

NOVEL TRANSFORMATIONS OF 2-HALOGENOPYRIDINES
IN BASIC MEDIUM YIELDING 8-CYANOQUINOLINES*

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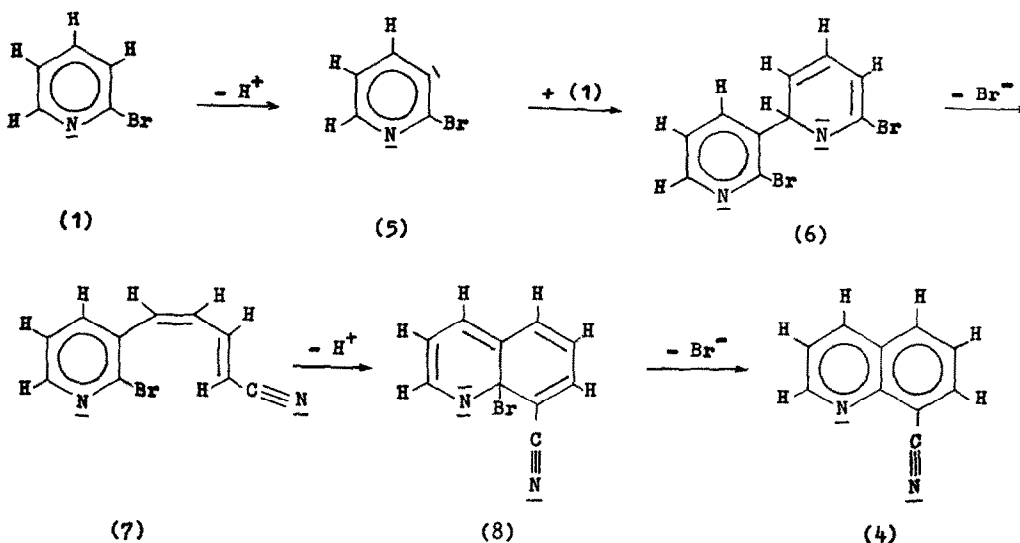
Reactions of 2-halogenopyridines and derivatives of these substances with strong bases were found to fall into several patterns. Together with substitutions, cine-substitutions¹ and formations of chain compounds^{1,2}, ring transformations were observed, i.a. conversions of 6-substituted 2-halogenopyridines into pyrimidine derivatives² and of 3-substituted 2-halogenopyridines into pyrrole derivatives³.

We now wish to report a novel type of ring transformation which occurs, together with the formation of a direct substitution product and a chain compound¹, when 2-bromo- and 2-chloropyridine are treated with lithiumpiperidide in a medium containing an excess of piperidine, i.e. the formation of a bicyclic product by abstraction of 2 molecules of hydrogen halide from 2 molecules of the substrate. As an example the reaction of 2-bromopyridine (1) is described.

A stirred solution of (1) (1 mmole) in piperidine (50 mmoles) was reacted at 35° under nitrogen by adding dropwise phenyllithium (4 mmoles) in 4 ml ether over 5 min, evaporating the ether during the procedure. The mixture was allowed to react with stirring for 6 h, whereupon by working up as usual⁴ along with 2-piperidinopyridine ((2), 2%) and 1-cyano-4-piperidino-1,3-butadiene ((3), trace), 8-cyanoquinoline (4) was obtained in a yield of 20%. The product (4) was separated by GLC using a column packed with 0.5 g FFAP on 2.6 g Diatoport-S (retention times of (2), (3) and (4) 1.4, 11.2 and 17.7 min respectively at 220° and F_o(N₂) 55 ml/min).

* XXXIIIrd Communication on Ring transformations from this laboratory; previous paper: J.Pomorski, H.J.den Hertog, D.J.Buurman and N.H.Bakker, Rec.Trav.Chim., in press.

The formation of (4) can be explained by the following scheme:



It is assumed that anion (5) adds to C-6 of a molecule of (1) yielding (6) after which ring fission affords (7), a sequence like that leading to the formation of (3) by the attack of the piperidide ion on C-6 of (5) followed by fission of the 1-6 bond¹. Finally (7) is converted into (4) by an internal addition elimination process via (8).

Similar transformations were found to occur when reacting derivatives of 2-bromopyridine such as 2-bromo-5-methyl- and 2-bromo-5-ethoxypyridine, together with other products the 3,6-dimethyl and 3,6-diethoxy derivatives of 8-cyanoquinoline being formed, melting at 125° and 120-122° respectively.

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4. Cf. H.C.van der Plas, T.Hijwegen and H.J.den Hertog, Rec.Trav.Chim. 84, 53 (1965)