Pergamon

Tetrahedron Letters 39 (1998) 1165–1168

TETRAHEDRON
LETTERS

Addition of sterically hindered Organolithium Compounds to *meso*-Tetraphenylporphyrin.

Bénédicte Krattinger and Henry J. Callot*

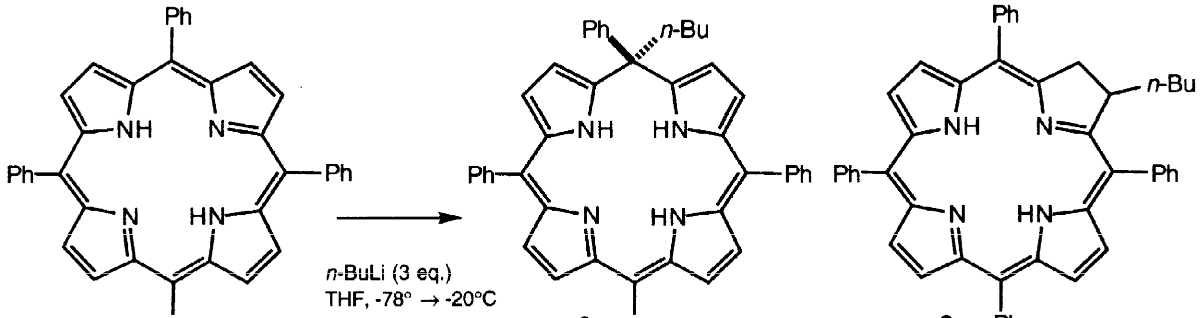
CNRS et Faculté de Chimie, Université Louis Pasteur,
1 rue Blaise Pascal, 67000 Strasbourg, France.

Received 30 October 1997; accepted 6 December 1997

Abstract: Reaction of *t*-butyllithium with *meso*-tetraphenylporphyrin gives two di-*t*-butyl-dihydroporphyrins, the addition occuring at positions 2,3 or 5,10. 5,10-di-*t*-butyl-5,10-dihydro-*meso*-tetraphenylporphyrin adopts a helicoidal structure as shown by its X-ray crystal structure.

Addition of nucleophiles to the *meso* position of a porphyrin should give a phlorin and this was demontrated in several examples[1]. We recently reported that stable phlorins can be isolated from the reduction of N-substituted porphyrin free bases[2]. Phlorin formation was extended to simple porphyrins like *meso*-tetraphenylporphyrin **1** (H_2TPP), whose alkylation with *n*-butyllithium gave **2**, however of moderate stability[3], likely *via* the lithium complex[4]. A β-addition product 2-*n*-butylTPchlorin **3** was also isolated. This last reaction, direct alkylation of an unactivated porphyrin free base is potentially promising since formation of Cβ-C bonds or nucleophilic addition to the pyrrolic positions is restricted to activated substrates[1,5].

To broaden the scope of the direct alkylation reaction and to influence the phlorin/chlorin ratio, we decided to use sterically more demanding reagents. This approach was also inspired by the known abnormal chemistry of *t*-butyl-substituted porphyrins[6].

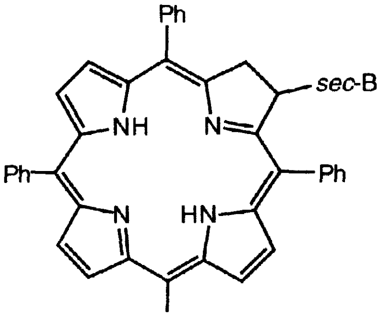


1 **2** **3**

e-mail callot@chimie.u-strasbg.fr fax (0)3 88 41 15 24

0040-4039/98/$19.00 © 1998 Published by Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(97)10792-4

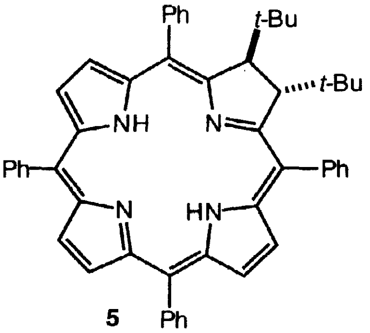
Addition of *sec*-butyllithium (3 eq.; -78° → -20°C; THF) to H_2TPP gave a complex mixture from which no phlorin could be isolated after the usual work-up. Only starting material (23%) and a monoalkylated chlorin **4** (22%; as a diastereomeric mixture) could be isolated in a pure state. The UV-visible and mass spectra of several fractions indicated the presence of additional chlorins (at least 3 dibutylated chlorins (8%) + polyalkylated mixtures), but the low amount of products, as well as their occurrence as diastereomeric mixtures precluded the isolation of any pure component. Compound **4** shows spectral data typical for a chlorin: long wavelength absorption (strong band at 652 nm), high-field protons, etc[7].



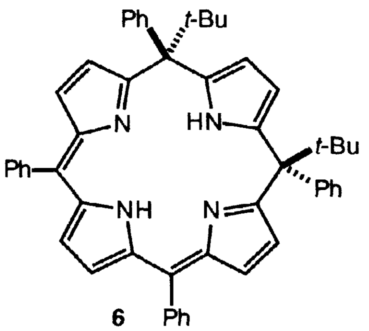
4

Reaction with *t*-butyllithium was expected to be more difficult in terms of approach of the reactive centers, but the structures of the products would be simpler to elucidate. The first hypothesis was verified when we recovered up to 70% starting material after reaction of *t*-butyllithium under the same conditions as with *n*- and *sec*-butyllithium. However, the only reaction products that could be fully characterized were both the result of a double addition.

Compound **5** (1%; racemic mixture if *trans*) is a typical chlorin whose UV-visible and NMR data[8] are similar to that of **2** and **4**. We suggest that the two *t*-butyl groups are in *trans* relationship: indeed, it is difficult to imagine the two groups positioned on the same face of the macrocycle without inducing a very large steric crowding involving the *t*-butyl groups and the *meso*-phenyl groups. In such a case, one would expect UV-visible data departing significantly from those of chlorins **2** and **4**.



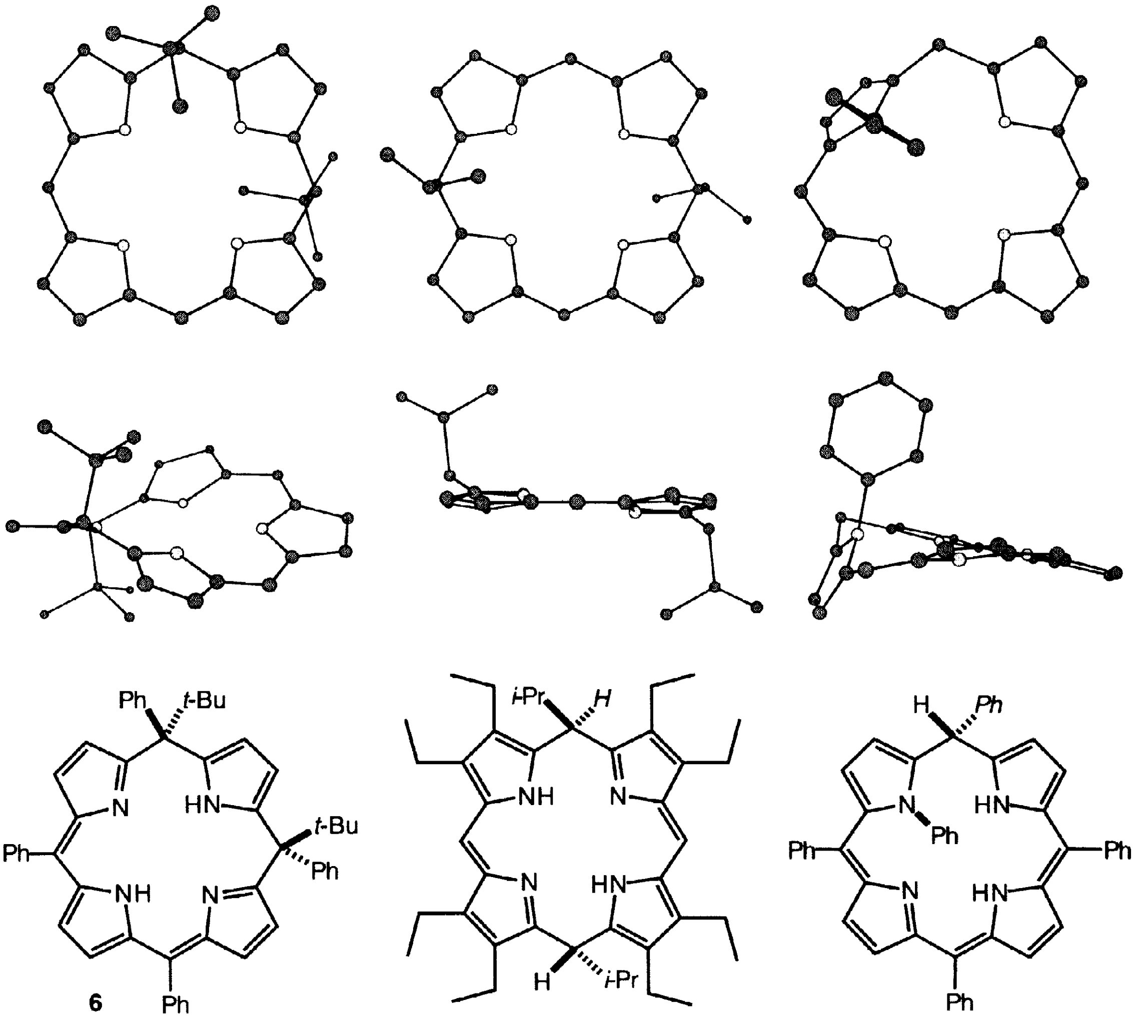
5



6

Compound **6** (5%) lost the 18π porphyrin conjugated system (N-H signals at 11.8 and 13.1 ppm) and showed several bands in the 350-550 nm range[9]. The presence of four intact pyrrole rings was illustrated by signals at 5.21 and 6.11 ppm (2d, 2+2 H, J = 2.3 Hz), and 5.60 and 6.42 ppm (2d, 2+2 H, J = 4.7 Hz), the J values strongly suggesting a 5,10 addition of *t*-butyl groups, the 2.3 Hz being due to a ß-H - NH coupling. The relative stereochemistry of the *t*-butyl groups was clarified by X-ray structure determination[10], using a single crystal grown by slow diffusion of CH_3OH into a CH_2Cl_2 solution of **6**.

Spontaneous resolution of **6** was observed. The shape of the molecule is that of a tripyrrolic helix, attached to an isolated pyrrole by two sp^3 carbons.The two *t*-butyl groups are arranged in an anti diaxial geometry. The bond lengths in the tripyrrolic unit define two pyrrolenine units with alternate single and double bonds and a central pyrrole with highly delocalized π system (see figure below).



6

Figure. Two orthogonal views of **6** and selected dihydroporphyrin derived compounds.
Meso-phenyl and β-ethyl groups have been ommitted for clarity. The figures in column 2 were generated using information downloaded from the Cambridge Crystallographic Data Centre and correspond to a structure originally reported in reference 11.

Only a few non-aromatic dihydroporphyrin bases have been structurally characterized, and compound **6** is the first fully characterized 5,10-dihydroporphyrin. In conclusion, it is interesting to underline the variety of shape adopted by these molecules. The tetrapyrrolic nucleus of 5,15-dihydroporphyrins is either almost flat, like in 5,15-di-*iso*-propyl-5,15-dihydro-octaethylporphyrin[11] (figure), or roof-shaped like a dication derived from *meso*-tetra-*t*-butylporphyrin[6], this geometry being often realized in metal complexes of the 5,15-dihydro series[12]. More unusual dihydroporphyrin bases show additional frameworks, with one pyrrolic rotated as in N-phenylphlorin[2] (figure), or resembling two dipyrromethenes in independent planes in a 1,2-dihydro structure[13].

The authors thank the "Service Commun de RX", Fédération de Recherche Chimie, Strasbourg, for the X-ray structural data.

References and notes

1. Sugimoto, H. *J. Chem. Soc. Dalton Trans.* **1982**, 1169-1171; Setsune, J.; Ikeda, T.; Iida, T.; Kitao, T. *J. Am. Chem. Soc.* **1988**, *110*, 6572-6574; Setsune, J.; Ishimaru, Y.; Kitao, T. *Chem. Lett.* **1990**, 1351-1354; Setsune, J.; Yamaji, H.; Kitao, T. *Tetrahedron Lett.* **1990**, *31*, 5057-5060; Setsune, J.; Wada, K.; Higashino, H. *Chem. Lett.* **1994**, 213-216; Segawa, H.; Azumi, R.; Shimidzu, T. *J. Am. Chem. Soc.* **1992**, *114*, 7564-7565; Jiang, X.; Nurco, D.J.; Smith, K.M. *Chem. Commun.* **1996**, 1759-1760.

2. Krattinger, B.; Callot, H.J. *Chem. Commun.* **1996**, 1341-1342.

3. Krattinger, B.; Callot, H.J. *Tetrahedron Lett.* **1996**, *37*, 7699-7702.

4. Arnold, J.; Dawson, D.Y.; Hoffman, C.G. *J. Am. Chem. Soc.* **1993**, *115*, 2707-2713; Brand, H.; Capriotti, J.A.; Arnold, J. *Inorg. Chem.* **1994**, *33*, 4334-4337; Tsuchiya, S. *J. Chem. Soc. Chem. Comm.* **1992**, 1475-1477.

5. Typical recent articles: Crossley, M.J.; King, L.G. *J. Org. Chem.* **1993**, *58*, 4370-4375; Crossley, M.J.; Harding, M.M.; Tansey, C.W. *J. Org. Chem.* **1994**, *59*, 4433-4437; Jaquinod, L.; Gros, C.; Olmstead, M.M.; Antolovich, M.; Smith, K.M. *Chem. Commun.* **1996**, 1475-1476; Jaquinod, L.; Gros, C.; Khoury, R.; Smith, K.M. *Chem. Commun.* **1996**, 2581-2582; Jiang, X.; Nurco, D.J.; Smith, K.M. *Chem. Commun.* **1996**, 1759-1760; DiMagno, S.G.; Lin, V.S.Y.; Therien, M.J. *J. Org. Chem.* **1993**, *58*, 5983-5993; LeCours, S.M.; Guan, H.W.; DiMagno, S.G.; Wang, C.H.; Therien, M.J. *J. Am. Chem. Soc.* **1996**, *118*, 1497-1503.

6. Ema, T.; Senge, M.O.; Nelson, N.Y.; Ogoshi, H.; Smith, K.M. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1879-1881.

7. **4**: UV-vis. (CH_2Cl_2): 418 nm (ε = 102000), 518 (16200), 548 (9900), 598 (6400), 652 (18400). ^1H NMR ($CDCl_3$; major or minor diastereomer): 8.56, 8.41, 8.17 (d+s+d, 2+2+2, pyrrole, maj + min), 8.3-7.5 (m, 22H, phenyl + 2 pyrrole maj+min), 4.91 and 4.78 (2d, H-3 syn/butyl, resp. maj and min), 4.1 (m, H-2, maj+min), 3.95 and 3.88 (2dd, H-3 anti/butyl, resp. maj+min, J = 17.6 and 1.8 Hz), 1.75 (m, H-2', maj+min), 1.13 and 0.85 (2m, CH_2, resp. maj and min), 0.78 and -0.09 (2d, CH_3, resp. min and maj), 0.57 and 0.16 (2t, terminal CH_3, resp. maj and min).

8. **5**: UV-vis. (CH_2Cl_2): 426 nm (ε = 96100), 530 (8600), 558 (7600), 612 (3800), 666 (14700). ^1H NMR ($CDCl_3$): 8.47 (2, 2H, pyrrole), 8.35 (s, 2H, pyrrole), 8.02 (d, 2H, pyrrole), 7.3-7.9 (m, 20H, *meso*-phenyl), 5.02 (s, 2H, 2-H + 3-H), 0.55 (slightly broadened s, 18, *t*-Bu), -0.6 (broad signal, 2H, N-H).

9. **6**: UV-vis. (CH_2Cl_2): 338 nm (ε = 65200), 356 (65000), 520 (42500), 556 (43800). ^1H NMR ($CDCl_3$): 13.1 and 11.8 (2 broad s, N-H), 7.70 and 7.32 (2d, 2+2 H, *o*-phenyl), 7.9-7.5 (m, 16H, remaining phenyl H), 6.42 (d, 2H, J = 4.7 Hz), 6.11 (d, 2H, J = 2.3 Hz), 5.60 (d, 2H, J = 4.7 Hz), 5.21 (d, 2H, J = 2.3 Hz), 1.24 (s, 18H, *t*-butyl). Data from single crystals indicate $\alpha_D > 3000$.

10. Crystal data for **6**: $C_{52}H_{48}N_4{\bullet}CH_2Cl_2$; M = 813.9, monoclinic, space group $P2_1$, a = 12.550(3), b = 13.381(4), c = 13.429(4) Å, β(deg) = 95.85(2), V = 2243.4 $Å^3$, Z = 2, Dc = 1.205 g cm^{-3}. A total of 4963 ± h ± k + l reflections was collected on a dark-purple crystal of dimensions 0.40 x 0.40 x 0.40 mm^3 using a Nonius CAD4-F diffractometer, graphite monochromated MoKα. 2588 unique reflexions having I > 3s(I) were used to determine (direct methods) and refine the structure. The absolute structure was determined by refining Flack's x parameter. Final results: $R(F) = 0.049$, $R_w(F) = 0.067$. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

11. Botulinski, A.; Buchler, J.W.; Abbes, N.E.; Scheidt, W.R. *Liebigs Ann.*, **1987**, 305-309.

12. Botulinski, A.; Buchler, J.W.; Lay, K.L.; Stoppa, H. *Liebigs Ann.*, **1984**, 1259-1269. Buchler, J.W.; Lay, K.L.; Lee, Y.J.; Scheidt, W.R. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 432-433 and references cited.

13. Crossley, M.J.; Hambley, T.W.; King, L.G. *Bull. Soc. Chim. Fr.*, **1996**, *133*, 735-742.