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Tetrahedron
Tetrahedron 62 (2006) 10039–10054

Tetrahedron report number 772

Synthetic routes to porphyrins bearing fused rings

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Received 31 July 2006
Available online 1 September 2006

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1. Introduction

Since the early work of Fischer, porphyrin chemistry has evolved dramatically allowing many exotic macrocycles to be synthesised.[1] Few boundaries restrict the porphyrin chemist, as the field overlaps with organic, inorganic and physical chemistry, as well as with many areas of biology and medicine. Within this diversity of porphyrin chemistry, there has been much interest in the synthesis of porphyrins bearing fused rings, whether as extensions of the conjugated macrocycle or fused alicyclic ring systems. They have proved to be valuable research tools and a fruitful area for the development of synthetic methodology. These fused rings can affect porphyrins by altering their optical properties, both ground and excited state, coordination chemistry and redox behaviour, and it is this potential that has captured the attention of many scientists.

The formation of porphyrins with 'exocyclic' rings fused to the macrocycle can be achieved by a variety of reactions, which will be discussed further. Generally, porphyrins bearing fused rings can be divided into two categories. Namely those formed by intramolecular cyclisation reactions and those formed by intermolecular cyclisation reactions. An extensive discussion of methods for the formation of porphyrins with fused rings from non-porphyrin starting materials is outside the scope of this review and these will only be mentioned if they give access to starting materials for further modification of the fused rings. Finally, examples of the formation of arrays in which porphyrins are fused to one another and the use of porphyrins bearing fused rings to synthesise heterodimers will be covered briefly.

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0040–4020/$ - see front matter
doi:10.1016/j.tet.2006.08.021

2. Porphyrins with fused rings formed via intramolecular cyclisations

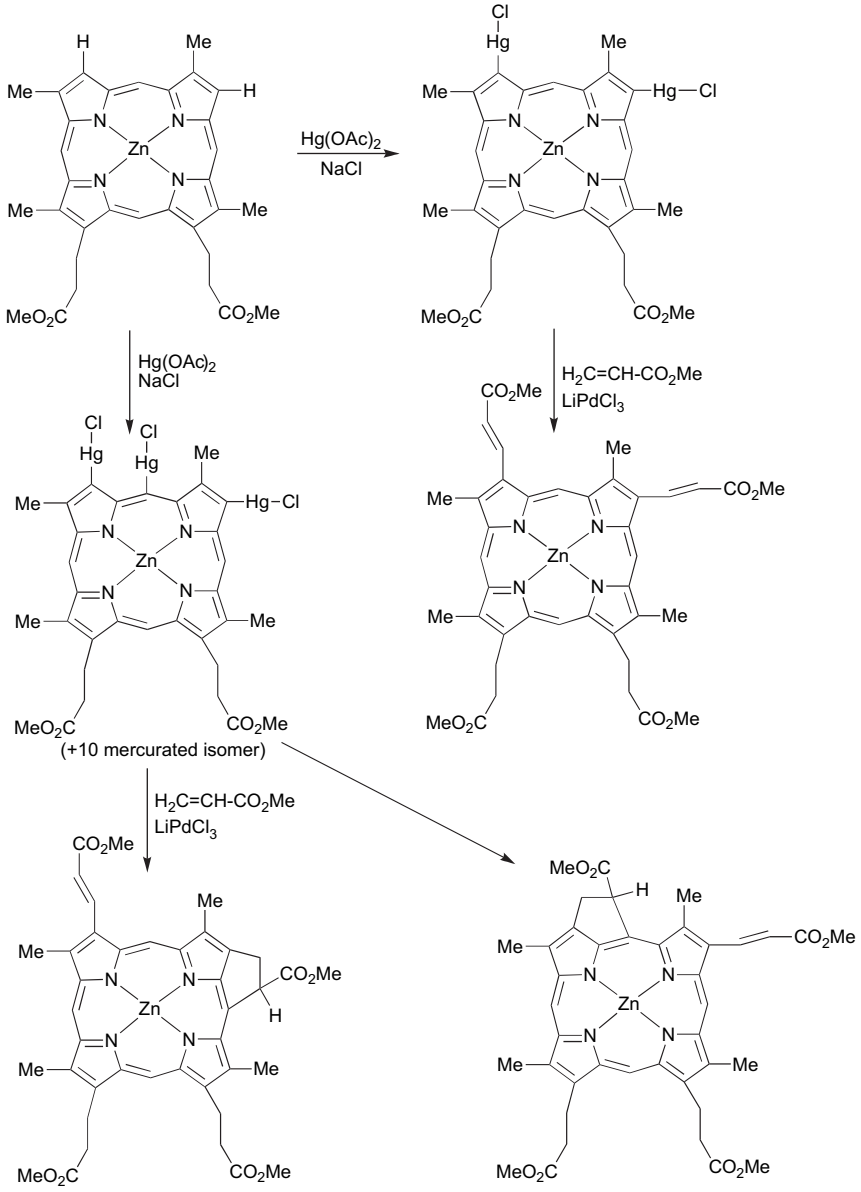
2.1. Metal-mediated cyclisations

In the 1980s, Smith et al. described a palladium-catalysed method that could be used to attach a number of unsaturated substituents directly to the periphery of mercurated porphyrins.[2–4] The first step was the mercuration of zinc(II) deuteroporphyrin IX dimethyl ester. Subsequent treatment with methyl acrylate and $LiPdCl_3$ gave the expected bis-acrylate, along with an unexpected by-product, which could be separated into two isomers (Scheme 1).

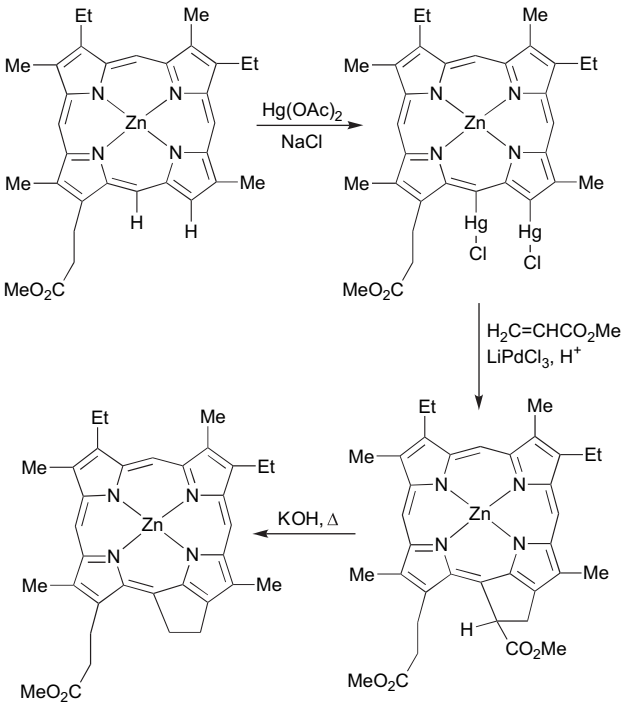
It was postulated that the bis-chloromercurated porphyrin product was contaminated with a tris-mercurated by-product in which mercuration had occurred at the 5- or 10-position. Subjecting these isomers to palladium-coupling conditions led to the formation of two products bearing fused five-membered exocyclic rings.[5] This synthetic method was then exploited to synthesise deoxyerythroetioporphyrin and deoxophylloerythrin methyl ester (Scheme 2).

Recently, Fox and Boyle[6] have developed a method for intramolecular cyclisation based on palladium-catalysed coupling of *meso*-(2-iodophenyl) porphyrins, which gives access to a variety of porphyrins in which the *meso*-phenyl rings are fused to adjacent β-positions (Scheme 3).

It is well documented that organozinc reagents can be easily prepared from organic bromides utilising metallic zinc.[7] Using this technique Chen et al.[8] discovered that treating 2-bromo-5,10,15,20-tetraphenylporphyrinatozinc with activated zinc metal[9] in DMSO at 60 °C for 30 min, resulted in the formation of a fused five-membered ring, similar to those accessed earlier by Fox and Boyle using intramolecular palladium coupling.



Scheme 1. Palladium-catalysed cross-couplings and cyclisations.



Scheme 2. Synthesis of deoxophylloerythrin methyl ester.

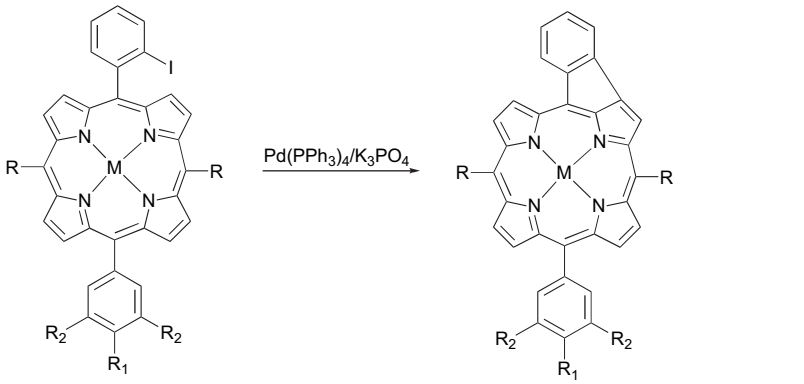
A further extension of this methodology led to the preparation and cyclisation of 2,3,12,13-tetrabromo-5,10,15,20-tetraphenylporphyrinatozinc (Scheme 4).

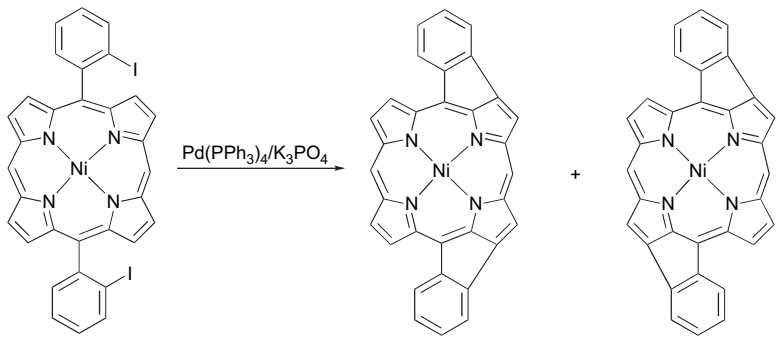
2.2. Acid- and base-catalysed intramolecular cyclisations

2.2.1. Naphthoporphyrins. Porphyrinoid systems with strong absorptions in the far red/near-infrared regions are of interest due to their potential applications, which range from sensors and novel optical materials[10] to the development of superior photosensitisers for photodynamic therapy.[11]

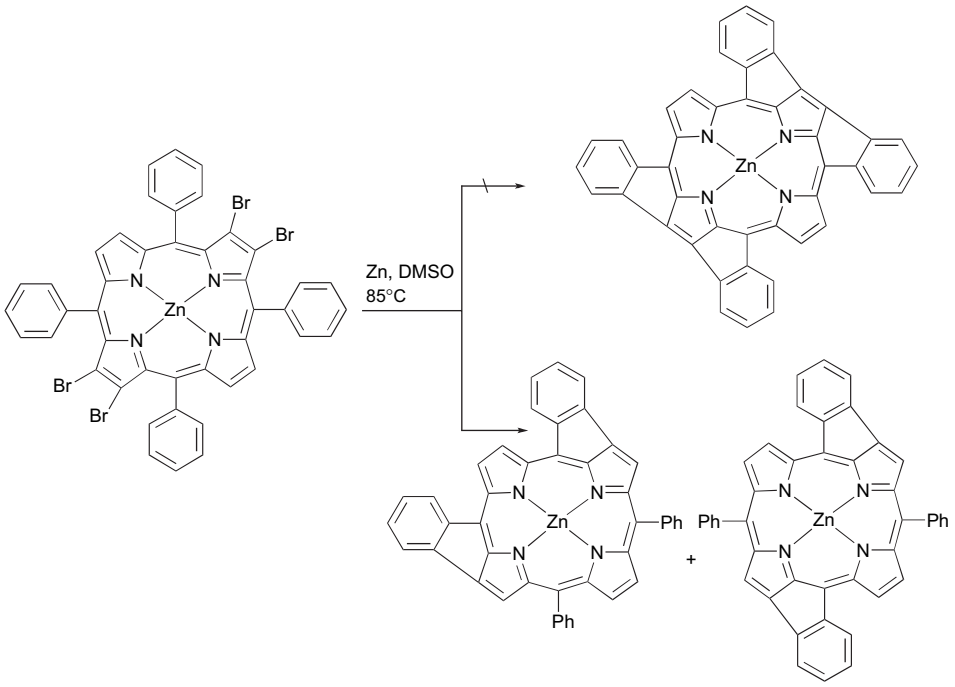
The synthesis of the so-called 'naphthoporphyrin' derivatives has been well documented in the literature by Callot, who used 2-formyl-5,10,15,20-tetraphenylporphyrinatocopper(II)[12] as an intermediate in an acid-catalysed condensation to yield oxonaphthoporphyrin.[13] In this reaction, the carbonyl carbon of the aldehyde group fuses to the *ortho* position of the adjacent phenyl group, producing, albeit in very low yield, an exocyclic six-membered ring containing a keto group (Scheme 5).

It was also found that substituted α-styryl-5,10,15,20-tetraphenylporphyrinatocobalt(III) could rearrange in the presence of low concentrations of acid to give the same naphthoporphyrin skeleton. The combination of air and TFA caused the cobalt(III)porphyrin to be oxidised to the corresponding π-cation radicals, which then suffered elimination followed by demetallation.[14] At low concentrations of acid, however, it was suggested that large amounts of starting material remained and reacted with either the cation radical or the α-styryl radical. The transfer of the styryl fragment

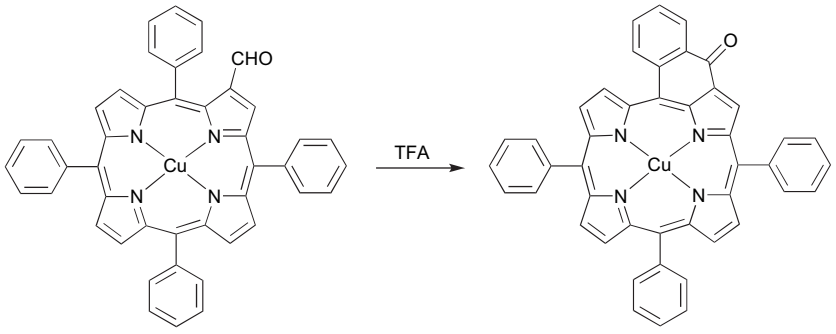




Scheme 3. Pd(0)-catalysed cyclisation of *meso*-(2-iodophenyl) porphyrins.



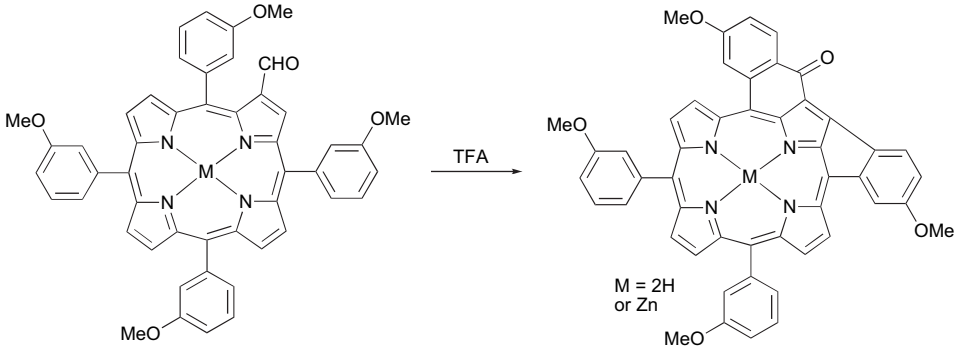
Scheme 4. Zinc-mediated intramolecular cyclisation of 2,3,12,13-tetrabromo-5,10,15,20-tetraphenylporphyrinatozinc.



Scheme 5. Callot's synthesis of an oxonaphthoporphyrin.

to the porphyrin β-position resulted in an olefinic intermediate, which underwent reaction with the adjacent phenyl group. In turn, the metal was lost, yielding a free-base naphthoporphyrin. The synthesis of these naphthoporphyrins provoked other studies into reactivity,[15] porphyrin oligomers,[16] and bis-acrylporphyrins with near-infrared absorbance.[17]

Much attention has been paid to naphthoporphyrin derivatives, due to their potential as photodynamic sensitisers. Dolphin et al.[18] synthesised a number of doubly cyclised derivatives (Scheme 6) that possessed enhanced absorptions in the far red region of the visible spectrum. This double cyclisation was attributed to electron-donating groups present on



Scheme 6. Synthesis of doubly cyclised naphthoporphyrin derivatives.

the *meta*-positions of the phenyl rings of the metallo-2-formyl-5,10,15,20-tetraphenylporphyrin starting material.

2.2.2. Purpurins. Purpurins are defined as tetrapyrrolic macrocycles containing a cyclopentyl ring fused to a reduced pyrrolic unit. They are formed by cyclisation of an appropriate side chain attached to the *meso*-position of the macrocycle, resulting in the formation of a five-membered ring. Like many porphyrins with modified optical properties, they received considerable interest as potential photodynamic sensitisers.[19]

Morgan et al.[19] presented results showing that *meso*-formylated etioporphyrinatonickel(II) could be converted into the corresponding purpurin in yields of up to 90%. This two-step procedure involved functional-group transformation of the aldehyde moiety into an unsaturated ester via a Wittig reaction and removal of the nickel, followed by the acid-catalysed cyclisation of the ester to form the five-membered ring and, hence, the purpurin (Scheme 7).

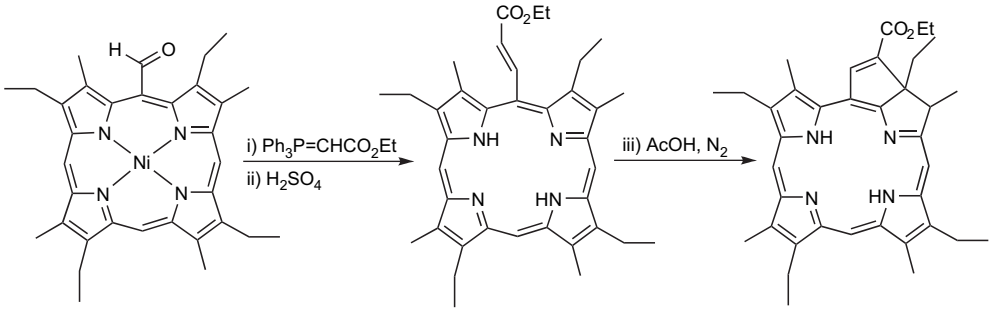
Gunter et al.[20] synthesised both type A and type B purpurins (Fig. 1) containing *meso*-phenyl substituents. Their findings were based on the theory that the purpurin yield was temperature dependent, e.g., purpurin B could be formed preferentially at higher temperatures.

By incorporating two vinylogous side chains, methods of synthesising doubly cyclised bacteriopurpurins have been investigated. Robinson[21] developed a new route to bacteriopurpurins from *meso*-substituted diacrylate octaalkylporphyrins (Scheme 8), and found that these compounds absorbed strongly in the region of 720–830 nm. Previously, Morgan et al.[19] had attempted to synthesise this class of compound via acidic catalysis. It was found, however, that the successful synthetic route required basic conditions, which resulted in the efficient cyclisation of *meso*-acrylate porphyrins to purpurins and bacteriopurpurins. Thus, 5,15-bis[β-(ethoxycarbonyl)vinyl]octaethylporphyrin was cyclised by refluxing in toluene/DBU for 6 h, producing two isomers of 5,15-octaethylbacteriopurpurin in 70% yield.

2.2.3. Benzochlorins. This class of compound is commonly synthesised by the acid-catalysed cyclisation of a corresponding metallo *meso*-(2-formylvinyl)porphyrin. Vicente and Smith[22] synthesised a series of porphyrins possessing 2-formylvinyl substituents by way of a modified Vilsmeier formylation developed by Inhoffen and co-workers.[23] Acid-promoted cyclisation of 2-formylvinyl porphyrins yielded a number of benzochlorins and benzobacteriochlorins. By incorporating two 2-formylvinyl groups into the porphyrin precursor, they were able to yield a mono-cyclised benzochlorin and a double-cyclised dibenzobacteriochlorin (Scheme 9). It was noted that, to achieve cyclisation, a divalent centrally chelated metal must be present.

Similar methods have been developed by Gunter and Robinson,[24] in an extension of previous work on purpurins.[20] Using the same 5,15-diphenylporphyrin skeleton, the group produced a number of 2-formylvinyl precursors and, in turn, synthesised the 5,15-diaryl-substituted benzochlorin derivatives (Scheme 10).

Other substituted benzochlorins have been synthesised and further modified by incorporating nonpolar side chains to increase the lipophilicity (Scheme 11).[25] Biologically, these



Scheme 7. Synthesis of etio purpurin.

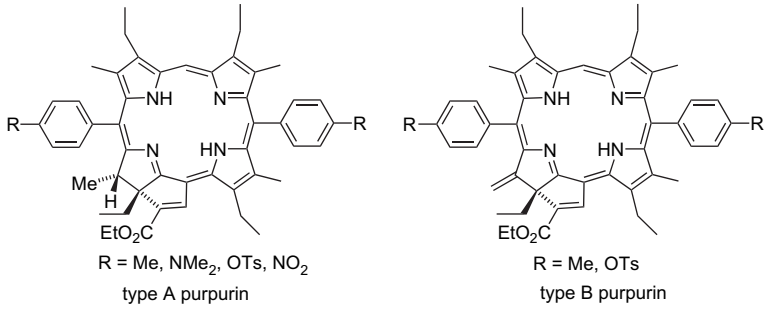
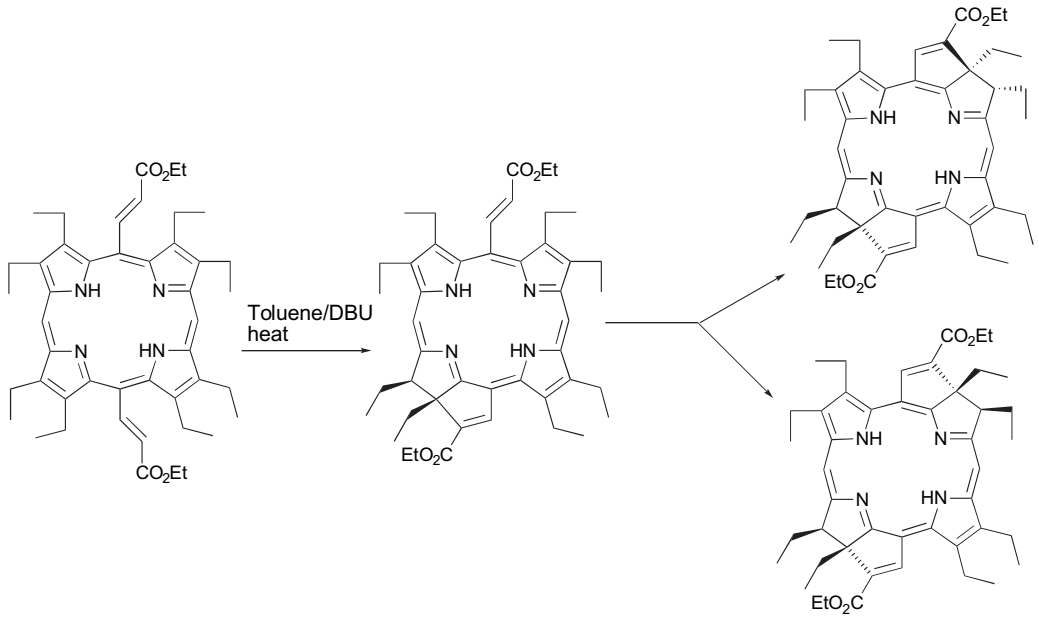
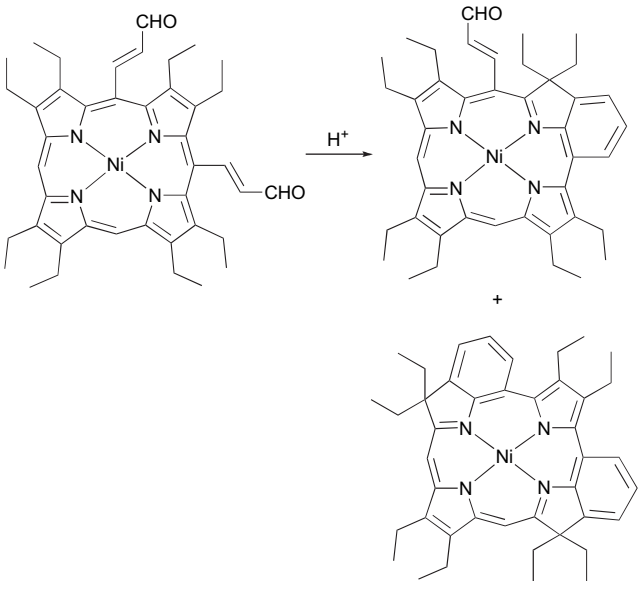


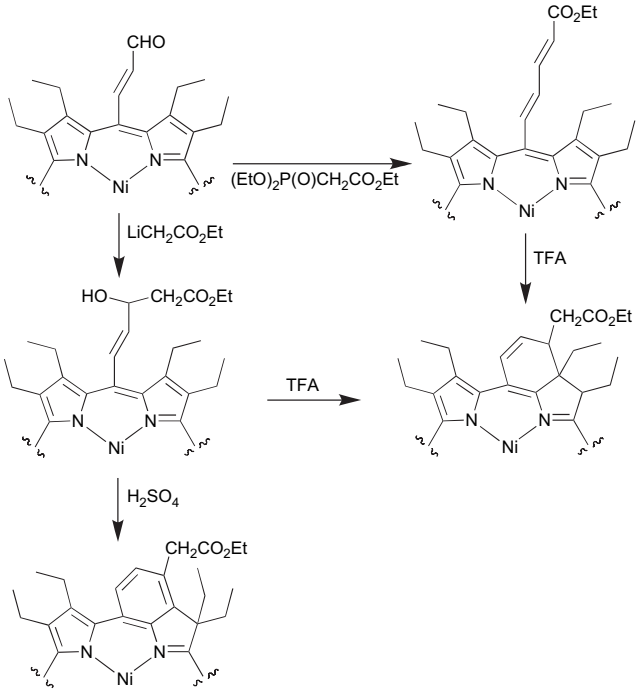
Figure 1. Types A and B purpurins.



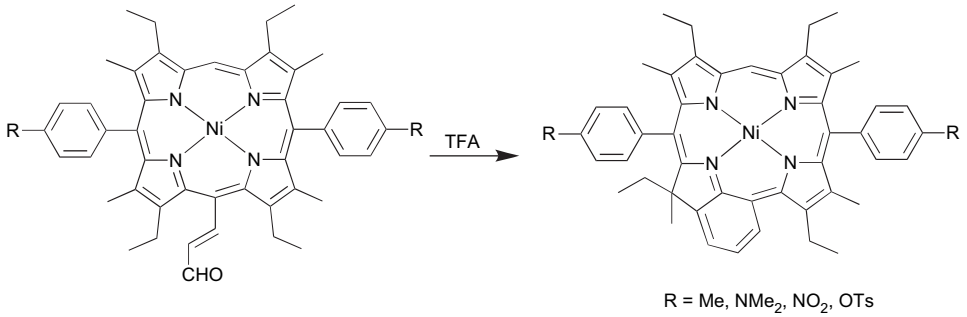
Scheme 8. Synthesis of 5,15-octaethylbacteriopurpurins.



Scheme 9. Synthesis of a benzochlorin and a dibenzobacteriochlorin.



Scheme 11. Preparation of lipophilic benzochlorins.



Scheme 10. Synthesis of 5,15-diphenyloctaalkylbenzochlorins.

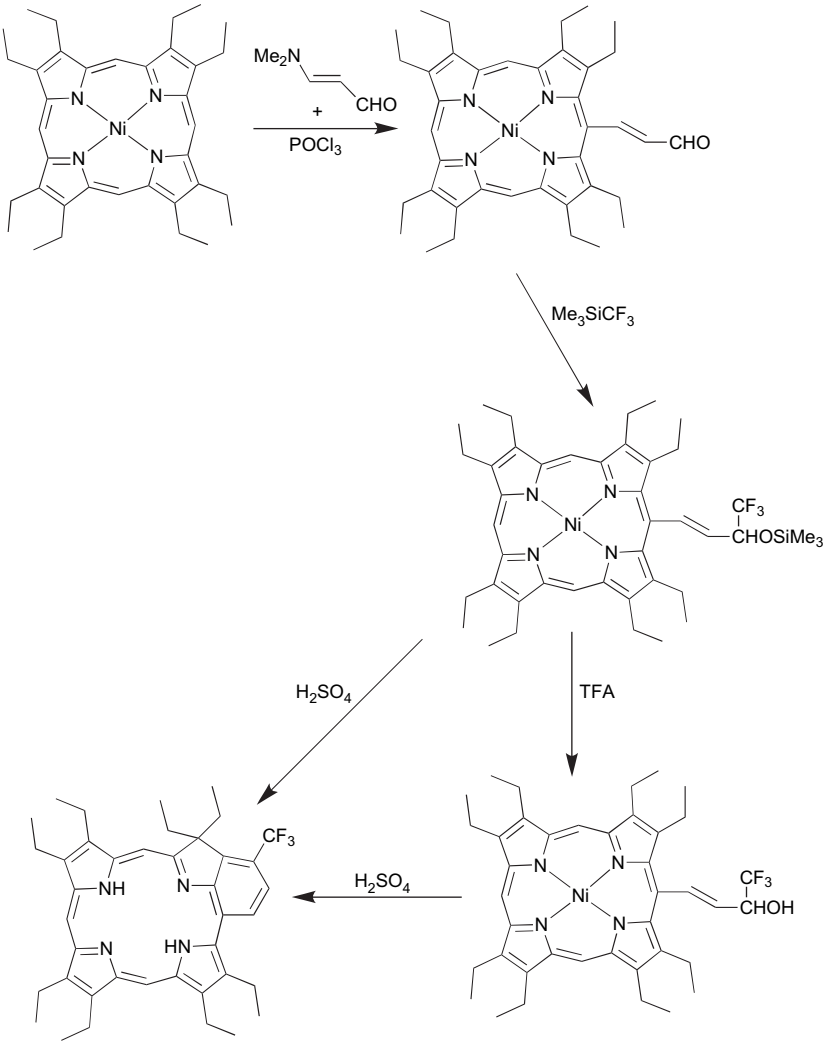
lipophilic benzochlorins were of great interest, and were produced in greater yield than the corresponding deuteroporphyrin derivatives.[22]

Many of the examples of benzochlorin synthesis are based on modification of octaethylporphyrin, as this compound is readily available commercially in both the free base and metallated forms, and is therefore a convenient starting material. Routes to fluorinated and non-fluorinated octaethylporphyrin-based benzochlorins have been developed by Pandey et al.[26] This work led to the synthesis of several benzochlorins with variable lipophilicity that were tested for their efficacy as drugs for photodynamic therapy. As with many of the examples discussed here, Vilsmeier formylation was initially used to attach a 2-formylvinyl group to one *meso*-position. The 2-formylvinyl side chain was then reacted with various fluorinated and non-fluorinated alkyl halides, yielding intermediates which, after acid-catalysed intramolecular cyclisation, generated the corresponding benzochlorins (Scheme 12).

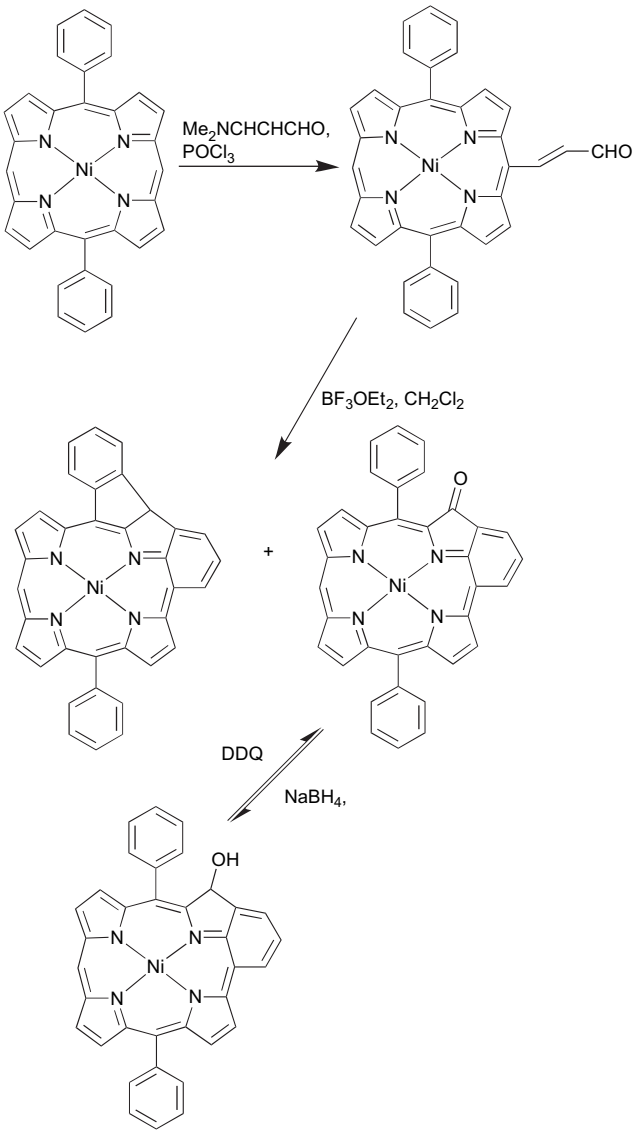
5,15-Diphenyloxobenzochlorins have been prepared by Boyle and Dolphin.[27] After vinylic formylation of 5,15-diphenylporphyrinatonickel(II), treatment with boron trifluoride etherate gave, unexpectedly, two products (Scheme 13), one of which was subsequently found to be an unusual multifused-ring benzochlorin.

2.2.4. Naphthochlorins. Until quite recently, the synthesis of naphthochlorins from octaalkylporphyrins had not been reported. Sengupta and Robinson[28,29] synthesised a number of *meso*-(2-hydroxymethylphenyl)octaalkyl-substituted porphyrins via methods developed by Johnson and Kay[30] and Grigg et al.,[31] and performed cyclisation reactions under acidic conditions. Interestingly, comparison of the octaethylnaphthochlorin with the octaethylbenzochlorin (Fig. 2) synthesised by Arnold et al.[32] revealed that the free base form of the naphthochlorin exhibited the greater long wavelength absorbance, but, conversely, when the metallated species were compared, the benzochlorin showed a greater bathochromic shift.

As mentioned above, the more common methods to access these molecules involve cyclisation of a vinylic group to yield the naphthochlorin. This method is facilitated by the ease with which the vinylic group can be formed from the corresponding formylporphyrins by way of the Wittig reaction.[12,32] Cavaleiro et al.[33] reported an intramolecular



Scheme 12. Synthesis of fluorinated benzochlorins.



Scheme 13. Synthesis of 5,15-diphenyl-7-oxobenzochlorins.

cyclisation of the Ni(II) complex of β-vinyl-5,10,15,20-tetraphenylporphyrins, resulting in naphthochlorins as the major products. In this case, treatment of 2-vinyl-5,10,15,20-tetraphenylporphyrins with dilute sulfuric acid did not afford the expected demetallated product, but, instead, the corresponding benzochlorins were formed in 60% yield (Scheme 14).

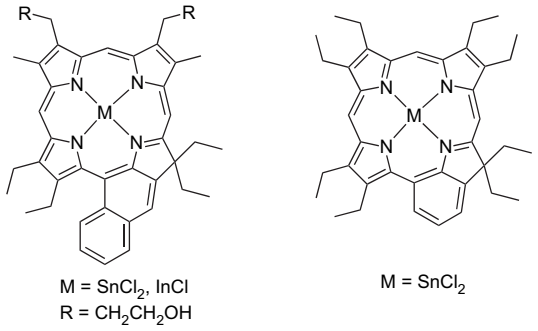


Figure 2. Synthesis of octaalkylbenzochlorins.

3. Porphyrins with fused rings formed via intermolecular reactions

3.1. Diels–Alder reactions

A versatile route to the synthesis of chlorins is the Diels–Alder reaction of vinylporphyrins with electron-deficient dienophiles,[34] and the same methodology can be applied to the synthesis of isobacteriochlorins and bacteriochlorins if divinylporphyrins are used.[35] Cavaleiro et al.[36] investigated [4+2] cycloadditions using the porphyrin exocyclic double bonds as the 2π-electron component. By heating 5,10,15,20-tetraphenyl porphyrin and an aromatic sulfone in trichlorobenzene for 7 h, a [4+2] cycloaddition reaction took place, yielding three products, a chlorin with a fused tetrahydronaphthalene ring (Scheme 15) as the major product, and two other naphthoporphyrins as the minor products.

3.2. Cycloaddition reactions

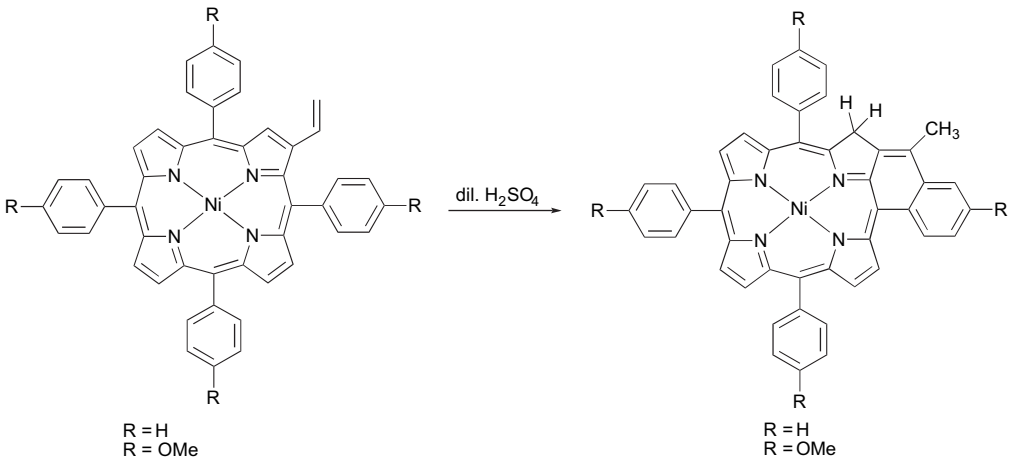
Azomethane ylides were reported by Cavaleiro et al.[37,38] to react with 5,10,15,20-tetraarylporphyrins as the dipolarophile in 1,3 cycloadditions, generating pyrrolidine-fused chlorins and bacteriochlorins in good yields (Scheme 16).

N-Protected pyrroles have been successfully used in a variety of [4+2] cycloaddition reactions with activated dienophiles, as described by Zhang and Trudell.[39] Smith et al.[40] synthesised β-fused pyrroloporphyrins from the Barton–Zard condensation[41] of metallo-2-nitro-5,10,15,20-tetraphenylporphyrins with isocyanoacetates. Studies on the cycloaddition reactions of β-fused metallopyrroloporphyrins with dimethyl acetylenedicarboxylate led to a synthetic route to benzoporphyrins and benzochlorins.[42] Interestingly, when synthesising benzoporphyrins by this route (Scheme 17), the Diels–Alder adduct was formed first, and then converted into the corresponding benzoporphyrin upon refluxing, conversion into the sole deaminated product (50–80% yield) occurring only after prolonged heating (overnight).

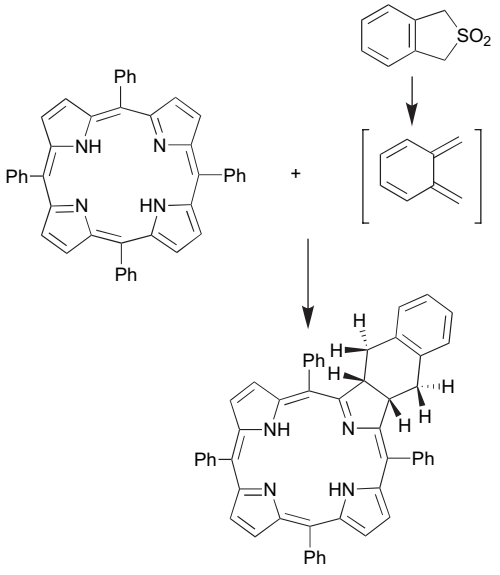
Mononitration of the corresponding benzoporphyrin and subsequent conjugate addition of malononitrile to the nitroalkene subunit of the benzoporphyrin in the presence of NaH in refluxing tetrahydrofuran[43] led to a β-fused benzochlorin as the major product (Fig. 3).

Similarly, as with *o*-quinodimethanes,[36] azomethine ylides[37] and nitrones,[43] it was found that sugar nitrones could be fused to porphyrin macrocycles. Carbohydrate derivatives of porphyrins have shown promise for applications in photodynamic therapy,[44] as these conjugates have demonstrated good water solubility and selectivity for cancer cells. By way of the 1,3-dipolar cycloaddition approach, Cavaleiro et al.[45] synthesised glyco derivatives of chlorins and bacteriochlorins by reacting several readily available sugar nitrones[46] with 5,10,15,20-tetra(pentafluorophenyl)porphyrin (Scheme 18).

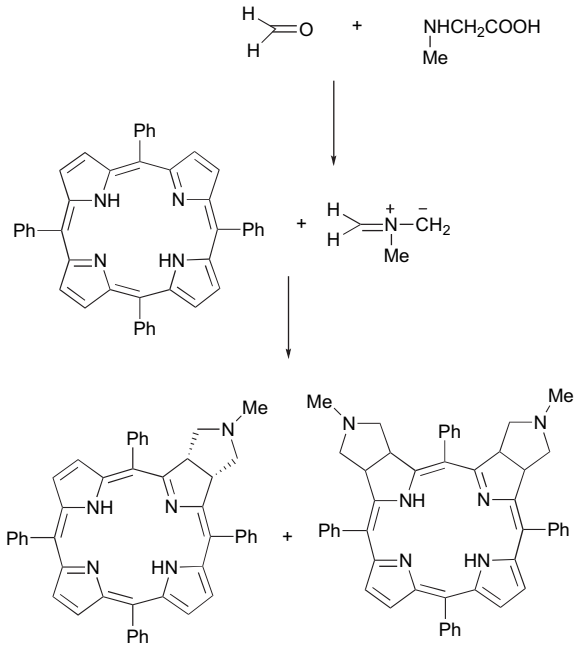
1,3-Dipolar [3+2] cycloaddition reactions are an effective method for the synthesis of five-membered heterocycles,[47] and these reactions have been successfully applied to



Scheme 14. Synthesis of naphthochlorins from 2-vinyl-5,10,15,20-tetraphenylporphyrins.



Scheme 15. 5,10,15,20-Tetraphenylporphyrin as a dienophile in the Diels–Alder reaction.



Scheme 16. Synthesis of pyrrolidine-fused chlorins and bacteriochlorins.

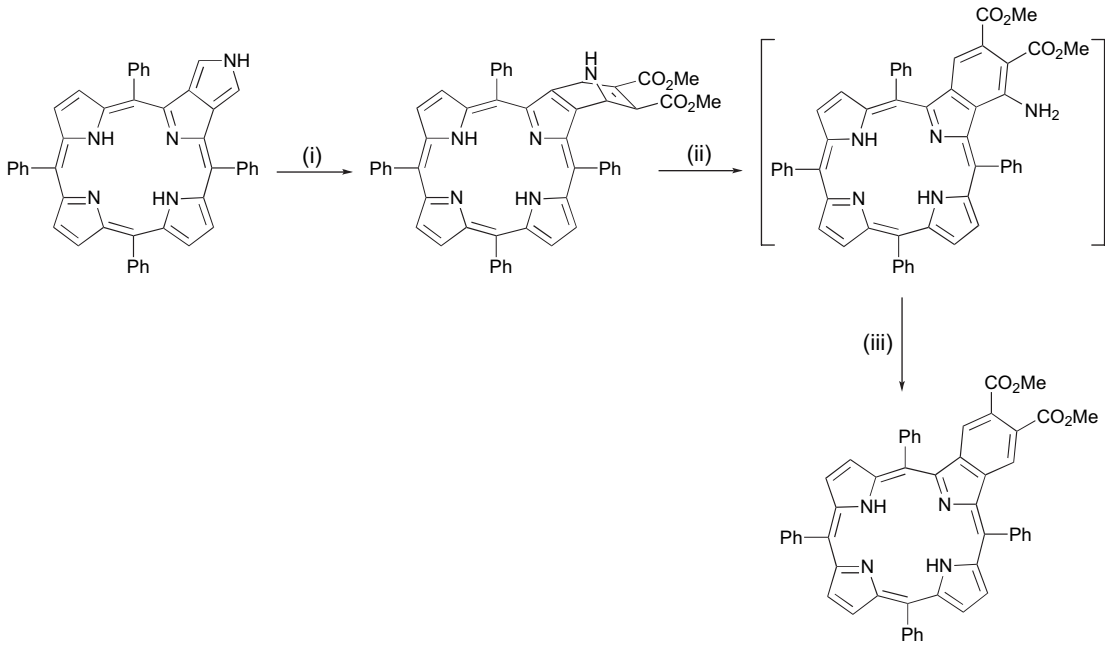
porphyrins by the group of Cavaleiro.[38] It has been noted that electron-deficient carbonyl ylides react with many dipolarophiles including aromatic systems.[48] More recently, non-stabilised carbonyl ylides have been shown to react with both electron-rich and electron-poor dipolarophiles.[49] Fleming and Dolphin[50] exploited these findings to devise a convenient route to chlorins via carbonyl ylides. On reacting 5,10,15,20-tetraphenylporphyrin with tetracyanoethylene oxide, the corresponding cycloadduct was produced in moderate yield (Scheme 19). It has been reported that the tetracyanoethylene oxide undergoes a first-order thermal electrocyclic ring opening to form the carbonyl ylide in refluxing toluene. The ylide then reacts via a 1,3-dipolar cycloaddition with the dipolarophile to yield a [3+2] adduct.[48]

Isoxazoline-fused chlorins have been synthesised as starting materials for further funtionalisation via chemical transformations of the isoxazoline ring by Li et al.[51] (Scheme 20).

The reaction of 5,10,15,20-tetra(4-chlorophenyl)porphyrin with an excess of 2,6-dichlorobenzonitrile oxide in benzene under reflux resulted in a mixture of three compounds. The chlorin was isolated as the major product in 53% yield. Interestingly, the reaction of porphyrins possessing electron-withdrawing aryl groups increased the yield, but porphyrins bearing electron-donating groups gave no cycloaddition adducts. This result obeyed the theory of reactivity of normal alkenes to nitrile oxide, whereby electron-withdrawing alkenes favour the cycloaddition reaction.[47]

3.3. Bergman cyclisation of porphyrin diynes

Only recently the Bergman cyclisation[52,53] has been applied to the synthesis of porphyrins bearing fused exocyclic rings.



Scheme 17. Synthesis of benzoporphyrins via [4+2] cycloaddition; reaction conditions: (i) dimethyl acetylenedicarboxylate, toluene, reflux; (ii) reflux overnight; (iii) continuous heating or reflux for 30 min in 1,2-trichlorobenzene.

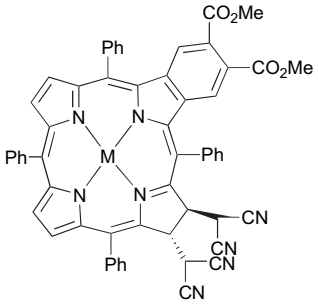
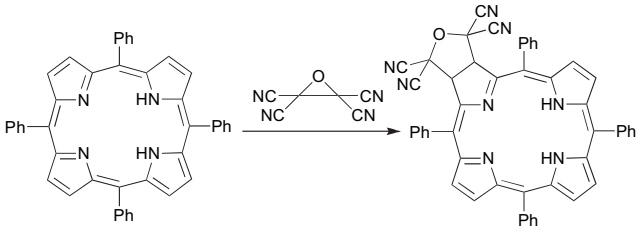


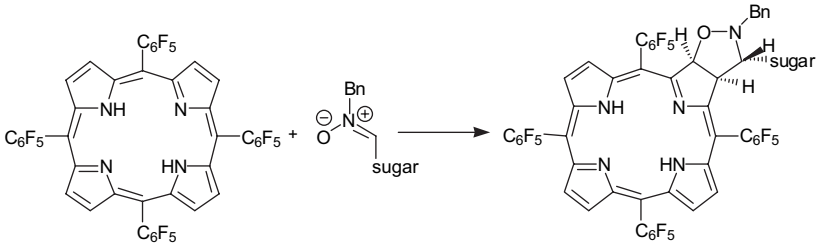
Figure 3. Benzochlorins generated by conjugate addition of malonitrile.



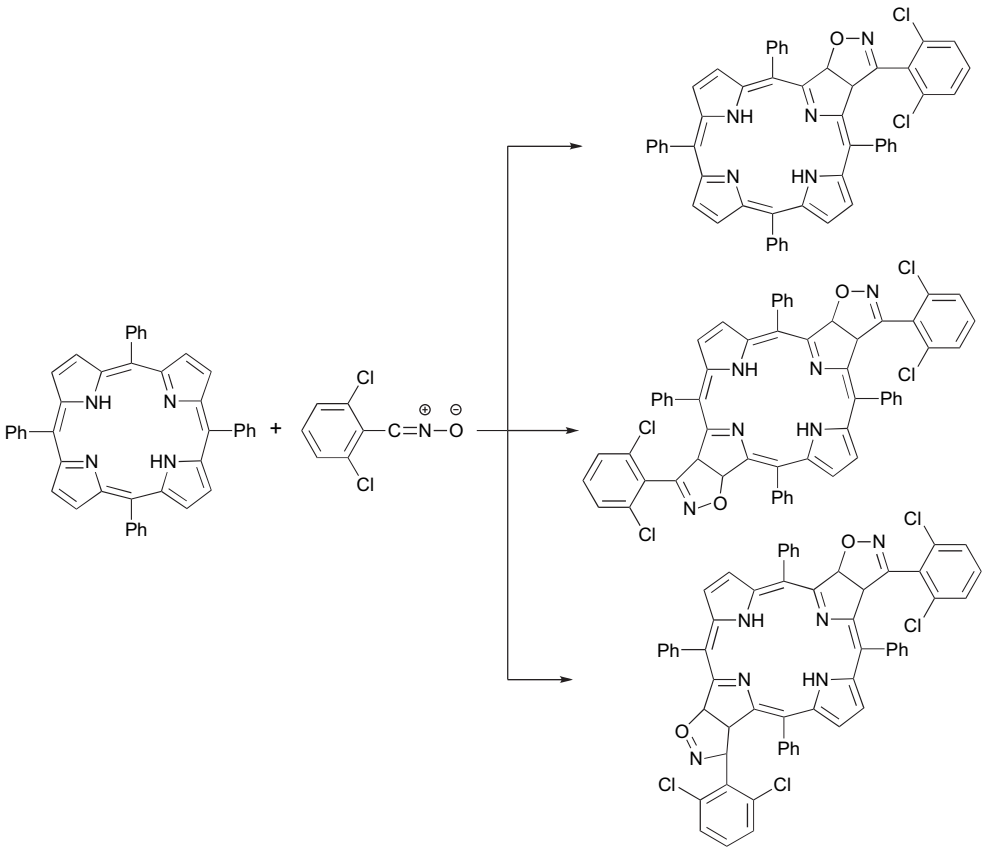
Scheme 19. 1,3-Dipolar cycloaddition of porphyrin and carbonyl ylide.

This method is described as a 'thermal benzoannulation' whereby the cyclisation of an enediyne is accomplished by heating the reaction mixture. The methodology was based on the realisation that two adjacent acetylenic moieties attached to the β-positions might behave in a similar fashion to components of an enediyne and cyclise under Bergman-type conditions. Smith et al.[54] proposed this theory and successfully demonstrated it experimentally. The first step in the synthesis involved a Pd(0)-catalysed cross-coupling[55] reaction with alkynyl-trimethylstannanes. In the second step the trimethylsilyl groups were cleaved, and then, finally, the porphyrin diyne was heated to reflux in cyclohexadiene/chlorobenzene at 190 °C to yield a picenoporphyrin. According to the literature, this was not the anticipated result, as only monobenzoporphyrin products were expected. In reality the reaction proceeded via a cascade tandem radical cyclisation to yield a multicarbocycle (Scheme 21).[54]

Zaleski et al.[56] discovered that this cascade tandem radical cyclisation could be performed at room temperature in the presence of DDQ. This indicated that the dehydrogenation step is rate limiting. To prevent the participation of *meso*-phenyl substituents in the reaction pathway, Spence et al.[57]

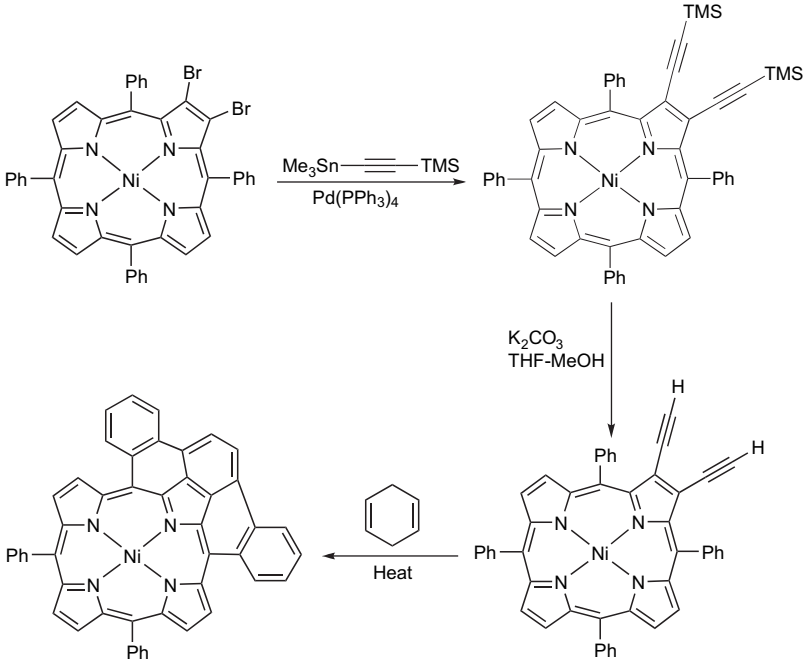


Scheme 18. Synthesis of glycoconjugated isoazolidine-fused chlorins.

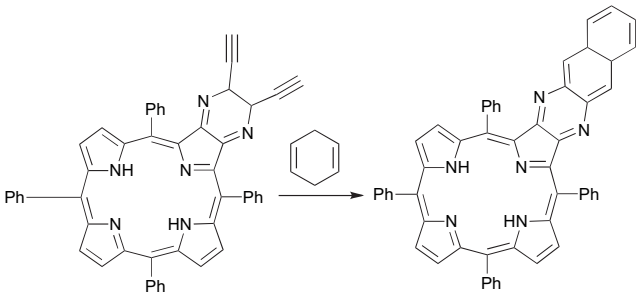


Scheme 20. Synthesis of isoxazoline-fused chlorins and bacteriochlorins.

prepared a porphyrin–enediyne that contained a conjugate quinoxaline spacer[58] between the enediyne core and the porphyrin macrocycle (Scheme 22). This spacer ensures that the endiyne is far enough away from the aromatic pathway of the macrocycle, thus suppressing tandem cyclisation to a picenoporphyrin.[54]



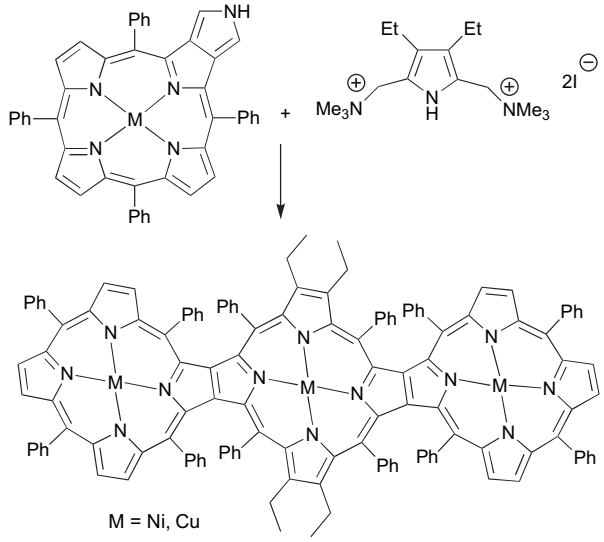
Scheme 21. Tandem radical cyclisation of 2,3-dialkynylporphyrins.



Scheme 22. Bergman cyclisation of porphyrin–enediyne.

4. Fused-ring systems incorporating multiple porphyrins

The syntheses of such covalently linked porphyrins have been investigated in order to examine their unique photoelectronic properties and potential applications as mimics of light harvesting in photosynthesis, and also as electron-transfer moieties in molecular wires.[59] Tetramerisation of pyrroloporphyrins is one possible way of producing cruciform porphyrins, but steric congestion undermines the viability and application of this method.[5] A synthesis of fully or directly fused oligoporphyrins that share a common extended π-electron system has been developed by Smith et al.[60] By reacting a nucleophilic, sterically hindered pyrrole with a pyrroloporphyrin, a porphyrin trimer was produced (Scheme 23).



Scheme 23. Synthesis of fused oligoporphyrins.

A cruciform pentamer was synthesised by Smith et al. [61] by acid-catalysed tetramerisation of a less sterically hindered 2*H*-dihydroisoindoloporphyrin. The pentamer (Scheme 24) contained two one-carbon linkages or 'spacers' between the pyrrolic rings and the porphyrin. The corresponding pyrroloporphyrin was synthesised via a [4+2] cycloaddition reaction of 1,1-sulfolano[3,4-*c*]pyrrole[36] and the *meso*-tetraarylporphyrin. This was then followed by acid-catalysed tetramerisation of the pyrroloporphyrin, and treatment of the pentamer with an excess of DDQ to give the fully conjugated pentamer.[61]

Recently, the properties of *meso–meso*-linked porphyrin arrays have been noted as possible photonic wires.[62–64] Osuka et al.[65] linked Cu(II)-porphyrins at both the *meso*- and β-positions with 2 equiv of tris(4-bromo-phenyl)aminium hexachloroantimonate (BA-HA) in C_6F_6 at room temperature for two days resulting in the triply linked diporphyrins in 62 and 6% yields (Fig. 4).

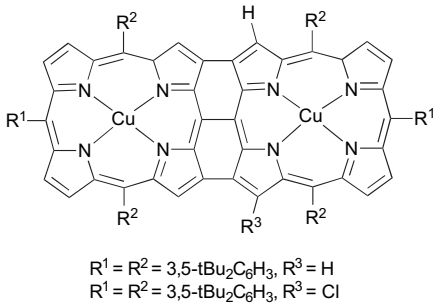
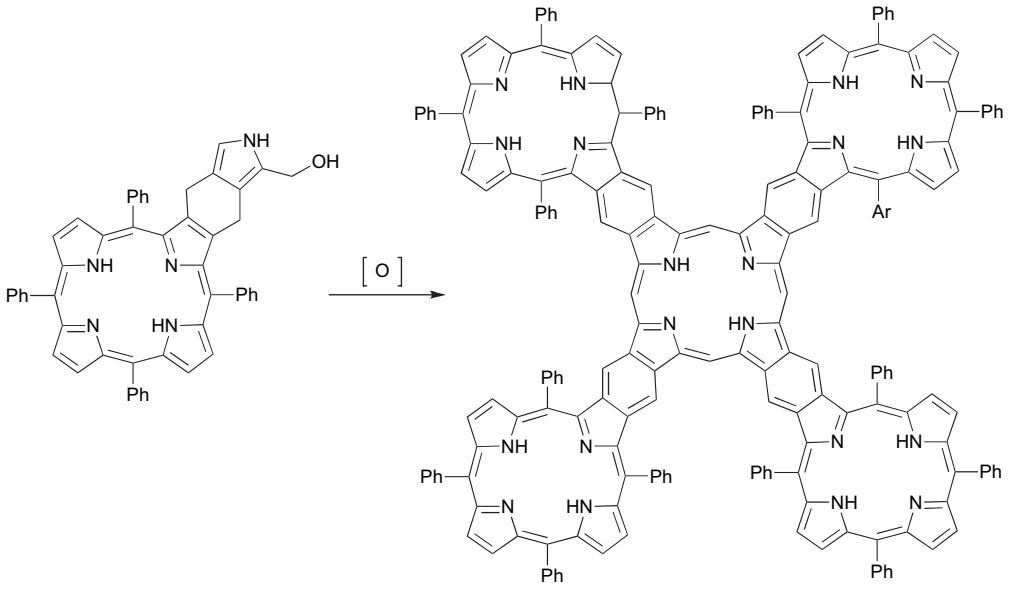


Figure 4. Triply fused diporphyrin.



Scheme 24. Synthesis of cruciform porphyrin pentamers.

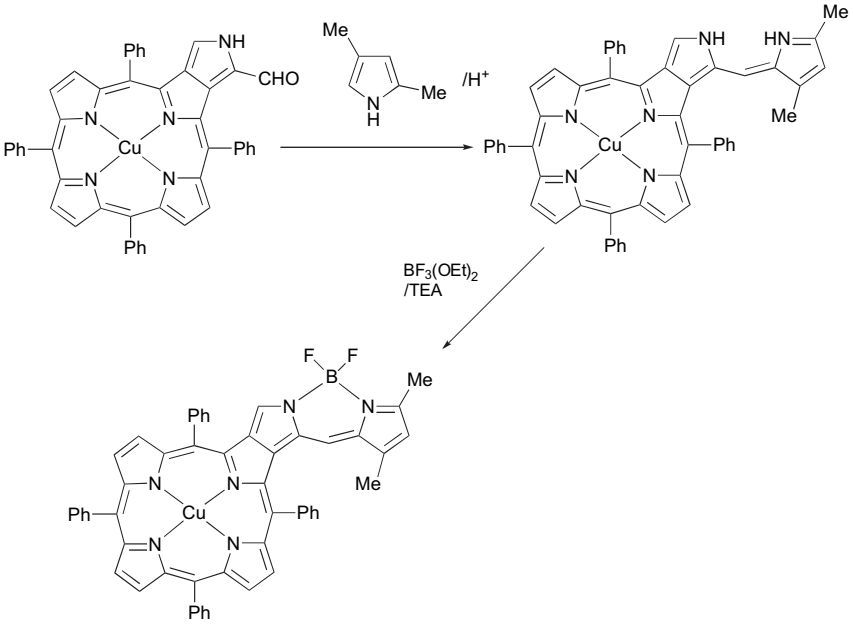
5. Use of porphyrins bearing fused rings to assemble heterodimeric systems

5.1. Fused porphyrin–BODIPY dyads

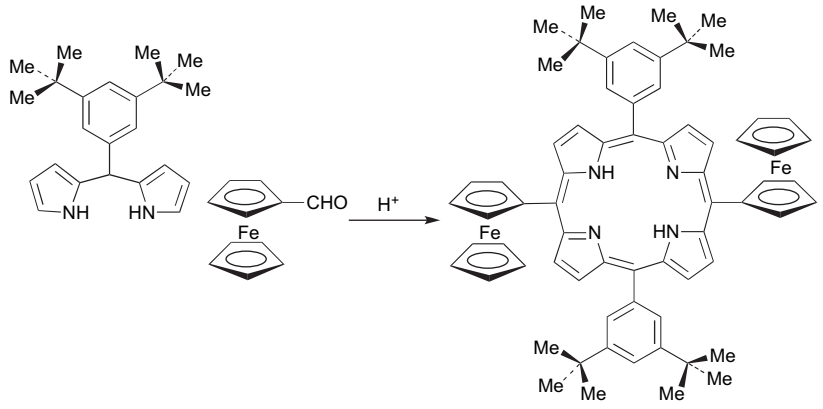
Fused porphyrin macrocycles are of great interest as potential molecular wires.[66–68] Smith's group had focused its attention on heterodyads, in which a porphyrin and another chromophore are fused through two neighbouring β-carbons, therefore giving rise to the extended conjugation of the aromatic π-system.[69] Among the different chromophores of interest, 4,4-difluoro-4-bora-3a,4a-diaza-*s*-indacene (BODIPY®) and related dyes had already been investigated for several applications.[70] In general, the pyrroloporphyrin[40] was used as the starting material in the synthesis of the fused BODIPY® and porphyrin moieties. The synthesis of CuTPP-BODIPY® began with the formylation of Cu-pyrroloporphyrin (Scheme 25).[71] The formylation of pyrroles is generally carried out by the Vilsmeier reaction, ($POCl_3$ and DMF), but the Vilsmeier reagents have been well documented as reacting with the β-positions of tetraarylporphyrins.[72] TFA and trimethyl orthoformate were used to selectively functionalise the pyrrole subunit.[73] The acid-catalysed condensation of formylpyrroloporphyrin gave dipyrromethenoporphyrin. Finally, treating the dipyrromethenoporphyrin with boron trifluoride etherate yielded the BODIPY® complex under basic conditions.[71]

5.2. Fused metallocenoporphyrins

In this final section, the synthesis of porphyrin/metallocene dyads will be discussed. The most commonly reported studies of porphyrin/metallocene dyads illustrate the metallocene part attached to the *meso*- or β-positions of the porphyrin through spacers,[74–82] or even directly through a central metal ion,[83] and the more uncommon direct linkages through a C–C bond at the *meso*-position have also been reported.[84,85] Smith et al. have synthesised a ferrocenylporphyrin via their previously reported work on Heck-type reactions and also via a 2+2 condensation (Scheme 26).



Scheme 25. Synthesis of CuTPP-BODIPY®.



Scheme 26. Synthesis of a 5,15-ferrocenylporphyrin.

Smith's group further investigated methods to synthesise the fused metallocenoporphyrins. Their aim was to synthesise the target compound (Fig. 5) via the corresponding tetrapropanoporphyrin.[86] The method used to obtain the precursors, however, had its limitations.[87]

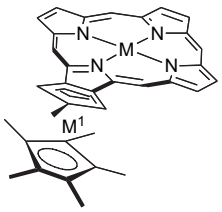
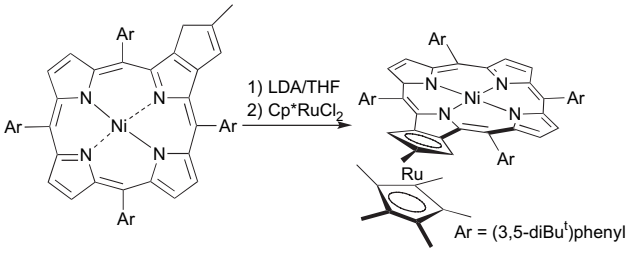


Figure 5. Fused metallocenoporphyrin.

After a consideration of the work by Holzapfel and van der Merwe,[88] Smith et al. subjected 2-nitro-5,10,15,20-tetra(3,5-di-*tert*-butylphenyl)porphyrinatonickel(II) to a palladium(0)-catalysed [3+2] cycloaddition with 2-[(trimethylsilyl)methyl]-2-propen-1-yl acetate, which gave the corresponding starting material. Formation of the anion by treatment with LDA and then addition of the Cp* resulted in the fused ruthenocenoporphyrin (Scheme 27).[69] Treatment of the methylcyclohexenylporphyrinatonickel(II) starting material with $FeCl_2$ yielded a bisporphyrinferrocene.[89,90]



Scheme 27. Synthesis of metallocenoporphyrins.

6. Conclusions

Reactions leading to porphyrins bearing fused rings have provided a wide range of novel and previously unknown macrocycles for study. The understanding of the spectroscopic, electrochemical and biological properties of porphyrin containing proteins and assemblies has thus been expanded at the fundamental level. On a practical level this has also led to the development of many new products, a particularly noteworthy example being the Diels–Alder adduct obtained from the reaction of protoporphyrin IX dimethyl ester with dimethyl acetylenedicarboxylate[91] followed by base-catalysed isomerisation and partial hydrolysis. The resulting chlorin bearing a six-membered ring fused to the A pyrrolic ring has now been developed into a successful drug for the photodynamic treatment of age related macular degeneration by QLT Inc. and Novartis. Under the trade name Visudyne® world-wide sales for 2005 were reported to be US$484.[92] In light of these intellectual and financial incentives it seems likely that this area of porphyrin synthetic chemistry will continue to be of great interest in the foreseeable future.

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Biographical sketch

Simon Fox was born in Beverley, UK. He graduated from the University of Hull with a B.Sc. (Hons) in Chemistry in 2002, after which he immediately started his Ph.D. under the supervision of Dr R. W. Boyle. During his time as a member of the Photomedicine and Photobiology group at the University of Hull, he investigated the synthesis of novel porphyrins bearing fused rings and related studies. He completed his doctoral thesis in 2005 and was awarded his Ph.D. in 2006.

Ross W. Boyle received his B.Sc. (Hons) in Chemistry and Ph.D. in Organic Chemistry from Paisley College of Technology under the supervision of Professor T. G. Truscott. Following this he spent six years in Canada, first as a postdoctoral research fellow in the MRC Group in Radiation Sciences, University of Sherbrooke with Professor J. E. van Lier, and then at the Department of Chemistry, University of British Columbia, working with Professor D. Dolphin. In 1996 he took up his first academic post as a Lecturer in Bioorganic Chemistry at University of Essex and in 2000 he moved to his current post of Reader in Biological Chemistry at Department of Chemistry, University of Hull. Research interests include porphyrin synthetic chemistry, photodynamic therapy and the application of light active molecules to image and modify biological systems.