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Stereochemical Study of the Allylation of 1-Phenylsulfinylethyl and 1-Phenylsulfinyl-2,2,2-trifluoroethyl Radicals

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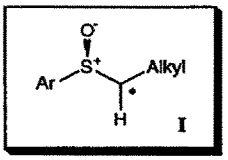
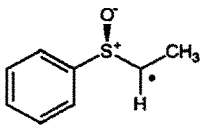
Abstract: The stereochemistry of the reactions of 1-phenylsulfinylethyl radical (**1r**) and 1-phenylsulfinyl-2,2,2-trifluoroethyl radical (**2r**) with allylstannanes has been examined. Preferential formation of products of opposite relative configuration has been observed. Conformational analysis of the radical intermediates (AM1 calculations) allows to rationalize the results.

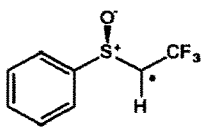
The control of stereoselectivity in the intermolecular reactions of acyclic radicals is presently a field of intensive research.[1] The use of sulfoxides[2-7] to induce stereoselectivity in radical reactions has recently attracted much attention. High stereoselectivities have been observed with acyclic sulfinylated radicals stabilized by a carbonyl group[6,7] and were attributed to the relative stability of one radical conformer over another by minimization of dipole-dipole interactions.[7,8] However, the reactions of simple alkyl substituted radicals (I) proceed with disappointingly low selectivities.[2,4] We report here an explanation for these results and a study of the importance of pure dipole effects. For our study, two simple model systems have been examined where the sulfinylated radical center is substituted by a methyl group (**1r**) and a trifluoromethyl group (**2r**).



I

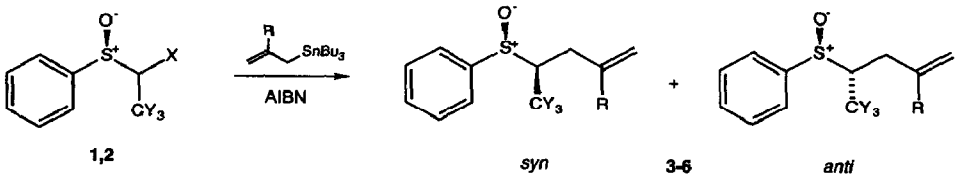


1r



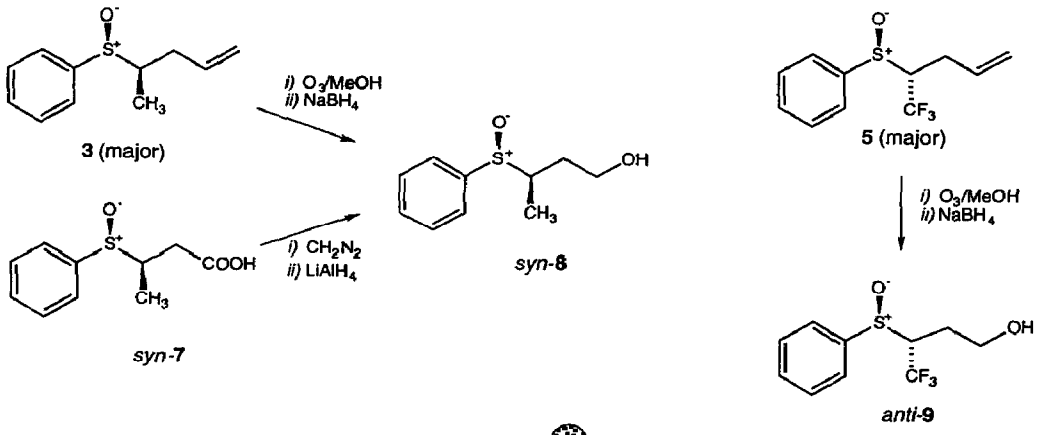
2r

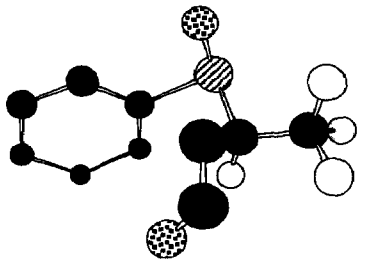
The methylated and trifluoromethylated radical precursors **1** and **2** were prepared in a straightforward manner.[9] Allylation[10] of **1** with 3-tributylstannylpropene[11] and 3-tributylstannyl-2-trimethylsilylpropene gave preferentially *syn*-**3** and *syn*-**4** with low stereoselectivities (61 % and 64 % ds, respectively). The trifluoromethylated radical precursor **2** gave preferentially *anti*-**5** and *anti*-**6** with diastereoselectivities of 81 % and 82 %, respectively.



Radical precursor	X	Y	R	Product	*syn/anti* (yield)
1	SePh	H	H	3	61:39 (64 %)
1	SePh	H	$SiMe_3$	4	64:36 (80 %)
2	Cl	F	H	5	19:81 (61 %)
2	Cl	F	$SiMe_3$	6	18:82 (83 %)

The relative *syn* configuration of the major diastereoisomer of **3** was proved by chemical correlation with compound *syn*-**7** of known stereochemistry.[12] For this purpose, **3** (major isomer) and *syn*-**7** were converted to the identical compound *syn*-**8**, using $O_3/NaBH_4$ and $CH_2N_2/LiAlH_4$ respectively. The *anti* configuration of **9**, obtained by ozonolysis ($O_3/NaBH_4$) of **5** (major isomer) was established by X-ray analysis.[13]





X-ray structure of *anti*-**9**
(H-omitted excepted at the stereogenic center)

AM1 calculations[14] indicate that radicals **1r** and **2r** possess the same two minimum energy conformations **a** and **b** (figure). These two conformations correspond to those predicted by stereoelectronic interactions, the singly occupied orbital is perpendicular to the S-O bond for optimal overlap,[15] and by the minimization of steric and eclipsing interactions. These latter are responsible for the small twisting (20°) of conformer **a**. In the case of radical **1r**, conformer **a** is more stable than **b** by 0.8 kcal/mol. For radical **2r** the situation is opposite, conformer **b** is more stable than **a** by 1.4 kcal/mol. We attribute this inversion of relative stability to a minimization of dipole-dipole interactions which favors conformer **b-2r** because the negative ends of the dipoles (the oxygen atom and the CF_3 group) are antiperiplanar. Reaction of conformer **b** from the less hindered face (opposite to the phenyl group) leads to *anti* products via transition state **B**.[16] We assumed that this pathway is the prefered one for radical **2r**. We also suggest also that reaction of the conformer **a** is responsible for the formation of *syn* compounds via a transition state **A**, this pathway being slightly prefered for the methylated radical **1r**.

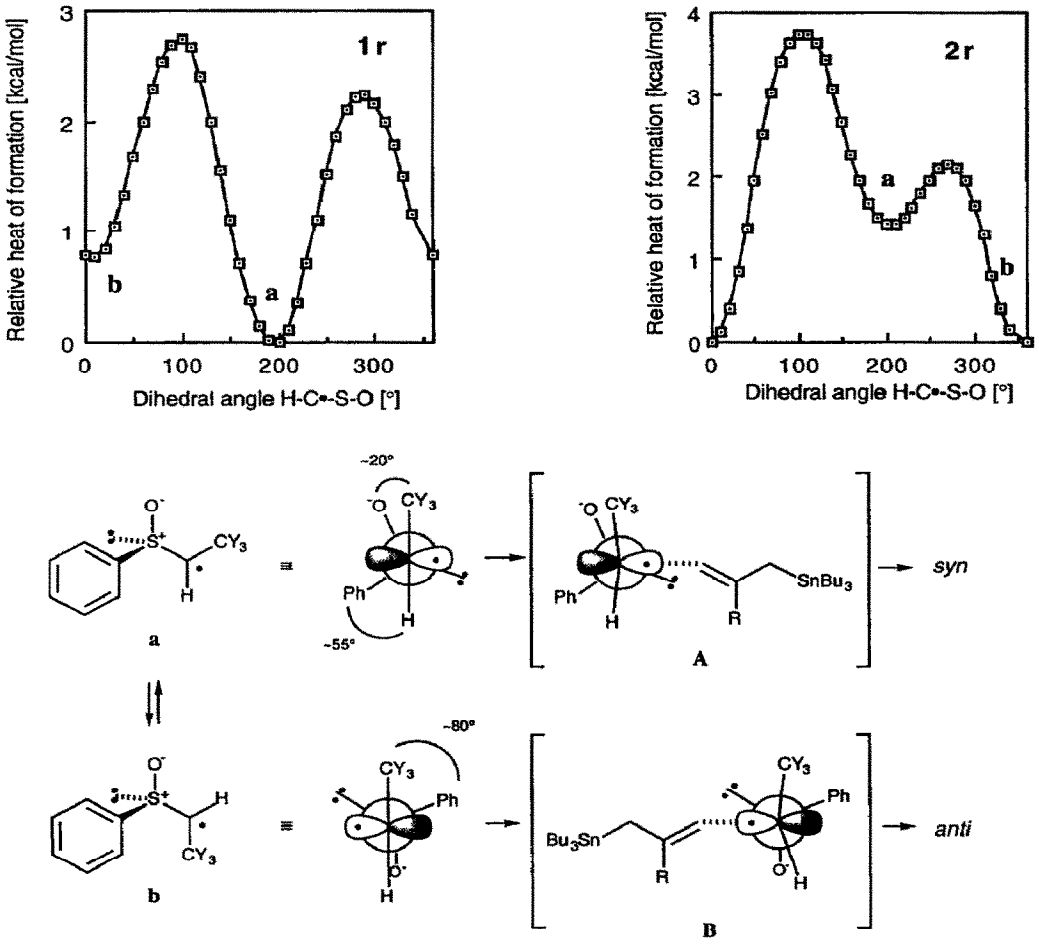


Figure: Conformational analysis of radicals **1r** and **2r** (AM1 calculations) and postulated transition states **A** and **B** for the allylation reaction.

In conclusion, our results demonstrate that for radicals of the type **I**, modest stereoselectivity may be obtained when electron withdrawing alkyl groups, such as the trifluoromethyl group, are used. For simple alkyl groups, the existence of two conformers **a** and **b** of similar energy leads to low diastereoselectivity. In order to obtain good stereoselectivities with alkyl substituted radicals of type **I**, it will be necessary to find a way of differentiating the energy level of these two conformers. Our efforts in that direction are presented in the next communication.

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8. Hart has recently suggested that his model developed for α–carbalkoxy radicals may also be applied to such cases: Hart, D. J.; Krishnamurthy, R. *J. Org. Chem.* **1992**, *57*, 4457-4470.
9. **1** was prepared from phenyl ethyl sulfoxide (2 equ. LiHMDS, PhSeSePh). **2** was obtained in three steps from thiophenol (i. CF_3CH_2I, Bu_4NI. ii. SO_2Cl_2. iii. mCPBA).
10. Typical procedure: A solution of the radical precursor **1** or **2** (1 mmol), allylstannane (1.5 mmol) and AIBN (10 mg) in degassed benzene (4 ml) was irradiated with a 300 W sunlamp at 10-15 °C for 12 h. Every 4 h, AIBN (10 mg) was added to the reaction mixture. Crude products (suitable for ^{1}-H-NMR ds determination) were isolated by filtration through silicagel (AcOEt/petroleum ether) and were further purified by flash chromatography.
    All new compounds have been characterized by ^{1}H, ^{13}C, MS, IR and elemental analysis. ^{1}H-NMR data (250 MHz, $CDCl_3$): *syn*-**4**: 0.08 (*s*, 9H); 1.00 (*d*, J = 7.0, 3H); 2.17 (*dd*, J = 15.5 and 11.0, 1H); 2.50-2.95 (*m*, 2H); 5.50 (*d*, J = 2.5, 1H); 5.65 (*m*, 1H); 7.40-7.70 (*m*, 5H). *anti*-**6**: -0.10 (*s*, 9H); 2.50 (*dd*, J = 9.0 and 17.0, 1H); 2.75 (*dm*, J = 17.0, 1H); 3.28 (*dquint.*, J = 4.0, 9.0, 1H); 5.28 (*m*, 1H); 5.35 (*m*, 1H); 7.40-7.70 (*m*, 1H).
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13. Suitable crystals for X-ray analysis were obtained by slow recrystallisation from ether/petroleum ether. Details of the structure have been deposited at the Cambridge Crystallographic Data Centre, Lensfield Road, Cambridge, England. More information will be furnished in a forthcoming full paper.
14 Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902-3909. The calculations were performed with the software *Mopac 5.0* (QCPE N° 445) on a *Silicon Graphics 4D-320* workstation. All optimizations were performed with the keyword PRECISE and for open-shell species, the UHF Hamiltonian was used.
15. Ab initio calculations on $HSOCH_2^{\bullet}$ have shown that sulfinylated radicals exist preferentially in a conformation where the singly occupied orbital is perfectly alligned for interaction with the S-O π system: Pasto, D. J.; Krasnansky, R.; Zercher, C. *J. Org. Chem.* **1987**, *52*, 3062-3072. Clark, T. In *Sulfur-Centered Reactive Intermediates in Chemistry and Biology*"; C. Chatgilialoglu and K. D. Asmos, Ed.; Plenum: New York, 1990; Vol. 197; pp 13-18.
16. We assume in this discussion that transition states are reactant-like. Dewar, M. J. S.; Olivella, S. *J. Am. Chem. Soc.* **1978**, *100*, 5290-5295.

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