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Helicity discrimination in diselenides by chiral substituents—a circular dichroism study

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Abstract—Diselenides substituted with chiral alkyl groups exhibit, in solution and in the crystal form, Cotton effects within the diselenide chromophore absorption region. The origin is traced to steric effects, leading to a non-uniform distribution of diastereomeric *P* and *M* forms of the diselenide chromophore. A DFT computational model presented herein allows us to predict the preferred helicity of the diselenide chromophore from the sign of the experimental n–σ^* Cotton effect, that is, a positive long-wavelength Cotton effect is due to a *P* conformer and a negative Cotton effect corresponds to an *M* conformer.
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1. Introduction

Diselenides exist in a *gauche* conformation analogous to that found in disulfides.[1] The repulsion between the lone pairs residing on each selenium atom results in the destabilization of the molecule when the torsion angle R–Se–Se–R (τ) is close to 0° or 180°. This destabilization is reduced when τ is close to 90° or −90°. For dimethyldiselenide, the torsion angle H_3C–Se–Se–CH_3 was found to be smaller than 90° (85° or 82° in the gas phase[2,3] and 65° in solution).[4] Therefore, the diselenide molecules are chiral, existing as an equilibrium mixture of *P* and *M* helical conformers. The rotational barrier of the diselenide moiety is low enough to enable unrestricted interchange of the two conformers. For example, diphenyl diselenide crystallizes as a single enantiomer, stable in the crystal form, whereas in solution it racemizes rapidly. For this molecule the Se–Se rotational barrier is estimated at 8.2 kcal/mol through a synperiplanar and 5.2 kcal/mol through an antiperiplanar transition state.[5,6]

The *gauche* conformation makes the diselenide chromophore inherently chiral. In the twisted diselenide chromophore, the HOMO energy level splits into the two n_a and n_b energy levels. The lowest-energy transitions are now $n_a \rightarrow \sigma^*$ and $n_b \rightarrow \sigma^*$ and are observed as a broad band between 285 and 315 nm in the UV spectra and two Cotton effects of opposite sign in the same wavelength range. Although there are examples of CD and ORD spectra of chiral diselenides reported in the literature,[7–10] no analysis of the influence of a chiral substituent on the distribution of diselenide *P* and *M* conformers was attempted. Herein, we report an experimental (CD)–computational (DFT) approach for the prediction of the preferred helicity of the diselenide chromophore from the sign and magnitude of the n–σ^* Cotton effect of dialkyl diselenides.

2. Results and discussion

Diselenides **1**–**7** substituted with the chiral alkyl groups are now available[11,12] and this enables the analysis of CD spectra, generated only by electronic transitions within the chiral diselenide chromophore (Chart 1).

From the CD data for dialkyl diselenides presented in Table 1, a tentative relationship between the chirality (*R* or *S*) of the carbon atom attached to the selenium atom and the sign of the long-wavelength (328–342 nm) Cotton effect can be envisaged, by assigning an (*S*)-absolute configuration to a positive Cotton effect and an (*R*)-absolute configuration to a negative Cotton effect. Further evidence for such a correlation can be obtained from the crystal structure and crystal powder CD determination.

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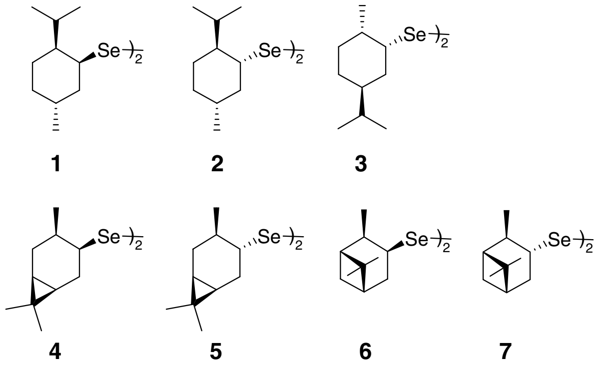

Chart 1.

Table 1. CD and UV data for the long-wavelength Cotton effect for dialkyl diselenides R–Se–Se–R

Compound	Configuration of the α carbon	CD Δε (nm)		UV ε (nm)
1	*S*	1.04 (334)	0.00[a] (284)	325 (316)
2	*R*	−0.18 (338)	0.12 (285)	500 (311)
3	*R*	−0.42 (341)	0.08 (296)	270 (311)
4	*S*	0.40 (339)	−0.32 (286)	340 (310)
5	*R*	−0.20 (333)	0.00[b] (285)	410 (306)
6	*S*	0.23 (342)	−0.36 (288)	370 (308)
7	*R*	−0.18 (328)	0.00[a] (278)	430 (305)

Spectra measured in cyclohexane.

[a] Minimum of the CD spectrum.

[b] Maximum of the CD spectrum.

Dineomenthyl diselenide **1** was the only compound obtained as a crystalline solid and the X-ray structure of this diselenide was determined.[12] The CD spectrum of the crystals of **1** was measured in a KBr pellet and compared to that measured in solution (Fig. 1).

Both spectra show a positive long wavelength Cotton effect. However, the CD spectrum measured in a KBr pellet displays a maximum shifted to a longer wavelength compared to the spectrum obtained for cyclohexane solution. Since the torsion angle τ in the crystal of **1** is −112°, the red shift can be explained as a result of the distortion by 22° from the ideal conformation of the diselenide chromophore (±90°). A similar shift of the UV maximum was observed for other diselenides having significantly distorted torsion angles τ, as in 9,10-diselenadecalin[13] and di-*tert*-butyldiselenide.[14]

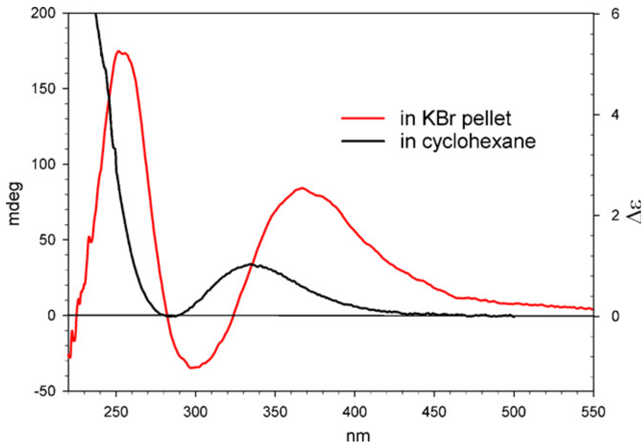

Figure 1. CD spectra of **1** in solution (right vertical scale) and in KBr pellet (left vertical scale).

In addition, we have found that an increase of solvent polarity (from cyclohexane to methanol) had no significant effect on the UV and CD signal strength and their position (Table 2). As a result, the effect of solvation on the conformation of the diselenide can be neglected. This allows us to directly transfer the results of structure calculation (see below) for a single molecule to the real solution system.

Table 2. CD and UV data for **1** and **2** in cyclohexane and methanol

Diselenide	Solvent	CD, Δε (nm)		UV, ε (nm)
1	Cyclohexane	1.04 (334)	0.00 (284)	325 (316)
1	Methanol	0.92 (331)	0.00 (283)	285 (313)
2	Cyclohexane	−0.18 (338)	0.12 (285)	500 (311)
2	Methanol	−0.16 (336)	0.14 (288)	425 (310)

To perform the conformational analysis of **1**, the DFT method[15] [b3lyp/6-31++g(d,p)] was chosen as giving reliable results within a short calculation time.[16] Starting geometries for the calculation of the structure of the dineomenthyl diselenide **1** were based on the X-ray structure reported for this compound.[12,17] By rotating the Se–Se bond, two stable conformers of opposite helicity were obtained (Table 3). It is noteworthy that the conformer with a negative torsion angle τ is of significantly higher energy.

Table 3. Calculated thermodynamic data for the minimum energy conformers of **1**

τ (°)	Heat of formation (kcal/mol)	Free energy (kcal/mol)
76	0.00	0.00
−78	2.98	1.70

From previous work on disulfides,[18,19] it is known that the sign of the long wavelength Cotton effect corresponds to the sign of the torsion angle C–S–S–C. We can now demonstrate that the same relationship can be used for diselenides by calculation of the rotational strength using TDDFT[15] (b3lyp/6-311g(df,2p)) for dimethyl diselenide, as shown in Figure 2. It is clear that the rotational strength of the diselenide $n \rightarrow \sigma^*$ transition increases following the increase of τ from 0° to 90° and it changes the sign from a positive to a negative at (around) $\tau = 90°$. The position of the maximum of the long-wavelength Cotton effect can be a measurement of non-planarity of the diselenide; the closer the value of τ to 90°, the higher the energy of the transition (λ_{max} 325 nm for $\tau = 90°$, vs 460 nm for a planar diselenide).

Thus from a comparison of the data in Table 1 and Figure 2, *P* helicity can be assigned to the lowest energy

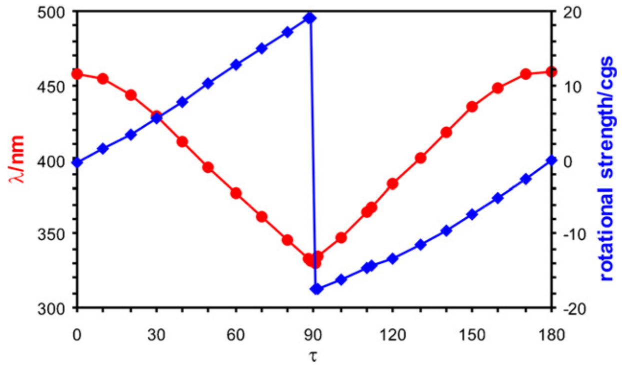

Figure 2. Calculated (b3lyp/6-311(df,2p)) positions of the long-wavelength Cotton effect (–●–) and rotational strength (–◆–) of dimethyl diselenide as a function of torsion angle τ.

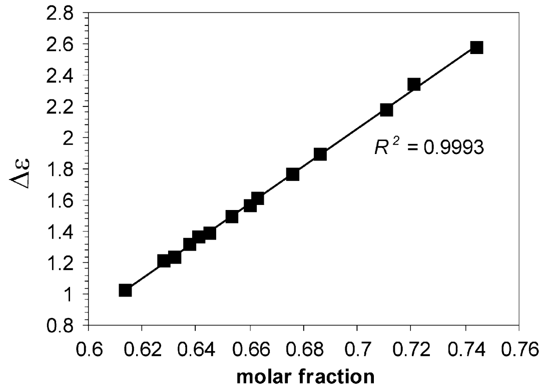

Figure 4. Plot of $\Delta\varepsilon$ against molar fraction of *P*-**1** for $\Delta G^0 = 0.27$ kcal/mol.

conformers of diselenides **1**, **4** and **6**, whereas *M* helical are those of **2**, **3**, **5** and **7**. In addition, these results provide rationalization for the same sign of the long-wavelength Cotton effect of dineomenthyl diselenide **1** in solution and in the crystals. Calculated long-wavelength Cotton effects for dimethyl diselenide having $\tau = 76°$ and $-112°$ are positive and located at 350 nm (for **1** at 334 nm in solution) and 368 (for **1** at 367 nm in KBr pellet), respectively.[20]

To estimate the experimental conformer distribution for **1** a collection of CD spectra measured at low temperatures was analyzed. As shown in Figure 3, lowering the temperature increased the CD signal.

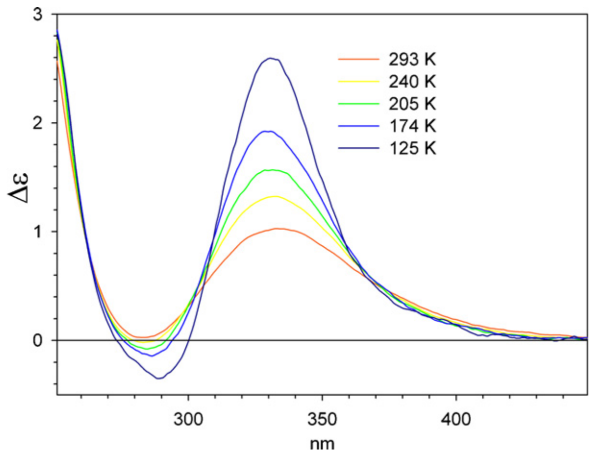

Figure 3. Variable temperature CD spectra of **1** in isooctane.

Using the method described by Moscowitz et al.,[21] an experimental difference of free energy of the two conformers in equilibrium and their population can be calculated. According to this method, the amplitude of the Cotton effects is plotted against the molar fraction *n* {calculated from the equation $n = [1 + \exp(-\Delta G^0/NkT)]^{-1}$}, for different values of ΔG^0. If ΔG^0 represents the experimental value, the plot is a straight line. Using regression analysis, the best correlation for the CD data of **1** was obtained with a ΔG^0 value of 0.27 kcal/mol (Fig. 4). This value is much lower than the calculated one (1.7 kcal/mol in Table 3). Calculated molar fraction (*n*) for *P*-**1** is then 0.61. This indicates that the degree of helical discrimination between the *P* and *M* conformers of the diselenide system due to chiral substitution and consequently the real energy difference between the diastereoisomeric conformers of the dialkyl diselenide molecule is, in fact, quite small.

Extrapolation of the regression line to the point where the molar fraction of *P*-**1** is 1 gives $\Delta\varepsilon = 5.66$. For a molar fraction at 0.5 the estimated value of $\Delta\varepsilon$ is -0.35; this leads to $\Delta\varepsilon = -6.01$ for pure *M*-**1**. The difference between absolute $\Delta\varepsilon$ values for *P*-**1** and *M*-**1** may be due to either a small difference of τ in both diastereoisomers of **1** or due to the contribution of the two neomenthyl substituents. According to CD spectra calculations (Fig. 2), a change of τ of about 5° in the 70–90° range is equivalent to a 5% change of $\Delta\varepsilon$. Lower magnitudes of the observed Cotton effects for compounds **2**–**7**, compared to **1**, can be explained as resulting from lower helicity discrimination in these compounds. Based on the assumption that magnitudes of the long-wavelength Cotton effects of pure *P* or *M* conformers are nearly equal ($\Delta\varepsilon \approx \pm 6$), calculated diastereoisomer ratios for compounds **2**–**7** are in the range 53:47 for $\Delta\varepsilon = \pm 0.42$ and 51:49 for $\Delta\varepsilon = \pm 0.18$.

The main factor leading to discrimination of diselenide conformers appears to be a steric repulsion of the alkyl substituents. Assuming that the C–Se–Se–C torsion angle is acute (less than 90°) in open chain molecules in solution[2–4,13,14] a general model for rationalization of the observed Cotton effects can be proposed, using diselenide **1** as an example (Fig. 5).

In molecule **1** (Fig. 5) with $\tau < 90°$ the groups labelled as large (L) and medium (M) point outside in a *P* conformer. In a situation where τ is negative (*M* conformer), there is a steric repulsion between the medium groups. Thus, a positive n–σ^* Cotton effect can be predicted for diselenide **1**. It appears that the sign of the long-wavelength Cotton effect of a diselenide is not only representative of the preferred helicity of the chromophore, but is also related to the absolute configuration of the α-carbon atom in open chain diselenide molecules. A similar rationalization applies to other diselenides having a secondary stereogenic carbon

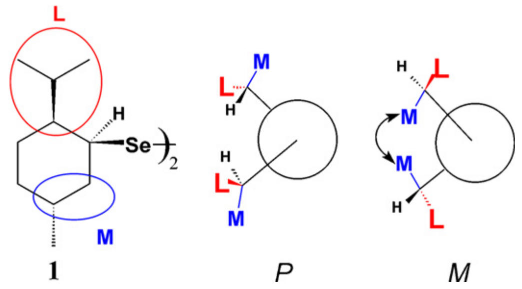

Figure 5. Proposed mechanism for conformer discrimination for dineomenthyl diselenide **1** based on the structures of calculated minimum energy conformers of **1**.

atom next to the selenium. However, in cases where the populations of *P* and *M* conformers are almost equal and the experimental Δε values are very low, the contributions of the other structural factors to the CD spectrum may become significant.

3. Conclusion

In conclusion, the results demonstrate that dialkyl diselenides are conformationally labile molecules, even at low temperatures. Nevertheless, chiral alkyl substituents of the diselenide moiety induce non-equal populations of conformers of *P* and *M* helicity. The sign of the long-wavelength Cotton effect appears to reflect the helicity of the preferred conformer (positive for *P* and negative for *M*). Moreover, the ratio of diastereoisomeric *P* and *M* conformers can be estimated on the basis of the magnitude of the observed n–σ^* long-wavelength Cotton effect of the diselenide chromophore.

4. Experimental

All diselenides investigated were obtained by Ścianowski et al.[12] CD and UV spectra were recorded in spectroscopic grade cyclohexane and methanol in either 0.1 or 1 cm pathlength cells at concentrations corresponding to a maximum absorbance 2, typically using four scans. Low temperature measurements were taken in spectroscopic grade isooctane. Solid state measurements were taken in a KBr pellet oriented perpendicularly to the light beam. The presented CD spectrum is the average of a set of spectra recorded for different orientations of the KBr pellet around the direction of the light beam. No significant differences between individual CD spectra in the KBr pellet were observed.

All excited-state calculations have been performed based upon the ground state geometries of the single molecules with the use of a Gaussian program package.[15] Thus, the results correspond to vertical transitions, and the excitation energies can be compared with the band maxima in the experimental spectra. Rotatory strengths were calculated using length and velocity representations. According to Grimme et al.,[16] the length representation provides better results in most cases, compared to the velocity representation. Length and velocity rotatory strengths are equal and origin-independent at the complete basis set limit. Herein, the differences between the length and velocity calculated values of rotatory strengths were quite small (less than 5%). The CD spectra were simulated by overlapping Gaussian functions for each transition according to the procedure described.[16]

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