Tetrahedron Letters No. 24, pp. 1125-1132, 1962. Pergamon Press Ltd.
Printed in Great Britain.

INTRAMOLECULAR INFLUENCE OF FIELD EFFECTS PROPAGATED WITHIN SULFUR-CONTAINING GROUPS.

III. BEHAVIOR OF CERTAIN SULFONE SYSTEMS[1]

Cal Y. Meyers

Istituto di Chimica Industriale, Università di Bologna, Italy

(Received 31 August 1962)

RECENT mention has been made of the intramolecular influence of field effects of thia, sulfinyl and sulfonyl groups on the acidity of phenols 2-substituted with these groups, respectively[2]. While these systems allowed facile rotation of the phenate plane[3], the most apparent influences observed were those of the negative field of the sulfonyl-oxygen atoms and the positive field of the sulfinyl-sulfur atom[2c].

This suggested that within rigid systems containing these groups *either* the negative oxygen atoms *or* positive sulfur atom might exert the dominating field effect, depending upon the fixed spacial positions of the S-O atoms relative to that of the group or atoms being studied in the specific system. A number of important phenomena have been reported in which the behavior of sulfones is anomalous in one way or another. Several of these may be accounted for on the basis of these field effects. Such an approach is attempted in this communication. It is hoped that the relationships proposed will be of special interest in current, related

---

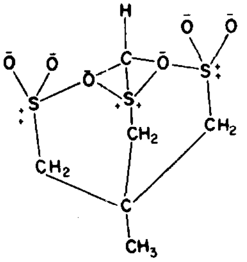
[1] This study is part of a series dealing with the nature of organic sulfur groups, supported by grants from the Petroleum Research Fund; the preceding communication is by C.Y. Meyers and G. Picciola, *Tetrahedron Letters* No. 21, 971 (1962).

[2] a C.Y. Meyers, *Ind. Chim. Belg.* 27, 538 (1962); b C.Y. Meyers, IXth National Chemical Congress of the Italian Chemical Society, Naples, May 27, 1962; c C.Y. Meyers, G. Lombardini and L. Bonoli, *J. Amer. Chem Soc.* 84 (December 1962).

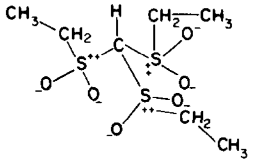
[3] That is, within the restrictions of conformational stability (see ref. 2c).

investigations.

In their classic report Doering and Levy[4] suggested that d-orbital resonance is diminished by strain in the bicyclic trisulfone, I, making it less acidic than the acyclic analog, II. But, a more recent related study[5] indicated that d-orbital stabilization of carbanions is rather



I



II

independent of geometric requirements. Moreover, in the sulfide analogs of I and II the bridgehead-hydrogen (deuterium) of the cyclic compound is much more labile than that in the corresponding position of the acyclic compound[6]. In accord with this is the observation that hydrogen atoms attached to strained cyclic systems are more acidic than those of the acyclic analogs[5].

Molecular models of I and II illustrate that the former is indeed a rigid structure whose oxygen atoms are held firmly in a position near - but not sterically blocking - the bridgehead-hydrogen atom. The situation is quite different in II in which rotation not only permits the oxygen atoms to lie as far as possible from the tertiary-hydrogen atom, but, because of steric reasons, would certainly favor this type of conformation. If, as has been indicated, conjugative-inductive effects within I are

---

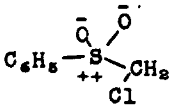
[4] W.E. Doering and L.K. Levy, J. Amer. Chem. Soc. 77, 509 (1955).

[5] H.E. Zimmerman and B.S. Thyagarajan, J. Amer. Chem. Soc. 82, 2505 (1960).

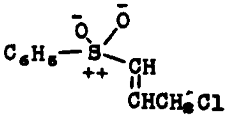
[6] S. Oae, W. Tagaki and A. Ohno, J. Amer. Chem. Soc. 83, 5036 (1961).

virtually equivalent to those within II, it is now suggested that the enforced influence of the negative field of the oxygens in I is the factor responsible for its lower acidity than II[7].

The negative field of the sulfonyl-oxygen atoms undoubtedly contributes to the extremely slow displacement of the chlorine atom by iodide ion in chloromethyl phenyl sulfone, III, in contrast to the rapid displacement in 1-benzenesulfonyl-3-chloro-1-propene, IV[8]. This explanation is in accord with the recent suggestion that the negative field of sulfonyl-oxygen atoms is important in repelling the approach of nucleophilic reagents in general[9].



III



IV

In contrast, the positive character of the sulfonyl-sulfur atom apparently becomes influential in 2,6-disubstituted diaryl sulfones. In such systems the aryl planes are easily twisted out of the more stable

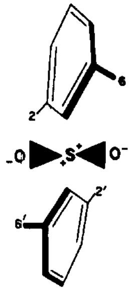
---

[7] The possibility of simple steric factors causing this difference in acidity appears unlikely as the acidic hydrogen atom of II, in fact, is blocked considerably more than is that of I.

[8] The investigators [F.G. Bordwell and G.D. Cooper, J. Amer. Chem. Soc. 73, 5184 (1951)] concluded, however, that the sulfonyl group of III physically blocked the attack by iodide, although they noted that this would not seem too important on the basis of molecular models. Furthermore, their assignment of steric rather than electric repulsion as being responsible does not seem justified on the basis of their experiments.

[9] J. Strating, Organic Sulfur Compounds (Edited by N. Kharasch) Vol. I, p. 150. Pergamon Press, New York (1961).

conformation in which they are more or less perpendicular to the C-S-C plane[10]. As a result the probability is increased of one substituent being in a position more strongly influenced by the positive field of the sulfur atom than by the negative field of the oxygens. In mesityl phenyl sulfone,V, [11a], the *o*-CH$_3$, but not *p*-CH$_3$, is metalated completely and rapidly by treatment with an equivalent of *n*-butyllithium; an excess of reagent causes a second metalation apparently at the *o*'-position. As suggested by the drawing the two positions attacked would be those influenced mainly by the positive field of the sulfur which would directly activate the respective hydrogen atoms toward protophilic attack[12]. It follows, then, that the 2-CH$_3$ and 2'-H (as designated in the drawing) are the reactive centers which are metalated. This conclusion is justified by related observations[13].



V **2, 4, 6 = CH$_3$**

VI **2 = O$^-$**
6 = CH$_3$ or Cl or Br
6' (or 2') = NO$_2$

---

[10] a/V. Baliah and V. Ramakrishnan, *J. Indian Chem. Soc.* **35**, 151 (1958); b/S.C. Abrahams, *Quart. Rev.* **10**, 407 (1956); c/J.F. Bunnett and R.E. Zahler, *Chem. Revs.* **49**, 369 (1951); d/G. Leandri, A. Mangini and R. Passerini, *Gazz. Chim. Ital.* **84**, 73 (1954).

[11] a/W.E. Truce, W.J. Ray, O.L. Norman and D.B. Eickemeyer, *J. Amer. Chem. Soc.* **80**, 3625 (1958); b/W.E. Truce and M.F. Amos, *Ibid.* **73**, 3013 (1951); c/W.E. Truce and O. Norman, *Ibid.* **75**, 6023 (1953).

[12] a/D. Bryce-Smith, *J. Chem. Soc.* 1079 (1954); b/G.E. Hall, R. Piccolini and J.D. Roberts, *J. Amer. Chem. Soc.* **77**, 4540 (1955).

[13] Truce (refs. 11*a*, *b*) suggested that the metalations might involve complexation at the oxygens (SO$_2$···Li+ Bu-) leading to attack on the H-atoms nearest the oxygens, *i.e.*, the 6- and 6'-positions. However, metalations seem to proceed by abstraction of the most acidic H-atom (ref. 12) and, in the above systems, those nearest the oxygens are probably the least acidic (ref. 2*c*). Moreover, this type of reaction

Likewise, the 100,000-fold increase in the rate of intramolecular rearrangement (Smiles) of certain 2-benzenesulfonylphenates when substituted in the 6-position[14], VI, may be partly associated with the positive charge on the sulfur atom, by virtue of its localized field effect. As elegantly described by Bunnett, *et al.*[10*c*, 14], the probability of a conformation in which the *o*-O$^-$ virtually lies next to the 1'-position, which it attacks, is greatly increased when a 6-group is introduced (as indicated by the drawing). This, they noted, was the major reason for the rapid rearrangement. In this conformation, moreover, the electron density *at* the *o*-O$^-$ is maintained (*i.e.*, localized) through the influence of the positive field around the sulfur atom[2*c*]. This, undoubtedly, is an additional factor responsible for the rapid reaction[15].

The influence of field effects is also suggested by the relative acidities of bicyclic carboxylic acids *β*-substituted with thia, sulfinyl and sulfonyl groups, respectively, VII[16]. In the *trans* series the order is that which would be expected on the basis of inductive effects. In the

---

[14] T. Okomoto and J.F. Bunnett, *J. Org. Chem.* **21**, 487 (1956).

[15] As in most nucleophilic reactions, this is also rather dependent upon a sufficiently high electron density at the attacking species; *viz.*, groups which withdraw electrons from the *o*-O$^-$ into the ring decrease the reaction rate (ref. 10c, pp. 368 ff.).

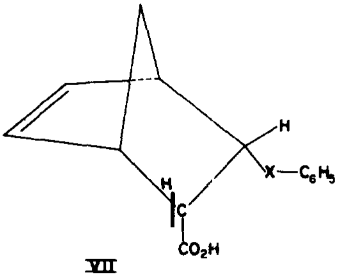
[16] The author is greatly indebted to Prof. F. Montanari and Dr. H. Hogeveen, of this Institute, for permission to use their data in this discussion. Their own studies will be published soon.

---

seems to be directly bimolecular, an *o*-position being favored because it is more positive as a result of inductive and field effects of the substituent, and a complex involving the latter and the reagent may be only incidental (ref. 12*b*). Finally, since V begins to rearrange (Smiles type) almost immediately following metalation (the sulfinate salt precipitates in a few minutes; ref. 11*a*), the *o*-CH_3 metalated must be already in the position favorable for this rearrangement, *viz.*, 2- and not 6- (*cf.* refs. 10*c*, 14).

TABLE 1

pK_a Values in 48% (Vol.) Aq. Ethanol at 25°[16]

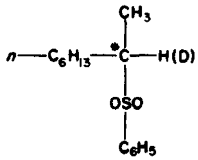


VII

X =	*Trans*	*Cis*
S	5.93	6.41
SO (*anti*-C=C, SO)	5.65	5.74
SO (*syn*-C=C, OS)	5.50	5.47
SO_2	5.36	6.23

cis series the negative field effect of the sulfonyl group on the carboxy is very noticeable, while that of thia is appreciable. Here it is interesting to speculate on the possibility that the negative influence of the sulfinyl-oxygen may be compensated to some extent in the *anti*-isomer, and perhaps superseded in the *syn*-isomer, by that of the positive field of its sulfur atom. Interestingly, in the *cis* series the sulfoxides are stronger acids than the corresponding sulfone, while the acidity of the latter approaches that of the sulfide[17].

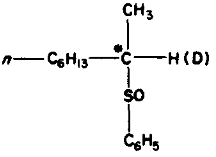
Cram, *et al.*[18], recently reported the striking contrast between the configurational stability of an asymmetric *a*-sulfonylcarbanion (from VIII) and the instability of the corresponding *a*-sulfinylcarbanion (from IX). One explanation for this contrast, they noted, might be associated with



$n{-}C_6H_{13}{-}\underset{\underset{\displaystyle C_6H_5}{|}}{\underset{\displaystyle OSO}{|}}{\overset{\overset{\displaystyle CH_3}{|}}{\overset{*}{C}}}{-}H(D)$

VIII

IX



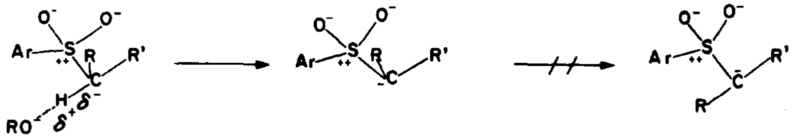
$n{-}C_6H_{13}{-}\underset{\underset{\displaystyle C_6H_5}{|}}{\underset{\displaystyle SO}{|}}{\overset{\overset{\displaystyle CH_3}{|}}{\overset{*}{C}}}{-}H(D)$

---

[17] These observations parallel those reported for the *o*- and *p*- phenols substituted by these groups (ref. 2*c*); *cis* // *o*, and trans // *p*. Only in the former pairs is the influence of field effects appreciable.

[18] D.J. Cram, R.D. Partos, S.H. Pine and H. Jäger, *J. Amer. Chem. Soc.* **84**, 1742 (1962); see also earlier papers by Cram, *et al.*

the much greater electrostatic effects within the sulfonyl anion than sulfinyl anion. On the basis of the preceding discussion this might be amplified by the suggestion that in the intact sulfone molecule the large negative field surrounding the oxygens may allow RO^- to attack the <u>a</u>-H only when the latter is as far as possible from the sulfonyl-oxygens; such an attack would be augmented by the positive field of the sulfur in this conformation[19]. Then, as also indicated by Cram, the resulting <u>a</u>-C^- would be stabilized in this conformation as well as configuration: energetically, inversion would be inhibited by the unfavorable negative-field influence of the oxygens[20]. The sulfoxide, having only one oxygen, affords a much wider spectrum of conformations favorable to attack and to the stability of the resulting carbanion. Consequently, the latter may undergo



inversion easily, both configurations being stable within the wider range of favorable conformations.

The author is pleased to acknowledge his fruitful discussions with Dr. H. Hogeveen on many of the points presented here.

<u>Note</u> - Immediately after this Letter had been submitted for publication the author became acquainted with the very recent report by Corey, <u>et al.</u>[21], concerning the stereochemistry of <u>a</u>-sulfonyl carbanions. It is especially important to note the close relationships between the comparative examples cited there and those discussed in this Letter. While it was not done, it is interesting to observe that their reported data <u>may</u> also be interpreted on the basis of sulfonyl-group field effects in virtually the same way as described in this Letter. The most interesting case in point

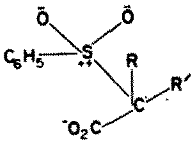
---

[19] <u>Cf</u>. refs. 8, 9, 13.

[20] In accord with this view is the observation that inversion (racemization) does become significant in a highly polar solvent (ref. 18). A polar medium apparently minimizes the relative importance of these field effects

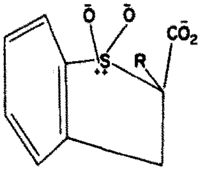
[21] E.J. Corey, H. König and T. Lowry, <u>Tetrahedron Letters</u> No. 12, 515 (1962).

is that of the optical stability of the sulfone derived from base-catalyzed decarboxylation of the optically active acyclic acid, X, but the complete racemization of the sulfone resulting from similarly-decarboxylated optically active cyclic acid, XI. The most favorable conformation of the



X anion

R = CH_3
R' = $n-C_6H_{13}$



XI anion

carboxylate anion of X would be that in which the CO_2^- group is remote from the negative sulfonyl-oxygens, and stabilized by the positive sulfur. The a-sulfonylcarbanion derived from this conformation (following decarboxylation) would be identical to that from VIII and, for the reasons suggested above, inversion would be inhibited. On the other hand, XI is a rigid structure whose predetermined conformation affords an a-sulfonylcarbanion also of fixed conformation in which, fortuitously, the a-C^- in both configurations is subjected to virtually the same magnitude of influence of the sulfonyl group's fields. Therefore, similar to the case noted above for the sulfoxide, IX, configurational equalization results (emanating, most likely, from the common planar anion suggested by Corey). Likewise, the variation in acidities of the b-disulfonyl systems (Table 2 in ref. 21) may be readily explained in terms of sulfonyl field effects in a manner similar to that proposed above in the discussion of I and II. It seems to this author that, fundamentally, there is much more similarity than difference between the explanatory approach described here and by Corey, *et al*.