Pergamon

Tetrahedron: Asymmetry, Vol. 7, No. 3, pp. 659-662, 1996

0957-4166/96 $15.00 + 0.00

S0957-4166(96)00058-4

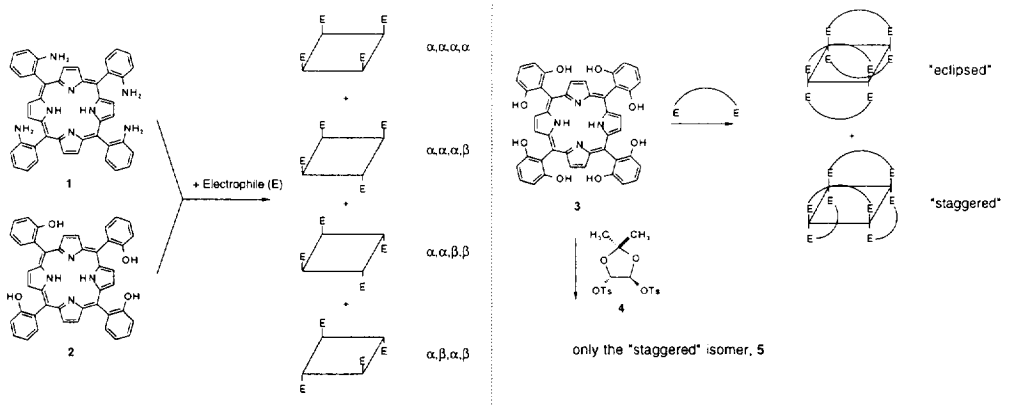
Self Assembly Assisted Preparation of a Homochiral Porphyrin

Santiago Ini,[a] Moshe Kapon,[a] Shmuel Cohen,[b] and Zeev Gross[a,*]

[a] Department of Chemistry, The Technion, Israel Institute of Technology, Haifa 32000, Israel
[b] Department of Inorganic and Analytical Chemistry, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

Abstract: The multiple alkylation of porphyrin **3** by four equivalents of the homochiral ditosylthreitol **4** proceeded in high yields, and only one of the two possible isomers was formed. The crystal structure of the product **5** suggests that that this novel phenomenon is a consequence of conformational changes, induced by the first alkylation. The formation of the first bridge completely eliminates the possibility of obtaining one of the isomers, while at the same time it seems to assist in the formation of the other isomer in a self assembly fashion.

Metal Complexes of homochiral ligands are frequently utilized as catalysts for asymmetric functionalization of hydrocarbons.[1] Utilization of homochiral metalloporphyrins as oxygenation catalysts is particularly important because of the biological relevance to catalysis by heme-dependant enzymes and the relatively well understood mechanistic aspects of their action.[2] The first utilization of homochiral metalloporphyrins for asymmetric induction was reported in 1983,[3] a few years after the pioneering demonstration of epoxidation of olefins via catalysis by synthetic iron[4] and manganese[5] porphyrin complexes. During the last decade more efficient and selective catalysts were developed, which also led to a higher level of knowledge about the requirements for effective asymmetric induction.[6]



Scheme 1

The most common approach for the preparation of homochiral porphyrins is by derivatization of free functional groups (-NH_2, -OH, -CO_2H) on the porphyrin periphery by readily available homochiral compounds (acid derivatives, alkyl halides or tosylates, amines). Ideally, a homochiral cavity must be built close to the metal center, which calls for derivatization of the *ortho*-phenyl positions of tetraphenylporphyrin. The three available precursors for these reactions are the tetraamino, tetrahydroxy, and octahydroxy derivatives, **1** - **3**, shown in

Scheme 1. Derivatisation of porphyrin **1** or **2** leads however to a mixture of four possible atropisomers, of which only two have the desired features (α,β,α,β and α,α,α,α in Scheme 1). In addition, in the α,α,α,α isomer all the homochiral groups are located on the same face of the porphyrin. To use such metal derivatives as catalysts requires blocking of the undesired site by bulky axial ligands, which because of mechanistic considerations is applicable only to manganese complexes. Utilization of porphyrin **3** appears quite appealing, since both sites will necessarily remain identical after functionalization of its OH groups. To our knowledge, only Naruta *et al* have so far prepared homochiral porphyrins from **3**, using derivatives of binaphtol.[7] The yields of coupling between **3** and these homochiral auxiliaries were however low, and in addition, two isomers– staggered and eclipsed– of these "twin coronet" porphyrins were formed in about equimolar ratio (Scheme 1).

In this account we report the coupling reaction of porphyrin **3** with commercially available (S,S)-(-)-1,4-di-*O*-tosyl-2,3-*O*-isopropylidene-L-threitol **4**, which was recently shown by Collman *et al* to be a quite effective alkylating agent for porphyrin **2** (combined yield of 37% of the two possible isomers).[8] In the present case, *the reaction proceeded with 60% yield and only one isomer, 5, was formed.* The crystal structure of **5** suggests that both the relatively high yield and the selectivity result from conformational changes in the porphyrin upon introduction of the first threitol unit, which direct the next incoming groups in a self assembly fashion.

The reaction was performed by treating porphyrin **3** with 5 equivalents of compound **4**,[9] following the procedure described by Collman *et al* for alkylation of porphyrin **2**. Flash chromatography afforded only one porphyrin, **5**, which was isolated in 60% yield. The structure of **5** was first elucidated from its ^{1}H NMR spectrum, based on symmetry considerations. Both possible isomers of the fully alkylated porphyrin have D_2 symmetry, but with different location of their $C_2(x)$ and $C_2(y)$ axes, considering $C_2(z)$ as perpendicular to the porphyrin plane. The β-pyrrole hydrogens appeared as two doublets in the ^{1}H NMR spectrum of **5**, which is only consistent with the staggered isomer, whose $C_2(x)$ and $C_2(y)$ axes penetrate the phenyl-carrying *meso* carbon atoms. For the eclipsed isomer the $C_2(x)$ and $C_2(y)$ axes bisect the pyrrole rings, leaving their adjacent hydrogens equivalent, which would result in two sets of singlets.

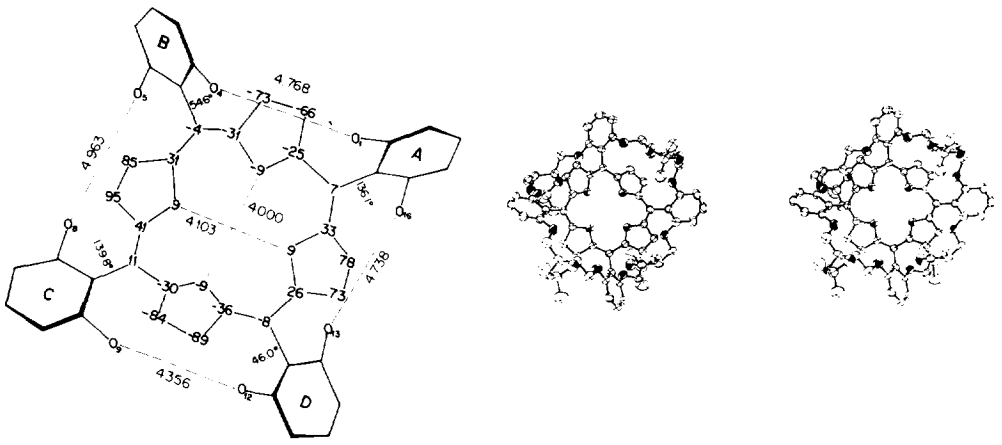


Figure 1. Formal diagram of the porphyrinato core and the phenyl rings (numbers are explained in text) and ORTEP stereoview of the structure of porphyrin **5**.

The crystal structure of **5** (Figure 1) confirmed its assignment as the staggered isomer.[10] Furthermore, critical examination of the structure revealed the reason for the selective formation of only the staggered, but not the eclipsed isomer. The most important structural parameters in the present context are the angles between the mean plane of the four *meso*-phenyl rings and the porphyrin plane. These angles were found to be 136.1, 54.6, 139.8, and 46.0° for rings A, B, C, and D of Figure 1, keeping a counterclockwise trend of the plane's normals around the porphyrin. Clearly, each two adjacent phenyl groups rotate in opposite directions in order to bring the bridging *ortho*-phenyl oxygens close enough in space for reaction with the ditosylthreitol groups. The distances between the four sets of bridging oxygens (O_1-O_4, O_5-O_8, O_9-O_{12}, O_{13}-O_{16}) in porphyrin **5** were found to be in the range of 4.66 ± 0.30 Å. The same rotations also move the two other *ortho*-phenyl oxygens of adjacent phenyl groups (O_1-O_{12}, O_4-O_9, O_5-O_{16}, O_8-O_{13}) away from each other to a range of 9.06 ± 0.15 Å, thus clearly avoiding the possibility of connecting a second threitol unit on the opposite porphyrin plane. Accordingly, the eclipsed isomer can not be formed. Furthermore, it seems likely that formation of the first bridge assists in formation of the next one. If for example the first reaction occurs between rings B and C, their free O_4 and O_9 *ortho*-phenyl hydroxides at the opposite porphyrin face will become closer to O_1 and O_{12} of rings A and D, respectively, thus encouraging the formation of the next bridge. This sequence of conformational changes seems to be responsible for the relatively high yield for the formation of **5**. Finally, the rotation of the phenyl groups and the formation of the bridges also appears to affect the final conformation of the porphyrin. It is well known that *ortho*-phenyl substituents and β-pyrrole CH's have strong steric interactions.[11] In the present case, each threitol bridge is expected to "push" the pyrrole unit encapsulated between the phenyl rings in order to relieve steric hindrance. For the staggered isomer this will result in deviation of the four pyrrole units from the porphyrin plane in an up-down-up-down fashion. This so-called saddle shaped porphyrin deformation[11] was indeed found to be very dominant for porphyrin **5**, as can be seen from Figure 1, in which the deviation of the 20 C and the 4 N atoms from the mean plane trough the four N atoms are shown in units of 0.01 Å.

In conclusion, the novel high-yield formation of only one isomer in the multiple alkylation of porphyrin **3** by four equivalents of ditosylthreitol **4** was found to be a consequence of conformational changes produced by the first alkylation. It completely eliminates the possibility of obtaining one of the isomers, while at the same time it seems to assist in the formation of the other. We trust that these observations will assist in future design of superstructured homochiral porphyrins.

Acknowledgments: This research was supported by the Israel Science Foundation, administered by The Israel Academy of Sciences and Humanities.

References and Notes

1. a) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1059-70. b) Johnson, R. A.; Sharpless, K. B. *Comprehensive Organic Synthesis*, Trost, B. M.; Fleming, I. Eds.; Pergamon Press: New York, 1991; Vol. 7, pp 389-436. c) Koenig, K. E. *Asymmetric Synthesis*, Morrison, J. D. Ed.; Academic Press: New York, 1985; Vol. 5, p. 71.
2. a) Meunier, B. *Metalloporphyrins Catalyzed Oxidations*; Montanari, F., Casella, L. Eds.; Kluwer Academic Publishers: Dordrecht, 1994; chapter 1. b) Mansuy, D. *Coord. Chem. Rev.* **1993**, *125*, 129. c)

Watanabe, Y.; Groves, J. T. *The Enzymes, vol. XX*; Sigman, D. S. Ed.; Academic Press: California, 1992; chapter 9.

3. Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5794.
4. Groves, J. T.; Nemo, T. E.; Meyers, R. S. *J. Am. Chem. Soc.* **1979**, *101*, 1032.
5. Chang, C. K.; Kuo, M. S. *J. Am. Chem. Soc.* **1979**, *101*, 3413.
6. Collman, J. P.; Zhang, X.; Lee, V. J.; Uffelman, E.; Brauman, J. I. *Science* **1993**, *261*, 1404-11.
7. Naruta, Y.; Ishihara, N.; Tani, F.; Haruyama, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 158-68 and earlier references therein.
8. Collman, J. P.; Lee, V. J.; Kellen-Yuen, C. J.; Zhang, X.; Ibers, J. A.; Brauman, J. I. *J. Am. Chem. Soc.* **1995**, *117*, 692-703.
9. Solid K_2CO_3 (285 mg, 2.9 mmol) was added to a 100 °C solution of **3** (86 mg, 0.114 mmol) and **4** (282 mg, 0.6 mmol) in 20 mL of dry DMF under N_2. After 18 hours at 100 °C the cool reaction mixture was diluted with 20 mL CH_2Cl_2 and washed with 40 mL H_2O. Drying by Na_2SO_4 and evaporation of the solvents, followed by flash chromatography on basic alumina with CH_2Cl_2/EtOAc/Et_3N (50:49:1) as eluents, afforded one fast moving fraction. By crystallization from $CHCl_3$/heptane, 87 mg (60.2%) of **5** were obtained. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.30 (d, *J*=4.7 Hz, 4H), 8.16 (d, *J*=4.7 Hz, 4H), 7.66 (t, *J*= 8.3 Hz, 4H), 7.24 (d, *J*= 7.7 Hz, 8H), 4.79 (dd, *J*= 10.8, 2.8 Hz, 4H), 4.42 (dd, *J*=10.9, 2.0 Hz, 4H), 4.35 (t, *J*= 8.3 Hz, 4H), 4.27 (dd, *J*=8.6, 2.0 Hz, 4H), 3.95 (d, *J*=8.1 Hz, 4H), 2.84 (t, *J*=8.2 Hz, 4H), 1.07 (s, 12H), 0.28 (s, 12H), -1.41 (s, 2H); R_f = 0.69 (alumina, CH_2Cl_2/EtOAc/Et_3N 50/49/1); λ_{max} (CH_2Cl_2, nm): 440 (soret), 540, 582, 678; FAB MS: m/z: 1247 ([M-H]$^+$, 100%).
10. Crystals of **5** , suitable for X-ray analysis were obtained by slow evaporation of a $CHCl_3$ solution of **5**. The crystals have the formula $C_{72}H_{70}N_4O_{16}\cdot 3.3CHCl_3\cdot 1.2H_2O$ and Formula Weight 1662.9. They are orthorhombic, a = 27.466(9), b = 19.240(6), c = 15.206(5) Å, space group $P2_12_12_1$, Z = 4, V = 8036Å^3, ρ_{calcd} = 1.375g·cm^{-3}, $2\theta_{max}$ = 120°, Cu Kα, = 1.5418Å, scan mode θ/2θ, T = 293K, No. of measured reflections 6524, No. of independent reflections 6491, No. of reflections included in the refinement 4919, Fo ≥ 4σ(Fo), LP corrections but not absorption applied, μ=3.71mm^{-1}. The structure was solved by directs methods using SHELXS86, and refined in full matrix using SHELXL93 program,[12] No. of refined parameters 755. Hydrogens were placed in calculated positions and shifted using the riding model, *R* = 0.088, ωR=0.234, refinement performed against $|F^2|$, residual electron density 0.79 e·Å-3. The porphyrin molecule was found to be well defined in the structure, while the $CHCl_3$ molecules occupy four different sites; two with full occupancies, one with partial occupancy of 0.5, and another in two occupancies of 0.39 and 0.40. The well defined porphyrin allows the critical elucidation of all important features, including the chirality centers on the threitol groups which were checked for the expected S,S configuration. The mean plane through the four N atoms, which was used in Figure 1 to demonstrate the saddle shape distortion of the porphyrin skeleton defined by its $C_{20}N_4$ group, is 23.837x + 0.556y + 7.541z + 3.838 = 0.
11. Scheidt, W. R.; Lee, Y. L. *Structure and Bonding (Berlin)* **1987**, *64*, 1-72.
12. Sheldrick, G. M. *Acta Cryst.* **1990**, *A46*, 467. Sheldrick, G. M.; SHELXL93 program for the refinement of crystal structures, University of Gottingen, Germany.

(*Received in UK* 19 *January* 1996)