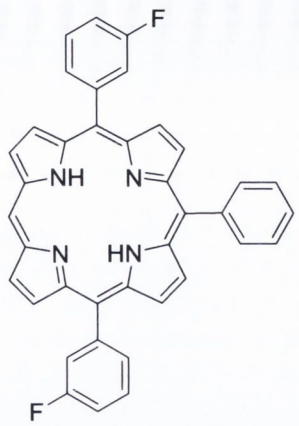
Synthesised *via* General Procedure 4 from **150c** (560 mg, 1.00 mmol) and PhLi (1.8 M, 3.30 mL, 6.00 mmol) in THF (300 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield a purple solid (607 mg, 0.95 mmol, 95 %). M.p.: >300 °C; R_f = 0.32 (*n*-hexane:CH_2Cl_2, 5:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = -2.87 (s, 2H, N*H*), 7.76-7.79 (m, 7H, Ar-C*H*), 8.14-8.16 (m, 2H, naph-C*H*), 8.23-8.26 (m, 6H, Ar-C*H*), 8.46 (d, $^3J_{H\text{-}H}$ = 8.3 Hz, 2H, naph-C*H*), 8.74 (s, 2H, naph-C*H*), 8.91 (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β), 8.95 (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β), 9.06 (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β), 9.37 (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β), 10.28 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 104.9, 119.5, 126.0, 126.6, 126.7, 127.0, 127.8, 128.0, 131.5, 132.3, 132.8, 133.9, 134.5, 139.3 and 142.5 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 416 (5.86), 511 (4.59), 546 (4.30), 584 (4.20), 642 nm (4.06); HRMS (ESI+) *m/z* calcd. for $C_{46}H_{31}N_4$ [M+H]: 639.2544, found 639.2549.

5,15-*Bis*(4-methoxyphenyl)-10-phenylporphyrin (151d):



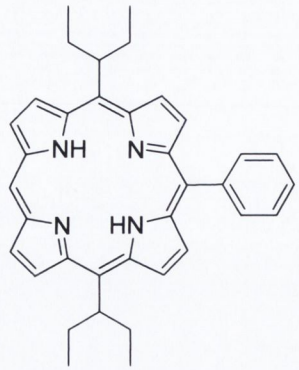
Synthesised *via* General Procedure 4 from **150d** (500 mg, 0.96 mmol) and PhLi (1.8 M, 3.20 mL, 5.76 mmol) in THF (300 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield a purple solid (517 mg, 0.86 mmol, 90 %). M.p.: 291-292 °C; R_f = 0.18 (*n*-hexane:CH_2Cl_2, 4:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = -2.95 (s, 2H, N*H*), 4.10 (s, 6H, OCH_3), 7.31 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 4H, C_6H_4OMe-*o*-C*H*), 7.74-7.78 (m, 3H, Ph-*o*/*p*-C*H*), 8.15 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 4H, C_6H_4OMe-*m*-C*H*), 8.20-8.23 (m, 2H, Ph-*m*-C*H*), 8.86 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*β), 8.93 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*β), 9.05 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*β), 9.31 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*β), 10.19 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 55.6, 104.7, 112.4, 119.4, 120.4, 126.5, 127.7, 131.4, 134.1, 134.5, 135.7, 142.7 and 159.4 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 415 (5.47), 452 (4.31), 511 (4.22), 547(3.89), 586 nm (3.78); HRMS (MALDI) *m/z* calcd. for $C_{40}H_{30}N_4O_2$ $[M]^+$: 598.2369, found 598.2385.

5,15-*Bis*(3-fluorophenyl)-10-phenylporphyrin (151e)



Synthesised *via* General Procedure 4 from **150e** (650 mg, 1.30 mmol) and PhLi (1.8 M, 4.40 mL, 7.80 mmol) in THF (300 mL). The title compound was obtained by column chromatography (silica; *n*-hexane:CH_2Cl_2, 4:1, v/v), solvents removed and recrystallised ($CHCl_3$/CH_3OH) to yield a purple solid (582 mg, 1.01 mmol, 78 %). M.p.: 190-191 °C; R_f = 0.29 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = -3.02 (s, 2H, N*H*), 7.51-7.56 (m, 2H, Ar-C*H*), 7.72-7.81 (m, 5H, Ar-C*H*), 7.98-8.05 (m, 4H, Ar-C*H*), 8.21-8.24 (m, 2H, Ar-C*H*), 8.92 (s, 4H, H_β), 9.02 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.33 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 10.21 ppm (s, 1H, H_{meso}); ^{19}F NMR (377 MHz, $CDCl_3$, 25 °C): -115.02 ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 105.0, 112.4, 114.8, 115.0, 118.0, 121.6, 121.8, 125.6, 126.6, 127.4, 127.5, 127.8, 128.1, 128.2, 129.0, 130.6, 130.7, 134.5, 134.6, 135.2, 142.4, 142.8, 142.9, 160.3 and 162.7 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 413 (5.48), 508 (4.21), 543 (3.76), 584 (3.76), 639 nm (3.46); HRMS (MALDI) *m/z* calcd. for $C_{38}H_{24}F_2N_4$ $[M]^+$: 574.1968, found 574.1974.

5,15-*Bis*(1-ethylpropyl)-10-phenylporphyrin (151f)

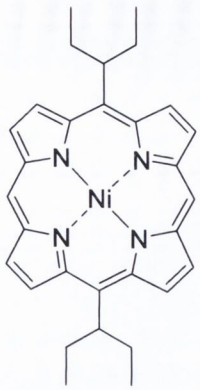


Synthesised *via* General Procedure 4 from **150f** (500 mg, 1.10 mmol) and PhLi (1.8 M, 3.70 mL, 6.60 mmol) in THF (300 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield a purple solid (561 mg, 1.07 mmol, 97 %). M.p.: >300 °C; R_f = 0.31 (*n*-hexane:CH_2Cl_2, 6:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = -2.47 (s, 2H, N*H*), 0.94 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 12H, alkyl-CH_3), 2.77-2.94 (m, 8H, alkyl-CH_2), 4.99-5.04 (m, 2H, alkyl-C*H*), 7.72-7.80 (m, 3H, Ph-*o*/*p*-C*H*), 8.18-8.20 (m, 2H, Ph-*m*-C*H*), 8.85 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.37 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.55 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.68 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 10.12 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.1, 34.5, 49.9, 126.2, 127.6, 131.7, 131.8 and 134.2 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 411 (5.62), 511 (4.36), 544 (3.88), 586 (3.88), 640 nm (3.65); HRMS (MALDI) *m/z* calcd. for $C_{36}H_{38}N_4$ $[M]^+$: 526.3096, found 526.3085.

General Procedure 5 (Nickel(II) insertion):

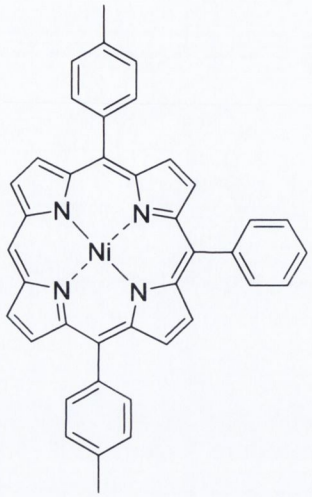
Free-base porphyrin (1 eq.) and $Ni(acac)_2$ (3 eq.) were dissolved in toluene and heated to reflux. The reaction process was monitored by TLC and once all the starting material was consumed the reaction flask was allowed to cool and filtered through silica gel using CH_2Cl_2 as eluent. Removal of the solvents was followed by recrystallisation from $CHCl_3/CH_3OH$.

[5,15-*Bis*(1-ethylpropyl)porphyrinato]nickel(II) (152)



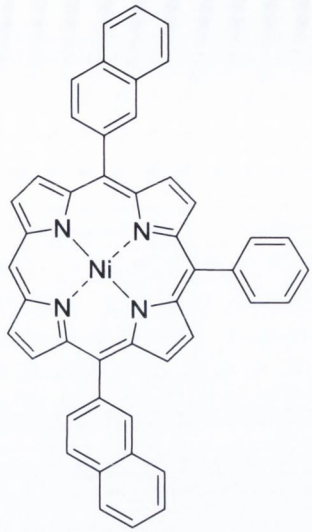
Synthesised *via* General Procedure 5 from **150f** (500 mg, 1.11 mmol) and $Ni(acac)_2$ (0.86 g, 3.33 mmol) in toluene (250 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield purple crystals (546 mg, 1.07 mmol, 97 %). M.p.: >300 °C; R_f = 0.37 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 12H, alkyl-C*H*$_3$), 2.62-2.79 (m, 8H, alkyl-C*H*$_2$), 4.48 (m, 2H, alkyl-C*H*), 9.09 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 4H, H_β), 9.49 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 4H, H_β), 9.57 ppm (s, 2H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.9, 33.6, 49.4, 103.4, 120.0, 130.9 and 131.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 405 (5.42), 525 (4.22), 560 nm (3.71); HRMS (MALDI) *m/z* calcd. for $C_{30}H_{32}N_4Ni$ $[M]^+$: 506.1980, found 506.1958.

[5,15-*Bis*(4-methylphenyl)-10-phenylporphyrinato]nickel(II) (153b):



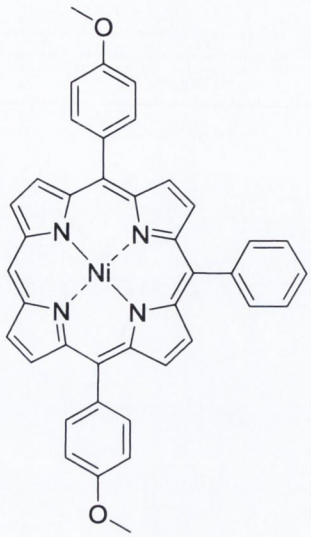
Synthesised *via* General Procedure 5 from **151b** (650 mg, 1.14 mmol) and $Ni(acac)_2$ (0.88 g, 3.44 mmol) in toluene (250 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield a purple solid (710 mg, 1.14 mmol, >99 %). M.p.: >300 °C; R_f = 0.68 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.66 (s, 6H, tolyl-C*H*$_3$), 7.49 (d, $^3J_{H\text{-}H}$ = 7.8 Hz, 4H, tolyl-*o*-C*H*), 7.66-7.68 (m, 3H, Ph-*o/p*-C*H*), 7.91 (d, $^3J_{H\text{-}H}$ = 7.8 Hz, 4H, tolyl-*m*-C*H*), 8.00-8.02 (m, 2H, Ph-*m*-C*H*), 8.75 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 8.79 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 8.91 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 9.12 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 9.82 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.5, 104.5, 118.7, 119.3, 126.8, 127.6, 131.9, 132.0, 132.1, 132.6, 133.7, 137.4, 138.0, 142.3, 142.7, 142.8 and 142.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 409 (5.70), 522 (4.56), 552 (4.02) nm; HRMS (MALDI) *m/z* calcd. for $C_{40}H_{28}N_4Ni$ $[M]^+$: 622.1667, found 622.1664.

[5,15-*Bis*(2-naphthyl)-10-phenylporphyrinato]nickel(II) (153c)



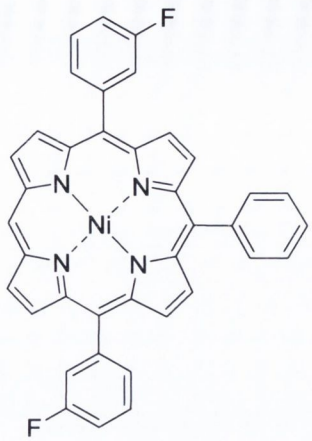
Synthesised *via* General Procedure 5 from **151c** (550 mg, 0.86 mmol) and $Ni(acac)_2$ (0.66 g, 2.58 mmol) in toluene (250 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield a purple solid (580 mg, 0.83 mmol, 97 %). M.p.: >300 °C; R_f = 0.35 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.69-7.74 (m, 7H, Ar-C*H*), 8.05-8.08 (m, 4H, Ar-C*H*), 8.17-8.19 (m, 4H, naph-C*H*), 8.25-8.27 (m, 2H, naph-C*H*), 8.52 (s, 2H, naph-C*H*), 8.81 (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β), 8.83 (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β), 8.93 (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β), 9.16 (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β), 9.88 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 104.8, 118.6, 119.6, 126.1, 126.6, 126.8, 126.9, 127.8, 128.0, 128.4, 131.9, 132.2, 132.3, 132.7, 132.8, 132.9, 133.7, 138.5, 142.5, 142.9 and 143.0 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 411 (5.69), 523 (4.58), 554 nm (4.10); HRMS (MALDI) *m/z* calcd. for $C_{46}H_{28}N_4Ni$ $[M]^+$: 694.1667, found 694.1678.

[5,15-*Bis*(4-methoxyphenyl)-10-phenylporphyrinato]nickel(II) (153d)



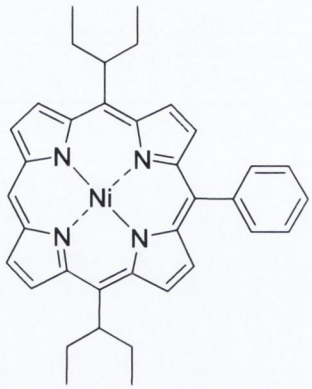
Synthesised *via* General Procedure 5 from **151d** (500 mg, 0.84 mmol) and $Ni(acac)_2$ (0.64 g, 2.52 mmol) in toluene (250 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield a purple solid (550 mg, 0.84 mmol, >99 %). M.p.: 270-272 °C; R_f = 0.25 (*n*-hexane:CH_2Cl_2, 4:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 4.05 (s, 6H, OCH_3), 7.22 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 4H, C_6H_4OMe-*o*-C*H*), 7.66-7.68 (m, 3H, Ph-*o*/*p*-C*H*), 7.94 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 4H, C_6H_4OMe-*m*-C*H*), 8.00-8.02 (m, 2H, Ph-*m*-C*H*), 8.76 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 8.80 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 8.91 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.11 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.80 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 55.5, 104.5, 112.4, 118.3, 119.3, 126.8, 127.7, 131.9, 132.0, 132.5, 133.3, 133.7, 134.8, 141.2, 142.3, 142.7, 143.1, 143.2 and 159.4 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 410 (5.36), 523 (4.25), 553 nm (3.77); HRMS (MALDI) *m/z* calcd. for $C_{40}H_{28}N_4NiO_2$ $[M]^+$: 654.1566, found 654.1586.

[5,15-*Bis*(3-fluorophenyl)-10-phenylporphyrinato]nickel(II) (153e)



Synthesised *via* General Procedure 5 from **151e** (550 mg, 0.96 mmol) and $Ni(acac)_2$ (0.74 g, 2.87 mmol) in toluene (250 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield a purple solid (594 mg, 0.94 mmol, 98 %). M.p.: 205-206 °C; R_f = 0.38 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.44-7.49 (m, 2H, Ar-C*H*), 7.61-7.73 (m, 5H, Ar-C*H*), 7.78-7.82 (m, 4H, Ar-C*H*), 8.04-8.06 (m, 2H, Ar-C*H*), 8.79 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 8.83 (m, 4H, H_β), 9.01 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.66 ppm (s, 1H, H_{meso}); ^{19}F NMR (377 MHz, $CDCl_3$, 25 °C): -115.38 ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 104.8, 114.8, 115.0, 117.1, 119.8, 120.8, 121.0, 126.9, 127.9, 128.2, 128.3, 129.8, 131.8, 132.2, 132.4, 133.7, 140.9, 142.3, 142.5, 142.6, 142.9, 143.0, 143.1, 160.3 and 162.7 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 406 (5.31), 521 (4.16), 551 nm (3.74); HRMS (MALDI) *m/z* calcd. for $C_{38}H_{22}F_2N_4Ni$ $[M]^+$: 630.1166, found 630.1143.

[5,15-*Bis*(1-ethylpropyl)-10-phenylporphyrinato]nickel(II) (153f)



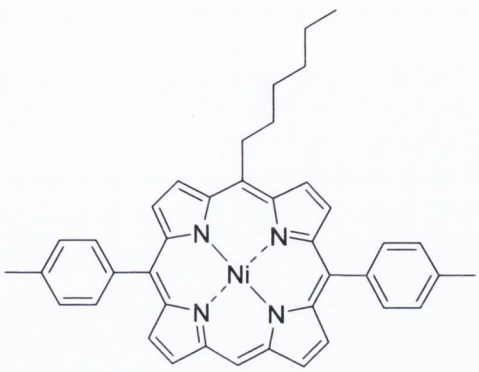
Synthesised *via* General Procedure 5 from **151f** (500 mg, 0.95 mmol) and $Ni(acac)_2$ (0.73 g, 2.85 mmol) in toluene (250 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield a purple solid (561 mg, 0.92 mmol, 97 %). M.p.: >300 °C; R_f = 0.62 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 12H, alkyl-C*H*$_3$), 2.59-2.74 (m, 8H, alkyl-C*H*$_2$), 4.40-4.44 (m, 2H, alkyl-C*H*), 7.65-7.67 (m, 3H, Ph-*o*/*p*-C*H*), 7.96-7.98 (m, 2H, Ph-*m*-C*H*), 8.71 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.05 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.36 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.44 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.48 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.0, 33.6, 49.4, 102.9, 117.7, 120.5, 126.8, 127.2, 128.7, 130.5, 131.1, 132.0, 133.5 and 140.1 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 413 (5.14), 532 nm (4.00); HRMS (MALDI) *m/z* calcd. for $C_{36}H_{36}N_4Ni$ $[M]^+$: 582.2293, found 582.2286.

General Procedure 6 (Reaction of porphyrins with alkyllithium reagents):

A nickel(II) porphyrin (1 eq.) was dissolved in anhydrous THF in an oven-dried Schlenk flask and degassed under high vacuum. The reaction vessel was then purged with argon and cooled to -78 °C. The appropriate alkyllithium reagent (6 eq.) was added dropwise over 10 minutes and the solution was stirred at -78 °C for 30 minutes before being quenched with a solution of water in THF (1:4, v/v). 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 3 eq.) was added in CH_2Cl_2 (10 mL) and the solution was allowed to warm to room temperature. The solvents were removed *in vacuo* and the crude product was filtered through

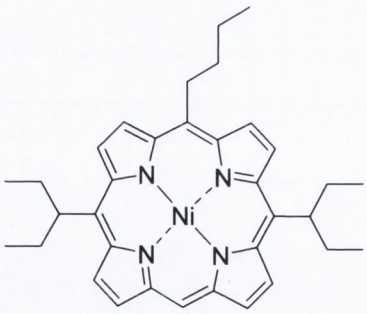
silica gel using CH_2Cl_2 as eluent. Removal of the solvents was followed by recrystallisation from $CHCl_3/CH_3OH$.

[5-(*n*-Hexyl)-10,20-*bis*(4-methylphenyl)porphyrinato]nickel(II) (153g)



Synthesised *via* General Procedure 6 from **127** (500 mg, 0.91 mmol) and *n*-hexyllithium (2.5 M, 2.20 mL, 5.46 mmol) in THF (250 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield purple crystals (530 mg, 0.84 mmol, 92 %). M.p.: 257-258 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.90 (t, $^3J_{H\text{-}H}$ = 7.3 Hz, 3H, hexyl-CH_3), 1.30-1.36 (m, 2H, hexyl-CH_2), 1.38-1.44 (m, 2H, hexyl-CH_2), 1.61-1.64 (m, 2H, hexyl-CH_2), 2.32-2.36 (m, 2H, hexyl-CH_2), 2.67 (s, 6H, tolyl-CH_3), 4.63 (m, 2H, hexyl-CH_2), 7.49 (d, $^3J_{H\text{-}H}$ = 7.6 Hz, 4H, tolyl-*o*-C*H*), 7.90 (d, $^3J_{H\text{-}H}$ = 7.6 Hz, 4H, tolyl-*m*-C*H*), 8.84 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 8.86 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.03 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.34 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.66 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.1, 21.5, 22.7, 30.1, 31.8, 34.5, 37.7, 103.7, 118.0, 119.2, 127.6, 129.2, 131.8, 132.3, 132.5, 133.7, 137.3, 138.0, 141.9, 142.2, 142.3 and 142.7 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 410 (5.08), 525 (3.95), 555 nm (3.57); HRMS (MALDI) *m/z* calcd. for $C_{40}H_{36}N_4Ni$ $[M]^+$: 630.2293, found 630.2289.

[5-(*n*-Butyl)-10,20-*bis*(1-ethylpropylporphyrinato]nickel(II) (153h)

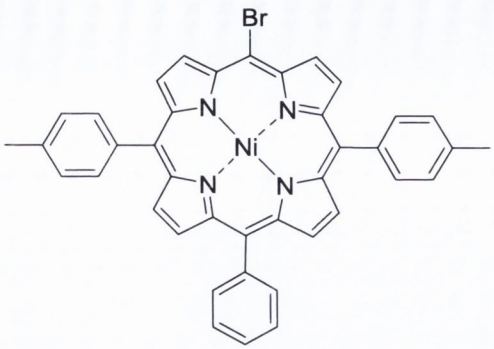


Synthesised *via* General Procedure 6 from **152** (500 mg, 0.99 mmol) and *n*-butyllithium (2.5 M, 2.40 mL, 5.94 mmol) in THF (250 mL) and recrystallised ($CHCl_3/CH_3OH$) to yield purple crystals (494 mg, 0.87 mmol, 89 %). M.p.: 143-145 °C; R_f = 0.30 (*n*-hexane:CH_2Cl_2, 5:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.90 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 12H, alkyl-C*H*$_3$), 1.03 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 3H, butyl-C*H*$_3$), 1.57 (m, 2H, butyl-C*H*$_2$), 2.27 (m, 2H, butyl-C*H*$_2$), 2.58-2.75 (m, 8H, alkyl-C*H*$_2$), 4.34-4.38 (m, 2H, alkyl-C*H*), 4.52 (t, $^3J_{H\text{-}H}$ = 8.0 Hz, 2H, butyl-C*H*$_2$), 8.98 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.28 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.36 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.38 (s, 1H, H_{meso}), 9.40 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.9, 14.0, 23.4, 33.5, 33.8, 39.5, 49.3, 102.2, 117.8, 120.0, 129.5, 130.7, 131.1, 131.8, 139.9, 140.6 and 141.6 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 414 (5.47), 534 nm (4.30); HRMS (MALDI) *m/z* calcd. for $C_{34}H_{40}N_4Ni$ $[M]^+$: 562.2606, found 562.2596.

General Procedure 7 (Bromination of porphyrins):

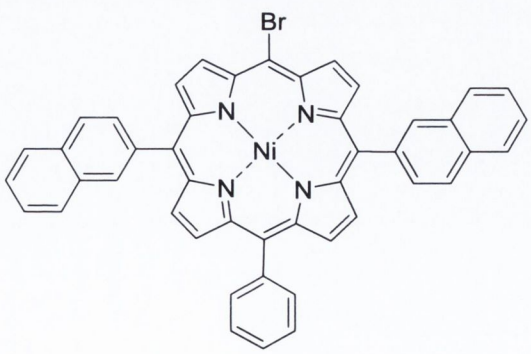
This procedure was adapted from Boyle and co-workers.[185] The trisubstituted porphyrin was dissolved in $CHCl_3$ and *N*-bromosuccinimide (NBS, 3 eq.) and pyridine (0.30 mL) were added. The progress of the reaction was monitored by TLC and once all starting material had been consumed the reaction mixture was filtered through silica gel using CH_2Cl_2 as eluent. The solvents were removed *in vacuo* and the crude product was purified by recrystallisation from $CHCl_3/CH_3OH$.

[5-Bromo-10,20-*bis*(4-methylphenyl)-15-phenylporphyrinato]nickel(II) (147b)



Synthesised *via* General Procedure 7 from **153b** (500 mg, 0.79 mmol) and NBS (420 mg, 2.37 mmol) in $CHCl_3$ (200 mL) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (521 mg, 0.74 mmol, 94 %). M.p.: 222-223 °C; R_f = 0.79 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.65 (s, 6H, tolyl-C*H*$_3$), 7.48 (d, $^3J_{H\text{-}H}$ = 7.8 Hz, 4H, tolyl-*o*-C*H*), 7.65-7.69 (m, 3H, Ph-*o*/*p*-C*H*), 7.85 (d, $^3J_{H\text{-}H}$ = 7.8 Hz, 4H, tolyl-*m*-C*H*), 7.96-7.98 (m, 2H, Ph-*m*-C*H*), 8.67 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 8.70 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 8.80 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 9.49 ppm (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.5, 102.1, 119.4, 119.5, 126.9, 127.1, 127.7, 127.8, 128.7, 132.4, 132.6, 133.0, 133.3, 133.55, 133.6, 137.5, 140.6, 142.3, 142.9 and 143.2 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 427 (5.10), 545 nm (3.99); HRMS (MALDI) *m/z* calcd. for $C_{40}H_{27}BrN_4Ni$ $[M]^+$: 700.0773, found 700.0748.

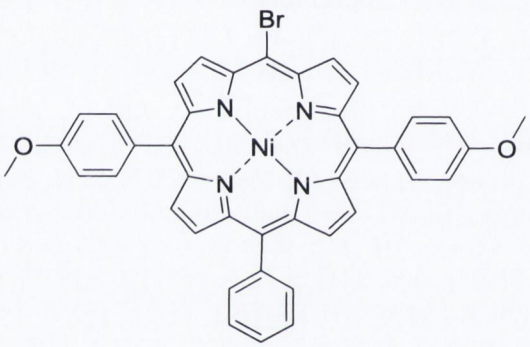
[5-Bromo-10,20-*bis*(2-naphthyl)-15-phenylporphyrinato]nickel(II) (147c)



Synthesised *via* General Procedure 7 from **153c** (500 mg, 0.72 mmol) and NBS (380 mg, 2.15 mmol) in $CHCl_3$ (200 mL) and recrystallised ($CHCl_3$/CH_3OH) to yield purple

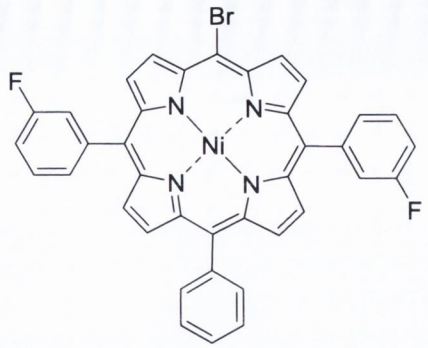
crystals (542 mg, 0.70 mmol, 97 %). M.p.: 254-255 °C; R_f = 0.25 (*n*-hexane:CH_2Cl_2, 4:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.65-7.70 (m, 7H, Ar-C*H*), 7.97-7.99 (m, 2H, naph-C*H*), 8.01-8.03 (m, 2H, naph-C*H*), 8.13-8.17 (m, 6H, Ar-C*H*), 8.43 (s, 2H, naph-C*H*), 8.67 (s, 4H, H_β), 8.80 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 8.95 ppm (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 102.4, 119.4, 119.7, 126.2, 126.7, 126.8, 126.9, 126.95, 127.9, 131.7, 132.2, 132.6, 132.7, 132.8, 133.3, 133.4, 133.6, 137.9, 140.5, 142.5, 143.0, 143.1 and 143.3 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 420 (5.38), 533 nm (4.28); HRMS (MALDI) *m/z* calcd. for $C_{46}H_{27}BrN_4Ni$ $[M]^+$: 772.0773, found 772.0739.

[5-Bromo-10,20-*bis*(4-methoxyphenyl)-15-phenylporphyrinato]nickel(II) (147d)



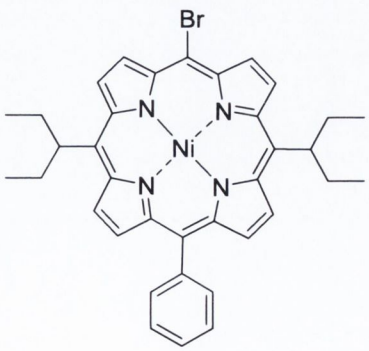
Synthesised *via* General Procedure 7 from **153d** (500 mg, 0.76 mmol) and NBS (407 mg, 2.29 mmol) in $CHCl_3$ (200 mL) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (530 mg, 0.72 mmol, 95 %). M.p.: 209-210 °C; R_f = 0.31 (*n*-hexane:CH_2Cl_2, 4:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 4.04 (s, 6H, OC*H*$_3$), 7.21 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 4H, C_6H_4OMe-*o*-C*H*), 7.65-7.67 (m, 3H, Ph-*o*/*p*-C*H*), 7.88 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 4H, C_6H_4OMe-*m*-C*H*), 7.96 (m, 2H, Ph-*m*-C*H*), 8.67 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 8.70 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 8.80 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.48 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 55.5, 112.5, 112.6, 119.2, 119.4, 126.9, 127.8, 132.4, 132.6, 132.8, 133.0, 133.3, 133.5, 133.6, 134.6, 134.7, 142.3, 142.9, 143.2, 143.4 and 159.5 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 421 (5.33), 536 nm (4.21); HRMS (MALDI) *m/z* calcd. for $C_{40}H_{27}BrN_4NiO_2$ $[M]^+$: 732.0671, found 732.0667.

[5-Bromo-10,20-*bis*(3-fluorophenyl)-15-phenylporphyrinato]nickel(II) (147e)



Synthesised *via* General Procedure 7 from **153e** (590 mg, 0.93 mmol) and NBS (496 mg, 2.79 mmol) in $CHCl_3$ (250 mL) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (614 mg, 0.86 mmol, 93 %). M.p.: 186-188 °C; R_f = 0.45 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, 25 °C): δ = 7.41-7.45 (m, 2H, Ar-C*H*), 7.59-7.73 (m, 9H, Ar-C*H*), 7.96 (m, 2H, Ar-C*H*), 8.66 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 8.71 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 8.72 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.45 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β); ^{19}F NMR (377 MHz, $CDCl_3$, 25 °C): -114.55 ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 102.5, 114.9, 115.1, 117.9, 119.9, 120.6, 120.9, 126.9, 127.9, 128.3, 128.4, 129.6, 132.3, 132.9, 133.0, 133.4, 133.5, 133.6, 140.3, 142.4, 142.5, 142.7, 143.2, 160.2 and 162.7 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 417 (5.36), 532 nm (4.23); HRMS (MALDI) *m/z* calcd. for $C_{38}H_{21}BrF_2N_4Ni$ $[M]^+$: 708.0271, found 708.0255.

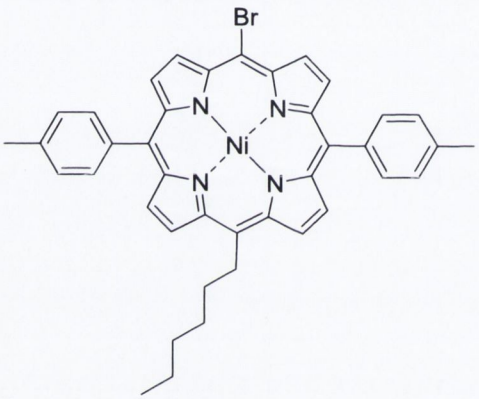
[5-Bromo-10,20-*bis*(1-ethylpropyl)-15-phenylporphyrinato]nickel(II) (147f)



Synthesised *via* General Procedure 7 from **153f** (500 mg, 0.86 mmol) and NBS (457 mg, 2.57 mmol) in $CHCl_3$ (250 mL) and recrystallised ($CHCl_3$/CH_3OH) to yield purple

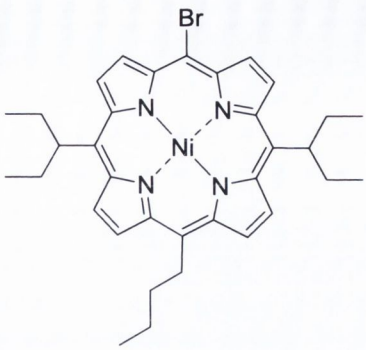
crystals (487 mg, 0.81 mmol, 94 %). M.p.: 231-232 °C; R_f = 0.51 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 12H, alkyl-C*H*$_3$), 2.55-2.67 (m, 8H, alkyl-C*H*$_2$), 4.31 (m, 2H, alkyl-C*H*), 7.64-7.66 (m, 3H, Ph-*o*/*p*-C*H*), 7.93-7.95 (m, 2H, Ph-*m*-C*H*), 8.65 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.26 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.36 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.43 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.9, 33.6, 49.4, 100.9, 118.1, 121.7, 126.9, 127.7, 131.0, 131.8, 132.5, 133.2, 133.4 and 140.4 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 424 (5.22), 548 (4.14), 589 nm (3.60); HRMS (MALDI) *m/z* calcd. for $C_{36}H_{35}BrN_4Ni$ $[M]^+$: 660.1399, found 660.1421.

[5-Bromo-10,20-*bis*(4-methylphenyl)-15-(*n*-hexyl)porphyrinato]nickel(II) (147g)



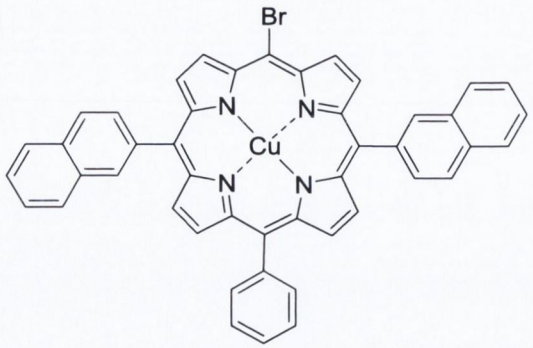
Synthesised *via* General Procedure 7 from **153g** (500 mg, 0.79 mmol) and NBS (423 mg, 2.37 mmol) in $CHCl_3$ (250 mL) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (516 mg, 0.73 mmol, 92 %). M.p.: 235-237 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.88 (t, $^3J_{H\text{-}H}$ = 7.2 Hz, 3H, hexyl-C*H*$_3$), 1.28-1.41 (m, 6H, hexyl-C*H*$_2$), 2.25 (m, 2H, hexyl-C*H*$_2$), 2.65 (s, 6H, tolyl-C*H*$_3$), 4.46 (m, 2H, hexyl-C*H*$_2$), 7.45 (d, $^3J_{H\text{-}H}$ = 7.6 Hz, 4H, tolyl-*o*-C*H*), 7.79 (d, $^3J_{H\text{-}H}$ = 7.6 Hz, 4H, tolyl-*m*-C*H*), 8.70 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 4H, H_β), 9.18 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.38 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.1, 21.5, 22.6, 30.0, 31.7, 34.2, 37.4, 118.8, 119.4, 127.6, 127.7, 129.7, 132.8, 133.2, 133.4, 133.5, 137.5, 142.1, 142.2 and 142.5 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 422 (5.28), 538 nm (4.17); HRMS (MALDI) *m/z* calcd. for $C_{40}H_{35}BrN_4Ni$ $[M]^+$: 708.1399, found 708.1406.

[5-Bromo-10,20-*bis*(1-ethylpropyl)-15-(*n*-butyl)porphyrinato]nickel(II) (147h)



Synthesised *via* General Procedure 7 from **153h** (500 mg, 0.89 mmol) and NBS (475 mg, 2.67 mmol) in $CHCl_3$ (250 mL) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (508 mg, 0.79 mmol, 89 %). M.p.: 188-190 °C; R_f = 0.47 (*n*-hexane:CH_2Cl_2, 5:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 12H, alkyl-C*H*$_3$), 1.01 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 3H, butyl-C*H*$_3$), 1.54 (m, 2H, butyl-C*H*$_2$), 2.20 (m, 2H, butyl-C*H*$_2$), 2.54-2.68 (m, 8H, alkyl-C*H*$_2$), 4.25 (m, 2H, alkyl-C*H*), 4.40 (t, $^3J_{H\text{-}H}$ = 8.0 Hz, 2H, butyl-C*H*$_2$), 9.18 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.28 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.30 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.35 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.9, 14.0, 23.4, 33.5, 33.6, 39.2, 49.3, 100.1, 118.2, 121.2, 130.0, 131.2, 131.8, 132.9, 140.2, 140.5, 141.6 and 141.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 423 (5.30), 546 (4.14), 588 nm (3.52); HRMS (MALDI) *m/z* calcd. for $C_{34}H_{39}BrN_4Ni$ $[M]^+$: 640.1712, found 640.1696.

[5-Bromo-10,20-*bis*(2-naphthyl)-15-phenylporphyrinato]copper(II) (147k)

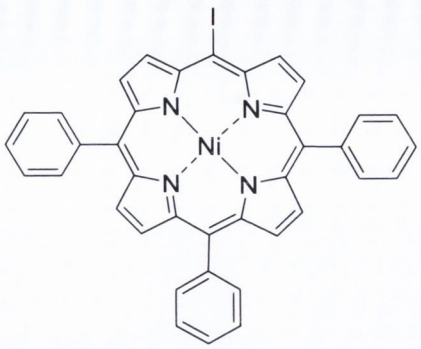


Porphyrin **154c** (270 mg, 0.38 mmol) and copper(II) acetylacetonate (306 mg, 1.14 mmol) were dissolved in toluene (200 mL) and heated to reflux. The reaction progress was monitored by TLC and once all the starting material had been consumed the reaction was quenched by filtration through silica using CH_2Cl_2 as eluent. The product was recrystallised from $CHCl_3/CH_3OH$ to yield purple crystals (273 mg, 0.35 mmol, 92 %). M.p.: >300 °C; R_f = 0.35 (*n*-hexane:CH_2Cl_2, 4:1, v/v); UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 422 (5.86), 546 (4.63), 583 nm (3.99); HRMS (MALDI) *m/z* calcd. for $C_{46}H_{27}BrN_4Cu$ $[M]^+$: 777.0715, found 777.0717.

General Procedure 8 (Iodination of porphyrins):

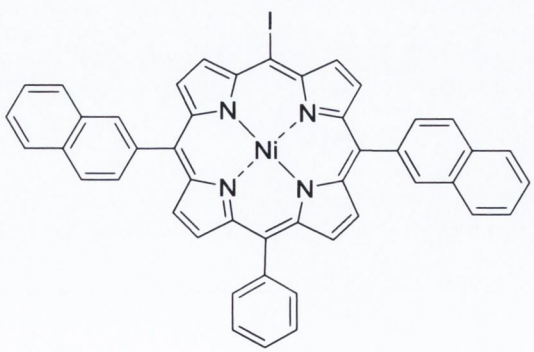
Following the procedure of Boyle and co-workers[185,287] the porphyrin (1 eq.) was dissolved in $CHCl_3$ and purged with argon. Iodine (1.5 eq.) and *bis*(trifluoroacetoxy)iodobenzene (1.1 eq.) were added and the flask shielded from light. The reaction mixture was left to stir at room temperature until consumption of the starting material was complete (typically ~48 h). The solution was then filtered through silica gel using CH_2Cl_2 as eluent, solvents were removed and the product was recrystallised from $CHCl_3/CH_3OH$.

(5-Iodo-10,15,20-triphenylporphyrinato)nickel(II) (155a)



Synthesised *via* General Procedure 8 from **151a** (200 mg, 0.34 mmol), I_2 (130 mg, 0.52 mmol) and $C_6H_5I(O_2CCF_3)_2$ (160 mg, 0.37 mmol) in $CHCl_3$ (200 mL) for 48 h before recrystallisation ($CHCl_3/CH_3OH$) to yield purple crystals (228 mg, 0.32 mmol, 93 %). M.p.: 264-265 °C; R_f = 0.53 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.65-7.71 (m, 9H, Ph-*o/p*-C*H*), 7.95-7.97 (m, 6H, Ph-*o*-C*H*), 8.66-8.70 (m, 4H, H_β), 8.73 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 9.47 ppm (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 119.4, 119.7, 126.9, 127.8, 127.9, 132.2, 132.6, 133.6, 133.7, 137.9, 140.3, 140.5, 140.9, 142.7, 142.8, 142.9, 143.4 and 144.5 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 419 (5.54), 533 nm (4.40); HRMS (MALDI) *m/z* calcd. for $C_{38}H_{23}IN_4Ni$ $[M]^+$: 720.0331, found 720.0321.

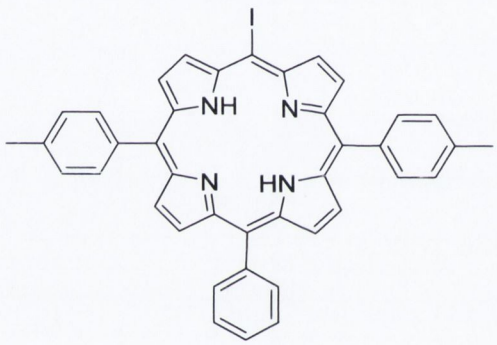
[5-Iodo-10,20-*bis*(2-naphthyl)-15-phenylporphyrinato]nickel(II) (155b)



Synthesised *via* General Procedure 8 from **153c** (300 mg, 0.43 mmol), I_2 (150 mg, 0.60 mmol) and $C_6H_5I(O_2CCF_3)_2$ (180 mg, 0.43 mmol) in $CHCl_3$ (200 mL) for 46 h before recrystallisation ($CHCl_3/CH_3OH$) to yield purple crystals (333 mg, 0.41 mmol, 95 %). M.p.:

289-291 °C; R_f = 0.35 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.68-7.73 (m, 7H, Ar-C*H*), 8.00 (m, 2H, naph-C*H*), 8.05 (m, 2H, naph-C*H*), 8.15-8.20 (m, 6H, Ar-C*H*), 8.44 (s, 2H, naph-C*H*), 8.71 (s, 4H, H_β), 8.78 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 9.53 ppm (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 119.4, 119.8, 126.2, 126.7, 126.9, 127.9, 128.2, 128.4, 129.0, 130.2, 131.7, 132.2, 132.3, 132.7, 132.8, 133.6, 133.7, 137.5, 137.9, 140.4, 142.8, 142.9, 143.0, 143.6 and 144.6 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 422 (5.37), 535 nm (4.25); HRMS (MALDI) *m/z* calcd. for $C_{46}H_{27}IN_4Ni$ $[M]^+$: 820.0634, found 820.0618.

5-Iodo-10,20-*bis*(4-methylphenyl)-15-phenylporphyrin (155c)



Synthesised *via* General Procedure 8 from **151b** (260 mg, 0.47 mmol), I_2 (165 mg, 0.65 mmol) and $C_6H_5I(O_2CCF_3)_2$ (205 mg, 0.48 mmol) in $CHCl_3$ (300 mL) for 48 h before recrystallisation ($CHCl_3$/CH_3OH) to yield purple crystals (270 mg, 0.39 mmol, 83 %). M.p.: >300 °C; R_f = 0.27 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = -2.72 (s, 2H, N*H*), 2.70 (s, 6H, tolyl-CH_3), 7.55 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 4H, tolyl-*o*-C*H*), 7.72-7.74 (m, 3H, Ph-*o*/*p*-C*H*), 8.05 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 4H, tolyl-*m*-C*H*), 8.15-8.17 (m, 2H, Ph-*m*-C*H*), 8.78 (m, 4H, H_β), 8.87 (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β), 9.65 ppm (d, $^3J_{H\text{-}H}$ = 4.8 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.5, 121.0, 126.8, 127.5, 127.8, 134.4, 134.5, 137.6, 138.9 and 141.8 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 423 (5.48), 522 (4.07), 558 (3.85), 598 (3.51), 655 nm (3.64); HRMS (MALDI) *m/z* calcd. for $C_{40}H_{29}IN_4$ $[M]^+$: 692.1437, found 692.1431.

7.6 Synthesis of allenylporphyrins

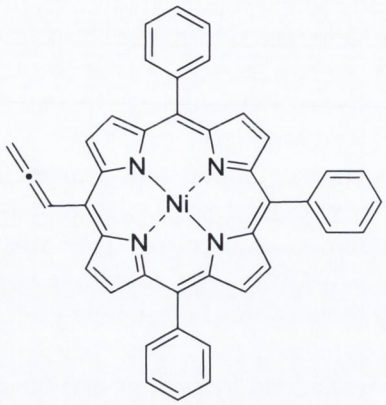
General Procedure 9 (Allenylporphyrins via Suzuki/Miyaura cross-coupling reactions):

The appropriate haloporphyrin, $PdCl_2(dppe)$ (15 mol %) and K_2CO_3 (10 eq.) were added to an oven-dried Schlenk flask equipped with a magnetic stirring bar. The contents of the flask were heated under vacuum. Anhydrous THF was added and the solution was subjected to three freeze-pump-thaw cycles before being released to argon. Allenylboronic acid pinacol ester **146** (10 eq.) was added by syringe and the contents of the flask were then heated to reflux for 72 h. The crude material was purified by filtration through a short silica plug using CH_2Cl_2 as eluent followed by column chromatography (silica) and recrystallisation from $CHCl_3/CH_3OH$.

General Procedure 10 (Allenylporphyrins via sequential Sonogashira and hydrogen transfer reactions):

The appropriate bromoporphyrin, $PdCl_2(PPh_3)_2$ (10 mol %) and CuI (30 mol %) were added to an oven-dried Schlenk flask equipped with a magnetic stirrer bar. The contents of the flask were heated under vacuum. Anhydrous THF and triethylamine (4:1, v/v) were added and the solution the solution was subjected to three freeze-pump-thaw cycles before being released to argon. *N,N*-Diisopropylprop-2-yn-1-amine **158** (6 eq.) was added and the contents of the flask were heated to 60 °C for 24 h. The crude material was purified by filtration through a short silica plug using CH_2Cl_2 as eluent to remove any unreacted starting material. Alteration of the eluent to EtOAc then provided crude alkyne-coupled porphyrin **159**, which was typically used without any further purification. This intermediate was dried *in vacuo* and transferred to a small RBF. Anhydrous $CHCl_3$, $Pd_2(dba)_3$ (10 mol %) and $P(C_6F_5)_3$ (40 mol %) were added and the solution purged with argon for 10 minutes before being the sealed reaction flask was heated to 90 °C for 24 h. The crude material was purified by filtration through silica gel using $CHCl_3$ as eluent followed by column chromatography (silica) and recrystallisation from $CHCl_3/CH_3OH$.

[5,10,15-Triphenyl-20-propadienylporphyrinato]nickel(II) (148a)[202]



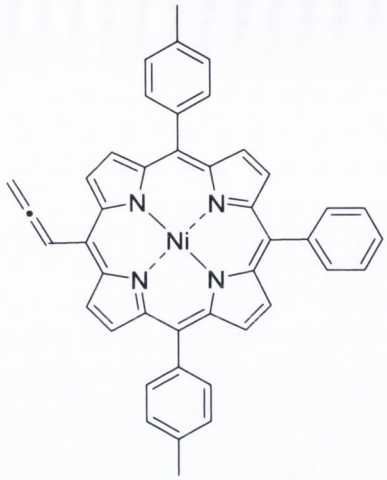
Method 1: Synthesised *via* General Procedure 9 from bromoporphyrin **147a** (100 mg, 163 μmol), $PdCl_2$(dppe) (14 mg, 25 μmol), K_2CO_3 (225 mg, 1.63 mmol) and **146** (0.29 mL, 1.63 mmol) in THF (15 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 3:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (91 mg, 143 μmol, 88 %).

Method 2: Synthesised *via* General Procedure 9 from iodoporphyrin **155a** (60 mg, 83 μmol), $PdCl_2$(dppe) (7 mg, 13 μmol), K_2CO_3 (110 mg, 0.83 mmol) and **146** (0.15 mL, 0.83 mmol) in THF (15 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 3:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (22 mg, 35 μmol, 42 %).

Method 3: Synthesised *via* General Procedure 10 from bromoporphyrin **147a** (185 mg, 0.30 mmol), $PdCl_2(PPh_3)_2$ (21 mg, 30 μmol), CuI (17 mg, 90 μmol) and **158** (208 mg, 1.50 mmol) in THF/NEt_3 (40 mL, 4:1, v/v). The title compound was obtained from crude **159a** with $Pd_2(dba)_3$ (27 mg, 30 μmol) and $P(C_6F_5)_3$ (64 mg, 0.12 mmol) in $CHCl_3$ (5 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 3:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (157 mg, 0.24 mmol, 79 %).

The product had analytical data consistent with that previously reported.[202]

[5,15-*Bis*(4-methylphenyl)-10-phenyl-20-propadienylporphyrinato]nickel(II) (148b)



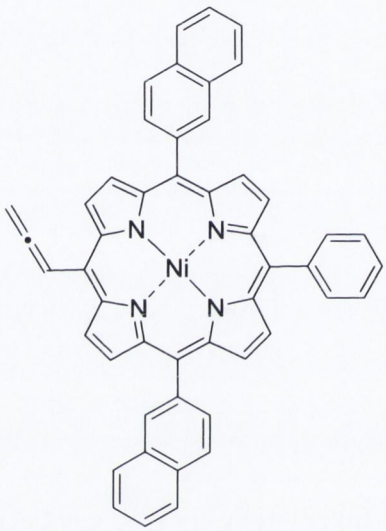
Method 1: Synthesised *via* General Procedure 9 from bromoporphyrin **147b** (55 mg, 78 μmol), $PdCl_2$(dppe) (7 mg, 12 μmol), K_2CO_3 (106 mg, 0.78 mmol) and **146** (0.14 mL, 0.78 mmol) in THF (10 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 6:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (41 mg, 61 μmol, 78 %).

Method 2: Synthesised *via* General Procedure 10 from bromoporphyrin **147b** (200 mg, 0.28 mmol), $PdCl_2(PPh_3)_2$ (20 mg, 28 μmol), CuI (16 mg, 84 μmol) and **158** (234 mg, 1.68 mmol) in THF/NEt_3 (40 mL, 4:1, v/v). The title compound was obtained from crude **159b** with $Pd_2(dba)_3$ (26 mg, 28 μmol) and $P(C_6F_5)_3$ (60 mg, 0.11 mmol) in $CHCl_3$ (5 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 6:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (155 mg, 0.24 mmol, 84 %).

M.p.: >300 °C; R_f = 0.34 (*n*-hexane:CH_2Cl_2, 4:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.64 (s, 6H, tolyl-C*H*$_3$), 5.28 (d, $^4J_{H\text{-}H}$ = 6.9 Hz, 2H, allene-C*H*$_2$), 7.47 (d, $^3J_{H\text{-}H}$ = 7.8 Hz, 4H, tolyl-*o*-C*H*), 7.65-7.67 (m, 3H, Ph-*o*/*p*-C*H*), 7.86 (d, $^3J_{H\text{-}H}$ = 7.8 Hz, 4H, tolyl-*m*-C*H*), 7.96-7.97 (m, 2H, Ph-*m*-C*H*), 8.26 (t, $^4J_{H\text{-}H}$ = 6.9 Hz, 1H, allene-C*H*), 8.65 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 8.68 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 8.80 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 9.41 ppm (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.5, 76.0, 92.5, 118.8, 118.9, 126.9, 127.6, 130.6, 132.0, 132.2, 132.6, 133.6, 137.4, 137.7, 140.7,

141.5, 142.0 142.4, 142.5 and 215.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 422 (5.10), 536 (4.07), 623 nm (3.42); IR (neat): $\bar{\nu}$ = 2963, 2918 and 1939 cm^{-1}; HRMS (MALDI) *m/z* calcd. for $C_{43}H_{30}N_4Ni$ $[M]^+$: 660.1824, found 660.1848; LRMS (ESI+, 150 V): 660.18 (30 %, M^+), 646.16 (38 %, M-CH_3), 569.13 (57 %, M-C_7H_7), 461.29 (100 %, M-$C_{15}H_{17}$), 446.27 (75 %, M-$C_{16}H_{20}$), 431.25 (61 %, M-$C_{17}H_{23}$), 331.20 (11 %, M-$C_{22}H_{21}Ni$), 243.13 (10 %, M-$C_{28}H_{25}NNi$), 171.08 (8 %, M-$C_{33}H_{28}N_2Ni$).

[5,15-*Bis*(2-naphthyl)-10-phenyl-20-propadienylporphyrinato]nickel(II) (148c)



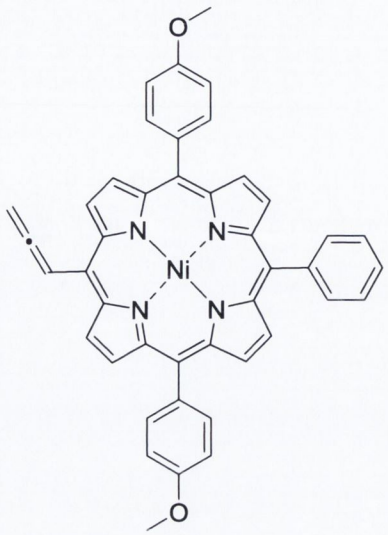
Method 1: Synthesised *via* General Procedure 9 from bromoporphyrin **147c** (100 mg, 130 µmol), $PdCl_2$(dppe) (11 mg, 20 µmol), K_2CO_3 (180 mg, 1.30 mmol) and **146** (0.23 mL, 1.30 mmol) in THF (15 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 6:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (87 mg, 124 µmol, 91 %).

Method 2: Synthesised *via* General Procedure 9 from iodoporphyrin **155b** (100 mg, 120 µmol), $PdCl_2$(dppe) (10 mg, 18 µmol), K_2CO_3 (165 mg, 1.20 mmol) and **146** (0.21 mL, 1.20 mmol) in THF (15 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 6:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (70 mg, 100 µmol, 73 %).

Method 3: Synthesised *via* General Procedure 10 from bromoporphyrin **147c** (230 mg, 0.30 mmol), $PdCl_2(PPh_3)_2$ (21 mg, 30 μmol), CuI (17 mg, 90 μmol) and **158** (208 mg, 1.50 mmol) in THF/NEt_3 (40 mL, 4:1, v/v). The title compound was obtained from crude **159c** with $Pd_2(dba)_3$ (27 mg, 30 μmol) and $P(C_6F_5)_3$ (64 mg, 0.12 mmol) in $CHCl_3$ (5 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 6:1, v/v) to yield purple crystals (180 mg, 0.25 mmol, 82 %).

M.p.: >300 °C; R_f = 0.15 (*n*-hexane:CH_2Cl_2, 5:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 5.27 (d, $^4J_{H\text{-}H}$ = 6.9 Hz, 2H, allene-C*H*$_2$), 7.40-7.42 (m, 2H, naph-C*H*), 7.65-7.70 (m, 7H, Ar-C*H*), 7.97-8.01 (m, 2H, naph-C*H*), 8.08-8.17 (m, 6H, Ar-C*H*), 8.23 (t, $^4J_{H\text{-}H}$ = 6.9 Hz, 1H, allene-C*H*), 8.42 (s, 2H, naph-C*H*), 8.69 (s, 4H, H_β), 8.78 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.39 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 76.0, 92.5, 118.8, 125.4, 126.1, 126.6, 126.8, 126.9, 127.7, 127.9, 128.4, 128.9, 130.5, 130.8, 131.8, 132.2, 132.3, 132.7, 133.6, 138.2, 140.7, 141.6, 142.1, 142.6, 143.3 and 216.0 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 423 (5.19), 536 nm (4.14); IR (neat): $\tilde{\nu}$ = 3051, 2963 and 1939 cm^{-1}; HRMS (MALDI) *m/z* calcd. for $C_{49}H_{30}N_4Ni$ $[M]^+$: 732.1824, found 732.1810; LRMS (ESI+, 150 V): 731.10 (8 %, M-H), 654.14 (6 %, M-C_6H_5), 602.21 (10 %, M-$C_{10}H_{10}$), 540.32 (8 %, M-$C_{15}H_{12}$), 466.41 (4 %, M-$C_{21}H_{14}$), 374.48 (17 %, M-$C_{24}H_{10}Ni$), 296.55 (16 %, M-$C_{30}H_{18}Ni$), 223.75 (89 %, M-$C_{35}H_{17}NNi$), 214.76 (100 %, M-$C_{36}H_{14}NNi$), 182.78 (24 %, M-$C_{38}H_{22}NNi$).

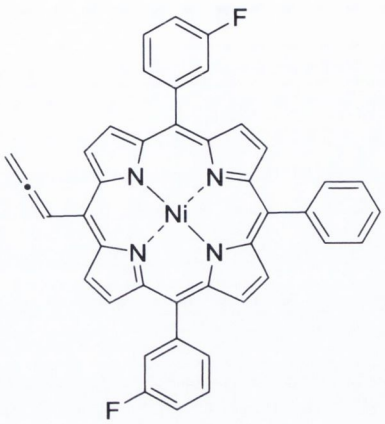
[5,15-*Bis*(4-methoxyphenyl)-10-phenyl-20-propadienylporphyrinato]nickel(II) (148d)



Synthesised *via* General Procedure 10 from bromoporphyrin **147d** (300 mg, 0.41 mmol), $PdCl_2(PPh_3)_2$ (29 mg, 41 µmol), CuI (23 mg, 123 µmol) and **158** (334 mg, 2.40 mmol) in THF/NEt_3 (50 mL, 4:1, v/v). The title compound was obtained from crude **159d** with $Pd_2(dba)_3$ (36 mg, 41 µmol) and $P(C_6F_5)_3$ (85 mg, 0.16 mmol) in $CHCl_3$ (7 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 4:1, v/v) and recrystallised ($CHCl_3/CH_3OH$) to yield purple crystals (189 mg, 0.27 mmol, 68 %). M.p.: 246-248 °C; R_f = 0.28 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 4.03 (s, 6H, OC*H*$_3$), 5.28 (d, $^4J_{H\text{-}H}$ = 6.8 Hz, 2H, allene-C*H*$_2$), 7.19 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, 4H, C_6H_4OMe-*o*-C*H*), 7.63-7.65 (m, 3H, Ph-*o*/*p*-C*H*), 7.87 (d, $^3J_{H\text{-}H}$ = 8.5 Hz, 4H, C_6H_4OMe-*m*-C*H*), 7.94-7.96 (m, 2H, Ph-*m*-C*H*), 8.27 (t, $^4J_{H\text{-}H}$ = 6.8 Hz, 1H, allene-C*H*), 8.63 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*$_\beta$), 8.67 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*$_\beta$), 8.78 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*$_\beta$), 9.40 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*$_\beta$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 55.5, 76.0, 92.5, 112.4, 118.6, 126.9, 127.7, 128.4, 128.9, 130.6, 132.0, 132.2, 132.6, 133.0, 133.6, 134.6, 140.7, 141.5, 142.2, 142.4, 142.7, 159.4 and 206.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 424 (5.19), 538 nm (4.09); IR (neat): $\tilde{\nu}$ = 2961, 2928, 2831 and 1944 cm^{-1}; HRMS (MALDI) *m/z* calcd. for $C_{43}H_{30}N_4NiO_2$ $[M]^+$: 692.1722, found 692.1722; LRMS (ESI+, 200 V): 692.15 (14 %,

M^+), 603.36 (43 %, M-CH_3NiO), 540.30 (80 %, M-$C_9H_{12}O_2$), 440.23 (100 %, M-$C_{17}H_{16}O_2$), 253.22 (56 %, M-$C_{27}H_{11}NNiO_2$).

[5,15-*Bis*(3-fluorophenyl)-10-phenyl-20-propadienylporphyrinato]nickel(II) (148e)



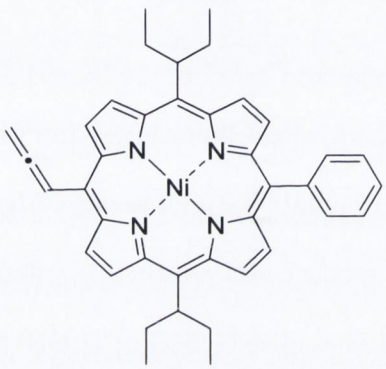
Method 1: Synthesised *via* General Procedure 9 from bromoporphyrin **147e** (50 mg, 70 µmol), $PdCl_2$(dppe) (6 mg, 10 µmol), K_2CO_3 (10 mg, 0.70 mmol) and **146** (0.13 mL, 0.70 mmol) in THF (10 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 5:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (30 mg, 45 µmol, 64 %).

Method 2: Synthesised *via* General Procedure 10 from bromoporphyrin **147e** (200 mg, 0.28 mmol), $PdCl_2(PPh_3)_2$ (20 mg, 28 µmol), CuI (16 mg, 84 µmol) and **158** (234 mg, 1.68 mmol) in THF/NEt_3 (40 mL, 4:1, v/v). The title compound was obtained from crude **159e** with $Pd_2(dba)_3$ (26 mg, 28 µmol) and $P(C_6F_5)_3$ (60 mg, 0.11 mmol) in $CHCl_3$ (5 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 5:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (137 mg, 0.20 mmol, 73 %).

M.p.: 284-285 °C; R_f = 0.79 (*n*-hexane:EtOAc, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 5.30 (d, $^4J_{H\text{-}H}$ = 6.9 Hz, 2H, allene-CH_2), 7.40-7.44 (m, 2H, Ar-C*H*), 7.61-7.76 (m, 9H, Ar-C*H*), 7.96 (m, 2H, Ar-C*H*), 8.27 (t, $^4J_{H\text{-}H}$ = 6.9 Hz, 1H, allene-C*H*), 8.63 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 8.68 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 8.75 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.43 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β); ^{19}F NMR (377 MHz, $CDCl_3$, 25 °C): -114.80 ppm; ^{13}C

NMR (100 MHz, $CDCl_3$, 25 °C): δ = 76.1, 92.4, 114.8, 120.8, 126.9, 129.6, 131.0, 131.9, 132.3, 132.5, 133.6, 140.5, 141.5, 141.7, 142.0, 142.7, 142.8 and 216.1 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 420 (5.18), 536 (4.15), 673 nm (3.34); IR (neat): $\tilde{\nu}$ = 2922, 2852 and 1939 cm^{-1}; HRMS (MALDI) *m/z* calcd. for $C_{41}H_{24}F_2N_4Ni$ $[M]^+$: 668.1323, found 668.1305; LRMS (ESI+, 150 V): 667.21 (7 %, M-H), 571.35 (9 %, M-C_6H_6F), 518.26 (9 %, M-$C_9H_4F_2$), 375.19 (15 %, M-$C_{19}H_{13}F_2N$), 295.12 (15 %, M-$C_{21}H_{11}F_2NNi$), 224.17 (81 %, M-$C_{27}H_{10}F_2NNi$), 215.17 (100 %, M-$C_{28}H_7F_2NNi$), 183.13 (25 %, M-$C_{30}H_{15}F_2NNi$).

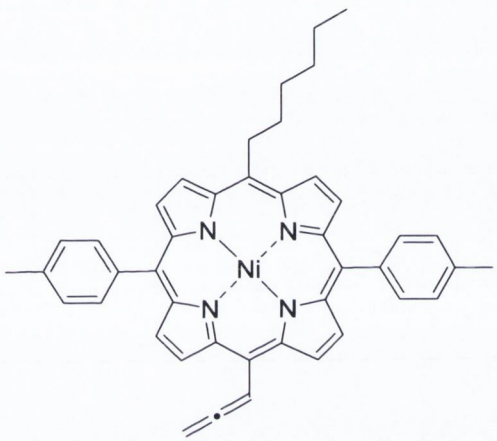
[5,15-*Bis*(1-ethylpropyl)-10-phenyl-20-propadienylporphyrinato]nickel(II) (148f)



Synthesised *via* General Procedure 10 from bromoporphyrin **147f** (265 mg, 0.40 mmol), $PdCl_2(PPh_3)_2$ (29 mg, 40 µmol), CuI (23 mg, 120 µmol) and **158** (334 mg, 2.40 mmol) in THF/NEt_3 (50 mL, 4:1, v/v). The title compound was obtained from crude **159f** with $Pd_2(dba)_3$ (36 mg, 40 µmol) and $P(C_6F_5)_3$ (85 mg, 0.16 mmol) in $CHCl_3$ (7 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 7:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (112 mg, 0.18 mmol, 45 %). M.p.: >300 °C; R_f = 0.39 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.88 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 12H, alkyl-C*H*$_3$), 2.54-2.69 (m, 8H, alkyl-C*H*$_2$), 4.24-4.32 (m, 2H, alkyl-C*H*), 5.25 (d, $^4J_{H\text{-}H}$ = 6.9 Hz, 2H, allene-C*H*$_2$), 7.63-7.66 (m, 3H, Ph-*o*/*p*-C*H*), 7.91-7.93 (m, 2H, Ph-*m*-C*H*), 8.16 (t, $^4J_{H\text{-}H}$ = 6.9 Hz, 1H, allene-C*H*), 8.60 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*$_\beta$), 9.21 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*$_\beta$), 9.32 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*$_\beta$), 9.36 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*$_\beta$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.9, 33.4, 49.3, 76.1, 92.4, 107.9,

117.6, 121.2, 126.8, 127.6, 130.6, 131.1, 132.1, 133.4, 140.6 and 215.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 428 (5.20), 549 (4.14), 595 nm (3.79); IR (neat): $\bar{\nu}$ = 2959, 2922, 2852 and 1938 cm^{-1}; HRMS (MALDI) *m/z* calcd. for $C_{39}H_{38}N_4Ni$ $[M]^+$: 620.245, found 620.2434; LRMS (ESI+, 200 V): 620.25 (4 %, M^+), 504.13 (100 %, M-C_9H_8), 427.95 (93 %, M-$C_{10}H_{14}Ni$), 253.64 (5 %, M-$C_{23}H_{19}NNi$).

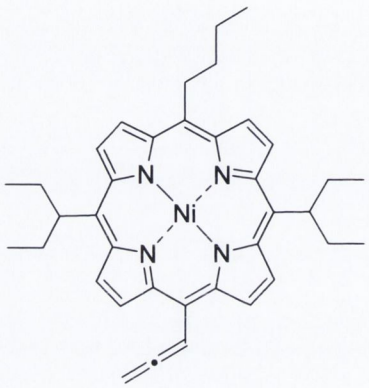
[5-(*n*-Hexyl)-10,20-*bis*(4-methylphenyl)-15-propadienylporphyrinato]nickel(II) (148g)



Synthesised *via* General Procedure 10 from bromoporphyrin **147g** (200 mg, 0.28 mmol), $PdCl_2(PPh_3)_2$ (20 mg, 28 µmol), CuI (16 mg, 85 µmol) and **158** (234 mg, 1.68 mmol) in THF/NEt_3 (20 mL, 4:1, v/v). The title compound was obtained from crude **159g** with $Pd_2(dba)_3$ (26 mg, 28 µmol) and $P(C_6F_5)_3$ (60 mg, 0.11 mmol) in $CHCl_3$ (5 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 8:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (105 mg, 0.15 mmol, 53 %). M.p.: > 300 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.92 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 3H, hexyl-C*H*$_3$), 1.28-1.40 (m, 6H, hexyl-C*H*$_2$), 2.22-2.28 (m, 2H, hexyl-C*H*$_2$), 2.64 (s, 6H, tolyl-C*H*$_3$), 4.49-4.54 (m, 2H, hexyl-C*H*$_2$), 5.25 (d, $^4J_{H\text{-}H}$ = 6.9 Hz, 2H, allene-C*H*$_2$), 7.46 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 4H, tolyl-*o*-C*H*), 7.83 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 4H, tolyl-*m*-C*H*), 8.21 (t, $^4J_{H\text{-}H}$ = 6.9 Hz, 1H, allene-C*H*), 8.71 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*β), 8.73 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*β), 9.21 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*β), 9.35 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, *H*β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.1, 21.5, 22.6, 29.7, 30.0, 31.7, 37.3, 76.0, 92.4, 118.3, 125.3, 128.2, 129.0, 130.4, 132.4,

132.6, 133.5, 137.3, 137.7, 141.3, 141.8, 142.1 and 215.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 424 (5.15), 541 (4.01), 587 nm (3.47); IR (neat): $\bar{\nu}$ = 2858, 2919, 2850 and 1939 cm^{-1}; HRMS (MALDI) *m/z* calcd. for $C_{43}H_{38}N_4Ni$ $[M]^+$: 668.2450, found 668.2465.

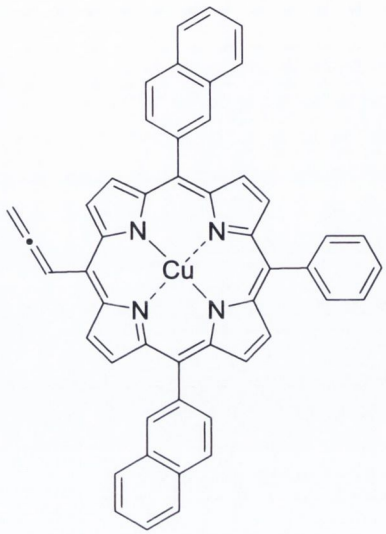
[5-(*n*-Butyl)-10,20-*bis*(1-ethylpropyl)-15-propadienylporphyrinato]nickel(II) (148h)



Synthesised *via* General Procedure 10 from bromoporphyrin **147h** (180 mg, 0.28 mmol), $PdCl_2(PPh_3)_2$ (20 mg, 28 µmol), CuI (16 mg, 84 µmol) and **158** (234 mg, 1.68 mmol) in THF/NEt_3 (40 mL, 4:1, v/v). The title compound was obtained from crude **159h** with $Pd_2(dba)_3$ (26 mg, 28 µmol) and $P(C_6F_5)_3$ (60 mg, 0.11 mmol) in $CHCl_3$ (5 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 8:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (74 mg, 0.12 mmol, 44 %). M.p.: 162-164 °C; R_f = 0.52 (*n*-hexane:CH_2Cl_2, 4:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.88 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 12H, alkyl-C*H*$_3$), 0.99 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 3H, butyl-C*H*$_3$), 1.51 (m, 2H, butyl-C*H*$_2$), 2.17 (m, 2H, butyl-C*H*$_2$), 2.53-2.68 (m, 8H, alkyl-C*H*$_2$), 4.23 (m, 2H, alkyl-C*H*), 4.40 (t, $^3J_{H\text{-}H}$ = 8.0 Hz, 2H, butyl-C*H*$_2$), 5.22 (d, $^4J_{H\text{-}H}$ = 6.9 Hz, 2H, allene-C*H*$_2$), 8.11 (t, $^4J_{H\text{-}H}$ = 6.9 Hz, 1H, allene-C*H*), 9.14 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.26 (m, 4H, H_β), 9.30 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.0, 23.3, 33.4, 33.5, 39.1, 49.3, 76.1, 92.4, 107.2, 117.7, 120.7, 129.6, 130.6, 130.8, 131.1, 139.3, 140.1, 140.6, 141.3 and 215.8 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 429 (5.24), 552 (4.17), 594 nm (3.82); IR (neat): $\bar{\nu}$ = 2957, 2924, 2867, 1938 and 1641 cm^{-1}; HRMS (MALDI) *m/z* calcd.

for $C_{37}H_{42}N_4Ni$ $[M]^+$: 600.2763, found 600.2755; LRMS (ESI+, 200 V): 600.35 (12 %, M^+), 440.13 (100 %, M-$C_{11}H_{28}$), 253.16 (10 %, M-$C_{21}H_{23}NNi$).

[5,15-*Bis*(2-naphthyl)-10-phenyl-20-propadienylporphyrinato]copper(II) (148k)



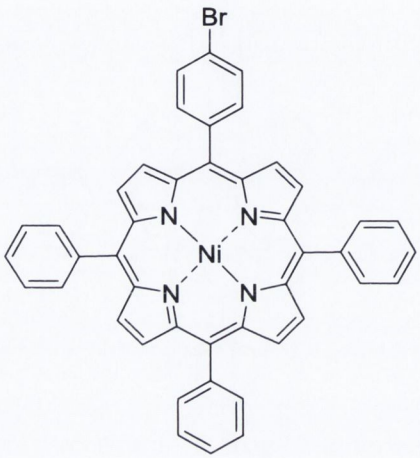
Synthesised *via* General Procedure 10 from bromoporphyrin **147k** (233 mg, 0.30 mmol), $PdCl_2(PPh_3)_2$ (21 mg, 30 μmol), CuI (17 mg, 90 μmol) and **158** (208 mg, 1.50 mmol) in THF/NEt_3 (40 mL, 4:1, v/v). The title compound was obtained from crude **159k** with $Pd_2(dba)_3$ (27 mg, 30 μmol) and $P(C_6F_5)_3$ (64 mg, 0.12 mmol) in $CHCl_3$ (5 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 6:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield red/purple crystals (104 mg, 0.14 mmol, 47 %). M.p.: >300 °C; R_f = 0.65 (*n*-hexane:EtOAc, 3:1, v/v); λ_{max} (log ε) = 427 (5.95), 549 (4.76), 585 nm (4.31); HRMS (MALDI) *m/z* calcd. for $C_{49}H_{30}N_4Cu$ $[M]^+$: 737.1766, found 737.1743; LRMS (ESI+, 150 V): 737.17 (16 %, M^+), 601.47 (20 %, M-C_6HCu), 462.04 (37 %, M-$C_{17}H_8Cu$), 387.85 (65 %, M-$C_{23}H_{11}Cu$), 253.61 (100 %, M-$C_{33}H_{11}CuN$).

General Procedure 11 (Introduction of 4-bromophenyl residue):

The appropriate bromoporphyrin was dissolved in dry THF in an oven-dried Schlenk flask and subjected to three freeze-pump-thaw cycles before being released to argon. 4-bromophenylboronic acid (5 eq.), $PdCl_2(PPh_3)_2$ (20 mol %), triphenylarsine (40 mol %) and

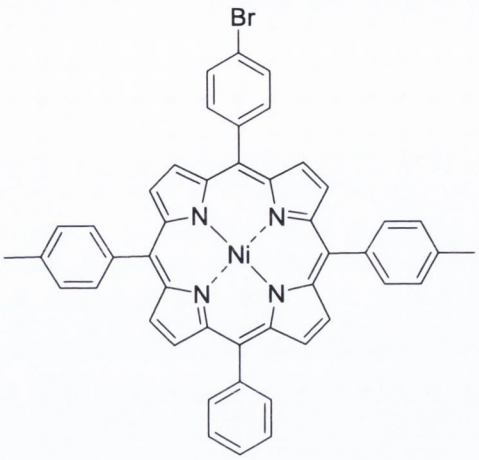
K_3PO_4 (5 eq.) were added and the solution was heated to 60 °C for 18 h. The product was filtered through silica gel using CH_2Cl_2 as eluent and then purified by column chromatography (silica gel) and recrystallised ($CHCl_3/CH_3OH$).

[5-(4-Bromophenyl)-10,15,20-triphenylporphyrinato]nickel(II) (162a)



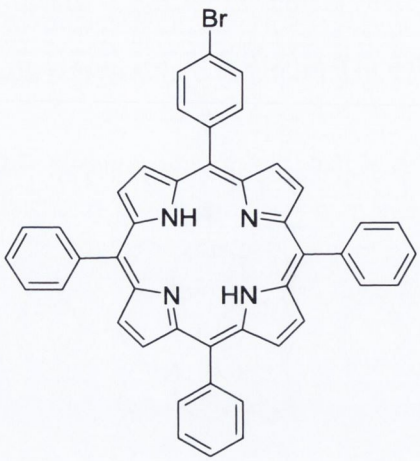
Synthesised *via* General Procedure 11 from **147a** (200 mg, 0.33 mmol), 4-bromophenylboronic acid (330 mg, 1.62 mmol), $PdCl_2(PPh_3)_2$ (46 mg, 66 µmol), $AsPh_3$ (40 mg, 0.13 mmol) and K_3PO_4 (346 mg, 1.62 mmol) in THF (50 mL). The product was purified by column chromatography on silica gel using *n*-hexane:CH_2Cl_2 (6:1, v/v) as eluent followed by crystallisation from $CHCl_3/CH_3OH$ to yield purple crystals (208 mg, 0.28 mmol, 84 %). M.p.: >300 °C; R_f = 0.42 (*n*-hexane:CH_2Cl_2, 5:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 7.66-7.73 (m, 9H, Ph-*o/p*-C*H*), 7.81 (d, $^3J_{H\text{-}H}$ = 8.3 Hz, 2H, *o*-C_6H_4Br), 7.89 (d, $^3J_{H\text{-}H}$ = 8.3 Hz, 2H, *m*-C_6H_4Br), 8.01-8.03 (m, 6H, Ph-*o*-C*H*), 8.73 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 8.77-8.78 ppm (m, 6H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 117.3, 119.1, 119.2, 122.4, 126.9, 127.3, 127.7, 127.8, 128.5, 130.1, 131.8, 131.9, 132.2, 132.3, 132.4, 133.7, 134.6, 135.1, 139.9, 140.8, 142.3, 142.7 and 142.8 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 414 (5.40), 528 nm (4.27); HRMS (MALDI) *m/z* calcd. for $C_{44}H_{27}BrN_4Ni$ $[M]^+$: 748.0773, found 748.0756.

[5-(4-Bromophenyl)-10,20-*bis*(4-methylphenyl)-15-phenylporphyrinato]nickel(II) (162b)



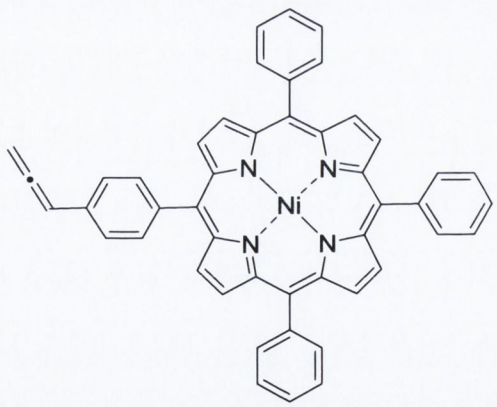
Synthesised *via* General Procedure 11 from **147b** (230 mg, 0.33 mmol), 4-bromophenylboronic acid (330 mg, 1.62 mmol), $PdCl_2(PPh_3)_2$ (46 mg, 66 μmol), $AsPh_3$ (40 mg, 0.13 mmol) and K_3PO_4 (346 mg, 1.62 mmol) in THF (50 mL). The product was purified by column chromatography on silica gel using *n*-hexane:CH_2Cl_2 (6:1, v/v) as eluent followed by crystallisation from $CHCl_3/CH_3OH$ to yield purple crystals (213 mg, 0.27 mmol, 83 %); M.p.: >300 °C; R_f = 0.45 (*n*-hexane:CH_2Cl_2, 4:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.64 (s, 6H, tolyl-C*H*$_3$), 7.47 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 4H, tolyl-*o*-C*H*), 7.66-7.67 (m, 3H, Ph-*o/p*-C*H*), 7.79 (d, $^3J_{H\text{-}H}$ = 8.3 Hz, 2H, *o*-C$_6$*H*$_4$Br), 7.86-7.89 (m, 6H, tolyl-*m*-C*H*, *m*-C$_6$*H*$_4$Br), 7.99-8.02 (m, 2H, Ph-*m*-C*H*), 8.70 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, *H*β), 8.73 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, *H*β), 8.78 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, *H*β), 8.79 ppm (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, *H*β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.5, 117.2, 119.0, 119.2, 121.9, 122.3, 126.8, 126.9, 127.3, 127.6, 128.4, 128.5, 130.0, 131.6, 131.9, 132.0, 132.2, 132.3, 132.4, 133.6, 133.7, 135.1, 137.5, 137.8, 138.8, 140.0, 140.9, 142.2, 142.7, 142.8 and 142.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 416 (5.23), 529 (4.09) nm; HRMS (MALDI) *m/z* calcd. for $C_{46}H_{31}BrN_4Ni$ $[M]^+$: 776.1086, found 776.1096.

5-(4-Bromophenyl)-10,15,20-triphenylporphyrin (162c)[364,365]



Synthesised *via* General Procedure 11 from **154a** (200 mg, 0.31 mmol), 4-bromophenylboronic acid (310 mg, 1.54 mmol), $PdCl_2(PPh_3)_2$ (40 mg, 60 μmol), $AsPh_3$ (30 mg, 0.10 mmol) and K_3PO_4 (328 mg, 1.54 mmol) in THF (50 mL). The product was purified by column chromatography on silica gel using *n*-hexane:CH_2Cl_2 (4:1, v/v) as eluent followed by crystallisation from $CHCl_3/CH_3OH$ to yield purple crystals (173 mg, 0.24 mmol, 78 %). The isolated product had analytical data consistent with the literature.[364,365]

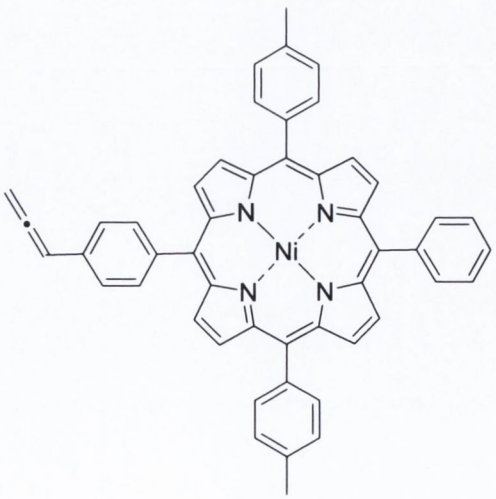
[5,10,15-Triphenyl-20-(4-propadienylphenyl)porphyrinato]nickel(II) (164a)



Synthesised *via* a modified General Procedure 10 from **162a** (400 mg, 0.53 mmol), $PdCl_2(PPh_3)_2$ (37 mg, 53 μmol), CuI (40 mg, 0.21 mmol), PPh_3 (55 mg, 0.21 mmol) and **158** (443 mg, 3.20 mmol) in DMF/Et_2NH (40 mL, 4:1, v/v). Intermediate **163a** was extracted with CH_2Cl_2 (300 mL) and washed with water (5 × 150 mL) to remove residual DMF before

filtration through silica gel using EtOAc as eluent. The title compound was obtained from crude **163a** with $Pd_2(dba)_3$ (48 mg, 53 μmol) and $P(C_6F_5)_3$ (112 mg, 0.21 mmol) in $CHCl_3$ (8 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 4:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (252 mg, 0.36 mmol, 67 %). M.p.: >300 °C; R_f = 0.55 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 5.25 (d, $^4J_{H\text{-}H}$ = 6.8 Hz, 2H, allene–C*H*$_2$), 6.38 (t, $^4J_{H\text{-}H}$ = 6.8 Hz, 1H, allene–C*H*), 7.55 (d, $^3J_{H\text{-}H}$ = 8.0 Hz, 2H, *o*-C$_6$*H*$_4$), 7.59-7.64 (m, 9H, Ph-*m*/*p*-C*H*), 7.90 (d, $^3J_{H\text{-}H}$ = 8.0 Hz, 2H, *m*-C$_6$*H*$_4$), 7.94-7.97 (m, 6H, Ph-*o*–C*H*), 8.69-8.73 ppm (m, 8H, *H*$_\beta$); ^{13}C NMR (150 MHz, $CDCl_3$): 79.1, 93.9, 119.0, 125.2, 126.9, 127.7, 132.1, 132.2, 133.5, 133.7, 134.0, 139.5, 140.9, 142.6, 142.7 and 210.2 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 416 (5.39), 529 nm (4.30); IR (neat): $\tilde{\nu}$ = 2924, 2850 and 1939 cm^{-1}; HRMS (MALDI) *m/z* calcd, for $C_{47}H_{30}N_4Ni$ $[M]^+$: 708.1824, found 708.1811; LRMS (ESI+, 200 V): 708.21 (23 %, M^+), 631.15 (52 %, M-C_6H_5), 591.36 (100 %, M-C_9H_9), 515.17 (81 %, M-$C_{15}H_{13}$), 412.88 (43 %, M-$C_{23}H_{19}$), 253.66 (46 %, M-$C_{31}H_{11}NNi$).

[5,15-*Bis*(4-methylphenyl)-10-phenyl-20-(4-propadienylphenyl)porphyrinato] nickel(II) (164b)



Synthesised *via* a modified General Procedure 10 from **162b** (300 mg, 0.39 mmol), $PdCl_2(PPh_3)_2$ (27 mg, 39 μmol), CuI (29 mg, 0.15 mmol), PPh_3 (40 mg, 0.15 mmol) and **158**

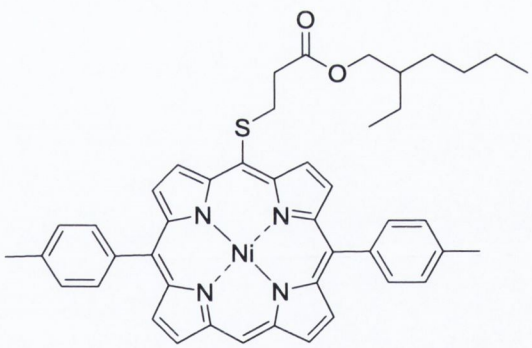
(230 mg, 1.54 mmol) in DMF/Et_2NH (30 mL, 4:1, v/v). Intermediate **163b** was extracted with CH_2Cl_2 (200 mL) and washed with water (5 × 100 mL) to remove residual DMF before filtration through silica gel using EtOAc as eluent. The title compound was obtained from crude **163b** with $Pd_2(dba)_3$ (35 mg, 39 μmol) and $P(C_6F_5)_3$ (80 mg, 0.16 mmol) in $CHCl_3$ (8 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 5:1, v/v) and recrystallised ($CHCl_3$/CH_3OH) to yield purple crystals (207 mg, 0.28 mmol, 72 %). M.p.: >300 °C; R_f = 0.33 (*n*-hexane:CH_2Cl_2, 7:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.63 (s, 6H, tolyl-CH_3), 5.29 (d, $^4J_{H\text{-}H}$ = 6.9 Hz, 2H, allene-CH_2), 6.43 (t, $^4J_{H\text{-}H}$ = 6.9 Hz, 1H, allene-C*H*), 7.46 (d, $^3J_{H\text{-}H}$ = 7.8 Hz, 4H, tolyl-*o*-C*H*), 7.60 (d, $^3J_{H\text{-}H}$ = 8.0 Hz, 2H, *o*-C$_6H_4$), 7.65-7.69 (m, 3H, Ph-*o*/*p*-C*H*), 7.89 (d, $^3J_{H\text{-}H}$ = 7.8 Hz, 4H, tolyl-*m*-C*H*), 7.95 (d, $^3J_{H\text{-}H}$ = 8.0 Hz, 2H, *m*-C$_6H_4$), 7.99-8.01 (m, 2H, Ph-*m*-C*H*), 8.73 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 8.76-8.77 ppm (m, 6H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.5, 79.1, 93.9, 118.6, 118.8, 119.0, 125.2, 126.8, 127.6, 131.9, 132.0, 132.2, 133.6, 134.0, 137.4, 137.9, 139.6, 140.9, 142.6, 142.8 and 210.2 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 417 (5.27), 529 nm (4.13); IR (neat): $\tilde{\nu}$ = 2921, 2854 and 1940 cm^{-1}; HRMS (MALDI) *m/z* calcd. for $C_{49}H_{34}N_4Ni$ $[M]^+$: 736.2137, found 736.2130; LRMS (ESI+, 200 V): 737.25 (100 %, M+H), 645.51 (76 %, M-C_7H_8), 605.38 (63 %, M-$C_{10}H_{11}$), 531.21 (40 %, M-$C_{16}H_{13}$), 440.98 (33 %, M-$C_{23}H_{29}$), 215.53 (71 %, M-$C_{36}H_{17}NNi$).

7.7 Synthesis of sulfur-substituted porphyrins

General Procedure 12 (Synthesis of thiol surrogates):

Bromoporphyrin (1 eq.) was added to a 100 mL oven-dried Schlenk tube and dried under high vacuum for 30 minutes. Anhydrous toluene and *N,N*-diisopropylethylamine were added and the solution was degassed *via* three freeze-pump-thaw cycles. 2-Ethylhexyl-3-mercaptopropanoate **93** (2 eq.), Xantphos (5 mol %) and $Pd_2(dba)_3$ (2.5 mol %) were added and the contents of the flask were heated to 110 °C for 16 h, while monitoring the reaction by TLC analysis. The solution was cooled to room temperature and the solvents were removed *in vacuo*. The crude residue was dissolved in CH_2Cl_2 and filtered through a plug of silica. The solvents were removed and the product was purified by column chromatography (silica gel).

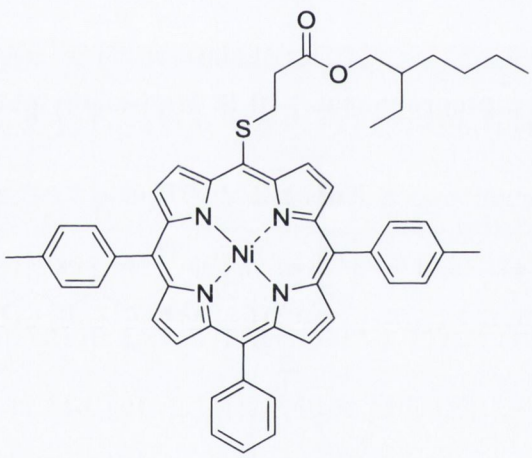
[5-(2-Ethylhexyl-3-mercaptopropanoate)-10,20-*bis*(4-methylphenyl)porphyrinato] nickel(II) (168f)



Synthesised *via* General Procedure 12 from **167c** (200 mg, 0.32 mmol), $Pd_2(dba)_3$ (14 mg, 16 μmol), Xantphos (19 mg, 32 μmol), *N,N*-diisopropylethylamine (0.10 mL) and **93** (0.15 mL, 0.64 mmol) in anhydrous toluene (20 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 2:1, v/v) and recrystallised (CH_2Cl_2/CH_3OH) to yield purple crystals (175 mg, 0.23 mmol, 72 %). M.p.: 138-140 °C; R_f = 0.31 (*n*-hexane:CH_2Cl_2, 5:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.69-0.77 (m, 6H, alkyl-C*H*$_3$), 1.09-1.15 (m, 9H, alkyl-C*H*$_2$/C*H*), 2.22 (t, $^3J_{H\text{-}H}$ = 7.2 Hz, 2H, SC*H*$_2$CH$_2$CO$_2$), 2.66

(s, 6H, tolyl-CH_3), 3.34 (t, $^3J_{H\text{-}H}$ = 7.2 Hz, 2H, SCH_2CH_2CO_2), 3.77-3.79 (m, 2H, CO_2CH_2CH), 7.48 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 4H, tolyl-*o*-C*H*), 7.87 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 4H, tolyl-*m*-C*H*), 8.83-8.86 (m, 4H, H_β), 9.06 (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β), 9.74 ppm (s, 1H, H_{meso}), 9.82 ppm (d, $^3J_{H\text{-}H}$ = 4.9 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 10.8, 13.9, 21.5, 22.8, 23.5, 28.7, 30.1, 34.7, 35.8, 38.5, 66.9, 105.5, 109.5, 118.9, 127.6, 132.3, 132.4, 132.6, 133.2, 133.6, 137.5, 137.6, 142.4, 143.0, 143.2, 146.5 and 171.8 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 413 (5.45), 526 (4.30), 556 nm (3.98); HRMS (MALDI) *m/z* calcd. for $C_{45}H_{60}N_4NiO_2S$ $[M]^+$: 762.2546, found 762.2538.

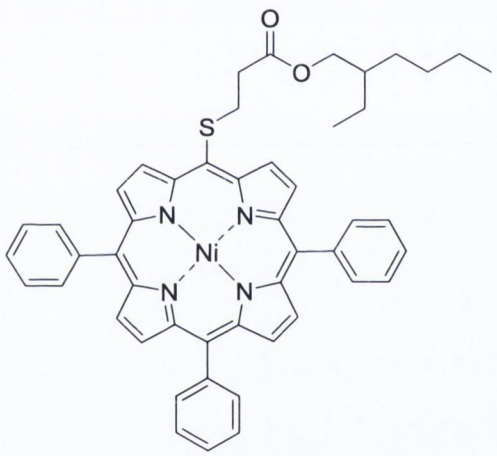
[5-(2-Ethylhexyl-3-mercaptopropanoate)-10,20-*bis*(4-methylphenyl)-15-phenylporphyrinato]nickel(II) (168g)



Synthesised *via* General Procedure 12 from **147b** (250 mg, 0.36 mmol), $Pd_2(dba)_3$ (16 mg, 18 μmol), Xantphos (21 mg, 36 μmol), *N,N*-diisopropylethylamine (0.10 mL) and **93** (0.16 mL, 0.72 mmol) in anhydrous toluene (20 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 3:1, v/v) and recrystallised (CH_2Cl_2/CH_3OH) to yield purple crystals (190 mg, 0.23 mmol, 63 %). M.p.: 154-156 °C; R_f = 0.50 (*n*-hexane:CH_2Cl_2, 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.72-0.80 (m, 6H, alkyl-CH_3), 1.11-1.30 (m, 9H, alkyl-CH_2/C*H*), 2.21 (t, $^3J_{H\text{-}H}$ = 7.2 Hz, 2H, SCH_2CH_2CO_2), 2.65 (s, 6H, tolyl-CH_3), 3.32 (t, $^3J_{H\text{-}H}$ = 7.2 Hz, 2H, SCH_2CH_2CO_2), 3.80-3.82 (m, 2H, CO_2CH_2CH), 7.47 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 4H, tolyl-*o*-C*H*), 7.64-7.67 (m, 3H, Ph-*o*/*p*-C*H*), 7.87

(d, $^{3}J_{H\text{-}H}$ = 7.7 Hz, 4H, tolyl-*m*-C*H*), 7.96-7.99 (m, 2H, Ph-*m*-C*H*), 8.69-8.73 (m, 4H, H_{β}), 8.83 (d, $^{3}J_{H\text{-}H}$ = 4.9 Hz, 2H, H_{β}), 9.78 ppm (d, $^{3}J_{H\text{-}H}$ = 4.9 Hz, 2H, H_{β}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 10.8, 13.9, 21.5, 22.8, 23.5, 28.8, 30.2, 34.7, 35.6, 38.5, 66.9, 108.9, 119.3, 120.0, 126.9, 127.6, 127.7, 127.8, 132.2, 132.4, 132.5, 133.3, 133.5, 133.6, 137.5, 140.6, 142.3, 143.0, 146.7 and 171.8 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 419 (5.39), 535 (4.27), 565 nm (3.88); HRMS (MALDI) *m/z* calcd. for $C_{51}H_{48}N_4NiO_2S$ $[M]^+$: 838.2851, found 838.2833.

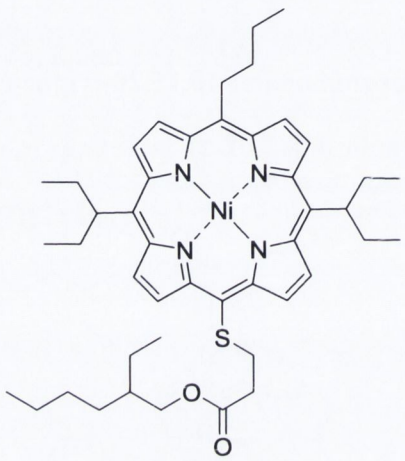
[5-(2-Ethylhexyl-3-mercaptopropanoate)-10,15,20-triphenylporphyrinato]nickel(II) (168h)



Synthesised *via* General Procedure 12 from **147a** (200 mg, 0.30 mmol), $Pd_2(dba)_3$ (14 mg, 15 µmol), Xantphos (18 mg, 30 µmol), *N,N*-diisopropylethylamine (0.10 mL) and **93** (0.14 mL, 0.60 mmol) in anhydrous toluene (20 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 3:1, v/v) and recrystallised (CH_2Cl_2/CH_3OH) to yield purple crystals (165 mg, 0.20 mmol, 68 %). M.p.: 166-167 °C; R_f = 0.44 (*n*-hexane:CH_2Cl_2, 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.69-0.77 (m, 6H, alkyl-C*H*$_3$), 1.11-1.33 (m, 9H, alkyl-C*H*$_2$/C*H*), 2.20 (t, $^{3}J_{H\text{-}H}$ = 7.2 Hz, 2H, SC*H*$_2$CH$_2$CO$_2$), 3.30 (t, $^{3}J_{H\text{-}H}$ = 7.2 Hz, 2H, SCH$_2$C*H*$_2$CO$_2$), 3.78-3.82 (m, 2H, CO$_2$C*H*$_2$CH), 7.64-7.67 (m, 9H, Ph-*o/p*-C*H*), 7.96-7.98 (m, 6H, Ph-*m*-C*H*), 8.68-8.69 (m, 4H, H_{β}), 8.79 (d, $^{3}J_{H\text{-}H}$ = 4.9 Hz, 2H, H_{β}), 9.78 ppm (d, $^{3}J_{H\text{-}H}$ = 4.9 Hz, 2H, H_{β}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 10.8,

13.9, 22.8, 23.5, 28.7, 30.1, 34.7, 35.6, 38.5, 66.9, 109.1, 119.2, 120.1, 126.8, 126.9, 127.8, 132.2, 132.5, 132.6, 133.3, 133.5, 133.6, 140.4, 140.5, 142.3, 142.8, 146.7 and 171.8 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 418 (5.42), 534 (4.27), 566 nm (3.84); HRMS (MALDI) *m/z* calcd. for $C_{49}H_{44}N_4NiO_2S$ $[M]^+$: 810.2538, found 810.2545.

[5-(*n*-Butyl)-10,20-*bis*(2-ethylpropyl)-15-(2-ethylhexyl-3-mercaptopropanoate)porphyrinato]nickel(II) (168i)



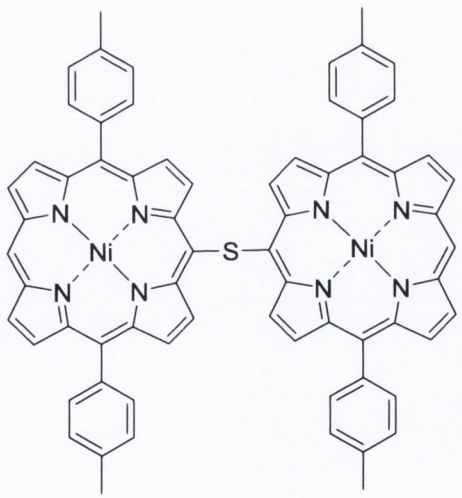
Synthesised *via* General Procedure 12 from **147h** (200 mg, 0.32 mmol), $Pd_2(dba)_3$ (14 mg, 16 μmol), Xantphos (18 mg, 32 μmol), *N,N*-diisopropylethylamine (0.10 mL) and **93** (0.14 mL, 0.62 mmol) in anhydrous toluene (20 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 5:1, v/v) and recrystallised (CH_2Cl_2/CH_3OH) to yield purple crystals (159 mg, 0.21 mmol, 65 %); M.p.: 137-138 °C; R_f = 0.53 (*n*-hexane:CH_2Cl_2, 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.73-0.81 (m, 6H, ethylhexyl-C*H*$_3$), 0.90 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 12H, ethylpropyl-C*H*$_3$), 1.01 (t, $^3J_{H\text{-}H}$ = 7.8 Hz, 3H, butyl-C*H*$_3$), 1.15-1.20 (m, 9H, ethylhexyl-C*H*$_2$/C*H*), 1.50-1.56 (m, 2H, butyl-$CH_2CH_2CH_3$), 2.13-2.19 (m, 4H, S$CH_2CH_2CO_2$/butyl-$CH_2CH_2CH_2CH_3$), 2.59-2.67 (m, 8H, ethylpropyl-C*H*$_2$), 3.16 (t, 2H, $^3J_{H\text{-}H}$ = 7.2 Hz, $SCH_2CH_2CO_2$), 3.82-3.84 (m, 2H, CO_2CH_2CH), 4.24-4.27 (m, 2H, ethylpropyl-C*H*), 4.45 (t, $^3J_{H\text{-}H}$ = 7.6 Hz, 2H, butyl-$CH_2CH_2CH_2CH_3$), 9.21 (d, $^3J_{H\text{-}H}$ = 5.1 Hz, 2H, H_β), 9.31 (d, $^3J_{H\text{-}H}$ = 5.1 Hz, 4H, H_β), 9.63 ppm (d, $^3J_{H\text{-}H}$ = 5.1 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 10.8, 13.9, 22.8, 23.3, 23.5, 28.8, 30.2, 33.5, 33.6, 34.7, 34.9,

38.5, 39.1, 49.3, 66.9, 106.8, 119.0, 121.1, 130.0, 130.8, 131.7, 132.5, 139.9, 141.7, 144.5 and 171.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 423 (5.35), 546 (4.20), 583 nm (3.69); HRMS (MALDI) *m/z* calcd. for $C_{45}H_{60}N_4NiO_2S$ $[M]^+$: 778.3790, found 778.3821.

General Procedure 13 (Synthesis of S-linked porphyrin dimers):

Thiol surrogate porphyrin **168** (1 eq.) was placed in an oven-dried Schlenk flask, charged with argon and dissolved in anhydrous toluene. NaOEt (21 % solution in EtOH, 2 eq.) was added dropwise and the mixture was stirred at room temperature for 4 h. Upon completion, the reaction mixture was poured onto H_2O (100 mL). The organic layer was extracted with CH_2Cl_2 (2 × 100 mL) and washed with H_2O (3 × 50 mL). The combined organic extracts were dried over Na_2SO_4, filtered and solvents removed *in vacuo*. The residue was purified by filtration through a plug of silica gel using CH_2Cl_2/ *n*-hexane as eluent and/or column chromatography (silica gel). The isolated product(s) were recrystallised from CH_2Cl_2/CH_3OH.

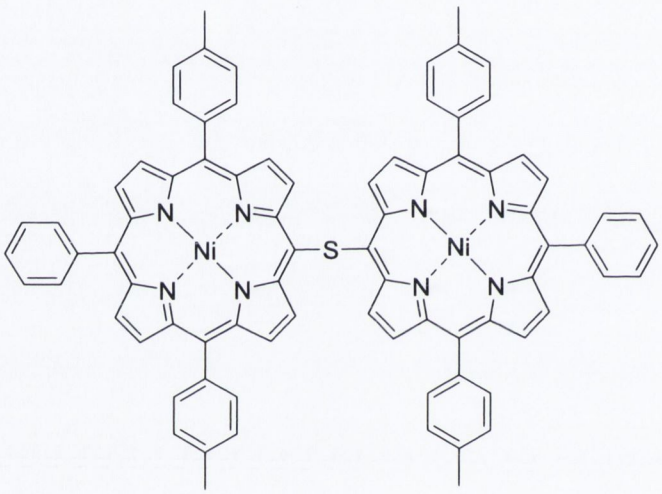
Bis[(10,20-bis(4-methylphenyl)porphyrinato-5-yl)nickel(II)]sulfane (169f)



Synthesised *via* General Procedure 13 from **168f** (50 mg, 65 µmol) and NaOEt (21 % solution, 0.10 mL) in anhydrous toluene (15 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 1:1, v/v) and recrystallised (CH_2Cl_2/*n*-hexane) to yield purple crystals (53 mg, 47 µmol, 72 %); M.p.: >300 °C; R_f = 0.52 (*n*-hexane:CH_2Cl_2,

1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.52 (s, 12H, tolyl-C*H*$_3$), 7.27 (d, $^{3}J_{H\text{-}H}$ = 7.6 Hz, 8H, tolyl-*o*-C*H*), 7.57 (d, $^{3}J_{H\text{-}H}$ = 7.6 Hz, 8H, tolyl-*m*-C*H*), 8.47 (d, $^{3}J_{H\text{-}H}$ = 5.0 Hz, 4H, H_β), 8.56 (d, $^{3}J_{H\text{-}H}$ = 4.7 Hz, 4H, H_β), 8.79 (d, $^{3}J_{H\text{-}H}$ = 4.7 Hz, 4H, H_β), 9.43 ppm (s, 2H, H_{meso}), 9.79 ppm (d, $^{3}J_{H\text{-}H}$ = 5.0 Hz, 4H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.3, 104.9, 115.4, 118.6, 127.4, 131.7, 131.9, 132.3, 133.4, 133.5, 137.2, 137.3, 142.1, 142.7 and 144.8 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 405 (4.92), 452[sh] (4.59), 539 (3.66), 587 nm (3.66); HRMS (MALDI) *m/z* calcd. for $C_{68}H_{46}N_8Ni_2S$ $[M]^+$: 1122.2273, found 1122.2277.

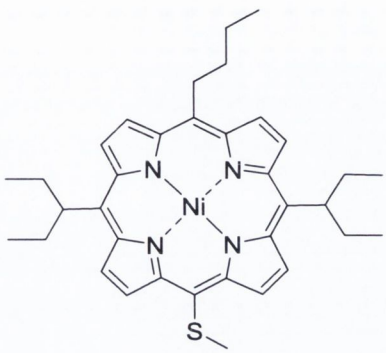
Bis[(10,20-bis(4-methylphenyl)-15-phenylporphyrinato-5-yl)nickel(II)]sulfane (169g)



Synthesised *via* General Procedure 13 from **168g** (50 mg, 60 µmol) and NaOEt (21 % solution, 0.10 mL) in anhydrous toluene (15 mL). The product was purified by column chromatography (silica; *n*-hexane:CH_2Cl_2, 5:2, v/v) and recrystallised (CH_2Cl_2/*n*-hexane) to yield purple crystals (52 mg, 41 µmol, 68 %); M.p.: >300 °C; R_f = 0.27 (*n*-hexane:CH_2Cl_2, 5:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.53 (s, 12H, tolyl-C*H*$_3$), 7.30 (d, $^{3}J_{H\text{-}H}$ = 7.4 Hz, 8H, tolyl-*o*-C*H*), 7.57-7.62 (m, 14H, tolyl-*m*-C*H*/Ph-*o/p*-C*H*), 7.84-7.85 (m, 4*H*, Ph-*m*-C*H*), 8.48-8.51 (m, 12H, H_β), 9.75 ppm (d, $^{3}J_{H\text{-}H}$ = 4.8 Hz, 4H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 21.3, 119.0, 119.5, 126.8, 127.4, 127.6, 131.8, 132.0, 132.1, 133.4, 133.5, 133.6, 137.2, 137.3, 140.4, 141.9, 142.0, 142.7 and 145.1 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log

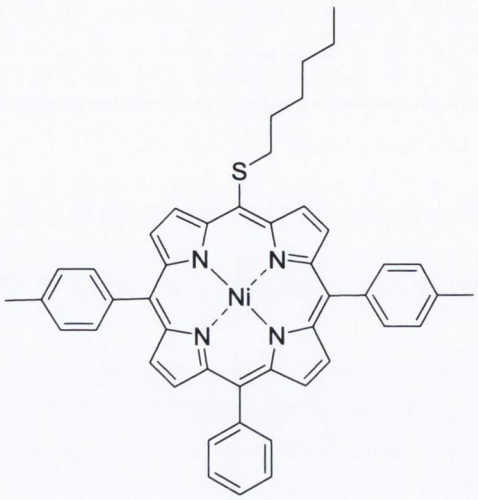
ε) = 409 (5.44), 457[sh] (5.06), 547 (4.55), 596 nm (4.21); HRMS (MALDI) *m/z* calcd. for $C_{80}H_{54}N_8Ni_2S$ $[M]^+$: 1274.2899, found 1274.2947.

[5-(*n*-Butyl)-10,20-bis(2-ethylpropyl)-15-methylthioporphyrinato]nickel(II) (171b)



Thiol surrogate **168i** (200 mg, 0.26 mmol) was dissolved in anhydrous toluene (20 mL) together with iodomethane (0.08 mL, 1.30 mmol). NaOEt (21 % solution, 0.20 mL) was added dropwise and the solution left to stir at room temperature for one hour. The reaction was quenched by adding H_2O (50 mL) and the organic layer was extracted with CH_2Cl_2 (3 × 50 mL). The title compound was obtained *via* recrystallisation (CH_2Cl_2/CH_3OH) to yield purple crystals (154 mg, 0.24 mmol, >95 %); M.p.: 215-216 °C; R_f = 0.63 (*n*-hexane:CH_2Cl_2, 4:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 12H, C*H*$_3$CH$_2$CH), 1.00 (t, $^3J_{H\text{-}H}$ = 7.4 Hz, 3H, butyl-C*H*$_3$), 1.50-1.56 (m, 2H, butyl-CH$_2$C*H*$_2$CH$_3$), 2.15-2.23 (m, 2H, butyl-CH$_2$C*H*$_2$CH$_2$), 2.55-2.69 (m, 8H, CH$_3$C*H*$_2$CH), 2.61 (s, 3H, SC*H*$_3$), 4.22-4.29 (m, 2H, CH$_3$CH$_2$C*H*), 4.44 (t, $^3J_{H\text{-}H}$ = 8.0 Hz, 2H, butyl-C*H*$_2$CH$_2$CH$_2$), 9.19 (d, $^3J_{H\text{-}H}$ = 5.1 Hz, 2H, *H*$_\beta$), 9.29-9.31 (m, 4H, *H*$_\beta$), 9.63 ppm (d, $^3J_{H\text{-}H}$ = 5.1 Hz, 2H, *H*$_\beta$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.9, 23.3, 24.5, 33.4, 33.6, 39.2, 49.3, 109.8, 118.8, 120.9, 129.9, 130.7, 131.7, 132.1, 139.9, 141.7 and 143.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 423 (5.29), 546 (4.14), 585 nm (3.60); HRMS (MALDI) *m/z* calcd. for $C_{35}H_{42}N_4NiS$ $[M]^+$: 608.2484, found 608.2509.

[5-(*n*-Hexylthio)-10,20-bis(4-methylphenyl)-15-phenylporphyrinato]nickel(II) (171c)

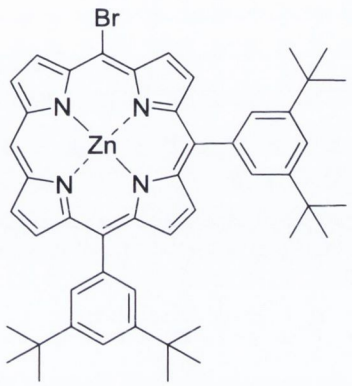


Thiol surrogate **168g** (50 mg, 60 μmol) was dissolved in anhydrous toluene (20 mL) together with 1-bromohexane (0.1 mL, 0.60 mmol). NaOEt (21 % solution, 0.20 mL) was added dropwise and the solution left to stir at room temperature for one hour. The reaction was quenched by adding H_2O (50 mL) and the organic layer was extracted with CH_2Cl_2 (3 × 50 mL). The title compound was obtained *via* recrystallisation (CH_2Cl_2/CH_3OH) to yield purple crystals (43 mg, 58 μmol, >95 %); M.p.: 241-243 °C; R_f = 0.54 (*n*-hexane:CH_2Cl_2, 4:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.72 (t, $^3J_{H\text{-}H}$ = 7.2 Hz, 3H, hexyl-C*H*$_3$), 1.02-1.04 (m, 2H, $CH_2CH_2CH_3$), 1.08-1.12 (m, 2H, $CH_2CH_2CH_3$), 1.26-1.32 (m, 4H, hexyl-CH_2), 2.64 (s, 6H, tolyl-C*H*$_3$), 3.07 (t, $^3J_{H\text{-}H}$ = 7.0 Hz, 2H, SCH_2CH_2), 7.48 (d, $^3J_{H\text{-}H}$ = 7.4 Hz, 4H, tolyl-*o*-C*H*), 7.64-7.67 (m, 3H, Ph-*o*/*p*-C*H*), 7.87 (d, $^3J_{H\text{-}H}$ = 7.7 Hz, 4H, tolyl-*m*-C*H*), 7.96-7.98 (m, 2H, Ph-*m*-C*H*), 8.67-8.71 (m, 4H, H_β), 8.82 (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β), 9.80 ppm (d, $^3J_{H\text{-}H}$ = 5.0 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.9, 21.5, 22.4, 28.2, 29.8, 31.2, 41.5, 119.1, 126.9, 127.3, 127.6, 127.7, 127.9, 131.6, 132.1, 132.3, 132.6, 133.0, 133.2, 133.6, 137.5, 137.6, 140.7, 142.2, 142.8, 142.9 and 146.7 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 420 (5.23), 536 (4.15), 569 nm (3.77); HRMS (MALDI) *m/z* calcd. for $C_{46}H_{40}N_4NiS$ $[M]^+$: 738.2327, found 738.2364.

7.8 Synthesis of 5,10-substituted porphyrins

2,5-Bis(hydroxymethyl)pyrrole **176**,[366] tripyrrane **177**,[160] and 5,10-bis(3,5-di-*tert*-butylphenyl)porphyrin **178a**[367] were all synthesised *via* standard procedures and had analytical data consistent with that reported in the literature.

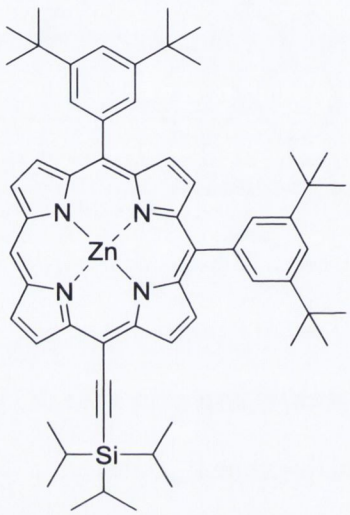
[5-Bromo-10,15-bis(3,5-di-*tert*-butylphenyl)porphyrinato]zinc(II) (179)



5,10-Bis(3,5-di-*tert*-butylphenyl)porphyrin **178a** (425 mg, 0.64 mmol) was dissolved in $CHCl_3$ (150 mL), purged with argon and cooled to 0 °C. Pyridine (0.50 mL) and NBS (100 mg, 0.58 mmol) were added and the solution stirred at 0 °C for one hour. Acetone (5 mL) was added to quench the reaction, the solvents were removed under vacuum and the product was purified by column chromatography (silica gel) using toluene/*n*-hexane (1:3, v/v) as eluent. The resultant monobromoporphyrin[368] (0.35 g, 0.46 mmol, 72 %) was dissolved in $CHCl_3$ (100 mL) at room temperature. Zinc(II) acetate (0.30 g, 1.38 mmol) was dissolved in methanol (5 mL) and added to the reaction. The reaction progress was monitored by TLC and, once complete, the reaction mixture was filtered through a plug of silica using CH_2Cl_2 as eluent. Removal of solvents and recrystallisation from $CHCl_3/CH_3OH$ gave purple crystals (373 mg, 0.45 mmol, 98 %). M.p.: >300 °C; R_f = 0.30 (*n*-hexane:CH_2Cl_2, 2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.55 (s, 36H, C*H*$_3$), 7.82 (s, 2H, Ar-*p*-C*H*), 8.09 (s, 4H, Ar-*o*-C*H*), 9.00-9.03 (m, 2H, *H*β), 9.04-9.07 (m, 2H, *H*β), 9.14 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, *H*β), 9.25 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, *H*β), 9.61 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, *H*β), 9.72 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, *H*β), 9.86 ppm (s, 1H, *H*$_{meso}$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ =

31.7, 35.0, 103.3, 105.7, 120.9, 123.5, 129.7, 131.8, 132.3, 132.5, 132.6, 132.8, 133.2, 133.5, 141.5, 141.6, 148.6, 148.7, 149.2, 149.3, 149.7, 149.8, 150.3, 150.4, 150.7 and 150.8 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 417 (5.46), 547 (4.04), 583 nm (3.30); HRMS (MALDI) *m/z* calcd. for $C_{48}H_{51}BrN_4Zn$ $[M]^+$: 826.2589, found 826.2562.

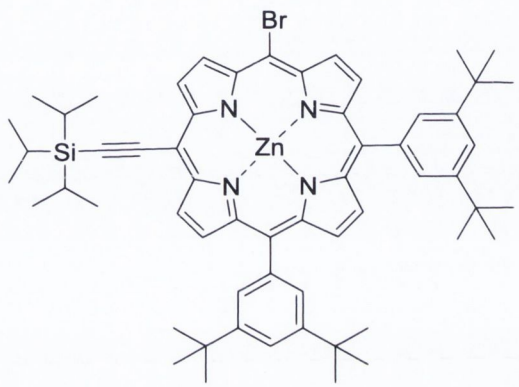
[5,10-Bis(3,5-di-*tert*-butylphenyl)-15-(triisopropylsilylethynyl)porphyrinato]zinc(II) (180)



Bromoporphyrin **179** (0.34 g, 0.41 mmol) was dissolved in anhydrous THF (30 mL) and NEt_3 (5 mL) in an oven-dried Schlenk flask and subjected to three freeze-pump-thaw cycles. Triisopropylsilylacetylene (0.27 mL, 1.23 mmol), $PdCl_2(PPh_3)_2$ (58 mg, 82 µmol) and CuI (26 mg, 0.14 mmol) were added and the solution was heated to reflux for 16 h. The solvent was removed under vacuum and the product was purified by column chromatography (silica gel) using CH_2Cl_2:*n*-hexane (1:3, v/v) as eluent. Recrystallisation from $CHCl_3/CH_3OH$ gave purple crystals (280 mg, 0.30 mmol, 73 %). M.p.: 203-204 °C; R_f = 0.36 (*n*-hexane:CH_2Cl_2, 2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.45-1.48 (m, 21H, SiC*H*(CH_3)$_3$), 1.53 (s, 36H, CH_3), 7.80 (s, 2H, Ar-*p*-C*H*), 8.05-8.06 (m, 4H, Ar-*o*-C*H*), 8.94-8.98 (m, 2H, H_β), 9.05-9.08 (m, 2H, H_β), 9.32 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, H_β), 9.42 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, H_β), 9.84 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, H_β), 9.91 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, H_β), 10.18 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 11.9, 19.2, 31.7, 35.0, 97.5,

99.5, 106.5, 109.4, 120.9, 121.0, 123.8, 129.4, 129.6, 130.8, 131.4, 131.6, 132.1, 132.4, 132.5, 133.2, 133.3, 141.4, 141.5, 148.5, 148.6, 149.6, 149.8, 150.0, 150.1, 150.3, 152.6 and 152.7 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 426 (5.78), 557 (4.29), 595 nm (4.21); HRMS (MALDI) *m/z* calcd. for $C_{59}H_{72}N_4SiZn$ $[M]^+$: 928.4818, found 928.4825.

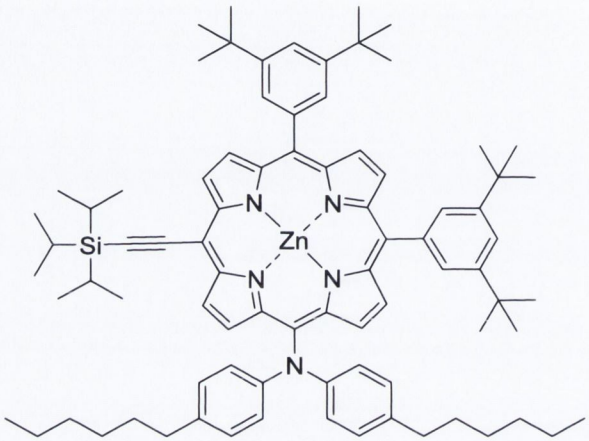
[5-Bromo-10,15-bis(3,5-di-*tert*-butylphenyl)-20-(triisopropylsilylethynyl) porphyrinato]zinc(II) (181)



Porphyrin **180** (200 mg, 0.22 mmol) was dissolved in $CHCl_3$ (150 mL). Pyridine (3 mL) and NBS (85 mg, 0.44 mmol) were added and the solution stirred at room temperature until TLC analyses indicated complete consumption of the starting material. The solvents were removed under vacuum and the product was purified by column chromatography (silica gel) using CH_2Cl_2:*n*-hexane (1:3, v/v) as eluent to give a purple solid (211 mg, 0.21 mmol, 95 %). M.p.: 178-180 °C; R_f = 0.41 (*n*-hexane:CH_2Cl_2, 2:1, v/v); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 1.46-1.49 (m, 21H, SiC*H*(CH_3)$_3$), 1.55 (s, 36H, CH_3), 7.81 (m, 2H, Ar-*p*-C*H*), 8.02-8.03 (m, 4H, Ar-*o*-C*H*), 8.87-8.89 (m, 2H, H_β), 8.97 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 8.98 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.71 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.76 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.81 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.86 ppm (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 11.9. 19.1, 31.7, 35.0, 97.8, 100.3, 105.0, 109.4, 120.9, 124.0, 124.8, 129.3, 129.6, 131.1, 132.1, 132.4, 132.7, 133.5, 133.6, 141.4, 149.6, 149.2, 149.7, 150.4, 150.5, 151.2, 152.9 and 153.0 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 434 (5.56), 567 (4.13),

609 nm (4.06); HRMS (MALDI) *m/z* calcd. for $C_{59}H_{71}BrN_4SiZn$ $[M]^+$: 1006.3923, found 1006.3917.

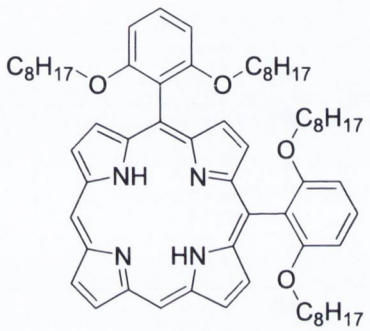
[5,10-Bis(3,5-di-*tert*-butylphenyl)-15-(bis(4-hexylphenyl)amino)-20-(triisopropylsilylethynyl)porphyrinato]zinc(II) (182)



Porphyrin **181** (330 mg, 0.33 mmol) was dissolved in dry THF (30 mL) and subjected to three freeze-pump-thaw cycles. Bis(4-hexylphenyl)amine (440 mg, 1.32 mmol), NaH (60 % dispersion, 50 mg, 1.32 mmol), $Pd(OAc)_2$ (15 mg, 66 µmol) and DPEPhos (54 mg, 0.10 mmol) were added and the solution was heated to reflux for 16 h. The solvent was removed under vacuum and the product was purified by column chromatography (silica gel) using CH_2Cl_2:*n*-hexane (1:4, v/v) as eluent. The first porphyrin containing fraction contained the title compound which was recrystallised from $CHCl_3/CH_3OH$ to give purple crystals (227 mg, 0.18 mmol, 56 %). The second porphyrin containing fraction contained debrominated starting material **180** (~30 %). M.p.: 192-193 °C; R_f = 0.40 (*n*-hexane:CH_2Cl_2, 3:1, v/v); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C): δ = 0.87 (t, $^3J_{H\text{-}H}$ = 6.8 Hz, 6H, hexyl-C*H*$_3$), 1.28-1.33 (m, 16H, hexyl-C*H*$_2$), 1.44-1.48 (m, 21H, SiC*H*(C*H*$_3$)$_3$), 1.52 (s, 18H, C*H*$_3$), 1.56 (s, 18H, C*H*$_3$), 2.51 (t, $^3J_{H\text{-}H}$ = 7.7 Hz, 4H, hexyl-C*H*$_2$), 7.01 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 4H, N-Ar-C*H*), 7.25 (d, $^3J_{H\text{-}H}$ = 8.7 Hz, 4H, N-Ar-C*H*), 7.78 (s, 1H, Ar-*p*-C*H*), 7.81 (s, 1H, Ar-*p*-C*H*), 8.01 (s, 2H, Ar-*o*-C*H*), 8.04 (s, 2H, Ar-*o*-C*H*), 8.83 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 8.85-8.87 (m, 2H, H_β), 8.98 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.30 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.40 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β),

9.73 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.75 ppm (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 11.9, 14.0, 19.1, 22.6, 29.0, 31.4, 31.7, 31.8, 35.0, 35.2, 97.5, 99.9, 109.2, 120.9, 121.9, 123.2, 123.9, 124.0, 128.9, 129.3, 130.8, 131.4, 132.0, 132.1, 132.4, 133.7, 134.9, 141.3, 148.6, 149.4, 150.2, 150.4, 150.7, 151.8, 152.4, 152.9 and 153.0 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 427 (5.37), 576 (4.05), 625 nm (4.05); HRMS (MALDI) *m/z* calcd. for $C_{83}H_{105}N_5SiZn$ $[M]^+$: 1263.7431, found 1263.7456.

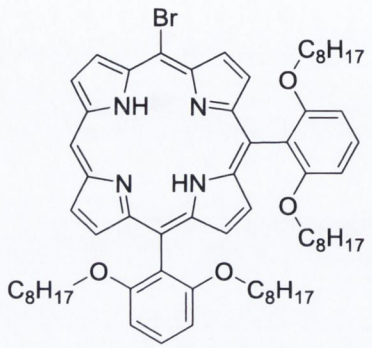
5,10-Bis(2,6-dioctyloxyphenyl)porphyrin (178b)



Tripyrrane **177** (0.92 g, 4.12 mmol), 2,6-dioctoxybenzaldehyde (2.96 g, 8.24 mmol) and pyrrole (0.28 mL, 4.12 mmol) were dissolved in anhydrous CH_2Cl_2 (2 L) and purged with argon for 30 minutes. TFA (1.50 mL, 20 mmol) was added and the solution was stirred with shielding from light for 18 h. DDQ (3.60 g, 15.86 mmol) was added followed after 30 minutes by NEt_3 (5 mL). The crude residue was filtered through a plug of silica gel using CH_2Cl_2 as eluent. Purification by column chromatography (silica gel; *n*-hexane:CH_2Cl_2, 2:1, v/v) and removal of solvents followed by recrystallisation ($CHCl_3$/CH_3OH) gave the title compound as purple crystals (256 mg, 0.26 mmol, 6.3 %). M.p 75-77 °C; R_f = 0.31 (*n*-hexane:CH_2Cl_2, 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = -3.22 (s, 2H, N*H*), 0.38-0.59 (m, 44H, CH_2/CH_3), 0.74-0.87 (m, 16H, CH_2), 3.75-3.78 (m, 8H, OCH_2), 6.97 (d, $^3J_{H\text{-}H}$ = 8.3 Hz, 4H, Ar-*m*-C*H*), 7.66 (t, $^3J_{H\text{-}H}$ = 8.3 Hz, 2H, Ar-*p*-C*H*), 8.78 (s, 2H, H_β), 8.92 (d, $^3J_{H\text{-}H}$ = 4.2 Hz, 2H, H_β), 9.22 (d, $^3J_{H\text{-}H}$ = 4.2 Hz, 2H, H_β), 9.38 (s, 2H, H_β), 10.10 ppm (s, 2H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.8, 22.2, 25.1, 28.4, 28.5, 28.6, 31.3, 68.7, 103.3, 105.3, 111.9, 120.9, 129.8, 129.9, 130.1, 130.2, 130.3, 130.4, 130.5, 130.6 and 160.1

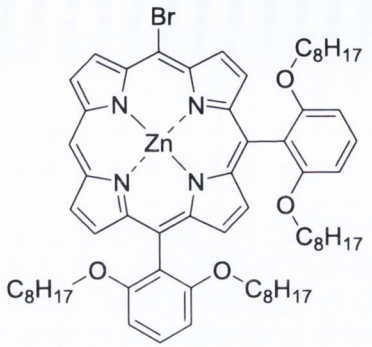
ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 407 (5.60), 502 (4.24), 576 nm (3.49); HRMS (MALDI) *m/z* calcd. for $C_{64}H_{86}N_4O_4$ $[M]^+$: 974.6649, found 974.6656.

5-Bromo-10,15-bis(2,6-dioctyloxyphenyl)porphyrin (186a)



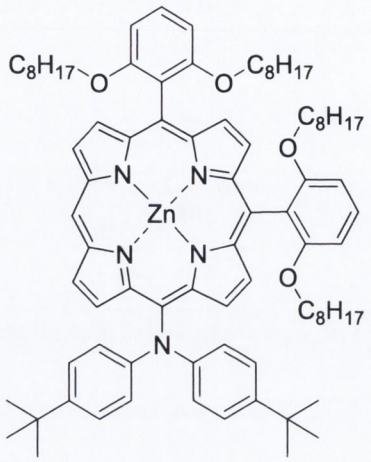
Porphyrin **178b** (400 mg, 0.38 mmol) was dissolved in $CHCl_3$ (150 mL), purged with argon and cooled to 0 °C. Pyridine (0.50 mL) and NBS (58 mg, 0.33 mmol) were added and the solution stirred at 0 °C for one hour. Acetone (5 mL) was added to quench the reaction, solvents were removed under vacuum and the product purified by column chromatography (silica gel) using toluene/*n*-hexane (1:3, v/v) as eluent. Target was obtained in the second porphyrin containing fraction as a purple solid (292 mg, 0.28 mmol, 73 %). M.p.: 72-74 °C; R_f = 0.44 (*n*-hexane:CH_2Cl_2, 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = -2.86 (s, 2H, N*H*), 0.37-0.57 (m, 44H, CH_2/CH_3), 0.71-0.77 (m, 8H, CH_2), 0.85-0.93 (m, 8H, CH_2), 3.76-3.79 (m, 8H, OCH_2), 6.94-6.97 (m, 4H, Ar-*m*-C*H*), 7.63-7.68 (m, 2H, Ar-*p*-C*H*), 8.70 (s, 2H, H_β), 8.83-8.85 (m, 2H, H_β), 9.14 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.30 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.54 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.68 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 10.00 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.8, 22.2, 25.1, 28.4, 28.5, 28.6,31.3, 68.6, 101.1, 104.5, 105.2, 105.3, 112.4, 113.2, 120.1, 120.8, 129.9, 130.0, 131.0, 131.1, 131.3, 159.9 and 160.0 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 415 (5.61), 511 (4.27), 546 (3.65), 587 (3.69), 641 nm (3.35); HRMS (MALDI) *m/z* calcd. for $C_{64}H_{85}BrN_4O_4$ $[M]^+$: 1052.5754, found 1052.5739.

[5-Bromo-10,15-bis(2,6-dioctyloxyphenyl)porphyrinato]zinc(II) (187a)



Bromoporphyrin **186a** (0.25 g, 0.24 mmol) was dissolved in $CHCl_3$ (70 mL) at room temperature. Zinc(II) acetate (0.15 g, 0.72 mmol) was dissolved in methanol (5 mL) and added to the reaction. The reaction progress was monitored by TLC and, once complete, the reaction products were filtered through a plug of silica using CH_2Cl_2 as eluent. The removal of solvents gave a quantitative yield of purple crystals (274 mg, 0.23 mmol, 97 %). M.p.: 88-91 °C; R_f = 0.39 (*n*-hexane:CH_2Cl_2, 1:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.40-0.56 (m, 44H, C*H*$_2$/C*H*$_3$), 0.71-0.78 (m, 8H, C*H*$_2$), 0.89-1.05 (m, 8H, C*H*$_2$), 3.85-3.88 (m, 8H, OC*H*$_2$), 7.02-7.04 (m, 4H, Ar-*m*-C*H*), 7.68-7.73 (m, 2H, Ar-*p*-C*H*), 8.68 (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 1H, H_β), 8.69 (s, 2H, H_β), 8.98-8.99 (m, 2H, H_β), 9.14 (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 1H, H_β), 9.23 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.57 (s, 1H, H_{meso}), 9.68 ppm (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 1H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.8, 22.2, 25.1, 25.2, 28.5, 28.6, 31.2, 31.3, 68.7, 102.9, 105.2, 105.3, 105.4, 105.5, 112.9, 113.8, 121.4, 121.5, 129.7, 131.2, 131.7, 131.8, 131.9, 132.1, 132.3, 148.1, 148.7, 149.3, 150.8, 150.9, 151.2, 151.4 and 160.0 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 417 (5.58), 546 (4.14), 583 nm (2.91); HRMS (MALDI) *m/z* calcd. for $C_{64}H_{85}BrN_4O_4Zn$ $[M]^+$: 1114.4889, found 1114.4885.

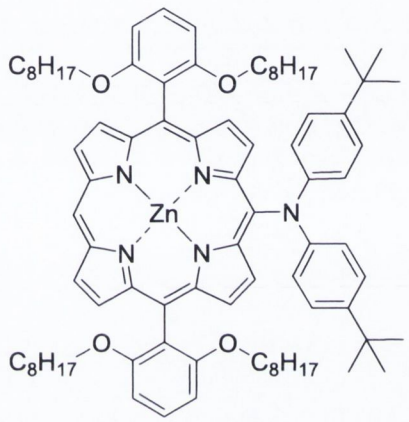
[5,10-Bis(2,6-dioctyloxyphenyl)-15-(bis(4-*tert*-butylphenyl)amino)porphyrinato] zinc(II) (188a)



Bromoporphyrin **187a** (210 mg, 0.19 mmol), *N,N*-bis(4-*tert*-butylphenyl)amine **184** (214 mg, 0.76 mmol), palladium(II) acetate (4 mg, 19 µmol), BINAP (25 mg, 38 µmol) and Cs_2CO_3 (246 mg, 0.76 mmol) were placed in an oven-dried Schlenk flask and heated under vacuum for 10 minutes. Anhydrous THF (20 mL) was added and the solution was subjected to three freeze-pump-thaw cycles before releasing to argon. The reaction mixture was heated to 65 °C for 16 h. The reaction was quenched by pouring into water (200 mL), extracted with CH_2Cl_2 (3 × 100 mL) and dried over $MgSO_4$. The solvents were removed *in vacuo* and the reaction mixture was filtered through a plug of silica using CH_2Cl_2 as eluent before column chromatography (silica gel) using *n*-hexane:CH_2Cl_2 (2:1, v/v) as eluent. Recrystallisation ($CHCl_3$/CH_3OH) gave purple crystals (170 mg, 0.13 mmol, 68 %). M.p.: 85-87 °C; R_f = 0.27 (*n*-hexane:CH_2Cl_2, 2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.37-0.55 (m, 44H, CH_2/CH_3), 0.67-0.75 (m, 8H, CH_2), 0.86-0.96 (m, 8H, CH_2), 1.23 (s, 18H, $C(CH_3)_3$), 3.76-3.80 (m, 8H, OCH_2), 6.93-6.99 (m, 4H, Ar-*m*-C*H*), 7.13 (d, $^3J_{H\text{-}H}$ = 8.9 Hz, 4H, N-Ar-*m*-C*H*), 7.24 (d, $^3J_{H\text{-}H}$ = 8.9 Hz, 4H, N-Ar-*o*-C*H*), 7.60-7.68 (m, 2H, Ar-*p*-C*H*), 8.78-8.80 (m, 3H, H_β), 8.92 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.21 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.23 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.28 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.41 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.99 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ =13.7, 13.8, 22.1, 22.2, 24.9, 25.1,

28.3, 28.5, 28.6, 28.7, 31.3, 31.4, 34.0, 68.6, 68.7, 105.0, 112.8, 112.9, 121.1, 121.3, 121.6, 125.5, 129.5, 130.2, 130.3, 131.1, 131.4, 131.6, 131.7, 131.9, 142.5, 148.3, 149.4, 149.8, 150.1, 150.8, 150.9, 151.6, 151.8, 151.9 and 160.0 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 410 (5.08), 555 (3.98), 600 nm (3.52); HRMS (MALDI) *m/z* calcd. for $C_{84}H_{109}N_5O_4Zn$ $[M]^+$: 1315.7771, found 1315.7756.

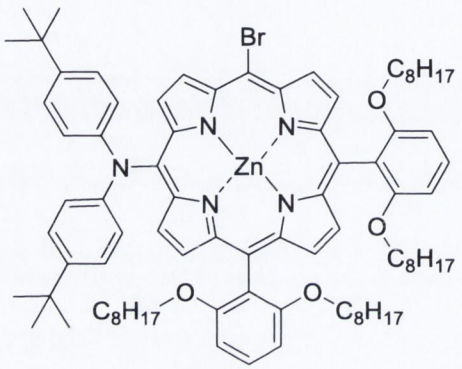
[5,15-Bis(2,6-dioctyloxyphenyl)-10-(bis(4-*tert*-butylphenyl)amino)porphyrinato]zinc(II) (188b)



Synthesised as per **188a** from bromoporphyrin **187b**[137] (250 mg, 0.24 mmol), **184** (268 mg, 95 mmol), palladium(II) acetate (5 mg, 24 µmol), BINAP (30 mg, 48 µmol) and Cs_2CO_3 (155 mg, 0.48 mmol). Purification by column chromatography (silica gel) using *n*-hexane:CH_2Cl_2 (2:1, v/v) as eluent and removal of solvents followed by recrystallisation ($CHCl_3$/CH_3OH) gave purple crystals (228 mg, 0.17 mmol, 72 %). M.p 81-83 °C, R_f = 0.28 (*n*-hexane:CH_2Cl_2, 3:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.42-0.60 (m, 44H, CH_2/CH_3), 0.76-0.80 (m, 8H, CH_2), 0.85-0.95 (m, 8H, CH_2), 1.21 (s, 18H, $C(CH_3)_3$), 3.81 (t, $^3J_{H\text{-}H}$ = 6.5 Hz, 8H, OCH_2), 6.96 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 4H, Ar-*m*-C*H*), 7.09 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 4H, N-Ar-*m*-C*H*), 7.22 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 4H, N-Ar-*o*-C*H*), 7.65 (t, $^3J_{H\text{-}H}$ = 8.6 Hz, 2H, Ar-*p*-C*H*), 8.81 (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 2H, H_β), 8.94 (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 2H, H_β), 9.22 (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 2H, H_β), 9.28 (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 2H, H_β), 10.03 ppm (s, 1H, H_{meso}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ =13.7, 14.1, 22.2, 25.0, 28.4, 28.5, 31.3, 31.4, 33.9, 68.6, 105.2,

112.7. 121.1, 121.4, 125.4, 129.6, 130.3, 131.1, 131.6, 132.0, 142.4, 149.4, 149.9, 105.0, 150.8, 151.9 and 159.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 408 (5.30), 554 (4.18), 602 nm (3.55); HRMS (MALDI) *m/z* calcd. for $C_{84}H_{109}N_5O_4Zn$ $[M]^+$: 1315.7771, found 1315.7787.

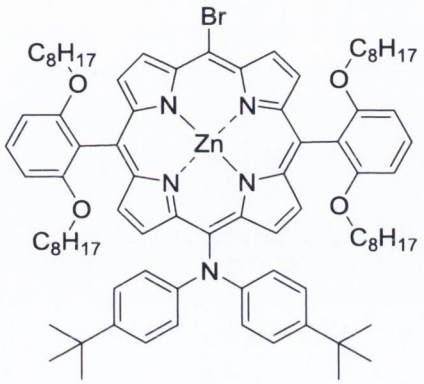
[5-Bromo-10,15-bis(2,6-dioctyloxyphenyl)-20-(bis(4-*tert*-butylphenyl)amino)porphyrinato]zinc(II) (189a)



Aminoporphyrin **188a** (200 mg, 0.15 mmol) was dissolved in $CHCl_3$ (50 mL), purged with argon and cooled to 0 °C. Pyridine (0.50 mL) and NBS (54 mg, 0.30 mmol) were added and the solution stirred until TLC analyses indicated complete consumption of the starting material. Acetone (5 mL) was added to quench the reaction, solvents were removed under vacuum and the product was purified by column chromatography (silica gel) using *n*-hexane:CH_2Cl_2 (2:1, v/v) as eluent. Recrystallisation ($CHCl_3$/CH_3OH) gave near quantitative yield of purple crystals (199 mg, 0.14 mmol, 95 %). M.p.: 79-82 °C; R_f = 0.49 (*n*-hexane:CH_2Cl_2, 2:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.43-0.55 (m, 44H, CH_2/CH_3), 0.67-0.77 (m, 8H, CH_2), 0.87-0.98 (m, 8H, CH_2), 1.22 (s, 18H, $C(CH_3)_3$), 3.75-3.80 (m, 8H, OCH_2), 6.90-6.96 (m, 4H, Ar-*m*-C*H*), 7.12 (d, $^3J_{H\text{-}H}$ = 8.9 Hz, 4H, N-Ar-*m*-C*H*), 7.20 (d, $^3J_{H\text{-}H}$ = 8.9 Hz, 4H, N-Ar-*o*-C*H*), 7.58-7.67 (m, 2H, Ar-*p*-C*H*), 8.69-8.70 (m, 3H, H_β), 8.82 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, H_β), 9.19 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, H_β), 9.32 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, H_β), 9.56 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.59 ppm (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β); ^{13}C NMR (150 MHz, $CDCl_3$/C_5D_5N, 25 °C): δ =13.9, 14.1, 22.3, 22.7, 24.9, 25.1, 28.3, 28.5, 28.6, 28.7, 29.4, 29.6, 31.3, 31.4, 31.5, 31.9, 68.4, 68.5, 105.3, 105.4, 117.4, 117.6, 121.3,

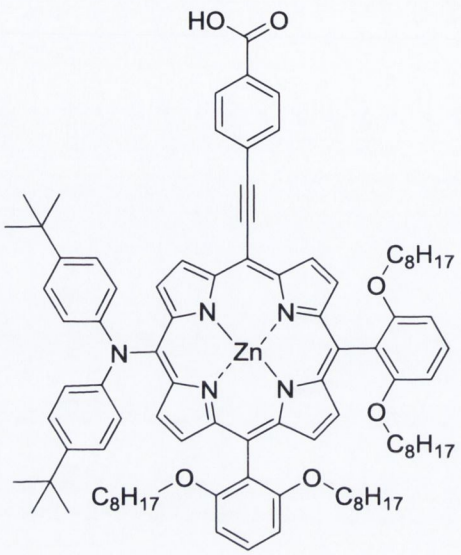
125.1, 125.5, 126.0, 129.4, 130.3, 130.7, 131.4, 131.5, 131.8, 132.1, 132.4 and 159.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 418 (5.30), 565 (4.12), 615 nm (3.84); HRMS (MALDI) *m/z* calcd. for $C_{84}H_{108}N_5O_4BrZn$ $[M]^+$: 1393.6876, found 1393.6910.

[5-Bromo-10,20-bis(2,6-dioctyloxyphenyl)-15-(bis(4-*tert*-butylphenyl)amino)porphyrinato]zinc(II) (189b)



Synthesised as per **189a** using **188b** (600 mg, 0.45 mmol), pyridine (0.50 mL) and NBS (162 mg, 0.90 mmol) in $CHCl_3$ (300 mL). Purification by column chromatography (silica gel) using n-hexane:CH_2Cl_2 (3:1, v/v), removal of solvents and recrystallisation ($CHCl_3$/CH_3OH) gave a quantitative yield of purple crystals (604 mg, 0.43 mmol, 96 %). M.p.: 139-141 °C; R_f = 0.48 (*n*-hexane:CH_2Cl_2, 3:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.40-0.61 (m, 44H, C*H*$_2$/C*H*$_3$), 0.76-0.82 (m, 8H, C*H*$_2$), 0.94-0.97 (m, 8H, C*H*$_2$), 1.20 (s, 18H, C(C*H*$_3$)$_3$), 3.81 (t, $^3J_{H\text{-}H}$ = 6.5 Hz, 8H, OC*H*$_2$), 6.93 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 4H, Ar-*m*-C*H*), 7.10 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 4H, N-Ar-*m*-C*H*), 7.20 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 4H, N-Ar-*o*-C*H*), 7.63 (t, $^3J_{H\text{-}H}$ = 8.6 Hz, 2H, Ar-*p*-C*H*), 8.71 (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 2H, H_β), 8.83 (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 2H, H_β), 9.20 (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 2H, H_β), 9.58 ppm (d, $^3J_{H\text{-}H}$ = 4.6 Hz, 2H, H_β); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ =13.7, 22.2, 25.1, 28.4, 28.5, 31.3, 31.4, 33.9, 68.5, 105.1, 113.9, 120.7, 121.4, 121.7, 125.5, 129.8, 130.7, 132.2, 132.3, 132.5, 142.6, 145.3, 149.1, 149.9, 150.2, 151.2, 152.8 and 159.8 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 417 (5.42), 568 (4.18), 616 nm (3.93); HRMS (MALDI) *m/z* calcd. for $C_{84}H_{108}N_5O_4BrZn$ $[M]^+$: 1393.6876, found 1393.6908.

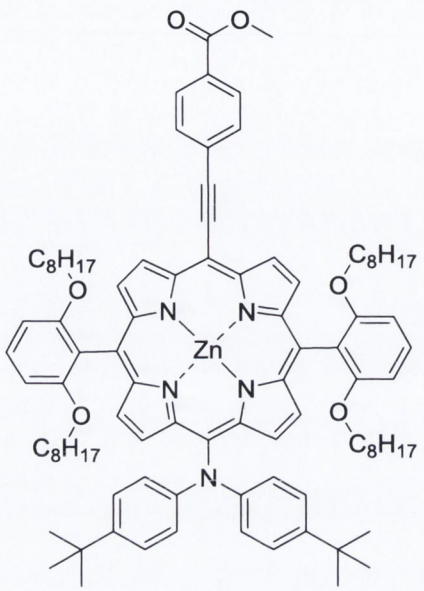
[5-(4-Carboxyphenylethynyl)-10,15-bis(2,6-dioctyloxyphenyl)-20-(bis(4-*tert*-butylphenyl)amino)porphyrinato]zinc(II) (191a)



Bromoporphyrin **189a** (150 mg, 107 μmol), methyl 4-ethynylbenzoate (87 mg, 0.54 mmol), $PdCl_2(PPh_3)_2$ (9 mg, 11 μmol) and CuI (6 mg, 33 μmol) were placed in an oven-dried Schlenk flask and heated under vacuum for 10 minutes. Anhydrous DMF (10 mL) and diethyl amine (3 mL) were added and the solution was subjected to three freeze-pump-thaw cycles before releasing to argon. The reaction mixture was heated to 120 °C for 16 h until TLC analyses indicated consumption of the starting material. The reaction was quenched by pouring into water (100 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were washed with brine (5 × 100 mL) before drying over $MgSO_4$. The solvents were removed and the reaction mixture was filtered through a plug of silica using CH_2Cl_2 as eluent before column chromatography (silica gel) using *n*-hexane:CH_2Cl_2 (3:2, v/v) as eluent gave a glossy purple solid (109 mg, 66 %) which was deprotected directly. The product was dissolved in anhydrous THF (13 mL). NaOH in methanol (2 M, 13 mL, 26 mmol) was added and the solution was heated to 70 °C under argon for 16 h. The solvents were removed *in vacuo* and water (700 mL) was added to give a green solution. HCl (1 M, 26 mL) was added dropwise until the pH reached 5. The green suspension was extracted with DCM (3 × 100 mL). The combined organic phases were washed with brine (1 × 100 mL) before drying over

$MgSO_4$. The solvents were removed and the product was purified by column chromatography (silica gel) using CH_2Cl_2:CH_3OH (19:1, v/v) as eluent to give a glossy purple solid (98 mg, 67 μmol, 96 %; 63 % over 2 steps). Analytical samples were obtained *via* recrystallisation ($CHCl_3$/CH_3OH). M.p 142-145 °C; R_f = 0.19 (CH_2Cl_2:CH_3OH, 19:1, v/v);^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.44-0.54 (m, 44H, C*H*$_2$/C*H*$_3$), 0.71-0.74 (m, 8H, C*H*$_2$), 0.91-1.00 (m, 8H, C*H*$_2$), 1.22 (s, 18H, C(C*H*$_3$)$_3$), 3.77-3.80 (m, 8H, OC*H*$_2$), 6.91-6.98 (m, 4H, Ar-*m*-C*H*), 7.13 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 4H, N-Ar-*m*-C*H*), 7.22 (d, $^3J_{H\text{-}H}$ = 8.9 Hz, 4H, N-Ar-*o*-C*H*), 7.59-7.66 (m, 2H, Ar-*p*-C*H*), 7.93 (d, $^3J_{H\text{-}H}$ = 7.5 Hz, 2H, alkynyl-Ar-*o*-C*H*), 8.07 (d, $^3J_{H\text{-}H}$ = 7.5 Hz, 2H, alkynyl-Ar-*m*-C*H*), 8.68 (br s, 3H, H_β), 8.86 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, H_β), 9.16 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.36 (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β), 9.63 (d, $^3J_{H\text{-}H}$ = 4.4 Hz, 1H, H_β), 9.66 ppm (d, $^3J_{H\text{-}H}$ = 4.5 Hz, 1H, H_β); ^{13}C NMR (150 MHz, $CDCl_3$/C_5D_5N, 25 °C): δ =13.9, 14.1, 22.3, 22.7, 24.9, 25.1, 28.3, 28.5, 28.6, 28.6, 28.7, 29.2, 29.3, 29.6, 29.7, 31.4, 31.5, 31.9, 34.0, 68.4, 68.5, 94.4, 96.9, 97.2, 105.3, 106.6, 114.2, 114.5, 117.3, 121.2, 121.3, 121.7, 121.8, 122.3, 125.4, 125.5, 126.0, 129.2, 129.4, 129.7, 129.8, 129.9, 130.0, 130.2, 130.3, 130.6, 130.8, 130.9, 131.3, 131.7, 131.9, 142.3, 149.7, 150.1, 150.4, 150.6, 150.7, 151.2, 151.3, 151.8, 152.0, 159.8 and 160.0 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 440 (5.31), 580 (4.17), 630 nm (4.23); HRMS (MALDI) *m/z* calcd. for $C_{93}H_{113}N_5O_6Zn$ $[M]^+$: 1459.7982, found 1459.7936.

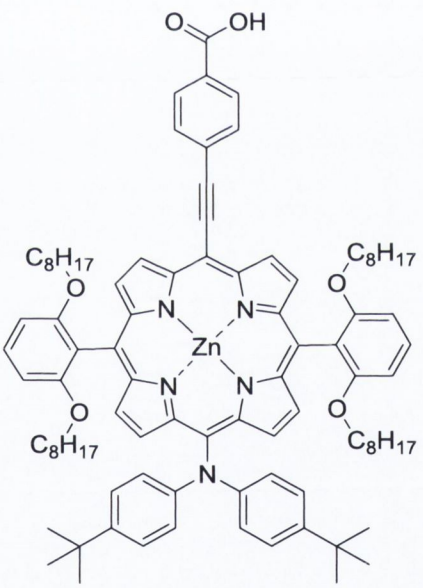
[5-(4-Carbomethoxyphenylethynyl)-10,20-bis(2,6-dioctyloxyphenyl)-15-(bis(4-*tert*-butylphenyl)amino)porphyrinato]zinc(II) (190b)



Bromoporphyrin **189b** (150 mg, 0.11 mmol), methyl 4-ethynylbenzoate (87 mg, 0.54 mmol), $PdCl_2(PPh_3)_2$ (9 mg, 11 µmol) and CuI (6 mg, 33 µmol) were placed in an oven-dried Schlenk flask and heated under vacuum for 10 minutes. Anhydrous DMF (10 mL) and diethyl amine (3 mL) were added and the solution was subjected to three freeze-pump-thaw cycles before releasing to argon. The reaction mixture was heated to 120 °C for 16 h until TLC analyses indicated complete consumption of the starting material. The reaction was quenched by pouring into water (100 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic phases were washed with brine (5 × 100 mL) before drying over $MgSO_4$. The solvents were removed *in vacuo* and the reaction mixture was filtered through a plug of silica using CH_2Cl_2 as eluent before column chromatography (silica gel) using *n*-hexane:CH_2Cl_2 (3:2, v/v) as eluent gave a glossy purple solid (135 mg, 91 µmol, 83 %). R_f = 0.16 (*n*-hexane:CH_2Cl_2, 3:2, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.45-0.63 (m, 44H, CH_2/CH_3), 0.74-0.80 (m, 8H, CH_2), 0.94-1.01 (m, 8H, CH_2), 1.21 (s, 18H, $C(CH_3)_3$), 3.82 (t, $^3J_{H\text{-}H}$ = 6.4 Hz, 8H, OCH_2), 3.98 (s, 3H, OCH_3), 6.95 (d, $^3J_{H\text{-}H}$ = 8.6 Hz, 4H, Ar-*m*-C*H*), 7.12 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 4H, N-Ar-*m*-C*H*), 7.21 (d, $^3J_{H\text{-}H}$ = 8.8 Hz, 4H, N-Ar-*o*-C*H*),

7.64 (t, $^{3}J_{H\text{-}H}$ = 8.6 Hz, 2H, Ar-*p*-C*H*), 8.02 (d, $^{3}J_{H\text{-}H}$ = 8.3 Hz, 2H, alkynyl-Ar-*o*-C*H*), 8.20 (d, $^{3}J_{H\text{-}H}$ = 8.3 Hz, 2H, alkynyl-Ar-*m*-C*H*), 8.69 (d, $^{3}J_{H\text{-}H}$ = 4.6 Hz, 2H, H_{β}), 8.87 (d, $^{3}J_{H\text{-}H}$ = 4.6 Hz, 2H, H_{β}), 9.18 (d, $^{3}J_{H\text{-}H}$ = 4.6 Hz, 2H, H_{β}), 9.65 ppm (d, $^{3}J_{H\text{-}H}$ = 4.6 Hz, 2H, H_{β}); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.7, 22.2, 25.1, 28.4, 28.6, 29.7, 31.3, 33.9, 52.2, 68.6, 94.5, 96.7, 98.1, 105.1, 114.5, 120.7, 121.5, 123.1. 125.5, 129.0, 129.4, 129.8, 130.1, 130.7, 131.2, 132.0, 132.2, 142.7, 149.9, 150.3, 150.5, 151.9, 152.0, 159.8 and 166.8 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 440 (5.18), 576 (3.95), 637 nm (4.25); HRMS (MALDI) *m/z* calcd. for $C_{94}H_{115}N_5O_6Zn$ $[M]^+$: 1473.8139, found 1473.8097.

[5-(4-Carboxyphenylethynyl)-10,20-bis(2,6-dioctyloxyphenyl)-15-(bis(4-*tert*-butylphenyl)amino)porphyrinato]zinc(II) (191b)



Methyl ester **190b** (100 mg, 68 µmol) was dissolved in anhydrous THF (13 mL). NaOH in methanol (2 M, 12 mL, 24 mmol) was added and the solution was heated to 70 °C under argon for 16 h. The solvents were removed *in vacuo* and water (600 mL) added to give a green solution. HCl (1 M, 24 mL) was added dropwise until the pH reached 5. The green suspension was extracted with DCM (3 × 100 mL). The combined organic phases were washed with brine (1 × 100 mL) before drying over $MgSO_4$. The solvents were removed *in vacuo* and the product was purified by column chromatography (silica gel) using

CH_2Cl_2:CH_3OH (19:1, v/v) as eluent to give a glossy purple solid (95 mg, 65 µmol, 96 %). Analytical samples were obtained *via* recrystallisation ($CHCl_3$/CH_3OH). M.p.: 112-115 °C; R_f = 0.21 (CH_2Cl_2:CH_3OH, 19:1, v/v); ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.45-0.64 (m, 44H, C*H*$_2$/C*H*$_3$), 0.77-0.87 (m, 8H, C*H*$_2$), 0.96-0.99 (m, 8H, C*H*$_2$), 1.21 (s, 18H, C(C*H*$_3$)$_3$), 3.83 (t, $^3J_{H-H}$ = 6.6 Hz, 8H, OC*H*$_2$), 6.95 (d, $^3J_{H-H}$ = 8.5 Hz, 4H, Ar-*m*-C*H*), 7.10 (d, $^3J_{H-H}$ = 8.7 Hz, 4H, N-Ar-*m*-C*H*), 7.21 (d, $^3J_{H-H}$ = 8.7 Hz, 4H, N-Ar-*o*-C*H*), 7.65 (t, $^3J_{H-H}$ = 8.5 Hz, 2H, Ar-*p*-C*H*), 8.06 (d, $^3J_{H-H}$ = 8.2 Hz, 2H, alkynyl-Ar-*o*-C*H*), 8.23 (d, $^3J_{H-H}$ = 8.2 Hz, 2H, alkynyl-Ar-*m*-C*H*), 8.68 (d, $^3J_{H-H}$ = 4.6 Hz, 2H, *H*$_\beta$), 8.87 (d, $^3J_{H-H}$ = 4.6 Hz, 2H, *H*$_\beta$), 9.18 (d, $^3J_{H-H}$ = 4.6 Hz, 2H, *H*$_\beta$), 9.64 ppm (d, $^3J_{H-H}$ = 4.6 Hz, 2H, *H*$_\beta$); ^{13}C NMR (150 MHz, $CDCl_3$/C_5D_5N, 25 °C): δ =13.9, 22.3, 25.1, 28.5, 28.6, 28.7, 31.4, 31.5, 33.9, 68.5, 97.2, 97.3, 105.2, 113.8, 121.1, 121.5, 125.2, 129.4, 129.8, 130.0, 130.4, 130.9, 131.5, 131.7, 142.1, 149.9, 150.1, 150.4, 151.5, 151.9 and 159.9 ppm; UV/Vis (CH_2Cl_2): λ_{max} (log ε) = 442 (5.28), 576 (4.09), 638 nm (4.36); HRMS (MALDI) *m/z* calcd. for $C_{93}H_{113}N_5O_6Zn$ $[M]^+$: 1459.7982, found 1459.7926.

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