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Synthesis and Characterization of a Stable Smaragdyrin Isomer

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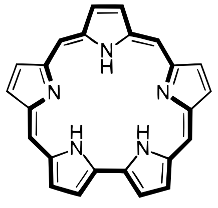
The synthesis of 16,20-dipropyl-2,3,6,7,10,11,15,21-octamethyl-[22]pentaphyrin-(1.1.1.0.0) (**8**), a stable isomer of smaragdyrin ([22]pentaphyrin(1.1.0.1.0)), and **9**, a furan-containing analogue of **8**, are reported. These two new expanded porphyrins were characterized in solution using UV−vis and ^{1}H and ^{13}C NMR spectroscopic means and in the solid state via single-crystal X-ray diffraction analysis.

Woodward first reported the discovery of sapphyrin (e.g., **1**) and smaragdyrin (e.g., **2**), two prototypic pentapyrrolic macrocycles, at the 1966 Aromaticity Conference.[1] While sapphyrins have been extensively studied,[2−12] little information about the properties of smaragdyrin is available in the open literature. In 1972, Broadhurst, Grigg, and Johnson, working independently of Woodward, reported spectral evidence consistent with the contention that smaragdyrin (a compound to which the trivial name "norsapphyrin" was given) could be obtained as the product of rational synthesis.[2] However, it was also reported that attempts at isolation resulted in decomposition of the macrocycle. Furan-containing analogues of smaragdyrin, of general structure **3**, were also reported in that paper. These latter systems proved much more stable than their all-aza systems analogues. Indeed, it was reported that, like sapphyrin, they could be stored for months in a freezer without significant decomposition. Unfortunately, while the oxasmaragdyrins could be characterized using NMR and UV−vis spectroscopic means, no X-ray structural data for these systems were ever reported.[2]



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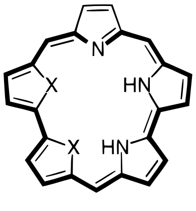
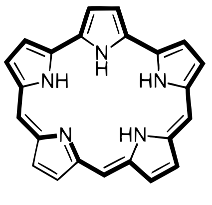


2 X = NH
3 X = O



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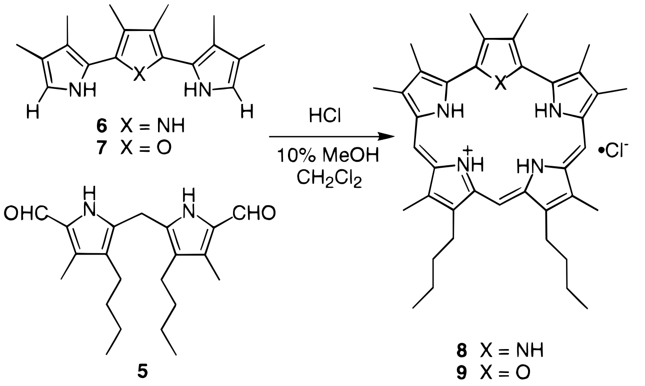
Scheme 1



Recent efforts in this group have confirmed the inherent instability of pentaazasmaragdyrin; it has a half-life on the order of a few hours in organic media under ambient conditions and decomposes in weeks in the solid state, even when stored under argon in a freezer.[13] However, these same studies led us to consider that "isosmaragdyrin", a macrocyclic system shown in its general, substituent-free form as structure **4**, might prove stable. In this paper, we discuss the synthesis of the dibutyloctamethyl derviative of isosmaragdyrin (compound **8**; Scheme 1) as well as that of its monoxa analogue, **9**. As detailed below, each of these materials is stable under a range of conditions. Accordingly, they have been characterized by solution-phase NMR, UV−visible spectroscopy, and mass spectrometry and, in the solid state, by X-ray crystallographic analysis.

Results and Discussion

Compounds **8** and **9** were synthesized via the acid-catalyzed condensation of bisformyl dipyrromethane **5**[14] with bis-α-free terpyrroles **6** and **7**, respectively (Scheme 1).[15] This afforded the macrocyclic products in ca. 40%

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(10) Iverson, B. L.; Shreder, K.; Král, V.; Sansom, P.; Lynch, V.; Sessler, J. L. *J. Am. Chem. Soc.* **1996**, *118*, 1608−1616.

(11) Sessler, J. L.; Cyr, M. J.; Lynch, V. *J. Am. Chem. Soc.* **1990**, *112*, 2810−2813.

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(13) Davis, J. M. A. Ph. D. Thesis, University of Texas at Austin, 1998. Briefly, the condensation of appropriate precursors led to the formation of a dark green species, presumed to be smaragdyrin, that displayed a UV−vis absorption maximum at ca. 453 nm. This finding, in conjunction with ^{1}H NMR data for the partially purified species, is consistent with the proposed pentapyrrolic, 22 π-electron system. However, no further characterization in our hands proved possible due to the rapid decomposition of the product when exposed to air.

(14) Sessler, J. L.; Hugdahl, J.; Johnson, M. R. *J. Org. Chem.* **1986**, *51*, 2838−2840 and references cited therein.

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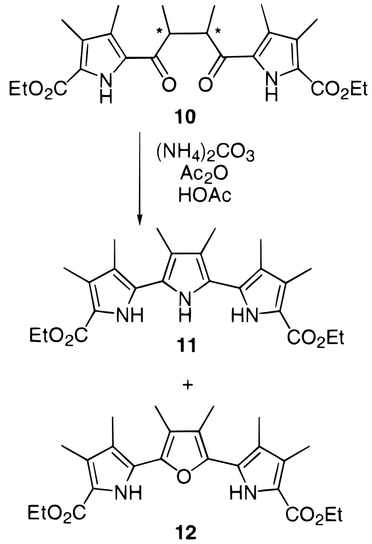
Scheme 2



yield after chromatographic purification. The key precursors **6** and **7** were, in turn, obtained from diketone **10** (Scheme 2).[15] Here, it was found that standard ring closure gave a mixture of the triaza- and diazamonoxa products **11** and **12**. This mixture was separated via column chromatography. Saponification and decarboxylation in hot ethylene glycol then afforded the bis-α-free terpyrroles **6** and **7** from **11** and **12**, respectively. It was also found that the furan-containing terpyrrole **12** could be prepared in high efficiency by simply heating diketone **10** to reflux in ethanol containing a trace quantity of sulfuric acid, following published procedures.[15,16]

Consistent with the stability trend noted in the case of the smaragdyrins and oxasmaragdyrins, the tetraazamonoxa isosmaragdyrin **9** proved more stable that its pentaaza analogue **8**. In this case, however, the difference is not as pronounced. Both **8** and **9** have half-lives on the order of several days in organic media under ambient conditions and can be stored for months as solids in a freezer without any signs of apparent decomposition.

The ^{1}H and ^{13}C NMR spectra of **8** and **9** are consistent with the proposed structures. The presence of an aromatic ring current is evidenced by the relative deshielding of the *meso* protons (peaks at δ 9.90 and 10.14 ppm for **8**; 9.93 and 10.27 ppm for **9**) and relative shielding of the internal NH protons (peaks at δ −3.69, −2.66, and −1.45 ppm for **8**; −1.67 ppm for **9**). These values are in accord with what would be expected on the basis of the NMR spectral data available for sapphyrin (*meso* proton peaks observed at δ 11.51 and 11.70 ppm, NH peaks at δ −5.46, −5.00, and −4.84 ppm for decamethylsapphyrin[17]) and pentaphyrin (*meso* protons resonating at δ 12.49 ppm, NH at δ −5.52 ppm for decamethylpentaphyrin[18]). Interestingly, the ring current effects (as judged by ^{1}H NMR shifts) appear to increase with increasing macrocycle core size, a result that is considered consistent with better net π orbital overlap being possible in the larger systems.

Table 1. UV−Vis Absorption Data for 8 and 9

8		9	
λ_{max} (nm)	log ϵ	λ_{max} (nm)	log ϵ
385	4.62	380	4.65
		391	4.66
453	4.83	426	4.87
		449	5.20
666	4.53	660	4.53
699	4.60	680	4.60

The UV−vis absorption spectrum of the all-aza isosmaragdyrin **8** (Table 1) is similar to that of sapphyrin (λ_{max} (log ϵ) = 456 (5.77), 624 (4.07), and 676 nm (4.15) for pentamethylsapphyrin[17]) but with a much smaller ratio of extinction coefficients for the main (but split) Soret-like band relative to those of the other Q-type bands. This effect, which presumably reflects critical differences in the electronics of these two aromatic pentapyrrolic systems, is not as pronounced in the case of the monooxa isosmaragdyrin **9** (Table 1), where the Soret-like band is more than 3 times as intense as that of **8**.[19] The splitting of the Soret-like absorbance observed for **8** and **9** is also seen in the spectra of oxasmaragdyrins, e.g., the hexalkyl derivative of **3** (λ_{max} (log ϵ) = 350 (4.40), 381 (4.35), 448 (5.26), 459 (5.33), 580 (3.90), 596 (3.92), 633 (4.21), 647 (4.17), and 707 nm (4.31)).[2] In this case, interestingly, the Soret-like absorptions are even more intense relative to the Q-type bands than in the case of **9**.

A single-crystal X-ray structure of the hydrochloride salt of **8** was obtained (Figure 1). It shows the macrocycle to be very nearly planar, a conformation that is consistent with the proposed aromaticity. The only notable deviation from planarity comes in the case of the central pyrrole of the terpyrrole moiety; this subunit is tilted out of the mean plane containing its neighbors by 23.2°, presumably as the result of steric interactions between the methyl groups on the β-positions of the pyrroles of the terpyrrolic subunit. The nitrogen of this pyrrole subunit is oriented away from the chloride anion (N−Cl distance of 3.367 Å). The other four nitrogen atoms are all within hydrogen-bonding distance of the chloride anion (N−Cl distances 3.155−3.219 Å). The chloride anion itself is found 1.919 Å out of the mean plane of the macrocycle.

The single-crystal X-ray structure of the HCl salt of **9** (Figure 2) proved to be very similar to that of the all-aza system. Again, the macrocyclic skeleton was found to be relatively flat, with the exception that the central furan is tilted up and away from the neighboring pyrroles (the dihedral angle is 21.2°). The N−Cl bond distances are between 3.140 and 3.225 Å, with the chloride counterion being bound 1.928 Å away from the mean N_4O heteroatom. The distance between the furan oxygen and the chloride anion is 3.354 Å.

An X-ray crystal structure for the trifluoroacetate salt of oxaisosmaragdyrin was also obtained (cf. Supporting Information). In this structure (not shown), the coordination of the anion is via one of the TFA oxygen atoms. This latter bound oxygen atom is found to lie within hydrogen-bonding distance of the four nitrogens (N−O bond distances all between 2.82 and 2.90 Å) but rather distant from the furan oxygen (the O−O distance is 2.98

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[18] Bauer, V. J.; Clive, D. L.; Dolphin, D.; Paine, J. B.; Harris, F. L.; King, M. M.; Loder, J.; Wang, S.-W. C.; Woodward, R. B. *J. Am. Chem. Soc.* **1983**, *105*, 6429−6436.

[19] Interestingly, in the case of the sapphyrins, the pentaaza macrocycle has a more intense Soret-like band than the monoxa analogue. See: Sessler, J. L.; Hoehner, M. C.; Gebauer, A.; Andrievsky, A.; Lynch, V. *J. Org. Chem.* **1997**, *62*, 9251−9260.

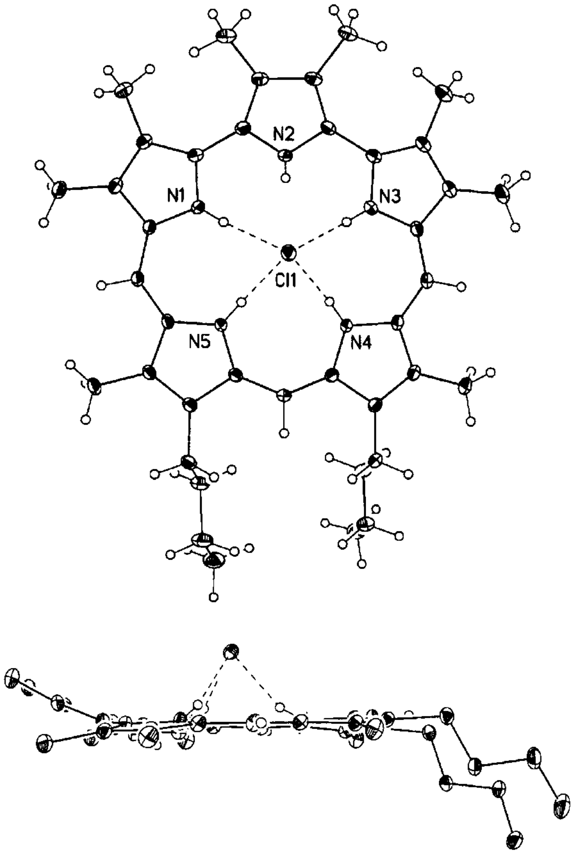

Figure 1. Top and side views of the single-crystal X-ray diffraction structure of the hydrochloride salt of isosmaragdyrin **8**.

Å). The distance from the hydrogen-bound acetate oxygen and the mean plane formed by the macrocyclic heteroatoms is 1.32 Å.

Conclusion

The synthesis of pentaazaisosmaragdyrin **8** represents the first example of a stable, doubly contracted pentapyrrolic macrocycle. The finding that this system, in contrast to smaragdyrin, is stable serves to underscore the emerging trend in porphyrin and expanded porphyrin chemistry that isomers can have properties dramatically different from those of their oftentimes better studied "parents".[20,21]

Experimental Section

General. All reagents were obtained commercially and used as received. The synthesis and characterization of **5**−**7** has been previously reported.[14,15]

16,20-Dipropyl-2,3,6,7,10,11,15,21-octamethyl-[22]pentaphyrin-(1.1.1.0.0) (8). In a 4-L round-bottomed flask, 2,5-bis(3,4-dimethyl-2-pyrryl)-3,4-dimethylpyrrole (**6**)[15] (385 mg, 1.37 mmol) and the bisformyl dipyrromethane **5**[14] (468 mg, 1.37 mmol) were dissolved in 2.5 L of a solution of 10% methanol in dichloromethane under an argon blanket. Hydrochloric acid (5 drops; 37% aqueous) was then added, and the reaction mixture was allowed to stir at room temperature in the dark overnight. The solvents were removed in vacuo. The resulting solid was purified by column chromatography using 230−400 mesh ASTM silica gel and chloroform as the eluent. The green fraction was collected, and the solvent was removed in vacuo. Recrystallization from chloroform layered with *n*-hexane afforded the hydrochloric acid salt of isosmaragdyrin in the form of blue crystals possessing a metallic luster. Yield: 312 mg (38%). ^{1}H NMR (300 MHz, $CDCl_3$): δ −3.69 (br, 1H), −2.66 (br, 2H), −1.45 (br, 2H, 1.19 (t, $J = 7.3$ Hz, 6H), 1.88 (m, $J = 7.4$ Hz, 4H), 2.35 (m, $J = 7.7$ Hz, 4H), 3.56 (s, 6H), 3.65 (s, 6H), 3.72 (s, 6H), 3.73 (s, 6H), 4.15 (t, $J = 7.7$ Hz, 4H), 9.90 (s, 1H), 10.14 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.0, 12.3, 13.8, 14.1, 14.3, 23.5, 26.9, 34.7, 84.8, 96.0, 119.9, 120.7, 121.9, 25.3, 125.8, 130.4, 130.7, 135.5, 135.7, 137.8. UV−vis (CH_2Cl_2) λ_{max} [nm] (ϵ): 385 (41 700), 453 (68 200), 666 (34 000), 699 (39 500). LRMS (FAB +) *m*/*e* [relative intensity]: 588 [100]. HRMS (FAB +) *m*/*z* calculated for $C_{39}H_{50}N_5$ (M^+): 588.4066, found 588.4056. Anal. Calcd for $C_{39}H_{50}N_5Cl$: C, 75.03; H, 8.07; N, 11.21. Found: C, 75.06; H, 8.15; N, 11.21.

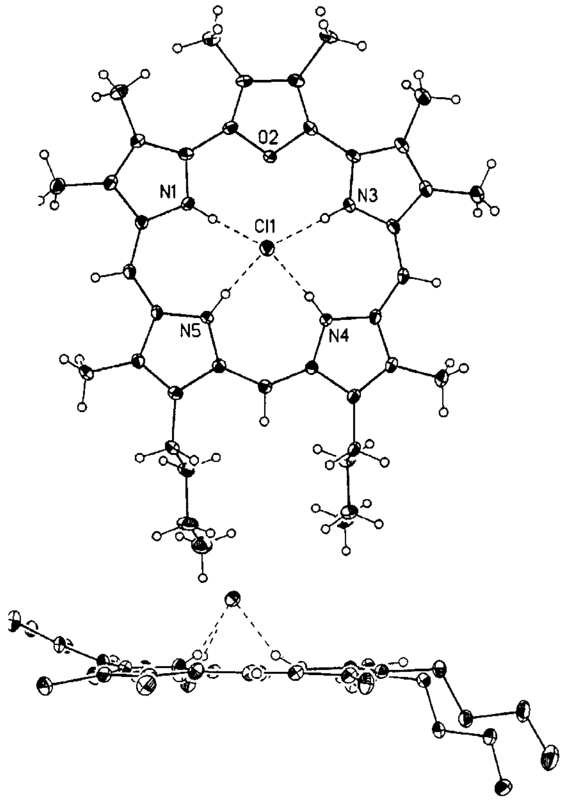

Figure 2. Top and side views of the single-crystal X-ray diffraction structure of the hydrochloride salt of oxaisosmaragdyrin **9**.

16,20-Dipropyl-2,3,6,7,10,11,15,21-octamethyl-5-oxa-[22]-pentaphyrin-(1.1.1.0.0) (9). Using the procedure detailed above, 2,5-bis(3,4-dimethyl-2-pyrryl)-3,4-dimethylfuran (**7**)[15] (141 mg, 0.50 mmol) and the bisformyl dipyrromethane **5**[14] (171 mg, 0.50 mmol) were used to synthesize the hydrochloric acid salt of monoxaisosmaragdyrin **9**, which was purified in accord with the procedure used to purify **8**. Yield: 124 mg (42%). ^{1}H NMR (300 MHz, $CDCl_3$): δ −1.68 (br, 2H), −1.66 (br, 2H), 1.19 (t, $J = 7.3$ Hz, 6H), 1.88 (m, $J = 7.4$ Hz, 4H), 2.36 (m, $J = 7.7$ Hz, 4H), 3.67 (s, 6H), 3.73 (s, 6H), 3.75 (s, 6H), 3.76 (s, 6H), 4.16 (t, $J = 7.8$ Hz, 4H), 9.93 (s, 1H), 10.27 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 12.1, 12.3, 13.5, 14.2, 14.5, 23.4, 26.9, 34.8, 83.9, 95.6, 121.6, 121.7, 123.8, 125.5, 130.6, 131.2, 135.7, 136.0, 137.5, 139.0. UV−vis (CH_2Cl_2) λ_{max} [nm] (ϵ): 380 (44 400), 391 (45 200), 426 (74 700), 449 (160 000), 660 (47 300), 680 (60 300). LRMS (FAB +) *m*/*e* [relative intensity]: 589 [100]. HRMS (FAB +) *m*/*z* calculated for $C_{39}H_{49}N_4O$ (M^+): 589.3906, found 589.3909. Anal. Calcd for $C_{39}H_{49}N_4OCl$: C, 74.91; H, 7.90; N, 8.96. Found: C, 74.74; H, 7.84; N, 8.96. The TFA salt was obtained via the same reaction

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(20) Sessler, J. L. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1348−1350.

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and purification methods described, above with the exception that TFA was used in place of HCl as the catalyst. UV−vis (CH_2Cl_2) λ_{max} [nm] (ϵ): 380 (63 100), 391 (36 700), 424 (63 900), 448 (150 000), 659 (40 900), 676 (48 100). HRMS (CI +) m/z calculated for $C_{39}H_{49}N_4O$ (M^+): 589.3906, found 589.3889. This complex was further characterized by X-ray diffraction analysis (cf. Supporting Information).

Acknowledgment. This work was supported by the National Science Foundation (Grant CHE 9725399 to J.L.S.).

Supporting Information Available: X-ray experimental details for **8**·Cl, **9**·Cl, and **9**·TFA and tables of crystallographic data, collection procedures, parameters, complete atomic coordinates, bond distances and angles, anisotropic thermal parameters, and torsion angles (98 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.

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