Pergamon

Tetrahedron, Vol. 52, No. 15, pp. 5441-5448, 1996

0040-4020/96 $15.00 + 0.00

S0040-4020(96)00174-3

Synthesis of Galactopyranosyl Substituted Porphyrins

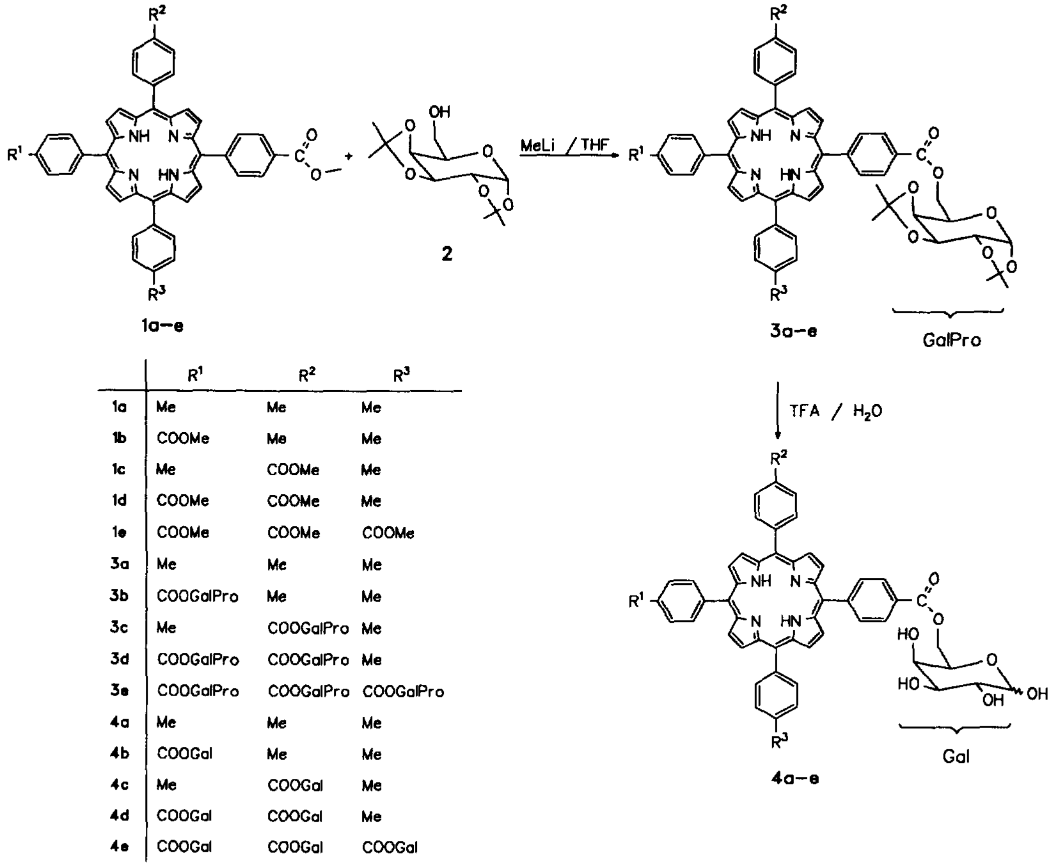
Hermann K. Hombrecher,* Stefan Ohm and Daniela Koll

Institut für Chemie der Medizinischen Universität zu Lübeck, Ratzeburger Allee 160, D-23538 Lübeck, Germany

Abstract: The synthesis of several galactopyranosyl substituted porphyrins is described. Starting from porphyrin carboxylic esters (**1**) di-O-isopropylidene-α-D-galactopyranosyl substituted porphyrins **3a** - **3e** were synthesised by a transesterification procedure. Treatment of **3a** - **3e** with TFA/ water leads to the formation of galactopyranosyl substituted porphyrins **4a** - **4e** in excellent yield. Furthermore porphyrin **3e** can be synthesised by reaction of di-O-isopropylidene-α-D-galactopyranosyl substituted benzaldehyde **7** with pyrrole. Aldehyde **7** was synthesised by a CsF catalysed condensation reaction of 6-desoxy-6-bromo-di-O-isopropylidene-α-D-galactopyranose **6** with 4-formyl benzoic acid.

One of the most interesting applications of porphyrins is photodynamic therapy (PDT) of tumours.[1] This treatment based on the interaction of the porphyrinic sensitizer with visible light, thus producing singlet oxygen directly in the cancer cell that causes cell death.[2] Today only a purified form of hematoporphyrin derivative (HpD), Photofrin II is used as photosensitizer in clinical studies and therapy. The main disadvantage of Photofrin II is its unknown composition of different porphyrins.[3] Therefore the synthesis of well-defined porphyrins is of great interest for the development of new photosensitizers for use in PDT.[4] One of the requirements a new photosensitizer has to fulfill is solubility in water. Therefore the synthesis of carbohydrate-substituted porphyrins is very interesting regarding PDT. Furthermore, a specific affinity of several carbohydrate substituted porphyrins to cancer cells was reported.[5] Therefore, a number of carbohydrate-substituted porphyrins were synthesised.[6] We now report here a new synthetic procedure for the synthesis of porphyrins bearing 1-4 carbohydrate substituents.

We recently reported the synthesis of porphyrins bearing long alkyl chains and cholesterol subunits by a transesterification procedure.[7] Herein we describe a modified procedure of this methodology for the synthesis of carbohydrate substituted porphyrins. In this modified procedure porphyrinic carboxylic esters **1** were treated with 1,2,3,4-di-O-isopropylidene-α-D-galactopyranose (**2**) and methyl lithium in THF (Scheme 1). The reaction proceeds in good yield (28 - 50%) at 80 - 90 °C for the synthesis of compounds **3a** - **3c**. Synthesis of **3d** and **3e**, respectively, was performed in lower yield (7%) due to the increased formation of



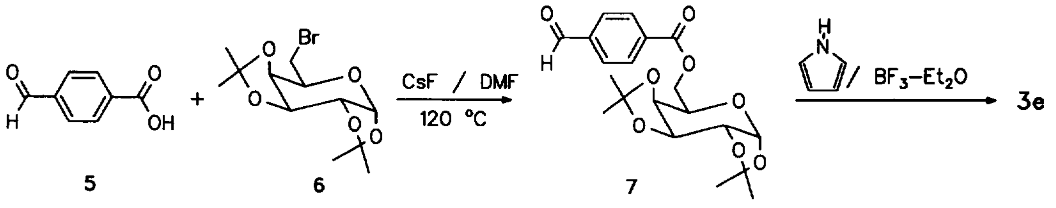
	R^1	R^2	R^3
1a	Me	Me	Me
1b	COOMe	Me	Me
1c	Me	COOMe	Me
1d	COOMe	COOMe	Me
1e	COOMe	COOMe	COOMe
3a	Me	Me	Me
3b	COOGalPro	Me	Me
3c	Me	COOGalPro	Me
3d	COOGalPro	COOGalPro	Me
3e	COOGalPro	COOGalPro	COOGalPro
4a	Me	Me	Me
4b	COOGal	Me	Me
4c	Me	COOGal	Me
4d	COOGal	COOGal	Me
4e	COOGal	COOGal	COOGal

Scheme 1

porphyrin carboxylic acids. Formation of these side-products can be explained by direct saponification of the starting compounds **1a** - **1e** or by thermal decomposition of products **3a** - **3e**. Due to the extreme water free reaction conditions a direct saponification of starting compounds is unlikely. However, investigation of the thermostability of compounds **3a** - **3e** showed, that these compounds are unstable and decompose to the observed side-products. We therefore carried out the reaction at lower temperature (40 °C). No formation of carboxylic acids was obtained under these reaction conditions; but unfortunately compounds **3a** - **3e** were obtained in lower yield at this temperature.

Alternatively, compound **3e** can be easily synthesised in nearly 20% yield by reacting aldehyde **7** with pyrrole. The di-O-isopropylidene-α-D-galactopyranosyl substituted aldehyde **7** was synthesised from **6** and 4-formyl benzoic acid (Scheme 2) in a CsF catalysed condensation reaction.[8] We also treated aldehyde **7** in a mixed condensation reaction with p-tolyl aldehyde and pyrrole using Lindsey's procedure.[9]

Although all porphyrins **3a** - **3e** were formed in this reaction the yields were very low (**3a** was formed in only 8% yield) compared with the yields obtained by the transesterification procedure.



Scheme 2

Deprotection of compounds **3a** - **3e** was performed in excellent yield (92 - 98%) with TFA/ H_2O (9:1) at room temperature. After neutralisation of the reaction mixture with Na_2CO_3 solution the porphyrins precipitated and were isolated by filtration. Purification of the deprotected porphyrins **4a** - **4d** was performed by column chromatography on silica gel using CH_2Cl_2/ MeOH (9:1) as eluent. TLC and NMR-spectroscopic studies showed, that all porphyrins **4a** - **4e** were formed as mixtures of α- and β-isomers.[10]

Identification of the synthesised carbohydrate substituted porphyrin derivatives was performed by ^1H NMR and ^{13}C NMR spectroscopy and FAB spectroscopy. The obtained analytical data are also in accordance with the proposed structures.

The synthesised porphyrins exhibit very different solubility properties. Compound **4a** is soluble in CH_2Cl_2 or $CHCl_3$, whereas compounds **4b** and **4c**, respectively, show better solubility in a mixture of $CHCl_3$ and methanol. In contrast to this **4c** is only soluble in methanol. Compound **4e** is only soluble in DMSO or in water or methanol without aggregation up to concentrations of approximately 10^{-4} M, as indicated by absorption spectroscopy.

EXPERIMENTAL SECTION

NMR spectra were obtained in $CDCl_3$ or DMSO-d_6 and recorded with a Varian XL 200 spectrometer or a Bruker DMX-500 spectrometer. Chemical shift values were given in ppm relative to TMS. Mass spectra were measured with a VG-Analytical VG70:250 E instrument. Electronic spectra were recorded on a Kontron Uvikon 860 instrument. IR spectra were recorded on a Shimadzu IR-435 spectrometer. 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.

Synthesis of 6′-deoxy-1′,2′: 3′,4′-di-O-isopropylidene-α-D-galactopyranosyl-4-formyl-benzoate (7)

To a solution of 1.30 g (4.02 mmol) **6** in 4 ml DMF 2.00 g (13.2 mmol) CsF and 336 mg (2.24 mmol) 4-formyl benzoic acid were added. The reaction mixture was stirred for 2 days at 120 °C. Then 40 ml CH_2Cl_2 were added. The mixture was poured into saturated $NaHCO_3$ solution (50 ml). The organic layer was separated and washed with water and dried (Na_2SO_4). The solvent was evaporated and the residue chromatographed on a silica gel column using CH_2Cl_2/ methanol (98:2) as eluent. Yield: 616 mg (70%) **7** (colourless oil).- ^{1}H NMR ($CDCl_3$): δ = 1.35, 1.37, 1.70, 1.73 (4 s, 12 H, $C(CH_3)_2$), 4.10 - 4.81 (m, 6 H, 2′-, 3′-, 4′-,5′-,6′-H), 5.60 (d, *J* = 5.4 Hz, 1 H, 1′-H), 7.95 (d, *J* = 8.3 Hz, 2 H, H_o), 8.24 (d, *J* = 8.3 Hz, 2 H, H_m), 10.12 (s, 1 H, CHO).- MS (70 eV): m/e = 394 (M^+ + 2).- Anal. Calc. for $C_{20}H_{24}O_8$ (392.40): C 61.22 H 6.16. Found: C 60.76 H 6.61.

5-(p-1′,2′:3′,4′-Di-O-isopropylidene-α-D-galactopyranoloxycarbonylphenyl)-10,15,20-tris(p-tolyl)-porphyrin (3a)

In a dry round bottom flask 1.27 g (4.88 mmol) 1,2-3,4-di-O-isopropylidene-α-D-galactopyranose (**2**) were added under nitrogen to 10 ml of dry THF. The mixture was cooled down to 1-2 °C. Then 3.00 ml (4.80 mmol) of a 1.6 M solution of methyllithium in ether were added. The reaction mixture was warmed up to room temperature and 241 mg (0.34 mmol) of porphyrin **1a** were added. The reaction mixture was stirred for 8 h at 80 - 90 °C. Then 70 ml CH_2Cl_2 were added and the reaction mixture was poured into water (40 ml). The organic layer was isolated and dried (Na_2SO_4). The solvent was evaporated and the residue chromatographed on a silica gel column using CH_2Cl_2/ methanol (98:2) as eluent. Yield: 114 mg (38%) **3a**. ^{1}H NMR ($CDCl_3$): δ = -2.78 (br s, 2 H, NH), 1.38, 1.42, 1.55, 1.63 (4 s, 12 H, $C(CH_3)_2$), 2.70 (s, 9 H, CH_3), 4.36 - 4.49, 4.64 - 4.76 (2 m, 6 H, 2′-, 3′-, 4′-, 5′-, 6′-H), 5.66 (d, *J* = 5.0 Hz, 1 H, 1′-H), 7.55 (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, $H_{o'}$), 8.78 (d, 8.3 Hz, 2 H, $H_{m'}$), 8.79 (d, *J* = 4.9 Hz, 2 H, 3-, 7-H), 8.87 (s, 4 H, 12-, 13-, 17-, 18-H), 8.88 (d, 2 H, 8-H).- ^{13}C NMR ($CDCl_3$): δ = 21.55 (q, CH_3), 24.61, 25.05, 26.10, 26.16 (4 q, $C(\mathit{C}H_3)_2$), 64.24 (t, C-6′), 66.26 (d, C-5′), 70.58. 70.81 (2 d, C-3′, C-4′), 71.25 (d, C-2′), 96.46 (d, C-1′), 108.92, 109.80 (2 s, $\mathit{C}(CH_3)_2$), 118.29, 120.41, 120.69 (3 s, C_{meso}), 127.44, 128.04 (2 d, C_m, $C_{m'}$), 129.40 (s, $C_{p'}$), 131.26 (br d, C_β), 134.51, 134.61 (2 d, C_o, $C_{o'}$), 137.41 (s, C_p), 139.15 (s, C_i), 147.29 (s, $C_{i'}$), 166.73 (s, CO).- IR (KBr): ν = 1717 cm^{-1} (CO).- UV-Vis. (CH_2Cl_2): λ = 419, 515, 551, 591, 646 nm.- FAB-MS: m/e = 944 (M^+ + 1), 701, 656.- Anal. Calc. for $C_{60}H_{54}N_4O_7$ (943.1): C 76.41, H 5.77, N 5.94. Found: C 76.43, H 5.78, N 5.59.

5-15-Bis(p-1′,2′:3′,4′-di-O-isopropylidene-α-D-galactopyranoloxycarbonylphenyl)-10,20-bis(p-tolyl)-porphyrin (3b)

According to the procedure given above, 44 mg (0.058 mmol) porphyrin **1b**, 625 mg (2.40 mmol) **2** and 1.00 ml (1.60 mmol) methyllithium were treated. Reaction time 2.5 h. Yield: 35 mg (50%) **3b**.- ^{1}H NMR ($CDCl_3$): δ = -2.79 (br s, 2 H, NH), 1.38, 1.42, 1.56, 1.63 (4 s, 24 H, $C(CH_3)_2$), 2.70 (s, 6 H, CH_3), 4.36 - 4.49, 4.64 - 4.76 (2 m, 12 H, 2′-, 3′-, 4′-, 5′-, 6′-H), 5.66 (d, *J* = 4.9 Hz, 2 H, 1′-H), 7.56 (d, *J* = 7.8 Hz, 4 H, H_m), 8.09 (d, *J* = 7. 8 Hz, 4 H, H_o), 8.30 (d, *J* = 8.3 Hz, 4 H, $H_{o'}$), 8.45 (d, *J* = 8.3 Hz, 4 H, $H_{m'}$), 8.79 (d, *J* = 4.8 Hz, 4 H, 3-, 7-, 13-, 17-H), 8.90 (d, *J* = 4.9 Hz, 4 H, 2-, 8-, 12-, 18-H).- ^{13}C NMR ($CDCl_3$): δ = 21.55 (q, CH_3), 24.58, 25.02, 26.06, 26.26 (4 q, $C(\mathit{C}H_3)_2$), 64.24 (t, C-6′), 66.23 (d, C-5′), 70.55, 70.80 (2 d, C-3′, C-4′), 71.25 (d, C-2′), 96.43 (d, C-1′), 108.92, 109.80 (2 s, $\mathit{C}(CH_3)_2$), 118.80, 120.69 (2 s, C_{meso}), 127.51, 128.01 (2 d, C_m, $C_{m'}$), 129.43 ($C_{p'}$), 131.20 (br d, C_β), 134.48, 134.52, (2 d, C_o, $C_{o'}$), 137.54 (s, C_p), 138.93 (s, C_i), 147.10 (s, $C_{i'}$), 166.66 (s, CO).- IR (KBr): ν = 1717 cm^{-1} (CO).- UV-Vis (CH_2Cl_2): λ = 419, 515, 551, 591, 646 nm.- FAB-MS: m/e = 1215 (M^+).- Anal. Calc. for C_{72} $H_{70}N_4O_{14}$ (1215.4): C 71.15 H 5.81 N 4.61. Found: C 71.12 H 5.87 N 4.54.

5,10-Bis(p-1´,2´:3´,4´-di-O-isopropylidene-α-D-galactopyranoloxycarbonylphenyl)-15,20-bis(p-tolyl)-porphyrin (3c)

According to the procedure given above 44 mg (0.058 mmol) porphyrin **1c**, 250 mg (0.96 mmol) **2** and 0.57 ml (0.91 mmol) methyllithium were treated. Reaction time 2.5 h. Purification of compound **3c** was performed by column chromatography on silica gel using CH_2Cl_2/ methanol (97:3) as eluent.Yield: 20 mg (28%) **3c**.- ^{1}H NMR ($CDCl_3$): δ = -2.78 (br s, 2 H, NH), 1.38, 1.42, 1.56, 1.63 (4 s, 24 H, $C(CH_3)_2$), 2.71 (s, 6 H, CH_3), 4.36 - 4.50, 4.64 - 4.76 (2 m, 12 H, 2´-, 3´-, 4´-, 5´, 6´-H), 5.66 (d, 4.9 Hz, 2 H, 1´-H), 7.56 (d, *J* = 7.8 Hz, 4 H, H_m), 8.10 (d, *J* = 7.8 Hz, 4 H, H_o), 8.30 (d, *J* = 7.8 Hz, 4 H, $H_{o'}$), 8.45 (d, *J* = 8.3 Hz, 4 H, $H_{m'}$), 8.78 (d, *J* = 4.9 Hz, 2 H, 3-H, 12-H), 8.80 (s, 2 H, 7-H, 8-H), 8.88 (s, 2 H, 17-H, 18-H), 8.89 (d, *J* = 6.3 Hz, 2 H, 2-H, 13-H).- ^{13}C NMR ($CDCl_3$): δ = 21.55 (q, CH_3), 24.61, 25.05, 26.06, 26.15 (4 q, $\mathrm{C}(\mathit{CH}_3)_2$), 64.24 (t, C-6´), 66.25 (d, C-5´), 70.58, 70.83 (2 d, C-3´, C-4´), 71.28 (d, C-2´), 96.45 (d, C-1´), 108.92, 109.83 (2 s, $\mathit{C}(\mathrm{CH}_3)_2$), 118.04, 118.57, 120.97 (3 s, C_{meso}), 127.50, 128.07 (2 d, C_m, $C_{m'}$), 129.46 (s, $C_{p'}$), 131.13 (br d, C_β), 134.51, 134.57 (2 d, C_o, $C_{o'}$), 137.54 (s, C_p), 139.02 (s, C_i), 147.00 (s, $C_{i'}$), 166.69 (s, CO).- IR (KBr): ν = 1717 cm^{-1} (CO).- UV-Vis (CH_2Cl_2): λ = 419, 515, 551, 591, 646 nm.- FAB-MS: m/e = 1214 (M$^+$).- Anal. Calc. for $C_{72}H_{70}N_4O_{14}$ (1215.4): C 71.15 H 5.81 N 4.61. Found: C 71.13 H 5.74 N 4.70.

5,10,15-Tris(p-1´,2´:3´,4´-di-O-isopropylidene-α-D-galactopyranoloxycarbonylphenyl)-20-(p-tolyl)-porphyrin (3d)

According to the procedure given above 240 mg (0.30 mmol) porphyrin **1d**, 1.60g (6.14 mmol) **2** and 3.8 ml (6.08 mmol) methyllithium solution were treated. Reaction time 5 h. Purification of compound **3d** was performed by column chromatography on silica gel using CH_2Cl_2/ methanol (97:3) as eluent. Yield. 31 mg (7%) **3d**.- ^{1}H NMR ($CDCl_3$): δ = -2.79 (br s, 2 H, NH), 1.38, 1.42, 1.56, 1.63 (4 s, 36 H, $C(CH_3)_2$), 2.71 (s, 3 H, CH_3), 4.36 - 4.50, 4.62 - 4.76 (2 m, 18 H, 2´-, 3´-, 4´-, 5´-, 6´-H), 5.67 (d, *J* = 4.8 Hz, 3 H, 1´-H), 7.57 (d, *J* = 7.8 Hz, 2 H, H_m), 8.10 (d, *J* = 7.8 Hz, 2 H, H_o), 8.31 (d, *J* = 8.3 Hz, 6 H, Ho´), 8.47 (d, *J* = 8.3 Hz, 6 H, Hm´), 8.81 (d, *J* = 4.8 Hz, 2 H, 3-H, 17-H), 8.84 (s, 4 H, 7-H, 8-H, 12-H, 13-H), 8.92 (s, 2 H, 17-H, 18-H), 8.89 (d, *J* = 4.9 Hz, 2 H, 2-H, 18-H).- ^{13}C NMR ($CDCl_3$): δ = 21.45 (q, CH_3), 24.58, 25.02, 26.06, 26.13 (4 q, $\mathrm{C}(\mathit{CH}_3)_2$), 64.27 (t, C-6´), 66.23 (d, C-5´), 70.55, 70.80 (d, C-3´, C-4´), 71.25 (d, C-2´), 96.43 (d, C-1´), 108.92, 109.80 (2 s, $\mathit{C}(\mathrm{CH}_3)_2$), 118.86, 119.11, 121.15 (3 s, C_{meso}), 127.54, 128.10 (2 d, C_m, $C_{m'}$), 129.52, 131.23 (br d, C_β), 134.54, 134.86 (2 d, C_o, $C_{o'}$), 137.63 (s, C_p), 139.12 (s, C_i), 146.91 (s, $C_{i'}$), 166.63 (s, CO).- IR (KBr): ν = 1717 cm^{-1}.- UV-Vis (CH_2Cl_2): λ = 419, 515, 550, 590, 647 nm.- FAB-MS: m/e = 1488 (M$^+$).- Anal. Calc. for $C_{84}H_{86}N_4O_{21}$ (1487.6): C 67.82 H 5.83 N 3.98. Found: C 67.50 H 6.27 N 3.75.

5,10,15,20-Tetrakis(p-1´,2´:3´,4´-di-O-isopropylidene-D-galactopyranoloxycarbonylphenyl)-porphyrin (3e)

Method A:

According to the procedure given for **3a** 150 mg (0.18 mmol) porphyrin **1e**, 1.38 g (5.30 mmol) **2** and 3.3 ml (5.28 mmol) methyllithium solution were treated. Reaction time 4.5 h. Purification of **3e** was performed on a silica gel column using CH_2Cl_2/ methanol (97:3) as eluent. Yield: 17 mg (5%) **3e**.- ^{1}H NMR ($CDCl_3$): δ = -2.78 (br s, 2 H, NH), 1.39, 1.43, 1.56, 1.64 (4 s, 48 H, $C(CH_3)_2$), 4.37 - 4.50, 4.65 - 4.77 (2 m, 24 H, 2´-, 3´-, 4´-, 5´-, 6´-H), 5.67 (d, *J* = 5.4 Hz, 4 H, 1´-H), 8.31 (d, *J* = 6.9 Hz, 8 H, H_o), 8.48 (d, *J* = 8.4 Hz, 8 H, H_m), 8.85 (s, 8 H, H_β).- ^{13}C NMR ($CDCl_3$): δ = 24.58, 25.02, 26.06, 26.13 (4 q, $\mathrm{C}(\mathit{CH}_3)_2$), 64.27, (t, C-6´), 66.23 (d, C-5´), 70.55, 70.80 (2 d, C-3´, C-4´), 71.25 (d, C-2´), 96.43 (d, C-1´), 108.92, 109.80 (2 s, $\mathit{C}(\mathrm{CH}_3)_2$), 119.40 (s, C_{meso}), 128.14 (d, C_m), 129.62 (s, C_p), 131.25 (C_β), 134.54 (d, C_o), 146.71 (s, C_i), 166.60 (s, CO).- IR (KBr): ν = 1718 cm^{-1}.- UV-Vis (CH_2Cl_2): λ = 419, 514, 549, 644,- FAB-MS: m/e = 1759 (M$^+$).- Anal. Calc. for $C_{96}H_{102}N_4O_{28}$ (1759.9): C 65.53 H 5.81 N 3.28. Found: C 65.56 H 5.85 N 3.19.

Method B:

To 500 ml dry CH_2Cl_2 1.77 g **7** (4.49 mmol) and 335 mg (0.50 mmol) pyrrole were added. Then 1 ml ethanol and 63 μl $BF_3{\cdot}EtO_2$ (50% solution) were added. The reaction mixture was stirred for 1 h at room temperature. Then 1.23 g (5 mmol) p-chloranile were added and the reaction mixture neutralised with NEt_3. The mixture was refluxed for 1 h. The solvent was evaporated and the residue chromatographed on a silica gel column using CH_2Cl_2/ methanol (99.5:0.5). The obtained crude porphyrinic fraction was purified by a MPLC on silica gel using CH_2Cl_2/ methanol (99.8:0.2) as eluent. Yield: 43.6 mg (19.8%) **3e**.

Synthesis of 5-(p-α/β-D-galactopyran-6´-oloxycarbonylphenyl)-10,15,20-tris(p-tolyl)- porphyrin (4a)

Porphyrin **3a** (28 mg, 0.032 mmol) was added to a mixture of CF_3COOH and water (9:1). The reaction mixture was stirred for 20 min at room temperature. Dichloromethane (20 ml) was added and the mixture cooled to 0°C. Then the mixture was poured into water (50 ml) and neutralised with Na_2CO_3-solution. The organic layer was separated and washed with water (30 ml) and dried (Na_2SO_4). The solvent was evaporated and the residue chromatographed on a silica gel column using CH_2Cl_2/ methanol (9:1) as eluent. Yield 26 mg (94%) **4a**.- ^1H NMR (DMSO-d_6): δ = -2.92 (br s, 2 H, NH), 2.65 (s, 9 H, CH_3), 3.60 - 4.15 (m, 4 H), 4.29 - 5.00 (m, 4 H), 5.05 - 5.14 (m, 1 H, 1´-H_α), 5.25 - 5.41 (m, 1 H), 6.37 (d, *J* = 4.9 Hz, 1 H, OH), 6.71 (d, *J* = 7.3 Hz, 1 H, OH), 7.59 (d, *J* = 7.8 Hz, 6 H, H_m), 8.07 (d, *J* = 7.8 Hz, 6 H, H_o), 8.31 - 8.48 (m, 4 H, $H_{o'}$, $H_{m'}$), 8.74 - 8.93 (m, 8 H, H_β).- ^{13}C NMR (DMSO-d_6): δ = 20.95 (q, CH_3), 64.75 (t, C-6´), 67.52 (d), 67.60 (d), 68.50 (d), 68.61 (d), 71.75 (d), 78.00 (d), 78.74 (d), 79.35 (d), 92.50 (d, αC-1´), 97.47 (d, βC-1´), 118.13 (s, C-5), 120.06 (s, C-10, C-20), 120.31 (s, C-15), 127.51, 127.69 (2 d, C_m, $C_{m'}$), 129.27 (s, $C_{p'}$), 131.32 (br d, C_β), 134.01, 134.42 (2d, C_o, $C_{o'}$), 137.22 (s, C_p), 138.14 (s, C_i), 146.09 (s, $C_{i'}$), 165.72 (s, CO).- IR (KBr): ν = 3395 (OH), 1700 (CO) cm^{-1}.- UV-Vis (CH_2Cl_2): λ = 418, 516, 550, 592, 647 nm.- FAB-MS: m/e = 863 (M^+ + 1).- Anal. Calc. for $C_{54}H_{46}N_4O_7$ (863.0): C 75.16 H 5.37 N 6.49. Found: C 75.47 H 5.51 N 6.63.

5,15-Bis(p-α/β-galactopyran-6´-oloxycarbonylphenyl)-10,20-bis(p-tolyl)porphyrin (4b)

According to the procedure given for **4a**, 35 mg (29 mmol) porphyrin **3b** were reacted. The reaction mixture was poured into water (50 ml) and neutralised with 20% Na_2CO_3 solution. The precipitated porphyrin **4b** was isolated by fitration (0.45 μm microfilter) washed with water and ethanol and dried. Yield: 28 mg (92%) **4b**.- ^1H NMR (DMSO-d_6): δ = -2.95 (br s, 2 H, NH), 2.65 (s, 6 H, CH_3), 3.60 - 4.10 (m, 8 H), 4.28 - 4.60 (m, 8 H), 4.80 - 4.88 (m, 2 H), 4.95 - 5.10 (m, 1 H, 1´-H_α), 5.20 - 5.35 (m, 1 H), 6.35 (m, 1H, OH), 6.68 (m, 1 H, OH), 7.60 (d, *J* = 6.7 Hz, 4 H, H_m), 8.07 (d, *J* = 6.7 Hz, 4 H, H_o), 8.33 - 8.45 (m, 8 H, $H_{o'}H_{m'}$), 8.80 (br s, 4 H, H_β), 8.88 (br s, 4 H, H_β).- ^{13}C NMR (DMSO): δ = 21.32 (q, CH_3), 65.02 (t, C-6´), 65.21 (t, C-6´), 67.88 (d), 68.14 (d), 68.98 (d), 69.01 (d), 69.50 (d), 69.61 (d), 69.99 (d), 72.27 (d), 72.31 (d), 73.46 (d), 81.77 (d), 83.04 (d), 93.11 (d, αC-1´), 97.88 (d, βC-1´), 102.19 (d), 119.05 (s, C-5, C-15), 120.71 (s, C-10, C-20), 127.95 (d, C_m), 128.00 (d, $C_{m'}$), 129.68 (s, $C_{p'}$), 133.00 (br d, C_β), 134.45 (d, C_o), 134.81 (d, $C_{o'}$), 137.74 (s, C_p), 138.44 (s, C_i), 146.46 (s, $C_{i'}$), 166.16 (s, CO).- IR (KBr): ν = 3400 (OH), 1705 (CO) cm^{-1}.- UV-Vis (CH_2Cl_2/ methanol): λ = 420, 515, 553, 592, 649 nm.- Anal. Calc. for $C_{60}H_{54}N_4O_{14}$ (1055.1): C 68.30 H 5.16 N 5.31. Found: C 68.13 H 5.21 N 5.19.

5-10-Bis(p-α/β-D-galactopyran-6´-oloxycarbonylphenyl)-15,20-bis(p-tolyl)porphyrin (4c)

According to the procedure given for the synthesis of **4a**, 48 mg (0.039 mmol) **3c** were reacted. The reaction mixture was poured into water (60 ml) and neutralised with 20% Na_2CO_3 solution. The precipitated porphyrin **4c** was isolated by filtration (0.45 μm microfilter) washed with water and ethanol and dried. Yield 39 mg (95%) **4c**.- ^1H NMR (DMSO-d_6): δ = -2.92 (br s, 2 H, NH), 2.65 (s, 6 H, CH_3), 3.56 - 4.17 (m, 8 H), 4.25 - 4.67 (m, 6 H), 4.80 - 4.86 (m, 4 H), 4.95 - 5.11 (m, 2 H, 1´-H, H_α), 5.20 - 5.35 (m, 1 H), 6.37 (d, *J* = 3.9 Hz, 2 H, OH), 6.71 (d, *J* = 6.9 Hz, 1 H, OH), 7.59 (br d, 4 H, H_m), 8.06 (br d, 4 H, H_o), 8.38 (br, 8 H, $H_{o',m'}$), 8.84 (br, 8 H, H_β).- ^{13}C NMR (DMSO-d_6): δ = 20.95 (q, CH_3), 64.25 (t, CH_2), 66.00 (t, C-6´), 66.25 (t, C-6´), 67.40 (d), 67.62 (d), 68.45 (d), 68.90 (d), 69.05 (d), 71.65 (d), 72.74 (d), 75.77 (d), 81.25 (d), 82.63 (d), 92.65 (d, αC-1´), 97.47 (d, βC-1´), 118.39 (s, C-5, C-10), 120.56 (s, C-15, C-20), 127.54, 127.73 (2 d, C_m, $C_{m'}$), 129.18 (s, $C_{p'}$), 131.48 (br d, C_β), 134.04, 134.42 (2 d, C_o, $C_{o'}$), 137.32 (s, C_p), 138.04 (s, C_i), 146.00 (s, $C_{i'}$), 165.65, 165.72 (2 s, CO).- IR (KBr): ν = 3395 (OH), 1705 cm^{-1}.- UV-Vis (CH_2Cl_2): λ = 418, 515, 550, 593, 645 nm.- FAB-MS: m/e = 1056 (M^+ + 1).- Anal. Calc. for $C_{60}H_{54}N_4O_{14}$ (1055.1): C 68.30 H 5.16 N 5.31. Found: C 68.63 H 5.22 N 5.12.

5,10,15-Tris(p-α/β-D-galactopyran-6´-oloxycarbonylphenyl)-20-(p-tolyl)porphyrin (4d)

According to the procedure given for the synthesis of **4a**, 23mg (0.016 mmol) **3d** were reacted. The reaction mixture was poured into water (40 ml) and neutralised with 20% Na_2CO_3 solution. The precipitated porphyrin **4d** was isolated by filtration (0.45 µm microfilter) washed with water and ethanol and dried. Yield: 19 mg (95%) **4d**.- ^{1}H NMR (DMSO-d_6): δ = -2.96 (br s, 2 H, NH), 2.64 (s, 3 H, CH_3), 3.56 - 4.14 (m, 12 H), 4.22 - 4.67 (m, 10 H), 4.80 - 4.86 (m, 4 H), 4.95 - 5.11 (m, 2 H, 1´-H_α), 5.20 - 5.37 (m, 2 H), 6.35 (d, *J* = 5.3 Hz, 3 H, 1´-Hα), 6.70 (d, *J* = 6.8 Hz, 3 H, 1´-H_β), 7.61 (d, *J* = 7.8 Hz, 2 H, H_m), 8.07 (d, *J* = 7.8 Hz, 2 H, H_o), 8.37 (m, 12 H, $H_{o'}$, $H_{m'}$), 8.85 (br, 8 H, Hβ).- ^{13}C NMR (DMSO-d_6): δ = 20.95 (q, CH_3), 64.65 (t, C-6´), 68.44 (d), 68.50 (d), 68.60 (d), 68.94 (d), 71.78 (d), 71.87 (d), 73.02 (d), 76.03 (d), 80.65 (d), 80.98 (d), 92.70 (d, αC-1´), 97.47 (d, βC-1´), 118.89, 120.05, 122.50 (3 s, C_{meso}), 127.60, 127.76 (2d, C_m, $C_{m'}$), 129.21 (s, $C_{p'}$), 131.50 (br d, C_β), 134.07, 134.45 (2 d, C_o, $C_{o'}$), 137.25 (C_p), 139.95 (s, C_i), 145.90 (s, $C_{i'}$), 165.68, 165.72 (2 s, CO).- IR (KBr): ν = 3390 (OH), 1700 (CO) cm^{-1}.- UV-Vis (CH_2Cl_2/methanol): λ = 418, 517, 550, 595, 648 nm.- FAB-MS: m/e = 1247 (M^+ + 1).- Anal. Calc. for $C_{66}H_{62}N_4O_{21}$ (1247.2): C63.56 H 5.01 N 4.49. Found: C 63.15 H 5.12 N 4.23.

5,10,15,20-Tetrakis(p-α/β-D-galactopyran-6´-oloxycarbonylphenyl)porphyrin (4e)

According to the procedure given above 35 mg (0.018 mmol) **3e** were reacted. The reaction mixture was poured into water (40 ml) and neutralised with 20% Na_2CO_3 solution. The porphyrin was isolated by filtration (0.45µm microfilter) washed with water and ethanol and dried.Yield 26 mg (91%) **4e**.- ^{1}H NMR (DMSO-d_6): δ = -2.95 (br s, 2 H, NH), 3.76 - 3.95 (m, 16 H), 4.32 - 4.58 (m, 16 H), 4.71 - 4.79 (m, 4 H), 5.02 (m, 2 H, 1´-H_α), 5.25 (m, 2 H), 6.29 (br m, 2 H, OH), 6.65 (br m, 2 H, OH), 8.40 (m, 16 H, H_0, H_m), 8.85 (br s, 8 H, H_β).- ^{13}C NMR (DMSO-d_6): δ = 65.04 (t, C-6´), 65.23 (t, C-6´), 66.84 (t, C-6´), 67.91 (d), 68.14 (d), 68.91 (d), 69.01 (d), 69.38 (d), 69.64 (d), 72.23 (d), 72.31 (d), 73.45 (d), 74.89 (d), 76.39 (d), 77.72 (d), 81.77 (d), 82.11 (d), 83.04 (d), 93.11 (d, αC-1´), 95.85 (d), 97.32 (d), 97.86 (d, βC-1´), 102.18 (d, C_m), 119.51 (s, C-5, C-10, C-15, C-20), 128.16 (d, C_m), 129.71 (s, C_p), 132.00 (d, C_β), 134.82 (d, C_o), 146.15 (s, C_i), 147.69 (br s, C_α), 166.07 (s, CO).- IR (KBr): ν = 3384 (OH), 1707 (CO) cm^{-1}.- UV-Vis (H_2O): λ = 418, 516, 554, 591, 645 nm.- FAB-MS: m/e = 1438 (M^+).- Anal. Calc. for $C_{72}H_{70}N_4O_{28}$ (1439.4): C 60.08 H 4.90 N 3.89. Found: C 59.66 H 4.75 N 3.88.

Acknowledgements. Financial support of this research by the Fonds der Chemischen Industrie is gratefully acknowledged.

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10. Besides the α- and β-isomers, the NMR spectra indicate the existance of several conformers of compounds **4a** - **4e**. The existance of these isomers is due to rotation around the C-6′-O bond and rotation around the CO-O bond.

(*Received in Germany* 11 *December* 1995; *revised* 30 *January* 1996; *accepted* 31 *January* 1996)