

tion of all the data, the free energy given above is probably accurate to 300 cal. and the entropy to one unit.

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p-Cyanostyrene

By C. G. OVERBERGER AND R. E. ALLEN¹

In a recent communication² a method of dehydrating *p*-cyanophenylmethylcarbinol to *p*-cyanostyrene was described. It has now been found that a much better yield can be obtained by first converting the carbinol to the acetate and then cracking the acetate by dropping it onto hot glass beads. The new method works best on quantities of less than 100 g.; with larger quantities polymerization during the deacetylation becomes serious.

Acetate of *p*-Cyanophenylmethylcarbinol.—Into a 200-cc. round-bottomed flask equipped with a condenser was placed 50 g. (0.34 mole) of *p*-cyanophenylmethylcarbinol and 70 g. (0.587 mole) of acetic anhydride. The mixture was treated for four hours under very gentle reflux and the contents of the flask were transferred to a 200-cc. distilling flask. The excess acetic anhydride and acetic acid were removed by distillation under water-pump pressures. The residue was then distilled through a helices-packed column. The product boiled at 154° (6 mm.); n_D^{20} 1.5156, d_4^{20} 1.0972. The yield was 58 g. (0.307 mole) or 90.3% of the theoretical amount.

*Anal.*³ Calcd. for C₁₁H₁₁O₂N: C, 69.82; H, 5.86. Found: C, 70.08; H, 5.82.

***p*-Cyanostyrene.**—Through a vertical fifteen inch, 20-mm. Pyrex tube, packed with solid glass beads heated to 575–600° by means of an electric furnace, was dropped 58 g. (0.307 mole) of the acetate of *p*-cyanophenylmethylcarbinol to which had been added a gram of *p*-*t*-butylcatechol, at the rate of one drop per second. The distillate was collected in an ice-cooled receiver, washed twice with 100 cc. of water and twice with 100-cc. of a 10% solution of sodium bicarbonate and dried over anhydrous sodium sulfate to which was added a small amount of *p*-*t*-butylcatechol. The product was distilled through a six-inch column packed with short pieces of glass rod. The yield was 30 g. (75.8%) b. p. 92–93° (3 mm.); n_D^{20} 1.5772.

(1) The work described in this note was done under the sponsorship of the Office of Rubber Reserve, Reconstruction Finance Corporation, in connection with the Government Synthetic Rubber Program.

(2) Marvel and Overberger, *THIS JOURNAL*, **67**, 2250 (1945).

(3) Microanalyses by Mr. H. S. Clark, Illinois State Geological Survey.

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The Hindered Phenols

By GORDON H. STILLSON

In an article entitled "The Hindered Phenols," by Stillson, Sawyer and Hunt,¹ an unfortunate misstatement was made. On page 304, at the conclusion of the paragraph which begins on page 303, it was stated that 2,6-di-*t*-butyl-4-methylphenol "... is insoluble in aqueous or alcoholic alkali of any strength." The statement intended was "... is insoluble in Claisen solution or in

(1) Stillson, Sawyer and Hunt, *THIS JOURNAL*, **67**, 303 (1945).

aqueous alkali of any strength." However, upon examining the latter statement critically, it occurred to us that the term "Claisen solution" does not accurately define this solvent. Claisen's directions call for dissolving 350 g. of potassium hydroxide in 250 g. of water, and making this up to 1 liter with methanol.² Frequently³ Claisen used a solution consisting of 350 g. of potassium hydroxide dissolved in 400 g. of water, made up to 1 liter with methanol. Niederl⁴ defines Claisen solution as "a mixture of equal parts of methanol and 50% aqueous potassium hydroxide solution." Neither author specifies the purity of the methanol used.

Now it has been found that the solubility of the hindered phenols in Claisen solution is strongly influenced by the proportion of water in the methanol which is added to the aqueous potassium hydroxide solution. Recent experiments have shown that 2,6-di-*t*-butyl-4-methylphenol is soluble to the extent of 6 g. per liter in fresh Claisen solution made up with absolute methanol. When 90 parts absolute methanol to 10 parts of water by weight is employed, the solubility drops off to only 2.7 g. per liter. 2,4,6-Tri-*t*-butyl-phenol is soluble in the amount of 2.3 g. per liter in absolute Claisen solution and 1.7 g. per liter in Claisen solution made up with 90% methanol. This solubility probably can be attributed entirely to the methanol present. The addition of water to these alcoholic alkali solutions precipitates the hindered phenols; when dilute hydrochloric acid is added to the clear filtrates from such precipitations, no further separation takes place.

On the other hand, when the isomer of 2,6-di-*t*-butyl-4-methylphenol, the so-called "crypto-phenol" 2,4-di-*t*-butyl-6-methylphenol, is dissolved in Claisen solution (absolute) at its limiting concentration of 20 g. per liter, the addition of water causes negligible precipitation. The subsequent acidification with dilute hydrochloric acid brings about complete precipitation of the alkylphenol. Thus it appears that the solubility of the crypto-phenol in Claisen solution comes as a result of alkali solubility rather than alcohol solubility. This Note is submitted with the approval of the co-authors.

(2) Claisen, *Ann.*, **418**, 96 (1919).

(3) Claisen, *ibid.*, **442**, 210 (1925).

(4) Niederl, *Ind. Eng. Chem.*, **30**, 1269 (1938).

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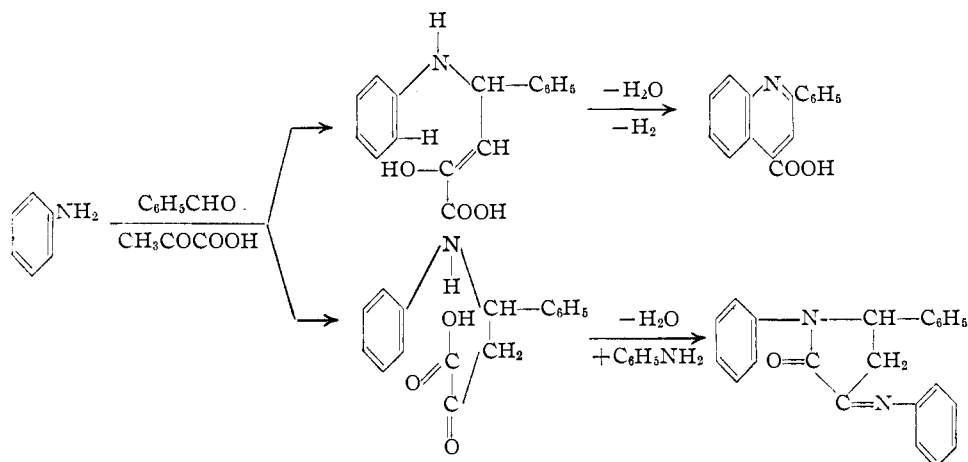
Failure of the Doebner Reaction with 2-Chloro-5-aminopyridine. Synthesis of a Pyrrolidine Derivative¹

By MARTIN J. WEISS AND CHARLES R. HAUSER

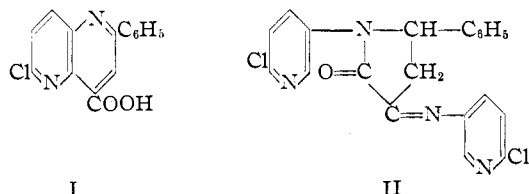
Aniline, benzaldehyde and pyruvic acid may undergo either the Doebner cyclization, involving

(1) The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Duke University.

the removal of hydrogen from the benzene ring to form a quinolinic acid, or a cyclization involving the removal of hydrogen from the amino group to form a pyrrolidine derivative.² The latter course may also involve reaction with an additional molecule of aniline.² These two courses of reaction may be represented thus³

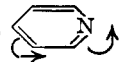


Räth⁴ has reported that with 2-chloro-5-aminopyridine, benzaldehyde and pyruvic acid the Doebner reaction occurs to form (I). However, under the conditions described by Räth, we have obtained an alkali insoluble product which analyzes correctly for the corresponding pyrrolidine (II). When the reaction was carried out at higher temperatures no identifiable product could be isolated. Although our yield of (II) has been satisfactory a better yield might be obtained under conditions which, with aniline, have been shown to favor the formation of the pyrrolidine.²



The Doebner reaction has also failed with 3-aminopyridine even though the anil, which is apparently the intermediate, was first prepared.

The failure of the Doebner reaction with 3-aminopyridine or 2-chloro-5-aminopyridine is not surprising, since the α and γ positions in the pyridine ring are deactivated as electron donors, in which capacity these positions would presumably function. Actually, because of the tendency for

the electronic shift, , the α or γ position in pyridine may function as an electron acceptor as it does, for example, in the reaction of pyridine with the amide ion.⁵

Procedure.—In a 100-ml. flask fitted with a reflux condenser having a calcium chloride tube were placed 30

ml. of commercial anhydrous ethanol, 10.3 g. (0.117 mole) of pyruvic acid and 12.4 g. (0.117 mole) of purified benzaldehyde. Some heat was developed on mixing these components. To this mixture was added 15 g. (0.117 mole) of 2-chloro-5-aminopyridine, prepared by the method of Cragoe and Hamilton,⁶ and the resulting solution was heated on a steam-bath. Within a few minutes a white precipitate had formed. Refluxing was continued for two and one-half hours, the mixture was cooled, suction-filtered and dried *in vacuo*. The solid (21 g., m. p. 180–190°) was recrystallized from dioxane-water yielding 10 g. (38%) of 2-keto-5-phenyl-1-(2-chloro-5-pyridyl)-3-(2-chloro-5-pyridimino)-pyrrolidine (II), melting at 234.4–236.4°, cor.

*Anal.*⁷ Calcd. for $C_{20}H_{14}Cl_2N_4O$: C, 60.46; H, 3.55; Cl, 17.85; N, 14.10. Found: C, 60.38; H, 3.81; Cl, 17.81; N, 14.06.

Attempts to isolate the Doebner product (I) by hot alkali extraction of the crude product, followed by acidification, failed. Räth observed that the product, m. p. 186°, after washing with methanol, was alkali insoluble, although he still considered this to be the acid (I).

When the Doebner reaction was attempted by adding pyruvic acid to a solution of 2-chloro-5-aminopyridine and benzaldehyde in methyl cellosolve at its reflux temperature or in *dow-therm* at 150°, no identifiable product could be isolated.

An unsuccessful attempt has been made to effect the Doebner reaction with 3-aminopyridine, benzaldehyde and pyruvic acid in refluxing methyl cellosolve. This reaction also failed when pyruvic acid was added to *N*-benzal-3-aminopyridine, prepared from the amine and aldehyde,⁸ in refluxing ethanol or benzene.

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(2) Bucherer and Russischwili, *J. prakt. Chem.*, [2] **128**, 89 (1930).

(3) These equations do not necessarily represent the mechanism of the reaction. See ref. 2 and Misani and Bogert, *J. Org. Chem.*, **10**, 458 (1945).

(4) British Patent 259,973 (1926); *Chem. Zentr.*, **99**, I, 2312 (1928).

(5) Deasy, *J. Org. Chem.*, **10**, 141 (1945).

(6) Cragoe and Hamilton, *THIS JOURNAL*, **67**, 536 (1945).

(7) Microanalysis by Dr. T. S. Ma, University of Chicago and by Arlington Laboratories, Fairfax, Virginia.

(8) Kirpal and Reiter, *Ber.*, **60**, 664 (1927).