

Alkylation and Acetal Formation Using Supercritical Alcohol without Catalyst

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The aromatic ring alkylation of phenols, *N*-alkylation of aniline, *O*-alkylation of phenols and acetal formation from acetaldehyde or acetone were examined using supercritical (SC) alcohol without any catalyst. Highly selective syntheses of monoalkylated compounds were achieved for the aromatic ring alkylation and *N*-alkylation. The *O*-alkylation proceeded more preferentially than the aromatic ring alkylation for phenols which have a deactivating group. The acetal formation went on in more than 96% selectivity.

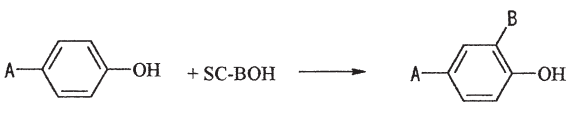
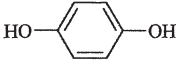
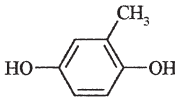
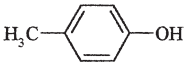
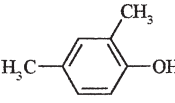
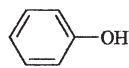
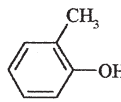
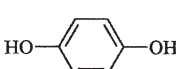
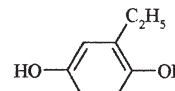
The alkylation of an aromatic ring or a functional group is an important reaction in the chemical industry. At the present time, toxic alkylating reagents, such as alkyl halides and dialkylsulfates, are often used along with a catalyst but have to change to less hazardous substances in the near future. Recently, supercritical alcohols have attracted much attention due to their high reactivity and relatively small impact on the environment. There are some literatures on the reactions of supercritical methanol or ethanol: the esterification of fatty acids,¹ the transesterification of polyethylene terephthalate² and the depolymerization of phenol resin³ without any catalyst. Supercritical alcohol can significantly accelerate the reaction, keeping a high selectivity. The analysis of the reaction mechanism begins on a molecular level. Several reports are available on the microscopic properties of supercritical alcohols which have been carried out mainly by spectroscopic techniques.^{4,5} For example, about 70% of the hydrogen bonding network among methanol molecules are broken at the critical point to produce dimers and monomers. As a result, the reactivity of the alcohol molecules increases significantly and the catalyst is not needed because the molecules can move fast and collide strongly with other molecules. Here, we report our preliminary results of the cleaner, uncatalyzed and selective alkylation and acetal formation with supercritical alcohol, where supercritical alcohol was used not only for an alkylating or acetal formation reagent but also for a reaction solvent.

The reactions with supercritical alcohol were conducted using a batch-type reactor made of 316 stainless steel and with an inner volume of 20 cm³. The experimental procedure was as follows: The test compound of 0.1 g and methanol of about 5.5 g were loaded into the reactor. The air in the reactor was replaced with argon gas. The reactor was sealed and immersed into a sand bath, which was already heated to the reaction temperature. A small amount of alcohol was added to the reactor to get the desired reaction pressure for a specified reaction temperature. After the desired reaction time, the reactor was removed from the sand bath and cooled quickly in water to stop the reaction. The reaction time was defined as the duration for which the reactor was kept in the sand bath. Subsequently, the solution sample was collected with alcohol and analyzed by GC, GC-MS, and LC.

The performance of supercritical methanol (critical temperature = 239.4 °C, critical pressure = 8.1 MPa)⁶ and ethanol

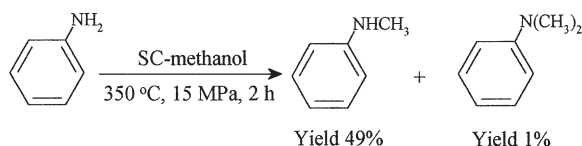
(critical temperature = 240.7 °C, critical pressure = 6.1 MPa)⁶ as alkylating reagents was investigated to evaluate the possibility of alternatives to hazardous compounds such as dimethylsulfate or methyl iodide. First, the alkylation of the aromatic ring of phenols was examined. The experimental results are given in Table 1. The Friedel-Crafts alkylation using a Lewis acid is well known. Compared with the traditional Friedel-Crafts reaction, alkylation using the supercritical alcohol did not require any catalyst. Furthermore it is remarkable that only a monoalkylated compound was synthesized in the reaction of hydroquinone with supercritical alcohol, while the Friedel-Crafts reaction gives the complex product mixture of mono- and polyalkylated compounds. A maximum yield of 15% was obtained for hydroquinone. The order of the reactivity of the aromatic compounds was hydroquinone > *p*-cresol > phenol, which agreed with the order of the activation of the aromatic ring by hydroxy and methyl-activating groups. On the other hand, the yield of the reaction of hydroquinone with supercritical ethanol was only 6% under the same conditions. The reactivity of supercritical ethanol was smaller than that of supercritical methanol.

Table 1. Alkylation of aromatic ring of phenols with supercritical alcohol^a

			
Aromatics	SC alcohol	Product	Yield / %
	CH ₃ OH		15
	CH ₃ OH		2
	CH ₃ OH		Trace
	C ₂ H ₅ OH		6

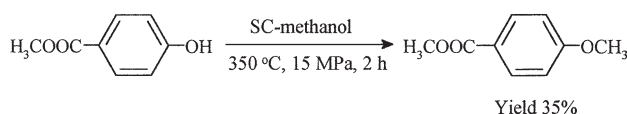
^aThe reaction was carried out at 350 °C, 15 MPa, and 2 h.

Secondly, *N*-alkylation was investigated. The *N*-alkylation of aniline proceeded using supercritical alcohol without any catalyst.



In the case of supercritical methanol, 49% of aniline was converted to *N*-methyl aniline with the selectivity of 98% and 1% of aniline to *N,N*-dimethyl aniline with the selectivity of only 2%, and methylated aromatic compounds were not detected. In the case of supercritical ethanol, the yields of *N*-ethyl aniline and *N,N*-diethyl aniline were 20% and zero at the same condition as that of methanol. The reactivity of supercritical ethanol was smaller than that of supercritical methanol.

The third example was the etherification of a phenol compound. Methyl *p*-hydroxybenzoate reacted with supercritical methanol to produce an ether compound.



The conversion was 35% and methylated aromatic compounds were not detected. The deactivating group, such as the ester group, could suppress the aromatic ring methylation. Figure 1 shows the temperature dependence of the product yield. The etherification did not occur until 270 °C, and then the yield increased steeply. The reaction of supercritical ethanol with the same hydroxy ester did not proceed at the same condition. The reactivity of supercritical ethanol was smaller than the supercritical methanol in the same manner as the alkylation of the

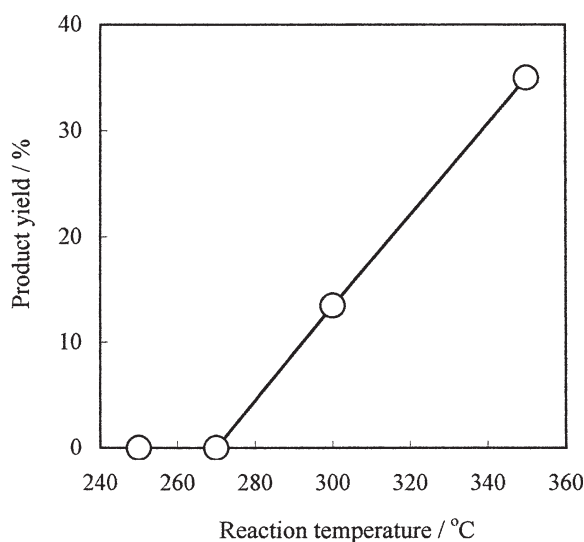
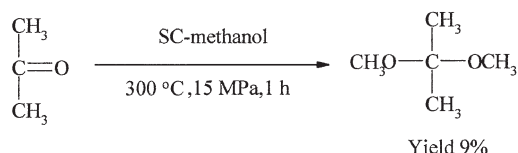


Figure 1. Temperature dependence of product yield of etherification of supercritical methanol and methyl *p*-hydroxybenzoate.

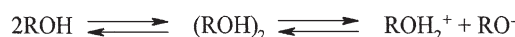
aromatic ring and *N*-alkylation.

The last example was acetal formation. Acetaldehyde and acetone converted to 1,1-dimethoxyethane with 10% of yield and 2,2-dimethoxypropane with 9% of yield by the supercritical methanol without catalyst respectively. The reactions proceeded a little more easily than the other methylations mentioned above. The reaction temperatures and times were lower and shorter than others.



The acetal formation of acetone with supercritical ethanol did not occur at the same condition of 300 °C and 15 MPa as supercritical methanol, but proceeded at 350 °C and 22 MPa for 1 h. The acetone conversion was 27%.

The reaction mechanism by the supercritical alcohol without catalyst is probably an electrophilic substitution for the alkylation and a nucleophilic addition for the acetal formation. One of the possible mechanisms of uncatalyzed alkylation and acetal formation can involve the autoprotolysis of the alcohol given by



The protonated alcohol cation may act as an electrophile for the alkylation of the aromatic ring, amino group and hydroxyl group. On the other hand, the alkoxide anion may act as a nucleophile for the acetal formation. The autoprotolysis constant, which is defined by $[\text{ROH}_2^+][\text{RO}^-]$, is related to the amount of protonated alcohol and alkoxide ions in the corresponding alcohol. Methanol⁷ with larger constant of 0.20×10^{-16} can produce more ions than ethanol with smaller constant of 0.79×10^{-19} . As a result, the product yields of supercritical methanol are always higher than those of supercritical ethanol.

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