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Chirality transfer through sulfur or selenium to chiral propellers[†]

Paweł Skowronek,*^a Jacek Ścianowski,^b Agata J. Pacuła^b and Jacek Gawroński^a

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The mechanism of chirality transfer from a chiral alkyl substituent to a trityl moiety through sulfur or selenium atoms is analysed and discussed on the basis of ECD measurements, DFT structure and ECD spectra calculations. It is shown that the presence of a chalcogen atom is manifested by elongation of the distance between the chiral and the trityl moieties as well as by the change of electronic properties of the trityl chromophore while maintaining its chiroptical response to the chirality of the molecule.

The trityl (triphenylmethyl) group is known to exist in two enantiomeric M, P conformations possessing C_3 symmetry (Fig. 1). Due to steric repulsion the three phenyl rings cannot be simultaneously perpendicular to the plane defined by the three *ipso* carbon atoms nor can be coplanar. On the other hand, in trityl cation coplanarity of the phenyl rings is crucial for efficient conjugation and charge distribution. When the trityl group is connected to a single atom (*i.e.* H, Cl or Br) or to CH₃, ⁺NH₃ groups of C_{∞} or C_3 symmetry, respectively, phenyl rings adopt a propeller shape and both enantiomeric M and P forms are equally abundant.

Investigations of dynamic stereochemistry of trityl group was started by Mislow and followed by other groups.¹⁻⁴ It was shown by dynamic NMR studies that both enantiomeric forms readily interchange through a low energy barrier what makes the separation of enantiomeric propeller-shaped conformers impossible.⁵

Introduction of substituent having symmetry different than C_{∞} or C_3 leads to significant conformational changes in the trityl group. For trityl ethers we observe breakdown of C_3 symmetry, *i.e.* the two dihedral angles C_{ortho} - C_{ipso} -C-X are of opposite sign to the sign of the third.⁶ Trityl group adopts a conformation which can be described as bevel gear" and is

similar to C_2 symmetry structure of the transition state between oppositely twisted propeller-like structures. Such a pattern was observed also for chiral *N*-tritylamines.⁷

We reasoned that the length of the Ph_3C-X bond in trityl chalcogenides significantly increases from oxygen to selenium (Table 1). In the case of chiral trityl substituted thiols and selenols, this elongation of the distance between chiral substituent and trityl group should lower steric hindrance and lead to less congested structures. Indeed, available data from X-ray diffraction determined crystal structures show a 27% longer C-X bond in dimethyl sulfide⁸ compared to dimethyl ether⁹ and a further 7% bond length increase on going from dimethyl disulfide to dimethyl diselenide.¹⁰ In ditrityl disulfide C-X bond length increase is even larger (31%), compared to ditrityl peroxide.¹¹

In order to observe the effect of chirality transmission to trityl groups we have chosen the prepare of three chiral sulfides (1a, 2a, 3a) and selenides (1b, 2b, 3b) with chiral substituents derived from *p*-menthane, carane and pinane terpenes.

Optically active terpenyl trityl sulfides (1a, 2a, 3a) were obtained by the reaction of the corresponding thiols with trityl chloride in the presence of pyridine. Using this method we could not obtain the corresponding terpenyl trityl selenides. Selenides 1b, 2b, 3b were prepared by the reaction of terpene selenolates, generated *in situ* from the terpene selenols and NaH, with trityl chloride. Starting terpene thiols and selenols were prepared according to the known procedures from terpenyl tosylates (Scheme 1).^{12–15}



Fig. 1 Two enantiomeric conformations of triphenylmethyl group.

^eDepartment of Chemistry, A. Mickiewicz University, Poznań, Poland. E-mail: Pawel. Skowronek@amu.edu.pl

^bDepartment of Organic Chemistry, Nicolaus Copernicus University, 7 Gagarin Street, 87-100 Torun, Poland. E-mail: jsch@chem.umk.pl

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Table 1 Lengths of the C-X bonds (in Å) in dimethyl and ditrityl monoand dichalcogenides based on X-ray diffraction data⁸⁻¹¹

	Ме-Х-Ме	Ме-Х-Х-Ме	Ph ₃ C-X-X-CPh ₃
$\mathbf{X} = \mathbf{O}$	1.41	n.a.	1.45
$\mathbf{X} = \mathbf{S}$	1.79	1.806	1.90
X = Se	n.a.	1.948, 1.938	n.a.

Measured ECD spectra of trityl sulfides and selenides show characteristic pattern of Cotton effects in the absorption range below 230 nm, corresponding to the trityl chromophore absorption,⁶ *i.e.* +/+/- for **1a**, **1b** and -/-/+ for **2a**, **3a**, **3b** (Table 2). Very large Cotton effects were recorded for neomenthyl derivatives 1a and 1b in which the X-CPh₃ substituent occupies an axial position (see below). Smaller Cotton effects were seen for the less sterically congested trityl derivatives 2a, 2b, 3a, 3b. For caranyl trityl selenide 2b measured ECD spectrum is weak (Table 2). This may be due to increased distance between the stereogenic center and the trityl group in the selenide 2b, compared to sulfide 2a. The C-S and C-Se bond lengths in 2a and 2b are not available, however reference bond lengths are available for published X-ray diffraction measurements for dimethyl and ditrityl chalcogens (Table 1). Surprisingly, even if the X-CPh₃ group is separated from the chiral substituent by a methylene group, as in pinane derivatives 3a and 3b, ECD spectra are still significant. However, no obvious correlation between the ECD spectra and the structures of trityl derivatives could be proposed, although they were previously established for trityl ethers6 and trityl amines.7

For neomenthyl derivatives **1a** and **1b** strong couplets (A = 87)and 134) at the wavelength of phenyl group ¹B band absorption

1a, X=S 2a, X=S 3a, X=S 1b, X=Se 2b, X=Se 3b. X=Se TsCl R-OTs R-OH Ρv Na₂Se₂ 1) CH₃COSK, DMSO DMF 2) LiAlH₄, Et₂O R-SH R-Se-Se-R CIC(Ph)₃ 1) NaBH₄, EtOH Py, DCM 2) 6N HC R-S-CPh₃ R-SeH 1) NaH. DCM 2) CICPha R-Se-CPh₃

Scheme 1 Synthesis of chiral tritylated sulfides and selenides.

Table 2 Experimental ECD data in $\Delta \varepsilon$ (nm) for trityl derivatives **1a**-**3a** and 1b-3b

-				
1a	-43.5(187)	+43.6 (202)	$+20.7(216)^{\rm sh}$	-2.8(236)
2a	+11.7 (184)	-13.8(203)	-5.5(215)	-2.0(231)
3a	+11.1 (186)	-11.1(202)	$-5.6(216)^{\rm sh}$	+0.5(234)
1b	-75.2(189)	+58.6(208)	+24.5(225)	—
2b	—	-2.3(200)	-1.9(223)	—
3b	+7.1 (188)	-4.6(202)	-4.1(224)	—

Table 3 Calculated conformers relative energies (kcal mol⁻¹) and twist of the phenyl rings, defined as Cortho-Cipso-C-X angle

		ΔG [kcal mol ⁻¹]	Abundance [%]	C _{ortho} –C _{ipso} –C–X [deg]
1a	Conf 1	0.00	57	-80, -36, -38
	Conf 2	0.16	42	-10, 42, 70
2a	Conf 1	0.00	56	-80, -36, -45
	Conf 2	0.14	44	-5, 51, 67

may suggest a strong preference toward one type of conformation. Molecular modelling using Monte Carlo search followed by DFT (B3LYP/6-311g(d,p)) method structure optimizations were performed for molecules 1a and 1b. Conformational rigidity of the neomenthyl moiety and axial position of the chalcogen atom strongly restrict the number of available low energy conformers. For **1a** only two conformers within 2 kcal mol^{-1} energy window were found, with almost the same energy $(0.16 \text{ kcal mol}^{-1} \text{ energy})$ difference) and abundance. For higher energy conformer 2 of 1a the trityl group has approximately C_s symmetry, similar to that observed earlier for chiral trityl ethers. The lowest energy conformer 1 has a propeller-like conformation of the trityl group. Planes of all three phenyl rings are twisted in the same direction. The phenyl ring sterically closest to the neomenthyl moiety is the most twisted (up to -80°) whereas next two have almost the same twist. Conformation of the selenide derivative 1b follows a similar pattern (Table 3 and Fig. 2).

Reliability of the conformers structures was confirmed by the calculation of their CD spectra. For the conformers of 1a and 1b Boltzmann averaged calculated CD spectra satisfactorily reproduce the experimental ones (Fig. 3).

The observed Cotton effects for the trityl sulfides and selenides are significantly larger when compared to the trityl ethers.



Fig. 2 Lowest energy (left) and next in energy (right) conformers of 1a.

CPh₃



Fig. 3 Experimental (solid line) and calculated (dashed line) CD spectra of **1a** (top) and **1b** (bottom).

Such behaviour can be explained by the electronic effect of sulfur and selenium atom. Calculated CD spectrum of triphenylmethane having the same conformation as in conformer 1 of **1a** showed different pattern and lower intensity of the Cotton effects (dotted line in Fig. 4) compared to that calculated for the



Fig. 4 Calculated CD spectra of conformer 1 of **1a** (solid line), trifenylmethane (dotted line), (+)-neomenthiol (dashed line), methyl trityl sulfide (dotted-dashed line), methyl trityl ether (long-dashed line). The conformation of triphenylmethyl moiety in all cases 2–5 was the same as in conformer 1 of **1a**.

entire molecule 1a. As expected, neomenthyl part of molecule 1a displays a negligible effect on the overall CD spectrum (dashed line in Fig. 4). The pattern and intensity of the spectrum of conformer 1 of 1a can be in satisfactory way reproduced when entire aliphatic moiety of the neomenthyl group is replaced by just a methyl group. This behaviour can be explained by conjugation of the lone pairs of the sulfur or selenium atom with triphenylmethyl chromophore. The lone pairs located on sulfur atom are very different in character. One, lower in energy, have dominant contribution of s orbital whereas second one, being the highest occupied NBO, constitutes of almost pure p orbital (see ESI, Table X2 and Fig. X2[†]). Higher energy lone pair orbital on sulfur atom interacts with antibonding orbitals located between sp³ carbon atom of the trityl group and *ipso* carbon atom of adjacent phenyl rings. Weaker interaction (lower than 1 kcal mol^{-1}) are estimated between higher energy lone pair orbital and NBOs located on closest Cortho-Hortho and Cipso-Cortho bonds on phenyl rings. Many transitions contributing to CD spectrum have significant participation of excitation from HOMO to orbitals placed on trityl phenyl rings. Thus CD spectrum of 1a depends on relative position between chalcogen lone pairs and phenyl rings of the trityl group. Similar effect is observed for methyl trityl ether of the conformation resembling that of conf 1 of 1a.

For comparison, there is seen only a weak effect of the heteroatom on the UV spectra of compounds of the structure Ph_3CXH , where X = O, S, NH, compared to UV spectrum of triphenylethane (Ph_3CCH_3), see ESI.[†] Increased absorption at around 260 nm was observed for Ph_3CSH and ascribed to electronic absorption involving *n* orbitals of the sulfur.

In chiral trityl derivatives, Ph_3CXR^* , chirality of the stereogenic carbon atom in R^* is efficiently transferred to the trityl group *via* the chalcogen atom X = S, Se. This is demonstrated by the CD spectra as well as by calculations of conformer structures and rotational strengths of their electronic transitions at the DFT level. CD active electronic transitions involve molecular orbitals located both on the phenyl rings and on the chalcogen atom. Less intense CD spectra are observed with trityl selenides, compared to trityl sulfides, on account of longer carbon–chalcogen bond in the former. Weaker steric demands result in preferred propeller type conformation of the trityl chromophore.

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