Sapphyrins

A Benzodipyrrole-Derived Sapphyrin**

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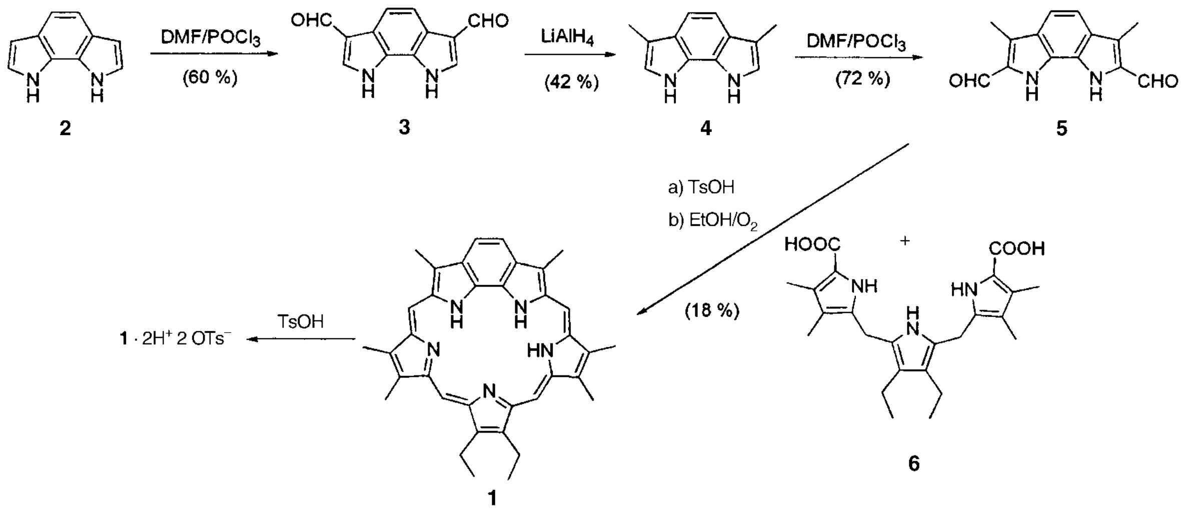
The discovery of expanded porphyrins has broadened the scope of porphyrin-related research. Since the first report of expanded porphyrins, namely a pentapyrrolic aromatic macrocycle referred to as sapphyrin,[1] various other oligopyrrole macrocycles including pentaphyrins, hexaphyrins, and rubyrins have been synthesized and characterized.[2] However, sapphyrins remain among the best studied of all the expanded porphyrins. For instance, they have been studied as hosts for anions[3,4] and as potential photosensitizers for photodynamic therapy,[5] and owing to their unique electronic features, which are exhibited in their narrow absorption bands, sapphyrins have also attracted interest as possible nonlinear optical materials. The synthesis and anion-binding properties of sapphyrins have been reviewed recently.[6] The most common synthesis of sapphyrins is the so-called 3+2 approach reported by Broadhurst et al.,[1] and this approach has successfully been employed to obtain a range of alkyl- and *meso*-substituted sapphyrins.[7–12] A less common but equally attractive approach is the so-called 4+1 approach, which relies on the use of a tetrapyrrolic precursor and formylpyrroles.[8,13,14] Despite these and other efforts, there has apparently been no report of a sapphyrin that imposes intrinsic conformational restriction on its pentapyrrolic core. In this light, we report here the synthesis and spectroscopic properties of what we believe is the first benzodipyrrole-derived sapphyrin system, **1**. As the corresponding benzo-extended sapphyrins[15] were found to exhibit red-shifted absorption bands, it was considered likely that the use of a benzodipyrrole unit such as **3** would provide another means of fine-tuning the electronic properties of sapphyrins.

Sapphyrin **1** was synthesized through a typical 3+2 condensation from the key precursors, diformylbenzodipyrrole derivative **5** and tripyrromethane dicarboxylic acid **6**. As shown in Scheme 1, 3,6-diformylbenzodipyyrole **3** was obtained by a Vilsmeier–Haack reaction of benzodipyrrole (**2**),[16] which upon reduction with $LiAlH_4$ yielded 3,6-dimethylbenzodipyrrole (**4**). A further Vilsmeier–Haack reaction of this intermediate afforded the required dialdehyde **5** in 72 % yield. Tripyrromethane dicarboxylic acid **6** was synthesized easily according to a reported procedure.[17] Acid-catalyzed condensation of benzodipyrrole derivative **5** and tripyrromethane dicarboxylic acid **6** followed by air oxidation provided the desired fused sapphyrin **1** in 18 % yield. A higher yield was expected as a result of the conformational restriction imposed by the fused dipyrrole moiety, but the isolated yield of **1** was rather low. Intermediate **5** proved to be less reactive than simple dipyrroles, and this lack of reactivity is thought to account, in part, for the low isolated yield of the sapphyrin product.[18] Sapphyrin **1** was characterized by standard spectroscopic methods, as well as single-crystal X-ray diffraction studies. The salt $\mathbf{1}\cdot 2H^+ 2OTs$ (OTs = *p*-



Scheme 1. Synthesis of sapphyrin **1**. DMF = *N*,*N*-dimethylformamide, TsOH = *p*-toluenesulfonic acid.

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$CH_3C_6H_4SO_3^-$ (tosylate)) was easily obtained by shaking a solution of **1** in dichloromethane with aqueous *p*-toluenesulfonic acid.

The ^{1}H NMR spectrum of the free-base sapphyrin **1** revealed three broadened signals at $\delta = -0.87$, -1.30, and -2.46 ppm for the inner NH protons which indicates that inner NH protons reside unsymmetrically as shown in Scheme 1. On the other hand, the ditosylate salt **1**·$2H^+2OTs$ showed distinctive resonances at $\delta = -3.65$, -3.78, and -4.79 ppm, with a respective ratio of integration of 2:1:2, which indicates C_{2v} symmetry for the diprotonated salt. The signals for the aromatic protons of *p*-toluenesulfonic acid appear as broad singlets at $\delta = 5.44$ and 2.59 ppm and indicate a strong diamagnetic influence from the sapphyrin.

Diffraction-grade crystals of **1**·$2H^+2OTs$ were obtained by the slow diffusion of hexane into a solution of the salt in chloroform. X-ray crystal structure analysis revealed the presence of one molecule of chloroform in the unit cell[19] and also showed that the oxygen atoms on one of the tosylate groups (upper) were disordered. As shown in Figure 1, the two oxygen atoms on the upper tosylate group are bound to three pyrrolic NH groups, with O–N distances of 2.830 (O1–N2), 2.932 (O1–N3), and 2.962 Å (O2–N5), while only a single oxygen atom (O1′) from the lower tosylate group is bound to the three NH groups at N1, N2, and N4 with respective O–N distances of 2.881, 2.927, and 2.838 Å. Presumably as a result of these interactions with the anions and possible steric congestion between the five inner N–H groups, the pyrrole ring that bears N5 is tilted upward relative to the mean plane of the macrocycle. This behavior is most unusual for a β-alkyl-substituted sapphyrin.

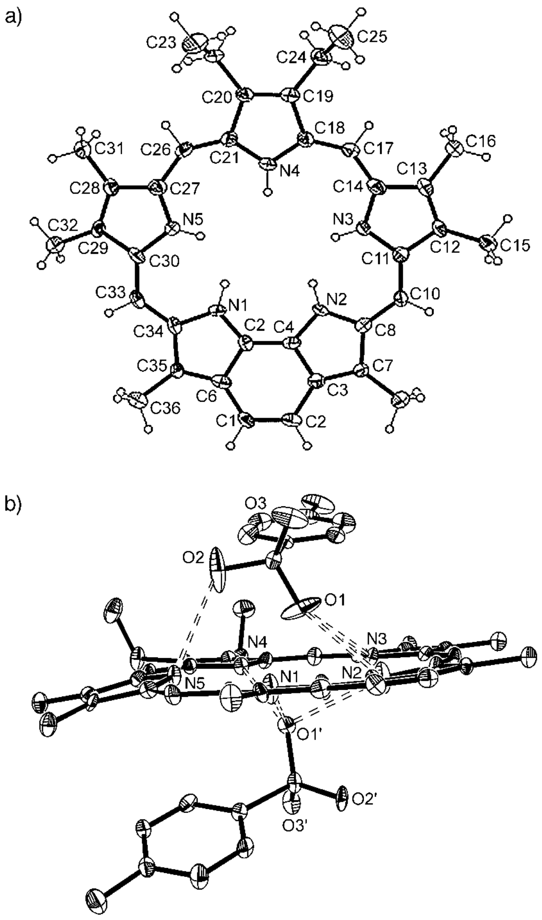

Figure 1. ORTEP views of the sapphyrin di-*p*-toluenesulfonic acid salt, **1**·$2H^+2OTs^-$. a) Top view with the tosylate groups omitted for clarity, and b) side view showing the unsymmetrical nature of the hydrogen-bonding interactions between the two anions and the protonated macrocycle.

The pyrrole–tosylate N–O distances range from 2.838 to 2.962 Å and are well within the range expected for effective hydrogen-bonding interactions. Further analysis of the 3D packing structure indicated that two tosylate groups are located between two sapphyrin molecules. The two tosylate anions lie slip-stacked one above the other in an antiparallel manner with the sulfonate groups pointing outwards to minimize electronic repulsion between them (see Figure 2). The distance between the uppermost hydrogen atom (H50) of the methyl group of the lower tosylate group and carbon atom C49 at the 4-position of the benzene ring in the upper tosylate is 2.941 Å.

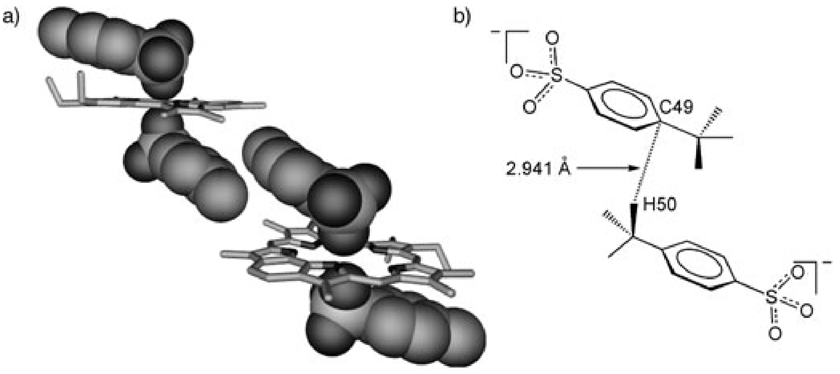

Figure 2. a) Arrangement of two diprotonated sapphyrin molecules (stick representations; C light gray, N dark gray) and their respective tosylate anions (space-filling representation; sulfonate oxygen atoms are shaded darker than S and C atoms) within the crystal structure. b) The two tosylate anions located between the two sapphyrins are packed antiparallel, with a distance of 2.941 Å separating atom C49 (*C*–C) of one OTs moiety and H50 (tolyl H_2C–*H*) of the other.

The absorption spectra of free-base **1** and its ditosylate salt **1**·$2H^+2OTs$ are shown in Figure 3. Sapphyrin **1** shows a Soret-like band at 466 nm, whereas the Soret-like band is slightly red-shifted and appears at 469 nm in the salt **1**·$2H^+2OTs$. The bands are also red-shifted relative to the values of 457 and 456 nm reported for decaalkylsapphyrin and its diprotonated form, respectively.[20] The strongest absorbing Q-band in free-base form **1** appears at 727 nm, whereas for the salt **1**·$2H^+2OTs$ the major Q-band at 703 nm is accompanied by a weaker band at 748 nm. The Q-bands are also significantly red-shifted relative to those of decaalkylsapphyrin.[14a] The Q-bands for **1** and its diprotonated salt are relatively less intense than those for other diprotonated

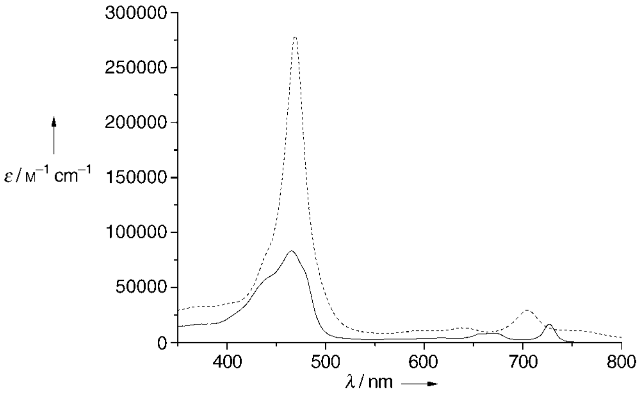

Figure 3. UV/Vis spectra of sapphyrin **1** (——; 1.99×10^{-5} M in $CHCl_3$ with 1% Et_3N) and $\mathbf{1}\cdot2H^+2OTs^-$ (-----; 6.79×10^{-5} M in $CHCl_3$).

sapphyrin species. The absorption spectrum of the dichloride salt of **1**, which was obtained by Sessler's method,[18,20] was compared directly with the spectra of some benzo-extended sapphyrins.[15] From the results obtained (data not shown), it appears that incorporation of the benzene ring directly into the sapphyrin, as in **1**, has a stronger effect on the electronic properties of the molecule than in benzo-extended analogues by extension of the overall π-electron conjugation (aromaticity) through the use of the diene part of the fused benzene unit.

In conclusion, we have introduced a new member to the family of extended porphyrins, a pyrrole-fused sapphyrin. The diprotonated benzodipyrrole-bridged sapphyrin **1** is slightly buckled presumably from a combination of conformational restriction about the fused benzodipyrrole moiety and through steric interactions between the five inner amine groups. Currently, we are exploring further extensions of this theme, for instance, by targeting the replacement of the dipyrrole moiety with other aromatic and heteroaromatic subunits.

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[1] M. J. Broadhurst, R. Grigg, A. W. Johnson, *Chem. Commun.* **1969**, 23–24.

[2] a) H. Rexhausen, A. Gossauer, *J. Chem. Soc. Chem. Commun.* **1983**, 275; b) R. Charriére, T. A. Jenny, H. Rexhausen, A. Gossauer, *Heterocycles* **1993**, *36*, 1561–1575; c) J. L. Sessler, T. Morishima, V. Lynch, *Angew. Chem.* **1991**, *103*, 1018–1020; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 977–980; d) M. G. P. M. S. Neves, R. M. Martins, A. C. Tomé, A. J. D. Silvestre, A. M. S. Silva, V. Félix, M. G. B. Drew, J. A. S. Cavaleiro, *Chem. Commun.* **1999**, 285–386; e) J.-Y. Shin, H. Furuta, K. Yoza, S. Igarashi, A. Osuka, *J. Am. Chem. Soc.* **2001**, *123*, 7190–7191.

[3] J. L. Sessler, M. Cyr, V. Lynch, E. McGhee, J. Ibers, *J. Am. Chem. Soc.* **1990**, *112*, 2810–2813.

[4] V. Kral, H. Furuta, K. Shreder, V. Lynch, J. L. Sessler, *J. Am. Chem. Soc.* **1996**, *118*, 1595–1607.

[5] B. G. Maiya, M. Cyr, A. Harriman, J. L. Sessler, *J. Phys. Chem.* **1990**, *94*, 3597–3601.

[6] J. L. Sessler, J. M. Davis, *Acc. Chem. Res.* **2001**, *34*, 989–997.

[7] M. J. Broadhurst, R. Grigg, A. W. Johnson, *J. Chem. Soc. Perkin Trans. 1* **1972**, 2111–2116.

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

[9] C. Bruckner, E. D. Sternberg, R. W. Boyle, D. Dolphin, *Chem. Commun.* **1997**, 1689–1690.

[10] A. Srinivasan, S. Mahajan, S. K. Pushpan, M. Ravikumar, T. K. Chandrashekar, *Tetrahedron Lett.* **1998**, *39*, 1961–1964.

[11] A. Srinivasan, S. K. Pushpan, M. R. Kumar, S. Mahajan, T. K. Chandrashekar, R. Roy, P. Ramamurthy, *J. Chem. Soc. Perkin Trans. 2* **1999**, 64, 961–968.

[12] A. Srinivasan, V. G. Anand, S. J. Narayanan, S. K. Pushpan, M. R. Kumar, T. K. Chandrashekar, K. I. Sugiura, Y. Sakata, *J. Org. Chem.* **1999**, *64*, 8693–8697.

[13] R. Paolesse, S. Licoccia, M. Spagnoli, T. Boschi, R. G. Khoury, K. M. Smith, *J. Org. Chem.* **1997**, *62*, 5133–5137.

[14] a) D. T. Richter, T. D. Lash, *J. Am. Chem. Soc.* **1998**, *120*, 9965–9966; b) D. T. Richter, T. D. Lash, *Tetrahedron Lett.* **1999**, *40*, 6735–6738; c) D. T. Richter, T. D. Lash, *J. Org. Chem.* **2004**, *69*, **8842–8850**.

[15] N. Ono, K. Kuroki, E. Watanabe, N. Ochi, H. Uno, *Heterocycles* **2004**, *62*, 365–373.

[16] A. Berlin, S. Bradamante, R. Ferraccioli, G. A. Pagani, F. Sannicolo, *J. Chem. Soc. Chem. Commun.* **1987**, 1176–1177.

[17] J. L. Sessler, M. R. Johnson, V. Lynch, *J. Org. Chem.* **1987**, *52*, 4394–4397.

[18] Spectroscopic data for free-base **1**: ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 10.64$ (br s, 2H), 10.49 (br s, 2H), 8.86 (s, 2H), 4.42 (m, 4H), 4.32 (s, 6H), 3.80 (s, 6H), 3.77 (s, 6H), 2.03 (t, 6H), −0.87 (br s, 1H), −1.30 (br s, 1H), −2.46 ppm (br s, 1H); FAB-MS *m/z* calcd for $C_{36}H_{37}N_5$: 539.30; found: 540.30 $[M+1]$; UV/Vis (1% Et_3N in $CHCl_3$): λ_{max} ($\log\varepsilon$) = 466 (4.92), 618 (3.59), 667 (3.92), 727 nm (4.22).

[19] Crystal data for $\mathbf{1}\cdot2H^+2OTs$: $C_{51}H_{54}Cl_3N_5O_6S_2$, triclinic, space group P-1, $a = 10.2266(8)$ Å, $b = 12.7492(10)$ Å, $c = 19.9972(16)$ Å, $\alpha = 108.042(2)°$, $\beta = 95.074(2)°$, $\gamma = 102.586(2)°$, $V = 2385.1(3)$ Å^3, $T = 173(2)$ K, $Z = 2$, GOF on $F^2 = 0.853$, R_1 $(I > 2\sigma(I)) = 0.0646$, $wR_2 = 0.1298$. The crystal was attached to glass fibers and mounted on a Bruker SMART diffractometer equipped with graphite monochromated $Mo_{K\alpha}$ ($\lambda = 0.71073$ Å) radiation, operating at 50 kV and 30 mA, and a CCD detector; 45 frames of two-dimensional diffraction images were collected and processed to obtain the cell parameters and orientation matrix. All data collections were performed at 173(2) K. The data collection 2θ range is 2.18–52.04°. No significant decay was observed during the data collection. The raw data were processed to give structure factors by using the SAINT program. The structure was solved by direct methods and refined by full-matrix least-squares against F^2 for all data by using SHELXTL software (version 5.14).[21] All non-hydrogen atoms were anisotropically refined. All other hydrogen atoms were included in their calculated positions and refined by using a riding model. CCDC 268397 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[20] J. L. Sessler, M. Cyr, A. K. Burrell, *Tetrahedron* **1992**, *48*, 9661–9672.

[21] SHELXTL NT Crystal Structure Analysis Package, Version 5.14; Bruker AXS, Analytical X-ray System, Madison, WI, **1999**.