

and water-ethanol-ethyl acetate, m.p. 258–259° (slow heating) or 278–281° (rapid heating), with decomposition. It gave a strong blue ninhydrin test.

*Anal.* Calcd. for  $C_8H_{10}N_2O_2Cl_2$ : C, 36.93; H, 7.36; Cl, 27.25. Found: C, 37.12; H, 7.86; Cl, 27.60.

**2-(4-Benzylpiperazino)-propanol.**—The reduction of 31 g. (0.112 mole) of ethyl 2-(4-benzylpiperazino)-propionate by 7.6 g. (0.2 mole) of lithium aluminum hydride in ether was carried out in the usual way. After 5 hours under reflux, the solution was treated with 18 ml. of water which must be added *dropwise* with stirring, initially at a maximum rate of one drop each few seconds, since the reaction mixture tends to foam as the hydrogen is involved. After the water had been added and the reaction mixture stirred an additional 10 minutes to ensure the destruction of all of the hydride, 9 g. of Dry Ice in small pieces was added through the condenser over 5 minutes with stirring, to decompose any lithium alkoxide. Filtration, washing of the solids with anhydrous ether, removal of the solvent and distillation of the remaining oil gave 22.5 g. (86%), b.p. 111–130° at 0.3 mm. The dihydrochloride was recrystallized from absolute ethanol, m.p. 239.8° dec.

*Anal.* Calcd. for  $C_{14}H_{24}N_2OCl_2$ : C, 54.72; H, 7.87. Found: C, 54.73; H, 8.20.

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### Hydroxylation of Benzene in a Solution of Hydrogen Peroxide and Copper Sulfate

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The formation and reactions of hydroxyl radicals in aqueous solutions have been the object of numerous investigations.<sup>1</sup> Wieland<sup>2</sup> observed that hydrogen peroxide in the presence of cupric ions degrades stable organic compounds, like benzoic acid, to carbon dioxide and water. Since Baxendale<sup>3</sup> reported that cuprous ions generate hydroxyl radicals from hydrogen peroxide, it seemed probable that the reaction described by Wieland proceeds through the intermediate formation of phenols. On treating benzene under suitable conditions with aqueous hydrogen peroxide and copper sulfate we were able to isolate phenol from the reaction mixture. Salicylic acid was obtained by treating sodium benzoate in a similar manner.

#### Experimental

**Hydroxylation of Benzene.**—Two grams of copper sulfate in 100 ml. of distilled water and 25 ml. of 30% hydrogen peroxide was vigorously agitated on a shaking machine for 14 hr. with 150 ml. of benzene. After 14 hours the mixture was filtered in order to break up the emulsion. The black aqueous layer was acidified with 6 *M* sulfuric acid and then extracted with successive portions of methylene chloride. The benzene and the methylene chloride were extracted with dilute sodium hydroxide and the alkaline extracts were acidified and treated with decolorizing carbon. The resulting clear solution was extracted with methylene chloride. The organic layer was dried and the solvent was removed leaving 0.14 g. of long needles, m.p. 37°, with the characteristic odor of phenol. It was converted into tribromophenol (0.30 g.) by bromine water, and recrystallized from dilute alcohol, m.p. 92° (uncor.). The experiment was repeated with a reaction time of 65 hr. and gave 0.37 g. of the crude product and 0.86 g. of the brominated derivative.

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**Hydroxylation of Sodium Benzoate.**—Fifty ml. of a 0.2 *M* solution of sodium benzoate, adjusted to pH 4 with excess acid, was mixed with an equal volume of a 0.4% solution of hydrated copper sulfate. On the addition of 12 ml. of 30% hydrogen peroxide the solution turned green and some green precipitate settled out. The volume of the system was made up to 500 ml. with distilled water and it was allowed to stand for 13 hr. At the end of that period the yellow brown solution was acidified with 6 *M* sulfuric acid and extracted with ethyl ether. After drying the extract the solvent was removed, leaving 1 g. of a light brown crystalline residue. On the addition of dilute ferric nitrate to an aqueous solution of the product, an intensely violet color developed. The absorption spectra in 0.00040 *M* aqueous ferric nitrate of a 0.014% solution of salicylic acid and a 0.19% solution of the product were compared. At the 530  $\mu$  absorption maximum the values of  $\log I/I_0$  were 0.63 and 0.55, respectively. The yield of 0.04 g. of salicylic acid was estimated colorimetrically.

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### Nitrohydroxy Aromatic Ketones. I. Nitrohydroxyacetophenones

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Though simple in structure, only a few nitrohydroxyacetophenones are described in the literature. These have been prepared in general by nitration of hydroxyketones or their derivatives and by acetylation of nitrophenols. By direct nitration, 3-nitro-4-hydroxy-,<sup>1</sup> 3-nitro-6-hydroxy-<sup>2</sup> and 3-nitro-2-hydroxy-5-methylacetophenones<sup>2,3</sup> were obtained. The oximes and acetyl derivatives of hydroxyacetophenones have also been employed.<sup>4–6</sup>

It has been reported that the nitro group inhibits direct acetylation<sup>7</sup> or migration of the acetyl group under the influence of aluminum chloride.<sup>8,9</sup> However, 3-nitro-4-hydroxyacetophenone has been obtained recently by both reactions.<sup>10</sup> It had been obtained earlier from 2-nitroanisole<sup>11,12</sup> and by hydrolysis of 4-bromo-3-nitroacetophenone.<sup>13</sup> The present investigation confirms other reports<sup>14,15</sup> that inhibition due to the nitro group may be overcome by proper experimental conditions.

The literature also records the formation of picric acid during the attempted dinitration of *o*-hydroxyacetophenone.<sup>5</sup> 3,5-Dinitro-6-hydroxyacetophenone was obtained in this Laboratory as a result of

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