Grignard Reagents of Sulfones. V. Preparation of Methyl and Ethyl Aryl Sulfones[1]

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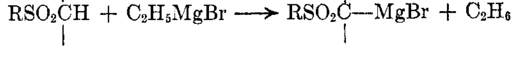
A Grignard reagent of a sulfone may be prepared by metalating a sulfone which contains an alkyl group having a hydrogen atom adjacent to the sulfone group. Such Grignard reagents are useful intermediates for preparing sulfones containing a variety of functional groups.[2] Since interest in the products afforded by these Grignard reagents frequently would be centered either about the sulfone group or the functional group introduced, simple starting materials often would suffice, such as methyl phenyl sulfone (I) or methyl *p*-tolyl sulfone (II). The synthetic utility of Grignard reagents of sulfones therefore frequently being a function of the ready availability of I or II, development of the best possible means for preparing I and II in quantity became desirable. Of the various preparations of methyl aryl sulfones,[3] that involving alkylation of an arenesulfinate provided the best compromise of economy, convenience, and adaptability to large scale.



$$\mathrm{RSO_2\overset{|}{\underset{|}{C}}H + C_2H_5MgBr \longrightarrow RSO_2\overset{|}{\underset{|}{C}}{-}MgBr + C_2H_6}$$

Oxley and coworkers prepared II by reducing *p*-toluenesulfonyl chloride with sodium sulfite to sodium *p*-toluenesulfinate and alkylating this product with methyl iodide.[4] Methyl iodide has the disadvantage, however, of expense, high volatility, and susceptibility to a side reaction which yields iodine and a thiol. Baldwin and Robinson, on the other hand, having prepared sodium benzenesulfinate in essentially the same way, isolated the sulfinic acid and then converted it to I by alkylation with methyl sulfate in the presence of aqueous sodium hydroxide.[5]

The procedures of this paper, based mainly on that of Baldwin and Robinson,[5] involve reduction of the sulfonyl chloride with sodium sulfite by a somewhat simplified process, followed by alkylation of the sulfinate salt using methyl sulfate, water, and sodium bicarbonate under vigorous conditions. Differences from the earlier procedure[5] require brief comment: (a) Only technical grades of organic reagents are specified. (b) The scale is increased eleven fold; one advantage of the present method is its presumed adaptability to further increase by minor modification. (c) The salt rather than the free sulfinic acid is used, thus eliminating the extra step of acidification and the copious evolution of sulfur dioxide (from excess sulfite) associated with it, as well as the necessity for alkylating the reduction product soon after its formation (the acid differs from the salt in being unstable). (d) A feature of more general interest and applicability is that the vigorous conditions of the present procedure seem to have caused methyl sodium sulfate to function as an alkylating agent, in contrast to the usual situation in alkylations where it is simply an inert by-product resulting after alkylation by methyl sulfate; thus, under vigorous conditions, the amount of methyl sulfate specified[5] for preparation of a given weight of sulfone could be reduced by more than one half. (e) A more concentrated solution was used for the alkylation to increase the temperature and rate of reaction. (f) Sodium bicarbonate was substituted for sodium hydroxide to prevent etching of glassware. (g) The sulfone was extracted from the reaction mixture with benzene, a modification which permits effective drying of the sulfone when it is to be used for organometallic reactions (recrystallization of the product from water[5] was unnecessary).

In preliminary work, essentially the procedure of Baldwin and Robinson was used (but with a molar ratio of methyl sulfate to benzenesulfinic acid of 1.7:1). Periods of reflux of 1–9 hr. during the alkylation gave I in yields of 53–59%. A study of the hydrolysis of methyl sulfate[6] strongly suggested that little or none of the sulfate would survive the 9-hr. period of reflux. On the other hand, since methyl potassium sulfate reportedly methylates sulfinates under vigorous conditions,[7] the possibility referred to in (d) above became attractive, *i.e.*, that the by-product, methyl sodium sulfate, could still be induced to effect alkylation. The fact that a reflux period of 18 hr. did result in an increase in the yield of I to 73% lends support to this viewpoint (since the yield increased only to 76% after a 36-hr. period, a 20-hr. period seemed optimum and was used in the modified procedure cited in the Experimental).

Alkylation 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.

The preparation reported in the Experimental for methyl phenyl sulfone (I) gave even better results when extended to methyl *p*-tolyl sulfone (II). Efforts to extend the alkylation step to the prep-

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[2] See Paper IV of this series and leading references there: L. Field, J. E. Lawson, and J. W. McFarland, *J. Am. Chem. Soc.*, **78**, 4389 (1956).

[3] C. M. Suter, *The Organic Chemistry of Sulfur*, p. 660 ff., John Wiley and Sons, Inc., New York, N. Y., 1944.

[4] P. Oxley, M. W. Partridge, T. D. Robson, and W. F. Short, *J. Chem. Soc.*, **1946**, 763.

[5] W. A. Baldwin and R. Robinson, *J. Chem. Soc.*, **1932**, 1445.

[6] H. F. Lewis, O'Neal Mason, and R. Morgan, *Ind. Eng. Chem.*, **16**, 811 (1924).

[7] R. Otto, *Ann.*, **284**, 300 (1895).

aration of the analogous ethyl aryl sulfones by substitution of ethyl sulfate, however, were less well rewarded. Despite a number of variations in the alkylation of sodium benzenesulfinate by ethyl sulfate, the yields could not be increased beyond about 34–48%; sodium *p*-toluenesulfinate gave ethyl *p*-tolyl sulfone in 45% yield. The route of choice for ethyl aryl sulfones, therefore, probably is ethylation of the sulfinate with an ethyl halide.

EXPERIMENTAL[8]

Methyl phenyl sulfone (I). The reduction was based on that of Oxley *et al.*[4] A mixture of 600 g. of anhydrous sodium sulfite, 420 g. of sodium bicarbonate, and 2.4 l. of water was heated on a hot plate at 70–80°. This temperature was maintained by switching off the hot plate occasionally, while 447 g. (325 ml.) of benzenesulfonyl chloride[9] was added with stirring during 3 hr. Heating and stirring were then continued until the volume did not exceed 2.4 l. (but at least for 1 hr.). The mixture was then allowed to stand overnight at room temperature, and the solid was collected by filtration. The filter cake was then used without further treatment in the alkylation step; moisture in the cake is unimportant, and salts other than the sulfinate probably have a desirable effect in reducing the rate of hydrolysis of methyl sulfate.[6]

In the alkylation procedure, suggested by that of Baldwin and Robinson,[5] the filter cake was mixed with 400 g. of sodium bicarbonate and 490 g. (370 ml.) of methyl sulfate[9,10] in a 3-necked flask provided with a stirrer, condenser, and dropping funnel containing 925 ml. of water. Enough of the water was added to permit stirring (*ca.* 100 ml.), and the remainder then added during 3 hr. with stirring. The mixture was then heated under reflux with stirring for 20 hr. It was then cooled to about 75°, and 200 ml. of benzene was added and the mixture was stirred briefly. All liquid was then decanted from solid into a separatory funnel. The aqueous layer was separated, extracted with 200 ml. more of benzene, and returned to the funnel. Solid remaining in the flask was washed into the separatory funnel with *ca.* 2 l. of water, after which the mixture was shaken with 200-ml. portions of benzene until all solid had been dissolved (three portions usually sufficed).

After the combined benzene extracts had been dried over calcium chloride, the benzene was removed by distillation under reduced pressure. (If the temperature was kept below 50°, well formed crystals were obtained.) The yield of colorless nicely crystalline I was 260 g. (66%), m.p. and mixture[11] m.p. 86–88°. Use of 134 g. of benzenesulfonyl chloride gave I in 69% yield, m.p. 86.5–87°.

The procedure of Baldwin and Robinson,[5] and our own experience on a small scale, suggests that if the I is not to be used in organometallic reactions, where the advantage of thorough drying of the extract is important, it can be isolated simply by allowing it to crystallize from the reaction mixture and washing with water. Carbon tetrachloride and 1:3 ethanol-water are convenient for recrystallization (or water[5] on a small scale), if this should be desired. The only limiting factor toward considerable increases in scale seems to be the extraction.

In exploring alkylation under other conditions, methyl sulfate[9,10] in a molar ratio of 1.7:1 was usually added over 1–2 hr. After the reaction, the excess was hydrolyzed and the I recrystallized. Benzenesulfinic acid in ether (reflux, 14 hr.) gave no crystalline product. Its salt (3 g.) in methyl sulfate[9,10] alone (5 ml.; 85°, 22 hr.) gave I in 24% yield, m.p. *ca.* 86°. Its salt in acetone (55°, 2.5–26 hr.) gave I with ranges in yield of 38–12% and in m.p. of 80–87°; in *t*-butyl alcohol containing 5% of water (reflux, 4.5 hr.), the salt gave I in 19% yield, m.p. 86–87.5°.

Methyl p-tolyl sulfone (II). The procedure given for I was followed exactly except that 484 g. of *p*-toluenesulfonyl chloride[9] was substituted for benzenesulfonyl chloride. In four experiments,[12] the II ranged in yield from 69 to 74%, and in m.p. from 83° to 87.5° (a typical product had m.p. and mixture[13] m.p. 86.5–87.5°).

A 20-hr. reflux period was established as sufficient for II by also effecting the alkylation using a 36-hr. period; the yield was 76% m.p. 86.5–87.5°.

Ethyl phenyl sulfone. A mixture of 20.0 g. of sodium benzenesulfinate, 20.1 g. of sodium bicarbonate, and 16.4 ml. of ethyl sulfate was heated at 50° with stirring while 50 ml. of water was added during 2 hr. The mixture was then heated under reflux for 20 hr. and the sulfone extracted with benzene; yield, 8.0 g. (39%), m.p. 41.5–42°; m.p. reported,[14] 41–42°.

Repetition of the procedure resulted in a yield of only 44% with twice the amount of ethyl sulfate and of only 48% with four times the amount both of ethyl sulfate and of sodium bicarbonate. Hydrolysis of the sulfate therefore does not seem to be the limiting factor. Indeed, when the procedure was repeated except that the mixture of the sulfinate and sulfate was heated and stirred alone at 120° for 4 hr. before addition (in one portion) of the sodium bicarbonate and water, only a dark oil, which could not be crystallized, was isolated. No favorable effect resulted either from interchanging the water and the sulfate in the original procedure (34%, m.p. 41.5–42°), from doubling the time of reflux (38%, m.p. 41.5–42°), or from other variations.

Ethyl p-tolyl sulfone. The procedure used for ethyl phenyl sulfone was repeated with 21.7 g. of sodium *p*-toluenesulfinate and 32.8 ml. of ethyl sulfate; yield 10.0 g. (45%), m.p. and mixture[13] m.p., 53–54°.

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[8] Melting points are corrected.

[9] Eastman Organic Chemicals, Yellow Label grade.

[10] Methyl sulfate is quite toxic and should be used in a hood; see N. I. Sax, *Handbook of Dangerous Materials*, p. 147, Reinhold Publishing Co., New York, N. Y., 1951. Glassware used for transfers may be cleaned with dilute ammonia water, containing detergent. It seems quite unlikely[6] that any methyl sulfate survives the 20-hr. period of reflux during alkylation, and no difficulty whatever has been experienced in handling the mixture after this period without gloves, hood, or other special precautions; nevertheless, the possible presence of methyl sulfate should be borne in mind.

[11] L. Field, *J. Am. Chem. Soc.*, **74**, 3919 (1952).

[12] We wish to thank O. D. Keaton and W. E. Stamper for two of these.

[13] L. Field and J. W. McFarland, *J. Am. Chem. Soc.*, **75**, 5582 (1953).

[14] R. Otto, *Ber.*, **13**, 1274 (1880).

Organic Polynitriles. II. 1,1,2,2-Tetracyanocyclopropanes and Their Conversion to Substituted Itaconic Acids[1]

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Several alkylidene bismalononitriles were prepared by the reaction of the appropriate aldehyde with malononitrile[4] (Table I).