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On the mechanism of the organocatalyzed Beckmann rearrangement of cyclohexanone oxime by trifluoroacetic acid in aprotic solvent

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ABSTRACT

The Beckmann rearrangement of cyclohexanone oxime to ε-caprolactam in high yield catalyzed by trifluoroacetic acid in aprotic solvents is described. The influence of the concentration of reagents, intermediates, solvents on reaction rate and selectivity in ε-caprolactam is studied. The identification of the key intermediate and its role in the catalysis are reported together with the influence of the acid on the reaction rate. In addition, the study of the hydrolysis reactions of reagent and intermediates highlights what are the parameters that influence the selectivity to ε-caprolactam. On the basis of these results a likely catalytic cycle based only on the experimentally verified intermediates is also given.

1. Introduction

Despite the environmental and the industrial concerns relating the production of ε-caprolactam [1–4] by Beckmann rearrangement of cyclohexanone oxime employing oleum as homogeneous catalyst, the new heterogeneous gas phase processes are far from being widely employed in the industrial production [3–6]. The reasons are both economical and technical and deeply related between them, indeed the fast catalyst deactivation needs of complex plant design for a continuum catalyst regeneration, which limits their practical application [6].

Recently, progresses on the homogeneous Beckmann rearrangement are observed by using organocatalysis [7,8]. Even though, these studies derive directly from the ones of Beckmann and Kuhara [9,10], and involved many researchers during the XX century, the argument is yet greatly studied due to its important practical application in the revamping of traditional processes [3,4]. The use of strong inorganic acids in the Beckmann rearrangement of cyclohexanone oxime is a common synthetic practice [11–14] and a more environmentally friendly approach may be attempted. For instance, recently the use of ionic liquids in combination with lewis acids give high yield and selectivity with some activated oxime but not really significantly in the rearrangement of the cyclohexanone oxime for this reasons a practical development of a process based on these catalytic systems seems to be, at the moment, impracticable [15,16]. On the contrary, use of quite mild acid with low protonation ability such methanesulfonic, sulfamic and more recently trifluoroacetic acid in non-aqueous solvent, showed high yield in ε-caprolactam and could be a useful approach to an ammonium sulfate-less process [7,8,17,18]. In the acid catalyzed Beckmann rearrangement the key points are the proton transfer from the nitrogen to the oxygen and the concerted extraction of the water molecule with the displacement of the carbon atom. This process is allowed by the formation of electron-poor nitrogen, which is the driving force for the rearrangement. According to this, the conversion of the oximes to more reactive ether or ester intermediates is a practical method to achieve the rearrangement under mild conditions [19–24]. As a matter of fact, these compounds, respect to the corresponding oximes, have a lower electronic density on the nitrogen atom and consequently a greater tendency to rearrange even without Brønsted acids [19–24]. For this reason a new catalytic pathway based on the rearrangement of acetyl cyclohexanone oxime, under mild acidic condition, to acetyl caprolactam was studied [17]. On the progress of these studies, bring us to study the reactivity of trifluoroacetyl cyclohexanone oxime and the reactivity of the neat oxime in the presence of trifluoroacetic acid as a catalyst: ε-caprolactam in high yield was obtained in non-aqueous solvent [18].

In the present paper we give new insight on the Beckmann rearrangement of cyclohexanone oxime catalyzed by CF_3COOH in aprotic solvent, a detailed study of the stages of the process and some data relative to the rate of reaction of the single step are studied, in order to discriminate what are the determining steps for the kinetics.

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2. Experimental

2.1. Materials

Reagents: cyclohexanone oxime, ε-caprolactam, trifluoroacetic acid, trifluoroacetic anhydride, were purchased from Aldrich. The purity of the commercially available samples was checked by the usual methods (melting point, TLC, HPLC, GC and GC–MS) and further purifications were carried out when necessary. In particular, cyclohexanone oxime was crystallized from cyclohexane, dried in vacuo and stored under nitrogen at 248 K. Reaction solvents were HPLC grade products used without further purifications. Deuterated acetonitrile was purchased from Euriso-Top.

2.2. Trifluoroacetyl cyclohexanone oxime and N-trifluoroacetyl caprolactam synthesis

The synthesis of trifluoroacetyl cyclohexanone oxime was carried out by drop wise addition of trifluoroacetic anhydride to a diethyl ether solution of cyclohexanone oxime at 273 K. Checked the conversion by CG analysis (completeness after few minutes) the reaction mixture is washed with a solution of $NaHCO_3$ at 273 K and desiccated with anhydrous Na_2SO_4. Finally distilled under vacuum with a final GC purity of *ca*. 96%.

The synthesis of N-trifluoroacetyl caprolactam is similar to that of the trifluoroacetyl cyclohexanone oxime except for the temperature of reaction, which is 298 K. In addition, the solution is not washed with aqueous $NaHCO_3$ because of the strong tendency of N-trifluoroacetyl caprolactam to hydrolyze and the solution is distilled under vacuum without any treatment. Both trifluoroacetyl cyclohexanone oxime and N-trifluoroacetyl caprolactam are characterized by GC–MS and NMR measurements and their purity (*ca*. 96%) are checked by GC analysis.

2.3. Reaction rates measurements

The kinetic runs were performed in a well stirred pressurized glass reactor thermostatted by a circulation bath in the range 354–383 K and containing weighed samples of the solvent and of the reagents. Small amounts (*ca*. 10 μl) of the reaction mixtures were drawn at different times and the samples were analyzed by GC and GC–MS, using an HP5 capillary column (300 μm i.d. 30 m long, 95% methyl, 5% phenyl silicone phase). The samples were also checked by HPLC using a PerkinElmer apparatus and a Lichrosphere 100 (RP-18, 5 μm) column with water acetonitrile 30/70 as eluent.

3. Results and discussion

The results reported below comprise some data already reported in preliminary works which have been included for a better comprehension of the argument.

3.1. Time concentration profiles and reaction steps

In Fig. 1 the typical time concentration profile in acetonitrile (ACN) as a solvent is reported. The formation of cyclohexanone, which is the major side reaction, will be extensively discussed in next section. Both trifluoroacetyl cyclohexanone oxime and N-trifluoroacetyl caprolactam are observed in small amount from the beginning of the reaction, thus suggesting their active involvement into the reaction mechanism.

The likely reaction steps inferred from the time concentration profile are reported in Scheme 1, as already discussed in previous work the esterification of the cyclohexanone oxime and its further rearrangement to the corresponding trifluoroacetyl caprolactam are key steps of the reaction. In fact, the rearrangement via

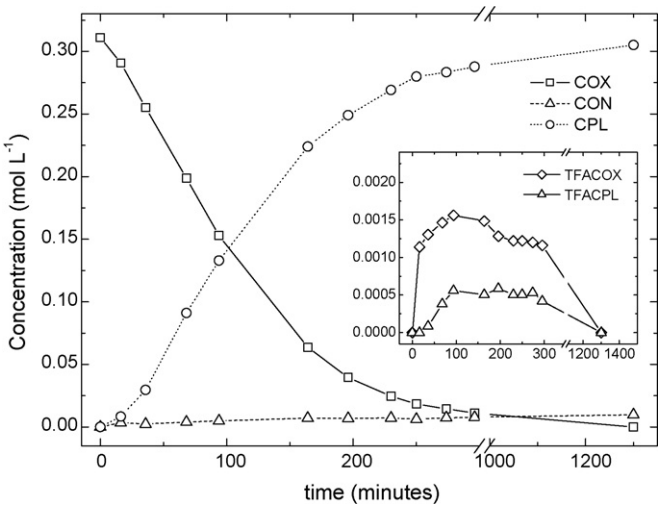

Fig. 1. Typical time concentration profiles in ACN as a solvent. Run conditions: T 363 K, cyclohexanone oxime concentration 0.31 mol L^{-1}, CF_3COOH concentration 1.0 mol L^{-1}, reaction volume 10 mL. COX = cyclohexanone oxime, CPL = ε-caprolactam, CON = cyclohexanone, TFACOX = trifluoroacetyl cyclohexanone oxime TFACPL = N-trifluoroacetyl caprolactam.

trifluoroacetyl cyclohexanone oxime is more facile than the direct rearrangement of the neat oxime due to the loosening of electronic density at the nitrogen induced to the electron withdrawing effect of the trifluoroacetyl group [19,22,23].

3.2. Influence of the solvent on reaction rate and selectivity

In Table 1 the influence of several solvents and mixture on initial reaction rate and selectivity is reported. It is noteworthy that the reaction rate, except in dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), moderately increases with the polarity of the solvent, while the selectivity to ε-caprolactam (except in benzonitrile, DMF and DMSO) are negligibly influenced, this behavior suggests a rate determining step whose active complex is poorly stabilized by solvation [25]. Different considerations must be accounted for DMF and DMSO, in which the reaction gives different products. As a matter of fact, in DMF reaction stops after 30 min with 60% of conversion of cyclohexanone oxime (Fig. 2), ε-caprolactam concentration reaches a maximum (after 15 min) then decreases, probably due to side reactions such as the polymerization of the lactam [26]. In DMSO the rearrangement does not occur at all and only the hydrolysis to cyclohexanone is observed. The results in DMSO are the contrary of what expected because it has been reported that in some cases the rearrangement rate slightly increases with the solvent polarity [18]. The reason of such a behavior is not clear, however, cage formation in which cation or anion are trapped is known to occur in DMSO, so that a specific solvent effect may be conjectured for this solvent [27].

The inhibiting effect of DMSO on the rearrangement is studied in order to highlight not only the solvent effect on the reaction but also the mechanism itself. In Fig. 3 the time concentration profile of the rearrangement in the presence of DMSO is reported, the shape of the profile does not differ significantly of what observed in neat ACN, except for the lower initial reaction rate and for the very low concentration of the trifluoroacetyl derivatives, which are detectable only in trace amount (about 10^{-5} mol L^{-1}, for this reason their concentration time profiles has been omitted due to the high uncertainty of the measure). The influence of the concentration of DMSO on both the initial reaction rate and the selectivity to ε-caprolactam is reported in Fig. 4. As expected, the initial rate diminishes as the concentration of DMSO increases, which confirms