

Chiroptical properties of some acyclic ketoses*

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Chiroptical properties of all tetrols, 2-pentuloses, D-3-pentulose and 4-deoxy-L-pentulose were investigated by means of circular dichroism. The compounds revealed overlapping ellipticity curves of opposite sign in the $n \rightarrow \pi^*$ transition region of the carbonyl group. The Octant Rule was employed to interpret signs of the Cotton effect. The existence of two bands is rationalized by the equilibrium of two dominating rotamers.

Применением кругового дихроизма изучались хироптические свойства всех тетраулоз, 2-пентулоз, D-3-пентулозы и 4-дезоксид-Л-пентулозы. Вещества давали перекрывающиеся эллиптические полосы противоположного знака в области $n \rightarrow \pi^*$ перехода карбонильной группы. При интерпретации знаков эффекта Коттона использовалось октантовое правило для карбонильных хромофоров. Существование двух полос объясняется равновесием двух преобладающих вращающихся изомеров.

A considerable attention is being paid to ketones in connection with their biological activity. Ketoses are the component of ketonucleosides [2], some antibodies [3] and hydrazones which inhibit the nucleo- and proteosynthesis in tumorous cells [4].

So far, acyclic ketones have not been frequently spectropolarimetrically studied [5—8] and acyclic saccharides even less [9—11]. The correlation between chiroptical properties and structure is rather complex because of the conformational flexibility. This phenomenon is evident from the experimentally determined low rotational power of these substances. The changeable systems of (+)-2-butyl alkyl ketones were studied more recently [12]; the conformation of the alkyl substituents was established for the first time using the Octant Rule. Optical rotatory dispersion was the tool by means of which we have studied some acyclic ketoses in aqueous solutions [10] and found the configuration of chiral centre adjacent to chromophore to be responsible for the sign of the Cotton effect.

In this paper we wish to report the results obtained with eight acyclic ketoses: D-glycero-tetrol (I), L-glycero-tetrol (II), D-threo-pentulose (III), L-threo-pentulose (IV), D-erythro-pentulose (V), L-erythro-pentulose (VI),

* Part XIV in the series *Studies on circular dichroism*. For Part XIII see Ref. [1].

Table 1

Spectral data of tetruloses and pentuloses as recorded in 1,1,1,3,3,3-hexafluoropropanol (HFP), methanol, and dioxan

No.	Hexafluoropropanol		Methanol		Dioxan		Ref.
	$\Delta\varepsilon$	λ	$\Delta\varepsilon$	λ	$\Delta\varepsilon$	λ	
I	<+0.01	313	+0.08	300	+0.01	307	[13]
	-0.80	268	-0.11	270	-0.37	272	
II	<-0.01	315	-0.09	300	-0.02	307	[14]
	+0.83	268	+0.11	269	+0.38	269	
III	-0.02	303	-0.06	296	-0.01	303	[15, 16]
	+0.48	265	+0.04	263	+0.15	269	
IV	+0.02	300	+0.05	295	+0.01	303	[17, 18]
	-0.48	264	-0.04	263	-0.14	269	
V	+	305	+	306	+	302	[15, 19]
	-0.10	270	-0.08	274	-0.14	274	
VI	-	304	-	304	-	303	[20, 21]
	+0.08	270	+0.08	275	+0.13	274	
VII	+0.01	329	+0.02	334	+0.02	333	[17]
	-2.28	276	-2.17	284	-2.53	278	
VIII	<-0.01	306	<-0.01	291	<-0.01	312	[22]
	+0.29	268	+0.06	264	+0.05	231	

D-threo-3-pentulose (VII), and 4-deoxy-L-glycero-pentulose (VIII). The ultraviolet spectra measured in methanol revealed a slight absorption band at 280 nm ($\varepsilon < 100$) due to the $n \rightarrow \pi^*$ transition of the carbonyl chromophore. Spectra of circular dichroism of tetruloses and pentuloses were taken in three solvents of various polarity; all showed two overlapping bands of opposite sign and different ellipticity (Table 1). The correlation of overlapping bands of opposite sign with the configuration of the chiral centre adjacent to chromophore showed that the long-wave band associated with the *R* configuration is positive, whilst that of the *S* configuration is negative. The long-wave less intense chiroptic band lies in the 310 nm region, the short-wave more intense one about 270 nm. The seeming positions (310 and 270 nm) of bands of opposite signs resulted from the superposition of two Cotton effects, the real maxima of which are much more close. The overlapping elliptic bands of opposite signs concentrated around simple electronic

transition can be ascribed to a dipole coupling of transition moments [23], or to a vibrational structure [24], or to both. This phenomenon has been rationalized with carboxylic acids [25] and ketohexoses [11] in terms of conformational equilibrium.

The long-wave chiroptic bands of D- and L-*erythro*-pentuloses (V and VI) could not be quantitatively evaluated. The rotational power of the short-wave band is more pronounced in the non-polar solvent than that of the long-wave band. The short-wave band corresponding to 3-pentulose is by two orders of magnitude more intense in all solvents employed.

As known, acyclic ketones exist quite frequently in an eclipsed conformation of the carbonyl group with substituents attached to the α -carbon [26, 27]. *E.g.* L-*glycero*-tetrulose ($R^1 = \text{CH}_2\text{OH}$, $R^2 = \text{OH}$) could be depicted by three eclipsed conformations A, B, and C (Fig. 1) the latter of which is very unfavourable

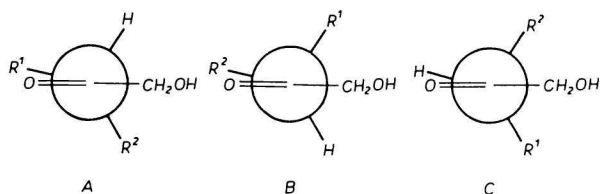


Fig. 1. Eclipsed conformation of tetruloses.

because of two gauche interactions. On the other hand, conformers A and B have only one such an interaction each. Considering the population of conformers the first two were taken into account. The Octant Rule [28] was also employed to determine the sign of the overlapping chiroptic bands of acyclic ketoses. Fig. 2 shows the octant drawing of two most populated conformers of L-*glycero*-tetrulose ($R = \text{CH}_2\text{OH}$). The *sec*-alcoholic group of the conformer A lies in the left lower (negative) octant. This conformer is predicted to reveal a negative Cotton effect.

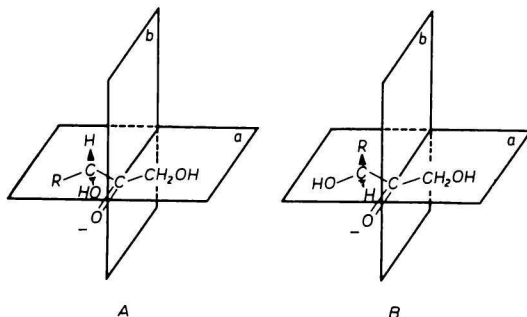


Fig. 2. Octant diagrams of favoured conformations (A and B) of L-*glycero*-tetrulose ($R = \text{CH}_2\text{OH}$).

Similarly, a positive Cotton effect could be anticipated for conformer *B* the R group (CH₂OH) of which positively contributes to the sign since it occupies the left upper (positive) octant. Other groups lying in planes *a* and *b* are of no contribution to the rotational power of the molecule.

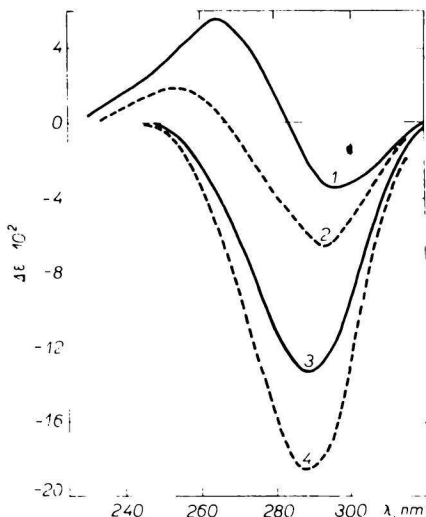


Fig. 3. Temperature dependence of CD of *D-threo*-pentulose in the mixture ethanol—methanol (4:1). 1. 40°C; 2. -20°C; 3. -80°C; 4. -140°C.

L-Glycero-tetulose could be assigned the conformation *A* on the basis of a negative Cotton effect in the 300 nm region and applying the Octant Rule. On the other hand, the positive Cotton effect in the 270 nm region belongs to the conformation *B* of *L-glycero*-tetulose. The single conformers of its antipode, *D-glycero*-tetulose, reveal opposite Cotton effects. The population of conformers *A* and *B* is shifted in 1,1,1,3,3,3-hexafluoropropane and dioxan at room temperature in favour of the conformer *A*, *i.e.* towards the long-wave band.

Fig. 3 shows the rotatory power of *D-threo*-pentulose dissolved in a mixture of ethanol—methanol (4:1) in the 40 to -140°C range. The positive Cotton effect disappears and the negative one increases with lower temperature and at -140°C only one energetically most favoured conformer was left in the solution. The position of the single negative minimum (288 nm) corresponds to the maximum of the absorption band $n \rightarrow \pi^*$ of the carbonyl transition [29].

The existence of two Cotton effects of opposite sign could not be comprehensively rationalized at the time being. Intramolecular interactions of molecules of acyclic ketoses in a non-polar solvent and intermolecular interactions of molecules with a polar solvent promote formation of rotamers and, consequently, the overlapping chiroptic bands of opposite sign. Substances measured in dioxan could intramolecularly interact to form hydrogen bonds. Therefore, the population of the

conformer *B* is favoured and the ellipticity of the short-wave band is greater as evident from Table 1. The population of both conformers in methanol is approximately equal and Cotton effect of the overlapping bands are of almost the same intensity. The obtained results show that conformer *A* is preferred with substances *III* and *IV*. In a strong proton-donating solvent (hexafluoropropanol) the intermolecular interactions result in preferring the conformer *B* this being evidenced by intense short-wave bands with the exception of those of *D-threo*-3-pentulose. The high ellipticity of the short-wave band is given by the inherent structure of this substance having two equivalent centres of chirality attached to the carbonyl group.

The presented results bring evidence that both preferred rotamers are equilibrated in dioxan, methanol, and hexafluoropropanol at room temperature.

Experimental

Syrupy substances *I*—*VIII* were prepared according to described methods (Table 1). Their physicochemical constants are in accordance with those reported. The spectra of ketoses were measured with an ORD/UV-5 JASCO spectropolarimeter, provided with a CD adapter, in dioxan, methanol, HFP, and in a mixture of ethanol—methanol (4:1) at a concentration 1—2 mg/ml, in 1 cm cells at room temperature. The CD spectra at low temperatures were recorded with a Roussel—Jouan dichrograph model 185.

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References

1. Bystrický, S., Sticzay, T., Kučár, Š., and Peciar, C., *Collect. Czech. Chem. Commun.* **41**, 2749 (1976).
2. Halmos, T. and Antonakis, K., *Carbohydr. Res.* **43**, 208 (1975).
3. Henessian, S. and Haskell, T. H., in *The Carbohydrates*. (W. Pigman and D. Horton, Editors.) Vol. *IIA*, p. 139. Academic Press, New York, 1970.
4. Fуска, J., Linek, K., and Buzinkay, Š., *Neoplasma* **21**, 561 (1974).
5. Levene, P. A. and Rothen, A., *J. Chem. Phys.* **4**, 48 (1936).
6. Djerassi, C. and Geller, L. E., *J. Amer. Chem. Soc.* **81**, 2789 (1959).
7. Robinson, M. J. T., *Chem. Ind.* **1964**, 932.
8. Lardicci, L., Salvadori, P., Botteghi, C., and Pino, P., *Chem. Commun.* **1968**, 381.
9. McGilvery, R. V., *Biochemistry* **4**, 1924 (1965).
10. Sticzay, T., Peciar, C., Babor, K., Fedoroňko, M., and Linek, K., *Carbohydr. Res.* **6**, 418 (1968).
11. Avigad, G., England, S., and Listowsky, I., *Carbohydr. Res.* **14**, 365 (1970).
12. Potapov, V. M., Demyanovich, V. M., and Zaytsev, V. P., *Dokl. Akad. Nauk SSSR* **223**, 875 (1975).
13. Linek, K., Fedoroňko, M., and Isbell, H. S., *Carbohydr. Res.* **21**, 326 (1972).
14. Whistler, R. L. and Underkofler, L. A., *J. Amer. Chem. Soc.* **60**, 2507 (1938).

15. Fedoroňko, M. and Linek, K., *Collect. Czech. Chem. Commun.* **32**, 2177 (1967).
16. Schmidt, O. T. and Treiber, R., *Ber.* **66**, 1765 (1933).
17. Stankovič, L., Linek, K., and Fedoroňko, M., *Carbohydr. Res.* **10**, 579 (1969).
18. Wolfrom, M. L. and Bennett, R. B., *J. Org. Chem.* **30**, 458 (1965).
19. Zinner, H. and Reppenning, W., *Carbohydr. Res.* **5**, 176 (1967).
20. Moses, V. and Ferrier, R. J., *Biochem. J.* **83**, 8 (1962).
21. Reichstein, T., *Helv. Chim. Acta* **17**, 996 (1934).
22. Linek, K., Šandtnerová, R., Kulhánek, M., and Tadra, M., *Czech. Appl.* 4585—75.
23. Schellman, J. A., *Accounts Chem. Res.* **1**, 144 (1968).
24. Weigang, O. E., *J. Chem. Phys.* **42**, 2244 (1965).
25. Listowsky, I., Avigad, G., and England, S., *J. Org. Chem.* **35**, 1080 (1970).
26. Cotteril, W. D. and Robinson, M. J. T., *Tetrahedron Lett.* **1963**, 1833.
27. Karabatsos, D. J., *J. Amer. Chem. Soc.* **89**, 1367 (1967).
28. Moffit, W., Woodward, R. B., Moscovitz, A., Klyne, W., and Djerassi, C., *J. Amer. Chem. Soc.* **83**, 4013 (1961).
29. Bystrický, S. and Sticzay, T., *Collect. Czech. Chem. Commun.*, in press.

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