[Contribution from the Chemical Laboratory of Stanford University]

DIRECT INTRODUCTION OF THE AMINO GROUP INTO THE AROMATIC AND HETEROCYCLIC NUCLEUS. IV. THE ACTION OF THE ALKALI AND ALKALINE EARTH AMIDES ON SOME SUBSTITUTED QUINOLINES*

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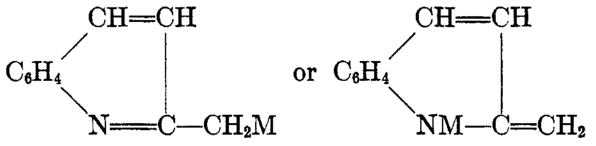
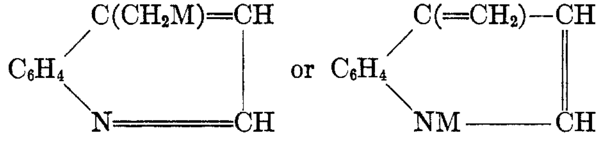
In continuation of previous work[1] a study has been made of the action of potassium amide on a number of substituted quinolines, with the ultimate goal in mind of determining the effect of various radicals on the rate of introduction of an amino group.

The methyl quinolines.—The alkali amides (MNH_2) react with solutions of 2- and 4-methylquinolines in liquid ammonia to form soluble salts of the formulas,[2]



Potassium quinaldyl
(Sodium)



Potassium lepidyl
(Sodium)

These salts did not react with an excess of potassium amide, alone, or in the presence of potassium nitrate, to form amino derivatives. The presence of the anionic charge in or near the nucleus has doubtless prevented the introduction of an amino group.

Potassium amide (in excess) reacts with 6-, 7- or 8-methylquinolines in liquid ammonia to form tars or resins, even when the reaction is carried out in the presence of potassium nitrate. Poor yields of 2-amino-8-

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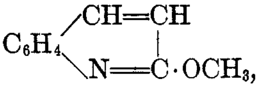
[1] (*a*) Bergstrom, *J. Am. Chem. Soc.*, **56**, 1748 (1934); (*b*) Bergstrom, *Ann.*, **515**, 34–42 (1934); (*c*) Bergstrom, J. Org. Chem., **2**, 411–430 (1937).

[2] (*a*) Bergstrom, *J. Am. Chem. Soc.*, **53**, 3027 (1931); (*b*) Chichibabin, *Ber.*, **60**, 1607 (1927), first suggested that quinaldine and lepidine are tautomeric substances.

methylquinoline and of amino-6-methylquinoline are obtained by the action of barium amide on 8- and 6-methylquinoline, respectively, in spite of the fact that approximately the theoretical amount of hydrogen is evolved. It has proven impossible to prepare amino-7-methylquinoline.

The alkoxy- and dimethylaminoquinolines.—6-Methoxyquinoline appears to be converted to two amino-6-methoxyquinolines by potassium amide and potassium nitrate in liquid ammonia, although probably only a single product is formed with barium amide. It will be recalled[1c] that under similar conditions a mixture of 2- and 4-aminoquinolines is obtained by the action of potassium amide and potassium nitrate on quinoline, while barium amide yields only 2-aminoquinoline.

Amino-6-dimethylaminoquinoline is prepared from 6-dimethylaminoquinoline with the use either of barium amide or of potassium amide and potassium nitrate at a slower rate than 2-aminoquinoline is similarly formed from quinoline.

2-Methoxyquinoline,  contains the grouping, —C(=N—)OCH_3, present also in the imido ethers of Pinner, and is therefore to be regarded as a neutral cyclic aquo ammono ester.[3] In accordance with expectation, it is readily saponified by a solution of potassium amide in liquid ammonia to potassium-2-aminoquinoline and potassium methylate, that is, to a salt of a cyclic ammono acid ester and to an aquo alcoholate. It has been found impossible to prepare an amino-2-methoxyquinoline, because of the greater rapidity of the saponification just described.

An amino-8-ethoxyquinoline is obtained in fairly good yield by the action of barium amide on 8-ethoxyquinoline in liquid ammonia, although practically none is formed when potassium amide and potassium nitrate are used. In the latter case, 8-hydroxyquinoline was the only definite product obtained. The removal of a methoxyl group in position 2 is a much more rapid reaction.

The hydroxy- and aminoquinolines.—Neither 2-hydroxyquinoline, 8-hydroxyquinoline nor 2-aminoquinoline can be converted to amino derivatives by potassium amide, potassium amide and potassium nitrate, or barium amide in liquid ammonia at temperatures up to 110°. The hydroxy and amino groups therefore decrease the rate of introduction of an amino group into the quinoline nucleus, even though they increase the rate of bromination, nitration and sulfonation of the benzene ring.

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[3] Franklin, "The Nitrogen System of Compounds." The Reinhold Publishing Co., New York, **1935**, p. 263.

To explain this difference in behavior, it has been assumed that bromine the nitro and sulfonic acid groups are positively polarized when introduced into a molecule while the amino group is negatively polarized.[4] Nitric and sulfuric acids are kationoid reagents, whereas potassium amide is anionoid.

The quinoline carboxylic acids.—Quinaldic acid and cinchoninic acid react with potassium amide and potassium nitrate in liquid ammonia to form, respectively, 4-amino-quinoline-2-carboxylic acid and 2-amino-quinoline-4-carboxylic acid. Competition experiments, to be described in a subsequent article, have shown that the carboxyl group increases the rate of introduction of the amino group into the quinoline nucleus. Cinchoninic acid does not appear to react with barium amide, beyond the formation of a barium salt of very low solubility in ammonia. An amino-quinoline-6-carboxylic acid of unknown orientation is obtained by treating quinoline-6-carboxylic acid with potassium amide and potassium nitrate in liquid ammonia.

Quinolinesulfonic acids.—Quinoline-2-sulfonic acid reacts readily with potassium amide or with a mixture of potassium amide and potassium nitrate to form 2-aminoquinoline and potassium sulfite. It is known that 2-hydroxyquinoline is easily made by heating quinoline-2-sulfonic acid with dilute aqueous alkali.[16] It will be recalled that chlorine in the 2-position also has an enhanced reactivity, since 2-chloroquinoline is a cyclic acid chloride-ester of the ammonia system.

An aminoquinoline-6-sulfonic acid is readily obtained by treating quinoline-6-sulfonic acid with barium amide, or with potassium amide and potassium nitrate in liquid ammonia. It is isolated as the monohydrate.

EXPERIMENTAL

Reactions were carried out in liquid ammonia solution at room temperatures, unless otherwise mentioned, and in accordance largely with the methods of references 1*a* and 1*c*. All temperatures are uncorrected. Microanalyses were made by Weiler and Straus, Oxford.

Amino-6-methylquinoline.—Eleven and nine-tenths millimoles of barium amide and 10.2 millimoles of 6-methylquinoline† reacted for thirty days at room temperature[1a]. Six and five-hundredths millimoles of hydrogen was collected (59%). The tarry hydrolysate was boiled with sodium sulfate solution and filtered hot, colorless crystals, m.p. 142–145°, separating from the filtrate. Yield, 1.72 millimoles or 16.9%; m.p. 145.7–146.7°, after several recrystallizations from water.

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[4] Ingold, *Rec. trav. chim.*, **48**, 809–810 (1929); Bradley and Robinson, *J. Chem. Soc.*, **1932**, 1254.

[16] Besthorn and Geiszelbrecht, *Ber.*, **53**, 1021–3 (1920).

† Obtained from the Eastman Kodak Company.

Anal. Calc'd for $C_{10}H_{10}N_2$: C, 75.89; H, 6.38; N, 17.72.
Found: C, 75.54; H, 6.30; N, 18.33.

Reaction also occurs with an excess of 6-methylquinoline, but more tar is formed.

Amino-8-methylquinoline.[6]—Fifteen and eight-tenths millimoles of barium amide reacted for 22 days with 10 millimoles of 8-methylquinoline.[1a] Seven and eighty-five-hundredths millimoles of hydrogen (78.4%) was obtained, the product being isolated as described above. Yield, 3.51 m. moles (35.1%); m.p. 85–7° crude, and 86.0–86.3°, after recrystallizations from water.

Anal. Calc'd for $C_{10}H_{10}N_2$: C, 75.89; H, 6.38; N, 17.72.
Found: C, 76.03; H, 6.29; N, 17.54.

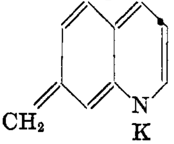
The picrate was prepared in alcohol and crystallized from the same solvent; m.p. 242–243.5°.

Anal. Calc'd for $C_{16}H_{13}N_5O_7$: C, 49.58; H, 3.38.
Found: C, 49.78; H, 3.52.

Amino-8-methylquinoline was diazotized in 25% sulfuric acid, and converted to hydroxy-8-methylquinoline by boiling; m.p. 214–215°, uncorr., as compared with 219–220° (corr.?) as given by Späth[5] for 2-hydroxy-8-methylquinoline. O. Fischer[6] prepared 2-amino-8-methylquinoline from 2-chloro-8-methylquinoline, but gave no melting point.

The rate of formation of hydrogen in the barium amide-8-methylquinoline reaction is somewhat increased by the addition of barium thiocyanate.

Barium amide reacts with an excess of 8-methylquinoline to form hydrogen and amino-8-methylquinoline, although more slowly than above.

7-Methylquinoline.—With a twofold excess of barium amide, hydrogen is formed (84.5%) but no amino derivative, or other definite product. Potassium amide reacts with 7-methylquinoline to form a solution which assumes several different colors, but no definite products were obtained therefrom. Attempts to prove (by alkylation) the presence of a potassium salt of a tautomeric form of 7-methylquinoline,  failed. No definite product was obtained by the action of an excess of potassium amide and potassium nitrate on 7-methylquinoline.

Amino-6-methoxyquinoline.—Seventeen and two-tenths millimoles of barium amide reacted for 26 days with 9.62 millimoles of 6-methoxyquinoline.†[1a] The hydrolysate of the reaction product was dissolved in dilute hydrochloric acid, and sulfuric acid added to precipitate barium. A crop of gray needles slowly separated from the filtrate of the barium sulfate upon addition of ammonia; m.p. 162–163°, crude, but 178.7–179.4° after several crystallizations from water (large volumes are required) and benzene. Yield, crude, 7.30 m. moles, or 75.9%; pure, 2.6 m. moles. The product is soluble in alcohol, and appears to be slowly oxidized by air.

Anal. Calc'd for $C_{10}H_{10}N_2O$: C, 68.93; H, 5.79; N, 16.09.
Found: C, 69.26; H, 5.89; N, 16.18.

Thirty-seven and six-tenths millimoles of potassium amide, 10.74 millimoles of 6-methoxyquinoline, and 18.0 millimoles of potassium nitrate reacted for 11 days (ref. 1*c*, expt. 11–15). The product, obtained in poor yield, and crystallized from

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[5] SPÄTH, *Monatsh.*, **40,** 125 (1919).

[6] FISCHER, *Ber.*, **35,** 3679 (1902).

water, consisted of two products, partially separated by further crystallizations into material melting at 119–121.5° (colorless needles), and at 160–175°. It is probable that both 2- and 4-amino-6-methoxyquinolines are formed.

2-Methoxyquinoline.—Addition of potassium amide (17.2 millimoles) to 2-methoxyquinoline[7] (6.75 millimoles) in a two-legged tube gave an opaque red solution from which much colorless precipitate (CH_3OK) separated on standing. Although the reaction appeared to be complete in about half an hour, the tube was allowed to stand for twelve hours before evaporation of the solvent. The 2-aminoquinoline (3.44 millimoles, or 51%, m.p. 127.8–129.1°) obtained from the hydrolysate was purified by crystallization from water and identified by the melting point of a mixture with authentic material.

In a repetition of this reaction, with the addition of potassium nitrate, a slightly lower yield of 2-aminoquinoline was obtained, but no other product was isolated.

Amino-8-ethoxyquinoline.—Potassium amide (25.3 millimoles) was added to a liquid ammonia solution of anhydrous barium thiocyanate (26.1 millimoles) and 8-ethoxyquinoline[8] (10.39 millimoles) with continual shaking until the precipitate, at first very voluminous, had become more compact. It is necessary to have all of the barium thiocyanate in solution before the addition of the potassium amide. To prevent or minimize caking, the ammonia is distilled into both legs of the reaction tube at once, but if a cake is formed, it may be slowly dissolved by evaporating some solvent into the other leg of the reaction tube, distilling ammonia back into the leg containing the thiocyanate, and repeating as long as necessary. Although the reaction was apparently complete at the end of about nine hours (no hydrogen evolution), the tube was allowed to stand for one day.

The hydrolysate was dissolved in hot dilute hydrochloric acid (about 1:3) and filtered. The nearly colorless crystals obtained on cooling consisted largely of aminoethoxyquinoline, formed by hydrolysis of the hydrochloride. These were filtered and treated with excess ammonia. An additional small amount of product was obtained by addition of ammonia to the hydrochloric acid filtrates. Yield, 7.90 millimoles, or 76.1%, m.p. 211–212° after recrystallization from benzene (in which it is not very soluble).

Anal. Calc'd for $C_{11}H_{12}N_2O$: C, 70.2; H, 6.4; N, 14.9.
Found: C, 70.08; H, 6.51; N, 14.77.

Less satisfactory results were obtained by using the coarser barium amide made from barium metal.

Thirty-nine and four-tenths millimoles of potassium amide, 12.19 millimoles of 8-ethoxyquinoline and 14.9 millimoles potassium nitrate reacted for two weeks (ref. 1c, expts. 11–15). A trace of amino-8-ethoxyquinoline was obtained, together with 2.02 millimoles of 8-hydroxyquinoline, m.p. 72.5–74°.

Amino-6-dimethylaminoquinoline.—6-Dimethylaminoquinoline[9] dissolves in liquid ammonia at room temperatures, but partially crystallizes at 0°. Potassium amide (27.8 millimoles) was added to a liquid ammonia solution of barium thiocyanate (13.8 millimoles) and 6-dimethylaminoquinoline (11.50 millimoles), in accordance with the method of the preceding section. The reaction was allowed to continue for 27 days. The hydrolysate of the reaction mixture was extracted several times with boiling benzene, the extracts being filtered and concentrated, whereupon silvery-

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[7] Friedländer and Ostermaier, *ibid.*, **15**, 336 (1882).

[8] Vis, *J. prakt. Chem.*, [2], **45**, 530 (1892).

[9] Knueppel, *Ber.*, **29**, 706 (1896). M.p. 59–61°; Knueppel found 56°.

gray needles separated; yield, 3.90 millimoles, or 33.9%, m.p. 162.5–165°; m.p. after several crystallizations from dilute alcohol, 168.5–169.5° (water is also a suitable solvent for crystallization). The product is soluble in dilute hydrochloric acid.

In a repetition of the above reaction, in the presence of excess barium thiocyanate, a 22.4% yield of aminodimethylaminoquinoline was obtained in a ten-day reaction. About half of the dimethylaminoquinoline was recovered as crude material. Quinoline then appears definitely to react more rapidly with barium amide than does 6-dimethylaminoquinoline.

Anal. Calc'd for $C_{11}H_{13}N_3$: C, 70.54; H, 7.00; N, 22.46.
Found: C, 70.29; H, 7.04; N, 22.4.

Considerable tar was formed in the reaction of excess potassium amide and potassium nitrate with 6-dimethylaminoquinoline, together with a trace (1%) of aminodimethylaminoquinoline. (Method of ref. 1c, expts. 11–15.)

8-Hydroxyquinoline.—8-Hydroxyquinoline† reacts with ammonia gas to form a yellow ammonium salt, which is sparingly soluble in liquid ammonia, but readily soluble in an excess of potassium amide, forming a yellow solution. Potassium amide (40 millimoles), 8-hydroxyquinoline (11 millimoles) and potassium nitrate (15 millimoles) did not react to form an amino derivative (10 days); 4.6 millimoles of 8-hydroxyquinoline was recovered unchanged.

2-Hydroxyquinoline.—2-Hydroxyquinoline,† although not very soluble in liquid ammonia at room temperatures, dissolves readily in an excess of potassium amide. In a 130-day reaction between 42.5 millimoles of potassium amide, 10.4 millimoles of 2-hydroxyquinoline and 14.6 millimoles of potassium nitrate, no amino derivative was formed, 9.25 millimoles (89%) of the hydroxyquinoline being recovered at the end. Considerable nitrogen was formed.‡ Similar results were obtained (but no nitrogen was evolved) when the potassium nitrate was omitted

2-Aminoquinoline.—2-Aminoquinoline[1a] (9.80 millimoles) was added to barium amide (14.0 millimoles) prepared in a straight tube in accordance with the method of reference 1c, this being followed by 8.19 millimoles of anhydrous barium thiocyanate to serve as a catalyst; 5.50 millimoles of 2-aminoquinoline was recovered at the end, and no other product was isolated. A slight reaction was indicated by the collection of 0.12 millimole of hydrogen.

Potassium amide (59.6 millimoles), 2-aminoquinoline (17.4 millimoles) and potassium nitrate (21.0 millimoles) were heated for four days at 100–125°,[12] in the presence of the iron oxide catalyst used in making the potassium amide. Nitrogen was formed,‡ and most of the aminoquinoline (12.9 millimoles) was recovered at the end of the experiment.

4-Aminoquinoline-2-carboxylic acid.—Potassium amide (36.0 millimoles), potassium nitrate (16.7 millimoles), and quinoline-2-carboxylic acid† (8.84 millimoles) reacted in a two-legged tube (ref. 1c, expts. 11–15) for 0.9 day. The iron-iron oxide catalyst was filtered from the cold hydrolysate of the reaction product, and the filtrate acidified with acetic acid. Cream-colored needles were obtained when this filtrate was concentrated; m.p. about 280.5–281°, (decomp., CO_2 evol.); yield, 7.19 millimoles or 81.4%. The product was soluble in dilute pyridine, or in aqueous alkalies, but insoluble in cold or hot ethyl alcohol, butyl alcohol, acetone, or anhydrous pyridine. It can be crystallized from water.

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‡ $3KNH_2 + 3KNO_3\ (+Fe_2O_3) = 3KNO_2 + 3KOH + N_2 + NH_3$. Bergstrom, unpublished work.

[12] Blair, *J. Am. Chem. Soc.*, **48**, 90–2 (1926).

The 4-aminoquinoline-2-carboxylic acid was not obtained entirely free from water. Drying *in vacuo* at 100° resulted in slight decomposition.

Anal. Calc'd for $C_{10}H_8N_2O_2$: C, 63.8; H, 4.3; N, 14.9.

Calc'd for $C_{10}H_8N_2O_2 \cdot 0.25\ H_2O$: C, 62.3; H, 4.45; N, 14.55.

Found (dried *in vacuo* at room temps.): C, 62.59; H, 4.50; N, 14.7.

Thirty-five-hundredths gram was heated in a test-tube just above the melting point for a few moments. The cooled melt was ground in a mortar, extracted with hot benzene, and filtered. From the cooled extracts, 0.12 g. of white crystals separated, m.p. 150–150.5°. Anhydrous 4-aminoquinoline melts at 154–155°.[10]

Anal. Calc'd for $C_9H_8N_2$: C, 75.0; H, 5.6; H, 19.4.

Found: C, 75.10; H, 5.64; N, 19.28.

Kynurenic acid—Fifty-two-hundredths gram of the amino acid was dissolved with warming in sulfuric acid (4 cc. of 1:1) and diazotized by slow addition of 0.25 g. sodium nitrite in 1 cc. of water. After half an hour at 0°, and an equal time at 100°, the solution was diluted with water, and the resultant light-yellow precipitate was collected by filtration. It was dissolved through the filter by dilute ammonia water, and reprecipitated by adding acetic acid; yield, 0.25 g.; m.p. within 2°, between about 260° and 290°,[11] depending upon the rate of heating.

Anal. Calc'd for $C_{10}H_7NO_3 \cdot H_2O$: C, 58.0; H, 4.3; N, 6.8.

Found: C, 58.25; H, 4.46; N, 6.57.

2-Aminoquinoline-4-carboxylic acid.—In accordance with the method of reference 1*c*, expts. 11–15, 52.4 millimoles of potassium amide, 16.7 millimoles of potassium nitrate and 13.05 millimoles of quinoline-4-carboxylic acid[13] were allowed to react for five days. The aqueous solution of the hydrolysate was filtered to remove the iron and iron oxide, and the filtrate was cooled and acidified with acetic acid. The light-brown precipitate was collected by filtration, and dissolved through the filter with dilute ammonia, leaving a small reddish residue. The filtrate was acidified with acetic acid, the resulting precipitate being dissolved in hot dilute hydrochloric acid. The hydrochloride separated as colorless needles which underwent partial hydrolysis when recrystallized from water. It was therefore dissolved in dilute ammonia, and the base was reprecipitated by addition of acetic acid; yield, 9.15 millimoles or 70.1%; m.p. 350–352°, crude.

Anal. Calc'd for $C_{10}H_8N_2O_2$: C, 63.80; H, 4.28; N, 14.90.

Found: C, 63.61; H, 4.39; N, 15.04.

The ethyl ester was prepared by refluxing the acid with a saturated alcoholic solution of hydrogen chloride gas, and crystallizing from alcohol; m.p. 191–2°.

Anal. Calc'd for $C_{12}H_{12}N_2O_2$: C, 66.66; H, 5.60.

Found: C, 66.59; H, 5.50.

A small amount of the acid was decomposed just above its melting point, the cooled melt being crystallized from water; the melting point 127–128°, as was the melting point of a mixture with authentic 2-aminoquinoline[1a], showing their identity. Koenigs[14] prepared 2-hydroxyquinoline-4-carboxylic acid by heating cinchoninic acid with potassium hydroxide.

Potassium amide (29.9 millimoles) was added to barium thiocyanate (18.55 milli-

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[10] KOENIGS, *Ber.*, **40**, 2880 (1907).

[11] SPÄTH, *Monatsh.* **42**, 92 (1921), observed the same behavior.

[13] KOENIGS, *Ber.*, **12**, 97 (1879); PFITZINGER, *J. prakt. Chem.*, [2], **56**, 311 (1897). Prepared by W. L. Coffin and H. A. Rooney.

[14] KOENIGS, *Ber.* **12**, 99 (1879); **16**, 2152 (1883).

moles) and cinchoninic acid (7.40 millimoles), in a two-legged tube, the reaction being allowed to continue for 26 days. The hydrolysate of the reaction product was treated with excess dilute ammonia and filtered. Aminocinchoninic acid was precipitated from the filtrate by addition of a slight excess of acetic acid; yield, 0.915 millimoles, or 12.4%; m.p. 349–52°, crude. In a repetition (49-day reaction), the isolable product was a small amount of colorless solid; m.p. 211.4–212.4°.

Anal. Calc'd for $C_{10}H_9N_3O$: C, 64.2; H, 4.8; N, 22.4.
Found: C, 63.54; H, 5.03; N, 22.47.

Possibly this is the amide of 2-aminoquinoline-4-carboxylic acid.

Aminoquinoline-6-carboxylic acid.—Potassium amide (29.2 millimoles) potassium nitrate (10.5 millimoles) and quinoline-6-carboxylic acid[15] (6.59 millimoles) reacted for three days, in accordance with the method of reference 1*c*, expts. 11–15. The filtered, cold aqueous hydrolysate was acidified with acetic acid, the light-brown precipitate being collected and dried at 110°; yield, 4.17 millimoles, or 60.4%; m.p. 322–4°. It was purified by dissolving in dilute ammonia, filtering, and reprecipitating by addition of dilute acetic acid; it then melted at 323–324°.

Anal. Calc'd for $C_{10}H_8N_2O_2 \cdot 0.5\ H_2O$: C, 60.88; H, 4.60; N, 14.22.
Found (dried *in vacuo* at 80°): C, 60.77; H, 4.67; N, 14.13.

Loss in weight when dried *in vacuo* at 80° (referred to weight when dried *in vacuo* over concentrated sulfuric acid at 20°), 4.26%; calc'd for loss of 0.5 H_2O from $C_{10}H_8N_2O_2 \cdot H_2O$, 4.37%.

The product is soluble in dilute hydrochloric acid, ammonia or alkali hydroxides, but insoluble or very slightly soluble in hot or cold alcohol or pyridine or in dilute acetic acid, although it may be crystallized from glacial acetic acid. Attempts to decarboxylate it failed.

Quinoline-2-sulfonic acid.—Quinoline-2-sulfonic acid (7.27 millimoles)[16] reacts with ammonia to form an ammonium salt, moderately soluble at 0°. This salt reacts rapidly with potassium amide (24.6 millimoles; ref. 1*c*, expts. 11–15, potassium nitrate omitted) to form a finely-divided yellow precipitate. At the end of a half-day, ammonia was evaporated from the reaction tube, the product was hydrolyzed, and the hydrolysate was filtered hot. 2-Aminoquinoline crystallized, and was identified by the melting point of a mixture with authentic material (m.p. 128–129°); yield, 5.36 millimoles, or 73.8%. The filtrate of the last crop was evaporated to dryness and extracted with boiling benzene, leaving a residue of potassium sulfite. From the benzene, a substance of unknown structure was obtained, which, after several recrystallizations from this solvent, melted at 209–210°.

Anal. Calc'd for $C_{18}H_{19}N_3O_2$: C, 69.84; H, 6.19; N, 13.59.
Found: C, 69.81; H, 6.11; N, 13.59.

No product other than 2-aminoquinoline was obtained when the above reaction was carried out in the presence of potassium nitrate.

Aminoquinoline-6-sulfonic acid.—Quinoline-6-sulfonic acid[17] (crystallized twice from water and dried at 120–140°) reacts with ammonia gas to form an ammonium salt which is moderately soluble in liquid ammonia at room temperatures. A small insoluble residue indicates that the original sulfonic acid was not quite homogeneous. Potassium amide (44.0 millimoles) and potassium nitrate (14.9 millimoles) react with the sulfonic acid (10.5 millimoles) (ref. 1*c*, expts. 11–15) to form a deep-brown or yellow-brown solution, from which a solid (potassium hydroxide?) is slowly deposited. The reaction appears to be relatively rapid (time of reaction, 1.1 days).

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[15] SCHLOSSER AND SKRAUP, *Monatsh.*, **2**, 526 (1881).

[17] KNUEPPEL, *ibid.*, **29**, 707 (1896); HEPP, *ibid.*, **17**, 191 (1884).

The aqueous solution of the reaction product was filtered to remove the catalyst. An excess of ammonium chloride was added, and the solution was held near the boiling point for several hours to precipitate the aminoquinolinesulfonic acid (the ammonium salt is slowly hydrolyzed). The procedure was repeated twice. Yield, 4.19 millimoles, or 39.8%, m.p. above 354°. The product is insoluble or very slightly soluble in cold or hot glacial acetic acid, or absolute pyridine, although it may be crystallized from water (large volumes are required).

Anal. Calc'd for $C_9H_8N_2O_3S \cdot H_2O$: C, 44.57; H, 4.16; N, 11.56; S, 13.24.
Found: C, 44.72; H, 4.10; N, 11.27; S, 12.98 (dried *in vacuo* at 100°).

Potassium amide (28.6 millimoles) was added to a solution of quinoline-6-sulfonic acid (9.56 millimoles) and barium thiocyanate (20.4 millimoles). Hydrogen was visibly formed, the reaction appearing sensibly complete in a day or less, though the tube stood for 6 days before the product was worked up. The hydrolysate was treated with excess sodium carbonate, the barium carbonate being filtered and washed with water. To the filtrate, an excess of ammonium chloride was added, and the aminoquinolinesulfonic acid hydrate was slowly precipitated by heating. Purification was accomplished as described in the previous section; yield, 7.95 millimoles, or 83.1%.

SUMMARY

(1) Substituted quinolines have been converted to amino derivatives by the following methods: (*a*) treatment with barium amide alone or in the presence of barium thiocyanate in liquid ammonia at room temperatures, and (*b*) treatment with potassium nitrate and an excess of potassium amide under the same conditions. Potassium amide alone converts many of the substituted quinolines studied into tars and resins.

(2) The following compounds have been prepared for the first time (the amino group is probably in the 2 position, unless otherwise stated): amino-6-methylquinoline, amino-8-methylquinoline, amino-6-methoxyquinoline, amino-8-ethoxyquinoline, amino-6-dimethylaminoquinoline, 4-aminoquinoline-2-carboxylic acid, 2-aminoquinoline-4-carboxylic acid, aminoquinoline-6-carboxylic acid monohydrate, aminoquinoline-6-sulfonic acid monohydrate. 7-Methylquinoline could not be converted to an amino derivative.

(3) Potassium amide, or potassium amide and potassium nitrate together, react with quinoline-2-sulfonic acid, or with 2-methoxyquinoline to form 2-aminoquinoline. It is considered that the reaction with 2-methoxyquinoline is analogous to saponification of an ester.

(4) The hydroxyl and amino groups in position 2 prevent the introduction of an amino group into quinoline. 8-Hydroxyquinoline cannot be converted to an amino derivative by any of the methods described in this article. The 2- or 4-carboxyl group, on the other hand, increases the rate of introduction of an amino group.