NUCLEOSIDE CONFORMATIONS

VI. Optical Properties of 1,3-diribofuranosyl-6-methyl-uracil *

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1. Introduction

The interest of using sterically hindered nucleoside analogues as models for optical studies has long been recognised [2]. In many cases, however, cyclonucleosides [2, 3] have been used to establish correlations between Cotton effects and nucleoside conformation. The question has arisen frequently, if the formation of an additional ring system implying the heterocyclic base would not change the electronic structure and consequently the orientation of the transition moment of the base in the cyclonucleoside compared with that in the parent compound. Also, it is not evident that the formation of another fixed asymmetric center would simply be additive or if more profound perturbances will occur. In the pyrimidine series, a proper substitution of the sugar residue [4–7] or the use of non-polar substitutents on the base should sterically fix a nucleoside in a certain conformation without the formation of another ring, nor the danger of large effects on the transition moment of the base. The latter case is demonstrated by 6-methyl-uridine (fig.1, I) [7].

We have therefore considered the possibility of establishing 2 independent asymmetric centers on a base, both of which will be sterically blocked. In the compounds shown in fig.1 this requirement is fulfilled and will permit the testing of the hypothesis whether or not 2 asymmetric contributions will add up or not. We have synthetized [8] the 3 components shown and have measured their absorption, CD and MCD spectra.

2. Experimental

The synthesis of the compounds in fig.1 is de-

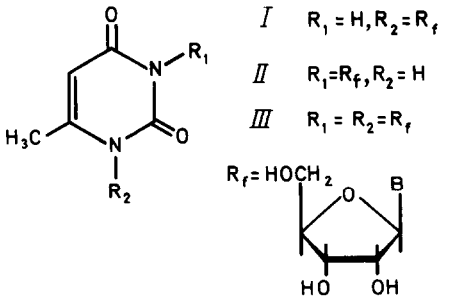

Fig.1. Structure of compounds studied. R_f = β-ribofuranosyl.

* part 5: see [1].
Abbreviations used:
CD: circular dichroism
MCD: magnetic circular dichroism.

Table 1
Circular dichroism and absorption characteristics of 6-methyl-uracil-nucleosides in water.

Compound and ref.	Circular dichroism								Absorbance	
	B_{2u}			B_{1u}			E_{1ua}			
	λ	$\theta \times 10^{-3}$ *	λ_0	λ	$\theta \times 10^{-3}$	λ_0	λ	$\theta \times 10^{-3}$	λ_{max}	$\times 10^{-3}$
I										
This work	271	−1.4	257	243	+1.8	231	213	− 7.1	261	11.2
[7]	260–270	−0.3	262	250	+1.0	238	214	−10.0	268	
II										
This work	270	−2.8	258	242	+3.7	227	210	− 3.8	263	8.7
[7]	268	−4.3		242	+6.2		214	− 3.8	265	
III										
This work	272	−4.2	260	245	+5.4	230	214	−10.0	263	10.0

* The CD values have an estimated error of ± 0.1 × 10^3 above 230 nm and about 0.5 × 10^3 around 220 nm.

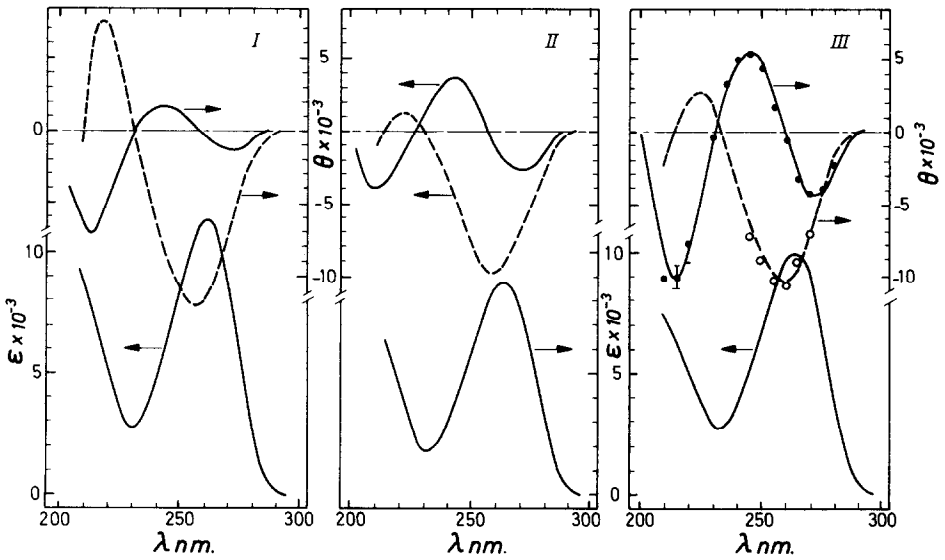

Fig.2. Optical properties of I, II and III in water. Bottom: UV absorption spectra; top: CD (———) and MCD (----) spectra. (•–•–•): *Sum* of CD spectra of I and II. (○–○–○): *Mean* of MCD spectra of I and II. (All MCD spectra were corrected for natural CD, but are presented at a field of 70 kG.)

scribed elsewhere [8]. The UV absorption and CD spectra were recorded on a Cary 14 spectrometer and a Roussel-Jouan 185 dichrograph, respectively. The MCD spectra were recorded on modified Roussel-Jouan 185 dichrograph at the Biophysics division in Saclay [11], equipped with a helium cooled superconducting magnet with a field of 70 kG. All MCD spectra were corrected for the natural CD, but are presented at 70 kG.

3. Results and discussion

The results of this investigation are summarized in table 1 and fig. 2. Although the molar ellipticities of I and II reported here are somewhat different from those measured by Miles et al. [7], the sum of these ellipticities describes well, within the experimental error, the CD spectrum of III. Both the absorbancy and MCD of III are the mean of those of I and II. This is

not surprising since these 2 properties depend essentially upon the base chromophore. The similarity of the absorbance and MCD spectra among each other and with that of Urd [9] indicate that the position and orientation of the transition moment are preserved in the substituted Urd analogues. The additivity of the CD spectra of I and II to yield the spectrum of III points out that the 2 asymmetric ribose units do not perturb seriously the electronic structure of the chromophore. Also they probably have the same conformation in respect to the ring as it is in I and II and act independently from each other upon the chromophore.

The fact that different contributions of optical activity appear to be additive suggests that modifications which do not perturb the electronic structure of the chromophore, but possess fixed asymmetric centers should yield useful information for defining rules correlating optical activity and conformation of nucleosides [10].

Acknowledgements

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References

[1] J.F. Chantot and W. Guschlbauer, in: The Purines. Theory and Experiment, Proc. 4th Jerusalem Symp. Quant. Chem. and Biochem., eds. E.D. Bergmann and B. Pullmann (Academic Press, New York) in press.
[2] T.R. Emerson, R.J. Swan and T.L.V. Ulbricht, Biochemistry 6 (1967) 843.
[3] M. Ikehara, Accounts Chem. Res. 2 (1969) 47.
[4] I. Frič, J. Šmejkal and J. Farkaš, Tetrahedron Letters (1966) 75.
[5] T. Nishimura, B. Shimizu and I. Iwai, Biochim. Biophys. Acta 157 (1968) 221.
[6] W. Guschlbauer and M. Privat de Garilhe, Bull. Soc. Chim. Biol. 52 (1969) 1511.
[7] D.W. Miles, M.J. Robbins, R.K. Robbins, M.W. Winkley and H. Eyring, J. Am. Chem. Soc. 91 (1969) 824.
[8] A. Holý, Coll. Czech. Chem. Comm., in press.
[9] W Voelter, R. Records, E. Bunnenberg and C. Djerassi, J. Amer. Chem. Soc. 90 (1968) 6163.
[10] W. Guschlbauer and J.M. Delabar, in preparation.
[11] Chr. Schneider and J.M. Thiéry, in preparation.