Supplementary Material (ESI) for Green Chemistry

Supporting Information

Efficient Green Synthesis of α-Aminonitriles, Precursors of α-Amino Acids

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Experimental

^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Varian NMR spectrometers at 400 MHz. ^{1}H NMR chemical shifts were determined relative to internal tetramethylsilane at δ 0.0 ppm or to the signal of a residual proton of the solvent in $CDCl_3$ at δ 7.24 ppm, ^{13}C NMR chemical shifts were determined relative to internal tetramethylsilane at δ 0.0 ppm or to the ^{13}C signal of $CDCl_3$ at δ 77.0 ppm. ^{19}F NMR chemical shifts were determined relative to internal $CFCl_3$ at δ 0.0 ppm.

Materials and Methods

Nafion®-H (perfluoroalkanesulfonic acid polymer) and Nafion® SAC-13, Silica gel, fumed silica, were used as environmentally benign catalysts. The aldehydes, ketones,

amines, and Nafion® SAC-13 were purchased from Sigma-Aldrich (Milwaukee, WI). Nafion®-H was prepared from Nafion®-K (potassium salt) following a literature procedure.[1] The fluorinated ketones, TMSCN, silica gel and fumed silica were purchased from other commercial sources. The solvent used in all the reactions was dichloromethane (CH_2Cl_2). Control experiment was conducted using $Ga(OTf)_3$ as the catalyst for comparison. Gallium triflate, prepared earlier following a literature procedure.[2]

Preparation of Nafion®-H from Nafion®-K

Nafion®-K (50 g) was stirred in boiling deionized water (150 mL) for 2 hours and filtered. The resin was then stirred with 20% nitric acid (200 mL) for 5h at room temperature and filtered. This step was repeated four times for maximum exchange of K^+ with H^+. The polymer was washed many times with deionized water till the filtrate became neutral, when tested with pH paper. It was then dried under vacuum at 105 ^oC for 24 h. The dry Nafion®-H polymer was finely ground in a grinder (by adding liquid nitrogen to make it brittle) and sieved in a testing sieve (VWR, USA standard testing sieve, No. 60 with 250 μm opening). This was further dried under vacuum and used for the reactions.

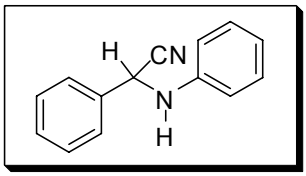
General procedure for the Strecker reaction of aldehydes and ketones

Aldehyde or ketone (2 mmol)/ fluorinated ketone (3 mmol), amine (2 mmol), TMSCN (3 mmol) and catalyst (200 mg) were taken in dichloromethane (5 mL) in a sealed pressure tube and the reaction mixture was stirred at the required temperature for several hours as indicated (refer Schemes and Tables). Completion of the reaction was monitored by ^1H or

^{19}F NMR. After completion, the mixture was then filtered and the residue was washed with CH_2Cl_2 (3 x 15 mL) and ethyl acetate (3 x 15 mL). The filtrate was collected and the solvent was removed under reduced pressure to obtain the crude product. Further purification can be carried out by trituration of the residue with excess hexane followed by evaporation of hexane. Products were characterized by spectral analysis (^{1}H NMR, ^{13}C NMR, ^{19}F NMR and GC/MS) and comparing them with those of the authentic samples.[3]

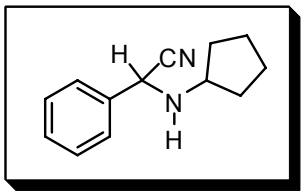
Spectral Data

2-phenyl-2-(phenylamino)acetonitrile (Table 1, entry 1)



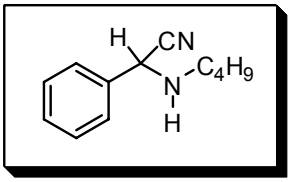
^{1}H NMR δ 4.08 (d, *J* = 7.51 Hz, 1H), 5.37 (d, *J* = 8.24 Hz, 1H), 6.73 (d, *J* = 7.69 Hz, 2H), 6.86 (t, *J* = 7.41 Hz, 1H), 7.23 (dd, *J* = 8.42 Hz, *J* = 0.91 Hz, 2H), 7.39-7.42 (m, 3H), 7.53-7.56 (m, 2H) ^{13}C NMR δ 50.2, 114.2, 118.3, 120.2, 127.3, 129.4, 129.5, 129.6, 134.0, 144.7.

2-(cyclopentylamino)-2-phenylacetonitrile (Table 1, entry 2)



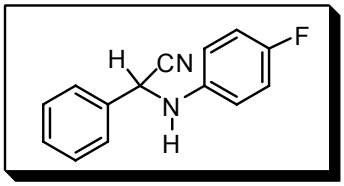
^{1}H NMR δ 1.36-1.45 (m, 2H), 1.56-1.62 (m, 2H), 1.68-1.75 (m, 3H), 1.84-1.92 (m, 2H), 3.42-3.46 (m, 1H), 4.70 (s, 1H), 7.34-7.42 (m, 3H), 7.49-7.52 (m, 2H); ^{13}C NMR δ 23.81, 23.87, 32.1, 33.5, 53.3, 57.8, 119.2, 127.1, 128.77, 128.82, 135.3.

2-(butylamino)-2-phenylacetonitrile (Table 1, entry 3)



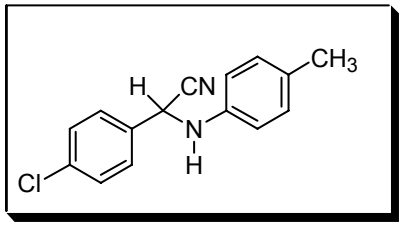
^{1}H NMR δ 0.91 (t, *J* = 7.14 Hz, 3H), 1.35-1.45 (m, 2H), 1.46-1.55 (m, 2H), 1.66 (brs, 1H), 2.68-2.87 (m, 2H), 4.77 (s, 1H), 7.32-7.40 (m, 3H), 7.50-7.53 (m, 2H); ^{13}C NMR δ 13.7, 20.1, 31.5, 46.9, 54.4, 118.9, 127.1, 128.7, 134.9.

2-(4-fluorophenylamino)-2-phenylacetonitrile (Table 1, entry 4)



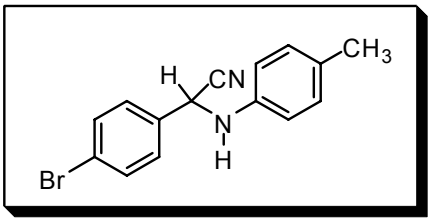
^{1}H NMR δ 4.02 (brs, 1H), 5.32 (s, 1H), 6.67- 6.70 (m, 2H), 6.93 (t, *J* = 8.6 Hz, 2H), 7.39-7.43 (m, 3H), 7.53-7.56 (m, 2H); ^{13}C NMR δ 50.7, 115.5 (d, $^{3}J_{C\text{-}F}$ = 7.64 Hz), 116.0 (d, $^{2}J_{C\text{-}F}$ = 22.89 Hz), 118.1, 127.1, 129.2, 129.4, 133.6, 140.8 (d, $^{4}J_{C\text{-}F}$ = 2.29 Hz),157.2 (d, $^{1}J_{C\text{-}F}$ = 238.8 Hz); ^{19}F NMR δ -124.58 (m).

2-(4-Chlorophenyl)-2-*p*-tolylaminoacetonitrile (Table 1, entry 5)



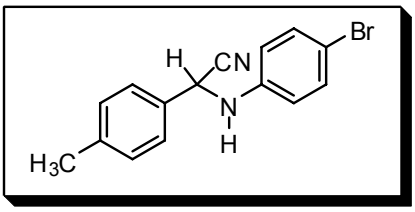
^{1}H NMR δ 2.27 (s, 3H), 3.87 (brs, 1H), 5.36 (s, 1H), 6.67 (d, *J* = 8.61 Hz, 2H), 7.07 (d, *J* = 8.61 Hz, 2H), 7.42 (d, *J* = 8.61 Hz, 2H), 7.53 (d, *J* = 8.61 Hz, 2H), ^{13}C NMR δ 20.5, 50.0, 114.6, 118.0, 128.5, 129.4, 129.9, 130.0, 132.5, 135.4, 142.0.

2-(4-bromophenyl)-2-(p-tolylamino)acetonitrile (Table 1, entry 6)



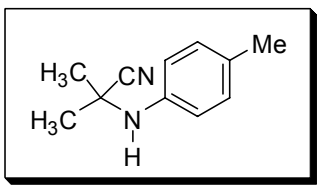
^{1}H NMR δ 2.27 (s, 3H), 3.91 (d, *J* = 8.0 Hz, 1H), 5.36 (d, *J* = 7.9 Hz, 1H), 6.67 (d, *J* = 8.61 Hz, 2H), 7.07 (d, *J* = 8.61 Hz, 2H), 7.47 (d, *J* = 8.61 Hz, 2H), 7.57 (d, *J* = 8.38 Hz, 2H), ^{13}C NMR δ 20.5, 50.1, 114.6, 117.9, 123.6, 128.8, 130.0, 132.4, 133.0, 142.0.

2-(4-bromophenylamino)-2-p-tolylacetonitrile (Table 1, entry 7)



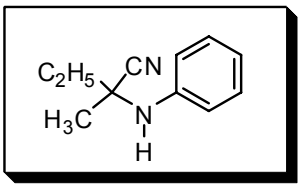
^{1}H NMR δ 2.38 (s, 3H), 4.06 (d, *J* = 6.0 Hz, 1H), 5.32 (d, *J* = 5.9 Hz, 1H), 6.67 (d, *J* = 8.98 Hz, 2H), 7.07 (d, *J* = 7.87 Hz, 2H), 7.47 (d, *J* = 8.79 Hz, 2H), 7.57 (d, *J* = 8.06 Hz, 2H), ^{13}C NMR δ 21.1, 49.8, 112.1, 115.7, 118.0, 127.0, 130.0, 130.4, 132.3, 139.7, 143.6.

2-Methyl-2-(*p*-tolylamino)propionitrile (Table 1, entry 8)



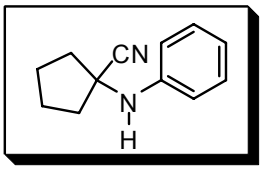
^{1}H NMR δ 1.65 (s, 6H), 2.28 (s, 3H), 3.59 (s, 1H), 6.86 (d, *J* = 8.42 Hz, 2H), 7.07 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR δ 20.5, 28.2, 49.6, 119.0, 122.2, 129.7, 131.0, 141.1.

2-methyl-2-(phenylamino)butanenitrile (Table 1, entry 9)



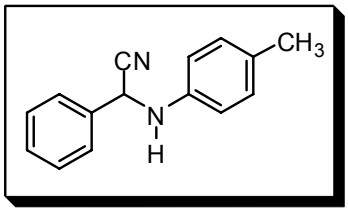
^{1}H NMR δ 1.1 (t, *J* = 7.33 Hz, 3H), 1.59 (s, 3H), 1.82-2.0 (m, 2H), 3.7 (brs, 1H), 6.86-6.91 (m, 3H), 7.20-7.25 (m, 2H); ^{13}C NMR δ 8.3, 24.9, 33.3, 53.3, 117.1, 120.3, 121.4, 129.1, 143.7.

1-(phenylamino)cyclopentanecarbonitrile (Table 1, entry 10)



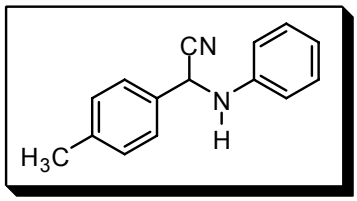
^{1}H NMR δ 1.85-1.95 (m, 4H), 2.10-2.20 (m, 2H), 2.30-2.40 (m, 2H), 3.94 (s, 1H), 6.80-6.91 (m, 3H), 7.20-7.30 (m, 2H); ^{13}C NMR δ 23.7, 40.0, 57.3, 115.4, 119.6, 122.2, 129.1, 144.0.

2-phenyl-2-(p-tolylamino)acetonitrile (Table 2, entry 2)



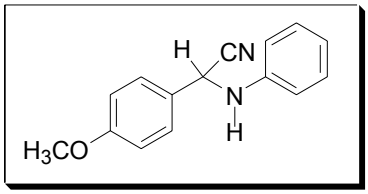
^{1}H NMR δ 2.25 (s, 3H), 3.92 (d, *J* = 8.24 Hz, 1H), 5.33 (d, *J* = 8.24 Hz, 1H), 6.65 (d, *J* = 8.61 Hz, 2H), 7.04 (d, *J* = 8.61 Hz, 2H), 7.38-7.42 (m, 3H), 7.53-7.55 (m, 2H), ^{13}C NMR δ 20.4, 50.4, 114.3, 118.0, 127.1, 129.1, 129.3, 129.5, 129.9, 133.9, 135.4, 142.3.

2-(phenylamino)-2-p-tolylacetonitrile (Table 2, entry 3)



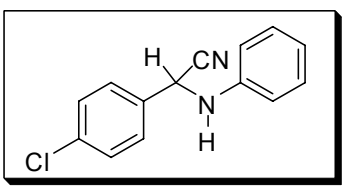
^{1}H NMR: δ 2.34 (s, 3H), 4.1 (brs, 1H), 5.30 (s, 1H), 6.70 (d, *J* = 7.69 Hz, 2H), 6.85 (t, *J* = 7.41 Hz, 1H), 7.19-7.24 (m, 4H), 7.41 (d, *J* = 8.24 Hz, 2H); ^{13}C NMR: δ 21.0, 49.7, 114.0, 118.3, 119.9, 127.0, 129.4, 129.8, 130.8, 139.3, 144.6.

2-(4-Methoxyphenyl)-2-(phenylamino)acetonitrile (Table 2, entry 4)



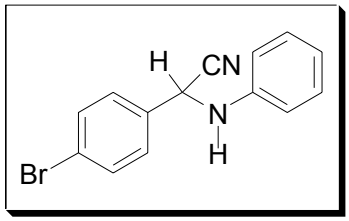
^{1}H NMR: δ 3.84 (s, 3H), 4.0 (brs, 1H), 5.36 (s, 1H), 6.77 (d, *J* = 8.61 Hz, 2H), 6.89 (t, *J* = 7.42 Hz, 1H), 6.96 (d, *J* = 8.79 Hz, 2H), 7.25-7.30 (m, 2H), 7.51 (d, *J* = 8.69 Hz, 2H); ^{13}C NMR: δ 49.6, 55.4, 114.1, 114.6, 118.4, 120.2, 125.9, 128.6, 129.5, 144.7, 160.4.

2-(4-chlorophenyl)-2-(phenylamino)acetonitrile (Table 2, entry 5)



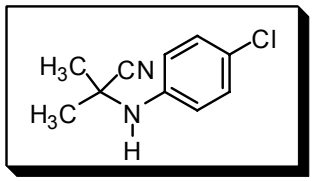
^{1}H NMR δ 4.08 (s, 1H), 5.39 (s, 1H), 6.73 (d, *J* = 7.69 Hz, 2H), 6.90 (t, *J* = 7.42 Hz, 1H), 7.22-7.28 (m, 2H), 7.39 (d, *J* = 8.61 Hz, 2H), 7.50 (d, *J* = 8.42 Hz, 2H); ^{13}C NMR δ 49.7, 114.4, 118.0, 120.6, 128.4, 129.6, 129.7, 132.5, 135.6, 144.5.

2-(4-Bromophenyl)-2-(phenylamino)acetonitrile (Table 2, entry 6)



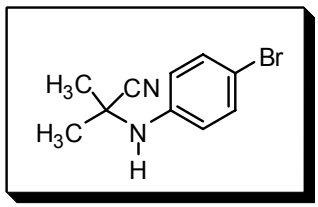
^{1}H NMR: δ 4.03 (brs, 1H), 5.38 (s, 1H), 6.73 (d, *J* = 7.69 Hz, 2H), 6.90 (t, *J* = 7.41 Hz, 1H), 7.23-7.28 (m, 2H), 7. 46 (d, *J* = 8.0 Hz, 2H), 7. 57 (d, *J* = 8.61 Hz, 2H); ^{13}C NMR: δ 49.7, 114.3, 117.7, 120.6, 123.7, 128.83, 129.6, 132.5, 132.9, 144.3.

2-(4-chlorophenylamino)-2-methylpropanenitrile (Table 2, entry 9)



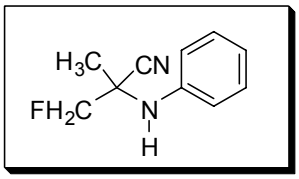
^{1}H NMR δ 1.67 (s, 6H), 3.71 (s, 1H), 6.83 (d, *J* = 8.79 Hz, 2H), 7.20 (d, *J* = 8.97 Hz, 2H); ^{13}C NMR δ 28.1, 49.0, 118.6, 121.7, 125.8, 129.2, 142.2.

2-(4-bromophenylamino)-2-methylpropanenitrile (Table 2, entry 10)



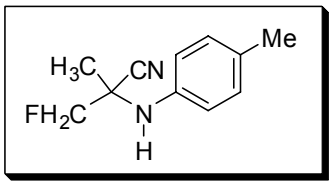
^{1}H NMR δ 1.69 (s, 6H), 3.7 (brs, 1H), 6.79 (d, J = 8.97 Hz, 2H), 7.35 (d, J = 8.98 Hz, 2H); ^{13}C NMR δ 28.1, 48.9, 113.8, 118.9, 121.6, 132.1, 142.7.

3-Fluoro-2-methyl-2-(phenylamino)propionitrile (Table 3, entry 1)



^{1}H NMR δ 1.64 (d, J = 2.01 Hz, 3H), 3.94 (s, 1H), 4.45 (ddd, J = 46.7 Hz, J = 17.58 Hz, J = 9.16 Hz, 2H), 6.92-6.99 (m, 3H), 7.23-7.29 (m, 2H); ^{13}C NMR δ 22.1 (d, $^{3}J_{C\text{-}F}$ = 3.81 Hz), 53.4 (d, $^{2}J_{C\text{-}F}$ = 19.84 Hz), 85.0 (d, $^{1}J_{C\text{-}F}$ = 185.4 Hz), 118.6, 119.0 (d, $^{3}J_{C\text{-}F}$ = 3.81 Hz), 121.9, 129.4, 142.7; ^{19}F NMR δ -223.1 (dd, J = 47.3 Hz, J = 45.78 Hz, 1F).

3-Fluoro-2-methyl-2-(*p*-tolylamino)propionitrile (Table 3, entry 2)



^{1}H NMR δ 1.57 (d, J = 2.0 Hz, 3H), 2.26 (s, 3H), 3.82 (s, 1H), 4.45 (ddd, J = 46.51, Hz, J = 17.58 Hz, J = 9.16 Hz, 2H), ^{13}C NMR δ 20.3, 21.7 (d, $^{3}J_{C\text{-}F}$ = 3.05 Hz), 53.8 (d, $^{2}J_{C\text{-}F}$ = 20.6 Hz), 85.0 (d, $^{1}J_{C\text{-}F}$ = 183.86 Hz), 119.1 (d, $^{3}J_{C\text{-}F}$ = 3.05 Hz),119.7, 129.6, 131.8, 140.1; ^{19}F NMR δ -223.4 (t, J = 46.51 Hz).

References

[1] G. A. Olah, P. S. Iyer and G. K. S. Prakash, *Synthesis,* 1986, 513.

[2] (a) G. A. Olah, O. Farooq, S. M. F. Farnia and J. A. Olah, *J. Am. Chem. Soc.,* 1988, **110**, 2560; (b) K. Boumizane, M. H. Herzog-Cance, D. J. Jones, J. L. Pascal, J. Potier and J. Roziere, *Polyhedron,* 1991, **10**, 2757.

[3] (a) G. K. S. Prakash, T. Mathew, C. Panja, S. Alconcel, H. Vaghoo, C. Do and G. A. Olah, *Proc. Natl. Acad. Sci., U. S. A.* 2007*,* **104***,* 3703; (b) G. K. S. Prakash, C. Panja, C. Do, T. Mathew and G. A. Olah, *Synlett,* 2007*,* 2395; (c) N. H. Khan, S. Agrawal, R. I. Kureshi, S. H. R. Abdi, S. Singh, E. Suresh and R. V. Jasra, *Tetrahedron Lett.,* 2008, **49**, 640; (d) S. Kobayashi, S. Nagayama and T. Busujima, *Tetrahedron Lett.,* 1996, **37**, 9221; (e) A. Heydari, P. Fatemi and A-A. Alizadeh, *Tetrahedron Lett.,* 1998, **39**, 3049; (f) J. S. Yadav, B. V. S. Reddy, B. Eshwaraiah, M. Sreenivas and P. Vishnumurthy, *New J. Chem.,* 2003, **27**, 462; (g) J. S. Yadav, B. V. S. Reddy, B. Eeshwaraiah, M. Srinivas, *Tetrahedron,* 2004, **60**, 1767; (h) S. K. De, R. A. Gibbs, *Tetrahedron Lett.,* 2004, **45**, 7407;(i) J. Mulzer, A. Meier, J. Buschmann and P. Luger, *Synthesis,* 1996, 123; (j) S. Kobayashi, T. Busujima and S. Nagayama, *Chem. Commun.,* 1998, 981; (k) L. Royer, S. K. De and R. A. Gibbs, *Tetrahedron Lett.,* 2005, **46**, 4595; (l) S. K. De, *J. Mol. Catal. A: Chem.,* 2005, **232**, 123; (m) G. Jenner, R. B. Salem, J. C. Kim and K. Matsumoto, *Tetrahedron Lett.,* 2003, **44**, 447; (n) K. Matsumoto, J. C. Kim, H. Iida, H. Hamana, K. Kumamoto, H. Kotsuki, and G. Jenner, *Helv. Chim. Acta.,* 2005, **88**, 1734.