apparatus. After the addition was complete, the mixture was warmed at 40–50° for 4 hours. The complex was decomposed with iced hydrochloric acid and the ketone I was isolated in the usual manner. Yield, 153 g. (72%), b.p. 152–155° (2 mm.).

Anal. Calc'd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.49; H, 5.88.

The *oxime* of the ketone melted at 164–165°.

Anal. Calc'd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77. Found: C, 73.71; H, 5.71.

The *diacetate of the oxime* was prepared by refluxing the oxime with acetic anhydride for 2 hours, yield 10.5 g. (65%), m.p. 123–124°.

Anal. Calc'd for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50. Found: C, 69.26; H, 5.69.

Reduction of 2-hydroxy-3-methylbenzophenone. In the copper liner of a conventional high pressure hydrogenation apparatus were placed 15 g. of I, 5 g. of Raney nickel, and 150 ml. of methylcyclohexane. The initial hydrogen pressure was 2500 p.s.i. at room temperature. After heating was started, there was some reduction at 65° but most of the reduction took place around 200°. When there was no further drop in pressure, the product was isolated in the usual manner, but it was partly soluble in base indicating incomplete reduction. This material was returned to the liner with fresh catalyst and solvent and heated until no further hydrogen was absorbed. This product distilled at 120–121° (2 mm.), yielded 5 g. (34%), n_D^{21} 1.4960. It solidified to yield III in the form of waxy white needles, m.p. 42–44°.

Anal. Calc'd for $C_{14}H_{26}O$: C, 79.93; H, 12.46. Found: C, 79.96; H, 12.56.

The *phenylurethan* of III melted at 138–139°.

Anal. Calc'd for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.48. Found: C, 76.62; H, 9.63.

7-Methyl-3-phenylbenzisoxazole (II). The crude mono acetate of the oxime of I was prepared as described by Lindenmann and Thiele.[4] The oxime (5 g.) was warmed with 20 ml. of acetic anhydride until the oxime dissolved, then the solution was poured onto ice. The white solid which separated was collected on a filter, washed, and dried, yield 4.5 g. (76%) m.p. 99–103°.

In a 25-ml. flask fitted for distillation was placed 6 g. of the crude oxime monoacetate. The flask was immersed in a metal bath preheated to 125° and evacuated with an oil pump. The reduced pressure was maintained with the pump for one hour, then the temperature of the bath was raised and the product was distilled. The benzisoxazole II distilled at 147–150° (1 mm.), yield 3.5 g. (76%) n_D^{21} 1.6235. It did not solidify.

Anal. Calc'd for $C_{14}H_{11}NO$: C, 80.36; H, 5.30. Found: C, 80.06; H, 5.44.

Nitration of II in an ice bath with fuming nitric acid[5] yielded a white solid, m.p. 225.5–226.5° after recrystallization from glacial acetic acid. The carbon and hydrogen percentages agreed with those calculated for a dinitro compound.

Anal. Calc'd for $C_{14}H_9N_3O_5$: C, 56.19; H, 3.03. Found: C, 56.51; H, 3.23.

Hydrogenation of 7-methyl-3-phenylbenzisoxazole. In the copper liner were placed 10 g. of II, 9 g. of Raney nickel, and 150 ml. of methylcyclohexane. The initial hydrogen pressure was 2400 p.s.i. at room temperature. After heating was started, reduction began at about 220° and that temperature was maintained until there was no further pressure drop. The product IV was isolated in the usual manner, yield 5 g. (30%), b.p. 110–113° (1 mm.), n_D^{20} 1.4900.

The *phenylurethan* of this product IV melted initially at 90–100°. After one recrystallization, the melting point was 99–105° and was unchanged after several recrystallizations from petroleum ether (b.p. 60–80°). The values from the carbon and hydrogen analyses agreed with those calculated for the phenylurethan of 2-methyl-6-(cyclohexylmethyl)-cyclohexanol.

Anal. Calc'd for $C_{21}H_{31}NO_2$: C, 76.55; H, 9.46. Found: C, 76.50; H, 9.51.

A mixture of this derivative and the same derivative of III melted at 98–107°.

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Addition Reactions of Chalcones. III. Some Basic Ketosulfides[1]

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In connection with a study of the pharmacological action of some sulfur-containing compounds, basically substituted alkyl mercaptans and aromatic thiols have been added to certain chalcones. Additions of this general type have been described previously;[2] the reactions have been effected in both acidic and basic media. In this study, the addition was unsuccessful when the basic catalysts piperidine and sodium methoxide were used with 2-diethylaminoethyl and 3-diethylaminopropyl mercaptans, respectively, and the chalcones. However, excellent yields of the ketosulfides were obtained when the hydrochlorides of these mercaptans were employed. The addition of the aromatic thiols to the unsaturated ketones proceeded smoothly in the presence of piperidine.

Some of these compounds and the intermediate chalcones were active in antituberculous tests. The authors are grateful to Parke, Davis and Company for arranging for the tests, the results of which will be reported elsewhere.

EXPERIMENTAL

2-Chloro-4'-acetylaminochalcone. Following a general procedure,[3a] 14.0 g. (0.10 mole) of *o*-chlorobenzaldehyde was condensed with 17.7 g. (0.10 mole) of *p*-acetylaminoacetophenone in the presence of sodium methoxide. The yield of the pure product was 21.3 g. (69%); m.p. 167°.

Anal. Calc'd for $C_{17}H_{14}ClNO_2$: N, 4.68. Found: N, 4.97.

4-Dimethylamino-4'-acetylaminochalcone,[3b] 4-methoxy-4'-acetylaminochalcone,[3c] 4-dimethylamino-4'-methoxychal

(1) For preceding paper of this series see H. Gilman and L. F. Cason, *J. Am. Chem. Soc.*, **73**, 1074 (1951).

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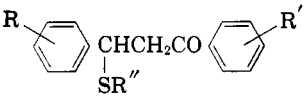
TABLE I

BASIC KETOSULFIDES 

R	R′	R″	M.p., °C.	Yield, %	Formula	Nitrogen Calc'd	Nitrogen Found
H	H	$(C_2H_5)_2NCH_2CH_2$	113–115	92	$C_{21}H_{28}ClNOS$[a]	3.71	3.67
H	H	$(C_2H_5)_2NCH_2CH_2CH_2$	112–113	—	$C_{23}H_{32}INOS$[b]	2.82	2.90
p-$(CH_3)_2N$	*p*-CH_3O	$(C_2H_5)_2NCH_2CH_2$	145–146	88	$C_{24}H_{35}ClN_2O_2S$[a]	6.22	6.28
p-$(CH_3)_2N$	*p*-Cl	$(C_2H_5)_2NCH_2CH_2$	142–143	71	$C_{23}H_{32}Cl_2N_2OS$[a]	6.16	6.14
p-$(CH_3)_2N$	*p*-CH_3CONH	$(C_2H_5)_2NCH_2CH_2$	153–154	87	$C_{25}H_{36}ClN_3O_2S$[a]	8.80	8.75
o-Cl	*p*-CH_3CONH	*p*-C_7H_7	148–149	85	$C_{24}H_{22}ClNO_2S$	3.32	3.57
p-CH_3O	*p*-CH_3CONH	*p*-C_7H_7	130–131	91	$C_{25}H_{25}NO_3S$	3.34	3.35

[a] Purified as the hydrochloride. [b] Methiodide.

cone,[3d] and 4-dimethylamino-4′-chlorochalcone[3e] have been reported.

The ketosulfides. The compounds listed in Table I were prepared by the following general procedure. Molar equivalents of the mercaptan and chalcone were refluxed for some hours (8–30) in absolute ethanol. The solution was concentrated, and the crystalline mass was filtered and washed with ethyl acetate. The basic ketosulfides could be recrystallized from ethanol, but the excess solvent had to be removed immediately upon isolating the product. If not, the crystals acquired a dark brown color on exposure to the air. Washing with ethyl acetate or petroleum ether gave a pure product.

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β-Ethylacrylamide

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The preparation and dehydration of β-ethylacrylamide to β-ethylacrylonitrile has been reported recently.[1] This potentially useful synthesis, however, falls short in one important respect, namely—low yields of β-ethylacrylamide. The need for relatively large quantities of β-ethylacrylonitrile as an intermediate in certain synthetic studies led us to reëxamine the condensation of malonmonoamide with propionaldehyde.

It is well known that the Knoevenagel reaction is reversible and, at the elevated temperatures often used, the water formed in the reaction can effect hydrolysis of the condensation product. Moreover, a not uncommon competing reaction is the removal of the reacting aldehyde through self-condensation (aldol).[2] Since the low boiling point of propionaldehyde precluded using continuous distillation as a means of water removal, it was thought that the gross reaction equilibrium might be favorably displaced by employing a larger proportion of propionaldehyde (which incidentally is more accessible than the other reactant, malonmonoamide). The use of an excess of aldehyde should also compensate for aldol losses.

It has been found that the yield of β-ethylacrylamide can be increased nearly four-fold by condensing malonmonoamide with 2 moles of propionaldehyde instead of with 0.5 mole as heretofore reported.

EXPERIMENTAL

To a mixture of 103 g. (1 mole) of malonmonoamide,[3] 100 ml. of dry pyridine, 2 ml. of piperidine, and 0.5 ml. of glacial acetic acid was added 116 g. (2 moles) of freshly distilled propionaldehyde and the system was heated under reflux (oil-bath at 80–82°) for 24 hours. As much pyridine as possible was distilled off (water pump) at 80°, and the cooled residue was triturated with alcohol-free ether and collected by filtration. After a second ether treatment, and air-drying, there remained 47.1 g. of practically colorless crystals, m.p. 150° (softening at 145°). Recrystallization from acetone afforded 42 g. (in two crops) of colorless plates, m.p. 151.5–153°. This represents a yield of 42.5% of *pure* material (based on malonmonoamide) as compared with 11.5% reported earlier.[1] A sample, sublimed at 120–130°/0.5 mm., melted at 152.5–154° (uncorr.), (lit.,[1,4] 148°, 152°).

Anal. Calc'd for C_5H_9NO: C, 60.6; H, 9.15. Found: C, 60.8; H, 9.14.

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