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OPTICAL ROTATORY DISPERSION OF ANOMERIC NUCLEOSIDES.[1]

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A recent publication,[2] describing the O.R.D. curves of the four main natural β-deoxyribonucleotides, prompts us to report our own results in this field. Yang and Samejima[2] found that the β-deoxyribonucleotides showed Cotton effects in the region of 260 mμ; an important difference was observed between the pyrimidine and purine compounds, which showed positive and negative Cotton effects respectively.

We have measured O.R.D. curves of a more extended range of nucleosides, which include three significant pairs of anomers. Our results parallel those of Yang and Samejima for the 5'-phosphates; our results also bring out the important (and not unexpected) finding, that the members of an anomeric pair give curves of opposite sign. For the measurements below 300 mμ, only 0.05 mg. of compound was required; hence the anomeric configuration of a nucleoside can be determined on a very small sample.

Our results also show that the presence or absence of a 2-hydroxy group in the sugar moiety (ribose or 2-deoxyribose) makes no major difference to the curve. This point is of considerable interest in connection with Hudson's isorotation rules[3], according to which the more dextrorotatory of a pair of anomeric-D-glycosides has the α-D-configuration. This is true of a wide variety of glycosides, including ribonucleosides, but does <u>not</u> apply to deoxyribonucleosides[4,5]. It is therefore not possible to assign anomeric configuration to deoxyribonucleosides on the

basis of $[\alpha]_D$ measurements. Our work shows that measurement of O.R.D. curves makes this possible; this is of particular importance since syntheses of deoxyribonucleosides from deoxyribosyl halides yield mixtures of the α- and β-anomers[6].

Results are given in the Table which includes amplitudes for the curves measures by Yang and Samejima[2] (translated into molecular rotations for comparison).

Measurements were made at Westfield College with the Bellingham & Stanley/Bendix-Ericsson spectropolarimeter "Polarmatic 62"[7]. Concentrations varied from $\underline{c}$. = 0.1 to $\underline{c}$. = 0.004, all rotations being determined in water at 18-22°C. The wavelength range was from 500 mμ - 220 mμ, and values of molecular rotations have an accuracy of approximately 10%. Optical densities were kept below 1.5 for most measurements, and the useful (non-stray) light transmission of the spectropolarimeter was continuously monitored during readings.

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TABLE +

Molecular Rotations of Nucleosides (in water).

tr = trough ; pk = peak

Amplitude $\underline{a}$ is (molecular rotation at first extremum minus molecular rotation at second extremum) divided by 100 (cf. ref.1).

Pyrimidine Nucleosides		Molecular Rotation			Amplitude
Compound	Anomeric Configuration	λ(mμ)	[Φ]		$\underline{a}$
Thymidine	β	282	+1890	pk	+95
		255	-7590	tr	
	α	286	-3660	tr	-104
		252	+6780	pk	

Pyrimidine Nucleosides	Anomeric Configuration	Molecular Rotation λ(mμ)	Molecular Rotation ∅	Amplitude a
Uridine	β	279	+4100 pk	+117
		247	-7600 tr	
Cytidine	β	282	+7250 pk	+152
		244	-7950 tr	
5-Fluorodeoxyuridine	β	281	+4350 pk	+120
		253	-7660 tr	
	α	286	-6300 tr	-159
		252	+9550 pk	
Deoxycytidine hydrochloride	β	290	+4630 pk	+111
		266	-6500 tr	
Pyrimidine Nucleotides				
Thymidine-5'-mono-phosphate diammonium salt	β	280	+1670 pk	+71*
		250	-5460 tr	
Values calculated from figures in Ref.2				
Thymidine-5'-mono-phosphoric acid	β	290	+1000 pk	+19*
		249	-850 tr	
Deoxycytidine-5'-mono-phosphoric acid	β	290	+6750 pk	+124
		250	-5650 tr	
Purine Nucleosides				
Adenosine	β	270	-2310 tr	-58
		238	+3450 pk	
Guanosine	β	294	-760 ‡*	-
Inosine	β	253	-2490 tr	-59
		228	+3380 pk	

Purine Nucleosides		Molecular Rotation		Amplitude
Compound	Anomeric Configuration	λ(mμ)	ø	a
Deoxyadenosine	β	286	-790 ‡	-
	α	271	+2700 pk	+80
		251	-5330 tr	
Deoxyguanosine	β	303	-800 ‡	-
Purine Nucleotides (values calculated from figures in Ref. 2)				
Deoxyadenosine-5'-monophosphoric acid	β	290	-1090 tr	-27
		240	+1650 pk	
Deoxyguanosine-5'-monophosphoric acid	β	290	-1460 tr	-29
		230	+1460 pk	

* The reason for the discrepancy between these two values is not understood.

‡ Neither extremum of the Cotton Effect was reached, but this value (at the lowest wavelength measured) indicates the trend of the curve.

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