

**MELAMINE TRISULFONIC ACID (MTSA) ON NEUTRAL ALUMINA CATALYZED AZA-MICHAEL ADDITION OF ALIPHATIC AMINES TO  $\alpha, \beta$  - UNSATURATED CARBONYL COMPOUNDS AND NITRILES****Deepali Mahajan**

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**Abstract:**

Melamine Trisulfonic Acid (MTSA) on Neutral Alumina is used as an efficient catalyst for aza-Michael addition of primary and secondary aliphatic amines to a series of  $\alpha, \beta$ -unsaturated carbonyl compounds and nitriles in acetonitrile to produce the corresponding  $\beta$ -amino derivatives in high yields. The method being simple and offers chemoselectivity, as aromatic amines were found to be unreactive.

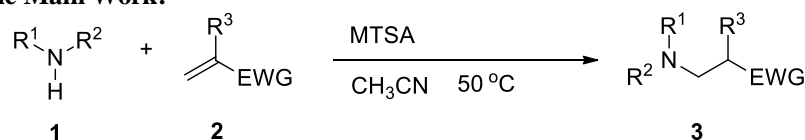
**Key Words:** Aza-Michael Addition, Aliphatic Amines,  $\alpha, \beta$ -Unsaturated Carbonyl Compounds, Nitriles & MTSA

**Introduction:**

The Aza-Michael addition is one of the widely used reactions for carbon-nitrogen bond formation in synthetic organic chemistry. It has been used for the synthesis of several nitrogen containing bioactive natural products<sup>1</sup>, chiral auxiliaries<sup>2</sup>, antibiotics<sup>3</sup> and a number of other drugs<sup>4</sup>. A variety of methods are known in the literature for the synthesis of  $\beta$ -amino carbonyl compounds and nitriles in the presence of an acid or a base catalyst<sup>5</sup>.

**Back Ground:**

Various Lewis acid catalysts have been reported to effect aza-Michael reaction and these include Yb(OTf)<sub>3</sub><sup>6</sup>, PtCl<sub>4</sub>·5H<sub>2</sub>O<sup>7</sup>, Cu(OTf)<sub>2</sub><sup>8</sup>, FeCl<sub>3</sub>·6H<sub>2</sub>O<sup>9</sup>, LiClO<sub>4</sub><sup>10</sup>, Bi(NO<sub>3</sub>)<sub>3</sub><sup>11</sup>, InCl<sub>3</sub><sup>12</sup>, CeCl<sub>3</sub>·7H<sub>2</sub>O<sup>13</sup>, MgO<sup>14</sup>, ZnO<sup>14</sup>, CAN<sup>15</sup>, MnCl<sub>2</sub><sup>16</sup> and SbCl<sub>3</sub>-HAP<sup>19</sup>. Most of these methods have one or more drawbacks such as the use of stoichiometric amount of Lewis acid catalyst, prolonged reaction time and drastic reaction conditions.

**Presentation of the Main Work:**

R<sup>1</sup> and R<sup>3</sup> = H/alkyl; R<sup>2</sup> = alkyl/benzyl/ phenyl/ COOEt;  
EWG = CN, COMe, COOEt.

Scheme 1: Aza-Michael addition reaction

**Scope of the Research:**

The use of reagents impregnated on inorganic supports offer various advantages such as simple work-up and product purification, enhanced or reduced reactivity of the functional groups in the substrates and manipulative simplicity, recovery and reuse of catalyst, long time persisting catalytic activity and environmentally friendliness. In continuation to our efforts<sup>17</sup> on the development of facile methods for organic synthesis and to explore the usage of newer greener catalyst in organic reactions,<sup>18,19</sup> we wished to employ Melamine Trisulfonic Acid (MTSA) on Neutral Alumina<sup>20</sup> for the synthesis of  $\beta$ -amino ketones and nitriles. In the present paper, we have used MTSA as an effective and eco-friendly catalyst for the conjugate addition of a variety of amines to different Michael acceptors (Scheme 1).

**Materials and Methods:**

All experiments were performed in an oven dried glass apparatus under nitrogen atmosphere. The progress of the reaction was monitored by thin layer chromatography (TLC) using silica gel pre-coated aluminium sheets (60 F254, Merck). The visualization of spots was effected by exposure to iodine vapours and 2,4-dinitrophenylhydrazine in ethanol containing few drops of conc. H<sub>2</sub>SO<sub>4</sub> and 5% anisaldehyde solution in acidic ethanol. Column chromatography was performed on silica gel (100-200 mesh) and the compounds were eluted with graded solvent systems of petroleum ether and ethyl acetate. NMR (<sup>1</sup>H and <sup>13</sup>C NMR) spectra were recorded on Bruker Ac-400 spectrophotometer at 400 MHz and 100 MHz respectively, with tetramethylsilane (TMS) as internal standard. The chemical shifts are expressed in  $\delta$  (ppm) downfield from TMS. J values are given in hertz (Hz). ESIMS spectra were recorded on Micro-Mass VG- 7070 H mass spectrometer. IR spectra

on KBr were recorded on Perkin-Elmer FTIR spectrophotometer. Elemental analysis was performed on Leco CHNS-932 analyser.

**General procedure for MTSA catalyzed synthesis of  $\beta$ -amino carbonyls and  $\beta$ -amino nitriles:** MTSA (5 mol%) was added to a mixture of an amine (1.0 mmol) and an  $\alpha,\beta$ -unsaturated compound (1.0 mmol) in acetonitrile (5 mL). The reaction mixture was stirred at 50 °C for about 1.5-10 hours till the completion of the reaction (TLC). Acetonitrile was distilled off under reduced pressure followed by dilution with diethylether (20 mL) and filtration to recover the catalyst. The combined organic layers were treated with brine, dried over  $\text{Na}_2\text{SO}_4$  and concentrated in vacuum. The column chromatography was performed on silica gel (100-200 mesh) and the compounds were eluted with graded solvent systems of *n*-hexane-EtOAc to afford the pure products.

**Spectral Data of the Products:**

3a. 3-(Benzylamino)propanenitrile Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 7.2-7.0 (5H, m), 3.8 (2H, s), 2.8 (2H, m), 2.1 (1H, br s), 2.5 (2H, m);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 117, 138, 128, 127, 126, 54, 44, 21; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3340, 2980, 1460; ESIMS ( $m/z$ ) = 161 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_{10}\text{H}_{12}\text{N}_2$ : C, 74.97, H, 7.55, N, 17.48; Found: C, 75.22, H, 7.79, N, 17.98.

3b. Ethyl 3-(benzylamino)propanoate Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 7.2- 7.0 (5H, m), 4.1 (2H, q,  $J = 7.2$  Hz), 3.6 (2H, s), 3.1-2.9 (2H, m), 2.7-2.6 (2H, t,  $J = 6.1$  Hz), 2.1 (1H, br s), 1.2 (3H, t,  $J = 7.2$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 172, 138, 128, 127, 126, 60, 55, 45, 14, 13; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3340, 2980, 1730; ESIMS ( $m/z$ ) = 208 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_{12}\text{H}_{17}\text{NO}_2$ : C, 69.54, H, 8.27, N, 6.76; Found: C, 69.88, H, 8.53, N, 7.02.

3c. 3-(Benzylamino)cyclohexanone Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 7.3- 7.2 (5H, m), 3.8 (2H, s), 3.7-3.6 (1H, s), 2.8 (1H, m), 2.4-2.2 (5H, m), 2.1 (1H, br s), 1.7-1.6 (2H, m);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 212, 140, 138, 136, 54, 51, 47, 40, 32, 19; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3335, 2960, 1705; ESIMS ( $m/z$ ) = 204 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_{13}\text{H}_{17}\text{NO}$ : C, 76.81, H, 8.43, N, 6.89; Found: C, 76.99, H, 8.62, N, 7.04.

3d. 3-(Benzylamino)-2-methyl-5-(prop-1-en-2-yl)cyclohexanone Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 7.4-7.2 (5H, m), 5.7-5.5 (2H, m), 3.8 (2H, s), 2.9 (1H, m), 2.7 (1H, m), 2.5-2.2 (6H, m), 2.1 (1H, br s), 1.3-1.1 (5H, m);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 212, 149, 140, 129, 127, 110, 59, 54, 38, 36, 21, 12; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3335, 2960, 1705; ESIMS ( $m/z$ ) = 258 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_{17}\text{H}_{23}\text{NO}$ : C, 79.33, H, 9.01, N, 5.44; Found: C, 79.66, H, 9.32, N, 5.78.

3e. 3-(Butylamino)propanenitrile Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 2.9 (2H, t,  $J = 6.6$  Hz), 2.6 (2H, t,  $J = 7.1$  Hz), 2.5 (2H, t,  $J = 6.6$  Hz), 2.1 (1H, br s), 1.7 -1.5 (2H, m), 1.3-1.1 (2H, m), 0.9 (3H, t,  $J = 7.3$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 112, 52, 46, 34, 30, 21, 14; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3310, 2960, 1465; ESIMS ( $m/z$ ) = 127 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_7\text{H}_{14}\text{N}_2$ : C, 66.62, H, 11.18, N, 22.20; Found: C, 66.92, H, 11.34, N, 22.47.

3f. Ethyl 3-(butylamino)propanoate Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 4.1 (2H, q,  $J = 7.5$  Hz), 2.9 (2H, t,  $J = 7.2$  Hz), 2.8 (2H, t,  $J = 6.8$  Hz), 2.6-2.5 (2H, m), 2.1 (1H, br s), 1.4-1.2 (4H, m), 1.0 (3H, t,  $J = 7.5$  Hz), 0.9 (3H, t,  $J = 7.5$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 172, 60, 49, 45, 36, 34, 21, 14, 13; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3410, 2960, 1730; ESIMS ( $m/z$ ) = 174 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_9\text{H}_{19}\text{NO}_2$ : C, 62.39, H, 11.05, N, 8.08; Found: C, 62.68, H, 11.26, N, 8.43.

3g. 3-(Butylamino)cyclohexanone Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 3.6 (1H, m), 3.0 (1H, m), 2.5 - 2.3 (4H, m), 2.2 - 2.1 (5H, m), 1.7-1.6 (4H, m), 0.9 (3H, t,  $J = 7.3$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 208, 51, 50, 47, 43, 39, 35, 22, 21, 14; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3340, 2970, 1700; ESIMS ( $m/z$ ) = 170 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_{10}\text{H}_{19}\text{NO}$ : C, 70.96, H, 11.31, N, 8.28; Found: C, 70.64, H, 11.02, N, 8.59.

3h. 3-(Isopropylamino)propanenitrile Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 2.8 (2H, t,  $J = 6.5$  Hz), 2.7 (1H, m), 2.4 (2H, t,  $J = 6.5$  Hz), 2.1 (1H, br s), 1.0 (6H, d,  $J = 6.2$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 119, 53, 42, 24, 19; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3340, 2960, 1450; ESIMS ( $m/z$ ) = 113 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_6\text{H}_{12}\text{N}_2$ : C, 64.24, H, 10.78, N, 24.97; Found: C, 64.56, H, 10.98, N, 25.21.

3i. Ethyl 3-(isopropylamino)propanoate Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 4.1 (2H, q,  $J = 7.2$  Hz), 2.9- 2.8 (1H, m), 2.7 (2H, t,  $J = 6.3$  Hz), 2.5 (2H, t,  $J = 6.3$  Hz), 2.1 (1H, br s), 1.2 (3H, t,  $J = 7.2$  Hz), 1.0 (6H, d,  $J = 6.1$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 174, 60, 36, 48, 42, 24, 14; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3345, 2960, 1740; ESIMS ( $m/z$ ) = 160 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_8\text{H}_{17}\text{NO}_2$ : C, 60.35, H, 10.76, N, 8.80; Found: C, 60.56, H, 10.94, N, 9.06.

3j. 3-((1-Phenylethyl)amino)propanenitrile Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 7.4 - 7.2 (5H, m), 3.6 (1H, q,  $J = 7.5$  Hz), 2.8 (2H, m), 2.7 (2H, m), 1.3 (3H, d,  $J = 6.8$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 138, 128, 127, 126, 118, 53, 42, 24, 21; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3320, 2245, 1490; ESIMS ( $m/z$ ) = 175 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_{11}\text{H}_{14}\text{N}_2$ : C, 75.82, H, 8.10, N, 16.08; Found: C, 76.03, H, 8.22, N, 16.26.

3k. Ethyl 2-((3-oxocyclohexyl)amino)acetate Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 4.2 (2H, q,  $J = 7.2$  Hz), 3.7 (1H, m), 3.4 (2H, s), 2.9 (1H, m), 2.5-2.3 (4H, m), 2.2-2.1 (5H, m), 1.7-1.6 (4H, m), 0.9 (3H, t,  $J = 7.3$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 211, 169, 63, 55, 49, 46, 41, 30, 19, 14; IR (KBr)  $\nu_{\text{max}}/\text{cm}^{-1}$ : 3340, 2950, 1620; ESIMS ( $m/z$ ) = 200 ( $\text{M}+\text{H}$ ) $^+$ ; Anal Calcd. for  $\text{C}_{10}\text{H}_{17}\text{NO}_3$ : C, 60.28, H, 8.60, N, 7.03; Found: C, 60.62, H, 8.94, N, 7.36.

3l. Ethyl 2-((2-cyanoethyl)amino)acetate Oil;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ , 400 MHz)  $\delta$ : 4.2 (2H, q  $J = 7.2$  Hz), 3.8 (2H, s), 2.6 (2H, t,  $J = 6.9$  Hz), 2.5 (2H, t,  $J = 6.8$  Hz), 1.1 (3H, t,  $J = 7.2$  Hz);  $^{13}\text{C NMR}$  ( $\text{CDCl}_3$ , 100 MHz)  $\delta$ : 171, 117,

63, 50, 47, 19, 14; IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$ : 3250, 1620, 1450; ESIMS ( $m/z$ ) = 157 (M+H)<sup>+</sup>; Anal Calcd. for C<sub>7</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>: C, 53.83, H, 7.74, N, 17.94; Found: C, 54.15, H, 8.06, N, 18.29.

3m. 3-(Piperidin-1-yl)propanenitrile Oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : 2.8 (2H, t,  $J$  = 6.7 Hz), 2.7-2.5 (6H, m), 1.3-1.1 (6H, m); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$ : 118, 52, 49, 26, 25, 18; IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$ : 2930, 1430; ESIMS ( $m/z$ ) = 139 (M+H)<sup>+</sup>; Anal Calcd. for C<sub>8</sub>H<sub>14</sub>N<sub>2</sub>: C, 69.52, H, 10.21, N, 20.27; Found: C, 69.84, H, 10.52, N, 20.63.

3n. Ethyl 3-(piperidin-1-yl)propanoate Oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : 4.1 (2H, q,  $J$  = 7.2 Hz), 2.9 (2H, t,  $J$  = 6.7 Hz), 2.7-2.5 (6H, m), 1.4-1.2 (6H, m) 1.1 (3H, t,  $J$  = 7.2 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$ : 172, 60, 52, 49, 33, 26, 25, 14; IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$ : 2950, 1730; ESIMS ( $m/z$ ) = 186 (M+H)<sup>+</sup>; Anal Calcd. for C<sub>10</sub>H<sub>19</sub>NO<sub>2</sub>: C, 64.83, H, 10.34, N, 7.56; Found: C, 64.47, H, 10.69, N, 7.88.

3o. 3-Morpholinopropanenitrile Oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : 3.7 (4H, t,  $J$  = 4.5 Hz), 2.8 (2H, t,  $J$  = 6.9 Hz), 2.6 (2H, t,  $J$  = 6.8 Hz), 2.5 (4H, t,  $J$  = 4.5 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$ : 118, 72, 56, 49, 18; IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$ : 2850, 1440; ESIMS ( $m/z$ ) = 141 (M+H)<sup>+</sup>; Anal Calcd. for C<sub>7</sub>H<sub>12</sub>N<sub>2</sub>O: C, 59.98, H, 8.63, N, 19.98; Found: C, 60.19, H, 8.98, N, 20.29.

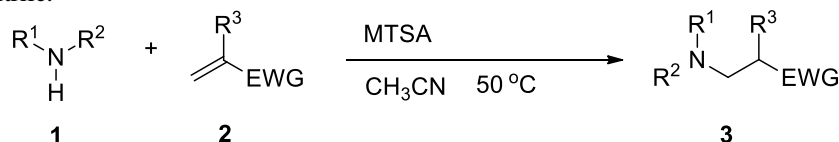
3p. Ethyl 3-morpholinopropanoate Oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : 4.1 (2H, q,  $J$  = 7.2 Hz), 3.8 (4H, t,  $J$  = 4.5 Hz), 2.9 (2H, t,  $J$  = 6.9 Hz), 2.7 (2H, t,  $J$  = 6.8 Hz), 2.5 (4H, t,  $J$  = 4.5 Hz), 1.2 (3H, t,  $J$  = 7.2 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$ : 172, 72, 60, 57, 49, 34, 14; IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$ : 2030, 1730; ESIMS ( $m/z$ ) = 188 (M+H)<sup>+</sup>; Anal Calcd. for C<sub>9</sub>H<sub>17</sub>NO<sub>3</sub>: C, 57.73, H, 9.15, N, 7.48; Found: C, 57.99, H, 9.47, N, 7.82.

3q. 3-Morpholinocyclohexanone Oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : 3.7 (4H, t,  $J$  = 4.6 Hz), 3.4-3.3 (1H, m), 2.6-2.5 (1H, m), 2.4 (4H, t,  $J$  = 4.6 Hz), 2.3-2.2 (3H, m), 2.1-2.0 (2H, m), 1.7-1.6 (2H, m); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$ : 209, 68, 65, 52, 42, 41, 29, 19; IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$ : 2030, 1520; ESIMS ( $m/z$ ) = 184 (M+H)<sup>+</sup>; Anal Calcd. for C<sub>10</sub>H<sub>17</sub>NO<sub>2</sub>: C, 65.54, H, 9.35, N, 7.64; Found: C, 65.89, H, 9.68, N, 7.97.

3r. 2-Methyl-3-morpholino-5-(prop-1-en-2-yl)cyclohexanone Oil; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : 7.4 - 7.2 (5H, m), 5.7-5.5 (2H, m), 3.9 (2H, s), 3.7 (2H, t,  $J$  = 4.5 Hz), 3.0-2.9 (1H, m), 2.8-2.7 (1H, m), 2.5 (4H, t,  $J$  = 4.5 Hz), 2.3-2.1 (6H, m), 1.3-1.1 (5H, m); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$ : 212, 148, 111, 80, 69, 54, 51, 47, 38, 36, 24, 13; IR (KBr)  $\nu_{\max}/\text{cm}^{-1}$ : 2950, 1520; ESIMS ( $m/z$ ) = 238 (M+H)<sup>+</sup>; Anal Calcd. for C<sub>14</sub>H<sub>23</sub>NO<sub>2</sub>: C, 70.85, H, 9.77, N, 5.90. Found: C, 71.18, H, 10.02, N, 6.24.

### Results and Discussion:

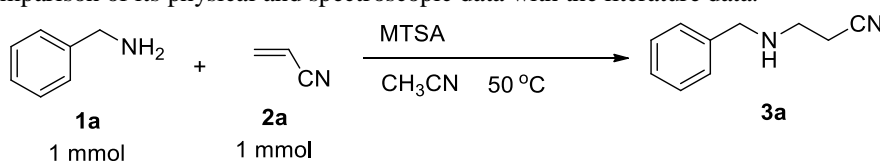
We herein report an efficient and simple method for the synthesis of  $\beta$ -amino ketones and nitriles by the aza-Michael addition of primary and secondary aliphatic amines to  $\alpha,\beta$ -unsaturated carbonyl compounds and nitriles in the presence of a non-toxic, inexpensive catalyst in acetonitrile at 50 °C (Scheme 1). In view of our earlier reported work,<sup>20</sup> we found that MTSA could catalyze the addition of a primary and secondary aliphatic amines to electron deficient  $\alpha,\beta$ -unsaturated carbonyl compounds and nitriles to produce the corresponding  $\beta$ -amino derivatives in excellent yields. The best result was achieved by carrying out the reaction with 5 mol% MTSA in acetonitrile.



$\text{R}^1$  and  $\text{R}^3$  = H/alkyl;  $\text{R}^2$  = alkyl/benzyl/ phenyl/ COOEt;  
EWG = CN, COMe, COOEt.

Scheme 1: Aza-Michael addition reaction

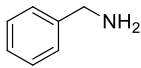

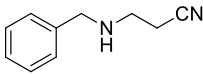
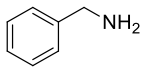
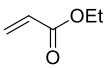
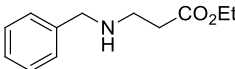
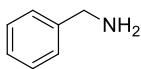
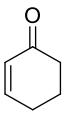
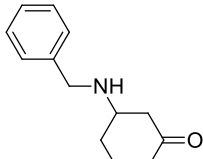
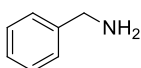
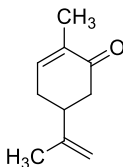
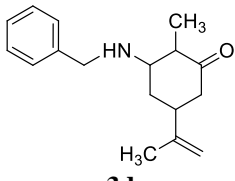
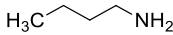

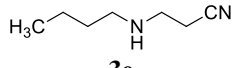
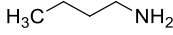
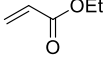
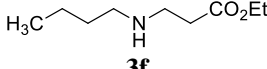
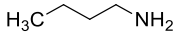
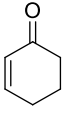
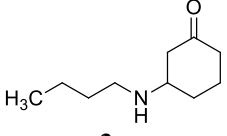
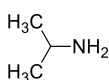

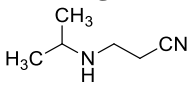
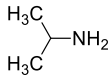
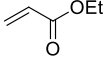
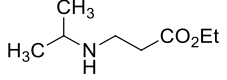
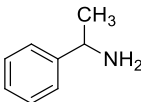

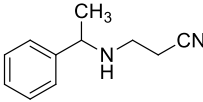
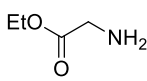
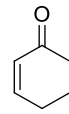
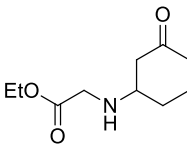
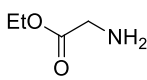

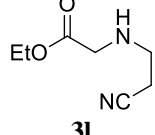
For optimization of the reaction conditions, a mixture of benzyl amine 1a (1.0 mmol), acrylonitrile 2a (1.0 mmol) and MTSA (5 mol%) was stirred in acetonitrile (5 mL) in an oven dried round bottom flask at 50 °C as shown in Scheme 2. After 2.0 hours of reaction run, the formation of a new compound was noticed on TLC which was isolated in 90% yield by column chromatography over silica gel (100-200 mesh using *n*-hexane:EtOAc (8:2) as eluent. The isolated compound was found to be 3-(butylamino)propanenitrile 3a as revealed by comparison of its physical and spectroscopic data with the literature data.<sup>10</sup>



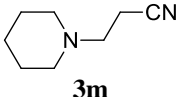

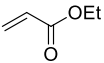
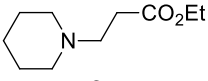


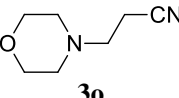

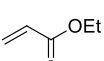
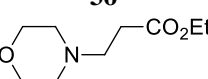

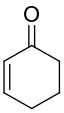
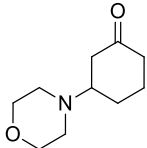

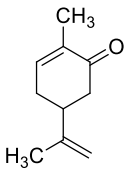
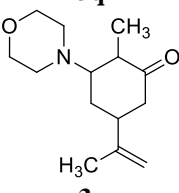
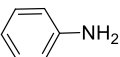

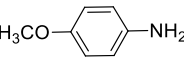



Scheme 2: MTSA catalyzed synthesis of 3-butylaminopropionitrile 3a.

Using the optimized reaction conditions, several structurally varied amines were coupled with a wide range of  $\alpha,\beta$ -unsaturated carbonyls and nitriles and the results are summarized in Table 1.

Table 1: MTSA catalyzed aza-Michael addition of  $\alpha,\beta$ -unsaturated carbonyls and nitriles with primary and secondary amines

Entry	Amine (1)	Unsaturated compound (2)	Product (3)	Time (hrs)	Yield (%) <sup>a</sup>
1			 <b>3a</b>	2.0	90
2			 <b>3b</b>	4.0	87
3			 <b>3c</b>	4.5	85
4			 <b>3d</b>	5.0	73
5			 <b>3e</b>	2.0	89
6			 <b>3f</b>	3.5	89
7			 <b>3g</b>	4.5	87
8			 <b>3h</b>	2.0	88
9			 <b>3i</b>	4.0	87
10			 <b>3j</b>	2.0	89
11			 <b>3k</b>	10	75
12			 <b>3l</b>	8	75

13			 <b>3m</b>	5.5	89
14			 <b>3n</b>	7.5	88
15			 <b>3o</b>	5.5	87
16			 <b>3p</b>	8	87
17			 <b>3q</b>	10	85
18			 <b>3r</b>	11	85
19			-	12	NR
20			-	12	NR

<sup>a</sup>Yield obtained after column chromatography purification; NR = No reaction.

#### Conclusion:

In summary, a simple, efficient aza-Michael addition of primary and secondary aliphatic amines to a series of  $\alpha,\beta$ -unsaturated carbonyl compounds and nitriles using MTSA catalyst to produce the corresponding  $\beta$ -amino derivatives has been achieved. The main advantages of this method are simplicity, mild and eco-friendly reaction conditions, high yields and use of inexpensive, non-toxic, easily available catalyst.

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