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ELECTRONIC EFFECTS IN ASYMMETRIC INDUCTION. REACTION OF *para*-SUBSTITUTED PHENYLSULFINYL CHLORIDES WITH S-(+)-1-(1-NAPHTHYL)-2,2,2-TRIFLUOROETHANOL.

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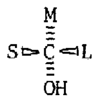
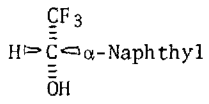
Mislow has reported[1] that when a chiral secondary alcohol corresponds to stereoformula **1**, treatment with *p*-tolyl sulfinyl chloride "at -78° in the presence of pyridine" gives an excess of the sulfinate diastereomer that, upon treatment with excess methyl magnesium bromide, affords *S*-(-) methyl *p*-tolyl sulfoxide. The success of this generalization depends upon the dominance of steric, as opposed to electronic, effects in determining the stereochemistry of the kinetically preferred reaction pathway.



$$\mathrm{S}\rhd\underset{\overset{\equiv}{\mathrm{OH}}}{\overset{\underset{\equiv}{\mathrm{M}}}{\mathrm{C}}}\lhd\mathrm{L}$$

1

S = Small
M = Medium
L = Large



$$\mathrm{H}\rhd\underset{\overset{\equiv}{\mathrm{OH}}}{\overset{\underset{\equiv}{\mathrm{CF_3}}}{\mathrm{C}}}\lhd\alpha\text{-Naphthyl}$$

2

Our interest in sulfinate chemistry led us to perform Mislow's sequence upon *S*-(+)-1-(1-naphthyl)-2,2,2-trifluoroethanol,[2] **2**, which corresponds to stereoformula **1**. Contrary to Mislow's generalization, *R*-(+)-enriched methyl *p*-tolyl sulfoxide is the product.

Mosher and co-workers have found instances[3] in which proximity of a trifluoromethyl group to the reaction center reverses the sense of asymmetric induction expected on steric grounds alone and explained these reversals on the basis of stereochemically dependent trifluoromethyl-phenyl repulsions. In the present reaction, varying the *p*-substituent on the phenyl sulfinyl chloride should have little steric consequence but could affect the outcome of the asymmetric induction if electronic effects play an important role in this type reaction. Guetté *et al*[4] have provided examples in which the electronic nature of *p*-substituents exerts control over the stereochemical outcome of an asymmetric reaction.

Reaction of *S*-(+)-**2** with a variety of *p*-substituted phenyl sulfinyl chlorides demonstrates the systematic electronic effect of these substituents in as much as the magnitude and sense of these asymmetric inductions appear to follow a Hammett linear free energy relationship (Fig. 1).

Diasteromeric purities of the sulfinates, determined by F^{19} and pmr, correspond closely with the enantiomeric purities of the sulfoxides subsequently derived by treatment of the sulfinates with excess methyl magnesium bromide. The enantiomeric composition and absolute configurations of these sulfoxides were determined by polarimetry and/or pmr in the presence of S-(+)-2 as previously described.[5] The diastereomeric sulfinates obtained from p-nitrophenyl sulfinyl chloride could not be converted into sulfoxide owing to side reactions attending the presence of the nitro substituent. Hence, in this instance, the configuration of the predominant diastereomer is not known rigorously, and the configurational assignment implicit in the tentative placement of this point in Figure 1 is reached on no basis other than the approximate fit of this point to the apparent trend of the data.

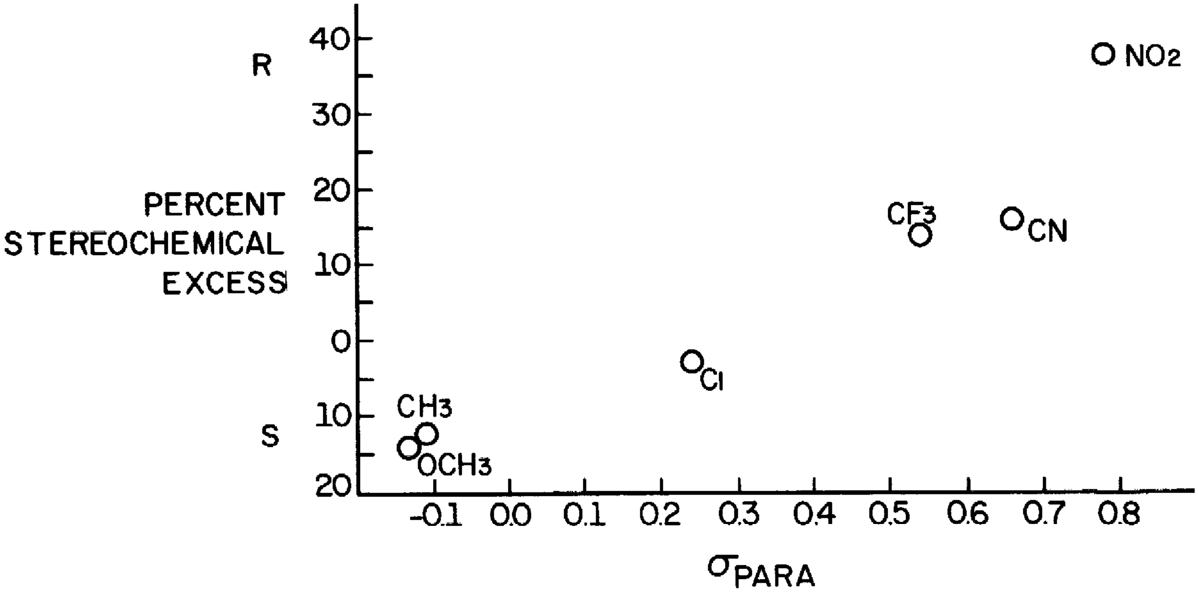
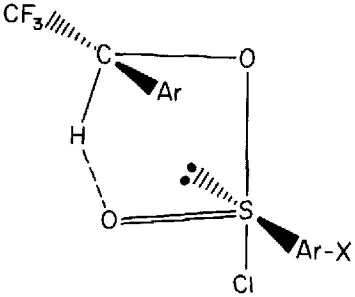
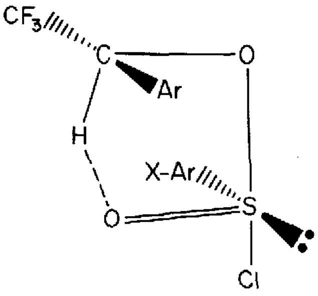


Figure 1. The magnitude and sense of the stereochemical preference of the asymmetry induced at sulfur upon reaction of p-substituted phenyl sulfinyl chlorides with S-(+)-2 plotted against the σ_p constants of the para substituents.

Presently, one can but speculate concerning the manner in which the electronic nature of the para-substituents affects the stereochemical outcome of these reactions. One might suppose that the transition states of these reactions involve approximate trigonal bipyrimidal geometry with the entering alcohol and the leaving halide occupying apical positions Further, assumption of a weakly bonding interaction between the carbinyl hydrogen of 2 and the sulfinyl oxygen, analogous to solvation interactions previously invoked,[6] allows the tentative formulation of 3a and 3b as favored "conformations" of the diastereomeric transition states. Drawings 3a and 3b illustrate the opportunity for differential interaction of trifluoromethyl and α-naphthyl substituents with the lone electron pair or the aromatic substituent of the sulfinyl chloride. Repulsive interactions between trifluoromethyl groups and aromatic rings have been suggested^3 and π-π interactions between aromatic groups are well known. Both such interactions would be influenced by the electronic nature of the *para*-substituent. Moreover, the *para*-substituent may influence relative extents of bond breaking and formation, thereby significantly altering the geometry of the transition states.



3a



3b

The use of alkyl sulfinyl chlorides eliminates the possibility of the aforementioned π-π and trifluoromethyl-π interactions. In the absence of dominating electronic effects, the hypothetical transition states 3a and 3b allow rationalization of Mislow's rule and accommodate his data. Experimentally, it is found that reaction of *i*-propyl sulfinyl chloride or *t*-butyl sulfinyl chloride with *S*-(+)-2 follows Mislow's generalization (41 and 8% diastereomeric purity respectively^7) whereas methyl sulfinyl chloride does not (14% diastereomeric purity), possibly because methyl is sufficiently small so that methyl-α-naphthyl steric interactions are less important than the interaction between the lone pair and the trifluoromethyl group.

We wish to emphasize that these transition states are speculative and, at best, are but approximations that take no specific cognizance of the role of the amine base,^{8} the solvent, or the leaving group, factors which can influence the stereoselectivity of these reactions.

A typical experiment is described as follows. *p*-Tolylsulfinyl chloride (0.785 g) was added portionwise to a -78° solution of *S*-(+)-2 (0.50 g) and pyridine (0.19 g) in 5 ml of CFCl$_3$. After 30 min, the cold reaction mixture was quickly filtered through a short column of silica gel (yield 90%) and the ratio of the diastereomeric sulfinates determined *via* F^{19} or pmr. Afterwards, an ethereal solution of the diastereomers was treated with a 2-3 fold excess of ethereal methyl magnesium bromide and the reaction worked up with aqueous ammonium chloride. The methyl *p*-tolyl sulfoxide was chromatographed on silica gel with ethyl acetate and the enantiomeric purity and absolute configuration determined by polarimetry or by pmr in the presence of *S*-(+)-**2**.

Methyl *p*-cyanophenyl sulfoxide, **3**, and methyl *p*-trifluoromethyl phenyl sulfoxide, **4**, not previously reported, gave satisfactory elemental analyses and nmr spectra. Sulfoxide **3** of $[\alpha]_D^{24}$ -22° (*c* 2.51 EtOH) was found[5] to be 16.8% *S*-enriched. Sulfoxide **4**, $[\alpha]_D^{24}$ -14° (*c* 2.51, EtOH) was found[5] to be 14.2% *S*-enriched.

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References and Notes

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2. W. H. Pirkle and M. S. Hoekstra, *J. Org. Chem.*, **39**, 3904 (1974).
3. For a recent review of this work, see "Asymmetric Organic Reactions", by J. D. Morrison and H. S. Mosher, Prentice Hall, Inc., Englewood Cliffs, 1971, pp 190-193.
4. J. P. Guetté, M. Perlat, J. Capillon, and D. Boucherot, *Tetrahedron Lett.*, 2409 (1974).
5. W. H. Pirkle, S. D. Beare, and R. L. Muntz, *Tetrahedron Lett.*, 2295 (1974).
6. W. H. Pirkle and J. R. Hauske, *J. Org. Chem.*, **41**, 0000 (1976).
7. On the basis of steric repulsion between the alkyl group of the sulfinyl chloride and the α-naphthyl group, one would expect greater asymmetric induction in the case of *t*-butyl than for *i*-propyl. For prior examples where similarly reasoned expectations are not realized, see ref 3, pp 183 and 188.
8. Chiral tertiary amines can afford chiral sulfinates from achiral sulfinyl chlorides and alcohols.[9] Hence, the amine clearly plays a role in the determination of stereochemistry at sulfur.
9. M. Mikolajczyk and J. Drabowicz, *Chem. Commun.*, 547 (1974).