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SUPPORTING INFORMATION

Title: A Novel and efficient one-pot strategy for the synthesis of 1,2,4-triazoles: An access to synthesis of Penipanoid A and its analogues.

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Contents

General information

Experimental Details

Copies of ^{1}H NMR and ^{13}C NMR Spectra of Compounds

LC-MS Data

General information:

The spectra were recorded with the following instruments: IR: Perkin-Elmer RX FT-IR spectrophotometer; ESIMS: VG-Auto spec micro mass spectrometer and HRMS: Hybrid MS system. ^{1}H NMR and ^{13} C NMR spectra were recorded on a 400 MHz, 500MHz and 100 MHz, 125 MHz spectrometers using the solvent peak as internal reference ($CDCl_3$, δ H: 7.26; δ C: 77.0, DMSO-d6). Data are reported in the following order: chemical shift (δ) in ppm; multiplicities are indicated s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constants *(J)* are in Hz. All reactions were monitored by thin-layer chromatography (TLC) using silica gel F_{254} pre-coated plates. Visualization was accomplished with UV-light or I_2 stain. Solvents for the catalytic reactions were technical grade. Solvents for chromatography (EtOAc, hexane) were technical grade and distilled prior to use. Melting points were determined on a Fischer-Johns melting point apparatus.

Experimental Details:

A. Typical procedure for synthesis of Penipanoid A (4a): [1]

To a stirred solution of 4-Hydroxyphenylacetic acid **1** (200 mg, 1.33 mmol, 1.0 equiv.) in DMF (5.0 mL) was added DIPEA (0.69 mL, 3.99 mmol, 3.0 equiv.) followed by the addition of formamidine hydrochloride **2** (160.0 mg, 1.97 mmol, 1.5 equiv.) and HATU (549.79 mg, 1.44 mmol, 1.1 equiv.) in a round bottom flask. The reaction was stirred at room temperature for 18 h and reaction was monitored by LC-MS and TLC for consumption of starting materials and formation of acylamidine intermediate **3**. After formation of the intermediate (18 h), 2-hydrazinylbenzoic acid hydrochloride (371.88 mg, 1.97 mmol, 1.5 equiv.) and acetic acid (0.75 mL, 13.14 mmol, 10.0 equiv.) were added and the reaction mixture was heated at 80 ^{o}C for 3 h and the reaction was monitored by LC-MS analysis for consumption of acylamidine intermediate as well formation of the product. After 3 h, the reaction was cooled to room temperature, diluted with EtOAc (20.0 mL) and work up with water (100 mL) and brine solution. The organic layer was collected and dried over $MgSO_4$, filtered and concentrated under reduced pressure. The

crude product was purified by flash column chromatography (CH_2Cl_2/MeOH: 100:0 to 9:1) to afford the Penipanoid A (287 mg, 74%) as a colorless crystalline solid.

B. General experimental procedure for gram scale synthesis of Penipanoid A (4a) :

To a stirred solution of 4-Hydroxy phenyl acetic acid 1 (0.5 g, 3.28 mmol, 1.0 equiv.) in DMF (10 mL) was added DIPEA (1.23 mL, 9.84 mmol, 3.0 equiv.) followed by the addition of formamidine hydrochloride **2** (395 mg, 4.93 mmol, 1.5 equiv.) and HATU (1.37 g, 3.6 mmol, 1.1 equiv.) in a round bottom flask. The reaction was stirred at room temperature and monitored by TLC for consumption of starting materials and formation of acylamidine intermediate **3**. After formation of the intermediate (18 h), 2-hydrazinylbenzoic acid hydrochloride (0.927 g, 4.93 mmol, 1.5 equiv.) and acetic acid (1.96 mL, 32.8 mmol, 10.0 equiv.) were added and the reaction mixture was heated at 80 ^oC and monitored by LC-MS analysis for consumption of acylamidine intermediate and formation of the product. After 3 h, the reaction was cooled to room temperature, diluted with EtOAc (50.0 mL) and washed with water (100 mL) and brine solution. The organic layer was collected and dried ($MgSO_4$), filtered and concentrated. The crude material was purified by flash column chromatography (CH_2Cl_2/MeOH: 100-0 to 90-10%) to afford the Penipanoid A (717 mg, 74%) as a colorless crystalline solid.

C. Analytical Data

2-(5-(4-hydroxybenzyl)-1H-1,2,4-triazol-1-yl) benzoic acid (4a):

Colorless solid; M.P. = 210-213 °C; FT-IR (KBr): *v* max = 3456, 2967, 2944, 1727, 1468, 1373, 1222, 1043, 703.; ^{1}H NMR (500 MHz, DMSO-d_6): δ 13.11 (brs, 1H), 9.25 (brs, 1H), 7.96 (d, J = 6.6 Hz, 2H), 7.66 (ddd, J = 6.5, 3.8, 1.9 Hz, 2H), 7.43–7.19 (m, 1H), 6.83 (d, J = 8.3 Hz, 2H), 6.59 (d, J = 8.4 Hz, 2H), 3.83 (s, 2H).; ^{13}C NMR (125 MHz, DMSO-*d* 6): δ 166.14, 155.91, 155.47, 150.56, 135.80, 132.25, 130.76, 129.96, 129.61, 128.52, 126.12, 114.99, 30.85.; LCMS: *m* /*z*: 296.1[M + H]; HRMS: found: *m* /*z* 296.1085, calcd. for $C_{16}H_{13}N_3O_3$: [M + H] 296.0990.

4-((1-cyclohexyl-1H-1,2,4-triazol-5-yl) methyl) phenol (4b):

Colorless solid; M.P. = 208-210 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.29 (s, 1H), 7.80 (s, 1H), 7.01 (d, J = 8.2 Hz, 2H), 6.68 (d, J = 8.4 Hz, 2H), 4.20 (tt, J = 11.2, 4.1 Hz, 1H), 4.06 (s, 2H), 1.81-1.46 (m, 7H), 1.40-1.03 (m, 3H).; ^{13}C NMR (100 MHz, DMSO-d_6): δ 155.97, 153.24, 149.84, 129.38, 126.80, 115.27, 56.04, 32.28, 30.19, 24.73, 24.68.; LCMS: *m* /*z*: 258.34 [M + H].

4-((1-(4-chlorophenyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4c):

Light yellow solid; M.P. = 196-200 °C.; ^{1}H NMR (400 MHz, DMSO): δ 9.32 (s, 1H), 8.09 (s, 1H), 7.68-7.56 (m, 2H), 7.56-7.43 (m, 2H), 6.96-6.78 (m, 2H), 6.72-6.52 (m, 2H), 4.08 (s, 2H).; 13C NMR (100 MHz, DMSO): δ 156.03, 154.85, 151.15, 135.94, 133.37, 129.46, 129.42, 126.71, 125.98, 115.22, 30.92.; LCMS: m /z: 286.73 [M + H].

4-((1-(p-tolyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4d):

Light yellow solid; M.P. = 180-185 °C.; ^{1}H NMR (500 MHz, DMSO) δ 9.28 (s, 1H), 8.05 (s, 1H), 7.34 (m, 4H), 6.89-6.83 (m, 2H), 6.67-6.60 (m, 2H), 4.03 (s, 2H), 2.38 (s, 3H).; 13C NMR (125 MHz, DMSO): δ 155.99, 154.50, 150.87, 138.61, 134.66, 130.05, 129.85, 129.61, 129.38, 126.30, 124.86, 115.21, 30.85, 20.75.; LCMS: m /z: 266.32 [M + H].

4-((1-(3-bromophenyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4e):
Brown solid; M.P. = 219-223 °C.; ^{1}H NMR (500 MHz, DMSO): δ 9.30 (s, 1H), 8.11 (s, 1H), 7.71 (dq, *J* = 6.9, 3.5 Hz, 2H), 7.58-7.43 (m, 2H), 6.96-6.80 (m, 2H), 6.74-6.55 (m, 2H), 4.11 (s, 2H).; ^{13}C NMR (125 MHz, DMSO) δ 156.03, 154.91, 151.20, 138.33, 131.77, 131.31, 129.45, 127.58, 125.95, 123.97, 121.78, 115.23, 31.03.; LCMS: m /z: 331.19 [M + H].

4-((1-(4-methoxyphenyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4f):
Off white solid; M.P. = 220-224 °C.; ^{1}H NMR (400 MHz, DMSO): δ 9.27 (s, 1H), 8.02 (s, 1H), 7.47-7.27 (m, 2H), 7.17-6.98 (m, 2H), 6.85 (d, *J* = 8.1 Hz, 2H), 6.64 (dd, *J* = 6.7, 4.6 Hz, 2H), 4.00 (s, 2H), 3.82 (s, 3H).; ^{13}C NMR (100 MHz, DMSO): δ 159.37, 155.96, 154.57, 150.71, 129.95, 129.35, 126.59, 126.30, 115.19, 114.47, 55.49, 30.78.; LCMS: m /z: 282.32 [M + H].

4-((1-(5-chloropyridin-2-yl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4g):
Off-white solid; M.P. = 190-194 °C.; 1H NMR (400 MHz, DMSO): δ 9.23 (s, 1H), 8.78-8.52 (m, 1H), 8.28-8.02 (m, 2H), 7.83 (d, *J* = 8.7 Hz, 1H), 7.00 (d, *J* = 8.0 Hz, 2H), 6.74-6.48 (m, 3H), 4.47 (s, 2H).; ^{13}C NMR (100 MHz, DMSO): δ 155.96, 155.93, 153.00, 152.81, 151.28, 149.73, 148.84, 146.63, 139.53, 129.96, 129.84, 126.50, 117.82, 115.64, 115.09, 32.53.; LCMS: m /z: 287.72 [M + H].

4-((1-([1,1'-biphenyl]-4-yl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4h):

Off white solid; M.P. = 170-173 °C.; ^{1}H NMR (400 MHz, DMSO): δ 9.33 (s, 1H), 8.10 (s, 1H), 7.84 (d, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 7.6 Hz, 2H), 7.61-7.35 (m, 5H), 6.91 (d, *J* = 8.0 Hz, 2H), 6.65 (d, *J* = 8.0 Hz, 2H), 4.12 (s, 2H).; ^{13}C NMR (100 MHz, DMSO): δ 156.05, 154.67, 151.09, 140.52, 138.79, 136.31, 129.44, 129.06, 128.88, 127.99, 127.60, 127.06, 126.83, 126.26, 126.21, 125.33, 115.25, 30.99.; LCMS: m /z: 328.39 [M + H].

4-((1-(pyrimidin-2-yl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4i):

Light yellow solid; M.P. = 197-200 °C; ^{1}H NMR (500 MHz, DMSO): δ 9.25 (s, 1H), 8.97 (d, *J* = 4.8 Hz, 2H), 8.13 (s, 1H), 7.61 (t, *J* = 4.9 Hz, 1H), 7.06-6.86 (m, 2H), 6.69-6.50 (m, 2H), 4.46 (s, 2H).; ^{13}C NMR (125 MHz, DMSO): δ 159.44, 156.93, 155.92, 155.19, 151.16, 129.74, 126.48, 120.84, 115.06, 32.55.; LCMS: m /z: 254.27 [M + H].

4-((1-benzyl-1H-1,2,4-triazol-5-yl) methyl) phenol (4j):

Off white solid; M.P. = 155-158 °C.; ^{1}H NMR (400 MHz, DMSO): δ 9.29 (s, 1H), 7.87 (s, 1H), 7.38-7.19 (m, 3H), 7.16-7.04 (m, 2H), 7.04-6.91 (m, 2H), 6.73-6.56 (m, 2H), 5.35 (s, 2H), 4.06 (s, 2H).; ^{13}C NMR (100 MHz, DMSO): δ 156.06, 154.64, 150.44, 136.22, 129.59, 128.50, 127.67, 127.45, 126.39, 115.21, 50.97, 30.17.; LCMS: m /z: 266.32 [M + H].

4-((1-(thiazol-2-yl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4k):

Light yellow solid; M.P. = 165-168 °C.; ^{1}H NMR (500 MHz, DMSO): δ 9.30 (s, 1H), 8.17 (s, 1H), 7.78 (d, *J* = 3.5 Hz, 1H), 7.72 (d, *J* = 3.5 Hz, 1H), 7.07 (d, *J* = 8.0 Hz, 2H), 6.66 (d, *J* = 8.1 Hz, 2H), 4.54 (s, 2H).; ^{13}C NMR (125 MHz, DMSO): δ 158.43, 156.12, 155.55, 151.88, 140.67, 129.85, 125.95, 119.58, 115.17, 31.74.; LCMS: m /z: 259.30 [M + H].

4-((1-(5-(trifluoromethyl) pyridin-2-yl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4l):

Light yellow solid; M.P. = 180-184 °C.; ^{1}H NMR (500 MHz, DMSO): δ 9.26 (s, 1H), 8.87 (d, *J* = 5.1 Hz, 1H), 8.20 (s, 1H), 8.08 (s, 1H), 7.88 (dd, *J* = 5.2, 1.5 Hz, 1H), 7.15-6.93 (m, 2H), 6.78-6.53 (m, 2H), 4.53 (s, 2H).; ^{13}C NMR (125 MHz, DMSO): δ 156.35, 155.97, 151.50, 151.14, 150.26, 139.61 (q, $J_{C,\,F}$ = 33.75 Hz), 129.87, 126.39, 125.62, 123.44, 121.27, 118.72 (q, $J_{C,\,F}$ = 3.75 Hz), 115.07, 111.86 (q, $J_{C,\,F}$ = 3.75 Hz), 32.74.; LCMS: m /z: 321.28 [M + H].

Benzyl 4-(5-(4-hydroxybenzyl)-1H-1,2,4-triazol-1-yl) piperidine-1-carboxylate (4m):

Off white solid; M.P. = 200-203 °C.; ^{1}H NMR (400 MHz, DMSO): δ 9.30 (s, 1H), 7.84 (s, 1H), 7.49-7.22 (m, 5H), 7.04 (d, *J* = 8.3 Hz, 2H), 6.80-6.59 (m, 2H), 5.09 (s, 2H), 4.55 (tt, *J* = 11.3, 4.1 Hz, 1H), 4.07 (d, *J* = 17.2 Hz, 4H), 2.93 (s, 2H), 1.76 (qd, *J* = 12.3, 4.3 Hz, 2H), 1.65-1.50 (m, 2H).; ^{13}C NMR (100 MHz, DMSO): δ 156.03, 154.34, 153.72, 150.15, 136.89, 129.47, 128.41, 127.82, 127.51, 126.65, 115.31, 66.27, 53.77, 42.46, 31.34, 30.07.; LCMS: m /z: 393.46 [M + H].

4-((1-(2-(trifluoromethoxy) phenyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4n):

Light yellow solid; M.P. = 186-189 °C.; ^{1}H NMR (500 MHz, DMSO): δ 9.26 (s, 1H), 8.13 (s, 1H), 7.75-7.68 (m, 1H), 7.66-7.60 (m, 1H), 7.59-7.54 (m, 2H), 6.87-6.73 (m, 2H), 6.68-6.49 (m, 2H), 3.88 (s, 2H).; ^{13}C NMR (125 MHz, DMSO): δ 156.05 (d, $J_{C,\,F}$ = 6.25 Hz), 156.03, 151.50, 143.20, 132.02, 129.59, 129.41, 129.30, 128.34, 125.57, 121.74, 120.65, 118.59, 116.53, 115.08, 30.60.; LCMS: m /z: 336.29 [M + H].

4-((1-(2,4-difluorophenyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4o):

Off white solid; M.P. = 203-205 °C.; ^{1}H NMR (500 MHz, DMSO): δ 9.28 (s, 1H), 8.13 (s, 1H), 7.63 (td, *J* = 8.8, 5.9 Hz, 1H), 7.56 (ddd, *J* = 10.4, 9.0, 2.8 Hz, 1H), 7.29 (tt, *J* = 8.8, 2.1 Hz, 1H), 6.87-6.70 (m, 2H), 6.67-6.52 (m, 2H), 3.93 (s, 2H).; ^{13}C NMR (125 MHz, DMSO): δ 163.64 (d, $J_{C,\,F}$ = 12.5 Hz), 161.64 (d, $J_{C,\,F}$ = 12.5 Hz), 157.76, 156.40, 156.02, 155.75, 151.60, 130.51 (d, $J_{C,\,F}$ = 11.25 Hz), 129.39, 125.56, 121.43 (d, $J_{C,\,F}$ = 8.75 Hz), 115.12, 112.57 (d, $J_{C,\,F}$ = 5.0 Hz), 112.39 (d, $J_{C,\,F}$ = 5.0 Hz), 105.43 (q, $J_{C,\,F}$ = 25.0 Hz), 30.60.; LCMS: m /z: 288.27 [M + H].

2-(5-benzyl-1H-1,2,4-triazol-1-yl) benzoic acid (5a):

Colorless solid; M.P. = 220-223 °C;, ^{1}H NMR (500 MHz, DMSO): δ 1H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.98 (s, 1H), 7.66-7.44 (m, 2H), 7.13 (qd, *J* = 6.2, 1.7 Hz, 4H), 6.95 (dd, *J* = 6.7, 2.8 Hz, 2H), 5.57 (s, 1H), 3.99 (s, 2H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.75, 149.97, 136.12, 135.06, 132.76, 132.03, 130.31, 128.85, 128.75, 128.56, 126.97, 77.32, 77.00, 76.68, 32.21, 29.68.; LCMS: m /z: 280.30 [M + H].

2-(5-(4-methoxybenzyl)-1H-1,2,4-triazol-1-yl) benzoic acid (5b):

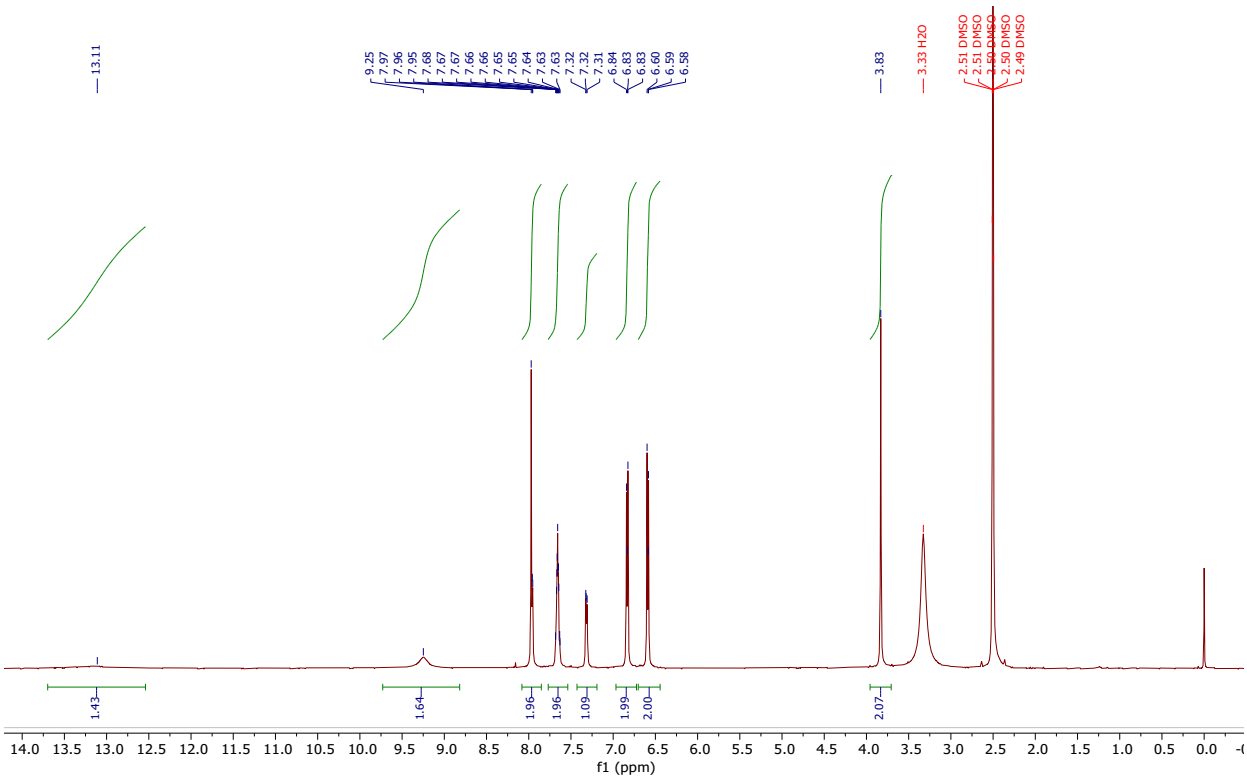
Off white solid; M.P. = 218-220 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 7.4, 2.0 Hz, 1H), 7.98 (s, 1H), 7.70-7.48 (m, 2H), 7.23-7.04 (m, 1H), 6.86 (d, *J* = 8.1 Hz, 2H), 6.68 (d, *J* = 8.6 Hz, 2H), 6.51 (s, 1H), 3.93 (s, 2H), 3.70 (s, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.65, 158.46, 155.97, 149.61, 136.08, 132.72, 132.03, 130.29, 129.80, 129.25, 128.87, 126.99, 113.95, 77.32, 77.00, 76.68, 55.18, 31.25.; LCMS: m /z: 310.33 [M + H].

2-(5-(4-methylbenzyl)-1H-1,2,4-triazol-1-yl) benzoic acid (5c):

Off white solid; M.P. = 215-218 °C; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.14 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.98 (s, 1H), 7.67-7.50 (m, 2H), 7.14 (dd, *J* = 7.6, 1.5 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.1 Hz, 2H), 3.95 (s, 2H), 2.23 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.68, 155.87, 149.66, 136.52, 136.08, 132.74, 132.03, 131.88, 130.27, 129.21, 128.90, 128.60, 77.25, 77.00, 76.75, 31.68, 20.97.; LCMS: m /z: 294.33 [M + H].

Copies of ^{1}H NMR and ^{13}C NMR Spectra of Compounds

2-(5-(4-hydroxybenzyl)-1H-1,2,4-triazol-1-yl) benzoic acid (4a)



FigureS1. 1HNMR spectrum of 4a (400 MHz, DMSO-d6)

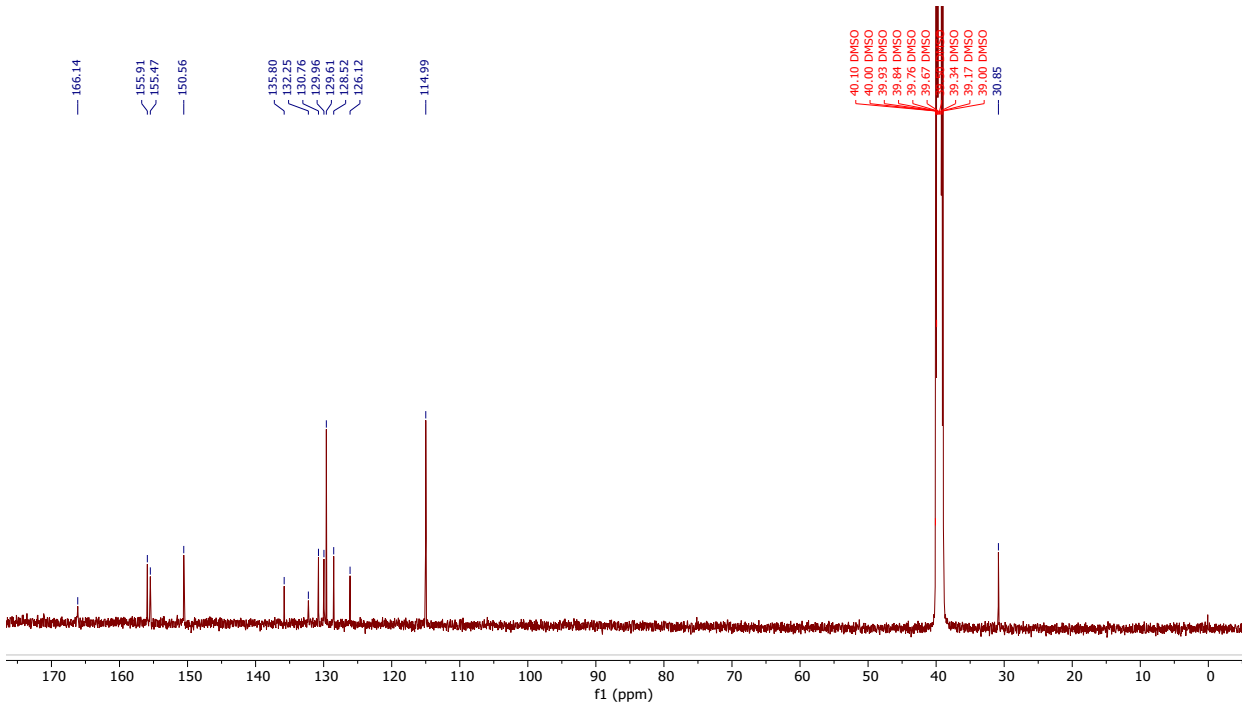
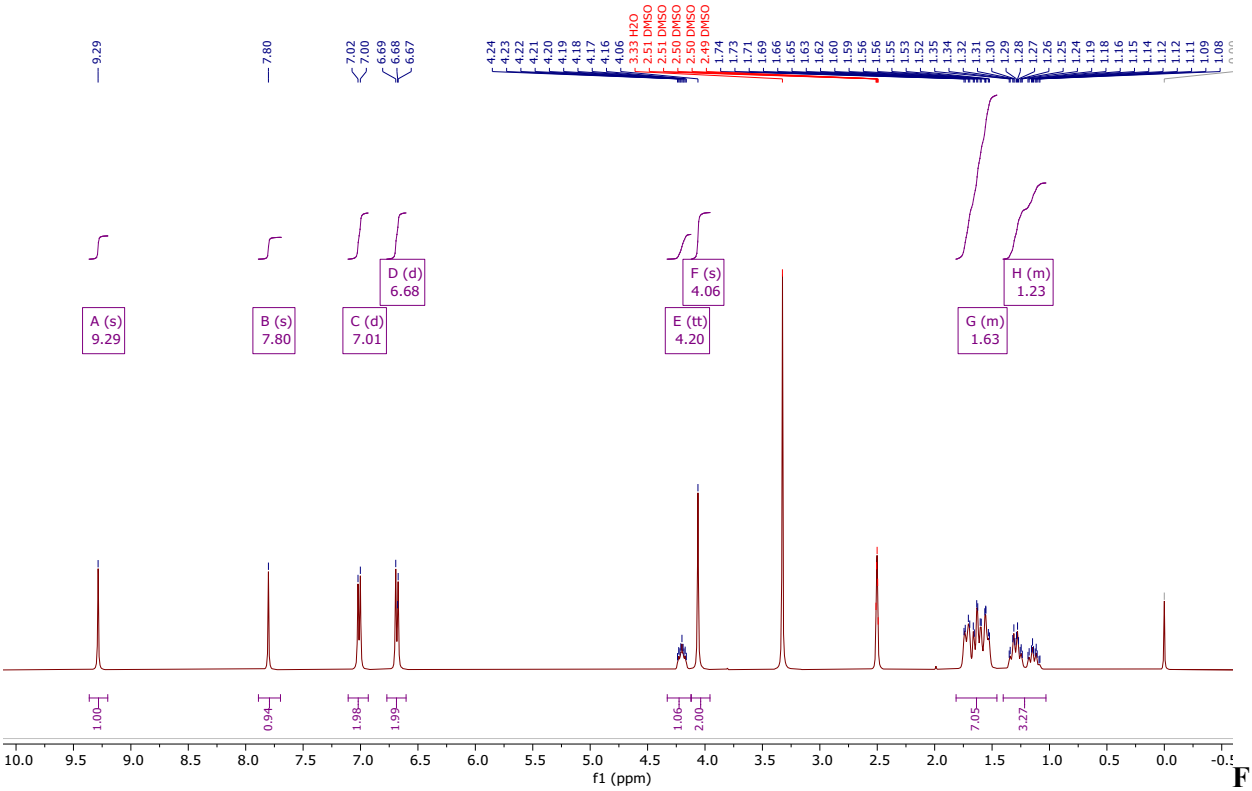


Figure S2. 13CNMR spectrum of 4a (100 MHz, DMSO-d6)

4-((1-cyclohexyl-1H-1,2,4-triazol-5-yl) methyl) phenol (4b):



FigureS3. 1HNMR spectrum of 4b (400 MHz, DMSO-d6)

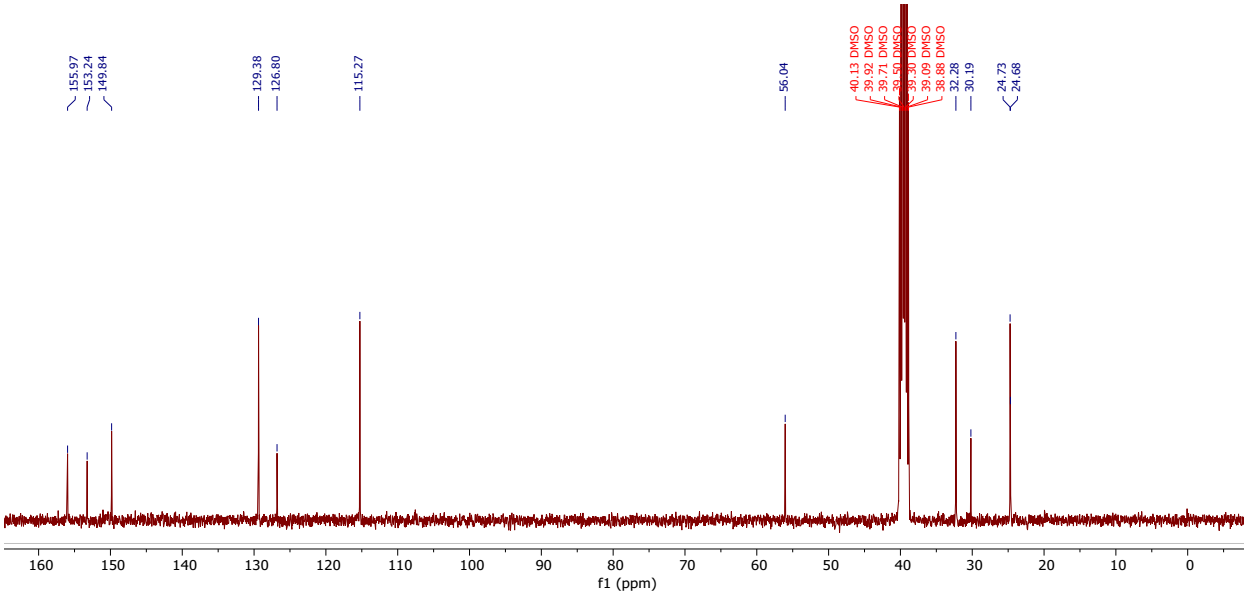


Figure S4. 13CNMR spectrum of 4b (100 MHz, DMSO-d6)

4-((1-(4-chlorophenyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4c):

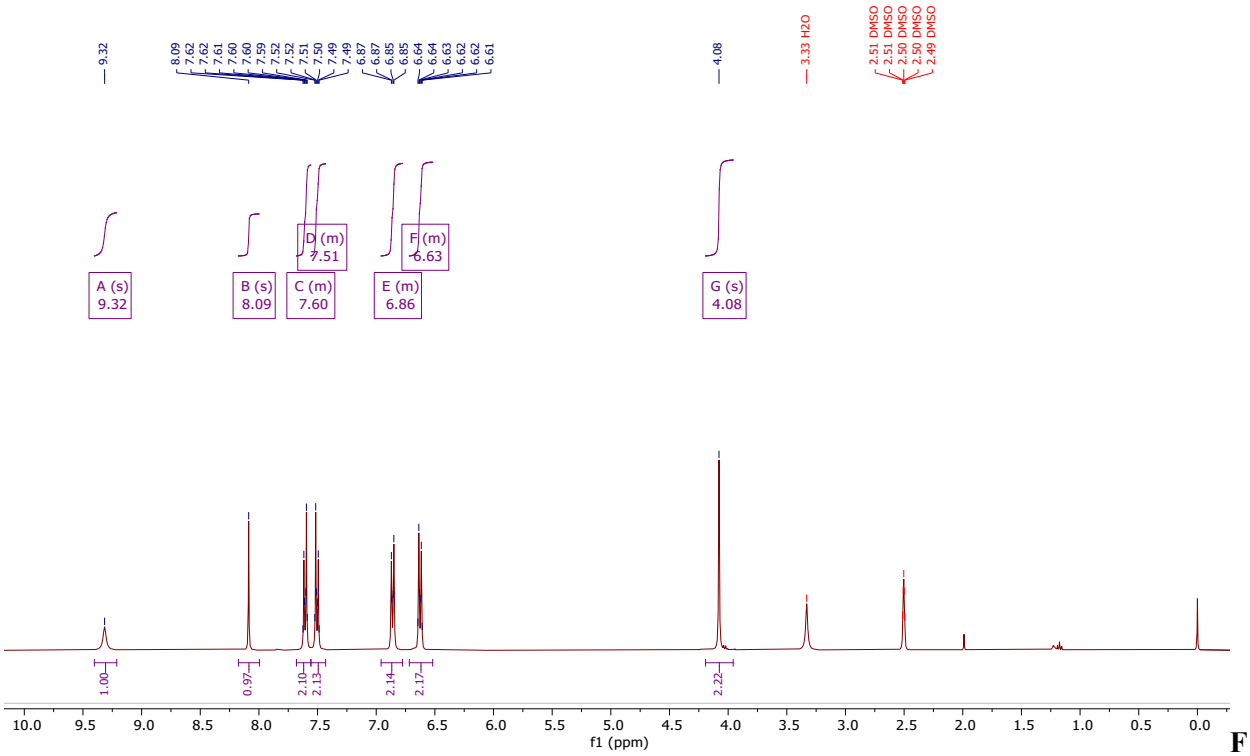


Figure S5. 1HNMR spectrum of 4c (400 MHz, DMSO-d6)

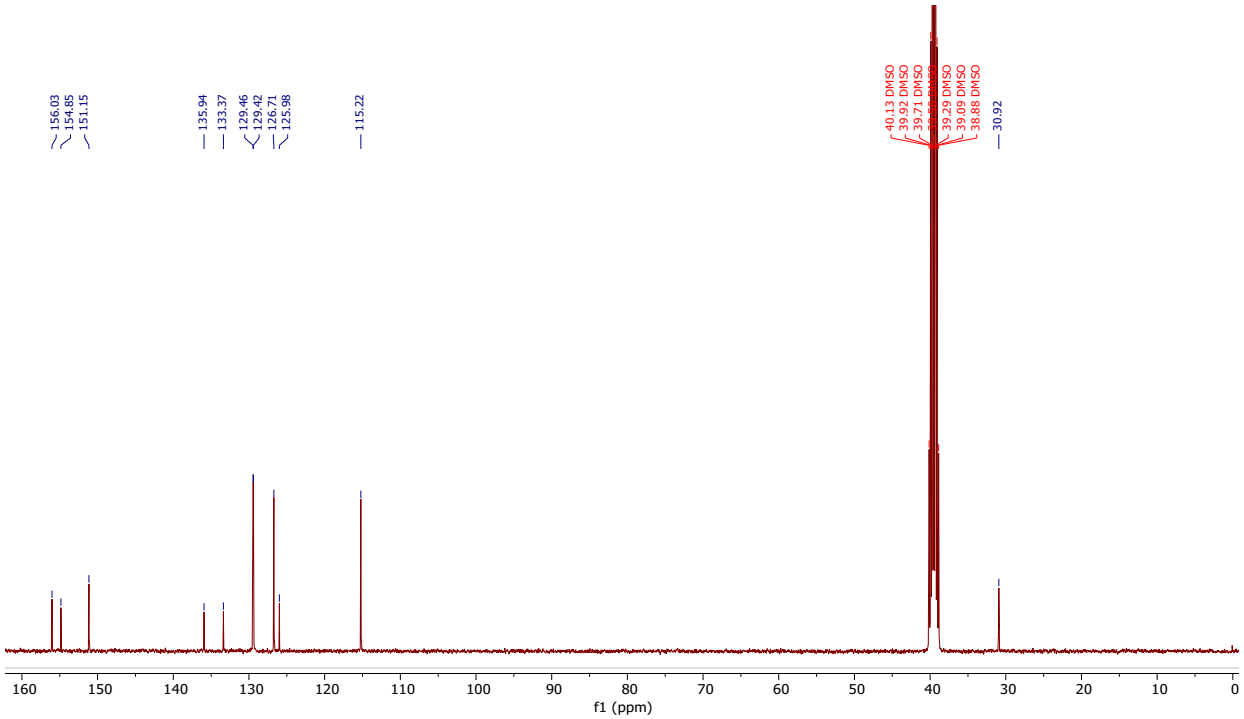


Figure S6. 13CNMR spectrum of 4c (100 MHz, DMSO-d6)

4-((1-(p-tolyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4d)

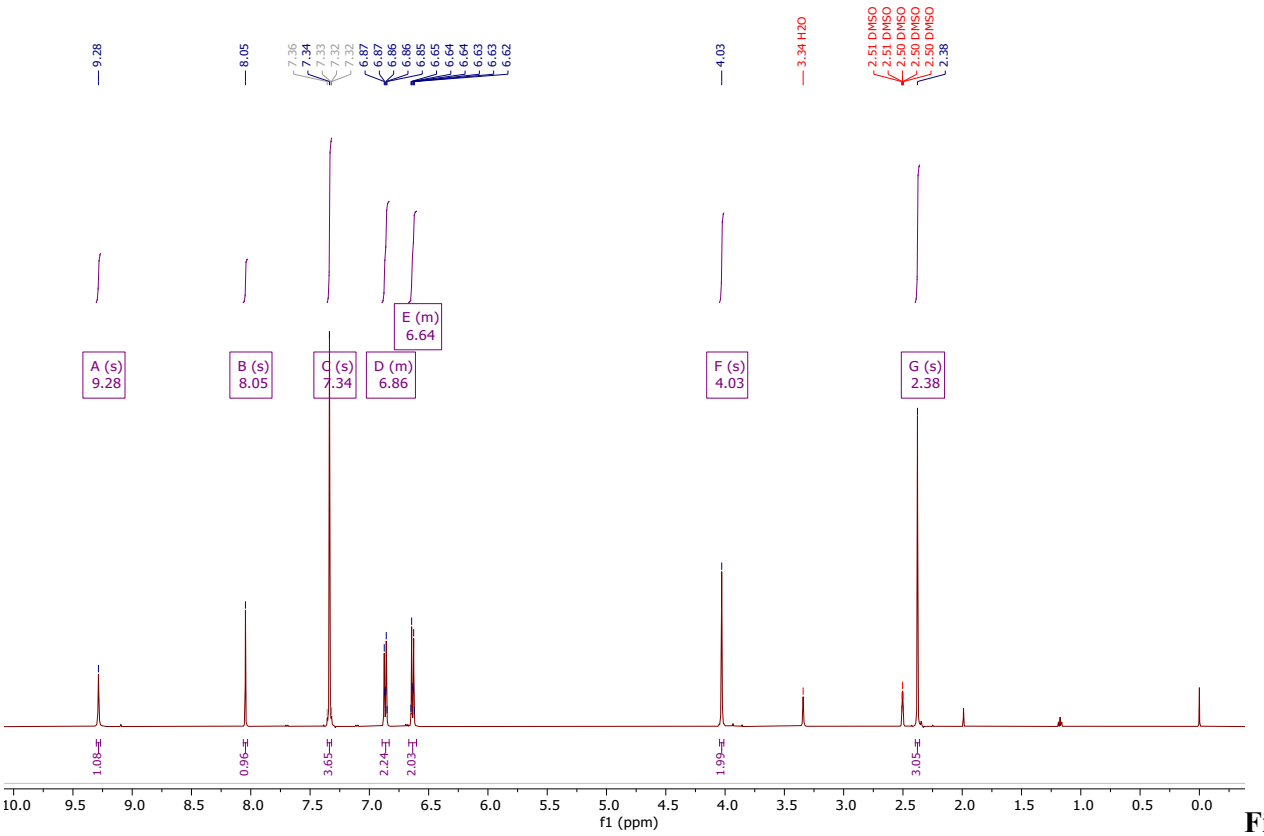


Fig ureS7. 1HNMR spectrum of 4d (500 MHz, DMSO-d6)

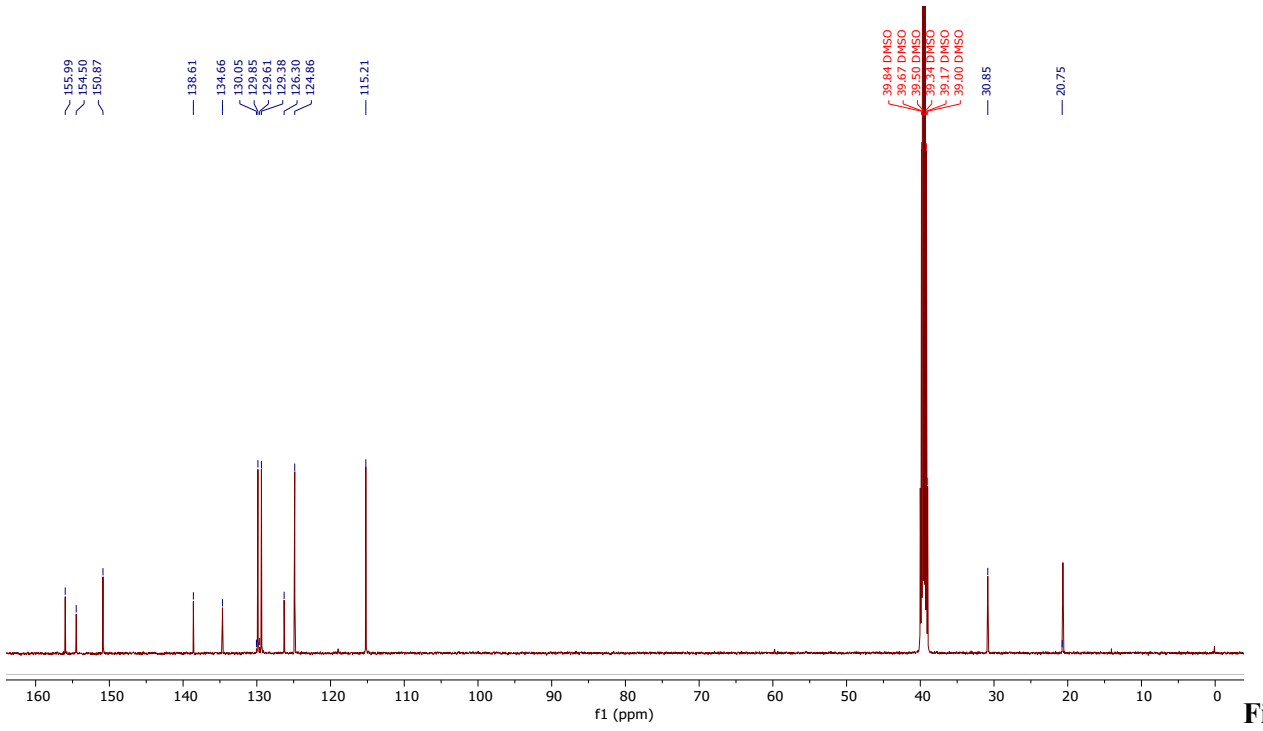


Fig ureS8. 13CNMR spectrum of 4d (125 MHz, DMSO-d6)

4-((1-(4-methoxyphenyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4e):

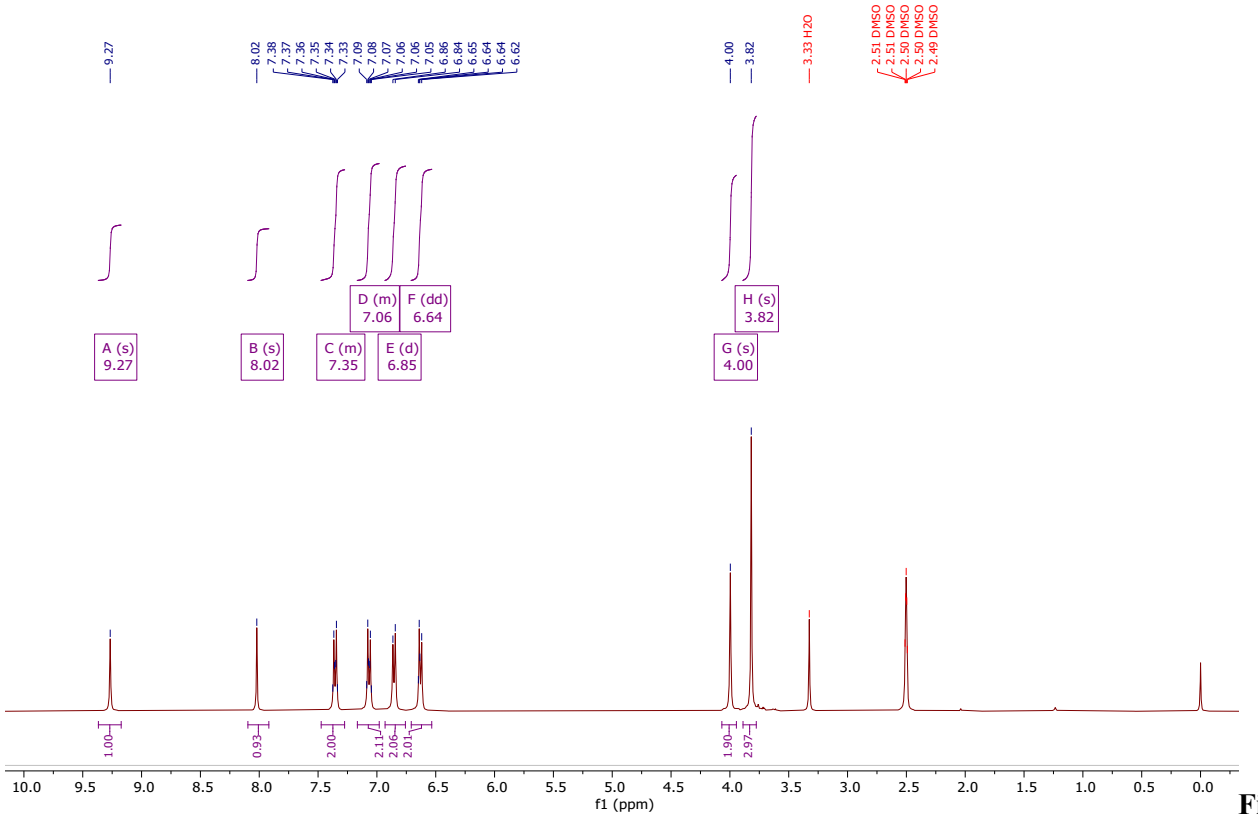
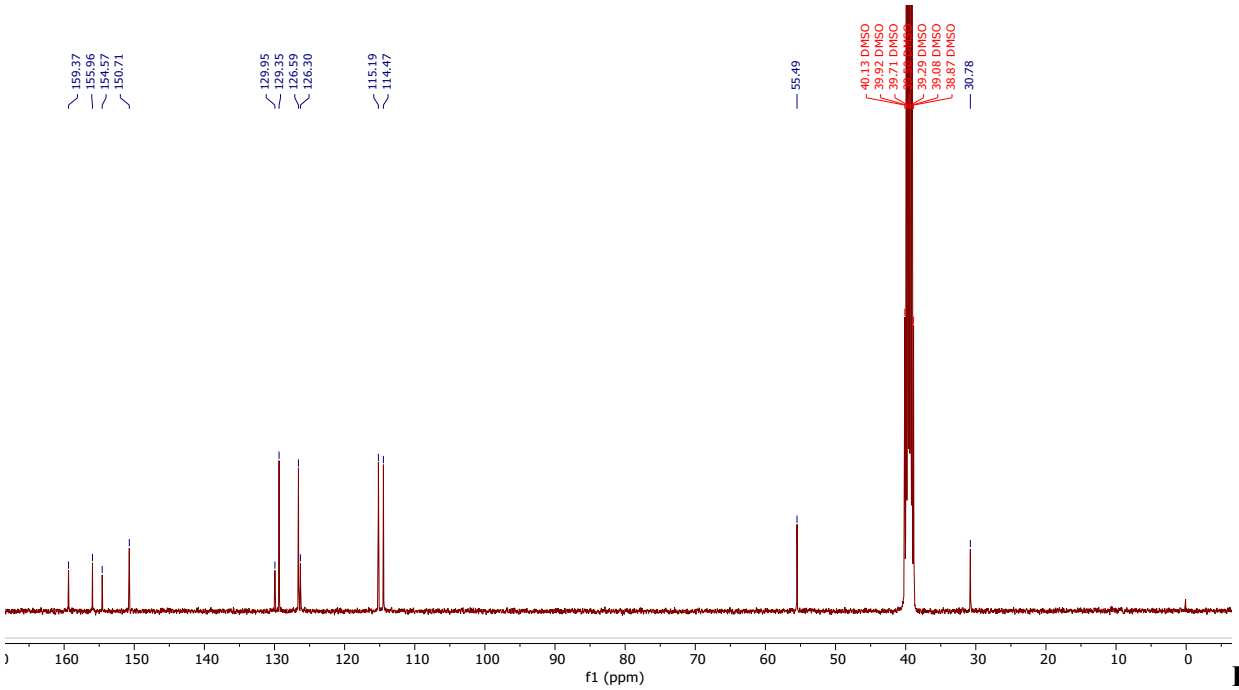
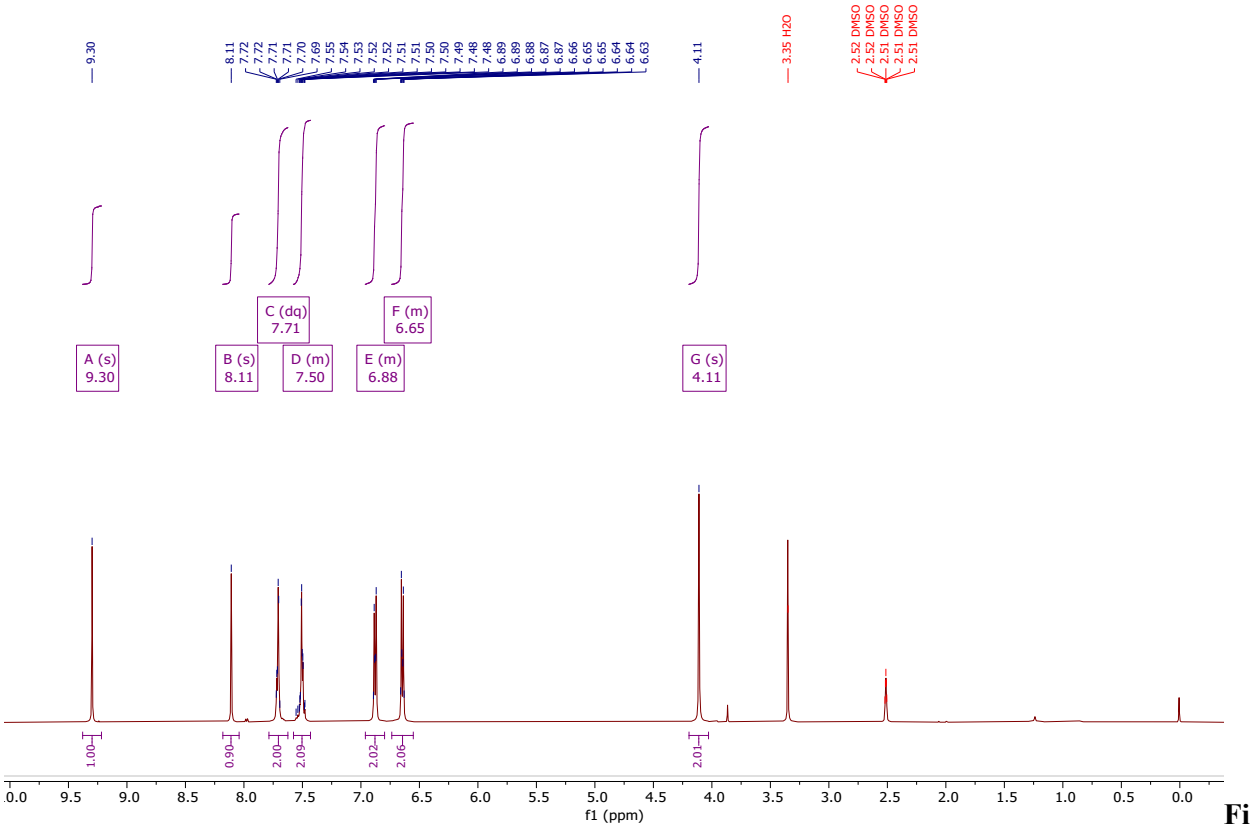


Fig ureS9. 1HNMR spectrum of 4e (400 MHz, DMSO-d6)

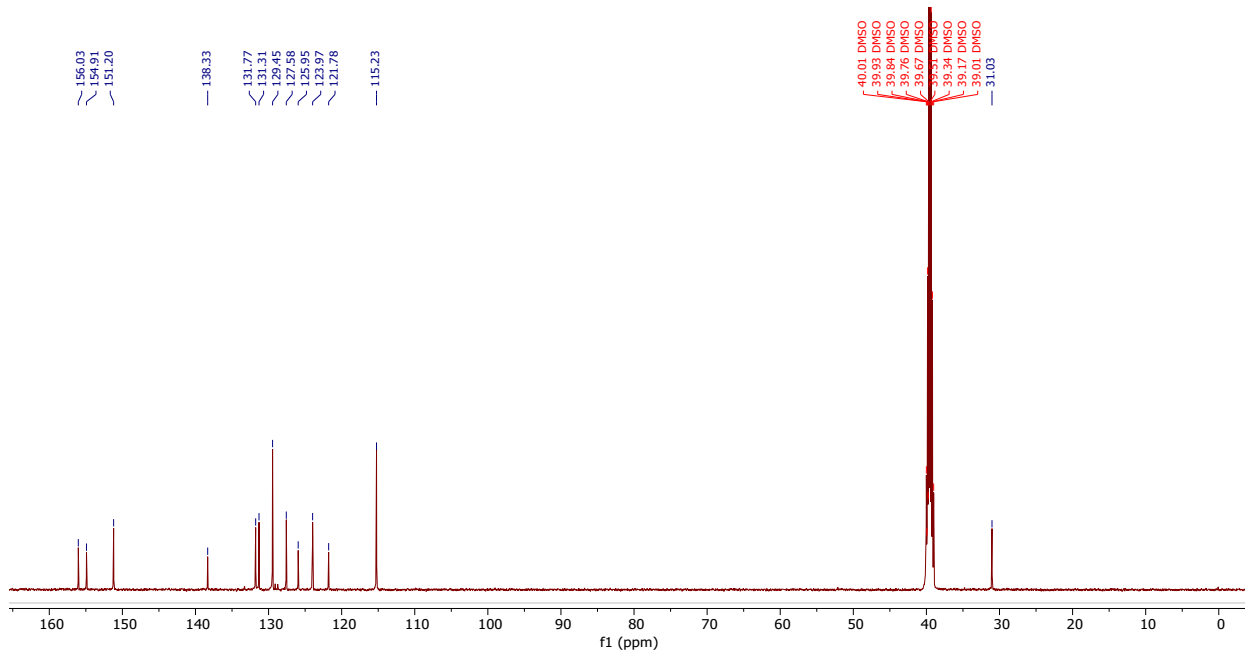


Figu re S10. 13CNMR spectrum of 4e (100 MHz, DMSO-d6)

4-((1-(3-bromophenyl)-1H-1,2,4-triazol-5-yl)methyl)phenol (4f):

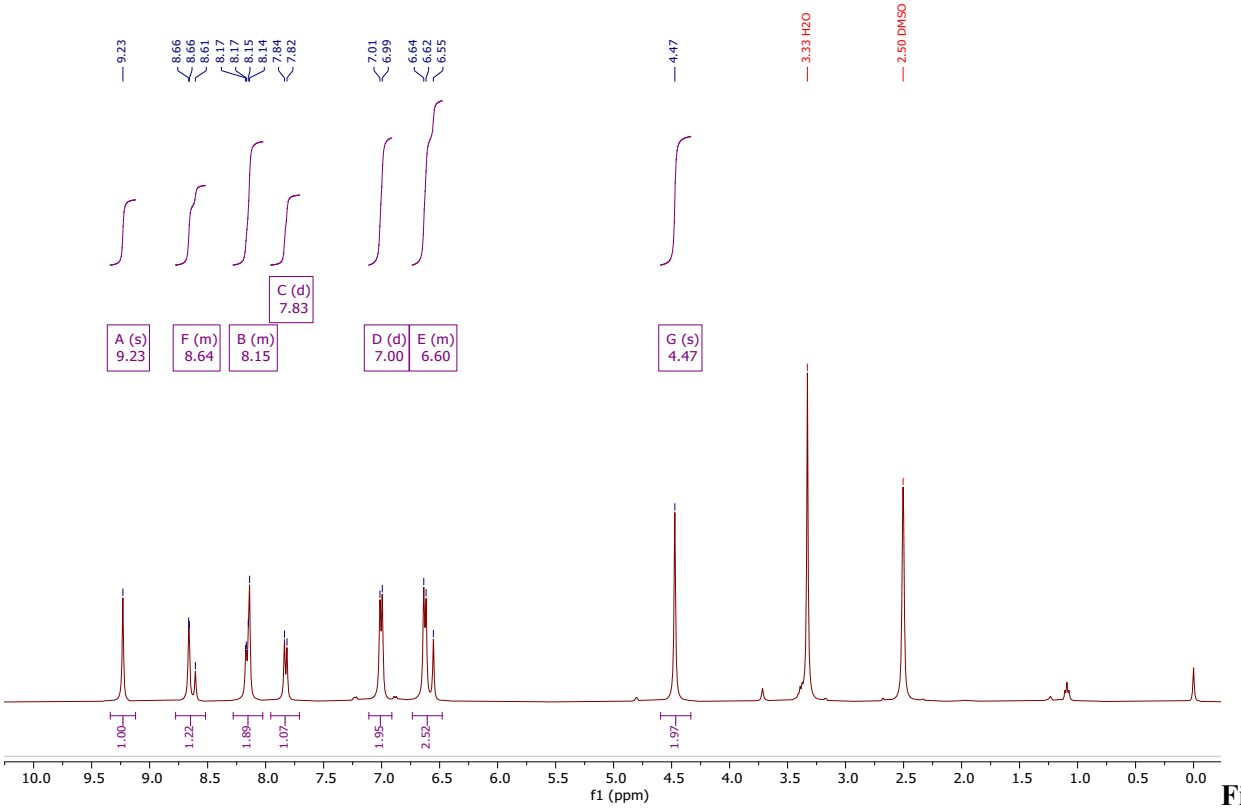


Fi gureS11. 1HNMR spectrum of 4f (500 MHz, DMSO-d6)

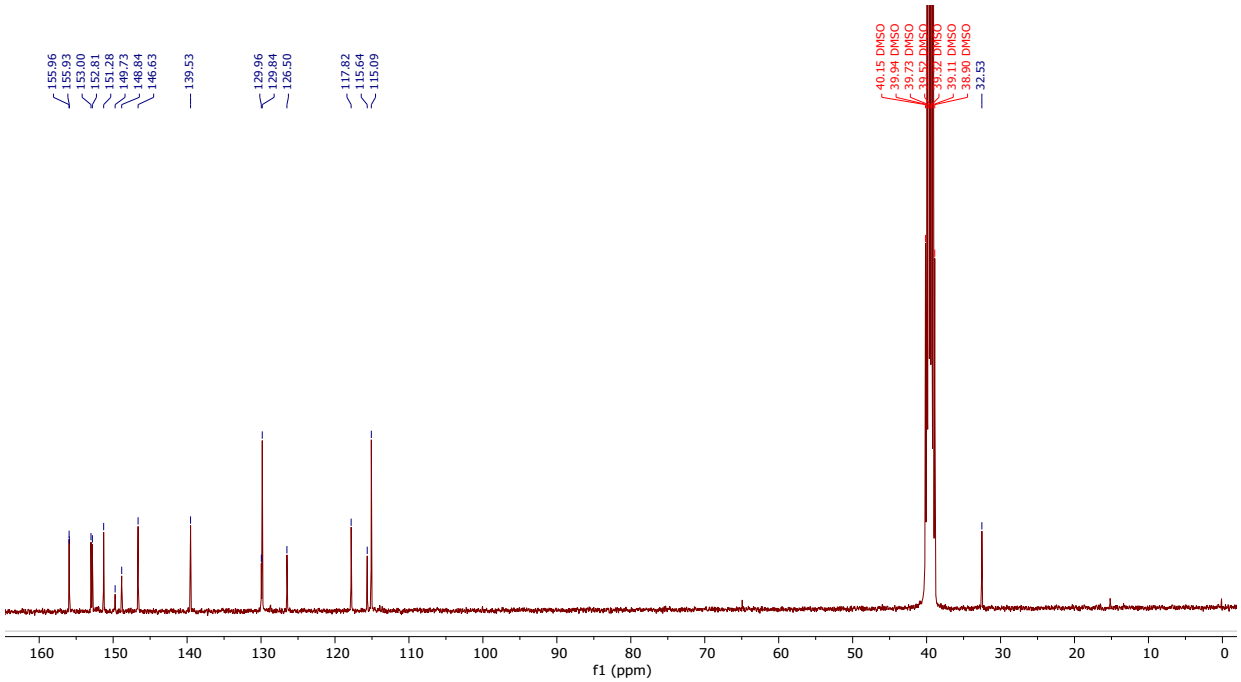


FigureS12. 13CNMR spectrum of 4f (125 MHz, DMSO-d6)

4-((1-(5-chloropyridin-2-yl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4g):

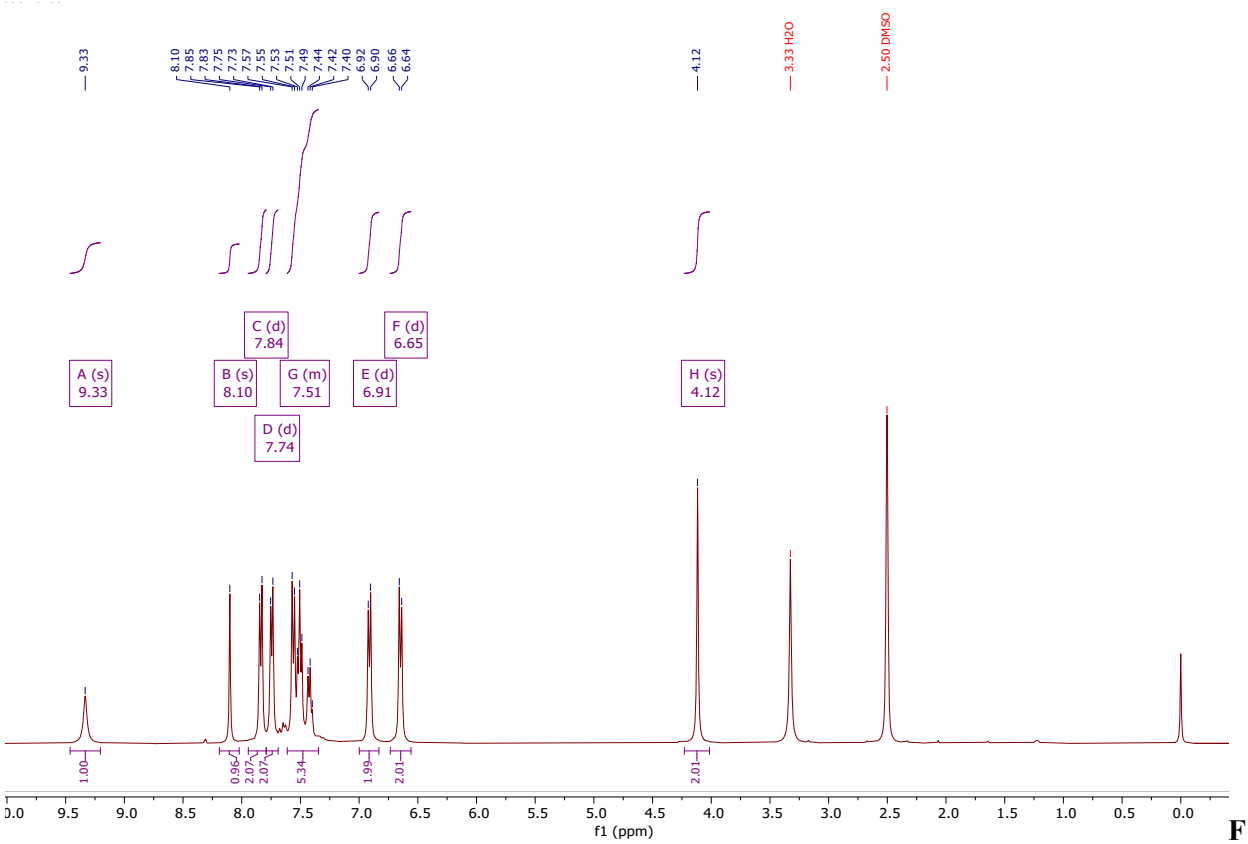


FigureS13. 1HNMR spectrum of 4g (400 MHz, DMSO-d6)

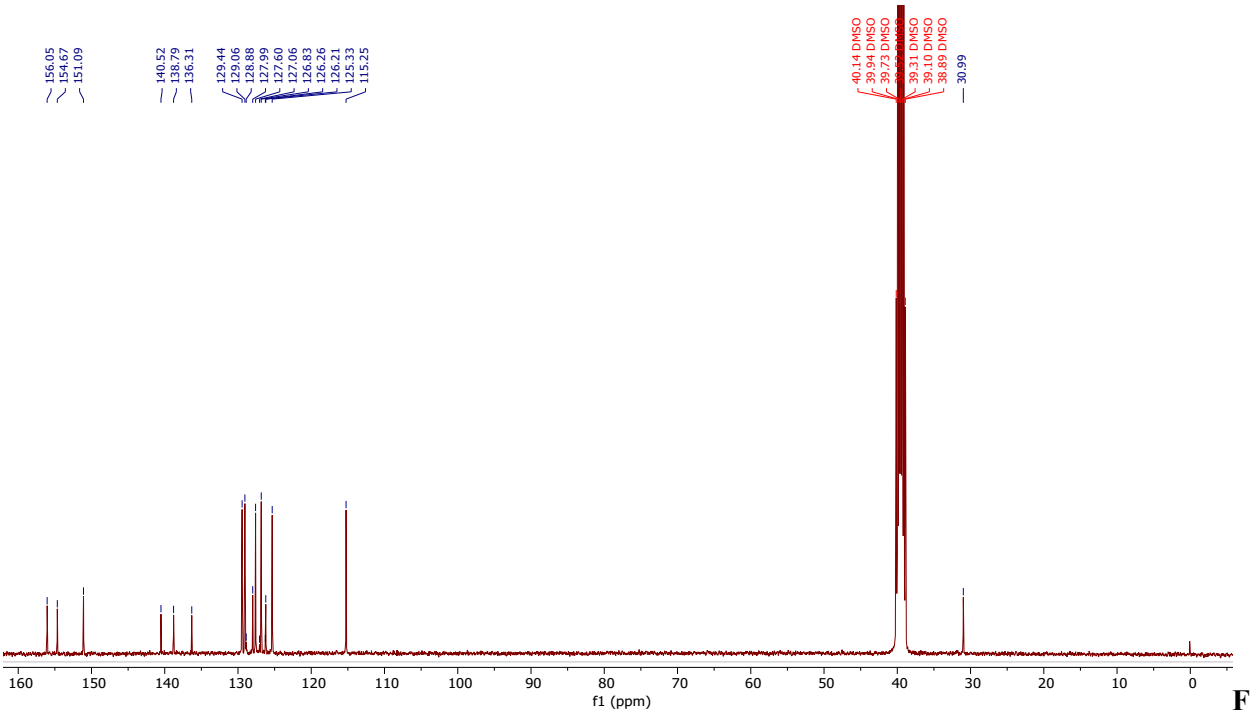


FigureS14. 13CNMR spectrum of 4g (100 MHz, DMSO-d6)

4-((1-([1,1'-biphenyl]-4-yl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4h):

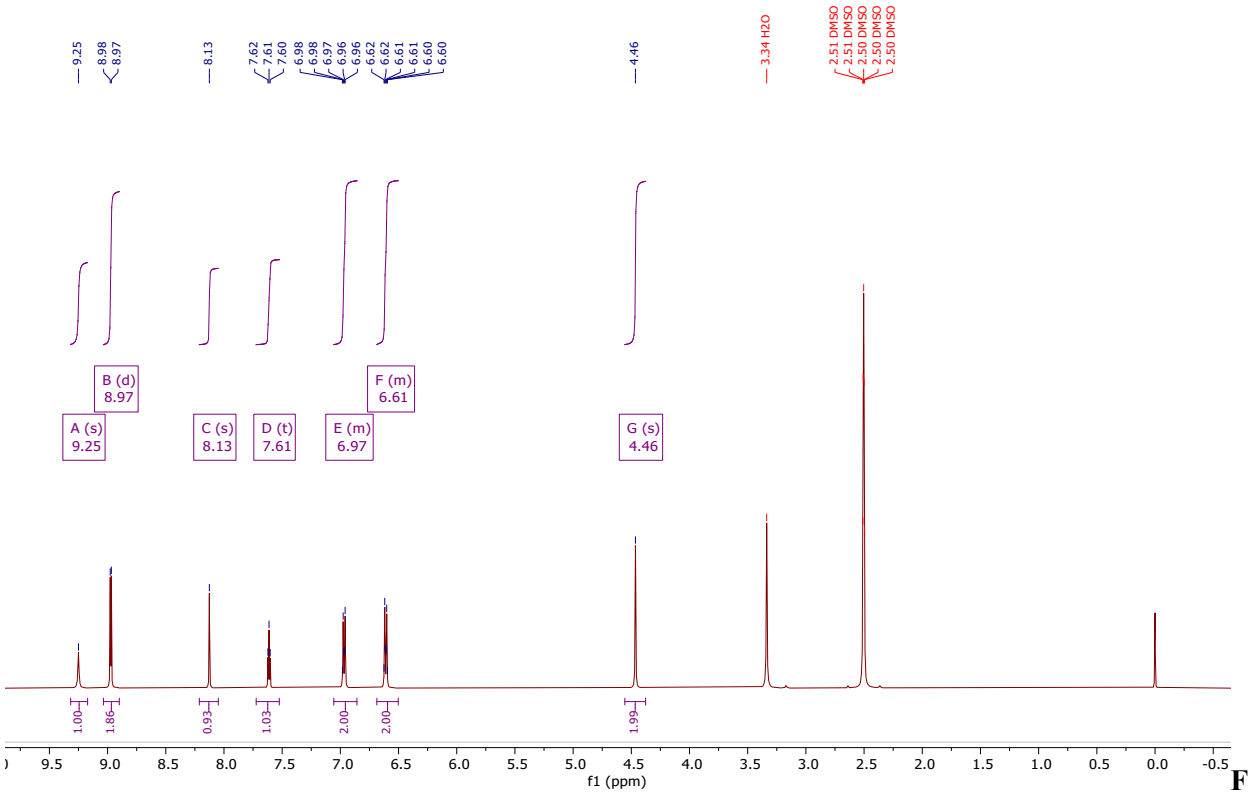


FigureS15. 1HNMR spectrum of 4h (400 MHz, DMSO-d6)

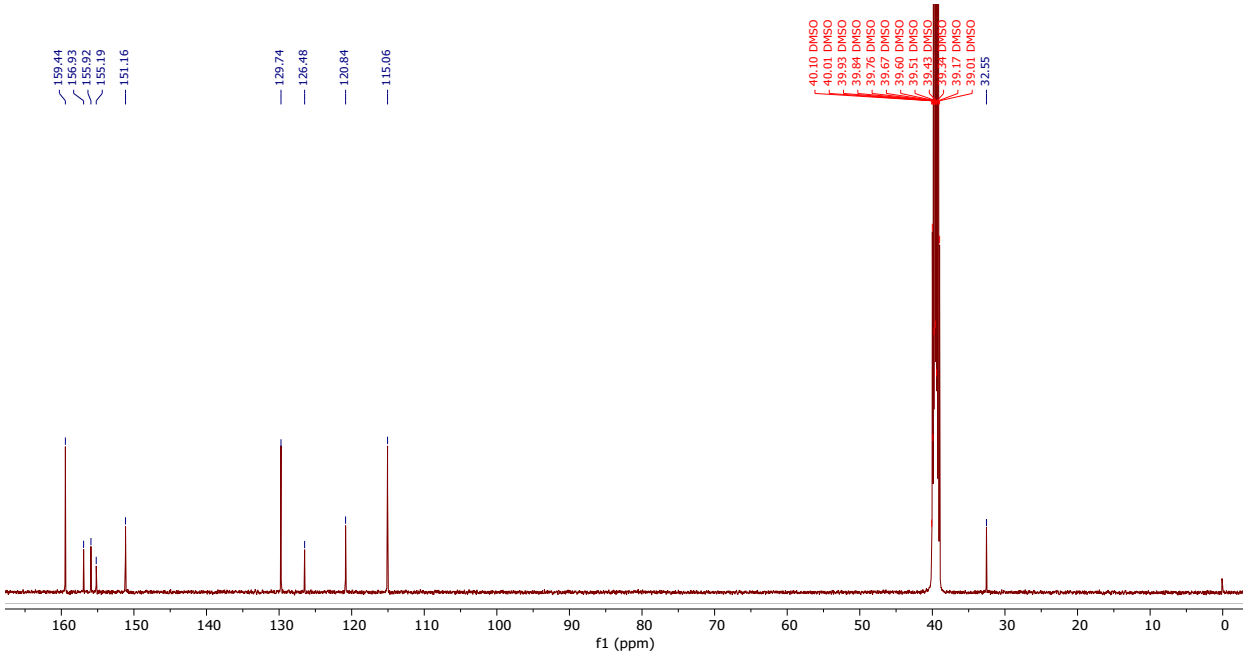


F igureS16. 13CNMR spectrum of 4h (100 MHz, DMSO-d6)

4-((1-(pyrimidin-2-yl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4i):

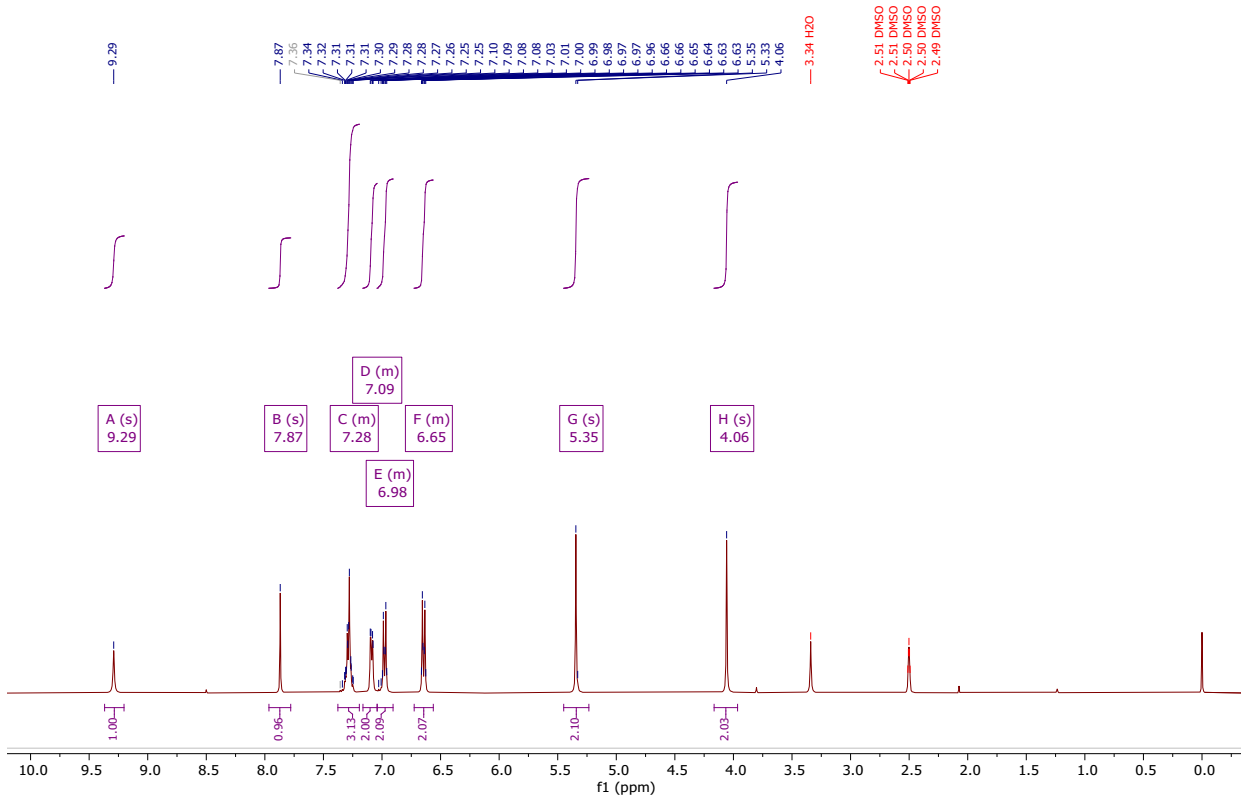


F igureS17. 1HNMR spectrum of 4i (500 MHz, DMSO-d6)

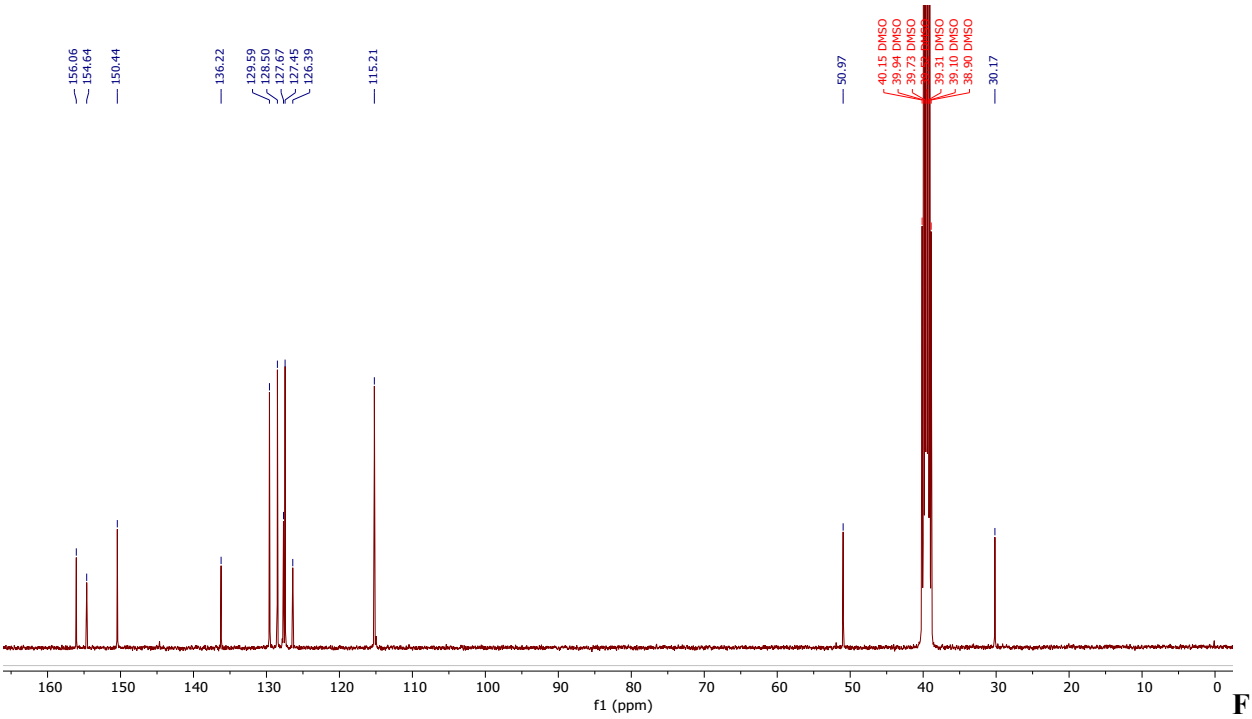


FigureS18. 13CNMR spectrum of 4i (125 MHz, DMSO-d6)

4-((1-benzyl-1H-1,2,4-triazol-5-yl) methyl) phenol (4j):

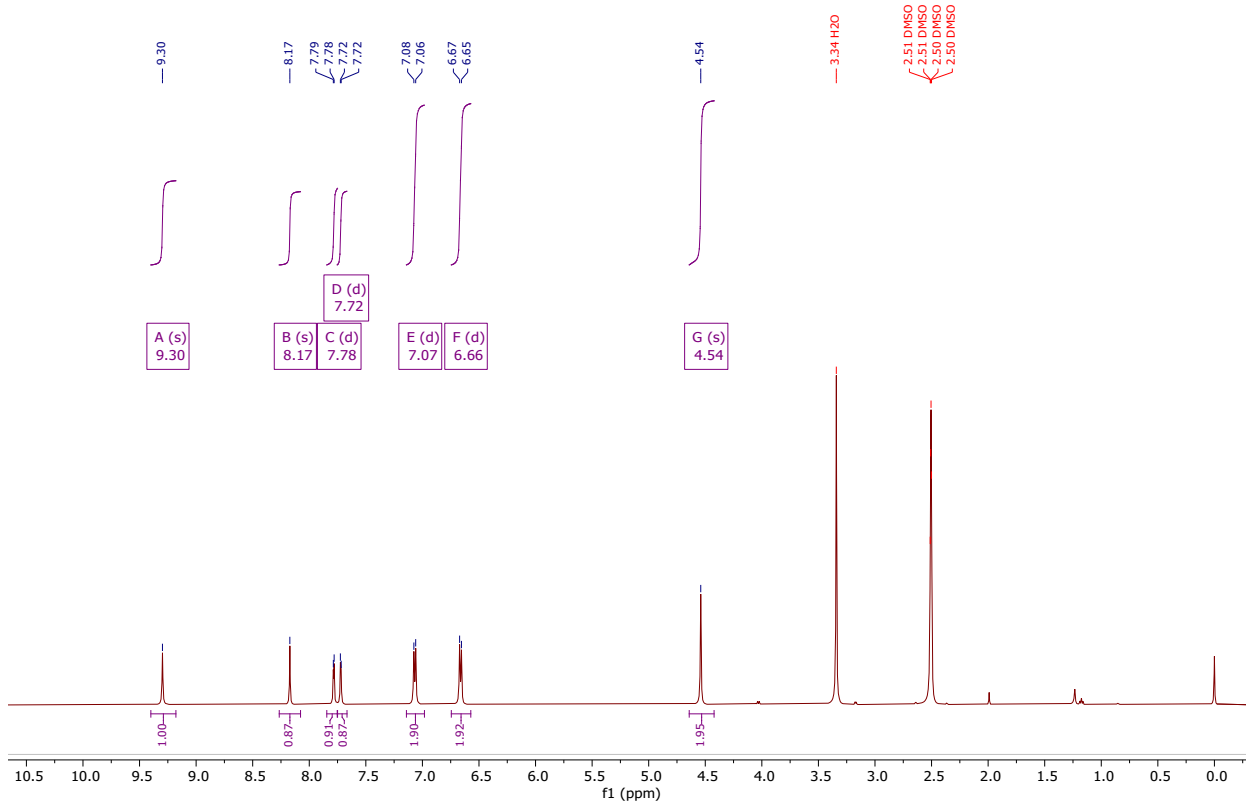


FigureS19. 1HNMR spectrum of 4j (400 MHz, DMSO-d6)



FigureS20. 13CNMR spectrum of 4j (100 MHz, DMSO-d6)

4-((1-(thiazol-2-yl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4k):



FigureS21. 1HNMR spectrum of 4k (500 MHz, DMSO-d6)

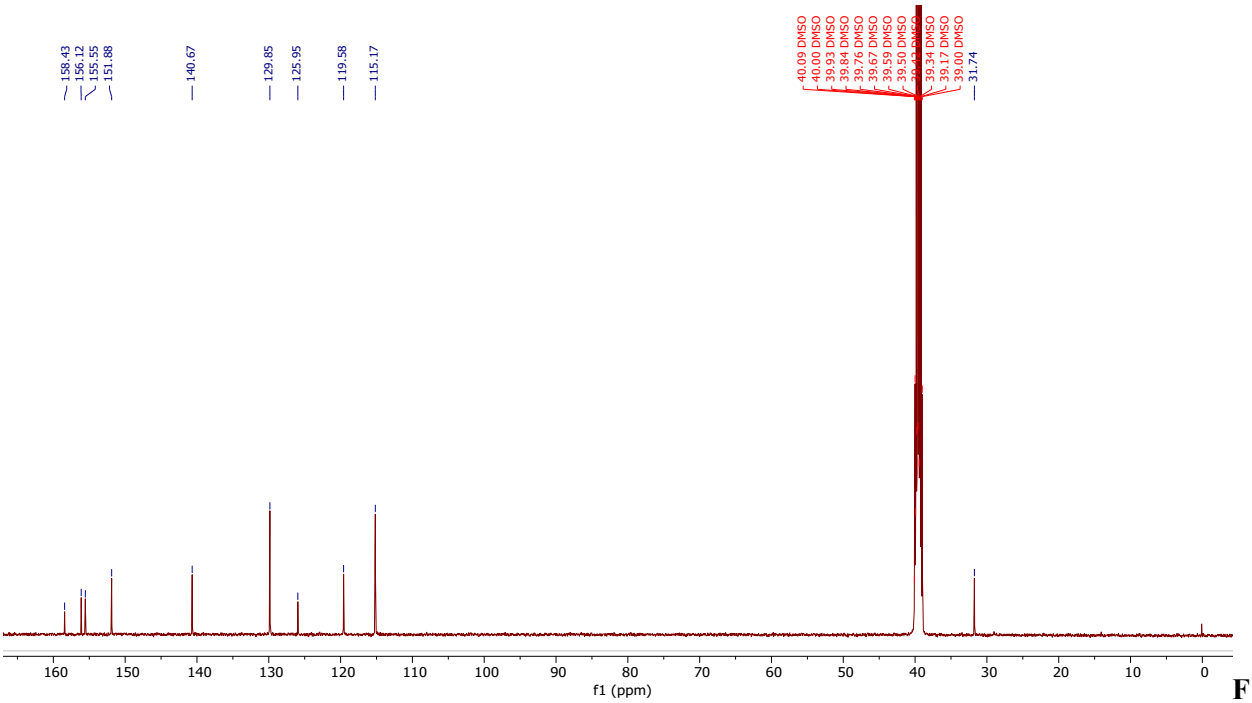


Figure S22. 13CNMR spectrum of 4k (125 MHz, DMSO-d6)

4-((1-(5-(trifluoromethyl) pyridin-2-yl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4l):

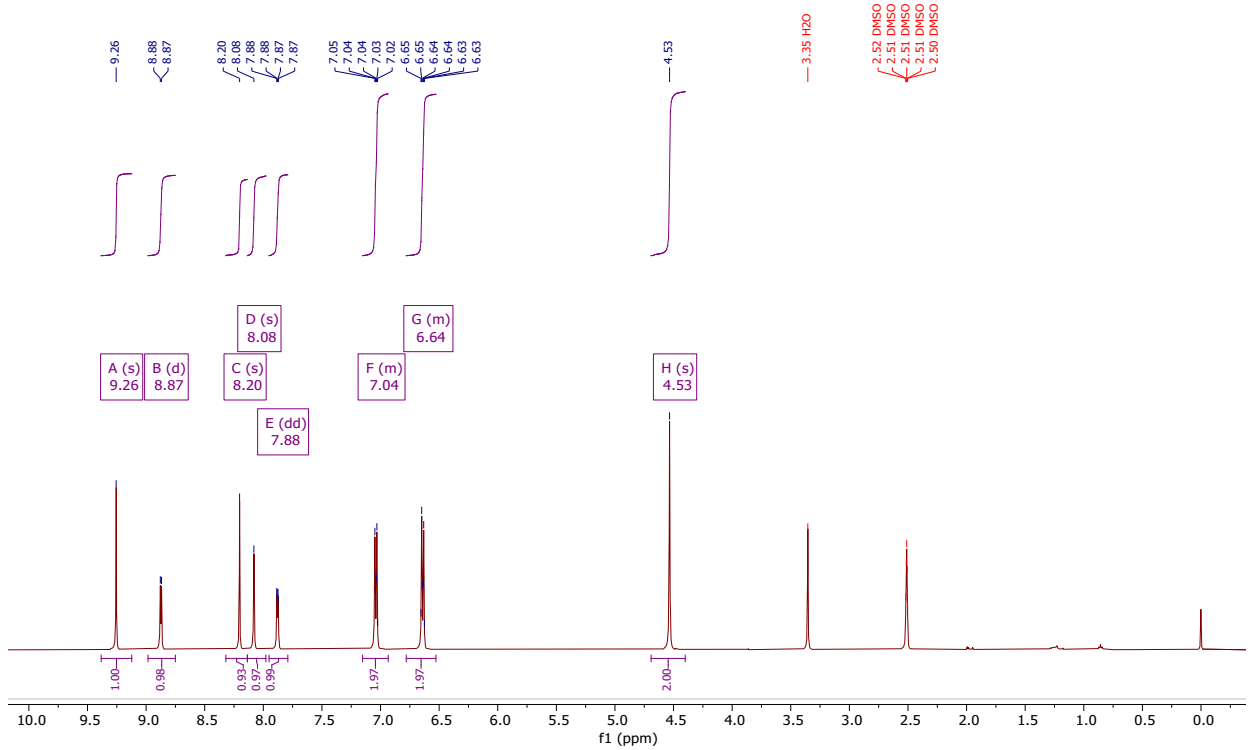


Figure S23. 1HNMR spectrum of 4l (500 MHz, DMSO-d6)

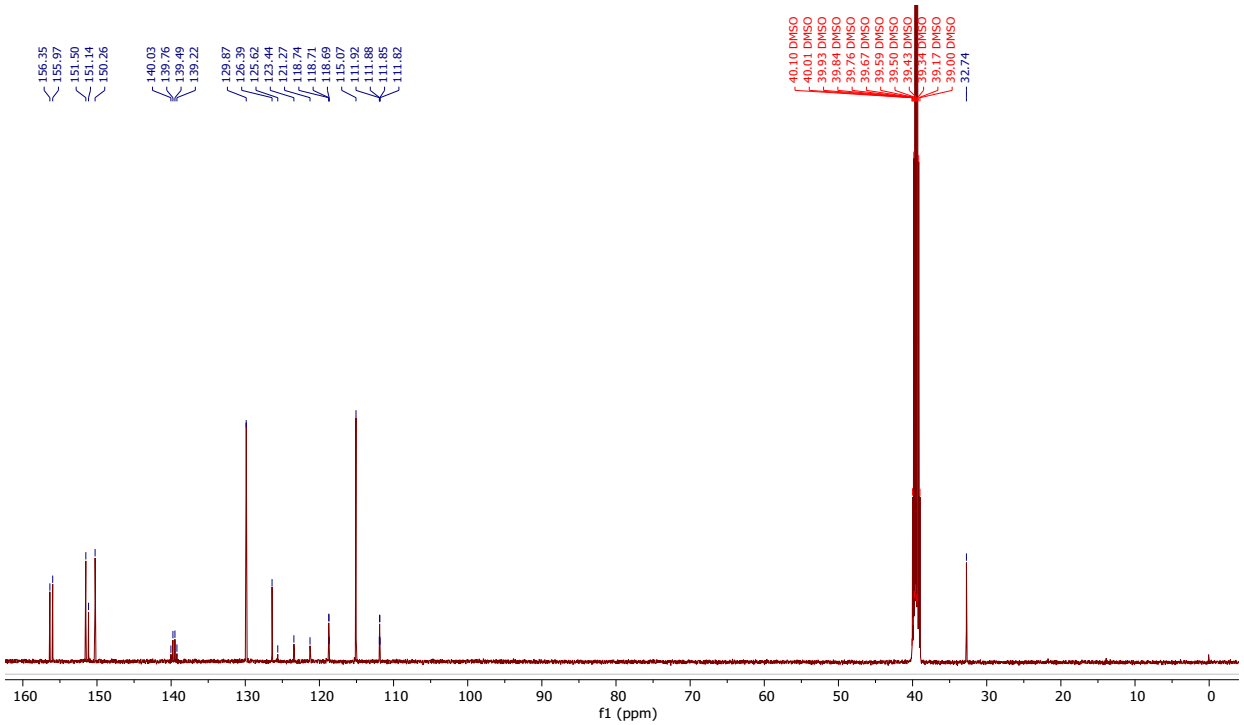


Figure S24. 13CNMR spectrum of 4l (125 MHz, DMSO-d6)

Benzyl 4-(5-(4-hydroxybenzyl)-1H-1,2,4-triazol-1-yl) piperidine-1-carboxylate (4m):

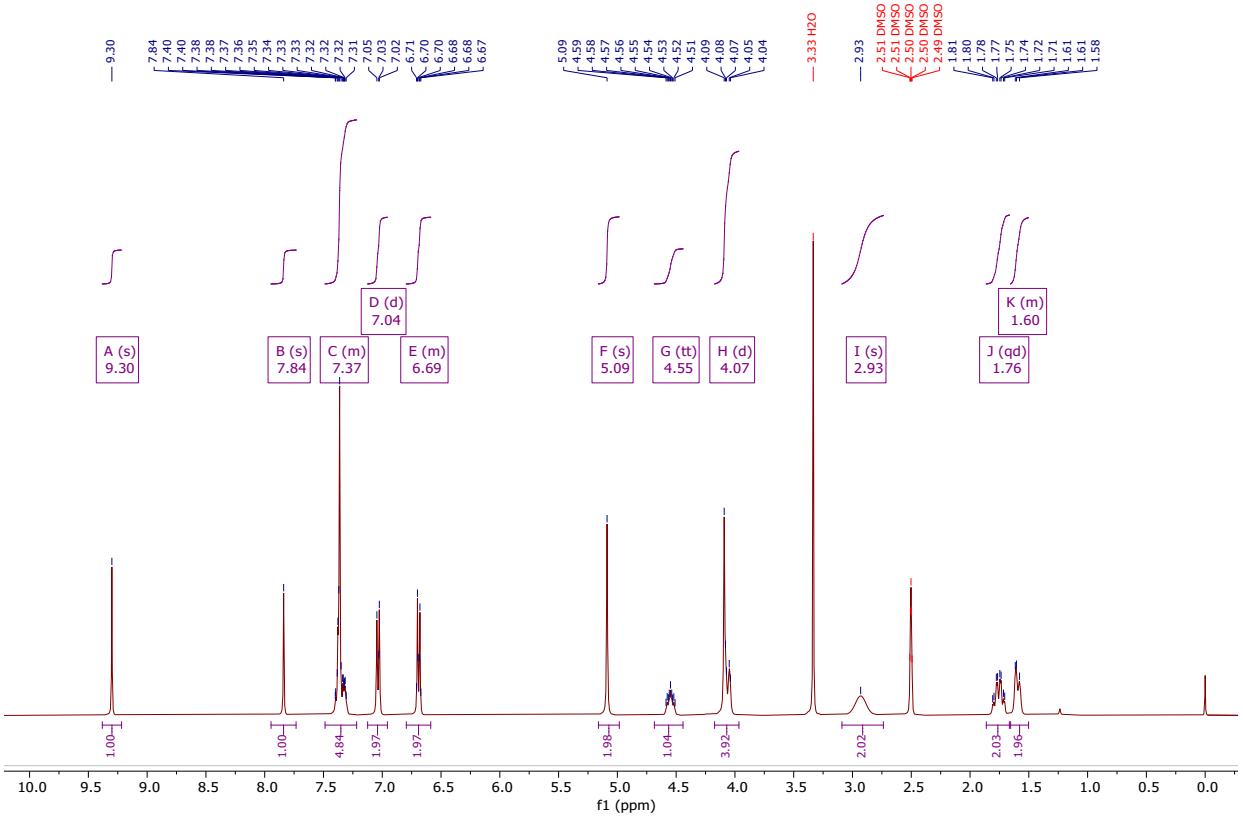


Figure S25. 1HNMR spectrum of 4m (400 MHz, DMSO-d6)

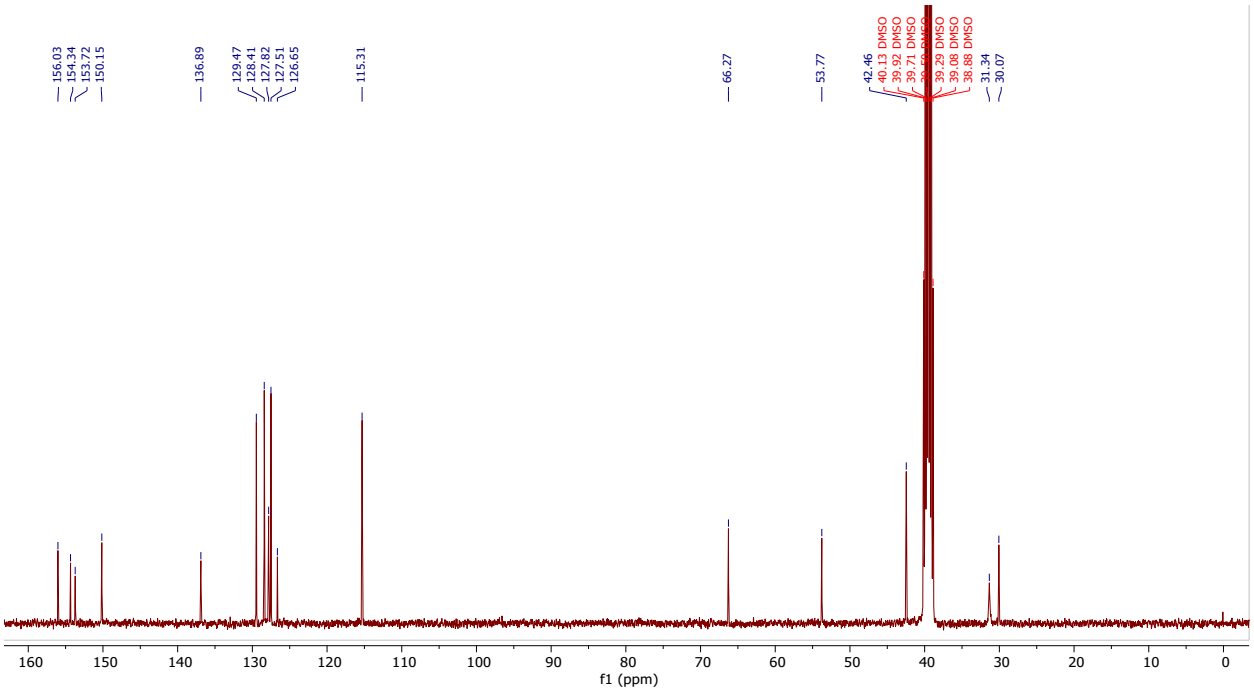


Figure S26. 13CNMR spectrum of 4m (100 MHz, DMSO-d6)

4-((1-(2-(trifluoromethoxy) phenyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (3n):

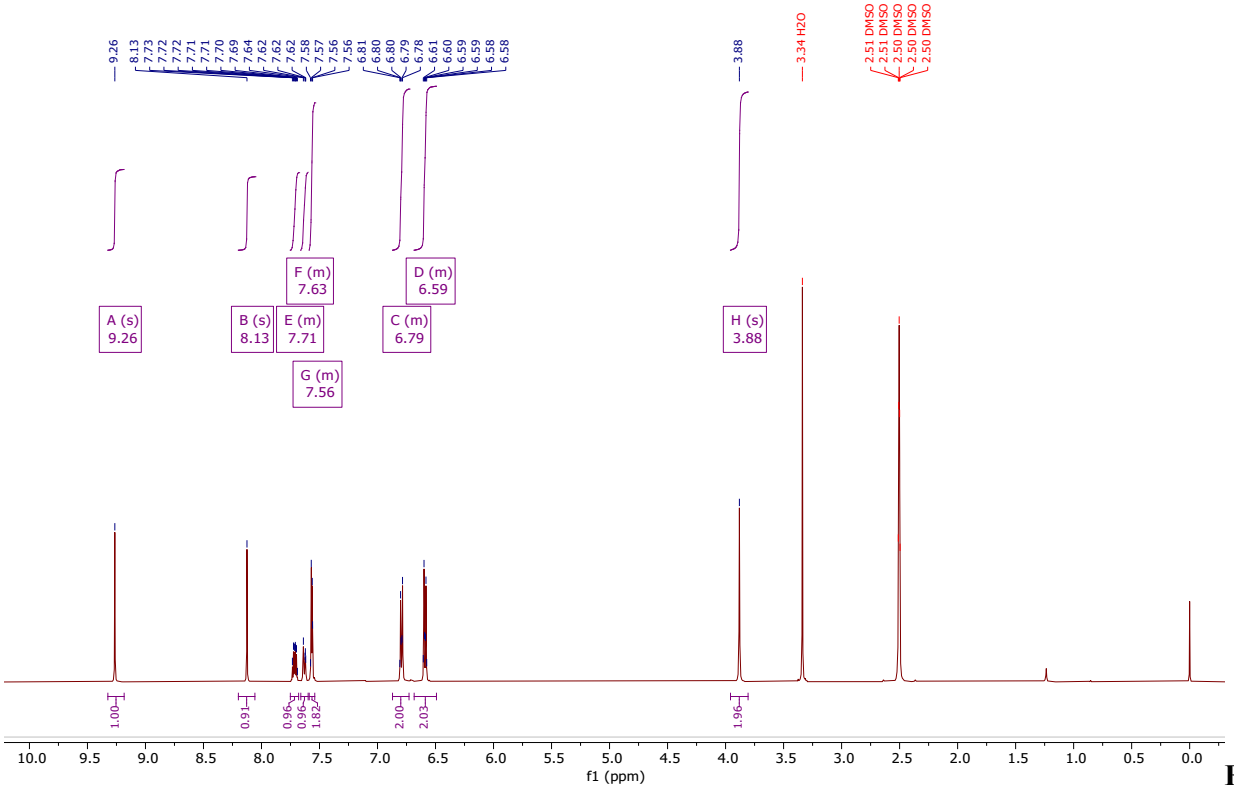


Figure S27. 1HNMR spectrum of 4n (500 MHz, DMSO-d6)

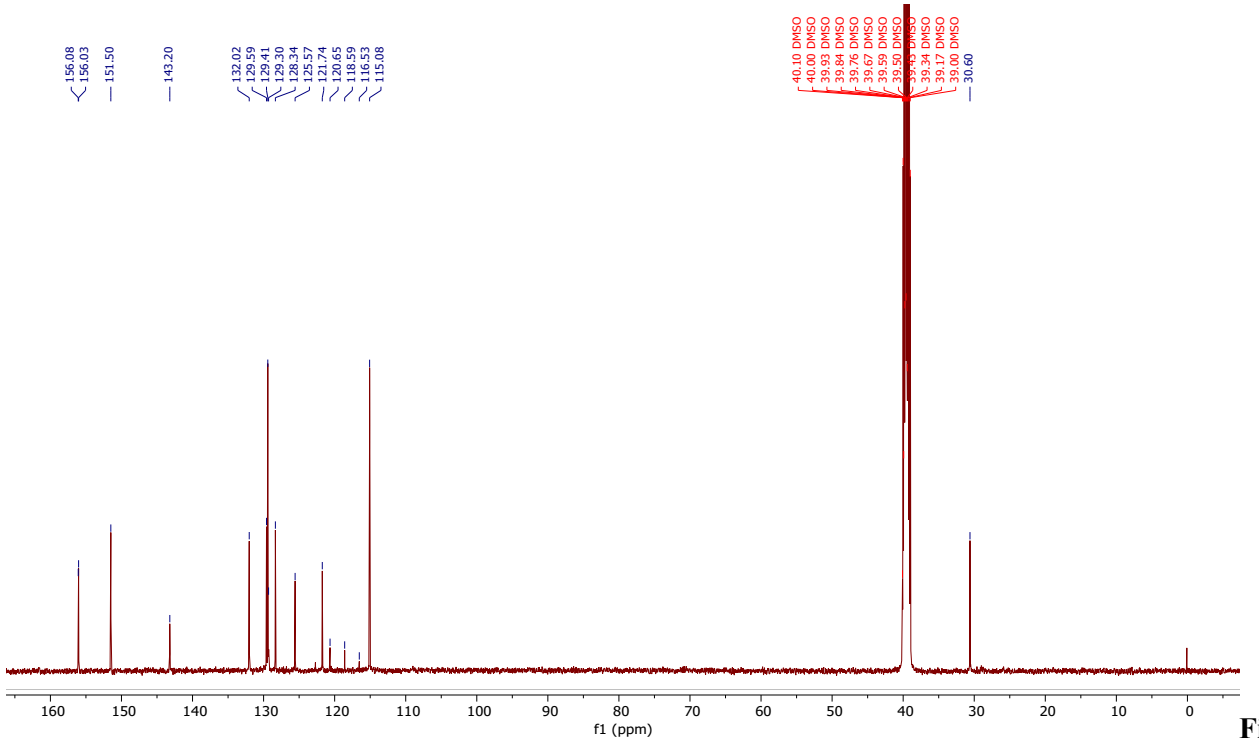


Figure S28. 13CNMR spectrum of 4n (125 MHz, DMSO-d6)

4-((1-(2,4-difluorophenyl)-1H-1,2,4-triazol-5-yl) methyl) phenol (4o):

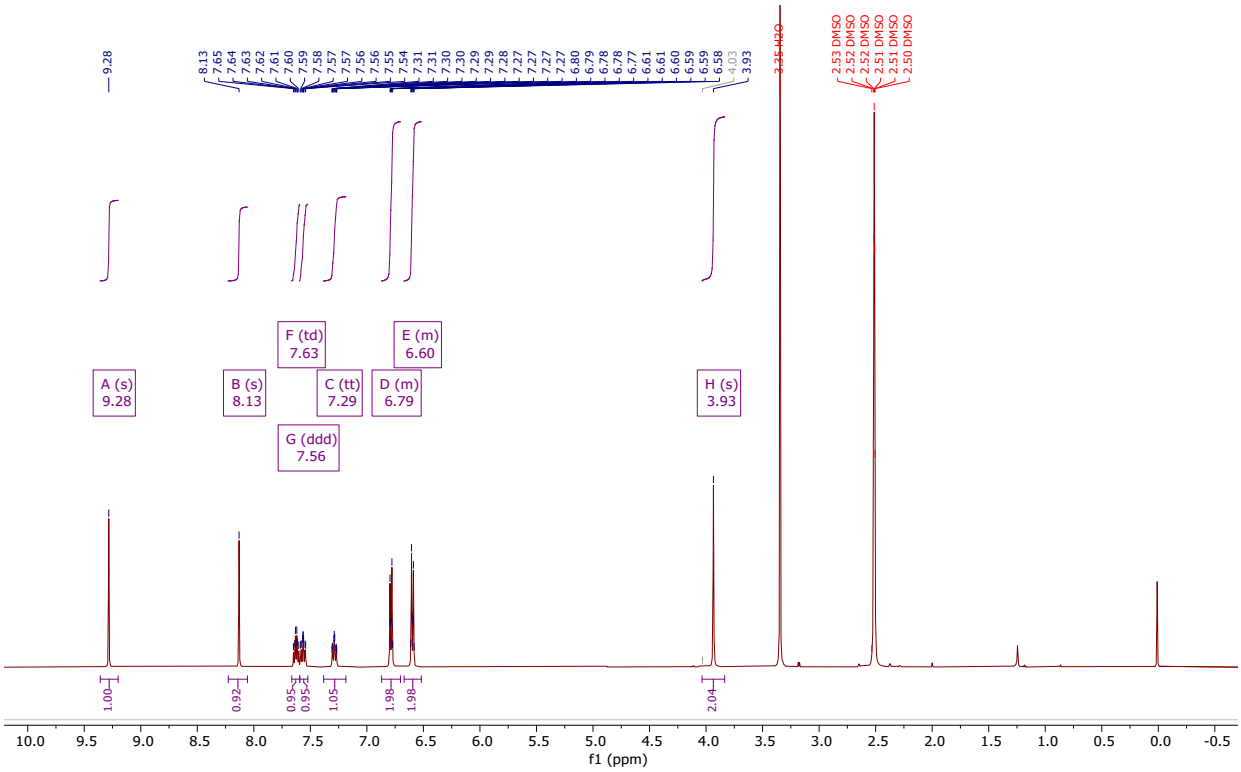


Figure S29. 1HNMR spectrum of 4o (500 MHz, DMSO-d6)

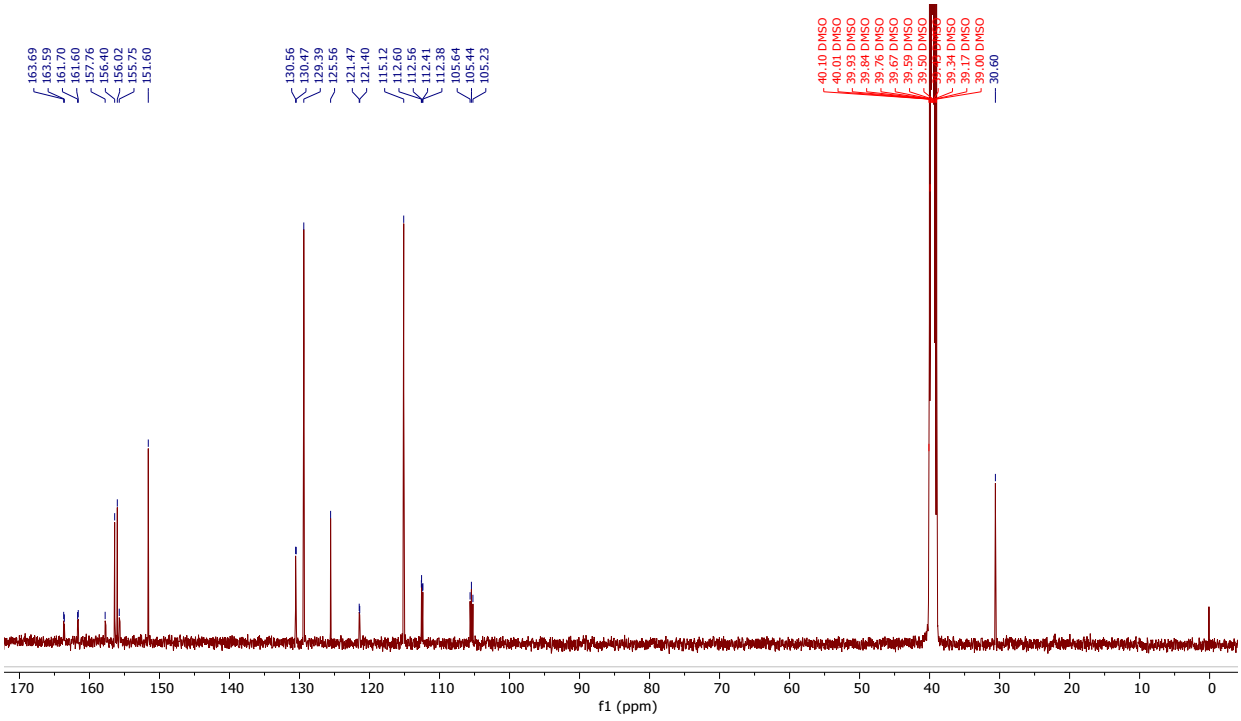


Figure S30. 13CNMR spectrum of 4o (125 MHz, DMSO-d6)

2-(5-benzyl-1H-1,2,4-triazol-1-yl) benzoic acid (5a):

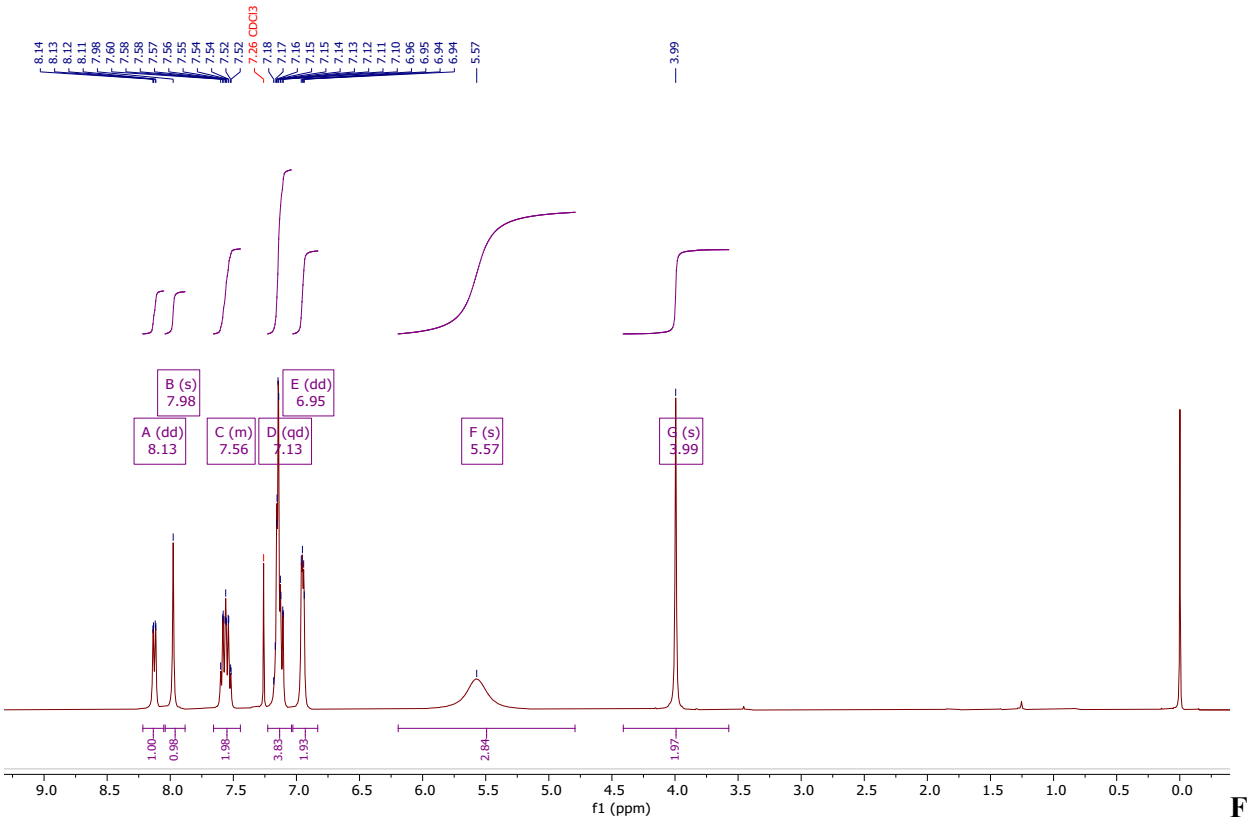


Figure S31. 1HNMR spectrum of 5a (400 MHz, $CDCl_3$)

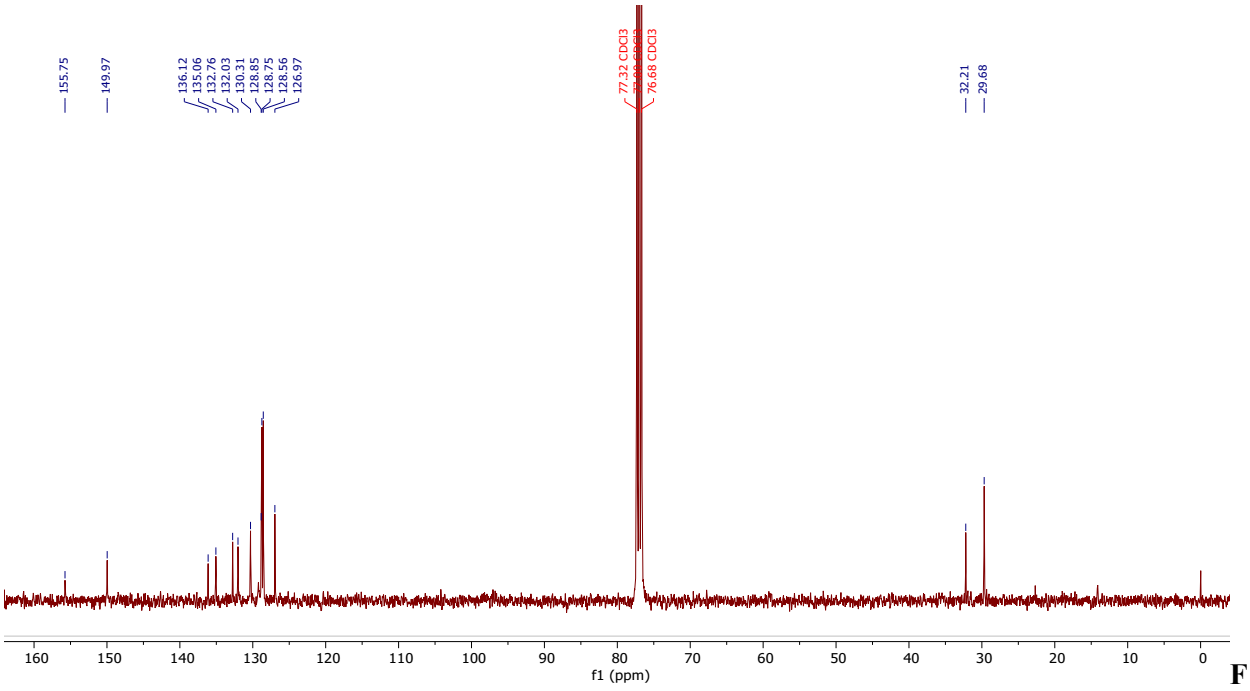


Figure S32. 13CNMR spectrum of 5a (100 MHz, CDCl3)

2-(5-benzyl-1H-1,2,4-triazol-1-yl) benzoic acid (5b):

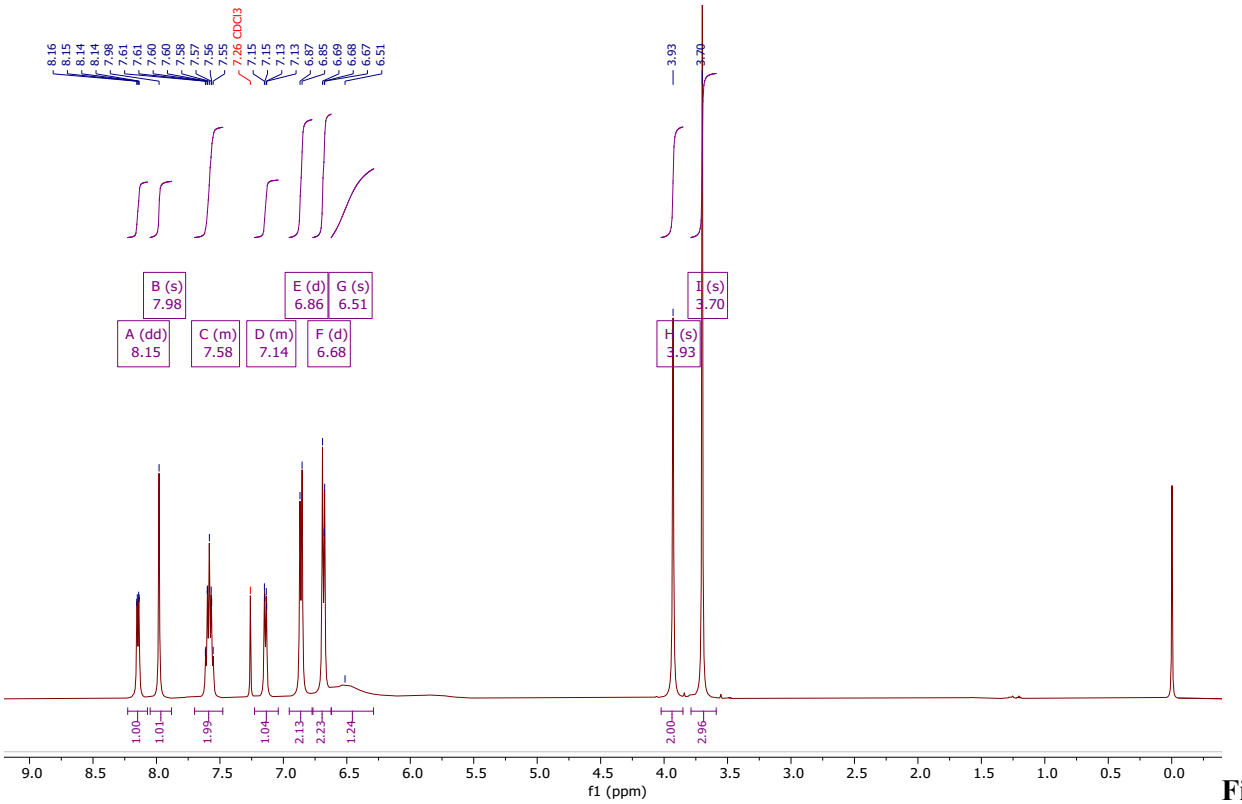


Figure S33. 1HNMR spectrum of 5b (500 MHz, $CDCl_3$)

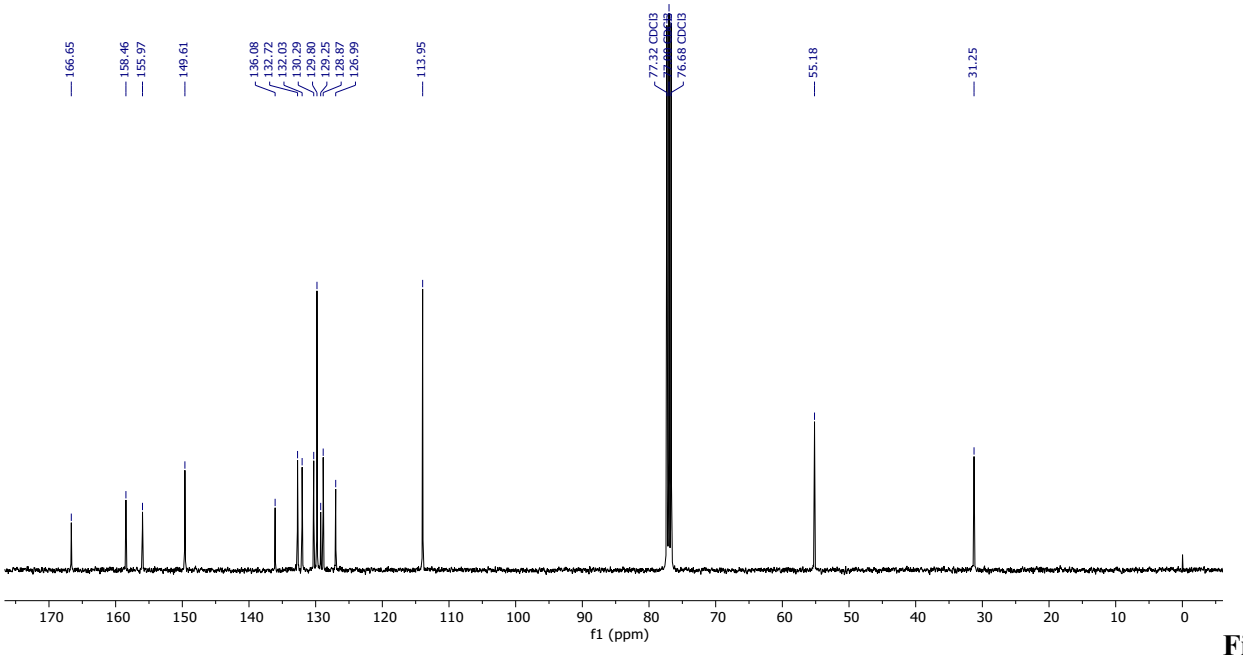


Figure S34. 13CNMR spectrum of 5b (100 MHz, CDCl3)

2-(5-(4-methylbenzyl)-1H-1,2,4-triazol-1-yl) benzoic acid (5c)

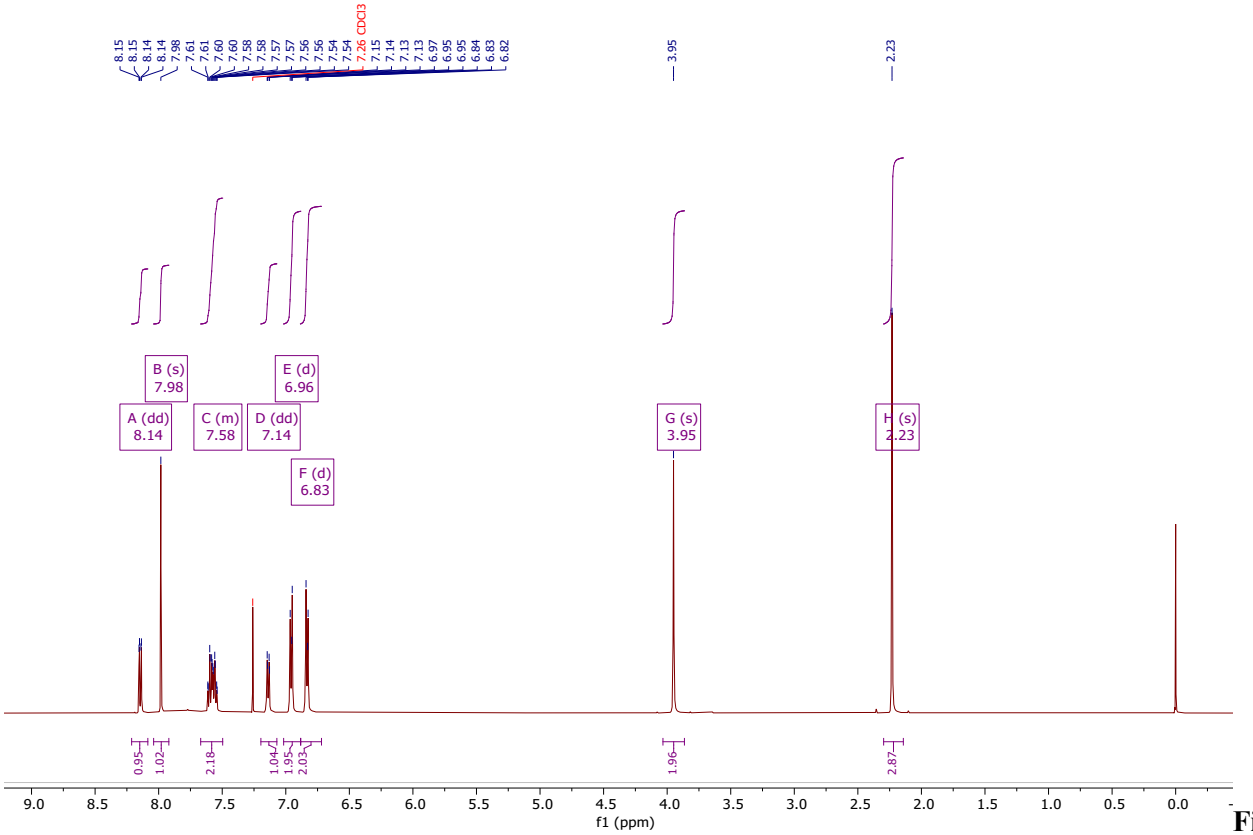


Figure S35. 1HNMR spectrum of 5c (500 MHz, $CDCl_3$)

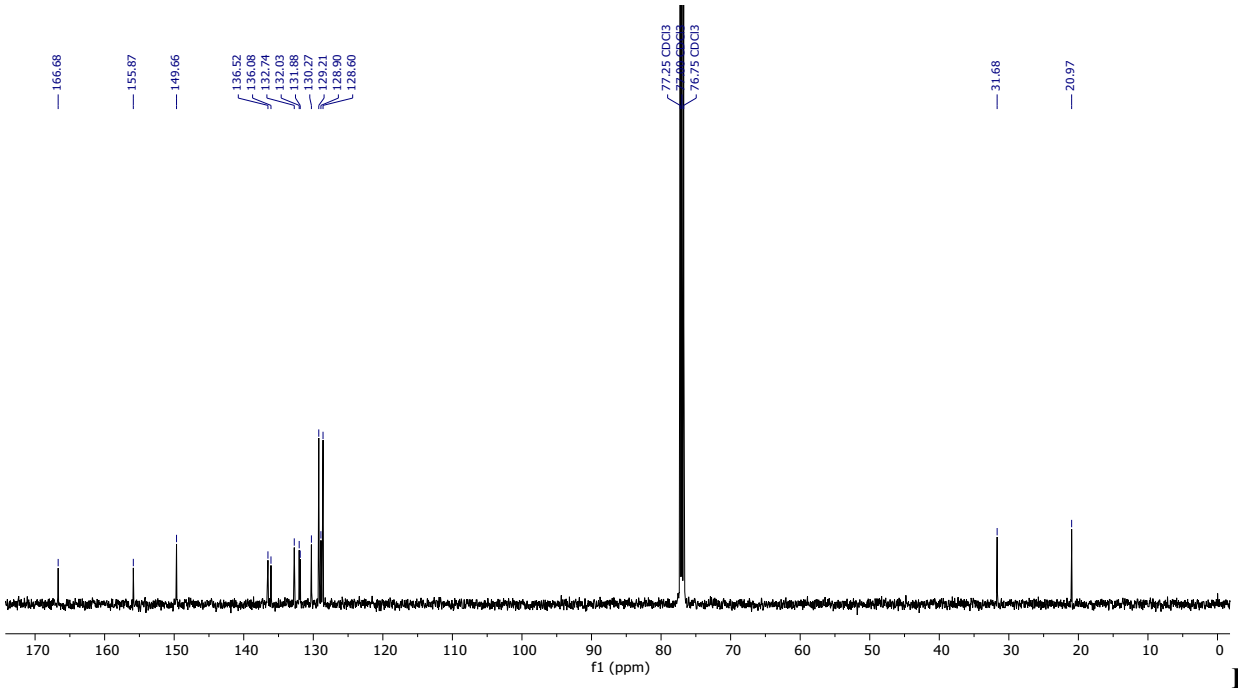


Figure S36. 13CNMR spectrum of 5c (100 MHz, CDCl3)