Supporting Information

Design and Optimization of 3'-(imidazo[1,2-a]pyrazin-3-yl)-[1,1'-biphenyl]-3-carboxamides as Selective DDR1 Inhibitors

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Contents of SI

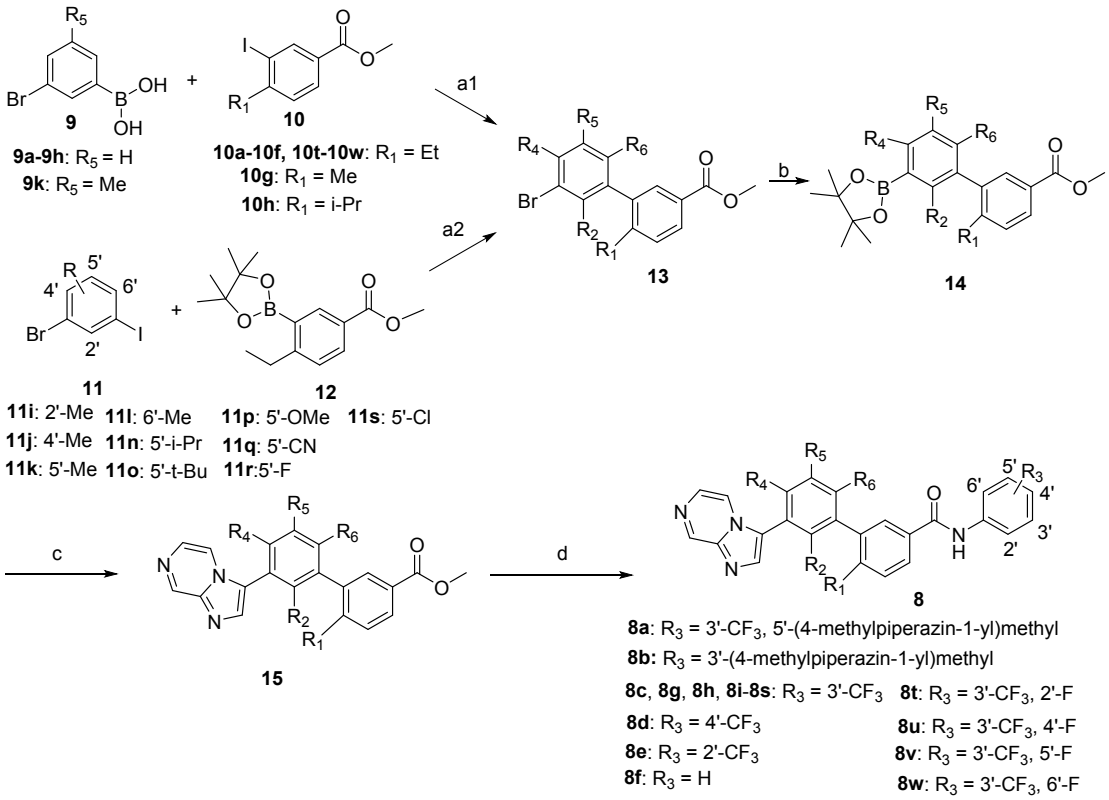
Synthetic procedures for compounds 8a-8w.

Synthesis of the designed compounds **8a-8l** and **8n-8w** was outlined in Scheme **S1.**

Briefly, the substituted methyl 3'-bromo-[1,1'-biphenyl]-3-carboxylate **13** was prepared by coupling substituted 3-bromophenylboronic acid **9a-9h**, **9k** and **9n-9w** with substituted methyl 3-iodobenzoate **10a**, **10g** and **10h** or by coupling substituted 1-bromo-3-iodobenzene **11i**, **11j** and **11l** with methyl

4-ethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate **12. 13** was further reacted with bis(pinacolato)diboron to give the intermediate **14**, which underwent the classical Suzuki coupling reaction to yield the key intermediate substituted methyl 3'-(imidazo[1,2-*a*]pyrazin-3-yl)-[1,1'-biphenyl]-3-carboxylate **15**. The designed compounds **8a-8l** and **8n-8w** were obtained by amidation of intermediate **15** with different anilines under basic condition in good or moderate yields.

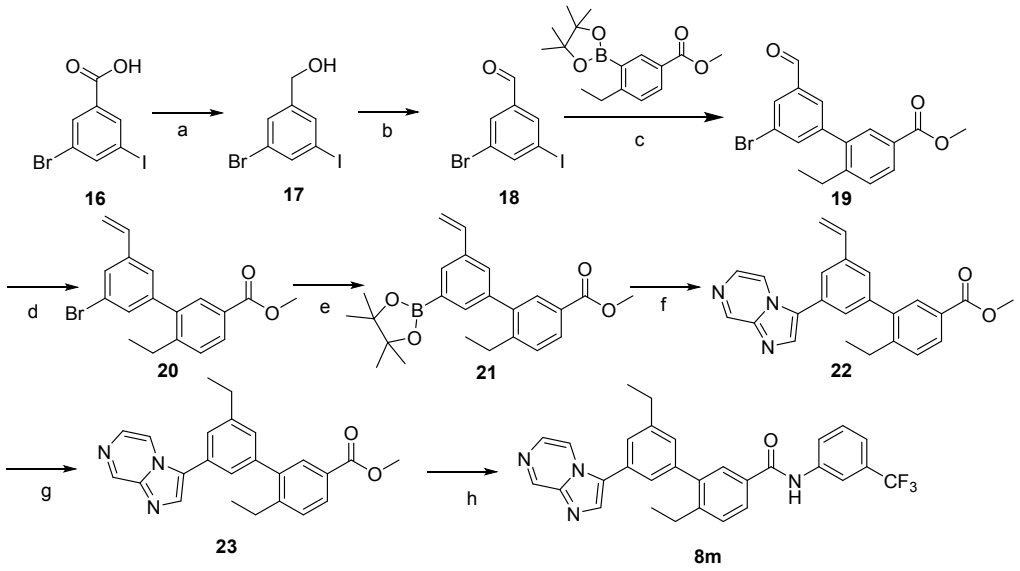
Scheme 1. Synthesis of Compounds **8a**-**8l** and **8n**-**8w**.



Reagents and conditions: (a1) $Pd(PPh_3)_4$, Na_2CO_3, PhMe/H_2O (3:1), Ar, 90℃, overnight, 58-98%; (a2) $Pd(PPh_3)_4$, K_3PO_4, Dioxane, Ar, 90℃, overnight, 55-91%; (b) $Pd(dffp)Cl_2$, KOAc, Bis(pinacolato)diboron, Dioxane, Ar, 90℃, overnight, 64-92%; (c) 3-bromoimidazo[1,2-a]pyrazine, $Pd(PPh_3)_4$, Na_2CO_3, PhMe/H_2O (3:1), Ar, 90℃, overnight, 42-82%; (d) t-BuOK, anilines, dry THF, -20℃, 4-79%.

Synthesis of the designed compound **8m** was outlined in Scheme **S2.**

Scheme **S2.** Synthesis of the compound **8m**.

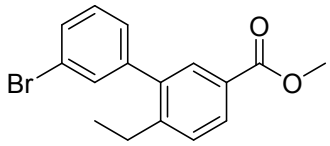


Reagents and conditions: (a) BH_3 (1M THF solution), THF, 0℃ to rt, 12h, 79%; (b) Dess-Martin periodinane, DCM, 0℃ to rt, 1h, 90%; (c) $Pd(PPh_3)_4$, K_3PO_4, Dioxane, Ar, 90℃, overnight, 64%; (d) Methyltriphenylphosphonium bromide, n-BuLi (2.4M THF solution), THF, -20℃ for 0.5h, overnight at rt, 50%; (e) $Pd(dffp)Cl_2$, KOAc, Bis(pinacolato)diboron, Dioxane, Ar, 90℃, overnight, 38%; (f) 3-bromoimidazo[1,2-a]pyrazine, $Pd(PPh_3)_4$, Na_2CO_3, PhMe/H_2O (3:1), Ar, 90℃, overnight, 79%; (g) 10% Pd/C, H_2, MeOH, rt, 4h, 50%; (h) t-BuOK, 3-(trifluoromethyl)aniline, dry THF, -20℃, 8%.

General Methods for Chemistry. All reagents and solvents were purchased from commercial sources without further purification. Flash chromatography was performed using 300 mesh silica gel. All reactions were monitored by thin-layer chromatography (TLC) using silica gel plates with fluorescence F254 and UV light visualization. 1H NMR spectra were recorded on a Bruker AV-400 spectrometer at 400 MHz or a Bruker AV-500 spectrometer at 500 MHz. ^{13}C NMR spectra were recorded on a Bruker AV-500 spectrometer at 125 MHz. Coupling constants (*J*) are expressed in hertz (Hz). Chemical shifts (δ) of NMR are reported in parts per million (ppm) units relative to an internal standard (TMS). Low resolution ESI-MS were recorded on an Agilent 1200 HPLC-MSD mass spectrometer and high resolution ESI-MS on an Applied Biosystems Q-STAR Elite ESI-LC-MS/MS mass spectrometer. Purity of compounds was determined by reverse-phase high

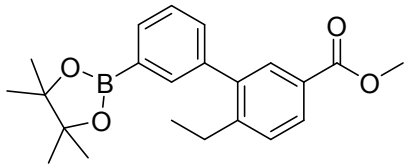
performance liquid chromatography [HPLC, Dionex Summit HPLC (Column: Diamonsil C18, 5.0 μm, 4.6 × 250 mm (Dikma Technologies); detector: PDA-100 photodiode array; injector: ASI-100 autoinjector; pump: p-680A)] to be >95%. A flow rate of 1.0 mL/min was used with mobile phase of 85%MeOH in H_2O with 0.1% modifier (ammonia, v/v).

Methyl 3'-bromo-6-ethyl-[1,1'-biphenyl]-3-carboxylate (**13a**)



To a solution of methyl 4-ethyl-3-iodo-benzoate (6.0 g, 20.66 mmol, 1.0 eq) in toluene/water (v/v, 3:1, 40 mL) was added 3-bromophenylboronic acid (4.36 g, 21.69 mmol, 1.05 eq), $Pd(PPh_3)_4$ (1.2 g, 1.03 mmol, 0.05 eq), Na_2CO_3 (6.58 g, 61.99 mmol, 3.0eq). The mixture was degassed and purged again with argon, then heated at 90℃ overnight. After cooling, the solvent was evaporated under reduced pressure. The residue was dissolved in DCM, washed with water and saturated salt water, dried over Na_2SO_4. The organic layer was concentrated and purified by column chromatography (PE/EA) through silica gel afforded the intermediate **13a** (3.8 g, yield: 58%). ^{1}H NMR (400 MHz, DMSO-d_6): δ(ppm) 7.98 (d, J = 8.0 Hz, 1H), 7.85 (s, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.47 (s, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.29 (t, J = 8.0 Hz, 1H), 7.23 (d, J = 7.6 Hz, 1H), 3.91 (s, 3H), 2.63 (q, J = 3.6 Hz, 2H), 1.12 (t, J = 3.6 Hz, 3H).

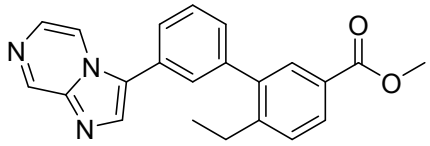
Methyl 6-ethyl-3'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-[1,1'-biphenyl]-3-carboxylate (**14a**)



To a solution of **13a** (2.61 g, 8.17 mmol, 1.0 eq) in dry dioxane (14 mL) was added bis(pinacolato)diboron (3.11 g, 12.2 6mmol, 1.5 eq), $Pd(dppf)Cl_2$(0.30 g, 0.41 mmol, 0.05 eq), KOAc (2.41 g, 24.52 mmol, 3.0 eq). The mixture was degassed and purged again with argon, then heated at 90℃ overnight. After cooling, the solvent was evaporated under reduced pressure. The residue was dissolved in DCM and filtered.

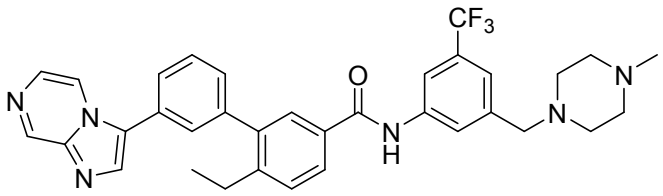
The filtrate was concentrated and purified by column chromatography (PE/EA) to give the intermediate **14a** (1.91 g, yield: 64%). ^{1}H NMR (400 MHz, DMSO-d_6): δ(ppm) 7.95 (d, J = 8.0 Hz, 1H), 7.88 (s, 1H), 7.81 (d, J = 6.8 Hz, 1H), 7.74 (s, 1H), 7.44-7.38 (m, 2H), 7.36 (t, J = 8.0 Hz, 1H), 3.89 (s, 3H), 2.62 (q, J = 3.6 Hz, 2H), 1.35 (s, 12H), 1.10 (t, J = 3.6 Hz, 3H).

Methyl 6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-[1,1'-biphenyl]-3-carboxylate (15a)



To a solution of **14a** (1.91 g, 5.23 mmol, 1.0 eq) and 3-bromoimidazo[1,2-a]pyrazine (0.98 g, 4.96 mmol, 0.95 eq) in Toluene/water (v/v, 3:1, 20ml) was added $Pd(PPh_3)_4$ (0.30 g, 0.26 mmol, 0.05 eq) and Na_2CO_3 (1.66 g, 15.68 mmol, 3.0 eq). The mixture was degassed and purged again with argon, then heated at 90℃ overnight. After cooling, the solvent was evaporated under reduced pressure. The residue was dissolved in DCM and filtered. The filtrate was concentrated and purified by column chromatography (PE/EA) through silica gel to give the intermediate **15a** (0.96 g, yield: 52%). ^{1}H NMR (400 MHz, DMSO-d_6): δ(ppm) 9.16 (s, 1H), 8.29 (d, J = 4.8 Hz, 1H), 8.00 (d, J = 12.0 Hz, 1H), 7.93-7.91 (m, 3H), 7.64-7.60 (m, 2H), 7.52 (s, 1H), 7.43-7.41 (m, 2H), 3.90 (s, 3H), 2.69 (q, J = 7.6 Hz, 2H), 1.10 (t, J = 7.6 Hz, 3H).

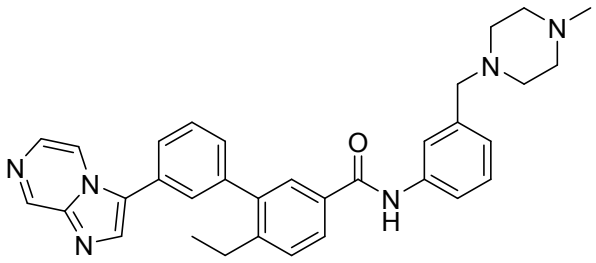
3-((4-methylpiperazin-1-yl)methyl)-5-(trifluoromethyl)phenyl-6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-[1,1'-biphenyl]-3-carboxylate (8a)



To a solution of **15a** (0.14 g, 0.39 mmol, 1.0 eq) and 3-((4-methylpiperazin-1-yl)methyl)-5-(trifluoromethyl)aniline (0.11 g, 0.39 mmol, 1.0 eq) in dry THF (5.0 mL) was added *t*-BuOK (0.17 g, 1.56 mmol, 4.0 eq) in portions at -20℃. The ice bath was removed after 1 hr. The reaction mixture was stirred at rt for

another 2h. The mixture was diluted with EA, washed with water and dried with anhydrous Na_2SO_4. The organic layer was concentrated. Purification by column chromatography (DCM/Methanol) through silica gel afforded the intermediate (0.077g, yield: 33 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.13 (s, 1H), 8.29 (d, *J* = 7.6 Hz, 1H), 8.24 (s, 1H), 7.93-7.91 (m, 3H), 7.88 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.80 (s, 2H), 7.65-7.59 (m, 2H), 7.53 (s, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.44 (dd, *J* = 7.2 Hz, 1.6 Hz, 1H), 7.34 (s, 1H), 3.55 (s, 2H), 2.71 (q, *J* = 7.6 Hz, 2H), 2.58 (br, 8H), 2.37 (s, 3H), 1.18 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.64, 146.08, 144.39, 142.22, 141.26, 140.87, 140.45, 138.75, 134.54, 131.93, 131.24, 129.99, 129.77, 129.43, 129.29, 128.74, 128.30, 127.78, 126.86, 126.60, 123.84, 123.68, 121.34, 116.29, 115.90, 62.21, 54.83, 52.77, 45.73, 26.24, 15.33. MS (ESI), m/z: 599 $[M+H]^+$. Purity: 98.18%, Rt 9.78 min.

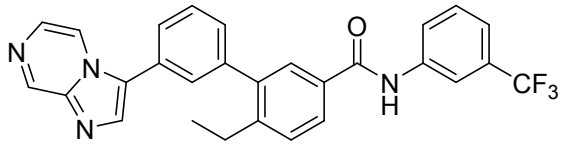
6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-*N*-(3-((4-methylpiperazin-1-yl)methyl)phenyl)-[1,1'-biphenyl]-3-carboxamide (8b)



Compound **8b** was prepared following similar procedure of **8a**, yield 20%. ^{1}H NMR (500 MHz, $CDCl_3$): δ(ppm) 9.10 (s, 1H), 8.27 (d, *J* = 4.3 Hz, 1H), 8.22 (s, 1H), 7.89 (d, *J* = 5.3 Hz, 2H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.78 (s, 1H), 7.64 – 7.55 (m, 3H), 7.53 (s, 1H), 7.50 (s, 1H), 7.43 (t, *J* = 8.6 Hz, 2H), 7.27 (dd, *J* = 10.2, 5.3 Hz, 1H), 7.06 (d, *J* = 7.5 Hz, 1H), 3.46 (s, 2H), 2.68 (q, *J* = 7.5 Hz, 2H), 2.48 (br, 8H), 2.25 (s, 3H), 1.15 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.49, 145.87, 144.67, 142.48, 141.49, 141.05, 139.34, 138.14, 134.80, 132.67, 130.17, 129.94, 129.58, 129.38, 129.04, 128.82, 128.54, 128.02, 126.77, 125.53, 120.96, 119.25, 116.44, 62.94, 55.07, 53.12, 46.01, 26.40, 15.54. HRMS (ESI) calcd for $C_{33}H_{34}N_6O$ $[M+H]^+$: 531.2866; found 531.2858. HPLC purity= 96.36%, Rt 13.26 min.

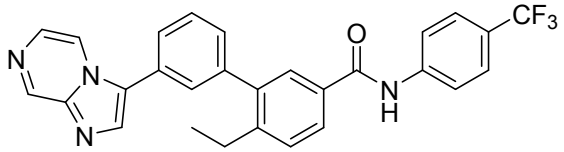
6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-*N*-(3-(trifluoromethyl)phenyl)-[1,1'-biphe

nyl]-3-carboxamide (8c)



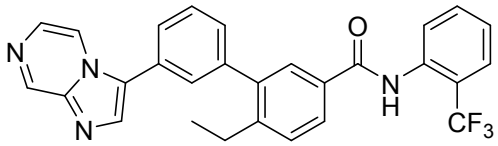
Compound **8c** was prepared following similar procedure of **8a**, yield 72%. ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.14 (s, 1H), 8.28 (d, *J* = 4.4 Hz, 1H), 8.05 (s, 1H), 7.91-7.93 (m, 3H), 7.86-7.89 (m, 2H), 7.78 (d, *J* = 1.6 Hz, 1H), 7.66-7.60 (m, 2H), 7.53-7.44 (m, 4H),7.40 (d, *J* = 0.4 Hz, 1H), 2.71 (q, *J* = 7.5 Hz, 2H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.70, 146.35, 144.67, 142.38, 141.50, 141.18, 138.76, 134.77, 132.12, 130.20, 129.93, 129.74, 129.64, 129.53, 128.85, 128.49, 128.04, 126.88, 126.83, 126.76, 123.44, 121.17, 121.14, 117.11, 117.08, 116.42, 26.45, 15.51. HRMS (ESI) calcd for $C_{28}H_{21}F_3N_4O$ $[M+H]^+$: 487.1740; found 487.1747. HPLC purity= 97.96%, Rt 6.57 min.

6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-*N*-(4-(trifluoromethyl)phenyl)-[1,1'-biphe nyl]-3-carboxamide (8d)



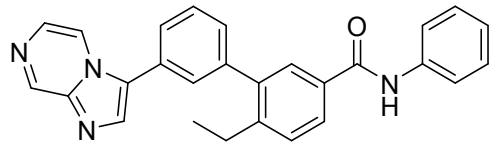
Compound **8c** was prepared following similar procedure of **8a**, yield 72%. ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.11 (s, 1H), 8.27-8.26 (s, 2H), 7.91-7.86 (m, 3H), 7.79-7.77 (m, 3H), 7.63-7.58 (m, 4H), 7.49-7.46 (m, 2H), 7.44-7.42 (m, 1H), 2.70 (q, *J* = 7.4 Hz, 2H), 1.17 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.88, 146.33, 144.55, 142.35, 141.41, 141.07, 134.68, 132.13, 130.15, 129.91, 129.53, 128.93, 128.38, 127.92, 127.00, 126.74, 126.36, 126.13, 125.26, 123.10, 120.00, 116.41, 26.41, 15.49. HRMS (ESI) calcd for $C_{28}H_{22}F_3N_4O$ $[M+H]^+$: 487.1740; found 487.1747. HPLC purity= 97.12%, Rt 11.14 min.

6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-*N*-(2-(trifluoromethyl)phenyl)-[1,1'-biphe nyl]-3-carboxamide (8e)



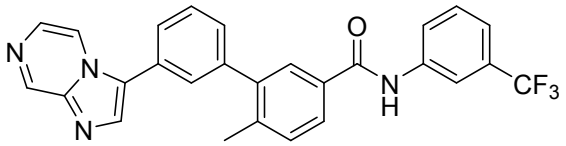
Compound **8d** was prepared following similar procedure of **8a**, yield 63%. ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.17 (s, 1H), 8.42 (d, *J* = 8.2 Hz, 1H), 8.31 (d, *J* = 4.3 Hz, 1H), 8.26 (s, 1H), 7.94-7.93 (m, 2H), 7.83-7.81 (m, 2H), 7.67-7.60 (m, 4H), 7.55 (s, 1H), 7.51 (d, *J* = 8.2 Hz, 1H), 7.46 (d, *J* = 6.8 Hz, 1H), 7.27 (t, *J* = 7.3 Hz, 1H), 2.72 (q, *J* = 7.4 Hz, 2H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.27, 146.52, 144.75, 142.31, 141.50, 135.63, 134.87, 133.17, 132.05, 130.19, 129.91, 129.62, 129.07, 128.50, 128.15, 126.94, 126.74, 126.28, 124.67, 124.42, 116.42, 26.45, 15.49. HRMS (ESI) calcd for $C_{28}H_{21}F_3N_4O$ $[M+H]^+$: 487.1740; found 487.1744. HPLC purity= 97.96%, Rt 6.57 min.

6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-*N*-phenyl-[1,1'-biphenyl]-3-carboxamide (8f)



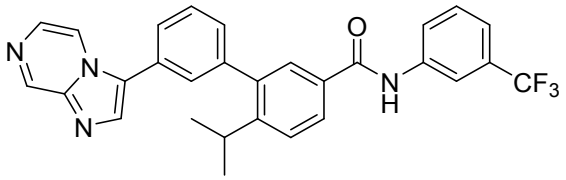
Compound **8f** was prepared following similar procedure of **8a**, yield 47%.^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.13 (d, *J* = 1.2 Hz, 1H), 8.28 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.01 – 7.88 (m, 3H), 7.85 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.78 (d, *J* = 1.8 Hz, 1H), 7.66 – 7.59 (m, 4H), 7.52 (s, 1H), 7.44 (dd, *J* = 11.8, 4.9 Hz, 2H), 7.35 (t, *J* = 7.9 Hz, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 2.70 (q, *J* = 7.5 Hz, 2H), 1.17 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.63, 145.79, 144.58, 142.46, 141.42, 140.96, 138.17, 134.73, 132.68, 130.12, 129.92, 129.54, 129.31, 129.11, 128.87, 128.45, 127.93, 126.98, 126.61, 124.60, 120.45, 116.42, 26.36, 15.53. HRMS (ESI) calcd for $C_{27}H_{21}N_4O$ $[M+H]^+$: 419.1866; found 419.1863. HPLC purity= 96.36%, Rt 13.26 min.

3'-(imidazo[1,2-*a*]pyrazin-3-yl)-6-methyl-*N*-(3-(trifluoromethyl)phenyl)-[1,1'-biphenyl]-3-carboxamide (8g)



Compound **8g** was prepared following similar procedure of **8a**, yield 65%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.14 (s, 1H), 8.29 (d, *J* = 4.4 Hz, 1H), 8.09 (s, 1H), 7.92-7.91 (m, 3H), 7.88 (d, *J* = 8.2 Hz, 1H), 7.83-7.81 (m, 2H), 7.67-7.59 (m, 2H), 7.53 (s, 1H), 7.50-7.43 (m, 3H), 7.39 (d, *J* = 8.0 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.70, 144.65, 142.37, 141.49, 141.19, 138.76, 134.75, 132.37, 131.23, 130.19, 129.92, 129.73, 129.68, 128.69, 128.52, 128.09, 126.87, 126.77, 126.59, 123.46, 121.16, 117.10, 116.43, 20.74. MS (ESI), m/z: 507 [M+Cl]+. HRMS (ESI) calcd for $C_{27}H_{19}F_3N_4O$ $[M+H]^+$: 473.1584; found 473.1578. Purity: 96.03%, Rt 6.82 min.

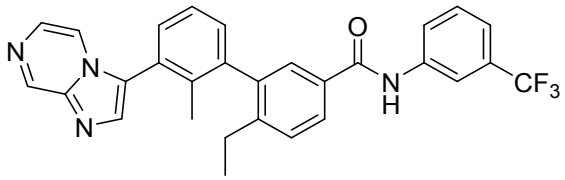
3'-(imidazo[1,2-*a*]pyrazin-3-yl)-6-isopropyl-N-(3-(trifluoromethyl)phenyl)-[1,1'-biphenyl]-3-carboxamide (8h)



Compound **8h** was prepared following similar procedure of **8a**, yield 7%. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.03 (d, *J* = 1.1 Hz, 1H), 8.69 (s, 1H), 8.23 (dd, *J* = 4.7, 1.2 Hz, 1H), 7.94 – 7.91 (m, 2H), 7.89 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 4.7 Hz, 1H), 7.83 (s, 1H), 7.79 (d, *J* = 1.8 Hz, 1H), 7.58 (dt, *J* = 15.3, 7.7 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 1H), 7.45 – 7.40 (m, 2H), 7.37 (dd, *J* = 11.5, 7.7 Hz, 2H), 3.13-3.08 (m, *J* = 6.8 Hz, 1H), 1.20 (d, *J* = 6.8 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$): δ(ppm) 165.79, 151.04, 144.60, 142.49, 141.45, 140.50, 138.83, 134.71, 131.84, 131.63, 131.38, 130.16, 129.99, 129.64, 128.86, 128.45, 127.92, 127.20, 126.75, 126.73, 125.04, 123.47, 122.87, 121.08, 117.11, 116.40, 29.93, 24.16. HRMS (ESI) calcd for $C_{29}H_{23}F_3N_4O$ [M+H]+ : 501.1897; found 501.1919. HPLC purity= 96.77%, Rt 11.95 min.

6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-2'-methyl-*N*-(3-(trifluoromethyl)phenyl)-[

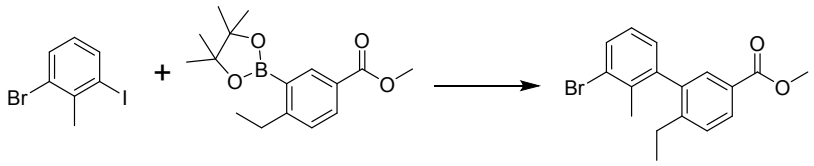
1,1'-biphenyl]-3-carboxamide（8i）



The title compound was synthesized following the procedure for compound **8a** substituting **13a** with **13i** (prepared by the method outlined below).

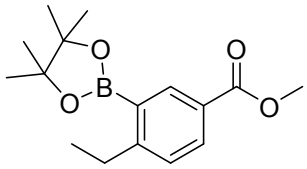
^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.14 (d, *J* = 1.3 Hz, 1H), 8.16 (s, 1H), 7.92 (s, 1H), 7.90 – 7.86 (m, 3H), 7.83 (s, 1H), 7.75 (dd, *J* = 4.6, 1.4 Hz, 1H), 7.71 (d, *J* = 1.9 Hz, 1H), 7.50-7.46 (m, 2H), 7.42-7.38 (m, 3H), 7.31 (dd, *J* = 6.8, 2.1 Hz, 1H), 2.58-2.44 (m, 2H), 1.82 (s, 3H), 1.13 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.81, 146.58, 144.25, 142.02, 141.06, 140.89, 138.82, 136.13, 135.22, 132.11, 131.36, 1301.49, 129.89, 129.70, 129.11, 128.55, 127.41, 126.76, 126.31, 125.03, 123.58, 122.86, 121.07, 117.28, 116.75, 26.39, 17.49, 14.92. HRMS (ESI) calcd for $C_{29}H_{23}F_3N_4O$ $[M+H]^+$: 501.1897; found 501.1914. HPLC purity= 99.57%, Rt 8.08 min.

methyl 3'-bromo-6-ethyl-2'-methyl-[1,1'-biphenyl]-3-carboxylate (**13i**)



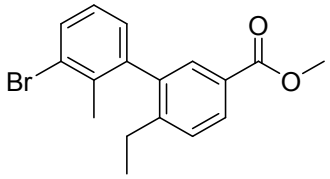
12 **13i**

methyl 4-ethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (**12**)



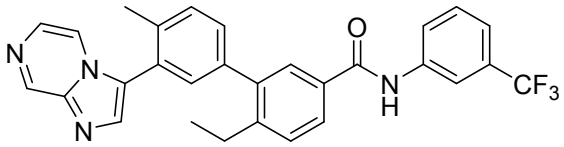
The title compound was synthesized following the procedure of compound **14a** starting with methyl 4-ethyl-3-iodobenzoate. ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 8.41 (s, 1H), 8.0 (d, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 1H), 3.90 (s, 3H), 2.96 (q, *J* = 7.6, 2H), 1.20 (t, *J* = 7.6 Hz, 3H).

methyl 3'-bromo-6-ethyl-2'-methyl-[1,1'-biphenyl]-3-carboxylate (**13i**)



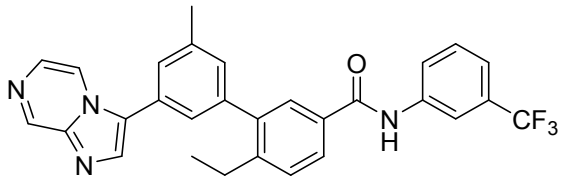
To a solution of methyl 4-ethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoate (**12**) (1.95g, 6.72mmol, 1.0eq) in dioxane (11mL) was added 1-bromo-3-iodo-2-methylbenzene (2.0g, 6.72mmol, 1.0eq), $Pd(PPh_3)_4$ (0.39g, 0.34mmol, 0.05eq), K_3PO_4 (5.38g, 20.16mmol, 3.0eq). The mixture was degassed and purged again with argon, then heated at 90℃ overnight. After cooling, the solvent was evaporated under reduced pressure. The residue was dissolved in DCM, washed with water and saturated salt water, dried with Na_2SO_4. The organic layer was concentrated. Purification by column chromatography (PE/EA) through silica gel afforded the intermediate **13i** (1.8g，yield: 80.37%).^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 7.97-7.93 (m, 2H), 7.37-7.32 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.12 (s, 1H), 3.90 (s, 3H), 2.70 (q, *J* = 8.0, 2H), 2.18 (s, 3H), 0.97 (t, *J* = 8.0 Hz, 3H).

6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-4'-methyl-*N*-(3-(trifluoromethyl)phenyl)-[1,1'-biphenyl]-3-carboxamide (**8j**)



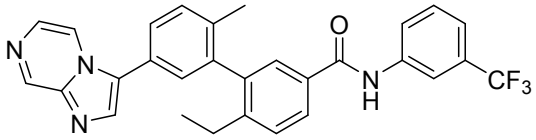
Compound **8j** was prepared following similar procedure of **8i**, yield 13%. ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.13 (d, *J* = 1.3 Hz, 1H), 8.12 (s, 1H), 7.91 (s, 1H), 7.88 (t, *J* = 6.5 Hz, 2H), 7.83 (dd, *J* = 7.3, 2.7 Hz, 2H), 7.78 (dd, *J* = 4.7, 1.5 Hz, 1H), 7.76 (d, *J* = 2.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.42 – 7.36 (m, 2H), 7.31 (d, *J* = 1.7 Hz, 1H), 2.70 (q, *J* = 7.5 Hz, 2H), 2.23 (s, 3H), 1.16 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 165.85, 146.35, 144.29, 140.95, 139.29, 138.83, 137.24, 135.20, 132.06, 131.63, 131.26, 130.65, 129.90, 129.68, 129.38, 129.01, 126.71, 125.82, 125.03, 123.48, 122.86, 121.06, 117.11, 116.73, 26.42, 19.62, 15.47. HRMS (ESI) calcd for $C_{29}H_{23}F_3N_4O$ $[M+H]^+$: 501.18967; found 501.18929. HPLC purity= 99.89%, Rt 8.52 min.

6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-5'-methyl-*N*-(3-(trifluoromethyl)phenyl)-[1,1'-biphenyl]-3-carboxamide (8k)



Compound **8k** was prepared following similar procedure of **8a**, yield 4%.^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 9.07 (d, *J* = 1.3 Hz, 1H), 8.38 (s, 1H), 8.24 (dd, *J* = 4.7, 1.4 Hz, 1H), 7.93 (s, 1H), 7.90 – 7.85 (m, 4H), 7.78 (d, *J* = 1.9 Hz, 1H), 7.48-7.44 (m, 2H), 7.39-7.38 (m, 2H), 7.27 (s, 1H), 7.23 (s, 1H), 2.69 (q, *J* = 7.6 Hz, 2H), 2.49 (s, 3H), 1.17 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.86, 146.25, 144.53, 142.28, 141.38, 141.21, 139.65, 138.89, 134.63, 132.04, 130.75, 130.09, 129.69, 129.41, 128.84, 127.77, 127.48, 126.91, 125.45, 123.47, 121.05, 117.12, 116.49, 26.43, 21.62, 15.51. HRMS (ESI) calcd for $C_{29}H_{23}F_3N_4O$ $[M+H]^+$: 501.1897; found 501.1893. HPLC purity= 99.47%, Rt 9.66 min.

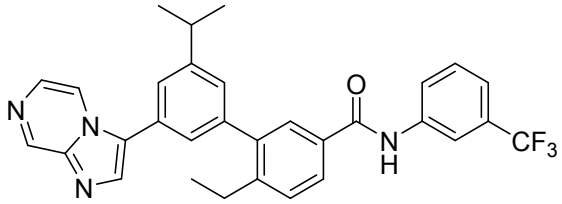
6-ethyl-5'-(imidazo[1,2-*a*]pyrazin-3-yl)-2'-methyl-*N*-(3-(trifluoromethyl)phenyl)-[1,1'-biphenyl]-3-carboxamide (8l)



Compound **8k** was prepared following similar procedure of **8a**, yield 4%. ^{1}H NMR (500 MHz, $CDCl_3$): δ(ppm) 8.99 (d, *J* = 1.3 Hz, 1H), 8.78 (s, 1H), 8.16 (dd, *J* = 4.6, 1.4 Hz, 1H), 7.94 (s, 1H), 7.91 (dd, *J* = 11.1, 5.0 Hz, 2H), 7.81 (d, *J* = 4.7 Hz, 1H), 7.77 (s, 1H), 7.74 (d, *J* = 1.7 Hz, 1H), 7.43 (dd, *J* = 14.9, 8.0 Hz, 4H), 7.35 (d, *J* = 7.4 Hz, 1H), 7.23 (s, 1H), 2.56-2.42 (m, 2H), 2.11 (s, 3H), 1.10 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 166.04, 146.77, 144.64, 141.87, 141.50, 140.66, 139.09, 137.64, 134.63, 132.31,132.07, 131.82, 131.55, 131.30, 130.22, 129.87, 129.38, 128.77, 128.59, 127.30, 127.00, 125.32, 125.24, 123.69, 123.07, 121.22, 120.91, 117.35, 116.62, 26.55, 20.25, 15.17. HRMS (ESI) calcd for $C_{29}H_{23}F_3N_4O$ $[M+H]^+$: 501.1897; found 501.1892. HPLC purity= 98.73%, Rt 8.76 min.

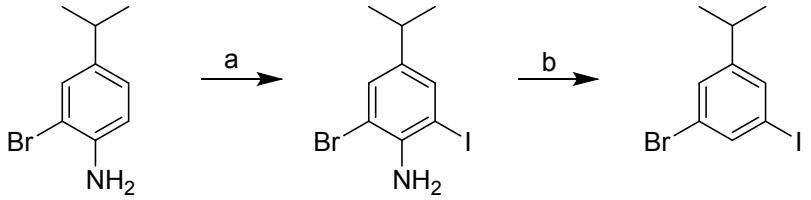
6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-5'-isopropyl-*N*-(3-(trifluoromethyl)phenyl

)-[1,1'-biphenyl]-3-carboxamide (8n)



Compound **8n** was prepared following similar procedure of **8i**, with 1-bromo-3-iodo-5-isopropylbenzene as starting material, yield 6%. ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.10 (s, 1H), 8.30 - 8.21 (m, 2H), 7.93 (s, 1H), 7.88 (d, *J* = 10.0 Hz, 4H), 7.80 (s, 1H), 7.51 - 7.44 (m, 2H), 7.43 (s, 1H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.30 (d, *J* = 5.1 Hz, 2H), 3.09-3.02 (m, 1H), 2.70 (q, *J* = 7.5 Hz, 2H), 1.35 (d, *J* = 6.9 Hz, 6H), 1.19 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.87, 150.66, 146.33, 144.55, 142.30, 141.44, 138.85, 134.64, 132.07, 131.64, 131.38, 130.09, 129.69, 129.45, 128.86, 128.62, 128.25, 127.85, 127.13, 126.82, 125.85, 125.10, 123.48, 122.88, 121.04, 117.12, 116.47, 34.32, 26.48, 24.08, 15.58. HRMS (ESI) calcd for $C_{31}H_{27}F_3N_4O$ $[M+H]^+$: 529.2209; found 529.2211. HPLC purity= 99.55%, Rt 11.40 min.

1-bromo-3-iodo-5-isopropylbenzene

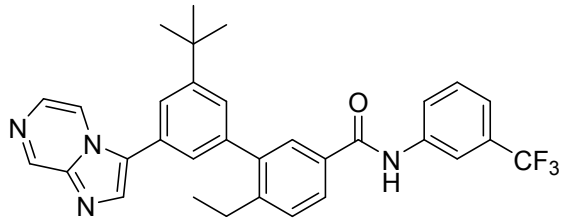


a. To a solution of 2-bromo-4-isopropylaniline (10g, 46.72mmol, 1.0eq) in DCM (66.6mL)/MeOH (26.65ml) was added $CaCO_3$ (8.13 g, 81.30 mmol, 1.74 eq) and benzyltrimethylammonium dichloroiodate (21.77 g, 2.60 mmol, 1.34 eq). The mixture was stirred at reflux for 3 h then cooled to ambient temperature, filtered. The filtration was concentrated under vacuum. Purification by column chromatography (PE/EA) through silica gel afforded the desired product 2-bromo-6-iodo-4-isopropylaniline (5.0 g, yield: 31%).^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 7.45 (s, 1H), 7.27 (s, 1H), 4.43 (brs, 2H), 2.69-2.78 (m, 1H), 1.18 (d, *J* = 7 Hz, 6H).

b. To a solution of 2-bromo-6-iodo-4-isopropylaniline (5.0g, 14.83mmol, 1.0eq) in toluene (7.8mL) and EtOH (23.6mL) was slowly added conc. H_2SO_4 (2.2ml) and

$NaNO_2$ (2.23g, 32.63mmol, 2.2eq). The mixture was stirred at reflux for 1.5h. The solvent was evaporated. The residue was dissolved in EA, then washed with water. The organic layer was concentrated under vacuum. Purification by column chromatography (PE/EA) through silica gel afforded the desired product 1-bromo-3-iodo-5-isopropylbenzene (2.31 g, yield: 48 %).^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 7.75 (s, 1H), 7.62 (s, 1H), 7.47 (s, 1H), 2.90 –2.83 (m, 1H), 1.16 (d, J = 6.8 Hz, 6H).

3'-(tert-butyl)-6-ethyl-5'-(imidazo[1,2-*a*]pyrazin-3-yl)-*N*-(3-(trifluoromethyl)phenyl)-[1,1'-biphenyl]-3-carboxamide （8o）



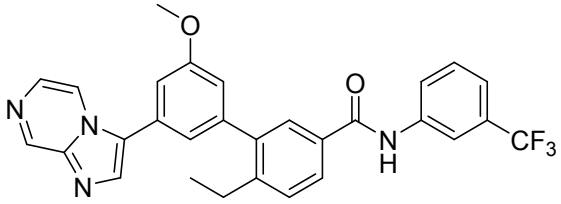
Compound **8o** was prepared following similar procedure of **8i** using1-bromo-3-(tert-butyl)-5-iodobenzene as starting material, yield 62%. ^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.10 (s, 1H), 8.24 (s, 2H), 7.91-7.87 (m, 5H), 7.81 (s, 1H), 7.58 (s, 1H), 7.48- 7.45 (m, 3H), 7.38 (d, *J* = 7.3 Hz, 1H), 7.30 (s, 1H), 2..69 (q, *J* = 7.4 Hz, 2H), 1.42 (s, 9H), 1.19 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 166.08, 153.15, 146.57, 144.72, 142.16, 141.85, 141.54, 139.04, 134.79, 132.27, 132.06, 131.80, 131.54, 131.29, 130.28, 129.88, 129.68, 129.08, 127.77, 127.54, 125.74, 125.23, 124.24, 123.70, 13.06, 121.25, 117.30, 116.62, 35.35, 31.63, 26.69, 15.83. HRMS (ESI) calcd for $C_{32}H_{29}F_3N_4O$ $[M+H]^+$: 543.2366; found 543.2364. HPLC purity= 99.90%, Rt 14.22 min.

1-bromo-3-(tert-butyl)-5-iodobenzene

n-BuLi (1.6M THF solution, 11.77 mL, 18.83 mmol, 1.1 eq) was added to the solution of 1,3-dibromo-5-(tert-butyl)benzene (5.0 g, 17.12 mmol, 1.0 eq) in dry THF (142 mL) at -78℃. The mixture was stirred at this temperature for 1 h, then a solution of 1,2-diiodoethane (5.85 g, 20.54 mmol, 1.2 eq) in dry THF (7.0 ml) was slowly added to the mixture. The temperature was allowed to rise to -45℃ in 4.5 h. Then, the cool bath was removed, and the mixture was stirred at room temperature for 2.5 h.

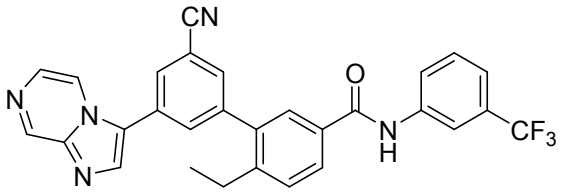
After that, the reaction was quenched with sat. $Na_2S_2O_3$ aqueous solution, extracted with EA, washed with water and sat. NaCl aqueous solution. The organic layer was concentrated under vacuum. Purification by column chromatography (PE/EA) through silica gel afforded the desired product 1-bromo-3-iodo-5-isopropylbenzene (2.15 g, yield: 37%). ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 7.67 (s, 1H), 7.62 (s, 1H), 7.46 (s, 1H), 1.28 (s, 9H).

6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-5'-methoxy-*N*-(3-(trifluoromethyl)phenyl)-[1,1'-biphenyl]-3-carboxamide (8p)



Compound **8p** was prepared following similar procedure of **8i**, yield 12%.^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.10 (s, 1H), 8.29-8.26 (m, 2H), 7.93 (s, 1H), 7.90 – 7.86 (m, 4H), 7.79 (d, *J* = 2.0 Hz, 1H), 7.49-7.45 (m, 2H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.10 – 7.09 (m, 1H), 7.06 (s, 1H), 6.94 (dd, *J* = 2.3, 1.4 Hz, 1H), 3.90 (s, 3H), 2.71 (q, *J* = 7.5 Hz, 2H), 1.18 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.85, 160.34, 146.21, 144.50, 143.70, 141.41, 141.04, 138.91, 134.69, 132.06, 131.61, 131.35, 130.14, 129.67, 129.46, 128.96, 128.69, 127.05, 126.71, 125.04, 123.51, 122.88, 121.04, 120.67, 117.15, 116.57, 115.30, 112.68, 55.70, 26.42, 15.56. HRMS (ESI) calcd for $C_{29}H_{23}F_3N_4O_2$ $[M+H]^+$: 517.1846; found 517.1847. HPLC purity= 99.85%, Rt 8.09 min.

3'-cyano-6-ethyl-5'-(imidazo[1,2-*a*]pyrazin-3-yl)-*N*-(3-(trifluoromethyl)phenyl)-[1,1'-biphenyl]-3-carboxamide (8q)



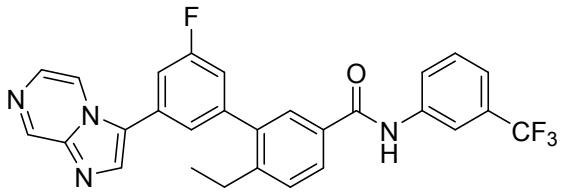
Compound **8p** was prepared following similar procedure of **8i** using3-bromo-5-iodobenzonitrile as starting material, yield 20%. ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.21 (s, 1H), 8.27 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.13 (s, 1H), 8.03 (d, *J* =

4.7 Hz, 1H), 7.99 (s, 1H), 7.93 – 7.90 (m, 4H), 7.82 – 7.80 (m, 2H), 7.73 (t, *J* = 1.5 Hz, 1H), 7.55-7.49 (m, 2H), 7.43 (d, *J* = 7.8 Hz, 1H), 2.70 (q, *J* = 7.5 Hz, 2H), 1.21 (t, *J* = 7.5 Hz, 3H).^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.16, 146.17, 145.12, 143.82, 141.93, 139.07, 138.49, 135.63, 132.93, 132.37, 131.83, 131.57, 130.92, 129.84, 128.94, 127.41, 125.02, 124.45, 123.47, 121.43, 117.82, 117.11, 116.08, 114.34, 26.43, 15.46. HRMS (ESI) calcd for $C_{29}H_{20}F_3N_5O$ $[M+H]^+$: 512.1692; found 512.1693. HPLC purity= 99.44%, Rt 6.61 min.

3-bromo-5-iodobenzonitrile

3-bromo-5-iodobenzoic acid (5.82 g, 17.80 mmol, 1.0 eq) was dissolved in $SOCl_2$ (25mL). The resulting mixture was stirred at 81℃ for 2h, then concentrated. The residual liquid was poured into ammonium hydroxide solution (~28%, 100mL) and stirred at room temperature for 3h. After that, the reaction mixture was filtrated, and the filter cake was dried under vacuum. Then, the dried solid was dissolved in $SOCl_2$ (25mL), and the resulting mixture was stirred under reflux for 18h. After that, the reaction mixture was concentrated, and the residue was dissolved in EA and washed with sat. sodium bicarbonate aqueous solution. The organic layer was concentrated under vacuum. Purification by column chromatography (PE/EA) through silica gel afforded the desired product 1-bromo-3-iodo-5-isopropylbenzene (4.25g, yield: 77 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 8.11 (s, 1H), 7.92 (s, 1H), 7.76 (s, 1H).

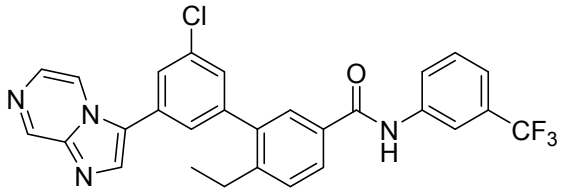
6-ethyl-3'-fluoro-5'-(imidazo[1,2-*a*]pyrazin-3-yl)-N-(3-(trifluoromethyl)phenyl)-[1,1'-biphenyl]-3-carboxamide (8r)



Compound **8r** was prepared following similar procedure of **8i**, yield 79%. ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.15 (d, *J* = 1.4 Hz, 1H), 8.28 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.12 (s, 1H), 7.95 (d, *J* = 4.7 Hz, 1H), 7.92-7.91 (m, 2H), 7.90 – 7.86 (m, 2H), 7.78 (d, *J* = 1.9 Hz, 1H), 7.50-7.46 (m, 2H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.34 – 7.31 (m, 2H), 7.17 – 7.13 (m, 1H), 2.71 (q, *J* = 7.5 Hz, 2H), 1.19 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (125

MHz, $CDCl_3$): δ(ppm) 165.43, 163.88, 161.89, 146.05, 144.63, 144.49, 144.42, 141.51, 139.88, 138.57, 134.98, 132.10, 131.55, 131.29, 130.37, 129.79, 129.72, 129.61, 129.47, 128.61, 127.09, 125.47, 124.88, 124.10, 123.36, 122.72, 121.07, 117.54, 116.98, 116.95, 116.87, 116.70, 113.59, 113.41, 26.25, 15.33. HRMS (ESI) calcd for $C_{28}H_{20}F_4N_4O$ $[M+H]^+$: 505.1646; found 505.1649. HPLC purity= 99.98%, Rt 12.9 min.

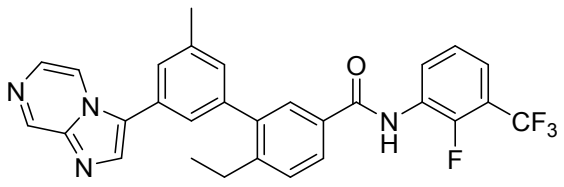
3'-chloro-6-ethyl-5'-(imidazo[1,2-*a*]pyrazin-3-yl)-*N*-(3-(trifluoromethyl)phenyl)-[1,1'-biphenyl]-3-carboxamide (**8s**)



Compound **8s** was prepared following similar procedure of **8i**, yield 15%. ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.15 (d, *J* = 1.4 Hz, 1H), 8.26 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.13 (s, 1H), 7.96 (d, *J* = 4.7 Hz, 1H), 7.92 (s, 2H), 7.90 – 7.86 (m, 2H), 7.77 (d, *J* = 1.9 Hz, 1H), 7.60 (t, *J* = 1.7 Hz, 1H), 7.50-7.46 (m, 2H), 7.43-7.39 (m, 3H), 2.70 (q, *J* = 7.5 Hz, 2H), 1.19 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ(ppm) 165.58, 146.15, 144.71, 144.00, 141.60, 139.77, 138.72, 135.56, 135.10, 132.23, 131.52, 131.37, 131.07, 130.50, 129.92, 129.39, 128.78, 127.33, 126.58, 125.40, 125.01, 123.51, 122.85, 121.16, 117.14, 116.34, 26.38, 15.44. HRMS (ESI) calcd for $C_{28}H_{20}ClF_3N_4O$ $[M+H]^+$: 521.1351; found 521.1347. HPLC purity= 99.71%, Rt 9.9 min.

Compounds **8t-8w** were synthesize according to procedures for compound **8k** with corresponding substituted aniline.

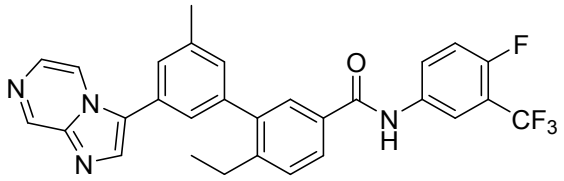
6-ethyl-*N*-(2-fluoro-3-(trifluoromethyl)phenyl)-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-5'-methyl-[1,1'-biphenyl]-3-carboxamide (8t)



Compound **8t** was prepared following similar procedure of **8k**, yield 71%. ^{1}H NMR

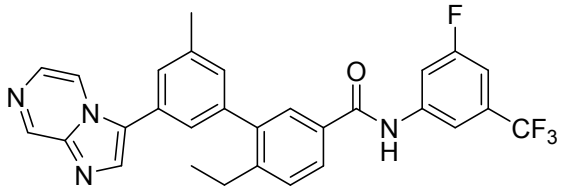
(400 MHz, $CDCl_3$): δ(ppm) 9.14 (d, *J* = 1.3 Hz, 1H), 8.70 (t, *J* = 7.6 Hz, 1H), 8.29 (dd, *J* = 4.7, 1.4 Hz, 1H), 8.17 (s, 1H), 7.92-7.91 (m, 2H), 7.86 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.77 (d, *J* = 1.9 Hz, 1H), 7.49 (d, *J* = 8.1 Hz, 1H), 7.43 (s, 1H), 7.37 – 7.27 (m, 3H), 7.27 (s, 1H), 2.72 (q, *J* = 7.5 Hz, 2H), 2.52 (s, 3H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.41, 146.74, 144.68, 142.13, 141.53, 139.67, 134.80, 131.63, 130.71, 130.10, 129.52, 128.91, 128.13, 127.72, 127.60, 126.85, 126.67, 125.81, 125.62, 124.64, 121.58, 120.96, 116.49, 26.47, 21.63, 15.48. HRMS (ESI) calcd for $C_{29}H_{22}F_4N_4O$ $[M+H]^+$: 519.1803; found 519.1811. HPLC purity= 97.31%, Rt 8.03 min.

6-ethyl-*N*-(4-fluoro-3-(trifluoromethyl)phenyl)-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-5'-methyl-[1,1'-biphenyl]-3-carboxamide (8u)



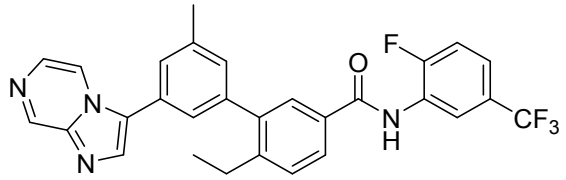
Compound **8t** was prepared following similar procedure of **8k**, yield 40%.^1H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.08 (d, *J* = 1.3 Hz, 1H), 8.38 (s, 1H), 8.24 (dd, *J* = 4.7, 1.4 Hz, 1H), 7.92 – 7.82 (m, 5H), 7.77 (d, *J* = 1.9 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H), 7.38 (s, 1H), 7.26 (s, 1H), 7.23 (s, 1H), 7.18 (t, *J* = 9.6 Hz, 1H), 2.70 (q, *J* = 7.5 Hz, 2H), 2.50 (s, 3H), 1.17 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.94, 157.15, 155.13, 146.33, 144.42, 142.25, 141.25, 139.66, 134.54, 131.77, 130.74, 130.07, 129.40, 128.85, 127.69, 127.45, 126.94, 125.84, 125.39, 123.50, 121.33, 119.22, 117.56, 117.39, 116.50, 26.41, 21.59, 15.47. HRMS (ESI) calcd for $C_{29}H_{22}F_4N_4O$ $[M+H]^+$: 519.1803; found 519.1798. HPLC purity= 97.99%, Rt 9.25 min.

6-ethyl-*N*-(3-fluoro-5-(trifluoromethyl)phenyl)-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-5'-methyl-[1,1'-biphenyl]-3-carboxamide (8v)



Compound **8t** was prepared following similar procedure of **8k**, yield 61%.^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.09 (d, *J* = 1.4 Hz, 1H), 8.39 (s, 1H), 8.24 (dd, *J* = 4.7, 1.4 Hz, 1H), 7.91-7.85 (m, 4H), 7.76 (d, *J* = 2.0 Hz, 1H), 7.58 (s, 1H), 7.48 (d, *J* = 8.1 Hz, 1H), 7.39 (s, 1H), 7.26 (s, 1H), 7.24 (s, 1H), 7.09 (d, *J* = 8.1 Hz, 1H), 2.70 (q, *J* = 7.5 Hz, 2H), 2.51 (s, 3H), 1.17 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.99, 163.87, 161.90, 146.52, 144.42, 142.20, 141.25, 140.79, 139.69, 134.52, 131.68, 130.73, 130.09, 129.47, 128.86, 127.68, 127.48, 127.01, 125.34, 116.49, 112.55, 110.96, 110.75, 108.32, 108.21, 107.83, 26.43, 21.61, 15.47. HRMS (ESI) calcd for $C_{29}H_{22}F_4N_4O$ $[M+H]^+$: 519.1803; found 519.1816. HPLC purity= 98.07%, Rt 11.37 min.

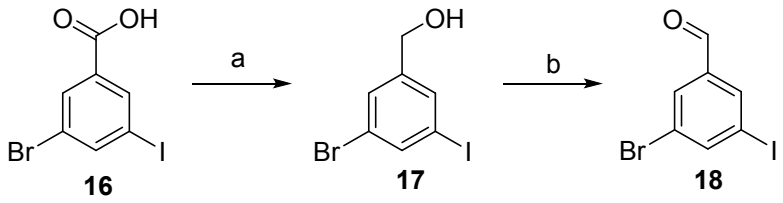
6-ethyl-*N*-(2-fluoro-5-(trifluoromethyl)phenyl)-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-5'-methyl-[1,1'-biphenyl]-3-carboxamide (8w)



Compound **8t** was prepared following similar procedure of **8k**, yield 58%.^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.14 (s, 1H), 8.86 (d, *J* = 6.0 Hz, 1H), 8.30 (d, *J* = 4.6 Hz, 1H), 8.21 (s, 1H), 7.92-7.90 (m, 2H), 7.86 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.78 (d, *J* = 1.5 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.43 (s, 1H), 7.37 (bs, 1H), 7.33 (s, 1H), 7.26 – 7.21 (m, 2H), 2.72 (q, *J* = 7.5 Hz, 2H), 2.52 (s, 3H), 1.18 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.36, 155.25, 153.28, 146.78, 144.69, 142.13, 141.53, 139.70, 134.81, 131.56, 130.74, 130.12, 129.54, 128.90, 128.00, 127.62, 127.33, 126.86, 126.62, 125.62, 124.79, 122.62, 121.73, 119.47, 116.50, 115.52, 115.36, 26.48, 21.64, 15.50. HRMS (ESI) calcd for $C_{29}H_{22}F_4N_4O$ $[M+H]^+$: 519.1803; found 519.1815. HPLC purity= 97.85%, Rt 8.12 min.

Synthesis of compound 8m

3-bromo-5-iodobenzaldehyde (**18**)

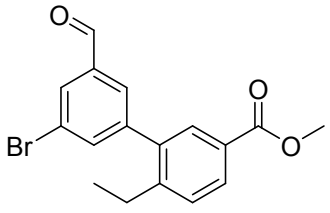


16 **17** **18**

a. To a solution of 3-bromo-5-iodobenzoic acid (10 g, 30.59 mmol, 1.0 eq) in dry THF under Ar at 0℃ was added 1M BH_3·THF solution (92 ml, 92 mmol, 3.0 eq). After addition, the ice bath was removed. The mixture was stirred at room temperature overnight. The reaction was quenched by added saturated sodium bicarbonate aqueous solution dropwise. The mixture was extracted with EA. The organic lay was concentrated. Purification by column chromatography (PE/EA) through silica gel afforded the (3-bromo-5-iodophenyl)methanol **17** (6.99 g, yield: 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.77 (s, 1H), 7.65 (s, 1H), 7.48 (s, 1H), 4.64 (s, 2H).

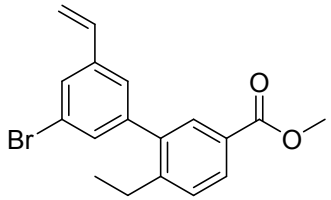
b. To a solution of (3-bromo-5-iodophenyl)methanol (**17**) (1.0 g, 3.19 mmol, 1.0 eq) in DCM was added Dess-Martin periodinane (1.63 g, 3.83 mmol, 1.2 eq) in portions. After addition, the ice bath was removed. The mixture was stirred at rt for 1h, and then filtered. The filtrate was concentrated. Purification by column chromatography (PE/EA) through silica gel afforded the 3-bromo-5-iodobenzaldehyde (**18**) (0.8993g, yield: 89%). ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.87 (s, 1H), 8.12 (t, J = 1.2 Hz, 1H), 8.10 (t, J = 1.6 Hz, 1H), 7.96 (t, J = 1.6 Hz, 1H).

methyl 3'-bromo-6-ethyl-5'-formyl-[1,1'-biphenyl]-3-carboxylate (**19**)



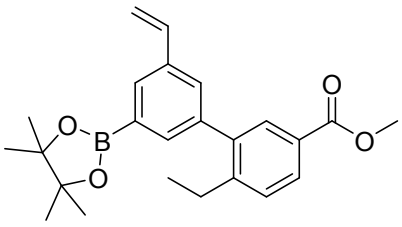
Compound **19** was prepared following similar procedure of **13i**, yield 64%. ^{1}H NMR (500 MHz, $CDCl_3$): δ(ppm) 10.00 (s, 1H), 8.03 (s, 1H), 8.02 (d, J = 8.0 Hz, 1H), 7.86 (s, 1H), 7.75 (s, 1H), 7.73 (s, 1H), 7.41 (d, J = 8.0 Hz, 1H), 2.62 (q, J = 7.5 Hz, 2H), 1.13 (t, J = 7.5 Hz, 3H).

methyl 3'-bromo-6-ethyl-5'-vinyl-[1,1'-biphenyl]-3-carboxylate (**20**)



To a solution of methyltriphenylphosphonium bromide (0.95g, 2.65mmol, 3.0eq) in dry THF (12mL) under Ar at -20℃ was added n-BuLi (2.66mmol, 2.4M, 3.0eq) dropwise. The mixture was stirred at this temperature for 0.5h. Then a solution of methyl 3'-bromo-6-ethyl-5'-formyl-[1,1'-biphenyl]-3-carboxylate (**19**) (0.31g, 0.88mmol, 1.0eq) in dry THF (1.6mL) was added to the reaction mixture dropwise. After addition, the cool bath was removed, and the mixture was stirred at rt overnight. Saturated NH_4Cl aqueous solution was added to the mixture dropwise. The mixture was extracted with EA. The organic layer was concentrated. Purification by column chromatography (PE/EA) through silica gel afforded methyl 3'-bromo-6-ethyl-5'-vinyl-[1,1'-biphenyl]-3-carboxylate (**20**) (0.1530g, yield: 50%). ^{1}H NMR (500 MHz, $CDCl_3$): δ(ppm) 7.98 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.85 (d, *J* = 1.6 Hz, 1H), 7.56 (s, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.34 (s, 1H), 7.25 (s, 1H), 6.68 (dd, *J* = 17.6 Hz, 10.8 Hz, 1H), 7.78 (d, *J* = 17.6 Hz, 1H), 7.78 (d, *J* = 10.8 Hz, 1H), 2.63 (q, *J* = 7.6 Hz, 2H), 1.13 (t, *J* = 7.6 Hz, 3H).

Methyl6-ethyl-3'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5'-vinyl-[1,1'-biphenyl]-3-carboxylate (21)

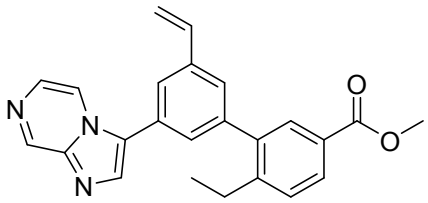


The title compound was synthesized following the procedure of compound **14a** substituting 13a with methyl 3'-bromo-6-ethyl-5'-vinyl-[1,1'-biphenyl]-3-carboxylate (**19**).

^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 7.96 (dd, *J* = 8.0 Hz, 1.6 Hz, 1H), 7.88 (s, 1H), 7.84 (s, 1H), 7.63 (s, 1H), 7.44 (s, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 6.77 (dd, *J* = 17.6 Hz, 10.8 Hz, 1H), 5.80 (d, *J* = 17.6 Hz, 1H), 5.27 (d, *J* = 10.8 Hz, 1H), 3.91 (s, 3H),

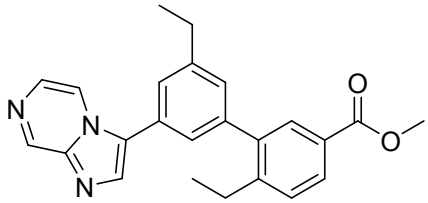
2.63 (q, *J* = 7.6 Hz, 2H), 1.36 (s, 12H), 1.11 (t, *J* = 7.6 Hz, 3H).

Methyl 6-ethyl-3'-(imidazo[1,2-*a*]pyrazin-3-yl)-5'-vinyl-[1,1'-biphenyl]-3-carboxylate (22)



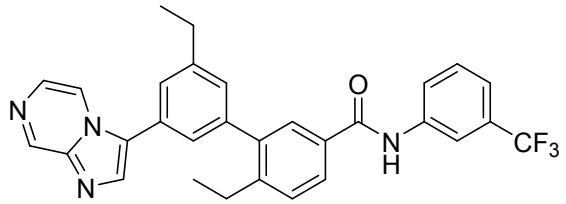
The title compound was synthesized following the procedure of compound **15a** substituting **14a** with methyl 6-ethyl-3'-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-5'-vinyl-[1,1'-biphenyl]-3-carboxylate (**21**). ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.16 (s, 1H), 8.28 (s, 1H), 8.01 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 7.94-7.92 (m, 2H), 7.60 (d, *J* = 1.6 Hz, 1H), 7.47-7.45 (m, 2H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 1.6 Hz, 1H), 6.82 (dd, *J* = 17.6 Hz, 10.8 Hz, 1H), 5.87 (d, *J* = 17.6 Hz, 1H), 5.41 (d, *J* = 10.8 Hz, 1H), 3.91 (s, 3H), 2.69 (q, *J* = 7.6 Hz, 2H), 1.17 (t, *J* = 7.6 Hz, 3H).

Methyl 3',6-diethyl-5'-(imidazo[1,2-*a*]pyrazin-3-yl)-[1,1'-biphenyl]-3-carboxylate (23)



To a solution of methyl 6-ethyl-3'-(imidazo[1,2-a]pyrazin-3-yl)-5'-vinyl-[1,1'-biphenyl]-3-carboxylate (0.9g, 2.34mmol, 1.0eq) in MeOH (8ml) was added 10% Pd/C (0.090g). The mixture was degassed and purged with hydrogen and stirred at rt overnight. The solution was filtered and concentrated. Purification by column chromatography (PE/EA) through silica gel afforded the intermediate **23** (0.456g, yield: 51%). ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.30 (s, 1H), 8.34 (d, *J* = 4.0 Hz, 1H), 8.04-7.99 (m, 3H), 7.92 (d, *J* = 2.0 Hz, 1H), 7.43-7.41 (m, 2H), 7.33 (s, 1H), 7.30 (s, 1H), 3.91 (s, 3H), 2.82 (q, *J* = 7.6 Hz, 2H), 2.68 (q, *J* = 7.2 Hz, 2H), 1.34 (t, *J* = 7.6 Hz, 3H), 1.17 (t, *J* = 7.2 Hz, 3H).

3',6-diethyl-5'-(imidazo[1,2-a]pyrazin-3-yl)-*N*-(3-(trifluoromethyl)phenyl)-[1,1'-*b*iphenyl]-3-carboxamide （8m）



Compound **8m** was prepared following similar procedure of **8a**, yield 8%. ^{1}H NMR (400 MHz, $CDCl_3$): δ(ppm) 9.10 (d, *J* = 1.4 Hz, 1H), 8.26 (dd, *J* = 4.7, 1.5 Hz, 1H), 8.23 (s, 1H), 7.93 (s, 1H), 7.90-7.85 (m, 4H), 7.79 (d, *J* = 1.9 Hz, 1H), 7.49-7.45 (m, 2H), 7.41 – 7.37 (m, 2H), 7.31 (s, 1H), 7.27 (s, 1H), 2.80 (q, *J* = 7.6 Hz, 2H), 2.70 (q, *J* = 7.5 Hz, 2H), 1.34 (t, *J* = 7.6 Hz, 3H), 1.18 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ(ppm) 165.72, 146.18, 145.85, 144.40, 142.20, 141.26, 141.24, 138.73, 134.51, 131.93, 131.52, 131.27, 129.96, 129.56, 129.49, 129.30, 128.73, 127.73, 126.91, 126.71, 126.29, 125.59, 124.93, 1243.35, 122.77, 120.93, 117.08, 116.37, 28.83, 26.33, 15.46, 15.40. HRMS (ESI) calcd for $C_{30}H_{25}F_3N_4O$ $[M+H]^+$: 515.2053; found 515.2058. HPLC purity= 97.85%, Rt 11.10 min.

Table S1 The results of the selectivity profiling study of compound 8v

Gene Symbol	%Ctrl @ 200nM
AAK1	100
ABL1(E255K)-phosphorylated	98
ABL1(F317I)-nonphosphorylated	72
ABL1(F317I)-phosphorylated	100
ABL1(F317L)-nonphosphorylated	73
ABL1(F317L)-phosphorylated	56
ABL1(H396P)-nonphosphorylated	95
ABL1(H396P)-phosphorylated	84
ABL1(M351T)-phosphorylated	74
ABL1(Q252H)-nonphosphorylated	85
ABL1(Q252H)-phosphorylated	79
ABL1(T315I)-nonphosphorylated	87
ABL1(T315I)-phosphorylated	62
ABL1(Y253F)-phosphorylated	79
ABL1-nonphosphorylated	94
ABL1-phosphorylated	82
ABL2	97
ACVR1	69
ACVR1B	80
ACVR2A	100
ACVR2B	100
ACVRL1	73
ADCK3	65
ADCK4	58
AKT1	69
AKT2	74
AKT3	100
ALK	91
ALK(C1156Y)	89
ALK(L1196M)	97
AMPK-alpha1	95
AMPK-alpha2	89
ANKK1	91
ARK5	89
ASK1	95
ASK2	82
AURKA	79
AURKB	97
AURKC	95
AXL	77
BIKE	100
BLK	91
BMPR1A	78
BMPR1B	80
BMPR2	99
BMX	58
BRAF	77
BRAF(V600E)	60

Gene Symbol	%Ctrl @ 200nM
BRK	80
BRSK1	75
BRSK2	94
BTK	99
BUB1	99
CAMK1	77
CAMK1B	91
CAMK1D	0.9
CAMK1G	93
CAMK2A	90
CAMK2B	93
CAMK2D	83
CAMK2G	97
CAMK4	78
CAMKK1	95
CAMKK2	88
CASK	77
CDC2L1	94
CDC2L2	92
CDC2L5	100
CDK11	84
CDK2	71
CDK3	92
CDK4	100
CDK4-cyclinD1	32
CDK4-cyclinD3	48
CDK5	74
CDK7	72
CDK8	82
CDK9	93
CDKL1	86
CDKL2	83
CDKL3	90
CDKL5	84
CHEK1	74
CHEK2	100
CIT	93
CLK1	71
CLK2	92
CLK3	73
CLK4	1.8
CSF1R	90
CSF1R-autoinhibited	93
CSK	91
CSNK1A1	92
CSNK1A1L	72
CSNK1D	63
CSNK1E	70
CSNK1G1	97

Gene Symbol	%Ctrl @ 200nM
CSNK1G2	95
CSNK1G3	72
CSNK2A1	68
CSNK2A2	67
CTK	70
DAPK1	100
DAPK2	93
DAPK3	98
DCAMKL1	100
DCAMKL2	86
DCAMKL3	76
DDR1	0
DDR2	15
DLK	100
DMPK	96
DMPK2	75
DRAK1	100
DRAK2	99
DYRK1A	87
DYRK1B	81
DYRK2	73
EGFR	89
EGFR(E746-A750del)	75
EGFR(G719C)	96
EGFR(G719S)	96
EGFR(L747-E749del, A750P)	82
EGFR(L747-S752del, P753S)	79
EGFR(L747-T751del,Sins)	99
EGFR(L858R)	83
EGFR(L858R,T790M)	100
EGFR(L861Q)	93
EGFR(S752-I759del)	92
EGFR(T790M)	95
EIF2AK1	90
EPHA1	71
EPHA2	60
EPHA3	80
EPHA4	71
EPHA5	71
EPHA6	67
EPHA7	99
EPHA8	75
EPHB1	100
EPHB2	92
EPHB3	75
EPHB4	65
EPHB6	11
ERBB2	91
ERBB3	99

Gene Symbol	%Ctrl @ 200nM
ERBB4	100
ERK1	97
ERK2	67
ERK3	76
ERK4	78
ERK5	94
ERK8	81
ERN1	75
FAK	79
FER	79
FES	84
FGFR1	93
FGFR2	88
FGFR3	70
FGFR3(G697C)	69
FGFR4	82
FGR	72
FLT1	97
FLT3	86
FLT3(D835H)	89
FLT3(D835V)	92
FLT3(D835Y)	97
FLT3(ITD)	100
FLT3(ITD,D835V)	100
FLT3(ITD,F691L)	100
FLT3(K663Q)	92
FLT3(N841I)	78
FLT3(R834Q)	95
FLT3-autoinhibited	94
FLT4	92
FRK	69
FYN	76
GAK	95
GCN2(Kin.Dom.2,S808G)	87
GRK1	94
GRK2	73
GRK3	96
GRK4	72
GRK7	73
GSK3A	96
GSK3B	89
HASPIN	86
HCK	99
HIPK1	96
HIPK2	100
HIPK3	100
HIPK4	74
HPK1	97
HUNK	98

Gene Symbol	%Ctrl @ 200nM
ICK	98
IGF1R	93
IKK-alpha	100
IKK-beta	98
IKK-epsilon	100
INSR	90
INSRR	87
IRAK1	100
IRAK3	95
IRAK4	97
ITK	100
JAK1(JH1domain-catalytic)	87
JAK1(JH2domain-pseudokinase)	100
JAK2(JH1domain-catalytic)	100
JAK3(JH1domain-catalytic)	100
JNK1	97
JNK2	79
JNK3	96
KIT	41
KIT(A829P)	100
KIT(D816H)	100
KIT(D816V)	73
KIT(L576P)	57
KIT(V559D)	39
KIT(V559D,T670I)	93
KIT(V559D,V654A)	100
KIT-autoinhibited	97
LATS1	98
LATS2	100
LCK	95
LIMK1	64
LIMK2	76
LKB1	80
LOK	58
LRRK2	100
LRRK2(G2019S)	100
LTK	93
LYN	95
LZK	84
MAK	100
MAP3K1	100
MAP3K15	76
MAP3K2	100
MAP3K3	99
MAP3K4	83
MAP4K2	99
MAP4K3	82
MAP4K4	100
MAP4K5	100

Gene Symbol	%Ctrl @ 200nM
MAPKAPK2	70
MAPKAPK5	70
MARK1	99
MARK2	95
MARK3	62
MARK4	97
MAST1	98
MEK1	90
MEK2	99
MEK3	96
MEK4	96
MEK5	100
MEK6	85
MELK	87
MERTK	78
MET	100
MET(M1250T)	73
MET(Y1235D)	74
MINK	95
MKK7	100
MKNK1	100
MKNK2	96
MLCK	98
MLK1	100
MLK2	74
MLK3	84
MRCKA	76
MRCKB	82
MST1	89
MST1R	69
MST2	95
MST3	93
MST4	84
MTOR	100
MUSK	83
MYLK	92
MYLK2	96
MYLK4	94
MYO3A	87
MYO3B	90
NDR1	90
NDR2	96
NEK1	92
NEK10	98
NEK11	100
NEK2	94
NEK3	98
NEK4	76
NEK5	93

Gene Symbol	%Ctrl @ 200nM
NEK6	78
NEK7	79
NEK9	77
NIK	74
NIM1	96
NLK	49
OSR1	92
p38-alpha	87
p38-beta	91
p38-delta	56
p38-gamma	100
PAK1	86
PAK2	82
PAK3	70
PAK4	100
PAK6	87
PAK7	89
PCTK1	94
PCTK2	71
PCTK3	94
PDGFRA	98
PDGFRB	69
PDPK1	97
PFCDPK1(P.falciparum)	76
PFPK5(P.falciparum)	65
PFTAIRE2	68
PFTK1	89
PHKG1	56
PHKG2	97
PIK3C2B	100
PIK3C2G	85
PIK3CA	100
PIK3CA(C420R)	97
PIK3CA(E542K)	84
PIK3CA(E545A)	97
PIK3CA(E545K)	88
PIK3CA(H1047L)	85
PIK3CA(H1047Y)	94
PIK3CA(I800L)	78
PIK3CA(M1043I)	94
PIK3CA(Q546K)	89
PIK3CB	100
PIK3CD	81
PIK3CG	100
PIK4CB	100
PIKFYVE	100
PIM1	94
PIM2	74
PIM3	87

Gene Symbol	%Ctrl @ 200nM
PIP5K1A	89
PIP5K1C	86
PIP5K2B	98
PIP5K2C	99
PKAC-alpha	88
PKAC-beta	90
PKMYT1	76
PKN1	100
PKN2	91
PKNB(M.tuberculosis)	91
PLK1	97
PLK2	93
PLK3	100
PLK4	89
PRKCD	94
PRKCE	100
PRKCH	55
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PRKCQ	75
PRKD1	74
PRKD2	96
PRKD3	96
PRKG1	98
PRKG2	87
PRKR	89
PRKX	44
PRP4	75
PYK2	57
QSK	81
RAF1	53
RET	83
RET(M918T)	81
RET(V804L)	95
RET(V804M)	96
RIOK1	100
RIOK2	64
RIOK3	99
RIPK1	97
RIPK2	79
RIPK4	99
RIPK5	89
ROCK1	95
ROCK2	91
ROS1	75
RPS6KA4(Kin.Dom.1-N-terminal)	84
RPS6KA4(Kin.Dom.2-C-terminal)	72
RPS6KA5(Kin.Dom.1-N-terminal)	71
RPS6KA5(Kin.Dom.2-C-terminal)	93
RSK1(Kin.Dom.1-N-terminal)	100

Gene Symbol	%Ctrl @ 200nM
RSK1(Kin.Dom.2-C-terminal)	92
RSK2(Kin.Dom.1-N-terminal)	100
RSK2(Kin.Dom.2-C-terminal)	89
RSK3(Kin.Dom.1-N-terminal)	72
RSK3(Kin.Dom.2-C-terminal)	80
RSK4(Kin.Dom.1-N-terminal)	100
RSK4(Kin.Dom.2-C-terminal)	100
S6K1	99
SBK1	100
SGK	80
SgK110	82
SGK2	99
SGK3	87
SIK	85
SIK2	82
SLK	99
SNARK	93
SNRK	84
SRC	90
SRMS	100
SRPK1	91
SRPK2	96
SRPK3	73
STK16	100
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STK35	81
STK36	96
STK39	97
SYK	93
TAK1	98
TAOK1	100
TAOK2	100
TAOK3	100
TBK1	91
TEC	100
TESK1	77
TGFBR1	71
TGFBR2	78
TIE1	76
TIE2	83
TLK1	93
TLK2	88
TNIK	93
TNK1	70
TNK2	81
TNNI3K	51
TRKA	94
TRKB	100
TRKC	90

Target	D2454
Gene Symbol	%Ctrl @ 200nM
TRPM6	88
TSSK1B	67
TSSK3	97
TTK	0
TXK	91
TYK2(JH1domain-catalytic)	100
TYK2(JH2domain-pseudokinase)	97
TYRO3	84
ULK1	95
ULK2	98
ULK3	98
VEGFR2	91
VPS34	78
VRK2	94
WEE1	100
WEE2	69
WNK1	99
WNK2	97
WNK3	98
WNK4	87
YANK1	73
YANK2	90
YANK3	65
YES	86
YSK1	81
YSK4	79
ZAK	70
ZAP70	84

Table S2. S-score table for **8v**

Compd	Selectivity Score Type	Number of hits	Number of Non-Mutant Kinases	Screening Concentration (nM)	Selectivity Score
8v	S(35)	7	403	200	0.017
	S(10)	4	403	200	0.01
	S(1)	3	403	200	0.007

Active-site dependent competition binding assay−Kinome*scan* Screening

The binding affinity of **8v** with DDR1 was analyzed by KINOME scan system conducted by Ambit Bioscience (San Diego, USA). Briefly, kinases were tagged with DNA. The ligands were biotinylated and immobilized to streptavidin-coated beads. The binding reactions were assembled by incubating DNA-tagged kinases, immobilized ligands, and test compounds in binding reactions (20% SeaBlock, 0.17 × PBS, 0.05% tween-20, 6 mM DTT) for 1.0 h at room temperature. The affinity beads were washed with washing buffer (1× PBS, 0.05% Tween-20) first and then elution buffer (1× PBS, 0.05% Tween 20, 0.5 μM nonbiotinylated affinity ligands). The kinase concentration in the eluate was determined by quantitative PCR of the DNA tagged to the kinase. The ability of the test compound to bind to the kinase was evaluated with percent control (%) as (test compound signal − positive control signal)/negative control signal – positive control signal) × 100%. Negative control is DMSO control (100% ctrl) and positive control is control compound (0% ctrl).

***In vitro* kinase assay**

The functional assays of compounds on the kinase activities of c-Kit and Abl were determined using the FRET-based Z′-Lyte assay system according to the manufacturer's instructions (Invitrogen, USA). Tyrosine 2 peptide was used as Abl substrate, and Ser/Thr 6 peptide was used as the substrate for c-Kit. The reactions were carried out in 384-well plates in a 10 μL of reaction volume with appropriate amount of kinases in 50 mM HEPES (pH 7.5), 10 mM $MgCl_2$, 1 mM EGTA, and

0.01% Brij-35. The reactions were incubated 1 h at room temperature in the presence of 2 μM of substrate with 10 mM of ATP (for Abl1 assays) or 300 μM of ATP (kit assay) and in the presence of various concentrations of the compounds. The development reagent was then added for a further 2 h room temperature incubation followed by the addition of stop solution. Fluorescence signal ratio of 445 nm (Coumarin)/520 nm (fluorescein) was examined on a EnVision Multilabel Reader (Perkin-Elmer, Inc.).

The effects of compounds on the kinases DDR1 and DDR2 were assessed by using a LanthaScreen Eu kinase activity assay technology (Invitrogen, USA). Kinase reactions were performed in a 10 μL solution in low-volume 384-well plates. The kinase reaction buffer consisted of 50 mM HEPES pH 7.5, 0.01% BRIJ-35, 10 mM MgCl2, and 1 mM EGTA; the concentration of Fluorescein-Poly GAT substrate (Invitrogen, USA) in the assay was 100 nM. Kinase reactions were initiated by the addition of 100 nM ATP in the presence of serially diluted compounds. The reactions were allowed to proceed for 1 h at room temperature before a 10 μL preparation of EDTA (20 mM) and Eu-labeled antibody (4 nM) in TR-FRET dilution buffer were added. The final concentration of antibody in the assay well was 2 nM, and the final concentration of EDTA was 10 mM. The plate was allowed to incubate at room temperature for one more hour before the TR-FRET emission ratios of 665 nm/340 nm were acquired on a PerkinElmer EnVision multilabel reader (Perkin-Elmer, Inc.). Data analysis and curve fitting were performed using GraphPad Prism4 software.

Colony formation assay

Cells were cultured in 6-well plates (1000 cell /well) for overnight and medium were replaced with the new one containing 8v of designated concentrations, and the plates were incubated at 37°C with 5% CO_2 for another 10 days. On the last day, the medium was removed. After being washed with 1X PBS and fixed with methanol, the colonies were stained with 0.25% crystal violet solution for 1 hr. at room temperature. The images were acquired with a scanner and colony numbers were counted after washing and air-drying.

Inhibition on H1299 cell proliferation by CCK-8 assay

H1299 Tumor cells were plated into 96-well plates (1500~3000/well) in complete medium. After incubation overnight, cells were exposed to various concentrations (0.0032~50μM) of 8v for further 72 hrs. Cell proliferation was evaluated by Cell Counting Kit 8(CCK-8, CK04, Dojindo laboratories, Japan). IC_{50} values were calculated by concentration-response cure fitting using GraphPad Prism 5.0 software. Each IC_{50} value was expressed as mean ± SD.

Wound healing assay

Cells were seeded in a 6-well plate and allowed to grow to nearly 100% confluence in culture medium. Subsequently, a cell-free line was manually created by scratching the confluent cell monolayers with a 200-μl pipette tip. The wounded cell monolayers were washed three times with PBS and incubated in RPMI-1640 with 10% FBS with different concentration of 8v for 24 h. Three scratched fields were randomly chosen and the images were captured by bright-field microscope (CKX41; Olympus). The percentage of wound closure was measured using Adobe Photoshop 7.0.1 (Adobe Systems Inc., San Jose, CA). The experiment was performed three times and in triplicate.

Transwell assay

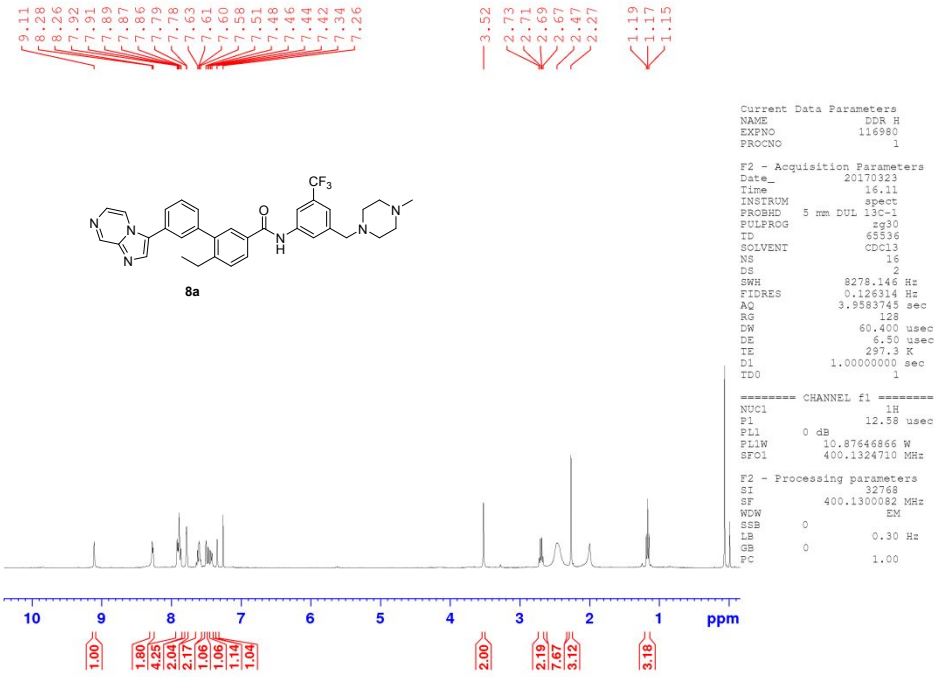
Cell migration assays were evaluated in Transwell chambers (353097, 353504; Corning Costar). Cell invasion assays were evaluated in Magrigel invasion chambers (354480; Corning Costar). 0.2~1 x 10^5 tumor cells were plated in the top chamber with medium without FBS. Culture medium containing 8v (0.625~5μmol/L) was added to the bottom chamber. After incubation for 24 hrs at 37℃, the cells were fixed in 100% methanol and stained with 0.25% crystal violet, then cotton swabs were used to remove the cells that had not migrated from the top surface of the filters. Migration cells were quantitated by counting cells in six randomly selected fields on each filter under a microscope at 200 magnification and graphed as the mean of three independent experiments.

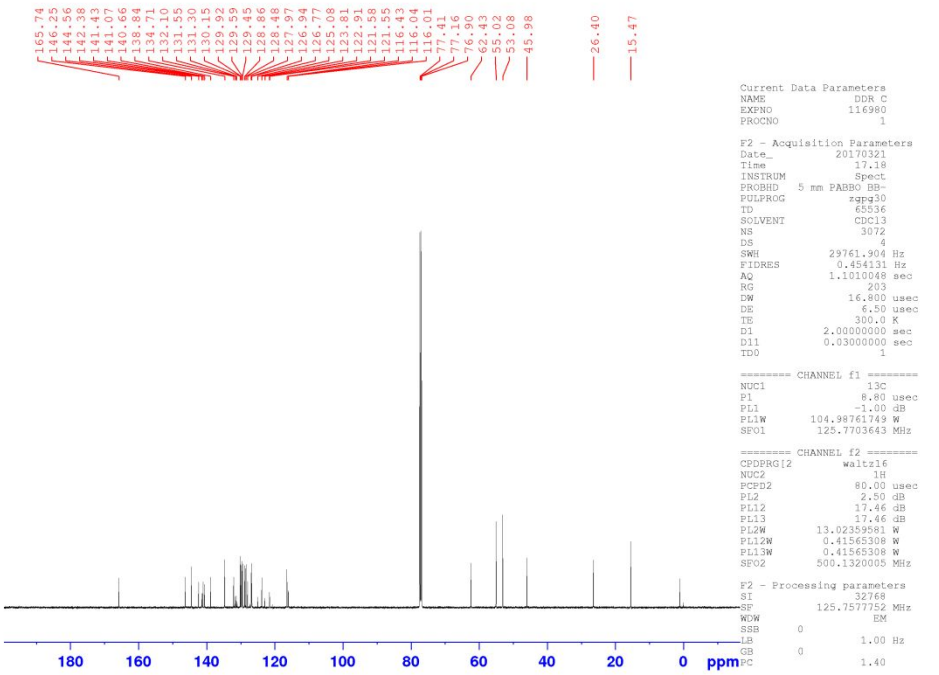
Computational study

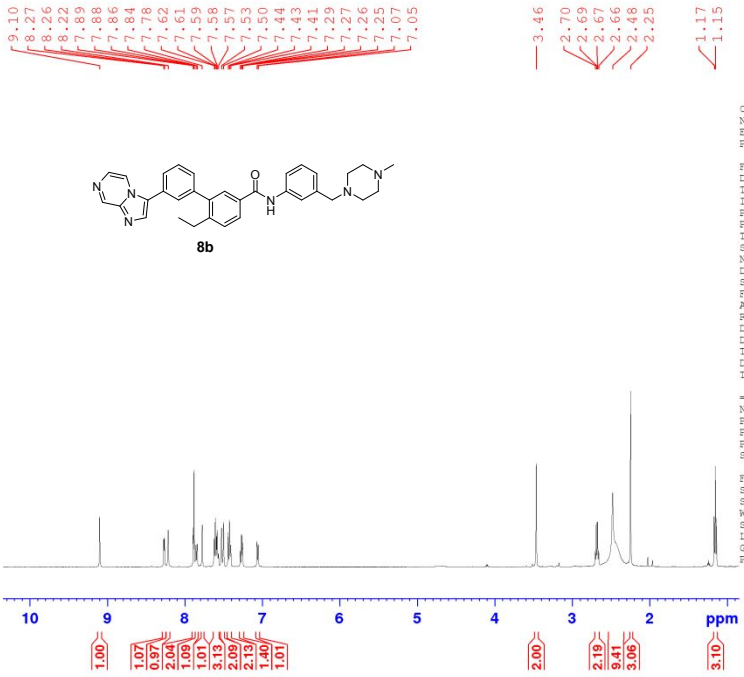
All the procedure was performed in Maestro 9.9 (Schrodinger LLC). The crystal structures of DDR1 protein with their corresponding inhibitors were taken from the

PDB (4BKJ). The protein was processed using the “Protein Preparation Wizard” workflow in Maestro 9.9 (Schrodinger LLC) to add bond orders and to add hydrogens. All heteroatom residues and crystal water molecules beyond 5 Å from het group were removed. Inhibitors 8a and 8c were built in the LigPrep module using the OPLS-2005 force field. Glide module was used as the docking program. The grid-enclosing box was placed on the centroid of the binding ligand in the optimized crystal structure as described above, and a scaling factor of 1.0 was set to van der Waals (VDW) radius of those receptor atoms with partial atomic charges of less than 0.25. Standard precision (SP) approach of Glide was adopted to dock 8a and 8c into DDR1 with the default parameters, and the top-ranking pose was selected for energy minimization using Prime MM-GBSA, under the solvation model of VSGB.

The ^{1}H and ^{13}C NMR spectra of compounds 8a-8w



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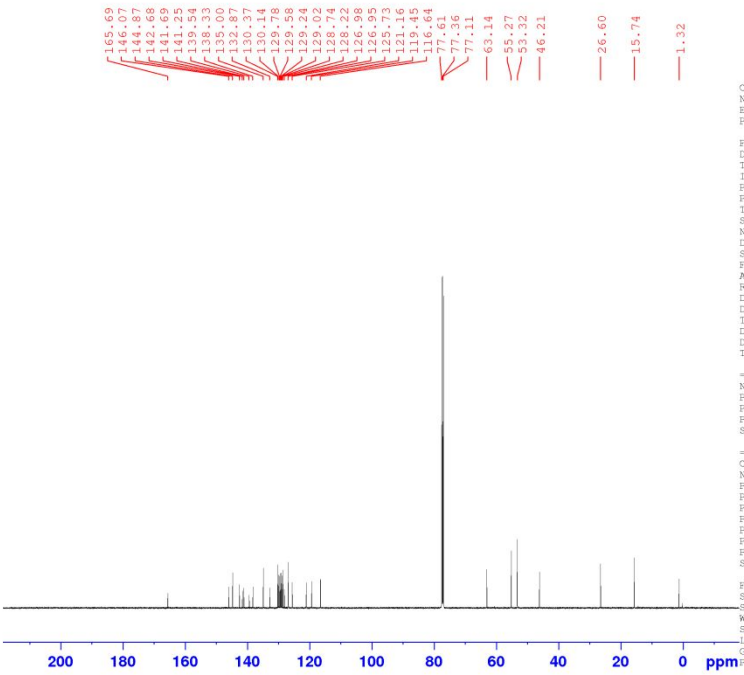
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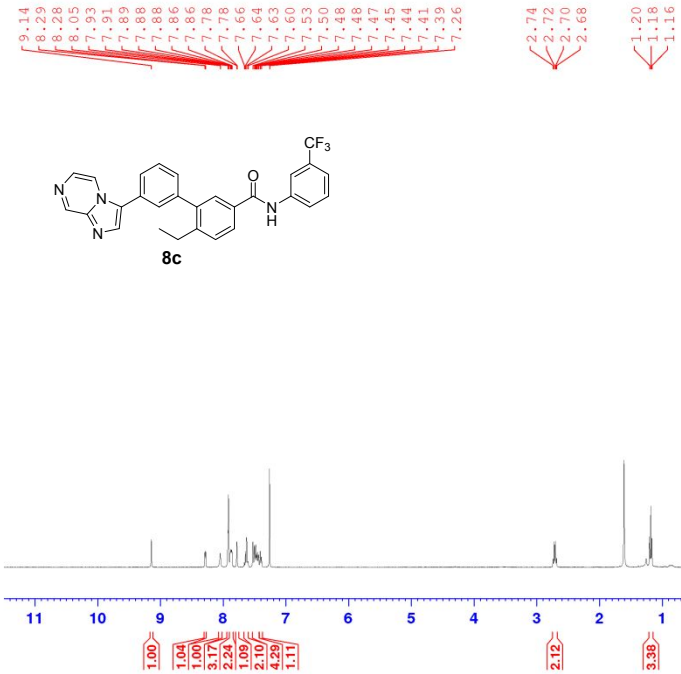
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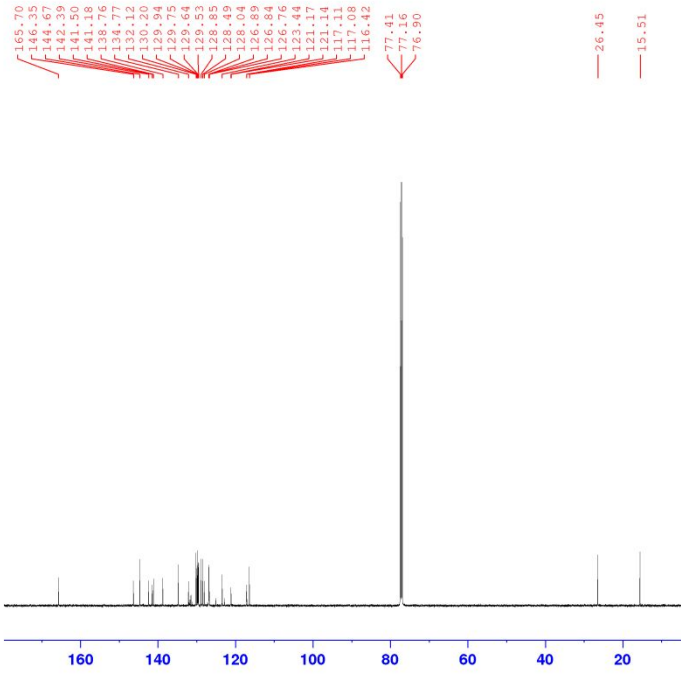
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TE 300.0 K
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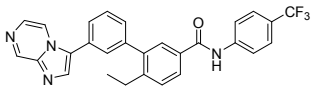
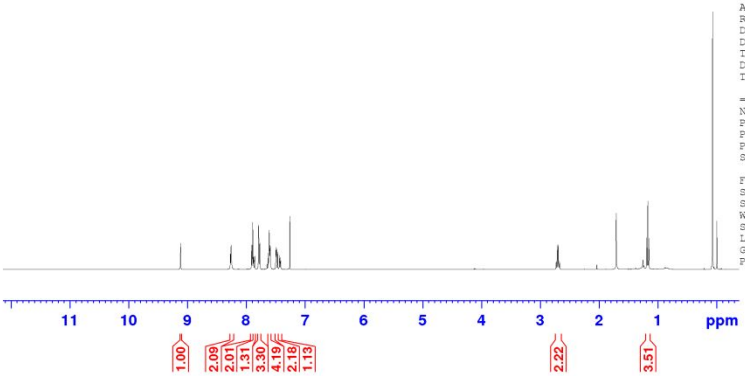
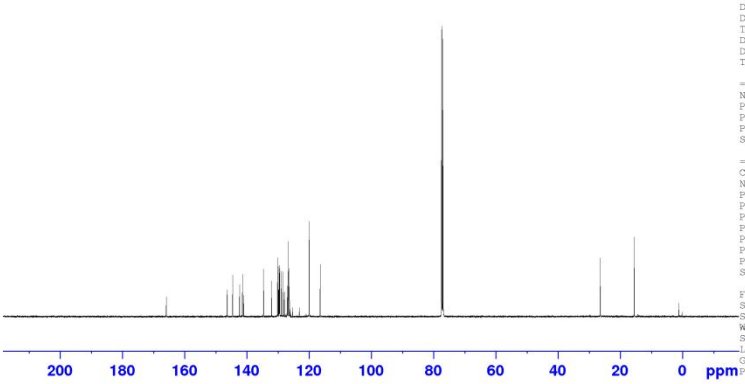
20
ppm



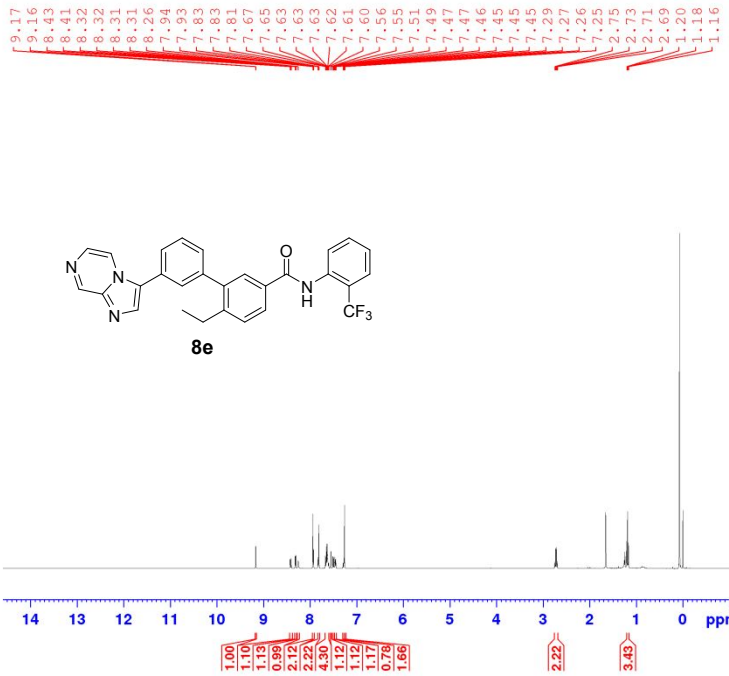
8d



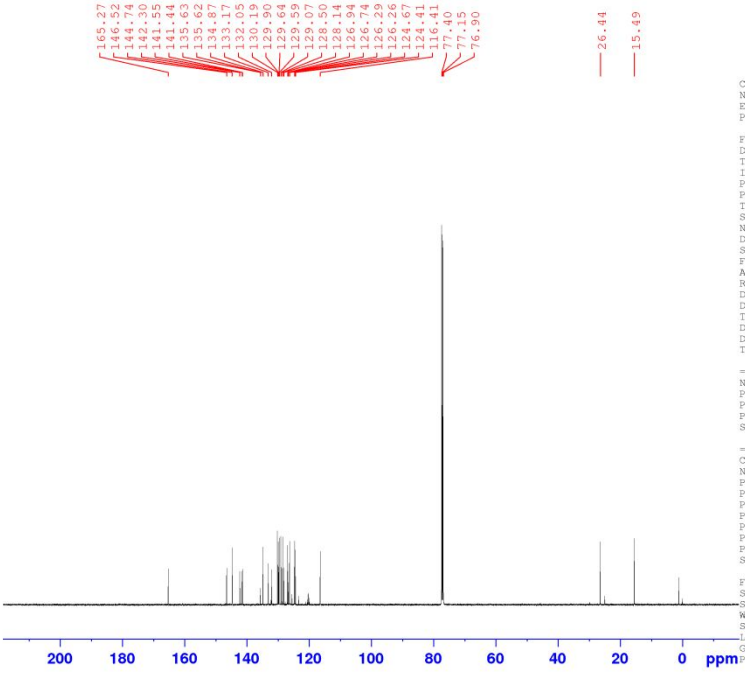

```
Current Data Parameters
NAME                  DDR H
EXPNO              70501592
PROCNO                    1

F2 - Acquisition Parameters
Date_              20170329
Time                 11.33
INSTRUM                spect
PROBHD    5 mm DUL 13C-1
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9583745 sec
RG                      256
DW                 60.400 usec
DE                  6.50 usec
TE                  296.8 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                 12.58 usec
PL1          0 dB
PL1W          10.87646866 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF            400.1300083 MHz
WDW                      EM
SSB          0
LB                  0.30 Hz
GB           0
PC                    1.00
```



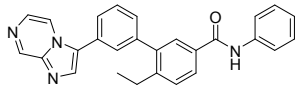

```
Current Data Parameters
NAME                  DDR C
EXPNO              70501592
PROCNO                    1

F2 - Acquisition Parameters
Date_              20170330
Time                 16.16
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     3048
DS                        4
SWH               29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010048 sec
RG                      203
DW                 16.800 usec
DE                  6.50 usec
TE                  298.8 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                  8.80 usec
PL1                -1.00 dB
PL1W          104.98761749 W
SFO1          125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                     1H
PCPD2               80.00 usec
PL2                  2.50 dB
PL12                17.46 dB
PL13                17.46 dB
PL2W          13.02359581 W
PL12W          0.41565308 W
PL13W          0.41565308 W
SFO2          500.1320005 MHz

F2 - Processing parameters
SI                    32768
SF            125.7577754 MHz
WDW                      EM
SSB          0
LB                  1.00 Hz
GB           0
PC                    1.40
```




```
Current Data Parameters
NAME                  DDR H
EXPNO              70501591
PROCNO                    1

F2 - Acquisition Parameters
Date_              20170329
Time                  11.27
INSTRUM               spect
PROBHD    5 mm DUL 13C-1
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9583745 sec
RG                    322.5
DW                   60.400 usec
DE                    6.50 usec
TE                   296.8 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                   12.58 usec
PL1          0 dB
PL1W           10.87646866 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF             400.1300083 MHz
WDW                      EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```

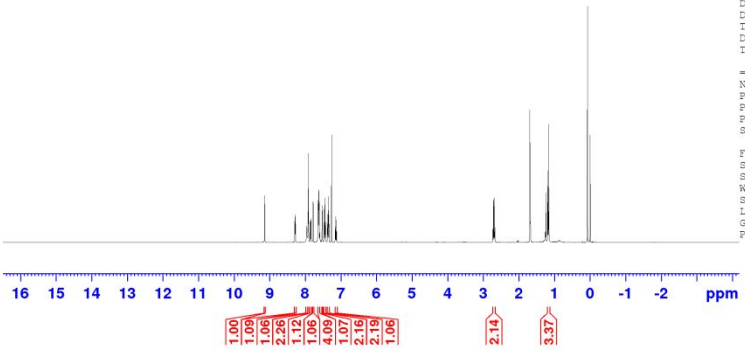


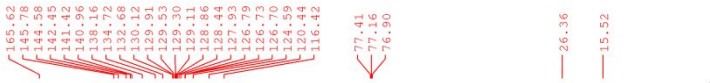

```
Current Data Parameters
NAME                  DDR C
EXPNO              70501591
PROCNO                    1

F2 - Acquisition Parameters
Date_              20170330
Time                  13.30
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    3048
DS                       4
SWH               29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010048 sec
RG                      203
DW                   16.800 usec
DE                    6.50 usec
TE                   296.8 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    8.80 usec
PL1                  -1.00 dB
PL1W          104.98761749 W
SFO1           125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   2.50 dB
PL12                 17.46 dB
PL13                 17.46 dB
PL2W          13.02359581 W
PL12W          0.41565308 W
PL13W          0.41565308 W
SFO2          500.1320005 MHz

F2 - Processing parameters
SI                    32768
SF             125.7577757 MHz
WDW                      EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```



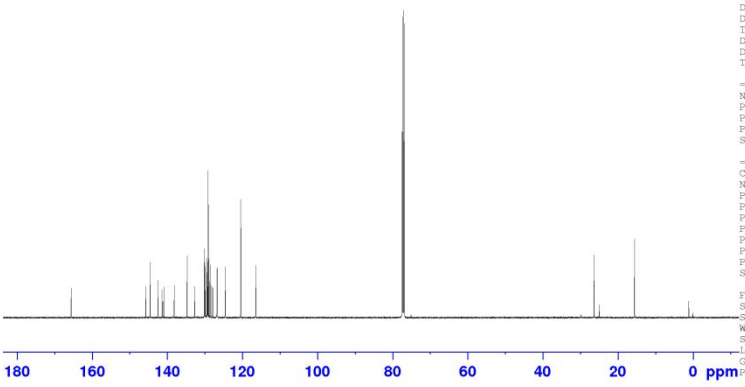
8f

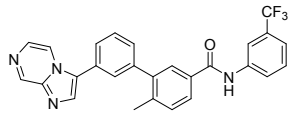
```
Current Data Parameters
NAME                  DDR H
EXPNO                340054
PROCNO                    1

F2 - Acquisition Parameters
Date_              20170328
Time                  11.38
INSTRUM               spect
PROBHD    5 mm DUL 13C-1
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES           0.126314 Hz
AQ                3.9583745 sec
RG                     256
DW                  60.400 usec
DE                   6.50 usec
TE                  296.0 K
D1               1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   12.58 usec
PL1          0 dB
PL1W          10.87646866 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF            400.1300085 MHz
WDW                     EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```



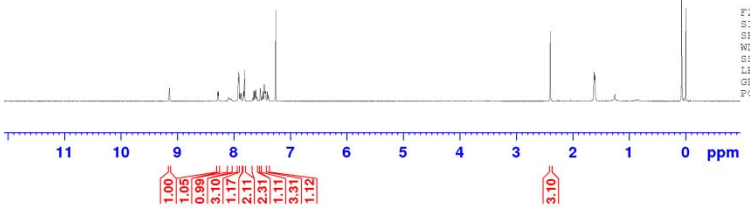



```
Current Data Parameters
NAME                  DDR C
EXPNO                340054
PROCNO                    1

F2 - Acquisition Parameters
Date_              20170402
Time                  11.27
INSTRUM               Spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    3072
DS                       4
SWH              29761.904 Hz
FIDRES           0.454131 Hz
AQ                1.1010048 sec
RG                     203
DW                  16.800 usec
DE                   6.50 usec
TE                  297.8 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                    8.80 usec
PL1                  -1.00 dB
PL1W        104.98761749 W
SFO1         125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2                80.00 usec
PL2                   2.50 dB
PL12                 17.46 dB
PL13                 17.46 dB
PL2W          13.02359581 W
PL12W          0.41565308 W
PL13W          0.41565308 W
SFO2         500.1320005 MHz

F2 - Processing parameters
SI                   32768
SF            125.7577790 MHz
WDW                     EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```

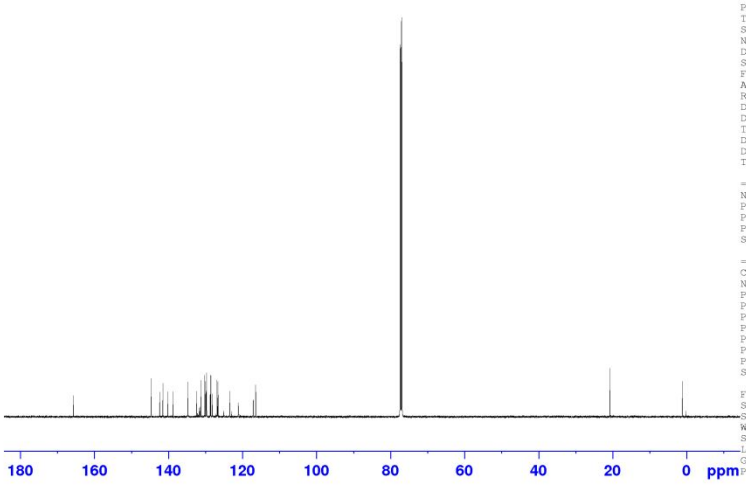




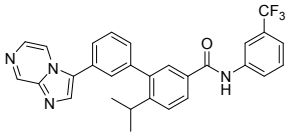
8g



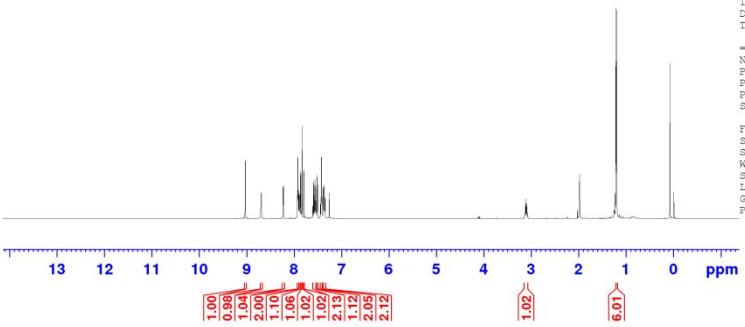

```
Current Data Parameters
NAME                  DDR H
EXPNO                116941
PROCNO                    1

F2 - Acquisition Parameters
Date_              20170323
Time                  16.06
INSTRUM               spect
PROBHD    5 mm DUL 13C-1
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9583745 sec
RG                      362
DW                   60.400 usec
DE                    6.50 usec
TE                   297.4 K
D1                1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                    12.58 usec
PL1          0 dB
PL1W           10.87646866 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF               400.1300084 MHz
WDW                      EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```



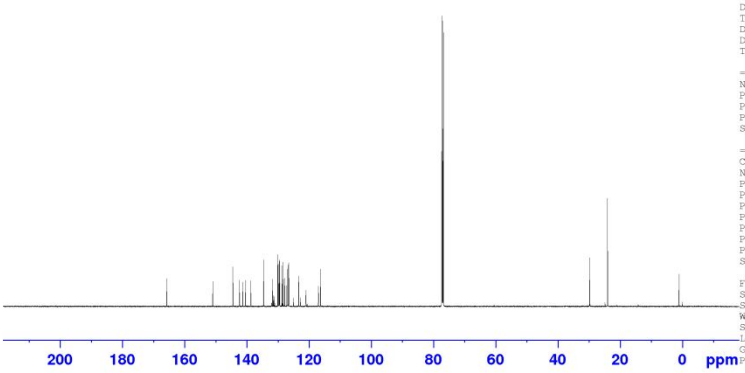

```
Current Data Parameters
NAME                  DDR C
EXPNO                116941
PROCNO                    1

F2 - Acquisition Parameters
Date_              20170321
Time                  14.32
INSTRUM               Spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     3072
DS                        4
SWH               29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010048 sec
RG                      203
DW                   16.800 usec
DE                    6.50 usec
TE                   300.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                    8.80 usec
PL1                  -1.00 dB
PL1W         104.98761749 W
SFO1          125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   2.50 dB
PL12                 17.46 dB
PL13                 17.46 dB
PL2W          13.02359561 W
PL12W          0.41565308 W
PL13W          0.41565308 W
SFO2          500.1320005 MHz

F2 - Processing parameters
SI                    32768
SF               125.7577719 MHz
WDW                      EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```



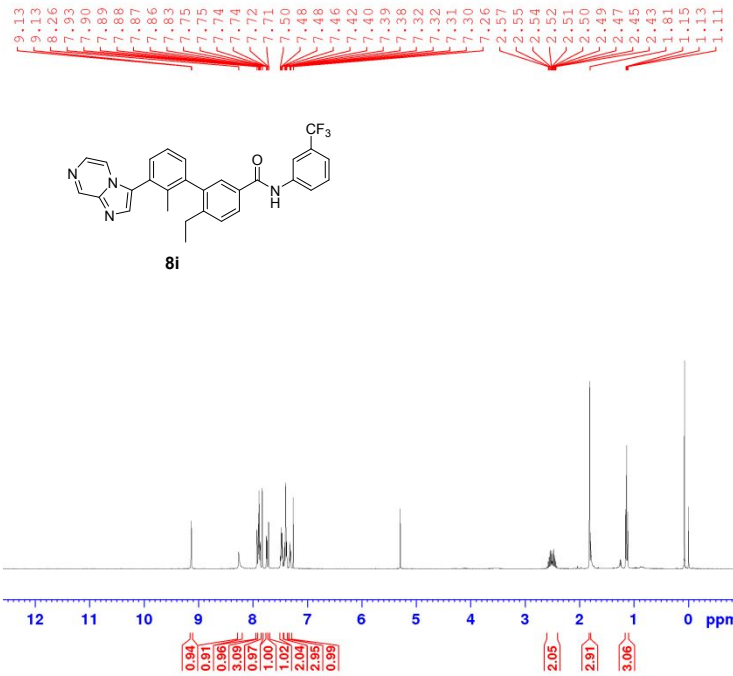
8h

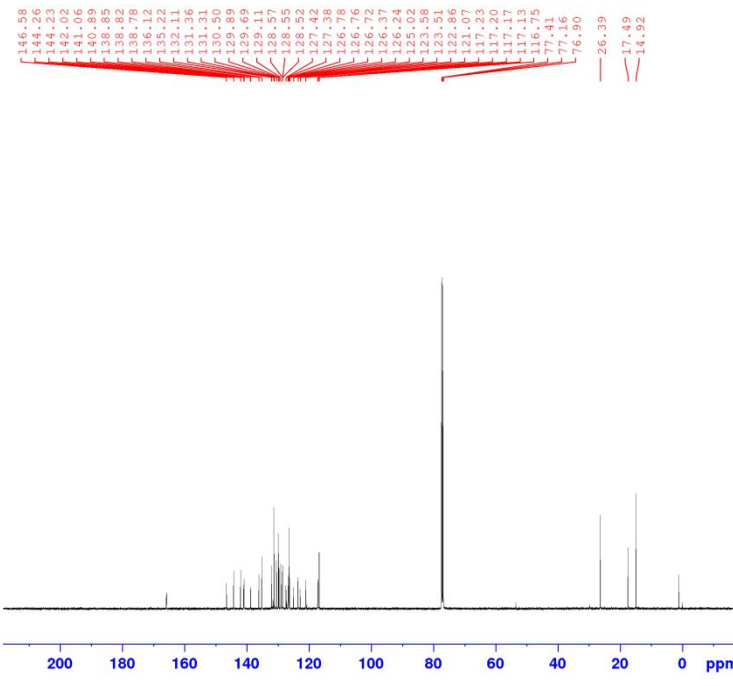


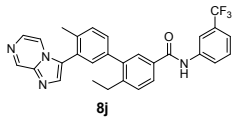

```
Current Data Parameters
NAME                  DDR_H
EXPNO               7050158
PROCNO                    1

F2 - Acquisition Parameters
Date_              20160314
Time                   3.50
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               10330.578 Hz
FIDRES            0.157632 Hz
AQ                3.1719425 sec
RG                      101
DW                 48.400 usec
DE                  6.50 usec
TE                  296.1 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                 14.00 usec
PL1                 2.50 dB
PL1W          13.02359581 W
SFO1          500.1330885 MHz

F2 - Processing parameters
SI                    32768
SF            500.1300227 MHz
WDW                      EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```



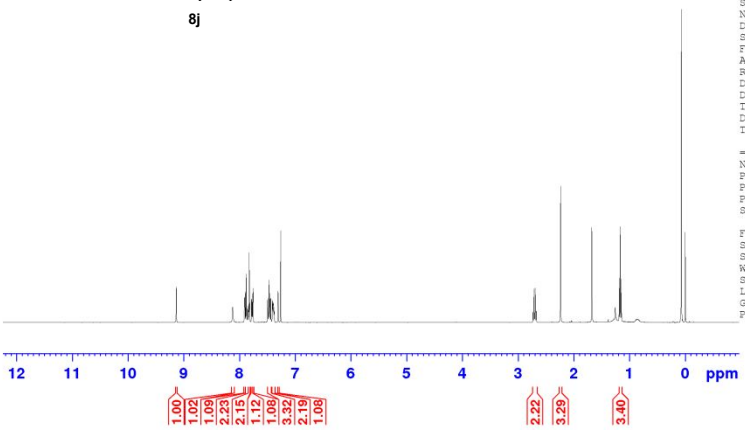

```
Current Data Parameters
NAME                  DDR_C
EXPNO               7050158
PROCNO                    1

F2 - Acquisition Parameters
Date_              20160314
Time                   8.21
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     5120
DS                        4
SWH               29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010048 sec
RG                      203
DW                 16.800 usec
DE                  6.50 usec
TE                  298.3 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     13C
P1                 13.84 usec
PL1                 2.50 dB
PL1W          46.89624786 W
SFO1          125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                     1H
PCPD2              80.00 usec
PL2                 2.50 dB
PL12               17.40 dB
PL13               17.40 dB
PL2W          13.02359581 W
PL12W          0.42143536 W
PL13W          0.42143536 W
SFO2          500.1320005 MHz

F2 - Processing parameters
SI                    32768
SF            125.7577769 MHz
WDW                      EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```


9.13
9.13
8.26
7.93
7.90
7.89
7.88
7.87
7.86
7.83
7.75
7.75
7.74
7.74
7.72
7.71
7.50
7.48
7.48
7.46
7.42
7.40
7.39
7.38
7.32
7.31
7.30
7.26
2.57
2.55
2.54
2.52
2.51
2.50
2.49
2.47
2.45
2.43
1.81
1.15
1.13
1.11
CF3
O
N
H
N
N
8i
Current Data Parameters
NAME DDR H
EXPNO 7050134
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170328
Time 16.10
INSTRUM spect
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9583745 sec
RG 128
DW 60.400 usec
DE 6.50 usec
TE 296.4 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.58 usec
PL1 0 dB
PL1W 10.87646866 W
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300082 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
0.94 0.91 0.96 3.09 0.97 1.00 1.02 2.04 2.95 0.99
2.05 2.91 3.06

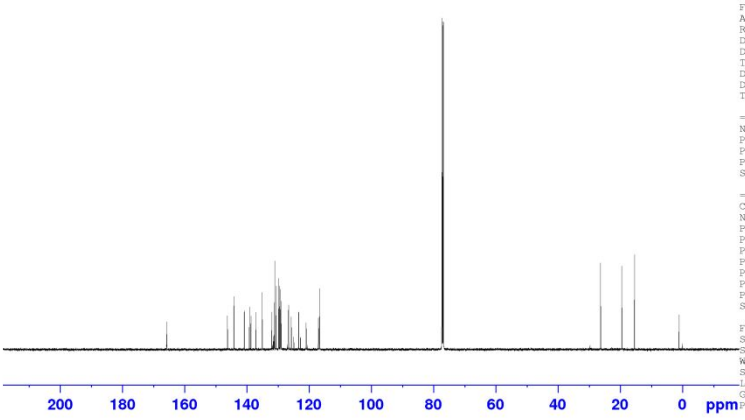

146.58
144.26
144.23
142.02
141.06
140.89
138.85
138.82
138.78
136.12
135.22
132.11
131.36
131.31
130.50
129.89
129.69
129.11
128.57
128.55
128.52
127.42
127.38
126.78
126.76
126.72
126.37
126.24
125.02
123.58
123.51
122.86
121.07
117.23
117.20
117.17
117.13
116.75
77.41
77.16
76.90
26.39
17.49
14.92
Current Data Parameters
NAME DDR C
EXPNO 7050134
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170330
Time 10.44
INSTRUM Spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3048
DS 4
SWH 29761.904 Hz
FIDRES 0.454131 Hz
AQ 1.1010048 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE 296.6 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.80 usec
PL1 -1.00 dB
PL1W 104.98761749 W
SFO1 125.7703643 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 2.50 dB
PL12 17.46 dB
PL13 17.46 dB
PL2W 13.02359581 W
PL12W 0.41565308 W
PL13W 0.41565308 W
SFO2 500.1320005 MHz
F2 - Processing parameters
SI 32768
SF 125.7577764 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm



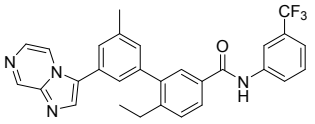
8j



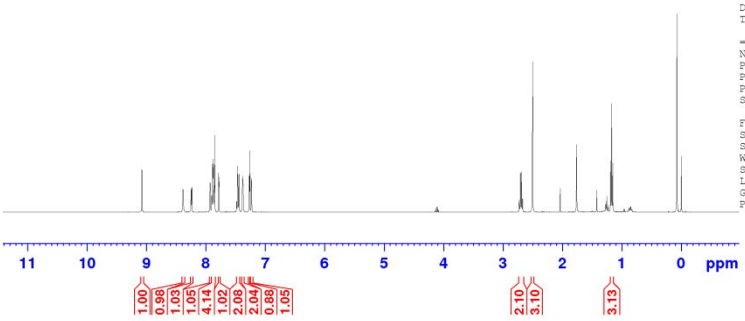

```
Current Data Parameters
NAME                  DDR H
EXPNO              7050135
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170329
Time                 11.38
INSTRUM              spect
PROBHD   5 mm DUL 13C-1
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9583745 sec
RG                    256
DW                 60.400 usec
DE                  6.50 usec
TE                296.7 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                  12.58 usec
PL1          0 dB
PL1W          10.87646866 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF           400.1300082 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```



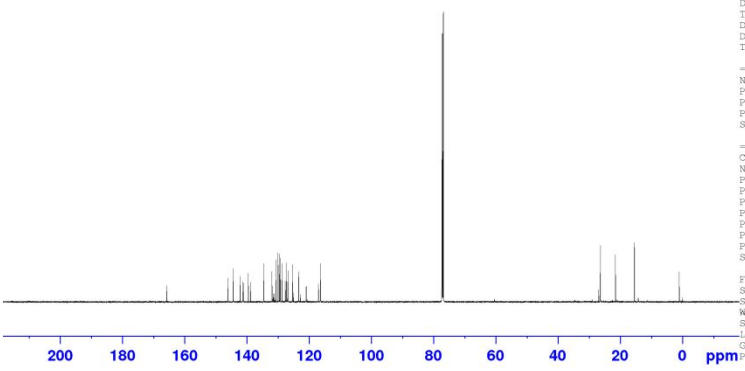

```
Current Data Parameters
NAME                  DDR C
EXPNO              7050135
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170330
Time                 19.01
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                   3048
DS                      4
SWH             29761.904 Hz
FIDRES           0.454131 Hz
AQ               1.1010048 sec
RG                    203
DW                 16.800 usec
DE                  6.50 usec
TE                298.8 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                   8.80 usec
PL1                 -1.00 dB
PL1W        104.98761749 W
SFO1         125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2               80.00 usec
PL2                  2.50 dB
PL12                17.46 dB
PL13                17.46 dB
PL2W          13.02359581 W
PL12W          0.41565308 W
PL13W          0.41565308 W
SFO2         500.1320005 MHz

F2 - Processing parameters
SI                  32768
SF           125.7577750 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```



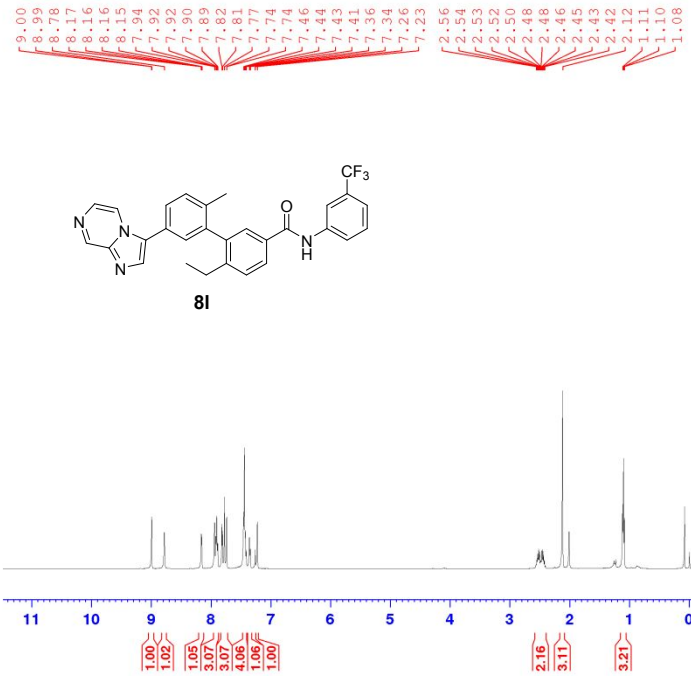
8k

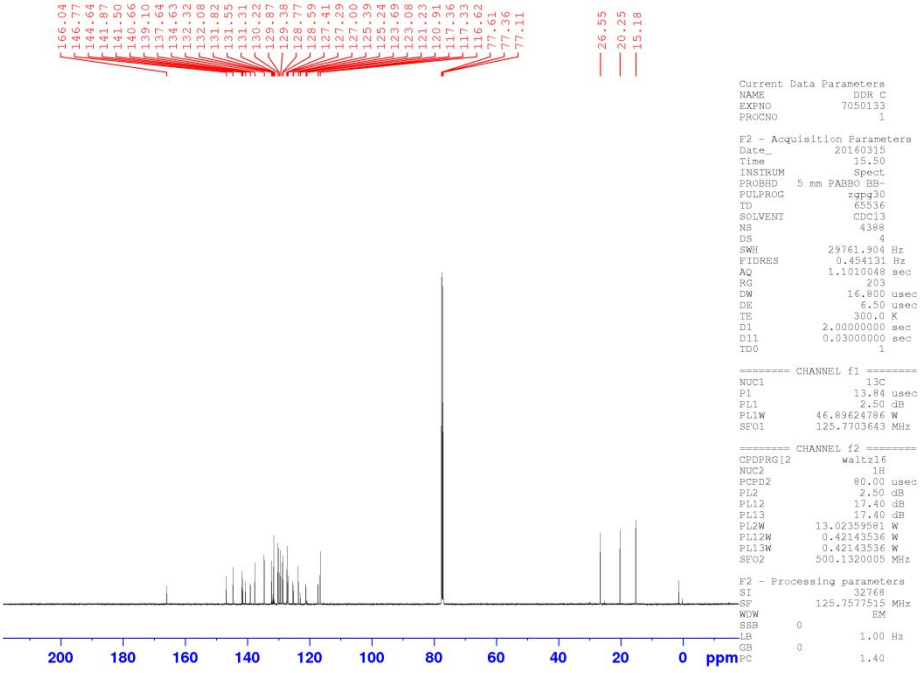


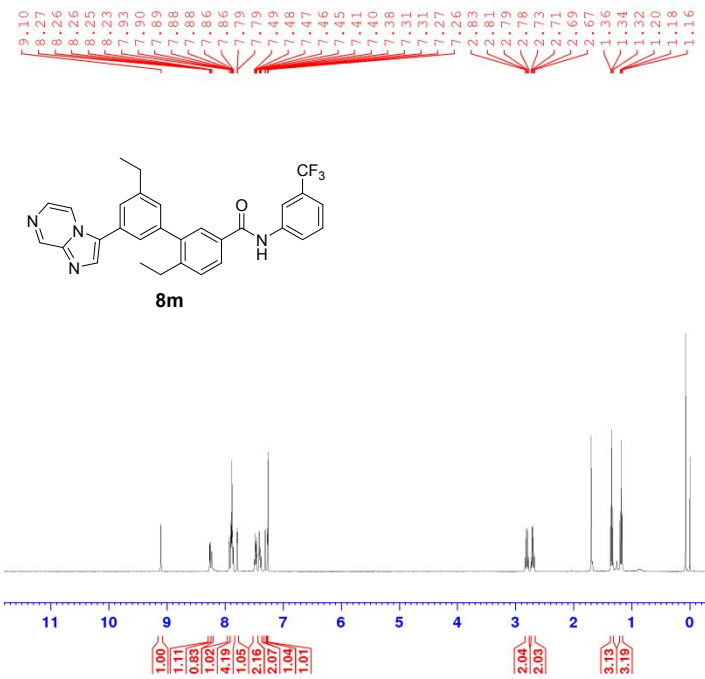

```
Current Data Parameters
NAME                  DDR H
EXPNO              7050136
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170328
Time                 16.16
INSTRUM              spect
PROBHD    5 mm DUL 13C-1
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9583745 sec
RG                      128
DW                   60.400 usec
DE                    6.50 usec
TE                   296.4 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                     1H
P1                   12.58 usec
PL1          0 dB
PL1W          10.87646866 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                    32768
SF           400.1300084 MHz
WDW                     EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```

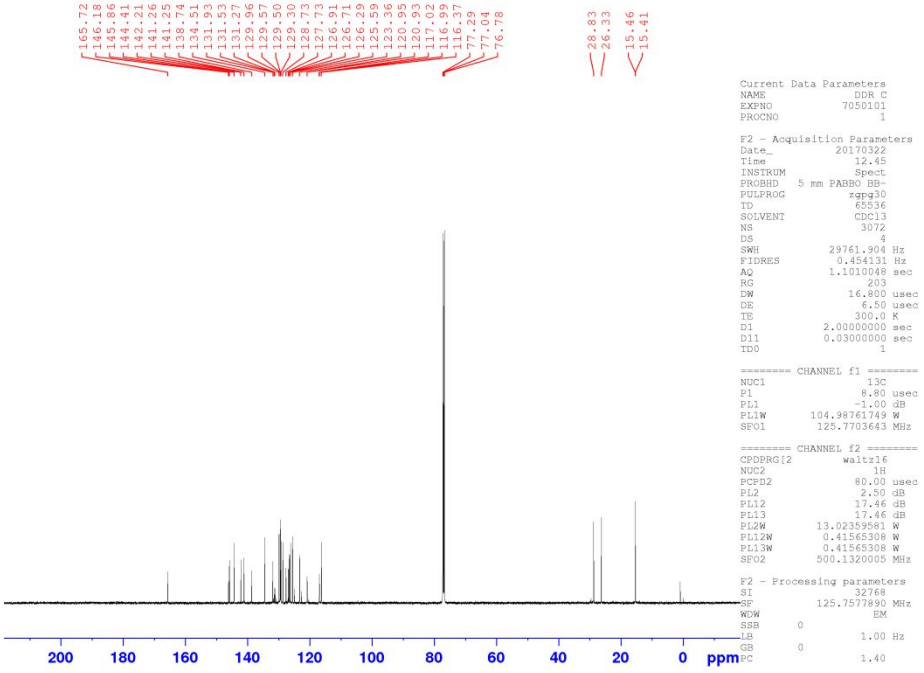


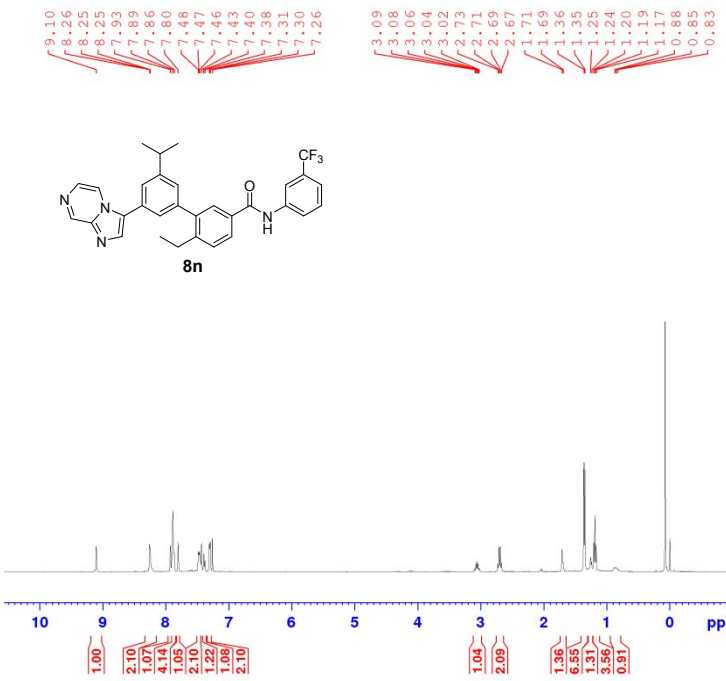

```
Current Data Parameters
NAME                  DDR C
EXPNO              7050136
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170331
Time                 14.23
INSTRUM              Spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     3048
DS                        4
SWH               29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010048 sec
RG                      203
DW                   16.800 usec
DE                    6.50 usec
TE                   298.0 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    13C
P1                    8.80 usec
PL1                  -1.00 dB
PL1W         104.98761749 W
SFO1         125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                    1H
PCPD2                80.00 usec
PL2                   2.50 dB
PL12                 17.46 dB
PL13                 17.46 dB
PL2W          13.02359561 W
PL12W          0.41565308 W
PL13W          0.41565308 W
SFO2         500.1320005 MHz

F2 - Processing parameters
SI                    32768
SF           125.7577740 MHz
WDW                     EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```

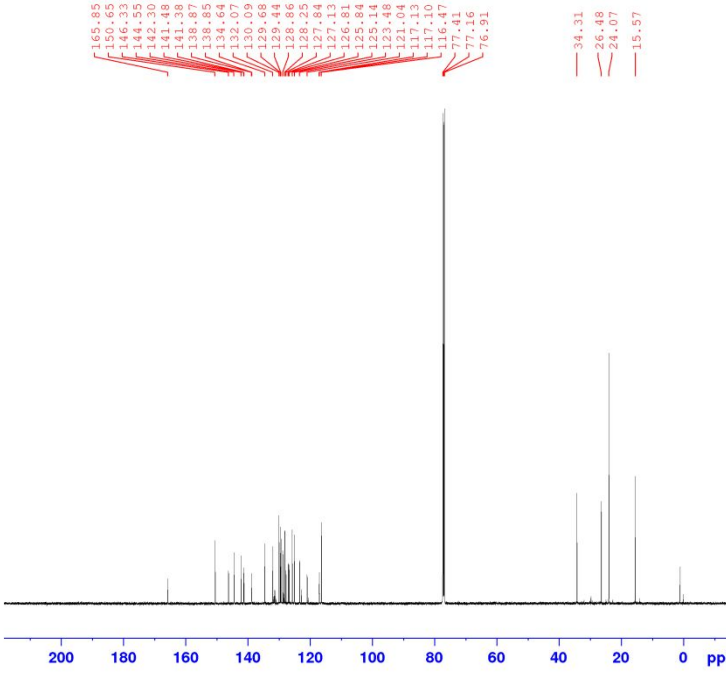

9.00
8.99
8.78
8.17
8.16
8.16
8.15
7.94
7.92
7.92
7.90
7.89
7.82
7.81
7.77
7.74
7.74
7.46
7.44
7.43
7.41
7.36
7.34
7.26
7.23
2.56
2.54
2.53
2.52
2.50
2.48
2.48
2.46
2.45
2.43
2.42
2.12
1.11
1.10
1.08
CF3
O
N
H
N
N
8l
Current Data Parameters
NAME DDR H
EXPNO 7050133
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160315
Time 15.52
INSTRUM Spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 10330.578 Hz
FIDRES 0.157632 Hz
AQ 3.1719425 sec
RG 101
DW 48.400 usec
DE 6.50 usec
TE 299.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 2.50 dB
PL1W 13.02359581 W
SFO1 500.1330885 MHz
F2 - Processing parameters
SI 32768
SF 500.1300212 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.00 1.02 1.05 3.07 3.07 4.06 1.06 1.00 2.16 3.11 3.21

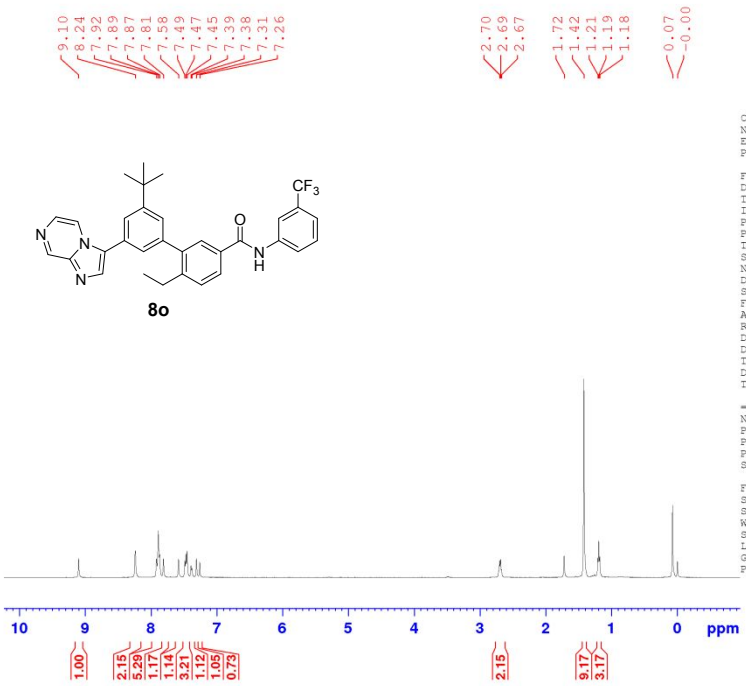

166.04
146.77
144.64
141.87
141.50
140.66
139.10
137.64
134.63
132.32
132.08
131.82
131.55
131.31
130.22
129.87
129.38
128.77
128.59
127.41
127.29
127.00
125.39
125.24
123.69
123.08
121.23
120.91
117.36
117.33
116.62
77.61
77.36
77.11
26.55
20.25
15.18
Current Data Parameters
NAME DDR C
EXPNO 7050133
PROCNO 1
F2 - Acquisition Parameters
Date_ 20160315
Time 15.50
INSTRUM Spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4388
DS 4
SWH 29761.904 Hz
FIDRES 0.454131 Hz
AQ 1.1010048 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 13.84 usec
PL1 2.50 dB
PL1W 46.89624786 W
SFO1 125.7703643 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 2.50 dB
PL12 17.40 dB
PL13 17.40 dB
PL2W 13.02359581 W
PL12W 0.42143536 W
PL13W 0.42143536 W
SFO2 500.1320005 MHz
F2 - Processing parameters
SI 32768
SF 125.7577515 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm


9.10
8.27
8.26
8.26
8.25
8.23
7.93
7.90
7.89
7.88
7.88
7.86
7.86
7.79
7.79
7.49
7.48
7.47
7.46
7.45
7.41
7.40
7.38
7.31
7.31
7.27
7.26
2.83
2.81
2.79
2.78
2.73
2.71
2.69
2.67
1.36
1.34
1.32
1.20
1.18
1.16
CF3
O
N
H
N
N
8m
Current Data Parameters
NAME DDR H
EXPNO 7050101
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170328
Time 12.54
INSTRUM spect
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9583745 sec
RG 256
DW 60.400 usec
DE 6.50 usec
TE 296.3 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.58 usec
PL1 0 dB
PL1W 10.87646866 W
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300083 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.00 1.11 0.83 1.02 4.19 1.05 2.16 2.07 1.04 1.01
2.04 2.03
3.13 3.19

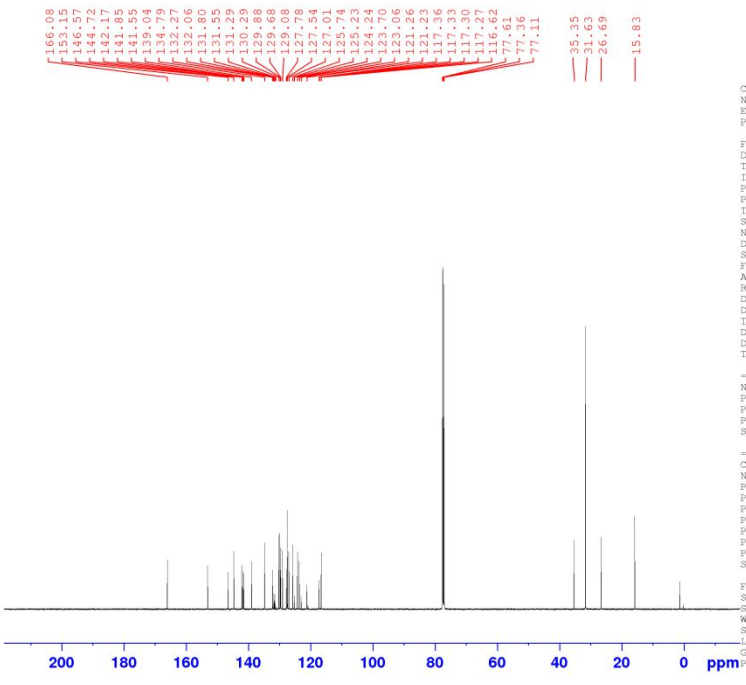

165.72
146.18
145.86
144.41
142.21
141.26
141.25
138.74
134.51
131.93
131.53
131.27
129.96
129.57
129.50
129.30
128.73
127.73
126.91
126.71
126.29
125.59
123.36
120.95
120.93
117.02
116.99
116.37
77.29
77.04
76.78
28.83
26.33
15.46
15.41
Current Data Parameters
NAME DDR C
EXPNO 7050101
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170322
Time 12.45
INSTRUM Spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3072
DS 4
SWH 29761.904 Hz
FIDRES 0.454131 Hz
AQ 1.1010048 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.80 usec
PL1 -1.00 dB
PL1W 104.98761749 W
SFO1 125.7703643 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 2.50 dB
PL12 17.46 dB
PL13 17.46 dB
PL2W 13.02359581 W
PL12W 0.41565308 W
PL13W 0.41565308 W
SFO2 500.1320005 MHz
F2 - Processing parameters
SI 32768
SF 125.7577890 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm


9.10
8.26
8.25
8.25
7.93
7.89
7.86
7.80
7.48
7.47
7.46
7.43
7.40
7.38
7.31
7.30
7.26
3.09
3.08
3.06
3.04
3.02
2.73
2.71
2.69
2.67
1.71
1.69
1.36
1.35
1.25
1.24
1.20
1.19
1.17
0.88
0.85
0.83
CF3
O
N
H
N
N
8n
Current Data Parameters
NAME DDR H
EXPNO 7050182
PROCNO 1
F2 - Acquisition Parameters
Date_ 20150128
Time 3.56
INSTRUM spect
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9583745 sec
RG 181
DW 60.400 usec
DE 6.50 usec
TE 296.3 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.58 usec
PL1 0 dB
PL1W 10.87646866 W
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10 9 8 7 6 5 4 3 2 1 0 ppm
1.00 2.10 1.07 4.14 1.05 2.10 1.22 1.08 2.10 1.04 2.09 1.36 6.55 1.31 3.56 0.91

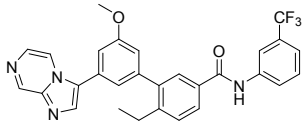

165.85
150.65
146.33
144.55
142.30
141.48
141.38
138.87
138.85
134.64
132.07
130.09
129.68
129.44
128.86
128.25
127.84
127.13
126.81
125.84
125.14
123.48
121.04
117.13
117.10
116.47
77.41
77.16
76.91
34.31
26.48
24.07
15.57
Current Data Parameters
NAME DDR C
EXPNO 7050182
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170331
Time 0.32
INSTRUM Spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3048
DS 4
SWH 29761.904 Hz
FIDRES 0.454131 Hz
AQ 1.1010048 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE 298.6 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.80 usec
PL1 -1.00 dB
PL1W 104.98761749 W
SFO1 125.7703643 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 2.50 dB
PL12 17.46 dB
PL13 17.46 dB
PL2W 13.02359581 W
PL12W 0.41565308 W
PL13W 0.41565308 W
SFO2 500.1320005 MHz
F2 - Processing parameters
SI 32768
SF 125.7577743 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm



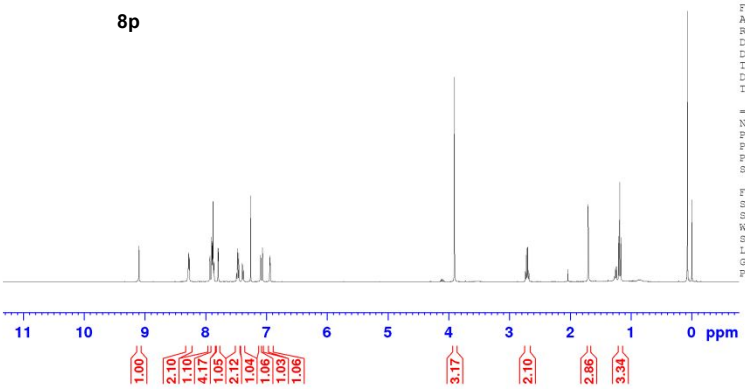

```
Current Data Parameters
NAME                  DDR H
EXPNO                340066
PROCNO                    1

F2 - Acquisition Parameters
Date_              20160311
Time                  19.10
INSTRUM               Spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH               10330.578 Hz
FIDRES            0.157632 Hz
AQ                3.1719425 sec
RG                      144
DW                 48.400 usec
DE                  6.50 usec
TE                  295.6 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    1H
P1                  14.00 usec
PL1                  2.50 dB
PL1W          13.02359581 W
SFO1          500.1330885 MHz

F2 - Processing parameters
SI                    32768
SF             500.1300227 MHz
WDW                      EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```



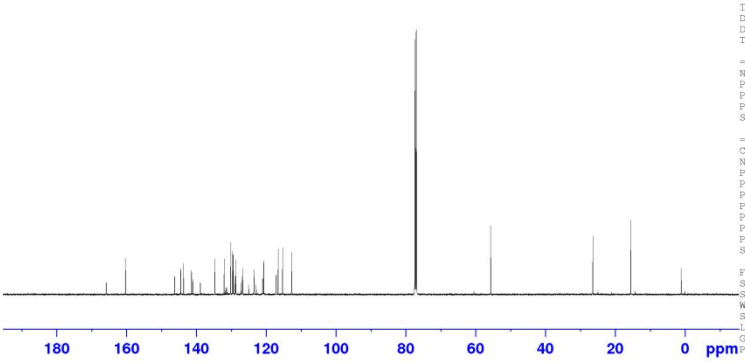

```
Current Data Parameters
NAME                  DDR C
EXPNO                340066
PROCNO                    1

F2 - Acquisition Parameters
Date_              20160313
Time                  11.07
INSTRUM               Spect
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                     5120
DS                        4
SWH               29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010048 sec
RG                      203
DW                 16.800 usec
DE                  6.50 usec
TE                  297.7 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                   13C
P1                  13.84 usec
PL1                  2.50 dB
PL1W          46.89624786 W
SFO1          125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2               80.00 usec
PL2                  2.50 dB
PL12                17.40 dB
PL13                17.40 dB
PL2W          13.02359581 W
PL12W          0.42143536 W
PL13W          0.42143536 W
SFO2          500.1320005 MHz

F2 - Processing parameters
SI                    32768
SF             125.7577523 MHz
WDW                      EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```



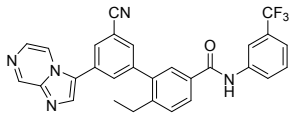
8p




```
Current Data Parameters
NAME                  DDR H
EXPNO                340045
PROCNO                    1

F2 - Acquisition Parameters
Date_              20170328
Time                  12.08
INSTRUM               spect
PROBHD    5 mm DUL 13C-1
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH                8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9583745 sec
RG                     256
DW                  60.400 usec
DE                   6.50 usec
TE                  296.0 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   12.58 usec
PL1          0 dB
PL1W           10.87646866 W
SFO1          400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF            400.1300082 MHz
WDW                     EM
SSB          0
LB                   0.30 Hz
GB           0
PC                   1.00
```

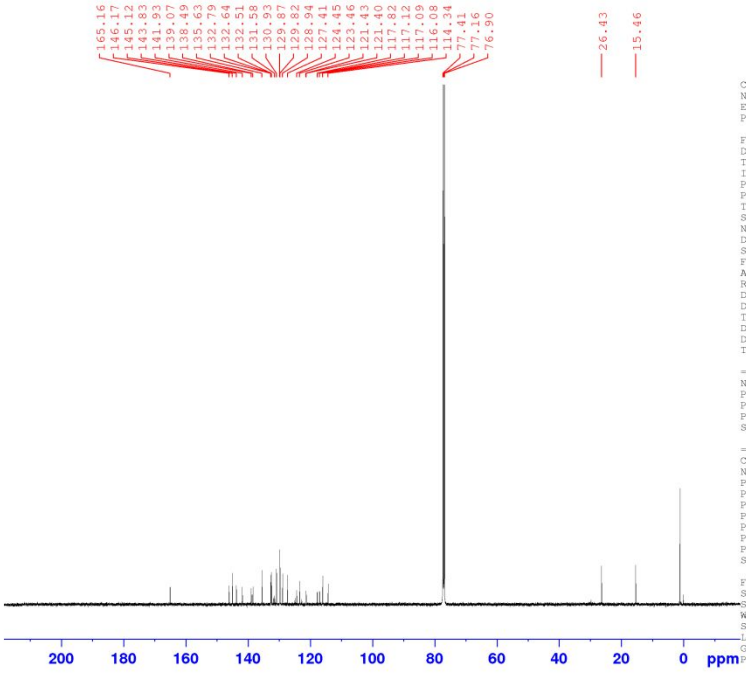



```
Current Data Parameters
NAME                  DDR C
EXPNO                340045
PROCNO                    1

F2 - Acquisition Parameters
Date_              20170322
Time                   9.58
INSTRUM               Spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    3072
DS                       4
SWH               29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010048 sec
RG                     203
DW                  16.800 usec
DE                   6.50 usec
TE                  300.0 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                   8.80 usec
PL1                 -1.00 dB
PL1W          104.98761749 W
SFO1          125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2                80.00 usec
PL2                  2.50 dB
PL12                17.46 dB
PL13                17.46 dB
PL2W          13.02359581 W
PL12W          0.41565308 W
PL13W          0.41565308 W
SFO2          500.1320005 MHz

F2 - Processing parameters
SI                   32768
SF            125.7577750 MHz
WDW                     EM
SSB          0
LB                   1.00 Hz
GB           0
PC                   1.40
```

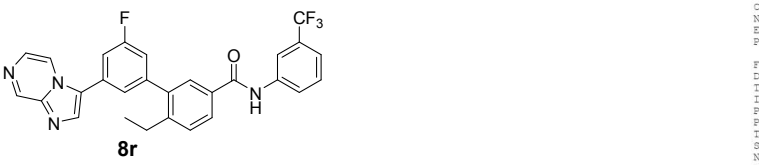


8q

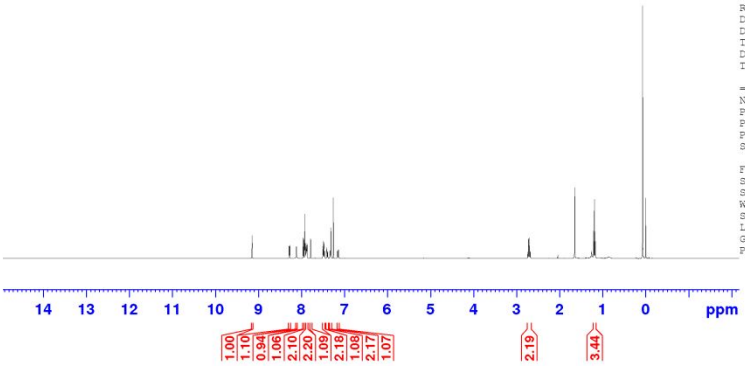

```
Current Data Parameters
NAME                  DDR H
EXPNO              7050167
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170328
Time                  9.57
INSTRUM              spect
PROBHD    5 mm DUL 13C-1
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      32
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9583745 sec
RG                     256
DW                60.400 usec
DE                 6.50 usec
TE                 295.9 K
D1              1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   1H
P1                 12.58 usec
PL1         0 dB
PL1W         10.87646866 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF              400.1299979 MHz
WDW                     EM
SSB         0
LB                  0.30 Hz
GB          0
PC                  1.00
```



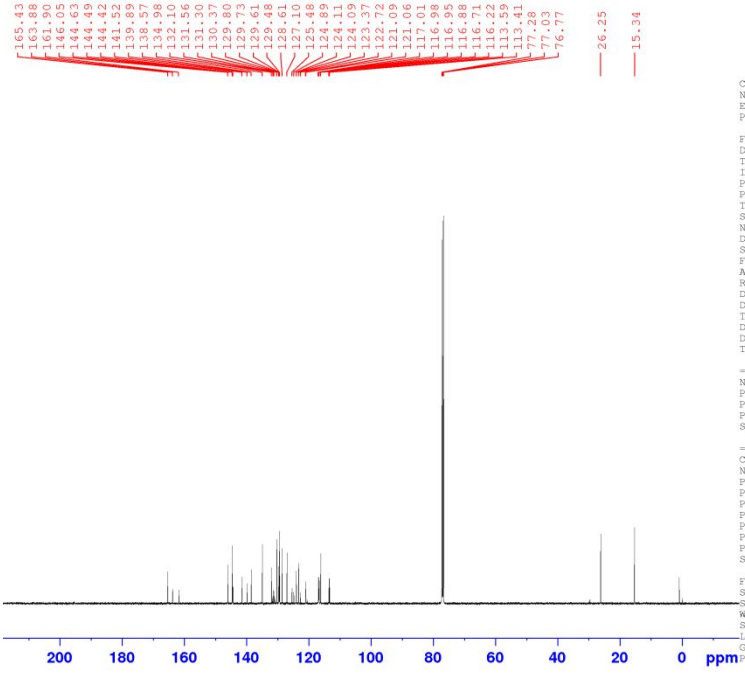

```
Current Data Parameters
NAME                  DDR C
EXPNO              7050167
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170324
Time                 17.36
INSTRUM              Spect
PROBHD    5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    5555
DS                       4
SWH              29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010048 sec
RG                     203
DW                16.800 usec
DE                 6.50 usec
TE                 300.0 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                  13C
P1                  8.80 usec
PL1                -1.00 dB
PL1W        104.98761749 W
SFO1        125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                 2.50 dB
PL12               17.46 dB
PL13               17.46 dB
PL2W        13.02359581 W
PL12W        0.41565308 W
PL13W        0.41565308 W
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                   32768
SF              125.7577699 MHz
WDW                     EM
SSB         0
LB                  1.00 Hz
GB          0
PC                  1.40
```



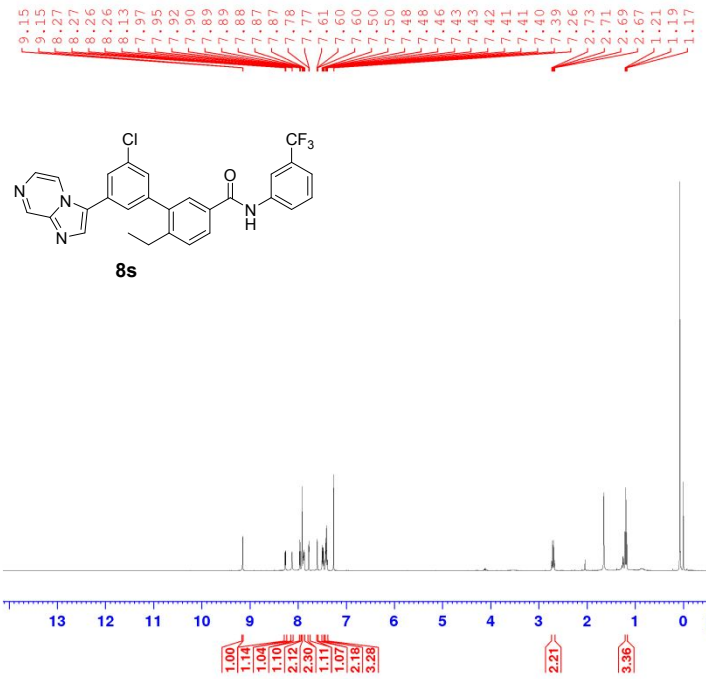
8r

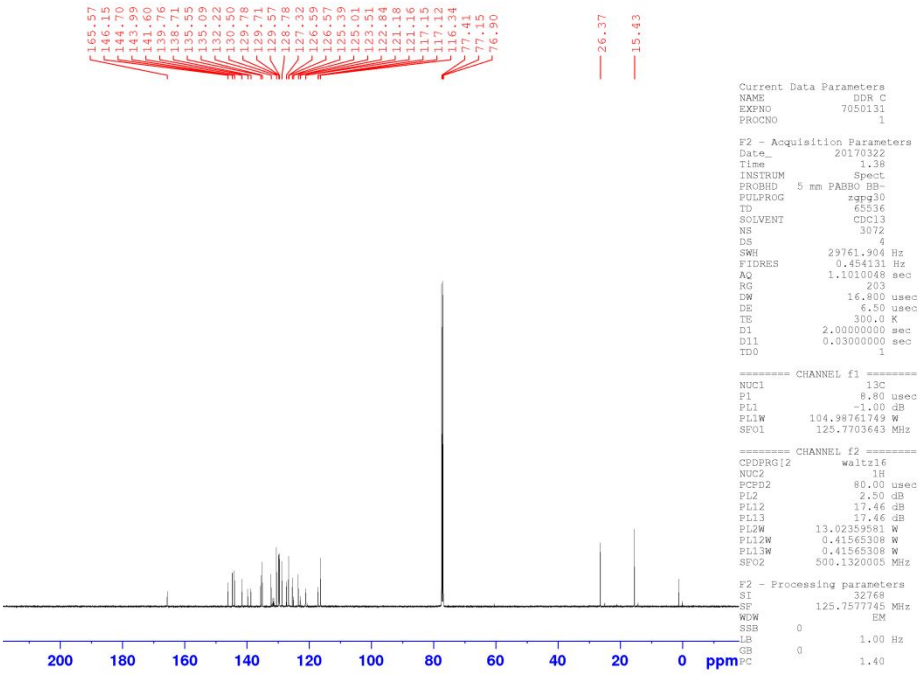


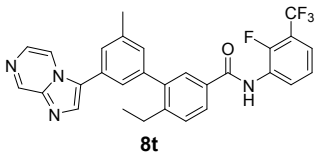

```
Current Data Parameters
NAME                  DDR H
EXPNO              7050130
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170328
Time                 11.45
INSTRUM              spect
PROBHD    5 mm DUL 13C-1
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                  322.5
DW                 60.400 usec
DE                  6.50 usec
TE                296.0 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 12.58 usec
PL1         0 dB
PL1W         10.87646866 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF          400.1300085 MHz
WDW                    EM
SSB         0
LB                  0.30 Hz
GB          0
PC                  1.00
```




```
Current Data Parameters
NAME                  DDR C
EXPNO              7050130
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170321
Time                 22.51
INSTRUM              Spect
PROBHD    5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                   3072
DS                      4
SWH            29761.904 Hz
FIDRES          0.454131 Hz
AQ              1.1010048 sec
RG                  203
DW                 16.800 usec
DE                  6.50 usec
TE                300.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  8.80 usec
PL1                -1.00 dB
PL1W        104.98761749 W
SFO1        125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2               80.00 usec
PL2                  2.50 dB
PL12                17.46 dB
PL13                17.46 dB
PL2W         13.02359561 W
PL12W         0.41565308 W
PL13W         0.41565308 W
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                  32768
SF          125.7577890 MHz
WDW                    EM
SSB         0
LB                  1.00 Hz
GB          0
PC                  1.40
```

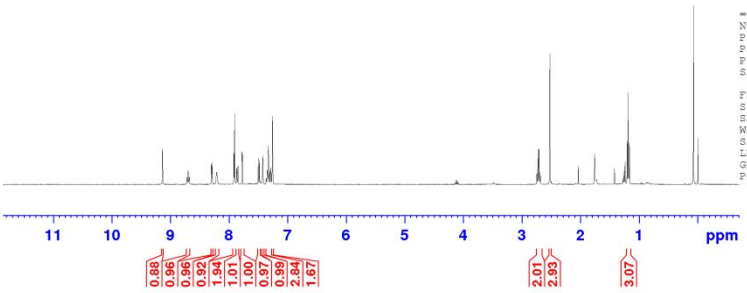

9.15
9.15
8.27
8.27
8.26
8.26
8.13
7.97
7.95
7.92
7.90
7.89
7.89
7.88
7.87
7.87
7.78
7.77
7.61
7.60
7.60
7.50
7.48
7.48
7.46
7.43
7.43
7.42
7.41
7.41
7.40
7.39
7.26
2.73
2.71
2.69
2.67
1.21
1.19
1.17
Cl
CF3
O
N
H
N
N
N
8s
Current Data Parameters
NAME DDR H
EXPNO 7050131
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170328
Time 11.51
INSTRUM spect
PROBHD 5 mm DUL 13C-1
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8278.146 Hz
FIDRES 0.126314 Hz
AQ 3.9583745 sec
RG 322.5
DW 60.400 usec
DE 6.50 usec
TE 296.1 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.58 usec
PL1 0 dB
PL1W 10.87646866 W
SFO1 400.1324710 MHz
F2 - Processing parameters
SI 32768
SF 400.1300083 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
1.00 1.14 1.04 1.10 2.12 2.30 1.11 1.07 2.18 3.28
2.21
3.36

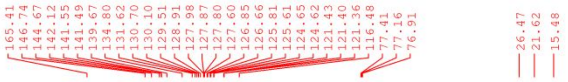

165.57
146.15
144.70
143.99
141.60
139.76
138.71
135.55
135.09
132.22
130.50
129.78
129.71
129.57
128.78
127.32
126.59
126.57
125.39
125.01
123.51
122.84
121.18
121.16
117.15
117.12
116.34
77.41
77.15
76.90
26.37
15.43
Current Data Parameters
NAME DDR C
EXPNO 7050131
PROCNO 1
F2 - Acquisition Parameters
Date_ 20170322
Time 1.38
INSTRUM Spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 3072
DS 4
SWH 29761.904 Hz
FIDRES 0.454131 Hz
AQ 1.1010048 sec
RG 203
DW 16.800 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.80 usec
PL1 -1.00 dB
PL1W 104.98761749 W
SFO1 125.7703643 MHz
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 2.50 dB
PL12 17.46 dB
PL13 17.46 dB
PL2W 13.02359561 W
PL12W 0.41565308 W
PL13W 0.41565308 W
SFO2 500.1320005 MHz
F2 - Processing parameters
SI 32768
SF 125.7577745 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm



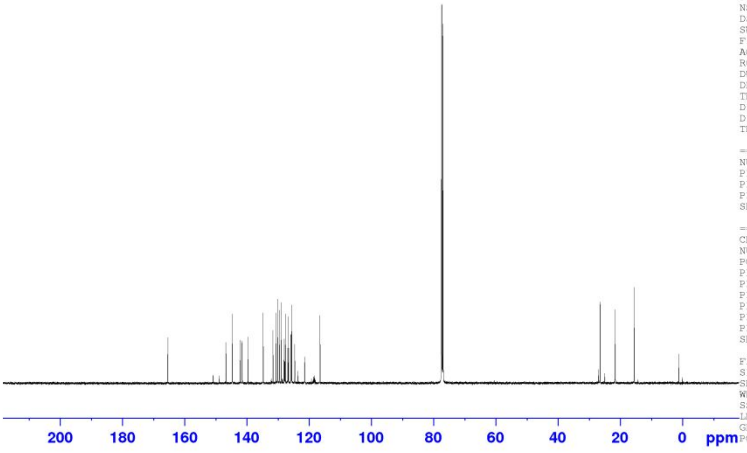
8t

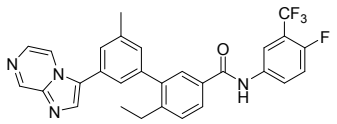
```
Current Data Parameters
NAME                  DDR H
EXPNO              7050172
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170328
Time                 16.21
INSTRUM              spect
PROBHD   5 mm DUL 13C-1
PULPROG              zg30
TD                  65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES               0.126314 Hz
AQ                3.9583745 sec
RG                     181
DW                  60.400 usec
DE                   6.50 usec
TE                  296.4 K
D1             1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   12.58 usec
PL1          0 dB
PL1W          10.87646866 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF            400.1300082 MHz
WDW                     EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```



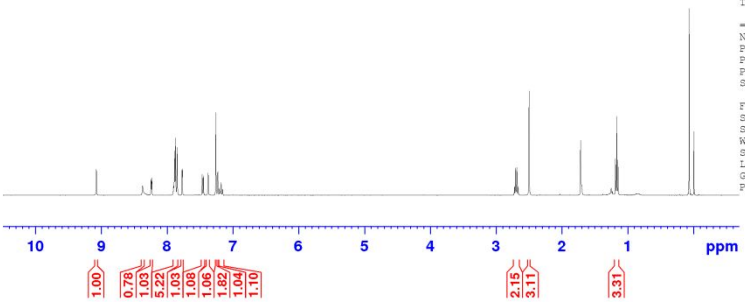



```
Current Data Parameters
NAME                  DDR C
EXPNO              7050172
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170331
Time                 11.36
INSTRUM              Spect
PROBHD   5 mm PABBO BB-
PULPROG            zgpg30
TD                  65536
SOLVENT              CDCl3
NS                    3048
DS                       4
SWH              29761.904 Hz
FIDRES               0.454131 Hz
AQ                1.1010048 sec
RG                     203
DW                  16.800 usec
DE                   6.50 usec
TE                  299.6 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                    8.80 usec
PL1                  -1.00 dB
PL1W        104.98761749 W
SFO1         125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2                80.00 usec
PL2                   2.50 dB
PL12                 17.46 dB
PL13                 17.46 dB
PL2W         13.02359561 W
PL12W         0.41565308 W
PL13W         0.41565308 W
SFO2         500.1320005 MHz

F2 - Processing parameters
SI                   32768
SF            125.7577748 MHz
WDW                     EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```

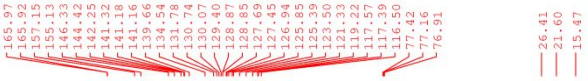


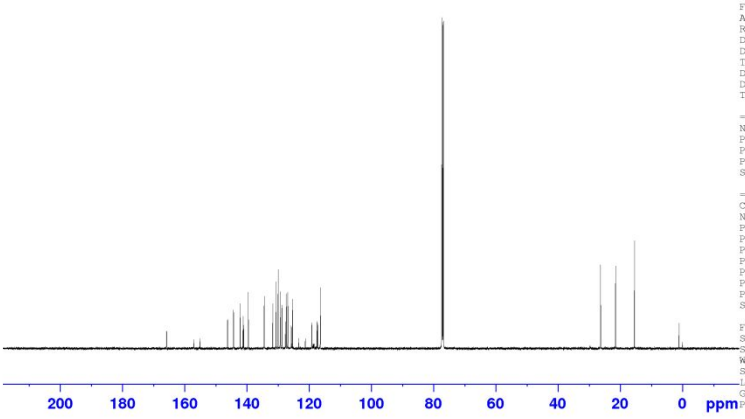


8u

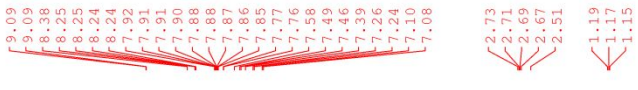


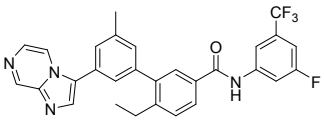

```
Current Data Parameters
NAME                  DDR H
EXPNO              7050171
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170328
Time                 11.56
INSTRUM              spect
PROBHD    5 mm DUL 13C-1
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH              8278.146 Hz
FIDRES           0.126314 Hz
AQ               3.9583745 sec
RG                    256
DW                60.400 usec
DE                 6.50 usec
TE                296.0 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 12.58 usec
PL1          0 dB
PL1W         10.87646866 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF           400.1300082 MHz
WDW                    EM
SSB          0
LB                  0.30 Hz
GB           0
PC                  1.00
```






```
Current Data Parameters
NAME                  DDR C
EXPNO              7050171
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170322
Time                  4.25
INSTRUM              Spect
PROBHD    5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                   3072
DS                      4
SWH             29761.904 Hz
FIDRES           0.454131 Hz
AQ               1.1010048 sec
RG                    203
DW                16.800 usec
DE                 6.50 usec
TE                300.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 8.80 usec
PL1               -1.00 dB
PL1W        104.98761749 W
SFO1        125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                2.50 dB
PL12              17.46 dB
PL13              17.46 dB
PL2W        13.02359561 W
PL12W        0.41565308 W
PL13W        0.41565308 W
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                  32768
SF           125.7577741 MHz
WDW                    EM
SSB          0
LB                  1.00 Hz
GB           0
PC                  1.40
```





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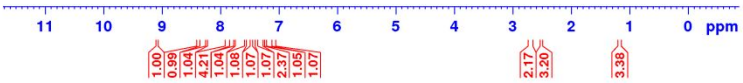
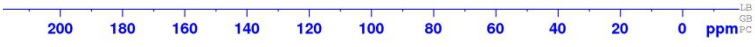
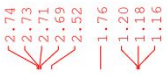
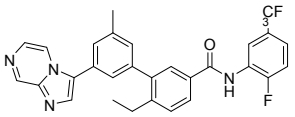
```
Current Data Parameters
NAME                  DDR H
EXPNO              7050175
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170328
Time                 12.03
INSTRUM              spect
PROBHD    5 mm DUL 13C-1
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     16
DS                      2
SWH             8278.146 Hz
FIDRES          0.126314 Hz
AQ              3.9583745 sec
RG                   322.5
DW                60.400 usec
DE                 6.50 usec
TE                296.1 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                 12.58 usec
PL1          0 dB
PL1W         10.87646866 W
SFO1        400.1324710 MHz

F2 - Processing parameters
SI                  32768
SF          400.1300082 MHz
WDW                    EM
SSB          0
LB                  0.30 Hz
GB           0
PC                  1.00
```




```
Current Data Parameters
NAME                  DDR C
EXPNO              7050175
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170322
Time                  7.11
INSTRUM              Spect
PROBHD    5 mm PABBO BB-
PULPROG           zgpg30
TD                  65536
SOLVENT             CDCl3
NS                   3072
DS                      4
SWH            29761.904 Hz
FIDRES          0.454131 Hz
AQ              1.1010048 sec
RG                    203
DW                16.800 usec
DE                 6.50 usec
TE                300.0 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                  8.80 usec
PL1                -1.00 dB
PL1W       104.98761749 W
SFO1        125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                 2.50 dB
PL12               17.46 dB
PL13               17.46 dB
PL2W        13.02359581 W
PL12W        0.41565308 W
PL13W        0.41565308 W
SFO2        500.1320005 MHz

F2 - Processing parameters
SI                  32768
SF          125.7577735 MHz
WDW                    EM
SSB          0
LB                  1.00 Hz
GB           0
PC                  1.40
```

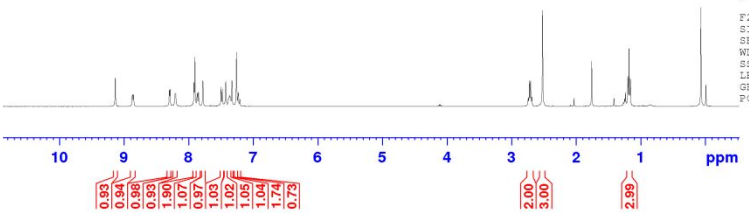


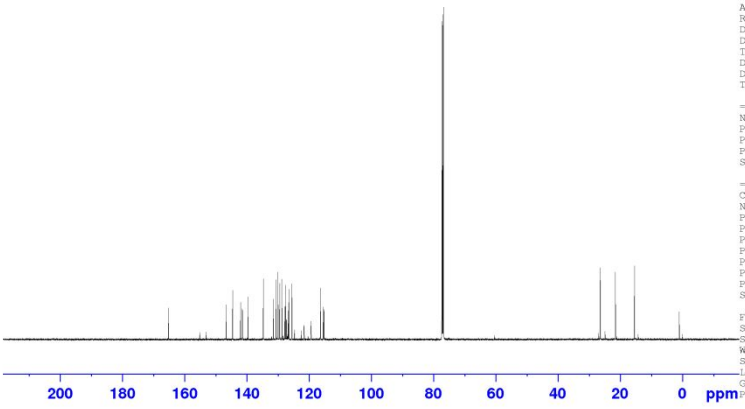




8w

```
Current Data Parameters
NAME                  DDR H
EXPNO              7050174
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170328
Time                 19.36
INSTRUM              spect
PROBHD   5 mm DUL 13C-1
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               8278.146 Hz
FIDRES            0.126314 Hz
AQ                3.9583745 sec
RG                     128
DW                  60.400 usec
DE                   6.50 usec
TE                  296.5 K
D1               1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   12.58 usec
PL1          0 dB
PL1W          10.87646866 W
SFO1         400.1324710 MHz

F2 - Processing parameters
SI                   32768
SF            400.1300074 MHz
WDW                     EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```






```
Current Data Parameters
NAME                  DDR C
EXPNO              7050174
PROCNO                   1

F2 - Acquisition Parameters
Date_              20170331
Time                  3.18
INSTRUM              Spect
PROBHD   5 mm PABBO BB-
PULPROG           zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    3048
DS                       4
SWH              29761.904 Hz
FIDRES            0.454131 Hz
AQ                1.1010048 sec
RG                     203
DW                  16.800 usec
DE                   6.50 usec
TE                  299.7 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                   13C
P1                    8.80 usec
PL1                  -1.00 dB
PL1W         104.98761749 W
SFO1          125.7703643 MHz

======== CHANNEL f2 ========
CPDPRG[2          waltz16
NUC2                   1H
PCPD2                80.00 usec
PL2                   2.50 dB
PL12                 17.46 dB
PL13                 17.46 dB
PL2W          13.02359581 W
PL12W          0.41565308 W
PL13W          0.41565308 W
SFO2          500.1320005 MHz

F2 - Processing parameters
SI                   32768
SF            125.7577740 MHz
WDW                     EM
SSB          0
LB                    1.00 Hz
GB           0
PC                    1.40
```