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Cross-selectivity in the catalytic ketonization of carboxylic acids

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ABSTRACT

A mixture of acetic and 2-methylpropanoic (isobutyric) acids representing non-branched and branched acids, respectively, was catalytically converted to a mixture of ketones in a set of statistically designed experiments (DOE). The selectivity toward the cross-ketonization product was analyzed depending on (a) temperature within 300–450 °C range, (b) molar fraction of each acid in the mixture, from 10% to 90%, and (c) liquid hourly space velocity (LHSV) within 2–12 h^{-1}, and compared against the selectivity toward two symmetrical ketones. Six metal oxide catalysts were tested and ranked on their ability to yield the cross-product as opposed to the self-condensation product. The catalysts were based on either the anatase form of titania or monoclinic form of zirconia and treated with either KOH or K_2HPO_4. The titania catalyst treated by KOH outperformed all other catalysts by providing the cross-selectivity above the statistically expected binomial distribution. The criterion for having a high cross-selectivity in the decarboxylative ketonization is formulated mathematically as the separation of roles of two acids, one being a more active enolic component, and the other being the preferred carbonyl component. According to the suggested criterion, the less branched acetic acid reacts as both the preferred carbonyl and enolic component with untreated catalysts. Therefore, untreated catalysts promote selective formation of the symmetrical ketone, acetone, thereby decreasing the selectivity to the cross-ketone. After alkaline treatment, both the anatase form of titania and monoclinic form of zirconia increase the isobutyric acid participation as the carbonyl component. Acetic acid remains as the preferred enolic component with all treated catalysts, thus increasing the selectivity toward the cross-product in the ketonization of a mixture of carboxylic acids. The condition for achieving a high cross-selectivity by polarizing roles of the two reactants can be extended to other types of cross-condensations.

1. Introduction

Increasing selectivity in catalytic reactions is one of the ultimate goals pursued in the design and preparation of catalysts [1]. Selectivity of chemical reactions can be classified into various types, such as chemo-, regio-, or stereo-selectivity [2]. A common strategy for improving the chemical selectivity of a catalyst is to minimize undesirable reactions by eliminating or blocking improper catalytic sites. In addition, selection of the best process conditions helps discriminate competing reactions. Perhaps, a more challenging problem in the catalyst design is to improve the selectivity toward just one of the several possible isomers in a particular reaction. Such selective catalysts may provide access to regio- or stereoisomers. A stereo selective catalyst must create kinetically favorable conditions for the formation of the preferred stereoisomer.

A less frequent type of selectivity appears in cross-coupling reactions between two reagents. Each reagent may condense either with itself to produce a symmetrical product, or with the other reagent to produce the cross-product. Obviously, each of the two symmetrical products may be produced separately starting from just a single reagent and for that reason often considered as a waste in cross-reactions. The intent of research and development on cross-reactions is to improve the selectivity to the cross-product, as for example, in aldol condensations [3]. Unfortunately, a broadening view on the subject of cross-selectivity combining diverse catalytic reactions has yet to be developed.

An example of an exceptionally high cross-selectivity can be illustrated by a recently discovered selective condensation of two different aldehydes to cross-coupled esters in a Ni(0) catalyzed Tishchenko reaction wherein different electronic factors of the alkyl versus the aryl group are responsible for the observed high selectivity [4]. A similar problem of the cross-selectivity exists in the industrial synthesis of unsymmetrical ketones, usually methyl

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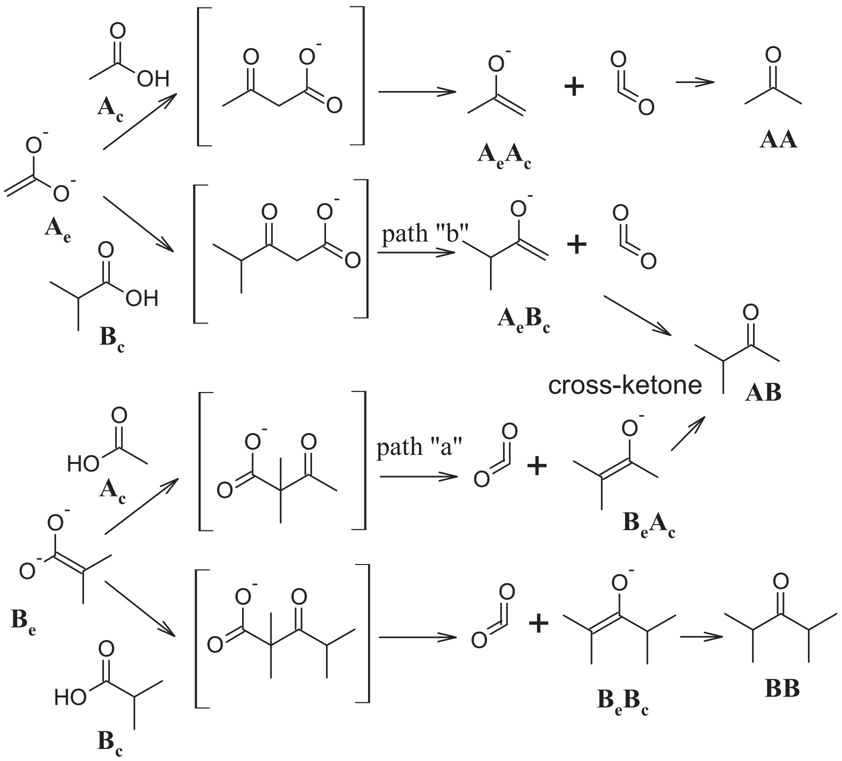

Scheme 1. Decarboxylative ketonization of a mixture of acetic (A) and isobutyric (B) acids yielding the cross-ketone (AB) and the two self-condensation products (AA and BB).

ketones, such as methyl cyclopropyl ketone [5], methyl nonyl ketone [6], methyl isopropyl ketone,[i] etc., from a mixture of two carboxylic acids by their cross-ketonization reaction (Scheme 1).

The ketonic decarboxylation, also known as the decarboxylative ketonization of carboxylic acids has a long history [8–11] and several versions, such as a non-catalytic pyrolysis reaction [12], or an industrial scale vapor phase catalytic process [11,13]. It has been rediscovered several times [8]. The literature on ketonization reactions has been extensively reviewed [9–11], but the discussion of the cross-selectivity was limited to just a few cases [14–16]. The interest to ketonization has been recently revived in connection with the bio-oil upgrading [17]. One possibility is to condense acetic acid with bio-derived fatty acids into methyl ketones [6,18]. In this process it is necessary to minimize consumption of acetic acid into the symmetrical ketone, acetone, which is an undesired by-product. The problem again, is to increase the selectivity to the cross-ketone. The importance of this problem urged us to examine the relative selectivity achieved with different catalysts toward the cross-product in the catalytic ketonization of carboxylic acids. Our goal is to understand the factors governing cross-selectivity and to improve it.

The cross-selectivity is closely related to and depends on the relative reactivity of the two carboxylic acids. In general, a higher degree of branching at the alpha-position decreases the carboxylic acid reactivity in the ketonization reaction [15,20]. The role of the catalyst, the molar ratio of two acids, and the process conditions affecting the cross-selectivity have not been sufficiently studied.

There are two components used for the construction of any ketone by the decarboxylative ketonization, the acyl group and the alkyl group coming from two different acids. We have recently suggested naming their sources as the carbonyl and enolic components, respectively by analogy with the aldol condensation [20]. However, unlike the aldol condensation or the Tishchenko reaction in which two cross-products can form, there is only one cross-product possible in the carboxylic acids ketonization reaction (Scheme 1). It has been shown that two different mechanistic pathways exist, and they both lead to the same cross-product [20]. Among two possible combinations for the construction of the cross-ketone, the preferred one is that utilizing the alkyl group from the less branched acid and the acyl group from the more branched acid. Mechanistically, it may occur through the preferred enolization of the less branched acid and its subsequent condensation with the more branched carbonyl component to a beta-ketoacid followed by the loss of CO_2 from the enolic component in the decarboxylation step [20].

The rate-limiting step of the catalytic ketonization has not been confirmed yet, but any variation of the cross-selectivity depending on the catalyst must be explained by the different influence of the employed catalysts on the substituents in the transition state structure. For this reason, cross-reaction becomes a valuable method in the study of the ketonization mechanism. In our previous work on the ketonization mechanism we proposed enolization of carboxylic acids on zirconia [19] and were able to analyze separately the effect of substituents on the reaction rates of the enolic and the carbonyl component [20]. Accordingly, in two competing reactions of a common enolic component with two different carbonyl components, a faster reaction rate is observed for a less substituted carbonyl component (Table 1). The same effect was found for a common carbonyl component reacting faster with a less substituted enolic component. In this approach, the cross-ketonization conditions are used to separate the effect of substituents on the enolic component from the carbonyl component of the same carboxylic acid.

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[i] There has been a surge of interest in the preparation of methyl isopropyl ketone for the past decade. See, for example, [7] available in the English language. The rest of the literature devoted to the preparation of this ketone as the single targeted product, about 20 publications from 1999 to 2012, is in the Chinese language.