Supporting Information

Synthesis of 6-Amino-2,4-dihydropyrano [2, 3-*c*] pyrazol-5-carbonitriles catalyzed by silica supported tetramethylguanidine under solvent free conditions

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Experimental

Materials and techniques

Chemicals were purchased from Aldrich, Merck and Alfa Aesar chemical companies. The NMR spectra were recorded in DMSO- d_6 on a Jeol JNM ECP 400 NMR instrument using TMS as an internal standard. The HRMS was recorded on a Jeol JMS-700 mass spectrometer. Melting points were taken in open capillaries on an Electrothermal-9100 instrument (Japan).

Preparation of silica supported tetramethylguanidine (SiO₂TMG) catalyst

A Silica supported tetramethylguanidine was prepared by adopting the literature precedent Daniel Brunel et al.^[31] 1,1,3,3-tetramethylguanidine (TMG, 0.2 mol) and mixed xylenes were mixed together and heated to 120 °C. Chloropropyl trimethoxysilane (0.081 mol) was added drop wise over 2 h, and the solution allowed to react for two more hours. Further it treated with activated silica in presence of triethyl amine and the solution allowed reacting for one hours. On cooling, a solid precipitates which is filtered, and dried at 85–90 °C, was the desired product.

General procedure for the synthesis of 6-Amino-2, 4-dihydropyrano [2, 3-c] pyrazol-5-carbonitriles

To a pre-stirred mixture of ethyl acetoacetate (1 mmol) hydrazine hydrate (1 mmol) was added aldehydes (1 mmol) and malononitrile (1 mmol) followed by SiO₂TMG (10 mol %). The reaction mixture was then heated at 100 °C. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature. The residue was treated with boiling ethanol and filtered through a sintered funnel and washed thoroughly with the same solvent. The combined filtrate was evaporated in vacuo to afford the crude product which was recrystallized from ethanol to afford pure compound **5**.

Characterization data of various 6-Amino-2, 4-dihydropyrano [2, 3-c] pyrazol-5-carbonitriles

1. 6-Amino-3-methyl-4-phenyl-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5a)

Yield 96%; White powder; mp 245-246 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.1 (s, 1H), 7.31 (t, *J* = 12 Hz, 2H), 7.22 (t, *J* = 8 Hz, 1H), 7.16 (d, *J* = 8 Hz, 2H), 6.88 (s, 2H), 4.59 (s, 1H), 1.77 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.9, 154.7, 144.4, 135.6, 128.4, 126.7, 120.8, 97.6, 57.2, 36.2, 9.7. HRMS (ESI, *m/z*): calcd for C₁₄H₁₂N₄O (*m/z*) 252.1011; found: 252.1011.

2. 6-Amino-3-methyl-4-(4-chlorophenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5b)

Yield 98%; Yellow powder; mp 233-234 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.19 (s, 1H), 7.49 (d, *J* = 8 Hz, 2H), 7.11 (d, *J* = 8 Hz, 2H), 6.95 (s, 2H), 4.64 (s, 1H), 1.76 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.4, 154.5, 143.6, 135.9, 132.0, 129.5, 118.7, 97.3, 56.8, 37.0, 9.4. HRMS (ESI, *m/z*): calcd for C₁₄H₁₁ClN₄O (*m/z*) 286.0621; found: 286.0623.

3. 6-Amino-3-methyl-4-(2-chlorophenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5c)

Yield 95%; White powder; mp 147-148 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.2 (s, 1H), 7.75-7.82 (m, 3H), 7.12-7.32 (m, 1H), 6.52 (s, 2H), 4.86 (s, 1H), 1.91 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 161.3, 154.8, 153.8, 135.6, 132.4, 131.8, 128.7, 127.9, 119.5, 96.3, 56.3, 31.7, 9.5. HRMS (ESI, *m/z*): calcd for C₁₄H₁₁ClN₄O (*m/z*) 286.0621; found: 286.0621.

4. 6-Amino-3-methyl-4-(4-fluorophenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5d)

Yield 96%; Yellow powder; mp 244-245 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.08 (s, 1H), 7.12-7.20 (m, 4H), 6.72 (s, 2H), 4.88 (s, 1H), 1.78 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 163.2, 160.5, 154.2, 141.6, 135.2, 129.6, 121.3, 116.4, 115.9, 98.6, 56.2, 34.6, 10.2. HRMS (ESI, *m/z*): calcd for C₁₄H₁₁FN₄O (*m/z*) 270.0917; found: 270.0920.

5. 6-Amino-3-methyl-4-(2-fluorophenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5e)

Yield 95%; Yellow powder; mp 260-262 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.13 (s, 1H), 7.59 (d, *J* = 8 Hz, 1H), 7.34 (d, *J* = 8 Hz, 1H), 7.16 (d, *J* = 8 Hz, 2H), 6.95 (s, 2H), 4.86 (s, 1H), 1.80 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 161.3, 155.1, 154.9, 135.4, 129.8, 127.8, 124.7, 116.4, 115.4, 96.6, 55.5, 30.1, 9.4. HRMS (ESI, *m/z*): calcd for C₁₄H₁₁FN₄O (*m/z*) 270.0917; found: 270.0920.

6. 6-Amino-3-methyl-4-(4-bromophenyl)-2,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**5f**)

Yield 95%; White powder; mp 179-180 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.14 (s, 1H), 7.51 (d, *J* = 8 Hz, 2H), 7.13 (d, *J* = 8 Hz, 2H), 6.94 (s, 2H), 4.62 (s, 1H), 1.79 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.9, 154.7, 143.9, 135.7, 131.3, 129.7, 119.7, 97.1, 56.6, 37.0, 9.7. HRMS (ESI, *m/z*): calcd for C₁₄H₁₁BrN₄O (*m/z*) 331.0116; found: 331.0118.

7. 6-Amino-3-methyl-4-(4-methoxyphenyl)-2,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**5g**)

Yield 92%; Pale yellow powder; mp 211-212 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.09 (s, 1H), 6.98-7.09 (m, 4H), 6.85 (s, 2H), 4.54 (s, 1H), 3.72 (s, 3H), 1.78 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 161.6, 157.9, 154.7, 136.4, 135.5, 128.5, 120.8, 113.7, 97.8, 54.9, 35.4, 9.7. HRMS (ESI, *m/z*): calcd for C₁₅H₁₄N₄O₂ (*m/z*) 282.1117; found: 282.1119.

8. 6-Amino-3-methyl-4-(2-bromophenyl)-2,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**5h**)

Yield 91%; Brown powder; mp 247-248 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.14 (s, 1H), 7.57 (d, *J* = 8 Hz, 2H), 7.34 (t, *J* = 8 Hz, 1H), 7.17 (t, *J* = 8 Hz, 1H), 6.97 (s, 2H), 5.06 (s, 1H), 1.76 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 161.3, 154.9, 135.4, 128.9, 127.8, 124.7, 120.6, 116.4, 96.6, 55.5, 30.1, 9.4. HRMS (ESI, *m/z*): calcd for C₁₄H₁₁BrN₄O (*m/z*) 331.0116; found: 331.0116.

9. 6-Amino-3-methyl-4-(4-isopropylphenyl)-2,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (**5i**)

Yield 89%; White powder; mp 182-183 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.09 (s, 1H), 7.16 (d, *J* = 8 Hz, 2H), 7.09 (d, *J* = 8 Hz, 2H), 6.72 (s, 2H), 4.53 (s, 1H), 2.70-2.90 (m, 1H), 1.81 (s, 3H), 1.20 (d, *J* = 12 Hz, 6H). ¹³C NMR (100 MHz, DMSO-d₆): 160.2, 153.4, 145.3, 142.0, 129.4, 124.2, 112.3, 89.5, 35.4, 24.5, 22.4, 10.8. HRMS (ESI, *m/z*): calcd for C₁₇H₁₈N₄O (*m/z*) 294.1481; found: 294.1481.

*10. 6-Amino-3-methyl-4-(4-nitrophenyl)-2,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5j)*

Yield 98%; White powder; mp 250-251 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.21 (s, 1H), 7.46 (d, *J* = 8 Hz, 2H), 7.37 (d, *J* = 8 Hz, 2H), 7.06 (s, 2H), 4.82 (s, 1H), 1.79 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.5, 155.2, 150.9, 142.2, 136.8, 129.4, 128.1, 125.4, 112.8, 97.5, 57.3, 29.4, 10.4. HRMS (ESI, *m/z*): calcd for C₁₄H₁₁N₅O₃ (*m/z*) 297.0862; found: 297.0864.

*11. 6-Amino-3-methyl-4-(4-ethoxyphenyl)-2,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5k)*

Yield 90%; Yellow powder; mp 189-190 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.08 (s, 1H), 7.05 (d, *J* = 8 Hz, 2H), 6.85 (s, 2H), 6.83 (d, *J* = 8 Hz, 2H), 4.52 (s, 1H), 3.95-4.00 (m, 2H), 1.77 (s, 3H), 1.30 (t, *J* = 8 Hz, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.7, 157.2, 136.3, 128.5, 114.2, 97.9, 62.9, 57.6, 35.2, 14.7, 9.7. HRMS (ESI, *m/z*): calcd for C₁₆H₁₆N₄O₂ (*m/z*) 296.1273; found: 296.1275.

*12. 6-Amino-3-methyl-4-(2-nitrophenyl)-2,4-dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5l)*

Yield 93%; White powder; mp 221-222 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.22 (s, 1H), 7.85 (d, *J* = 4 Hz, 1H), 7.65 (d, *J* = 4 Hz, 1H), 7.48 (t, *J* = 8 Hz, 1H), 7.32 (d, *J* = 8 Hz, 1H), 7.04 (s, 2H), 5.09 (s, 1H), 1.76 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 161.1, 149.1, 135.7, 133.3, 131.2, 128.3, 123.8, 96.3, 56.0, 31.4, 9.4. HRMS (ESI, *m/z*): calcd for C₁₄H₁₁N₅O₃ (*m/z*) 297.0862; found: 297.0862.

13. *6-Amino-3-methyl-4-(4-dimethylaminophenyl)-2,4 dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5m)*

Yield 90%; Pale yellow powder; mp 168-169 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.03 (s, 1H), 6.96 (d, *J* = 8 Hz, 2H), 6.76 (s, 2H), 6.65 (d, *J* = 8 Hz, 2H), 4.44 (s, 1H), 2.85 (s, 6H), 1.78 (s, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 160.5, 154.7, 149.2, 135.4, 132.0, 127.9, 120.9, 112.3, 98.1, 57.9, 35.4, 9.7. HRMS (ESI, *m/z*): calcd for C₁₆H₁₇N₅O (*m/z*) 295.1433; found: 295.1433.

14. *6-Amino-3-methyl-4-(2-methoxyphenyl)-2,4 dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5n)*

Yield 88%; White powder; mp 250-252 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.03 (s, 1H), 7.19 (t, *J* = 8 Hz, 1H), 7.05-6.98 (m, 2H), 6.89 (t, *J* = 8 Hz, 1H), 6.82 (s, 2H), 4.98 (s, 1H), 3.77 (s, 3H), 1.79 (s, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 162.9, 158.0, 134.5, 130.1, 128.0, 122.3, 113.4, 112.7, 99.3, 57.2, 57.0, 30.6, 11.0. HRMS (ESI, *m/z*): calcd for C₁₅H₁₄N₄O₂ (*m/z*) 282.1117; found: 282.1119.

15. *6-Amino-3-methyl-4-(perfluorophenyl)-2,4 dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5o)*

Yield 98%; Green powder; mp 249-250 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.23 (s, 1H), 7.18 (s, 2H), 5.11 (s, 1H), 1.91 (s, 3H). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 161.9, 154.8, 135.7, 120.1, 94.1, 52.5, 26.0, 9.2. HRMS (ESI, *m/z*): calcd for C₁₄H₇F₅N₄O (*m/z*) 342.0540; found: 342.0540.

16. *6-Amino-3-methyl-4-(3,4,5 methoxyphenyl)-2,4 dihydropyrano[2,3-*c*]pyrazole-5-carbonitrile (5p)*

Yield 90%; White powder; mp 210-211 °C. ¹H NMR (400 MHz, DMSO-*d*₆): δ 12.10 (s, 1H), 6.88 (s, 2H), 6.47 (s, 2H), 4.58 (s, 1H), 3.71 (s, 6H), 3.64 (s, 3H), 1.87 (s, 3H). ¹³C NMR (100

MHz, DMSO-d₆): δ 161.0, 154.7, 152.8, 140.1, 136.1, 135.7, 120.9, 104.6, 97.3, 59.9, 56.9, 55.8, 35.2, 9.9. HRMS (ESI, m/z): calcd for C₁₇H₁₈N₄O₄ (m/z) 342.1328; found: 342.1328.

17. 6-Amino-3-methyl-4-propyl-2,4 dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5q)

Yield 79%; Brown powder; mp 143-144 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.01 (s, 1H), 6.73 (s, 2H), 3.23-3.28 (m, 1H), 1.94 (s, 3H), 1.61-1.71 (m, 2H), 1.18-1.22 (m, 2H), 0.75-0.83 (m, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 169.2, 159.4, 139.7, 112.5, 97.2, 40.8, 36.5, 32.1, 19.3, 13.6, 9.8. HRMS (ESI, m/z): calcd for C₁₁H₁₄N₄O (m/z) 218.1168; found: 218.1168.

18. 6-Amino-3-methyl-4-(3-hydroxyphenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5r)

Yield 92%; White powder; mp 259-260 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.09 (s, 1H), 9.32 (s, 1H), 7.09 (t, *J* = 12 Hz, 1H), 6.86 (s, 2H), 6.61 (t, *J* = 12 Hz, 1H), 6.54 (s, 1H), 4.48 (s, 1H), 1.82 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.8, 157.4, 154.8, 146.0, 135.6, 129.3, 120.9, 118.2, 114.1, 113.9, 97.7, 57.3, 36.2, 9.8. HRMS (ESI, m/z): calcd for C₁₄H₁₂N₄O₂ (m/z) 268.0960; found: 268.0960.

19. 6-Amino-3-methyl-4-(4-hydroxyphenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5s)

Yield 93%; White powder; mp 225-226 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.05 (s, 1H), 9.29 (s, 1H), 6.95 (d, *J* = 8 Hz, 2H), 6.80 (s, 2H), 6.68 (d, *J* = 8 Hz, 2H), 4.47 (s, 1H), 1.78 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.6, 156.0, 154.7, 135.5, 134.7, 128.4, 120.9, 115.1, 98.0, 57.7, 35.5, 9.7. HRMS (ESI, m/z): calcd for C₁₄H₁₂N₄O₂ (m/z) 268.0960; found: 268.0960.

20. 6-Amino-3-methyl-4-(1-hydroxynaphthalen-1-yl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5t)

Yield 85%; Yellow powder; mp 248-250 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.2 (s, 1H), 7.92-7.92 (m, 3H), 7.41-7.48 (m, 2H), 7.21 (d, *J* = 8 Hz, 1H), 6.77 (s, 2H), 5.45 (s, 1H), 5.08 (s, 1H), 1.89 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.6, 155.3, 145.6, 142.5, 141.7, 136.4,

132.4, 130.8, 129.6, 127.2, 120.3, 114.2, 97.6, 59.3, 36.2, 10.0. HRMS (ESI, m/z): calcd for C₁₈H₁₄N₄O₂ (m/z) 318.1117; found: 318.1117.

21. 6-Amino-3-methyl-4-(thiophen-2-yl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5u)

Yield 85%; Pale yellow powder; mp 190-191 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.18 (s, 1H), 7.36 (d, *J* = 4 Hz, 1H), 7.01 (d, *J* = 4 Hz, 1H), 6.96 (s, 2H), 6.93 (dd, *J*₁ = 4 Hz, *J*₂ = 8 Hz, 1H), 4.99 (s, 1H), 1.91 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.6, 154.3, 149.7, 136.0, 126.5, 124.9, 124.3, 97.5, 57.5, 31.4, 9.7. HRMS (ESI, m/z): calcd for C₁₂H₁₀N₄OS (m/z) 258.0575; found: 258.0575.

22. 6-Amino-3-methyl-4-(4-methylphenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5v)

Yield 87%; White powder; mp 175-176 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.05 (s, 1H), 7.09 (d, *J* = 8 Hz, 2H), 6.83 (d, *J* = 8 Hz, 2H), 6.29 (s, 2H), 4.51 (s, 1H), 2.09 (s, 3H), 1.89 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.2, 153.8, 142.5, 141.3, 135.1, 129.0, 128.3, 112.8, 89.4, 58.2, 30.4, 23.8, 10.9. HRMS (ESI, m/z): calcd for C₁₅H₁₄N₄O (m/z) 266.1168; found: 266.1168.

23. 6-Amino-3-methyl-4-(4-trifluoromethylphenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5w)

Yield 95%; Pale green powder; mp 244-245 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.10 (s, 1H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.09 ((d, *J* = 8.5 Hz, 2H), 6.85 (s, 2H), 4.67 (s, 1H), 1.85 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 161.2, 155.2, 147.5, 145.7, 136.4, 135.7, 128.4, 127.6, 123.6, 121.3, 112.8, 98.3, 62.3, 35.8, 10.2. HRMS (ESI, m/z): calcd for C₁₅H₁₁F₃N₄O (m/z) 320.0885; found: 320.0885.

24. 6-Amino-3-methyl-4-(2-hydroxyphenyl)-2,4-dihydropyrano[2,3-c]pyrazole-5-carbonitrile (5x)

Yield 90%; White powder; mp 209-211 °C. ¹H NMR (400 MHz, DMSO-d₆): δ 12.07 (s, 1H), 8.67 (s, 1H), 7.54-7.76 (m, 2H), 6.65-6.89 (m, 2H), 6.21 (s, 2H), 4.86 (s, 1H), 1.98 (s, 3H). ¹³C NMR (100 MHz, DMSO-d₆): δ 160.8, 154.3, 154.0, 141.0, 131.2, 129.6, 126.7, 124.5, 121.8, 120.5, 112.6, 69.4, 10.2. HRMS (ESI, m/z): calcd for C₁₄H₁₂N₄O₂ (m/z) 268.0960; found: 268.0960.

¹H and ¹³C NMR spectra of some compounds