A Catalytic Method for Room-Temperature Michael Additions Using 12-Tungstophosphoric Acid as a Reusable Catalyst in Water

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Abstract: 12-Tungstophosphoric acid ($H_3PW_{12}O_{40}$) has been found to be an efficient and recyclable catalyst in promoting room temperature Michael additions of amines and aryl thiols to α,β-unsaturated esters and acrylonitrile in water to afford the corresponding saturated amines in good to excellent yields.

Key words: 12-tungstophosphoric acid, Michael addition, α,β-unsaturated ester, acrylonitrile, recyclable catalyst, aqueous medium

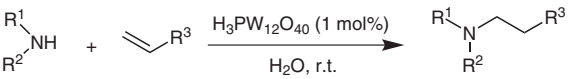
β-Amino carbonyl and nitrile compounds have attracted considerable attention in organic synthesis because of their wide range of biological activities[1] and pharmacological properties.[2] An alternative method for preparing these compounds is via Michael addition, which is a perfectly atom-economic and inherently green C–N bond-forming reaction involving the conjugate addition of nitrogen nucleophiles to α,β-unsaturated carbonyl or nitrile compounds.[3]

Several procedures for the conjugate addition of amines to electron-deficient olefins have been developed in the past few years.[4] Recently, additional procedures have been reported for such additions, including those promoted by $Me_2S^+BrBr^-$,[5a] basic ionic liquid,[5b] Amberlyst-5,[5c] borax–water,[5d] acetic acid/microwave,[5e,f] AlSBA-15,[5g] imidazolium-based polymer supported $Gd(OTf)_3$,[5h] DBU–acetonitrile,[5i] and SiO_2–acetonitrile.[5j] Despite their remarkable success, many of these methods still suffer from certain drawbacks, such as: low yields, the requirement for high temperatures and stoichiometric amounts of costly and inaccessible and/or non-recyclable catalysts, substrate selectivity and most require the use of hazardous solvents. Many of the methods are also generally limited with regard to aryl amines. Thus, the development of greener and more efficient pathways is still highly desirable.

Recently, water has become the preferred medium for organic reactions,[6] both from an environment-friendly point of view as well as from those of economization and safety. Reactions in water are even more attractive if they can be performed using reusable catalysts. In this respect, few of the aforementioned procedures can meet this criterion of green chemistry. Therefore, there is still scope for new recyclable catalysts to be used in Michael addition reactions. Heteropolyacids (HPAs), which are well known for their reusability, flexibility in modifying the acid strength, ease of handling, environmental compatibility, non-toxicity and experimental simplicity, have been reported to efficiently catalyze many organic reactions.[7]

In continuation of our work[8] on the application of 12-tungstophosphoric acid ($H_3PW_{12}O_{40}$) in pure water for the development of useful synthetic methodologies, we recently observed that a catalytic amount (0.01 equiv) of this acid can efficiently promote the conjugate addition of aliphatic and aromatic amines to α,β-unsaturated esters and acrylonitrile at room temperature in water. To the best of our knowledge, there have been only three reports on the aza-Michael addition of amines to α,β-unsaturated esters and acrylonitrile mediated by catalysts in water, such as Borax–water,[5d] boric acid–water,[4a] and β-cyclodextrin–water–acetone.[4b] However, aromatic amines can not effectively participate in the reaction when using Borax–water and boric acid–water, while stoichiometric amounts of catalyst was needed when using β-cyclodextrin–water–acetone.

Initially, addition of various aliphatic and aromatic amines (1.2 mmol) to α,β-unsaturated esters and acrylonitrile (1 mmol) with $H_3PW_{12}O_{40}$ (1% mmol) in pure water (2 mL) was examined (Scheme 1 and entries 1–19 in Table 1). Aliphatic amines reacted efficiently with α,β-unsaturated esters and acrylonitrile to afford the saturated amines in excellent yields (entries 1–5). Moreover, aromatic amines could also effectively participate in the reaction to afford good to excellent yields of the desired products after 40 hours at room temperature (entries 6–19). Additional experiments indicated that the same yields of products could be afforded after eight hours at 60 °C (entries 6, 8 and 18).



R^1 = Bn, alkyl, aryl; R^2 = H, alkyl; R^3 = COOMe, CN

Scheme 1 12-Tungstophosphoric acid catalyzed Michael addition between amines with α,β-unsaturated esters and acrylonitrile

Finally, this protocol was also extended to the conjugate addition of aryl thiols to α,β-unsaturated esters and acrylonitrile under similar conditions (Scheme 2 and entries 20–22 in Table 1). The reactions proceeded at room temperature efficiently and delivered excellent yields.

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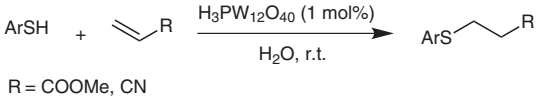


Scheme 2 12-Tungstophosphoric acid catalyzed Michael addition between aryl thiols with α,β-unsaturated esters and acrylonitrile

The possibility of recycling the catalyst was then examined. For this reason, the reaction of benzylamine and methyl acrylate was studied further (entry 1, Table 1). When the reaction was complete, ethyl acetate (2 × 2 mL) was added, the organic materials were extracted and the aqueous solution was saved. This solution, containing the used catalyst, could be reused and subjected to a second run of the reaction. The results of the first and subsequent experiments were almost consistent in yields. Even after five runs, the catalytic activity of $H_3PW_{12}O_{40}$ was almost the same as that of fresh catalyst.

In conclusion, we have developed a green and efficient approach for the room temperature Michael additions of various aliphatic and aromatic amines and aryl thiols to α,β-unsaturated esters and acrylonitrile in pure water in the presence of a catalytic amounts of $H_3PW_{12}O_{40}$ as a reusable catalyst. The aqueous medium, simple experimental procedure, mild conditions, high yields, participation of wide range of substrates, employment of catalytic amounts of the catalyst, and reusability of the catalyst are the noteworthy advantages of the protocol.

Table 1 12-Tungstophosphoric Acid Catalyzed Michael Additions of Aliphatic and Aromatic Amines and Aryl Thiols to α,β-Unsaturated Esters and Acrylonitrile[a]

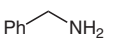
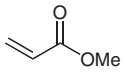
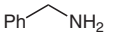
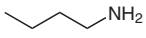
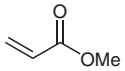
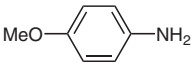
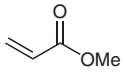
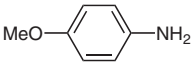
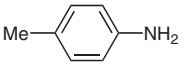
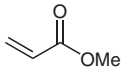
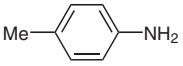
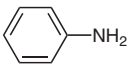
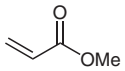
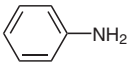
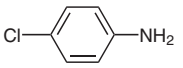
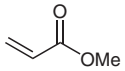
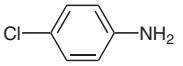
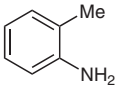
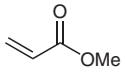
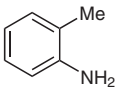
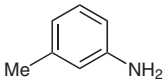
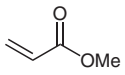
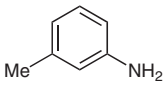
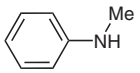
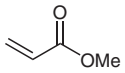
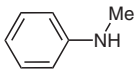
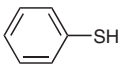
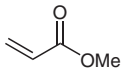
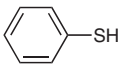
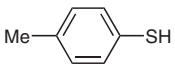
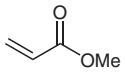
Entry	Donor	Acceptor	Product	Time (h)	Yield (%)[b]
1			**1a**	2.5	94 (95, 93, 94, 94, 95)[c]
2			**2a**	2.5	94
3			**3a**	2.5	96
4			**4a**	2.5	96
5			**5a**	2.5	95
6			**6a**	40 (8)[d]	86 (85)[d]
7			**7a**	40	84
8			**8a**	40 (8)[d]	86 (87)[d]
9			**9a**	40	85
10			**10a**	40	82
11			**11a**	40	80
12			**12a**	40	65
13			**13a**	40	60
14			**14a**	40	74
15			**15a**	40	72

Table 1 12-Tungstophosphoric Acid Catalyzed Michael Additions of Aliphatic and Aromatic Amines and Aryl Thiols to α,β-Unsaturated Esters and Acrylonitrile[a] (continued)

Entry	Donor	Acceptor	Product	Time (h)	Yield (%)[b]
16			**16a**	40	76
17			**17a**	40	73
18			**18a**	40 (8)[d]	76 (78)[d]
19			**19a**	40	75
20			**20a**	2.5	97
21			**21a**	2.5	97
22			**22a**	2.5	98

[a] Reactions performed at r.t. with α,β-unsaturated ester/acrylonitrile (1.0 mmol), amine/aryl thiol (1.2 mmol), $H_3PW_{12}O_{40}$ (1% mmol) in H_2O (2 mL).
[b] Isolated yields after column chromatography.
[c] Yields for 2nd, 3rd, 4th, 5th and 6th cycles.
[d] Reactions at 60 °C.

All chemicals were purchased from Aldrich. Petroleum ether (PE), where used, had a boiling range 60–90 °C. NMR spectra were recorded on a Bruker Avance DMX 400 MHz (^{1}H, 400 MHz; ^{13}C, 100 MHz) spectrometer in $CDCl_3$ solution. Low-resolution MS analyses were measured on a Bruker Esquire 3000 spectrometer using electrospray ionization (ESI). Elemental analyses were measured on an EA 1112. IR spectra were recorded on a Nicolet Nexus 470 FT IR.

Michael Addition; General Procedure

The α,β-unsaturated esters (acrylonitrile) (1 mmol) and amines (aryl thiols) (1.2 mmol) were placed in a 5 mL glass tube with pure H_2O (2 mL). $H_3PW_{12}O_{40}$ (1% mmol) was added and the mixture was stirred at r.t. for the time indicated in Table 1. The mixture was extracted into EtOAc (3 × 2 mL), dried (Na_2SO_4), and the solvent was evaporated. The product was purified by column chromatography (EtOAc–PE, 1:10).

Methyl 3-(Benzylamino)propanoate (1a)[5b,d,9a]

Yellow oil.

^{1}H NMR ($CDCl_3$): δ = 1.86 (s, 1 H, NH), 2.48–2.51 (t, *J* = 6.8 Hz, 2 H, CH_2), 2.85–2.88 (t, *J* = 6.8 Hz, 2 H, CH_2), 3.67 (s, 2 H, CH_2), 3.77 (s, 3 H, OCH_3), 7.23–7.30 (m, 5 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 32.49, 49.08, 51.40, 58.23, 126.93, 128.11, 128.60, 138.87, 172.79.

MS (ESI): *m*/*z* = 194 $[M + H]^+$.

3-(Benzylamino)propanenitrile (2a)[5d,9b]

Yellow oil.

^{1}H NMR ($CDCl_3$): δ = 1.66 (s, 1 H, NH), 2.49–2.52 (t, *J* = 6.6 Hz, 2 H, CH_2), 2.91–2.94 (t, *J* = 6.8 Hz, 2 H, CH_2), 3.84 (s, 2 H, CH_2), 7.28–7.38 (m, 5 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 18.67, 44.26, 53.06, 118.69, 127.19, 127.99, 128.47, 139.46.

MS (ESI): *m*/*z* = 161 $[M + H]^+$.

3-(Butylamino)propanenitrile (3a)[9b,c]

Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 0.86–1.90 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.27–1.36 (m, 3 H, CH_2 and NH), 1.40–1.47 (m, 2 H, CH_2), 2.46–250 (t, *J* = 6.4 Hz, 2 H, CH_2), 2.57–2.61 (t, *J* = 7.2 Hz, 2 H, CH_2), 2.87–2.90 (d, *J* = 6.8 Hz, 2 H, CH_2).

^{13}C NMR ($CDCl_3$): δ = 13.86, 18.63, 20.26, 30.05, 45.03, 48.83, 118.72.

MS (ESI): *m*/*z* = 127 $[M + H]^+$.

Methyl 3-(Piperidin-1-yl)propanoate (4a)[5b]

Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 1.41–1.43 (m, 2 H, CH_2), 1.55–1.59 (m, 4 H, CH_2), 2.37–2.39 (t, *J* = 5.2 Hz, 4 H, CH_2), 2.49–2.52 (t, *J* = 7 Hz, 2 H, CH_2), 2.64–2.74 (d, *J* = 7 Hz, 2 H, CH_2), 3.67 (s, 3 H, OCH_3).

^{13}C NMR ($CDCl_3$): δ = 24.90, 26.23, 31.94, 51.54, 54.32, 55.62, 173.10.

MS (ESI): *m*/*z* = 172 $[M + H]^+$.

3-(Piperidin-1-yl)propanenitrile (5a)[5b,d,9b]

Colorless oil.

^{1}H NMR ($CDCl_3$): δ = 1.37–1.42 (m, 2 H, CH_2), 1.52–1.58 (m, 4 H, CH_2), 2.38–2.40 (t, *J* = 5.2 Hz, 4 H, CH_2), 2.44–2.48 (t, *J* = 7 Hz, 2 H, CH_2), 2.61–2.65 (d, *J* = 7.4 Hz, 2 H, CH_2).

^{13}C NMR ($CDCl_3$): δ = 15.60, 24.02, 25.76, 53.93, 54.10, 119.00.

MS (ESI): *m*/*z* = 139 $[M + H]^+$.

Methyl 3-(4-Methoxyphenylamino)propanoate (6a)
Brown solid; mp 59–60 °C.

IR (KBr): 3392, 3039, 2996, 2952, 2834, 1734, 1620, 1515, 1462, 1439, 1366, 1238, 1176, 1121, 1092, 1036, 823 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.59–2.62 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.38–3.41 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.63 (br s, 1 H, NH), 3.69 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 6.59–6.61 (d, *J* = 9.2 Hz, 2 H, Ph), 6.77–6.80 (d, *J* = 9.2 Hz, 2 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 33.65, 40.42, 51.60, 55.65, 114.48, 114.83, 141.65, 152.32, 172.79.

MS (ESI): *m*/*z* = 210 $[M + H]^+$.

Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.01; H, 7.15; N, 6.86.

3-(4-Methoxyphenylamino)propanenitrile (7a)[9b,d]
Brown solid; mp 58–59 °C.

^1H NMR ($CDCl_3$): δ = 2.59–2.62 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.44–3.48 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.29–3.64 (br s, 1 H, NH), 3.77 (s, 3 H, OCH_3), 6.60–6.62 (d, *J* = 9.2 Hz, 2 H, Ph), 6.81–6.83 (d, *J* = 8.8 Hz, 2 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 18.05, 40.77, 55.68, 114.69, 115.04, 118.31, 140.15, 152.87.

MS (ESI): *m*/*z* = 177 $[M + H]^+$.

Methyl 3-(*p*-Toluidino)propanoate (8a)[9e]
Yellow solid; mp 54–56 °C.

^1H NMR ($CDCl_3$): δ = 2.26 (s, 3 H, CH_3), 2.61–2.65 (t, *J* = 6.2 Hz, 2 H, CH_2), 3.43–3.46 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.71 (s, 3 H, OCH_3), 3.30–4.12 (br s, 1 H, NH), 6.56–6.58 (d, *J* = 7.6 Hz, 2 H, Ph), 7.00–7.02 (d, *J* = 8.0 Hz, 2 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 20.28, 33.63, 39.74, 51.61, 113.23, 126.96, 129.72, 145.14, 172.79.

MS (ESI): *m*/*z* = 194 $[M + H]^+$.

3-(*p*-Toluidino)propanenitrile (9a)[9f]
White solid; mp 102–103 °C.

^1H NMR ($CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 2.61–2.64 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.49–3.52 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.60 (br s, 1 H, NH), 6.57–6.59 (d, *J* = 8.4 Hz, 2 H, Ph), 7.05–7.07 (d, *J* = 8 Hz, 2 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 18.02, 20.31, 40.10, 113.28, 118.30, 127.86, 129.96, 143.81.

MS (ESI): *m*/*z* = 161 $[M + H]^+$.

Methyl 3-(Phenylamino)propanoate (10a)[5f]
Brown solid; mp 37–38 °C.

^1H NMR ($CDCl_3$): δ = 2.63–2.66 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.46–3.49 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.72 (s, 3 H, OCH_3), 3.98 (br s, 1 H, NH), 6.64–7.22 (m, 5 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 33.62, 39.33, 51.64, 112.97, 117.67, 129.24, 147.46, 172.73.

MS (ESI): *m*/*z* = 180 $[M + H]^+$.

3-(Phenylamino)propanenitrile (11a)[9g]
White solid; mp 47–48 °C.

^1H NMR ($CDCl_3$): δ = 2.61–2.65 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.50–3.53 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.93 (br s, 1 H, NH), 6.64–7.27 (m, 5 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 18.02, 39.70, 113.02, 118.31, 118.50, 129.41, 146.21.

MS (ESI): *m*/*z* = 147 $[M + H]^+$.

Methyl 3-(4-Chlorophenylamino)propanoate (12a)[9h]
Yellow solid; mp 56–57 °C.

^1H NMR ($CDCl_3$): δ = 2.60–2.63 (t, *J* = 6 Hz, 2 H, CH_2), 3.41–3.44 (t, *J* = 6.2 Hz, 2 H, CH_2), 3.71 (s, 3 H, OCH_3), 4.05 (br s, 1 H, NH), 6.53–6.56 (d, *J* = 8.8 Hz, 2 H, Ph), 7.11–7.14 (d, *J* = 8.8 Hz, 2 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 33.42, 39.42, 51.71, 114.02, 122.25, 129.03, 146.01, 172.59.

MS (ESI): *m*/*z* = 214 $[M + H]^+$.

3-(4-Chlorophenylamino)propanenitrile (13a)
White solid; mp 72–73 °C.

IR (KBr): 3363, 3050, 2913, 2853, 2255, 1599, 1515, 1493, 1477, 1407, 1316, 1295, 1265, 1216, 1125, 1090, 1061, 824 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.62–2.66 (t, *J* = 6.6 Hz, 2 H, CH_2), 3.48–3.52 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.99 (br s, 1 H, NH), 6.55–6.57 (d, *J* = 8.8 Hz, 2 H, Ph), 7.16–7.18 (d, *J* = 9.2 Hz, 2 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 18.00, 39.78, 114.11, 117.93, 123.22, 129.31, 144.70.

MS (ESI): *m*/*z* = 181 $[M + H]^+$.

Anal. Calcd for $C_9H_9ClN_2$: C, 59.84; H, 5.02; N, 15.51. Found: C, 59.67; H, 4.94; N, 15.68.

Methyl 3-(*o*-Toluidino)propanoate (14a)
Yellow oil.

IR (KBr): 3428, 3056, 3020, 2924, 1733, 1606, 1587, 1514, 1439, 1369, 1317, 1256, 1194, 1174, 1130, 1052, 748, 665 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.16 (s, 3 H, CH_3), 2.68–2.71 (t, *J* = 6.0 Hz, 2 H, CH_2), 3.51–3.54 (t, *J* = 6.6 Hz, 2 H, CH_2), 3.73 (s, 3 H, OCH_3), 4.00 (br s, 1 H, NH), 6.65–7.16 (m, 4 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 17.32, 33.59, 29.29, 51.64, 109.64, 117.22, 122.40, 127.04, 130.18, 145.45, 172.83.

MS (ESI): *m*/*z* = 194 $[M + H]^+$.

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.21; H, 7.75; N, 7.43.

3-(*o*-Toluidino)propanenitrile (15a)
Brown oil.

IR (KBr): 3423, 3055, 3019, 2927, 2248, 1605, 1588, 1516, 1475, 1452, 1371, 1314, 1264, 1211, 1135, 1082, 1057, 987, 751 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.20 (s, 3 H, CH_3), 2.67–2.70 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.58–3.62 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.89 (br s, 1 H, NH), 6.59–7.28 (m, 4 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 17.30, 18.07, 39.59, 109.47, 118.13, 127.74, 127.13, 130.62, 144.02.

MS (ESI): *m*/*z* = 161 $[M + H]^+$.

Anal. Calcd for $C_{10}H_{12}N_2$: C, 74.97; H, 7.55; N, 17.48. Found: C, 74.81; H, 7.47; N, 17.65.

Methyl 3-(*m*-Toluidino)propanoate (16a)
Yellow oil.

IR (KBr): 3401, 3027, 2952, 2920, 2859, 1732, 1606, 1514, 1492, 1436, 1366, 1326, 1255, 1171, 1110, 1054, 844, 772, 694 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.30 (s, 3 H, CH_3), 2.62–2.65 (t, *J* = 6.2 Hz, 2 H, CH_2), 3.45–3.49 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.71 (s, 3 H, OCH_3), 3.10–4.19 (br s, 1 H, NH), 6.45–7.11 (m, 4 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 21.51, 33.67, 39.35, 51.63, 110.09, 113.78, 118.61, 129.09, 139.01, 147.49, 172.76.

MS (ESI): *m*/*z* = 194 $[M + H]^+$.

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.20; H, 7.76; N, 7.44.

3-(*m*-Toluidino)propanenitrile (17a)
Yellow solid; mp 46–47 °C.

IR (KBr): 3406, 3036, 2948, 2248, 1605, 1515, 1452, 1370, 1323, 1256, 1170, 1112, 850, 775, 696 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.33 (s, 3 H, CH_3), 2.62–2.65 (t, *J* = 6.6 Hz, 2 H, CH_2), 3.50–3.53 (t, *J* = 6.4 Hz, 2 H, CH_2), 3.73 (br s, 1 H, NH), 6.45–7.15 (m, 4 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 10.05, 21.53, 39.76, 110.12, 113.87, 118.28, 119.48, 129.34, 139.34, 146.17.

MS (ESI): *m*/*z* = 161 $[M + H]^+$.

Anal. Calcd for $C_{10}H_{12}N_2$: C, 74.97; H, 7.55; N, 17.48. Found: C, 74.80; H, 7.48; N, 17.66.

Methyl 3-[Methyl(phenyl)amino]propanoate (18a)
Yellow oil.

IR (KBr): 3059, 3026, 2951, 1735, 1600, 1505, 1436, 1366, 1324, 1287, 1195, 1171, 1113, 1044, 991, 749, 692 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.58–2.61 (t, *J* = 7 Hz, 2 H, CH_2), 2.95 (s, 3 H, CH_3), 3.68–3.72 (m, 5 H, CH_2 and OCH_3), 6.73–7.28 (m, 5 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 31.41, 38.12, 48.53, 51.60, 112.43, 116.71, 129.10, 148.49, 172.63.

MS (ESI): *m*/*z* = 194 $[M + H]^+$.

Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.22; H, 7.75; N, 7.41.

3-[Methyl(phenyl)amino]propanenitrile (19a)
Brown oil.

IR (KBr): 3061, 3028, 2919, 2825, 2247, 1601, 1505, 1452, 1433, 1361, 1287, 1235, 1196, 1160, 1121, 992, 960, 752, 694 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.57–2.60 (t, *J* = 7.0 Hz, 2 H, CH_2), 3.05 (s, 3 H, CH_3), 3.72–3.75 (t, *J* = 6.8 Hz, 2 H, CH_2), 6.74–7.32 (m, 5 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 15.15, 38.58, 48.93, 112.55, 117.67, 118.41, 129.45, 147.58.

MS (ESI): *m*/*z* = 161 $[M + H]^+$.

Anal. Calcd for $C_{10}H_{12}N_2$: C, 74.97; H, 7.55; N, 17.48. Found: C, 74.82; H, 7.47; N, 17.66.

Methyl 3-(Phenylthio)propanoate (20a)[9i]
Yellow oil.

^1H NMR ($CDCl_3$): δ = 2.61–2.65 (t, *J* = 7.8 Hz, 2 H, CH_2), 3.15–3.18 (t, *J* = 7.2 Hz, 2 H, CH_2), 3.67 (s, 3 H, OCH_3), 7.19–7.38 (m, 5 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 29.03, 34.21, 51.77, 126.56, 129.00, 130.09, 135.17, 172.13.

MS (ESI): *m*/*z* = 197 $[M + H]^+$.

3-(Phenylthio)propanenitrile (21a)[9b]
Yellow oil.

^1H NMR ($CDCl_3$): δ = 2.57–2.61 (t, *J* = 7.4 Hz, 2 H, CH_2), 3.11–3.14 (t, *J* = 7 Hz, 2 H, CH_2), 7.26–7.43 (m, 5 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 18.23, 30.29, 117.91, 127.75, 129.38, 131.46, 133.14.

MS (ESI): *m*/*z* = 164 $[M + H]^+$.

Methyl 3-(*p*-Tolylthio)propanoate (22a)[9j]
Yellow oil.

^1H NMR ($CDCl_3$): δ = 2.32 (s, 3 H, CH_3), 2.58–2.62 (t, *J* = 7.2 Hz, 2 H, CH_2), 3.09–3.13 (t, *J* = 7.2 Hz, 2 H, CH_2), 3.67 (s, 3 H, OCH_3), 7.10–7.12 (d, *J* = 8 Hz, 2 H, Ph), 7.27–7.30 (d, *J* = 8.4 Hz, 2 H, Ph).

^{13}C NMR ($CDCl_3$): δ = 20.99, 29.75, 34.29, 51.72, 129.78, 131.04, 131.29, 136.85, 172.21.

MS (ESI): *m*/*z* = 211 $[M + H]^+$.

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