Peripheral Mercuration of Metalloporphyrins: Novel Syntheses of Deoxophylloerythroetioporphyrin and Deoxophylloerythrin Methyl Ester

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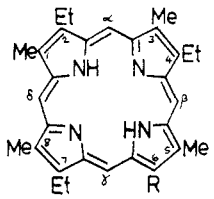
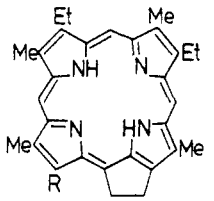
Zinc(II) porphyrins bearing unsubstituted β positions can be mercurated at the β position and at an adjacent meso position. Palladium/olefin reactions with the dimercurated porphyrins produce products possessing a five-membered isocyclic ring bridging the β and meso positions and resembling that found in chlorophyll derivatives. With use of this methodology, novel syntheses of deoxophylloerythroetioporphyrin (2) and deoxophylloerythrin methyl ester (3), two degradation products of chlorophyll, are described.

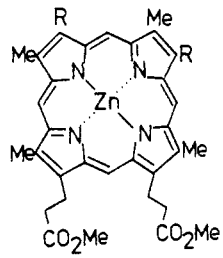
The petroporphyrins are porphyrins, usually isolated as metal complexes, which occur in petroleum and related deposits.[1] Three series of petroporphyrins have been identified as (a) those homologous series related to etioporphyrin III (1), (b) a series related to deoxophyllo-



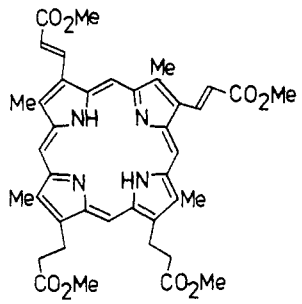
1 R = Et
4 R = H



2 R = Et
3 R = $CH_2CH_2CO_2Me$



5 R = H
6 R = HgCl



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erythroetioporphyrin (2) (DPEP), and (c) a "rhodo-type" series, which has been shown[2] to possess a benzoporphyrin skeleton. Recently, a γ,7-butanoporphyrin has been isolated from Serpiano and other oil shales,[3] and the nickel(II) complexes of 2-desethyl-DPEP and three γ,7-butanoporphyrins have been isolated from Julia Creek oil shales.[4]

Porphyrins which occur in petroleum deposits have long been believed to be derived by degradation of chlorophyll over the course of time,[5-7] and recent evidence[4] appears to support this contention. Spectroscopic work has resulted in the conclusion[8] that DPEP (2), deoxophylloerythrin, and its methyl ester, 3, are present in German Messel oil shale. Indeed, DPEP has been prepared in very low yield from pheophytin.[9] In response to a need for pure petroporphyrin markers, several syntheses of DPEP from monopyrroles have been described. Two approaches from pyrromethenes[10,11] gave DPEP in miniscule yields and with differing electronic absorption spectra. A third synthesis,[12] in 6% yield, from a *b*-bilene bearing the intact exocyclic ring represented a dramatic improvement; most recently, Clezy and co-workers[13] have described a synthesis of DPEP in which the exocyclic ring was added to a preformed porphyrin by way of a keto ester and thallium(III)-promoted cyclization. In this paper we describe a novel synthesis of DPEP (2) [by way of pyrroetioporphyrin XV (4)] and deoxyphylloerythrin methyl ester (3) in which the troublesome exocyclic ring is constructed on preformed porphyrins by way of a mercuration/palladium–olefin reaction.

Results and Discussion

It has previously been shown[14] that zinc(II) or copper(II) derivatives of β-unsubstituted porphyrins [such as zinc(II) deuteroporphyrin IX dimethyl ester, (5)] react with mercuric acetate to give the corresponding mercurated porphyrin, e.g., 6. Subsequent reaction with $LiPdCl_3$ in acetonitrile and then with methyl acrylate gave the bis acrylate 7. Demercuration of 6 with $NaBD_4$ showed[14] that the excessively high yields (approximately 125%) of 6 from 5 were due to contamination of the required product with the corresponding meso-mercurated derivatives; moreover, formation of two "monoacrylate" byproducts, the structures of which were at that time unassigned, provided evidence of some unexpected side reactions in the otherwise clean acrylate formation from the mercurated porphyrin. In the earlier work[14] 4 molar equiv of mercuric acetate were used and a 37% yield of the bis acrylate 7 was obtained, compared with a combined yield of 25% for the "monoacrylates". Subsequent use of 6 molar equiv of mercuric acetate afforded a combined yield of 48% of the "monoacrylates", compared with only 25% of the bis acrylate 7. Larger excesses of mercuric acetate resulted in lowering of yields of all products.

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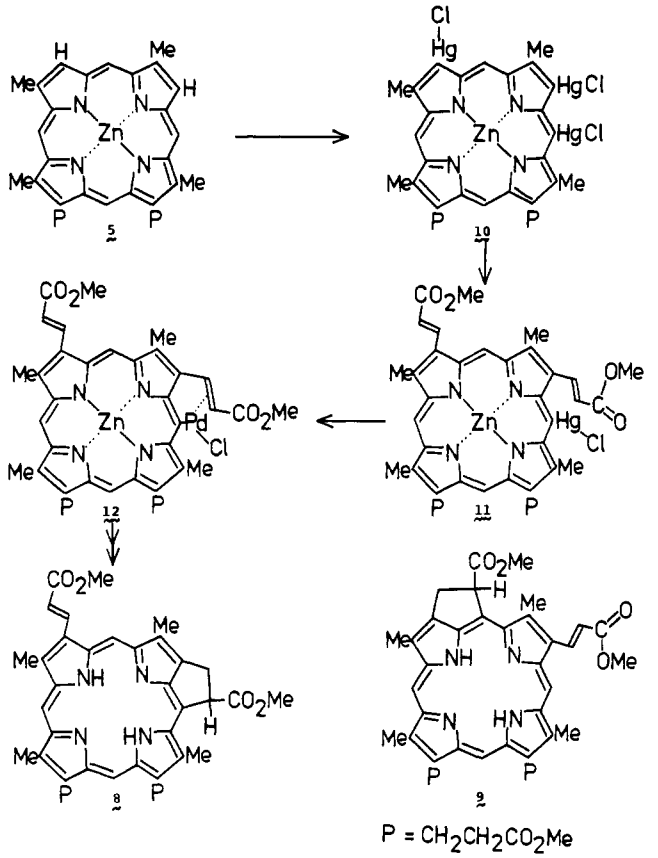
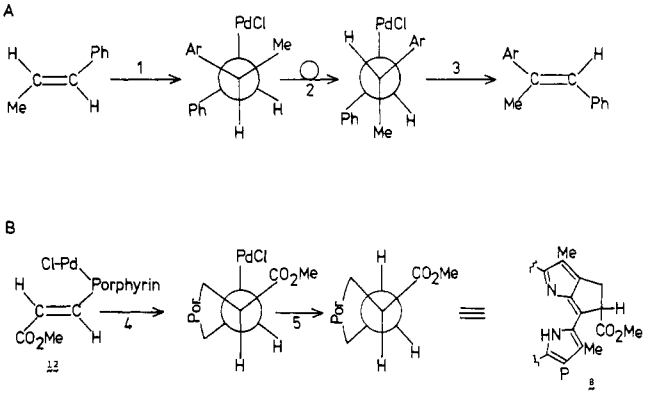
Scheme I. Anomalous Palladium/Olefin Reaction on Trimercurated Zinc(II) Porphyrin 10. The Stage at Which the Meso-Mercury Atom is Transmetalated with Palladium is not Established



The two readily separated byproducts ("monoacrylates") from the palladium/olefin reaction are now assigned structures 8 and 9 on the basis of electronic absorption, NMR, and mass spectroscopic evidence, as well as elemental combustion analysis. The electronic absorption spectra were alike for the two isomers and were of the "mesorhodin" type,[15] indicating possible cyclization of a β substituent to a meso position, combined with the presence of an electron-withdrawing substituent. Proton NMR spectra of the two isomers 8 and 9 were also similar, showing notably only three meso protons and a trans acrylate with characteristic doublets (J = 16 Hz) at ca. 9.3 and 7.2 ppm and the acrylate methyl ester at ca. 4.1 ppm. The spectra also showed a doublet (J = 8 Hz) at 6.59 ppm for the chromatographically most mobile pigment (6.36 ppm for the least mobile one) and integration evidence for obscured resonances (2 protons) beneath the methylene resonances between 4.0 and 4.5 ppm. The mass spectra of the two structurally unidentified compounds were also compatible with structures 8 and 9 and possessed a molecular ion at m/e 706 with expected fragmentation patterns.[16]

The spectroscopic evidence was entirely in agreement with structures 8 and 9 for the monoacrylate porphyrins. Bearing in mind the >100% yield in the mercuration step, and the fact that increase in the excess of mercuric acetate also increased the yield of 8 and 9 relative to 7, a likely mechanistic pathway to these compounds is shown (for compound 8) in Scheme I. The key step is proposed to

Scheme II. (A) Normal Mode of cis Oxidative Addition of Aryl Palladium Salts and Subsequent cis Reductive Elimination. (B) Restricted Rotation of Porphyrin-Palladium System Prohibits cis Elimination, Thereby Permitting Acid Hydrolysis of the Pd-Carbon Bond. Steps: 1, cis Addition of ArPdCl; 2, Rotation; 3, Loss of PdHCl via cis Elimination; 4, Intramolecular Addition of PorPdCl; 5, Hydrolysis, + HX, then −PdClX, Owing to Restricted Rotation. Por = Porphyrin



involve *trimercuration* of zinc(II) deuteroporphyrin IX dimethyl ester (5) to give 10. With $LiPdCl_3$ and methyl acrylate, the species 11 is formed; subsequent palladation of 11 would yield 12, which has its reactive meso-palladium atom close the the β-acrylate where it would be capable of inducing an intramolecular coupling reaction to form the isocyclic ring in 8.

In normal palladium coupling reactions[17] the addition of the metal to the olefin results in the metal locating itself on the most hindered carbon of the alkene because the organic group predominantly adds to the least substituted carbon. In the system shown in Scheme I, not only does the ester function have the smaller steric requirement to favor ring formation at the methylene α to the ester but also spatial constraints favor a five-membered ring over four. Such conditions require that the palladium migrate to the methylene adjacent to the porphyrin in the newly formed isocyclic ring system (Scheme I); the molecular weight (m/e 706, mass spectrometry) indicates that there is no reductive elimination of HPdCl (which would give an olefin, m/e 704). In the usual palladium coupling reaction (Scheme IIA) the stereochemistry of the addition is cis, as is the reductive elimination of HPdCl.[17] Scheme IIB, however, shows that in the case under discussion, cis elimination is prohibited by restricted rotation as a result of the prior ring closure. Thus, we propose that the PdCl group is lost by simple acid hydrolysis (Scheme IIB) rather than by reductive elimination, and the product is compound 8.

The isomeric identities of 8 and 9 were established by using the previously synthesized[14] zinc(II) porphyrin 13, an intermediate in the synthesis of S-411 porphyrin. Mercuration of 13 gave 14 and 15 as a mixture, which was treated with $LiPdCl_3$ and methyl acrylate to give a readily separable mixture of the acrylate 16 and the porphyrin 17 bearing a five-membered isocyclic ring. This compound was identified (by NMR and analytical HPLC with coinjections) with the product obtained by catalytic hydrogenation of the lower (i.e., compound 9) of the two "monoacrylates". Thus, the structures assigned to compounds 8 and 9 are unambiguously those depicted in the structural formulas.

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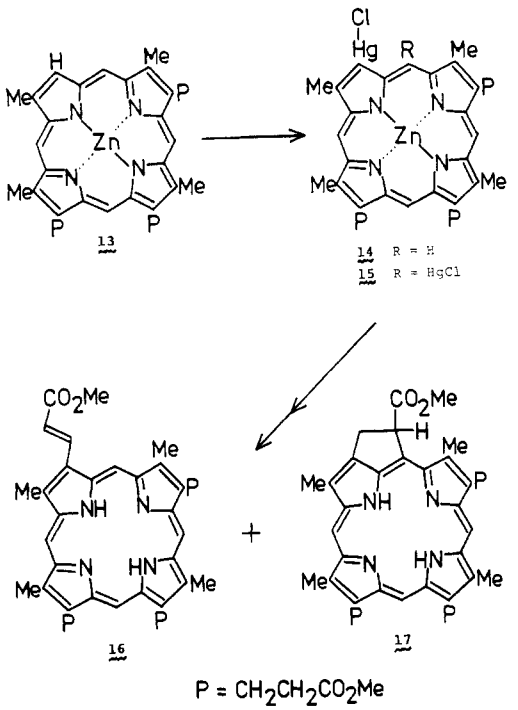
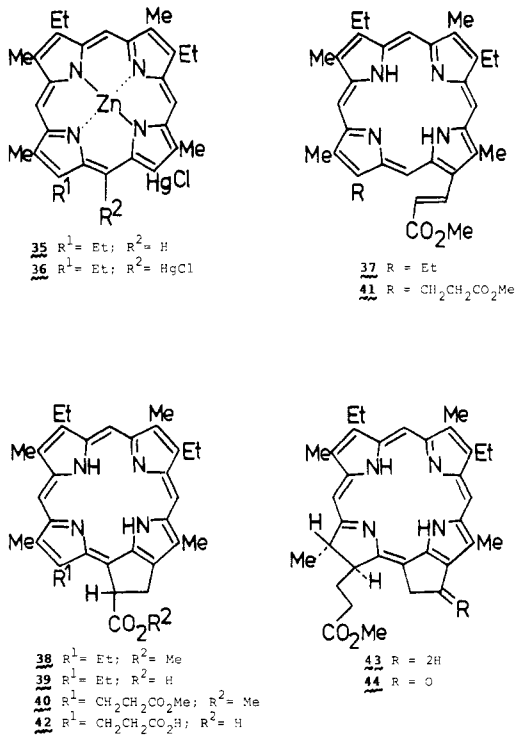


P = $CH_2CH_2CO_2Me$

Syntheses of DPEP (2) and Deoxophylloerythrin Methyl Ester (3). Syntheses of the two porphyrins to be further elaborated by the mercuration procedure, namely, pyrroetioporphyrin XV (4) (for DPEP) and 31 (for deoxophylloerythrin), were accomplished in an uneventful manner, as shown in Scheme III. An alternate, more efficient synthesis of 4, involving iodine-mediated cyclization of a 1′-methyl-8′-unsubstituted-*a*,*c*-biladiene salt in hot *o*-dichlorobenzene,[18] is shown in Scheme IV. Zinc(II) insertion[19] into pyrroetioporphyrin XV (4) was quantitative, and treatment with 4 molar equiv of mercuric acetate gave the two mercurated porphyrins 35 and 36. With



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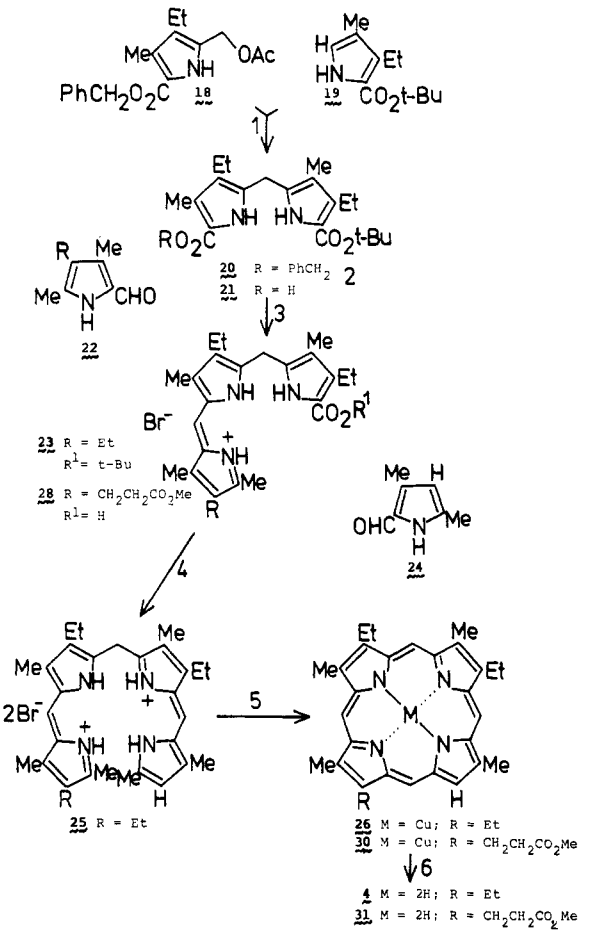
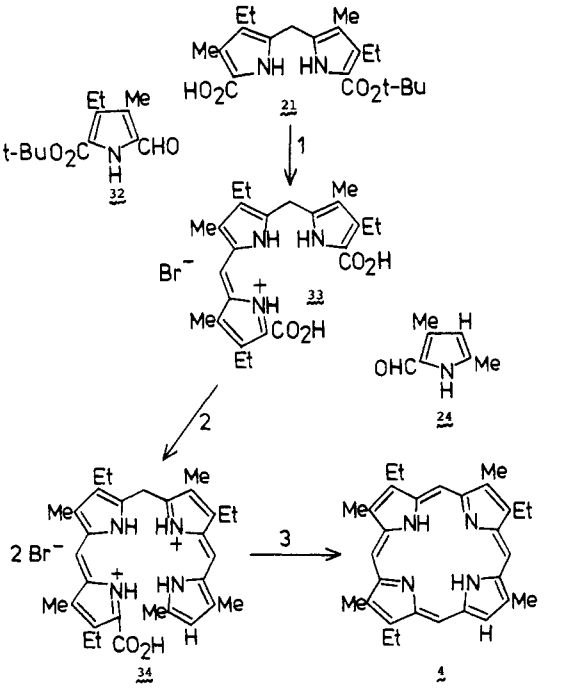
Scheme III. Synthetic Scheme for 4 and 31. Reagents: 1, TosOH in AcOH; 2, H_2/Pd-C; 3, 22 + TosOH/MeOH, then HBr; 4, 24 + TFA, then HBr; 5, $CuSO_4$/DMF; 6, H_2SO_4/TFA



Scheme IV. Synthetic Scheme for 3 Using *o*-Dichlorobenzene Cyclization of *a*,*c*-Biladiene 34. Reagents: 1, 32 + TosOH/MeOH, then HBr; 2, 24 + TFA, then HBr; 3, Hot *o*-Dichlorobenzene/I_2



$LiPdCl_3$ and methyl acrylate in acetonitrile, 35 and 36 gave the corresponding acrylate, 37, and ring-closed, 38, por-

phyrins in 60% and 24% yields, respectively. These were separated by chromatography, and the porphyrin **38** was hydrolyzed (KOH/MeOH/H_2O; 100% yield) to give **39** and then decarboxylated (in a sealed tube, 180 °C, AcOH/HCl) to give a 69% yield of DPEP (**2**). In an exactly analogous manner, deoxophylloerythrin methyl ester (**3**) was obtained from **31** by zinc(II) insertion (100%), mercuration, olefination [to give **40** (5.9%),[20] with the monoacrylate **41** (62%)], hydrolysis to afford **42**, (100%) and decarboxylatation followed by esterification (72%). Both DPEP (**2**) and deoxophylloerythrin methyl ester (**3**) were characterized by normal spectroscopic techniques, including combustion analysis (DPEP) or HRMS (**3**). Confusion appears to have arisen, in past syntheses, concerning the electronic absorption spectrum of DPEP; for example, the spectrum described in Fischer and Hoffmann,[10] Baker et al.,[9] and Flaugh and Rapoport[12] possessed a longest wavelength absorption (619 nm) which was larger in intensity than the adjacent one at lower wavelength (562 nm). On the other hand, the compounds prepared by Sugihara and McGee[11] and Clezy et al.[13] had the peak at 616 nm smaller than that at 563 nm. This apparent inconsistency, which has previously been pointed out by Rapoport,[12] appears to be due to the presence, in the latter samples,[11,13] of small amounts of metallic impurities which have the effect of raising the intensity of the shorter wavelength peaks. Our own absorption spectra initially resembled those of Sugihara, MeGee, and Clezy, but after treatment of the product with trifluoroacetic acid (to remove chelated zinc picked up from silicagel plates) the spectra reverted to those of Fischer, Baker, Rapoport, and co-workers.

The deoxophylloerythrin methyl ester (**3**) was shown to be identical with an authentic sample prepared by dehydrogenation of methyl 9-deoxomesopyropheophorbide *a* (**43**), which in turn was obtained from methyl mesopyropheophorbide *a* (**44**),[21] a readily available degradation product from chlorophyll *a*.

Experimental Section

Melting points were measured on a hot-stage apparatus and are uncorrected. Neutral alumina (Merck) or silica gel 60 (70–230 mesh) (Merck) were used for column chromatography, and preparative TLC was carried out on 20 × 20 cm glass plates coated with Merck GF 254 silica gel (1-mm thick). Analytical TLC was performed by using Merck silica gel 60 F 254 precoated sheets (0.2 mm). High-pressure liquid chromatography (HPLC) was performed on a Waters Associates chromatograph, with a Model 6000A solvent delivery system, a U6K injector, a Perkin-Elmer LC 55B variable wavelength detector (set at 405 nm), and a microporasil (250 × 4.6 mm i.d.) column eluted with 1% tetrahydrofuran in dichloromethane. Electronic absorption spectra were measured on a Hewlett-Packard 8450A spectrophotometer (solutions in dichloromethane), proton NMR spectra were measured at 360 MHz on a Nicolet NT-360 spectrometer (solutions in $CDCl_3$), and low-resolution mass spectra were measured (direct insertion probe, 70 eV, 50 μA, source temperature ca. 200 °C) on a Finnegan 3200 mass spectrometer. High-resolution mass spectra were measured at the Department of Pharmaceutical Chemistry, UC San Francisco. Elemental analyses were performed at the Berkeley Microanalytical Laboratory, Department of Chemistry, UC Berkeley.

6,7-Bis[2-(methoxycarbonyl)ethyl]-2,4-bis[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin (7), 6,7-Bis[2-(methoxycarbonyl)ethyl]-β,4-[β′-(methoxycarbonyl)ethylene]-2-[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin (8), and 6,7-Bis[2-(methoxycarbonyl)ethyl]-α,2-[α′-(methoxycarbonyl)ethylene]-4-[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin (9). Mercury(II) acetate (2.7 g) in methanol (25 mL) was added dropwise rapidly, under nitrogen, to zinc(II) deuteroporphyrin IX dimethyl ester[19] (**5**) (850 mg) in tetrahydrofuran (100 mL) at 60 °C. The mixture was stirred for 5 h and then treated with saturated aqueous sodium chloride (100 mL) and shaken vigorously for 10 min. After dilution with dichloromethane (100 mL), the solution was collected (along with precipitated porphyrin) and washed with water (4 × 100 mL). The organic phase, still containing the precipitated porphyrin, was evaporated to dryness and was treated with 95% ethanol (50 mL) and heated until it boiled gently. The dark blue shiny metalloporphyrin was scraped from the wall of the vessel, filtered off, and dried at room temperature and high vacuum to give 1.78 g of mercurated porphyrin [λ_{max} (relative intensity), 397 nm (1.00), 550 (0.08), 582 (0.61)]. The foregoing mercurated porphyrin (610 mg) was treated in dimethyl sulfoxide, as described previously[14] with methyl acrylate (10 mL), triethylamine (0.5 mL), and $LiPdCl_3$ [from $PdCl_2$ (250 mg) and LiCl (20 mg)] in acetonitrile. After preparative thick layer chromatography (silica, elution with 3.5% methanol in dichloromethane), the least mobile fraction afforded 6,7-bis[2-(methoxycarbonyl)ethyl]-2,4-bis[2-(methoxycarbonyl)-vinyl]-1,3,5,8-tetramethylporphyrin (**7**) (111 mg, 25%), mp 259–261 °C, after recrystallization from dichloromethane/heptane. It was identical in all respects with an authentic sample.[14] The two more mobile bands were further purified by rechromatography under the same conditions as above; of these, the more mobile mobile band afforded the cyclic monoacrylate, 6,7-bis[2-(methoxycarbonyl)ethyl]-β,4-[β′-(methoxycarbonyl)ethylene]-2-[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin (**8**) (124 mg, 28%): mp 258–259 °C dec; NMR δ −3.55 and −2.65 (each br s, 1 H, NH), 3.23 (t, 4 H, CH_2CH_2CO), 3.50, 3.54, 3.57, and 3.79 (each s, 3 H, Me), 3.65 (s, 9 H, $CH_2CH_2CO_2CH_3$), 4.07 (s, 3 H, $CH{=}CHCO_2CH_3$), 4.12, (d, 1 H, CH of isocyclic ring CH_2), 4.34 and 4.43 (each t, 2 H, CH_2CH_2CO), 4.40–4.55 (dd, CH of isocyclic ring CH_2), 6.59 (d, J = 8 Hz, 1 H, $CHCO_2Me$), 7.19 and 9.36 (each d, J = 16 Hz, 1 H, CH=CH), 9.88, 9.91, and 10.00 (each s, 1 H, meso-H); vis λ_{max} 416 nm (ε 189 000), 508 (17 540), 544 (8300), 580 (7300), 636 (15 000); MS, *m/e* (relative intensity) 706 (49), 647 (74), 633 (9), 573 (5), 559 (3), 515 (10), 501 (32), 257 (100). Anal. Calcd for $C_{40}H_{42}N_4O_8 \cdot {}^1/_2H_2O$: C, 67.11; H, 6.06; N, 7.83. Found: C, 67.20; H, 6.08; N, 7.72.

The least mobile monoacrylate band afforded 89 mg (20%) of 6,7-bis[2-(methoxycarbonyl)ethyl]-α,2-[α′-(methoxycarbonyl)-ethylene]-4-[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin (**9**): mp 283.5–285 °C; NMR δ −3.56 and −2.65 (each br s, 1 H, NH), 3.26 (m, 4 H, CH_2CH_2CO), 3.45, 3.50, 3.55, and 3.63 (each s, 3 H, Me), 3.63 and 3.67 (each s, 6 H, 3 H, $CH_2CH_2CO_2CH_3$)e, 4.08 (s, 3 H, $CH{=}CHCO_2CH_3$), 4.31, 4.40 (each t, 2 H, CH_2CH_2CO), 4.26–4.46 (dd, 2 H, isocyclic CH_2), 6.36 (d, 1 H, $CHCO_2Me$), 7.07 and 9.27 (each d, J = 16 Hz, 1 H, CH=CH), 9.85, 9.92, and 10.05 (each s, 1 H, meso-H); vis λ_{max} 416 nm (ε 164 000), 508 (15 600), 546 (8000), 580 (6800), 632 (12 700); MS, *m/e* (relative intensity) 706 (100), 647 (57), 633 (10), 587 (3), 573 (6), 559 (5), 515 (6), 501 (13). Anal. Calcd for $C_{40}H_{42}N_4O_8$: C, 67.97; H, 5.99; N, 7.93. Found: C, 67.75; H, 6.06; N, 7.76.

The unique isomeric identities assigned to **8** and **9** were established by using the experiments described below.

4,6,7-Tris[2-(methoxycarbonyl)ethyl]-α,2-[α′-(methoxycarbonyl)ethylene]-1,3,5,8-tetramethylporphyrin (17). (A) By Hydrogenation of Zinc(II) 6,7-Bis[2-(methoxycarbonyl)ethyl]-α,2-[α′-(methoxycarbonyl)ethylene]-4-[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin. The foregoing least mobile monoacrylate isomer (**9**) was converted into the corresponding zinc(II) complex by using the zinc(II) acetate method,[19] and 32 mg of this in tetrahydrofuran (30 mL) and triethylamine (0.1 mL) was hydrogenated at room temperature and atmospheric pressure over 10% palladized charcoal (25 mg) until uptake of hydrogen ceased. The catalyst was removed by filtration through a bed of Celite, and the filtrate was evaporated to dryness to give a bright red solid. This was purified by chromatography on preparative thick layer plates (silica, elution with 3% methanol in dichloromethane), and elution of the major red band from the silica gel (5% methanol in dichloromethane)

(20) The lower than expected yield of cyclized material is presumably a consequence of the greater steric requirement of propionate (relative to ethyl) at position 7, thus reducing the amount of dimercurated intermediate.

(21) Goff, D. A.; Smith, K. M., unpublished results.

gave the zinc complex of **17**. This was dissolved in trifluoroacetic acid (3 mL), set aside for 5 min, and then diluted with water, extracted with dichloromethane (50 mL), which was then washed with aqueous sodium bicarbonate and then water, dried (Na_2SO_4), and evaporated to dryness. The product was recrystallized from dichloromethane/hexane and gave 29 mg (69%): mp 185–186 °C; NMR δ −3.01 (br s, 2 H, NH), 3.24, 3.26, and 3.31 (each t, 2 H, CH_2CH_2CO), 3.52, 3.56, 3.60, 3.65 (each s, 3 H, Me), 3.67, 3.678, 3.682 (each s, 3 H, 3 H, 6 H, OMe), 4.15 (d, J = 17.3 Hz, 1 H, isocyclic ring CH_2), 4.52 (dd, J = 8.3 and 17.3 Hz, 1 H, isocyclic ring CH_2), 4.36, 4.46, and 4.48 (each t, 2 H, CH_2CH_2CO), 6.61 (d, 1 H, $CHCO_2Me$), 9.99, 10.06, and 10.09 (each s, 1 H, meso-H); vis λ_{max} 399 nm (ϵ 302 000), 500 (23 800), 534 (7100), 564 (9200), 619 (8700). MS, m/e (relative intensity) 708 (93), 678 (7), 650 (100), 577 (5), 561 (4), 517 (4), 503 (19). Anal. Calcd for $C_{40}H_{44}N_4O_8$: C, 67.78; H, 6.26; N, 7.90. Found: C, 68.06; H, 6.42; N, 7.80.

(B) By Transformation of Zinc(II) 4,6,7-Tris[2-(methoxycarbonyl)ethyl]-1,3,5,8-tetramethylporphyrin (13). Zinc(II) 4,6,7-tris[2-(methoxycarbonyl)ethyl]-1,3,5,8-tetramethylporphyrin (**13**) was synthesized from 2-acetyldeuteroporphyrin IX dimethyl ester, as described previously.[14] It was transformed into the title compound (5.4-mg scale, 28% yield) by mercuration and subsequent treatment with methyl acrylate and $LiPdCl_3$ in acetonitrile as described above. The product was identical, in all respects, with the title compound synthesized by using method A; since the isomeric identity of the product from method B has been previously established,[14] this sequence definitively differentiates between the two monoacrylate isomers **8** and **9**, with structure **8** corresponding with the chromatographically most mobile isomer.

2,6,7-Tris[2-(methoxycarbonyl)ethyl]-β,4-[β'-(methoxycarbonyl)ethylene]-1,3,5,8-tetramethylporphyrin. This porphyrin was likewise prepared by catalytic hydrogenation of the zinc(II) complex of 6,7-bis[2-(methoxycarbonyl)ethyl]-β,4-[β'-(methoxycarbonyl)ethylene]-2-[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin (**8**) (45 mg) to give 38.7 mg (94%) of the title compound: mp 215–216 °C; NMR δ −3.78 and −2.99 (each br s, 1 H, NH), 3.25, 3.27, and 3.39 (each t, 2 H, CH_2CH_2CO), 3.56, 3.58, 3.59, and 3.65 (each s, 3 H, Me), 3.670, 3.673, and 3.70 (each s, 3 H, OMe), 4.17 (d, J = 17.3 Hz, 1 H, isocyclic ring CH_2), 4.52 (dd, J = 8.3 and 17.3 Hz, 1 H, isocyclic ring CH_2), 4.36, 4.46, and 4.49 (each t, 2 H, CH_2CH_2CO), 6.66 (d, J = 8.3 Hz, 1 H, $CHCO_2Me$), 9.99, 10.07, and 10.11 (each s, 1 H, meso-H); vis λ_{max} 400 nm (ϵ 235 000), 500 (18 700), 534 (5000), 564 (7700), 618 (7600). Anal. Calcd for $C_{40}H_{44}N_4O_8$: C, 67.78; H, 6.26; N, 7.90. Found: C, 68.04; H, 6.41; N, 8.03.

Syntheses of DPEP (2) and Deoxophylloerythrin Methyl Ester (3). Ethyl 3,5-Dimethylpyrrole-2-carboxylate. A solution of sodium nitrite (200 g) in water (600 mL) was added to a cooled, stirred solution of diethyl malonate (Aldrich, 256 mL) in acetic acid (600 mL) at a rate such that the temperature remained below 10 °C. After being stirred for 3 h at room temperature, the mixture was extracted with dichloromethane (600 mL), washed with water (2 × 200mL), dried (Na_2SO_4), and evaporated to give an orange liquid. This material (ethyl oximinoacetoacetate) was diluted with acetic acid (600 mL) and then added slowly to a mixture of pentane-2,4-dione (Aldrich, 113 mL) in acetic acid (550 mL) at 95 °C, while a mixture of zinc dust (260 g) and anhydrous sodium acetate (304.5 g) was simultaneously added. The mixture was then heated under reflux for an additional 1 h and then poured into ice–water, and the precipitated solid was filtered, washed with water, and dried (vacuum oven). The resulting solid was recrystallized from dichloromethane/heptane to give fine white crystals (146 g; 80%. lit.[22] yield, 49%): mp 122–123 °C (lit.[22] mp 123–124 °C); NMR δ 1.33 (t, 3 H, CH_3CH_2, 2.24 and 2.30 (each s, 3 H, Me), 4.30 q, 2 H, CH_3CH_2), 5.79 (d, 1 H, 4-H), 9.5 (br s, 1 H, NH).

2-Formyl-3,5-dimethylpyrrole (24). 3,5-Dimethylpyrrole-2-carboxylic acid (600 mg, obtained by saponification[23] of the above ethyl ester) was added portionwise, at room temperature with stirring, to trifluoroacetic acid (7 mL), and the mixture was then stirred for a further 5 min. It was cooled to 0 °C and treated with trimethyl orthoformate (3.8 mL). After 5 min the solution was warmed to room temperature, diluted with water (40 mL), and extracted with dichloromethane (3 × 50 mL). The combined organic phases were washed with water, dried (Na_4SO_4), and evaporated to dryness to give a pale brown solid. After chromatography (silica, elution with dichloromethane), the appropriate eluates were evaporated to yield 430 mg (80%) of the product: mp 89–90 °C (lit.[24] mp 90 °C); NMR δ 2.33 (s, 6 H, Me), 5.84 (s, 1 H, 4-H), 9.47 (s, 1 H, CHO), 11.14 (br s, 1 H, NH).

***tert*-Butyl 3-Ethyl-5-formyl-4-methylpyrrole-2-carboxylate (32).** 2-(*tert*-Butoxycarbonyl)-3-ethyl-4-methylpyrrole-5-carboxylic acid[25] (2.0 g) in dichloromethane (25 mL) was treated with the Vilsmeier complex prepared from phosphoryl chloride (2.45 mL) and dimethylformamide (2.08 mL). The mixture was stirred at room temperature for 30 min until analytical TLC (silica, elution with dichloromethane) showed all material to be retained at the origin. Aqueous sodium acetate (50 mL) was cautiously added, followed by aqueous sodium bicarbonate until the solution reached pH 8. The mixture was then stirred at 30 °C for 30 min before being extracted with dichloromethane (3 × 25 mL), washed with water, dried (Na_2SO_4), and evaporated to dryness to give white needles (2.22 g, 99%); mp 96–97 °C, NMR δ 1.18 (t, 3 H, CH_2CH_3), 1.65, (s, 9 H, *t*-Bu), 2.40 (s, 3 H, Me), 2.78 (q, 2 H, CH_2CH_3), 9.70 (br s, 1 H, NH), 9.82 (s, 1 H, CHO). Anal. Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.67; H, 8.13; N, 5.88.

5′-(*tert*-Butoxycarbonyl)-3,4′-diethyl-3′,4-dimethylpyrromethane-5-carboxylic Acid (21). Benzyl 5′-(*tert*-butoxycarbonyl)-3,4′-diethyl-3′,4-dimethylpyrromethane-5-carboxylate (**20**)[25] (3.0 g) in acetone (100 mL) containing triethylamine (0.1 mL) and 10% palladized charcoal (500 mg) was hydrogenated at room temperature and atmospheric pressure until uptake of hydrogen ceased. The catalyst was removed by filtration through Celite and the filtrate was evaporated to dryness to give a white solid. Recrystallization from dichloromethane/cyclohexane gave 2.3 g (91%): mp 156–157 °C dec; NMR δ 0.98 and 1.03 (each t, 3 H, CH_2CH_3), 1.55 (s, 9 H, *t*-Bu), 2.07 and 2.28 (each s, 3 H, Me), 2.51 (m, 4 H, CH_2CH_3), 3.82 (s, 2 H, CH_2); 10.86 and 11.53 (each br s, 1 H, NH). Anal. Calcd for $C_{21}H_{30}N_2O_4 \cdot {}^1/_4H_2O$: C, 66.38; H, 8.36; N, 7.37. Found: C, 66.51; H, 8.05; N, 7.22.

***tert*-Butyl 1,3,6-Triethyl-2,4,5,6′-tetramethyltripyrrene-*b*-1′-carboxylate Hydrobromide (23).** The foregoing pyrromethanecarboxylic acid (**21**) (245 mg) and 4-ethyl-2-formyl-3,5-dimethylpyrrole (**22**) (134 mg) in dichloromethane (30 mL) were stirred with a solution of toluene-*p*-sulfonic acid hydrate (278 mg) in methanol (3 mL) for 40 min. The solution was washed with water, aqueous sodium bicarbonate, and water again and then dried (Na_2SO_4) and evaporated to dryness. Dry dichloromethane (15 mL) was added, and then dry HBr gas was passed through the solution for 9 s (color: orange to red). Diethyl ether (70 mL) was added dropwise while stirring at 0 °C, and the product was filtered off to give 334 mg (90%): mp 224–245 °C dec; NMR δ 0.94, 1.07, and 1.08 (each t, 3 H, CH_2CH_3), 2.05, 2.24, 2.28, and 2.70 (each s, 3 H, Me), 2.41, 2.46, and 2.71 (each q, 2 H, CH_2CH_3), 4.33 (s, 2 H, CH_2), 7.07 (s, 1 H, CH=), 10.25, 12.97, and 12.98 (each br s, 1 H, NH); vis λ_{max} 494 nm (ϵ 87 700); Anal. Calcd for $C_{25}H_{33}BrN_3O_2 \cdot {}^1/_2H_2O$: 60.48; H, 6.90; N, 8.47. Found: C, 60.05; H, 6.73; N, 8.22.

1,3-Diethyl-6-[2-(methoxycarbonyl)ethyl]-2,4,5,6′-tetramethyltripyrrene-*b*-1′-carboxylic Acid Hydrobromide (28). This tripyrrene salt was likewise prepared from **21** (558 mg) and 2-formyl-4-[2-(methoxycarbonyl)ethyl]-3,5-dimethylpyrrole[26] (**27**) (374 mg). In this case the HBr gas caused cleavage of the *tert*-butyl ester, so the product (797 mg; 98%) was isolated as the 1′-carboxylic acid, mp 210–211 °C dec, NMR δ 0.02 and 1.07 (each t, 2 H, CH_2CH_3), 2.05, 2.24, 2.30, and 2.70 (each s, 3 H, Me), 2.27 (t, 2 H, CH_2CH_2CO), 2.39 and 2.75 (each q, 2 H, CH_2CH_3), 2.47 (t, 2 H, CH_2CH_2CO), 3.66 (s, 3 H, OMe), 4.34 (s, 2 H, CH_2), 7.08

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(s, 1 H, CH=), 10.17, 13.01, and 13.09 (each br s, 1 H, NH); vis λ_{max} 494 nm (ϵ 87 300). Anal. Calcd for $C_{27}H_{35}BrN_3O_4 \cdot {}^1/_2H_2O$: C, 58.48; H, 6.54; N, 7.58. Found: C, 58.68; H, 6.55; N, 7.34.

1,3,6-Triethyl-2,4,5-trimethyltripyrrene-*b*-1′,6′-dicarboxylic Acid Hydrobromide (33). This tripyrrene salt was likewise prepared in 84% yield (594 mg) from 5′-(*tert*-butoxycarbonyl)-3,4′-diethyl-3′,4-dimethylpyrromethane-5-carboxylic acid (**20**) (513 mg) and *tert*-butyl 3-ethyl-5-formyl-4-methylpyrrole-2-carboxylate (**32**) (415 mg): mp 169–170 °C; NMR δ 1.08, 1.15, and 1.19 (each t, 3 H, CH_2CH_3), 2.05, 2.27, and 2.32 (each s, 3 H, Me), 2.47, 2.48, and 2.68 (each q, 2 H, CH_2CH_3), 4.25 (s, 2 H, CH_2), 6.52 (s, 1 H, CH=); 10.15, 12.92, and 13.27 (each br s, 1 H, NH); the carboxylic acid protons were not observed; vis λ_{max} 490 nm (ϵ 28 800). Anal. Calcd for $C_{25}H_{31}BrN_3O_4$: C, 58.03; H, 6.04; N, 8.12. Found: C, 57.86; H, 6.32; N, 8.31.

3,5,8-Triethyl-1′,2,4,6,7,8′-hexamethyl-*a*,*c*-biladiene Dihydrobromide (25). *tert*-Butyl 1,3,6-triethyl-2,4,5,6′-tetramethyltripyrrene-*b*-1′-carboxylate hydrobromide (**23**) (370 mg) was stirred in trifluoroacetic acid (5 mL) for 5 min before addition of 2-formyl-3,5-dimethylpyrrole (**24**) (92 mg) and then 30% HBr in acetic acid (3.0 mL). After stirring for 1 h, ether (80 mL) was added dropwise with continued stirring. The *a*,*c*-biladiene salt was filtered off and washed with ether to give greenish brown microprisms (308 mg; 72%): mp 258–260 °C dec; NMR δ 0.67, 1.09, and 1.16 (each t, 3 H, CH_2CH_3), 1.94, 2.26, 2.31, 2.40, 2.69, and 2.70 (each s, 3 H, Me), 2.46, 2.47, and 2.64 (each q, 2 H, CH_2CH_3), 5.10 (s, 2 H, CH_2), 6.25 (s, 1 H, 1-H), 7.13 (s, 2 H, CH=), 12.96, 12.99, 13.03, and 13.20 (each br s, 1 H, NH); vis λ_{max} 446 nm (ϵ 104 300), 522 (122 000). Anal. Calcd for $C_{31}H_{42}Br_2N_4$: C, 59.05; H, 6.71; N, 8.89. Found: C, 58.82; H, 6.53; N, 8.64.

3,5-Diethyl-8-[2-(methoxycarbonyl)ethyl]-1′,2,4,6,7,8′-hexamethyl-*a*,*c*-biladiene Dihydrobromide (29). This *a*,*c*-biladiene salt was likewise prepared in 86% yield (747 mg) from 1,3-diethyl-6-[2-(methoxycarbonyl)ethyl]-2,4,5,6′-tetramethyltripyrrene-*b*-1′-carboxylic acid (**28**) (689 mg) and 2-formyl-3,5-dimethylpyrrole (187 mg) (**24**): mp 209–210 °C dec; NMR δ 0.63, 1.11 (each t, 3 H, CH_2CH_3), 1.92, 2.25, 2.32, 2.70, and 2.72 (each s, 3 H, Me), 2.47, 2.62 (each q, 2 H, CH_2CH_3), 2.48 (t, 2 H, CH_2CH_2CO), 2.77 (t, 2 H, CH_2CH_2CO), 3.67 (s, 3 H, OMe), 5.21 (s, 2 H, CH_2), 6.22 (s, 1 H, 1-H), 7.10 and 7.11 (each s, 1 H, CH=), 13.20, 13.34, and 13.4) (each br s, 2 H, 1 H, 1 H, NH); vis λ_{max} 446 nm (ϵ 108 500), 522 (59 100). Anal. Calcd for $C_{33}H_{43}Br_2N_4O_2 \cdot H_2O$: C, 56.39; H, 6.31; N, 7.97. Found: C, 56.63; H, 6.26; N, 7.82.

3,5,8-Triethyl-1′,2,4,6,7-pentamethyl-*a*,*c*-biladiene-6′-carboxylic Acid Dihydrobromide (34). This *a*,*c*-biladiene salt was likewise prepared from 1,3,6-triethyl-2,4,5-trimethyltripyrrene-*b*-1′,6′-dicarboxylic acid hydrobromide (**33**) (502 mg) and 2-formyl-3,5-dimethylpyrrole (**24**) (143 mg). The yield was 95% (609 mg): mp 260–261 °C dec; NMR δ 0.65, 1.14, and 1.20 (each t, 3 H, CH_2CH_3), 2.26, 2.28, 2.31, 2.39, and 2.71 (each s, 3 H, Me), 2.48, 2.51, and 2.65 (each q, 2 H, CH_2CH_3), 5.24 (s, 2 H, CH_2), 6.23 (s, 1 H, 1-H), 7.105 and 7.11 (each s, 1 H, CH=), 7.67 (s, 1 H, 8′-H), 13.20 and 13.42 (each br s, 2 H, NH); vis λ_{max} 444 nm (ϵ 123 000), 520 (105 000). Anal. Calcd for $C_{30}H_{38}Br_2N_4 \cdot {}^1/_2H_2O$: C, 57.79; H, 6.31; N, 8.99. Found: C, 57.80; H, 6.44; N, 8.88.

2,4,7-Triethyl-1,3,5,8-tetramethylporphyrin, "Pyrroetioporphyrin XV" (4). (A) From the 1′,8′-Dimethyl-*a*,*c*-biladiene (25). 3,5,8-Triethyl-1′,2,4,6,7,8′-hexamethyl-*a*,*c*-biladiene dihydrobromide (**25**) (500 mg) in dry dimethylformamide (60 mL) containing anhydrous copper(II) sulfate (1.35 g; 10 equiv) was stirred under nitrogen at 160 °C for 4 min. After being cooled, the solution was poured into water (100 mL) and extracted with dichloromethane (2 × 50 mL). The organic phase was dried (Na_2SO_4) and evaporated to dryness under vacuum to give a residue which was chromatographed (Alumina, Brockmann Grade III; elution with dichloromethane). The red fractions (compound **26**) were evaporated to dryness, and the residue was taken up in trifluoroacetic acid (8.5 mL) and concentrated sulfuric acid (1.5 mL) and set aside for 45 min. The mixture was then diluted with water (50 mL), extracted with dichloromethane (3 × 50 mL), and then dried (Na_2SO_4) and evaporated to dryness. The residue was chromatographed on preparative plates (silica, elution with dichloromethane) and the red band was extracted from the silica. The residue was recrystallized from dichloromethane/hexane to give bright red microprisms (87 mg, 24%): mp 269–270 °C; NMR δ −3.80 (br s, 2 H, N H), 1.86 and 1.88 (each t, 6 H, 3 H, CH_2CH_3), 3.62, 3.64, 3.66, and 3.75 (each s, 3 H, Me), 4.09 (q, 6 H, CH_2CH_3), 9.08 (s, 1 H, 6-H), 10.03, 10.09, and 10.13 (each s, 1 H, 2 H, 1 H, meso-H); vis λ_{max} 385 nm (ϵ 149 000), 496 (18 900), 530 (12 700), 566 (9200), 620 (6000); MS, *m*/*e* (relative intensity) 450 (100), 435 (33), 422 (11), 391 (8), 375 (3), 250 (14). Anal. Calcd for $C_{30}H_{34}N_4$: C, 79.96; H, 7.61; N, 12.43. Found: C, 80.12; H, 7.88; N, 12.02.

(B) From the 1′-Methyl-*a*,*c*-biladiene-8′-carboxylic Acid (34). 3,5,8-Triethyl-1′,2,4,6,7-pentamethyl-*a*,*c*-biladiene-8′-carboxylic acid dihydrobromide (**34**) (100 mg) in *o*-dichlorobenzene (20 mL) was heated to 190 °C. Iodine (384 mg; 10 equiv) was added and the mixture was refluxed for 20 min before being cooled. The mixture was chromatographed on alumina (Brockmann Grade I, elution with hexane, followed by 5% methanol in dichloromethane), and the red fractions were collected and evaporated to dryness, and the residue was subjected to further purification by preparative TLC (silica gel, elution with dichloromethane). Extraction of the major red band with 5% methanol in dichloromethane gave the porphyrin (20 mg; 25%) identical with the material obtained in method A.

2,4-Diethyl-7-[2-(methoxycarbonyl)ethyl]-1,3,5,8-tetramethylporphyrin (31). This porphyrin was prepared by way of the copper(II) complex **30** as described above (method A), from 3,5-diethyl-8-[2-(methoxycarbonyl)ethyl]-2,3,5,7-tetramethyl-*a*,*c*-biladiene dihydrobromide (**29**) (605 mg) and copper(II) acetate (3.50 g; 20 equiv) in dry dimethylformamide (60 mL) at 160 °C for 4 min. After removal of the chelating copper, the product was obtained in 24% yield (108 mg): mp 240–241 °C; NMR δ −3.80 (br s, 2 H, NH), 1.87 and 1.88 (each t, 3 H, CH_2CH_3), 3.28 (t, 2 H, CH_2CH_2CO), 3.63, 3.65, 3.67, and 3.77 (each s, 3 H, 6 H, 3 H, 3 H, Me and OMe), 4.09 and 4.11 (each q, 2 H, CH_2CH_3), 4.41 (t, 2 H, CH_2CH_2CO), 9.11 (s, 1 H, 6-H), 10.02, 10.09, 10.11, and 10.13 (each s, 1 H, meso-H); vis λ_{max} 398 (ϵ 182 000), 496 (14 300), 530 (9000), 566 (6700), 620 (4500); MS, *m*/*e* (relative intensity) 508 (100), 493 (5), 478 (7), 450 (9), 436 (26), 420 (27). Anal. Calcd for $C_{32}H_{36}N_4O_2$: C, 75.56; H, 7.13; N, 11.01. Found: C, 75.32; H, 7.09; N, 10.96.

2,4,7-Triethyl-6,γ-[γ′-(methoxycarbonyl)ethylene]-1,3,5,8-tetramethylporphyrin (38) and 2,4,7-Triethyl-6-[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin (37). Under an atmosphere of nitrogen, mercuric acetate (158 mg; 4 equiv) in methanol (25 mL) was added to zinc(II) 2,4,7-triethyl-1,3,5,8-tetramethylporphyrin (obtained from the corresponding free base porphyrin **4** using the zinc acetate method[19]) (78.6 mg) in dry tetrahydrofuran (20 mL) at 60 °C. After 4 h, saturated aqueous sodium chloride (50 mL) was added and the biphasic mixture was stirred vigorously for 10 min. The mixture was then diluted with dichloromethane (50 mL) and the organic layer was collected, washed with water (4 × 100 mL), dried (Na_2SO_4), and evaporated to dryness to give a deep purple solid. To this solid was added 95% ethanol (20 mL), and the mixture was brought to boiling; the solid was scraped from the walls of the vessel and was collected by filtration. The blue flakes were dried under vacuum to give the mercurated porphyrins **35** and **36** (114 mg; 84%); vis λ_{max} (relative intensity) 408 nm (1.00), 540 (0.06), 576 (0.06). Without further purification the mercurated zinc porphyrins (100 mg) were dissolved in dimethyl sulfoxide (10 mL), tetrahydrofuran (20 mL), and freshly distilled methyl acrylate (5 mL), and the mixture was stirred under nitrogen at 50 °C. Following addition of triethylamine (0.5 mL), a solution of $LiPdCl_3$ [prepared by refluxing, for 30 min, $PdCl_2$ (45 mg) and LiCl (5.0 mg) in acetonitrile (10 mL)] was added dropwise. After 30 min the reaction mixture was cooled and filtered through a 4-cm thick pad of Celite, and the filtrate was diluted with dichloromethane (50 mL), washed with water (50 mL), dried (Na_2SO_4), and evaporated to dryness. The residue was chromatographed on thick layer plates (silica gel, elution with dichloromethane) and two principal bands were collected. After removal of the porphyrins from the silica gel with 5% methanol in dichloromethane and evaporation of the solvents, the separate bands were dissolved in trifluoroacetic acid (5 mL) and stirred for 5 min. The mixtures were diluted with dichloromethane (50 mL), washed with water (3 × 100 mL), dried (Na_2SO_4), and evaporated to dryness. The most mobile fraction was crystallized from chloroform/hexane and afforded the ring-cyclized porphyrin **38** (11.6 mg; 24%): mp

263–264 °C; NMR δ −3.80 and −3.00 (each br s, 1 H, NH), 1.70, 1.85, and 1.88 (each t, 3 H, CH_2CH_3), 3.57, 3.59, 3.60, and 3.70 (each s, 3 H, Me), 4.02, 4.06, and 4.15 (each q, 2 H, CH_2CH_3), 4.19 (d, J = 17.3 Hz, 1 H, 6′-H), 4.59 (dd, J = 8.3, 17.3 Hz, 6′-H), 6.69 (d, J = 8.3 Hz, 1 H, γ′-H), 10.02, 10.05, and 10.12 (each s, 1 H, meso-H); vis λ_{max} 399 nm (ε 246 000), 498 (17 500), 536 (5200), 564 (7900), 616 (7150); MS, m/e (relative intensity) 534 (100), 519 (4), 475 (69), 460 (5), 445 (8), 431 (9), 429 (6). Anal. Calcd for $C_{34}H_{38}N_4O_2$: C, 76.37; H, 7.16; N, 10.48. Found: C, 76.16; H, 7.16; N, 10.26.

The least mobile band afforded, after recrystallization from chloroform/hexane, 29.4 mg (60%) of 2,4,7-triethyl-6-[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin (**37**): mp 258–259 °C dec; NMR δ −3.68 (br s, 2 H, NH), 1.85, 1.86, and 1.88 (each t, 3 H, CH_2CH_3), 3.56, 3.67, 3.68, and 3.81 (each s, 3 H, Me), 4.02, 4.14, and 4.15 (each q, 2 H, CH_2CH_3), 4.07 (s, 3 H, OMe), 7.12 and 9.42 (each d, J = 16 Hz, CH=CH); 10.04, 10.05, 10.17, and 10.21 (each s, 1 H, meso-H); vis λ_{max} 412 nm (ε 163 000), 508 (10 900), 550 (18 700), 574 (11 300), 636 (2700); MS, m/e (relative intensity) 534 (100), 519 (19), 503 (4), 475 (8); $C_{34}H_{38}N_4O$ requires 534.299, found 534.300.

2,4-Diethyl-7-[2-(methoxycarbonyl)ethyl]-6,γ-[γ′-(methoxycarbonyl)ethyl]-1,3,5,8-tetramethylporphyrin (40) and 2,4-Diethyl-6-[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin (41). These porphyrins were also prepared, as described above, from the zinc(II) complex of 2,4-diethyl-7-[2-(methoxycarbonyl)ethyl]-1,3,5,8-tetramethylporphyrin (**31**), (82 mg). The most mobile chromatographic band afforded 2,4-diethyl-7-[2-(methoxycarbonyl)ethyl]-6,γ-[γ′-(methoxycarbonyl)ethylene]-1,3,5,8-tetramethylporphyrin (**40**) (5 mg; 5.9%): mp 283–284 °C; NMR δ −3.98 and −3.73 (each br s, 1 H, NH), 1.84 and 1.88 (each t, 3 H, CH_2CH_3), 3.02 and 3.17 (each m, 1 H, $CH_2CH_AH_BCO$), 3.56, 3.59, 3.64, and 3.69 (each s, 3 H, Me), 3.72 and 3.73 (each s, 3 H, OMe), 4.01 and 4.14 (each q, 2 H, CH_2CH_3), 4.20 and 4.58 (d and dd, each 1 H, CH_2 in isocyclic ring), 4.33 and 4.46 (each m, 1 H, $CH_AH_BCH_2CO$), 6.74 (d, J = 6.4 Hz, 1 H, $CHCO_2Me$), 10.00, 10.05, and 10.12 (each s, 1 H, meso-H); vis λ_{max} 400 nm (ε 181 000), 498 (13 700), 532 (3800), 568 (5500), 616 (6000); MS, m/e (relative intensity) 592 (100), 577 (7), 563 (2), 549 (7), 534 (84), 519 (10), 505 (3); $C_{36}H_{40}N_4O_4$ requires 592.305, found 592.309.

The least mobile band afforded 2,4-diethyl-6-[2-(methoxycarbonyl)vinyl]-1,3,5,8-tetramethylporphyrin (**41**) (52 mg; 62%): mp 263–264 °C; NMR δ −3.75 (br s, 2 H, NH), 1.85 and 1.87 (each t, 3 H, CH_2CH_3), 3.27 (t, 2 H, CH_2CH_2CO), 3.55, 3.65, and 3.68 (each s, 3 H, 6 H, 3 H, Me), 3.77 (s, $CH_2CH_2CO_2CH_3$), 4.01 and 4.11 (each q, 2 H, CH_2CH_3), 4.08 (s, 3 H, $CH=CHCO_2CH_3$), 4.43 (t, 2 H, CH_2CO), 7.13 and 9.37 (each d, J = 16.2 Hz, CH=CH), 10.00, 10.01, 10.11, and 10.13 (each s, 1 H, meso-H); vis λ_{max} 414 nm (ε 167 000), 510 (13 700), 552 (19 500), 176 (12 900), 638 (4900); MS, m/e (relative intensity) 592 (100), 577 (11), 563 (4), 548 (1), 533 (7), 519 (28), 504 (7); $C_{36}H_{40}N_4O_4$ requires 592.305, found 592.304.

Deoxophylloerythroetioporphyrin (DPEP) (2). 2,4,7-Triethyl-6,γ-[γ′-(methoxycarbonyl)ethylene]-1,3,5,8-tetramethylporphyrin (**38**) (8.45 mg) was dissolved in methanol (24 mL) and water (1 mL) containing potassium hydroxide (250 mg) and then heated under reflux for 6 h. The mixture was then acidified to pH 4 with dilute hydrochloric acid, extracted with ether (3 × 50 mL), dried (Na_2SO_4), and evaporated to dryness to give a deep purple solid (porphyrin carboxylic acid, **39**) in quantitative yield. Without further purification, the porphyrin was dissolved in acetic acid (1.5 mL) and placed in a Carius tube. The mixture was then diluted with 1% hydrochloric acid (3 mL) and degassed under nitrogen with 3 freeze–thaw cycles. The tube was sealed under vacuum, heated at 180 °C for 2.5 h, and reopened, and the solution was neutralized and extracted with dichloromethane. The organic phase was washed with aqueous sodium bicarbonate and water and then dried (Na_2SO_4) and evaporated to give a purple residue. This was purified on preparative silica gel TLC plates (elution with dichloromethane). The major band was eluted from the silica gel with 3% methanol in dichloromethane, which was evaporated and recrystallized from chloroform/methanol to give DPEP, **2** (5.2 mg; 69%): mp >300 °C dec. A sample was prepared for spectrophotometry by dissolving a small amount of DPEP in trifluoroacetic acid, stirring for 5 min, then addition of dichloromethane, water, and aqueous sodium bicarbonate. Extraction and drying gave a metal-free sample: NMR δ (in $CDCl_3$) −3.80 and −2.95 (each br s, 1 H, NH), 1.78, 1.85, and 1.88 (each t, 3 H, CH_2CH_3), 3.57, 3.59, and 3.69 (each s, 3 H, 3 H, 6 H, Me), 4.02, 4.11, and 4.14 (each q, 2 H, CH_2CH_3), 4.10 (m, 2 H, 9-CH_2), 5.43 (m, 2 H, 10-CH_2), 9.99, 10.00, and 10.06 (each s, 1 H, meso-H); NMR δ (in CF_3CO_2H) 1.79, 1.85, and 1.86 (each t, 3 H, CH_2CH_3), 3.75, 3.76, and 3.78 (each s, 3 H, 6 H, 3 H, Me), 4.26 (q, 6 H, CH_2CH_3), 4.49 (m, 2 H, 9-CH_2), 5.83 (m, 2 H, 10-CH_2), 10.75, 10.76, and 10.85 (each s, 1 H, meso-H); vis λ_{max} 400 nm (ε 210 000), 498 (16 000), 534 (3900), 564 (6400), 618 (6600); MS, m/e (relative intensity) 476 (100), 461 (25), 446 (5), 431 (7). Anal. Calcd for $C_{32}H_{36}N_4$: C, 80.63; H, 7.61; N, 11.75. Found: C, 80.51; H, 7.63; N, 11.73.

Deoxophylloerythrin Methyl Ester (3). (A) From the Mercuration Route. This compound was prepared, as described above, from 2,4-diethyl-7-[2-(methoxycarbonyl)ethyl]-6,γ-[γ′-(methoxycarbonyl)ethylene]-1,3,5,8-tetramethylporphyrin (**40**) (3.8 mg). Prior to the silica gel TLC chromatography, the purple residue was esterified with 5% sulfuric acid in methanol (40 mL) for 20 h, and this solution was then neutralized (sodium bicarbonate) and extracted with chloroform (50 mL). After preparative TLC purification (silica, elution with dichloromethane) the product was crystallized from dichloromethane/hexane to give 2.5 mg (72%): mp 261 °C (lit.[9,27] mp 262 °C, 264 °C); NMR δ −3.71 and −2.92 (each br s, 1 H, NH), 1.85 and 1.89 (each t, 3 H, CH_2CH_3), 3.12 (t, 2 H, CH_2CH_2CO), 3.56, 3.58, 3.67, and 3.69 (each s, 3 H, Me), 3.79 (s, 3 H, OMe), 4.02 and 4.14 (each q, 2 H, CH_2CH_3), 4.05 and 5.37 (each m, 2 H, isocyclic CH_2CH_2), 4.38 (t, 2 H, CH_2CH_2CO), 9.97, 10.00, and 10.03 (each s, 1 H, meso-H); vis λ_{max} 400 nm (ε 233 000), 498 (17 000), 532 (4000), 564 (6600), 616 (6900); MS, m/e (relative intensity) 534 (100), 519 (4), 503 (1), 492 (2), 475 (8), 461 (17), 446 (4); $C_{34}H_{38}N_4O_2$ requires 534.299, found 534.301.

(B) From Methyl 9-Deoxomesopyropheophorbide *a*.[28] Methyl 9-deoxomesopyropheophorbide *a*[21] (**43**) (30 mg) in dichloromethane (20 mL) was stirred at 0 °C (ice bath) and titrated, dropwise, with 8.5 mL of a solution of dichlorodicyanobenzoquinone (Aldrich) (19 mg) in benzene (25 mL). The procedure was monitored by using analytical TLC and by spectrophotometry, the reaction being complete when the green chlorin spot on TLC had completely changed into a red spot, and when the absorption maximum at 654 nm had concomitantly disappeared. The mixture was filtered through a short bed of alumina (Brockmann Grade III) and the red filtrate was evaporated to dryness. The residue was chromatographed on preparative TLC plates (silica gel, elution with 2.5% methanol in dichloromethane), and the fast running red band was collected. After removal from the silica gel and crystallization from dichloromethane/hexane, 7 mg (23%) of deoxophylloerythrin methyl ester (**3**) was obtained. This material was in all respects identical with the compound prepared in method A.

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92284-87-2; **43**, 13566-43-3; 2,6,7-tris[(2-(methoxycarbonyl)-ethyl]-β,4-[(β-(methoxycarbonyl)ethylene]-1,3,5,8-tetramethylporphrin, 62786-79-2; methyl acrylate, 96-33-3; diethyl malonate, 105-53-3; ethyl oximinoacetoacetate, 5447-76-7; pentane-2,4-dione, 123-54-6; ethyl 3,5-dimethylpyrrole-2-carboxylate, 2199-44-2; 3,5-dimethylpyrrole-2-carboxylic acid, 4513-93-3; 2-(*tert*-butoxycarbonyl)-3-ethyl-4-methylpyrrole-5-carboxylic acid, 52459-88-8.

Photostimulated Reaction of 1-Haloadamantane and 9-Bromotriptycene with Nucleophiles. A Nucleophilic Substitution by $S_{RN}1$ at the Bridgehead Position

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1-Haloadamantanes and 9-bromotriptycene react under irradiation with diphenylphosphide and diphenylarsenide ions to give the substitution product in good yields. 1-Iodoadamantane (8) also reacts with disodium telluride and disodium selenide under irradiation to give di-1-adamantyl ditelluride and di-1-adamantyl diselenide, respectively. 9,10-Dibromotriptycene with diphenylphosphide gives a good yield of the disubstitution product. It seems that all these reactions occur by the $S_{RN}1$ mechanism. Substrate 8 reacts under irradiation with carbanionic nucleophiles and diethyl phosphite ion, but the products are adamantane and 1,1'-biadamantyl rather than substitution products. These nucleophiles transfer an electron to 8 to form radical anions which fragment to 1-adamantyl radicals. The radicals are reduced or dimerized. In contrast, amide ions do not react with 8. The ease of the halogen nucleofugality is I > Br > Cl, the same as in the aromatic system.

It is well-known that 1-halo-substituted bridgehead compounds are very unreactive toward nucleophilic substitution reactions (S_N1 or S_N2 type mechanism),[1] but we have recently reported that 1-bromoadamantane reacts with nucleophiles by the $S_{RN}1$ mechanism.[2]

$$\underset{\mathbf{1}}{\text{1-BrAd}} + \underset{\substack{\mathbf{2},\ M = P\\ \mathbf{3},\ M = As}}{Ph_2M^-} \xrightarrow{h\nu} \underset{\mathbf{4}}{\text{1-AdMPh}_2} + \underset{\mathbf{5}}{\text{AdH}} + \underset{\mathbf{6}}{\text{(1-Ad)}_2} \quad (1)$$

Ad = adamantyl

This novel nucleophilic substitution on a bridgehead position opens an interesting field, not only from the mechanistic point of view but also as a synthetic route for this type of compounds.

We report here the photostimulated reaction of 1-X-adamantane (X = Cl, Br, I) with several nucleophiles as well as the photostimulated reactions of 9-bromo- and 9,10-dibromotriptycene with nucleophiles in order to determine the scope of this novel nucleophilic substitution at bridgehead carbon.

Results and Discussion

Reactions of 1-Haloadamantanes with Amide Ions. In the photostimulated reaction of **1** with **3** in liquid ammonia, we found a small amount of 1-aminoadamantane (**7**).[2] But when we performed a photostimulated reaction of **1** with amide ions, no reaction occurred. This result might suggest that amide ions failed to initiate the reaction (eq 2), but would propagate it (eq 3–5). However, when

$$1 + NH_2^- \overset{h\nu}{\not\rightarrow} (\text{1-BrAd})^{-\cdot} + NH_2\cdot \quad (2)$$

$$(\text{1-BrAd})^{-\cdot} \rightarrow \text{1-Ad}\cdot + Br^- \quad (3)$$

$$\text{1-Ad}\cdot + NH_2^- \rightarrow (\text{1-NH}_2\text{Ad})^{-\cdot} \quad (4)$$

$$(\text{1-NH}_2\text{Ad})^{-\cdot} + 1 \rightarrow (\text{1-BrAd})^{-\cdot} + \underset{\mathbf{7}}{\text{1-NH}_2\text{Ad}} \quad (5)$$

1-adamantyl radicals were formed by reaction of **1** with sodium metal in liquid ammonia[3] or by photostimulation with carbanionic nucleophiles (see below) together with amide ions, no **7** was found, but only **5** and **6** were formed (Table I, expt 2, 5, 6).

These results suggest that amide ions do not react either with 1-adamantyl radicals or with **1**, but **7** is formed in the reaction of **1** with **2** or **3** in the presence of amide ions (Table I, expt 3, 4). Then, **7** might be formed by the reaction of amide ions with the substitution product **4** in a consecutive reaction (eq 6 and 7).

$$1 + Ph_2M^- \xrightarrow[S_{RN}1]{h\nu} \underset{\mathbf{4}}{\text{1-AdMPh}_2} \quad (6)$$

$$4 + NH_2^- \rightarrow \underset{\mathbf{7}}{\text{1-NH}_2\text{Ad}} \quad (7)$$

4 reacted with amide ions (M = As) to give **7** (Table I, expt 7, 8) in photostimulated as well as in dark conditions, thus suggesting that the formation of **7** is derived from the attack of amide ions on **4**.

Reaction of 1-Haloadamantane with Carbanionic Nucleophiles. Carbanionic nucleophiles, such as ketone enolated ions, cyanomethyl anion, etc., react with aryl radicals to give good yields of substitution products by the $S_{RN}1$ mechanism.[3]

In the photostimulated reaction of 1-iodoadamantane with several carbanionic nucleophiles, the only products formed were the reduction product adamantane and the dimeric product **6**. No coupling products were formed (eq 8) (Table II).

$$\underset{\mathbf{8}}{\text{1-IAd}} + {}^-CH_2Z \xrightarrow{h\nu} \underset{\mathbf{5}}{\text{AdH}} + \underset{\mathbf{6}}{\text{(1-Ad)}_2} \quad (8)$$

Because there was no dark reaction, and because **5** and **6** were the only products formed from **8** in the photostimulated reactions, carbanionic nucleophiles probably

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