proposed by Bodforss,[27] following a suggestion by Wieland,[28] to explain the rapid fall in phenylhydrazine concentration and the slow formation of colored phenylhydrazone which was observed on mixing phenylhydrazine and *m*-nitrobenzaldehyde. Phenylhydrazone formation was found to follow monomolecular kinetics, as would be expected if the aldehyde were almost completely converted to addition compound in an initial fast reaction. In the analogous reaction with acetophenone, bimolecular kinetics was observed at low phenylhydrazine concentration, as would be expected if the concentration of addition compound in equilibrium with starting materials were low. Similar shifts from first- to second-order kinetics, depending on the concentration of nitrogen base and the equilibrium constant for addition compound formation, are described above (*cf.* Fig. 2) and account for the varying order of reaction described by other workers for phenylhydrazine reactions.[29]

The acid and alkaline hydrolysis of esters and amides has been shown by Bender to be accompanied in many cases by incorporation of O^{18} from water into unreacted ester or amide, suggesting that an intermediate addition product has some stability in these reactions.[30] The even greater importance of a tetrahedral addition product in these reactions of aldehydes and ketones suggests that rate-acceleration by enzymes and other catalysts of the reactions of a number of carbonyl compounds may be due to an acceleration of the decomposition of addition compounds rather than to acceleration of the addition of a nucleophilic reagent to the carbonyl group.

Acknowledgments.—The author is greatly indebted to the National Science Foundation, the National Cancer Institute of the National Institutes of Health (Grant C-3975) and the Lilly Research Laboratories for financial support, to Mrs. Reba Chakrabarti, Miss Marion Hyatt and Miss Joan Carriuolo for technical assistance in various phases of this investigation, and to Dr. Henry Linschitz for helpful discussions on kinetic problems.

WALTHAM, MASS.

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[27] S. Bodforss, *Z. physik. Chem.*, **109**, 223 (1924).

[28] H. Wieland, "Die Hydrazine," Ferdinand Enke, Stuttgart, 1913, p. 84.

[29] E. G. R. Ardagh and F. C. Rutherford, THIS JOURNAL, **57**, 1085 (1935); J. Compton and M. L. Wolfrom, *ibid.*, **56**, 1157 (1934); U. Grassi, *Gazz. chim. ital.*, **40**, II, 139 (1910).

[30] M. L. Bender, THIS JOURNAL, **73**, 1626 (1951); **77**, 348 (1955).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

Rearrangements of Aryl Sulfones. II. The Synthesis and Rearrangement of Several *o*-Methyldiaryl Sulfones to *o*-Benzylbenzenesulfinic Acids[1]

BY WILLIAM E. TRUCE AND WILLIAM J. RAY, JR.

RECEIVED JUNE 2, 1958

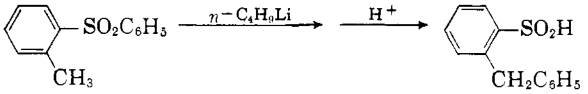
The synthesis and *n*-butyllithium-induced rearrangement of phenyl *o*-tolyl sulfone and some of its methylated homologs to the corresponding substituted *o*-benzylbenzenesulfinic acids is reported.

The synthesis of phenyl *o*-tolyl sulfone by the Friedel–Crafts reaction of *o*-toluenesulfonyl chloride with benzene is reported in the literature.[2] We have also carried out this reaction obtaining results similar to those described. Because of the difficulty in preparing sizable amounts of the sulfonyl chloride completely free of the *para* isomer, however, an alternate procedure was investigated. This involved treatment of *o*-tolyllithium with phenyl disulfide according to the method of Burton and Davey.[3] Oxidation of the product gave phenyl *o*-tolyl sulfone in good over-all yield. The sulfone prepared in this manner was identical to that prepared by the Friedel–Crafts reaction.

The preparation of phenyl 2,4-xylyl sulfone is also described in the literature.[4] The reported reaction of 2,4-dimethylbenzenesulfonyl fluoride with phenylmagnesium bromide, however, seemed less attractive than the Friedel–Crafts reaction of the corresponding sulfonyl chloride with benzene; hence, the latter preparation was used.

Phenyl 2,6-xylyl sulfone was prepared in good yield *via* the sulfide in a reaction sequence similar to that used to prepare phenyl *o*-tolyl sulfone. In the preparation of this sulfide, however, the reaction of 2,6-dimethylphenyllithium with benzenesulfenyl chloride[5] instead of phenyl disulfide was employed.

The reaction of solutions of these sulfones in refluxing ether with a 5% excess of *n*-butyllithium gave the corresponding *o*-benzylbenzenesulfinic acids, *e.g.*



Both mesityl sulfone and phenyl 2,6-xylyl sulfone rearranged almost completely, while phenyl *o*-tolyl sulfone and phenyl 2,4-xylyl sulfones gave only a 65–70% conversion to the corresponding sulfinic acids, most of the remainder being recovered as starting sulfone on hydrolysis. These low conversions might be the result of a reaction concurrent with rearrangement whereby the common intermediate, I, is used up. This is doubtful,

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[1] Abstracted from W. J. R.'s Ph.D. Thesis.

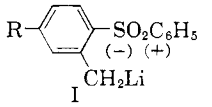
[2] F. Ullmann and A. Lehrner, *Ber.*, **38**, 734 (1905).

[3] H. Burton and W. A. Davey, *J. Chem. Soc.*, 528 (1948).

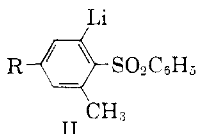
[4] W. Steinkopf and R. Heubner, *J. prakt. Chem.*, **141**, 197 (1934).

[5] Sulfenyl chlorides may be used to good advantage in place of disulfides in such preparations where a product free of the starting disulfide is desired. This is unnecessary, however, if the sulfide is to be oxidized to the sulfone.

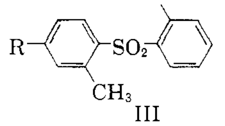
however, since simple, first-order kinetics were observed for the over-all reaction of both of these sulfones with *n*-butyllithium.[6] Although such kinetics might still be observed if the side reaction of I is cleavage of the ether solvent,[7] this possibility is discounted by the fact that the rearrangement of the metalation intermediate from mesityl sulfone, a reaction which proceeds much more slowly than does the rearrangement of the intermediates from either of the sulfones in question,[6] results in a high conversion to the corresponding sulfinic acid.



I



II



III

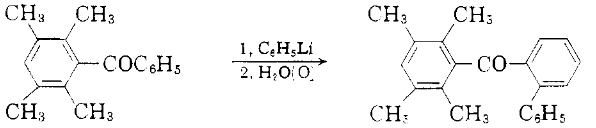
Apparently, then, phenyl *o*-tolyl and phenyl 2,4-xylyl sulfones are metalated to give I (R = H– and CH_3–, respectively) in 65 to 70% conversion, the remainder of the metalation occurring at other positions, perhaps at the unsubstituted *o*-positions to give II and III by analogy with the metalation of diphenyl sulfone.[8] Both II and III, being incapable of rearrangement, would give rise to unreacted sulfone on hydrolysis.

The formation of II is obviously excluded in mesityl phenyl and phenyl 2,6-xylyl sulfones, and metalation of these sulfones to give a homolog of III apparently does not occur, in view of the almost complete rearrangement of these sulfones, unless III may be rapidly transformed into I *via* hydrogen–metal interchange. It seems possible that in these 2,6-disubstituted sulfones the *o*-hydrogens of the phenyl ring are effectively shielded from metalation by the two *o*-methyl groups of the 2,6-xylyl-type ring.

2-Benzyl-4-methylbenzenesulfinic acid and 2-benzylbenzenesulfinic acid have been prepared by replacing the amino group of 2-benzyl-4-methylaniline[9] and 2-benzylaniline,[10] respectively, by the sulfinic acid group according to the method of Gattermann.[11a,b] These acids were shown to be identical to the rearrangement products of phenyl 2,4-xylyl and phenyl *o*-tolyl sulfones, respectively. The chloromercuric derivatives[12] of the acids were used in the comparison because of the instability of the parent acids.

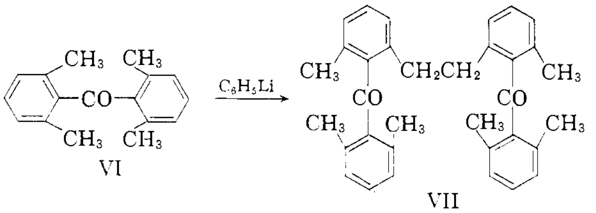
By analogy with the rearrangement of these sulfones and of mesityl phenyl and mesityl *p*-tolyl sulfones,[13] the rearrangement products of phenyl 2,6-xylyl and mesityl sulfones are assumed to be 2-benzyl-6-methylbenzenesulfinic acid and 2,4-dimethyl-6-(2,4,6-trimethylbenzyl)-benzenesulfinic acid, respectively. Both of these sulfinic acids together with the sulfinic acids from phenyl *o*-tolyl and phenyl 2,4-xylyl sulfones exhibited the expected neutral equivalents after isolation and purification.

It seems appropriate to note here the difference in behavior between hindered aryl ketones and similarly substituted aryl sulfones toward organolithium reagents. Whereas 2,3,5,6-tetramethylbenzophenone (IV) reacts with phenyllithium to give V[14] mesityl phenyl sulfone, as described previously,[13] is metalated in the *o*-methyl group and gives a sulfinic acid *via* rearrangement. The more highly hindered ketone, 2,2′,6,6′-tetramethylbenzophenone (VI), however, reacts to give VII,[15]



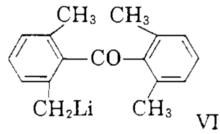
IV V

while mesityl sulfone behaves like mesityl phenyl sulfone. (The homologous 2,2′,4,4′,6,6′-hexamethylbenzophenone behaves like VI.)[15]



VI VII

The mechanism postulated[15] for the ketone reaction leading to VII involves the intermediate VIII which is analogous to our intermediate I.



VIII

In spite of the similarity between I and VIII, the reactions obviously take quite different courses. However, considering the expected difference in the relative stabilities of the two anions, $ArSO_2^-$ and $ArCO^-$, which would result from the rearrangement of I and VIII, respectively, this difference in behavior is not surprising.

Since the herein-described rearrangements of *o*-methyl-diaryl sulfones frequently proceed in high yield, such sulfones might well be utilized in syntheses of *o*-substituted diarylmethanes, some of which might be useful in cyclization reactions, *e.g.*, phenyl *o*-tolyl sulfone could be converted to thiaxanthene dioxide *via* rearrangement and subsequent oxidation and cyclization. *o*-Chloromer-

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(6) W. E. Truce and W. J. Ray, Jr., THIS JOURNAL, **81**, 484 (1959).

(7) H. Gilman, A. H. Haubein and H. Hartzfeld, *J. Org. Chem.*, **19**, 1034 (1954), have shown that such ether cleavage by a number of organolithium compounds is a pseudo first-order reaction.

(8) W. E. Truce and M. F. Amos, THIS JOURNAL, **73**, 3013 (1951).

(9) R. E. Davies, H. T. Openshaw, F. S. Spring, R. T. Stanley and A. R. Todd, *J. Chem. Soc.*, 295 (1948).

(10) C. L. Hewett, L. J. Lermit, H. T. Openshaw, A. R. Todd, A. H. Williams and F. N. Woodward, *ibid.*, 292 (1948).

(11) (a) L. Gattermann. *Ber.*, **32**, 1136 (1899); (b) M. E. Hanke, THIS JOURNAL, **45**, 1321 (1923).

(12) F. C. Whitmore, F. H. Hamilton and N. Thurman, *ibid.*, **45**, 1066 (1923).

(13) W. E. Truce, W. J. Ray, Jr., O. L. Norman and D. B. Eickemeyer, *ibid.*, **80**, 3625 (1958).

(14) R. C. Fuson, G. P. Speranza and R. Gaertner, *J. Org. Chem.*, **15**, 1155 (1950).

(15) A. C. Faber and W. T. Nauta, *Rec. trav. chim.*, **62**, 469 (1943); **70**, 659 (1951).

curi-[12] and *o*-acetoxymercuridiphenylmethanes[11b] are also readily available *via* the rearrangement products. The –HgCl and –HgOAc substituents can in turn be replaced, for example, by the nitro, halo or acetyl group.[16]

Experimental[17]

Phenyl *o*-Tolyl Sulfide and Its Sulfone.—A solution of *o*-tolyllithium from 53.7 g. (0.314 mole) of *o*-bromotoluene[18] and 4.72 g. (0.680 mole) of lithium wire in 500 ml. of anhydrous ether was filtered through a glass wool plug and treated dropwise with 67.0 g. (0.307 mole) of phenyl disulfide in 400 ml. of benzene over a period of about one hour, refluxing and stirring being maintained throughout.[3] The solvent was distilled off through a Claisen head until the temperature of the vapor reached 67°. After refluxing for one additional hour, the solution was hydrolyzed with hydrochloric acid and ice. The organic layer was separated, washed once with water, twice with 75-ml. portions of 5% aqueous sodium hydroxide and again with water. The ether was distilled off, after which the product boiled at 107–125° (0.5 mm.), reported[19] 160.5° (11 mm.). Although the product probably contained some phenyl disulfide, it was oxidized with hydrogen peroxide in refluxing acetic acid without further purification. The sulfone was isolated by pouring the oxidation mixture over crushed ice and filtering; weight 49 g. (69% of theory based on phenyl disulfide), m.p. 79.5–80.5°, reported[2] 80–81°.

Phenyl 2,4-Xylyl Sulfone.—A solution of 44.6 g. (0.218 mole) of 2,4-dimethylbenzenesulfonyl chloride[20] and 66.0 g. (0.872 mole) of benzene was treated with 29.6 g. (0.223 mole) of aluminum chloride in small amounts over a period of about 0.5 hour. Refluxing and stirring were maintained for 2 additional hours after which the reaction mixture was hydrolyzed with hydrochloric acid and ice. The layers were separated with the aid of additional benzene and the organic layer was washed once with water and once with dilute ammonia. After filtering and drying, the solvent was distilled off and the product vacuum distilled, b.p. 150–155° (0.2 mm.), weight 38 g. (71% of theory). The light yellow oil rapidly solidified in the receivers, m.p. 86–87° after crystallizing once from methanol and once from 60–70° petroleum ether, reported[4] m.p. 87°.

Phenyl 2,6-Xylyl Sulfide and Its Sulfone.—A solution of 2,6-dimethylphenyllithium from 88 g. (0.47 mole) of 2,6-dimethylbromobenzene[21] and 7.15 g. (1.03 g. atoms) of lithium wire in 60 ml. of ether was filtered and treated dropwise with an ethereal solution containing 67.7 g. (0.468 mole) of benzenesulfenyl chloride. After refluxing for 10 minutes the mixture was hydrolyzed with dilute hydrochloric acid and ice. The organic layer was washed once with water and extracted twice with 75-ml. portions of 4% sodium hydroxide and again with water. The ether was evaporated and the product distilled under vacuum. The light yellow oil boiling at 112–122° (1 mm.) was oxidized with hydrogen peroxide in acetic acid to give 77 g. (66% of theory based on 2,6-dimethylbromobenzene) of the corresponding sulfone, m.p. 101–102° after crystallization from methanol.

Anal. Calcd. for $C_{14}H_{14}O_2S$: C, 68.27; H, 5.73. Found: C, 68.07; H, 5.78.

The Reaction of *o*-Methyldiaryl Sulfones with *n*-Butyllithium.—The metalation and rearrangement of phenyl 2,4-xylyl, phenyl *o*-tolyl, phenyl 2,6-xylyl and mesityl sulfones was carried out in refluxing ether employing a 5% excess of *n*-butyllithium as described for the rearrangement of mesityl phenyl sulfone in the preceding paper of this series.[13] The reaction times required for these sulfones were 4, 4, 1 and 24 hours, respectively. The sulfinic acids were isolated by acidifying the basic solution resulting from the hydrolysis of the reaction mixture with water. The acid then was extracted from the water layer with ether. If the ether solution was yellow, the acid was extracted into an aqueous sodium bicarbonate solution which was decolorized by shaking with charcoal. The acid was then re-isolated as before. The 2,6-disubstituted acids were crystallized easily from aqueous acetone as described previously[13] while the acids containing a single *o*-substituent were crystallized from an ether–petroleum ether mixture.

TABLE I

Substituted benzenesulfinic acid	Conversion, %	M.p., °C., dec.	Neut. equiv. Calcd.	Neut. equiv. Found
2-Benzyl-	65–70	70–72	232.3	232.9
2-Benzyl-4-methyl	65–70	81–83	246.3	246.3
2-Benzyl-6-methyl	98	92–94	246.3	247.6
2,4-Dimethyl-6-(2,4,6-trimethylbenzyl)-	95		302.3	304.3

2-Benzylbenzenesulfinic Acid.—Using the procedure of Hewett, *et al.*,[10] 6.0 g. (0.030 mole) of 2-benzoylaniline was reduced to 2-benzylaniline with sodium in alcohol. A small portion of the almost colorless ether solution of this product was evaporated to dryness and the 2-benzylaniline so obtained melted at 49–53° after one crystallization from petroleum ether; reported[10] m.p. 52–53°. Since the aniline became colored in contact with air, the remainder of the ether solution was run, dropwise, into 120 g. of hot, 30% sulfuric acid. After cooling, diazotization was accomplished with 2.40 g. (0.0348 mole) of sodium nitrite in 12 ml. of water. A cold solution of 45 g. of 60% sulfuric acid was slowly added and the resulting solution cooled to –5°. Sulfur dioxide was added until the gain in weight was 22 g. The coolant was removed and the solution allowed to warm to 10° with the frequent addition of small amounts of copper bronze, vigorous stirring being maintained throughout.[11]

The unreacted copper and the organic residue were filtered off and the sulfinic acid was extracted with base. The acid was isolated as the ferric salt by precipitation from a neutral aqueous solution with ferric chloride.[22] The ferric salt was used below without further purification.

2-Chloromercuridiphenylmethane.—A portion of the above ferric sulfinate was dissolved in hot, aqueous base. After digesting and filtering off the excess ferric hydroxide, the solution was neutralized and treated with a hot solution of mercuric chloride according to the method of Whitmore, *et al.*[12] The resulting flocculent, white precipitate was filtered while the solution was still hot and the acetone-soluble residue was crystallized from methanol. The resulting white crystals melted at 147–148°. This derivative was identical with that prepared from the sulfinic acid obtained by the rearrangement of phenyl *o*-tolyl sulfone.

Anal. Calcd. for $C_{13}H_{11}ClHg$: Cl, 8.79. Found: Cl, 8.95.

2-Benzyl-4-methylbenzenesulfinic Acid.—2-Benzyl-4-methylaniline was prepared in the manner described by Davies, *et al.*[19]; b.p. 135–155° (0.5 mm). The product was further purified by dissolving 28 g. (0.142 mole) of the yellow oil in ether and precipitating as the hydrochloride, which was filtered off, washed with ether and dissolved in 600 ml. of hot water. After cooling somewhat, several grams of a dark, oily solid were filtered off. The solution was cooled further, made basic, and extracted with ether. The ether solution was added dropwise to 400 g. of hot 30% sulfuric acid and the resulting solution diazotized and treated with sulfur dioxide and copper as in the preparation of 2-benzylbenzenesulfinic acid. The following quantities of reagents were used: 20% aqueous sodium nitrite added portionwise until a starch—iodide test showed the presence of nitrous acid for 15 minutes after the last addition, 200 g. of cold 60% sulfuric acid, 125 g. of sulfur dioxide and several grams of copper bronze. The sulfinic acid was isolated *via* the ferric salt as before. On air drying, the salt weighed 30 g. (79% of theory).

2-Chloromercuri-4-methyldiphenylmethane.—The chloromercuric derivative of the above sulfinic acid, prepared as

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(16) H. Gilman, "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1938, p. 550.

(17) All melting and boiling points are uncorrected.

(18) Commercial *o*-bromotoluene was used after careful rectification, f.p. –27.0°. J. Timmermans, "Physico-Chemical Constants of Pure Organic Compounds," Elsevier Publishing Co., Inc., New York, N. Y., 1950, p. 298, reports –28.1°.

(19) E. Bourgeois, *Ber.*, **28**, 2322 (1895).

(20) Prepared by the chlorosulfonation of purified *m*-xylene. The *m*-xylene employed had a freezing point of –47.8°. The value reported by J. White and W. Rose, Jr., *J. Research Natl. Bur. Standards*, **9**, 711 (1932), is –47.89°.

(21) Prepared from commercial 2,6-xylidine. The purity of the bromo compound which froze at –12.3°, after careful rectification, was estimated at >99% by the freezing curve.

(22) J. Thomas, *J. Chem. Soc.*, **95**, 342 (1909).

described before, melted at 147–148°, after crystallization from methanol. Admixture with the same derivative of the sulfinic acid obtained by the rearrangement of phenyl 2,4-xylyl sulfone did not depress the melting point.

Anal. Calcd. for $C_{14}H_{13}ClHg$: Cl, 8.53. Found: Cl, 8.51, 8.80.

Acknowledgment.—We wish to acknowledge gratefully the support of this work by the National Science Foundation and by the Union Carbide and Carbon Chemicals Co.

Lafayette, Ind.

[Contribution from the Department of Chemistry, Purdue University]

Rearrangements of Aryl Sulfones. III. The Kinetics of the Reaction of *o*-Methyldiaryl Sulfones with *n*-Butyllithium[1]

By William E. Truce and William J. Ray, Jr.

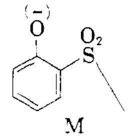
Received June 2, 1958

A marked difference in the kinetics of the reaction of phenyl *o*-tolyl- and phenyl 2,6-xylyl-type sulfones was observed. This difference is attributed to the steric influence of the 6-methyl group on the latter reaction.

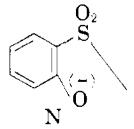
Introduction

In 1937, McClement and Smiles[2] reported that the rate of the base-induced rearrangement of 2-hydroxy-2′-nitrodiphenyl sulfones was accelerated by a methyl group in the 6-position. This acceleration was attributed by them to the electron-releasing ability of the methyl group. Bunnett and Zahler,[3] however, later pointed out that this acceleration can best be explained as the result of a steric rather than an electronic effect, and Bunnett and Okamoto[4] recently have presented convincing evidence in support of this view. These workers found that chloro and bromo as well as methyl substituents in the 6-position exerted a tremendous accelerating effect on the reaction, their presence increasing the first-order rate constant of the rearrangement by as much as 500,000-fold over that of the unsubstituted sulfone. Since the electronically opposite halo and methyl substituents produced a similar accelerating effect on the rearrangement, this effect was taken to be steric in nature and a consequence of the size of the substituent.

These workers also showed that the entropy of activation in all cases examined approached zero and that, "... the changes in rate, owing both to electronic and steric effects, arise principally from changes in the energy of activation."[4] They also reasoned that, "Since in the transition state...the 6-substituent is in an open and relatively uncrowded situation, it is unlikely that the enthalpy of the transition state is greatly dependent on the bulk of a 6-substituent. Therefore, a 6-substituent must change the energy of activation mainly by increasing the enthalpy of the unrearranged sulfone anions."[4] This change in enthalpy is explained as the result of steric factors which favor conformations similar to M over those similar to N in sulfones lacking a 6-substituent, while favoring conformations such as N over those such as M when a bulky 6-substituent is present. The enthalpy of the favored conformations in the latter case must be substantially greater than the enthalpy of the favored conformations in the former case due to "...steric repulsions between the solvated ionized hydroxyl group and the carbon atoms of the other ring...."[4] Since the rearrangement occurs from conformations such as N, there will be a net difference between the energy required for the rearrangement of these two classes of sulfones equal to the energy necessary to bring about the transformation M→N, prior to rearrangement, in sulfones lacking a bulky 6-substituent.



M

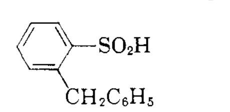


N

With this in mind, it was of interest to examine the kinetics of the related rearrangement of *o*-methyldiaryl sulfones described in parts I[5a] and II[5b] of this series. Of special interest was the fact that in sulfones such as mesityl phenyl sulfone, the two *o*-substituents are of the same size and both are possible sites for metalation and subsequent rearrangement.

Results and Discussion

A mechanism has been postulated for the reaction of *o*-methyldiaryl sulfones with *n*-butyllithium[5a]



If the metalation reaction is rate determining, the over-all reaction rate should be proportional to the sulfone concentration, other variables remaining constant. That this is contrary to fact is indicated by the rate studies involving mesityl phenyl, phenyl 2,4-xylyl and phenyl *o*-tolyl sulfones, the results of which are summarized in Table I.

---

[1] Abstracted from Ph.D. thesis of W. J. Ray, Jr.

[2] C. S. McClement and S. Smiles, *J. Chem. Soc.*, 1016 (1937).

[3] J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 369 (1951).

[4] J. F. Bunnett and T. Okamoto, This Journal, **78**, 5363 (1956).

[5] (a) W. E. Truce, W. J. Ray, Jr., O. L. Norman and D. B. Eickemeyer, *ibid.*, **80**, 3625 (1958); (b) W. E. Truce and W. J. Ray, Jr., *ibid.*, **81**, 481 (1959).