SYNTHESIS OF MIXED SECONDARY AMINO ALCOHOLS FROM OXAZOLIDINE DERIVATIVES

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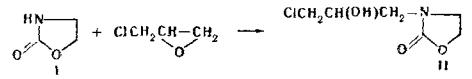
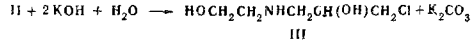
The reaction of oxides (epichlorohydrin, glycidol methyl ether, and ethylene oxide) with oxazolid-2-one and 2-imino-5-methyloxazolidine has been studied. It has been established that the oxides add in position 3 of the oxazolidine ring with the formation of the corresponding 3-(β-hydroxyalkyl) derivatives, the alkaline cleavage of which leads to mixed secondary amino alcohols.

The reaction of 2-imino-5-methyl-1,3-oxazolidine with propylene oxide [1] and the reactions of some alkylene oxides with 2-imino-1,3-oxazolidine [1] and oxazolid-2-one [4] and their derivatives have been described previously. In the present work it has been shown that oxazolid-2-one (I) reacts with epichlorohydrin in an aqueous medium [7] in a ratio of 1 : 1.5 : 1.8 at 98–100° C in 4 hr giving a 98.3% yield of 3-(γ-chloro-β-hydroxypropyl)oxazolid-2-one (II).





Heating the reactants in this ratio at 55° C led to no reaction even over 52 hr, heating at 75° C for 24 hr gave a yield of II of 68–69%, and heating at 98–100° C for 2 hr one of 87–89%. The yield of II when I was heated with epichlorohydrin in a ratio of 1 : 1 to 98–100° C for 2 hr amounted to only 76–78%. It was also found that calcium hydroxide and caustic potash have no appreciable influence on the reaction. Compound II dissolves in water, methanol, and dimethylformamide. It is insoluble in other solvents. This excludes the possibility of its identification by adsorption chromatography. It was isolated in the pure state by high-vacuum distillation; however, under these conditions a considerable part of it resinifies. The composition of compound II was confirmed by a determination of its molecular weight by the method of nonaqueous titration [5], by its molecular refraction, and by its nitrogen content. Its structure was shown by alkaline cleavage [2], which yielded γ-chloro-β-hydroxypropyl(β-hydroxyethyl)amine and carbon dioxide, obtained in the form of barium carbonate. The synthesis of II is considerably simplified if the stage of the isolation of I is eliminated. After the preparation of I by the reaction of calcium cyanamide and ethylene chlorohydrin [6], epichlorohydrin is added to the mixture and it is heated at 100° C for 4 hr, after which the II is isolated. The reaction of I with epichlorohydrin in the absence of a solvent gives not an individual substance but a complex mixture.

To obtain the mixed amino alcohols, the corresponding 3-(β-hydroxyalkyl)-substituted oxazolidines again need not be isolated in the pure state. After their synthesis, they are decomposed in the reaction mixture and the corresponding amino alcohols are isolated from it. In this way we have also obtained β-hydroxy-γ-methoxypropyl(β-hydroxyethyl)amine (IV) by the reaction of the methyl ether of glycidol and I. β-Hydroxyethyl(β-hydroxypropyl)amine (V) [3] was obtained by the reaction of ethylene oxide with 2-imino-5-methoxy-1,3-oxazolidine in an autoclave with subsequent cleavage of the reaction product to give V.

The mixed amino alcohols were obtained in the pure state by three or four fractional distillations.

EXPERIMENTAL

3-(γ-Chloro-β-hydroxypropyl)oxazolid-2-one (II). a) A mixture of 87 g (1 mole) of I, 116 ml (1.48 mole) of epichlorohydrin, and 210 ml of water was heated at 100° C for 4 hr and then the water was distilled of in vacuum. The yield of II was 176 g (98.3%). Bp 100–101° C (0.01 mm); d_4^{20} 1.2790; n_D^{20} 1.4770. Found, %: N 7.84; g-eq 177.20, 181.37; MR_D 39.67. Calculated, %: N 7.80; g-eq 179.60; MR_D 39.70.

b) With vigorous stirring at 40–45°C, 35 ml (0.5 mole) of ethylene chlorohydrin was added over 1 hr to a mixture of 80 g (0.5 mole) of technical 50% calcium cyanamide and 230 ml of water. The mixture was stirred for 3 hr, after which 59 ml (0.75 mole) of epichlorohydrin was carefully added and heating was carried out at 98–100°C for 4 hr. After the reaction mixture had cooled, the II was extracted with methanol. The methanolic solution was neutralized with carbon dioxide and filtered, and the methanol and water were distilled off from the filtrate. The yield of II was 65 g (70%). Bp 100–101° C (0.1 mm); d_4^{20} 1.2790; n_D^{20} 1.4770. Found, %: N 7.76; MR_D 39.67.

γ-Chloro-β-hydroxypropyl-(β-hydroxyethyl)amine (III). A mixture of 179.6 g (1 mole) of II and 420 g (3 mole) of a 40% solution of potassium hydroxide was heated to the boil for 3 hr, was neutralized with carbon dioxide, and the water was distilled off; the residue was dissolved in methanol, the potassium carbonate being filtered off. The filtrate was neutralized with concentrated H_2SO_4, the potassium sulfate was filtered off, and the methanol and water were distilled off from the filtrate (finally under vacuum). The yield of III was 144 g (94%). The distilled product consisted of a colorless sirupy liquid. Bp 158° C (6 mm); d_4^{20} 1.2178; n_D^{20} 1.4835. Found, %: N 9.09; MR_D 36.81. Calculated for $C_5H_{12}NO_2Cl$, %: N 9.12; MR_D 36.81. On the hydrolysis of 0.882 and 0.934 g of II, found: $BaCO_3$ 0.931 and 0.984 g; calculated: 0.969 and 1.007 g.

β-Hydroxyethyl(β-hydroxy-γ-methoxypropyl)amine (IV). With continuous stirring, 40 ml (0.6 mole) of epichlorohydrin was added at 35–40° C over 1.5 hr to a mixture of 80 g (0.5 mole) of technical calcium cyanamide and 230 ml of water. The mixture was left to stand for 18 hr, after which 46 ml (0.6 mole) of the methyl ether of glycidol was added and it was heated at 98–100° C with continuous stirring for 3 hr. Then 168 g of a 50% aqueous solution of potassium hydroxide (1.5 mole) was added and it was heated at 110–115°C with stirring for 3 hr. After the reaction mixture had been cooled, the IV was extracted with methanol. The aqueous methanolic solution was neutralized with carbon dioxide and the potassium carbonate was filtered off. The methanol and water were distilled off from the filtrate, the resulting mixture was dissolved in methanol, the potassium carbonate was

filtered off, the solution was neutralized with concentrated H_2SO_4, and the potassium sulfate was filtered off. The methanol and water were distilled off from the filtrate (finally under vacuum), giving **IV**. Yield 55 g (73.82%). Mp 126.5–127° C (4 mm); d_4^{20} 1.1100; n_D^{20} 1.4752. Found, %: N 9.37; MR_D 37.85. Calculated, %: N 9.39; MR_D 38.20.

β-Hydroxyethyl(β-hydroxypropyl)amine (V). A 0.5-liter autoclave with a stirrer was charged with 102 g (1 mole) of 2-imino-5-methyl-1,3-oxazolidine and 56 ml (1.14 mole) of ethylene oxide. With constant stirring, the mixture was heated at 55–60° C for 4.5 hr. The resulting sirupy liquid was dissolved in a mixture (1:1) of acetone and chloroform to eliminate the unchanged 2-imino-5-methoxyl-1,3-oxazolidine. The solvent was distilled off from the filtrate and the product was subjected to alkaline decomposition as described above. The yield of **V** was 102 g (85.71%). Bp 124–236° C (749 mm); d_4^{20} 1.0382; n_D^{20} 1.4596. Found, %: N 11.85; MR_D 31.41. Calculated, %: N 11.75; MR_D 31.94.

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