Vibrational Circular Dichroism

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Abstract: Vibrational circular dichroism (VCD) has been observed in the fundamental C–H, O–H, and N–H stretching bands of a number of chiral molecules in the liquid phase. VCD spectra are reported for α-methylbenzylamine, *N,N*,α-trimethylbenzylamine, 2,2,2-trifluoro-1-phenylethanol, 3-methylcyclohexanone, 3-methylcyclopentanone, menthol, α- and β-pinene, camphor, 3-bromocamphor, borneol, tris(3-trifluoromethylhydroxymethylene-*d*-camphorato)praseodymium and -europium, poly(1-methylpropyl vinyl ether), and poly(4-methyl-1-hexene). Our results for 2,2,2-trifluoro-1-phenylethanol are compared with the earlier work, experimental and theoretical, on this compound by Holzwarth et al.

We report observations of natural vibrational circular dichroism (VCD) in chiral molecules. Our results demonstrate that VCD is measurable with good signal-to-noise ratio in unexceptional chiral molecules with currently accessible instrumentation.

The contribution of vibrational motion to natural optical activity has been studied sporadically for many years. On the experimental side, in 1935 Lowry[1] reviewed existing measurements of infrared (ir) optical rotatory dispersion (ORD), a few of which encompassed vibrational absorptions, and commented: "very few measurements of rotatory dispersion have been made in the infrared, since this phenomenon shows no points of outstanding interest, the rotatory power decreasing steadily with increasing wavelength, even when passing through an infrared absorption band". In 1951, Gutowsky[2] reported anomalous ORD in α-quartz, but this work was challenged by West.[3] Günthard et al. also reported ORD anomalies in organic compounds, but subsequently attributed these to instrumental artefacts.[4] Katzin[5] concluded that the monotonic near-ir ORD of α-quartz contains a contribution from vibrational transitions and Chirgadze, Venyaminov, and Lobachev[6] reached a similar conclusion with regard to a number of polymers. More recently, in 1973 Hsu and Holzwarth[7] reported VCD in single crystals of $NiSO_4 \cdot 6H_2O$, $NiSO_4 \cdot 6D_2O$, and $ZnSeO_4 \cdot 6H_2O$. Further, in 1974, Holzwarth et al.[8] reported the observation of VCD in the 2920-cm^{-1} band of 2,2,2-trifluoro-1-phenylethanol, due to the C*–H stretching motion and in the 2204-cm^{-1} band of neopentyl-*l*-*d* chloride due to the C*–D stretching motion.

Theoretical calculations of vibrational optical activity have also been published. Fickett,[9] and later Cohan and Hameka,[10] investigated molecules optically active due to isotopic substitution. Deutsche and Moscowitz[11] studied model polymers. Schellman[12] reported calculations for methyl pyrrolidones and Snir, Frankel, and Schellman[13] discussed the amide bands of polypeptides of varying structure. Holzwarth and Chabay[14] investigated dimers using the coupled oscillator model. Faulkner et al.[15] have also reported calculations on the molecules in which VCD was observed by Holzwarth et al.,[8] the only work directly comparing theory and experiment.

In our work we have utilized an existing near-ir CD instrument,[16] extended into the medium-ir and enhanced in sensitivity. With this instrumentation, we have been able to observe VCD in a wide variety of chiral organic molecules.[17] In this paper we present and discuss experimental data obtained to date.

Instrumental Section

In this section we describe the modifications made to the previously described near-ir CD instrument[16] for VCD experiments. These have extended its long wavelength limit and significantly improved its sensitivity.

The extension of the wavelength range was accomplished by replacement of the InAs detector by a 77 °K InSb photovoltaic detector usable to ~5.5 μm (Santa Barbara Research Center). A 750 W tungsten–halogen lamp (Sylvania 750 Q/CL) provides greater throughput than the earlier 500 W source.

The polarization optics have been completely reconstructed. In the 2.0–4.5-μm region a 15-mm aperture $LiIO_3$ Glan-Foucault prism polarizer (Interactive Radiation Inc) has been substituted for the gold wire grid polarizer, the former having a much greater polarization efficiency. The fused quartz photoelastic modulator (PEM) has been replaced by a polycrystalline ZnSe unit designed in our laboratory,[18] oscillating at ~50 kHz. ZnSe transmits to much longer wavelengths than quartz. It also possesses superior stress-optic properties permitting quarter-wave retardation to be achieved to much longer wavelengths than quartz.

In addition, we have introduced a second ZnSe PEM immediately after the sample. This modulator operates at a different frequency from the first (by a few hundred hertz) and is used to scramble the polarization of the light beam prior to reaching the ellipsoidal mirror and detector, thereby reducing artefact CD signals. The theory and practice of this polarization scrambling system is described more fully in a separate publication.[19]

The signal processing electronics have also been redesigned (Figure 1). In our CD experiments the signal at the detector contains a component of frequency ω_C (~500 Hz) due to mechanical chopping of the light beam and a component of frequency ω_M (~50 kHz) due to the polarization modulation and the CD of the sample. To determine the CD it is necessary to measure the ratio of the latter to the former.[16] Previously this was accomplished by direct division of the outputs of two lock-in amplifiers tuned to ω_M and ω_C. Now, an automatic normalization circuit is used, which adjusts the amplification of both the ω_C and ω_M signals so that the ω_C signal output is kept constant. The output of the normalization circuit is passed through a tuned LRC filter and into the ω_M lock-in amplifier (Princeton Applied Research, Inc. 124A) whose output is then directly proportional to the CD.

In addition, in high sensitivity experiments a third lock-in amplifier (PAR HR-8) tuned to the chopping frequency ω_C is connected to the output of the PAR 124A which is operated with minimum time constant (1 ms). The output of the PAR 124A due to CD then varies at ω_C and this is measured by the PAR HR-8.

All VCD experiments reported here lie in the range 2.5–4.0 μm. The 3.0 μm blaze, 300 lines/mm grating (Bausch and Lomb), was used throughout with maximum 3 mm monochromator slit widths giving a spectral band pass in the range 2.5–4.0 μm of ~0.012 μm (~7–20 cm^{-1}). Filtering was achieved by a sharp cut-off, long-wave-pass filter (Optical

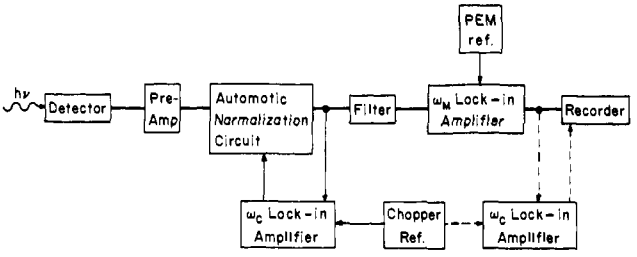

Figure 1. Electronics block diagram. Dashed lines connect the optional three lock-in amplifier system.

Coating Laboratory, Inc.) with greater than 10^3 rejection at λ <2.0 μm. Except where indicated the $LiIO_3$ polarizer and the three-lock-in amplifier system were used. Most of the instrument was evacuated to reduce atmospheric absorption (due principally to H_2O).

The first PEM was held at a constant oscillation voltage and its retardation therefore varied with wavelength. The retardation was set to maximize the CD signal in the range scanned. The second scrambling modulator was tuned with wavelength to the constant retardation level at which $J_0(\delta_0) = 0$, where $\delta = \delta_0 \sin \omega_M t$ is the modulator retardation and J_0 is the zero-order Bessel function. This was accomplished by slaving the PEM power supply to the monochromator wavelength drive.

Calibration of the magnitude of CD signals was carried out by an absolute method described earlier,[16] modified as described in Appendix I. Calibration of the sign of CD was carried out by reference to the 1.1-μm band of a nickel(II) tartrate-*d* complex whose sign has been previously established.[16]

At the high sensitivity level required for the measurement of VCD and in the 2.5-4.0-μm range our experiments have been limited primarily by artefact signals rather than by intrinsic detector noise. These can originate both optically and electronically and a variety of approaches have been used in order to reduce their magnitude. Artefacts arising from imperfect polarizing optics have been minimized by the introduction of the second scrambling modulator and by the use of as high quality components as possible. The scrambling modulator greatly reduces artefact signals originating in optical components subsequent to the sample (the ellipsoidal mirror and the detector). The improvement of the purity of the initial linear polarization by replacement of the grid polarizer with the $LiIO_3$ crystal polarizer was found to reduce artefacts significantly. We have also found that the optical quality of both PEM optical elements is important, different modulators giving different CD baselines. Pick-up of stray ω_M signals, either due to background ir radiation or electronic in origin, can create artefact signals. The use of the three-lock-in-amplifier electronic system reduces such signals by detecting only signals chopped at ω_C.

The data presented below illustrate the level at which artefacts remain currently. Ideally, CD measured with a *dl* sample is zero at all wavelengths and the CD of *d* and *l* compounds are equal in magnitude and opposite in sign. In practice, these expectations are rarely exactly realized. However, data are not regarded as acceptable unless (i) the *dl* baseline is essentially the same as the instrumental baseline, (ii) *d* and/or *l* spectra differ from the *dl* baseline by appreciably more than the baseline fluctuations, (iii) *d* and *l* spectra, where both obtainable, are close to equal and opposite, and (iv) the spectra do not change qualitatively on varying the pathlength (absorbance).

Experimental Section

All of the compounds for which data are presented here are commercially available as resolved optical isomers, with the exception of two polymers. *N,N,α*-Trimethylbenzylamine (TMBA) (*d,l*) was obtained from Hoffmann-LaRoche Inc. 2,2,2-Trifluoro-1-phenylethanol (TPE: Pirkle's solvent) (*d,l,dl*) was obtained from Burdick and Jackson Labs. *α*-Methylbenzylamine (MBA) (*d,l,dl*), 3-methylcyclohexanone (MCH) (*d,dl*), 3-methylcyclopentanone (MCP) (*d,dl*), menthol (*l*), *α*-pinene (*d,l,dl*), *β*-pinene (*l*), camphor (*d,l,dl*), 3-bromocamphor (*d*), and borneol (*l*) were obtained from Aldrich Chemical Co. Tris(3-trifluoromethylhydroxymethylene-*d*-camphorato)europium and -praseodymium (Eu-Opt and Pra-Opt) were obtained from Ventron (Alpha Products). The two polymers, poly((*S*)-1-methylpropyl vinyl ether) (P1) and poly((*S*)-4-methyl-1-hexene) (P2), were kindly given to us by Dr. E. Chiellini and Professor F. Ciardelli.

All compounds were used as obtained without further purification. Optical rotations and ir spectra were checked against published data. Compounds were studied either as neat liquids or in CCl_4 solution in a variable pathlength cell with CaF_2 windows. The latter enables variation of the sample absorption to achieve optimum signal-to-noise ratio, which we found to be obtained with absorbances in the range 0.5-1.0. In practice the maximum absorbance was usually set close to 0.7 (~20% transmission). With neat liquids this requires very short pathlengths and in some cases stronger absorption bands could not be studied, their absorbance being excessive even at the minimum cell pathlength. Transmission and CD baselines of the CCl_4 indicate no signals in the regions studied. Solutions of MBA in CCl_4 were observed to deteriorate with time; all spectra were obtained with freshly prepared solutions.

Results

In this section we present VCD spectra for a variety of molecules in the spectral region 2.5-4.0 μm. Absorption in this range is predominantly due to fundamental C-H, O-H, and N-H stretching modes.

In all cases experimental spectra are directly reproduced without further processing. VCD spectra are shown for all isomers available (+, −, and ± in figures indicating *d*, *l*, and *dl* isomers). Single beam transmission spectra are also shown to facilitate comparison of VCD and absorption spectra. All VCD and transmission spectra for a specific system were run in a consecutive sequence under identical conditions of pathlength and spectral resolution. In the case of compounds for which *dl* mixtures were not available, CD baselines were obtained with racemic compounds having closely similar absorption spectra. Such baselines were run under identical instrumental conditions and with transmission spectra as closely matched to the sample transmission as possible. Because of the limited wavelength range over which VCD spectra are scanned and the PEM retardations used, CD scales are independent of wavelength within experimental error. The CD ΔA is defined to be $A_L - A_R$, where A_L and A_R are the absorbances for left and right circularly polarized light, in accordance with standard convention.[20] The frequencies of principal absorption bands are indicated in the figures. These are also tabulated in Table I, together with their assignments and absorbances.[20] The spectral resolution used was chosen to be as low as possible consistent with the observation of all spectral features. Comparison with transmission spectra at higher resolution indicates sharper features in some cases to be slightly under-resolved.

In comparing the magnitudes of VCD signals between different bands, the significant quantity is the ratio of CD, ΔA, to absorbance, A, and not the absolute magnitude of ΔA which depends on the concentration, pathlength, and transition intensity. Statements below regarding the magnitude of the VCD thus refer to this "normalized" quantity rather than to ΔA itself. This distinction is of particular importance in the case of weaker transitions, where a small ΔA signal may still reflect a $\Delta A/A$ value as large as that obtained from a larger ΔA associated with a stronger transition.

The VCD data shown in Figures 2 and 3 were obtained using a gold grid polarizer and two lock-in amplifiers, as were the previously published data.[17] VCD data in Figures 4-13 were

Table I. Frequencies, Absorbances and Assignments of Observed Vibrational Bands

Compd	Freq, cm^{-1}	Absorbance[a]	Assignment[b]
α-Methylbenzylamine (0.31 M solution)	3083	0.26	C_6H_5
	3064	0.33	C_6H_5
	3028	0.50	C_6H_5
	2964	0.75	CH_3 (as)
	2923	0.41	CH (?)
	2866	0.38	CH_3 (s)
	2808	0.14	?
α-Methylbenzylamine (neat)	3362	0.34	NH_2
	3281	0.29	NH_2
	3078	0.29	C_6H_5
	3058	0.40	C_6H_5
	3022	0.57	C_6H_5
	2961	1.04	CH_3 (as)
	2922	0.44	CH (?)
	2864	0.45	CH_3 (s)
	2807	0.15	?
*N,N,*α-Trimethylbenzylamine	3084	0.1	C_6H_5
	3065	0.1	C_6H_5
	3030	0.2	C_6H_5
	2978	0.7	
	2955	0.5	C-CH_3,
	2939	0.4	N-CH_3
	2861	0.4	C-CH_3
	2817	0.7	N-CH_3
	2770	1.0	N-CH_3
2,2,2-Trifluoro-1-phenylethanol (neat)	3093	0.48	C_6H_5
	3069	0.75	C_6H_5
	3038	0.85	C_6H_5
	2916	0.48	CH
2,2,2-Trifluoro-1-phenylethanol (0.14 M solution)	3093	0.27	C_6H_5
	3070	0.50	C_6H_5
	3038	0.68	C_6H_5
	2908	0.43	CH
2,2,2-Trifluoro-1-phenylethanol (0.70 M solution)	3614	0.83	OH
3-Methylcyclopentanone	2959	0.68	CH_3 (as)
	2929	0.28	CH_2 (as)
	2875	0.25	CH_3 (s), CH_2 (s)
3-Methylcyclohexanone	2957	0.70	CH_3 (as)
	2928	0.62	CH_2 (as)
	2871	0.36	CH_3 (s)
	2847	0.20	CH_2 (s)
Menthol	2957	0.70	CH_3 (as)
	2922	0.61	CH_2 (as)
	2871	0.42	CH_3 (s)
	2849	0.25	CH_2 (s)
β-Pinene	3070	0.08	=CH_2
	2976	0.35	?
	2946	0.49	?
	2920	0.62	?
	2868	0.26	?
α-Pinene	3024	0.07	=CH
	2984	0.31	?
	2948	0.38	?
	2917	0.61	?
	2878	0.29	?
	2833	0.16	?
3-Bromocamphor	2966	0.60	CH_3 (as)
	2930	0.26	CH_2 (as)
	2876	0.18	CH_3 (s), CH_2 (s)
Camphor	2962	0.74	CH_3 (as)
	2931	0.36	CH_2 (as)
	2875	0.22	CH_3 (s), CH_2 (s)
Borneol	2983	0.65	?
	2952	0.89	CH_3 (as)
	2876	0.38	CH_3 (s), CH_2 (s)
Pra-Opt	2962	0.76	CH_3 (as)
	2928	0.39	CH_2 (as)
	2872	0.28	CH_3 (s), CH_2 (s)
Eu-Opt	2961	0.65	CH_3 (as)
	2928	0.34	CH_2 (as)
	2871	0.25	CH_3 (s), CH_2 (s)
Poly((*S*)-1-methylpropyl vinyl ether)	2967	0.57	CH_3 (as)
	2928	0.46	CH_2 (as)
	2879	0.25	CH_3 (s)
	2852	0.14	CH_2 (s)
Poly((*S*)-4-methyl-1-hexene)	2959	0.64	CH_3 (as)
	2919	0.66	CH_2 (as)
	2873	0.32	CH_3 (s)
	2849	0.30	CH_2 (s)

[a] Obtained from the transmission spectra of Figures 2-12. [b] Based on the standard vibrational spectroscopy literature.

obtained using the $LiIO_3$ polarizer and three lock-in amplifiers.

Figure 2 shows spectra for α-methylbenzylamine (MBA), both neat and in dilute solution. VCD is observable in neat MBA (Figure 2b) over a wide wavelength range which includes both the N-H and C-H stretching regions. The bands above 3100 cm^{-1} are primarily due to N-H stretching modes, broadened by intermolecular interactions; bands in the region 2850-3100 cm^{-1} are due to C-H stretching modes. The VCD in the region of the 2961-cm^{-1} band is not shown due to excessive absorbance.

The spectra of MBA in dilute solution are shown in Figure 2a. At the pathlength and concentration used no VCD was observed in the N-H stretching region. In the C-H stretching region, however, both absorption and VCD remain essentially unchanged from the neat liquid. The VCD of the antisymmetric methyl stretching band at 2964 cm^{-1} is now observed.

Figure 3 shows spectra of *N,N,*α-trimethylbenzylamine (TMBA) in dilute solution. The VCD of the 2770-cm^{-1} band is not shown due to its excessive absorbance.

Figure 4 shows spectra for 2,2,2-trifluoro-1-phenylethanol (TPE), both neat and in dilute solution, in the C-H stretching region. The VCD associated with the C*-H stretching band in neat TPE (Figure 4a) has been published previously,[17] but was remeasured for the sake of direct comparison to the solution spectra (Figure 4b). Spectra in the phenyl C-H stretching region, not previously shown, are also included. The VCD of the C*-H stretching band changes dramatically on dilution, in contrast to the absorption which undergoes little change. Figure 4 shows spectra for 100 and 2% solutions; the spectra change continuously between these extremes at intermediate dilutions. The smaller VCD of the phenyl C-H stretching bands appears to alter little upon dilution, although the appearance of the spectrum in this region is modified by the changing background due to the O-H stretching band. On dilution from neat liquid to a 0.1% solution the absorption spectrum in the O-H stretching region changes from a broad band, peaking at 3400 cm^{-1}, to a narrow band, at 3614 cm^{-1}. With a 10% solution an intermediate spectrum is observed. The neat liquid VCD has been published earlier.[17] Figure 5 shows

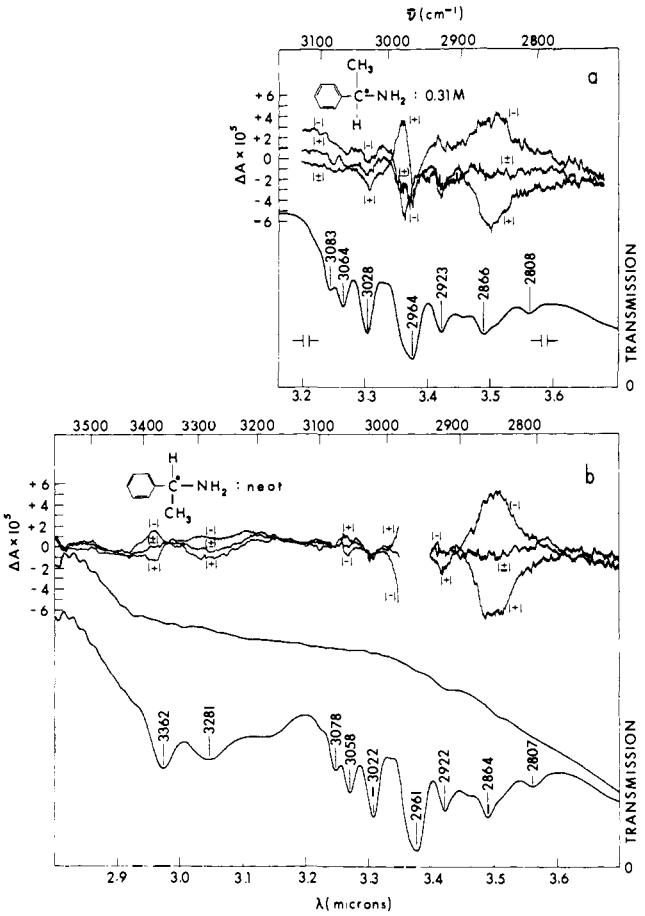

Figure 2. VCD and single-beam transmission spectra of α-methylbenzylamine (MBA): (a) 0.31 M (4% by volume) in CCl_4 (pathlength 380 μm, VCD time constant 3 s); (b) neat liquid (pathlength 30 μm, VCD time constant 3 s). +, −, and ± on VCD spectra denote *d*, *l*, and *dl* isomers, respectively. Lower curves are single-beam transmission spectra, obtained under identical conditions to the VCD spectra. Frequencies (in cm^{-1}) of principal absorption peaks are indicated. In Figure 2b the corresponding instrument baseline is also shown. The spectral resolution of 0.012 μm is shown in Figure 2a.

the 3614-cm^{-1} band in a 10% solution, together with the tail of the broader, lower energy band. Since the instrumental transmission in this region shows significant atmospheric water vapor absorption a baseline transmission is also included.

In Figure 6 spectra of dilute solutions of 3-methylcyclopentanone (MCP) and 3-methylcyclohexanone (MCH) are shown. These homologous molecules have quite different VCD spectra in both form and magnitude.

Spectra of a dilute solution of *l*-menthol in the C-H stretching region are shown in Figure 7. Since neither *d* nor *dl* menthol was available, a solution of *dl*-MCH was used to provide a VCD baseline. No VCD signals have been observed in the O-H stretching region.

Figure 8 contains spectra of dilute solutions of α- and β-pinene. The *dl*-α-pinene VCD spectrum may be used as a baseline for the β-pinene spectrum, *dl*-β-pinene being unavailable. The transmission spectra of the two compounds are quite similar. Their VCD, however, differ significantly, β-pinene giving large signals, while the VCD of α-pinene is barely measurable. No VCD is observed in the ethylenic C-H stretching bands at 3070 cm^{-1} in β-pinene or at 3024 cm^{-1} in α-pinene.

The spectra of camphor and 3-bromocamphor in dilute solution are shown in Figure 9. Only *d*-3-bromocamphor was available, and the *dl*-camphor VCD spectrum may be used as a baseline for the 3-bromocamphor spectrum.

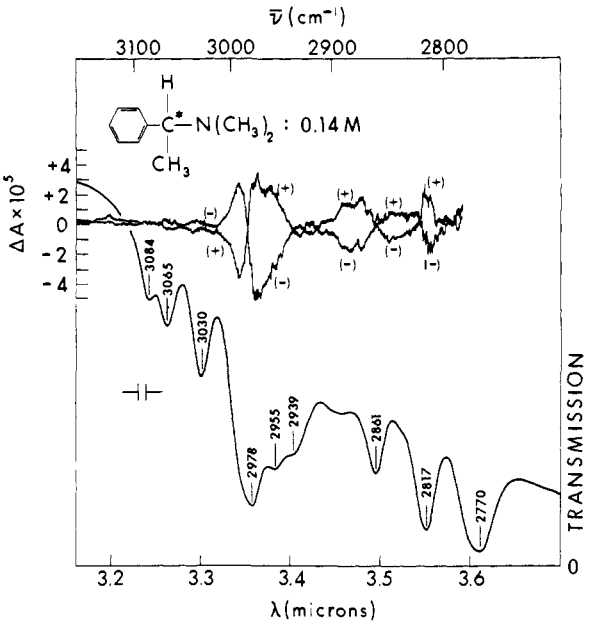

Figure 3. VCD and single-beam transmission spectra of *N,N,*α-trimethylbenzylamine (TMBA), 0.14 M (2% by volume) in CCl_4 (VCD time constant 3 s).

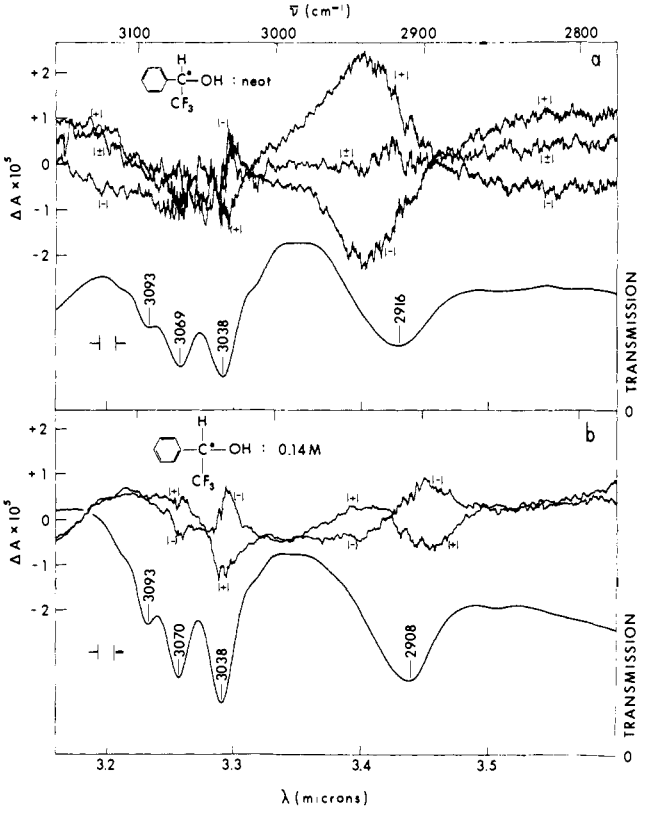

Figure 4. VCD and single-beam transmission spectra of 2,2,2-trifluoro-1-phenylethanol (TPE): (a) neat liquid (pathlength 80 μm, VCD time constant 10 s); (b) 0.14 M (2% by volume) in CCl_4 (pathlength 2 mm, VCD time constant 10 s).

Spectra of borneol in dilute solution are shown in Figure 10. A *dl*-camphor solution provides a baseline in the absence of *dl*-borneol. No VCD has been observed in the O-H stretching region of borneol.

Figure 11 shows the spectra of the commonly used NMR shift reagents tris(3-trifluoromethylhydroxymethylene-*d*-camphorato)praseodymium, Pra-Opt, and its europium analogue, Eu-Opt. VCD baselines are obtained with *dl*-camphor.

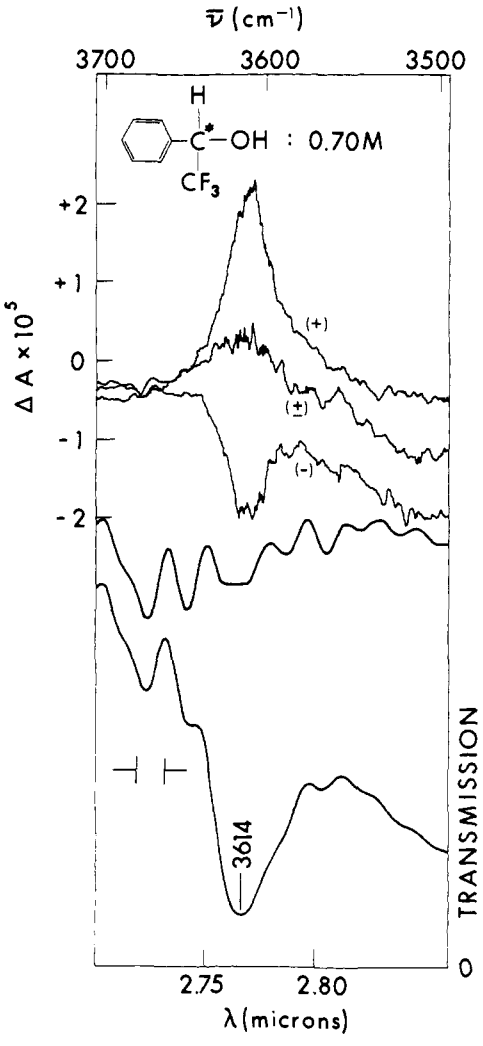

Figure 5. VCD and single-beam transmission spectra of 2,2,2-trifluoro-1-phenylethanol (TPE), 0.70 M (10% by volume) in CCl_4 (pathlength 230 μm, VCD time-constant 10 s). The instrument transmission baseline is also shown.

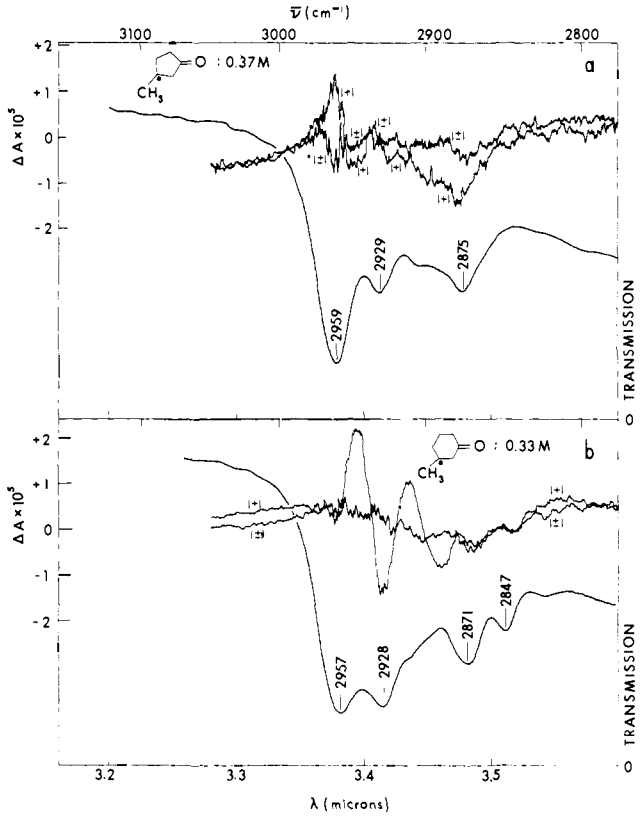

Figure 6. VCD and single-beam transmission spectra of (a) 3-methylcyclopentanone (MCP), 0.37 M (4% by volume) in CCl_4 (pathlength 150 μm, VCD time constant 10 s); (b) 3-methylcyclohexanone (MCH), 0.33 M (4% by volume) in CCl_4 (pathlength 150 μm, VCD time constant 10 s).

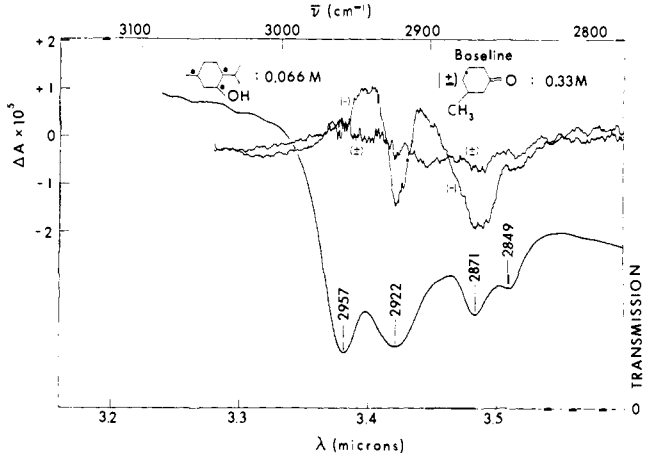

Figure 7. VCD and single-beam transmission spectra of menthol, 0.066 M in CCl_4 (pathlength 330 μm, time constant 10 s). The VCD baseline is obtained with a 0.33 M *dl*-3-methylcyclohexanone solution.

Lastly, Figure 12 shows spectra from two stereo-regular polymers, poly((*S*)-1-methylpropyl vinyl ether) (P1) and poly((*S*)-4-methyl-1-hexene) (P2). These polymers differ only in the substitution of a side chain $-CH_2-$ linkage for an ether linkage. In spite of the close similarity in formula structure, the pure hydrocarbon polymer gives a significantly more intense VCD spectrum.

In addition to the compounds in which VCD signals have been observed we have also examined the alcohols 2-butanol, 2-pentanol, and 2-octanol in both C–H and O–H stretching regions. At most very small VCD was observed.

Discussion

Our primary purpose in this work has been to investigate the measurability of VCD with conventional CD instrumentation techniques. At present, we have established, first, that in the 2.5–4.0-μm region, a CD sensitivity in the range $2\text{–}5 \times 10^{-6}$ is attainable with optimum absorbances at a resolution adequate for the study of vibrational bands in liquids. Second, we have shown that, with this sensitivity, VCD is measurable in the C–H, O–H, and N–H stretching bands of a variety of chiral organic molecules. These results were not wholly predictable at the outset. The high instrumental sensitivity was achieved only following the development of a new, high-quality ZnSe PEM and of the polarization scrambling method of reducing artefact CD signals. Although theoretical calculations had predicted the magnitudes of VCD signals, their accuracy had not been established. With only slightly lower sensitivity and smaller VCD signals, VCD would not have been observed.

During the course of this work, Holzwarth et al. published VCD data[7,8] obtained using fundamentally similar instrumentation.[21] In particular, one spectrum of VCD in a chiral organic molecule in the liquid phase was presented.[8] This spectrum, for the C*–H stretching band of neat TPE, can be compared with our earlier spectrum[17] and with Figure 4a. While the spectra are qualitatively similar, in particular, agreeing in sign, the signal-to-noise ratio in the spectrum of Holzwarth et al. is appreciably lower than in our spectra.

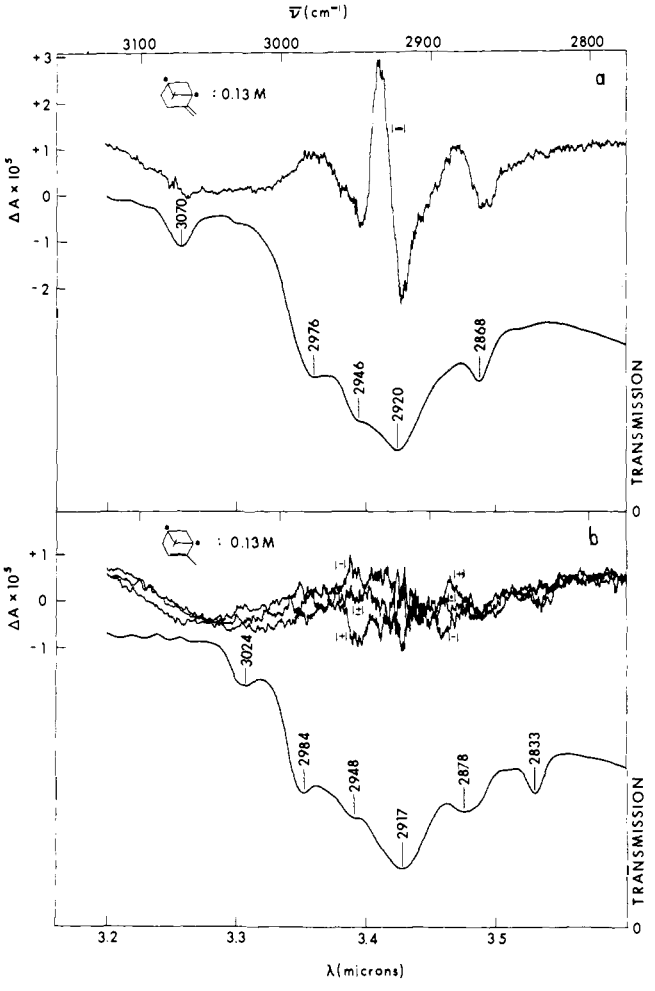

Figure 8. VCD and single-beam transmission spectra of (a) β-pinene, 0.13 M (2% by volume) in CCl_4 (pathlength 200 μm, VCD time constant 10 s); (b) α-pinene, 0.13 M (2% by volume) in CCl_4 (pathlength 200 μm, VCD time constant 10 s). The VCD of *dl*-α-pinene may be used as a VCD baseline for β-pinene.

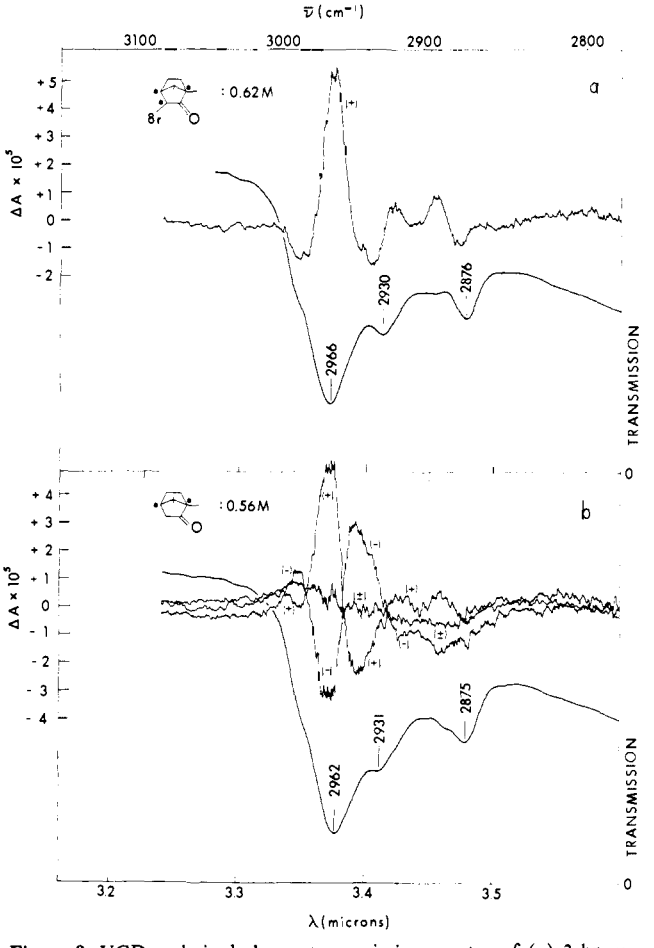

Figure 9. VCD and single-beam transmission spectra of (a) 3-bromocamphor 0.62 M in CCl_4 (pathlength 80 μm, VCD time constant 3 s); (b) camphor 0.56 M in CCl_4 (pathlength 80 μm, VCD time constant 3 s). The VCD of *dl*-camphor may be used as a VCD baseline for 3-bromocamphor.

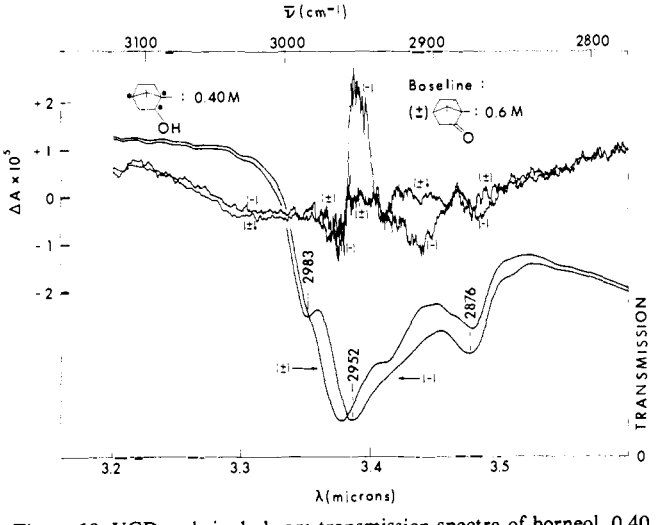

Figure 10. VCD and single-beam transmission spectra of borneol, 0.40 M in CCl_4 (pathlength 90 μm, VCD time constant 10 s). The VCD baseline is obtained with 0.6 M *dl*-camphor.

Consequently, only the main feature is observed. A quantitative comparison can be made by normalizing our data to the same pathlength as used by Holzwarth et al.[22] From Figure 4a we obtain $\Delta A = 1.6 \times 10^{-5}$, compared with $\Delta A = 2 \times 10^{-5}$ observed by Holzwarth et al. Considering the magnitude of the signal, the problems in absolute CD measurement and the differences in calibration techniques employed,[21] the agreement is excellent.

The detailed interpretation of the VCD spectra obtained requires both the experimental determination and the theoretical calculation of the VCD associated with individual vibrational bands. On the experimental side, this analysis is complicated by the lack of complete resolution of bands lying close in energy. For example, all C-H stretching bands from CH_3, CH_2, and CH groups generally overlap, forming one, structured continuum. In addition, a number of compounds exist in several conformations, each of which can give quite different VCD. These effects together are presumably responsible for the lack of correlation between VCD and absorption band maxima observed quite frequently in our spectra.

On the theoretical side, there exist two major problems. First, any VCD analysis is predicated upon a satisfactory normal mode calculation, which is not trivial for the large molecules involved. Second, and more fundamentally, VCD calculations for such molecules have so far always been carried out using a heuristic, vibrating-effective-charge theory.[11,12,15] This has not been derived from the basic theory of optical activity.[23] It also requires empirical choice of effective-charge parameters. Its adequacy can therefore be questioned.

As a consequence of these problems we have not yet carried out a detailed analysis of our spectra and we shall restrict the following discussion to qualitative and empirical observations.

Marked changes occur in the spectra of TPE on dilution of the neat liquid in both O-H and C-H stretching regions. In the O-H stretching region the VCD follows the absorption

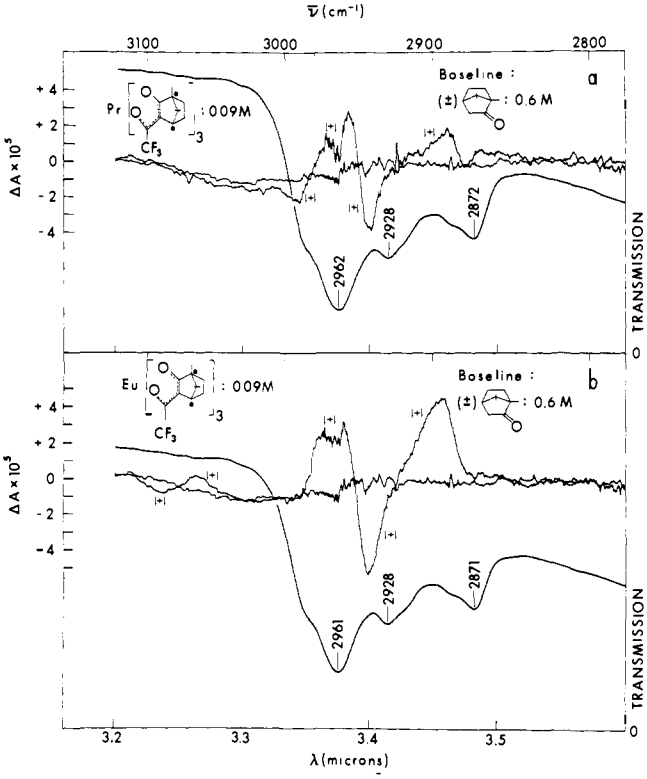

Figure 11. VCD and single-beam transmission spectra of (a) tris(3-trifluoromethylhydroxymethylene-*d*-camphorato)praseodymium (Pra-Opt), 0.09 M in CCl_4 (pathlength 120 μm, VCD time constant 3 s); (b) Eu-Opt, 0.09 M in CCl_4 (pathlength 140 μm, VCD time constant 3 s). VCD baselines are obtained with 0.6 M *dl*-camphor.

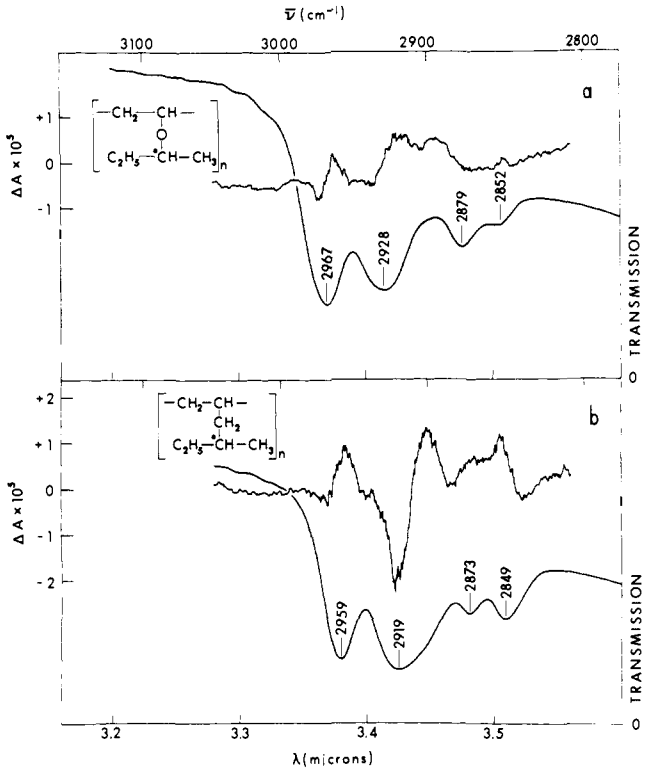

Figure 12. VCD and single-beam transmission spectra of (a) poly((*S*)-1-methylpropyl vinyl ether) (P1) 0.35 M (per monomer) in CCl_4 (pathlength 180 μm, VCD time constant 10 s); (b) poly((*S*)-4-methyl-1-hexene) (P2) 0.61 M (per monomer) in CCl_4 (pathlength 180 μm, VCD time constant 10 s).

qualitatively: due to intermolecular hydrogen bonding, a broad unstructured band exists in the neat liquid[17]; on dilution the broad band weakens, and a sharp band due to non-hydrogen-bonded molecules appears. The VCD of the sharp and broad bands are of the same sign and are of similar magnitude; $\Delta A/A$[24] for the 3614-cm^{-1} band is 2.5×10^{-5}. In the C*-H band, while the absorption changes only slightly on dilution of the neat liquid shifting to lower energy and narrowing on the high energy side, the VCD is radically altered. The band observed in the neat liquid, peaking 23 cm^{-1} higher than the absorption and with $\Delta A/A = 4.8 \times 10^{-5}$, diminishes in intensity on dilution. At the same time a band of opposite sign and of considerably smaller magnitude appears peaking slightly lower in energy than the absorption maximum. The simplest interpretation of this change is to ascribe the former band to hydrogen-bonded molecules and the latter to free molecules. However, since in the most dilute solution examined so far (2%) a significant fraction of molecules remain hydrogen bonded, this analysis could yet require modification and the identification of the isolated molecule spectrum requires more careful studies as a function of, and at lower, concentration. In contrast to both O-H and C*-H bands, the VCD of the phenyl C-H bands, although small, appears to vary little on dilution when the changing background due to the O-H band is taken into account. VCD is observed in the 3038- and 3070-cm^{-1} bands with opposite sign and $\Delta A/A$ values in dilute solution of 1.3×10^{-5} and 0.8×10^{-5}, respectively.

These results show that in comparing VCD data on molecules capable of aggregation with calculations for isolated molecules it is important to establish experimentally that aggregation effects are absent, even in the case of vibrations of groups not participating directly in the aggregation. Thus, the analysis by Faulkner et al.[15] of the VCD of the C*-H band of neat liquid TPE, on the basis of a calculation for the free TPE molecule, is invalidated by our experimental data on dilute solutions. This calculation predicted VCD of the sign observed by Holzwarth, et al.;[8] if the predominant VCD band of TPE in dilute solution arises from the free molecule, this calculation gives the VCD sign incorrectly. Unfortunately no predictions were published for the O-H band and none could have been given for the phenyl modes since the phenyl group was replaced by a single effective mass and charge. Further comparison of our data with the calculation of Faulkner et al. is thus not possible.

By contrast, the VCD of MBA in the C-H stretching region, due primarily to the CH_3 bands, changes very little on dilution of the neat liquid. The weaker C*-H band is not definitely identifiable, and its sensitivity to dilution cannot therefore be reliably gauged. The small VCD correlating with the 2922-cm^{-1} absorption, and possibly due to the C*-H stretching mode, does not change sign on dilution and has the opposite sign to the VCD in neat TPE.

The O-H bands of menthol and borneol have so far yielded no definite VCD signals. Excepting TPE and MBA, therefore, all VCD observed lies in the C-H region. In general, very similar molecules give similar VCD, while appreciable changes in structure cause major changes in VCD. For example, camphor and 3-bromocamphor have clearly similar VCD spectra. On the other hand, α- and β-pinene give very different spectra, as do MBA and TMBA, MCP and MCH, and P1 and P2. In all cases, unsurprisingly, the VCD is much more sensitive to structural change than is the absorption spectrum.

In Pra-Opt and Eu-Opt the possibility exists of CD due to f → f electronic transitions in addition to VCD. In view of the known electronic transitions of Pr^{3+},[25] including those detected in Pr^{3+} tartrate complexes by Chabay, Hsu, and Holzwarth,[21] it is unlikely that the VCD of Pra-Opt contains electronic CD. Eu^{3+}, on the other hand, is known to have excited states in the 2500-3500-cm^{-1} region,[25] and the difference in CD from Pra-Opt may well originate in transitions to these levels.

In the compounds so far studied, we have found little correlation between the VCD magnitude observed and the electronic optical activity, as gauged by $[\alpha]_D$. *d*-MCH and *d*-MCP have literature $[\alpha]_D$ values of 14 and 148°, respectively, while the VCD of MCH is larger than that of MCP. *l*-α- and *l*-β-pinene have $[\alpha]_D$ 48 and 21°, respectively, while the VCD of β-pinene is much larger than that of α-pinene. The very similar VCD of camphor and 3-bromocamphor contrasts with respective $[\alpha]_D$ values of 44 and 132° for the *d* isomers. On the other hand, it may be significant that the stereoregular polymers P1 and P2 have both very large $[\alpha]_D$[26] and VCD, while the aliphatic alcohols 2-butanol, 2-pentanol, and 2-octanol have both very small $[\alpha]_D$ and VCD.

Conclusion

We have shown that VCD measurements on ordinary chiral organic molecules are now technically feasible with good signal-to-noise ratio in the 2.5–4.0-μm region. Further work is required both to improve the sensitivity in this spectral region and to develop instrumentation for VCD measurement at longer wavelengths. CD sensitivity is intimately related to source power, detector sensitivity, and quality of polarizing optics. Simultaneous optimization of these parameters is of crucial importance in such development.

On the theoretical front it is now important both to develop the formal theory of VCD to a more definitive level and to explore the accuracy of calculations on simple, well-defined systems for which unambiguous calculations and experiments can both be performed. Such work is prerequisite to the application of a priori theory to larger, complex molecules.

Applications of VCD to chemical problems can now be looked for. It is to be expected that, like electronic CD, VCD will be sensitive to and provide molecular stereochemistry information concerning structure, conformation, and absolute configuration. An advantage of VCD over electronic CD is the greater variety of accessible chromophores.

Differential Raman scattering of left and right circularly polarized light by chiral molecules (Raman CID) has recently been reported.[27] Although premature at the present time, detailed comparisons of Raman CID and VCD data will be of great interest.

Acknowledgment. We are greatly indebted to Dr. J. C. Cheng who made important contributions to the development of the instrumentation used in this work. We also thank Professor F. Ciardelli and Dr. E. Chiellini of the Università di Pisa for providing us with samples of stereoregular polymers, Professor O. Schnepp for the use of a lock-in amplifier and several compounds and the National Institutes of Health, the National Science Foundation and the Research Corporation for financial support.

Appendix I

The calibration of our CD instrument is still carried out by the earlier method using a birefringent (sapphire) plate and a second linear polarizer. However, the equation given previously for the pseudo-CD signal generated (ref 16, eq 6) is incorrect and should be replaced by[19]

$$I_{ac}^{\omega_M}/I_{dc} = \frac{2J_1(\delta_0)\sin\alpha_B \sin\omega_M t}{1 - J_0(\delta_0)\cos\alpha_B} \quad \text{(A1)}$$

where α_B is the retardation of the sapphire place, $\delta_0 \sin \omega_M t$ is the modulator retardation, and J_0 and J_1 are Bessel functions of order 0 and 1, respectively. $I_{ac}^{\omega_M}$ is the $\sin \omega_M t$ component of the light flux at the detector, and I_{dc} is the static component, which in our instrument is converted to an ac signal of frequency ω_C by mechanical chopping. For comparison, a sample with CD of ΔA ($=A_L - A_R$) gives

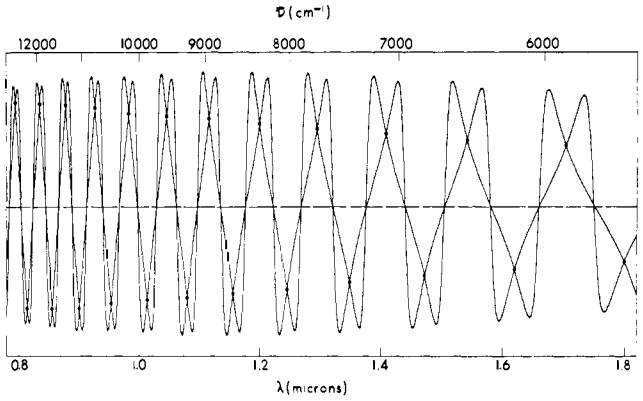

Figure 13. Sample instrumental calibration spectra, obtained using an infrasil quartz PEM.

$$I_{ac}^{\omega_M}/I_{dc} = 2J_1(\delta_0)\tanh\left[\frac{\ln 10}{2}\Delta A\right]\sin\omega_M t \quad \text{(A2)}$$

Since $\alpha_B = 2\pi(\Delta n)l/\lambda$, where Δn and l are the birefringence and thickness of the sapphire plate, the calibration signal given by eq A1 oscillates with wavelength. However, the extrema do not occur at $\alpha_B = n\pi/2$ (n = odd integer), as previously indicated.[16] To find the wavelengths at which this condition occurs ($\sin\alpha_B = \pm 1$, $\cos\alpha_B = 0$) we instead rotate both the sapphire plate and polarizer by $\pi/2$, thereby reversing the sign of α_B and making the two linear polarizers parallel instead of crossed. Equation A1 then becomes

$$\frac{I_{ac}^{\omega_M}}{I_{dc}} = \frac{2J_1(\delta_0)\sin\alpha_B \sin\omega_M t}{1 + J_0(\delta_0)\cos\alpha_B} \quad \text{(A3)}$$

Equations 1 and 3 are equal when $\cos\alpha_B = 0$, and hence $\sin\alpha_B = \pm 1$.

To calibrate a CD spectrum, therefore, two calibration spectra are obtained with orientations of the sapphire plate and polarizer unit differing by $\pi/2$. At their intersection points, the signals correspond to $\tanh((\ln 10)\,\Delta A/2) = \pm 1$. Calibration at other wavelengths is then carried out by interpolation. An example of a calibration spectrum is shown in Figure 13.

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Nuclear Magnetic Resonance Spectroscopy. Spin–Lattice Relaxation of the Acetic Acid Carboxyl Carbon[1]

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Abstract: The carbon-13 spin–lattice relaxation times of the carboxyl carbons of acetic acid and its deuterated analogues (CH_3COOD, CD_3COOH, CD_3COOD) have been measured by nuclear magnetic resonance spectroscopy. These measurements reveal that the methyl protons and the hydroxyl proton contribute roughly equally to the total dipolar relaxation of neat acetic acid. Spin–rotation relaxation is also observed in these molecules. The T_1 and NOE values for the carboxyl carbon of acetic acid in aqueous solution each demonstrate a small concentration dependence in the region of high acid concentration. Although samples of 1 M acetic acid contaminated with paramagnetic metal ions show a marked pH dependence of T_1 and NOE, the T_1 and NOE values for purified samples are invariant with respect to pH. Some chemical implications of the above behavior are discussed.

Traditionally, nuclear magnetic resonance spectroscopists have usually been concerned with the measurement of chemical shifts, resonance intensities, and coupling constants. In recent years, yet another parameter, the spin–lattice relaxation time (T_1), has become of interest in carbon-13 NMR spectroscopy.[2] Although T_1 values may yield important information concerning molecular dynamics, their measurement is often fraught with difficulties. The presence of oxygen in solution, contamination by other paramagnetic impurities, vortex formation in the sample, temperature variation, and instrumental problems often lead to variable results for T_1 studies of the same molecule performed under different conditions. The value of T_1 for the carboxyl carbon of neat acetic acid, for example, has been determined by several groups[3] under various conditions, and the reported values range from 18.5 to 41.1 s.

A more detailed study of the spin–lattice relaxation behavior of acetic acid is reported here. Such a study is particularly appropriate in view of the recently discovered extreme sensitivity of carboxyl carbon T_1 values to contamination by trace paramagnetic metal ion impurities.[3e,4,5] By means of selective deuteration experiments, the relative contributions of various mechanisms to the relaxation of the acetic acid carboxyl carbon atom have been studied, and in addition the effects of dilution and pH changes upon the values of T_1 for this nucleus have been investigated.

Results and Discussion

Acetic Acid and Its Deuterated Analogues. In order to investigate the relative contributions to dipole–dipole relaxation (T_1^{DD}) from the methyl and hydroxyl protons of neat acetic acid, T_1 values (T_1^{obsd}) and nuclear Overhauser enhancements (NOE $(1 + \eta)$) for the carboxyl carbon atom of the molecules CH_3COOH, CH_3COOD, CD_3COOH, and CD_3COOD were measured. In each case, the dipole–dipole relaxation arising from the protons and the spin–lattice relaxation due to other mechanisms (T_1^{other}) were calculated by use of eq 1 and 2.

$$T_1^{DD} = T_1^{obsd}\frac{1.988}{\eta} \quad (1)$$

$$\frac{1}{T_1^{obsd}} = \frac{1}{T_1^{DD}} + \frac{1}{T_1^{other}} \quad (2)$$

The T_1 values were measured at 15.09 MHz on our "Brukarian" spectrometer by the progressive saturation technique, and are deemed accurate to ±10%[6] (see Experimental Section). The accuracy of the NOE measurements is approximately ±5%. Because carboxyl carbon T_1 values are known to be extremely sensitive to paramagnetic metal ion impurities, the samples (obtained from commercial sources) were distilled three or more times, and all glassware, vortex plugs, etc., were decontaminated as described elsewhere,[4] and in the Experimental Section. Deoxygenation was achieved by purging with nitrogen, or by the freeze–thaw technique.

The results of this study are presented in Table I. It must be emphasized at this point that in spite of the rigorous purification procedures employed, all T_1 values reported in Table I and elsewhere in this paper may be only lower limits. If residual contamination by paramagnetic metal ions or by oxygen is great enough, T_1 values in the absence of contamination may be larger than reported. However, in all cases the reported values are reproducible for multiple samples, and other evidence (see below) indicates that even if some individual T_1 or NOE values are somewhat in error, the trends observed cannot be ascribed to contamination by paramagnetic impurities.

The first line of the table reports results for CH_3COOH. These values for T_1 and NOE agree, within experimental error, with those reported by Farrar et al.[3d] Other values for T_1 and NOE reported in the literature are smaller than