O and S Methylation of the Ambident *p*-Toluenesulfinate Anion

JOHN S. MEEK AND JOANNA S. FOWLER[1]

Department of Chemistry, University of Colorado, Boulder, Colorado 80302

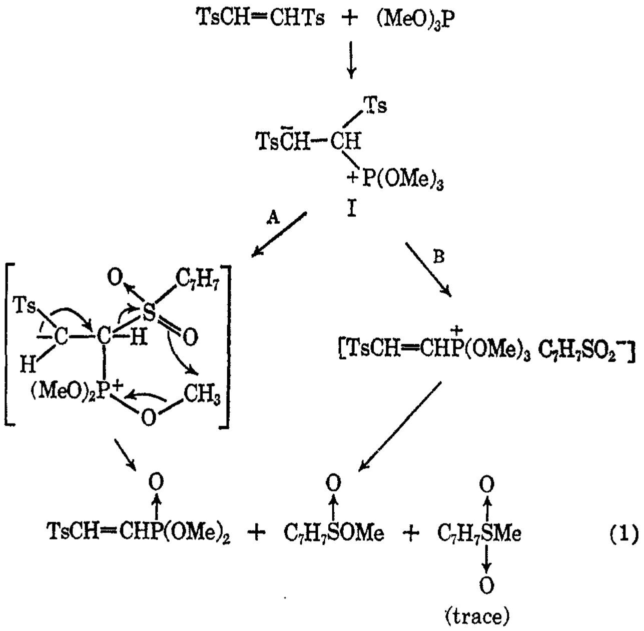
Received December 7, 1967

The alkylation of the *p*-toluenesulfinate anion in methanol or dimethylformamide by methyl iodide, methyl sulfate, and methyl *p*-toluenesulfonate gives both methyl *p*-toluenesulfinate and methyl *p*-tolyl sulfone. Alkylation of the ambident anion with hard alkylating agents gives predominantly the ester, whereas a soft alkylating agent gives predominantly the sulfone.

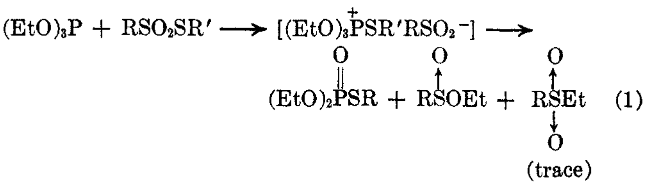
The assertion that the alkali metal salts of sulfinic acids on alkylation with alkyl halides give only sulfones has been made repeatedly.[2-5] Such reactions have led so far only to the detection of sulfones although the possible formation of sulfinate esters has been recognized from the beginning to the present.[6] Indeed, in addition to the reactions with alkyl halides[5,7] only sulfones, and not esters, have been reported in the reaction of a sulfinic acid or its salt with such alkylating or arylating agents as quaternary ammonium ions,[8] sulfonium ions,[8] methyl sulfate,[9] ethylene oxide,[10] β-propiolactone,[11] sultones,[12] aldehydes,[13,14] aniline, catechol, and hydroquinone[15] 2,3-diphenyl-2H-azirine,[16] activated aromatic halides,[17] and α,β-unsaturated compounds such as quinones,[15] esters,[13] aldehydes,[13] acids,[13] ketones,[13] sulfones,[15] and nitriles.[18,19]

Since in all of these reactions, only sulfones were reported, the observation that the reaction of trimethyl phosphite and 1,2-di-*p*-toluenesulfonylethene gave rise almost exclusively to methyl *p*-toluenesulfinate[20] (Scheme I) led us to consider the possibility of an intramolecular decomposition (path A) of the intermediate (I) to give the products rather than the decomposition to a salt (path B). By running the reaction in methyl iodide the formation of the salt (path B) was shown since the yield of the ester decreased and a 20–30% yield of methyl *p*-tolyl sulfone was obtained.

SCHEME I



This result suggested that a sulfinate anion on alkylation with a hard alkylating agent such as an alkoxyphosphonium ion gives rise primarily to ester formation, whereas a soft alkylating agent such as methyl iodide gives rise mainly to sulfone formation. This would be in accord with the findings of Michalski, Modro, and Wieczorkowski[21] and supports their mechanism (eq 1). Although the intramolecular mechanism (path A, Scheme I) is not ruled out, there is no longer any reason to propose it nor to invoke one to fit Michalski's reaction.



$$(\mathrm{EtO})_3\mathrm{P} + \mathrm{RSO_2SR'} \longrightarrow [(\mathrm{EtO})_3\overset{+}{\mathrm{P}}\mathrm{SR'RSO_2}^-] \longrightarrow (\mathrm{EtO})_2\overset{\overset{\mathrm{O}}{\|}}{\mathrm{P}}\mathrm{SR} + \mathrm{R}\overset{\overset{\mathrm{O}}{\uparrow}}{\mathrm{S}}\mathrm{OEt} + \mathrm{R}\underset{\underset{\mathrm{O}}{\downarrow}}{\overset{\overset{\mathrm{O}}{\uparrow}}{\mathrm{S}}}\mathrm{Et} \quad (1)$$

(trace)

The observations that the rates of some nucleophilic displacements depend on the proton basicity of the nucleophile while others depend on the polarizability are well known. The experimental facts have been compiled recently and certain generalizations were made. These generalizations have been termed the principle of hard and soft acids and bases (HSAB principle)[22] and have found successful application to the reactions of ambident anions.[23]

Since only Michalski's and our work have given reactions in which both a sulfone and a sulfinate ester have been isolated there has been no examination of the ratio of O- and S-alkylated products in the reaction

---

[1] National Institutes of Health Predoctoral Fellow, 1966–1967.

[2] R. Otto, *Ber.*, **13**, 1272 (1880).

[3] F. Arndt and A. Scholz, *Ann.*, **510**, 62 (1934).

[4] "Chemistry of Carbon Compounds," Vol. 3, E. H. Rodd, Ed., Elsevier Publishing Co., New York, N. Y., 1954, p 243.

[5] B. Lindberg, *Acta Chem. Scand.*, **17**, 393 (1963).

[6] K. Schank, *Ann.*, **702**, 75 (1967).

[7] A listing of the alkyl halides which give sulfones has been made: C. M. Suter, "The Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1948, p 668 ff.

[8] E. v. Meyer, *Chem. Zentr.*, **80**, Part II, 1800 (1909).

[9] L. Field and R. D. Clark in "Organic Syntheses," Coll. Vol. IV, N. Rabjohn, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, p 674.

[10] C. C. J. Culvenor, W. Davies, and N. S. Heath, *J. Amer. Chem. Soc.*, **71**, 278 (1949).

[11] T. L. Gresham, J. E. Jensen, F. W. Shaver, M. R. Frederick, F. T. Fiedorek, R. A. Bankert, J. T. Gregory, and W. L. Beears, *ibid.*, **74**, 1323 (1952).

[12] Johann H. Helberger and W. Grublewsky (B. Fettchemie, G.m.b.H.), German Patent 901,288 (Jan 11, 1954); *Chem. Abstr.*, **49**, 3249*a* (1955).

[13] E. P. Kohler and M. Reimer, *J. Amer. Chem. Soc.*, **31**, 163 (1904).

[14] T. Olijnsma, J. B. F. M. Engberts, and J. Strating, *Rec. Trav. Chim. Pays Bas*, **86**, 463 (1967).

[15] O. Hinsberg, *Ber.*, **36**, 107 (1903).

[16] J. S. Meek and J. S. Fowler, *J. Org. Chem.*, **33**, 3418 (1968).

[17] C. J. M. Stirling, *J. Chem. Soc.*, 5856, 5857 (1964).

[18] M. V. Kalnins and B. Miller, *Chem. Ind.* (London), 555 (1966).

[19] V. N. Mikhailova and A. I. Filippova, *Russ. J. Org. Chem.*, **1**, 1641 (1965).

[20] J. S. Meek and J. S. Fowler, *J. Org. Chem.*, **33**, 985 (1968).

[21] J. Michalski, T. Modro, and J. Wieczorkowski, *J. Chem. Soc.*, 1665 (1960).

[22] R. G. Pearson and J. Songstad, *J. Amer. Chem. Soc.*, **89**, 1827 (1967).

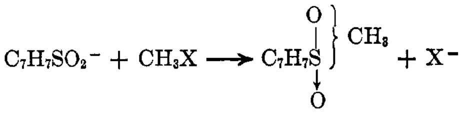
[23] R. G. Pearson and J. Songstad, *J. Org. Chem.*, **32**, 2899 (1967).

TABLE I
REACTION CONDITIONS AND YIELD DATA

Substrate	Alkylating agent	Solvent	Temp, °C	Time, hr	Yield, %	Ester, %	Sulfone, %
$C_7H_7SO_2H$	CH_2N_2	10% MeOH in ether	25	1	100	100	0
$C_7H_7SO_2^-$	$TsCH{=}CH\overset{+}{P}(OMe)_3$	None	25	0.03	100	95	5
$C_7H_7SO_2Na$	$(MeO)_2SO_2$	DMF	25	17	80	88	12
$C_7H_7SO_2Na$	$MeOSO_2C_7H_7$	DMF	25	23	66	77	23
$C_7H_7SO_2^-$	$TsCH{=}CH\overset{+}{P}(OMe)_3$	CH_3I	25	0.5	100	70	30
$C_7H_7SO_2Na$	$(MeO)_2SO_2$	MeOH	Reflux	20	70	69	31
$C_7H_7SO_2Na$	$MeOSO_2C_7H_7$	MeOH	Reflux	25	83	54	46
$C_7H_7SO_2Ag$	MeI	DMF	25	33	73	9	91
$C_7H_7SO_2Na$	MeI	DMF	25	22	50	7	93
$C_7H_7SO_2Na$	MeI	MeOH	Reflux	23	77	2	98
$C_7H_7SO_2Na$	$Me\overset{O}{\underset{O}{S}}C_7H_7$	DMF	25	20	87	0	100[a]
$C_7H_7SO_2Na$	$MeO\overset{O}{S}C_7H_7$	DMF	25	20	100	100	0[a]
$C_7H_7SO_2Na$	$MeOSO_2C_7H_7$	DMF	25	0.5	54% had reacted	78	22[b]
$C_7H_7SO_2Na$	$(MeO)_2SO_2$	DMF	25	0.5	98% had reacted	84	16[b]

[a] These two experiments demonstrated that the sulfone and ester were not interconvertible under the reaction conditions. [b] These two experiments demonstrated that the product isomer content did not vary during the course of the reaction.

of the *p*-toluenesulfinate anion with various methylating agents. It is the purpose of this paper to report our findings on the alkylation of *p*-toluenesulfinate anion as a function of the leaving group X in the alkylating agent (eq 2).



$$C_7H_7SO_2^- + CH_3X \longrightarrow C_7H_7\overset{\overset{O}{\|}}{\underset{\underset{O}{\downarrow}}{S}}\Big\}CH_3 + X^- \qquad (2)$$

Results

Table I summarizes the products of the alkylation of *p*-toluenesulfinate anion with various alkylating agents in methanol and in dimethylformamide. The ratio of O- and S-alkylated products was obtained from the nmr spectrum of the crude product which shows a signal for the $-OCH_3$ group of methyl *p*-toluenesulfinate as a sharp singlet at 3.42 ppm from TMS and a signal for the methyl group of methyl *p*-tolyl sulfone as a sharp singlet at 3.02 ppm. In addition, the presence of methyl *p*-tolyl sulfone in Scheme I was confirmed by comparing glpc retention time with that of an authentic sample of the sulfone.

Discussion

The reaction of *p*-toluenesulfinic acid with diazomethane has been reported to give only methyl *p*-toluenesulfinate.[3] In this reaction, proton transfer gives the sulfinate anion and the methanediazonium ion. This cation is a hard alkylating agent but might give some S alkylation. Reinvestigation of the product failed to reveal any sulfone and only O alkylation as claimed was found.

At first, Field's preparation for methyl *p*-tolyl sulfone[9] appeared to be an exception to the HSAB correlation for it involves the alkylation of sodium *p*-toluenesulfinate with methyl sulfate, a hard alkylating agent. By carrying out the reaction with methyl sulfate in dimethylformamide, we found that O alkylation does indeed occur as predicted by the HSAB principle. The difference in products is attributable to the difference in reaction media. Field's[9] method uses aqueous bicarbonate which should saponify the methyl ester and regenerate the sulfinate anion for further alkylation. The procedure calls for an excess of alkylating agent. Field and Clark[24] mention that the alkylation of sodium arylsulfinates with methyl sulfate in organic solvents was examined as a matter of interest connected with the general preparation of methyl aryl sulfones but proved rather unpromising. We suspect, that in the organic solvents the yield of sulfone was low and was further reduced in the crystallization needed to separate it from the ester. Methyl benzenesulfinate and methyl *p*-toluenesulfinate are readily hydrolyzed by heating with water and in alkaline solution are rapidly and completely saponified.[25] The hydrolysis of methyl *p*-toluenesulfinate in neutral aqueous dioxane is very slow but is autocatalyzed by the sulfinic acid produced, and in alkali the saponification is too fast to be measured by conventional means.[26]

Lindberg[5] has studied the kinetics of the reaction of sodium *p*-toluenesulfinate with bromoacetate ion in aqueous solution to give sulfone. Under these conditions it was observed that the sulfinate anion catalyzed the solvolysis of bromoacetate ion. No explanation of the catalysis was given but it appears that the catalytic effect can be explained by the formation of a sulfinate ester which, as others, would be quickly saponified in the alkaline solution to regenerate the sulfinate anion and the solvolysis product of the bromacetate ion.

The percentage of S alkylation observed in technical methanol was higher than that found in N,N-dimethylformamide and probably is due to hydrolysis of some of the methyl *p*-toluenesulfinate. Refluxing some methyl *p*-toluenesulfinate in excess technical methanol for 21 hr caused hydrolysis to an extent of 30%. Since hydrogen bonding is a hard acid-hard base interaction, an alternative explanation for the high percentage of sulfone in methanol is that a protic solvent such as methanol is capable of hydrogen bonding with the oxygen atoms of the sulfinate anion making them less available for alkylation.

With methyl iodide, the sulfone is the kinetic product as well as the thermodynamically more stable product.

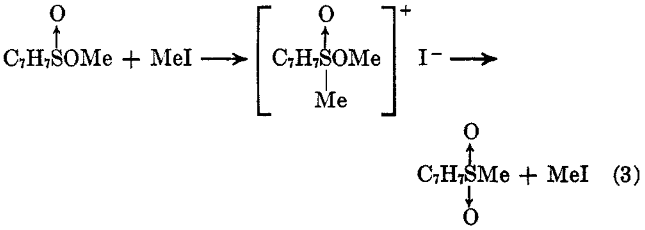
---

[24] L. Field and R. D. Clark, *J. Org. Chem.*, **22**, 1129 (1957).

[25] R. Otto and A. Rossing, *J. Prakt. Chem.*, **47**, 152 (1893).

[26] C. A. Bunton and B. W. Hendy, *Chem. Ind.* (London), 466 (1960).

The possibility of isomerization of the ester to the sulfone *via* eq 3 was suggested to us by Professor Saul



$$C_7H_7\overset{\overset{O}{\uparrow}}{S}OMe + MeI \longrightarrow \left[C_7H_7\underset{\underset{Me}{|}}{\overset{\overset{O}{\uparrow}}{S}}OMe \right]^+ I^- \longrightarrow C_7H_7\underset{\underset{O}{\downarrow}}{\overset{\overset{O}{\uparrow}}{S}}Me + MeI \quad (3)$$

Winstein during a discussion of the applicability of the HSAB principle to the formation and isomerization of O-methylsulfonium salts to sulfoxonium salts[27] but was ruled out since methyl iodide and methyl *p*-toluenesulfinate in dimethylformamide did not give sulfone.

Silver salts of sulfinic acids have been reported to give sulfones.[28-32] Since there are differences in the alkylation of sodium and silver nitrite and cyanide, silver *p*-toluenesulfinate was allowed to react with methyl iodide in N,N-dimethylformamide. Both the ester and sulfone were formed and their relative amounts were almost the same as when the sodium salt was used.

Using the experimental facts gained from this study, one could predict that methyl *p*-toluenesulfinate would be the predominant product in Scheme I. Since in the phosphonium salt (Scheme I, path B) the acceptor atom, carbon, is of high positive charge and small size, it is a hard alkylating agent and the reaction would be predicted to occur at the oxygen atom of *p*-toluenesulfinate anion. The term used by Jorgensen[33] for the mutual stabilizing effect imparted to a species when several soft or several hard ligands are attached to it is symbiosis, and application of this generalization to the ambident anions is useful in predicting the products of many reactions. Hard alkylating agents such as diazomethane, dimethyl sulfate, methyl *p*-toluenesulfonate, and alkoxyphosphonium salts react with the *p*-toluenesulfinate anion to give mainly sulfinate esters while methyl iodide, a soft alkylating agent, gives mainly the sulfone. In summary there exists a definite correlation between the hardness or softness of the alkylating agent and the amount of O or S alkylation which further supports the applicability of the HSAB principle to the alkylation of ambident ions, and thus the claim that metal salts of sulfinic acids on alkylation with alkyl halides give only sulfones can no longer be made.

This study has indicated that one can use one procedure to prepare either a sulfinate ester or a sulfone by varying the alkylating agent. The reaction is easily carried out at room temperature in DMF and the product can be isolated by diluting with water and extracting with ether. The simplicity of the reaction of hard alkylating agents such as methyl sulfate and methyl *p*-toluenesulfonate with sodium *p*-toluenesulfinate to give the methyl ester in high yield compliments other methods used to prepare this ester.[34,35]

Experimental Section

Nmr spectra were run using a Varian A-60A spectrometer with deuteriochloroform as a solvent and tetramethylsilane as an internal standard.

General Procedure for the Reaction of Sodium *p*-Toluenesulfinate with Alkylating Agents.—Equimolar amounts of sodium *p*-toluenesulfinate dihydrate and the alkylating agent were used in either methanol or DMF (25 ml of solvent/2 g of reactants) for the time and at the temperature specified in Table I. The reaction mixtures were then diluted with water and extracted three times with 100 ml of ether. The ether extracts were combined, washed several times with water (total volume, 300 ml), and dried over anhydrous magnesium sulfate. Removal of the solvent left a crude product which was weighed; then an nmr spectrum was obtained. All of the nmr analyses showed that the sulfone and the ester were the only components of the crude reaction mixture.

Reaction of *p*-Toluenesulfinic Acid with Diazomethane.—To 0.5 g of *p*-toluenesulfinic acid (prepared by acidifying sodium *p*-toluenesulfinate dihydrate) in 20 ml of methanol was added 200 ml of an ethereal solution of diazomethane (prepared from nitrosomethylurea and dried over KOH pellets). The mixture was allowed to stand for 1 hr at room temperature and the solvent was removed giving a quantitative yield of methyl *p*-toluenesulfinate.

Reaction of 1,2-Di-*p*-toluenesulfonylethene with Trimethyl Phosphite.—Equimolar quantities of the disulfone and trimethyl phosphite were allowed to react in methyl iodide solvent (2 ml of methyl iodide/1 g of reactants) for 30 min. The excess methyl iodide was removed under reduced pressure and the crude product was analyzed by nmr and glpc. Glpc analyses were run on an Aerograph 200 instrument using an SE-52 column at 130°.

Reaction of Silver *p*-Toluenesulfinate with Methyl Iodide.—A 1-g sample of silver *p*-toluenesulfinate (prepared from sodium *p*-toluenesulfinate and silver nitrate) and 2 ml of methyl iodide in 25 ml of DMF was stirred at room temperature for 33 hr. The solution was poured into water and extracted with ether. The ethereal extracts were combined, washed with water, and dried over anhydrous magnesium sulfate. The ether was removed under reduced pressure. Yield and product isomer content are summarized in Table I.

Registry No.—*p*-Toluenesulfinate anion, 17223-96-0.

---

(27) S. G. Smith and S. Winstein, *Tetrahedron*, **3**, 317 (1958).

(28) T. Zincke and F. Farr, *Ann.*, **391**, 74 (1912).

(29) T. Zincke and S. Lenhardt, *ibid.*, **400**, 16 (1913).

(30) T. Zincke and J. Baeumer, *ibid.*, **416**, 86 (1918).

(31) T. Zincke and K. Eismayer, *Ber.*, **51**, 758 (1918).

(32) H. Reinholdt, F. Mott, and E. Motzkus, *J. Prakt. Chem.*, **134**, 257 (1932).

(33) C. K. Jorgensen, *Inorg. Chem.*, **3**, 1201 (1964).

(34) I. B. Douglass, *J. Org. Chem.*, **30**, 633 (1965).

(35) L. Field, C. B. Hoelzel, and J. M. Locke, *J. Amer. Chem. Soc.*, **84**, 847 (1962).