Supplemental Materials and Methods

**1. Chemistry**

All reagents and solvents used were analytical grades. Fourier transform infrared (FT-IR) absorption spectra were recorded on a Shimadzu mode IR Prestige-21 spectrophotometer. The melting points (m.p.) were measured employing the Büchi model B-545. The BRUKER Avance instrument was used to obtain the spectras of 1H, 13C and 19F nuclear magnetic resonance (NMR) in frequences of 400.00,100.00 and 376.00 MHz MHz respectively. The chemical shifts (δ) are presented in ppm, and the coupling constants (*J*) are stated in Hertz. High- Resolution Mass Spectrometry (HRMS) spectras were made by an LC-MS Bruker Daltonics MicroTOF. The reactions were accompanied by TLC (thin layer chromatography) silica gel F-254 glass plate (20 x 20 cm).

**1.1 General procedure for preparation of ethyl 5-amino-1-(1,3,4-thiadiazol-2-yl)-1*H*-pyrazole-4-carboxylate (9a-h)**

The respective 2-hydrazinyl-1,3,4-thiadiazole (**7**) (2 mmol) and (ethoxymethylene)malononitrile (**8a**) or ethyl (ethoxymethylene)cyanoacetate (**8b**) were dissolved in 40 mL of ethanol and the mixture was stirred and refluxed for 2-4 h. The reactions were accompanied by TLC (CHCl3/MeOH 9:1). After detecting the end of the reaction, the reaction medium was poured onto ice-cold water (50 mL). The product was precipitated, filtered, washed with cold water and recrystallized using the solvent mixture ethanol/water (3:1) to produce 9a-h at 55-91% yield.

5-amino-1-(5-phenyl-1,3,4-thiadiazol-2-yl)-1*H*-pyrazole-4-carbonitrile **(9a)**. Yield: 85%. brown solid. MP: 234-235 ºC. IR (cm-1): 3398; 3312; 2364; 2342; 2219; 1708; 1628; 1579; 1560; 1508; 1459; 1425; 1360; 1221; 1092; 982; 932; 763; 688; 669; 616; 589; 578; 559; 542; 533. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 7.55-7.60 (m, 3H, C-3´´, C-4´´ and C-5´´); 7.98-8.00 (m, 2H, C-2´´ and C-6´´); 8.07 (s, 1H, H-3´); 8.11 (s, 2H, NH2). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 73.3 (C-4´); 113.4 (CN); 127.3 (C-4´´); 128.9 (C-3´´ and C-5´´); 129.4 (C-2´´ and C-6´´) ; 131.5 (C-1´´); 145.7 (C-3´); 151.9 (C-5´); 163.0 (C-2); 164.3 (C-5). HRMS (ESI) calc. for C12H8N6SNa= 291.0429; found [M+Na]+ 291.0431.

5-amino-1-(5-(2-chlorophenyl)-1,3,4-thiadiazol-2-yl)-1*H*-pyrazole-4-carbonitrile **(9b)**. Yield: 55%. brown solid. MP: 250-251 ºC. IR (cm-1): 3388; 3295; 3232; 3190; 3143; 2924; 2359; 2223; 1628; 1576; 1506; 1479; 1431; 1407; 1368; 1294; 1228; 1193; 1162; 1127; 1064; 1039; 981; 921; 899; 873. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 7.55-7.65 (m, 2H, H-4´and H-5´); 7.71-7.73 (m, 1H, H-3´´); 8.07 (s, 1H, H-3´); 8.13 (s, 2H, NH2); 8.17-8.20 (m, 1H, H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 73.4 (C-4´); 113.4 (CN); 127.6 (C-5´´); 127.9 (C-6´´); 130.7 (C-3´´); 131.4 (C-4´´); 132.6 (C-2´´); 145.9 (C-3´); 152.0 (C-5´); 159.6 (C-2); 164.2 (C-5). HRMS (ESI) calc. for C12H7ClN6SNa= 325.0039; found [M+Na]+ 325.0046.

5-amino-1-(5-(4-fluorophenyl)-1,3,4-thiadiazol-2-yl)-1*H*-pyrazole-4-carbonitrile **(9c)**. Yield: 91%. white solid. MP: 262-263 ºC. IR (cm-1): 3400; 3296; 3234; 3186; 3084; 2230; 1628; 1602; 1569; 1530; 1507; 1449; 1427; 1406; 1368; 1311; 1292; 1262; 1228; 1205; 1170; 1077; 984; 926; 882; 841; 812. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 7.40-7.44 (m, 2H, H-3´´ and H-5´´); 8.04-8.08 (m, 2H, H-2´´ and H-6´´); 8.07 (s, 1H, H-3´); 8.11 (s, 2H, NH2). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 73.4 (C-4´); 113.5 (CN); 116.6 (d, *J* = 22.3 Hz, C-3´´ and C-5´´); 125.6 (d, *J* = 3.2 Hz, C-2´´ and C-6´´); 129.9 (d, *J* = 9.0 Hz, C-1´´); 145.9 (C-3´), 152.0 (C-5´), 163.2 (C-2), 163.3 (C-5); 163.9 (d, *J* = 248 Hz, C-4´´). HRMS (ESI) calc. for C12H7FN6SNa= 309.0335; found [M+Na]+ 309.0344.

5-amino-1-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl)-1*H*-pyrazole-4-carbonitrile **(9d)**. Yield: 75%. white solid. MP: >300 ºC. IR (cm-1): 3402; 3295; 3234; 3186; 2920; 2233; 2030; 1979; 1630; 1596; 1575; 1530; 1510; 1444; 1428; 1399; 1384; 1367; 1297; 1265; 1214; 1165; 1091; 1075; 1024, 1014, 999; 983; 967; 931; 877; 835. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 7.65 (d, 2H, *J* = 6.8 Hz, H-3´´ and H-5´´); 8.02 (d, 2H, J = 6.8 Hz, H-2´´ and H-6´´); 8.08 (s, 1H, H-3´); 8.12 (s, 2H, NH2). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 73.2 (C-4´); 113.4 (CN); 127.8 (C-2´ and C-6´); 129.0 (C-3´´ and C-5´´); 129.5 (C-1´´); 136.2 (C-4´´); 145.9 (C-3´); 151.9 (C-5´); 163.2 (C-2); 163.3 (C-5). HRMS (ESI) calc. for C12H7ClN6SNa= 325.0039; found [M+Na]+ 325.0034

Ethyl 5-amino-1-(5-phenyl-1,3,4-thiadiazol-2-yl)-1*H*-pyrazole-4-carboxylate **(9e)**. Yield: 85%. brown solid. MP: 165-167 ºC. IR (cm-1): 3445; 3302; 3116; 3064; 2980; 2928; 2905; 2359; 2162; 1811; 1672; 1614; 155; 1539; 1519; 1501; 1462; 1428; 1398; 1376; 1353; 1315; 1285; 1264; 1205; 1157; 1111; 1074; 1030; 977; 920; 834. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 1,28 (t, 3H, *J* = 7.1 Hz, CH3); 4.24 (q, 2H, *J* = 7.1 Hz, CH2); 7.46 (s, 2H, NH2); 7.55-7.60 (m, 3H, H-3´´, H-4´´ and H-5´´); 7.92 (s, 1H, H-3´); 7.98-8.00 (m, 2H, H-2´´ and H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 14.3 (CH3); 59.3 (CH2); 94.5 (C-4´); 127.3 (C-4´´); 128.9 (C-3´´ and C-5´´); 129.4 (C-2´´ and C-6´´); 131.5 (C-1´´); 144.3 (C-3´); 150.2 (C-5´); 162.5 (C-2); 163.3 (CO); 164.0 (C-5). HRMS (ESI) calc. for C14H13N5O2SNa= 3338.0688; found [M+Na]+ 338.0689.

Ethyl 5-amino-1-(5-(2-chlorophenyl)-1,3,4-thiadiazol-2-yl)-1*H*-pyrazole-4-carboxylate **(9f)**. Yield: 55%. brown solid. MP: 190-191 ºC. IR (cm-1): 3463; 3351; 3069; 2993; 2917; 2850; 2358; 2161; 2035; 1757; 1691; 1628; 1590; 1559; 1523; 1505; 1429; 1410; 1380; 1354; 1317; 1281; 1271; 1206; 1152; 1111; 1061; 1037; 979; 930; 879; 835; 810. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 1.30 (t, 3H, *J* = 7.1Hz, CH3); 4.25 (q, 2H, *J* = 7.1 Hz, CH2); 7.50 (s, 2H, NH2); 7.56-7.66 (m, 2H, H-4´´ and H-5´´); 7.72-7.75 (m, 1H, H-2´´); 7.95 (s, 1H, H-3´); 8.18-8.20 (m, 1H, H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 14.3 (CH3); 59.4 (CH2); 94.5 (C-4´); 127.7 (C-5´´); 128.0 (C-6´´); 130.6 (C-3´´); 130.7 (C-4´´); 131.3 (C-2´´); 132.6 (C-1´´); 144.3 (C-3´); 150.3 (C-5´); 159.3 (C-2); 162.5 (CO); 164.5 (C-5). HRMS (ESI) calc. for C14H12ClN5O2SNa= 372.0298; found [M+Na]+  372.0292.

Ethyl 5-amino-1-(5-(4-fluorophenyl)-1,3,4-thiadiazol-2-yl)-1*H*-pyrazole-4-carboxylate **(9g)**. Yield: 77%. white solid. MP: 250-251 ºC. IR (cm-1): 3338; 3004; 2363; 1676; 1568; 1519; 1419; 1358; 1220; 1093; 903; 835. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 1.29 (t, 3H, *J* = 7.1Hz, CH3); 4.25 (q, 2H, *J =* 7.1 Hz, CH2); 7.41-7.46 (m, 2H, H-3); 7.48 (s, 2H); 7.95 (s, 1H); 8.05-8.09 (m, 2H). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 14.3 (CH3), 59.4 (CH2), 94.5 (C-4´), 116.6 (d, *J* = 22.3 Hz) (C-3´´ and C-5´´); 125.6 (C-1´´); 129.9 (d, *J* = 8.9 Hz) (C-2´´ and C-6´´); 144.3 (C-3´); 150.2 (C-5´); 162.5 (C-2); 162.9 (C-5); 163.4 (CO); 163.7 (d, *J* = 252.7 Hz) (C-4´´). HRMS (ESI) calc. for C14H12FN5O2SNa= 356.0594; found [M+Na]+  356.0604.

Ethyl 5-amino-1-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl)-1*H*-pyrazole-4-carboxylate **(9h)**. Yield: 77%. white solid. MP: 252-253 ºC. IR (cm-1): 3005; 2360; 2342; 1709; 1421; 1359; 1220; 1092; 902. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 1.29 (t, 3H, *J* = 5.4 Hz, CH3); 4.25 (q, 2H, *J* = 5.4 Hz, CH2); 7.48 (s, 2H, NH2); 7.65-7.67 (m, 2H, H-3´´ and H-5´´); 7.96 (s, 1H, H-3´); 8.02-8.04 (m, 2H, H-2´´ and H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 14.3 (CH3); 59.4 (CH2); 94.5 (C-4´); 127.8 (C-3´´ and C-5´´); 129.0 (C-2´´ and C-6´´); 129.5 (C-1´´); 136.1 (C-4´´); 144.4 (C-3´); 150.2 (C-5´); 162.5 (C-2); 162.9 (CO); 163.6 (C-5). HRMS (ESI) calc. for C14H12ClN5O2SNa= 372.0298; found [M+Na]+  372.0292.

**1.2 General method for preparation of 2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3,4-thiadiazole (11a-d)**

The respective 2-hydrazinyl-1,3,4-thiadiazole (**7**) (2 mmol) and 2,4-pentanedione **(10)** (2.4 mmol) were dissolved in 40 mL of ethanol and the mixture was stirred and refluxed for 2-4 h. The reactions were accompanied by TLC (CHCl3/MeOH 9:1). After detecting the end of the reaction, the reaction medium was poured onto ice-cold water (50 mL). The product was precipitated, filtered, washed with cold water and recrystallized using the solvent mixture ethanol/water (3:1) to produce **11a-d** at 77- 95% yield.

2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-5-phenyl-1,3,4-thiadiazole **(11a)**. Yield: 95%. brown solid. MP: 170-171 ºC. IR (cm-1): 3101; 2162; 1965; 1574; 1515; 1458; 1433; 1405; 1377; 1364; 1267; 1151; 1065; 1028; 998; 974; 910; 825. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.22 (s, 3H, CH3); 2.67 (s, 3H, CH3); 6.29 (s, 1H, H-4´); 7.57-7.58 (m, 3H, H-3´´, H-4´´ and H-5´´); 7.97-7.99 (m, 2H, H-2´´ and H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 13.3 (CH3); 13.4 (CH3); 110.8 (C-4´); 127.4 (C-4´´); 129.5 (C-3´´ and C-5´´); 129.7 (C-2´´ and C-6´´); 131.6 (C-1´´); 142.4 (C-3´); 153.0 (C-5´); 163.6 (C-2); 164.7 (C-5). HRMS (ESI) calc. for C13H12N4SNa= 279.0681; found [M+Na]+ 279.0679.

2-(2-chlorophenyl)-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3,4-thiadiazole **(11b)**. Yield: 82%. yellow solid. MP: 163-165 ºC. IR (cm-1): 3066; 2729; 2358; 1642; 1568; 1514; 1435; 1423; 1388; 1316; 1284; 1176; 1073; 1043; 994; 964; 884; 849. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.23 (s, 3H, CH3); 2.69 (s, 3H, CH3); 6.30 (s, 1H, H-4´); 7.55-7.64 (m, 2H, H-4´´ and H-5´´); 7.72 (dd, 1H, *J* = 8.0 and 1.2 Hz, H-3´´); 8.16 (dd, 1H, *J* = 7.6 and 1.6 Hz, H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 13.2 (CH3); 13.2 (CH3); 110.7 (C-4´); 128.0 (C-5´´); 128.1 (C-6´´); 130.6 (C-3´´); 130.7 (C-4´´); 131.3 (C-2´´); 132.5 (C-1´´); 142.4 (C-3´); 153.0 (C-5´); 159.8 (C-2); 164.8 (C-5). HRMS (ESI) calc. for C13H11ClN4SNa= 313.0291; found [M+Na]+ 313.0283.

2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-5-(4-fluorophenyl)-1,3,4-thiadiazole **(11c)**. Yield: 79%. white solid. MP: 174-174 ºC. IR (cm-1): 3081; 2919; 2850; 2359; 1596; 1577; 1558; 1515; 1450; 1406; 1385; 1297; 1266; 1218; 1165; 1134; 1105; 1075; 1024; 998; 966; 834; 810. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.23 (s, 3H, CH3); 2.67 (s, 3H, CH3); 6.30 (s, 1H, H-4´); 7.41-7.45 (m, 2H, H-3´´ and H-5´´); 8.03-8.07 (m, 2H, H-2´´ and H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 13.1 (CH3); 13.1 (CH3); 110.5 (C-4´); 116.5 (d, *J* = 22.1 Hz) (C-3´´ and C-5´´); 126.0 (d, *J* = 3.3 Hz) (C-1´´); 129.6 (d, *J* = 8.8 Hz) (C-2´´ and C-6´´); 142.1 (C-3´); 152.7 (C-5´); 163.3 (C-2); 163.4 (C-5); 163.6 (d, *J* = 248.0 Hz) (C-4´´). HRMS (ESI) calc. for C13H11FN4SNa= 297.0586; found [M+Na]+ 297.0585.

2-(4-chlorophenyl)-5-(3,5-dimethyl-1*H*-pyrazol-1-yl)-1,3,4-thiadiazole **(11d)**. Yield: 77%. white solid. MP: 202-203 ºC. IR (cm-1): 3089; 2932; 2360; 2344; 2163; 1980; 1904; 1593; 1578; 1519; 1446; 1398; 1382; 1302; 1264; 1177; 1137; 1120; 1088; 1073; 1026; 985; 969; 826. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.23 (s, 3H, CH3); 2.67 (s, 3H, CH3); 6.30 (s, 1H, H-4´); 7.64-7.66 (m, 2H, H-3´´ and H-5´´); 7.99-8.02 (m, 2H, H2´´ and H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 13.1 (CH3); 13.1(CH3); 110.6 (C-4´); 128.2 (C-2´ and C-6´); 128.8 (C-3´´ and C-5´´); 129.4 (C-1´´); 135.8 (C-4´´); 142.2 (C-3´); 152.8 (C-5´); 163.2 (C-2); 163.6 (C-5). HRMS (ESI) calc. for C13H11ClN4SNa= 313.0291; found [M+Na]+ 313.0286.

**1.3 General procedure for preparation of 5-methyl-1-(5-phenyl-1,3,4-thiadiazol-2-yl)-3-(trifluoromethyl)-4,5-dihydro-1*H*-pyrazol-5-ol (13a-d)**

A mixture of respective 2-hydrazinyl-5-phenyl-1,3,4-thiadiazoles **(7)** (2.0 mmol) and 1,1,1-trifluoropentane-2,4-dione **(10)** (2.4 mmol) and 40 mL of ethanol was kept under stirring and reflux for 2-6 h. The advance of the reaction was monitored using TLC (CHCl3/MeOH 9:1). After detecting the end of the reaction, the reaction medium was poured onto ice-cold water (50 mL). The precipitate produced was selected by filtration, washed with water and recrystallized from ethanol/water (3:1) to produce **13a-d** at 54- 90% yield.

5-methyl-1-(5-phenyl-1,3,4-thiadiazol-2-yl)-3-(trifluoromethyl)-4,5-dihydro-1*H*-pyrazol-5-ol **(13a)**. Yield: 79%. yellow solid. MP: 183-185 ºC. IR (cm-1): 3005; 2364; 2338; 1713; 1646; 1577; 1521; 1465; 1438; 1363; 1310; 1280; 1222; 1197; 1173; 1159; 1078; 995. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.07 (s, 3H, CH3); 3.23 (d, 1H, *J* = 19.2 Hz, Ha4´ or Hb4´); 3.63 (d, 1H, *J* = 19.2 Hz, Ha4´ or Hb4´); 7.50-7.53 (m, 3H, H-3´´, H-4´´ and H-5´´); 7.86-7.88 (m, 2H, H-2´´ and H-6´´); 8.31 (s, 1H, OH). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 15.5 (CH3); 48.5 (C-4´); 92.3 (q, *J* = 33.7 Hz) (C-3´); 123.2 (q, *J* = 271.6 Hz) (CF3); 126.8 (C-4´´); 129.3 (C-3´´ and C-5´´); 130.2 (C-2´´ and C-6´´); 130.5 (C-1´´); 155.9 (C-5´); 161.1 (C-2); 164.9 (C-5). HRMS (ESI) calc. for C13H11F3N4OSNa= 351.0504; found [M+Na]+ 351.0500.

1-(5-(2-chlorophenyl)-1,3,4-thiadiazol-2-yl)-5-methyl-3-(trifluoromethyl)-4,5-dihydro-1*H*-pyrazol-5-ol **(13b)**. Yield: 54%. white solid. MP: 163-165 ºC. IR (cm-1): 3065; 2728; 2358; 1642; 1567; 1514; 1435; 1432; 1387; 1316; 1283; 1175; 1073; 1092; 994; 964; 887; 850. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.08 (s, 3H, CH3); 3.24 (d, 1H, *J* = 19,2 Hz, Ha4´ or Hb4´); 3.64 (d, 1H, *J* = 19.2 Hz, Ha4´ or Hb4´); 7.52-7.57 (m, 2H, H-4´´ and H-5´´); 7.65-7.67 (m, 1H, H-3´´); 8.07-8.10 (m, 1H, H-6´´); 8.35 (s, 1H, OH). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 15.2 (CH3); 48.5 (C-4´); 92.3 (q, *J* = 33.0 Hz, C-3´); 123.1 (q, *J* = 281.1 Hz, CF3); 127.8 (C-5´´); 128.9 (C-6´´); 130.5 (C-3´´); 130.5 (C-4´´); 131.0 (C-2´´); 131.7 (C-1´´); 155.9 (C-5´); 156.2 (C-2); 166.1 (C-5). HRMS (ESI) calc. for C13H10ClF3N4OSH= 363.0284; found [M+H]+ 363.0295.

1-(5-(4-fluorophenyl)-1,3,4-thiadiazol-2-yl)-5-methyl-3-(trifluoromethyl)-4,5-dihydro-1*H*-pyrazol-5-ol **(13c)**. Yield: 90%. white solid. MP: 182-183 ºC. IR (cm-1): 3077; 1713; 1601; 1592; 1526; 1467; 1388; 1362; 1311; 1279; 1266; 1240; 1202; 1171; 1162; 1154; 1129; 1099; 1074; 1046; 985; 841; 816. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.07 (s, 3H, CH3); 3.23 (d, 1H, *J* = 19.2 Hz, Ha4´ or Hb4´ ); 3.63 (d, *1H*, *J* = 19.2 Hz, Ha4´ or Hb4´); 7.35-7.38 (m, 2H, H-3´´ and H-5´´); 7.92-7.95 (m, 2H, H-2´´ and H-6´´); 8.33 (s, 1H, OH). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 15.1 (CH3); 48.4 (C-4´); 92.2 (q, *J* = 33.1 Hz, C-3´); 116.3 (d, *J* = 22.0 Hz, C-3´´ and C-5´´); 123.0 (q, *J* = 283.3 Hz, CF3); 126.7 (d, *J* = 3.0 Hz, C-1´´); 129.0 (d, *J* = 8.7 Hz, C-2´´ and C-6´´); 155.7 (C-5´); 159.7 (C-2); 163.3 (d, *J =* 274.0 Hz, C-4´´); 164.4 (C-5). HRMS (ESI) calc. for C13H10F4N4OSNa= 369.0409; found [M+Na]+ 369.0410.

1-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl)-5-methyl-3-(trifluoromethyl)-4,5-dihydro-1*H*-pyrazol-5-ol **(13d)**. Yield: 62%. white solid. MP: 184-185 ºC. IR (cm-1): 3056; 2360; 1640; 1595; 1569; 1526; 1459; 1387; 1349; 1313; 1274; 1197; 1179; 1173; 1160; 11301; 1105; 1095; 1073; 1015; 994; 983; 960; 882; 839; 822. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.08 (s, 3H, CH3); 3,24 (d, 1H, *J* = 19.2 Hz, Ha4´ or Hb4´); 3.65 (d, 1H, *J* = 19.2 Hz, Ha4´ or Hb4´); 7.57-7.60 (m, 2H, H-3´´ and H-5´´); 7.88-7.92 (m, 2H, H-2´´ and H-6´´); 8.36 (s, 1H, OH). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 15.1 (CH3); 48.3 (C-4´); 92.2 (q, *J* = 33.2 Hz, C-3´); 123.0 (q, *J* = 283.4 Hz, CF3); 128.3 (C-2´´ and C-6´´); 129.0 (C-3´´ and C-5´´); 129.3 (C-1´´); 134.9 (C-4´´); 155.8 (C-5´); 159.6 (C-2); 164.8 (C-5). HRMS (ESI) calc. for C13H10ClF3N4OSNa= 385.0114; found [M+Na]+ 385.0106.

**1.4 General procedure for preparation of 2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-1,3,4-thiadiazole (14a-d)**

The respective 5-methyl-1-(5-phenyl-1,3,4-thiadiazol-2-yl)-3-(trifluoromethyl)-4,5-dihydro-1*H*-pyrazol-5-ol (**13a-d**) (1.0 mmol) was dissolved in 5 mL of pyridine and the reaction was maintained at 0 oC and 1.5 mL of thionyl chloride was added slowly. The reaction mixture was stirred in room temperature for 12 h. The reactions were accompanied by TLC (CHCl3/MeOH 9:1). After detecting the end of the reaction, was added 22 mL of HCl 3 M, washed with water (30 mL) and extracted with chloroform (3 × 30 mL). The organic phase was dried (magnesium sulfate), filtered, and evaporated under vacuum. Compounds **14a-d** were obtained in 60-96% yield.

2-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-5-phenyl-1,3,4-thiadiazole **(14a)**. Yield: 96%. yellow solid. MP: 163-164 ºC. IR (cm-1): 3119; 2936; 2163; 1980; 1600; 1579; 1522; 1460; 1435; 1388; 1298; 1189; 1141; 1064; 1021; 951; 921; 839; 762; 688; 621; 587; 537. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.35 (s, 3H, CH3); 7.24 (s, 1H, H-4´); 7.55-7.61 (m, 3H, H-3´´, H-4´´ and H-5´´); 7.99-8.02 (m, 2H, H-2´´ and H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 13.4 (CH3); 112.7 (q, *J* = 2.7 Hz, C-4´); 119.1 (q, *J* = 267.9 Hz, CF3); 127.6 (C-4´´); 129.2 (C-3´´ and C-5´´); 129.7 (C-2´´ and C-6´´); 131.5 (C-1´´); 133.4 (q, *J* = 41.7 Hz, C-3´); 152.3 (C-5´); 161.0 (C-2), 167.0 (C-5). HRMS (ESI) calc. for C13H9F3N4SNa= 333.0398; found [M+Na]+ 333.0408.

2-(2-chlorophenyl)-5-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-1,3,4-thiadiazole **(14b)**. Yield: 60%. white solid. MP: 139-140 ºC. IR (cm-1): 3170; 3122; 2925; 2856; 2163; 1984; 1942; 1916; 1830; 1747; 1653; 1586; 1519; 1474; 1389; 1367; 1230; 1221; 1134; 1069; 982; 956; 841; 761; 729; 662; 526. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.40 (s, 3H, CH3); 6.75 (s, 1H, H-4´); 7.42-7.48 (m, 2H, H-4´´ and H-5´´); 7.53-7.56 (m, 1H, H-3´´); 8.41-8.43 (m, 1H, H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 13.5; 112.7-112.8 (m, C-4´); 119.1 (q, *J* = 267.7 Hz, CF3); 127.5 (C-5´´); 128.6 (C-6´´); 130.6 (C-3´´); 130.7 (C-4´´); 131.9 (C-2´´); 132.4 (C-1´´); 133.5 (q, *J =* 41.7 Hz, C-3´); 152.4 (C-5´); 162.2 (C-2); 162.7 (C-5). HRMS (ESI) calc. for C13H8ClF3N4SNa= 367.0008; found [M+Na]+ 366.9992.

2-(4-fluorophenyl)-5-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-1,3,4-thiadiazole **(14c)**. Yield: 79%. white solid. MP: 149-150 ºC. IR (cm-1): 3167; 3085; 2161; 2034; 1752; 1670; 1597; 1577; 1514; 1447; 1390; 1369; 1291; 1224; 1135; 1066; 983; 955; 817; 762; 667; 620; 584; 527. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.35 (s, 3H, CH3); 7.26 (s, 1H, H-4´); 7.41-7.47 (m, 2H, H-3´´ and H-5´´); 8.06-8.11 (m, 2H). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 13.0; 113.9-114.0 (m, C-4´); 116.7 (d, *J* = 22.3 Hz) (C-3´´ and C-5´´); 119.1 (q, *J* = 267.4 Hz, CF3); 125.7 (d, *J* = 3.0 Hz, C-1´´); 130.0 (d, *J* = 8.9 Hz, C-2´´ and C-6´´); 131.6 (q, *J* = 41.0 Hz, C-3´); 152.9 (C-5´); 161.0 (C-2); 164.0 (d, *J* = 248.7 Hz, C-4´´); 165.5 (C-5) (d, *J* = 21.7 Hz). HRMS (ESI) calc. for C13H8F4N4SNa= 351.0304; found [M+Na]+ 351.0298.

2-(4-chlorophenyl)-5-(5-methyl-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)-1,3,4-thiadiazole **(14d)**. Yield: 70%. brown solid. MP: 147-148 ºC. IR (cm-1): 3156; 3081; 2162; 1963; 1594; 1576; 1525; 1445; 1390; 1368; 1294; 1219; 1182; 1140; 1090; 1066; 981; 953; 852; 818; 777; 732; 656; 581; 538. 1H NMR (400 MHz, DMSO-d6, TMS, *δ* in ppm): 2.35 (s, 3H, CH3); 7.26 (s, 1H, H-4´); 7.64-7.67 (m, 2H, H-3´´ and H-5´´); 8.02-8.05 (m, 2H, H-2´´ and H-6´´). 13C NMR (100 MHz, DMSO-d6, TMS, *δ* in ppm): 13.0 (CH3); 114.0; 119.1 (q, *J* = 267.4 Hz) (CF3); 127.9 (C-2´´ and C-6´´); 129.*2* (C-3´´ and C-5´´); 129.6 (C-1´´); 131.6 (q, *J* = 41.4 Hz) (C-3´); 136.4 (C-4´´); 152.9 (C-5´); 161.2 (C-2); 165.4 (C-5). HRMS (ESI) calc. for C13H8ClF3N4SNa= 367.0008; found [M+Na]+ 367,0003.