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

Action of potassium amide on 2-bromo- and 2,6-dibromo-3-hydroxypyridine

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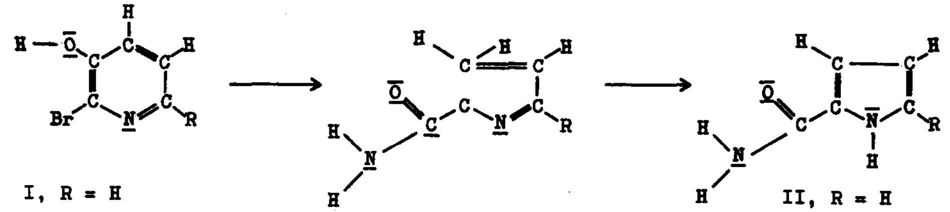
Previously it has been shown that 3-amino-2-bromopyridine (2) and 5-amino-4-bromo-2-phenylpyrimidine (3) are converted into compounds containing a 5-membered ringsystem (3-cyanopyrrole and 4-cyano-2-phenylimidazole) and studying the analogous conversion of 3-amino-2-bromoquinoline we succeeded in elucidating the course of the ring transformation (1). As it is likely that reactions of this type are initiated by abstraction of a proton from the amino group, it was especially of interest to study what would happen when reacting 2-bromo-3-hydroxypyridine with potassium amide.

2-Bromo-3-hydroxypyridine (I, prepared from 3-ethoxy-2-nitropyridine (4)) was reacted for 2 hrs at -33° with the eightfold molar amount of potassium amide in liquid ammonia. After evaporation of the ammonia a solid was left from which by extraction with ether pyrrole-2-carbonamide (II) was isolated in a yield of 85%. The identity of the reaction product (m.p.172.5-174°) was established by microanalysis (found: C 54.7, H 5.6, N 25.7; calc.for $C_5H_6N_2O$(110.11): C 54.53, H 5.49, N 25.44), determination of IR-spectrum (absorptions in accordance with the presence of $-NH_2$, $>$NH and $>$C=O) and of NMR-spectrum (absorptions = 2 broad singlets (τ = -1.4 and 3.1) and 2 multiplets (τ = 3.2 and 4.05; ratio of peak areas 2 : 1) corresponding to $>$NH, $-NH_2$, H^3+ H^5 and H^4) and by mixed melting point determination with an authentic specimen (m.p.173-175°) synthesized from pyrrole-2-carboxylic acid according to Fischer and Van Slyke (5).

In an analogous reaction 2,6-dibromo-3-hydroxypyridine (III, prepared from 3-hydroxypyridine (6)) was converted under similar conditions. In a yield of 80% 5-bromo-pyrrole-2-carbonamide (IV, m.p.136-138°) was formed. IV was identified by microanalysis (found: C 32.0, H 2.7, N 14.9; calc.for $C_5H_5BrN_2O$(189.02): C 31.77, H 2.63, N 14.82), its IR-spectrum (nearly identical with that of II) and its NMR-spectrum (together with

>NH and $-NH_2$ absorptions (τ = -2.17 and 2.63) the spectrum showed 2 doublets (τ = 3.15 and 3.75) characteristic for β-protons in the pyrrole nucleus).

Thus, it appears that in the reactions of both I and III there is no bond fission between carbon atoms 2 and 3 as in the transformations of 3-amino-2-bromopyridine and 3-amino-2-bromoquinoline, but the rings are broken between carbon atoms 3 and 4. Awaiting more experimental data on the course of reactions of bromohydroxypyridines only a tentative reaction scheme for the conversion of 2-bromo-3-hydroxypyridine (I) and 2,6-dibromo-3-hydroxypyridine (III) with potassium amide is given:



I, R = H
III, R = Br

II, R = H
IV, R = Br

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