Efficient Preparation of the α,α,β,β-Atropoisomer of *meso*-Tetrakis(*o*-aminophenyl)porphyrin

Eric Rose,* Aurélien Cardon-Pilotaz, Mélanie Quelquejeu, Nicolas Bernard, and Alain Kossanyi

Laboratoire de Chimie Organique, URA CNRS 408, Tour 44, 4 Place Jussieu, 75230 Paris Cedex 05, France

Bernard Desmazières

Laboratoire de Chimie Organique Structurale 2, ERS CNRS 73, Bâtiment F, Boite 45, 4 Place Jussieu, 75252 Paris Cedex 05, France

Received February 15, 1995

Synthetic chiral porphyrins have attracted much interest as models for heme proteins.[1,2] The building blocks are usually achiral atropoisomeric *meso*-5,10,15,20-tetrakis(*o*-substituted phenyl)porphyrins. The first superstructured Collman's "picket-fence" porphyrin is prepared from the pure α,α,α,α-atropoisomer of *meso*-tetrakis(2-aminophenyl)porphyrins, $TAPPH_2$.[3a,b] Then, "basket-handle",[1j,4] "pocket",[3c] "picnic-basket" [3d] gyroscope,[1b,c,e,j] octopus,[5a] "twin-coronet",[2c] and many other porphyrins[5b–e] have been described. In most cases, the α,β,α,β-$TAPPH_2$ atropoisomer represents the starting material: its content in the atropoisomeric mixture under equilibrium is only 12.5%. Recently, Nishino et al.[6] and our group[7a] described the preparation of this isomer by thermal treatment of the *meso*-5,10,15,20-tetrakis(*o*-nitrophenyl)-porphyrin atropoisomers $TNPPH_2$ in toluene and naphthalene in 63.7%[6] and 72%[7a] abundances as determined by HPLC. In order to know if better results could be obtained, we undertook the same study with the Zn complexes of tetrakis(*o*-nitrophenyl)porphyrin isomers, TNPPZn.[4a]

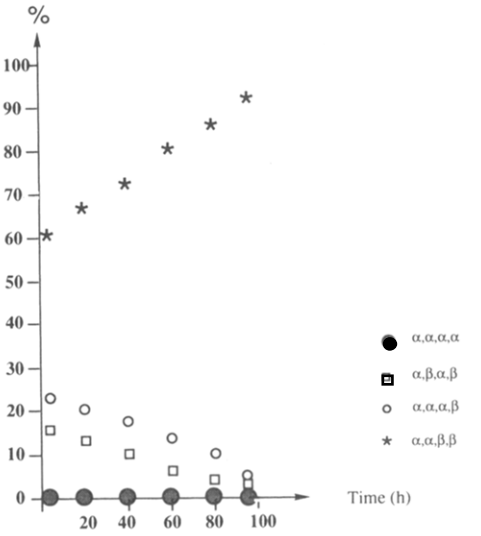

Figure 1. Thermal isomerization of the statistic ratio of crude TNPPZn at 120 °C.

Table 1 Ratio of the Atropoisomers of TNPPZn in Naphthalene

T (°C)	α,β,α,β	α,α,β,β	α,α,α,β	α,α,α,α
110	7	76	15	ϵ
120	2	92	6	ϵ
145	13	68	19	ϵ
160	23	42	35	ϵ

Crude TNPPZn[4a] (2 g) and naphthalene (400 g) were heated at 120 °C under vigorous stirring for 4 days giving an homogeneous solution **A**. Unexpectedly, by analyzing the mixture by HPLC,[8] we found that the α,α,β,β-atropoisomer was the major product (92%) and not the α,β,α,β one! (See Table 1 and Figures 1 and 2.) The hot solution **A** was poured into a concentrated HCl solution (400 mL) at −10 °C. CH_2Cl_2 (1l at 0 °C) and $SnCl_2{\cdot}2H_2O$ (6.5 g)[7b] were slowly added, and the two-phase solution was magnetically stirred for 20h at rt.[7] Naphthalene was removed in the CH_2Cl_2 organic phase and could be recovered almost quantitatively (380 g). The HCl phase

(1) (a) Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983,** *105,* 5791. (b) Lecas, A.; Levisalles, J.; Renko, Z.; Rose, E. *Tetrahedron Lett.* **1984,** *25,* 1563. (c) Lecas, A.; Renko, Z.; Rose, E. *Tetrahedron Lett.* **1985,** *26,* 1019. (d) Mansuy, D.; Battioni, P.; Renaud, J.-P.; Guerin, P. *J. Chem. Soc., Chem. Commun.* **1985,** 155. (e) Boitrel, B.; Lecas, A.; Renko, Z.; Rose, E. *J. Chem. Soc., Chem. Commun.* **1985,** 1820. (f) Ogoshi, H.; Saita, K.; Sakurai, K.; Watanabe, T.; Toi, H.; Aoyama, Y.; Okamoto, Y. *Tetrahedron Lett.* **1986,** *27,* 6365. (g) Naruta, Y.; Maruyama, K. *Tetrahedron Lett.* **1987,** *28,* 4553. (h) Aoyama, Y.; Saita, K.; Toi, H.; Ogoshi, H.; Okamoto, Y. *Tetrahedron Lett.* **1987,** *28,* 4853. (i) Groves, J. T.; Neumann, R. *J. Am. Chem. Soc.* **1987,** *109,* 5045. (j) Boitrel, B.; Lecas, A.; Rose, E. *Tetrahedron Lett.* **1988,** *29,* 5653. (k) Boitrel, B.; Lecas, A.; Renko, Z.; Rose, E. *New J. Chem.* **1989,** *13,* 73. (l) Boitrel, B.; Camilleri, E.; Fleche, Y.; Lecas, A.; Rose, E. *Tetrahedron Lett.* **1989,** *30,* 2923. (m) Maillard, P.; Guerquin-Kern, J. L.; Momenteau, M.; Gaspard, S. *J. Am. Chem. Soc.* **1989,** *111,* 9125. (n) Boitrel, B.; Lecas, A.; Rose, E. *J. Chem. Soc., Chem. Commun.* **1989,** 349. (o) Tetreau, C.; Boitrel, B.; Rose, E.; Lavalette, D. *J. Chem. Soc., Chem. Commun.* **1989,** 1805. (p) O'Malley, S.; Kodadek, T. *J. Am. Chem. Soc.* **1989,** *111,* 9116.

(2) (a) Boitrel, B.; Lecas, A.; Rose, E. *Tetrahedron Lett.* **1991,** *32,* 2129. (b) Konishi, K.; Sugino, T.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1991,** *113,* 6487. (c) Naruta, Y.; Tani, F.; Ishihara, N.; Maruyama, K. *J. Am. Chem. Soc.* **1991,** *113,* 6865. (d) Le Maux, P.; Bahri, H.; Simonneaux, G. *J. Chem. Soc., Chem. Commun.* **1991,** 1350. (e) Maillard, P.; Huel, C.; Momenteau, M. *Tetrahedron Lett.* **1992,** *33,* 8081. (f) Boitrel, B.; Lecas, A.; Rose, E. *Tetrahedron Lett.* **1992,** *33,* 227. (g) Le Maux, P.; Bahri, H.; Simmoneaux, G. *Tetrahedron* **1993,** *49,* 1401. (h) Rose, E.; Boitrel, B.; Quelquejeu, M.; Kossanyi, A. *Tetrahedron Lett.* **1993,** *34,* 7267. (i) Kuroda, Y.; Kato, Y.; Higashioji, T.; Ogoshi, H. *Angew. Chem., Int. Ed. Engl.* **1993,** *32,* 723. (j) Maillard, P.; Guerquin-Kern, J. L.; Huel, C.; Momenteau, M. *J. Org. Chem.* **1993,** *58,* 2774. (k) Collman, J. P.; Zhang, X.; Lee, V. J.; Uffelman, E. S.; Brauman, J. I. *Science* **1993,** *261,* 1404. (l) Mizutani, T.; Ema, T.; Tomita, T.; Kuroda, Y.; Ogoshi, H. *J. Chem. Soc., Chem. Commun.* **1993,** 520. (m) Konishi, K.; Yahara, K.; Toshishige, H.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1994,** *116,* 1337. (n) Le Maux, P.; Bahri, H.; Simonneaux, G. *J. Chem. Soc., Chem. Commun.* **1994,** 1287.

(3) (a) Collman, J. P.; Gagne, R. R.; Reed, C. A.; Halbert, T. R.; Lang, G.; Robinson, W. T. *J. Am. Chem. Soc.* **1975,** *97,* 1427. (b) Sorrell, T. N. *Inorganic Synthesis;* McGraw-Hill: New York, 1980; Vol. XX, p 161. (c) Collman, J. P.; Brauman, J. I.; Collins, T. J.; Iverson, B. L.; Lang, G.; Pettman, R. B.; Sessler, J. L.; Walters, M. A. *J. Am. Chem. Soc.* **1983,** *105,* 3038. (d) Collman, J. P.; Brauman, J. I.; Fitzgerald, J. P.; Hampton, P. D.; Naruta, Y.; Sparapany, J. W.; Ibers, J. A. *J. Am. Chem. Soc.* **1988,** *110,* 3477.

(4) (a) Momenteau, M.; Mispelter, J.; Loock, B.; Lhoste, J. M. *J. Chem. Soc., Perkin Trans. 1* **1985,** 221. (b) Stäubli, B.; Fretz, H.; Piantini, U.; Woggon, W. D. *Helv. Chim. Acta* **1987,** *70,* 1173.

(5) (a) Komatsu, T.; Nakao, K.; Nishide, H.; Tsuchida, E. *J. Chem. Soc., Chem. Commun.* **1993,** 728. (b) Baldwin, J. E.; Perlmutter, P. *Top. Curr. Chem.* **1984,** *121,* 181. (c) Osuka, A.; Nagata, T.; Maruyama, K. *Chem. Lett.* **1991,** 1687. (d) Nagata, T. *Bull. Chem. Soc. Jpn.* **1992,** *65,* 385. (e) Collman, J. P.; Zhang, X.; Herrmann, P. C.; Uffelman, E. S.; Boitrel, B.; Straumanis, A.; Brauman, J. I. *J. Am. Chem. Soc.* **1994,** *116,* 2681. See also some articles described in references 1 and 2, but of course this list is not exhaustive!

(6) Nishino, N.; Kobata, K.; Mihara, H.; Fujimoto, T. *Chem. Lett.* **1992,** 1991.

(7) (a) Rose, E.; Quelquejeu, M.; Pochet, C.; Julien, N.; Kossanyi, A.; Hamon, L. *J. Org. Chem.* **1993,** *58,* 5030. (b) Lecas, A.; Boitrel, B.; Rose. E. *Bull. Soc. Chim. Fr.* **1991,** *128,* 407.

(8) α,β,α,β-Atropoisomer, t = 10.48 min; α,α,α,β-atropoisomer, t = 11.04 min; α,α,β,β-atropoisomer, t = 13.46 min; α,α,α,α-atropoisomer, t =13.98 min; column cyano-bonded silica; internal diameter = 4.6 mm, l = 300 mm; dp = 10 μm; flow rate 1 mL/min; eluent 25–45% THF/heptane for 15 min; detection UV–vis, 420 nm; injections, 10 μL of the mixture dissolved in acetone.

0022-3263/95/1960-3919$09.00/0

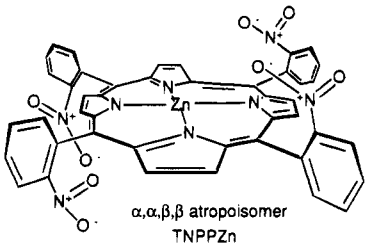

Figure 2.

was extracted twice with 100 mL of CH_2Cl_2 and neutralized slowly with NH_4OH until neutral pH. After five extractions (5 × 250 mL CH_2Cl_2) and finally another one with magnetic stirring for one night, the combined organic phases were dried over $MgSO_4$, evaporated under reduced pressure, and chromatographed on silica gel (15 μm) with CH_2Cl_2 and ether (60/40). The *meso*-α,α,β,β-tetrakis(*o*-aminophenyl)porphyrin atropoisomer (TAP-PH_2) was precipitated by adding petroleum ether to the CH_2Cl_2 solution to give 804 mg (63% yield).

At 160 °C and at 145 °C in naphthalene, 42% and 68% of the α,α,β,β-TNPPZn isomer were respectively obtained as observed by HPLC study (Table 1). At 110 °C, 76% of this isomer was observed. At the same temperature, crude TNPPZn was refluxed for 7 days in toluene but only 35% of the α,α,β,β-isomer was formed; this shed light on the crucial role of the naphthalene. In the case of the free base $TNPPH_2$ at 130 °C in naphthalene, 72% of the α,β,α,β-atropoisomer was determined by HPLC after only 20 min,[7a] and such a ratio cannot be obtained in xylene for example.

The statistic ratio 1/1/2/4 = αβαβ/αααα/ααββ/αααβ of crude $TNPPH_2$ and of $TAPPH_2$ are recovered by condensation of pyrrole and *o*-nitrobenzaldehyde and also after the reduction of the nitro isomers.[3a] The α,α,α,β nitro derivative represents the more abundant product. The α,α,α,α-isomer has been obtained as the major one by Elliott[9a] and Lindsey[9b] by treating the mixture in silica gel. The atropoisomerization of the mixture in toluene or naphthalene readily gives principally the α,β,α,β-isomer.[6,7a] Finally, we describe the obtention of the last (useful)[2g,i,3a] atropoisomer, α,α,β,β, by appropriate rotation of the other isomers of the TNPPZn mixture at 120 °C in naphthalene for 4 days followed by reduction at rt. The reasons for the high relative yield of the α,α,β,β-atropoisomer are currently unknown.[10] Work is in progress to elucidate such recognition of one atropoisomer to gain an insight of this process.

JO9502920

(9) (a) Elliott, C. M. *Anal. Chem.* **1980**, *52*, 660. (b) Lindsey, J.,*J. Org. Chem.* **1980**, *45*, 5215. Momenteau et al. obtained an α,α,α,α-atropoisomer in the case of *meso*-tetrakis(2,3,4,6-tetraacetyl-*O*-β-glucosylphenyl)porphyrin by treating also the mixture of isomers in the presence of silica gel.[9c] (c) Maillard, P.; Vilain, S.; Huel, C.; Momenteau, M. *J. Org. Chem.* **1994**, *59*, 2887. Hayashi and Ogoshi et al. described also a shift of another equilibrium of atropoisomers to the α,α,α,α-isomer in homogeneous solution.[9d] (d) Hayashi, T.; Asai, T.; Hokazono, H.; Ogoshi, H. *J. Am. Chem. Soc.* **1993**, *115*, 12210.

(10) The 92% abundance could be interpreted by a stabilization of two nitro groups by a polar water molecule and/or by ligation of the Zn complex by a water molecule which could favor the α,α,β,β-atropoisomer by means of hydrogen bonds. In order to prove it, α,α,β,β-TNPPZn was crystallized in a mixture of CH_2Cl_2 and pentane, but unfortunately, the cristals did not diffract yet and in solution ^1H NMR study did not show a water molecule signal.