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Indium(III) iodide-mediated Strecker reaction in water: an efficient and environmentally friendly approach for the synthesis of α-aminonitrile via a three-component condensation

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ABSTRACT

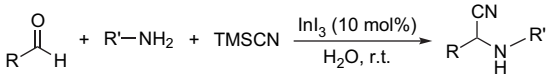
A mild, efficient and environmentally friendly method has been developed for the synthesis of α-aminonitriles via a three-component condensation of aldehyde, amine and TMSCN in the presence of a catalytic amount of indium(III) iodide in water. The reactions proceeded smoothly at room temperature in water to generate the corresponding products in moderate to excellent yields.

1. Introduction

α-Aminonitriles are significantly important intermediates for the synthesis of a wide variety of amino acids, amides, diamines and nitrogen-containing heterocycles.[1] Among the methods reported for the synthesis of α-aminonitriles, Strecker reaction, which proceeded via the addition of HCN to imine proved to be an effective one for the preparation of α-aminonitrile.[2] Recently, modified method using one-pot procedure via a three-component condensation of aldehyde, amine and trimethylsilyl cyanide (TMSCN, a promising alternative to HCN and alkali cyanide due to its nature as an effective, safe and easily-handled cyanation reagent) catalyzed by Lewis acids (or protic acids) in conventional organic solvents has been described.[3] However, many of these reported methods involve the use of expensive reagents, toxic organic solvent, tedious workup procedure and longer reaction times. Therefore, it is still desirable to develop an efficient and practical method for the Strecker reaction under mild conditions.

In recent decades, water has aroused considerable attention in synthetic community and proved to be a promising solvent in organic synthesis due to its economic, environmentally friendly and polar nature.[4] In relation to this, significant efforts have been dedicated to developing organic reactions in water with many inherent advantages over reactions in conventional organic solvents. Therefore, if the Strecker reaction can be developed to operate in water, it will be of practical value and contribute to the area of water chemistry.

More recently, indium(III) compounds have been demonstrated to be mild, efficient and water-tolerant Lewis acids for various organic transformations.[5] In contrast to classical Lewis acids, which often are required in stoichiometric quantities, indium(III) compounds readily promote a wide variety of organic reactions in catalytic quantities soluble both in organic solvents and in aqueous media. In continuation of our work to apply indium(III) compound as catalyst to organic reactions in water,[6] herein, we report an efficient and environmentally friendly method for the synthesis of α-aminonitriles catalyzed by indium(III) iodide (InI_3) in water (Scheme 1).



Scheme 1. Strecker reaction in water.

2. Results and discussion

Initial research was focused on the reaction of benzaldehyde, aniline and TMSCN in acetonitrile using different catalysts (10 mol %). As shown in Table 1, the one-pot reaction proceeded

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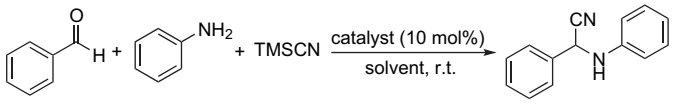
Table 1
One-pot synthesis of α-aminonitrile using different catalysts



Entry	Catalyst	Solvent	Time	Yield[a] (%)
1	InF_3	CH_3CN	24 h	94
2	$InCl_3$	CH_3CN	24 h	93
3	$InBr_3$	CH_3CN	24 h	91
4	$In(OTf)_3$	CH_3CN	24 h	93
5	$In(OH)_3$	CH_3CN	24 h	72
6	InI_3	CH_3CN	24 h	98
7	InI_3	—[b]	10 min	95
8	InI_3	H_2O	30 min	95 (89)[c]
9	Pyridine	CH_3CN	24 h	87
10	DABCO[d]	CH_3CN	24 h	89
11	DMAP[e]	CH_3CN	24 h	76
12	HMT[f]	CH_3CN	24 h	67
13	MIM[g]	CH_3CN	24 h	87

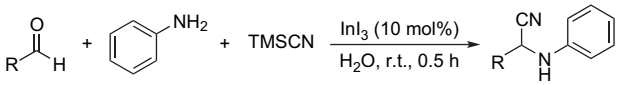
[a] Isolated yield.
[b] Solvent-free condition.
[c] With catalyst loading of 5 mol%.
[d] DABCO=1,8-diazabicyclo[5.4.0]undec-7-ene.
[e] DMAP=4-*N*,*N*-dimethylamino pyridine.
[f] HMT=hexamethylenetetramine.
[g] MIM=1-methyl imidazole.

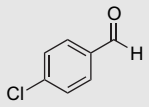
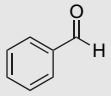
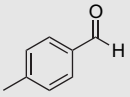
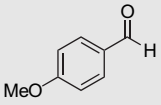
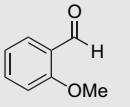
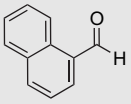
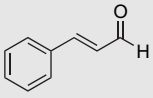
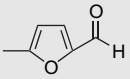
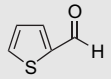
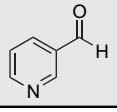
efficiently in the presence of various indium(III) compounds at room temperature. Among the various catalysts used, InI_3 proved to be the best one and 98% yield of the corresponding product was afforded (entry 6, Table 1). In the meantime, employing InI_3 as catalyst, it was found that the three-component reaction could also take place efficiently in water or under solvent-free condition to furnish the desired product both in 95% yields within a short reaction time of 30 min (entries 7 and 8, Table 1). Considering the advantages provided by using water as reaction solvent, following reactions were carried out in water. In addition, it was worthy of noting that the one-pot reaction could also work well in acetonitrile in the presence of different nitrogen-containing organocatalysts, good yields were obtained when utilizing pyridine, 1,8-diazabicyclo[5.4.0]undec-7-ene (DABCO) and 1-methyl imidazole (MIM) as catalysts (entries 9, 10 and 13, Table 1).

In the following work, a series of α-aminonitriles were synthesized by using different aldehydes, amines and TMSCN in the presence of InI_3 (10 mol%) in water. As shown in Table 2, all aldehydes could react effectively with aniline and TMSCN in water catalyzed by InI_3 to afford the corresponding products with excellent yields of 81–97%. The catalytic system also worked well with acid sensitive heterocyclic aldehydes such as 5-methyl-furaldehyde, 2-thiophenecarboxaldehyde and 3-pyridinecarboxaldehyde to generate the corresponding products with good yields of 93%, 97% and 83% (entries 8, 9 and 10, Table 2). Even for α,β-unsaturated aldehyde, a good yield of the desired product (81%) was obtained without observing the formation of other side products (Table 2, entry 7).

Encouraged by above results, we continued our task to explore the reactivity of different amines with benzaldehyde and TMSCN under similar reaction conditions. As shown in Table 3, all aromatic amines could efficiently undergo reactions with benzaldehyde and TMSCN to give the products in excellent yields (entries 1–4, Table 3). When it came to aliphatic amines such as benzyl amine, pyrrolidine and morpholine, relatively slow reaction rate occurred due to the unstable nature of the formed aliphatic imines in the presence of water (entries 5–7, Table 3). However, if the reaction time was prolonged to 10 h, moderate to good yields of the desired products could be obtained.

Table 2
One-pot synthesis of α-aminonitrile in water[a]



Entry	Aldehyde	Yield[b] (%)
1		91
2		95
3		90
4		93
5		93
6		92
7		81
8		93
9		97
10		83

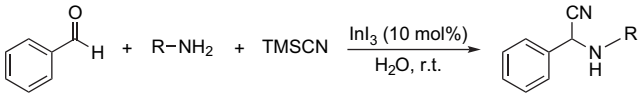
[a] The reactions were operated at room temperature for 0.5 h catalyzed by InI_3 in water.
[b] Isolated yield.

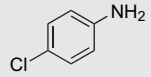
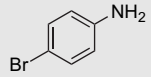
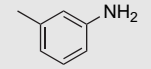
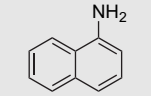
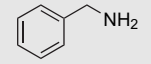
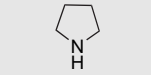
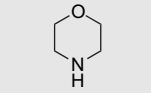
The three-component condensation is proposed to proceed via two-step reactions. Firstly, InI_3 serves as a Lewis acid to promote the formation of imine, which derived from the condensation of aldehyde and amine. Then the formed imine is further activated by InI_3 to produce a more electrophilic C=N intermediate, which facilitates the following attack of TMSCN to the carbon–nitrogen double bond, and thus forms the desired product α-aminonitrile after hydrolysis with water.

3. Conclusion

In summary, we have developed a mild, efficient and environmentally friendly method for the synthesis of α-aminonitriles via a three-component condensation of aldehydes, amines and TMSCN catalyzed by a catalytic amount of water-stable Lewis acid InI_3 in water. This method is quite general and it works well with a wide variety of aldehydes and amines at room temperature. The mild reaction conditions, short reaction time, good yields, the simplicity

Table 3
One-pot synthesis of α-aminonitrile via a three-component condensation of benzaldehyde, TMSCN and various amines[a]



Entry	Amine	Time (h)	Yield[b] (%)
1		0.5	91
2		1	90
3		1	82
4		0.5	86
5		10	81
6		10	73
7		10	78

[a] The reactions were operated at room temperature catalyzed by InI_3 in water.
[b] Isolated yield.

of the reaction procedure and environmentally friendly feature make this method attractive for scale-up purposes.

4. Experimental

4.1. General method

Analytical thin layer chromatography (TLC) was performed using Merck 60 F_{254} precoated silica gel plate (0.2 mm thickness). Subsequent to elution, plates were visualized using UV radiation (254 nm) on Spectroline Model ENF-24061/F 254 nm. Further visualization was possible by staining with acidic solution of ceric molybdate or ethanolic solution of ninhydrin. Flash-column chromatography was performed using Merck silica gel 60 with freshly distilled solvents. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance DPX 300 and Bruker AMX 400 spectrophotometers using TMS as an internal standard. Chemical shifts for ^{1}H NMR spectra are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-*d* (δ 7.2600, s). Multiplicities were given as: s (singlet); d (doublet); t (triplet); q (quartet); or m (multiplets). The number of protons (*n*) for a given resonance is indicated by *n*H. Coupling constants are reported as a *J* value in hertz. Carbon nuclear magnetic resonance spectra (^{13}C NMR) are reported as δ in units of parts per million (ppm) downfield from $SiMe_4$ (δ 0.0) and relative to the signal of chloroform-*d* (δ 77.03, t). HRMS spectra were obtained using Finnigan MAT95XP GC/HRMS (Thermo Electron Corporation). IR spectra were recorded on a Bio-Rad FTS 165 FTIR spectrometer.

4.2. Representative experimental procedure

To a 10 mL round-bottomed flask were added aldehyde (1.0 mmol), amine (1.0 mmol), TMSCN (1.2 mmol), H_2O (0.5 mL) and InI_3 (0.1 mmol) sequentially. The reaction was stirred vigorously at room temperature and the progress of the reaction was monitored by TLC. After stirring for a special time as shown in Tables 2 and 3, the reaction system was extracted by diethyl ether (15 mL×3), washed with brine. Following dry over anhydrous $MgSO_4$, removal of the solvent and passage through a column of silica gel gave the desired product α-aminonitriles.

4.2.1. 2-(N-Anilino)-2-(4-chlorophenyl)acetonitrile (Table 2, entry 1)

R_f=0.61 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3381, 2236 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.10 (d, *J*=8.43 Hz, 1H), 5.36 (d, *J*=8.43 Hz, 1H), 6.72 (d, *J*=7.65 Hz, 2H), 6.88 (t, *J*=7.43 Hz, 1H), 7.24 (t, *J*=7.83 Hz, 2H), 7.37 (d, *J*=8.43 Hz, 2H), 7.47 (d, *J*=8.22 Hz, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 144.4 (C), 135.4 (C), 132.4 (C), 129.5 (CH×2), 129.4 (CH×2), 128.5 (CH×2), 120.4 (CH), 117.9 (CN), 114.3 (CH×2), 49.5 (CH) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{14}H_{11}ClN_2$: 242.0611, found: 242.0602.

4.2.2. 2-(N-Anilino)-2-phenylacetonitrile (Table 2, entry 2)

R_f=0.23 (ethyl acetate/hexane=1:6); FTIR (NaCl, neat): ν 3369, 2235 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.03 (d, *J*=8.34 Hz, 1H), 5.42 (d, *J*=8.34 Hz, 1H), 6.77 (d, *J*=7.65 Hz, 2H), 6.90 (t, *J*=7.32 Hz, 1H), 7.29 (m, 2H), 7.46 (m, 3H), 7.59 (m, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 50.3 (CH), 114.2 (CH×2), 118.2 (CN), 120.3 (CH), 127.3 (CH×2), 129.3 (CH×2), 129.5 (CH), 129.6 (CH×2), 134.0 (CH), 144.7 (CH) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{14}H_{12}N_2$: 208.1000, found: 208.0996.

4.2.3. 2-(N-Anilino)-2-(4-methylphenyl)acetonitrile (Table 2, entry 3)

R_f=0.56 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3339, 2235 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (s, 3H), 4.15 (d, *J*=8.04 Hz, 1H), 5.40 (d, *J*=8.01 Hz, 1H), 6.81 (d, *J*=8.43 Hz, 2H), 6.95 (m, 1H), 7.28–7.35 (m, 4H), 7.51 (d, *J*=8.04 Hz, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 144.7 (C), 139.3 (C), 130.9 (C), 129.8 (CH×2), 129.4 (CH×2), 127.0 (CH×2), 119.9 (CH), 118.3 (CN), 114.0 (CH×2), 49.7 (CH), 21.0 (CH_3) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{15}H_{14}N_2$: 222.1157, found: 222.1158.

4.2.4. 2-(N-Anilino)-2-(4-methoxyphenyl)acetonitrile (Table 2, entry 4)

R_f=0.59 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3361, 2234 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.84 (s, 3H), 4.15 (d, *J*=8.43 Hz, 1H), 5.36 (d, *J*=8.04 Hz, 1H), 6.79 (d, *J*=8.43 Hz, 2H), 6.90–6.99 (m, 3H), 7.29 (t, *J*=8.03 Hz, 2H), 7.50 (d, *J*=8.01 Hz, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 160.2 (C), 144.7 (C), 129.4 (CH×2), 128.5 (CH×2), 125.8 (C), 119.9 (CH), 118.4 (CN), 114.4 (CH×2), 114.0 (CH×2), 55.3 (CH_3), 49.4 (CH) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{15}H_{14}N_2O$: 238.1106, found: 238.1100.

4.2.5. 2-(N-Anilino)-2-(2-methoxyphenyl)acetonitrile (Table 2, entry 5)

R_f=0.44 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3372, 2233 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.91 (s, 3H), 4.44 (d, *J*=8.82 Hz, 1H), 5.65 (d, *J*=8.43 Hz, 1H), 6.83–7.08 (m, 5H), 7.29–7.54 (m, 4H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 156.6 (C), 144.9 (C), 130.8 (CH), 129.3 (CH×2), 128.5 (CH), 122.2 (C), 121.0 (CH), 119.7 (CH), 118.6 (CN), 114.2 (CH×2), 111.3 (CH), 55.6 (CH), 45.5 (CH_3) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{15}H_{14}N_2O$: 238.1106, found: 238.1104.

4.2.6. 2-(N-Anilino)-2-(1-naphthyl)acetonitrile (Table 2, entry 6)

R_f=0.46 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3359, 2236 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.15 (d, *J*=8.04 Hz, 1H), 5.96 (d, *J*=8.01 Hz, 1H), 6.83 (d, *J*=8.85 Hz, 2H), 6.98 (m, 1H), 7.35 (t, *J*=7.62 Hz, 2H), 7.50–7.60 (m, 3H), 7.92–7.97 (m, 4H) ppm; ^{13}C NMR

(75.4 MHz, $CDCl_3$): δ 144.7 (C), 133.8 (C), 130.5 (CH), 130.0 (C), 129.5 (CH×2), 129.0 (CH), 128.9 (C), 127.2 (CH), 126.4 (CH), 126.1 (CH), 125.1 (CH), 122.7 (CH), 120.0 (CH), 118.2 (CN), 113.6 (CH×2), 48.1 (CH) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{18}H_{14}N_2$: 258.1157, found: 258.1157.

4.2.7. 2-(N-Anilino)-4-phenyl-butenenitrile (Table 2, entry 7)

R_f=0.55 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3428, 2225 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.91 (d, *J*=9.24 Hz, 1H), 5.04 (m, 1H), 6.25 (dd, *J*=16.05, 5.22 Hz, 1H), 6.76 (q, *J*=3.21 Hz, 2H), 6.89 (t, *J*=7.43 Hz, 1H), 7.03 (dd, *J*=15.63, 1.59 Hz, 1H), 7.23–7.39 (m, 7H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 144.5 (C), 135.1 (CH), 134.9 (C), 129.6 (CH×2), 128.9 (CH), 128.8 (CH×2), 126.9 (CH×2), 121.0 (CH), 120.4 (CH), 117.7 (CN), 114.4 (CH×2), 47.7 (CH) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{16}H_{14}N_2$: 234.1157, found: 234.1154.

4.2.8. 2-(N-Anilino)-2-(5-methyl-2-furyl)acetonitrile (Table 2, entry 8)

R_f=0.56 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3420, 2242 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H), 4.21 (d, *J*=8.82 Hz, 1H), 5.43 (d, *J*=8.85 Hz, 1H), 6.01 (q, *J*=1.07 Hz, 1H), 6.46 (d, *J*=2.82 Hz, 1H), 6.79 (d, *J*=8.43 Hz, 2H), 6.92 (m, 1H), 7.29 (m, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 154.0 (C), 144.2 (C), 144.0 (C), 129.5 (CH×2), 120.4 (CH), 116.7 (CN), 114.4 (CH×2), 110.4 (CH), 106.8 (CH), 44.3 (CH), 13.5 (CH_3) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{13}H_{12}N_2O$: 212.0950, found: 212.0948.

4.2.9. 2-(N-Anilino)-2-(2-thienyl)acetonitrile (Table 2, entry 9)

R_f=0.5 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3335, 2238 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.20 (d, *J*=8.85 Hz, 1H), 5.58 (d, *J*=9.24 Hz, 1H), 6.74 (d, *J*=7.62 Hz, 2H), 6.89 (t, *J*=7.43 Hz, 1H), 7.00 (q, *J*=2.81 Hz, 1H), 7.21–7.33 (m, 4H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 144.1 (C), 136.8 (C), 129.5 (CH×2), 127.13 (CH), 127.07 (CH), 127.01 (CH), 120.6 (CH), 117.5 (CN), 114.5 (CH×2), 46.1 (CH) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{12}H_{10}N_2S$: 214.0565, found: 214.0561.

4.2.10. 2-(N-Anilino)-2-(3-pyridyl)acetonitrile (Table 2, entry 10)

R_f=0.24 (ethyl acetate/hexane=1:2); FTIR (NaCl, neat): ν 3324, 2235 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.81 (d, *J*=8.82 Hz, 1H), 5.46 (d, *J*=8.82 Hz, 1H), 6.75 (d, *J*=7.62 Hz, 2H), 6.88 (m, 1H), 7.21–7.31 (m, 3H), 7.86 (m, 1H), 8.55 (d, *J*=3.21 Hz, 1H), 8.71 (s, 1H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 150.2 (CH), 148.2 (CH), 144.3 (C), 134.9 (CH), 130.0 (C), 129.4 (CH×2), 123.8 (CH), 120.3 (CH), 117.3 (CN), 114.2 (CH×2), 47.8 (CH) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{13}H_{11}N_3$: 209.0953, found: 209.0943.

4.2.11. 2-[N-(4-Chloroanilino)]-2-phenylacetonitrile (Table 3, entry 1)

R_f=0.5 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3335, 2235 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.25 (d, *J*=8.43 Hz, 1H), 5.38 (d, *J*=8.43 Hz, 1H), 6.69 (d, *J*=8.43 Hz, 2H), 7.21 (d, *J*=8.85 Hz, 2H), 7.44–7.58 (m, 5H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 143.2 (C), 133.4 (C), 129.5 (CH), 129.3 (CH×2), 129.2 (CH×2), 127.0 (CH×2), 124.8 (C), 117.9 (CN), 115.3 (CH×2), 50.0 (CH) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{14}H_{11}ClN_2$: 242.0611, found: 242.0603.

4.2.12. 2-[N-(4-Bromoanilino)]-2-phenylacetonitrile (Table 3, entry 2)

R_f=0.5 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3348, 2236 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.17 (d, *J*=8.04 Hz, 1H), 5.33 (d, *J*=8.43 Hz, 1H), 6.60 (d, *J*=8.82 Hz, 2H), 7.28–7.54 (m, 7H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 143.6 (C), 133.4 (C), 132.2 (CH×2), 129.5 (CH), 129.3 (CH×2), 127.1 (CH×2), 117.9 (C), 115.7 (CH×2), 112.1 (CN), 50.0 (CH) ppm; HRMS (EI, *m*/*z*): $[M-HCN]^+$, Calcd for $C_{13}H_{10}BrN$: 258.9985, found: 258.9991.

4.2.13. 2-[N-(2-Methylanilino)]-2-phenylacetonitrile (Table 3, entry 3)

R_f=0.53 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3360, 2236 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.21 (s, 3H), 3.90 (d, *J*=8.29 Hz, 1H), 5.29 (d, *J*=8.44 Hz, 1H), 6.45–6.48 (m, 2H), 6.61 (d, *J*=7.47 Hz, 1H), 7.05 (t, *J*=7.58 Hz, 1H), 7.32–7.34 (m, 3H), 7.46–7.47 (m, 2H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 144.6 (C), 139.4 (C), 133.9 (C), 129.4 (CH), 129.3 (CH), 129.2 (CH×2), 127.1 (CH×2), 121.0 (CH), 118.2 (CN), 114.8 (CH), 111.2 (CH), 50.1 (CH), 21.5 (CH_3) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{15}H_{14}N_2$: 222.1157, found: 222.1151.

4.2.14. 2-[N-(1-Naphthylamino)]-2-phenylacetonitrile (Table 3, entry 4)

R_f=0.53 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3365, 2236 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 4.62 (d, *J*=8.43 Hz, 1H), 5.47 (d, *J*=8.04 Hz, 1H), 6.83 (dd, *J*=6.83, 1.62 Hz, 1H), 7.32–7.80 (m, 11H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 139.8 (C), 134.2 (C), 133.9 (C), 129.5 (CH), 129.3 (CH×2), 128.7 (CH), 127.3 (CH×2), 126.11 (CH), 126.08 (CH), 125.4 (CH), 123.9 (C), 120.6 (CH), 119.8 (CH), 118.1 (CN), 107.3 (CH), 50.1 (CH) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{18}H_{14}N_2$: 258.1157, found: 258.1158.

4.2.15. 2-(N-Benzylamino)-2-phenylacetonitrile (Table 3, entry 5)

R_f=0.62 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 3332, 2228 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.83 (br s, 1H), 3.95 (q, *J*=14.85 Hz, 2H), 4.69 (s, 1H), 7.27–7.51 (m, 10H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 138.1 (C), 134.7 (C), 128.9 (CH), 128.8 (CH×2), 128.5 (CH×2), 128.3 (CH×2), 127.5 (CH), 127.2 (CH×2), 118.6 (CN), 53.3 (CH), 51.1 (CH_2) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{15}H_{14}N_2$: 222.1157, found: 222.1147.

4.2.16. 2-(N-Pyrrolidino)-2-phenylacetonitrile (Table 3, entry 6)

R_f=0.67 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 2226 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.82 (m, 4H), 2.64 (m, 4H), 5.04 (s, 1H), 7.34–7.53 (m, 5H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 134.2 (C), 128.7 (CH×3), 127.6 (CH×2), 116.0 (CN), 59.2 (CH), 50.1 (CH_2×2), 23.3 (CH_2×2) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{12}H_{14}N_2$: 186.1157, found: 186.1149.

4.2.17. 2-(N-Morpholino)-2-phenylacetonitrile (Table 3, entry 7)

R_f=0.43 (ethyl acetate/hexane=1:4); FTIR (NaCl, neat): ν 2228 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 2.57 (t, *J*=4.62 Hz, 4H), 3.72 (t, *J*=4.62 Hz, 4H), 4.81 (s, 1H), 7.37–7.54 (m, 5H) ppm; ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 132.4 (C), 129.0 (CH), 128.7 (CH×2), 127.9 (CH×2), 115.1 (CN), 66.5 (CH), 62.3 (CH_2×2), 49.8 (CH_2×2) ppm; HRMS (EI, *m*/*z*): $[M]^+$, Calcd for $C_{12}H_{14}N_2O$: 202.1106, found: 202.1099.

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