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Abstract

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CHEMISTRY

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CONVERSION OF ESTERS OF γ-KETOCARBOXYLIC ACIDS INTO LACTAMS

The simple method we have found for the catalytic synthesis of esters of γ-ketocarboxylic acids ([1]) opens up new possibilities for further interesting syntheses based on the high reactivity of the carbonyl and carboalkoxy groups.

The present work is devoted to the conversion of esters of γ-ketocarboxylic acids into the corresponding lactams under conditions of reductive amination. The indicated catalytic synthesis of lactams, which are formed in 60–70% yield, amounts to converting esters of γ-ketocarboxylic acids in an autoclave in the presence of skeletal Ni–Al catalyst at a temperature of 100–110°. To explain the course of the synthesis described, we propose the following scheme:

$$CH_3{-}CH_2{-}CH_2{-}C(=O){-}CH_2{-}CH(R){-}COOR' \xrightarrow[-R'OH]{NH_3,\ Ni{-}Al} [CH_3{-}CH_2{-}CH_2{-}C(=O){-}CH_2{-}CH(R){-}C($$

$$\xrightarrow[H_2]{-H_2O} CH_3{-}CH_2{-}CH_2{-} \text{-lactam ring}$$

$$(I) \qquad (II) \qquad (III)$$

$$R = H,\ CH_3$$

$$R' = CH_3,\ C_2H_5$$

The validity of the proposed reaction mechanism was also proved by additional experiments:

$$CH_3COOC_6H_{11} \xrightarrow[100^\circ]{H_2,\ Ni{-}Al} \text{did not change}$$

$$CH_3COOC_6H_{11} \xrightarrow[100^\circ]{H_2,\ NH_3,\ Ni-Al} C_6H_{11}OH + CH_3CONH_2$$

$$CH_3COOC_6H_{11} \xrightarrow[100^\circ]{NH_3,\ Ni-Al} C_6H_{11}OH + CH_3CONH_2$$

This scheme is also confirmed by the fact that ethyl alcohol was isolated from the catalyst during conversion of the ethyl ester of γ-ketoenanthic acid.

The totality of the data obtained leads to the conclusion that from the ester of the γ-keto acid (I) the corresponding amide (II) is first formed, which, as a result of dehydration, hydrogenation, and cyclization reactions, is converted into the corresponding γ-lactam (III). The transition from esters of β-furylacrylic acids to γ-lactams can be carried out in one stage, bypassing the isolation of the esters of γ-keto acids. In this case, the conversion of esters of β-furylacrylic acids is carried out on a platinum catalyst with simultaneous introduction of hydrogen and ammonia into the reactor. As a result of a consecutively proceeding series of reactions, a γ-lactam is formed in a yield of about 30%:

$$\text{furyl}-CH{=}CH-COOR \xrightarrow[300^\circ]{H_2,\ NH_3,\ Pt-C} CH_3-CH_2-CH_2-C(=O)-CH_2-CH_2-COOR \longrightarrow$$

$$\longrightarrow CH_3-CH_2-CH_2- \text{-lactam ring}$$

Experimental Section

Synthesis of starting materials. Ethyl ester of γ-ketoenanthic acid and methyl ester of α-methyl-γ-ketoenanthic acid were obtained according to the following scheme (1):

$$\text{furfural} + RCH_2COOR' \longrightarrow \text{furylidene ester} \xrightarrow[130^\circ]{H_2,\ Cu-Al} \text{furylalkyl ester} \xrightarrow[250^\circ]{H_2,\ Pt-C} CH_3-CH_2-CH_2-C(=O)-C$$

$$R = H,\ CH_3; \quad R' = CH_3,\ C_2H_5 \qquad (1)$$

The yield of the esters of γ-ketoenanthic acids was 90-92%. Ethyl ester of γ-ketoenanthic acid: b.p. 93° (10 mm), n_D^{20} 1.4310. Methyl ester of α-methyl-γ-ketoenanthic acid: b.p. 95-96° (11 mm), n_D^{20} 1.4320.

Catalysts. Platinized charcoal was prepared by impregnating activated birch charcoal with the calculated amount of a solution of chloroplatinic acid, followed by reduction with formalin in alkaline medium (KOH) while cooling with ice water. The excess potassium hydroxide was neutralized with dilute hydrochloric

acid (Congo paper test), after which the material was washed with water until a negative reaction for Cl′. The catalyst obtained contained 10% finely dispersed platinum. Skeletal Ni–Al catalyst was prepared by leaching aluminum from a Ni–Al alloy with a 25% NaOH solution. For leaching 100 g of alloy, 115 g of caustic soda was used. The catalyst was washed with water until neutral to phenolphthalein.

Preparation of γ-lactams. Into an autoclave were charged 40 g of the keto-acid ester, 100 ml of methyl alcohol saturated with ammonia at 0°, 10 g of skeletal Ni–Al catalyst, and, at an initial hydrogen pressure of 50 atm, the mixture was heated for 6 h at 100–110°. After distilling off the solvent–methyl alcohol–and the low-boiling fractions, the catalyzate was distilled under vacuum. In the catalysis of the ethyl ester of γ-ketoenanthic acid, ethyl alcohol was isolated among the other reaction products.

5-Propylbutyrolactam, b.p. 148–150° (13 mm), m.p. 53–54°, n_D^{58} 1.4625. Yield 68%.

Found, %: C 65.95, 65.89; H 10.22, 10.30; N 10.53, 10.62
Calculated, %: C 66.10; H 10.30; N 11.01

In the IR spectrum of 5-propylbutyrolactam, bands are observed at frequencies of 3120 cm^{-1} and 3214 cm^{-1}, characteristic of vibrations of the NH group in the lactam ring, and a band at 1707 cm^{-1}, characteristic of C=O vibrations in a lactam.

3-Methyl-5-propylbutyrolactam, b.p. 143–145° (10 mm), m.p. 48–49°, n_D^{58} 1.4640. The yield is 68%.

Found, %: C 67.98, 68.06; H 10.44, 10.38; N 9.99, 10.32
Calculated, %: C 68.04; H 10.70; N 9.92

In the IR spectrum, bands are observed at frequencies of 3100 cm^{-1} and 3216 cm^{-1}, characteristic of vibrations of the NH group in the lactam ring.

Conversion of hexyl acetate under the action of hydrogen and ammonia.

The conversion of hexyl acetate in an autoclave over skeletal Ni–Al catalyst at 100–110° was investigated under the action of: 1) hydrogen (initial pressure 50 atm.)–no changes occurred; 2) hydrogen (initial pressure 50 atm.) and ammonia dissolved in methanol. Hexyl alcohol and acetamide were obtained; 3) ammonia dissolved in methanol. Hexyl alcohol and acetamide were obtained.

Reductive amination of ethyl β-furylacrylate in the vapor phase. 70 g of ethyl β-furylacrylate was passed in the vapor phase through a layer of 10% Pt–C at 300° with a space velocity of 0.1 h^{-1} in a stream of hydrogen mixed with ammonia (2:1). 63 g of catalyzate was obtained, from which a fraction consisting of 5-propylbutyrolactam was isolated, b.p. 146–147° (10 mm), m.p. 53–54°; yield 31%.

On the basis of the foregoing, the following conclusions may be drawn: under the action of hydrogen and ammonia at 100–110° over a skeletal Ni—Al catalyst, esters of γ-ketoenanthic acid and its α-alkyl homologs are converted into the corresponding lactams (5-propyl- and 3-alkyl-5-propylpyrrolidin-2-ones) in 60–70% yield; reductive amination of esters of β-furylacrylic acids in the vapor phase over Pt—C at 300° leads to the formation of lactams in 30% yield.

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Note: Figure translations are in progress. See original paper for figures.