

A Novel Stepwise Degradation of Porphyrins. Synthesis and Structural Characterization of *meso*-Tetraphenylchlorophinato Nickel(II) and *meso*-Tetraphenylsecochlorinato Nickel(II)

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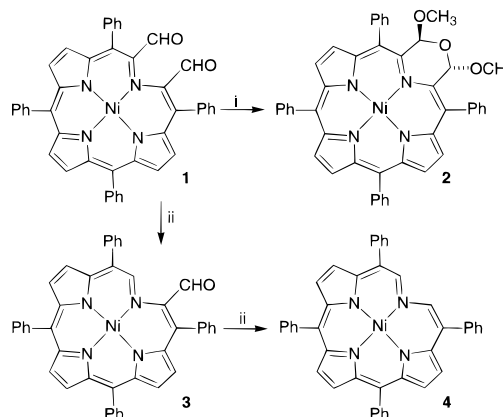
The search for novel photosensitizers for photodynamic therapy (PDT)¹ as well as basic research interests has led to the synthesis of expanded porphyrins,² porphyrin isomers,^{2a,3} and porphyrins containing moieties other than pyrroles as building blocks.^{4,5} A current topic of interest in porphyrin chemistry is the study of nonplanar porphyrins⁶ for its relevance to the understanding of porphyrin-containing enzymes and light harvesting pigments.

We reported on the synthesis of secochlorinato Ni **1**, a metallochlorin-like pigment which was derived from *meso*-tetraphenylporphyrinato Ni by cleavage of one peripheral β,β' -double bond. We also described^{4a} its conversion into the nonplanar homoporphyrin **2**, in which one pyrrolic unit of a porphyrin is formally replaced by an oxazoline moiety (Scheme 1). Its X-ray crystal structure^{4a} revealed that it was severely twisted (ruffled).^{6c}

We now report the X-ray crystal structure of the Ni secochlorin **1** and its stepwise decarbonylation. The structure of the resulting novel *meso*-tetraphenylchlorophinato⁷ Ni **4** was confirmed by single-crystal X-ray crystallography. The crystal structures of **1** and **4** revealed that, surprisingly, both compounds also exist in severely ruffled^{6c} conformations comparable to that of **2**.

In the course of our continuing work with the secochlorin dialdehyde **1**, we were able to grow crystals suitable for an X-ray crystal structure determination.⁸ This provided the ultimate proof of the proposed structure (Figure 1).^{4a} It also showed that the

Scheme 1^a



^a Reaction conditions: (i) CHCl₃, MeOH, H⁺, 25 °C, chromatography;^{4a} (ii) (Ph₃P)₃RhCl, PhCN, reflux, chromatography (silica gel–CH₂Cl₂/hexane 1:1).

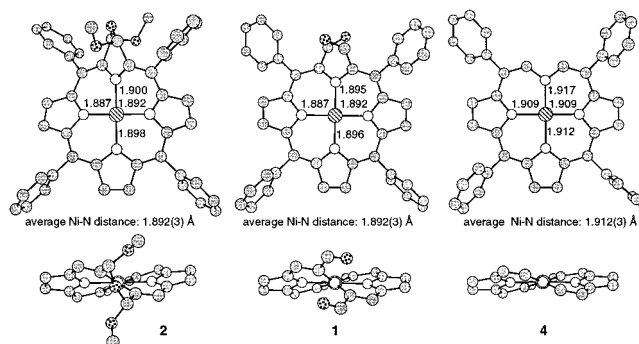


Figure 1. Top view (hydrogen atoms omitted for clarity) and edge-on view (along a Ni–N axis, the hydrogen atoms and the *meso*-phenyl substituents have been omitted for clarity) of the X-ray crystal structures of **1**,^{4a} **2**, **4** with Ni–N bond lengths. The Ni–N bond lengths for **4** have been determined by averaging the equivalent bond lengths of the two molecules present in the asymmetric unit.

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(1) (a) *Photodynamic Theory: Basic Principles and Clinical Applications*; Henderson, B. W.; Dougherty, T. J., Eds.; Marcel Dekker: New York, 1992. For overview articles of PDT, see: (b) Bonnett, R. *Chem. Soc. Rev.* **1995**, 19. (c) Sternberg, E. D.; Dolphin, D.; Brückner, C. *Tetrahedron Reports Number 447* **1998**, 54, 4151.

(2) (a) *Expanded, Contracted and Isomeric Porphyrins*, Sessler, J. L.; Weghorn, S. J. Pergamon: New York, 1997 and references therein. (b) Jasat, A.; Dolphin, D. *Chem. Rev.* **1997**, 97, 2267.

(3) For brief overviews, see: (a) Vogel, E. *Pure Appl. Chem.* **1996**, 68, 1355.

(4) (a) Brückner, C.; Rettig, S. J.; Dolphin, D. *J. Org. Chem.* **1998**, 63, 2095. (b) Lash, T. D.; Hayes, M. J. *Angew. Chem., Int. Ed. Engl.* **1997**, 36, 840. (c) Lash, T. D.; Chaney, S. T. *Angew. Chem., Int. Ed. Engl.* **1997**, 36, 839. (d) Lash, T. D.; Chaney, S. T. *Chem. Eur. J.* **1996**, 2, 944. (e) Berlin, K. *Angew. Chem., Int. Ed. Engl.* **1996**, 35, 1820 and references therein.

(5) The crystal structure of the octaethylporphyrin-derived analogue to **1** has been determined, although details have not yet been published: (a) Adams, K. R.; Bonnett, R.; Burke, P. J.; Salgado, A.; Asunción Vallés, M. *J. Chem. Soc., Perkin 1* **1997**, 1769. (b) Adams, K. R.; Bonnett, R.; Burke, P. J.; Salgado, A.; Vallés, M. A. *J. Chem. Soc., Chem. Commun.* **1993**, 1860.

(6) (a) Shelnutz, J. A.; Song, X.-Z.; Ma, J.-G.; Jia, S.-L.; Jantzen, W.; Medforth, C. J. *Chem. Soc. Rev.* **1998**, 27, 31. (b) Ravikanth, M.; Chandrashekar, T. K. *Struct. Bonding (Berlin)* **1995**, 82, 107. Classification of porphyrin distortion modes: (c) Scheidt, W. R.; Lee, Y. *J. Struct. Bonding (Berlin)* **1987**, 64, 1. For recent developments see: (d) Nurco, D. J.; Medforth, C. J.; Forsyth, T. P.; Olmstead, M. M.; Smith, K. M. *J. Am. Chem. Soc.* **1996**, 118, 10918. (e) Cheng, B.; Munro, O. Q.; Marques, H. M.; Scheidt, W. R. *J. Am. Chem. Soc.* **1997**, 119, 10732. (f) Senge, M. O.; Kalisch, W. W.; Runge, S. *Liebigs Ann./Recueil* **1997**, 1345.

(7) We follow the trivial nomenclature suggested by Flitsch (ref 22) and propagated by Chang et al. (ref 21a). Systematic nomenclature: **4**, [1,4-didecarbo-1*H*,4*H*-1,5,10,15-tetraphenylporphyrinato]Ni(II); **3**, [1-decarbo-1*H*-3-oxo-3*H*-1,5,10,15-tetraphenylporphyrinato]Ni(II).

plane of the metallosecochlorin, while retaining a square planar coordination sphere around the central metal, was severely twisted along an N–Ni–N axis resulting in a ruffled conformation of the porphyrin core (rms of the C₁₈N₄Ni mean plane, 0.465 Å). The conformation is very similar to that observed in **2** (rms of the C₁₈N₄Ni mean plane, 0.468 Å). This was unexpected since the intramolecular steric constraints imparted by the nonplanar six-membered ring in **2** are absent in **1**. The conformation of **1** allows the carboxaldehyde moieties to be arranged paralleled to each other, allowing for π - π -stacking interactions (average distance of the C=O bonds, 2.85 Å). However, this interaction should not be strong enough to distort the pigment into the observed extremes.

(8) C₄₄H₂₈N₄NiO₂ (**1**) crystallized by diffusion of MeOH into a CH₂Cl₂ solution. Burgundy prisms. Monoclinic C-centered lattice, space group C2/c (No. 15) with $a = 31.928(3)$ Å, $b = 20.807(1)$ Å, $c = 13.302(2)$ Å, $\beta = 101.86(1)$, $V = 8648(1)$ Å³, $Z = 8$. Data were collected at 21.0 °C on a Rigaku AFC6S diffractometer with graphite monochromated Cu K α radiation up to $2\theta_{max}$ of 155.7°. A total of 9227 reflections were measured, 9065 of which were unique ($R_{int} = 0.032$) and 5267 with $I > 3\sigma(I)$. Reflection-to-parameter ratio, 10.62. The structure was solved by direct methods (SIR92) and expanded using Fourier techniques. The C(33–38) phenyl ring was modeled as 2-fold disordered with respect to rotation about the C(15)–C(33) bond. The C(27–32) phenyl ring shows a relatively high degree of thermal motion and may also be disordered, but no satisfactory disordered model could be refined. The full-matrix least-squares refinement (anisotropic for all non-hydrogen atoms) yielded $R = 0.047$, $R_w = 0.051$. Additional details are available in the Supporting Information.

Aromatic aldehydes decarbonylate in the presence of $(\text{Ph}_3\text{P})_3\text{-RhCl}$.⁹ A solution of the dialdehyde **1** in benzonitrile when reacted with a stoichiometric excess of $(\text{Ph}_3\text{P})_3\text{RhCl}$, under reflux for 45 min, produced, along with small amounts of starting material and side products, the monodecarbonylated pigment **3** in 10% and the bisdecarbonylated pigment **4** in 40% yield (Scheme 1). The structures of the blue-green pigments are supported by their spectroscopic and analytical data.¹⁰ Their UV-vis spectra indicate the presence of metalated chlorin-like systems (λ_{max} [log ϵ] for **3**: 448 [4.06], 630 [3.15], 678 [3.34]; λ_{max} [log ϵ] for **4**: 422 [4.33], 576 [3.28], 612 [3.58]). The stepwise loss of the carbonyl groups which served to extend the chromophore is also reflected in the hypsochromic shift of the Soret band of **1** (λ_{max} [log ϵ] 466 [4.78]).^{4a} This shift can also be taken as an indication for some reduction of the ruffling of the macrocycle.^{6b} The HR mass spectra (EI) of the pigments (**3**: *m/e* calcd for $\text{C}_{43}\text{H}_{28}\text{N}_4\text{NiO}$ 674.16168, found 674.16024; **4**: *m/e* calcd for $\text{C}_{42}\text{H}_{28}\text{N}_4\text{Ni}$ 646.16675, found 646.16652) as well as elemental analysis corroborate the proposed composition. The ¹H NMR spectra show the stepwise loss of the signals attributed to the carbonyl group (**1**: 9.50 ppm;^{5a} **3**: δ 9.85 ppm) and its concomitant replacement by a singlet at δ 9.80 ppm with an integration corresponding to 1H and 2H for **3** and **4**, respectively.¹⁰ This diatropic shift for the α -protons is comparable to those measured for β - and *meso*-protons of other 18π -electron porphyrinic systems, for instance, 5,15-diphenyl-porphyrin.¹¹

A single-crystal X-ray diffraction study was performed on **4**.¹² This unequivocally proved its assigned chlorophinato structure. One pyrrolic unit of the parent porphyrin has been degraded to an aldimine linkage, without any other change in the connectivity of the macrocycle. Aldimine linkages in polypyrrolic macrocycles are known, albeit their establishment and position within the macrocycle are fundamentally different.¹³ The bond lengths and notably the bond angle found here (C–N 1.366(4) Å, $\angle\text{C–N–C}$ 110.9(3)°) vary significantly from those found in the larger macrocycles, texaphyrins and porphocyanines.^{2a,13} The C–C and C–N bond lengths found in **2** and **4** (with the exception of the Ni–bond lengths, vide infra) are within expectation for a fully conjugated chromophore, and are close to those found in **1**.

Examination of the conformation of **4** reveals that it also deviates to an astonishing degree from planarity. In a manner similar to that of **1** and **2**, it takes up a ruffled conformation (rms of the $\text{C}_{18}\text{N}_4\text{Ni}$ mean plane, 0.368 Å) (Figure 1), albeit somewhat

less pronounced than **1**. Due to the absence of any sterically incumbering moieties we surmise that this conformation is caused by the presence of Ni as the central metal. The Ni–N distances found in diamagnetic planar Ni porphyrins average about 1.95 Å.^{14,15} Bond distances of severely distorted porphyrins are reduced to 1.90 Å^{14,16} whereas the average Ni–N distance of imine type ligands are approximately 1.85 Å.¹⁷ The Ni–N bond distances found in **1** and **4** average 1.892(3) and 1.912(3). The longest bond length in each set is found between the metal and the nitrogen of the imine unit (Figure 1) analogous to precedents found in the solid-state structures of chlorinato Ni complexes.¹⁸

The flexibility of the hydroporphyrins allows them to adopt a ruffled conformation upon binding to a low spin nickel(II) center which has been noted before.¹⁹ The conformations of compounds **1–4** exhibit particularly strong ruffling which we attribute to the increased flexibility of the degraded porphyrin framework. Unfortunately, the attempted acid-induced demetalation of pigments **3** and **4** led only to their decomposition; hence, no direct comparisons can be made with their free base analogues. Molecular modeling studies suggest that the free base of **4** is planar.²⁰

Synthesis of the parent chlorophin²¹ as well as that of tetraphenylchlorophin²² (**4**) has been unsuccessfully attempted before. Two other closely related chromophores have been reported by Fritsch and co-workers.^{21,23} These compounds are the bacteriochlorin and isobacteriochlorin (*meso*-unsubstituted) analogues of chlorophin **4**. In contrast to our facile preparation of **4**, however, their total syntheses were very low yielding ($\ll 0.1\%$ over several steps).

To conclude, we have shown that the stepwise decarbonylation of secochlorin **1** produces the new homoporphyrins **3** and **4**. Thus, we have shown how to degrade one pyrrolic unit of the ultimate starting material *meso*-tetraphenylporphyrin in three steps (dihydroxylation, diol cleavage, decarbonylation) to an aldimine linkage. Although other porphyrin degradation pathways have been reported before, mainly involving cleavages at the *meso*-position,^{5,24} this degradation of the β -positions is novel to the field of porphyrin chemistry. Furthermore, the X-ray crystal structure determination of **1** and **4** revealed their severely central-metal induced ruffled conformations.

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Supporting Information Available: Procedures for the preparation of **3** and **4**, experimental crystallographic details, positional and anisotropic thermal parameters for **1** and **4** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA981417W

- (9) James, B. R.; Young, C. G. *J. Organomet. Chem.* **1985**, 285, 321.
 (10) Selected analytical and spectroscopic data for **3**: ¹H NMR (400 MHz, CDCl_3) δ 7.42 (tt, 7.5, 1.0 Hz, 2H), 7.55–7.65 (m, 16H), 7.78 (d, 4.8 Hz, 1H), 7.95 (d, 7.1 Hz, 2H), 8.05, (d, 4.8 Hz, 1H), 8.07 (d, 4.8 Hz, 1H), 8.15 (d, 4.7 Hz, 1H), 8.22 (d, 4.9 Hz, 1H), 8.28 (d, 5.0 Hz, 1H), 9.80 (s, 1H), 9.85 (s, 1H); IR (film) 1657 (s, C=O), 1548 (m, C=C), 1439 (m); LR MS (EI) *m/e* (%) 674 (M^+ , 100), 646 ($\text{M}^+ - \text{CO}$, 85), 597 ($\text{M}^+ - \text{C}_6\text{H}_5$, 55), 568 ($\text{M}^+ - \text{C}_6\text{H}_5 - \text{CO}$, 72), 492 ($\text{M}^+ - 2 \text{C}_6\text{H}_5 - \text{CO}$, 35). **4**: mp > 310 °C sublimation; ¹H NMR (400 MHz, CDCl_3) δ 7.49 (tt, $J = 7.2, 1.1$ Hz, 1H), 7.55–7.65 (m, 5H), 7.78 (d, $J = 7.7$ Hz, 2H), 7.86 (dd, 7.6, 1.8 Hz, 2H), 8.15 (s, 1H), 8.20 (d, 4.8 Hz, 1H), 8.38 (d, 5.0 Hz, 1H), 9.8 (s, 1H). ¹³C NMR (75 MHz, CDCl_3) δ 112.36, 123.75, 126.04, 126.96, 127.35, 128.88, 129.24, 128.20, 130.51, 131.84, 132.34, 133.24, 134.03, 134.66, 138.17, 138.93, 139.84, 140.30, 141.16, 141.56, 145.57. IR (film) 3400 (s, CH_2 stretch), 1570 (w, C=C), 1050 (m) cm^{-1} ; LR MS (EI) *m/e* (%) 646 (M^+ , 100), 568 ($\text{M}^+ - \text{C}_6\text{H}_5$, 18). Anal. Calcd (found) for $\text{C}_{42}\text{H}_{28}\text{N}_4\text{Ni}\cdot\text{H}_2\text{O}$ (from $\text{CH}_2\text{Cl}_2/\text{wet MeOH}$) C 75.81 (75.89), H 4.54 (4.55), N 8.42 (8.30).
 (11) Manka, J. S.; Lawrence, D. S. *Tetrahedron Lett.* **1989**, 30, 7341.
 (12) $\text{C}_{42}\text{H}_{28}\text{N}_4\text{Ni}$ (**4**) crystallized by diffusion of hexane into a THF solution of **4**. Purple prisms. Space group tridinic *P* 1 (No. 2) with $a = 13.676(3)$ Å, $b = 18.858(2)$ Å, $c = 12.764(4)$ Å, $\alpha = 102.58(1)^\circ$, $\beta = 91.49(1)^\circ$, $\gamma = 102.56^\circ$, $V = 3126.5(9)$ Å³, $Z = 4$. Data were collected at 21.0 °C on a Rigaku AFC6S diffractometer with graphite monochromated Cu K α radiation up to $2\theta_{\text{max}}$ of 155°. A total of 13337 reflections were measured, 12754 of which were unique ($R_{\text{int}} = 0.028$) and 6094 with $I > 3\sigma(I)$. Reflection-to-parameter ratio: 6.97. The structure was solved by Patterson methods. The full-matrix least-squares refinement (anisotropic for all non-hydrogen atoms) yielded $R = 0.042$, $R_w = 0.038$. Additional details are available in the Supporting Information.
 (13) Dolphin, D.; Rettig, S. J.; Tang, H.; Wijesekera, T.; Xie, L. Y. *J. Am. Chem. Soc.* **1993**, 115, 9301.

- (14) Hoard, J. L. *Ann. N.Y. Acad. Sci.* **1973**, 206, 18.
 (15) Jentzen, W.; Turowska-Tyrk, I.; Scheidt, W. R.; Shelnutt, J. A. *Inorg. Chem.* **1996**, 35, 3559.
 (16) Barkigia, K. M.; Renner, M. W.; Furenliid, L. R.; Medforth, C. J.; Smith, K. M.; Fajer, J. *J. Am. Chem. Soc.* **1993**, 115, 3627.
 (17) (a) Henrick, K.; Tasker, P. A.; Lindoy, L. F. *Prog. Inorg. Chem.* **1985**, 33, 1. (b) Ni–N bond distance in bis(*meso*-phenyl)dipyrrinato Ni(II) 1.879(2) Å: Brückner, C.; Karunaratne, V.; Rettig, S. J.; Dolphin, D. *Can. J. Chem.* **1996**, 27, 2182.
 (18) Gallucci, J. C.; Swepston, P. N.; Ibers, J. A. *Acta Crystallogr., Sect. B* **1982**, 38, 2134.
 (19) Stolzenberg, A. M.; Stershic, M. T. *J. Am. Chem. Soc.* **1988**, 110, 6391.
 (20) MM2 force field, CAChe System, Oxford Molecular Systems, V.3.9, 1996.
 (21) Bohusch, M.; Flitsch, W.; Kneip, H.-G. *Liebigs Ann. Chem.* **1991**, 67.
 (22) (a) Crossley, M. J.; King, L. G. *J. Chem. Soc., Chem. Commun.* **1984**, 920. (b) Crossley, M. J.; Hambley, T. W.; King, L. G. *Bull. Soc. Chim. Fr.* **1996**, 133, 735.
 (23) (a) Flitsch, W. *Pure Appl. Chem.* **1986**, 58, 153. (b) Flitsch, W. *Adv. Heterocycl. Chem.* **1988**, 43, 73.
 (24) Isaak, M.; Senge, M. O.; Smith, K. M. *J. Chem. Soc., Perkin Trans I* **1995**, 705, and references therein.