Vibrational Circular Dichroism and Absolute Configuration of Chiral Sulfoxides: *tert*-Butyl Methyl Sulfoxide

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Dedicated to Professor Kurt Schank on the occasion of his 65th birthday

Abstract: Mid-infrared vibrational unpolarised absorption and vibrational circular dichroism (VCD) spectra of CCl_4 solutions of *tert*-butyl methyl sulfoxide (**1**) are reported. The spectra are compared to ab initio density functional theory (DFT) calculations carried out using two functionals, B3PW91 and B3LYP, and two basis sets, 6-31G* and TZ2P. The VCD spectra are calculated using Gauge-invariant atomic orbitals (GIAOs). The analysis of the VCD spectrum confirms the *R*(−)/*S*(+) absolute configuration of **1**. The advantages and disadvantages of VCD spectroscopy in determining the absolute configurations of chiral sulfoxides are discussed.

Keywords: absolute configuration · chiral sulfoxides · circular dichroism · density functional calculations

Introduction

We report a study of the vibrational circular dichroism (VCD) spectrum of the chiral sulfoxide, *tert*-butyl methyl sulfoxide (**1**). The mid-IR VCD spectrum of **1** is analysed using the recently developed DFT/GIAO methodology for the prediction of vibrational rotational strengths.[1–5]

Optically active **1** was first synthesised by Axelrod et al.[6] via Grignard reaction from *O*-menthyl-methanesulfinate. The known reaction stereochemistry (inversion)[7] led to the absolute configuration (AC): *R*(−)/*S*(+). Subsequently, additional methods for the synthesis of enantiomers of **1** have been reported;[8–16] **1** has been used in evaluating the efficacy of a variety of chiral shift reagents for the determination of enantiomeric excess (*ee*) in chiral sulfoxides;[17–19] and the AC of **1** has been confirmed through X-ray crystallography of the derivative (1*R*,2*S*)-ephedrinium-(*S*)-*tert*-butylsulfinylacetate.[20]

The purpose of this work is to investigate the utility of VCD spectroscopy[4, 21, 22] in elucidating the AC of chiral sulfoxides. There have been no prior VCD studies of chiral sulfoxides. The dialkyl sulfoxide **1** is a convenient target for initial study. Its small size and conformational rigidity facilitate analysis of its VCD spectrum and the evaluation of the DFT/GIAO methodology.

Vibrational unpolarised absorption ("IR") spectra are automatically measured and calculated simultaneously with the measurement and calculation of VCD spectra. The analysis of VCD spectra is substantially enhanced by simultaneous analysis of unpolarized absorption spectra. Accordingly, we study the unpolarized absorption spectrum of **1** in addition to its VCD spectrum.

Results

The mid-IR absorption spectra of three solutions of (±)-**1** in CCl_4 of varying concentration are shown in Figure 1. Significant variation with concentration is observed in the region 975 – 1100 cm^{-1}. At the highest concentration (1.08 M) a shoulder is observed to low frequency of the strong band at ~1060 cm^{-1}. As the concentration decreases, the intensity of this shoulder decreases, showing that it originates in molecular aggregates, whose fractional concentration diminishes with diminishing concentration of **1**. Some variation with concentration is also observed in the bands at ~1300 cm^{-1}. Otherwise, the absorption spectrum of **1** varies very little with concentration from 1.08 to 0.06 M.

The mid-IR VCD spectra of (+)-**1** corresponding to the absorption spectra in Figure 1 are shown in Figure 2. The signal-to-noise (S:N) ratios of the experimental VCD spectra are much lower than those of the absorption spectra; as a

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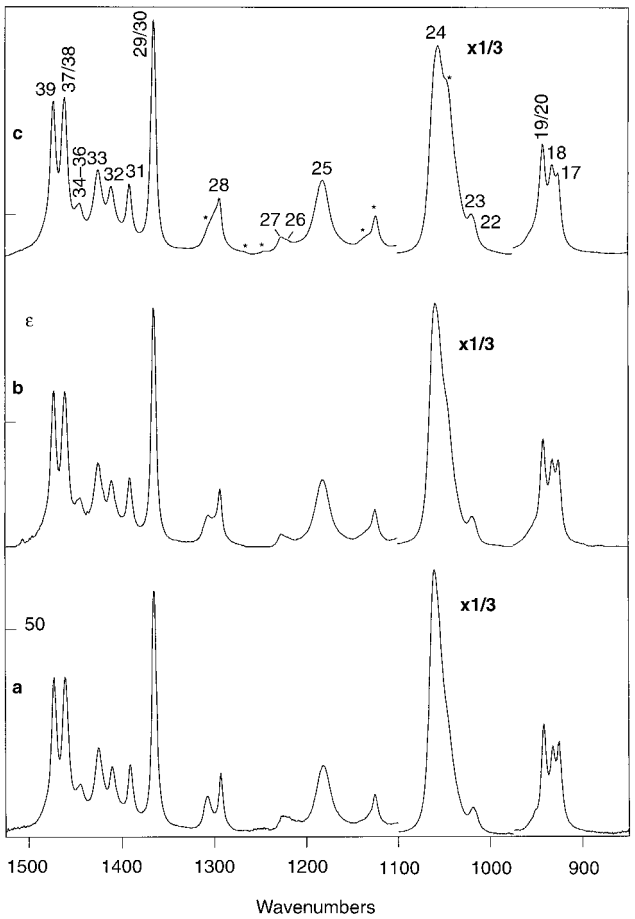

Figure 1. Experimental mid-IR absorption spectrum of (±)-**1** in CCl_4 solution: a) 0.06 M, 597 μm path; b) 0.42 M, 109 μm path; c) 1.08 M, 109 μm path. Assignments of fundamentals are indicated in c). Asterisks indicate bands not assigned as fundamentals (see text).

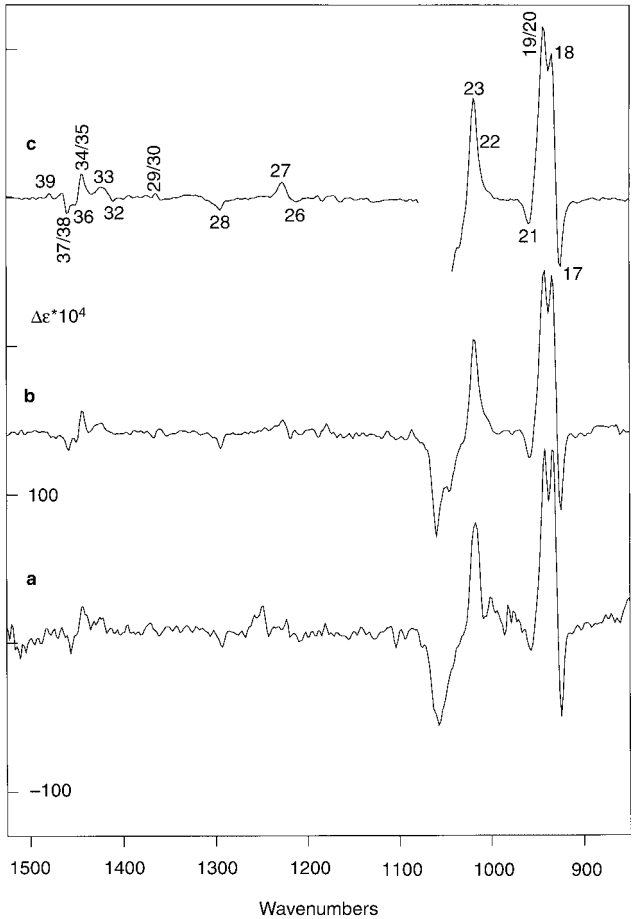

Figure 2. Experimental mid-IR VCD spectrum of *S*(+)-**1** in CCl_4 solution: a) 0.06 M, 597μm path; b) 0.52 (+)/0.48 (−) M, 109 μm path; c) 1.22 (+)/1.11 (−) M, 109 μm path. The spectra are half-difference spectra (see text). Assignments of fundamentals are indicated in c). The lower signal-to-noise ratio in a) is attributable to the much greater solvent absorption. Note that in c), the VCD of fundamental 24 is not shown; the absorbance at this concentration–pathlength combination was too great to permit artefact-free VCD measurement.

result, the concentration dependence of the VCD is less easily quantitated than that of the absorption spectrum. With the exception of the region 975–1100 cm^{-1}, concentration dependence is not detectable. In the case of the band at ~1060 cm^{-1}, a shoulder is observed at ~0.5 M and ~1.1 M while at 0.06 M no shoulder is apparent; as with the absorption spectrum, this shoulder can be attributed to molecular aggregation.

In our analysis of the absorption and VCD spectra of **1**, we utilize the spectra shown in Figures 1c and 2c, with the exception of the region 975–1100 cm^{-1}, where the spectra shown in Figures 1a and 2a are used.

Equilibrium geometries of **1** have been obtained at the B3PW91/TZ2P, B3LYP/TZ2P, B3PW91/6-31G*, and B3LYP/6-31G* levels. The B3PW91/TZ2P structure is shown in Figure 3. Selected structural parameters are given in Table 1. The O and C1 atoms are staggered with respect to C3, C4, C5 when viewed along the SC2 bond. The bond angles within the C1S(O)C2 moiety are approximately tetrahedral; it is noteworthy, however, that they are uniformly smaller than 109°, the C1SC2 angle being the smallest (100–101°). There have been no experimental structural studies of **1**. In the closely related molecule, DMSO, the CSO and CSC angles were determined by microwave spectroscopy to be 106.6° and 96.6°, respectively.[23]

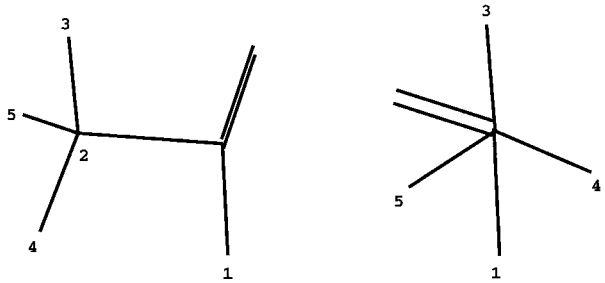

Figure 3. B3PW91/TZ2P structure of **1** (H atoms are not shown). C atoms are numbered. In the right-hand view, the S and C2 atoms are superimposed.

Harmonic vibrational frequencies, dipole strengths and rotational strengths predicted for fundamentals 17–39 using the B3PW91 and B3LYP functionals and the TZ2P basis set are given in Table 2. Absorption and VCD spectra predicted thence are shown in Figures 4 and 5. Rotational strengths and VCD spectra are for the *S* enantiomer. The B3PW91/TZ2P and B3LYP/TZ2P absorption spectra are very similar to each other and in excellent qualitative agreement with the

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Table 1. Structural parameters of **1**.[a]

	B3PW91/ 6-31G*	B3LYP/ 6-31G*	B3PW91/ TZ2P	B3LYP/ TZ2P
bond lengths				
SO	1.513	1.518	1.504	1.509
SC1	1.824	1.838	1.819	1.833
SC2	1.882	1.899	1.879	1.899
bond angles				
C1SO	106.3	106.2	105.6	105.4
C2SO	106.5	106.4	106.7	106.6
C1SC2	100.4	100.4	100.7	100.8
dihedral angles[b]				
C1SC2C3	179.4	179.5	177.8	177.8
C1SC2C4	– 62.7	– 62.5	– 64.5	– 64.4
C1SC2C5	61.9	62.0	59.9	59.8
OSC2C3	68.8	69.0	67.8	68.0
OSC2C4	– 173.3	– 173.1	-174.5	– 174.3
OSC2C5	– 48.7	– 48.5	-50.0	– 50.0

[a] Bond lengths in Å; bond angles and dihedral angles in degrees. [b] *S* enantiomer.

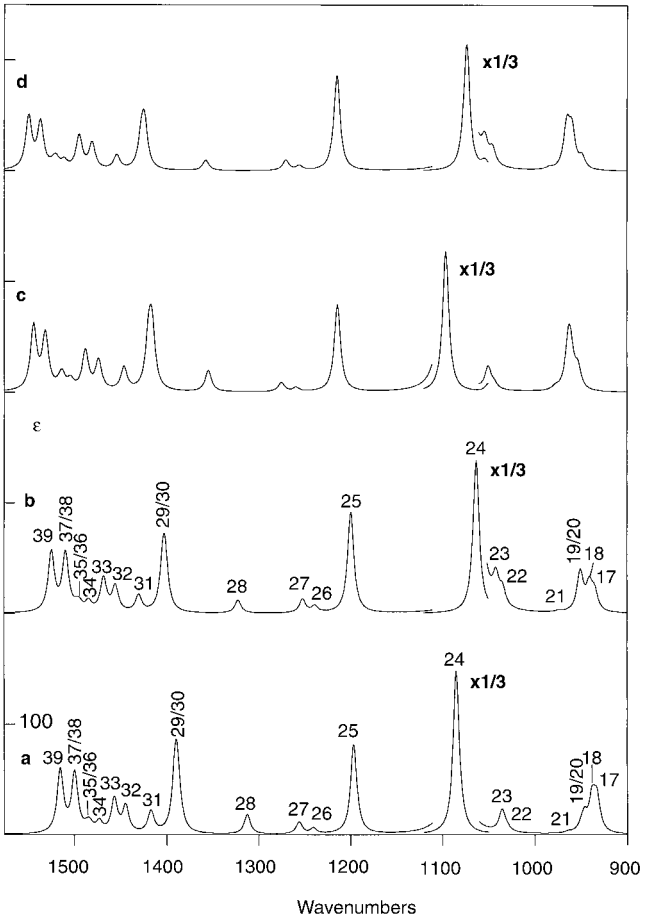

Figure 4. Calculated mid-IR absorption spectrum of **1**: a) B3PW91/TZ2P; b) B3LYP/TZ2P; c) B3PW91/6-31G*; d) B3LYP/6-31G*. Band shapes are Lorentzian; $\gamma = 4.0\ cm^{-1}$. Fundamentals are numbered.

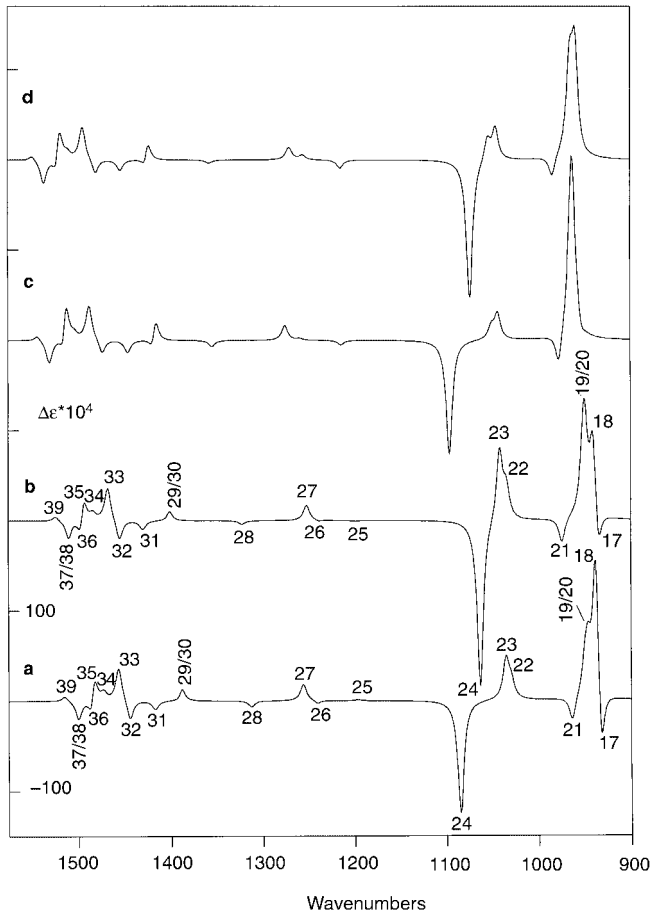

Figure 5. Calculated mid-IR VCD spectrum of *S*(+)-**1**: a) B3PW91/TZ2P; b) B3LYP/TZ2P; c) B3PW91/6-31G*; d) B3LYP/6-31G*. Band shapes are Lorentzian; $\gamma = 4.0\ cm^{-1}$. Fundamentals are numbered.

experimental spectrum, allowing for the overall shift of the calculated spectra to higher frequencies due principally to the neglect of anharmonicity in the calculations.[24] Assignment of fundamentals 17–39 in the experimental absorption spectrum is straightforward, as shown in Figures 1c and 6e. Fundamentals 17, 18, 24, 25–28, 31–33 and 39 are resolved. Fundamentals 19/20, 22/23, 29/30, 34/35/36 and 37/38 are not resolved, consistent with the small predicted frequency separations. Fundamental 21 is not clearly visible. Assignment of the VCD spectrum follows from that of the absorption spectrum as shown in Figures 2c and 6f. The B3PW91/TZ2P and B3LYP/TZ2P VCD spectra are very similar; both are in excellent qualitative agreement with the experimental VCD. In the region of fundamentals 17–24 VCD is predicted to be substantially larger than in the region of fundamentals 25–39, as is observed experimentally. Fundamentals 17, 18, 21, 24, 26–28, 32, 33, 36 and 39 are resolved and give measurable VCD. Fundamentals 19/20, 22/23, 29/30, 34/35 and 37/38 are not resolved, but give measurable VCD. Fundamentals 25 and 31 are not detectable.

Experimental and calculated frequencies are compared in Table 2 and Figure 7. Experimental frequencies for modes 17–24 are obtained by Lorentzian fitting of the experimental absorption and VCD spectra; for modes 25–39 they are peak absorption frequencies. Percentage deviations of calculated and experimental frequencies are in the range 0–4%, typical of B3PW91/TZ2P and B3LYP/TZ2P calculations,[25–27] supporting the assignment of the fundamentals arrived at the above. Experimental dipole and rotational strengths for

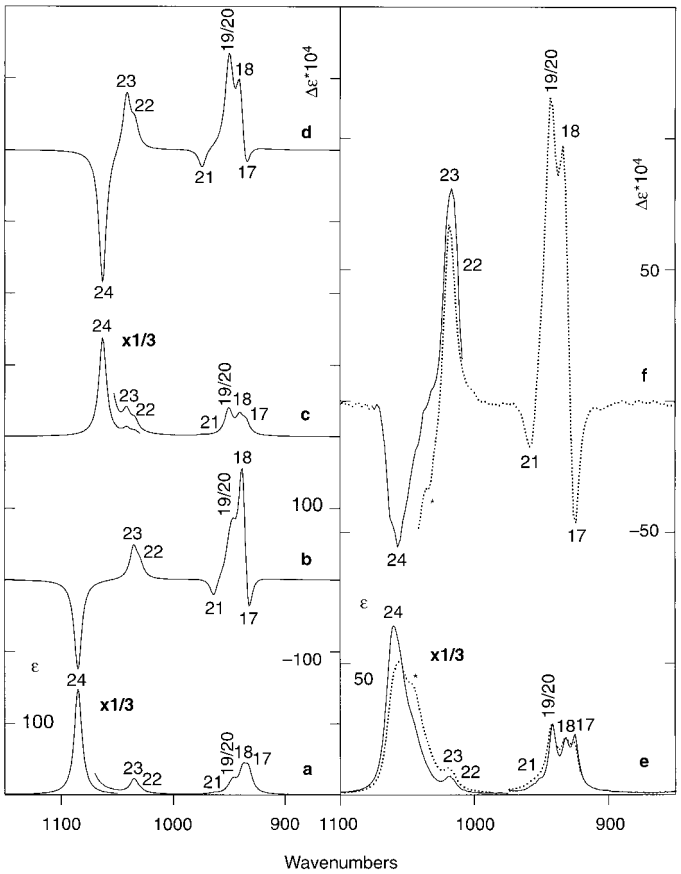

Figure 6. Absorption and VCD spectra of fundamentals 17–24: a) B3PW91/TZ2P absorption; b) B3PW91/TZ2P VCD; c) B3LYP/TZ2P absorption; d) B3LYP/TZ2P VCD; e) experimental absorption (—— from Figure 1a; ---- from Figure 1c); f) experimental VCD (—— from Figure 2a; ---- from Figure 2c). Band shapes in a)–d) are Lorentzian; $\gamma = 4.0\ cm^{-1}$. All VCD spectra are for *S*(+)-**1**. Fundamentals are numbered. Asterisks indicate features attributed to aggregates of **1** (see text).

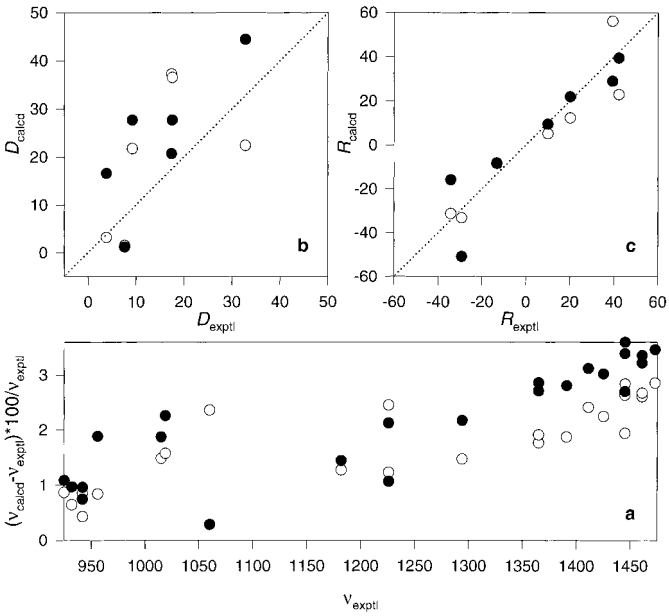

Figure 7. Comparison of calculated and experimental frequencies, a) (modes 17–39); dipole strengths, b) (modes 17–23); rotational strengths, c) (modes 17–24). $\tilde{\nu}$, *D*, *R* are in cm^{-1}, $10^{-40}\ esu^2cm^2$ and $10^{-44}\ esu^2cm^2$, respectively. Rotational strengths are for *S*(+)-**1**. ○ and ● are for B3PW91/TZ2P and B3LYP/TZ2P calculations, respectively. Dashed lines in b) and c) have slope +1.

fundamentals 17–24 obtained by Lorentzian fitting are also compared to calculated values in Figure 7. Again, agreement is consistent with prior experience.[25–27] Note, particularly, the excellent agreement of calculated and experimental rotational strengths.

We have compared calculated VCD spectra for *S*-**1** to experimental spectra of (+)-**1** (Figures 2, 5 and 6) and calculated rotational strengths for *S*-**1** to experimental rotational strengths of (+)-**1** (Figure 7). The excellent agreement confirms the *R*(−)/*S*(+) AC of **1**.

The B3PW91/6-31G* and B3LYP/6-31G* absorption and VCD spectra (Figures 4c, 4d and 5c, 5d) are qualitatively very similar, overall, to the corresponding TZ2P spectra. The changes with basis set are most marked for the fundamentals 17–20, 25 and 26. Where the 6-31G* and TZ2P spectra are different, the 6-31G* spectra agree less well with the experimental spectra.

As noted above, the VCD originating in fundamentals 17–24 is substantially larger than that of fundamentals 25–39. Mode 24 is predominantly S–O stretching; modes 17–23 are predominantly C–H bending modes. At the present time, we cannot provide a qualitative explanation of the much larger rotational strengths of these modes.

Discussion

The goal of this work is to evaluate the accuracy of the DFT/GIAO methodology in predicting the solution VCD spectrum of **1**. Since the DFT/GIAO calculations are carried out for isolated ("gas phase") molecules, it is important that comparison be made with the experimental spectrum at concentrations where Beer's law applies, that is the spectrum at infinite dilution. Our studies have been carried out using CCl_4 solutions, since CCl_4 is a relatively non-perturbing solvent and since it is also a very convenient solvent for IR spectroscopy. Initial studies of the mid-IR absorption spectrum of CCl_4 solutions of **1** showed that above ~0.1M the spectrum becomes significantly concentration dependent. In particular, the very strong S–O stretching band at $\sim 1060\ cm^{-1}$ exhibits a shoulder to low frequency whose intensity increases with increasing concentration. This behavior can be attributed to aggregation of **1**. Aggregation in sulfoxides is precedented. Infrared spectroscopy of DMSO in CCl_4 solution demonstrated aggregation at concentrations $\gtrsim$0.01M.[28] Up to ~0.1M dimerisation occurs; at higher concentrations, additional aggregates are formed. A symmetrical, "head-to-tail" structure for the dimer was proposed. The formation of an analogous dimer in 2-thiaindane-2-oxide was inferred from NMR and freezing point depression studies in $CDCl_3$ and cyclohexane solutions, respectively.[29] Dimerisation of methyl *n*-butyl sulfoxide in cyclohexane solution was demonstrated by vapor phase osmometry.[7, 30] In the specific case of **1**, the specific rotation in acetone has been reported to be concentration dependent, indicating aggregation.[13] Our finding that aggregation also occurs in CCl_4 solutions of **1** is therefore

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Table 2. Frequencies, dipole strengths, and rotational strengths of **1**.[a]

	B3PW91/TZ2P			B3LYP/TZ2P			exptl[b]		
mode	ν	D	R	ν	D	R	ν	D	R
39	1515	43.6	1.1	1524	40.8	1.0	1473		
38	1500	23.5	−5.7	1510	22.8	−5.8			
							1461		
37	1499	18.5	1.7	1508	18.1	2.3			
36	1486	3.1	−5.5	1497	2.8	−5.3			
35	1483	5.1	7.2	1494	4.3	6.7	1445		
34	1473	7.4	1.8	1484	6.7	1.5			
33	1457	24.3	7.4	1468	23.9	7.4	1425		
32	1445	19.3	−4.6	1455	18.3	−4.5	1411		
31	1417	16.0	−2.0	1430	12.2	−1.9	1391		
30	1391	35.3	−1.1	1404	29.4	−0.8			
							1365		
29	1389	42.3	3.5	1402	34.6	2.7			
28	1313	15.8	−1.5	1322	10.3	−0.9	1294		
27	1256	9.8	4.2	1252	11.3	3.9			
							1226		
26	1241	4.6	−0.8	1239	5.7	−0.4			
25	1197	78.9	0.3	1199	88.6	−0.2	1182		
24	1085	472.5	−33.3	1063	448.6	−50.9	1060	309.3	−29.2
23	1035	21.8	12.2	1042	27.7	21.8	1019	9.2	20.1
22	1030	3.2	5.1	1034	16.6	9.4	1015	3.8	10.0
21	964	1.5	−8.4	974	1.2	−8.2	956	7.6	−13.2
20	950	4.7	8.6	951	37.4	23.5			
							942	32.8	42.2
19	946	17.7	14.3	949	7.0	15.9			
18	938	36.5	56.1	941	27.7	28.9	932	17.6	39.3
17	933	37.2	−31.3	935	20.7	−15.9	925	17.4	−34.3

[a] ν in cm^{-1}; D in 10^{-40} esu^2cm^2; R in 10^{-44} esu^2cm^2. Rotational strengths are for $S(+)$-**1**. [b] From Lorentzian fitting of spectra from Figures 1c and 2c for modes 17–21 and of spectra from Figures 1a and 2a for modes 22–24; frequencies for modes 25–39 are peak frequencies from Figure 1a.

unsurprising. The IR spectra of CCl_4 solutions of **1** over the concentration range 0.01–1M do not exhibit an isosbestic point, leading to the conclusion that more than one aggregate species exists. The expectation that aggregation involves the intermolecular interactions of sulfoxide groups is supported by the fact that the most prominent concentration-dependent feature of the spectrum is associated with the S–O stretching band. However, neither the stoichiometries nor the structures of the aggregates are defined at this time. The concentration dependence of the VCD spectrum parallels that of the absorption spectrum. The shoulder visible at ~0.5M and ~1.1M is greatly reduced at ~0.06M showing that the aggregates exhibit measurable VCD. Elsewhere, the VCD spectrum is independent of concentration. In our analysis of the IR and VCD spectra of **1**, we have used spectra measured at concentrations where Beer's law applies.

DFT spectra depend on the density functional and basis set employed. As in several previous studies,[25–27] we have carried out calculations using the hybrid functionals B3PW91 and B3LYP and the basis sets 6-31G* and TZ2P. The mid-IR absorption and VCD spectra predicted by the two functionals and two basis sets are very similar. The largest differences are observed in the region of modes 17–24. The TZ2P spectra are in better agreement with the experimental spectra than are the 6-31G* spectra, consistent with the expectation of significantly improved accuracy in calculations using the larger basis set. Similar differences have been observed in previous studies.[25–27]

The B3PW91/TZ2P and B3LYP/TZ2P absorption and VCD spectra are in excellent overall qualitative agreement with the experimental spectra in the mid-IR region. Assignment of fundamentals 17–39 is straightforward. Predicted and experimental absorption and VCD intensities are in excellent qualitative agreement. Quantitative comparison of frequencies, dipole strengths, and rotational strengths, insofar as carried out, yields agreement comparable to that found in previous studies.[25–27] In particular, calculated rotational strengths for S-**1** are in excellent agreement with experimental rotational strengths for (+)-**1**.

We have reported mid-IR VCD spectra of CCl_4 solutions of **1** at frequencies $\gtrsim 800\ cm^{-1}$. The lower frequency limit is determined by CCl_4 absorption. However, the lower limit of the VCD instrumentation is $\sim 700\ cm^{-1}$ and experiments in other solvents would extend the lower frequency limit very little. Of the fundamentals 1–16, only mode 16 is predicted to lie in the range 700–800 cm^{-1} and its VCD is predicted to be very weak. Accordingly, we have limited our studies to CCl_4 solutions and frequencies $\gtrsim 800\ cm^{-1}$. We have not measured VCD spectra of **1** in the C–H stretching region. The complexity of this region generally precludes detailed analysis.

The analysis of the VCD spectrum of **1** reconfirms the $R(-)/S(+)$ AC of **1**. The work of Drabowicz et al.[20] confirmed the AC deduced by Axelrod et al.[6] and eliminated the possibility that this might be in error. The utility of our study thus lies principally in demonstrating both the reliability

and the convenience of VCD spectroscopy as an alternative technique for determining the AC of chiral sulfoxides. A number of methodologies have been used in determining ACs for chiral sulfoxides, including ultraviolet chiroptical spectroscopies (optical rotatory dispersion and circular dichroism), X-ray crystallography, NMR spectroscopy, and chemical synthesis.[31] The VCD technique offers several advantages: 1) It is a "direct" method, involving study of the molecule of interest alone; 2) it is a solution method; 3) measurement is rapid. These advantages exist equally for electronic circular dichroism (ECD), of course. However, VCD spectra generally exhibit a much larger number of bands, of much higher resolution, than ECD spectra. As a result, analysis of VCD spectra is generally more straightforward than of ECD spectra. In addition, theoretical prediction of VCD spectra is intrinsically easier, since only the ground electronic state is involved, in contrast to ECD where excited state properties must also be calculated. Theoretical analysis of VCD spectra is therefore easier. At the same time, it must be noted that vibrational absorption is intrinsically weaker than electronic absorption and that VCD is intrinsically weaker than ECD. Optimum circular dichroism measurements (with standard instrumentation) are generally made with absorbance values of $\sim 0.1-1$. For comparable pathlengths, this generally requires much higher concentrations for vibrational spectroscopy than for electronic spectroscopy. In addition, anisotropy ratios ($\Delta A:A = \Delta\varepsilon:\varepsilon$) are generally much lower for VCD than for ECD. As a result, S:N ratios are lower in VCD spectra. The present study of **1** illustrates this feature of VCD spectroscopy: for practical pathlengths (up to ~ 1 mm) concentrations $\gtrsim 0.01$M are required for mid-IR VCD measurement. VCD signals are comparable to the instrumental sensitivity for a number of bands. For molecules which are soluble in convenient IR solvents (such as CCl_4) up to concentrations of 1M and whose spectra obey Beer's law up to 1M, the relative insensitivity of VCD poses no difficulty. However, for molecules of more limited solubility and/or whose spectra are concentration dependent at concentrations required for VCD measurement, the use of VCD becomes more difficult. In the present study of **1** we have shown that aggregation occurs in CCl_4 solution at concentrations $\gtrsim 0.1$M. Single molecule spectra—that is Beer's law spectra—thus require concentrations $\lesssim 0.1$M. As aggregation becomes greater, the concentration range for VCD spectroscopy further decreases.

In addition to the issues of solubility and aggregation discussed above, two further factors affect the practical application of VCD spectroscopy in determining AC. First, the size of the molecule determines the computational time required for VCD prediction. Second, conformational flexibility introduces additional complexity in the analysis of the VCD spectrum. At the present time, 6-31G* calculations (the minimum basis set level for which useful predictions can be obtained[4, 5]) can be easily carried out for molecules with 50–100 atoms using standard work-stations and larger molecules have been studied on supercomputers. Future increases in speed of computational hardware and software will further accelerate VCD computations. Thus, for a large fraction of non-polymeric organic molecules, computational demands will not be limiting. In the case of conformationally flexible molecules, the structures, relative energies, and VCD spectra of all conformers must be calculated and population-weighted spectra obtained thence. The analysis of the vibrational spectra of conformationally flexible molecules is more complex than for rigid molecules. However, studies of a number of such molecules have shown that, when the number of significantly populated conformations is relatively small such analysis is practicable.[32] With respect to this issue, we note that it arises equally in ECD spectroscopy and that analysis is easier for VCD as a result of the much narrower bandwidths and, hence, much greater resolution of VCD spectra.

X-ray crystallography provides an alternative technique for determining the AC of chiral sulfoxides.[31] An advantage of VCD is that diffraction quality single crystals are not required. NMR methods have also been used for determining the AC of chiral sulfoxides.[31] Such methods generally rely on empirical correlation with AC of chemical shifts induced in protons neighboring the sulfoxide group by chiral environments.[33–36] In comparison, VCD is a non-empirical methodology.

The first assignment of AC in **1** by Axelrod et al.[6] relied on the knowledge of the AC of its synthetic precursor, *O*-menthyl methanesulfinate, together with the assumption that the Grignard reaction leading to **1** occurs with inversion of configuration, as had been established for other sulfoxides.[7] The use of VCD does not require the knowledge of the AC of synthetic precursors (or, alternatively, of synthetic derivatives) and of the stereochemistry of reactions used in synthesising (or derivatising) the chiral sulfoxide of interest.

Conclusion

Our study of **1** demonstrates that VCD spectroscopy constitutes a practical alternative technique for determining the AC of chiral sulfoxides, which in some cases may be more convenient and efficient than established techniques. The availability of both commercial instrumentation for the measurement of VCD and of commercial software for the calculation of VCD spectra using the DFT/GIAO methodology renders its application routine at this time. VCD studies of other chiral sulfoxides are currently in progress.[37, 38]

Experimental Section

Synthesis

Racemic *tert*-butyl methyl sulfoxide [(±)-**1**] was prepared according to the literature procedure.[39] The dextro- and levorotatory enantiomers of *tert*-butyl methyl sulfoxide (**1**) were prepared using the diastereomeric sulfinates derived from (−) diacetone glucose (DAG).[12, 13] Since we were not able to obtain these sulfinates having the reported diastereomeric ratio in the Łódź laboratory the detailed synthetic procedures for the preparation of the enantiomerically pure dextrorotatory enantiomer of **1** and the levorotatory enantiomer of **1** having 50.8% *ee* are described below:

The dextrorotatory enantiomer (+)-1

a) 1,2,5,6-Di-*O*-isopropylidene-*α*-D-glucofuranosyl (+)-(*R*)-*tert*-butanesulfinate: A solution of DAG (7.2 g, 27.6 mmol) and pyridine (2.4 g, 30 mmol) in THF (15 mL) was added dropwise with vigorous stirring to a solution of *tert*-butanesulfinyl chloride (3.86 g, 27.5 mmol) in THF (20 mL) at 70 °C.

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After the reaction mixture was stirred for 6 h at 70 °C and 42 h at room temperature, the solution was diluted with diethyl ether (500 mL) and quenched with water. The organic phase was separated and washed with 5% H_2SO_4 solution, 5% K_2CO_3 solution and water and dried over $MgSO_4$. After the solvent was removed in vacuo, the crude sulfinate (10.15 g) with $[\alpha]_D = -1.34$ ($c = 1.78$, acetone) was purified by column chromatography on silica gel (120 g) with petroleum ether/diethyl ether 1:1 as an eluent giving the dextrorotatory diastereomer (5.322 g) with $[\alpha]_D = +10.60$ ($c = 2.02$, acetone) and the levorotatory diastereomer (1.267 g) with $[\alpha]_D = -34.5$ ($c = 1.3$, acetone). The dextrorotatory diastereomer was purified again by silica gel (60 g) chromatography affording the sulfinate (4.446 g) with $[\alpha]_D = +11.3$ (1.67, acetone).

b) (+)-*tert*-Butyl methyl sulfoxide (1): A 3 M solution of methylmagnesium bromide in diethyl ether (15 mL) was added dropwise at room temperature was added to a solution of the dextrorotatory sulfinate obtained above in diethyl ether (30 mL). After the reaction mixture was stirred for 72 h at room temperature, the reaction mixture was quenched with 5% H_2SO_4 solution and diluted with water (200 mL). The organic solution was separated from the aqueous phase, and the aqueous phase was extracted with chloroform (6×50 mL). The organic extracts were dried over $MgSO_4$. Evaporation of the solvent gave the crude *tert*-butyl methyl sulfoxide (1.2 g), which was purified by column chromatography on silica gel (40 g). The column was washed subsequently with petroleum ether/diethyl ether 1:1 (200 mL), and diethyl ether (200 mL), methylene chloride (200 mL), and acetone (200 mL). Evaporation of the acetone solution gave the pure sulfoxide (0.438 g) with $[\alpha]_D = +12.0$ ($c = 1.52$, MeOH) and $[\alpha]_D = +1.6$ ($c = 1.27$, $CHCl_3$).

The levorotatory enantiomer [(−)-1]

a) 1,2,5,6-Di-*O*-isopropylidene-α-D-glucofuranose (+)-(*R*)-methanesulfinate: A solution of methanesulfinyl chloride (4.7 g, 47 mmol) in THF (10 mL) was added dropwise with vigorous stirring to a solution of DAG (10.4 g, 40 mmol) and pyridine (4 mL, 50 mmol) in THF (100 mL) at 70 °C. After the reaction mixture was stirred for 5 h at 70 °C, the solution was diluted with CH_2Cl_2 (300 mL) and quenched with water. The organic phase was washed with 5% H_2SO_4 solution and 5% K_2CO_3 solution and dried over $MgSO_4$. Evaporation of the solvent gave the crude sulfinate (13.06 g) with $[\alpha]_D = +4.2$ ($c = 2.37$, acetone).

b) (−)-*tert*-Butyl methyl sulfoxide (1): A solution of the dextrorotatory sulfinate prepared above (13.06 g) in toluene (30 mL) was added dropwise at 0 °C to a solution of *tert*-butylmagnesium chloride prepared in situ from *tert*-butyl chloride (7.36 g) and magnesium (1.92 g, 80 mmol) in diethyl ether (50 mL). After the reaction mixture was stirred at room temperature for 24 h, the solution was quenched with 5% H_2SO_4 solution and diluted with water (200 mL). The organic solution was separated from the aqueous phase, which was later extracted with chloroform (6×50 mL). The chloroform extracts were dried over $MgSO_4$. Evaporation of the solvent gave the crude *tert*-butyl methyl sulfoxide (2.2 g). The crude sulfoxide was purified by column chromatography on silica gel (70 g). The column was washed out subsequently with diethyl ether (250 mL), CH_2Cl_2 (250 mL) and acetone (350 mL). Evaporation of the acetone solution gave the pure sulfoxide (1.09 g) with $[\alpha]_D = -8.25$ (1.66, MeOH).

The enantiomeric excess was measured by ^{1}H-NMR spectroscopy using optically active *tert*-butylphenyl phosphinothioic acid as a chiral solvating agent.[19] *ee* values for (+)-**1** and (−)-**1** were 100% and 50.8%, respectively. Specific rotations were measured for the 0.06 M CCl_4 solutions of **1** used for VCD spectroscopy (see below). $[\alpha]_D^{30}$ values for (+)-**1** and (−)-**1** were +13.7° and −8.3°, respectively. Assuming that the *ee* of (+)-**1** is 100%, this leads to an *ee* of (−)-**1** of 61%.

IR and VCD spectroscopy

Absorption spectra of CCl_4 solutions of **1** were measured at 1 cm^{-1} resolution using a Nicolet MX-1 spectrometer. VCD spectra of CCl_4 solutions of **1** were measured at 4 cm^{-1} resolution using a Bomem/BioTools ChiralIR spectrometer. VCD scan times were 1 h. The VCD spectrum of **1** at a given concentration and pathlength was obtained from the VCD spectra of (+)-**1**, (−)-**1**, and (±)-**1**, measured at the same concentration and pathlength. The spectrum of (±)-**1** was used as the baseline for the (+)-**1** and (−)-**1** spectra. After conversion to $\Delta\varepsilon$ units, the spectra of (+)-**1** and (−)-**1** were normalized to 100% *ee*. Subsequently, the half-difference and half-sum spectra, $\frac{1}{2}[\Delta\varepsilon(+) - \Delta\varepsilon(-)]$ and $\frac{1}{2}[\Delta\varepsilon(+) + \Delta\varepsilon(-)]$, were calculated. The former provides the final VCD spectrum of (+)-**1**. The latter provides a gauge of the reliability of the VCD spectrum; it is non-zero due to noise and to artifact signals which are not reproducible in the original (+), (−), and (±) spectra.

The VCD spectrum of (+)-**1** was substantially more intense than the spectrum of (−)-**1** (at a given concentration) due to the greater *ee* of (+)-**1**. Quantitative comparison of the VCD spectra exhibiting the highest S:N ratio leads to *ee*-(+): *ee*-(−) ~1.65, identical (within experimental error) to the ratio obtained from the measured rotations of the ~0.06 M CCl_4 solutions (see above). In calculating the half-difference VCD spectrum, we have therefore used the ee values: *ee*-(+) = 100%; *ee*-(−) = 100:1.65 = 61%.

The absorption spectra of (+)-**1**, (−)-**1**, and (±)-**1** in CCl_4 were very similar but not identical. The sample of (±)-**1** exhibited the smallest number of bands and was therefore the most chemically pure. However, the 1125 cm^{-1} band of (±)-**1** was not exhibited by (−)-**1** and is attributable to an impurity.

Experimental vibrational frequencies, dipole strengths, and rotational strengths were obtained from experimental absorption and VCD spectra through Lorentzian fitting, as described previously.[25, 26]

Computational methods

DFT calculations were carried out using GAUSSIAN 98[40] as described previously.[1, 2, 25, 26] All calculations of harmonic force fields (HFFs), atomic polar tensors (APTs), and atomic axial tensors (AATs) are carried out using analytical derivative (AD) techniques and perturbation-dependent (PD) basis sets. The functionals B3PW91[41, 42] and B3LYP[42] were used, together with the basis sets 6-31G*[43] and TZ2P.[44] Calculated harmonic vibrational frequencies, dipole strengths, and rotational strengths were used to predict absorption and VCD spectra assuming Lorentzian band shapes, as described previously.[25, 26]

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