Asymmetricaly substituted calix[4]pyrrole with chiral substituents

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Supplementary material

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Experimental

TLC was performed on HF254 plates (Merck), detection by UV light or by spraying with a solution of 5 g of Ce(SO4)2 in 50 ml 10 % H2SO4 and subsequent heating. Flash column chromatography was performed on silica gel (MERCK, 100-160 μm) in solvents, distilled prior to use. Optical rotations were measured in CHCl3 solutions on a Rudolph Research Autopol VI polarimeter at 25 °C and [α]D values are given in 10-1 deg.cm 2.g-1 with concentration in 10 g.l-1, unless stated otherwise. UV spectra were recorded on a Specord 210 spectrometer (Analytik Jena) (with δ given in dm3.cm-1.mol-1). IR spectra (wavenumbers in cm -1) were recorded on a Perkin-Elmer PE 580 spectrometer in CHCl3 solutions (temperature 23 °C), unless stated otherwise. 1H and 13C NMR spectra were taken on a Bruker AVANCE 500 (500.1 MHz for 1H and 125.8 MHz for 13C) FT NMR spectrometer at 300 K if not stated otherwise. As standard the internal signal of tetramethylsilane (δ 0.0) for 1H and central line of solvent (δ 77.0) for 13C were used. Chemical shifts are presented in ppm (δ), coupling constants in Hz (J). Mass spectra were taken on a TOF LQ spectrometer with direct inlet (ESI) or on a ZAB-EQ (VG Analytical) instrument (FAB) with Xe ionization, accelerating voltage 8 kV.

To a solution of pyrrole (2.9 ml, 42 mmol) and ketone 2 (ref, 11, 400 mg, 1.05 mmol) in 14 ml of dry CH2Cl2, was added trifluoroacetic acid (5 μl 0.2 mmol). The solution was stirred in the dark at ambient temperature under Ar for 20 hours. The reaction mixture was extracted with NaHCO3, dried, the solvent was evaporated and residue was subjected to chromatography on silica gel (cyclohexane-ethyl acetate 4:1) to give the dipyrrole 1 (320 mg, 60 %; [α]D +3.0 (c 0.5); UV spectrum: λmax(EtOH)/nm 209 (c 5.9 × 1010); IR spectrum: umax/cm-1 -OAc: 1750vs, br; 1255vs, br; 1049s, sh; 1034vs; 599m; 1376vs, 1368vs, 1143m; 978m; 2-subst. pyrrole: 3459s; 3386m, br; 3105w; 1556m; 1415s, 1H NMR spectrum: δH (300 MHz) 1.62 (3H, s, H-1), 2.01-1.83(13H, m, H-3b, 4xCH2CO), 2.35 (1H, m, H-3a), 3.16 (1H, dd, J = 8.7, J 8.9, H-4), 3.32 (1H, ddd, J = 1.8, J = 5.6, J 9.6, H-8), 3.90 (1H, dd, J = 1.8, J = 12.2, H-9b), 4.03 (1H, dd, J = 5.6, J = 12.2, H-9a), 4.81 (1H, dd, J = 9.3, J = 9.5, H-5), 4.89 (1H, dd, J = 9.5, J = 9.5, H-7), 4.98 (1H, dd, J = 9.1, J = 9.1, H-6), 6.06-5.93 (4H, m, H-4', H-4", H-3', H-3"), 6.45 (1H, d, H-5"), 6.51 (1H, d, J = 1.3, H-5'), 7.78 (1H, bs, H-NH), 8.01 (1H, bs, H-NH); 13C NMR spectrum 8C (75 MHz) 21.0, 21.0, 21.1, 21.1 (4xCH3CO); For C35H32N2O37 (504.52) calculated 527.2005 [M+Na]+. Found: C, 59.7; H, 6.2; N, 5.4. C35H32N2O37 requires C, 59.5; H, 6.4; N, 5.55%.

5,6,7,9-Tetra-O-acetyl-4,8-anhydro-1,2,3-trideoxy-2',2''-di-O-acetyl-4,8-anhydro-1-deoxy-1-deoxy-1-((5,10,15,15,20,20-heptamethyl-5,10,15,20,22,24-hexahydro-3,4,5,7-tetra-1-(5,10,15,15,20,20-heptamethyl-5,10,15,20,22,24-hexahydro-porphyrin-5-yl)-D-glycero-D-gulo-heptitol 4

and a mixture of 5,10-cis and trans 3,4,5,7-tetra-O-acetyl-2,6-anhydro-1-deoxy-1-(5,10,15,15,20,20-heptamethyl-5,10,15,20,22,24-hexahydro-porphyrin-5,10-diyll)-bis-D-glycero-D-gulo-heptitol 3

To a solution of dipyrrolmethane 1 (200 mg, 0.39 mmol) in 16 ml of dry CH2Cl2 was added acetone (44 μl, 0.6 mmol). Then trifluoroacetic acid (5 μl, 0.07 mmol) was added as catalyst. The reaction vessel was shielded from light and stirring under Ar at ambient temperature for one night then acetone (44 μl, 0.6 mmol) and trifluoroacetic acid (5 μl, 0.06 mmol) and the reaction mixture was stirred for additional night. Then the Et3N (15 μl, 0.1 mmol) and silica gel were added and the solvent was evaporated under vacuum. The resulting powder was posed at the top of a small silica gel column. Increasing polarity elution with cyclohexane:ethylacetate 6:1→4:1 gave derivative 4 (50 mg, 16 %) in the first major fraction.

[a]D - 3.6 (c 0.25). UV spectrum: λmax(EtOH)/nm 210 (c 8.07 × 1010). IR spectrum: -OAc: 1752vs; 1710m, sh; 1254s, br; 1144w; 977w; pyrrole: 3438s; 3111w; 1576w; 1501w; 1417m; gem. 90 sh; 1230vs; 1041m; 1033m, sh; 600w; 1376m; 1367m; 1144w; 977w; pyrrole: 3438s; 3111w; 1576w; 1501w; 1417m; gem. Me2: 2973s; 1383m, sh; 1367m. 1H NMR (300 MHz) δ (ppm) 7.03 (bs, 2H, H-NH); 6.96 (bs, 2H, H-NH); 5.88-5.73 (m, 8H, H-pyrrole); 4.97 (dd, 1H, J = 9.2 Hz, J = 8.8 Hz, H-7); 4.91 (dd, 1H, J = 10.8 Hz, J = 9.3 Hz, H-6); 4.81 (dd, 1H, J = 9.7 Hz, J = 8.9 Hz, H-5); 4.03 (dd, 1H, J = 5.2 Hz, J = 12.2 Hz, H-9a); 3.81 (dd, 1H, J = 2.2 Hz, J = 12.2 Hz, H-9b);
Further elucidation of the above column gave amorphous mixture of isomers 3 (70 mg, 16%).

UV spectrum: λ\text{max}(\text{EtOH})/nm 210 (ε 1.02 × 10^11). IR spectrum: -OAc: 1752 vs; 1251 vs; 1043 vs; 1034 vs. HRMS (TOF/ES+) m/z 1089.54 [M+H]^+. Found: C, 66.0; H, 7.1; N, 8.4. C_{34}H_{46}N_{4}O_{5} requires C, 66.6; H, 7.4; N, 7.4%.

4,8-anhydro-1,2,3-trideoxy-2′,2″-di-1H-pyrryl-2-yl-D-glucero-β-D-gulo-olitido-1-yl-calicin[4]pyrrole 7

Reaction A: To a solution of dipyrrylmethane 6 (400 mg, 1.19 mmol) in 50 ml of dry methanol was added acetone (320 μl, 4.36 mmol). Then methanesulfonic acid (27 μl, 0.35 mmol) was added as catalyst. The reaction vessel was sealed from light and stirring was continued for 3 hours under Ar at ambient temperature. Then pyridine (40 μl, 0.5 mmol) and silica gel were added and the solvent was evaporated under vacuum. The resulting powder was pose at the top of a short silica gel column. Increasing polarity elution with CHCl3, CHCl3/Methanol 4:1 gave product 7 (80 mg, 11 %) as white solid.
Notes and references
