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FIRST REPRESENTATIVES OF PORPHYRINYLNUCLEOSIDES

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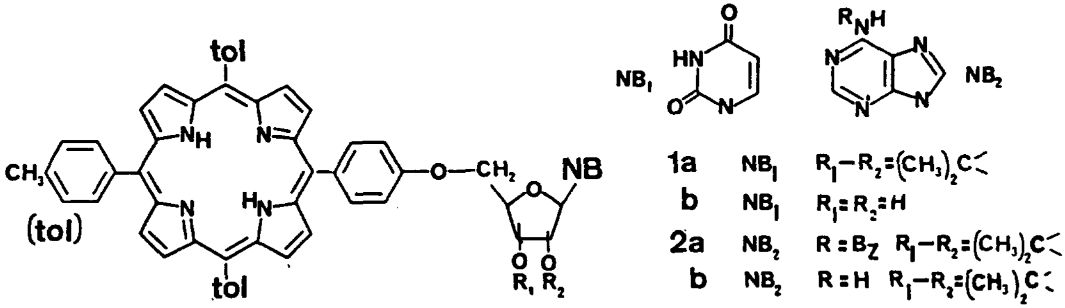
Summary: 5'-0-(5-p-Phenylene-10,15,20-tri-p-tolylporphyrin)uridine and similarly substituted(2',3'-0-isopropylidene)adenosine were obtained as first representatives of nucleosides containing covalently bonded porphyrin.

There have been reports in the literature of porphyrins substituted with monosaccharides (1) but none describing the synthesis of a porphyrin covalently bonded to either a nucleoside or a nucleotide.

We now report the synthesis of 5'-0-substituted: uridine, (2',3'-0-protected)uridine and (2',3'-0-protected)adenosine,containing meso-5-p-phenylene-10,15,20-tri-p-tolylporphyrin as substituent.



The 5'-0-(5-p-phenylene-10,15,20-tri-p-tolylporphyrin)uridine,1a, was obtained as follows. Meso-p-hydroxyphenyl-tri-p-tolylporphyrin(2), 5'-0-tosyl-2',3'-0-isopropylideneuridine(3) and sodium hydride were mixed in DMF at room temperature. After removal of DMF, the residue was dissolved in $CHCl_3$, washed with 5% $NH_{3\ aq}$, then water, dried and chromatographed on a silica-gel column, $CHCl_3$/MeOH 100:1 as eluent. The last of three fractions eluted represented 1a, yield 42%, while the second fraction contained the unreacted meso-p-hydroxyphenyl-tri-p-tolylporphyrin. The protective group was removed by mixing 1a in trifluoroacetic acid (80% solution in methanol) at room temperature. After removal of solvent, the residue was dissolved in CH_2Cl_2, washed with 5% $NH_{3\ aq}$, water, then dried and chromatographed on a silica-gel column with CH_2Cl_2/MeOH 5:1; yield of 1b 36%.

The porphyrinylnucleosides containing adenosine, 2a and 2b, were obtained from tosylated(4) N-benzyl-2',3'-0-isopropylideneadenosine and 2',3'-0-isopropylideneadenosine, respectively, in the same way as 1a. Separation of 2a gave the main fraction that was preceeded by two smaller fractions; yield 31% as the TsO^-

salt. Separation of 2b was achieved on a silica-gel column. Elution which began with $CHCl_3$ gave the unreacted meso-p-hydroxyphenyl-tri-p-tolylporphyrin. Addition of 1% v/v MeOH to the eluent yielded two additional fractions, the second one representing 2b, yield 18%.

The spectral data are in compliance with the expected structures.

1a. FAB-MS,$(M+2)^+$ 940, 3-nitrobenzyl alcohol matrix; 1H NMR (300 MHz) in $CDCl_3$,ppm: 8.84(m,8H,pyr),8.54(bs,1H,H-3),8.07 and 7.52(dd,7.7Hz,12H,H_{ar}tol),8.07 and 7.15(dd,8.6Hz,4H,C_6H_4), 7.58(d,8.1Hz,1H,H-6),5.94(d,2.3Hz,1H,H-1'),5.77 (d,8.11Hz,1H,H-5),5.07(m,2H,H-2',H-3'),4.66(m,1H, H-4'),4.36(m,2H,H-5'),2.68(s,9H,H_{al}tol),1.58(s,3H,H iprop),1.43(s,3H,H iprop), -2.78(s,2H,NHporph); UV-vis in $CHCl_3$, nm: 648,592,553,517,420 Soret,298,256.

1b. FAB-MS,$(M+2)^+$ 900; 1H NMR in $CDCl_3$,ppm: 8.83(m,8H,pyr),8.12 and 7.23(dd,8.6Hz,4H,C_6H_4), 8.07 and 7.53(dd,7.9Hz,12H_{ar}tol),7.98(d,8.2Hz,1H,H-6),5.95(d,2.3Hz,1H,H-1'),5.86(d,8.2Hz,1H,H-5),4.63-4.40(m,5H,H-2',H-3',H-4',2'-0H,3'-0H),2.68(s,9H,H_{al}tol),-2.81(s,2H,NHporph); UV-vis in CHCl3, nm: 648,591,553,517,420 Soret,300,256,239.

2a. FAB-MS,$(M+TsOH)^+$ 1224; 1H NMR in $CDCl_3$,ppm:8.83(m,8H,pyr),8.50(s,1H,H-8),8.39(s,1H,H-2),8.07 and 7.53(dd,7.9Hz,12H,H_{ar}tol),8.07(d) and 7.4-7.1(m, 4H,C_6H_4;5H,H Bz;4H,H_{ar}Ts),6.30(d, 2.2Hz,1H,H-1'),5.65 and 5.37(m, 2H,H-2',H-3'),4.83(m,1H,H-4'),4.50(m,2H,H-5'),1.72(s,3H,Hiprop),1.54 (s,3H,Hiprop),-2.81(s,2H,NHporph); UV-vis in CHCl3, nm: 647,591,553,517,418 Soret,272,239.

2b. FAB-MS,$(M+2)^+$ 964, 1H NMR in $CDCl_3$,ppm: 8.83(m,8H,pyr),8.63(s,1H,H-8),8.21(s,1H,H-2),8.06 and 7.55(dd,7.8Hz,12HH_{ar}tol),8.06 and 7.16(dd,8.6Hz,4H,C_6H_4),6.43(d,2.2Hz,1H,H-1),5.62(m) and 5.38(m) (2H,H-2',H-3'),4.86(m,1H,H-4'),4.48(m,2H,H-5'),2.68(s,9H,H_{al}tol),1.73(s,3H,H iprop),1.49(s,3H,Hiprop), -2.81(s,2H,NHporph); UV-vis in $CHCl_3$, nm: 647,591,553,517,420 Soret.

In addition to the ions listed, the porphyrin fragment $(M_{porph} + 2)^+$ 673 (5) is found in all FAB-MS spectra.

Further synthetic work is presently underway which will lead to formation of water-soluble porphyrinylnucleosides, compounds of potential importance to researchers in biochemistry, physiology and physiotherapy.

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