THE PROPERTIES AND SOME REACTIONS OF 4-OXO-1, 5-DIAZABICYCLO[4, 4, 0]DECANE AND 5-OXO-1, 4-DIAZABICYCLO[4, 4, 0]DECANE

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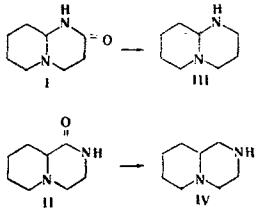
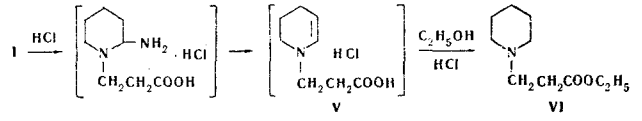
The chemical properties of 1,4- and 1,5-diazabicyclo[4,4,0]decanes and their 5- and 4-oxo derivatives, respectively, have been studied.

The present paper is devoted to a comparative study of the properties of the isomeric bicyclic lactams 4-oxo-1, 5-diazabicyclo[4, 4, 0]decane (I) and 5-oxo-1, 4-diazabicyclo[4, 4, 0]decane (II) and also the products of their reduction by lithium aluminum hydride—1, 5- and 1, 4-diazabicyclo[4, 4, 0]decanes (III and IV).

Lactam I was obtained by the Beckmann rearrangement of the oxime of 7-oxo-1-azabicyclo[4, 3, 0]nonane [1], and lactam II by the reaction of 2-ethoxycarbonylpiperidine and ethyleneimine [2]. 1, 5- and 1, 4-diazabicyclo[4, 4, 0]decanes (III and IV) were synthesized by the reduction of the lactams I and II with lithium aluminum hydride.



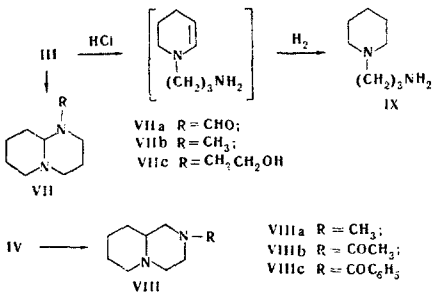
Compound I readily hydrolyzes on being heated with hydrochloric acid to 100° C, giving the unsaturated acid V and ammonium chloride, which apparently arise as a result of the cleavage of the initial hydrolysis product—2-amino-1-(β-carboxyethyl)piperidine.



Attempts to recrystallize the technical acid V and also to esterify it led to resinification. Consequently, the mixture of substances obtained in the hydrolysis of the lactam I was subjected, without purification, to catalytic hydrogenation and subsequent esterification. The 1-(β-ethoxycarbonylethyl)piperidine (VI) formed proved to be identical in its physical constants and IR spectrum with the compound obtained by the alkylation of piperidine with ethyl β-chloropropionate.

The lactam II could not be saponified on being heated with hydrochloric acid to 180° C.

Acylation of compound I with acetic anhydride, and also methylation with a mixture of formaldehyde and formic acid at 100° C led to resinous substances. Consequently, to synthesize 5-methyl-1, 5-diazabicyclo [4, 4, 0]decane (VIIb), compound III was converted into the 5-formyl derivative (VIIa), which was then reduced to (VIIb). The reaction of compound III with ethylene oxide enabled 5-(β-hydroxyethyl)-1, 5-diazabicyclo[4, 4, 0]decane (VIIc) to be obtained



The resinification processes observed in the acylation and alkylation of compound III in an acid medium are possibly connected with an increase in the partial positive charge on the C_6 atom through the protonation of the N_1 atom and the appearance of an electron-accepting substituent on the N_5—C_6 bond and the appearance of Δ^2-tetrahydropyridines, which readily undergo change.

Conversely, the alkylation and acylation of compound IV under similar conditions took place, as was to be expected, with good yields giving its 4-substituted derivatives (VIIIa–VIIIc).

The hydrolytic cleavage of compound III was achieved only by heating it with hydrochloric acid at 150° C. The high temperature required in this case for the cleavage of the N_5—C_6 bond is apparently due to the absence of an electron-accepting substituent promoting this process on the N_5 atom in the bicyclic compound III. The 1-(γ-aminopropyl)-Δ^2-tetrahydropyridine dihydrochloride formed in the hydrolysis was reduced to 1-(γ-aminopropyl)piperidine (IX), the structure of which was confirmed by analysis and its IR spectrum.

EXPERIMENTAL

Hydrolysis of 4-oxo-1, 5-diazabicyclo[4, 4, 0]decane (I). A solution of 3 g (0.0195 mole) of the lactam I [1] in 35 ml of conc HCl was boiled for 9 hr and was then evaporated to dryness in vacuum. The technical product was dissolved in 50 ml of 1 N HCl, 0.2 g of platinum oxide was added, and the mixture was shaken in a current of hydrogen. Hydrogenation ceased after the absorption of one mole of hydrogen. The platinum black was filtered off, the hydrochloric acid solution was evaporated in vacuum, and the residue was dried and was then esterified by being heated with alcoholic hydrogen chloride. This gave 1.2 g (33%) of 1-(β-ethoxycarbonylethyl)piperidine (VI). Bp 105–106° C (11 mm). Found, %: C 64.53; H 10.33; N 7.41. Calculated for $C_{10}H_{19}NO_2$, %: C 64.83; H 10.29; N 7.57. The substance proved to be identical with the ester obtained previously [3].

1, 5-Diazabicyclo[4, 4, 0]decane (III). With stirring, a solution of 8 g (0.0515 mole) of the lactam I in 240 ml of anhydrous benzene was added gradually to a suspension of 8 g (0.21 mole) of lithium aluminum hydride in 240 ml of anhydrous ether. The reaction mixture

was boiled for 12 hr, cooled, and treated with 18 ml of water. The lithium and aluminum hydroxides were filtered off and carefully washed with benzene. This yielded 5.25 g (72.3%) of compound III in the form of a colorless very volatile liquid with an ammoniacal odor. Bp 83–84° C (10 mm). IR spectrum: 3290 cm^{-1} (NH). Found, %: C 67.96; H 11.36; N 19.80. Calculated for $C_8H_{16}N_2$, %: C 68.52; H 11.50; N 19.97.

5-Formyl-1,5-diazabicyclo[4,4,0]decane (VIIa). A mixture of 2.26 g (0.023 mole) of acetic anhydride and 0.9 g (0.02 mole) of formic acid was heated at 60° C for 2 hr. Then, with cooling, a solution of 2 g (0.0144 mole) of III in 10 ml of ether was added. The mixture was left at room temperature for 20 hr, and then 20 ml of chloroform was added to give a homogeneous mass and it was left for a further 24 hr. Then it was evaporated in vacuum and the residue was made alkaline with 50% potassium carbonate solution and extracted with benzene. Yield 0.7 g (29%). Bp 100–101° C (0.5 mm). Found, %: C 64.22; H 9.51; N 16.39. Calculated for $C_9H_{16}N_2O$, %: C 64.25; H 9.58; N 16.65.

5-Methyl-1,5-diazabicyclo[4,4,0]decane (VIIb). With stirring, a solution of 0.8 g (4.8 mM) of compound VIIa in 30 ml of anhydrous benzene was added to a suspension of 1 g (26 mM) of lithium aluminum hydride in 30 ml of anhydrous ether. The mixture was boiled for 20 hr and was treated as described above. Yield 0.4 g (55%), bp 118–120° C (50 mm). Found, %: C 69.77; H 11.46; N 17.96. Calculated for $C_9H_{18}N_2$, %: C 70.07; H 11.76; N 18.16.

5-(β-Hydroxyethyl)-1,5-diazabicyclo[4,4,0]decane (VIIc). With cooling, a solution of 0.4 g (0.1 mole) of ethylene oxide in 10 ml of methanol was added to a solution of 6.5 g (0.046 mole) of III in 30 ml of methanol. The reaction mixture was kept with ice cooling for 2 hr and then at room temperature for 72 hr. The ethanol was driven off in vacuum and the substance was distilled to give 3.5 g (41%) of VIIc in the form of a viscous liquid with bp 121–122° C (1 mm). Found, %: C 64.88; H 11.02; N 15.25. Calculated for $C_{10}H_{22}N_2O$, %: C 65.18; H 10.94; N 15.20.

Hydrolysis of 1,5-diazabicyclo[4,4,0]decane (III). A solution of 2 g (0.0144 mole) of III in 20 ml of 17% HCl was heated in a sealed tube at 150° C for 10 hr and was then evaporated in vacuum. The residue was dissolved in 20 ml of 1 N HCl, 0.2 g of platinum oxide was added, and the mixture was shaken in a current of hydrogen. Hydrogenation ceased after the absorption of 1 mole of hydrogen. The platinum black was filtered off, the hydrochloric acid solution was evaporated in vacuum, and the residue was made alkaline with 50% potassium carbonate solution and extracted with chloroform. After the extracts had been dried, the solvent was distilled off and the residue was fractionated in vacuum. Two fractions were collected: fraction I (0.4 g, bp 95° C (20 mm)—a mobile colorless liquid with an ammoniacal smell—1-(γ-aminopropyl)piperidine (IX). Found, %: C 67.24; H 12.79; N 19.51. Calculated for $C_8H_{18}N_2$, %: C 67.55; H 12.75; N 19.69.

Dihydrochloride—white crystals, mp 196–197° C (from a mixture of ethanol and acetone). Found, %: Cl 30.42; N 12.15. Calculated for $C_8H_{18}N_2 \cdot 2HCl \cdot H_2O$, %: Cl 30.41; N 12.01. IR spectrum: 3300 and 3370 cm^{-1} (ν NH_2), 1600 cm^{-1} (δ NH_2).

2nd fraction (0.4 g), bp 156–158° C (0.3 mm), apparently consisting of a dimer of the amine IX. Found, %: C 67.41; H 12.40; N 19.40. Calculated for $(C_8H_{18}N_2)_2$, %: C 67.55; H 12.75; N 19.69. IR spectrum: 3300 and 3370 cm^{-1} (ν NH_2), 1600 cm^{-1} (δ NH_2).

4-Methyl-1,4-diazabicyclo[4,4,0]decane (VIIIa). With cooling, 0.7 g (8.6 mM) of 37% formalin and 1 g (21 mM) of formic acid were added to a mixture of 1 g (7 mM) of compound IV [2] and 0.7 ml of water. The reaction mixture was heated at 100° C for 15 hr and was then concentrated in vacuum, made alkaline with potassium carbonate, and extracted with benzene. Yield 0.7 g (63.7%), bp 120–122° C (65 mm). Found, %: C 70.03; H 11.60; N 17.82. Calculated for $C_9H_{18}N_2$, %: C 70.07; H 11.76; N 18.16.

4-Acetyl-1,4-diazabicyclo[4,4,0]decane (VIIIb). With ice water cooling, 1 g (7.2 mM) of IV was mixed with 3 g of acetic anhydride, and the mixture was left at room temperature for 4 hr. The excess of acetic anhydride was decomposed with water, with cooling, and the mixture was made alkaline with 50% potassium carbonate solution and extracted with benzene. Yield 1.1 g (84.7%), bp 110° C (0.8 mm). Found, %: C 65.49; H 10.10; N 15.21. Calculated for $C_{10}H_{18}N_2O$, %: C 65.89; H 9.96; N 15.37.

4-Benzoyl-1,4-diazabicyclo[4,4,0]decane (VIIIc). At 0 to 2° C, 1.13 g (0.0107 mole) of sodium carbonate and 1.5 g (0.0107 mole) of benzoyl chloride were added to a solution of 1.5 g (0.0107 mole) of IV in 3 ml of water. The mixture was kept at 0° C for 1 hr and was then diluted with 4 ml of water and the oil that separated out was extracted with benzene. Yield 1.6 g (61.5%), bp 153–154° C (0.35 mm). Found, %: C 73.70; H 8.19; N 11.33. Calculated for $C_{15}H_{20}N_2O$, %: C 73.73; H 8.25; N 11.46.

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