SYNTHESIS OF CYCLIC γ-DIMAINES

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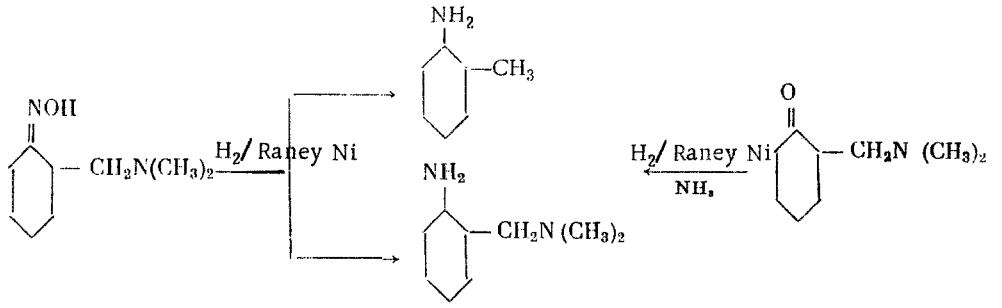
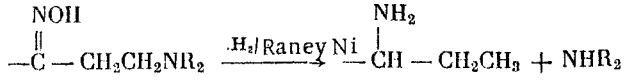
In the development of methods of synthesizing dienes having a fixed transoid system of bonds, such as 3-methyl--enecyclohexene, we were faced with the necessity of preparing cyclic γ-diamines, which were not readily accessible. It appeared that it would be possible to prepare cyclic diamines either by the reduction of oximes of β-amino ketones or by reductive amination of the β-amino ketones themselves, which are fairly readily prepared by the Mannich method [1, 2]:



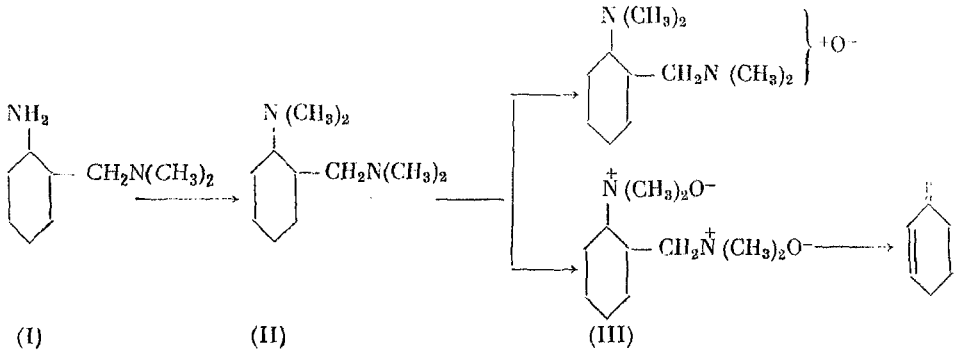
Several cases of the catalytic hydrogenation of oximes of β-amino ketones have been described [3-5], but the reaction is accompanied by hydrogenolysis of the molecule with elimination of an amine:



and no γ-diamines have been prepared in this way. The reduction of oximes of β-amino ketones with sodium amalgam [6] or sodium and alcohol [4] gives γ-diamines in very low yield (less than 30%). All these considerations apply also to the preparation of γ-diamines by the reductive amination of β-amino ketones: either γ-diamines are not obtained at all, or they are obtained in very low yields [7]. Hence, no convenient methods for the synthesis of γ-diamines have been described.

It was shown that the hydrogenation of oximes must be carried out in a small amount of methanol saturated with ammonia in presence of a large amount of Raney nickel at temperatures not above 40°. Hydrogenation of the oxime of 2-(dimethylaminomethyl)cyclohexanone [8] under these conditions gives 2-(dimethylaminomethyl)cyclohexylamine in about 70% yield, and the oxime of 2-(dimethylaminomethyl)cyclopentanone gives the corresponding diamine in 50% yield. The diamines obtained were methylated with formaldehyde and formic acid to give bis-dimethylamino compounds [8].

The bisdimethylamino compound (II) was oxidized with 30% hydrogen peroxide, and a mono- or di-oxide (III) was formed according to the amount of hydrogen peroxide added:



(I) (II) (III)

The dioxides were isolated in the form of their picrates. When the dioxide (III) was heated to 100-120° under reduced pressure (20 mm), it was converted into 3-methylenecyclohexene in a yield of about 50%. We studied also the reductive amination of 2-(dimethylaminomethyl)cyclohexanone. It was found that in aqueous ammonia the yield of 2-(dimethylamino)cyclohexylamine (I) was about 65%.

EXPERIMENTAL

Oxime of 2-(Dimethylaminomethyl)cyclopentanone. A mixture of 170 g of cyclopentanone, 82 g of dimethylamine hydrochloride, and 100 ml of 35% formaldehyde solution was boiled for ten minutes and then cooled with ice water. After treatment with water as in the case of the reaction with cyclohexanone [8], we obtained 75 g of unchanged ketone, m.p. 125-130°, and 130 g of the oxime of 2-(dimethylaminomethyl)cyclopentanone. After recrystallization from methanol the substance had m.p. 177-178°. The literature [9] gives m.p. 184°.

Hydrogenation of the Oxime of 2-(Dimethylaminomethyl)cyclopentanone. The oxime of 2-(dimethylaminomethyl)cyclopentanone (31.2 g) was hydrogenated in 30 ml of methanol saturated with ammonia in presence of 8 g of Raney nickel. The reaction was carried out at 40°, and the initial hydrogen pressure was 120 atm. The product, amounting to 13 g (46.5%) was 2-(dimethylaminomethyl)cyclopentylamine, b.p. 92-94° (15 mm); $n^{20}D$ 1.4830.

Methylation of 2-(Dimethylaminomethyl)cyclopentylamine. A mixture of 8 g of the amine, 15 ml of 35% formaldehyde solution, and 30 ml of 85% formic acid was heated at 100° for 16 hours [8]. The product, amounting to 8 g, was 2-(dimethylaminomethyl)-N,N-dimethylcyclopentylamine, b.p. 106-108° (15 mm); $n^{20}D$ 1.4895.

Hydrogenation of the Oxime of 2-(Dimethylaminomethyl)cyclohexanone. 1) Hydrogenation of 50 g of the oxime [3] (m.p. 111-112°) was carried out as a solution in 50 ml of methanol saturated with ammonia in presence of 20 g of Raney nickel; an autoclave was used. The reaction temperature was 45°, the initial hydrogen pressure was 130 atm, and the reaction was continued for four hours. The product, amounting to 30 g, was the substance (I), b.p. 112-113° (30 mm) and $n^{20}D$ 1.4780; its dipicrate had m.p. 216-217° (with decomposition).

2) The oxime (170 g; m.p. 111-112°) was hydrogenated in 500 ml of methanol saturated with ammonia in presence of 15 g of Raney nickel at an initial hydrogen pressure of 100 atm and a reaction temperature of 70-80°. The products were 67 g of 2-methylcyclohexylamine, b.p. 56-61° (15 mm), and 37 g of (I), b.p. 101-103° (15 mm).

Reductive Amination of 2-(Dimethylaminomethyl)cyclohexanone Hydrochloride. 1) Hydrogenation of 20 g of the hydrochloride of the Mannich base (prepared according to [1]) in 100 ml of saturated alcoholic ammonia in presence of 10 g of Raney nickel at 60° and an initial hydrogen pressure of 100 atm gave 3 g (16.7%) of (I), b.p. 104-106° (20 mm) and $n^{20}D$ 1.4780.

2) Hydrogenation of 20 g of the hydrochloride of the Mannich base in 60 ml of saturated aqueous ammonia in presence of 20 g of Raney nickel at 40° and an initial hydrogen pressure of 100 atm gave 10 g (65%) of (I), b.p. 103-105° (20 mm), and $n^{20}D$ 1.4775.

Oxidation of 2-(Dimethylaminomethyl)-N,N-dimethylcyclohexylamine with Hydrogen Peroxide. a) With stirring and cooling 7.5 g of 30% hydrogen peroxide was added to 5 g of the substance (II) (which was prepared previously [8]) in 10 ml of methanol; the hydrogen peroxide partially decomposed with evolution of oxygen, and after 30 minutes a further 15 g of 30% hydrogen peroxide was added. After 24 hours the excess of hydrogen

peroxide was decomposed by stirring the mixture with a little platinum black. After being recrystallized from ethanol, the dipicrate of the monoxide of (II) had m.p. 83-85° (with decomposition).

b) To 5 g of the same diamine in 10 ml of methanol we added 7.5 ml of 30% hydrogen peroxide. The addition was repeated six times more at intervals of 30 seconds with stirring and cooling with ice water. After one day the excess of hydrogen peroxide was removed by shaking the mixture with platinum black. The dipicrate of (III) was crystallized from ethanol; it melted at 112-115° (with decomposition).

Pyrolysis of the Diamine Dioxide (III). The above experiment (b) was repeated, and a solution of the combined reaction products from the two experiments was evaporated down at a residual pressure of 10 mm and a temperature of less than 45°. The residue was decomposed by heating it to 100° at a residual pressure of 20 mm, and the reaction products were condensed in a trap cooled with a mixture of solid carbon dioxide and acetone. The usual treatment gave 1.5 g of 3-methylenecyclohexene, b.p. 108-112°; $n^{20}D$ 1.4920; λ_{max} 231 mμ; ε 8250 (heptane).

SUMMARY

1. A method was developed for the preparation of γ-diamines by the reductive amination of Mannich bases and also by the reduction of their oximes.

2. It was shown that the dioxide (III) is readily converted into 3-methylenecyclohexene.

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