

**Conjugated Macrocycles Related to the Porphyrins.**  
**Part 2 [1]. Further Synthetic and Spectroscopic Studies**  
**on Difuryl Analogs of the Oxophlorins [2]**

Timothy D. Lash\* and Yoek Lin See-Tow Armiger

Department of Chemistry, Illinois State University,  
 Normal, Illinois 61761-6901 U.S.A.

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The synthesis of three difuryl analogs of the oxophlorins is described. In common with the tetrapyrrolic oxophlorins, these compounds favor the keto tautomers and little, if any, of the enol tautomers are present in neutral solutions. Unlike the tetrapyrrolic systems, the difuryl oxophlorins give well resolved nmr spectra. Attempts to extend these studies to the synthesis of dithienyl oxophlorin analogs were unsuccessful.

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Conjugated macrocycles related to the porphyrins have been the subject of extensive investigations [3]. However, analogs of the hydroxyporphyrins/oxophlorins have received little attention. Oxophlorins **1a** are important intermediates in the total synthesis of porphyrins [4], and an iron complex of the hydroxy tautomer **2a** is believed to be an intermediate in heme catabolism [5]. Although the hydroxy tautomers **2a** are fully conjugated aromatic structures, uv, ir and nmr data are consistent with the oxophlorin structure **1a** being the sole species present in neutral organic solvents [6]. However, the hydroxy form is favored by the dications and metal complexes of this system [7].

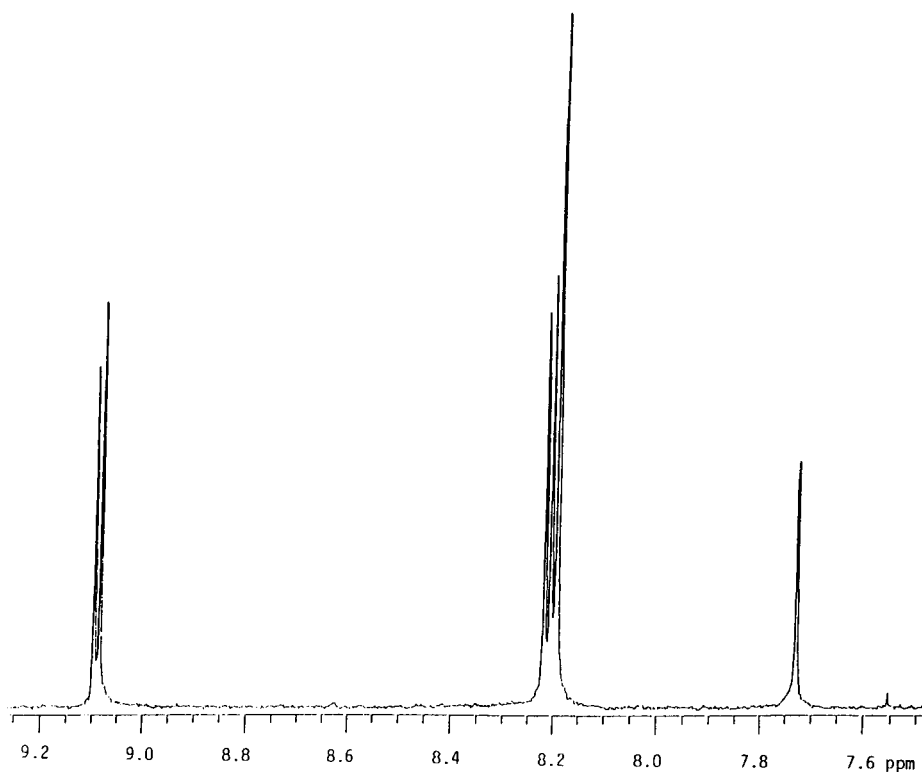
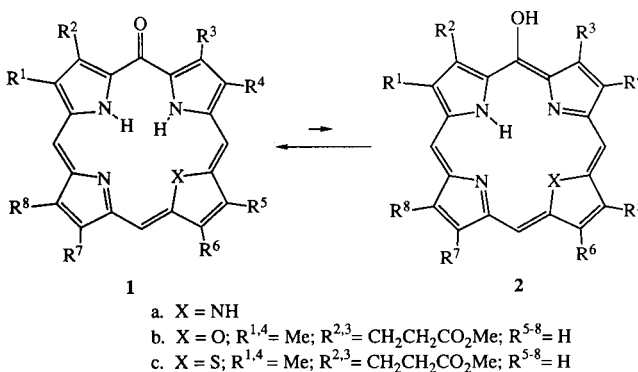
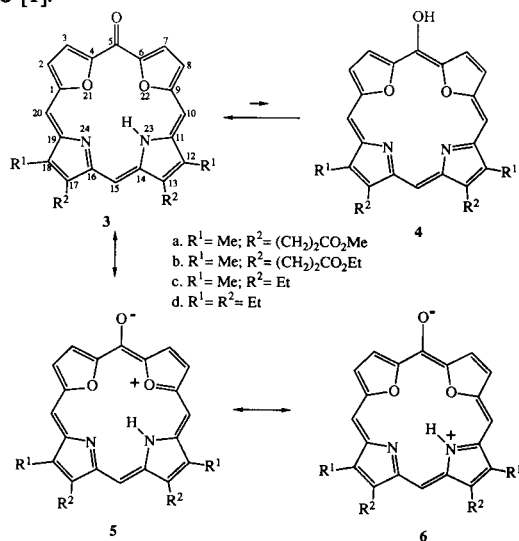


Figure 1. Partial 360 MHz proton nmr spectrum of **3b** in deuteriochloroform.

Furan and thiophene analogs, **1b** and **1c**, have been reported [8] and these compounds also favor the keto tautomers. We have previously reported [1] the synthesis of a difuryl oxophlorin analog **3b**. The ir and uv data suggested that this structure favored the keto form, and little, if any, of the hydroxyporphyrin analog **4** was present in solution. In the ir spectrum of **3a**, a carbonyl absorption close to  $1550\text{ cm}^{-1}$  was observed, which was consistent with the proposed cross-conjugated structure where dipolar resonance contributors such as **5** and **6** are involved. Similar carbonyl absorptions were also reported [6,7] for the tetrapyrrolic oxophlorins **1a**, as well as for the furan and thiophene analogs **1b** and **1c** [8]. Organic solutions containing **1a** are paramagnetic, probably due to the presence of radical species [7]; as a result, nmr spectra are poorly resolved [6,7]. By contrast, the oxophlorin analogs **1b** and **1c** gave well resolved proton nmr spectra [8]. The difuryl oxophlorin analog **3a** was sparingly soluble in organic solvents and in our initial study [1] the proton nmr spectrum was recorded for the dication in deuterated trifluoroacetic acid solution. Subsequently, **3a** was transesterified to give the diethyl ester **3b**. The proton nmr spectrum of **3b** in deuteriochloroform was well resolved (Figure 1) and gave no indication of the hydroxy tautomer **4b** being present [2b]. The chemical shifts were consistent with the keto structure **3b**; the low field doublet at 9.08 ppm corresponds to the two furyl protons flanking the carbonyl function. The nmr and uv data (Figure 2) for the dication of **3a** was fully consistent with the hydroxy structure **7** [1]. However, the monocation of **3a** appeared to favor the keto form **8** [1].



In order to extend these studies, a related oxophlorin analog **3c** was also synthesized [9]. Reaction of 5-bromofuran-2-carboxaldehyde with ethylene glycol in the presence of trace *p*-toluenesulfonic acid gave the cyclic acetal **9** (Scheme 1). Treatment with *n*-butyllithium, followed by reaction with ethyl *N,N*-dimethylcarbamate in ether at

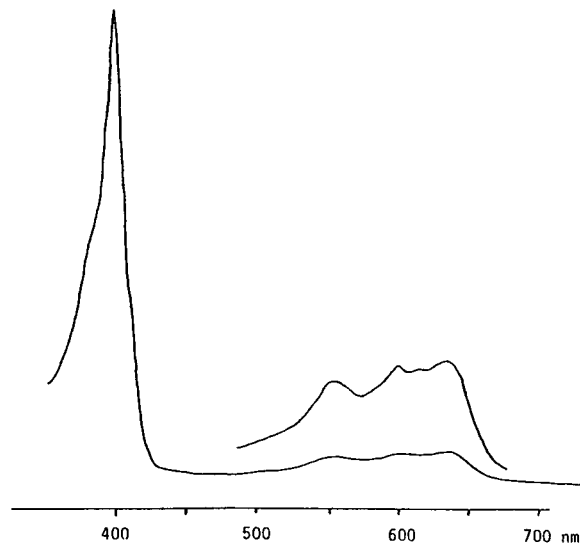
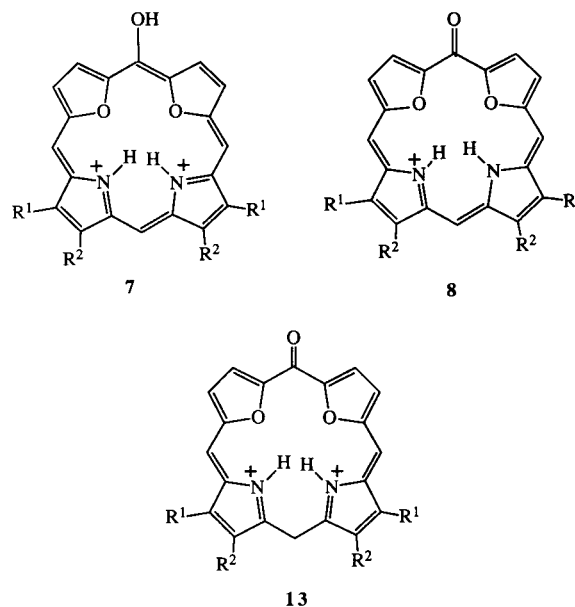


Figure 2.

Uv spectrum of dication **7a** in 10% trifluoroacetic acid-chloroform.

$-20^\circ$ , gave the difuryl ketone **10** [10,11]. Subsequent acid hydrolysis gave the corresponding dialdehyde **11**. The difuryl methanone dialdehyde **11** was condensed with the dipyrromethane dicarboxylic acid **12** in trifluoroacetic acid solution (this is a variation on the MacDonald porphyrin condensation [12]) to give **3c** in 44% yield. The lower yield previously reported [1] for **3a** was attributed to losses during chromatography due to the low solubility of



this compound. The spectral characteristics of **3c** were similar to those previously noted for **3a** [1]; in the ir spectrum, a carbonyl absorption was observed at  $1552\text{ cm}^{-1}$ . Macrocycle **3c** was reasonably soluble in organic solvents,

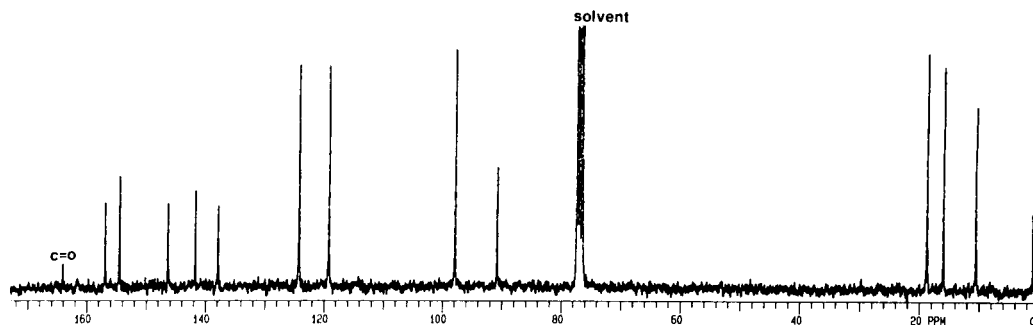


Figure 3. Carbon-13 nmr spectrum of **3a** in deuteriochloroform.

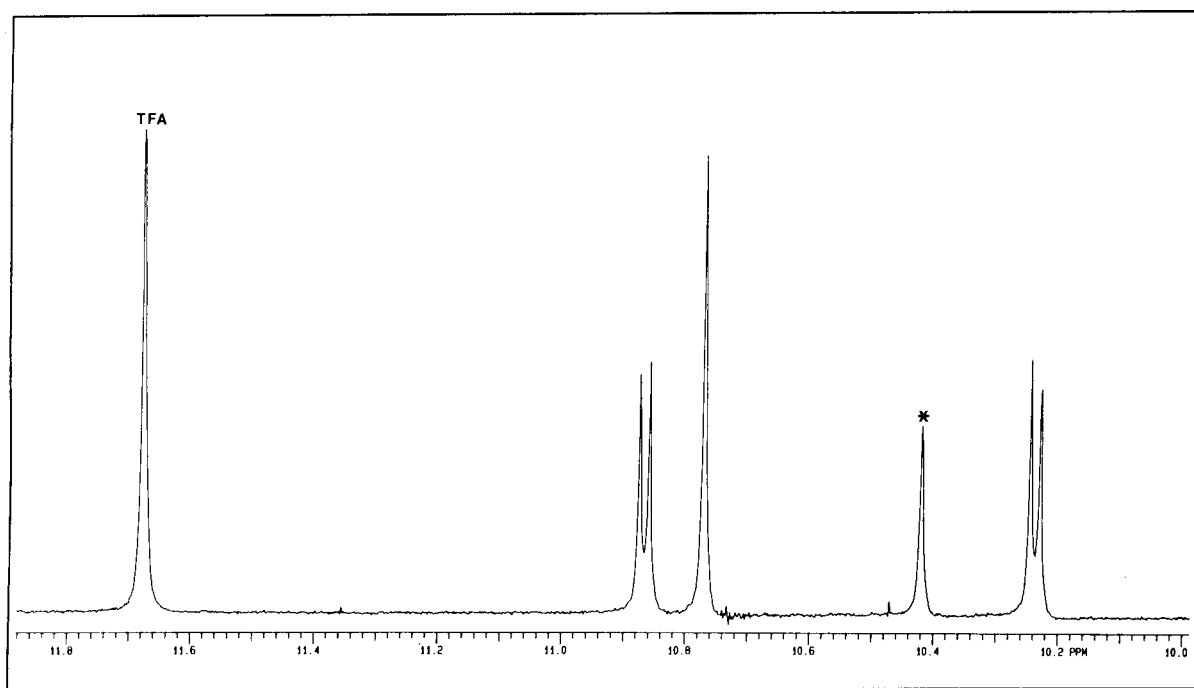
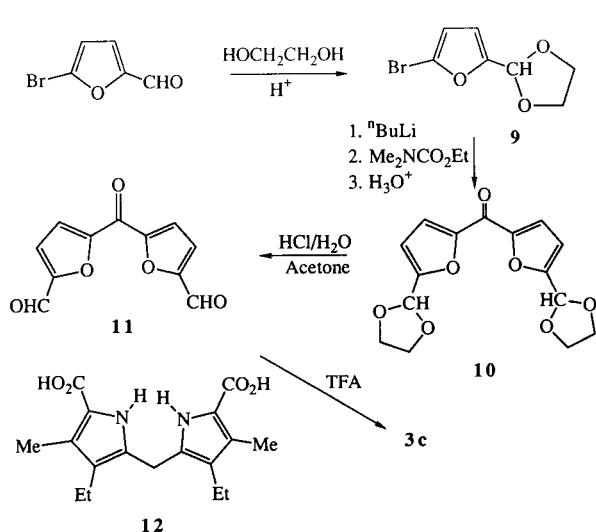


Figure 4. Partial 300 MHz proton nmr spectrum of dication **7c** in 20% trifluoroacetic acid-d-deuteriochloroform. \*The signal due to the C-15 methine proton is gradually lost due to deuterium exchange.

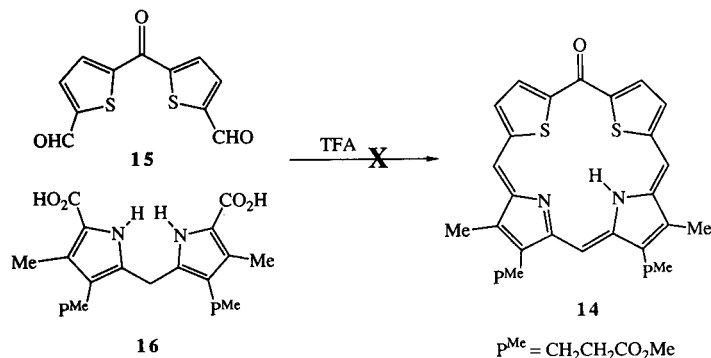
such as dichloromethane, and gave deep blue solutions which displayed red porphyrin-like fluorescence under long wavelength ultraviolet light. The proton and carbon-13 (Figure 3) nmr spectra of **3c** are consistent with the keto tautomer. The proton nmr spectrum of **3c** in 20% deuterated trifluoroacetic acid-deuteriochloroform (Figure 4) demonstrated an enhanced ring current consistent with the fully aromatic dication **7c**. The three methine protons and the four furyl protons are severely deshielded (Figure 4); a similar spectrum was obtained in neat deuterated trifluoroacetic acid. In our earlier study [1], a proton nmr spectrum of **3a** was obtained using deuterated trifluoroacetic acid as a solvent. The methine proton at C-15 appeared to be absent and we interpreted this as being due

to deuterium exchange with a C-protonated species **13a**. However, the original data was poorly resolved and this interpretation was in error. The 300 MHz proton nmr of **3a** in deuterated trifluoroacetic acid also clearly shows the presence of the C-15 methine proton. None-the-less, slow deuterium exchange with the C-15 methine proton of **3a**, or **3c**, was observed after several days at room temperature or at elevated temperatures. Hence, selective deuterium exchange, presumably involving equilibration with the minor tautomer **13**, does indeed take place, although the process is not quite as facile as our earlier paper [1] suggested. Tetrapyrrolic oxophlorins also undergo deuterium exchange in deuterated trifluoroacetic acid at the C-15 meso carbon [6a].

Scheme 1



Scheme 2



## EXPERIMENTAL

We were also interested in the synthesis of the related dithienyl oxophlorin **14**. However, attempts to condense dialdehyde **15** [11] with dipyrromethane dicarboxylic acid **16** failed to give even trace amounts of the oxophlorin analogs (Scheme 2). Clezy and Diakiw reported that the oxophlorin analog **1c** was exceedingly photosensitive [8], and it may be that **14** decomposes under the reaction conditions employed. However, we have some evidence to suggest that the bulky sulfur atoms inhibit macrocyclic ring formation [9,13].

Very recently, Breitmaier and co-workers reported [14] the synthesis of two oxophlorin analogs **3c** and **3d**. These workers employed the same approach described in this paper, although they utilized 5,5'-diunsubstituted dipyrromethanes and carried out the "MacDonald condensations" in the presence of acetic acid-dichloromethane. Breitmaier *et al.* also concluded that the keto tautomers **3c** and **3d** were favored. The nmr and ir data were in reasonable agreement with our work, although the reported molar absorptivities for uv-visible maxima appear to be in error [15]. Surprisingly, detailed proton and carbon-13 nmr data were also reported for a tetrapyrrolic oxophlorin **1a** ( $R^{1,4,5,8} = \text{Me}$ ,  $R^{2,3,6,7} = \text{Et}$ ), although the authors do not comment on the paramagnetic nature of this species [7]. It may be that this data was obtained at low temperatures, since the proton nmr spectra of oxophlorins are reported to be partially resolved under these conditions [16].

Note added in proof: After this paper had been submitted for publication, we received a short note from Dr. Breitmaier, dated February 4, 1991, in response to a letter of enquiry that we sent on December 12, 1990. He kindly sent us copies of several original nmr spectra for compounds **3c** and **3d**, and these data are in good agreement with our results. However, Dr. Breitmaier did not comment on the discrepancies noted in our paper.

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 710B spectrometer. The uv spectra were obtained on a Perkin-Elmer 330 or a Beckmann DU-40 spectrophotometer. The nmr spectra were recorded on a Hitachi-Perkin Elmer R24B 60 MHz nmr spectrometer or a Varian Gemini-300 nmr spectrometer, chemical shifts are reported using the  $\delta$  scale in ppm relative to tetramethylsilane. Mass spectral data were obtained at the Midwest Center for Mass Spectrometry at the University of Nebraska-Lincoln or at the Washington University Mass Spectrometry Resource, which is supported by a grant from the National Institutes of Health (RR00954). Elemental analyses were obtained from Micro-analysis, Inc., Wilmington, DE 19808.

## 2-(5-Bromo-2-furyl)-1,3-dioxalan (9).

*p*-Toluenesulfonic acid monohydrate (2.5 mg) was added to a mixture of 5-bromofuran-2-carboxaldehyde [17] (9.53 g, 0.054 mole) and ethylene glycol (5.34 g, 0.086 mole) in toluene (74 ml). The solution was refluxed using a Dean and Stark apparatus to azeotropically remove the water as it formed in the reaction. The mixture was cooled, diluted with ether, and washed successively with saturated sodium bicarbonate, water and saturated sodium chloride solution. The etherial phase was dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure. The residue was distilled *in vacuo* to give the dioxalan as a pale yellow oil (10.04 g, 85%) bp 57.5-58.5° at 0.3 torr (lit bp [11] 110-112° at 6 torr); pmr (deuteriochloroform):  $\delta$  3.97 (4H, m,  $-\text{OCH}_2\text{CH}_2\text{O}-$ ), 5.80 (1H, s,  $-\text{CH}-\text{O}$ ), 6.25 (1H, d,  $J = 4$  Hz, 4-H), 6.36 (1H, d,  $J = 4$  Hz, 3-H).

## 5,5'-Diformyl-2,2'-difuryl-methanone (11).

A solution of the foregoing dioxalan (18.0 g) in anhydrous ether (50 ml) was added dropwise over 15 minutes to a stirred solution of *n*-butyllithium (10.9 ml, 10 M solution in hexane) in ether (100 ml), under nitrogen, maintaining the temperature at  $-20^\circ$ . After 10 minutes a solution of ethyl *N,N*-dimethylcarbamate [11] (4.64 g) in anhydrous ether (20 ml) was added over a 10 minute period. The mixture was stirred for 45 minutes at  $-15^\circ$  to  $-20^\circ$ . A solution of saturated aqueous ammonium chloride (75 ml) was cautiously added to the mixture. After several minutes of stirring a brown precipitate formed. The solid was filtered

off, dissolved in acetone (240 ml)-10% aqueous hydrochloric acid (80 ml) and stirred for 2 hours. The acetone was evaporated under reduced pressure, the residue dissolved in chloroform and washed with water, 5% aqueous sodium bicarbonate solution and water. The solution was dried over magnesium sulfate, evaporated under reduced pressure and chromatographed on silica, eluting first with dichloromethane and then with 5% methanol-dichloromethane. Crystallization from dichloromethane-petroleum ether (60-80°) gave the dialdehyde as a yellow powder (10.5 g, 68%), mp 182-184° (lit mp [11] 189°); ms: (m/e) 218 (M<sup>+</sup>, 44%), 217 (22%), 190 (25%), 162 (10%), 134 (10%), 123 (100%), 105 (16%), 95 (23%); ir (Nujol mull):  $\nu$  1668 (aldehyde C=O str), 1630 (bridging C=O str); pmr (DMSO-d<sub>6</sub>-deuteriochloroform):  $\delta$  7.44 (2H, d, J = 3.8 Hz, 3,3'-H), 7.77 (2H, d, J = 3.8 Hz, 4,4'-H), 9.90 (2H, s, 2 x CHO); cmr (DMSO-d<sub>6</sub>-deuteriochloroform): 120.15, 121.04 (4 x  $\beta$ -furyl C), 152.55, 153.93 (4 x  $\alpha$ -furyl C), 168.77 (bridge C=O), 178.95 (2 x CHO).

Dibenzyl 3,3'-Diethyl-4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylate.

Concentrated hydrochloric acid (6 ml) was added to a solution of benzyl 5-acetoxymethyl-4-ethyl-3-methylpyrrole-2-carboxylate [18] (10.13 g, 0.03 mole) in methanol (70 ml) and the mixture heated under reflux for 3 hours. The mixture was cooled and stored in the freezer overnight. The resulting yellow crystals were collected by suction filtration and recrystallized from ethanol to give white needles (7.0 g, 88%), mp 130-131° (lit mp [18] 131°); ir (Nujol mull):  $\nu$  3320 (NH str), 1690 (C=O str); pmr (deuteriochloroform):  $\delta$  1.03 (6H, t, 2 x CH<sub>2</sub>CH<sub>3</sub>), 2.27 (6H, s, 2 x pyrrole-CH<sub>3</sub>), 2.42 (4H, q, 2 x CH<sub>2</sub>CH<sub>3</sub>), 3.75 (2H, s, bridging CH<sub>2</sub>), 5.18 (4H, s, 2 x OCH<sub>2</sub>Ph), 7.33 (10H, m, 2 x C<sub>6</sub>H<sub>5</sub>), 9.8 (2H, br, 2 x NH); cmr (deuteriochloroform): 10.86 (4,4'-CH<sub>3</sub>), 15.64 (2 x CH<sub>2</sub>CH<sub>3</sub>), 17.39 (2 x CH<sub>2</sub>CH<sub>3</sub>), 22.66 (bridge CH<sub>2</sub>), 65.76 (2 x OCH<sub>2</sub>Ph), 117.53 (5,5'-C), 124.07 (3,3'-C), 127.63 (4,4'-C), 127.78 (4 x *ortho* C), 127.93 (2 x *para* C), 128.47 (4 x *meta* C), 130.38 (2,2'-C), 136.40 (2 x Ph C<sub>ar</sub>), 162.10 (2 x C=O).

Dibenzyl 3,3'-Bis(2-methoxycarbonyl)ethyl-4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylate.

Prepared from benzyl 5-acetoxymethyl-4(2-methoxycarbonyl)ethyl-3-methylpyrrole-2-carboxylate [21] (12.0 g, 0.032 mole) by the procedure detailed above. Recrystallization from ethanol gave the title dipyrromethane as pale pink crystals (8.28 g, 83%), mp 102-103° (lit mp [20] 101-102°); ir (Nujol mull):  $\nu$  3350 (NH str), 1732 (methyl ester C=O str), 1700 (benzyl ester C=O str); pmr (deuteriochloroform) 2.27 (6H, s, 2 x pyrrole-CH<sub>3</sub>), 2.46 (4H, t, 2 x CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me), 2.75 (4H, t, 2 x CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me), 3.58 (6H, s, 2 x OCH<sub>3</sub>), 3.97 (2H, s, bridging CH<sub>2</sub>), 5.21 (4H, s, 2 x CH<sub>2</sub>Ph), 7.36 (10H, m, 2 x C<sub>6</sub>H<sub>5</sub>), 9.6 (2H, b, 2 x NH); cmr (deuteriochloroform): 10.88 (4,4'-CH<sub>3</sub>), 19.35 (3,3'-CH<sub>2</sub>CH<sub>2</sub>CO), 22.52 (bridge CH<sub>2</sub>), 34.59 (3,3'-CH<sub>2</sub>CH<sub>2</sub>CO), 51.74 (2 x OCH<sub>3</sub>), 65.62 (2 x OCH<sub>2</sub>Ph), 117.99 (5,5'-C), 120.26 (3,3'-C), 127.31 (4,4'-C), 127.93 (2 x *para* C), 128.00 (4 x *ortho* C), 128.51 (4 x *meta* C), 131.08 (2,2'-C), 136.08 (2 x Ph C<sub>ar</sub>), 161.60 (2 x CO<sub>2</sub>CH<sub>2</sub>Ph), 173.82 (2 x CO<sub>2</sub>Me).

13,17-Diethyl-12,18-dimethyl-21,22-dioxaphlorin (3c).

Dibenzyl 3,3'-diethyl-4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylate (10.00 g, 0.021 mole) was dissolved in acetone (148

ml) containing 20 drops of triethylamine. The solution was flushed with nitrogen and 10% palladium-charcoal (1.0 g) was added. The mixture was shaken under an atmosphere of hydrogen at 30 psi and ambient temperature overnight. The catalyst was removed by suction filtration and evaporated under reduced pressure. The residue was taken up in a 5% ammonia solution and cooled to 0°. The mixture was cautiously neutralized with glacial acetic acid, maintaining the temperature between 0-5°, and resulting precipitate filtered, washed thoroughly with water, and dried *in vacuo*. 3,3'-Diethyl-4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylic acid (12) was obtained as a white powder (5.91 g, 88%), mp 158-159° (lit mp [19] 166-170°); pmr (DMSO-d<sub>6</sub>-deuteriochloroform):  $\delta$  1.00 (6H, t, 2 x CH<sub>2</sub>CH<sub>3</sub>), 2.20 (6H, 2 x pyrrole-CH<sub>3</sub>), 2.42 (4H, q, 2 x -CH<sub>2</sub>CH<sub>3</sub>), 3.73 (2H, s, bridging CH<sub>2</sub>), 11.85 (2H, s, 2 x CO<sub>2</sub>H).

5,5'-Diformyl-2,2'-difurylmethanone (284 mg, 1.3 mmoles) was added portionwise over 10 minutes to a stirred solution of the foregoing dipyrromethane dicarboxylic acid (293 mg, 0.92 mmole) in trifluoroacetic acid (10 ml) at room temperature. The wine red colored solution was allowed to stir at room temperature for 1 hour. An 8:2 v/v mixture of chloroform-methanol (20 ml) was added to the mixture and the resulting green solution washed with 5% ammonia solution (20 ml) and water (2 x 20 ml). The organic solution was evaporated under reduced pressure and the resulting green residue chromatographed on neutral grade 3 alumina (150 g), eluting with chloroform-dichloromethane (1:1 v/v). The title compound was collected as a blue fraction which exhibited red porphyrin-like fluorescence under long wave ultraviolet light. Crystallization from dichloromethane-methanol gave purple needles (166.6 mg, 44%), mp > 300°; ms: (electron impact) m/e 412 (M<sup>+</sup>; 100%), 397 (9%); hrms: Calcd. for C<sub>26</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub>: 412.1788. Found: 412.1776; ir (potassium bromide):  $\nu$  1552 (C=O str); uv (dichloromethane):  $\lambda$  max (log<sub>10</sub>  $\epsilon$ ) 382 (4.72), 397 (4.71), 424 (sh, 4.43), 586 (4.11), 632 (4.24); uv (10% trifluoroacetic acid-dichloromethane):  $\lambda$  max (log<sub>10</sub>  $\epsilon$ ) 399 (5.21), 554 (3.93), 597 (4.03), 631 (4.13); pmr (deuteriochloroform):  $\delta$  1.52 (6H, t, J = 7.5 Hz, 2 x CH<sub>2</sub>CH<sub>3</sub>), 2.86 (6H, s, 2 x CH<sub>3</sub>), 3.27 (4H, q, 2 x CH<sub>2</sub>CH<sub>3</sub>), 4.27 (1H, br, NH), 7.73 (1H, s, 15-H), 8.19 (2H, s, 10,20-H), 8.21 (2H, d, J = 4 Hz, 2,8-H), 9.11 (2H, d, J = 4 Hz, 3,7-H); pmr (1% trifluoroacetic acid-d-deuteriochloroform):  $\delta$  1.52 (6H, t, J = 7.6 Hz, 2 x CH<sub>2</sub>CH<sub>3</sub>), 2.92 (6H, s, 2 x CH<sub>3</sub>), 3.35 (4H, q, J = 7.6 Hz, 2 x CH<sub>2</sub>CH<sub>3</sub>), 7.94 (1H, s, 15-H), 8.41 (2H, d, 2,8-H), 8.44 (2H, s, 10,20-H), 9.07 (2H, d, 3,7-H); pmr (20% trifluoroacetic acid-d-deuteriochloroform):  $\delta$  1.89 (6H, t, 7.7 Hz, 2 x CH<sub>2</sub>CH<sub>3</sub>), 3.72 (6H, s, 2 x CH<sub>3</sub>), 4.20 (4H, q, J = 7.7 Hz, 2 x CH<sub>2</sub>CH<sub>3</sub>), 10.25 (2H, d, J = 4.8 Hz, 2,8-H), 10.43 (1H, s, 15-H) [22], 10.78 (2H, s, 10,20-H), 10.88 (2H, d, J = 4.8 Hz, 3,7-H); cmr (deuteriochloroform): 10.55, 15.98 (4 x CH<sub>3</sub>), 18.76 (2 x CH<sub>2</sub>), 90.86 (15-C), 97.94 (10,20-C), 119.24, 124.31 (2,3,7,8-C), 137.89, 141.75, 146.38, 154.51, 156.95 (quaternary furan and pyrrole C), 164.09 (C=O); cmr (20% trifluoroacetic acid-d-deuteriochloroform): 11.70, 16.60, 20.43, 96.88 [22], 102.50, 131.12, 134.12, 141.99, 143.57, 147.26, 147.84, 152.67, 157.62.

Anal. Calcd. for C<sub>26</sub>H<sub>24</sub>N<sub>2</sub>O<sub>3</sub>·H<sub>2</sub>O (430.50): C, 72.54; H, 6.09; N, 6.51. Found: C, 72.79; H, 5.95; N, 6.34.

13,17-Bis(2-methoxycarbonyl)ethyl-12,18-dimethyl-21,22-dioxaphlorin (3a).

Dibenzyl 3,3'-bis(2-methoxycarbonyl)ethyl-4,4'-dimethyl-2,2'-dipyrromethane-5,5'-dicarboxylate (10.0 g, 16 mmoles) was dissolved in acetone (120 ml) containing 16 drops of triethylamine.

The resulting solution was shaken with 10% palladium-charcoal (1.0 g) under an atmosphere of hydrogen at 30 psi and ambient temperature overnight. The catalyst was removed by suction filtration, the acetone solution evaporated under reduced pressure and the residue taken up in a 5% ammonia solution. The aqueous solution was cooled in a salt/ice bath and neutralized with glacial acetic acid whilst maintaining the temperature between 0-5° throughout. The resulting white precipitate was filtered, washed thoroughly with water and dried *in vacuo* overnight. The dicarboxylic acid **16** was obtained as a white powder (6.78 g, 96%) that darkened slightly on standing for several days, mp 190-191° (lit mp [21] 190-191°); pmr (DMSO- $d_6$ ):  $\delta$  2.12 (6H, s, 2 x pyrrole-CH<sub>3</sub>), 2.13 (4H, t, 2 x CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me), 2.56 (4H, t, 2 x CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me), 3.56 (6H, s, 2 x OCH<sub>3</sub>), 3.80 (2H, s, bridging CH<sub>2</sub>), 11.10 (2H, s, 2 x CO<sub>2</sub>H), 12.0 (2H, br, 2 x NH).

5,5'-Diformyl-2,2'-difurylmethanone (0.284 g) was added in portions to a stirred solution of the foregoing dipyrromethane dicarboxylic acid in trifluoroacetic acid (10 ml) over 10 minutes. The mixture was allowed to stir for a further 1 hour at room temperature. Dichloromethane (50 ml) was added to the deep purple solution, and the resulting mixture was washed with water, 5% aqueous ammonia solution and water. The solvent was evaporated off under reduced pressure and the residue chromatographed on grade 3 alumina, eluting first with dichloromethane, and then with 2% methanol-dichloromethane. Some problems were encountered at this stage, due to precipitation on the column. The blue fractions were collected and crystallized from dichloromethane-methanol to yield purple microneedles (102 mg, 15%), mp > 300°; ir (potassium bromide):  $\nu$  1551 (C=O str); uv (chloroform):  $\lambda$  max (log<sub>10</sub>  $\epsilon$ ) 385 (4.78), 396 (4.78), 423 (sh, 4.45), 587 (4.16), 635 (4.28); uv (0.1% trifluoroacetic acid-chloroform):  $\lambda$  max log<sub>10</sub>  $\epsilon$  384 (4.84), 395 (4.85), 604 (4.09), 658 (4.38); uv (10% trifluoroacetic acid-chloroform):  $\lambda$  max (log<sub>10</sub>  $\epsilon$ ) 400 (5.25), 555 (4.01), 600 (4.07), 636 (4.09); pmr (trifluoroacetic acid- $d$ ):  $\delta$  3.53 (4H, t, (J = 7.5 Hz), -CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me), 3.84 (6H, s), 3.89 (6H, s) (ring and ester CH<sub>3</sub>), 4.76 (4H, t, J = 7.5 Hz, CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me), 10.55 (2H, d, J = 4.7 Hz, 2,8-H), 11.09 (1H, s, 15-H) [22], 11.14 (2H, d, J = 4.7 Hz, 3,7-H), 11.18 (2H, s, 10,20-meso-H); pmr (deuteriochloroform):  $\delta$  2.79 (6H, s, 2 x ring-CH<sub>3</sub>), 2.92 (4H, t, J = 7.5 Hz, CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me), 3.60 (4H, t, J = 7.5 Hz, CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me), 3.68 (6H, s, 2 x OCH<sub>3</sub>), 4.38 (1H, b, NH), 7.73 (1H, s, 15-meso-H), 8.20 (2H, s, 10,20-meso-H), 8.22 (2H, d, J = 4.1 Hz, 2,8-H), 9.09 (2H, d, J = 4.1 Hz, 3,7-H).

Anal. Calcd. for C<sub>30</sub>H<sub>28</sub>N<sub>2</sub>O<sub>7</sub> (528.56): C, 68.17; H, 5.34. Found: C, 67.67; H, 5.60.

13,17-Bis(2-ethoxycarbonyl-ethyl)-12,18-dimethyl-21,22-dioxaphlorin (**3b**).

The foregoing dimethyl ester (100 mg) was dissolved in 5% sulfuric acid-methanol and stirred in the dark for 2 days at room temperature. Dichloromethane (80 ml) was added to the deep inky-blue solution and the mixture was washed with water, 5% aqueous ammonia and water. Crystallization from dichloromethane-methanol gave lustrous purple microneedles (92 mg, 87%), mp > 300°; hrms: Calcd. for C<sub>32</sub>H<sub>32</sub>N<sub>2</sub>O<sub>7</sub>: 556.2211. Found: 556.2222; pmr (deuteriochloroform):  $\delta$  1.21 (6H, t, J = 7 Hz, 2 x OCH<sub>2</sub>CH<sub>3</sub>), 1.57 (1H, br, NH), 2.87 (6H, s, 2 x pyrrole-CH<sub>3</sub>), 2.89 (4H, t, J = 7.6 Hz, 2 x CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et), 3.58 (4H, t, J = 7.6 Hz, 2 x CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Et), 4.13 (4H, q, J = 7 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 7.72 (1H, s,

15-H), 8.17 (2H, s, 10,20-H), 8.19 (2H, d, J = 4.0 Hz, 2,8-H), 9.08 (2H, d, J = 4.0 Hz, 3,7-H).

Anal. Calcd. for C<sub>32</sub>H<sub>32</sub>N<sub>2</sub>O<sub>7</sub>· $\frac{3}{4}$ H<sub>2</sub>O (570.12): C, 67.41; H, 5.92; N, 4.91. Found: C, 67.37; H, 5.49; N, 5.12.

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