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Absolute Configuration and Conformational Stability of (+)-2,5-Dimethylthiolane and (−)-2,5-Dimethylsulfolane

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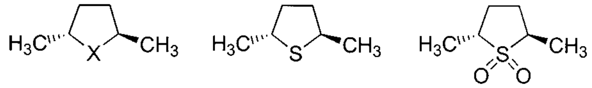
Enantiopure (+)-2,5-dimethylthiolane and (−)-2,5-dimethylsulfolane were prepared using literature procedures and investigated using vibrational circular dichroism (VCD). Experimental absorption and VCD spectra of (+)-2,5-dimethylthiolane and (−)-2,5-dimethylsulfolane in CCl_4 solution in the 2000−900 cm^{-1} region were compared with the ab initio predictions of absorption and VCD spectra obtained with density functional theory using the B3LYP/6-311G(2d, 2p) basis set for different conformers of (2*R*,5*R*)-2,5-dimethylthiolane and (2*R*,5*R*)-2,5-dimethylsulfolane. This comparison indicates that (+)-2,5-dimethylthiolane is of the (2*R*,5*R*)-configuration and has two predominant conformations in CCl_4 solution. In addition, (−)-2,5-dimethylsulfolane is of (*2R*,*5R*)-configuration and has only one predominant conformation. The stereochemical assignment is in agreement with literature.

Introduction

C_2-Symmetric heterocycles such as (2*R*,5*R*)-2,5-dimethylpyrrolidine **1a**[1] (see Figure 1), (2*R*,5*R*)-2,5-dimethylphosphalane **1b**,[2](2*R*,5*R*)-2,5-dimethylborolane **1c**,[3] and (2*R*,5*R*)-2,5-dimethyltetrahydrofuran **1d**[4] have been used successfully for several applications.[5] Analogous (2*R*,5*R*)-2,5-dimethylthiolane **2** is a member of the rich family of chiral thioethers, which are important auxiliaries used in asymmetric and stereoselective syntheses such as the nonracemic preparation of epoxides via sulfur ylides[6] or the electrophilic sulfenylation of unsaturated carbon−carbon bonds.[7] For these reasons, synthesis and characterization of chiral thioethers and C_2-symmetric heterocycles have attracted much attention in recent years.[8]

(+)-2,5-Dimethylthiolane **2** was assigned the (2*R*,5*R*)-configuration by chemical correlation.[8] To prove the absolute stereochemistry of (+)-2,5-dimethylthiolane, **2** was oxidized with *m*-chloroperbenzoic acid in dichloromethane to obtain the corresponding 2,5-dimethylsulfolane **3**, which was then analyzed by X-ray crystallography. It was reported initially that the oxidation of (+)-2,5-dimethylthiolane resulted in (+)-2,5-dimethylsulfolane,[8a] but later this was corrected as (−)-2,5-dimethylsulfolane.[8b] On the basis of this correction and X-ray crystal structure, (−)-2,5-dimethylsulfolane **3** is assigned the (2*R*,5*R*)-configuration; consequently, (+)-2,5-dimethylthiolane is assigned the (2*R*,5*R*)-configuration.



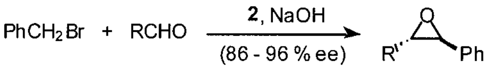
1a: X= NH
b: X= P-R
c: X= BH
d: X= O

2

3

Figure 1. C_2-Symmetric heterocycles.

Scheme 1



Vibrational circular dichroism (VCD) is a spectroscopic method without dependency on chemical methods to determine the absolute configuration and predominant conformations of chiral molecules in solution phase. Combined with density functional theory,[9−11] it is possible to use VCD for a confident determination of the absolute configurations and/or conformations in solution phase.[12,13] Both the absolute configurations and predominant conformations of 1,2,2,2-tetrafluoroethylmethyl ether,[12a] desflurane,[12b] epichlorohydrin,[12c] *tert*-butylphenylphosphine oxide,[12d] Troger's base,[13a] and phenyloxirane [13b] in solution phase have been investigated, and the results reflect the reliability of VCD method. Recently, thiolane

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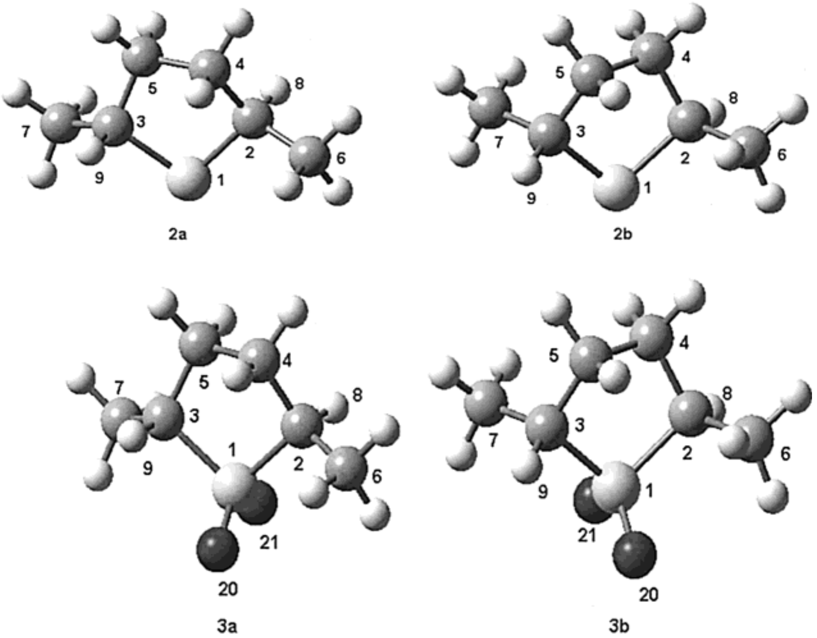

Figure 2. Two different conformations of (2*R*,5*R*)-2,5-dimethylthiolane (**2a**, **2b**) and of (2*R*,5*R*)-2,5-dimethylsulfolane (**3a, 3b**).

Table 1. Conformations and Energies of (2*R*,5*R*)-2,5-Dimethylthiolane 2 and -sulfolane 3

molecule	conformer	$C_6-C_2-C_4-C_5$[a]	$C_7-C_3-C_5-C_4$[a]	energy[b] electronic	energy[b] Gibbs	ΔE[c] (kcal/mol)	pop.[d] (%)
thiolane	**1a**	−160.0	−160.0	−634.171597	−634.034515	0	92.1
	1b	−86.7	−86.7	−634.169698	−634.032191	1.5	7.9
sulfolane	**2a**	−159.6	−159.6	−784.630728	−784.487831	0	98.5
	2b	−85.9	−85.9	−784.627257	−784.483906	2.5	1.5

[a] Dihedral angle in degrees. [b] In Hartrees. [c] Relative energy difference. [d] Population based on Gibbs energies.

2 has been used to mediate the asymmetric condensation of benzyl bromide with aldehydes to give epoxides in high enantiomeric excess (Scheme 1).[6a,b] Unambiguous determination of the absolute stereochemistry of **2** and detailed information regarding its conformation would aid in the development of this synthetic method. We use the vibrational circular dichroism (VCD) method here for the independent verification of the absolute configuration and the determination of the predominant conformations of chiral 2,5-dimethylthiolane and sulfolane.

The VCD investigation of chiral thioethers and the ab initio predictions of vibrational properties of chiral 2,5-dimethylthiolane and 2,5-dimethylsulfolane have not been undertaken before. Therefore, the VCD spectra of (+)-2,5-dimethylthiolane and (−)-2,5-dimethylsulfolane were measured, and the state-of-the-art ab initio theoretical VCD investigations was undertaken by using the B3LYP/6-311G(2d,2p) basis set. The absolute configurations and predominant conformations of (+)-2,5-dimethylthiolane and (−)-2,5-dimethylsulfolane are elucidated from these results.

Results and Discussion

The geometries were optimized with the B3LYP/6-311G(2d,2p) basis set using the standard dihedral angles of 180° and −60° for the $C_6-C_2-C_4-C_5$ and $C_7-C_3-C_5-C_4$ segments (see Figure 2) of (2*R*,5*R*)-2,5-dimethylthiolane. These starting geometries converged to two conformations, as summarized in Table 1 and shown in Figure 2. The converged $C_6-C_2-C_4-C_5$ and $C_7-C_3-C_5-C_4$ dihedral angles, optimized electronic energies, Gibbs energies, and relative populations are listed in Table 1. Both trans C−C−C−C and gauche C−C−C−C conformations have C_2-symmetry, and the trans C−C−C−C form has significantly lower energy than the gauche C−C−C−C form. Thus, the trans form is expected to be the predominant conformation for isolated (2*R*,5*R*)-2,5-dimethylthiolane.

The converged trans and gauche forms (labeled as **2a** and **2b**, respectively) were found to have potential energy minima (i.e., all vibrational frequencies are real) at the B3LYP/6-311G(2d,2p) level. The absorption and VCD intensities were calculated for these two conformations

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Table 2. Ab Initio Predicted Vibrational Frequencies and Intensities for (2*R*,5*R*)-2,5-Dimethylthiolane 2[a]

	conformer **a**				conformer **b**			
labels	calcd[b]	pred.[c]	*A*	*R*	calcd[b]	pred.[c]	*A*	*R*
1	1505.5	1467.9	0.33	2.37	1508.1	1470.4	0.95	−5.76
2	1505.4	1467.8	11.25	−9.67	1508.0	1470.3	15.42	−7.31
3	1501.6	1464.1	2.31	0.59	1501.8	1464.3	0.04	0.32
4	1496.7	1459.3	6.29	5.95	1497.7	1460.3	0.31	1.40
5	1495.1	1457.7	4.12	−0.13	1495.5	1458.1	9.00	1.93
6	1490.9	1453.6	1.16	−0.84	1490.4	1453.1	1.53	0.26
7	1417.7	1382.3	0.98	0.37	1419.1	1383.6	9.89	−5.07
8	1417.7	1382.3	5.16	−0.18	1417.0	1381.6	0.22	−1.21
9	1383.4	1348.8	0.00	1.04	1380.3	1345.8	0.02	2.88
10	1381.6	1347.1	4.46	33.09	1362.7	1328.6	14.07	47.00
11	1346.3	1312.6	0.02	−0.26	1353.0	1319.2	1.74	2.79
12	1329.1	1295.9	0.30	−0.73	1346.4	1312.7	5.91	0.02
13	1291.7	1259.4	8.55	24.54	1294.5	1262.1	1.55	19.17
14	1285.4	1253.3	30.04	−50.12	1241.0	1210.0	0.15	−2.85
15	1223.0	1192.4	0.84	22.34	1211.8	1181.5	24.88	−40.91
16	1188.7	1159.0	13.15	−35.09	1190.0	1160.2	0.00	0.21
17	1153.7	1124.9	0.61	4.37	1162.3	1133.2	4.54	−24.67
18	1110.0	1082.3	0.39	−4.44	1100.5	1073.0	0.01	0.93
19	1093.9	1066.6	0.85	7.72	1081.6	1054.6	0.01	−1.75
20	1066.2	1039.5	6.22	−10.34	1039.5	1013.5	0.08	0.47
21	1029.2	1003.5	4.76	1.40	1037.2	1011.3	3.83	8.96
22	1005.8	980.7	0.05	−0.08	1007.9	982.7	11.85	18.93
23	1004.4	979.3	6.07	−7.02	963.7	939.6	0.51	−2.15
24	949.8	926.1	1.70	−8.47	945.5	921.9	2.51	21.85

[a] Frequencies in cm^{-1}, absorption intensities (*A*) in Km/mol, and rotational strengths (*R*) in 10^{-44} esu^2 cm^2. [b] Obtained with the B3LYP/6-311G(2d,2p) basis set. [c] Scaled the calculated value by 0.975.

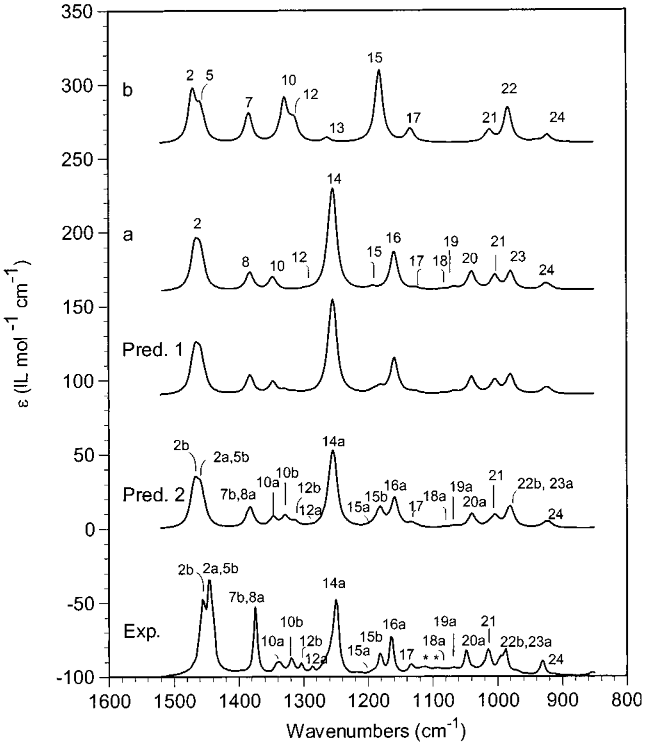

Figure 3. Comparison of the experimental absorption spectrum of (+)-2,5-dimethylthiolane at 0.342 M in CCl_4 solution (bottom trace) with the predicted absorption spectra for (2*R*,5*R*)-configuration. Bands marked with asterisks come from impurities. Ab initio vibrational absorption spectra for two conformers of (2*R*,5*R*)-2,5-dimethylthiolane were obtained with the B3LYP/6-311G(2d, 2p) basis set. The labels on the traces are the conformation labels (Figure 2). The trace labeled as Pred. 1 is obtained with 92.1% conformation **a** and 7.9% conformation **b**, while the trace labeled as Pred. 2 is obtained with 73.3% conformation **a** and 26.7% conformation **b**.

at the B3LYP/6-311G(2d, 2p) level (see Table 2). The predicted absorption and VCD spectra were simulated with 5 cm^{-1} half-widths and Lorentzian band shapes (shown in Figure 3 and 4). The population-weighted theoretical spectra can be compared to the experimental spectra in Table 3 and Figures 3 and 4.

Using the predicted absorption intensities in Table 2 and the correspondence between experimental and predicted band positions in Table 3, one can set up equations relating the areas of the experimentally observed bands at 1181 (no. 15b) and 1164 (no. 16a) cm^{-1} to the percent population of conformers in CCl_4 solution. These equations, along with the constraint that the sum of the populations for both conformers is 100%, permit us to calculate the individual conformer populations from the experimental absorption band areas. The same procedure has also been used with the VCD bands at 1343 (no. 10a) and 1338 (no. 10b) cm^{-1}. This analysis from absorption spectra suggested that the populations for (2*R*,5*R*)-2,5-dimethylthiolane in CCl_4 solution are 73.3% conformation **a** and 26.7% conformation **b**. The analysis from VCD spectra agrees with this result within the experimental uncertainties. Because the difference in the dipole moments of the two conformations of (2*R*,5*R*)-2,5-dimethylthiolane is very small (2.0464 D for conformation **a** and 2.0226 D for conformation **b**), the difference of the populations obtained for (2*R*,5*R*)-2,5-dimethylthiolane in CCl_4 solution and those predicted for isolated molecules may not be coming from the dipole−induced dipole interaction between solute and solvent.

The experimental absorption spectrum of (+)-2,5-dimethylthiolane obtained for a 0.342 M solution in CCl_4 is shown in Figure 3, where the absorption spectrum of the solvent has been subtracted. Bands at 1114 and 1094 cm^{-1} (marked with asterisks in Figure 3) come from impurities; ethers present as impurities could not be completely removed from (+)-2,5-dimethylthiolane in the purification process. The absorption bands in the predicted spectrum show one-to-one correspondence with the absorption bands in the experimental spectrum, and the Pred.2 (73.3% **a**, 26.7% **b**) spectrum matches the experimental spectrum much better than the Pred.1 (92.1% **a**, 7.9% **b**) spectrum [especially compare bands at 1319 cm^{-1} (no. 10b), 1304 cm^{-1} (no. 12b), and 1181 cm^{-1} (no. 15b) in Figure 3]. The notable differences between predicted and experimental absorption spectra are the following: (a) the two closely spaced experimental bands (nos. 2b, 2a−5b) at 1455 and 1445 cm^{-1} correspond to one poorly resolved band at 1469 cm^{-1} in the predicted spectrum; (b) the experimental absorption band (nos. 7b−8a) at 1375 cm^{-1} is sharper than the corresponding band at 1383 cm^{-1} in the predicted spectrum; and (c) the experimental bands (nos. 22b−23a) at 994 and 988 cm^{-1} are clearly resolved but the corresponding bands in the predicted spectra are not. Except for these differences, the experimental spectra in CCl_4 are considered to be in good agreement with the absorption spectrum predicted for mixture of ~73% **a** and ~27% **b**.

The experimental VCD spectrum of (+)-2,5-dimethylthiolane obtained for a 0.342 M solution in CCl_4 is shown in Figure 4, where the VCD spectrum of the solvent has been subtracted. The significant VCD bands in the observed (+)-2,5-dimethylthiolane spectrum are two positive bands at 1340 cm^{-1} (no. 10a) and 1319 cm^{-1} (no. 10b), a negative band at 1248 cm^{-1} (no. 14a), and a

Table 3. Comparison of Predicted and Observed Frequencies and Vibrational Assignments for (2*R*,5*R*)-2,5-Dimethylthiolane 2

band no.[a]	Exp. (cm^{-1})[b]	Pred. (cm^{-1})[c,d]	calcd (cm^{-1})[c,e]	assignment[f]
ν_{2b}	1455	1470	1508	asym. *HCH bend, CH_3 deformation
$\nu_{2a,5b}$	1445	1468	1505	asym. CH_3 deformation, *HCH Bend
		1458	1496	
$\nu_{7b,8a}$	1375	1384	1419	asym. CH_3 rock
		1382	1418	
ν_{10a}	1343	1347	1382	asym. ring deformation, in-plane CH bend, CH(*CH_2) out-of-plane bend
ν_{10b}	1338	1329	1363	asym. In-plane CH bend, out-of-plane CH(*CH_2) bend
ν_{12b}	1304	1313	1346	asym. ring deformation, *CH_2 wag
ν_{12a}	1286	1296	1329	asym. ring deformation,*CH_2 wag
ν_{14a}	1250	1253	1285	sym. CH out-of-plane bend, *CH_2 twist
ν_{15a}	1193*	1192	1223	sym. CH_2 twist, CH out-of-plane bend
ν_{15b}	1181	1182	1212	asym. CH out-of-plane bend, *CH_2 twist
ν_{16a}	1164	1159	1189	asym. CH out-of-plane bend, *CH_2 twist
$\nu_{17b,a}$	1133	1133	1162	sym. ring deformation, CH_3 wag
		1125	1154	
ν_{18a}	1080	1082	1110	sym. ring breath, CH out-of-plane bend
ν_{19a}	1069	1067	1094	asym. ring deformation, CH out-of-plane bend
ν_{20a}	1048	1040	1066	asym. *CH_2 twist, CH_3 wag
$\nu_{21b,a}$	1014	1011	1037	sym. *CH_2, CH_3 wag
		1004	1029	
ν_{22b}	994*	983	1008	asym. *CH_2 twist
ν_{23a}	988	979	1004	asym. CH in-plane bend, *CH_2 twist
$\nu_{24a,b}$	931	926	950	sym. *CH_2, *CH and CH_3 wag, ring def.
		922	946	

[a] These numbers derived from those in Figure 3, and the subscript indicates which conformation contributes to the intensity of the band. [b] Experimental wavenumbers obtained from the absorption spectrum at concentration of 0.342 M; asterisks (*) denote those bands that appear as shoulders in the spectrum. [c] Band positions from the simulated spectra with populations given in Figure 3. [d] Ab initio wavenumbers scaled with 0.975. [e] Unscaled ab initio wavenumbers. [f] Deduced from Gaussview (version 2.1); asterisks (*) denote ring mode.

Table 4. Ab Initio Predicted Vibrational Frequencies and Intensities for (2*R*,5*R*)-2,5-Dimethylsulfolane 3[a]

	conformer **a**				conformer **b**			
labels	calcd[b]	pred.[c]	*A*	*R*	calcd[b]	pred.[c]	*A*	*R*
1	1507.0	1469.3	0.00	−0.17	1510.1	1472.3	0.31	−3.14
2	1505.4	1467.8	15.59	−18.37	1510.0	1472.3	21.67	−26.85
3	1503.9	1466.3	8.62	6.77	1502.5	1464.9	3.93	1.18
4	1500.0	1462.5	6.17	9.40	1499.6	1462.2	0.14	1.86
5	1496.0	1458.6	5.61	1.83	1494.2	1456.8	12.27	0.61
6	1493.5	1456.1	1.31	3.74	1489.4	1452.2	2.42	1.81
7	1423.7	1388.1	0.01	−0.06	1426.7	1391.0	4.96	5.99
8	1423.1	1387.5	2.80	4.38	1424.3	1388.7	0.20	1.51
9	1376.9	1342.5	0.11	4.80	1374.2	1339.9	0.01	0.05
10	1372.0	1337.7	0.00	−0.01	1354.4	1320.6	6.94	32.62
11	1336.2	1302.8	0.05	1.53	1351.0	1317.2	2.66	8.91
12	1328.7	1295.5	4.37	−25.50	1341.8	1308.2	0.61	6.89
13	1323.7	1290.6	97.42	52.42	1306.6	1273.9	151.60	29.45
14	1289.9	1257.6	2.45	−11.86	1292.0	1259.7	7.11	−45.71
15	1270.3	1238.5	68.15	−35.95	1242.4	1211.4	0.72	1.40
16	1213.9	1183.5	0.04	−4.84	1223.3	1192.7	22.45	−35.09
17	1202.3	1172.3	6.33	10.71	1184.5	1154.9	11.71	−34.85
18	1156.3	1127.4	13.32	−22.04	1161.8	1132.8	7.10	20.30
19	1115.4	1087.5	82.82	64.81	1110.5	1082.8	98.21	44.56
20	1109.6	1081.8	5.71	2.53	1093.3	1066.0	1.63	−14.33
21	1104.4	1076.8	53.82	−43.97	1092.0	1064.7	44.39	−47.60
22	1071.3	1044.5	2.10	−0.82	1048.0	1021.8	0.25	3.23
23	1025.2	999.6	10.83	14.87	1028.1	1002.4	4.76	21.90
24	1011.9	986.6	2.75	−12.32	1025.6	1000.0	0.46	−1.82
25	987.7	963.0	0.03	−0.50	957.3	933.4	0.52	−20.69
26	954.8	930.9	1.94	15.04	956.1	932.2	0.92	−1.86
27	945.5	921.9	1.39	−8.72	941.4	917.9	0.10	−1.76

[a] Frequencies in cm^{-1}, absorption intensities (*A*) in Km/mol, and rotational strengths (*R*) in 10^{-44} esu^2 cm^2. [b] Obtained with the B3LYP/6-311G(2d,2p) basis set. [c] Scaled the calculated value by 0.975.

positive−negative couplet with peak maxima at 1193 (no. 15a) and 1164 cm^{-1} (no. 16a). The same features are seen in the predicted VCD spectra of (2*R*,5*R*)-2,5-dimethylthiolane. The major VCD features observed for (+)-2,5-dimethylthiolane are reproduced in the Pred.2 (73.3% **a**, 26.7% **b**) VCD spectrum much better than in the Pred.1 (92.1% **a**, 7.9% **b**) VCD spectrum for the (2*R*,5*R*)-2,5-dimethylthiolane, as reflected by the relative intensities of bands no. 10a and no. 10b. This is in agreement with what we observed earlier in the comparison of absorption spectra.

The optimized structures for (2*R*,5*R*)-2,5-dimethylsulfolane are shown in Figure 2 (labeled as **3a** and **3b**) and Table 1. This molecule also has C_2-symmetry, but only one conformation is predominant for the isolated molecule. The experimental absorption and VCD spectra for (−)-2,5-dimethylsulfolane are compared to the predicted ones for (2*R*,5*R*)-2,5-dimethylsulfolane in Figure 5 and Figure 6 (Tables 4 and 5). One-to-one correspondence can be observed between the experimental absorption spectrum and the predicted one for conformation **a**, except for the three bands (nos. 19, 21, 22) seen around 1100 cm^{-1}, two of which are attributed to the S═O stretch. The difference here may be attributed to the interaction between (−)-2,5-dimethylsulfolane and trace water due to the polar nature of (−)-2,5-dimethylsulfolane.

The one-to-one correspondence observed between the experimental and predicted spectra for sulfolane (Figures 5 and 6) is not as good as that for thiolane but is reasonable enough to conclude that (−)-2,5-dimethylsulfolane is of (2*R*,5*R*)-configuration and only one conformation is predominant in CCl_4 solution.

Since C−S bonds are a part of the ring structure, the C−S stretching vibrations are strongly coupled to the C−C stretching vibrations. Therefore, it was not possible to assign any of the experimentally observed bands to a pure C−S stretching vibration in both molecules studied.

Table 5. Comparison of Predicted and Observed Frequencies and Vibrational Assignments for (2*R*,5*R*)-2,5-Dimethylsulfolane 3

band no.[a]	Exp. (cm^{-1})[b]	Pred. (cm^{-1})[c,d]	calcd (cm^{-1})[c,e]	assignment[f]
ν_{2-4a}	1454	1466	1504	asym. CH_3 deformation
ν_{8a}	1382	1387	1423	asym. CH_3 deformation
ν_{13a}	1315	1291	1324	asym. *CH_2 twist, *CH out-of-plane bend, S=O stretch
ν_{15a}	1250	1238	1270	asym. S=O stretch, *CH_2 twist, *CH out-of-plane bend
ν_{17a}	1185	1172	1202	asym. ring deformation, CH_3 wag, *CH_2 twist
ν_{18a}	1164	1127	1156	sym. ring deformation
ν_{19a}	1139	1087	1115	sym. ring breath, S=O stretch
ν_{21a}	1119	1076	1104	sym. S=O stretch, ring breath
ν_{22a}	1094	1044	1071	asym. CH_3 wag, *CH_2 twist, ring deformation
ν_{23a}	1010	999	1025	sym. CH_3, *CH_2, *CH wag, ring breath
ν_{24a}	998	986	1011	asym. CH_3 wag, *CH_2 twist
ν_{26a}	944	931	955	asym. CH_3 wag, ring deformation
ν_{27a}	930	921	945	sym. CH_3 wag, ring deformation

[a] These numbers derived from those in Figure 5, and the subscript indicates which conformation contributes to the intensity of the band. [b] Experimental wavenumbers obtained from the absorption spectrum at concentration of 0.257 M. [c] Band positions from the simulated spectra for conformation **a**. [d] Ab initio wavenumbers scaled with 0.975. [e] Unscaled ab initio wavenumbers. [f] Deduced from Gaussview (2.1); asterisks (*) denote ring mode.

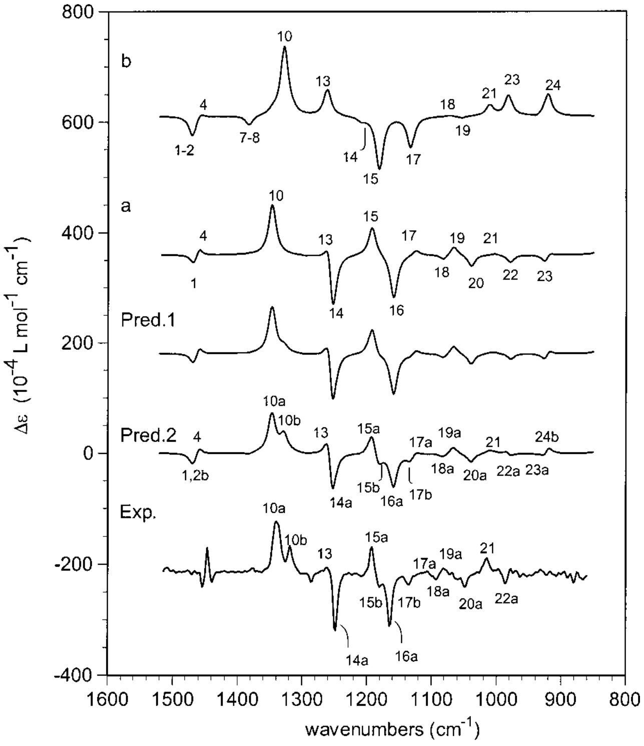

Figure 4. Comparison of the experimental VCD spectrum of (+)-2,5-dimethylthiolane at 0.342 M in CCl_4 solution (bottom trace) with the predicted VCD spectra for (2*R*,5*R*)-configuration. Ab initio VCD spectra for two conformers of (2*R*,5*R*)-2,5-dimethylthiolane were obtained with the B3LYP/6-311G(2d, 2p) basis set. The labels on the traces are the conformation labels (Figure 2). The trace labeled as Pred. 1 is obtained with 92.1% conformation **a** and 7.9% conformation **b**, while the trace labeled as Pred. 2 is obtained with 73.3% conformation **a** and 26.7% conformation **b**.

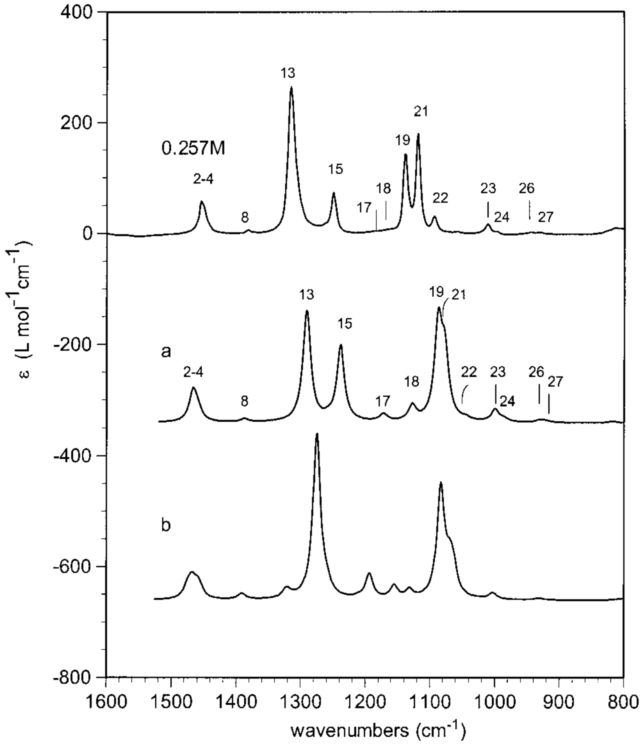

Figure 5. Comparison of the experimental absorption spectrum of (−)-2,5-dimethylsulfolane at 0.257 M in CCl_4 solution with the predicted absorption spectra (bottom traces) for two conformations (**a**, **b**; see Figure 2) of (2*R*,5*R*)-configuration obtained with the B3LYP/6-311G(2d,2p) basis set.

Conclusion

The comparison of experimental and ab initio predicted absorption and VCD spectra indicates that (a) (+)-2,5-dimethylthiolane is of (2*R*,5*R*)-configuration, in agreement with the known absolute configuration;[6a,8] (b) two conformations are predominant for (2*R*,5*R*)-(+)-2,5-dimethylthiolane in CCl_4 solution; and (c) (−)-2,5-dimethylsulfolane is of (2*R*,5*R*)-configuration and one conformation is predominant in CCl_4 solution.

Experimental Section

Synthesis. All reagents and solvents were purified and dried, if necessary, according to standard procedures. (+)-2,5-Dimethylthiolane **2** and (−)-2,5-dimethylsulfolane **3** were synthesized using literature procedures[6a,8] from (+)-(2*S*,5*S*)-2,5-hexanediol (Strem Chemicals).

Measurements. ^1H NMR spectra were recorded at 300 MHz in $CDCl_3$. Thin-layer chromatography was performed on silica gel (Silica Gel 60 F254 glass plates). Visualization was accomplished by staining with an anisaldehyde stain followed by heating or with I_2. Column chromatography was performed using silica gel (70−230 mesh). GC -MS was performed on a Hewlett-Packard 5890 Series II gas chromatograph with a 5971 Series mass selective detector. Optical rotations were measured on an Autopol III polarimeter with a Na lamp.

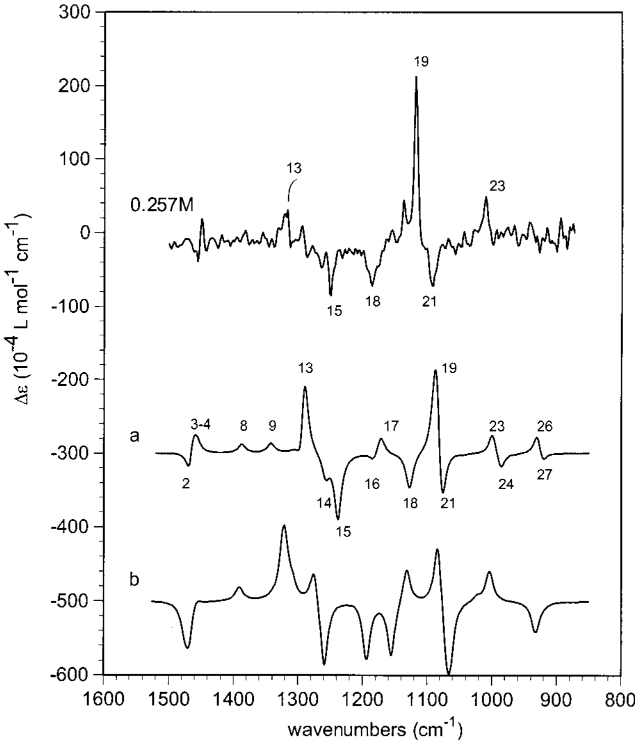

Figure 6. Comparison of the experimental VCD spectrum of (−)-2,5-dimethylsulfolane at 0.257 M in CCl_4 solution with the predicted VCD spectra (bottom traces) for two conformations (**a**, **b**; see Figure 2) of (2*R*,5*R*)-configuration obtained with the B3LYP/6-311G(2d,2p) basis set.

The infrared and VCD spectra were recorded[12] on a commercial Fourier transform VCD spectrometer, Chiralir. The VCD spectra were recorded with a 3 h data collection time at 4 cm^{-1} resolution. For (+)-2,5-dimethylthiolane, spectra were measured in CCl_4 solvent at 0.342 and 0.102 M. No significant differences were found in the spectra at these two concentrations. For (−)-2,5-dimethylsulfolane, spectra were measured in CCl_4 solvent at 0.257 M, 0.122 M, and 0.061 M. Small differences in the absorption spectra were found in the 1070−1040 cm^{-1} region, but VCD spectra are identical at these three concentrations. The absorption and VCD spectra obtained for (−)-2,5-dimethylsulfolane as neat liquid (not shown here), however, are quite different from those in the CCl_4 solutions mentioned above, possibly due to aggregation in neat liquid. The sample was held in a variable path length cell with BaF_2 windows. In the presented absorption spectra, the solvent absorption was subtracted out. In the presented VCD spectra the raw VCD spectrum of the solvent was subtracted.

Calculations. The ab initio vibrational frequencies, absorption, and VCD intensities for (2*R*,5*R*)-2,5-dimethylthiolane were calculated using the Gaussian 98 program[11] on a Pentium II 300 MHz PC. The calculations used the density functional theory with B3LYP functional[9] and 6-311G(2d, 2p) basis set.[14] The procedure for calculating the VCD intensities using DFT theory is due to Cheeseman et al.[10] as implemented in the Gaussian 98 program.[11] The theoretical absorption and VCD spectra were simulated with Lorentzian band shapes and 5 cm^{-1} full width at half-height. Since the ab initio predicted band positions are higher than the experimental values, the ab initio frequencies were scaled with 0.975.

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Supporting Information Available: Synthetic procedure for (+)-2,5-dimethylthiolane and (−)-2,5-dimethylsulfolane and Cartesian coordinates for the two conformations each of (2*R*,5*R*)-2,5-dimethylthiolane and (2*R*,5*R*)-2,5-dimethylsulfolane. This material is available free of charge via the Internet at http://pubs.acs.org.

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