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Journal Name

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Chirality transfer through sulfur or selenium to chiral propellers

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Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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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.

Trityl (triphenylmethyl) group is known to exist in two enantiomeric *M, P* conformations possessing C_3 symmetry (Figure 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 CH_3, $^+NH_3$ groups of C_∞ or C_3 symmetry, respectively, phenyl rings adopt a propeller shape and both enantiomeric *M* and *P* forms are equally abundant.

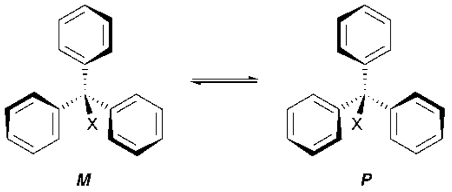


Fig. 1 Two enantiomeric conformations of triphenylmethyl group

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]

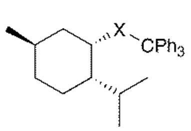
Table 1 Lengths of the C-X bonds (in Å) in dimethyl and ditrityl mono- and dichalcogenides based on X-ray diffraction data [8-11].

	Me-X-Me	Me-X-X-Me	Ph_3C-X-X-CPh_3
X = O	1.41	n.a.	1.45
X = S	1,79	1.806	1.90
X = Se	n.a.	1.948, 1.938	n.a.

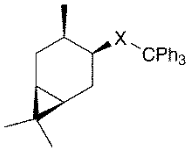
Introduction of substituent having symmetry different than C_∞ or C_3 leads to significant conformational changes in the trityl group. For trityl ethers we observe breakdown of C_3 symmetry, i.e. the two dihedral angles C_{ortho}-C_{ipso}-C-X are of opposite sign to the sign of the third.[6] Trityl group 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-li 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 the 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 sulfide[8] compared to dimethyl ether[9] 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]

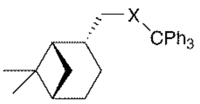
In order to observe the effect of chirality transmission to trityl groups we have chosen the prepare of three chiral sulfides (**1a**, **2a**, **3a**) and selenides (**1b, 2b**, **3b**) with chiral substituents derived from



1a, X=S
1b, X=Se



2a, X=S
2b, X=Se



3a, X=S
3b, X=Se

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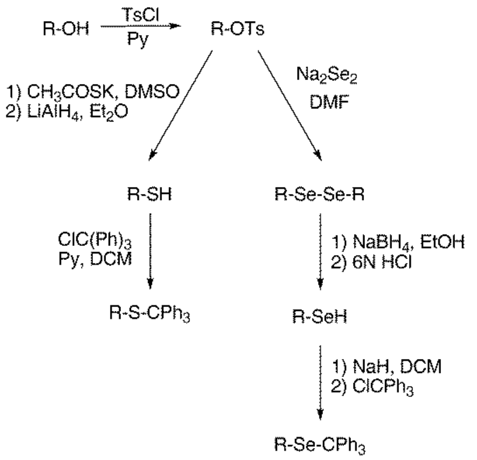
† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x



Scheme 1 Synthesis of chiral tritylated sulfides and selenides

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]

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-CPh$_3$ 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 (Table1). Surprisingly, even if the X-CPh$_3$ 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 ethers[6] and trityl amines.[7]

For neomenthyl derivatives **1a** and **1b** strong couplets (A = 87 and 134) at the wavelength of phenyl group ^{1}B band absorption 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 kcal mol^{-1} 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 Figure 2).

Table 2 Experimental ECD data in Δε (nm) for trityl derivatives **1a** – **3a** and **1b** – **3b**

1a	-43.5 (187)	+43.6 (202)	+20.7 (216)^{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)^{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 C$_{ortho}$-C$_{ipso}$-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

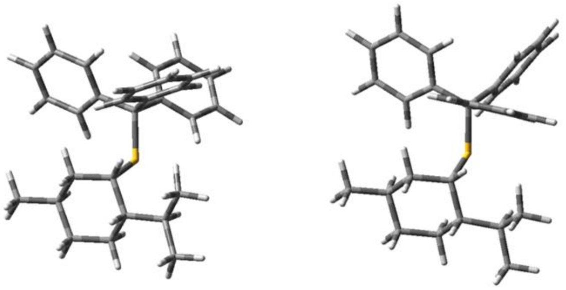


Fig. 2 Lowest energy (left) and next in energy (right) conformers of **1a**.

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 (Figure 3).

The observed Cotton effects for the trityl sulfides and selenides are significantly larger when compared to the trityl ethers. 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 Figure 4) compared to that calculated for the entire molecule **1a**. As expected, neomenthyl part of molecule **1a** displays a negligible effect on the overall CD spectrum (dashed line in Figure 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

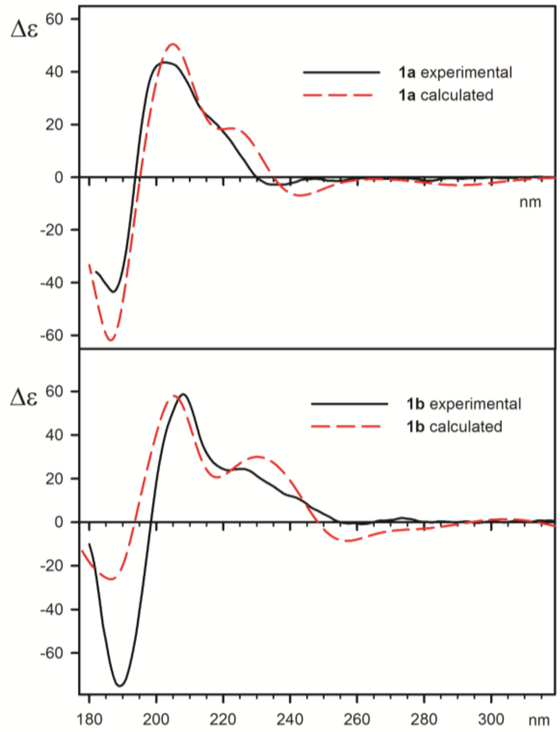


Fig. 3 Experimental (solid line) and calculated (dashed line) CD spectra of **1a** (top) and **1b** (bottom)

whereas second one, being the highest occupied NBO, constitutes of almost pure *p* orbital (see ESI, table X2, figure X2). Higher energy lone pair orbital on sulfur atom interacts with antibonding orbitals located between sp^3 carbon atom of the trityl group and *ipso* carbon atom of adjacent phenyl rings. Weaker interaction (lower than 1 kcal/mol) are estimated between higher energy lone pair orbital and NBOs located on closest C$_{ortho}$-H$_{ortho}$ and C$_{ipso}$-C$_{ortho}$ bonds on phenyl rings. Many transitions contributing to CD spectrum have significant participation of excitation from HOMO to obitals placed on trityl phenyl rings. Thus CD spectrum of **1a** depends on relative position between chalcogene 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**.

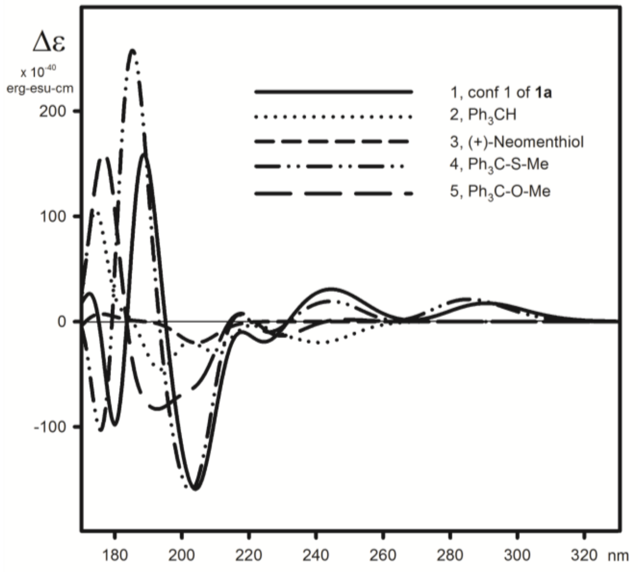


Fig. 4 Calculated CD spectra of conformer 1 of **1a** (solid line), trifenylmethane (dotted line), (+)-neomenthiol (dashed line), methyl trityl sulfide (dotted-dashed line), methyl trityl ether (long-dashed line) The conformation of triphenylmethyl moiety in all cases 2-5 was the same as in conformer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

For comparison, there is seen only a weak effect of the heteroatom on the UV spectra of compounds of the structure Ph$_3$CXH, where X = O, S, NH, compared to UV spectrum of triphenylethane (Ph$_3$CCH$_3$), see ESI. Increased absorption at around 260 nm was observed for Ph$_3$CSH and ascribed to electronic absorbtion involving n orbitals of the sulfur.

In chiral trityl derivatives, Ph$_3$CXR*, 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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This work was supported by Grant no. 2011/03/B/ST5/01011 from National Center for Science (NCN), Poland. All calculations were performed at Poznan Supercomputing and Networking Center.

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