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Catalytic Condensation of Ketones with Carboxylic Acids

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Catalytic Condensation of Ketones with Carboxylic Acids

Abstract

It is found that use of acetone in place of acetic acid in the reaction with isobutyric acid is effective for the synthesis of the cross-ketonization product, methyl isopropyl ketone (MIPK). Rate of MIPK formation is of the same order of magnitude, but slightly lower for acetone compared to acetic acid under similar conditions (Fig. 1). The most active catalyst is KOH-treated titania. The second product of this reaction, DIPK, results from the ketonic decarboxylative condensation of isobutyric acid with itself. The ^{13}C labeled carbonyl group from isobutyric acid is almost exclusively (within the detection error) transferred to the MIPK product (Scheme 2). In the reaction of acetic acid with a more branched ketone, DIPK, only a negligible amount of MIPK is produced with all studied catalysts. Based on the experimental data, the proposed mechanism most likely includes enolization of acetone, followed by its condensation as the nucleophile with isobutyric acid as the electrophile, and completed by the retro-condensation to MIPK (Scheme 2). The order of the enolic components activity, acetic acid \geq isobutyric acid $>$ acetone \gg DIPK, is generally consistent with the order of their adsorption energies on metal oxides. Low or non-branched ketones could be efficiently used in place of one of the acids in the cross-ketonization reaction. Because of the relatively high reaction rate, this process needs to be accounted for in the kinetic scheme of the decarboxylative ketonization.

Keywords

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Comments

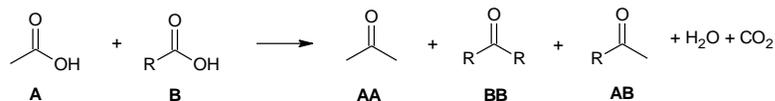
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Catalytic Condensation of Ketones with Carboxylic Acids

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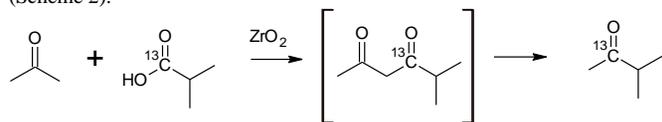
Introduction

Ketones can be prepared from carboxylic acids by their catalytic decarboxylation on metal oxides, also known as the ketonic decarboxylation or the decarboxylative ketonization (Scheme 1) [1]. Debates on the reaction mechanism have been actively continued in the literature since 1910 [1, 2]. At the same time, very little is known about catalytic condensation of ketones with carboxylic acids, which may be taking place as a side process during ketones preparation from carboxylic acids. Kinetic data for the ketonic decarboxylation of carboxylic acids are an important argument in the mechanistic discussions, but the condensation of the product ketone with the starting carboxylic acid has not been accounted for in a kinetic scheme. Yet, it may significantly affect the overall rate of the decarboxylative ketonization.



Scheme 1. Decarboxylative cross-ketonization of two carboxylic acids.

In the current study, reaction rates of the catalytic condensation of ketones with carboxylic acids are measured depending on the degree of substitution in the alpha position of both reagents. This unexplored catalytic condensation could be used for the production of unsymmetrical ketones by replacing one of the acids with its ketone equivalent, for example, using acetone instead of acetic acid in the cross-ketonization reaction with another acid (Scheme 2).



Scheme 2. Condensation of acetone with isotubutyric acid.

Materials and Methods

Reaction rates for the condensation of acetone with isotubutyric acid and also for the condensation of diisopropyl ketone (DIPK) with acetic acid were measured in a continuous flow differential reactor, 6.4 mm in diameter, 250 mm in length, under conditions free of any diffusion limitations. Products were quantitatively analyzed by gas chromatography (GC) using flame ionization detector and identified by comparison with the known standards. Catalytic condensation of acetone with isotubutyric acid labeled by ¹³C isotope on its carbonyl group was studied in a pulse microreactor inside a Thermo Scientific TRACE 1300 GC equipped with a

Thermo Scientific ISQ Single Quadrupole mass-selective detector. Zirconium and titanium metal oxides, in monoclinic and anatase form (Alfa Aesar), untreated, and KOH-treated [3], were used as the catalyst.

Results and Discussion

It was found that using acetone in place of acetic acid in the reaction with isotubutyric acid is efficient for the synthesis of the cross-ketonization product, methyl isopropyl ketone (MIPK). Rate of MIPK formation is of the same order of magnitude, but slightly lower for acetone compared to acetic acid under similar conditions (Fig. 1). The most active catalyst is KOH-treated titania. The second product of this reaction, DIPK, results from the ketonic decarboxylative condensation of isotubutyric acid with itself. The ¹³C labeled carbonyl group from isotubutyric acid almost exclusively (within the detection error) was transferred to the MIPK product (Scheme 2). In the reaction of acetic acid with a more branched ketone, DIPK, only a negligible amount of MIPK was produced with all studied catalysts.

Based on the experimental data, the proposed mechanism most likely includes enolization of acetone, followed by its condensation as the nucleophile with isotubutyric acid as the electrophile, and completed by the retro-condensation to MIPK (Scheme 2). The order of the enolic components activity, acetic acid \geq isotubutyric acid $>$ acetone \gg DIPK, is generally consistent with the order of their adsorption energies on metal oxides.

Significance

Low or non-branched ketones could be efficiently used in place of one of the acids in the cross-ketonization reaction. Because of the relatively high reaction rate, this process needs to be accounted for in the kinetic scheme of the decarboxylative ketonization.

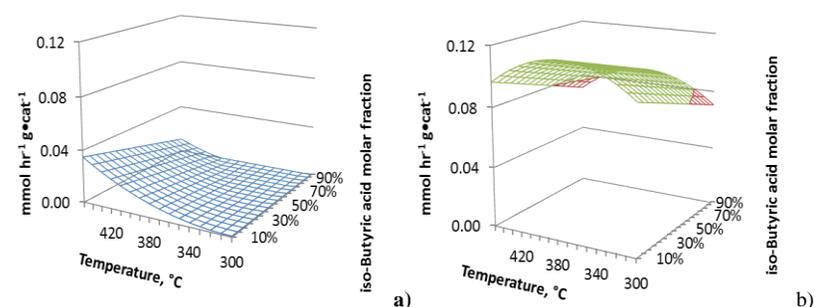


Figure 1. Rates of MIPK formation for the ZrO₂ catalyzed reaction of isotubutyric acid with a) acetone, or b) acetic acid.

References

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3. Ignatchenko, A.V., Kozliak, E.I. *ACS Catal.* 2, 1555 (2012)