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Supporting Information

Unusual Rearrangement of Imidazo[1,5-*a*]imidazoles and Imidazo[1,2-*b*]pyrazoles into Imidazo[1,5-*a*]pyrimidines and Pyrazolo[1,5-*a*]pyrimidines

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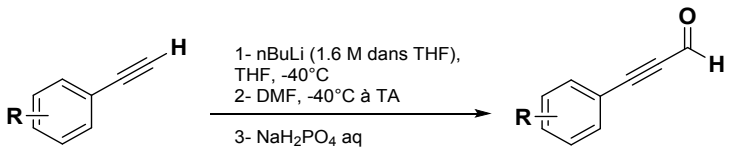
General experimental information:

The reactions were monitored by thin-layer chromatography (TLC) analysis using silica gel (60 F254) plates. Compounds were visualized by UV irradiation. Flash column chromatography was performed on silica gel 60 (230– 400.13 mesh, 0.040, 0.063 mm). Melting points (mp [°C]) were taken on samples in open capillary tubes and are uncorrected. The infrared spectra of compounds were recorded on a Thermo Scientific Nicolet iS10 are given in cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance II 400 MHz (13C, 100 MHz) or on a Bruker Avance DPX 250 MHz (13C, 62.9 MHz). Chemical shifts are given in parts per million from tetramethylsilane (TMS) as internal standard. The multiplicities of the spectra are reported as follows: singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Coupling constants (J) are reported in hertz (Hz). High-resolution mass spectra (HRMS) were performed on a Maxis Bruker 4G. Propargylic aldehydes were all synthesized through a literature procedure[1].

General procedure: Preparation of propargylic aldehydes[1]



A well-stirred solution of alkyne (1.0 equiv.) in anhydrous THF (0.4 M) was cooled down to -40 °C. *n*-BuLi (1.6 M solution in hexanes, 1.1 equiv.) was then added dropwise via syringe. The solution was stirred at -40 °C for 15 min, and anhydrous DMF (2.0 equiv.) was added in one portion. The mixture was allowed to slowly reach ambient temperature. After stirring for further 1 h, the reaction mixture was poured into a vigorously stirred mixture of KH_2PO_4 aqueous solution and *tert*-butyl methyl ether. The layers were separated and the aqueous layer was extracted with *tert*-butyl methyl ether. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude oil was purified by flash chromatography on silica gel using n-hexane/EtOAc as eluent.

3-(4-(Trifluoromethyl)phenyl)propiolaldehyde (3e): Yellow oil, yield: 72%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.43 (s, 1H), 7.85 – 7.58 (m, 4H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.4, 133.5 (2C), 132.8 (q, $^{2}J_{Cq\text{-}F}$ = 33.0 Hz, $C_{q\text{-}F}$),125.8 (q, $^{3}J_{CHAr\text{-}F}$= 3.8 Hz, 2C, C_{HAr}), 123.5, 121.3 (q, $^{1}J_{C\text{-}F}$ = 272.3 Hz, CF_3), 92.2, 89.3; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.9; HRMS (m/z) [M+H]+ calculated mass for $C_{10}H_6F_3O$ 199.0365 mass found 199.0367.

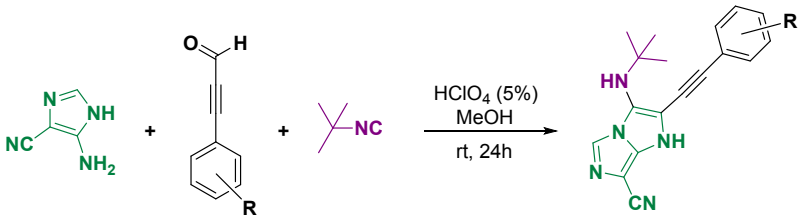
3-(3-Methoxyphenyl)propiolaldehyde (3f): Orange oil, yield: 85%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.37 (s, 1H), 7.29 - 6.96 (m, 4H), 3.77 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.7, 159.5, 129.9, 125.8, 120.3, 118.1, 117.7, 95.0, 88.1, 55.4; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{10}H_9O_2$ 161.0597 mass found 161.0595.

3-(3-Fluorophenyl)propiolaldehyde (3g): Yellow oil, yield: 55%; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.44 (s, 1H), δ 7.95 – 7.16 (m, 4H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 178.5, 161.7 (d, *J* = 246.0 Hz), 131.3 (d, *J* = 8.7 Hz), 129.3 (d, *J* = 3.1 Hz), 120.5 (d, *J* = 9.8 Hz), 119.4 (d, *J* = 23.5 Hz), 119.0 (d, *J* = 21.1 Hz), 91.5 (d, *J* = 3.5 Hz), 88.3; ^{19}F NMR (376 MHz, DMSO-d_6) δ -111.5; HRMS (m/z) $[M+H]^+$ calculated mass for C_9H_6FO 149.0397 mass found 149.0396.

3-(2-Fluorophenyl)propiolaldehyde (3i): Yellow oil, yield: 56%; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.42 (s, 1H), 7.55 (ddd, *J* = 7.8, 6.9, 1.8 Hz, 1H), 7.51 – 7.43 (m, 1H), 7.20 – 7.09 (m, 2H); ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.4, 163.7 (d, *J* = 256.4 Hz), 134.9, 133.4 (d, *J* = 8.4 Hz), 124.5 (d, *J* = 3.9 Hz), 116.0 (d, *J* = 20.3 Hz), 108.4 (d, *J* = 15.3 Hz), 92.5 (d, *J* = 3.2 Hz),

88.2; ^{19}F NMR (376 MHz, Chloroform-*d*) δ -106.6; HRMS (m/z) $[M+H]^+$ calculated mass for C_9H_6FO 149.0397 mass found 149.0399.

General procedure A: Synthesis of imidazo[1,5-*a*]imidazole derivatives



In a round bottomed flask, a mixture of 5-aminoimidazole-4-carbonitrile (0.92 mmol, 100 mg, 1.0 equiv.), propargylic aldehydes (1.1 equiv.) and *tert*-butyl isocyanide (1.37 mmol, 156 µL,.5 equiv.) in MeOH (1 mL) was stirred at room temperature for 5 min. Perchloric acid (0.046 mmol, 2.78 µL, 0.05 equiv.) was added dropwise and the mixture was further stirred for 24h. The reaction was filtered and the filtrate was washed with dichloromethane to give the product **4**. No further purification was needed.

3-(*tert*-Butylamino)-2-(phenylethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4a): Prepared according to the general procedure **A**; isolated as beige solid, yield: 72%; Mp: 171-172°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.10 (s, 1H), 7.75 (s, 1H), 7.54–7.43 (m, 5H), 4.96 (s, 1H), 1.23 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 139.4, 130.9 (2C), 129.2, 128.9 (2C), 127.8, 121.5, 120.2, 116.9, 108.8, 94.9, 80.9, 79.3, 55.5, 29.7 (3C); IR (neat, cm^{-1}): 750, 1207, 1492, 1627, 2201, 2962, 3336; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{18}H_{18}N_5$ 304.1557, mass found 304.1556.

3-(*N*-*tert*-Butylamino)-2-(*p*-tolylethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4b): Prepared according to the general procedure **A**; isolated as beige solid, yield: 61%, Mp: 183-184°C ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.08 (s, 1H), 7.74 (s, 1H), 7.42 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 4.92 (s, 1H), 2.34 (s, 3H), 1.22 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 139.3 , 139.1 , 130.9 (2C), 129.5 (2C), 127.5 , 120.2 , 118.4 , 116.9 , 109.1 , 95.0 , 80.8 , 78.6 , 55.4 , 29.7 (3C), 21.0; IR (neat, cm^{-1}): 813, 1207, 1510, 1623, 2201, 2965, 3312. HRMS (m/z) $[M+H]^+$ calculated mass for $C_{19}H_{20}N_5$ 318.1713, mass found 318.1713.

3-(*tert*-Butylamino)-2-((4-methoxyphenyl)ethynyl)-1*H* imidazo[1,5-*a*]imidazole-7-carbonitrile (4c):
Prepared according to the general procedure **A**; isolated as beige solid, yield: 68%. Mp: 177-178°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 7.73 (s, 1H), 7.48 (d, *J* = 8.7 Hz, 2H), 7.02 (d, *J* = 8.7 Hz, 2H), 4.88 (s, 1H), 3.80 (s, 3H), 1.22 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 159.9, 139.2, 132.7 (2C), 127.2, 120.2, 116.9, 114.6 (2C), 113.3, 109.4, 94.9, 80.8, 77.7, 55.4, 55.3, 29.7 (3C); IR (neat, cm^{-1}): 776, 827, 1168, 1509, 1614, 2200, 2967, 3321. HRMS (m/z) $[M+H]^+$ calculated mass for $C_{19}H_{20}N_5O$ 334.1662 mass found 334.1662.

3-(*N*-*tert*-Butylamino)-2-((4-fluorophenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4d): Prepared according to the general procedure **A**; isolated as beige solid, yield: 73%. Mp: 186-187°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.10 (s, 1H), 7.75 (s, 1H), 7.59 (dd, *J* = 8.8, 5.4 Hz, 2H), 7.32 (t, *J* = 8.8 Hz, 2H), 4.97 (s, 1H), 1.22 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.2 (d, $J_{C\text{-}F}$ = 248.5 Hz), 139.4, 133.4 (d, *J* = 8.8 Hz, 2C), 127.8, 120.2, 118.0 (d, *J* = 3.3 Hz), 116.9, 116.3 (d, *J* = 22.3 Hz, 2C), 108.7, 93.8, 80.8, 79.0, 55.4, 29.7 (3C); 19F NMR (376 MHz, DMSO-d_6) δ -117.5; IR (neat, cm^{-1}): 836, 1208, 1231, 1365, 1506, 1627, 2204, 2968, 3122, 3336; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{18}H_{17}FN_5$, 322.1463 mass found 322.1461.

3-(*N*-*tert*-Butylamino)-2-((4-(trifluoromethyl)phenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrle (4e): Prepared according to the general procedure A; isolated as beige solid, yield: 81%; Mp: 188-189°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.16 (s, 1H), 7.85 – 7.68 (m, 5H), 5.13 (s, 1H), 1.24 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 139.6, 131.5 (2C) , 128.7, 128.8 (q, $J_{Cq\text{-}F}$ = 32.3 Hz, $C_{q\text{-}F}$), 125.8 (q, $^{3}J_{CHAr\text{-}F}$= 3.8 Hz, 2C, C_{HAr}), 123.9 (q, $^{1}J_{C\text{-}F}$ = 272.1 Hz, CF_3), 120.3, 116.8, 107.6 (2C), 93.7, 82.2, 80.9, 55.4, 29.6 (3C); ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.4; IR (neat, cm^{-1}): 840, 1121, 1320, 1454, 1615, 2202, 2973, 3143, 3316; HRMS (m/z) [M+H]$^+$ calculated mass for $C_{19}H_{17}F_3N_5$ 371.1431 mass found 371.1430.

3-(*N*-*tert*-Butylamino)-2-((3-methoxyphenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4f): Prepared according to the general procedure **A**; isolated as beige solid, yield: 43%; Mp: 178-179°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.10 (s, 1H), 7.75 (s, 1H), 7.42 – 7.32 (m, 1H), 7.16 – 6.98 (m, 3H), 4.97 (s, 1H), 3.79 (s, 3H), 1.23 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 159.2 , 139.4, 130.1, 127.9, 123.3, 122.5, 120.2, 116.9, 115.8, 115.4, 108.6, 94.8, 80.8, 79.2, 55.4, 55.2, 29.7 (3C); IR (neat, cm^{-1}): 780, 1201, 1451, 1607, 1627, 2207, 2965, 3331; HRMS (m/z) [M+H]$^+$ calculated mass for $C_{19}H_{20}N_5O$ 334.1662 mass found 334.1661.

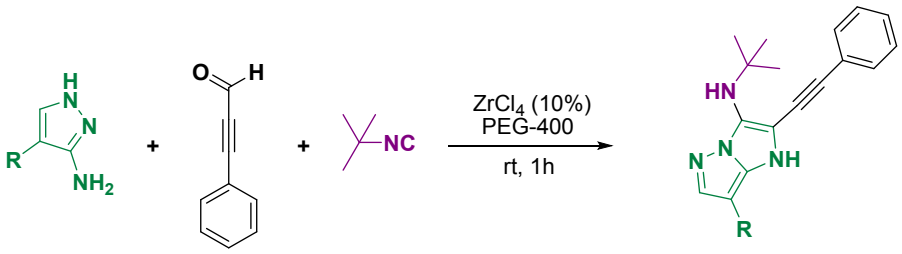
3-(*tert*-Butylamino)-2-((3-fluorophenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4g): Prepared according to the general procedure **A**; isolated as beige solid, yield: 71%; Mp: 181-182°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.13 (s, 1H), 7.76 (s, 1H), 7.51 (td, *J* = 8.1, 5.9 Hz, 1H), 7.40 – 7.28 (m, 3H), 5.03 (s, 1H), 1.23 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.8 (d, $J_{C\text{-}F}$= 244,3 Hz), 139.5, 131.1(d, *J* = 8.9 Hz), 128.4, 127.3 (d, *J* = 2.9 Hz), 123.4 (d, *J* = 2.6 Hz), 120.3, 117.3 (d, *J* = 23.1 Hz), 116.8, 116.4 (d, *J* = 22.0 Hz), 108.0, 93.6, 80.8, 80.4, 55.4, 29.6 (3C); ^{19}F NMR (376 MHz, DMSO-d_6) δ -112.1; IR (neat, cm^{-1}): 679, 781, 965, 1204, 1447, 1579, 1626, 2204, 2968, 3121, 3337; HRMS (m/z) [M+H]$^+$ calculated mass for $C_{18}H_{17}FN_5$ 322.1463 mass found 322.1461.

3-(*N*-*tert*-Butylamino)-2-((2-methoxyphenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4h): Prepared according to the general procedure **A**; isolated as beige solid; yield: 38%; Mp: 170-171°C; ^{1}H NMR (250 MHz, DMSO-d_6) δ 12.08 (s, 1H), 7.73 (s, 1H), 7.49 – 7.37 (m, 2H), 7.11 (d, *J* = 8.4 Hz, 1H), 7.01 (td, *J* = 7.5, 1.0 Hz, 1H), 4.84 (s, 1H), 3.85 (s, 3H), 1.23 (s, 9H); ^{13}C NMR (2.9 MHz, DMSO-d_6) δ 159.6, 139.4, 132.8, 130.9, 127.3, 120.6, 120.2, 116.9, 111.5, 110.5, 109.3, 91.9, 82.6, 80.9, 55.6, 55.4, 29.7 (3C); IR (neat, cm^{-1}): 748, 1027, 1205, 1496, 1625, 2205, 2965; HRMS (m/z) [M+H]$^+$ calculated mass for $C_{19}H_{20}N_5O$ 334.1662 mass found 334.1661.

3-(*N*-*tert*-Butylamino)-2-((2-fluorophenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4i): Prepared according to the general procedure **A**; isolated as beige solid; yield: 72%; Mp: 180-181°C; ^{1}H NMR (250 MHz, DMSO-d_6) δ 12.16 (s, 1H), 7.76 (s, 1H), 7.65 – 7.24 (m, 4H), 5.01 (s, 1H), 1.23 (s, 9H); ^{13}C NMR (2.9 MHz, DMSO-d_6)) δ 161.6 (d, *J* = 250.2 Hz), 139.5, 133.0, 131.4 (d, *J* = 8.1 Hz), 128.2, 125.0 (d, *J* = 3.7 Hz), 120.2, 116.8, 115.9 (d, *J* = 20.3 Hz), 110.0 (d, *J* = 15.4 Hz), 108.1, 88.4, 84.2 (d, *J* = 3.0 Hz), 80.9, 55.4, 29.7 (3C); ^{19}F NMR (376 MHz, DMSO-*d6*) δ -118.2; IR (neat, cm^{-1}): 781, 965, 1204, 1447, 1579, 1626, 2968, 3121, 3337; HRMS (m/z) [M+H]$^+$ calculated mass for $C_{18}H_{17}FN_5$ 322.1463 mass found 322.1460.

3-(*N*-*tert*-Butylamino)-2-(hept-1-yn-1-yl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4j): Prepared according to the general procedure **A**; isolated as beige solid; yield: 75%; Mp: 169-170°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (s, 1H), 7.66 (s, 1H), 4.59 (s, 1H), 2.47 (t, *J* = 7.2 Hz, 2H), 1.58 – 1.50 (m, 2H), 1.44 – 1.37 (m, 2H), 1.34 – 1.28 (m, 2H), 1.16 (s, 9H), 0.88 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 138.9, 126.4, 120.1, 117.0, 110.4, 96.8, 80.7, 70.0, 55.3, 30.3, 29.7 (3C), 27.4, 21.6, 18.7, 13.8; IR (neat, cm^{-1}): 706, 1093, 1204, 1364, 1600, 2207, 2961, 3138, 3311; HRMS (m/z) [M+H]$^+$ calculated mass for $C_{17}H_{24}N_5$ 298.2026 mass found 298.2024.

General procedure B: synthesis of imidazo[1,2-*b*]pyrazole derivatives



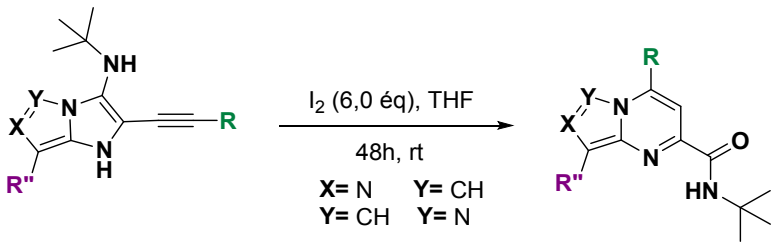
A flask containing a stirring bar was charged with the 5-amino-1*H*-pyrazole-4-carbonitrile (100 mg, 1.0 equiv.), phenyl propargyl aldehyde (1.1 equiv.) and *tert*-butyl isocyanide (1.1 equiv.) in PEG^{400} (1 mL). Zirconium tetrachloride (0.1 equiv.) was added and the mixture was stirred at room temperature for 1 hour. Next, 10 mL of AcOEt and 10 mL of water were added. The organic layer was separated, washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel using 30% ethyl acetate in petroleum ether as eluent to provide the desired products.

3-(*N*-*tert*-Butylamino)-2-(phenylethynyl)-1*H*-imidazo[1,2-*b*]pyrazole-7-carbonitrile (4k): Prepared according to the general procedure **B**; isolated as beige solid; Yield: 76%; Mp: 173-174°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.52 (s, 1H), 8.11 (s, 1H), 7.56 – 7.41 (m, 5H), 4.87 (s, 1H), 1.25 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 146.7, 138.3, 130.9, 130.7 (2C), 128.9, 128.8 (2C), 121.7, 114.7, 105.2, 94.9, 79.6, 65.3, 54.9, 29.9 (3C); IR (neat, cm^{-1}): 750, 1205, 1488, 1621, 2215, 2737, 2970, 3100, 3356; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{18}H_{18}N_5$ 304.1557 mass found 304.1555.

3-(*N*-*tert*-Butylamino)-7-phenyl-2-(phenylethynyl)-1*H*-imidazo[1,2-*b*]pyrazole (4l): Prepared according to the general procedure **B**; isolated as beige solid; yield: 37%; Mp: 181-182°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.63 (s, 1H), 8.11 (s, 1H), 7.66 – 7.30 (m, 10H), 4.64 (s, 1H), 1.32 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 141.0, 135.5, 132.8, 130.5 (2C), 130.1, 128.8 (2C), 128.6 (2C), 128.5, 123.7, 123.3 (2C), 122.3, 103.7, 96.4, 94.6, 81.2, 54.6, 30.0 (3C); IR (neat, cm^{-1}): 750, 1205, 1488, 1621, 2737, 2970, 3100, 3356. HRMS (m/z) $[M+H]^+$ calculated mass for $C_{23}H_{23}N_4$ 355.1917 mass found 355.1913.

Ethyl-3-(*tert*-butylamino)-2-(phenylethynyl)-1*H*-imidazo[1,2-*b*]pyrazole-7-carboxylate (4m): Prepared according to the general procedure **B**; isolated as beige solid; yield : 44%; Mp: 178-179°C, ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.10 (s, 1H), 7.96 (s, 1H), 7.56 – 7.42 (m, 5H), 4.75 (s, 1H), 4.21 (q, J = 7.1 Hz, 2H), 1.30 (d, J = 7.1 Hz, 3H), 1.26 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.9, 144.9, 137.7, 130.6 (2C), 128.8 (2C), 128.7, 122.1, 104.8, 99.5, 94.7, 89.8, 80.3, 58.8, 54.8, 29.9 (3C); IR (neat, cm^{-1}): 688, 751, 770, 1060, 1140, 1284, 1376, 1487, 1669, 2972, 3302. HRMS (m/z) $[M+H]^+$ calculated mass for $C_{20}H_{23}N_4O_2$ 351.1816 mass found 351.1816.

General procedure C: synthesis of imidazo[1,5-*a*]pyrimidine 5a-i and pyrazolo[1,5-*a*]pyrimidine derivatives 5k-m



Iodine (6.0 equiv.) was added to a solution of the imidazo[1,5-*a*]pyrimidine or pyrazolo[1,5-*a*]pyrimidine (100 mg, 1.0 equiv.) derivatives in 3 mL of tetrahydrofuran at room temperature. After 48h, the reaction mixture was poured into an aqueous saturated solution of $Na_2S_2O_3$ and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. The residue was purified by flash chromatography (using 10% ethyl acetate in petroleum ether) to provide the desired products.

***N*-(*tert*-Butyl)-8-cyano-4-phenylimidazo[1,5-*a*]pyrimidine-2-carboxamide (5a):** Prepared according to the general procedure **C**; isolated as orange solid; yield: 71%. Mp: 220-221°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.67 (s, 1H), 8.09 (s, 1H), 7.88 (dd, J = 7.5, 2.1 Hz, 2H), 7.74 – 7.63 (m, 3H), 7.52 (s, 1H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$)) δ 160.8, 151.9, 145.3, 142.9, 132.4, 130.1, 130.0 (2C), 128.0 (2C), 126.2, 114.1, 107.3, 105.2, 51.9, 28.7 (3C); IR (neat, cm^{-1}): 694, 747, 1223, 1480, 1491, 1677, 2221, 2918, 3133, 3387. HRMS (m/z) $[M+H]^+$ calculated mass for $C_{18}H_{18}N_5O$ 320.1506 mass found 320.1507.

***N*-(*tert*-Butyl)-8-cyano-4-(4-methoxyphenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5b):** Prepared according to the general procedure **C**; isolated as yellow solid; yield: 67%; Mp: 221-222°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.69 (s, 1H), 8.07 (s, 1H), 7.90 (d, J = 8.8 Hz, 2H), 7.48 (s, 1H), 7.21 (d, J = 8.8 Hz, 2H), 3.89 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.9, 161.3, 151.9, 145.6, 143.3, 130.3 (2C), 127.8, 121.9, 115.0, 114.9 (2C), 106.3, 102.1, 55.5, 51.0, 28.1 (3C); IR (neat, cm^{-1}): 675, 839, 1027, 1254, 1495, 1681, 2223, 2961, 3139, 3376; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{19}H_{20}N_5O_2$ 350.1612 mass found 350.1610.

***N*-(*tert*-Butyl)-8-cyano-4-(4-fluorophenyl)imidazo[1,5-*a*] pyrimidine-2-carboxamide (5c):** Prepared according to the general procedure C; isolated as yellow solid; yield: 53%. Mp: 229-230°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.67 (s, 1H), 8.10 (s, 1H), 8.00 (dd, J = 8.7, 5.5 Hz, 2H), 7.55 – 7.49 (m, 3H), 1.46 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 164.0 (d, J = 247.3 Hz) 161.26 , 152.0 , 144.7 , 143.1 , 131.4 (d, J = 9.1 Hz), 128.0 , 126.4 (d, J = 3.1 Hz, 2C), 116.7 , 116.6 (d, J = 22.1 Hz, 2C), 114.9 , 107.1, 102.4 , 51.4, 28.1 (3C); ^{19}F NMR (376 MHz, DMSO-d_6) δ -105.9 (s); IR (neat, cm^{-1}): 560, 855, 1160, 1498, 1673, 2221, 2979, 3131, 3391; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{18}H_{15}FN_5O$ 338.1412 mass found 338.1408.

***N*-(*tert*-Butyl)-8-cyano-4-(*p*-tolyl)imidazo[1,5-*a*]pyrimidine -2-carboxamide (5d):** Prepared according to the general procedure **C**; isolated as yellow solid; yield: 48%; Mp: 239-240°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.67 (s, 1H), 8.08 (s, 1H), 7.82 (d, J = 8.2 Hz, 2H), 7.49 (d, J = 7.9 Hz, 3H), 2.45 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.3, 152.0, 145.7, 143.2, 142.1, 130.1 (2C), 128.5 (2C), 127.9, 127.0, 115.0, 106.7, 102.3, 51.1, 28.2 (3C), 21.1; IR (neat, cm^{-1}): 689, 790, 1116, 1213, 1496, 1515, 1676, 2222, 2972, 3131, 3387; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{19}H_{20}N_5O$ 334.1662 mass found 334.1661.

***N*-(*tert*-Butyl)-8-cyano-4-(4-(trifluoromethyl)phenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5e):** Prepared according to the general procedure C; isolated as yellow solid; yield: 38%; Mp: 251-252°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.69 (s, 1H), 8.16 – 8.12 (m, 3H), 8.04 (d, J = 8.3 Hz, 2H), 7.60 (s, 1H), 1.46 (s, 9H); ^{13}C NMR (62.9 MHz, DMSO-d_6) δ 162.5, 141.9, 132.5, 131.0, 130.5, 130.4 (q, $^2J_{Cq\text{-}F}$ = 43.8, 32.5 Hz, $C_{q\text{-}F}$), 127.9 (d, J = 3.7 Hz, 2C), 126.6, 125.6 (q, $^3J_{CHAr\text{-}F}$ = 3.8 Hz, $2C_{HAr}$), 123.7 (q, $^1J_{C\text{-}F}$ = 272.7 Hz), 115.3, 112.1, 99.4, 51.0, 24.4 (3C); ^{19}F NMR (376 MHz, DMSO-d_6) δ -61.5 ; IR (neat, cm-1): 702, 841, 1126, 1323, 1521, 1678, 2224, 2923, 3133, 3383; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{19}H_{17}F_3N_5O$ 388.1380 mass found 388.1379.

***N*-(*tert*-Butyl)-8-cyano-4-(3-methoxyphenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5f):** Prepared according to the general procedure **C**; isolated as yellow solid; yield: 30%, Mp: 211-212°C; ^{1}H NMR (250 MHz, DMSO-d_6) δ 8.69 (s, 1H), 8.09 (s, 1H), 7.62 – 7.52 (m, 2H), 7.45 (d, J = 6.8 Hz, 2H), 7.26 (d, J = 8.0 Hz, 1H), 3.86 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (62.9 MHz,

DMSO-d_6) δ 161.2, 159.7, 152.0, 145.4, 143.1, 131.1, 130.7, 128.0, 120.6, 118.1, 114.9, 113.3, 107.0, 102.4, 55.4, 51.1, 28.1 (3C); IR (neat, cm^{-1}): 746, 862, 1247, 1505, 1675, 2223, 2920, 3134, 3396; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{19}H_{20}N_5O_2$ 350.1612 mass found 350.1612.

***N*-(*tert*-Butyl)-8-cyano-4-(2-methoxyphenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5g):** Prepared according to the general procedure **C**; isolated as yellow solid; yield: 15%; Mp: 196-197°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.29 (s, 1H), 8.11 (s, 1H), 7.70 (ddd, *J* = 8.6, 7.5, 1.7 Hz, 1H), 7.63 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.49 (s, 1H), 7.33 (d, *J* = 8.6 Hz, 1H), 7.21 (td, *J* = 7.5, 1.7 Hz, 1H), 3.81 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.3, 156.7, 151.1 , 143.7, 142.2, 133.5 , 131.1, 129.3, 121.1, 118.2, 114.9, 112.3, 108.2, 102.1, 55.7, 51.1, 28.1 (3C); IR (neat, cm^{-1}): 548, 747, 1246, 1520, 1672, 2227, 2972, 3111, 3390. HRMS (m/z) $[M+H]^+$ calculated mass for $C_{19}H_{20}N_5O_2$ 350.1612 mass found 350.1613.

***N*-(*tert*-Butyl)-8-cyano-4-(3-fluorophenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5h):** Prepared according to the general procedure C; isolated as yellow solid; yield: 12%. Mp: 216-217°C; ^{1}H (400 MHz, DMSO-d_6) δ 8.71 (s, 1H), 8.10 (s, 1H), 7.82 (dt, *J* = 9.5, 2.1 Hz, 1H), 7.73 (td, *J* = 7.8, 5.7 Hz, 2H), 7.59 – 7.52 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 162.3 (d, *J* = 248.1 Hz), 161.2, 152.1, 144.2, 143.0, 131.8 (d, *J* = 9.6 Hz), 128.2, 124.9 (d, *J* = 2.9 Hz), 118.7 (d, *J* = 20.9 Hz), 115.8 (d, *J* = 24.0 Hz), 114.9, 107.5, 102.6, 69.6 (d, *J* = 11.4 Hz), 51.2, 28.2 (3C); ^{19}F NMR (376 MHz, DMSO-d_6) δ -110.9; IR (neat, cm^{-1}): 699, 797, 1486, 1510, 1676, 2223, 2923, 3073, 3133, 3391; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{18}H_{17}FN_5O$ 338.1412 mass found 338.1412.

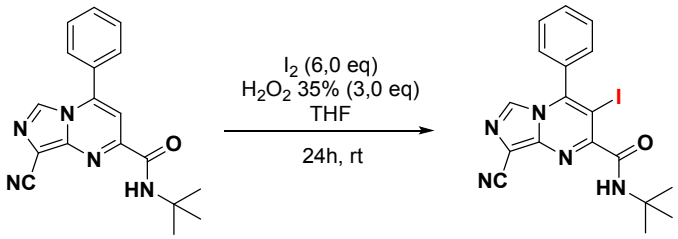
***N*-(*tert*-Butyl)-8-cyano-4-(2-fluorophenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5i):** Prepared according to the general procedure **C**; isolated as yellow solid, yield: traces, HRMS (m/z) $[M+H]^+$ calculated mass for $C_{18}H_{17}FN_5O$ 338.1412 mass found 338.1410.

***N*-(*tert*-Butyl)-3-cyano-7-phenylpyrazolo[1,5-*a*]pyrimidine-5-carboxamide (5k):** Prepared according to the general procedure C; isolated as beige solid; yield: 35%; Mp: 220-221°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.97 (s, 1H), 8.18 – 8.10 (m, 3H), 7.89 (s, 1H), 7.71 – 7.62 (m, 3H), 1.47 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 161.1, 153.2, 149.6, 148.9, 148.5, 131.9, 129.8 (2C), 129.4, 128.6 (2C), 113.2, 107.6, 82.3, 51.1, 28.2 (3C); IR (neat, cm^{-1}): 689, 897, 1449, 1529, 1682, 2231, 2924, 3070, 3382; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{18}H_{18}N_5O$ 320.1506 mass found 320.1507

N-(tert-Butyl)-3,7-diphenylpyrazolo[1,5-a]pyrimidine-5-carboxamide (5l): Prepared according to the general procedure **C**; isolated as beige solid; yield : 56%; Mp: 228-229°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.61 (s, 1H), 8.37 (s, 1H), 8.10 – 8.05 (m, 2H), 7.63 (dd, *J* = 5.3, 1.8 Hz, 3H), 7.56 – 7.43 (m, 4H), 7.44 (s, 1H), 7.28 (t, *J* = 7.4 Hz, 1H), 1.43 (s, 9H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.0, 157.6, 149.6, 143.0, 142.5, 133.8, 131.3, 130.2, 129.2 (2C), 128.78 (2C), 128.71 (2C), 126.4, 125.9 (2C), 109.8, 77.2, 51.2, 28.4 (3C); IR (neat, cm^{-1}): 755, 1012, 1196, 1217, 1457, 1644, 2929, 2961, 3271; HRMS (m/z) $[M+H]^+$ calculated mass for $C_{23}H_{23}N_4O$ 371.1866 mass found 371.1849.

Ethyl 5-(*tert*-butylcarbamoyl)-7-phenylpyrazolo[1,5-*a*]pyrimidine-3-carboxylate (5m): Prepared according to the general procedure **C**; isolated as beige solid; yield: 67%; Mp: 190-191°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.48 (s, 1H), 8.36 (s, 1H), 7.62 (dd, *J* = 5.1, 1.9 Hz, 4H), 7.49 (dd, *J* = 6.7, 3.0 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.43 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.6, 161.2, 160.4, 150.6, 147.0, 145.7, 133.3, 130.4, 129.2 (2C), 128.6 (2C), 102.0, 79.7, 59.7, 51.2, 28.3 (3C), 14.3; IR (neat, cm^{-1}): 694, 749, 1063, 1128, 1477, 1520, 1669, 1694, 2973, 3325. HRMS (m/z) $[M+H]^+$ calculated mass for $C_{20}H_{23}N_4O_3$ 367.1765 mass found 367.1762.

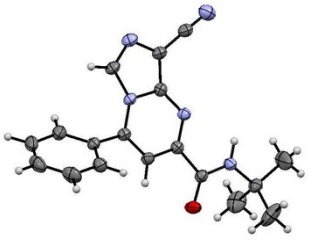
Synthesis of imidazo[1,5-*a*]pyrimidine 6a



Iodine (6.0 equiv.) and H_2O_2 35% (3.0 equiv.) were added to a solution of the imidazo[1,5-a]pyrimidine **5a** (50 mg, 1.0 equiv.) in 2 mL of tetrahydrofuran at room temperature under argon. After 24h, the reaction mixture was poured into an aqueous saturated solution of $Na_2S_2O_3$ and extracted with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered off and concentrated under reduced pressure. The residue was purified by flash chromatography (using 10% ethyl acetate in petroleum ether) to provide the desired product.

***N*-(*tert*-Butyl)-8-cyano-3-iodo-4-phenylimidazo[1,5-a]pyrimidine-2-carboxamide (6a):** isolated as yellow solid; yield: 31%; Mp: 282-283°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.44 (s, 1H, NH), 7.87 (s, 1H, Himidazole), 7.73 – 7.68 (m, 3H, HAr), 7.61 – 7.57 (m, 2H, HAr), 1.43 (s, 9H, 3CH_3); ^{13}C NMR (101 MHz, DMSO-d_6) δ 165.5, 159.8, 147.2, 142.8, 132.9, 131.8, 130.1 (2C), 129.3 (2C), 128.4, 115.2, 101.9, 81.4, 51.9, 28.8 (3C); IR (neat, cm^{-1}): 697, 736, 1214, 1415, 1468, 1524, 1580, 1655, 2237, 2926, 3135. HRMS (m/z) $[M+H]^+$ calculated mass for $C_{18}H_{17}IN_5O$ 446.1203, mass found 446.1218.

Structure of 5a by a single-crystal X-ray study.



Crystallographic studies for compound **5a** were performed at **170** K. Single crystals were mounted on a Xcalibur equipped with monochromatized Mo-K radiation (0.71073 Å). The data collection, unit cell refinement, and data reduction were performed using the CrysAlis CCD, Oxford Diffraction Ltd. software package[1].

The structural determination was carried out by direct methods, and the refinement of atomic parameters based on full-matrix least-squares on F^2 were performed using the SHELX-2014 programs[2] within the WINGX package[3]. The positions of non-H atoms were determined and refinement by SHELX-2014 program[2]. A summary of crystallographic data for **5a** was resumed in table 1.

The positions of the H atoms were deduced from coordinates of the non-H atoms and Fourier synthesis. H atoms were included for structure factor calculations but not refined. Supplementary crystallographic data can be found in the CCDC deposit (CCDC 1900146), and obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif/.

Table 1. Crystal data and structure refinement for compound 5a.

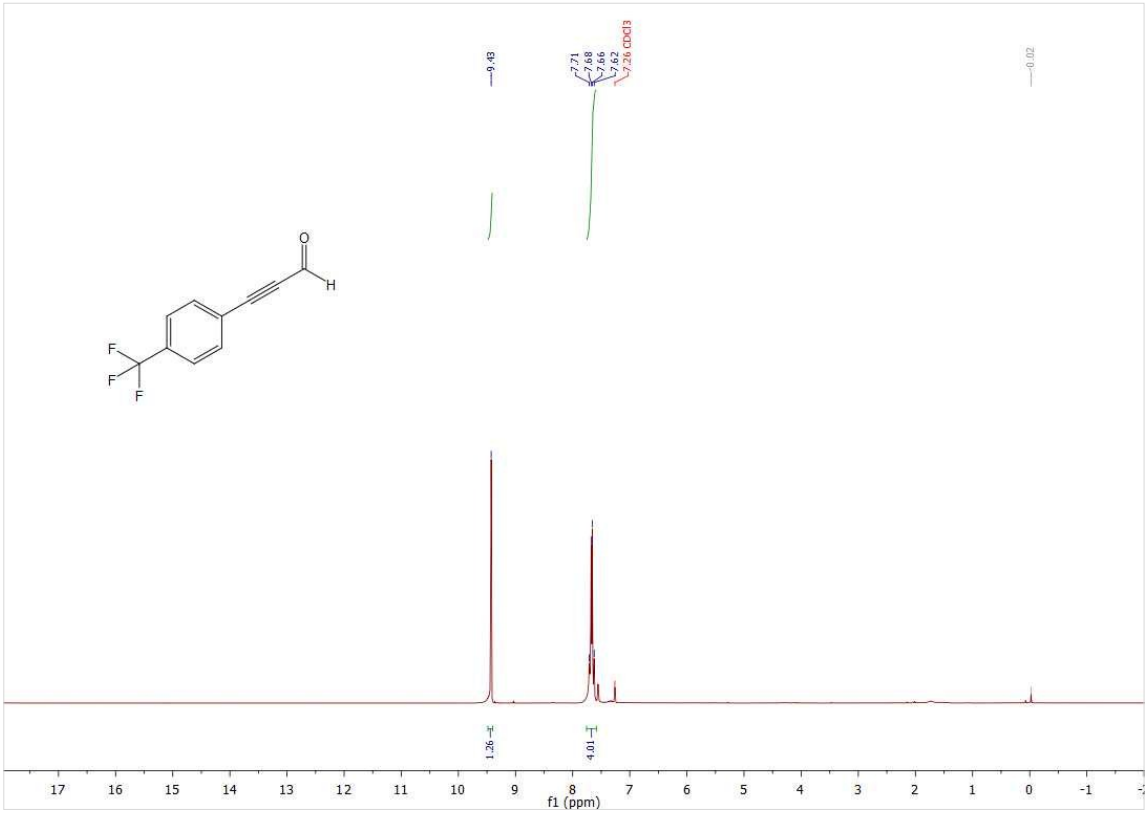
CCDC number deposit	CCDC 1900146
Empirical formula	C_{18} H_{17} N_5 O
Formula weight	319.36
Temperature	170(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P 21/c
Unit cell dimensions	a = 10.7895(4) Å
	b = 14.8634(7) Å
	c = 10.0794(5) Å
	= 92.246(4)°
Volume	1615.18(13) $Å^3$
Z	4
D_c	1.313 g/cm^3
Absorption coefficient	0.086 mm^{-1}
F(000)	672
Crystal size	0.300 x 0.230 x 0.160 mm
Theta range for data collection	3.407 - 26.368°
Index ranges	-13≤ h ≤ 13 -17≤ k≤ 18 -10≤ l≤ 12
Reflections collected	9923
Independent reflections	3302 [R_{int} = 0.0755]
Completeness	99.7 %
Refinement method	Full-matrix least-squares on F^2
Data / parameters	3302 / 220
Goodness-of-fit on F^2	1.021
Final R indices [I > 2 (I)]	R1 = 0.0521, wR2 = 0.1025
R indices (all data)	R1 = 0.0884, wR2 = 0.1223
Largest diff. peak and hole	0.235 and -0.285 $e.Å^{-3}$

References:

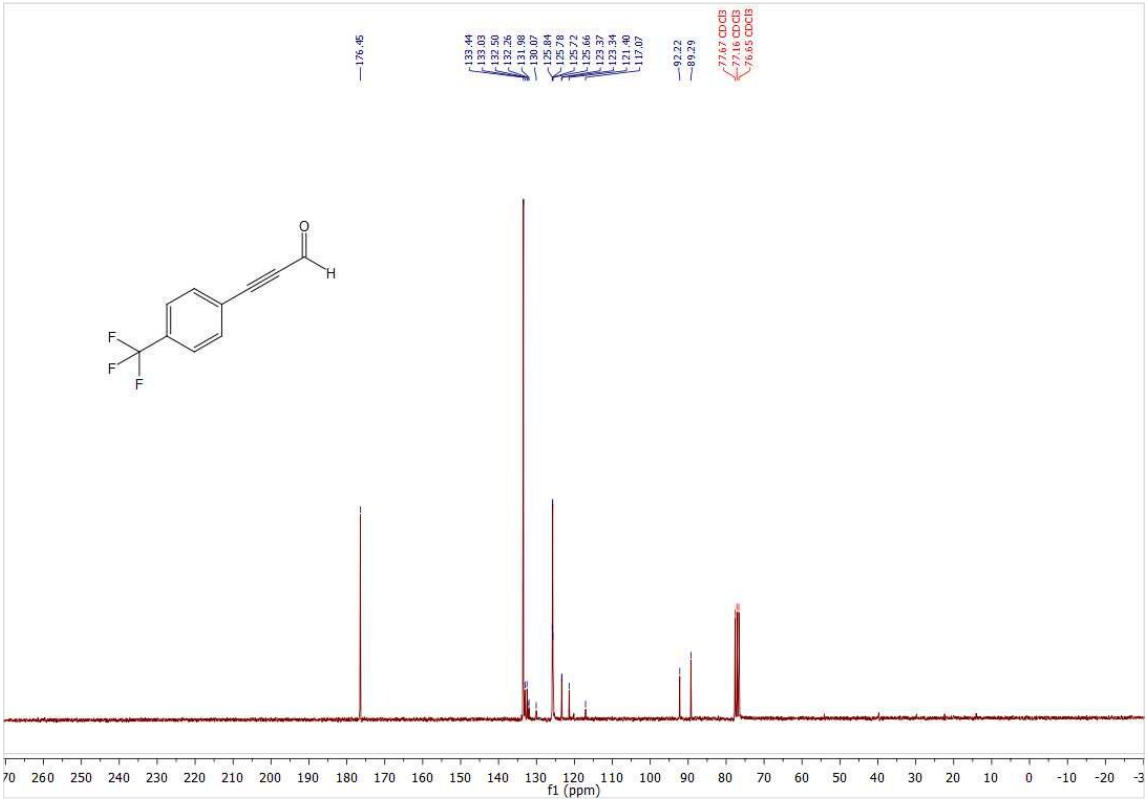
1- F. R. Michailidis, C. Besnard, A. Alexakis, *Org. Lett.* 2012, **14**, **18**, 4906-4909
2- CrysAlis CCD, Oxford Diffraction Ltd., Version 1.171.33.46.
3- G. M. Sheldrick, Programs for Crystal Structure Analysis; University of Göttingen: Göttingen, Germany, 2014.
4- L. J. Farrugia, WinGX, *J. Appl. Cryst*. 2012, **45**, 849-854.

3-(4-(trifluoromethyl)phenyl)propiolaldehyde (3e):

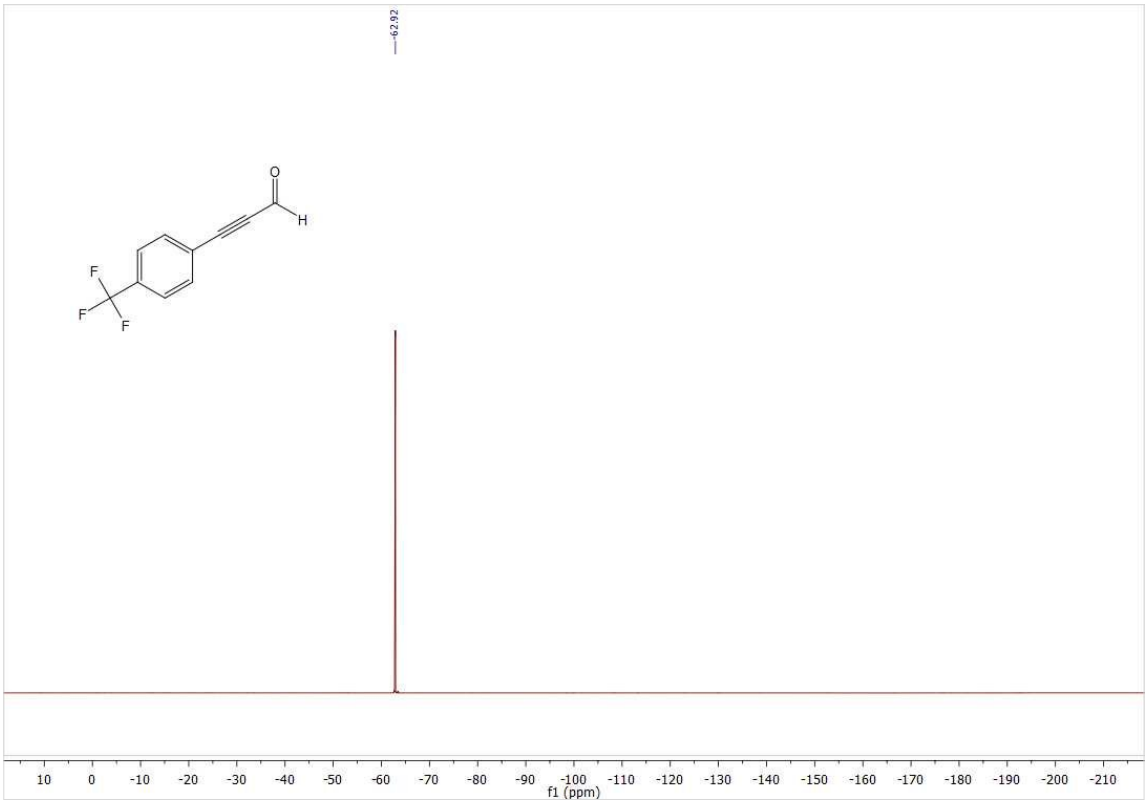
^{1}H NMR (400 MHz, Chloroform-*d*) *δ*



^{13}C NMR (101 MHz, Chloroform-*d*) *δ*

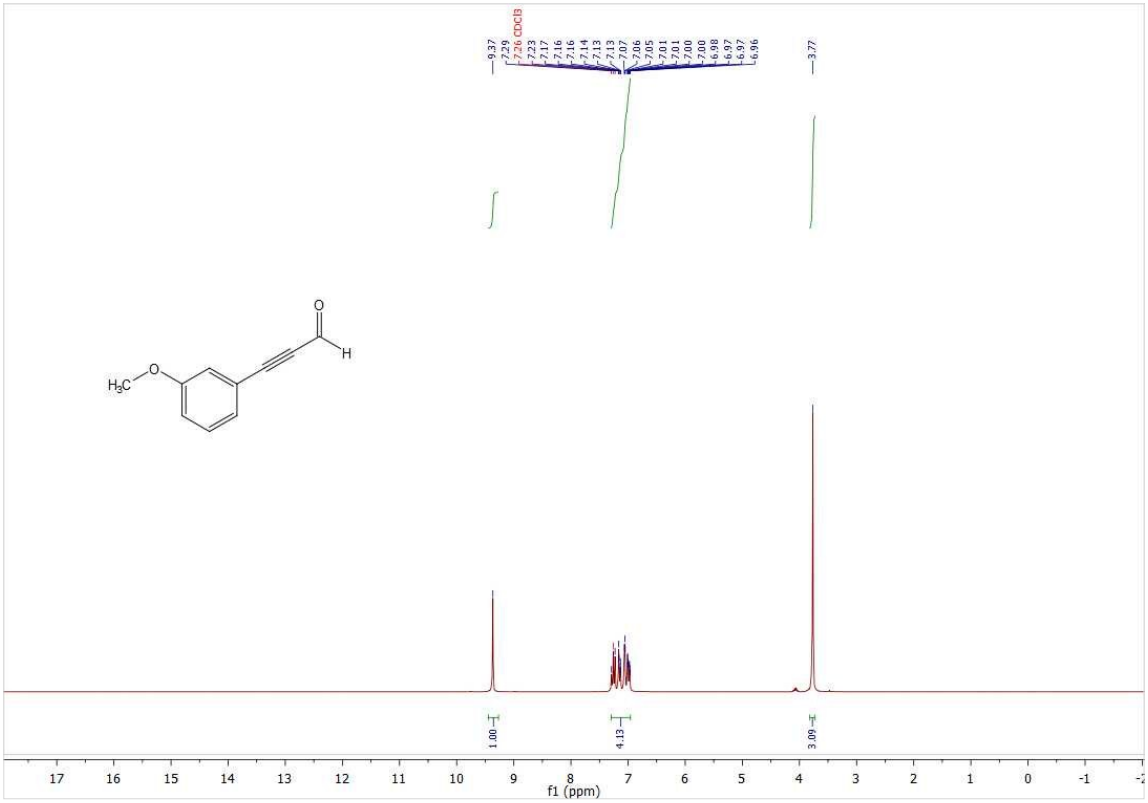


^{19}F NMR (376 MHz, Chloroform-*d*) *δ*

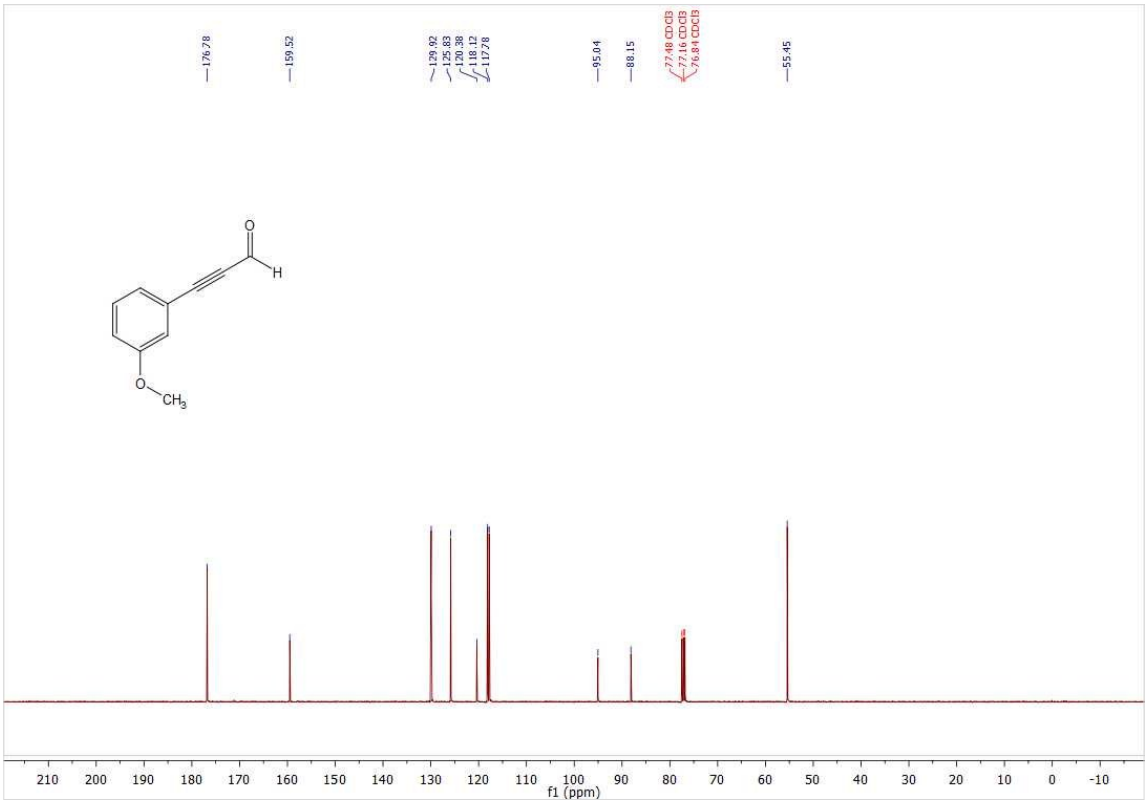


3-(3-methoxyphenyl)propiolaldehyde (3f):

^{1}H NMR (400 MHz, Chloroform-*d*) *δ*

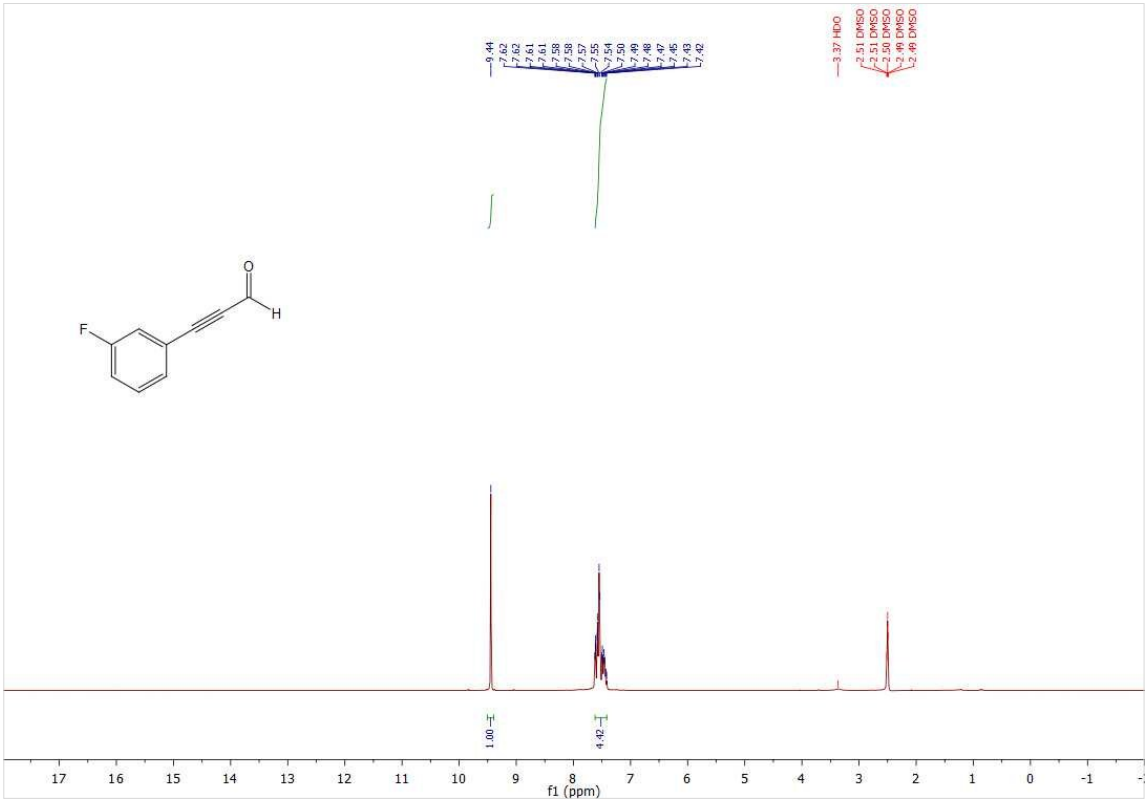


^{13}C NMR (101 MHz, Chloroform-*d*) *δ*

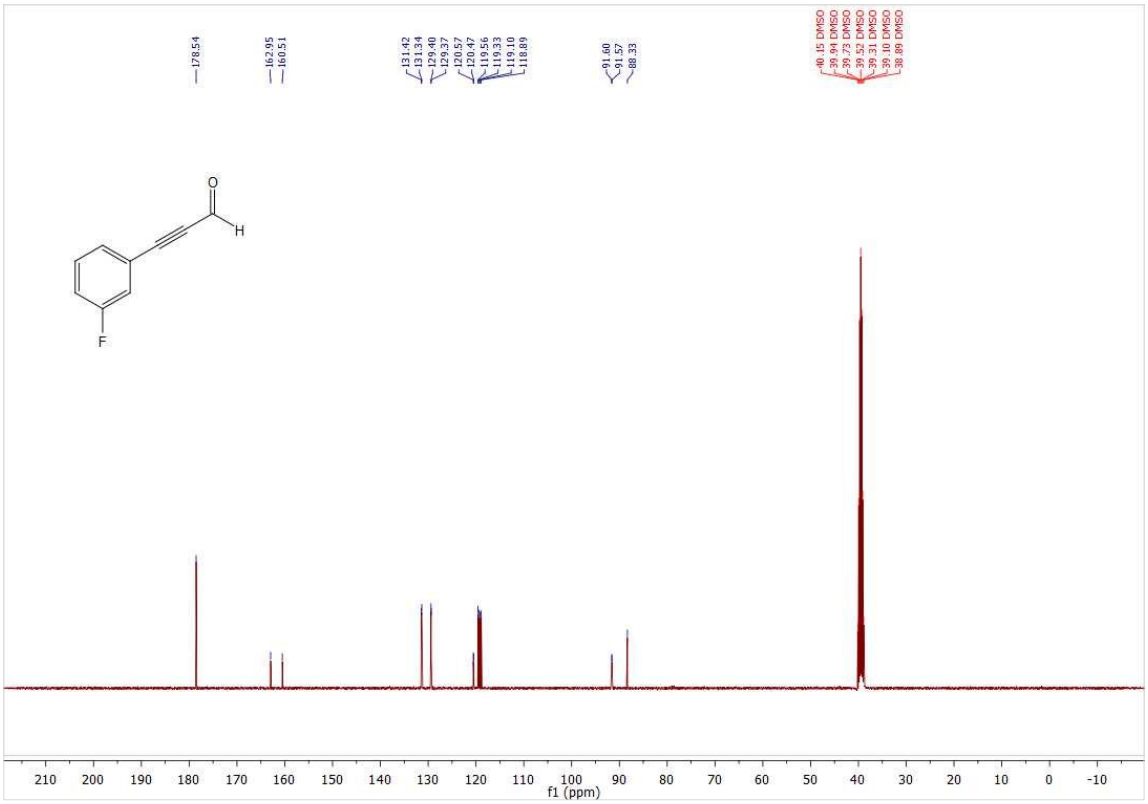


3-(3-fluorophenyl)propiolaldehyde (3g):

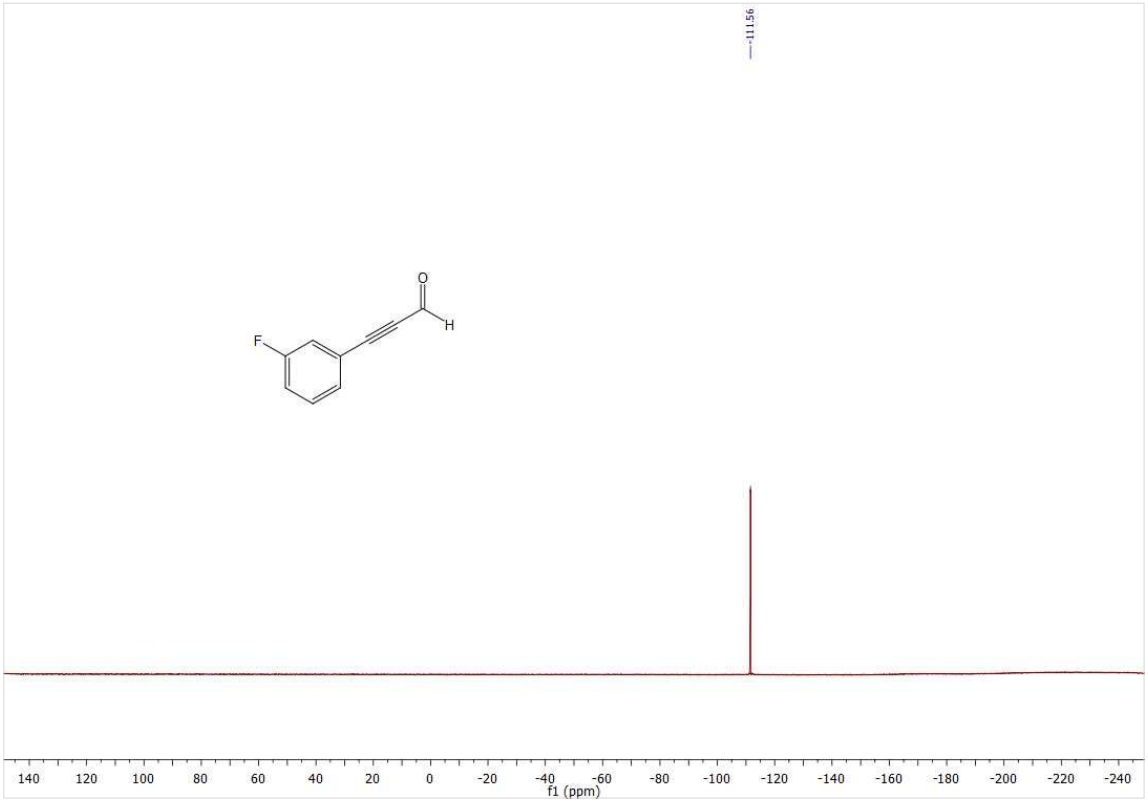
^{1}H NMR (400 MHz, DMSO-*d*$_6$) *δ*



^{13}C NMR (101 MHz, DMSO-d_6) δ

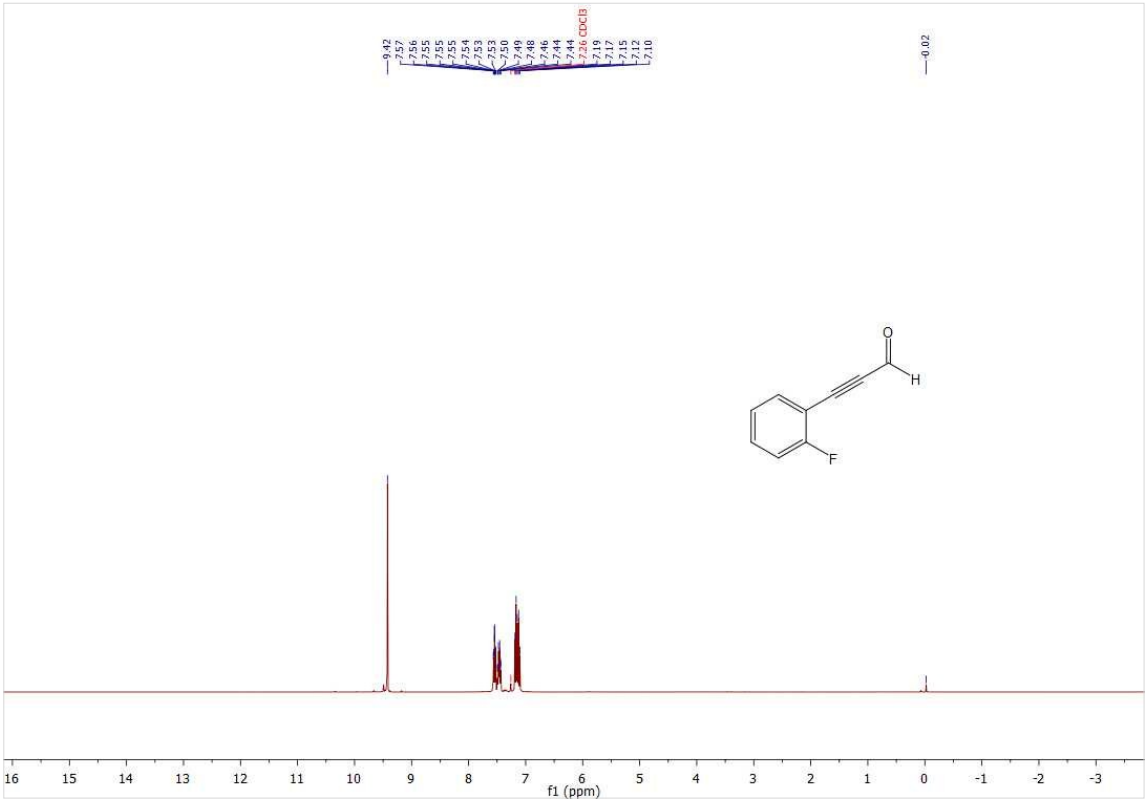


^{19}F NMR (376 MHz, Chloroform-d) δ

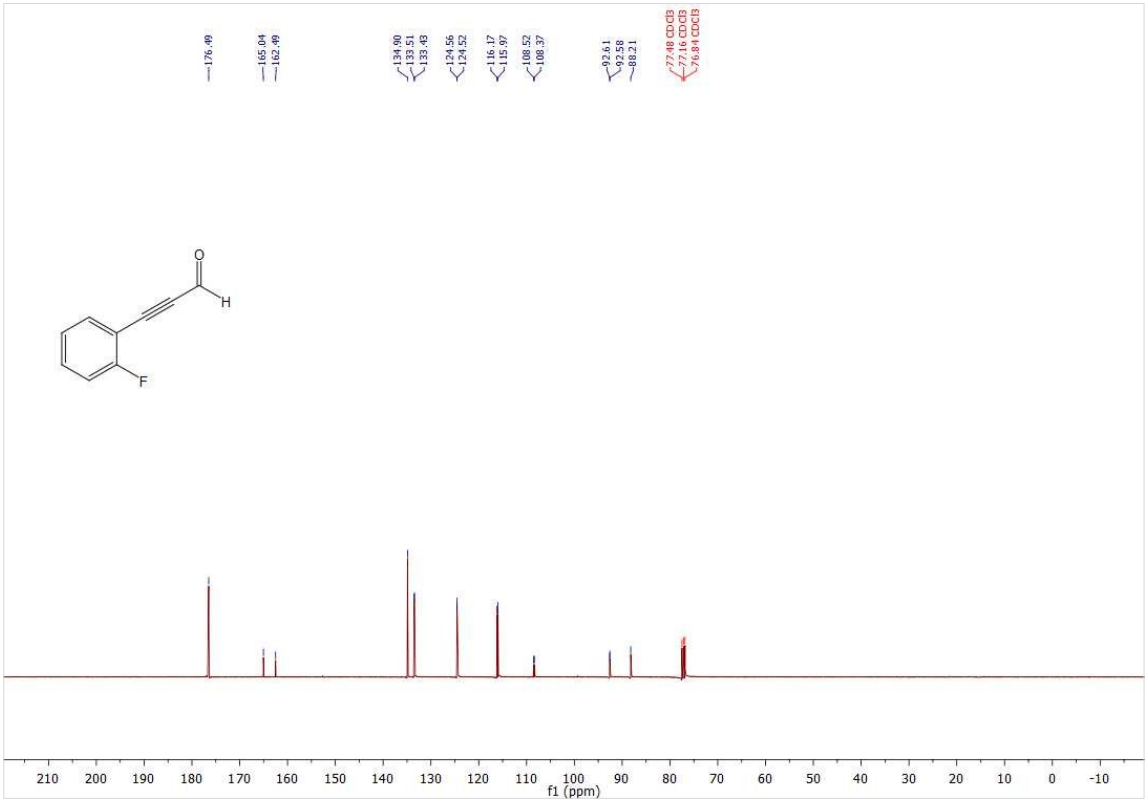


3-(2-fluorophenyl)propiolaldehyde (3i):

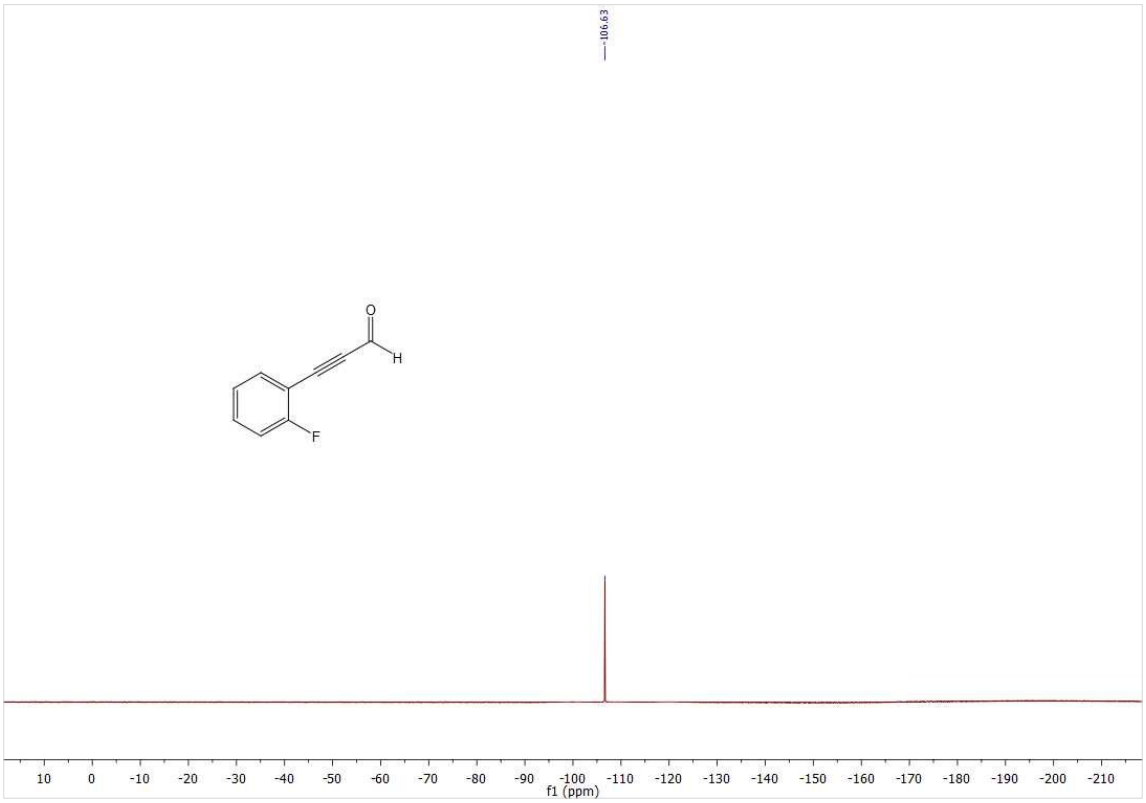
^{1}H NMR (400 MHz, DMSO-d_6) δ



^{13}C NMR (101 MHz, DMSO-d_6) δ



^{19}F NMR (376 MHz, Chloroform-*d*) *δ*



3-(3-methoxyphenyl)propiolaldehyde (3f):

^{1}H NMR (400 MHz, Chloroform-*d*) *δ*

^{13}C NMR (101 MHz, Chloroform-*d*) *δ*

3-(3-fluorophenyl)propiolaldehyde (3g):

^{1}H NMR (400 MHz, DMSO-d_6) *δ*

^{13}C NMR (101 MHz, DMSO-d_6) δ

^{19}F NMR (376 MHz, Chloroform-d) δ

3-(2-fluorophenyl)propiolaldehyde (3i):

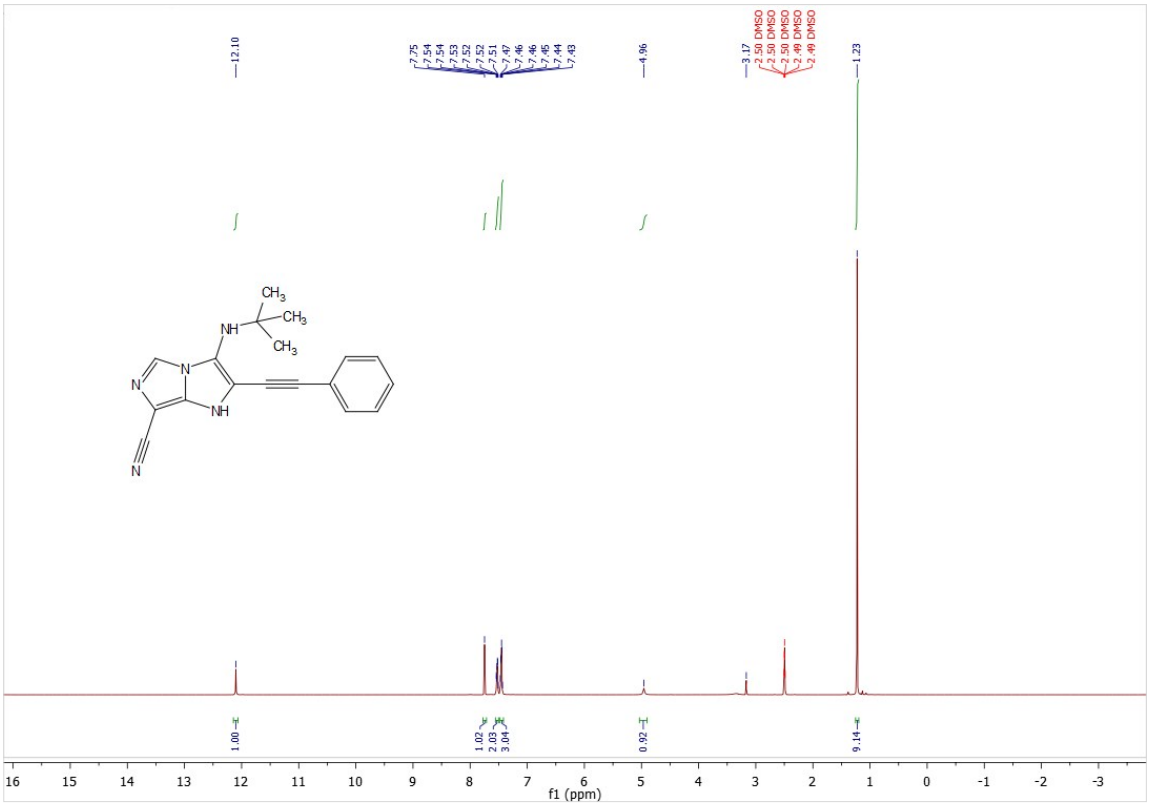
^{1}H NMR (400 MHz, DMSO-d_6) δ

^{13}C NMR (101 MHz, DMSO-d_6) δ

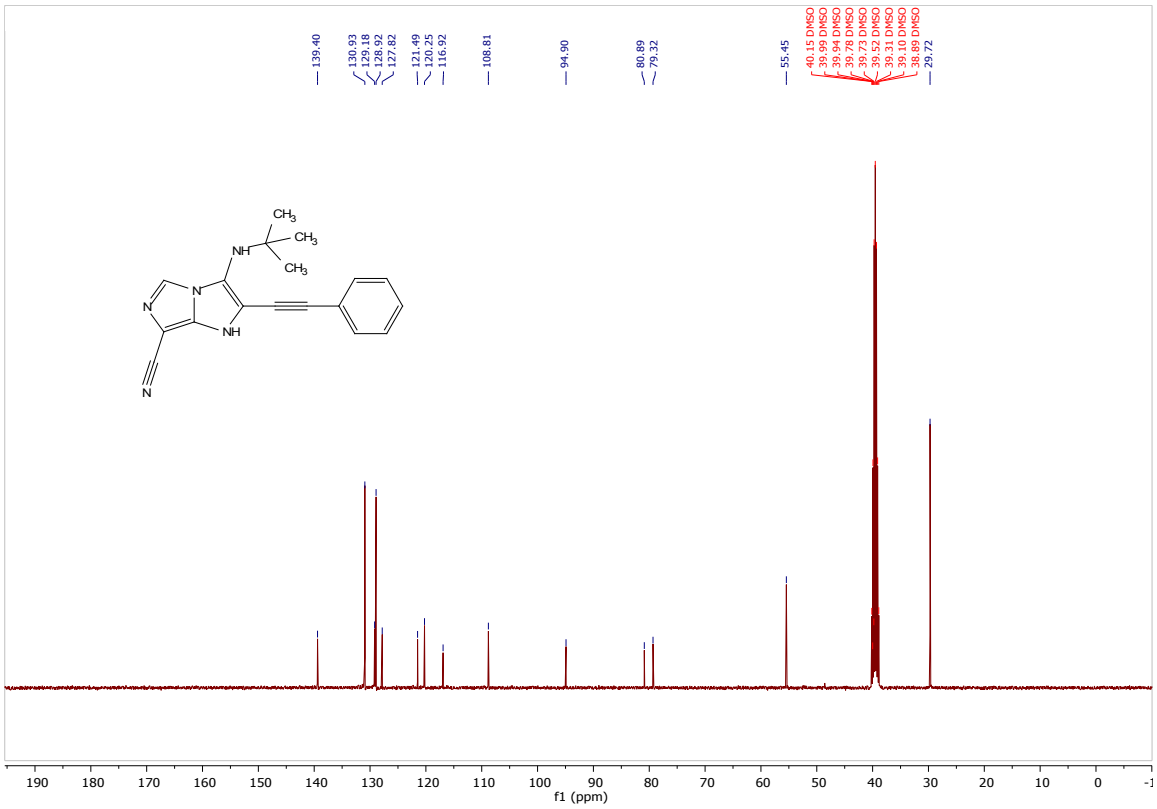
^{19}F NMR (376 MHz, Chloroform-*d*) δ

3-(*tert*-Butylamino)-2-(phenylethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4a):

^{1}H NMR (400 MHz, DMSO-d_6)

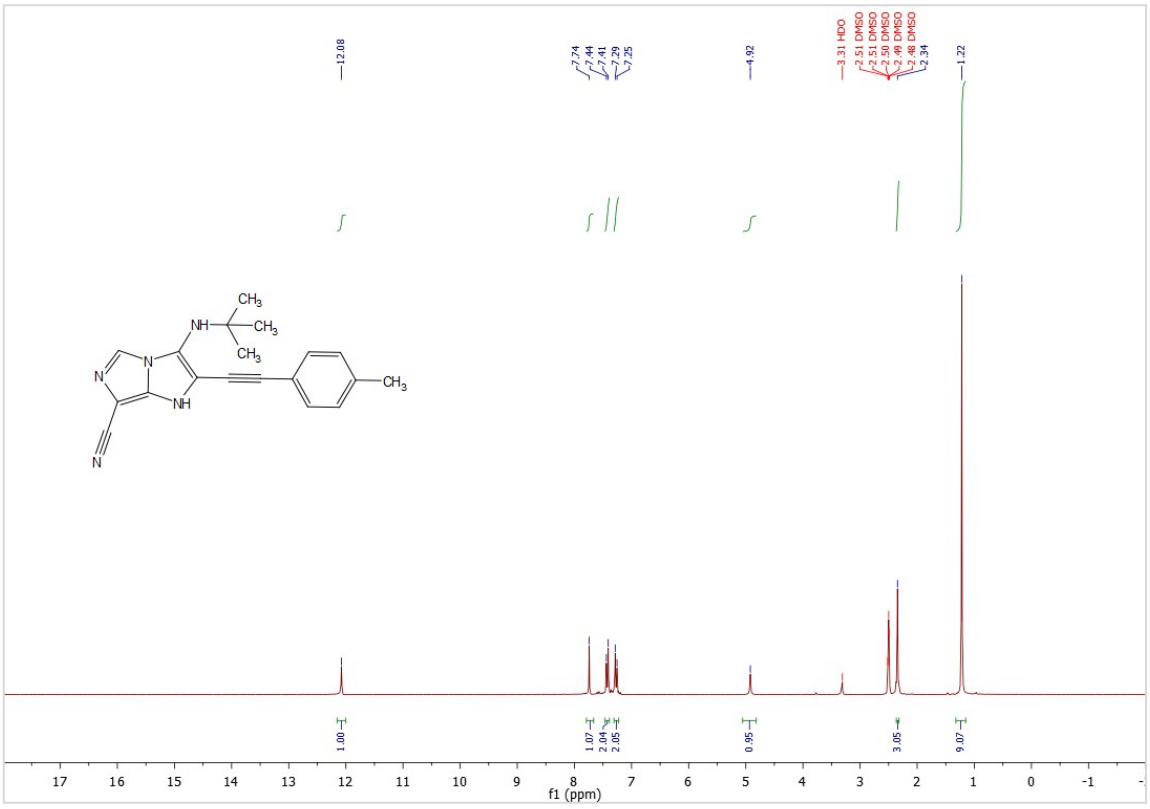


^{13}C NMR (101 MHz, DMSO-d_6)

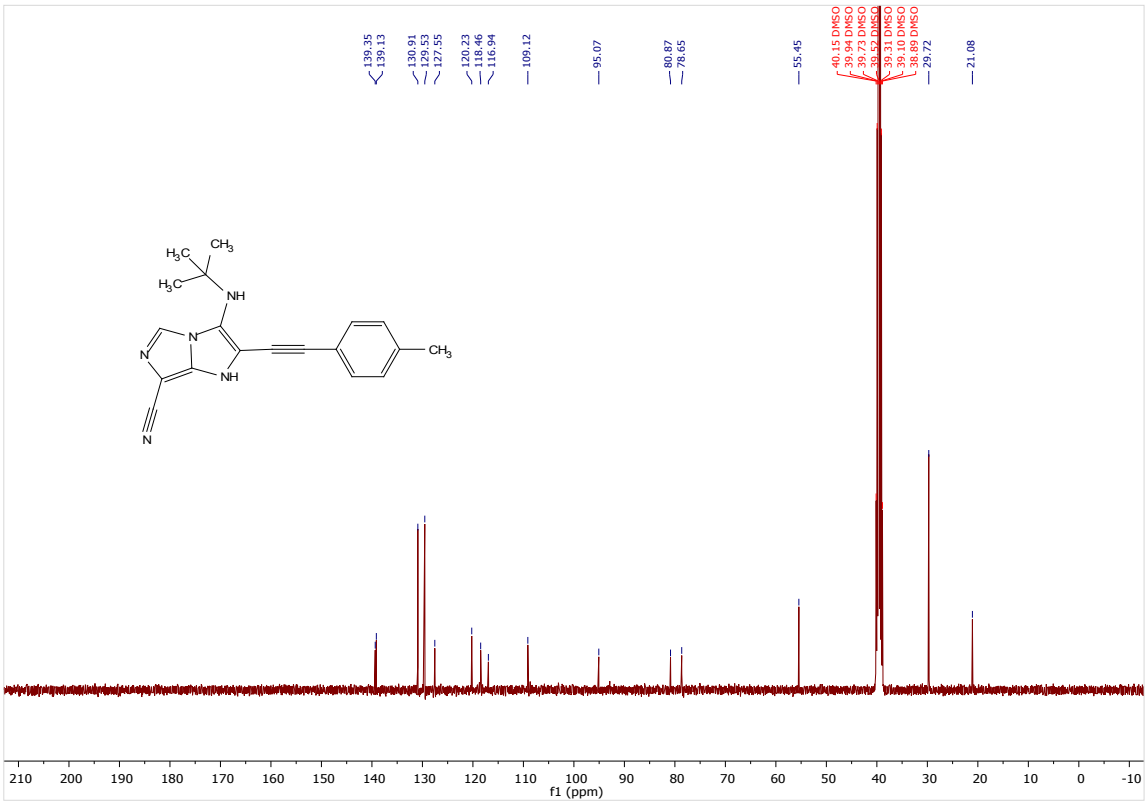


3-(*tert*-Butylamino)-2-(*p*-tolylethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4b):

^{1}H NMR (400 MHz, DMSO-d_6)

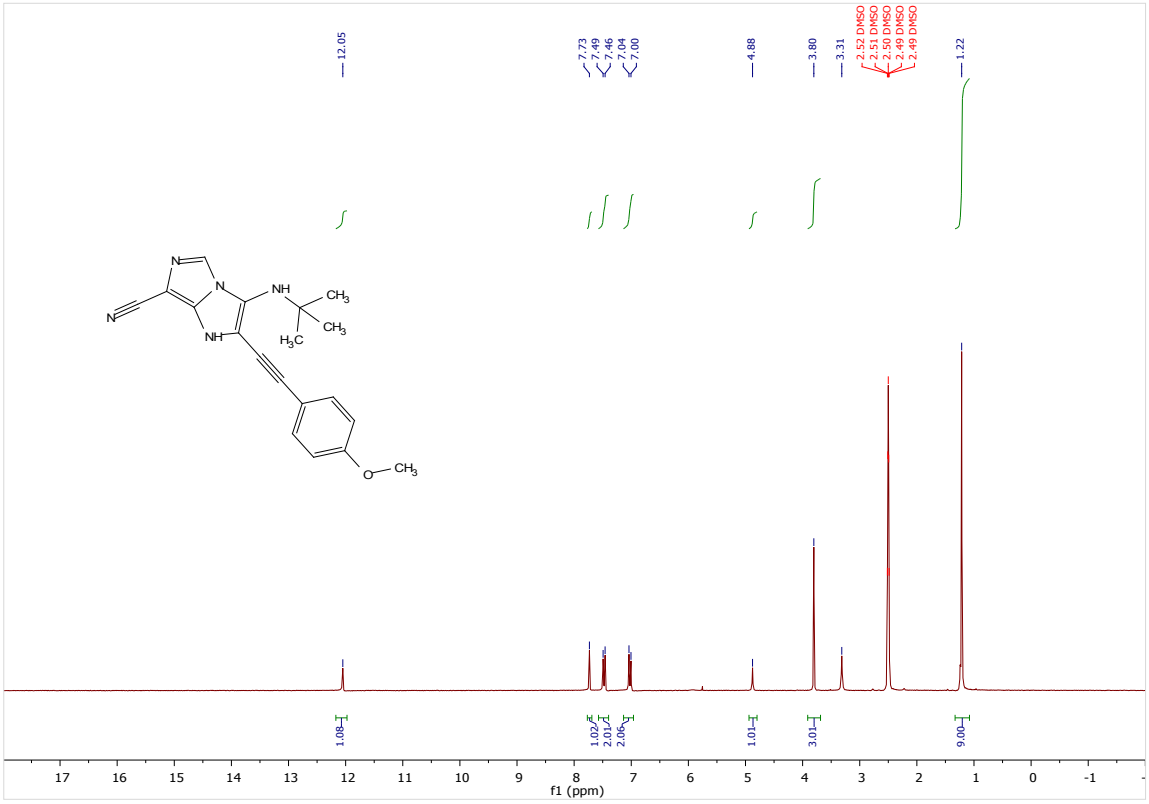


^{13}C NMR (101 MHz, DMSO-d_6)

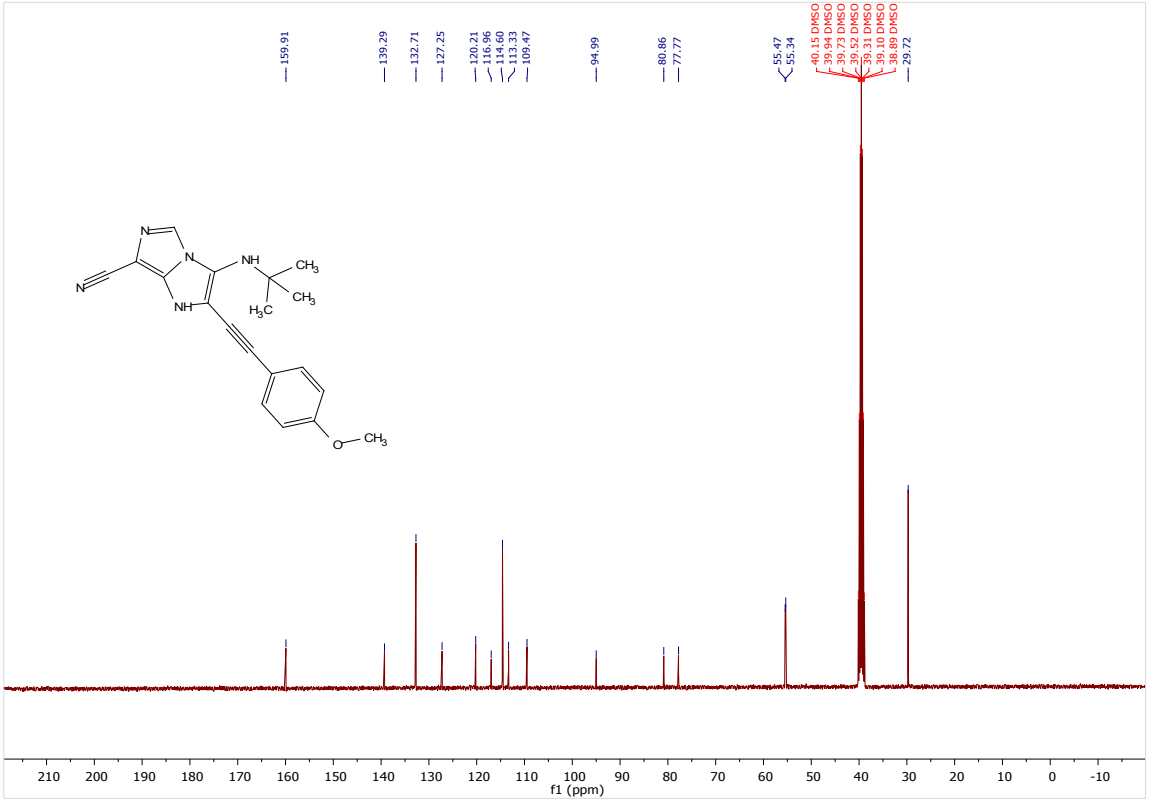


3-(*tert*-Butylamino)-2-((4-methoxyphenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4c):

^{1}H NMR (400 MHz, DMSO-d_6)

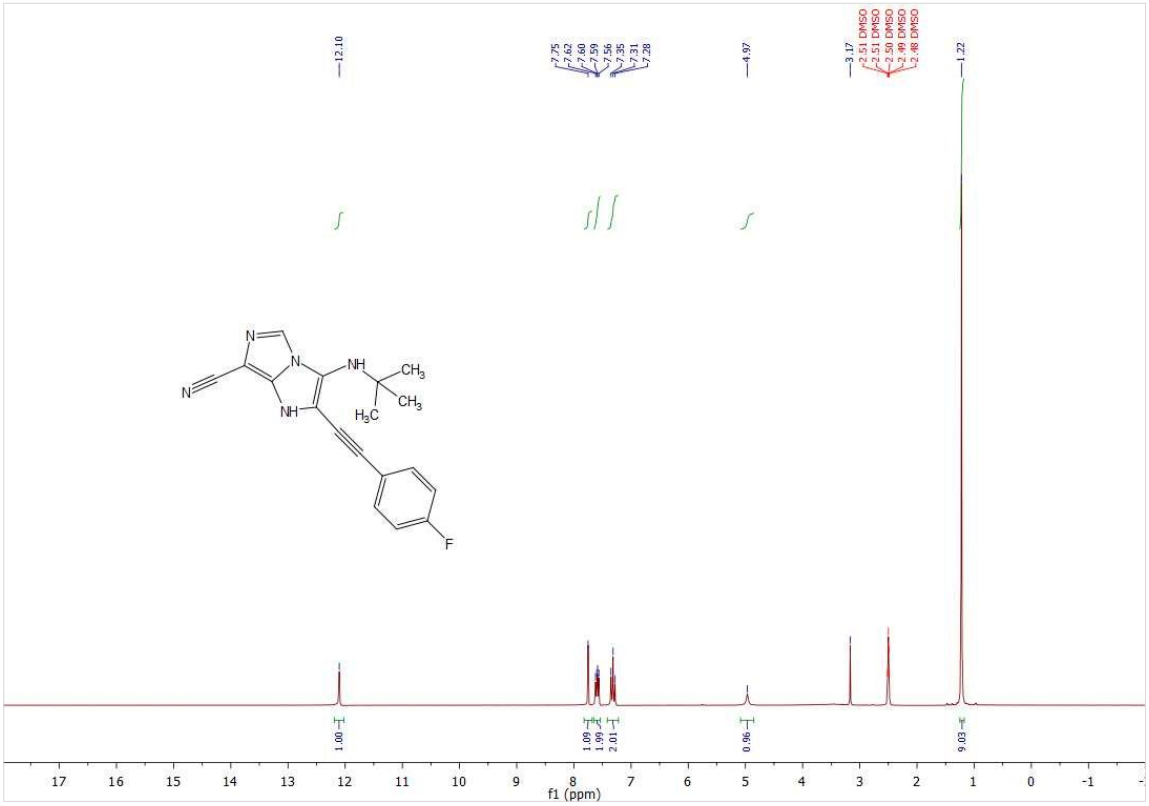


^{13}C NMR (101 MHz, DMSO-d_6)

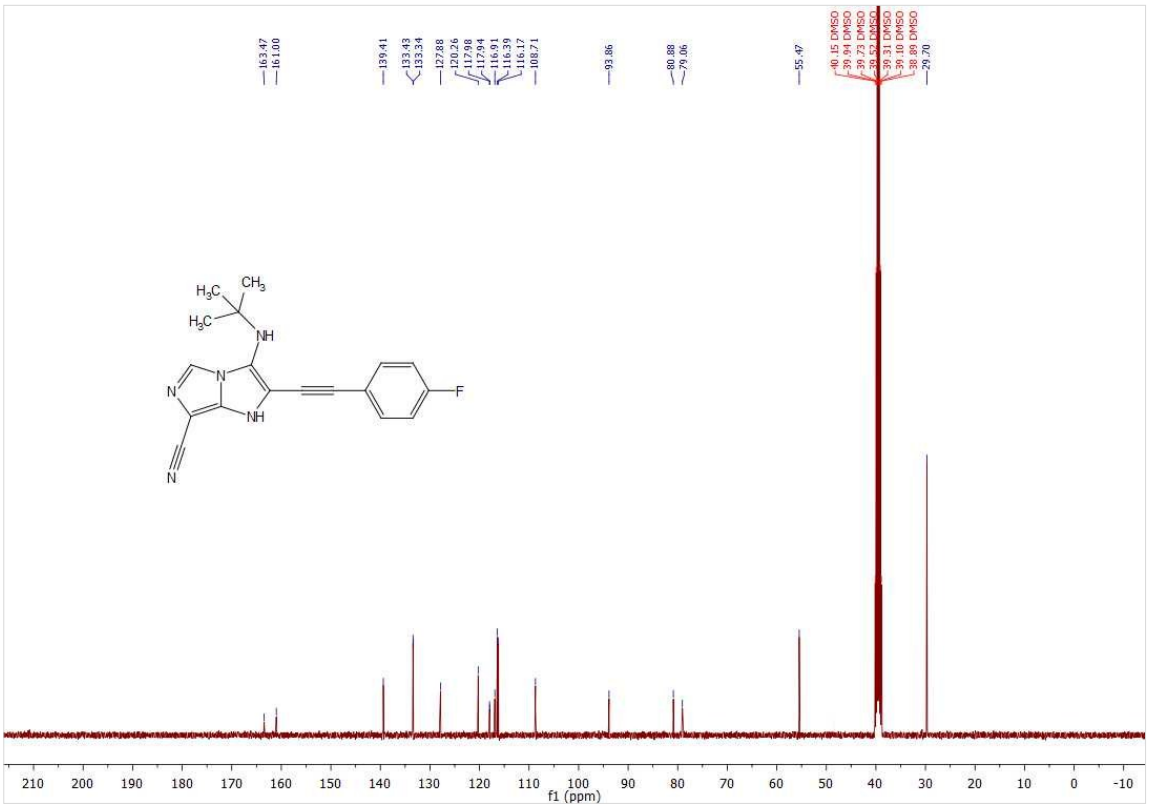


3-(*tert*-Butylamino)-2-((4-fluorophenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4d):

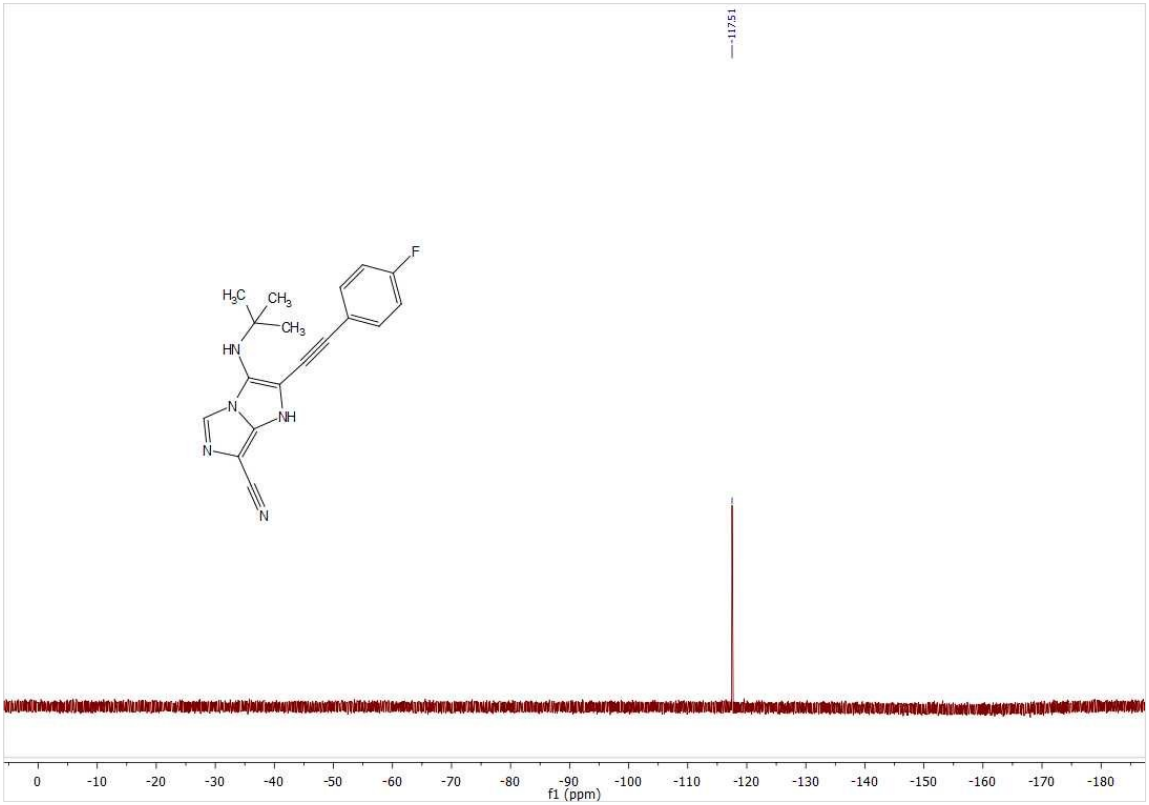
^{1}H NMR (400 MHz, DMSO-d_6)



^{13}C NMR (101 MHz, DMSO-d_6)

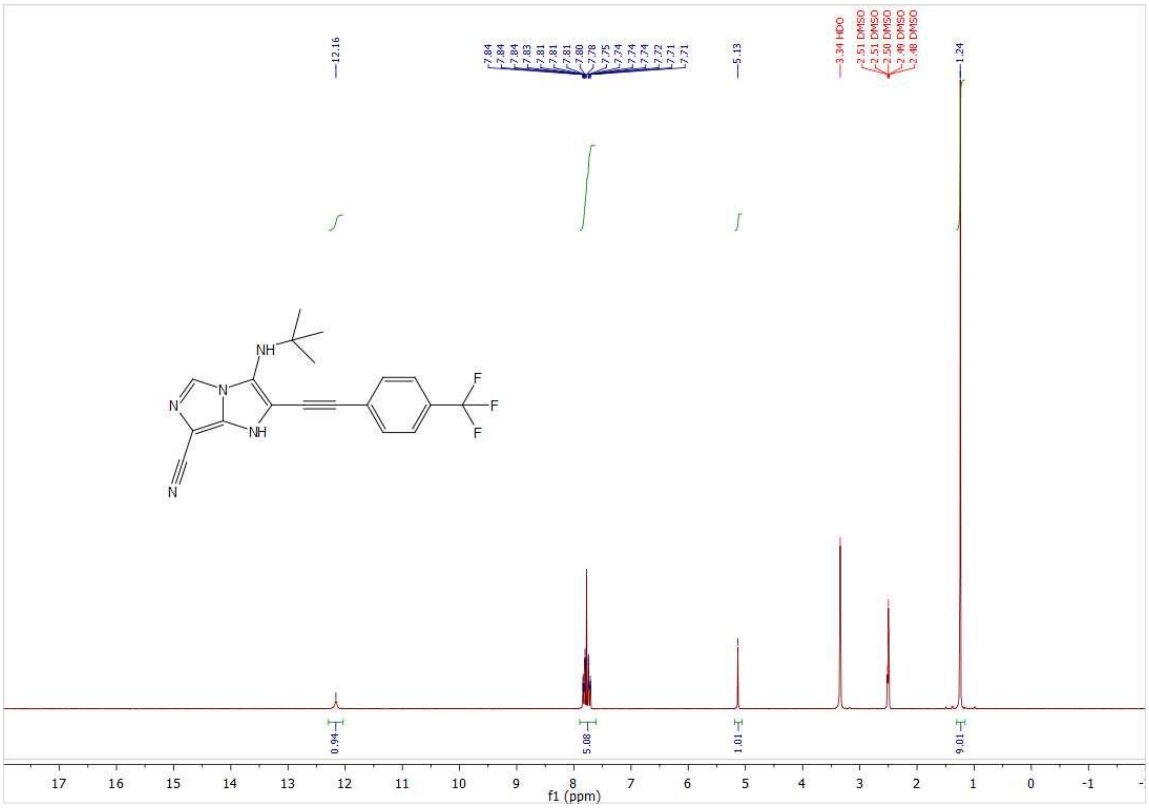


^{19}F NMR (376 MHz, DMSO-d_6)

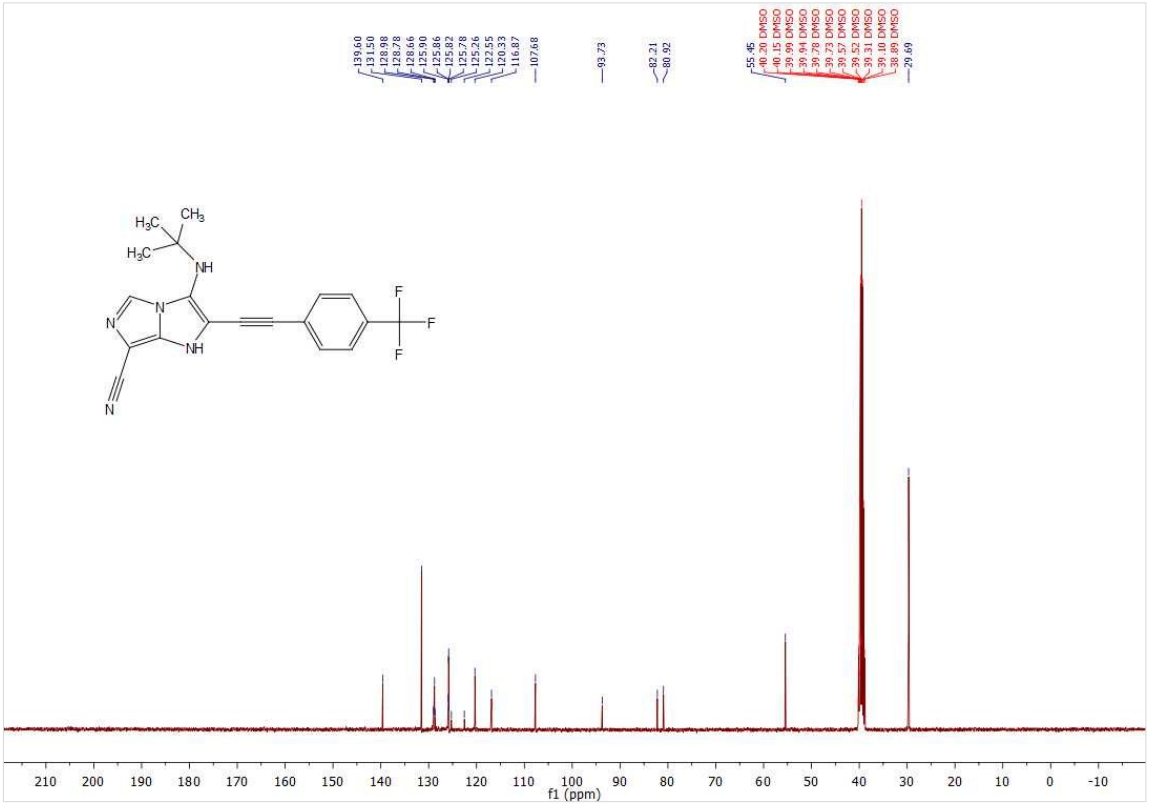


3-(*tert*-Butylamino)-2-((4-(trifluoromethyl)phenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4e):

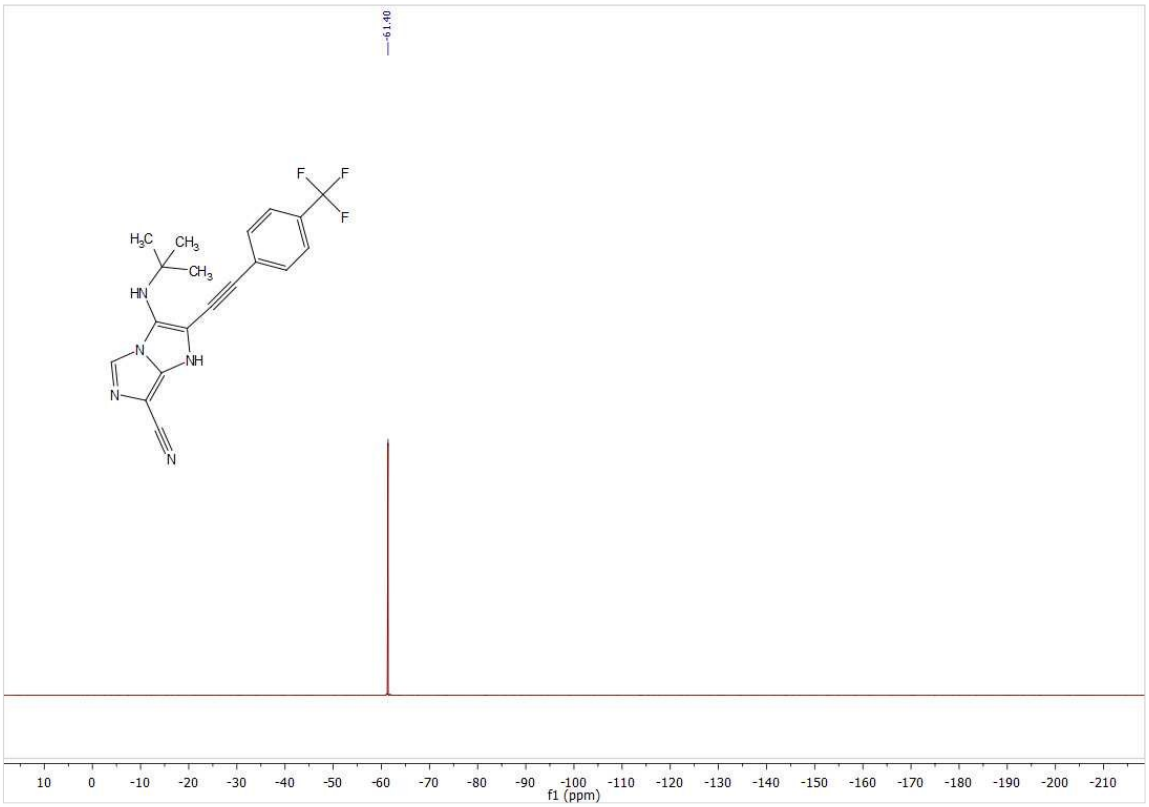
^{1}H NMR (400 MHz, DMSO-d_6)



^{13}C NMR (101 MHz, DMSO-d_6)

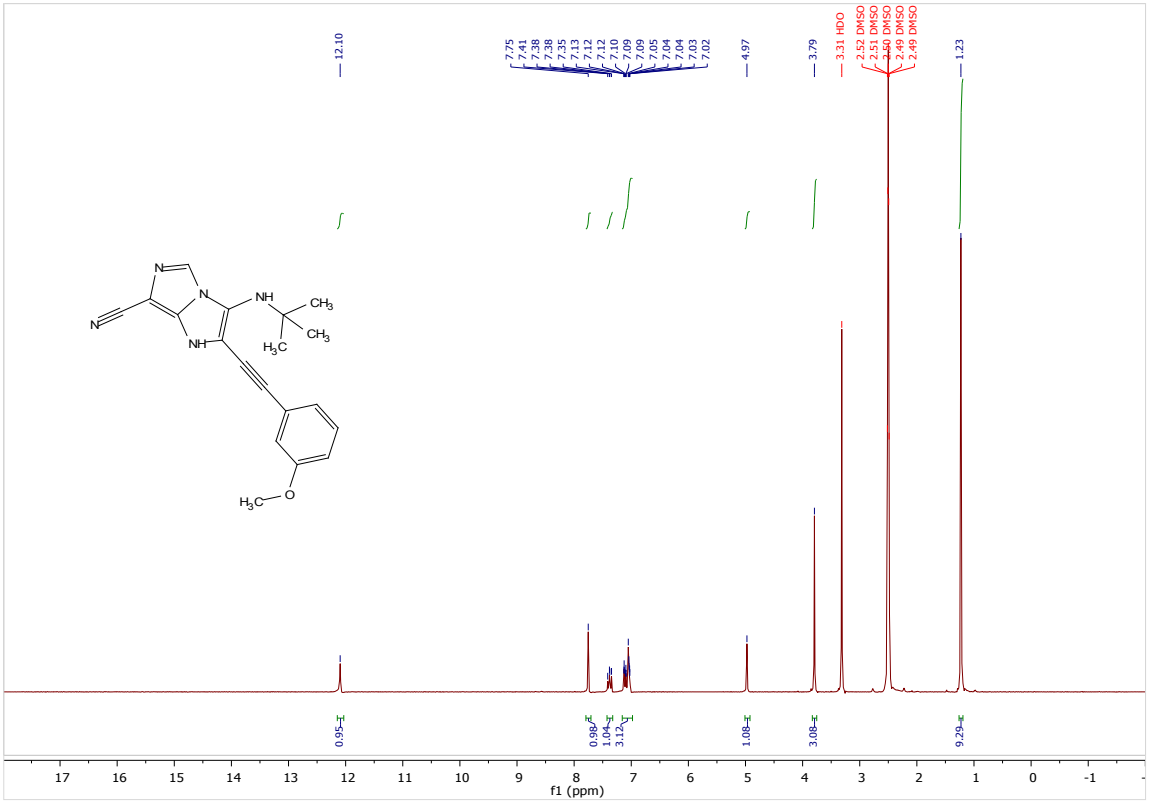


^{19}F NMR (376 MHz, DMSO-d_6)

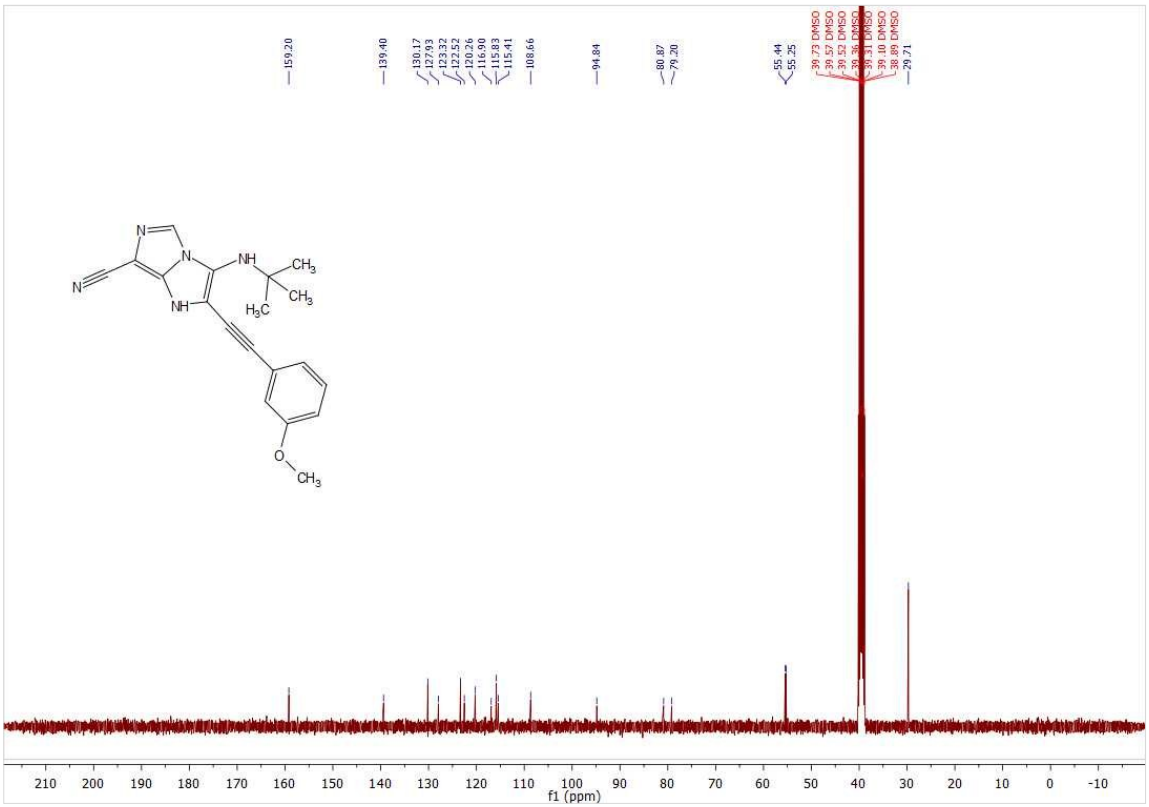


3-(*tert*-Butylamino)-2-((3-methoxyphenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4f):

^{1}H NMR (400 MHz, DMSO-d_6)

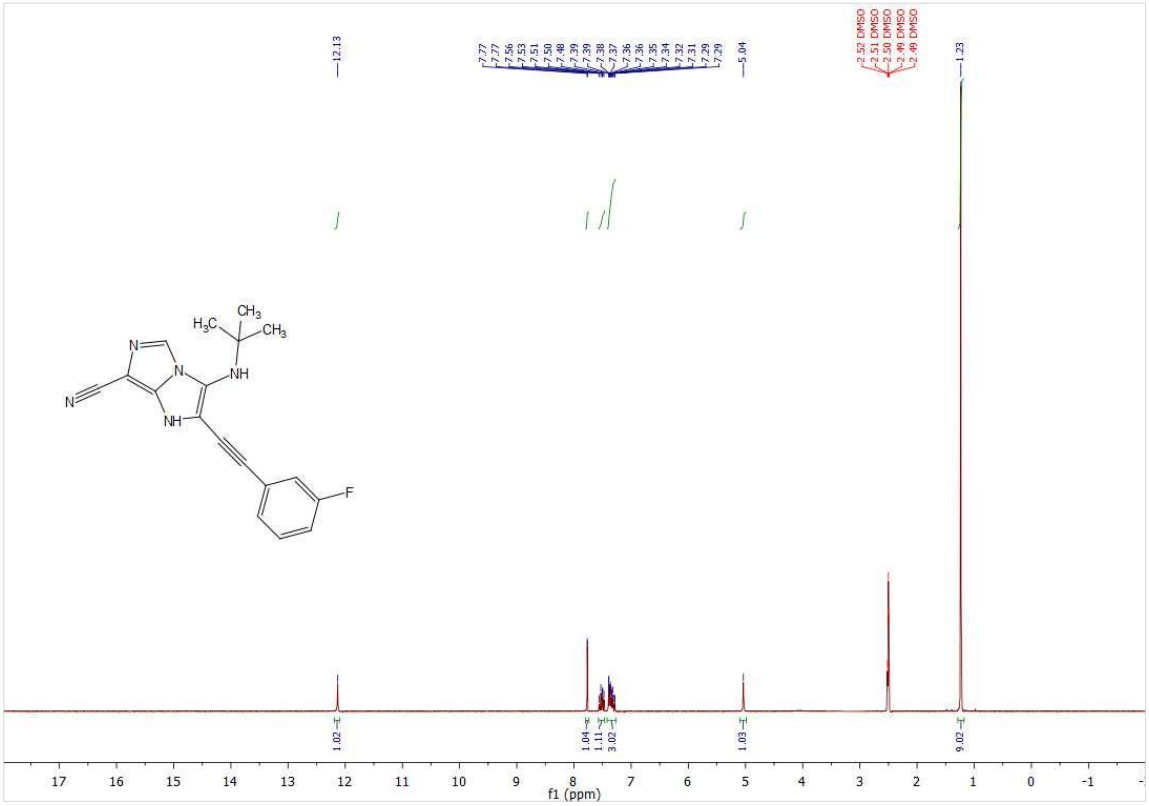


^{13}C NMR (101 MHz, DMSO-d_6)

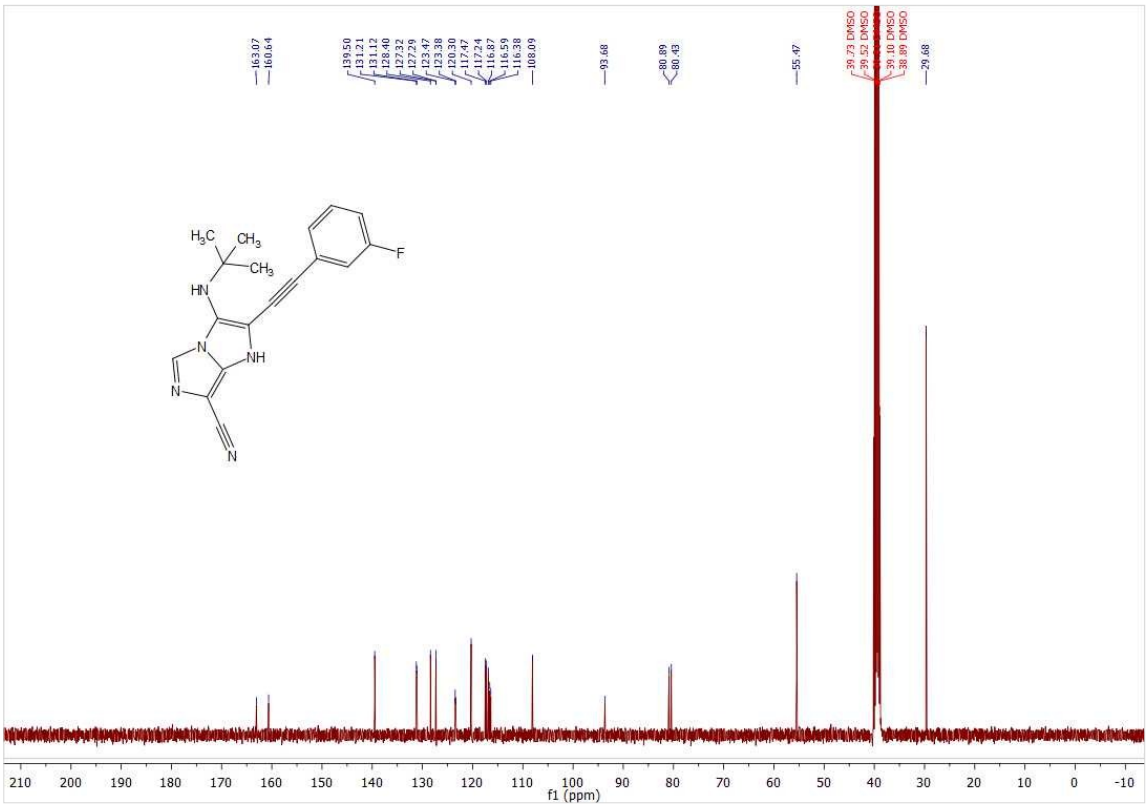


3-(*tert*-Butylamino)-2-((3-fluorophenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4g):

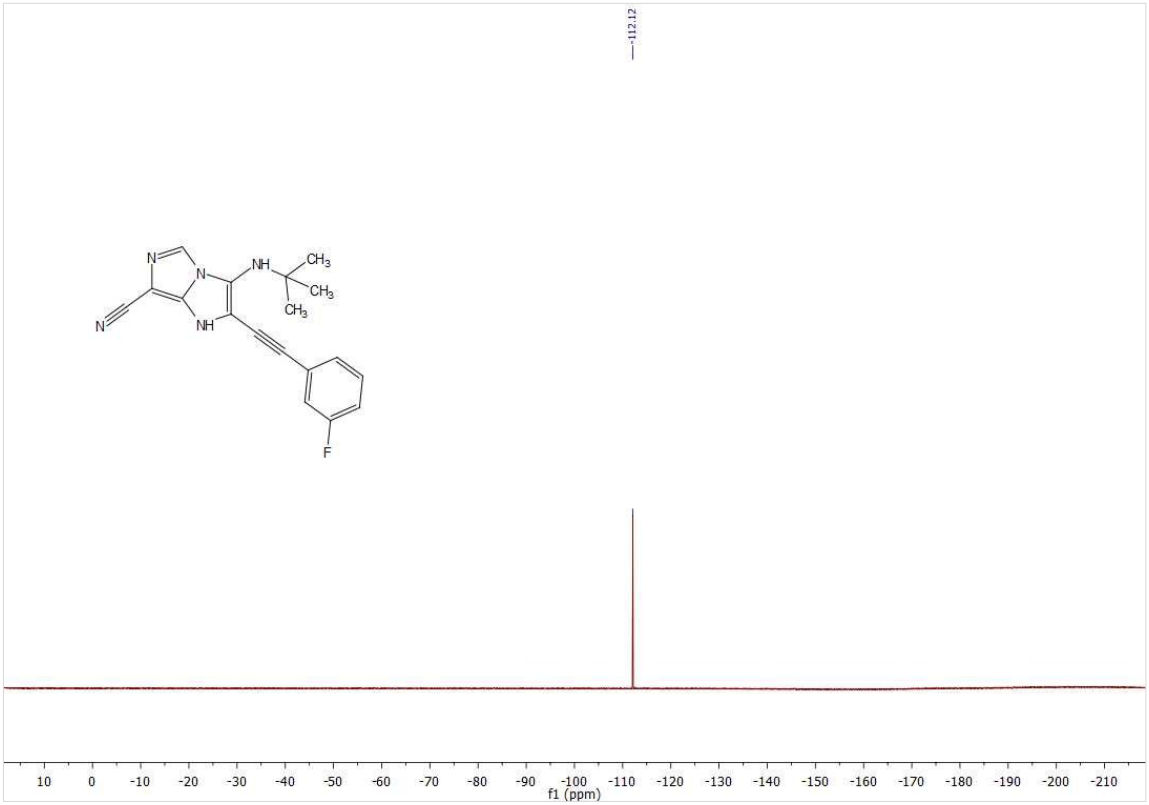
^{1}H NMR (400 MHz, DMSO-d_6)



^{13}C NMR (101 MHz, DMSO-d_6)

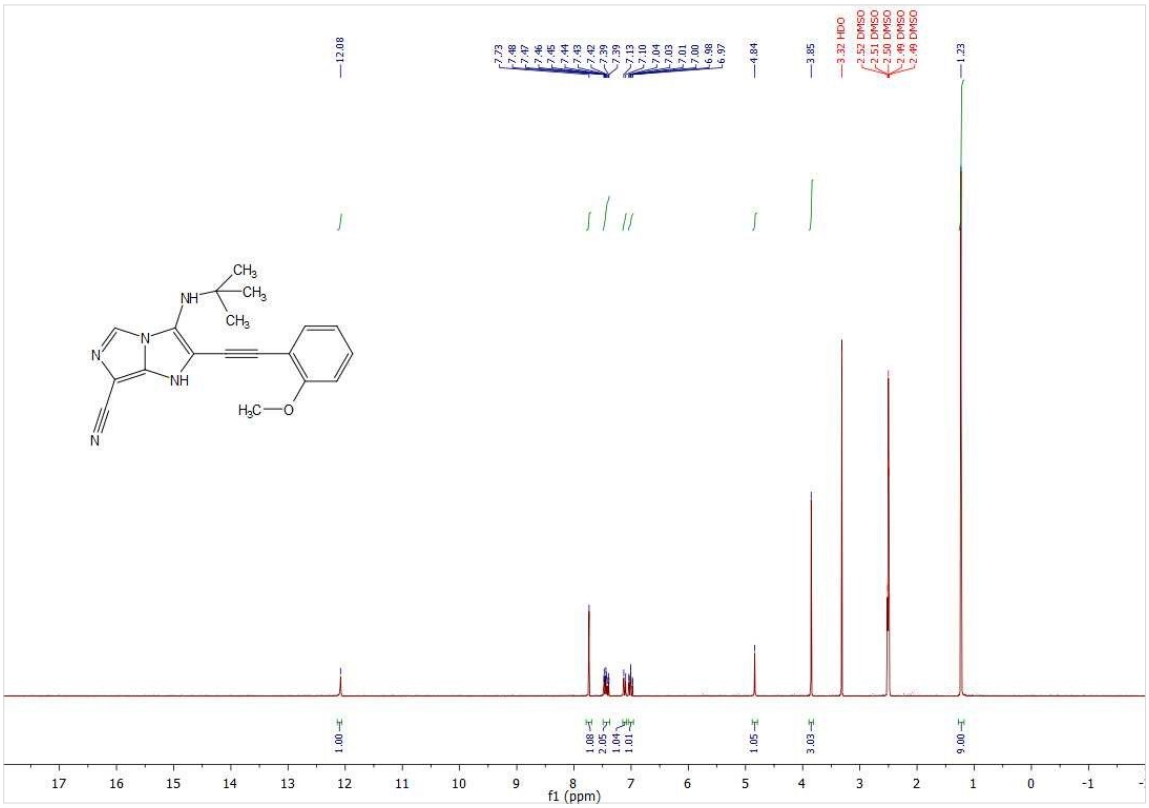


^{19}F NMR (376 MHz, DMSO-d_6)

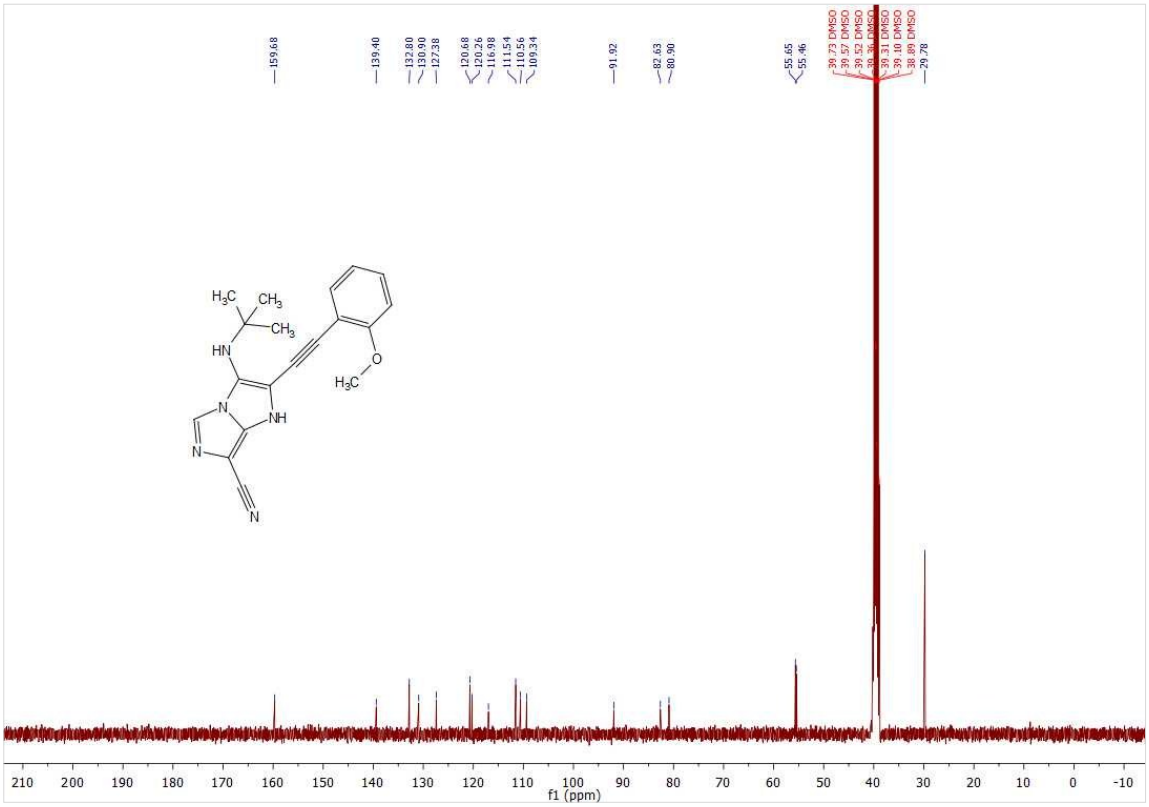


3-(*tert*-Butylamino)-2-((2-methoxyphenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4h):

^{1}H NMR (250 MHz, DMSO-d_6)

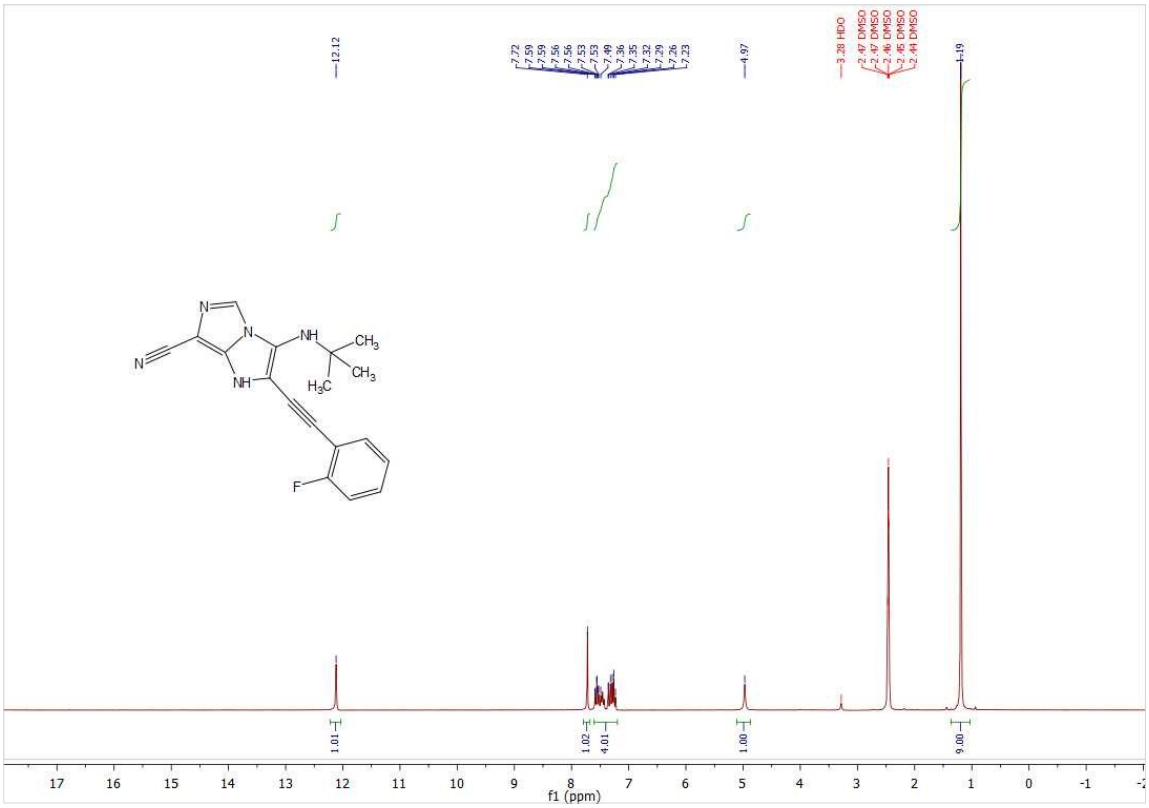


^{13}C NMR (62.9 MHz, DMSO-d_6)

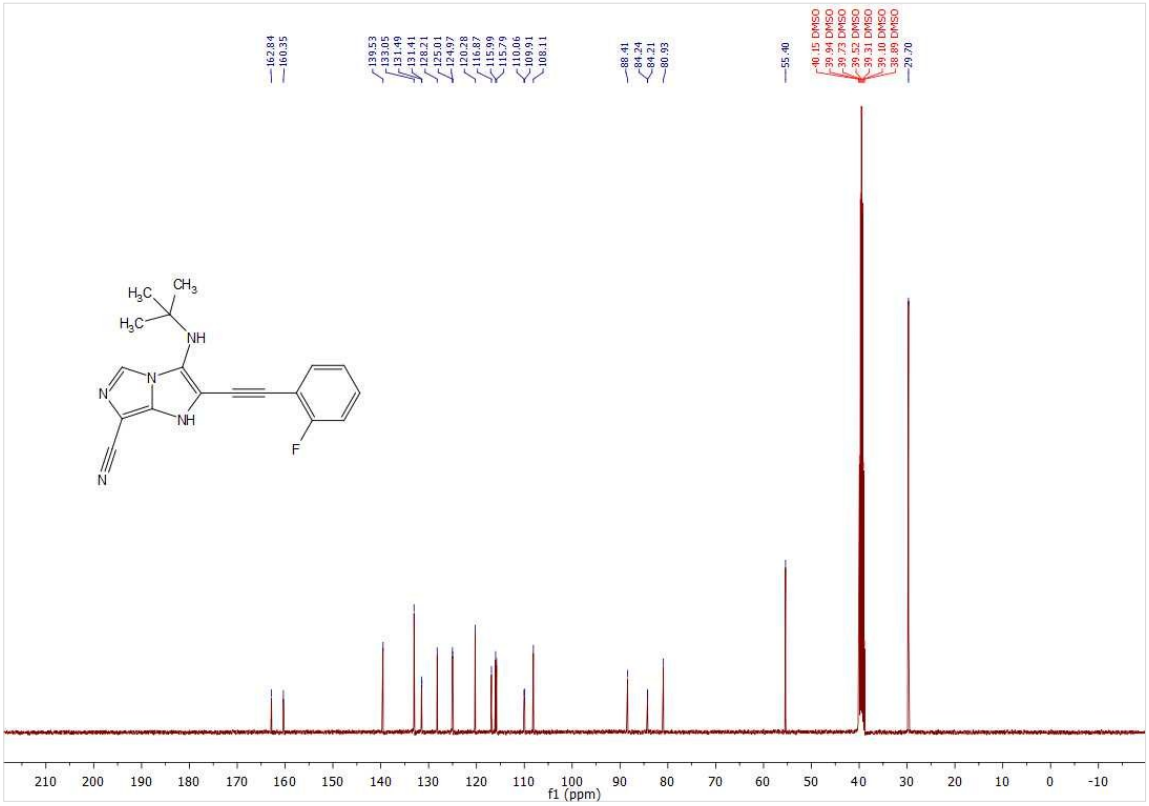


3-(*tert*-Butylamino)-2-((2-fluorophenyl)ethynyl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4i):

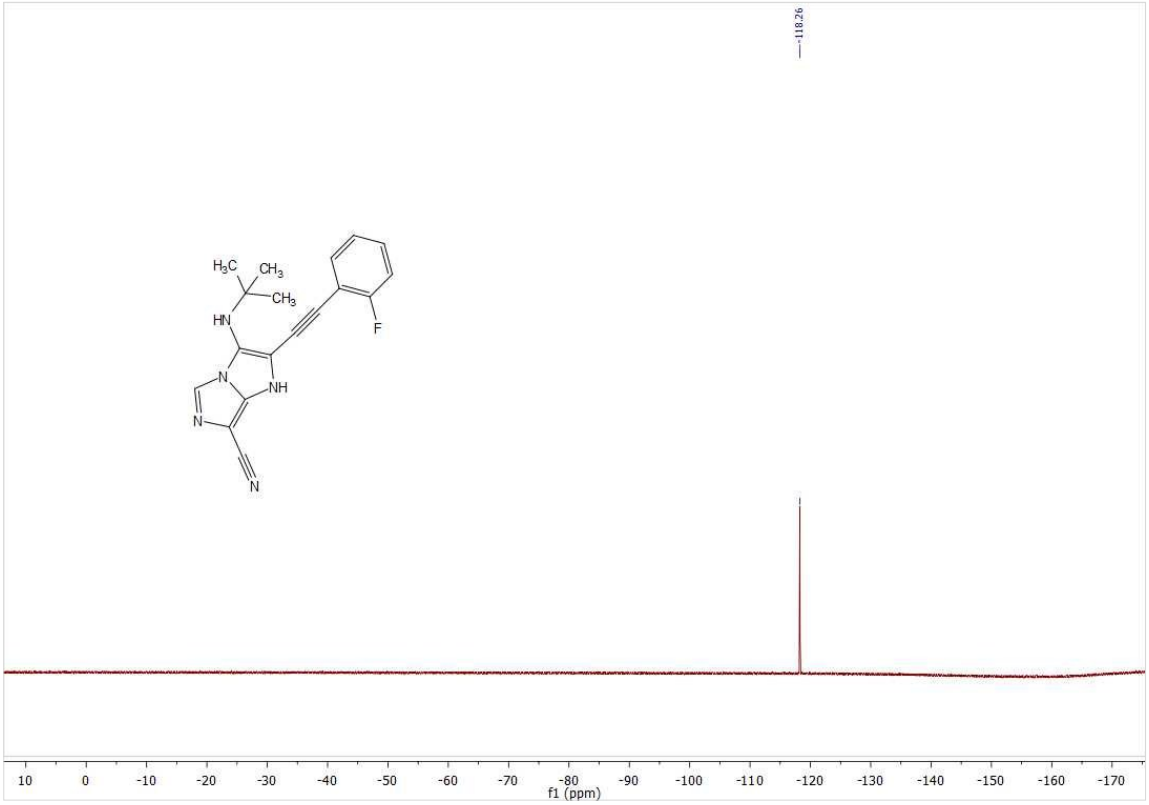
^{1}H NMR (400 MHz, DMSO-d_6)



^{13}C NMR (101 MHz, DMSO-d_6)

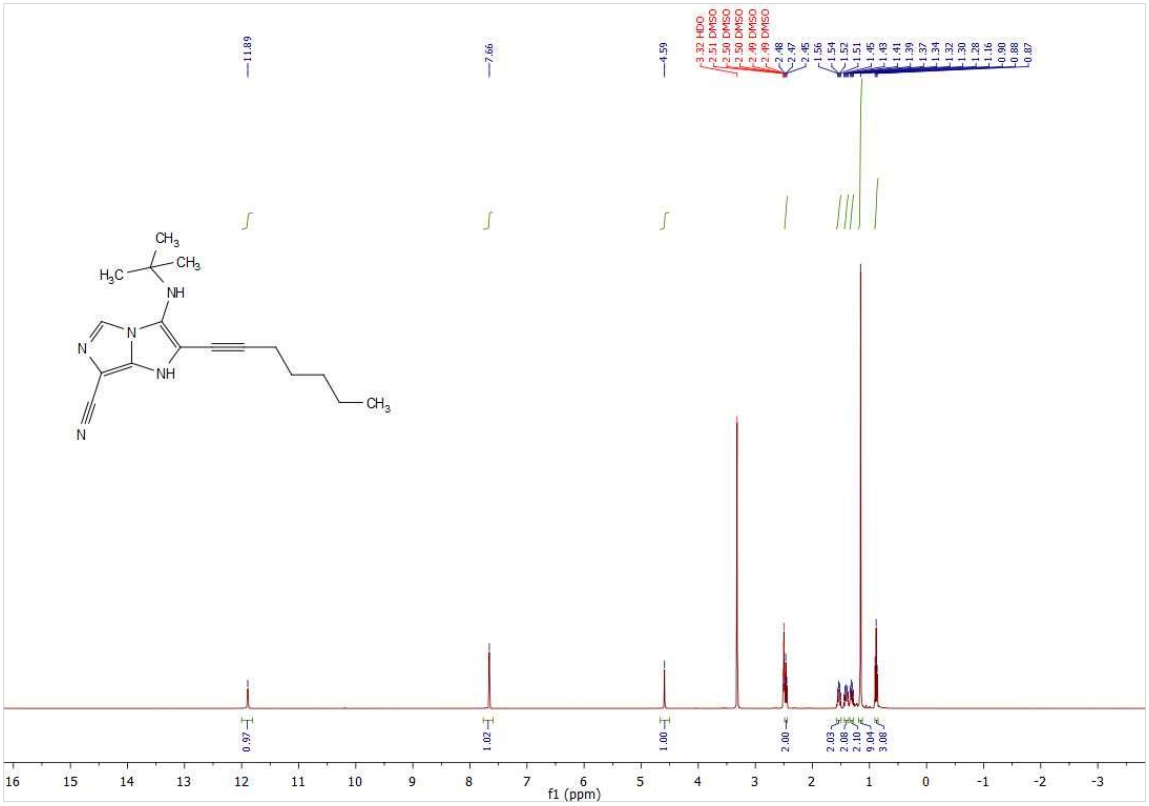


^{19}F NMR (376 MHz, DMSO-d_6)

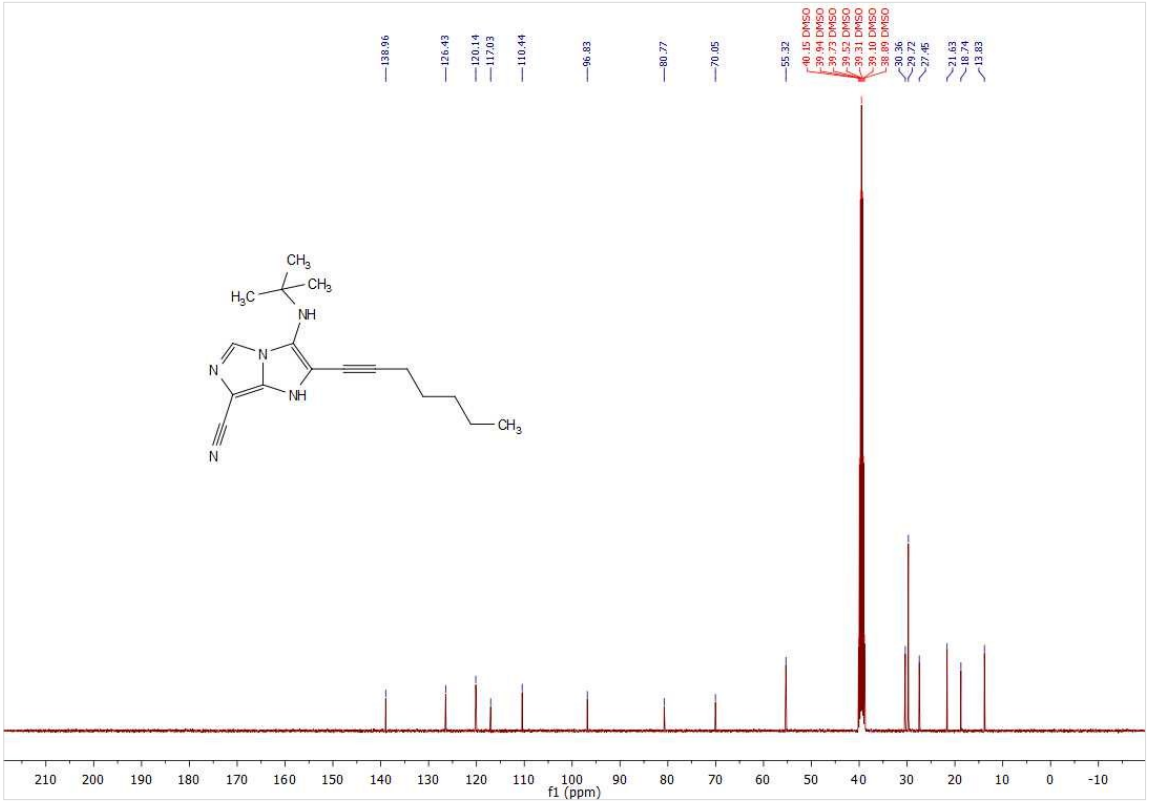


3-(*tert*-Butylamino)-2-(hept-1-yn-1-yl)-1*H*-imidazo[1,5-*a*]imidazole-7-carbonitrile (4j):

^{1}H NMR (400 MHz, DMSO-d_6)

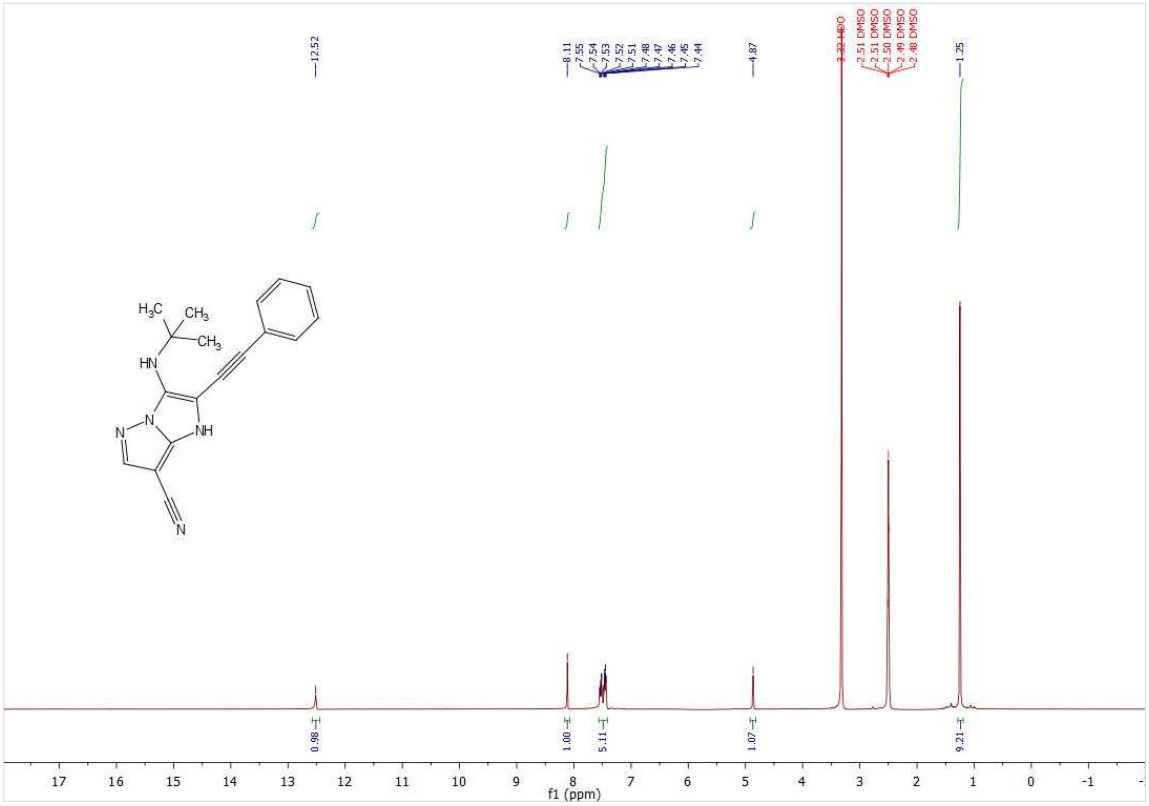


^{13}C NMR (101 MHz, DMSO-d_6)

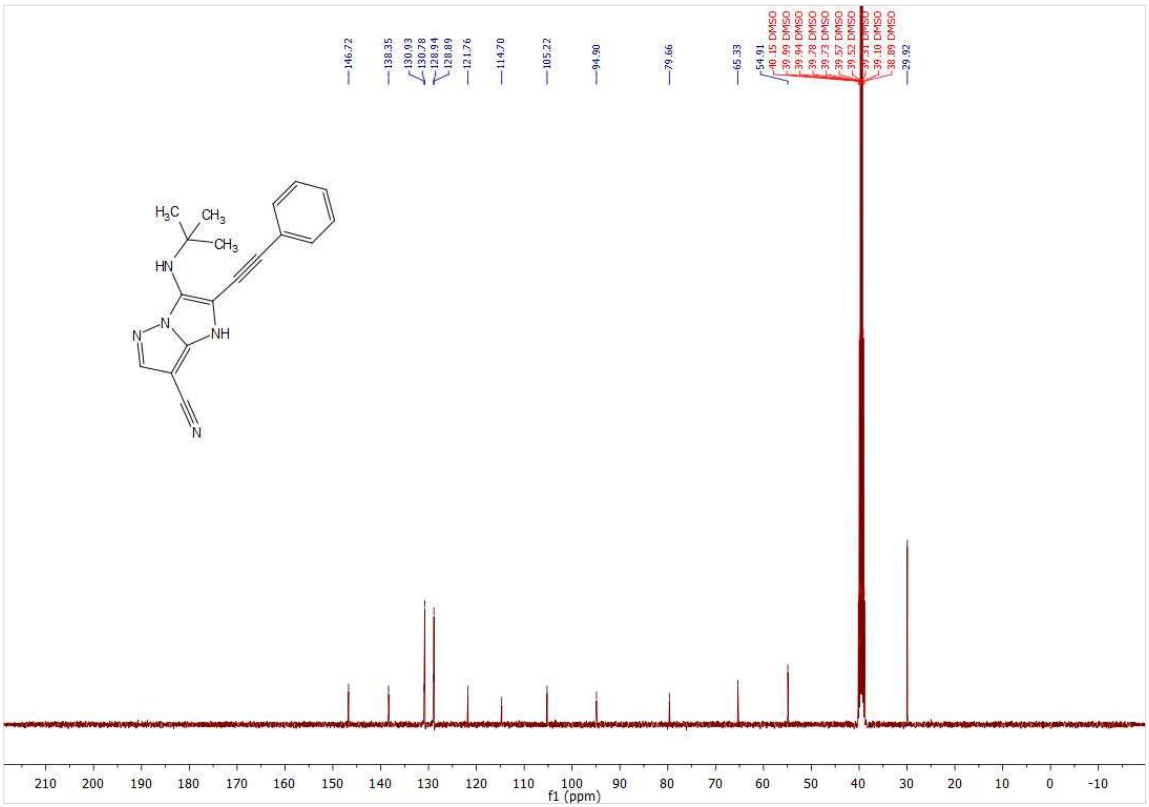


3-(*tert*-Butylamino)-2-(phenylethynyl)-1*H*-imidazo[1,2-*b*] pyrazole-7-carbonitrile (4k):

^{1}H NMR (400 MHz, DMSO-d_6)

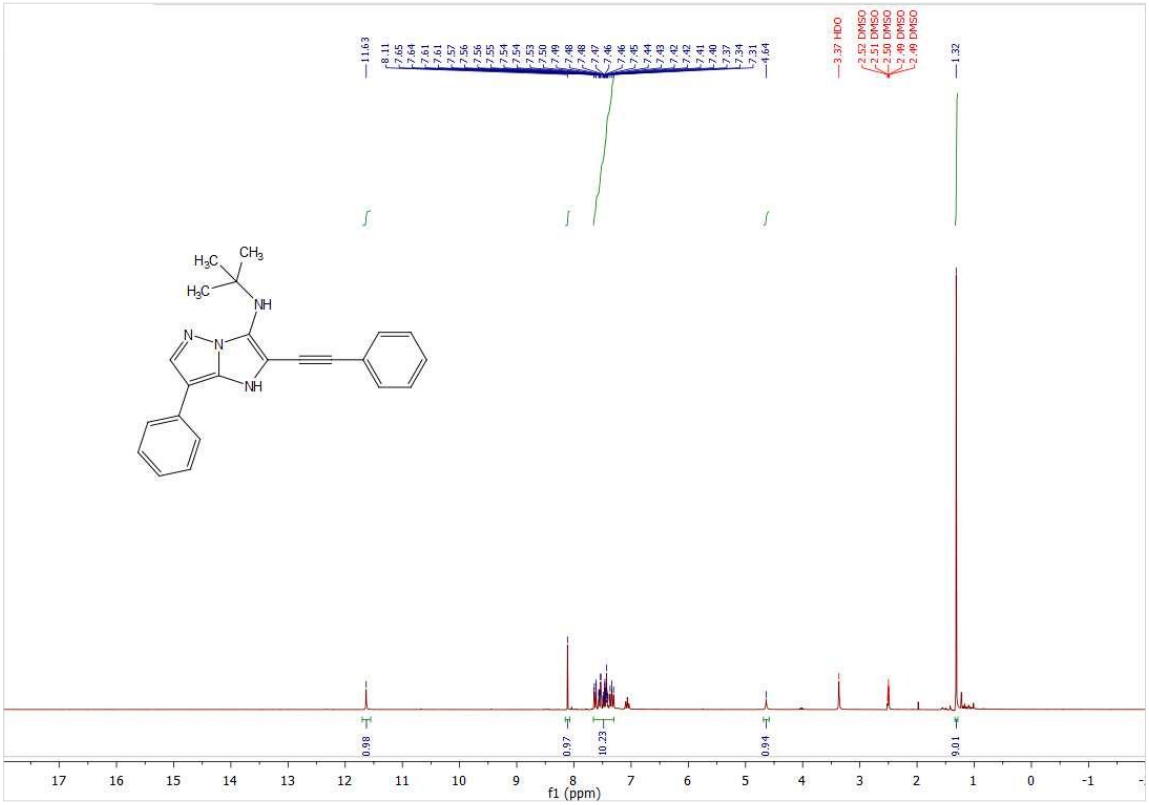


^{13}C NMR (101 MHz, DMSO-d_6)

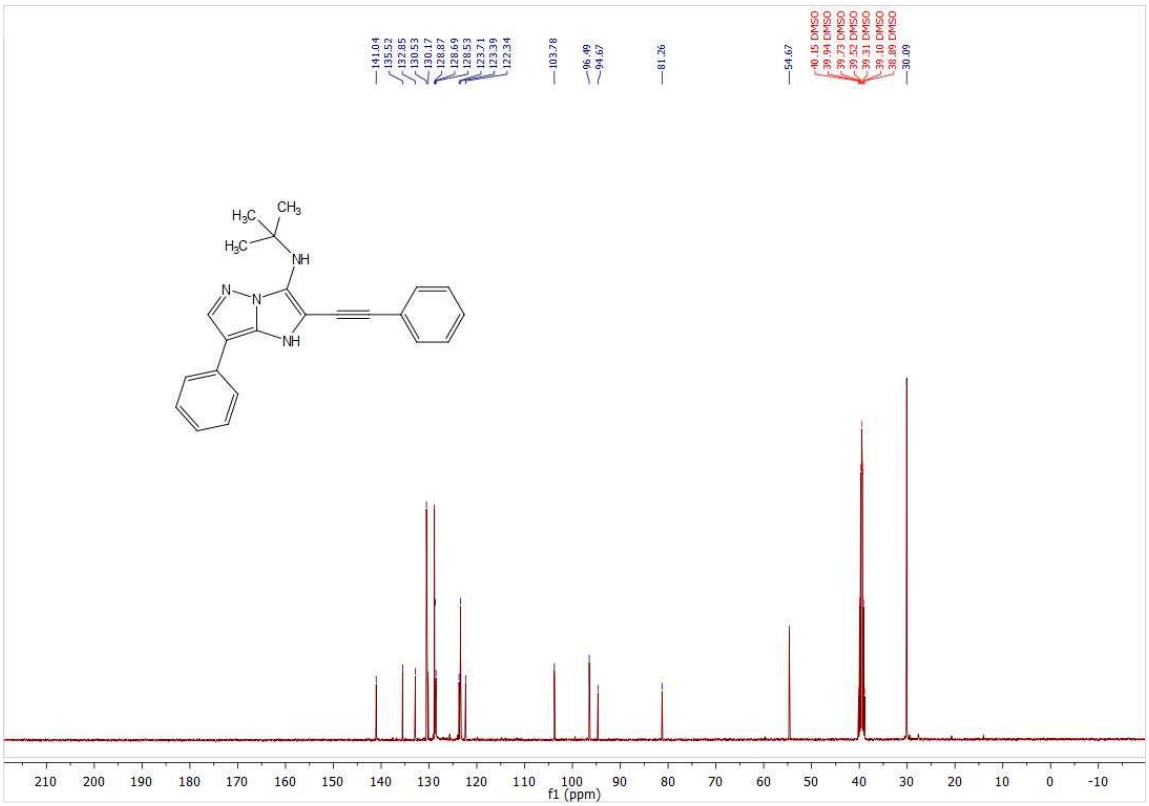


N-(*tert*-Butyl)-7-phenyl-2-(phenylethynyl)-1*H*-imidazo[1,2-*b*]pyrazol-3-amine (4l)

^{1}H NMR (400 MHz, DMSO-d_6)

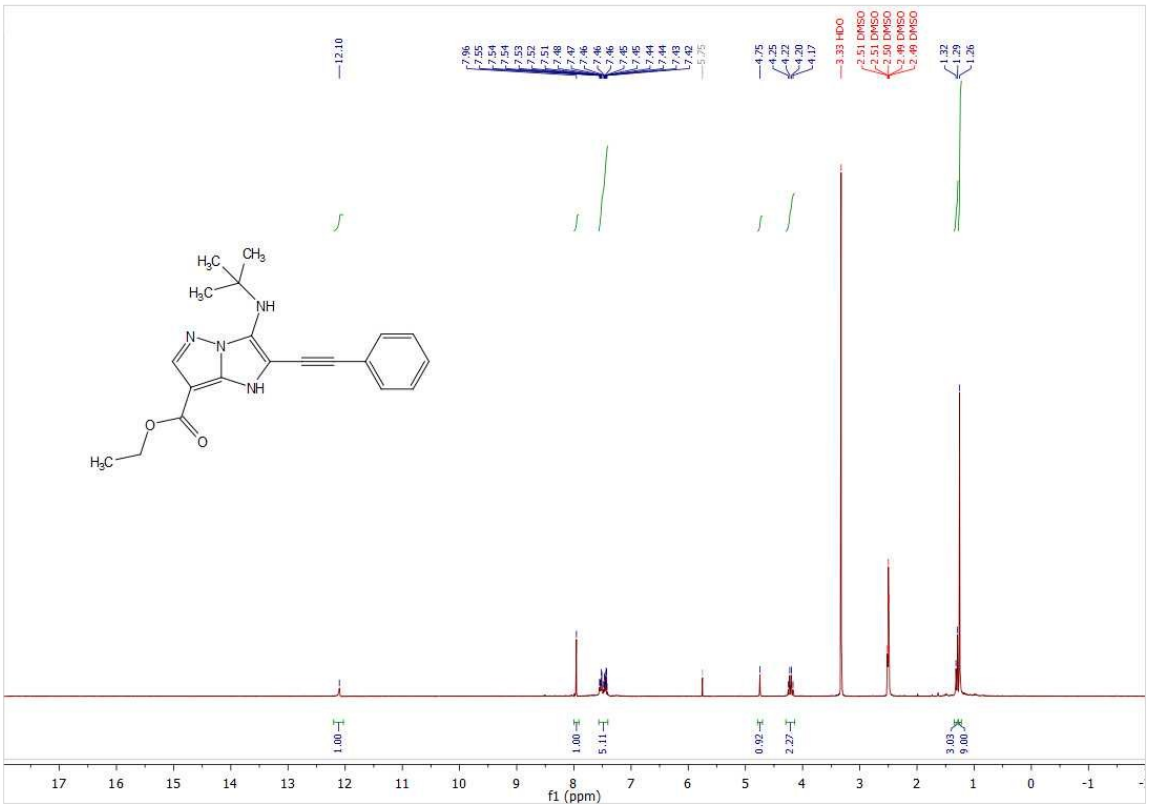


^{13}C NMR (101 MHz, DMSO-d_6)

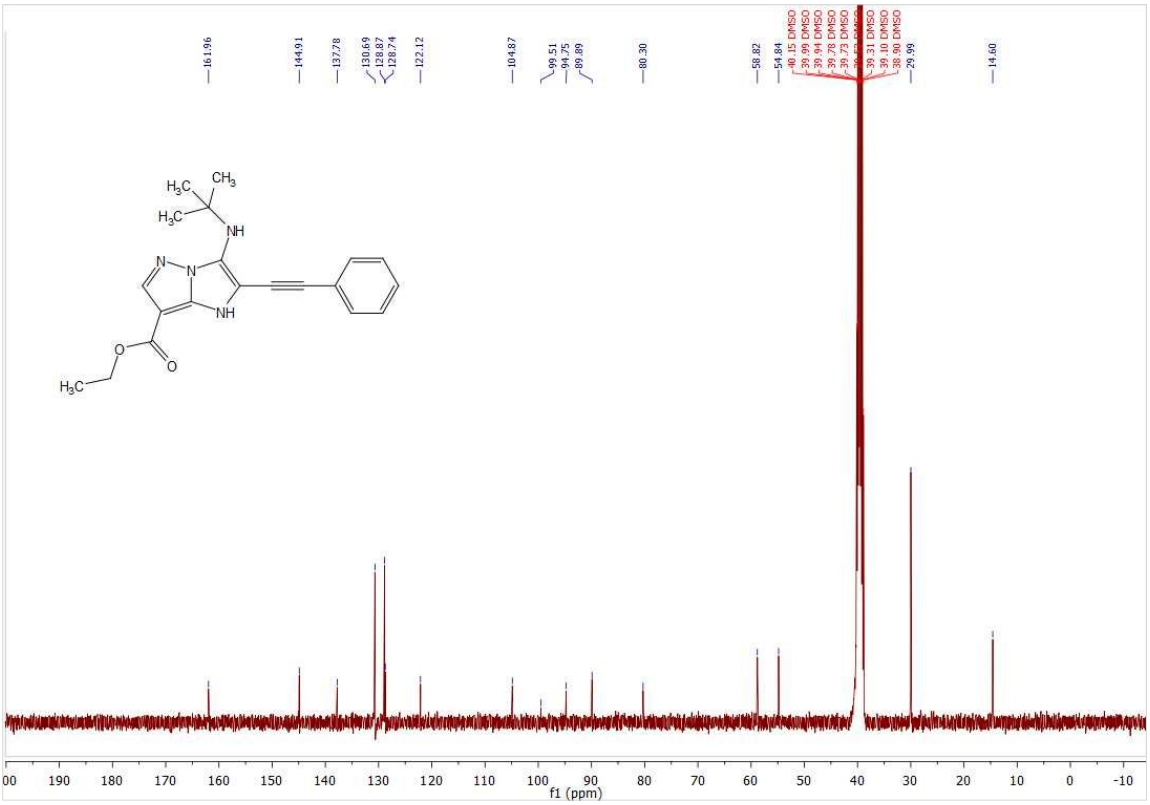


Ethyl 3-(tert-Butylamino)-2-(phenylethynyl)-1*H*-imidazo[1,2-*b*]pyrazole-7-carboxylate (4m):

^{1}H NMR (400 MHz, DMSO-d_6)

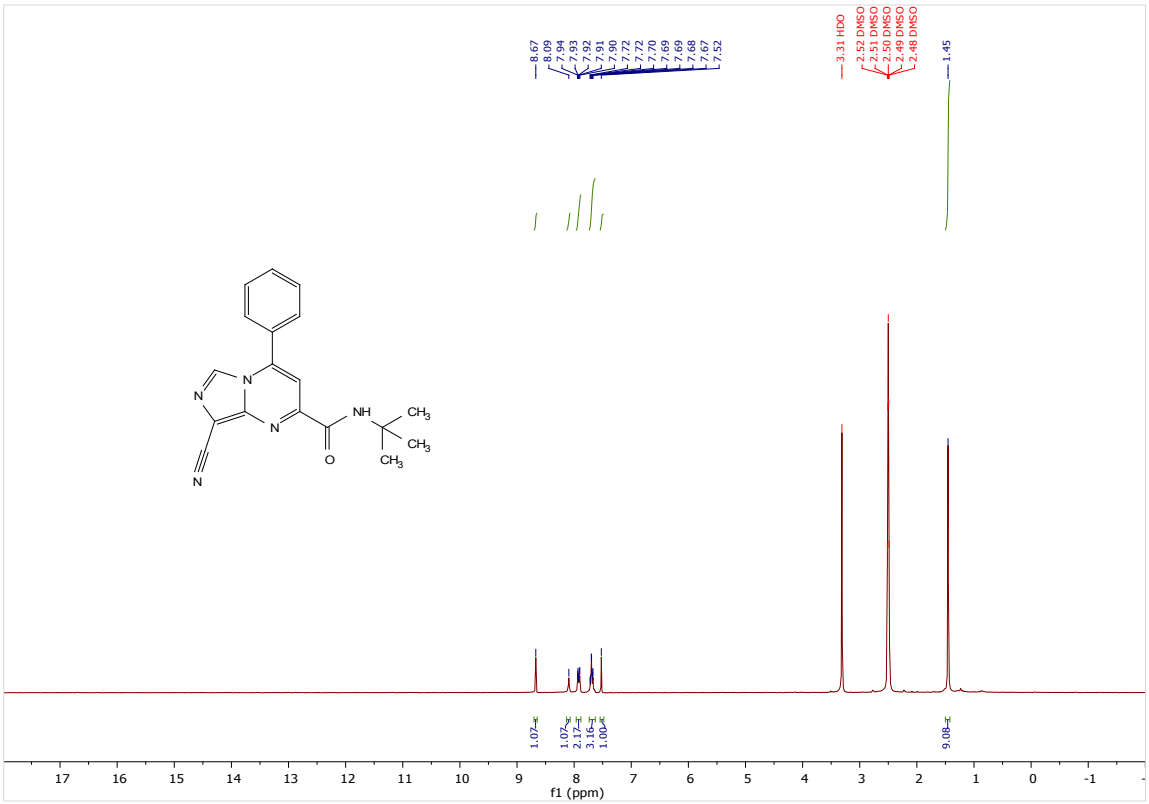


^{13}C NMR (101 MHz, DMSO-d_6)

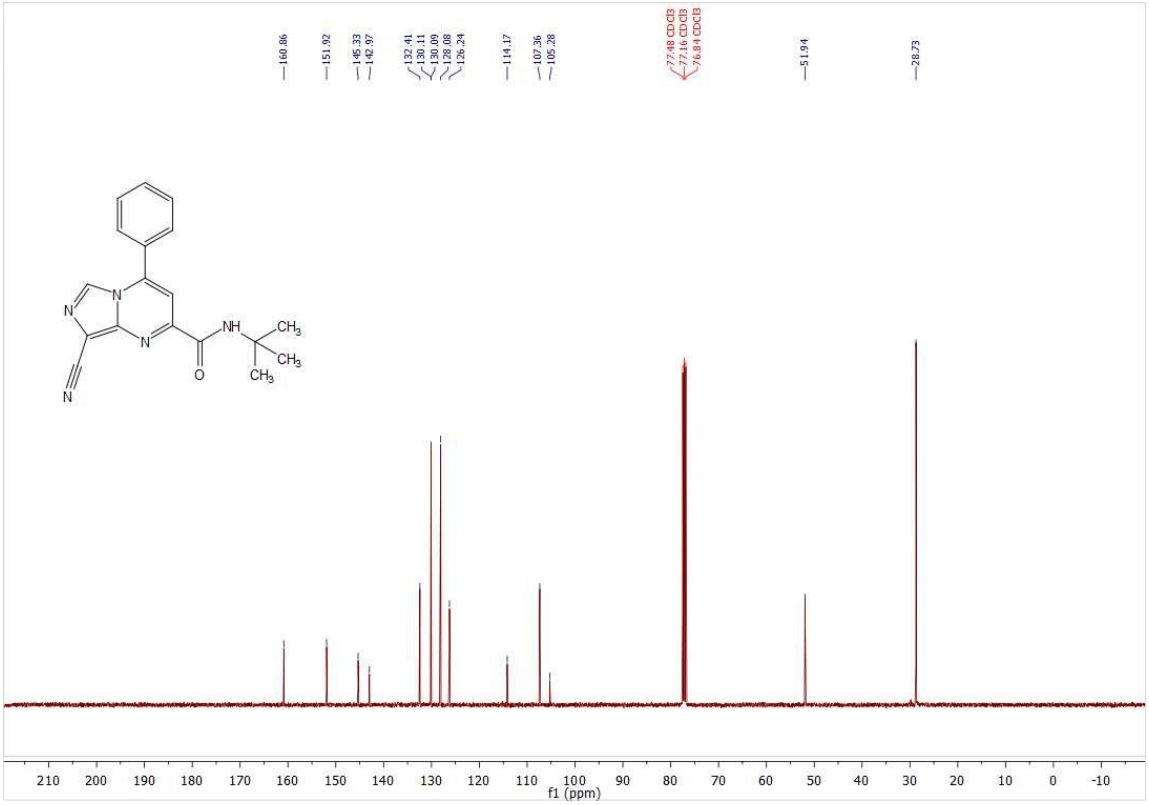


***N*-(*tert*-Butyl)-8-cyano-4-phenylimidazo[1,5-*a*]pyrimidine-2-carboxamide (5a)**

^{1}H NMR (400 MHz, DMSO-d_6)

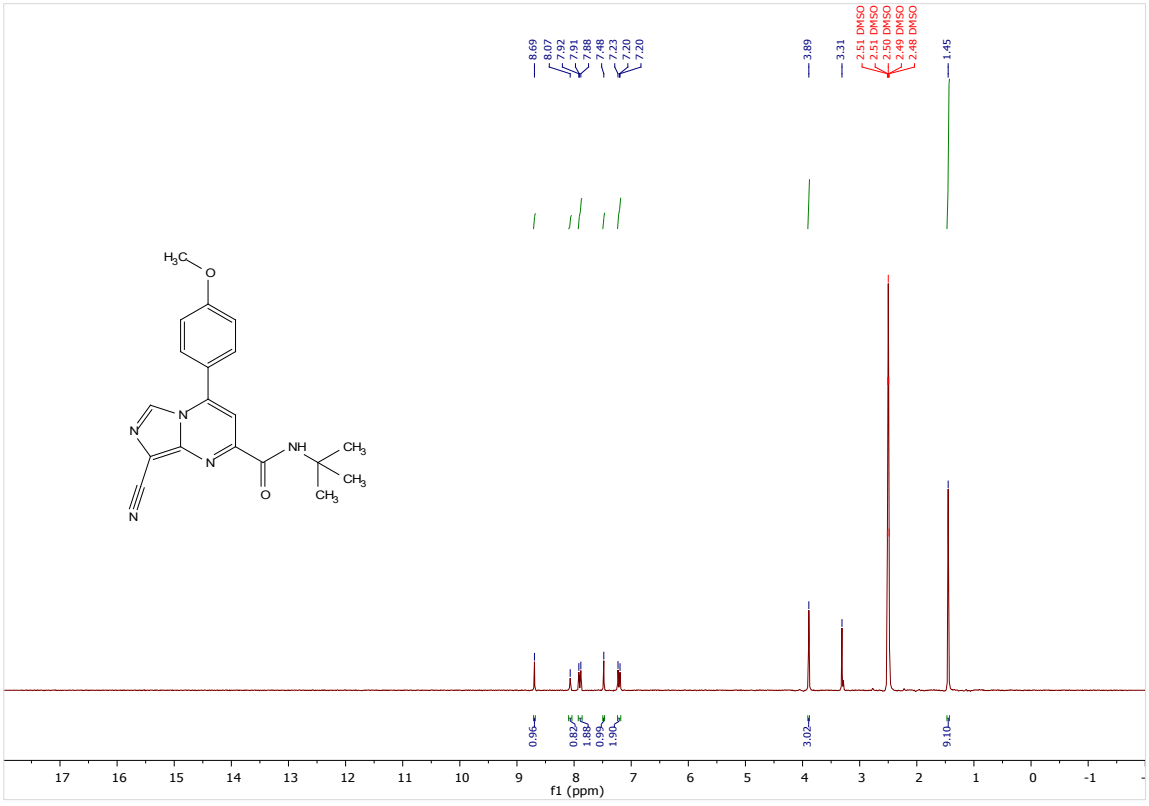


^{13}C NMR (101 MHz, $CDCl_3$)

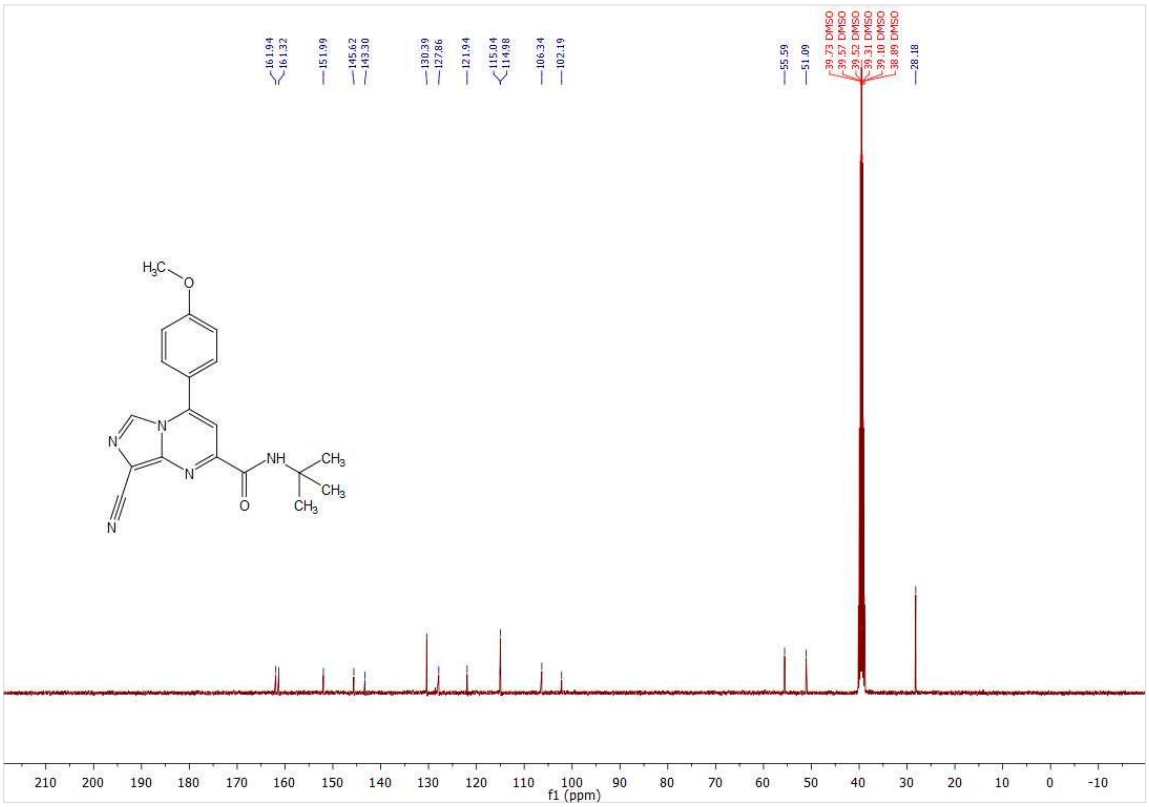


***N*-(*tert*-Butyl)-8-cyano-4-(4-methoxyphenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5b):**

^{1}H NMR (400 MHz, DMSO-d_6)

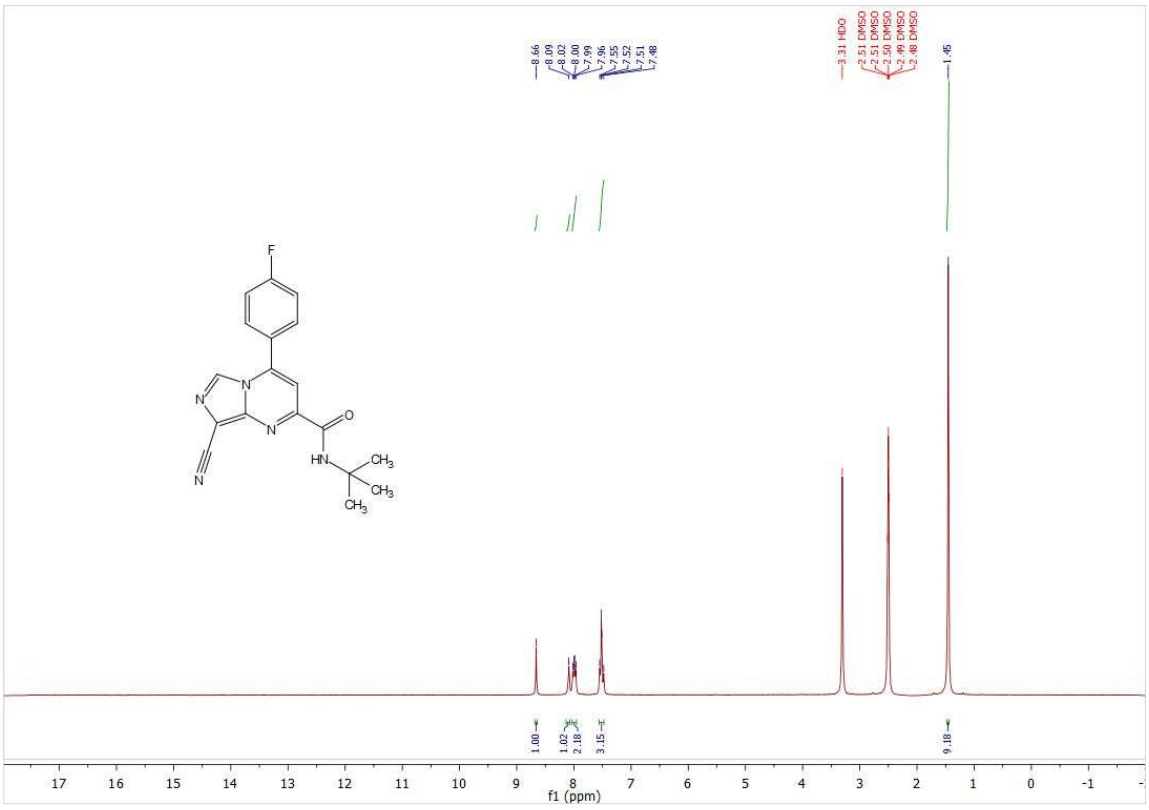


^{13}C NMR (101 MHz, DMSO-d_6)

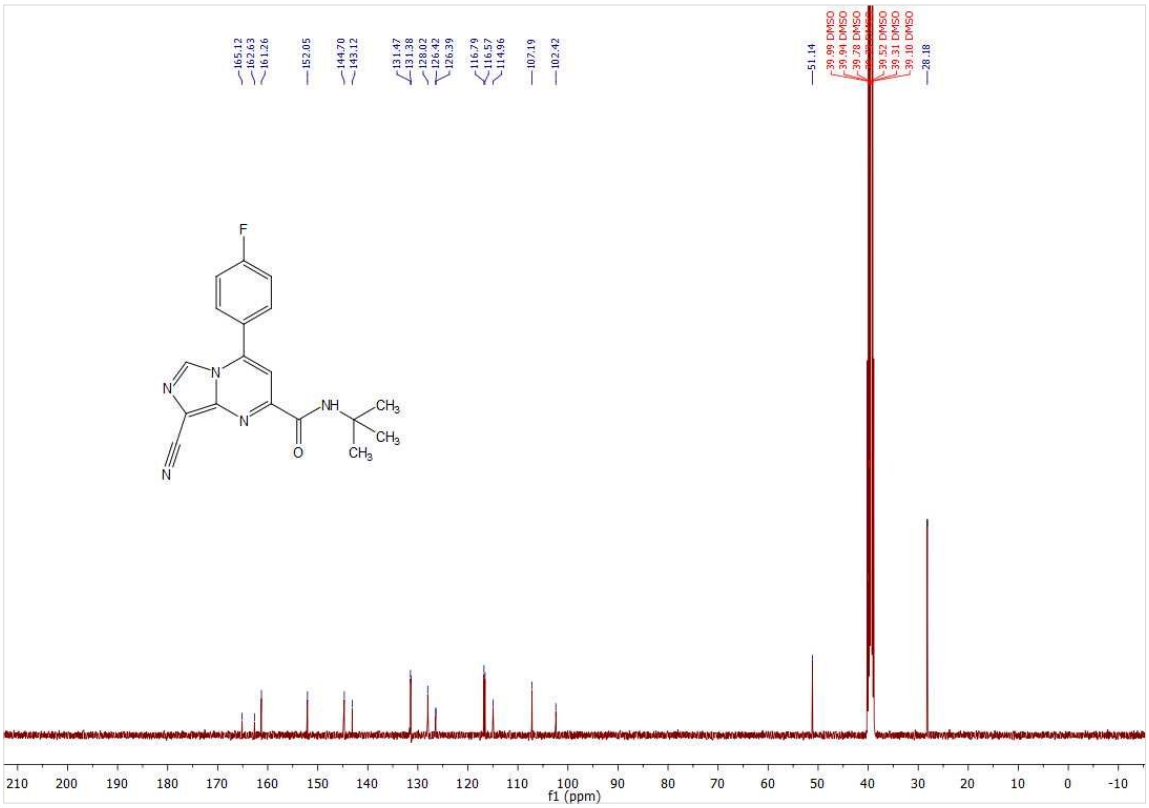


***N*-(*tert*-Butyl)-8-cyano-4-(4-fluorophenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5c) :**

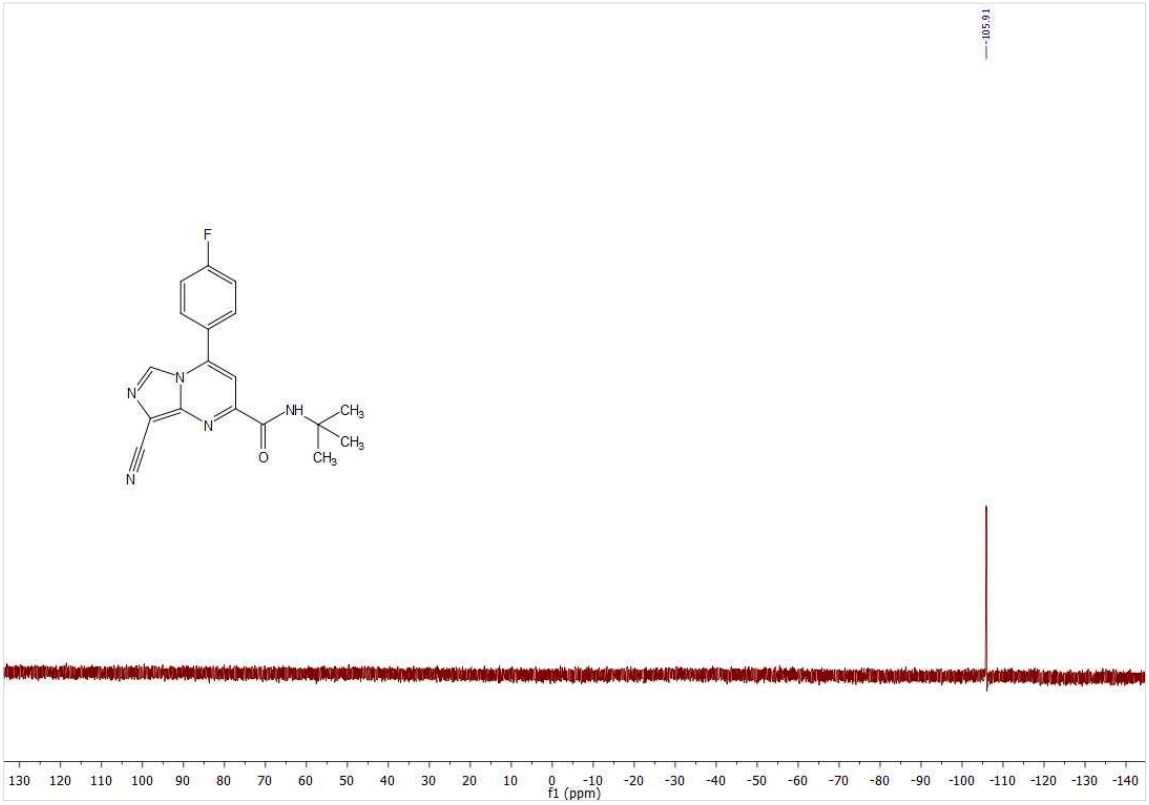
^{1}H NMR (400 MHz, DMSO-*d6*)



^{13}C NMR (101 MHz, DMSO-d_6)

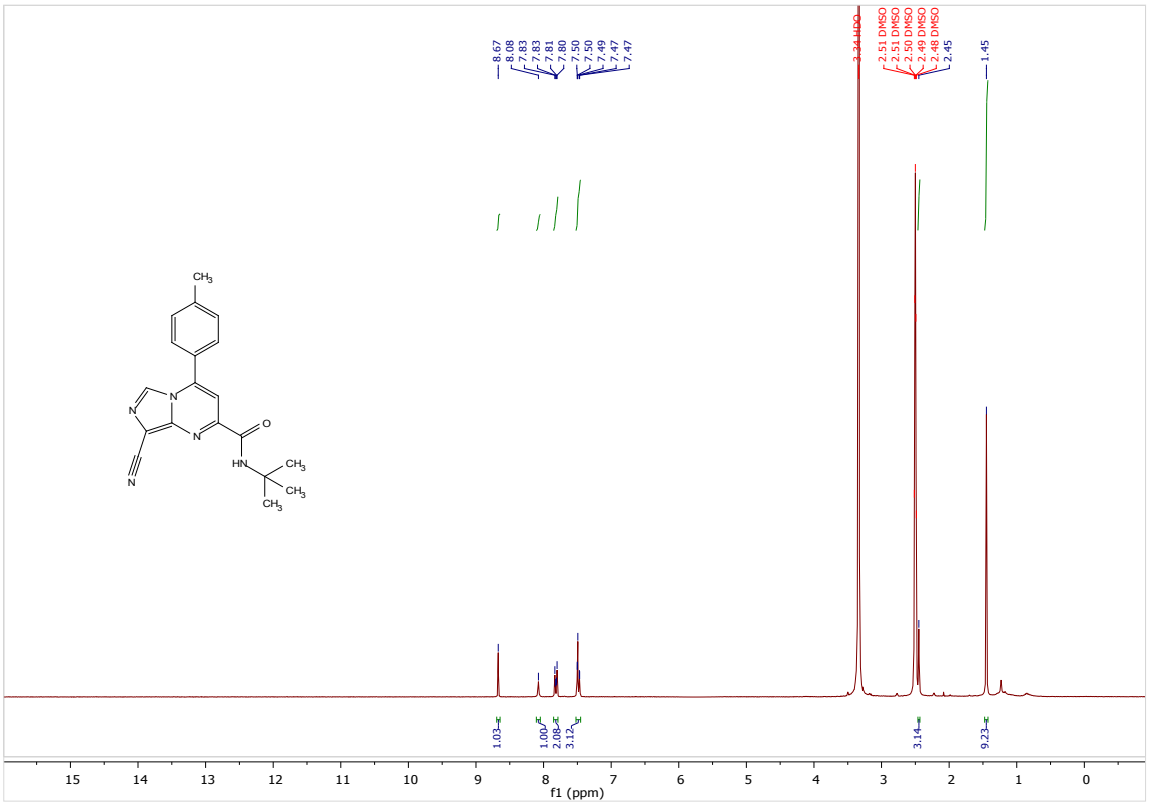


^{19}F NMR (376 MHz, DMSO-d_6)

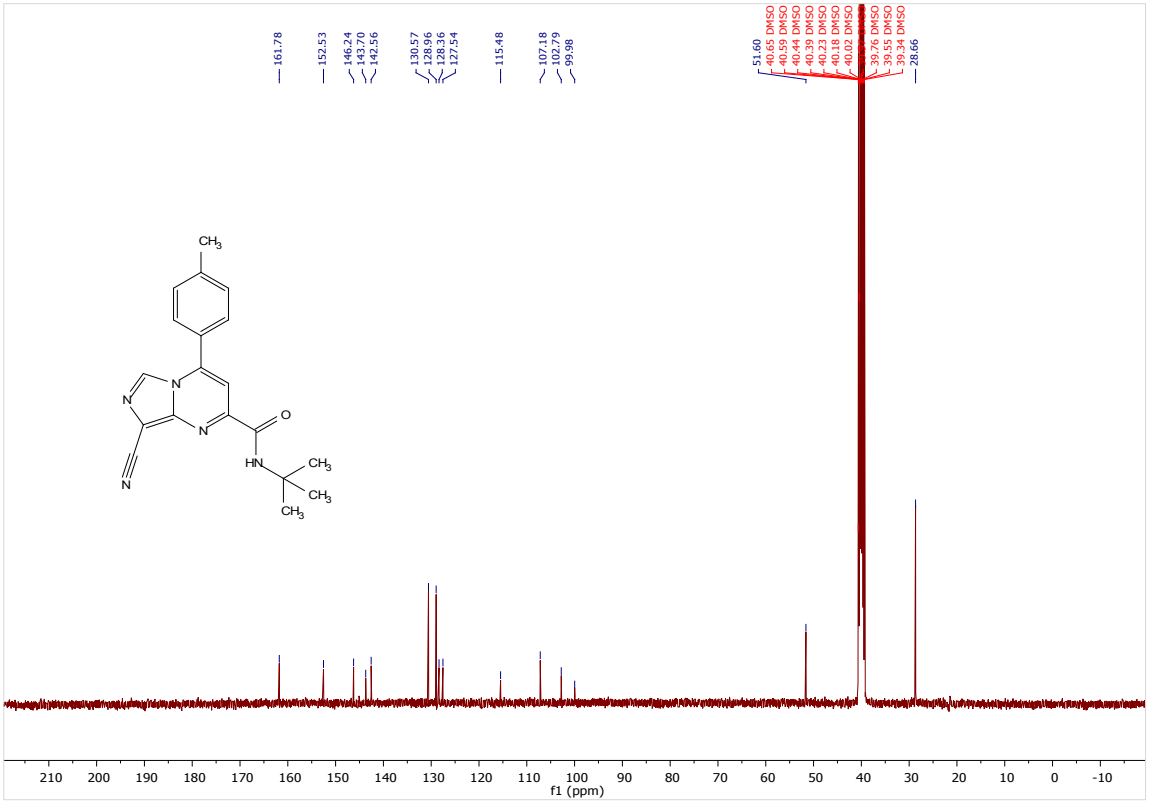


***N*-(*tert*-Butyl)-8-cyano-4-(*p*-tolyl)imidazo[1,5-a]pyrimidine-2-carboxamide (5d):**

^{1}H NMR (400 MHz, DMSO-d_6)

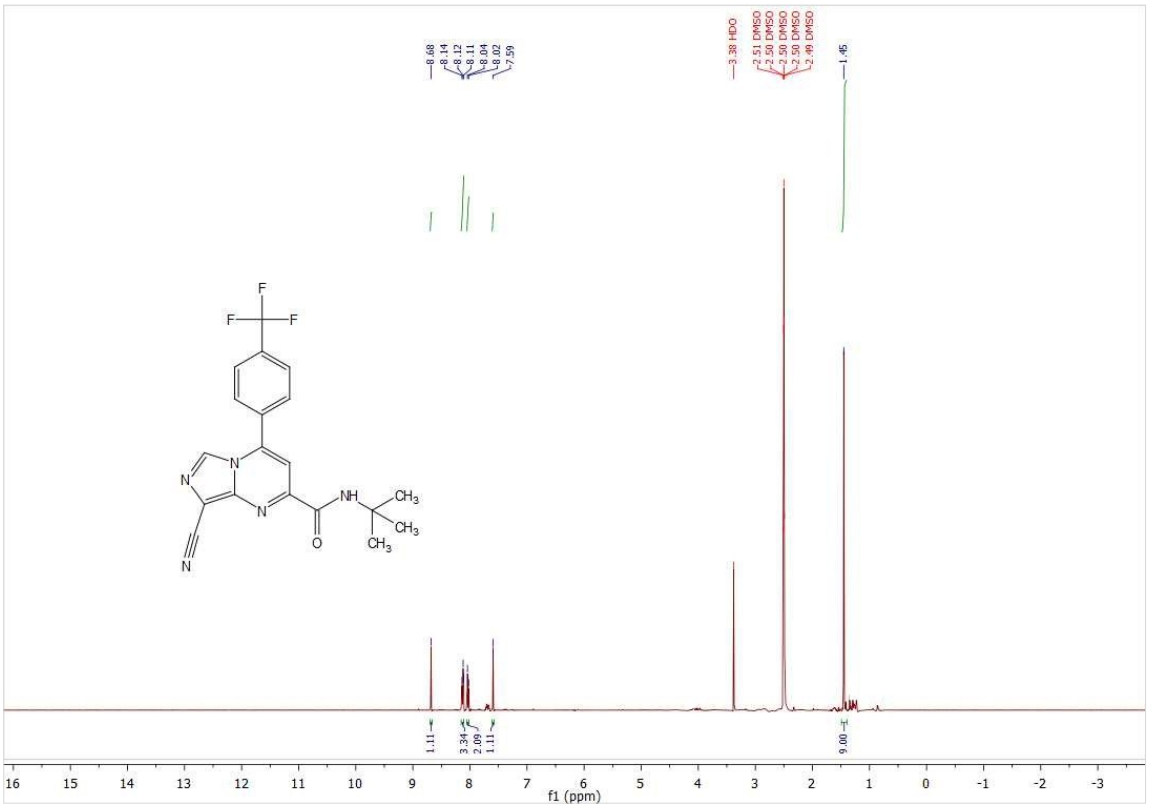


^{13}C NMR (101 MHz, DMSO-d_6)

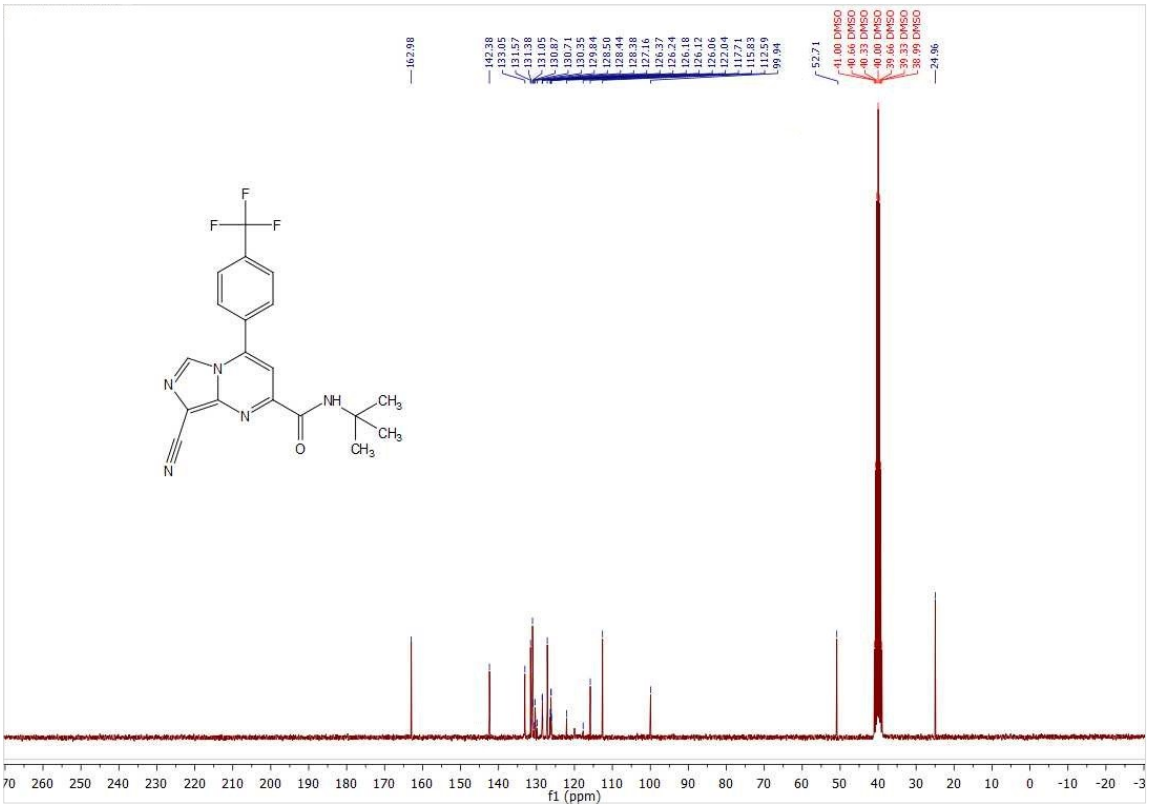


***N*-(*tert*-Butyl)-8-cyano-4-(4-(trifluoromethyl)phenyl)imidazo[1,5-a]pyrimidine-2-carboxamide (5e) :**

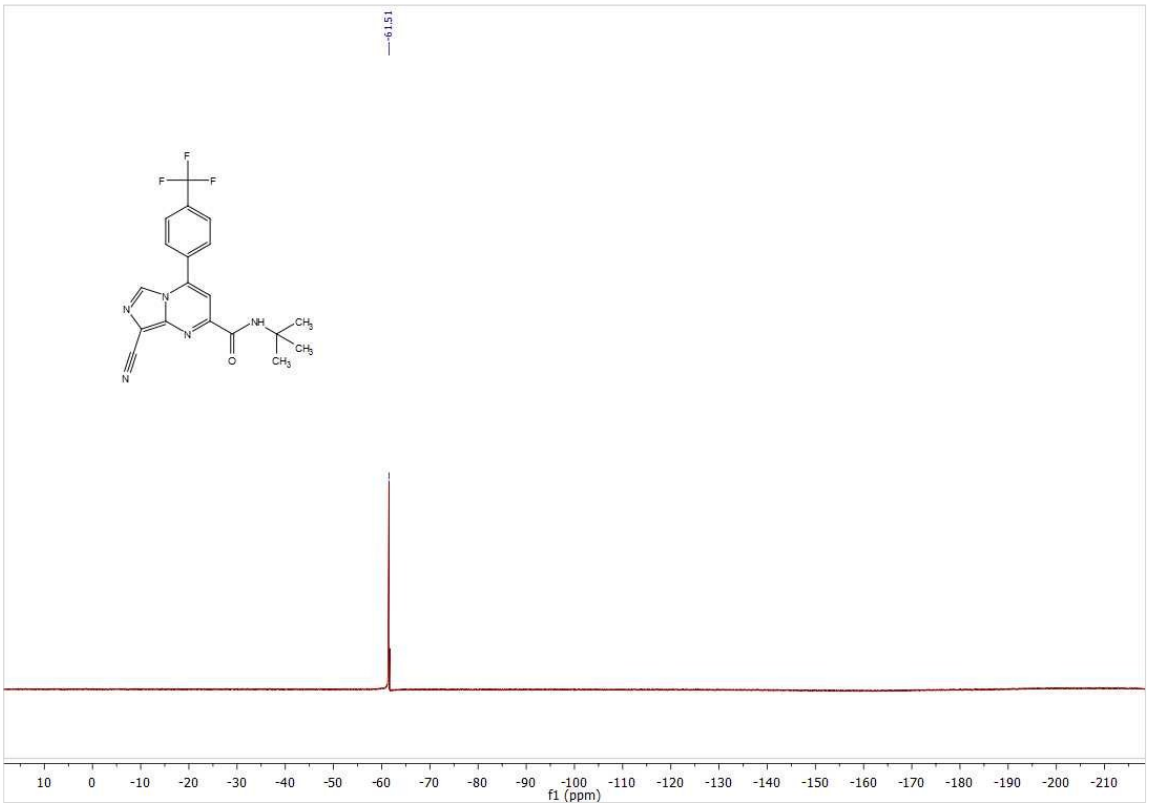
^{1}H NMR (400 MHz, DMSO-d_6)



^{13}C NMR (62.9 MHz, DMSO-d_6)

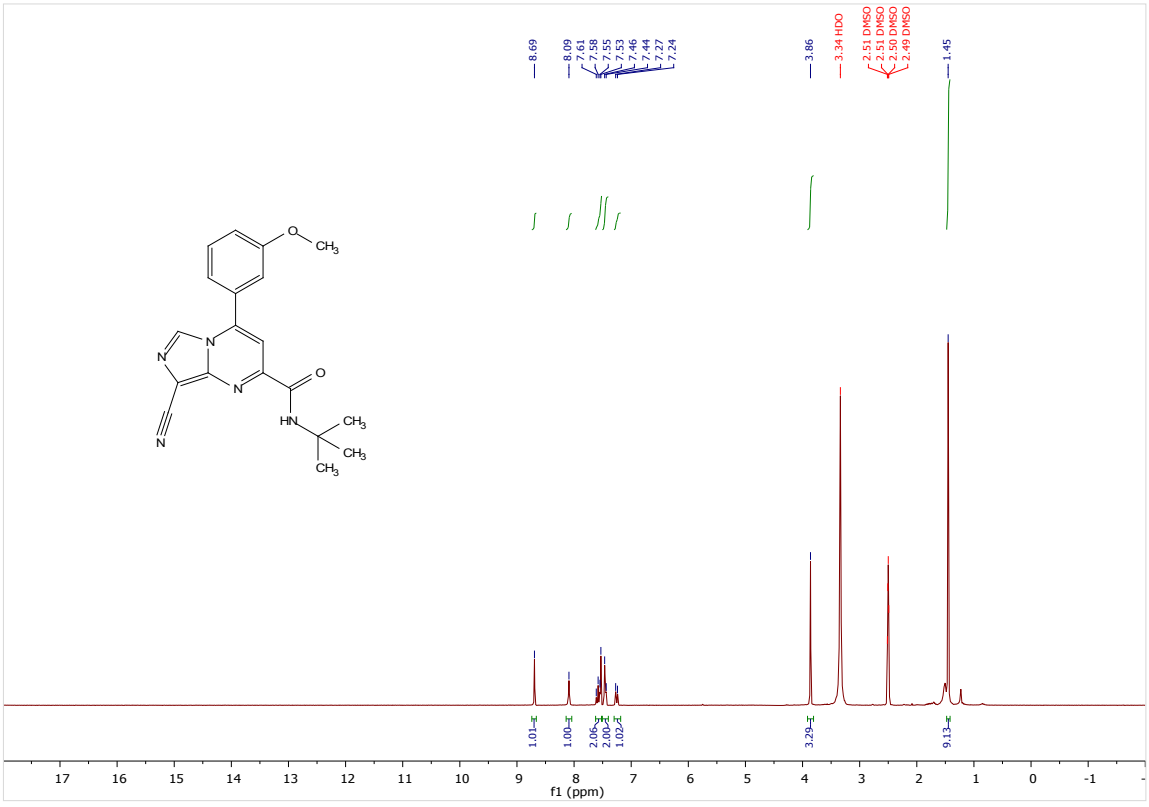


^{19}F NMR (376 MHz, DMSO-d_6)

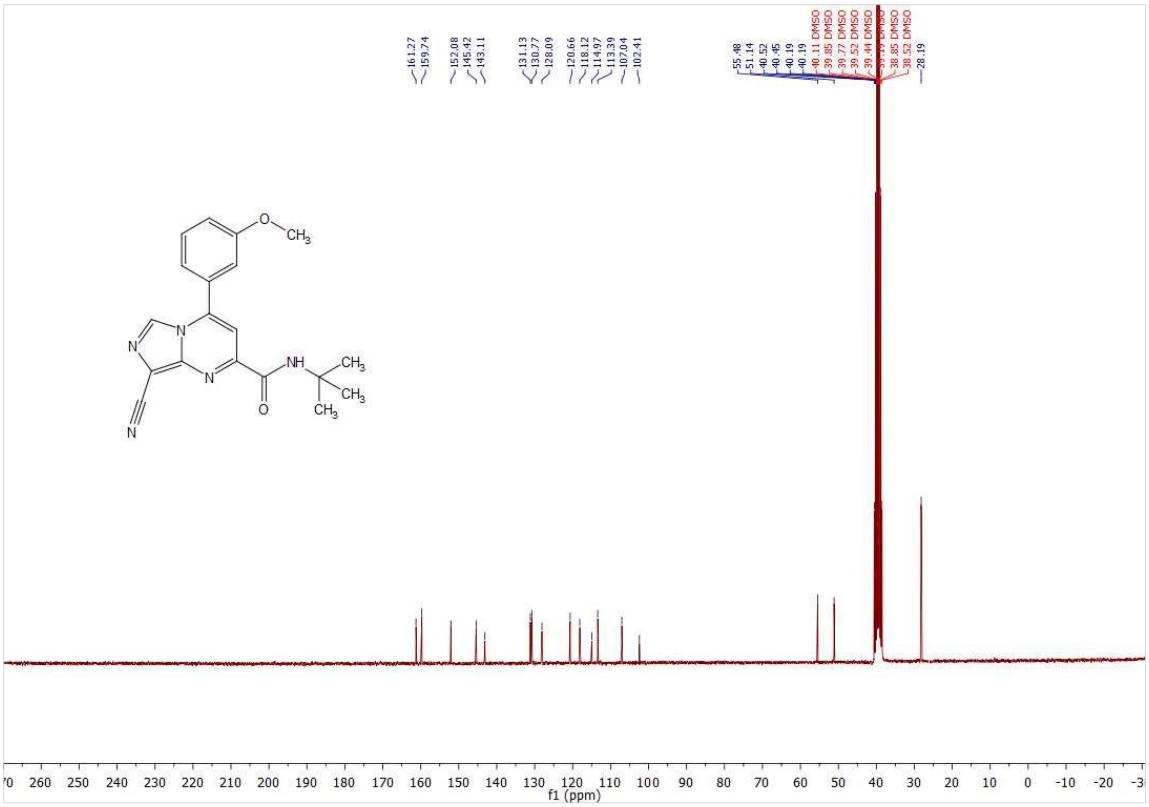


***N*-(*tert*-Butyl)-8-cyano-4-(3-methoxyphenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5f) :**

^{1}H NMR (250 MHz, DMSO-d_6)

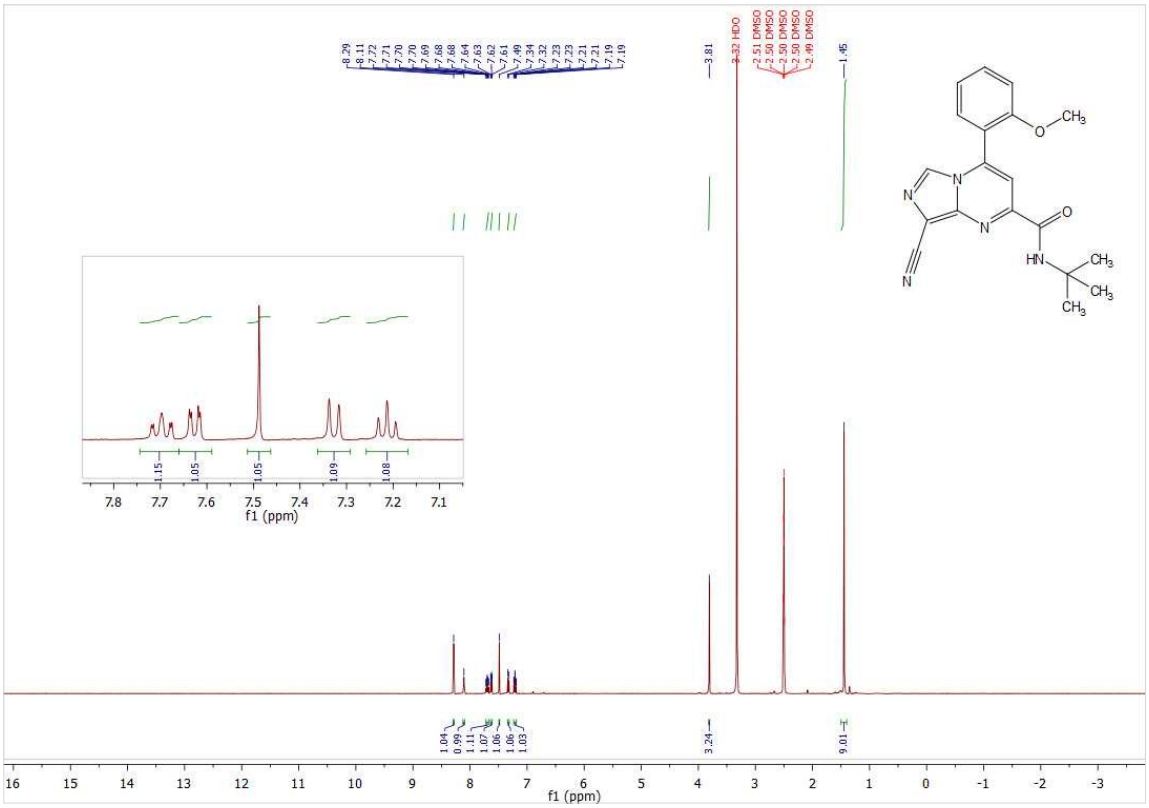


^{13}C NMR (62.9 MHz, DMSO-d_6)

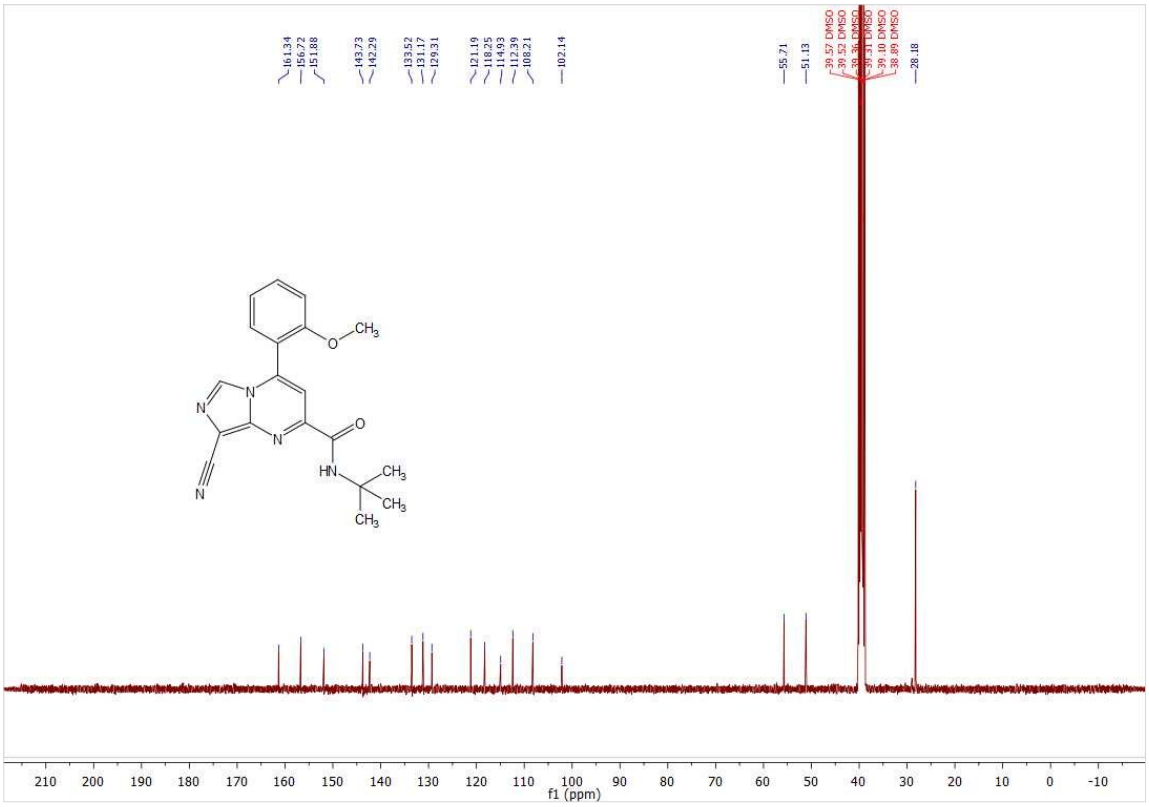


***N*-(*tert*-Butyl)-8-cyano-4-(2-methoxyphenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5g) :**

^{1}H NMR (400 MHz, DMSO-d_6)

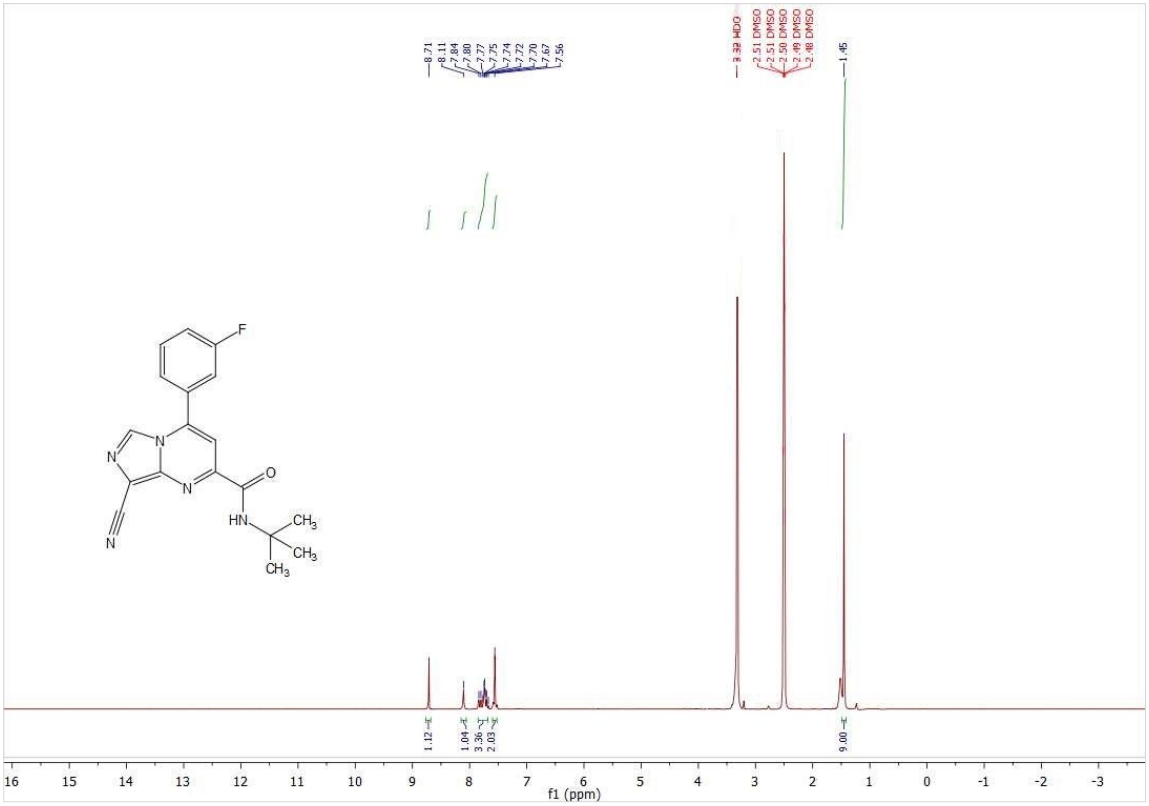


^{13}C NMR (62.9 MHz (101 MHz, DMSO-d_6)

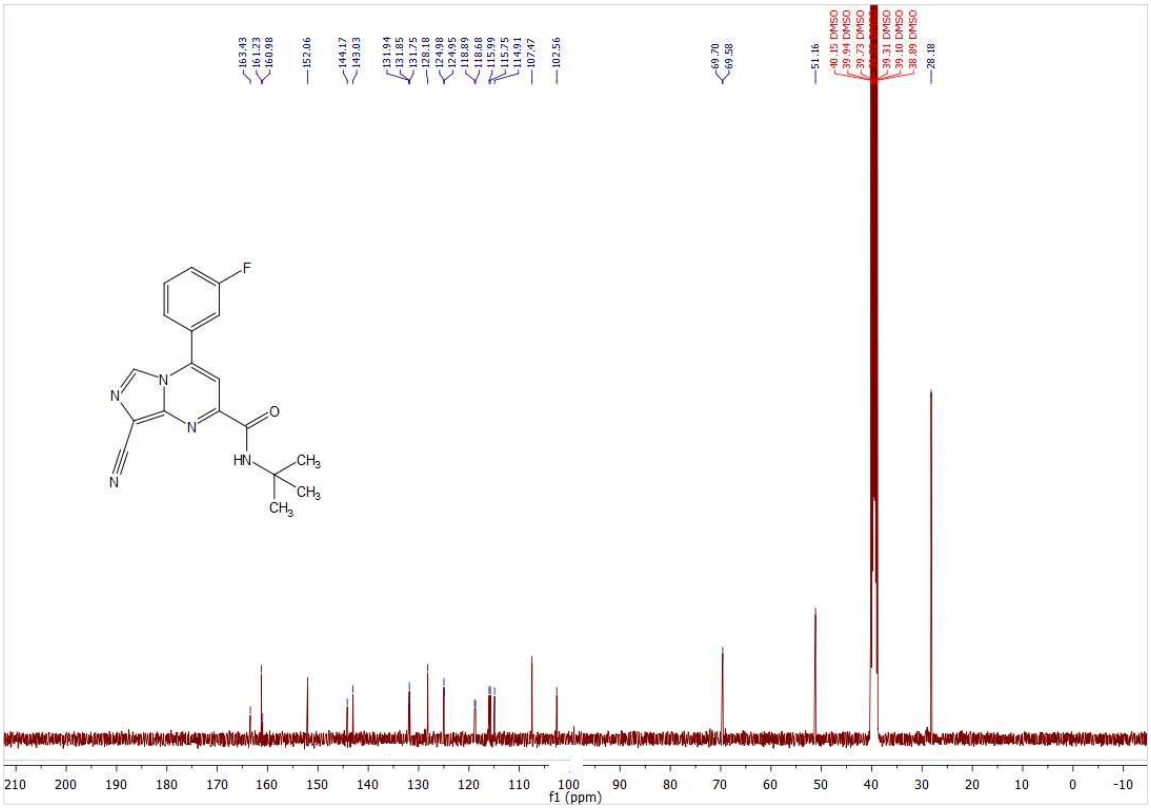


***N*-(tert-Butyl)-8-cyano-4-(3-fluorophenyl)imidazo[1,5-*a*]pyrimidine-2-carboxamide (5h):**

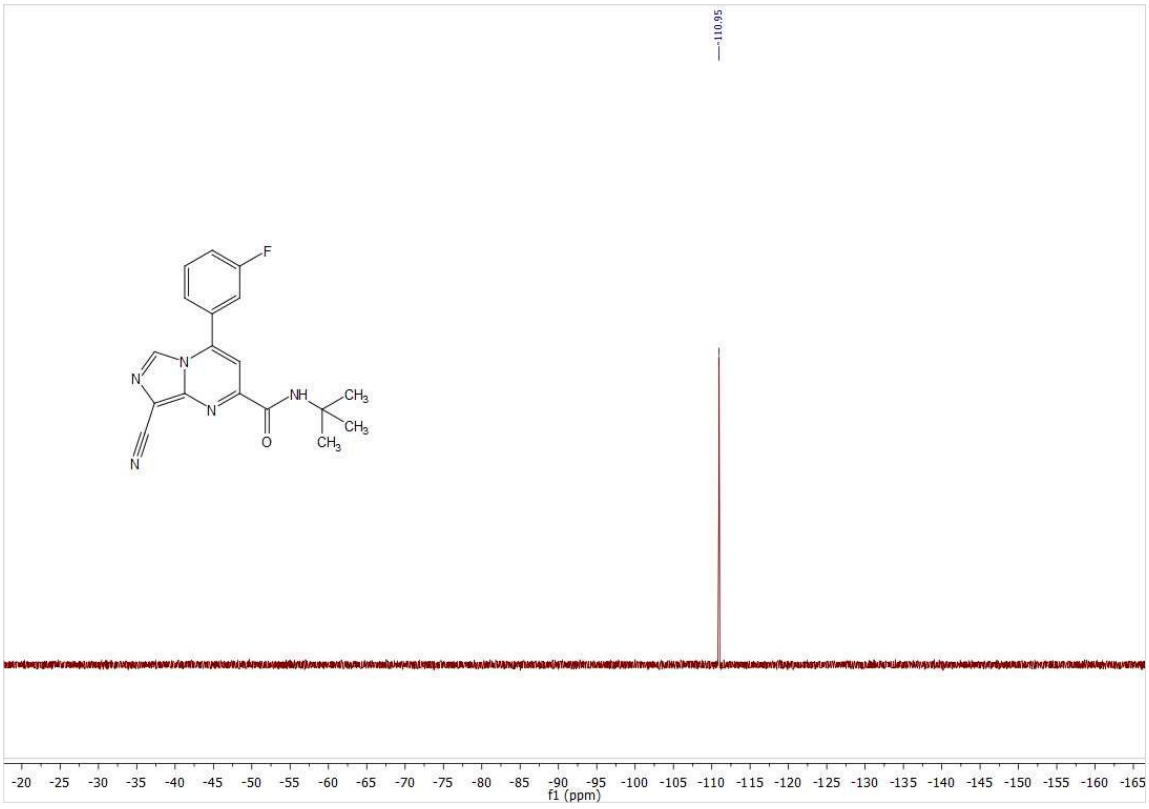
^{1}H NMR (62.9 MHz (400 MHz, DMSO-d$_6$)



^{13}C NMR (62.9 MHz (101 MHz, DMSO-*d*$_6$)



^{19}F NMR (376 MHz, DMSO-d_6)

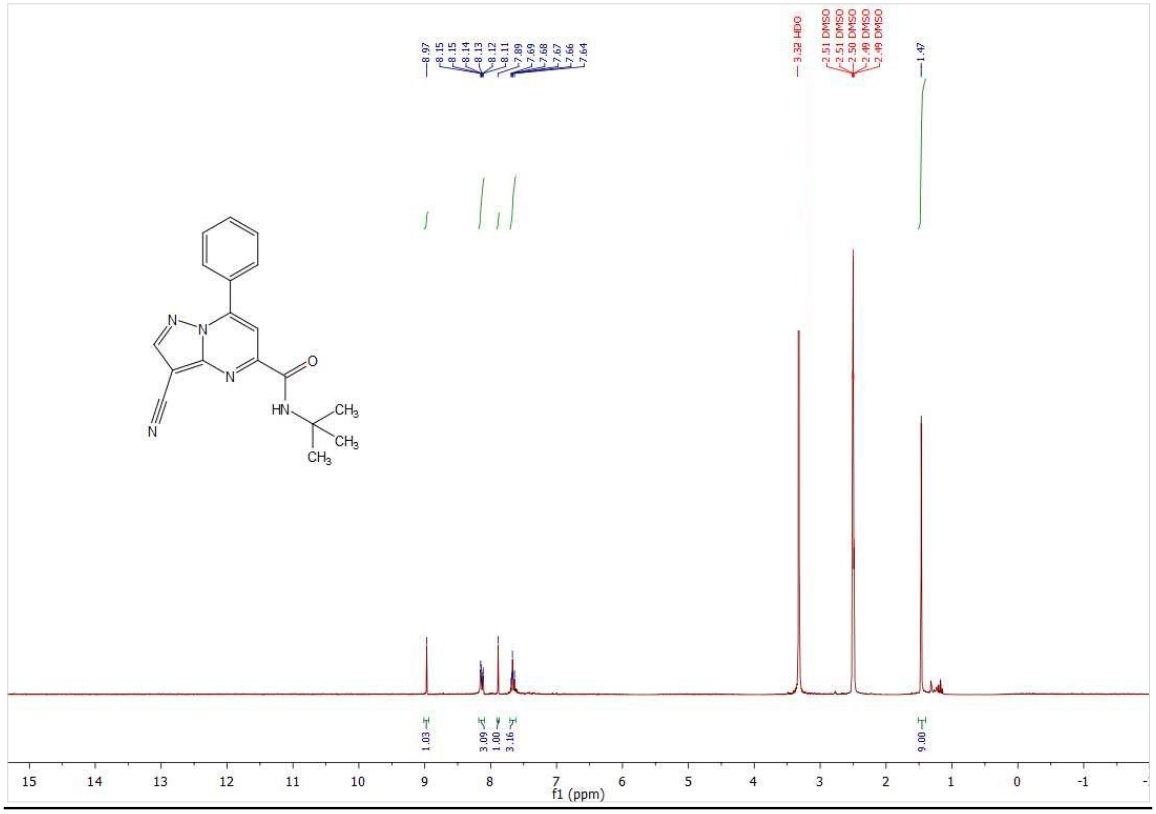


N-(tert-Butyl)-8-cyano-4-(2-fluorophenyl)imidazo[1,5-a]pyrimidine-2-carboxamide (5i):

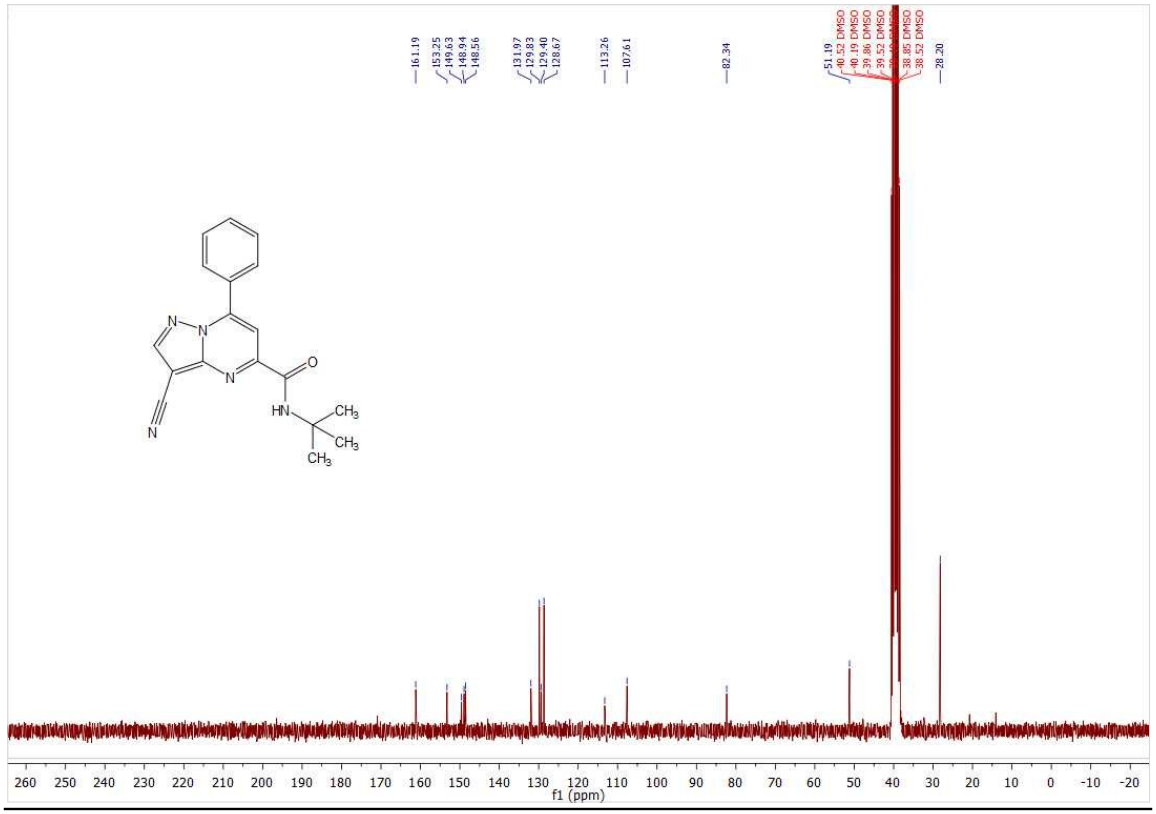
HRMS (m/z) calculated mass for $C_{18}H_{17}FN_5O$ 338.1412 $[M+H]^+$, mass found 338.1410 $[M+H]^+$.

N-(*tert*-Butyl)-3-cyano-7-phenylpyrazolo[1,5-*a*]pyrimidine-5-carboxamide (5k) :

^{1}H NMR (400 MHz, DMSO-d_6)

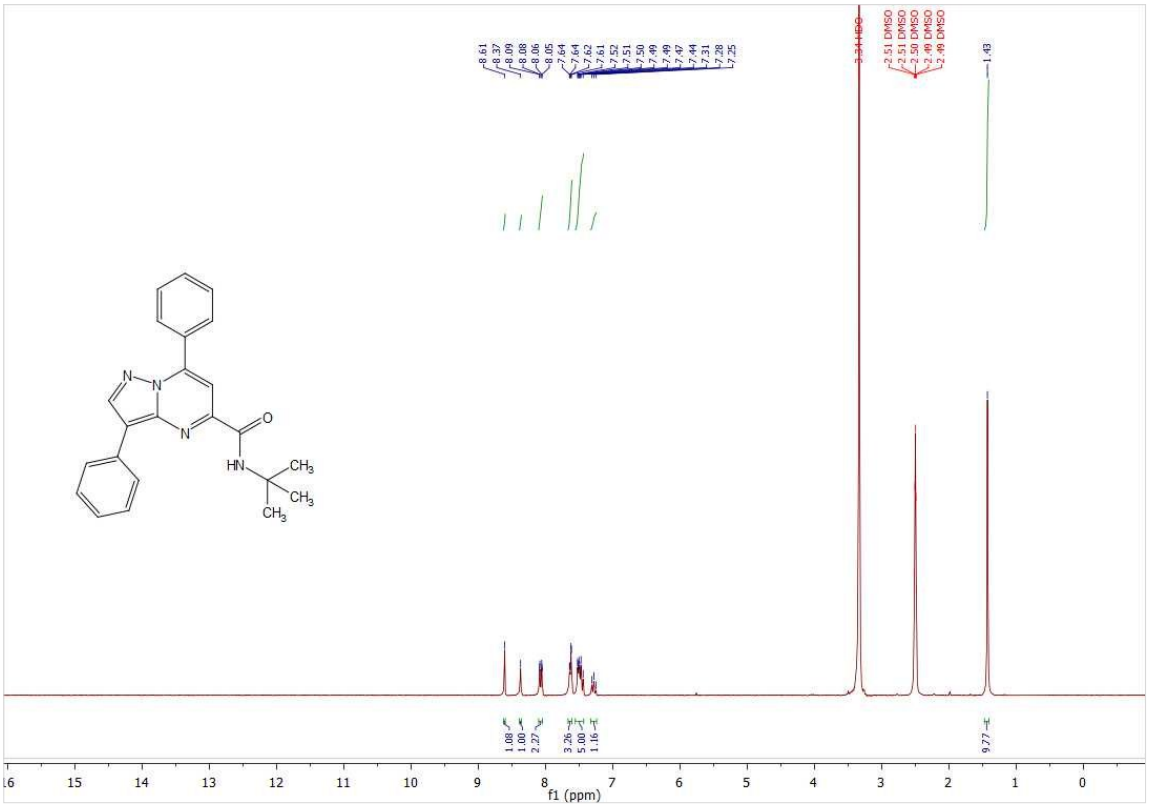


^{13}C NMR (101 MHz, DMSO-d_6)

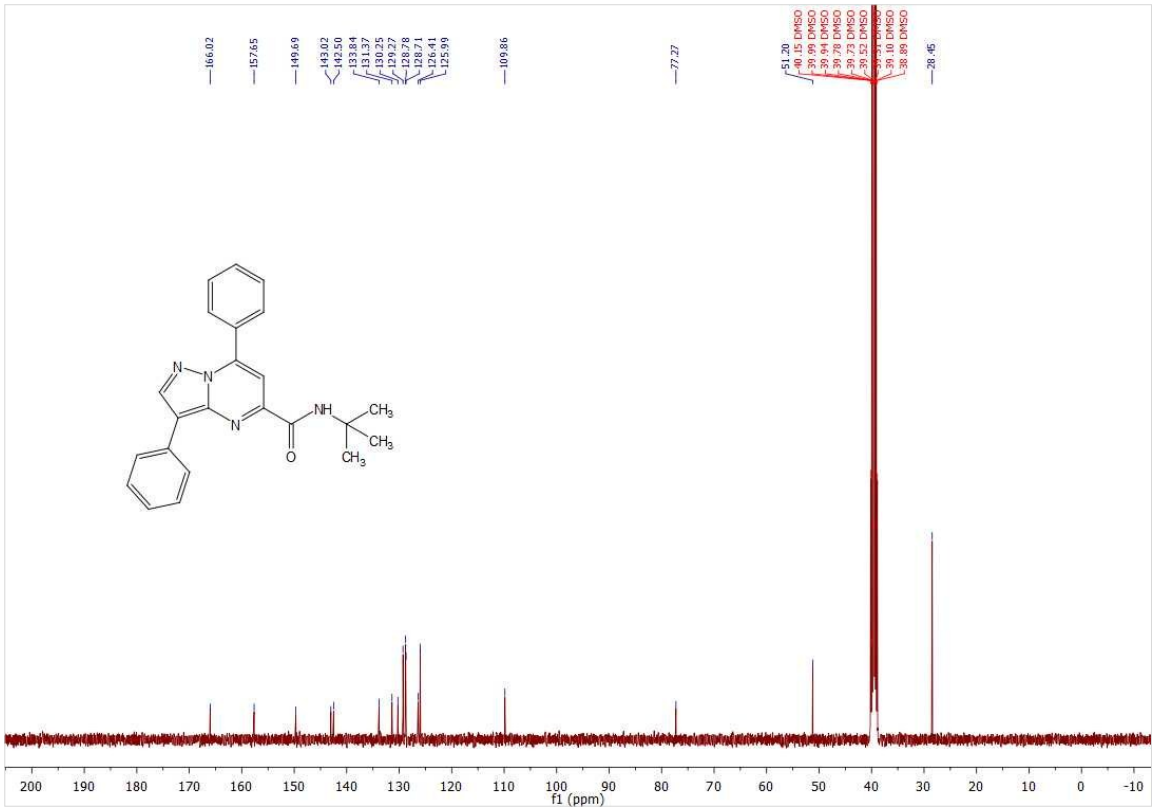


***N*-(*tert*-Butyl)-3,7-diphenylpyrazolo[1,5-*a*]pyrimidine-5-carboxamide (5l) :**

^{1}H NMR (400 MHz, DMSO-d_6)

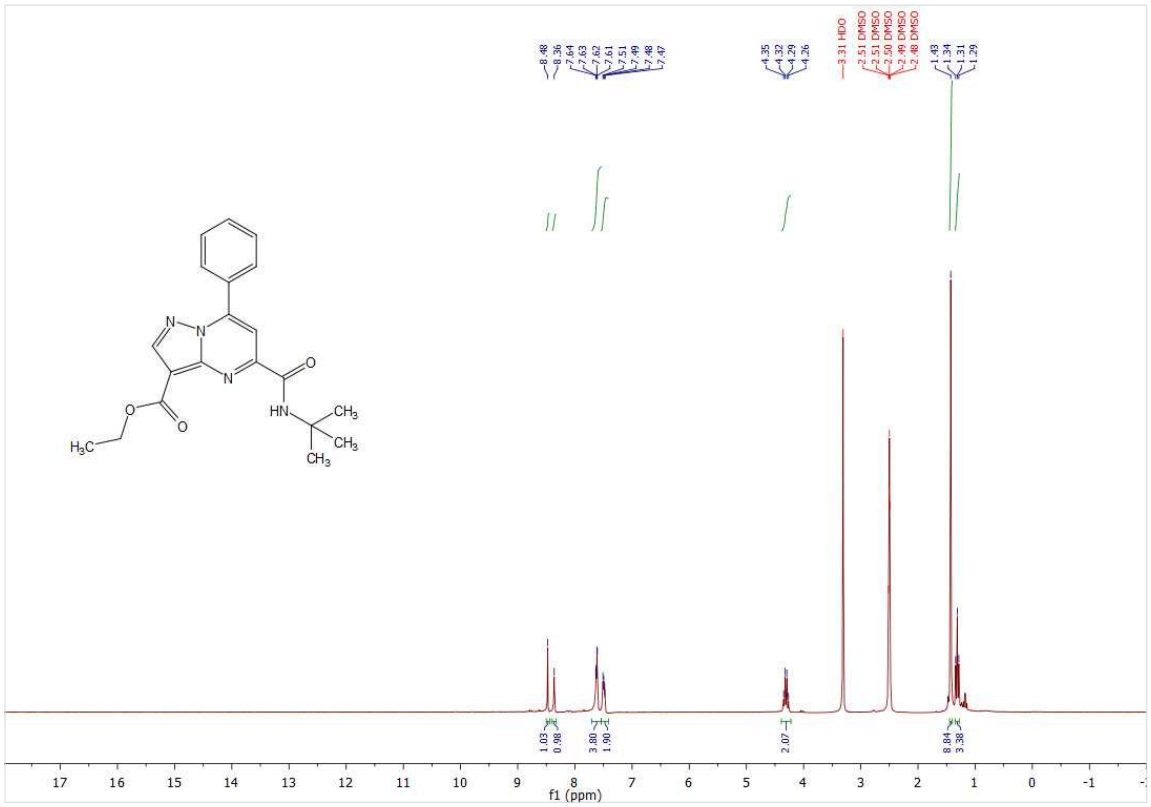


^{13}C NMR (101 MHz, DMSO)

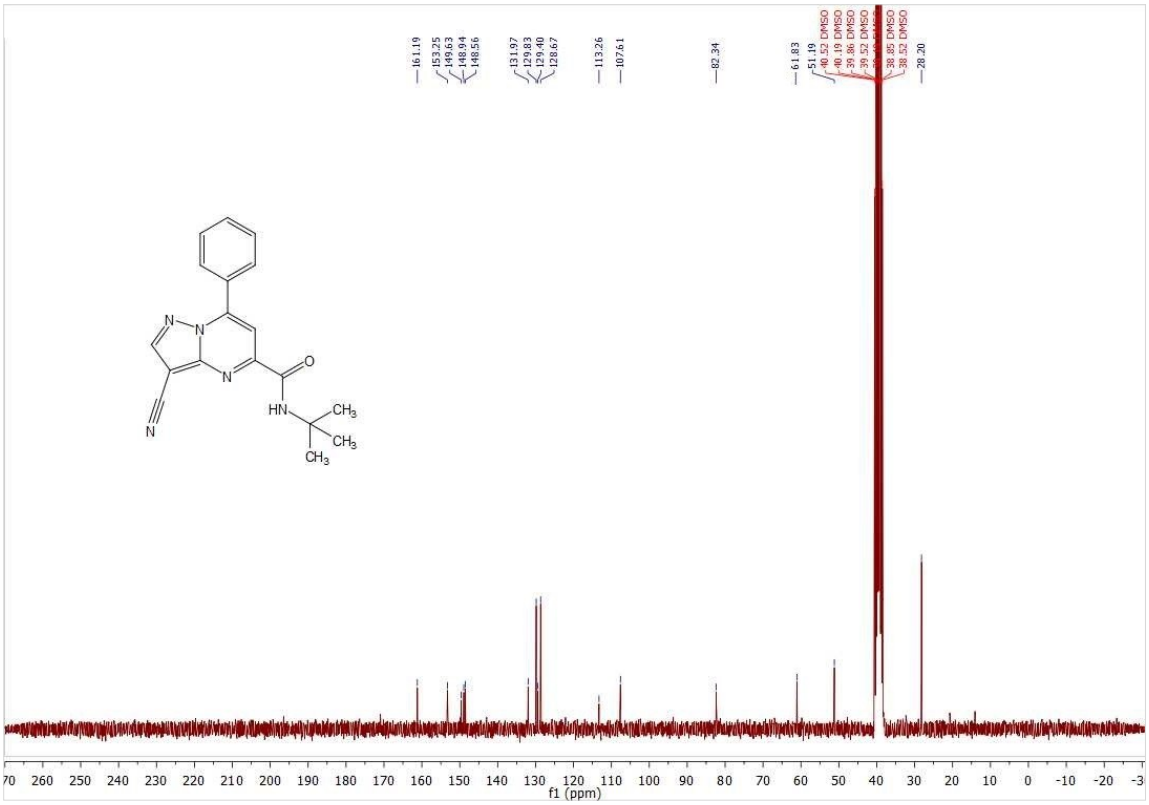


Ethyl 5-(*tert*-butylcarbamoyl)-7-phenylpyrazolo[1,5-*a*]pyrimidine-3-carboxylate (5m) :

^{1}H NMR (400 MHz, DMSO-d_6)

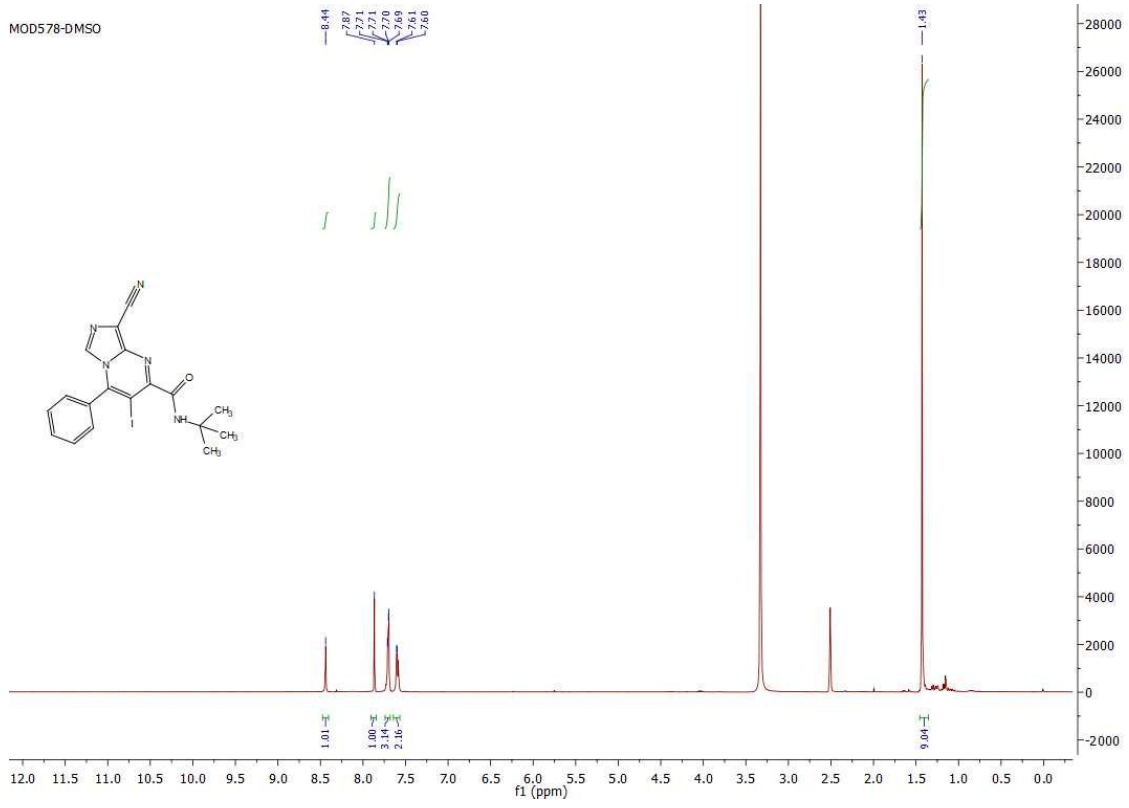


^{13}C NMR (101 MHz, DMSO)

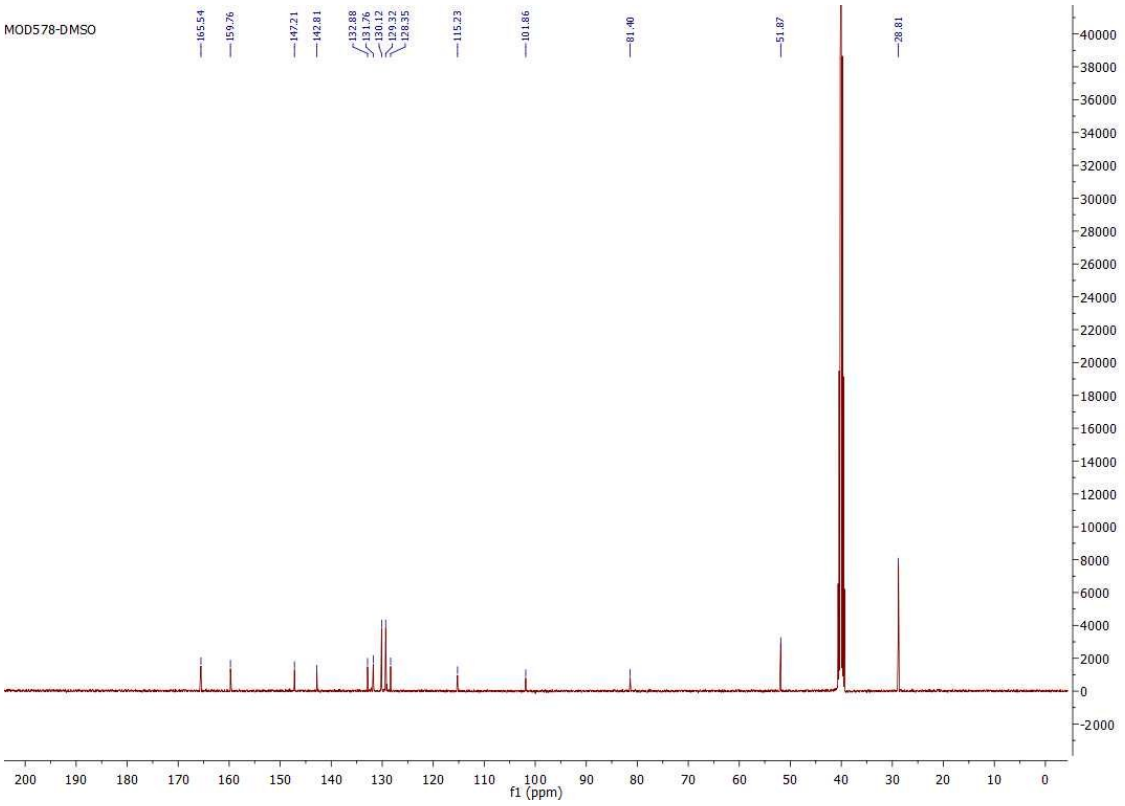


***N*-(*tert*-Butyl)-8-cyano-3-iodo-4-phenylimidazo[1,5-a]pyrimidine-2-carboxamide (6a):**

^{1}H NMR (400 MHz, DMSO-d_6)



^{13}C NMR (101 MHz, DMSO)


MOD578-DMSO
165.54
159.76
147.21
142.81
132.88
131.76
130.12
129.32
128.35
115.23
101.86
81.40
51.87
28.81
f1 (ppm)