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Conformational Analysis of (*S*)-(+)-1-Bromo-2-methylbutane and the Influence of Bromine on Conformational Stability

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(*S*)-(+)-1-bromo-2-methylbutane was investigated using vibrational circular dichroism (VCD). Experimental absorption and VCD spectra of (+)-1-bromo-2-methylbutane in $CDCl_3$ solution were recorded in the 2000−900 cm^{-1} region, and they were compared with the ab initio predictions of absorption and VCD spectra obtained with density functional theory using the B3LYP/6-31G* basis set for (*S*)-1-bromo-2-methylbutane. This comparison indicates that (+)-1-bromo-2-methylbutane is of the (*S*) configuration and exists in several conformations. The results obtained for (*S*)-(+)-1-bromo-2-methylbutane are also compared to those for (*S*)-(+)-3-(2-methylbutyl)thiophene, which indicates that the predominant conformations are influenced by the substitution of bromine with thiophene ring.

Introduction

(+)-1-Bromo-2-methylbutane is the starting material in the synthesis of (+)-3-(2-methylbutyl)thiophene whose polymer can serve as asymmetric electrodes for chiral electrosynthesis.[1] A comparison of the absolute configuration and predominant conformations of a homologous series of molecules is helpful to understand the influence of substituents on the molecular structures and in turn on their absorption and VCD spectra. In addition, an understanding of the structure of monomer units is important to elucidate the structures of polymers derived from these monomers.

There have been no prior studies on the conformational analysis of 1-bromo-2-methylbutane. A relevant literature report[2] is on the conformations of 1-chloro-2-methylbutane, where qualitative information on the plausible conformations was deduced using infrared and Raman spectra measured for liquid, crystal and glass samples. The experimental vibrational frequencies were compared to those obtained in vibrational analysis that used transferred force constants. Such vibrational analyses, however, are no longer considered to be reliable. Modern quantum mechanical methods can provide accurate information on the molecular conformations and vibrational properties.

Three different independent approaches which have been recently developed for determining the structures of chiral molecules are vibrational circular dichroism (VCD),[3] vibrational Raman optical activity (VROA),[4] and ab initio optical rotation.[5] All three methods derive their strength from the advances made in quantum mechanical methods for the prediction of these properties. A reliable prediction of the appropriate property for a given structure of the molecule is a prerequisite for its application in molecular structure determination. Among these three methods, VCD has been the most widely used method due in part to its reliable prediction by density functional theory.

A combination of improved instrumental performance for experimental measurement and accurate theoretical predictions with density functional theory[6−8] made VCD a reliable tool for confident determination of the conformations in solution phase. Recently, the absolute configurations and predominant conformations of chiral molecules, such as *tert*-butyl *n*-butyl sulfoxide,[9] 2,5-dimethylthiolane and sulfolane[10a] and *tert*-butylphenylphosphineoxide,[10b] and epichlorohydrin[11] have been studied successfully in the solution phase using the VCD technique. Structures of polymers [12,13] have also been investigated using VCD.

In the present study, we use state-of-the-art experimental and ab initio theoretical VCD results for an independent verification of the absolute configuration and to determine the predominant conformations of (+)-1-bromo-2-methylbutane. A similar approach was used[13] for (+)-3-(2-methylbutyl)thiophene, where the configuration has been confirmed to be (*S*), and it was further determined that an isolated molecule exists in six different conformations. Another motivation for this study is to investigate the influence of the substituent (Br vs thiophene) on the structure of the carbon skeleton of 2-methylbutane. A knowledge of such influence is important for understanding or deducing the structures of corresponding polymers. For this purpose, we compare the results obtained for (+)-1-bromo-2-methylbutane with those reported earlier[13] for (+)-3-(2-methylbutyl)thiophene.

Procedures

The infrared and VCD spectra were recorded on a commercial Fourier transform VCD spectrometer, Chiralir. The VCD spectra were recorded with 3 h data collection time at 4 cm^{-1} resolution. Spectra were measured in $CDCl_3$ solvent at 0.306 M and a path length of ∼250 μm for (+)-1-bromo-2-methylbutane. The sample was held in a variable path length cell with BaF_2 windows. In the absorption spectra presented, the solvent

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TABLE 1: Conformations and Energies of (*S*)-(+)-1-Bromo-2-methylbutane

conformer[a]	converged[b] CC*CBr	converged[b] CCC*C	energy[c] electronic	energy[c] Gibbs	Δ*E* [d] (kcal/mol)	pop.[e] (%)
G^+g^+	59.3	53.3	−2768.877296	−2768.758255	0.000	29.5
G^+t	64.4	168.8	−2768.876532	−2768.757957	0.187	21.5
G^-t	−65.2	171.9	−2768.876237	−2768.757759	0.311	17.4
Tt	−170.9	173.0	−2768.876153	−2768.757619	0.399	15.0
Tg^+	−171.8	67.3	−2768.875932	−2768.757440	0.511	12.4
G^-g^-	−57.0	−54.9	−2768.875301	−2768.756399	1.165	4.2

[a] See Figure 1 for the labels. [b] Dihedral angle. [c] In Hartrees. [d] Relative energy difference, in kcal/mol. [e] Population based on Gibbs energies.

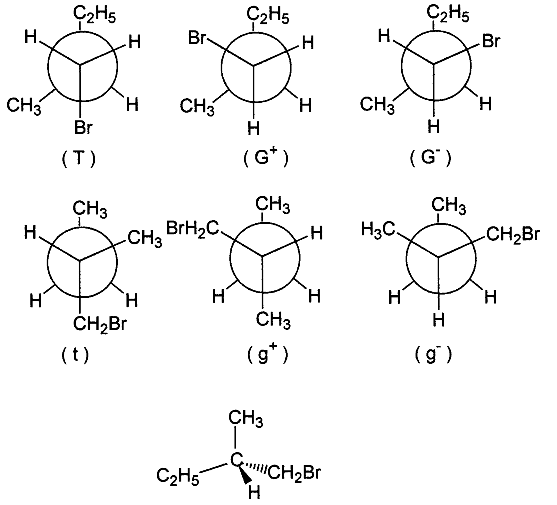

Figure 1. Different conformations of (*S*)-1-bromo-2-methylbutane, based on the dihedral angles of Br−C−C*−C and C−C*−C−C segements.

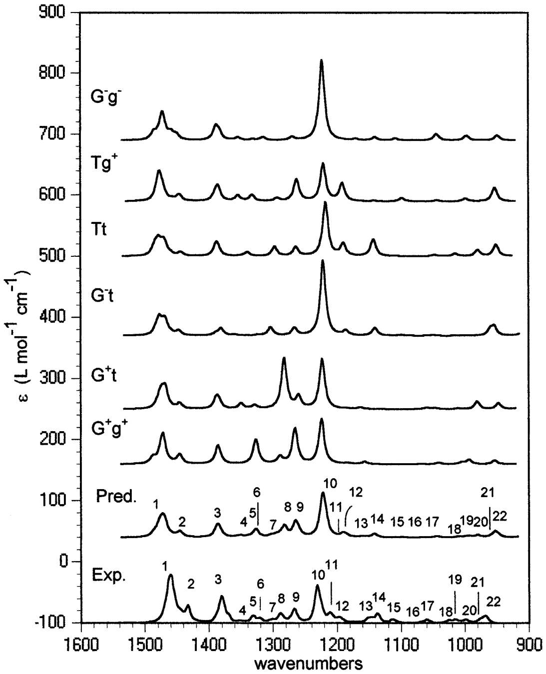

Figure 2. Comparison of the experimental absorption spectrum (bottom trace) with the predicted (population weighted) absorption spectrum of 1-bromo-2-methylbutane obtained with B3LYP/6-31G* basis set. Ab initio vibrational absorption spectra for the six conformers of 1-bromo-2-methylbutane were obtained with the B3LYP/6-31G* basis set. The spectra were simulated with Lorentzian band shapes, and 8 cm^{-1} half-widths and frequencies were multiplied with 0.96. The labels on the top six traces are the conformation labels (Table 1). The final predicted absorption spectrum is obtained by adding the population weighted absorption spectra of all conformers.

absorption was subtracted out. In the VCD spectra presented, the raw VCD spectrum of the solvent was subtracted.

The ab initio vibrational frequencies, absorption, and VCD intensities for (+)-1-bromo-2-methylbutane were calculated using the Gaussian 98 program.[8] The calculations used the density functional theory with B3LYP functional[6] and 6-31G* basis set.[14] The procedure for calculating the VCD intensities using DFT theory is due to Cheeseman et al.[7] as implemented in Gaussian 98 program.[8] The theoretical absorption and VCD spectra of (*S*)-1-bromo-2-methylbutane were simulated with Lorentzian band shapes and 8 cm^{-1} full width at half-height. Because the ab initio predicted band positions are higher than the experimental values, the ab initio frequencies were scaled with 0.96.

Results and Discussion

The geometries were optimized with the B3LYP/6-31G* basis set using the standard dihedral angles of 60, 180, and 300° for both CCC*C and CC*CBr segments (see Figure 1) of (*S*)-1-bromo-2-methylbutane. The six most stable conformations are summarized in Table 1 and shown in Figure 1. Each conformation is labeled with a two-letter designation with these letters representing the conformation of CC*CBr and CCC*C dihedral segments, respectively. The converged CC*CBr and CCC*C dihedral angles, optimized electronic energies, Gibbs energies, and relative populations are listed in Table 1. These data suggest that an isolated (+)-1-bromo-2-methylbutane molecule exists in six conformations (namely, G^+g^+, G^+t, G^-t, Tt and Tg^+, and G^-g^-). Of these, the G^+g^+ conformation is expected to be the most stable, and the first five conformations have a population greater than 10% each.

The absorption and VCD intensities were calculated for the six most stable conformations at the B3LYP/6-31G* level, and all of these conformations were found to have potential energy minima (i.e., all vibrational frequencies are real) at the B3LYP/6-31G* level. The predicted absorption and VCD spectra for all six conformations of (*S*)-1-bromo-2-methylbutane were simulated with 8 cm^{-1} half widths and Lorentzian band shapes (shown in Figures 2 and 3). The unpolarized absorption spectrum is independent of the absolute configuration. The predicted absorption spectrum, obtained as population weighted sum of the absorption spectra of different conformers, is compared to the experimental absorption spectrum in Figure 2 and Table 2. The population-weighted theoretical VCD spectra for chiral 1-bromo-2-methylbutane with (*S*)-configuration can be compared to the experimental VCD spectra in Figure 3.

The experimental absorption spectra of (*S*)-1-bromo-2-methylbutane obtained in $CDCl_3$ are shown in Figure 2, where the absorption spectrum of the solvent has been subtracted. The absorption bands in the predicted spectrum of (*S*)-1-bromo-2-methylbutane show one-to-one correspondence with the absorption bands in the experimental spectrum of (*S*)-1-bromo-2-methylbutane. The notable differences between predicted and experimental absorption spectra are that the experimental bands

TABLE 2: Comparison of Predicted and Observed Frequencies and Vibrational Assignments for 1-Bromo-2-methylbutane[a]

band no.	exp.[b] (cm^{-1})	pred.[c] (cm^{-1})	calcd.[d] (cm^{-1})	assignment[e]
1	1460	1475	1535	CH_3 def., CH_2 bend
		1470	1529	CH_3 def., CH_2 bend
2	1434	1446	1504	CH_2 bend, CH_3 def.
3	1380	1386	1442	CH_3 def.
4	1357	1350	1404	CH_2 and CH wag
5	1331	1340	1394	CH_2 wag
6	1322	1328	1381	CH_2 twist, CH and CH_2 wag
7	1301	1296	1348	CH, CH_2 and CH_3 wag
8	1289	1282	1334	CH wag
9	1267	1262	1313	CH_2 twist, CH wag
10	1231	1221	1270	CH_2 wag, C−Br and C−C stretch, and CH wag
11	1211	1191	1239	CH, CH_2 and CH_3 wag, CH_2 twist
12	1197	1185	1233	CH, CH_2 and CH_3 wag, CH_2 twist
13	1169	1163	1210	CH_2 twist, C−C stretch, and CH_3 and CH_2 wag
14	1137	1141	1187	CH_2 twist, CH_2 and CH_3 wag
15	1114	1100	1144	CH, CH_2 and CH_3 wag
16	1083	1058	1100	CH_2 twist, CH_3 and CH_2 wag
17	1060	1046	1088	CH_2 twist, CH_3 and CH_2 wag
18	1025	1014	1055	C−C stretch, CH_3 and CH_2 wag
19	1015	1005	1045	C−C stretch, CH_3 and CH_2 wag
20	999	980	1019	CH_3, CH_2 wag, C−C stretch
21	976	959	997	CH_2 twist, CH_2 and CH_3 wag
22	969	951	989	CH_2 twist, CH_2 and CH_3 wag

[a] Experimental wavenumbers obtained from the absorption spectrum at concentration of 0.306 M. [b] Band positions from the simulated spectra in Figure 2. [c] Ab initio wavenumbers scaled with 0.96. [d] Unscaled ab initio wavenumbers. [e] Deduced from Gaussview (version 2.1).

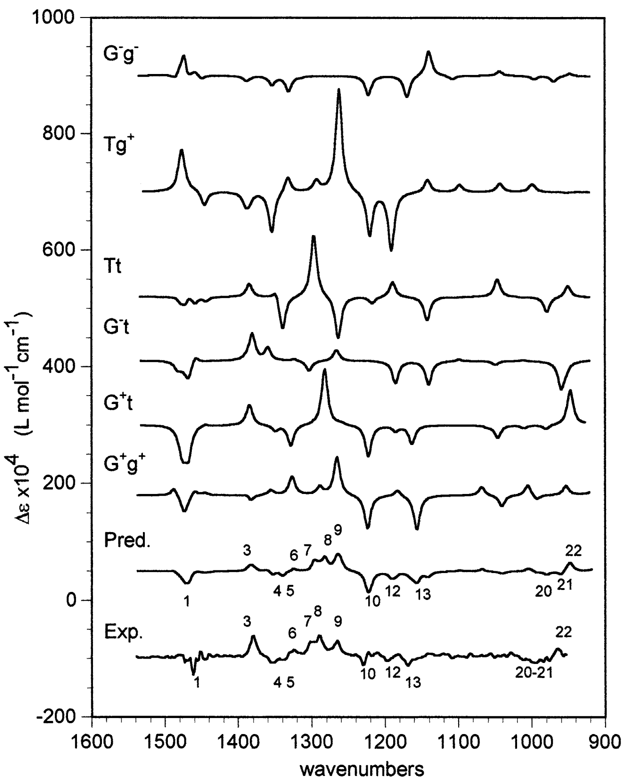

Figure 3. Comparison of the experimental VCD spectrum of (+)-1-bromo-2-methylbutane (bottom trace) with the predicted (population weighted) VCD spectrum of (*S*)-1-bromo-2-methylbutane obtained with the B3LYP/6-31G* basis set. Ab initio vibrational VCD spectra for the six conformers of (*S*)-1-bromo-2-methylbutane were obtained with the B3LYP/6-31G* basis set. The spectra were simulated with Lorentzian band shapes, and 8 cm^{-1} half-widths and frequencies were multiplied with 0.96. The labels on the top six traces are the conformation labels (Table 1). The predicted VCD spectrum is obtained by adding the population weighted absorption spectra of all conformers.

at 1331 (#5) and 1322(#6) and 1211(#11) and 1197(#12) cm^{-1} are well separated, whereas the corresponding bands in the predicted spectrum overlap each other. Except for these differences, the experimental spectra in $CDCl_3$ are considered to be in good agreement with the absorption spectrum predicted for 1-bromo-2-methylbutane.

The experimental VCD spectra of (+)-1-bromo-2-methylbutane obtained in $CDCl_3$ are shown in Figure 3, where the VCD spectrum of the solvent has been subtracted. The significant VCD bands in the observed spectrum of (+)-1-bromo-2-methylbutane are 1460(−, #1), 1380 (+, #3), 1357 (−, #4), 1331(−, #5), 1322(+, #6), 1301(+, #7), 1289(+, #8), 1267 (+, #9), 1231 (−, #10), 1197 (−, #12), 1169 (−, #13), 999(−, #20), 976 (−, #21), and 969 (+, #22) cm^{-1}. The major VCD features observed for (+)-1-bromo-2-methylbutane are reproduced in the predicted VCD spectrum of (*S*)-1-bromo-2-methylbutane. This agreement indicates that (+)-1-bromo-2-methylbutane is of (*S*) configuration.

The data in Table 1 indicate that the isolated 1-bromo-2-methylbutane molecule exists in six different conformations. The populations of these conformations in $CDCl_3$ solution can be different from that for isolated molecule. To establish the percent populations of individual conformations in solution, it is necessary to identify the bands that are characteristic to each conformation, as was done for epichlorohydrin.[11] However, the individual conformer spectra shown in Figures 2 and 3 do not reveal such conformer characteristic bands in the 1600−900 cm^{-1} region. As a result, we can only deduce the conformers in $CDCl_3$ solution by inference as follows. (a) Because none of the individual conformer spectra in Figures 2 and 3 alone can satisfactorily explain the experimental spectra, but a combination of conformer spectra can, it is imperative that more than one conformer should be present in $CDCl_3$ solution. (b) Because the population weighted predicted spectra in Figures 2 and 3 reproduce the experimental spectra reasonably well, it is possible that the populations given in Table 1 for isolated molecule, to a good approximation, reflect the compositions in $CDCl_3$ solution as well. (c) However, it is possible that the population weighted spectra with some modified population compositions can also satisfactorily reproduce the experimental spectra. Such possibility makes the determination of populations in $CDCl_3$ solution somewhat uncertain.

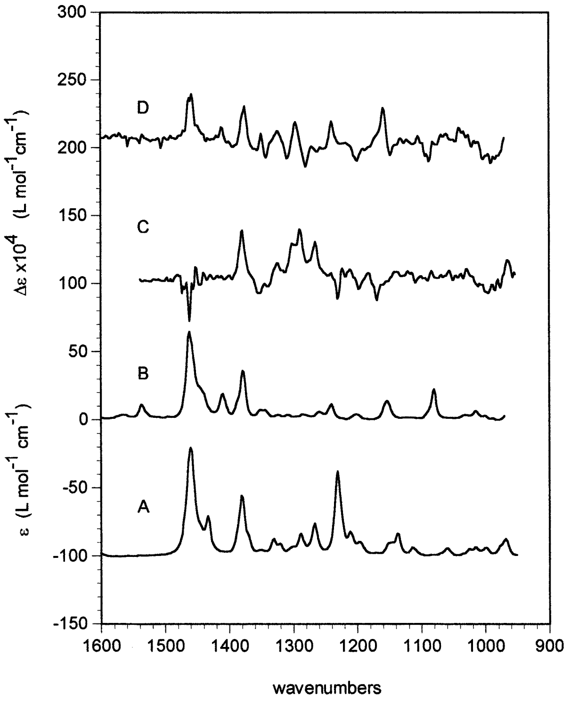

Figure 4. Comparison of the experimental absorption (traces A and B) and VCD (traces C and D) spectra of (+)-1-bromo-2-methylbutane (traces A and C) with those of (+)-3-(2-methylbutyl)thiophene (traces B and D).

The experimental absorption and VCD spectra for (+)-3-(2-methylbutyl)thiophene (at ~0.25 M and path length of ~100 μm) were reported earlier.[13] These spectra are compared to those of (+)-1-bromo-2-methylbutane in Figure 4. Large differences in absorption and VCD spectra are observed for these two molecules: (a) the main differences in the absorption spectra are in the 1200−1300 cm^{-1} region; notably the band at 1231 cm^{-1} is much more intense in the bromine case; (b) there are more differences in the VCD spectra- besides large differences in the 1200−1300 cm^{-1} region, there is an overall inversion of the VCD band at about 1460 cm^{-1}; furthermore, the band at about 1150 cm^{-1} is also inverted in the two spectra (a negative VCD band at 1169 cm^{-1} for the bromo compound and a positive band at 1153 cm^{-1} for the thiophene compound). On comparing the lowest energy structures of these two molecules, it becomes clear that the substitution of bromine with thiophene ring has a large influence on the conformational stability. The six most stable conformations for (*R*)-3-(2-methylbutyl)thiophene[13] are g^+Tt (24%), g^-G^+t (21%), g^+Tg^- (20%), g^-Tt (10%), g^+G^+t (7%), and g^-Tg^- (7%) (the three letters here represent the conformation of $C_{t1}C_{t2}CC^*$, $C_{t2}CC^*C$, and CC^*CC dihedral segments, respectively, where C_{t1} and C_{t2} are carbon atoms of thiophene ring and C_{t2} corresponds to Br in 1-bromo-2-methylbutane; thus, in three letter designation, the first letter has no counterpart in 1-bromo-2-methylbutane). For (*S*)-3-(2-methylbutyl)thiophene,[13] these stable conformations correspond to g^-Tt, g^+G^-t, g^-Tg^+, g^+Tt, g^-G^-t, and g^+Tg^+. Then, although Tt (34%), G^-t (28%), and Tg^+ (27%) conformations are dominant in (*S*)-3-(2-methylbutyl)thiophene,[13] G^+g^+ (29%) G^+t (21%), G^-t (17%), Tt (15%), Tg^+ (12%), and G^-g^- (4%) are dominant in (*S*)-1-bromo-2-methylbutane. Thus, G^+g^+, G^+t, and G^-g^- conformations of (*S*)-1-bromo-2-methylbutane become energetically unfavorable upon substitution of Br with thiophene ring. Because the gauche-plus orientation of Br−C−C*-C segment is the preferred conformation of (*S*)-1-bromo-2-methylbutane and the trans orientation of thiophene-C−C*-C segment is the preferred conformation in (*S*)-3-(2-methylbutyl)-thiophene (see Figure 5),[13] it is clear that the thiophene ring keeps the first four carbon atom segment in extended orientation, whereas bromine prefers that segment to curl-up. This is one reason for the large differences seen in the absorption and VCD spectra of (*S*)-1-bromo-2-methylbutane and (*S*)-3-(2-methylbutyl)thiophene (Figure 4). Other influences of Br vs thiophene substitution can be discerned from a comparison of the spectra predicted for the same conformation in two molecules. Such comparison (not shown here) indicates large differences in the absorption and VCD spectra for a given conformation in the two molecules, which indicates that the substitution of bromine with thiophene ring also has a large influence because of the changes in the composition of the vibrational normal modes. The large difference in the intensity at the 1231 cm^{-1} (1270 cm^{-1} in predicted spectrum) band may come from the contribution of C−Br stretching motion in the bromine case. The above observations suggest that the thiophene ring has a large influence not only on the predominant conformations, but also on the normal mode compositions and hence on the electronic properties.

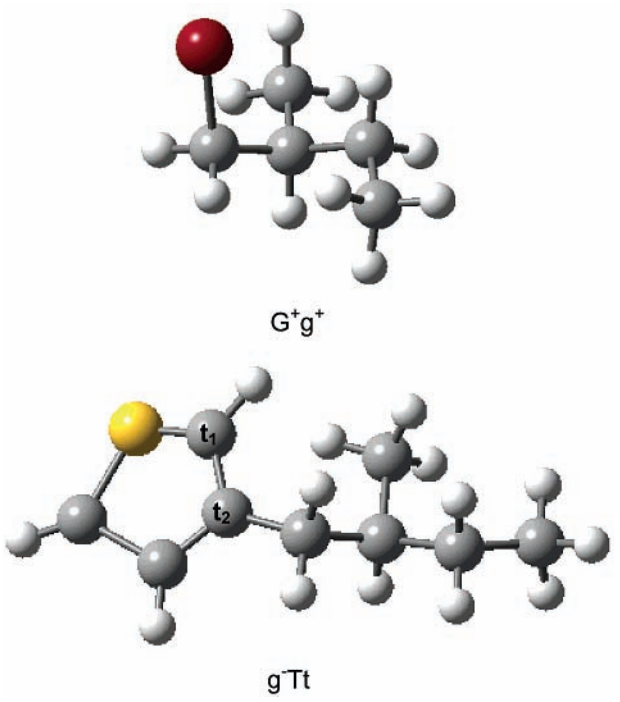

Figure 5. G^+g^+ conformation of (*S*)-1-bromo-2-methylbutane and g^-Tt conformation of (*S*)-3-(2-methylbutylthiophene).

Conclusion

The comparison of experimental and ab initio predicted absorption and VCD spectra indicates the following: (a) (+)-1-Bromo-2-methylbutane is of (*S*) configuration, in agreement with the known absolute configuration. (b) At least six conformations are present for isolated (*S*)-1-bromo-2-methylbutane molecule. The same six conformations are considered to be present in $CDCl_3$ solution, although this statement requires additional support. (c) The substitution of bromine with thiophene ring has a large influence on the conformational stability, and on vibrational properties including normal mode compositions, vibrational absorption and circular dichroism.

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