Porphodimethylidenes from porphyrin-fused 3-sulfolenes—versatile porphyrin dienes for cycloadditions

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A porphyrin with a β-fused 3-sulfolene on one of the pyrroles acts as a porphodimethylidene precusor which can be used for a variety of Diels–Alder cycloaddition reactions.

The need for molecular assemblies that will match the increasingly sophisticated design demands of supramolecular chemistry has been the motive for the production of modular components that can be assembled readily and predictably. This is especially so for custom-designed porphyrins which can be utilised in an impressive variety of systems.[1]

For some applications it has been necessary to constrain rotational freedom of the porphyrin nucleus within the assembly, and this has most effectively been achieved by a 1,2-linkage at adjacent β-pyrrole positions. Hence the construction of many rigid porphyrin-containing systems has commonly utilised Schiff base formation with preformed porphyrin diamines or diones.[2] However, the Diels–Alder reaction is a classic cycloaddition reaction which leads to fused ring systems and is ideally suited to the construction of well-defined molecular assemblies with limited flexibilities.

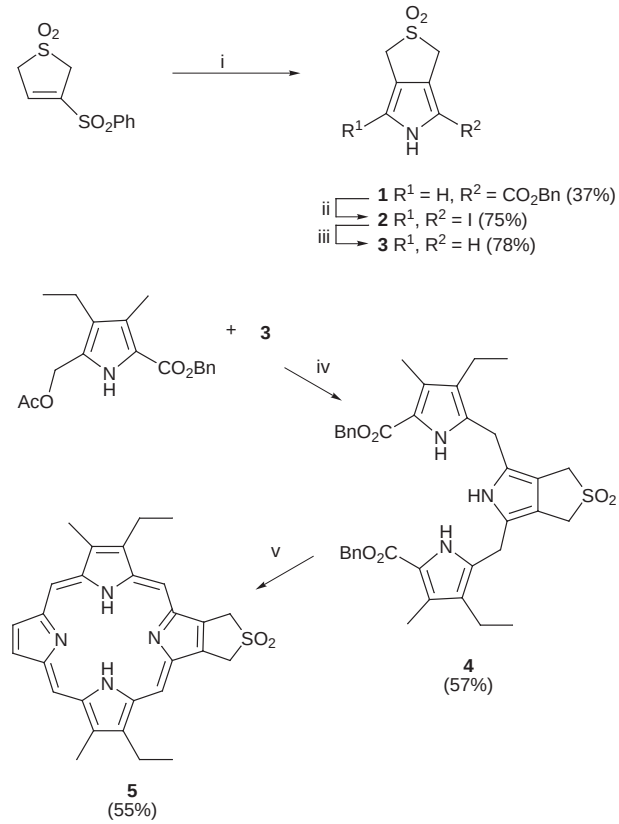
There have been few reports of Diels–Alder chemistry involving porphyrins and related macrocycles. Of these, several have used β-vinyl porphyrins as the diene,[3] and a related tetramethine-bridged porphyrin has also been shown to undergo cycloaddition reactions.[4] Alternatively, tetraaryl porphyrins have been used as dienophiles, giving a mixture of products with reactive dienes under forcing conditions,[5] and Diels-Alder methodology has been used in the construction of benzoporphyrins.[6] More recently, *N*-substituted β-fused pyrroloporphyrins have been used as dienes for certain cycloaddition reactions.[7] We have shown that cycloaddition reactions provide an excellent method for geometric control in certain made-to-order rigid assemblies which incorporate porphyrins.[8]

Aromatic fused 3-sulfolenes have been used as precursors for highly reactive *o*-quinodimethanes.[9] Thermal extrusion of sulfur dioxide from the sulfolenes is usually performed in the presence of a dienophile so that the quinodimethane is trapped as a Diels–Alder adduct.[10] While *N*-substituted pyrrole-fused 3-sulfolenes have been used as a source of annelated pyrroles,[11] some of which have been subsequently used in the synthesis of pyrroloporphyrins[12] and symmetrical tetra-substituted porphyrins,[6] reported here is the first example to the best of our knowledge of a porphyrin with a β-fused sulfolene that allows subsequent chemistry at only *one* of the pyrroles. This is a key precusor for a range of cycloadducts resulting from Diels–Alder reaction of the intermediate porphodimethylidene which is formed by elimination of sulfur dioxide under mild conditions.

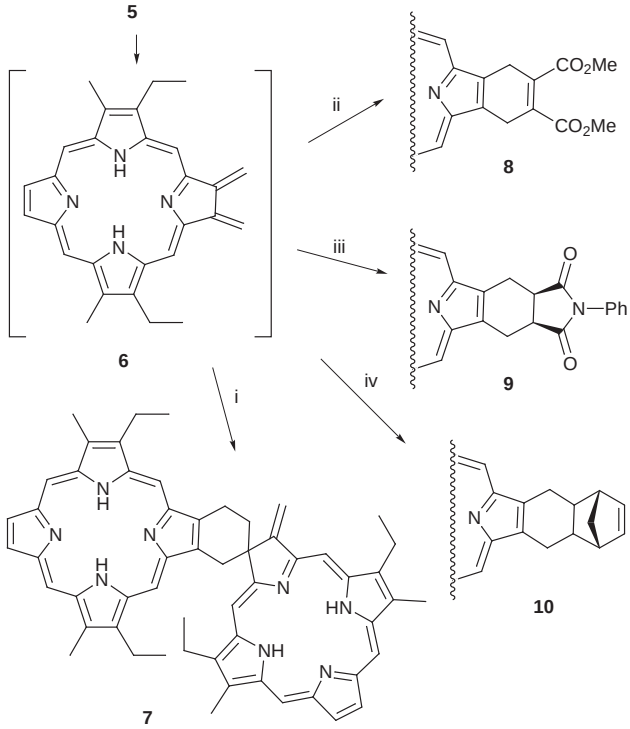
The pyrrole-fused 3-sulfolene **1** was prepared by a modification of the Barton–Zard reaction[13] using benzyl isocyanoacetate and 3-phenylsulfonyl-2,5-dihydrothiophene 1,1-dioxide (Scheme 1),[14] in an analogous manner to that for the corresponding ethyl ester reported by Vicente *et al*.[6] Hydrogenolysis (H_2, 10% Pd–C) and oxidative iodination (I_3^-, room temperature, 2 h) to give **2** followed by reduction (H_2, 10% Pd–C, NaOAc, 3 atm) produced **3**. Condensation (Montmorillonite clay, CH_2Cl_2, room temperature, 10 h) with benzyl 5-acetoxymethyl-4-ethyl-3-methylpyrrole-2-carboxylate resulted in the tripyrrane **4**, which was subsequently hydrogenolysed and subjected to a '3 + 1' porphyrin synthesis[15] with pyrrole-2,5-dicarbaldehyde (TFA, CH_2Cl_2, room temperature, 2 h, followed by DDQ, 1 h) to form the desired porphyrin **5**.†

While **5** is indefinitely stable at ambient temperatures, on heating above 80 °C it readily loses SO_2 to form the reactive porphodimethylidene **6**. Although it was not possible to isolate **6**, it could be trapped as Diels–Alder adducts in the presence of suitable dienophiles. In the absence of a dienophile and at moderate temperatures (80–110 °C, toluene) it cleanly produced the dimer **7**.

Compound **7** is analogous to the previously identified dimeric product formed from *o*-quinodimethane itself,[9] and its structure was established from its ^{1}H NMR spectrum and mass spectrum [*m/z* 841.5 $(M + H)^+$]. In particular the NMR spectrum (C_6D_6) showed a clear lack of simple symmetry, and individual



Scheme 1 *Reagents and conditions*: i, $NCCH_2CO_2Bn$, KOBu^t, THF, −15–25 °C, 2 h; ii, H_2, Pd–C (10%), 3 atm, 7 h, room temp., then I_2, KI(aq. EtOH), 5 h, room temp.; iii H_2, Pd–C (10%), NaOAc, 3 atm, 22 h, room temp.; iv, Montmorillonite clay K-10, CH_2Cl_2, N_2, 10 h, room temp.; v, H_2, Pd–C (10%), 3 atm, 3 h, then pyrrole-2,5-dicarbaldehyde, TFA, CH_2Cl_2, 2 h, then DDQ, 1 h, room temp.



Scheme 2 *Reagents and conditions*: i, Δ, toluene, 80–110 °C, 2 h; ii, $MeO_2CC{\equiv}CCO_2Me$, Δ, toluene, 110 °C, 4.5 h; iii, *N*-phenylmaleimide, Δ, 85 °C, 3 h; iv, norbornadiene, Δ, 80 °C, 2 h.

resonances for each of the substituents on the porphyrin and chlorin rings.† For example, there are four distinct ethyl and methyl resonances, two AB quartets for the β-pyrrole protons, eight singlets for the *meso*-protons, and two NH singlets at high field. The exocyclic methylene is defined by two singlets (δ 6.16 and 6.95) significantly deshielded by the neighbouring porphyrin while the deshielded single bridging methylene is a clear AB quartet at δ 5.18 and 5.56. The remaining ethylene of the spiro-linked cyclohexene bridge is a series of complex multiplets at δ 3.05, 3.34 and 4.68. The UV-visible spectrum of **7** is a composite of both porphyrin and chlorin-type rings and not surprisingly shows little evidence of electronic communication between the linked macrocycles.

On heating **5** in toluene at 80–110 °C in the presence of various dienophiles shown in Scheme 2, the corresponding Diels–Alder adducts were isolated in good yields (65–95%).† The C_{2_v} symmetry of each is clear from the ^{1}H NMR spectra. In the case of **10**, only a single stereoisomer was isolated, and both a lack of vicinal H, H-coupling and no significant shielding of the ethylenic protons indicates it to be the *exo*-product (molecular modelling indicates a close proximity of the ethylenic protons to the shielding region of the porphyrin in the *endo*-isomer, although the environments of the bridge methylenes are little different in either isomer). Each of these suggests considerable potential as building blocks for higher level structures. For example **8** can be utilised in further cycloaddition reactions using its activated double bond, **9** *via* a variety of associated *N*-substituted derivatives can provide a single attachment point on a *meso*-unsubstituted porphyrin, and the formation of **10** indicates the possibility for more elaborate architectures. Although these few reactions demonstrate the utility of **5**, its potential is clearly much more extensive and can now be explored.

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Notes and references

† *Selected data* for **5**: δ_H($CDCl_3$) −4.0 [2H, br s, NH], 1.84 [6H, t, CH_2CH_3], 3.70 [6H, s, CH_3], 4.12 [4H, q, CH_2CH_3], 5.67 [4H, s, CH_2], 9.38 [2H, s, pyrrole β-H], 9.87 [2H, s, *meso*-H], 10.21 [2H, s, *meso*-H]; λ_{max}($CHCl_3$)/nm 392, 502, 539, 561; ν_{max}/cm^{-1} 1216(S=O); *m/z* (FAB) 485.20074 (M^+ + 1). For **7**: δ_H(300 MHz, C_6D_6, dashed (′) numbering for chlorin ring) −1.62 [2H, br s, N′H], −2.76 [2H, s, NH], 0.82 [3H, t, C(7′)CH_2CH_3], 1.67 [3H, t, C(18′)CH_2CH_3], 1.76 [3H, t, C(13)CH_2CH_3], 1.95 [3H, t, C(2)CH_2CH_3], 2.93 [3H, s, C(8′)CH_3], 3.28 [3H, s, C(17′)CH_3], 3.34 [3H, s, C(12)CH_3], 3.48 [3H, s, C(3)CH_3], 2.83 [2H, m, C(7′)CH_2CH_3], 3.05 [1H, m, C(22′)CH_2], 3.34 [1H, m, C(22′)CH_2], 3.84 [4H, m, C(18′, 13)CH_2CH_3], 4.11 [2H, m, C(2)CH_2CH_3], 4.68 [2H, m, C(21)CH_2CH_2], 5.18 [1H, d, *J* 21, C(23) CH_2], 5.56 [1H, d, *J* 21, C(23) CH_2], 6.16 [1H, s, C(3′)=CH_2], 6.95 [1H, s, C(3′)=CH_2], 9.21 [1H, d, C(7)H], 9.23 [1H, d, C(12′)H], 9.45 [1H, d, C(8)H], 9.46 [1H, d, C(13′)H], 9.50. 9.75, 9.80, 9.87, 10.20, 10.27, 10.38, 10.48 [1H each, s, *meso*-H′s]; *m/z* (FAB) 841.47036 (M^{+}+1). For **8**: δ_H($CDCl_3$) −4.01 [2H, br s, NH], 1.86 [6H, t, CH_2CH_3], 3.68 [6H, s, CH_3], 4.08 [6H, s, OCH_3], 4.12 [4H, q, CH_2CH_3], 5.10 [4H, s, CH_2], 9.36 [2H, s, pyrrole β-H], 9.93 [2H, s, *meso*-H], 10.17 [2H, s, *meso*-H]; *m/z* (EI) 562.25886 (M^+). For **9**: δ_H($CDCl_3$) −3.95 [2H, br s, NH], 1.88 [6H, t, CH_2CH_3], 3.68 [6H, s, CH_3], 4.15 [6H, m, CH_2CH_3, CH], 4.30, 4.36 [2H, m, CH_2], 4.84 [2H, d, CH_2′], 6.86 [2H, m, Ar–H], 7.10 [3H, m, Ar–H], 9.38 [2H, s, pyrrole β-H], 10.11 [2H, s, *meso*-H], 10.19 [2H, s, *meso*-H]; *m/z* (EI) 593.27971 (M^+). For **10**: δ_H($CDCl_3$) −3.90 [2H, br s, NH], 1.84 [6H, t, CH_2CH_3], 1.86 [1H, d, *J* 10, CH_2], 2.35 [1H, d, *J* 10, CH_2], 2.57 2H, m, CH], 3.13 [2H, s, CH], 3.45 [2H, dd, CH_2], 3.64 [6H, s, CH_3], 4.12 [4H, q, CH_2CH_3], 4.69 [2H, dd, CH_2], 6.38 [2H, s, =CH], 9.40 [2H, s, pyrrole β-H], 10.09 [2H, s, *meso*-H], 10.18 [2H, s, *meso*-H].

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