N-Acetyl-3-acetoxymethylindole (VI).—A mixture of 5.0 g. of gramine, 50 ml. of redistilled acetic anhydride and 10 g. of dry sodium acetate was refluxed for 4 hours and poured into a mixture of ice and 5% sodium carbonate solution. After the excess acetic anhydride had decomposed the mixture was extracted with benzene. The dried and decolorized (Norite) benzene extract was evaporated and the oily residue dissolved in ethanol (60 ml.). After removal of about a gram of tarry material the ethanol solution was diluted with water (500 ml.) and cooled. The crystalline product (0.87 g., m.p. 87–89°) was recrystallized from ligroin from which it formed colorless needles, m.p. 90–90.5°.

Anal. Calcd. for $C_{13}H_{13}O_3N$: C, 67.52; H, 5.66. Found: C, 67.43; H, 5.80.

The infrared spectrum of VI (Fig. 3) showed no absorption in the region of 2.9 μ, and showed a two-banded absorption peak at about 5.9 μ, indicative of the two acyl carbonyl groups. The infrared spectrum of skatole (Fig. 3) shows the 2.9-μ band; and that of N-acetylskatole (Fig. 3) resembles that of VI except for a sharper 5.9-μ band.

N-Acetylskatole was prepared for comparison of its ultraviolet and infrared spectra with those of VI. This compound has been described by Oddo,[13] who prepared it by the action of acetyl chloride on indolylmagnesium bromide. A simpler method of preparation is as follows: A solution of 2.0 g. of skatole in 20 ml. of acetic anhydride was heated at 180–200° for 7 hours. The excess acetic anhydride was removed by distillation under reduced pressure and the black residue distilled with steam. The crystalline material in the cooled distillate had m.p. 63–66° and after two recrystallizations from aqueous ethanol afforded pure N-acetylskatole, m.p. 66–67°.[13] The spectra of this compound have been referred to above.

NOTE ADDED IN PROOF.—In an article which appeared after this paper had been accepted for publication, J. Thesing and F. Schülde [*Ber.*, **85**, 324 (1952)] described the use of gramine methosulfate for the preparation of 3-indolylacetonitrile, and referred to a preliminary announcement in which the preparation of gramine methiodide is accomplished *via* the methosulfate [C. Schöpf and J. Thesing, *Angew. Chem.*, **63**, 377 (1951)]. Although the details of the latter work have not been reported in detail, it appears that Schöpf and Thesing have reached conclusions in agreement with ours.

Acknowledgments.—The authors' thanks are due Mr. Wm. Netusil for the determination of the spectra and Mr. David Wilson for carbon–hydrogen analyses.

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[13] B. Oddo, *Gazz. chim. ital.*, **43**, II, 190 (1913); *C. A.*, **8**, 85 (1914).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF VANDERBILT UNIVERSITY]

Grignard Reagents of Sulfones. I. Preparation and Reactions of β-Phenyl-β-hydroxyethyl Phenyl Sulfone[1]

BY LAMAR FIELD

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The reaction of phenylsulfonylmethylmagnesium bromide with benzaldehyde yields β-phenyl-β-hydroxyethyl phenyl sulfone (I). The possible utility of compounds such as I for the synthesis of several classes of sulfones is suggested by the conversion of I in good yields to the corresponding keto, chloro, unsaturated and saturated sulfones.

α-Halomagnesium derivatives of sulfones undergo several reactions typical of Grignard reagents including acylation,[2–4] carbonation,[2,5] alkylation,[3] halogenolysis[2,6] and hydrolysis.[2,6] Previous interest in these sulfone derivatives which may be regarded as Grignard reagents of sulfones has apparently originated largely incidentally to other problems. A more direct study appeared to be worthwhile because of the possibility that the reactions of these compounds might provide unique and useful routes to a wide variety of classes of sulfones, many of which would otherwise be difficultly obtainable. Furthermore, the effect which the highly electronegative but relatively unreactive sulfonyl group might have upon the adjacent organometallic bond is of considerable theoretical interest.

Phenylsulfonylmethylmagnesium bromide was found to react with benzaldehyde to give the hydroxysulfone (I) in 90% yield. Intermediates such as I clearly provide attractive routes to several general classes of sulfones, especially unsaturated ones.[7] The reactions described in this paper were carried out to confirm this apparent utility. Studies of the generality of the addition reaction are now in progress.

$$C_6H_5SO_2CH_3 \xrightarrow[\text{(2) } C_6H_5CHO]{\text{(1) } C_2H_5MgBr} \underset{\text{I}}{C_6H_5SO_2CH_2CH(OH)C_6H_5}$$

The hydroxysulfone I is formed in a mildly exothermic reaction. It is stable in boiling water, possibly because of its insolubility, but upon treatment with potassium hydroxide[8] gives methyl phenyl sulfone and benzaldehyde. Further characterization of I is afforded by its oxidation to the corresponding ketone, ω-phenylsulfonylacetophenone (II), in 79% yield. Ashworth and Burkhardt[9] found that II is isomerized to phenyl α-phenylethyl sulfone by reduction using acidic conditions followed by reoxidation with chromic acid. In order to eliminate any possibility that a similar rearrangement had occurred in the present instance, II was catalytically reduced to a hydroxysulfone identical with I.

The formation of an unsaturated sulfone such as III by the condensation of benzaldehyde and an

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[1] Presented at the 121st Meeting of the American Chemical Society at Milwaukee, Wis., March 30–April 3, 1952.

[2] E. P. Kohler and H. A. Potter, THIS JOURNAL, **57**, 1316 (1935).

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

[4] E. P. Kohler and H. A. Potter, *ibid.*, **58**, 2166 (1936).

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

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

[7] A referee directed our attention to a report of H. A. Potter at the Spring (1951) Meeting of the Midland Section of the A.C.S. in which, as Dr. Potter has kindly informed us, the addition of *p*-tolylsulfonylmethylmagnesium bromide to benzophenone and the dehydration of the product were described. Conversions of hydroxysulfones, somewhat similar to some presently described but seemingly used mainly for characterization, were recently reported by H. J. Backer, *et al.* [*Rec. trav. chim.*, **70**, 365 (1951)], and C. C. J. Culvenor, *et al.* [*J. Chem. Soc.*, 2198 (1949)].

[8] E. Rothstein, *ibid.*, 684 (1934).

[9] F. Ashworth and G. N. Burkhardt, *ibid.*, 1791 (1928).

alkyl aryl sulfone[2] or an arylsulfonylacetic acid[10] generally occurs in low yield. The use of I as an intermediate, on the other hand, provides an effective conversion of an alkyl aryl sulfone to an unsaturated sulfone inasmuch as the dehydration of I was found to give styryl phenyl sulfone (III) in 100% yield.

$$C_6H_5SO_2CH_2CH(OH)C_6H_5 \xrightarrow{H_3PO_4} \underset{III}{C_6H_5SO_2CH{=}CH{-}C_6H_5}$$

The non-occurrence of rearrangement in the dehydration was established by the catalytic reduction of III to phenyl β-phenylethylsulfone (IV). Apparently only one geometrical isomer is formed in the dehydration.

Treatment of I with thionyl chloride and a small amount of pyridine[11] gives the corresponding β-chlorosulfone (V, 71% yield) which upon catalytic reduction yields IV (98% yield). Dehydrohalogenation of V occurs readily in collidine even at room temperature, and after brief heating the unsaturated sulfone III is obtained in 100% yield.

The conversion of the benzoate of I to the unsaturated sulfone III by heating in dimethylaniline was also investigated since this method[12] might permit formation of an unsaturated sulfone under non-acidic conditions. Crude III was obtained in 56% yield, but was difficult to purify. The vigorous conditions required are also disadvantageous since III appears to decompose slowly at high temperatures.

Acknowledgment.—The author wishes to express his appreciation to the Research Corporation of New York for generous grants in support of this work.

Experimental[13]

β-Phenyl-β-hydroxyethyl Phenyl Sulfone (I).—Methyl phenyl sulfone, m.p. 86.5–88°, was obtained in 68% yield by modification of a method of Michael and Palmer.[14]

Phenylsulfonylmethylmagnesium bromide was prepared using a procedure based on one of Ziegler and Connor.[6] A solution of 15.00 g. of well-dried methyl phenyl sulfone in 100 ml. of dry benzene was added during ten minutes to the ethylmagnesium bromide prepared in 30 ml. of ether from 14.5 g. of ethyl bromide and 3.05 g. of magnesium. The mixture was stirred for ten minutes, diluted with 60 ml. of benzene and then heated rapidly to the reflux temperature at which it was held for three minutes. It was then cooled quickly.

A solution of 12.72 g. of purified[15] benzaldehyde in 20 ml. of dry benzene was added with stirring during one hour at a temperature of about 20–35°. The white precipitate changed to a gummy solid which was difficult to stir; material which caked on the flask wall was dislodged occasionally. After the mixture had been stirred for two hours at room temperature it was chilled and 20 ml. of ice-water followed by 40 ml. of iced 3 *N* hydrochloric acid was added. It was necessary to break up the solid to effect solution. The aqueous layer was washed with benzene and the benzene extract was washed with water until neutral, dried and concentrated. After trituration with cold petroleum ether the resulting solid amounted to 22.7 g. (90%) of slightly yellow I, m.p. 79–91°. Recrystallization from carbon tetrachloride gave 19.1 g. (76%) of white powdery crystals, m.p. 89.5–93.5°, which after a second crystallization amounted to 18.5 g. (73%), m.p. 92–94°. A similarly prepared sample after recrystallization from aqueous methanol, carbon tetrachloride, and benzene–petroleum ether had a constant m.p. of 93–94°.

Anal. Calcd. for $C_{14}H_{14}O_3S$: C, 64.10; H, 5.38; S, 12.22; mol. wt., 262. Found: C, 64.40; H, 5.28; S, 11.84; mol. wt. (Rast), 260.

When the reaction mixture was heated under reflux after completion of the addition, a lower yield of less pure product was obtained.

I was unaffected by stirring in boiling water for four hours (97% recovery, m.p. and mixture m.p. 91–93.5°). Reverse aldolization was effected, however, by distilling a mixture of 4.57 g. of I and 3 *N* aqueous potassium hydroxide. An ether extract of the steam distillate yielded 1.24 g. (67%) of benzaldehyde, $n^{20}D$ 1.5376; the phenylhydrazone (55% yield) after recrystallization had a constant m.p. of 153.5–156.5°. An ether extract of the distillation residue gave 2.71 g. of solid, m.p. 43–54°, from which ethanol–water separated 0.28 g. (10%) of methyl phenyl sulfone, m.p. and mixture m.p. 87–88°.

ω-Phenylsulfonylacetophenone (II).—A solution of 1.87 g. of chromium trioxide in aqueous acetic acid was added during 1.5 hours to 7.00 g. of I in acetic acid. The temperature was maintained at 55° during this period and an additional one-half hour. Water was then added to the mixture and a solution of the resulting solid in aqueous sodium hydroxide was washed with ether and acidified; yield of II, 5.48 g. (79%), m.p. 92.5–94°. Recrystallization from ethanol gave 5.41 g. (78%), m.p. 93–94° undepressed by authentic[16] II (constant m.p. 93–94°) from sodium benzenesulfinate and phenacyl chloride.

The oxidation product II gave a colorless phenylhydrazone with a constant m.p. of 165.5–167.5°, undepressed by authentic material.

In the reduction of II to I, 2.50 g. of palladium catalyst[17] in dioxane[18] was saturated with hydrogen at room temperature and atmospheric pressure, after which a solution of 5.00 g. of II in dioxane was added. After shaking for five hours at room temperature and pressure, 421 ml. of hydrogen was absorbed (S.T.P., 98% of one molar equivalent). Separation of the catalyst followed by concentration of the filtrate gave 4.88 g. (97%) of solid, m.p. 85–91°. Two recrystallizations from carbon tetrachloride gave 4.36 g. (87%), m.p. 90–94°, which after further recrystallization had constant m.p. 93–94°, undepressed by I but depressed to 70–87° by II.

Styryl Phenyl Sulfone (III).—A mixture of 30.0 g. of finely ground I and 150 ml. of 85% phosphoric acid was stirred vigorously and heated to the reflux temperature (168°) during one hour, and was maintained at this temperature for 15 minutes. The mixture was then cooled and 400 g. of ice was added. A benzene extract was washed with water, dried and concentrated; yield 28.0 g. (100%), m.p. 70–73.5°. Recrystallization from isopropyl alcohol and cyclohexane–benzene gave material of constant m.p. 74–75°, an acetone solution of which rapidly decolorized 2% aqueous potassium permanganate.

Anal. Calcd. for $C_{14}H_{12}O_2S$: C, 68.83; H, 4.95. Found: C, 68.93; H, 4.86.

Longer heating periods during the dehydration gave lower yields of less pure III.

A solution of 3.00 g. of III in acetic acid was reduced as described above using 2.0 g. of palladium catalyst[17]; hydrogen absorption after 36 minutes, 286 ml. (S.T.P., 104% of one molar equivalent). Concentration yielded 2.77 g. (92%) of slightly greasy solid, m.p. 38–40°. Recrystallization from aqueous ethanol gave 2.57 g. (85%) of IV, m.p. 57.5–58.5°, unchanged by recrystallization from

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[10] S. Chodroff and W. F. Whitmore, This Journal, **72**, 1073 (1950).

[11] W. Gerrard and K. H. V. French, *Nature*, **159**, 263 (1947).

[12] G. A. D. Haslewood, *J. Chem. Soc.*, 224 (1938).

[13] Melting points are corrected and boiling points are uncorrected. Anhydrous magnesium sulfate was used as a drying agent except where otherwise specified; concentrations were effected by distillation under reduced pressure. Analyses are by Clark Microanalytical Laboratory, Urbana, Ill.

[14] A. Michael and G. M. Palmer, *Am. Chem. J.*, **6**, 255 (1884).

[15] L. F. Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., New York, N. Y., 1941, p. 224.

[16] J. Tröger and O. Beck, *J. prakt. Chem.*, [2] **87**, 295 (1913) [*C. A.*, **7**, 2543 (1913)].

[17] E. Alexander and A. C. Cope, "Organic Syntheses," Vol. 26, John Wiley and Sons, Inc., New York, N. Y., 1946, p. 32.

[18] Ref. 15, p. 369.

pure ethanol and undepressed by authentic IV.[9] Further evidence for the identity of these two samples is provided by their identical infrared spectra[19] (in Nujol mulls) which were as follows:

Wave length, μ	Frequency, cm.$^{-1}$	Relative intensity[a]	Wave length, μ	Frequency, cm.$^{-1}$	Relative intensity
6.27	1595	mw	9.91	1009	mw
7.14	1400	mw	10.04	996	mw
7.66	1305	VS	10.74	931	M
7.77	1287	M	11.01	908	mw
7.97	1255	MS	11.75	851	w
8.09	1236	w	12.76	784	VS
8.33	1200	w	13.12	762	MS
8.54	1171	w	13.56	737	S
8.78	1139	VS	13.92	718	S
9.23	1083	S	14.28	700	MS
9.35	1070	MS	14.50	690	MS
9.75	1026	mw			

[a] VS, very strong; S, strong; MS, medium strong; M, medium; mw, medium weak; w, weak.

β-Phenyl-β-chloroethyl Phenyl Sulfone (V).—A suspension of 5.00 g. of I in 20 ml. of dry benzene containing 0.03 ml. of dry pyridine was cooled to 5°. A solution of 2.61 g. of thionyl chloride in 5 ml. of benzene was added, the cooling bath was removed, and the mixture allowed to stand for 1.5 hours. The mixture was then heated to the reflux temperature during 1.5 hours and there maintained during 1.5 hours. It was then concentrated. Two portions of benzene were added and likewise removed by concentration. A solution in carbon tetrachloride of the solid obtained was filtered, and gave after crystallization 3.78 g. (71%) of V, m.p. 87.5–88.5°. Further recrystallization from carbon tetrachloride and benzene–petroleum ether gave a colorless solid having a constant m.p. of 88–89°.

Anal. Calcd. for $C_{14}H_{13}O_2SCl$: C, 59.89; H, 4.67. Found: C, 60.09; H, 4.77.

A solution of 3.00 g. of V in dioxane[18] was reduced to IV in the manner described using 1.49 g. of palladium catalyst.[17] In 18 minutes, 243 ml. of hydrogen was absorbed (S.T.P., 101% of one molar equivalent). Concentration gave 2.58 g. (98%) of IV, m.p. 56.5–58°. Recrystallization from aqueous ethanol gave IV with a constant m.p. of 58–58.5°, undepressed by authentic[9] IV.

For the conversion of V to III, 3.00 g. in 15 ml. of dry benzene and 4.5 ml. of 2,4,6-collidine was allowed to stand for 19 hours, and was then heated under reflux for 1.5 hours. The cooled mixture was diluted with benzene, washed with water, 25 ml. of cold 3 *N* hydrochloric acid, and again with water. Drying and concentration gave 2.60 g. (100%) of III, m.p. 73–75°. Recrystallization from isopropyl alcohol gave colorless prisms which had a constant m.p. of 74.5–75° undepressed by the III prepared from I using phosphoric acid.

Filtration of the insoluble collidine hydrochloride in another experiment showed that the reaction was about 78% complete after standing overnight.

β-Phenyl-β-hydroxyethyl Phenyl Sulfone Benzoate (VI).—Benzoyl chloride (18 ml.) was added to 30 ml. of pyridine and the mixture then added to an ice-cold solution of 10.00 g. of I in 30 ml. of pyridine. This mixture after standing at 5° for 24 hours and at room temperature for 24 hours was heated on a steam-bath for 2.5 hours, cooled and poured onto ice. A chloroform extract was washed with hydrochloric acid, aqueous sodium bicarbonate and water. Drying and concentration gave an oily solid which was washed with petroleum ether and recrystallized from isopropyl alcohol; yield 13.18 g. (94%), m.p. 144.5–145°. A similarly prepared sample after recrystallization from isopropyl alcohol, carbon tetrachloride and methanol was colorless and had a constant m.p. of 144.5–145°.

Anal. Calcd. for $C_{21}H_{18}O_4S$: C, 68.83; H, 4.95. Found: C, 68.73; H, 4.76.

Appreciable reduction of the time of heating of the reaction mixture resulted in lower yields.

A solution of 6.00 g. of VI in purified[20] dimethylaniline was heated at gentle reflux under dry nitrogen for six hours. The solution was then diluted with benzene, washed with hydrochloric acid, aqueous sodium bicarbonate and water. Drying and concentration gave a greasy solid (3.64 g.) which was triturated with cold petroleum ether and mixed with 30 ml. of carbon tetrachloride. Filtration separated unchanged VI (5%). The filtrate gave 2.25 g. (56%) of crude III, m.p. 57–69°. Recrystallization from isopropyl alcohol yielded 1.84 g. (46%), m.p. 67.5–74°. Two further recrystallizations did not affect the m.p. of the III. Evaporative distillation (145°, 0.006 mm.) and recrystallization then gave an 84% recovery of the III, m.p. 71.5–74.5°, lowered to 70–74° by a second recrystallization. This m.p. was undepressed (mixture m.p. 72–75°) by III prepared from I using phosphoric acid. An acetone solution of the product rapidly decolorized 2% aqueous potassium permanganate. Inasmuch as distillation failed to effect complete purification it seems possible that the impurity which remained may be a geometrical isomer of the principal product.

When VI was heated in dimethylaniline to the reflux temperature during one hour and held at this temperature for one hour, the carbon tetrachloride treatment separated 53% of VI; 20% of III was obtained, m.p. and mixture m.p. 67–73°.

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[19] We are indebted to Dr. Nelson Fuson and Dr. M. L. Josien of Fisk University for these data.

[20] Reference 15, p. 382.