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Abstract

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SYNTHESIS OF 2-SUBSTITUTED DEHYDROQUINOLIZINIUM SALTS

In a number of papers the authors, together with N. K. Kochetkov, reported on the use of β-chlorovinyl ketones as an extremely useful starting material for the synthesis of various five- and six-membered heterocyclic systems. In our latest paper on this topic, the synthesis of 4-alkyl-1-azadehydroquinolizinium salts was reported (^{1}).

In the present work, the synthesis of dehydroquinolizinium salts has also been carried out. In this case, the lithium derivative of α-picoline was used in the reaction with acetals of acylacetaldehydes, readily obtained from β-chlorovinyl ketones by the method developed by us and N. K. Kochetkov (^{2}). The reaction proceeded according to the scheme:

(reaction scheme)

α-picolyllithium + dimethyl acetal of an acylacetaldehyde $\longrightarrow$ [lithium alcoholate II] $\xrightarrow{\text{HBr}}$ 2-hydroxy-2-substitu

$\xrightarrow{(\text{CH}_3\text{CO})_2\text{O}}$ 2-substituted dehydroquinolizinium bromide I

where $R = \text{CH}_3—,\ \text{C}_3\text{H}_7—,\ \text{C}_6\text{H}_5—$.

α-Picolyllithium, reacting in the cold with dimethyl acetals of acylacetaldehydes, gives lithium alcoholates of alcohol II, sparingly soluble in ether, which can be filtered off and washed with ether, thereby freeing them from impurities of the starting α-picoline and acetal, and then decomposed with water. The resulting alcohols II were not isolated in the free state. They were subjected to cyclization by boiling with an excess of concentrated hydrobromic acid, as a result of which salts of 2-hydroxy-2-methyl- and 2-hydroxy-2-phenylquinolizinium $(1H, 2H)$ (III) were obtained. The latter are readily soluble in water and rapidly decolorize a solution of potassium permanganate. The corresponding salt for $R = \text{C}_3\text{H}_7$ could not be isolated in crystalline form; therefore, without preliminary purification, it was used in the next stage. The last stage, dehydration by boiling with acetic anhydride, proceeds extremely readily.

Thus, the method developed by us makes it possible to obtain previously unknown 2-substituted dehydroquinolizinium salts rather simply. The yields of these salts, calculated on the starting acetal of the acylacetaldehyde, range within 20–30%.

The method we propose for the synthesis of dehydroquinolizinium salts substituted in the 2-position is simpler, in terms of the starting materials, than those described in the literature ($^{3-7}$).

The 2-substituted dehydroquinolizinium bromides obtained are colorless crystalline substances, readily soluble in water.

The perchlorate and picrate of 2-phenyldehydroquinolizinium are poorly soluble in water and alcohol and can be obtained by the action of perchloric or picric acid on the corresponding bromide.

The dehydroquinolizinium salts obtained do not decolorize potassium permanganate solution and, consequently, do not contain nonaromatic double bonds. On hydrogenation over platinum black, 2-methyldehydroquinolizinium bromide absorbs five moles of hydrogen, which indicates the presence of five double bonds in the condensed nucleus.

The bromohydrate of 2-methylquinolizidine obtained as a result of hydrogenation was converted into the picrate, whose melting point coincided with the melting point of the picrate of 2-methylquinolizidine isolated by Clemo and Metcalfe (^{8}).

The absorption spectrum of 2-methyldehydroquinolizinium bromide in aqueous solution, recorded in the ultraviolet region, agrees well with the spectrum recorded by Boekelheide and Gall (^{4}) for the dehydroquinolizinium ion.

$\lambda_{\max}$ 325; 317; 310; 306; 298; 294; 286; 283; 272; 261; 244; 233; 277 mμ

ε 0.9; 0.51; 0.6; 0.35; 0.3; 0.2; 0.18; 0.18; 0.17; 0.15; 0.21; [0.7; $1.0 \cdot 10^{-3}$

Experimental Part

2-Methyldehydroquinolizinium bromide. To 13.2 g (0.1 mole) of dimethyl acetal of acetoacetaldehyde in 100 ml of absolute ether, under a stream of nitrogen, there was added dropwise, with cooling by ice and salt and vigorous stirring, an ethereal solution of α-picolyllithium prepared from 9.3 g (0.1 mole) of α-picoline (^{9}). A colorless precipitate separated, which gradually turned orange-red. The precipitate was stirred for 1 hour at room temperature, rapidly filtered off, and thoroughly washed with absolute ether. If a precipitate again separated from the filtrate, it was also filtered off and washed with ether. The collected precipitate was decomposed with water under ether. The ether layer was separated, and the aqueous layer was extracted twice with ether. The ether extracts were dried over potash. To the oily residue obtained after distilling off the ether, 30 ml of concentrated hydrobromic acid was added, and the mixture was heated on a water bath under a reflux condenser for 3 hours. The excess hydrobromic acid was then distilled off in vacuo. The residue was dissolved in 300–150 ml of water and extracted several times with chloroform. The aqueous layer was again evaporated in vacuo. The residue was a viscous brownish mass, which crystallized on standing and on rubbing the wall with a rod. The crystals were filtered off. Yield: 6.5 g (27% of theory) of 2-oxo-2-methylquinolizinium bromide (1H, 2H), m.p. 156–158° (reprecipitation from alcohol with ether).

$$\text{Found, \%: C 49.88; H 4.92; N 5.61; Br 33.40}$$

$$C_{10}H_{12}NOBr,\ \text{calculated, \%: C 49.58; H 4.95; N 5.78; Br 33.05}$$

Colorless crystals, readily soluble in water and alcohol, decolorize potassium permanganate solution.

To a mixture of 1.1 g of 2-oxo-2-methylquinolizinium bromide (1H, 2H) and 30 ml of acetic anhydride, a drop of concentrated sulfuric acid was added. The mixture was boiled for 20 min.; after cooling, 2-methyldehydroquinolizinium bromide ···

lizinium was precipitated with ether. Yield 1 g (98% of theory), m.p. 185–186° (reprecipitation from alcohol with ether).

Found, %: C 53.50; H 4.59; N 6.06; Br 35.57
$C_{10}H_{10}NBr$. Calculated, %: C 53.50; H 4.46; N 6.30; Br 35.66

Colorless crystals, readily soluble in water, do not decolorize potassium permanganate solution.

2-Propyldehydroquinolizinium bromide. Obtained analogously from 12.0 g of the dimethyl acetal of propionaldehyde and 7.0 g of α-picoline. Yield of 2-propyldehydroquinolizinium bromide 5.9 g (31.2% of theory), m.p. 133–135° after reprecipitation from alcohol with ether and drying in vacuo at 100°/5 mm. Very hygroscopic, forms crystalline hydrates.

Found, %: C 57.23; H 5.80; N 5.32; Br 31.59
$C_{12}H_{14}NBr$. Calculated, %: C 57.14; H 5.55; N 5.55; Br 31.74

The intermediate 2-hydroxy-2-propylquinolizinium (1H, 2H) bromide was not isolated in pure form, since it could not be crystallized. Therefore the viscous mass obtained after cyclization was directly subjected to dehydration with acetic anhydride.

2-Phenyldehydroquinolizinium bromide. Obtained analogously from 17.5 g of the dimethyl acetal of benzoylacetaldehyde and 8.4 g of α-picoline. Yield of 2-phenyldehydroquinolizinium bromide 5.9 g (21% of theory); hydrate m.p. 193–194° (reprecipitation from alcohol with ether).

Found, %: C 59.24; H 4.61; N 4.69; Br 26.38
$C_{15}H_{12}NBr \cdot H_2O$. Calculated, %: C 59.21; H 4.60; N 4.60; Br 26.31

Perchlorate m.p. 168–169.5° (from water, drying in vacuo).

Found, %: C 59.00; H 4.04; Cl 11.55
$C_{15}H_{12}NO_4Cl$. Calculated, %: C 58.92; H 3.92; Cl 11.61

Picrate m.p. 168–170° (from methanol).

Found, %: C 58.22; H 3.32; N 12.98
$C_{12}H_{14}N_4O_7$. Calculated, %: C 58.06; H 3.45; N 13.13

The intermediate 2-hydroxy-2-phenylquinolizinium (1H, 2H) bromide: yellow needle-like crystals with m.p. 150–153° (reprecipitation from alcohol with ether). Yield 6.3 g (22.4% of theory).

Found, %: C 59.31; H 4.66; N 4.49; Br 26.50
$C_{15}H_{14}NOBr$. Calculated, %: C 59.21; H 4.60; N 4.60; Br 26.31

Perchlorate m.p. 145–146° (from methanol).

Found, %: C 55.88; H 4.33; N 4.36; Cl 10.81
$C_{15}H_{14}NO_5Cl$. Calculated, %: C 55.64; H 4.32; N 4.32; Cl 10.97

Hydrogenation of 2-methyldehydroquinolizinium bromide. 0.239 g of 2-methyldehydroquinolizinium bromide was hydrogenated in a solution of 50 ml of alcohol over platinum black at room temperature and atmospheric pressure. 5 mol of hydrogen was absorbed. The catalyst was filtered off, and the filtrate was evaporated in vacuo to dryness. The residue after twofold reprecipitation from alcohol with ether has m.p. 221–223°.

Found, %: C 51.34; H 8.64; N 5.93; Br 34.20
$C_{10}H_{20}NBr$. Calculated, %: C 51.28; H 8.54; N 5.98; Br 34.18

Picrate, m.p. 154–156° (from alcohol).
Literature data ([8]): m.p. 158°.

The spectroscopic part of the work was carried out in the optical laboratory of Corresponding Member of the Academy of Sciences of the USSR I. V. Obreimov at the Institute of Organoelement Compounds of the Academy of Sciences of the USSR.

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