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# Intermolecular hydroamination of vinyl arenes using tungstophosphoric acid as a simple and efficient catalyst

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**Abstract**—The intermolecular hydroamination of vinyl arene derivatives has been efficiently carried out using a tungstophosphoric acid (TPA) catalyst under solvent free and mild reaction conditions. The present protocol provides an environmentally benign, easy to handle and highly active solid acid catalyst for hydroamination of vinyl arenes. The catalyst yields both hydroamination and hydroarylation products and the selectivity mostly depends on the reaction conditions.


## 1. Introduction

The reaction between an alkene and an amine for the synthesis of substituted amines involves multiple steps.[1] The addition of amines to unsaturated carbon–carbon multiple bonds, a process termed hydroamination, has proved to be the best method for preparing highly substituted amines. This methodology has attained considerable interest from both industry and academia. It is well known that acid catalyzed addition of amines to alkenes is generally unsuccessful due to the buffering effect of the amine substrate.[2] Also Friedel–Crafts alkylations of aryl amines are hindered by coordination of the amine to the Lewis acid catalyst.[3a] Therefore the development of these reactions remains an intriguing challenge for chemists. In previous studies, hydroamination of alkenes with amine derivatives has been carried using various ligand mediated acid catalysts.[3b–d] Hartwig and Schlummer[4] reported that several common Brönsted acids catalyze the intermolecular hydroamination of tosyl-protected amino olefins. Beller et al.[5] reported alkylation of electron rich anilines with styrene promoted by $HBF_4{\cdot}Et_2O$. Furthermore, Anderson et al. described the proton catalyzed hydroamination and hydroarylation of an alkene with an amine,[6] whereas Kaspar et al. reported $TiCl_4$ catalyzed hydroamination and hydroarylation reactions.[7] A number of significant contributions have been made on the use of late-transition metal complexes for the hydroamination of olefins using iridium,[8] rhodium,[9] nickel,[10] palladium,[11] platinum[12] and ruthenium.[13] The high cost of these complexes and their stabilizing ligands or the additives constitute limitations of these protocols. Indeed, the hydroamination mainly proceeds over long reaction times and at high reaction temperatures. Recently, several Brönsted acids such as triflic acid and H-montmorillonite have been reported for the hydroamination of activated and unactivated alkenes with numerous reactive amide derivatives.[14] However, the hydroamination of styrene and aniline derivatives is limited due to rapid oligomerization of the styrene. Thus, it remains an intriguing challenge for researchers to develop improved catalytic systems for the hydroamination of vinyl arenes with substituted aniline derivatives.

In the present Letter, we disclose an environmentally benign, efficient, reusable tungstophosphoric acid (TPA) catalyst for intermolecular hydroamination of alkenes under mild and solvent-free conditions (Scheme 1). The present catalyst promotes the complete reaction within reasonable reaction times and affords high product yields.

## 2. Results and discussion

Experimental results showed that 1 mmol of the styrene derivative reacts with 2 mmol of the aromatic amine in the presence of TPA under solvent-free conditions.

*Keywords*: Hydroamination; Vinyl arene; Solvent free; TPA.
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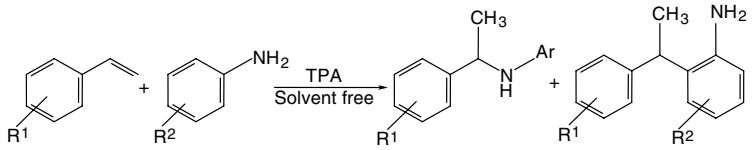
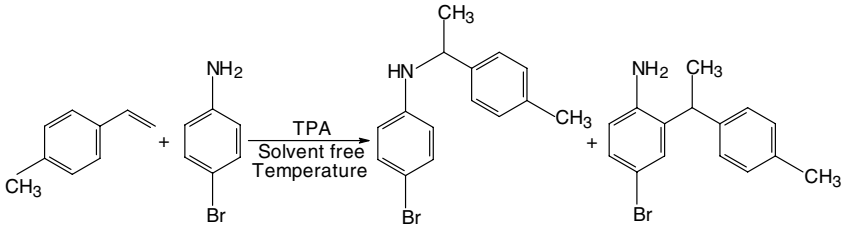



**Scheme 1.** Catalytic intermolecular hydroamination of vinyl arenes.

**Table 1.** Acid catalyzed hydoamination of 4-methyl styrene[a]




**1** **2** **3** **4**

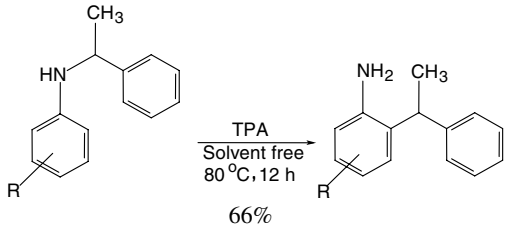
| Entry | Catalyst | Time (h) | (%) Yield **3**[c] | (%) Yield **4**[c] |
|---|---|---|---|---|
| 1 | TPA | 3[b] | 82 | Trace |
| 2 | TPA | 1.5 | 75 | Trace |
| 3 | TPA | 6 | 25 | 70 |
| 4 | $H_2SO_4$ | 18 | — | — |
| 5 | TFA | 12 | — | — |
| 6 | $CH_3COOH$ | 18 | — | — |
| 7 | $Cp_2TiCl_4$ | 18 | — | — |

[a] Reaction conditions: 4-methylstyrene (1.0 mmol); 4-bromoaniline, (2 mmol); catalyst wt: 30 mg; reaction temperature, 80 °C.
[b] Reaction temperature, 60 °C.
[c] Yields were determined by $^1H$ NMR spectroscopy.

Initially, the hydroamination of 4-methylstyrene with 4-bromoaniline (Table 1) was carried out using TPA and its activity was compared with other acid reagents such as $H_2SO_4$, triflic acid (TFA) and $CH_3COOH$. TPA catalyzed the reaction within a reasonable time, whereas simple Brönsted acids did not catalyze this reaction (Table 1, entries 4–6). These results are in agreement with observations made by Hartwig and Schlummer.[4]

Under the present reaction conditions, a mixture of hydroamination and *ortho*-hydroarylation products was obtained. In order to study the ratio of these products, the reaction conditions were varied with respect to reaction time and temperature. Experiments showed that the yield of the *ortho*-alkylated hydroarylation product increased with an increase in reaction time and temperature. Prolonged reaction times resulted in rearrangement of the hydroamination product to give the *ortho*-alkylated hydroarylation product.

In order to confirm the rearrangement of the hydroamination product over time, we prepared the secondary amine independently[15] and subjected it to the present reaction conditions (Scheme 2). Indeed, the secondary amine was converted quantitatively into the hydroarylation product by a Hofmann–Martius rearrangement.[16] Marcsekova and Doye[17] reported that the hydroamination reaction is favourable for aliphatic alkenes and the hydroarylation becomes more favourable for styrene derivatives. In the present studies, it was also found that

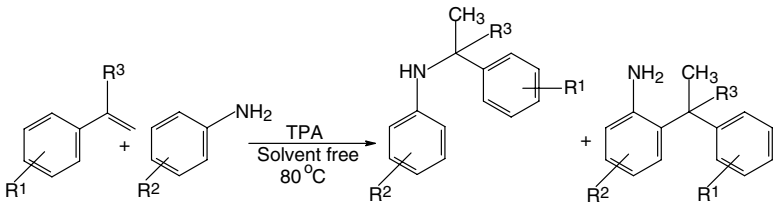



**Scheme 2.** TPA catalyzed rearrangement of the hydroamination product.

the product selectivity varied with reaction time (Table 1, entries 2, 3 and Table 2, entry 11) and our results are in good agreement with those reported.[17]

Catalytic intermolecular hydroaminations of styrene derivatives were carried out using TPA to study the scope of this catalyst (Table 2). A number of vinyl arenes **1** and aniline derivatives **2** were converted to hydroaminated **3** and hydroarylated **4** products in high yields. It is interesting to note that anilines with electron withdrawing groups present on the aromatic ring reacted smoothly. In marked contrast, vinyl arenes with an electron donating substituent (4-methyl) present on the aromatic ring reacted at a faster rate compared to those with electron withdrawing groups such as 4-chloro or 4-bromo. Additionally, α-methylstyrene (Table 2, entry 14) was converted into **3** and **4** (70:30). TPA also catalyzed the reaction of a sterically demanding aniline

**Table 2.** Study of the hydroamination reaction of various aniline and vinyl arene derivatives with the TPA catalyst[a]




**1** **2** **3** **4**

| Entry | $R^1$ | $R^3$ | Amine | Time (h) | (%) Yield **3**[b] | (%) Yield **4**[b] | Combined (%) Yield (**3** + **4**)[b,e] |
|---|---|---|---|---|---|---|---|
| 1 | H | H | 4-Br·$C_6H_4NH_2$ | 1 | 75 | Trace | 75 (99:1) |
| 2 | 4-Br | H | 4-Br·$C_6H_4NH_2$ | 12 | 66 | 30 | 96 (69:31) |
| 3 | 4-Me | H | 4-Br·$C_6H_4NH_2$ | 6 | 25 | 70 | 95 (27:73) |
| 4 | H | H | 4-Cl·$C_6H_4NH_2$ | 3 | 62 | 33 | 95 (65:35) |
| 5 | 4-Cl | H | 4-Cl·$C_6H_4NH_2$ | 12 | 52 | 42 | 94 (55:45) |
| 6 | 4-Me | H | 4-Cl·$C_6H_4NH_2$ | 1.5 | 70 | 25 | 95 (75:25) |
| 7 | H | H | 4-F·$C_6H_4NH_2$ | 4 | 48 | 50 | 98 (50:50) |
| 8 | H | H | 4-$NO_2$·$C_6H_4NH_2$ | 4 | 96 | Trace | 96, 89[c] (99:1) |
| 9 | H | H | 3-$NO_2$·$C_6H_4NH_2$ | 5 | 93 | Trace | 93 (99:1) |
| 10 | H | H | 3-$CF_3$·$C_6H_4NH_2$ | 3 | 55 | 25 | 80 (69:31) |
| 11 | H | H | 3-$CF_3$·$C_6H_4NH_2$ | 12 | Trace | 85 | 85 (1:99)[f] |
| 12 | H | H | 2-$CH_3$·$C_6H_4NH_2$ | 12 | 35 | 54 | 89 (40:60) |
| 13 | H | H | 4-$CH_3O$·$C_6H_4NH_2$ | 12 | 28 | 62 | 90 (32:68) |
| 14 | H | $CH_3$ | 2-Cl·$C_6H_4NH_2$ | 4 | 60 | 25 | 85 (70:30) |
| 15 | H | H | 2,4-$F_2$·$C_6H_4NH_2$ | 6 | 45 | 40 | 85 (52:48) |
| 16 | H | H | 2,4,6-$Cl_3$·$C_6H_4NH_2$ | 24 | — | — | — |
| 17 | H | H | $C_6H_5NHMe$ | 6 | Trace | 89 | 89, 82[c] (1:99) |
| 18 | H | H | 1-Napthylamine | 6 | Trace | 95 | 95 (1:99) |
| 19 | H | H | $C_6H_5NHMe$ | 14 | 82[d] | Trace | 82 (99:1) |
| 20 | H | H | 1-Napthylamine | 14 | 78[d] | Trace | 78 (99:1) |

[a] Reaction conditions: alkene derivative (1 mmol); aniline derivative (2 mmol); temperature, 80 °C; catalyst, 30 mg.
[b] Isolated yields.
[c] Yields obtained after 4th cycle.
[d] Reaction temperature: 45 °C.
[e] Values in parentheses denotes the selectivity ratio of products **3** and **4**.
[f] At a longer reaction time, the hydroarylation product **4** was formed as the major product.

(Table 2, entry 15) with styrene affording both hydroamination and hydroarylated products. However, the di-*ortho*-substituted aniline derivative, 2,4,6-trichloroaniline did not react with styrene under the present conditions (Table 2, entry 16).

On the other hand TPA catalyzed the reaction of an aniline with an electron withdrawing group at the *meta* position (Table 2, entry 10) with styrene affording both hydroamination and hydroarylation products (Table 2). 3-Nitroaniline reacted with styrene to afford only the hydroamination product (Table 2, entry 9). A similar observation was noticed in the reaction of *para*-nitroaniline with styrene (Table 2, entry 8). Aniline derivatives with electron donating substituents present at the *ortho* and *para* positions also reacted with vinyl arene derivatives. However, the rates of the reactions were slow compared to reactions with anilines with electron withdrawing substituents (Table 2, entries 12 and 13). Styrene reacted rapidly with *N*-methylaniline and 1-napthylamine to afford *ortho*-hydroarylation products in high yields under the stated reaction conditions (Table 2, entries 17 and 18). However, when the reaction was conducted at a lower temperature, hydroamination of styrene was observed in high yield (Table 2, entries 19 and 20).

To investigate the reusability of the TPA catalyst, recycling was carried out for two examples where one gave a high hydroamination yield and the other gave the hydroarylation product. For both reactions, no appreciable loss in activity was observed and analogous products were obtained (Table 2, entries 8 and 17).

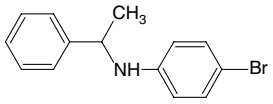
In summary, TPA catalyzes the hydroamination of styrene derivatives with a variety of aryl amines. Control experiments showed that facile N–H addition took place quickly and at low temperatures, whereas C–H addition (the Hofmann–Martius rearrangement) was favoured by longer reaction times and elevated temperatures. The catalyst can be recovered easily and reused four times without any significant loss in activity.

## 3. Typical procedure for the hydroamination reaction

TPA (30 mg) was added to a mixture of styrene (1 mmol) and 4-bromoaniline (2 mmol). The mixture was stirred for 6 h at 80 °C under solvent-free conditions. The progress of the reaction was monitored by TLC and, on completion, the reaction mixture was filtered and the filtrate concentrated under reduced pressure to afford the crude product, which, after

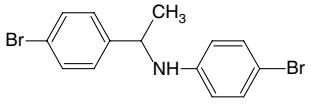
chromatography on silica gel, gave 4-bromo-*N*-(1-(4-methylphenyl)ethyl)aniline and 4-bromo-2-(1-(4-methylphenyl)ethyl)aniline, eluent: *n*-hexane/ethyl acetate (9.5:0.5 v/v).

### 3.1. 4-Bromo-*N*-((1-phenyl)ethyl)aniline: (Table 2, entry 1, product 3)




$^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.32–7.18 (m, 5H), 7.10 (dd, $J = 8.3$, 2.2 Hz, 2H), 6.34 (d, $J = 8.9$ Hz, 2H), 4.41 (q, $J = 6.8$ Hz, 1H), 3.90 (br s, 1H), 1.51 (d, $J = 6.79$ Hz, 3H); $^{13}$C NMR (75 MHz, DEPT, $CDCl_3$): $\delta$ 146.2 (Cq), 145.3 (Cq), 143.5 (Cq), 131.5 (CH), 128.2 (CH), 127.0 (CH), 125.0 (CH), 114.8 (CH), 53.0 (CH), 24.8 ($CH_3$). EI-MS: *m*/*z* (relative intensity) [$M^+$] 276.15 (100). Anal. Calcd for $C_{14}H_{14}BrN$: C, 60.89; H, 5.11; N, 5.07. Found: C, 60.91; H, 5.05; N, 5.10.

### 3.2. 4-Bromo-*N*-(1-(4-bromophenyl)ethyl)aniline: (Table 2, entry 2, product 3)




$^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.48–7.12 (m, 4H), 6.31 (m, 4H), 4.38 (q, $J = 6.8$ Hz, 1H), 3.94 (br s, 1H), 1.51 (d, $J = 6.8$ Hz, 3H). $^{13}$C NMR (75 MHz, DEPT, $CDCl_3$): $\delta$ 146.0 (Cq), 144.0 (Cq), 132.2 (CH), 130.5 (CH), 127.7 (CH), 120.8 (Cq), 115.2 (CH), 109.8 (Cq), 53.5 (CH), 24.9 ($CH_3$). EI-MS: *m*/*z* (relative intensity) [$M^+$] 355.09 (100). Anal. Calcd for $C_{14}H_{13}Br_2N$: C, 47.36; H, 3.69; N, 3.94. Found: C, 47.52; H, 3.55; N, 3.92.

## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.08.120.

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