

Ready Syntheses of Benzoporphyrins *via* Diels–Alder Reactions with Protoporphyrin IX

Alan R. Morgan, Veronica Scherrer Pangka, and David Dolphin

Department of Chemistry, University of British Columbia, 2036 Main Mall, Vancouver, B.C. V6T 1Y6, Canada

Reaction of protoporphyrin IX dimethyl ester with strongly activated dienophiles causes a Diels–Alder reaction to occur with the porphyrin periphery; elimination of the angular methyl group from these adducts gives monobenzoporphyrins.

The occurrence of monobenzoporphyrins as constituents of petroleum deposits was first proposed in 1967¹ and has recently received experimental support by Clezy *et al.*^{2,3} who have prepared benzoporphyrins from pyrrolic precursors and showed them to have rhodo-type electronic spectra[†] similar to some petroporphyrins. It has been suggested³ that an intramolecular cyclization of two β -substituents to a cyclohexane moiety followed by dehydrations and dehydrogenations would account for the benzo ring formation. Baker and Palmer,⁴ on the other hand, suggested that a Diels–Alder reaction between the vinyl and β - β' double bonds of a tetrapyrrolic macrocycle and some natural dienophile, such as plastoquinone, could initiate benzo ring formation.

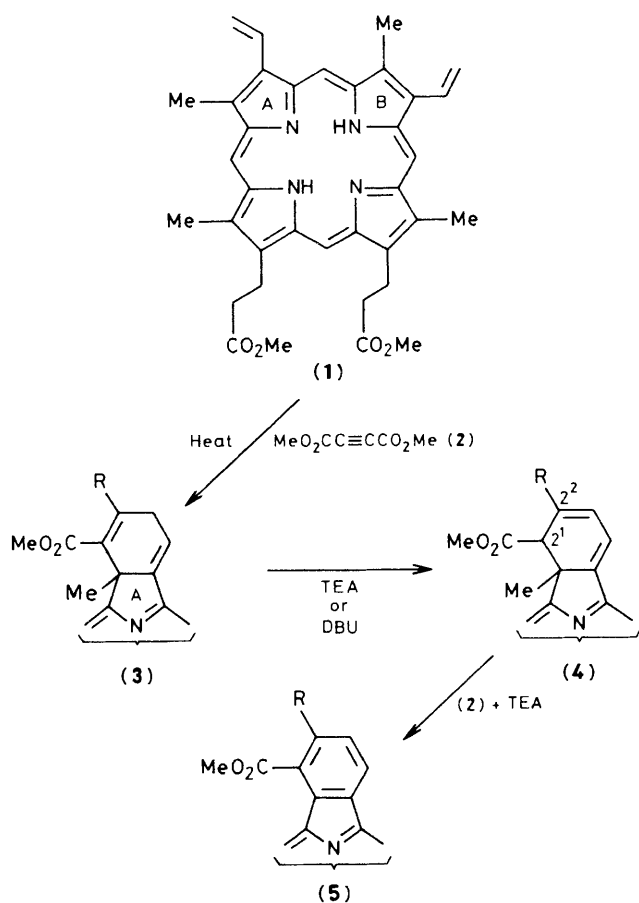
We report here two facile syntheses of monobenzoporphyrins both starting with Diels–Alder reactions on protoporphyrin IX dimethyl ester (**1**). Johnson and his colleagues^{5,6} reported that (**1**) reacted with both tetracyanoethylene (TCNE) and acetylenedicarboxylic esters involving both vinyl-bearing groups of rings A and B to give only the corresponding isobacteriochlorins. We subsequently found that this was not the case with TCNE,⁷ nor, as we show here, with acetylenes.

Reaction of (**1**) with dimethyl acetylenedicarboxylate (**2**) gave the corresponding 4 + 2 addition product [the chlorin (**3**; R = CO₂Me)] in moderate yield[‡] (Scheme 1). Treatment of this adduct with excess of dienophile led only to the recovery of (**3**) with no isobacteriochlorin formation. Treatment of (**3**) with triethylamine (TEA) brought about the quantitative rearrangement of (**3**) to (**4**) (R = CO₂Me). However, the combination of excess of (**2**) with (**3**), or (**4**), and TEA regenerates a porphyrin, detected by the change in colour from green to red. The visible spectrum was of the rhodo type although band I was unusually strong, a characteristic noted previously for benzoporphyrins. ¹H N.m.r. and mass spectrometry showed that aromatization (with the loss of the angular methyl group) had occurred to give (**5**; R = CO₂Me). Treatment of (**4**) with excess of dienophile in the absence of base causes no further reaction.

When (**3**; R = CO₂Me) is treated with diethyl acetylenedicarboxylate and base the methyl ester (**5**) is still obtained. The role of excess of acetylenedicarboxylic ester appears to be that of an electron acceptor since the yield of benzoporphyrin can be increased from 25 to 60% by replacing the excess of acetylenedicarboxylic ester with *p*-benzoquinone.

[†] In rhodo-type porphyrin spectra the intensity of the four visible bands is III > IV > II > I.

[‡] Reaction occurs to give both ring A and ring B isomers. In every case reported here the two isomers have been isolated and characterized spectroscopically (mass; ¹H n.m.r.).

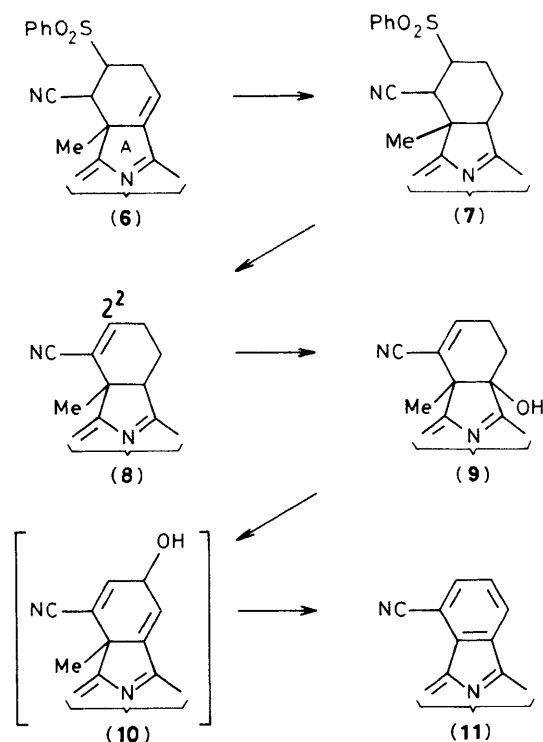


The mechanism by which aromatization occurs is under investigation but we suspect that oxidation of (4; R = CO₂Me) to a cation⁸ followed by base-catalysed elimination of the angular methyl group will be key features of the reaction.

The reaction appears to be a general one. Thus reaction of (1) with methyl β-phenylsulphonylpropiolate⁹ gives the phenylsulphonyl derivative (3; R = SO₂Ph) which under the same conditions of excess of electron acceptor and base gives the benzoporphyrin (5; R = SO₂Ph) which has an optical spectrum similar to that of the methyl ester analogue.

Treatment of (3; R = CO₂Me) with TEA gives the rearranged product (4; R = CO₂Me) with the angular methyl group and adjacent C-2¹ methoxycarbonyl group in a *cis* geometry (determined by nuclear Overhauser enhancement experiments). The *cis*-compound is the kinetically controlled product and treatment of (3) or the *cis*-product (4), from TEA treatment, with 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) gives the thermodynamic *trans*-product. In (3; R = CO₂Me) the methoxy groups at C-2¹ and C-2² appear in the n.m.r. spectrum at δ 4.03 and 3.91 respectively. However, in the DBU rearranged product (4; R = CO₂Me) the methoxy group at C-2¹ now appears at δ 2.95 while that at C-2² remains at δ 3.99.

Compound (3; R = SO₂Ph) exhibits a signal at δ *ca.* 3.65 for the methoxy group. After rearrangement with DBU the *trans*-product (4; R = SO₂Ph) shows the methoxy signal at δ 2.58. These changes in the n.m.r. resonances of the methoxycarbonyl groups in compounds (3) and their rearranged partners (4) show that in (3) and (4) (R = SO₂Ph) the methoxy carbonyl group is at C-2¹ and that the regiospecificity of the Diels-Alder reaction, between (1) and methyl β-phenylsulphonylpropiolate, is as shown in Scheme 1.



A second serendipitous route to benzoporphyrins has also arisen from our studies of Diels-Alder reactions of (1). Treatment of (1) with β-phenylsulphonylacrylonitrile gives the Diels-Alder adduct (6) (Scheme 2). Reduction of (6) using Pd/C-H₂ removed both the exocyclic and vinylic double bonds to give (7). Base-catalysed elimination of the phenylsulphonyl group gives (8). The olefinic proton in (8) at C-2² appears as a triplet (*J* 4 Hz) at δ 6.54. This confirms the regioselectivity of the initial Diels-Alder reaction to generate (6). Attempted chromatography of (8) on silica gel causes autoxidation to give (9). Treatment of (9) with pyridine-acetic anhydride gives the benzoporphyrin (11) which again has a characteristic optical spectrum. A putative intermediate (10) has been isolated from the aromatization reaction. Thus the second reaction differs dramatically from the initial aromatization in being two consecutive oxidation-dehydration reactions.

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