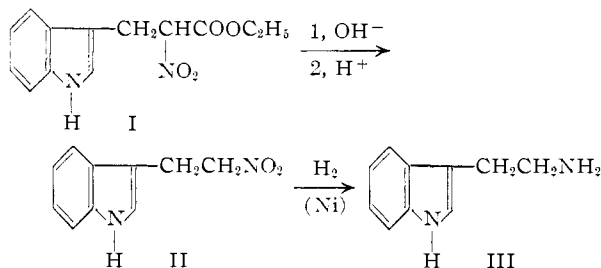


gramine. The scheme below represents a convenient method for the preparation of tryptamine from this compound (I)



Hydrolysis of I is carried out at room temperature using alcoholic sodium hydroxide. A solid sodium salt is collected, dissolved in water and treated with an excess of acid to give 3-(2-nitroethyl)-indole<sup>1,3</sup> (II) in 83% yield. The melting points we found for two dimorphic forms of this compound (55.5–56.1° and 68.3–69.2°) agree with those reported by Noland and Hartman<sup>3</sup> (56.5–57° and 68–68.5°). Catalytic reduction of II (Raney Ni) gave tryptamine, isolated as the hydrochloride, in 81.6% yield.

#### Experimental

**3-(2-Nitroethyl)-indole (II).**—A solution of sodium hydroxide (32.0 g., 0.8 mole) in 64 ml. of water was added to 78.6 g. (0.30 mole) of ethyl  $\alpha$ -nitro- $\beta$ -(3-indole)-propionate (I) in 200 ml. of ethanol. The resulting solution was allowed to stand at room temperature for 44 hours. Solvent was removed under reduced pressure until the flask contained a mass of solid, semi-crystalline material. Ethanol (400 ml.) was added, the mixture was slurried well and the solid was collected on a filter. It was washed with ethanol, then with ether and dried on the filter. The solid was dissolved in 600 ml. of water, the solution was cooled in ice and acidified by slowly adding 20% hydrochloric acid until the pH was between 4 and 5. Crystalline material began to separate and the flask was cooled at 4° overnight. The light pink crystals were collected, washed with water and dried under vacuum. The yield of 3-(2-nitroethyl)-indole was 47.4 g. (83.2%). Material of analytical purity was obtained from the "practical grade" product described above by dissolving it in 200 ml. of ethanol, treating the solution with charcoal, filtering and adding 95 ml. of warm water to the warm (60°) filtrate. The flask was allowed to cool slowly to room temperature and was then placed in the refrigerator for 2 days. The large, sparkling plates were collected on a filter and washed with two 40-ml. portions of 50% ethanol. The product, dried under vacuum, weighed 39.14 g. (68.5%) and melted at 55.5–56.1°. Two months later the melting point of the same material was 68.3–69.2°. It was shown by analysis and infrared spectra that these are dimorphic forms.

*Anal.* Calcd. for  $C_{10}H_{10}N_2O_2$ : C, 63.14; H, 5.30; N, 14.73. Found: C, 62.80; H, 5.20; N, 14.71.

**Tryptamine (3-(2-Aminoethyl)-indole) (III).**—In a Parr rocking autoclave of 250-ml. void volume was placed 25.8 g. of 3-(2-nitroethyl)-indole, 102 ml. of ethanol, approximately 3.8 g. of Raney nickel catalyst and hydrogen under a pressure of 1520 p.s.i. at 23°. The autoclave was heated as rapidly as possible. Very little reduction occurred until the temperature reached 85°, when it was complete in about 3 minutes. Heating was discontinued, the temperature continued to rise to 100°, and the autoclave was allowed to cool slowly to room temperature. Catalyst was removed by filtration and the filtrate was concentrated under vacuum to 75 ml. An excess of 10% alcoholic hydrogen chloride was added, causing crystalline material to precipitate. The mixture was chilled at 4° overnight, the crystals were collected on a filter and washed with a little cold ethanol, then ether. The light brown, crystalline material weighed 21.77 g. (81.6%), m.p. 240° dec. An analytical sample

(3) W. E. Noland and P. J. Hartman, *THIS JOURNAL*, **76**, 3227 (1954).

was prepared by recrystallizing the above material twice from ethanol; m.p. 242–248°.

*Anal.* Calcd. for  $C_{10}H_{13}ClN_2$ : C, 61.06; H, 6.66; N, 14.25. Found: C, 61.33; H, 6.41; N, 14.23.

The reduction was also carried out under the same conditions in the presence of a slight excess of acetic acid. The solvent was removed under reduced pressure and the residual solid was recrystallized from ethanol to give 60% of pure tryptamine acetate, m.p. 134–135°. Free base prepared from the acetate melted at 114–115° (uncor.).

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## Hydroxylation of Benzene in Aqueous Solution in the Presence of Hydroxylamine Hydrochloride

By JAN O. KONECNY

RECEIVED FEBRUARY 21, 1955

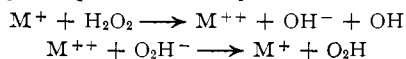
The formation of *o*-nitrosophenol at room temperature by the action of aqueous hydrogen peroxide, hydroxylamine hydrochloride and copper sulfate on benzene or phenol has been described in the literature.<sup>1</sup> Other *o*-nitrosophenols have been prepared<sup>2</sup> in the same manner from numerous aromatic hydrocarbons, phenols and their derivatives. *o*-Nitrosophenols, formed in small quantities, are identified readily owing to their formation of characteristic and intensely colored complexes<sup>3</sup> with the ions of transitional metals. The reaction has been attributed to the formation of  $-NOH$  radicals and their attack on the organic molecule. In order to explain the seemingly specific catalytic action of copper ions, it has been postulated<sup>3</sup> that they react with and stabilize the free radicals.

The present investigation revealed that ferrous sulfate, cuprous chloride and metallic copper also catalyzed the reaction. Traces of *o*-nitrosophenol were found to be formed from benzene even in the absence of a catalyst, and under such conditions the reaction rate was increased by exposing the solution to X-rays. Phenol, however, reacted readily with the solution of hydroxylamine hydrochloride and hydrogen peroxide. The formation of  $-NOH$  radicals in the system has so far remained conjectural. However, ample evidence is available concerning the formation of hydroxyl radicals from hydrogen peroxide by the action of short wave radiation,<sup>4</sup> of copper<sup>5</sup> and iron salts<sup>6</sup> and metallic silver and mercury.<sup>7</sup> It has been shown<sup>4,6,8</sup> that such systems oxidize benzene to phenol. It also has been shown<sup>9</sup> that hydroxylamine hydrochloride is oxidized to nitric acid by hydrogen peroxide, and it is very probable that nitrous acid is formed in the reaction as an intermediate. *p*-Nitrosophenol<sup>9</sup> has been prepared by the action of these reagents on phenol, and the formation of *o*-nitrosophenol from phenol and nitrous acid is described in this work.

- (1) O. Baudisch, *Science*, **92**, 336 (1940).
- (2) G. Cronheim, *J. Org. Chem.*, **12**, 1 (1947).
- (3) O. Baudisch, *Science*, **108**, 443 (1948).
- (4) H. G. C. Bates, M. G. Evans and N. Uri, *Nature*, **166**, 869 (1950).
- (5) J. H. Baxendale, M. G. Evans and G. S. Park, *Trans. Faraday Soc.*, **42**, 155 (1946).
- (6) H. Loeb, G. Stein and D. Weiss, *J. Chem. Soc.*, 2074 (1949).
- (7) J. Weiss, *Trans. Faraday Soc.*, **31**, 1547 (1935).
- (8) J. O. Konecny, *THIS JOURNAL*, **76**, 4993 (1954).
- (9) C. Wurster, *Ber.*, **20**, 2631 (1887).

Halfpenny<sup>10</sup> reported the formation of pernitrous acid by the action of hydrogen peroxide on oxides of nitrogen, which is capable of simultaneously hydroxylating and nitrating benzene. All evidence available so far indicates that the conversion of benzene to *o*-nitrosophenol is an oxidation of the hydrocarbon to phenol by hydroxyl radicals, followed by nitrosation.

The assumption accounts for the different reactivities of phenol and benzene with aqueous hydroxylamine hydrochloride and hydrogen peroxide. Nitrous acid, formed by the oxidation of hydroxylamine, nitrosates the phenol readily. However, the presence of a catalyst, like copper sulfate, is required to generate hydroxyl radicals from hydrogen peroxide, and to convert the benzene into phenol, before the nitrosation can take place. The large increase of the yield of *o*-nitrosophenol, which resulted on substituting a cuprous for a cupric salt, and the inhibition of the reaction rate by hydrogen ions, are explained readily in terms of this mechanism. According to Haber<sup>11</sup> the generation of hydroxyl radicals from hydrogen peroxide and a metal ion catalyst depends on the cycle



Cupric ions must be reduced by the second reaction, before the generation of the hydroxyl radicals can take place. The rate of the second reaction is inversely proportional to the hydrogen ion concentration. The predictions of the Haber theory were verified also by comparing the yield of phenol formed from benzene, hydrogen peroxide and ferrous sulfate in neutral and acid solutions.

#### Experimental

**Identification and Determination of *o*-Nitrosophenol.**—The *o*-nitrosophenol was isolated by extracting the acidified reaction mixtures with chloroform. The compound was identified by the intensely yellow-green color of its organic solutions, and the characteristic colors of its cupric, ferrous and cobaltous complexes, formed quantitatively<sup>2</sup> on shaking the organic solution of the material with the aqueous salt solutions. The spectrum of the red cupric complex in water agreed with that described by Cronheim,<sup>3</sup> and was characterized by transmission minima at 339, 420 and 520  $\mu$ . The solution of *o*-nitrosophenol in 0.50% aqueous copper sulfate obeyed Beer's law over the experimental range. The reaction mixtures containing benzene were made up at room temperature by adding the reagents to 100 ml. of a 1.0% solution of hydroxylamine hydrochloride, which was saturated with benzene. One ml. of the 30% stabilizer free hydrogen peroxide was added last. The reaction time was measured from the addition of the hydrogen peroxide to the addition of 40 ml. of 1 *N* sulfuric acid to the reaction mixture. A suitable portion of the acidified solution was extracted rapidly with chloroform until no more yellow material passed into the organic phase. The *o*-nitrosophenol was removed from the combined organic extracts by shaking with 0.50% aqueous copper sulfate, leaving usually a yellow organic layer. The process was discontinued when the equilibration with fresh copper sulfate failed to turn the aqueous layer pink. The product was purified further by extracting the *o*-nitrosophenol into chloroform from the acidified copper sulfate solution, and then back into copper sulfate again, leaving a colorless organic layer. The final extract was made up to a suitable volume with 0.50% copper sulfate, and the optical density of the solution was determined at the 520  $\mu$  adsorption maximum. The values of  $\log I_0/I$ , given at the end of

each experiment, were calculated for solutions made up to the volume of the extracted reaction mixture. In order to establish the extent of interference due to impurities in the final copper sulfate solution, another portion of the reaction mixture was treated in the same manner, but the second chloroform solution was equilibrated with distilled water in place of aqueous copper sulfate. The aqueous extract obtained in this manner was generally transparent to light at 520  $\mu$ .

**Reaction of Benzene in the Presence of Copper Sulfate.**—To 100 ml. of the hydroxylamine hydrochloride solution was added 5 ml. of 0.5% copper sulfate and 1 ml. of hydrogen peroxide. The solution turned pink in a few seconds, and became orange-red on standing. The value of  $\log I_0/I$ , corresponding to the reaction time of 10 min., was 0.145. The experiment was repeated with 0.60 g. of copper sulfate and a reaction time of 5 min. The solution turned deep red on standing. The value of  $\log I_0/I$  was 0.486. When the latter experiment was carried out in a solution which was 0.1 *M* in hydrochloric acid, the mixture turned pink on prolonged standing. The value of  $\log I_0/I$  was 0.085 for a reaction time of 12 hr.

**Reaction of Benzene in the Presence of Ferrous Sulfate.**—In place of the copper sulfate, 5 ml. of 0.5% ferrous sulfate was used. The neutral solution turned orange on adding the hydrogen peroxide, became brown in 1 min. and dark brown and turbid in 5 min. The second solution which was 0.1 *M* in hydrochloric acid, turned first bright yellow and then orange. The values of  $\log I_0/I$  were, respectively, 0.197 and 0.030 for a reaction time of 5 min.

**Reaction of Benzene in the Presence of Cuprous Chloride and Metallic Copper.**—To 100 ml. of the hydroxylamine hydrochloride solution was added 0.20 g. of finely powdered cuprous chloride, and the system was stirred vigorously. The solution turned deep red on adding the peroxide and the color grew more intense on standing. The reaction proceeded in the same manner, when metallic copper was substituted for cuprous chloride. The metal, prepared by dissolving 0.20 g. of zinc in a copper sulfate solution, was washed with dilute sulfuric acid and then with water, before using. The values of  $\log I_0/I$  were 1.46 and 0.900, respectively, for reaction times of 5 min.

**Reaction of Benzene Under Irradiation with X-Rays.**—One hundred ml. of the hydroxylamine hydrochloride solution, containing 1 ml. of hydrogen peroxide, was exposed to X-rays for 1 hr. An identical solution was allowed to stand in the dark for the same period of time. Both systems turned pale yellow; the color of the first solution was more intense. The values of  $\log I_0/I$  were, respectively, 0.004 and 0.002.

**Reaction of Phenol with Hydrogen Peroxide and Hydroxylamine Hydrochloride.**—One ml. of hydrogen peroxide was added to 100 ml. of a solution, which was 0.1% in phenol and 1.0% in hydroxylamine hydrochloride. The system turned yellow in 4 min. and the color grew more intense on standing. Extractions were carried out in 15 and 30 min.; the values of  $\log I_0/I$  were 0.110 and 0.230, respectively.

**Reaction of Phenol with Nitrous Acid.**—To 100 ml. of a solution, which was 0.10% in phenol and sodium nitrite, was added 0.60 g. of copper sulfate. When the green solution was acidified with 5 ml. of 1 *M* sulfuric acid, the color faded, the system became colorless for a few seconds, turning pink and then red on standing. In the absence of copper sulfate, the solution turned yellow after acidification. The values of  $\log I_0/I$  were 0.225 and 0.167, respectively, for a reaction time of 10 min. Similar changes were observed when a stream of nitric oxide, containing some nitrogen dioxide, was passed through a solution of phenol. In the presence of copper sulfate the system turned red on standing and exposure to air.

**The Hydroxylation of Benzene by Ferrous Sulfate and Hydrogen Peroxide.**—To 20 ml. of 3% hydrogen peroxide and 25 ml. of benzene was added 5 ml. of freshly made up 2% ferrous sulfate and the mixture was shaken vigorously throughout the course of the reaction. The temperature rose slowly from 25 to 29° in 6 minutes. No oxygen was evolved. In the next minute a fast reaction occurred in which all hydrogen peroxide was used up and the temperature rose to 56°. The aqueous layer was black and the benzene orange-brown. The odor of phenol was discernible when the solvent was removed. Ten ml. of a gas, probably oxygen, was evolved during the last phase of the reaction,

(10) E. Halfpenny and P. L. Robinson, *J. Chem. Soc.*, 928 (1952).

(11) F. Haber and J. Weiss, *Proc. Roy. Soc. (London)*, **147A**, 333 (1934).

when the experiment was carried out in a 25° bath with constant agitation. The experiment was repeated with different quantities of benzene and "neutral" solutions of ferrous sulfate and hydrogen peroxide. For a fixed volume and composition of the aqueous phase the reaction time increased markedly with the volume of benzene. For a given volume of benzene and the aqueous phase the time decreased with increasing concentrations of hydrogen peroxide and ferrous sulfate. The violent oxidation did not occur in the presence of 0.1 *N* sulfuric acid. When the first experiment was repeated with a 0.15% solution of phenol in benzene the fast oxidation took place in two minutes.

TABLE I  
YIELD OF PHENOL AS A FUNCTION OF REACTION CONDITIONS<sup>2</sup>

The time was measured from the addition of ferrous sulfate to the addition of the 1 *N* sulfuric acid. In experiments 3 and 6 the rapid final oxidation, and the accompanying temperature rise, commenced after 50 min. In the third experiment, the temperature was kept below 26° by the addition of ice to the mixture during the final stage of the reaction.

H <sub>2</sub> O <sub>2</sub> , ml.	FeSO <sub>4</sub> , ml.	Reacn. time, min.	Wt. of phenol, g.
100	20	10	0.05
100	20	30	0.36
100	20	55	1.13
50	10	60	0.09
50	10	30	.03
50 <sup>b</sup>	10	55	.46
50 <sup>b</sup>	10	30	.07
200°	20	240	.76
200 <sup>d</sup>	20	1800	.17

<sup>a</sup> Temperature 23° (water bath), pH 3, volume of benzene 500 ml. except as otherwise noted. <sup>b</sup> 250 ml. of benzene. <sup>c</sup> Temperature in this experiment maintained at 6°. <sup>d</sup> pH 1.

The following method was used to study the formation of phenol: A 2.0% solution of ferrous sulfate was added to a mixture of benzene and 3.0% hydrogen peroxide, which was vigorously stirred in a Morton flask, immersed in a bath at a suitable temperature. Before the mixture was allowed to separate at the end of the experiment, it was acidified with 10 ml. of 1 *N* sulfuric acid. In a few runs it was necessary to break up the emulsion by centrifuging. The aqueous layer was discarded and the phenol was isolated from the organic phase by a method described earlier.<sup>8</sup> The phenol, m.p. 38° (uncor.), crystallized in long needles and was in most cases colorless or pale yellow. The yield was calculated from the weight of tribromophenol, m.p. 93° (uncor.), obtained by treating the product with bromine water.

Table I summarizes a number of experiments. The pH of the systems obtained by mixing "neutral" solutions of ferrous sulfate and hydrogen peroxide was approximately 3. In one experiment the solution was adjusted to pH 1 with sulfuric acid.

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### Piscidic Acid from *Narcissus poeticus*<sup>1</sup>

BY F. SHIGEO OKUMURA, R. R. SMEBY AND F. M. STRONG  
RECEIVED JUNE 4, 1955

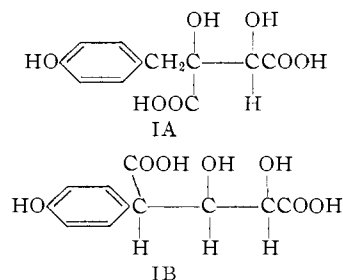
The isolation and partial characterization of several apparently new acids from *Narcissus poeticus* bulbs has recently been reported.<sup>2</sup> The most

(1) Published with the approval of the Director of the Wisconsin Agricultural Experiment Station. Supported in part by the Research Committee of the Graduate School from funds supplied by the Wisconsin Research Foundation.

(2) R. R. Smeby, V. Zbinovsky, R. H. Burris and F. M. Strong, *This Journal*, **76**, 6127 (1954).

stable acid, C<sub>11</sub>H<sub>12</sub>O<sub>7</sub> (I), obtained in relatively large amounts, was found to contain one phenolic hydroxyl, two alcoholic hydroxyl and two carboxyl groups.<sup>3</sup>

In further work it has been established that alkali fusion of I results in the formation of *p*-hydroxybenzoic and *p*-hydroxyphenylacetic acids, and that periodate oxidation yields formic and oxalic acids. In the light of these findings it was tentatively concluded that I has either the structure IA or IB



At this point in the study the similarity of I to piscidic acid, obtained by A. Robertson and co-workers from *Piscidia erythrina*,<sup>4</sup> was noted. A comparison of some of the properties of the two substances and their derivatives is given in Table I.<sup>5</sup> At first only free piscidic acid and its dimethyl ester were available for comparison, and it will be seen from Table I that appreciable differences were observed, particularly in the properties of the two free acids. Infrared spectra of the acids were determined as micromulls in mineral oil, and, although the tracings were generally very similar, distinct differences were again apparent. Another point of disagreement noted at first was a 12° difference in the m.p. of the two dimethyl esters. However, it was found that this discrepancy was due to the existence of two polymorphic forms of this ester, one melting at 115° and the other at 127°. Neither gave any m.p. depression with dimethyl piscidate.

TABLE I  
COMPARISON OF PISCIDIC ACID AND AN ORGANIC ACID OBTAINED FROM *Narcissus Poeticus* BULBS

Property	Piscidic acid		Compound I Obsd.
	Lit. <sup>4</sup>	Obsd.	
M.p., °C. <sup>a</sup>	186-187	183-184 dec.	184-184.5 dec.
[α] <sub>D</sub> (c 2.6, water)	+41.02° (20°)	...	+48.88° (28°)
Dimethyl ester, m.p., °C.	127	127	115, 127 <sup>b,c</sup>
Dimethyl ester triacetate, m.p., °C. <sup>d</sup>	84	81-82	82-83
R <sub>f</sub> value <sup>e</sup> of free acid	...	0.56	0.42
dimethyl ester	...	0.72	0.72

<sup>a</sup> Mixed m.p. 166-170°. <sup>b</sup> Apparently polymorphic forms, see text. <sup>c</sup> Mixed m.p. with either form, 126-127°. <sup>d</sup> Mixed m.p. 81-82°. <sup>e</sup> Paper chromatograms carried out as previously described.<sup>2</sup>

When the triacetate was prepared from the dimethyl ester of piscidic acid, the m.p. was found to be very nearly the same as that of the corresponding

(3) This acid was designated compound III in the previous paper.<sup>2</sup> It was obtained only after alkali treatment of extracts of narcissus bulbs and probably does not exist as such in the plant.

(4) W. Bridge, F. Coleman and A. Robertson *J. Chem. Soc.*, 257 (1948).

(5) Samples of piscidic acid and its dimethyl ester were kindly provided by Dr. A. McCookin, University of Liverpool.