Configurational and Conformational Studies of Sugars by the Aromatic Chirality Method

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Summary The dibenzoate chirality method can be extended to the sugar series and enables the hydroxyl configurations of sugar conformations to be determined unambiguously.

THE following data indicate that the dibenzoate chirality method[1] or its extension,[2] for which we suggest the more general term "The Aromatic Chirality Method"[3] (since it is applicable to aromatic chromophores other than benzoates[2,3]), can be applied in a straightforward manner to various diols and triols. The chiralities of these aromatic chromophores are in agreement with results of nonempirical calculations.[3,4]

The data permit assignments of relative configurations or enables one to determine the preferred conformation (1*C* or *C*1); it also reflects subtle conformational distortions caused by steric interactions. Only a few mg of sugar are required for this method because the great intensities of Cotton effects necessitate usage of very dilute solutions; furthermore, the benzoates can readily be separated from unreacted sugars by t.l.c.

Pyranose and furanose diols. Two interacting benzoate chromophores give rise to a Davydov-type splitting in the c.d. spectra, the wavelengths and amplitudes of Cotton effects of which depend on the nature of the particular benzoate group as summarised in Table 1.

The *p*-chlorobenzoates have been used in the present studies because the two Cotton effects appear in a region more readily measurable as compared to unsubstituted benzoates (Table 1). Other *para*-substituted benzoates exhibiting Cotton effects at even longer wavelengths,[1,5] could have been used but as the long axis (intramolecular charge-transfer transition) and short axis ($^1A_{1g} \rightarrow {}^1B_{2u}$)

transitions overlap, theoretical treatment becomes more complex (for practical purposes, however, this aspect is no obstacle).

TABLE 1. *Positions of u.v. and c.d. peaks of benzoates*

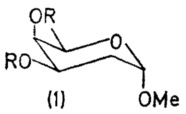
Benzoates	U.v. maxima	C.d. of noninteracting monobenzoate	C.d. of interacting dibenzoates 1st	2nd
Unsubstituted dibenzoates	230 nm	227 nm ($\Delta\epsilon$ *ca.* 3)	233 ($\Delta\epsilon$ 10—15)	219 ($\Delta\epsilon$ 10—15)
Di-*p*-chlorobenzoates	240 nm	235 nm ($\Delta\epsilon$ *ca.* 5)	247 ($\Delta\epsilon$ *ca.* 20)	229 ($\Delta\epsilon$ *ca.* 20)

TABLE 2. *Di-*p *chlorobenzoate Cotton effects of sugars in methanol*[a]

	Compound[b,c]	Chirality	Cotton effects $\Delta\epsilon$ (nm) 1st	2nd
(1)	α-Methyl-2,6-dideoxy-D-galactopyranoside 3,4-[8,9]	(+)	+17·2(246)	− 7·2(229)
(2)	β-Methyl-2,6-dideoxy-D-galactopyranoside 3,4-[8,9]	(+)	+28·9(246)	−7·5(229)
(3)	β-Methyl-2,6-dideoxy-D-glucopyranoside 3,4-[8,9]	(−)	−29·0(245)	+14·5(230)
(4)	α-Methyl-2,6-dideoxy-D-glucopyranoside 3,4-[8,9]	(−)	−37·1(246)	+17·1(229)

[a] Glycosides received from Drs. Berlin, Kolosov (Moscow). [b] Positions of the *p*-chlorobenzoyloxy-groups follow compound name. [c] R; *p*-Cl·C_6H_4CO·.

As seen from Table 2, the predicted and observed chiralities are in agreement without exception. However, the $\Delta\epsilon$ values are spread over a wide range, *i.e.*, from 17·2 to 37·1, and are in general larger than values encountered in other diols[1] of more rigid systems, such as steroids. This is due to distortion of the monocyclic ring from the standard chair conformation. When the dihedral angle between the benzoate groups is 180°, theoretically no interaction should occur.[3] The c.d. of the diaxial di-*p*-chlorobenzoate of α-methyl-4-*O*-methyl-6-deoxy-D-altroside (11; R = *p*-Cl·-C_6H_4CO·), showed only a single Cotton effect at the perturbed wavelength of 247 nm ($\Delta\epsilon$ −10·5). The wavelength and negative sign of the relatively weak Cotton effect suggests that the diaxial benzoate groups are distorted in the direction expected from models.[6] The second Cotton effect is presumably too weak to be observed. A similar case has been encountered in a steroidal 2β,3α-diaxial dibenzoate.[7]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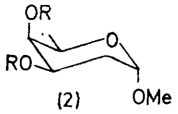
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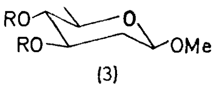
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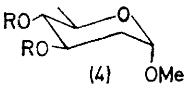
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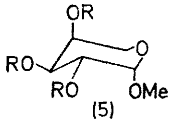
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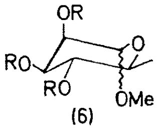
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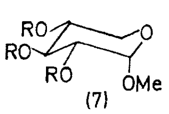
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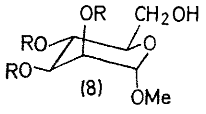
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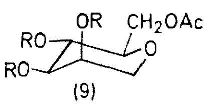
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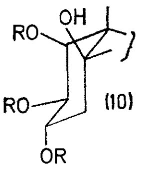
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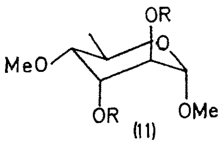
(11)

For furanose systems, we have already reported[1] that two anomeric methyl riboside dibenzoates adopt inverse conformations.

Triols. In the case of triols, two aspects of practical importance are apparent. Namely, if the 1,2,3-triol moiety is such that the chiralities between the 1,2-, 2,3-, and 1,3-dihydroxy-groups are all negative or positive, the first Cotton effect amplitudes are greatly augmented and have large values of minus or plus *ca.* 80. In contrast, when opposing chiralities are present, the rotatory powers of interacting chromophores cancel out and no clearcut Davydov-split Cotton effects are observed (Figure).

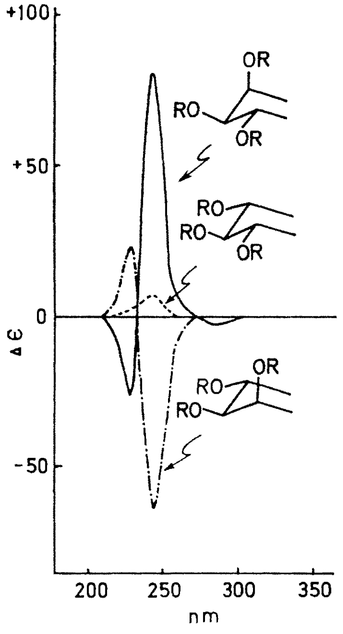

FIGURE. *C.d. spectra of tri-*p*-chlorobenzoate of sugars.* (———), *α-methyl-L-arabinoside 2,3,4-tri-*p*-chlorobenzoate*; (– – – – – –) *α-methyl-D-xyloside 2,3,4-tri-*p*-chlorobenzoate*; (-·-·-·-·-), *α-methyl-D-mannoside 2,3,4-tri-*p*-chlorobenzoate.*

The present rule is applicable in exactly the same manner to more rigid systems (kogagenin,[10] a 1β,2β,3α-steroidal saponin, Table 3). The interaction still operates between more remotely located benzoate groups, as exemplified by

TABLE 3. *C.d Cotton effects of tri-*p*-chlorobenzoates*

Entry	Compound[a,b,c]	Chirality	$\Delta\epsilon$ (nm) 1st	2nd	Solvent[d]
(5)	α-Methyl-L-arabinopyranoside 2,3,4-	(+)	+81·3(246)	−25·6(230)	H
(6)	Methyl-L-rhamnopyranoside 2,3,4-	(+)	+78·1(245)	−17·3(230)	H
(7)	α-Methyl-D-xylopyranoside 2,3,4-	0	+8·3(244)		E
(8)	α-Methyl-D-mannopyranoside 2,3,4-	(−)	−62·8(248)	+24·7(230)	E
(9)	α-Methyl-D-mannopyranoside 6-acetate 2,3,4- ..	(−)	−63·8(247)	+30·0(231)	E
(10)	Kogagenin 1,2,3- (T)	(+)	+85·6(247)	−36·6(230)	E

[a] Positions of *p*-chlorobenzoyloxy-groups follow compound name. [b] R; *p*-Cl·C_6H_4CO·. [c] Sample received from: (T), Dr. K. Takeda, Shionogi Co. [d] H, n-hexane; E, ethanol.

ajugasterone C, which has three benzoate groups on C-3, C-2, and C-11 of the steroid nucleus.[10]

A theoretical treatment of the triol benzoates is in agreement with the present experimental results.[3]

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[7] Ref. 1, Table I, Entry 3: (5α-cholestane-2β, 3α-diol dibenzoate).

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