PMA/SiO_2 — An efficient recyclable heterogeneous catalyst for the synthesis of homoallyl alcohols and amines under solvent-free conditions[1]

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Abstract: Aldehydes and imines can efficiently undergo nucleophilic addition reaction with allyltributylstannane in the presence of phosphomolybdic acid supported on silica (PMA/SiO_2) under solvent free-conditions to form the corresponding homoallyl alcohols and amines respectively at room temperature in excellent yields. The catalyst can be easily recovered and re-used.

Key words: homoallyl alcohol, homoallyl amine, phosphomolybdic acid, heterogeneous catalyst, allyltributylstannane, solvent-free conditions.

Résumé : Opérant à la température ambiante et des conditions sans solvant, les aldéhydes et les imines peuvent donner lieu à des réactions efficaces d'addition nucléophile avec l'allyltributylstannane, en présence d'acide phosphomolybdique supporté sur de la silice (APM/SiO_2) pour conduire à la formation respectivement d'alcools et d'amines homoallyliques avec d'excellents rendements. Le catalyseur peut facilement être récupéré et réutilisé.

Mots-clés : alcool homoallylique, amine homoallylique, acide phosphomolybdique, catalyseur hétérogène, allyltributylstannane, conditions sans solvant.

[Traduit par la Rédaction]

Introduction

Homoallylic alcohols (1) and amines (2) are important building blocks for the construction of various biologically active compounds, and hence the syntheses of these compounds are highly useful. Lewis acid promoted nucleophilic addition of allyltin reagent to carbonyl compounds and imines is one of the straightforward methods for the synthesis of homoallyl alcohols and amines. Various Lewis acids such as metal halides (3), metal triflates (4), I_2 (5), (bromodimethyl)sulfonium bromide (6), and cyanuric chloride (7) can catalyze this reaction. However, most of the methods employing these catalysts suffer from certain disadvantages such as high temperature, prolonged reaction times, harsh reaction conditions, and the use of hazardous and expensive acid catalysts. Some of the catalysts are extremely moisture sensitive and can cause inconvenience in performing the reaction. In recent years, the use of solid acids as heterogeneous catalysts has gained tremendous interest in different areas of organic synthesis. These catalysts are advantageous over conventional homogeneous acid catalysts as they can be easily recovered from the reaction mixture by simple filtration and can be re-used after activation or without activation, thereby making the process more economically viable. Here we report the utilization of a solid acid as a catalyst for the preparation of homoallylic alcohols and amines.

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[1]Part 150 in a series of studies on novel synthetic methodologies.

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Results and discussion

In continuation of our work (8) on the application of heterogeneous catalysts for the development of useful synthetic methodologies, we have observed that phosphomolybdic acid supported on silica (PMA/SiO_2) (9) is very suitable to catalyze the allylation of aldehydes and imines with allyltributylstannane to form the corresponding homoallyl alcohols and amines at room temperature (RT) under solvent-free conditions (Scheme 1). This catalyst possesses excellent activity, low toxicity, and high stability towards humidity. It can be recovered from the reaction mixture and recycled.

Initially we studied the reaction of benzaldehyde, aniline, and allyltributylstananne in CH_3CN in the presence of PMA/SiO_2 at RT. The desired homoallylamine was obtained in good yield (85%) within 80 min (Table 1, entry a). In absence of the catalyst the product was not formed. We studied the effect of different solvent systems such as THF, Et_2O, MeOH, CH_3CN, CH_2Cl_2, and $CHCl_3$ for the reaction, but the conversion proceeded best in the absence of any solvent. A wide variety of aromatic and aliphatic aldehydes

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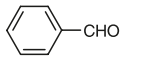
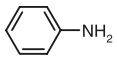
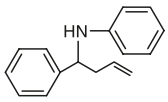
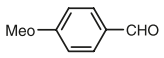
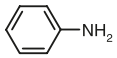
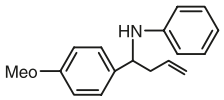
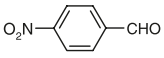
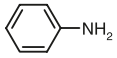
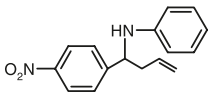
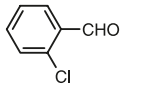
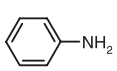
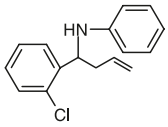
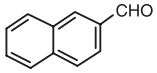
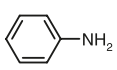
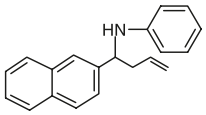
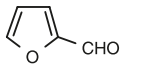
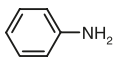
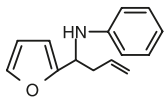
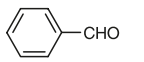
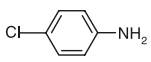
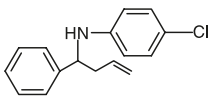
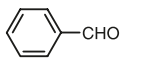
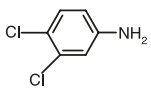
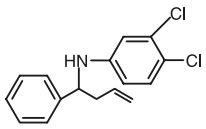
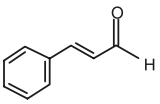
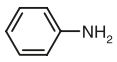
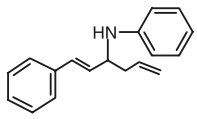
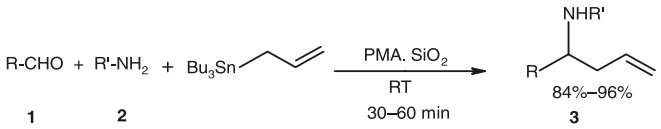
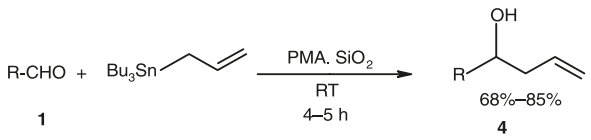
Table 1. Preparation of homoallylic amines using PMA/SiO_2.

Entry	Aldehyde (**1**)	Amine (**2**)	Product (**3**)	Time (min)	Isolated yield (%)
a				35	92
b				30	96
c				45	87
d				45	89
e				30	93
f				55	84
g				40	90
h				45	88
i				50	87

Scheme 1. Preparation of homoallylic amines using PMA/SiO_2.



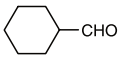
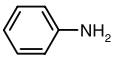
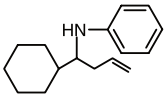
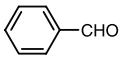
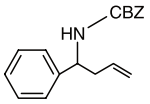
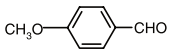
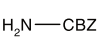
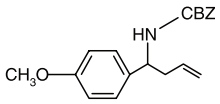
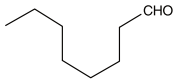
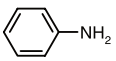
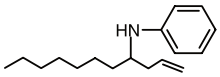
Scheme 2. Preparation of homoallylic alcohols using PMA/SiO_2.



containing electron-donating (Table 1, entries b and l) and electron-withdrawing substituents (Table 1, entries c and d) underwent the transformation smoothly. An acid sensitive aldehyde such as α,β-unsaturated aldehydes (Table 1, entry i), furfuraldehyde (Table 1, entry f), and a sterically hindered aldehyde such as 2-naphthaldehyde (Table 1, entry e) worked well to produce their corresponding homoallylic amines. The imines (formed in situ from aldehydes and amines in the presence of the catalyst) underwent facile reaction with allyltributylstannane to form these compounds. Previously, some methods were found to be unsuitable for the preparation of homoallylic amines from enolizable aldehydes. Interestingly the reaction of aldehydes, benzylcarbamate ($CbzNH_2$), and allyltributylstannane yielded the corresponding Cbz-protected allylamines in excellent yield (79%–83%) (Table 1, entries k and l).

The other application of the present method is the preparation of homoallyl alcohols from the corresponding aldehydes on treatment with allyltributylstannane using

Table 1 (*concluded*).

Entry	Aldehyde (**1**)	Amine (**2**)	Product (**3**)	Time (min)	Isolated yield (%)
j				50	86
k				45	79
l				45	83
m				60	87

Note: The structures of the homoallylic amines were settled from their spectral (^{1}H NMR and MS) data.

PMA/SiO_2 under solvent- free conditions (Scheme 2). The reaction proceeded at RT and the products were formed within 4–5 h (Table 2). Both aromatic and aliphatic aldehydes were used for the preparation of homoallylic alcohols. The aldehydes containing electron-donating (Table 2, entry b) and electron-withdrawing groups (Table 2, entry c) in the aromatic rings were found to undergo the conversion smoothly. Acid-sensitive aldehydes such as furfural (Table 2, entry f) and cinnamaldehyde (Table 2, entry e) also smoothly reacted to afford the corresponding homoallyl alcohols.

We extended this method for the conversion of ketones and carried out the reaction using acetophenone, cyclohexanone, and β-ketoesters. None of the ketones gave homoallylic alcohols and amines even after prolonging the reaction times. The chemoselectivity of the present allylation method is remarkable, providing allylation of only aldehydes in the presence of ketones (Table 2, entries i–k). The times required for the preparation of homoallylic alcohols (4–5 h) are somewhat more than those required for the preparation of homoallylic amines (30–60 min).

Conclusion

In conclusion, we have developed a simple and efficient method for the allylation of aldehydes and amines using PMA/SiO_2 as a heterogeneous catalyst. The main features of this methodology are (*i*) operational simplicity, (*ii*) short reaction times, (*iii*) mild reaction conditions, (*iv*) excellent yields, (*v*) application of an inexpensive heterogeneous catalyst, (*vi*) high chemoselectivity, (*vii*) high stability towards humidity, and (*viii*) reusability of the catalyst.

Experimental

Preparation of PMA/SiO_2 catalyst (9)

Slica gel (100–200 mesh, 450 mg) was added slowly to a solution of $H_3PMo_{12}O_{40}{\cdot}24H_2O$ (50 mg) in methanol (5 mL). The mixture was stirred at RT for 6 h. Methanol was evaporated under reduced pressure to attain the catalyst (PMA/SiO_2) as an yellowish powder.

General experimental procedure for the synthesis of homoallyl amines

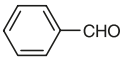
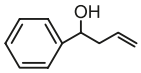
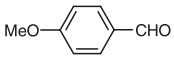
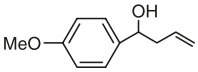
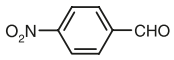
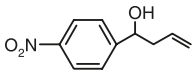
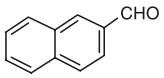
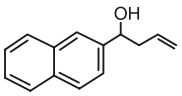
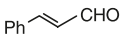
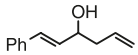
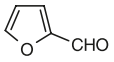
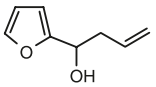
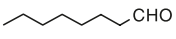
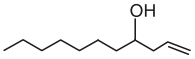
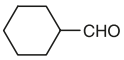
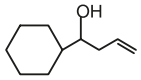
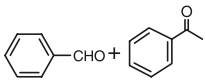
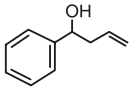
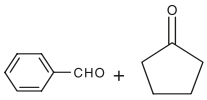
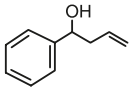
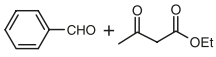
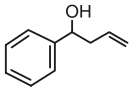
To a mixture of an aldehyde (2 mmol), amine (2 mmol), and allyltributylstannane (2.5 mmol), PMA/SiO_2 (113 mg) was added under solvent-free conditions at RT. The mixture was stirred and the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the catalyst was recovered quantitatively after washing the residue with dry methanol (2 × 5 mL). The filtrate (containing the product in methanol) was concentrated and the residue was subjected to column chromatography (silica gel, hexane) to obtain pure homoallyl amine. The recovered catalyst was re-used three times subsequently for the same reaction without affecting the yield of the product.

General experimental procedure for the synthesis of homoallyl alcohols

To a mixture of an aldehydes (2 mmol) and allyltributylstannane (2.5 mmol), PMA/SiO_2 (113 mg) was added under solvent-free conditions at RT. The mixture was stirred and the reaction was followed by TLC. After completion, the mixture was filtered and the residue was washed with dry methanol (2 × 5 mL) to recover the catalyst quantitatively. The filtrate (containing the product in methanol) was concentrated and the viscous mass was subjected to column chromatography (silica gel, 35% EtOAc and hexane) to afford pure homoallyl alcohol. The recovered catalyst was re-used three times subsequently in this case also for the same reaction without affecting the yield of the product.

All the prepared compounds (except **3b**, **3f**, and **4b**) are known (3*c*, 3*d*, 4*b*, 4*c*, and 6). The spectral and analytical data of representative products are given below.

Table 2. Preparation of homoallylic alcohols using PMA/SiO_2.

Entry	Aldehyde (**1**)	Product (**4**)	Time (h)	Isolated yield (%)
a			4.0	85
b			4.0	85
c			5.0	68
d			4.5	80
e			5.0	78
f			5.0	74
g			5.0	69
h			4.0	70
i			4.0	85
j			4.0	83
k			4.0	85

Note: The structures of the homoallylic alcohols were settled from their spectral (^{1}H NMR and MS) data.

3b

Oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.27 (2H, d, J = 8.0 Hz), 7.03 (2H, t, J = 8.0 Hz), 6.82 (2H, d, J = 8.0 Hz), 6.59 (1H, t, J = 8.0 Hz), 6.42 (2H, d, J = 8.0 Hz), 5.75 (1H, m), 5.21–5.09 (2H, m), 4.31 (1H, td, J = 5.5, 1.5 Hz), 4.03 (1H, m), 3.78 (3H, s), 2.61–2.40 (2H, m). FABMS m/z: 254 (M^+ + 1). Anal. calcd. for $C_{17}H_{19}$ NO: C 80.63, H 7.50, N 5.53; found: C 80.58, H 7.54, N 5.49.

3f

Oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.30 (1H, d, J = 1.8 Hz), 7.06 (2H, t, J = 8.0 Hz), 6.64 (1H, t, J = 8.0 Hz), 6.52 (2H, d, J = 8.0 Hz), 6.23 (1H, dd, J = 2.0, 1.8 Hz), 6.09 (1H, d, J = 2.0 Hz), 5.72 (1H, m), 5.20–5.08 (2H, m), 4.52 (1H, t, J = 5.5 Hz), 3.89 (1H, brs), 2.64 (2H, t, J = 5.5 Hz). FABMS m/z: 214 (M^+ + 1). Anal. calcd. for $C_{14}H_{16}NO$: C 78.50, H 7.47; found: C 78.56, H 7.51.

4b

Oil. ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.20 (2H, d, J = 8.0 Hz), 6.80 (2H, d, J = 8.0 Hz), 5.67–5.80 (1H, m), 5.08 (2H, m), 6.42 (1H, t, J = 12.5, 6.0 Hz), 3.77 (3H, s), 2.43 (2H, J = 12.5, 6.5 Hz), 2.08 (brs, OH). FABMS m/z: 179 (M^+ + 1). Anal. calcd. for $C_{11}H_{14}O$: C 74.15, H 7.86; found: C 74.22, H 7.80.

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References

1. (*a*) K.R. Hoenberer, C.L. Hamblet, and J.L. Leighton. J. Am.

Chem. Soc. **122**, 12894 (2000); (*b*) K.C. Nicolaou, D.W. Khim, and R. Baati. Angew. Chem., Int. Ed. **41**, 3701 (2002).
2. (*a*) R.D. Enders and U. Reinhold. Tetrahedron: Asymmetry, **8**, 1895 (1997); (*b*) R. Bloch. Chem. Rev. **98**, 1407 (1998).
3. (*a*) T. Akiyama, J. Iwai, Y. Onuma, and H. Kagoshima. J. Chem. Soc. Chem. Commun. 2191 (1999); (*b*) T. Akiyama and Y. Onuma. J. Chem. Soc. Perkin Trans. 1, 1157 (2002); (*c*) J.S. Yadav, B.V.S. Reddy, G. Kondaji, and S.S.J. Redyy. Tetrahedron, **61**, 879 (2005); (*d*) N.V. Lingaaih, G. Ezikiel, T. Yakaaih, G.V. Reddy, and P.S. Rao. Tetrahedron Lett. **47**, 4315 (2006).
4. (*a*) S. Kobayashi, T. Busujima, and S. Nagayama. J. Chem. Soc. Chem. Commun. 19 (1998); (*b*) H.C. Aspinall, J.S. Bissett, N. Greeves, and D. Levin. Tetrahedron Lett. **43**, 323 (2002); (*c*) J.S. Yadav, B.V.S. Reddy, and A.K. Raju. Synthesis, 883 (2003); (*d*) T. Ollevier and T. Ba. Tetrahedron Lett. **44**, 9003 (2003); (*e*) H.C. Aspinall, J.S. Bissett, N. Greeves, and D. Levin. Tetrahedron Lett. **43**, 319 (2002).
5. H. Nakamura, H. Iwama, and Y. Yamamoto. J. Am. Chem. Soc. **118**, 6641 (1996).
6. B. Das, B. Ravikanth, P. Thirupathi, and B.V. Rao. Tetrahedron Lett. **47**, 5041 (2006).
7. B. Das, K. Laxminarayana, B. Ravikanth, and B. Rama Rao. Tetrahedron Lett. **47**, 9103 (2006).
8. (*a*) B. Das, B. Ramu, B. Ravikanth, and K.R. Reddy. Tetrahedron Lett. **47**, 779 (2006); (*b*) B. Das, P. Thirupathi, V.S. Reddy, and Y.K. Rao. J. Mol. Catal. A Chem. **247**, 233 (2006); (*c*) B. Das, A. Majhi, J. Benerjee, N. Chowdhury, K.H. Kishore, and U.S.N. Murty. Chem. Pharm. Bull. **54**, 403 (2006).
9. G.D. Kishore Kumar and S. Basakaran. J. Org. Chem. **70**, 4520 (2005).