

Additive-assisted Rupe rearrangement of 1-ethynylcyclohexan-1-ol in near-critical water

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Received 2 April 2011; Revised 29 July 2011; Accepted 21 August 2011

We performed the Rupe rearrangement of 1-ethynylcyclohexan-1-ol in near-critical water to study the reaction under high temperature conditions. The final product thus obtained was primarily 1cyclohexen-1-ylethanone which was identified by GC-MS. The influences of reaction time, temperature, and initial reactant-to-water ratio on the yield of 1-cyclohexen-1-ylethanone were examined. The yield of 1-cyclohexen-1-ylethanone was 49 % in pure water at 260 °C for a reaction time of 60 min. However, when additives such as $ZnSO_4$, $FeCl_3$, and $NaHSO_4$, respectively, were introduced to the water to investigate the effect of salts on the Rupe rearrangement reaction, the yield increased markedly to as much as 88 % in 5 mole % $NaHSO_4$ aqueous solution under the same conditions. The catalytic ability of the additives decreased in order: $NaHSO_4$, $FeCl_3$, $ZnSO_4$. On the basis of these results, a possible reaction mechanism of the Rupe rearrangement of 1-ethynylcyclohexan-1-ol in near-critical water was proposed.

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Keywords: Rupe rearrangement, 1-ethynylcyclohexan-1-ol, additives, near-critical water, mechanism

Introduction

Water near its critical region, namely near-critical water (NCW, 150-370°C, 0.4-21.8 MPa), can serve as an environmentally benign solvent, a reactant, and catalyst in organic chemical reactions because of its special physical and chemical properties, such as high ion product, low dielectric constant, and the good solubility of various materials (Watanabe et al., 2004; Savage, 1999; Weingärtner & Franck, 2005; Kruse & Dinjus, 2007; Fraga-Dubreuil & Poliakoff, 2006; Anastas & Williamson, 1998). Parsons (1996), Katritzky et al. (1996), An et al. (1997), and Simoneit (1995) provide very good overviews of the types of syntheses in organic chemistry that have been demonstrated in near-critical and supercritical water. For example, ethers and esters, which are unreactive to heat alone, undergo facile hydrolysis in water at 250-350 °C (Siskin et al., 1990).

The Rupe rearrangement is an acid-catalysed rear-

rangement of tertiary α,β -acetylenic alcohols leading to the formation, predominantly, of α,β -unsaturated ketones, which traditionally were synthesised in boiling formic acid, with a tendency for low yields of labile reaction products. A rearrangement of 1ethynylcyclohexan-1-ol described in the literature was conducted in 90 % formic acid under reflux to give 1-cyclohexen-1-ylethanone in 49 % yield (Hassner & Stumer, 1994). An et al. (1997) noted that 1-ethynylcyclohexan-1-ol underwent the Rupe rearrangement (Swaminathan & Narayanan, 1971) in high-temperature water at 290 °C for 60 min, affording 1-cyclohexen-1-ylethanone in moderate yield (45 %). In this study we selected 1-ethynylcyclohexan-1-ol as a model compound to investigate the Rupe rearrangement reaction assisted by various additives in NCW.

The strong self-dissociation ability of water, when it approaches the critical point, can offer rich sources of both H^+ and OH^- with a concentration three orders of magnitude greater than at room temper-

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ature, and which is abundantly available and nontoxic (Watanabe et al., 2004). Therefore, it is potentially safe to handle an environmentally compatible solvent, catalyst, and reactant in which to conduct the rearrangement and hydrolysis reactions. However, problems such as slow reaction rate and poor selectivity exist for these non-catalysed organic reactions in NCW, which substantially restrict the application of this attractive technique in processes of interest to industry. For example, Katritzky et al. (1990) heated ethynylbenzene in NCW for up to 5 days, and their best result showed a 51 % conversion to 1-phenylethanone. Jerome and Parsons (1993) heated alkynes in supercritical water without catalyst up to 2 h, and they obtained no ketone but some lowmolecular weight oligomers. Torry et al. (1992) explored the effects of salts on the hydrolysis of phenylmethoxymethylbenzene and N-benzylaniline in supercritical and NCW. Our co-worker examined the hydration of ethynylbenzene in NCW with ZnCl₂, FeCl₃, and $NaHSO_4$ as additives to improve the yield of 1phenylethanone (Li et al., 2011). In recent years, some Brønsted acid catalysts have been developed (Fukuda & Utimoto, 1991; Fukuda et al., 1991) and some less toxic metal catalysts, such as gold, platinum, palladium, and ruthenium are not economically viable. Consequently, in this paper, Lewis acid $FeCl_3$ and salts ZnSO₄, NaHSO₄ which would intensify the selfdissociation of water were chosen to investigate the effects of additives and reaction conditions on the Rupe rearrangement reaction of 1-ethynylcyclohexan-1-ol in NCW. A high yield of 1-cyclohexen-1-ylethanone was obtained under optimal conditions. We also suggested a possible reaction mechanism for the rearrangement reaction of 1-ethynylcyclohexan-1-ol in NCW.

Experimental

All reagents were commercially available from China National Medicines Corporation Ltd. (Shanghai, China) with purity higher than 99 mass % and were used as received. Pure water was redistilled after deionisation. The solutions of additives were prepared based on mole % by dissolving the respective additive in double-distilled water.

The reaction was conducted in a high-pressure stainless steel bath reactor (Shandong Precision and Scientific Instrument Co., China) with a volume of 500 μ L. The total amount of stock solution was calculated so as to generate the pressure inside the reactor to correspond to the saturated water vapour pressure at any given temperature, as we reported previously (Duan et al., 2009). The reactant and solution were fed via microliter syringes in terms of the mole ratio of 1 : 40. The loaded reactor was placed into the salt bath which was preheated to a temperature 60 °C higher than the desired reaction temperature to ensure that the reaction system rapidly reached the desired



Fig. 1. Yield of 1-cyclohexen-1-ylethanone at: 260 °C, 60 min with different r/w mole ratio in NCW without additives.

temperature. Once the desired reaction time had expired, the reactor was removed from the salt bath and immersed in a cooled water bath to quench the reaction. The reaction mixture was rinsed with toluene using microliter syringes and transferred into a volumetric flask with 7 μ L of dodecane. Four replicate experiments were conducted and the points given in the plots were the average values of the experimental data.

The liquid sample was analysed quantitatively using an Agilent 6890GC (Agilent Technologies, USA) spectrometer by comparing the peak area with the peak area of the dodecane internal standard. Product identification was achieved by matching the retention time to those of the authentic compounds and by inspecting mass spectra.

The experiments were conducted at different batch holding temperatures, reaction times, reactant-towater (r/w) mole ratios, and additives, to determine the influence of these parameters on the reaction. The experimental conditions were: temperature ranges of 220-290 °C, time ranges of 30-150 min, and r/w mole ratio from 1 : 20 to 1 : 45. The reaction environment under the conditions investigated represented almost a single phase system.

Results and discussion

Dependence of yield of 1-cyclohexen-1ylethanone on r/w ratio

Fig. 1 depicts the dependence of the yield of 1cyclohexen-1-ylethanone in NCW without any additives on different r/w mole ratios ranging from 1 : 20 to 1 : 45, maintaining temperature at 260 °C, and reaction time at 60 min. The trend of the curve in



Fig. 2. Yield of 1-cyclohexen-1-ylethanone at r/w = 1 : 40 with different temperature and time in NCW without additives; ■ - 240 °C, ● - 260 °C, ▲ - 270 °C, ▼ - 290 °C.

this figure shows that the yield of 1-cyclohexen-1ylethanone increased slightly with the increasing r/w mole ratio from 1:20 to 1:35, then increased rapidly and achieved the highest yield of 49 % when the r/w mole ratio was 1 : 40. However, the content of water increased further when the yield dropped rapidly. Although water near the critical temperature could boast a much higher concentration of H⁺ resulting from its self-dissociation, the increase in the content of water was disadvantageous for the Rupe rearrangement reaction in accordance with Le Chatelier's principle (if a chemical system at equilibrium experiences a change in concentration, temperature, volume, or partial pressure, then the equilibrium shifts to counter the imposed change and a new equilibrium is established) when it increased beyond the most advantageous content of water. In accordance with the molecular collision theory, the reaction rate would increase with the increasing content of water, since the probability of the collision between the H⁺ and OH⁻ originating from the reactant or NCW self-dissociation in the volume unit will be higher. On the other hand, the rapid accumulation of products could also accelerate the reaction rate with a higher reactant concentration, but the noted effect caused by the products accumulation was inferior to the collision effect. The yield decreased when the r/w mole ratio exceeded 1:40 as there was a limit to the collision effect.

Dependence of yield of 1-cyclohexen-1ylethanone on temperature or time without additives

All the experiments were conducted in NCW with no additives, keeping as constant the following parameters: r/w mole ratio (1 : 40), reaction time (30 min, 60 min, 90 min, 120 min, and 150 min, respectively) or a varied reaction temperature.

Fig. 2 shows that the yield of 1-cyclohexen-1-

95 90 85 75 70 65 60 0 2 4 6 8 10 NaHSO4 concentration/mole %

Fig. 3. Dependence of yield of 1-cyclohexen-1-ylethanone on different concentrations of NaHSO₄ solution with r/w mole ratio (1 : 40) in NCW at 260 °C, after 60 min.

ylethanone increased with prolonging reaction time or increasing the temperature, but gradually decreased with prolongation of the reaction time; the same was observed with the temperature. The yield of 1-cyclohexen-1-ylethanone achieved its maximum at different temperatures within about 60 min and approached a value as high as 49 % at 260°C. This illustrated that the formation of 1-cyclohexen-1-vlethanone was more rapid than its decomposition and the formation rate was more rapid than that of side reaction under the condition $260\,^{\circ}$ C within 60 min. On the other hand, the ionisation constant of water approached its maximum at about 260 °C (Marshall & Franck, 1981; Connolly, 1966), which meant that the dissociation of water itself near the critical point 260 °C generated a sufficiently high H⁺ concentration to be involved in some acid-catalysed organic reactions without the addition of an acid. However, the H⁺ concentration decreased dramatically once the critical point was exceeded.

Dependence of yield of 1-cyclohexen-1ylethanone with additives on time

Since the volume of the reactor was too small to introduce additives directly into the reaction mixture, we prepared solutions based on mole % by dissolving the additives in the double-distilled water. Fig. 3 presents the yield of 1-cyclohexen-1-ylethanone depending on different concentrations of the NaHSO₄ solution at 260 °C, after 60 min at the same r/w mole ratio (1 : 40). As the highest yield of the reaction was 87 % in the 5 mole % of the NaHSO₄ solution, the concentration of additives used in the following experiments was 5 mole %.

Fig. 4 illustrates the influence of reaction time (30 min, 60 min, 90 min, 120 min, and 150 min, respectively) on the yield of 1-cyclohexen-1-ylethanone. All the experiments were conducted at $260 \,^{\circ}$ C, r/w mole



Fig. 4. Dependence of yield of 1-cyclohexen-1-ylethanon on time at 260 °C with additives in NCW; ■ - NaHSO₄,
● - FeCl₃, ▲ - ZnSO₄, ♥ - no additive.

ratio of 1 : 40 in the solution of NaHSO₄, FeCl₃, or ZnSO₄ to investigate the effect of these salts on the Rupe rearrangement reaction.

These curves demonstrate that 60 min was the most appropriate reaction time under the same conditions and that the NaHSO₄ solution presented the best catalytic activity with the highest yield of 88 %. When the reaction was prolonged beyond 60 min, all yields decreased to some extent, irrespective of the type of additive or its presence. With an even greater prolongation of the reaction time, the H⁺ concentration would have decreased and would not have provided enough H⁺ ions for the acid-catalysed reaction to continue. Besides the rearrangement of 1ethynylcyclohexan-1-ol yielded by-products cyclohexanone, 1-ethynylcyclohex-1-ene, etc., there was a possible equilibrium between the reactant and the products, which could be explained by Le Chatelier's principle. Since the equilibrium pertained among them, it was difficult to convert all the 1-ethynylcyclohexan-1ol to products, and the products might also undergo a reciprocal transformation.

The dissociation of NaHSO₄ generated H^+ as also did the hydrolysis of ZnSO₄ and FeCl₃. Moreover, the self-dissociation of NCW would be intensified by the introduction of NaHSO₄, ZnSO₄, and FeCl₃ as the additives. As a result, the yield increased significantly in the presence of the additives. The concentration of H^+ formed by the ionisation or hydrolysis was in the order: NaHSO₄, FeCl₃, ZnSO₄ under the same conditions in the NCW system. As a consequence, the catalytic ability of the additives decreased in order: NaHSO₄, FeCl₃, ZnSO₄.

Dependence of yield of 1-cyclohexen-1ylethanon on temperature with additives

As can be seen from the tendency of the curves in the experiments in Fig. 5 conducted with the addi-



Fig. 5. Dependence of yield of 1-cyclohexen-1-ylethanon on temperature and 60 min reaction time with additives in NCW; ■ - NaHSO₄, ● - FeCl₃, ▲ - ZnSO₄, ▼ - no additive.

tive introduced into water by setting the parameters at r/w mole ratio (1:40), reaction time (30 min, 60 min)min, 90 min, 120 min, and 150 min) while varying the reaction temperature, the yield improved with the temperature increase from $220 \,^{\circ}$ C to $260 \,^{\circ}$ C. Then the yield decreased with temperature reaching the range of NCW. The shift in the yields lies in two effects: first, with the increase in temperature, the ionisation constant of water increased and NCW generated more H⁺ ions which could accelerate the rearrangement reaction. Around 260 °C, the ionisation constant of water approached the maximum (Connolly, 1966). The ion product or dissociation constant for the water, as it approached the critical point, was about 3 orders of magnitude higher than that of ambient liquid water. This means that water can produce the largest amounts of H^+ at 260 °C, resulting in the highest yield. Second, the increase in temperature $(> 260 \,^{\circ}\text{C})$ accelerated side reactions and induced the decomposition of 1-cyclohexen-1-ylethanon, so the selectivity towards 1-cyclohexen-1-ylethanon decreased.

As discussed above, the yields with additives were much higher than those without additives and the effect of additives on the yield was in the order: NaHSO₄, FeCl₃, ZnSO₄, with the highest yields of 88 %, 77 %, and 73 %, respectively, at 260 °C, under the same reaction condition.

Reaction mechanisms

Based on the product detected and the results of the experiment, a probable reaction mechanism of the rearrangement of 1-ethynylcyclohexan-1-ol in NCW is proposed and presented in Fig. 6. The NCW could provide a rich source of H^+ because of its selfdissociation and this self-dissociation could be intensified by the introduction of NaHSO₄, FeCl₃, and



Fig. 1. Formation of 1-cyclohexen-1-ylethanon in NCW.

 ${\rm ZnSO}_{4,}$ all of which generated a high concentration of ${\rm H}^+.$

Initially, alcohol, I attacked by a proton originating from NCW results in the formation of a tertiary carbonium ion which then expels a proton from an adjacent carbon atom, giving 1-ethynylcyclohex-1-ene, II. Next, electrophilic attack produces a secondary carbonium ion, which is attacked by H₂O and results in III. Subsequently, III eventually forms α,β -unsaturated ketone, IV via tautomerisation. Such enyne intermediates have been detected spectroscopically (Parham et al., 1954) and they have even been isolated (Ansell et al., 1956; Smissmann et al., 1956) on several occasions.

However, a mechanism not involving an enyne as intermediate was also probable in NCW. A proton from NCW attacks the triple bond of I to form a carbonium ion, then through the cation exchange it forms a tertiary carbonium ion which then expels a proton from an adjacent carbon atom, generating *III*, which then forms IV through tautomerisation.

Conclusions

We performed the Rupe rearrangement of 1ethynylcyclohexan-1-ol in NCW in order to obtain 1cyclohexen-1-ylethanon as the main product and examine the influence of reaction r/w mole ratio, temperature, and time on the product yield. The yield was low (50 %) at 260 $^{\circ}$ C with the reaction time set at 60 min. However, when NaHSO₄, FeCl₃, or ZnSO₄ was introduced, the yield increased markedly and reached as high as 88 % in the NaHSO₄ aqueous solution under the same reaction conditions. The catalytic ability of additives decreased in the order: $NaHSO_4$, $FeCl_3$, ZnSO₄. A probable mechanism of the Rupe rearrangement reaction of 1-ethynylcyclohexan-1-ol was proposed based on the reaction products and reaction principles. Compared with the traditional method, this simple experimental procedure, rapid reaction, high yield, and easy product detection could be expected to contribute to the development of a clean and environmentally benign strategy for the rearrangement of 1-ethynylcyclohexan-1-ol.

Acknowledgements. This research was supported by the Na-

tional Natural Science Foundation of China (Nos. 21073064, 21003049).

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