CHIROPTICAL PROPERTIES OF MONOSACCHARIDE ACETYL DERIVATIVES

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Received November 17th, 1984

Circular dichroism of positional isomers of acetylated methyl β-D-xylopyranosides, 1,6-anhydro--β-D-glucopyranoses and methyl α-L-rhamnopyranosides is discussed considering the mechanism of optical rotatory strength nature. Interactions determining the signs are influenced by the character of the solvent. Magnitude of the effect depends on the spatial arrangement of the chromophore environment. This effect is lowered with diacetyl derivatives, where the interaction of transitional dipole moments of acetyl groups is the main source of optical rotational strength.

The presence of an acetyl group at various positions of the pyranose ring of saccharides challenges to study the structural properties by means of circular dichroism spectra. A conventional measurement displays at about 210 nm an optically active band of $n \rightarrow \pi^*$ electronic transition[1]. A subsequent absorption band appears below 190 nm (ref.[2]). Optical activity of the chromophore is induced by the chiral moiety of the molecule. A planar sector rule with nodal plane in the chromophore plane was deduced and employed for isoelectric carboxyl chromophore of uronic acids[3,4]. The molecular skeleton of derivatives having an acetyl group at the pyranose ring in an extended arrangement[5] is divided by an analogous nodal plane into two more or less compensating parts. A simple interpretation of circular dichroism of acetyl derivatives has been reported[6,7]. By chiral action of the surrounding, the influence of an oxygen atom of neighbouring groups oriented gauche to the bond of the chromophore and to the rest of the molecule is understood. Arrangement *A* makes a positive, arrangement *B* a negative sign of the Cotton effect. The order of decreasing influence of the particular groups is as follows: $CH_2OH > CH_2OAc > O(5) > OH > OCH_3 > OAc$. An empirical correlation of the sign of circular dichroism and the sign of dihedral angle was used for various hexopyranosides and pentopyranosides[6-8].

Mechanism of origination of a rotational strength due to the above-mentioned groups of various electronic nature is obviously not equal. A series of chosen acetyl derivatives of glycopyranosides (Fig. 1) offers a possibility to study these correla-

tions. It seems to be advantageous to evaluate a series of data obtained by measurement of circular dichroism spectra at various solvation and temperature conditions.

EXPERIMENTAL

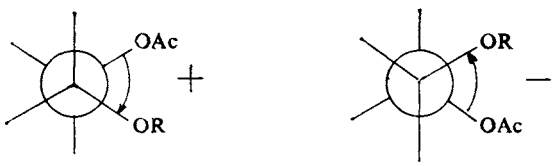
Methyl β-D-xylopyranosides, 1,6-anhydro-β-D-glucopyranoses and methyl α-L-rhamnopyranosides were prepared according to[9-15]. The CD spectra were recorded in 2,2,2-trifluoroethanol or acetonitrile (both Merck) solutions. Monoacetyl derivatives of methyl α-L-rhamnopyranoside were also measured in 2-methylbutane (Merck). The low-temperature measurements down to −160°C were performed with derivatives of xylopyranoside and glucopyranose in methanol–ethanol (1 : 4). Concentration of the solutions (measured with Dichrographe III Jobin-Yvon, equipped with a cryostat) was 0·5—2 mg ml^{-1} at a cell length 1 and 5 mm.

RESULTS AND DISCUSSION

Monoacetyl Derivatives

The circular dichroism (CD) parameters of monoacetyl derivatives are listed in Table I. All derivatives displayed a single dichroic band associated with an $n\rightarrow\pi^*$ electronic transition. Position of its maximum is located at 205 – 220 nm. Due to 2,2,2-trifluoroethanol a greater shift of the maximum of the dichroic band $n\rightarrow\pi^*$ was observed, as a result of an interaction of the solvent with the carbonyl group chromophore, where the solvent acts as proton donor. The presented data let us suggest that circular dichroism is considerably influenced by a relative configuration of the acetyl group in relation to vicinal substituents. The predicted sign of CD according to the afore-mentioned empirical correlation[6] is listed in the last column of Table I.

It is probable that the optical rotatory strength of the $n\rightarrow\pi^*$ transition of monoacetyl derivatives originates by a one-electron mechanism[16]. The electronic transition $n\rightarrow\pi^*$ has its own magnetic dipole transition moment. The required parallel component of the electric dipole transition moment originates by a perturbance interaction associated with the $\pi\rightarrow\pi^*$ transition of the same chromophore under influence of the vicinal hydroxyl or methoxyl group charges. It could be deduced that change in orientation of vicinal oxygen-containing group connected with the change



A *B*

of dihedral angle (see *A*, *B*) resulted in an orientation change of the electric transition moment[17]. Consequently, a change of the CD sign takes place.

All CD spectra of monoacetyl derivatives under investigation show a dominant effect of charge at the neighbouring oxygen atom. Intensity of this effect depends upon the magnitude and distance of the charge; the intensity could be, however, enhanced or lowered by the solvent effect. The decisive role plays here the sign

TABLE I

The CD parameters of saccharide acetates

Acetyl	$\Delta\varepsilon$ (λ, nm)		$\Delta\varepsilon$ (215 nm)[b]		Predicted sign, ref.[6]
	CH_3CN	TFE[a]	20°C	−140°C	
		Methyl β-D-xylopyranosides			
2-O-	−0·219 (211)	−0·303 (207)	−0·243	−0·487	−
3-O-	−0·016 (214)	−0·063 (207)	−0·022	−0·080	+−
4-O-	0·371 (212)	0·275 (209)	0·439	0·942	+
2,3-Di-O-	−0·315 (212)	−0·503 (207)	0·054	−0·291	+
2,4-Di-O-	0·423 (214)	0·176 (206)	0·302	0·586	+
3,4-Di-O-	0·371 (212)	0·619 (208)	0·065	0·307	−
2,3,4-Tri-O-	0·068 (215)	−0·110 (210)	0·025	0·817	+
		1,6-Anhydro-β-D-glucopyranoses			
2-O-	−0·034 (218)	0·128 (207)	−0·088	0·022	−
3-O-	−0·087 (210)	0·073 (210)	0·015	−0·265	
4-O-	0·050 (215)	−0·057 (205)	0·103	−0·181	+
2,3-Di-O-	−0·365 (214)	−0·257 (209)	−0·197	−0·611	−
2,4-Di-O-	0·173 (214)	—	0·251	0·780	+−
3,4-Di-O-	0·201 (213)	0·389 (208)	0·212	0·080	+
2,3,4-Tri-O-	−0·450 (215)	0·076 (205)	0·117	−0·421	+−
		Methyl di-O-methyl- and mono-O-methyl-α-L-rhamnosides			
2-O-	−0·165 (212)	−0·101 (208)			−
3-O-	−0·258 (214)	−0·189 (214)			−
4-O-	0·194 (212)	0·214 (212)			−
2,3-Di-O-	−0·488 (210)	−0·190 (207)			−
2,4-Di-O-	−0·288 (213)	−0·166 (210)			−
3,4-Di-O-	−0·146 (219)	−0·112 (215)			−

[a] 2,2,2-Trifluoroethanol; [b] measured in methanol–ethanol (1 : 4).

of dihedral angle what is in line with preceding findings[6-8]. The ($^1C_4$, $^4C_1$) conformation of the pyranose ring is implicite manifested at this dihedral angle.

A concurrent effect of the $C_{(1)}$ methoxyl group and $C_{(3)}$ hydroxyl group charges was observed with methyl 2-O-acetyl-β-D-xylopyranoside. The observed CD is negative, what indicates, in line with the preceding finding, the prevalent influence of the hydroxyl group. The methoxyl group in given orientation contributes to a positive sign of CD. As known[18], a delocalization of charge occurs with acetate grouping, so that the effective charge at the glycoside oxygen is smoller in comparison with the localized charge in other positions of the pyranose ring. A noticeable manifestation of this effect has been observed with analogous 2-N-acetylglycosides[19,20]. The sign of the long-wavelength CD of these compounds is not sensitive towards a change of anomeric configuration; it undergoes, however, change when rotating around the $C_{(3)}$—OH bond. The negative CD of methyl 2-O-acetyl-D-glucopyranosides and methyl 2-O-acetyl-D-galactopyranosides[6] proves this conception, as well. Considering the one-electron mechanism, the decisive role obviously plays the magnitude of the charge of the vicinal oxygen atom, whilst the minor one belongs to the type of this group (OH or OCH_3).

Interaction of the solvent weakens, as a rule, the intramolecular interactions. No sign change of CD has been observed due to a solvent change in a series of *xylo*-monoacetyl derivatives in contrast to N-acetyl analogues[19-21], what can be rationalized by a possibility to form inherently chiral non-planar conformations of N-acetyl group. These conformations are sensitive to the influence of surroundings[22,23] in contrast to O-acetyl grouping, where this kind of conformations has not been found as yet.

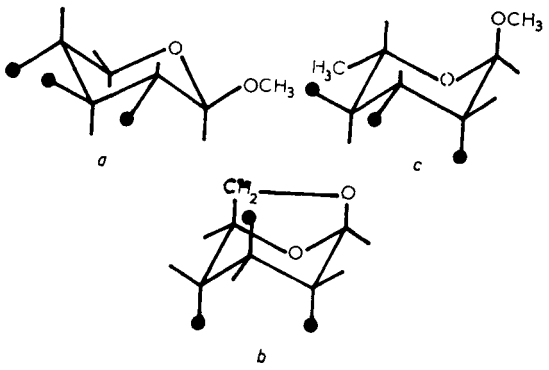


FIG. 1

Structures of *a* methyl β-D-xylopyranoside ($^4C_1$); *b* 1,6-anhydro-β-D-glucopyranose ($^1C_4$); *c* methyl α-L-rhamnopyranoside ($^1C_4$) with indicated (●) potential positions of acetyl group

The 1,6-anhydro-D-glucose derivatives display a low intensity of dichroic absorption. The decisive perturbance action of the charge in 2-O-acetyl and 4-O-acetyl derivatives, comes from the vicinal oxygen of the pyranose ring whilst in 3-O-acetyl derivative responsible for this action is probably the spatially close $O_{(6)}$ oxygen of the anhydroring. The $(^1C_4)$ conformation with functional groups in axial positions makes the attack of the solvent easier. The change of the solvent character changes also the CD sign. In acetonitrile, which does not interact with the chromphore, the signs of CD are in agreement with the above-mentioned spatial correlation of the perturbance action of the charge and, at the same time, in accordance with signs of the respective position isomers of *xylo*-derivatives. On the other hand, reverse signs of CD were observed in 2,2,2-trifluoroethanol, which meaningfully interacts with an acetyl group, due to change of interactions and possibly to conformations of functional groups.

The conformational equilibrium of methyl α-L-rhamnopyranoside derivatives is shifted to $^1C_4$ conformation (Fig. 1). The 2-O-acetyl- and 3-O-acetyl derivatives have their CD signs in line with the theoretical consideration, the 4-O-acetyl derivative, where a negative CD sign would be anticipated, displays a positive dichroic band in both polar solvents. Measurement in 2-methylbutane afforded, however, the expected negative CD ($\Delta\varepsilon = -0{\cdot}09$; 219 nm). The 2-O-acetyl and 3-O-acetyl derivatives showed in this solvent following values: $\Delta\varepsilon = -0{\cdot}18$ at 214 nm and $\Delta\varepsilon = -1{\cdot}13$ at 218 nm. This was caused by solvatation, the effect of which eliminated with 4-O-acetyl derivative the vicinal methoxyl group charge effect.

Di- and Tri-Acetyl Derivatives

The CD parameters of diacetyl- and peracetyl derivatives are presented in Table I. All compounds reveal only one dichroic band of $n\rightarrow\pi^*$ transition which obviously embodies optically active electronic transition of two or three acetyl groups. The sign of CD predicted by employing the empirical rule[6,7] is given in the last column in Table I. This rule, based in principle on the application of one-electron mechanism is not, in some cases (2,3-di-O-acetyl- and 3,4-di-O-acetyl-β-D-xylopyranoside) reliable. It is our opinion that a mutual electronic interaction of two close acetyl groups has to be taken into account. Due to this, the predominant mechanism of rotational strength probably becomes the $\mu-m$ one ($n\rightarrow\pi^*$ transition), alternatively the mechanism of coupled oscillators ($\pi\rightarrow\pi^*$ transition); the mutual orientation of acetyl groups is anyway decisive for both mechanisms. According to qualitative MO theory[17] the orientation of the appropriate electric ($\boldsymbol{\mu}$) and magnetic ($\boldsymbol{m}$) dipole transition moments can be deduced (Fig. 2). The induced magnetic moment ($\boldsymbol{m}$) of the $n\rightarrow\pi^*$ transition originates by an attractive dipole–quadrupole interaction, since the $n\rightarrow\pi^*$ transition is of lower energy. Different orientation of acetyl groups (various dihedral angle) plotted in Fig. 2 leads to a different orientation of transitional

moments. The consonant orientation of $\boldsymbol{m}$ and $\boldsymbol{\mu}$ (right side, Fig. 2) results in a positive Cotton effect, the inconsonant one of $\boldsymbol{m}$ and $\boldsymbol{\mu}$ (left hand side, Fig. 2) in a negative Cotton effect. This correlation is in a formal accord with the preceding correlation[6,7]. Nevertheless, we consider the mutual effect of acetyl groups in a *gauche* orientation as dominant, exceeding the effect of other vicinal groups. It leads, with the above-mentioned diacetylxylopyranosides to CD signs according with experimental observations.

Derivatives of 1,6-anhydro-β-D-glucopyranose have the neighbouring acetyl groups in a *trans*-axial position, so that their mutual interaction does not take place. The optical activity is induced, similarly as with monoacetyl derivatives, due to the charge of vicinal oxygen atoms of rings. The increments of optical rotatory strength of 2,3- and 3,4-di-O-acetyl derivatives coming from the interaction of acetyl groups and those associated with the vicinal methoxyl groups are of the same negative sign.

Low-Temperature Measurements

The low-temperature measurement can evidence whether the CD sign found really represents the manifestation of predominant conformation. Low temperature makes the preferred conformation stabilized, although the inter- or intramolecular inteactions increase. As a rule, the optical activity of a given sign becomes more pregnant when dropping the temperature of *xylo*-derivatives (CD positive with 2,3,4-tri-O-acetyl, *xylo*-derivative). Noteworthy is the course of methyl 2,3-di-O-acetyl-β-D-xylopyranoside, which is homomorphous with methyl 2,3-di-O-acetyl-β-D-glucopyranoside[7]. The positive CD of low intensity decreases with lowered temperature and becomes negative. The more stable structure even in a mixture of alcohols is that with an opposite CD sign, than found at room temperature.

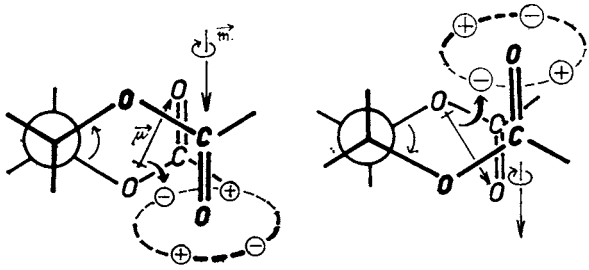


FIG. 2

Arising of optical activity of diacetyl derivatives of saccharides by μ–m mechanism — interaction of a dipole of electrically allowed transition ($\pi \rightarrow \pi^*$) with an electric quadrupole of magnetically allowed transition ($n \rightarrow \pi^*$)

Several derivatives of 1,6-anhydroglucopyranose show a change of the CD sign, when cooled; this is associated with a more significant effect of interactions with the solvent. The 2-O-acetyl- and 4-O-acetyl derivatives changed their CD sign, which was originally found in 2,2,2-trifluoroethanol solutions. On the other hand, the sign of 3-O-acetyl- and 2,3,4-tri-O-acetyl derivatives changes into that determined in acetonitrile.

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Translated by Z. Votický.