Notes

Synthesis and Characterization of New "Expanded" Thiophene- and Furan-Containing Macrocycles

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Reports of new porphyrin-like, aromatic macrocycles have appeared in increasing numbers in the last few years.[1-8] These macrocycles generally consist of five-membered rings linked together by zero, one, or two sp-hybridized (methine) atoms to form a cyclic extended aromatic network. Previously, we suggested the use of the term "pentaplanar" to describe these two common features.[9] We report here the synthesis and characterization of two new expanded macrocycles, oxobronzaphyrin (**5**) and thioozaphyrin (**6**). These compounds are additional examples of stable, neutral thiophene- and furan-containing macrocycles that contain 22 or 26 conjugated π-electrons. The electrochemistry of a related macrocycle, bronzaphyrin (**2**), is reported.

Results and Discussion

The precursor dialdehydes[9,10] used for the syntheses of the three macrocycles discussed here were made by a modified version of the method of Merrill and LeGoff.[11] Macrocycle **2** was prepared by a McMurry homo-coupling of thiophene dialdehyde **1**.[9] The initial product rapidly oxidizes when dissolved in chloroform to give **2**. In the same spirit of appellation as rubyrin,[2] sapphyrin,[8,12-16] rosarin,[17] and ozaphyrin,[18] we christen macrocycle **2** "bronzaphyrin" for its distinctive bronze color in chloroform solution.

The furan-substituted analogue of bronzaphyrin, oxobronzaphyrin (**5**), was synthesized by a McMurry coupling of furan dialdehyde **3** with thiophene dialdehyde **1** (Scheme 1). The homo-coupled product of **3** is produced, but is apparently unstable. Only bronzaphyrin (**2**) and oxobronzaphyrin (**5**) are isolated. Both ^{1}H NMR and UV-vis spectra indicate an aromatic electronic structure for oxobronzaphyrin, as was also the case for bronzaphyrin.[9] In the ^{1}H NMR spectrum the sharp peak at 0.41 ppm is consistent with the diamagnetically shielded internal pyrrole proton, and the peaks in the range of 9.96 to 11.32 ppm correspond to the external and deshielded furan, methine, pyrrole, and thiophene resonances. The UV-vis spectrum of oxobronzaphyrin, which is consistent with the lowered symmetry (C_{2v}) of the macrocycle, is similar to that of bronzaphyrin,[9] with split Soret-like bands at 455 and 489 nm and three Q-like transitions at 745, 783, and 855 nm. This spectrum closely resembles the spectra of porphycenes, which also have highly intense Q-like transitions relative to the Soret-like bands.[10] The UV-vis spectrum of oxobronzaphyrin is red-shifted from that of free-base tetrapropylporphycene, consistent with the increase of conjugated π-electrons from 18 to 26.[19] Oxobronzaphyrin is a potential photosensitizing agent for photodynamic therapy,[20-22] because of its highly intense electronic absorption band at 855 nm.

Oxobronzaphyrin (**5**) is an isomeric analogue of rubyrin[2] and hexaphyrin,[12] two recently synthesized hexapyrrolic macrocycles whose methine groups are arranged in the order [1.1.0.1.1.0] and [1.1.1.1.1.1], respectively.[23] Oxobronzaphyrin (**5**), by contrast, has methine groups in the order [2.0.0.2.0.0] and has two pyrrole groups replaced by thiophene and furan groups. Among known furan-containing macrocycles[4] are furan analogues of porphycene[24-26] and porphyrin.[27-30] Thiophene-containing aromatic macrocycles are also known.[6,30-35] These furan-

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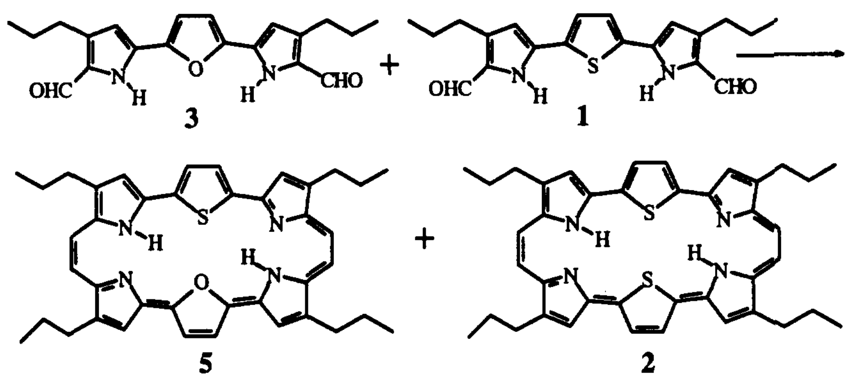
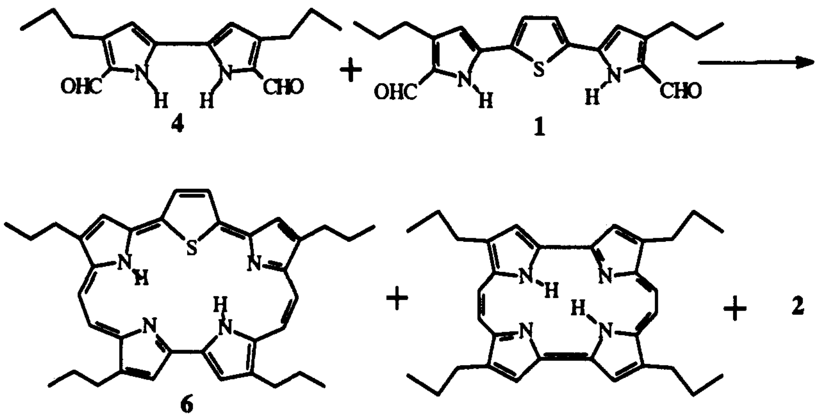
Scheme 1



Scheme 2



and thiophene-containing macrocycles are mostly variants of the well-known porphyrin or [1.1.1.1]-type system, norsapphyrin and thiosapphyrin being two exceptions.[36]

Thioozaphyrin (**6**), the thiophene analogue of ozaphyrin,[18] was synthesized by a McMurry coupling of bipyrrole dialdehyde **4** with thiophene dialdehyde **1** (Scheme 2). All three major coupling products of the dialdehydes are stable and can be separated by extensive chromatography. Thioozaphyrin is aromatic, as evidenced by ^{1}H NMR spectroscopy and UV–vis spectroscopy. The ^{1}H NMR spectrum of thioozaphyrin is consistent with the aromatic nature of the macrocycle; the spectrum is nearly identical to that of ozaphyrin, which also has diamagnetically shielded protons and is planar, as established by X-ray crystallography.[18] The resonance of the diamagnetically shielded internal proton of thioozaphyrin occurs at −2.7 ppm, while the deshielded external methine, pyrrole, and thiophene proton resonances occur at 10.13, 10.32, 10.53, and 10.88 ppm. The UV–vis spectrum of thioozaphyrin is slightly red-shifted from that of ozaphyrin[18] and is consistent with C_{2v} symmetry for the macrocycle. The red shift exhibited in the UV–vis spectrum of thioozaphyrin relative to that of porphycene is consistent with the increase of conjugated π-electrons from 18 to 22.[37] Thioozaphyrin (**6**) is an isomeric analogue of sapphyrin,[36] which has methine groups arranged around the ring in the order [1.1.1.1.0]. Thioozaphyrin, in contrast, has methine groups arranged in the order [2.0.0.2.0], with one of the pyrrole rings replaced with a thiophene ring. Both oxobronzaphyrin and thioozaphyrin are stable as the free-base, neutral species, in contrast to many expanded macrocycles that are only stable as polycationic species, for example, rubyrin.[2]

The electrochemistry of bronzaphyrin (**2**) has been examined by cyclic voltammetry. The compound exhibits one quasi-reversible electrochemical reduction at −0.794 V and two quasi-reversible oxidations at +0.272 V and +0.723 V versus SCE (Figure 1).[38] The reduction peak may be composed of two overlapping one-electron reductions. The oxidation peaks have more complicated shapes than normal. The potentials for the oxidations and reduction of bronzaphyrin are lower than those for porphyrins,[39] porphycenes,[40] and ozaphyrin.[18] The low first-oxidation potential of bronzaphyrin is comparable to that of polypyrrole.[41] Thus bronzaphyrin may be potentially useful as a donor in one-dimensional molecular conductors.

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(38) The peak potential difference of a solution of bronzaphyrin in CH_2Cl_2 is constant and close to 90 mV from scan rates of 400 mV/s to 1200 mV/s. A plot of the peak currents I_{pc} and I_{pa} vs the square root of the scan rate is a line that crosses near the origin; I_{pa}/I_{pc} is ≈1. For ferrocene in CH_2Cl_2 (with 0.1 mM $[NBu_4][PF_6]$) $E_{1/2}$ = +0.432 V vs SCE.

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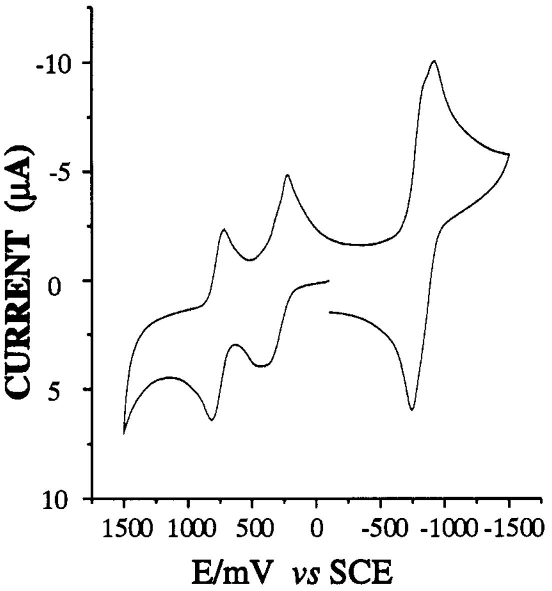

Figure 1. Cyclic voltammogram of bronzaphyrin (**2**) (~1 mM + 0.1 M $[NBu_4][PF_6]$, CH_2Cl_2, 800 mV/s).

Experimental Section

THF was dried by distillation under Ar from sodium–benzophenone ketyl. CH_2Cl_2 for the electrochemistry was dried by distillation under N_2 over CaH_2. Pyridine was stored over NaOH pellets. $TiCl_4$, ferrocene, and Zn dust were obtained from Aldrich Chemical Co. and used as received. Electrochemical grade tetrabutylammonium hexafluorophosphate was obtained from Fluka Chemical Co. and used as received.

^1H and ^{13}C NMR measurements were made with deuteriochloroform as solvent at 300 and 75.4 MHz, respectively. Chemical shifts (δ) are reported in parts per million, with the solvent peak or TMS as reference. FAB low- and high-resolution mass spectra were recorded by Doris Hung of the Analytical Services Laboratory at Northwestern University. UV–vis spectra are reported in nanometers.

2,5-Bis(5-formyl-4-propyl-2-pyrrolyl)thiophene (1). This compound was prepared as reported previously.[9]

Bronzaphyrin (2). This compound was prepared as reported previously.[9]

2,5-Bis(5-formyl-4-propyl-2-pyrrolyl)furan (3). This compound was prepared as reported previously.[18]

5,5′-Diformyl-4,4′-dipropyl-2,2′-bipyrrole (4). This compound was prepared as reported previously.[10]

Oxobronzaphyrin (5). A solution of $TiCl_4$ (2.57 g) in THF (900 mL) was added under an Ar atmosphere to Zn dust (1.8 g) with stirring, and the suspension was held at reflux for 0.5 h. Thiophene dialdehyde 1 (0.251 g), furan dialdehyde 3 (0.240 g), and pyridine (7 mL) in THF (500 mL) were added dropwise over a 1.5-h period to the gently refluxing suspension. The resulting mixture was refluxed with stirring for 16 h. A quenching solution of 10% K_2CO_3 in water (125 mL) was then carefully introduced. The reaction mixture was filtered through Celite and the filtrate was concentrated on a rotary evaporator. The solution was extracted with $CHCl_3$, was washed three times with water, and was concentrated to dryness on a rotary evaporator, and the resultant solid was dried *in vacuo* overnight. The solid was redissolved in $CHCl_3$ and eluted through a silica gel column. The fast running band, bronzaphyrin (2), was isolated first. The second band was collected and was recrystallized from $CHCl_3$/hexane to give the product, oxobronzaphyrin (5), as a metallic green solid with a bronze color in $CHCl_3$ solution (40 mg, 7%): mp >300 °C dec; UV–vis λ_{max} (log ϵ) (THF/MeOH 1:1 v/v) 455 (5.10), 489 (4.81), 745 (4.61), 783 (4.64), 855 (4.72); ^1H NMR ($CDCl_3/d_6$-DMSO) δ 0.41 (s, 2H, N*H*), 1.43, 1.46 (t, t, 6H, 6H, J = 7.3 Hz), 2.53 (m, 8H), 4.22 (dd, J = 7.6 Hz, 8H), 9.96 (dd, 4H), 9.99, 10.03, 10.17, 10.20, 11.32 (5 s, 10H); ^{13}C NMR δ 14.6, 14.7, 24.9, 25.3, 30.5, 30.6, 107.9, 111.5, 118.8, 122.0, 123.3, 128.2, 130.8, 135.3, 137.4, 140.9, 141.7, 145.2, 148.0, 158.2; FAB MS *m/e* 628 (100); FAB HRMS calcd for $C_{40}H_{43}N_4OS$ $(m + 1)/z$ 627.3158, found 627.3139.

Thioozaphyrin (6). A solution of $TiCl_4$ (5.42 g) in THF (900 mL) was added under an Ar atmosphere to Zn dust (3.736 g) with stirring, and the suspension was held at reflux for 0.5 h. Thiophene dialdehyde 1 (0.501 g), bipyrrole dialdehyde 4 (0.384 g), and pyridine (5.5 mL) in THF (450 mL) were then added dropwise over a 20-min period to the gently refluxing suspension. The resulting mixture was stirred at reflux for 20 h. A quenching solution of 10% K_2CO_3 in water (250 mL) was then carefully introduced. The crude reaction mixture was placed in a refrigerator overnight. Next the THF layer was removed on a rotary evaporator. The remaining $CHCl_3$ solution was filtered and concentrated to dryness on a rotary evaporator. Chromatography of the redissolved solid on an alumina TLC plate (3:1 v/v CCl_4:$CHCl_3$) resulted in three major bands for bronzaphyrin, porphycene, and thioozaphyrin. Thioozaphyrin (6) was isolated with the use of a Chromatotron (1:1 v/v $CHCl_3$:hexane) as a purple solid, which is emerald green color in solution ($CHCl_3$) (14.2 mg, 2.6%): mp >250 °C dec; UV–vis λ_{max} (log ϵ) (THF/MeOH 1:1 v/v) 367 (4.32), 425 (5.00), 447 sh (4.87), 660 (4.48), 697 (4.46), 713 (4.46), 755 (4.70); ^1H NMR δ −2.72 (s, 2H, N*H*), 1.47 (t, J = 7.3 Hz, 12H), 2.60 (m, J = 8.0 Hz, 8H), 4.22 and 4.37 (t, t, 4H, 4H, J = 7.7 Hz), 9.63 (s, 2H), 10.13 and 10.32 (d, d, 4H, J = 11.6 Hz), 10.53 and 10.88 (s, s, 2H, 2H); ^{13}C NMR δ 14.7, 14.8, 25.3, 25.6, 30.8, 31.5, 107.2, 111.0, 112.0, 127.8, 128.8, 129.6, 134.4, 139.8, 141.6, 143.1, 145.9, 147.6; FAB MS *m/e* 561 (100), 517 (37), 281 (21); FAB HRMS calcd for $C_{36}H_{40}N_4S$ m/z 560.2974, found 560.2896.

Electrochemical Measurements. Electrochemical measurements were carried out on a solution under an N_2 atmosphere. A conventional three-electrode system was used, comprising of a platinum-wire working electrode, a silver-wire counter electrode, and a silver-wire reference electrode. The cyclic voltammogram was obtained from a CH_2Cl_2 solution containing ~1 mM bronzaphyrin and 0.1 mM $[NBu_4][PF_6]$. The scan rate was varied from 400 mV/s to 1200 mV/s, and the ferrocene/ferrocenium couple was used as the internal standard.

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Supplementary Material Available: ^1H NMR and ^{13}C NMR spectra of **5** and **6** and UV–vis spectra of **2**, **5**, and **6** (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.