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Direct determination of the absolute configuration of a cyclic thiolsulfinate by VCD spectroscopy

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Abstract—Experimental and calculated vibrational circular dichroism (VCD) spectra of the enantiomers of the conformationally rigid thiolsulfinate, naphtho[1,8-*cd*]-1,2-dithiole 1-oxide **1**, obtained by chromatographic resolution of the racemate, were in excellent agreement, showing a (+)-(*S*)-**1**/(−)-(*R*)-**1** relationship.

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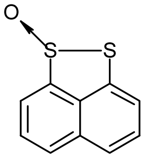
1. Introduction

In connection with our previous studies of enantiomer interconversion barriers in *S*-oxides, we prepared the enantiomers of naphtho[1,8-*cd*]-1,2-dithiole 1-oxide **1** by small scale enantioselective chromatographic resolution.[1] The high specific rotations of (+)- and (−)-**1** (±1540 at 546 nm in CH_2Cl_2), together with their rigid structures, made them of interest for theoretical calculations of specific rotations. As described in a recent paper,[2] specific rotation values at discrete wavelengths, obtained by polarimetric determination and by density functional calculation (DFT), showed an agreement that permitted a determination of absolute configuration.



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Herein we report on the use of vibrational circular dichroism (VCD) spectroscopy for the same purpose. Our VCD study unequivocally confirms the specific rotation results.

2. Results and discussion

The optimized B3LYP/6-31G** structure of (*S*)-**1** is shown in Figure 1. The S–S bridge shows a slight non-planarity, whereas the atoms in naphthalene moiety are all lying nearly in the same plane. This is in agreement with the results of Stephens et al. who used the B3LYP/6-31G* method for geometry optimization.[2]

When increasing the basis set to the 6-311G** level, the degree of nonplanarity increases slightly. From the calculated structures we estimate the C–S–S–O dihedral angle to be ca. 100°

In Figure 2, the experimental IR spectrum (+)-**1** and the calculated absorption spectrum of (*S*)-**1** are presented. After scaling the calculated frequencies by a single scale factor of 0.975, there is a perfect agreement between experimental and calculated spectra, both in terms of energies and band intensities and each observable band can be assigned straightforwardly. This is a strong indication that the optimized structure is a good description of the geometry of **1**.

Figure 1. Side view of a stick representation of (*S*)-**1**.

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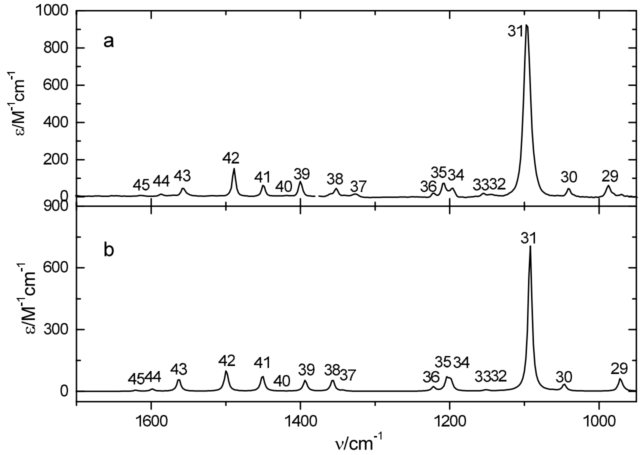

Figure 2. a) Experimental mid-IR absorption spectrum of **1** in CS_2 (0.015 M, 950–1375 cm^{-1}) and in $CDCl_3$ (0.24 M, 1380–1700 cm^{-1}). b) Calculated spectrum of (*S*)-**1** at the B3LYP/6-31G** level. Lorentzian band shapes are used with $\gamma = 3$ cm^{-1}. Frequencies have been scaled by a factor of 0.975. Fundamentals are numbered.

The strongest band at 1096 cm^{-1} (mode 31) is assigned to the pure S–O stretch. The modes 45–32 and 30–29 are due to in-plane C–C stretching and C–H bending vibrations of the naphthalene moiety.

The corresponding VCD spectra are shown in Figure 3. The S–O stretch exhibits a strong positive VCD, while the remaining modes in the observed region exhibit VCD signals that are too weak to be observed under our conditions. This is in agreement with the calculation for (*S*)-**1** where the S–O stretch is calculated to have a large positive VCD and the other modes have much weaker VCD.

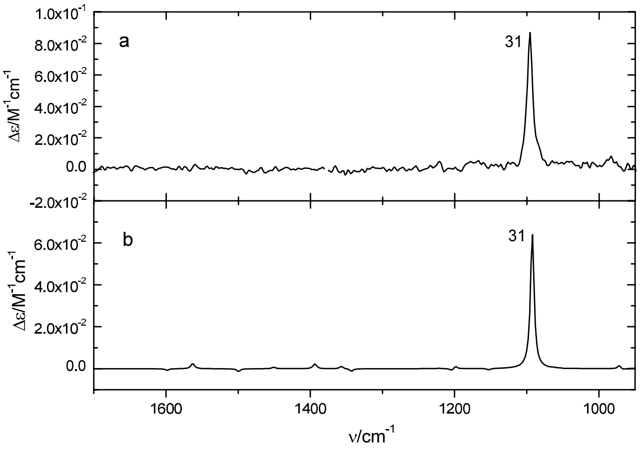

Figure 3. (a) Experimental mid-IR VCD spectrum of (+)-**1** in CS_2 (0.015 M, 950–1375 cm^{-1}) and in $CDCl_3$ (0.24 M, 1380–1700 cm^{-1}). The spectrum is the half-difference spectrum: $1/2\{[\Delta\varepsilon(+)-\Delta\varepsilon(\pm)]-[\Delta\varepsilon(-)-\Delta\varepsilon(\pm)]\}$. (b) Calculated VCD spectrum of (*S*)-**1** at the B3LYP/6-31G** level. Lorentzian band shapes are used with $\gamma = 3$ cm^{-1}. Frequencies have been scaled by a factor of 0.975.

When extending the analysis of the VCD spectrum to vibrations outside the observed region, we predict from the calculation that the C–H stretches will exhibit very weak VCD and some vibrations in the 500–300 cm^{-1} region with in-plane or out-of-plane motions of the S–S–O part will give rise to intermediate VCD intensity. Thus, we have a case where only vibrations that directly involve the movement of the stereogenic sulfur atom give rise to appreciable VCD.

Calculations with both smaller (3-21G**) and larger (6-311G**) basis sets and a different functional (B3PW91) all give the same results regarding the positive VCD of the S–O stretch in (*S*)-**1** (Table 1). Thus, there is a robust prediction of the sign of the VCD for this band.

Table 1. Calculated frequencies, dipole strengths and rotational strengths for the S–O stretch of (*S*)-**1** using different computational methods

Method	ν^a	D^b	R^c
B3LYP/3-21G**	1112.5	427.3	97.4
B3LYP/6-31G**	1120.4	585.7	131.9
B3LYP/6-311G**	1101.0	675.4	145.3
B3PW91/6-31G**	1142.7	586.7	132.0

[a] Unscaled frequencies in cm^{-1}.
[b] Dipole strengths in 10^{-40} esu^2 cm^2.
[c] Rotational strengths in 10^{-44} esu^2 cm^2.

3. Conclusions

The conformationally rigid cyclic thiolsulfinate **1** has a VCD spectrum with a single dominating VCD band due to the S–O stretching vibration. For (+)-**1,** this band has a positive sign, which is the calculated result for (*S*)-**1**. The calculated sign is robust with respect to the size of the basis set and DFT functional. Therefore, the absolute configuration of the studied enantiomers can be unambiguously established as (+)-(*S*)-**1**/(–)-(*R*)-**1** confirming the results obtained by Stephens et al. using DFT predictions of specific rotation.[2]

4. Experimental

4.1. Synthesis and chromatographic resolution

(±)-**1** was prepared by oxidation of the dithiole with *m*-chloroperbenzoic acid in chloroform at –20°C followed by flash chromatography of the crude product.[1] The pure racemate had mp 87–89°C (lit.[3] 91–92°C, lit.[4] 93–95°C). Resolution of 180 mg racemate into enantiomers was achieved by the use of a 20×250 mm (3*S*,4*R*)-Whelk-O1 preparative column, using 2% 2-propanol in methyl *tert*-butyl ether as the mobile phase. Evaporation and drying gave 80 mg of the first eluted (+)-enantiomer in >99.5% e.e. and 82 mg of the (–)-form in 99% e.e. E.e.'s were determined by the use of a 4.6×250 mm column containing the same chiral sorbent. Both enantiomers gave mp 108.5–109.5°C.[5]

4.2. Spectroscopy

IR and VCD spectra were recorded at 4 cm^{-1} resolution using a variable pathlength liquid cell with BaF_2 windows and a ChiralIR VCD instrument from ABB Bomem/Biotools (Quebec, Canada) optimized for measurements at 1200 cm^{-1}. The VCD spectrum was recorded for 2 h. Samples were dissolved either in $CDCl_3$ (0.24 M) or in CS_2 (0.014 M). The reported VCD spectrum is the half difference spectrum, $\Delta\varepsilon = 1/2\{[\Delta\varepsilon(+)-\Delta\varepsilon(\pm)]-[\Delta\varepsilon(-)-\Delta\varepsilon(\pm)]\}$, calculated from the raw VCD spectra of the (+)- and (−)-forms and the racemate.

4.3. Quantum chemical calculations

Density functional theory calculations of isotropic IR absorption and VCD spectra were performed using the Gaussian 98 quantum chemistry package. The B3LYP and B3PW91 hybrid functionals was used together with the 3-21G**, 6-31G** and 6-311G** basis sets.[6]

The absorption and VCD spectral profiles were simulated, using an in-house Matlab[7] code, from the calculated scaled frequencies (scale factor = 0.975), the dipole (D_i) and rotational (R_i) strengths using the following equations:[8]

$$\varepsilon(\tilde{\nu}) = \frac{8\pi^3 N_A \tilde{\nu}}{3000hc2.303}\sum_i D_i f_i(\tilde{\nu},\tilde{\nu}_i) \tag{1}$$

$$\Delta\varepsilon(\tilde{\nu}) = \frac{32\pi^3 N_A \tilde{\nu}}{3000hc2.303}\sum_i R_i f_i(\tilde{\nu},\tilde{\nu}_i) \tag{2}$$

The lineshape, $f_i(\tilde{\nu}, \tilde{\nu}_i)$, is assumed to be Lorentzian:[8]

$$f(\tilde{\nu},\tilde{\nu}_i) = \frac{\tilde{\gamma}}{\pi\left[(\tilde{\nu}-\tilde{\nu}_i)^2 - \tilde{\gamma}^2\right]} \tag{3}$$

with a half width at half height, $\tilde{\gamma}$, equal to 3 cm^{-1}.

Acknowledgements

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