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Iron-Containing Mesoporous Aluminosilicate: A Highly Active and Reusable Heterogeneous Catalyst for Hydroarylation of Styrenes

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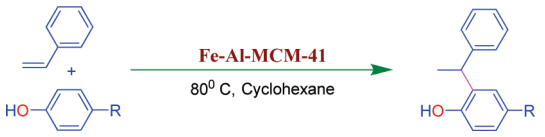

Hydroarylation of various styrene derivatives has been successfully carried out in excellent yield using Fe−Al-MCM-41 catalyst. The C−H functionalization using solid heterogeneous catalyst provides a straightforward access to a series of important 1,1-diarylalkane products. The catalyst can be recovered and reused at least three times without any significant loss in its catalytic activity.

The modified and tailored arenes and heteroarenes have attracted a considerable attention for its synthetic application in the field of pharmaceutical, agricultural, and fine chemical industries. Traditionally, Friedel−Crafts alkylation and acylation is one of the most powerful methods for such carbon−carbon bond-forming reactions.[1] These reactions are performed using strong Lewis acids such as $TiCl_4$, $BF_3 \cdot OEt_2$, and $AlCl_3$ and Brönsted acids such as HF and H_2SO_4. There are ongoing investigation programs to identify catalysts that address problems like high catalyst loading, low selectivity, overalkylation, formation of byproducts (salt), and sensitivity toward moisture and strong acid medium.

During the past decade, studies of iron-catalyzed C−C coupling reactions grew immensely.[2] "Iron-exploited catalysts" have been proven to be the most effective and green system in modern organic synthesis because of their lower toxicity and easy accessibility.[3]

Though the use of $FeCl_3$ as Lewis acid catalyst in carbon−carbon coupling reactions has been studied using alkyl or acyl halides, there are lacunas in the product selectivity and its widespread applicability. Recent development involves the utilization of esters, aldehydes, olefins, or alkynes as the alkylating reagent.[4] However, the use of aromatic olefins has been found to be very useful and practical as the resulting diarylalkane block represents an important part in biologically active compounds and pharmaceuticals substrates such as dimetindene, haplopappin, phenprocoumone, papaverine, or afenopin (Figure 1). In addition, diarylmethanes are utilized for the preparation of fluorenyl-based electroactive and photoactive oligomers and polymers.[5]

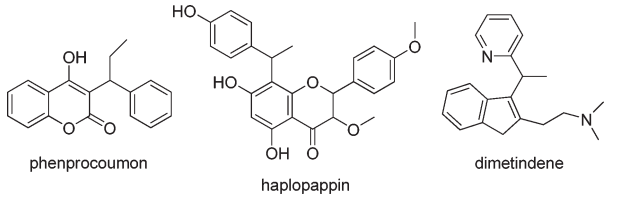

FIGURE 1. Biologically active compounds and pharmaceutical substrates.

Reactions being carried out in homogeneous media using $FeCl_3$, these methods, while useful, suffer from serious limitations including high catalyst loading, difficulty in recovery, reusability of the catalyst, and tedious workup procedures. Therefore, development of highly active and recoverable heterogeneous catalysts for such C−C coupling reactions is still an open challenge.

In the last few decades, mesoporous materials have received much attention in the field of catalysis, especially for their use as solid supports.[6] Supported catalysts have attracted increased attention in organic transformation due to their easy separation from the reaction mixture and possible reuse. Toward this end, mesoporous aluminosilicates (Al-MCM-41) have been employed in different organic reactions.[7] Although Al-MCM-41 has been successfully employed in heterogeneous C−C coupling reactions, most of the reactions have involved alkyl or acyl halides,[8] whereas

(1) (a) Olah, G. A. In *Friedel−Crafts Chemistry*; Wiley: New York, 1973. (b) Olah, G. A.; Krishnamurti, R.; Prakash, G. K. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, p 293. (c) Bandini, M.; Melloni, A.; Ronchi, A. U. *Angew. Chem., Int. Ed.* **2004**, *43*, 550–556.

(2) Czaplik, W. M.; Mayer, M.; Cvengroš, J.; von Wangelin, A. J. *ChemSusChem* **2009**, *2*, 396–417.

(3) Bolm, C.; Legros, J.; Paih, J. L.; Zani, L. *Chem. Rev.* **2004**, *104*, 6217–6254.

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(7) (a) Corma, A.; Fornes, V.; Navarro, M. T.; Perezpariente, J. *J. Catal.* **1994**, *148*, 569–574. (b) Corma, A. *Chem. Rev.* **1997**, *97*, 2373–2420. (c) De Vos, D. E.; Dams, M.; Sels, B. F.; Jacobs, P. A. *Chem. Rev.* **2002**, *102*, 3615–3640. (d) Iwanami, K.; Choi, J.-C.; Lu, B.; Sakakura, T.; Yasuda, H. *Chem. Commun.* **2008**, *8*, 1002–1004.

(8) (a) Hu, X.; Chuah, G. K.; Jaenicke, S. *Appl. Catal. A: Gen.* **2001**, *217*, 1–9. (b) Choudhary, V. R.; Jana, S. K.; Mamman, A. S. *Microporous Mesoporous Mater.* **2002**, *56*, 65–71. (c) Sartori, G.; Maggi, R. *Chem. Rev.* **2006**, *106*, 1077–1104.

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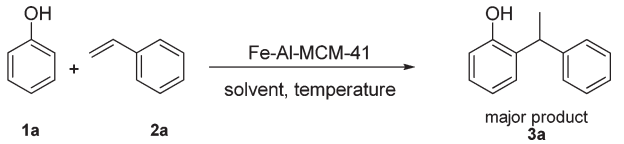
the use of olefins as the alkylating reagent is mainly restricted to the homogeneous system.[4d] However, there are examples for the synthesis of alkylbenzene using heterogeneous catalysts.[4g] Further, the catalytic activity of such aluminosilicates can be increased via incorporation of metal ions such as Cu^{II}, Zn^{II}, Fe^{III}, etc., which causes the generation of highly active Lewis acid sites.[9] The combination of such active Lewis acid site along with the available Brönsted acid site in metal-exchanged Al-MCM-41 together with their high surface area are known to facilitate reactions by localizing the reactants in their pore surfaces and providing high local concentration.[7c,10]

In the course of our continuing investigation of different organic reactions using ordered mesoporous silica materials as heterogeneous catalytic support we have found that the hybrid organic−inorganic material demonstrates desirable catalytic efficacy.[11] Herein, we report a facile and reusable heterogeneous catalyst, which is not sensitive to moisture, for the synthesis of diarylethane through C−H functionalization. The catalyst demonstrates high yield of products with good selectivity under mild conditions in a short reaction time.

MCM-41 and Al-MCM- 41 were prepared following the method described in a previous report.[12] The BET surface area and the BJH pore diameter of Fe−Al-MCM-41 were 917 $m^2 g^{-1}$ and 3.3 nm, respectively. The hexagonal pore structures of MCM-41 and Al-MCM-41 were confirmed from the XRD pattern.[12] Fe^{III} was immobilized into Al-MCM-41 by the conventional ion-exchange method.[13] The catalyst is hereinafter abbreviated as Fe−Al-MCM-41. The aluminum and iron content of the Fe−Al-MCM-41 was 5 wt % and 0.75 wt %, respectively, as estimated by atomic absorption spectrometer. Initial experiments focused on optimizing the solvent and temperature for the reaction of styrene with phenol using Fe−Al-MCM-41 (Table 1). The reaction was monitored by GC analysis. Considerable solvent dependence was revealed for this reaction (Table 1, entry 1−5). While the reaction yielded no product in acetonitrile or tetrahydrofuran, a rapid conversion of styrene was observed in dichloromethane. However, no arylated product of phenol is produced in dichloromethane. The yield of desired product in nitromethane was relatively less. Almost complete conversion of styrene to its desired product was observed in cyclohexane within a remarkably short reaction time (Table 1, entry 5). The optimum temperature of the reaction was 80 °C. On reduction of the reaction temperature, the yield is also reduced. For example,when the temperature was reduced to 70 °C, the yield of diarylethane was only 55% in 4 h (Table 1, entry 6). Notably, the coupling reaction did not take place below 60 °C in 24 h (Table 1, entry 7−9).

In order to understand the role of the iron center in Fe−Al-MCM-41, the coupling reaction of phenol and styrene was carried out using a variety of other prospective catalysts, like microporous, mesoporous, and amorphous silica and alumina in cyclohexane at 80 °C (Table 2). The well-known solid acid catalyst, HY zeolite could not activate the substrates (Table 2, entry 3). An analogous result was obtained using a strong mineral (Brönsted) acid like HCl (Table 2, entry 1). Similarly, mesoporous silica MCM-41 also does not catalyze the reaction (Table 2, entry 4). This is, however, expected as there is no acid site in silicious MCM-41. Mesoporous aluminosilicates are known for their catalytic efficiency for a number of reactions.[8] Catalytic activity normally originates owing to the presence of mild Brönsted acid centers as well as Lewis acid centers in aluminosilicates. Notably, when Al-MCM-41 was used in this reaction no conversion was observed (Table 2, entry 5). To understand the role of aluminum, reactions were performed using different amorphous alumina (Table 2, entries 6−8). The three types of alumina (acidic, basic, and neutral) were catalytically inactive in this reaction. However, Fe−Al-MCM-41 demonstrates remarkable performance showing a high yield of products

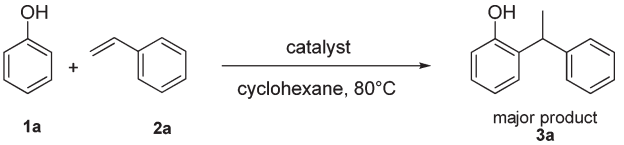
TABLE 1. Fe−Al-MCM-41-Catalyzed Reaction of Styrene and Phenol[a]



entry	T (°C)	solvent	time (h)	conversion[b] (%)	yield[c] (%)
1	80	CH_3CN	4	6	0
2	80	THF	4	8	0
3	40	CH_2Cl_2	4	90	0
4	80	CH_3NO_2	4	82	75
5	80	cyclohexane	3	100	95
6	70	cyclohexane	4	55	93
7	rt	cyclohexane	24	2	0
8	60	cyclohexane	24	9	0
9	40	cyclohexane	24	5	0

[a]Reaction conditions: 0.5 mmol of styrene, 2 mmol of phenol, 65 mg of catalyst, 5 mL of solvent. [b]GC conversion of styrene. [c]GC yield of arylated products.

TABLE 2. Reactions of Phenol with Styrene[a]



entry	catalyst	time (h)	conversion[b] (%)	yield[c] (%)
1[e]	HCl (10 mol %)	20	8	0
2[e]	$FeCl_3 \cdot 6H_2O$ (10 mol %)	20	94	88
3	HY	24	3	0
4	MCM-41	24	1	0
5	Al-MCM-41	24	4	0
6	basic alumina	24	2	0
7	Acidic alumina	24	5	0
8	Neutral alumina	24	1	0
9	Fe−Al-MCM-41	3	100	95
10[f]	$FeCl_3 \cdot 6H_2O$	(a) 3	(a) < 1	(a) < 1
	(0.008 mmol)	(b) 20	(b) 3	(b) < 3

[a]Reaction conditions: 0.5 mmol of styrene, 2 mmol of phenol, 65 mg of catalyst, 5 mL of cyclohexane, 80 °C. [b]GC conversion of styrene. [c]GC yield of arylated products. [e]10 mmol % of catalyst, ref 4d. [f]Catalyst: 2.32 mg of $FeCl_3 \cdot 6H_2O$ (0.008 mmol)

(9) Luan, Z.; Hatmann, M.; Zhao, D.; Zhou, W.; Kevan, L. *Chem. Mater.* **1999**, *11*, 1621–1627.
(10) Taguchi, A.; Schüth, F. *Microporous Mesoporous Mater.* **2005**, *77*, 1–45.
(11) (a) Jana, S.; Dutta, B.; Bera, R.; Koner, S. *Langmuir* **2007**, *23*, 2492–2496. (b) Jana, S.; Dutta, B.; Bera, R.; Koner, S. *Inorg. Chem.* **2008**, *47*, 5512–5520. (c) Jana, S.; Haldar, S; Koner, S. *Tetrahedron Lett.* **2009**, *50*, 4820–4823.
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with good selectivity within a very short time (Table 2, entry 9). These results indicate that the mesoporous aluminosilicate itself does not catalyze the reaction. Nevertheless, its catalytic activity was remarkably enhanced when Fe^{III} was immobilized into it. In fact, only 65 mg of Fe−Al-MCM-41 was enough to complete the reaction at 3 h. Thus, the catalytic efficacy of mesoporous catalyst Fe−Al-MCM-41 was found to be much higher than the corresponding homogeneous $FeCl_3 \cdot 6H_2O$ catalyst under the same conditions (Table 2, entry 10). Notably, iron-doped commercially available silica remained virtually inactive in this reaction[14] and so also did iron-doped microporous aluminosilicates (see Table S2,Supporting Information).

To explore the scope and limitation of the reaction, the optimized conditions were subsequently applied to several other substituted phenols (Table 3). The reactions proceeded smoothly, and the desired products were obtained in high yields within 2.5−7.5 h. Analysis reveals that the substituted phenols with electron-donating groups quickly reacted to afford full conversion of the styrene, and the corresponding diarylethanes were obtained in high yield. The catalyst was active enough in the C−C coupling reactions of electron deficient arenes like *p*-chlorophenol and *p*-nitrophenol with styrene. However, salicylaldehyde was totally inactive toward this reaction under the reaction condition.

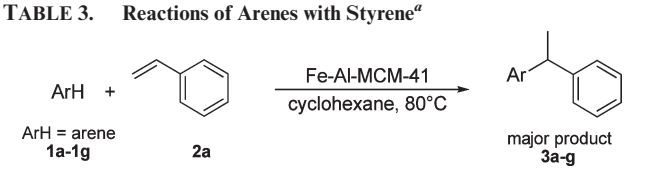
Further, to explore the general applicability of the reaction, different methyl-substituted styrenes were examined (Table 4). 4-Methylstyrene reacted adequately with phenol and *p*-cresol with a complete conversion with a shorter time period (Table 4, entries 3 and 4). In the case of 3-methylstyrene, 81% and 91% arylated products were obtained with phenol and *p*-cresol, respectively. Thus, both styrene and the substituted styrene reacted smoothly with different arenes to produce the Markownikoff adduct in high conversion and selectivity in a reasonable time frame.

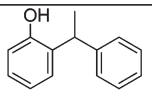
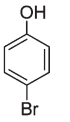
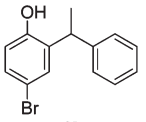
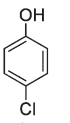
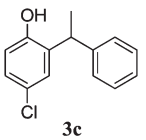
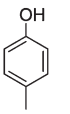
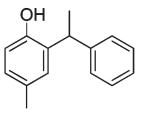
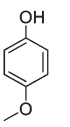
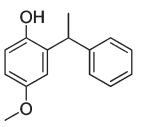
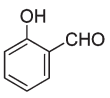
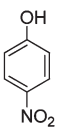
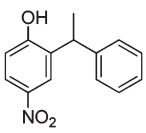
To test the recycling of the catalyst, the C−C coupling reaction of phenol and styrene was performed using the recovered catalyst (Table 5). After each cycle, the reaction mixture was allowed to cool to room temperature, and catalyst was separated by filtration. Recovered catalyst was then washed with cyclohexane and methanol followed by dichloromethane and dried at 80 °C for 1 h. The catalyst was then reused without any further treatment. The recycled catalyst exhibited 100% conversion in 3−4 h (Table 5). Fe−Al-MCM-41 also demonstrates good mechanical stability (see Table S1 and Figure S4 in the Supporting Information).

In order to confirm the true heterogeneity of the catalyst, the "hot filtration method" was employed as described by Lempers and Sheldon.[15] Catalyst was separated from the reaction mixture by filtration when approximately 22% conversion had taken place (after around 1 h) in a coupling reaction of styrene and phenol. The "catalyst-free" filtrate was then kept under the reaction conditions. Analysis of the filtrate showed no further progress of reaction even after 24 h. Catalyst was filtered off at the reaction temperature (80 °C) in order to avoid readsorption of leached iron on the catalyst surface on cooling. Leaching of the metal from the catalyst during reaction was examined by AAS analysis. Upon completion of the coupling reaction catalyzed by Fe−Al-MCM-41, the reaction mixture was filtered through a dried Celite pad under the reaction temperature (80 °C) to remove the solid catalyst. The AAS analysis of the clear filtrate did not show any leached iron.

In conclusion, we have succeeded in preparing a heterogeneous solid catalyst, Fe−Al-MCM-41, for hydroarylation of styrenes. The catalyst has shown notable activity in the carbon−carbon coupling reaction toward a variety of substituted phenols and olefins in an extraordinarily short time. Thus, the Fe−Al-MCM-41 offered an effective and facile catalytic method

TABLE 3. Reactions of Arenes with Styrene[a]



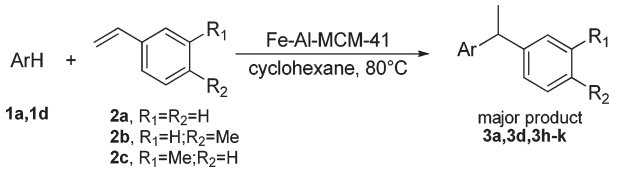
Ent.	Arene	Product[b]	Time [h]	Conv [%][c]	Yield [%][d]	Sel.[e]
1	 1a	 3a	3	100	95	95:5
2	 1b	 3b	2.5	100	96	>99:1
3	 1c	 3c	3.5	93	87	>99:1
4	 1d	 3d	2.5	100	>99	>99:1
5	 1e	 3e	3.5	100	98	96:4
6	 1f	-	12	-	-	-
7	 1g	 3g	7.5	73	65[f]	>99:1

[a]Reaction condition: 0.5 mmol of styrene, 2 mmol of arene, 5 mL of cyclohexane, 65 mg of Fe−Al-MCM-41, 80 °C. [b]Main product. [c]GC conversion of styrene. [d]GC yield of arylated products. [e]Main product: other isomers. [f]Yield after column chromatography.

(14) Reaction of phenol and styrene using different iron doped silica (reaction conditions: 0.5 mmol of styrene, 2 mmol of phenol, 65 mg of modified silica, 5 mL of cyclohexane, 80 °C): Fe−silica gel 60−120 mesh, 24 h, 1% conversion (based on GC conversion of styrene), 0% yield (based on GC yield of arylated products); Fe−silica gel 230−400 mesh, 24 h, 2% conversion (based on GC conversion of styrene), 0% yield (based on GC yield of arylated products).

(15) Lempers, H. E. B.; Sheldon, R. A. *J. Catal.* **1998**, *175*, 62–69.

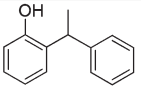
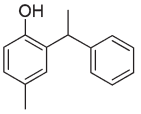
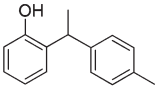
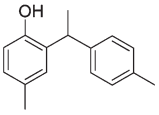
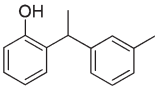
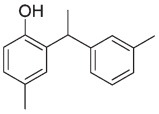
TABLE 4. Reaction of Phenol and p-Cresol with Styrene Derivatives[a]



1a,1d

2a, $R_1=R_2=H$
2b, $R_1=H;R_2=Me$
2c, $R_1=Me;R_2=H$

major product
3a,3d,3h-k

Ent.	Reactant	Product[b]	Time [h]	Conv. [%][c]	Yield [%][d]	Sel.[e]
1	**1a + 2a**	 **3a**	3	100	95	95:5
2	**1d + 2a**	 **3d**	2.5	100	>99	>99:1
3	**1a + 2b**	 **3h**	2.5	100	96	96:4
4	**1d + 2b**	 **3i**	2	100	>99	>99:1
5	**1a + 2c**	 **3j**	7	91	81	97:3
6	**1d + 2c**	 **3k**	6	95	91	>99:1

[a]Reaction conditions: 0.5 mmol of 4/3-methylstyrene or styrene, 2 mmol of arene, 5 mL of cyclohexane, 65 mg of Fe−Al-MCM-41, 80 °C. [b]Main product. [c]GC conversion of 4/3-methyl styrene or styrene. [d]GC yield of arylated products. [e]Main product: other isomers.

for the synthesis of a wide variety of diarylethanes. The catalyst can be recovered by filtration and reused several times without any loss of activity. The catalytic reaction can be performed under "open-flask" conditions. The enhanced efficacy of Fe−Al-MCM-41 in the catalytic C−C coupling reaction is attributed to the high internal surface area of the nanoporous catalyst that provides enough space for organic substrate to interact with active sites present on the solid surface inside the ordered mesopore.

TABLE 5. Recycling of Fe−Al-MCM-41 Catalyst for the Reaction of Phenol with Styrene

	cycle			
	1	2	3	4
conversion (%)[a]	100	100	100	100
time (h)	3	3.5	4	3.5
yield (%)[b]	95	96	93	91

[a]GC conversion of styrene. [b]GC yield of arylated products.

Experimental Section

Typical Procedure for Catalytic Reaction. The coupling reaction was carried out in a glass batch reactor. Styrene (0.5 mmol) was added to a mixture of phenol (2 mmol) and Fe−Al-MCM-41 (0.065 g) in 5 mL of cyclohexane. The mixture was stirred at 80 °C in an oil bath. To study the progress of the reaction, the products were collected at different time intervals and identified and quantified by gas chromatograph. After completion of the reaction, the solution was cooled, and the catalyst was removed by filtration. The resulting crude mixture was gently evaporated under vacuo and purified by column chromatography on silica gel using an appropriate solvent.

2-(1-Phenylethyl)phenol (**1a**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 −7.19 (m, 6H, C*H*), 7.17 −7.11 (m, 1H, C*H*), 6.98 −6.93 (m, 1H, C*H*), 6.78 −6.75 (m, 1H, C*H*), 4.69 (s, 1H, O*H*), 4.39 (q, *J* (H,H) = 7.2 Hz, 1H, C*H*CH_3), 1.64 (d, *J* (H,H) = 7.2 Hz, 3H, CH_3CH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 144.8, 131.4, 128.1, 127.4, 126.9, 125.9, 120.3, 115.4, 38.2, 20.4.

Synthesis of the Catalyst (Fe−Al-MCM-41). Iron was incorporated into the mesoporous aluminosilicate (Al-MCM-41) by the ion-exchange method. Al-MCM-41 (0.5 g) was added to 100 mL of a 0.001 M methanolic solution of $FeCl_3 \cdot 6H_2O$ and stirred vigorously for 12 h. The resultant solid was then filtered. To remove the excess $FeCl_3$, the isolated solid was washed with Soxhlet extraction using methanol. The resulting solid was dried in oven at 80 °C and characterized. The catalyst then used directly in reactions without any further activation.

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Supporting Information Available: Experimental procedures and compound characterization data of all unknown compounds as well as known compounds. This material is available free of charge via the Internet at http://pubs.acs.org.