[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Metalation of Diaryl Sulfones. I[1]

BY WILLIAM E. TRUCE AND M. FREDERICK AMOS[2]

The metalation of diaryl sulfones by *n*-butyllithium has been realized. Diphenyl sulfone gave, after carbonation, *o*-benzenesulfonylbenzoic acid in 80% yield and *o*-bromophenyl phenyl sulfone gave the same acid in 64% yield. *m*-Bromophenyl phenyl sulfone gave a 54% yield of 3-bromo-2-carboxydiphenyl sulfone. *p*-Bromophenyl phenyl sulfone yielded 52% of 4-bromo-2-carboxydiphenyl sulfone, and in one experiment, 2% of *p*-benzenesulfonylbenzoic acid. Phenyl 2-thienyl sulfone gave a 60% yield of 2-benzenesulfonyl-5-thiophenecarboxylic acid. Explanations for the results obtained are offered.

Methods of forming organometallic derivatives of sulfones are limited. The reaction of a halogenated monosulfone with magnesium under the usual conditions for the formation of a Grignard reagent has to date been unsuccessful. For example, when *p*-bromophenyl methyl sulfone is treated with magnesium, no reaction occurs.[3] Furthermore, we found that the bromophenyl phenyl sulfones do not react with magnesium or lithium under the usual conditions. However, Kohler and Tishler[4] formed Grignard reagents from both the monobromo and the dibromo derivative of bis-(benzenesulfonyl)-methane, *i.e.*, $(C_6H_5SO_2)_2CHBr$ and $(C_6H_5SO_2)_2CBr_2$. Moreover, when methyl *p*-tolyl sulfone is treated with ethylmagnesium bromide, metalation occurs with the formation of *p*-toluenesulfonylmethylmagnesium bromide.[5] Analogous results are obtained when methyl phenyl sulfone is treated with *n*-butyllithium.[6] On treating bromomethyl *p*-tolyl sulfone with phenylmagnesium bromide, halogen–metal interchange occurs and *p*-toluenesulfonylmethylmagnesium bromide is obtained.[5]

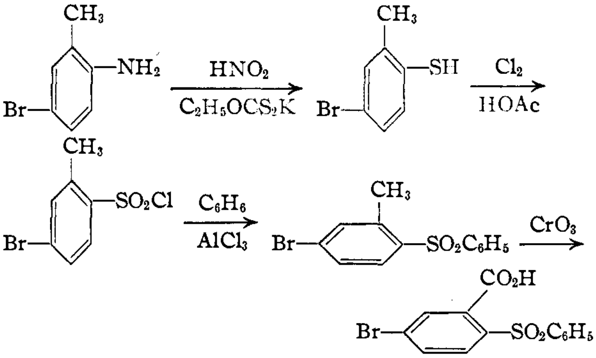
Many instances of metalations by *n*-butyllithium have been reported.[7] The metalation of aromatic compounds containing substituents, which normally direct electrophilic agents to the meta position, has been limited to two cases. The metalation of trifluoromethylbenzene yielded, after carbonation, both the ortho and meta acids in the ratio of about five to one.[8] Gilman and Webb[6] reported that after carbonating the metalation product of diphenyl sulfone, an acidic material, which they were unable to purify, was isolated.

This paper reports on the reaction of *n*-butyllithium with diphenyl sulfone,[9] *p*-bromophenyl phenyl sulfone,[10] phenyl 2-thienyl sulfone,[11] *o*-bromophenyl phenyl sulfone and *m*-bromophenyl phenyl sulfone. The last two compounds are reported here for the first time.

By carbonating the metalation product of diphenyl sulfone, *o*-benzenesulfonylbenzoic acid was obtained in 80% yield and 61% conversion. The proof of structure consisted of comparing this product with an authentic sample.[12]

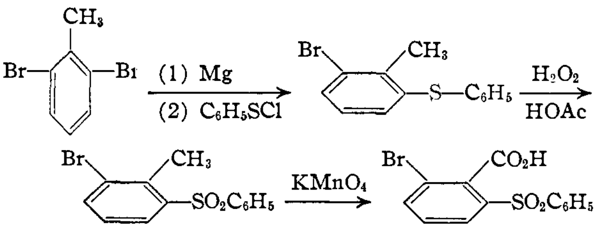
The action of *n*-butyllithium on *o*-bromophenyl phenyl sulfone gave, after carbonation, a 64.5% yield of *o*-benzenesulfonylbenzoic acid.

When *p*-bromophenyl phenyl sulfone was metalated, *p*-benzenesulfonylbenzoic acid[13] was obtained in only trace (1.9%) quantities. The principal product was 4-bromo-2-carboxydiphenyl sulfone, obtained in 52% yield. The structure of this compound was determined by preparing an authentic sample in the following manner



4-Bromo-2′-carboxydiphenyl sulfone was also prepared and found to be different from the metalation product.

The metalation product of *m*-bromophenyl phenyl sulfone, obtained in 54% yield, was shown to be 3-bromo-2-carboxydiphenyl sulfone, an authentic sample of which was obtained as indicated.



In addition, the following bromo-carboxydiphenyl sulfones were also prepared and found to be different from the metalation product: 3-bromo-5-carboxydiphenyl sulfone, 5-bromo-2-carboxydiphenyl sulfone and 3-bromo-2′-carboxydiphenyl sulfone.

The metalation of phenyl 2-thienyl sulfone gave an acid, identified as 2-benzenesulfonyl-5-thiophenecarboxylic acid, in 60% yield and 41.6% conversion. An authentic sample of this acid was prepared by the series of reactions

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[3] H. S. Holt and E. E. Reid, THIS JOURNAL, **46**, 2329 (1924).

[4] E. P. Kohler and M. Tishler, *ibid.*, **57**, 217 (1935).

[5] W. M. Ziegler and R. Conner, *ibid.*, **62**, 2596 (1940).

[6] H. Gilman and F. J. Webb, *ibid.*, **71**, 4062 (1949).

[7] A. A. Morton, *Chem. Revs.*, **35**, 1 (1944).

[8] J. D. Roberts and D. Y. Curtin, THIS JOURNAL, **68**, 1658 (1946).

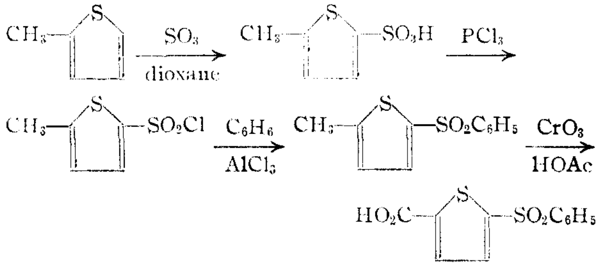
[9] H. Beckurts and R. Otto, *Ber.*, **11**, 2066 (1878).

[10] J. Olivier, *Rec. trav. chim.*, **33**, 119 (1914).

[11] N. Burton and W. A. Davy, *J. Chem. Soc.*, 526 (1948).

[12] W. S. Weedon and H. W. Doughty, *Am. Chem. J.*, **33**, 417 (1905).

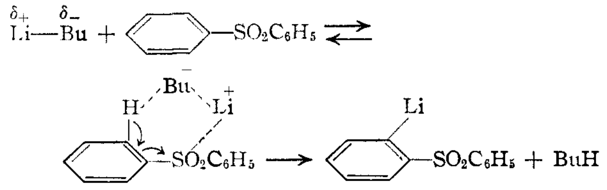
[13] L. C. Newell, *ibid.*, **20**, 304 (1898).



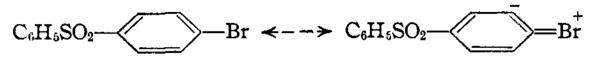
Muhlert[14] reported the preparation of 2-methyl-5-thiophenesulfonic acid by the cleavage of 2-methyl-5-acetylthiophene with oleum. His material yielded a sulfonamide which melted at 78–80°. We found that the sulfonation of 2-methylthiophene with dioxane sulfotrioxide yielded an acid which gave a sulfonamide melting at 119–121°. That this product was 2-methyl-5-thiophenesulfonic acid was demonstrated by subjecting it to the series of reactions given above. The final acid was identical with that obtained by the metalation of phenyl 2-thienyl sulfone. Muhlert[14] did not establish the position of the sulfonic acid group. He assumed that it took up the position of the ketonic group, which was removed. In the light of the present work, it appears that further study on the cleavage of ketones by oleum would be desirable.

In explaining metalation reactions, Roberts and Curtin[8] emphasize nucleophilic attack while Morton[7,15] emphasizes electrophilic attack. Both postulate an intermediate complex resulting from attack by the lithium portion of *n*-butyllithium on an electron rich substituent, *e.g.*, trifluoromethyl, with accompanying attack by the butyl portion of *n*-butyllithium at the most acidic position on the benzene ring.

The sulfone group is ordinarily thought of as a meta director to electrophilic attacking agents, but when diphenyl sulfone was metalated, attack took place ortho to the sulfone group. The same explanation employed for trifluoromethylbenzene can be used here, *i.e.*



In *p*-bromophenyl phenyl sulfone, the inductive effect of the sulfone group on the position ortho to it in the brominated ring would be strengthened by the inductive effect of the bromine substituent. Resonance interaction of the latter group with the ring would have no appreciable effect on these positions as

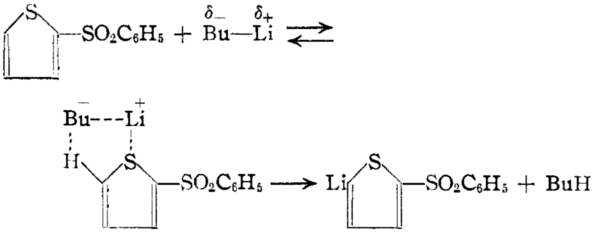


This reasoning leads to the prediction that *p*-bromophenyl phenyl sulfone would be attacked by *n*-butyllithium in the positions ortho to the sulfone group in the bromine-substituted ring. This was borne out by the experimental results since the main metalation product was 4-bromo-2-carboxydiphenyl sulfone.

With *m*-bromophenyl phenyl sulfone, the inductive effect of the bromine atom reinforces that of the sulfone group at the position ortho to both groups. Although the resonance effect of the bromine atom would tend to counteract its inductive effect at this position, the latter effect should predominate. This would be anticipated on the basis that in electrophilic substitutions on bromobenzene, the orientation is ortho–para (explained by the resonance theory) but with deactivation (explained by the inductive effect). The prediction is borne out by experimental evidence since metalation occurs on the carbon atom ortho to both the bromine atom and the sulfone group yielding 3-bromo-2-carboxydiphenyl sulfone.

In the metalation of *o*-bromophenyl phenyl sulfone, halogen–metal interchange occurs and, on carbonation, *o*-benzenesulfonylbenzoic acid is formed. Here again the inductive effect of the sulfone group would withdraw electrons from the ring. This tendency would be further increased if the metal portion of *n*-butyllithium formed the intermediate complex with the sulfone group. Nucleophilic displacement by the butyl portion of *n*-butyllithium would result in the formation of *n*-butyl bromide and *o*-benzenesulfonylphenyllithium.

The metalation of phenyl 2-thienyl sulfone occurs with attack at the 5-position of the thiophene nucleus rather than in positions ortho to the sulfone group. Presumably the reaction proceeds



Experimental[16]

***m*-Bromophenyl Phenyl Sulfone.**—*m*-Nitrophenyl phenyl sulfone[17] was prepared by a Friedel–Crafts reaction of *m*-nitrobenzenesulfonyl chloride[18] with benzene in 68.5% yield. The nitrosulfone was reduced to the aminosulfone with tin and hydrochloric acid in 89% yield; m.p. 110–112°.

m-Aminophenyl phenyl sulfone (208.4 g., 0.9 mole) in 470 ml. of 48% hydrobromic acid was cooled below 5° and diazotized with a solution of 63 g. (0.9 mole) of sodium nitrite in 100 ml. of water. The cold diazonium solution was added to a cold cuprous bromide solution (prepared in a manner analogous to that used for cuprous chloride[19]) with stirring. A heavy brown precipitate was formed. The mixture was allowed to come to room temperature, during which time nitrogen was freely evolved. When the evolution of nitrogen slackened, the mixture was warmed on a steam-cone for 15 minutes, cooled and filtered. A solid, which melted at 121.5–123.5° after two recrystallizations from a 50–50 ethanol–water mixture, was obtained; yield 46 g. (17.2%).

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[14] F. Muhlert *Ber.*, **19**, 1621 (1886).

[15] A. A Morton, THIS JOURNAL, **69**, 969 (1947).

[16] All melting points are corrected unless otherwise indicated.

[17] J. Olivier, *Rec. trav. chim.*, **35**, 110 (1915).

[18] H. H. Hodgson and J. S. Whitehurst, *J. Chem. Soc.*, 482 (1944).

[19] A. H. Blatt, "Organic Syntheses," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p. 170.

Anal. Calcd. for $C_{12}H_9O_2SBr$: C, 48.48; H, 3.03; Br, 26.9. Found: C, 48.55; H, 3.06; Br, 26.7.

o-Bromophenyl Phenyl Sulfone.—*o*-Nitrophenyl phenyl sulfide[20] was oxidized to the sulfone with 30% hydrogen peroxide in 99% yield. The nitrosulfone was reduced to the aminosulfone with tin and hydrochloric acid in 84% yield.

When 0.1 mole of the aminosulfone was subjected to the Sandmeyer reaction, following the procedure used for the meta isomer, a 17% yield of *o*-bromophenyl phenyl sulfone, m.p. 117–119°, was obtained.

Anal. Calcd. for $C_{12}H_9O_2SBr$: C, 48.48; H, 3.03; Br, 26.8. Found: C, 48.55; H, 2.80; Br, 26.8.

Starting with 0.5 mole of the aminosulfone, a large amount of solid melting at 84–95° was obtained. All attempts to purify this solid failed.

o-Bromobenzenesulfonyl chloride was prepared in 50% yield from *o*-bromothiophenol[21] by chlorination in acetic acid solution.[22]

A Friedel–Crafts reaction between *o*-bromobenzenesulfonyl chloride and benzene gave a 63.5% yield of *o*-bromophenyl phenyl sulfone, m.p. 118–119° after recrystallization from ethanol.

General Metalation Procedure.—An ether solution of *n*-butyllithium prepared in the usual manner[23] was added over a half-hour period to 30 g. of the sulfone in 500 ml. of anhydrous ether at ice-bath temperature. A nitrogen atmosphere was used. The mixture was stirred in the ice-bath for two hours and for one hour after removal of the ice-bath. Excess Dry Ice was added and the mixture was hydrolyzed with dilute (3 *N*) hydrochloric acid. The ether layer was extracted with 5% sodium hydroxide solution and then evaporated yielding unreacted sulfone and/or small amounts of non-acidic material.

Acidification of the basic ether extract yielded the acid either as a solid or as an oil which solidified on standing in an ice-bath for two or three hours. Concentration of the acid layer sometimes yielded traces of acidic material.

Metalation of Diphenyl Sulfone.—Thirty grams (0.137 mole) of diphenyl sulfone was treated with *n*-butyllithium prepared from 17 g. (0.184 mole) of *n*-butyl chloride and 2.8 g. (0.4 g. atom) of lithium. The product, *o*-benzenesulfonylbenzoic acid, recrystallized from benzene and melting at 143–144°, weighed 22 g. (Seven grams of diphenyl sulfone was recovered from the ether layer.) Conversion was 61%, yield 80%. The melting point was not depressed by an authentic sample.[12]

Anal. Calcd. for $C_{13}H_{10}O_4S$: C, 59.54; H, 3.81. Found: C, 59.55; H, 3.85.

Metalation of o-Bromophenyl Phenyl Sulfone.—Thirty grams (0.101 mole) of *o*-bromophenyl phenyl sulfone was treated with *n*-butyllithium prepared from 13.6 g. (0.148 mole) of *n*-butyl chloride and 2.1 g. (0.3 g. atom) of lithium. The product, *o*-benzenesulfonylbenzoic acid, recrystallized from benzene and melting at 142.5–143.5°, weighed 17 g. (64.5% yield). The melting point was not depressed by an authentic sample.[12] The ether layer yielded 2 g. of a non-acidic material melting at 73–100°. Repeated recrystallizations from ethanol yielded a small amount of diphenyl sulfone.

Metalation of p-Bromophenyl Phenyl Sulfone.—Thirty grams (0.101 mole) of *p*-bromophenyl phenyl sulfone was treated with *n*-butyllithium prepared from 13.6 g. (0.148 mole) of *n*-butyl chloride and 2.1 g. (0.3 g. atom) of lithium. Evaporation of the ether layer gave 3 g. of a pale yellow solid (I), m.p. 79–80° after recrystallization from alcohol.

Anal. (I) Found: C, 55.4, 55.2; H, 3.80, 3.90; S, 12.41, 12.27.

The main product was 4-bromo-2-carboxydiphenyl sulfone, m.p. 153–154°; yield 18 g. (52.2%). The m.p. was not depressed when mixed with an authentic sample prepared as described below.

Anal. Calcd. for $C_{13}H_9O_4BrS$: C, 45.74; H, 2.64; Br, 23.46. Found: C, 45.74; H, 2.87; Br, 23.38.

Concentration of the acid layer from which the main product had been isolated gave 0.5 g. (1.88% yield) of *p*-benzenesulfonylbenzoic acid, m.p. 273–276°. The m.p. was not depressed by an authentic sample prepared by the method of Newell.[13]

When a duplicate experiment was run, no trace of compound I was found. Evaporation of the ether layer yielded 3 g. of crude material from which, by recrystallization from ethanol, 0.35 g. of material (II), m.p. 222–224°, was obtained.

Anal. (II) Found: C, 49.00; H, 1.90; Br, 29.03.

4-Bromo-2-carboxydiphenylsulfone was still the main product but no trace of *p*-benzenesulfonylbenzoic acid was found.

4-Bromo-2-methylbenzenesulfonyl Chloride.—One hundred and twenty-two grams (0.60 mole) of 4-bromo-2-methylthiophenol, prepared by the xanthogenate method[21] from 4-bromo-2-methylaniline,[24] was treated with chlorine in acetic acid solution following a known procedure.[16] The product was recrystallized from acetic acid; m.p. 64–65°, yield 41 g. (25.5%).

Anal. Calcd. for $C_7H_6O_2SBrCl$: C, 31.2; H, 2.22; halogen (as Br), 52.50. Found: C, 31.42; H, 2.30; halogen (as Br), 52.55.

By adding liquid ammonia to a small amount of 4-bromo-2-methylbenzenesulfonyl chloride, the sulfonamide was prepared. Recrystallization from ethanol gave a solid, m.p. 179.5–180°.

Anal. Calcd. for $C_7H_8O_2NBr$: N, 5.65. Found: N, 5.69.

4-Bromo-2-methyldiphenyl Sulfone.—This was prepared by the Friedel–Crafts reaction with 41 g. (0.152 mole) of 4-bromo-2-methylbenzenesulfonyl chloride, 100 ml. of benzene and 22 g. (0.165 mole) of aluminum chloride. The yield of material melting at 106–106.5° after recrystallization from ethanol was 35 g. (74%).

Anal. Calcd. for $C_{13}H_{11}O_2SBr$: C, 50.01; H, 3.57; Br, 25.6. Found: C, 50.32; H, 3.62; Br, 25.55.

4-Bromo-2-carboxydiphenyl Sulfone.—This was prepared from 4-bromo-2-methyldiphenyl sulfone by the oxidation procedure of Newell.[13] The product was recrystallized from benzene and melted at 153–154°.

p-Bromobenzenesulfenyl Chloride.—Forty-eight and six-tenths grams (0.257 mole) of *p*-bromothiophenol (m.p. 70–74°, prepared by the xanthogenate method[21] from *p*-bromoaniline) was treated with chlorine in carbon tetrachloride following a known procedure for the preparation of sulfenyl chlorides.[25] The product boiled at 105–107° (4 mm.); yield 37 g. (64.5%).

Anal. Calcd. for C_6H_4SBrCl: C, 32.3; H, 1.79; halogen (as Br), 63.30. Found: C, 32.35; H, 1.70; halogen (as Br), 63.05.

4-Bromo-2′-methyldiphenyl Sulfone.—A Grignard reagent was prepared from 40.6 g. (0.238) of *o*-bromotoluene and 5.9 g. (0.243 g. atom) of magnesium. An ether solution of 38.5 g. (0.164 mole) of *p*-bromobenzenesulfenyl chloride was added following the procedure of Lecher, *et al.*,[26] for the preparation of diphenyl sulfide. The crude 4-bromo-2′-methyldiphenyl sulfide, obtained by evaporation of the ether layer, was dissolved in acetic acid and oxidized to the sulfone with 30% hydrogen peroxide.[20] The product, after recrystallization from ethanol, melted at 82–83.5° and weighed 26.5 g. (54% based on the sulfenyl chloride).

Anal. Calcd. for $C_{13}H_{11}O_2SBr$: C, 50.01; H, 3.54; Br, 25.6. Found: C, 50.18; H, 3.51; Br, 25.78.

4-Bromo-2′-carboxydiphenyl Sulfone.—This was prepared from 4-bromo-2′-methyldiphenyl sulfone by the oxidation procedure of Newell[13]; m.p. 166.5–168.5°.

Anal. Calcd. for $C_{13}H_9O_4SBr$: C, 45.74; H, 2.64; Br, 23.46. Found: C, 45.55; H, 2.56; Br, 23.62.

m-Tolyl Phenyl Sulfone.—The Friedel–Crafts procedure starting with 69 g. (0.36 mole) of *m*-toluenesulfonyl chloride (prepared by chlorinating *m*-thiocresol[22]), 100 ml. of benzene and 48.6 g. (0.364 mole) of aluminum chloride was

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(20) H. Gilman and H. S. Broadbent, THIS JOURNAL, **69**, 2053 (1947).

(21) G. Schwarzenbach and H. Egli, *Helv. Chim. Acta*, **17**, 1176 (1934).

(22) T. Zincke and W. Frohneberg, *Ber.*, **43**, 840 (1910).

(23) G. Wittig, "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 575.

(24) H. Alt, *Ann.*, **252**, 319 (1889).

(25) E. Gebauer-Fulnegg, THIS JOURNAL, **49**, 2274 (1927).

(26) H. Lecher, F. Holschneider, K. Koberle, W. Speer and P. Stocklin, *Ber.*, **58**, 414 (1926).

used. The product, after recrystallization from ethanol, melted at 119–120.5°; yield 52 g. (62%).

Anal. Calcd. for $C_{13}H_{12}O_2S$: C, 67.24; H, 5.17. Found: C, 67.15; H, 5.19.

***m*-Benzenesulfonylbenzoic Acid.**—This was prepared from *m*-tolyl phenyl sulfone using the oxidation procedure of Newell[13]; m.p. 186–187°.

Anal. Calcd. for $C_{13}H_{10}O_4S$: C, 59.54; H, 3.81. Found: C, 59.50; H, 3.70.

Metalation of *m*-Bromophenyl Phenyl Sulfone.—Thirty grams (0.101 mole) of *m*-bromophenyl phenyl sulfone was treated with *n*-butyllithium prepared from 13.6 g. (0.148 mole) of *n*-butyl chloride and 2.1 g. (0.3 g. atom) of lithium. The main product, recrystallized from a 50–50 alcohol-water mixture and melting at 242–244° (uncor.), was 3-bromo-2-carboxydiphenyl sulfone; yield 18 g. (54%). The m.p. was not depressed when mixed with an authentic sample, prepared as outlined below.

Anal. Calcd. for $C_{13}H_9O_4SBr$: C, 45.74; H, 2.64; Br, 23.46. Found: C, 45.80; H, 2.74; Br, 23.57.

Concentration of the acid layer from which 3-bromo-2-carboxydiphenyl sulfone was isolated, yielded 0.5 g. of material melting at 208–222°. Attempts to purify this were unsuccessful.

Evaporation of the ether layer yielded 2 g. of material melting at 100–120°. Purification attempts were unsuccessful.

3,5-Dibromo-4-methylnitrobenzene.—Two moles of *p*-nitrotoluene and 3.2 g. of small nails were placed in a one-liter flask. The flask was warmed with steam until the nitrotoluene melted and then 700 g. (4.38 moles) of bromine was added dropwise. Evolution of hydrogen bromide began in a few moments and continued vigorously throughout the addition. After the addition was complete, the mixture was heated on a steam-cone until no more hydrogen bromide was evolved. The mixture was poured into water and the excess bromine destroyed with sodium thiosulfate. The product was extracted with ether, dried over drierite and distilled. Four fractions were obtained of which three solidified on standing a short time.

Fraction	B.p. °C.	B.p. Mm.	M.p., °C.
1	107–111	1	68–75
2	111–118	1	...
3	122–128	1	52–56
4	130–138	1	51.5–55.5

Fraction 1 appears to be mainly 3-bromo-4-methylnitrobenzene, m.p. 77.5°.[27] Fractions 3 and 4 were combined and recrystallized from ethanol yielding 127.8 g. (21.6%) of the dibromo compound, m.p. 54–56°. The reported m.p. is 57°.[27]

2,6-Dibromotoluene.—This was obtained by deaminating 3,5-dibromo-4-methylaniline (prepared by reducing 3,5-dibromo-4-methylnitrobenzene with tin and hydrochloric acid) using the procedure of Adams and Johnson[28]; b.p. 110.5–112° (12 mm.); yield 22.4%.

3-Bromo-2-methyldiphenyl Sulfone.—A Grignard reagent was prepared from 23.2 g. (0.093 mole) of 2,6-dibromotoluene and 2.25 g. (0.093 g. atom) of magnesium. An ether solution of 13.4 g. (0.093 mole) of benzenesulfenyl chloride[29] was added following the procedure of Lecher, *et al.*,[26] for the preparation of diphenyl sulfide. The crude 3-bromo-2-methyldiphenyl sulfide, obtained by evaporation of the ether layer, was dissolved in acetic acid and oxidized to the sulfone with 30% hydrogen peroxide.[20] The yield of product melting at 101–102.5°, after recrystallization from ethanol, was 9.7 g. (33.5%).

Anal. Calcd. for $C_{13}H_{11}O_2SBr$: C, 50.01; H, 3.57; Br, 25.6. Found: C, 49.98; H, 3.56; Br, 25.82.

3-Bromo-2-carboxydiphenyl Sulfone.—Four grams of 3-bromo-2-methyldiphenyl sulfone, 5 g. of potassium permanganate, one pellet of sodium hydroxide and 100 ml. of water were refluxed for nine hours. Excess permanganate was destroyed with ethanol. The manganese dioxide was filtered off and on acidification of the filtrate the product separated. Recrystallization from a 50–50 ethanol–water mixture gave an acid melting at 243–245° (uncor.).

5-Bromo-2-methylaniline.—This was prepared by reducing 200 g. (0.93 mole) of 4-bromo-2-nitrotoluene[30] with tin and hydrochloric acid, b.p. 102.5–103.5° (1.5 mm.); yield 109.8 g. (64%).

5-Bromo-2-methyldiphenyl Sulfone.—Forty-three grams (0.16 mole) of 5-bromo-2-methylbenzenesulfonyl chloride, prepared from 5-bromo-2-methylthiophenol (from 5-bromo-2-methylaniline by the xanthogenate method[21]) by chlorination,[22] was treated in a Friedel–Crafts reaction with 100 ml. of benzene and 23 g. (0.172 mole) of aluminum chloride. The product was recrystallized from ethanol, m.p. 120–121°; yield 11 g. (22%).

Anal. Calcd. for $C_{13}H_{11}O_2SBr$: C, 50.01; H, 3.57; Br, 25.6. Found: C, 49.99; H, 3.77; Br, 25.86.

5-Bromo-2-carboxydiphenyl Sulfone.—This was prepared from 5-bromo-2-methyldiphenyl sulfone by the oxidation method of Newell,[13] m.p. 199–200.5° after recrystallization from benzene.

Anal. Calcd. for $C_{13}H_9O_4SBr$: C, 45.74; H, 2.64. Found: C, 45.75; H, 2.58.

***m*-Bromobenzenesulfenyl Chloride.**—Forty-eight and six-tenths grams (0.256 mole) of *m*-bromothiophenol, prepared from *m*-bromoaniline by the xanthogenate method,[21] was treated with chlorine in carbon tetrachloride following a general procedure for preparing sulfenyl chlorides.[25] The yield of material boiling at 92–93° (1 mm.) was 27.3 g. (45.8%).

Anal. Calcd. for C_6H_4SBrCl: C, 32.2; H, 1.79. Found: C, 32.3; H, 1.89.

3-Bromo-2′-methyldiphenyl Sulfone.—A Grignard reagent was prepared from 31.2 g. (0.182 mole) of *o*-bromotoluene and 4.5 g. (0.185 g. atom) of magnesium. An ether solution of 27 g. (0.121 mole) of *m*-bromobenzenesulfenyl chloride was added following the procedure of Lecher, *et al.*,[26] for the preparation of diphenyl sulfide. The crude 3-bromo-2′-methyldiphenyl sulfide, obtained by evaporation of the ether layer, was dissolved in acetic acid and oxidized to the sulfone with 30% hydrogen peroxide.[20] The yield of material, melting at 60–61° after recrystallization from ethanol, was 18 g. (52%).

Anal. Calcd. for $C_{13}H_{11}O_2SBr$: C, 50.01; H, 3.57; Br, 25.6. Found: C, 50.2; H, 3.55; Br, 25.42.

3-Bromo-2′-carboxydiphenyl Sulfone.—This was prepared by oxidation of 3-bromo-2′-methyldiphenyl sulfone with potassium permanganate using the procedure outlined for 3-bromo-2-carboxydiphenyl sulfone; m.p. 153.5–155°.

Anal. Calcd. for $C_{13}H_9O_4SBr$: C, 45.74; H, 2.64; Br, 23.46. Found: C, 46.0; H, 2.78; Br, 23.3.

3,5-Dibromotoluene.—2,6-Dibromo-4-methylaniline[31] was deaminated following a procedure of Adams and Johnson.[28] The product was recrystallized from ethanol, m.p. 39–39.5° (reported m.p. 39°[32]); yield 68.2%.

3-Bromo-5-methyldiphenyl Sulfone.—A Grignard reagent was prepared from 65 g. (0.26 mole) of 3,5-dibromotoluene and 6.35 g. (0.26 g. atom) of magnesium. An ether solution of 25 g. (0.173 mole) of benzenesulfenyl chloride[29] was added following the procedure of Lecher, *et al.*,[26] for the preparation of diphenyl sulfide. The crude 3-bromo-5-methyldiphenyl sulfide, obtained by evaporation of the ether layer, was dissolved in acetic acid and oxidized to the sulfone with 30% hydrogen peroxide.[20] The product was recrystallized from ethanol and melted at 117–118°; yield 30 g., 55%.

Anal. Calcd. for $C_{13}H_{11}O_2SBr$: C, 50.01; H, 3.57; Br, 25.6. Found: C, 50.25; H, 3.43; Br, 25.7.

3-Bromo-5-carboxydiphenyl Sulfone.—This was prepared by oxidation of 3-bromo-5-methyldiphenyl sulfone with potassium permanganate using the procedure outlined for 3-bromo-2-carboxydiphenyl sulfone. Recrystallization from benzene yielded the acid, m.p. 198–199.5°.

Anal. Calcd. for $C_{13}H_9O_4SBr$: C, 45.74; H, 2.64; Br, 23.46. Found: C, 45.60; H, 2.69; Br, 23.5.

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Metalation of Phenyl 2-Thienyl Sulfone.—Thirty grams (0.134 mole) of phenyl 2-thienyl sulfone was treated with *n*-butyllithium prepared from 16.5 g. (0.179 mole) of *n*-butyl chloride and 2.6 g. (0.362 g. atom) of lithium. Nine grams of unreacted sulfone was recovered from the ether layer. The product, 2-benzenesulfonyl-5-thiophenecarboxylic acid, was recrystallized from a 50–50 mixture of ethanol and water; m.p. 205–207.5° (uncor.); weight 15 g.; conversion 41.6%, yield 60%. The m.p. was not lowered when mixed with an authentic sample prepared as outlined below.

Anal. Calcd. for $C_{11}H_8O_4S_2$: C, 49.25; H, 2.98. Found: C, 49.55; H, 3.07.

Sodium 2-Methyl-5-thiophenesulfonate.—Forty grams (0.5 mole) of sulfur trioxide was distilled into 200 ml. of dry ethylene chloride. With the temperature below 15°, 42 g. (0.5 mole) of dry dioxane was added slowly. With the temperature below 20°, 49 g. (0.5 mole) of 2-methylthiophene was added. When the addition was complete, the ice-bath was removed and the mixture stirred for two hours. It was then poured into water and the water layer separated and neutralized with sodium hydroxide to a *p*H of 7 using hydrion paper as the indicator. The aqueous layer was evaporated and the solid obtained was extracted with hot 95% ethanol. On cooling the alcohol, the product separated; yield 49.2 g. (49.2%).

Two grams of sodium 2-methyl-5-thiophenesulfonate was heated for three hours on a steam-bath with 4 g. of phosphorus pentachloride. The mixture was poured on ice and an oily layer separated. Five milliliters of liquid ammonia was added to the oil. The resulting solid, 2-methyl-5-thiophenesulfonamide, after recrystallization from 95% ethanol, melted at 119.5–121°.

Anal. Calcd. for $C_5H_7O_2NS_2$: N, 7.91. Found: N, 7.94.

2-Benzenesulfonyl-5-methylthiophene.—2-Methyl-5-thiophenesulfonyl chloride (41.8 g., 0.212 mole), prepared by treating sodium 2-methyl-5-thiophenesulfonate with phosphorus pentachloride, was treated with 75 ml. of benzene and 28.5 g. of aluminum chloride. The product was recrystallized from 95% ethanol; m.p. 91–92.5°, yield 26 g. (51.4%).

Anal. Calcd. for $C_{11}H_{10}O_2S_2$: C, 55.46; H, 4.20. Found: C, 55.50; H, 4.20.

2-Benzenesulfonyl-5-thiophenecarboxylic Acid.—This was prepared from 2-benzenesulfonyl-5-methylthiophene following the oxidation procedure of Newell.[13] The product was recrystallized from a 50–50 ethanol-water mixture and melted at 204–207° (uncor.).

Action of Lithium on the Bromophenyl Phenyl Sulfones.—One gram of lithium and 10 g. of *o*-bromophenyl phenyl sulfone were refluxed in ether under a dry nitrogen atmosphere for ten hours. Excess Dry Ice was then added. The mixture was hydrolyzed with dilute acid. The ether layer was extracted with 5% sodium hydroxide and evaporated. A quantitative recovery of unreacted sulfone was made. Acidification of the basic extract yielded no acidic material. The same results were obtained with *m*- and *p*-bromophenyl phenyl sulfones.

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Stobbe Condensation with Methyl γ-Benzoylbutyrate

BY D. L. TURNER

The Stobbe condensation with methyl γ-benzoylbutyrate gives a cyclized product Ia, together with a product of the normal type. Both substances are utilized to prepare the ester III, a valuable intermediate for steroid synthesis.

Recently, the Stobbe condensation with methyl γ-anisoylbutyrate was shown to produce both cyclized and normal products.[1] The cyclized half-ester (Ia) from methyl γ-benzoylbutyrate was obtained as a liquid in about 15% yield. It was purified by distillation of its methyl ester, which was obtained by the mild esterification procedure of Freudenberg and Jakob.[2] Hydrolysis of this gave a liquid acid, which was esterified with diazomethane to give the crystalline ester Ib. The structure of this substance, except for the position of the double-bond, was shown by its cyclization with sulfuric acid to 9-hydroxy-1-keto-1,2,3,4-tetrahydrophenanthrene, identified as its methyl ether IIa by comparison with an authentic sample.[3]

The position of the double-bond indicated in the structures Ia and Ib is supported by the absorption spectra, which show maxima at positions to be expected from the data for the cyclized ester from methyl γ-anisoylbutyrate (see Table II of the earlier paper).[1]

The dimethyl ester Ic was converted to the homologous reduced ester III by methods employed previously.[1] The structure of this ester is demonstrated below.

The crude cyclic product from the Stobbe condensation was also reduced by the Raney alloy procedure[4] to give a lactone acid presumed to be IV.

After the separation of the cyclic half-ester from the products of the Stobbe condensation, the normal Stobbe product was isolated as the unsaturated tricarboxylic acid V. The position of the double-bond in this acid was demonstrated by oxidation to γ-benzoylbutyric acid,[5] using a procedure of Johnson and Hunt.[6]

The unsaturated acid was converted to a crystalline dimethyl ester; the trimethyl ester was a liquid. The nature of the dimethyl ester can be deduced from the known difficulty of esterifying α,β-unsaturated acids.[7] It was reduced and cyclized to a product which should therefore be VI. The substance obtained from this by hydrogenolysis of the carbonyl group did not give recognizable

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[5] The ultraviolet absorption spectrum of V, ($\lambda_{max.}$ 237 mμ, log ε 3.92) and that of the similar acid of W. S. Johnson, A. R. Jones and W. P. Schneider, THIS JOURNAL, **72**, 2395 (1950), ($\lambda_{max.}$ 259 mμ, log ε 3.85), determined in 95% ethanol, differ from the absorption of cinnamic acid, probably as a result of steric inhibition of resonance. *Cf.* Y. Hirschberg, THIS JOURNAL, **71**, 3241 (1949), and P. Ramart-Lucas, *Bull. soc. chim.*, **9**, 850 (1942).

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