Tetrahedron Letters No.38, pp. 3657-3659, 1967. Pergamon Press Ltd. Printed in Great Britain.

RING TRANSFORMATIONS IN REACTIONS OF HETEROCYCLIC HALOGENO COMPOUNDS WITH NUCLEOPHILES (XI) (1)

Reaction of 3-amino-2-bromoquinoline with potassium amide in liquid ammonia

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(Received in UK 28 June 1967)

In previous investigations in this laboratory it has been found that ring transformations occur when 3-amino-2-bromopyridine (I) or 5-amino-4-chloro-2-phenylpyrimidine (II) is treated with potassium amide in liquid ammonia, I yielding 3-cyanopyrrole (2) and II 4-cyano-2-phenylimidazole (3). Mechanisms for these reactions were proposed in which the formation of chain compounds as intermediates was assumed. In two reactions of another type, the conversions of 5-methoxy- and 5-ethoxy-4-chloro-2-phenylpyrimidine by potassium amide, chain compounds were shown to be generated which changed into 5-alkoxy-6-amino-2-phenylpyrimidines by heating (3). Whereas such intermediates were not detected in the transformations of I and II mentioned above, we succeeded now in isolating such a product in an analogous reaction i.e. the conversion of 3-amino-2-bromoquinoline (III) with potassium amide in liquid ammonia.

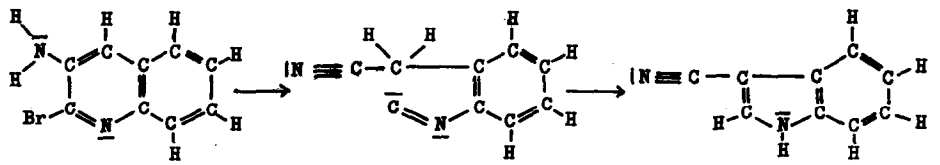
3-Amino-2-bromoquinoline (III; m.p. 157-158°; analysis: C 48.7, H 3.1, N 12.7; calc. for $C_9H_7BrN_2$ (223.08): C 48.45, H 3.16, N 12.50) was synthesized from 2-hydroxyquinoline-3-carboxylic acid (4) by reacting this substance with phosphorus oxybromide at 135°, converting the product obtained with liquid ammonia into 2-bromoquinoline-3-carbonamide (m.p. 207-208°; analysis: C 48.1, H 2.8, N 11.3; calc.for $C_{10}H_7BrN_2O$ (251.09): C 47.83, H 2.81, N 11.16) and treating the carbonamide with a solution of bromine in aqueous potassium hydroxide.

3-Amino-2-bromoquinoline (III) was reacted with the fourfold molar amount of potassium amide in liquid ammonia at -33° for 4 hrs. The reaction mixture was separated by chromatography in a column filled with aluminum oxide, using chloroform and absolute ethanol as eluents subsequently. It appeared that together with 3-cyanoindole (IV, m.p. 178-179°), ortho-cyanomethylphenyl isocyanide (V, m.p. 63-64°) was formed. Yields: 20 and 70% respectively.

IV was identified by microanalysis (found: C 76.0, H 4.0, N 20.1; calc. for $C_9H_6N_2$ (142.15): C 76.04, H 4.25, N 19.71) and comparison of its physical properties with a specimen (m.p. 177,5-179°) prepared from indole-3-carboxylic acid (5).

The structure of V (analysis: found C 76.1, H 4.0, N 19.7; calc.for $C_9H_6N_2$ (142.15): C 76.04, H 4.25, N 19.71) was established by its formation and, in collaboration with P.Smit, by spectrometry (IR absorptions at 2260 and 2130 cm^{-1} in accordance with the presence of $-CH_2-C\equiv N|$ and $-\bar{N}=C|$; NMR absorptions: τ = 6.05 (singlet) and 2.53 (multiplet), the ratio of areas being 1 : 2, showing that only the pyridine nucleus was opened). In an attempt to synthesize V from ortho-cyanomethylaniline (6) by reacting this substance with chloroform and potassium hydroxide, instead of V, IV was obtained by ring closure in the basic medium of the primarily formed isocyanide.

The course of the reaction of potassium amide on 3-amino-2-bromoquinoline (III) can be explained by the following sequence:



III V IV

This pathway was affirmed by the fact that V, when treated with potassium amide in liquid ammonia under equal conditions as III, changed into IV for 20%.

The mixture of 3-cyanoindole (IV) and ortho-cyanomethylphenyl isocyanide (V) could not be separated by gas chromatography using a column filled with Polyphenyl ether (LP-103) on Chromosorb (60-80)(weight ratio = 1 : 20) at 200° as V is transformed into IV during this procedure.

The investigation is being continued.

Acknowledgement We are indebted to Drs.P.Smit for his help in determining the structures of the reaction products, Drs.C.A.Landheer for advice on the chromatographic analyses and Messrs. W.P.Combé and A.Koudijs for carrying out the microanalyses.

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