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Ribofuranosides N-Substituted with meso-Porphyrin as Nucleoside-Like Compounds

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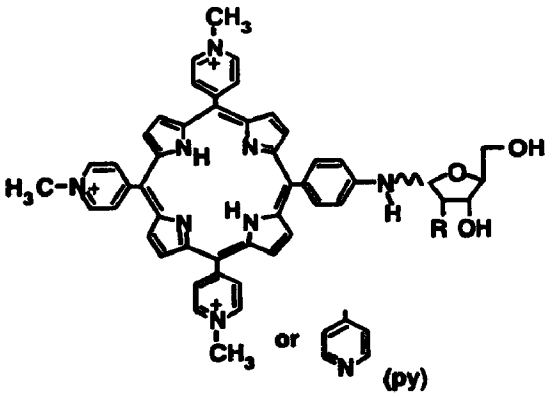
Abstract: Meso-tri(4-pyridyl)porphyrin-p-phenylene-1'-amino-D-ribose and the respective D-2-deoxyribose derivative were synthesized as first representatives of porphyrinyl-N-glycosides.

An earlier report described the synthesis of porphyrins containing O-glycosyl substituents either at all meso-positions or at some β-carbon centers.[1] In this study we describe the synthesis of the first representatives of porphyrinyl-N-glycosides. In these compounds, meso-position is occupied by p-phenylene-1'-aminoribose or p-phenylene-1'-2-deoxyribose. The other three meso-positions contain the 4-pyridyl-or N-methyl-4-pyridinium substituents which are responsible for the solubility of these compounds in water. These porphyrin N-substituted (deoxy)ribofuranosides 3-6, can be formally considered to be nucleoside-like structures in which a nucleobase is replaced by p-aminophenylporphyrin. Our interest in these compounds represents a continuation of our synthetic efforts toward water-soluble porphyrinyl-nucleosides,[2-4] some of which show tumoricidal activity.[5] The presence of a furanose unit containing the 3'-and 5'-OH groups creates a potential for further synthesis of the analogs of oligonucleotides containing a number of porphyrin units.



3 py, R=OH
4 py, R=H
5 N-Mepy, R=OH
6 N-Mepy, R=H

The starting porphyrin was the meso-4-acetamidophenyl-tri(4-pyridyl)porphyrin 1 obtained by condensation of pyrrole, pyridine-4-carboxaldehyde and 4-acetanidobenzaldehyde by the Rothemund reaction.[6] The product was isolated as a fourth fraction from a silica gel column, $CHCl_3/CH_3OH$ 60:1 as an eluent. Even with the use of an extremely pure 4-acetamidobenzaldehyde the yield did not exceed 5%. Hydrolysis of acetamido group in CF_3COOH solution by conc. HCl at 80°C for 36 h[7] resulted in the respective aminophenylporphyrin 2 which was purified like 1 with $CHCl_3/CH_3OH$ 80:1 as eluent; yield, 79%. D-ribose

(D-2-deoxyribose) in absolute ethanol solution was then stirred with 2 and anhydrous NH_4Cl at room temperature for 36 h. After removing excess NH_4Cl, solvent and washing out ribose (deoxyribose) with water, the dry product was dissolved in $CHCl_3$ and chromatographed using $CHCl_3/CH_3OH$ 40:1 as an eluent. The products were collected as the second fractions with the yields of 64% for meso-tri(4-pyridyl)porphyrin-p-phenylene-1'-amino-D-ribose 3 (37% α and 63% β anomers) and 54% for the respective D-2-deoxyribose derivative 4 (34% α and 66% β). The ratio of anomers was determined for 3 and 4 dissolved in H_2O/CH_3CN 30:70 by C-18 reverse phase separation, microbore spheresorb S5ODS2 as a supporting matrix, G 414 nm. Stirring the DMF solutions of 3 and 4 with excess CH_3I at room temperature for 1 h[8] resulted in N-methylation of 4-pyridyl substituents. The products, 5 and 6, respectively, were precipitated with diethyl ether from methanol solution; yield 78%.

1. ^{1}HNMR ($CDCl_3$), ppm: 9.05(m,6H,2,6-py;2H,β-pyr),8.85(s,6H,β-pyr),8.10(m,6H,3,5-py),8.00(d,2H,2,6-NH-Ph),7.10(d,2H,3,5-NH-Ph),1.95(s,3H,COCH3),-2.95(s,2H,porph).
2. FAB-MS,(3-nitrobenzyl alcohol matrix),m/z:633 M+;^{1}HNMR,200MHz($CDCl_3$),ppm:9.10(m,6H,2,6-py;2H,β-pyr),8.23(m,6H,3,5-py),8.05(d,2H,2,6-NH-Ph),7.15(d,2H,3,5-NH2-Ph),-2.85(s,2H,porph). UV-vis (CH_3OH) λ_{max} nm:646,589,551,514,413(S),247,203.
3. FAB-MS,m/z:763(M-2)+;^{1}HNMR (DMSO-d_6), ppm:8.99(m,6H,2,6-py,2H,β-pyr),8.80(m,6H,β-pyr),8.18(m,6H,3,5-py),7.90(d,2H,2,6-NH-Ph),7.10(d,2H,3,5-NH-Ph),5.05(m,1H,H-1'),4.90(m,2H,H-2', H-3'),4.76(m,1H,H-4'),4.34(m,2H,H-5'),-3.00(s,2H,porph); UV-vis(CH3OH), λ_{max} nm:646,589,551, 514,414(S),248,209.
4. FAB-MS,m/z:747(M-2)+; ^{1}HNMR(DMSO-d_6), ppm:9.00(m,6H,2,6-py,2H,β-pyr),8.82(m,6H,β-pyr),8.21(m,6H,3,5-py),7.92(d,2H,2,6-NH-Ph),7.10(d,2H,3,5-NH-Ph),5.20(m,1H,H-1'),4.70(m,1H,H-3'), 4.05(m,1H,H-4'),3.60(m,2H,H-5'),1.95(m,2H,H-2'),-3.00(s,2H,porph); UV-vis(CH_3OH), λ_{max} nm: 646,589,551,514,414(S),252,216.
5. ^{1}HNMR(DMSO-d_6), ppm:9.45(m,6H,2,6-py),9.00(m,6H,3,5-py;8H,β-pyr),7.15(m,4H,NH-Ph), 5.85(m,1H,H-1'),5.25(m,2H,H-2',H-3'),4.95(m,1H,H-4'),4.00(m,2H,H-5'),4.65(s,9H,N-CH_3); UV-vis(CH_3OH), λ_{max} nm: 653,591,562,519,426(S),253,216.
6. ^{1}HNMR(DMSO-d_6), ppm:9.42(m,6H,2,6-py),9.10(8H,β-pyr),8.95(6H,3,5-py),7.10(m,4H,NH-Ph), 5.25(m,1H,H-1'),4.60(s,9H,NCH_3),4.25(m,2H,H-3',H-4'),3.40(m,2H,H-5'),1.95(m,2H,H-2'), UV-vis(CH_3OH), λ_{max} nm: 651,593,559,517,424(S),221.

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