Origin of the Stereoselectivity in (Ethoxycarbonyl)-, Cyano-, and Phenyl-Substituted (Arylsulfinyl)methyl Radicals

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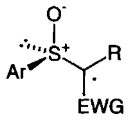
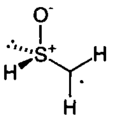
An explanation for the very high diastereoselectivity observed for the reactions of carbonyl-substituted (arylsulfinyl)methyl radicals is presented, based on experimental results and semiempirical calculations. The influence of dipole-dipole interactions, allylic 1,3-strain ($A^{1,3}$ strain), allylic 1,2-strain ($A^{1,2}$ strain), and coulombic interactions is discussed based on stereoselectivities observed with (alkoxycarbonyl)-, cyano-, and aryl-substituted (arylsulfinyl)methyl radicals. In the second part, the effect of solvents and *Lewis* acids on the stereoselectivity of reactions of (arylsulfinyl)- and (alkylsulfinyl)benzyl radicals has been examined.

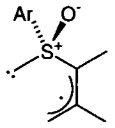
1. Introduction. – Recent reports have shown that sulfoxides are very effective for the induction of diastereoselectivity in radical reactions when the radical center is further substituted by an electron-withdrawing group (EWG) such as an ester, an amide, or a ketone [1–3][1]). The high stereoselectivities have been attributed to intramolecular dipole-dipole interactions which favor the radical conformer having the S–O and the C–EWG bonds *anti* (= s-*trans*) to each other (see **I**). The coplanarity of the radical center and the S–O bond is also predicted by *ab initio* calculations for the simple sulfoxide model system **II** [7][8]. However, we anticipate for delocalized radicals that allylic 1,3-strain ($A^{1,3}$ strain) could also play a crucial role for the level of induction[2]). For instance, it is expected that the lone electron pair at the S-atom and the pseudo-double bond are eclipsed in order to minimize $A^{1,3}$ strain (**III**). We disclose here experimental results and calculations which allow a better understanding of the behavior of radicals of type **III** in their uniquely highly diastereoselective radical reactions. In the second part of this paper, we will discuss the influence of external factors such as solvent and *Lewis* acids on the stereoselectivity of reactions mediated by sulfinylated benzyl radicals[3]).



I (s-*trans*)
dipole-dipole
interactions



II
ab initio
calculations



III
$A^{1,3}$ strain

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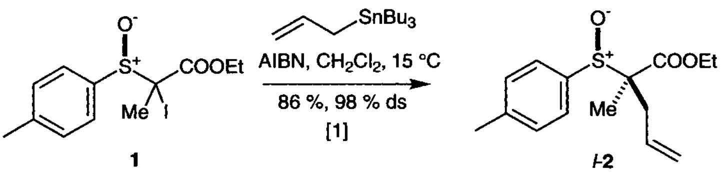
[1]) Reactions of other types of 1-sulfinyl-substituted radicals have been described [4][5]. Radical additions to α,β-unsaturated sulfoxides have also been reported [6].

[2]) For a general review on the stereoselectivity of radical reactions, see [9]. For general reviews on allylic strain, see [10][11]. For reviews dealing specifically with allylic strain in radical reactions, see [12][13].

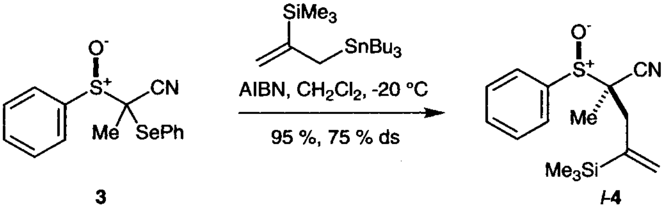
[3]) This part of the work was partially published as a communication [14].

2. Radical Reactions in Non-coordinating Solvent. – To minimize the solvent effects, we decided to run the radical reactions in CH_2Cl_2, a solvent which does not complex sulfoxides[4]). Thus, the reaction starting from the iodide **1** and allyltributylstannane in the presence of AIBN (2,2'-azobis[isobutyronitrile]) was repeated in CH_2Cl_2 according to the *Beckwith* procedure [1]. As reported for the reaction in benzene, *l*-**2** was isolated in 86% yield and 98% diastereoselectivity (*Eqn. 1*). To investigate separately the influence of dipole-dipole interactions and allylic strain, we prepared the radical precursors **3** and **5**–**8** (*Eqns. 2* and *3*) of the cyano- and aryl-substituted radicals (see below, **3r** and **5r**–**8r**, resp.), respectively. The latter are simple models for pure dipole-dipole interactions (**3r**), $A^{1,3}$ strain (**5r** and **6r**), $A^{1,3}$ strain and dipole-dipole interactions (**7r**), and finally $A^{1,3}$ and $A^{1,2}$ strain (**8r**).

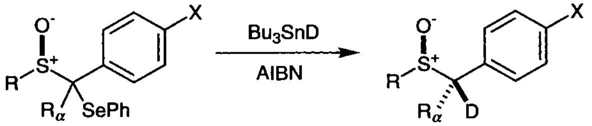
The nitrile **3** was allylated in CH_2Cl_2 with tributyl[2-(trimethylsilyl)prop-2-enyl]-stannane to give *l*-**4** in 75% ds (*Eqn. 2*). The reaction was run at –20° to avoid the facile elimination of sulfenic acid. The observed selectivity was considerably lower than the one determined for the allylation of **1** to *l*-**2** (98% ds, *Eqn. 1*). Since dipole effects are stronger for a cyano than for an (alkoxycarbonyl) group, our results indicate that at least one other important factor is involved in the stereochemistry control. The relative configuration of *l*-**4** was established by analogies of the NMR spectra with those of *l*-**2**. Due to the instability of *l*-**4**, no chemical correlation between the two compounds was possible.



1 *l*-**2** (1)



3 *l*-**4** (2)



(3)

5 R=Ph, X=H, R_α=H
6 R=Me, X=H, R_α=H
7 R=Ph, X=CF_3, R_α=H
8 R=Ph, X=H, R_α=Me

9 R=Ph, X=H, R_α=H
10 R=Me, X=H, R_α=H
11 R=Ph, X=CF_3, R_α=H
12 R=Ph, X=H, R_α=Me

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[4]) Aromatic solvents, alcohols, and ethers are known to form complexes with sulfoxides by coordination at the S-atom (aromatic solvents and ethers) [15] or by H-bonding at the O-atom (alcohols) [16][17].

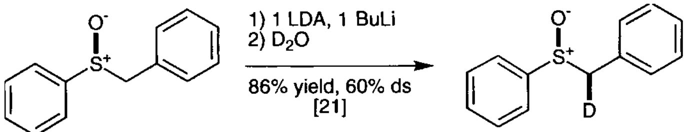
The effect of $A^{1,3}$ strain was investigated next with the aryl-substituted radical precursors **5**–**8** (*Eqn. 3*, *Table 1*). The deuteration reaction of **5** in CH_2Cl_2 gave *u*-**9** (66% ds, *Entry 1*). The reduction of the methyl sulfoxide **6** was not stereoselective (50% ds, *Entry 2*). This demonstrates that $A^{1,3}$ strain effects alone are not sufficient to obtain a high diastereocontrol. Similar conclusions have been drawn from cycloaddition reactions of vinyl sulfoxides [18][19]. The radical deuteration of **7** was marginally more selective in CH_2Cl_2 (71% ds, *Entry 3*) due to the presence of the electron-withdrawing CF_3 group in *para* position. A great improvement in stereoselectivity was observed when the H-atom at C(α) was replaced by a Me group[5]). Thus, upon treatment with Bu_3SnD/AIBN, **8** gave the deuterated sulfoxide *l*-**12** with a selectivity of 93% ds in CH_2Cl_2 (*Table 1*, *Entry 4*).

Table 1. *Reduction of (Arylsulfinyl)- and (Alkylsulfinyl)benzyl Radicals According to* Eqn. 3. Reactions performed in CH_2Cl_2 at 15°.

Entry	Precursor	R	X	R_α	Product	Yield [%]	ds [%]ᵃ)
1	**5**	Ph	H	H	**9**	87	66 (*u*)
2	**6**	Me	H	H	**10**	59	50 (*l*)
3	**7**	Ph	CF_3	H	**11**	94	71 (*u*)
4	**8**	Ph	H	Me	**12**	59	80 (*l*)

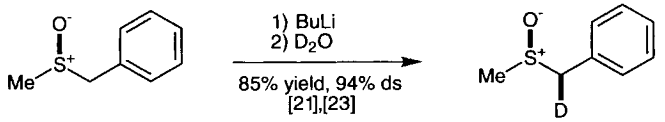
[a]) Stereochemical descriptor in parentheses. Change of the descriptor is caused by changes in the order of priority of the substituents at the S-atom. All major isomers correspond to the one drawn in *Eqn. 3*.

The relative configuration of *u*-**9** was attributed by comparison with the product issued from the deuteration of deprotonated benzyl phenyl sulfoxide (1 equiv. of lithium diisopropylamide (LDA)/1 equiv. of BuLi at −78°, then D_2O; 86% yield, 60% ds) which is known to be *u*-**9** (*Eqn. 4*) [21][22]. This was further confirmed by comparison of the ^{1}H-NMR spectra of *u*-**9** with those of the known *l*-**10** prepared from methyl benzyl sulfoxide according to the *Durst-Ohno* procedure (*Eqn. 5*) [21][23]. The relative configuration of *u*-**11** was assessed by comparison of NMR spectra with those of *u*-**9**. The relative configuration of *l*-**12** has been established by *Modena* and coworkers [24].



u-**9**

(4)



l-**10**

(5)

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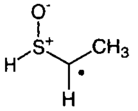
[5]) For a related effect with (alkoxycarbonyl)-substituted radicals, see [12] and [20] and the discussion in [13].

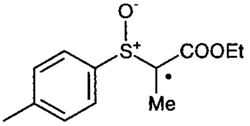
3. Calculations. – To understand the stereochemical results, we decided to investigate the conformation of the radical intermediates involved in the reactions described in *Eqns. 1–3*. This approach has been applied with success to many radical reactions, because they are known to proceed *via* early transition states [25].

3.1. *Calculation Method.* In a preliminary study, we investigated the hypothetical radical **13r** using different calculation methods with the aim to compare *ab initio* and semiempirical methods and to choose a suitable method to calculate more complicated systems. All calculations were performed using the Spartan 4.1 program [26] running on a *Silicon Graphics* workstation *Iris 4400*. *Ab initio* calculations were performed using the 6-31G** and STO-3G* basis sets. Semiempirical calculations were done using the MNDO/d parametrization developed by *Thiel* and coworkers [27]. In the case of the open-shells species, the unrestricted *Hartree-Fock* (UHF) hamiltonian was used for the geometry optimization. All defaults criteria for both the SCF and geometry optimization were used. *Table 2* reports the results of *ab initio* and semi-empirical calculations for the simplest radical H–SO–CH(Me)$^{\cdot}$ (**13r**).

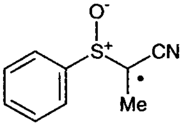
All four calculation methods gave a similar qualitative result: the radical H–SO–CH(Me)$^{\cdot}$ exists in two conformations s-*cis*-**13r** (Me and O-atom *cis*) and s-*trans*-**13r** (Me and O-atom *trans*). It is worth noting that the S–O bond is not perfectly



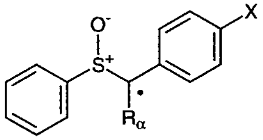
13r



1r



3r



5r $R_\alpha = X = H$
7r $R_\alpha = H, X = CF_3$
8r $R_\alpha = Me, X = H$

Table 2. *Comparison between* ab initio *and Semiempirical Calculations for Radical* **13r**

	6-31G**	STO-3G*	MNDO/d	AM1
s-*cis*-**13r**				
Energy	−550.90645a)	−544.70262a)	−17.75b)	−12.36
d(S=O [Å]	1.482	1.483	1.514	1.494
d(S–C) [Å]	1.765	1.784	1.742	1.664
∠ (O–S–C–Me) [°]	−32.3	−11.2	−29.2	−21.6
∠ (O–S–C–H) [°]	170.4	171.3	154.7	162.0
s-*trans*-**13r**				
Energy	−550.90490a)	−544.70198a)	−17.67b)	−12.40
d(S=O) [Å]	1.481	1.483	1.514	1.493
d(S–C) [Å]	1.762	1.784	1.743	1.660
∠ (O–S–C–Me) [°]	175.0	170.1	158.3	153.4
∠ (O–S–C–H) [°]	−27.2	−37.4	−26.1	−29.9
Δ [kcal/mol]c)	−0.97	−0.40	−0.08	+0.04

a) Total energy in hartrees. b) Heat of formation in kcal/mol. c) *Δ* = Energy difference between the two conformers (*Δ* > 0 ⇒ *trans*-**13r** more stable than *cis*-**13r**).

orthogonal to the SOMO orbital, the dihedral angle ∠(O–S–C–Me) lies between 11 and 37°. This is different to what was previously reported by *Clark* and *Pasto* based on *ab initio* calculations [7] [8]. Moreover, it is apparent from *ab initio* calculations that the SOMO of the radical tends to be parallel to the electron pair at the S-atom; this demonstrates that the SOMO-n_S interactions are an important factor of stabilization. Although the small energy difference between the two conformers is reproduced by all the methods (within 1 kcal/mol), variations are noted for the geometry. *Ab initio* calculations predict a slightly pyramidal radical[6]), whereas the semiempirical calculations predict a planar geometry (*Fig. 1*). Moreover, AM1 calculations predict too short S–C bond lengths. Therefore, for the large systems investigated here, we chose the MNDO/d method which represents a good compromise between accuracy and calculation time.

3.2. *Conformational Analysis of the Radicals* **1r**, **3r**, **5r**, **7r**, *and* **8r**. Interestingly, the calculations predict that radicals **1r** and **3r** exist in the same conformations s-*cis* and


s-*cis*-13r **s-*trans*-13r**

Fig. 1. *Minimum-energy conformations of radical* **13r** (6-31G**)

Table 3. *Conformational Analysis of Radicals* **1r**, **3r**, **5r**, **7r**, *and* **8r** (Ar–SO–C(R_z)(Z)˙) *Using MNDO/d Methods*

	R_z	Z	ΔH_f [kcal/mol]	∠(O–S–C–R_z) [°]	∠(O–S–C–Z) [°]
s-*cis*-**1r**	Me	COOEt	–74.21	164.7	–20.1
s-*trans*-**1r**	Me	COOEt	–76.63	–14.0	171.3
Diff.[a])			**2.24**		
s-*cis*-**3r**	Me	CN	39.64	166.0	–17.9
s-*trans*-**3r**	Me	CN	38.15	–20.6	163.6
Diff.[a])			**1.49**		
s-*cis*-**5r**	H	Ph	34.85	126.9	–57.0
s-*trans*-**5r**(1)	H	Ph	35.01	47.5	–130.0
s-*trans*-**5r**(2)	H	Ph	34.73	–26.4	150.4
Diff.[a])			**0.12/–0.16**		
s-*cis*-**7r**(1)	H	p-CF_3–C_6H_4	–113.54	144.1	–40.8
s-*cis*-**7r**(2)	H	p-CF_3–C_6H_4	–113.13	129.2	–54.9
s-*trans*-**7r**(1)	H	p-CF_3–C_6H_4	–112.77	38.6	–138.1
s-*trans*-**7r**(2)	H	p-CF_3–C_6H_4	–112.50	27.2	–149.7
Diff.[a])			**–0.63/–0.77**		
s-*cis*-**8r**(1)	Me	Ph	32.71	–129.1	46.6
s-*cis*-**8r**(2)	Me	Ph	31.35	167.3	–19.4
s-*trans*-**8r**(1)	Me	Ph	31.04	44.0	–134.8
s-*trans*-**8r**(2)	Me	Ph	30.90	–2.2	178.3
Diff.[a])			**0.45/1.67**		

[a]) Difference = ΔH_f(s-*cis*) – ΔH_f(s-*trans*) (Diff. > 0 ⇒ *trans* more stable than *cis*).

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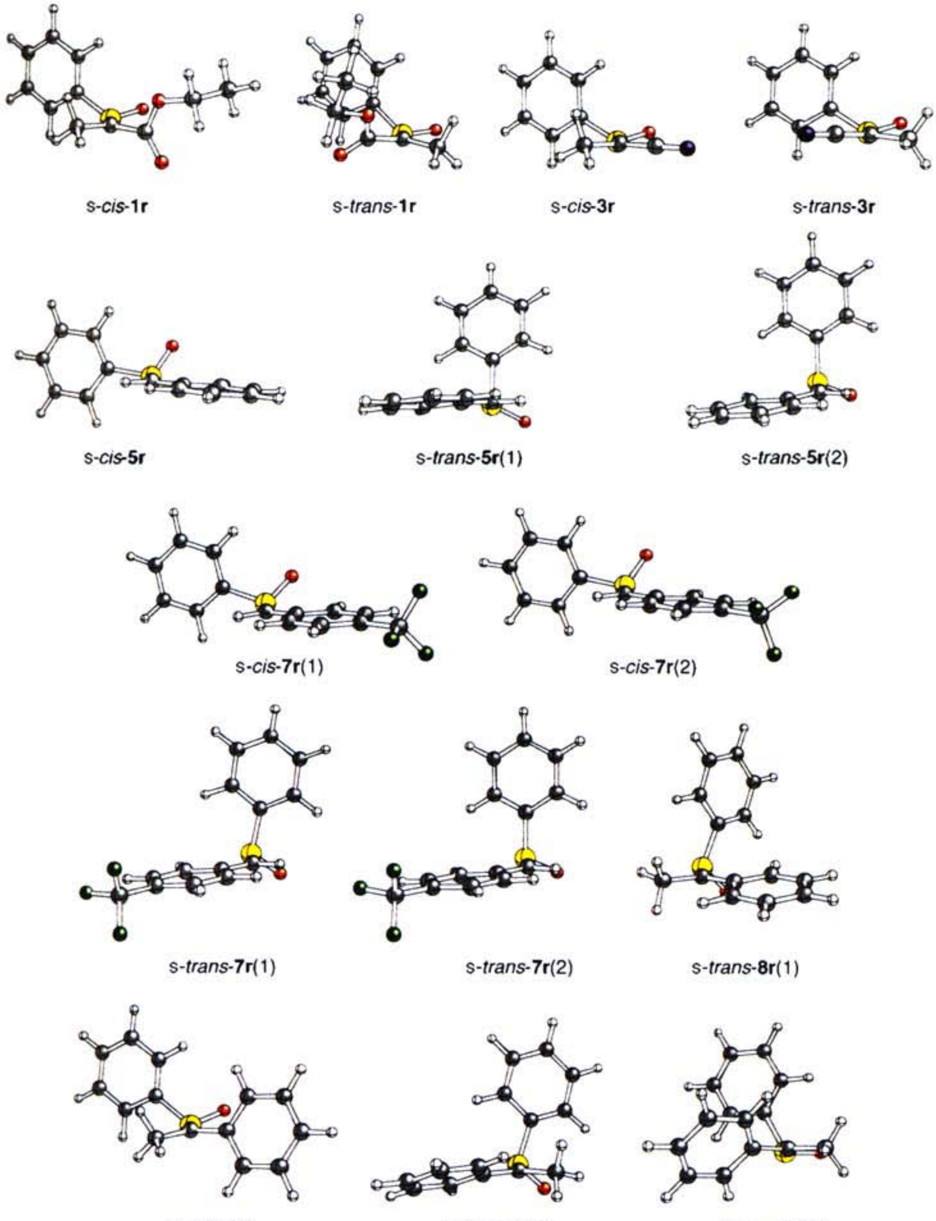
[6]) The pyramidalization is such that the largest lobe of the SOMO orbital is *anti*-periplanar to the electron pair at the S-atom. This conformation minimizes the eclipsing interactions.

s-*trans* as the model system **13r**. For the radicals **5r**, **7r**, and **8r**, the situation is somewhat more complicated due to the existence of several conformers; however, they still can be categorized in s-*cis* and s-*trans* conformations. The results of the calculations are summarized in *Table 3*, and models are depicted in *Fig. 2*.



s-*cis*-**1r** s-*trans*-**1r** s-*cis*-**3r** s-*trans*-**3r**

s-*cis*-**5r** s-*trans*-**5r**(1) s-*trans*-**5r**(2)

s-*cis*-**7r**(1) s-*cis*-**7r**(2)

s-*trans*-**7r**(1) s-*trans*-**7r**(2) s-*trans*-**8r**(1)

s-*cis*-**8r**(2) s-*trans*-**8r**(1) s-*trans*-**8r**(2)

Fig. 2. *Minimum-energy conformations of radicals* **1r**, **3r**, **5r**, **7r**, *and* **8r** (MNDO/d)

Radical **1r**: The s-*trans* conformer of the ethoxycarbonyl derivative **1r** is more stable than the s-*cis* one by *ca.* 2.2 kcal/mol. This can be attributed partially to minimization of dipole-dipole interactions and to the fact the COOEt group stabilizes the radical only in the s-*trans* conformer. Indeed, in the s-*cis* conformer, the π system of the COOEt group is orthogonal to the SOMO of the radical due to electrostatic repulsion between the ester and the sulfoxide O-atoms. This type of interactions is best described by the term allylic coulombic 1,3-repulsion ($A^{1,3}$ coulombic repulsion) by analogy to the term $A^{1,3}$ strain.

Radical **3r**: Compared to **1r**, the energy difference is smaller in the case of the cyano derivative **3r**: the s-*trans* conformer is more stable than the s-*cis* by only 1.5 kcal/mol. This result is surprising because dipole-dipole interactions are stronger in the case of the CN-substituted radical **3r** than in the case of the COOEt-substituted radical **1r**. This result can be attributed to the fact that both conformations of the radical are equally stabilized by the CN group. Indeed, $A^{1,3}$ coulombic repulsion is not occurring because of the linearity of the CN group[7]).

Radical **5r**: Three minimum-energy conformations have been found. One s-*cis* conformation and two very similar s-*trans* conformations; in all conformations, the radical is stabilized by the Ph group. The s-*cis* conformer is comparable to s-*cis*-**13r**. The two s-*trans* conformers are characterized by a S–C(arom.) bond orthogonal to the radical plane and by a perfect minimization of $A^{1,3}$ strain (the electron pair at the S-atom and the Ph group are coplanar). All three conformations are, within 0.3 kcal/mol, similar in energy.

Radical **7r**: This radical exists in two s-*cis* and two s-*trans* conformations. However, the s-*cis* conformers are perceptibly more stable than the s-*trans* ones by 0.6 kcal/mol. This cannot be explained by dipole interactions which should favor the s-*trans* conformers. The CF_3 group is supposed to enhance the SOMO-n_s interactios due to its electron-withdrawing effect.

Radical **8r**: The conformational analysis of this radical is more complicated than the preceding cases. It exists in 4 conformations, two s-*cis* and two s-*trans* ones, as depicted in *Fig. 2*. The s-*trans* conformers are noticeably more stable than the s-*cis* ones. Conformer s-*cis*-**8r**(1) shows stabilization by delocalization into the Ph ring, but no stabilization by SOMO-n_s interactions. Conformer s-*cis*-**8r**(2) corresponds to the conformation s-*cis*-**1r** where optimal SOMO-n_s overlap occurs, with the Ph group being now orthogonal to the radical center and thus not participating in the stabilization. Moreover, this conformation is destabilized by $A^{1,2}$ strain (interaction between the Me group and the Ph group at the S-atom). The two s-*trans* conformers resemble the conformers s-*trans*-**5r** and -**7r**.

3.3. *Rationalization of the Observed Stereoselectivities.* The major isomer of the reaction of the allylation of **1** and **3** can be explained by attack of the radical intermediates **1r** and **3r** in their most stable s-*trans* conformation from the less hindered face (*ul* topicity, *Fig. 3*). The difference of selectivity for these two reactions is directly related to the difference of stability of the two conformers. This difference of stability is not due to dipole-dipole interactions but is caused by destabilizing allylic coulombic 1,3-interactions destabilizing s-*cis*-**1r**. This destabilization does not exist with the linear CN group in s-*cis*-**3r**.

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[7]) Comparison of COOR- and CN-substituted radicals has already been used as probe for the allylic-strain effects [20][28].

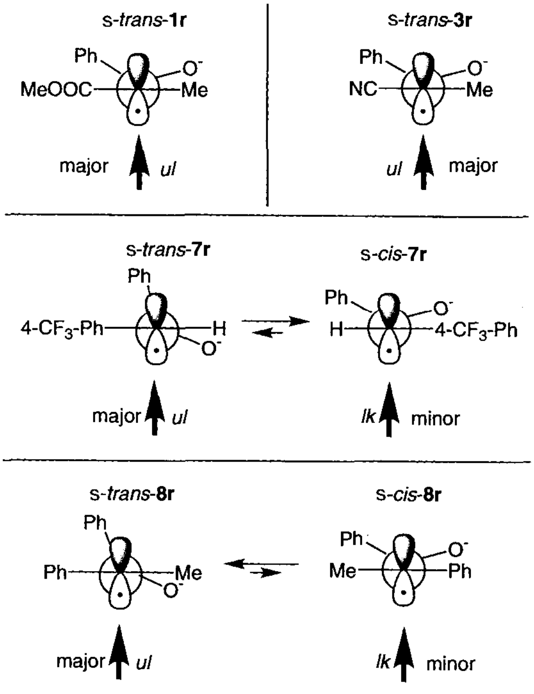

Fig. 3. *Proposed models for the stereochemical outcome of reactions of radicals* **1r**, **3r**, **7r**, *and* **8r**

For the deuteration of **5** and **6**, the low selectivity is explained by the absence of energy discrimination between the conformers.

The stereoselectivity of the reduction of **7r** by Bu_3SnD cannot be explained based on conformer stability. The main isomer is coming from the attack of the minor s-*trans* conformations leading to staggered transition states (*ul* topicity, *Fig. 3*). Attack of the s-*cis* conformers (*lk* topicity) is leading to eclipsed transition states which is less favorable. Moreover, the two faces of the s-*cis* conformers are almost equally shielded by the Ph group at the S-atom (see *Fig. 2*).

Finally, the good stereoselectivities observed for the reduction of **8** can be explained by the greater stability of s-*trans*-**8r** and by formation of a staggered transition state (*ul* topicity, *Fig. 3*). The s-*cis* conformer is leading to eclipsed interactions in the transition state (*lk* topicity, *Fig. 3*).

Solvent Effects. – The reactions described in *Eqns. 1–3* were repeated in different solvents. For all reactions, except for the allylation of **1r** which is already almost completely stereoselective, an increase of the stereoselectivity was noticed when the reactions were run in aromatic solvents or THF (see *Table 4*, *Entries 1–5*, *8*, and *9*). The steric bulk of the solvent also played a role, indeed, for the reduction of **5**, the selectivity varying from 82% ds in benzene to 85% in mesitylene. Propanenitrile (*Entry 6*) produced no change of the deuteration of **5** as compared to the deuteration in CH_2Cl_2. Interestingly, an inversion of selectivity was observed in CF_3CH_2OH, a solvent known to form H-bonds with the O-atom of the sulfoxide [17].

Table 4. *Effect of Solvents on the Reactions of* Eqns. 1–3 *at 15°*

Entry	Precursor	Product	Solvent	Yield [%]	ds [%][a])
1	**1**	**2**	C_6H_6	86	98 (*l*)
2	**3**	**4**	toluene[c])	81	90 (*l*)
3	**5**	**9**	C_6H_6	51	81 (*u*)
4			mesitylene	66	85 (*u*)
5			THF	51	82 (*u*)
6			$MeCH_2Cn$	58	69 (*u*)
7	**5**	**8**	CF_3CH_2OH	79	65 (*l*)[b])
8	**6**	**10**	C_6H_6	74	77 (*l*)
9	**8**	**12**	C_6H_6	67	96 (*l*)

[a]) Stereochemical descriptor in parentheses. Change of the descriptor is caused by changes in the order of priority of the substituents at the S-atom. All major isomers, except for *Entry 7*, correspond to the one drawn in *Eqns. 1–3*. [b]) Inversion of selectivity observed in this case. [c]) Reaction performed at −20°.

The rationalization of these solvent effects is not straightforward. Aromatic solvents are known to complex efficiently sulfoxides at the S-atom *anti* to the S–O bond [15] and, therefore, they have been shown to induce steric hindrance which modify the stereoselectivity of radical reactions in cyclic sulfoxides [29][30]. The same kind of effect is expected with acyclic sulfoxides, and the coordination is going to modify the conformational equilibrium as well as the reactivity of the different conformers. The first point is difficult to evaluate by calculations; however, a simple analysis of the conformers can help to understand the effect. Radical **5r** exists in the s-*cis* and two s-*trans* conformations. Complexation by aromatic solvents (or THF) should reduce the reactivity of the s-*cis* conformer since the solvent is coordinated exactly on the trajectory of the incoming radical trap (see *Fig. 4*). The s-*trans* conformers are much less influenced by the solvation which is occurring on the face opposite to the radical reactions. In case of 2,2,2-trifluoroethanol, the reversal of the stereoselectivity can be explained by H-bonding at the S–O O-atom [17] which disfavors the reaction of the s-*trans* conformers (*Fig. 4*).

Effect of *Lewis* Acids. – *Lewis* acids have been shown to be spectacularly effective in the control of the stereoselectivity with cyclic sulfinylated radicals [14][29][8]). Therefore, we decided to investigate their use in the reactions depicted in *Eqns. 1–3*. The ethoxycarbonyl and the cyano derivatives (*Eqn. 1* and *2*, resp.) were not suitable for this study since all the acids tested catalyzed the elimination of sulfenic acid. However, with the reactions depicted in *Eqn. 3*, dramatic results were obtained; they are summarized in *Table 5*.

Lithium perchlorate and [Eu(dpm)$_3$] (dpm = 2,2,6,6-tetramethylheptane-3,5-dione), which are efficient for the control of the stereoselectivity in cyclic systems, reduced strongly the diastereoselectivity of the deuteration reaction. However, the major stereoisomer formed was still *u*-**9** (*Table 5*, *Entries 1* and *2*). With the very bulky and oxophilic bis[2,6-di(*tert*-butyl)-4-methylphenolato]methylaluminium (MAD) and bis-[4-bromo-2,6-di(*tert*-butyl)phenolato]methylaluminium (MABR) [32], an excellent selec-

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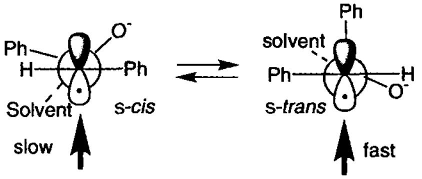
[8]) For a general review on the use of *Lewis* acids in radical reactions, see [31].

Reduction of **5r** in aromatic solvent and THF



Reduction of **5r** in 2,2,2-trifluoroethanol

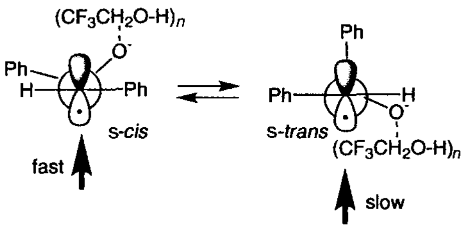


Fig. 4. *Solvent effect in the reduction of radical* **5r**

Table 5. *Effect of* Lewis *Acids on the Deuteration Reactions of* Eqn. 3 *at 15° in Different Solvents*

Entry	Precursor	Product	Solvent	*Lewis* acid (mol-equiv.)	Yield [%]	ds [%][a])
1	**5**	**9**	$MeCH_2CN$	$LiClO_4$ (1.2)	51	58 *u*)
2	**5**	**9**	CH_2Cl_2	[Eu(dpm)$_3$] (1.1)	95	54 (*u*)
3	**5**	**9**	CH_2Cl_2	MAD (1.1)	85	*97.5 (l)*
4	**5**	**9**	CH_2Cl_2	MAD (0.1)	89	62 (*u*)
5	**5**	**9**	CH_2Cl_2	MABR (1.1)	84	>*97 (l)*
6	**5**	**9**	CH_2Cl_2	MABR (0.1)	91	52 (*u*)
7	**6**	**10**	CH_2Cl_2	MAD (1.1)	77	*96 (u)*
8	**8**	**12**	C_6H_6	MAD (1.1)	86	*58 (u)*
9	**8**	**12**	CH_2Cl_2	MAD (1.1)	73	*86 (u)*

[a]) Stereochemical descriptor in parentheses. Change of the descriptor is caused by changes in the order of priority of the substituents at the S-atom or by a real change of the relative configuration. This last case is indicated in italics.

tivity (> 97% ds, *Entries 3* and *5*) was obtained for **5**, with preferential formation of *l*-**9**. Deuteration of **6**, which was not selective in CH_2Cl_2, gave preferentially *u*-**10** with 96% ds in the presence of 1.1 equiv. of MAD (*Entry 7*). The inversion of the stereochemical outcome was also observed with **8**, but to a lesser degree (*Entry 9*, 86% ds). Unlike what we observed in cyclic systems [29][30], the effect of the *Lewis* acid is not catalytic. In the presence of 10 mol-% of MAD or MABR, a nearly 1:1 mixture of isomers was formed (*Entries 4* and *6*).

The effect of methyldi(phenolato)aluminium derivatives can be understood by considering the models depicted in *Fig. 5*. Due to the tremendous size of the *Lewis* acids used, the complexed O-atom is expected to be orthogonal to the radical plan. In model **A**, the system possesses a minimum $A^{1,3}$ strain (the electron pair at the S-atom is coplanar with the Ph–C$^{\bullet}$ bond), and reaction with Bu_3SnD is occurring *anti* to the bulky $OAlMeX_2$ group. This leads to the formation of the major isomers *l*-**9**, *u*-**10**, and *u*-**12** (inversion of the stereochemical outcome as compared to the reaction in the absence of *Lewis* acid). The minor isomer is expected to be formed according to model **B** which is less stable due to strong $A^{1,3}$ interactions between the R group (= Ph or Me) and the Ph substituent at the radical center. Interestingly, the lower level of induction obtained with the radical leading to **12** is easily explained by our model. Indeed, for **8r**, the transition state **A** is destabilized by allylic 1,2-strain between R_{α} (= Me) and R (= Ph). Therefore, the contribution of **B** to the stereoselectivity becomes more important.

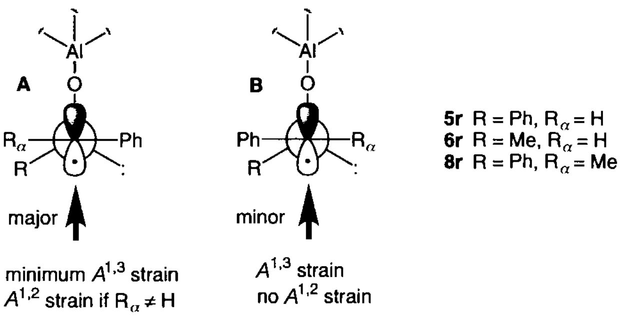


Fig. 5. *Reduction of radical* **5r**, **6r**, *and* **8r** *in the presence of bulky* Lewis *acids*

In conclusion, we have demonstrated that dipole-dipole interactions are not sufficient to explain the very high stereoselectivities obtained with 1-(alkoxycarbonyl)-1-(arylsulfinyl)methyl radicals. Destabilizing $A^{1,3}$ coulombic interactions are an important factor which disfavor the formation of the minor isomer in the case of the alkoxycarbonyl group. For sulfinylated benzyl radicals, we have demonstrated that $A^{1,3}$ strain effects are not sufficient to produce a good stereoselectivity control. Incorporation of substituents which generate $A^{1,2}$ strain is necessary for a good stereocontrol. Interestingly, the sense of the stereoselectivity can be controlled by solvent effects and by *Lewis*-acid additives.

The authors are grateful to Prof. *Walter Thiel*, University of Zurich, for providing the d-parameters for sulfur prior to their publications. This work was supported by the *Swiss National Science Foundation* (project CHiral2 No. 2027-048164.96) and by the *Office Fédéral pour l'Education et la Science (OFES)* within a *European COST-D2* program.

Experimental Part

General. All the commercially available reagents (*Fluka* or *Aldrich*) were used as received unless otherwise specified. THF was freshly distilled from K under N_2, CH_2Cl_2 and benzene from CaH_2. Irradiations were conducted using a sun lamp *Osram Ultra-Vitalux 300 W*. Flash column chromatography (FC) and filtration: *Baker* silica gel (0.063–0.200 mm); elution with AcOEt and hexane. TLC: *Merck* silica gel *60* F_{254} anal. plates; detection with UV, I_2, or by spraying with a soln. of phosphomolybdic acid (25 g), $Ce(So_4)_2 \cdot 4\,H_2O$ (10 g) conc. H_2SO_4 soln. (60 ml), and H_2O (940 ml) with subsequent heating. M.p.: *Büchi-Tottoli* apparatus and *Reichert Thermovar Kofler* hot stage; not corrected. IR: *Perkin-Elmer-297* spectrophotometer. FT-IR: *Mattson*

Unicam 5020. NMR: *Varian Gemini 200* (^{1}H 200 MHz, ^{13}C 50.3 MHz), *Bruker AC-250* (^{1}H 250 MHz, ^{13}C 62.9 MHz), *Bruker AM-360* (^{1}H 360.13 MHz, ^{13}C 90.56 MHz), or *Bruker AMX-400* (^{1}H 400 MHz, ^{13}C 100.5 MHz); unless otherwise indicated, $CDCl_3$ soln.; chemical shifts δ in ppm rel. to $CHCl_3$ (= 7.27 ppm). MS: *Finnigan 1020*; *Nermag R10-10C*; *Vacuum Generators Micromass E70/70*, and *Hewlett-Packard 5988A*, CI: chemical ionization with NH_3; EI: electron ionization at 70 eV. Elemental analysis: *Ilse Beetz*, Mikroanalytisches Laboratorium, D-8640 Kronach, and *Ciba-Geigy*, Mikrolabor, CH-1700 Fribourg-Marly.

General Procedure 1: *Preparation of Sulfides*. A soln. of the thiol (45 mmol) and the alkyl halide (48 mmol) in benzene (20 ml) was added to a soln. containing NaOH (3.0 g, 75 mmol) and Bu_4NI (500 mg, 1.4 mmol) in H_2O (25 ml). The biphasic system was stirred vigorously during 12 h. The aq. phase was extracted with Et_2O (3 × 20 ml) and the combined org. phase washed with 1N NaOH (20 ml) and brine (50 ml), dried ($MgSO_4$), and evaporated: crude product which was used without further purification for the oxidation step.

General Procedure 2: *Oxidation of Sulfides*. A soln. of the sulfide (1.0 mmol) in CH_2Cl_2 (20 ml) was treated at $-10°$ with a dried ($MgSO_4$) soln. of 3-chlorobenzenecarboperoxoic acid (1.0 mmol) in CH_2Cl_2 (10 ml). The soln. was stirred for 1 h at $-10°$ and warmed to r.t. Solid KF (174 mg, 3.0 mmol) was added, and the resulting suspension was stirred overnight and then filtered through *Celite*. After solvent removal, the residue was purified by FC.

General Procedure 3: *Oxidation of Sulfides*. A soln. of sulfide (10.0 mmol) in $MeOH/H_2O$ 95:5 (35 ml) was treated with $NaIO_4$ (2.24 g, 10.5 mmol). The mixture was stirred at r.t. until reaction completion (TLC monitoring), filtered, and poured into H_2O. The soln. was extracted with CH_2Cl_2 (3 × 100 ml), washed with 1M $Na_2S_2O_3$, and dried ($MgSO_4$). After solvent removal, the residue was purified by FC.

General Procedure 4: *Selanylation of the Sulfoxides*. A soln. of hexamethyldisilazane (HMDS; 0.23 ml, 1.1 mmol) in dry THF (10 ml) was cooled to $-78°$ and treated with 1.6M BuLi in hexanes (0.70 ml, 1.1 mmol). After 15 min stirring at $-78°$, a soln. of the sulfoxide (1.0 mmol) in THF (2 ml) was added dropwise. After 30 min stirring, a soln. of benzeneselenenyl chloride (200 mg, 1.05 mmol) in THF (2 ml) was added dropwise. The mixture was stirred for 1 h at $-78°$, allowed to warm to r.t., then poured into 10% NH_4Cl soln. (10 ml), and extracted with Et_2O (3 × 10 ml). The extract was washed with brine (20 ml), dried ($MgSO_4$), and evaporated and the residue purified by FC.

General Procedure 5: *Radical Allylation*. The radical precursor (1.0 mmol) and AIBN (= 2,2′-dimethyl-2,2′-azobis[propanenitrile] or 2,2′-azobis[isobutyronitrile]; 10 mg) were dissolved in the solvent (10 ml). Allyltributylstannane derivative (2.0 mmol) was added, and the resulting soln. was irradiated with a 300-W sun lamp until completion of the reaction (TLC monitoring). After solvent removal, the residue was purified by FC.

General Procedure 6: *Radical Deuteration*. Bu_3SnD (307 mg, 1.5 mmol) was added to a soln. of the radical precursor (1.0 mmol) and AIBN (10 mg) in the solvent (10 ml). The soln. was irradiated with a 300-W sun lamp until completion of the reaction (TLC monitoring). After solvent removal, the residue was purified by FC.

General Procedure 7: *Radical Deuteration in the Presence of* Lewis *Acids*. A soln. of the sulfoxide (2 mmol), Bu_3SnD (642 mg, 2.2 mmol), and AIBN (15 mg) in the indicated solvent (4 ml) was added to a soln. of the *Lewis* acid (0.2–2.4 mmol) prepared as described below. The soln. was irradiated with a 300-W sun lamp at 10° for 12 h. Et_2O (100 ml) was added and the soln. washed with 1M NaOH (3 × 30 ml) and H_2O (30 ml), dried ($MgSO_4$), and evaporated. The residue was filtered through a short pad of silica gel before determination of the diastereoselectivity. The crude product was further purified by FC.

Lewis-*Acid Solutions*. $LiClO_4$ (255 mg, 2.4 mmol) was dissolved in propanenitrile (1 ml). $[Eu(dpm)_3]$ (1.54 g, 2.2 mmol) was dissolved in CH_2Cl_2 (1 ml). MAD: 2,6-Di(*tert*-butyl)-4-methylphenol (485 mg, 2.2 mmol) in CH_2Cl_2 or benzene (1.1 ml) was treated at r.t. with 2M Me_3Al (0.55 ml, 1.1 ml) in heptane [32]. MABR: 4-Bromo-2,6-di(*tert*-butyl)phenol (627 mg, 2.2 mmol) in CH_2Cl_2 (1.1 ml) was treated at r.t. with 2M Me_3Al (0.55 ml, 1.1 ml) in heptane [32].

*Ethyl 2-(*p*-Tolylsulfinyl)propanoate* [1]. A soln. of *p*-thiocresol (20 g, 0.165 mol) and ethyl 2-bromopropanoate (20.0 ml, 0.153 mmol) in Et_2O (300 ml) was treated with Et_3N (18.2 g, 0.180 mmol, 25.1 ml), heated under reflux for 12 h, then poured into 1M NaOH (250 ml), and extracted with Et_2O (3 × 200 ml). The collected org. layers were washed with H_2O (250 ml) and brine (2 × 200 ml), dried ($MgSO_4$), and evaporated. The crude product (33.0 g, 96%) was used for the next step without further purification. ^{1}H-NMR (200 MHz): 7.38 (*m*, 2 arom. H); 7.12 (*m*, 2 arom. H); 4.10 (*q*, J = 7.0, $MeCH_2O$); 3.70 (*q*, J = 7.0, CHS); 2.33 (*s*, MeC_6H_4); 1.45 (*d*, J = 7.0, Me–(2)); 1.20 (*t*, J = 7.0, $MeCH_2O$).

The crude sulfide (30.0 g, 134 mmol) was treated according to *GP 2*. FC (AcOEt/hexane 1:5 → 1:3): ethyl 2-(*p*-tolylsulfinyl)propanoate (29.6 g, 92%; diastereoisomer mixture). Pale yellow oil. IR (film): 2983, 2937, 1731, 1450, 1320, 1087, 1054, 813. ^{1}H-NMR (200 MHz): 7.55–7.43 (*m*, 2 arom. H); 7.35–7.25 (*m*, 2 arom. H); 4.12, 4.08 (2*q*, J = 7.0, H–C(2)); 3.78, 3.45 (2*q*, J = 7.0, $MeCH_2O$); 2.39 (*s*, MeC_6H_4); 1.46, 1.25 (2*d*, J = 7.0, Me–C(2)); 1.18, 1.15 (*2q*, $J = 7.0$, *Me*CH$_2$O). ^{13}C-NMR (50.3 MHz): 168.35 (*s*); 167.66 (*s*); 142.08 (*s*); 141.89 (*s*); 138.76 (*s*); 137.16 (*s*); 129.59 (*d*); 129.45 (*d*); 124.93 (*d*); 124.46 (*d*); 65.50 (*d*); 63.31 (*d*); 61.46 (*t*); 61.38 (*t*); 21.20 (*q*); 13.76 (*q*); 9.34 (*q*); 8.50 (*q*). CI-MS: 241 (100, $[M + 1]^+$), 240 (14, M^+), 224 (5), 195 (5), 139 (9), 129 (2), 123 (2), 101 (2), 73 (1), 41 (1). Anal. calc. for $C_{12}H_{16}O_3S$ (240.30): C 59.98, H 6.71, S 13.34; found: C 59.81, H 6.85, S 13.01.

*Ethyl 2-Iodo-2-(*p*-tolylsulfinyl)propanoate* (**1**). A soln. of ethyl 2-(*p*-tolylsulfinyl)propanoate (1.20 g, 5.0 mmol; prepared as described above) in dry THF (5 ml) was added dropwise at –78° to a soln. of LiHMDS (5.05 mmol), prepared at –78° from 1.6M BuLi in hexanes (3.15 ml, 5.05 mmol) and hexamethyldisilazane (1.25 ml, 6.0 mmol) in THF (50 ml). After 30 min, a soln. of I_2 (1.27 g, 5.0 mmol) in THF (5 ml) was added, and stirring was continued for 30 min. The mixture was allowed to warm to r.t. and poured into 10% NH_4Cl soln. (30 ml). The soln. was extracted with Et_2O (3 × 50 ml), washed with 10% $Na_2S_2O_5$ soln. (10 ml) and brine (50 ml), dried ($MgSO_4$), and evaporated. The residue was purified by FC (AcOEt/hexane 1:4) giving unstable **1** (0.95 g, 52; 6:4 diastereoisomer mixture). Pale red oil. ^{1}H-NMR (250 MHz): 7.78 (*m*, 1 arom. H); 7.54 (*m*, 1 arom. H); 7.38–7.32 (*m*, 2 arom. H); 4.43–4.08 (*m*, MeC*H*$_2$O); 2.42 (*s*, *Me*C$_6$H$_4$, minor); 2.38 (*s*, *Me*C$_6$H$_4$, major); 2.05 (*s*, Me–C(2), minor); 1.98 (*s*, Me–C(2), major); 1.35 (*t*, $J = 7.0$, *Me*CH$_2$O, minor); 1.28 (*t*, $J = 7.0$, *Me*CH$_2$O, major).

*Ethyl 2-Methyl-2-(*p*-tolylsulfinyl)pent-4-enoate* (**2**). From **1** (395 mg, 1.08 mmol) and allyltributyltin (713 mg, 2.16 mmol) according to *GP 5* (30 min irradiation). FC (AcOEt/hexane 1:5): **2** (260 mg, 86%; 98:2 *l/u* mixture). Yellow oil. Not stable.

l-**2**: IR (film): 2981, 2936, 1735, 1717, 1451, 1213, 1053, 925, 813. ^{1}H-NMR (250 MHz): 7.40 (*m*, 2 arom. H); 7.36 (*m*, 2 arom. H); 5.70 (*m*, CH$_2$=C*H*); 5.15 (*m*, C*H*$_2$=CH); 4.05 (*qd*, $J = 7.0$, 2.0, MeC*H*$_2$O); 3.03 (*dd*, $J = 13.5$, 6.5, 1 H–C(3)); 2.57 (*dd*, $J = 13.5$, 7.5, 1 H–C(3)); 2.38 (*s*, *Me*C$_6$H$_4$); 1.18 (*t*, $J = 7.0$, *Me*CH$_2$O); 1.15 (*s*, Me–C(2)). ^{13}C-NMR (50.3 MHz): 169.45 (*s*); 142.00 (*s*); 136.54 (*s*); 131.43 (*s*); 129.20 (*d*); 125.44 (*d*); 119.70 (*t*); 69.86 (*s*); 61.25 (*t*); 39.58 (*t*); 21.24 (*q*); 13.85 (*q*); 10.83 (*q*). CI-MS: 281 (70, $[M + 1]^+$), 280 (2, M^+), 263 (20), 246 (7), 214 (3), 169 (10), 141 (100), 113 (13), 95 (11).

u-**2**: ^{1}H-NMR (250 MHz): 7.49 (*m*, 2 arom. H); 7.25 (*m*, 2 arom. H); 5.66 (*m*, CH$_2$=C*H*); 5.15 (*m*, C*H*$_2$=CH); 4.08 (*q*, $J = 7.0$, MeC*H*$_2$O); 2.70 (*dd*, $J = 13.5$, 6.5, 1 H–C(3)); 2.40 (*s*, *Me*C$_6$H$_4$); 2.26 (*dd*, $J = 13.5$, 8.0, 1 H–C(3)); 1.38 (*s*, Me–C(2)); 1.18 (*t*, $J = 7.0$, MeCH$_2$O).

2-(Phenylselanyl)-2-(phenylsulfinyl)propanenitrile (**3**). Propanenitrile (1.00 g, 18.0 mmol) in dry THF (10 ml) was added at –78° to a soln. of LDA prepared from $(i\text{-}Pr)_2NH$ (1.41 ml, 10.0 mmol) and 1.6M BuLi in hexanes (6.25 ml, 10.0 mmol) in THF (50 ml). After 30 min, a soln. of diphenyl disulfide (4.36 g, 20.0 mmol) in THF (20 ml) was added dropwise. The mixture was allowed to warm up to r.t. and poured into 10% NH_4Cl soln. (80 ml). The aq. phase was extracted with Et_2O (3 × 100 ml), the combined org. phase washed with 1M NaOH (80 ml), dried ($MgSO_4$), and evaporated, and the residue purified by FC (AcOEt/hexane 1:8) affording 2-(phenylthio)propanenitrile (1.91 g, 65%). Pale yellow liquid. ^{1}H-NMR (60 MHz): 7.0–7.8 (*m*, 5 arom. H); 3.8 (*q*, $J = 8$, H–C(2)); 1.55 (*d*, $J = 8$, Me).

2-(Phenylthio)propanenitrile (9.14 g, 56.0 mmol) was treated according to *GP 3* (3 days stirring at r.t.). FC (AcOEt/hexane 1:4) of the crude product gave 2-(phenylsulfinyl)propanenitrile (6.75 g, 675; diastereoisomer mixture). Yellow liquid. ^{1}H-NMR (60 MHz): 7.95–7.35 (*m*, 5 arom. H); 3.74 (*q*, $J = 8.0$, H–C(2), major); 3.69 (*q*, $J = 8.0$, H–C(2), minor); 1.55 (*d*, $J = 8.0$, Me, major); 1.53 ($J = 8.0$, Me, minor).

2-(Phenylsulfinyl)propanenitrile (6.7 g, 37 mmol) was then treated according to *GP 4*. FC (AcOEt/hexane 1:2) and recrystallization (Et_2O/hexane) gave **3** (7.7 g, 61%; 93:7 diastereoisomer mixture). White solid. M.p. 87–92°. ^{1}H-NMR (250 MHz): 7.95–7.30 (*m*, 10 arom. H); 1.75 (*s*, Me, minor); 1.65 (*s*, Me, major). ^{13}C-NMR (50.3 MHz): 138.61 (*s*); 138.10 (*d*); 132.72 (*d*); 130.86 (*d*); 129.56 (*d*); 128.85 (*d*); 126.24 (*d*); 124.58 (*s*); 116.74 (*s*); 55.14 (*s*); 21.55 (*q*, minor); 16.87 (*q*, major). EI-MS: 325 (< 1, M^+), 314 (5), 266 (12), 209 (29), 186 (28), 157 (60), 125 (93), 77 (100), 51 (65). Anal. calc. for $C_{15}H_{13}NO_3SSe$ (334.30): C 53.89, H 3.92, N 4.19, S 9.59, Se 23.62; found: C 53.80, H 3.98, N 4.28, S 9.64, Se 23.50.

2-Methyl-2-(phenylsulfinyl)-4-(trimethylsilyl)pent-4-enenitrile (**4**). From **3** (100 mg, 0.30 mmol) and tributyl[2-(trimethylsilyl)prop-2-enyl]tin (137 mg, 0.33 mmol) in CH_2Cl_2 (1 ml) at –20° for 2 h according to *GP 5*. FC (AcOEt/hexane 1:5) gave **4** (80 mg, 95%; *l/u* 75:25 mixture). White solid. Not stable. The reaction in toluene according to *GP 5* gave **4** (69 mg, 81%; *l/u* 90:10 mixture).

l-**4**: ^{1}H-NMR (250 MHz): 7.80–7.72 (*m*, 2 arom. H); 7.63–7.52 (*m*, 3 arom. H); 6.05 (*dd*, $J = 3.0$, 1.5, 1 H, CH$_2$=C); 5.75 (*dm*, $J = 1.5$, 1 H, CH$_2$=C); 2.79 (*d*, $J = 15.0$, 1 H–C(3)); 2.58 (*dd*, $J = 15.0$, 1.5, 1 H–C(3)); 1.32 (*s*, Me–C(2)); 0.15 (*s*, MeSi). ^{13}C-NMR (50.3 MHz): 144.66 (*s*); 138.33 (*s*); 132.44 (*d*); 131.56 (*t*); 128.72 (*d*); 126.03 (*d*); 118.60 (*s*); 58.42 (*s*); 38.43 (*t*); 15.21 (*q*); –1.32 (*q*).

u-**4**: ^{1}H-NMR (250 MHz): 7.80–7.72 (*m*, 2 arom. H); 7.63–7.52 (*m*, 3 arom. H); 5.90 (*m*, 1 H, $CH_2{=}C$); 5.68 (*m*, 1 H, $CH_2{=}C$); 2.79 (*d*, *J* = 15.0, 1 H–C(3)); 2.52 (*m*, 1 H–C(3)); 1.52 (*s*, Me–C(2)); 0.09 (*s*, MeSi).

Phenyl Phenyl(phenylselanyl)methyl Sulfoxide (**5**). From thiophenol (5.00 g, 45.4 mmol) and benzyl bromide (8.15 g, 47.7 mmol), according to *GP 1* (24 h). Workup afforded crude benzyl phenyl sulfide (8.90 g, 98%). Pale yellow solid. ^{1}H-NMR (60 MHz): 7.55–7.15 (*m*, 10 arom. H); 4.15 (*s*, $PhCH_2$).

The crude sulfide (2.00 g, 10.0 mmol) was oxidized according to *GP 3* (24 h). Workup afforded crude benzyl phenyl sulfoxide (1.95 g, 90%). Pale yellow solid. ^{1}H-NMR (60 MHz): 7.65–6.75 (*m*, 10 arom. H); 4.05 (*s*, CH_2S).

The crude sulfoxide (6.50 g, 30.1 mmol) was selanylated according to *GP 4*. FC (AcOEt/hexane 1:2) and recrystallization (AcOEt/hexane) gave **5** (10.5 g, 94%; diastereoisomer mixture). White solid. M.p. 105–120°. IR ($CHCl_3$): 3060, 3000, 1580, 1210, 1080, 1045, 1000, 745, 690, 665. ^{1}H-NMR (250 MHz): 7.68–6.81 (*m*, 10 arom. H); 5.09 (*s*, CHS, minor); 4.95 (*s*, CHS, major). ^{13}C-NMR (62.9 MHz): 135.29; 131.37; 131.25; 129.32; 129.22; 128.68; 128.57; 128.43; 128.11; 125.7; 125.2; 71.61; 70.65. EI-MS: 314 (4, $[M-57]^+$), 266 (23), 247 (100), 245 (62), 243 (22), 167 (36), 109 (1), 106 (48), 105 (64), 78 (11). Anal. calc. for $C_{19}H_{16}OSSe$ (371.36): C 61.45, H 4.34, S 8.63; found: C 61.36, H 4.30, S 8.68.

Methyl Phenyl(phenylselanyl)methyl Sulfoxide (**6**). From benzenemethanethiol (5.3 g, 42 mmol) and MeI (4.0 g, 28 mmol) according to *GP 1* (20 h). Workup afforded crude benzyl methyl sulfide (3.6 g, 93%). Colorless liquid. ^{1}H-NMR (60 MHz): 6.65–7.70 (*m*, 5 arom. H); 3.6 (*s*, CH_2); 1.95 (*s*, Me).

The crude sulfide (3.5 g, 25 mmol) was oxidized according to *GP 3* (22 h). Workup afforded crude benzyl methyl sulfoxide (3.6 g, 91%). Pale yellow solid. ^{1}H-NMR (60 MHz): 6.8–7.8 (*m*, 5 arom H); 3.95 (*s*, CH_2); 2.45 (*s*, Me).

The crude sulfoxide (0.70 g, 4.54 mmol) was selanylated according to *GP 4*. FC (AcOEt/hexane 1:1) and recrystallization (AcOEt/hexane) gave **6** (1.28 g, 88%; diastereoisomer mixture). M.p. 104–106° (major isomer). ^{1}H-NMR (250 MHz): 7.7–7.15 (*m*, 10 arom. H); 5.05 (*s*, CHSe, minor); 4.90 (*s*, CHSe, major); 2.45 (*s*, Me, major); 2.40 (*s*, Me, minor). ^{13}C-NMR (90.55 MHz; major): 135.62, 133.09, 129.39, 129.29, 129.15, 128.93, 128.78, 67.5, 37.1.

Phenyl (Phenylselanyl)[4-(trifluoromethyl)phenyl]methyl Sulfoxide (**7**). From thiophenol (2.00 g, 18.2 mmol) and 4-(trifluoromethyl)benzyl bromide according to *GP 1* (24 h stirring at r.t.): phenyl [4-(trifluoromethyl)phenyl]methyl sulfide (4.70 g, 96%). White solid. ^{1}H-NMR (60 MHz): 7.75–7.10 (*m*, 9 arom. H); 4.15 (*s*, CH_2S).

The sulfide (1.00 g, 3.73 mmol) was oxidized according to *GP 3* (40 h). FC (AcOEt/hexane 1:1) and recrystallization (Et_2O/hexane) gave phenyl [4-(trifluoromethyl)phenyl]methyl sulfoxide (300 mg, 28%). White solid. ^{1}H-NMR (250 MHz): 7.55–7.05 (*m*, 9 arom. H); 4.15 (*B* of *AB*, J_{AB} = 13.0, 1 H, CH_2SO); 4.02 (*A* of *AB*, J_{AB} = 13.0, 1 *H*, CH_2SO).

The sulfoxide (200 mg, 0.70 mmol) was selanylated according to *GP 4*. FC (AcOEt/hexane 1:2) and recrystallization from AcOEt/hexane gave **7** (250 mg, 81%; isomer mixture). White solid. M.p. 128–132°. IR (KBr): 2940, 1580, 1480, 1440, 1410, 1325, 1160, 1085, 1075, 1020, 1000, 850, 740, 690. ^{1}H-NMR (250 MHz): 7.64–6.92 (*m*, 14 arom H); 5.11 (*s*, CHSO, minor); 4.91 (*s*, CHSO, major). ^{13}C-NMR (62.9 MHz): 135.55; 135.40; 131.78; 131.52; 129.59; 129.07; 128.67; 128.40; 125.64; 124.99; 124.88; 70.45 (minor); 69.50 (major). EI-MS: 317 (19, $[M-122]^+$), 315 (100), 313 (58), 312 (21), 311 (24), 236 (16), 235 (75), 159 (16), 109 (23), 78 (67), 77 (26). Anal. calc. for $C_{20}H_{15}F_3OSSe$: C 54.68, H 3.44, S 7.30, Se 17.97; found: C 54.53, H 3.50, S 7.15, Se 17.85.

Phenyl 1-Phenyl-1-(phenylselanyl)ethyl Sulfoxide (**8**). A soln. of benzyl phenyl sulfoxide (12.0 g, 54.97 mmol; prepared as described above) in THF (150 ml) was treated with LiHMDS (55 mmol; prepared according to *GP 4*) at −78°. After 30 min stirring at −78°, MeI (3.40 ml, 55.0 mmol) was added and the mixture allowed to warm to r.t. After 1 h at r.t., the mixture was poured into 10% NH_4Cl soln. (100 ml), extracted with Et_2O (3 × 100 ml), washed (brine), and dried ($MgSO_4$). Evaporation followed by FC (AcOEt/hexane 1:4) of the crude product gave phenyl 1-phenylethyl sulfoxide (10.84 g, 85%; 80:20 diastereoisomer mixture). White solid. M.p. 95–100°. IR (KBr): 3056, 2974, 1575, 1441, 1082, 1042, 744, 692. ^{1}H-NMR (200 MHz): 7.50–6.90 (*m*, 10 arom. H); 4.05 (*q*, *J* = 7.0, Me, major); 3.80 (*q*, *J* = 7.0, Me, minor); 1.70 (*d*, *J* = 7.0, minor); 1.60 (*d*, *J* = 7.0, major). ^{13}C-NMR (50.3 MHz): 140.48 (*s*, major); 135.50 (*s*, minor); 133.86 (*s*, minor); 130.76 (*d*); 128.69 (*d*); 128.51 (*d*); 128.34 (*d*); 128.14 (*d*); 127.97 (*d*); 125.02 (*d*); 124.96 (*s*, major); 124.80 (*d*); 67.00 (*d*, minor); 64.28 (*d*, major); 13.93 (*q*, minor); 12.11 (*q*, major). CI-MS: 231 (46, $[M+1]^+$), 155 (4), 133 (4), 127 (12), 109 (5), 105 (100), 91 (2), 41 (3). Anal. calc. for $C_{14}H_{14}OS$ (230.33): C 73.01, H 6.13, S 13.92; found: C 73.21, H 6.14, S 13.99.

Phenyl 1-phenylethyl sulfoxide (8.0 g, 34.7 mmol) was selanylated according to *GP 4*. FC (AcOEt/hexane 1:4) gave **8** (11.68 g, 87%; diastereoisomer mixture). White solid. A sample of each diastereoisomer was obtained by further FC.

8 (major): M.p. 95–98°. ^{1}H-NMR (200 MHz): 7.78 (*m*, 2 arom. H); 7.45–7.08 (*m*, 11 arom. H); 6.95 (*m*, 2 arom. H); 1.62 (*s*, Me). ^{13}C-NMR (50.3 MHz): 140.25 (*s*); 138.33 (*d*); 130.69 (*s*); 129.31 (*d*); 128.86 (*d*); 128.64 (*d*); 128.46 (*d*); 128.32 (*d*); 127.73 (*d*); 127.36 (*d*); 127.33 (*s*); 125.77 (*d*); 71.65 (*s*); 21.88 (*q*). EI-MS: 260 (19), 234 (2), 218 (5), 186 (10), 158 (8), 125 (33), 103 (100), 77 (59), 51 (30). Anal. calc. for $C_{20}H_{18}OSSe$ (385.39): C 62.33, H 4.71; found: C 62.45, H 4.60.

8 (minor): ^{1}H-NMR (200 MHz): 7.78 (*m*, 2 arom. H); 7.45–7.08 (*m*, 11 arom. H); 6.95 (*m*, 2 arom. H); 1.70 (*s*, Me).

Phenyl Phenyl($^2H_1$)methyl Sulfoxide (**9**). *a*) Radical deuteration: From **5** (100 mg, 0.27 mmol) and Bu_3SnD (134 mg, 0.46 mmol) according to *GP 6*. FC gave **9** (55 mg, 93%; *u*/*l* 66:34 mixture). *b*) Anionic deuteration [21]: At −78°, 1M LDA (2.1 ml, 2.1 mmol) in THF/hexane was added to a soln. of benzyl phenyl sulfoxide (350 mg, 1.62 mmol) in THF (5 ml). After 30 min at −78°, 1.6M BuLi in hexanes (2.0 ml, 3.2 mmol) was added followed by D_2O (1 ml) in THF (4 ml). The soln. was allowed to warm to r.t. Et_2O (100 ml) and H_2O (50 ml) were added. The aq. phase was further extracted with Et_2O (2 × 100 ml) and the org. phase dried ($MgSO_4$) and evaporated. FC of the residue gave **9** (304 mg, 86%; *u*/*l* 1.2:1 mixture). Yellow oil. IR (KBr): 2940, 1495, 1450, 1440, 1305, 1090, 1070, 1040, 1000, 920, 900, 745. ^{1}H-NMR (200 MHz): 7.55–7.18 (*m*, 8 arom. H); 7.05–6.95 (*m*, 2 arom. H); 4.08 (*s*, PhC*H*, minor *l*); 3.96 (*s*, PhC*H*, major *u*). EI-MS: 217 (1, M^+), 125 (3), 97 (4), 92 (100), 77 (5), 66 (8), 65 (5), 51 (6). Anal. calc. for $C_{13}H_{11}DOS$ (217.31): C 71.85, H 5.57, S 14.75; found: C 72.02, H 5.56, S 14.7.

Methyl Phenyl($^2H_1$)methyl Sulfoxide (**10**). From **6** (500 mg, 1.62 mmol) and Bu_3SnD (710 mg, 2.43 mmol) according to *GP 6*. FC (AcOEt) gave **10** (in CH_2Cl_2: 148 mg, 59%, 50% ds; in benzene: 186 mg, 74%, 77% ds). ^{1}H-NMR (250 MHz): 7.4–7.2 (*m*, 5 arom. H); 4.0 (*s*, CHD, minor); 3.9 (*s*, CHD, major); 2.45 (*s*, Me).

Phenyl [4-(Trifluoromethyl)phenyl](^2H)methyl Sulfoxide (**11**). From **7** (100 mg, 0.23 mmol) in CH_2Cl_2 according to *GP 6* (3 days of irradiation at 15°). FC (AcOEt/hexane 1:2) gave **11** (610 mg, 94%; *l*/*u* 71:29 mixture). White solid. M.p. 199–201°. IR (KBr): 2930, 2200, 1440, 1410, 1335, 1130-1100, 1135, 1120, 1035, 1020, 1000, 850, 740, 690, 620. ^{1}H-NMR (250 MHz): 7.55–7.05 (*m*, 8 arom. H); 4.11 (*s*, CHSO, major); 4.01 (*s*, CHSO, minor). EI-MS: 285 (14, M^+), 161 (9), 160 (100), 125 (6), 110 (21), 97 (8), 78 (7), 77 (10). Anal. calc. for $C_{14}H_{10}DF_3OS$ (285.30): C 58.94, H 3.89, S 11.24; found: C 59.09, H 3.77, S 11.36

Phenyl 1-Phenyl(1-^2H)ethyl Sulfoxide (**12**). From **8** (200 mg, 0.52 mmol) in CH_2Cl_2 according to *GP 6* (4 h). FC (AcOEt/hexane 1:4) gave **12** mg (70 mg, 59%; *l*/*u* 93:7 mixture). The reaction in benzene according to *GP 6* yielded **12** (80 mg, 67%; *l*/*u* 96:4 mixture). IR (KBr): 3061, 2963, 1495, 1444, 1090, 1038, 748, 688.

l-**12**. ^{1}H-NMR (200 MHz): 7.45–6.92 (*m*, 10 arom. H); 1.58 (*s*, Me). ^{13}C-NMR (50.3 MHz): 140.43 (*s*); 133.81 (*s*); 130.76 (*d*); 128.68 (*d*); 128.14 (*d*); 127.99 (*d*); 127.81 (*d*); 125.07 (*d*); 63.82 (*t*, J (^{13}C,^{2}H) = 22.4); 11.99 (*q*). EI-MS: 232 (3, $[M + 1]^+$), 231 (1, M^+), 126 (8), 106 (100), 80 (13), 77 (27), 51 (20). Anal. calc. for $C_{14}H_{13}DOS$ (231.08): C 72.69, H 6.53, S 13.86; found: C 72.62, H 6.31, S 13.81.

u-**12**: ^{1}H-NMR (200 MHz): 7.45–6.92 (*m*, 10 arom. H); 1.58 (*s*, Me).

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