

## Heteropoly Acid Catalyzed Micheal Addition of Benzene Sulfonamide to Ethyl Acrylate

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The solvent-free aza-Michael addition reaction of benzene sulfonamide to ethyl acrylate carried out in presence of catalytic amount of different Keggin type heteropoly acids as reusable catalyst in solvent-free condition has been investigated. Pure N-alkylsulfonamide was obtained and the structure of N-alkylsulfonamide was identified by GC-MS, FT-IR and <sup>1</sup>H NMR spectra. It is found that H<sub>3</sub>PW<sub>12</sub> had the best activity affording N-alkylsulfonamide with excellent yield of 93 %. The effects of experimental factors on the catalytic aza-Michael addition reaction and the catalytic recycling of H<sub>3</sub>PW<sub>12</sub> catalyst were studied. H<sub>3</sub>PW<sub>12</sub> catalyst exhibited good catalytic activity after 5 times of running. The undemanding catalytic separation and the reusability of the H<sub>3</sub>PW<sub>12</sub> catalyst is hopefully to be beneficial to the exploration of green chemistry and environmental benign procedure for the synthesis of N-alkylsulfonamide.

**Key Words:** Heteropoly acid, Aza-Michael addition, Synthetic method, Sulfonamide.

### INTRODUCTION

N-Alkylsulfonamides have attracted considerable attention in organic synthesis because of their wide range of biological activities and pharmacological properties<sup>1,2</sup>. N-Alkylsulfonamides are useful synthons for the preparation of several nitrogen containing bioactive natural products, antibiotics and chiral auxiliaries. A large number of other biologically active compounds contain N-alkylsulfonamide moiety<sup>3</sup>. The development of novel synthetic methodologies for the preparation of these compounds is an attractive area of research in synthetic organic chemistry. A general method for preparing these compounds is *via* aza-Michael addition of sulfonamides to electrophilic alkenes, which is a perfectly atom-economic and intrinsically green C-N bond formation reaction<sup>4,5</sup>. In general, the aza-Michael reaction needs a basic condition or some special reaction condition<sup>6</sup>. As a result, a great quantity of catalytic system has been explored for the conjugate addition of sulfonamides to electron-deficient olefins, including basic ionic liquid, MgO/[bmim]Br<sup>7</sup>, KF/Al<sub>2</sub>O<sub>3</sub><sup>8</sup>, acetic acid/microwave<sup>9</sup>, SiO<sub>2</sub>-acetonitrile<sup>10</sup> and imidazolium-based polymer supported Gd(OTf)<sub>3</sub><sup>11</sup>. Despite their remarkable progress, many of these methods are associated with some certain drawbacks, such as large number of reagent, low yields, requirement of high temperature and stoichiometric amount of catalyst and hazardous solvents. Therefore, the development for an

alternative method which is greener and more efficient is still highly desirable.

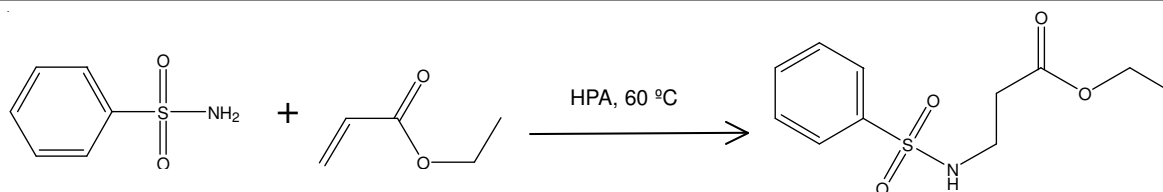
Keggin type heteropoly acids (also known as polyoxo-metalate acids) are promising solid acids which are ease of modifying the acid strength, act as catalyst both under homogeneous and under heterogeneous conditions and present high capacity and selectivity in various synthetically useful transformations<sup>12,13</sup>. Heteropoly acid are often regard as green catalyst in view of nontoxicity, environmental benign and clean reaction process<sup>14</sup>. The Michael addition of different nucleophile and  $\alpha:\beta$  unsaturated ketone or ester catalyzed by heteropoly acid had been reported<sup>15</sup>, but the heteropoly acid catalyzed aza-Michael addition of benzene sulfonamide and ethyl acrylate ester has not been reported (**Scheme-I**).

Herein, we reported a new green chemistry procedure for the synthesis of N-alkylsulfonamide by the aza-Michael addition of benzene sulfonamide and ethyl acrylate catalyzed by heteropoly acid.

### EXPERIMENTAL

Four kinds of heteropoly acids: H<sub>3</sub>PW<sub>12</sub>, H<sub>4</sub>SiW<sub>12</sub>, H<sub>4</sub>PMo<sub>12</sub>, H<sub>5</sub>PMo<sub>10</sub>V<sub>2</sub>, were synthesized according the literature, respectively<sup>16-19</sup>. *p*-Toluene sulfonamide and benzaldehyde are commercially available.

**General procedure:** A well-ground mixture of benzene sulfonamide (2 mmol) and heteropoly acid (100 mg) were



placed in a 25 mL round bottom flask. Then ethyl acrylate (2.2 mmol) was added and the mixture was stirred and heated in oil bath for the times investigated. Subsequently, the reaction mixture was cooled to room temperature, transferred to a sintered glass funnel and washed with chloroform (60 mL). After evaporating the solvent from filtrate, the crude product was purified by column chromatography on silica gel eluting with EtOAc: *n*-hexane (1:3). The catalyst remained on the funnel was dried and used for the next run under identical reaction conditions.

**Detection method:** The product was analyzed by  $^1\text{H}$  NMR, GC/MS, FT-IR.

## RESULTS AND DISCUSSION

**Spectra of product:** Colorless oil like ethyl 3-(phenylsulfonamido)-propionate was obtained and analyzed. GC/MS:  $m/z$  (%) 257 (22.7 M $^+$ );  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  1.26 (t, 3H,  $J = 7.0$  Hz), 2.58 (t, 2H,  $J = 5.0$  Hz), 3.24 (t, 2H,  $J = 5.0$  Hz), 4.11 (q, 2H,  $J = 7.0$  Hz), 5.65 (s, 1H), 7.52-7.62 (m, 3H), 7.89 (m, 2H); FT-IR:  $\text{cm}^{-1}$  3286, 3059, 2975, 1732, 1447, 1329.

**Effect of catalyst:** The effect of different heteropoly acid on the aza-Michael addition of benzene sulfonamide to ethyl acrylate is investigated in solvent-free condition and the results are shown in Table-1. Four kinds of heteropoly acid had been investigated, among which the  $\text{H}_3\text{PW}_{12}$  exhibited the best catalytic activity offering a yield of 93 % in solvent-free condition. The activity decreased in the order  $\text{H}_3\text{PW}_{12} > \text{H}_4\text{SiW}_{12} > \text{H}_4\text{PMo}_{12} > \text{H}_5\text{PMo}_{10}\text{V}_2$  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 a very important role in determining the catalytic performance.

**Effect of catalyst amount:** The effect of  $\text{H}_3\text{PW}_{12}$  amount (mol %) on the aza-Michael addition of benzene sulfonamide to ethyl acrylate had been investigated and the results are shown in Fig. 1. The yield of N-alkylsulfonamide increased from 34-93 % as the pw12 mol per cent increased from 0.4-1.7 %. To keep on increasing the pw12 mol % did not lead to noticeable 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 temperature and time:** Effect of reaction temperature on the aza-Michael addition of benzene sulfonamide to

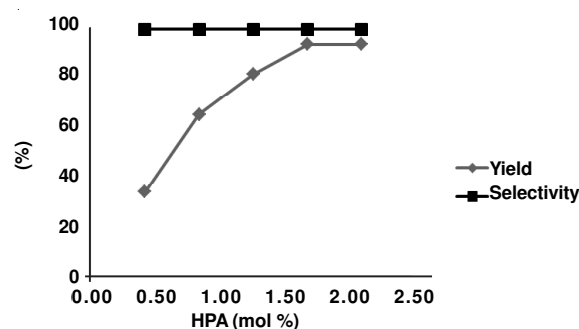


Fig. 1. Effect of catalyst amount. Reaction condition: benzene sulfonamide 2 mmol, ethyl acrylate 2.2 mmol, no solvent. Reaction temperature is 60 °C. Reaction time is 2 h

ethyl acrylate had been investigated as the temperature verifying from room temperature to 80 °C and the results are shown in Table-2. The yield was low at low temperature and increased drastically as the temp increased from 25-60 °C. Rising up the temp after 60 °C, the yield up rose slightly, so the suitable reaction temperature is 60 °C.

Effect of the reaction time was investigated in a range of 0.5-2.5 h. The results are shown in Table-2. The yield of N-alkylsulfonamide raised as the reaction time increased from 0.5-2.0 h and then the yield increased slightly upon further increasing the reaction time from 2.0-2.5 h.

**Reusability of heteropoly acid:** The reusability of heteropoly acid catalyst on the aza-Michael addition of benzene sulfonamide to ethyl acrylate has been investigated through conducting recycling experiments. The results are shown in Fig. 2. As can

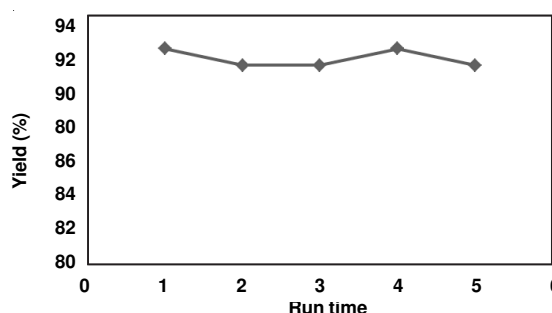


Fig. 2. Reusability of heteropoly acid. Reaction condition: benzene sulfonamide 2 mmol, ethyl acrylate 2.2 mmol, heteropoly acid 100 mg (1.7 mol %), no solvent

TABLE-1  
CATALYTIC ACTIVITIES OF HETEROPOLY ACIDS IN THE AZA-MICHAEL ADDITION OF BSA TO ETHYL ACRYLATE

Entry	Catalyst	Time	Temperature (°C)	Yield (%)	Selectivity (%)
1	$\text{H}_3\text{PW}_{12} \cdot n\text{H}_2\text{O}$	2	60	93	99
2	$\text{H}_4\text{SiW}_{12} \cdot n\text{H}_2\text{O}$	2	60	87	99
3	$\text{H}_4\text{PMo}_{12} \cdot n\text{H}_2\text{O}$	2	60	75	99
4	$\text{H}_5\text{PMo}_{10}\text{V}_2 \cdot n\text{H}_2\text{O}$	2	60	62	99

Reaction condition: BSA 2mmol, ethyl acrylate 2.2mmol, heteropoly acid 100mg (1.7mol %), no solvent.

TABLE-2  
EFFECT OF REACTION TEMPERATURE AND TIME ON THE  
AZA-MICHAEL ADDITION OF BENZENE SULFONAMIDE  
TO ETHYL ACRYLATE

Entry	Temp. (%)	Time (h)	Yield (%)	Selectivity (%)
1	25	2.0	22	99
2	40	2.0	49	99
3	60	2.0	93	99
4	80	2.0	95	99
5	60	0.5	36	99
6	60	1.0	59	99
7	60	1.5	74	99
8	60	2.0	93	99
9	60	2.5	94	99

Reaction condition: BSA 2 mmol, ethyl acrylate 2.2 mmol, no solvent, heteropoly acid 100 mg (1.7 mol %).

be seen, the yield of N-alkylsulfonamide remained almost unchanged after the catalyst had been recycled for 5 times. This may due to the stability and high activity of the H<sub>3</sub>PW<sub>12</sub> catalyst. The result demonstrated that H<sub>3</sub>PW<sub>12</sub> is a recyclable and environmental friendly catalyst for the synthesis of N-alkyl-sulfonamide.

### Conclusion

The aza-Michael addition of benzene sulfonamide to ethyl acrylate can be effectively catalyzed by heteropoly acid in solvent-free condition. H<sub>3</sub>PW<sub>12</sub> has been proved to be the most efficient catalyst for the synthesis of N-alkyl sulfonamide with good yield and selectivity and ease of product isolation, reusability of the catalyst as well as compliance with green chemistry protocols.

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