[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Metalation of Diaryl Sulfones. II. Phenyl *p*-Tolyl Sulfone and Dimesityl Sulfone[1]

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In accord with the known weak inductive effect of a methyl substituent, metalation of phenyl *p*-tolyl sulfone by *n*-butyllithium results in a slight preference for metalation in the *o'*-position over the ortho *o*-position. Similar metalation and subsequent carbonation of dimesityl sulfone resulted in an acid whose structure could not be established.

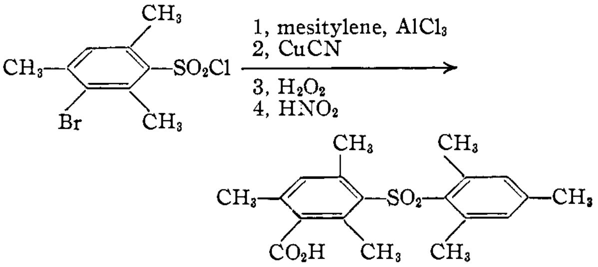
While both alkyl aryl sulfones and diaryl sulfones have been metalated[3] with *n*-butyllithium, and subsequently carbonated, an identifiable product, phenylsulfonylacetic acid, was obtained from methyl phenyl sulfone only. Recently[4] diaryl sulfones were successfully metalated with *n*-butyllithium, producing *o*-phenylsulfonylbenzoic acid from diphenyl sulfone and *o*-bromodiphenyl sulfone, and 4-bromo-2-carboxydiphenyl sulfone and 3-bromo-2-carboxydiphenyl sulfone from 4-bromodiphenyl sulfone and 3-bromodiphenyl sulfone, respectively. Explanations for the consistent metalation in the ortho positions of diphenyl sulfones, and the preferred metalation in the bromine-substituted ring have been previously proposed,[4] based on inductive effects of substituents and considerations of the nucleophilic character of the attack by butyllithium.

The present work concerns the metalation of two methyl-substituted diphenyl sulfones. The methyl substituent was chosen because its inductive effect is opposite in sign to that of a bromine substituent. Furthermore, it should neither undergo cleavage from the ring, as did the bromine substituent in 2-bromodiphenyl sulfone, nor should it enter into competition with the sulfone group by complexing with *n*-butyllithium as might other groups, such as alkoxyls, etc.

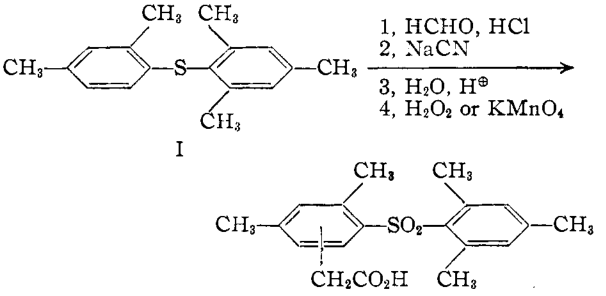
When phenyl *p*-tolyl sulfone was metalated and then carbonated, a mixture of the two possible ortho-carboxy sulfones was obtained, as indicated by its ready conversion to 2-methylthioxanthone-10-dioxide. This mixture consisted of about 41% of 2-carboxy-4-methyldiphenyl sulfone and 59% of 2-carboxy-4'-methyldiphenyl sulfone, as determined by preparing a melting point composition curve from authentic samples of the two isomers. The metalation also gave a small amount of a dicarboxylic acid, presumably[5] 2,2'-dicarboxy-4-methyldiphenyl sulfone.

On comparing the metalations of 4-bromodiphenyl sulfone[4] and 4-methyldiphenyl sulfone, it is striking that the former gives only one isomer while the latter sulfone gives a mixture of isomers whose composition approaches that expected on the basis of statistical distribution. However, the stronger directive influence of a bromine substituent over a methyl substituent in the metalation reaction is not surprising when one considers the well known greater inductive effect of the former group.[6]

The metalation of dimesityl sulfone gave 25% of a carboxydimesityl sulfone. One of the possible isomers, 3-carboxydimesityl sulfone, was prepared as outlined.



However, the product of this sequence of reactions was different from that obtained by metalating dimesityl sulfone. Furthermore, both of these products were different from the compound II formed from chloromethylated mesityl xylyl sulfide.



I

II

If chloromethylation of I had definitely occurred ortho to the sulfide group, the possibility of metalation at an ortho methyl group on dimesityl sulfone could have been tested. However, although a sulfide group is a more powerful orienting group than methyl in electrophilic substitutions,[7] the fact that mesitylene[8] and bromomesitylene[9] are readily chloromethylated under practically the same conditions as those used with simple sulfides,[7] places in doubt the orientation obtained in the present chloromethylation reaction. Attempts to clarify the structure of II by decarboxylation were unsuccessful.

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[1] Taken from Mr. Norman's Ph.D. thesis. Presented at the Chicago Meeting of the American Chemical Society, September, 1953.

[2] National Institutes of Public Health Fellow, 1951–1952.

[3] H. Gilman and F. J. Webb, THIS JOURNAL, **71**, 4062 (1949).

[4] W. E. Truce and M. F. Amos, *ibid.*, **73**, 3013 (1951).

[5] H. Gilman and D. L. Esmay, *ibid.*, **75**, 278 (1953).

[6] L. E. Sutton, *Proc. Roy. Soc.* (*London*), **A133**, 668 (1931); J. Kendall, THIS JOURNAL, **36**, 1069 (1914); W. Ostwald, *Z. physik. Chem.*, **3**, 369 (1889).

[7] E. G. Howard, E. Campaigne and R. L. Shriner, THIS JOURNAL, **70**, 4251 (1948); J. H. Wood, M. A. Perry and C. C. Tung, *ibid.*, **72**, 2989 (1950).

[8] R. C. Fuson and N. Rabjohn, *Org. Syntheses*, **25**, 65 (1945).

[9] G. Vavon, J. Bolle and J. Calin, *Bull. soc. chim.*, [5] **6**, 1025 (1920).

During the early work on the synthesis of II the question arose as to whether or not a "hindered" sulfide, such as dimesityl sulfide, could be oxidized to the corresponding sulfone.[10] It was found that dimesityl sulfide, prepared by the reaction of mesitylmagnesium bromide with mesitylenesulfenyl chloride, is readily oxidized by hydrogen peroxide in the usual manner to the corresponding sulfone.

In the preparation of mesitylenesulfonyl chloride by the chlorination of thiomesitol, trichloromesitylene [$C_6Cl_3(CH_3)_3$] was isolated as a by-product. This represents another example of the cleavage of carbon–sulfur bonds by chlorine, which has previously been observed with several sulfonic acids.[11]

Experimental[12]

Metalation of Phenyl *p*-Tolyl Sulfone.—A filtered solution of *n*-butyllithium, prepared in the usual manner[13] from 17.1 g. (0.125 mole) of *n*-butyl bromide, 1.94 g. (0.28 mole) of lithium wire and 135 ml. of ether, was added during *ca.* 15 minutes and with ice-bath cooling to 23.2 g. (0.10 mole) of phenyl *p*-tolyl sulfone (m.p. 126–126.5°) in *ca.* 500 ml. of ether. After 1.5 hours in the ice-bath, the reaction mixture was allowed to reach room temperature during an additional hour and under constant stirring. A large excess of Dry Ice was added in small pieces as rapidly as the bubbling and frothing would permit. The resulting mixture was hydrolyzed with 100 ml. of 3 *N* hydrochloric acid. After washing the ether layer once with water, it was extracted with two 50-ml. portions of 5% sodium hydroxide solution and 50 ml. of water. The ether layer yielded 6 g. of unreacted sulfone. On acidification, the combined aqueous extracts deposited a colorless oil, which slowly crystallized in a desiccator and left a white solid when taken up in boiling benzene. The solid weighed 1.9 g. after recrystallization from water; m.p. 245–251°, neut. equiv. 168, calcd. for 2,2′-dicarboxy-4-methyldiphenyl sulfone, 160. On evaporating the benzene solution to a small volume, 13.5 g. of solid was deposited; m.p. 115–135°, 122–132° after several recrystallizations from benzene.

A solution of 0.5 g. of the preceding solid in 10 ml. of concd. sulfuric acid kept at 190° for 15 minutes gave 0.34 g. (72%) of 2-methylthioxanthone-10-dioxide, m.p. 197–198°, reported[15] 199°.

Anal. Calcd. for $C_{14}H_{12}O_4S$: C, 60.85; H, 4.38. Found: C, 60.31, 60.29; H, 4.44, 4.38.

2-Carboxy-4-methyldiphenyl Sulfone.—A mixture of 6.2 g. (0.025 mole) of potassium 2-bromo-5-methylbenzoate,[14] 7.9 g. (0.044 mole) of potassium benzenesulfinate, 0.35 g. of copper powder and 40 ml. of *n*-amyl alcohol was held at reflux temperature, 136–139°, for 3.5 hours. The mixture was cooled and, after 50 ml. of water was added, filtered. The layers were separated, and the aqueous layer was acidified and extracted with three small portions of ether. These were combined and evaporated to a residue which was kept on a steam-bath and under vacuum for 1.5 hours. Recrystallization from benzene gave 1.7 g. (25% yield) of 2-carboxy-4-methyldiphenyl sulfone, m.p. 168.5–169°. A similar run gave a 41% yield.

Anal. Calcd. for $C_{14}H_{12}O_4S$: C, 60.85; H, 4.38. Found: C, 60.89; H, 4.42.

2-Carboxy-4′-methyldiphenyl Sulfone.—This material was prepared similarly as the 2,4-isomer. From 4.0 g. (0.017 mole) of potassium *o*-bromobenzoate, 5.8 g. (0.025 mole) of potassium *p*-toluenesulfinate, 0.25 g. of copper powder and 20 ml. of *n*-amyl alcohol there was obtained 1.45 g. (31% yield) of 2-carboxy-4′-methyldiphenyl sulfone. Another preparation starting with 5.9 g. of the *o*-bromobenzoate, 8.5 g. of sulfinate, 0.35 g. of copper powder and 40 ml. of amyl alcohol gave 1.9 g. (19% yield) of the acid. The product melted at 161–162° after recrystallizations from benzene; reported[15] m.p. 155°.

Anal. Calcd. for $C_{14}H_{12}O_4S$: C, 60.85; H, 4.38. Found: C, 60.92, 60.98; H, 4.76, 4.65.

Mixed Melting Points of 2-Carboxy-4-methyldiphenyl Sulfone and 2-Carboxy-4′-methyldiphenyl Sulfone.—Samples of these two acids were weighed together to give mixtures of varying composition. These were dissolved in minimum boiling benzene, and the resulting solutions evaporated slowly to dryness. Melting points of these mixtures were determined, and the upper values (representing complete melt) plotted. The unknown mixture corresponded to either 51–49 or 41–59% of the 2,4- and 2,4′-isomers, respectively, the eutectic occurring between these two points. Since addition of a small amount of the 2,4-isomer to the unknown lowered the m.p., while the 2,4′-isomer raised the m.p., the composition of the unknown was established as the latter possibility. A mixture of the authentic isomers having this composition did not alter the m.p. on admixture with the unknown.

Weight of 2,4-isomer in mg.	Weight of 2,4′-isomer in mg.	Composition, %	Melting point, °C.
58.3	6.5	90–10	163
48.1	12.0	80–20	158
43.0	18.3	70–30	149
35.4	23.5	60–40	140
29.6	29.8	50–50	129
24.5	36.6	40–60	132
22.7	49.8	31–69	140
13.9	68.6	17–83	150
7.5	67.6	10–90	155
	Unknown and 2,4-isomer		128
	Unknown and 2,4′-isomer		137
	Unknown and known mixture		132

The Metalation of Dimesityl Sulfone.—A suspension of 22.8 g. (0.075 mole) of dimesityl sulfone[16] in 500 ml. of ether was metalated in the usual way with *n*-butyllithium prepared in a proportionate quantity. After the usual isolation procedure, 6.6 g. (25% yield) of acid, which melted at 265–267° dec., was obtained. A sample for analysis was recrystallized from glacial acetic acid.

Anal. Calcd. for $C_{19}H_{22}O_4S$: C, 65.87; H, 6.40. Found: C, 65.62; H, 6.26.

There was also obtained 4.5 g. of non-acidic material from which no dimesityl sulfone could be obtained nor could it be recrystallized to a sharp melting product.

3-Carboxydimesityl Sulfone.—Following the procedure used to prepare dimesityl sulfone, a mixture of 60.7 g. (0.205 mole) of bromomesitylenesulfonyl chloride, prepared by the method of Huntress and Autenreith,[17] 33.3 g. (0.277 mole) of mesitylene, 33.3 g. (0.25 mole) of anhydrous aluminum chloride and 300 ml. of carbon disulfide gave 40.8 g. (52% of theory) of 3-bromodimesityl sulfone melting at 137–138°.

Anal. Calcd. for $C_{18}H_{21}BrO_2S$: C, 56.69; H, 5.55. Found: C, 57.05; H, 5.86.

A mixture of 19 g. (0.05 mole) of 3-bromodimesityl sulfone, 5.1 g. of cuprous cyanide and a small crystal of cupric sulfate pentahydrate was heated at 250° for 6 hours. The reaction mixture was extracted with small portions of boiling ethanol. The ethanol solution was partially decolorized with charcoal and cooled to give yellowish-brown fine crystals. Recrystallization from methanol gave 8 g. (49%) of a colorless 3-cyanodimesityl sulfone, m.p. 156–157.5°.

Anal. Calcd. for $C_{19}H_{21}NO_2S$: N, 4.28. Found: N, 4.32.

Following a general hydrolysis procedure[18] with slight modifications, a mixture of 3.9 g. of 3-cyanodimesityl sulfone in 57 ml. of 95% ethanol was made alkaline to litmus with sodium hydroxide solution. After adding 15 ml. of 30% hydrogen peroxide, the mixture was kept in a vapor-

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[10] J. E. Woodbridge, THIS JOURNAL, **75**, 2528 (1953), oxidized *t*-butyl sulfide to *t*-butyl sulfone in moderate yield with hydrogen peroxide.

[11] C. M. Suter, "Organic Chemistry of Sulfur," John Wiley and Sons, Inc., New York, N. Y., 1944, p. 394.

[12] All melting points are corrected.

[13] H. Gilman, *et al.*, THIS JOURNAL, **71**, 1499 (1949).

[14] W. Borsche and W. Scriba, *Ann.*, **541**, 288 (1939).

[15] F. Ullmann and A. Lehner, *Ber.*, **38**, 741 (1905).

[16] M. E. Maclean and R. Adams, THIS JOURNAL, **55**, 4685 (1933).

[17] E. H. Huntress and F. H. Carten, *ibid.*, **62**, 511 (1940).

[18] L. McMaster and C. Noller, *J. Indian Chem. Soc.*, **12**, 632 (1932).

bath of refluxing chloroform for 2 hours. An additional 15-ml. quantity of 30% hydrogen peroxide was added and heating was continued for 5 hours. The reaction mixture was cooled and carefully neutralized to litmus with 5% sulfuric acid. The solvent was evaporated almost to dryness, water was added and the resulting solid was recrystallized from 95% ethanol; yield 3.46 g., m.p. 112–126°. When recrystallized twice from water–acetic acid solution the solid softened at 113° and finally melted at 189–192°. A portion (3.2 g.) of this solid was hydrolyzed[19] to give 2.0 g. (48% based on 3-cyanodimesityl sulfone) of an acid with m.p. 177.5–179.5° after recrystallization from acetic acid.

Anal. Calcd. for $C_{19}H_{22}O_4S$: C, 65.87; H, 6.40. Found: C, 65.98; H, 6.01.

2,4-Dimethylphenyl Mesityl Sulfide.—From 155 g. (0.76 mole) of 2,4-dimethylbenzenesulfonyl chloride and 268 g. of zinc dust[20] there was obtained 74.3 g. (71% yield) of 2,4-dimethylthiophenol, b.p. 92–94° (15 mm.), reported b.p. 207–208°[21] and 212–214°.[22] A slow stream of chlorine[23] was passed into 150 ml. of carbon tetrachloride while 74.3 g. (0.54 mole) of 2,4-dimethylthiophenol in 470 ml. of carbon tetrachloride was added slowly over a period of 3 hours at *ca.* −3° and in the dark to yield 79.8 g. (86% yield) of 2,4-dimethylbenzenesulfenyl chloride, b.p. 92–96° (3 mm.). To a Grignard reagent,[24] prepared from 70.1 g. (0.352 mole) of mesityl bromide, 8.6 g. (0.352 mole) of magnesium turnings and 275 ml. of ether, was added dropwise 51.8 g. (0.30 mole) of 2,4-dimethylbenzenesulfenyl chloride in 2–3 times its volume of ether. After standing overnight the mixture was hydrolyzed and the ether layer was separated, dried over calcium chloride, and distilled to give 59.0 g. (77% yield) of product, b.p. 173–174° (4 mm.), m.p. 58–59°.

Anal. Calcd. for $C_{17}H_{20}S$: C, 79.63; H, 7.86. Found: C, 80.37, 80.39; H, 8.16, 8.15.

Oxidation of 1 g. of mesityl *m*-xylyl sulfide in about 20 ml. of glacial acetic acid with 6 ml. of 30% hydrogen peroxide gave a white solid which was recrystallized from methanol and had m.p. 156–157.5°, reported[25] 149°.

Anal. Calcd. for $C_{17}H_{20}O_2S$: C, 70.79; H, 6.99. Found: C, 70.80; H, 6.85.

Chloromethylated 2,4-Dimethylphenyl Mesityl Sulfide.—While bubbling hydrogen chloride through a mixture of 23.2 g. (0.09 mole) of mesityl *m*-xylyl sulfide in 60 ml. of glacial acetic acid and 75 ml. of concd. hydrochloric acid maintained at 60–65°, two separate 1.5-g. portions of trioxymethylene were added at an interval of 2.5 hr. After maintaining the temperature and passage of gas for 2.5 hr. more, heating was stopped and the gas was bubbled through for another hour. Next day the mixture was poured over ice and extracted with ether. The ether extract was washed with sodium bicarbonate solution until neutral, dried over calcium chloride and evaporated to a non-crystallizable solid, which gave a precipitate with alcoholic silver nitrate. A mixture of this solid, 7.7 g. (0.157 mole) of sodium cyanide, 10 ml. of water and 20 ml. of 95% ethanol was refluxed for 5 hours. On pouring the mixture over ice there was formed a solid, which was taken up in ether and washed several times with water. The ether was evaporated to give 20.8 g. of an oily solid, which contained nitrogen and sulfur but no halogen.

A mixture of 5.8 g. of the preceding nitrile, 22.5 ml. of water and 18.8 ml. of concd. sulfuric acid was refluxed for 6 hours. The mixture was poured over ice and extracted with ether. Alkaline extraction of the ether solution with subsequent acidification gave 1.4 g. of crude acid. The remainder of the solid containing the nitrile was hydrolyzed in the same manner to give 3.75 g. (18% based on mesityl *m*-xylyl sulfide) of crude acid. A small amount of this acid was recrystallized from a methanol-water solution to give white needles melting at 163–164°; neut. equiv. 307.6, calculated 314.

Anal. Calcd. for $C_{19}H_{22}O_2S$: C, 72.57; H, 7.05. Found: C, 72.21; H, 7.14.

To a solution of 0.3 g. of the acid in 15 ml. of 80% acetic acid was added a solution of 0.48 g. of potassium permanganate in 7 ml. of water. After standing for about 2 hours with occasional shaking, the resulting brown mixture was decolorized with a few drops of 30% hydrogen peroxide. The solid obtained by adding 45 ml. of water, cooling and filtering, was recrystallized from aqueous acetic acid. Three crops of crystals were obtained, all of which melted at 148–153° after first softening at about 100°. The combined material was recrystallized from methanol to give an acid with m.p. 156–158° and mixed with preceding sulfide m.p. 141–156°; neut. equiv. 347.5, calculated 346. The same product was obtained by oxidizing a solution of 0.5 g. of the preceding sulfide in 6 ml. of glacial acetic acid with 3 ml. of 30% hydrogen peroxide at reflux temperature for 1.5 hours.

Anal. Calcd. for $C_{19}H_{22}O_4S$: C, 65.87; H, 6.40. Found: C, 65.89; H, 6.54.

Dimesityl Sulfide.—Mesitylenesulfonyl chloride (160 g., 0.75 mole) was reduced to 73.8 g. (66% yield) of thiomesitol, b.p. 109.5–111.5° (18 mm.), reported[26] b.p. 228–229°. After treating[24] thiomesitol (38 g., 0.25 mole) with chlorine in carbon tetrachloride at a temperature of −8 to −10°, there was isolated 29.8 g. of mesitylenesulfenyl chloride, b.p. 95–101° (2.5–3.5 mm.), and trichloromesitylene, m.p. 209.5–210.5° with sublimation, reported[27] 207°, mixed m.p. with authentic[28] sample 209–210°.

To a Grignard reagent, prepared from 37.4 g. (0.187 mole) of mesityl bromide, 4.58 g. (0.188 mole) of magnesium and 125 ml. of ether, was added 29.8 g. of mesitylenesulfenyl chloride in about 2.5 times its volume of ether.[24] The resulting distillate, b.p. 173–174° (2 mm.), solidified and was recrystallized from 95% ethanol as flat, square, colorless crystals with m.p. 91–92°.

Anal. Calcd. for $C_{18}H_{22}S$: C, 79.94; H, 8.20. Found: C, 80.40, 80.39; H, 8.01, 8.00.

A solution of 1 g. of dimesityl sulfide in 20 ml. of glacial acetic acid when treated in the usual manner with 5 ml. of 30% hydrogen peroxide gave a solid, which was recrystallized from aqueous acetic acid in the form of small white needles, identical in appearance with dimesityl sulfone, m.p. 202.5–204°, m.p. of an authentic sample of dimesityl sulfone 203.5–205°, mixed m.p. 203.5–205°.

Attempted Decarboxylations of Sulfide Corresponding to (II).—(1) Three-tenths of a gram of acid was dissolved in 1 g. of quinoline and 0.1 g. of copper bronze was added.[29] The temperature was raised to the reflux point and maintained there for 15 minutes. No alkali-insoluble product was isolated. (2) A mixture of 1.6 g. of the sodium salt of the acid and 6 g. of powdered sodium hydroxide was heated under reduced pressure at a temperature of 195–210°. No alkali-insoluble product was isolated. (3) A mixture of 5 g. of 100 mesh powdered soft glass, 0.2 g. of powdered iron and 1 g. of the acid was heated for 2 hours at 195°. No alkali-insoluble product was isolated.

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