The Anomeric Configuration of 6-Methyl-3-D-glycosyluracil

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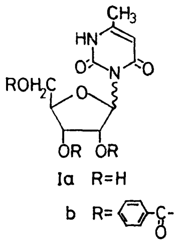
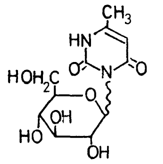
Recent papers[1,2] in which Lemieux's PMR method was applied to determine the anomeric configuration of pyrimidine nucleosides prompt us to suggest the limitations of the method. The use of a seeming coupling constant in high-resolution PMR might be a mistake for the assignment of the anomeric proton of acylated ribofuranosyl nucleosides without consideration of the half-height width of the absorption peak,[3] since two heavily overlapped broad peaks seem to be one broad peak. We wish now to report the anomeric proton assignment of 6-methyl-3-D-glycosyluracils (Ia, b, and II) synthesized by the condensation of 6-methyluracil with acylglycosyl halide in nitromethane containing a hydrogen halide acceptor.[4]

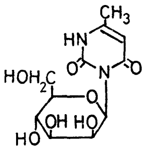


Ia R=H

b R=



II



III

6-Methyl-3-D-ribofuranosyluracil (Ia) [$[\alpha]_D^{22}=-18°$ (c 0.083, H_2O), $\lambda_{max}^{H_2O}=266$, $\lambda_{min}^{H_2O}=234$ mμ (Found: C, 46.56: H, 5.59; N, 11.08; Calcd for $C_{10}H_{14}N_2O_6$: C, 46.51; H, 5.47; N, 10.85; mol wt, 258.23): NMR data (DMSO-d_6) δ 6.10 (d, $J_{1',2'}=3.7$ Hz, H-1')] and 6-methyl-3-(tri-*O*-benzoyl-D-ribofuranosyl) uracil (Ib) [NMR data (DMSO-d_6) δ 6.55 (s, half-height width 3 Hz, H-1')] seemed to be pure β anomer judging from the NMR data.[1,2] 6-Methyl-3-D-glucopyranosyluracil [II, mp 196—200°C, $[\alpha]_D^{22}=0°$ (c 0.091, H_2O), $[M]_{350}^{22}=0°$ (c 0.0032 M, H_2O), $\lambda_{max}^{H_2O}=266$ (ε 9370), $\lambda_{min}^{H_2O}=234$ mμ (ε 2036): (Found: C, 45.48; H, 5.64; N, 9.52; Calcd for $C_{11}H_{16}N_2O_7$: C, 45.83; H, 5.59; N, 9.72; mol wt 288.25): NMR data (D_2O) δ 5.65 (d, $J_{1',2'}=9.67$ Hz, H-1'), 5.76 (d, $J_{1',2'}=9.33$ Hz, H-1'), 5.62 (q, $J_{5,6}=0.7$ Hz, H-5)] was an anomeric mixture. In order to prepare the pure anomer to give clear data, II was converted into 6-methyl-3-β-D-mannopyranosyluracil (III) [mp 237—238°C, $[\alpha]_D^{22}=-32.8°$ (c 0.091, H_2O), $\lambda_{max}^{H_2O}=267$, $\lambda_{min}^{H_2O}=235$ mμ: (Found: C, 45.83; H, 5.59; N, 9.79; Calcd for $C_{11}H_{16}N_2O_7$: C, 45.83; H, 5.60; N, 9.72; mol wt 288.25): NMR data (D_2O) δ 6.08 (d, $J_{1',2'}=0.6$ Hz, H-1')] in several steps.

The optical rotatory dispersion of the dialdehydes formed from a 0.01 mol solution of the free nucleosides (Ia, II, and III) containing excess sodium metaperiodate[5] gave the following data:

Ia,	$[M]_{589}^{22}=-80°$,	$[M]_{350}^{22}=-410°$
II,	$[M]_{589}^{22}=-85°$,	$[M]_{350}^{22}=-400°$
III,	$[M]_{589}^{22}=-25°$,	$[M]_{350}^{22}=-230°$

The anomeric configuration of furanosyl nucleoside could not be assigned only from the seeming PMR coupling constant of less than 1 Hz without a consideration of the broad half-height width of the absorption peak of the anomeric proton.

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[4] N. Yamaoka, K. Aso, and K. Matsuda, *J. Org. Chem.*, **30**, 149 (1965).

[5] B. Lythgoe, H. Smith, and A. R. Todd, *J. Chem. Soc.*, **1947**, 355.