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Organic synthesis in subcritical water Oxidation of alkyl aromatics

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Abstract

The ability of sub- and supercritical water to solubilize both functionalized aromatic compounds and molecular oxygen was exploited for its use as a solvent to perform oxidative modification of a number of compounds. Alkyl aromatic compounds were oxidized to aldehydes, ketones and acids by molecular oxygen mediated by transition metal catalysts in subcritical water. A number of alkyl aromatics were oxidized directly to their acids, including *p*-xylene, *o*-xylene, *m*-xylene, ethylbenzene, and toluene. Alternatively, conditions were discovered which allowed the oxidation reactions to stop at the aldehyde stage. In addition, several aromatic methylenes could be oxidized to ketones, and anthracene could be oxidized to anthraquinone under the same conditions. The syntheses were performed in 10 ml stainless steel and Hastelloy-C 276 batch reactors between 300 and 355°C with up to five equivalents of O₂. The reactions were found to be very sensitive to the nature of the catalysts, with MnBr₂ and CoBr₂ providing the cleanest reactions and highest yields. Other metal salts led to severe charring or coupling reactions. © 1998 Elsevier Science B.V. All rights reserved.

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1. Introduction

The use of supercritical fluids as a medium for chemical reactions has recently received a great deal of attention [1–3]. The dramatic decrease in solvent viscosity, increase in substrate solubility, and enhanced sensitivity of solvating properties of the supercritical fluid to temperature and pressure make them attractive as potential solvents. Many studies have focused on the use of supercritical CO₂ as a solvent [4,5], however, its limited polarity

impairs its ability to solubilize functional substrates although recent work has shown that CO₂ can solubilize polar compounds with the aid of surfactants and polymers [6].

In this research, we have focused on the use of sub/supercritical water as a solvent for organic reactions. The dielectric constant of water decreases dramatically as it approaches its critical point (374°C and 218 atm), allowing it to solubilize organic molecules. Most polar organics become completely miscible, while many non-polar compounds also dissolve sufficiently [7,8]. This property suggests that subcritical or supercritical water may be used as a possible replacement for environ-

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mentally unacceptable solvents for a number of synthetic organic reactions. Here, we report on the successful use of subcritical water as a solvent for a number of important synthetic oxidation reactions.

Oxidation in supercritical water has previously been used for the destruction of toxic organic waste, and recent studies have shown that such reactions are efficient and clean processes [2,9]. A recent review illustrates the usefulness of metal catalyst in the destructive oxidation of organic compounds in supercritical water [10]. However, limited synthetic chemistry has been carried out in sub- or supercritical water [11–14]. Oxidation is of particular interest since oxygen is highly soluble in sub- and supercritical water, and many homogeneous organic oxidations of industrial importance have been traditionally performed in either aromatic or halogenated solvents. To demonstrate that sub- or supercritical water can be a viable replacement for such environmentally undesirable solvents, we have undertaken the study of some simple synthetic organic oxidations, i.e. the selective oxidation of alkyl aromatics in subcritical water using molecular oxygen as the oxidant. A major concern in using subcritical water is that the high temperatures and relatively harsh conditions might lead to a complex mixture of products, or massive decomposition of the substrate, particularly in the presence of molecular oxygen. Preliminary results indicated, however, that under the proper conditions the desired products can be isolated in high purity and good yields, thereby demonstrating that subcritical water is an attractive medium for synthetic oxidations.

2. Materials and methods

The water used in the reported experiments was distilled over KMnO_4 , neutralized, degassed with argon and stored under argon to eliminate CO_2 and any other organic impurities. All organic reagents were ordered from Aldrich Chemical, Inc. (Milwaukee, WI) and used as received. The metal catalysts were obtained from Strem Chemical Inc. (Newburyport, MA) and used as received. Oxygen was obtained from Sunox Gases (Charlotte, NC)

at a 99.99% purity. The reactor consisted of a 9/16 in OD, 5/16 in ID, 8 in long tube capped at one end with a reducing adapter to a valve at the other end (High Pressure Equipment, Erie, PA). The total volume of a completely assembled vessel was 10.1 ml having a pressure rating of 20 000 psi (at 40°C), utilizing coned and threaded seats. Vessels were constructed of either 316 stainless steel and Hastelloy-C 276 alloy. A thermocouple (1/16 in, type K, Inconel sheath) can be placed inside the vessel through the capped end to measure the temperature of the water. Microanalyses were performed at Atlantic Microlabs, Norcross, GA. GC/MS analysis was performed on a Hewlett Packard 5890 GC using a 10 m SE-30 column coupled to a Hewlett Packard 5970 Mass Selective Detector. Proton NMR was performed on a 300 MHz Bruker AC 300 NMR.

In a typical reaction, i.e. the oxidation of *p*-xylene to terephthalic acid, the oxidation was performed by adding 4.0 ml water, 0.5 ml (4.1 mmol) *p*-xylene and 0.21 mmol catalyst into a high pressure reaction vessel under nitrogen. The vessel was pressurized with 1000 psi (16.4 mmol) oxygen and placed in a tube furnace preheated to 375°C. The internal operating pressure of this vessel is about 3500 psi at its maximum operating temperature. This estimate is based on the initial water volume, oxygen pressure, and the temperature of the system. (Extreme caution should always be exercised when working at high temperatures and pressures. It is imperative that only the best quality components are employed, and great care is used in designing experiments to provide generous margins of safety.) After an appropriate amount of time (see Table 1), the vessel was removed from the oven and cooled under a stream of air until cool to the touch (approximately 15 min), and the product was separated from the water layer by traditional organic techniques (i.e. filtration, extraction, etc.). Oxidation of *o*-xylene, *m*-xylene, 1,3,5-trimethylbenzene (mesitylene), toluene, ethylbenzene, fluorene, diphenyl methane, anthracene, and dibenzyl was performed in a similar manner. The reaction products were analyzed and their identity verified by use of GC/MS, NMR, thin layer chromatography, and elemental analysis.

Table 1
Reaction conditions and yields for subcritical water oxidations

Reactant	Catalyst (eq.) ^a	O ₂ (eq.) ^b	Time (min)	% Yield product(s)
<i>p</i> -xylene	0.05 ^c	4.0	40	64% terephthalic acid ^c 14% <i>p</i> -toluic acid ^d 3% <i>p</i> -tolualdehyde ^d
	0.05 ^g	3.0	25	24% <i>p</i> -tolualdehyde ^d 24% <i>p</i> -toluic acid ^d
<i>m</i> -xylene	0.05 ^c	3.2	60	16% isophthalic acid ^c 4% <i>m</i> -tolualdehyde ^d
	0.025 ^c	3.0	30	20% <i>m</i> -tolualdehyde ^d 10% <i>m</i> -toluic acid ^d
	0.01 ⁱ			
<i>o</i> -xylene	0.06 ^c	4.0	60	62% benzoic acid ^d 26% <i>o</i> -toluic acid ^d 1% <i>o</i> -tolualdehyde ^d
mesitylene	0.075 ^c	3.6	50	3.5% trimesic acid ^c
toluene	0.025 ^c	4.5	50	63% benzoic acid ^d 1% benzaldehyde ^d
	0.015 ^h	1.5	25	30% benzaldehyde ^d 10% benzoic acid ^d
ethylbenzene	0.05 ^c	1.5	60	24% acetophenone ^d 1% benzoic acid ^d
fluorene	0.09 ^f	1	30	63% fluorenone ^c
anthracene	0.09 ^f	2	40	50% anthraquinone ^d
diphenylmethane	0.18 ^f	1	30	65% benzophenone ^d <1% benzaldehyde ^d
dibenzyl	0.18 ^f	2	60	50% benzoic acid ^d <1% diphenylethandione ^d 1% benzophenone ^d

^a Molar equivalents of catalyst.

^b Molar equivalents of molecular oxygen.

^c Yield based on gravimetric analysis.

^d Relative yield based on GC/MS analysis.

^e MnBr₂ as catalyst.

^f CoBr₂ as catalyst.

^g Co(OAc)₂ as catalyst.

^h CuBr as catalyst.

ⁱ Mn(OAc)₃ as catalyst.

Unreacted starting materials account for remaining material balance.

3. Results and discussion

A listing of the reagents, times, and results used in the reactions can be seen in Table 1. This table shows that a number of alkyl aromatic compounds were oxidized to aldehydes, ketones, and acids by molecular oxygen in subcritical water mediated by various transition metal catalysts. Most of the alkyl aromatics were oxidized to their corresponding acids in reasonable yields between 40 and 60 min. Additionally, conditions, such as time of reaction, type of catalyst, and amount of oxygen,

could be altered to yield partial oxidation products like aldehydes. Aromatic methylenes were oxidized to ketones in reasonable yields between 30 and 40 min.

The actual temperature of the water utilized for conducting these reactions is time dependent and listed in Table 2. The final temperature of the water is dependent on the length of time the vessel is in the oven. In this particular set-up, the vessel never truly reaches supercritical conditions. However, reactions are occurring at subcritical conditions. The lowest temperature at which a

Table 2
Rise of reaction vessel temperature inside oven^a

Time (min)	Temperature (°C)
10	198
20	268
30	313
35	324
40	333
45	341
50	346
55	350
60	352
65	354

^a Reaction vessel fitted with a thermocouple containing 4 ml water placed in a furnace preheated to 375°C. Time equals the time of reaction; temperature is actual reading of water inside the vessel.

noticeable reaction occurred was $\sim 300^\circ\text{C}$, where the hottest temperature needed for these oxidations was 350°C . These aromatic compounds become completely soluble in water at or above 300°C [8], hence temperatures above the critical point of water are not needed to initiate these reactions. Further, this eliminates or limits the pyrolysis of reactants or products in the system. In addition, subcritical water is also more attractive for industrial use because it requires less energy input and limits metallurgical corrosion seen at higher temperatures.

The stainless steel vessels used in the above reactions showed slight signs of deterioration after a large number of reactions (40–50) and a brown powder started to contaminate the reactions after this time. Energy dispersive X-ray analysis in a scanning electron microscope of the brown powder indicated that it had approximately the same metal composition as 316 stainless steel. The use of a Hastelloy-C vessel (316 stainless steel is an iron based alloy whereas Hastelloy-C is a nickel based superalloy that is much more resistant to oxidation than stainless steel) eliminated this contamination, producing much cleaner reactions and a slight improvement in yields. Hastelloy-C's resistance to oxidation means there is more oxygen available for the reactions compared to stainless steel. This could account for the slight increase in yields in the Hastelloy vessels. In addition, these vessels

show no sign of deterioration even after a large number (50–60) of reactions.

In the presence of an appropriate catalyst, a variety of methyl aromatics could be cleanly oxidized to the corresponding aromatic acids, as shown in Fig. 1. These reactions are assumed to occur through a free radical mechanism [15]. A number of different catalyst systems were investigated, and these studies showed that the bromide salt of either Mn(II) or Co(II) must be utilized in order to facilitate the complete oxidation of the alkyl methyl to the carboxylic acid. These catalysts are similar to those used in the industrial production of terephthalic acid (TPA) using acetic acid as a solvent [16]. If KBr was used as the catalyst, the yield of the desired products was almost non-existent. A wide variety of first row transition metal halides, in particular bromide salts, were investigated, and Mn(II) was found to provide the best yield to the acid. The use of Fe(II) or Ni(II) salts produced large amounts of carbonaceous material. If $\text{Mn}(\text{OAc})_2$ was used instead of the bromide salt, the yield of acid was reduced significantly. This suggests that the mechanism is free radical in nature, with the metal acting as an initiator in the process, and the bromide as a chain propagator. However, it is difficult to study the reaction mechanism in such a non-traditional solvent system. In the absence of a catalyst, control of the reaction is lost, and the starting materials are either recovered unchanged or pyrolyzed to char. It should be noted that one of the useful properties of water near its supercritical state is its very high heat capacity [17]. This ability of supercritical water to absorb heat may be responsible for our observation that the reactions can be controlled, and do not undergo runaway oxidation, even at high oxygen pressure.

Of particular interest was the oxidation of *o*-xylene, in which the major product was benzoic acid instead of phthalic acid. There was a noticeable amount of head pressure after the reaction was completed, and further analysis showed that it was mostly carbon dioxide. From this observation, the *o*-xylene is most likely first oxidized to the diacid, followed by thermal decarboxylation at the *ortho* position. In support of this postulate we found that a phthalic acid standard decarboxylates

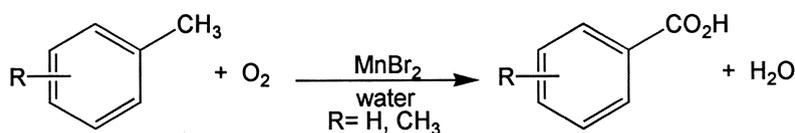


Fig. 1. Oxidation of methyl aromatics to acids.

in subcritical water to form CO₂ and benzoic acid. By contrast, *m*-xylene is not readily oxidized; with the diacid being formed only in low yield. This may be attributed to the fact that there is no resonance stabilization of the radical intermediate at the *meta* position as seen at the *ortho* and *para* position.

A number of other alkyl aromatics can be selectively oxidized at the alpha position. For example, the reaction of ethylbenzene leads to clean formation of acetophenone with no evidence of the formation of phenylethanoic acid (Fig. 2). In this case, increasing the oxygen pressure or using longer reaction times leads to the formation of benzoic acid. The oxidation of ethylbenzene to acetophenone shows a selectivity toward oxidation of the alpha carbon. This suggests the formation of the more stable benzylic carbon radical intermediate rather than the formation of a primary carbon radical intermediate.

Aromatic methylenes can also be selectively oxidized to ketones. Use of MnBr₂ as a catalyst leads to oxidation to the corresponding aromatic acids. However, the use of CoBr₂ as an alternative catalyst leads to the desired ketone products. Although relatively good yields of ketones were obtained, it appears that these products are somewhat unstable in the batch reactor, as they start to decompose after 30 to 40 min reaction time. Such decompositions are why the reaction yield never exceeds 65% in this type of reaction. This result suggests that yields could be increased sub-

stantially if a flow reactor were used instead of a batch reactor, due to the flow system's ability to remove the product from the heated zone before it had time to decompose.

It was also noted that toluene could be selectively oxidized to benzaldehyde in modest yield. The most efficient catalyst for this reaction was found to be CuBr. For production of the aldehyde, it was found that the reaction time and amount of oxygen had to be reduced relative to that needed for benzoic acid formation. In the case of the oxidation of dibenzyl, however, it appears that the desired product, diphenylethandione, is unstable under the reaction conditions employed. Apparently, it is rapidly oxidized to benzoic acid through cleavage of the ethylene bridge and our attempts to terminate the reaction at the diketone stage were unsuccessful. It was also noted that anthracene could be oxidized cleanly to anthraquinone using the same conditions. This reaction occurred readily despite the fact that the aromaticity of the center ring is destroyed in the oxidation.

4. Conclusions

In summary, we have shown that subcritical water can be used as a synthetic medium for reactions involving highly non-polar substrates. This research also demonstrates that selective oxidation can be performed and controlled in subcritical water on a number of different aromatic

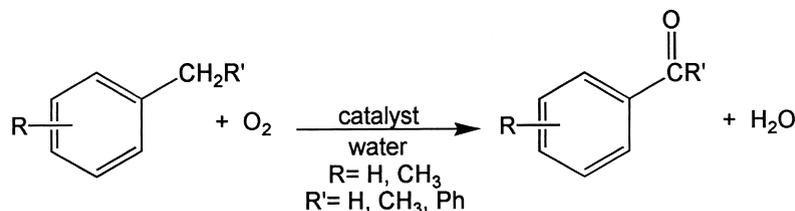


Fig. 2. Oxidation of alkyl aromatics.

substrates, leading to formation of oxidized products. The large heat capacity of subcritical water facilitated control of the oxidation of the reaction substrates and prevented irreversible pyrolysis of the substrate to CO₂ or char in the presence of heat and oxygen. Research is continuing in our laboratories to determine the scope and limitations of subcritical and supercritical water as a solvent for conducting organic oxidations as well as other traditionally non-aqueous organic reactions.

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