

BASE-CATALYZED REACTIONS IN NEAR-CRITICAL WATER FOR ENVIRONMENTALLY BENIGN CHEMICAL PROCESSING

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INTRODUCTION

Water has recently attracted much interest as an environmentally benign solvent for organic syntheses [1,2]. While many of the previous studies have been devoted to water near ambient conditions, it exhibits more favorable characteristics as a medium for organic reactions when it is closer to its critical point (near-critical water) but still in the liquid state. First, the solubility of organic substances in water increases considerably with increasing temperature due to a decrease in dielectric constant. For liquid water at 250 °C the dielectric constant is comparable to that of ambient acetone [3]. Conversely to acetone, product separation from the solvent can occur simply by phase separation upon returning to ambient conditions. Secondly, the ionization constant of near-critical water is several orders of magnitude higher than that of ambient water, thus providing a source of hydronium and hydroxide ions, which can act as catalytically active species in chemical conversions. As shown in previous studies in our group [4,5] acid catalyzed reactions, such as Friedel-Crafts alkylations, can be successfully accomplished in near-critical water with less or even without added catalyst. Thirdly, while reactions in supercritical water have mainly been applied in chemical reactions to break up bonds, e.g., for waste destruction by supercritical water oxidation (SCWO) [6,7], the milder temperature regime of hot liquid water allows for bond formation, i.e., the synthesis of organic compounds.

In this study we aimed at scouting the opportunities to perform organic syntheses in near-critical water that are usually conducted in the presence of base. Based on earlier work by *Katritzky, Siskin et al.* [8], aldol condensations have been chosen as first examples because the reactants are not subject to immediate hydrolysis, and different products can be formed. In the classical preparation methods the selectivity for the products is determined, e.g., by the reaction temperature and by the pH during the work-up procedure. Selectivity for those products might therefore give insight into the effect of water as the reaction medium on product distribution. The aldol condensation of phenylacetaldehyde has been studied in further detail, including different reaction times, reactant concentrations, and in the presence of added acid and base. The scope of this type of reaction has also been explored for some condensations between different reactants. Other synthetically important C-C bond formation reactions involve hydrolyzable compounds, such as esters, and as examples the Dieckmann condensation and typical malonic ester syntheses have been included in the present study to encompass the scope of reactions accessible in near-critical water.

EXPERIMENTAL SECTION

The reactions have been carried out in the batch mode using Titanium vessels (rated to 1 kbar at 500 °C) with an inner volume of 3 ml. After loading, these reactors have been placed in a preheated aluminum block where they reached the desired reaction temperature within ca. 5 min. After stopping the reaction by quenching the reactors in a room temperature water bath, the reactor contents were dissolved in acetone and diluted to a known volume. For determination of product distribution versus time several vessels were loaded in the same manner and have been quenched at different reaction periods. Product analysis was achieved via temperature-programmed capillary GC equipped with an FID or an MS detector and product distribution are given in terms of mole fractions.

All chemicals were ACS grade (Aldrich) and were used as received. Water to be used as reaction solvent was HPLC grade (Aldrich) and was used without further purification. As shown in previous experiments, both deoxygenation of the water and loading under nitrogen atmosphere did not afford a change in the obtained product of more than experimental accuracy.

In a typical run at 275 °C a reactor is loaded at ambient conditions with 1.8 ml liquid reactant/water mixture with a molar ratio of 1/47. Accounting for the expansion of the water with increasing temperature the reactor at 275 °C contains 2.6 ml liquid phase and a small gas phase.

RESULTS AND DISCUSSION

Aldol condensations

The aldol condensation of *n*-butyraldehyde is industrially carried out in the presence of caustic sodium to produce 2-ethyl-2-hexenal. This is later hydrogenated to 2-ethylhexanol which is esterified with phthalic acid to give the plasticizer dioctylphthalate (DOP) [9]. If *n*-butyraldehyde is reacted for 15 hrs at 275 °C in water, essentially complete conversion is obtained without the addition of any catalyst. The main product is, like in the conventional synthesis, 2-ethylhexanal (selectivity 85 %). Some 2-butyl-2-butanone is also formed by double

bond isomerization of the former. Other byproducts with selectivities < 2 % are the dialdolization product, triethylnaphthalene and cis/trans isomers of the formed olefins.

As already pointed out by *Katritzky et al.* [10] phenylacetaldehyde (PAA) is a highly reactive compound and a reaction scheme (Figure 2) has been provided by these authors. The distribution of some key intermediates for the conversion of PAA in water at 275 °C as a function of reaction time is shown in Figure 1. From this Figure it can be clearly seen that products **1** and **2** formed by two aldol reaction steps and subsequent double bond isomerization are intermediate products in the formation of 1,3,5-triphenylbenzene as proposed by the reaction scheme. In addition to the main reaction products observed by *Katritzky et al.* [10] we have also found 2-phenylnaphthalene which can be formed by ring closure of the aldol reaction and subsequent dehydration and isomerization. The presence of small amounts of 2-phenyldihydronaphthalene provides further evidence for the formation of 2-phenylnaphthalene. 2-Phenylnaphthalene is the major reaction product when PAA is converted in the presence of hydrochloric acid (Table 1) and otherwise constant reaction conditions. With added NaOH as a base, however, 1,3-diphenylpropane is the main reaction product and no 2-phenylnaphthalene is observed. Table 1 also shows the influence of the PAA concentration: While higher dilution of the reactant does not afford a considerable change in the product distribution, a higher reactant concentration leads to a lower conversion and lower mole fractions of products formed in subsequent reactions.

Ketones are less reactive in aldol-type reactions than aldehydes. Although acetone is readily converted in near-critical water to mainly mesityloxide, 1-phenyl-2-butanone (PBO) does not undergo any reaction at 275 °C after 24 hrs, and a conversion of only about 15 % is reached in the presence of added NaOH ($n_{\text{PBO}}/n_{\text{NaOH}} = 1/0.5$). Nearly 50 % conversion of PBO is obtained without further addition of base, when it is reacted with benzaldehyde as a more active carbonyl compound. Table 2 summarizes the main products resulting from aldol type C-C bond formations in the conversions of acetone and PBO with benzaldehyde. In accordance with the results reported by *Katritzky, et al.* [11] benzaldehyde alone undergoes primarily Cannizzaro reaction and disproportionation in an overall low conversion (< 5 %) to yield benzoic acid, benzylalcohol, and toluene, respectively.

Dieckmann condensation

Many base catalyzed involve the conversion of hydrolyzable compounds, such as esters in the Claisen condensation [12]. To test whether such reactions can be carried out in near-critical water at 275 °C the Dieckmann condensation of adipic acid and its dimethyl and diethyl ester has been attempted without any added catalyst. Both esters undergo hydrolysis to the monoester and adipic acid, respectively, and, the diethyl ester hydrolyzes slower than the methyl derivative, as expected. It should be noted, however, that even after 16 hrs at 275 °C this hydrolysis is not complete, leaving about a third of the overall adipic acid at the mono- or the diester. Besides hydrolysis the main products were cyclopentanone and benzoic acid. Cyclopentanone is the expected product, if the base-catalyzed ring closure is followed by decarboxylation, which is facilitated at the elevated temperature. More cyclopentanone is formed when the ester hydrolysis is less pronounced, i.e., with diethyl adipate as reactant. With adipic acid the formation of benzoic acid is strongly favored over the formation of cyclopentanone, but the cyclopentanone yield is comparable to the one achieved with the esters. The overall yield of cyclopentanone in all cases is, however, comparably low (< 2 %).

Knoevenagel condensation

The condensation of a carbonyl compound with a malonic ester is a useful tool in the synthesis of substituted organic acids, often referred to as "malonic ester syntheses" [12]. By this method cinnamic acid can be obtained from the conversion of a malonic acid ester with benzaldehyde followed by hydrolysis and decarboxylation. With malonic acid as the reactant, water as the solvent and in the absence of added base, the main product of the conversion is styrene as well as the products arising from self reaction of benzaldehyde (Table 3). Although the desired C-C bond formation has occurred, decarboxylation apparently is the strongly favored reaction under these reaction conditions. In addition to an overall higher conversion than with malonic acid, the use of disodium malonate instead of malonic acid resulted predominantly in an increased formation of benzylalcohol most probably due to the reduction of benzaldehyde, accompanied by the production of carbon dioxide. 2-Methyl-1-propenylbenzene and isobutyric acid were the major products in the conversion of benzaldehyde with dimethyl malonate in near-critical water. The formation of these products involve a series of condensation, hydrolysis, and decarboxylation reactions.

The conversion of benzylaldehyde with diphenylmethane in water at 275 °C did not result in the formation of any detectable condensation product. Presumably the ions from the dissociation of water can neither deprotonate diphenylmethane, nor activate the benzaldehyde carbonyl group to an extent sufficient to bring about the desired reaction.

CONCLUSIONS

Near-critical water is a promising and environmentally benign reaction medium for a number of synthetically important conversions that are conventionally carried out in the presence of base. Due to the high ionization of water these conversions may be accomplished without further addition of base, especially in the when reactive carbonyl compounds and substrates with sufficiently high C-H acidity are involved.

It has been shown that C-C bond formations can be brought about in near-critical water in syntheses that involve hydrolyzable compounds like esters. Decarboxylation, which was indicated to be a limiting factor in these reactions, might be reduced by pressurizing the reaction vessels with carbon dioxide and lowering the reaction temperature. At lower temperature the solubility of the organic reactants might, however, also be considerably reduced. Therefore, more detailed information on the phase behavior of organic substances relevant to chemical synthesis is needed. Investigations are currently underway in our laboratory.

Although the spectrum of prospective reactants might be limited to those thermally stable at temperatures up to ca. 300 °C, the lower cost of the reactants and the solvent, the ease of carrying out the reaction and product separation as well as the opportunity to reduce, if not completely avoid the addition of a catalyst render near-critical water an profitable alternative to many less favorable solvents currently used in chemical processes.

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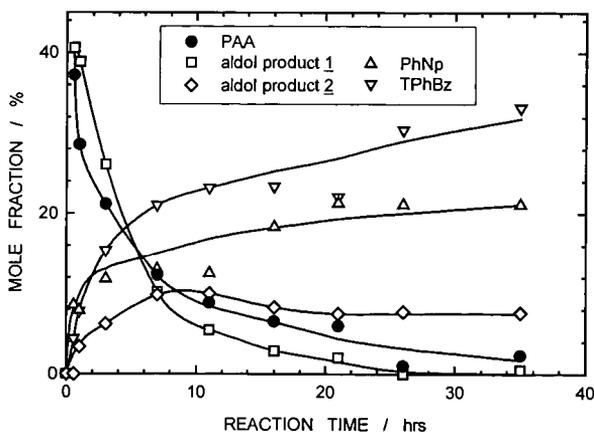


Figure 1: Distribution of major products as a function of reaction time for the conversion of phenylacetaldehyde (PAA) in near-critical water at 275 °C ($n_{\text{PAA}}/n_{\text{H}_2\text{O}} = 1/50$); PhNp: 2-phenylnaphthalene, TPhBz: 1,3,5-triphenylbenzene, aldol product 1 and 2: see Figure 2.

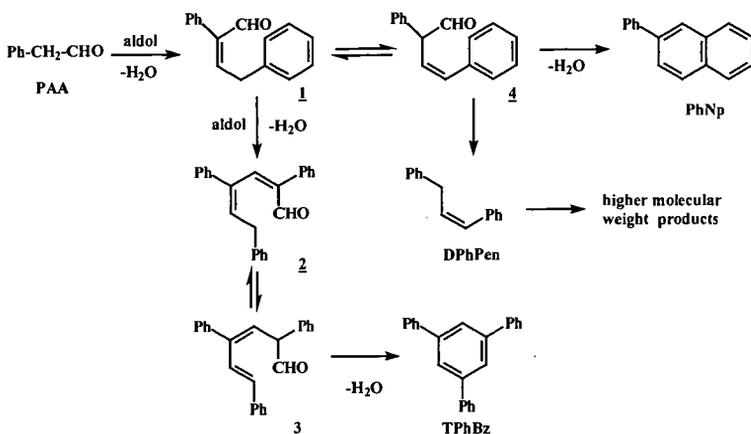


Figure 2: Reaction scheme of major condensation products in the conversion of phenylacetaldehyde after [10]; PAA: phenylacetaldehyde, PhNp: 2-phenylnaphthalene, TPhBz: 1,3,5-triphenylbenzene, DPhPen: 1,3-diphenylpropene.

Table 1: Mole fractions (in %) of key products in the conversion of PAA in near-critical water at 275 °C ($n_{PAA}/n_{H_2O} = 1/50$) after 16 hrs in the absence and presence of added acid and base and at different starting concentrations of PAA.

compound	pure water	added NaOH;		added HCl;	PAA concentration	
		n_{PAA}/n_{NaOH} 1/0.5	1/0.05		n_{PAA}/n_{H_2O} 1/100	1/25
PAA	6.5	0.9	1.0	< 0.1	7.0	22.6
PhNp	18.3	< 0.1	< 0.1	91.5	18.0	25.3
DPhPen	6.9	53.2	30.7	0.2	11.2	15.7
TPhBz	23.3	17.1	24.2	0.8	27.3	13.4
aldol product <u>2</u>	8.3	< 0.1	2.9	4.9	5.3	3.2

Table 2: Main Products in crossed aldol condensations of benzaldehyde in near-critical water at 275 °C ($n_{PAA}/n_{H_2O} = 1/50$) after 16 hrs.

reactants	Main products (mole % of total product)
PhCHO/ PhCH ₂ COCH ₂ CH ₃	PhCH=C(Ph)COCH ₂ CH ₃ (16); PhCH=C(Ph)CO(CH ₂) ₂ CH ₂ C=CH(Ph) (30); PhCH=CH(Ph) (31)
PhCHO/H ₃ CCOCH ₃	PhCH=CHCH ₂ COCH ₃ (69); PhCH=CHCH ₂ COCH ₂ CH=CH(Ph) (9)

Table 3: Products in the conversion of benzaldehyde with malonic acid and disodium malonate in near-critical water at 275 °C after 16 hrs (mole % of total product).

reactants	PhCH=CH ₂	PhCH ₂ OH	PhCOOH
PhCHO/CH ₂ (COOH) ₂	52	25	9
PhCHO/CH ₂ (COONa) ₂	3	3	1