Acid−Base Chemistry of the Metal-Bonded Porphyrinogen Tetraanion: A Novel Methodology for the Metal-Assisted Deuteration, Alkylation, and Functionalization of the Porphyrinogen Skeleton

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Within the context of the porphyrin chemistry, two major properties of the porphyrinogen precursor[1] are quite hard to define; namely, the redox and acid−base chemistry. This difficulty is due to the high tendency of porphyrinogen to oxidize to the corresponding porphyrin.[2] Quite recently we used a stable form of porphyrinogen, the *meso*-octaalkylporphyrinogen in its fully deprotonated form complexed to a transition metal[3] for inspecting both kinds of chemistry. This approach enabled us to study the stepwise oxidation to artificial porphyrins[4] and porphodimethenes.[3c,5] We report here a modeling study, using Ni(II)−*meso*-octaethylporphyrinogen (complex **1**[3b,4a] in Scheme 1), for exploring the acid−base chemistry of the porphyrinogen tetraanion, which proved to be a remarkably useful methodology, leading to the metal-assisted functionalization of the porphyrinogen skeleton.[6]

The reaction of **1**[3b] (see Scheme 1) with PyHCl (1:2 molar ratio) under rigorously anhydrous conditions led to the formation of dihydro species. The two dihydro (2,12 and 2,13) [**2a** + **2b**] isomers[7,8] derived from the protonation of two pyrroles trans to each other are detected in a 1:1 ratio in solution. The isolation from the solution mixture of a solid gave the **2a** isomer only,[8] as confirmed by the X-ray analysis. The NMR spectrum of the **2a** dissolved in benzene showed the 1:1 mixture of **2a** + **2b**. The two isomers in solution are deprotonated using either LiBu (see **1**) or 1,4-diazabicyclo[2.2.2]octane (see **3**). The reversible protonation−deprotonation accounts for the formation of the deuterated form **4**,[8] when **2** was dissolved in CD_3OD or in C_5D_5N. The deprotonation of **4** led to the 2,3,7,8,12,13,17,18-octadeutero derivative, **5**.[8] The protonation−deprotonation of the porphyrinogen is a key step for determining its metal-assisted functionalization. The reaction of **1** at room temperature with $Me_3O^+BF_4^-$ led to 1,11-dihydro-2,12-dimethyl derivative **6** which, upon heating, gave 2,12,-dimethyl-3,13-dihydro derivative **7**.[8] Complex **7** was then deprotonated to **8**,[8] which was protonated to a mixture of **6** and **7** using 2 equiv of PyHCl at room temperature. Complex **8** underwent a further methylation to the 2,3,12,13-tetramethyl-4,14-dihydro derivative **9**[8] and subsequently was deprotonated to **10** (Scheme 1).[8]

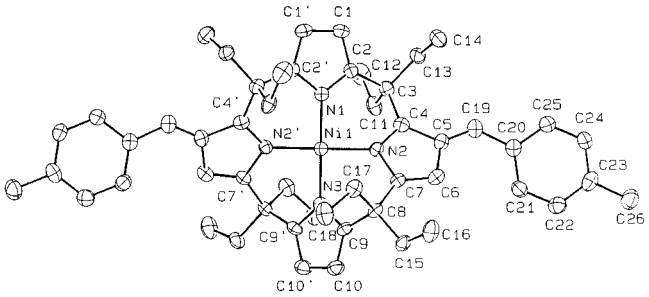

Figure 1. ORTEP view (50% probability ellipsoids) of complex **14**. Selected bond distances (Å): Ni−N_{av}, 1.862; N(2)−C(4), 1.307(4); N(2)−C(7), 1.430(5); C(4)−C(5), 1.480(5); C(5)−C(6), 1.449(4); C(6)−C(7), 1.341(5); C(5)−C(19), 1.343(5). A prime denotes a transformation of $-x, y, 0.5 - z$.

The results mentioned above showed a stepwise direct and selective methylation of the porphyrinogen. The same methodology allowed the functionalization of the porphyrinogen skeleton. This is exemplified in Scheme 2 by the reaction of **1** with benzoyl chloride and *p*-tolyl aldehyde. In the former case, the reaction led to the 8,18-dihydro-3,12-dibenzoyl derivative **11**,[8] which was deprotonated to **12**.[8] In the reaction with an excess of *p*-tolyl aldehyde, complex **1** led to the formation of the 2,13-divinylidene derivative **14**,[8] via the plausible intermediate **12**, which was not identified. *All of the compounds in Schemes 1 and 2 were obtained at the preparative level (>60% yield) and in gram amount with high selectivity.* In particular, the reactions leading to **6**, **11**, and **14** are totally selective with respect to the β-carbon substitution. A full account of the synthetic sequence is given in the Supporting Information.[8] All of the compounds displayed in Schemes 1 and 2, except for **13**, were fully characterized, including the X-ray analysis on **2**, **6**, **9**, **11**, and **14**, although only the structure of **14** is reported here and displayed in Figure 1.[9] A detailed description of the structures of **9**, **11**, and **14** is reported in the Supporting Information. The structural parameters confirm both the atom connectivity, the bonding sequence, and the isomeric forms reported in Schemes 1 and 2. In all of the complexes the ligand has a so-called saddle-shape conformation, and the hydrogens from four methylenes of the *meso*-ethyl groups provide a flattened tetrahedral cage for the metal. The N_4 core which is planar in **11** and **14** has a relevant tetrahedral distortion in complex **9**. The results reported here show an unprecedented

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(1) (a) *The Porphyrins*; Dolphin, D., Ed., Academic: New York, 1978; Vols. I and II. (b) Smith, K. M. *Porphyrins and Metalloporphyrins*; Elsevier: Amsterdam, 1975.

(2) Mauzerall, D. The Porphyrinogens. Chapter 3, Vol. II of ref 1a.

(3) (a) Floriani, C. *Chem. Commun.* **1996**, 1257 and references therein. (b) Jubb, J.; Jacoby, D.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *Inorg. Chem.* **1992**, *31*, 1306. (c) Solari, E.; Musso, F.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *J. Chem. Soc., Dalton Trans.* **1994**, 2015. (d) Jacoby, D.; Isoz, S.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *J. Am. Chem. Soc.* **1995**, *117*, 2793 and 2805. (e) De Angelis, S.; Solari, E.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *Organometallics* **1995**, *14*, 4505. (f) Isoz, S.; Floriani, C.; Schenk, K.; Chiesi-Villa, A.; Rizzoli, C. *Organometallics* **1996**, *15*, 337. (g) Floriani, C. *Pure Appl. Chem.* **1996**, *68*, 1.

(4) (a) De Angelis, S.; Solari, E.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *J. Am. Chem. Soc.* **1994**, *116*, 5691. (b) De Angelis, S.; Solari, E.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *J. Am. Chem. Soc.* **1994**, *116*, 5701. (c) Piarulli, U.; Solari, E.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *J. Am. Chem. Soc.* **1996**, *118*, 3634. (d) Floriani, C. In *Transition Metals in Supramolecular Chemistry*; Fabbrizzi, L., Poggi, A., Eds.; Kluwer: Dordrecht, The Netherlands, 1994; Vol. 448, p 191.

(5) Piarulli, U.; Floriani, C.; Chiesi-Villa, A.; Rizzoli, C. *J. Chem. Soc., Chem. Commun.* **1994**, 895.

(6) For related earlier work on peripheral functionalization of porphyrinogen and hexahydroporphyrins close to naturally occurring systems, see the contributions from Eschenmoser's group: Johansen, J. E.; Piermattie, V.; Angst, C.; Diener, E.; Kratky, C.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 261. Waditschatka, R.; Diener, E.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 631. Waditschatka, R.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 630. Waditschatka, R.; Angst, C.; Johansen, J. E.; Plaquevent, J. C.; Schreiber, J.; Eschenmoser, A. *Helv. Chim. Acta* **1985**, *68*, 1312. Angst, C.; Kajiwara, M.; Zass, E.; Eschenmoser, A. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 140.

(7) For the numbering scheme of the porphyrinogen skeleton, see: Bonnett, R. Vol. I, Chapter 1, p 9 of ref 1a.

(8) For synthesis and analytical data, see Supporting Information.

(9) Crystal data for **14**: $C_{52}H_{62}N_4Ni$, $M = 801.8$, monoclinic, space group $C2/c$, $a = 15.100(2)$ Å, $b = 17.249(2)$ Å, $c = 17.720(2)$ Å, $\beta = 113.35(2)°$, $V = 4237.4(11)$ Å^3, $Z = 4$, $D_{calcd} = 1.257$ g/cm^3, $F(000) = 1720$, λ(Cu Kα) = 1.54178 Å, μ(Cu Kα) = 9.29 cm^{-1}, crystal dimensions 0.10 × 0.22 × 0.40 mm. For 2272 unique observed reflections [$I > 2\sigma(I)$] collected at $T =$ 143 K on a Rigaku AFC6S diffractometer ($5 < 2\theta < 140°$) and corrected for absorption the conventional R is 0.052 (wR2 = 0.127 calculated over 3455 unique total data having $I > 0$).

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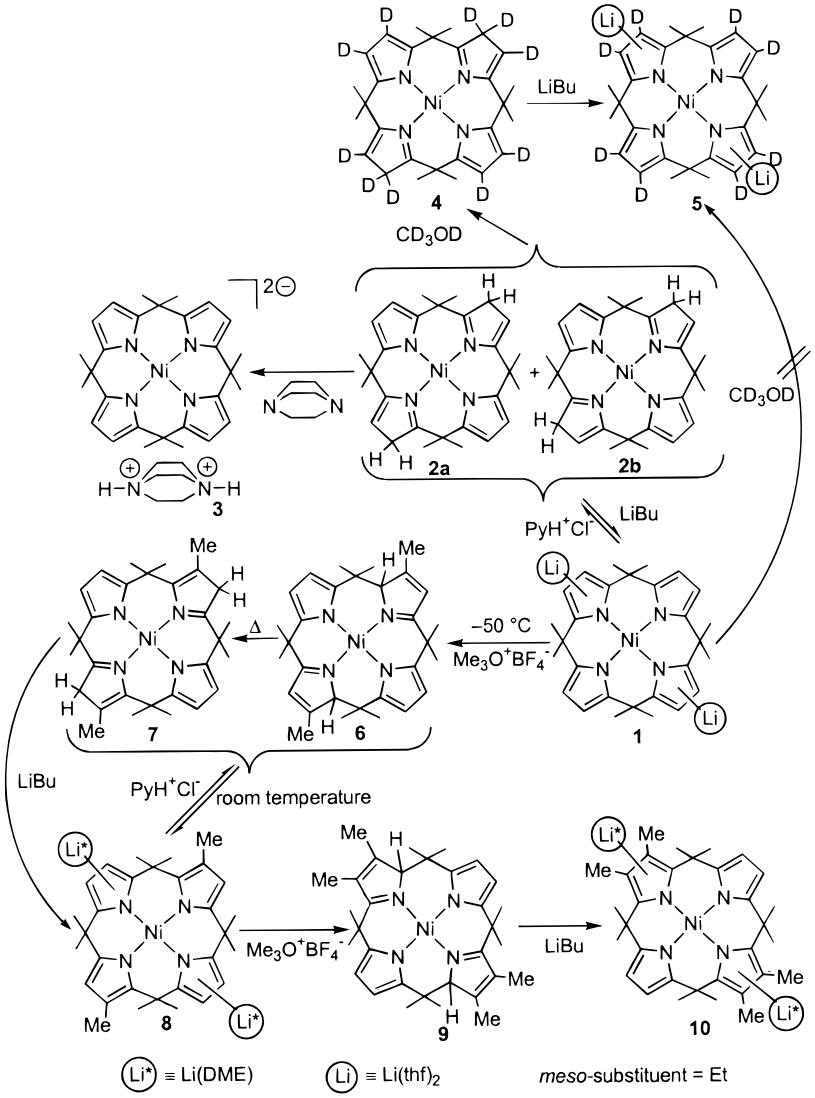
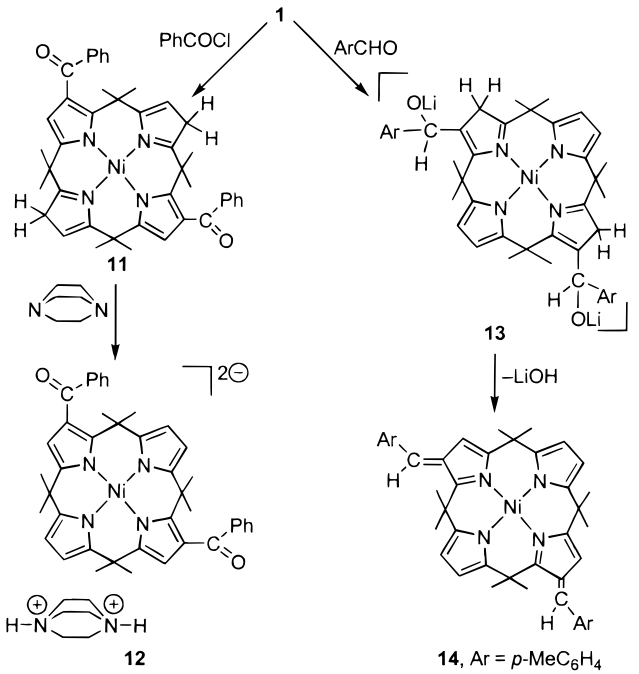
Scheme 1



Scheme 2



acid−base protic chemistry of porphyrinogen skeleton which is the basis for determining its functionalization. In addition, they show (i) how significant is the difference between metal-assisted and metal-nonassisted electrophilic reaction at the porphyrinogen anion.[10] Several of the functionalization reactions reported here and performed on the lithium derivative $[Et_8N_4Li_4thf_4]$[3] gave untractable mixtures of uncharacterizable compounds; (ii) how the functionalization can be carried out on the porphyrinogen rather than on the initial pyrroles; (iii) the possibility of getting regiochemically controlled partially substituted porphyrinogen, including the introduction of reactive functionalities; and (iv) the functionalization reaction is at the preparative level.

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Supporting Information Available: SCHAKAL and ORTEP drawings, description of the structures, tables giving crystal data and details of the structure determination, atomic coordinates, anisotropic thermal parameters, and bond distances and angles for **9**, **11**, and **14**; synthesis and analytical data of **2**−**14** (27 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

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(10) A single example of metal nonassisted functionalization of *meso*-octamethylporphyrinogen leading to a mixture of mono- (20%) and disubstituted (3%) derivatives, R being CH_2COOEt, has been reported: Gale, P. A.; Sessler, J. L.; Allen, W. E.; Tvermoes, N. A.; Lynch, V. *Chem. Commun.* **1997**, 665.