Recrystallization from alcohol gave light yellow needles, melting at 230–231°.

Anal. Calc'd for $C_{14}H_{12}N_2O_2$: C, 70.0; H, 5.04. Found: C, 69.5; H, 4.88.

2,7-DIBROMOPHENAZINE[6]

(*a*). *4,5'-Dibromo-2'-methoxy-2-nitrodiphenylamine.* When a mixture of 28.1 g. of 2,5-dibromonitrobenzene, 20.2 g. of 5-bromo-2-anisidine,[11] and 30 g. of anhydrous sodium acetate was heated for 40 hours in an oil-bath at 200–210°, followed by steam-distillation of the unreacted material, etc., there was obtained 30.2 g. of crude, dark red product. Recrystallized several times from absolute alcohol (Norit), this gave small, red-orange needles, m.p. 198–200°.

Anal. Calc'd for $C_{13}H_{10}Br_2N_2O_3$: C, 38.8; H, 2.51. Found: C, 39.0; H, 2.50.

(*b*). *2,7-Dibromophenazine.* An intimate mixture of 2.0 g. of crude 4,5'-dibromo-2'-methoxy-2-nitrodiphenylamine, 2.6 g. of ferrous oxalate dihydrate, and 20 g. of granulated lead heated for 12 minutes in a bath at 260° gave 0.8 g. of crude 2,7-dibromophenazine on vacuum sublimation. Purified by chromatography from benzene on alumina, the compound formed bright yellow needles or prisms, m.p. 251–252°; lit.[6] m.p. 242.5° (d).

Anal. Calc'd for $C_{12}H_6Br_2N_2$: C, 42.6; H, 1.80. Found: C, 42.7; H, 1.99.

7-CHLORO-1-METHYLPHENAZINE

(*a*). *4-Chloro-2'-methyl-2-nitrodiphenylamine.* A mixture of 200 g. each of 2,5-dichloronitrobenzene, *o*-toluidine, and anhydrous sodium acetate was heated for 40 hours at 180°. The usual working-up (steam-distillation, addition of HCl, and continued steam-distillation, etc.) gave a yield of only 51 g. (20.5%), of the crude, as cocoa-colored solid. Several recrystallizations from absolute alcohol gave sparkling orange prisms, m.p. 103–105°.

Anal. Calc'd for $C_{13}H_{11}ClN_2O_2$: C, 59.4; H, 4.24. Found: C, 59.7; H, 4.39.

(*b*). *7-Chloro-1-methylphenazine.* An intimate mixture of 10.0 g. of the cocoa-colored crude product, above, 12 g. of ferrous oxalate dihydrate, and 100 g. of granulated lead, heated for 12 minutes in a bath at 270°, produced a maximum internal temperature of 314°. Vacuum sublimation gave 3.5 g. of product, which on several recrystallizations from ethanol formed yellow needles, m.p. 128–129°.

Anal. Calc'd for $C_{13}H_9ClN_2$: N, 12.3. Found: N, 12.3.

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[11] Madesani, *Gazz. chim. ital.*, **62**, 51 (1932).

The Preparation of 3-Phenyl-7-methylbenzisoxazole

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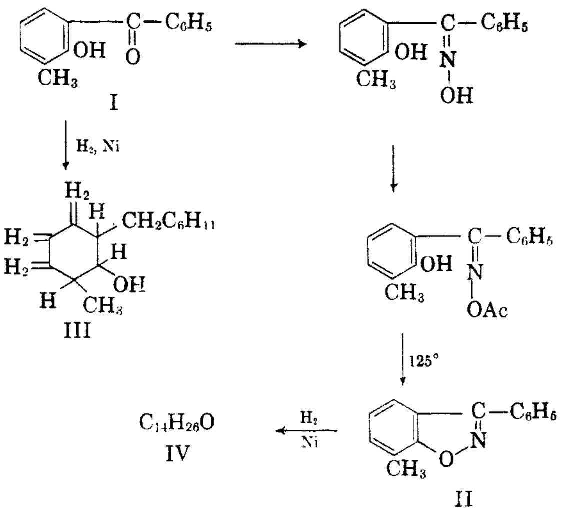
3-Phenyl-7-methylbenzisoxazole, not described in the literature, was needed as a reference compound in connection with another problem. The chosen method of preparation was that of Lindenmann and Thiele[2] as shown in Chart I. Yields were good at each step.

Nitration of II with fuming nitric acid in the cold yielded a dinitro compound, the orientation of which was not determined. Hydrogenation of both I and II over Raney nickel should yield 2-methyl-6-(cyclohexylmethyl)cyclohexanol III. The phenylurethan of III obtained from I melted at 138.5–139.5° but the same derivative of product IV from the hydrogenation of II melted at 99–105° after several recrystallizations. A mixture of the two derivatives melted at 98–107°. The values from the carbon and hydrogen analyses of the two derivatives agree closely with the calculated values. Product IV may be a mixture of stereo isomers, one component of which should be III.

EXPERIMENTAL[3]

CHART I



2-Hydroxy-3-methylbenzophenone[4] (I). Technical 2-hydroxy-3-methylbenzoic acid from Distillation Products was purified by recrystallization from aqueous alcohol, and converted to the acid chloride by means of thionyl chloride. A benzene solution of the crude acid chloride from 153 g. of purified acid was added with stirring to 1 l. of thiophene-free benzene and 200 g. of aluminum chloride in the usual

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[1] Abstracted from the Ph.D. dissertation of Donald A. Reich, June, 1956.

[2] H. Lindenmann and H. Thiele, *Ann.*, **449**, 63 (1926).

[3] The carbon and hydrogen analyses were done by R. E. Bolin and R. L. Elliott.

[4] C. Hamada, *Science Repts. Tohoku Imp. Univ., First Ser.*, **22**, 55 (1933), *Chem. Abstr.*, **27**, 3928 (1933), reported the formation of 2-hydroxy-3-methylbenzophenone from benzotrichloride and *p*-cresol, but the melting point he lists for his ketone is the same as that reported for 6-hydroxy-3-methylbenzophenone. By his method of synthesis, Hamada's ketone would have the hydroxyl group in the 6 position. The melting point of the oxime of 6-hydroxy-3-methylbenzophenone is reported in Heilbron, *Dictionary of Organic Compounds*, II, p. 290, as 126–129° whereas the oxime of I prepared in the present investigation melted at 164–165°.

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.[2] 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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(5) V. Cathcart B. Meyer, *Ber.* **25**, 3296 (1892).

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

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

(2) References to earlier work on the addition of sulfur compounds are cited in papers by F. Kipnis and J. Ornfelt, *J. Am. Chem. Soc.*, **71**, 3554 (1949) and H. Gilman and L. F. Cason, *J. Am. Chem. Soc.*, **72**, 3469 (1950).

(3) (a) E. Rohrmann, R. G. Jones, and H. A. Shonle, *J. Am. Chem. Soc.*, **66**, 1856 (1944); (b) M. J. S. Dewar, *J. Chem. Soc.*, 619 (1944); (c) W. Dilthey, L. Neuhaus, E. Reis, and W. Schommer, *J. prakt. Chem.*, **124**, 81 (1930); (d) P. Pfeiffer, *Ann.*, **441**, 228 (1925); (e) P. Pfeiffer and H. Kleu, *Ber.*, **66**, 1704 (1933).