[Contribution from the Department of Chemistry, Duquesne University]

SOME DERIVATIVES OF *p*-PHENYLMERCAPTOACETOPHENONE

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In continuation of the study of the chemistry of phenyl sulfide (1, 2) there was investigated the preparation of a number of derivatives of *p*-phenylmercaptoacetophenone (I).

In spite of numerous attempts to bring about the Mannich reaction between I and several secondary amines only the condensation products of morpholine (II), piperidine, and dimethylamine could be isolated. Diethyl-, di-*n*-butyl-, and diisobutyl-amine failed to give the Mannich condensation products and from the reaction mixtures there could be recovered the respective amine (as the hydrochloride) and a low-melting material which was difficult to purify by crystallization. This material was suspected to be a mixture of I and *p*-phenylmercaptoacrylophenone (III), and when the latter was prepared by the base-catalyzed decomposition of II it proved to be a low-melting solid (m.p. 51–52°). In view of the structural similarity between I and III and the fact that both of these compounds are rather low-melting solids it is not surprising that it was impossible to recover either component from the unsuccessful Mannich reactions. The yields of the successful Mannich reactions were found to decrease when a large excess of hydrochloric acid was employed.

The sulfone of I was found to undergo the Mannich condensation with morpholine rather slowly but the unreacted ketone could be recovered from the partially completed reaction and there was no evidence of the formation of the corresponding acrylophenone.

The complete failure of the Mannich reaction of I with diethyl- and the higher dialkyl-amines is surprising since these amines have been successfully employed in the condensation of acetophenone and substituted acetophenones (3). Apparently the failure of these reactions lies in the facile decomposition reactions of the condensation products to the unsaturated ketone (III). The role of the *p*-phenylmercapto substituent in hindering the Mannich reaction of acetophenone and the role of the *p*-phenylsulfonyl substituent in facilitating the isolation of the Mannich condensation product are currently being investigated.

The reduction of I to the corresponding alcohol was brought about with aluminum isopropoxide or lithium aluminum hydride. The second reagent also reduced the carbonyl function of II. The attempted reduction of the condensation product of the sulfone of I and morpholine with Raney nickel resulted in the cleavage of the amino group and gave *p*-phenylsulfonylpropiophenone.

The oxidation of the alcohol of I with peroxyacetic acid gave the expected sulfone alcohol, but several attempts to oxidize II gave unidentified degradation products.

EXPERIMENTAL[1]

p-Phenylmercapto-β-N-morpholinopropiophenone hydrochloride (II). A solution of 13 g. (0.06 mole) of I, 7.41 g. of morpholine hydrochloride (0.06 mole), 8 g. of paraformaldehyde (0.24 mole), 15 cc. of concentrated hydrochloric acid, and 150 cc. of 95% ethanol was refluxed for four hours and then was allowed to stand for 12 hours. The resulting precipitate was filtered, dried, and recrystallized to give 10 g. (73%) of pure product, m.p. 189–190°.

Anal. Calc'd for $C_{19}H_{22}ClNO_2S$: C, 62.63; H, 6.13; Cl, 9.75.
Found: C, 62.25; H, 5.43; Cl, 9.76.

p-Phenylmercapto-β-dimethylaminopropiophenone hydrochloride. A solution of 22.8 g. of I, 8.2 g. of dimethylamine hydrochloride, 4.7 g. of paraformaldehyde, 2 cc. of concentrated hydrochloric acid, and 75 cc. of 95% ethanol was refluxed for three hours, allowed to come to room temperature and then mixed with 250 cc. of boiling acetone. On standing in an ice chest there was obtained 5 g. (15%) of product, m.p. 149–150°.

Anal. Calc'd for $C_{17}H_{20}ClNOS$: C, 63.43; H, 6.26; Cl, 11.1.
Found: C, 63.45; H, 6.27; Cl, 11.1.

Variations in the procedure gave lower yields of the product and the formation of oily byproducts which refused to crystallize.

p-Phenylmercapto-β-N-piperidinopropiophenone hydrochloride. A solution of 22.8 g. of I, 12.2 g. of piperidine hydrochloride, 4.5 g. of paraformaldehyde, 1 cc. of concentrated hydrochloric acid, and 50 cc. of 95% ethanol was refluxed one hour, an additional 1.5 g. of paraformaldehyde was added, and the refluxing was continued for another two hours. Boiling acetone (250 cc.) was then added and the reaction mixture was allowed to stand in an ice chest. There was obtained 3 g. (8.3%) of product, m.p. 169–170°.

Anal. Calc'd for $C_{20}H_{25}ClNOS$: C, 66.36; H, 6.68; Cl, 9.8.
Found: C, 66.34; H, 6.22; Cl, 9.7.

p-Phenylsulfonyl-β-N-morpholinopropiophenone. A solution of 5 g. of the sulfone of I (1), 4.6 g. of morpholine hydrochloride, 5 g. of paraformaldehyde, 15 cc. of concentrated hydrochloric acid, and 100 cc. of 95% ethanol was refluxed for one hour, an additional 1.5 g. of paraformaldehyde and 5 cc. of hydrochloric acid was then added, and the reaction mixture was refluxed 3.5 hours longer. Since standing at room temperature failed to show any precipitate, the reaction mixture was concentrated to approximately ¼ of its original volume whereupon there was obtained 1.7 g. of the unreacted starting material. Further concentration of the reaction mixture gave 5 g. (100%) of the product, m.p. 189–190°.

Anal. Calc'd for $C_{19}H_{22}ClNO_4S$: C, 57.80; H, 5.62.
Found: C, 57.69; H, 5.50.

1-p-Phenylmercaptophenylethanol. A. The Meerwein-Pondorf method: A mixture of 15 g. of I, 25 cc. of aluminum isopropoxide solution (2.02 g. *per* cc. of toluene), and 50 cc. of isopropyl alcohol was refluxed for four hours, cooled, and hydrolyzed with 10% sulfuric acid. The hydrolysis mixture was extracted with ether, and the ethereal extract was dried and distilled. The product was obtained in the fraction b_1 150–151°.

B. The lithium aluminum hydride method: A solution of 22.8 g. of I in 175 cc. of ether was added slowly to a solution of 1 g. of lithium aluminum hydride in 200 ml. of ether. The reaction mixture was refluxed under a nitrogen atmosphere for 30 minutes, and, after the addition of a few drops of water, it was poured on ice. The ethereal solution was dried and distilled and the product was collected at 197–198° (3 mm.), n_D^{25} 1.6220, yield 53%.

Anal. Calc'd for $C_{14}H_{14}OS$: C, 73.00; H, 6.10.
Found: C, 72.87; H, 5.62.

1-p-Phenylmercaptophenyl-3-N-morpholino-2-propanol. A suspension of 5 g. of II in 100 cc. of ether was treated with a solution of 5 g. of lithium aluminum hydride in 200 cc. of ether. The reaction mixture was refluxed for 90 minutes and was hydrolyzed. The ethereal solution was dried and saturated with hydrogen chloride to give 3 g. of the desired product

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[1] The microanalyses were carried out by Mr. G. Stragand of the Microanalytical Laboratories of the University of Pittsburgh. All melting points are uncorrected.

as the hydrochloride, m.p. 195–196°. A mixture of this product and of the starting material gave a depression of the melting point by some twenty degrees.

Anal. Calc'd for $C_{19}H_{24}ClNO_2S$: C, 62.40; H, 6.61.

Found: C, 62.53; H, 6.41.

p-Phenylsulfonylpropiophenone. From a mixture of *p*-phenylsulfonyl-β-N-morpholinopropiophenone hydrochloride (1.5 g.), 25 cc. of ethanol, and Raney nickel subjected to hydrogenation at 60 p.s.i. there was isolated a neutral product, m.p. 97–98°.

Anal. Calc'd for $C_{15}H_{14}O_3S$: C, 65.50; H, 5.09.

Found: C, 65.48; H, 4.86.

The *2,4-dinitrophenylhydrazone* was prepared in the usual way, m.p. 220–221°.

Anal. Calc'd for $C_{21}H_{18}N_4O_6S$: C, 55.80; H, 3.95.

Found: C, 55.61; H, 3.69.

1-p-Phenylsulfonylphenylethanol. The corresponding sulfide, 5 g., was dissolved in 50 cc. of acetic acid and was treated with 5 g. of 30% hydrogen peroxide. The mixture was allowed to stand for one week and then was hydrolyzed and neutralized with 5% sodium hydroxide. The product obtained in essentially quantitative yield was crystallized from ethanol to the constant m.p. 80–81°.

Anal. Calc'd for $C_{14}H_{14}O_3S$: C, 64.45; H, 5.37.

Found: C, 64.06; H, 5.31.

p-Phenylmercaptoacrylophenone. Compound II (5 g.) was dissolved in water and the solution was made basic with 5% sodium hydroxide. The mixture was steam-distilled until the distillate was free of morpholine, and the residue was separated and crystallized from ethanol to the constant m.p. 51–52°.

Anal. Calc'd for $C_{15}H_{12}OS$: C, 74.90; H, 5.03.

Found: C, 74.43; H, 5.31.

The *2,4-dinitrophenylhydrazone* was prepared in the usual way, m.p. 151–152°.

Anal. Calc'd for $C_{21}H_{16}N_4O_4S$: C, 60.50; H, 3.81.

Found: C, 60.37; H, 3.64.

SUMMARY

The Mannich condensations of *p*-phenylmercaptoacetophenone and of the corresponding sulfone are described. The sulfide ketone can be reduced to the corresponding alcohol and the latter oxidized to the corresponding sulfone alcohol. One of the Mannich condensation products of the sulfide was reduced to the alcohol, but an attempt to reduce the sulfone caused hydrogenolysis of the amino group. Under alkaline conditions the Mannich condensation product of the sulfide gave *p*-phenylmercaptoacrylophenone.

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