Vibrational Optical Activity. Circular Differential Raman Scattering from a Series of Chiral Sulfoxides

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Abstract: Circular differential Raman scattering is the difference in scattering intensity that is observed for left and right circularly polarized incident light impinging upon an optically active medium. The differential scattering associated with the various vibrational modes of chiral molecules is related to their absolute configurations. Differential scattering from a series of simple optically active sulfoxides is reported and a correlation between the absolute configurations and the differential scattering associated with common vibrational modes is discussed. The effect may ultimately provide a routine method for determining absolute configurations.

Of all the stereochemical features of molecules, the determination of absolute configuration remains the last structural characteristic which, as yet, is not subject to routine spectroscopic determination. Only the anomalous x-ray scattering method is capable of providing unambiguous assignments for crystalline chiral substances.

With the advent of commercial dichrographs and the preceding spectroscopic developments, electronic circular dichroism aroused high expectations, particularly with the initial success of the octant rule for cyclic ketones and the use of nonempirical methods.[1] It soon became apparent, however, that the nonempirical methods encompassed only a narrow range of chromophores and that the empirical methods were limited by the growing number of exceptions to the postulated regional rules. The essential problem with the empirical rules is that the nature of the electronic modifications to the inherently symmetric chromophores by distant substituents is poorly understood. Thus, generally electronic circular dichroism provides absolute stereochemical information in an indirect way; the molecular dissymmetry is sampled, as it were, through the "eyes" of the slightly modified chromophore.

It is clear that a possible solution to this problem of indirect sampling of the dissymmetry is the development of spectroscopic techniques which would sample and respond to the groups and atoms which make up the molecular chirality. The most obvious spectroscopic methods, therefore, are those which are associated with molecular vibrations, infrared and Raman spectroscopy. The circular differential absorption and circular differential scattering which these techniques produce are weak and therefore difficult to observe with current instrumentation.

Theoretical calculations suggest that the infrared circular dichroism (IR-CD) is likely to be about two orders of magnitude smaller than the circular differential Raman scattering (CID).[3-8] Despite the smallness of these effects, Holzwarth[9] was the first to report IR-CD originating in the vibrations of a chiral molecule and, recently, Stephens[10] reported superb IR-CD spectra for a range of organic systems.

Some time ago we reported[11] CID's in α-phenylethylamine which were later confirmed by others.[12] We, however, were mistaken; the reported effects arose from the optical rotation of elliptically polarized light which gave the observed effect a deceptive plausibility in that the effect switched sign with enantiomers. The first genuine CID's were reported by Barron and Buckingham[13,14] and these were latter substantially confirmed by Hug.[15]

In this paper we confirm the major CID's of α-pinene reported previously and, in addition, we describe the CID's associated with a series of chiral sulfoxides which all have the same (known) absolute configuration (Figure 1). The sulfox-

ides were chosen because of their optical stability, their high scattering power, and because they provide a homologous series of related molecules. The ultimate object was to see whether a series of closely related molecules would give similar CID's for equivalent or similar vibrational modes.

I. Experimental Section

Preparation of Sulfoxides. The chiral sulfoxides were prepared by similar methods to those described elsewhere.[16] Those sulfoxides which were solids were purified by crystallization from cyclohexane after decoloring with animal charcoal. The liquids were purified by molecular distillation.

The spectra were run on the neat liquids and on nearly saturated methanol and methylene chloride solutions of the solids. Results obtained with the two solvents were in good agreement.

Data Collection. Raman scattering was excited with Ar^+ laser radiation and was collected at right angles to the incident beam by an $f/1$ lens after passing through a polarizer. Only scattered light polarized parallel to the scattering plane was collected and focused on the slit of a SPEX 1401 monochrometer. The photon counting system consisted of a cooled RCA photomultiplier tube, amplifier, and discriminator. Output pulses were routed to a synchronous counter which, when the laser beam was modulated, directed counts registered in each of the modulation half-cycles to two separate memories.

In order to observe circular differential scattering, the incident laser radiation was modulated between left- and right-circular polarization by means of a pockels cell (Lasermetrics). The modulation voltage was provided by a square wave generator switched at 200 Hz and stepped up to the required level by a transformer made for that purpose (Hammond Engineering, Waterloo, Ont.). Data were accumulated for a preset time, (usually 7 min) at a spectral location. Then a stepping motor advanced the grating to the next location. Photon counts were routed into the appropriate memory according to the sense of rotation of the electric vector of the circularly polarized incident light. The sum and difference of the two memories were printed in digital and analog form. Counts were only collected during a digitally clocked fraction of each half-cycle (approximately 80%) in order to avoid the slight initial voltage overshoot imposed on the pockels cell immediately after switching and in order to ensure identical accumulation times during the two half-cycles of conjugate polarization.

The digital output was used to plot the sum, a smoothed difference, and the smoothed difference divided by the sum as a function of reciprocal wavelength.

The alignment of the pockels cell is critical since large artifacts are generated if it is not properly aligned and fixed. The alignment was accomplished by passing the emergent laser beam through a glan polarizer, and then allowing the light to fall on a silicon photovoltaic cell. The tilt and yaw of the pockels cell was adjusted until identical signals were obtained for each of the two half-cycles for various analyzer settings.

Samples were contained in low strain quartz cells whose tilt and rotation could be adjusted. Cells were fixed to the sample table with a small disk of double sided tape so as to avoid clamping which could
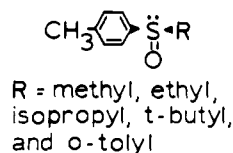
$$R = \text{methyl, ethyl,}$$
$$\text{isopropyl, t-butyl,}$$
$$\text{and o-tolyl}$$

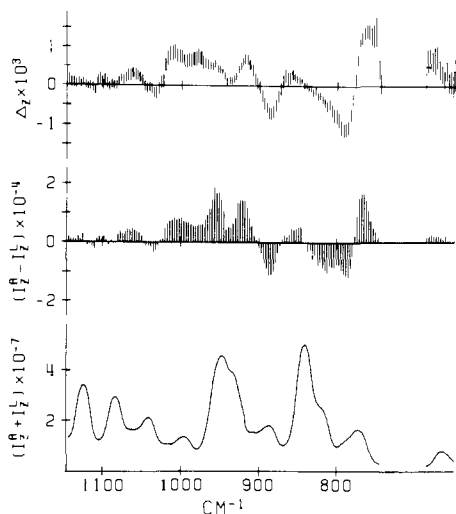**Figure 1.** The absolute configuration of the sulfoxides.

Figure 2. The sum, difference, and CID spectra of "neat" $(-)$-α-pinene recorded in parallel polarization. The isolated feature on the right is the strongly polarized 665-cm^{-1} band of α-pinene.

introduce visible changes in polarization of both the transmitted and scattered light.

II. Results

A. Artifacts. Raman circular differential scattering may be obtained either in parallel or perpendicular polarization with respect to the scattering plane. These are conventionally referred to as the depolarized and polarized components. We have found, as have others,[7,15] that the perpendicular scattering is subject to large artifacts which are critically dependent on the polarization state of the incident light. So far, we have been unable to control these artifacts in perpendicular polarization sufficiently to obtain reliable spectra and all the data given herein refer to the light vector scattered parallel to the scattering plane. Even for this polorization, large artifacts can be observed with bands which are strongly polarized. Despite the fact that we were able to control the artifacts for strongly polarized bands to within a few parts in 10^4, we make no claim to the authenticity of the effects observed associated with bands

marked p (polarized) in the spectra. Further, CID's which are less than 3×10^{-4} are not considered significant; CID's which we believe to be genuine are marked with an asterisk.

The CID is defined[6] as the dimensionless quantity Δ, which for the parallel (depolarized) scattering component is

$$\Delta_z = \frac{I_z{}^R - I_z{}^L}{I_z{}^R + I_z{}^L}$$

where $I_z{}^R$ and $I_z{}^L$ refer to the parallel intensity components for right and left circularly polarized incident light, respectively.

We present the data as three quantities in each diagram: the Raman spectrum $(I_z{}^R + I_z{}^L)$ at low resolution (15-cm^{-1} slit width), the difference spectrum $(I_z{}^R - I_z{}^L)$ smoothed over five points, and the corresponding Δ_z curves.

Figure 2 shows the results obtained for $(-)$-α-pinene in the regions where substantial CID's are observed. We have found that $(+)$-α-pinene gives an enantiomorphic CID spectrum and that $(\pm)$-α-pinene gives no detectable CID. The features shown in Figure 2 are in essential agreement with those published previously[14,15] although the magnitudes of the corresponding CID's are about one half of those reported. Figure 2 also shows the magnitude of the "CID" observed associated with the strongly polarized band at $\sim$665 cm^{-1} of $(-)$-α-pinene during the time the data shown were collected. It is significant that although the artifacts associated with the 665-cm^{-1} band have not been as well controlled previously, the same basic CID pattern has been observed with the unpolarized or weakly polarized bands. In fact, we obtained essentially the same Δ_z CID spectrum when the 665-cm^{-1} artifact was skewed either positive or negative up to about 3 parts in 10^3; further misalignment "lifted" the genuine CID's positively or negatively according to the sign of the induced artifact and also began to generate spurious effects in bands having CID's less than 3×10^{-4}. We have also reproduced the reported spectrum of active phenylethyl alcohol[7] but, again, our CID's were about half as intense.

B. Sulfoxides. Figure 3 shows the spectra for R-p-tolylethyl sulfoxide run as the "neat" liquid. Raman bands which have a depolarization ratio (ρ) of $\sim$0.1 or less for linearly polarized incident light are marked "p" and it can be seen that artifacts which tend to be associated with strongly polarized bands have been controlled. Differential effects which are observed below $\sim$200 cm^{-1} are subject to artifacts carried by the (polarized) Rayleigh line and may not be reliable. The negative CID at 296 cm^{-1} and the two positive CID's at 335 and 368 cm^{-1} are associated with Raman bands which have ρ values of about 0.35, 0.7, and 0.45, respectively. These three CID's and particularly the two positive features are easily obtained and are not greatly sensitive to alignment and we are confident of their authen-
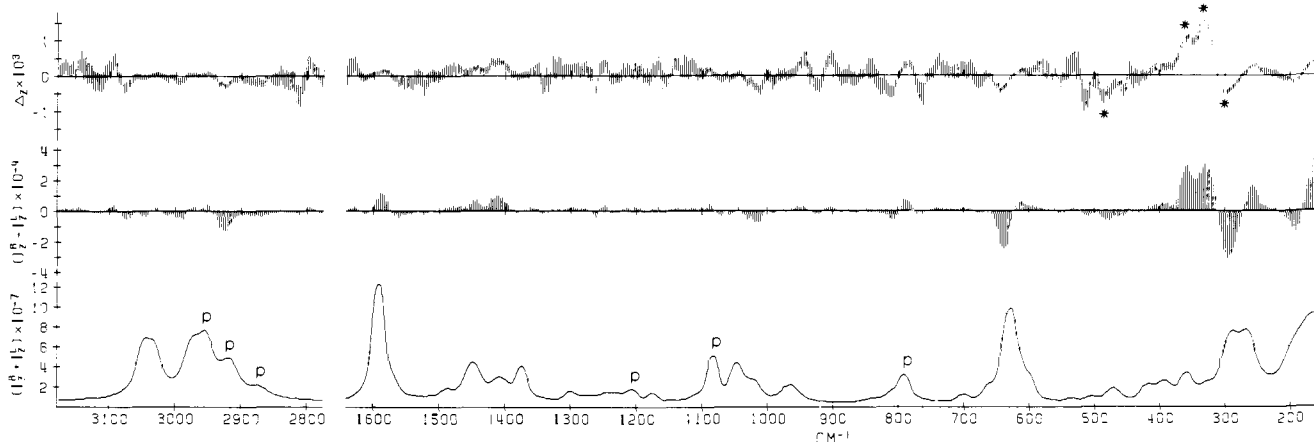

Figure 3. The sum, difference, and CID spectra of "neat" R-p-tolylethyl sulfoxide recorded in parallel polarization.
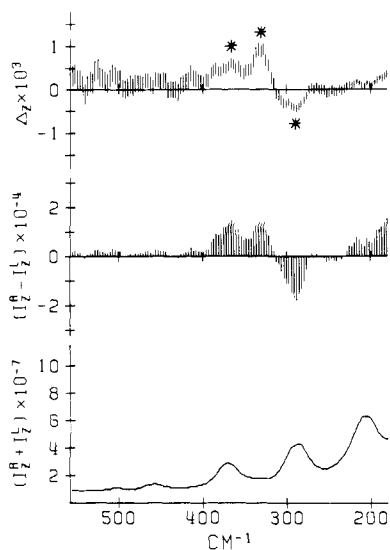
Figure 4. The sum, difference, and CID spectra of a saturated methanol solution of R-p-tolylmethyl sulfoxide in parallel polarization.
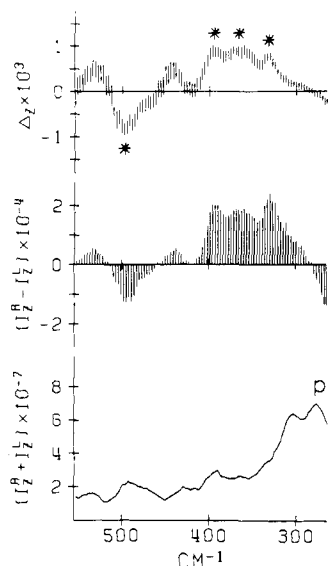

Figure 5. The sum, difference, and CID spectra of "neat" R-p-tolylisopropyl sulfoxide recorded in parallel polarization.

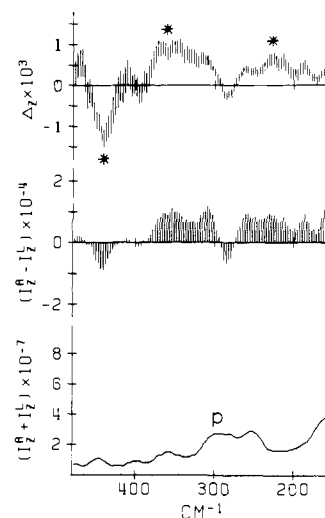
Figure 6. The sum, difference, and CID spectra of a saturated methanol solution of R-p-tolyl-tert-butyl sulfoxide recorded in parallel polarization.
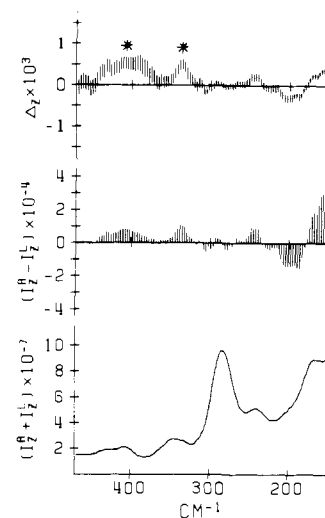

Figure 7. The sum, difference, and CID spectra of a saturated methylene chloride solution of S-p-tolyl-o-tolyl sulfoxide recorded in parallel polarization.

ticity. At around 500 cm^{-1}, the very weak Raman bands (ρ ~0.5) show weak negative CID which was confirmed after a longer count time than that shown in the figure. None of the other features in the CID spectrum are significant at the present level of detection. Indeed none of the other sulfoxides showed any strong CID above 600 cm^{-1}.

In Figures 4, 5, and 6, we show the spectra obtained for R-p-tolylmethyl sulfoxide, R-p-tolylisopropyl sulfoxide, and R-p-tolyl-tert-butyl sulfoxide in the low-frequency regions. The p-tolylmethyl sulfoxide shows three significant CID's, a negative band at 294 cm^{-1} (ρ ~0.4), and two positive bands at 363 cm^{-1} (ρ ~0.2) and 375 cm^{-1} (ρ ~0.3) in methanol solution. The p-tolylisopropyl sulfoxide, run as the "neat" liquid, has a strongly polarized band (ρ ~0.1) at 276 cm^{-1} and two moderately polarized features at 431 cm^{-1} and 443 cm^{-1} (ρ ~0.15). Moreover, the other bands are also more polarized than in the other homologues. The values are 498, 492, 356 cm^{-1} (ρ ~0.2), 401, 395, 341 cm^{-1} (ρ ~0.3), 539, 477 cm^{-1} (ρ ~0.4), and 372 cm^{-1} (ρ ~0.5). Thus the richer CID displayed by this sulfoxide is complicated by the intrusion of polarized bands although those marked (*) are reproducible and are probably free of artifact. The p-tolyl-tert-butyl sulfoxide spectrum obtained in methanol solution has a strongly polar-

ized band at 312 cm^{-1} (ρ ~0.1), but the other bands which show appreciable CID's are much less polarized.

The CID spectrum of S-p-tolyl-o-tolyl sulfoxide was difficult to obtain because of its insolubility in suitable solvents and because of the weakness of the effect (Figure 7). The most prominent Raman feature, at 283 cm^{-1}, is a CH_2Cl_2 solvent peak. The only reproducible CID effects were the positive differentials at 335 cm^{-1} (ρ ~0.5), 410 cm^{-1} (ρ ~0.3), and 431 cm^{-1} (ρ ~0.8). Even these are barely within significance.

III. Discussion

The acquisition of CID data is not a simple matter with the present state of instrumentation although the technical difficulties could be overcome were it not for the potential artifacts which are peculiar to the method. Briefly, birefringence in any of the elements of the incoming optical train generates artifacts which are most pronounced for strongly polarized lines in parallel polarization and are present in all lines in perpendicular polarization. For certain inclinations of the axis of birefringence, artifacts may arise which change sign for enantiomers and are zero (or very small) for racemic and archiral substances. The artifacts in the present spectra have been reduced considerably over previously published data. Even so, drift in the instrumental settings over the long acquisition times
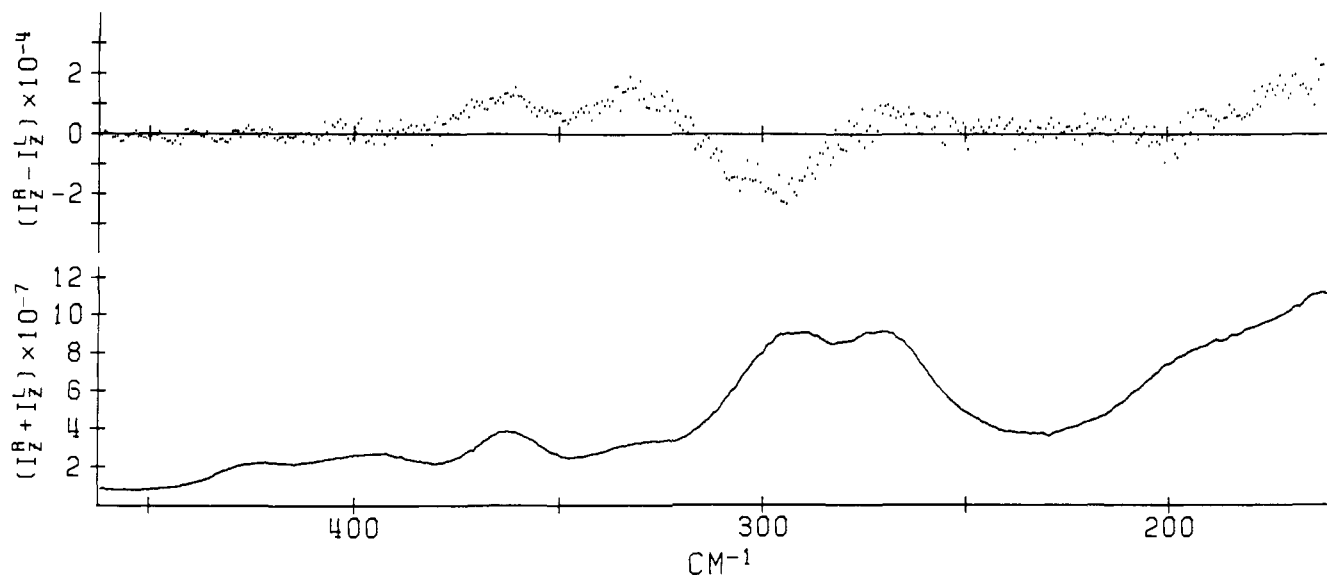
Figure 8. The sum and difference spectra of "neat" R-*p*-tolylethyl sulfoxide recorded in parallel polarization with the new multichannel system. The difference spectrum, which required 2 h to collect, is the actual "raw" data output.

compels us to reject differentials associated with highly polarized bands ($\rho < 0.1$) and effects associated with depolarized bands of less than 3 parts in 10^4.

The present sulfoxides all have the same absolute configuration in the sense that the oxygen atom, the *p*-tolyl group, and the R-group are related in the same absolute disposition. It is gratifying to note, therefore, that all the substances show a common (positive) CID feature in the 300 to 400-cm^{-1} region.

Bands in the low-frequency regions are difficult to assign uniquely since vibrational modes associated with various groups of the molecule strongly interact. It seems reasonable, however, to assign bands in the 368 to 378-cm^{-1} region for the four alkyl sulfoxides, where substantial CID is observed in all cases, to carbon–sulfur–oxygen deformations.[17,18] Other bands in this general region include deformational modes which involve the carbon–sulfur–carbon bonds as well as some which belong to distortional modes in the aryl group.[19] Except for the methyl *p*-tolyl sulfoxide, all of the other alkyl substituted sulfoxides show substantial negative CID's in the 450–510-cm^{-1} regions. Bands in this region are normally assigned to alkyl carbon skeletal deformations,[18] which in the case of sulfoxides may involve the sulfur atom as well. In addition, a certain degree of coupling between these modes and the low symmetry distortional vibrations of the aryl group is expected.

It appears, therefore, that those modes which either tend to invert the molecule or otherwise modulate its chirality about the chiral center, display the largest CID's while modes, such as stretching vibrations, which affect the chirality indirectly, show small CID's. The generality of this notion, however, will have to await further study on simple chiral molecules.

Finally, we note that the *p*-tolyl-*o*-tolyl sulfoxide shows the weakest CID spectrum. This may have been intuitively expected since it differs from the achiral entity only by virtue of the positions of the methyl groups attached to the phenyl rings. The fact that CID's are observed at all for this sulfoxide is encouraging for it suggests that subtle structural changes are detectable by this technique.

The present results indicate that future systematic studies may reveal certain consistent patterns in the CID's shown by simple chiral molecules. In particular the classical asymmetric molecules which are devoid of electronic chromophores in the accessible spectral regions may be susceptible to this technique. It would appear, however, that until the origins of the CID are

more clearly perceived, empirical correlations will require caution. The difficulties with eliminating artifacts can, to some extent, be ameliorated by the development of multichannel detection systems which are capable of acquiring data of a wide spectral span at one time. Such devices tend to eliminate the frustrations associated with instrumentral drift. We shall report shortly on such a system which we have developed and which we believe will make the acquisition of CID data a relatively routine matter. A spectrum recorded with this recently developed instrument is shown in Figure 8. It required roughly one-tenth of the acquisition time that the same region of the spectrum with the single channel system required and it provides better signal to noise and better resolution as well.

References and Notes

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