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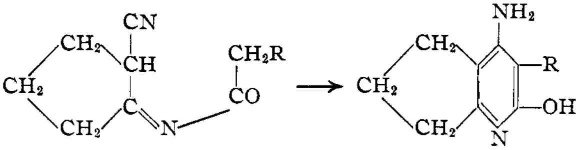
The Cyclization of Acetylated β-Iminonitriles: 4-Amino-2-hydroxy-6,7-dihydropyrindine

BY H. E. SCHROEDER AND G. W. RIGBY

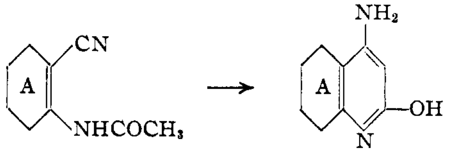
The intramolecular condensation of dinitriles under the influence of sodium ethoxide[1] or alkali metal amides[2] to give 3-iminonitriles has been reported previously. Acyl derivatives of certain 3-iminonitriles have been converted to derivatives of 4-amino-2-hydroxypyridine.[3] In this reaction 2-(acylimino)-cyclopentanecarbonitriles (I), obtained by acylation of 2-iminocyclopentanecarbonitrile, on treatment with sodamide in liquid ammonia at −33° gave excellent yields of 4-amino-2-hydroxy-6,7-dihydropyrindine derivatives in the following manner



I, R = H
III, R = CH_3
V, R = Cl
VII, R = $COCH_3$

II, R = H
IV, R = CH_3
VI, R = Cl
VIII, R = $COCH_3$

Detailed study of this cyclization has revealed that while sodamide effects the condensation at elevated temperatures in inert solvents such as paraffin wax, finely divided sodamide prepared in liquid ammonia by the procedure of Vaughn, Vogt and Nieuwland[4] is a particularly effective agent for the intramolecular cyclization of acylated iminonitriles at the boiling point of liquid ammonia. The majority of the species evaluated gave high yields of the desired pyridine derivatives. Thus, the N-acetylimine (I) was cyclized in 93–97% yield to the pyrindine (II), m. p. 321–322° and the N-propionylimine (III) in 97% yield to the corresponding 3-methylpyrindine (IV), m. p. 287°; even the chloroacetyl- (V) and acetoacetyl- (VII) imines condensed smoothly to form the 3-chloro (VI) and 3-acetyl (VIII) pyrindines in yields of 92 and 85%, respectively. The latter examples illustrate the ease of condensation, for in neither case was there any appreciable evidence of side reactions involving the normally sensitive chlorine atom or the acetyl group. Further extensions of this reaction involving replacement of the cyclopentane ring by either cyclohexane or benzene apparently did not alter the course of the reaction since 2-acetamidobenzonitrile (XXV) was readily cyclized in 93% yield to form 4-aminocarbostyril (XXVI), m. p. 308°, previously obtained[5] only from 4-amino-2-ethoxyquinoline or from 4-hydroxycarbostyril on treatment with ammonia. In similar fashion 2-(acetylimino)-cyclohexanecarbonitrile (XXVII) apparently afforded the desired 4-amino-2-hydroxy-Bz-tetrahydroquinoline (XXVIII). The analytical data and chemical properties of the latter compound appear consistent with the structure indicated, but the melting point (130°) is surprisingly low for members of this series.



XXV A = benzene XXVI A = benzene
XXVII A = cyclohexene XXVIII A = cyclohexene

In view of the dearth of information on materials possessing the 4-amino-2-hydroxypyridine structure, and their ready accessibility by this new route, the chemical behavior of 4-amino-2-hydroxy-6,7-dihydropyrindine (II) was investigated in some detail. Although this compound resembles meta-aminophenol in most respects, the amino group is typical of 4-aminopyridines in its lowered reactivity and lack of basic character. The aminohydroxypyrindine (II) is a monoacid base, crystallizable from water, in which it is soluble hot and sparingly soluble cold, in the form of a monohydrate which loses water of crystallization on heating above 100°. (This behavior is typical of all of these compounds; they are also obtainable from acetic acid as monoacetates.) The pyrindine is readily soluble in cold sodium hydroxide or in cold dilute hydrochloric acid and gives a red color with aqueous or alcoholic ferric chloride solutions indicating the presence of a phenolic hydroxyl group.

Both the amino and hydroxyl groups can be acylated or the acylation can be directed to protect whichever group is desired. Thus, treatment with warm acetic anhydride affords 2-acetoxy-4-acetamido-6,7-dihydropyrindine (IX), m. p. 232°, in which the 2-acetoxy group is readily hydrolyzed by ammonia in methanol to form the 2-hydroxy-4-acetamido derivative (X), m. p. 314°. *p*-Nitrobenzoyl chloride in aqueous potassium hydroxide yields the 2-*p*-nitrobenzoxy derivative (XI), m. p. 203°, which fails to give the characteristic red color with ferric chloride. This amine can be diazotized with sodium nitrite in glacial acetic acid to yield a product which will couple with 1-naphthol. The 4-*p*-nitrobenzoylamino compound (XII) (m. p. 218–219°) is obtained when the free base is heated with *p*-nitrobenzoyl

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[1] Thorpe, *J. Chem. Soc.*, **95**, 1903 (1909).

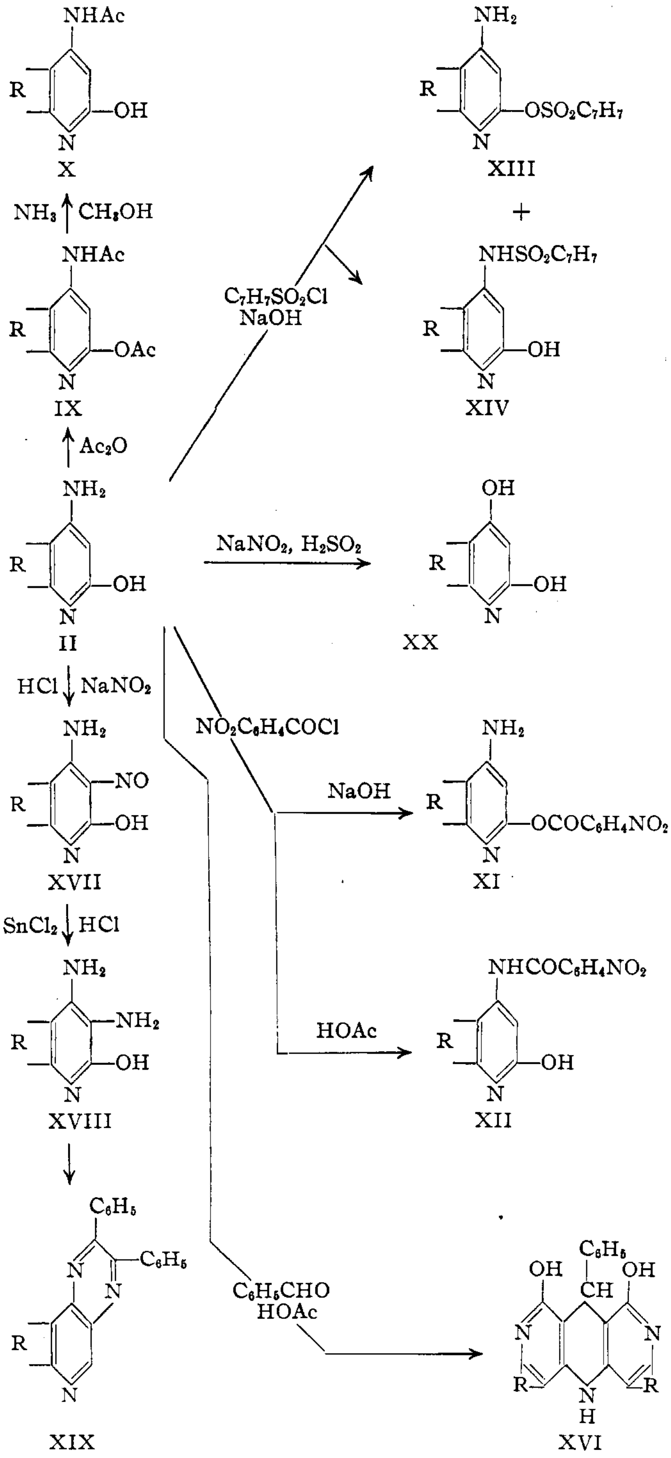
[2] Ziegler, Eberle and Ohlinger, *Ann.*, **504**, 94 (1933); also U. S. Patent 2,068,284, 2,068,586.

[3] Rigby, U. S. Patent 2,333,493.

[4] Vaughn, Vogt and Nieuwland, THIS JOURNAL, **56**, 2120 (1934).

[5] Buchmann and Hamilton, *ibid.*, **64**, 1357 (1942); German Patent 681,980.

Chart I



chloride in glacial acetic acid. This compound gives a characteristic red color with ferric chloride and shows no sign of free amino group on treatment with sodium nitrite in either glacial acetic or cold concentrated sulfuric acid. *p*-Toluenesulfonyl chloride in aqueous potassium hydroxide at 55–60° gives a 49% conversion to the 2-*p*-toluenesulfonate (XIII), m. p. 167°. On concentration of the mother liquors, the more soluble 4-*p*-toluenesulfonamide (XIV), m. p. 168°, is obtained in 12% conversion.

The 3-position ortho to both the hydroxyl and amino groups is reactive. Bromination or chlorination in cold glacial acetic proceeds instantaneously to form the 3-bromo (XV) or 3-chloro (VI) derivatives in high yield. Diazotized aromatic amines couple readily to yield the corresponding azo compounds and reaction with benzaldehyde (or formaldehyde) proceeds smoothly as in the case of *m*-aminophenol to give a dipyrido-pyridine derivative (XVI). Attempted diazotization of 4-amino-2-hydroxy-6,7-dihydropyrindine with sodium nitrite in cold dilute hydrochloric acid proceeded very rapidly to form the bright green 3-nitroso derivative (XVII), m. p. 260° dec. This relatively unstable material precipitates almost immediately in the form of the bright red hydrochloride. Neutralization with sodium hydroxide then affords the green nitroso compound which on further treatment with sodium hydroxide is converted to the blood-red sodium salt, presumably of the isonitroso form. The location of the nitroso substituent was readily confirmed by reduction with stannous chloride to the ortho diamine (XVIII), m. p. 286–287° and subsequent condensation with benzil in glacial acetic acid to form the bright yellow pyrido-(3,4)-pyrazine derivative (XIX).

Diazotization of the aminohydroxypyrindine (II) with sodium nitrite in cold concentrated sulfuric acid yielded the unstable diazonium salt which spontaneously lost nitrogen to form 2,4-dihydroxy-6,7-dihydropyrindine (XX), which chars at 305–310° but exhibits an instantaneous (block) melting point of about 380°. This compound has also been prepared by Prelog.[6] Further confirmation of the structure of the dihydroxy compound is its ready acetylation to the 2,4-diacetoxy derivative (XXI), m. p. 92°, and its nitrosation to form the green 2,4-dihydroxy-3-nitroso-6,7-dihydropyrindine (XXII). It is of interest that the corresponding 3-amine (XXIII) obtainable by stannous chloride reduction is readily diazotized like 3-aminopyridines in general and may be coupled with typical phenols.

It has also been found possible to convert 4-amino-2-hydroxy-6,7-dihydropyrindine to the 2-

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[6] Prelog and Szpilfogel, *Helv. chim. acta*, **28**, 1684 (1945); *C. A.*, **40**, 1835 (1946).

TABLE I

No.	Acylimino-cyclopentane carbonitrile derivatives	M. p., °C.	Nitrogen, % Calcd.	Nitrogen, % Found	No.	2-Hydroxy-6,7-dihydro-pyrindine derivative	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
I	Acetyl	127	18.65	18.55	II	4-Amino-	322	64.1	64.0	6.74	6.66	18.69	18.7
II	Propionyl[a]	116	17.1	17.7	IV	4-Amino-3-methyl	287	65.96	65.96	7.41	7.32	17.08	17.1
VII	Acetoacetyl[b]	94	14.57	14.63	VIII	3-Acetyl-4-amino	>330	....	....	..	..	14.57	14.43
V	Chloroacetyl[c]	166–167	[d]	[d]	VI	4-Amino-3-chloro	324[e]	49.01[f]	49.01[f]	5.3[f]	5.1[f]	11.43[f]	11.85[f]

[a] From the corresponding anhydride—four hours at 90°. [b] From the iminonitrile and acetoacetic ester by boiling in toluene for six hours. [c] From chloroacetyl chloride in pyridine at 20–25°. [d] Calcd.: Cl, 19.1. Found: Cl, 18.7. [e] M. p. and analysis as the acetate. [f] Calcd.: Cl, 14.5. Found: Cl, 14.32.

chloro compound (XXIV) (m. p. 167°) by treatment of the monohydrochloride with phosphorus pentachloride at 150°.

The reactions which have been described above are illustrated in the chart.

Experimental

2-Iminocyclopentanecarbonitrile.—Although the cyclization of adiponitrile with alkali metal amides proceeds in excellent yield,[2] the following method has been found more convenient for the preparation of large amounts in the laboratory. A mixture of 255 g. of metallic sodium and 2500 ml. of dry toluene was heated at 100° under an atmosphere of deoxidized nitrogen to melt the sodium. Adiponitrile (1100 g.) was then introduced slowly with efficient stirring over a period of six hours. After the first addition a white solid separated and some gas was evolved. Addition was carefully continued at such a rate that the mixture maintained a gentle reflux. After a total of ten hours of heating the mixture was cooled, filtered and washed with benzene. The white solid was then suspended in benzene and decomposed by cautious addition of water with stirring. The mixture was then cooled, filtered, and the residual solid extracted with three successive two-liter portions of boiling benzene. On concentration and cooling there was obtained 720 g. (64%) of purified material, m. p. 148°.

2-(Acetylimino)-cyclopentanecarbonitrile (I).—2-Iminocyclopentanecarbonitrile (100 g.) was dissolved in 700 g. of acetic anhydride by gentle warming on the steam-bath. The flask was stoppered lightly and left overnight at room temperature. After cooling to 0° the solid which separated was collected and air dried (104.1 g.). An additional 21.6 g. was recovered by concentrating the mother liquors *in vacuo;* total yield, 90.6%. After recrystallization from ligroin the acetyl compound melted at 127°.

Anal. Calcd. for $C_8H_{10}N_2O$: N, 18.65. Found: N, 18.55.

When the acetic anhydride mixture was allowed to stand two to three weeks, fractional crystallization from benzene–petroleum ether gave the above acetyl compound and in addition another solid, m. p. 171°. The latter compound was obtained in high yield when a trace of catalyst such as zinc chloride or hydrochloric acid was added to the acetic anhydride.

Analyses indicated addition of a molecule of acetic acid to the acetamido compound. This material was not studied further.

Anal. Calcd. for $C_{10}H_{14}N_2O_3$: N, 13.3. Found: N, 13.48.

4-Amino-2-hydroxy-6,7-dihydropyrindine (II). (a) **Low Temperature Cyclization.**—To a well-stirred suspension of 191 g. (4.9 moles) of sodamide in 4,000 ml. of liquid ammonia prepared by the procedure of Vaughn, Vogt and Nieuwland,[5] there was added 300 g. (2 moles) of 2-(acetylimino)-cyclopentanecarbonitrile (I) during forty to sixty minutes. The ammonia was maintained at the original level and stirring continued for three and one-half hours. During this time the mixture changed in color from dark gray to gray-green to light gray. The sodamide was then cautiously neutralized with 320 g. (6 moles) of dry ammonium chloride. After spontaneous evaporation of the ammonia, the residual solid was slurried in 1,000 ml. of water for thirty minutes at 90°, cooled to 0° and filtered. After decolorization with charcoal the grayish solid was crystallized from 8,000 ml. of water to yield long white needles of the monohydrate, which after oven drying (110°) gave 298 g. (96%) of anhydrous material melting at 321–322° (block).

Anal. Calcd. for $C_8H_{10}ON_2$: C, 64.1; H, 6.74; N, 18.69. Found: C, 64.0; H, 6.66; N, 18.7.

(b) **High Temperature Cyclization.**—A mixture of 5 g. of 2-(acetylimino)-cyclopentanecarbonitrile, 5 g. of sodamide, and 115 g. of paraffin wax was slowly heated with stirring to about 200°. After about one hour, during which time the mixture darkened with evolution of some ammonia the mixture was cooled to 100° and filtered. The black solid was further washed with petroleum ether and extracted with several portions of boiling benzene. On concentration there were obtained crystals, m. p. 319° which after recrystallization from water melted at 322–323°, 64% yield.

An aqueous solution of the aminohydroxypyrindine is neutral to methyl red; however, a monohydrochloride is readily formed either by adding hydrogen chloride to the pulverized solid material or by dissolving the solid in concentrated hydrochloric acid and evaporating to dryness.

Anal. Calcd. for $C_8H_{10}N_2O \cdot HCl$: Cl, 19.0. Found: Cl, 18.9.

The free base gives a dark red color with ferric chloride or with Millon reagent, indicating the presence of a hydroxyl group of phenolic character.

The pyrindine derivatives prepared by the low temperature procedure are summarized in Table I.

2-Acetamidobenzonitrile (XXV).—A mixture of 65 g. (0.55 mole) of 2-aminobenzonitrile, 306 g. (3.0 moles) of acetic anhydride, and a drop of 85% phosphoric acid was heated at 90° for one hour and then set aside for fifteen hours at room temperature when the entire contents of the flask solidified. On filtration and washing with ether there was obtained 50.1 g. of amide (m. p. 132°). Hydrolysis of the mother liquors with hot water afforded on cooling an additional 24.2 g. (m. p. 132°); total yield 84.2%. The amide was recrystallized from methanol; m. p. 133°.

Anal. Calcd. for $C_9H_8N_2O$: N, 17.5. Found: N, 17.52.

4-Aminocarbostyril (XXVI).—By the procedure outlined above, 64 g. of acetamidobenzonitrile was cyclized with 54 g. of sodamide in 1500 ml. of liquid ammonia. There was obtained 60 g. (93%) of 4-amino-2-hydroxyquinoline (m. p. 308°) crystallizing in needles from water.

Anal. Calcd. for $C_9H_8N_2O$: N, 17.49. Found: N, 17.39.

4-Amino-2-hydroxy-5,6,7,8-tetrahydroquinoline (XXVIII).—A mixture of 11.7 g. of 2-iminocyclohexanecarbonitrile and 100 g. of acetic anhydride was allowed to stand at room temperature for three days when the excess acetic anhydride was removed *in vacuo.* The residual oil (XXVII) was slowly added to a suspension of 25 g. of sodamide in 500 ml. of liquid ammonia. After the usual procedure (see above) the product was recrystallized from 200 ml. of water after decolorization with charcoal to yield a white crystalline solid (XXVIII), m. p. 130°.

Anal. Calcd. for $C_9H_{12}N_2O$: C, 65.8; H, 7.32; N, 17.02. Found: C, 65.7; H, 7.42; N, 17.65.

TABLE II

No.	6,7-Dihydropyrindine derivative	Reagent	Yield, %	M. p., °C.	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
IX	4-Acetamido-2-acetoxy	Acetic anhydride[a]	92	232	61.1	60.76	5.98	5.41	11.95	11.84
XI[b]	4-Amino-2-(*p*-nitrobenzoxy)-[b]	*p*-Nitrobenzoyl Cl + KOH[c]	86	203	60.2	59.95	4.34	4.41	14.05	14.17
XII	2-Hydroxy-4-(*p*-nitrobenzamido)-	*p*-Nitrobenzoyl Cl + CH_3CO_2H[a]	92	218–219	60.2	60.36	4.34	4.48	14.05	14.01
XIII[d]	4-Amino-2-(*p*-toluenesulfonato)-[d]	*p*-Toluenesulfonyl Cl + KOH[e]	74	167	..	...	..	..	9.22[f]	9.30[f]
XIV[d]	2-Hydroxy-4-(*p*-toluenesulfonato)-[d]	*p*-Toluenesulfonyl Cl + KOH	19	168	[g]	[g]	..	..	....	....

[a] At reflux. [b] This compound is diazotizable in acetic acid and gives no color with ferric chloride. [c] At 60°. [d] This acylation gives a 62% conversion (93% yield) and the total acylated product on recrystallization from methanol gives 80% (XIII) and then from the mother liquor 19% (XIV). XIII is diazotizable in cold acetic acid and shows no ferric chloride color; XIV gives a red color with ferric chloride and is not diazotizable. [e] At 50–55°. [f] Calcd.: S, 10.5. Found: S, 10.21. [g] Calcd.: S, 10.5. Found: S, 10.2.

Reactions of 4-Amino-2-hydroxy-6,7-dihydropyrindine

1. **Acylation.**—Acylation may be directed toward either the amino or hydroxyl group as indicated in Table II. In the case of the diacetyl compound the acetoxy group is readily saponified.

4-Acetamido-2-hydroxy-5,6-dihydropyrindine (X).—A mixture of 2.1 g. of the diacetyl compound, 20 ml. of methanol and 20 g. of methanol saturated with dry ammonia was allowed to stand twenty minutes and then the crystals which had separated were filtered and washed with methanol. On drying in air there was obtained 1.6 g. (94% yield) of the 2-hydroxy compound, m. p. 314°.

Anal. Calcd. for $C_{16}H_{12}N_2O_2H_2O$: C, 57.2; H, 6.68. Found: C, 57.0; H, 7.2.

2. Nuclear Substitutions and Replacements

(a) **Halogenation. 4-Amino-3-bromo-2-hydroxy-6,7-dihydropyrindine (XV).**—To a solution of 15 g. of the pyrindine in 150 ml. of acetic acid at 15° there was added slowly with vigorous stirring 16 g. of bromine in 25 ml. of acetic acid. Reaction was instantaneous and a white solid separated; addition of bromine was continued until the bromine color was permanent. The white bromo hydrobromide which separated was collected, washed with acetic acid and acetone and dried. The dry product was stirred into 200 ml. of water, and neutralized with sodium carbonate. The precipitated white solid melted with decomposition at 204–205° and contained one molecule of water of crystallization. Further purification by recrystallization from acetic acid did not alter the melting point.

Anal. Calcd. for $C_8H_9ON_2Br \cdot H_2O$: Br, 32.38. Found: Br, 32.36.

Attempted condensations of this halogen with potassium cyanide, or cuprous cyanide in pyridine were unsuccessful. Similar treatment with a solution of chlorine in cold acetic acid yielded the 3-chloro compound (VI) described above.

(b) **Nitrosation. 4-Amino-2-hydroxy-3-nitroso-6,7-dihydropyrindine (XVII).**—To a cold (0–5°) solution of 7.5 g. of the pyrindine in 250 ml. of water containing 20 ml. of concentrated hydrochloric acid there was added slowly 3.5 g. of sodium nitrite in 10 ml. of water. The bright red hydrochloride of the nitroso compound began to separate almost immediately. When all the nitrite had been added the mixture was neutralized with sodium carbonate to precipitate the bright green nitroso compound which was filtered and washed with ice-water and acetone. The nitroso compound itself was too unstable for successful recrystallization, but the material could be purified by recrystallization and clarification of the red sodium salt from cold water followed by neutralization. The yield of purified nitroso compound, m. p. 260° dec., was 78%.

Anal. Calcd. for $C_8H_9N_3O_2 \cdot H_2O$: N, 21.43. Found: N, 22.07.

3,4-Diamino-2-hydroxy-6,7-dihydropyrindine (XVIII).—The wet filter cake from the nitrosation above was slowly added to cold (0°) concentrated hydrochloric acid containing an excess of stannous chloride. The mixture was stirred for thirty minutes at 0–5° after discharge of the red color and the precipitated white solid collected and washed with cold (0°) concentrated hydrochloric acid. The wet filter cake was then dissolved in water and neutralized with potassium carbonate. The cream colored solid which separated was recrystallized from water containing a small amount of sodium hydrosulfite to prevent oxidation. The yield of pure diamine, m. p. 286–287°, which crystallized in long silky needles darkening on exposure to air, was 90%.

Anal. Calcd. for $C_8H_{11}ON_3 \cdot H_2O$: N, 22.9. Found: N, 22.4.

The location of the amino groups was confirmed by condensation with benzil to form the pyrazine (XIX). A solution of 1.65 g. of the diamine and 2.1 g. of benzil in 25 ml. of hot (100°) acetic acid deposited yellow crystals in a few minutes. On recrystallization from acetic acid there was obtained 3 g. of bright yellow needles, m. p. 362°.

Anal. Calcd. for $C_{22}H_{17}N_3O \cdot C_2H_4O_2$: N, 10.55. Found: N, 10.66.

(c) **Diazotization. 2,4-Dihydroxy-6,7-dihydropyrindine (XX).**—To 300 g. of cold 96% sulfuric acid was added with stirring 50 g. of the aminohydroxypyrindine. At 35–45°, 23 g. of sodium nitrite was slowly added with immediate evolution of nitrogen. The yellow solution was then heated at 60° until a drop no longer turned red on addition of 1 ml. of water (one hour) (free nitrous acid nitrosates either the starting material or the product to give the red sulfate of the nitroso compound). The solution was poured into 1 liter of ice-water containing 40 g. of boric acid, then heated at 100° for thirty minutes, and finally just neutralized with ammonium hydroxide, cooled to 0° and filtered. On recrystallization from water or acetic acid there was obtained 37 g. (74%) of material melting above 380°.

Anal. Calcd. for $C_8H_9NO_2$: N, 9.38. Found: N, 9.76.

2,4-Diacetoxy-6,7-dihydropyrindine (XXI).—A mixture of 10 g. of dihydroxypyrindine and 40 g. of acetic anhydride was heated at 90–100° for one hour, excess reagent removed under diminished pressure, and the residue recrystallized from acetone–petroleum ether; m. p. 92°.

Anal. Calcd. for $C_{12}H_{13}O_4N$: C, 61.4; H, 5.53; N, 6.1. Found: C, 61.55; H, 5.58; N, 6.28.

2,4-Dihydroxy-3-nitroso-6,7-dihydropyrindine (XXII).—Treatment of the dihydroxy compound with 1.2 equiv. of sodium nitrite by the same procedure as originally employed in the preparation of (XVII) above afforded the 3-nitroso compound (green), m. p. *ca.* 250° dec.

Anal. Calcd. for $C_8H_8O_3N$: N, 15.55. Found: N, 15.38.

On reduction with stannous chloride there was obtained an amine which could be diazotized and coupled to phenols.

(d) **Replacement of the Hydroxy Group. 4-Amino-2-Chloro-6,7-dihydropyrindine (XXIV).**—The aminohydroxypyrindine (5.0 g.) was treated with hydrogen chloride until 1 g. was adsorbed; 7.0 g. of phosphorus pentachloride was then added and the mixture was heated at

105° until evolution of hydrogen chloride ceased. The product was then carefully mixed with crushed ice and stirred to decompose excess phosphorus halides. The collected solid was washed acid free with water, dried at 100° and finally extracted with boiling benzene. On concentration of the extract, the chloro compound separated as small rosettes; m. p. 167°.

Anal. Calcd. for $C_8H_9N_2Cl$: Cl, 21.05. Found: Cl, 20.8.

(e) **Reaction with Aldehydes.** (1) **Formaldehyde.**—A mixture of 3 g. of aminohydroxypyrindine in 20 ml. of glacial acetic acid containing 0.11 ml. of concentrated hydrochloric acid and 0.9 g. 37% aqueous formaldehyde was boiled for one hour. Almost immediately a white solid began to separate; on cooling the reaction mixture to 25° and filtering there was obtained 2.7 g. of product; m. p. 360° dec. after drying in a vacuum desiccator. Analyses indicated that this product probably was 3,3'-methylene-bis-(2-hydroxy-4-amino-6,7-dihydropyrindine) containing one molecule of acetic acid of crystallization.

Anal. Calcd. for $C_{17}H_{20}N_4O_2 \cdot C_2H_4O_2$: C, 61.3; H, 6.45; N, 15.05. Found: C, 60.91; H, 6.90; N, 15.11.

(2) **Benzaldehyde (XVI).**—A solution of 3 g. of aminohydroxypyrindine (II) in 20 ml. of glacial acetic acid containing 0.1 ml. of concentrated hydrochloric acid and 1.06 g. of benzaldehyde was heated for two hours at reflux with stirring. The precipitate which formed almost immediately was collected and washed with acetic acid and dried in a vacuum desiccator; m. p. 360°. The analysis corresponds to the structure of a phenyl dipyridopyridine indicated by the formula XVI on the chart. No attempt was made to identify the product.

Anal. Calcd. for $C_{23}H_{21}N_3O_2$: N, 11.35. Found: N, 11.49.

Acknowledgment.—The authors wish to acknowledge the advice and many helpful suggestions of Dr. W. A. Lazier.

Summary

Acyl derivatives of iminonitriles (cyanoimines) of the cyclopentane, cyclohexane and benzene series have been found to undergo a ready condensation with sodamide to give 4-amino-2-hydroxypyridine derivatives in excellent yield. Some chemical reactions of these materials, which resemble meta-aminophenol, are described.

WILMINGTON, DELAWARE RECEIVED NOVEMBER 22, 1948

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF MISSOURI]

The Reaction of Aromatic Aldehydes with Aluminum Chloride and Benzene[1]

BY HERBERT E. UNGNADE AND ELBERT W. CRANDALL[2]

Certain aromatic aldehydes lose carbon monoxide when heated with aluminum chloride and benzene.[3,4,5,6,7] The reaction products include the aromatic residue corresponding to the aldehyde, anthracene and triphenylcarbinol.[8] The present investigation is concerned with the conditions of this reaction, the effect of substituents in the aldehyde and the nature of the solvent.

An exhaustive study with *o*-chlorobenzaldehyde indicates that the highest yields of chlorobenzene and triphenylcarbinol are obtained with two to three moles of aluminum chloride per mole of aldehyde and a reaction time of four hours at 60°.

The course of the reaction depends upon the substituents in the aldehyde. Nitrobenzaldehydes fail to lose carbon monoxide and give good yields of nitrotriphenylmethanes. Ortho–para directing groups facilitate the elimination of carbon monoxide and thus the formation of anthracene and triphenylcarbinol. Veratric aldehyde behaves abnormally since it yields only a small amount of guaiacol, the main product being vanillin which in turn is recovered when heated with benzene and aluminum chloride. A similar stability has been observed for 3-phenoxy-4-hydroxybenzaldehyde.[6]

When benzene is replaced by chlorobenzene or nitrobenzene, the aldehyde is recovered unchanged. Even a mixture of equal volumes of benzene and nitrobenzene fails to give a reaction with benzaldehyde. Toluene, however, can be substituted for benzene, giving a mixture of dimethylanthracenes but no triarylcarbinol.

Experimental[9]

Starting Materials.—*m*-Methoxybenzaldehyde was prepared by the methylation of *m*-hydroxybenzaldehyde with dimethyl sulfate. *o*-Nitrobenzaldehyde was obtained from *o*-nitrotoluene[10] and *m*-chlorobenzaldehyde from *m*-nitrobenzaldehyde.[11] The remaining aldehydes were commercial products.[12]

Procedure.—The reaction of aromatic aldehydes with benzene and aluminum chloride was carried out according to a standardized procedure which is given in detail for *o*-chlorobenzaldehyde.

A solution of *o*-chlorobenzaldehyde (25 g., 0.18 mole) in 150 cc. of thiophene-free benzene was added to 75 g. (0.56 mole) of anhydrous aluminum chloride contained in a three-necked flask equipped with stirrer, condenser and thermometer. The resulting mixture was stirred for six hours at a constant temperature of 60°. During the course of the reaction the mixture turned black. The reaction mixture was poured onto ice and concentrated hydrochloric acid and was steam-distilled. The volatile

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[1] Presented before the Division of Organic Chemistry of the American Chemical Society, Chicago, April, 1948.

[2] In part from the Master's thesis of E. W. Crandall, 1948.

[3] Hey, *J. Chem. Soc.*, 72 (1935).

[4] Schaarschmidt, Hermann and Szemo, *Ber.*, **58**, 1914 (1925).

[5] Ellison and Hey, *J. Chem. Soc.*, 1847 (1938).

[6] Ungnade and Orwoll, THIS JOURNAL, **65**, 1736 (1943).

[7] Dewar and Jones, *J. Chem. Soc.*, **85**, 212 (1904).

[8] Triphenylmethane reported instead by the earlier workers[3,4,5] was undoubtedly a secondary product formed by reduction of the triphenylcarbinol.

[9] All temperatures uncorrected.

[10] "Organic Syntheses," **24**, 75 (1944).

[11] Buck and Ide, *ibid.*, **13**, 28 (1933).

[12] The authors are indebted to the Heyden Chemical Corporation, Garfield, N. J., for generous samples of *o*-chloro-, *p*-chloro-, 2,4-dichloro- and 3,4-dichlorobenzaldehyde.