

Mesoporous Silicates as Green Tools for Organic Synthesis

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Abstract: Solid catalysis is a promising way for green organic chemical processes. Our recent works on solid catalysis for organic synthesis based on ordered mesoporous silicates are reviewed on the following topics: 1. the esterification of fatty acid and alcohol over multi-valent metal salt hydrates, 2. the *tert*-butylation of *p*-cresol with *tert*-butyl alcohol over tungstophosphoric acid (HPW), and 3. the base catalysis of silicate-organic composite materials (SOCMs), such as as-synthesized [Si]-MCM-41.

Multi-valent metal salt hydrates (cation: Al³⁺, Fe³⁺, and Zr⁴⁺, *etc.*; anion: Cl⁻, SO₄²⁻, NO₃⁻, OAc⁻, ClO₄⁻, *etc.*) were highly active for the esterification of equimolar mixtures of fatty acids and alcohols. The heterogenization of ZrOCl₂·8H₂O on [Si]-MCM-41 enhanced the catalytic activity because of the acceleration of water removal by their hydrophobic properties of [Si]-MCM-41. Even esters of bulky branched acid and alcohols can be synthesized from equimolar substrates.

The *tert*-butylation of *p*-cresol with *tert*-butyl alcohol over HPW supported on [Si]-MCM-41 occurred effectively in supercritical CO₂ medium (*sc*-CO₂), resulting in high yield of 2-*tert*-butyl-4-methylphenol and 2,6-di-*tert*-butyl-4-methylphenol. Coke-precursors are eliminated from acidic sites by their rapid dissolution in *sc*-CO₂ to minimize the deactivation of the *tert*-butylation.

SOCMs were active for base catalysis, such as Knoevenagel, Aldol, and Michael reactions. Knoevenagel reaction of benzaldehyde with ethyl cyanoacetate gave ethyl 1-cyanocinnamate in quantitative yield. Michael reaction of 4-methoxychalcone with diethyl malonate gave an adduct, diethyl 1-(4-anisyl)-3-phenyl-3-oxopropylmalonate, in high yield. SOCMs have higher activities than amine-functionalized [Si]-MCM-41. The catalytic activity of secondary amines of Aldol reaction was enhanced by the addition of mesoporous silicates, such as [Si]-FSM-16 and [Si]-MCM-41.

Keywords: mesoporous silicate, esterification, fatty acid, fatty alcohol, multi-valent metal cation cluster, *tert*-butylation, *p*-cresol, supercritical carbon monoxide, silicate-organic composite materials, Knoevenagel reaction, Michael reaction, Aldol reaction.

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Introduction

It is urgent issue to reduce CO₂ generation from chemical industry. Green chemistry principles are the guideline for chemical processes [1]. One of the important targets to green chemical processes is the replacement of liquid acid or base catalysts to solid catalysts in manufacturing specialty and/or fine chemicals [2,3]. Ordered mesoporous materials, such as MCM-41 [4,5] and FSM-16 [6,7], open new era for developing green catalytic processes. Mesoporous materials have very high surface area up to 1600 m²/g with mono-dispersed pore diameters in the range of 2–10 nm and ordered array of channels due to surfactant micelle templates [4-8].

The merits of mesoporous materials for solid catalysis are classified to several ways. Microporous materials can be used for the support of active species. High surface area with ordered channels of the materials can be attained high dispersion of active species, and easy contact of the

active species with reactants is highly enhanced resulting in high activity [9-17]. They are also versatile supports for grafting catalytic active centre [12,18-20]. Bulky reactants and catalytic active species, which can not enter microporous pores of zeolitic materials, can accommodate in mesoporous materials. The catalysis proceeds effectively inside channels without choke of mesoporous pores. Hydrophobic characters of mesoporous materials, in particular, for silicates accelerate the reaction accompanying removal of water.

Mesoporous materials are high performance supports for acids, such as heteropolyacids, rare-earth triflates, sulfuric acid, phosphoric acid, *etc.* [14-17]. Particularly, heteropolyacids, such as tungstophosphoric acid and molybdphosphoric acid, supported on mesoporous materials are versatile tools for acid catalyzed reaction. Grafting active species on mesoporous materials are also versatile method for the immobilization of acid,

base, and metal complexes. Among them, grafting of amine catalysts has been paid attention to by many workers [12,13,18,21-24], and examined for base catalyzed organic reactions such as Knoevenagel, Aldol, and Michael reactions.

Recent topics on the mesoporous materials are the base character of Silicate-Organic Composite Materials (SOCMs) such as as-synthesized [Si]-MCM-41, which are composites of silicate and structure-directing agents (SDA) [21-28]. They work as versatile and green tools for base-catalyzed organic reactions, in which their active sites are supposed silica-organic ionic pair.

In this paper, we describe our recent works on acid and base catalyses using mesoporous materials: 1. the esterification of fatty acid and alcohol over multi-valent metal salts, 2. the *tert*-butylation of *p*-cresol with *tert*-butyl alcohol over tungstophosphoric acid, and 3. SOCMs for base catalyzed reactions, and 4. amine-functionalized molecular sieves for base catalyzed reactions 5. the acceleration of amine-catalyzed Aldol reaction mesoporous silica.

Experimental

Catalysts

All chemicals were obtained commercially and used without any purification. Impregnation of metal salts and tungstophosphoric acid (HPW) was carried out in EtOH solution. Silicate organic composite materials (SOCMs) were as as-synthesized [Si]-MCM-41 [29], [Si]-SBA-15 [30], [Si]-SBA-1 [31], [Si]-C8-H [32], and [Al]-BEA [33] prepared according to the literatures.

Amine functionalized molecular sieves were prepared according to the literatures [34,35]. Typical example for aminopropylsilylated [Si]-MCM-41 is as follows: [Si]-MCM-41 (2.0 g) vacuum dried at 250 °C for 1 h was suspended in anhydrous toluene (30 ml). To this suspension, 494 mg (2.75 mmol) of 3-aminopropyltrimethoxysilane (TCI, Tokyo, Japan) was added, and the mixture was stirred under reflux for 2 h. Toluene containing MeOH (\approx 10 ml) was distilled off and toluene (10 ml) was added again; the reflux was continued for another 0.5 h. The product was recovered by filtration, washed with de-ionized water, and then dried at room temperature to give 2.44 g of aminopropylsilylated [Si]-MCM-41 (denoted AP-[Si]-MCM-41) as white powder. The content of amine moiety was estimated to be 1.31 mmol/g based on elemental and thermogravimetric analysis. 3-Piperazinopropylsilyl- (PZP), *N*-methyl-aminopropylsilyl- (MAP), *N,N*-dimethylaminopropylsilyl- (DMAP), and piperidinopropylsilyl- (PDP) functionalized materials were also prepared using corresponding aminoalkyltrimethoxysilanes.

Catalytic Reactions.

Esterification. The esterification of fatty acids and alcohols was carried out in a single-

necked, round-bottomed flask (100 ml) equipped with a Teflon-coated magnetic stirring bar and a Dean-Stark apparatus surmounted with a reflux condenser. An equimolar mixture of substrates (acid and alcohol; 6 mmol) and catalyst (ZrOCl₂(20wt%)/[Si]-MCM-41: 0.115 g; ZrOCl₂·8H₂O: 0.12 mmol) in 40 ml of solvent (benzene, toluene, *m*-xylene, mesitylene, diethylbenzene, and tetralin) were charged into the round-bottomed flask. The mixture was heated to reflux temperature and water generated by the reaction removed as an azeotropic mixture. After 12 or 24 h, resulting reaction mixture was cooled to ambient temperature, and the catalyst was separated by filtration. GC analysis (GC-14A, Shimadzu Corporation, Kyoto, Japan; column Ultra-1(25 m × 0.3 mm; 0.33 μm thick layer; Agilent Technologies, MA, USA) determined the conversion and product yield. Product purification was achieved by column chromatography using silica gel (70–230 mesh) eluted by 10% ethyl acetate in hexane.

The *tert*-Butylation of *p*-Cresol. In a typical reaction, *p*-cresol (9.24 mmol), *tert*-butyl alcohol (36.9 mmol), and dried catalyst (100 mg) were placed in a 100 ml SUS-316 autoclave, and dry ice was loaded into the reactor. The amount of CO₂ for required pressures was calculated from empty volume of the reactor. The reactor was heated to a required reaction temperature, and then, the reaction was started with agitation. The reactor was cooled with cold water after the completion of the reaction, and CO₂ was slowly released. The contents of the reactor were washed with acetone, the products were analyzed by GC using an Ultra-1 column (25 m × 0.3 mm; 0.33 μm thick layer), and also compared with authentic samples.

Knoevenagel, Aldol, and Michael Reactions.

These reactions were carried out according to the similar procedures. Typically, Knoevenagel reaction was carried out as follows: to a solution of benzaldehyde (**1a**, 1.25 mmol) and ethyl cyanoacetate (**2b**, 1.3 mmol) in toluene (1.0 ml), solid catalyst (100 mg) was added and stirred for 1–6 h. The reaction was monitored by thin-layer chromatography (TLC) on silica (eluent: ethyl acetate–hexane). After completion of the reaction, the catalyst was filtrated, washed thoroughly with benzene, and recovered. The filtrate was analyzed by GC (Ultra-1 (25 m × 0.3 mm; 0.33 μm thick layer), ¹H- and ¹³C-NMR spectroscopies, and then ethyl (*E*)-2-cyanocinnamate (**3ab**) was isolated from the filtrate by column chromatography (hexane/ethyl acetate = 4/1). Products were confirmed by means of ¹H and ¹³C NMR spectroscopy. Since the GC results were consistent with isolated weight and the selectivity was almost 100% in all cases, the isolated yields were used for the evaluation of activity.

Amine-catalyzed Aldol Reaction in the Presence of Mesoporous Silica. The typical reaction in the presence of amine and solid additive

was carried out as follows: a solution of 4-nitrobenzaldehyde (**4**, 1.0 mmol) in acetone (5 ml) was maintained at 30 °C with stirring. To this solution, piperazine (0.1 mmol) and FSM-16 (120 mg) were added successively, and whole mixture was stirred for further 6 h. Solid additive was separated by filtration, and the residue was washed with benzene (100 ml). Combined filtrate was washed with chilled 10% citric acid solution (in order to avoid further catalysis by the remaining amine), saturated NaHCO₃ solution followed by brine, and then dried over anhydrous Na₂SO₄. The product analysis was done in the same way as described in previous section. Filtration and evaporation gave yellow crude solid, which was purified by column chromatography on silica gel (eluent: hexane-ethyl acetate) to give 1.1 mg (0.7%) of **4**, 191.1 mg (90.8%) of 4-(4-nitrophenyl)-4-hydroxy-2-butanone (**5**), and 7.0 mg (3.6%) of (*E*)-4-(4-nitrophenyl)-3-buten-2-one (**6**).

Results and Discussion

Esterification of Fatty Acids and Alcohols with Multi-valent Metal Salts Supported on [Si]-MCM-41

Recently, there has been attention to the esterification of equimolar carboxylic acid alcohols using homogeneous and heterogeneous catalysis [36]. Rare earth metal triflates, ZrCl₄, and Zn(ClO₄)₂ are successful examples of the catalysts recently proposed [37-39].

We examined the esterification of fatty acids and alcohols (C₁₂-C₁₈) with multi-valent metal salts as catalysts [40-42]. Table 1 shows activities of metal salts for the esterification of palmitic acid with cetyl alcohol. Catalytic activities were observed in the wide range of metal hydrates. Particularly, Fe³⁺, Ga³⁺, In³⁺, Zn²⁺, Zr⁴⁺, Hf⁴⁺ chlorides showed excellent activities. Al³⁺, Co²⁺, Ni²⁺, Mn³⁺, Cr³⁺, and Cu²⁺ chlorides gave moderate

Scheme 1.

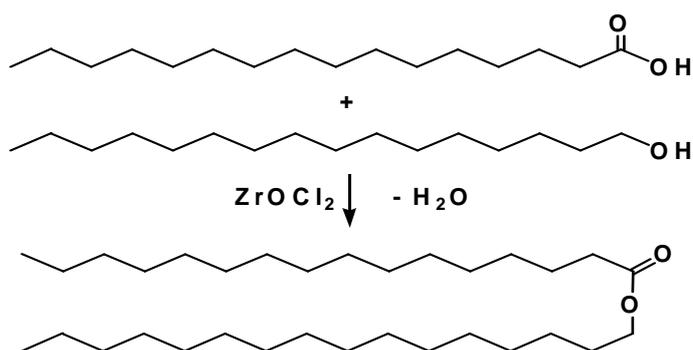


Table 1 : Esterification of Palmitic Acid and Cetyl Alcohol with Metal Chlorides^{a)}

Run	Metal salt	Yield (%)
1	FeCl ₃ ·6H ₂ O	95.8
2	AlCl ₃ ·6H ₂ O	73.8
3	GaCl ₃	97.5
4	InCl ₃	98.6
5	ZnCl ₂	81.5
6	ZrOCl ₂ ·8H ₂ O	86.2
7	HfOCl ₂ ·8H ₂ O	98.7
8	CoCl ₂ ·6H ₂ O	70.5
9	CrCl ₃ ·6H ₂ O	48.8
10	MnCl ₂ ·4H ₂ O	53.8
11	NiCl ₂ ·6H ₂ O	32.3
12	CuCl ₂ ·2H ₂ O	37.7
13	MgCl ₂ ·6H ₂ O	12.5
14	CaCl ₂ ·2H ₂ O	14.0
15	NaCl	13.0
16	--	12.8

^{a)} Reaction conditions: catalyst, 0.12 mmol; palmitic acid, 6 mmol; cetyl alcohol, 6 mmol; mesitylene (solvent), 40 ml; temperature, 162 °C; period, 24 h.

Table 2: The Esterification of Palmitic Acid and Cetyl Alcohol with Metal Salt Hydrates^{a)}.

Metal salt	Yield (%)			
	Chloride	Nitrate	Sulfate	Acetate
Fe(III)	95.8	93.5	88.2	
Al(III)	73.8	53.6	49.2	72.4 ^{b)}
Ga(III)	97.5	98.0		
In(III)	98.6	95.6	89.1	
ZrO(II)	92.5	92.5	84.3	88.0
Zn(II)	81.5	76.6	79.5	78.2
Co(II)	70.5	71.8	72.2	65.0

a) Reaction conditions: catalyst, 0.12 mmol; palmitic acid, 6 mmol; cetyl alcohol, 6 mmol; mesitylene (solvent), 40 ml; temperature, 162 °C; period, 24 h.

b) $\text{Al}_2\text{O}(\text{OAc})_4 \cdot n\text{H}_2\text{O}$

Table 3: The Esterification of Palmitic Acid with Cetyl Alcohol with $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ over Inorganic Supports^{a)}

Run	Support	Conversion (%)
1	none	59.3
2	[Si]-MCM-41	89.3
3	[Si]-FSM-16	85.0
4	[Si]-SBA-15	87.2
5	Amorphous SiO_2	71.2
6	Al_2O_3	62.0
7	ZrO_2	62.5
8	Activated charcoal	77.5

a) Reaction conditions: catalyst: $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$, 0.12 mmol; substrate: acid, 6 mmol, alcohol, 6 mmol; mesitylene (solvent), 40 ml; temperature, 162 °C; period, 12 h.

yields of cetyl palmitate; however, Mg^{2+} , Ca^{2+} , and Na^+ chlorides had no catalytic activities.

Table 2 summarizes catalytic activities of metal salt hydrates in the esterification of palmitic acid and cetyl alcohol. Chlorides had higher activities among the salts, and catalytic activities of nitrate, sulfate, and acetate were moderate to high. The order of the activity of these salts was also very similar to that of the chlorides. These results suggest that cationic metal moieties play an important role on catalytically active species.

We examined the supporting of $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ on inorganic supports, including [Si]-MCM-41, silica gel, γ -alumina, zirconia, and activated charcoal (Table 3). Among these supports, hydrophobic supports, such as [Si]-MCM-41, silica gel, and activated charcoal, had the higher activities for the esterification.

Figure 1 shows the influences of reaction period on the yield of cetyl palmitate in the esterification of palmitic acid and cetyl alcohol with $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$. Supporting on [Si]-MCM-41 enhances the rate of the esterification. The reaction using supported catalysts was completed at least half period of unsupported salts.

Table 4 shows typical results of the

esterification of C_{12} - C_{18} acids and alcohols. With the increase in chain length, the yields of esters were decreased to some extent; however, they were reasonably good to excellent. Supported catalyst was recyclable without significant loss of activity.

The supporting of $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ on [Si]-MCM-41 also enhanced the esterification of less reactive acids and alcohols (Table 5). The esterification of palmitic acid with 2-alkanol with C_{10} - C_{16} was also enhanced by the supporting. Bulky acid, isostearic acid (2-heptylundecanoic acid) also yielded the esters with C_{10} - C_{18} alcohols in good to excellent yield. However, the yield of esters from isostearic acid and 2-alkanol was too low for their efficient syntheses although the rates were increased by supporting.

Unsaturated acids, oleic acid, elaidic acid, linoleic acid also gave corresponding esters by the esterification with cetyl alcohol (see also Table 5). No isomerization of double bonds occurred during the esterification although extensive isomerization occurs in the case of conventional acid catalysts.

The recyclability of $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ and $\text{ZrOCl}_2(20)/[\text{Si}]\text{-MCM-41}$ catalysts for the esterification of palmitic acid and cetyl alcohol is shown in Table 6. A slight decrease in the yield of

cetyl palmitate was observed in second recycle for unsupported and supported $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$; however, there was no further decrease during third and fourth recycles. $\text{ZrOCl}_2(20\text{wt}\%)/[\text{Si}]\text{-MCM-41}$ catalysts maintained higher activity than unsupported $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ during the recycling. Unsupported $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ catalysts were recovered as white paste after the reaction, and white dry solid was separated from reaction mixtures for supported $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ catalysts.

These results show that there is no coke-formation during the catalysis. For other active

multi-valent metal salts, similar results were obtained in the esterification of fatty acids and alcohols. Catalytic activity is principally owed to cationic parts of the metals. It is well known that these metal cations were easily hydrolyzed to form metal cationic clusters in appropriate conditions [43]. Some of typical examples are $[\text{Zr}_4(\text{OH})_8]^{8+}$, $[\text{Fe}_3(\text{OH})_4]^{5+}$, and $[\text{Al}_3(\text{OH})_4]^{5+}$, which have hydrated water on the metal centers. We can propose that these cationic clusters are catalytic species of the esterification, which was suggested by Yamamoto *et al.* for ZrCl_4 [38].

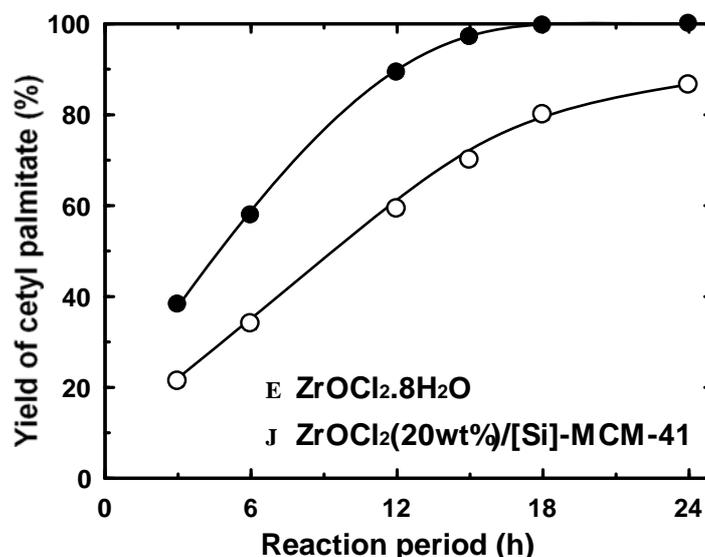


Figure 1 : Time on Course of the Esterification of Palmitic Acid with Cetyl Alcohols. Reaction conditions: substrate: acid, 6 mmol, alcohol, 6 mmol; solvent: mesitylene, 40 ml; $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$, 39 mg (12 mmol); $\text{ZrOCl}_2(20\text{wt}\%)/[\text{Si}]\text{-MCM-41}$, 0.155 g; mesitylene (solvent), 40 ml; temperature, 162 °C.

Table 4 : The Esterification of Primary Acid with Primary Alcohol of Different Chain Length the $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ and $\text{ZrOCl}_2(20\text{wt}\%)/[\text{Si}]\text{-MCM-41}$ ^{a)}

Run	Acid	Alcohol	Yield (%)	
			$\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ ^{b)}	$\text{ZrOCl}_2(20\text{wt}\%)/[\text{Si}]\text{-MCM-41}$ ^{c)}
1	Palmitic acid	Capryl alcohol	>99.9	>99.9
2	Palmitic acid	Lauryl alcohol	>99.9	>99.9
3	Palmitic acid	Myristyl alcohol	90.5	92.5
4	Palmitic acid	Cetyl alcohol	86.2	89.3
5	Palmitic acid	Stearyl alcohol	85.3	88.5
6	Capric acid	Cetyl alcohol	>99.9	>99.9
7	Lauric acid	Cetyl alcohol	99.9	>99.9
8	Myristic acid	Cetyl alcohol	99.5	94.5
9	Palmitic acid	Cetyl alcohol	86.2	89.3
10	Stearic acid	Cetyl alcohol	83.3	87.8

^{a)} Reaction conditions: catalyst, $\text{ZrOCl}_2(20\text{wt}\%)/\text{MCM-41}$, 0.155 g ($\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$, 0.12 mmol); acid, 6 mmol; alcohol, 6 mmol; mesitylene (solvent), 40 ml; temperature, 162 °C.

^{b)} reaction period: 24 h.

^{c)} reaction period: 12 h.

Table 5 : The Esterification of Various Acids and Alcohols with $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ and $\text{ZrOCl}_2(20\text{wt}\%)/[\text{Si}]\text{-MCM-41}^{\text{a)}$

Run	Acid	Alcohols	Yield (%)	
			$\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}^{\text{b)}$	$\text{ZrOCl}_2(20\text{wt}\%)/[\text{Si}]\text{-MCM-41}^{\text{c)}$
1	Palmitic acid	2-Decanol	70.8	>99.9
2	Palmitic acid	2-Dodecanol	60.2	99.3
3	Palmitic acid	2-Tetradecanol	41.2	75.8
4	Palmitic acid	2-Hexadecanol	33.1	70.1
5	Isostearic acid	Capryl alcohol	42.4	>99.9
6	Isostearic acid	Lauryl alcohol	35.2	99.2
7	Isostearic acid	Myristyl alcohol	33.5	96.1
8	Isostearic acid	Cetyl alcohol	30.7	84.4
9	Isostearic acid	Stearyl alcohol	28.5	67.8
10	Isostearic acid	2-Decanol	7.1	30.2
11	Isostearic acid	2-Dodecanol	5.1	28.8
12	Isostearic acid	2-Tetradecanol	6.2	23.5
13	Isostearic acid	2-Hexadecanol	No reaction ^d	21.6
14	Oleic acid	Cetyl alcohol	>99.9	97.8
15	Elaidic acid	Cetyl alcohol	>99.9	99.4
16	Linoleic acid	Cetyl alcohol	70.1	62.5

^{a)} Reaction conditions: catalyst: 0.12 mmol as $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$; acid and alcohol, 6 mmol; mesitylene (solvent), 40 ml; temperature, 162 °C.

^{b)} reaction eperiod: 24 h.

^{c)} reaction period: 12 h.

^{d)} Acid to $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ molar ratio = 10.

Table 6 : The Recycle and Reuse of $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$ and $\text{ZrOCl}_2(20\text{wt}\%)/[\text{Si}]\text{-MCM-41}$ Catalyst in the Esterification of Palmitic Acid and Cetyl Alcohol^{a)}

Run	Fresh/recycled catalysts	Yield (%)	
		$\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}^{\text{b)}$	$\text{ZrOCl}_2(20)/[\text{Si}]\text{-MCM-41}^{\text{c)}$
1	Fresh	86.2	89.3
2	First recycle	84.5	88.0
3	Second recycle	84.3	88.5
4	Third recycle	84.8	88.6
5	Fourth recycle	84.2	89.0

^{a)} Reaction conditions: substrate: palmitic acid, 6 mmol, cetyl alcohol, 6 mmol; catalyst: $\text{ZrOCl}_2 \cdot 8\text{H}_2\text{O}$, 0.12 mmol. $\text{ZrOCl}_2(20\text{wt}\%)/[\text{Si}]\text{-MCM-41}$, 0.115 g; mesitylene (solvent) 40 ml mesitylene; reaction temperature, 162 °C.

^{b)} reaction period: 24 h.

^{c)} reaction period: 12 h.

The enhancement of catalytic activity of the metal salts supporting on MCM-41 is explained by their easy contact with substrate because the cationic cluster is highly dispersed on MCM-41 with a high surface area. We also suggest that the hydrophobic properties of mesoporous silica accelerate the removal of water by controlling hydrated water in the cluster. The decrease in amounts of water proximately to catalytic center accelerates the esterification because of favorite equilibrium to ester. There have been similar environments by organic modified mesoporous silicates [44] or O/W micelles with surfactants [45,46].

The *tert*-Butylation of *p*-Cresol by HPW on [Si]-MCM-41

It is important to synthesize bulky organic functional molecules over solid catalysts. *tert*-Butylphenols are typical molecules with bulky substituents. There has been much attention to the *tert*-butylation of phenols, using solid acid catalysts including zeolites and mesoporous materials, under liquid and vapor phase reaction conditions [47]. However, the products were principally mono-*tert*-butylphenols, and no literatures describe selective synthesis of di- and tri-*tert*-butylated products. The drawbacks of these catalysts are severe coke-formation during the catalysis.

Supercritical fluids are important reaction media which are being used extensively in recent years for organic transformations [48-50]. Supercritical fluids provide the advantages, such as higher dissolution power to remove coke-precursors from catalytically active sites during heterogeneous catalysis. They also possess intermediate characteristics between the reaction under liquid and vapor phase conditions, which facilitate better mass transfer of reactants and products, thus maintaining catalytic activity with considerably lower deactivation even at longer reaction periods. *sc*-CO₂ also has advantages of tunable dissolving power based on the solubility of reactants and products by the variation of pressure and temperature [48-50].

Recently, there have been increasing interests in the area of heterogeneous catalysis in *sc*-CO₂ because the deactivation caused by coke-formation during heterogeneous catalysis in *sc*-CO₂ can be minimized compared to the other reaction media [50]. Other merits of using *sc*-CO₂ as a reaction medium are recyclability, non-corrosiveness, exclusion of hazardous organic solvents, minimal generation of waste, and easy separation of products from catalytic system. These advantages of *sc*-CO₂ offered to heterogeneous catalysis have prompted us to study the *tert*-butylation of phenols in *sc*-CO₂.

We examined the *tert*-butylation of *p*-cresol in *sc*-CO₂ by using HPW supported on [Si]-MCM-41 (HPW/[Si]-MCM-41) in order to reduce the coke-formation during the catalysis (Table 7) [47,52]. The *tert*-butylation of *p*-cresol gave 2,6-di-*tert*-butyl-4-methylphenol (2,6-DTBPC) in high yield in *sc*-CO₂; however, zeolites, H-Y and H-β, gave only 2-*tert*-butyl-4-methylphenol (2-TBPC) because of their limitation in pore size. The yield of 2,6-DTBPC over HPW(30wt%)/[Si]-MCM-41 was maximum at 110 °C, and further increase in temperature decreased the yield as shown in Figure 2. There was the optimal CO₂ pressure on the yield of 2,6-DTBPC at 10 MPa, and further increase of the pressure resulted in rapid decrease of the yield. Thermogravimetric analysis of used catalysts showed that the deactivation by coke-formation is minimized in *sc*-CO₂ compared to the other reaction media such as hexane as solvent or without solvent under N₂ atmosphere. HPW(30wt%)/[Si]-

MCM-41 was recyclable in *sc*-CO₂ without significant loss of catalytic activity, and retained mesoporous structure after the reaction.

The recyclability of the catalyst is important for a green catalysis. The *tert*-butylation of *p*-cresol over HPW(30wt%)/[Si]-MCM-41 was carried out for three recycles to examine the recyclability in *sc*-CO₂, and typical results are shown in Table 8. The catalysts after the reaction were separated from reaction mixtures, and washed with acetone, and used after drying at 120 °C overnight. Only 6–8% decreases in the conversion and yield of 2,6-DTBPC was observed after three recycles. The excellent recyclability of HPW(30wt%)/[Si]-MCM-41 in the *tert*-butylation of *p*-cresol is mainly due to low coke-formation in *sc*-CO₂ because catalytic active sites of HPW(30wt%)/[Si]-MCM-41 remained free from coke-precursors. Surface area of HPW(30wt%)/[Si]-MCM-41 was decreased from 645 m²/g for fresh catalyst to 618m²/g for recovered catalysts: this change in surface area during the catalysis suggests that there is almost no collapse of catalyst structure.

The *tert*-butylation of phenol was also examined over Sc(OTf)₃ supported on [Si]-MCM-41 (Sc(OTf)₃/[Si]-MCM-41) in *sc*-CO₂ [53]. Phenol gave 2,4,6-tri-*tert*-butylphenol (2,4,6-TTBP) in 36% yield and 2,4-di-*tert*-butylphenol (2,4-DTBP) in 34% yield over Sc(OTf)₃(30wt%)/[Si]-MCM-41 at 130 °C under CO₂ pressure of 10 MPa. The coke formation in supercritical CO₂ was much lower than that in other reaction media.

The spatial requirement for catalytic active sites is important for the selective synthesis of 2,6-DTBPC and 2,4,6-TTBP. Sc(OTf)₃/[Si]-MCM-41 can allow the formation of 2,6-DTBPC and 2,4,6-TTBP, and subsequent diffusion of the products from the channels. H-Y zeolite was also highly active for the *tert*-butylation of *p*-cresol and phenol in *sc*-CO₂. However the principal products were 2-TBPC from *p*-cresol, and 2,4-DTBP from phenol. H-Y zeolites can afford reaction environment to allow the formation of 2-TBPC from *p*-cresol and 2,4-DTBP from phenol, but not 2,6-DTBPC and 2,4,6-TTBP. 2-TBPC and 2,4-DTBP can be easily formed inside H-Y zeolites and diffuse out from their 12-membered pores.

Scheme 2

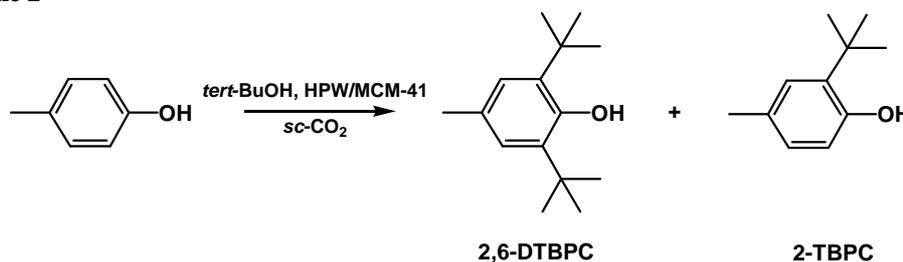


Table 7 : The *tert*-Butylation of *p*-Cresol over HPW in *sc*-CO₂^{a)}

Run	Catalyst	Conversion (%)	Yield (%)	
			2,6-DTBC	2-TBC
1	HPW(30)/[Si]-MCM-41 ^{b)}	99	53	46
2	HSiW(30)/[Si]-MCM-41	98	24	71
3	[Si]-MCM-41	1.0	-	1.0
4	[Al]-MCM-41(30) ^{c)}	47	4.0	41
5	HPW(30)/ZrO ₂	93	26	65
6	ZrO ₂	1.0	-	1.0
7	HPW(30)/[Si]-MCM-41 ^{d)}	85	6.7	78
8	HPW(30)/[Si]-MCM-41 ^{e)}	93	24	69
9	H-Y(5.2) ^{e)}	99	3.4	96
10	H-Y(30) ^{e)}	98	3.7	95
11	H-β(25) ^{e)}	56	1.0	53

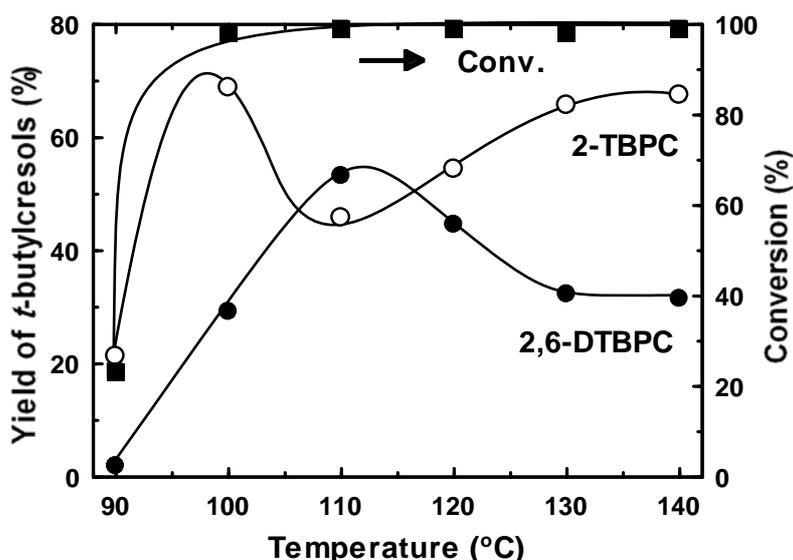
a) Reaction conditions: catalyst, 100 mg; *p*-cresol 1.00 g (9.24 mmol); *t*-butyl alcohol, 2.73 g (36.9 mmol); temperature, 110 °C; period, 5 h; CO₂ pressure, 10 MPa.

b) Loading amounts are 30% against the support.

c) value in parentheses is SiO₂/Al₂O₃.

d) Hexane (15 mL) was used as solvent. Reaction conditions were the same except CO₂ pressure.

e) The reaction was carried out without solvent under N₂ pressure. Reaction conditions were the same except CO₂ pressure.

**Figure 2** : The Influence of Reaction Temperature on the *t*-Butylation of *p*-Cresol over HPW(30wt%)/[Si]-MCM-41. Reaction conditions: catalyst, 100 mg; *p*-cresol 1.00 g (9.24 mmol); *tert*-butyl alcohol, 2.73 g (36.9 mmol); period, 5 h; CO₂ pressure, 10 MPa.**Table 8** : Recyclability of HPW(30wt%)/[Si]-MCM-41 in the *t*-Butylation of *p*-Cresol in *sc*-CO₂^{a)}

Run	Cycle	Conversion (%)	Yield (%)	
			2,6-DTBPC	2-TBPC
1	Fresh	99	53	46
2	First recycle	95	51	45
3	Second recycle	93	49	44
4	Third recycle	93	47	46

a) Reaction conditions: catalyst: HPW(30wt%)/[Si]-MCM-41, 100 mg; *p*-cresol, 1.0 g (9.24 mmol); *tert*-butyl alcohol, 2.73 g (36.9 mmol); temperature, 110 °C; CO₂ pressure: 10 MPa; period, 5 h.

These high performances of *sc*-CO₂ are due to high solubility of reactants and products and to minimal coke formation. *Sc*-CO₂ works as reaction medium, and removes coke-precursors, which are heavy aromatics from the phenols and/or isobutene oligomers before they convert to coke materials, and keeps catalytic sites clean during the catalysis. The yields of 2,6-DTBPC and 2,4,6-TTBP were significantly influenced by reaction conditions, particularly, CO₂ pressure. The optimum CO₂ pressure was 10 MPa at 110 °C for *p*-cresol and at 130 °C for phenol. However, a further increase in CO₂ pressure rapidly decreased the formation of 2,6-DTBPC and 2,4,6-TTBP. Highly dense CO₂ may also decelerate the catalysis by preventing access of reactants to catalytic active sites.

Silicate-Organic Composite Materials for Base Catalyzed Reactions

In comparison with solid acid catalysis, solid base catalyses have been less interested in chemical industry although they are highly potential for the important reactions [18,54]. However, growing efforts in the investigation of new type of basic microporous and mesoporous materials are opening new era in solid base catalysis [11-13,18-28]. Among them, mesoporous silicates, such as [Si]-MCM-41, [Si]-FSM-16, [Si]-SBA-15, *etc.*, have very large surface area with ordered channels of 2–10 nm although they do not have acid and base characters. The introduction of base moieties is essential for the appearance of base catalysis. Many of researchers have examined the introduction of base center by the impregnation and/or the grafting [11-13,18-20,34,35].

We found silicate-organic composite materials (SOCMs), such as as-synthesized [Si]-MCM-41, [Si]-SBA-15, and [Si]- and [Al]-BEA, have basic sites originated of silica and organic moieties from SDA, which work as base catalysts [21,22,24-27]. These are completely new type of catalysts, although they have not microporous and mesoporous characters. Here, we describe the catalytic properties of SOCMs in base catalyzed reactions, Knoevenagel, Aldol, and Michael reactions (Schemes 3-5).

Knoevenagel Reaction. Table 9 summarizes typical results of Knoevenagel reaction of benzaldehyde (**1a**) with ethyl cyanoacetate (**2b**) by using SOCMs. (CTMA⁺)-[Si]-MCM-41, an as-synthesized [Si]-MCM-41, showed high catalytic activity, and the reaction proceeded smoothly under mild conditions to give ethyl (*E*)-2-cyanocinnamate (**3ab**) in high yields. The reactions catalyzed by (TEA⁺)-[Al]-BEA and (TMBP²⁺)-[Si]-BEA, which are as-synthesized β -zeolite, gave **3ab** in moderate yields. On the other hand, calcined SDA-free materials such as [Si]-MCM-41 and [Al]-BEA showed no catalytic activity even at elevated temperatures. CTMA⁺Br⁻ and TEA⁺Br⁻, which are raw materials for hydrothermal synthesis of SOCMs, exhibit only low activities. The yield of

3ab was low by using TEA⁺OH⁻, which is stronger base than halides. These results suggest that high activity appears only by SOCMs, in which silicate and quaternary ammonium moiety coexist proximately. However, (TEA⁺F⁻)-[Si]-BEA synthesized by fluoride method had very low activities.

(CTMA⁺)-[Si]-MCM-41 was reusable and the product yield was remained very high even at second recycle. Unlike recovered catalyst, the filtrate demonstrated no activity after adding fresh substrates. These results show that homogeneous catalysis by any leached species (including amine) did not occur in our SOCMs catalysts. It was confirmed by means of XRD, elemental analysis, and TG-DTA analysis that framework structure and organic content in recovered catalysts were unchanged from fresh catalyst. However, the activity significantly decreased after second recycle. From TG-DTA analysis, it suggested that the loss of catalytically active component occurs mainly from near surface.

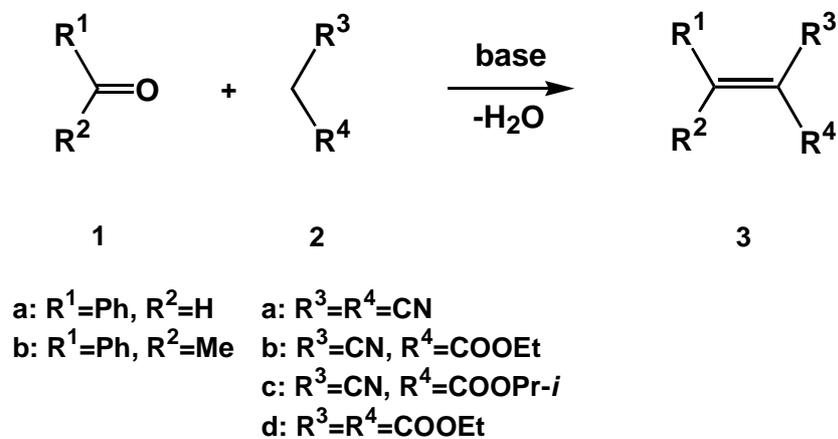
Table 10 summarizes typical results of Knoevenagel reaction with (CTMA⁺)-[Si]-MCM-41. Malononitrile (**2a**), ethyl and isopropyl cyanoacetates (**2b,c**) were easily reacted with **1a** although lower reactivity was observed for bulky esters of cyanoacetic acid. Reactivity of diethyl malonate (**2d**) with **1a** was considerably low, suggesting that one or two cyano-groups in **2a** are necessary for the effective catalysis. Further, less reactive acetophenone (**1b**) gave lower yield than benzaldehyde (**1a**), and did not react with **2b**.

Activity of (CTMA⁺)-[Si]-MCM-41 increased significantly when the reaction was carried out without solvent. The increase in the activity was also observed in the reaction catalyzed by (TEA⁺)-[Al]-BEA, which is less active in benzene or toluene. The enhancement of catalytic activity suggests that active sites is located closer to the external surface on the catalyst and promote solid-liquid interfacial reaction without solvent.

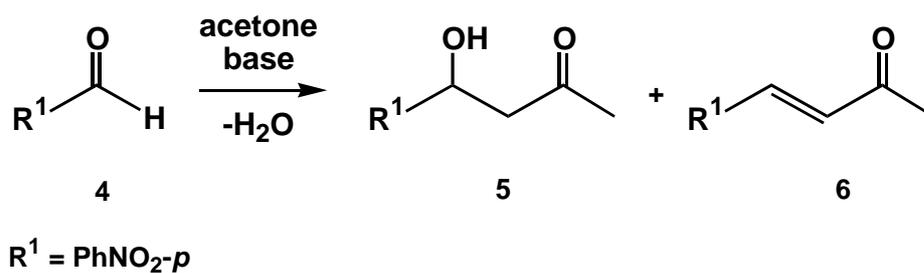
Aldol Reaction. (CTMA⁺)-[Si]-MCM-41 catalyst was also effective for Aldol reaction of aromatic aldehyde and ketone. Some typical results are shown in Table 11. The reaction of 4-nitrophenylbenzaldehyde (**4**) with acetone gave 4-nitrophenyl-3-hydroxy-2-butanone (**5**) in high yields accompanying small amount of 4-nitrophenyl-3-buten-2-one (**6**) even at 20 °C. On the other hand, calcined SDA-free materials such as [Si]-MCM-41 showed no catalytic activity. CTMA⁺Br⁻ and CTMA⁺Cl⁻ did not show any activity, either. These results suggest that the cooperation of silicate and quaternary ammonium moiety is necessary for high catalytic activity of Aldol reactions.

Michael Reaction. Table 12 summarizes typical results of Michael reaction of 4-methoxyhalocone (**7c**) with diethyl malonate (**8a**) in EtOH by using SOCMs catalysts. The reaction of **7c** with **8a** readily occurred by (CTMA⁺)-[Si]-

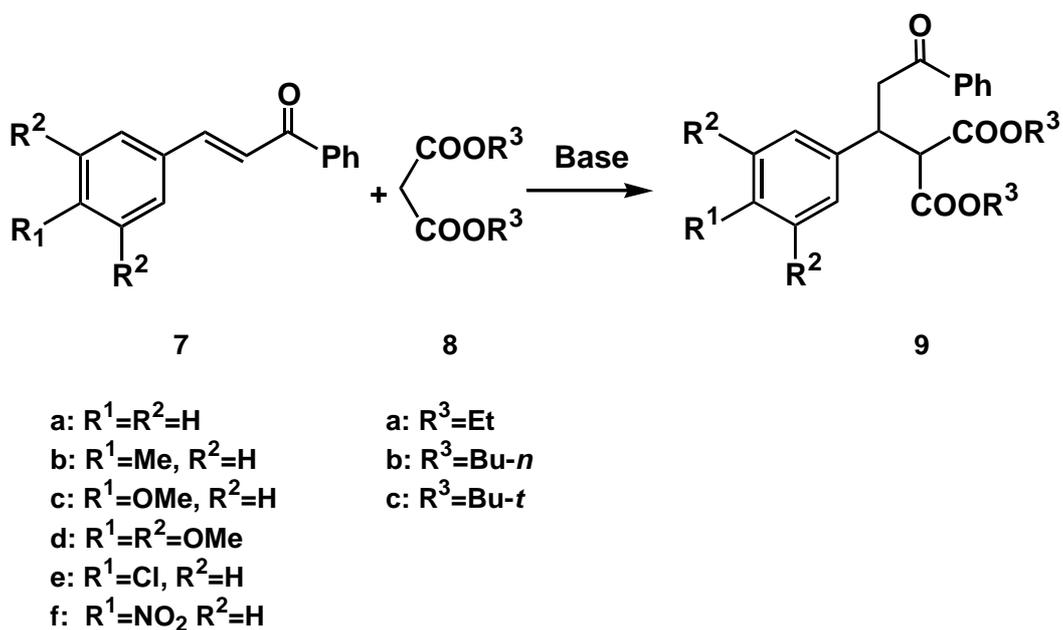
Scheme 3



Scheme 4



Scheme 5



MCM-41 catalyst under mild conditions, resulting in the formation of a product, diethyl 1-(4-anisyl)-3-phenyl-3-oxopropylmalonate (**9ca**) in moderate to high yields. On the other hand, calcined SDA-free materials such as [Si]-MCM-41 showed no catalytic activity. CTMA⁺Br⁻ did not show any activity, either. These results suggest that the cooperation of silicate and quaternary ammonium moiety is necessary for high activity as discussed on Knoevenagel and Aldol reactions.

Table 13 shows the influences of the substitution of chalcone by using (CTMA⁺)-[Si]-MCM-41. The reaction of **7a-f** with **8a** in EtOH gave the products **9aa-9fa** in high yields. The product yield decreased with the increase in the bulkiness of alkoxy group: **8a** ≥ **8b** > **8c**. When dibutyl malonate (**8b**) was used as a Michael donor, the transesterification partially took place in EtOH, resulting in lower yield of desired products. This side-reaction was able to be avoided by using benzene as a solvent. This result indicates that non-polar solvent is excellent in the catalytic system.

Reusability of (CTMA⁺)-[Si]-MCM-41 was examined for the reactions (**7a** with **8a**, and **7c** with **8a**) in benzene. Catalytic activity of recovered catalysts was decreased after recycling: Only slight loss of the activity was observed for the reaction of **7a** with **8a**, whereas there was significant loss of activity in the reaction of **7c** with **8a**. The decrease in organic content after the second recycle in benzene was less than 5 and 2 wt% of initial weight, respectively. Less reactive substrate **7c** is more sensitive to slight change in the surface conditions of the catalyst. It was confirmed by means of XRD that framework structures of recovered catalysts were unchanged after the reactions. However, it is

still unclear for the reasons of the loss of activity.

After the reaction of **7c** with **8a**, the filtrate had no activity when fresh substrates were added and the reaction was carried out at 80 °C for 2 h; ¹H NMR spectra of the reaction mixture taken every 30 min showed that no further reaction occurred. This result indicates that, even if there are leached species, they do not act as effective homogeneous catalyst similar to the results of Knoevenagel reactions.

Mechanistic Aspects on Base Catalysis over SOCMs Nitrogen adsorption measurement of active (CTMA⁺)-[Si]-MCM-41 did not give Type-IV isotherm and BET surface area was less than 20 m²/g, whereas typical Type IV isotherm and large BET surface area (1013 m²/g) were obtained from catalytically inactive [Si]-MCM-41. These results indicate that large surface area and complete porosity are not indispensable in this reaction system, and the reaction takes place near pore-entrance of silicates, not deeply inside the pore. Efficient catalysis by SOCMs may be due to more exposed catalytic sites at the pore-entrance as compared to zeolite-based materials, such as (TEA⁺)-[Al]-BEA.

Solid-state ²⁹Si MAS NMR spectra of as-synthesized [Si]-MCM-41 and [Si]- and [Al]-BEA materials are shown in Figure 3. The resonances corresponding to Si(3-OSi, 1-OH), i.e. Q³, are obviously observed in the spectra of (CTMA⁺)-[Si]-MCM-41, (TEA⁺)-[Al]-BEA and (TMBP²⁺)-[Si]-BEA, whereas only small Si(3-OSi, 1-OH) resonance appears in the spectrum of (TEA⁺F⁻)-[Si]-BEA. These results suggest that actual catalytic sites are basic (SiO)₃SiO⁻ moieties in SOCMs. It seems that the SiO⁻ moiety works an

Table 9 : Knoevenagel Reaction of Benzaldehyde (**1a**) and Ethyl Cyanoacetate (**2b**) over SOCMs^{a)}

Run	Catalyst	Temp. (°C)	Period (h)	Yield of 3ab ^{b)} (%)
1	(CTMA ⁺)-[Si]-MCM-41 ^{c)}	20	1	82
2	(CTMA ⁺)-[Si]-MCM-41 ^{c)}	20	6	97,94 ^{d)} , 80 ^{e)} , 60 ^{f)}
3	(TEA ⁺)-[Al]-BEA ^{g)}	20	6	51
4	(TMBP ²⁺)-[Si]-BEA	20	6	49
5	[Si]-MCM-41	80	6	0
6	[Al]-BEA ^{g)}	80	6	0
7	HDTMA ⁺ Br ⁻	20	6	6
8	TEA ⁺ Br ⁻ ^{h)}	20	6	6
9	TEA ⁺ OH ⁻ ⁱ⁾	20	6	24
10	(TEA ⁺ F ⁻)-[Si]-BEA	20	6	0

a) Reactions conditions: catalyst: 200 mg; **1a**: 1.5 mmol; **2b**: 2.6 mmol.

b) isolated yield.

c) Amount of CTMA⁺ occluded is 1.6 mmol/g-composite.

d) first recycle.

e) second recycle.

f) third recycle.

g) SiO₂/Al₂O₃=105.

h) 0.30 mmol of each catalyst was used.

i) 0.96 mmol.

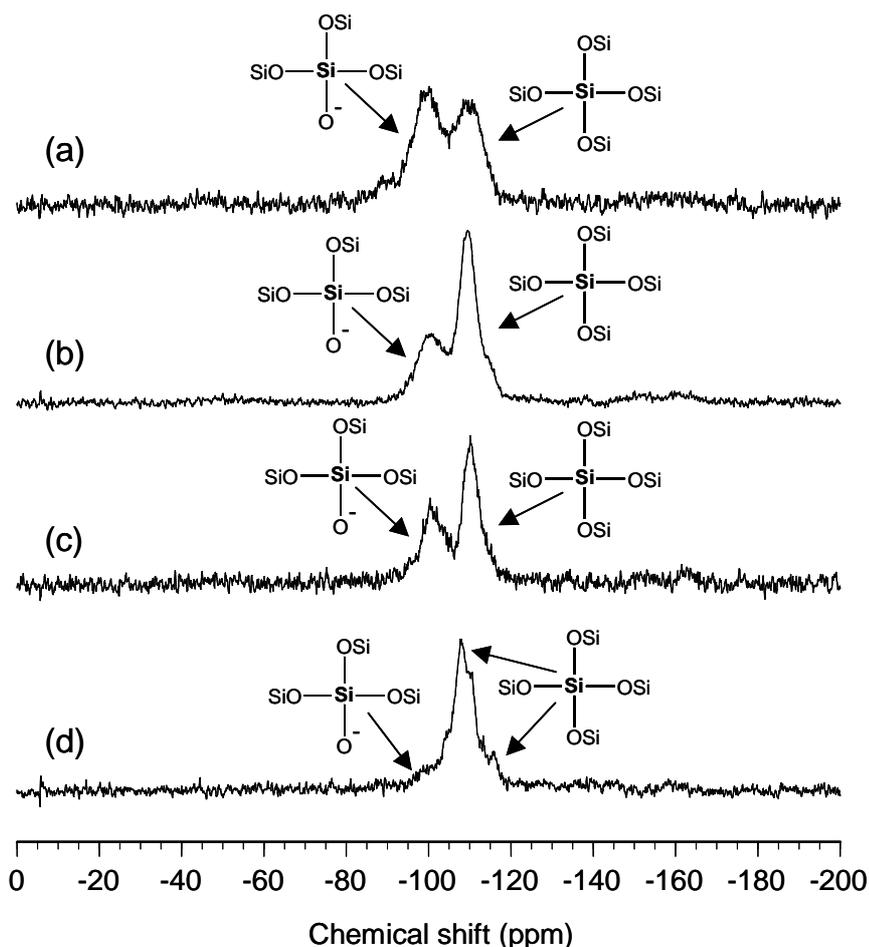


Figure 3 : Solid-state ^{29}Si -MAS NMR spectra of SOCMs. (a) (CTMA^+) -[Si]-MCM-41, (b) (TEA^+) -[Al]-BEA, (c) (TMBP^{2+}) -[Si]-BEA, and (TEA^+F^-) -[Si]-BEA

effective base with assistance of proximate quaternary ammonium cation in non-polar medium. This is quite different from hydroxide or alkoxide, which are generated from metal cation in aqueous or alcoholic media. The ion pair $(\text{SiO})_3\text{SiO}^-(^+\text{NR}_4)$, which works as a basic active site on SOCMs, is not mobile and located on both sides at the entrance of parent silicate framework.

Such a ion-pair $(\text{SiO})_3\text{SiO}^-(^+\text{NR}_4)$ is considered as active species in Knoevenagel, Aldol, and Michael reactions. A possible mechanism of Michael reaction is shown in Scheme 6. Generally, Michael reaction starts from the abstraction of a proton by a base (B^-M^+) from the active methylene compound such as diethyl malonate (step 1) [56]. The carbanion thus formed attacks the β -carbon of α,β -unsaturated ketone such as chalcone to form a carbon-carbon bond (step 2). The last step (step 3) consists of the formation of final product and the regeneration of base. B^-M^+ in Scheme 6 corresponds to the ion pair $(\text{SiO})_3\text{SiO}^-(^+\text{NR}_4)$ for SOCM catalyst. It is possible that the steps 1–3 proceed on the solid surface or in its close proximity.

Similar type of the mechanism, in which the ion pair $(\text{SiO})_3\text{SiO}^-(^+\text{NR}_4)$ works as catalytic active

species, operates similarly in Knoevenagel and Aldol reactions.

Amine-functionalized molecular sieves for Base Catalyzed Reactions

In the previous section, we described our findings on base catalyzed properties of SOCMs, such as as-synthesized [Si]-MCM-41. It is important to compare the catalysis of SOCMs to amine immobilized mesoporous silicates catalysts, recently reported by many workers.

Knoevenagel Reaction. Table 14 summarizes the results of Knoevenagel reaction of benzaldehyde (**1a**) with ethyl cyanoacetate (**2b**) by using AP-functionalized mesoporous and mesoporous materials. AP-[Si]-MCM-41 and AP-[Si]-SBA-15 showed high activity and gave **3ab** in high yield within 1 h. The yield decreased roughly depending on surface area and pore volume values for silicate supports. The use of AP-[Si]-SBA-1, which has much smaller pores than those of AP-[Si]-MCM-41 and AP-[Si]-SBA-15, resulted in slower reaction; however, the activity was enough high to give the product in high yield after 6 h. This is probably by the benefit of three-dimensional pore system of [Si]-SBA-1. Hexagonally ordered

Table 10. : Influences of the Substitution of Substrates on Knoevenagel Reaction with (CTMA⁺)-[Si]-MCM-41^{a)}

Run	1	2	Temp (°C)	Period (h)	Yield of 3 ^{b)} (%)
1	1a	2a	r.t.	6	94
2	1a	2b	r.t.	6	97
3	1a	2b	r.t.	2	92
4	1a	2c	r.t.	6	60
5	1a	2c	80	6	95
6	1a	2d	110	6	8
7	1b	2a	r.t.	6	37
8	1b	2a	r.t.	6	45
9	1b	2b	110	6	5

^{a)} Reaction conditions: (CTMA⁺)-[Si]-MCM-41, 100 mg; **1a-b**, 1.25 mmol; **2a-d**, 1.30 mmol; benzene (solvent), 1 ml.

^{b)} isolated yield.

Table 11 : Aldol Reaction of 4-Nitrobenzaldehyde (**4**) and Acetone over (CTMA⁺)-[Si]-MCM-41^{a)}

Run	Catalyst	Temp. (°C)	Conv. (%)	Yield (%) ^{b)}	
				5	6
1	(CTMA ⁺)-[Si]-MCM-41	20	98	78	3
2	[Si]-MCM-41	20	0	-	-
3	CTMA ⁺ Br ⁻	20	0	-	-
4	CTMA ⁺ Cl ⁻	20	0	-	-

^{a)} Reaction conditions: catalyst, 120 mg; **4**: 1.0 mmol; Acetone 5 ml; temperature 20 °C; period, 6 h.

^{b)} isolated yield.

Table 12 : Michael Reaction of 4-Methoxychalcone (**7c**) and Diethyl Malonate (**8a**) over SOCMs^{a)}

Run	Catalyst	Solvent	Temperature (°C)	Conversion (%)	Yield of 9ca (%) ^{b)}
1	(CTMA ⁺)-[Si]-MCM-41	EtOH	80	93	92
2	(CTMA ⁺)-[Si]-MCM-41	EtOH	30	69	68
3	(CTMA ⁺)-[Si]-MCM-41	Benzene	80	90	90
4	(CTMA ⁺)-[Si]-MCM-41	Benzene	30	28	26
5	[Si]-MCM-41	EtOH	80	0	0
6	CTMA ⁺ Br ^{-c)}	EtOH	80	0	0
7	(TEA ⁺)-[Al]-BEA	EtOH	80	15	11
8	(TEA ⁺ F ⁻)-[Si]-BEA	EtOH	80	0	0

^{a)} Reaction conditions: catalyst, 100 mg; **7c**, 1.25 mmol; **8a**, 1.375 mmol. solvent: 0.5 ml; reaction period: 2 h.

^{b)} isolated yield.

^{c)} catalyst amount: 0.30 mmol.

Table 13 : The Influences of the Substitution of Substrates on Michael Reaction Catalyzed by (CTMA⁺)-[Si]-MCM-41^{a)}

Run	Substrate		Solvent	Conversion (%)	Yield of 9 ^{b)} (%)
	7	8			
1	7a	8a	EtOH	99	98
2	7b	8a	EtOH	98	96
3	7c	8a	EtOH	93	92
4	7c	8a	Benzene	90	90
5	7d	8a	EtOH	99	99
6	7e	8a	EtOH	99	98
7	7f	8a	EtOH	99	97
8	7c	8b	EtOH	80	68 (11) ^{c)}
9	7c	8b	Benzene	81	80
10	7c	8c	EtOH	59	58
11	7c	8c	Benzene	61	61

a) Reaction conditions: catalyst, (CTMA⁺)-[Si]-MCM-41, 100 mg; **7a-f**: 1.25 mmol; **8a-c**: 1.375 mmol; solvent, 0.5 ml; temperature: 80 °C; period: 2 h; under N₂ atmosphere.

b) isolated yield.

c) The value in parentheses is a combined yield of ethyl and butyl esters.

Table 14 : Knoevenagel Reaction of Benzaldehyde (**1a**) and Ethyl Cyanoacetate (**2b**) Catalyzed by AP-functionalized Catalysts^{a)}

Run	Catalyst	AP-content ^{b)} (mmol/g-cat)	Period (h)	Yield of 3ab ^{c)} (%)	TOF (1/h)
1	AP-[Si]-MCM-41	1.31	0.25	78	29.8
2	AP-[Si]-MCM-41	1.31	1	99	
3	AP-[Si]-SBA-15	1.45	0.25	73	25.1
4	AP-[Si]-SBA-15	1.45	1	99	
5	AP-[Si]-SBA-1	1.40	0.5	43	7.7
6	AP-[Si]-SBA-1	1.40	3	72	
7	AP-[Si]-C8-H	1.27	6	68	1.1
8	AP-[Al]-FAU	0.55	6	59	2.2
9	AP-[Al]-BEA	0.95	6	52	1.1
10	AP-[Al]-MOR	0.53	6	6	0.2

a) Reaction conditions: catalyst, 100 mg; **1a**, 1.25 mmol; **2b**, 1.30 mmol; solvent: toluene, 1 ml; temperature 20 °C.

b) determined by elemental and thermogravimetric analyses.

c) Isolated yield.

d) moles of product per mol of catalysts /hour.

[Si]-C8-H, whose pore size is the border of micro- and mesoporous region, gave the product in lower yields. Although the product yields depend on pore structures, microporous materials generally showed lower activities. On the basis of turnover frequency (TOF), it is obvious that multi-dimensional pore systems are advantageous. AP-FAU and AP-BEA had much higher activities than those of AP-MOR.

Table 15 shows the influences of immobilized amine moieties on [Si]-MCM-41 in Knoevenagel reaction of **1a** with **2b**. Secondary amine, such as MAP and PZP moieties had lower activities than AP-[Si]-MCM-41. No activity was observed for tertiary amine such as DMAP, DEAP, and PDP moieties. These results mean that formation of

imine-type intermediate is involved as a key step for the Knoevenagel reaction. There have also been some discussions on roles of imine-type intermediate in the reaction [25,34,55].

Aldol Reaction. Aldol reaction of 4-nitrobenzaldehyde (**4**) and acetone by using AP-, PZP-, MAP-, and DMAP-functionalized [Si]-FSM-16 and [Si]-MCM-41 is shown in Figure 4. Secondary amine, MAP and PZP showed high catalytic activity among the amine-immobilized silicates, particularly, MAP gave the highest activity (yield of **5** and **6** after 1 h were 86% and 7%, respectively). AP is also moderately active; however, DMAP has no catalytic activity for Aldol reaction. The highest catalytic activity of

secondaryamines suggests that the formation of enamine is a key step for Aldol reaction. There are some differences in roles of amine as base catalyst between Aldol and Knoevenagel reactions.

There were some differences in catalytic activity of AP among the supports. [Si]-MCM-41 \approx [Si]-FSM-16 $>$ SiO₂. The differences are due to the advantages of surface area of ordered mesoporous structure.

Michael Reaction. Table 16 shows typical results of Michael reaction of chalcone (**7a**) with diethyl malonate (**8a**) catalyzed by various 3-aminopropylsilylated molecular sieves using EtOH as solvent. The molecular sieves with larger pores show higher activity. AP-[Si]-MCM-41 showed high activity, and gave the product in high yield. The yield decreased roughly depending on the surface area and pore volume values for silicate supports. The use of AP-[Si]-SBA-1 having much smaller pores than those of AP-[Si]-MCM-41

resulted in slower reaction. Among microporous materials, AP-FAU showed the highest activity, which is comparable to that of AP-[Si]-MCM-41. Other microporous catalysts showed much lower activities. These differences of catalytic activity suggest that the circumstance of mesoporous silicate is more appropriate than those of microporous materials.

Catalytic activity of Michael reaction was highly dependent on the type of solvent. The yield of the adduct in polar solvent of solvent such as EtOH and DMF was higher than non-polar benzene. These results suggest that the polarity plays more important roles in the catalysis than ethoxide anion (EtO⁻) formed under basic conditions. This may be a reason of different features of solvent in Michael reaction from Knoevenagel reaction.

Michael reaction of 4-methoxychalcone (**7c**) and diethyl malonate (**8a**) was examined by using AP-, PZP-, MAP-, and DMAP-functionalized [Si]-

Table 15 : Knoevenagel Reaction of Benzaldehyde (**1a**) and Ethyl Cyanoacetate (**2b**) over AP-functional Molecular sieves^{a)}

Run	Catalyst	Temp (°C)	Period (h)	Yield of 3ab ^{b)} (%)
1	AP-[Si]-MCM-41	r.t.	1	99
2	MAP-[Si]-MCM-41	r.t.	1	70
3	PZP-[Si]-MCM-41	80	6	13
4	DMAP-[Si]-MCM-41	80	6	0
5	DEAP-[Si]-MCM-41	80	6	0
6	PDP-[Si]-MCM-41	80	6	0

^{a)} Reaction conditions: catalyst, 100 mg; **1a**, 1.25 mmol; **2b**, 1.30 mmol; solvent, toluene, 1 ml.

^{b)} isolated yield.

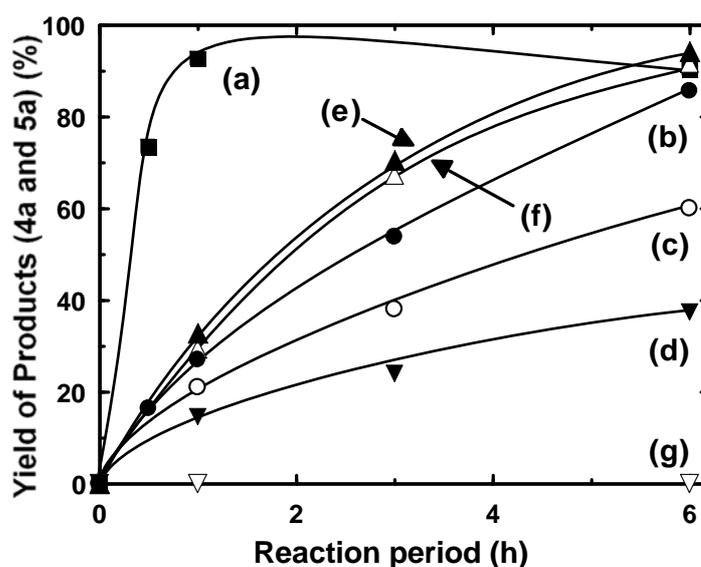


Figure 4 : Time-course of Aldol reaction of 4-nitrobenzaldehyde (**4**) with acetone catalyzed by AP-functionalized silicates. (a) MAP-[Si]-FSM-16, (b) AP-[Si]-MCM-41, (c) AP-[Si]-FSM-16, (d) AP-SiO₂, (e) PzP-[Si]-MCM-41, (f) PzP-[Si]-FSM-16, and (g) DMAP-[Si]-FSM-16. Reaction conditions: catalyst, 100 mg; **7a**, 1.25 mmol; **8b**, 1.30 mmol; solvent, toluene; temperature, 20 °C.

Table 16 : Michael Reaction of Chalcone (**7a**) and Diethyl Malonate (**8a**) over Aminopropyl-functionalized Molecular Sieves in Different Solvents^{a)}

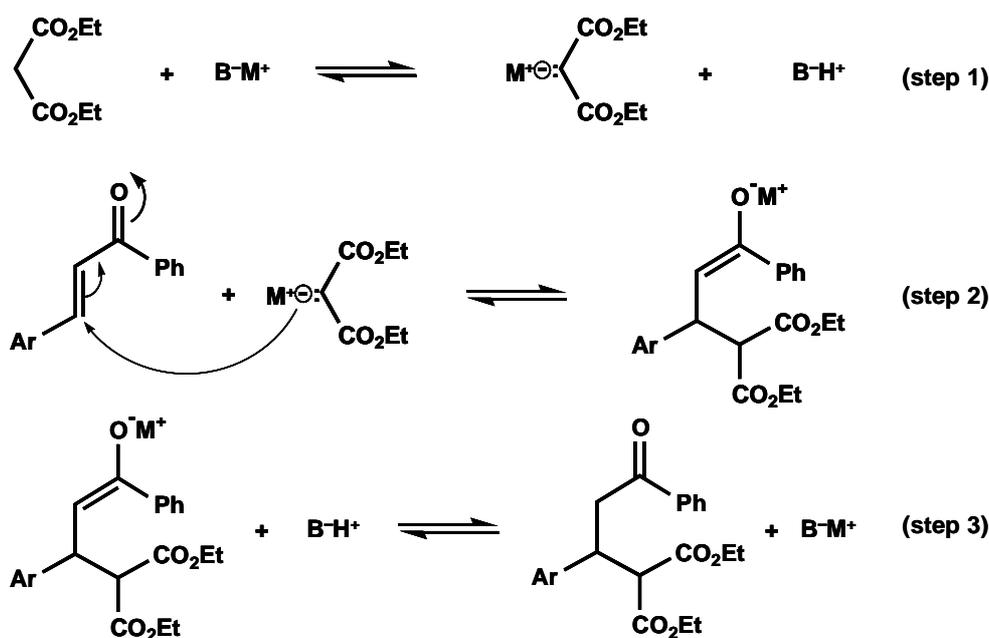
Run	Catalyst	AP ^{b)} (mmol/g)	Solvent	Yield of 9ab ^{c)} (%)	TOF ^{d)} (1/h)
1	AP-[Si]-MCM-41	1.31	EtOH	43	2.1
2	AP-[Si]MCM-41	1.31	DMF	46	2.2
3	AP-[Si]MCM-41	1.31	Benzene	3	0.1
4	AP-[Al]-FAU	0.61	EtOH	41	4.2
5	AP-[Al]-FAU	0.61	DMF	50	5.1
6	AP-[Al]-FAU	0.61	Benzene	1	0.1
7	AP-[Al]-BEA	0.95	EtOH	6	0.4
8	AP-[Al]-BEA	0.95	DMF	7	0.5
9	AP-[Al]-BEA	0.95	Benzene	1	0.1

^{a)} Reaction conditions: catalyst, 100 mg; **7a**, 1.25 mmol; **8b**, 1.30 mmol; solvent, toluene, temperature, 20 °C; period, 2 h.

^{b)} determined by elemental and thermogravimetric analyses.

^{c)} isolated yields.

^{d)} product(mol)/AP(mol)/h.

**Scheme 6** : A Proposed Mechanism of Michael Reaction over SOCMs Catalyst

MCM-41. All amine-immobilized silicates showed low activity for the reaction even in EtOH as a polar solvent. These activities of catalysts are totally different from that observed for Knoevenagel and Aldol reactions, in which primary and secondary amines are particularly active [34,56]. These results suggest that neither imine- nor enamine-type intermediate is involved in the mechanism of Michael reaction.

There have been differences between SOCMs and AP-functionalized molecular sieves. The differences of catalytic activity are dependent on the reaction. SOCMs have high activities for Knoevenagel, Michael, and Aldol reactions in benzene and EtOH as solvent. These results suggest

the role of $(\text{SiO})_3\text{SiO}^-(\text{NR}_4)^+$ ion pair is key for catalytic performances. The ion pair should activate the active methylene compounds, and then activated species attack the carbonyl group for unsaturated compounds for Michael reaction as shown in Scheme 6. On the other hand, imine is a key intermediate in the case of AP-functionalized molecular sieves judging from the influences of amine moieties on Knoevenagel and Aldol reactions. In these reactions, carbonyl group is more strongly activated by imine- or enamine-formation with primary or secondary amine moieties of the molecular sieves. However, the formation of imine or enamine of chalcone is not involved in Michael reaction, but the amines work

as conventional base catalysts. This should be one of reasons why AP-functionalized molecular sieves are not much active for Michael reaction.

Acceleration of Amine-catalyzed Aldol Reaction by Mesoporous Silica

It is interesting to know the influence of silicate, particularly, on hydrophobic properties and silanols, in base catalyzed reactions. We examined the addition of mesoporous silica on the amine catalyzed Aldol reaction.

Table 17 shows the influences of secondary and primary amines on Aldol reaction of 4-nitrobenzaldehyde (**4**) with acetone. The activities using amines in Aldol reaction were generally low and the yields of 4-nitrophenyl-3-hydroxy-2-butanone (**5**) were not exceeding 5%. However, the yield of **5** enormously increased by addition of [Si]-FSM-16 to reaction mixture containing 10% of piperidine, piperazine, or dipropylamine (*n*-Pr₂NH) although 4-nitrophenyl-3-buten-2-one (**6**) was accompanied in small amounts. [Si]-MCM-41 also accelerated similarly the reaction; however, they were totally inert in the absence of amine. Sterically hindered secondary amines, such as diisopropylamine (*i*-Pr₂NH), showed no activity with or without [Si]-FSM-16 because of steric hindrance of bulky isopropyl groups. Primary amines, such as propylamine (*n*-PrNH₂), hexylamine (*n*-HexNH₂), benzylamine, and cyclohexylamine (*c*-HexNH₂), showed only low

activity (conversion < 20%), and the activity did not change in these cases even by the addition of [Si]-FSM-16. The use of tertiary amine, such as triethylamine, tributylamine, diisopropylethylamine, 1,4-diazabicyclo[2.2.2]octane (DABCO), pyridine, and 2,6-lutidine, either with or without [Si]-FSM-16, did not give any product, and only **4** was quantitatively recovered.

The activity of this catalytic system is primarily governed by the type of amines besides the presence or absence of silicate additive: secondary > primary > tertiary. The order is reasonable from view points of the mechanism via enamine formation [34,57]. However, the addition of silicates also played important role on the catalysis. Catalytic activities of [Si]-FSM-16, [Si]-MCM-41, and silica gel (Davison #57; surface area: 370 m²/g) versus surface area were similar level; however, the reaction was less accelerated by activated charcoal. These results indicate that co-existence of secondary amine and silicate is important for acceleration of Aldol reaction. The increase in reactant concentration on hydrophobic surface of silicate should be one of reasons of acceleration of the reaction by silicate addition. The coexistent acidic and basic sites also play important roles in Aldol reaction. Silanols on the silicate may work as acidic sites and synergistically accelerate amine catalysis.

Table 17 : Aldol Reaction of 4-Nitrobenzaldehyde(**4**) and Acetone Catalyzed by Amine^{a)}

Run	Amine	Additive ^{b)}	Conversion (%)	Yield ^{c)} (%)	
				5	6
1	Piperidine	-	7	3	0
2	Piperidine	[Si]-FSM-16	98	80	5
3	-	[Si]-FSM-16	0	0	0
4	Piperidine	[Si]-MCM-41	97	79	6
5	Piperidine	SiO ₂	59	59	0
6	Piperazine	-	11	47	2
7	Piperazine	[Si]-FSM-16	99	91	4
8	<i>n</i> -Pr ₂ NH	-	6	2	0
9	<i>n</i> -Pr ₂ NH	[Si]-FSM-16	79	48	5 ^d
10	<i>i</i> -Pr ₂ NH	-	0	0	0
11	<i>i</i> -Pr ₂ NH	[Si]-FSM-16	0	0	0
12	<i>n</i> -PrNH ₂	-	18	12	0
13	<i>n</i> -PrNH ₂	[Si]-FSM-16	18	13	3
14	<i>n</i> -HexNH ₂	-	13	8	0
15	<i>n</i> -HexNH ₂	[Si]-FSM-16	9	6	0
16	PhCH ₂ NH ₂	-	13	5	1
17	PhCH ₂ NH ₂	[Si]-FSM-16	9	5	1
18	<i>c</i> -HexNH ₂	-	10	3	1
19	<i>c</i> -HexNH ₂	[Si]-FSM-16	9	3	1

^{a)} Reaction conditions: amine, 0.1 mmol; silicate, 120 mg; **4**, 1.0 mmol; acetone, 5 ml. temperature, 30 °C; period: 6 h.

^{b)} 0 mol% of each amine was used.

^{c)} isolated yield.

^{d)} 18% of 2,6-di(4-nitrophenyl)tetrahydropyran-4-one was also obtained as a further reacted product.

AP-[Si]-FSM-16 discussed previously gave higher product yield than a physical mixture of *n*-PrNH₂ and [Si]-FSM-16: 18% (Run 13 in Table 17) and > 50%, respectively (amine amount is 14% of *n*-PrNH₂). These results mean that “immobilization” enhances the reactivity much better than “simple physical mixing”.

Conclusion

Heterogeneous catalysis for the organic synthesis is a key technology for green chemical processes. Ordered mesoporous materials are the important materials for the purposes. Because they have originally no acid and base characters, it is necessary to introduce catalytic active species in their channels. In this paper, we discuss our recent works on 1. the introduction of acid center to achieve high catalytic activity in acid catalyzed reaction high and 2. the use of Silicate-organic composite materials (SOCMS), such as-synthesized [Si]-MCM-41 for the typical base catalyzed reactions and a comparison with amine-functionalized mesoporous silica. 3. the acceleration of the amine-catalyzed Aldol reaction by hydrophobic character of mesoporous silica. The principal results thus obtained are follows:

Multi-valent metal salts (cation: Al³⁺, Fe³⁺, and Zr⁴⁺, etc.; anion: Cl⁻, SO₄²⁻, NO₃⁻, OAc⁻, etc.) were highly active for the esterification of equimolar fatty acids and alcohols. The heterogenization of the salts on [Si]-MCM-41 enhanced the catalytic activity because of the acceleration of water removal from the salts by their hydrophobic properties. Even esters of bulky branched acid and alcohols can be synthesized from equimolar substrates.

The *tert*-butylation of *p*-cresol with *tert*-butyl alcohol over [Si]-MCM-41-supported HPW occurred effectively in supercritical CO₂, resulting in high yield of 2-*tert*-butyl-4-methylphenol (2-TBPC) and 2,6-di-*tert*-butyl-4-methylphenol (2,6-DTBPC). Coke-precursors are eliminated by their dissolution in supercritical CO₂ to minimize the deactivation of the *tert*-butylation to 2-TBPC and 2,6-DTBPC. We could achieve the highest yield of 2,6-DTBPC in the literature.

Silicate-organic composite materials (SOCMs), such as synthesized [Si]-MCM-41, were active for base catalysis, such as Knoevenagel, Aldol, and Michael reactions. These catalysts are quite new types of catalysts. They are highly active for these reactions, and reusable for further reaction. (SiO)₃SiO⁻(NR₄⁺), the ion pair of silicate and organic moiety in as-synthesized materials plays key roles in the catalysis. They have much higher catalytic performances than amine-functionalized materials under the same conditions.

Mesoporous silica accelerates the amine-catalyzed Aldol reaction. Amines adsorbed on the hydrophobic surface catalyzes effectively with the assistance of silanol moieties with slightly acidic

characters.

These examples of catalysts for organic catalysis in mesoporous environment show the promising ways to apply for the green synthesis for specialty and fine chemicals.

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