allowed to stir for 7 days at room temperature before being diluted with dichloromethane, neutralized with aqueous saturated sodium bicarbonate, washed with water, and dried (Na_2SO_4). The product was purified by preparative TLC on silica gel (elution with 3% tetrahydrofuran in dichloromethane), giving less than 1 mg of demetalated product (**27**) and mostly unreacted nickel(II) complex (**27b**).

Copper(II) Methyl δ-*meso*-[(Methylthio)methyl]-2-(2-chloroethyl)-2-devinylpyropheophorbide *a* (26a). Methyl 2-(2-chloroethyl)-2-devinylpyropheophorbide *a* (**24**) (55 mg) was dissolved in dichloromethane (6 mL), and saturated copper(II) acetate hydrate in methanol (3 mL) was added. The resulting solution was refluxed under nitrogen for 6.5 h before being diluted with dichloromethane, washed with water, dried, and evaporated. The resulting copper(II) complex (**25a**) was crystallized from dichloromethane/hexane and had mp 186-190 °C: UV λ_{max} 400 nm (ϵ 6.4 × 10^4), 420 (9.6 × 10^4), 504 (4.1 × 10^3), 548 (5.1 × 10^3), 598 (1.2 × 10^4), 646 (6.15 × 10^4). This material, without further purification, was dissolved in dry dichloromethane (10 mL), and chloromethyl methyl sulfide (80 μL) was added under nitrogen before the solution was cooled to -15 °C. $TiCl_4$ (80 μL; 1.1 M solution in dichloromethane) was added dropwise via a syringe, and after 15 min, the mixture was allowed to warm to room temperature. After 2 h, the reaction was determined by spectrophotometry to be incomplete so the mixture was cooled to -15 °C and an additional 80 μL of $TiCl_4$ solution was added. After 1 h at room temperature, the mixture was heated to 40 °C for 1 h, after which the reaction was determined by spectrophotometry to be complete. The reaction mixture was then diluted with dichloromethane (75 mL), washed with aqueous saturated sodium bicarbonate (50 mL) and water (2 × 50 mL), dried, and evaporated. The product was purified by flash column chromatography on silica gel (elution with 3% tetrahydrofuran in dichloromethane), giving 45 mg (68% yield from methyl 2-(2-chloroethyl)-2-devinylpyropheophorbide *a*), mp 117-121 °C: UV λ_{max} 424 nm (ϵ 6.1 × 10^4), 610 (4.2 × 10^3), 658 (3.6 × 10^4).

Copper(II) Methyl δ-*meso*-Methyl-2-(2-chloroethyl)-2-devinylpyropheophorbide *a* (27a). Copper(II) methyl δ-*meso*-[(methylthio)methyl]-2-(2-chloroethyl)-2-devinylpyropheophoride *a* (**26a**) (40 mg) was dissolved in acetone (15 mL); Raney Ni (pH 10 slurry; 700 mg) was added, and the stoppered flask was stirred for 1 h at 40 °C. The Raney Ni was then filtered off and the product was purified by preparative TLC on silica gel (elution with 3% tetrahydrofuran in dichloromethane), giving 20 mg (59%) of the required *meso*-methylchlorin, mp 113-117 °C: UV λ_{max} 424 nm (ϵ 5.9 × 10^4), 612 (1.2 × 10^3), 658 (3.5 × 10^4).

Methyl δ-*meso*-Methyl-2-(2-chloroethyl)-2-devinylpyropheophorbide *a* (27). Copper(II) methyl δ-*meso*-methyl-2-(2-chloroethyl)-2-devinylpyropheophorbide (**27a**) (20 mg) was dissolved in dichloromethane (5 mL), and HCl (g) was bubbled through the solution for 5 min. The reaction mixture was then stirred in a stoppered flask for 30 min at room temperature before being opened carefully and the contents poured into iced saturated aqueous sodium acetate/dichloromethane. Then, saturated aqueous sodium bicarbonate was added to the vigorously stirred solution to pH 7. The organic layer was separated, washed with water, dried (Na_2SO_4), and evaporated to give a residue which was purified by silica gel TLC (elution with 3% tetrahydrofuran in dichloromethane), and the product was crystallized from dichloromethane/methanol, giving 10 mg (55% yield). [This material was identical with an authentic sample which had previously been converted into the corresponding Bmph-*c* [Et, Me] (**4**)]: mp 211-212 C [lit.[6] mp 212-213 °C]: NMR (500 MHz, $CDCl_3$) 9.34, 9.52 (each s, 1 H, α- and β-meso-H), 5.25 (ABq, J = 19.5 Hz, 10-CH_2), 4.60 (q, 1 H, 8-H), 4.18-4.23, 4.40 (m, t, 5 H, 2a,b-CH_2CH_2, 7-H), 3.92 (s, 3 H, δ-meso-Me), 3.73 (q, 2 H, 4a-CH_2), 3.31, 3.49, 3.58, 3.70 (each s, 3 H, 3-, 1-, 5-Me, 7d-OMe), 2.10-2.23, 2.50-2.55 (each m, 2 H, 7a,b-CH_2CH_2), 1.72 (t, 3 H, 4b-Me), 1.53 (d, 3 H, 8-Me), -1.72 (br s, 2 H, NH); UV λ_{max} 412 nm (ϵ 1.12 × 10^5), 484 (3.5 × 10^3), 516 (9.4 × 10^3), 550 (1.3 × 10^4), 612 (6.8 × 1/3), 670 (5.04 × 10^4).

Acknowledgment. This research was supported by a grant from the National Science Foundation (CHE 81-20891).

Registry No. 3, 68464-68-6; **3a**, 96806-69-8; **3b**, 96806-63-2; **4** (isomer 1), 59924-02-6; **4** (isomer 2), 73365-61-4; **7**, 36151-62-9; **7a**, 96806-58-5; **7d**, 15634-17-0; **8**, 5594-30-9; **9**, 6453-67-4; **11**, 96806-59-6; **13**, 96806-70-1; **13a**, 96806-60-9; **16**, 33719-95-8; **17**, 51742-45-1; **18**, 96806-71-2; **18a**, 96825-30-8; **19a**, 96806-61-0; **19b**, 96806-62-1; **20**, 96806-72-3; **21**, 66229-98-9; **22**, 66229-99-0; **23**, 66230-00-0; **23** (acid), 66230-01-1; **24**, 96806-73-4; **25a**, 96806-67-6; **25b**, 96806-64-3; **26a**, 96825-31-9; **26b**, 96806-65-4; **27**, 73333-66-1; **27a**, 96806-68-7; **27b**, 96806-66-5; pheophytin *a*, 603-17-8; pheophytin *a* (7-propionic acid), 57458-59-0; pyropheophytin *a*, 14409-87-1.

Synthesis of Nickel(II) Isobacteriochlorins from Nickel(II) Complexes of Chlorophyll Derivatives

Kevin M. Smith* and Dane A. Goff

Contribution from the Department of Chemistry, University of California, Davis, California 95616. *Received November 16, 1984*

Abstract: Treatment of nickel(II) methyl δ-*meso*-[(methylthio)methyl]mesopyropheophorbide *a* (**1c**) with Raney Ni gives the expected nickel(II) δ-*meso*-methyl compound **5** as well as byproducts, which are shown to be the nickel(II) isobacteriochlorin **2b**, nickel(II) hexahydroporphyrin **4**, and methyl nickel(II) δ-*meso*-methyldeoxomesopyropheophorbide *a* **3c**. The nickel(II) isobacteriochlorin is shown to consist substantially of one isomer (**2b**, "tcc") by using HPLC and high-field NMR spectroscopy. When the same reaction is carried out with the δ-meso-unsubstituted nickel(II) compound **9b**, similar isobacteriochlorin **11a**, hexahydroporphyrin **12**, and deoxo compound **10b** are obtained. In this case, the isobacteriochlorin is separated by HPLC into approximately equal amounts of two isomers. On the basis of extensive NMR experiments, structures for the two isomeric nickel(II) isobacteriochlorins are proposed. Variation of the solvent used in the Raney Ni reduction allows preferential formation of either the isobacteriochlorins **11a** or the deoxo compound **10b**, but under no circumstances are materials formed in which both the 9-ketocarbonyl and the ring A pyrrole subunit have been reduced. The presence of the δ-*meso*-methyl substituent (e.g., in **1c**) also has an effect on the Raney Ni reaction such that significantly higher yields of nickel(II) isobacteriochlorin **2b** are obtained (compared with reduction of **9b** to give **11a**).

The recent discovery of the nitrite and sulfite reductases containing the isobacteriochlorin prosthetic group, siroheme,[1a] and the structure elucidation of the nickel-containing factor 430 from methanogenic bacteria[1b] have sparked a resurgence of interest in highly reduced porphyrin systems. As mentioned in the preceding paper[2] Raney Ni desulfurization of copper(II) methyl δ-*meso*-[(methylthio)methyl]mesopyropheophorbide *a* (**1b**) in methanol at 70 °C gave rise to a major side product tentatively identified

(1) (a) Scott, A. I.; Irwin, A. J.; Siegel, L. M.; Shoolery, J. N. *J. Am. Chem. Soc.* **1978**, *100*, 7987-7994. (b) Pfalz, A.; Jaun, B.; Fässler, A.; Eschenmoser, A.; Jaenchen, R.; Gilles, H. H.; Diekert, G.; Thauer, R. K. *Helv. Chim. Acta* **1982**, *65*, 828-865.

(2) Smith, K. M.; Goff, D. A.; Simpson, D. J. *J. Am. Chem. Soc.*, preceding paper in this issue.

0002-7863/85/1507-4954$01.50/0

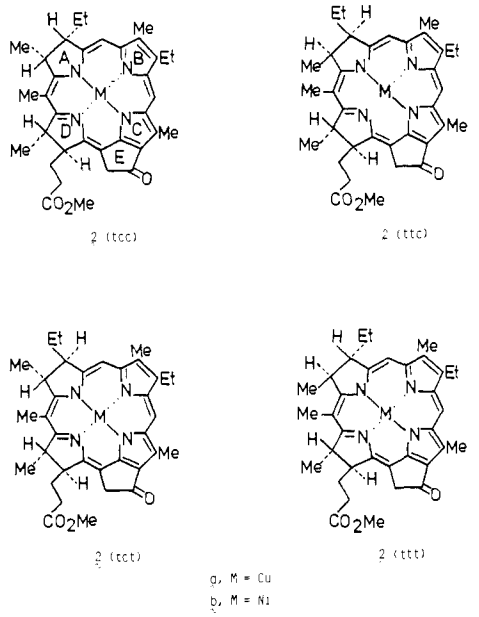
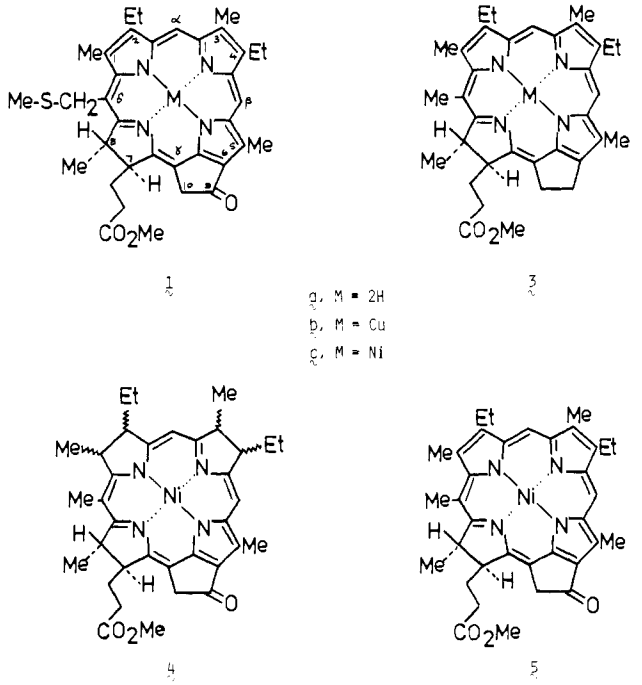


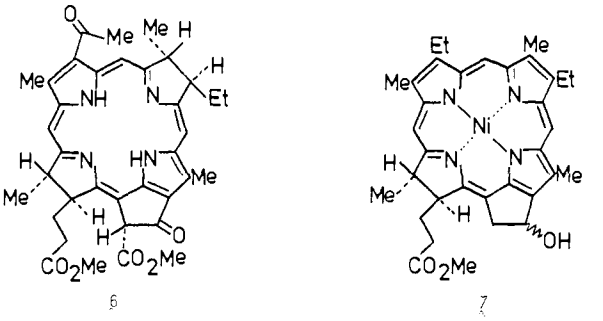
Figure 1. Structural formulas for the four possible δ-*meso*-methylisobacteriochlorins **2** derived from **1b** or **1c**.

as the copper(II) isobacteriochlorin (or a-tetrahydroporphyrin) **2a**. Assuming that the stereochemistry at ring D was unaffected,



compounds of type **2** could exist as four diastereomers: tcc or ttc (ring A cis) and tct or ttt (ring A trans) (see Figure 1).[3] When the nickel(II) complex **1c** was heated with 28 mass equiv of Raney Ni in methanol at 70 °C for 1.5 h, the starting material was completely consumed. The major gray–blue product (45%) was a nickel(II) isobacteriochlorin **2b**. In addition, royal-blue nickel(II) methyl δ-*meso*-methyl-9-deoxomesopyropheophorbide *a* (**3c**) was formed in 7% yield. A small amount of a purple material **4** (<2%) was also produced. This appeared to be a mixture of two nickel hexahydroporphyrins (three reduced rings). The three products were easily separable from each other (and the starting material) by using silica TLC and appeared to suffer little decomposition.

Nickel(II) isobacteriochlorin, **2b**, has a distinctive visible absorption spectrum with a strongly blue-shifted Q_y absorption at 598 nm (vs. 654 nm for starting material **1c**). The Soret band is split into two peaks at 414 and 393 nm. The effect of converting the dihydroporphyrin (chlorin) chromophore into a tetrahydroporphyrin has been calculated;[4] according to these calculations, the isobacteriochlorin chromophore, which has two adjacent rings reduced, should (and does) show a pronounced blue shift of the Q_y band relative to the parent chlorin, while a bacteriochlorin such as methyl bacteriopheophorbide *a* (**6**), which has opposite rings reduced, should show a pronounced red shift of the Q_y band to ca. 750 nm. No red shifted materials of this type were observed.



The Q_y band of the nickel(II) 9-deoxo compound **3c** at 600 nm also showed a strong blue shift, but the Soret band at 402 nm was not split. The spectrum of the nickel(II) hexahydroporphyrin **4** resembles that of nickel(II) isobacteriochlorin **2b** (see Experimental Section), though it is even more blue-shifted.

The mass spectra of **2b** and **3c** showed the expected parent ions at *m/e* 623 (84.6%) and 606 (47.0%), as did the nickel(II) hexahydroporphyrin fraction at *m/e* 625 (73.2%). The NMR spectra of **2b** and **3c** are informative and will be discussed in detail later. The most striking fact revealed by NMR is that **2b** is produced as mainly one diastereomer (>90%). This was also the case when the reduction was carried out in acetone at 40 °C or in THF under 1 atm of hydrogen at room temperature. In the latter cases, the stereoselectivity was also demonstrated by HPLC.

Nickel(II) hexahydroporphyrin **4** appeared to be a mixture of two compounds by NMR spectroscopy. In this case, repeated separation by silica TLC followed by reverse-phase high-performance liquid chromatography (RP HPLC) gave a major fraction, but efforts to obtain a clean NMR spectrum of this material were unsuccessful.

When the desulfurization of **1c** was performed in acetone at 40 °C for 1 h with 29 mass equiv of Raney Ni, the yield of **2b** (1%) was greatly reduced and no carbonyl reduction product **3c** was observed. The use of acetone to deactivate Raney Ni is well-known,[5] and it was thought that here the acetone might serve as a competitive substrate for carbonyl reduction, hence favoring production of the isobacteriochlorin. However, treatment of **1c** with 16 mass equiv of Raney Ni at 40° C for 26 h led only to production of a small amount of **2b**; the major product, **5**, was that of desulfurization alone. Retreatment with 46 mass equiv of Raney Ni for 53 h led to no significant increase in the amount of **2b** produced relative to **5** although, as before, no **3c** was observed (TLC). Therefore, the use of acetone at 40 °C appeared impractical for selectively obtaining a reasonable yield of **2b**. It must be noted that the reaction of the methylthiomethyl group of **1c** with Raney Ni is probably free-radical in nature and proceeds in 20 min or less at room temperature, while isobacteriochlorin formation and carbonyl reduction resemble catalytic hydrogenations. No 9-hydroxy compounds **7** were isolated, though they may well be intermediates in the production of **3c**. It is well-known (vide infra) that under the conditions used in our experiments,

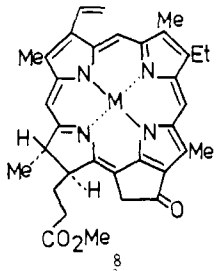
(3) The nomenclature is adapted from Eschenmoser and co-workers and refers to the stereochemical relationship between the 8-Me and 7-propionic side chain, 8-Me and 1-Me, and 1-Me and 2-Et groups, respectively: Angst, C.; Kajiwara, M.; Zass, E.; Eschenmoser, A. *Angew. Chem.* **1980**, *92*, 139–141.

(4) Barnard, J. R.; Jackman, L. M. *J. Chem. Soc.* **1956**, 1172–1178. Chang, C. K.; Hanson, L. K.; Richardson, P. F.; Young, R.; Fajer, J. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 2652–2656.

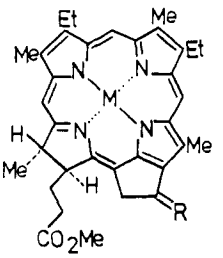
(5) Petit, G. R.; van Tamelen, E. E. *Org. React.* **1962**, *12*, 356–529.

Raney Ni will reduce a conjugated vinyl group at the 2-position to ethyl.

Prior to our initial observations in the δ-meso-substituted series, Mengler had investigated the Raney Ni reduction of nickel(II) methyl pyropheophorbide *a* (**8b**).[6] Thus, when **8b** was subjected



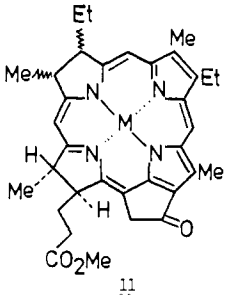
8



9, R = O
10, R = H_2
13, R = H,OH

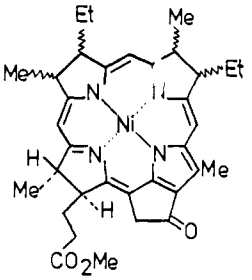
a, M = 2H
b, M = Ni
c, M = Zn

(400 mg) in diethyl ether to 6–6.5 g of ethanolic RaneyNi[7] under 1 atm of hydrogen for 18–20 h, nickel(II) methyl mesopyropheophorbide *a* (**9b**) (40%), nickel(II) methyl 9-deoxomesopyropheophorbide *a* (**10b**) (20%), a mixture of two inseparable nickel(II) isobacteriochlorins **11a** (20%) and a nickel(II) hexa-



11

a, M = Ni
b, M = Zn

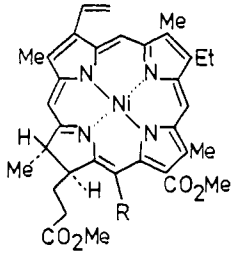


12

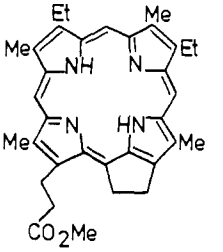
hydroporphyrin band **12** (<3%) were obtained, as well as some nickel(II) methyl 9-hydroxymesopyropheophorbide *a* (**13b**) (<3%).

Reduction of the 2-vinyl group of **8b** to give fully characterized 2-ethyl (meso) compound **9b** is not surprising. We have found that the 2-vinyl group of nickel(II) 2-vinylrhodochlorin dimethyl ester (**14**) and nickel(II) chlorin e_6 trimethyl ester (**15**) are similarly reduced by Raney Ni (see later).

The C-9 carbonyl reduction product **10b** was also fully characterized. Particularly significant were the mass spectrum, the blue-shifted Q_y band in the visible absorption spectrum, the loss



14, R = H
15, R = CH_2CO_2Me

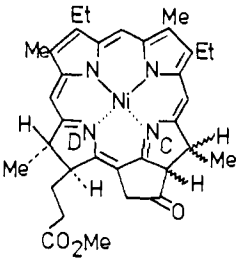


16

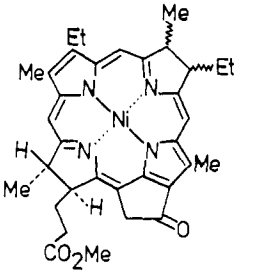
of the C-9 carbonyl stretch in the IR spectrum, and the appearance of a new (C-9) methylene group in the NMR spectrum, accompanied by a radical alteration in the appearance and chemical shift of the C-10 methylene group (see later). This compound was identical with that prepared by sodium borohydride reduction of methyl mesopyropheophorbide *a* (**9a**) to give 9-hydroxy compound **13a**, followed by hydrogenation over palladium on carbon and insertion of nickel(II). The benzoquinone oxidation of **10b**, synthesized by either route, followed by demetallation, gave the known porphyrin, deoxophylloerthyrin methyl ester (**16**).[8]

The empirical formula of the nickel(II) isobacteriochlorin fraction **11a** was established by elemental analysis. This fraction consisted of a 1:1 mixture of two diastereomers as judged by NMR spectroscopy. The presence of four methyl doublets, two for each isomer, clearly demonstrated the reduction of two rings in each compound. This mixture of isobacteriochlorins was stable to oxidation with *p*-benzoquinone in refluxing benzene; however, a trace of acid rapidly caused reoxidation to the chlorin (dihydroporphyrin) **9b**. Thus, removal of the nickel(II) with acid without reoxidation to the chlorin proved impossible.

Mengler[6] justified his assignment of structure **11a** (A and D rings reduced) rather than isomer **17** (C and D rings reduced) on three grounds: (1) the C-9 carbonyl stretch of the nickel(II) isobacteriochlorin fraction at 1665 cm^{-1} was only slightly different from that of nickel(II) methyl mesopyropheophorbide *a* (1685 cm^{-1}). Reduction of ring C would remove from C-9 carbonyl



17



18

from conjugation with the aromatic ring and should shift the absorbance to a significantly larger wavenumber.[9] (2) Inspection of Dreiding models suggested that reduction of ring C would even further increase the strain on the aromatic nucleus caused by the presence of isocyclic ring E. (3) The β-, α-, and δ-*meso* proton resonance of nickel(II) methyl mesopyropheophorbide *a* (**9b**) were assigned to 9.13, 8.79, and 8.0 ppm, respectively. The β-, α-, and δ-*meso* proton resonances of the **11a** diastereomeric mixture were assigned to 8.19, 7.02/7.08, and 6.48/6.39 ppm. Thus, Δδ for the δ-*meso* resonance was 0.94 ppm, for the α-*meso* ca. 1.7 ppm, and for the δ-*meso* 1.6 ppm. It was reasoned that the larger 1.6–1.7 ppm shifts were caused by a decrease in the local aromatic ring current due to reduction of the ring adjoining the *meso* protons in question. Such a large effect on *two* (the α and δ) *meso* protons could only happen if ring A was reduced. If ring C was reduced, the β-*meso* proton should show a much larger shift than the other two. The problem, of course, is that none of the assignments of the *meso* protons in **9b** and **11a** were certain, except for the δ-*meso* proton of **9b**. Thus, the assignment of the α- and β-*meso* proton resonances of **9b** to 9.13 and 8.79 ppm, respectively ($CDCl_3$, 50 mM), were not thoroughly justified.[6] At lower concentration (8.1 mM, $CDCl_3$, see later) the α- and β-*meso* protons of **9b** are shifted downfield to 9.26 and 8.99 ppm, suggesting aggregation at the higher concentration.[10] A better argument for reduction at ring A is that the 2-H (assigned independently) shows a 1.1–1.2-Hz coupling to the *meso* proton resonance at 7.03 ppm in one of the two **11a** diastereomers (see later). Thus, the original assignment of the 7.0 ppm resonance to the α-*meso* proton was correct.

It was also suggested[6] that the reduction of ring A proceeds in a cis fashion. Thus, the **11a** mixture would consist of the tcc and ttc isomers (Figure 1). This suggestion was based on the

(6) Mengler, C. D. Dissertation, Braunschweig, 1966.
(7) Pavlic, A. A.; Adkins, H. *J. Am. Chem. Soc.* **1946**, *68*, 1471.
(8) Smith, K. M.; Langry, K. C.; Minnetian, O. M. *J. Org. Chem.* **1984**, *49*, 4602–4609.
(9) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. "Spectrometric Identification of Organic Compounds", 4th ed.; Wiley: New York, 1981; p 117.
(10) Abraham, R. J.; Smith, K. M. *J. Am. Chem. Soc.* **1983**, *105*, 5734–5741.

Table I. Reductions of Nickel(II) Methyl Mesopyropheophorbide *a* (**9b**) with Raney Nickel

entry	**9b** mass, mg	Raney Ni mass, g	H_2, psi	solvent	*T*, °C	time, h	Ni 9-desoxo-**10b**, %	Ni iBc-**11a**, %	recovd **9b**, %
1	50.5	0.96		MeOH	70	3	22	7	37
2	269.0	4.42	12	$MeOH/CH_2Cl_2$	RT[b]	19	52		10
3	74.2	1.55	15	Et_2O/acetone	RT	15.5	17	9	46
4	44.5	0.98	20	acetone	RT	19		22	35
5	49.6	0.95	20	THF	RT	18.5	4	25	21
6	44.2	2.11	20	THF	RT	17.5	4	2	7
7	50.1	0.24	20	THF	RT	18.5		<25[a]	63
8	1088	17.3	20	THF	RT	16	52	18	

[a] Compound was impure. [b] Room temperature.

reported hydrogenation of magnesium(II) octamethyltetraazaporphyrin in the presence of palladium black, followed by demetallation with acetic acid, to give a tetrahydrotetraazaporphyrin.[11] The blue shift of the Q_y transition in the visible spectrum suggested the formation of the isobacteriochlorin analogue rather than bacteriochlorin analogue. Oxidative degradation of the tetrahydrotetraazaporphyrin product gave 2 mol of α,α-*meso*-dimethylsuccinimide, indicating that the hydrogenation proceeds in a syn fashion in this system. Since no dihydrotetraazaporphyrins were observed by visible spectroscopy during the reaction, Ficken et al. concluded that the addition of four hydrogen atoms to the same face of the tetraazaporphyrin occurs simultaneously, resulting in a cis–syn–cis stereochemical arrangement. Better evidence for the cis stereochemistry of the Raney Ni reduction in the isobacteriochlorin series is found in the NMR coupling constants of the vicinal hydrogens attached to reduced ring A (see later). Mengler also isolated a small amount of a polar, reddish-purple compound which was assigned nickel(II) hexahydroporphyrin structure **12**. This assignment was based on the similarity of its visible absorption spectrum to that observed by Eisner for a hexahydroporphyrin produced by sodium/isoamyl alcohol reduction of iron(II) octaethylporphyrin chloride[12] and by its partial reoxidation with *p*-benzoquinone in chloroform to give **11a** as the major product, plus a small amount of nickel(II) methyl mesopyropheophorbide *a* (**9**) and bacteriochlorin **18**. The reoxidation experiment established that the additional reduction occurred at ring B rather than ring C. Eschenmoser and co-workers have recently shown that the octaethylhexahydroporphyrin species originally characterized by Eisner is actually a mixture of four diastereomers.[13] However, the NMR spectrum of **12** supports a structure in which the three peripheral double bonds of rings A, B, and D are reduced (see later).

In view of recent interest in reduced porphyrin macrocycles, a further examination of the Raney Ni reduction of chlorins seemed desirable. One objective was to increase the selectivity of the reaction toward either the nickel(II) 9-deoxo compounds or the nickel(II) isobacteriochlorins. Separation of the two *meso*-unsubstituted diastereomeric nickel(II) isobacteriochlorins **11a** by HPLC seemed desirable, and examination of these and the major isomer **2b** produced in the *meso*-methyl series by NMR might allow an assignment of the stereochemistry of ring A reduction. Preparative HPLC would then allow isolation of sufficient quantities of all three isobacteriochlorins to crystallize for X-ray analysis. (Crystal studies of synthetic nickel(II) isobacteriochlorins have proven very interesting.[14]) Finally, we sought to establish whether nickel(II) hexahydroporphyrin **12** is produced as a single compound or as a mixture, and to identify the structures.

The experiments with nickel(II) methyl mesopyropheophorbide *a* (**9b**) (*meso*-unsubstituted) are summarized in Table I. Four basic sets of reaction conditions were investigated: (1) methanol at 70 °C; (2) methanol; (3) acetone; and, (4) THF at room temperature under hydrogen. The presence of water in the commercial Raney Ni slurry made use of diethyl ether as the solvent impractical.

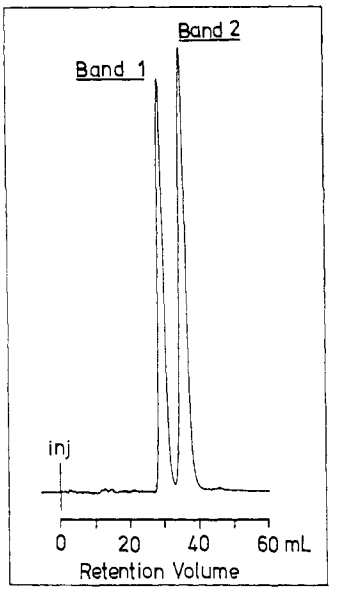


Figure 2. Semipreparative HPLC separation of nickel(II) δ-*meso*-unsubstituted isobacteriochlorins **11a** band 1 and **11a** band 2. Conditions: C-18 RP, 10 μM, Waters Z-module, 70/30 acetone/water, 1.0 mL/min, detector set at 594 nm.

Small-scale reduction of **9b** with 19 mass equiv of Raney Ni in methanol at 70 °C in a sealed tube, followed by preparative TLC, gave nickel(II) 9-deoxo compound **10b** (22%) and recovered starting material (37%) as the major products. Complete consumption of the starting material was never observed in any of the experiments listed in Table I. Nickel(II) isobacteriochlorin **11a** (7%) consisted of a 1:1 mixture of two isomers (NMR). These are cleanly separated by reversed-phase HPLC with 70/30 acetone/water as the eluent (Figure 2). The visible absorption spectra of the two diastereomers were indistinguishable. The NMR spectra are discussed later. A large-scale reaction (437 mg of **9b**, 7.8 g of Raney Ni, 70 °C, 2 h), followed by flash chromatography, gave mostly recovered starting material (ca. 60%), along with some **10b** and a low yield of **11a**. The nickel(II) isobacteriochlorins could not be obtained pure by preparative TLC. The first plating gave some starting material **9b**, plus a major blue–gray band which darkened considerably upon drying. This major blue–gray band contained nickel(II) isobacteriochlorins (596 nm, dichloromethane) as well as methyl mesopyropheophorbide *a* (**9a**) (656 nm). When the nickel(II) isobacteriochlorin-containing band was replated, two fractions were obtained; the faster-running band (656, 408 nm) appeared to be methyl mesopyropheophorbide *a*, while the slower-running blue–gray band was once again a mixture of methyl mesopyropheophorbide *a* (656 nm) and nickel(II) isobacteriochlorins (596 nm). One explanation for these observations is that some overreduction of **9b** to colorless compounds such as porphyrinogens (octahydroporphyrins) occurred. These colorless compounds apparently separated with nickel(II) isobacteriochlorin mixture **11a** on TLC and, upon exposure to air, were reoxidized to the dihydroporphyrin stage. The

(11) Ficken, G. E.; Linstead, R. P.; Stephen, E.; Whalley, M. *J. Chem. Soc.* 1958, *3879*–3886.
(12) Eisner, U. *J. Chem. Soc.* **1957**, 3461–3469.
(13) Johansen, J. E.; Angst, C.; Kratky, C.; Eschenmoser, A. *Angew. Chem.* **1980**, *92*, 141–143.
(14) Kratky, C.; Angst, C.; Johansen, J. *Angew. Chem.* **1981**, *93*, 204–205.

Table II. Proton NMR Spectra of Nickel(II) Isobacteriochlorins[a]

reson	Ni iBc (band 1) **11a**	Ni iBc (band 2) **11a**	Ni δ-Me-iBc **2b**	Ni Me-mesopyro *a*[b] **9b**
meso				
β	8.185	8.203	8.201	9.26
α	7.086 (s)	7.033 (d, $J_{2,\alpha}$ = 1.1 Hz)	6.994 (d, $J_{2,\alpha}$ = 1.2 Hz)	8.99
δ	6.399	6.506		8.08
10-CH_2				
H_a	4.220 ($J_{a,b}$ = 19.6 Hz)	4.203 ($J_{a,b}$ = 19.7 Hz)	4.227 ($J_{a,b}$ = 19.6 Hz)	4.85 ($J_{a,b}$ = 19.7 Hz)
H_b	4.172	4.173	4.180	4.75
1-H	3.878 ($J_{1,2}$ = 7.8, $J_{1,1a}$ = 8.0 Hz)	3.762 ($J_{1,2}$ = 7.7, $J_{1,1a}$ = 7.0 Hz)	3.875 ($J_{1,2}$ = 7.4, $J_{1,1a}$ = 6.9 Hz)	
7d-OMe	3.641	3.637	3.626	3.60
2-H	3.479 ($J_{2,2a}$ = 4.6, $J_{2,2a'}$ = 4.0 Hz)	3.570 ($J_{2,2a}$ = 3.9, $J_{2,2a'}$ = 10.6 Hz)	3.510 ($J_{2,2a}$ = 3.8, $J_{2,2a'}$ = 10.9 Hz)	
8-H	3.520 ($J_{7,8}$ = 1.0, $J_{8,8a}$ = 7.2 Hz)	3.503 ($J_{7,8}$ = 1.0, $J_{8,8a}$ = 7.2 Hz)	3.63 ($J_{8,8a}$ = 6.9 Hz)	4.25 "q", ($J_{7,8}$ < 1.0, $J_{8,8a}$ = 7.2 Hz)
7-H	3.280 ($J_{7,7a}$ = $J_{7,7a'}$ = 7.1 Hz)	3.284 ($J_{7,7a}$ = 6.9 Hz)	3.220 ($J_{7,7a}$ = 6.0, $J_{7,7a'}$ = 8.2 Hz)	3.96 (m)
4a-CH_2				
H_a	3.157 ($J_{4a,4a'}$ = −14.1 Hz)	3.163 ($J_{4a,4a'}$ = −14.0 Hz)	3.172 ($J_{4a,4a'}$ = −14.4 Hz)	3.54 (q)[d]
H_b	3.127 ($J_{4a,4b}$ = $J_{4a',4b}$ = 7.5 Hz)	3.133 ($J_{4a,4b}$ = $J_{4a',4b}$ = 7.5 Hz)	3.135 ($J_{4a,4b}$ = $J_{4a',4b}$ = 7.4 Hz)	
δ-Me			2.680	
5-Me	2.986[c]	2.992[c]	2.997[c]	3.46[c]
3-Me	2.589[c]	2.594[c]	2.561[c]	3.02[c]
7b-CH_2				
H_b	2.356 ("t")	2.339 ("t")	2.339 ($J_{7a,7b}$ = $J_{7a',7b'}$ = 6.0;	2.1–2.4 (m)
$H_{b'}$			2.293 ($J_{7a',7b}$ = $J_{7a,7b'}$ = 8.8; $J_{7b,7b'}$ = −15.2)	
2a-CH_2				
H_a	1.76 ($J_{2a,2a'}$ = −13.6, $J_{2a,2b}$ = $J_{2a',2b}$ = 7.2 Hz)	2.26 ($J_{2a,2a'}$ = −14, $J_{2a,2b}$ = $J_{2a',2b}$ = 7.3 Hz)	2.30 ($J_{2a,2a'}$ = −13.4, $J_{2a,2b}$ = $J_{2a',2b}$ = 7.3 Hz)	3.53 (q)[d]
$H_{a'}$	1.35	2.01	2.08	
7a-CH_2				
H_a	1.973 ($J_{7a,7b}$ = 6.8 Hz)	1.96 (center of (m))	1.961 ($J_{7a,7a'}$ = −14.0 Hz)	2.1–2.4 (m)
$H_{a'}$	1.962 ($J_{7a',7b}$ = 8.2 Hz)		1.787	
4b-Me	1.384 (t, J = 7.5 Hz)	1.395 (t, J = 7.5 Hz)	1.398 (t, J = 7.4 Hz)	1.60 (t, J = 7.6 Hz)[e]
8-Me	1.273 (d, $J_{8,8a}$ = 7.2 Hz)	1.278 (d, $J_{8,8a}$ = 7.2 Hz)	1.188 (d, $J_{8,8a}$ = 6.9 Hz)	1.53 (d, $J_{8,8a}$ = 7.2 Hz)
2b-Me	0.817 (t, J = 7.2 Hz)	1.261 (t, J = 7.3 Hz)	1.291 (t, J = 7.3 Hz)	1.60 (t, J = 7.6 Hz)[e]
1-Me	1.615 (d, $J_{1,1a}$ = 8.0 Hz)	1.088 (d, $J_{1,1a}$ = 7.0 Hz)	1.013 (d, $J_{1,1a}$ = 6.9 Hz)	3.12[c]

[a] In $CDCl_3$ with TMS as reference. Concentrations (mM): Ni iBc band 1 (16.5); Ni iBc band 2 (5.8); Ni δ-Me-iBc (23.4); Ni Me-mesopyro *a* (8.1). Multiplets in quotes (" ") indicate deceptively simple multiplets which were not completely analyzed. The signs of the geminal couplings were not determined. [b] Chemical shifts unchanged upon addition of excess pyridine-d_5. [c] The assignment of the Me singlets is tentative. [d] Overlapping quartets. [e] Overlapping triplets.

nickel(II) was probably lost at the porphyrinogen stage, so that reoxidation gave metal-free material (**9a**) rather than **9b**. Similar results were obtained when reduction of zinc(II) methyl mesopyropheophorbide *a* (**9c**) was attempted under these conditions. The initial TLC separation of zinc(II) methyl 9-deoxomesopyropheophorbide *a* (**10c**), unreacted starting material, and zinc(II) isobacteriochlorins **11b** appeared clean. However, spectrophotometry showed that the alleged zinc(II) isobacteriochlorins (598 nm) were contaminated with a material absorbing at 644 nm (dichloromethane), probably zinc(II) methyl mesopyropheophorbide *a*. When the mixed band was rechromatographed, at least four products were observed.

Finally, metal-free methyl mesopyropheophorbide *a* (**9a**) was reacted with 16 mass equiv of Raney Ni in THF under 20 psi of hydrogen at room temperature for 23 h. Preparative TLC gave a major gray–blue band running distinctly slower than the starting material. This band darkened on the plate and appeared to be a mixture of at least two compounds (656 and 594 nm). An attempt to further purify this material by flash chromatography under nitrogen resulted only in the isolation of methyl mesopyropheophorbide *a* (TLC and visible spectrum identical with an authentic sample). Mengler also reported that Raney Ni reduction of **9a** led to porphyrinogen, which reoxidized to a chlorin–phlorin.[6]

Fortunately, the difficulties described above were not encountered when the reaction of **9b** with Raney Ni was carried out under hydrogen at room temperature. Four features of these experiments deserve comment: (1) The use of methanol as solvent definitely favors production of nickel(II) 9-deoxo compound **10b** over nickel(II) isobacteriochlorin **11a** (Table I, entry 2). (2) Use of acetone as the solvent favored production of **11a** over **10b**; however, the solvent reacted with the Raney Ni to give isopropyl alcohol, and this may have contributed to the poor conversion. (3) There is probably an optimal "catalyst" loading (compare entries 5, 6, and 7); too much Raney Ni can lead to loss of substrate due to adsorption, while too little leads to poor conversion. (4) It appeared that hydrogen pressure affected the product distribution.

The results of a large-scale reduction of **9b** are shown in Table I, entry 8. The reduction was first carried out with 16 mass equiv of Raney Ni in THF under 20 psi of hydrogen for 16 h. The catalyst was then filtered off and the crude product purified by flash chromatography on silica under nitrogen. The unreacted starting material was resubjected to Raney Ni under 24 psi of hydrogen for 16.5 h. This time, **10b** was the major product and virtually no **11a** was produced. Thus, the subtle change from 20 to 24 psi of hydrogen may have affected the product distribution. The overall 52% yield of **10b** (entry 8, Table I) is clearly inconsistent with the trend for the smaller-scale reactions in THF (entries 5, 6, and 7). The nickel(II) isobacteriochlorin fraction (18%) was, as expected, a mixture of two diastereomers. This mixture was separated by preparative RP HPLC without suffering any apparent decomposition. Similarly, δ-*meso*-methylthiomethyl-substituted nickel(II) complex **1c** (459 mg) was reacted with 15 mass equiv of Raney Ni in THF under 15 psi of hydrogen for 15.5 h to give nickel(II) 9-deoxo compound **3c** (ca. 30%), some unreacted starting material, and nickel(II) isobacteriochlorin **2b** (30%). Again, the nickel(II) δ-*meso*-methylisobacteriochlorin fraction showed only a single peak on analytical HPLC.

NMR Spectra of Isobacteriochlorins and Hexahydroporphyrins. The NMR spectral data for δ-*meso*-unsubstituted nickel(II) isobacteriochlorins **11a** (bands 1 and 2), nickel(II) methyl δ-*meso*-methylisobacteriochlorin **2b**, and nickel(II) methyl mesopyropheophorbide *a* **9b** are presented in Table II. The assignments were made on the basis of exhaustive decoupling experi-

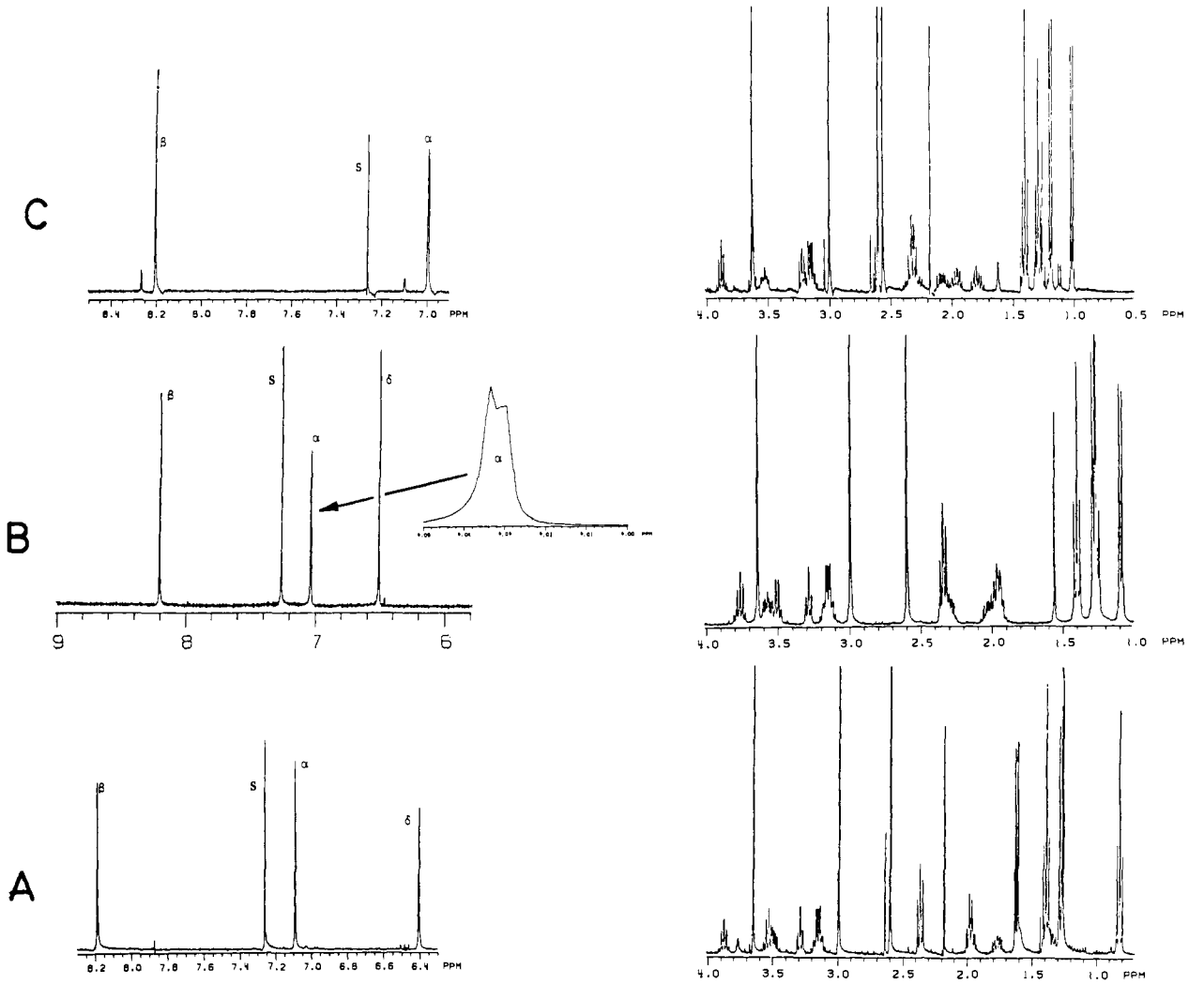


Figure 3. Meso (left) and high-field (right) proton regions in the 360-MHz NMR spectra of nickel(II) isobacteriochlorins. A, **11a** band 1; B, **11a** band 2; C, δ-*meso*-methyl compound **2b**. (S = $CHCl_3$.)

ments. Coupling constants were determined by inspection or, in the case of the more complex multiplets such as the 2-H, 2a-H, 2a′-H, 4a-CH_2, 7a-CH_2, and 7b-CH_2, from computer simulation. The couplings obtained from these analyses are considered accurate to 0.5 Hz or better, and were internally self-consistent: that is, the couplings common to the analysis of different multiplets, for example, the 2-H and 2a-H, were found to be the same in each case to this degree of accuracy. The high-field and *meso* proton regions of the NMR spectra of the three isobacteriochlorins are shown in Figure 3. Two high-field doublets in each compound are due to the 1-Me and 8-Me. One set of doublets appears at 1.19–1.27 ppm in the three compounds, while the second set has two doublets at 1.01 (**2b**) and 1.09 (**11a** band 2) and the third at 1.61 ppm (**11a** band *1*). Since the difference between **11a** bands 1 and 2 lies in the stereochemistry of reduction at ring A, these data strongly suggest that the second set of doublets belongs to the 1-Me, as assigned. Furthermore, the similarity of the 1-Me shifts for **11a** band 2 and **2b** suggests that they have the same relative stereochemistry at ring A, while **11a** band 1 has the opposite relative stereochemistry.

The assignments of the 1- and 8-Me groups were confirmed independently. Decoupling the multiplets at 3.88 (**11a** band 1), 3.76 (**11a** band 2), and 3.88 ppm (**2b**) collapsed the doublets provisionally assigned to the 1-Me at 1.61, 1.09, and 1.01 ppm, respectively, to singlets. Similarly, decoupling the multiplets at 3.52 (**11a** band 1), 3.50 (**11a** band 2), and 3.63 ppm (**2b**) collapsed the doublets provisionally assigned to the 8-Me at 1.27, 1.28, and 1.19 ppm, respectively. Thus, the two sets of lower field multiplets represent H-1 and H-8. The question of unique identity can be answered if one assumes that the stereochemistry at ring D has not changed during the course of the Raney Ni reduction. With this assumption, the trans $J_{7,8}$ coupling constant should be 2 Hz or less. Thus, decoupling H-8 will only have a small effect on H-7 and vice versa. It also means that decoupling the 8-Me will show H-8 either as a doublet, J = 1–2 Hz, or, if $J_{7,8}$ is even smaller, as a broadened singlet. Decoupling the high-field doublets assigned to the 8-Me collapsed the muliplets assigned to H-8 to broadened *singlets* in all three cases. Decoupling the high-field doublets assigned to the 1-Me collapsed the multiplets assigned to the 1-H into *doublets*, with J = 7.4–7.8 Hz. Thus, the original assignments were confirmed, and the $J_{1,2}$ coupling was found to be ca. 7.5 Hz. This suggests that the stereochemistry of A ring reduction is cis.

The assignment of H-1 and H-8 made it possible to assign H-2 and H-7 by examination of the remaining decoupling experiments. In **11a** band 2 and **2b**, H-2 shows a 1.1–1.2-Hz coupling to a low-field doublet at ca. 7.0 ppm: this must be the α-*meso* proton. Assuming the β-*meso* proton to be the least affected by ring A reduction, and hence to lowest field, this allows complete assignment of the *meso* resonances.

The protons of the 2a-CH_2 group are diastereotopic, occurring at 1.76 and 1.35 ppm in **11a** band 1, 2.26 and 2.01 ppm in **11a** band 2, and at 2.30 and 2.08 ppm in **2b**. The 2b-Me groups resonate at 0.82 (**11a** band 1), 1.26 (**11a** band 2), and 1.29 ppm (**2b**). Again, the similarity between **11a** band 2 and **2b** is apparent. All the protons of the 2-Et group are deshielded in **11a** band 2 and **2b** relative to **11a** band 1. The assignments of the 2a-H and 2a′-H were made by decoupling experiments with the 2-H and the 2b-Me. The 2a-H resonances in **11a** band 2 and **2b** were

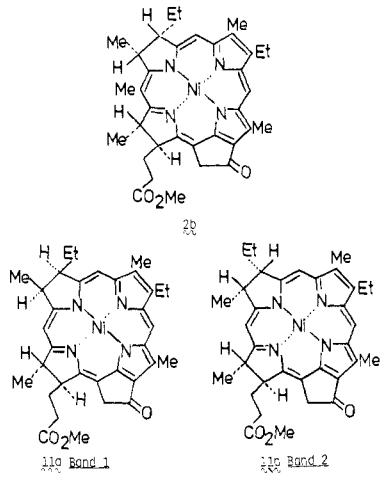


Figure 4. Proposed structures for nickel(II) isobacteriochlorins.

partially obscured by the 7a-CH_2, but decoupling of the 7b-CH_2 allowed the chemical shifts of the 2a-H to be determined.

The 4a-CH_2 protons are also diastereotopic, giving an ABX_3 pattern in all three cases. The 7b-CH_2 appears as a pseudotriplet at ca. 2.3 ppm in all three cases, while the 7a-CH_2 is a multiplet at ca. 1.96 ppm in **11a** bands 1 and 2. In **2b**, the 7a-CH_2 protons are more clearly diastereotopic, resonating at 1.96 and 1.79 ppm. Thus, the isobacteriochlorins differ from chlorins, which generally show four distinct absorbances for the 7a,b-CH_2CH_2-group, i.e., the anisochrony is considerably reduced in this region. This could be due to a lack of conformational preference about the C7a–C7b bond, leading to more equal rotamer populations.

Finally, the 3- and 5-Me groups occur as singlets at 2.56–2.59 and 2.99 ppm in all three isobacteriochlorins. The exact assignments are only tentative. The remaining singlet at 2.68 ppm in **2b** was assigned to the *δ-meso*-Me. Thus, the *δ-meso*-Me experiences a 0.75 ppm upfield shift upon reduction of ring A (compared with the *δ-meso*-Me of nickel(II) meso-Bmph-*d*[Et, Me] **5** assigned to 3.44 ppm). This is consistent with the general upfield shifts experienced by the other peripheral substituents in the isobacteriochlorins (Table II). The *meso* protons, bonded directly to the conjugated π system, are more strongly affected.

The conformation of the 2-Et side chain about C-2 appears to be quite different in **11a** band 1 from **11a** band 2 and **2b**. Thus, the $^3J_{2,2a}$ and $^3J_{2,2a'}$ couplings are approximately equal (4.0 and 4.6 Hz) in **11a** band 1, while they are quite different (10.6–10.9, 3.8–3.9 Hz) in **11a** band 2 and **2b**. The latter values are similar to those of the 7a- and 7a′-H about C-7 in chlorins and suggest a preferred conformation for the 2-Et group in these cases. Without more knowledge of the bond angles at C-2, it is difficult to calculate rotamer populations, however.[15]

The proposed structures for the three nickel(II) isobacteriochlorins shown in Figure 4 are based on the similarities between **11a** band 2 and **2b** in the NMR and the assumption that steric repulsion between the 8-Me and the *δ-meso*-Me would trend to push the latter "above" the plane of the molecule. Cis hydrogenation of **5** from the β-face would then be preferred in order to prevent crowding between the *δ-meso*-Me and 1-Me groups in nickel(II) isobacteriochlorin **2b**. The preliminary results of an X-ray crystal structure analysis[16] of **11a** band 2 have confirmed this hypothesis.

The NMR spectrum of the *meso*-unsubstituted nickel(II) hexahydroporphyrin **12** is shown in Figure 5, and the assignments are presented in Table III. Only a small amount of material was available, but extensive decoupling experiments were performed, and the coupling network was completely established. The spectrum of **12** shows the presence of a small amount of another compound. Judging by the three small *meso* resonances at ca. 6.8 and 6.1–6.2 ppm, this compound is another nickel(II) hexahydroporphyrin, rather than a nickel(II) tetrahydroporphyrin. The discussion which follows concerns only the major isomer of **12**. Three doublets assigned to the 1-, 3-, and 8-Me groups appear at 1.46, 1.04, and 1.20 ppm. This is convincing evidence that the hydrogenation has occurred across the peripheral double bonds of **9b** rather than across a methine bridge as proposed by Eschenmoser and co-workers for their octaethylhexahydroporphyrin. The assignment of the ring Me groups once again hinges on the same logic as in the case of the isobacteriochlorins; namely, we assume that the reduction has not affected the trans stereo-

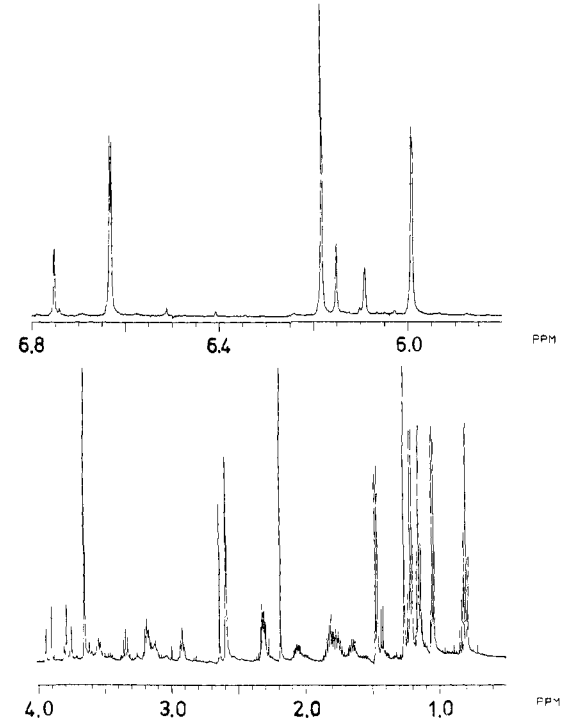


Figure 5. Proton NMR spectra (360 MHz) of nickel(II) hexahydroporphyrin, **12**.

Table III. Proton NMR Spectra of Hexahydroporphyrin **12**[a]

resonance	shift	(coupling)
meso		
β	6.63	(d, $J_{\beta,4}$ = 1.8 Hz)
α	6.18	(s)
δ	5.99	(d, $J_{\delta,1}$ = 1.1 Hz)
10-CH_2		
Ha	3.91	(AB q, J = 19.3 Hz)
Hb	3.77	
7d-OMe	3.65	
1-H	3.54	(m, $J_{1,2}$ = 7.3, $J_{1,1a}$ = 7.0 Hz)
3-H	3.34	(m, $J_{3,4}$ = 7.8, $J_{3,3a}$ = 7.0 Hz)
8-H	3.19	(m, $J_{7,8}$ < 1.0, $J_{8,8a}$ = 7.2 Hz)
2-H	3.16	(m, $J_{2,2a'}$ = 8.5 Hz)
4-H	3.11	(m)
7-H	2.91	(t, J = 7.0 Hz)
7b-CH_2	2.31	(m)
4a-H	2.06	(m, $J_{4,4a}$ = 4.1, $J_{4a,4a'}$ = −13.4, $J_{4a,4b}$ = 7.3 Hz)
7a-CH_2	1.72–1.86	(m)
4a′-H	1.78	(m)
2a-H	1.64	(m, $J_{2,2a}$ = 4.6, $J_{2a,2a'}$ = −13.9, $J_{2a,2b}$ = 7.4 Hz)
2a′-H	1.1–1.2	(obsc m)
1a-Me	1.46	(d, J = 7.0 Hz)
8a-Me	1.20	(d, J = 7.2 Hz)
4b-Me	1.15	(t, J = 7.3 Hz)
3a-Me	1.04	(d, J = 7.0 Hz)
2b-Me	0.79	(t, J = 7.4 Hz)

[a] In $CDCl_3$, chemical shifts relative to TMS, coupling constants in hertz.

(15) Smith, K. M.; Goff, D. A.; Abraham, R. J. *Tetrahedron Lett.* **1981**, *22*, 4873–4876.
(16) Fajer, J.; Barkigia, K. M.; Smith, K. M.; Goff, D. A. unpublished results.

Table IV. Proton NMR Spectra of Methyl 9-Deoxomesopyropheophorbide *a* (**10a**) and Derivatives[a]

resonance	[Ni δ-*meso*-Me(**10a**)] **3c**	[δ-*meso*-Me(**10a**)] **3a**	[Ni(**10a**)] **10b**	**10a**
meso				
α	9.13	9.81	9.26	9.82
β	9.07	9.45	9.25	9.64
δ			8.30	8.92
10-CH_2				
H_a	4.48 ($J_{10a,10b}$ = 15.6, $J_{10a,9a}$ = $J_{10b,9b}$ = 8.0 Hz)	4.87 (m, 2 H)	4.46 ($J_{10a,10b}$ = 15.4, $J_{10a,9a}$ = 8.0 Hz)	4.95 ($J_{10a,10b}$ = 16.0, $J_{10a,9a}$ = $J_{10b,9b}$ = 6.9 Hz)
H_b	4.09 ($J_{10a,9b}$ = 2.6, $J_{10b,9a}$ = 3.0 Hz)		4.30 ($J_{10a,9b}$ = 2.9, $J_{10b,9a}$ = 3.4, $J_{10b,9b}$ = 8.1 Hz)	4.83 ($J_{10a,9b}$ = 3.6, $J_{10b,9a}$ = 3.2 Hz)
9-CH_2				
H_a	3.80	ca. 4.04 (obsc)	3.65–3.75 (obsc)	4.07 (overlapped)
H_b	ca. 3.6–3.7	ca. 4.04 (obsc)	3.65–3.75 (obsc)	4.07 (overlapped)
8-H	4.34 (q, $J_{8,8a}$ = 7.0, $J_{7,8}$ < 1.0 Hz)	4.67 (q, $J_{8,8a}$ = 7.1, $J_{7,8}$ < 1.0 Hz)	4.34 (q, $J_{8,8a}$ = 7.2, $J_{7,8}$ < 1.0 Hz)	4.68 (AMX_3, $J_{8,8a}$ = 7.2, $J_{7,8}$ = 2.1 Hz)
7-H	4.22 (t)[b]	4.32 (dd, $J_{7,7a}$ = 3.1, $J_{7,7a'}$ = 8.7 Hz)	4.09 (dd, $J_{7,7a}$ = 4.6, $J_{7,7a'}$ = 8.3 Hz)	4.51 (AMXY, $J_{7,7a}$ = 2.8, $J_{7,7a'}$ = 9.0 Hz)
2a-CH_2	3.6–3.7 (m)	4.06 (q, J = 7.7 Hz)	3.67–3.72 (m)	4.07 (m, overlapped) and
4a-CH_2	3.6–3.7 (m)	3.84 (q, J = 7.7 Hz)	3.67–3.72 (m)	3.90 (q, J = 7.6 Hz)
7d-OMe	3.61	3.54	3.58	3.58
δ-Me	3.30	4.03		
1-Me	3.21	3.53	3.27	3.53
3-Me	3.20	3.46	3.25	3.49
5-Me	3.18	3.45	3.13	3.48
7a	2.0–2.5	2.58	2.30	2.81
7a′	2.0–2.5	2.21	2.13	2.39
7b	2.0–2.5	2.56	2.48	2.60
7b′	2.0–2.5	2.11	2.24	2.20
2b-Me	1.60 (t, J = 7.6 Hz)	1.750 (t, J = 7.7 Hz)	1.64 (t, J = 7.7 Hz)	1.81 (t, J = 7.5 Hz)
4b-Me	1.60 (t, J = 7.6 Hz)	1.754 (t, J = 7.7 Hz)	1.64 (t, J = 7.7 Hz)	1.79 (t, J = 7.5 Hz)
8-Me	1.13 (d, J = 7.0 Hz)	1.52 (d, J = 7.1 Hz)	1.51 (d, J = 7.2 Hz)	1.86 (d, J = 7.2 Hz)
NH		−0.47, −3.02		−1.66 −3.50

[a] In $CDCl_3$ solution, with TMS (**3c**) or $CHCl_3$ (7.260 ppm) as reference. Concentrations (mM): **3c** (11.0); **3a** (22.0); **10a** (3.0). [b] Assignment uncertain.

chemistry of ring D and, therefore, that $J_{7,8}$ in the hexahydroporphyrin remains 2 Hz or less. Decoupling the multiplets at 3.19, 3.34, and 3.54 ppm, respectively, collapsed the doublets at 1.20, 1.04, and 1.46 ppm. Conversely, decoupling the doublet at 1.20 collapsed the multiplet at 3.19 ppm to a broad singlet; decoupling the doublet at 1.04 collapsed the multiplet at 3.34 ppm to a doublet, J = 7.8 Hz, while irradiating the doublet at 1.46 ppm collapsed the multiplet at 3.54 ppm to a doublet, J = 7.3 Hz. Thus, the assignment of the 8-Me at 1.20 ppm and the 8-H at 3.19 ppm was confirmed. The remaining two sets of resonances at 1.46 (d) and 3.54 (m) ppm and 1.04 (d) and 3.34 (m) ppm are due to the 1-H and 1-Me and the 3-H and 3-Me.

The assignment of the multiplet at 2.91 ppm to the 7-H was based on the following: decoupling the multiplet at ca. 1.8 ppm assigned to the 7a-CH_2 collapses the resonance at 2.91 ppm to a doublet with a small (<2 Hz) coupling. If the signal at 2.91 ppm was due to either the 2-H or the 4-H, decoupling the adjacent 2a- or 4a-CH_2 would give a doublet with J = 7.3–7.8 Hz ($J_{1,2}$ or $J_{3,4}$), which is clearly not the case. Thus, by elimination, the three-proton multiplet at 3.1–3.2 ppm consists of the 2-H, 4-H, and 8-H. A careful examination of this region shows that the three protons can be distinguished. The proton at 3.19 ppm is the 8-H. The proton at ca. 3.16 ppm is coupled to a one-proton multiplet at 1.64 ppm. This multiplet is in turn coupled to a multiplet buried at 1.1–1.2 ppm and to the triplet at 0.79 ppm. Decoupling experiments on each of these resonances showed complete internal consistency. Similarly, the proton at 3.11 ppm was coupled to one-proton multiplets at 2.06 and ca. 1.78 ppm, which were both coupled to the triplet at 1.15 ppm. Thus, the two sets, 3.16, 1.64, 1.1–1.2, and 0.79 and 3.11, 2.06, 1.78, and 1.15 ppm, represent the 2-H, 2a-H, 2a′-H, and 2b-Me and the 4-H, 4a-H, 4a′-H, and 4b-Me.

There are two additional pieces of information. The multiplet at 3.54 ppm (1-H or 3-H) is coupled with the *meso* proton doublet at 5.99 ppm (J = 1.1 Hz, α- or δ-*meso* H). Similarly, the multiplet at 3.11 ppm (2-H or 4-H) is coupled to the *meso* proton doublet at 6.6 ppm (J = 1.8 Hz, α- or β-*meso* H). Since the β-*meso* position is the only one not flanked by two reduced rings, the lowest field doublet at 6.6 ppm is assigned to the β-*meso* H. Thus, the 3.11 ppm signal is due to the 4-H, while that at 3.16 ppm is due to the 2-H.

The assignments of the protons of the 2- and 4-Et groups then follow accordingly. To complete the assignment of the 1-H, 1-Me and 3-H, 3-Me pairs, the two remaining *meso* proton resonances at 5.99 ppm (d, coupled to the multiplet at 3.54 ppm) and 6.17 (s) ppm need to be assigned. It seems reasonable to assume that the lowest field resonance at 5.99 ppm is due to the δ-*meso* H, but this is insufficient proof. However, decoupling the multiplet at 3.54 ppm affects the multiplet at 3.16 ppm (assigned to the 2-H) but does not affect the multiplet at 3.11 ppm (assigned to the 4-H). Thus, the multiplet at 3.54 ppm is assigned to the 1-H, from which the rest of the assignments in Table III follow automatically. Thus, the δ-*meso* proton at 5.99 ppm is coupled to the 1-H at 3.55 ppm and the β-*meso* proton at 6.6 ppm is coupled to the 4-H at 3.11 ppm.

The differences between **12** and the two nickel(II) tetrahydroporphyrins **11a** band 2 and **2b**, which show coupling between the 2-H and the α-*meso* proton, is intriguing. If one adopts the suggestion of Linstead et al.[11] and Mengler[6] that the four additional hydrogen atoms are attached to the same face of **9b**, then that leaves two possible structures, tcccc and ttccc, for **12**.

The NMR spectral data of methyl 9-deoxomesopyropheophorbide *a* (**10a**) and its δ-*meso*-methyl-substituted and nickel(II)-complexed derivatives are presented in Table IV. The new methylene group created by reduction of the C-9 carbonyl was assigned to the broad absorbances at ca. 4 ppm in the metal-free compounds and at 3.6–3.75 ppm in the nickel(II) complexes. Unfortunately, in each case, this multiplet was overlapped by the 2a- or 4a-methylene absorption. Decoupling this region, however, simplified the signals assigned to the 10-CH_2 at lower field. This assignment is intuitive but seems reasonable in light of the overlap of the 9-CH_2 with the similarly situated β-pyrrolic 2a- and 4a-CH_2 groups. The straightforward analysis of the downfield 10-CH_2 gives all the coupling constants except $J_{9a,9b}$. In the case of δ-*meso*-methyl free-base **3a**, the 10a,b-H were too closely coupled to allow an analysis.

Table V. Proton NMR Data for Some Chl-*a* Derivatives: Methyl-Free vs. Ni Complex[a]

resonance	**8a** Me pyropheo *a*	**9a** Me mesopyropheo *a*	**9b** Ni Me mesopyro *a*	meso-Bmph-[Et, Me]	**5** Ni meso-Bmph-*c* [Et, Me]
meso					
α	9.40	9.20	8.99	9.36[f]	8.83[f]
β	9.52	9.47	9.26	9.47[f]	9.17[f]
δ	8.56	8.45	8.08		
2a	8.02	3.83	3.53[d]	3.92	3.53
2b	6.29	1.73[c]	1.60	1.72[c]	1.58[c]
2b′	6.18	1.73[c]	1.60	1.72[c]	1.58[c]
10-CH_2	5.27	5.24	4.85	5.26	4.85
	5.11	5.09	4.75	5.21	4.63
8-H	4.49	4.45	4.25	4.58	4.28
7-H	4.30	4.27	3.96	4.19	3.81
4a-CH_2	3.70	3.68	3.54[d]	3.72	3.53
7d-OMe	3.61	3.61	3.60	3.58	3.61
δ-Me				3.90	3.44[e]
5-Me	3.68	3.66	3.46	3.68	3.22[e]
1-Me	3.41	3.29	3.12	3.43	3.10
3-Me	3.25	3.25	3.02	3.30	3.10
7a	2.70	2.64–2.74[b]	2.12–2.4	2.48–2.53	2.01
7a′	2.31	2.22–2.36	2.12–2.4	2.48–2.53	2.01
7b	2.56	2.50–2.60	2.12–2.4	2.15–2.21	2.38
7b′	2.29	2.2–2.36	2.12–2.4	2.15–2.21	2.32
4b-Me	1.70	1.70[c]	1.60	1.71[c]	1.57[c]
8-Me	1.81	1.80	1.53	1.52	1.22
NH	0.48, −1.67	0.63, −1.60		−1.65	

[a] Concentrations ($CDCl_3$; mM): **8a** (7.0), **9b** (8.1), **5** (5.4). [b] Assignment of the 7a,b-CH_2CH_2 by analogy to **8a**.[15] [c–f] Assignments of these pairs may be interchanged.

The general effect of reducing the C-9 carbonyl is to shift most of the resonances 0.3–0.4 ppm downfield. This can be seen by comparison of the 9-deoxo compounds with the corresponding 9-keto compounds (Table V). This effect agrees with the observed increase of ca. 10% in the aromatic ring current when the 9-carbonyl group was converted into its ethylene ketal.[17] The only significant effect of the *meso*-methyl group is to deshield the neighboring 8-Me. This steric effect has been previously observed with bulky *meso* substituents such as bromine.[18]

The insertion of nickel(II) into the macrocycle causes significant changes. Addition of 5 mol equiv of pyrrolidine or pyridine to the $CDCl_3$ solutions of the nickel(II) 9-deoxo derivatives did not alter the chemical shifts, thereby excluding aggregation as the source. A comparison of the pairs **3c**/**3a** and **10b**/**10a** shows that most of the resonances in the nickel(II) 9-deoxo compounds are shifted upfield 0.1–0.5 ppm relative to the 9-deoxo compounds. The largest effect was observed for the δ-*meso*-methyl group of **3c** which is shielded by at least 0.7 ppm. This general effect could be due to electron donation by the Ni atom and/or buckling of the chlorin ring. The effect also extends to a comparison of the 9-keto compounds (Table V). Thus, most of the resonances of nickel(II) methyl mesopyropheophorbide *a* (**9b**) and nickel(II) methyl δ-*meso*-methyl-Bmph-*c* [Et, Me] (**5**) experience 0.1–0.6 ppm upfield shifts relative to the corresponding free bases.

When zinc(II) octaethylporphyrin or nickel(II) octaethylchlorin was subjected to Raney Ni in THF under hydrogen overnight, only starting material was recovered. In the case of nickel(II) 2-vinylrhodochlorin dimethyl ester (**14**) and nickel(II) chlorin e_6 trimethyl ester (**15**), NMR spectra showed that the 2-vinyl group was reduced cleanly to ethyl, but no isobacteriochlorins were produced. Similarly, the nickel(II) 9-deoxo compound **10b** gave no nickel(II) 9-deoxoisobacteriochlorin when retreated with Raney Ni under these conditions; rather, starting material was recovered cleanly. No nickel(II) 9-deoxoisobacteriochlorins were ever observed as products of the Raney Ni reduction of nickel(II) methyl mesopyropheophoribde *a*; a carbonyl or other electron-withdrawing group conjugated to the macrocycle seems to be required. Apparently the 6-nuclear ester groups of **14** and **15** are either not sufficiently electron-withdrawing or are not conjugated to the aromatic π system. Undoubtedly, the electron-withdrawing effect of the C-9 carbonyl increases the oxidation potential of **8b**. The 9-deoxo compound **10b** is more easily oxidized to the corresponding porphyrin than is nickel(II) methyl mesopyropheophorbide *a* (**9b**), again suggesting that the effect of the C-9 carbonyl is to increase the oxidation potential of the chlorin macrocycle.

Meso substituents can also affect the delicate balance of the Raney Ni reduction. Thus, δ-*meso*-methylthiomethyl substrate **1c** gave a significantly higher yield of isobacteriochlorin than did *meso*-unsubstituted compound **9b**. However, a single *meso* substituent, as in nickel(II) chlorin e_6 trimethyl ester (**15**), does not replace the isocyclic five-membered ring with its conjugated ketone. It should be noted, however, that low yields of isobacteriochlorins were obtained from the Raney Ni reduction of *meso*-tetraphenylchlorin.[19]

Experimental Section

General conditions were as described in the preceding paper in this issue.[2]

Small-Scale Reduction of Nickel(II) Methyl Mesopyropheophorbide *a* (9b) with Raney Ni in Methanol. Nickel(II) methyl mesopyropheophorbide *a* (**9b**) (50.5 mg) was dissolved in 15 mL of methanol and placed in a heavy-walled glass tube equipped with a metal screw cap. Raney Ni slurry (0.96 g) was added, and the suspension was heated with magnetic stirring at a 70 °C bath temperature for 3 h in dim light and then at room temperature overnight (11 h). TLC of the reaction mixture at 75 and 155 min was very similar; there were three spots: R_f = 0.65 (royal-blue, **10b**), 0.3 (bright green, **9b**), and 0.25 (blue-gray, **11a**). The ratio of the visible absorbances at 640 nm (**9b**) and 606 nm (**10b**, **11a**) decreased from 1.52 at 75 min to 1.05 at 155 min. To workup, the Raney Ni was first filtered off on a sintered glass funnel and washed well with methanol. The solvent was evaporated, and the residue was redissolved in dichloromethane, rinsed with water, dried, and evaporated to give the crude product. Preparative TLC on silica, eluting with 97/3 dichloromethane/THF gave **10b** (11.0 mg, 22%), recovered starting material **9b** (18.7 mg, 37%), and **11a** (3.7 mg, 7%).

10b: UV λ_{max} (CH_2Cl_2, rel absorbance) 608 nm (37.0), 562 (6.0), 524 (3.4), 490 (4.1), 399 (100); MS, *m/e* (%) 595 (15%), 594 (24), 593 (12), 592 (74, M^+, ^{58}Ni), 476 (24) + Ni isotope cluster; NMR (360 MHz, $CDCl_3$) see Table IV.

11a: UV λ_{max} (CH_2Cl_2, rel absorbance) 594 nm (80.4), 554 (26.3), 470 (15.0), 410 (77.8), 380 (100); MS, *m/e* (%) 611 (17%), 610 (21), 609 (49), 608 (31, M^+, ^{58}Ni), 607 (25), 606 (18), 493 (30) + Ni isotope cluster. The NMR were identical with the products of the large-scale

(17) Abraham, R. J.; Smith, K. M.; Goff, D. A.; Lai, J.-J. *J. Am. Chem. Soc.* **1982**, *104*, 4332–4337.

(18) Trowitzsch, W. Dissertation, Braunschweig, 1974.

(19) Dorough, G. D.; Miller, J. R. *J. Am. Chem. Soc.* **1952**, *74*, 6106–6109.

Raney Ni reduction of **9b** in THF under H_2 at room temperature; see Table II. **11a** consisted of a 1:1 mixture of two diastereomers as judged by NMR: HPLC (C-18 reversed-phase, Z-Module, 70/30 acetone/H_2O, 1.5 mL/min, retention times (min)) **11a** band 1 (20.1), **11a** band 2 (24.7). See also Figure 2.

Small-Scale Raney Ni Reductions of 9b in THF under H_2 (Table I, Entries 4–7). In a typical procedure, nickel(II) methyl mesopyropheophorbide *a* (**9b**) (50 mg) was dissolved in 30 mL of freshly distilled THF. The solution was placed in a pressure bottle with the specified amount of Raney Ni slurry and hydrogenated under the indicated pressure of H_2 at room temperature. The reaction was worked up by filtration of the suspension through a sintered glass funnel and washing the Raney Ni well with acetone or dichloromethane (CAUTION: catalyst may spark). The resulting solution was transferred to a separatory funnel and washed with water. The organic layer was dried and evaporated, and the crude products were purified by silica TLC, eluting with 97/3 dichloromethane/THF.

Large-Scale Raney Ni Reduction of Nickel(II) Methyl Mesopyropheophorbide *a* (9b). Nickel(II) methyl mesopyropheophorbide *a* (**9b**) (1.088 g) was dissolved in 60 mL of freshly distilled THF and treated with 17.3 g of Raney Ni slurry under 20 psi of H_2 at room temperature on a Parr shaker for 16 h. The catalyst was filtered off on a sintered glass funnel and rinsed well with dichloromethane (CAUTION: catalyst may spark). The resulting solution was rinsed with water, dried, and evaporated. TLC of the crude product (97/3 dichloromethane/THF) showed royal-blue 9-deoxo compound **10b** [R_f = 0.7—turns red after standing on the plate, presumably due to oxidation to nickel(II) deoxophyllo-erythrin], unreacted starting material (R_f = 0.23–0.31, bright green), isobacteriochlorin mixture **11a** (blue-gray, R_f = 0.13), hexahydroporphyrin **12** (red), and a faint orange spot (R_f = 0–0.05). The crude product was purified by flash chromatography on silica under nitrogen, eluting first with 98.5/1.5 dichloromethane/THF to obtain **10b**, followed by starting material **9b**, a mixed fraction of **9b** and nickel(II) isobacteriochlorins, and finally a pure nickel(II) isobacteriochlorin fraction. Increasing the amount of THF gave two further fractions: the impure red nickel(II) hexahydroporphyrin **12**, and an orange band (not further characterized). The recovered starting material was again treated with Raney Ni (6.57 g) in 50 mL of THF for 16.5 h under 24 psi of H_2. The initial workup and chromatography were repeated. The major product in this case was 9-deoxo compound **10b**; only a small amount of **11a** was obtained. The mixed fraction of **11a** and starting material was rechromatographed, eluting with 98.5/1.5 dichloromethane/THF to remove **9b** and then increasing the amount of THF to obtain **11a**. The pure nickel(II) isobacteriochlorin fractions were combined and evaporated to give 191 mg (18%). The Ni 9-deoxo compound **10b** was obtained as a dark-blue viscous oil (ca. 566 mg, 52%) which could not be induced to crystallize, even at −70 °C. A sample of this material was subsequently repurified by TLC and obtained as a solid from methanol. The nickel(II) hexahydrophorphyrin fraction **12** was analyzed by HPLC (C-18 RP, Z-Module, 70/30 acetone/water, 1.0 mL/min, detection at 586 nm). This revealed the presence of some slower-running nickel(II) isobacteriochlorin impurities. Thus, **12** was repurified by silica TLC, eluting with 95/5 dichloromethane/THF. The purified **12** was then resubjected to semipreparative HPLC under the same conditions. The major fraction, R_t = 20 min, 9.8 mg (dried film), is further described below. Two other minor components (R_t = 17.4 and 23.3 min) as well as small amounts of **11a** band 1 (31.0 min) and **11a** band 2 (38.0 min) [visible absorptions for bands 1 and 2 in 70/30 acetone/water: 592, 406, and 380 nm] were also present. It is not clear whether the nickel(II) isobacteriochlorins were contaminants not removed during the TLC purification or whether they are oxidation products formed during the handling of **12**. The nickel(II) isobacteriochlorin fraction was separated into **11a** bands 1 and 2 by preparative HPLC on the Waters Prep 500A. The separation gave several cuts of each band, plus 34 mg of recovered **11a** mixture. **11a** band 2 was crystallized from dichloromethane/hexane. Numerous attempts to obtain crystals of **11a** band 1 failed. The spectroscopic data reported for this compound were therefore obtained from the dried pure solid.

10b: Obtained as a solid from methanol, mp 152–156 °C [lit.[6] 154–156 °C]; UV λ_{max} (CH_2Cl_2) 608 nm (ϵ 4.40 × 10^4), 562 (7.49 × 10^3), 522 (5.13 × 10^3), 490 (5.63 × 10^3), 398 (1.24 × 10^5); NMR (360 MHz, $CDCl_3$) see Table IV.

11a Band 1: solid, mp 106–108 °C; UV λ_{max} (CH_2Cl_2) 638 nm (ϵ 4.22 × 10^3—chlorin impurity ?), 594 (2.67 × 10^4), 552 (9.67 × 10^3), 406 (3.23 × 10^4), 381 (4.01 × 10^4); NMR (360 MHz, $CDCl_3$) see Table II; HPLC retention time (70/30 acetone/water, 1.5 mL/min) 20.5 min.

11a Band 2: crystallized from dichloromethane/*n*-hexane, mp 192 °C UV λ_{max} (CH_2Cl_2) 638 nm (ϵ 4.13 × 10^3—chlorin impurity ?), 594 (3.65 × 10^4), 1.24 × 10^4), 468 (6.87 × 10^3), 408 (3.59 × 10^4), 380 (4.72 × 10^4); NMR spectrum (360 MHz, $CDCl_3$) see Table II; HPLC retention time (70/30 acetone/water, 1.5 mL/min) 25.1 min. Anal. Calcd for $C_{34}H_{38}N_4NiO_3$: C, 67.01; H, 6.29; N 9.19. Found: C, 66.78; H, 6.41; N, 9.22.

12: UV λ_{max} (CH_2Cl_2, rel absorbance): 580 nm (39.3), 536 (35.3), 454 (19.2), 448 (19.6), 399 (90.4), 380 (73.8), 346 (100). MS, m/e (%): 612 (52%, M^+,^{60}Ni), 610 (100, M^+,^{58}Ni), 609 (34), 608 (40), 606 (14), 551 (54), 495 (17), 493 (22), 463 (16), 451 (21), 499 (29), 437 (12), 435 (20). NMR spectrum (360 MHz, $CDCl_3$): see Table III.

Preparation of Methyl 9-Deoxomesopyropheophorbide *a* (10a). Nickel(II) methyl mesopyropheophorbide *a* (**9b**) (269 mg) was dissolved in 7 mL of dichloromethane and 50 mL of methanol (solubility is poor in methanol alone). Raney Ni slurry (4.42 g) was added, and the mixture was shaken on a Parr apparatus at room temperature under 20 psi of H_2 for 19 h. The starting material was almost completely consumed, and the major product was nickel(II) methyl 9-deoxomesopyropheophorbide *a* (**10b**). The hydrogenation was continued for 7 h at 50 psi of H_2. The TLC of the reaction mixture was hardly changed. The Raney Ni was filtered off on a sintered glass funnel, and the filtrate was diluted with dichloromethane, washed with water, dried, and evaporated. The crude product was purified by flash chromatography on silica, eluting with 98.5/1.5 dichloromethane/THF to give **10b** (141 mg, 52%) and recovered starting material (28 mg, 10%), plus a small amount of nickel(II) isobacteriochlorin mixture **11a**. The Ni was removed by treatment of **10b** (141 mg) in TFA (16 mL) with 0.25 mL of 1,2-ethanedithiol[20] with stirring under Ar for 2 h. The reaction appeared to be complete by visible spectroscopy (606 nm goes to 638 nm) and TLC (**10b**, R_f = 0.62; **10a**, R_f = 0.26; 98.5/1.5 dichloromethane/THF) and was worked up by pouring into dichloromethane/water, rinsing with saturated aqueous sodium bicarbonate, drying, and evaporating. Flash chromatography on silica gave **10a** plus a small amount of starting material **10b**, which was resubjected to TFA/1,2-ethanedithiol. The product was crystallized from dichloromethane/methanol to give **10a** as a green solid (102 mg, 81%): mp 177 °C [lit.[6] 180–182 °C]; UV λ_{max} (CH_2Cl_2) 638 nm (ϵ 5.01 × 10^4), 584 (6.14 × 10^3), 526 (5.37 × 10^3), 498 (1.73 × 10^4), 394 (2.10 × 10^5); NMR (360 MHz, $CDCl_3$) see Table IV.

Large-Scale Raney Ni Reduction (δ-*meso*-Methyl Series). Nickel(II) methyl δ-*meso*-[(methylthio)methyl]mesopyrophorbide *a* (**1c**) (459 mg) was dissolved in 50 mL freshly distilled THF. Raney Ni slurry (6.85 g) was added and hydrogenation carried out at 15 psi of H_2 on a Parr apparatus for 15.5 h. The catalyst was filtered off and then washed with acetone and dichloromethane. The resulting solution was rinsed with water, dried, and evaporated. Flash chromatography on silica under nitrogen, eluting first with dichloromethane, gave the nickel(II) 9-deoxo compound **3c**. Increasing the THF to 3% gave recovered starting material, followed by a mixed fraction of starting material and nickel(II) isobacteriochlorin **2b** and then pure **2b**. Increasing the percentage of THF gave a crude fraction of what were suspected to be nickel(II) hexahydroporphyrins **4**. The recovered starting material was resubjected to Raney Ni reduction, but this time little **2b** was obtained and the major product was unreacted starting material (58 mg), contaminated with five other minor, faster-running spots. The nickel(II) isobacteriochlorin fraction (128 mg, 30%) appeared to be a single isomer by HPLC, although NMR spectroscopy indicated the presence of another isomer (<10%). Recrystallization of **2b** was attempted unsuccessfully from dichloromethane/*n*-hexane and diethyl ether/*n*-hexane. Finally, the product was precipitated as a purplish solid from acetone with water. The material was stable as a solid and gave a satisfactory elemental analysis. Nickel(II) 9-deoxo compound **3c** was obtained as a dried film (140 mg, 30%). The NMR and visible spectra were similar to those of the same compound obtained previously in the reduction of **1c** with Raney Ni in methanol at 70 °C. It was decided to remove the Ni and characterize the free-base **3a** fully. Therefore, **3c** was dissolved in TFA (15 mL) and treated with 0.1mL of 1,2-ethanedithiol at room temperature for 3 h under Ar.[20] TLC showed formation of an unexpectedly complex product mixture, and the visible spectrum suggested that some oxidation to porphyrin had taken place. The reaction mixture was poured into a mixture of dichloromethane/saturated aqueous sodium acetate. The organic layer was then rinsed with saturated aqueous sodium bicarbonate solution, dried, and evaporated. TLC (97/3 dichloromethane/THF) showed the desired greenish-brown **10a** (R_f = 0.33) and two major reddish-brown spots (ca. 50%) at R_f = 0.5–0.6. Flash chromatography on silica, eluting with dichloromethane, gave a porphyrin mixture (not further investigated) and **10a** (7.0 mg). The nickel(II) hexahydroporphyrin **4** fraction was further purified twice by silica TLC (8% and 12% THF in dichloromethane). Several bands were obtained. The major fraction [626 nm (19.4), 592 (39.1), 552 (21.3), 404 (100), 358 (55.6), dichloromethane] was subjected to C-18 RP HPLC, eluting

(20) Battersby, A. R.; Jones, K.; Snow, R. J. *Angew. Chem.* **1983**, *95*, 742–743.

with 70/30 acetone/water at 1.2 mL/min. Two major and at least four minor compounds were present in this fraction. The first major compound (R_f = 13.9 min) had a visible spectrum reminiscent of a tetrahydroporphyrin [594 nm (71), 554 (26), 486 (14) 472 (16), 454 (15), 410 (78), 384 (100), 80/20 acetone/water], but the HPLC retention time was much less than would be expected for **2b**. Thus, it might be a minor isomeric nickel(II) isobacteriochlorin. The second major product (R_f = 17.9 min) appeared to be a nickel(II) hexahydrophorphyrin by its visible spectrum [586 nm (37), 556 (29), 538 (32), 462 (18), 430 (13), 402 (84), 385 (72), 353 (100), 80/20 acetone/water] and was reinjected to provide pure material for NMR study. However, the NMR spectrum was not clean, and further attempts to characterize the δ-*meso*-methylhexahydrophorphyrins were abandoned. A previous Raney Ni reduction of **1c** in methanol at 70 °C had also yielded as small amount of a similar compound: UV λ_{max} (CH_2Cl_2) 582 nm (32), 546 (27), 460 (13), 402 (92), 387 (73), 371 (61), 356 (100); MS, *m/e* (%) 625 (73, M^+, ^{58}Ni).

Analytical Data. 3c: UV λ_{max} (CH_2Cl_2, rel absorbance) 600 nm (38.2), (10), 520 (7.3), 402 (100); MS, *m/e* (%) 611 (20%), 609 (34), 608 (39), 607 (47, M^+, ^{58}Ni), 606 (47), 507 (11), 506 (16), 504 (36), 492 (16), 491 (19), 489 (37); NMR (360 MHz, $CDCl_3$ see Table IV.

3a: UV λ_{max} (CH_2Cl_2, rel absorbance) 644 nm (20.3), 588 (3.3), 502 (9.5), 400 (100); MS, *m/e* (%) 551 (100%, bp, M^+), 536 (19, $M^+ - CH_3$), 463 (12, $M^+ - CH_2CH_2CO_2Me$); NMR (360 MHz, $CDCl_3$) see Table IV.

2b: obtained as a solid from acetone/water, mp, 142-144 °C; UV λ_{max} (CH_2Cl_2) 598 nm (ϵ 3.58 × 10^4), 554 (1.45 × 10^4), 478 (1.09 × 10^4), 414 (4.10 × 10^4), 393 (5.90 × 10^4); MS *m/e* (%) 625 (32%), 624 (28, M^+, ^{60}Ni), 623 (85), 622 (37, M^+, ^{58}Ni), 621 (22), 520 (14), 508 (11), 507 (11), 477 (12), 465 (12), 464 (18), 463 (23), 462 (13); NMR (360 MHz, $CDCl_3$) see Table II. Anal. Calcd for $C_{35}H_{40}N_4NiO_3$: C, 67.43; H, 6.46; N, 8.99. Found: C, 67.09; H, 6.43; N, 8.83.

Acknowledgment. This research was supported by grants from the National Science Foundation (CHE 81-20891) and the National Institutes of Health (HL 22252).

Registry No. 1c, 96806-62-1; **2b** (tcc), 96866-31-8; **3a**, 96896-95-6; **3c**, 96866-32-9; **4**, 96866-33-0; **5**, 96806-63-2; **9b**, 96893-69-5; **10a**, 13566-43-3; **10b**, 47823-49-4; **10c**, 96866-35-2; **11a**, 96866-34-1; **12**, 96896-96-7.

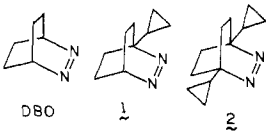
"Spring-Loaded" Biradicals. The Radical and Electron-Transfer Photochemistry of Bridgehead Cyclopropyl-Substituted 2,3-Diazabicyclo[2.2.2]oct-2-enes (DBO's)

Paul S. Engel,* Dalen E. Keys, and Akihide Kitamura

Contribution from the Department of Chemistry, Rice University, Houston, Texas 77251.
Received December 26, 1984

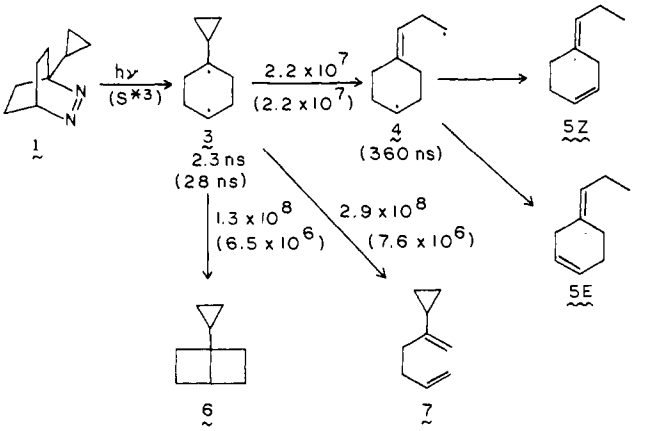
Abstract: Bridgehead cyclopropyl-substituted 2,3-diazabicyclo[2.2.2]oct-2-enes **1** and **2** have been synthesized from 1-cyclopropyl-1,3-cyclohexadiene and 1,4-dicyclopropyl-1,3-cyclohexadiene. Irradiation of these azoalkanes leads to 1,4-biradicals which undergo single- and double-cyclopropylcarbinyl rearrangement. The lifetime of the resulting 1,7- and 1,10-biradicals has been determined by using a combination of "free radical clock" and trapping techniques. Irradiation of **1** in CCl_4 provides the first case of photochemically induced electron-transfer fragmentation of an azoalkane and the first bimolecular reaction of an azoalkane triplet state. Even the triplet state of the unsubstituted 2,3-diazabicyclo[2.2.2]oct-2-ene can be intercepted by a good hydrogen donor such as 1,4-cyclohexadiene.

When the azo group is part of a bicyclo[2.2.2] skeleton as in 2,3-diazabicyclo[2.2.2]oct-2-ene (DBO), loss of nitrogen is difficult both thermally and photochemically.[1-5] Photolysis of such



"reluctant" azoalkanes can be accelerated by employing elevated temperatures[6-8] and short-wavelength irradiation[9] or by modifying the structure to make the compounds more labile thermally.[8,10]

Scheme I. Biradical Rate Constants (s^{-1}) and Lifetimes for Direct and (Triplet-Sensitized) Photolysis of 1



In the course of studying the photochemistry of bridgehead-substituted DBO's, we prepared compounds **1** and **2**, whose cyclopropyl groups not only enhance photoreactivity but also have a drastic effect on the product distribution. We already reported[11]

(1) Turro, N. J.; Liu, K. C.; Cherry, W.; Liu, J. M.; Jacobson, B. *Tetrahedron Lett.* **1978**, 555.
(2) Berson, J. A.; Davis, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 3658.
(3) Snyder, J. P. *Diss. Abstr.* **1966**, 26, 5728.
(4) Allred, E. L.; Beck, B. R. *Tetrahedron Lett.* **1974**, 437.
(5) Turro, N. J.; Renner, C. A.; Waddell, W. H.; Katz, T. J. *J. Am. Chem. Soc.* **1976**, *98*, 4320.
(6) Engel, P. S.; Nalepa, C. J.; Leckonby, R. A.; Chae, W. K. *J. Am. Chem. Soc.* **1979**, *101*, 6435.
(7) Engel, P. S.; Nalepa, C. J. *Pure Appl. Chem.* **1980**, *52*, 2621.
(8) Engel, P. S.; Horsey, D. W.; Keys, D. E.; Nalepa, C. J.; Soltero, L. R. *J. Am. Chem. Soc.* **1983**, *105*, 7108.
(9) Adam, W.; Mazenod, F. P. *J. Am. Chem. Soc.* **1980**, *102*, 7131.
(10) McElwee-White, L.; Dougherty, D. A. *J. Am. Chem. Soc.* **1984**, *106*, 3466.
(11) Engel, P. S.; Keys, D. E. *J. Am. Chem. Soc.* **1982**, *104*, 6860.

0002-7863/85/1507-4964$01.50/0