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Abstract

Full Text

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ON SOME CHEMICAL FEATURES OF 2,6-DICHLORO DERIVATIVES OF PYRIDINE

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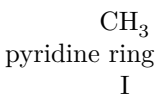
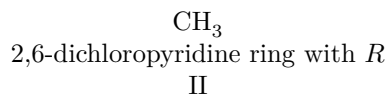
In the course of the synthesis of quinuclidine derivatives, a series of 3,4-disubstituted pyridines (I) and their 2,6-dichloro derivatives (II) were obtained ([1–2]).



pyridine ring with R

I



2,6-dichloropyridine ring with R

II

$R =$ $-C_2H_5$; $-CH{=}CH_2$; $-CH_2CH_2Cl$; $-CH_2CH_2OH$; $-CH_2CH_2OCH_3$; $-C$ $-COOH$; $-COOC_2H_5$; $-COCH_3$.

Comparison of the properties of these compounds made it possible to reveal certain chemical features of the 2,6-dichloro derivatives of pyridine II, associated with the presence of α, α'-halogen atoms. II, in contrast to the corresponding dehalogenated compounds I, do not form salts with mineral acids and do not give picrates.

These data are in agreement with the absence in the literature of reports on hydrochlorides or picrates of any 2,6-dihalo derivatives of pyridine and with the statement of Sell and Dootson ([3]) that 2,6-dichloropyridine does not form a chloroplatinate or a complex salt with mercuric chloride.

It should be noted that elimination of only one α-chloro substituent already leads to a compound forming a hydrochloride. We synthesized 2-chloro-4-methyl-3-(β-chloroethyl)-pyridine ([2]) and obtained its hydrochloride (III) by treating an ethereal solution of the base with alcoholic hydrogen chloride.

2-chloro-4-methyl-3-(β-chloroethyl)pyridine · HCl

III

The hydrochloride is stable in air, but is readily hydrolyzed by water.

Another feature of the 2,6-dichloro derivatives of pyridine is that they do not form quaternary salts upon many hours' boiling in acetone solution with methyl iodide. At the same time, the corresponding dehalogenated compounds I readily form iodomethylates with methyl iodide in acetone at room temperature.

In accordance with these data is the report of Wibaut ([4]), who succeeded in obtaining the iodomethylate of 2,6-dibromopyridine in insignificant yield only when the reaction was carried out in a tube at 100° for 6 hours.

The third feature of 2,6-dichloro derivatives of pyridine II is their inability to form N-oxides, which, in the case of dehalogenated compounds I, are readily obtained by heating with hydrogen peroxide in glacial acetic acid.

Difficulties in the formation of salts, quaternary salts, N-oxides, and nitrogen complex compounds in 2,6-dichloro derivatives of pyridine may be associated both with steric hindrance and with suppression of the basic properties of nitrogen by a decrease in electron density at the nitrogen atom due to the α, α'-halogen atoms, which are electron acceptors. The latter factor is also supported by the absence of reactivity of the methyl group in position 4 in 2,6-dichloro derivatives of pyridine II.

Examples. A. II, unlike I, do not enter into condensation reactions with carbonyl compounds (aldehydes, mesoxalic ester).

B. II are not changed on heating with selenium dioxide under various conditions, whereas the γ-methyl group of I is readily oxidized by selenium dioxide. For example, 3-(β-acetoxyethyl)-4-methylpyridine, when heated with selenium dioxide in boiling toluene for 25 min, forms 3-(β-acetoxyethyl)-isonicotinic acid. M.p. 155–156° (from toluene).

Found %:	C 57.13; 57.29; H 5.61; 5.64; N 6.30
$C_{10}H_{11}O_4N$. Calculated %:	C 57.41; H 5.26; N 6.69

2,6-Dichloro-3-(β-acetoxyethyl)-4-methylpyridine (II, R = $-CH_2CH_2\cdot OOCCH_3$) is recovered quantitatively unchanged when heated with selenium dioxide in boiling toluene for 3 hr, and also without solvent for ½ hr at 160–165° or at 250° for 10 min.

N. A. Preobrazhenskii and A. A. Beer ([5]) indicate that when 4-methylnicotinic acid is heated with an excess of thionyl chloride, along with formation of the acid chloride, replacement of hydrogen atoms in the γ-methyl group by chlorine atoms occurs. Saponification of the resulting acid chloride of 4-trichloromethylnicotinic acid gives cinchomeronic acid.

It was to be expected that, in the corresponding 2,6-dichloro-4-methylnicotinic acid, the hydrogen atoms in the γ-methyl group would be less mobile.

Indeed, when the 2,6-dichloro-4-methylnicotinic acid obtained by us (II, R = −COOH) was heated with an excess of thionyl chloride under the same conditions, only the acid chloride of 2,6-dichloro-4-methylnicotinic acid was obtained; by heating with absolute alcohol it was converted into the ethyl ester of 2,6-dichloro-4-methylnicotinic acid, in a yield of 91% based on the starting acid.

Finally, it should be noted that, according to literature data ([6]), the Rosenmund reaction is applicable only to the acid chlorides of 2,6- (or 2,4-) dichloropyridinecarboxylic acids. The corresponding dehalogenated acids of the pyridine series are not converted into aldehydes by this route.

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Note: Figure translations are in progress. See original paper for figures.