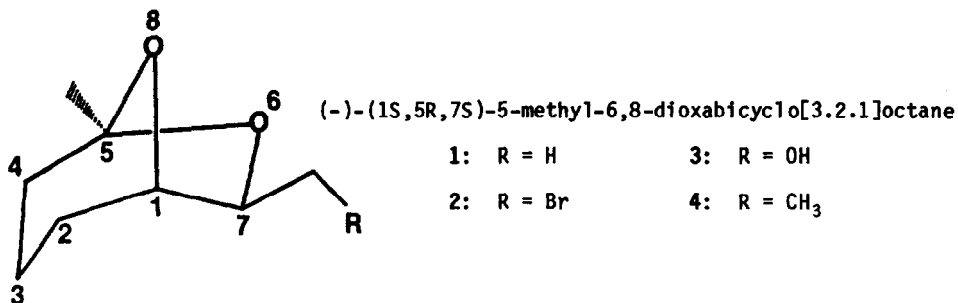


**DETERMINING THE ABSOLUTE CONFIGURATION OF EXO-7  
DERIVATIVES OF 5-METHYL-6,8-DIOXABICYCLO[3.2.1]OCTANE BY VCD**

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**Abstract.** The VCD spectra in the region of 1100-1400  $\text{cm}^{-1}$  of four derivatives of 5-methyl-6,8-dioxabicyclo[3.2.1]octane reveal common features which indicate the absolute configuration of the bicyclic ketal ring system. One of these in particular can serve as a more general configurational marker for the chiral unit  $-\text{C}^*\text{H}(\text{CH}_2\text{R})\text{X}-$ , X = O and S, when contained in different size ring molecules.

Vibrational circular dichroism (VCD) spectra offer the unique opportunity to determine relatively quickly and easily the absolute configuration of a chiral compound. While this can be achieved in principle by theoretical means in conjunction with the observed spectra, problems of exact formulation for the magnetic dipole transition moment and computational complexities still preclude such calculations for any but the smallest of chiral compounds.<sup>1</sup> Moreover, it is unlikely that such calculations will become routine within the foreseeable future. Alternatively, the VCD spectra for molecules with similar structure can be compared in order to isolate those VCD bands and/or sign patterns which are characteristic of certain common structural features.<sup>1</sup> We wish to report here the observation of VCD bands for four exo-7 derivatives of 5-methyl-6,8-dioxabicyclo[3.2.1]octane which have sign patterns that are characteristic of specific enantiomers.



The synthesis of the compounds will be described in detail elsewhere. The chirality was induced by Sharpless epoxidation of (Z)-7-oxo-2-octen-1-ol using chiral diethyl

tartrates.<sup>2</sup> The enantiomeric purity was at least 90% ee as determined by chiral complexation chromatography (25 m × 0.25 mm fused silica OV-1, 0.25 micron coated with Ni-4-Pin, supplied by CC & CC, FRG). The VCD spectra were obtained with a Nicolet 8000 FT spectrometer incorporating the VCD attachments specified by Nafie and Diem.<sup>3</sup> For each enantiomer, in CCl<sub>4</sub> solution in convenient concentrations (0.2 to 0.5 M) and contained in 0.1 mm KBr cells, 20 000 scans were accumulated with a nominal unapodized resolution of 4 cm<sup>-1</sup>. The appropriate sections of the VCD spectra are displayed in Fig. 1.

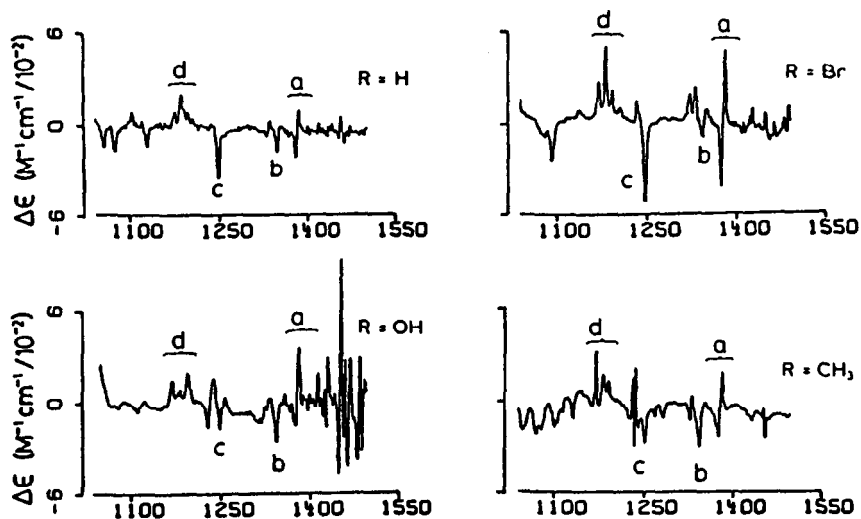
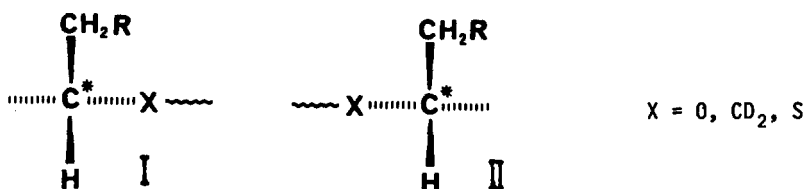


Figure 1. VCD spectra of the (-)-(1S,5R,7S) enantiomers of derivatives of 5-methyl-6,8-dioxabicyclo[3.2.1]octane. The region above 1400 cm<sup>-1</sup> is unreliable particularly for R = OH due to atmospheric absorptions.

The most prominent common feature is the bisignate band near 1380 cm<sup>-1</sup>, labelled a in Fig. 1. The negative lobe at lower frequency, for the (-)-(1S,5R,7S) enantiomer, can be assigned unambiguously to a vibration which consists principally of the "out-of-plane" C-H bend on C(7), based on STO-3G *ab initio* force field calculations for 1 and the C(7)D<sub>3</sub> isotopomer, and on the vibrational spectra of the completely unsubstituted analog.<sup>4</sup> Clearly this band serves to indicate the absolute configuration of this series of bicyclic ketals. Moreover, we suggest that it is more widely applicable as a configurational marker for other ring molecules. Namely, the same vibration in 2-methyloxetan, 3-methyloxetan-2,2-d<sub>2</sub>, and

2-methylthietan, assigned on the basis of extensive analyses of the vibrational spectra of deuterated isotopomers and 3-21G scaled *ab initio* force fields, gives rise to similar prominent bands in the less congested spectra, always negative for the configuration I below and positive for II.<sup>4</sup> Further confirmation is afforded by the VCD spectra of propylene oxide<sup>5</sup> and sulfide<sup>6</sup> for which the same correlation exists.



The positive lobe of the a-couplet, for the (-)-(1S,5R,7S) configuration, clearly arises from the symmetric CH<sub>3</sub> deformation of the methyl group on C(5). It is a conspicuous band in a position which is normally clear from interference. The deformation of the additional methyl group in 4 and that on C(7) in 1 appear to have little or no VCD intensity. In 2-methyloxetan<sup>4</sup> and propylene oxide<sup>5</sup> the same vibration results in an equally prominent VCD band. In 2-methylthietan<sup>4</sup> and propylene sulfide,<sup>6</sup> however, its VCD intensity is near zero, while for 3-methyloxetan-2,2-d<sub>2</sub> it shows the opposite VCD sign to that for 2-methyloxetan with the same configuration at the asymmetric carbon.<sup>4</sup> Evidently electronic effects contribute to the VCD intensity of the CH<sub>3</sub> symmetric deformation mode and the mechanism of this contribution is not clear at this stage. The usefulness of this VCD band as a configurational marker is therefore limited for the moment, providing consistent VCD signs only within certain series of molecules, such as the derivatives of 5-methyl-6,8-dioxabicyclo[3.2.1]octane, or monocyclic ethers containing the chiral unit -C\*H(CH<sub>3</sub>)O-.

The spectra in Fig. 1 show additional common features. While approximate assignments can be provided with the help of the *ab initio* force field, the modes appear to be mixed to a greater extent than the two previously mentioned. In the absence of other corroborative evidence these bands cannot yet be classified as marker bands in general, although they may be useful for indicating the configuration of the derivatives of 5-methyl-6,8-dioxabicyclo[3.2.1]octane and perhaps also of related bicyclic ketals. These bands are labelled b

( $\sim 1350\text{ cm}^{-1}$ ), c ( $\sim 1250\text{ cm}^{-1}$ ), and d ( $\sim 1175, 1185, 1200\text{ cm}^{-1}$ ) in Fig. 1, approximately corresponding, respectively, to C(1)-H "out-of-plane" bend, C(1) and/or C(7) C-H "in-plane" bend, and wagging/twisting vibrations of the  $\text{CH}_2$  groups on the 6-membered ring. Further investigations in order to properly characterize these bands by also varying the methyl substitution are in progress.

Similar characteristic VCD bands which in certain instances may be used for identifying absolute configurations have been observed for methine and methyl C-H stretching vibrations when either one or both groups are attached to an asymmetric centre. The intensity of such VCD signals is particularly enhanced if the chiral unit is part either of a covalently or hydrogen bonded ring, and is sensitive to the unit's inter- and intramolecular environment.<sup>7,8</sup>

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