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Dimethoxytetraphenylbenziporphyrins☆,☆☆

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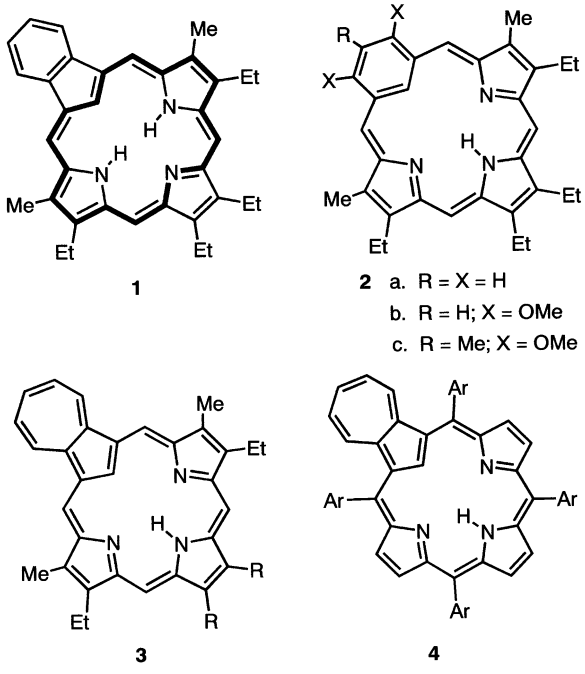
Abstract—A two step synthesis of dimethoxytetraphenylbenziporphyrins is reported. Although these porphyrin analogues are cross-conjugated, addition of TFA affords diprotonated species that show a significant diamagnetic ring current. In addition, reaction with nickel(II) acetate also affords organometallic derivatives with borderline aromatic characteristics.

Carbaporphyrinoids,[1] porphyrin analogues where one or more of the pyrrolic units have been replaced by carbocyclic rings, are an important group of conjugated macrocycles that exhibit unusual chemistry such as the ability to form stable organometallic derivatives.[2] As is the case for true porphyrins, many of these macrocycles, including the benzocarbaporphyrins **1**,[3] are aromatic and exhibit strong diamagnetic ring currents in their proton NMR spectra. However, benziporphyrin **2a**[4,5] is non-aromatic showing no indication of diatropicity by proton NMR spectroscopy due to the interruption of the usual 18π electron delocalization pathway by the cross-conjugated benzene moiety.[5b] Azuliporphyrins **3** and **4** have intermediary characteristics showing a significant amount of aromatic character despite the presence of a cross-conjugated azulene unit.[6,7] This was attributed to dipolar resonance contributors that give the system tropylium character while simultaneously generating a carbaporphyrin-like 18π electron delocalization pathway. The aromatic character for **3** and **4** is considerably enhanced in the protonated forms where this type of resonance contributor aids in charge delocalization.[6,7] Dimethoxybenziporphyrin **2b**, and to a lesser extent the related 3-methyl species **2c**, also shows borderline aromatic character by proton NMR spectroscopy that again is significantly enhanced in the presence of acid.[5c] Carbaporphyrinoids such as **1**–**3** can be obtained via the '3+1' methodology[8] from tripyrranes and aromatic dialdehydes



in good yields, although these multistep routes only provide limited quantities of these interesting systems for further investigation. For this reason, there has been some incentive for the development of more direct routes to carbaporphyrinoids. Recently, we reported the synthesis of tetraarylazuliporphyrins **4**[7] in a one-pot procedure from aryl aldehydes, pyrrole and azulene under Lindsey–Rothemund conditions.[9] In independent work by Stepien and Latos–Grazynski, tetraphenylbenziporphyrin was prepared in two steps from isophthalaldehyde (Scheme 1).[10] Reaction of the dialdehyde with phenyl magnesium bromide afforded a dicarbinol and this reacted with

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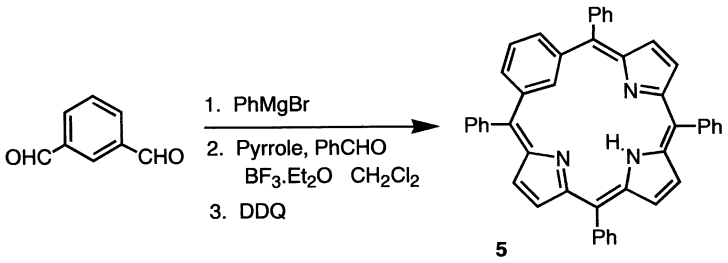
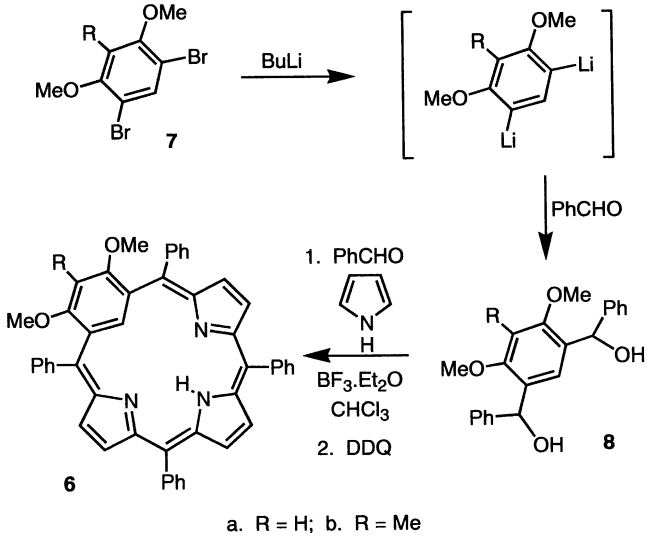


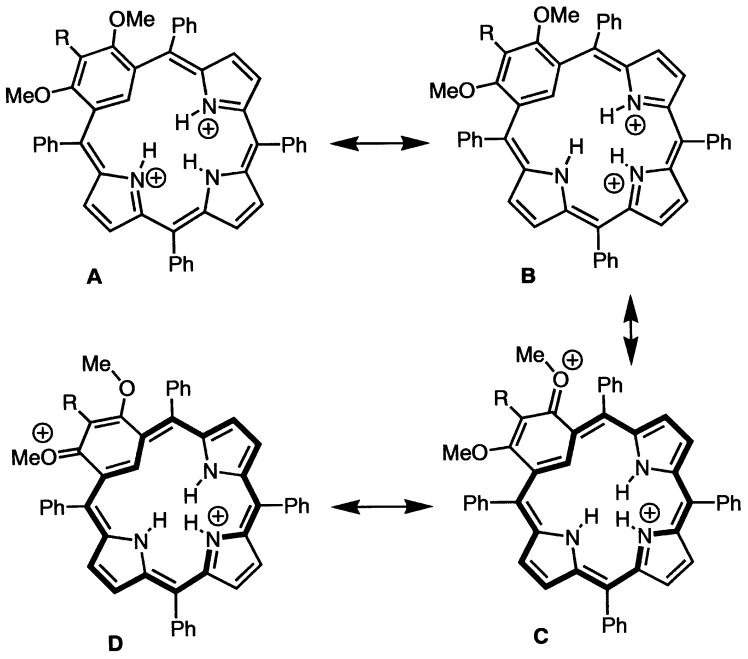
Scheme 1.

pyrrole and benzaldehyde in the presence of boron trifluoride etherate to give, following an oxidation step, the nonaromatic benziporphyrin **5** in moderate yield. The unique properties observed for dimethoxybenziporphyrins **2b** and **2c**, and their relationship to the azuliporphyrins **3** and **4**, inspired us to develop a straightforward route to related tetraphenyl substituted macrocycles **6** (Scheme 2). 1,3-Dimethoxybenzene and 2,6-dimethoxytoluene are easily dibrominated to give **7a** and **7b**, respectively.[11] Following lithium–halogen exchange, reaction with 2 equiv. of benzaldehyde afforded the dicarbinols **8**. The dimethoxybenzene derivative **8a** was isolated as small white needles in >70% yield, while the methyl substituted version **8b** afforded the corresponding dialcohol in 62% yield. In both cases, the proton and ^{13}C NMR spectra indicated that the products had been isolated as a mixture of two diastereomers, but this was not important as the stereochemistry is not retained in the targeted benziporphyrins. The synthesis of **6a** was initially attempted by reacting **8a** with 2 equiv. of benzaldehyde and 3 equiv. of pyrrole using $BF_3{\cdot}Et_2O$ as the catalyst and dichloromethane as the solvent. Following oxidation with DDQ, chromatography on silica and recrystallization from chloroform–methanol, the dimethoxybenziporphyrin **6a** was isolated in 5% yield. As has been observed for syntheses of many sterically hindered porphyrins,[9b,12] as well as tetraarylazuliporphyrins,[7] chloroform proved to be a superior solvent for this chemistry. Under optimized conditions using chloroform, the yield of **6a** was raised to 15%. Significantly, under the same conditions **8b** reacted with pyrrole and benzaldehyde to give the related porphyrinoid **6b** in 25% yield. These represent very respectable results when one takes into account the small number of steps involved in these syntheses.

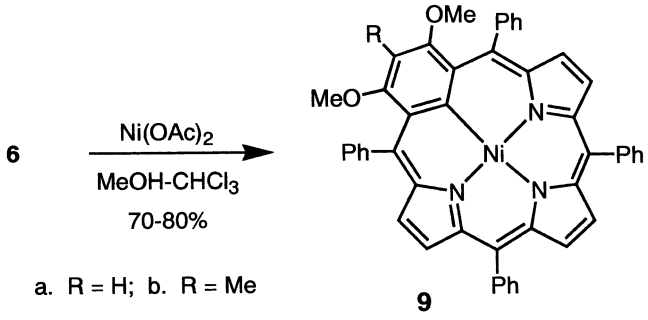


Scheme 2.

As the benziporphyrins are cross-conjugated, the macrocycles would not be expected to exhibit diatropic ring currents in their proton NMR spectra. In addition, the *meso*-aryl substituents adjacent to the methoxy units would be expected to significantly distort the ring system further decreasing the possibilities for aromatic character. However, the internal CH of **6a** resonates at 5.84 ppm, hinting at the presence of a small diamagnetic ring current, while the NH gives rise to a broad peak at 9.2 ppm. In the proton NMR spectrum for **6b**, these resonances show up at 6.42 and 9.9 ppm, respectively, indicating that **6a** is more aromatic than **6b**. Although these shifts are relatively small, the corresponding dications $\mathbf{6}H_2^{2+}$ that are formed by addition of TFA showed far more pronounced effects. In the proton NMR spectrum of $\mathbf{6a}H_2^{2+}$ in TFA–$CDCl_3$, the internal CH shifts upfield to 3.5 ppm, while the NHs give rise to two resonances at 8.4 (2H) and 6.8 ppm (1H). The external pyrrolic protons also shift downfield by ca. 0.5 ppm. This effect is much reduced for the 2-methylbenziporphyrin dication $\mathbf{6b}H_2^{2+}$, where the interior CH was observed at 4.7 ppm and the NH resonances appeared at 8.2 and 9.9 ppm. Even so, these shifts clearly point to the presence of a diamagnetic ring current for $\mathbf{6b}H_2^{2+}$ as well as for $\mathbf{6a}H_2^{2+}$. The origin of the aromatic character observed for the dimethoxybenziporphyrins most likely derives from the electron-donating influence of the methoxy groupings. These allow for better charge delocalization in the protonated species $\mathbf{6}H_2^{2+}$ (Scheme 3). A series of canonical forms (e.g. **A**–**D**) can be used to describe these dications, and in contributors such as **C** and **D**, electron-donation leads to the presence of an 18π-electron delocalization pathway. These electronic interactions require the oxygen atoms to take on sp^2 hydrid character and this requires the methoxy groups to lie in the same plane as the macrocycle. The methyl substituted system is too sterically crowded to easily allow the methoxy units to take on the required geometry, although the associated electronic interaction must still occur to a limited extent. The free base molecules can have similar dipolar resonance contributors, but these are less favored due to the associated need for charge separation. Hence,



Scheme 3.



Scheme 4.

dimethoxytetraphenylbenziporphyrins are intriguing systems that have properties that are intermediary between tetraphenylbenziporphyrin **5** and tetraphenylazuliporphyrin **4**. It is noteworthy that the free base and dicationic forms for these macrocycles show increasing aromatic character going from **5** to **6b** to **6a** to **4**. For instance, the proton NMR spectra for the free base forms in $CDCl_3$ show the internal CHs at 7.33,[10] 6.42, 5.84 and 3.35 ppm, respectively. These differences cannot be simply due to electron-donating effects, andare paralleled by a downfield shift of the external pyrrolic protons. The dications for **6b**, **6a** and azuliporphyrin **4** show a more pronounced trend for the inner CH, giving resonances at 4.73, 3.5 and –0.33 ppm,[7a] respectively. Again the upfield shifts for the internal CHs is paralleled by a downfield shift for the external pyrrolic protons.

The UV–vis spectra for the free base forms of **6a**, **6b** and **5** are similar to one another, showing a weak Soret-like band slightly above 400 nm, and a broad absorption near 700 nm. However, there is a bathochromic shift for the shorter wavelength band going from **5** to **6b** to **6a**, giving λ_{max} values of 437, 422 and 411 nm, respectively. The dications of **6b**, **6a** and **4** in 1% TFA–chloroform all show a show a strong broad absorption in the near IR, although in this case there is a hypsochromic shift for the series with the λ_{max} values at 889, 876 and 850 nm.[7a] The dication of **5** gives data that are agreement with this trend, showing the equivalent absorption at >900 nm (Scheme 4).[10]

Azuliporphyrins undergo metallation with nickel(II) or palladium(II) acetate,[2b] and it was of some interest to see whether it is also possible to synthesize organometallic derivatives for **6a** and **6b**. Nickel(II) acetate in chloroform–methanol cleanly reacted with **6** to afford the related organometallic derivatives **9** in 70–80% yield (Scheme 4). However, in our hands palladium(II) acetate failed to give the anticipated palladium(II) benziporphyrins, and considerable decomposition was noted for prolonged reaction times. Nonetheless, these results confirm that these dimethoxybenziporphyrins are suitable ligands for organometallic chemistry. The proton NMR spectrum for **9a** in $CDCl_3$ gave resonances for the pyrrolic protons that were ca. 0.6 ppm further downfield than the free base **6a**, and similar, albeit smaller, shifts were noted for the **9b** as well. These results imply that the metallo-derivatives have significantly higher diatropic character than the free base dimethoxybenziporphyrins, a feature that may be due in part to a conformational change associated with binding to the nickel(II) cation.

In conclusion, a straightforward route to electron-rich tetraphenylbenziporphyrins **6** has been developed. These novel porphyrin analogues show enhanced diatropic character under acidic conditions that parallels the results obtained for azuliporphyrins.[7] In addition,

these macrocycles readily form nickel(II) complexes and show great promise as organometallic ligands. Further studies on this family of tetraarylporphyrinoids are in progress.

Acknowledgements

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References

1. (a) Lash, T. D. *Synlett* **2000**, 279; (b) Lash, T. D. In *The Porphyrin Handbook*; Kadish, K. M.; Smith, K. M.; Guilard, R., Eds.; San Diego: Academic Press, 2000; Vol. 2, pp. 125–199.
2. (a) Muckey, M. A.; Szczepura, L. F.; Ferrence, G. M.; Lash, T. D. *Inorg. Chem.* **2002**, *41*, 4840; (b) Graham, S. R.; Ferrence, G. M.; Lash, T. D. *Chem. Commun.* **2002**, 894; (c) Stepien, M.; Latos-Grazynski, L.; Lash, T. D.; Szterenberg, L. *Inorg. Chem.* **2001**, *40*, 6892.
3. (a) Lash, T. D.; Hayes, M. J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 840; (b) Lash, T. D.; Hayes, M. J.; Spence, J. D.; Muckey, M. A.; Ferrence, G. M.; Szczepura, L. F. *J. Org. Chem.* **2002**, *67*, 4860; (c) Liu, D.; Lash, T. D. *J. Org. Chem.* **2003**, *68*, 1755.
4. Berlin, K.; Breitmaier, E. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1246.
5. (a) Lash, T. D. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2533; (b) Lash, T. D.; Chaney, S. T.; Richter, D. T. *J. Org. Chem.* **1998**, *63*, 9076; (c) Richter, D. T.; Lash, T. D. *Tetrahedron* **2001**, *57*, 3659.
6. (a) Lash, T. D.; Chaney, S. T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 839; (b) Graham, S. R.; Colby, D. A.; Lash, T. D. *Angew. Chem., Int. Ed. Engl.* **2002**, *41*, 1371.
7. (a) Colby, D. A.; Lash, T. D. *Chem. Eur. J.* **2002**, *8*, 5397; (b) Lash, T. D.; Colby, D. A.; Ferrence, G. M. *Eur. J. Org. Chem.* **2003**, in press. See also: Colby, D. A.; Lash, T. D. *J. Org. Chem.* **2002**, *67*, 1031.
8. Lash, T. D. *Chem. Eur. J.* **1996**, *2*, 1197.
9. (a) Lindsey, J. S.; Schreiman, I. C.; Hsu, H. C.; Keaney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827; (b) Lindsey, J. S.; Wagner, R. W. *J. Org. Chem.* **1989**, *54*, 828.
10. Stepien, M.; Latos-Grazynski, L. *Chem. Eur. J.* **2001**, *7*, 5113.
11. Worden, L. R.; Kaufman, K. D.; Smith, P. J.; Widiger, G. N. *J. Chem. Soc. (C)* **1969**, 227.
12. (a) Lash, T. D.; Novak, B. H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 683; (b) Lash, T. D.; Chandrasekar, P. *J. Am. Chem. Soc.* **1996**, *118*, 8767; (c) Spence, J. D.; Lash, T. D. *J. Org. Chem.* **2000**, *65*, 1530.