Synthesis of a Porphyrin-2,3-diacrylic Acid using a New '3 + 1' Type Procedure

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A porphyrin with two acrylic acid substituents on the same pyrrole ring was synthesized using a '3 + 1' type procedure; the electronic state of the porphyrin macrocycle was strongly affected by their presence.

The construction of the porphyrin macrocycle can usually be accomplished using one of three different methods: (*i*) stepwise condensation of monopyrroles with aliphatic or aromatic aldehydes; this procedure was initiated and developed by Rothemund[1] and recently reinvestigated by Lindsey *et al.*;[2] (*ii*) '2 + 2' type synthesis based on dipyrromethane or dipyrromethene condensation suggested by MacDonald *et al.*;[3] (*iii*) cyclization of linear tetrapyrrole compounds (bilanes, bilenes and biladienes) obtained by multistep condensation of pyrroles.[4]

To the best of our knowledge, the condensation of tripyrranes with 2,5-diformylpyrroles has not been reported for the synthesis of porphyrins. However, tripyrranes have been used in the preparation of porphyrinoid derivatives which possess a thiophene,[5] furan[5] or pyridine[6] ring replacing one of the pyrrole rings and in the preparation of extended macrocycles such as sapphyrins.[7,8]

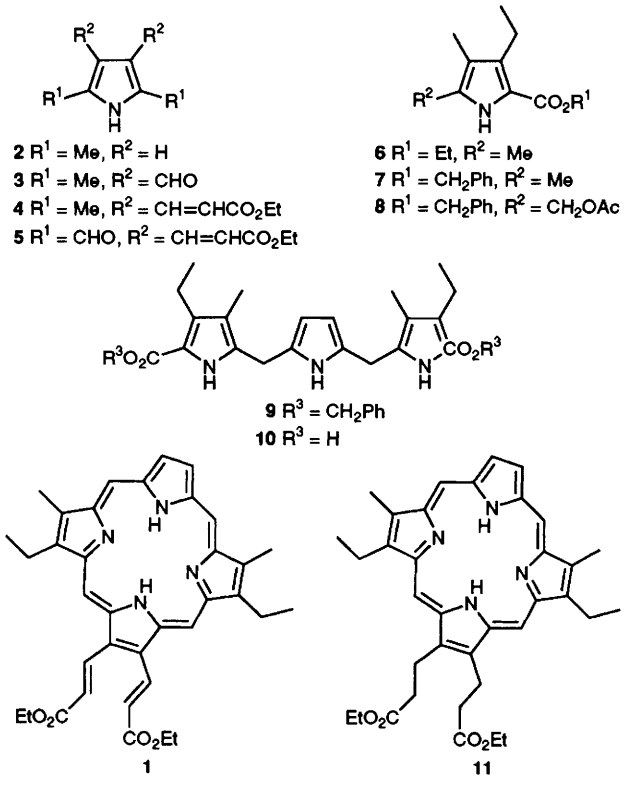
We now report the synthesis of the first example of a porphyrin functionalized by two acrylic acid moieties linked to the same pyrrole, using this '3 + 1' strategy. The presence of these substituents induces an oxorhodo-type UV–visible absorption spectrum.

The new porphyrin **1** was obtained by acid-catalysed condensation of 2,5-diformyl-3,4-bis(ethoxycarbonylvinyl) pyrrole **5** with tripyrrane **10**. The pyrrole **5** was prepared as follows. The commercially available 2,5-dimethylpyrrole **2** was formylated using the Vilsmeier–Haack reaction to give **3** in 62% yield.[9] The diacrylic derivative **4** was directly obtained by treating **3** with triethylphosphonoacetate by a Wittig type reaction in 83% yield. The ^{1}H NMR coupling constants (J_{HH} 16 Hz) of the ethylenic protons of the two acrylic acid groups allow the *trans*-conformation to be assigned to the unique isomer obtained. The α,α′-methyl groups of the pyrrole **4** were then oxidized by $Pb(OAc)_4$–PbO_2 in acetic acid at room temperature for 72 h. Hydrolysis in the presence of water at reflux[10] led to the desired diformylpyrrole **5** in 8.2% yield.

Prepared according to the method described by Chang,[11] compound **6** was firstly benzylated by transesterification and then treated with $Pb(OAc)_4$ to afford the ester **8** in 90% overall yield. Tripyrrane **9** was prepared by condensation of unsubstituted pyrrole (1 equiv.) with **8** (2 equiv.) using an excess of montmorillonite K-10 acidic clay in CH_2Cl_2 at room temperature[12] in 64% yield. Benzyl protecting groups were removed by catalytic hydrogenation (Pd/C 10%) in THF to give the α,α′-dicarboxylic acid tripyrrane **10**.

Cyclization to give the macrocycle was achieved by mixing equimolar amounts of **5** and **10** in CH_2Cl_2 in the presence of trifluoroacetic acid under argon. After neutralization of the reaction mixture by addition of triethylamine, the porphyrinogen was oxidized with DDQ. Porphyrin **1**, purified on a silica gel column (eluent CH_2Cl_2), was obtained in 33% yield. Catalytic hydrogenation of acrylic acid groups over 30% palladium on charcoal in formic acid gave the dipropionic acid porphyrin **11**. All physico-chemical data (elemental analysis, ^{1}H NMR, UV–VIS) were in agreement with the proposed structure.†

The UV–VIS spectrum of porphyrin **1** is characterized in the visible region by two main bands at 564 and 588 nm (bands III and II) and two less intense bands at 518 and 630 nm (bands IV and I) (Fig. 1). This oxorhodo-type absorption pattern[13] with band intensities III > II > IV > I is generally observed when two electron-withdrawing groups are present on diagonally opposite pyrrole rings.[13] On the other hand, when two acrylic acid side chains are linked to adjacent pyrroles, Clezy *et al.*[14] observed a rodho-type visible absorption spectrum (band III > IV > II > I). In contrast, the porphyrin **11** in which the side chains are saturated, shows a UV–VIS absorption spectrum of the well known etio type (band IV > III > II > I). Thus, a striking influence on the Q transitions is exercised not only by



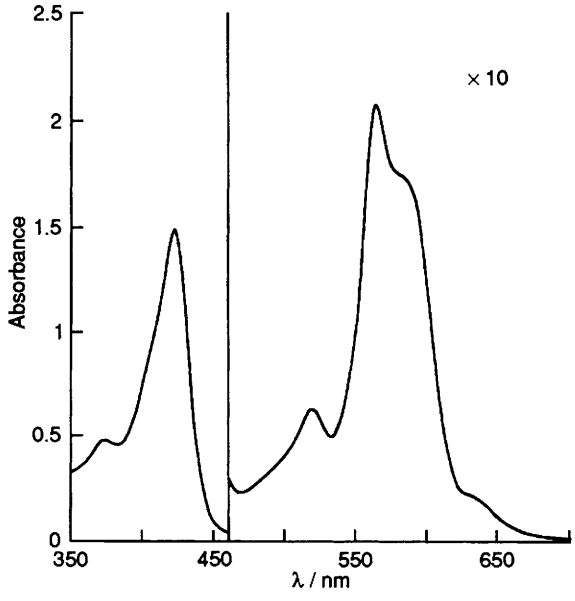


Fig. 1 Optical absorption spectrum of compound **1** in CH_2Cl_2

chemical nature of the substituents but also by the peripheral linkage positions.

In conclusion, we have succeeded in the synthesis of porphyrins employing the '3 + 1' type procedure which could be extended to the preparation of *meso*-unsubstituted porphyrins. However, note that this strategy should be particularly convenient if one component, either the tripyrrane or diformylpyrrole, is symmetrical. We have also demonstrated the possibility of inducing significant bathochromic shifts in the absorption spectra when two acrylic acid groups are linked to the same pyrrole ring.

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Footnote

† *Spectroscopic data*: **5**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.62 (1H, br, NH), 9.96 (2H, s, CHO), 7.86 (2H, d, –CH=), 6.27 (2H, d, =CH–), 4.26 (4H, q, OCH_2Me), 1.32 (6H, t, OCH_2Me). **9**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.85 (2H, br, 2 NH), 9.12 (1H, br, NH), 7.24–7.03 (10 H, m, Ph), 5.86 (2H, d, *J* 2.5 Hz, H_β), 4.41 (4H, s, CH_2Ph), 3.67 (4H, s, CH_2), 2.64 (4H, q, CH_2Me), 1.87 (6H, s, Me), 0.99 (6H, t, CH_2Me). **1**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.11, 10.0 (4H, 2s, H *meso*), 9.28 (2H, s, H_β), 9.22 (2H, d, *J* 16 Hz, –CH=), 7.01 (2H, d, *J* 16 Hz, =CH–), 4.55 (4H, q, OCH_2Me), 4.09 (4H, q, CH_2Me), 3.63 (6H, s, Me), 1.84 (6H, t, OCH_2Me), 1.55 (6H, t, CH_2Me), −4.17 (2H, s, 2 NH); UV–VIS λ_{max} nm (ε cm^{-1} mmol l^{-1}) (CH_2Cl_2) 422 (134.6), 518.5 (5.605) 563.5 (18.824), 588 (15.99), 630 (1.889). **11**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 10.15, 10.10 (4H, 2s, H *meso*), 9.37 (2H, s, H_β), 4.41 (4H, t, $CH_2CH_2CO_2$), 4.19 (8H, m, CH_2Me and OCH_2Me), 3.67 (6H, s, Me), 3.28 (4H, t, $CH_2CH_2CO_2$), 1.88 (6H, t, OCH_2Me), 1.20 (6H, t, CH_2Me), −3.89 (2H, s, 2 NH); UV–VIS λ_{max} nm (ε cm^{-1} mmol l^{-1}) (CH_2Cl_2) 398 (177.6), 499 (10.2), 535 (8.5), 564 (6.2), 621 (1.5).

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