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An Efficient Synthesis of Tetraaryl Porphyrins Substituted with Ester Groups Bearing Long Alkyl Chains

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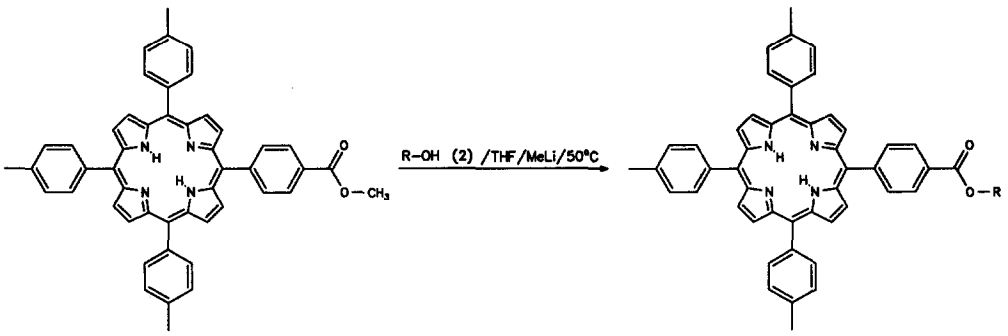
Abstract. *The synthesis of tetraaryl porphyrins substituted with long chain ester groups is described. The compounds are conveniently prepared from the methyl ester* ***1a*** *via a base induced transesterification procedure. The method is also applicable for the synthesis of ester linked diporphyrins.*

Porphyrins substituted with long alkyl chains are of interest due to their nonlinear optical properties,[1] their surfactant like structure[2] and their membrane spanning capabilities.[3] Furthermore some long chain substituted derivatives show liquid crystalline properties[4] and are of interest as model systems for study the electron and energy transfer mechanisms in self organized assemblies.[5] During our studies directed towards the synthesis of porphyrins for use in photodynamic therapy (PDT),[6] we become interested in the synthesis of porphyrins substituted with ester groups bearing long alkyl chains. We thought it usefull to introduce the long alkyl chains by classical transesterification procedures. Though there are many methods for transfering ester groups,[7] most of them are not applicable to our systems. This is mainly due to the decreased solubility of the porphyrins and the long chain alcohols in the solvents used in those methods.

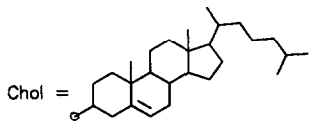
We now wish to report a very convenient synthetic method for the preparation of those compounds. The procedure based on a method described by Meth-Cohn[8] for the synthesis of aryl esters. The synthesis is outlined in scheme 1. To a suspension of the long chain alcohol **2** in THF methyllithium (MeLi) or n-butyllithium (n-BuLi) is added. After complete formation of the alkoxide the porphyrin ester **1a** is added and the reaction mixture is stirred for several hours and quenched by addition of NH_4Cl. After a standard work up procedure the reaction products were isolated and purified by chromatography and recrystallized from MeOH. If n-BuLi is used instead of MeLi the yield decreased strongly with increasing chain length of the alcohol. If MeLi is used this dependency from the chain lenght is not found. Furthermore, we obtained the butyloxycarbonyl derivative **3a** as a side product if n-BuLi is used. Our new method is not limited to linear and primary alcohols. For example, we were able to prepare porphyrin **4** bearing a highly lipophilic cholesteryl group in a yield of 64%. Those cholesterol and steroid substituted porphyrins recently gained



1 a

3 a – f, 4

	R	MeLi Yield (%)	BuLi Yield (%)
3a	$CH_3(CH_2)_4$–	–	4 – 10
3b	$CH_3(CH_2)_{13}$–	82	62
3c	$CH_3(CH_2)_{15}$–	72	50
3d	$CH_3(CH_2)_{17}$–	82	30
3e	$CH_3(CH_2)_{19}$–	71	7
3f	$CH_3(CH_2)_{21}$–	79	7
4	Chol.	64	–

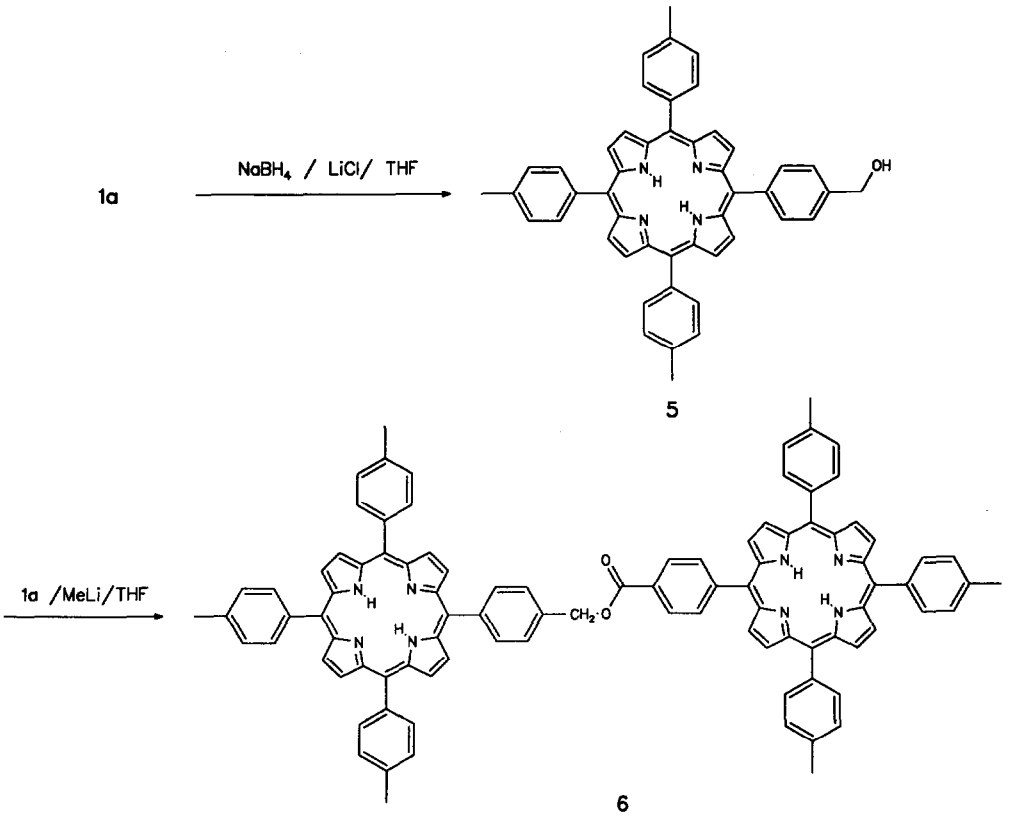


Scheme 1

much attention for the synthesis of model systems mimicking some aspects of P-450.[9)]

We made also use of this transesterification procedure in the synthesis of the ester bridged diporphyrin **6** (scheme 2). The porphyrin **5** is easily available from **1a** by reduction with $NaBH_4$ / LiCl in THF. Reacting **5** in the same manner as described previously, the diporphyrin **6** is formed in 20% yield. This relatively low yield may be due to the extremely low solubility of compound **5** and the alkoxide in THF thus giving rise to a more heterogenous reaction medium and enhanced reaction time. Furthermore **6** has a low solubility in the solvents used in the purification steps.

Nevertheless, the described method is very easy to use and gives good yields for most of the investigated systems. The procedure is applicable to different types of alcohols as illustrated by the formation of compounds **4** and **6**. Furthermore the starting methoxy substituted porphyrin is easily available by standard procedures. In our opinion this method is an attractive alternative to existing procedures, especially if the solubility of the starting compounds is limited. The synthesized porphyrins are currently investigated with respect to their lipophilic properties and their membrane penetrating capabilities.



Scheme 2

EXPERIMENTAL SECTION

NMR spectra were obtained in $CDCl_3$ and recorded with a Varian XL 200 spectrometer. Chemical shift values were given in ppm relative to TMS. Coupling constants were given in Hz. Mass spectra were measured with a VG-Analytical VG70:250 E instrument. Electronic spectra were recorded on a Kontron Uvikon 860 instrument. Melting points were measured on a Büchi 510 apparatus and are uncorrected. Column chromatography was carried out with Merck silica gel mesh size 0.060 - 0.2 mm. MPLC separations were done on a silica gel column with a Gilson Avimed model 302 pump and a Gilson Avimed model 304 C manometric unit.

***Synthesis of 5-(p-Methoxycarbonylphenyl)-10,15,20-tri(p-methylphenyl)porphine* (1a):**

To a solution of 1.24 g (5.91 mmol) 4-methoxybenzaldehyde dimethyl acetal and 3.56 g (29.6 mmol) 4-tolylaldehyde in 370 ml propionic acid were added at 130°C 2.38 g (35.5 mmol) pyrrole dissolved in 70 ml propionic acid. The reaction mixture was refluxed for 1h. Then 300 ml of propionic acid were removed by distillation. After standing at 5°C for 24 h a precipitate was formed, which was isolated by filtration (precipitate A). To the propionic acid solution hexane was added until a black precipitate was formed. This precipitate (B) contained mainly oligomeric products. The remaining solution was washed with water (3 x). The solvent was evaporated and the residue poured into CH_2Cl_2 and dried ($MgSO_4$). The solution was filtered over a plug of silica gel and the solvent evaporated. The obtained residue and precipitate A were chromatographed on a silica gel column with CH_2Cl_2 as eluent. The first porphyrinic fraction was TTP (tetratolylporphyrin), the second fraction was the ester **1a** and the third fraction consists of a mixture of esters **1b** and **1c**. The isomeric esters **1b** and **1c** were separated on a second silica gel column. All products were recrystallized from methanol.

***5-(p-Methoxycarbonylphenyl)-10,15,20-tri(p-methylphenyl)porphine* (1a):**

Yield: 634 mg (15%).

^{1}H-NMR ($CDCl_3$): δ = -2.79 (br s, 2 H, -NH), 2.65 (s, 9 H, $ArCH_3$), 4.07 (s, 3 H, $-COOCH_3$), 7.50 (d, J = 7.9 Hz, 6 H, H_m), 8.07 (d, J = 7.9 Hz, 6 H, H_o), 8.28 (d, J = 8.3 Hz, 2 H, H_o'), 8.41 (d, J = 8.3 Hz, 2 H, H_m'), 8.77 (d, J = 4.8 Hz, 2H, H-2, H-7), 8.86 (s, 4 H, H-12, H-13, H-17, H-18), 8.87 (d, J = 4.8 Hz, 2 H, H-2, H-8).- ^{13}C-NMR ($CDCl_3$):[10] δ = 21.77 (q, $ArCH_3$), 52.41 (q, $COOCH_3$), 118.26, 120.45, 120.69 (3 x s, C_{meso}), 127.47, 127.91 (2 x d, C_m , C_m'), 129.48 (s, C_p'), 131.25 (br s, C_β), 134.53, 134.60 (2 x d, C_o , C_o'), 137.43 (s, C_p), 139.15 (s, C_{ipso}), 147.22 (s, C_{ipso}'), 167.40 (s, -COO-).- FAB-MS: m/e = 715 (M^+).- UV-Vis (CH_2Cl_2): λ = 418, 516, 551, 590, 647 nm.- Anal. Calc. for $C_{49}H_{38}N_4O_2$ (714.9): C 82.32 H 5.36 N 7.84. Found: C 82.09 H 5.11 N 7.62.

We obtained TTP (Tetratolylporphyrin) and **1b** and **1c** as side products. The spectroscopic data of TTP are those reported in the literature.

***5,15-Di(p-methoxycarbonylphenyl)-10,20-di(p-methylphenyl)porphine* (1b):**

Yield: 44.9 mg (2%).

^{1}H-NMR ($CDCl_3$): δ = -2.79 (br s, 2 H, -NH), 2.71 (s, 6 H, $ArCH_3$), 4.11 (s, 6 H, $-COOCH_3$), 7.56 (d, J = 7.9 Hz, 4 H, H_m), 8.09 (d, J = 7.9 Hz, 4 H, H_o), 8.30 (d, J = 8.3 Hz, 4 H, H_o'), 8.44 (d, J = 8.3 Hz, 4 H, H_m'), 8.78 (d, J = 4.9 Hz, 4 H, H-3, H-7, H-13, H-17), 8.89 (d, J = 4.9 Hz, 4 H, H-2, H-8, H-12, H-18).- ^{13}C-NMR ($CDCl_3$): δ = 21.51 (q, $ArCH_3$), 52.42 (q, $-COOCH_3$), 118.52, 120.96 (2 x s, C_{meso}), 127.46, 127.90 (2 x d, C_m , C_m'), 129.80 (s, C_p'), 131.45 (d, C_β), 134.47, 134.53 (d, C_o , C_o'), 137.50 (s, C_p), 138.97 (s, C_{ipso}), 146.95 (s, C_{ipso}'), 167.30 (s, -COO-).- FAB-MS: m/e = 758 (M^+).- UV-Vis (CH_2Cl_2): λ = 418, 515, 550, 591, 648 nm.- Anal. Calc. for $C_{50}H_{38}N_4O_4$ (758.9): C 79.14 H 5.05 N 7.38. Found: C 77.88 H 5.17 N 7.12.

5,10-Di(p-methoxycarbonylphenyl)-15,20-di(p-methylphenyl)porphine **(1c):**

Yield: 89.7 mg (4%).

^{1}H-NMR ($CDCl_3$): δ = -2.78 (br s, 2 H, -NH), 2.68 (s, 6 H, $ArCH_3$), 4.09 (s, 6 H, $-COOCH_3$), 7.52 (d, J = 7.9 Hz, 4 H, H_m), 8.06 (d, J = 7.9 Hz, 4 H, H_o), 8.27 (d, J = 8.0 Hz, 4 H, H_o'), 8.41 (d, J = 8.0 Hz, 4 H, H_m'), 8.76 (d, J = 6.4 Hz, 2 H, H-3, H-12), 8.78 (s, 2 H, H-7, H-8), 8.86 (s, 2 H, H-17, H-18), 8.87 (d, J = 5.3 Hz, 2 H, H-2, H-13).- ^{13}C-NMR ($CDCl_3$): δ = 21.52 (q, $ArCH_3$), 52.43 (q, $-COOCH_3$), 118.80, 120.69 (2 x s, C_{meso}), 127.48, 127.88 (2 x d, C_m , C_m'), 129.54 (s, C_p'), 131.45 (d, C_β), 134.47, 134.53 (2 x d, C_o, C_o'), 137.52 (s, C_p), 138.92 (s, C_{ipso}), 147.01 (s, C_{ipso}'), 167.33 (s, -COO-).- FAB-MS: m/e = 759 (M^++1).- UV-Vis (CH_2Cl_2): λ = 418, 525, 551, 590, 647 nm.- Anal. Calc. for $C_{50}H_{38}N_4O_4$ (758.9): C 79.14 H 5.05 N 7.38. Found: C 79.23 H 5.41 N 7.14 O 8.11.

Synthesis of 5-(p-Hydroxymethylphenyl)-10,15,20-(p-methylphenyl)porphine **(5):**

To a suspension of 10.0 mmol (380 mg) $NaBH_4$ and 9.2 mmol (390 mg) LiCl in 15 ml THF (dried) 0.28 mmol (200 mg) **1a** were added. The reaction mixture was heated to reflux for 1.5 h. Then 15 ml water was added carefully. The mixture was extracted 3 times with CH_2Cl_2 (containing 1% methanol). The combined organic layers were dried over $MgSO_4$ and the solvent evaporated. The residue was chromatographed on a silica gel column with CH_2Cl_2 as eluent. Two porphyrinic fractions were collected. The first one contains unreacted starting material, the second fraction was the expected product.

Yield: 182 mg (95%).

^{1}H-NMR ($CDCl_3$): δ = -2.78 (br 2 H, -NH), 2.71 (s, 9 H, $ArCH_3$) 5.07 (d, J = 5 Hz, 2 H, $-CH_2$-OH), 7.55 (d, J = 7.8 Hz, 6 H, H_m), 7.75 (d, J = 7.8 Hz, 2 H, H_m'), 8.10 (d, J = 7.8 Hz, 6 H, H_o), 8.21 (d, J = 7.8 Hz, 2 H, H_o'), 8.82 (d, J = 4.9 Hz, 2 H, H-3, H-7), 8.86 (s, 4 H, H-12, H-13, H-17, H-18), 8.87 (d, J = 4.9 Hz, 2 H, H-2, H-8).- ^{13}C-NMR ($CDCl_3$): δ = 21.54 (q, $ArCH_3$), 65.80 (t, CH_2-O-), 118.00, 120.00 (s, C_{meso}), 125.30 (d, C_m'), 127.40 (d, C_m), 131.52 (br d, C_β), 134.50, 134.73 (2 x d, C_o , C_o'), 137.33 (s, C_p), 139.22 (s, C_{ipso} , C_p'), 140.76 (s, C_{ipso}').- FAB-MS: m/e = 687 (M^+).- UV-Vis (CH_2Cl_2): λ = 418, 516, 551, 591, 646 nm.- Anal. Calc. for $C_{48}H_{38}N_4O_1$ (686.9): C 83.9 H 5.58 N 8.16. Found: C 84.01 H 5.66 N 8.01.

Synthesis of Porphyrins **3a - 3f** ***and*** **4.**

General Transesterification Procedure: Method A:

In a dried round bottom flask were added under nitrogen (dried) 0.75 mmol of the appropriate alcohol. The flask was heated under vacuum to 50°C for at least 4 h. Then 0.5 - 0.7 ml THF (dried) were added and the mixture was stirred until a homogenous suspension was formed. The mixture was cooled to 3 - 4°C and then carefully 0.75 mmol MeLi (0.50 ml of a 1.5 M MeLi-solution in diethyl ether) were added. The reaction mixture was warmed up gently to room temperature and stirred for 30 min. Then 0.3 - 0.4 ml THF and 0.15 mmol (107 mg) **1a** were added. The mixture was warmed to 50°C and stirred for 2.5 h. After adding 30 ml CH_2Cl_2 and 50 ml of a 2 M NH_4Cl solution the organic layer was separated and dried over Na_2SO_4. The

solution was filtered over a plug of silica gel. The solvent was evaporated and the residue chromatographed by MPLC on a silica gel column (25 x 300 mm) with hexane/CH_2Cl_2 (3:1) as eluent. All products were recrystallized from methanol.

Method B:

In a dried 10 ml round bottom flask were added under nitrogen 0.75 mmol of the appopropriate alcohol and 2 ml THF (dried). Then 0.75 mmol n-BuLi (49.5 mg, 0.47 ml of a 1.6 M hexane-solution) were added at 4 - 5°C. After warming up the reaction mixture gently to room temperature 0.15 mmol (107 mg) of **1a** dissolved in 3 ml THF were added. The mixture was stirred for 4 h at room temperature. Then 25 ml CH_2Cl_2 and 50 ml of a 2 M NH_4Cl solution were added. The organic layer was separated and dried over Na_2SO_4. The solvent was evaporated and the residue chromatographed by MPLC on a silica gel column with hexane/CH_2Cl_2 (3:1) as eluent. All products were recrystallized from methanol.

5-(p-Tetradecyloxycarbonylphenyl)-10,15,20-tri(p-methylphenyl)-porphine (3b):

Method A: Yield: 111 mg (82%). Method B: Yield: 84 mg (62%).

^{1}H-NMR ($CDCl_3$): δ = -2.76 (br s, 2 H, -NH), 0.78 - 0.90 (m, 3 H, alkyl-CH_3), 1.08 - 1.65 (m, 22 H, -$(CH_2)_{11}$-), 1.82 - 2.03 (m, 2 H, $COOCH_2$-CH_2-), 2.67 (s, 9 H, $ArCH_3$), 4.48 (t, J = 6.3 Hz, 2 H, $COOCH_2$-), 7.51 (d, J = 7.9 Hz, 6 H, H_m), 8.07 (d, J = 7.9 Hz, 6 H, H_o), 8.28 (d, J = 8.0 Hz, 2 H, $H_{o'}$), 8.42 (d, J = 8.0 Hz, 2 H, $H_{m'}$), 8.76 (d, J = 4.6 Hz, 2 H, H-3, H-7), 8.86 (s, 4 H, H-12, H-13, H-17, H-18), 8.87 (d, 2 H, J = 4.6 Hz, H-2, H-8).- ^{13}C-NMR ($CDCl_3$): δ = 14.12 (q, C-14 side chain), 21.51 (q, $ArCH_3$), 22.68, 26.17, 28.87, 29.38, 29.64, 29.65, 29.69, 31.91 (8 x t, -CH_2- side chain), 65.49 (t, C-1 side chain), 118.29, 120.36, 120.63 (3 x s, C_{meso}), 127.41, 127.82 (2 x d, C_m , $C_{m'}$), 129.83 (s, $C_{p'}$), 131.35 (br., d, C_β), 134.47 (d, C_o), 137.37 (s, C_p), 139.10 (s, C_{ipso}), 147.03 (s, $C_{ipso'}$), 166.94 (s, -COO).- FAB-MS: m/e = 897 (M^+).- UV-Vis (CH_2Cl_2): λ = 419, 515, 551, 591, 646 nm.- Anal. Calc. for $C_{62}H_{64}N_4O_2$ (897.2): C 83.00 H 7.19 N 6.24. Found: C 82.12 H 7.28 N 6.05.

Using method B, we obtained always ***5-(p-Butyloxycarbonylphenyl)-10,15,20-tri(p-methylphenyl)porphine*** (**3 a**) as a byproduct. Yield 4 - 10%.

^{1}H-NMR ($CDCl_3$): δ = -2.78 (br s, 2 H, -NH), 1.08 (t, J = 7.3 Hz, 3 H, alkyl-CH_3), 1.43 - 1.68 (m, 2 H, -CH_2-CH_3), 1.80 - 1.98 (m, 2 H, $COOCH_2$-CH_2-), 2.70 (s, 9 H, $ArCH_3$), 4.52 (t, J =6.6 Hz, $COOCH_2$-), 7.55 (d, J = 7.9 Hz, 6 H, H_m), 8.09 (d, J = 7.9 Hz, H_o), 8.30 (d, J = 8.2 Hz, $H_{o'}$), 8.44 (d. J = 8.2 Hz, 2 H, $H_{m'}$), 8.77 (d, J = 4.8 Hz, 2 H, H-3, H-7), 8.86 (s, 4 H, H-12, H-13, H-17, H-18), 8.88 (d, J = 4.8 Hz, H-2, H-8).- ^{13}C-NMR ($CDCl_3$): δ = 13.84 (q, CH_3 side chain), 21.46 (t, C-3 side chain), 21.59 (q, $ArCH_3$), 30.92 (t, C-2 side chain), 65.17 (t, C-1 side chain),118.28, 120.36, 120.61 (3 x s, C_{meso}), 127.43, 127.81 (2 x d, C_m , $C_{m'}$), 129.54 (s, $C_{p'}$), 131.28 (br s, C_β), 134.47, 134.53 (2 x d, C_o , $C_{o'}$), 137.40 (s, C_p), 139.10 (s, C_{ipso}), 147.03 (s, $C_{ipso'}$), 166.95 (s, -COO-).- FAB-MS: m/e = 757 (M^+).- UV-Vis (CH_2Cl_2): λ = 418, 516, 551, 591, 646 nm.- Anal. Calc. for $C_{52}H_{44}N_4O_2$ (756.9): C 82.52 H 5.86 N 7.40. Found: C 81.78 H 5.86 N 7.20.

5-(p-Hexadecyloxycarbonylphenyl)-10,15,20-tri(p-methylphenyl)porphine **(3c):**

Method A: Yield: 100 mg (72%). Method B: Yield: 83 mg (60%).

^{1}H-NMR ($CDCl_3$): δ = -2.77 (br s, 2 H, -NH), 0.74 - 0.93 (m, 3 H, alkyl-CH_3), 1.09 - 1.66 (m, 26 H, -$(CH_2)_{13}$-), 1.78 - 1.99 (m, 2 H, $COOCH_2$-$C\underline{H}_2$-), 2.69 (s, 9 H, $ArCH_3$), 4.50 (t, J = 6.3 Hz, $COOCH_2$-), 7.54 (d, J = 7.9 Hz, 6 H, H_m), 8.09 (d, J = 7.9 Hz, 6 H, H_o), 8.30 (d, J = 8.3 Hz, 2 H, H_o'), 8.44 (d, J = 8.3 Hz, 2 H, H_m'), 8.78 (d, J = 4.8 Hz, 2 H, H-3, H-7), 8.87 (s, 4 H, H-12, H-13, H-17, H-18), 8.88 (d, 2 H, J = 4.8 Hz, 2 H, H-2, H-8).- ^{13}C-NMR ($CDCl_3$): δ = 14.11 (q, C-16 side chain), 21.52 (q, $ArCH_3$), 22.67, 26.18, 28.89, 29.35, 29.39, 29.70, 29.93, 31.90 (8 x t, -CH_2- side chain), 65.50 (t, C-1 side chain), 118.30, 120.37, 120.62 (3 x s, C_{meso}), 127.42, 127.82 (2 x d, C_m , C_m'), 129.84 (s, C_p'), 131.15 (br d, C_β), 134.48 (d, C_o), 137.38 (s, C_p), 139.13 (s, C_{ipso}), 147.05 (s, C_{ipso}'), 166.95 (s, -COO-).- FAB-MS: m/e = 925 (M^+), 657 (35 %).- UV-Vis (CH_2Cl_2): λ = 419, 516, 551, 591, 647 nm.- Anal. Calc. for $C_{64}H_{68}N_4O_2$ (925.3): C 83.08 H 7.41 N 6.06. Found: C 83.61 H 7.42 N 5.83.

5-(p-Octadecyloxycarbonylphenyl)-10,15,20-tri(p-methylphenyl)porphine **(3d):**

Method a: Yield: 117 mg (82%). Method B: 43 mg (30%).

^{1}H-NMR ($CDCl_3$): δ = -2.75 (br s, 2 H, -NH), 0.79 - 0.95 (m, 3 H, alkyl-CH_3), 1.11 - 1.68 (m, 30 H, -$(CH_2)_{15}$-), 1.81 - 2.01 (m, 2 H, $COOCH_2$-$C\underline{H}_2$-), 2.65 (s, 9 H, $ArCH_3$), 4.48 (t, J = 6.6 Hz, 2 H, $COOCH_2$-), 7.50 (d, J = 7.9 Hz, 6 H, H_m), 8.07 (d, J = 7.9 Hz, 6 H, H_o), 8.30 (d, J = 8.3 Hz, 2 H, H_o'), 8.44 (d, J = 8.3 Hz, 2 H, H_m'), 8.79 (d, J = 4.9 Hz, 2 H, H-3, H-7), 8.86 (s, 4 H, H-12, H-13, H-17, H-18), 8.88 (d, J = 4.9 Hz, 2 H, H-2, H-8).- ^{13}C-NMR ($CDCl_3$): δ = 14.12 (q, C-18 side chain), 21.50 (q, $ArCH_3$), 22.67, 26.17, 28.87, 29.35, 29.39, 29.70, 31.90 (7 x t, -CH_2- side chain), 65.48 (t, C-1 side chain), 118.20, 120.36, 120.61 (3 x t, C_{meso}), 127.41, 127.82 (2 x d, C_m , C_m'), 129.82 (s, C_p'), 131.19 (br d, C_β), 134.47 (d, C_o), 137.36 (s, C_p), 139.11 (s, C_{ipso}), 147.05 (s, C_{ipso}'), 166.93 (s, -COO-).- FAB-MS: m/e = 954 (M^++1).- UV-Vis (CH_2Cl_2): λ = 419, 515, 551, 591, 647 nm.- Anal. Calc. for $C_{66}H_{72}N_4O_2$ (953.3): C 83.15 H 7.61 N 5.88. Found: C 83.37 H 7.53 N 5.87.

5-(p-Eicosyloxycarbonylphenyl)-10,15,20-tri(p-methylphenyl)porphine **(3e):**

Method A: Yield: 105 mg (71%). Method B: 11 mg (7%).

^{1}H-NMR ($CDCl_3$): δ = -2.77 (br s, 2 H, -NH), 0.76 - 0.92 (m, 3 H, alkyl-CH_3), 1.10 - 1.65 (m, 34 H, -$(CH_2)_{17}$-), 1.78 - 2.02 (m, 2 H, $COOCH_2$-$C\underline{H}_2$-), 2.68 (s, 9 H, $ArCH_3$), 4.49 (br t, J = 6.5 Hz, 2 H, $COOCH_2$-), 7.53 (d, J = 7.9 Hz, 6 H, H_m), 8.08 (d, J = 7.9 Hz, 6 H, H_o), 8.30 (d, J = 8.2 Hz, 2 H, H_o'), 8.44 (d, J = 8.2 Hz, 2 H, H_m'), 8.78 (d, J = 4.5 Hz, 2 H, H-3, H-7), 8.86 (s, 4 H, H-12, H-13, H-17, H-18), 8.88 (d, J = 4.5 Hz, 2 H, H-2, H-8).- ^{13}C-NMR ($CDCl_3$): δ = 14.12 (q, C-20 side chain), 21.52 (q, $ArCH_3$), 22.69, 26.18, 28.88, 29.39, 29.70, 31.91 (6 x t, -CH_2- side chain), 65.49 (t, C-1 side chain), 118.29, 120.36 (2 x s, C_{meso}), 127.42, 127.83 (2 x d, C_m , C_m'), 129.83 (s, C_p'), 131.26 (br d, C_β), 134.48 (d, C_o), 137.37 (s, C_p), 139.12 (s, C_{ipso}), 147.04 (s, C_{ipso}'), 166.94 (s, -COO-).- FAB-MS: m/e = 982 (M^++1).- UV-Vis

(CH_2Cl_2): λ = 419, 516, 551, 591, 647 nm.- Anal. Calc. for $C_{68}H_{76}N_4O_2$ (981.4): C 83.22 H 7.81 N 5.71. Found: C 83.05 H 7.84 N 6.03.

5-(p-Docosyloxycarbonylphenyl)-10,15,20-tri(p-methylphenyl)porphine **(3f):**

Method A: Yield: 120 mg (79%). Method B: 11 mg (7%).

^{1}H-NMR ($CDCl_3$): δ = -2.78 (br s, 2 H, -NH), 0.77 - 0.90 (m, 3 H, alkyl-CH_3), 1.05 - 1.63 (m, 38 H, -$(CH_2)_{19}$-), 1.80 - 1.98 (m, 2 H, $COOCH_2$-CH_2-), 2.70 (s, 9 H, $ArCH_3$), 4.50 (br t, J = 6.5 Hz, 2 H, $COOCH_2$-CH_2-), 7.55 (d, J = 7.9 Hz, 6 H, H_m), 8.08 (d, J = 7.9 Hz, 6 H, H_o), 8.30 (d, J = 8.3 Hz, 2 H, $H_{o'}$), 8.44 (d, J = 8.3 Hz, 2 H, $H_{m'}$), 8.78 (d, J = 4.9 Hz, 2 H, H-3, H-7), 8.86 (s, 4 H, H-12, H-13, H-17, H-18), 8.87 (d, J = 4.9 Hz, 2 H, H-2, H-8). ^{13}C-NMR ($CDCl_3$): δ = 14.14 (q, C-22 side chain), 21.52 (q, $ArCH_3$), 22.69, 26.19, 28.87, 29.34, 29.69, 31.90 (6 x t, -CH_2- side chain), 65.50 (t, C-1 side chain), 118.29, 120.37, 120.63 (3 x s, C_{meso}), 127.41, 127.82 (2 x d, C_m , $C_{m'}$), 129.81 (s, $C_{p'}$), 131.00 (br d, C_β), 134.48 (d, C_o), 137.38 (s, C_p), 139.12 (s, C_{ipso}), 147.04 (s, $C_{ipso'}$), 166.95 (s, -COO-).- FAB-MS: m/e = 1010 (M^++1).- UV-Vis (CH_2Cl_2): λ = 419, 516, 551, 591, 647 nm.- Anal. Calc. for $C_{70}H_{80}N_4O_2$ (1009.4): C 83.29 H 7.99 N 5.55. Found: C 83.30 H 7.93 N 5.15.

5-(p-Cholesteryloxycarbonylphenyl)-10,15,20-tri(p-methylphenyl)porphine **(4)**

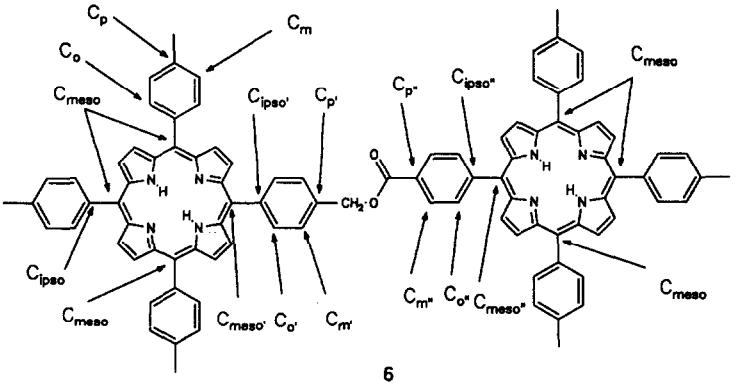
Method A: Yield: 103 mg (67%).

^{1}H-NMR ($CDCl_3$):[11] δ = -2.86 (br s, 2 H, -NH), 0.61 (s, 3 H, CH_3-18 Chol.), 0.80 (d, J = 6.7 Hz, 6H, CH_3-26, CH_3-27 Chol.), 0.85 (d, J = 6.4 Hz, 3 H, CH_3-21 Chol.), 1.02 (s, 3 H, CH_3-19 Chol.), 1.10 - 1.65 (br., m, CH_2- Chol.), 1.70 - 2.20 (br m, CH- Chol.), 2.57 (d, J = 7,3 Hz, 2 H, CH_2- Chol.), 2.61 (s, 9 H, Ph-CH_3), 4.95 - 5.15 (br., m, 1 H, -CH-O- Chol.), 5.42 (m, 1 H, -CH= Chol.), 7.54 (d, J = 7.8 Hz, 6 H, H_m), 8.09 (d, J = 7.8 Hz, 6 H, H_o), 8.29 (d, J = 7.9 Hz, 2 H, $H_{o'}$), 8.44 (d, J = 7.9, 2 H, $H_{m'}$), 8.78 (d, J = 4.8 Hz, H-3, H-7), 8.86 (s, 4 H, H-12, H-13, H-17, H-18), 8.88 (d, J = 4.8 Hz, 2 H, H-2, H-8).- ^{13}C-NMR ($CDCl_3$):[11] δ = 11.87 (q, C-18 Chol.), 18.73 (q, C-21 Chol.), 19.43 (q, C-19 Chol.), 21.07 (t, C-11 Chol.), 21.53 (q, $ArCH_3$), 22.58 (q, C-26 Chol.), 22.85 (q, C-27 Chol.), 23.84 (t, C-23 Chol.), 24.30 (t, C-15 Chol.), 28.03 (d, C-25 Chol.), 28.25 (t, C-16 Chol.), 29.84 (t, C-2 Chol.), 31.89 (d, C-8 Chol.), 31.96 (t, C-7 Chol.), 35.81 (s, C-20 Chol.), 36.12 (t, C-22 Chol.), 36.71 (s, C-10 Chol.), 37.11 (t, C-1 Chol.), 38.36 (t, C-4 Chol.), 39.52 (t, C-24 Chol.), 39.73 (t, C-12 Chol.), 42.32 (s, C-13 Chol.), 50.05 (s, C-9 Chol.), 56.11 (s, C-17 Chol.), 56.68 (s, C-14 Chol.), 74.93 (d, C-3 Chol.), 118.34, 120.35, 120.60 (3 x s, C_{meso}), 122.90 (d, C-6 Chol.), 127.43 (d, C_m), 127.83 (d, $C_{m'}$), 129.83 (s, $C_{p'}$), 131.49 (br d, C_β), 134.50 (d, C_o , $C_{o'}$), 137.40 (s, C_p), 139.20 (s, C_{ipso}), 139.64 (s, C-5 Chol.), 147.04 (s, $C_{ipso'}$), 166.96 (s, -COO-).- FAB-MS: m/e = 1070 (M^+).- UV-Vis (CH_2Cl_2): λ = 418, 516, 551, 596, 646 nm.- Anal. Calc. for $C_{75}H_{80}N_4O_2$ (1069.5): C 84.23 H 7.54 N 5.24. Found: C 84.21 H 7.65 N 5.27.

***Synthesis of the Diporphyrin* (6):**

According to method A, 40 mg (0.056 mmol) **1a** and 190 mg (0.28 mmol) **5** were treated with 6.16 mg MeLi (0.28 mmol, 0.175 ml of a 1.6 M MeLi solution in diethyl ether). Reaction time 5 h. Yield: 17 mg (22%).

^{1}H-NMR ($CDCl_3$): δ = -2.76 (br s, 4 H, -NH), 2.69 (s, 18 H, $ArCH_3$), 5.91 (br., s, 2 H, $COO-CH_2$-), 7.54 (d, J = 7.8 Hz, 12 H, H_m), 7.96 (d, J = 7.9 Hz, 2 H, H_o') 8.10 (d, J = 7.7 Hz, 12 H, H_o), 8.31 (d, J = 7.9 Hz, 2 H, H_m'), 8.39 (d, J = 8.3 Hz, 2 H, H_o''), 8.64 (d, J = 8.3 Hz, 2 H, H_m''), 8.81 - 8.93 (m, 16 H, H_β).- ^{13}C-NMR ($CDCl_3$): 21.55 (q, $ArCH_3$), 67.11 (t, $-CH_2$-O-), 118.26, 120.34, 120.47, 120.53, 120.83 (5 x s, C_{meso}), 126.69 (d, C_m''), 127.57 (d, C_m , C_m'), 128.29 (s, C_p'), 131.08 (br d, C_β), 134.57, 134.79, 134.92 (3 x d, C_o , C_o' , C_o''), 135.65 (s, C_p''), 137.57 (s, C_p), 139.09 (s, C_{ipso}), 142.30 (s, C_{ipso}' ,), 147.45 (s, C_{ipso}'), 167.07 (s, -COO-) no differentiation was possible between the different meso carbons substituted with a tolyl group. Also no differentiation was possible between the different ortho, meta, and para carbons in the different tolyl substituents.- FAB-MS: m/e = 1370 (M^+).- UV-Vis (CH_2Cl_2): λ = 419, 515, 551, 590, 646 nm.- Anal. Calc. for $C_{96}H_{72}N_8O_2$ (1369.7): C 84.18 H 5.30 N 8.18. Found: C 83.28 H 5.80 N 8.39.



6

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