

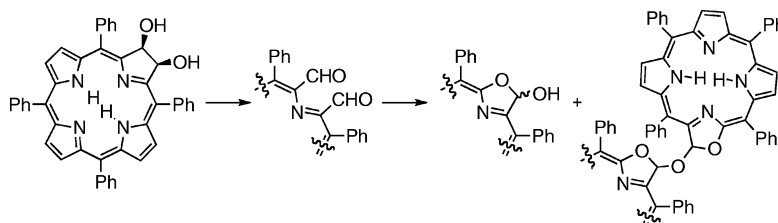
Oxazolochlorins. 2. Intramolecular Cannizzaro Reaction of *meso*-Tetraphenylsecochlorin Bisaldehyde[†]

Joshua Akhigbe,[‡] Claudia Ryppa,[‡] Matthias Zeller,[§] and Christian Brückner^{*,‡}

Department of Chemistry, University of Connecticut, Storrs, Connecticut 06269-3060, and Department of Chemistry, Youngstown State University, One University Plaza, Youngstown, Ohio 44555-3663

c.bruckner@uconn.edu

Received March 20, 2009



Using mildly basic reaction conditions, the periodate-induced diol cleavage of *meso*-tetraphenyl-2,3-diolchlorin allows for the generation and isolation of the corresponding hitherto elusive free base secochlorin bisaldehyde. An intramolecular Cannizzaro reaction of this porphyrinoid generates three pyrrole-modified, oxazole-based porphyrins: the known porpholactol (2-oxa-3-hydroxychlorin) as the major product, known porpholactone (2-oxa-3-oxoporphyrin), and a novel porpholactol dimer that is linked through an acetal functionality. The structure of the dimer was confirmed by ¹H NMR spectroscopy, X-ray diffractometry, and ESI(+) collision-induced fragmentation mass spectrometry. The chromophores in the dimer are coupled electronically only to a minor extent. A mechanism to rationalize the formation of all products is advanced.

Introduction

The development of novel synthetic methodologies toward chlorins and related oligopyrrolic macrocycles constitutes a significant portion of current porphyrin research. Two principal approaches can be pursued:¹ total synthesis or the conversion of a porphyrin. Particularly owing to the recent efforts by the group of Lindsey, the total synthesis and derivatization of chlorins (and bacteriochlorins) has recently become very efficient,² but methods that induce the conversion of a porphyrin to a chlorin promise also to be versatile and scaleable as the readily synthesized *meso*-tetraarylporphyrins³ or octaalkylporphyrin⁴ can be used as starting materials.⁵

The synthetic manipulation of the β,β' -bonds of porphyrins offers also many options to convert one (or more) pyrrole to a nonpyrrolic heterocycle, generating chlorin-like chromophores or, more generally, pyrrole-modified porphyrins. Early examples of pyrrole-modified porphyrins using this synthetic strategy were discovered by serendipity,^{6,7} but work by the groups of Callot,⁸

* To whom correspondence should be addressed. Tel: (+1) 860 486-2743. Fax: (+1) 860 486-2981.

[†] Oxazolochlorins. 1. See: McCarthy, J. R.; Melfi, P. J.; Capetta, S. H.; Brückner, C. *Tetrahedron* **2003**, 59, 9137–9146.

[‡] University of Connecticut.

[§] Youngstown State University.

(1) (a) Sessler, J. L.; Gebauer, A.; Vogel, E. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guillard, R., Eds.; Academic Press: San Diego, 2000; Vol. 2, pp 1–54. (b) Sessler, J. L.; Gebauer, A.; Weghorn, S. J. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guillard, R., Eds.; Academic Press: San Diego, 2000; Vol. 2, pp 55–124. (c) Lash, T. D. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guillard, R., Eds.; Academic Press: San Diego, 2000; Vol. 2, pp 125–200.

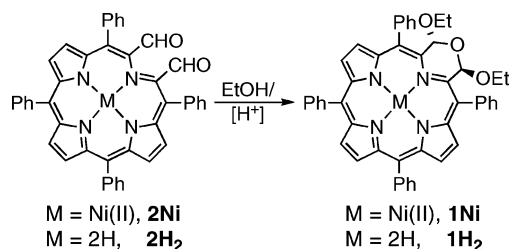
(2) For recent leading examples, see: (a) Muthiah, C.; Bhaumik, J.; Lindsey, J. S. *J. Org. Chem.* **2007**, 72, 5839–5842. (b) Ptaszek, M.; McDowell, B. E.; Taniguchi, M.; Kim, H.-J.; Lindsey, J. S. *Tetrahedron* **2007**, 63, 3826–3839. (c) Taniguchi, M.; Ptaszek, M.; McDowell, B. E.; Lindsey, J. S. *Tetrahedron* **2007**, 63, 3840–3849. (d) Taniguchi, M.; Ptaszek, M.; McDowell, B. E.; Boyle, P. D.; Lindsey, J. S. *Tetrahedron* **2007**, 63, 3850–3863. (e) O'Neal, W. G.; Jacobi, P. A. *J. Am. Chem. Soc.* **2008**, 130, 1102–1108. (f) Borbas, K. E.; Ruzić, C.; Lindsey, J. S. *Org. Lett.* **2008**, 10, 1931–1934. (g) Muthiah, C.; Ptaszek, M.; Nguyen, T. M.; Flack, K. M.; Lindsey, J. S. *J. Org. Chem.* **2007**, 72, 7736–7749. (h) Ruzić, C.; Krayner, M.; Balasubramanian, T.; Lindsey, J. S. *J. Org. Chem.* **2008**, 73, 5806–5820, and references therein.

(3) Adler, A. D.; Longo, F. R.; Finarelli, J. D.; Goldmacher, J.; Assour, J.; Korsakoff, L. *J. Org. Chem.* **1967**, 32, 476.

(4) Sessler, J. L.; Mozaffari, A.; Johnson, M. R. *Org. Synth.* **1992**, 70, 68–78.

(5) For reviews covering chlorin syntheses, see: (a) Flitsch, W. *Adv. Heterocycl. Chem.* **1988**, 43, 73–126. (b) Sternberg, E. D.; Dolphin, D.; Brückner, C. *Tetrahedron* **1998**, 54, 4151–4202. (c) Galezowski, M.; Gryko, D. T. *Curr. Org. Chem.* **2007**, 11, 1310–1338.

(6) Chang, C. K.; Wu, W.; Chern, S.-S.; Peng, S.-M. *Angew. Chem., Int. Ed. Engl.* **1992**, 31, 70–72.

SCHEME 1. Synthesis of Morpholinochlorins^{13,14}

Crossley,⁹ Bonnett,¹⁰ Pandey,¹¹ Zaleski,¹² and us^{13–20} point toward the wide potential of a controlled, stepwise transformation of a porphyrinic β,β' -bond.

We demonstrated the synthesis of *meso*-tetraphenylmorpholinochlorin (**1Ni**) and noticed a profound metal-templating effect.^{13,14} While the $\text{Pb}(\text{OAc})_4$ - or IO_4^- -mediated oxidations of [*meso*-tetraaryl-2,3-diolchlorinato]Ni(II) generate the stable and crystallographically characterized bisaldehyde **2Ni**,^{15,16} and in a subsequent reaction **1Ni**,¹³ the high reactivity of free base **2H₂** allowed only its in situ preparation, whereby it can be trapped in high yields as a stable double-acetal, free base morpholinochlorin **1H₂** (Scheme 1).¹⁴

Another area of interest in current porphyrin research is the synthesis and photophysical characterization of porphyrinoid dimers and oligomers. Typically, two or more tetrapyrrolic macrocycles, such as porphyrins, chlorins, or corroles, are linked directly or via a spacer of various lengths.²¹ The study of the energy-transfer processes in these models promises to lead to a better understanding of photosynthetic pigment assemblies.

(7) Gouterman, M.; Hall, R. J.; Khalil, G.-E.; Martin, P. C.; Shankland, E. G.; Cerny, R. L. *J. Am. Chem. Soc.* **1989**, *111*, 3702–3707.

(8) (a) Callot, H. *Bull. Chem. Soc. Chim. Fr.* **1972**, *11*, 4387–4391. (b) Callot, H. J.; Schaeffer, E. *Tetrahedron* **1978**, *34*, 2295–2300. (c) Callot, H. J. *Dalton Trans.* **2008**, 6346–6357.

(9) Crossley, M. J.; King, L. G. *J. Chem. Soc., Chem. Commun.* **1984**, 920–922.

(10) (a) Adams, K. R.; Bonnett, R.; Burke, P. J.; Salgado, A.; Vallés, M. A. *J. Chem. Soc., Chem. Commun.* **1993**, 1860–1861. (b) Adams, K. R.; Bonnett, R.; Burke, P. J.; Salgado, A.; Vallés, M. A. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1769–1772.

(11) Kozyrev, A. N.; Alderfer, J. L.; Dougherty, T. J.; Pandey, R. K. *Angew. Chem., Int. Ed.* **1999**, *38*, 126–128.

(12) (a) Köpke, T.; Pink, M.; Zaleski, J. M. *Org. Biomol. Chem.* **2006**, *4*, 4059–4062. (b) Köpke, T.; Pink, M.; Zaleski, J. M. *Chem. Commun.* **2006**, 4940–4942.

(13) Brückner, C.; Rettig, S. J.; Dolphin, D. *J. Org. Chem.* **1998**, *63*, 2094–2098.

(14) McCarthy, J. R.; Jenkins, H. A.; Brückner, C. *Org. Lett.* **2003**, *5*, 19–22.

(15) Brückner, C.; Sternberg, E. D.; MacAlpine, J. K.; Rettig, S. J.; Dolphin, D. *J. Am. Chem. Soc.* **1999**, *121*, 2609–2610.

(16) Brückner, C.; Hyland, M. A.; Sternberg, E. D.; MacAlpine, J.; Rettig, S. J.; Patrick, B. O.; Dolphin, D. *Inorg. Chim. Acta* **2005**, *358*, 2943–2953.

(17) McCarthy, J. R.; Hyland, M. A.; Brückner, C. *Org. Biomol. Chem.* **2004**, *2*, 1484–1491.

(18) Daniell, H. W.; Brückner, C. *Angew. Chem., Int. Ed.* **2004**, *43*, 1688–1691.

(19) Lara, K. K.; Rinaldo, C. K.; Brückner, C. *Tetrahedron* **2005**, *61*, 2529–2539.

(20) Ryppa, C.; Niedzwiedzki, D.; Morozowich, N. L.; Rapole, S.; Zeller, M.; Frank, H. A.; Brückner, C. *Chem.—Eur. J.* **2009**, *15*, 5749–5762.

(21) For recent representative examples, see: (a) Matano, Y.; Matsumoto, K.; Nakao, Y.; Uno, H.; Sakaki, S.; Imahori, H. *J. Am. Chem. Soc.* **2008**, *130*, 4588–4589. (b) Hisaki, I.; Hiroto, S.; Kim, K. S.; Noh, S. B.; Kim, D.; Shinokubo, H.; Osuka, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 5125–5128. (c) Kelley, R. F.; Lee, S. J.; Wilson, T. M.; Nakamura, Y.; Tiede, D. M.; Osuka, A.; Hupp, J. T.; Wasielewski, M. R. *J. Am. Chem. Soc.* **2008**, *130*, 4277–4284. (d) Esdaile, L. J.; Jensen, P.; McMurtrie, J. C.; Arnold, D. P. *Angew. Chem., Int. Ed.* **2007**, *46*, 2090–2093. (e) Lysenko, A. B.; Thamyongkit, P.; Schmidt, I.; Diers, J. R.; Bocian, D. F.; Lindsey, J. S. *J. Porphyrins Phthalocyanines* **2006**, *10*, 22–32. (f) Song, H.; Kirmaier, C.; Taniguchi, M.; Diers, J. R.; Bocian, D. F.; Lindsey, J. S.; Holten, D. *J. Am. Chem. Soc.* **2008**, *130*, 15636–15648, and references therein.

We report here a method toward the synthesis and isolation of free base secochlorin bisaldehyde **2H₂**. Furthermore, we introduce an intramolecular Cannizzaro reaction of **2H₂**. This new synthetic methodology generates known monomeric and a new dimeric oxazolochlorins, pyrrole-modified porphyrins in which one of the pyrroles was formally replaced by an oxazole moiety.

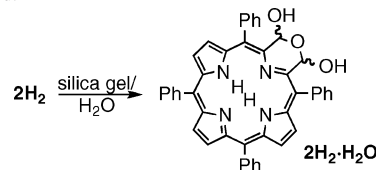
Results and Discussion

Synthesis of Free Base *meso*-Tetraphenylsecochlorin Bisaldehyde (2H₂**).** We previously explored the in situ preparation¹⁴ and reactivity¹⁷ of **2H₂** under acidic reaction conditions and realized its high reactivity. We therefore decided to test its formation and reactivity using Lewis and Brønsted basic reaction conditions. Thus, reaction of the purple, polar ($R_f = 0.12$, silica– CH_2Cl_2) diolchlorin **3H₂** in THF containing 1–2 vol % Et_3N with IO_4^- , heterogenized onto silica gel, converts it in essentially quantitative yields into a brown, nonpolar pigment ($R_f = 0.61$, silica– CH_2Cl_2) (Scheme 2).

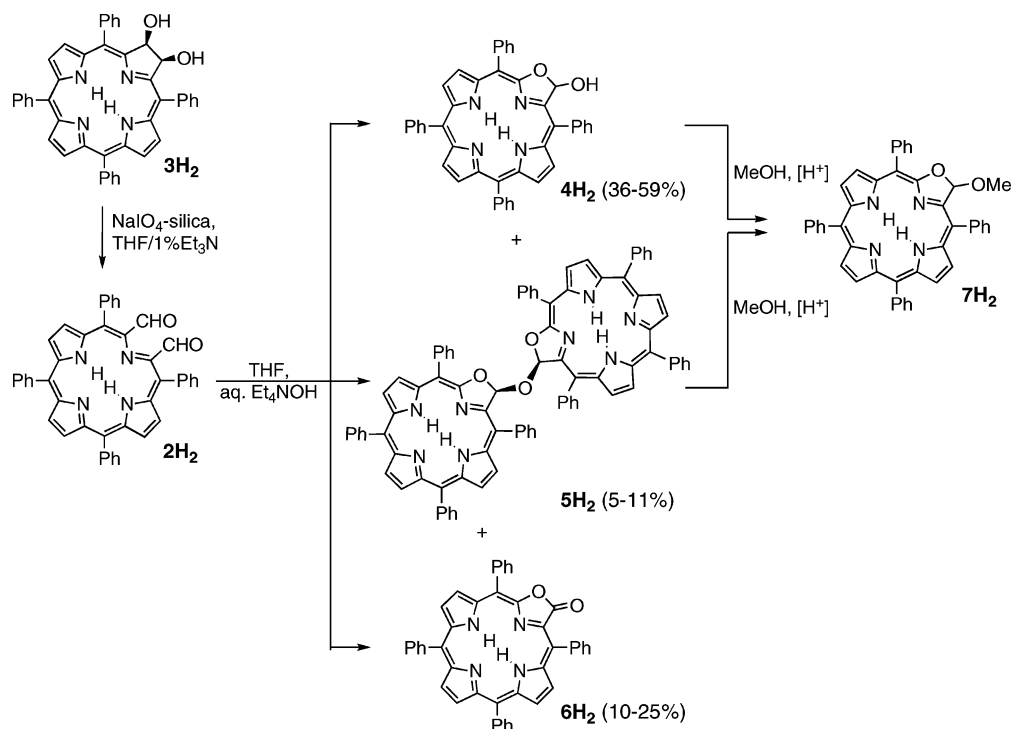
Column chromatography (silica gel, CH_2Cl_2 –0.1% Et_3N) allows the isolation of a reactive compound with the spectroscopic properties that characterize it as bisaldehyde **2H₂**. Notably, its nonchlorin-like UV–vis spectrum displays a split Soret band and broad side bands that also have been observed to be diagnostic features for the Ni(II) complex of secochlorin bisaldehydes (**2Ni**) and related compounds (Figure 1).^{15,16} The NMR spectra of **2H₂** reflect its 2-fold symmetry and show the signals for an aldehyde group ($\delta = 9.64$ ppm for CHO and 188 ppm for CHO , respectively) that is also evident in its IR spectrum (neat, $\nu_{\text{C=O}} = 1675\text{ cm}^{-1}$). In solution, particularly in acidic and/or wet solvents or on silica gel, this bisaldehyde tends to decompose within several hours.²² Evaporated to dryness and kept in a freezer at $-18\text{ }^\circ\text{C}$, **2H₂** is stable over several months. Filtration of the crude reaction mixture to remove the oxidant (with or without being followed by a removal of the solvent by rotary evaporation) produces suitably pure secochlorin bisaldehyde **2H₂** for subsequent transformations. For instance, morpholinochlorin **1H₂** is formed upon reaction with an alcohol and catalytic amounts of acid (HCl fumes).¹⁴

Cannizzaro Reaction of *meso*-Tetraphenylsecochlorin Bisaldehyde (2H₂**).** Aldehydes lacking α -hydrogens are susceptible to a Cannizzaro reaction, a Brønsted base-induced disproportionation reaction of 2 equiv of, for instance, benzaldehyde, to generate 1 equiv each of benzyl alcohol and benzoic acid.²³ Bisaldehyde **2H₂** could potentially undergo an intramo-

(22) The decomposition is often accompanied by the forming of a green, polar ($R_f = 0.10$, silica– CH_2Cl_2), and unstable compound. We tentatively assigned it, based on its morpholinochlorin-like UV–vis spectrum and mass (ESI+ HR-MS, 100% MeCN, m/z found 665.2548, corresponding to $\text{C}_{44}\text{H}_{33}\text{N}_4\text{O}_3$, expected mass 665.2553), as the hydrate structure **2H₂·H₂O**. Correspondingly, it can be converted by addition of EtOH, under acid catalysis, in high yield to morpholinochlorin **1H₂**. However, attempts to isolate and fully characterize this compound failed.



(23) (a) Cannizzaro, S. *Liebigs Ann. Chem.* **1853**, *88*, 129–130. Intramolecular Cannizzaro reactions of aromatic *vic*-bisaldehydes: (b) McDonald, R. S.; Sibley, C. E. *Can. J. Chem.* **1981**, *59*, 1061–1067. (c) Bowden, K.; El-Kaissi, F. A.; Ranson, R. J. *J. Chem. Soc., Perkin Trans. 2* **1990**, 2089–2092. (d) Anvia, F.; Bowden, K. *J. Chem. Soc., Perkin Trans. 2* **1990**, 2093–2098.

SCHEME 2. Synthesis and Cannizzaro Reaction Products of Secochlorin Bisaldehyde **2H₂**

molecular Cannizzaro reaction. When a solution of brown, nonpolar **2H₂** in THF is treated with a large molar excess of a 30% aqueous solution of Et₄NOH in THF, three purple products are formed in varying yields (Scheme 2). The product of intermediate polarity ($R_f = 0.78$, silica-CH₂Cl₂) could be identified as known porpholactone **6H₂**.^{14,24} Its formation has no diagnostic value whether a Cannizzaro reaction has taken place, or not, as we have observed its occurrence in a range of reactions involving diol **3**, secochlorins **2** or other pyrrole-modified porphyrins.²⁵ It appears that this compound is a thermodynamic sink in the oxidative β,β' -degradation pathways of porphyrins.^{7,9,11,14,25}

The most polar compound ($R_f = 0.41$, silica-CH₂Cl₂), formed in up to 59% isolated yields, showed a chlorin-like UV-vis spectrum (Figure 1) and could be identified as known porpholactol **4H₂**.^{24,26} Considering that this oxazolochlorin derivative **4H₂** was previously made by reduction of **6H₂**, which itself was made by oxidation of diol **3H₂**,^{14,24} the Cannizzaro pathway to free base porpholactol is more direct. Alas, the overall yields from diol **3H₂** along both methods are comparable.

An acid-catalyzed reaction of **4H₂** in the presence of MeOH converts it in high yields to the corresponding methyl acetal

7H₂.²⁵ Of note are the greater chemical stability of the methyl acetal compared to the hemiacetal and the fact that this transformation is not reflected in the optical properties of the compound (Figures 1 and 2).

The third, least polar ($R_f = 0.90$, silica-CH₂Cl₂) compound, **5H₂**, is isolated in yields up to 11%. Its UV-vis spectrum is chlorin-like and similar to that of porpholactol **4H₂** (or its methyl acetal **7H₂**), with the exception of the presence of a 9 nm red-shifted Soret band that also displays a distinct shoulder at 400 nm (Figure 2).

The NMR spectrum of **5H₂** reflects its lack of any plane of symmetry, rendering, for instance, all six β -protons nonequivalent. Also, the splitting of the signals assigned to the phenyl *o*-protons is suggestive of the lack of a plane of symmetry parallel to the mean plane of the chromophore and is indicative of the presence of a chlorin-type sp³-carbon carrying four different substituents. In all of these aspects, the ¹H NMR spectrum is similar to that of **7H₂**, but stark differences exist also. For instance, the signals assigned to one phenyl group are spread and shifted high field between 4.9 and 7.7 ppm. In comparison, the corresponding signals for **7H₂** are found within

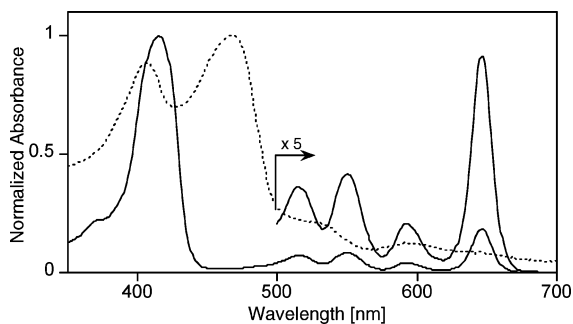


FIGURE 1. UV-vis spectra (CH₂Cl₂) of **2H₂** (dotted trace) and **4H₂** (solid trace).

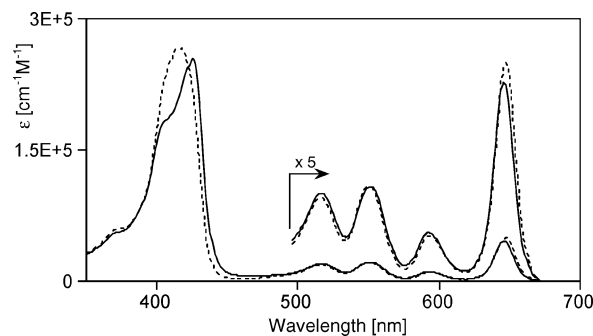


FIGURE 2. Overlay of UV-vis spectra (CHCl₃) of **7H₂** (broken trace) and **5H₂** (solid trace).

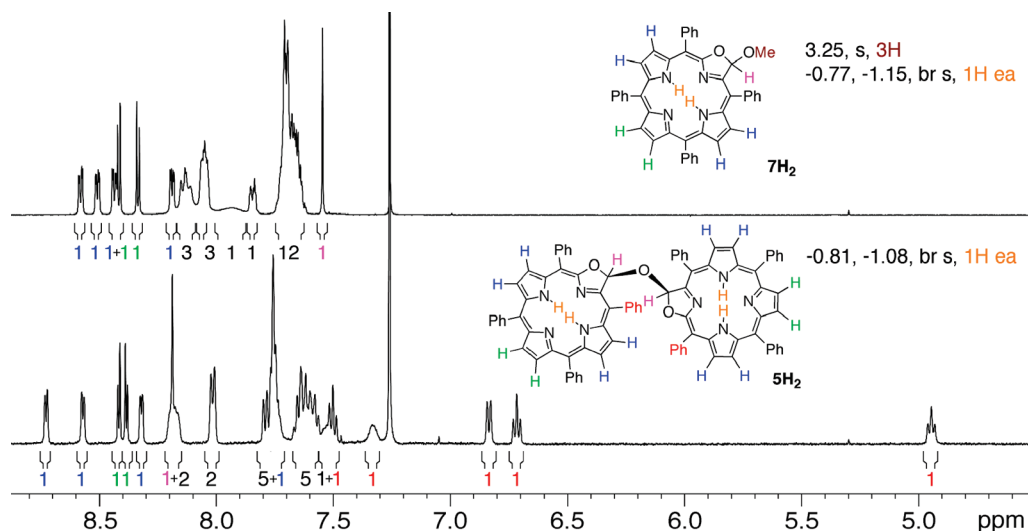


FIGURE 3. Low-field region of ^1H NMR (500 MHz, CDCl_3 , rt) of 5H_2 and 7H_2 .

a 0.5 ppm span between 7.6 and 8.1 ppm.²⁷ This type of shift and spread has been shown to be characteristic for a β -to-phenyl ring-closure reaction.^{17,18,28} However, such reactions are generally also characterized by a significant bathochromic shift of λ_{max} as a result of the increased conjugation of the phenyl group with the chromophore,¹⁸ but this is not observed here (Figure 2).

Compared to the position of the signals of the corresponding protons in 7H_2 , a number of other changes are notable: a 0.6 ppm low-field-shifted signal for the oxazole proton and a 0.5 ppm high-field-shifted β -proton signal. Dramatic shifts of the NMR signals can be the result of two interacting aromatic π -systems, suggestive of a dimeric structure of 7H_2 .²⁹ In support of this, reaction of 5H_2 with MeOH and catalytic quantities of acid generated quantitatively acetal 7H_2 (Scheme 2), indicative of the presence of a acetal-type dimer structure of 5H_2 .

Mass spectrometry also provides a number of clear indications for the structural assignment of 5H_2 . The ESI(+) mass spectra of porpholactol 4H_2 and its acetal 7H_2 display a minor signal for $[4\text{H}_2\cdot\text{H}]^+$ and $[7\text{H}_2\cdot\text{H}]^+$ respectively, and a dominating signal for 8^+ , the carbocation resulting from the protonated parent compound after the loss of H_2O or MeOH, respectively (Figure 4). The high abundance of 8^+ corresponds well with the projected stability of this highly stabilized carbocation. The ESI(+) mass spectrum of $[5\text{H}_2\cdot\text{H}]^+$ indicates a mass that is nearly twice as high as that for 4H_2 . Its composition, as determined by ESI(+) HR-MS, is $\text{C}_{86}\text{H}_{59}\text{O}_3$, i.e., corresponding to $[(2 \times 4\text{H}_2) - \text{H}_2\text{O}] \cdot \text{H}^+$. Moreover, another peak corre-

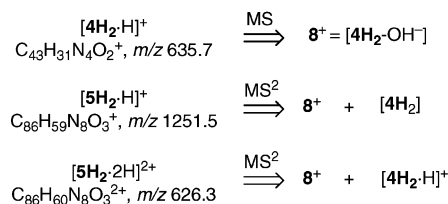
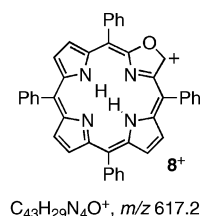


FIGURE 4. Interpreted ESI(+) MS and MS^2 data for 4H_2 and 5H_2 (100% CH_3CN , 30 V cone voltage).

sponding to the diprotonated species $[5\text{H}_2\cdot 2\text{H}]^{2+}$ (at $m/z = 626.3$; dicationic charge indicated by the $1/2$ amu isotope pattern separation) is visible, providing further support for the presence of a structure containing two porphyrinoid moieties. The tandem ESI(+) mass spectrum of the putative dimer $[5\text{H}_2\cdot\text{H}]^+$ (at $m/z = 1251.5$) displays one signal corresponding to 8^+ , whereas the tandem ESI(+) mass spectrum for the diprotonated species shows a signal for 8^+ and $[4\text{H}_2\cdot\text{H}]^+$ (Figure 4), suggestive of 5H_2 indeed being the acetal dimer of 4H_2 .

This interpretation rationalizes also all spectroscopic findings. The altered UV-vis spectrum of 5H_2 compared to that of $4\text{H}_2/7\text{H}_2$ reflects only a small exciton coupling between the chromophores, suggestive of the absence of, for instance, a cofacial dimer and a possible orthogonal relative arrangement of the two chromophores.³⁰ In fact, since the single sp^3 -oxygen atom is linking two sp^3 -carbons, the two chromophores cannot be arranged coplanar to each other. The NMR data are reflective of the short linkage as the diatropic ring current of one oxazolochlorin affects the shifts of the protons on the other oxazolochlorin, and particularly those that are in between the two chromophores (the oxazole hydrogen and one phenyl group). The presence of both high- and low-field shifted proton

(24) McCarthy, J. R. Ph.D. Thesis, University of Connecticut, 2003.

(25) McCarthy, J. R.; Melfi, P. J.; Capetta, S. H.; Brückner, C. *Tetrahedron* **2003**, 59, 9137–9146.

(26) Brückner, C.; McCarthy, J. R.; Daniell, H. W.; Pendon, Z. D.; Ilagan, R. P.; Francis, T. M.; Ren, L.; Birge, R. R.; Frank, H. A. *Chem. Phys.* **2003**, 294, 285–303.

(27) All the assignments were backed by H,H and H,C-COSY measurements; see the Supporting Information.

(28) (a) Barloy, L.; Dolphin, D.; Dupré, D.; Wijesekera, T. P. *J. Org. Chem.* **1994**, 59, 7976–7985. (b) Review article: Fox, S.; Boyle, R. W. *Tetrahedron* **2006**, 62, 10039–10054.

(29) For an example of a chlorin dimer, see: (a) Jaquinod, L.; Nurco, D. J.; Medforth, C. J.; Pandey, R. K.; Forsyth, T. P.; Olmstead, M. M.; Smith, K. M. *Angew. Chem., Int. Ed. Engl.* **1996**, 35, 1013–1016. For examples of the ^1H NMR shifts expressed by directly β,β' -linked porphyrin dimers, see: (b) Bringmann, G.; Götz, D. C. G.; Gulder, T. A. M.; Gehrke, T. H.; Bruhn, T.; Kupfer, T.; Radacki, K.; Braunschweig, H.; Heckmann, A.; Lambert, C. *J. Am. Chem. Soc.* **2008**, 133, 17812–17825.

(30) Hunter, C. A.; Sanders, J. K. M.; Stone, A. *J. Chem. Phys.* **1989**, 133, 395–404.

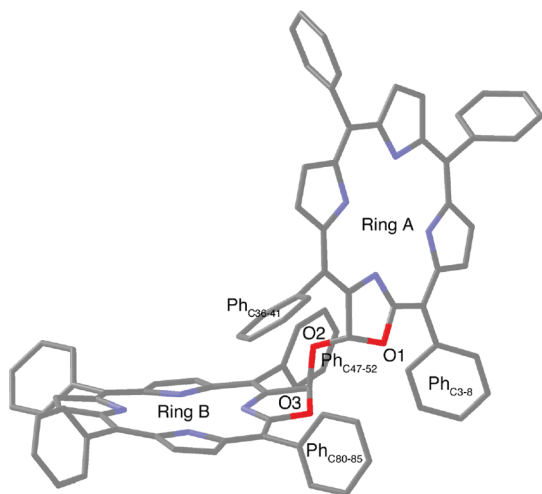


FIGURE 5. Stick representation of the single-crystal structure of **5H₂**. All hydrogen atoms were omitted for clarity.

signals is indicative of a relative arrangement of the two porphyrinoids that exposes one oxazolochlorin moiety to the shielding and deshielding regions of the other π -system. Interestingly, the NMRs do not indicate the formation of diastereomers despite the presence of two chiral carbons in the dimer.

The synthesis of porphyrin dimers is frequently rather involved,²¹ but one other serendipitous, photochemically induced, formation of a (metallo)chlorin-type chromophore was recently reported,¹² as well as chlorin dimers,^{29a} and a directly linked β,β' -porphyrin dimers prepared in one step.^{29b}

Structural Characterization of Dimer 5H₂. The ultimate proof of the spectroscopically derived dimeric structure for **5H₂** was provided by single-crystal X-ray diffractometry. Figure 5 shows a stick representation of the result. Indeed, two oxazole-derived chlorin-like moieties are linked via an acetal-type oxygen. As a result of the sterics imposed by the sequence of the three sp^3 -hybridized atoms making up the linkage and the large size of the linked moieties, the two mean planes of the chromophores are nearly perpendicular to each other (79° angle between the two C₁₉N₄O oxazolochlorin mean planes), whereby the two pairs of *meso*-phenyl groups flanking the linking oxazole (PhC₃₋₈/PhC₃₆₋₄₁ and PhC₄₇₋₅₂/PhC₈₀₋₈₅, respectively) are arranged in a cog-wheeled fashion, allowing the expression of multiple π -edge-to- π -center interactions. This tight packing mode may also be suggestive of a low conformational flexibility of the linkage. In fact, low-temperature (−10 °C) ¹H NMR studies lead to a minor sharpening of a few signals but to no further shifts.

The solid-state structure is idealized 2-fold symmetric, with an axis of rotation projecting between the molecules through the linking acetal oxygen. As demonstrated above, the two chromophores are equivalent by NMR. However, in the crystal structure, the conformations of rings A and B differ from each other. The root-mean-square (rms) deviation from planarity of the C₁₉N₄O moiety of ring A is 0.0617 Å, while it is 0.2073 Å for the corresponding plane in ring B. However, their modes of nonplanarity, as analyzed by the normal-coordinate structural decomposition (NSD) procedure, are not fundamentally different from each other (Figure 6).³¹

Both rings are predominantly saddled, with some ruffled and a minor waving (x) contribution. The previously structurally characterized Ag(II) complex of **7H₂** was nearly planar, with

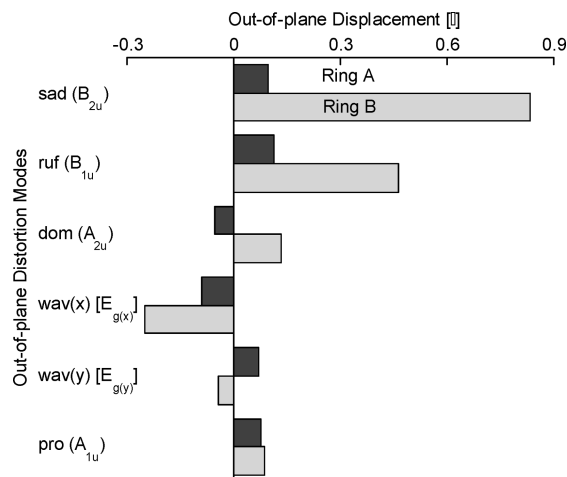
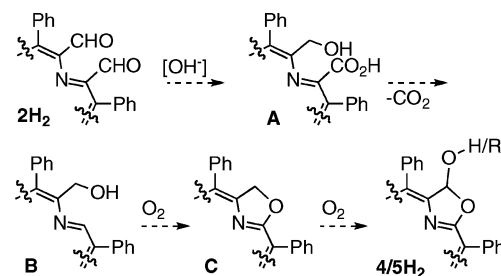


FIGURE 6. Lowest frequency normal-coordinate structural decomposition results for the C₁₉N₄O macrocycles of ring A and ring B of **5H₂**.²⁶

SCHEME 3. Proposed Cannizzaro Reaction Sequence and Consecutive Fundamental Steps toward the Formation of the Oxazole-Derived Chromophores



an overall rms of the C₁₉N₄OAg macrocycle of only 0.0551 Å.³² With the caveat that the conformational differences in all these three oxazolochlorins are relatively small, we believe that they are nevertheless indicative of a significant structural flexibility of the free base oxazolochlorin macrocycles.

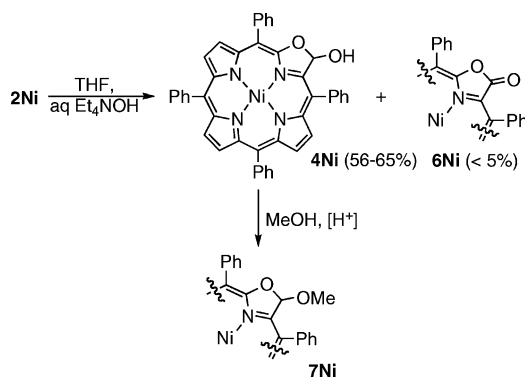
Dimer **5H₂** is chiral, containing two homochiral centers (both sp^3 oxazolochlorin carbons) but crystallizes as a racemic mixture in the (nonchiral) centrosymmetric space group *P* $\bar{1}$. Evidently, establishment of the chirality of the first chiral center enforces the homochirality of the second. Molecular models show that a heterochiral linkage appears to cause more steric inhibition and does not allow for the observed cog-wheeled arrangement of the phenyl groups.

Mechanistic Considerations. Are the occurrence of products **4H₂** and **5H₂** an indication that an intramolecular Cannizzaro reaction has taken place? We suggest that this question can be answered in the affirmative. An intramolecular Cannizzaro reaction of **2H₂** generates the benzyl alcohol carboxylic acid intermediate **A** (Scheme 3). We suggest that acid **A** decarboxylates to form putative intermediate **B** before undergoing an oxidative ring-closure step to form **C**. The decarboxylation step has its parallel in the decarboxylation of the putative diacid compound formed by MnO₄[−]-oxidation of diol **3H₂** and that

(31) (a) Shelnutt, J. A. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guillard, R., Eds.; Academic Press: San Diego, 2000; Vol. 7, pp 167–224. (b) Jentzen, W.; Song, X.-Z.; Shelnutt, J. A. *J. Phys. Chem. B* **1997**, *101*, 1684–1699. (c) Song, L.; Shelnutt, J. A. NSD Engine Version 3.0 (<http://jasheln.unm.edu/jasheln/content/nsd/NSDengine/start.htm>).

(32) Zeller, M.; Hunter, A. D.; McCarthy, J. R.; Capetta, S. H.; Brückner, C. *J. Chem. Crystallogr.* **2005**, *35*, 935–942.

SCHEME 4. Results of the Cannizzaro Reaction of the Ni(II) Complex of Secochlorin Bisaldehyde 2Ni



ring closes to generate porpholactone **6H₂** (though nothing is known about the exact mechanism of this reaction).^{9,24} Previous results reported by us have also shown that the benzylic position in the oxazole-derived chromophore **C** is very sensitive toward further (air) oxidation.²⁴ Further considering that free base chlorins are generally good photosensitizers, the formation of the observed oxidation products is readily rationalized. Correspondingly, the formation of **5H₂** can be suppressed significantly by running the reaction under anaerobic conditions (though the workup still took place under regular light and aerobic conditions).

Cannizzaro Reaction on [*meso*-Tetraphenylsecochlorinato]Ni(II) (1Ni). Exposure of the stable Ni(II) complex of secochlorin **2Ni** to the identical strongly basic conditions described above (THF, aq Et₄NOH) also elicits a Cannizzaro reaction (Scheme 4). However, next to the hemiacetal oxazolochlorin Ni(II) complex **4Ni** as the main product (56–65% isolated yields) and some porpholactone **6Ni** (<5%), traces of a few other products are observed, but none of them could be assigned a Ni₂-dimer structure corresponding to **5H₂**. This result again highlights the influence of the central metal on the outcome of a reaction on the β -positions of porphyrins.^{17,33} Hemiacetal **4Ni** could be converted in high yields to its corresponding methyl acetal **7Ni**.

Conclusions

We have demonstrated that free base secochlorin **2H₂** can be prepared. Secochlorin bisaldehydes are susceptible to an intramolecular Cannizzaro reaction, a novel pathway toward the generation of pyrrole-modified porphyrins. This method represents an alternative to the established syntheses of monomeric porpholactol **4H₂** but offers also an all together novel pathway toward chiral dimeric chlorin-type chromophores (**5H₂**).

Experimental Section

X-ray Single-Crystal Diffractometry of 5H₂. All experimental details are provided in the Supporting Information.

***meso*-Tetraphenylsecochlorin Bisaldehyde (2H₂).** *meso*-Tetraphenyl-2,3-dihydroxychlorin (**3H₂**) (30 mg, 4.62 $\times 10^{-5}$ mol) was dissolved in THF (10 mL) containing Et₃N (5 drops) at rt in a round-bottom flask equipped with a magnetic stirring bar. The flask was shielded from ambient light with aluminum foil. Silica gel-supported NaIO₄ (~0.9 g) was added to the stirring reaction mixture and

allowed to react for ~3 h. Additional oxidant (~0.2 g) was added until all starting material, as monitored by TLC, was consumed. Upon completion, the reaction mixture was passed through a glass frit (M) containing some neutral alumina, and the filter cake was washed with THF until the filtrate was nearly colorless. The combined filtrates were evaporated to dryness by rotary evaporation. Product **2H₂** was generally used immediately without any further purification. A 100% conversion of **3H₂** was assumed (30 mg crude **2H₂**). Spectroscopic data for **2H₂**: *R_f* (silica–CH₂Cl₂) 0.61; ¹H NMR (400 MHz, CDCl₃) 9.81 (s, 1H), 9.0 (br s, 1H), 8.41 (d, ³*J* = 4 Hz, 1H), 8.2 (d, ³*J* = 4 Hz, 1H), 7.7–7.3 (overlapping signals, 10H), 1.1 (s, 1H); ¹H NMR (400 MHz, DMSO) 9.64 (s, 1H), 8.32 (d, ³*J* = 4 Hz, 1H), 8.16 (d, ³*J* = 4 Hz, 1H), 8.07 (s, 1H), 7.98–7.18 (m, 10H), 0.96 (s, 1H, exchangeable with D₂O); ¹³C NMR (100 MHz, DMSO) 187.9, 153.7, 151.9, 143.0, 139.8, 139.6, 137.9, 133.8, 133.7, 129.7, 129.4, 128.8, 128.6, 127.8, 127.2, 125.4, 124.5, 120.8; UV–vis (CHCl₃) λ_{max} (rel intens) 407 (0.89), 467 (1.00), 532 (0.21), 596 nm (0.12); MS (ESI, 100% CH₃CN, cone voltage 30 eV) *m/z* 647 ([M·H]⁺); HR-MS (ESI+, 100% CH₃CN) calcd for C₄₄H₃₁N₄O₂ ([M·H]⁺) 647.2442, found 647.2433.

Cannizzaro Reaction of 2H₂ to Generate *meso*-Tetraphenyl-2-hydroxy-3-oxachlorin (4H₂), *meso*-Tetraphenyl-2-oxa-3-oxochlorinato (6H₂), and (*meso*-Tetraphenyl-3-oxa-2-yl-chlorin)₂O (5H₂). Crude bisaldehyde (30 mg, 4.64 $\times 10^{-5}$ mol) was dissolved in THF (10 mL) in a round-bottom flask equipped with a magnetic stirring bar and a N₂ inlet/bubbler. Et₄NOH (1.0 mL of a 30 wt % solution in H₂O) was added and the mixture stirred at ambient temperature for 10–15 min. When the starting material was consumed (reaction control by UV–vis and TLC), the reaction mixture was washed with water (2 \times 10 mL), dried over anhyd Na₂SO₄, and evaporated to dryness by rotary evaporation. The resulting mixture was separated on a preparative TLC plate (silica, CH₂Cl₂–petroleum ether 1:1). Isolated yields for **4H₂** ranged from 36 to 59% yield (10.5 to 17.8 mg), for **5H₂** from 5 to 11% (3.0 to 6.5 mg; note: the more rigorously oxygen was excluded, the lower the yield of this products), and for **6H₂** from 10 to 25% (3.0 to 7.4 mg).

Spectroscopic data for **5H₂**: *R_f* (silica–CH₂Cl₂) 0.90; ¹H NMR (500 MHz, CDCl₃) 8.73 (d, ³*J* = 5.0 Hz, 1H), 8.57 (d, ³*J* = 4.5 Hz, 1H), 8.42 (d, ³*J* = 4.5 Hz, 1H), 8.38 (d, ³*J* = 4.5 Hz, 1H), 8.32 (d, ³*J* = 4.5 Hz, 1H), 8.18–8.22 (m, 3H), 8.02–8.00 (d, ³*J* = 7.5 Hz, 2H), 7.80–7.74 (m, 6H), 7.67–7.56 (m, 5H), 7.53 (br s, 1H), 7.50 (t, ³*J* = 7.5 Hz, 1H), 7.33 (br s, 1H), 6.83 (d, ³*J* = 7.5 Hz, 1H), 6.72 (t, ³*J* = 7.5 Hz, 1H), 4.95 (t, ³*J* = 7.5 Hz, 1H), –0.79 (s, 1H, exchangeable with D₂O), –1.06 (s, 1H, exchangeable with D₂O); ¹³C NMR (125 MHz, CDCl₃) 164.0, 154.9, 151.6, 149.9, 142.6, 141.7, 141.6, 140.8, 138.5, 138.2, 136.7, 134.4, 134.1, 133.9, 133.6, 133.5, 133.4, 132.1, 131.7, 129.6, 127.7, 127.5, 127.3, 127.2, 126.9, 126.7, 126.6, 125.9, 125.8, 125.1, 122.0, 121.1, 112.0, 100.5, 99.7; for FT-IR (neat) see the Supporting Information; UV–vis (CHCl₂) λ_{max} (log Σ) 425 (5.42), 516 (4.32), 552 (4.35), 593 (4.06), 646 (4.68) nm; Fl (CH₂Cl₂, $\lambda_{\text{excitation}}$ = 418 nm) λ_{max} (rel intensity): 651 (1.0), 709 (0.07) nm; HR-MS (ESI+, 100% CH₃CN) *m/e* calcd for C₈₆H₅₉N₈O₃ ([M·H]⁺) 1251.4710, found 1251.4888 (Δ = 14 ppm); HR-MS (FAB, PEG) *m/e* calcd for C₈₆H₅₈N₈NaO₃ ([M·Na]⁺) 1273.4530, found 1273.4590.

Spectroscopic data for **4H₂** and **6H₂** were identical to those reported in the literature.^{20,22,24}

***meso*-Tetraphenyl-2-methoxy-3-oxachlorin (7H₂).** Excess MeOH (1 mL) was added to a stirring solution of **4H₂** (100 mg, 15.7 mmol) in CH₂Cl₂ (20 mL). Traces of TFA vapors (from a TFA bottle head space, delivered via pipet) were added, and the reaction was monitored by TLC for completion. The acid was then neutralized with Et₃N (1 drop) and the solution washed, dried over anhyd MgSO₄, evaporated to dryness, purified by column or preparative plate chromatography, and recrystallized by slow solvent exchange from CH₂Cl₂ to MeOH to provide 90% (92 mg) isolated yield: *R_f* = 0.91 (silica–CH₂Cl₂); ¹H NMR (400 MHz, CDCl₃) δ 8.60 (dd, ³*J* = 5.0, ⁴*J* = 1.6 Hz, 1H), 8.52 (dd, ³*J* = 4.6, ⁴*J* = 1.8 Hz, 1H), 8.45 (dd, ³*J* = 5.0, ⁴*J* = 1.6 Hz, 1H), 8.43 (d, ³*J* = 4.6 Hz, 1H),

(33) Buchler, J. W.; Dreher, C.; Herget, G. *Liebigs Ann. Chem.* **1988**, 43–54.

8.35 (d, $^3J = 4.4$ Hz, 1H), 8.21 (dd, $^3J = 4.6$, $^4J = 1.8$ Hz, 1H), 8.07 (br s, 3H), 8.14 (m, 3H), 7.95 (br s, 1H), 7.85 (m, 1H), 7.71 (m, 12H), 7.56 (s, 1H), 3.28 (s, 3H), -0.73 (s, 1H), -1.11 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.0, 155.1, 152.0, 150.0, 142.0, 136.8, 134.8, 134.0, 133.9, 133.6, 131.9, 131.3, 129.8, 128.1, 128.0, 127.9, 127.7, 127.6, 127.1, 126.9, 125.2, 122.1, 112.3, 106.5, 100.3, 54.9; for FT-IR (neat), see the Supporting Information; UV-vis (CH_2Cl_2) λ_{max} (log ϵ): 418 (5.20), 515 (4.00), 550 (4.07), 592 (3.83), 646 (4.38) nm; FI (CH_2Cl_2 , $\lambda_{\text{excitation}} = 420$ nm) λ_{max} (rel intensity): 653 (1.0), 705 (0.08) nm; HR-MS (FAB+, PEG) m/z calcd for $\text{C}_{44}\text{H}_{33}\text{O}_2\text{N}_4$ ($[\text{M}\cdot\text{H}]^+$) 649.2604, found 649.2629.

[*meso*-Tetraphenyl-2-hydroxy-2-oxachlorinato]Ni(II) (4Ni). Prepared, next to porpholactone Ni(II) complex **6Ni**, according to the general Cannizzaro procedure. The reaction mixture was separated by preparative TLC (silica, CH_2Cl_2 –petroleum ether 90:10). At a 4.2×10^{-5} mol scale: 5% of **6Ni** and **4Ni** in 56 to 65% isolated yields: R_f (silica– CH_2Cl_2) 0.69; ^1H NMR (500 MHz, CDCl_3) δ 8.33 (d, $^3J = 5.0$ Hz, 1H), 8.31 (d, $^3J = 4.5$ Hz, 1H), 8.24 (d, $^3J = 4.8$ Hz, 1H), 8.17 (d, $^3J = 4.4$ Hz, 1H), 8.10 (d, $^3J = 4.8$ Hz, 1H), 7.98 (d, $^3J = 4.8$ Hz, 1H), 7.82–7.81 (m, 5H), 7.68–7.54 (m, 16H), 3.47 (d, $^3J = 7.6$ Hz, 1H, exchangeable with D_2O); ^{13}C NMR (100 MHz, $\text{CDCl}_3/10\% \text{CD}_3\text{OD}$) δ 160.3, 154.9, 150.2, 146.2, 143.7, 143.4, 143.0, 141.8, 141.5, 140.6, 139.7, 136.5, 136.3, 136.1, 135.1, 133.1, 132.4, 131.5, 131.1, 130.9, 130.6, 130.3, 130.2, 129.1, 128.9, 124.7, 115.9, 108.6, 100.0; UV-vis (CH_2Cl_2) λ_{max} (log ϵ) 408 (4.93), 499 (3.53), 567 (3.74), 607 (4.39) nm; HR-MS (ESI^+ , 100% CH_3CN) m/z calcd for $\text{C}_{43}\text{H}_{28}\text{N}_4\text{NiO}_2$ ($[\text{M}]^+$) 690.1566, found 690.1582.

[*meso*-Tetraphenyl-2-oxa-3-oxoporphyrinato]Ni(II) ([*meso*-tetraphenylporpholactonato]Ni(II), 6Ni): R_f (silica– CH_2Cl_2) 0.74; ^1H NMR (400 MHz, $\text{CDCl}_3/10\% \text{MeOD}$) δ 8.55 (d, $^3J = 4.0$ Hz, 1H), 8.51–8.47 (two overlapping d, $^3J = 4.0$ Hz, 2H), 8.45–8.41 (two overlapping d, $^3J = 4.0$ Hz, 2H), 8.33 (d, $^3J = 4.0$ Hz, 1H), 7.90–7.85 (m, 6H), 7.75–7.73 (d, 2H), 7.66–7.60 (m, 12H); ^{13}C NMR (100 MHz, $\text{CDCl}_3/10\% \text{MeOD}$) δ 149.3, 144.9, 144.5, 141.4, 140.9, 139.9, 137.1, 136.0, 133.5, 133.3, 133.0, 131.8, 128.1, 127.7,

127.4, 127.0, 126.9, 124.9, 121.2, 120.3, 100.7; UV-vis (CHCl_3) λ_{max} (log ϵ) 415 (5.24), 543 (3.96), 586 (4.49) nm; HR-MS (ESI^+ , 100% CH_3CN) m/z calcd for $\text{C}_{43}\text{H}_{27}\text{N}_4\text{NiO}_2$ ($[\text{M}\cdot\text{H}]^+$) 689.1487, found 689.1536.

[*meso*-Tetraphenyl-2-methoxy-2-oxachlorinato]Ni(II) (7Ni). Prepared from **4Ni** (30 mg, 4.33×10^{-2} mmol) as described for the preparation of **7H₂** from **4H₂**. Yield after recrystallization by slow solvent exchange from CH_2Cl_2 to MeOH, 94% (28.6 mg): R_f (silica– CH_2Cl_2) 0.86; ^1H NMR (500 MHz, CDCl_3) δ 8.32 (d, $^3J = 5.0$ Hz, 1H), 8.31 (d, $^3J = 5.0$ Hz, 1H), 8.23 (d, $^3J = 5.0$ Hz, 1H), 8.16 (d, $^3J = 5.0$ Hz, 1H), 8.08 (d, $^3J = 5.0$ Hz, 1H), 8.01 (d, $^3J = 5.0$ Hz, 1H), 7.99–7.72 (br, 5H), 7.71–7.45 (m, 15H), 7.31 (s, 1H), 3.28 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.0, 151.6, 146.9, 142.9, 140.5, 140.1, 139.7, 138.5, 138.2, 137.4, 136.4, 133.3, 133.1, 132.8, 131.8, 129.8, 129.2, 128.2, 127.9, 127.8, 127.7, 127.6, 127.3, 127.0, 126.9, 125.8, 125.5, 121.4, 112.6, 105.4, 96.6, 54.7; UV-vis (CH_2Cl_2) λ_{max} (log ϵ) 408 (5.02), 499 (3.58), 567 (3.80), 607 (4.47) nm; MS (ESI^+ , 100% CH_3CN) m/z 704.2 ($\text{M}\cdot\text{H}^+$), 673.2 ($\text{M} - \text{OMe}^+$); HR-MS (ESI^+ , 100% CH_3CN) m/z calcd for $\text{C}_{43}\text{H}_{27}\text{N}_4\text{NiO}$ ($[\text{M} - \text{OMe}]^+$) 673.1538, found 673.1611.

Acknowledgment. This work was supported by the US National Science Foundation under Grant Nos. 0517782 and 0730826 (to C.B.). The diffractometer was funded by NSF Grant No. 0087210, by the Ohio Board of Regents Grant No. CAP-491, and by YSU.

Supporting Information Available: ^1H , ^{13}C NMR, and IR spectra of all novel compounds obtained, (tandem) $\text{ESI}(+)$ spectra for select compounds, and experimental details for the crystal structure determination of **5H₂**, including the CIF file. This material is available free of charge via the Internet at <http://pubs.acs.org>.

JO9006046