ISOMERIZATION OF α-(β-CYANOETHYLAMINO)KETONES INTO FUNCTIONAL PYRROLIDINE DERIVATIVES

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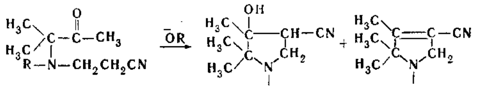
We have previously shown [1–3] that β-cyanoethyl ethers of α-hydroxy ketones isomerize under the action of basic reagents into 3-cyano-4-hydroxytetrahydrofurans.

In order to develop a method of synthesizing functional pyrrolidine derivatives, we have investigated the behavior of α-(β-cyanoethylamino)ketones (I) under conditions of basic catalysis. It was found that, like the β-cyanoethyl ethers of α-hydroxyketones, these compounds are converted by the action of basic catalysts into the corresponding derivatives of pyrrolidine (II) and of 3-pyrroline (III).



Ia, b IIa, b IIIa, b

I–III a R = H; b R = CH_3

The composition and structure of the starting materials and also of the heterocyclic compounds obtained were shown by elementary analysis, functional group analysis, and IR, UV, and PMR spectroscopy.

6-Oxo-5, 5-dimethyl-4-azapentanonitrile (Ia): mp 42–43° C. Found, %: C 61.79; H 9.25; N 17.89. Calculated for $C_8H_{14}N_2O$, %: C 62.06; H 9.09; N 18.18.

6-Oxo-4, 5, 5-trimethyl-4-azapentanonitrile (Ib): bp 99–100° C (1 mm); n_D^{20} 1.4579; d_4^{20} 0.9585. Found, %: C 64.09; H 9.80; N 16.41; MR_D 47.39. Calculated for $C_9H_{16}N_2O$, %: C 64.25; H 9.58; N 16.65: MR_D 47.44.

A mixture of 2 g of Ia, 50 ml of absolute ether, and a catalytic amount of caustic potash was heated at 35° C for 6 hr. After the end of the reaction, the mixture was decomposed with a small amount of water and was extracted with ether. The ethereal extracts were neutralized with carbon dioxide. The residue from the elimination of the ether crystallized on standing.

4-Cyano-3-hydroxy-2, 2, 3-trimethylpyrrolidine (IIa): yield 20%, mp 114–115° C. Found, %: C 62.06; H 9.21; N 18.05. Calculated for $C_8H_{14}N_2O$, %: C 62.33; H 9.09; N 18.18.

A solution of 4 g of Ib in 20 ml of ethanol containing 0.5 g of sodium ethoxide was left to stand, and the course of the reaction was followed by thin-layer chromatography. After 2 days, the complete isomerization of Ib and the formation of two transformation products was observed. The reaction mixture was neutralized with carbon dioxide. After the elimination of the solvent, the reaction products (IIb and IIIb) were isolated by preparative thin-layer chromatography on alumina of activity grade II.

4-Cyano-3-hydroxy-1, 2, 2, 3-tetramethylpyrrolidine (IIb): mp 36–37° C. Found, %: C 64.07; H 9.63; N 16.55. Calculated for $C_9H_{16}N_2O$, %: C 64.25; H 9.58; N 16.65.

4-Cyano-1, 2, 2, 3-tetramethyl-3-pyrroline (IIIb): bp 86–87° C (7 mm); n_D^{20} 1.4795; d_4^{20} 0.9439. Found, %: C 72.27; H 9.39; N 18.80; MR_D 45.16. Calculated for $C_9H_{14}N_2$, %: 72.00; H 9.30; N 18.66; MR_D 45.08.

When the concentration of sodium alkoxide was increased and the time of the reaction was extended, the yield of IIIb rose.

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