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# Unexpected Methylation and Propylation of Porphyrin E-ring during the Hemisynthesis of Deoxophylloerythroetioporphyrin (DPEP)

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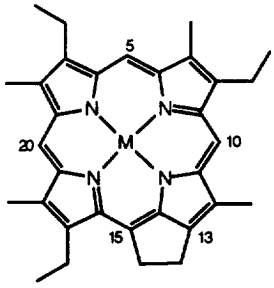
*Key Words*: porphyrins, petroporphyrins, DPEP, synthesis, triazabicyclodecene, ring E alkylation.

***Abstract:*** An improved hemisynthesis of DPEP from chlorophyll *a* is described. Hydrogenation of the vinyl group avoided the cleavage to a 3-H porphyrin, while heating in triazabicyclodecene performed the decarboxylation of the side-chain and the aromatization of ring D. Under these conditions extensive methylation and propylation of ring E occurred in the presence of $CH_2X_2$ (X = Cl, Br). © 1997 Elsevier Science Ltd.

Deoxophylloerythroetioporphyrin **1** (DPEP) is a chlorophyll fossil found in most sediments containing organic matter, such as crude oils and oil shales.[1] Since this compound is often the major component of the mixture of porphyrins that can be isolated from geological sources, it is also a reference compound for all studies related to the structure determination of these fossil pigments.




DPEP **1**
M = $H_2$ (free base) or metal ion

The total synthesis of DPEP has been carried out by several groups,[2] but hemisynthesis from the readily available chlorophyll *a* **2** provides by far the simplest access to DPEP.[3] We carried out such a hemisynthesis,[4] and have now improved several steps. During the initial work, a highly unexpected methylation of the five-membered ring E occurred, which was due to adventitious traces of dichloromethane interfering with the decarboxylation-dismutation reaction described by Kämpfen and Eschenmoser.[5] Further work showed this reaction to give additional products, including propylated porphyrins. This article presents the full account of the improved hemisynthesis of DPEP as well as a reinvestigation of the alkylation processes occurring under Eschenmoser's conditions.

## *1. Hemisynthesis of DPEP*

Crude chlorophyll *a* was extracted from *Spirulina*[6] to avoid a separation from chlorophyll *b*, and was transformed in three classical steps (acid catalyzed demetallation, transesterification, refluxing in collidine) into methyl pyropheophorbide *a* **3**.[7] Reduction[8] of the keto group gave ester **4**.

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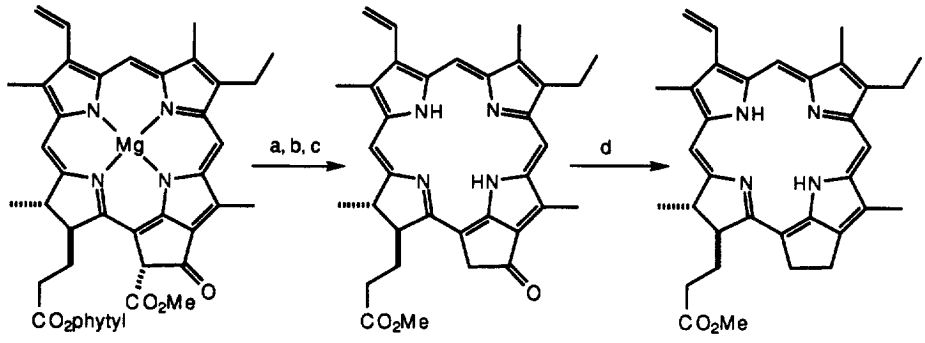



2
Chlorophyll *a*

3
Methyl pyropheophorbide *a*

4

Figure 1. Reagents: a. 2N HCl; b. MeOH + 5% $H_2SO_4$; c. collidine, reflux; d. $NaBH_4$, $CF_3CO_2H$

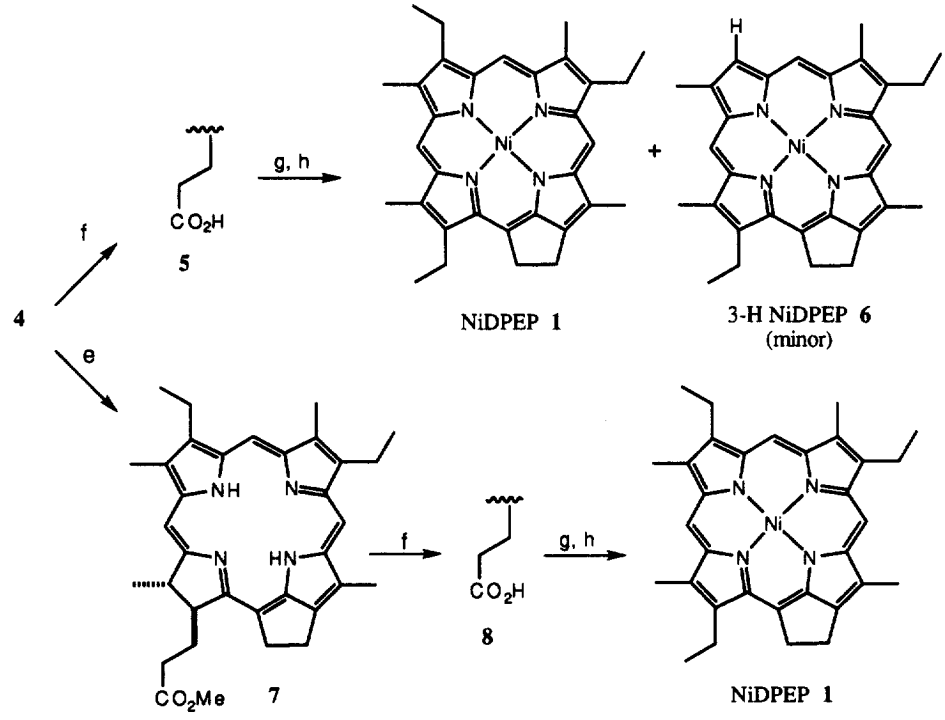



Figure 2. Reagents: e. Pd/C, $H_2$, THF; f. KOH, EtOH; g. TBD, 200°C; h. $Ni(acac)_2$, benzene, reflux.

The vinyl group could in principle be carried as such to the last step since, under Eschenmoser's conditions (triazabicyclodecene = TBD; 200°C),[5] it is reduced to an ethyl group. However, a careful examination of the nickel complex of DPEP, produced at the end of our initial reaction sequence, revealed the presence of *ca* 10 % 3-H NiDPEP **6**. HPLC purification of this compound allowed us to compare its NMR data and

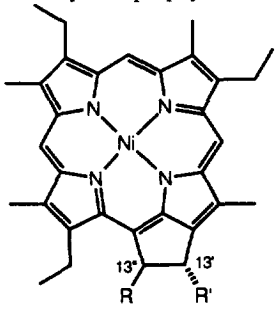
chromatographic behavior with those of a sample of 3-H NiDPEP, a widely distributed fossil porphyrin,[1] isolated from a natural source.[9] This proved that, during the last step, the vinyl group of acid **5** could be cleaved, which recalls the Schumm reaction,[10] *viz.* cleavage of vinyl groups of porphyrin free bases in hot resorcinol. It was suggested[5] that the reduction of the vinyl group may proceed similarly, by way of an intermediate with TBD added at C-3' and we suggest that the cleavage of the C-3 side-chain may proceed *via* such an intermediate. To avoid this side-reaction the vinyl group of **4** was hydrogenated to an ethyl group to give **7**. We also found that the two reduction steps (reduction of the 13'-ketone and hydrogenation of the 3-vinyl group) can be reversed.

The three last steps, hydrolysis of the ester group to give acid **8** and reaction with TBD and immediate metallation with $Ni(acac)_2$ to avoid the oxidation of the very sensitive DPEP free base,[1] were carried out as reported earlier. DPEP, as its stable nickel complex **1**, was thus produced in 20 % overall yield from methyl pyropheophorbide *a*, in five highly reliable steps.

### *2. Methylation and propylation of DPEP under the conditions of Eschenmoser's reaction*

In our preliminary report[4] we drew attention to the fact that when traces of $CH_2Cl_2$ were inadvertently introduced into the reaction mixture, another product, 13"-methyl DPEP **9**, was obtained (the yield reported in our preliminary communication should read 6 % (/ starting material) and not 60 % which refers to the ratio of **9** / total porphyrin fraction). We suspected that the additional carbon originated from $CH_2Cl_2$ and wished to investigate further this new and unexpected reaction. We also noted that **9** is be identical to a porphyrin isolated from an oil shale.[11]

The results of preliminary experiments using $CH_2Cl_2$ proved to be erratic. This is likely due to the volatility of $CH_2Cl_2$, which was expected to be partially lost under the conditions required for sealing the reaction tube under vacuum. To control the amount of added reagent we used instead the less volatile $CH_2Br_2$ and found that alkylated porphyrins were also reproducibly produced and that the relative amount of alkylated / non-alkylated porphyrins was in the main sensitive to the relative amount of added $CH_2Br_2$.




| | | |
|---|---|---|
| **1** | R = H | R' = H |
| **9** | R = Me | R' = H |
| **10** | R = *n*-Pr | R' = H |
| **11** | R = Me | R' = Me |
| **12** | R, R' = Me, *n*-Pr | |

Using 4 equivalents of $CH_2Br_2$, standard reaction conditions (ca 150 eq. TBD; 200°C; 4 h) and the usual work-up, including metallation with nickel, we recovered a porphyrin mixture (54 %, based on an average molecular weight of 560) containing five isolable products. NiDPEP **1** represented only 6.8 % of the mixture. The remaining components all contained one or more additional $CH_2$ groups, as measured by mass spectrometry. HPLC separation allowed us to isolate two major components, Ni-13"-methyl DPEP **9** (62.6 %) and **10** (18.6 %) containing three additional carbons, while two minor porphyrins **11** (1.6 %) and **12** (3.8 %) contained respectively 2 or 4 additional $CH_2$. Mass spectra (12 and 70 eV) gave crucial information: peaks corresponding to the loss of methyl or propyl were observed and there was no evidence for loss of an ethyl group from **10**, **11** or **12** , or of a butyl group from **12** (under the conditions used the ethyl groups at C-3, C-8 and C-17 are almost untouched).

The NMR data ($^1$H and DEPT 135) for **9-12** confirmed the substitution patterns. In **9** and **10**, there remain 3 protons in the E ring, their relative chemical shifts indicating that substitution had occurred on carbon 13". In **11**, two doublets at high field indicated the presence of a -CH($CH_3$)-CH($CH_3$)- substitution pattern on the ring, the absence of significant coupling between the two 13' and 13" protons confirming a trans stereochemistry. $^{13}$C data also fully support the proposed structures for **9** and **10**. Product **12** is a mixture of the two isomers in a 5:1 ratio.

These results rule out a reaction mechanism involving successive methylations. Instead, we require a one carbon - $CH_2Br_2$ or $CH_2Cl_2$ being good candidates - and a 3 carbon unit to be added to the E-ring. The only 3 carbon fragment available is part of the TBD reagent.

TBD is a strong base, used in large excess under drastic thermal conditions; for example all the hydrogens of octaethylporphyrin are exchanged for deuterium under Eschenmoser's conditions.[5] Accordingly, the formation of an anion at the benzylic positions 13' or 13" of DPEP should be easy. Moreover, the high reactivity at position 13" (or 15' if not cyclized) has been documented.[12] The porphyrin anion has then to react with an appropriate electrophile, generated by the reaction of $CH_2X_2$ (X = Cl, Br) with TBD. Alkylation of TBD would lead first to a iminium salt, which in turn may eliminate HX. The resulting iminium salt may then equilibrate with an endocyclic isomer. Attack of an anionic porphyrin on the iminium carbons would subsequently give intermediates in which the amine is bound to the porphyrin E ring.

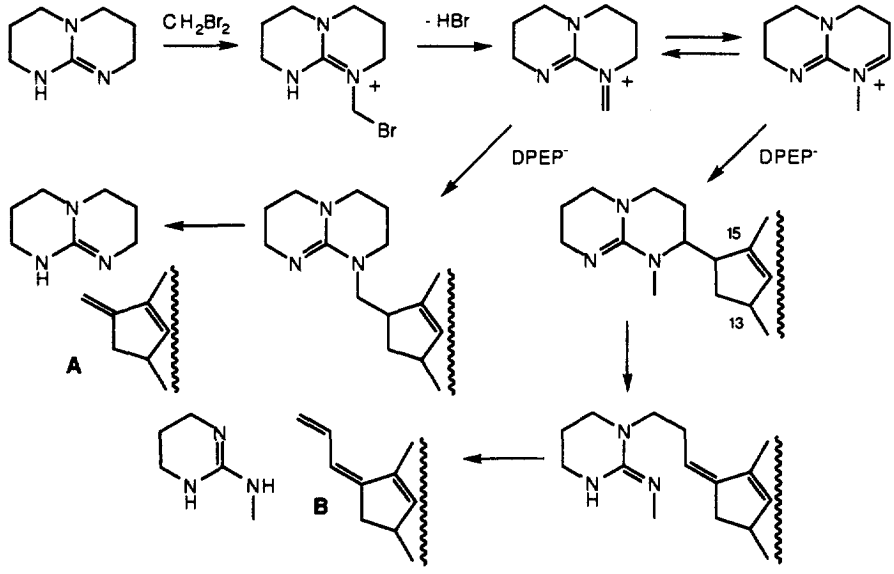



Figure 3. Proposed mechanism for the alkylation of DPEP by $CH_2Br_2$ / TBD (the cyclopentene represents DPEP E ring, attached to positions 13,15).

We suggest that the next steps are either elimination of TBD to give **A**, or two successive eliminations to give a monocyclic amine and **B**. **A** is comparable to β-vinylporphyrins, known to be reduced in hot TBD, while analogue **B** would be expected to behave similarly in two successive reduction steps. This sequence may then be

repeated at position 13', leading to dialkylation of DPEP. During the TBD reaction, the formation of very polar products possessing the porphyrin chromophore was observed. This not only accounts for the incomplete recovery of the alkylporphyrins, but also suggests that the cleavage of nitrogen containing highly basic intermediates was not complete.

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## *Experimental Section*

### *General*

NMR spectra were obtained in $CDCl_3$ (unless otherwise stated) on Bruker SY 200 (200 MHz) and Bruker AC 300 (300 MHz) instruments. Chemical shifts (δ) are expressed in ppm from TMS and coupling constants in Hz (vicinal coupling constants in ethyl groups are in the 7 Hz range). Mass spectra were recorded on a Finnigan TSQ 70 spectrometer, while high resolution data were measured on a VG Analytical ZAB-HF spectrometer (FAB mode). UV-visible spectra were obtained in $CH_2Cl_2$ using a Hewlett-Packard HP 8453 spectrometer. Elemental analyses were performed by the "Service de Microanalyse du Centre de Recherche Chimie de Strasbourg". Chromatographic separations were obtained using Merck 60 silica gel columns. HPLC separations were run on Waters 6000 A and 590 instruments (Hewlett-Packard DAD HP 1100 and Waters 440 detectors) using Du Pont RP-18 Zorbax ODS columns (analytical scale: 250 x 4.6 mm, 5µm, eluent: methanol-$CH_2Cl_2$ 96:4, 1mL/min; preparative scale: 250 x 21.6 mm, 8µm, eluent: methanol-$CH_2Cl_2$ 9:1, 19mL/min).

### *Methyl pyropheophorbide a 3 from Spirulina*

Lyophilized *Spirulina*[6] powder (500 g) was extracted overnight in refluxing acetone / ethanol (resp. 0.5 and 1.0 L). Filtration (paper) gave a green solution which was treated with 2 N HCl (150 mL) for 5 min, diluted with water (2 L) and extracted with $CH_2Cl_2$ (400 mL). The organic phase was dried over $Na_2SO_4$ and the solvent evaporated under vacuum. The residue was treated with methanol containing 5 % $H_2SO_4$ (250 mL). The resulting blue solution was kept overnight, filtered through sintered glass (por. 4) and extracted with $CH_2Cl_2$ (200 mL). The organic phase was washed with water (2 x 1 L), dried over $Na_2SO_4$ and concentrated. Crystallization ($CH_2Cl_2$-hexane) gave methyl pheophorbide *a* (2.6 g).

Methyl pheophorbide *a* (1.055 g) was dissolved in collidine (110 mL; redistilled and stored over KOH) and refluxed for 1 h. After cooling the solution was diluted with $CH_2Cl_2$ and washed with 2N HCl (4 x 200 mL) and water (2 x 200 mL). The solution was dried ($Na_2SO_4$) and evaporated. The residue was purified by silica gel chromatography (150 mL). Methyl pyropheophorbide *a* **3** was eluted with $CH_2Cl_2$-AcOEt (9:1) and crystallized from $CH_2Cl_2$-hexane (887 mg; 93 %).

### *Methyl 13'-Deoxopyropheophorbide a 4 and methyl 13'-deoxomesopyropheophorbide a 7*

A round-bottom flask containing trifluoroacetic acid (100 mL) was cooled to 0°C. Successively were added sodium borohydride (3.3 g; caution: gas evolution) and, dropwise, a solution of **3** in $CH_2Cl_2$ (16 mL). The mixture turned blue. At the end of the addition the ice bath was removed and the solution stirred overnight at

20°C. Dilution with $CH_2Cl_2$ (100 mL), addition of NaOH pellets until neutral, water washing (3 x 600 mL), drying ($Na_2SO_4$) and concentration under vacuum gave a solid residue which was chromatographed (silica gel; 200 mL). Elution with $CH_2Cl_2$-AcOEt (95:5), evaporation and crystallization from $CH_2Cl_2$-MeOH gave **4** (672 mg; 86 %). Compound 4 was used as such for the hydrogenation step.

**4**. $^1$H NMR: 9.95, 9.59, 8.95 (3s, 1+1+1H, *meso*), 8.29, 6.29, 6.22 (3 dd, 1+1+1H, vinyl), 4.89 (m, 2H, 13"-$CH_2$), 4.67 (m, 1H, 18-H), 4.49 (m, 1H, 17-H), 4.07 (m, 2H, 13'-$CH_2$), 3.87 (q, 2H, 8-ethyl $CH_2$), 3.59 (s, 3H, ester $CH_3$), 3.58, 3.51, 3.44 (3s, 3+3+3H, 2-, 7-, 12-$CH_3$), 2.9-2.1 (m, 4H, 17-$CH_2$-$CH_2$), 1.85 (d, 3H, 18-ethyl $CH_3$), 1.77 (t, 3H, 8-ethyl $CH_3$), -1.6, -3.3 (2 broad s, 1+1H, NH). UV-visible: $\lambda_{max}$ 404 ($\varepsilon$ = 145 600), 504 (15 300), 532 (5 300), 594 (6 300), 648 (37 600).

To a solution of **4** (400 mg) in freshly distilled THF (100 mL) was added palladium on charcoal (10 %; 15 mg). After stirring at 20°C and normal hydrogen pressure for 1.5 h, the filtered solution was evaporated and product **7** purified on silica gel (200 mL; elution with $CH_2Cl_2$-AcOEt 95:5) and crystallized from $CH_2Cl_2$-MeOH (367 mg; 91 %). Its physical data were identical with those reported in the literature.[13]

**7**. $^1$H NMR: 9.80, 9.63, 8.90 (3s, 1+1+1H, *meso*), 4.89 (m, 2H, 13"-$CH_2$), 4.67 (dq, 1H, 18-H), 4.57 (m, 1H, 17-H), 4.08 (m, 2H, 13'-$CH_2$), 4.06, 3.89 (2q, 2+2H, ethyl $CH_2$), 3.58 (s, 3H, ester $CH_3$), 3.53, 3.48, 3.47 (3s, 3+3+3H, 2-, 7-, 12-$CH_3$), 2.9-2.1 (m, 4H, 17-$CH_2$-$CH_2$), 1.85 (d, 3H, 18-$CH_3$), 1.80, 1.78 (2t, 3+3H, ethyl $CH_3$), -1.7, -3.5 (2 broad s, 1+1H, NH). UV-visible: $\lambda_{max}$ 395 nm ($\varepsilon$ = 153 000), 498 (12 300), 527 (3 600), 585 (4 300), 638 (37 700).

*13'-Deoxomesopyropheophorbide a* ***8***

Ester **7** (928 mg) and KOH (195 mg) were dissolved in ethanol (350 mL) and refluxed overnight. After being diluted with $CH_2Cl_2$ (150 mL) and washed with water (500 mL) containing AcOH (5 mL), followed by pure water (500 mL), the solution was dried ($Na_2SO_4$) and evaporated. The residue was purified on silica gel (300 mL) and eluted with $CH_2Cl_2$-MeOH (95:5). Acid **8** did not crystallize and was pumped under vacuum ($10^{-2}$ Torr) and used as such.

**8**. $^1$H NMR: NMR: 9.80, 9.62, 8.90 (3s, 1+1+1H, *meso*), 4.85 (m, 2H, 13"-$CH_2$), 4.66 (dq, 1H, 18-H), 4.51 (m, 1H, 17-H), 4.05 (m, 2H, 13'-$CH_2$), 4.05, 3.88 (2q, 2+2H, ethyl $CH_2$), 3.51 (s, 3H, 12-$CH_3$), 3.48, 3.46 (2s, 3+3H, 2-, 7-$CH_3$), 2.9-2.10 (m, 4H, 17-$CH_2$-$CH_2$), 1.85 (d, 3H, 18-$CH_3$), 1.81, 1.77 (2t, 3+3H, ethyl $CH_3$), -3.4 (very broad signal, 2H, NH). UV-visible: $\lambda_{max}$ (rel. int.): 395 nm (1), 499 (0.100), 527 (0.053), 585 (0.053), 638 (0.232).

*Nickel deoxophylloerythroetioporphyrin (NiDPEP)* ***1*** *(M = Ni)*

A mixture of **8** (50 mg) and TBD (1.95 g) was sealed in a glass tube under argon vacuum and heated at 200°C for 4 h. The resulting product was dissolved in $CH_2Cl_2$ (150 mL), washed with water (3 x 250 mL), dried over $Na_2SO_4$ and evaporated under vacuum. The residue and Ni(acac)$_2$ (100 mg) were refluxed in benzene (15 mL) under argon for 6 h. The solution was filtered on a short silica gel column (eluent $CH_2Cl_2$) and the product purified on alumina (50 mL; eluent $CH_2Cl_2$-hexane 1:1) and crystallized from $CH_2Cl_2$-MeOH to give **1** (24 mg; 47 %). All physical data for this product were identical with those described in the literature.

**1** (M = Ni) $^1$H NMR: 9.76, 9.74, 9.73 (3s, 1+1+1H, *meso*), 5.06 (m, 2H, 13"-$CH_2$), 3.94, 3.92 (2q, 2+2H, 3,8-ethyl $CH_2$), 3.89 (m, 2H, 13'-$CH_2$), 3.78 (q, 2H, 17-ethyl $CH_2$), 3.50, 3.48, 3.44, 3.43 (4s, 3+3+3+3H, $CH_3$), 1.80, 1.79 (2t, 3+3H, 3-,8-ethyl $CH_3$), 1.63 (t, 3H, 17-ethyl $CH_3$). DEPT 135 (75 MHz) $^{13}$C: 97.1,

97.0, 95.8 (meso CH), 37.1, 24.3 (E ring $CH_2$), 20.8, 19.9, 19.8 (ethyl $CH_2$), 17.6, 17.5, 16.5, 12.3, 11.5, 11.3, ethyl $CH_3$). UV-visible: $\lambda_{max}$ 393 nm ($\varepsilon$ = 186 000), 514 (11 300), 552 (21 900).

*Formation of NiDPEP **1** and 3-H-NiDPEP **6** from acid **5** in TBD*

Ester **4** was hydrolyzed as described above (**7** to **8**). The crude acid **5** (80 %) did not crystallize and was pumped under vacuum ($10^{-2}$ Torr) and used as such.

**5**. $^1H$ NMR: 9.95, 9.60, 8.96 (3s, 1+1+1H, *meso*), 8.28, 6.29, 6.21 (3dd, 1+1+1H, vinyl), 4.89 (m, 2H, 13"-$CH_2$), 4.68 (m, 1H, 18-H), 4.55 (m, 1H, 17-H), 4.07 (m, 2H, 13'-$CH_2$), 3.86 (q, 2H, 8-ethyl $CH_2$), 3.59, 3.51, 3.44 (3s, 3+3+3H, $CH_3$), 2.9-2.1 (m, 4H, 17-$CH_2$-$CH_2$), 1.86 (d, 3H, 18-$CH_3$), 1.76 (t, 3H, ethyl $CH_3$). UV-visible (rel. int.): $\lambda_{max}$ 402 (1), 502 (0.089), 516 (0.042), 646 (0.113).

Reaction in TBD under standard conditions (15 mg **5**, 625 mg TBD, sealed tube, 200°C, 4 h), followed by metallation with $Ni(acac)_2$ gave a mixture of nickel porphyrins **1** and **6** (ratio *ca* 9:1), which were separated by HPLC (conditions above). The products were identical to reference samples from various geochemical sources.

*Reaction of **8** in the presence of TBD + $CH_2Br_2$*

Acid **8** (50 mg), TBD (1.95 g) and $CH_2Br_2$ (27 µl; 4 eq.) were placed in a glass tube, cooled to -78°C, sealed under argon vacuum, and heated to 200°C for 4h. After the isolation and metallation steps described above, the residue (29 mg) was analyzed by analytical HPLC to measure the relative abundance of the porphyrins (**1**, 6.8%; **9**, 62.6 %; **10**, 18.6 %; **11**, 1.6 %; **12**, 3.8 %). It was first purified on a silica gel plate (2 mm thick; eluent $CH_2Cl_2$-hexane 1:2) to eliminate **1**, then the individual alkylated porphyrins were separated by preparative HPLC. Nickel 13"-methylDPEP **9** and nickel 13"-*n*-propylDPEP **10** could be crystallized from $CH_2Cl_2$-MeOH (9 and 3 mg; 17 and 5 % recovery respectively).

*Nickel 13"-methyl DPEP **9**.* $^1H$ NMR: 9.79, 9.78, 9.76 (3s, 1+1+1H, *meso*), 5.80 (q, 1H, 13"-H, J = 6.8), 4.39 (dd, 1H, 13'-H, J = 16.8 and 5.3), 4.07 (m, 1H from 17-ethyl $CH_2$), 3.93 (m, 6H, 3-, 8-ethyl $CH_2$, 1H from 17-ethyl $CH_2$ and 13'-H), 3.51, 3.50, 3.48 (3s, 3+3+6H, 2-,7-,12-,18-$CH_3$), 1.82 (d, 3H, 13"-$CH_3$, J = 6.8 Hz), 1.79, 1.78 (2t, 3+3H, 3-,8-ethyl $CH_3$), 1.69 (t, 3H, 17-ethyl $CH_3$). DEPT 135 (75 MHz) $^{13}C$: 97.1, 97.0, 96.0 (meso CH), 44.7 (13"-CH), 34.2 (13'-$CH_2$), 27.2 (13"-$CH_3$), 21.0, 19.9, 19.0 (ethyl $CH_2$), 17.6, 17.5, 17.2, 12.3, 11.6, 11.5 (2-,7-,12-,18-$CH_3$ and ethyl $CH_3$). UV-visible: $\lambda_{max}$ 394 nm ($\varepsilon$ = 177 000), 515 (11 600), 553 (21 200). HRMS calcd for $C_{33}H_{36}N_4{}^{58}Ni$: 546.2293. Found: 546.2279.

*Nickel 13"-n-propyl DPEP **10**.* $^1H$ NMR: 9.79, 9.77, 9.75 (3s, 1+1+1, *meso*), 5.67 (m, 1H, 13"-H), 4.27 (dd, 1H, 13'-H, J = 5.9 and 16.5 Hz), 3.94 (m, 6H, 3-,8-,17-ethyl $CH_2$), 3.67 (d, 1H, 13'-H, J = 16.5 Hz), 3.51, 3.50, 3.48 (3s, 3+3+6H, 2-,7-,12-,18-$CH_3$), 2.36 (m, 2H, propyl $CH_2$), 1.79, 1.78 (2t, 3+3H, 3-,8-ethyl $CH_3$), ca 1.8 (m, 2H, propyl $CH_2$), 1.67 (t, 3H, 17-ethyl $CH_3$), 0.98 (t, 3H, propyl $CH_3$). DEPT 135 (75 MHz) $^{13}C$: 97.1, 97.0, 96.0 (meso CH), 50.0 (13"-CH), 43.9 (13'''-$CH_2$), 31.4 (13'-$CH_2$), 22.1 (13''''-$CH_2$), 20.9, 19.9, 19.8 (ethyl $CH_2$), 17.6, 17.5, 17.0, 12.3, 11.6, 11.5 (2-,7-,12-,18-$CH_3$ and ethyl $CH_3$), 14.3 (propyl $CH_3$). UV-visible: $\lambda_{max}$ 395 nm ($\varepsilon$ = 200 000), 515 (12 300), 553 (22 700). MS (70 eV): 574 (100 %, $M^{+\cdot}$), 531 (36 %, $M^{+\cdot}$-propyl). HRMS, calcd for $C_{35}H_{40}N_4{}^{58}Ni$: 574.2606. Found: 574.2606.

*Nickel 13',13"-dimethyl DPEP* ***11***. $^1$H NMR: 9.78, 9.77, 9.75 (3s, 1+1+1H, *meso*), 5.35 (q, 1H, 13'- or 13"-H, J = 6.1 Hz), 5.25 (q, 1H, 13'- or 13"-H, J = 7.0 Hz), 3.93 (m, 6H, ethyl $CH_2$), 3.51, 3.50, 3.49, 3.48 (4s, 3+3+3+3H, 2-,7-,12-,18-$CH_3$), 1.95, 1.81 (2d, 3+3H, 13'- and 13"-$CH_3$), 1.79, 1.78 (2t, 3+3H, 3-,8-ethyl $CH_3$), 1.69 (t, 3H, 17-ethyl $CH_3$). UV-visible (rel. int.): $\lambda_{max}$ 395 nm (1), 515 (0.58), 553 (0.114). MS (70 eV): 560 (100 %, $M^{+\cdot}$), 545 (20 %, $M^{+\cdot}$-$CH_3$), 530 (6 %, $M^{+\cdot}$-2$CH_3$). HRMS, calcd for $C_{34}H_{38}N_4{}^{58}Ni$: 560.2449. Found: 560.2441.

*Nickel methyl,n-propyl DPEP* ***12***. The ratio between the two isomers was estimated at *ca* 5:1 and the signals were assigned to each isomer when possible and accordingly the number of H refer to each product or to the mixture of both. $^1$H NMR: 9.78, 9.75 (2s, 2+1H, major, *meso*), 9.79, 9.77, 9.74 (3s, 1+1+1H, minor, *meso*), 5.35 (m, 13'- and 13"-H), 3.92 (m, 6H, ethyl $CH_2$), 3.53 (d, 3H, major, 12-$CH_3$, J = 0.6 Hz), 3.52, 3.50, 3.48 (3s, 3+3+3H, major, 2-, 7-, 18-$CH_3$), 2.3 and 2.0 (2m, propyl $CH_2$), 1.8 (m, 9H, 3-, 8-ethyl $CH_3$ and ring E $CH_3$), 1.70 (t, 3H, major, 17-ethyl $CH_3$), 1.69 (t, 3H, minor, 17-ethyl $CH_3$), 1.14 (t, 3H, minor, propyl $CH_3$), 1.12 (t, 3H, major, propyl $CH_3$). UV-visible (rel. int.): 395 nm (1), 515 (0.59), 553 (0.116). MS (70 eV): 588 (100 %, $M^{+\cdot}$), 573 (4 %, $M^{+\cdot}$-$CH_3$), 545 (15 %, $M^{+\cdot}$-propyl). HRMS, calcd for $C_{36}H_{42}N_4{}^{58}Ni$: 588.2763. Found: 588.2744.

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