and ethyl alcohols. In a few cases where the hydrochloride was only very slightly soluble in water, the picrate was prepared by adding an excess of alcoholic picric acid solution to an alcoholic solution of the hydrochloride. The picrate was allowed to crystallize, then was washed with water and recrystallized from ethyl alcohol after air drying.

Invert Soaps.—The quaternary methosulfates were prepared by refluxing equivalent quantities of the free base and di-methyl sulfate and half the total volume of dry benzene for four hours. They were finally crystallized from methyl alcohol or ethyl acetate.

The melting points were determined on Fisher–Johns electrical melting point apparatus, and the point of complete liquefaction was determined.

Acknowledgment.—The authors desire to express their appreciation to the Commanding Officer of Edgewood Arsenal for the mustard gas, and to the Chemical Division of Armour and Company for the amines used in this work.

Summary

Studies in the utilization of mustard gas for peace time industrial purposes have now been extended also to its oxidation products. Thus far, these compounds were used in the preparation of a series of "invert soaps" containing a thiamorpholine nucleus and possessing rather promising properties.

NOTES

The Reversible Inactivation of Gliotoxin by Thiols

BY CHESTER J. CAVALLITO, JOHN HAYS BAILEY AND WILLIAM F. WARNER

In a recent publication, Dutcher, Johnson and Bruce[1] reported results at variance with the observation[2] that cysteine inactivates gliotoxin. The inactivation of gliotoxin has been investigated with a number of thiols at several pH values and is readily observable when antibacterial activity is tested by both the dilution and the cylinder-plate method. In any inactivation studies of this type one obviously includes control tests which would determine the inactivating action of pH alone.

Dilute solutions of gliotoxin buffered at pH values of 6, 7 or 8 rapidly lost their antibacterial activity when treated with an excess of cysteine, N-acetylcysteine or thioglycolate, but not with S-methylcysteine. Longer standing than ten minutes prior to testing produced no further inactivation. When the reaction mixture was allowed to stand in air rather than under nitrogen, antibacterial activity as measured by the plate method, was slowly regenerated. Addition of more thiol again eliminated this activity. It therefore appeared that the thiol inactivation of gliotoxin was reversible by oxidation. This could be shown by treating gliotoxin with cysteine to produce an inactive mixture which after titration with iodine solution (to the starch–iodine end-point) showed complete regeneration of antibacterial activity.

The observed reversible inactivation of gliotoxin by means of reactive thiol compounds favors the dithio structures for gliotoxin rather than the thiosulfinate structure, which latter should not be capable of reversible reduction–oxidation. Whether gliotoxin is merely reduced to the dithiol structure or forms an intermediate product with the inactivating thiol was not shown, as a result of limited quantities of the antibiotic available. However, it would appear that the reaction represents an equilibrium between active (oxidized or dithio-) gliotoxin and inactive (reduced or dithiol-) gliotoxin and the thiol and dithio forms of the inactivator. This would be in agreement with the observed reaction[1] of gliotoxin with alkaline thioglycolate.

The reaction of gliotoxin with thiol groups is in agreement with our postulated mode of action for a large group of antibiotics and would be an example of method 1 (oxidation) discussed in an earlier paper,[3] in which an antibiotic disulfide could oxidize —SH groups essential to certain enzymes to enzyme —S—S— groups.

The failure of Dutcher, Johnson and Bruce to observe the reaction of cysteine with gliotoxin might result from testing for antibacterial action under conditions which would allow reoxidation of reduced gliotoxin to the active dithio-form.

Experimental

Gliotoxin was dissolved in a minimum of ethanol, and diluted with 0.5 M potassium phosphate buffer of the pH desired. The thiol compound was also dissolved in 0.5 M phosphate buffer of corresponding pH values. The two solutions were mixed so that each cc. of mixture contained 0.1 mg. of gliotoxin, not more than 5% ethanol and variable quantities of the thiol. The mixture was allowed to stand at room temperature for various periods of time, then tested for antibacterial activity against *Staphylococcus aureus* by the usual dilution and cylinder-plate methods. Buffer alone at pH of 6, 7 or 8 produced no loss of antibacterial activity in twenty-four hours; 0.1 mg. per cc. of cysteine produced a noticeable loss, 0.4 mg. per cc., nearly complete loss and 1.0 mg. per cc., total loss of antibacterial activity after ten minutes reaction time.

(1) Dutcher, Johnson and Bruce, THIS JOURNAL, **67**, 1736 (1945).
(2) Cavallito and Bailey, *Science*, **100**, 390 (1944).
(3) Cavallito, Bailey, Haskell, McCormick and Warner, *J. Bact.*, **50**, 61 (1945).

Further reaction time (up to twenty-four hours) did not produce significant changes. Under similar conditions, N-acetylcysteine and thioglycolate also inactivated gliotoxin, whereas 10 mg. per cc. of S-methylcysteine had no effect.

The antibacterial activity of reduced gliotoxin could be regenerated immediately by titration with iodine solution or slowly by exposure to oxygen.

RESEARCH LABORATORIES
WINTHROP CHEMICAL COMPANY, INC.
RENSSELAER, NEW YORK   RECEIVED FEBRUARY 1, 1946

Catalytic Conversion of Aldols over Chromia Catalysts

BY J. R. COLEY AND V. I. KOMAREWSKY

Recently it has been shown[1] that branched aldehydes having an *alpha*-substituted carbon atom do not undergo the complex dehydrogenation-condensation reactions when subjected to catalytic conversion over a chromia catalyst at 400° to give either ketones and olefins or unsaturated aldehydes. This was unexpected since the catalytic condensation had been assumed to be similar to a conventional liquid phase aldol condensation.

It has therefore been of interest to examine the behavior of several aldols when subjected to these conditions.

Procedure.—The aldols were prepared by the procedure of Batalin and Slavina.[2] They were vaporized and passed over a chromia catalyst at 400° in a vertical furnace at a space velocity of 0.1 as previously described.[3] The products were distilled in a 36-inch super-cal Heli Grid Podbielniak Column.

Results.—The results obtained are given in the following table.

Aldol	Ketone	B. p., °C.	Yield, %
CH₃CH(OH)C(CH₃)₂CHO	CH₃COCH(CH₃)₂	95	12.0^a
(CH₃)₂CHCHOHC(CH₃)₂CHO	[(CH₃)₂CH]₂CO	124	6.5^b
(C₂H₅)CH₃CHOHCH(C₂H₅)CHO	(C₃H₇)₂CO	144	61.0^c
(C₄H₉)CH₃CHOHCH(C₄H₉)CHO	(C₅H₁₁)₂CO	^{e}	82.8^d

^{a} 2,4-Dinitrophenylhydrazone, m. p. 116–117°. ^{b} 2,4-Dinitrophenylhydrazone, m. p. 85–86°. ^{c} Semicarbazone, m. p. 134–135°. ^{d} Dihexylcarbinol, m. p. 40.0–40.5°. ^{e} M. p. 32.0–32.5°.

These results indicate that the step blocking the conversion of *alpha*-substituted aldehydes is not the primary condensation step but the secondary decarbonylation and dehydrogenation step. The major product obtained from the catalytic conversion of the aldols of *alpha*-substituted aldehydes was the original aldehyde. This is the product normally expected from thermal decomposition of aldols.

DEPARTMENT OF CHEMICAL ENGINEERING
ILLINOIS INSTITUTE OF TECHNOLOGY
CHICAGO, ILLINOIS   RECEIVED DECEMBER 28, 1945

(1) V. I. Komarewsky and L. G. Smith, THIS JOURNAL, **66**, 1116 (1944).

(2) V. S. Batalin and S. E. Slavina, J. Gen. Chem. U. S. S. R., **7**, 202 (1937).

(3) V. I. Komarewsky and J. R. Coley. THIS JOURNAL, **63**, 700, 3269 (1941); V. I. Komarewsky and T. H. Kritchevsky, ibid., **65**, 547 (1943).

The α-Naphthyl Isocyanate Derivative of n-Butylaniline[1]

BY DAVID CRAIG

Kharasch, Richlin and Mayo[2] have described the reaction of butyraldehyde with aniline to produce n-butylaniline among other products. They reported that α-naphthyl isocyanate[3] reacted with this n-butylaniline as well as with a known sample to form N-n-butyl-N-phenyl-N'-α-naphthylurea.

We have found that equivalent weights of the n-butylaniline and α-naphthyl isocyanate do react to form almost the theoretical yield of the expected urea which, however, instead of melting at 277° as stated by Kharasch, et al., actually melts at 97–98°. A mixed melting point of this derivative with that prepared from n-butylaniline isolated from the reaction of butyraldehyde with aniline showed no depression. Hexane was a satisfactory solvent for recrystallization.

Anal. Calcd. for C₂₁H₂₂N₂O: C, 79.20; H, 6.98; N, 8.79. Found: C, 79.18, 79.23; H, 7.01, 6.95; N, 8.67, 8.78.

The single analysis reported by Kharasch and others was 9.03 for nitrogen. This value which is in excellent agreement with 8.97, the nitrogen content of N,N'-di-α-naphthylurea, and the very high melting point of 277° reported by them suggest that under their conditions of reaction, water may have been present or a disproportionation of the expected urea may have occurred. In either case N,N'-di-α-naphthylurea would be expected as a product. The formation of this urea is sometimes troublesome when conducting reactions of α-naphthyl isocyanate with amines in the presence of tertiary amines.[2] Thus n-butylaniline (2.0 g.) and 3-ethyl-2-propylquinoline (0.5 g.) reacted with the isocyanate (1.7 g.) at room temperature to form small amounts of N,N'-di-α-naphthylurea, N-n-butyl-N-phenyl-N'-α-naphthylurea and presumably N,N'-di-n-butyl-N,N'-diphenylurea reported by Wahl.[4] In a subsequent experiment 0.8 g. of N-n-butyl-N-phenyl-N'-α-naphthylurea was heated for two hours at 100° with 0.4 g. of 3-ethyl-2-propylquinoline. By extraction with hexane 0.1 g. of N,N'-di-α-naphthylurea was obtained. Fortunately N,N'-di-α-naphthylurea is easily isolated due to its extreme insolubility in hexane and other solvents. It melts when pure at 296°. The investigation described here suggests that one feature of the effect of tertiary amines on the reaction of α-naphthyl isocyanate with other amines is the formation of N,N'-di-α-naphthylurea.

RESEARCH LABORATORY
B. F. GOODRICH CO.
AKRON, OHIO   RECEIVED DECEMBER 26, 1945

(1) Editor's footnote.—A copy of this Note was sent on its receipt to Dr. M. S. Kharasch for his information. In reply Dr. Kharasch promptly submitted the following statement for publication: "The writer has been aware for a few years that through an error on his part (and not of his co-workers) the melting point of the derivative of n-butylaniline with α-naphthyl isocyanate (isolated in the reaction of n-butyraldehyde and aniline) had been incorrectly reported [Kharasch, Richlin and Mayo, THIS JOURNAL, **62**, 497 (1940)]. Due to pressure of other work this oversight had not been corrected. The melting point of the derivative as obtained by us was 87–89°. By some unexplainable lapse of intelligence, the melting point of the N,N'-di-α-naphthylurea prepared in the course of that work was confused in the writing of the text with that of N-n-butyl-N-phenyl-N',α-naphthylurea. The writer is grateful to Dr. Craig for making the appropriate correction, but he wishes to point out that none of the results or conclusions of that article are thereby invalidated." M. S. KHARASCH.

(2) Kharasch, Richlin and Mayo, THIS JOURNAL, **62**, 497 (1940).

(3) French and Wirtel, ibid., **48**, 1736 (1926).

(4) Wahl, Bull. Soc. Chim., [5] **1**, 246 (1934)

April, 1946

NOTES

717

The Reactions of Acetophenone and Iodine with Some Nitrogenous Bases[1]

By L. Carroll King and Margaret McWhirter

In recent papers from this Laboratory[2] the reaction of ketones with iodine and pyridine to give substituted β-ketoalkylpyridinium iodides was reported. This reaction has now been extended to certain other bases, namely, α, β and γ-picoline, quinoline, isoquinoline and 4-amylpyridine. A suitable excess of each of these bases reacted with iodine and acetophenone to give a quaternary salt corresponding to the base used. The course of the reactions was analogous to that reported in previous papers[2] and may be formulated as
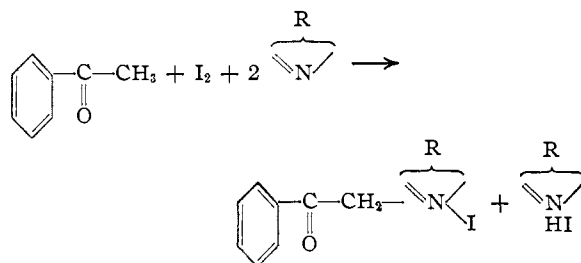
where $\overset{R}{\overbrace{\quad}}\!\!\underset{N}{}$ represents α, β ·or γ-picoline, quinoline, isoquinoline or 4-amylpyridine,

tive and on the fact that alkaline cleavage of each of these gave benzoic acid.[5] The structure of I was confirmed by conversion to 2-phenylpyrrocoline.[6] The structure of V was identified by comparison of the melting point of its perchlorate derivative, Va, with that of the corresponding substance prepared by Krohnke.[7] The structure of VI depends on the mode of formation and on the analyses of the iodide and perchlorate derivative.

The reactions used for preparation of the quaternary iodides described in this paper, when considered in connection with the more extensive survey of similar reactions wherein pyridinium salts were prepared,[2] establish the generality of this type of reaction. Further work is in progress.

This work was partially supported by a grant from the Abbott Fund of Northwestern University.

Experimental

The preparation of each of the quaternary salts was effected in about the same way.

To a solution of 0.1 mole of acetophenone in 30 g. of the appropriate base, 0.1 mole of iodine was added. The reaction mixture was heated overnight on the steam-bath, cooled and thoroughly washed with ethyl ether. Each quaternary salt was separated from the appropriate crude reaction products by one of the methods described below.

I and IV separated slowly from a clarified acetone solution of the appropriate crude reaction products. Both of them were recrystallized from acetone–alcohol containing a small amount of water. V and VI crystallized from an acetone–alcohol solution of the appropriate crude reaction products. III crystallized slowly from the mother

· TABLE I

Iodide	Compound Number	Formula	M. p.,[a] °C.	Yield,[b] %	Analyses, % [c]			
					Nitrogen		Iodide	
					Calcd.	Found	Calcd.	Found
1-Phenacyl-2-picolinium	I	$C_{14}H_{14}INO$	200–202	24	4.13	4.24	37.5	37.5
1-Phenacyl-3-picolinium	II	$C_{14}H_{14}INO$	182–184	56	4.13	3.97	37.4	37.3
1-Phenacyl-4-picolinium	III	$C_{14}H_{14}INO$	195–198	12	4.13	3.93	37.5	37.8
1-Phenacylquinolinium	IV	$C_{17}H_{14}INO$	187–192	43	3.76	3.83	33.8	33.4
2-Phenacylisoquinolinium	V	$C_{17}H_{14}INO$	178–180	95	3.76	3.60	33.8	33.9
1-Phenacyl-4-amylpyridinium	VI	$C_{18}H_{22}INO$	173–175	20	3.53	3.52	32.1	32.6
Perchlorate								
1-Phenacyl-2-picolinium	Ia	$C_{14}H_{14}ClNO_5$	185–189	d	4.49	4.40		
1-Phenacyl-3-picolinium	IIa	$C_{14}H_{14}ClNO_5$	180–181	d	4.49	4.48		
1-Phenacyl-4-picolinium	IIIa	$C_{14}H_{14}ClNO_5$	175–176	d	4.49	4.52		
1-Phenylacylquinolinium	IVa	$C_{17}H_{14}ClNO_9$	193–195	d	4.03	4.21		
2-Phenacylisoquinolinium	Va	$C_{17}H_{14}ClNO_4$	194–197	d	4.03	4.10		
1-Phenacyl-4-amylpyridinium	VIa	$C_{18}H_{22}ClNO_5$	130–131	d	3.81	4.22		

[a] All melting points were observed on a Fisher–Jones melting point block and represent the range where the crystalline salt becomes an orange to black liquid. [b] Yield of pure product isolated based on the ketone. [c] Nitrogen analysis by M. Ledyard. [d] See note 3.

The analytical, melting point and yield data for each of the iodides produced and for the corresponding perchlorate[3] derivative of each is listed in the Table I. The structures[4] of II, III and IV depend on the mode of formation, on the analyses of the iodide and of a perchlorate deriva-

liquors after removal of most of the γ-picoline hydroiodide from an acetone solution of the crude reaction products. II crystallized from a water solution of the clarified crude reaction products.

Chemistry Department
Northwestern University
Evanston, Illinois   Received February 2, 1946

(1) Some of the compounds described in this paper were prepared independently and simultaneously by Dr. Jonathan L. Hartwell and Sylvia R. L. Kornberg, This Journal, 68, in press (1946).

(2) L. C. King, This Journal, 66, 894 (1944); 66, 1612 (1944); 67, 2089 (1945).

(3) Prepared as described in previous papers (ref. 2). The yield was 90–95% in each case.

(4) For identification of compounds see the table.

(5) The cleavage reactions were effected in a manner similar to that described previously (ref. 2). Only about 10% of the theoretical yield of benzoic acid was obtained from IV and V.

(6) The method of Tschitschibabin, Ber., 60, 1607 (1927), was used. The product obtained in this Laboratory melted at 214–215° after crystallization from acetone–alcohol. Anal. Calcd. for C₁₆H₁₁N: N, 7.24. Found: N, 7.40.

(7) Krohnke, Ber., 68, 1177 (1935).

Tetrahydrofuran Compounds. III. Some Acid Derivatives

BY RICHARD D. KLEENE[1]

For the preparation of the following esters, Eastman Kodak Co. furoic acid was used. Tetrahydrofuroic acid was obtained by hydrogenation of furoic acid with a nickel catalyst according to the directions of Paul and Hilly.[2]

Phenacyl ester of furoic acid and the following esters were prepared according to the directions of Shriner and Fuson.[3] The ester was twice recrystallized from water-alcohol solutions; small cream-colored needles, m. p. 85–86°.

Anal. Calcd. for $C_{13}H_{10}O_4$: C, 67.82; H, 4.35. Found: C, 67.96; H, 4.59.

No solid phenacyl ester was obtained from tetrahydro-furoic acid.

p-Phenylphenacyl ester of furoic acid was recrystallized from water and alcohol; crystalline white powder, m. p. 110–111°.

Anal. Calcd. for $C_{19}H_{14}O_4$: C, 74.51; H, 4.57. Found: C, 74.35; H, 4.63.

p-Phenylphenacyl ester of tetrahydrofuroic acid was recrystallized from water and alcohol; m. p. 100.5°.

Anal. Calcd. for $C_{19}H_{18}O_4$: C, 73.55; H, 5.81. Found: C, 73.50; H, 5.59.

p-Phenylphenacyl Ester of *β*-Tetrahydrofurylpropionic Acid.—The acid was obtained by hydrogenation of ethyl *β*-furylacrylate, followed by saponification with aqueous sodium hydroxide. The derivative was obtained as glistening white needles, recrystallized from water and alcohol; m. p. 97–98°.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.55; H, 6.52. Found: C, 74.86; H, 6.57.

The analyses were performed by Dr. T. S. Ma.

(1) Formerly 1st Lt. CWS, Army of the United States.

(2) Paul and Hilly, *Compt. rend.*, **208**, 359 (1939).

(3) Shriner and Fuson, "Identification of Organic Compounds," 2nd ed., John Wiley and Sons, New York, 1940, p. 132.

2211 BURLING STREET
CHICAGO, ILLINOIS   RECEIVED DECEMBER 26, 1945

The Preparation of 2-(4-Hydroxybenzoyl)-benzoic Acid

BY M. H. HUBACHER

In the synthesis of various phthaleins, a relatively large quantity of 2-(4-hydroxybenzoyl)-benzoic acid was needed. This acid has been prepared by heating 2-(4-halobenzoyl)-benzoic acid with sodium hydroxide,[1] or 2-(4-methoxybenzoyl)-benzoic acid with hydrobromic acid.[2] It has also been shown that when a solution of phenolphthalein in 0.2 N sodium hydroxide is slowly oxidized by air, then the 2-(4-hydroxybenzoyl)-benzoic acid is obtained in a yield of 41–46%.[3] Ullmann and Schmidt produced 2-(4-hydroxybenzoyl)-benzoic acid by treating phthalic anhydride with an excess of phenol in *s*-tetrachloroethane in the presence of aluminum chloride[4]; some 2-(2-hydroxybenzoyl)-benzoic acid and

(1) I. Gubelmann, H. J. Weiland and O. Stallmann, U. S. Patent 1,654,289 [C. A., **22**, 788 (1928)].

(2) L. C. Kin, *Ann. chim.*, **13**, 332 (1940).

(3) M. H. Hubacher, THIS JOURNAL, **65**, 2097 (1943).

(4) F. Ullmann and W. Schmidt, *Ber.*, **52**, 2107 (1919).

phthalein are also formed in this reaction. By the same method, Blicke and Weinkauff obtained a yield of 55% based on the phthalic anhydride,[5] a figure confirmed in this Laboratory. The best method, however, for the production of this acid is clearly that discovered by Friedlaender, who found that the "phenolphthalein oxime" could easily be split into 2-(4-hydroxybenzoyl)-benzoic acid and *p*-aminophenol.[6] The mechanism of this somewhat unusual reaction was cleared up by Orndorff, Murray and Yang[7]; first a rearrangement of the "oxime" takes place and then a splitting
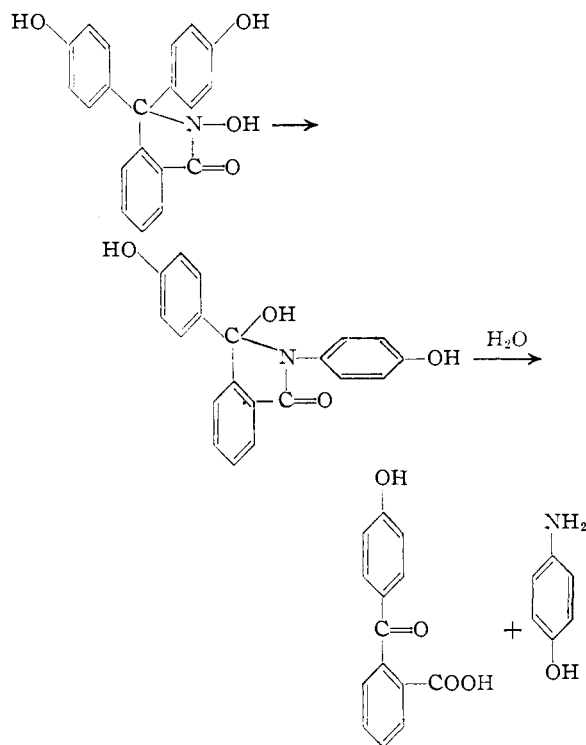
The Friedlaender method was thoroughly investigated and the following procedure evolved, which was found to give consistent and almost quantitative yields of an acid of high purity.

Phenolphthalein Oxime.—Into a 500-ml. three-necked round-bottom flask fitted with a stirrer and a thermometer are placed 31.8 g. (0.10 mole) of phenolphthalein (m. p. 259–263°) and 160 ml. (0.40 mole) of 2.5 N sodium hydroxide. The mixture is heated to 65° and as soon as the phenolphthalein has dissolved, the flame is removed and a solution of 7.6 g. (0.105 mole) of hydroxylamine hydrochloride (96%) or 9.0 g. of hydroxylamine sulfate (95–98%) in 30 ml. of water is added in one portion. The temperature will go up from 65° to 72–79° within two and one-half to three minutes and the color will change from distinct red to a brownish red. The solution is stirred for an additional fifteen minutes at 75–80° and then poured, while still warm, into 690–710 ml. of 0.5 N sulfuric acid. The yellow precipitate is filtered off, using

(5) F. F. Blicke and O. J. Weinkauff, THIS JOURNAL, **54**, 1450 (1932).

(6) P. Friedlaender, *Ber.*, **26**, 174 (1893).

(7) W. R. Orndorff and R. R. Murray, THIS JOURNAL, **39**, 679 (1917); W. R. Orndorff and S. T. Yang, *ibid.*, **45**, 1926 (1923).

a hardened filter paper or a funnel with a sintered glass disc, washed with water, and pressed in order to squeeze out most of the water. It is not necessary to wash it free from SO_4^-. For the subsequent step, the wet cake, weighing from 109–143 g., is used.

2-(4-Hydroxybenzoyl)-benzoic Acid.—The wet, yellow cake of "phenolphthalein oxime" is placed into a flask or a beaker of 500 ml., fitted with a stirrer and a thermometer. One-hundred ml. 5 N of sulfuric acid, prewarmed to 90–104°, is then added in such a way as to wash down any oxime adhering to the neck of the flask or the side of the beaker. The stirrer is started and the yellow slurry rapidly heated. Within three minutes after the temperature has reached 96–102°, a dark yellow solution is formed. After one to three minutes from this point on, the solution first becomes turbid and then crystals of the acid appear. The reaction mixture is stirred for an additional ten minutes at 97–103°, gradually becoming brown. After cooling to 20°, the sandy crystals of 2-(4-hydroxybenzoyl)-benzoic acid are filtered off and washed with three portions of 20 ml. of water. After drying at 100–120°, the acid, of moderate greenish yellow color, weighs from 22.1–23.0 g. and melts at 209–213° cor. (sl. dec.); (yield 91.3–95.0% based on the phenolphthalein).

If a purer product is required, 20 g. of the acid, 0.5 g. of decolorizing carbon (Norit-A) and 1 liter of water are refluxed for fifteen minutes, filtered through a preheated funnel and the filtrate cooled to 5°. From 18.0–18.4 g. of acid, which melts at 211–215° cor. (sl. dec.), is obtained. This purified acid dissolves in ethanol (1 g. in 20 ml.) with but faint yellow color; its solution in 0.1 N sodium hydroxide (0.2 g. in 20 ml.) is clear and either light yellowish or faintly red.

From the filtrate of the acid, together with 75 ml. of wash-water, there can be obtained, after neutralization with 80 ml. of 5 N sodium hydroxide and about 60 ml. of 20% sodium sulfite solution and subsequent extraction with ether, 8.6–9.6 g. of p-aminophenol (m. p. 182–187°).

Equally good yields are obtainable with batches from 0.5 to 1.0 mole of phenolphthalein.

RESEARCH LABORATORY
EX-LAX, INC.
BROOKLYN 17, N. Y.   RECEIVED, JANUARY 3, 1946

Habit Modification of Ammonium Oxalate Monohydrate Crystals During Growth from Solution

BY HARRY J. KOLB[1] AND JOSEPH J. COMER[2]

In a previous paper,[3] the habit modification of ammonium dihydrogen phosphate was described. Additional investigations on the habit modification of ammonium oxalate monohydrate are presented here.

Procedure.—Ammonium oxalate monohydrate crystals were grown in the large water-bath described previously.[3] Each of the tanks was filled with 7.5 liters of ammonium oxalate solution saturated at 40°. Two crystal seeds, about 0.3 sq. cm. in the z-plane and 2 cm. along the z-axis, were suspended in each tank and grown, as before, by reduction of the temperature in the thermostat until the seeds were 4-cm. long. The cations which were added to the saturated oxalate solution containing the growing crystals are the eight listed in Table I. The concentrations of the cations were 0.1 g./liter of solution. Modification tests were also made at the following concentrations of magnesium ion: 0.001, 0.005, 0.01, 0.03, 0.05, 1.0, 2.0, 5.0 g./liter.

(1) Present address: E. I. du Pont de Nemours and Company, Rayon Dept., Pioneering Research, Buffalo, N. Y.
(2) Present address: Pennsylvania State College, State College, Pa.
(3) Kolb and Comer, THIS JOURNAL, 67, 894 (1945).

Results.—The ammonium oxalate monohydrate crystals normally show the (001), (110) and (010) planes. The modifications of the growing crystal by the cations are listed in Table I, *i. e.*, development of (021), (110) and (111) planes.

TABLE I

Development of planes	Zn++	Cu++	Mg++	Sc+++	Co++a	Ni++a	Cd++	Mn++
(110)	+	0	0	0	0	0	+	+
(111)	+	+	+	+	0	0	0	0
(021)	+	+	+	+	+	+	0	0

a Crystal tapered toward z-axis, obscuring the identity of individual planes.

In the series of experiments using magnesium ion, the (021) and (0$\bar{2}$1) planes became more fully developed as the metal ion concentration increased until the (001) plane was finally eliminated. At the magnesium ion concentration of 5 g./liter, the growth of the crystal seed was completely inhibited.

The habit modification may be due to adsorption of foreign metal ions at the crystal–solution interface. This adsorption with subsequent habit modification could be explained by the insolubility interpretation (oxalate in this case) suggested in the previous paper.[3]

The oxalate reticular densities of the crystal planes were calculated and found to be (110), 3.54; (010), 2.87; (111), 1.83; (021), 1.71; (001), 1.06. All are relative to the (011) plane as 1.00. Thus, the appearance of the (021) plane rather than the (011) plane could be accounted for by the density sequence. The removal of the (001) plane could also be explained. In cases where the (110) plane was not developed (given in the table), no growth was noted on either the (110) or (010) planes. The cessation of all growth at high foreign cation concentrations supports a strongly adsorbed ion interpretation. However, it must be stated that we have no direct evidence of an adsorbed metal ion layer.

NAVAL RESEARCH LABORATORY
OFFICE OF RESEARCH AND INVENTION
WASHINGTON, D. C.   RECEIVED SEPTEMBER 24, 1945

The Molecular Structure of Trimethyl Silicon Chloride

BY R. L. LIVINGSTON[1] AND L. O. BROCKWAY

The silicon–carbon bond distances have been determined in several compounds and found to be less than the value of 1.93 Å. obtained for tetramethyl silicon.[2] For example, in hexamethyl disilicon[3] and in SiC,[4] the silicon–carbon distance

(1) Present address: Department of Chemistry, Purdue University, West Lafayette, Indiana.
(2) L. O. Brockway and H. O. Jenkins, THIS JOURNAL, 58, 2036 (1936).
(3) L. O. Brockway and N. R. Davidson, ibid., 63, 3287 (1941).
(4) Ewald and Hermann, "Structurbericht," Akademische Verlagsgesell., 1931, 146.

is 1.90 Å. while in dimethyl silicon dichloride[5] this distance is 1.83 Å. if one assumes a tetrahedral angle for carbon–silicon–carbon. Trimethyl silicon chloride affords an opportunity for further study of the effect of chlorine substitution and for the determination of the silicon–chlorine distance which has been shown to vary somewhat from one chlorosilane to another.

Electron diffraction photographs of trimethyl silicon chloride were prepared using samples provided by W. F. Gilliam[6] of the General Electric Research Laboratory and by E. L. Warrick of the Mellon Institute. An electron wave length of 0.0592 Å. and a camera distance of 102.6 mm, were used. The photographs give rise to the s_0 values listed in Table I and qualitatively resemble curves E and F of Fig. 1. The features
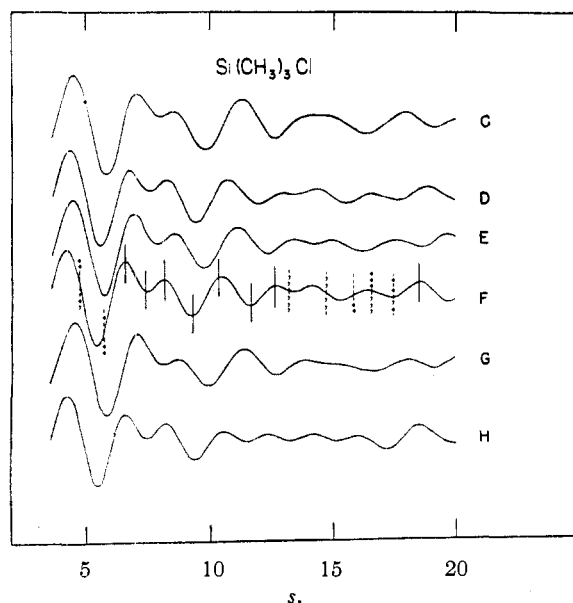

Fig. 1.—Theoretical electron scattering curves for trimethyl silicon chloride. The positions of the maxima and minima observed on the photographs are indicated by vertical lines.

on the photographs beyond $s = 13$ (with the exception of a peak at 18.5) cannot be measured with a satisfactory reproducibility although the qualitative appearance is quite definite. Unreliable measurements are enclosed in parentheses and are not used in the quantitative comparisons.

Scattering curves were calculated for the models shown in Table II. In all but model F the scale was fixed by a C–C distance of 2.96 Å.; the Si–Cl bond was assumed to lie on a trigonal axis of symmetry and C–H was set at 1.09 with $\angle HCH = 109^1/_2°$. Model F differs from E by a scale shift which fixes Si–C at 1.88 Å. and by having the trigonal axes of the methyl groups lie on the Si–C bonds. Of the calculated curves,

(5) R. L. Livingston and L. O. Brockway, THIS JOURNAL, 66, 94 (1944).

(6) W. F. Gilliam and R. D. Sauer, ibid., 66, 1793 (1944).

CALCULATED AND OBSERVED DIFFRACTION MAXIMA FOR TRIMETHYL SILICON CHLORIDE

Max.	Min.	s_0	s_F/s_0	s_E/s_0
1		(4.76)		
	1	(5.71)		
2		6.53	1.006	1.060
	2	7.40	1.011	1.065
3		8.14	0.997	1.050
	3	9.30	0.995	1.048
4		10.34	1.012	1.075
	4	11.63	1.001	1.062
5		12.61	1.007	1.063
	5	(13.16)		
6		(14.70)		
	6	(15.80)		
7		(16.53)		
	7	(17.43)		
8		18.48	1.000	1.065
	8	(20.25)		
9		(21.57)		
	9	(22.87)		
10		(24.88)		
Average			1.004	1.061
Average deviation			0.005	0.006
Si–C, Å.			1.89	1.88
Si–Cl, Å.			2.09	2.08
$\angle$ C–Si–C, deg.			114	114

only E and F agree qualitatively with the photographs. Models with Si–Cl/Si–C 1.07 or less (as in model C) fail to resolve the fifth and sixth maxima. This resolution is also poor in D which has the sixth peak too strong. Models with Si–Cl/Si–C 1.145 (as H) have the fourth maximum too weak or have one peak completely missing. In curve G the sixth maximum is almost completely missing.

CALCULATED MODELS FOR TRIMETHYL SILICON CHLORIDE

$\angle$ C–Si–C, deg.	(Si–Cl/Si–C)			
	1.030	1.070	1.105	1.145
$109^1/_2$	A	B	D	H
114		C	E, F	J
116			G	

The quantitative comparison for model E (Table I) leads to an s/s_0 ratio which is 6% greater than unity. Since C–H was chosen as 1.09 Å. in this model, this gives rise to somewhat large values for the distances between the hydrogens and other atoms. To check the effect of this on the final results, curves C, D, E, G and J were recalculated from models with the scale fixed by setting Si–C at 1.88 Å. and C–H = 1.09 Å. These curves do not differ qualitatively from the original ones and final quantitative results are based on F which gives results only slightly different from E. The final results are: Si–C = 1.89 ± 0.03 Å.; Si–Cl = 2.09 ± 0.03 Å, and $\angle$ C–Si–C = 113 ± 2°.

Discussion

The Si–Cl bond lengths in the chloromethyl silanes are: 2.09 ± 0.03 Å. in $Si(CH_3)_3Cl$, 1.99 ± 0.03 Å. in $Si(CH_3)_2Cl_2$,[5] 2.01 ± 0.02 Å. in $SiCH_3$-Cl_3[5] and 2.02 ± 0.02 Å. in $SiCl_4$.[7] The distances in the chlorosilanes are (in the same order): 2.06 ± 0.05 Å.,[8] 2.02 ± 0.03 Å.,[7] 2.01 ± 0.03 Å.[9] and 2.02 ± 0.02 Å. In both series of compounds the chlorine bond is longer when only one chlorine is attached to the silicon than when two or more chlorine atoms occur in the same molecule. This observation is similar to the effect found in the C–F bonds in fluorocarbons, where the available data are far more extensive. On the basis of the Si–Cl distances reported we should expect the two monochlorosilanes to react more readily than the polychlorosilanes in reactions involving the removal of chlorine.

The Si–C distance reported in $Si(CH_3)_3Cl$ (1.89 ± 0.03 Å.) is intermediate between the values reported in $Si(CH_3)_4$ (1.93 ± 0.03 Å.) and in $Si(CH_3)_2Cl_2$ (1.83 ± 0.06 Å. with a regular tetrahedral angle assumed for C–Si–C).

(7) L. O. Brockway and F. T. Wall, This Journal, **56**, 2373 (1934).

(8) L. O. Brockway and I. E. Coop, Trans. Faraday Soc., **34**, 1429 (1938).

(9) L. O. Brockway and J. Y. Beach, This Journal, **60**, 1836 (1938).

CHEMISTRY LABORATORY
UNIV. OF MICHIGAN
ANN ARBOR, MICH.   RECEIVED FEBRUARY 12, 1946

An Improved Synthesis of Glutaconic Ester

By H. L. LOCHTE AND P. L. PICKARD[1]

Considerable quantities of glutaconic ester were required in connection with a synthetic problem, and previously described methods[2,3,4] were found tedious and expensive. A synthesis starting with citric acid was developed and found to give an over-all yield of 24%, based on the citric acid used. The citric acid was converted to acetone-dicarboxylic ester, which was hydrogenated by Raney nickel to the hydroxy ester. This was dehydrated by thionyl chloride in pyridine. It was found that the hydrogenation either fails completely or proceeds very slowly except with a freshly prepared catalyst.

Diethyl Glutaconate.—One hundred grams of acetone-dicarboxylic ester, prepared by the well-known method,[5] and about 1 g. of freshly prepared Raney nickel were hydrogenated at 1500 lb. pressure and 150°. Reduction was complete in four hours when the catalyst was very active, but in case of catalyst which had been stored under ethanol for long periods of time, or which had not been carefully prepared, hydrogenation either failed completely or was very slow. The catalyst was filtered off and dis-

(1) General Aniline Fellow, 1944–1945.

(2) Conrad and Gutzeit, Ber., **15**, 2841 (1882).

(3) Pechman and Jenisch, ibid., **24**, 3250 (1891).

(4) Blaise, Bull. soc. chim., [3] **29**, 1014, 1028 (1903).

(5) "Organic Syntheses," Coll. Vol. I, 1941, John Wiley and Sons, Inc., New York, N. Y., 10, 237.

carded and the filtrate distilled at 2 mm. pressure. Seventy-seven grams (76%) of β-hydroxyglutaric ester was obtained, b. p. 105–107° (2 mm.), 133° (8 mm.), $n^{20}D$ 1.4381. This ester was dehydrated by the method of Gidvani[6] to yield 62 g. (88%) of glutaconic ester, b. p. 115° (4 mm.), $n^{20}D$ 1.4465. Saponification equivalent: found, 92.8; calculated, 93.1.

(6) Gidvani, J. Chem. Soc., 2666 (1932).

CHEMISTRY DEPARTMENT
THE UNIVERSITY OF TEXAS
AUSTIN, TEXAS   RECEIVED JANUARY 14, 1946

The Standard Free Energy of Formation and Entropy of the Aqueous Magnesium Ion

By C. C. STEPHENSON

Improved calculations of the standard free energy of formation and entropy of the aqueous magnesium ion are made possible by recent thermodynamic data concerning some magnesium compounds.

The standard free energy of solution of $MgCl_2 \cdot 6H_2O$ is given by the equation $\Delta F° = -RT \ln 4(\gamma m)^3 a_1^6$, in which γ, the activity coefficient[1] of magnesium chloride in the saturated solution at 25° is 32.2, the solubility is $5.84\ m$ and the activity of the water is 0.3296; hence, $\Delta F°_{298.1} = -6,180$ cal. The free energies of formation of $MgCl_2 \cdot 6H_2O$,[2] H_2O and the chloride ion are $-505,410 \pm 320$ cal., $-56,693$ cal. and $-31,340$ cal., respectively; from these values and the standard free energy of solution, the standard free energy of formation of the aqueous magnesium ion at 25° is $-108,760$ cal. The corresponding electrode potential is 2.358 volts.

The standard heat of formation of the magnesium ion may be calculated from the heats of formation[3] of $Mg(NO_3)_2$ $-188,770$ cal., and $Mg(NO_3)_2 \cdot 6H_2O$, $-624,410$ cal., and the standard heats of solution,[4] $-21,530$ cal. and $4,340$ cal., respectively. The heats of formation of the nitrate ion,[5] $-49,320$, and water, $-68,318$ cal., are consistent with the heats of formation of the solids. The heat of formation of the magnesium ion is $-111,660$ cal. calculated from the heat of formation and solution of $Mg(NO_3)_2$ and $-111,520$ cal. is obtained from the corresponding data for $Mg(NO_3)_2 \cdot 6H_2O$. With the latter value and the free energy of formation, $\Delta S°_{298.1} = -9.3$ is calculated for the reaction $Mg + 2H^+ = Mg^{++} + H_2$, and the standard entropy of the magnesium ion is -32.7 cal. deg.$^{-1}$ mole^{-1}.

Additional values for the entropy and free energy of formation of the magnesium ion, derived from the solubility products of $Mg(OH)_2$, $MgCO_3$ and $Mg(NO_3)_2 \cdot 6H_2O$, are in good agreement, although less accurate. From a considera-

(1) R. H. Stokes, Trans. Faraday Soc., **41**, 642 (1945).

(2) K. K. Kelley and G. E. Moore, This Journal, **65**, 2340 (1943).

(3) F. E. Young, ibid., **66**, 773 (1944).

(4) W. W. Ewing, E. Klinger and J. D. Brandner, ibid., **56**, 1053 (1934).

(5) W. R. Forsythe and W. F. Giauque, ibid., **64**, 48 (1942).

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

p-Cyanostyrene

BY C. G. OVERBERGER AND R. E. ALLEN[1]

In a recent communication[2] 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. (0.687 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^{20}D 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 $C_{11}H_{11}O_2N$: 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^{20}D 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.

NOYES CHEMICAL LABORATORY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS   RECEIVED FEBRUARY 4, 1946

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] Frequently[3] Claisen used a solution consisting of 350 g. of potassium hydroxide dissolved in 400 g. of water, made up to 1 liter with methanol. Niederl[4] 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).

GULF RESEARCH AND DEVELOPMENT COMPANY
PITTSBURGH 30, PA.   RECEIVED DECEMBER 8, 1945

Failure of the Doebner Reaction with 2-Chloro-5-aminopyridine. Synthesis of a Pyrrolidine Derivative[1]
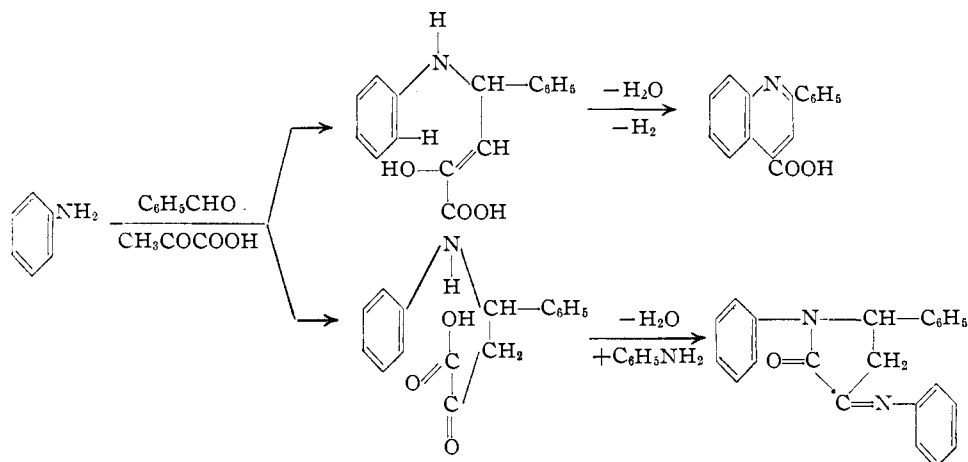
BY MARTIN J. WEISS AND CHARLES R. HAUSER

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 thus[3]

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

Räth[4] 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]
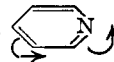

I   II
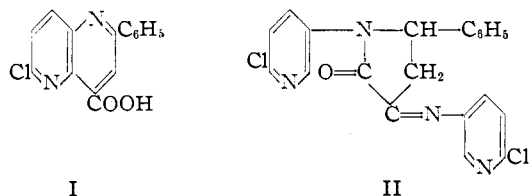
The Doebner reaction has also failed with 3-aminopyridine even though the anil, which is apparently the intermediate, was first prepared.

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

ml. of commerical 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-pyridoimino)-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.

DEPARTMENT OF CHEMISTRY
DUKE UNIVERSITY   RECEIVED JANUARY 28, 1946
DURHAM, NORTH CAROLINA

(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).