Strong Base Catalysis of Sulfated Mesoporous Alumina for the Tishchenko Reaction in Supercritical Carbon Dioxide

Tsunetake Seki and Makoto Onaka*

Department of Chemistry, Graduate School of Arts and Sciences, The University of Tokyo, Komaba, Meguro, Tokyo 153-8902

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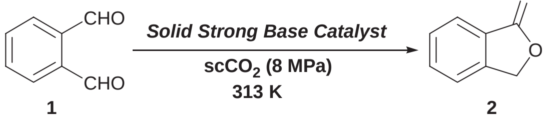
Heterogeneous strong base catalysis for the Tishchenko reaction in acidic $scCO_2$ solvent has been realized with mesoporous alumina modified with SO_4^{2-}, while a conventional solid base like CaO showed almost no catalytic performance in $scCO_2$.

The supercritical fluid (SCF) medium has recently attracted much attention as the fourth phase for performing chemical synthesis besides gas, liquid, and solid phases. The physical properties of an SCF can be continuously varied from those analogous to gases to those to liquids by manipulating its pressure and temperature, hence SCFs are expected to comprise a unique heterogeneous catalytic system that enhances reaction rate and product selectivity in comparison with conventional organic solvents.[1] Among the SCFs, supercritical carbon dioxide ($scCO_2$) is the most attractive as a reaction medium because of the low critical temperature (304 K) and pressure (7.4 MPa), as well as the nontoxic and nonflammable nature and low cost. The following characteristics of $scCO_2$ are advantageous especially for heterogeneous catalytic reactions that proceed in the nano-sized pores of zeolites and mesoporous materials: 1) the high ability to dissolve or extract a variety of organic compounds, 2) the high diffusivity and the low viscosity that improve mass transfer of reactants and products, and 3) the high thermal conductivity that can efficiently eliminate the reaction heat.

CO_2 is notorious as a poison for heterogeneous base-catalyzed reactions:[2] upon exposure of a solid base to CO_2, the acidic CO_2 molecules are promptly adsorbed on basic sites of the solid base, and hinder its base catalysis. Therefore, an attempt to perform base-catalyzed reactions in $scCO_2$ seems reckless, but is certainly a challenging theme in catalysis chemistry.

Here we wish to report that sulfated mesoporous alumina (designated as $meso\mathrm{Al_2O_3/SO_4^{2-}}$) can act as a solid strong base catalyst even in acidic $scCO_2$; $meso\mathrm{Al_2O_3/SO_4^{2-}}$ exhibits the highest catalytic performance in $scCO_2$ for the intramolecular Tishchenko reaction of aromatic dialdehydes, which is a typical solid base-catalyzed reaction and normally performed by strong base sites (O^{2-}) on metal oxides (Scheme 1).[2,3]

Firstly, we applied CaO prepared by thermal decomposition of $Ca(OH)_2$ to the transformation of *o*-phthalaldehyde (**1**) into phthalide (**2**) in $scCO_2$ (Table 1, Entry 1), because CaO exhibited the highest activity for this reaction in benzene solvent.[3c,3d] However, the reaction in $scCO_2$ hardly proceeded presumably due to the prompt formation of the inert material of $CaCO_3$ on the CaO surface. This result indicated that solid strong bases like alkaline earth oxides[2] were inadequate for base-catalyzed reactions in acidic $scCO_2$. We next tested three types of γ-aluminas, ALO-2, -3, and -4[5] in the reaction: ALO-2 is contaminated with a few weight percent of SO_4^{2-} ions; ALO-3 includes Na^+ ions; and ALO-4 is almost pure γ-alumina. The three aluminas showed noticeable differences in the catalytic activity, depending on the kind of impurities: ALO-2 showed quite high activity in $scCO_2$ (Entry 2), while more basic aluminas, ALO-3 and -4, gave poor catalysis (Entries 3 and 4).



Scheme 1.

Table 1. Catalytic activities of CaO, aluminas, and sulfated aluminas for the intramolecular Tishchenko reaction of *o*-phthalaldehyde (**1**) to phthalide (**2**) in supercritical carbon dioxide[a]

Entry	Catalyst[b] (Al/SO_4^{2-})[c]	Surface area[d] /$m^2 g^{-1}$	Pore diameter[e] /nm	Yield[f]/%
1	CaO[g]	48	—	1
2	ALO-2	312	—	62 (64[h])
3	ALO-3	129	—	<1
4	ALO-4	173	—	12 (15[h])
5	$meso\mathrm{Al_2O_3}$	474	2.7	51 (59[h])
6	$meso\mathrm{Al_2O_3/SO_4^{2-}}$-I (89)[c]	532	2.9	66
7	$meso\mathrm{Al_2O_3/SO_4^{2-}}$-II (45)[c]	567	2.4	62
8	$meso\mathrm{Al_2O_3/SO_4^{2-}}$-III (6)[c]	570	3.4	73 (81[h])

[a] In a 10-mL stainless steel autoclave, an activated solid base catalyst (0.050 g) and **1** (1.00 mmol) were stirred in $scCO_2$ at 8.0 ± 0.2 MPa at 313 K for 2 h.[4] [b] Each catalyst was pretreated at 773 K for 2 h under vacuum (10^{-2} Pa) prior to use. [c] Initial mixing molar ratios of $Al(O\text{-}sec\text{-}Bu)_3/SO_4^{2-}$ in preparation. [d] Determined by BET method. [e] Determined by DH method. [f] Determined by ^1H NMR using Ph_3CH as an internal standard. [g] Prepared from $Ca(OH)_2$ at 873 K for 2 h under vacuum (10^{-2} Pa). [h] Reaction time was 4 h.

It seems that SO_4^{2-} ions in ALO-2 decrease the basic nature of the alumina surface through the electron-withdrawing inductive effects,[2a,6] resulting in the prevention of the adsorption of acidic CO_2 onto the surface. The nature of ALO-2 has guided our investigation to develop a new solid strong base catalyst that would efficiently function in acidic $scCO_2$.

Interestingly, we found that mesoporous alumina ($meso\mathrm{Al_2O_3}$) possessing uniform nano-sized pores prepared from $Al(O\text{-}sec\text{-}Bu)_3$ through sol–gel process[7] promoted the reaction (Entry 5), even though the $meso\mathrm{Al_2O_3}$ included no sulfate ions.[8] The yield of 51% with $meso\mathrm{Al_2O_3}$ was much higher than that of 12% with pure γ-alumina, ALO-4.

This finding encouraged us to further develop $meso\mathrm{Al_2O_3}$-based solid base *intentionally* modified with SO_4^{2-} ions to achieve higher catalytic performance. We introduced sulfate ions into the framework of *meso*Al_2O_3, not on its surface, in a similar way as in the preparation of sulfated zirconia aerogels,[9] because **1** requires close contact with a metal oxide surface in the Tishchenko reaction.[2,3] A mesoporous alumina containing $SO_4{}^{2-}$ ions (*meso*$Al_2O_3/SO_4{}^{2-}$-I) was successfully synthesized by the hydrolysis of Al(O-*sec*-Bu)$_3$ with deionized water containing H_2SO_4,[8] and it showed a higher yield of 66% than the non-sulfated *meso*Al_2O_3 (Entry 5 vs 6). It is noteworthy that an increase in the amount of $SO_4{}^{2-}$ in *meso*Al_2O_3 (*meso*$Al_2O_3/SO_4{}^{2-}$-II)[8] brought about an increase in the surface area, but a decrease in the yield, presumably owing to some reduction of the surface basicity (Entry 7). *meso*$Al_2O_3/SO_4{}^{2-}$-III was synthesized with relatively a large amount of $Al_2(SO_4)_3$ in place of H_2SO_4 as a sulfate source,[8] having a higher surface area than the other aluminas. With *meso*$Al_2O_3/SO_4{}^{2-}$-III an introduction of sulfate ions into the alumina framework[8] led to not only an expansion of a surface area of mesoporous alumina, but also the highest yield of **2** (Entry 8), indicating that *meso*$Al_2O_3/SO_4{}^{2-}$-III has the most suitable basic character for the Tishchenko reaction in acidic $scCO_2$.

Although $scCO_2$ is an ideal reaction medium for organic reactions, in some cases we encounter lack of dissolving power of $scCO_2$ for polar organic substrates. The use of a co-solvent is one of workable solutions to overcome the problem.[1] Table 2 shows the effect of co-solvents on the *meso*$Al_2O_3/SO_4{}^{2-}$-III-catalyzed reaction. It should be noted that a drastic increase in the reaction rate was observed when a small amount of benzene or tetrahydrofuran (THF) was added as a co-solvent (Entries 2 and 3). Especially, the reaction in the $scCO_2$-THF system was almost twice as fast as that in pure $scCO_2$. In contrast, the addition of protic solvents brought about remarkable decreases in the reaction rates (Entries 4 and 5). The poisoning effect of methanol ($pK_a = 15.5$) clearly demonstrated that the Tishchenko reaction in $scCO_2$ proceeded by the action of strong base sites on *meso*$Al_2O_3/SO_4{}^{2-}$-III.

In summary, we have designed a new strong base material of *meso*$Al_2O_3/SO_4{}^{2-}$ capable of catalyzing the Tishchenko reaction in $scCO_2$. Two key factors were considered to realize the strong base catalysis in acidic $scCO_2$; 1) a metal oxide that does not form a metal carbonate was chosen, and 2) the surface basicity of the metal oxide was adjusted by the introduction of sulfate ions into its oxide framework in order to suppress the strong CO_2 adsorption that quenches the reaction. The *meso*$Al_2O_3/SO_4{}^{2-}$ was demonstrated to transform **1** into **2** effectively in $scCO_2$ under mild reaction conditions. The addition of a small amount of tetrahydrofuran as a co-solvent led to a remarkable increase in the reaction rate through the enhancement of the solubility of **1** in $scCO_2$. The present heterogeneous solid base-catalyzed Tishchenko reaction in $scCO_2$ will realize the clean production of pharmaceutically promising phthalide derivatives[10] from the viewpoint of green chemistry.

Table 2. Effect of co-solvent on the *meso*$Al_2O_3/SO_4{}^{2-}$-III-catalyzed intramolecular Tishchenko reaction of *o*-phthalaldehyde (**1**) to phthalide (**2**) in supercritical carbon dioxide[a]

Entry	Co-solvent	Yield/%
1	None	31
2	Benzene	48
3	Tetrahydrofuran	58
4	Acetic acid	<1
5	Methanol	6

[a] Reaction conditions are as follows: a 10-mL stainless steel autoclave; catalyst, 0.050 g (activated at 773 K for 2 h under vacuum (10^{-2} Pa)); **1**, 1.00 mmol; $scCO_2$, 8.0 ± 0.2 MPa;[4] co-solvent, 0.1 mL; reaction temp., 313 K; reaction time, 15 min.

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References and Notes

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4 Operators of high-pressure equipment should take proper precautions to minimize the risk of personal injury.

5 ALO-2, -3, and -4 are the reference alumina catalysts supplied from the Catalysis Society of Japan, and contain the following impurities. ALO-2: 0.03% Fe_2O_3, 0.22% SiO_2, 0.04% Na_2O, 1.72% $SO_4{}^{2-}$; ALO-3: 0.01% Fe_2O_3, 0.01% SiO_2, 0.3% Na_2O, 0.01% TiO_2; ALO-4: 0.01% Fe_2O_3, 0.01% SiO_2, 0.01% Na_2O.

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8 Preparation methods of mesoporous alumina catalysts: *meso*Al_2O_3, *meso*$Al_2O_3/SO_4{}^{2-}$-I, -II, and -III were synthesized in one-half the literature scale.[7a] In the preparation of *meso*$Al_2O_3/SO_4{}^{2-}$-I and -II, Al(O-*sec*-Bu)$_3$ was hydrolyzed by deionized water containing 0.1 and 0.2 g of H_2SO_4, respectively. In the preparation of *meso*$Al_2O_3/SO_4{}^{2-}$-III, 19.5 g (79.0 mmol) of Al(O-*sec*-Bu)$_3$ and 1.7 g (5.0 mmol) of $Al_2(SO_4)_3$ were used. The XRD spectrum attributed to mesopores of *meso*$Al_2O_3/SO_4{}^{2-}$-III appeared at a higher *d*-spacing than that of pure *meso*Al_2O_3, indicating that the sulfur atoms in the alumina framework brought about the partial structural collapse.[7a] The absence of IR absorption bands assigned to surface $SO_4{}^{2-}$ species[2a,6] implied that $SO_4{}^{2-}$ ions in *meso*$Al_2O_3/SO_4{}^{2-}$-III were incorporated into the alumina framework.

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