CATALYTIC REDUCTIVE CYCLIZATION OF POTASSIUM SALT OF ETHYL ESTER OF o-NITROPHENYLPYRUVIC ACID

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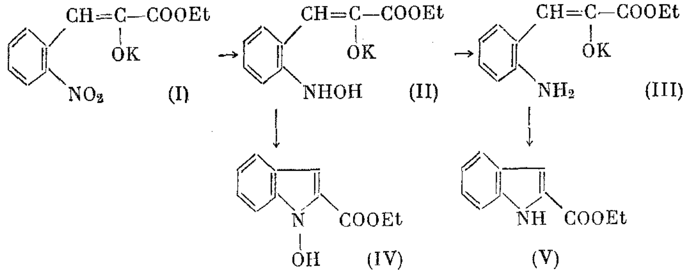
In the hydrogenation of the K salt of the ethyl ester of o-nitrophenylpyruvic acid (I) in the presence of Pt (from PtO_2) in order to obtain 2-carbethoxyindole (V) [1] it was found that, together with the latter, substantial amounts of a low-melting product with a constant melting point are formed, which is composed of (V) and 2-carbethoxy-1-hydroxyindole (IV), as is evidenced by the following data. 1) Compound (V) was extracted with ether from an alkaline solution of this product: 1-hydroxyindole-2-carboxylic acid (IV acid) [2, 3] was isolated after acidification of the alkaline solution. 2) A band at 1820 cm^{-1} was detected in the IR spectrum of the acylation product, which band is characteristic for the $O-COCH_3$ group [4]. 3) Two intense fragments with m/e 189 and 205 [molecular ions, corresponding to (V) and (IV)], were detected in the mass spectrum of this product. 4) The investigated product is hydrogenated in the presence of nickel boride catalyst, with the absorption of 0.6 mole of H_2, to give (V). We will mention that the hydrogenation of this product does not go in the presence of Pt. 5) The GLC analysis of this product gives the peak of (V), the amount of which is 40%.



The formation of the product with a constant melting point is apparently associated with the comparatively strong reaction of the weakly acid (IV) with the weakly basic (V). However, these compounds behave as monomers in solution; the mol. wt. is 200 (cryoscopically in benzene) and 213 (ebullioscopically in the same solution).

A study of other catalysts disclosed that Pd/C, the same as Pt, gives a mixture of 2-carbethoxyindole and 2-carbethoxy-1-hydroxyindole, which are capable of forming an associate with the same melting point, when the hydrogenation of (I) is run in either alcohol or CH_3COOH. Nickel catalysts (both Raney and the boride) give the pure (V), while Ru-black leads to the formation of (IV) (acid). The formation of the acid instead of the ester (IV) in this case is explained by the easy saponification of the latter during the reduction process in alkaline medium [2].

The formation of 1-hydroxyindole derivatives during the hydrogenation of (I) testifies to the fact that the cyclization can occur not only at the stage of forming the amine (III), but also at the stage of forming the hydroxylamine (II). Cases are known for the formation of (IV) (the acid) during the hydrogenation of the oximes, semicarbazone and phenylhydrazone of o-nitrophenylpyruvic acid in the presence of Pt (PtO_2) [5]. However, the ethyl ester of o-nitrophenylpyruvic acid gave (V) exclusively under the conditions given in [5]. According to [6], $NaBH_4$ in the presence of Pd/C reduces o-nitrophenylpyruvic acid and its methyl ester to (IV) (the acid).

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As a result, cyclization to the indole system during the catalytic reduction of the corresponding aromatic nitro compounds also makes it possible to record the stage of forming the hydroxylamine.

EXPERIMENTAL METHOD

The K salt of the ethyl ester of o-nitrophenylpyruvic acid (I) was obtained as described in [1]. The catalysts were: Adams Pt (from PtO_2), 5% Pd/C, Raney nickel, nickel boride [7] and Ru-black, which was obtained by the reduction of ruthenium oxychloride with $NaBH_4$ [8].

The GLC analysis was run on an LKhM-5 chromatograph using a 1 m × 3 mm column filled with 0.5% of poly(ethylene glycol adipate) deposited on NaCl, a temperature of 152°, a helium flow rate of 32 ml/min, a katharometer as the detector, and 1,9-nonanediol as the internal standard.

Hydrogenation in the Presence of Platinum. A solution of 45 g of (I) in 300 ml of glacial acetic acid was hydrogenated in an autoclave in the presence of 0.3 g of PtO_2 at 20° and an initial H_2 pressure of 50 atm. The catalyzate was poured into water; the obtained precipitate was recrystallized from hexane. We obtained 3 g of (V), mp 122°. The IR and UV spectra coincide with the data given in [1]. From the filtrate after evaporation we isolated 9 g of product with mp 57-59°, which could not be separated by fractional crystallization using heptane, CH_2Cl_2, petroleum, or benzene. The acetate was obtained when the product was heated with acetic anhydride, which had an absorption band at 1820 cm^{-1} in the IR spectrum. Treatment of the product with mp 57-59° with caustic solution, followed by extraction with ether gave (V) with mp 122°. After the extraction of (V), the solution was acidified and extracted with ether to give 1-hydroxyindole-2-carboxylic acid with mp 159° (decompn.). The color reactions and the IR spectrum coincide with the literature data [2, 3]. The hydrogenation of (I) at atmospheric pressure leads to the same products.

Hydrogenation in the Presence of Pd/C. A solution of 0.3 g of (I) in 10 ml of alcohol was hydrogenated in the presence of 0.2 g of 5% Pd/C at 20° and atmospheric pressure until the H_2 absorption ceased. The catalyzate was filtered, evaporated in vacuo, and the residue was treated with water. The obtained precipitate, which melted at 90-107°, was recrystallized from hexane. We obtained a small amount of (V), mp 122°. A product with mp 58-60° was isolated from the filtrate.

Hydrogenation in the Presence of Nickel Catalysts. A solution of 0.5 g of (I) in 10 ml of alcohol was hydrogenated in the presence of 0.3 g of either Raney Ni or nickel boride catalyst at 20° and atmospheric pressure until the H_2 absorption ceased. The catalyzate was filtered and the filtrate was evaporated in vacuo to dryness. We obtained (V) with mp 122°.

Hydrogenation in the Presence of Ruthenium. A solution of 0.3 g of (I) in 10 ml of alcohol was hydrogenated in the presence of 15 mg of Ru catalyst. Here 2 moles of H_2 was absorbed. The catalyzate was filtered, evaporated in vacuo to dryness, and the residue was dissolved in water, acidified with HCl solution, and extracted with ether to give (IV) (the acid).

CONCLUSIONS

In the presence of nickel catalysts, the reductive cyclization of the K salt of the ethyl ester of o-nitrophenylpyruvic acid gives 2-carbethoxyindole, while 1-hydroxyindole-2-carboxylic acid is obtained in the presence of ruthenium, and a mixture of 2-carbethoxyindole and 1-hydroxy-2-carbethoxyindole in the presence of either platinum or palladium.

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