Circular Dichroism of the Isotopically Dissymmetric Molecules (1R,2S)-[1-²H]- and (1R,2S)-[1-¹⁸O]-1,2-Dihydroxy-1,2-diphenylethane

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Summary The circular dichroism of the related pair of isotopically dissymmetric molecules (1R,2S)-[1-²H] and (1R,2S)-[1-¹⁸O]-1,2-dihydroxy-1,2-diphenylethane allows the time-averaged conformation of achiral *meso*-hydrobenzoin to be rather closely defined.

(1)   (2)

(3)   (4)

Optical activity of isotopically dissymmetric molecules has been widely observed,[1] and the c.d. of such molecules possessing a chromophoric group can provide information concerning their conformation.[2] Only the carbonyl group has been used as a chromophore in such studies so far and the isotope has been almost invariably deuterium, although molecular dissymmetry due to isotopic oxygen can give rise to measurable optical activity[3] and c.d. [4,5] The elegant study of the Leiden school on the synthesis and c.d. of (1R)-[1-²H]- and (1R)-[2-¹⁸O]-α-fenchocamphoronequinone (1 and 2)[4,6] together with theoretical calculations on these systems,[7] is the first reported investigation by c.d. of a pair of related isotopically dissymmetric molecules. With a view to exploring a conformationally mobile system by c.d. the isotopically dissymmetric diol (3) was prepared; the related diol (4) was available from a previous investigation.[5]
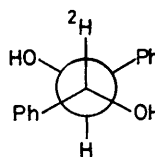
Reduction of benzoin with lithium aluminium hydride at 0 °C gives *meso*-hydrobenzoin in high yield.[8] (1R,2S)-[1-²H]-1,2 Dihydroxy-1,2-diphenylethane (3) was prepared
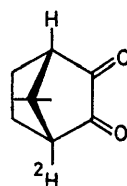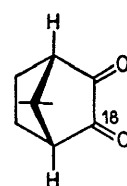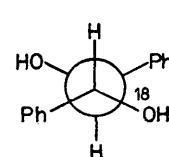
(81%) by reduction of (S)-benzoin[5] with lithium aluminium deuteride; (1R,2S)-[1-¹⁸O]-1,2-dihydroxy-1,2-diphenylethane (4) had been prepared by reducing (1S)-[2-¹⁸O]-benzoin with lithium aluminium hydride.[5] The u.v. and c.d. spectra of the diols (3) and (4) are shown in Figure 1 and the data are
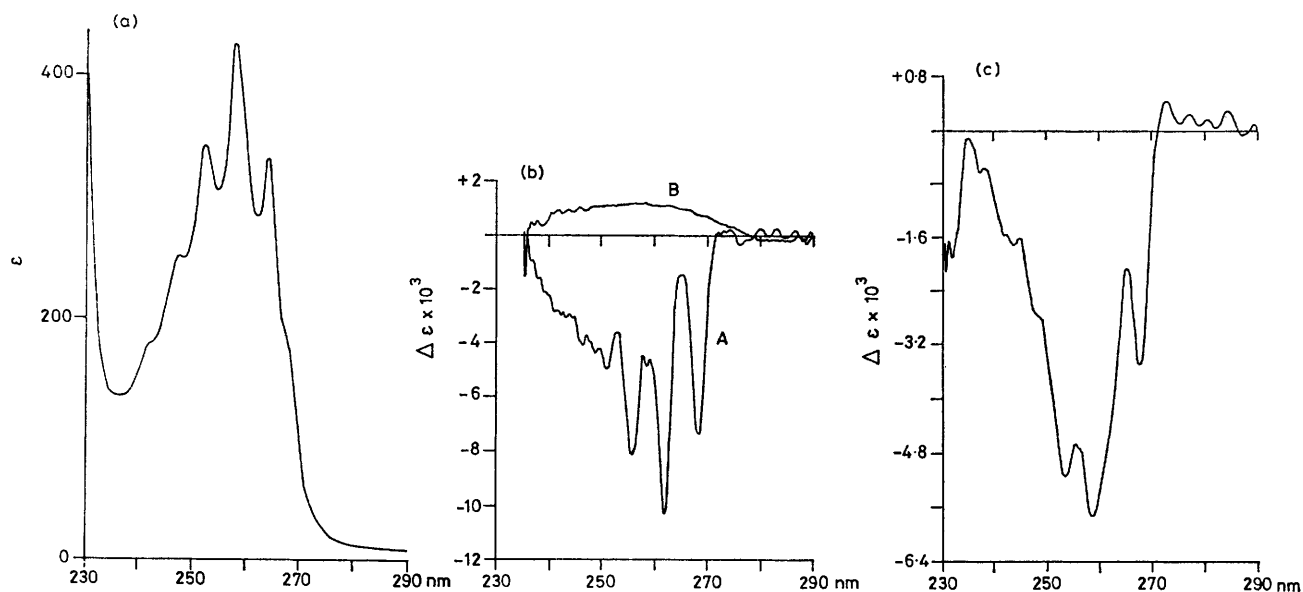
FIGURE 1. (a) The u.v. spectrum of $(1R,2S)$-$[1$-$^2H]$-1,2-dihydroxy-1,2-diphenylethane (3); (b) the c.d. spectra of (3) (A, 2·29 mM) and *meso*-hydrobenzoin (B, 3·21 mM) formed by LiAlH$_4$ reduction of (S)-benzoin (each spectrum is the average of 4 scans with the baseline subtracted); (c) the c.d. spectrum of $(1R,2S)$-$[1$-$^{18}O]$-1,2-dihydroxy-1,2-diphenylethane (4) (2·50 mM) (the spectrum is the average of 24 scans with the baseline subtracted). The c.d. spectra were determined in ethanol (1 cm path length) on a Jasco J41C spectrometer with a 16 s time constant and are smoothed. The limit of error is best represented by the c.d. spectrum of *meso*-hydrobenzoin (b, B).

analysed in the Table. To establish that the c.d. spectra were not due to trace impurities, (S)-benzoin was reduced with lithium aluminium hydride; the *meso*-hydrobenzoin obtained showed no fine structure in the c.d. spectrum (figure 1b, B) which would have been indicative of (1S,2S)-1,2-dihydroxy-1,2-diphenylethane.

The sector rule governing the ^1L_b electronic transition (centred at *ca.* 260 nm) for monosubstituted benzenoid molecules is depicted in Figure 2a.[9] Since benzylic substituents will in general fall into four sectors defined by the nodal planes passing through C(1), C(2), C(6), and the plane of the ring itself, the quadrant rule depicted in Figure 2b is satisfactory.

Deuterium gives rise to a lower bond polarizability than hydrogen,[10] which is principally caused by its shorter average bond length.[7] Likewise ^{18}O should give rise to a lower bond polarizability than ^{16}O. If this is so, since both
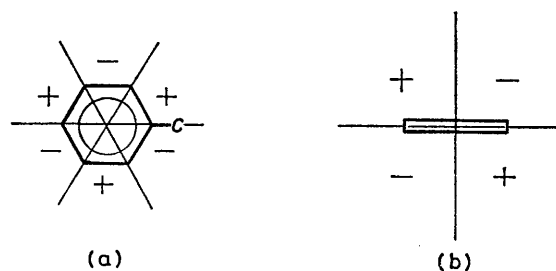

FIGURE 2. (a) The sector rule for the c.d. of the ^1L_b band of a benzyl chromophore; the plane of the ring is also a nodal plane. The signs shown are for the sectors above the plane of the ring, those below are of the opposite sign. (b) The simplified sector rule showing the signs of the sectors into which benzylic substituents will generally fall; the observer is *para* to the benzylic group.

TABLE. Spectroscopic data for $(1R,2S)$-$[1$-$^2H]$-1,2-dihydroxy-1,2-diphenylethane (3) and $(1R,2S)$-$[1$-$^{18}O]$-1,2-dihydroxy-1,2-diphenylethane (4) in ethanol

Compound (3)							Compound (4)						
u.v.			c.d.				u.v.			c.d.			
$\lambda_{max}/$ nm	$\bar\nu/$ cm^{-1}	$\Delta\bar\nu/$ cm^{-1}	$\lambda_{max}/$ nm	$\Delta\epsilon$ $\times 10^3$	$\bar\nu/$ cm^{-1}	$\Delta\bar\nu/$ cm^{-1}	$\lambda_{max}/$ nm	$\bar\nu/$ cm^{-1}	$\Delta\bar\nu/$ cm^{-1}	$\lambda_{max}/$ nm	$\Delta\epsilon$ $\times 10^3$	$\bar\nu/$ cm^{-1}	$\Delta\bar\nu/$ cm^{-1}
267·5	37380		268·4	−6·25	37260		267·5	37380		267·5	−3·40	37380	
		560				960			570				1300
263·6	37940		261·6	−7·40	38220		263·5	37950		258·5	−5·68	38680	
		880				960			880				840
257·6	38820		255·2	−6·02	39180		257·5	38830		253	−5·08	39520	
		860							850				800
252	39680						252	39680		248	−2·80	40320	
		810							810				830
247	40490						247	40490		243	−1·60	41150	
		830							830				
242	41320						242	41320					

the diols (3) and (4) show negative c.d. the C–²H bond in the diol (3) and the C–¹⁸OH bond in the diol (4) must fall into a positive quadrant and hence the C–H bond in the diol (3) and the C–OH bond in the diol (4) into a negative quadrant in the time-averaged conformation. Making the reasonable assumption that the time-averaged conformation of the diols (3) and (4) are the same, then the C–²H bond in the diol (3) and the C–¹⁸OH bond in the diol (4) must fall into the two alternative positive quadrants.

The absence of a c.d. couplet in the c.d. spectra of the diols (3) and (4) indicates a lack of interaction between the benzene rings, suggesting that the potential hydrogen-bonding between the hydroxy groups which would hold the two phenyl groups in close proximity is effectively suppressed by solvent ethanol. Since the differential dichroic absorption ($\Delta\epsilon$) is only slightly greater for the diol (3) than for the diol (4) the C–²H bond in the diol (3) must be closer to a nodal plane than the C–¹⁸OH in the diol (4). These considerations make it possible to rather closely define the time-averaged conformation of the achiral *meso*-hydrobenzoin (Figure 3) from the c.d. of the diols (3) and (4).
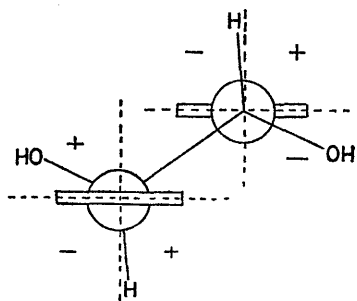

FIGURE 3. The approximate time-averaged conformation of *meso*-hydrobenzoin deduced from the related isotopically dissymmetric diols (3) and (4), showing also the sign of the quadrants associated with each benzylic species.

The simplicity of the vibronic fine structure in the c.d. spectrum of the diol (3) allows the spectrum to be readily analysed (Figure 1b, A). The 268·4 nm peak is assignable to the O–O transition of the ^1L_b band and the spacings between the higher energy transitions are 960 cm⁻¹. This c.d. active vibronic transition is assignable to the $A_{1g}(\nu_2)$ totally symmetric 'breathing' vibration of the excited state of the benzyl chromophore. The O–O transition as expected is absent from the u.v. spectrum which consists of a series of overlapping progressions (Figure 1a), none of which correspond with that observed in the c.d. spectrum. Although the frequencies can be determined from the low energy end of the spectrum (Table), their assignment to particular vibrational modes is uncertain.

By contrast, the vibronic transitions in the c.d. spectrum of the diol (4) are strikingly similar to those in the u.v. spectrum (Figure 1c and Table). The dominant progression in each spectrum has a frequency of *ca*. 830 cm⁻¹. The apparent absence of a peak near 264 nm in the c.d. spectrum could well be due to a weaker progression preventing its resolution; an inflection of this wavelength is evident. Thus the c.d. spectrum is more complex than that of the diol (3) and is dominated by a different vibronic transition.

This investigation shows for the first time that c.d. of the inherently achiral benzyl chromophore can be observed where chirality is caused by isotopic dissymmetry. The study of pairs of related isotopically dissymmetric molecules such as the diols (3) and (4) provides a useful approach to the study of the conformation in solution of otherwise achiral molecules.

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