



Green Synthesis of *N*-Sulfonylimine in Solvent-Free Condition with Heteropoly Acid as Catalyst

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A new method for the synthesis of *N*-sulfonylimine directly from benzaldehyde and *p*-methylphenyl sulphonylamine with Keggin type heteropoly acid as reusable catalyst in solvent-less condition had been investigated. H₃PW₁₂ is found to be the most efficient activity and affording *N*-sulfonylimine in the yield of 86 %. H₃PW₁₂ catalyst reserved its' activity and the yield decreased slightly after running for 5 times. The facial catalytic separation and the reusability of the H₃PW₁₂ may hopefully contribute to the development of green chemistry and the environmental benign strategy for the synthesis of *N*-sulfonylimine.

Key Words: Heteropoly acid, Condensation, Synthetic method, Sulfonamide, Solvent free.

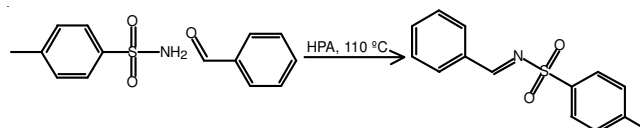
INTRODUCTION

Imines bearing electron-withdrawing *N*-substituents are useful intermediates in organic synthesis¹. Among them, sulfonylimines have been increasingly focused in the last decades for they are easy to separated and the sulfonyl moiety has ability to activate C = N bond sincerely which is reactive enough to undergo addition reactions². Therefore, *N*-sulfonylimines have been widely used in organic synthesis, mainly nucleophilic additions³, reductions, aza-Diels-Alder reactions, aziridine⁴ and oxaziridine synthesis and ene reactions. Some synthesis routes toward *N*-sulfonylimine have been developed, mainly isomerization or rearrangement of *N*-sulfonylaziridines, generation of sulfonamide sulfones by three-components condensation of aldehydes⁵, Lewis acid catalyzed reactions of sulfonamides with aldehydes, sulfonamides and sulfinic acid⁶, subsequently base catalyzed elimination, rearrangement of oxime *O*-sulfinates, tellurium mediated reaction of aldehydes with chloramines T by utilization of *in situ* generated *N,N'*-ditosyltellurodiimide, application of *N*-sulfinyl sulfonamides instead of sulfonamides to generate sulfonyl imine *in situ* via a [2+2] cyclo-addition and extrusion of sulfur dioxide.

However, there exist some drawbacks in these methods, for instance the formation of contaminative by-products, long reaction times, unsatisfactory yields, tedious purification and the use of expensive and hazardous reagents as well as solvents.

Furthermore, some other procedures need cumbersome experimental and multi-step procedure. Therefore, there is high demand for the seeking of one step and inexpensive protocol for the direct synthesis of *N*-sulfonylimines.

Keggin type heteropoly acids (also known as polyoxo-metalate acids) have been paid much attention in recent years for their flexibility in modifying the acid strength, ease of handling, nontoxicity, environmental compatibility and experimental simplicity^{7,8}. Heteropoly acids have been applied to efficiently catalyze many organic reactions as heterogeneous acid and oxidation catalyst^{9,10}. Heteropoly acid catalyzed condensation of ketone or aldehydes with all kinds of nucleophiles had been reported intensively¹¹⁻¹³. But to the best of our knowledge, the condensation of *p*-toluene sulfonamide and benzaldehyde catalyzed by heteropoly acid has never been reported earlier (**Scheme-I**).



Scheme-I: the condensation of *p*-toluene sulfonamide and benzaldehyde

Herein, we explored the application of heteropoly acid in the synthesis of *N*-sulfonylimine through the condensation of *p*-toluene sulfonamide and benzaldehyde with green chemistry protocol.

EXPERIMENTAL

Four kinds of heteropoly acids: H_3PW_{12} , H_4SiW_{12} , H_4PMo_{12} , $H_5PMo_{10}V_2$, were synthesized according the literature, respectively¹⁴⁻¹⁷. *p*-toluene sulfonamide and benzaldehyde are commercially available.

To a well ground mixture of the *p*-toluene sulfonamide (2 mmol) and heteropoly acid (100 mg) in a 25 mL round-bottomed flask connected to a reflux condenser was added the benzaldehyde (2.5 mmol). The mixture was stirred in an oil bath (110 °C) for a certain time as been investigated. Afterward, the reaction mixture was cooled to room temperature, evaporated in vacuum and was transferred to a sintered glass funnel and washed with acetone (40 mL). The solvent was evaporated from the filtrate and the crude product was dissolved in warm ethyl acetate (4 mL), *n*-hexane (6 mL) was added and allowed to stand at room temperature for 5-6 h. During this time, crystals of the product which had formed were collected on a sintered glass funnel, washed with *n*-hexane and dried. The catalyst remained on the funnel was dried and used for the next run under identical reaction conditions. The product was analyzed by ¹H NMR.

RESULTS AND DISCUSSION

Colourless solid *N*-benzylidene-4-methylbenzenesulfonamide was obtained and characterized. ¹H NMR (CDCl₃): δ 2.43 (s, 3H), 7.35 (d, 2H, *J* = 8.2 Hz), 7.49 (t, 2H, *J* = 7.8Hz), 7.61 (t, 1H, *J* = 6.2Hz), 7.90- 7.94 (m, 4H), 9.04 (s, 1H).

Effect of heteropoly acid and solvent: The yield of the condensation of *p*-toluene sulfonamide and benzaldehyde catalyzed by different heteropoly acid and in different solvent condition are shown in Table-1. Four kinds of heteropoly acid had been investigated, among which the H_3PW_{12} exhibited the best catalytic activity offering a yield of 86 % in solvent-free condition. The activity decreased in the order $H_3PW_{12} > H_4SiW_{12} > H_4PMo_{12} > H_5PMo_{10}V_2$ as the same as the acidic order decreased. From Table-1, it can be inferred that the acid properties of the heteropoly acid catalysts play an important role in determining the catalytic performance.

To compare the efficiency of the capacity of the solvent-free conditions with respect to solution conditions, the condensation was performed in the presence of H_3PW_{12} in several solvents (Table-1). As can be seen, the solvent-free method is more efficient than those in solution.

Effect of catalyst amount: The effect of H_3PW_{12} amount (mol per cent mol %) on the condensation of *p*-toluene sulfonamide and benzaldehyde had been investigated and the results are shown in Fig. 1. The yield of *N*-sulfonylimine increased from 11 to 86 % as the H_3PW_{12} mol per cent increased from 0.8 to 1.7 %. To keep on increasing the H_3PW_{12} mol per cent did not lead to conspicuous change on the yield. This may due to the fact that exceeding a certain quantity, the additional catalyst did not participate in the reaction and had no influence on the yield.

Effect of the mol ratio of benzaldehyde and *p*-toluene sulfonamide: The effect of the mol ratio of benzaldehyde and *p*-toluene sulfonamide on the the condensation of *p*-toluene sulfonamide and benzaldehyde had been investigated and the results are shown in Fig. 2. The yield increased constantly

from 65 % to 86 % as the mol ratio of benzaldehyde and *p*-toluene sulfonamide increased from 1 to 1.25. Continuously increasing the mol ratio from 1.25 to 1.3, the yield exhibited no further increasing. It is demonstrated that exceeded benzaldehyde in this procedure is requisite. The mol ratio of benzaldehyde and *p*-toluene sulfonamide of 1.25 is beneficial to the formation of *N*-sulfonylimine.

TABLE-1
CATALYTIC ACTIVITY OF DIFFERENT HETEROPOLY ACIDS AND IN DIFFERENT SOLVENT AND NO SOLVENT CONDITIONS

Entry	Catalyst	Solvent	Temperature	Yield (%)
1	$H_4SiW_{12} \cdot nH_2O$	None	110	65
2	$H_4PMo_{12} \cdot nH_2O$	None	110	59
3	$H_5PMo_{10}V_2 \cdot nH_2O$	None	110	47
4	$H_3PW_{12} \cdot nH_2O$	None	110	86
5	$H_3PW_{12} \cdot nH_2O$	DMF	110	42
6	$H_3PW_{12} \cdot nH_2O$	Toluene	110	54
7	$H_3PW_{12} \cdot nH_2O$	CH ₃ Cl	Reflux	27
8	$H_3PW_{12} \cdot nH_2O$	CH ₃ CN	Reflux	36
9	$H_3PW_{12} \cdot nH_2O$	EtOAc	Reflux	13
10	$H_3PW_{12} \cdot nH_2O$	THF	Reflux	18

Reaction condition: PTSA 2 mmol, benzaldehyde 2.5 mmol, heteropoly acid 100 mg (1.7 mol %), reaction time 6 h

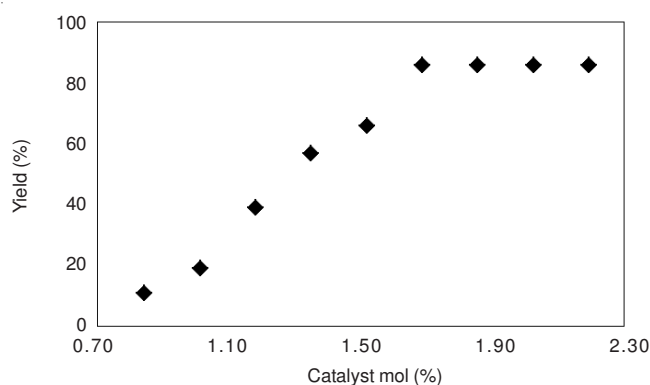


Fig. 1. Effect of heteropoly acid amount. Reaction condition: PTSA 2 mmol, benzaldehyde 2.5 mmol, reaction time 6 h, reaction temperature 60 °C.

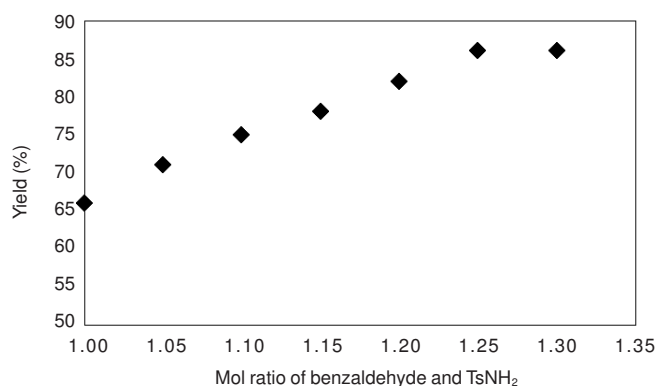


Fig. 2. Effect of heteropoly acid amount. Reaction condition: PTSA 2 mmol, benzaldehyde 2.5 mmol, reaction time 6 h, reaction temperature 60 °C, heteropoly acid 100 mg (1.7 mol %)

Effect of reaction temperature and time: Effect of reaction temperature on the condensation of *p*-toluene sulfonamide and benzaldehyde had been investigated as the temperature

verifying from 50 °C to 120 °C and the results are shown in Table-2. The yield was low at low temperature and increased drastically as the temp increased from 70 °C to 110 °C. Rising up the temp after 110 °C, the yield barely unchanged.

Effect of the reaction time was investigated in a rang of 2-8 h. The results are shown in Table-2. The yield of *N*-sulfonylimine raised as the reaction time increased from 2 to 6 h, and then the yield did not increased any more upon further increasing the reaction time from 6 to 8 h.

Entry	Temperature (°C)	Time (h)	Yield (%)
1	50	6	11
2	70	6	27
3	90	6	71
4	110	6	86
5	120	6	86
6	110	2	37
7	110	4	69
8	110	6	86
9	110	8	86

Reaction condition: *p*-toluene sulfonamide 2 mmol, benzaldehyde 2.5 mmol, heteropoly acid 100 mg (1.7 mol %)

The reusability of heteropoly acid catalyst has been investigated through conducting recycling experiments. The results are shown in Fig 3. As can be seen, the yield of *N*-sulfonylimine decreased a little after the catalyst had been recycled for 5 times. This may be due to the wastage during the catalyst recovery. The result demonstrated that H₃PW₁₂ is a recyclable and environmental friendly catalyst for the synthesis of *N*-sulfonylimine.

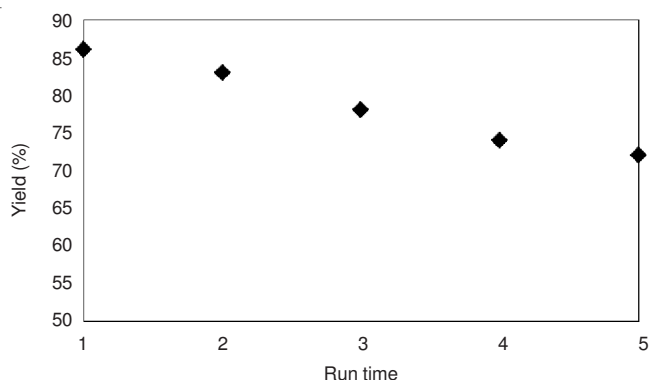


Fig. 3. Catalyst recycling, reaction condition: *p*-toluene sulfonamide 2 mmol, benzaldehyde 2.5 mmol, reaction time 6 h, reaction temperature 60 °C, heteropoly acid 100 mg (1.7 mol %)

Conclusion

In summary, we have successfully developed an efficient and eco-friendly method for the synthesis of *N*-sulfonylimine via the condensation of *p*-toluene sulfonamide with benzaldehyde using heteropoly acid catalyst under mild and solvent free conditions. H₃PW₁₂ was found to be the most efficient, reusable solid acid catalyst for the synthesis of *N*-sulfonylimine. Good yield, low cost, simple experimental and isolation procedures, and green chemistry protocols make this protocol complementary to the existing methods.

REFERENCES

1. R. Bloch, *Chem. Rev.*, **98**, 1407 (1998).
2. D. Enders and U. Reinhold, *Tetrahedron: Asymm.*, **8**, 1895 (1997).
3. M. Gunter and H.J. Gais, *J. Org. Chem.*, **68**, 8037 (2003).
4. L.G. Arini, A. Sinclair and P. Szeto, *Tetrahedron Lett.*, **45**, 1589 (2004).
5. Z. Li, X.H. Ren, P. Wei, H.G. Wan and Y.H. Shi, *Green Chem.*, **8**, 433 (2006).
6. T.S. Jin, G.L. Feng and M.T.S. Yang, *Synth. Commun.*, **34**, 1277 (2004).
7. N. Mizuno and M. Misono, *Curr. Opin. Solid State Mater.*, **2**, 84 (1997).
8. N. Mizuno and M. Misono, *Chem. Rev.*, **98**, 199 (1998).
9. M. Misono, *Topics Catal.*, **21**, 89 (2002).
10. M. Misono, *Chem. Commun.*, 1141 (2001).
11. R. Fazaeli and H. Aliyan, *Appl. Catal. A-Gen.*, **331**, 78 (2007).
12. I.M. Baltork, M. Moghadam, S. Tangestaninejad, V. Mirkhani, Z. Eskandari, *J. Chem. Sci.*, **65**, 461 (2010).
13. B.F. Mirjalili and Z. Zaghaghi, *J. Chin. Chem. Soc.*, **55**, 694 (2008).
14. H. Wang, *J. Biol. Chem.*, **43** (1920).
15. A. Tézé and G. Hervé, *Inorg. Synth.*, **27**, 85 (1990).
16. J. Ma and Y. Wu, *Acta Chim. Sin.*, **51**, 860 (1993).
17. A.M. Khenkin, A. Rosenberger and R. Neumann, *J. Catal.*, **182**, 82 (1999).