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OPTICAL ROTATORY DISPERSION OF ANOMERIC PYRIMIDINE NUCLEOSIDES

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As suggested recently by Ulbricht et al.[1], the O.R.D. curves can be applied to determine the configuration of pyrimidine nucleosides at the anomeric centre. It appeared of interest to use this method with some other nucleosides containing a different sugar moiety. In the present paper, anomeric pairs of 1-glycosylthymines derived from D-aldopentoses and D-glucose have been used as model compounds.

Results of measurements are listed in Table I and II. It may be seen that all compounds therein show a simple Cotton effect. Its sign is negative with α-anomers and positive with β-anomers, in accordance with the findings of Ulbricht et al.[1] This effect holds for nucleosides with the sugar moiety both in the furanose and in the pyranose form except 1-(α-D-glucopyranosyl)thymine which shows, contrary to expectations, a positive Cotton effect. This anomaly is probably due to the bulky pyrimidine substituent in the axial position and the consequent lower stability of the C1 conformation of the pyrane ring; the conformation 1C (or B) becomes thus energetically more advantageous.

(The 1C conformation has been found by Lemieux[2] for N-(tetra-O-acetyl-α-D-glucopyranosyl) pyridinium bromide by the method of nuclear magnetic resonance. A flexible B conformation is assumed by Stevens[3] for some pyrimidine nucleosides). Moreover, it is apparent from the Table I that the hydroxylic function at 2′-position exerts a strong influence on the magnitude of the amplitude of the Cotton effect but not on its sign. Nucleosides with a cis-oriented hydroxylic function in respect to the pyrimidine ring show considerably higher amplitude values than those with a trans-oriented hydroxylic function. This effect might be ascribed to a restricted free rotation of the pyrimidine ring (due to the steric hindrance of the cis-oriented hydroxylic function or to the $2'\text{-OH} \longrightarrow 2 = \text{O}$ hydrogen bonding), leading to an increase of the optical rotation values (the Kauzmann-Eyring rule[4,5]). In a lesser degree, this effect may be observed also with a hydroxylic function at 3′-position. This effect, expressed by a ratio of amplitude of the corresponding anomers, depends also on the character of the chromophoric groups as shown in the case of the anomeric pairs of thymidines and 5-fluoro-2′-deoxyuridines (Table II).

As shown by our results, the assignment of the anomeric configuration of pyrimidine nucleosides by the method of the O.R.D. curves may be reliably performed only in those cases when both the measured compound and the reference

TABLE I

O.R.D. Measurements of Anomeric 1-D-Glycosylthymines

cis-(2′-OH-Thymine)				trans-(2′-OH-Thymine)				
Compound	λ^b (mμ)	[M]	a^c	Compound	λ (mμ)	[M]	a	$\frac{\|a_{cis}\|}{\|a_{trans}\|}$
β-D-ArFuThy[a,d]	287 251	+ 9920 -19350	+293	α-D-ArFuThy	288 256	-2200 +8110	-103	2.8
β-D-LyFuThy[d]	287 252	+11700 -19300	+310	α-D-LyFuThy	288 261	0 +8260	- 83	3.7
α-D-RiFuThy	286 254	-10630 +20530	-312	β-D-RiFuThy	291 256	+2940 -8390	+113	2.8
α-D-XyFuThy	286 253	-11250 +19000	-302	β-D-XyFuThy	290 254	+4110 -6360	+104	2.9
α-D-RiPyThy	286 252	- 8960 +11920	-209	β-D-RiPyThy	291 260	+ 720 -3870	+ 46	4.6
α-D-XyPyThy	286 253	-10200 +13300	-235	β-D-XyPyThy	285 255	+3590 -4460	+ 81	2.9
α-D-GluPyThy	280 240	+ 3450 - 3220	+ 67	β-D-GluPyThy	290 257	+1350 -3020	+ 44	1.5

[a] Abbreviation β-D-ArFuThy means 1-β-D-arabinofuranosylthymine and other abbreviations were formed analogously; [b] extremum positions of the O.R.D. curves; [c] definition of the molar amplitude a see the paper of Ulbricht et al.[1]; [d] the sample was provided by Dr Jack J. Fox (Sloan-Kettering Institute, New York).

TABLE II

O.R.D. Measurements of Anomeric 2′-Deoxy-Nucleosides

Compound		λ[a] (mμ)	[M]	a[b]
2′-Deoxy-D-ribofuranosyl-thymine	α	289.5 257.5	- 3710 +10040	-138
	β	292 259	+ 1700 - 6830	+ 85
2′-Deoxy-D-ribofuranosyl-5-fluorouracil[c]	α	288 252	- 7700 +15550	-232
	β	293 257	+ 3690 - 5540	+ 92

[a] Extremum positions of the O.R.D. curves; [b] definition of molar amplitude see in paper of Ulbricht et al.[1]; [c] the samples were provided by Dr Jack J. Fox (Sloan-Kettering Institute, New York).

specimen possess an identical chromophore and an identical conformation of the sugar moiety.

Optical rotatory dispersions were measured with the Jasco spectropolarimeter, model O.R.D./U.V.-5 in the wavelength range from 350 to 220 mμ at 25 - 28°C. In the absorption band region, the measurements were performed with a cell length 0.01 dm and concentrations of 0.01 - - 0.03 g/100 ml (maximum slit width 1.5 mm). Under these conditions, the maximum absorbances of solutions were approximately 1. Values of molecular rotations have an accuracy of approximately 10 %.

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