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## Direct addition of supercritical alcohols, acetone or acetonitrile to the alkenes without catalysts

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**Abstract**—The reactions of the alkenes with supercritical organic compounds under non-catalytic conditions were investigated. The H and CR<sub>2</sub>OH, CH<sub>2</sub>C=OCH<sub>3</sub> or CH<sub>2</sub>C $\equiv$ N of supercritical alcohols (CHR<sub>2</sub>OH), acetone (CH<sub>3</sub>C=OCH<sub>3</sub>) or acetonitrile (CH<sub>3</sub>C $\equiv$ N) added to the C=C bonds of alkenes form C–C bonds between the  $\alpha$ -carbons of the supercritical organic compounds and the sp<sup>2</sup> carbons of the alkenes.

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To build carbon skeletons from smaller units, it is absolutely necessary to form carbon-carbon bonds between them. Consequently, C-C bond forming reactions are among the most important organic reactions. Recently, the applications of supercritical fluids<sup>1</sup> were used for the C–C bond forming reactions. For example, the Heck reaction,<sup>2</sup> the Friedel–Crafts reactions,<sup>3,4</sup> the Cannizzaro-type reaction,<sup>5</sup> and Diels-Alder reaction<sup>6</sup> were successfully attempted using supercritical water as the reaction medium without catalysts. The C-C bond forming reactions in hot water (below the critical temperature) were also reported. For example, dichloromethane converts to glycolic acid via the C-C bond forming reaction in hot water.<sup>7</sup> The C–C bond forming reactions in supercritical or hot water afforded the expected products in sufficient yields and selectivities. The use of supercritical fluids for the C–C bond forming reactions as reaction media or reaction species is a promising version-up of the reactions from an environmental point of view.

We have previously reported the reduction of unsaturated bonds with supercritical alcohols.<sup>8-10</sup> The C=C

and C=O bonds were reduced to the CH–CH and CH–OH bonds, respectively. When supercritical 2-propanol (critical temperature:  $T_c = 508$  K, critical pressure:  $P_c = 4.76$  MPa) was used as the reducing reagent, the reduction of C=O to CH–OH proceeded smoothly,<sup>9,10</sup> but the reduction of the C=C bond to the CH–CH bond did not proceed smoothly.<sup>8</sup> One of the major reactions of the C=C bond with supercritical alcohol was a C–C bond forming reaction (Scheme 1). For example, the H and CH<sub>3</sub>CHOH group of supercritical ethanol ( $T_c = 514$  K,  $P_c = 6.15$  MPa) added to the C=C bond of styrene to afford its  $\alpha$ -hydroxyethylated derivative, 4-phenyl-2-butanol.

In a previous paper, we reported that the hydroxyalkylation of the C=C bonds of alkenes or alkynes containing conjugate phenyl group(s) proceeded more smoothly than that of the C=C bonds of alkenes containing an



Scheme 1. Hydroxyalkylation of styrene with supercritical alcohols.

*Keywords*: Carbon–carbon bond forming reaction; Supercritical fluid; Hydroxyalkylation; Acetonylation; Uncatalyzed reaction.

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unconjugated phenyl group. Herein, we now report the hydroxyalkylation of the C=C bonds of styrene and alkenes containing no phenyl group. Moreover, we also report the C-C bond forming reaction between the C=C bond and supercritical acetone ( $T_c = 508 \text{ K}$ ,  $P_c = 4.70 \text{ MPa}$ ) or acetonitrile ( $T_c = 548 \text{ K}$ ,  $P_c = 4.83 \text{ MPa}$ ).

The reactions were conducted using glass capillary tubes (0.2 cm inner diameter, 7.0 cm length). The reaction solutions of the alkenes were loaded into the tubes. The air in the tube was replaced with argon gas and the tube was sealed by fusing. The tube was placed in an autoclave (stainless 316) with methanol that prevents breaking of the tube due to high pressure during the reaction. The autoclave was heated by electric furnace and maintained at 623 K. After 2-20 h, the autoclave was cooled to quench the reaction. Quantitative analysis of the products was conducted by GC-FID using the internal standard method. The products were identified by the GC-retention times to those of the authentic samples. Some products were separated by thin layer chromatography and identified by the <sup>1</sup>H NMR and GC-MS.

Table 1 shows the results of the hydroxyalkylation of styrene and aliphatic alkenes with supercritical alcohols.

As previously reported,<sup>8</sup> the hydroxyalkylation of styrene (**1a**) with supercritical methanol ( $T_c = 513$  K,  $P_c = 8.10$  MPa), ethanol and 2-propanol proceeded at 623 K (entries 1–3). Although most of the C–C bond forming reactions require reagents and/or catalysts to activate the reaction position of the reagents, this reaction requires no reagents and catalysts other than the alcohols and the alkenes. Thus, the post-treatment is

extremely simple. In these reaction systems, ethylbenzene and toluene were generated. Dehydrogenation of methanol to give formaldehyde was also confirmed.<sup>11</sup> Ether formation between the alcohol molecules is also a possible side reaction.<sup>12</sup> However, the concentrations of these compounds are negligible to that of the hydroxyalkylated products.

Recently, the rhodium-catalyzed hydroxyalkylation of the C=C bond with alcohols was reported in which the styrenes were converted to the corresponding hydroxyalkyl derivatives with up to approximately 70% yields.<sup>13</sup> In spite of the fairly good yields, this procedure has the problem of recycling the Rh catalyst. As far as aliphatic alkenes are concerned, one example is described in the report (2-methylpropene, yield: 31%).

The hydroxyalkylation of the C=C bond with supercritical alcohol occurs by the fission of  $\alpha$ -C-H bond of supercritical alcohol. We examined the reaction of styrene with supercritical  $\alpha$ -deuterio-2-propanol. The yield of the hydroxyalkyl derivative **3c** (entry 4) was much lower than the yield with the non-deuterated 2-propanol under the same reaction conditions. This indicates that the fission of the  $\alpha$ -C-H bond of 2-propanol occurs during the rate determining step.

Next, we attempted the hydroxyalkylation of aliphatic alkenes to extend the application of this reaction. Two aliphatic alkenes, **1b** and **1c**, were employed as the substrates of the hydroxylalkylation with supercritical ethanol and 2-propanol at 623 K (entries 5–7). The yields were much lower than the yield from the hydroxy-alkylation of styrene (**1a**) with ethanol or 2-propanol.

Table 1. Hydroxyalkylation of C=C bonds using supercritical alcohols under non-catalytic conditions<sup>a</sup>

Entry	Substrate	Supercritical alcohol	Reaction time (h)	Conversion (%)	Product	Yield <sup>c</sup> (%)
1	Ph 1a	CH <sub>3</sub> OH <b>2a</b>	2	39	Ph OH 3a	6
2	Ph 1a	СН <sub>3</sub> СН <sub>2</sub> ОН <b>2b</b>	2	>99	Ph OH 3b	56
3	Ph 1a	(CH <sub>3</sub> ) <sub>2</sub> CHOH <b>2c</b>	2	>99	Ph OH 3c	70
4	Ph 1a	(CH <sub>3</sub> ) <sub>2</sub> CDOH <b>2d</b>	2	65	Ph OH 3c	27
5	() 3 1b	СН <sub>3</sub> СН <sub>2</sub> ОН <b>2</b> b	20	n.d. <sup>b</sup>	←) <sub>5</sub> OH 3d	37
6	() 3 1b	(CH <sub>3</sub> ) <sub>3</sub> CHOH <b>2c</b>	20	n.d. <sup>b</sup>	CH 3e	12
7	$\left\langle \cdot \right\rangle_{7}$ 1c	(CH <sub>3</sub> ) <sub>3</sub> CHOH <b>2c</b>	20	100	() <sub>9</sub> OH 3f	13
8	Ph 1a	CF <sub>3</sub> CH <sub>2</sub> OH 2e	20	100	Ph OH 3g	26

<sup>a</sup> Reaction conditions: concentration of alkene in the alcohol at room temperature was  $0.10 \text{ mol dm}^{-3}$ , a 0.14-mL portion of the alcoholic solution was enclosed in the glass tube (inner diameter 2.0 mm, length 70 mm), the reaction temperature was 623 K.

<sup>b</sup> Conversion could not be determined because the GC-peak of the substrate overlapped with that of the diluent for the GC analysis.

<sup>c</sup> Yields were evaluated by GC (Shimadzu GC-15 A, capillary column DB-17); the yields were calculated based on the alkenes.

Table 2. Direct addition of	supercritical acetor	he and acetonitrile to	the alkenes <sup>a</sup>
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Entry	Substrate	Supercritical fluid	Reaction time (h)	Conversion (%)	Product	Yield <sup>b</sup> (%)
1	Ph 1a	(CH <sub>3</sub> ) <sub>2</sub> C=O <b>4</b>	2	91	Ph 6a	40
2	$\begin{pmatrix} \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\$	(CH <sub>3</sub> ) <sub>2</sub> C=O 4	2	85		63
3	→ 1d	(CH <sub>3</sub> ) <sub>2</sub> C=O 4	2	78	()5	49
4	Ph 1a	CH <sub>3</sub> CN 5	10	97	Ph CN 7	44

<sup>a</sup> Reaction conditions: temperature, 623 K; concentration of alkenes in the solution at room temperature, 0.10 mol dm<sup>-3</sup>.

<sup>b</sup> Yields were evaluated by GC (Shimadzu GC-15A, capillary column DB-17); the yields were calculated on the basis of the alkenes.

The compounds possessing CF<sub>3</sub> groups have been a subject of growing interest from both chemical and biological points of view due to their characteristic chemical properties and medicinal uses.<sup>14</sup> Thus, we carried out the reaction of **1a** with 2,2,2-trifluoroethanol (**2e**:  $T_c = 499 \text{ K}$ ,  $P_c = 4.87 \text{ MPa})^{15}$  to determine if the 1,1,1-trifluoro-2-alkanols can be obtained by the reaction of the terminal alkene with 2,2,2-trifluoroethanol. The reaction was carried out under the same conditions as the reaction of 1a with 2b. The product 3g possessing a CF<sub>3</sub> group was obtained in the yield of 26% (entry 8). Generally, the introduction of a CF<sub>3</sub> group into organic molecules is complicated.<sup>16</sup> For example, 1,1,1-trifluoro-2-alkanols can be prepared in 60-80% overall yield by the reaction between alkyl magnesium bromide and lithium trifluoroacetate, and the successive NaBH4 reduction of the C=O group.<sup>17</sup> The Grignard reaction and the NaBH<sub>4</sub> reduction are not suitable for a large scale preparation. On the other hand, the hydroxyalkylation of the C=C bond with supercritical 2,2,2-trifluoroethanol is a promising procedure for the large scale preparation of 1,1,1-trifluoro-2-alkanols because the 1,1,1-trifluoro-2-alkanols can be prepared in one step without reagents other than the terminal alkene and 2,2,2-trifluoroethanol. However, the optimization of the reaction conditions should be required for improving the reaction yield.

Several reports have described that acetone can be directly added to alkenes using a silver catalyst<sup>18</sup> or by photo-irradiation.<sup>19</sup> Based on the findings that a supercritical alcohol can be directly added to the C=C bond, we expected the direct addition of supercritical acetone to the C=C bond without a catalyst and by photo-irradiation. When the alkenes were treated with supercritical acetone, the alkenes were acetonylated in moderate yields; that is,  $C=C+CH_3C=OCH_3 \rightarrow$ CH-C-CH<sub>2</sub>COCH<sub>3</sub>. These results are shown in entries 1–3 in Table 2. The alkenes containing no conjugate phenyl group were more smoothly acetonylated than styrene. The formations of the aldol products between the acetone molecules were also confirmed.<sup>20</sup> Like the reaction of styrene with supercritical alcohols or acetone, acetonitrile under supercritical conditions can

also be directly added to 1a to afford 7 in 44% yield (entry 4).^{21}  $\,$ 

In summary, we have developed new C–C bond forming reactions with alkenes via the fission of the  $\alpha$ -C–H bond of supercritical alcohols, acetone and acetonitrile. Our results showed that the supercritical fluids can act not only as unique reaction media, but also as powerful reagents for organic syntheses. A more detailed and wide-spread investigation of these reactions is now in progress.

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concentration of formaldehyde in the methanol recovered from the supercritical reaction was higher than that of the authentic methanol. Nash's method, see: Nash, T. *Biochem. J.* **1953**, *55*, 416–421.

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- Formation of toluene was confirmed as a by-product in 21% yield. Condensation products of acetonitrile molecules were not detected by the GC analysis.