Syntheses of Quadruply Two- and Three-Atom, Aza-Bridged, Cofacial Bis(5,10,15,20-tetraphenylporphyrins)

Brett C. Bookser and Thomas C. Bruice*

Contribution from the Department of Chemistry, University of California at Santa Barbara, Santa Barbara, California 93106. *Received October 3, 1990*

Abstract: Several syntheses for quadruply aza-bridged, cofacial bis(5,10,15,20-tetraphenylporphyrins) were investigated. Reaction of 5,10,15,20-tetrakis(α-bromo-*m*-tolyl)porphyrin (**2**) with *p*-toluenesulfonamide or cyanamide and Cs_2CO_3 at high dilution in dimethylformamide produced the tosyl and cyano dimers **3a** and **3b** in 8% yield each. The method of choice was the reaction of porphyrin **2** with tosylamido porphyrin **5a** under the same conditions to give dimer **3a** in 38% yield. Biphenyl radical anion induced desulfonylation of **3a** provided the amino dimer **3c** (41%). Reaction of porphyrin **2** with tosylamido porphyrin **13** provided the dimer **14** (of reduced bridge length) in 1% yield. Other methods for the synthesis of **3a** and **3c** are also discussed. UV/vis and ^1H NMR spectroscopic results suggest an eclipsed "screwed-down" preferred conformation for these dimers, and molecular models are used to illustrate this conformational possibility.

Introduction

Many metabolic processes involve catalysis by multimetal proteins. Covalently linked, cofacial or *strati*-bisporphyrins[1-5] and their metallo complexes have been explored in the modeling of a number of these systems. The groups of Chang and Collman have carried out extensive studies upon the four-electron reduction of dioxygen to water as a model for cytochrome-*c* oxidase with use of cofacial bisporphyrins with relatively small internal cavities.[6,7] Dioxygen and carbon monoxide binding affinities have been determined.[8] The antiferromagnetic coupling in superoxide dismutase and cytochrome-*c* oxidase has been mimicked by employing such systems.[5d,e] Several cofacial bisporphyrins have been employed in studies to mimic the aspects of energy storage and electron transfer that occur in the photosynthetic reaction center.[9]

(1) Several terms have been used to describe the orientation of one porphyrin ring parallel and coplanar on top of another (i.e., strati by Kagen,[5b] face to face by Collman,[5a] and cofacial by Chang[3b]). Whereas the term cofacial is now generally the most commonly used descriptor, we prefer the usage of strati (from stratum, Latin for covering) for the specific naming of compounds, since it allows for more detailed structural information than simple letter-number shorthand abreviations. Moreover, a new shorthand naming system will be presented in the body of this account,[17] which derives naturally from the strati terminology used in the Experimental Section.

(2) For a partial review of the literature prior to 1980, see: Dolphin, D.; Hiom, J.; Paine, J. B., III. *Heterocycles* **1981**, *16*, 417.

(3) For syntheses of covalently linked cofacial bisporphyrins with unsubstituted meso positions, see: (a) Ogoshi, H.; Sugimoto, H.; Yoshida, Z.-i. *Tetrahedron Lett.* **1977**, 169. (b) Chang, C. K.; Kuo, M.-S.; Wang, C.-B. *J. Heterocycl. Chem.* **1977**, *14*, 943. (c) Chang, C. K. *Ibid.* **1977**, *14*, 1285. (d) Chang, C. K. *Adv. Chem. Ser.* **1979**, *173*, 162. (e) Chang, C. K.; Abdalmuhdi, I. *J. Org. Chem.* **1983**, *48*, 5388. (f) *Idem. Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 164. (g) Eaton, S. S.; Eaton, G. R.; Chang, C. K. *J. Am. Chem. Soc.* **1985**, *107*, 3177. (h) Traylor, T. G.; Tatsuno, Y.; Powell, D. W.; Cannon, J. P. *J. Chem. Soc., Chem. Commun.* **1977**, 732. (i) Collman, J. P.; Denisevich, P.; Konai, Y.; Marrocco, M.; Koval, C.; Anson, F. C. *Ibid.* **1980**, *102*, 6027. (j) Collman, J. P.; Anson, F. C.; Bencosme, S.; Chong, A.; Collins, T.; Denisevich, P.; Evitt, E.; Geiger, T.; Ibers, J. A.; Jameson, G.; Konai, Y.; Koval, C.; Meier, K.; Oakley, P.; Pettman, R.; Schmittou, E.; Sessler, J. In *Organic Synthesis Today and Tomorrow*; Trost, B. M., Hutchinson, C. R., Eds.; Pergamon Press: Oxford, 1981; pp 29-45. (k) Collman, J. P.; Chong, A. O.; Jameson, G. B.; Oakley, R. T.; Rose, E.; Schmittou, E. R.; Ibers, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 516. (l) Collman, J. P.; Bencosme, C. S.; Durand, R. R., Jr.; Kreh, R. P.; Anson, F. C. *Ibid.* **1983**, *105*, 2699. (m) Collman, J. P.; Bencosme, C. S.; Barnes, C. E.; Miller, B. D. *Ibid.* **1983**, *105*, 2704. (n) Hiom, J.; Paine, J. B., III; Zapf, U.; Dolphin, D. *Can. J. Chem.* **1983**, *61*, 2220. (o) Hamilton, A. D.; Lehn, J.-M.; Sessler, J. L. *J. Chem. Soc., Chem. Commun.* **1984**, 311. (p) *Idem. J. Am. Chem. Soc.* **1986**, *108*, 5158. (q) Nishide, H.; Maeda, H.; Wang, S.-g.; Tsuchida, E. *J. Chem. Soc., Chem. Commun.* **1985**, 573. (r) Dubowchik, G. M.; Hamilton, A. D. *Ibid.* **1985**, 904. (s) Cowan, J. A.; Sanders, J. K. M. *Ibid.* **1985**, 1213. (t) *Idem. Ibid.* **1985**, 1214. (u) *Idem. Tetrahedron Lett.* **1986**, *27*, 1201. (v) Cowan, J. A.; Sanders, J. K. M.; Beddard, G. S.; Harrison, R. J. *J. Chem. Soc., Chem. Commun.* **1987**, 55. (w) Leighton, P.; Sanders, J. K. M. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2385. (x) Cowan, J. A.; Sanders, J. K. M. *Ibid.* **1987**, 2395. (y) Leighton, P.; Cowan, J. A.; Abraham, R. J.; Sanders, J. K. M. *J. Org. Chem.* **1988**, *53*, 733. (z) Hunter, C. A.; Meah, M. N.; Sanders, J. K. M. *J. Chem. Soc., Chem. Commun.* **1988**, 692. (a') Anderson, H. L.; Hunter, C. A.; Meah, M. N.; Sanders, J. K. M. *J. Am. Chem. Soc.* **1990**, *112*, 5780.

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(5) For syntheses of covalently linked cofacial bis(5,10,15,20-tetraphenylporphyrins), see: (a) Collman, J. P.; Elliot, C. M.; Halbert, T. R.; Tovrog, B. S. *Proc. Natl. Acad. Sci. U.S.A.* **1977**, *74*, 18. (b) Kagan, N. E.; Mauzerall, D.; Merrifield, R. B. *J. Am. Chem. Soc.* **1977**, *99*, 5484. (c) Kagan, N. E. In *Porphyrin Chemistry Advances*; Longo, F. R., Ed.; Ann Arbor Science Publishers, Inc.: Ann Arbor, MI, 1979; pp 43-50. (d) Landrum, J. T.; Reed, C. A.; Hatano, K.; Scheidt, W. R. *J. Am. Chem. Soc.* **1978**, *100*, 3232. (e) Landrum, J. T.; Grimmett, D.; Haller, K. J.; Scheidt, W. R.; Reed, C. A. *Ibid.* **1981**, *103*, 2640. (f) Neumann, K. H.; Vögle, F. *J. Chem. Soc., Chem. Commun.* **1988**, 520. (g) Golubchikov, O. A.; Korovina, S. G.; Kuvshinova, E. M.; Semeikin, A. S.; Shul'ga, A. M.; Perfil'ev, V. A.; Syrbu, S. A.; Berezin, B. D. *J. Org. Chem. USSR (Engl. Transl.)* **1989**, *88*, 2144.

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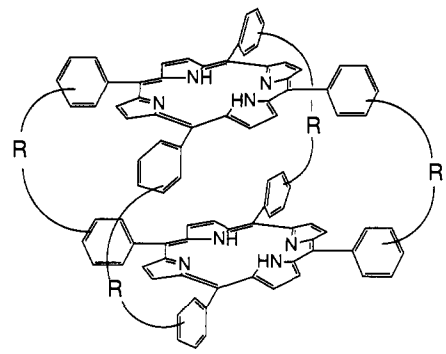
The dimers with relatively large cavities have been used as molecular receptors[10] and also as models of $\pi-\pi$ aggregation[11] by neutral metalated and freebase porphyrins and by metalloporphyrin π cation radicals. Cofacial bisporphyrins have been suggested as useful reagents in the exploration of the mechanisms of cytochrome c_3,[12] nitrogenase,[13] and other multimetal proteins[14] as well as metallo–sandwich complexes[15] and metal–metal multiple bonds.[16] Given this broad spectrum of applications, further advances in the synthesis of cofacial bisporphyrins of fixed geometry may well lend greatly to the understanding of a number of biological and physical phenomena.

The porphyrin moieties of most synthesized cofacial bisporphyrins are linked together by two bridges at transoid β-positions of the porphyrin ring, and their syntheses require the formation of amide or ester linkages in the bridging units from reaction of an acid chloride monomer with another monomer containing amine or alcohol side chains under high dilution conditions. With the single- and double-bridge designs, the flexability of movement of the porphyrin planes is such that they need not remain eclipsed. A drawback in many of these dimers is that they have unsubstituted meso positions, making them susceptible to oxidation.[3i] Substitution of phenyl groups at the meso 5-, 10-, 15-, and 20-positions of the porphyrin ring provides increased resistance to oxidation. The early assumption[3c] that the synthesis of covalently linked, cofacial bis(5,10,15,20-tetraphenylporphyrins) (R-$((TPP)H_2)_2$s),[17] with relatively small internal cavities, would be difficult if not impossible has been supported by experimental work.[3j,5a] With the exception of the elegant work of Kagan,[5b,c] tightly linked, closely interspaced R-$((TPP)H_2)_2$s are unknown.[18]

We present in this paper several practical methods for the synthesis of some new quadruply bridged, cofacial bis(5,10,15,20-tetraphenylporphyrins) with two- and three-atom separations between the *meso*-phenyl substituents. Additionally, the bridging units are made up of central substituents that are potentially useful for further modification of the character of the dimer. These molecules promise to be strong candidates for many of the type studies alluded to at the beginning of this section because of the reinforced geometry of the porphyrin rings.

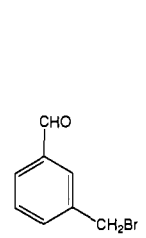


R-$(TPPH_2)_2$

Results and Discussion

Quadruply Three-Atom, Aza-Bridged, Cofacial Bis(5,10,15,20-tetraphenylporphyrins). In order to make the resulting R-$((TPP)H_2)_2$ molecules flexible toward further functionalization at the central bridging unit, a bridge that contained a secondary amine was chosen as the primary objective. With this in mind, standard polyazamacrocycle synthesis techniques could be envisioned.[19] We chose the meta position of the *meso*-phenyl groups as the points from which to anchor the bridges since this position appeared least likely to lead to steric problems in a short bridge. To this end, a monomeric tetraphenylporphyrin having a bromomethyl substituent at the meta position of each *meso*-phenyl group was synthesized[20] and its reactivity toward dimerization investigated as follows.

Reduction of α-bromo-*m*-tolunitrile with diisobutylaluminum hydride (DIBAL–H) provided α-bromo-*m*-tolualdehyde (**1**) (82%), precursor to the porphyrin. The requisite porphyrin *m*-$CH_2Br(TPP)H_2$ (**2**) was prepared in 35% yield by reacting aldehyde **1** with pyrrole according to the Lindsey protocol (catalytic boron trifluoride etherate [$BF_3{\cdot}Et_2O$], 10^{-2} M substrate concentration in $CHCl_3$; tetrachloro-1,4-benzoquinone).[21]



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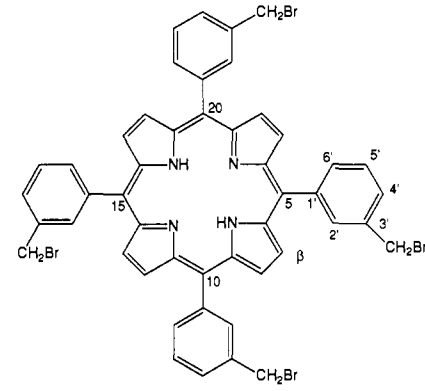

2

Two geometric barriers must be overcome in order to achieve a successful cofacial quadrupole coupling of two tetraphenylporphyrin units in competition with polymer formation. These are (i) the appropriate cofacial alignment of the two reacting monomeric porphyrins and (ii) the rotation of the phenyl groups about the *meso*-carbons of the two so aligned porphyrin rings to bring their respective meta substituents within proximity of each other[22] (the monomer *m*-$CH_2Br(TPP)H_2$ (**2**) illustrates free ro-

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(15) Donohoe, R. J.; Duchowski, J. K.; Bocian. *J. Am. Chem. Soc.* **1988**, *110*, 6119.

(16) Collman, J. P.; Garner, J. M. *J. Am. Chem. Soc.* **1990**, *112*, 166.

(17) In the shorthand nomenclature presented in this paper, R is the substituent that makes up the bridging unit that runs between the *meso*-phenyl groups of the cofacial bisporphyrin R-$((TPP)H_2)_2$ (where $(TPP)H_2$ represents 5,10,15,20-tetraphenylporphyrin with two exchangeable pyrrole H's). In cases of increased symmetry such as R-(*m*-$CH_2(TPP)H_2)_2$, R is the bridging unit that runs between the methylene groups, which are meta-substituted on the *meso*-phenyls. Lastly in cases of unsymmetrical bridges such as *m,m'*-$\overline{TsNCH_2}$-$((TPP)H_2)_2$, the bridging unit is $TsNCH_2$ connected to the *meso*-phenyls at the meta and meta' positions through the nitrogen and methylene groups, respectively.

(18) We arbitrarily define tightly linked as four bridges spaced equally between two porphyrin rings and closely interspaced at a 3.5–6-Å separation between the planes. Two examples exist of R-$((TPP)H_2)_2$-type molecules with large internal cavities (i.e., ref 5f and 5g).

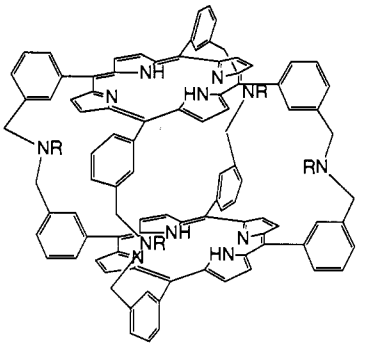
(19) Rossa, L.; Vögtle, F. *Top. Curr. Chem.* **1983**, *113*, 1. For relevant discussion on the synthesis of cyclophanes, see: Boekelheide, V. *Ibid.* **1983**, *113*, 87.

(20) One other halomethyl-substituted $(TPP)H_2$ has been reported—that being 5,10,15,20-tetrakis(α-chloro-*p*-tolyl)porphyrin: Petrova, R. A.; Berezin, B. D.; Potapova, T. I.; Toropova, E. L. *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.* **1986**, *29*, 55; *Chem. Abstr.* **1987**, *107*, 197906g.

(21) Lindsey, J. S.; Wagner, R. W. *J. Org. Chem.* **1989**, *54*, 828.

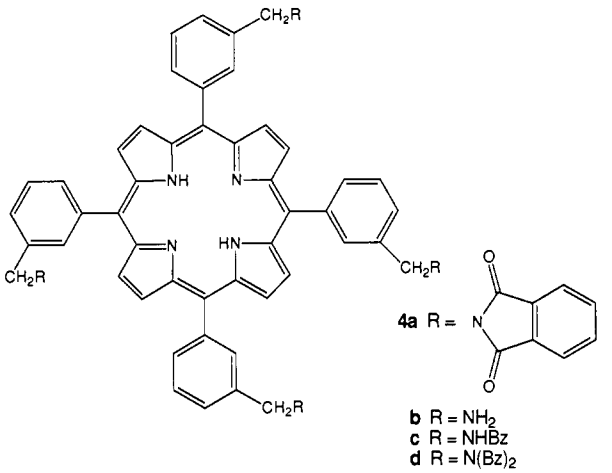
tation of its *meso*-phenyls in its well-resolved ^1H NMR spectrum in $CDCl_3$ at room temperature (see supplementary material), which indicates perfect C_{4v} symmetry). Fortunately, these geometric obstacles were not prohibitive since 2 equiv of the tetrabromide *m*-$CH_2Br(TPP)H_2$ (**2**) on reaction with 4 equiv of *p*-toluenesulfonamide or 4 equiv of cyanamide, in dimethylformamide (DMF) (10^{-3} M solution) containing Cs_2CO_3, provided the cofacial quadruply bridged $TPPH_2$ dimers TsN-(*m*-CH_2-$(TPP)H_2)_2$ (**3a**)[24] and NCN-(*m*-$CH_2(TPP)H_2)_2$ (**3b**) in 8% yield each. Increasing the concentration of the solution by a factor of 10 (DMF, 10^{-2} M in **2**) decreased the yield to 2% in the case of **3a**. The tosyl dimer **3a** was carefully reduced with sodium biphenylide in DME[25] to give the tetraamino-bridged dimer HN-(*m*-$CH_2(TPP)H_2)_2$ (**3c**) (41%).[26]

Heterobimolecular routes to the synthesis of **3c** were also investigated. The advantage of the use of such a procedure is the potential to prepare mixed-bimetallic complexes, as this area has



3a, R = SO_2-(Ts)
b, R = CN
c, R = H

literature precedent.[31s,w] The tetrabromide *m*-$CH_2Br(TPP)H_2$ (**2**) was reacted with potassium phthalimide to give the tetraphthalimide **4a** (95%)[24] followed by hydrazinolysis (85% aqueous hydrazine, catalytic benzyltriethylammonium chloride and chloroform) to provide the tetraamine *m*-$CH_2NH_2(TPP)H_2$ (**4b**)[26] (74%). Before the coupling of *m*-$CH_2Br(TPP)H_2$ (**2**) with



4a R =

b R = NH_2
c R = NHBz
d R = $N(Bz)_2$

m-$CH_2NH_2(TPP)H_2$ (**4b**) was explored, their individual alkylation chemistries were investigated. The tetrabromide **2** reacted with excess benzylamine in DMF in the presence of K_2CO_3 to give the tetrabenzylamine adduct **4c** (88%). The tetraamine **4b** when reacted similarly with 4 equiv of benzyl bromide gave the tetrakis(dibenzylamine) adduct **4d** (39%).

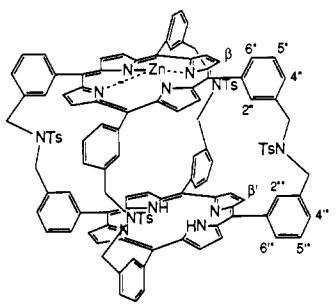
Thus, with the necessary reactivity established (although overalkylation was seen a potential hazard that would increase polymerization over dimerization), the tetraamine *m*-CH_2NH_2-$(TPP)H_2$ (**4b**) was reacted with the tetrabromide *m*-CH_2Br-$(TPP)H_2$ (**2**) in DMF (10^{-3} M) in the presence of Cs_2CO_3 and indeed produced the amino dimer HN-(*m*-$CH_2(TPP)H_2)_2$ (**3c**), albeit in only 2.4% isolated yield (eq 1).[27] The amino dimer **3c** produced in this manner had spectral characteristics (500-MHz ^1H NMR and UV/vis spectra) identical with that obtained from reduction of the tosyl dimer **3a**.

The *p*-toluenesulfonamide derivative *m*-$CH_2NH(Ts)(TPP)H_2$ (**5a**) was next investigated as a potential dimerization partner since initial localization of sulfonamide functionality on one porphyrin is expected to increase the coupling efficiency whereas the homobinuclear route suffers from the potential of a dimer pair from being over substituted with Ts groups, which will decrease the overall quadruple coupling.[19] When the amino monomer **4b** was reacted with *p*-toluenesulfonyl chloride in the presence of triethylamine, the desired tetratosylamide *m*-$CH_2NH(Ts)(TPP)H_2$ (**5a**) and accompanying pentatosylamide **5b** were obtained in 28 and 24% yields, respectively.

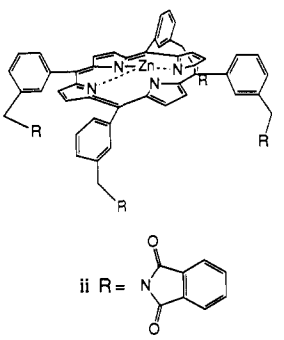
(22) The three other known quadruply bridged cofacial bisporphyrins have each been synthesized by a different technique. The first was by the intramolecular synthesis of a porphyrin underneath a second preformed porphyrin ring (8%).[5b,c] The second utilized 2 equiv of Collman's *meso*-tetrakis($\alpha,\alpha,\alpha,\alpha$-*o*-aminophenyl)porphyrin[23] to couple with acyl groups on both ends of a long bridging unit in a stepwise fashion (18%).[5f] The third condensed 4 equiv of a dibenzaldehyde (linked through six atoms at the meta and meta' positions) with 8 equiv of pyrrole to give a cofacial bisporphyrin (no yield reported).[5g] Our approach most resembles the second (although ours uses alkylation reactions and the second uses acylation reactions), but the second approach did not require consideration of *meso*-phenyl rotation since all of the reacting amino groups are fixed on one face of the molecule and the phenyl groups do not rotate freely.

(23) Collman, J. P.; Gagne, C. A.; Reed, C. A.; Halbert, T. R.; Lang, G.; Robinson, T. W. *J. Am. Chem. Soc.* **1975**, *97*, 1427.

(24) Of unusual note, a zinc ion was inserted into some of these porphyrins during preparative TLC (the zinc presumably present as a trace metal contaminant in the silica gel). Only monometalation was observed in the dimeric porphyrin **3a** to give TsN-(*m*-$CH_2(TPP))_2H_2Zn$ (i). Also, this phenomena was not restricted to dimers since the tetraphthalimide zinc complex ii was also isolated after preparative TLC of **4a** on silica gel. The complexes were



i



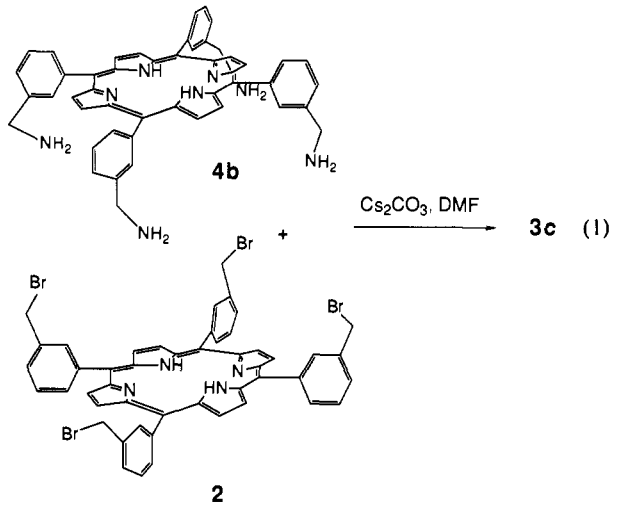
ii R =

very distinctly colored violet during TLC and were converted back to their respective freebases by stirring in CF_3CO_2H for 15 min, then diluting with $CHCl_3$, washing this solution with aqueous NH_4OH, water, and brine, then drying (Na_2SO_4), and evaporating to optimize the yields. The complexes were characterized as follows. TsN-(*m*-$CH_2(TPP))_2H_2Zn$ (i): ^1H NMR ($CDCl_3$ (no pyrrolic NH observed) δ 2.53 (s, 12, tosyl CH_3), 4.74, 4.76 (s, 8 each, CH_2 groups), 7.48, 7.56 (t, 4 each, J = 8 Hz, H-5' and H-5''), 7.49 (d, 8, J = 8 Hz, tosyl *m*-H), 7.55 (br s, 8, H-2' and H-2''), 7.60, 7.78 (d, 4 each, J = 8 Hz, H-6' and H-6''), 7.65, 7.68 (d, 4 each, J = 8 Hz, H-4' and H-4''), 8.02 (d, 8, J = 7.5 Hz, tosyl *o*-H), 8.18, 8.21 (s, 8 each, β-pyrrolic H's); UV/vis λ_{max} ($\epsilon \times 10^{-3}$ cm^{-1} M^{-1}) 408 nm (sh, 411), 415 (546), 516 (34.1), 551 (40.2), 592 (18.2), 646 (7.43); FABMS calcd for $C_{124}H_{94}N_{12}O_8S_4Zn$ (M^+) cluster *m/z* (% int) 2071 (54), 2072 (80), 2073 (100), 2074 (95), 2075 (90), 2076 (72), 2077 (48), 2078 (27), 2079 (13); found 2071 (37), 2072 (82), 2073 (100), 2074 (98), 2075 (90), 2076 (63), 2077 (57), 2078 (45), 2079 (24). Tetraphthalimidozinc complex ii: ^1H NMR ($CDCl_3$) δ 4.96, 4.99, 5.02 (all s, 8, CH_2), 7.49–7.66 (m, 24), 8.06–8.10 (m, 4), 8.20–8.28 (m, 4), 8.85, 8.87 (ea s, 8, β-pyrrolic H); UV/vis λ_{max} 423 nm, 552, 593; FABMS calcd for $C_{80}H_{48}N_8O_8Zn$ (M^+) cluster *m/z* (% int) 1312 (97), 1313 (92), 1314 (100), 1315 (75), 1316 (74), 1317 (48), 1318 (22), 1319 (8), 1320 (2); found 1312 (76), 1313 (100), 1314 (97), 1315 (89), 1316 (79), 1317 (61), 1318 (26), 1319 (14), 1320 (3).

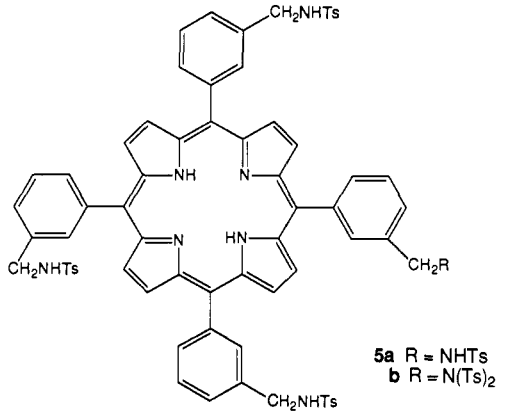
(25) Closson, W. D.; Ji, S.; Schulenberg, S. *J. Am. Chem. Soc.* **1970**, *92*, 650.

(26) This compound decomposes slowly to a dark, insoluble solid when exposed to light and air and should be used in the next reaction immediately after isolation or stored as a solid under argon in the dark.

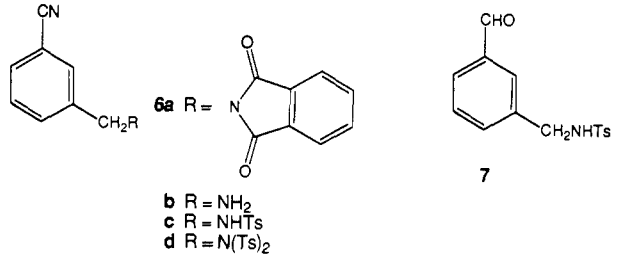
(27) In the equations and the scheme, the porphyrin monomers are presented in a view that represents only the $\alpha,\alpha,\alpha,\alpha$-atropisomer for ease of understanding since this would be the ideal rotomer population for dimerization. Moreover, all of these monomers exhibit ^1H NMR spectra indicative of freely rotating phenyl groups at room temperature.



This poor yield prompted the more satisfactory preparation of the tosyl monomer **5a** in the following manner. α-Bromo-*m*-tolunitrile was converted to the phthalimide **6a** (87%), which in



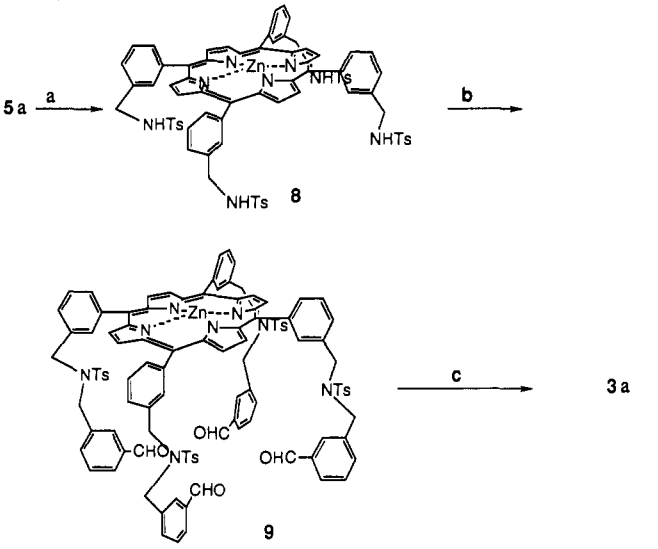
turn was hydrazinolyzed to the amine **6b** (77%). This amine was exclusively monotosylated to **6c** (62%) (the ditosyl derivative **6d** being obtained competitively when the reaction was conducted in the presence of γ-(dimethylamino)pyridine).[28] DIBAL-H reduction of the nitrile **6c** produced the porphyrin precursor **7** (68%). The porphyrin *m*-$CH_2NH(Ts)(TPP)H_2$ (**5a**) was obtained from condensation of **7** with pyrrole according to the Lindsey method (18%).[21]



The following reaction provided the method of choice for the synthesis of TsN-(*m*-$CH_2(TPP)H_2)_2$ (**3a**). When the two porphyrin monomers *m*-$CH_2NH(Ts)(TPP)H_2$ (**5a**) and *m*-CH_2Br-$(TPP)H_2$, (**2**) were allowed to react in the presence of Cs_2CO_3,

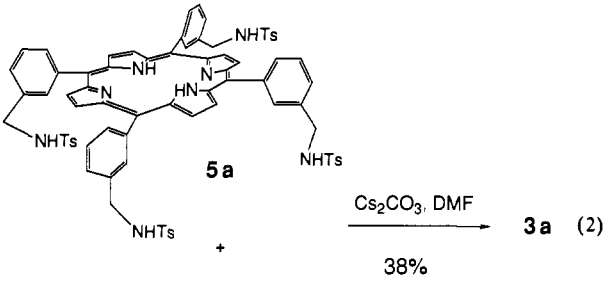
(28) This sulfonylation was conducted under the same conditions that led to overtosylation of the porphyrin amine **4b**. Since the acylation catalyst γ-(dimethylamino)pyridine (DMAP) induced production of the ditosyl derivative **6d**, then it would appear that the pyrrolic portion of the porphyrin substrate **4b** acted similarly during its overtosylation. α-[Bis(*p*-tolylsulfonyl)imino]-*m*-tolunitrile (**6d**): mp 156–157 °C; ^1H NMR δ 2.42 (s, 6, tosyl CH_3), 4.90 (s, 2, CH_2), 7.24 (d, 4, J = 8 Hz, tosyl *m*-H), 7.34 (t, 1, J = 8 Hz, H-5), 7.51 (br s, 1, H-2), 7.52 (d, 1, J = 8 Hz, H-6), 7.58 (d, 1, J = 8 Hz, H-4), 7.68 (d, 4, J = 8 Hz, tosyl *o*-H); IR ν 2250 (m, C≡N), 1595 (m, C=C), 1180 (s, SO_2) cm^{-1}; low-resolution MS *m/z* 440 (calcd for $C_{22}H_{20}N_2O_4S_2$ (M^+) 440).

Scheme I[a]



[a] Key: (a) $ZnCl_2$, DMF, Δ (42%), (b) I, K_2CO_3, DMF, Δ (48%), (c) pyrrole, $BF_3{\cdot}Et_2O$, $CHCl_3$ (10^{-2} M), Δ; NEt_3, tetrachloro-1,4-benzoquinone, Δ (43%); H_3O^+.

under high dilution conditions in DMF (10^{-3} M), the desired dimer **3a** was obtained *in 38% yield* (see eq 2). This is more than double

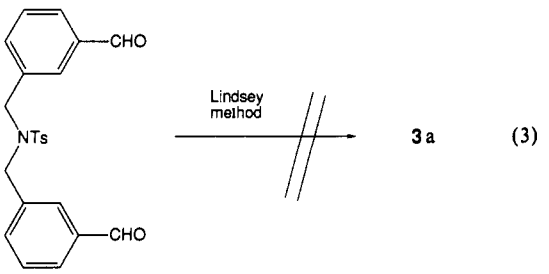


the highest yield for a similar dimer[22] and is remarkable considering that not too long ago quadruply bridged cofacial tetraphenylporphyrin dimers were judged to be near to impossible to synthesize.[3c,j,5a] This moves the tosyl dimer **3a** from the realm of being a novel compound to being a preparatively available novel compound.

Another approach to TsN-(*m*-$CH_2(TPP)H_2)_2$ (**3a**) was realized according to the Kagan approach as shown in Scheme I.[27] The tosyl monomer **5a** was metalated with $ZnCl_2$ in hot DMF to give the zinc complex **8** (42%), which in turn was alkylated by bromoaldehyde **1** (Cs_2CO_3, DMF) to give the tetraaldehyde precursor to intramolecular porphyrin synthesis **9** (48%). This compound was reacted with 4 equiv of pyrrole according to the method of Lindsey[21] to provide, after preparative TLC and acid-induced demetalation, the tosyl dimer **3a** in 20% yield (43% after correcting for recovered tetraaldehyde **9**). Thus, this approach is also credible.

One last approach was tested to synthesize the tosyl dimer TsN-(*m*-$CH_2(TPP)H_2)_2$ (**3a**) based on a recently published technique of condensing 4 equiv of a bridged dibenzaldehyde with 8 equiv of pyrrole to give directly a cofacial bisporphyrin.[5g] Thus, the dibenzaldehyde **10** was synthesized (*p*-toluenesulfonamide, 2 equiv of bromoaldehyde **1**, and Cs_2CO_3 in DMF) in 59% yield and condensed with pyrrole according to the conditions of Lindsey.[21] Absolutely no porphyrin product could be detected by UV/vis spectroscopy (see eq 3).

Quadruply Two-Atom, Aza-Bridged, Cofacial Bis(5,10,15,20-tetraphenylporphyrin). With the strategy for constructing the three-atom bridge established, we decided to test if the heterobimolecular technique could be extended to the synthesis of a cofacial bisporphyrin with a bridging unit shorter by one atom.



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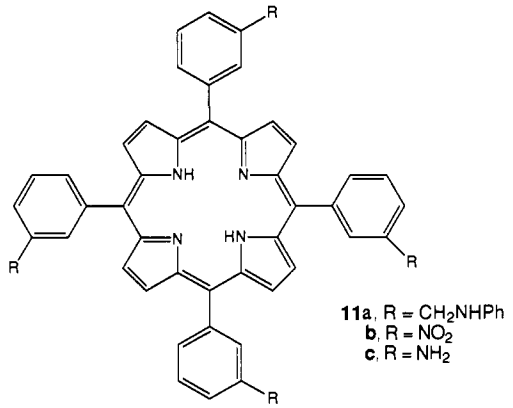
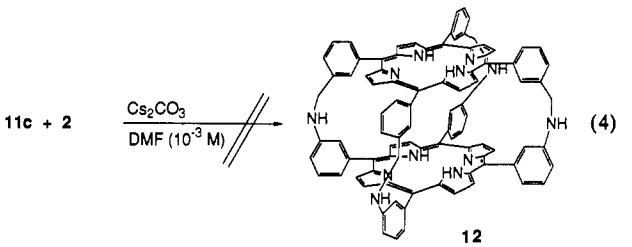
The tetrakis(bromomethyl)porphyrin *m*-$CH_2Br(TPP)H_2$ (**2**) was readily substituted by aniline (Cs_2CO_3, DMF) to give the amine *m*-$CH_2(NHPh)(TPP)H_2$ (**11a**), (43%). Hence, the *m*-NH_2-



$(TPP)H_2$ (**11c**) monomer was synthesized (by way of reduction of *m*-$NO_2(TPP)H_2$ (**11b**);[29] see Experimental Section) and its reaction with *m*-$CH_2Br(TPP)H_2$ (**2**) tested (Cs_2CO_3, DMF (10^{-3} M); see eq 4).[27] Although the reactants were consumed, none of the five isolated major products (preparative silica TLC) displayed any spectral evidence for being the cofacial bisporphyrin **12**.



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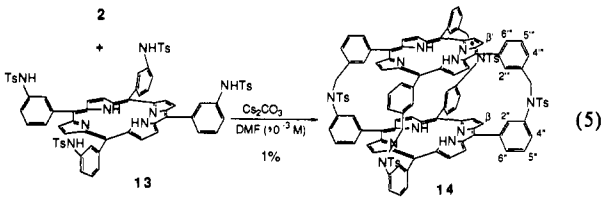
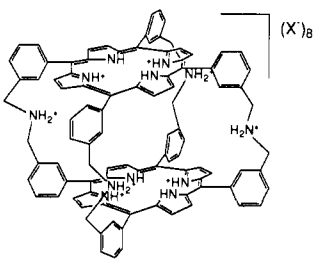
Next, the tetrasulfonamide *m*-(NHTs)$(TPP)H_2$ (**13**) was synthesized from **11c** (*p*-toluenesulfonyl chloride, triethylamine, THF) in 87% yield and reacted with *m*-$CH_2Br(TPP)H_2$ (**2**) (Cs_2CO_3, DMF (10^{-3} M); see eq 5).[27] The desired dimer *m*,*m*'-$TsNCH_2$-$((TPP)H_2)_2$ (**14**) was obtained, although in the poor yield of 1%.



13 14

Solubilities. Solubility has previously been a serious concern for other tightly packed porphyrin oligomeric systems. The quadruply bridged dimers **3a**, **3b**, **3c**, and **14** are soluble in chloroform and more polar organic solvents excluding aliphatic alcohols. If solubility in alcohols is desired, they are soluble in ethylene glycol monoethyl ether and *o*-chlorophenol. The amino dimer HN-(*m*-$CH_2(TPP)H_2)_2$ (**3c**) and amino monomer *m*-$CH_2NH_2(TPP)H_2$ (**4b**) are solubilized in acidic aqueous solutions (pH < 5), presumably as the octacation $[H_2N$-(*m*-CH_2-$(TPP)H_4)_2]^{8+}\cdot(X^-)_8$ (**15**) and hexacation $[m$-CH_2NH_3-$(TPP)H_4]^{6+}\cdot(X^-)_6$ (**16**).[30]



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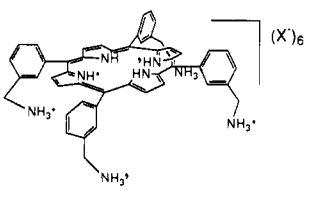

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(29) See the experimental section for improved preparations of these porphyrins (**11b** and **11c**) based on the preparations in Bettelheim, A.; White, B. A.; Raybuck, S. A.; Murray, R. W. *Inorg. Chem.* **1987**, *26*, 1009.

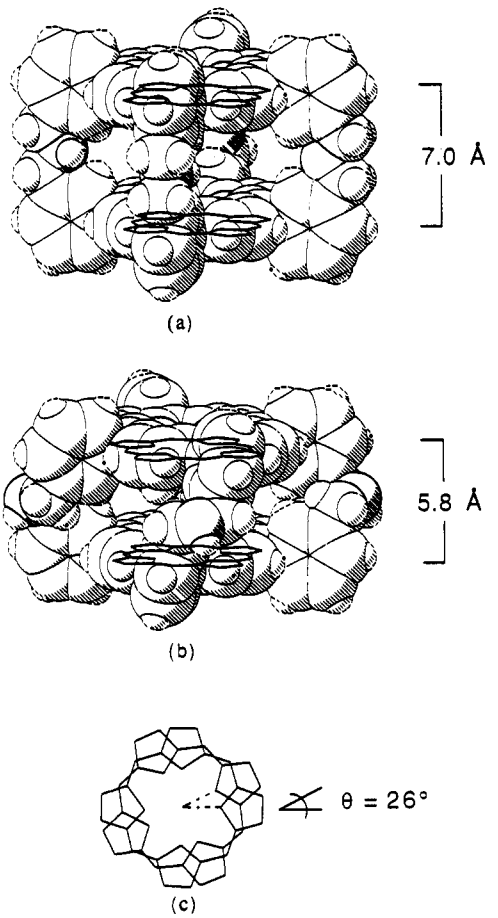

Figure 1. Molecular models of the dimer **3c** undergoing a screwing-down conformational change. In the shaded CPK models, the atoms are displayed with "textured" shading (i.e., C is shaded with normal lines, H with broken lines, and N with dark lines). Also in the shaded CPK models, an overlapped line drawing of the porphyrin rings is displayed: (a) shaded CPK model of the fully extended unscrewed form, (b) shaded CPK model of the totally screwed-down form, (c) distal view line drawing of the porphyrin rings of the totally screwed-down form illustrating the angle of radial turn. (The molecules were constructed on a Silicon Graphics 4D/220 GTX Molecular Graphics Workstation with QUANTA 2.1A (Polygen Corp.). The file PORPHYRINH.RTF was used to generate the porphyrin ring.[31] Dibenzylamine was constructed in the 2-D molecular construction routine of QUANTA and transferred to 3-D molecular modeling where it was subjected to torsions in order to be docked onto the two suitably juxtaposed porphyrin rings and 1.49-Å bonds made between the *meso*-carbons of the porphyrins and the *meta*-carbons of the dibenzylamine. The four bridges are identical so the same bridge was bonded four times at the 5, 10, 15, and 20 positions of the cofacial porphyrin rings. In order to avoid strong nonbonded repulsions within the molecule, no two nonbonded atoms are closer than 2 Å to each other.)

Table I. UV/Vis Spectral Data on the Dimers as Compared to Monomers

compound	Soret half-bandwidth (nm)	UV/vis λ_{max} (nm) ($\epsilon \times 10^{-3}$ cm^{-1} M^{-1})
(TPP)H$_2$	12	418 (411), 515 (17.3), 551 (8.06), 590 (6.40), 645 (6.22)
m-CH$_2$Br(TPP)H$_2$ (**2**)	12	419 (324), 515 (16.1), 549 (7.21), 589 (5.50), 646 (3.42)
TsN-(*m*-CH$_2$(TPP)H$_2$)$_2$ (**3a**)	19	414[a] (447), 516 (22.3), 550 (9.33), 591 (7.53), 649 (5.67)
NCN-(*m*-CH$_2$(TPP)H$_2$)$_2$ (**3b**)	18	415[b] (454), 514 (20.5), 550 (9.87), 591 (6.4), 645 (3.47)
HN-(*m*-CH$_2$(TPP)H$_2$)$_2$ (**3c**)	20	414[c] (258), 515 (15.9), 550 (9.51), 590 (7.78), 646 (5.85)
m,m'-TsNCH$_2$-((TPP)H$_2$)$_2$ (**14**)	20	415[d] (314), 517 (16.6), 552 (7.71), 593 (5.69), 650 (4.03)

[a] Soret band of dimer has shoulder at 407 (350). [b] Shoulder at 407 (293). [c] Shoulder at 406 (137). [d] Shoulder at 407 (204).

Table II. Selected ^{1}H NMR Shifts of the Dimers as Compared to Monomers

compound	^{1}H NMR (δ) pyrrolic NH	H-2′	β-pyrrolic H
(TPP)H$_2$	−2.76	8.21	8.84
m-CH$_2$Br(TPP)H$_2$ (**2**)	−2.81	8.25	8.86
TsN-(*m*-CH$_2$(TPP)H$_2$)$_2$ (**3a**)	−4.42	7.14	8.17
NCN-(*m*-CH$_2$(TPP)H$_2$)$_2$ (**3b**)	−3.99	7.31	8.38
HN-(*m*-CH$_2$(TPP)H$_2$)$_2$ (**3c**)	−3.78, −3.68, −2.8 (br)	7.81	8.43, 8.46, 8.8 (br)
m,m'-TsNCH$_2$-((TPP)H$_2$)$_2$ (**14**)	−4.11, −4.07	6.95, 7.78	8.25, 8.43

Structure Models. Molecular models were constructed to explore the potential conformational flexibility available to the three- and two-atom-bridged tetraphenylporphyrin dimers as shown in Figures 1 and 2. To simplify the view, the secondary amine bridged dimers **3c** and **12** were examined even though the latter was not synthesized. These models can be extrapolated to those derivatives where the hydrogen connected to the amine nitrogen is substituted by other groups. We propose that the primary conformational mobility available to these molecules is one that involves a "screwing-down" action, and this is illustrated by proceeding from Figures 1a to 1b and 2a to 2b. This allows an interporphyrin distance range of 7.0–5.8 Å for the three-atom-bridged dimer and a 5.7–5.3-Å range for the two-atom-bridged dimer. The distal view of the eclipsing porphyrin ring skeletons in Figures 1c and 2c shows clearly that the three-atom-bridged dimer enjoys a greater freedom of motion than does the two-atom-bridged dimer since twice as large a radial turn is possible.

Most cofacial bisporphyrins tend to assume an offset geometry that maximizes their intramolecular π–π interactions as witnessed from X-ray crystallographic[3j,6b,g,11c] and solution ^{1}H NMR studies.[3y] Also in solution at room temperature, ^{1}H NMR studies show that some will exist in a number of conformational isomers.[3j] Hence, other conformations were examined such as offset and clamshell conformations; however, these led inevitably to severe nonbonded repulsions of the 2′-hydrogens of the three-atom-bridge case (and the 2″- and 2‴-hydrogens in the two-atom-bridge case) with each other and the methylene hydrogens. In fact, the screwed-down conformations in general are supported by (i) calculations that suggest a rotated eclipsed dimer has great van der Waals binding energy compared to the offset form[32] and (ii) an X-ray crystal structure of a tightly linked porphyrin dimer that illustrates a 40° screwed-down dimer.[7k] ^{1}H NMR and UV/vis spectroscopic results lend support to this proposed conformational flexability (vide infra).

UV/Vis and ^{1}H NMR Spectra. Tables I and II exhibit UV/vis and selected ^{1}H NMR shifts of the synthesized freebase cofacial bisporphyrins as compared to a representative monomer (*m*-CH$_2$Br(TPP)H$_2$ (**2**)) as well as 5,10,15,20-tetraphenylporphyrin ((TPP)H$_2$). As previously witnessed,[3-5] the relative positioning of two porphyrin rings in a cofacial orientation has a distinct effect on their electronic and magnetic properties, which often becomes more pronounced as the interporphyrin separation decreases. This is the first report of a family of quadruply bridged (TPP)H$_2$ dimers, and spectral comparison illustrates clearly the effect of eclipsing porphyrin rings in close proximity.

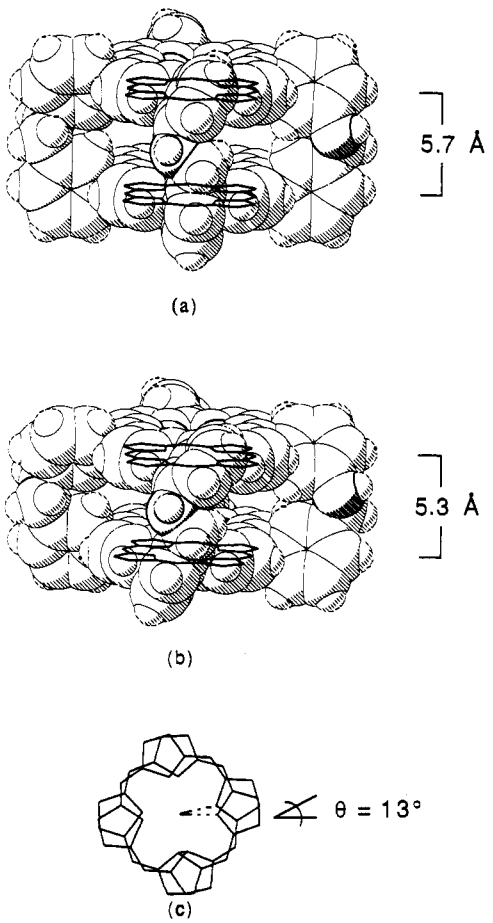

Figure 2. Molecular models of the dimer **12** undergoing a screwing-down conformational change: (a) shaded CPK model of the fully extended unscrewed form, (b) shaded CPK model of the totally screwed-down form, (c) distal view line drawing of the porphyrin rings of the totally screwed-down form illustrating the angle of radial turn. (*N*-Benzylaniline was constructed in the 2-D molecular construction routine of QUANTA and transfered to 3-D molecular modeling where it was torsioned and bonded to the two cofacial porphyrins as described in Figure 1.)

(30) The amino dimer HN-(*m*-CH$_2$(TPP)H$_2$)$_2$ (**3c**) was solubilized by first dissolving in a minimal amount of THF and then adding 0.05 M aqueous HCl to create the emerald green octacation solution. Then the pH can be raised to the desired level with the appropriate buffer system. When the pH was raised to the endpoint (the solution changes from green to red and the porphyrin freebase is formed), the porphyrin precipitates out of solution as a red solid. The amino monomer *m*-CH$_2$NH$_2$(TPP)H$_2$ (**4b**) could be extracted directly into dilute aqueous HCl solutions from chloroform.

(31) This file, available from Polygen Corp., was derived from the X-ray crystal structure of protoporphyrin IX: Caughey, W. S.; Ibers, J. A. *J. Am. Chem. Soc.* **1977**, *99*, 6639.

(32) Sudhindra, B. S.; Fuhrhop, J.-H. *Int. J. Quantum Chem.* **1981**, *20*, 747.

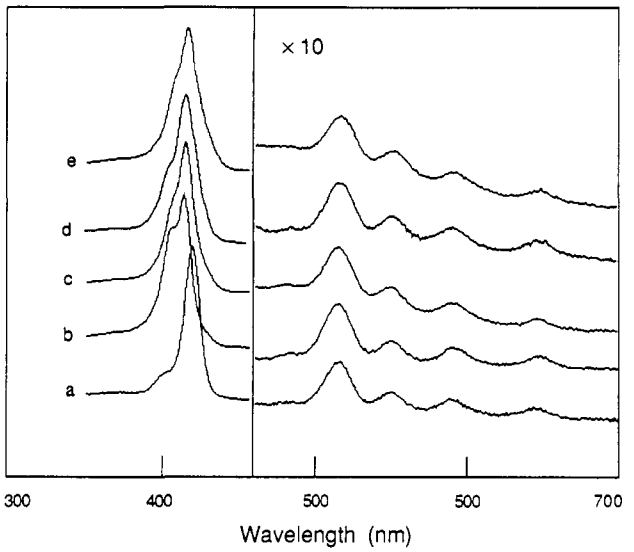

Figure 3. UV/vis spectroscopy in $CHCl_3$. The Soret band absorptions were normalized, and the spectra were amplified 10× in the Q-band region. See Table I for extinction coefficients: (a) *m*-$CH_2Br(TPP)H_2$ (**2**), (b) TsN–(*m*-$CH_2(TPP)H_2)_2$ (**3a**), (c) NCN–(*m*-$CH_2(TPP)H_2)_2$ (**3b**), (d) HN–(*m*-$CH_2(TPP)H_2)_2$ (**3c**), (e) *m,m'*-TsNCH$_2$–((TPP)$H_2)_2$ (**14**).

As can be seen in Table I and Figure 3, the Soret bands in the UV/vis spectra of these dimers are blue-shifted by 4–5 nm and split when compared to the monomer *m*-$CH_2Br(TPP)H_2$ (**2**). The splitting is most distinct in the case of the tosyl dimer **3a** (Figure 3b) and appears as a shoulder on the blue side of the Soret for the other dimers. This splitting results in a broadened Soret band, hence, the increased half-bandwidth. The visible (Q) bands are slightly shifted to the red for the dimers when compared to the monomer **2**. The blue shift, the red shifts, and the band splitting are from exciton splitting, which results when the interacting transition dipoles of two coplanar chromophores are at an angle other than 0 or 180° to each other.[33] Thus, this observable band splitting leads to the assignment of the screwed-down conformations (shown in Figures 1b and 2b) as the preferred solution conformers.

The ^{1}H NMR spectral assignments displayed in Table II show the distinctive shielding effects on the shifts of protons lying above the plane of the neighboring porphyrin ring. The pyrrolic NH has a $\Delta\delta$ = −0.87 to −1.61. The phenyl ring H-2′ is the most strongly shielded of the phenyl protons ($\Delta\delta$ = −0.4 to −1.3), which is to be expected since it is pointing into the core of the interspacial cavity. The β-pyrrolic H is also significantly shielded ($\Delta\delta$ = −0.40 to −0.69) but less so because of its increased distance from the anisotropically shielding region. It is apparent, when comparing the three dimers **3a**, **3b**, and **3c**, that when the substituent on the bridging nitrogen is made bulkier (i.e., sizewise Ts > CN > H), then the more these protons are shielded. One explanation for this is that the bulkier the group the more screwed-down the preferred conformation becomes because the bulky group encounters less steric congestion when it is pointed outside the dimer cavity (see Figure 1b) than when it is pointed inside the cavity (see Figure 1a). Thus, the more screwed-down conformation leads to a shorter interporphyrin separation, which results in stronger shielding effects. This argument assigns the tosyl dimer **3a** as having the most screwed-down preferred conformation and is supported by the distinct splitting of this compound's Soret band (see Figure 3b), which indicates that the transition dipoles of the two porphyrin rings are further away from parallelism than **3b**, **3c**, or **14**.

(33) (a) Kasha, M.; Rawls, H. R.; El-Bayoumi, M. A. *Pure Appl. Chem.* **1965**, *11*, 371. (b) Cantor, C. R.; Schimmel, P. R. *Biophysical Chemistry Part II: Techniques for the Study of Biological Structure and Function*; W. H. Freeman and Company: San Francisco, 1980; pp 390–398. See also ref 3c.

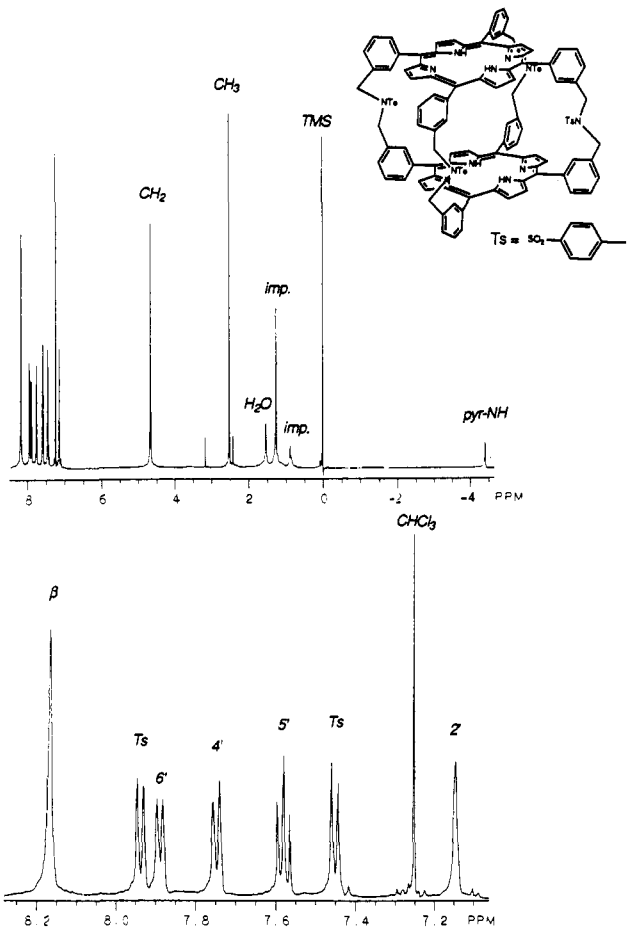

Figure 4. 500-MHz ^{1}H NMR of TsN–(*m*-$CH_2(TPP)H_2)_2$ (**3a**) in $CDCl_3$: top, complete spectrum; bottom, expansion of the aromatic region.

The distinct proton shift splitting patterns of the dimers **3a**, **3b**, and **14** (see Figure 4 for **3a** and supplementary material for **3b** and **14**) are indicative of D_{4h} symmetry for **3a** and **3b** and C_{4v} symmetry for **14**. These high symmetries are not possible in the frozen screwed-down conformations depicted in Figures 1b and 2b. Thus, the screwed-down conformation is preferred, but the molecule is in equilibration with its racemate (Figures 1b and 2b depict single enantiomers) in solution at room temperature. The equilibration most probably results from nitrogen inversion in the screwed-down conformation, unscrewing, and then screwing down again in the opposite direction.

The amino-bridged dimer **3c** exhibits broadened signals in its ^{1}H NMR spectrum (see Figure 5), which most probably reflect its ability, with its more flexible amine bridges, to exist in several interconverting conformational minima. When trifluoroacetic acid was added to a $CDCl_3$ solution of this dimer, the aromatic region resolved into the multiplicity expected for the D_{4h} symmetric dimer $[H_2N–(m\text{-}CH_2(TPP)H_4)_2]^{8+}\cdot(X^-)_8$ (**15**), where X = $CF_3CO_2^-$ (i.e., ^{1}H NMR ($CDCl_3$) δ 7.75 (s, 4 H-2′), 7.81 (d, 4, *J* = 8 Hz, H-4′), 7.93 (t, 4, *J* = 8 Hz, H-5′), 8.51 (d, 4, *J* = 8 Hz, H-6′), 8.58 (s, 8, β-pyrrolic H); see supplementary material). In the protonated form, it is expected that the charge–charge repulsions will force the molecule into one preferred solution conformer that maximizes the distances between the intramolecular charges.

Summary. Several methods have been investigated for the synthesis of quadruply bridged, cofacial tetraphenylporphyrin dimers, with the most successful being the coupling of an electrophilic monomer (*m*-$CH_2Br(TPP)H_2$ (**2**)) with a nucleophilic monomer (*m*-$CH_2NH(Ts)(TPP)H_2$ (**5a**)) to provide the dimer TsN–(*m*-$CH_2(TPP)H_2)_2$ (**3a**) in 38% yield. This dimer and its derivative amine HN–(*m*-$CH_2(TPP)H_2)_2$ (**3c**) as well as **3b** and **14** hold significant promise in some of the studies described in the introduction. Additionally, the monomers **2** and **5a** are po-

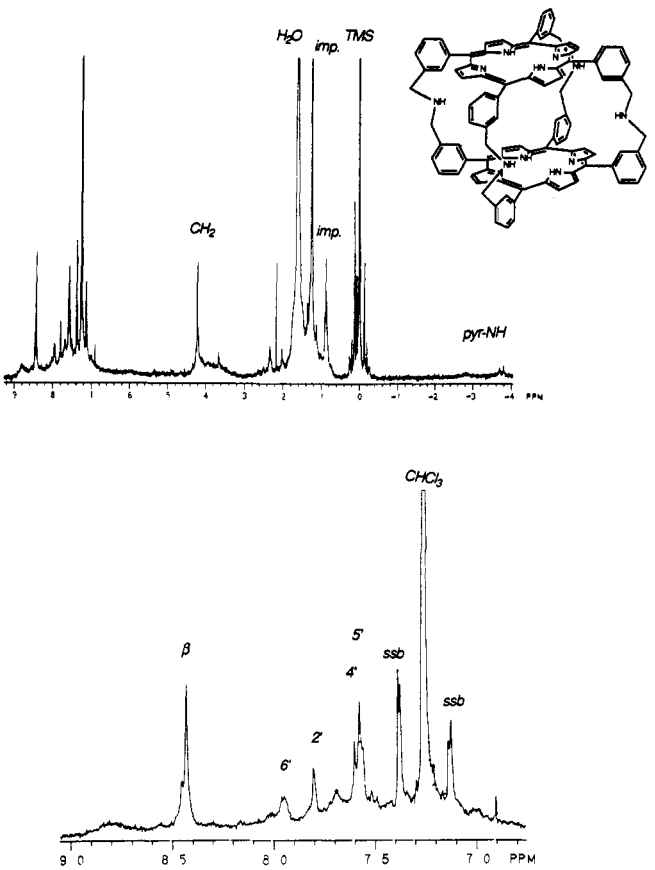

Figure 5. 300-MHz ^1H NMR of HN-(*m*-CH_2(TPP)H_2)$_2$ (**3c**) in $CDCl_3$: top, complete spectrum; bottom, expansion of the aromatic region (ssb stands for spinning side bands).

tential key starting materials for other types of unusual biomimetic porphyrins.[34] Progress in these areas is currently underway.

Experimental Section

Melting points were taken on a Laboratory Devices MEL-TEMP apparatus and are uncorrected. R_f values were obtained on E. M. Sciences 0.2-mm-thick precoated, plastic-backed silica gel 60 F-254 plates. ^1H NMR spectra of deuteriochloroform or where noted dimethyl-d_6 sulfoxide solutions (Me_4Si as internal standard) were measured on Nicolet NT-300 and General Electric GN-500 spectrophotometers and ^{13}C NMR spectra of deuteriochloroform solutions on the latter instrument, operating at 125.7 MHz in the Fourier transform mode. The carbon shifts are in parts per million downfield from Me_4Si; $\delta(Me_4Si) = \delta(CDCl_3) + 77.0$ ppm. Infrared spectra of chloroform solutions were recorded on a Perkin-Elmer 1330 spectrophotometer. UV/vis spectra of chloroform solutions were obtained on Perkin-Elmer 553 Fast Scan and Cary 14 spectrophotometers. Fast atom bombardment (FAB) mass spectroscopy was performed at UCSB by Dr. Hugh Webb with use of *m*-nitrobenzyl alcohol as the matrix and a parallel run of cesium rubidium iodide for the reference. Laser desorption mass spectroscopy was performed in the laboratory of Professor Charles Wilkins at UCR. Elemental analyses were performed at Galbraith Laboratories, Inc. All reactions were carried out with purified reagents in dry, purified solvents[35] under an atmosphere of argon or nitrogen unless noted otherwise. The standard workup procedure refers to washing the organic extract with water and brine, drying (Na_2SO_4 for porphyrins, $MgSO_4$ for all other compounds), and evaporation under vacuum. Column chromatography was performed with Fischer type 60A (200–425 mesh) silica gel and Aldrich neutral aluminum oxide (150 mesh, converted to Brockmann III activity level unless noted otherwise). Preparative thin-layer chromatography (TLC) was performed with E. M. Sciences Kieselgel 60 F_{254} and aluminiumoxid 60 F_{254} (Typ E) glass-backed plates.

α-Bromo-*m*-tolualdehyde (1). A 1 M solution of diisobutylaluminum hydride (DIBAL-H) in hexanes (36.8 mL) was added in a dropwise manner over a period of 20 min to a solution of α-bromo-*m*-tolunitrile (6.00 g, 30.6 mmol) in 60 mL of chlorobenzene at 0 °C. The resulting mixture was stirred at 0 °C for 1 h and then diluted with 100 mL of $CHCl_3$. This solution was shaken with 10% aqueous HCl for ca. 10 min. The layers were separated and the aqueous layer extracted with $CHCl_3$ (2×). The organic solutions were combined and worked up in the usual manner, and the resultant crystalline residue was recrystallized by dissolving in a minimal amount of ether (ca. 5 mL) and layering this solution with hexanes (ca. 30 mL). The resulting spiney, white crystals were collected and washed with a small amount of ice-cold hexanes to yield 4.98 g (82%) of aldehyde **1** having mp and ^1H NMR in agreement with previously prepared **1**:[36] mp 46–49 °C; ^1H NMR δ 4.54 (s, 1, CH_2Br), 7.52 (t, 1, J = 8 Hz, H-5), 7.67 (br d, 1, J = 8 Hz, H-4), 7.82 (dt, 1, J = 8, 1 Hz, H-6), 7.90 (br s, 1, H-2), 10.02 (s, 1, CHO); ^{13}C NMR δ 32.0 (CH_2Br), 129.6, 129.7, and 129.8 (C-2, C-5, and C-6), 134.8 (C-4), 136.8 (C-1), 138.9 (C-3), 191.6 (CHO); IR ν 1595 and 1610 (m, C=C), 1710 (s, C=O), 2740 and 2820 (m, CHO) cm^{-1}. Anal. Calcd for C_8H_7OBr: C, 48.27; H, 3.54. Found: C, 48.05; H, 3.48.

5,10,15,20-Tetrakis(α-bromo-*m*-tolyl)porphyrin (2) (*m*-CH_2Br-(TPP)H_2). A 2.5 M solution of boron trifluoride etherate ($BF_3{\cdot}ET_2O$) in $CHCl_3$ (1.98 mL, 4.95 mmol) was added to a mixture of aldehyde **1** (2.98 g, 15.0 mmol) and pyrrole (1.04 mL, 15.0 mmol) in 1.5 L of dry $CHCl_3$ and the resulting solution stirred at room temperature for 1 h. Triethylamine (0.85 mL, 6.0 mmol) and then tetrachloro-1,4-benzoquinone (2.77 g, 11.3 mmol) were added and the mixture refluxed for 1 h. The solvent was evaporated and the residue triturated with diethyl ether and then filtered. The filtrate was evaporated and the residue triturated with CH_2Cl_2 and then filtered. The filtrate was concentrated down to ca. 50 mL, and ca. 75 mL of methanol was added. Precipitation was induced by rotary evaporation of this solution down to ca. 20 mL. The resulting purple solid was collected by filtration, washed with methanol, and then dried at 110 °C (0.2 mmHg) over P_2O_5 for 1 h to yield 1.29 g (35%) of the bromide **2** as a bright purple solid: ^1H NMR δ −2.81 (s, 2, NH), 4.77 (s, 8, CH_2Br), 7.73 (t, 4, J = 8 Hz, H-5′), 7.81 (d, 4, J = 8 Hz, H-6′), 8.15 (d, 4, J = 8 Hz, H-4′), 8.25 (s, 4, H-2′), 8.86 (s, 8, β-pyrrolic H); ^{13}C NMR δ 33.5 (t, CH_2Br), 119.5 (s, *meso*-C), 127.2 (d), 128.4 (d), 131.3 (br s), 143.5 (d), 135.0 (d), 136.4 (s, C-3′), 142.5 (s, C-1′); IR ν 3330 (w, N—H), 1610, 1590, and 1565 (m, C=C) cm^{-1}; UV/vis λ_{max} (ε × 10^{-3} cm^{-1} M^{-1}), 4195 nm (324), 515 (16.1), 549 (7.21), 589 (5.50), 646 (3.42); FABMS *m/z* 982 (calcd for $C_{48}H_{34}Br_4N_4$ (M^+) 982). Anal. Calcd for $C_{48}H_{34}Br_4N_4$: C, 58.45; H, 3.47; N, 5.68. Found: C, 58.03; H, 3.42; N, 5.57.

5,10,15,20-Tetrakis(α-*N*-phthalimido-*m*-tolyl)porphyrin (4a). A mixture of *m*-CH_2Br(TPP)H_2 (**2**) (470 mg, 0.476 mmol) and potassium phthalimide (882 mg, 4.76 mmol) in 8 mL of dimethylformamide (DMF) was stirred for 14 h at room temperature and then diluted with water and the resulting precipitate collected and dried at 110 °C for 4 h to give 566 mg (95%) of **4a** as a purple solid: ^1H NMR δ −2.90 (s, 2, NH), 5.14 (m, 8, CH_2), 7.68 (m, 16, phthalimide H's), 7.83 (m, 8, H-5′ and H-6′), 8.10 (m, 4, H-4′), 8.28 (m, 4, H-2′), 8.79 and 8.81 (s, 8, β-pyrrolic H); IR ν 3320 (w, N—H), 1765 (w, C=O), 1715 (s, C=O), 1600 (m, C=C) cm^{-1}; UV/vis λ_{max} (ε × 10^{-3} cm^{-1} M^{-1}) 420 nm (304), 516 (15.8), 550 (6.76), 590 (4.79), 646 (3.24); FABMS *m/z* 1250 (calcd for $C_{80}H_{50}N_8O_8$ (M^+) 1250).

5,10,15,20-Tetrakis(α-amino-*m*-tolyl)porphyrin (4b) (*m*-CH_2NH_2-(TPP)H_2). A mixture of tetraphthalimide **4a** (534 mg, 0.427 mmol), benzyltriethylammonium chloride (97 mg, 0.427 mmol), 85% hydrazine (5 mL), and 43 mL of $CHCl_3$ was stirred for 14 h at room temperature, then diluted with $CHCl_3$, and washed with 5% NaOH followed by the usual workup. The purple solid obtained was dried at 110 °C (0.2 mmHg) for 3 h to give 232 mg (74%) of **4b** as a purple solid: ^1H NMR δ −2.78 (s, 2, pyrrolic NH), 1.80 (br s, 8, amino NH_2), 4.16 (s, 8, CH_2), 7.71 (br s, 8, H-5′ and H-6′), 8.14 (br s, 8, H-2′ and H-4′), 8.84 (s, 8, β-pyrrolic H); IR ν 3300 (w, N—H), 1590 and 1570 (m, C=C) cm^{-1}; UV/vis λ_{max} (ε × 10^{-3} cm^{-1} M^{-1}) 419.5 nm (178), 516 (9.71), 554 (4.85), 591 (3.64), 648 (3.81); FABMS *m/z* 730 (calcd for $C_{48}H_{42}N_8$ (M^+) 730).

5,10,15,20-Tetrakis[α-(benzylamino)-*m*-tolyl]porphyrin (4c) (*m*-CH_2NHBz(TPP)H_2). A mixture of *m*-CH_2Br(TPP)H_2 (**2**) (200 mg, 0.203 mmol), benzylamine (0.22 mL, 2.03 mmol) and K_2CO_3 (141 mg, 1.02 mmol) in 8 mL of DMF was stirred for 14 h at room temperature and then diluted with water and the resulting precipitate collected. It was dried overnight at 110 °C (0.2 mmHg) to give 194 mg (88%) of **4c** as a purple powder, which was ca. 90% pure by ^1H NMR and UV/vis spectral analysis. Absolute purity was obtained by subjecting 180 mg of this residue to chromatography on basic alumina(III) eluting with 200:1 CH_2Cl_2/methanol to give initially an unidentified green band and

(34) (a) Baldwin, J. E.; Perlmutter, P. *Top. Curr. Chem.* **1984**, *121*, 181. (b) Morgan, B.; Dolphin, D. *Struct. Bonding (Berlin)* **1987**, *64*, 115.

(35) Perrin, D. D.; Perrin, D. R.; Armarego, W. L. F. *Purification of Laboratory Chemicals*; Pergamon Press: Oxford, 1980. $CHCl_3$ for porphyrin syntheses was distilled from K_2CO_3 and stored over 3-Å molecular sieves. $CHCl_3$ for other reactions was distilled from P_2O_5.

(36) Sun, Y.; Martell, A. E.; Chen, D.; Macfarlane, R. D.; McNeal, C. J. *J. Heterocycl. Chem.* **1986**, *23*, 1565.

then **4c** as a red band. The residue obtained was caused to precipitate from a CH_2Cl_2/methanol solution by rotary evaporation. This material was collected and again induced to precipitate from a CH_2Cl_2/heptane solution by rotary evaporation to provide 44 mg (20%) of **4c** as a purple solid: ^{1}H NMR δ −2.76 (s, 2, pyrrolic NH), 1.73 (br s, 4, amino NH), 3.97, 4.10 (s, 8 each, CH_2 groups), 7.23 (t, 4, J = 8 Hz, H-4″), 7.29 (t, 8, J = 8 Hz, H-3″ and H-5″), 7.39 (d, 8, J = 8 Hz, H-2″ and H-6″), 7.71 (t, 4, J = 8 Hz, H-5′), 7.77 (t, 4, J = 8 Hz, H-6′), 8.11 (d, 4, J = 8 Hz, H-4′), 8.18 (s, 4, H-2′), 8.84 (s, 8, β-pyrrolic H's); IR ν 3320 (m, NH), 1585 and 1610 (m, C=C) cm^{-1}; UV/vis λ_{max} ($\epsilon \times 10^{-3}$ cm^{-1} M^{-1}) 419 nm (256), 516 (17), 551 (7.8), 590 (5.2), 646 (3.9); FABMS m/z 1090 (calcd for $C_{76}H_{66}N_8$ (M^+) 1090). Anal. Calcd for $C_{76}H_{66}N_8$: C, 83.64; H, 6.10; N, 10.27. Found: C, 83.34; H, 6.02; N, 10.23.

5,10,15,20-Tetrakis[α-(dibenzylamino)-m-tolyl]porphyrin (4d) (m-$CH_2N(Bz)_2$(TPP)H_2). To a mixture of m-CH_2NH_2(TPP)H_2 (18 mg, 0.025 mmol), K_2CO_3 (14 mg, 0.1 mmol), and DMF (1 mL) was added benzyl bromide (12 μL, 0.1 mmol), and the resulting solution was stirred at room temperature for 14 h and then diluted with water. The precipitate was collected and dried at 110 °C (0.2 mmHg) for 2 h to give 14 mg (39%) of **4d** as a purple solid: ^{1}H NMR δ −2.72, −2.76, (both s, 4, NH), 3.74 (s, 16, CH_2), 3.84 (s, 8, CH_2), 7.18–7.22 and 7.45 (m, 40, phenyl H's), 7.69 (m, 4, H-5′), 7.83 (m, 4, C-4′), 8.12 (m, 4, H-6′), 8.27 (s, H-2′), 8.79 (m, 8, β-pyrrolic H); FABMS m/z 1453 (calcd for $C_{104}H_{90}N_8$ (M^+) 1451).

α-Phthalimido-m-tolunitrile (6a). A mixture of α-bromo-m-tolunitrile (5.00 g, 25.5 mmol) and potassium phthalimide (4.96 g, 26.8 mmol) in 50 mL of DMF was stirred at room temperature for 14 h and the resulting suspension diluted with 200 mL of water. The crystalline precipitate that resulted was collected by filtration and then recrystallized by layering a saturated CH_2Cl_2 solution of it with ethanol to yield 5.81 (87%) of colorless crystalline phthalimide **6a**: mp 146–148 °C; ^{1}H NMR δ 4.79 (s, 2, CH_2), 7.36 (t, 1, J = 8 Hz, H-5), 7.50 (dt, 1, J = 8, 1 Hz, H-6), 7.63 (t, 1, J = 1 Hz, H-2), 7.65–7.69 (m, 2, H-3′ and H-4′), 7.76–7.82 (m, 2, H-2′ and H-5′); IR ν 2250 (m, C≡N), 1760, (m, C=O), 1700 (s, C=O), 1600, 1575 (m, C=C) cm^{-1}; exact mass m/z 262.0746 (calcd for $C_{16}H_{10}N_2O_2$ (M^+) 262.0742).

α-Amino-m-tolunitrile (6b). A mixture of phthalimide **6a** (5.56 g, 21.2 mmol), 3.9 mL of an 85% aqueous solution of hydrazine, and 100 mL of THF was vigorously stirred at room temperature for 14 h. The resulting suspension was diluted with 100 mL of $CHCl_3$ and the resulting organic solution washed with an aqueous 5% NaOH solution and water. The organic layer was next extracted with aqueous 5% HCl (3×). The acidic aqueous extracts were combined and washed with $CHCl_3$ (3×) and then made basic (pH 14) with an aqueous 5% NaOH solution. The resulting oily aqueous layer was extracted with $CHCl_3$ (3×) and the combined organic extract worked up in the usual manner to yield 2.17 g (77%) of amine **6b** as a colorless oil: ^{1}H NMR δ 1.60 (br s, 2, NH_2), 3.92 (s, 2, CH_2), 7.43 (t, 1, J = 8 Hz, H-5), 7.53 (d, 1, J = 8 Hz, H-6), 7.57 (d, 1, J = 8 Hz, H-4), 7.65 (br s, 1, H-2); IR ν 3390, 3310 (w, N—H), 2250 (m, C≡N), 1605, 1590 (w, C=C) cm^{-1}; exact mass m/z 132.0680 (calcd for $C_8H_8N_2$ (M^+) 132.0688).

α-(p-Toluenesulfonamido)-m-tolunitrile (6c). To a stirring mixture of amine **7b** (162 mg, 1.23 mmol) and triethylamine (0.21 mL, 1.48 mmol) in 6 mL of dry purified $CHCl_3$ at 0 °C was added p-toluenesulfonyl chloride (234 mg, 1.23 mmol). The temperature of the resulting solution was allowed to rise to room temperature, after stirring for 6 h it was washed with aqueous 5% HCl and then worked up in the usual manner. The resulting crystalline residue was recrystallized from ethanol to yield 219 mg (62%) of amide **6c** as a colorless crystalline solid: mp 112–114 °C; ^{1}H NMR δ 2.43 (s, 3, CH_3), 4.14 (d, 2, J = 7 Hz, CH_2), 5.65 (t, 1, J = 7 Hz, NH), 7.27 (d, 2, J = 8 Hz, tosyl m-H), 7.36 (t, 1, J = 7 Hz, H-5), 7.40 (d, 1, J = 7 Hz, H-4), 7.47 (s, 1, H-2), 7.48 (d, 1, J = 7 Hz, H-6), 7.70 (d, 2, J = 8 Hz, tosyl o-H); IR ν 3290 (m br, N—H), 2250 (m, C≡N), 1600 (m, C=C), 1165 (s, SO_2) cm^{-1}; exact mass m/z 286.0756 (calcd for $C_{15}N_{14}N_2O_2S$ (M^+) 286.0776).

α-(p-Toluenesulfonamido)-m-tolualdehyde (7). The amide **6c** (2.59 g, 9.04 mmol) was dissolved in 90 mL of warm, dry chlorobenzene and the mixture cooled with a water bath at room temperature. Then 21.5 mL of a 1 M solution of DIBAL-H in hexanes was added in a dropwise manner over 15 min to this mixture and the resulting solution stirred for an additional 45 min at room temperature. The resulting mixture was diluted with 30 mL of $CHCl_3$, then aqueous 5% HCl was added carefully, and the mixture was agitated vigorously for ca. 10 min. The layers were separated, and the aqueous solution was extracted with $CHCl_3$. The combined organics were worked up in the usual manner and the crystalline residue obtained recrystallized from ethanol to yield 1.77 g (68%) of colorless crystalline aldehyde **7**: mp 102–104 °C; ^{1}H NMR δ 2.43 (s, 3, CH_3), 4.22 (d, 2, J = 6 Hz, CH_2), 4.97 (t, 1, J = 6 Hz, NH), 7.29 (d, 2, J = 8 Hz, tosyl m-H), 7.46 (t, 1, J = 8 Hz, H-5), 7.53 (d, 1, J = 8 Hz, H-4), 7.66 (s, 1, H-2), 7.74 (d, 2, J = 8 Hz, tosyl o-H), 7.66 (d, 1, J = 8 Hz, H-6), 9.92 (s, 1, CHO); IR ν 3290 (m br, N—H), 2850, 2750 (w, OC—H), 1695 (s, C=O), 1600, 1595 (s, C=C); exact mass m/z 289.0793 (calcd for $C_{15}H_{15}NO_3S$ (M^+) 289.0773).

5,10,15,20-Tetrakis[α-(N-p-toluenesulfonamido)-m-tolyl]porphyrin (5a) (m-$CH_2NH(Ts)$(TPP)H_2) from Porphyrin 4b. A mixture of m-CH_2NH_2TPPH_2 (**4b**) (70 mg, 0.096 mmol), p-toluenesulfonyl chloride (183 mg, 0.96 mmol) and triethylamine (0.2 mL, 1.44 mmol) in 10 mL of purified $CHCl_3$ was stirred at room temperature for 24 h, then diluted with $CHCl_3$, and washed with 5% aqueous NaOH followed by the usual workup. The residue was subjected to preparative TLC on a 1.5 × 200 × 200 mm alumina plate eluting with 50:1 $CHCl_3$/methanol, and the two major bands were collected. The less polar band provided 34 mg (24%) of the pentatosylated porphyrin **5b**: R_f 0.20 (50:1 $CHCl_3$/methanol); ^{1}H NMR δ −2.92, −2.91, −1.58 (all s, 2, pyrrolic NH), 1.97–2.05 and 2.23 (m, 15, tosyl CH_3), 4.29–4.35 (m, 8, CH_2), 5.17–5.38 (m, 3, tosyl NH), 7.00 (m, 8, tosyl m-H), 7.18 (d, 2, J = 8 Hz, tosyl m-H), 7.52–7.79 (m, 16, H-4′, H-5′, and tosyl o-H), 7.81 (d, 2, J = 8 Hz, tosyl o-H), 7.93–8.05 (m, 8, H-2′ and H-6′), 8.68–8.78 (m, 8, β-pyrrolic H); UV/vis λ_{max} ($\epsilon \times 10^{-3}$ cm^{-1} M^{-1}) 420 nm (227), 516 (10.6), 550 (5.07), 591 (3.04), 652 (5.41); FABMS m/z 1500 (calcd for $C_{83}H_{72}N_8O_{10}S_5$ (M^+) 1500).

The more polar band provided 36 mg (28%) of m-CH_2NH(Ts)-(TPP)H_2 (**5a**): R_f 0.14 (50:1 $CHCl_3$/methanol), ^{1}H NMR δ −3.03 to −2.96 (m) and −1.64 (s) (2, pyrrolic NH), 1.85–1.99 (m, 12, tosyl CH_3), 4.21–4.28 (m, 8, CH_2), 5.45, 5.60, 5.74 (all br s, 4, tosyl NH), 6.84–6.95 (m, 8, tosyl m-H), 7.43–7.65 (m, 16, H-4′, H-5′ and tosyl o-H), 7.90–7.97 (m, 8, H-2′ and H-6′), 8.64–8.66 (m, 8, β-pyrrolic H); UV/vis λ_{max} ($\epsilon \times 10^{-3}$ cm^{-1} M^{-1}) 419.5 nm (229), 516 (13.0), 550 (6.64), 590 (5.51), 647 (3.73); FABMS m/z 1346 (calcd for $C_{76}H_{66}N_8O_8S_4$ (M^+) 1346).

From Aldehyde 7. The procedure described previously for the synthesis of porphyrin m-CH_2Br(TPP)H_2 (**2**) was applied with use of aldehyde **7** (200 mg, 0.69 mmol), pyrrole (48 μL, 0.69 mmol), 90 μL of a 2.5 M solution of BF_3·Et_2O in $CHCl_3$ (0.23 mmol), triethylamine (39 μL, 0.28 mmol), tetrachloro-1,4-benzoquinone (127 mg, 0.52 mmol), and 69 mL of dry $CHCl_3$. The crude residue obtained was subjected to chromatography on neutral alumina(I) eluting initially with $CHCl_3$, which removed an unidentified yellow band that was discarded. Elution was continued with 100:1 $CHCl_3$/methanol and the porphyrin-containing red band collected. This material was subjected to flash chromatography on silica eluting initially with $CHCl_3$, which removed unidentified pigments that were discarded. Elution was continued with 200:1 $CHCl_3$/methanol and the red band isolated to provide 41 mg (18%) of porphyrin **5a**, which was spectrally identical (500-MHz ^{1}H NMR) with the above sample.

[5,10,15,20-Tetrakis[α-(N-p-toluenesulfonamido)-m-tolyl]-porphyrin]zinc(II) Complex (8) (m-CH_2NH(Ts)(TPP)Zn). A mixture of m-CH_2NH(Ts)(TPP)H_2 (**5a**) (36 mg, 0.027 mmol) and $ZnCl_2$ (36 mg, 0.27 mmol) in 1 mL of DMF was stirred at 100 °C for 2 h and then cooled and diluted with $CHCl_3$. The resulting solution was worked up in the usual manner. The residue was separated into two fractions, each fraction was subjected to preparative TLC on a 200 × 100 × 0.25 mm silica plate eluting with 50:1 $CHCl_3$/methanol along the short axis, and the bright magenta band was collected and dried at 110 °C (0.2 mmHg) over P_2O_5 to give 16 mg (42%) of m-CH_2NH(Ts)(TPP)Zn (**8**) as a red solid: ^{1}H NMR δ 2.02–2.08 (m, 12, tosyl CH_3), 4.13–4.27 (m, 8, CH_2), 5.06–5.24 (m, 4, tosyl NH), 6.96–7.04 (m, 8, m-tosyl H), 7.45–7.52 (m, o-tosyl H), 7.59 (t, 4, J = 8 Hz, H-5′), 7.64 (d, 4, J = 8 Hz, H-4′), 7.87 (s, 4, H-2′), 7.91–7.96 (m, 4, H-6′), 8.67–8.75 (m, 8, β-pyrrolic H); UV/vis λ_{max} ($\epsilon \times 10^{-3}$ cm^{-1} M^{-1}) 423.5 nm (268), 516 (6.10), 551 (13.4), 590 (5.08), 652 (6.10); FABMS m/z 1410 (calcd for $C_{76}H_{64}N_8O_8S_4Zn$ (M^+) 1410).

[5,10,15,20-Tetrakis[α-[N-(m-formyl-α-tolyl)-N-p-toluenesulfonamido]-m-tolyl]porphyrin]zinc(II) Complex (9) (m-CH_2N(Ts)(m-CH_2PhCHO)(TPP)Zn). A mixture of tetrasulfonamide **8** (18 mg, 0.013 mmol), α-bromo-m-tolualdehyde (**1**) (12 mg, 0.06 mmol), and Cs_2CO_3 (50 mg, 0.153 mmol) in 1 mL of DMF was stirred at 80 °C for 2 h. Then the solution was cooled, diluted with $CHCl_3$, and worked up in the usual manner. The resulting residue was subjected to preparative TLC on a 1.0 × 100 × 100 mm silica plate and eluted with 50:1 $CHCl_3$/methanol. The fastest running magenta band was collected to provide 12 mg (48%) of the title tetraaldehyde **9**: R_f 0.32 (50:1 $CHCl_3$/methanol); ^{1}H NMR δ 2.03–2.16 (m, 12, tosyl CH_3), 4.60–4.67 (m, 16, CH_2 groups), 7.12–7.21 (m, 8, tosyl m-H), 7.37 (t, 4, J = 8 Hz, phenyl H), 7.56–7.66 (m, 24, phenyl H's), 7.76–7.79 (m, 8, tosyl o-H), 7.86, 7.94 (all s, 4, H-2′), 8.02, 8.07, 8.11 (all d, 4, J = 8 Hz, H-6′), 8.68, 8.69 (all s, 8, β-pyrrolic H), 9.67–9.71 (m, 4, CHO); IR ν 1705 (s, C=O), 1600 (m, C=C) 1170, 1100, and 1080 (s, SO_2) cm^{-1}; UV/vis λ_{max} ($\epsilon \times 10^{-3}$ cm^{-1} M^{-1}) 426 nm (311), 516 (5.54), 556 (15.7), 595 (6.57); FABMS m/z 1881 (calcd for $C_{108}H_{88}N_8O_{12}S_4Zn$ (M^+) 1881).

Tetrakis[*m*,*m*-[[methylene(*p*-tolylsulfonyl)imino]methylene]]-*strati*-bis(5,10,15,20-tetraphenylporphyrin) (3a) (TsN-(*m*-CH_2(TPP)H_2)$_2$). **Method A.** A mixture of *m*-$CH_2Br(TPP)H_2$ (**2**) (237 mg, 0.24 mmol), *p*-toluenesulfonamide (82 mg, 0.48 mmol) and Cs_2CO_3 (469 mg, 1.44 mmol) in 240 mL of DMF was stirred at room temperature for 14 h, then diluted with 100 mL of $CHCl_3$, and worked up in the usual manner. The purple residue was further dried at 110 °C (0.2 mmHg) to give 192 mg of purple solid. This was subjected to flash chromatography through a short column (4 × 0.75 in.) of silica eluting with $CHCl_3$ to give 125 mg of purple solid. This was divided into two fractions, and each fraction was subjected to preparative TLC on a 0.5 × 200 × 200 mm silica plate eluting with $CHCl_3$ (developing twice). The major purple band and trailing green-brown band were collected, and the residue obtained was stirred in a solution of trifluoroacetic acid (0.5 mL) for 20 min. This green solution was diluted with $CHCl_3$ and washed with a 5% aqueous NH_4OH solution followed by the usual workup to give 18 mg (8%) of TsN-(*m*-CH_2(TPP)H_2)$_2$ (**3a**) as a purple solid: R_f 0.42 (100:1 $CHCl_3$/methanol); ^1H NMR δ −4.42 (s, 4, NH), 2.51 (s, 12, tosyl CH_3), 4.66 (s, 16, CH_2), 7.14 (s, 8, H-2′), 7.45 (d, 8, J = 8 Hz, tosyl *m*-H), 7.58 (t, 8, J = 8 Hz, H-5′), 7.75 (d, 8, J = 8 Hz, H-4′), 7.89 (d, 8, J = 8 Hz, H-6′), 8.02 (d, 8, J = 8 Hz, tosyl *o*-H), 8.17 (s, 16, β-pyrrolic H); ^{13}C NMR δ 21.6 (tosyl CH_3), 49.3 (CH_2), 118.4 (*meso*-C), 127.2 (d, J = 160 Hz), 127.6 (d, J = 161 Hz), 128.7 (d, J = 156 Hz), 129.8 (d, J = 160 Hz), 133.2 (d, J = 160 Hz), 133.4 (tosyl *p*-C), 135.1 (d, J = 156 Hz), 138.4 (C-3′), 141.7 (C-1′), 143.6 (tosyl *ipso*-C), 153.1 (br s); IR ν 3322 (w, N—H), 1601 (m, C=C), 1156 and 1090 (s, SO_2) cm^{-1}; UV/vis λ_{max} (ϵ × 10^{-3} cm^{-1} M^{-1}) 408 nm (sh, 368), 415 (470), 516 (49.2), 551 (21.5), 592 (16.0), 648 (5.21); FABMS m/z 2008 (calcd for $C_{124}H_{96}N_{12}O_8S_4$ (M^+) 2009); laser desorption MS m/z 2009.6726 (calcd for $^{12}C_{123}{}^{13}C_1H_{96}N_{12}O_8S_4$ (M^+) 2009.6391).

Method B. A mixture of *m*-$CH_2Br(TPP)H_2$ (**2**) (9.8 mg, 9.9 μmol), *m*-$CH_2NH(Ts)(TPP)H_2$ (**5a**) (14.0 mg, 9.9 μmol), and Cs_2CO_3 (19.4 mg, 60 μmol) and 10 mL of DMF were stirred at room temperature for 14 h, and the resulting suspension was diluted with $CHCl_3$ and worked up in the usual manner. The crude residue obtained was subjected to preparative TLC on a 0.5 × 200 × 200 mm silica plate eluting with $CHCl_3$. The purple band and the green-brown band following directly behind it were collected, and the residue obtained was stirred in a solution of trifluoroacetic acid (0.5 ml) for 20 min. This green solution was diluted with $CHCl_3$ and washed with a 5% aqueous NH_4OH solution followed by the usual workup to provide 7.6 mg (38%) of the dimer **3a** spectrally identical (UV/vis 500-MHz ^1H NMR) with the sample previously prepared.

Method C. A mixture of tetraaldehyde **9** (predried overnight in a 5-mL round-bottom flask at 110 °C (0.2 mmHg) over P_2O_5) (7 mg, 0.0037 mmol), pyrrole (1 μL, 0.0149 mmol), and BF_3·Et_2O (2 μL of a 2.5 M solution in $CHCl_3$, 0.005 mmol) in 1.5 mL of $CHCl_3$ (distilled off of K_2CO_3) in the above flask, glass-stoppered (stopper secured in place with a plastic crimp), was heated with stirring in a 65 °C oil bath for 3.5 h during which the solution became dark green. Then the solution was cooled to room temperature and triethylamine (2 μL, 0.010 mmol) was added, which caused the solution color to change to red. After 15 min of stirring at room temperature, tetrachloro-1,4-benzoquinone (2.7 mg, 0.0112 mmol) was added and the resulting mixture again heated with stirring (65 °C oil bath) for 1 h. Then the solvent was evaporated and the residue obtained subjected to preparative TLC on a 0.25 × 200 × 200 mm silica plate eluting with 50:1 $CHCl_3$/methanol to give two nonpolar red bands and one polar red band. The polar band was collected to give 3 mg (43%) of starting tetraaldehyde **9** (identified by ^1H NMR). The nonpolar bands were combined and treated as previously stated for demetalation to give 1.5 mg (20%, 43% corrected for recovered tetraaldehyde **9**) of TsN-(*m*-CH_2(TPP)H_2)$_2$ (**3a**) spectrally identical (500-MHz ^1H NMR, laser desorption MS) with the previously prepared sample.

Tetrakis[*m*,*m*-[(methylenecyanoimino)methylene]]-*strati*-bis-(5,10,15,20-tetraphenylporphyrin) (3b) (NCN-(*m*-CH_2(TPP)H_2)$_2$). Prepared in a manner parallel to method A for the preparation of **3a** by using *m*-$CH_2Br(TPP)H_2$ (**2**) (228 mg, 0.23 mmol), cyanamide (19.4 mg, 0.46 mmol) in place of *p*-toluenesulfonamide, Cs_2CO_3 (450 mg, 1.38 mmol), and DMF (230 mL). The initial crude residue (144 mg after drying) weighed 58 mg after short column chromatography. This was subjected to preparative TLC on a 0.5 × 200 × 200 mm silica plate eluting with 150:1 $CHCl_3$/methanol, and the second most nonpolar purple band was isolated to give 13 mg (8%) of NCN-(*m*-CH_2-(TPP)H_2)$_2$ (**3b**) as a purple solid: R_f 0.20 (100:1 $CHCl_3$/methanol); ^1H NMR δ −3.99 (s, 4, NH), 4.43 (s, 16, CH_2), 7.31 (s, 8, H-2′), 7.74 (t, 8, J = 8 Hz, H-5′), 7.84 (d, 8, J = 8 Hz, H-4′), 8.13 (d, 8, J = 8 Hz, H-6′), 8.38 (s, 16, β-pyrrolic H); IR ν 3320 (w, N—H), 2230 (s, C≡N) 1600 and 1580 (m, C=C) cm^{-1}; UV/vis λ_{max} (ϵ × 10^{-3} cm^{-1} M^{-1}) 415 nm (454), 514 (20.5), 550 (9.87), 591 (6.40), 645 (3.47); FABMS m/z 1492 (calcd for $C_{100}H_{68}N_{16}$ (M^+) 1493).

Tetrakis[*m*,*m*-[(methyleneimino)methylene]]-*strati*-bis(5,10,15,20-tetraphenylporphyrin) (3c) (HN-(*m*-CH_2(TPP)H_2)$_2$) from Dimer 3a. To a solution of TsN-(*m*-CH_2(TPP)H_2)$_2$ (**3a**) in 0.5 mL of dry dimethoxyethane (DME) at −60 °C was added a solution of sodium biphenyl radical anion in DME (prepared by mixing biphenyl (382 mg, 2.5 mmol) with sodium metal (57 mg, 2.5 mmol) in 20 mL of DME overnight at room temperature and found to be 0.028 M immediately prior to this reaction by titration against *N*,*N*-methylphenyl-*p*-toluenesulfonamide),[25] and the progress of the reaction was monitored by TLC at intervals after every 0.2-mL addition of biphenyl radical anion solution after an initial 0.8-mL addition. The reaction was quenched with wet ether when TLC analysis (100:1 $CHCl_3$/methanol) showed no (or very little) fast-running **3a** remaining (the product stays at the baseline) (1.7 mL total of biphenyl radical anion solution). The solution was diluted with $CHCl_3$ and then worked up in the usual manner to give a residue that was dissolved in a minimal amount of $CHCl_3$ and then caused to precipitate by addition of hexanes. The precipitate was collected on a small (0.5 × 1 cm) pad of Celite in a pipet and rinsed with hexanes. The precipitate was then washed off of the Celite with $CHCl_3$ and the filtrate evaporated to give 2.3 mg (41%) of HN-(*m*-CH_2(TPP)H_2)$_2$ (**3c**) as a purple solid: ^1H NMR δ −3.78, −3.68, −2.8 (br) (all s, 4, pyrrolic NH), 3.8 (br s), 4.19 (sh), 4.21 (all s, 16, CH_2), 7.56–7.60 (m, 16 H-4′ and H-5′), 7.81 (s, 8, H-2′), 7.95 (br d, 8, J = 7 Hz, H-6′), 8.43, 8.46 (sh), 8.8 (br) (all s, 16, β-pyrrolic H); IR ν 3320 (w, N—H), 1600 (m, C=C) cm^{-1}; UV/vis λ_{max} (ϵ × 10^{-3} cm^{-1} M^{-1}) 406 nm (sh, 137), 414 (258), 515 (15.9), 550 (9.51), 590 (7.78), 646 (5.85); laser desorption MS m/z 1393.7149 (calcd for $^{12}C_{95}{}^{13}CH_{72}N_{12}$ (M^-) 1393.6036).

From the Alkylation of 4b with 2. A solution of *m*-$CH_2Br(TPP)H_2$ (**2**) (60 mg, 0.061 mmol), *m*-$CH_2NH_2(TPP)H_2$ (**4b**) (44 mg, 0.061 mmol), and Cs_2CO_3 (159 mg, 0.49 mmol) in 60 mL of DMF was stirred at room temperature for 14 h and then diluted with 60 mL of $CHCl_3$. The resulting solution was worked up in the usual manner. The residue was dissolved in $CHCl_3$ and filtered. The filtrate was concentrated and then subjected to preparative TLC on a 0.25 × 200 × 200 mm alumina plate eluting with 100:20:1 $CHCl_3$/hexanes/methanol. The baseline band was collected to give 1 mg (2.4%) of HN-(*m*-CH_2(TPP)H_2)$_2$ (**3c**) as a purple solid, which was spectrally identical (500-MHz ^1H NMR, UV/vis) with the previously prepared sample.

***N*,*N*-Bis(*m*-formyl-α-tolyl)-*p*-toluenesulfonamide (10).** A mixture of *p*-toluenesulfonamide (100 mg, 0.585 mmol), α-bromo-*m*-tolualdehyde (**1**) (232 mg, 1.17 mmol), and Cs_2CO_3 (760 mg, 2.34 mmol) in 12 mL of DMF was stirred at 90 °C for 90 min, then cooled, and diluted with ether followed by the usual workup. The crude white solid obtained was recrystallized from ether to provide 141 mg (59%) of white crystalline **10**: mp 97–99 °C; ^1H NMR δ 2.47 (s, 3, tosyl CH_3), 4.39 (s, 4, CH_2), 7.32–7.40 (m, 8), 7.43 (s, 2, *o*-H), 7.77 (d, 2, J = 8 Hz, tosyl *o*-H), 9.83 (s, 2, CHO); exact mass m/z 407.1183 (calcd for $C_{23}H_{21}NO_4S$ (M^+) 407.1164).

5,10,15,20-Tetrakis(α-anilino-*m*-tolyl)porphyrin (11a) (*m*-CH_2-(NHPh)(TPP)H_2). A mixture of *m*-$CH_2Br(TPP)H_2$ (20 mg, 0.020 mmol), aniline (15 μL, 0.16 mmol), and Cs_2CO_3 (26 mg, 0.08 mmol) in 1 mL of DMF was stirred at room temperature for 14 h, then diluted with $CHCl_3$ (20 mL), and worked up in the usual manner. After the residue was dried further at 110 °C (0.2 mmHg) over P_2O_5 for 2 h, the resulting purple solid (21 mg) was subjected to preparative TLC on a 0.5 × 200 × 200 mm silica plate eluting with 200:1 $CHCl_3$/methanol and the major band collected to give 9 mg (43%) of *m*-CH_2(NHPh)(TPP)H_2 (**11a**): R_f 0.69 (50:1 $CHCl_3$/methanol); ^1H NMR δ −2.83 (s, 2, pyrrolic NH), 4.58 (s, 8, CH_2), 6.70 (t, 4, J = 7.5 Hz, H-4″), 6.75 (d, 8, J = 7.5 Hz, H-2″), 7.20 (t, 8, J = 7.5 Hz, H-3″), 7.71 (t, 4, J = 7.5 Hz, H-5′), 7.77 (d, 4, J = 7.5 Hz, H-4′), 8.11 (d, 4, J = 7.5 Hz, H-6′), 8.18 (s, 4, H-2′), 8.78 (s, 8, β-pyrrolic H); FABMS m/z 1035 (calcd for $C_{72}H_{58}N_8$ (M^+) 1035).

5,10,15,20-Tetrakis(*m*-aminophenyl)porphyrin (11c) (*m*-NH_2-(TPP)H_2). The earlier preparation[29] of porphyrin **11c** was improved by modifying the isolations in the following manner.

The reagents *m*-nitrobenzaldehyde (20.0 g, 132 mmol), acetic anhydride (21.8 mL, 231 mmol), 660 mL of propionic acid, and pyrrole (9.2 mL, 132 mmol) were combined as previously reported,[29] and the resulting precipitate was collected by filtration and washed with water and methanol. This red cake was dissolved portionwise in CH_2Cl_2 and filtered through silica gel eluting with CH_2Cl_2. The filtrate was concentrated down to 150 mL, and 100 mL of methanol was added. This solution was reduced to ca. 90 mL by rotary evaporation and the precipitate collected by filtration, then stirred thoroughly with ca. 30 mL of CH_2Cl_2, and filtered again. The resulting solid was dried at 110 °C (0.2 mmHg) for 14 h over P_2O_5 to give 2.89 g (11%) of *m*-$NO_2(TPP)H_2$ (**11b**) as a purple powder: R_f 0.66 (3:1 THF/hexanes); ^1H NMR (DMSO-d_6) δ −2.83 (s, 2, pyrrolic NH), 8.00 (t, 4, J = 7 Hz, H-5′), 8.57 (d, 4, J = 7 Hz, H-6′),

8.72 (d, 4, J = 7 Hz, H-4'), 8.82 (s, 8, β-pyrrolic H), 9.09 (s, 4, H-2').

The porphyrin *m*-NO_2(TPP)H_2 (**11b**) (2.72 g, 3.42 mmol), 137 mL of concentrated aqueous HCl, and stannous chloride dihydrate (12.3 g, 54.8 mmol) were combined as previously reported.[29] The resulting mixture was made basic (140 mL of NH_4OH), and 50 mL of CH_2Cl_2 was added. After the suspension was thoroughly mixed, the resulting precipitate was collected by filtration. The dark solid collected was crushed to a powder and extracted with THF (4 × 150 mL). The resulting THF extract was filtered through a pad of silica gel. The filtrate was reduced to 30 mL, 50 mL of $CHCl_3$ was added, and the solution was again reduced to 30 mL when another 50 mL of $CHCl_3$ was added. After the solution was reduced to a final 20 mL, the precipitate was filtered and washed with $CHCl_3$ to give 2.00 g (87%) of *m*-NH_2-(TPP)H_2 (**11c**) as a fine purple microcrystals: R_f 0.46 (3:1 THF/hexanes); ^{1}H NMR (DMSO-d_6) δ −2.96 (s, 2, pyrrolic NH), 5.48 (br s, 8, NH_2), 7.01 (d, 4, J = 7 Hz, H-4'), 7.36-7.46 (m, 12, H-2', H-5', and H-6'), 8.92 (s, 8, β-pyrrolic H); FABMS m/z 675 (calcd for $C_{44}H_{34}N_8$ (M^+) 675).

5,10,15,20-Tetrakis[*m*-(*p*-tolylsulfonamido)phenyl]porphyrin (13) (*m*-(NHTs)(TPP)H_2). A mixture of *m*-NH_2(TPP)H_2 (**11a**) (100 mg, 0.148 mmol), *p*-toluenesulfonyl chloride (565 mg, 2.96 mmol), and triethylamine (0.52 mL, 3.7 mmol) in 30 mL of THF was stirred at room temperature for 72 h, then 10 mL of methanol was added, and the solution was stirred for an additional 14 h. The mixture was then diluted with ethyl acetate followed by the usual workup. The residue was dissolved in a minimal amount of CH_2Cl_2, and this solution was layered with benzene. The resulting red-purple crystals were collected by filtration and dried at 110 °C (0.2 mmHg) over P_2O_5 for 14 h to give 166 mg (87%) of *m*-(NHTs)(TPP)H_2 (**13**): R_f 0.62 (3:1 THF/hexanes); ^{1}H NMR (DMSO-d_6) δ −3.17 (s, 2, pyrrolic NH), 2.34 (s, 12, tosyl CH_3), 7.46 (d, 8, J = 7.5 Hz, tosyl *m*-H), 7.65 (br s, 4), 7.70-7.82 (m, 16), 7.87-7.96 (m, 4), 8.42-8.51 (m, 8, β-pyrrolic H), 10.55-10.62 (m, 4, tosyl NH); FABMS m/z 1290 (calcd for $C_{72}H_{58}N_8O_8S_4$ (M^+) 1290).

Tetrakis[*m*,*m*'-[methylene-(*p*-tolylsulfonyl)imino]]-*strati*-bis-(5,10,15,20-tetraphenylporphyrin) (14b) (*m*,*m*'-TsNCH$_2$-(TPP)H_2)$_2$). A mixture of *m*-(NHTs)(TPP) (**13**) (160 mg, 0.124 mmol), *m*-CH_2Br-(TPP)H_2 (**2**) (122 mg, 0.124 mmol), and Cs_2CO_3 (242 mg, 0.744 mmol) in 125 mL of DMF was stirred at room temperature for 14 h, then diluted with 50 mL of $CHCl_3$, and worked up in the usual manner. The residue obtained was dried further at 110 °C (0.05 mmHg) over P_2O_5 for 45 min. The residue (220 mg) was subjected to flash chromatography on silica, and elution with 100:1 $CHCl_3$/methanol provided 55 mg of a purple residue.

To simplify the preparative TLC,[24] the material thus obtained was metalated in the following manner.[37] To a refluxing $CHCl_3$ solution (8 mL) of this crude residue was added 5 mL of a methanolic solution containing 15 mg of potassium acetate (0.15 mmol) and 15 mg of Zn-$(OAc)_2 \cdot 2H_2O$ (0.68 mmol). This mixture was refluxed for 30 min, and then the solvent was evaporated. The residue was dissolved in $CHCl_3$ and filtered over Celite. The filtrate was subjected to preparative TLC on a 0.5 × 200 × 200 mm silica plate eluting with 100:1 $CHCl_3$/methanol, and the second most nonpolar magenta band was isolated. This residue was dissolved in 0.3 mL of trifluoroacetic acid, and this solution was stirred for 15 min at room temperature, then diluted with $CHCl_3$, and washed with 5% aqueous NH_4OH solution followed by the standard workup to give 1.3 mg (1%) of *m*,*m*'-TsNCH$_2$-((TPP)H_2)$_2$ (**14**) as a purple solid: R_f 0.46 (100:1 $CHCl_3$/methanol); ^{1}H NMR δ −4.11, −4.07 (s, 2 each, pyrrolic NH), 2.25 (s, 12, tosyl CH_3), 5.19 (s, 8, CH_2), 6.95 (s, 4, H-2'''), 7.26 (d, 8, J = 8 Hz, tosyl *m*-H), 7.50 (d, 4, J = 8 Hz, H-4'''), 7.60 (t, 4, J = 8 Hz, H-5'''), 7.66 (d, 4, J = 8 Hz, H-4''), 7.76 (t, 4, J = 8 Hz, H-5''), 7.78 (s, 4, H-2''), 7.79 (d, 8, J = 8 Hz, tosyl *o*-H), 7.96 (d, 4, J = 8 Hz, H-6'''), 8.25 (br s, 8, β'-pyrrolic H), 8.35 (d, 4, J = 8 Hz, H-6''), 8.43 (s, 8, β-pyrrolic H); IR ν 3320 (w, N—H), 1600 (m, C=C) 1270, 1170, and 1100 (s, SO_2) cm^{-1}; UV/vis λ_{max} ($\epsilon \times 10^{-3}$ cm^{-1} M^{-1}) 415 nm (314), 517 (16.6), 552 (7.71), 593 (5.69), 650 (4.03); FABMS m/z 1953 (calcd for $C_{120}H_{88}N_{12}O_8S_4$ (M^+) 1953).

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Supplementary Material Available: ^{1}H NMR spectra of compounds **2**, **3b**, and **15** (X = $CF_3CO_2^-$, the aromatic region as compared to **3c**) each in $CDCl_3$ and **14** in $CDCl_3$ and CD_2Cl_2 (5 pages). Ordering information is given on any current masthead page.

(37) *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier Scientific Publishing Co.: New York, 1975; p 798.

Highly Felkin-Anh Selective Hiyama Additions of Chiral Allylic Bromides to Aldehydes. Application to the First Synthesis of Nephromopsinic Acid and Its Enantiomer

Johann Mulzer,*,† Lars Kattner,† Achim R. Strecker,† Christian Schröder,†,§ Jürgen Buschmann,‡ Christian Lehmann,‡ and Peter Luger‡,⊥

Contribution from the Institut für Organische Chemie der Freien Universität Berlin, Takustrasse 3, D-1000 Berlin 33, FRG, and Institut für Kristallographie der Freien Universität Berlin, Takustrasse 6, D-1000 Berlin 33, FRG. *Received October 15, 1990*

Abstract: The chromium(II)-mediated addition ("Hiyama reaction") of the chiral allylic bromides **13**, **15**, **19**, **22**, **24**, and **27** to achiral and chiral aldehydes proceeds with high Felkin-Anh selectivity with respect to the stereocenter at Cγ in the bromide (Table II). By double stereodifferentiation experiments (Tables III/IV) it was shown that the bromide is the stereodominating component in the addition. The methodology was applied to the first synthesis of nephromopsinic acid (−)-**69**, found in the lichen species *nephromopsis stracheyi*, and its enantiomer.

Allyl transfer reactions from reagents **1a-g** to aldehydes have acquired a central importance in natural product synthesis, due to their high regio- and stereochemical predictability.[1] The C-C connection regioselectively occurs at the γ-position of the double bond with concomitant allylic shift and migration of X to the aldehyde oxygen, from where it is removed by hydrolysis. The simple diastereoselection (syn or anti configuration at the newly

† Institut für Organische Chemie der Freien Universität Berlin.
‡ Institut für Kristallographie der Freien Universität Berlin.
§ Preparative work.
⊥ Crystal structure analysis of compounds **44** and **57**.

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