at 17.1 ppm and the pair at 13.5 and 12.5 ppm each correspond to 4 protons. Although it is impossible definitively to assign these resonances without further experiments, they most likely arise from pyrazolyl H4 and H5 protons since, in the analogous binuclear compound **5**, the H3 proton resonance is broad and occurs farther upfield in the spectrum. Although there are two symmetrically inequivalent sets of pyrazole rings in **1**, the resonances for either the H4 or the H5 protons must be coincident, forming the peak at 17.1 ppm, while the other set of protons gives rise to the pair of peaks at 13.5 and 12.5 ppm. Similarly, in the spectrum of **2**, signals are observed at 17.3, 13.5, and 12.4 ppm, but they are overlapped by two broader signals at 16.9 and 14.2 ppm (Figure 7). The spectrum of **2** in CD_2Cl_2 exhibits two additional broad resonances at 10.9 and 8.0 ppm. Either of these latter two bands could arise from the pyrazole ring H3 proton; the remaining three of this set of four resonances arise from methyl groups of the bridging acetates. In CD_3CN, the pyrazole ring resonances appear sharper but are still overlapped by the methyl resonances. Also, the broad band at 8.1 ppm appears much sharper and occurs at 7.7 ppm, and an additional small resonance is apparent at 6.6 ppm.

The H3 pyrazole ring resonances cannot be observed in the spectrum of **1**, owing to the occurrence of numerous broad bands between 5 and 11 ppm arising from phenyl ring protons of the bridging benzoates. Three relatively sharp peaks at 7.3, 6.5, and 6.0 ppm are probably due to the para protons, which are farthest from the paramagnetic iron centers. From the ratio of intensities it appears that the para protons of two of the symmetrically distinct benzoates must be accidentally coincident at 6.5 ppm. When the spectrum is recorded in CD_3CN, a shoulder is visible on the peak at 6.5 ppm.

The very broad signals at 2.1 and 0.6 ppm in the spectrum of **1** dissolved in CD_2Cl_2 are those most dramatically affected by a change in solvent. In CD_3CN, these peaks appear with line widths only one-fourth of the values seen in CD_2Cl_2 and at chemical shift values of 2.9 and 1.0 ppm. These resonances, the first of which lies on top of the broad B-H resonances of the $H_2B(pz)_2^-$ ligands, are assigned to the methylene and methyl protons, respectively, of the Et_4N^+ cation. The effects on the analogous peaks at 3.1 and 1.2 ppm in the spectrum of **2** are similar but less dramatic. These two peaks become sharper, but no significant change in chemical shift is observed.

The room-temperature magnetic susceptibility of **1** in solution was measured by the Evans method.[22] A value for μ_{Fe} of 2.34 μ_B at 295 K calculated by this method is in close agreement with the solid-state value of 2.33 μ_B at 300 K. A value of 2.41 μ_B was measured for **2**. The results are consistent with retention of the tetranuclear $\{Fe_4O_2\}^{8+}$ core in solution, especially with respect to dissociation into $\{Fe_2O\}^{4+}$ units. The larger magnetic moment of the tetranuclear compared to dinuclear complexes is reflected in the magnitude of the isotropic shifts observed for pyrazolyl protons. The most shifted resonance is found at 17.1 ppm in **1**, compared with 12.2 ppm in **5**.[4b]

Conclusions

Conceptually, the residual donating capacity of a μ-oxo atom in the $\{Fe_2O\}^{4+}$ core results in dimerization to form $\{Fe_4O_2\}^{8+}$. This reaction pathway is not available to the $\{Fe_2O\}^{4+}$ core in hemerythrin, since it is sterically protected by the polypeptide chain. From the present study, it appears that steric hindrance may be required in order to obtain functional models for Hr and RR, as was the case for hemoglobin models.[34] The tetranuclear complex obtained from the present work was characterized by crystallographic, spectroscopic, Mössbauer, and preliminary magnetic measurements. Distortions from the planarity manifest in a similar compound, $[Fe_4O_2(O_2CCF_3)_8(H_2O)_6]$, presumably are caused by strain induced by additional bridging carboxylate groups in **1**. Paramagnetically shifted NMR spectra and solution magnetic susceptibility results provide strong evidence that the tetranuclear structure of $[Fe_4O_2(O_2CR)_7(H_2B(pz)_2)_2]^-$, where R = Ph or Me, persists in solution.

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Supplementary Material Available: Tables of non-hydrogen atom thermal parameters, hydrogen atom positional and thermal parameters, ligand, cation, and solvent molecular geometry, and magnetic susceptibility data (Tables S2-S5) (11 pages); table of observed and calculated structure factor amplitudes (Table S1) (23 pages). Ordering information is given on any current masthead page.

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Raney Nickel Reductions of Chlorophyll Derivatives: Hydroporphyrins in the Anhydro Series

Kevin M. Smith* and Daniel J. Simpson

Contribution from the Department of Chemistry, University of California, Davis, California 95616. *Received February 23, 1987*

Abstract: Raney nickel reductions of nickel(II) anhydromesorhodoporphyrin XV (**17**) provide a series of readily separable nickel(II) hydroporphyrins. Apart from the two expected isobacteriochlorins **19** and **22**, two hexahydroporphyrins **20** and **21** were obtained as the major reduction product (32%). Hexahydroporphyrins of the pyrrocorphin type (**7**) observed in Raney nickel reductions of pheophorbides were not observed. The most novel hydroporphyrin isolated was an octahydroporphyrin **23** obtained in 5% yield by further reduction of the hexahydroporphyrin isomers.

There are a variety of porphyrinoid macrocycles in which the chromophore is in some reducted state. The most common of these, the dihydroporphyrins (chlorins), are generally associated with magnesium-containing photosynthetic pigments. However,

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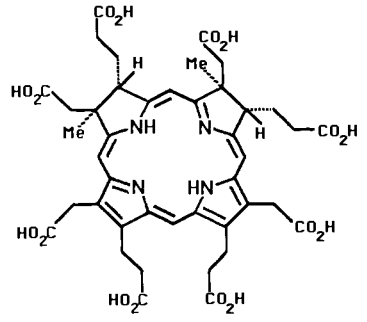
evidence for reduced porphyrins as prosthetic groups in other living systems has been emerging recently.[1-11] Of interest here are the tetrahydroporphyrins for which there are two primary forms: Bacteriochlorins (BC), such as bacteriochlorophyll *a*, are tetrahydroporphyrins with two reduced pyrrolic rings opposite each other. Isobacteriochlorins (iBC), such as sirohydrochlorin, have two reduced rings adjacent to each other.

Isobacteriochlorins (iBC) were first reported[12,13] as side products in sodium reductions of metalloporphyrins in the early 1950s. However, it was not until the isolation[7,14,15] of sirohydrochlorin (**1**) that iBCs came of interest from a biological standpoint.



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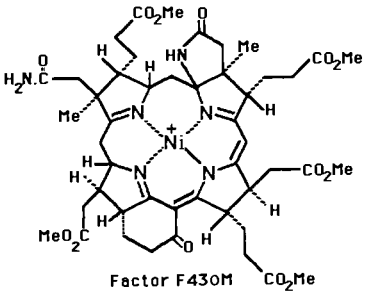

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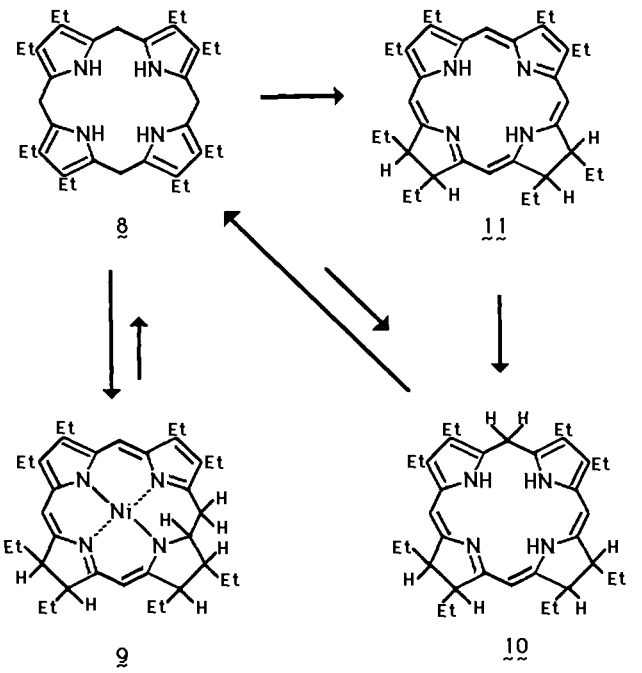
Sirohydrochlorin was first reported in 1973 by Murphy et al.[7,14,15] who isolated it from ferredoxin-nitrite reductase of spinach. The structure of sirohydrochlorin,[16] first determined in 1977, was based primarily on spectroscopic evidence. The iron complex of sirohydrochlorin is the prosthetic group of certain assimilatory and dissimilatory sulfite and nitrite reductase enzymes. A dihydro

Scheme I



derivative of sirohydrochlorin has been shown to be an intermediate in the biosynthetic pathway to vitamin B_{12};[17,18] thus, it has been suggested that sirohydrochlorin may provide an evolutionary link between sulfite and nitrite reductases and vitamin B_{12}. In addition, sirohydrochlorin has also been reported as an intermediate on the biosynthetic pathway of factor F430 (**2**), the prosthetic group of methanogenic bacteria.[19] More recently, the prosthetic group of heme d_1 has been proposed to possess the iron iBC chromophore, though in this case a dioxo acrylate.[11]

Apart from the tetrahydroporphyrins, several isomeric hexahydroporphyrins have also been isolated as synthetic products and intermediates. However, to date hexahydroporphyrins have not been isolated as such from nature. The most common type of hexahydroporphyrin, the porphyrinogen, is a known intermediate of the biosynthesis of many important porphyrins. Eschenmoser has shown[20,21] that three additional hexahydroporphyrins can be accessed (either directly or indirectly) from the porphyrinogen. The pyrrocorphin-type hexahydroporphyrin has been prepared by tautomerization of a porphyrinogen as well as by the Raney nickel reduction.[22] Tautomerization of octaethylporphyrinogen (**8**) (Scheme I) in nonpolar media in the presence of nickel(II) salts gives hexahydroporphyrin **9**.[20] In this case saturation is across a meso carbon and a pyrrole α-position adjacent to a reduced ring. In this same paper Eschenmoser repeated the classical sodium reductions of Eisner and found by NMR spectroscopy that the hexahydroporphyrin produced in this reaction was not the pyrrocorphin type previously reported but of the same type (**9**) as found in these tautomerization studies. Thus although this hexahydro ligand system seems to be a thermodynamically and kinetically favored type of structure, it has not yet been found in nature.

Eschenmoser has also prepared[21] the hexahydroporphyrin **10** where the parent iBC **11** is reduced across a meso position and an adjacent pyrrole nitrogen but opposite the reduced iBC pyrroles. Following this preparation, it was demonstrated that equilibrium

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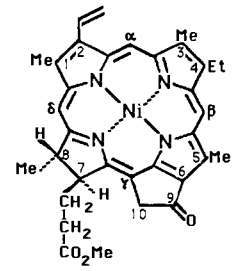
between this hexahydroporphyrin and the corresponding porphyrinogen heavily favors the porphyrinogen.

As mentioned earlier the synthesis of IBCs from parent porphyrins has, in general, been limited to sodium reduction in isoamyl alcohol and Raney nickel reduction of certain porphyrins. To avoid isomer formation,[23] both of these methods (employed in chlorin synthesis) have, in the past, been limited to symmetrical molecules. Several iBC model compounds,[24-27] as well as the sirohydrochlorin macrocycle,[26] have also been prepared by total synthesis, which provide the iBC ring system without any reduction of the macrocycle. However, this method is limited in that the reduced pyrrole ring(s) must be geminally disubstituted in one of the two saturated pyrrole β-positions to prevent oxidation. This requirement limits unsymmetrical iBC synthesis to reductive methods of which few are well-known.

Recent investigations have prompted us to look in more detail at Raney nickel reduction of metallochlorins as a viable method for unsymmetrical iBC synthesis. The reduction of certain metallochlorins has recently been exploited for the synthesis of nickel(II) iBCs in yields generally between 20 and 30%. In this investigation,[23] when nickel(II) methyl pyropheophorbide *a* (**3**) was treated with Raney nickel, a diastereomeric mixture of nickel(II) iBCs (**4**) was obtained. The two diastereomers differed in absolute stereochemistry at the 1- and 2-positions and were separable by preparative reversed-phase HPLC. The structure was determined both by NMR spectroscopy and for one diastereomer, by X-ray crystallography.[28] However, the Raney nickel reduction of a δ meso substituted nickel(II) pheophorbide (**5**) gave the nickel(II) iBC **6**, obtained as one diastereomer (>95%). Presumably because of steric interactions with the substituted meso position, the reduction occurred preferentially from the top to the macrocycle to give the diastereomer where the 1-Me and the 2-Et groups are behind the plane of the iBC. Also isolated from the Raney nickel reduction were small amounts of the pyrrocorphin-type hexahydroporphyrin **7**.

Specific substituents were necessary in order the Raney nickel reductions[23] to occur. Either a carbonyl (such as the 9-keto group) or some other electron-withdrawing group must be rigidly conjugated to the macrocycle in order for ring reduction to occur. While the application of the Raney nickel reduction to form iBCs is limited by the electronic characteristics of the macrocycle, it still appeared to be potentially useful. We felt that a compound such as anhydromesorhodochlorin (**12**) should contain the necessary substituents to affect facile reduction. Moreover, after the anhydro compound had been reduced to iBC, the six-membered ring might be reopened[29,30] to a propionic ester, thereby removing the earlier requirement for an exocyclic five-membered ring (E) to facilitate the reduction. In addition, the anhydro ring is in exactly the same position as is found in factor F430M (**2**), and so this series of compounds possessed potential for synthesis of models of the complex F430 chromophore, not only because reduced products were isolated as nickel(II) complexes.

Fischer has reported[29] that anhydroporphyrins or anhydrochlorins (e.g. **12**) can be formed reversibly from an acid-catalyzed cyclization of propionic-substituted porphyrins or chlorins (e.g. **13**). Rhodochlorin XV dimethyl ester (**14**) was obtained[31] by



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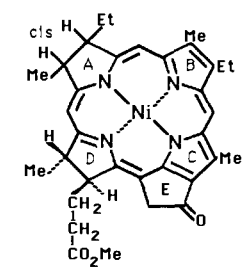

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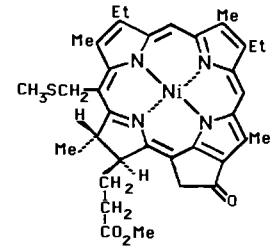

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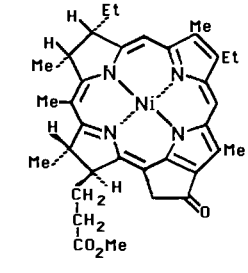

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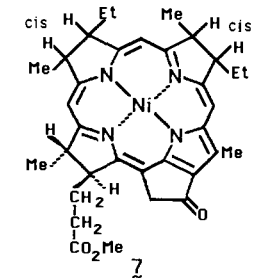

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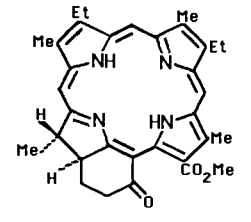

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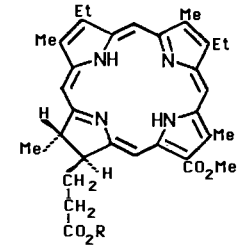
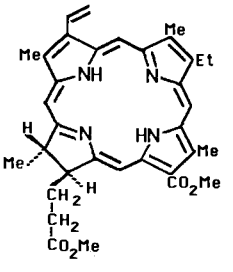


13 R = H
16 R = Me



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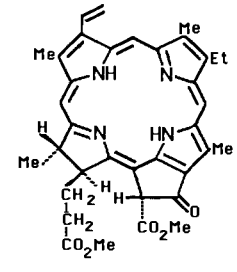

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treating methyl pheophorbide *a* (**15**) in a strongly basic solution (25% KOH/MeH) with O_2 at or below 0 °C. After workup and chromatography, three products were usually obtained. Rhodochlorin dimethyl ester (**14**) was obtained in yields of 20–40%. Also isolated from the reaction was 2-vinylrhodoporphyrin XV dimethyl ester, obtained presumably from oxidation of rhodochlorin. The last product, which depended largely on the reaction temperature, was chlorin e_6 trimethyl ester which was probably a result of base-catalyzed nucleophilic attack on the 9-carbonyl of pheophorbide *a*.

Rhodochlorin XV dimethyl ester (**14**) was then hydrogenated (H_2, Pd/C) to give mesorhodochlorin XV dimethyl ester (**16**) and

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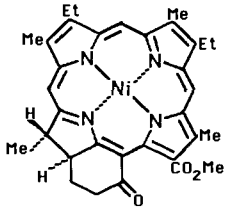
subjected to acid hydrolysis to selectively hydrolyze the 7-propionic ester to the corresponding monoacid **13**. Anhydromesorhodochlorin (**12**) was obtained by briefly treating the crude acid with oleum.[32] After chromatography the anhydro compound **12** was obtained in 77% yield from **16**. Attempts to form it directly from the mesorhodochlorin XV diester **16** were disappointing. Yields were on the order of 10% at best, and it was apparent that ester hydrolysis is necessary prior to treating with oleum. Nickel acetate was used to make the nickel(II) complex **17**, and this compound (188 mg) was treated with Raney nickel.



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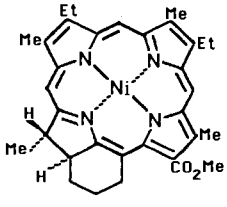
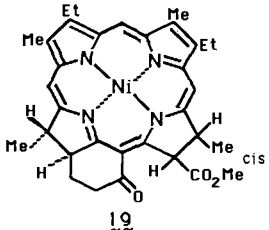
A detailed optimization of the reduction conditions was not performed because of the limited availability of material. Instead, the conditions that gave[23] the optimal yield of iBC from nickel(II) methyl pyropheophorbide *a* were used. Thus nickel(II) anhydromesorhodochlorin (**17**) was treated with 20 mass equiv of Raney nickel at room temperature under 20 psi of H_2 pressure in a Parr shaker for a total of 19 h. TLC of the reaction mixture at this time showed five distinctly different products, none of which had the same retention time as the starting material.

The five products were separated on a chromatotron. The first product, a purplish blue compound that ran just behind the solvent front and was recovered in less than 5% yield, appeared to be a mixture of products by spectrophotometry. The main blue-shifted absorption at 622 nm and its chromatographic behavior suggested that it may be a deoxo type compound **18** similar to that observed in the methyl pheophorbide *a* reductions. It was not characterized further.



18

Band 2 (R_f 0.56) was royal blue and was obtained in 21% yield. Visible absorption spectra (608 nm) and low-resolution mass spectra suggested that it was an iBC. NMR spectra of this compound confirmed this and, more definitely, that ring C was the site of reduction. This conclusion was based initially on the chemical shift pattern observed for the meso protons and substantiated by decoupling and nuclear Overhauser enhancement (NOE) studies. Since the γ meso position between the two reduced rings was substituted, the absence of an upfield meso proton (6.0–6.5 ppm) suggested that ring C had been reduced. The two protons at 7.00 and 7.02 ppm could be tentatively assigned as the β and δ meso protons. The α meso proton (8.06 ppm) was at lowest field as expected for the iBC **19** When the molecule was



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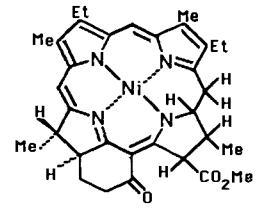
irradiated at 3.00 ppm (q, 2 protons), enhancement was observed at 7.00 ppm, thus assigning the enhanced peak as the β meso proton. Irradiation at 3.12 ppm (q, 2 protons) resulted in enhancement at 8.06 ppm. This same peak was also enhanced when the singlet at 2.68 ppm (3 protons) was irradiated, confirming this meso proton as the α at 8.06 ppm, the methylene at 3.12 ppm as the 2-CH_2, and the methyl at 2.68 ppm as the 3-Me. Enhancement as observed for the last meso proton, the δ (7.02 ppm), when the methyl singlet at 2.57 ppm was irradiated. The remaining assignments were based on decoupling assuming that the doublet at 4.81 ppm is the 6-H, geminal to the carbomethoxy group. This assumption is consistent with the NMR data and is the basis for determining the chemical shifts of several of the five products of the reaction. Thus the presence of this nuclear ester greatly simplified the NMR analysis.

When this 6-H was irradiated, the multiplet at 3.95 ppm collapsed to a quartet. In turn, when this multiplet was irradiated, the doublet at 4.81 ppm, as well as the doublet (1.69 ppm) in the methyl region, collapsed to a singlet. The ring C assignments could all be inferred from these two decoupled spectra. The remaining protons were assigned by decoupling and by analogy to the spectra of nickel(II) anhydromesorhodochlorin (**17**). The coupling of the 5-H and 6-H, J_{5-6} = 10 Hz, strongly suggested that the new ring had cis relative stereochemistry as expected from the results of the pheophorbide *a* reductions.[23] Furthermore, it appears from the spectra that the product may only be one diastereomer since only one set of signals was observed. The exact stereochemical assignment cannot be made without X-ray analysis, but to date no crystals suitable for analysis have been obtained. Attempts to separate any diastereomers by HPLC were fruitless.

Band 3 (R_f 0.48 was greenish blue and was the major product, obtained in 32% yield. The long-wavelength absorption (640 nm) of this product was only 12-nm blue-shifted from the nickel(II) chlorin starting material, unlike the iBC **19**, which was 34-nm shifted. Mass spectra showed a molecular ion 4 mass units greater than the chlorin, suggesting that the major product was a hexahydroporphyrin.

As shown by NMR spectroscopy, band 3 was a mixture of two very similar components, as is illustrated by two sets of signals for most of the resonances. The meso region showed four protons in the same general area (7.0–5.5 ppm) as reported for the meso protons of hexahydroporphyrin **9** prepared by Eschenmoser.[20] The mixture could be separated into two components, bands 3A and 3B, the latter of which suffered oxidation (back to the chlorin) upon excessive handling. Oxidation was confirmed by both spectrophotometry and NMR spectroscopy. Analytical HPLC was useful in allowing the separation without oxidation of either of the two components, but the more polar product (band 3B) suffered decomposition at some point after initial separation. Band 3A constituted about 70% of the mixture by HPLC. This separation allowed us to obtain data for the individual components; however, because of the small quantities and isolation problems only band 3A was looked at in any detail.

The long-wavelength absorptions of the two components, as separated by HPLC, varied slightly, with band 3A at 634 nm and 3B at 642 nm. The NMR spectra of both bands were assigned based on the assumption that the 6-H doublet of the compound saturated across the nearby 5′- to meso position (**20**) is observed at higher than their the field than the other hexahydroporphyrin **21**. The structure of **20** was thus assigned to the material from band 3A.



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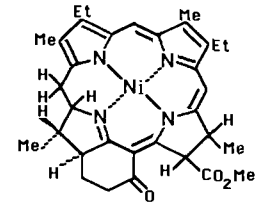


21

(32) Fischer, H.; Orth, H. *Die Chemie des Pyrrols*; Akademische Verlag: Leipzig, 1940; Vol. 2, Part 2, p 136.

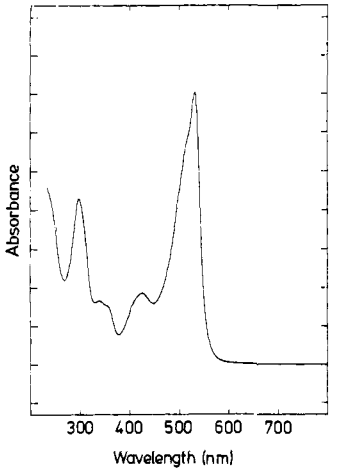
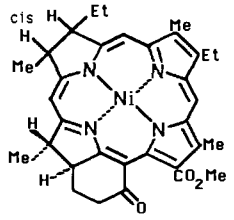


Figure 1. Optical spectrum, in dichloromethane, of nickel(II) octahydroporphyrin **23**.

If the reduction of the chlorin is nonstereospecific as would be expected, then two iBCs corresponding to **19** should be formed. A second reduction of **19** to give band 3A and 3B (**20** and **21**) could produce up to four stereoisomers. As in **19** the NMR spectra of band 3 showed no indication that more that one diastereomer was present; the NMR spectra have been interpreted by assuming that the second reduction would occur from the least hindered face of the molecule. If this is true, the 5′-H and 5-H should have a cis relationship. The NMR spectrum for band 3A (**20**) was interpreted as follows: When the 6-H doublet (3.86 ppm, J = 9.8 Hz) was irradiated, decoupling was observed at 2.65 ppm, thus allowing this multiplet to be assigned as the 5-H. This 5-H (2.65 ppm) proton was also coupled with the multiplet at 4.5 ppm (tentatively assigned as the 5′-H) and with a methyl doublet (5-Me) at 1.11 ppm. When the 4.5 ppm multiplet was irradiated, decoupling was observed at 2.85, 2.65 (5-H), and 2.54 ppm. The previous assignment of the 5-H suggests that the signals at 2.85 and 2.45 ppm are diastereotopic β protons. The remaining chemical shifts were assigned by straightforward decoupling and chemical shift assumptions based on the proximity of the protons to the reduced portion of the molecule. They are summarized in Table I. Because of the presence of up to four possible diasteromers, the coupling constants, in most cases, were not measured.

As mentioned earlier, band 3B (**21**) was sensitive toward oxidation than band 3A, making it too difficult to obtain sufficient pure material to run decoupling experiments. The NMR spectrum assignments for **21** are by analogy with **20** and are given in Table I.

Band 4 (R_f 0.38), obtained in 11% yield as a purple compound, had an electronic absorption at 588 nm, and its mass spectrum was similar to that of band 2 (**19**), suggesting it was an iBC. The NMR spectrum confirmed this initial suggestion, as observed by the meso protons (8.10, 6.94, and 6.44 ppm), which bore close resemblance to those of the iBC **4**. Thus, band 4 appeared to be the iBC **22** in which ring A is the newly reduced ring. As with



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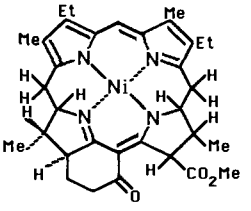

23

the other products, the structure of this compound was based on low-resolution mass spectra, NMR decoupling, and NOE experiments. The primary assumption used in interpretation of the NMR spectra was that the triplet of the terminal methyl of the

Table I. 360-MHz Proton NMR Spectra, in $CDCl_3$ of Nickel(II) Hydroporphyrins **20**, **21**, and **23**

proton	Ni hexahydro **20**	Ni hexahydro **21**	Ni octahydro **23**
α	6.75	6.79	6.69
β		5.87	
δ	5.84		
6-CO_2Me	3.81	3.70	3.81
5′-H	4.50		3.68
8′-H		4.12	3.49
5-H	2.54[a]	3.20	2.55[d]
6-H	3.90	4.24 (d, J = 9.9 Hz)	3.90 (d, J = 10 Hz)
7-H	2.68–2.42[a]	2.20, 2.00	2.05
8-H			1.92
β-CH_2	2.85, 2.45		2.61, 2.53[a,d]
δ-CH_2		2.62–2.30[a]	2.61, 2.30[a,d]
2a-CH_2	2.58[b]	2.62–2.30[a]	2.50
4a-CH_2	2.30[b]		2.22[d]
1-Me	2.05[a,b]	1.92[b]	1.85
3-Me	2.15[a,b]	2.16[b]	2.10
5-Me	1.13 (d, J = 7.6 Hz)	1.26 (d)	1.06 (d, J = 7.3 Hz)
8-Me	1.33 (d, J = 5.7 Hz)[c]	1.13 (d, J = 6.9 Hz)	1.08 (d, J = 6.7 Hz)
7-CH_2CH_2	2.68–2.42, 1.61[a]	2.62–2.30, 1.50[a]	2.43, 1.38–1.25[a]
2b-Me	1.10 (t, J = 7.1 Hz)	1.11, 1.09 (overlapping t, J = 7.5 and 7.5 Hz)	1.08 (t, J = 7.1 Hz)
4b-Me	1.00 (t, J = 7.3 Hz)		0.95 (t, J = 7.5 Hz)

[a] Tentative assignment. [b] Based on proximity to reduced ring(s). [c] Coupling estimated from overlapping signals. [d] Chemical shifts extrapolated from contour plots.

Table II. 360-MHz Proton NMR Spectra, in $CDCl_3$ of Nickel(II) Hydroporphyrins **17**, **19**, and **22**

proton	Ni anhydro **17**	Ni iBc **19**	Ni iBc **22**
α	8.61	8.06	6.94
β	8.86	7.00	8.10
δ	7.62	7.02	6.44
6-CO_2Me	4.05	3.66	3.92
1-H			3.70
2-H			3.52
5-H		3.95	
6-H		4.81 (d, J = 10 Hz)	
7-H	3.67	3.28	3.27
8-H	4.00	3.50	3.45
2a-CH_2	3.40	3.12 (q, J = 7.6 Hz)	1.90, 2.25
4a-CH_2	3.40	3.00	3.10
1-Me		2.57	1.00 (d, J = 7 Hz)
3-Me	3.18, 2.97, 2.84	2.68	2.52[a,b]
5-Me		1.69 (d, J = 6.8 Hz)	2.86[a,b]
8-Me	2.01 (d, J = 6.5 Hz)	1.74 (d, J = 6.4 Hz)	1.55 (d, J = 6.6 Hz)
7-CH_2CH_2	3.13, 2.70, 2.50[a]	2.87, 2.45, 2.23[a]	2.95, 2.41[a]
2b-Me	1.53 (t, J = 7.6 Hz)	1.39 (t, J = 7.6 Hz)	1.25 (t, J = 7.2 Hz)
4b-Me	1.50 (t, J = 7.7 Hz)	1.29 (t, J = 7.5 Hz)	1.36 (t, J = 7.6 Hz)

[a] Tentative assignment. [b] Based on proximity to reduced ring(s).

2-Et (on the reduced ring) was at higher field than the 4-Et terminal methyl triplet. This was confirmed by an NOE experiment where the 4-Me (1.4 ppm) was irradiated, and a small positive enhancement was noted for the lowest field (β) meso proton at 8.10 ppm. Having assigned the 2- and 4-Me, the remaining protons could be assigned by decoupling, beginning at these methyls. The chemical shift assignments are summarized in Table II. The 1-H appeared as a one-proton quintet (doublet of quartets) at 3.69 ppm, which collapsed to a doublet (J = 7.3 Hz) when the 1-Me (1.00 ppm) was irradiated. Thus the ring was reduced to give the expected cis product. Once again, no absolute stereochemical information could be inferred from the

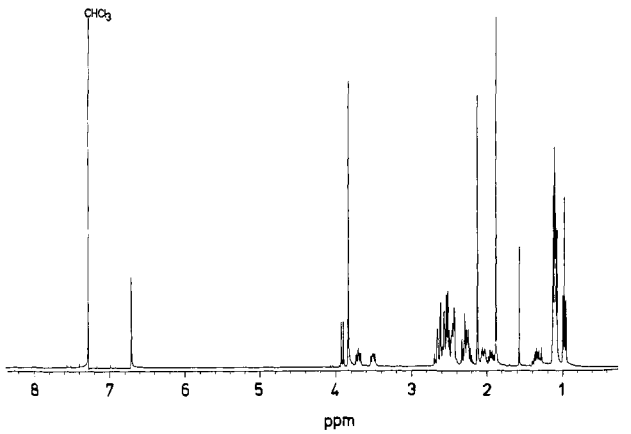

Figure 2. Proton NMR spectrum (360 MHz, in $CDCl_3$) of nickel(II) octahydroporphyrin **23**.

NMR spectra because only one set of signals were observed.

The most novel of the five reduction products isolated was band 5 (R_f 0.30); this was an orange compound obtained in 5% yield. The visible absorption spectrum of band 5 (Figure 1) showed only one absorption centered at 532 nm with a shoulder around 510 nm. Low-resolution mass spectroscopy suggested that band 5 was an octahydroporphyrin. In light of the other reduced compounds isolated, the octahydroporphyrin structure **23** seemed a likely candidate. The NMR spectrum (Figure 2) also suggested that band 5 was a highly saturated porphyrin. Above 3 ppm the spectrum was simple, with only one proton in the meso region (6.69 ppm) and with evidence that ring C was reduced by the 6-H (d, 3.90 ppm, J = 10.4 Hz). However, below 3 ppm in the saturated methylene region, the spectrum was complex. The observation of two aromatic methyl signals (2.10 and 1.90 ppm) also favored structure **23** with ring A and B both being fully aromatic.

The combination of data from three different NMR techniques, namely decoupling, COSY, and NOESY experiments, all generally agreed with the postulated structure and are interpreted as follows. The NOESY spectra helped assign several peaks conclusively and led to speculative assignments for others. The meso proton at 6.69 ppm showed a significant cross peak with a methylene (2.5 ppm) and the methyl group at 2.10 ppm. Since ring C is assumed to be reduced, the meso proton must be the α in order to show these cross peaks. The methylene is thus assigned as the 2-CH_2 and the methyl as the 3-Me. Three remaining significant cross peaks could not be assigned at this point and are left for further interpretation.

The decoupling and COSY data were also interpreted from the 6-H (3.90 ppm) doublet. The cross peak associated with the 6-H identified part of the multiplet at 2.55 ppm as the 5-H. As expected this was the only cross peak noted for the 6-H. This 2.55 ppm multiplet was also coupled with the 3.68 ppm multiplet. By analogy with the hexahydroporphyrins the 3.68 and 3.49 ppm multiplets were assigned to the 5′-H (3.68 ppm) and the 8′-H (3.49 ppm) for the octahydro structure **23**. The 5-H multiplet also showed the expected large cross peak with the 1.10 ppm aliphatic methyl region. Thus the assignments for ring C were confirmed. The ring D assignments follow from the tentative assignment of the 8′-H (3.48 ppm). Although the COSY cross peak was absent, when this 3.48 ppm multiplet was irradiated alone in a 1D spectrum, the multiplet at 1.92 ppm collapsed to approximately a quartet. This multiplet in turn was coupled to the1.10 ppm methyl region and thus assigned the 8-H. The adjacent multiplet at 2.05 ppm was weakly coupled with the 8-H and assigned as the 7-H.

The chemical shifts of the two β and two δ protons were inferred from coupling with the respective 5′ and 8′ protons at 3.68 and 3.49 ppm. The diastereotopic β protons appear at 2.61 and 2.53 ppm and display significant geminal coupling (between 13 and 16 Hz). The two δ protons are found at 2.65 and 2.30 ppm. This coupling was best observed in the 1D decoupling spectra when the 8′-H was irradiated.

The remaining unassigned cross peaks in the NOESY spectra were interpreted from the assignments of the decoupling but are not conclusive because of close chemical shift proximities. A cross peak of 3.68 and 2.5 ppm may be an enhancement between the 5′-H and either the 5-H (2.55 ppm) or one of the β meso protons (2.53 ppm). In either case the proton is probably cis to the 5′-H because of the magnitude of the cross peak. The other large cross peak of 2.3 and 2.6 ppm appears to be between the 4-CH_2 (2.27 and 2.21 ppm) and one of the adjacent β meso protons.

The two-dimensional J-resolved contour plots obtained resolved both complex areas of the spectra and allowed us to make precise assignments of the chemical shifts (based on peak multiplicities) of the β-, δ-, 5-, 5′-, and 8′-H and 2- and 4-CH_2. The coupling constants inferred from these plots were in some cases quite close to those measured in the 1D spectra and in other cases varied by as much as 13% from the expected values. While the coupling information was at best approximate, the observed peak multiplicities, which were resolved, seem to fit into the general scheme of our interpretation of this data.

Conclusions

The major products of the Raney nickel reduction of **17**, the nickel(II) hexahydroporphyrins **20** and **21**, together with the octahydroporphyrin **23** are obviously products of further reduction of the nickel(II) iBC **19**. While the reaction conditions were not varied, it is apparent that the nickel(II) anhydrochlorin **7** undergoes much more facile ring reduction than any other chlorin system reduced in the same manner. The overall yield of reduced products is 70%. Reduction of the C ring is obviously favored, as reflected by the yield of reduced C ring products, 58% versus 11% for ring A reduced iBC. On the basis of the products of the reduction of nickel(II) pyropheophorbide a,[23] the results for the anhydro system were somewhat surprising at first. However, if one takes into account the steric and electronic effects that could direct the selectivity to ring C, the results appear logical. The issue of absolute stereochemistry of the two iBCs **19** and **22** is still unresolved. All of the data collected, including that from attempts at separation by reversed-phase HPLC, suggest that both of these products are, surprisingly, formed stereospecifically. However, without hard evidence such as X-ray analysis one has to assume that both may still be mixtures of diastereomers. The same holds true for the hexa- and octahydroporphyrins, which may be further complicated by additional asymmetric centers. Attempts are still under way to obtain crystals for analysis.

Fischer has reported[33] that anhydroporphyrins can be converted back to the propionic acid porphyrins by heating with succinic acid. This method failed to produce any recognizable products when either the anhydrochlorin **12** or the nickel(II) complex **17** was heated in a succinic acid melt. Thus, alternate methods were investigated. Deacylation of certain acyl- and formylpyrroles, as well as some β-substituted porphyrins, has been achieved by a method employing formation of a ketal or dithioketal or acetal, which is followed by deacylation in the presence of boron trifluoride etherate.[30] Several variations of this method were attempted on nickel(II) anhydromesorhodochlorin methyl ester (**17**) but with no success. The formation of the dithioketal could be observed by both TLC and spectrophotometry, but no evidence of ring opening was ever obtained.

Experimental Section

General Procedures. Melting points, which are uncorrected, were measured on a Thomas/Bristoline microscopic hot-stage apparatus. Electronic absorption spectra were measured on a Hewlett-Packard 8450A spectrophotometer using solutions in dichloromethane, and mass spectra were measured on a ZAB instrument in the FAB mode. Proton NMR spectra were obtained at 360 and 500 MHz on Nicolet NT-360 and NT-500 spectometers; the chemical shifts are reported relative to $CHCl_3$ at 7.260 ppm. The phrase "dried and evaporated" means drying with sodium sulfate, followed by evacuation with a Buchi rotary evaporator under house or oil pump vacuum. Elemental analyses were de-

(33) Fischer, H.; Schroder, C. G. *Justus Liebigs Ann. Chem.* **1939**, *537*, 250–286.

termined by the Microchemical Analysis Laboratory at the University of California, Berkeley.

Reactions were monitored by thin-layer chromatography (TLC) by using cut strips (approximately 2 cm by 6 cm) of E. Merck silica gel 60 F254 precoated (0.25-mm thickness) plastic-backed sheets. Two types of packing material were employed in column chromatography; E. Merck neutral alumina (70–230 mesh) and Merck silica gel 60. The alumina was deactivated with either 6% H_2O (Brockmann grade III) or 15% H_2O (Brockmann grade V) before use. A 250-mL J. T. Baker column was used for flash chromatography. Chromatotron separations were performed on a Harrison Research Model 7924 chromatotron equipped with an FMI pump; disk thickness, flow rate, and solvents are specified where appropriate, and in all cases the circular disks were coated with Kieselgel 60 PF254 (E. Merck). Analytical high-performance liquid chromatography (HPLC) was performed on a Waters Associates instrument equipped with a Model 6000A solvent delivery system, a Valco Model C6U injector, and a Perkin-Elmer LC55B variable-wavelength detector. A Waters Z-Module system equipped with a 10-μm μ-Porasil normal-phase cartridge was used. The solvent systems used are specified where appropriate. All solvents were reagent grade and were filtered through a 0.45-μm Millipore filter before use.

Rhodochlorin XV Dimethyl Ester (14). A 25% KOH/methanol (w/v) solution (140 mL) was cooled to −5 °C (sodium chloride/ice water bath). Methyl pheophorbide *a* (**15**) (1.00 g) in pyridine (8 mL) was added dropwise to the basic solution while oxygen was also bubbled into the reaction. After pheophorbide addition was complete, oxygen was further bubbled into the solution for 15 min. This was followed by stirring for 30 min while the temperature was kept at or below 0 °C. Nitrogen was then bubbled into the reaction for 20 min, after which the mixture was heated to reflux for 10 min under N_2. The reaction mixture was cooled in an ice bath and poured into water (150 mL) and methylene chloride (200 mL), which was previously cooled in an ice bath. Concentrated HCl was then added to adjust the aqueous layer to pH 3 (pH paper). The organic layer was then separted from the aqueous layer, which was further extracted until the extracts were colorless. The aqueous layer remained somewhat green and cloudy. The organic layers were combined, washed with water (3 × 200 mL), dried, and evaporated to dryness. The crude product was dissolved in methylene chloride with methanol and treated with excess ethereal diazomethane. The product mixture was then put on a short silica column (eluting with 3% tetrahydrofuran/methylene chloride) to remove base-line impurities. The mixture was then purified on a Chromatotron with a 4-mm silica disk (elution with 3% tetrahydrofuran/methylene chloride, flow rate 8 mL/min). Rhodochlorin dimethyl ester was obtained as a shiny blue solid from methylene chloride/*n*-hexane, giving 395 mg (42%). Mp: 200–204 °C (lit. mp 206–208 °C,[32] 207 °C[34]). Vis: 400 nm (ϵ 142 000), 498 (10 700), 528 (2900), 612 (3900), 666 (50 700). NMR (500 MHz, ppm): 9.80, 9.77, 9.64 (s, α, β, and γ meso H); 8.74 (s, δ meso H); 8.09 (X of ABX, 2a-H); 6.20 (AB of ABX, 2b- and 2b′-H), 4.50 (m, 7- and 8-H); 4.35, 3.83, 3.62, 3.48, 3.32 (s, 1-, 3-, and 5-Me, 6a- and 7d-OMe); 3.80 (m, 4-CH_2); 2.74–2.35 (m, 7-CH_2CH_2); 1.89 (d, 8-Me, J = 7.1 Hz); 1.73 (t, 4b-Me, J = 7.6 Hz); −1.62 (br s, NH). Also isolated in varying yields was a red product identified as 2-vinylrhodoporphyrin XV dimethyl ester and a green product identified as chlorin e_6 trimethyl ester. 2-Vinylrhodoporphyrin XV Dimethyl Ester. Vis: 404 nm (ϵ 196 000), 512 (10 700), 552 (19 300), 576 (11 300). NMR (500 MHz, ppm): 11.05, 10.15, 10.10, 10.00 (br s, α, β, γ, and δ meso H); 8.23 (X of ABX, 2a-H); 6.24 (AB of ABX, 2b- and 2b′-H), 4.43, 3.94, 3.69, 3.64 (s, 1-, 3-, 5-, and 8-Me, 6a- and 7d-OMe); 3.67 (4a-CH_2); 4.12, 3.35 (both m, 7-CH_2CH_2); 1.87 (m, 4b-Me); −3.79 (br s, NH). Chlorin e_6 Trimethyl Ester. Mp: 205–207 °C (lit.[35] 211 °C). Vis: 402 nm (ϵ 144 000), 500 (10 300), 530 (2400), 608 (2100), 664 (42 000).

Mesorhodochlorin XV Dimethyl Ester (16). Rhodochlorin dimethyl ester (**14**) (200 mg) was dissolved in acetone (20 mL) in a Parr bottle, and 10% Pd/C (25 mg) was added. This mixture was hydrogenated in a Parr apparatus at 14 psi H_2 for 1 h. The Pd/C was filtered off, and the crude product was evaporated to dryness. The product was purified on a flash silica column (eluting with 2–3% tetrahydrofuran/methylene chloride) and obtained as a solid (165 mg, 82% yield) from methylene chloride/methanol. Mp: 176–178 °C (lit.[36] 176 °C). Vis: 398 nm (ϵ 155 000), 494 (24 400), 598 (17 000), 654 (55 200). NMR (360 MHz, ppm): 9.77, 9.75, 9.45 (s, α, β, and γ meso H); 8.65 (s, δ meso H); 4.48 (m, 7- and 8-H); 4.35, 3.82, 3.35, 3.33 (s, 1-, 3-, and 5-Me, 6a-OMe); 3.61 (s, 7d-OMe); 3.90, 3.80 (m, 2- and -CH_2); 2.72–2.31 (m, 7-CH_2CH_2); 1.87 (d, 8-Me, J = 7.1 Hz); 1.74 (overlapping t, 4b-Me); −1.60 (br s, NH).

(34) Reference 32, p 133.
(35) Reference 32, p 64.
(36) Reference 32, p 134.

Anhydromesorhodochlorin XV Methyl Ester (12). Mesorhodochlorin XV dimethyl ester (**16**) (180 mg) was dissolved in methylene chloride (9 mL) and tetrahydrofuran (40 mL) to which was added HCl/H_2O (1.5/2.0 mL). This mixture was refluxed under N_2 and monitored by TLC. After 45 min the reaction was cooled, diluted with methylene chloride (100 mL), and washed with water (1 × 50 mL), with saturated sodium acetate (1 × 50 mL), and then again with water (1 × 50 mL). After drying, the product was evaporated to dryness. The NMR spectrum confirmed the product as the monoacid **13** (loss of the 7d-OMe signal previously obsered at 3.61 ppm). NMR (360 MHz, ppm, $CDCl_3$): 9.77, 9.75, 9.45 (s, α, β, and γ meso H); 8.65 (s, δ meso H); 4.48 (m, 7- and 8-H); 4.35, 3.82, 3.35, 3.33 (s, 1-, 3-, and 5-Me, 6a-OMe); 3.90, 3.80 (m, 2- and 4-CH_2); 2.72–2.31 (m, 7-CH_2CH_2); 1.87 (d, 8-Me, J = 7.1 Hz); 1.74 (overlapping t, 4b-Me); −1.60 (br s, NH). Without further purification, the monoacid **13** was dissolved in concentrated H_2SO_4 (6 mL), and oleum (1.5 mL) was added dropwise. This mixture was capped and stirred for 15 min. It was then poured into cold, saturated sodium acetate (150 mL) with water to aid in the transfer. Cold, concentrated NH_3 was used to adjust this solution to pH 3–4 (pH paper). Methylene chloride (200 mL) was added and shaken with the aqueous phase. The brown organic layer was separated, and the almost clear aqueous layer was discarded. The organic layer was washed with water (3 × 100 mL), dried, and evaporated to dryness. The product was purified on alumina (grade III, eluting with methylene chloride). The product, 130 mg (77% yield) of blue powder, was obtained as a solid from methylene chloride/methanol. Mp: >300 °C (lit.[32] 279 °C). Vis: 406 nm (ϵ 124 000), 504 (8400), 536 (9900), 624 (6600), 680 (42 000). NMR (360 MHz, ppm): 9.46, 9.12, (s, α and β meso H); 8.28 (s, δ meso H); 4.39 (t, 7-H); 4.13 (s, 6a-OMe); 4.02 (q, 8-H); 3.72, 3.64 (q, m, 2a- and 4a-CH_2); 3.48, 3.18, 3.16 (s, 1-, 3-, and 5-Me); 3.44, 3.40, 3.03–2.90 (m, 7-CH_2CH_2); 2.23 (d, 8-Me, J = 6.8 Hz); 1.66 (overlapping t, 4b-Me, J = 8.1 and 7.7 Hz); 0.26 (br s, NH).

Nickel(II) Anhydromesorhodochlorin XV Methyl Ester (17). Anhydromesorhodochlorin XV methyl ester (**12**) (193 mg) was dissolved in chloroform (20 mL) to which saturated nickel(II) acetate in methanol (8 mL) was added. This mixture was refluxed for 20 h under N_2 before cooling to room temperature. The cooled solution was diluted with methylene chloride (100 mL), washed with water (3 × 75 mL), dried, and evaporated to dryness. The product was purified by flash column chromatography on silica (3 × 20 cm, 4% tetrahydrofuran/methylene chloride). The product, 198 mg (93% yield), was obtained as a solid from methylene chloride/*n*-hexane. Mp: >290 °C. Vis: 408 nm (ϵ 89 100), 500 (4600), 538 (4900), 652 (31 800). NMR (360 MHz): see Table I. Anal. Calcd for $C_{33}H_{34}N_4NiO_3$: C, 66.80; H, 5.80; N, 9.44. Found: C, 67.01; H, 5.77; N, 9.51.

Raney Nickel Reduction of 17. The nickel complex **17** (188 mg) was dissolved in tetrahydrofuran (24 mL) in a Parr bottle, and Raney nickel (3.84 g, 20.4 mass equiv), in a pH 10 slurry (Aldrich), was added. This mixture was hydrogenated at 20 psi H_2 on a Parr apparatus for 19 h. The Raney nickel was then filtered off on Celite, and the filtrate was diluted with methylene chloride, washed with water, dried, and evaporated to dryness. The crude product was separated into five bands on a chromatotron with a 2-mm silica disk (eluting with 2% methanol/methylene chloride). Bands 2–5 were all obtained as solids from methylene chloride/methanol was reported below.

Band 1 (18). Obtained in less than 5% yield. Band not obtained as a solid and appeared by spectrophotometry to be a mixture. Vis (relative absorbance): 416 nm (1.00), 548 (0.050), 586 (0.026), 622 (0.055).

Band 2 (19). R_f 0.56. Obtained (40 mg; 21% yield) as a royal blue solid, a portion of which was recrystallized from $CHCl_3$/ methanol, giving dark blue needles. Mp: >300 °C. Vis: 400 nm (ϵ 40 900), 608 (50 900). NMR (360 MHz): see Table I. Anal. Calcd for $C_{33}H_{36}N_4NiO_3$: C, 66.57; H, 6.09; N, 9.41. Found: C, 66.85; H, 5.89; N, 9.52. MS (FAB positive ion, thioglycerol matrix): 595 [100, $(M + H)^+$], 561 (22.6), 535 (17.9, $M^+ - CO_2Me$).

Band 3 (20 and 21). R_f 0.48. Obtained (60 mg; 32% yield) as a greenish blue solid, as a mixture of two products. Vis (relative absorbance of mixture): 383 nm (0.909), 640 (1.00). Anal. Calcd for $C_{33}H_{38}N_4NiO_3$: C, 66.35; H, 6.41; N, 9.38. Found: C, 66.41; H, 6.25; N, 9.51. MS (FAB positive ion, thioglycerol matrix): 597 [100, $(M + H)^+$], 581 (7.8), 568 (7.9), 537 (17.4, $M^+ - CO_2Me$).

Band 3A (20). Separated by normal-phase HPLC with a Waters Z-module radial compression column fitted with a 10-μm μ-porasil column insert (1% tetrahydrofuran/methylene chloride at 1.5 mL/min with a variable-wavelength detector (Waters) set at 640 nm). Vis (relative absorbance): 366 nm (0.582), 376 (0.590), 440 (0.334), 594 (0.447), 634 (1.00). NMR (360 MHz): see Table I for chemical shift assignments.

Band 3B (21). Vis (relative absorbance): 382 nm (1.00), 642 (0.931). NMR (360 MHz): see Table I for chemical shift assignments.

Band 4 (22). R_f 0.38. obtained (20 mg; 11% yield) as a purple solid. Small portion recrystallized from $CHCl_3$/methanol, giving small red needles. Mp: >300 °C. Vis: 404 nm (ϵ 43 800), 588 (35 300). NMR (360 MHz): see Table II for chemical shift assignments. Anal. Calcd for $C_{33}H_{36}N_4NiO_3$: C, 66.57; H, 6.09; N, 9.41. Found: C, 66.78; H, 5.68; N, 9.48. MS (FAB positive ion, thioglycerol matrix): 595 [22.2, $(M + H)^+$], 594 (23.6, M^+), 563 (37.4, M^+ - OMe), 181 (100, bp, thioglycerol).

Band 5 (23). R_f 0.30. obtained (10 mg; 5% yield) as an orange solid. Vis (Figure 2): 298 nm (ϵ 17 600); 426 (7800), 532 (29 000). NMR (360 MHz): see Figure 2 for spectra and Table I for chemical shift assignments. MS (FAB positive ion, thioglycerol matrix): 599 [100, $(M + H)^+$], 583 (7.2), 567 (22.0, M^+ - OMe), 539 (8.8, $M^+ - CO_2Me$).

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Spontaneous and Olefin-Promoted Reductive Elimination of η^3-Allyl(organo)palladium(II) Complexes: Mechanistic and Molecular Orbital Analysis

Hideo Kurosawa,*[1a] Mitsuhiro Emoto,[1a] Hiroaki Ohnishi,[1a] Kunio Miki,[1a] Nobutami Kasai,[1a] Kazuyuki Tatsumi,[1b] and Akira Nakamura[1b]

Contribution from the Department of Applied Chemistry, Osaka University, Suita, Osaka 565, Japan, and the Department of Macromolecular Science, Osaka University, Toyonaka, Osaka 560, Japan. *Received March 11, 1987*

Abstract: Kinetic studies are reported on spontaneous and olefin-promoted reductive elimination of complexes of Pd(η^3-allyl)(Ar)(L) (**1**: Ar = $C_6H_3Cl_2$-2,5; L = PR_3, AsR_3), which affords high yields of the coupling products, allylbenzene derivatives. The rate of the spontaneous process was not affected by addition of free ligands, L, suggesting no significant participation of a η^1-allylpalladium species nor of a 14-electron intermediate arising from ligand dissociation during the C–C bond-forming step. Reductive elimination of structurally rigid Pd(η^1-allyl)(Ar)(dppe) proceeded more slowly than that of **1**. The rate of the olefin-promoted process for **1** (L = AsR_3) showed first-order dependence on the concentration of olefins and inverse dependence on that of AsR_3. A reaction scheme consistent with this observation has been proposed which involves initial ligand exchange between AsR_3 of **1** and olefins to form an intermediate, Pd(η^3-allyl)(Ar)(olefin), followed by the C–C coupling step. These types of olefin complexes for Ar = C_6HCl_4-2,3,5,6 were generated separately in solution at low temperature and characterized by ^1H NMR spectra. Reactivity patterns of the reductive elimination of these olefin complexes unambiguously confirmed the kinetically implicated trend described above, namely they are by far more reactive than the corresponding $AsPh_3$ complex, and the complex having the more electron-withdrawing olefin gives the coupling product more rapidly. Extended Hückel molecular orbital calculations on Pd(η^3-CH_2CHCH_2)(CH_3)L (L = PH_3, $CH_2{=}CH_2$) and related species have been carried out. The MO analyses satisfactorily explain the origin of the above-mentioned reactivity patterns, which are apparently specific to the η^3-allyl complexes.

η^3-Allyl complexes of transition metals are important reagents and intermediates in many organic transformations.[2-5] Recently, increasing attention has been paid to the synthetic value of reductive elimination of η^3-allylmetal complexes.[3-5] Nevertheless, mechanistic studies of this process are scarce aside from some stereochemical examinations,[6] in contrast to remarkable progress concerning mechanistic understanding of the reductive elimination of those complexes that contain only η^1-bound alkyl and aryl ligands.[7-9] However, knowledge in the latter field cannot always be transferable to the η^3-allylmetal chemistry, for the intrinsic difference between the nature of the η^3-allyl–metal and the η^1-alkyl–metal bond may lead to a considerable difference in reactivity patterns of two classes of complexes. Well-known examples include the attack of certain nucleophiles at the metal-bound η^3-allyl ligand from the anti side,[2] whereas very few equivalents of this step are found in the chemistry of the η^1-alkyl complexes.

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