much significance should not be attributed to the temperatures of melting given, since these, as well as their limits, can be made to vary considerably by changes in the rate of heating.

Laboratory of Chemical Pharmacology
National Cancer Institute
Bethesda 14, Maryland

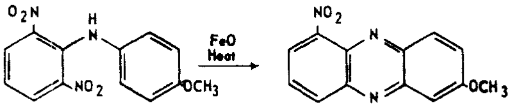
Phenazine Syntheses. VII.[1] Certain Disubstituted Phenazines

Donald L. Vivian

Received March 30, 1956

The compounds given in this paper continue the illustration of the applicability of ring closure through the nitro group to the synthesis of several types of phenazines. These compounds were prepared during the course of work directed toward the chemistry of vital stains.

One of the compounds described, 7-methoxy-1-nitrophenazine, is of special interest because its formation, although in lower than average yield, furnishes the first reported example of a ring closure by this method in which one nitro group remains unchanged:[2]



Another of the compounds reported, 2-chloro-8-N,N-dimethylaminophenazine, is an alternative intermediate for the preparation of 2-amino-8-N,N-dimethylaminophenazine, which can be modified to form a vital stain.[3] referred to in German usage as "Neutral Violet."

Slack and Slack[4] have reported the formation of 2,3-dimethoxyphenazine by the same method given herein, but do not give the melting point and analysis.

Another of the compounds included in this paper, 2,7-dibromophenazine, is also a known compound,[5] but has not been reported before as having been made by nitro-group ring closure.

EXPERIMENTAL[6]

7-METHOXY-1-NITROPHENAZINE

(*a*). *2,6-Dinitro-4'-methoxydiphenylamine.* A mixture of 25 g. of 1-chloro-2,6-dinitrobenzene,[7] 24 g. of *p*-anisidine, 37.5 g. of sodium acetate trihydrate, and 375 cc. of 95% ethanol was refluxed for 16 hours. The precipitate formed on cooling to room temperature was washed once with 125 cc. of ethanol, then with water, and air-dried. The dull, brick-red crude so obtained weighed 32.6 g. (91%), and on recrystallization from absolute alcohol formed small, yellowish-red needles, m.p. 171–173°.

Anal.[8] Calc'd for $C_{13}H_{11}N_3O_5$: C, 54.0; H, 3.81. Found: C, 53.9; H, 3.80.

(*b*). *7-Methoxy-1-nitrophenazine.* When a mixture of 1.0 g. of crude 2,6-dinitro-4'-methoxydiphenylamine, 1.3 g. of ferrous oxalate dihydrate, and 10 g. of granulated lead was heated in an open flask in an oil-bath at 250–262° for 20 minutes, no internal temperature rise above that of the bath occurred. Vacuum sublimation from the entire reaction mixture gave 0.15 g. of greenish-yellow needles, m.p. 235–236°.

Anal. Calc'd for $C_{13}H_9N_3O_3$: C, 61.2; H, 3.55. Found: C, 61.3; H, 3.61.

2-CHLORO-8-N,N-DIMETHYLAMINOPHENAZINE

(*a*). *4-Chloro-4'-N,N-dimethylamino-2-nitrodiphenylamine.* A mixture of 76.5 g. of N,N-dimethyl-*p*-phenylenediamine, 96.0 g. of 2,5-dichloronitrobenzene, and 90 g. of anhydrous sodium acetate was heated for 40 hours in an oil-bath at 195–210°. Steam-distillation to remove unchanged dichloronitrobenzene was followed by the addition of 100 cc. of HCl, and further steam-distillation until all acid was removed. Extraction of the residue with ether after air-drying gave about 60 g. of very crude, semi-soft product, which was nevertheless satisfactory for ring closure. Recrystallization from alcohol (Norit) gave brick-red microcrystals, m.p. 144–146°.

Anal. Calc'd for $C_{14}H_{14}ClN_3O_2$: C, 57.7; H, 4.84. Found: C, 57.6; H, 5.08.

(*b*). *2-Chloro-8-N,N-dimethylaminophenazine.* When 1.0 g. of the preceding crude compound was heated for 10–15 minutes with 1.3 g. of ferrous oxalate dihydrate and 10 g. of granulated lead, in an open flask immersed in an oil-bath at 250–260°, vacuum sublimation of the whole reaction mixture yielded 0.4 g. of crude product. Recrystallization from ethanol gave brownish-red needles of the 2-chloro-8-N,N-dimethylaminophenazine, m.p. 194–195°.

Anal. Calc'd for $C_{14}H_{12}ClN_3$: C, 65.3; H, 4.70. Found: C, 65.5; H, 4.92.

2,3-DIMETHOXYPHENAZINE[4]

(*a*). *4,5-Dimethoxy-2-nitrodiphenylamine.* A mixture of 20 g. of 4,5-dinitroveratrole,[9] 24.5 g. of aniline, and 40 cc. of absolute alcohol was refluxed for three weeks, and the unreacted material was removed by steam-distillation. Chromatography on alumina from a benzene solution gave 17.4 g. of dull red-orange crude product melting at 111–117°. Three recrystallizations from 95% alcohol gave orange needles, m.p. 120.5–121.5°, Lit.,[10] 91°.

Anal. Calc'd for $C_{14}H_{14}N_2O_4$: C, 61.3; H, 5.14; N, 10.2. Found: C, 61.5; H, 4.83; N, 10.2.

(*b*). *2,3-Dimethoxyphenazine.* A mixture of 2.0 g. of 4,5-dimethoxy-2-nitrodiphenylamine, 2.6 g. of ferrous oxalate dihydrate, and 20 g. of granulated lead gave 0.43 g. of crude 2,3-dimethoxyphenazine on vacuum sublimation after 15 minutes' heating in an oil-bath at 255–260°. During the reaction the internal temperature rose to a maximum of 320°.

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(1) Paper VI: Vivian, *J. Org. Chem.*, **21**, 822 (1956).

(2) Efforts to prepare 1-nitrophenazine by nitro group ring closure with 2,6-dinitrodiphenylamine have so far yielded no definite product.

(3) Vivian and Belkin, *Nature*, in press.

(4) Slack and Slack, *Nature*, **160**, 437 (1947).

(5) Bamburger and Ham, *Ann.*, **382**, 106 (1911).

(6) All melting points reported by the author are corrected.

(7) *Org. Syntheses*, **32**, 23 (1952).

(8) Microanalyses by the Microanalytical Laboratory of the National Institutes of Health, under the supervision of Dr. W. C. Alford.

(9) Erlich and Bogert, *J. Org. Chem.*, **8**, 331 (1943).

(10) Hughes, Lions, Maunsell, and Wright, *J. Proc. Roy. Soc. N. S. Wales*, **71**, 428 (1938).

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.

LABORATORY OF CHEMICAL PHARMACOLOGY
NATIONAL CANCER INSTITUTE
BETHESDA 14, MARYLAND

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

The Preparation of 3-Phenyl-7-methylbenzisoxazole

DONALD A. REICH[1] AND DOROTHY V. NIGHTINGALE

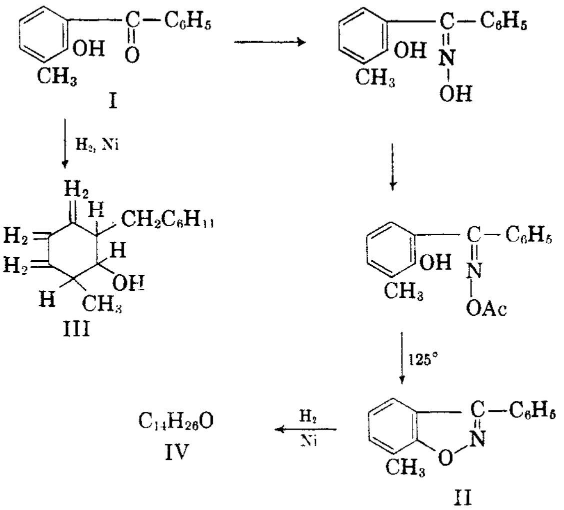
Received April 2, 1956

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°.