

the filtrate were converted to the chloride and a small amount of platinum salt was obtained. *Anal.* Found: Pt, 28.5. Calcd. for $[(\text{CH}_3)_3\text{N}-\text{C}(\text{CH}_3)_2-\text{OC}_2\text{H}_5]_2\text{PtCl}_6$, Pt, 27.9.

Reaction with Cyanide Ion.—Alcoholic solutions of $(\text{CH}_3)_2\text{C}=\text{N}^+(\text{CH}_3)_2\text{NO}_3^-$ were shaken with dry potassium cyanide for several hours, then filtered and the filtrate fractionated. There was little evidence of amino nitrile or vinyl amine formation on the basis of the analysis described above. In one such experiment the total yield of acetone recovered was 37% while the amine was 72%. In another experiment treatment of the residue with methyl iodide after distilling off the amine and ketone, gave a quaternary salt (1.3 g.). After recrystallization from 85% propyl alcohol it gave on analysis, 41.2, 41.3% iodine; calcd. for $\text{C}_9\text{H}_{13}\text{N}(\text{CH}_3)_3\text{I}$, 41.3%.

The previous experiment was repeated using liquid hydrogen cyanide as the solvent. On treatment of the high boiling fraction with methyl iodide a quaternized salt was obtained. *Anal.* Iodine content 51.0%. M. p. (dec.) 260–265°; calcd. for $(\text{CH}_3)_2\text{C}=\text{N}^+(\text{CH}_3)_3\text{I}$, I, 50.0; m. p.⁸ 234–236°.

Reaction with a Grignard Reagent.—Methylmagnesium iodide (0.1 mole) prepared in the usual manner was added slowly to 8.2 g. (0.034 equiv.) of $(\text{CH}_3)_2\text{C}=\text{N}^+(\text{C}_2\text{H}_5)_2\text{I}^-$ held in suspension in ether by vigorous stirring. The solid salt disappeared quite rapidly but the mixture was refluxed for about two hours. After hydrolysis at 0° the solution was acidified and distilled to remove the ether. The residue was made alkaline and the amine (0.033 equiv.) dis-

tilled into 1 N hydrochloric acid. This was given two treatments with phenylsulfonyl chloride in alkaline solution to remove the secondary amine; yield of tertiary amine, 0.0036 equiv. The platinum double salt was recrystallized from absolute alcohol; decomposition point 223–225°; % Pt, 29.2, 29.4; calcd. for $[(\text{CH}_3)_2\text{C}=\text{N}(\text{C}_2\text{H}_5)_2]_2\text{H}_2\text{PtCl}_6$, 29.2.

Since this salt is not described in the literature, it was prepared from tertiary butylamine and ethyl iodide, and purified as described above. The platinum salt of this contained 29.1% Pt, m. p. 223–224°. Mixed melting points confirmed the identification.

Summary

We have isolated a number of tetra substituted methylene immonium salts and proved their structure by identifying the products of the hydrolysis of the immonium ion, and by the isolation of the expected tertiary amine when treated with a Grignard reagent. A preliminary study of the reactions of such immonium ions with hydroxide, cyanide, ethylate, and hydroxylammonium ions has been made. Some evidence for the existence of the vinylammonium ion in alcohol solutions has been offered and a possible tool for its detection has been suggested.

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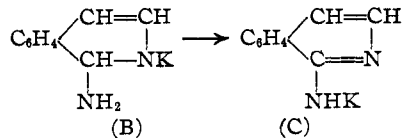
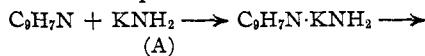
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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF STANFORD UNIVERSITY]

The Preparation and Properties of Some 4-Substituted Isoquinolines¹

BY F. W. BERGSTROM AND J. H. RODDA

Previous work has indicated that potassium amide and isoquinoline react in the sense of the following series of equations to form potassium 1-aminoisoquinoline:



The reaction can be regarded as being initiated by the addition of an amide ion, NH_2^- , to the 1-carbon atom (formula B), this being followed by the loss of H^- under the influence of an excess of potassium amide.^{1a} Substituents in the 4-position of the isoquinoline nucleus are in the proper position to exert a maximum effect upon

the addition of an amide ion to the 1-carbon atom with a minimum of steric influences, since the effect of a group is transmitted as a rule primarily to the ortho and para positions.² The present work describes the synthesis of some derivatives of isoquinoline with substituents in the 4-position.

4-Bromoisoquinoline is ammonolyzed by heating with aqueous or liquid ammonia in the presence of copper and copper salts to 4-aminoisoquinoline in poor yield. At elevated temperatures, and under pressure, a solution of sodium methylate or potassium *t*-butylate in the corresponding alcohol converts 4-bromoisoquinoline to isoquinoline in 43–54% yield. Isoquinoline-4-carboxylic acid reacts with excess potassium amide in liquid ammonia to give a sparingly soluble potassium salt, which slowly passes into solution with the evolution of hydrogen and the

(1) Original manuscript received June 3, 1940.
(1a) Bergstrom, *Ann.*, **515**, 35, 38 (1934); *J. Org. Chem.*, **2**, 412 (1937).

(2) Watson, "Modern Theories of Organic Chemistry," the Clarendon Press, Oxford, 1937, pp. 57–80.

formation of the potassium salt of 1-aminoisoquinoline-4-carboxylic acid. The rate of hydrogen evolution is definitely slower than in the potassium amide-isoquinoline reaction, unquestionably because of the initial precipitation of potassium isoquinoline-4-carboxylate. It is therefore evident that no true estimate can be made of the effect of the carboxyl group on the rate of introduction of an amino group into the isoquinoline nucleus.

Experimental

4-Bromoisquinoline.—The method of Edinger and Bossung³ for the preparation of 4-bromoisquinoline is lacking in sufficient detail. The following directions have been found to give fairly satisfactory results.

Three moles (387 g.) of purified isoquinoline⁴ was dissolved in 350 cc. of 48% hydrobromic acid, and evaporated almost to dryness. Six atoms (480 g.) of bromine was added slowly, and the mixture was heated (air reflux condenser) for seven hours at 180–190°, until practical cessation of hydrogen bromide evolution (water was lost as steam from the top of the reflux condenser). Excess sodium hydroxide solution was added, and the liberated bromoisquinoline steam distilled. All but five liters of the water was decanted from the distilled oil. The latter was dissolved while hot by addition of nitric acid, 4-bromoisquinoline nitrate crystallizing out on cooling. A second crop was obtained in the usual manner. The crystals were filtered, dissolved in hot water, and treated with an excess of ammonia water. The 4-bromoisquinoline separating on cooling was crystallized from ether; m. p. 39–40°; yield, 460 g. or 73.7%. In most of the runs the yield for some reason was closer to 45%.

4-Aminoisquinoline.—4-Bromoisquinoline (30 g.), concd. ammonia water (150 cc.), copper sulfate (0.1 g.) and a strip of copper gauze (5 sq. cm.) were heated in a closed steel tube with a glass liner for sixteen hours at 250°. The portion of the reaction mixture insoluble in cold water was extracted with hot benzene, and the latter concentrated to crystallize 4-aminoisoquinoline. Much of the tar surrounding the crystals could be absorbed on filter paper or drying paper. The yield, after several crystallizations from benzene and decolorization with animal charcoal, was 3.5 g. (16%); m. p. 108°, uncor. For unknown reasons, nothing but tar was obtained in about half of the runs. *Anal.* Calcd. for C₉H₈N₂: C, 74.99; H, 5.59; N, 19.44. Found: C, 75.10; H, 5.45; N, 19.50.

Aminoisquinoline may be formed somewhat more rapidly in the following manner: 4-bromoisquinoline (10 g.), cupric nitrate (0.1 g.), copper gauze, and liquid ammonia (about 20 cc.) were heated in a steel bomb with glass liner at 106° for seven hours. The yield was 1.2 g., or 17%, purified as described above.

Attempts to prepare 4-aminoisoquinoline by adding 4-bromoisquinoline to an excess of a liquid ammonia solu-

tion of potassium amide or sodium amide, in accordance with a previously described method, yielded only a tar.⁵

Isoquinoline-4-carboxylic Acid.—Tyson⁶ hydrolyzed 4-cyanoisoquinoline to the corresponding acid by heating with a concentrated hydrochloric acid in a sealed tube. The following method is somewhat simpler.

4-Cyanoisoquinoline^{6,7} (10 g.) and 75 cc. of sodium hydroxide solution (about 20%) were refluxed for twenty minutes in a 200-cc. round-bottomed flask. The reaction mixture was acidified with 6 *N* acetic acid and concentrated somewhat by evaporation. The isoquinoline-4-carboxylic acid separated on cooling and was recrystallized from water, in which it was only slightly soluble. The yield was 11.0 g. (98%), m. p. 263–265°, uncor.

Ethyl Ester.—The chloride (1.9 g.) of isoquinoline-4-carboxylic acid⁶ was refluxed for one hour with absolute ethanol (25 cc.), the latter then being concentrated. The hydrochloride of the ester (m. p. 160°, uncor.) separated on cooling. Treated in aqueous solution with excess ammonia, the ester itself was liberated, and then crystallized from petroleum ether (b. p. 60–70°); yield, 2 g. or 50%; m. p. 47–48°. *Anal.* Calcd. for C₁₂H₁₁O₂N: C, 71.64; H, 5.56. Found: C, 71.30; H, 5.47.

The same ethyl ester was prepared in approximately 30% yields by refluxing (for about five hours) alcohol and isoquinoline-4-carboxylic acid with hydrochloric acid gas, or with a few cc. of concentrated sulfuric acid.

Amide.—4-Cyanoisoquinoline (1.54 g.), hydrogen peroxide (5 cc. of 30% in 20 cc. water) and sodium hydroxide (2 pellets, or 0.2 g.) were heated for fifteen minutes on a boiling water-bath. The precipitate separating on cooling was filtered and washed with water; m. p. 168–172° crude, and 174.5–175.5° after twelve crystallizations from water; crude yield, 1.1 g., or 64%. *Anal.* Calcd. for C₁₀H₈NO₂: C, 69.75; H, 4.68; N, 16.28. Found: C, 69.47; H, 4.44; N, 16.7.

1-Aminoisoquinoline-4-carboxylic Acid.—Potassium amide, made in one leg of a two-legged reaction tube by the action of liquid ammonia on 1.17 g. (0.03 atom) of potassium in the presence of iron oxide as a catalyst, was slowly added to 1.73 g. (0.01 mole) of isoquinoline-4-carboxylic acid in the other leg.⁸ A vigorous reaction ensued with liberation of hydrogen and the slow formation of a quantity of yellow precipitate, tentatively identified as the monopotassium salt of isoquinoline-4-carboxylic acid. The precipitate slowly disappeared on standing with evolution of hydrogen and the production of a green solution, the entire reaction consuming about eight hours. After evaporation of the ammonia the tube was cut open, the reaction mixture hydrolyzed with alcohol and benzene, water added, and the two organic solvents evaporated. From the cold filtered aqueous solution, acetic acid precipitated aminoisoquinolinecarboxylic acid, which was purified by crystallization from water (three liters of hot water dissolve about a gram of the acid); yield, 1.4 g., or 71%;

(5) Bergstrom, Wright, Chandler and Gilkey, *J. Org. Chem.*, **1**, 172–174 (1936).

(6) Tyson, *THIS JOURNAL*, **61**, 183–185 (1939).

(7) Cf. method of Jansen and Wibaut, *Rec. trav. chim.*, **56**, 711 (1937).

(8) Franklin, *THIS JOURNAL*, **27**, 831–833 (1905); **35**, 1460–1462 (1913); *J. Phys. Chem.*, **15**, 511–517 (1911); and other articles. Cf. expt. 10, *J. Org. Chem.*, **2**, 421 (1937).

(3) Edinger and Bossung, *J. prakt. Chem.*, **43**, 191–192 (1891); cf. Ukai, *Chem. Abstr.*, **23**, 1642 (1929).

(4) Harris and Pope, *J. Chem. Soc.*, **121**, 1031 (1922). The starting material was a 70% isoquinoline concentrate.

m. p. 249–250°, uncor., gas evolution. *Anal.* Calcd. for $C_{10}H_9O_2N_2$: C, 63.83; H, 4.28; N, 14.89. Found: C, 63.98; H, 4.08; N, 14.70.

One-half gram of the amino acid was heated in a test-tube just above the melting point until gas evolution ceased. The resulting product, crystallized from water, proved to be 1-aminoisoquinoline (m. p. and mixed m. p. 120–121°).

From 0.01 mole of isoquinoline-4-carboxylic acid and 0.03 mole of potassium amide in a straight reaction tube⁹ there was obtained 167.7 cc. of hydrogen, standard conditions (74.8%).

The bulky precipitate formed by treating isoquinoline-4-carboxylic acid with excess potassium amide in a two-legged reaction tube was washed with liquid ammonia and analyzed,¹⁰ after drying *in vacuo* at room temperature. *Anal.* Calcd. for $C_9H_8NO_2K$: K, 19.62. Found: K, 17.0. Calcd. for the diammonate, K, 16.8.

Aminoisoquinoline-carboxylic acid reacts with potassium amide (3 equivalents) in liquid ammonia to form a colorless salt, but no diamino derivative is formed in a one week reaction.

The Action of Sodium Alcoholates on 4-Bromoisquinoline.—4-Bromoisquinoline (6.24 g., 0.03 mole) was heated in a glass-lined steel tube autoclave with a solution of 1.15 g. of sodium in 50 cc. of methyl alcohol for seven hours at 235°. Alcohol was evaporated from the reaction product, and the residue steam distilled (some tar remained behind). The water insoluble oil that distilled over was con-

(9) Bergstrom, *This Journal*, **56**, 1748 (1934).

(10) Bergstrom, *ibid.*, **46**, 1556 (1924).

verted to a picrate, m. p. 220–222°, which proved to be identical with isoquinoline picrate, m. p. 222–223.5°; yield 5.80 g. or 0.54 mole per mole of bromoisquinoline.

Under the same conditions, bromoisquinoline was heated with a solution of 1.95 g. of potassium in 50 cc. of *t*-butyl alcohol; yield of crude isoquinoline (separated as picrate), 0.43 mole per mole of bromoisquinoline. Reiterations of this experiment at 190–212° and 180–190° gave 48% and 51% yields of isoquinoline, respectively.

Blau¹¹ reports the formation of benzene (small yield) and anisole (32.4%) by heating bromobenzene with sodium methylate under pressure at 220–230°.

Summary

1. Isoquinoline-4-carboxylic acid reacts with excess potassium amide in liquid ammonia to form hydrogen and the potassium salt of 1-aminoisoquinoline-4-carboxylic acid.

2. 4-Aminoisoquinoline is prepared in very poor yield by heating 4-bromoisquinoline with aqueous ammonia, copper and a copper salt in an autoclave.

3. Sodium methylate and potassium *t*-butylate react with 4-bromoisquinoline when heated under pressure to form isoquinoline in yields approximating 50% of the theoretical.

(11) Blau, *Monatsh.*, **7**, 622 (1886).

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[CONTRIBUTION FROM THE BASIC SCIENCE RESEARCH LABORATORY OF THE UNIVERSITY OF CINCINNATI]

Viscosities of Polyester Solutions and the Staudinger Equation^{1a}

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Introduction

Staudinger and co-workers^{2,3} have advanced the following relationship between viscosities of dilute solutions of linear polymers and their molecular weights

$$\eta_{sp}/c = K_m M \quad (1)$$

where the specific viscosity η_{sp} equals the relative viscosity η_r minus one, c is the concentration in moles of recurring unit per liter and M is the molecular weight. Staudinger has advocated the use of (1) for determining the molecular

weights of such substances as polystyrenes, cellulose and its derivatives, polyoxymethylenes and polyethylene oxides. This method has had much appeal because of its exceptional simplicity compared with the few other known methods which are applicable to high molecular weight substances. However, the validity of the Staudinger equation has been the subject of much controversy during the past eight years.⁴

Staudinger originally presented as the basis for (1) viscosities of solutions of monomeric long chain compounds, *e. g.*, *n*-paraffins, esters, and ketones. However, very careful measurements carried out by Meyer and van der Wijk⁵ have shown that the viscosities of carbon tetrachloride

(4) See, for example, H. Staudinger, K. H. Meyer and others, *Z. Elektrochem.*, **40**, 434, 446, 449 (1934); I. Sakurada, *Ber.*, **67B**, 1045 (1934); H. Staudinger, *Helv. Chim. Acta*, **19**, 204 (1936); K. H. Meyer and A. van der Wijk, *ibid.*, **19**, 218 (1936).

(5) K. H. Meyer and A. van der Wijk, *Helv. Chim. Acta*, **18**, 1067 (1935).

(1a) This paper was presented before the Organic Plastics Section, Paint and Varnish Division, of the American Chemical Society at the Cincinnati meeting, April, 1940.

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(2) H. Staudinger and W. Heuer, *Ber.*, **63**, 222 (1930); H. Staudinger and R. Nodza, *ibid.*, **63**, 721 (1930).

(3) H. Staudinger, "Die hochmolekularen organischen Verbindungen," Verlag von Julius Springer, Berlin, 1932.