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Highly Efficient Procedure for the Conjugate Addition of Amines to Electron Deficient Alkenes[1]

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Abstract—The novel efficient procedure has been developed for the conjugate addition of amines to electron deficient alkenes. The results showed that the catalyst was very efficient for the reactions with the excellent yields in several minutes. Operational simplicity, without need of any solvent, low cost of the catalyst used, high yields, reusability, excellent chemoselectivity, applicability to large-scale reactions are the key features of this methodology.

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The addition of nitrogen compounds across carbon-carbon multiple bonds is an unsolved synthetically important problem for both basic research and for the chemical industry [1]. An alternative method for preparing these compounds is via Michael addition. It is a very straightforward approach for the synthesis of substituted amines and their derivatives with 100% atom efficiency and without any byproduct formation [2]. Although a number of alternative procedures have been reported recently using a variety of reagents such as Pd compounds, $InCl_3$, $CeCl_3$, $Yb(OTf)_3$, $Bi(NO_3)_3$, $Bi(OTf)_3$, $Cu(OAc)_2$, $LiClO_4$, Clay, Silica gel, SmI_2, $FeCl_3$, $CrCl_3$, $SnCl_4$, et al. [3–23]. Many suffer from limitations such as the requirement for a large excess of reagents, long reaction times, harsh reaction conditions and also involvement of toxic solvents such as acetonitrile or 1,2-dichloroethane. Hence, the development of less expensive, simpler, "greener" catalysts for the reactions is still highly desirable. Aiming to these advantages, we developed a solvent-free protocol for the conjugate addition of amines to electron deficient alkenes using a novel heterogeneous acid catalyst. The catalyst has been synthesized through the copolymerization of p-toluenesulfonic acid (PTSA) and paraformaldehyde with sulfuric acid as catalyst (Scheme 1). The results showed that the catalysts were efficient for the reaction with the excellent yields.

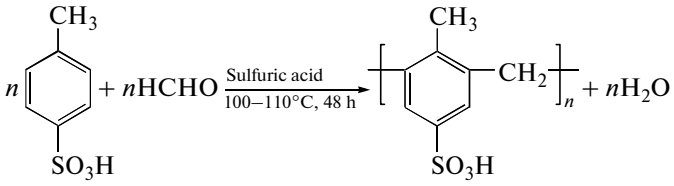
EXPERIMENTAL

All organic reagents were commercial products with the highest purity available (>98%) and used for the reaction without further purification.

The catalyst was synthesized through the polymerization of p-toluenesulfonic acid (PTSA) and paraformaldehyde catalyzed by sulfuric acid (Scheme 1). In the typical procedure: The mixture of p-toluenesulfonic acid (10 g), paraformaldehyde (2 g), and sulfuric acid (0.2 g) was heated to 100–110°C in a three necked round bottomed flask equipped with a magnetic stirrer, a thermometer, and a funnel. The reaction was kept in the range of 100–110°C for 48 h to form black solid. The solid was washed with hot water (>80°C) and filtrated until no SO_4^{2-} was detected in the filtrate. The catalyst was obtained after drying at 120°C overnight in an oven.

The Conjugate Addition of Amines to Electron Deficient Alkenes

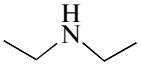
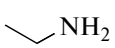
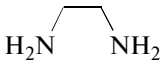
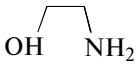
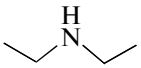
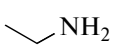
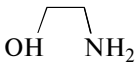
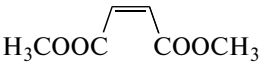
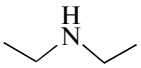
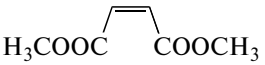
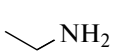
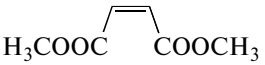
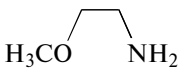
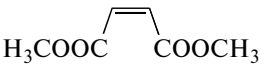
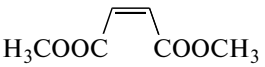
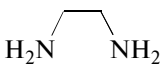
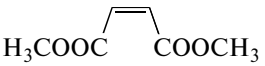
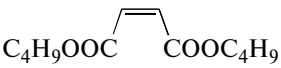
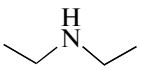
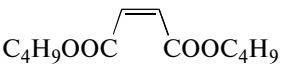
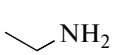
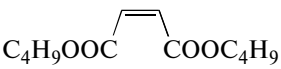
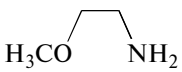
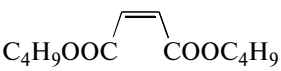
Typical procedure for the conjugate addition of amines: To a mixture of amines (20 mmol), alkenes (24 mmol) and the catalyst (50 mg) was stirred at room temperature for the certain time as shown below. The process of the reaction was monitored by GC analysis. The reaction mixture was extracted with ethyl acetate (2 × 20 ml) and the combined extract was dried over Na_2SO_4 and evaporated to leave a crude product, the product was separated by column chromatography



Scheme 1. The synthetic route of the novel catalyst.

[1] The article is published in the original.

Conjugate additions of various amines with alkenes

Entry	Amines	Alkenes	Reaction time, min	Yield, %*
1			5	98
2			10	96
3			10	97
4			15	94
5			25	92
6			5	97
7			20	95
8			10	96
9			25	92
10			5	98
11			25	93
12			15	94
13			20	95
14			25	92
15			30	92
16			5	98
17			20	94
18			15	92
19			25	91

Note: Reaction conditions: amine 20 mmol, alkenes 20 mmol, catalyst 50 mg, R.T. (25°C).
* Isolated yield.

using neutral alumina as stationary phase and (petroleum ether/ethyl acetate 95 : 5) as eluent to give the corresponding products.

RESULTS AND DISCUSSION

Characterization of the Catalyst

The acidity of the catalyst determined through the neutralization titration gave the results of 224 mg (KOH)/g. The acid strength of the catalyst was determined by thermodesorption of chemisorbed ammonia (NH_3-TPD). The results showed that the catalyst had high acid strength in which ammonia desorbed ranging from 673 to 873 K. The elemental analyst gave the results: C 59.7%; H 7.3%; S 12.8%; O 20.2%. The results indicating that almost all the element S existed in the catalyst in the form of sulfuric groups. The IR spectra of the catalyst showed the sulfuric group absorbability at 1030 and 970 cm^{-1} which confirmed the existence of the sulfuric groups. The BET surface area using nitrogen adsorption-desorption isotherms at the temperature of liquid nitrogen which gave the result of 23 m^2/g. The TG analysis gives the decomposed temperature of 200°C, which showed that the catalyst holds great potential for the high temperature reactions (Fig. 1).

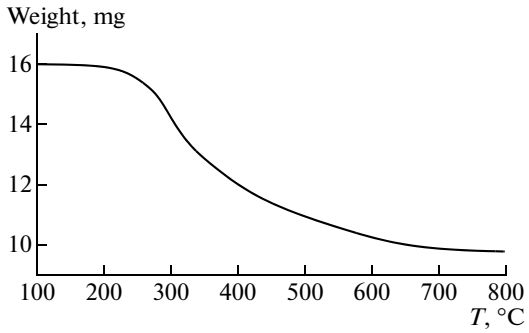
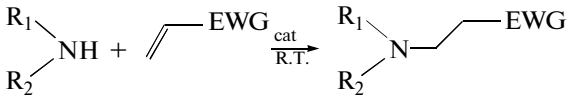


Fig. 1. The TG curve of the novel catalyst.

Catalytic Procedure for the Conjugate Addition

The conjugate additions of various amines with alkenes under solvent-free condition were investigated first (Table 1). The results showed that the reactions underwent smoothly at room temperature within several minutes. The dimethylamine showed extremely high activity for all kinds of electron deficient alkenes with almost complete conversion within 5 min (Entries 1, 6, 10, 16). The yields slightly dropped with the carbon atomicity of the amines added because of the steric hinderance (Entries 2, 3, 7, 8, 11, 12, 17, 18). Here the catalyst was also efficient for the multi-amino compound such as ethanediamine (Entries 4, 15). Both amino groups reacted with the alkenes the yield over 90% in short time. The primary amines underwent the single substitution reaction under the reaction condition (Entries 3, 8, 12, 18). These results indicated the usefulness of the novel catalyst for the reactions and the reaction conditions are mild and not sufficient to cause double substitution reaction. The multi-substitution reaction could also be activated when more alkenes and high temperature applied, then the double substituted products were obtained with high yields. Ethanolamine and 3-methoxy ethylamine also converted to the corresponding products without destroy the hydroxyl and methoxy groups (Entries 5, 9, 13, 14, 19). As to the alkenes, the reactivity was affected by the EWG and the steric hindrance also had the certain effect on the reaction.



The Spectroscopic Data for Products

Entry 1:

^{1}H NMR ($CDCl_3$, 500 MHz, δ, ppm): 3.685 (*s*, 3H), 2.612 (*t*, 2H), 2.486 (*t*, 2H), 2.243 (*t*, 6H).

Entry 2:

^{1}H NMR ($CDCl_3$, 500 MHz, δ, ppm): 3.68 (*s*, 3H), 2.80 (*t*, 2H, J = 7.30 Hz), 2.52 (*q*, 4H, J = 7.18 Hz), 2.46 (*t*, 2H, J = 7.30 Hz), 1.03 (*t*, 3H, J = 7.18 Hz).

^{13}C NMR ($CDCl_3$, 125 MHz, δ, ppm): 173.5, 51.8, 48.2, 47.1, 32.1, 12.2.

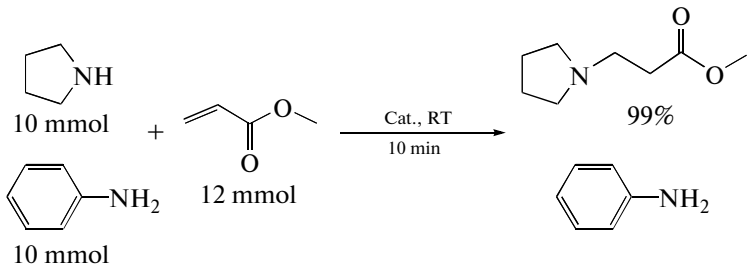
Entry 7:

^{1}H NMR ($CDCl_3$, TMS): δ(0.993 (*t*, 6H, J = 7.2 Hz), 2.426 (*t*, 2H, J = 7.2 Hz), 2.477 (*q*, 4H, J = 7.2 Hz), 2.765 (*t*, 2H, J = 7.2 Hz), 3.649 (*s*, 3H). GC–MS: m/z 159 (M+ –1), 144, 130, 116, 102, 86 (100%), 72, 58, 42, 30.

The other separated products were then tested by ^{1}H NMR and results agreed well with that of authentic samples.

The Reuse of the Catalyst

One property of the catalyst is the heterogeneous catalytic process. Thus, recovery of the catalyst is very convenient. After reactions, the catalyst was recovered by filtration. The recovered activities were investigated through the reaction of dibutylamine and methyl acrylate carefully (Fig. 2). The yield remained unchanged even after the catalyst had been recycled for a sixth time.



Scheme 2. The chemoselectivity of the catalyst.

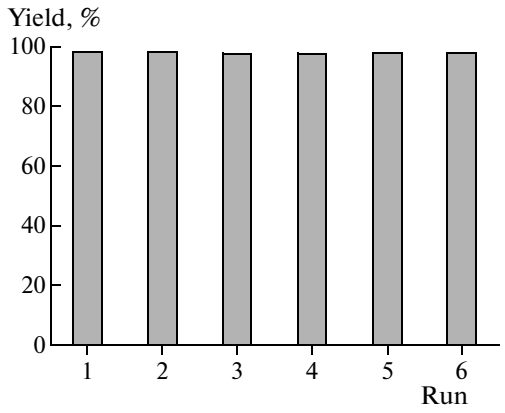


Fig. 2. The reuse of the catalyst.

The Chemoselectivity of the Catalyst

It is noteworthy that aromatic amines did not undergo the reaction under the same reaction conditions (Scheme 2). This result indicated that the present protocol could be applicable to the chemoselective addition of aliphatic amines in the presence of aromatic amines.

CONCLUSIONS

In conclusion, a novel efficient procedure has been developed for the conjugate addition of amines to electron deficient alkenes. Operational simplicity, without need of any solvent, low cost of the catalyst used, high yields, excellent chemoselectivity, applicability to large-scale reactions are the key features of this methodology.

REFERENCES

1. Zhang, D., Wang, G., and Zhu, R., *Tetrahedron: Asymmetry*, 2008, vol. 19, p. 568.
2. Singh, R. and Goswami, T., *J. Phys. Org. Chem.*, 2008, vol. 21, p. 225.
3. Wang, C.J., Zhang, Z.H., Dong, X.Q., and Wu, X.J., *Chem. Commun.*, 2008, p. 1431.
4. Xu, L.W., Yang, M.S., Qiu, H.Y., Lai, G.Q., and Jiang, J.X., *Synth. Commun.*, 2008, vol. 38, p. 1011.
5. Miao, T. and Wang, L., *Tetrahedron Lett.*, 2008, vol. 49, p. 2173.
6. Wang, Y., Li, P., Liang, X., Zhang, T.Y., and Ye, J., *Chem. Commun.*, 2008, p. 1232.
7. Bhanushali, M.J., Nandurkar, N.S., Jagtap, S.R., and Bhanage, B.M., *Catal. Commun.*, 2008, vol. 9, p. 1189.
8. Shirakawa, S. and Shimizu, S., *Synlett.*, 2007, p. 3160.
9. Zhu, S., Yu, S., and Ma, D., *Angew. Chem. Int. Ed. Engl.*, 2008, vol. 47, p. 545.
10. Chen, F.X., Shao, C., Wang, Q., Gong, P., and Zhang, D.Y., *Tetrahedron Lett.*, 2008, vol. 49, p. 1282.
11. Ni, B., Zhang, Q., and Headley, A.D., *Tetrahedron Lett.*, 2008, vol. 49, p. 1249.
12. Azim, Z.H. and Saidi, M.R., *Tetrahedron Lett.*, 2008, vol. 49, p. 1244.
13. Li, X., Cun, L., Lian, C., Zhong, L., Chen, Y., Liao, J., Zhu, J., and Deng, J., *Org. Biomol. Chem.*, 2008, vol. 6, p. 349.
14. Attanasi, O.A., Favi, G., Filippone, P., Golobic, A., Perrulli, F.R., Stanovnik, B., and Svete, J., *Synlett.*, 2007, p. 2971.
15. Micheletti, G., Pollicino, S., Ricci, A., Berionni, G., and Cahiez, G., *Synlett*, 2007, p. 2829.
16. Esteban, J., Costa, A.M., Gomez, A., and Vilarrasa, J., *Org. Lett.*, 2008, vol. 10, p. 65.
17. Bi, X., Zhang, J., Liu, Q., Tan, J., and Li, B., *Adv. Synth. Catal.*, 2007, vol. 349, p. 2301.
18. Chen, F.X., Shao, C., Wang, Q., Gong, P., Zhang, D.Y., Zhang, B.Z., and Wang, R., *Tetrahedron Lett.*, 2007, vol. 48, p. 8456.
19. Luo, S., Zhang, L., Mi, X., Qiao, Y., and Cheng, J., *J. Org. Chem.*, 2007, vol. 72, p. 9350.
20. Fustero, S., Chiva, G., Piera, J., Volonterio, A., Zanda, M., Gonzalez, J., and Ramallal, A.M., *Chem. Eur. J.,* 2007, vol. 13, p. 8530.
21. Deb, I., John, S., and Namboothiri, I.N.N., *Tetrahedron,* 2007, vol. 63, p. 1991.
22. Sharma, Y.O. and Degani, M.S., *J. Mol. Catal. A: Chem.*, 2007, vol. 277, p. 215.
23. Xu, D.Q., Luo, S.P., Wang, Y.F., Xia, A.B., Yue, H.D., Wang, L.P., and Xu, Z.Y., *Chem. Commun.*, 2007, p. 4393.