(1.0 mL), and the reaction was allowed to proceed for 17 h at room temperature. The solvents were removed from the reaction mixture in vacuo and the products separated on a silica Sep-pak (Waters) using ethyl acetate/methanol (94:6) as eluant. The product appeared as a mixture by ^{1}H NMR spectroscopy, and separation was attempted by HPLC on μ-Partisil using ethyl acetate as eluant. This yielded a single peak, which was determined to be a 6:4 mixture of syn and anti isomers of the acetamide 7 (0.9 mg, 73% yield).

Chelonin A acetamide (7): clear oil; IR ($CHCl_3$) 3480, 1640, 1630, 1595, 1510, 1460, 1420, 1130 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.18 (s, ~1.8 H), 2.19 (s, ~1.2 H), 2.74 (dd, 1 H, J = 13.5, 10.8 Hz), 3.05 (dd, 1 H, J = 13.0, 11.0 Hz), 3.29 (dd, 1 H, J = 13.5, 11.6 Hz), 3.54 (dd, 1 H, J = 13.0, 10.9 Hz), 3.80 (s, 3 H), 3.84 (s, 3 H), 3.87 (s, 3 H), 4.84 (dd, 1 H, J = 11.6, 10.9 Hz), 4.95 (dd, 1 H, J = 11.0, 10.8 Hz), 6.68 (s, 2 H), 7.18 (m, 3 H), 7.37 (d, ~0.4 H, J = 6.8 Hz), 7.40 (d, ~0.6 H, J = 7.2 Hz), 7.79 (d, ~0.4 H, J = 7.4 Hz), 7.83 (d, ~0.6 H, J = 7.2 Hz), 8.15 (br s, ~0.4 H), 8.20 (br s, ~0.6 H); LREIMS m/z = 410 (12%, M$^+$).

Acetylation of Chelonin B (4). Acetic anhydride (0.1 mL) was added to a stirred solution of chelonin B (4, 1.7 mg) in pyridine (1.0 mL), and the reaction was allowed to proceed for 21 h at room temperature. The solvents were removed from the reaction mixture in vacuo and the products separated on a silica Sep-Pak (Waters) in ethyl acetate. The product was purified by HPLC on μ-Partisil using hexane/ethyl acetate (1:9) as eluant to obtain a single peak, which was determined to be a mixture of conformational isomers of the N,O-diacetate 8 (1.7 mg, 84% yield).

Chelonin B N,O-diacetate (8): clear oil; IR ($CHCl_3$) 3475, 1745, 1635, 1605, 1500, 1455, 1440, 1420, 1375, 1260, 1225, 1055, 905 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.93 (s, ~2 H), 2.06 (s, 3 H), 2.09 (s, ~1 H), 2.99 (m, ~3 H), 3.14 (dd, ~0.3 H, J = 14.9, 4.6 Hz), 3.57 (m, ~3 H), 3.87 (s, 3 H), 5.72 (dd, ~0.4 H, J = 8.4, 4.8 Hz), 5.96 (dd, ~0.6 H, J = 7.6, 5.5 Hz), 6.81 (d, ~0.4 H, J = 8.2 Hz), 6.84 (d, ~0.6 H, J = 8.3 Hz), 6.97 (d, ~0.6 H, J = 2.3 Hz), 7.02 (d, ~0.4 H, J = 2.0 Hz), 7.21 (m, 3 H), 7.38 (m, ~1.4 H), 7.51 (d, ~0.6 H, J = 2.0 Hz), 7.56 (br d, ~0.6 H, J = 8.4 Hz), 7.67 (br d, ~0.4 H, J = 7.2 Hz), 8.00 (br s, ~0.4 H), 8.07 (br s, 0.6 H).

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Supplementary Material Available: ^{1}H NMR spectra of compounds 3–8 and ^{13}C NMR spectra of compounds 3–6 (10 pages). Ordering information is given on any current masthead page.

Vilsmeier Reactions of Porphyrins and Chlorins with 3-(Dimethylamino)acrolein To Give *meso*-(2-Formylvinyl)porphyrins: New Syntheses of Benzochlorins, Benzoisobacteriochlorins, and Benzobacteriochlorins and Reductive Coupling of Porphyrins and Chlorins Using Low-Valent Titanium Complexes

M. Graça H. Vicente and Kevin M. Smith*

Department of Chemistry, University of California, Davis, Davis, California 95616

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Vilsmeier reactions between nickel(II) or copper(II) porphyrins or chlorins and 3-(dimethylamino)-acrolein/phosphoryl chloride (3-DMA/$POCl_3$) are described. For example, copper(II) octaethylporphyrin **5** affords the *meso*-(2-formylvinyl) derivative **7**, which cyclizes in strong acid to give the benzochlorin **10**. Treatment of the nickel(II) benzochlorin **9** with 3-DMA/$POCl_3$ gives the *meso*-(2-formylvinyl) derivative **14**, which is cyclized in acid to give the dibenzoisobacteriochlorin **16**. Prolonged treatment of nickel(II) octaethylporphyrin (**4**) with 3-DMA/$POCl_3$ gives the disubstituted compound **17** in which the acrolein substituents are on adjacent rather than opposite meso positions. Acid-promoted cyclization of **17** afforded the monocyclized product **15** as well as the dibenzobacteriochlorin **18**. The reaction is extended to obtain spiro benzochlorins (**37**, **38**) from (tetrabutano- and -pentanoporphyrinato)nickel(II) complexes, as well as benzoisobacteriochlorins (e.g., **28**, **29**) from nickel(II) mesochlorin e_6 trimethyl ester (**19**) and nickel(II) octaethylchlorin (**26**), respectively. Nickel(II) deuteroporphyrin IX dimethyl ester (**11**) also affords benzochlorins (**12**, **13**) resulting from the corresponding *meso*-(2-formylvinyl)porphyrin. A centrally chelated metal is shown to be essential in order to accomplish cyclization of the 2-formylvinyl substituents to afford benzo derivatives. Porphyrin and chlorin dimers joined by one or three carbon–carbon double bond linkages are formed in good yields via reductive coupling by low valent titanium complexes of nickel(II) or copper(II) porphyrins or chlorins containing a formyl or an acrolein side chain. For example, nickel(II) α-(formylvinyl)octaethylporphyrin (**6**) reacts with the active titanium reagent to produce dimer **48** in 96% yield. When two different porphyrins or chlorins are cross-reacted under the same conditions, a mixture of products is obtained. The acrolein group seems to be more reactive in reductive coupling reactions than does the corresponding formyl substituent.

Introduction

The Vilsmeier formylation reaction was first introduced into porphyrin chemistry, in 1966, by Inhoffen and coworkers.[1] Since that time it has been routinely exploited as a highly efficient means for introduction of substituents into the meso positions of numerous copper(II) and nickel(II) porphyrins and chlorins. An interesting vinylogous Vilsmeier formylation of pyrrole **1** [with 3-(dimethylamino)acrolein and phosphoryl chloride (3-DMA/$POCl_3$)] to give an acrolein-substituted analogue **2** was reported by Gosmann and Franck[2] in 1986. In this paper we describe

(1) Inhoffen, H. H.; Fuhrhop, J.-H.; Voigt, H.; Brockmann, H., Jr. *Justus Liebigs Ann. Chem.* **1966**, *695*, 133.

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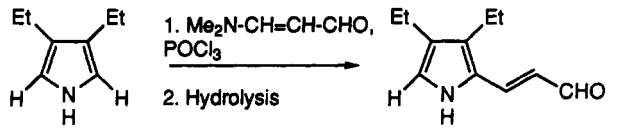
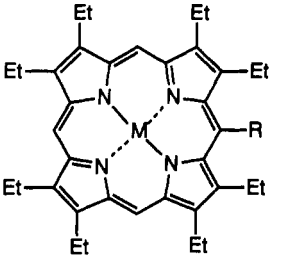


1 2

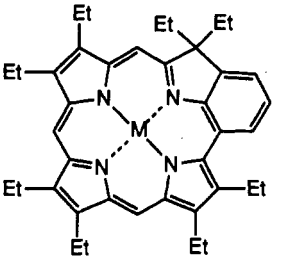
the application of this same Vilsmeier reagent to porphyrin and chlorin systems; the chemistry developed is particularly interesting in that it provides ready access to "benzochlorin" systems[3-5] which have been shown to be important sensitizers[5] for photodynamic therapy (PDT) of tumors.[6] PDT involves the selective retention of a photosensitizer in tumor tissue and its ability to be activated by penetrating light. Currently, the most widely used photosensitizer in PDT is Photofrin-II, a purified form of hematoporphyrin derivative (HpD) that consists of a complex mixture of porphyrin dimers and higher oligomers linked by ether, ester, or carbon–carbon bonds. In the last four years it has been observed that porphyrin dimers with ether[7] or ester linkages[8] are not efficient in vivo photosensitizers, so their use in PDT is limited; this has increased the interest in porphyrin dimers linked by carbon–carbon bonds.[9,10] In order to synthesize new porphyrin and chlorin dimers with carbon–carbon bond linkages suitable for use in PDT, we have developed an efficient procedure for the coupling of porphyrins and chlorins using $TiCl_3(DME)_{1.5}$ and a Zn–Cu couple.[11] This same type of coupling reaction has been used by Vogel and co-workers[12] in their ingenious syntheses of porphycenes.

Vinylogous Vilsmeier Formylations of Porphyrins and Chlorins

Treatment of the nickel(II) complex 4 of octaethylporphyrin (3) with 3-DMA/$POCl_3$ gave compound 6 in 85% yield after the normal hydrolysis of the imine salt intermediate. This compound has previously been prepared by Johnson et al.[3] by a much longer process, consisting of formylation with DMF/phosphoryl chloride followed by Wittig reaction and another formylation with DMF/phosphoryl chloride. The cyclization of the acrolein group onto the adjacent pyrrole subunit β-position occurred by treatment of compound 6 with concentrated sulfuric acid (2 h at room temperature). Compound 9 was produced in 50% yield and has also been reported by Johnson et al.[3] Removal of the robust central nickel(II) ion from 9 was accomplished by using trifluoroacetic acid and 1,3-propanedithiol, and a 10% yield of the metal-free benzochlorin 10 was obtained, along with a 70% recovery



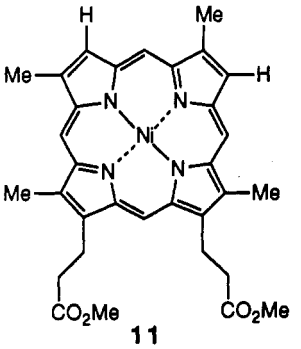
3 R = H; M = 2H
4 R = H; M = Ni
5 R = H; M = Cu
6 R = CH=CH-CHO; M = Ni
7 R = CH=CH-CHO; M = Cu
8 R = CH=CH-CHO; M = 2H



9 M = Ni
10 M = 2H

of the nickel(II) complex 9. However, a better way to produce 10 is by treatment of copper(II) octaethylporphyrin (5) with 3-DMA/$POCl_3$, which gave compound 7 in 57% yield. Treatment of 7 with 18% sulfuric acid/TFA (15 min at room temperature) gave 10 in 70% yield. The UV/vis and proton NMR data (aromatic proton region) for this compound are given in Figure 1. Characteristically, the protons in the geminal diethyl groups are shifted upfield (CH_3CH_2, 0.08 and 2.66 ppm, respectively) due to the anisotropic effect of the neighboring benzene ring. When 7 was treated with 15% sulfuric acid/TFA, the free base 8 was the only product obtained in 66% yield (84% based on recovered starting material).

In order to investigate the relative reactivities of meso versus pyrrole unsubstituted β-positions, nickel(II) deuteroporphyrin IX dimethyl ester (11) was chosen to react with 3-DMA and phosphoryl chloride. A mixture of products containing the acrolein group only at the meso positions (and mostly at the β-meso position) was obtained from this reaction. Upon treatment with concentrated sulfuric acid (10 min at room temperature), two main benzochlorins, 12 and 13, were obtained. Many other green products were formed but in much lower yields, and their separation and identification were very difficult.



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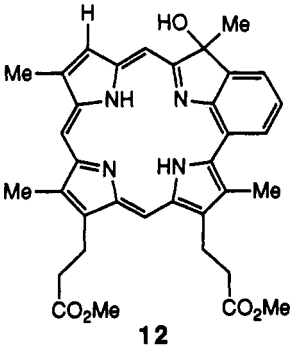

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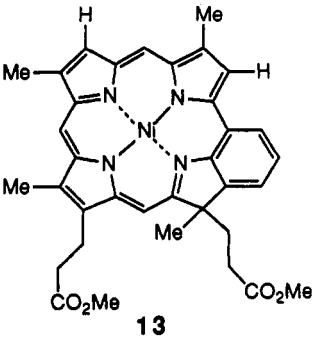

13

When nickel(II) octaethylbenzochlorin (9) was treated with 3-DMA/$POCl_3$, compound 14 was obtained in 90%

(2) Gosmann, M.; Franck, B. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1100.
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(10) Morris, I. K.; Ward, A. D. *Tetrahedron Lett.* **1988**, *29*, 2501.
(11) McMurry, J. E.; Lectka, T.; Rico, J. G. *J. Org. Chem.* **1989**, *54*, 3748. McMurry, J. E. *Chem. Rev.* **1989**, *89*, 1513.
(12) Vogel, E.; Kocher, M.; Schmickler, H.; Lex, J. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 257.

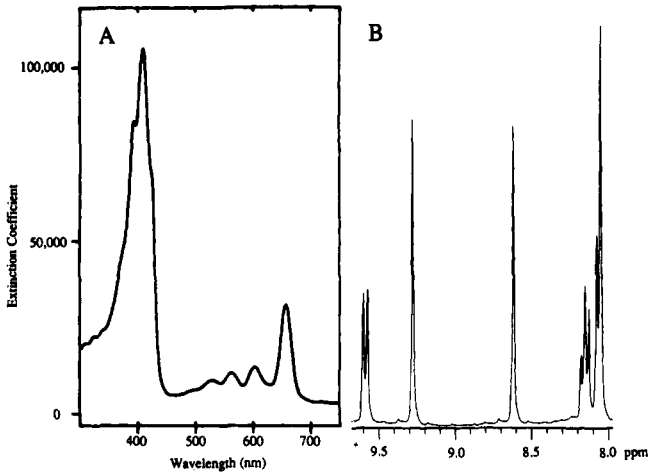
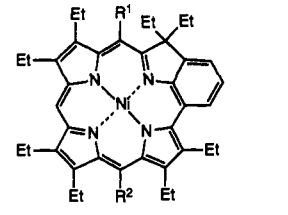
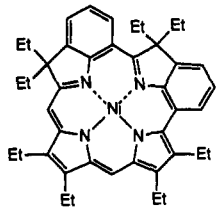


Figure 1. (A) Optical spectrum (in CH_2Cl_2) and (B) proton NMR spectrum (aromatic region only, in $CDCl_3$ at 300 MHz) of benzochlorin **10**.

yield. The benzochlorin reacted much faster than the porphyrin, due to the "activated" meso position, and **14** was the only regioisomer obtained. Treatment of compound **14** with concentrated sulfuric acid gave the dibenzoisobacteriochlorin **16** in 13% yield. Unfortunately, proton NMR data for this compound could not be obtained because it was paramagnetic [high-spin nickel(II)], but its structure was determined on the basis of high-resolution mass spectrometry and spectrophotometry (Figure 2A).



14 R^1 = CH=CH-CHO; R^2 = H
15 R^1 = H; R^2 = CH=CH-CHO



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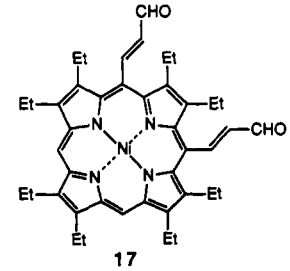
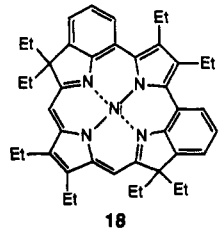
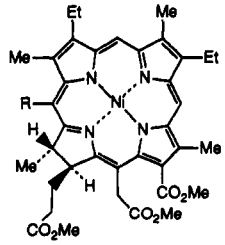


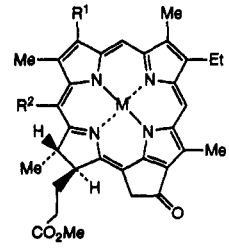
17



18



19 R = H
20 R = CH=CH-CHO



21 R^1 = Et; R^2 = H; M = Ni
22 R^1 = CH=CH_2; R^2 = H; M = Ni
23 R^1 = Et; R^2 = CH=CH-CHO; M = Ni
24 R^1 = Et; R^2 = CH=CH-CHO; M = 2H
25 R^1 = CH=CH_2; R^2 = CH=CH-CHO; M = Ni

When nickel(II) octaethylporphyrin (**4**) was exposed to a large excess of the Vilsmeier complex from 3-DMA/$POCl_3$, nickel(II) bis(2-formylvinyl)octaethylporphyrin (**17**) was formed in 55% yield. The two acrolein groups are in adjacent meso positions, as indicated by the existence of four different ethyl groups in the ^{13}C NMR spectrum. The presence of one (or more) acrolein groups on the porphyrin ring decreases its reactivity toward the Vilsmeier reagent. Upon acid treatment, compound **17** yielded several products, but mainly the monocyclized product **15** and the dibenzobacteriochlorin **18**. Compound **18** was also paramagnetic, so its structure is based upon high-resolution mass spectrometry and spectrophotometry (Figure 2B).

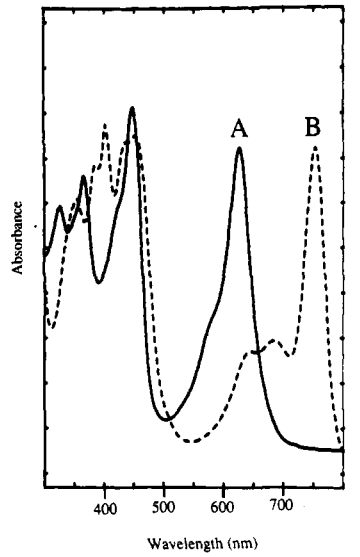


Figure 2. Optical spectrum, in CH_2Cl_2, of (A) nickel(II) dibenzoisobacteriochlorin **16** and (B) nickel(II) dibenzobacteriochlorin **18**. See Experimental Section for molar extinction coefficients.

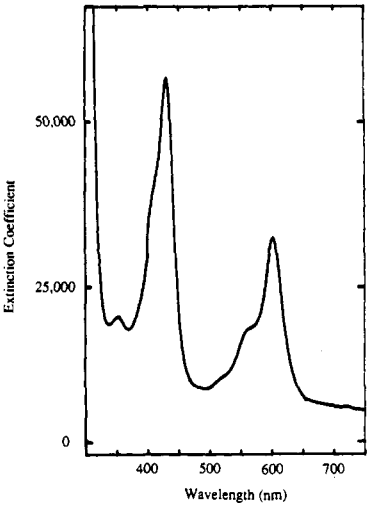


Figure 3. Optical spectrum, in CH_2Cl_2, of nickel(II) benzoisobacteriochlorin **28**.

Benzoisobacteriochlorins can be readily formed by the reaction of natural chlorins with 3-DMA/$POCl_3$, even those containing vinyl side chains and/or exocyclic rings. Nickel(II) mesochlorin e_6 trimethyl ester (**19**) reacted with 3-DMA/$POCl_3$ to produce nickel(II) δ-(2-formylvinyl)-mesochlorin e_6 trimethyl ester (**20**) in 89% yield. Nickel(II) mesopyropheophorbide *a* methyl ester (**21**) gave nickel(II) δ-(2-formylvinyl)mesopyropheophorbide *a* methyl ester (**23**) in 83% yield, and nickel(II) pyropheophorbide *a* methyl ester (**22**) produced **25** in 63% yield. Products resulting from reaction of the peripheral vinyl group in **22** and the exocyclic ring E in **21** and **22** with the Vilsmeier reagent were not detected. Nickel(II) octaethylchlorin (**26**)

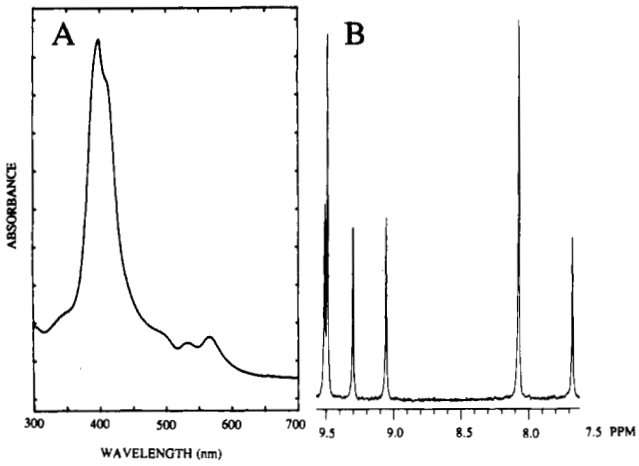
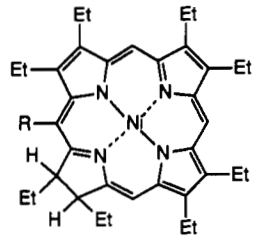
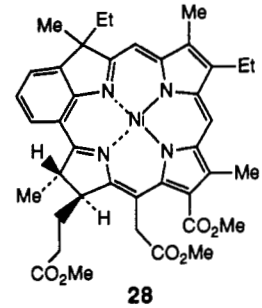


Figure 4. (A) Electronic absorption spectrum and (B) proton NMR spectrum (in $CDCl_3$; 300 MHz; low-field region only) of dimer **51**.

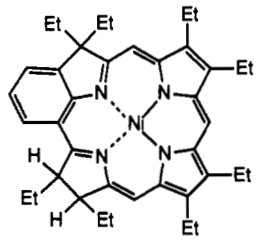
also reacted with 3-DMA/$POCl_3$ to give nickel(II) γ-(2-formylvinyl)octaethylchlorin (**27**) in 81% yield; under the reaction conditions 10% of the chlorin was oxidized to porphyrin. Upon treatment with concentrated sulfuric



26 R = H
27 R = CH=CH-CHO



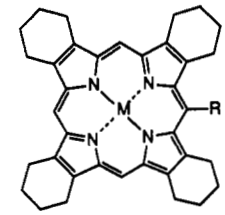
28



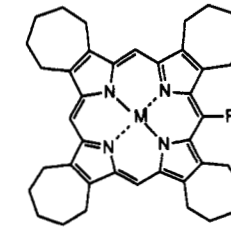
29

acid (2.5 h at room temperature), compound **20** gave the benzoisobacteriochlorin **28** in 55% yield (UV/vis data, Figure 3). Acid treatment of **23** and **25** only caused the extrusion of the chelated nickel(II), and no isobacteriochlorin was thus produced. A centrally chelated metal is required for the cyclization step to occur to prevent protonation from curtailing the electrophilic cyclization of the meso acrolein group to the macrocyclic δ-position. Upon acid treatment, compound **27** produced the benzoisobacteriochlorin **29** in 15% yield.

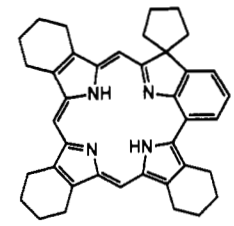
Spiro benzochlorins were also obtained by reacting porphyrins containing cyclic side chains with the above Vilsmeier complex reagent followed by cyclization of the meso acrolein group. The tetrabutanoporphyrin (**30**) and the tetrapentanoporphyrin (**33**) were obtained from the respective α-unsubstituted pyrroles, prepared by the nitroalkene method.[13] Treatment of the nickel(II) tetrabutanoporphyrin (**31**) with 3-DMA/$POCl_3$ gave nickel(II) *meso*-(2-formylvinyl)tetrabutanoporphyrin (**32**) in 65% yield, and nickel(II) *meso*-(2-formylvinyl)tetrapentanoporphyrin (**35**) was produced in 72% yield from the nickel(II) tetrapentanoporphyrin (**34**). Acid treatment of **32** gave the spiro benzochlorin **37** in 55% yield. Upon acid treatment, compound **35** gave the spiro benzochlorin **38** in 30% yield, along with its nickel(II) complex **39** and the metal-free *meso*-(2-formylvinyl)tetrapentanoporphyrin (**36**).



30 R = H; M = 2H
31 R = H; M = Ni
32 R = CH=CH-CHO; M = Ni



33 R = H; M = 2H
34 R = H; M = Ni
35 R = CH=CH-CHO; M = Ni
36 R = CH=CH-CHO; M = 2H



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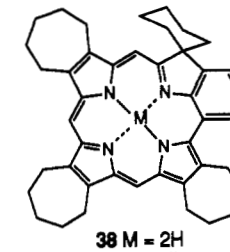
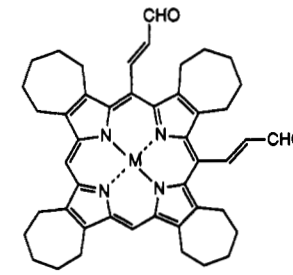
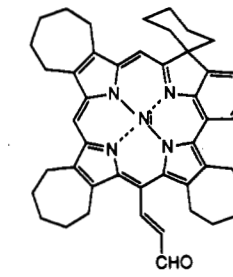


38 M = 2H
39 M = Ni



40 M = Ni
41 M = 2H



42

Treatment of the nickel(II) tetrapentanoporphyrin (**34**) with an excess of the Vilsmeier complex reagent produced the diacrolein-substituted porphyrin **40** in 44% yield. Acid treatment of **40** gave mainly the corresponding free base **41** in 43% yield, along with 10% of the monocyclized compound **42**. No bacteriochlorin was detected in this case, probably because of the extrusion of the chelated nickel(II) atom before and second cyclization could take place.

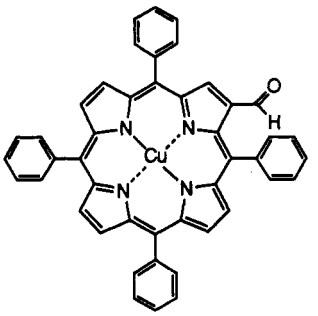
Reductive Dimerizations of Porphyrins and Chlorins

In 1988, Zhilina et al.[14] reported the first reductive dimerization of the copper(II) complex of 1-formyl-α,β,γ,δ-tetraphenylporphyrin (**43**) using low valent titanium complexes. The reaction took place at room temperature over 18–20 h in the presence of 2 equiv of $TiCl_4$/Zn(Hg) and produced a 20% yield of dimer **44**. When 10 equiv of

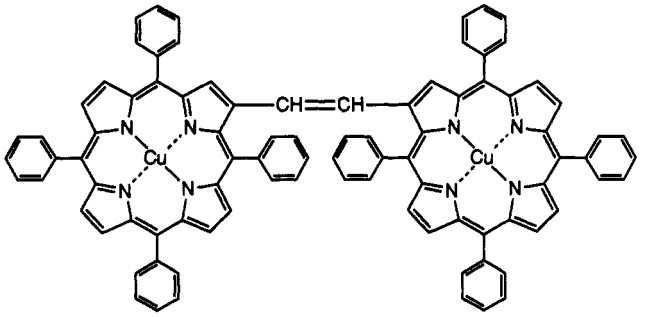
(13) Ono, N.; Maruyama, K. *Chem. Lett.* **1988**, 1511.

(14) Zhilina, Z. I.; Ishkov, Y. V.; Voloshanovskii, I. S.; Andronati, A. S. A. *Dokl. Akad. Nauk SSSR (Engl. Transl.)* **1988**, *303*, 326.

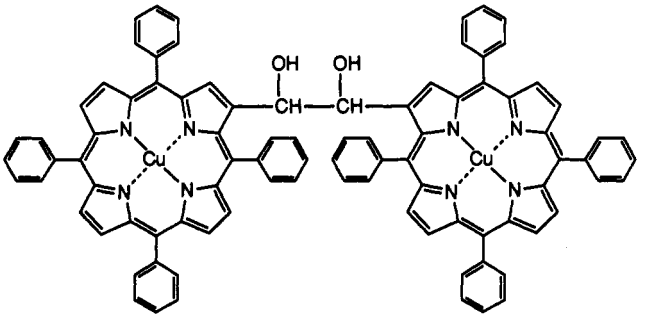
$TiCl_4/Zn(Hg)$ was used, the reaction took 2 h at room temperature and produced dimer **44** in 15% yield. Decreasing the temperature of the reaction to 12 °C caused the formation of the diol **45**, and only 3% of dimer **44** was formed.



43

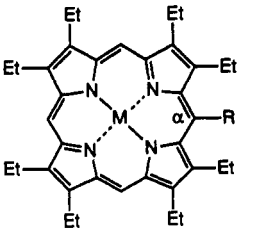


44

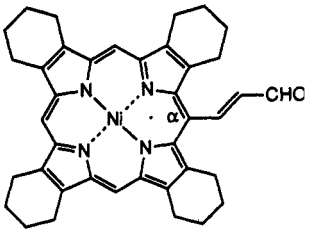


45

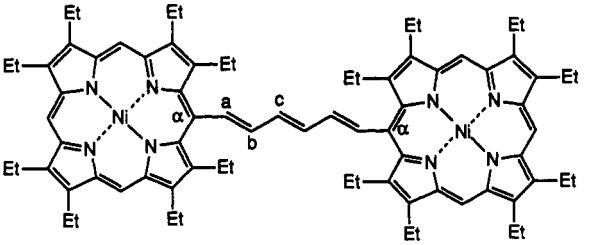
We decided to further investigate the reductive coupling reaction of porphyrins and chlorins bearing a formyl or acrolein side chain and chose nickel(II) α-(2-formylvinyl)octaethylporphyrin (**6**) as a model compound. The active titanium reagent was prepared by refluxing a slurry containing 9.9 equiv of $TiCl_3(DME)_{1.5}$ and 37.5 equiv of Zn–Cu couple for 2 h in dry 1,2-dimethoxyethane (DME). Compound **6** was carefully added via syringe to the refluxing slurry under argon partially dissolved in DME. The formation of a very mobile compound was observed by TLC just a few minutes after addition of the porphyrin, and 30 min later no residual starting material was detected. The mixture was filtered through a short silica gel column; the only brown and nonpolar product obtained was further purified by chromatography on silica gel followed by crystallization, yielding 96% of dimer **48**. In the ^1H NMR spectrum the alkene protons appear as a doublet (H_a) at 8.66 ppm, as a dd (H_c) at 6.43 ppm, and as a ddd (H_b) at 5.47 ppm. Decoupling experiments were performed to assign the above proton NMR resonances. Irradiation of the doublet at 8.66 ppm caused the simplification of the ddd signal to dd, while the dd at 6.43 ppm remained unchanged. The irradiation of the dd at 6.43 ppm caused the simplification of the ddd signal to a doublet (J = 15 Hz) while the doublet at 8.66 ppm was unchanged.



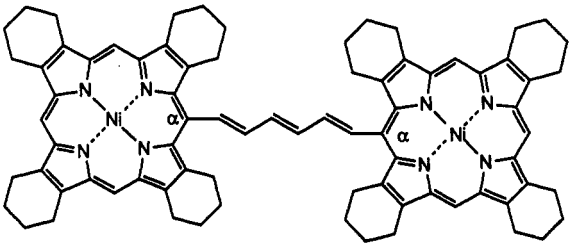
4 R = H, M=Ni
6 R=CH=CH-CHO, M=Ni
46 R=CHO, M=Ni
47 R=CHO, M=Cu



49



48



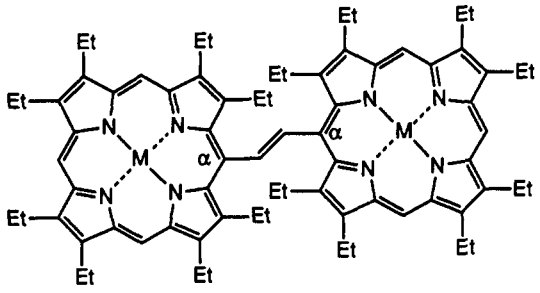
50

The same reductive coupling procedure was used to form dimer **50** in 55% yield from nickel(II) α-(2-formylvinyl)-tetrabutanoporphyrin (**49**). This compound was found to be less stable on silica gel than dimer **48**. Although a single nonpolar spot was observed by TLC 1 h after addition of the porphyrin, only a 55% yield of **50** was obtained after purification.

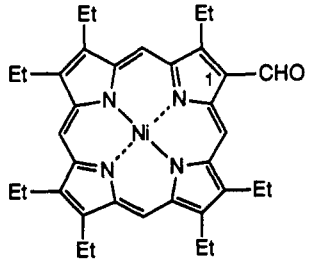
In order to obtain dimers of porphyrins with only one carbon–carbon double bond linkage, we used nickel(II) α-formyloctaethylporphyrin (**46**) and copper(II) α-formyloctaethylporphyrin (**47**) as starting materials. In a similar procedure, 6.6 equiv of $TiCl_3(DME)_{1.5}$ and 24.7 equiv of Zn–Cu were used to form the active slurry. Compound **46** was added, and 1 h later no more starting material was observed by TLC. Dimer **51** was obtained in 49% yield. In the ^1H NMR spectrum the alkene protons appear as a singlet at 8.07 ppm (Figure 4), which indicates that they are magnetically equivalent and that the dimer molecule has an element of symmetry. When the copper(II) complex **47** was used along with 8.4 equiv of $TiCl_3(DME)_{1.5}$ and 33.8 equiv of Zn–Cu, dimer **52** was obtained in 64% yield. Attempts to remove the chelated copper atom with H_2SO_4/TFA resulted only in decomposition.

Synthesis of an unexpected β,β′-linked dimer was accomplished by using[15] nickel(II) 1-formyl-2,3,4,5,6,7,8-heptaethylporphyrin (**53**). The same procedure was followed, with 8.8 equiv of $TiCl_3(DME)_{1.5}$ and 33.4 equiv of Zn–Cu, to prepare the active titanium species. The main

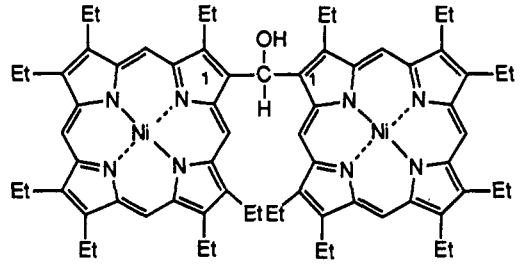
(15) Vicente, M. G. H.; Smith, K. M. *Synlett* **1990**, 579.



51 M=Ni
52 M=Cu



53



54

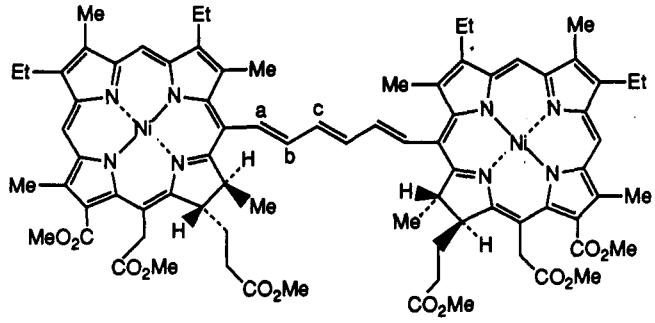
red product was isolated in 61% yield and was found[16] to be dimer **54**.

The coupling reaction was also used for the dimerization of chlorins bearing an acrolein side group at the δ-meso position. Nickel(II) δ-(2-formylvinyl)mesochlorin e_6 trimethyl ester (**20**) was coupled under the same reaction conditions to give dimer **55** in 84% yield. This compound is more polar than the above dimers due to its three methyl ester side chains. By TLC, the polarities of compounds **20** and **55** were very similar, so the reaction was followed by UV/vis in addition to TLC (for UV/vis data of dimer **55**, see Figure 5).

Reductive coupling of nickel(II) γ-(2-formylvinyl)octaethylchlorin (**27**) gave dimer **56** in 72% yield. Compound **56** has a strong UV/vis absorption at λ = 630 nm (see Figure 5). Under the same conditions, nickel(II) γ-(2-formylvinyl)octaethylbenzochlorin (**14**) coupled to produce dimer **57** in 56% yield. The lower yield in this case is probably due to the insolubility of compound **14** compared with all other starting materials, which required use of a more dilute reaction mixture. Of all dimers that were prepared, dimer **57** shows its second strongest UV/vis absorption at higher wavelength, λ = 706 nm (see Figure 5).

The intermolecular carbonyl-coupling reaction has not yet been accomplished on metal-free porphyrins and is usually limited to the preparation of symmetrical olefins.

(16) Though a dimeric olefin was anticipated from this reaction, the product was identified by single-crystal X-ray study to be the dimeric porphyrin carbinol **54**. Details of the X-ray structure will be reported elsewhere (M. O. Senge, M. G. H. Vicente, and K. M. Smith, manuscript in preparation).



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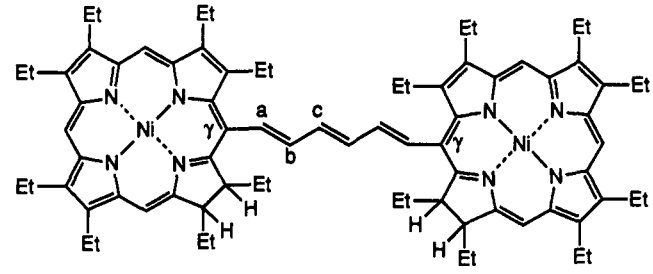
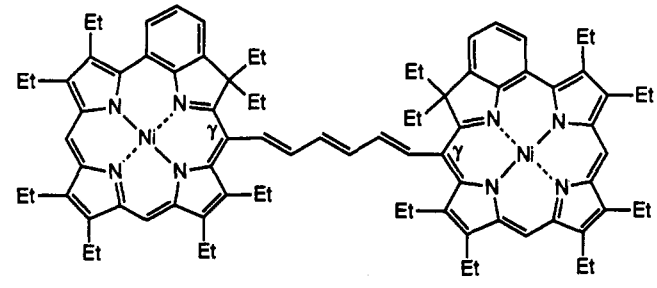


56



57

When a mixture of two different carbonyl compounds is allowed to react with Ti(0), a roughly statistical mixture of the possible alkene coupling products is normally obtained. When a 1:1 mixture of nickel(II) α-formyloctaethylporphyrin (**46**) and nickel(II) δ-(2-formylvinyl)mesochlorin e_6 trimethyl ester (**20**) were reacted under the usual reaction conditions, a mixed dimer was formed together with dimer **55** in ~1:2 ratio. Only traces of dimer **51** were detected along with nickel(II) octaethylporphyrin (**4**) and unreacted starting material **46**. This suggests that the unsaturated aldehyde of the acrolein group is more labile than the formyl group of **46**, but one has also to take into account the difference in solubilities of the two compounds involved.

Experimental Section

Melting points were measured on a hot-stage apparatus and were uncorrected. Silica gel 60 (70–230 mesh, Merck) or neutral alumina (Merck; usually Brockmann grade III, i.e., deactivated with 6% water) were used for column chromatography. Preparative thin-layer chromatography was carried out on 20 × 20 cm glass plates coated with Merck G 254 silica gel (1 mm thick). Analytical thin-layer chromatography was performed by using Merck 60 F254 silica gel (precoated sheets, 0.2 mm thick). Reactions were monitored by thin-layer chromatography and spectrophotometry and were carried out under nitrogen and in the dark. Proton NMR spectra were obtained in deuteriochloroform solution at 300 MHz on a General Electric QE300 spectrometer; chemical shifts are expressed in parts per million relative to chloroform (7.258 ppm). Elemental analyses were performed at the Microchemical Analysis Laboratory, University of California, Berkeley. Electronic absorption spectra were measured in dichloromethane solution on a Hewlett-Packard

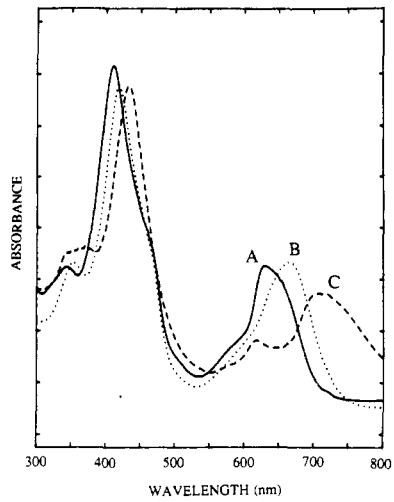


Figure 5. Electronic absorption spectra, in CH_2Cl_2, of dimers **56** (A; solid line), **55** (B; dotted line), and **57** (C; dashed line).

8450A spectrophotometer. Mass spectra were obtained on a VG Analytical ZAB-HS instrument.

The preparation of the $TiCl_3(DME)_{1.5}$ and Zn–Cu reagents was achieved accordingly to literature procedures.[11] The reagents were stored and weighed under an atmosphere of nitrogen, in a glovebox. 1,2-Dimethoxyethane (DME) was distilled from potassium metal and in the presence of benzoquinone, under an argon atmosphere. Compound **53** was obtained by oxidation of 1-*trans*-(2-bromovinyl)-1-desethyloctaethylporphyrin with osmium tetraoxide.[15]

Copper(II) *meso*-(2-Formylvinyl)octaethylporphyrin (7). Phosphorus oxychloride (0.40 mL, 4.0 mmol) was added dropwise to a solution of 3-(dimethylamino)acrolein (0.40 mL, 4.0 mmol) in dichloromethane (4.0 mL), and the mixture was kept at 0 °C for 15 min. This mixture was then added to a solution of copper(II) octaethylporphyrin (**5**) (80.7 mg, 0.135 mmol) in dichloromethane (20.0 mL) with continuous stirring, at 0 °C. The final mixture was then warmed up to room temperature and stirred for 18 h. Saturated aqueous sodium carbonate (100 mL) was then added, and the solution was stirred overnight. The mixture was extracted with dichloromethane, the combined organic layers were washed with water (3 × 200 mL) and dried over anhydrous sodium sulfate, and the solvent was removed under vacuum. The resulting residue was chromatographed on silica gel (elution with 30% petroleum ether in dichloromethane), and the desired compound was collected and recrystallized from dichloromethane/methanol to give 50.2 mg (57%) of the title compound: mp 230–231 °C; vis λ_{max} 331 nm (ϵ 22 100), 408 (139 500), 534 (12 100), and 568 (14 200); MS, *m/e* (%) 649 (100), 620 (24), and 591 (34). Anal. Calcd for $C_{39}H_{46}CuN_4O$: C, 72.02; H, 7.14; N, 8.61. Found: C, 71.81; H, 7.14; N, 8.53.

Nickel(II) *meso*-(2-Formylvinyl)octaethylporphyrin (6). The same procedure was followed as for the synthesis of compound **7**. After addition of the Vilsmeier complex mixture [containing 1.0 mL, 10 mmol each of 3-(dimethylamino)acrolein and phosphorus oxychloride in 4.0 mL of dry methylene chloride] to the nickel(II) octaethylporphyrin (**4**) (200 mg, 0.338 mmol) at 0 °C, the final solution was then stirred at room temperature for 8 h. After basic hydrolysis, the final neutralized residue was chromatographed on silica gel (elution with dichloromethane) and was further purified on preparative TLC silica gel plates, 20% petroleum ether in dichloromethane being used for elution. The less polar compound was separated and crystallized from dichloromethane/methanol, giving an 85% yield (186 mg) of the title compound: mp 245–246 °C; vis λ_{max} 406 nm (ϵ 70 800), 536 (15 850), 564 (17 900), and 582 (17 200); NMR δ_H 9.84 (d, CHO, J = 7.7 Hz), 9.69 (d, β-H of acrylaldehyde, J = 15.2 Hz), 9.36 (s, 3 meso H), 5.53 (dd, α-H of acrylaldehyde), 3.65–3.86 (overlapping q, CH_2 of peripheral Et, 16 H), 1.66–1.79 (overlapping t, CH_3 of peripheral Et, 24 H); δ_C 17.32, 18.26, and 18.39 (q, CH_3 of Et), 19.68, 19.72, 19.82, and 22.40 (t, CH_2 of Et), 98.25 (d, 1 meso C), 98.29 (d, 2 meso C), 105.32 (s, quaternary meso C), 138.44, 138.99, 140.48, 140.57, 143.26, 144.00, 144.06, and 146.94 (all s, 2 C each, ring C's), 142.70 and 149.98 (both d, vinyl C's), 190.87 (d, CHO); MS, *m/e* (%) 645 (100), 616 (29), 587 (37), and 559 (25). Anal. Calcd for $C_{39}H_{46}N_4NiO$: C, 72.64; H, 7.20; N, 8.69. Found: C, 72.74; H, 7.20; N, 8.95.

***meso*-(2-Formylvinyl)octaethylporphyrin (8).** Copper(II) *meso*-(2-formylvinyl)octaethylporphyrin (**7**) (50 mg, 0.077 mmol) was dissolved in 20 mL of 15% sulfuric acid in TFA, immediately neutralized with 20% saturated sodium bicarbonate, washed with water (4 × 200 mL), and extracted with dichloromethane. The organic layer was dried over anhydrous sodium sulfate, and the solvent was removed under vacuum. The resulting residue was chromatographed on silica gel (elution with 10% petroleum ether in dichloromethane), and the desired band was collected and recrystallized from dichloromethane/methanol, yielding 30 mg (66%) of the title compound (84% based on recovered starting material that was obtained in 21% yield): mp 218–219 °C; vis λ_{max} 410 nm (ϵ 87 000), 506 (11 700), 540 (9000), 578 (9200), 626 (7000), and 666 (6500); NMR (360 MHz, $CDCl_3$) δ_H 10.08 (s, β- and δ-meso H, 2 H), 9.93 (s, γ-meso H, 1 H), 10.25 (d, CHO, $J_{\alpha H-CHO}$ = 7.5 Hz), 10.29 (d, β-H of acrylaldehyde, $J_{\beta H-\alpha H}$ = 15.1 Hz), 6.47 (dd, α-H of acrylaldehyde), 3.95, 4.06 (overlapping q, CH_2 of peripheral Et, 16 H), 1.92, 1.85, and 1.72 (overlapping t, CH_3 of peripheral Et, 24 H), −2.83 (NH, br, 2 H); MS, *m/e* (%) 588 (100), 560 (70), and 531 (75). Anal. Calcd for $C_{39}H_{48}N_4O$: C, 79.55; H, 8.22; N, 9.52. Found: C, 79.77; H, 8.00; N, 9.41.

Nickel(II) 1,2,3,4,5,6,7,7-Octaethylbenzochlorin (9). Nickel *meso*-(2-formylvinyl)octaethylporphyrin (**6**) (200 mg, 0.31 mmol) was stirred at room temperature for 2 h in concentrated sulfuric acid (15 mL). The mixture was poured into ice/water (300 mL), neutralized with 50% aqueous saturated sodium bicarbonate, and then extracted with dichloromethane. The organic layers were washed with water (2 × 200 mL) and dried over anhydrous sodium sulfate, and the solvent was removed under vacuum. The residue was chromatographed on silica gel, 22% dichloromethane/petroleum ether being used for elution. The desired green band was collected and crystallized from dichloromethane/methanol, yielding 92 mg (47%) of the title compound: mp 224–225 °C; vis λ_{max} 373 nm (ϵ 14 300), 414 (37 100), 508 (4600), 564 (4200), 618 (6800), and 670 (20 000); NMR δ_H 8.98 (dd, 1 H of benzene ring), 8.89, 8.54, and 7.83 (s, 3 meso H), 7.82 (dd, 1 H of benzene ring), 7.79 (t, 1 H of benzene ring), 3.35–3.71 (overlapping q, CH_2 of peripheral Et, 12 H), 2.41 and 2.46 (q, CH_2 of *gem*-Et_2, 4 H), 1.54–1.70 (overlapping t, CH_3 of peripheral Et, 18 H), 0.16 (t, CH_3 of *gem*-Et_2, 6 H); MS, *m/e* (%) 628 (100), 599 (86), 569 (37), and 314 (38). Anal. Calcd for $C_{39}H_{46}N_4Ni$: C, 74.41; H, 7.36; N, 8.90. Found: C, 74.35; H, 7.35; N, 9.00.

1,2,3,4,5,6,7,7-Octaethylbenzochlorin (10). Copper(II) *meso*-(2-formylvinyl)octaethylporphyrin (**7**) (50 mg, 0.077 mmol) was stirred in 18% sulfuric acid/TFA (10 mL) for 15 min. The mixture was then neutralized with 20% aqueous saturated sodium bicarbonate (100 mL) and extracted with dichloromethane, and the combined organic layers were washed with water (3 × 200 mL). The solution was dried over anhydrous sodium sulfate, the solvent was evaporated, and the resulting residue was chromatographed on silica gel (elution with 70% petroleum ether/dichloromethane). The desired product was collected and recrystallized from dichloromethane/methanol, yielding 32 mg (70%) of the title compound: mp 241–243 °C; vis λ_{max} 392 nm (ϵ 87 200), 412 (107 500), 530 (13 700), 564 (15 400), 604 (17 000), and 658 nm (35 000); NMR (360 MHz, $CDCl_3$) δ_H 9.23, 8.57, and 8.01 (each s, 3 meso H), 9.54 (d, 1 benzo H, J = 8.1 Hz), 8.12 (t, 1 benzo H, J = 7.8 Hz), 8.04 (d, 1 benzo H, J = 7.6 Hz), 3.51–3.69 and 3.80–3.99 (overlapping q, CH_2 of peripheral Et, 12 H), 2.57–2.76 (overlapping q, CH_2 of *gem*-Et_2, 4 H), 1.63–1.79 and 1.85–1.94 (overlapping t, CH_3 of peripheral Et, 18 H), 0.08 (t, CH_3 of *gem*-Et_2, 6 H); δ_C 8.15 (q, CH_3 of *gem*-Et_2), 15.76–21.34 (peripheral Et), 34.09 (t, CH_2 of *gem*-Et_2), 61.74 (s, C bearing *gem*-Et_2), 87.48, 94.86, and 106.93 (all d, 3 meso C), 115.35 (s, quaternary meso C), 117.84, 121.60, and 124.98 (all d, C of benzene ring), 127.06, 128.99, 134.51, 137.96, 138.97, 139.71, 139.87, 140.37, 142.45, 143.32, 145.30, 146.81, 152.95, 157.18, and 175.44 (all s, ring C's); MS, *m/e* (%) 573 (100), 543 (19). Anal. Calcd for $C_{39}H_{49}N_4$: C, 81.77; H, 8.44; N, 9.78. Found: C, 81.85; H, 8.31; N, 9.81.

3-Hydroxydeuterobenzochlorin (12) and Nickel(II) 6-Methyldeuterobenzochlorin (13). Nickel(II) deuteroporphyrin IX dimethyl ester (**11**) (114.8 mg, 0.193 mmol), phosphorus ox-

ychloride (0.57 mL, 5.7 mmol), and 3-(dimethylamino)acrolein (0.57 mL, 5.7 mmol) were used. After 21 h of stirring at room temperature and basic hydrolysis, the organic product was treated with diazomethane and neutralized. The residue was chromatographed on silica gel with 3% acetone/methylene chloride and further purified on preparative TLC silica gel plates with 4% acetone in methylene chloride being used for elution. A brown product was obtained which was a mixture of two compounds having the 2-formylvinyl group at different meso positions. This mixture (20 mg) (17%) was dissolved in concentrated sulfuric acid (3 mL) and stirred at room temperature for 10 min. After neutralization, the product was chromatographed on preparative TLC silica gel plates with 1% acetone in methylene chloride being used for elution. The two main fractions were collected and recrystallized from methylene chloride/methanol, yielding 3-hydroxydeuterobenzochlorin (12) (10%) and nickel(II) 6-methyldeuterobenzochlorin (13) (7%). **3-Hydroxydeuterobenzochlorin (12)**: mp 162–163 °C; vis λ_{max} 331 nm (ϵ 17 700), 410 (56 200), 538 (7150), 572 (8200), 614 (8100), and 670 (17 550); NMR δ_H 9.45 (d, 1 benzo H, J = 8.4 Hz), 9.12, 8.63, and 8.27 (s, 3 meso H), 8.24 (d, 1 benzo H, J = 6.9 Hz), 8.19 (s, 1 β-H), 7.98 (t, 1 benzo H, J = 7.5 Hz), 3.93 and 3.79 (t, each 2 H, 6,7-CH_2CH_2), 3.65 and 3.64 (s, each 3 H, 6,7-CO_2CH_3), 3.31, 3.26, and 3.02 (s, each 3 H, 1,5,8-CH_3), 2.96 and 2.93 (t, each 2 H, 6,7-CH_2CH_2), 2.03 (s, 3 H, 3-CH_3); MS, m/e (%) 592.7 (100), 575.7 (13), 418.7 (90), and 390.7 (17). **Nickel(II) 6-methyldeuterobenzochlorin (13)**: mp 101–103 °C; vis λ_{max} 305 nm (ϵ 10 600), 412 (51 000), 508 (4000), 564 (3400), 616 (7250), and 668 (26 200); NMR δ_H 8.97 (d, 1 benzo H, J = 8.6 Hz), 8.88, 8.57, and 7.94 (s, 3 meso H), 8.24 and 8.18 (s, 2 β-H), 7.86 (m, 2 benzo H), 4.00 (t, 2 H, 7-CH_2CH_2), 3.80 (s, 3 H, 7-CO_2CH_3), 3.32 (s, 3 H, 6-CO_2CH_3), 3.12 (m, 2 H, 6-CH_2CH_2), 3.10, 3.09, and 3.06 (s, each 3 H, 1,3,8-CH_3), 3.01 (t, 2 H, 7-CH_2CH_2), 2.82 (m, 1 H, of 6-CH_2CH_2), 1.91 (s, 3 H, 6-CH_3), 1.35 (m, 1 H of 6-CH_2CH_2); MS, m/e (%) 633.2 (100), 545.1 (35), and 458.9 (38).

Nickel(II) γ-*meso*-(2-Formylvinyl)-1,2,3,4,5,6,7,7-octaethylbenzochlorin (14). The same procedure as above was followed, with nickel(II) 1,2,3,4,5,6,7,7-octaethylbenzochlorin (9) (232 mg, 0.37 mmol), 3-(dimethylamino)acrolein (0.90 mL, 9.0 mmol), and phosphorus oxychloride (0.90 mL, 9.0 mmol). The reaction mixture was stirred at 0 °C for 20 min, and after basic hydrolysis and neutralization, the residue was chromatographed on silica gel with 2% acetone/methylene chloride being used for elution. The major product was collected and recrystallized from methylene chloride/hexane, yielding 227 mg (90%) of the title compound: mp 298–299 °C; vis λ_{max} 376 nm (ϵ 46 700), 444 (70 500), and 726 (47 900); NMR δ_H 9.68 (d, CHO, J = 7.8 Hz), 8.69 (d, β-H of acrylaldehyde, J = 15.0 Hz), 8.63 (d, 1 benzo H, J = 8.1 Hz), 8.49 and 8.21 (s, 2 meso H), 7.70 (t, 1 benzo H), 7.63 (d, 1 benzo H), 5.72 (dd, α-H of acrylaldehyde), 3.25–3.49 (overlapping q, CH_2 of peripheral Et, 12 H), 2.79 and 2.46 (sext, 2 H each, CH_2 of *gem*-Et_2), 1.39–1.59 (overlapping t, CH_3 of peripheral Et, 18 H), 0.13 (t, CH_3 of *gem*-Et_2, 6 H); δ_C, 9.19 (q, CH_3 of *gem*-Et_2), 16.03, 16.32, 17.69, 17.94, 18.20, 18.40, 19.00, 19.11, 19.38, 19.54, 21.05, and 21.48 (peripheral Et), 36.51 (t, CH_2 of *gem*-Et_2), 62.28 (s, C bearing *gem*-Et_2), 82.15 (s, quaternary meso C bearing acrolein group), 99.68 and 113.13 (both d, 2 meso C), 134.58 (s, quaternary meso C), 102.84, 109.85, and 121.56 (all d, C of benzene ring), 118.95 and 123.87 (both d, vinyl C's), 136.63, 136.77, 137.13, 138.21, 138.70, 140.03, 141.33, 141.76, 142.08, 142.36, 144.89, 146.81, 147.47, 149.00, and 164.10 (all s, ring C's), 191.02 (d, CHO); MS, m/e (%) 683 (100), 655 (19), and 309 (29). Anal. Calcd for $C_{42}H_{48}N_4NiO$: C, 73.80; H, 7.08; N, 8.20. Found: C, 73.63; H, 6.99; N, 8.19.

Nickel(II) α-*meso*-(2-Formylvinyl)-1,2,3,4,5,6,7,7-octaethylbenzochlorin (15) and Nickel(II) 1,2,4,4,5,6,7,7-Octaethyldibenzobacteriochlorin (18). Nickel(II) α,β-*meso*-bis(2-formylvinyl)octaethylporphyrin (17) (78 mg, 0.112 mmol) was dissolved in concentrated sulfuric acid (10 mL) and stirred for 5 min before it was poured into ice/water, extracted with methylene chloride, and neutralized. The resulting neutralized residue was chromatographed on a silica column (elution with 1:1 petroleum ether/methylene chloride) and further purified on preparative TLC silica plates with methylene chloride being used for elution. Compound 15 was the second least polar band, and it was recrystallized from methylene chloride/methanol to give 13 mg (17%). The least polar band was recrystallized from methylene chloride/methanol to give 4 mg (5%) of compound 18. For nickel(II) α-*meso*-(2-formylvinyl)-1,2,3,4,5,6,7,7-octaethylbenzochlorin (15): mp 220–221 °C; vis λ_{max} 346 nm (ϵ 44 400), 430 (89 400), and 690 (38 700); NMR δ_H 9.94 (d, CHO, J = 7.5 Hz), 9.43 (d, β-H of acrylaldehyde, J = 15.6 Hz), 8.72 (d, 1 benzo H, J = 7.5 Hz), 8.34 and 7.73 (s, 2 meso H), 7.71 (d, 1 benzo H), 7.69 (t, 1 benzo H), 5.96 (dd, α-H of acrylaldehyde), 3.54, 3.45, and 3.34 (q, CH_2 of peripheral Et, 12 H), 2.39 (q, 4 H, CH_2 of *gem*-Et_2), 1.59–1.44 (overlapping t, CH_3 of peripheral Et, 18 H), 0.22 (t, CH_3 of *gem*-Et_2, 6 H); MS, m/e 682.3 (100), 653.3 (12), and 498 (60). For nickel(II) 1,2,4,4,5,6,7,7-octaethyldibenzobacteriochlorin (18): mp 139–140 °C; vis λ_{max} 352 nm (ϵ 38 200), 384 (41 000), 402 (45 200), 452 (44 000), 644 (18 500), 686 (19 500), 752 (41 800); HRMS m/e $C_{42}H_{48}N_4Ni$ requires 666.3227, found 664.3222.

Nickel(II) 1,1,3,3,5,6,7,8-Octaethyldibenzoisobacteriochlorin (16). The same general procedure was followed for the cyclization of the acrolein side chain. Nickel(II) γ-*meso*-(2-formylvinyl)-1,2,3,4,5,6,7,7-octaethylbenzochlorin (14) (40 mg) was dissolved in 5 mL of concentrated sulfuric acid and stirred at room temperature for 1.5 h. The acidic solution was then diluted with water and extracted with methylene chloride (20 × 25 mL). The organic extracts were neutralized, washed with water, and dried over anhydrous sodium sulfate, and the solvent was evaporated under vacuum. The residue was purified on preparative TLC alumina plates with 10% methylene chloride in petroleum ether being used for elution. The least polar band was collected and recrystallized from methylene chloride/methanol to give 5 mg (13%) of the above compound: mp 292–302 °C vis λ_{max} 340 nm (ϵ 37 000), 444 (45 600), and 634 nm (38 600); HRMS m/e (%) $C_{42}H_{48}N_4Ni$ requires 666.3227, found 666.3218 (100).

Nickel(II) α,β-*meso*-Bis(2-formylvinyl)octaethylporphyrin (17). The same procedure as above was followed, with nickel(II) octaethylporphyrin (4) (347 mg, 0.587 mmol), 3-(dimethylamino)acrolein (4.9 mL, 49 mmol), and phosphorus oxychloride (4.9 mL, 49 mmol). The reaction mixture was stirred at room temperature for 8 h and then refluxed at 40 °C for 24 h. After basic hydrolysis and neutralization, the residue was chromatographed on silica gel and the title compound was collected and recrystallized from methylene chloride/hexane to give 226 mg (55%), along with 95 mg (25%) of nickel(II) *meso*-(2-formylvinyl)octaethylporphyrin (6). For the title compound: mp 236–237 °C; vis λ_{max} 338 nm (ϵ 58 800), 458 (156 700), and 616 (29 900); NMR δ_H 9.87 (d, 2 CHO, J = 7.8 Hz), 9.56 (d, 2 H, β-H of acrylaldehyde, J = 15.3 Hz), 9.14 (s, 2 meso H), 5.58 (dd, 2 H, α-H of acrylaldehyde), 3.53–3.71 (overlapping q, CH_2 of peripheral Et, 16 H), 1.59–1.71 (overlapping t, CH_3 of peripheral Et, 24 H); δ_C 13.82; 14.06, 15.03, 15.15, 16.46, 16.61, 19.02, and 19.30 (peripheral Et), 96.57 (d, 2 meso C), 104.94 (s, 2 quaternary meso C), 133.38, 135.50, 136.21, 137.74, 139.09, 141.13, 141.33, 144.79, and 144.89 (all s, 2 C each, ring C's), 139.09 and 146.13 (both d, vinyl C's), 187.84 (d, CHO); MS, m/e (%) 698.9 (100). Anal. Calcd for $C_{42}H_{48}N_4NiO_2$: C, 72.11; H, 6.91; N, 8.00. Found: C, 71.92; H, 6.87; N, 7.99.

Nickel(II) δ-(2-Formylvinyl)mesochlorin e_6 Trimethyl Ester (20). The same procedure as above was followed, with nickel(II) mesochlorin e_6 trimethyl ester (19) (99 mg, 0.14 mmol), 3-(dimethylamino)acrolein (0.41 mL, 4.1 mmol), and phosphorus oxychloride (0.41 mL, 4.1 mmol). The mixture was stirred at room temperature for 4 h, and after basic hydrolysis it was treated with diazomethane at 0 °C. The final neutralized residue was chromatographed on silica gel, 4% acetone/dichloromethane being used for elution. The major green band was collected and recrystallized from dichloromethane/methanol, giving 95 mg (89%) of the title compound: mp 126–127 °C; vis λ_{max} 428 nm (ϵ 99 800), 574 (16 000), 582 (15 650), and 672 (42 150); NMR δ_H 9.69 (d, CHO, J = 7.8 Hz), 8.72 and 8.62 (s, 2 meso H), 8.36 (d, β-H of acrylaldehyde, J = 15.4 Hz), 5.72 (dd, α-H of acrylaldehyde), 4.35, 4.40, 4.53, and 4.59 (AB q, 2 H, γ-CH_2), 4.36 (q, 1 H, 8-H), 4.09 (s, 3 H, 6-CO_2CH_3), 3.88 (dd, 1 H, 7-H), 3.75 and 3.67 (s, each 3 H, CO_2CH_3), 3.35–3.40 (overlapping q, 4 H, CH_2 of Et), 3.09, 2.96, and 2.80 (all s, each 3 H, 1,3,5-CH_3), 2.44–2.50 (m, 2 H, 7-CH_2CH_2), 1.66–1.85 (m, 2 H, 7-CH_2CH_2), 1.53 and 1.48 (t, each 3 H, CH_3 of Et), 1.35 (d, 3 H, 8-CH_3); MS, m/e (%) 751 (100) and 692 (12). Anal. Calcd for $C_{40}H_{44}N_4NiO_7$: C, 63.98; H, 5.90; N, 7.47. Found: C, 63.97; H, 5.90; N, 7.56.

Nickel(II) δ-(2-Formylvinyl)mesopyropheophorbide *a* Methyl Ester (23). The same general procedure was followed: nickel(II) mesopyropheophorbide *a* methyl ester (21) (173.2 mg, 0.285 mmol), 3-(dimethylamino)acrolein (0.69 mL, 6.9 mmol), and phosphorus oxychloride (0.69 mL, 6.9 mmol) were used. After 5 h of stirring at room temperature followed by the basic hydrolysis, the mixture was treated with diazomethane at 0 °C. The final neutralized residue was chromatographed on silica gel (elution with 2% acetone/dichloromethane), and it was further purified on preparative TLC silica gel plates, 2% acetone in dichloromethane being used for elution. The main product was collected and recrystallized from dichloromethane/methanol, yielding 122 mg (65%) of the title compound [83% based on recovered mesopyropheophorbide *a* methyl ester, which was also recovered in 22% (34 mg) yield]. **23**: mp 161–163 °C; vis λ_{max} 430 nm (ε 46850), 682 nm (26600), and 752 (7800); NMR δ_H 9.79 (d, CHO, J = 7.8 Hz), 8.96 and 8.67 (s, 2 meso H), 8.49 (d, β-H of acrylaldehyde, J = 15.3 Hz), 5.83 (dd, α-H of acrylaldehyde), 4.72, 4.66, 4.52, and 4.46 (AB q, 2 H, γ-CH_2), 4.48 (q, 1 H, 8-H), 3.77 (q, 1 H, 7-H), 3.64 (s, 3 H, CO_2CH_3), 3.41 (overlapping q, 4 H, CH_2 of Et), 3.31, 2.99, and 2.78 (s, each 3 H, 1,3,5-CH_3), 2.40 (m, 2 H, 7-CH_2CH$_2$), 2.19 and 2.03 (m, each 1 H, 7-CH$_2$CH_2), 1.52 and 1.51 (t, each 3 H, CH_3 of Et), 1.25 (d, 3 H, 8-CH_3); MS, m/e (%) 661 (100), 574 (17), and 487 (20). Anal. Calcd for $C_{37}H_{38}N_4NiO_4$: C, 67.19; H, 5.79; N, 8.47. Found: C, 67.11; H, 5.73; N, 8.33.

δ-(2-Formylvinyl)mesopyropheophorbide *a* Methyl Ester (24). Nickel(II) δ-(2-formylvinyl)mesopyropheophorbide *a* methyl ester (23) (40 mg, 0.060 mmol) was dissolved in concentrated sulfuric acid (5 mL) and stirred at room temperature for 2 h. The resulting solution was neutralized with 20% aqueous saturated sodium bicarbonate and extracted with dichloromethane, and the organic layers were washed with water (3 × 100 mL) and dried over anhydrous sodium sulfate. The main product was purified on preparative TLC silica gel plates (6% acetone/dichloromethane for elution) and crystallized from dichloromethane/methanol, yielding 24 mg (65%) of the title compound: mp 244–245 °C; vis λ_{max} 414 nm (ε 118000), 564 (17800), 620 (11000), and 680 (26900); NMR δ_H 10.10 (d, CHO, J = 7.8 Hz), 9.40 and 9.33 (s, 2 meso H), 9.12 (d, β-H of acrylaldehyde, J = 15.6 Hz), 6.57 (dd, α-H of acrylaldehyde), 5.18, 5.12, 5.10, and 5.04 (AB q, 2 H, γ-CH_2), 4.67 (q, 1 H, 8-H), 4.15 (dd, 1 H, 7-H), 3.79 and 3.64 (q, each 2 H, CH_2 of Et), 3.62 (s, 3 H, CO_2CH_3), 3.61, 3.23, and 3.09 (s, each 3 H, 1,3,5-CH_3), 2.54 (m, 2 H, 7-CH_2CH$_2$), 2.34 and 2.23 (m, each 1 H, 7-CH$_2$CH_2), 1.68 and 1.66 (t, each 3 H, CH_3 of Et), 1.43 (d, 3 H, 8-CH_3), −0.91 (br, 2 NH); δ_C 11.27 (q, 3-CH_3), 12.11 (q, 5-CH_3), 16.95 (q, 2 C, CH_3 of Et), 17.48 (q, 1-CH_3), 19.45 and 19.70 (t, 2 C, CH_2 of Et), 21.42 (q, 8-CH_3), 30.01 (t, 7-CH_2CH_2), 31.32 (t, 7-CH_2CH_2), 48.46 and 48.58 (d, C7 and C8), 51.88 (m, overlap of CO_2CH_3 and C10), 99.99 (d, α-meso C), 104.16 (s, δ-meso C), 105.54 (d, β-meso C), 106.55 (s, γ-meso C), 129.78, 129.97, 131.40, 134.66, 136.44, 139.25, 141.13, 144.98, 149.29, 151.64, 153.88, 160.47, and 170.35 (all s, ring C's), 137.10 and 149.74 (both d, vinyl C's), 173.44 (s, CO_2CH_3), 192.50 (d, CHO), 195.91 (s, C9); MS, m/e (%) 604 (100), 589 (31), 517 (34), and 480 (18). Anal. Calcd for $C_{37}H_{40}N_4O_4$: C, 73.49; H, 6.67; N, 9.26. Found: C, 73.61; H, 6.63; N, 9.23.

Nickel(II) δ-(2-Formylvinyl)pyropheophorbide *a* Methyl Ester (25). The same general procedure was followed, with nickel(II) pyropheophorbide *a* methyl ester (22) (45 mg, 0.074 mmol), 3-(dimethylamino)acrolein (0.20 mL, 2.0 mmol), and phosphorus oxychloride (0.20 mL, 2.0 mmol). After 8 h of stirring at room temperature and basic hydrolysis, the mixture was treated with diazomethane and neutralized. The residue was chromatographed on silica gel, 3% acetone/methylene chloride being used for elution. The major green fraction was collected and recrystallized from methylene chloride/methanol to give 31 mg (63%) of the title compound: mp 149–150 °C; vis λ_{max} 430 nm (ε 111100), 588 (30950), and 694 (82100); NMR δ_H 9.77 (d, CHO, J = 7.8 Hz), 8.99 and 8.80 (s, 2 meso H), 8.46 (d, β-H of acrylaldehyde, J = 15.3 Hz), 7.52 (dd, 1 H, internal vinyl), 5.96 (d, 1 H, terminal vinyl, J = 11.5 Hz), 5.84 (d, 1 H, terminal vinyl, J = 18.0 Hz), 5.84 (dd, α-H of acrylaldehyde), 4.73, 4.66, 4.53, and 4.46 (AB q, 2 H, γ-CH_2), 4.50 (q, 1 H, 8-H), 3.79 (t, 1 H, 7-H), 3.63 (s, 3 H, CO_2CH_3), 3.45 (m, 2 H, CH_2 of Et), 3.33, 2.98, and 2.88 (s, each 3 H, 1,3,5-CH_3), 2.40 (q, 2 H, 7-CH_2CH$_2$), 2.18 and 2.03 (m, each 1 H, 7-CH$_2$CH_2), 1.51 (t, 3 H, CH_3 of Et), 1.24 (d, 3 H, 8-CH_3); MS, m/e (%) 658 (100) and 604 (43). Anal. Calcd for $C_{37}H_{38}N_4NiO_4$: C, 67.39; H, 5.50; N, 8.51. Found: C, 66.76; H, 5.31; N, 8.39.

Nickel(II) γ-*meso*-(2-Formylvinyl)octaethylchlorin (27). The same general procedure was followed, with nickel(II) octaethylchlorin (26) (151.5 mg, 0.255 mmol), 3-(dimethylamino)acrolein (0.58 mL, 5.8 mmol), and phosphorus oxychloride (0.58 mL, 5.8 mmol). The final solution was stirred at room temperature for 3.5 h before it was hydrolyzed with saturated aqueous sodium carbonate. The final neutralized residue was chromatographed on a silica column, 30% petroleum ether in methylene chloride being used for elution. The title compound was collected and recrystallized from methylene chloride/methanol to give 133 mg (81%) along with 17 mg (10%) of nickel(II) *meso*-(2-formylvinyl)octaethylporphyrin (6). For the title compound: mp 115–116 °C; vis λ_{max} 428 nm (105300), 506 (15000), 562 (17200), 654 (36850), and 660 (36400); NMR δ_H 9.90 (d, CHO, J = 7.8 Hz), 8.92, 8.81, and 7.87 (all s, 3 meso H), 8.61 (d, β-H of acrylaldehyde, J = 15.3 Hz), 6.07 (dd, α-H of acrylaldehyde), 4.36 (dd, H-8), 4.00 (t, H-7), 3.64–3.37 (overlapping q, 12 H, CH_2 of Et), 1.96–1.87 (m, 4 H, 7,8-CH_2 of Et), 1.76–1.50 (overlapping t, 18 H, CH_3 of Et), 1.13 and 1.07 (t, 3 H each, 7,8-CH_3 of Et); δ_C 11.81 and 11.96 (q, 7,8-CH_3 of Et), 16.73, 17.47, 18.18, 18.23, 18.42, 19.15, 19.35, 19.52, 19.70, 21.27, 26.47, and 27.81 (overlapping t and q, CH_2 and CH_3 of Et), 54.36 and 55.29 (d, C7 and C8), 94.35, 102.88, and 105.07 (d, 3 meso C), 101.40 (s, quaternary meso C), 135.63, 137.72, 138.54, 139.15, 139.32, 140.20, 140.35, 143.96, 145.20, 146.56, 147.05, 154.29, and 155.09 (all s, ring C's), 138.77 and 149.98 (both d, vinyl C's), 192.07 (d, CHO); MS, m/e 646 (%) (100), 618 (22), and 592 (20). Anal. Calcd for $C_{39}H_{46}N_4ONi$: C, 72.41; H, 7.49; N, 8.65. Found: C, 72.42; H, 7.57; N, 8.59.

Nickel(II) Benzoisobacteriomesochlorin e_6 Trimethyl Ester (28). Nickel(II) (2-formylvinyl)mesochlorin e_6 trimethyl ester (20) (60 mg, 0.08 mmol) was dissolved in concentrated sulfuric acid (10 mL) and stirred at room temperature for 2.5 h. The solution was neutralized with 50% aqueous saturated sodium bicarbonate and extracted with dichloromethane, and the combined organic layers were washed with water (3 × 100 mL). After drying over anhydrous sodium sulfate and evaporation of the solvent, the residue was purified by preparative TLC silica gel plates, 3% acetone in dichloromethane being used for elution. The title product was recrystallized from dichloromethane/methanol/water, and it was obtained in 55% yield (32 mg): mp 123–124 °C; vis λ_{max} 354 nm (ε 23300), 432 (57000), and 602 (32100); NMR δ_H 8.06 (d, 1 H of benzene ring, J = 8.4 Hz), 7.98 and 6.99 (s, 2 meso H), 7.58 (d, 1 H of benzene ring, J = 6.6 Hz), 7.44 (t, 1 H of benzene ring, J = 7.5 Hz), 4.11 (s, 2 H, γ-CH_2), 3.97, 3.75, and 3.56 (s, each 3 H, CO_2CH_3), 3.83 (q, 1 H, 8-H), 3.66 (dd, 1 H, 7-H), 3.10 (q, 2 H, 4-CH_2), 2.83 and 2.60 (s, each 3 H, 3,5-CH_3), 2.20 (q, 2 H, 2-CH_2), 2.13 (m, 2 H, 7-CH_2CH$_2$), 1.66 (d, 3 H, 8-CH_3), 1.62 (s, 3 H, 2-CH_3), 1.39 (t, 3 H, 4-CH_3), 1.33 (m, 2 H, 7-CH$_2$CH_2), 0.16 (t, 3 H, 2-CH_3 of Et); δ_C 9.02 (q, 2-CH_3), 10.53 (q, 3-CH_3), 12.12 (q, 5-CH_3), 16.88 and 17.75 (q, CH_3 of Et), 18.95 (q, 8-CH_3), 27.19 and 27.97 (t, CH_2 of Et), 30.91 (t, 7-CH_2CH_2), 35.96 (t, 7-CH_2CH$_2$), 38.17 (t, γ-CH_2), 47.24 and 50.50 (d, C_7 and C_8), 51.77, 51.94, and 52.03 (q, CO_2CH_3), 52.52 (s, C_2), 88.27 (d, α-meso C), 107.03 (d, β-meso C), 109.06 and 110.56 (s, γ- and δ-meso C), 120.22, 121.94 and 125.11 (d, C of benzene ring), 129.98, 132.41, 133.37, 137.05, 139.71, 141.70, 144.66, 146.36, 146.48, 151.49, 166.55, and 168.71 (all s, ring C's), 163.65 (s, 6-CO_2CH_3), 172.10 (s, γ-CO_2CH_3), 173.43 (s, 7-CO_2CH_3); MS, m/e (%) 735 (100), 705 (25), and 545 (16). Anal. Calcd for $C_{40}H_{44}N_4NiO_6$: C, 65.37; H, 6.03; N, 7.62. Found: C, 65.38; H, 5.99; N, 7.39.

Nickel(II) 2,2,3,4,5,6,7,8-Octaethylbenzoisobacteriochlorin (29). The same general procedure was followed: nickel(II) γ-*meso*-(2-formylvinyl)octaethylchlorin (27) (40 mg) was dissolved in concentrated sulfuric acid (5 mL) and stirred at room temperature for 1.5 h. After extractions, neutralizations, and washings, the resulting residue was chromatographed on a silica gel column, 30% methylene chloride/petroleum ether being used for elution, and the fast running band collected. The title compound was recrystallized from methylene chloride/methanol to give 5.8 mg (15%) along with 10 mg (28%) of the free-base from 27. For the title compound: mp 129–135 °C; vis λ_{max} 335 nm (ε 33000), 416 (55600), 616 (20300), 634 (19700), 668 (26700); NMR δ_H 8.99 (d, 1 benzo H, J = 7.4 Hz), 8.89, 8.55, and 7.83 (s, 3 meso H), 7.81 (d, 1 benzo H, J = 7.8 Hz), 7.79 (t, 1 benzo H), 3.30–3.66 (m, 8 H + 2 H, CH_2 of Et and 7,8-H), 2.39–2.45 (m, 4 H, 7,8-CH_2 of

Et), 2.01–2.15 (m, 4 H, CH_2 of *gem*-Et_2), 1.43–1.68 (overlapping t, 12 H, CH_3 of Et), 1.19 and 0.78 (t, 3 H each, 7,8-CH_3 of Et), 0.26 and 0.16 (t, 3 H each, CH_3 of *gem*-Et_2); MS, *m/e* (%) 630 (100), 601 (27), and 548 (29).

Nickel(II) *meso*-(2-Formylvinyl)-1,2:3,4:5,6:7,8-tetrabutanoporphyrin (32). The same general procedure was followed, with nickel(II) tetrabutanoporphyrin (31) (107 mg, 0.183 mmol), 3-(dimethylamino)acrolein (0.45 mL, 4.5 mmol), and phosphorus oxychloride (0.45 mL, 4.5 mmol). After stirring at room temperature for 11 h and basic hydrolysis, the neutralized residue was chromatographed on a silica gel column, 20% petroleum ether in dichloromethane being used for elution. The desired product was collected and recrystallized from dichloromethane/methanol, giving 75 mg (65%) of the title compound: mp >350 °C; vis λ_{max} 335 nm (ϵ 27 400), 404 (128 400), 528 (14 400), and 558 (21 600); NMR δ_H 9.97 (d, CHO, J = 8.1 Hz), 9.71 (d, C*H*=CHCHO, J = 15.6 Hz), 9.26 (s, 3 meso H), 5.80 (dd, CH=C*H*CHO), 3.80 and 3.76 (s, br, 16 H, α-CH_2), 2.34 and 2.23 (s, br, 16 H, β-CH_2); MS, *m/e* (%) 636 (100), 607 (8), 581 (10), and 304 (15). Anal. Calcd for $C_{39}H_{38}N_4NiO$: C, 73.48; H, 6.02; N, 8.78. Found: C, 73.49; H, 6.06; N, 8.59.

Nickel(II) *meso*-(2-Formylvinyl)-1,2:3,4:5,6:7,8-tetrapentanoporphyrin (35). The same general procedure was followed, with nickel(II) tetrapentanoporphyrin (34) (143 mg, 0.224 mmol), 3-(dimethylamino)acrolein (0.65 mL, 6.5 mmol), and phosphorus oxychloride (0.65 mL, 6.5 mmol). The reaction mixture was stirred at room temperature for 11 h, hydrolyzed with saturated aqueous sodium carbonate, washed with water, and dried over sodium sulfate, and the solvent was evaporated. The final residue was chromatographed on a silica gel column, 20% petroleum ether in methylene chloride being used for elution. The title product was collected and recrystallized from methylene chloride/methanol, to give 110 mg (72%) along with 13 mg (8%) of compound 40. For the title compound: mp >350 °C; vis λ_{max} 452 nm (ϵ 125 300) and 608 (26 900); NMR δ_H 9.64 (d, CHO, J = 8.1 Hz), 9.36 (s, 1 meso H), 9.34 (s, 2 meso H), 9.13 (d, C*H*=CHCHO, J = 15.0 Hz), 5.37 (dd, CH=C*H*CHO), 4.04 and 3.88 (br, 16 H, α-CH_2), 2.23 and 2.17 (br, 24 H, β- and γ-CH_2); MS, *m/e* 692 (%) (100). Anal. Calcd for $C_{43}H_{46}N_4NiO$: C, 74.53; H, 6.70; N, 8.09. Found: C, 74.48; H, 6.83; N, 8.12.

***meso*-(2-Formylvinyl)-1,2:3,4:5,6:7,8-tetrapentanoporphyrin (36), Cyclohexanespirotripentanobenzochlorin (38), and Nickel(II) Cyclohexanespirotripentanobenzochlorin (39).** A solution of nickel(II) *meso*-(2-formylvinyl)tetrapentanoporphyrin (35) (200 mg, 0.288 mmol) in 100 mL of concentrated sulfuric acid was stirred at room temperature for 1 h. The acidic mixture was neutralized, washed with water, and extracted with methylene chloride, before it was dried over anhydrous sodium sulfate and the solvent evaporated. The residue was chromatographed on a silica gel column (starting elution with 40% petroleum ether in methylene chloride and then increasing the percentage of methylene chloride). Compound 36 was isolated and recrystallized from methylene chloride/hexane, giving 60 mg (33%), compound 38 was recrystallized from methylene chloride/methanol to give 54 mg (30%), and compound 39 was recrystallized from methylene chloride/methanol to give 10 mg (5%). For *meso*-(2-formylvinyl)tetrapentanoporphyrin (36): mp >350 °C; vis λ_{max} 420 nm (ϵ 208 800), 508 (26 100), and 586 (27 100); NMR δ_H 10.04 (d, CHO, J = 7.8 Hz), 10.00 (d, β-H of acrylaldehyde, J = 15.3 Hz), 9.98 (s, 2 meso H), 9.91 (s, 1 meso H), 6.15 (dd, α-H of acrylaldehyde), 4.16 and 4.08 (br, 16 H, α-CH_2), 2.30 and 2.15 (br, 24H, β- and γ-CH_2); δ_C, 27.68, 28.03, 28.23, 28.32, 28.99, 32.13, 32.19, and 33.21 (all t, peripheral CH_2), 98.66 (d, 2 meso C), 98.89 (d, 1 meso C), 107.65 (s, quaternary meso C), 141.35–156.75 (br, ring C's), 143.20 and 152.87 (both d, vinyl C's), 191.23 (d, CHO); MS, *m/e* (%) 636 (100), 608 (58), and 593 (28). Anal. Calcd for $C_{43}H_{48}N_4O$: C, 81.08; H, 7.60; N, 8.80. Found: C, 81.04; H, 7.65; N, 8.78. For cyclohexanespirotripentanobenzochlorin (38): mp >340 °C; vis λ_{max} 408 nm (ϵ 104 400), 534 (9000), 566 (11 000), 604 (14 000), 656 (32 300); NMR δ_H 9.25 (d, 1 benzo H, J = 8.4 Hz), 9.09, 8.44, and 7.93 (s, 1 H each, 3 meso H), 8.09 (d, 1 benzo H, J = 6.9 Hz), 7.92 (t, 1 benzo H), 4.02, 3.83, and 3.67 (br, 12 H, α-CH_2), 2.65, 2.46, 2.20, and 2.11 (br, 18 H, β- and γ-CH_2), 1.82 (br, 4 H, α-CH_2 of spiro ring), 0.25 and 0.23 (br, 6 H, β- and γ-CH_2 of spiro ring): δ_C 14.55, 24.55, 27.25, 27.79, 27.98, 28.31, 28.69, 28.75, 28.90, 30.03, 32.53, 32.67, 33.04, 33.77, 35.73, 40.13, and 48.19 (all t, CH_2 of pentano and cyclohexane rings), 67.40 (s, C bearing cyclohexane ring), 87.65, 94.59, and 107.60 (all d, 3 meso C), 115.09 (s, quaternary meso C), 119.78, 120.56, and 126.92 (all d, C of benzene ring), 127.62, 129.48, 134.86, 139.06, 139.31, 140.17, 141.12, 141.73, 143.51, 144.84, 146.55, 147.58, 151.90, 157.42, and 178.04 (all s, ring C's); MS, *m/e* 620.2 (100). Anal. Calcd for $C_{43}H_{48}N_4$: C, 83.17; H, 7.79; N, 9.02. Found: C, 82.71; H, 7.79; N, 8.92. For nickel(II) cyclohexanespirotripentanobenzochlorin (39): mp >350 °C; vis λ_{max} 336 nm (31 700), 420 (99 300), 508 (11 300), 562 (10 900), 622 (17 400), and 672 (51 000); NMR δ_H 8.86, 8.49, and 7.86 (s, 1 H each, 3 meso H), 8.68 (d, 1 benzo H, J = 8.1 Hz), 8.25 (d, 1 benzo H, J = 6.9 Hz), 7.60 (t, 1 benzo H, J = 7.6 Hz), 3.81 and 3.57 (br, 12 H, α-CH_2), 2.44, 2.14, and 2.03 (br, 18 H, β- and γ-CH_2), 1.86 (br, 4 H, α-CH_2 of spiro ring), 0.86 (m, 6 H, β- and γ-CH_2 of spiro ring); MS, *m/e* 676 (100).

Cyclopentanespirotributanobenzochlorin (37). Nickel(II) *meso*-(2-formylvinyl)-tetrabutanoporphyrin (32) (35 mg, 0.055 mmol) was dissolved in 5 mL of concentrated sulfuric acid, and the acidic solution was stirred at room temperature for 1.5 h. After neutralization and extraction with dichloromethane, the organic residue was chromatographed on a silica gel column, 1:1 petroleum ether/dichloromethane being used for elution. The desired compound was collected and recrystallized from dichloromethane/methanol, giving 17 mg (55%) of the title compound: mp >350 °C; vis λ_{max} 410 nm (ϵ 135 900), 526 (14 750), 562 (16 800), 604 (18 400), and 660 (40 600); NMR δ_H 9.43 (d, 1 H of benzene ring), 9.00, 8.36, and 7.95 (s, 3 meso H), 8.16 (d, 1 H of benzene ring), 8.03 (t, 1 H of benzene ring), 3.97, 3.82, 3.59, and 3.51 (s, br, α-CH_2), 2.80, 2.58, 2.31, and 2.24 (s, br, β-CH_2), 1.25 (s, br, α-CH_2 of reduced ring), 0.88 (s, br, β-CH_2 of reduced ring); MS, *m/e* (%) 564 (100) and 503 (35). Anal. Calcd for $C_{39}H_{40}N_4$: C, 82.93; H, 7.14; N, 9.92. Found: C, 82.55; H, 7.25; N, 9.85.

Nickel(II) α,β-*meso*-Bis(2-formylvinyl)tetrapentanoporphyrin (40). The same procedure as above was followed, with nickel(II) tetrapentanoporphyrin (34) (110 mg, 0.172 mmol), 3-(dimethylamino)acrolein (1.20 mL, 12.0 mmol), and phosphorus oxychloride (1.20 mL, 12.0 mmol). The reaction mixture was stirred at room temperature for 8 h and was then refluxed at 40 °C for 24 h. After basic hydrolysis and neutralization, the residue was chromatographed on silica gel (20% petroleum ether/methylene chloride for elution). The title product was collected and recrystallized from methylene chloride/methanol to give 55 mg (44%) along with 33 mg (28%) of nickel(II) *meso*-(2-formylvinyl)tetrapentanoporphyrin (35). For the title compound: mp >350 °C; vis λ_{max} 348 nm (42 200), 478 (87 950), and 640 (19 700); NMR δ_H 9.69 (d, 2 CHO, J = 7.5 Hz), 9.06 (s, 2 meso H), 9.07 (d, 2 H, β-H of acrylaldehyde, J = 15.3 Hz), 5.45 (dd, 2 H, α-H of acrylaldehyde), 3.88, 3.78, and 3.72 (br, 16 H, α-CH_2), 2.16 (br, 24H, β- and γ-CH_2); δ_C 27.27, 27.58, 27.90, 28.07, 28.16, 28.72, 30.69, 31.21, 31.40, 32.00, and 32.93 (peripheral CH_2), 101.69 (d, 2 meso C), 106.72 (s, 2 quaternary meso C), 138.48, 138.73, 141.24, 142.83, 144.92, 145.14, 149.37, and 149.87 (all s, ring C's), 141.44 and 148.21 (both d, vinyl C's), 190.80 (d, CHO); MS, *m/e* 746 (%) (100). Anal. Calcd for $C_{46}H_{46}N_4NiO_2$: C, 73.90; H, 6.48; N, 7.49. Found: C, 73.68; H, 6.53; N, 7.48.

Nickel(II) α-*meso*-(2-Formylvinyl)cyclohexanespirotripentanobenzochlorin (42) and α,β-*meso*-Bis(2-formylvinyl)tetrapentanoporphyrin (41). Nickel(II) α,β-*meso*-bis(2-formylvinyl)tetrapentanoporphyrin (40) (50 mg) was dissolved in concentrated sulfuric acid (5 mL) and stirred at room temperature for 5 min. After neutralization, the resulting residue was chromatographed on a silica gel column, 30% petroleum ether/methylene chloride being used for elution. The less polar band was collected and recrystallized from methylene chloride/methanol to give 5 mg (10%) of nickel(II) α-*meso*-(2-formylvinyl)cyclohexanespirotripentanobenzochlorin (42). The major band was eluted with 4% acetone/methylene chloride and after recrystallization from methylene chloride/hexane gave 20 mg (43%) of the free-base α,β-*meso*-bis(2-formylvinyl)tetrapentanoporphyrin (41). For nickel(II) α-*meso*-(2-formylvinyl)cyclohexanespirotripentanobenzochlorin (42): mp >350 °C; vis λ_{max} 340 nm (ϵ 28 600), 395 (42 700), 436 (46 800), and 708 (21 800); NMR δ_H 9.92 (d, CHO, J = 7.8 Hz), 9.14 (d, β-H of acrylaldehyde, J = 15.3 Hz), 8.52 (d, 1 benzo H, J = 8.1 Hz), 8.36 and 7.77 (s, 2 meso H), 8.18 (d, 1 benzo H, J = 6.9 Hz), 7.54 (t, 1 benzo H), 6.03

(dd, α-H of acrylaldehyde), 3.65, 3.51, 3.43, and 3.35 (br, 12 H, α-CH_2), 2.39, 2.09, and 2.02 (br, 18 H, β- and γ-CH_2), 1.84 (br, 4 H, α-CH_2 of spiro ring), 1.21 (br, 6 H, β- and γ-CH_2 of spiro ring); MS, *m/e* (%) 730 (100). Anal. Calcd for $C_{46}H_{48}N_4NiO$: C, 75.52; H, 6.62; N, 7.65. Found: C, 75.30; H, 6.78; N, 7.56. For α,β-*meso*-bis(2-formylvinyl)tetrapentanoporphyrin (41): mp >350 °C; vis λ_{max} 400 nm (ε 32300), 424 (32900), and 656 (12000); NMR δ_H 10.13 (d, 2 CHO, J = 7.8 Hz), 9.68 (d, 2 H, β-H of acrylaldehyde, J = 15.3 Hz), 9.46 (s, 2 meso H), 6.60 (dd, 2 H, α-H of acrylaldehyde), 3.95, 3.91, and 3.12 (br, 16 H, α-CH_2), 2.24, 2.07, and 1.86 (br, 24 H, β- and γ-CH_2), −1.29 (s, br, 2 NH); δ_C 26.70, 27.18, 27.87, 27.99, 28.09, 28.77, 31.29, 31.53, 31.91, 32.64, and 32.91 (peripheral CH_2), 99.68 (d, 2 meso C), 112.54 (s, 2 quaternary meso C), 141.30–152.78 (s, br, ring C's), 142.68 and 151.77 (both d, vinyl C's), 192.01 (d, CHO); MS, *m/e* (%) 690 (100).

***trans,trans,trans*-1,6-Bis{α-[nickel(II) octaethylporphyrinyl]}-1,3,5-hexatriene (48).** $TiCl_3(DME)_{1.5}$ (450 mg, 1.55 mmol) and Zn–Cu couple (415 mg, 5.85 mmol) were added to a dry nitrogen-filled flask in a dry box. DME (10 mL) was added to the reaction flask, and the resulting mixture was refluxed for 2 h under an atmosphere of nitrogen to yield a black suspension. Nickel(II) α-(2-formylvinyl)octaethylporphyrin (6) (101.5 mg, 0.156 mmol) in 10 mL of DME was added and the mixture refluxed for 45 min. After being cooled to room temperature, the reaction mixture was chromatographed on a short silica gel column, methylene chloride being used for elution. The resulting residue was further purified by chromatography on a silica gel column (elution with 33% methylene chloride/petroleum ether), and the main brown fraction was collected and recrystallized from methylene chloride/methanol, yielding 94 mg (96%) of the title dimer: mp >340 °C; vis λ_{max} 340 nm (ε 47300), 404 (175800), and 562 (31200); NMR δ_H (ppm) 9.38 (s, 6 meso H), 8.66 (d, 2 H_a, J = 15.0 Hz), 6.43 (dd, 2 H_c, J_1 = 7.2 Hz, J_2 = 3.0 Hz), 5.47 (ddd, 2 H_b, J_1 = 15.0 Hz, J_2 = 7.2 Hz, J_3 = 3.0 Hz), 3.79 (m, 32 H, CH_2 of Et), 1.78, 1.68, and 1.60 (all t, 18 H, 15 H, and 15 H, respectively, CH_3 of Et); δ_C (ppm) 17.23, 17.27, 18.49, 18.55, 19.95, and 22.62 (peripheral Et), 96.60 (d, 2 meso C), 97.41 (d, 4 meso C), 111.72 (s, 2 quaternary meso C), 132.15, 134.23, and 143.98 (all d, 2 C each, vinyl C's), 138.34, 139.42, 139.89, 140.56, 143.17, 143.46, 144.88, and 145.59 (ring C's); MS, *m/e* 1257.3 (100). Anal. Calcd for $C_{78}H_{92}N_8Ni_2 \cdot H_2O$: C, 73.43; H, 7.43; N, 8.79. Found: C, 73.47; H, 7.48; N, 8.83.

***trans,trans,trans*-1,6-Bis{α-[nickel(II) tetrabutanoporphyrinyl]}-1,3,5-hexatriene (50).** The same general procedure was followed, with $TiCl_3(DME)_{1.5}$ (300 mg, 1.03 mmol), Zn–Cu (275 mg, 3.87 mmol), and DME (8.0 mL). After 2 h of refluxing, nickel(II) α-(2-formylvinyl)tetrabutanoporphyrin (49) (65 mg, 0.10 mmol) in 8 mL of DME was added and the resulting mixture was refluxed for 1 h. The product was purified by chromatography on a silica gel column (elution with 30% methylene chloride in petroleum ether). The main fraction was collected and recrystallized from methylene chloride/methanol to give 34 mg (55%) of the title dimer: mp >350 °C; vis λ_{max} 332 nm (ε 24340), 402 (194000), 524 (17340), and 558 (27690); NMR δ_H (ppm) 9.31 (s, 4 meso H), 9.29 (s, 2 meso H), 8.52 (d, 2 H_a, J = 15.3 Hz), 6.61 (dd, 2 H_c), 5.62 (dd, 2 H_b), 3.74 and 3.86 (br, 32 H, α-CH_2), 2.24 and 2.36 (br, 32 H, β-CH_2); MS, *m/e* 1241.8 (2) and 1216.5 (100). Anal. Calcd for $C_{78}H_{76}N_8Ni_2 \cdot H_2O$: C, 74.29; H, 6.24; N, 8.88. Found: C, 74.00; H, 6.43; N, 8.44.

1,2-Bis{α-[nickel(II) octaethylporphyrinyl]}ethene (51). The same general procedure was followed. $TiCl_3(DME)_{1.5}$ (180 mg, 0.62 mmol), Zn–Cu couple (165 mg, 2.32 mmol), and DME (5.0 mL) were used. After 2 h of refluxing, nickel(II) α-formyloctaethylporphyrin (46) (58 mg, 0.09 mmol) in 5 mL of DME was added and the final mixture was refluxed for 1 h. The product was purified by chromatography on a silica gel column, 9:1 petroleum ether/methylene chloride being used for elution. The main fraction was collected and recrystallized from methylene chloride/methanol to give 28 mg (49%) of the title compound: mp >350 °C; vis λ_{max} 398 nm (ε 161800), 534 (25250), and 566 (28200); NMR δ_H (ppm) 9.51, 9.30, 9.06, and 7.67 (all s, 4 meso H), 9.49 (s, 2 meso H), 8.07 (s, 2 H, CH=CH), 4.04, 3.59, 3.49, and 2.89 (q, 2 H each, CH_2 of Et), 3.88 and 3.76 (m, 8 H each, CH_2 of Et), 3.38 and 2.63 (m, 4 H each, CH_2 of Et), 1.75–1.85 (overlapping t, 24 H, CH_3 of Et), 1.43–1.53 (overlapping t, 12 H, CH_3 of Et), 1.02 and 0.69 (t, 6 H each, CH_3 of Et); MS, *m/e* 1206.3 (100) and 601.1 (10). Anal. Calcd for $C_{74}H_{88}N_8Ni_2$: C, 73.64; H, 7.35; N, 9.28. Found: C, 73.69; H, 7.27; N, 9.27.

1,2-Bis{α-[copper(II) octaethylporphyrinyl]}ethene (52). The same general procedure was followed. $TiCl_3(DME)_{1.5}$ (790 mg, 2.72 mmol), Zn–Cu couple (773 mg, 10.9 mmol), and DME (20.0 mL) were used. After 2 h of refluxing, copper(II) α-formyloctaethylporphyrin (47) (200 mg, 0.32 mmol) in 15 mL of DME was added and the final mixture was refluxed for 1 h. The residue after evaporation was further purified by chromatography on a silica gel column, 20% methylene chloride/petroleum ether being used for elution. The main brown fraction was collected and recrystallized from methylene chloride/methanol to give 125 mg (64%) of the title compound: mp >350 °C; vis λ_{max} 334 nm (ε 30400), 391 (182400), 546 (13460), and 572 (13180); MS, *m/e* 1216.7 (100) and 606.2 (56). Anal. Calcd for $C_{74}H_{88}Cu_2N_8$: C, 73.04; H, 7.30; N, 9.21. Found: C, 73.11; H, 7.32; N, 9.19.

Bis{1-[nickel(II) 2,3,4,5,6,7,8-heptaethylporphyrinyl]}methanol (54). The same general procedure was followed. $TiCl_3(DME)_{1.5}$ (620 mg, 2.13 mmol), Zn–Cu couple (576 mg, 8.1 mmol), and DME (12.0 mL) were used. After 2 h of refluxing, nickel(II) 1-formylheptaethylporphyrin (53) (144 mg, 0.24 mmol) in 14 mL of DME was added and the final mixture was refluxed for 1 h. The residue after evaporation was further purified by chromatography on a silica gel column, 40% methylene chloride/petroleum ether being used for elution. The main compound was collected and recrystallized from methylene chloride/methanol to give 85 mg (61%) of the title dimer: mp 219–221 °C; vis λ_{max} 334 nm (ε 27820), 399 (180200), 520 (20040), and 562 (35630); NMR δ_H (ppm) 11.55, 9.97, 9.74, 9.69, 9.57, and 9.41 (all s, 6 meso H), 9.81 (s, 2 meso H), 10.02 (s, C*H*OH), 4.04–3.82 (overlapping q, 22 H, CH_2 of Et), 3.75, 3.57, and 2.83 (q, 2 H each, CH_2 of Et), 1.91–1.65 (overlapping t, 39 H, CH_3 of Et), 0.55 (t, 3 H, CH_3 of Et); MS, *m/e* 1152.4 (25) and 589.1 (100). Anal. Calcd for $C_{69}H_{80}N_8Ni_2O$: C, 71.76; H, 6.98; N, 9.70. Found: C, 71.77; H, 6.90; N, 9.63.

***trans,trans,trans*-1,6-Bis{δ-[nickel(II) mesochlorin e_6 trimethyl ester]}-1,3,5-hexatriene (55).** The same general procedure was followed, with $TiCl_3(DME)_{1.5}$ (350 mg, 1.20 mmol), Zn–Cu (325 mg, 4.58 mmol), and DME (8.0 mL). After 2 h of refluxing, nickel(II) δ-(2-formylvinyl)mesochlorin e_6 trimethyl ester (20) (90 mg, 0.12 mmol) in 8 mL of DME was added and the final mixture refluxed for 45 min. The resulting residue was further purified by chromatography on a silica gel column, 3% acetone/methylene chloride being used for elution. The main compound was collected and recrystallized from methylene chloride/methanol/water to give 74 mg (84%) of the title dimer: mp 197–199 °C; vis λ_{max} 360 nm (ε 48500), 420 (87700), and 666 (50300); NMR δ_H (ppm) 8.86 and 8.75 (s, 2 H each, 4 meso H), 7.53 (d, 2 H_a, J = 15.0 Hz), 6.42 (dd, 2 H_c, J_1 = 7.0 Hz, J_2 = 3.0 Hz), 5.63 (ddd, 2 H_b, J_1 = 15.0 Hz, J_2 = 7.0 Hz, J_3 = 3.0 Hz), 4.68, 4.62, 4.45, and 4.39 (AB q, 4 H, γ-CH_2), 4.22 (q, 2 H, 8,8′-H), 4.10 (s, 6 H, 6,6′-CO_2CH_3), 3.86 (dd, 2 H, 7,7′-H), 3.72 and 3.65 (s, 6 H each, 4 CO_2CH_3), 3.44–3.54 (m, 8 H, CH_2 of Et), 3.17, 3.07, and 2.93 (s, 6 H each, 1,1′,3,3′,5,5′-CH_3), 2.44 (m, 4 H, 7,7′-C$H_2$$CH_2$), 1.79–1.84 (m, 4 H, 7,7′-CH_2CH_2), 1.63 and 1.54 (t, 6 H each, CH_3 of Et), 1.20 (d, 6 H, 8,8′-CH_3); δ_C (ppm) 10.56, 10.71, and 12.23 (q, 2 C each, 1,1′,3,3′,5,5′-CH_3 respectively), 16.40, 16.90, 17.11, 18.05, 19.09, and 19.46 (q, 2 C each, CH_3 of Et and 8,8′-CH_3), 26.63 and 29.67 (t, 2 C each, CH_2 of Et), 31.29 and 31.39 (t, 2 C each, 7,7′-CH_2CH_2), 36.90 (t, 2 C, γ-CH_2), 46.70 and 51.65 (d, 2 C each, $C_{7,7'}$ and $C_{8,8'}$), 51.68, 51.90, and 51.94 (q, 2 C each, CO_2CH_3), 52.42 (s, 2 C, $C_{2,2'}$), 100.17, 100.50, 104.23, and 104.43 (d, 4 C, α,α′,β,β′-meso C), 103.91 (s, 2 C, γ,γ′-meso C), 111.69 (s, 2 C, δ,δ′-meso C), 129.24, 133.48, and 142.35 (d, 2 C each, vinyl C's), 127.58, 129.78, 132.76, 132.93, 134.01, 134.40, 137.24, 137.71, 140.49, 141.49, 142.00, 142.05, 142.20, 144.96, 147.50, 147.69, 150.13, 150.35, and 154.74 (all s, ring C's), 169.30 and 169.36 (s, 6,6′-CO_2CH_3), 172.41 and 172.46 (s, γ,γ′-CO_2CH_3), 173.35 and 173.38 (s, 7,7′-CO_2CH_3); MS, *m/e* 1470.5 (100) and 1262.6 (41). Anal. Calcd for $C_{80}H_{88}N_8Ni_2O_{12}$: C, 65.37; H, 6.04; N, 7.62. Found: C, 65.47; H, 6.13; N, 7.58.

***trans,trans,trans*-1,6-Bis{γ-[nickel(II) *trans*-7,8-dihydrooctaethylporphyrinyl]}-1,3,5-hexatriene (56).** The same general procedure was followed. $TiCl_3(DME)_{1.5}$ (205 mg, 0.71 mmol), Zn–Cu (192 mg, 2.70 mmol), and DME (5.0 mL) were used. After 2 h of refluxing, nickel(II) γ-(2-formylvinyl)octaethylchlorin

(27) (46 mg, 0.07 mmol) in 5 mL of DME was added and the final mixture refluxed for 1 h. The resulting residue was further purified by chromatography on a silica gel column, 20% methylene chloride/petroleum ether being used for elution. The main compound was collected and recrystallized from methylene chloride/methanol to give 32 mg (72%) of the title dimer: mp 199-200 °C; vis λ_{max} 347 nm (ϵ 45 600), 412 (118 100), and 630 (51 610); NMR δ_H (ppm) 8.90, 8.87, 8.83, 8.82, 7.85, and 7.83 (all s, 6 meso H), 7.60 and 7.58 (both d, 2 H_a, J = 15.1 Hz), 6.44 (dd, 2 H_c, J_1 = 7.2 Hz, J_2 = 3.0 Hz), 5.81 (ddd, 2 H_b, J_1 = 15.0 Hz, J_2 = 7.2 Hz, J_3 = 3.0 Hz), 4.10 (m, 2 H, 8,8'-H), 3.88 (m, 2 H, 7,7'-H), 3.25-3.57 (overlapping q, 24 H, CH_2 of Et), 1.76 (overlapping q, 8 H, 7,7',8,8'-CH_2 of Et), 1.46-1.68 (overlapping t, 36 H, CH_3 of Et), 0.98 and 0.93 (t, 12 H, 7,7',8,8'-CH_3 of Et); MS, m/e 1261.9 (100). Anal. Calcd for $C_{78}H_{98}N_8Ni_2$: C, 74.17; H, 7.66; N, 8.87. Found: C, 74.20; H, 7.58; N, 8.88.

***trans,trans,trans*-1,6-Bis{δ-[nickel(II) benzochlorin]}-1,3,5-hexatriene (57).** The same general procedure was followed. $TiCl_3(DME)_{1.5}$ (336 mg, 1.16 mmol), Zn-Cu (311 mg, 4.38 mmol), and DME (10.0 mL) were used. After 2 h of refluxing, nickel(II) γ-(2-formylvinyl)octaethylbenzochlorin (14) (76 mg, 0.11 mmol) in 15 mL of DME was added and the final mixture was refluxed for 1 h. The resulting residue was chromatographed on a silica gel column, 40% methylene chloride/petroleum ether being used for elution. The second least polar band was collected and recrystallized from methylene chloride/methanol to give 42 mg (56%) of the title compound: mp 239-241 °C; vis λ_{max} 371 nm (ϵ 54 500), 434 (95 700), 618 (28 800) and 706 (42 400); NMR δ_H (ppm) 8.66 (d, 2 benzo H, J = 8.1 Hz), 8.63 and 8.27 (s, 2 H each, 4 meso H), 7.86 (d, 2 H_a, J = 14.7 Hz), 7.68 (t, 2 benzo H), 7.60 (d, 2 benzo H, J = 6.9 Hz), 6.35 (dd, 2 H_c, J_1 = 7.2 Hz, J_2 = 3.0 Hz), 5.55 (ddd, 2 H_b, J_1 = 15.0 Hz, J_2 = 7.2 Hz, J_3 = 3.0 Hz), 3.27-3.55 (m, 24 H, CH_2 of Et), 2.77 and 2.32 (q, 4 H each, CH_2 of *gem*-Et_2), 1.56, 1.53, and 1.36 (t, 36 H, CH_3 of Et), 0.07 and 0.04 (t, 6 H each, CH_3 of *gem*-Et_2); MS, m/e 1334.5 (100). Anal. Calcd for $C_{84}H_{98}N_8Ni_2 \cdot H_2O$: C, 74.56; H, 7.30; N, 8.28. Found: C, 74.60; H, 7.36; N, 8.12.

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Preparation of 3-Alkyl β-Lactams via the Ketene-Imine Cycloaddition Reaction Using α-(Phenylthio)alkanoyl Halides as Starting Materials: Application to the Synthesis of (±)-Carbapenem Building Blocks and Related Compounds

Claudio Palomo,* Fernando P. Cossio, Jose M. Odiozola, Mikel Oiarbide, and Jesús M. Ontoria

Departamento de Quimica Orgánica, Facultad de Química, Universidad del Pais Vasco. Apdo. 1072, 20080 San Sebastián, Spain

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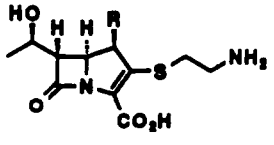
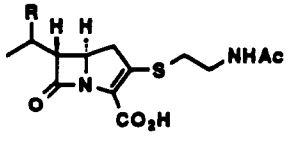
Preparation of appropriately substituted 3-alkyl β-lactams via the ketene (or equivalent)-imine cycloaddition reaction is described. The dehydrochlorination reaction of α-(phenylthio)alkanoyl chlorides with triethylamine in the presence of imines derived from cinnamaldehydes and *p*-anisidine produced a high-yield formation of α-phenylthio β-lactams, which upon desulfuration furnished a variety of 3-alkyl β-lactams in a highly stereoselective fashion. In contrast, reaction between α-haloalkanoyl chlorides and cinnamylideneamines in the presence of triethylamine furnished the corresponding [4 + 2] cycloadducts as main products. Preparation of highly functionalized α-alkylidene β-lactams through thermal decomposition of the corresponding β-lactam sulfoxides or by cycloaddition of α,β-unsaturated acid chlorides to imino esters in the presence of triethylamine is also described. Addition of Flemming's silylcuprate reagent to α-alkylidene β-lactams furnished the corresponding 3-(1'-(dimethylphenylsilyl)ethyl) β-lactams as (±)-thienamycin intermediates.

Carbapenem antibiotics, such as thienamycin (1), 1-β-methylthienamycin (2), and the closely related structures PS-5 (3) and PS-6 (4), have attracted a great deal of interest from both a biological and a synthetic point of view.[1]



1 R: H Thienamycin
2 R: Me 1-β-Methylcarbapenems



3 R: H PS-5
4 R: Me PS-6

Because of the inherent chemical instability of the bicyclic ring system, the main strategies toward their synthesis (Figure 1) usually involve the preparation of an appropriately substituted monocyclic 3-alkyl β-lactam with the correct stereochemistry at C_3-C_4 of the β-lactam ring, followed by chemical manipulations at N_1 and C_4 and subsequent ring closure to form the bicyclic carbapenem system in the last steps of the synthesis.[2] Of the existing methods to carry out an efficient ring closure, the carbene insertion reaction developed by the Merck group[3] for thienamycin synthesis (Figure 2) seems to be the most widely employed method for the construction of bicyclic

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