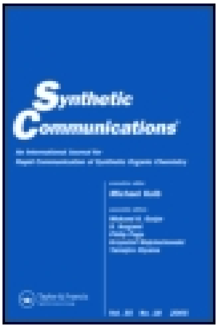

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Highly Efficient Michael Addition Reaction of Amines Catalyzed by Silica-Supported Aluminum Chloride

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Highly Efficient Michael Addition Reaction of Amines Catalyzed by Silica-Supported Aluminum Chloride

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Abstract: Aliphatic and aromatic amines undergo smooth nucleophilic addition to α,β-unsaturated compounds in the presence of a catalytic amount of silica-supported aluminum chloride at 60 °C and under solvent-free conditions to produce the corresponding β-amino compounds in excellent yields. This method is simple and convenient and works efficiently under mild conditions. This catalyst can used again without losing its activity three times.

Keywords: Amines, Michael addition, silica-supported aluminum chloride, α,β-unsaturated olefins

INTRODUCTION

Interest in developing environmentally benign and solvent-free reactions has increased dramatically. Consequently, operationally simple catalytic processes, which circumvent the use of toxic materials, have become a powerful tool in constructing an organic transformation.[1–5] One problem for using solvent-free reactions is high catalyst loading, which is generally required to effect the desired transformations in a reasonable time scale.

The Michael reaction is one of the most important carbon–carbon bond-forming reactions. A variety of Michael acceptors, such as α, β-unsaturated ketones, aldehydes, esters, and nitrils, can be used in this

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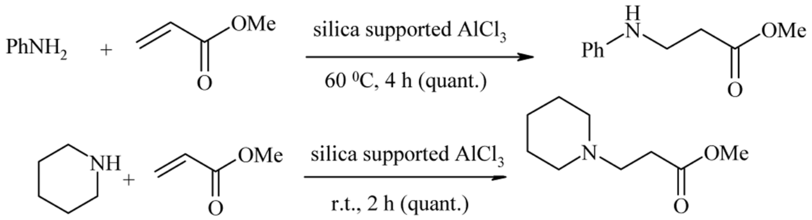
reaction, which can be readily transformed into a range of different functionalities.[6] A large number of methods have been reported quite recently for 1,4-conjugate addition to electron-deficient olefins.

This reaction has been investigated using catalysts such as lanthanum trichloride ($LaCl_3$),[6] bromodimethylsulfonium bromide,[7] silica-supported perchloric acid,[8] cerium(IV) ammonium nitrate (CAN),[9,10] β-cyclodextrin,[11] zirconium(IV) chloride,[12] samarium(III) triflate,[13] $ZrOCl_2 \cdot 8H_2O$ on montmorillonite K10,[14] *N*-methylimidazole,[15] amberlyst-15,[16] 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU),[17] bismuth (III) triflate,[18] cadmium chloride ($CdCl_2$),[19] $Y(NO_3)_3 \cdot 6H_2O$,[20] and cellulose-supported copper(0).[21] However, there are various limitations with the reported methodologies, especially when using aromatic amines, such as long reaction times, low yields for aromatic amines, use of halogenated solvents, difficulty in recovery of high-boiling solvents, high temperatures, requirement of special efforts for preparation of the catalysts, use of costly catalysts, and moderate yields.

In the past few years, the use of silica-supported aluminum chloride as a reusable, heterogeneous, inexpensive solid Brønsted acid catalyst has been widely used and received much attention.[22–26] Aluminum chloride is a very active Lewis acid that is soluble in many organic solvents and produces unwanted side reactions. By using silica-supported aluminum chloride, the high reactivity of this active Lewis acid is under control. Silica-supported aluminum chloride is a strong Brønsted and Lewis acid, presumably arising from the formation of $SiOAlCl_2$ sites on the surface.[27] This heterogeneous catalyst can be easily separated from the reaction media, has greater selectivity, and is recyclable, easier to handle, more stable, nontoxic, and insoluble in organic solvents.

RESULTS AND DISCUSSION

Because of our interest in studying the Michael reaction under solvent-free and environmentally benign methods,[28–32] herein we report a mild, easy, and catalytic process for Michael addition of aromatic amines at 60 °C and aliphatic amines at room temperature in excellent to quantitative yields using silica-supported aluminum chloride as catalyst. At first, we examined the reaction of aniline with methyl acrylate and 0.2 g of silica-supported aluminum chloride at room temperature under solvent-free conditions. Partial conversion took place within 4 h, leading to Michael adduct. When the temperature was raised to 60 °C, complete conversation took place after 4 h (Scheme 1).[33] By using 0.1 g of silica-supported aluminum chloride, the reaction was not complete after 4 h at 60 °C. When 0.3 g of catalyst was used, some polymeric materials were



Scheme 1. Michael addition of aromatic and aliphatic amines with methyl acrylate.

also formed as by-products. In the next step, we used piperidine with methyl acrylate and 0.2 g of catalyst at room temperature under solvent-free conditions. After 2 h, the reaction was complete with quantitative yields of the Michael adduct.

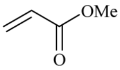
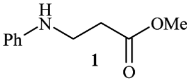
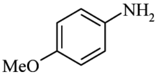
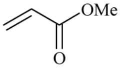
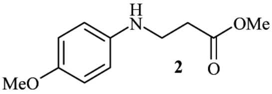
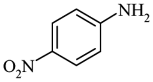
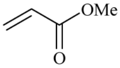
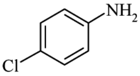
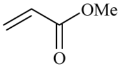
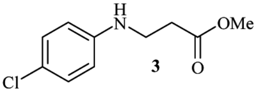
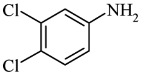
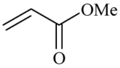
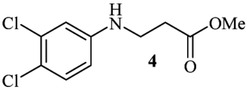
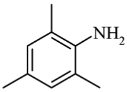
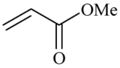
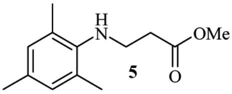
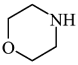
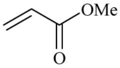
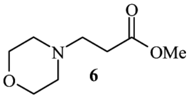
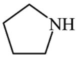
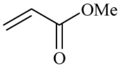
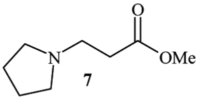
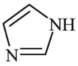
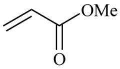
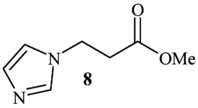
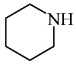
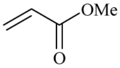
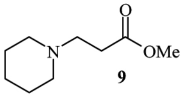
These results encouraged us to exploit the generality and scope of this reaction by using other Michael acceptors with various aromatic and aliphatic amines under catalytic amounts of silica-supported aluminum chloride. The reaction proceeded well with aromatic and aliphatic amines. As shown in Table 1, by this method, Michael addition of various aliphatic amines and aryl amines carrying either electron-donating or electron-withdrawing substituents were successfully reacted with α,β-unsaturated olefins to produce their corresponding Michael adducts in high to excellent yields. By using this method, Michael addition of 2,4,6-trimethylaniline and imidazole proceeded effectively with α,β-unsaturated compounds, but in low yields of products. Longer reaction times did not improve the yields of the products. The reaction with 4-nitroaniline did not proceed at all, even at higher temperatures. Michael addition with 2-naphthylamine in the presence of 0.2 g of catalyst gave quantitative yield after 20 h at 60 °C.

Methyl vinyl ketone (MVK) undergoes Michael addition under these reaction conditions. When aromatic amine was used with MVK, a mono-adduct was formed within shorter reaction time (Table 1, entry 19; mixture of 96% of mono- and 4% bis-adducts were formed after 4 h). In the case of 4-chloroaniline and 3,4-dichloroaniline, by using 1.5 equivalent of MVK, less than 10% of bis-adduct was formed after 4 h. When 3 equivalents of MVK was used, bis-adduct was formed with a longer reaction time (Table 1, entries 20 and 24).

We also examined the reaction of aniline with methyl acrylate using different protic and aprotic solvents in the presence of silica-supported aluminum chloride at 50–60 °C. The results showed that solvent-free conditions gave a better yield of β-amino compound (Table 2).

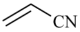
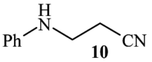
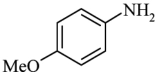
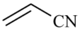
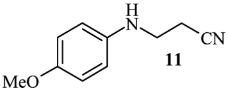
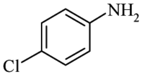
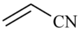
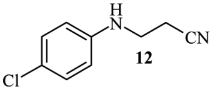
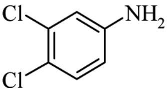
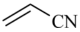
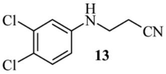
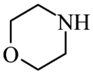
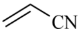
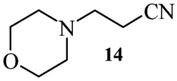
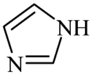
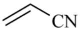
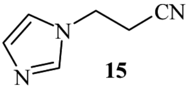
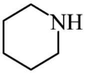
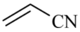
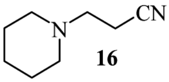
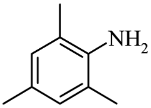
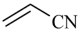
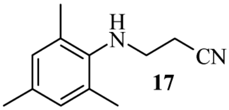
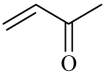
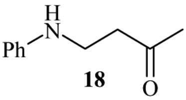
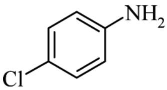
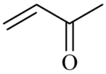
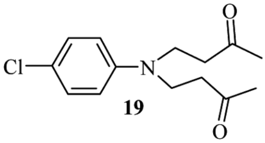
Silica-supported aluminum chloride catalyst can be used three times without losing its activity. The recovered silica-supported aluminum

Table 1. Michael addition of amines catalyzed by silica-supported aluminum chloride under solvent-free conditions

Entry	Amine	Michael acceptor	Product	Time (h)	Yield (%)
1	PhNH$_2$		 **1**	4.0	Quant.
2			 **2**	1.5	Quant.
3			N. R		
4			 **3**	4.0	97
5			 **4**	5.5	85
6			 **5**	8.0	50
7			 **6**	2.0	Quant.
8			 **7**	2.0	Quant.
9			 **8**	4.0	52
10			 **9**	2.0	Quant.

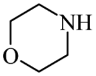
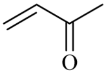
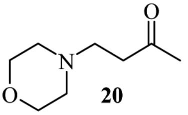
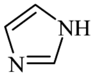
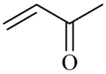
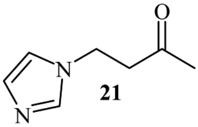
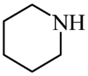
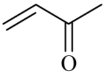
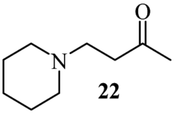
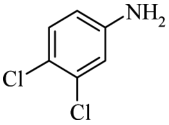
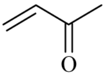
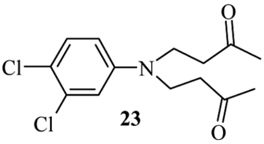
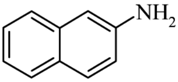
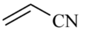
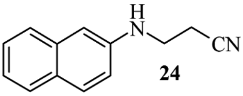
(*Continued*)

Table 1. Continued

Entry	Amine	Michael acceptor	Product	Time (h)	Yield (%)
11	$PhNH_2$		 **10**	6.0	75
12			 **11**	1.5	63
13			 **12**	6.5	90
14			 **13**	7.0	60
15			 **14**	2.0	86
16			 **15**	5.0	40
17			 **16**	2.0	72.5
18			 **17**	10.0	15
19	$PhNH_2$		 **18**	4.0	Quant.[a]
20			 **19**	7.0	Quant.[a,b]

(*Continued*)

Table 1. Continued

Entry	Amine	Michael acceptor	Product	Time (h)	Yield (%)
21			 **20**	2.0	90
22			 **21**	5.0	44
23			 **22**	2.0	77.5
24			 **23**	8.0	Quant.[b],[c]
25			 **24**	20.0	Quant.

[a] 96% mono-substitution and 4% bis-substitution products.

[b] 100% bis-substitution.

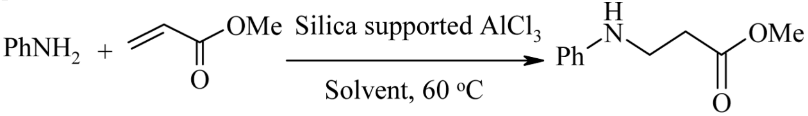
[c] Three equivalents of Michael acceptor were used.

chloride was tested in the reaction of aniline and methyl acrylate. The catalyst was still active when it was used for the third time, but the yield of the product decreased each time (Table 3).

A competition reaction was also carried out by using aniline (1 mmol), morpholine (1 mmol), and methyl acrylate (1 mmol) in the presence of silica-supported aluminum chloride at room temperature. After 3 h, compound **6** was formed as major product with small amount of **1** (Scheme 2).

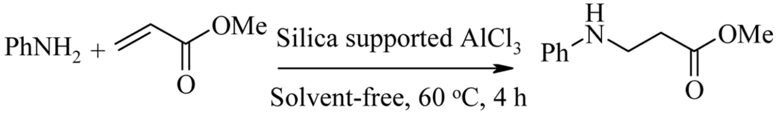
The silica-supported aluminum chloride catalyst was prepared according to the reported procedure in the literature.[6]

Table 2. Michael addition reaction of methyl acrlylate with aniline in protic and aprotic solvent



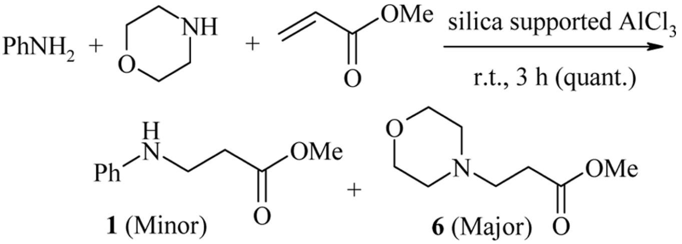
Solvent	Yield (%)
C_2H_5OH	28
H_2O	50
$ClCH_2CH_2Cl$	89
$PhCH_3$	55
CH_3CN	83

Table 3. Activity of the recovered silica-supported aluminum chloride[a]



Run	Yield (%)
1	97
2	69
3	65

[a] 1 mmol aniline, 1.5 mmol methyl acrylate, and 0.2 g silica-supported aluminum chloride were used each time.



1 (Minor)

6 (Major)

Scheme 2. Competition reaction of aniline and morpholine with methyl acrylate.

CONCLUSION

In conclusion, silica-supported aluminum chloride is among the most efficient catalysts for Michael addition of amines, especially aromatic amines, with different Michael acceptors under solvent-free conditions. This process avoids the use of organic solvent to carry out the reaction, and the catalyst can be separated from the product very easily after the reaction. Handling of the catalyst is easy, and it can be used again.

EXPERIMENTAL

General Procedure for the Synthesis of Compounds 1

Aniline (1 mmol), methyl acrylate (1.5 mmol), and 0.2 g of catalyst were placed into a small flask (or a test tube) and stirred at 60 °C for 4 h. The progress of the reaction was monitored with thin-layer chromatography (TLC). Then ethyl acetate (10 mL) was added, and the solution was filtered. The solid material was washed with 5 mL ethyl acetate, and the combined organic filtrates were dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was analyzed by its NMR spectra. In most cases, pure product was obtained. If needed, the residue was separated by silica gel (Merck 80–240 mesh) column chromatography using a 4:1 n-hexane–EtOAc mixture as eluent to afford the pure product. All of the products are known, and the structure of the products were determined from their NMR and IR spectra and by comparison with those reported in the literature.

Selected Spectroscopic Data

Compound **5**: ^1H NMR (500 MHz, $CDCl_3$, CCl_4) δ: 2.20 (s, 9H), 2.64 (t, $J = 6.1$ Hz, 2H), 3.24 (t, $J = 6.1$ Hz, 2H), 3.49 (br, 1H), 3.74 (s, 3H), 6.80 (s, 2H).

Compound **6**: ^1H NMR (500 MHz, $CDCl_3$, CCl_4) δ: 2.39 (t, $J = 4.4$ Hz, 4H), 2.42 (t, $J = 7.2$ Hz, 2H), 2.60 (t, $J = 7.2$ Hz, 2H), 3.61 (t, $J = 4.4$ Hz, 4H), 3.63 (s, 3H).

Compound **10**: ^1H NMR (500 MHz, $CDCl_3$, CCl_4) δ: 2.77 (t, $J = 6.6$ Hz, 2H), 3.28 (t, $J = 6.6$ Hz, 2H), 3.60 (br, 1H), 6.90–7.48 (m, 5H).

Compound **12**: ^1H NMR (500 MHz, $CDCl_3$, CCl_4) δ: 2.65 (t, $J = 6.1$ Hz, 2H), 3.53 (t, $J = 6.1$ Hz, 2H), 4.00 (br, 1H), 6.55 (d, $J = 8.3$ Hz, 2H), 7.14 (d, $J = 8.3$ Hz, 2H).

Compound **19**: ^{1}H NMR (500 MHz, $CDCl_3$, CCl_4) δ: 2.20 (s, 6H), 2.71 (t, $J = 6.8$ Hz, 4H), 3.58 (t, $J = 6.8$ Hz, 4H), 6.60 (d, $J = 7.4$ Hz, 2H), 7.18 (d, $J = 7.4$ Hz, 2H).

REFERENCES

1. Azizi, N.; Saidi, M. R. Novel and efficient method for the silylation of hydroxyl groups with hexamethyldisilazane (HMDS) under solvent-free and neutral conditions. *Organometallics* **2004**, *23*, 1457–1458.
2. Azizi, N.; Saidi, M. R. $LiClO_4$ accelerated Michael addition of amines to α,β-unsaturated olefins under solvent-free conditions. *Tetrahedron* **2004**, *60*, 383–387.
3. Azizi, N.; Saidi, M. R. Lithium perchlorate–catalyzed three–component coupling: A facile and general method for the synthesis of α-aminophosphonates under solvent-free condition. *Eur. J. Org. Chem.* **2003**, 4630–4633.
4. Azizi, N.; Saidi, M. R. Highly chemoselective addition of amines to epoxides in water. *Org. Lett.* **2005**, *7*, 3649–3651.
5. Yang, L.; Xu, L.-W.; Zhou, W.; Li, L.; Xia, C.-G. Highly efficient aza-Michael reactions of aromatic amines and *N*-heterocycles catalyzed by a basic ionic liquid under solvent-free conditions. *Tetrahedron Lett.* **2006**, *47*, 7723–7726.
6. Yadav, J. S.; Ramesh Reddy, A.; Gopal Rao, Y.; Narsaiah, A. V.; Reddy, B. V. S. Lanthanum trichloride ($LaCl_3$): An efficient catalyst for conjugate addition of amines to electron-deficient olefins. *Lett. Org. Chem.* **2007**, *4*, 462–464.
7. Khan, A. T.; Parvin, T.; Gazi, S.; Choudhury, L. H. Bromodimethylsulfonium bromide-mediated Michael addition of amines to electron deficient alkenes. *Tetrahedron Lett.* **2007**, *48*, 3805–3808.
8. Mukherjee, C.; Misra, A. K. Aza-Michael addition of amines to activated alkenes catalyzed by silica supported perchloric acid under a solvent-free condition. *Lett. Org. Chem.* **2007**, *4*, 54–59.
9. Duan, Z.; Xuan, X.; Li, T.; Yang, C.; Wu, Y. Cerium(IV) ammonium nitrate (CAN) catalyzed aza-Michael addition of amines to α,β-unsaturated electrophiles. *Tetrahedron Lett.* **2006**, *47*, 5433–5436.
10. Varala, R.; Sreelatha, N.; Adapa, S. R. Ceric ammonium nitrate catalyzed aza-Michael addition of aliphatic amines to α,β-unsaturated carbonyl compounds and nitriles in water. *Synlett* **2006**, 1549–1553.
11. Surendra, K.; Krishnaveni, N. S.; Sridhar, R.; Rao, K. R. β-Cyclodextrin promoted aza-Michael addition of amines to conjugated alkenes in water. *Tetrahedron Lett.* **2006**, *47*, 2125–2127.
12. Meshram, H. M.; Lakshindra, C.; Reddy, P. N.; Sadashiv, K.; Yadav, J. S. Zirconium(IV) chloride–mediated chemoselective conjugate addition of aliphatic amines to α,β-ethylenic compounds. *Synth. Commu.* **2006**, *36*, 795–801.
13. Yadav, J. S.; Ramesh Reddy, A.; Gopal Rao, Y.; Narsaiah, A. V.; Subba Reddy, B. V. Samarium(III) triflate catalyzed conjugate addition of amines to electron-deficient alkenes. *Synthesis* **2007**, 3447–3450.

14. Hashemi, M. M.; Eftekhari-Sis, B.; Abdollahifar, A.; Khalili, B. $ZrOCl_2 \cdot 8H_2O$ on montmorillonite K10 accelerated conjugate addition of amines to α,β-unsaturated alkenes under solvent-free conditions. *Tetrahedron* **2006**, *62*, 672–677.
15. Bo, K. L.; Wu, Q.; Xue, Q. Q.; De, S. L.; Xian, F. L. *N*-methyl-imidazole as a promising catalyst for the aza-Michael addition reaction of *N*-heterocycles. *Synthesis* **2007**, 2653–2659.
16. Das, B.; Chowdhury, N. Amberlyst-15: An efficient reusable heterogeneous catalyst for aza-Michael reactions under solvent-free conditions. *J. Mol. Catal. A: Chem.* **2007**, *263*, 212–215.
17. Yeom, C.-E.; Kim, M. J.; Kim, B. M.; Choudhury, L. H. 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU)-promoted efficient and versatile aza-Michael addition. *Tetrahedron* **2007**, *63*, 904–909.
18. Monfray, J.; Koskinen, A. M. P. Aza-Michael additons on α,β-unsaturated esters catalyzed by bismuth(III) triflate in conventional chemistry and under microwave irradiation. *Lett. Org. Chem.* **2006**, *3*, 324–327.
19. Vijender, M.; Kishore, P.; Satyanarayana, B. Cadmium chloride ($CdCl_2$): An efficient catalyst for conjugate addition of amines to electron-poor alkenes. *Synth. Commun.* **2007**, *37*, 591–594.
20. Bhanushali, M. J.; Nandurkar, N. S.; Jagtap, S. R.; Bhanage, B. M. $Y(NO_3)_3 \cdot 6H_2O$ catalyzed aza-Michael addition of aromatic/hetero-aromatic amines under solvent-free conditions. *Catal. Commun.* **2008**, *9*, 1189–1195.
21. Reddy, K. R.; Kumar, N. S. Cellulose-supported copper(0) catalyst for aza-Michael addition. *Synlett* **2006**, 2246–2250.
22. Borujeni, K. P.; Tamami, B. Polystyrene and silica gel supported $AlCl_3$ as highly chemoselective heterogeneous Lewis acid catalysts for Friedel–Crafts sulfonylation of aromatic compounds. *Catal. Commun.* **2007**, *8*, 1191–1196.
23. Borujeni, K. P. Silica-gel-supported aluminum chloride: A stable, efficient, selective, and reusable catalyst for tetrahydropyranylation of alcohols and phenols. *Synth. Commun.* **2006**, *36*, 2705–2710.
24. Tamami, B.; Borujeny, K. P. Chemoselective protection of carbonyl compounds as dithioacetals using silica gel supported aluminum chloride. *Synth. Commun.* **2003**, *33*, 4253–4258.
25. Tamami, B.; Borujeny, K. P. Chemoselective protection of carbonyl compounds as dithioacetals using polystyrene and silica gel supported $AlCl_3$ and $FeCl_3$. *Iran. Polym. J.* **2003**, *12*, 507–513.
26. Li, Z.; Ma, X.; Liu, J.; Feng, X.; Tian, G.; Li Zhu, A. Silica-supported aluminum chloride: A recyclable and reusable catalyst for one-pot three-component Mannich-type reactions. *J. Mol. Catal. A: Chem.* **2007**, *272*, 132–135.
27. Clark, J. H. Solid acids for green chemistry. *Acc. Chem. Res.* **2002**, *35*, 791–797.
28. Ziyaei-Halimjani, A.; Saidi, M. R. An efficient one-pot Michael addition of dithiocarbamate anion to α,β-unsaturated olefins. *J. Sulfur Chem.* **2005**, *26*, 149–154.

29. Rajabi, F.; Saidi, M. R. Solid lithium perchlorate-mediated conjugate addition of thiols and indoles to α,β-unsaturated carbony compounds. *J. Sulfur Chem.* **2005**, *26*, 251–259.
30. Saidi, M. R.; Rajabi, F.; Brown, R. S. Enantioselective conjugate addition to α,β-unsaturated esters and amides mediated by lithium perchlorate. *J. Iran. Chem. Soc.* **2005**, *2*, 300–304.
31. Azizi, N.; Arynasab, F.; Saidi, M. R. Efficient Friedel-Crafts alkylation of indoles and pyrrole with enones and nitroalkene in water. *Org. & Biomol. Chem.* **2006**, 4275–4277.
32. Azizi, N.; Aryanadab, F.; Torkian, L.; Ziyaei-Halimjani, A.; Saidi, M. R. One-pot synthesis of dithiocarbamates accelerated in water. *J. Org. Chem.* **2006**, *71*, 3634–3635.
33. Xu, T.; Kob, N.; Drago, R. S.; Nicholas, J. B.; Haw, J. F. A solid acid catalyst at the threshold of superacid strength: NMR, calorimetry, and density functional theory studies of silica-supported aluminum chloride. *J. Am. Chem. Soc.* **1977**, *119*, 12231–12239.