Tetrahedron Letters 51 (2010) 4243–4245

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Mesoporous aluminosilicate-catalyzed Sakurai allylation and Mukaiyama aldol reaction of acetals

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ARTICLE INFO

Article history:
Received 21 April 2010
Revised 2 June 2010
Accepted 7 June 2010
Available online 11 June 2010

Keywords:
Al-MCM-41
Solid acid catalyst
Sakurai allylation
Mukaiyama aldol reaction

ABSTRACT

In the presence of a catalytic amount of mesoporous aluminosilicate (Al-MCM-41), both allyltrimethylsilane and silyl enol ether reacted with various acetals under mild reaction conditions to afford the corresponding homoallyl ethers and β-alkoxy ketones, respectively. The catalyst was easily recovered from the reaction mixture and could be reused in the same reaction without a significant loss of catalytic activity. Moreover, Al-MCM-41 exhibited high chemoselectivity for acetal over aldehyde in the reactions.

Acetals are generally inert toward nucleophiles under basic conditions, therefore they have been widely used as the protective group of carbonyl compounds.[1] On the other hand, acetals react with allylsilanes (Sakurai allylation) or silyl enol ethers (Mukaiyama aldol reaction) in the presence of Lewis acids to afford homoallyl ethers or β-alkoxy carbonyl compounds.[2,3] These reactions are recognized as valuable carbon–carbon bond-forming reactions in organic synthesis because of the high synthetic utility of the products.[4] Although a wide variety of catalysts are known to be effective for these reactions,[5,6] the recovery and reuse of the catalysts are generally difficult because most of them decompose during work up of the reaction.

Along with the increasing attention to the development of environmentally benign reaction systems, the replacement of conventional Lewis acids to heterogeneous solid acids is important in the current field of synthetic organic chemistry. Nevertheless, there have been only few reports on allylation or aldol reaction of acetals with allylsilanes or silyl enol ethers catalyzed by heterogeneous catalysts.[7,8]

In 2003, Iwamoto and co-workers reported that ordered mesoporous silica MCM-41 catalyzed Mukaiyama aldol reaction of silyl enol ethers with acetals under heterogeneous conditions.[8c] MCM-41 possesses large uniform pores (2–10 nm) and a high surface area,[9] and it is well known that the catalytic activity of MCM-41 increases by incorporating metals, such as Ti, Sn, and Al, into its structure.[10] Among them, aluminum incorporated MCM-41 (Al-MCM-41) has been found to catalyze several synthetic reactions under mild reaction conditions, recently.[11] Herein, we report mild and efficient catalytic systems for chemoselective reactions of acetals and allylsilane or silyl enol ether by using Al-MCM-41.

At first, Sakurai allylation of benzaldehyde dimethyl acetal (**1a**) with allyltrimethylsilane (**2**) was investigated (Table 1). In the presence of Al-MCM-41 (30 mg, Si/Al = 26, dried prior to use at 120 °C for 1 h under vacuum),[12,13] the reaction of **1a** (1.0 mmol) with **2** (1.5 mmol) in dichloromethane at 30 °C for 45 min afforded 4-methoxy-4-phenylbut-1-ene (**3a**) in 86% yield along with 7% yield of 1-phenylbuta-1,3-diene (**4**) (entry 1). When the reaction was carried out by using amorphous silica–alumina (SiO_2–Al_2O_3)[14] or aluminum-free MCM-41[15] in place of Al-MCM-41, homoallyl ether **3a** was not obtained (entries 2 and 3). Therefore, it turned out that both the mesoporous structure and the presence of aluminum moiety were necessary for the high catalytic activity of Al-MCM-41 as was observed in the case of Al-MCM-41-catalyzed allylation of aldehydes. By reducing the aluminum content of the catalyst, the amount of **4** produced in the reaction decreased and only **3a** was obtained in 96% yield by using Al-MCM-41 (Si/Al = 48) (entries 4 and 5).[16]

As high yield was achieved in the reaction of **1a**, Al-MCM-41-catalyzed allylation of various acetals was examined (Table 2). Electron-withdrawing or electron-donating groups on the aromatic ring did not affect the reaction, and the corresponding homoallyl methyl ethers were obtained in 76–98% yields (entries 2–12). Allylation of acetals derived from naphthaldehydes, (*E*)-cinnamaldehyde, and aliphatic aldehydes also proceeded to give the corresponding product in good yields (entries 13–17). Benzaldehyde diethyl acetal was allylated as well, and the corresponding homoallyl ethyl ether was obtained in 85% yield (entry 18). The

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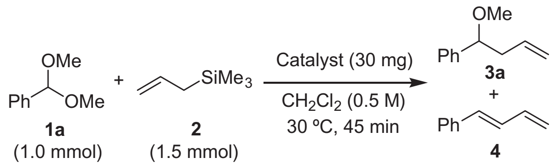
doi:10.1016/j.tetlet.2010.06.034

Table 1
Allylation of benzaldehyde dimethyl acetal (**1a**) with allyltrimethylsilane (**2**)



Entry	Catalyst	Si/Al	**3a**[a] (%)	**4**[a] (%)
1	Al-MCM-41	26	86	7
2	SiO_2–Al_2O_3	31	0	0
3	MCM-41	∞	0	0
4	Al-MCM-41	34	91	4
5	Al-MCM-41	48	96	Trace

[a] Determined by ^{1}H NMR analysis of the crude product using nitromethane as an internal standard.

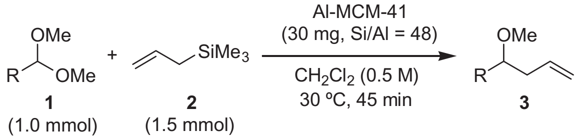
reaction of a ketal, cyclohexanone dimethyl ketal (**5**), with 3 equiv of **2** afforded 1-allyl-1-methoxycyclohexane (**6**) in 95% yield (Scheme 1).

The recovery and reuse of the catalyst were examined in the reaction of **1a** with **2** (Table 3).[17] After the reaction was completed, the catalyst was recovered by filtration and dried at 70 °C for 15 min. The catalyst was then treated in the same manner as the first run. The recovered catalyst could be reused three times for the same reaction without significant loss of catalytic activity.

Next, a reaction of various acetals with 1-phenyl-1-trimethylsiloxyethene (**7**) (Mukaiyama aldol reaction) was investigated (Table 4). The reaction of benzaldehyde dimethyl acetal (**1a**) with **7** under an optimized reaction condition of Al-MCM-41-catalyzed aldol reaction of aldehydes[11e,18] afforded 3-methoxy-1,3-diphenylpropan-1-one in 95% yield, and the catalyst was reusable at least three times (entry 1).[19] The reaction did not proceed in the presence of SiO_2–Al_2O_3 or MCM-41 under the same reaction conditions (entries 2 and 3), though it was reported that MCM-41 could catalyze the same reaction in toluene.[8c] The difference in catalytic activity between the present MCM-41 and previously reported one[8c] is probably due to the difference of silica sources of MCM-41.[20] Other aromatic and aliphatic acetals and ketal were also reacted with **7** to afford the corresponding β-methoxy ketones **8** in good yields (entries 4–9).

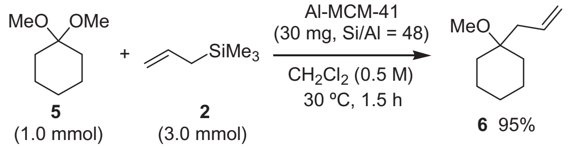
To estimate the chemoselectivity of the reactions, Al-MCM-41-catalyzed allylation and aldol reaction of acetal **1a** (1.0 mmol) were carried out in the presence of benzaldehyde (**9**) (1.0 mmol) using **2** (1.0 mmol) and **7** (1.0 mmol), respectively. As shown in Scheme 2, both reactions proceeded chemoselectively. Only **1a** reacted with **2** or **7** to afford **3a** or **8a**, although the reactions of **9** with **2** or **7** proceeded smoothly under the same reaction conditions in the absence of **1a**.[11d,e] With regard to the chemoselectivity of the reaction, typical strong Lewis acids (e.g., $TiCl_4$, $BF_3 \cdot OEt_2$, and $AlCl_3$) are known to show poor chemoselectivity.[6i] Trimethylsilyl trifluoromethanesulfonate (TMSOTf) and MCM-41 were reported to catalyze the aldol reaction of acetals in the presence of aldehydes,[6a,i,8c] because they usually could not promote the reaction of aldehydes and silyl enol ethers. Only MgI_2 etherate was reported to show chemoselectivity for acetals over aldehydes in the reaction despite the fact that it could activate both acetals and aldehydes.[21] Among the catalysts that activate both acetals and

Table 2
Allylation of various acetals **1** with allyltrimethylsilane (**2**) catalyzed by Al-MCM-41



Entry	R	Yield[a] (%)
1	Ph	93
2	$4\text{-}NO_2C_6H_4$	98
3	$4\text{-}BrC_6H_4$	90
4	$2\text{-}BrC_6H_4$	92
5	$4\text{-}ClC_6H_4$	96
6	$3\text{-}ClC_6H_4$	86
7	$2\text{-}ClC_6H_4$	92
8	$4\text{-}MeC_6H_4$	93
9	$3\text{-}MeC_6H_4$	92
10	$2\text{-}MeC_6H_4$	95
11[b]	$4\text{-}MeOC_6H_4$	76
12	$2\text{-}MeOC_6H_4$	88
13	2-Naphthyl	89
14	1-Naphthyl	80
15	(*E*)-PhCH=CH	74
16	*c*-C_6H_{11}	93
17	$PhCH_2CH_2$	93
18[c]	Ph	85

[a] Isolated yield.
[b] Allyltrimethylsilane (3.0 mmol) was used.
[c] Benzaldehyde diethyl acetal was used.



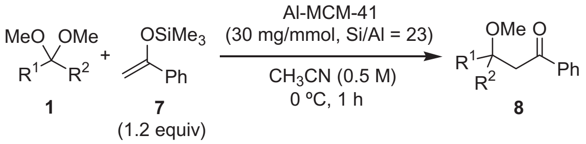
Scheme 1. Allylation of cyclohexanone dimethyl ketal (**5**) with allyltrimethylsilane (**2**).

Table 3
Reuse of Al-MCM-41[a]

Run	Al-MCM-41 (mg)	**1a** (mmol)	Time (min)	Yield[b] (%)
1	60	2.0	45	93
2	50	1.7	45	94
3	34	1.1	45	94
4	20	0.7	90	94

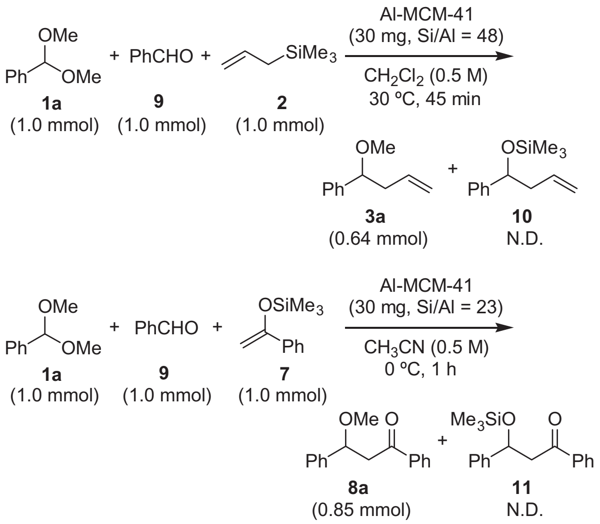
[a] In the presence of Al-MCM-41 (30 mg/mmol, Si/Al = 48) the reaction of benzaldehyde dimethyl acetal (**1a**) with 1.5 equiv of allyltrimethylsilane (**2**) was carried out in dichloromethane (0.5 M) at 30 °C.
[b] Isolated yield.

Table 4
Aldol reaction of various acetals **1** with 1-phenyl-1-trimethylsiloxyethene (**7**)



Entry	R^1	R^2	Yield[a] (%)
1	Ph	H	95 (1st run) 92 (4th run)[b]
2[c]	Ph	H	0
3[d]	Ph	H	0
4	$2\text{-}ClC_6H_4$	H	90
5	$3\text{-}ClC_6H_4$	H	78
6	$4\text{-}MeC_6H_4$	H	89
7	$4\text{-}MeOC_6H_4$	H	90
8	*c*-C_6H_{11}	H	89
9	–$(CH_2)_5$–		85

[a] Isolated yield.
[b] Recovered catalyst was used.
[c] SiO_2–Al_2O_3 (30 mg/mmol, Si/Al = 31) was used in place of Al-MCM-41.
[d] MCM-41 (30 mg/mmol, Si/Al = ∞) was used in place of Al-MCM-41.



Scheme 2. Chemoselective allylation and aldol reaction of benzaldehyde dimethyl acetal (**1a**).

aldehydes in Sakurai allylation, no catalyst has been reported to exhibit high acetal selectivity in the reaction, to the best of our knowledge.

In summary, the reactions of allyltrimethylsilane and silyl enol ether of acetophenone with various acetals were promoted under mild reaction conditions by using Al-MCM-41 as a reusable solid acid catalyst. Furthermore, it should be noted that Al-MCM-41 effected an interesting chemoselective activation of acetal over aldehyde in Sakurai allylation and Mukaiyama aldol reaction.

Acknowledgment

Y.K. thanks New Energy and Industrial Technology Development Organization (NEDO) for financial support.

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13. The specific surface area (BET) and the average pore diameter (BJH) were 1120 m^2/g and 2.7 nm, respectively.
14. Amorphous silica–alumina was synthesized according to the same procedure as the one used in the synthesis of Al-MCM-41 without the addition of surfactant, cethyltrimethylammonium bromide. The specific surface area (BET) was 385 m^2/g.
15. Aluminum-free MCM-41 was synthesized according to the same procedure as the one used in the synthesis of Al-MCM-41 without the addition of aluminum source, $Al(O^iPr)_3$. The specific surface area (BET) and the average pore diameter (BJH) were 1080 m^2/g and 2.6 nm, respectively.
16. The specific surface areas of Al-MCM-41 (Si/Al = 34) and Al-MCM-41 (Si/Al = 48) were 1101 and 1135 m^2/g, respectively. The average pore diameter (BJH) was 2.7 nm.
17. *Typical experimental procedure for Al-MCM-41-catalyzed Sakurai allylation*: Under an atmosphere of argon, to a mixture of benzaldehyde dimethyl acetal (0.304 g, 2.0 mmol) and Al-MCM-41 (60 mg, Si/Al = 48, dried prior to use at 120 °C for 1 h under vacuum) in dichloromethane (3.0 mL), allyltrimethylsilane (0.343 g, 3.0 mmol) in dichloromethane (1.0 mL) was added through a syringe at 30 °C. The reaction mixture was stirred at 30 °C for 45 min and the catalyst was removed by filtration. After the filtrate was concentrated under reduced pressure, almost pure homoallyl methyl ether was obtained. Further purification by silica-gel column chromatography (hexane to hexane/Et_2O = 10:1) afforded 4-methoxy-4-phenylbut-1-ene[5j] as a colorless oil (0.301 g, 93%). The product gave satisfactory IR and ^1H, ^{13}C NMR spectra. The recovered catalyst was dried at 70 °C for 15 min. Then, the catalyst (50 mg) was dried at 120 °C for 1 h under vacuum and used in a second run.
18. Al-MCM-41 was newly synthesized according to the same manner as the one used in allylation and previous aldol reaction of aldehydes. However, Si/Al ratio was slightly different from each other. It was confirmed that there had been no difference in catalytic activity between Al-MCM-41 (Si/Al = 26) and Al-MCM-41 (Si/Al = 23).
19. *Typical experimental procedure for Al-MCM-41-catalyzed Mukaiyama aldol reaction*: Under an atmosphere of argon, to a mixture of benzaldehyde dimethyl acetal (0.304 g, 2.0 mmol) and Al-MCM-41 (60 mg, Si/Al = 23, dried prior to use at 120 °C for 1 h under vacuum) in acetonitrile (3.0 mL), 1-phenyl-1-trimethylsiloxyethene (0.462 g, 2.4 mmol) in acetonitrile (1.0 mL) was added through a syringe at 0 °C. The reaction mixture was stirred at 0 °C for 1 h and the catalyst was removed by filtration. After the filtrate was concentrated under reduced pressure, the crude product was purified by silica-gel column chromatography (hexane/Et_2O = 8:1) to afford 3-methoxy-1,3-diphenylpropan-1-one[22] as a colorless oil (0.456 g, 95%). The product gave satisfactory IR and ^1H, ^{13}C NMR spectra. The recovered catalyst was dried at 70 °C for 15 min. Then, the catalyst (50 mg) was dried at 120 °C for 1 h under vacuum and used in a second run.
20. Silica sources of present and previous MCM-41 were tetraethyl orthosilicate and colloidal silica, respectively.
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