

A HOFMANN TYPE REARRANGEMENT IN LIQUID AMMONIA<sup>1</sup>

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Potassium amide and potassium nitrate dissolved in liquid ammonia at room temperatures react with 2-phenylquinoline-4-carboxylic acid (cinchophen) to give 2-phenylindole in good yield (1). During this rather peculiar reaction, the ring is opened, two carbon atoms are lost, and the indole derivative then formed by ring closure. In an attempt by us to extend this reaction to derivatives of cinchophen, it was found that the corresponding amide (2-phenylquinoline-4-carbonamide) rather unexpectedly reacted with potassium amide and potassium nitrate in liquid ammonia to give 4-amino-2-phenylquinoline in yields of 90–98%, together with a corresponding amount of potassium nitrite and potassium cyanate. It is with this reaction that the present paper is concerned.

Excellent yields of 4-amino-2-phenylquinoline and potassium cyanate may also be obtained by shaking 2-phenylquinoline-4-carbonamide with an excess of potassium amide in the presence of mercury. A dilute potassium amalgam is formed at the same time. Potassium nitrate or mercury are both highly desirable in the above reactions, since in their absence the yield of product drops to about 40%.

Homologs of 4-amino-2-phenylquinoline were formed in fair amount by the action of potassium amide and potassium nitrate on 6-methyl-2-phenylquinoline-4-carbonamide and 2-phenylbenzoquinoline-4-carbonamide (2-phenyl- $\beta$ -naphthocinchoninamide). Benzamide, phenylacetamide, stearamide, and 2-*n*-propyl-2-phenyl-4-methylpentane amide are not converted in this manner to the corresponding amine. The only other amide found to undergo this type of reaction was *o*-benzoylbenzamide, from which *o*-aminobenzophenone was obtained in 20% yield.

2- $\beta$ -Naphthylquinoline-4-carbonamide, 2-*p*-tolylquinoline-4-carbonamide, and 2-*p*-methoxyphenylquinoline-4-carbonamide all react readily with potassium amide and potassium nitrate in liquid ammonia, but without the formation of definite products.

Potassium amide and potassium nitrate react with 9-phenyl-9-fluorylamine in liquid ammonia to give 9-aminophenanthridine, while triphenylmethylamine is changed under similar conditions to benzamide. The latter appears to result from the hydrolysis of primarily formed benzamidine (ammonobenzoic acid). Both of these reactions may be interpreted as Stieglitz rearrangements (2, 3).

Quinoline-4-carbonamide (cinchoninamide) reacts with potassium amide and potassium nitrate, in accordance with an earlier type of reaction (4), to form 2-aminoquinoline-4-carbonamide instead of the anticipated 4-aminoquinoline.

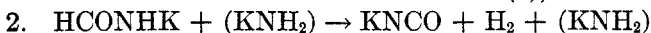
<sup>1</sup> From the Doctorate Thesis of H. C. White, Stanford University, 1940.

## MECHANISM OF THE REACTIONS

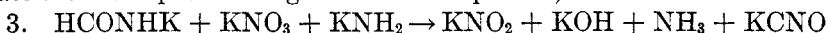
The most obvious mechanism is one involving the direct replacement of the carbonamide group,  $\text{CONH}_2$ , by an amine group in accordance with the equations,



Hydrolysis of the potassium salts on the right hand side of the equation above will give an amine,  $\text{RNH}_2$ , and formamide. The failure to isolate the latter is understandable in view of the known reaction (5),

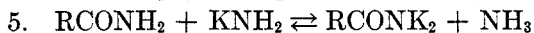
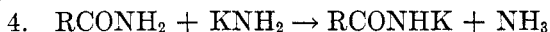


which occurs only in the presence of potassium amide. Perhaps with potassium nitrate the decomposition might follow the equation,

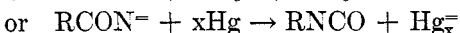
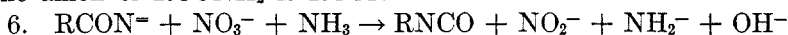


Reaction 3 was however ruled out, because excess potassium amide reacts with potassium nitrate and formamide in liquid ammonia to yield hydrogen in almost theoretical quantity. Hydrogen is not a product of the reaction between potassium amide, potassium nitrate, and 2-phenylquinoline-4-carbonamide, in which 2-phenyl-4-aminoquinoline and potassium nitrite are formed to the exclusion of reduced quinoline derivatives. Accordingly, the entire mechanism above can be ruled out.

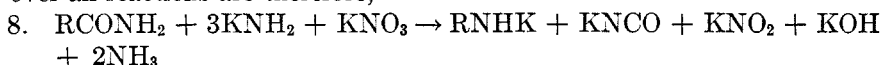
It is more probable that the reaction proceeds by a mechanism having some formal similarity to the Hofmann rearrangement of acid amides to amines, and also to the formation of 2-aminoquinoline from quinoline with potassium amide and potassium nitrate in liquid ammonia (6). The following equations are proposed.



The anion of  $\text{RCONK}_2$  is  $\text{RCON}^-$



The over-all reactions are therefore,

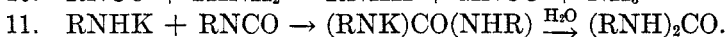
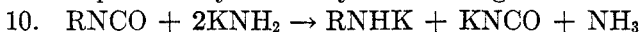


Equation 5 represents the formation of the dipotassium salt of the acid amide as reversible, since most acid amides of the type  $\text{RCONH}_2$  are known only to form stable monopotassium salts (7). It is known that three or more equivalents of potassium amide are necessary for a good yield in the reaction expressed by equation 8, and it is logical to assume that one of its functions is to produce the doubly charged anion,  $\text{RCON}^-$ , of equation 5. The removal of the two negative charges and the formation of the isocyanic ester,  $\text{RNCO}$ , is doubtless a continuous process, as Wallis and Moyer (8) have suggested to be the case in the true Hofmann rearrangement. It is highly improbable that the monovalent nitrogen intermediate of Stieglitz,  $\text{RCON}$ , is formed at any stage of the reaction.

Attempts to isolate the intermediate 2-phenylquinoline-4-isocyanic ester (an aquo-ammono ester) in the reaction between potassium amide, potassium nitrate,

and 2-phenylquinoline-4-carbonamide have proved fruitless. The ester, formed by other means, reacts much more slowly with potassium amide and potassium nitrate than does 2-phenylquinoline-4-carbonamide, suggesting either that the latter reaction is a continuous process in which the aquo-ammono ester does not appear as such, or else the ester is much more easily saponified immediately after it is formed.

Phenylisocyanate reacts with liquid ammonia to form monophenylurea, as expected, since the same well known reaction occurs with gaseous ammonia. Both phenylisocyanate and  $\alpha$ -naphthylisocyanate react with a liquid ammonia solution of potassium amide to give both the mono- and the di-substituted urea. The latter is presumably formed by the following series of reactions,

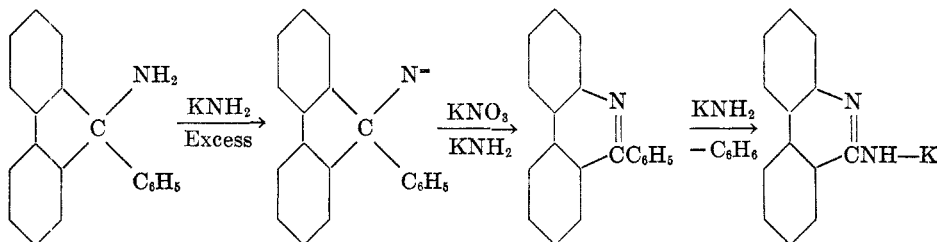


In support of equation 11, it was found that potassium  $\alpha$ -naphthylamide reacts with a liquid ammonia solution of  $\alpha$ -naphthylisocyanate to form both mono- and di- $\alpha$ -naphthylurea, the former probably the result of a reaction with liquid ammonia alone. There is accordingly some basis for saying that the amine of equations 8 and 9 can be formed by the reaction of equation 7, but it is necessary to make the plausible assumption that the potassium salt of the amine does not readily add to these comparatively unreactive isocyanates to form substituted ureas.

4-Amino-2-phenylquinoline is formed in about 20% yield by the action of potassium amide and potassium nitrate on 2-phenylquinoline-4-carbondimethylamide and in 70% yield from the monomethylamide, probably because these compounds, mixed aquo-ammono esters, are saponified by the potassium amide to dimethylamine, or monomethylamine, and 2-phenylquinoline-4-carbonamide.

The reason for the failure of some 2-substituted quinoline-4-carbonamides to undergo this type of reaction is unknown. Apparently side reactions that lead to the formation of tars and resins predominate over the ones expressed by equations 4-9. Since the two open-chain acid amides failed to react at all with potassium amide and potassium nitrate, it seems that some type of activation of the  $\text{CONH}_2$  group is necessary, as by  $\text{C}=\text{O}$  or  $\text{C}=\text{N}$  in the ortho or para position with respect to  $\text{CONH}_2$ .

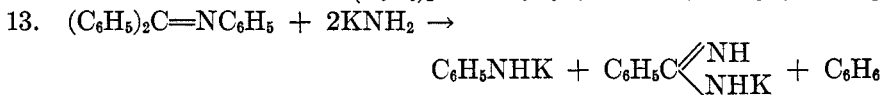
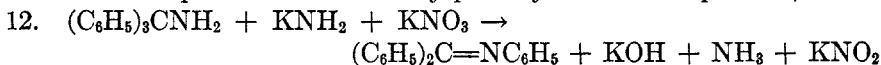
9-Aminophenanthridine (as a potassium salt) is possibly formed from 9-phenyl-9-fluorylamine in accordance with the equations,



The mechanism therefore resembles that suggested by Pinck and Hilbert (2) for the conversion of 9-phenyl-9-fluorylamine to 9-phenylphenanthridine out-

side of liquid ammonia, in the same way that the reactions of equations 4-9 resemble the Hofmann rearrangement. Since potassium amide reacts with 9-phenylphenanthridine to form 9-aminophenanthridine (9), the latter product is the only one isolated in the liquid ammonia reaction.

The conversion of triphenylmethylamine to benzamide by the action of potassium amide and potassium nitrate may possibly follow the equations,



In support of this mechanism, it was found that benzophenone anil when heated with potassium amide and potassium nitrate in liquid ammonia gave, after hydrolysis and steam distillation, aniline and benzoic acid in fair yield. The benzoic acid represents the last step in the hydrolysis of benzamidine. Equation 13 recalls the similar scission of benzophenone by heated sodium amide, to benzene and potassium benzamide, or by heated potassium hydroxide to benzene and potassium benzoate (10). Benzophenone anil is an ammono ketone-ether (11).

#### EXPERIMENTAL PART

##### PREPARATION OF ACID AMIDES

With the exception of 2-phenylquinoline-4-carbonamide, none of the compounds below have been described in the literature.

*2-Phenylquinoline-4-carbonamide.*<sup>2</sup> Isatin (22.1 g., 0.15 mole), ammonium chloride (16 g., 0.30 mole), concentrated aqueous ammonia (180 cc.), and acetophenone (20 g., 0.17 mole) were gently refluxed for fifty minutes with good mechanical stirring. After cooling, the precipitate was collected and recrystallized from alcohol; yield, 18.5 g., or 49.7%; m.p. 195-197°.

*Anal.* Calc'd for  $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}$ : C, 77.40; H, 4.87; N, 11.29.

Found: C, 77.70; H, 4.72; N, 11.50.

The product was found by mixed melting point determinations to be identical with the 2-phenylquinoline-4-carbonamide previously prepared (12).

*2-β-Naphthylquinoline-4-carbonamide.* 2-β-Naphthylquinoline-4-carboxylic acid (7 g., Ref. 14) was refluxed for thirty minutes (water-bath) with thionyl chloride (50 cc.). The excess thionyl chloride was distilled off, first at atmospheric pressure, and then under a partial vacuum. One hundred cubic centimeters of concentrated ammonia water was added and the mixture allowed to stand for one hour. The tan reaction product was twice crystallized from dil. alcohol; yield, 5.5 g. of colorless crystals, m.p. 250.5-251.0°, uncorr.

*Anal.* Calc'd for  $\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}$ : C, 80.50; H, 4.69; N, 9.40.

Found: C, 80.43; H, 4.53; N, 9.42.

Other acid chlorides were prepared in the same manner from 7-8 g. of the carboxylic acid and 50 cc. of thionyl chloride, and converted to the amide by the action of ammonia water (100 cc.).

*2-p-Methoxyphenylquinoline-4-carbonamide.* The product after crystallization from cellosolve (ethylene glycol monoethyl ether) melted at 245-246°, uncorr.; yield, 9 g. from 12 g. of 2-p-methoxyphenylquinoline-4-carboxylic acid (15) and 85 g. of thionyl chloride.

<sup>2</sup> This preparation was first worked out by Dreisbach in these laboratories (13).

*Anal.* Calc'd for  $C_{17}H_{14}N_2O_2$ : C, 73.37; H, 5.07.

Found: C, 73.18; H, 5.02.

*2-Phenylbenzo[h]quinoline-4-carbonamide* (16). The crude amide, crystallized from dilute cellosolve, melted at 268–269° uncorr.; yield, 67%.

*Anal.* Calc'd for  $C_{20}H_{14}N_2O$ : C, 80.54, H, 4.69; N, 9.43.

Found: C, 80.74; H, 4.73; N, 9.42.

*2-p-Xenylquinoline-4-carboxylic acid and its amide.* *p*-Phenylacetophenone (10 grams) and isatin (9 grams) were refluxed in 100 cc. of 33% potassium hydroxide solution with mechanical stirring for five hours. To the cooled mixture of solid and solution, an excess of dilute acetic acid was added, forming a bulky yellow precipitate. This was collected, washed, and crystallized twice from cellosolve; it then melted at 292–293°, uncorr. The yield was 11 g. Analytical figures for hydrogen and nitrogen were close to the theoretical, but carbon was for some reason low, in all analyses.

*Anal.* Calc'd for  $C_{22}H_{15}NO_2$ : C, 81.23; H, 4.65; N, 4.31.

Found: C, 80.23, 79.90, 79.77, 80.03; H, 4.60, 4.60, 4.54, 4.61; N, 4.34.

The acid chloride, prepared in the usual way with thionyl chloride, was converted by treatment with conc'd ammonium hydroxide to the amide, which was twice crystallized from cellosolve. The yield was 4 g. from 8 g. of the acid; m.p. 245.5–246°, uncorr.:

*Anal.* Calc'd for  $C_{22}H_{16}N_2O$ : C, 81.46; H, 4.93.

Found: C, 81.33; H, 4.73.

*3-Phenylbenzo[f]quinoline-1-carbonamide.* The amide, crystallized from alcohol using Norit, melted at 239–240°, uncorr.; yield, 81%.

*Anal.* Calc'd for  $C_{20}H_{14}N_2O$ : C, 80.54; H, 4.69; N, 9.43.

Found: C, 80.37; H, 4.82; N, 9.30.

*Reactions in liquid ammonia. General procedure.* Reactions in two-legged glass ammonia tubes were carried out in a previously described manner (17). A liquid ammonia solution of potassium amide, prepared in one leg from metallic potassium with an iron oxide catalyst, was added to an ammonia solution or suspension of potassium nitrate and the acid amide in the other leg. Strongly colored solutions resulted. After evaporation of ammonia, the reaction products were treated in the tube with benzene and alcohol to destroy reactive potassium salts, water was added and the first two solvents evaporated. The solid was filtered and crystallized from an appropriate solvent.

*2-Phenylquinoline-4-carbonamide and potassium amide.* In a straight tube (18) was prepared the potassium amide from 1.17 g. (30 milliatoms) of potassium with an iron wire catalyst. After cooling and removing the catalyst, 2.48 g. (10.0 millimoles) of 2-phenylquinoline-4-carbonamide was introduced, the tube sealed, and allowed to stand at room temperatures for 23 days. The solution at various stages was colored green, reddish-brown, and greenish-brown. Gases obtained during the reaction were insignificant ( $H_2$ , 0.4 cc.;  $N_2$ , 1.1 cc., standard conditions). The ammonia solution of the reaction product (at  $-78^\circ$ ) was poured into a beaker, and excess ammonium chloride added to destroy potassium amide. After evaporation of solvent, the solid was washed with water and the dried residue then extracted with hot benzene, the extracts concentrated and cooled to obtain 2-phenyl-4-aminoquinoline. The yield was 0.932 g., m.p. 163.0–170.0°, uncorr., or 43.4%. It was identified after recrystallization as 2-phenyl-4-aminoquinoline (m.p. 163–164°) by mixed melting point determinations. A small amount (0.15 g., m.p. 264–275°) of benzene-insoluble material was also isolated.

*2-Phenylquinoline-4-carbonamide, potassium amide, and potassium nitrate.* (a) 2-Phenylquinoline-4-carbonamide (1.695 g., 6.82 millimoles), potassium nitrate (1.20 g., 11.9 millimoles), and the potassium amide from 1.20 g. (28.1 milliatoms) of potassium reacted for one day at room temperatures in a two-legged reaction tube, as in the general procedure; yield, 1.342 g., or 89.6%, m.p. 162.5–163.5°, uncorr. In other experiments, yields up to 98% (m.p. 162.5–164°) were obtained. The melting point when the compound was mixed with known 2-phenyl-4-aminoquinoline (19) was 163.5–164.5°, showing their identity.

(b) The above experiment was repeated with an iron wire catalyst for making the potassium amide, since iron oxide catalyzes the formation of potassium nitrite from potassium

nitrate (20). The reaction product was hydrolyzed in the tube with water vapor (21), then treated with water (after breaking open the tube) and the solid collected on a filter. The yield was 1.420 g. or 94.9%. The aqueous filtrate was diluted to 50 cc. and nitrite (22) and cyanate determined on aliquot portions.

One-tenth aliquot gave 14.24 cc.  $N_2$ , standard conditions, or 93.2% on the basis of equation 8.

One-half aliquot was treated with excess silver nitrate in very dilute nitric acid, and then with 10 cc. of conc'd sodium nitrite to dissolve possible silver nitrite in the precipitate. The washed silver cyanate collected on a Gooch filter weighed 0.446 g. (88.3%).

(c) In a two-legged tube, 1.63 g. of 2-phenylquinoline-4-carbonamide (6.56 millimoles) reacted with 1.05 g. (10.4 millimoles) of potassium nitrate and the potassium amide from 1.02 g. of potassium (26.1 milliatoms) for 9 days. The solvent was evaporated and the reaction mixture hydrolyzed with benzene and alcohol, and then worked over in the usual way. The yield of 2-phenyl-4-aminoquinoline was 1.394 g., (6.43 millimoles or 97.9%), m.p. 163-164.5°.

(d) In a repetition of reaction (a) at -33° (five hours, round-bottomed flask), 83% of the 2-phenylquinoline-4-carbonamide was recovered unchanged.

(e) In a steel autoclave (22), 128 millimoles of potassium amide reacted for five hours (at 55°) with 60.4 millimoles of 2-phenylquinoline-4-carbonamide and 99 millimoles of potassium nitrate. Considerable resinous material was formed, together with 6.7 g. of solid, m.p. 137-142°, after several crystallizations from alcohol. No pure reaction product was isolated.

(f) *2-Phenylquinoline-4-carbonamide and barium amide.* The chief isolable product is 2-phenylquinoline. Details of this peculiar reaction are reserved for a future article.

*2-Phenylquinoline-4-carbonamide, potassium amide, and mercury.* In a two-legged glass tube (23) the potassium amide from 1.1 g. (28.2 milliatoms) of potassium was rocked for two days at room temperatures with 1.695 g. (6.82 millimoles) of 2-phenylquinoline-4-carbonamide and 3 cc. of purified mercury. At the end of the reaction, the mercury was well washed with ammonia. Negligible amounts of water-insoluble gases were formed (0.3 cc.  $H_2$ , 0.3 cc.  $N_2$ ). Thirteen and two-tenths milliatoms of potassium was found in the mercury, or 96.8% (equation 9). The yield of 2-phenyl-4-aminoquinoline was 1.401 g. (92.7%).

To the aqueous filtrate of the above, made barely acid with dil. nitric acid, was added excess silver nitrate solution;  $AgCNO$ , 0.9180 g. or 90%,  $AgCl$  from the  $AgCNO$ , 0.8740 g. as against a theoretical 0.8770 g.

*2-Phenyl-6-methylquinoline-4-carbonamide, potassium amide, and potassium nitrate.* The acid amide (1.20 g., 4.57 millimoles), potassium amide (19.2 millimoles from 0.75 g. of potassium), and potassium nitrate (0.90 g., 7.9 millimoles) reacted for four days at room temperatures.

The tarry precipitate left after evaporation of the benzene-alcohol was freed from water and extracted with petroleum ether. The reddish-brown solid, m.p. 150-160°, that remained was twice crystallized from dilute alcohol with the addition of Norit. It then melted at 184-185°. 2-Phenyl-4-amino-6-methylquinoline melts at 188-189° (24).

*2-Phenylbenzo[h]quinoline-4-carbonamide, potassium amide, and potassium nitrate.* The acid amide (1.31 g., 4.35 millimoles), potassium amide (17.9 millimoles from 0.70 g. potassium), and potassium nitrate (7.9 millimoles) reacted for three days at room temperatures. The yield of 2-phenyl-4-aminobenzo[h]quinoline (m.p. 162.5-163°) was 0.60 g., or 54%. It was crystallized from alcohol with the use of Norit.

*Anal.* Calc'd for  $C_{18}H_{14}N_2$ : C, 84.42; H, 5.20; N, 10.37.

Found: C, 84.20; H, 5.54; N, 10.50.

*2-Phenylquinoline-4-carbonmethylamide, potassium amide, and potassium nitrate.* The methylamide was prepared by the action of methylamine on the acid chloride of 2-phenylquinoline-4-carboxylic acid. Five millimoles, reacting for four days (20°) with 20.5 millimoles of potassium amide and 8.9 millimoles of potassium nitrate, yielded 0.264 g. (78.5%) of 2-phenyl-4-aminoquinoline (m.p. 162-163° uncorr.).

*2-Phenylquinoline-4-carbondimethylamide, potassium amide, and potassium nitrate.* The dimethylamide was prepared from the acid chloride of cinchophen and dimethylamine. Five millimoles reacted for two days (20°) with 20 millimoles of potassium amide and 9 millimoles of potassium nitrate. The yield of 2-phenyl-4-aminoquinoline (m.p. 160–162°) was 0.243 g., or 23.3%.

*o-Benzoylbenzamide, potassium amide, and potassium nitrate.* *o*-Benzoylbenzamide, (1.059 g., 4.71 millimoles) (25) potassium amide (19.2 millimoles), and potassium nitrate (0.80 g., 7.9 millimoles) reacted for six days at 20° in a two-legged tube.

The hydrolysate, freed from benzene and alcohol, was concentrated to about 25 cc. and an excess of dilute hydrochloric acid added. The crystals that separated after standing overnight were added to aqueous sodium hydroxide. The yield of slowly forming yellow crystals was 0.23 g. (20%), m.p. 105–107°. Fifty-one per cent of the theoretical quantity of nitrite was formed (equation 8). *o*-Aminobenzophenone melts at 105° (26). In a repetition of this experiment at –33° (six hours), only a trace of *o*-aminobenzophenone was isolated.

#### OTHER ACID AMIDES WITH POTASSIUM AMIDE AND POTASSIUM NITRATE

Under the conditions of the preceding experiments (general method), *2-p*-tolylquinoline-4-carbonamide, *2-β*-naphthylquinoline-4-carbonamide, *2-p*-xenylquinoline-4-carbonamide, and *2-p*-methoxyphenylquinoline-4-carbonamide were converted to tar. Benzamide did not react with four equivalents of potassium amide and two equivalents of potassium nitrate in liquid ammonia at room temperatures during three weeks. Phenylacetamide dissolves in excess potassium amide with a deep red color, indicating possibly that a dipotassium salt,  $C_6H_5CHKCONHK$ , is formed. Under the usual conditions, with the addition of potassium nitrate, no appreciable reaction had occurred within one week (74% of the phenylacetamide was recovered and no nitrite was formed). Stearamide (6.82 millimoles), potassium amide (23 millimoles) and potassium nitrate (9.9 millimoles) did not react at all in liquid ammonia at 90° (18 hours). *2-n*-Propyl-2-phenyl-4-methylpentanamide (27) failed to react in three days at 20° with excess potassium amide and potassium nitrate. It was hoped that an optically active amine would be formed.

In all of the above cases, failure to observe a reaction signifies that nothing occurred beyond the formation of a potassium salt, such as  $RCONHK$ , from which the acid amide was regenerated on hydrolysis.

*Quinoline-4-carbonamide, potassium amide, and potassium nitrate.* Quinoline-4-carbonamide<sup>3</sup> (0.30 g., 1.74 millimoles), potassium nitrate (0.30 g., 3.0 millimoles) reacted for two days in a two-legged reaction tube with the potassium amide from 0.30 g. (7.7 millimoles) of potassium (iron wire catalyst). The product, crystallized from water, had the composition of 2-aminoquinoline-4-carbonamide; yield, 0.175 g. (54%), m.p. 218–218.5°, uncorr.; picrate, m.p. 278–280°, uncorr., decomp. Six hundred fourteen thousandths of a mole of nitrite were formed per mole of quinolinecarbonamide.

*Anal.* Calc'd for  $C_{10}H_8N_2O$ : C, 64.09; H, 4.85.

Found: C, 63.89; H, 4.99.

One gram was refluxed with dilute hydrochloric acid (about 10%) for one hour, then dil. sodium hydroxide was added to neutrality. The resulting precipitate was filtered cold and washed. The yield was 0.80 g.; m.p. 349–353°, uncorr., depending upon the rate of heating. These properties are those of 2-aminoquinoline-4-carboxylic acid (29).

#### THE ACTION OF POTASSIUM AMIDE AND LIQUID AMMONIA ON ISOCYANATES

*2-Phenylquinoline-4-isocyanic ester, potassium amide, and potassium nitrate.* 2-Phenylquinoline-4-isocyanic ester (30) (m.p. 230–231°, uncorr.; 0.71 g. or 2.85 millimoles), potas-

<sup>3</sup> Prepared from cinchoninic acid chloride and aqueous ammonia. The physical properties are the same as those described by Wenzel (28), who prepared the substance by another method.

sium nitrate (0.4 g., 4.0 millimoles), and the potassium amide from 0.35 g. of potassium (9.0 milliatoms) reacted for two days at room temperatures in a two-legged tube. Most of the isocyanate (77%) was recovered from the hydrolysate of the reaction mixture.

In another experiment, five equivalents of potassium amide reacted with 1.23 g. of the isocyanic ester and one equivalent of potassium nitrate for 36 hours at room temperatures. The hydrolyzed product, when crystallized from alcohol, gave 0.75 g. (62%) of the original isocyanic ester, and 0.22 g. (20%) of 2-phenyl-4-aminoquinoline, m.p. 161–162° uncorr.

*2-Phenyl-6-methylquinolyl-4-isocyanic ester.* This was prepared through the acid azide by the method of John (31) but melted at 246–247°, instead of the reported 214°, even though the melting points of the intermediate hydrazide and acid azide agreed with the values of John.

*Anal.* Calc'd for  $C_{17}H_{12}N_2O$ : C, 78.44; H, 4.65.

Found: C, 78.15; H, 4.85.

Mol. wt. (Rast): Calc'd, 260; found, 267.

When refluxed for ten hours with 33% alcoholic potassium hydroxide, 2-phenyl-4-amino-6-methylquinoline was formed (0.6 g. from 1.0 g. isocyanate); m.p. 188.5–189.3°, uncorr.; picrate, m.p. 206–207° (John reports 208°). The substance in hand therefore had the properties of the isocyanic ester, in spite of the different melting point of John (a misprint?).

2-Phenyl-6-methylquinolyl-4-isocyanic ester (1.23 g.), potassium nitrate (1.0 g.), and the potassium amide from 0.9 g. of potassium (0.02 g.  $Fe_2O_3$  catalyst) reacted for two days in a two-legged tube at room temperatures. One and five hundredths grams of the isocyanic ester was recovered unchanged from the hydrolysate.

*Phenylisocyanate and potassium amide.* (a) Fifty cubic centimeters of liquid ammonia was added to 4.5 g. of phenylisocyanate in a 200-cc. round-bottomed flask, forming a colorless solution. After the ammonia had evaporated (about four hours) there was left an almost solid colorless residue, which was crystallized from alcohol. The yield was 4.5 g., m.p. 144–145°, uncorr. (87.5%). It was identified as phenylurea by a mixed melting point.

(b) Five grams of phenylisocyanate was added to a liquid ammonia solution (75 cc.) of the potassium amide prepared from 2 g. of potassium with an iron oxide catalyst. A vigorous reaction took place with the formation of a voluminous light purple precipitate. After the ammonia had evaporated (about four hours), the solid was treated with benzene-alcohol mixture, boiled with Norit, and filtered. Colorless crystals (3.7 g.) of sym. diphenylurea, m.p. 233–234°, were obtained and identified by the melting point of a mixture with authentic material. Varying amounts of monophenylurea were also obtained. Under the same conditions, monophenylurea reacted with potassium amide only to form a salt, and not to form diphenylurea.

*$\alpha$ -Naphthylisocyanate and potassium amide.* Four grams of  $\alpha$ -naphthylisocyanate was added to a liquid ammonia solution of the potassium amide from 1.0 g. of potassium in 75 cc. of liquid ammonia at  $-33^\circ$ . A copious yellow precipitate formed. An excess of ammonium chloride (1.5 g.) was added after five minutes. The reaction product remaining after evaporation of the ammonia was fractionally crystallized from alcohol, thereby yielding 2.1 g. (48%) of  $\alpha$ -naphthylurea (m.p. 211–212° uncorr.) and 1.4 g. (38%) of di- $\alpha$ -naphthylurea (m.p. 283–285°, uncorr.). Identification was by mixed melting point.

*Potassium  $\alpha$ -naphthylamide and  $\alpha$ -naphthylisocyanate.* Potassium amide was prepared from a liquid ammonia solution of 2 g. of potassium in the presence of an iron wire catalyst, in an Erlenmeyer flask. To this was added 4 g. of  $\alpha$ -naphthylamine, to form potassium  $\alpha$ -naphthylamide, whose liquid ammonia solution was orange-red in color. Four grams of  $\alpha$ -naphthylisocyanate was slowly introduced, resulting in the formation of a yellow solution and a yellow precipitate. The reaction was stopped after ten minutes by the addition of 3 g. of ammonium chloride. The precipitate remaining after the evaporation of the solvent ammonia was treated with water, filtered, and dissolved in hot alcohol. Addition of conc'd hydrochloric acid gave a precipitate of  $\alpha$ -naphthylamine hydrochloride (1.5 g., or 30%). From the filtrate, two fractions were obtained by concentration:  $\alpha$ -naphthylurea, 2.4 g., 55%, melting at 210–212°, and di- $\alpha$ -naphthylurea, 2.8 g., or 38%, melting at 282–284°.



*Formamide, potassium amide, and potassium nitrate.* In a two-legged reaction tube, the potassium amide from 0.75 g. (19 milliatoms) of potassium (iron wire catalyst) was added to a liquid ammonia solution of 0.384 g. (8.53 millimoles) of formamide and 1.10 g. (11 millimoles) of potassium nitrate. Gases were collected at irregular intervals for 18 hours, but little or none was obtained after the first three hours (32). There was obtained 176.6 cc. of gas, standard conditions, consisting of H<sub>2</sub>, 97.5%; yield 90%. Small losses of gas always occur when two-legged reaction tubes with stopcock are used, as in the present case.

*Pinck and Hilbert type rearrangement.* 9-Amino-9-phenylfluorene (1.47 g., 5.00 millimoles), potassium nitrate (0.80 g., 7.9 millimoles), and the potassium amide from 1.0 g. (25.6 milliatoms) of potassium (iron wire catalyst) reacted for two days in a liquid ammonia reaction tube at room temperatures. The product, crystallized from alcohol, proved to be 9-aminophenanthridine, m.p. 190–190.5°, uncorr. The mixed melting point with 9-aminophenanthridine prepared by the action of potassium amide on 9-phenylphenanthridine (9) was the same. The yield was 0.689 g., or 61%. Potassium nitrite was also a reaction product.

*Stieglitz type rearrangement.* Triphenylmethylamine was not appreciably attacked by potassium amide and potassium nitrate in liquid ammonia at room temperatures; accordingly, it was necessary to apply heat.

Triphenylmethylamine (1.003 g., 3.84 millimoles), potassium nitrate (0.75 g., 7.4 millimoles), and the potassium amide from 0.70 g. (18 milliatoms) of potassium (with 0.02 g. of iron oxide as a catalyst) were rocked in a steel bomb (33)<sup>4</sup> for fourteen hours at 80°. The product was treated with alcohol-benzene mixture, then with water, and the first two solvents evaporated. Benzamide (0.202 g., crude or 43%) was obtained by concentrating and cooling the aqueous solution. The recrystallized material was identified as benzamide by its melting point alone and in mixture with authentic benzamide.

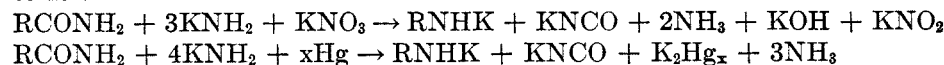
#### SUMMARY

1. 2-Phenylquinoline-4-carbonamide is converted in about 40–50% yields to 2-phenyl-4-aminoquinoline by reaction with potassium amide in liquid ammonia. Almost quantitative yields are obtained in the presence of potassium nitrate or of mercury.

2. Only a few of the homologs of 2-phenylquinoline-4-carbonamide behave similarly. Open-chain acid amides studied failed to react. The amide of *o*-benzoylbenzoic acid is converted in poor yield to *o*-aminobenzophenone by potassium amide and potassium nitrate. It is thus apparent that a reaction of the above type occurs only if the –CONH<sub>2</sub> group is activated by C=O or C=N at a favorable position in the molecule.

3. The direct replacement of the –CONH<sub>2</sub> group by –NH<sub>2</sub> is very improbable.

4. A more probable mechanism is the following: RCONH<sub>2</sub> (2-phenylquinoline-4-carbonamide, etc.) reacts with potassium amide reversibly to form some of the ion, RCON<sup>–</sup>. This loses two electrons to potassium nitrate or to mercury to give the rearranged product, RNCO, which excess potassium amide converts to RNHK and KNCO. The over-all reactions are



<sup>4</sup> A sealed glass tube was enclosed in a steel bomb tube containing liquid ammonia to counterbalance the internal pressure.

2-Phenylquinoline-4-isocyanic ester and 2-phenyl-6-methylquinolyl-4-isocyanic ester react more slowly with potassium amide to form the corresponding amine than this latter is produced in accordance with the equations above from quinoline-4-carbonamide derivatives. Isocyanate is, therefore, either not a true intermediate in the reactions, or it is much more readily saponified by potassium amide immediately after its formation.

5. Phenyl- and naphthyl-isocyanates react with liquid ammonia at  $-33^{\circ}$  to form monosubstituted ureas, but disubstituted ureas are also formed in the presence of potassium amide. This can be interpreted as involving the intermediate formation of a salt of a primary amine, *e.g.*,  $C_6H_5NHK$ , which adds to the isocyanate to form the disubstituted urea. Accordingly, the assumption of the formation of the isocyanic ester (paragraph 4 of summary) receives some support.

6. 9-Phenyl-9-fluorylamine reacts with potassium amide and potassium nitrate to form 9-aminophenanthridine by a method related to the Pinck-Hilbert modification of the Stieglitz rearrangement. The expected primary product, 9-phenylphenanthridine, has been converted by potassium amide to 9-amino-phenanthridine.

7. Potassium amide and potassium nitrate react with triphenylmethylamine to form benzamide. It is assumed that a Stieglitz-type rearrangement takes place with the formation of benzophenone anil, which is cleaved by potassium amide to potassium benzamidine. The latter is hydrolyzed to benzamide.

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