Electronic Supplementary Material (ESI)
This journal is © The Royal Society of Chemistry 2012

Supporting information

Application of a multi-SO_3H Brönsted acidic ionic liquid in water: A highly efficient and reusable catalyst for regioselective and scale-up synthesis of pyrazoles under mild condition

Shirin Safaei,[a] Iraj Mohammadpoor-Baltork,*[a] Ahmad R. Khosropour,*[a] Majid Moghadam,[a] Shahram Tangestaninejad,[a] Valiollah Mirkhani,[a] Reza Kia[b]

[a] *Catalysis Division, Department of Chemistry, University of Isfahan, Isfahan 81746-7344, Iran*

[b]*Department of Chemistry, Science and Research Branch, Islamic Azad University, Tehran, Iran*
E-mail: *imbaltork@sci.ui.ac.ir; khosropour@chem.ui.ac.ir*

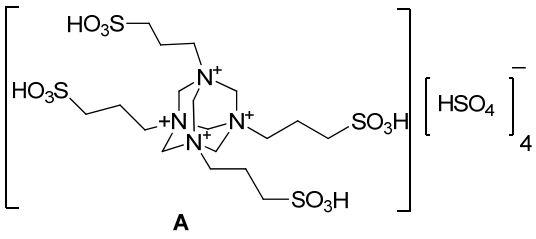
Contents:

General information:

Melting points were determined using Stuart Scientific SMP2 apparatus. Yields refer to isolated products. FT-IR spectra were recorded on a Nicolet-Impact 400D instrument in the range of 400-4000 cm^{-1}. ^{1}H and ^{13}C NMR (400 and 100 MHz) spectra were recorded in a $CDCl_3$ solution on a Bruker-AC 400 spectrometer. Mass spectra were obtained on a Platform II spectrometer from Micromass using EI mode at 70 eV. Elemental analysis was done on LECO, CHNS-932.

Synthesis of multi-SO_3H Brönsted acidic ionic liquid (A):

The catalyst was prepared according to known process.[34a] Hexamethylentetramine (10 mmol) and 1,3-propanesultone (40 mmol) was stirred in dry THF (40 ml) for 72 h at room temperature to form white solid zwitterion. After washing the salt with Et_2O to remove any unreacted starting materials, the solid was derided in vacuo. Then, sulfuric acid (40 mmol) was added and the mixture was stirred for 10 h at 120 ^{o}C during which time the solid zwitterion liquefied.



A

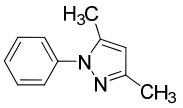
Spectroscopic data of zwitterion: Mp 185 °C (decomp.). IR (KBr): ν_{max} = 1469, 1266, 1212, 1177, 1043, 824, 638 cm^{-1}. ^{1}H NMR (400 MHz, D_2O): δ = 5.05 (s, 3H), 3.04 (t, J = 7.6 Hz, 2H), 2.90 (t, J = 7.4 Hz, 2H), 1.96-2.04 (m, 2H). ^{13}C NMR (100 MHz, D_2O): δ = 78.28, 55.34, 47.83, 22.35. Anal. calcd for $C_{18}H_{36}N_4O_{12}S_4$: C, 34.38; H, 5.77; N, 8.91; S, 20.40%. Found: C, 34.23; H, 5.71; N, 9.01, S, 20.19%.

Spectroscopic data of **A**: Oil. IR (neat): ν_{max} = 1433, 1291, 1199, 1167, 1050, 876, 581 cm^{-1}. ^{1}H NMR (400 MHz, D_2O): δ = 4.71 (s, 3H), 3.01 (t, J = 7.6 Hz, 2H), 2.88 (t, J = 7.6 Hz, 2H), 1.94-2.01 (m, 2H). ^{13}C NMR (100 MHz, D_2O): δ = 62.66, 50.38, 40.77, 24.89. Anal. calcd for $C_{18}H_{44}N_4O_{28}S_8$: C, 21.17; H, 4.34; N, 5.49; S, 25.12%. Found: C, 20.99; H, 4.40; N, 5.39; S, 24.96%.

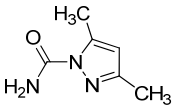
General procedure for regioselective synthesis of pyrazoles:

A mixture of 1,3-diketone (1 mmol), arylhydrazine/hydrazide (1 mmol) and catalyst (15 mol%) was stirred at room temperature for the appropriate time according to Table 2. After completion of the reaction, in the case of solid products, the mixture was filtered and dried. In the case of liquid products, the mixture was extracted with Et_2O and the organic phase was dried over $MgSO_4$ and evaporated. In all cases, the product was pure enough for identification. If necessary, the crude product was purified by recrystallization from ethanol. All products were characterized by IR, mass, ^{1}H NMR and ^{13}C NMR spectral data and elemental analysis.

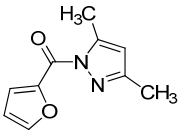
Spectroscopic data of products 3a-l, 4a,b:



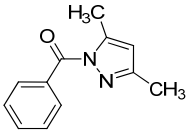
3,5-Dimethyl-1-phenyl-1H-pyrazole (3a)[2]: Oil. IR (neat): ν_{max} = 3060, 2922, 1597, 1502, 1381, 1026, 891, 782, 755 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47-7.42 (m, 5H), 6.00 (s, 1H), 2.30 (s, 6H).



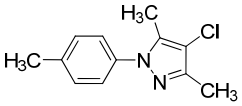
3,5-Dimethyl-1H-pyrazole-1-carbohydrazide (3b)[3]: Mp 88-90 °C. IR (KBr): ν_{max} = 3254, 3071, 2925, 1690, 1601, 1581, 1453, 1324, 1292, 1070, 800, 709 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.12 (s, 1H), 5.92 (s, 1H), 5.32 (s, 1H), 2.55 (s, 3H), 2.21 (s, 3H).



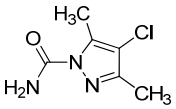
(Furan-2-yl)(3,5-dimethyl-1H-pyrazol-1-yl)methanone (3c)[2]: Mp 94-95 °C. IR (KBr): ν_{max} = 3118, 2924, 1684, 1560, 1461, 1353, 1287, 1034, 866, 789 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.93 (d, *J* = 3.6 Hz, 1H), 7.73 (s, 1H), 6.60 (t, *J* = 1.8 Hz, 1H), 6.04 (s, 1H), 2.63 (s, 3H), 2.30 (s, 3H).



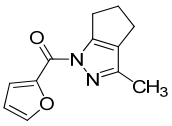
(3,5-Dimethyl-1H-pyrazol-1-yl)(phenyl)methanone (3d)[2]: Oil. IR (neat): ν_{max} = 3061, 2928, 1697, 1583, 1448, 1340, 1278, 1121, 916, 713 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.0 (d, *J* = 7.6 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 6.07 (s, 1H), 2.64 (s, 3H), 2.26 (s, 3H).



4-Chloro-3,5-dimethyl-1-*p*-tolyl-1H-pyrazole (3e): Oil. IR (neat): ν_{max} = 3008, 2925, 1744, 1504, 1463, 1379, 1160, 831, 724 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.29-7.24 (m, 4H), 2.40 (s, 3H), 2.29 (s, 3H), 2.27 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.75, 137.71, 137.31, 135.68, 129.71, 124.48, 109.47, 21.10, 11.40, 10.75. MS: *m/z* = 222.02 ($[M+2]^+$, 31.44), 220.02 ($[M]^+$, 100), 185.08 (9.82), 168.04 (15.64), 132.08 (12.88), 90.98 (95.71), 76.98 (30.67), 64.98 (85.89). Anal. calcd for $C_{12}H_{13}ClN_2$: C, 65.31; H, 5.94; N, 12.69%. Found: C, 64.55; H, 6.07; N, 12.53%.

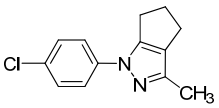


4-Chloro-3,5-dimethyl-1H-pyrazole-1-carboxamide (3f): Mp 141-142 °C. IR (KBr): ν_{max} = 3423, 3244, 2931, 1742, 1595, 1491, 1394, 1216, 1071, 760, 716 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.09 (s, 1H), 5.44 (s, 1H), 2.55 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.82, 149.12, 138.05, 111.19, 10.62, 10.14. MS: *m/z* = 174.93 ($[M+2]^+$, 7.41), 172.92 ($[M]^+$, 21.61), 128.95 (76.88), 94.91 (100), 64.96 (60.80). Anal. calcd for $C_6H_8ClN_3O$: C, 41.51; H, 4.64; N, 24.21%. Found: C, 41.45; H, 4.78; N, 24.33%.



(Furan-2-yl)(5,6-dihydro-3-methylcyclopenta[c]pyrazol-1(4H)-yl)methanone (3g):

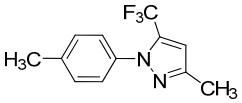
Mp 145-147 °C. IR (KBr): ν_{max} = 3080, 2924, 1744, 1464, 1378, 1159, 1110, 873, 722 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 3.6 Hz, 1H), 7.72 (s, 1H), 6.61-6.58 (m, 1H), 3.12 3.08 (m, 2H), 2.60-2.55 (m, 4H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.01, 153.73, 148.89, 147.47, 145.20, 130.75, 123.59, 112.33, 31.91, 27.22, 22.07, 13.19. MS: *m/z* = 218.11 ($[M+2]^+$, 4.09), 216.05 ($[M]^+$, 86.75), 188.09 (65.38), 159.05 (74.79), 134.08 (72.65), 94.99 (100), 67.04 (73.50). Anal. calcd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96%. Found: C, 66.32; H, 5.68; N, 12.80%.



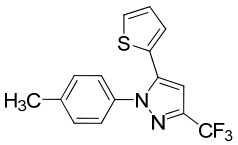
1-(4-Chlorophenyl)-1,4,5,6-tetrahydro-3-methylcyclopenta[c]pyrazole (3h):

Mp 48-50 °C. IR (KBr): ν_{max} = 3060, 2925, 1735, 1597, 1500, 1462, 1274, 1118, 829, 808 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.8 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 2.98-2.95 (m, 2H), 2.61-2.58 (m, 4H), 2.25 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.79, 144.34, 139.01,

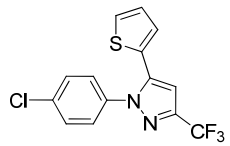
130.25, 129.22, 128.76, 119.58, 30.96, 26.88, 22.27, 12.71. MS: *m*/*z* = 232.09 ([M]$^+$, 93.33), 197.13 (85.88), 177.08 (26.27), 148.95 (90.98), 110.84 (100), 74.98 (100). Anal. calcd for $C_{13}H_{13}ClN_2$: C, 67.10; H, 5.63; N, 12.04%. Found: C, 66.96; H, 5.67; N, 12.13%.



5-(Trifluoromethyl)-3-methyl-1-*p*-tolyl-1H-pyrazole (3i): Oil. IR (neat): ν_{max} = 3005, 2926, 1632, 1465, 1293, 1138, 798, 726 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33-7.28 (m, 4H), 6.45 (s, 1H), 2.42 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.42 (q, $^2J_{C\text{-}F}$ = 37), 140.68, 138.81, 136.43, 129.80, 125.12, 121.49 (q, $^1J_{C\text{-}F}$ = 272), 104.59, 21.07, 12.18. MS: *m*/*z* = 241.10 ([M+1]$^+$, 9.54), 240.10 ([M]$^+$, 34.98), 171.12 (27.54), 149.08 (69.34), 91.15 (54.32), 65.17 (97.17), 57.21 (100). Anal. calcd for $C_{12}H_{11}F_3N_2$: C, 60.00; H, 4.62; N, 11.66%. Found: C, 59.09; H, 4.74; N, 11.75%.

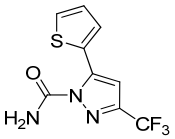


3-(Trifluoromethyl)-5-(thiophen-2-yl)-1-*p*-tolyl-1H-pyrazole (3j): Mp 112-115 °C. IR (KBr): ν_{max} = 3098, 2923, 1512, 1471, 1385, 1251, 1133, 975, 800, 712 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33-7.23 (m, 5H), 6.97 (dd, ^1J = 5.0 Hz, ^2J = 3.8 Hz, 1H), 6.87 (dd, ^1J = 3.6 Hz, ^2J = 0.8 Hz, 1H), 6.80 (S, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.92 (q, $^2J_{C\text{-}F}$ = 38), 139.53, 138.75, 136.46, 129.82, 127.97, 127.50, 127.35, 126.20, 121.18 (q, $^1J_{C\text{-}F}$ = 267), 105.01, 21.27. MS: *m*/*z* = 309.97 ([M+2]$^+$, 9.79), 307.95 ([M]$^+$, 100), 238.03 (4.57), 224.02 (4.90), 143.02 (20.62), 91.07 (52.58), 65.07 (79.90). Anal. calcd for $C_{15}H_{11}F_3N_2S$: C, 58.43; H, 3.60; N, 9.09; S, 10.40%. Found: C, 58.27; H, 3.78; N, 9.33, S, 10.35%.

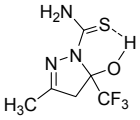


1-(4-Chlorophenyl)-3-(trifluoromethyl)-5-(thiophen-2-yl)-1H-pyrazole (3k):

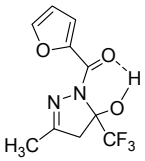
Mp 91-93 °C. IR (KBr): ν_{max} = 3096, 2921, 1497, 1385, 1253, 1129, 974, 843, 713 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.4 Hz, 2H), 7.01 (t, *J* = 6.0 Hz, 1H), 6.90 (s, 1H), 6.80 (S, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.45 (q, $^2J_{C\text{-}F}$ = 39), 138.76, 137.39, 135.18, 129.45, 129.27, 128.41, 127.84, 127.71, 127.42, 120.36 (q, $^1J_{C\text{-}F}$ = 267), 105.79. MS: *m*/*z* = 329.86 ([M+2]$^+$, 37.90), 327.88 ([M]$^+$, 100), 292.95 (7.16), 260.03 (3.83), 224.04 (3.68), 136.39 (20.56), 111.03 (25.40), 75.05 (41.73). Anal. calcd for $C_{14}H_8ClF_3N_2S$: C, 51.15; H, 2.45; N, 8.52; S, 9.75%. Found: C, 51.17; H, 2.52; N, 8.57, S, 9.86%.



3-(Trifluoromethyl)-5-(thiophen-2-yl)-1H-pyrazole-1-carboxamide (3l): Mp 115-117 °C. IR (KBr): ν_{max} = 3204, 3135, 2983, 1599, 1455, 1340, 1257, 1135, 983, 849, 707 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.47 (s, 2H), 7.40 (d, J = 4.8 Hz, 1H), 7.31 (d, J = 2.8 Hz, 1H), 7.11 (t, J = 4.8 Hz, 1H), 6.69 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.95 (q, $^{2}J_{C\text{-}F}$ = 36), 139.91, 129.76, 128.05, 127.78, 126.46, 125.48, 120.85 (q, $^{1}J_{C\text{-}F}$ = 267), 101.21. MS: m/z = 217.79 (100), 169.80 (82.35), 148.89 (32.94), 120.85 (63.92), 68.73 (98.82). Anal. calcd for $C_9H_6F_3N_3OS$: C, 41.38; H, 2.32; N, 16.09; S, 12.27%. Found: C, 41.12; H, 2.35; N, 16.35, S, 12.09%.



5-(Trifluoromethyl)-4,5-dihydro-5-hydroxy-3-methylpyrazole-1-carbothioamide (4a): Mp 140-142 °C. IR (KBr): ν_{max} = 3400, 3288, 3174, 3002, 2920, 1605, 1477, 1388, 1285, 1174, 882, 743 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 (s, 1H), 7.13 (s, 1H), 6.19 (s, 1H), 3.31 (AB-q, J = 19.2 Hz, 2H), 2.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.33, 156.32, 123.88 (q, $^{1}J_{C\text{-}F}$ = 288), 92.46 (q, $^{2}J_{C\text{-}F}$ = 33), 47.56, 14.72. MS: m/z = 229.09 ($[M+2]^+$, 73.33), 227.45 ($[M]^+$, 100), 211.06 (61.18), 168.09 (92.16), 158.08 (82.35), 99.12 (100), 69.05 (100). Anal. calcd for $C_6H_8F_3N_3OS$: C, 31.72; H, 3.55; N, 18.49; S, 14.11%. Found: C, 31.92; H, 3.64; N, 18.38; S, 14.04%.



5-(Trifluoromethyl)-4,5-dihydro-5-hydroxy-3-methylpyrazol-1-yl)(furan-2-yl)methanone (4b): Mp 90-92 °C. IR (KBr): ν_{max} = 3360, 2938, 1643, 1476, 1316, 1164, 1022, 867, 751 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (s, 1H), 7.57 (d, , J = 2.8 Hz 1H), 6.55 (s, 1H), 6.49 (s, 1H), 3.22 (AB-q, J = 18.8 Hz, 2H), 2.14 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.99, 155.71, 146.50, 144.94, 123.17 (q, $^{1}J_{C\text{-}F}$ = 286), 121.27, 111.91, 92.65 (q, $^{2}J_{C\text{-}F}$ = 34), 46.36, 15.48. MS: m/z = 262.02 ($[M]^+$, 9.87), 207.00 (4.31), 177.01 (2.16), 150.04 (10.94), 95.02 (100). Anal. calcd for $C_{10}H_9F_3N_2O_3$: C, 45.81; H, 3.46; N, 10.68%. Found: C, 45.72; H, 3.54; N, 10.79%.

References:

1 X. Liang and J. Yang, *Green Chem.*, 2010, **12**, 201

2 V. Polshettiwar and R. S. Varma, *Tetrahedron Lett.*, 2008, **49**, 397.

3 W. Ried and *B.* Schleimer, *Angew. Chem.*, 1958, **70**, 164.

Crystal data and structure refinement for **3h**

Empirical formula	$C_{13}H_{13}ClN_2$	
Formula weight	232.70	
Temperature	291(2) K	
Wavelength	0.71069 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 7.115(5) Å	α = 73.839(5)°
	b = 12.488(5) Å	β = 87.734(5)°
	c = 14.141(5) Å	γ = 81.732(5)°
Volume	1194.3(11) $Å^3$	
Z	4	
Density (calculated)	1.294 Mg/m^3	
Absorption coefficient	0.293 mm^{-1}	
F(000)	488	
Crystal size	0.18 x 0.12 x 0.01 mm^3	
Theta range for data collection	1.94 to 29.29°	
Index ranges	-9<=h<=9, -17<=k<=17, -16<=l<=19	
Reflections collected	9389	
Independent reflections	5862 [R(int) = 0.1026]	
Completeness to theta = 29.29°	89.8%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.952	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5862 / 0 / 291	
Goodness-of-fit on F^2	0.475	
Final R indices [I>2sigma(I)]	R1 = 0.0396, wR2 = 0.0348	
R indices (all data)	R1 = 0.3999, wR2 = 0.0578	
Largest diff. peak and hole	0.110 and -0.106 $e.Å^{-3}$	

Crystal data and structure refinement for **3k**

Empirical formula	$C_{14}H_8ClF_3N_2S$	
Formula weight	328.73	
Temperature	291(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P c a 21	
Unit cell dimensions	a = 25.542(5) Å	$\alpha = 90°$
	b = 9.4168(19) Å	$\beta = 90°$
	c = 6.0399(12) Å	$\gamma = 90°$
Volume	1452.8(5) $Å^3$	
Z	4	
Density (calculated)	1.503 Mg/m^3	
Absorption coefficient	0.432 mm^{-1}	
F(000)	664	
Crystal size	0.35 x 0.14 x 0.08 mm^3	
Theta range for data collection	2.69 to 29.20°	
Index ranges	-34<=h<=34, -12<=k<=5, -8<=l<=6	
Reflections collected	6269	
Independent reflections	3222 [R(int) = 0.0652]	
Completeness to theta = 29.20°	92.1%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9662 and 0.8634	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3222 / 1 / 190	
Goodness-of-fit on F^2	0.767	
Final R indices [I>2sigma(I)]	R1 = 0.0505, wR2 = 0.1211	
R indices (all data)	R1 = 0.1070, wR2 = 0.1331	
Absolute structure parameter	-0.08(11)	
Largest diff. peak and hole	0.266 and -0.207 $e.Å^{-3}$	

Crystal data and structure refinement for **4a**

Empirical formula	$C_6H_8F_3N_3OS$	
Formula weight	227.21	
Temperature	291(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 2/c	
Unit cell dimensions	a = 11.767(2) Å	α = 90°
	b = 6.7984(14) Å	β = 115.03(3)°
	c = 13.303(3) Å	γ = 90°
Volume	964.3(3) $Å^3$	
Z	4	
Density (calculated)	1.565 Mg/m^3	
Absorption coefficient	0.353 mm^{-1}	
F(000)	464	
Crystal size	0.16 x 0.12 x 0.10 mm^3	
Theta range for data collection	3.00 to 26.00°	
Index ranges	-14<=h<=11, -7<=k<=8, -16<=l<=16	
Reflections collected	4251	
Independent reflections	1766 [R(int) = 0.0371]	
Completeness to theta = 26.00°	92.8%	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.978	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1766 / 0 / 128	
Goodness-of-fit on F^2	0.795	
Final R indices [I>2sigma(I)]	R1 = 0.0323, wR2 = 0.0605	
R indices (all data)	R1 = 0.0713, wR2 = 0.0662	
Largest diff. peak and hole	0.140 and -0.203 $e.Å^{-3}$	