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Transformation of benzonitrile into benzyl alcohol and benzoate esters in supercritical alcohols

Takashi Kamitanaka[a,b,*], Kenji Yamamoto[b], Tomoko Matsuda[c], Tadao Harada[b,*]

[a] Industrial Research Center of Shiga Prefecture, Kamitoyama, Ritto, Shiga 520-3004, Japan
[b] Department of Materials Chemistry, Ryukoku University, Seta, Otsu, Shiga 520-2194, Japan
[c] Department of Bioengineering, Graduate School of Bioscience and Biotechnology, Tokyo Institute of Technology, Yokohama 226-8501, Japan

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ABSTRACT

The reactions of benzonitrile in supercritical methanol, ethanol, and 2-propanol were investigated under non-catalytic conditions. In supercritical methanol, benzonitrile was converted to methyl benzoate in high yield. The esterification reaction also occurred in supercritical ethanol to afford ethyl benzoate in moderate yield. The esterification could occur via a route analogous to the Pinner reaction. On the other hand, benzonitrile in supercritical 2-propanol yielded no ester. Benzyl alcohol was the major product in supercritical 2-propanol. We investigated the reaction of the C=N bond in supercritical 2-propanol. In supercritical 2-propanol, *N*-benzylideneaniline was transferred to the reduction product (*N*-benzylaniline) and hydrolysis products (benzyl alcohol and aniline). The hydrolysis reaction was restricted when the reaction was carried out in supercritical 2-propanol with a low water content. This indicates that the water in the 2-propanol acts as a reagent for the hydrolysis of the C=N bond. These results suggested the following reaction process: $C_6H_5C{\equiv}N \rightarrow C_6H_5CH{=}NH \rightarrow C_6H_5CHO \rightarrow C_6H_5CH_2OH$.

1. Introduction

Supercritical or high-temperature water is a candidate reagent for the transformation of nitrile into the corresponding amide or carboxylic acid at high temperature.[1] Izzo et al. investigated the kinetics and mechanisms for the hydrolysis of aliphatic and aromatic nitriles in high-temperature water.[2] They proposed an autocatalytic mechanism. This process requires no further addition of a catalyst to promote the reaction because of high acidity of the supercritical water.

Supercritical alcohols tend to be reactive with nitriles as well as supercritical water. Supercritical alcohols function as reducing agents for ketones and aldehydes.[3–5] We have reported the direct additions of alcohol molecules to alkenes or alkynes to form a carbon–carbon bond.[6] Poly(ethylene terephthalate) is depolymerized by methanolysis in supercritical methanol.[7] Surprisingly, these reactions are carried out under non-catalyzed conditions. This indicates that supercritical alcohols have high reactivities toward unsaturated bonds.

As mentioned above, the reactions of the C=O, C=C, C≡C or COOR group with supercritical alcohols have been reported. However, no reactions of the C≡N bonds with supercritical alcohols have been reported. We now report the reactions of benzonitrile with supercritical alcohols to afford benzoate esters or/and benzyl alcohol. The preferential products were dependent on the kind of supercritical alcohol.

The critical conditions of the alcohols used in this study are as follows: methanol (critical temperature T_c=513 K, critical pressure p_c=8.1 MPa, critical density ρ_c=0.272 g cm^{-3}), ethanol (T_c=516 K, p_c=6.3 MPa, ρ_c=0.276 g cm^{-3}), and 2-propanol (T_c=508 K, p_c=4.8 MPa, ρ_c=0.273 g cm^{-3}).

2. Results and discussion

2.1. Reactions of benzonitrile in supercritical methanol, ethanol, and 2-propanol

The behavior of benzonitrile in supercritical methanol, ethanol or 2-propanol was examined in detail, and it was found that the transformation of benzonitrile occurred in the supercritical alcohols. The preferential product was strongly dependent on the kind of supercritical alcohol. The time courses of the reactions of benzonitrile in supercritical methanol, ethanol, and 2-propanol are shown in Figure 1a–c, respectively. The rate of disappearance of the benzonitrile in supercritical methanol was much higher than that in supercritical ethanol or supercritical 2-propanol. Benzonitrile in supercritical methanol exclusively afforded methyl benzoate

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* Corresponding authors. Tel.: +81 77 558 1500; fax: +81 77 558 1373 (T.K); tel.: +81 77 543 7461; fax: +81 77 543 7483 (T.H).

E-mail addresses: kamitanaka.takashi@shiga-irc.go.jp (T. Kamitanaka), harada@rins.ryukoku.ac.jp (T. Harada).

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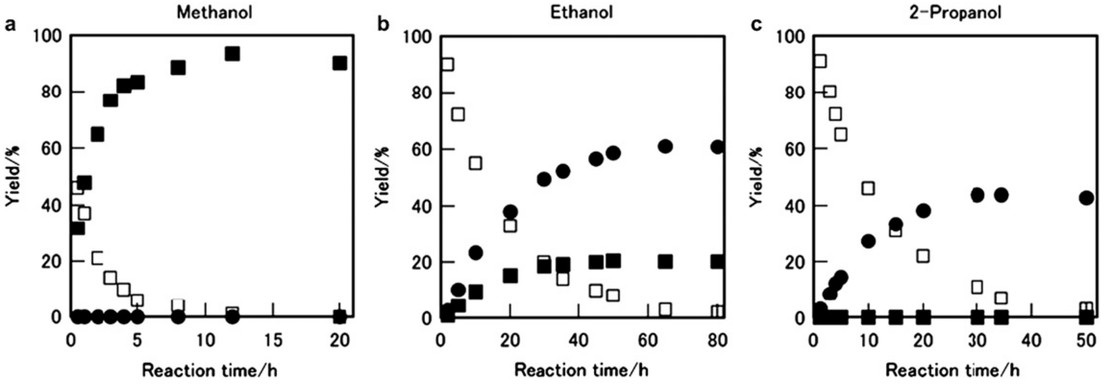


Figure 1. Time courses of the reactions of benzonitrile in supercritical (a) methanol, (b) ethanol, and (c) 2-propanol at 623 K; □ benzonitrile, ● benzyl alcohol, ■ benzoate ester.

(around 95% yield). On the other hand, the major product of the reactions between benzonitrile and supercritical ethanol or 2-propanol was benzyl alcohol. The reactions in supercritical 2-propanol afforded no ester. We found that the esterification also proceeded for an aliphatic nitrile, i.e., lauronitrile, in supercritical methanol. However, the maximum yield was much lower than that for benzonitrile. The yield was 24% at 623 K for a 6-h reaction.

The effects of the density of supercritical alcohol on the conversion of benzonitrile and yield of benzoate ester were investigated by carrying out the reactions of benzonitrile in supercritical methanol. These results are shown in Table 1. At the reaction time of 5 h, an increase in the density of supercritical methanol (0.20→0.30 g cm^{-3}) resulted in a drastic increase in the conversion (39→94%) and the yield (31→83%).

2.2. Mechanistic aspects

2.2.1. *Esterification*

There have been various reports on the transformation of the C≡N bond into COOR. One of the well-known reactions is the Pinner reaction.[8,9] When a nitrile is treated with hydrochloric acid in an alcohol, the nitrile is converted into an ester. Scheme 1 shows a plausible mechanism. The HCl functions as a H$^+$ donor to the C≡N bond, and the primary or secondary alcohol functions as an alcoholysis agent for the C≡N$^+$ bond. The resulting intermediate (hydrochloride salt of iminoester) can be converted into the carboxylic ester with H_2O and HCl, which functions as a catalyst in this step.

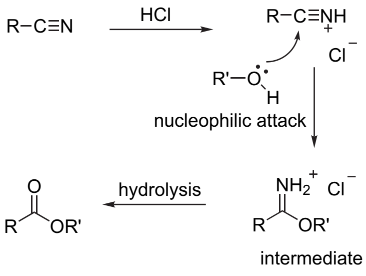
Table 1
Effects of the density of supercritical methanol on conversion of benzonitrile and yield of methyl benzoate

Density[a] (g cm^{-3})	Conversion[b] (%)	Yield[b] (%)
0.20	39	31
0.25	75	68
0.30	94	83

Reaction conditions: temperature 623 K, reaction time 5 h.

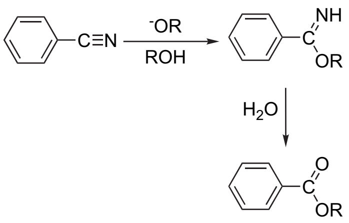
[a] Density of methanol solution in the reactor tube during the reaction.

[b] Conversion and the yield of methyl benzoate were determined by gas chromatography.



Scheme 1. Plausible mechanism for esterification of nitriles (Pinner reaction).

Based on the mechanism for the Pinner reaction, the following mechanism can be proposed for the esterification of benzonitrile in supercritical methanol (Scheme 2). During the first step, protonation on the C≡N nitrogen and attack of the alkoxide ions in an alcoholic solution to the C≡N carbon occur to form an imino ester. The imino ester is then hydrolyzed to a carboxylic ester with water in the reaction system.

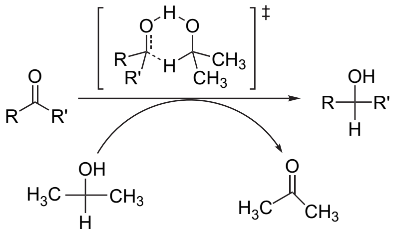


Scheme 2. Plausible mechanism for the esterification of benzonitrile using supercritical alcohol.

The concentrations of the alcohols are 24.7 mol/l for methanol, 17.2 mol/l for ethanol, and 13.1 mol/l for 2-propanol at 298 K. In addition, Reeve et al. reported that the relative acidity of the alcohols for methanol, ethanol, and 2-propanol are 4.4, 1.0, and 0.24, respectively.[10] These indicate that the concentration of alkoxide ion in methanol is much higher than those in ethanol and 2-propanol. The alkoxide concentration order may also be valid for the alcohols in the supercritical state. It can be assumed that the high concentration of methoxide ion in supercritical methanol is responsible for the rapid formation of methyl benzoate. On the other hand, in supercritical ethanol, the concentration of the alkoxide ion is much lower, and then the rate of esterification is slower; it is likely that another reaction (benzyl alcohol formation) also occurs in parallel to the esterification. In supercritical 2-propanol, the concentration of the alkoxide ion may be too low for the esterification. Indeed, acetone is converted into 2,2-dimethoxypropane with a high selectivity through attack on the carbonyl carbon by methoxide ions in supercritical methanol,[11] whereas no acetal was obtained in supercritical 2-propanol.[3–5] Steric hindrance with alkyl substituents of alcohols might also be ascribed to the product distribution; the more bulky substituents there are at the hydroxyl-bearing carbon, the less likely the alcohol will approach the C≡N carbon. From the viewpoint of steric-hindrance, the reactivity order is also methanol>ethanol>2-propanol. This is the same order as that of the alkoxide concentration mentioned above.

2.2.2. Benzyl alcohol forming reaction

We reported the non-catalytic reduction of carbonyls to the corresponding alcohols using supercritical 2-propanol.[3–5] This involves the simultaneous hydrogen transfer via a six-membered transition state analogous to that of the Meerwein–Ponndorf–Verley reduction (Scheme 3). It could be expected that the reduction of nitriles to the corresponding amines occurs by a similar mechanism. However, no amine generation was observed in the reactions of benzonitrile in supercritical 2-propanol (Fig. 1c). Alternatively, benzyl alcohol was obtained as the main product in 43% yield for a 40-h reaction. Concerning the reduction of nitriles to alcohols, Takahashi et al. reported that the reaction of nitriles in 2-propanol over hydrous zirconium oxide in the vapor phase afforded the corresponding alcohols.[12] These facts suggest that it is unlikely for nitriles to be reduced to the corresponding amines by alcohols.



Scheme 3. Meerwein–Ponndorf–Verley type reduction of ketone using supercritical 2-propanol.

Taking into account that the C=O bond is hydrogenated to CH–OH by supercritical alcohols, the C≡N bond would be hydrogenated to CH=NH by supercritical alcohols. Thus, it can be presumed that benzonitrile in supercritical alcohol is transformed into the benzyl alcohol through the following route: $C_6H_5C{\equiv}N \rightarrow C_6H_5CH{=}NH \rightarrow C_6H_5CH{=}O \rightarrow C_6H_5CH_2OH$. Imines can be easily hydrolyzed to the corresponding aldehydes and amines.[13] Hence, the transformation of $C_6H_5CH{=}NH$ to $C_6H_5CH{=}O$ will occur with H_2O in 2-propanol (less than 0.2%). Unfortunately, $C_6H_5CH{=}NH$ is unstable for investigating its reactivity. We selected substituted $C_6H_5CH{=}NC_6H_5$ (*N*-benzilideneaniline) instead of naked $C_6H_5CH{=}NH$ to investigate the reactivity of the C=N bond in supercritical 2-propanol, because the C=N bond in substituted $C_6H_5CH{=}NC_6H_5$ is more resistant than in the naked $C_6H_5CH{=}NH$ due to conjugation of the C=N bond with two phenyl groups. Table 2 shows the results of the reaction of $C_6H_5CH{=}NC_6H_5$ in supercritical 2-propanol at 623 K.

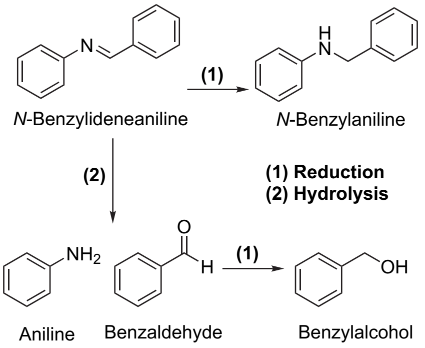
N-Benzylideneaniline was converted into *N*-benzylaniline, benzyl alcohol, and aniline. The resistance of *N*-benzylideneaniline to hydrolysis would result in the formation of *N*-benzylaniline. Plausible reaction routes of *N*-benzylideneaniline to *N*-benzylaniline, aniline, and benzyl alcohol are shown in Scheme 4.

To investigate the hydrolysis step for the reaction of benzonitrile to benzyl alcohol, we carried out the reaction of *N*-benzylideneaniline in dehydrated 2-propanol (H_2O content: less than 0.005%).[14] This result is also shown in Table 2. The generation of benzyl alcohol and aniline was suppressed under the dehydrated conditions. This indicates that the water in the reaction system functions as a reagent for the benzyl alcohol formation.

Table 2
Reaction of *N*-benzylideneaniline in supercritical 2-propanol

Alcohol	Conversion (%)	Yield (%)		
		N-Benzyl aniline	Aniline	Benzyl alcohol
2-Propanol	84	32	23	29
Dehydrated 2-propanol	67	41	4	3

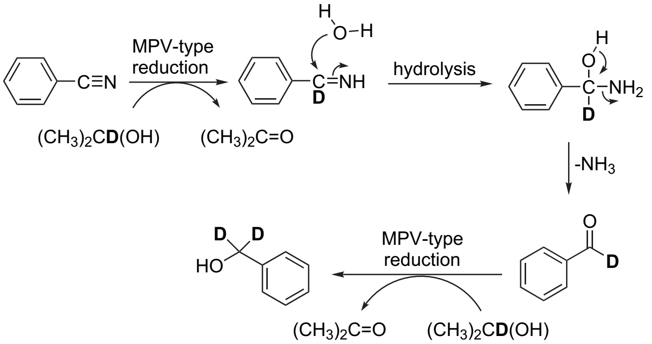
Reaction conditions: temperature 623 K, reaction time 3 h.



Scheme 4. Plausible reactions of *N*-benzylideneaniline with supercritical 2-propanol.

It is well known that the transformation of $C_6H_5CH{=}NH$ to $C_6H_5CH{=}O$ is extremely easy in the presence of water. Nevertheless, there was no detectable peak of benzaldehyde in the GC analysis.[15] This finding suggests that $C_6H_5CH{=}O$ readily reacts with supercritical 2-propanol to yield $C_6H_5CH_2OH$, and the step of $C_6H_5C{\equiv}N$ to $C_6H_5CH{=}NH$ is the rate-determining one in the transformation of $C_6H_5C{\equiv}N$ to $C_6H_5CH_2OH$.

The deuterium tracer study using $(CH_3)_2CD(OH)$ was applied to the reactions of benzonitrile with supercritical 2-propanol with the expectation of proving the reaction route from benzonitrile to benzyl alcohol via $C_6H_5CH{=}NH$ and $C_6H_5CH{=}O$. If the transformation of benzonitrile to benzyl alcohol proceeds through the above route, the two D atoms will be incorporated into the benzylic position of the benzyl alcohol as shown in Scheme 5. The results are shown in Table 3. The integration of the peak area for the benzylic position on the ^1H NMR spectrum suggested that deuterium atom was indeed incorporated into the benzylic position by around 80%. No H/D exchange occurred on the benzyl alcohol, when it was treated with supercritical $(CH_3)_2CD(OH)$ at 623 K (entry 2 in Table 3). This fact indicated that the deuterium atom was incorporated into the benzyl alcohol during the reaction route from benzonitrile to benzyl alcohol. These results support the idea that the benzyl



Scheme 5. Plausible mechanism for the benzyl alcohol formation (deuterium trace reaction).

Table 3
Deuterium contents at benzylic position of benzyl alcohol[a]

Entry	Reaction	D at benzyl position (%)
1[b]	Ph–CN → Ph–CH_2OH	80
2[c]	Ph–CH_2–OH in sc $(CH_3)_2CD(OH)$	0

[a] Deuterium contents were quantified by ^1H NMR.

[b] Benzonitrile was reacted in supercritical $(CH_3)_2CD(OH)$ at 623 K for 8 h. The benzyl alcohol was isolated by thin layer chromatography (Merck silica gel precoated plate, eluent: *n*-hexane/AcOEt=5:1, R_f=0.24 (benzyl alcohol), 0.45 (benzonitrile)).

[c] $(CH_3)_2CD(OH)$ solution of benzyl alcohol was maintained at 623 K for 8 h.

alcohol forming reaction mainly proceeds via the route shown in Scheme 5.

3. Conclusions

The treatment of benzonitrile with supercritical methanol, ethanol or 2-propanol resulted in the formations of the benzoate ester or/and benzyl alcohol. The esterification of benzonitrile in supercritical methanol and ethanol occurred in high (up to 93%) and low (up to 20%) yields, respectively. On the other hand, no ester generation was observed in supercritical 2-propanol. The rate of ester formation may depend on the amount of the alkoxide ion in the alcohol solution. The transformation of benzonitrile into esters is explained on the basis of a mechanism analogous to that for the Pinner reaction. The benzyl alcohol generation occurred in supercritical 2-propanol and ethanol. The study under dehydrated conditions and the deuterium tracing one suggested that the transformation from benzonitrile to benzyl alcohol proceeded via the route of $C_6H_5C{\equiv}N \rightarrow C_6H_5CH{=}NH \rightarrow C_6H_5CH{=}O \rightarrow C_6H_5CH_2OH$.

4. Experimental section

4.1. Materials

Materials were purchased from Nacalai Tesque, Inc. and used without further purification. Dehydrated 2-propanol was purchased from Wako Pure Chemical Industry. The water content was below 50 ppm.

4.2. Procedure for the reaction of benzonitrile in supercritical alcohol

Alcoholic solutions of benzonitrile were prepared at a concentration of 10 mmol dm^{-3}. A 0.12 ml portion of the alcoholic solution was pipetted into a Pyrex glass tube, and the air in the tube was replaced by argon gas and fused shut under reduced pressure in order to close the open end of the tube (2.0-mm i.d., 4.0-mm o.d., ca. 70-mm length). The tube and appropriate amounts of methanol, to prevent the tube from breaking during the reaction, were placed in an autoclave (stainless steel 316, 30 ml of inner volume). The autoclave was heated by an electric furnace. The reaction time was set to zero when the temperature reached the desired value. The temperature in the autoclave reached 623 K in 20 min. After a specific reaction time had elapsed, the autoclave was removed from the furnace and cooled by a strong air stream to quench the reaction.

4.3. Analysis

A 25 μl portion of the reaction solution in the tube was poured into a test tube and a 25 μl aliquot of the solution of bibenzyl (internal standard; 10 mmol dm^{-3}) was added to the tube. The solution was subjected to analysis by the gas chromatography (Shimadzu GC-15A, capillary column, i.d. 0.32-mm, liquid phase DB-17, film thickness 0.5-μm, length 30-m). The quantitative analyses were performed by the internal standard method. The identification of the products was performed by GC–MS and ^1H NMR analyses, if necessary.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.04.029.

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14. Water content in commercially available 2-propanol is less than 0.5%.
15. For gas chromatogram of the reaction solution and authentic benzaldehyde, see Supplementary data.