

Discovery of (1*H*-Pyrazolo[3,4-*c*]pyridin-5-yl)sulfonamide Analogs as Hepatitis B Virus Capsid Assembly Modulators by Conformation Constraint

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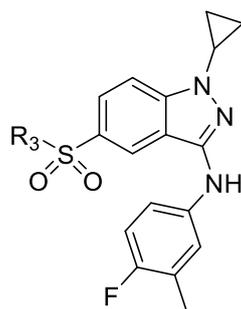
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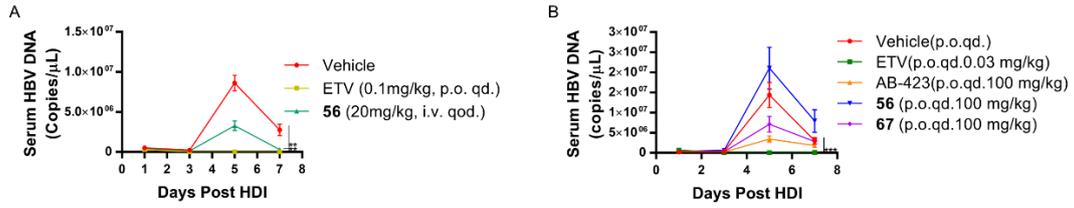
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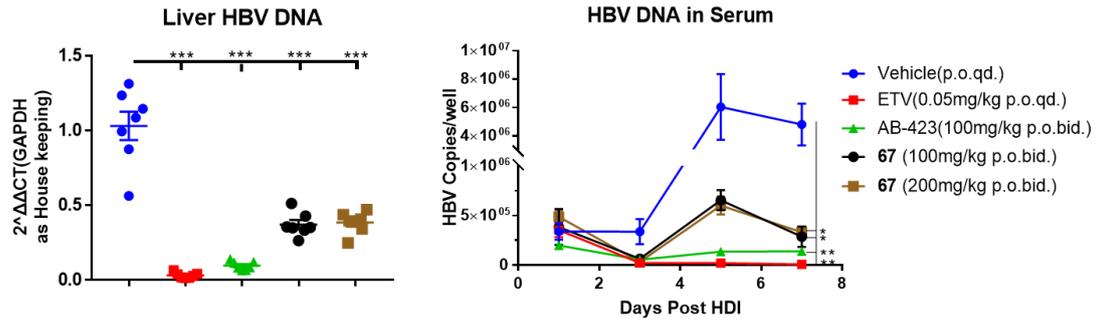
Supplementary Table S1: Anti-HBV activity and cytotoxicity in HepAD38 cells of compounds with various substituents at the sulfonamide moiety.



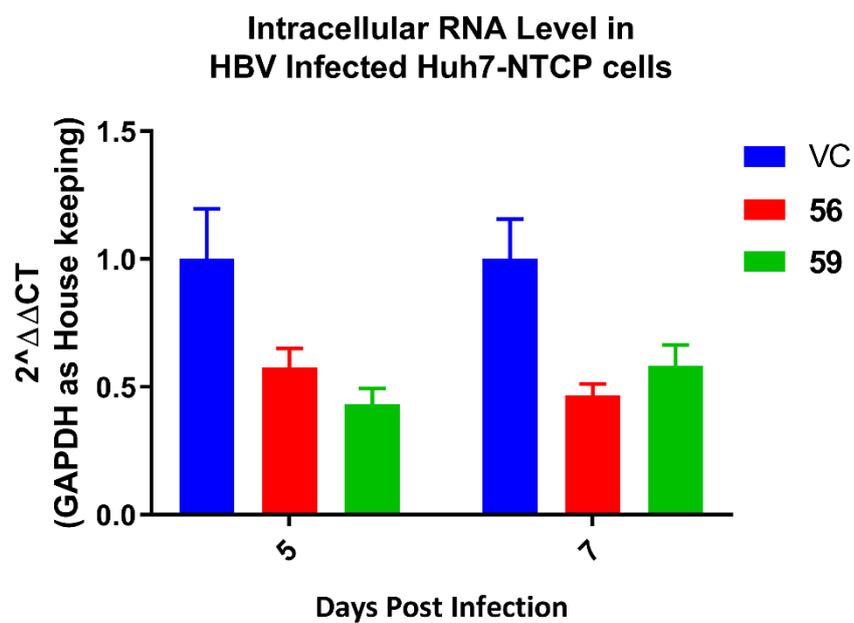
Compd.	R ₃	IC ₅₀ (μM)	CC ₅₀ (μM)
S1		0.17	23.23
S2		0.083	13.5
S3		0.22	14.06
S4		0.21	19.34
S5		0.23	>100
S6		0.070	8.85
S7		0.079	27.8



Supplementary Figure S1. *In vivo* anti-HBV activity of **56** and **67** in HDI mouse model. (A) *In vivo* anti-HBV activity of **56** administered intravascularly. (B) *In vivo* anti-HBV activity of **56** and **67**. Results are presented as mean±SEM. $N=7$; **, $P < 0.01$; ***, $P < 0.001$.



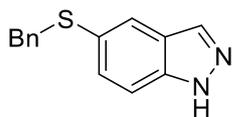
Supplementary Figure S2. In vivo anti-HBV activity of **56** and **57** (p.o. bid.) in HDI mouse model. Results are presented as mean±SEM. $N=7$; *, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$.



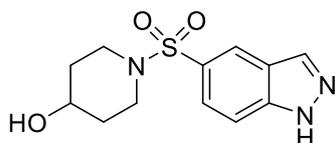
Supplementary Figure S3. Inhibition of intracellular HBV RNA in HBV infected Huh7-NTCP cells. The Huh7-NTCP cells (2×10^5 cells/well in 24 micro-well plate) were infected by HBV (200MOI) for 24h, and then treated with 1.0 μ M compounds or DMSO (VC) for 5 or 7 days. Cells were collected and intracellular RNA was extracted and detected by qPCR. The data is presented as mean \pm SD.

Synthesis of the intermediates

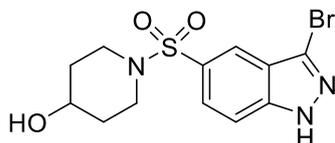
Synthesis of **72-75**.



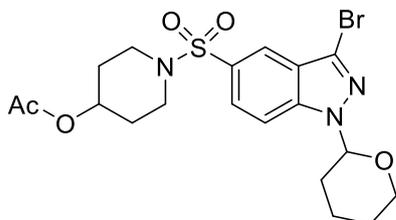
5-(benzylthio)-1H-indazole (72). 5-Bromoindazole (390 mg, 2 mmol), Pd₂(dba)₃ (91 mg, 0.1 mmol), Xantphos (117 mg, 0.2 mmol) were dissolved in 20 mL 1,4-dioxane. Then DIPEA (660 μL, 4 mmol) and benzyl mercaptan (372 mg, 3 mmol) were added. The mixture was heated at 90 °C under argon atmosphere for 4h. After that, the mixture was filtered and the filtrate was concentrated under vacuum. The residue was purified by column chromatography on silica gel (eluted with PE/EA, 2/1) to get 440 mg 1-2 as orange oil. Yield: 92%.



1-((1H-indazol-5-yl)sulfonyl)piperidin-4-ol (73). 420 mg (1.75 mmol) **72** was dissolved in mixture of 10 mL acetonitrile, 100 μL H₂O and 100 μL AcOH. After the mixture was cooled to -30 °C, 5,5-dimethylhydantoin (520 mg, 2.62 mmol) was added portion wise. Then the mixture was warmed to -15 °C and stirred for another hour. The mixture was diluted with EA and washed with brine. The organic layer was dried using anhydrous sodium sulfate. EA was removed under vacuum. The residue was dissolved with DCM. 4-hydroxypiperidine (520 mg, 5.2 mmol) and TEA (1.0 ml, 7.86 mmol) were added. The mixture was stirred at room temperature for 30 mins and water was added. The organic layer was separated, washed with brine and dried using anhydrous sodium sulfate. DCM was evaporated under vacuum. The residue was then purified using flash chromatography on C₁₈ silica gel (eluted with water/methanol) to give 200 mg **73** as white powder. Yield 41%.

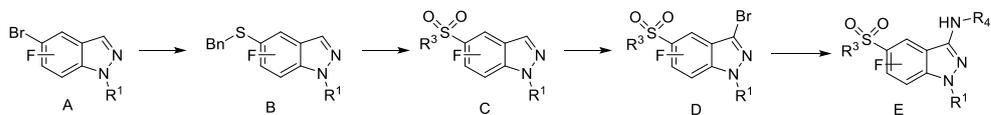


1-((3-bromo-1H-indazol-5-yl)sulfonyl)piperidin-4-ol (74). To the mixture of **73** (93 mg, 0.33 mmol) in chloroform was added NBS (65 mg, 0.37 mmol). The resulting mixture was stirred at 60 °C. After completion, saturated Na₂S₂O₃ solution was added. The organic phase was separated, washed with brine and dried using anhydrous sodium sulfate. DCM was evaporated under vacuum to give **74** which was used for next step without purification.

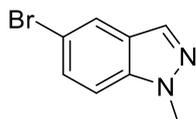


1-((3-bromo-1-(tetrahydro-2H-pyran-2-yl)-1H-indazol-5-yl)sulfonyl)piperidin-4-yl acetate (75). To the solution of 1-4 obtained above in EA was added 3,4-Dihydro-2H-pyran (55 mg, 0.66 mmol) and *p*-Toluenesulfonic acid monohydrate (19 mg, 0.1 mmol). The resulting mixture was stirred under reflux for 16 h. Ac₂O (67 μL, 0.66 mmol) was then added. After completion, the mixture was washed

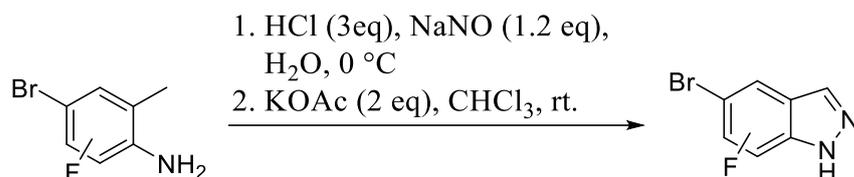
with water, brine and dried by anhydrous sodium sulfate. After evaporation, the residue was then purified using flash chromatography on silica gel (eluted with PE/EA) to give 138 mg **65** as white powder. Yield 86%.



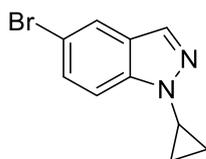
Synthesis of intermediate A.



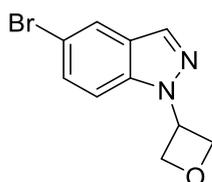
5-bromo-1-methyl-1H-indazole. To the solution of 5-bromo-1H-indazole (394 mg, 2 mmol) in acetone was added CH₃I (870 mg, 6 mmol) and K₂CO₃ (552 mg, 4 mmol). The resulting mixture was stirred at 80 °C for 12 h. After filtration, acetone was evaporated under vacuum. Purification by column chromatography on silico gel (eluted with PE/EA, 2/1) afforded the 220 mg product as white powder. Yield: 59%. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.95 (d, *J* = 1.0 Hz, 1H), 7.89 (dd, *J* = 1.8, 0.7 Hz, 1H), 7.49 (dd, *J* = 8.9, 1.8 Hz, 1H), 7.31 (dt, *J* = 8.9, 0.9 Hz, 1H), 4.09 (s, 3H).



To the mixture of the aniline (6 mmol) in H₂O and hydrochloric acid (2.5 mL) at 0 °C under stirring was added aqueous NaNO (7.2 mmol). After 30 min, H₂O was evaporated under vacuum. The residues were dispersed in CHCl₃. To the mixture, KOAc (18 mmol) was added. The resulting mixture was stirred at room temperature until completion. CHCl₃ was evaporated under vacuum. The residue was washed with water and dried under vacuum to afford the product.

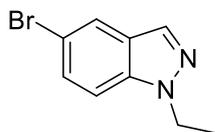


5-bromo-1-cyclopropyl-1H-indazole. The mixture of 5-bromo-1H-indazole (985 mg, 5 mmol), cyclopropylboronic acid (859 mg, 10 mmol), Cu(OAc)₂ (900 mg, 5 mmol), 2,2'-Bipyridine (780 mg, 5 mmol) and Na₂CO₃ (1.0 g, 10 mmol) in 30 mL 1,2-DCE was stirred at 70 °C for 2 h. After filtration, the filtrate was concentrated under vacuum. The residue was dissolved in EA and washed with saturated aqueous CuSO₄, brine and dried using anhydrous sodium sulfate. EA was evaporated under vacuum. The product was used for next step without purification.

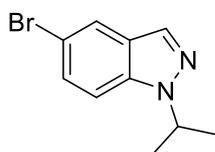


5-bromo-1-(oxetan-3-yl)-1H-indazole. To the solution of 5-bromo-1H-indazole (329 mg, 1.67 mmol) in DMF were added oxetan-3-yl 4-methylbenzenesulfonate (570mg, 2.5 mmol) and K₂CO₃ (691 mg,

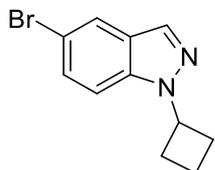
5 mmol). The resulting mixture was stirred at 110 °C for 12 h. After filtration, DMF was evaporated under vacuum. Purification by column chromatography on silico gel (eluted with PE/EA, 4/1) afforded the product.



5-bromo-1-ethyl-1H-indazole. To the solution of 5-bromo-1H-indazole (591 mg, 3 mmol) in DMF were added CH₃CH₂I (936 mg, 6 mmol) and K₂CO₃ (1.24 g, 9 mmol). The resulting mixture was stirred at 40 °C for 12 h. After filtration, DMF was evaporated under vacuum. Purification by column chromatography on silico gel (eluted with PE/EA, 8/1) afforded 125 mg product. Yield: 19%. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.94 (d, *J* = 1.1 Hz, 1H), 7.88 (d, *J* = 1.8 Hz, 1H), 7.46 (dd, *J* = 8.9, 1.8 Hz, 1H), 7.31 (d, *J* = 8.9 Hz, 1H), 4.43 (q, *J* = 7.3 Hz, 2H), 1.52 (t, *J* = 7.3 Hz, 3H).



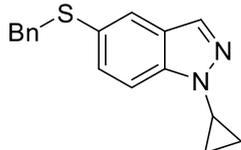
5-bromo-1-isopropyl-1H-indazole. To the solution of 5-bromo-1H-indazole (296 mg, 1.5 mmol) in 10 mL DMF were added *i*-PrI (510 mg, 3 mmol) and DBU (456 mg, 3 mmol). The mixture was stirred at room temperature for 48 h. After evaporation under vacuum, the residue was purified by column chromatography on silico gel (eluted with PE/EA, 10/1) to afford 160 mg product. Yield: 45%. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.94 (s, 1H), 7.86 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.43 (dd, *J* = 8.9, 1.7 Hz, 1H), 7.33 (d, *J* = 8.9 Hz, 1H), 4.81 (hept, *J* = 6.7 Hz, 1H), 1.59 (d, *J* = 6.6 Hz, 6H).



5-bromo-1-cyclobutyl-1H-indazole. To the solution of 5-bromo-1H-indazole (296 mg, 1.5 mmol) in 10 mL DMF were added cyclobutyl bromide (405 mg, 3 mmol) and NaH (180 mg (60%), 4.5 mmol). The mixture was stirred at 50 °C for 12 h. After evaporation under vacuum, the residue was purified by column chromatography on silico gel (eluted with PE/EA, 10/1) to afford 170 mg product. Yield: 45%.

Synthesis of intermediate B.

Examples:

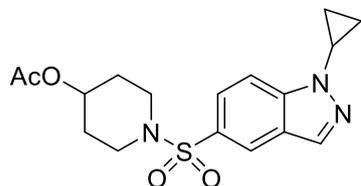


5-(benzylthio)-1-cyclopropyl-1H-indazole. To the solution of 5-bromo-1-cyclopropyl-1H-indazole (crude product, 5 mmol) was added Pd₂(dba)₃ (229 mg, 0.025 mmol), Xantphos (289 mg, 0.5 mmol), DIPEA (1650 μL, 10 mmol) and benzyl mercaptan (930 mg, 7.5 mmol). The resulting mixture was stirred at 90 °C for 4 h. After filtration and evaporation, the residue was purified by column chromatography on silico gel (eluted with PE/EA, 8/1) to afford 854 mg product as yellow solid.

Yield: 61% for 2 steps. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.84 (d, J = 0.9 Hz, 1H), 7.66 (dd, J = 1.7, 0.8 Hz, 1H), 7.48 (dt, J = 8.7, 0.9 Hz, 1H), 7.35 (dd, J = 8.7, 1.6 Hz, 1H), 7.28 – 7.16 (m, 5H), 4.06 (s, 2H), 3.56 (tt, J = 7.1, 3.7 Hz, 1H), 1.24 – 1.18 (m, 2H), 1.18 – 1.10 (m, 2H).

Synthesis of intermediate C

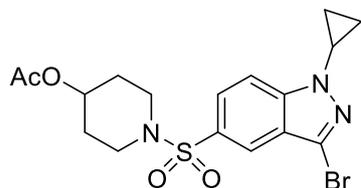
Example:



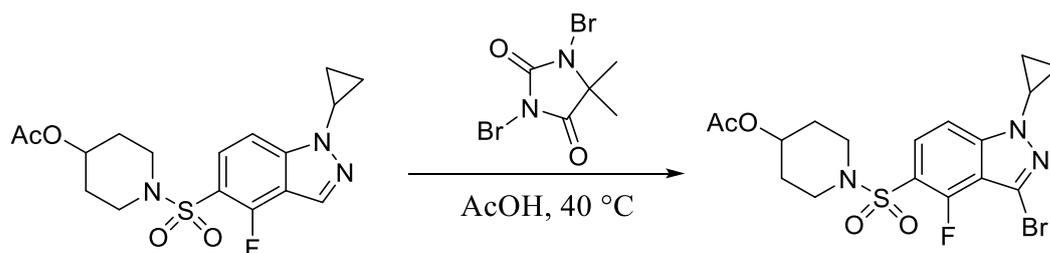
1-((3-bromo-1-cyclopropyl-1H-indazol-5-yl)sulfonyl)piperidin-4-yl acetate. To the solution of 5-(benzylthio)-1-cyclopropyl-1H-indazole (140 mg, 0.5 mmol) in 5 mL CH_3CN , 100 μL H_2O and 100 μL AcOH was added 5,5-dimethylhydantoin (200 mg, 1.0 mmol) slowly at -15°C under stirring. The mixture was kept at -15°C for 1 h. EA was added; the organic phase was washed with brine and dried by anhydrous sodium sulfate. EA was evaporated under vacuum. To the solution of the above product in DCM was added 4-hydroxypiperidine (100 mg, 1 mmol) and TEA (277 μL , 1 mmol). The mixture was stirred at room temperature for 30 min. Then it was washed with water and brine, and dried using anhydrous sodium sulfate. DCM was evaporated under vacuum. To the solution of the above product in EA was added Ac_2O (600 μL , 5 mmol) and pyridine (160 μL , 5 mmol). The mixture was stirred at reflux until disappearance of the substrate. The organic phase was washed with saturated aqueous CuSO_4 , brine and dried using anhydrous sodium sulfate. EA was evaporated under vacuum to afford the product, which can be used for next step without further purification.

Synthesis of intermediate D

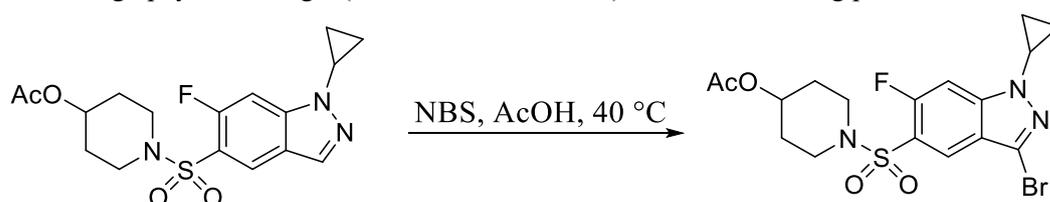
Examples:



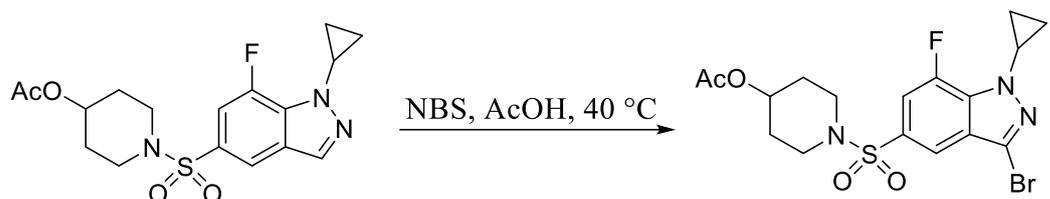
To the solution of the substrate (crude product, 0.5 mmol) in the mixture of 4 mL CH_3CN and 2 mL AcOH was added NBS (133mg, 0.75 mmol) at room temperature under stirring. The reaction was monitored using LC-MS. Upon the disappearance of the substrate, EA was added. The organic phase was washed with saturated aqueous NaHCO_3 and brine. After evaporation, the residue was purified by column chromatography on silico gel (eluted with PE/EA, 8/1) to afford 140 mg product as white powder. Yield: 64%. ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.00 (d, J = 8.9 Hz, 1H), 7.94 (s, 1H), 7.85 (d, J = 9.0 Hz, 1H), 4.67 (s, 1H), 3.89 (p, J = 5.2 Hz, 1H), 3.31 – 3.12 (m, 3H), 2.87 (d, J = 10.3 Hz, 2H), 2.02 – 1.80 (m, 5H), 1.61 (q, J = 9.9 Hz, 2H), 1.19 (d, J = 8.1 Hz, 4H).



To the solution of the substrate (76mg, 0.2 mmol) in 3 mL AcOH was added dibromo-5,5-dimethylhydantoin (86 mg, 0.3 mmol) at 40 °C under stirring. Upon the disappearance of the substrate, AcOH was evaporated under vacuum. The residue was purified with thin layer chromatography on silico gel (eluted with PE/EA, 2/1) to afford the 64 mg product. Yield: 70%.

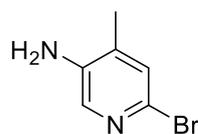


To the solution of the substrate (350 mg, 0.92 mmol) in 10 mL AcOH was added NBS (481 mg, 2.7 mmol) at 40 °C under stirring. Upon the disappearance of the substrate, AcOH was evaporated under vacuum. The residue was purified with column chromatography on silico gel (eluted with PE/EA, 3/1) to afford the 180 mg product. Yield: 42%.

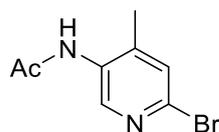


To the solution of the substrate (133 mg, 0.35 mmol) in 10 mL AcOH was added NBS (187 mg, 1.05 mmol) at 40 °C under stirring. Upon the disappearance of the substrate, AcOH was evaporated under vacuum. The residue was purified with thin layer chromatography on silico gel (eluted with PE/EA, 4/1) to afford the 45 mg product. Yield: 28%.

Synthesis of 78-84.

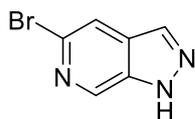


6-bromo-4-methylpyridin-3-amine (78). To the solution of 2-Bromo-5-nitro-4-picoline (2.0 g, 9.3 mmol) in methanol was added Raney Ni. The resulting mixture was stirred at room temperature under hydrogen atmosphere for 48 h. Raney Ni was removed through filtration; the filtrate was evaporated to afford **78**, which was used for next step without purification.

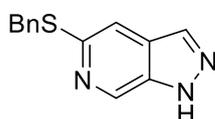


N-(6-bromo-4-methylpyridin-3-yl)acetamide (79). The mixture of **78** (crude product, 9.3 mmol) and Ac₂O (2.86 mL, 28 mmol) in PhCH₃ was stirred at 100 °C for 2 h. PhCH₃ was evaporated under

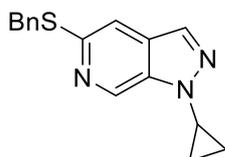
vacuum. The residue was purified with column chromatography on silico gel to afford 1.7 g compound **79** as white powder. Yield: 85% for 2 steps.



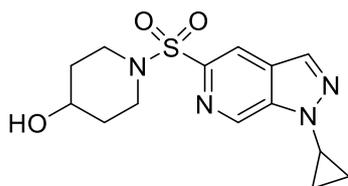
5-bromo-1H-pyrazolo[3,4-c]pyridine (80). To the solution of **79** in 20 mL PhCH₃ was added isoamyl nitrite (2.34 g, 20 mmol), Ac₂O (1.6 mL, 16 mmol), KOAc (1.44 g, 16 mmol) and 18-crown-6 (211 mmol, 16 mmol). The resulting mixture was stirred at 80 °C for 20 h. PhCH₃ was evaporated and the residue was dissolved in EA. The organic phase was washed with water and brine. EA was evaporated under vacuum. The residue was purified with column chromatography on silico gel. The product obtained above was dissolved in THF/water (10/10 mL). NaOH (1.28 g, 32 mmol) was added. The resulting mixture was stirred at room temperature for 2 h. After evaporating the THF under vacuum, 1N HCl was added slowly to the aqueous phase to make the pH ≈ 7. The solid was collected through filtration and dried under vacuum. Yield: 1.03 g, 63%. ¹H NMR (400 MHz, DMSO-*d*₆) δ 13.83 (s, 1H), 8.88 (s, 1H), 8.21 (d, *J* = 1.2 Hz, 1H), 8.04 (d, *J* = 1.0 Hz, 1H).



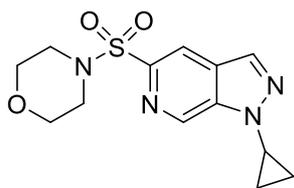
5-(benzylthio)-1H-pyrazolo[3,4-c]pyridine (81). To the solution of **80** (1.0 g, 5 mmol) was added Pd(dba)₂ (144 mg, 0.25 mmol), Xantphos (144 mg, 0.25 mmol), DIPEA (1650 μL, 10 mmol) and benzyl mercaptan (930 mg, 7.5 mmol). The resulting mixture was stirred at 90 °C for 4 h. After filtration and evaporation, the residue was purified by column chromatography on silico gel (eluted with PE/EA, 2/1) to afford 1.22 g product as yellow solid. Yield: 87%. ¹H NMR (400 MHz, Chloroform-*d*) δ 10.62 (s, 1H), 9.00 (s, 1H), 8.02 (s, 1H), 7.57 (d, *J* = 1.2 Hz, 1H), 7.39 – 7.32 (m, 2H), 7.29 – 7.24 (m, 2H), 7.23 – 7.18 (m, 1H), 4.42 (s, 2H).



5-(benzylthio)-1-cyclopropyl-1H-pyrazolo[3,4-c]pyridine (82). The mixture of **81** (1.2 g, 5 mmol), cyclopropylboronic acid (859 mg, 10 mmol), Cu(OAc)₂ (900 mg, 5 mmol), 2,2'-Bipyridine (780 mg, 5 mmol) and Na₂CO₃ (1.0 g, 10 mmol) in 30 mL 1,2-DCE was stirred at 70 °C for 2 h. After filtration, the filtrate was concentrated under vacuum. The residue was dissolved in EA and washed with water for 4 times and dried using anhydrous sodium sulfate. EA was evaporated under vacuum. The residue was purified by column chromatography on silico gel (eluted with PE/EA, 2/1) to afford 714 mg product as yellow solid. Yield: 51%.



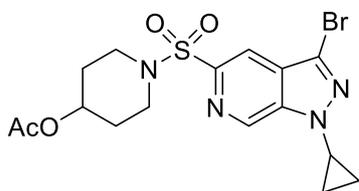
1-((1-cyclopropyl-1H-pyrazolo[3,4-c]pyridin-5-yl)sulfonyl)piperidin-4-ol (83a).



4-((1-cyclopropyl-1H-pyrazolo[3,4-c]pyridin-5-yl)sulfonyl)morpholine (**83b**).

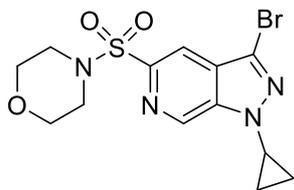
To the solution of **82** (140 mg, 0.5 mmol) in 5 mL CH₃CN, 100 μ L H₂O and 100 μ L AcOH was added 5,5-dimethylhydantoin (200 mg, 1.0 mmol) slowly at -15 °C under stirring. The mixture was kept at -15 °C for 1 h. EA was added; the organic phase was washed with brine and dried by anhydrous sodium sulfate. EA was evaporated under vacuum.

To the solution of the above product in DCM was added 4-hydroxypiperidine (100 mg, 1 mmol, for **83a**) or morpholine (87 mg, 1 mmol, for **83b**) and TEA (277 μ L, 1 mmol). The mixture was stirred at room temperature for 30 min. Then it was washed with water and brine, and dried using anhydrous sodium sulfate. DCM was evaporated under vacuum to afford the product, which can be used for next step without further purification.



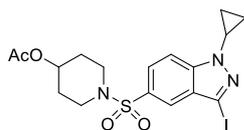
1-((3-bromo-1-cyclopropyl-1H-pyrazolo[3,4-c]pyridin-5-yl)sulfonyl)piperidin-4-yl acetate (**84a**).

To the solution of **83a** (crude product, 4 mmol) in EA was added Ac₂O (2.0 mL, 20 mmol) and pyridine (1480 μ L, 16 mmol). The mixture was stirred at reflux until disappearance of the substrate. The organic phase was washed with water and brine and dried using anhydrous sodium sulfate. EA was evaporated under vacuum. The crude product was dissolved in TFA/AcOH (8/8 mL). To the solution was added NBS (1.42 g, 8 mmol). The mixture was stirred overnight at 50 °C. The solvent was evaporated under vacuum. The residue was dissolved in ethyl acetate and washed with saturated aqueous NaHCO₃ and brine. After evaporation, the residue was purified by column chromatography on silico gel (eluted with PE/EA, 2/1) to afford 900 mg **74a** as white powder. Yield: 51% for two steps. ¹H NMR (400 MHz, Chloroform-*d*) δ 9.13 (d, *J* = 1.2 Hz, 1H), 8.24 (d, *J* = 1.2 Hz, 1H), 4.82 (tt, *J* = 7.9, 3.8 Hz, 1H), 3.86 – 3.71 (m, 1H), 3.61 (ddd, *J* = 11.7, 7.0, 4.0 Hz, 2H), 3.21 (ddd, *J* = 12.4, 8.5, 3.6 Hz, 2H), 2.01 (s, 3H), 1.95 (ddd, *J* = 13.9, 7.2, 3.6 Hz, 2H), 1.76 (dtd, *J* = 12.5, 8.3, 3.8 Hz, 2H), 1.32 (tq, *J* = 6.9, 2.6, 2.0 Hz, 4H).

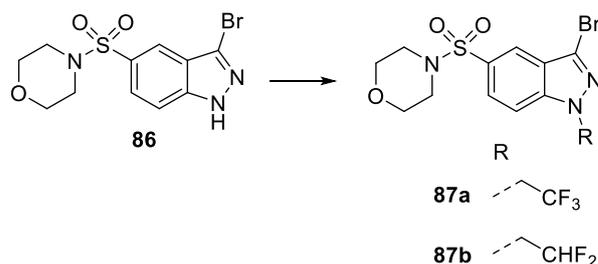


4-((3-bromo-1-cyclopropyl-1H-pyrazolo[3,4-c]pyridin-5-yl)sulfonyl)morpholine (**84b**). To the solution of **83b** (97 mg, 0.3 mmol) in CH₃CN/AcOH (3/3 mL) was added dibromo-5,5-dimethylhydantoin (129 mg, 0.45 mmol). The mixture was stirred at room temperature. Upon the disappearance of **83b**, EA was added. The organic phase was washed with saturated aqueous NaHCO₃ and brine. After evaporation, the residue was purified by column chromatography on silico

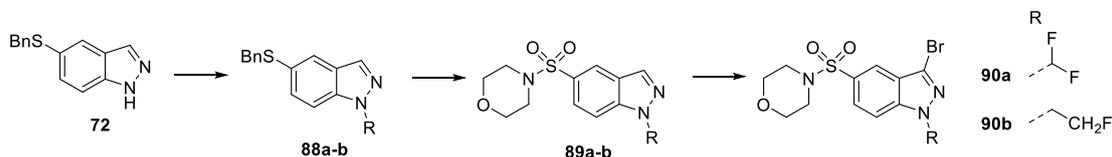
gel to afford 68 mg 84b as white powder. Yield: 59%.



1-((1-cyclopropyl-3-iodo-1H-indazol-5-yl)sulfonyl)piperidin-4-yl acetate (85). To the solution of the substrate (crude product, 1 mmol) in CH₃CN/H₂SO₄ (8/2 mL) was added NIS (562 mg, 2.5 mmol). The mixture was stirred at room temperature for 48 h. EA was added. The organic phase was washed with sat. aq. NaHCO₃ and brine and dried with Na₂SO₄. After evaporating the EA, the residue was purified with column chromatography on silico gel (eluted with PE/EA, 2/1) to afford 180 mg product as white powder. Yield: 37%



To the solution of 86 (70 mg, 0.2 mmol) in 2 mL DMF was added 2-iodo-1,1,1-trifluoroethane (for **87a**, 84 mg, 0.4 mmol) or 2-iodo-1,1-difluoroethane (for **87b**, 76 mg, 0.4 mmol) and K₂CO₃ (56 mg, 0.4 mmol). The mixture was stirred at 80 °C overnight. After filtration, the filtrate was concentrated under vacuum and the residue was purified with column chromatography on silico gel (eluted with PE/EA, 3/2) to afford the product **87a** (39 mg, yield 45%), **87b** (47 mg, yield 58%).



5-(benzylthio)-1-(difluoromethyl)-1H-indazole (88a). To the solution of **72** (240 mg, 1 mmol) in CH₃CN was added Diethyl bromodifluoromethanephosphonate (534 mg, 2 mmol) and KF (116 mg, 2 mmol). The mixture was stirred at 40 °C for 48h. After filtration, the filtrate was concentrated under vacuum and the residue was purified with column chromatography on silico gel (eluted with PE/EA, 12/1) to afford the product **88a** (245 mg, yield 84%). ¹H NMR (400 MHz, Chloroform-*d*) δ 8.24 (s, 1H), 7.65 (d, *J* = 9.1 Hz, 1H), 7.61 – 7.23 (m, 8H), 4.16 (s, 2H).

5-(benzylthio)-1-(2-fluoroethyl)-1H-indazole (88b). To the solution of **72** (240 mg, 1 mmol) in DMF was added 1-Fluoro-2-iodoethane (348 mg, 2 mmol) and K₂CO₃ (276 mg, 2 mmol). The mixture was stirred at 80 °C overnight. After filtration, the filtrate was concentrated under vacuum and the residue was purified with column chromatography on silico gel (eluted with PE/EA, 2/1) to afford the product **88b**, 186 mg, yield 65%.

The procedure for synthesis of **89a-b** was as the described in the synthesis of **83b**.

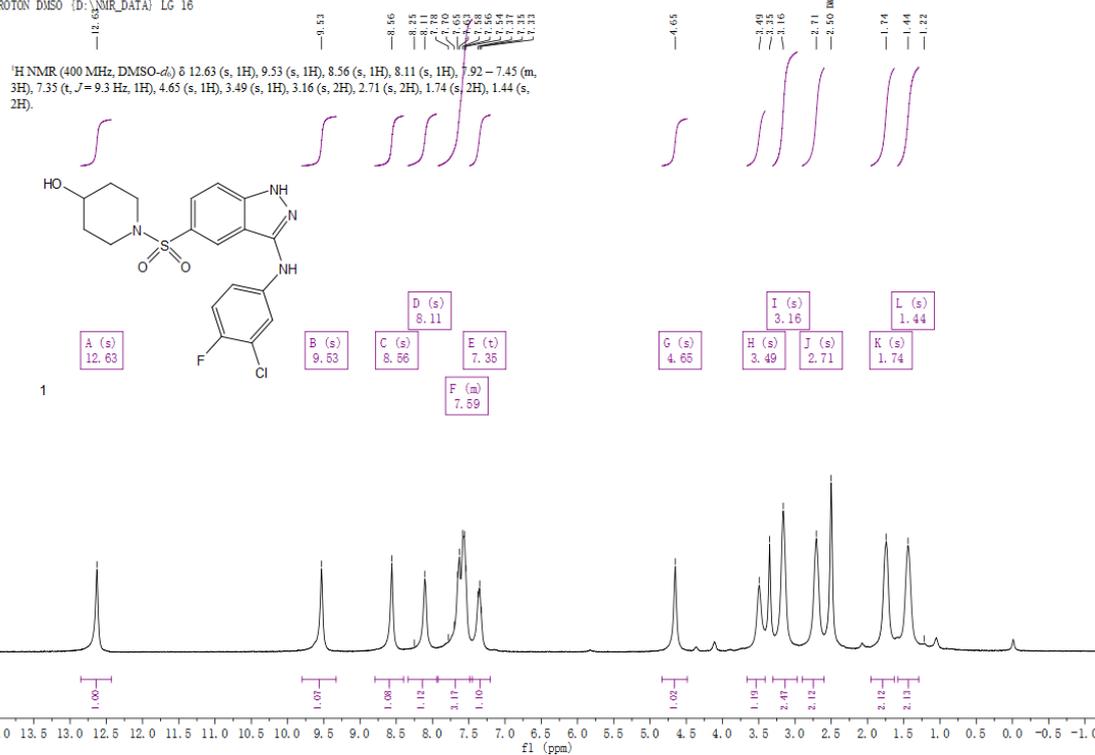
4-((3-bromo-1-(difluoromethyl)-1H-indazol-5-yl)sulfonyl)morpholine (90a). To the solution of **89a** (98 mg, 0.31 mmol) in 4 mL CH₃CN and 2 mL TFA was added NBS (83 mg, 0.465 mmol). The mixture was stirred at 80 °C. Upon the disappearance of **89a**, ethyl acetate was added. The organic phase was washed with saturated aqueous NaHCO₃ and brine. After evaporation, the residue was purified by column chromatography on silico gel to afford 61 mg **90a**. Yield: 50%.

4-((3-bromo-1-(2-fluoroethyl)-1H-indazol-5-yl)sulfonyl)morpholine (**90b**). To the solution of **89b** (0.30 mmol, crude product) in 4 mL CH₃CN and 2 mL AcOH was added NBS (169 mg, 0.95 mmol). The mixture was stirred at 40 °C overnight. Ethyl acetate was added. The organic phase was washed with saturated aqueous NaHCO₃ and brine. After evaporation, the residue was purified by column chromatography on silico gel to afford 87 mg **90b**. Yield: 74%.

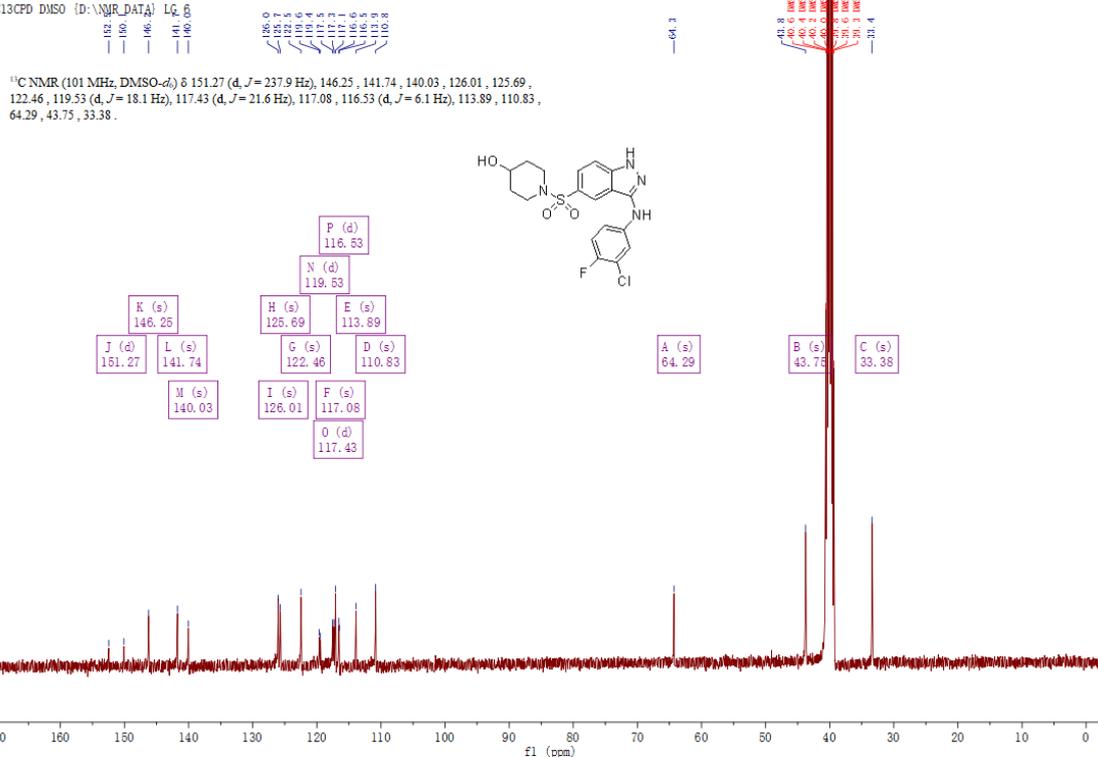
¹H NMR and ¹³C NMR spectrum

Compound 1

20190306-wet-1095-1-H/10
PROTON DMSO [D:\NMR_DATA] LG 16



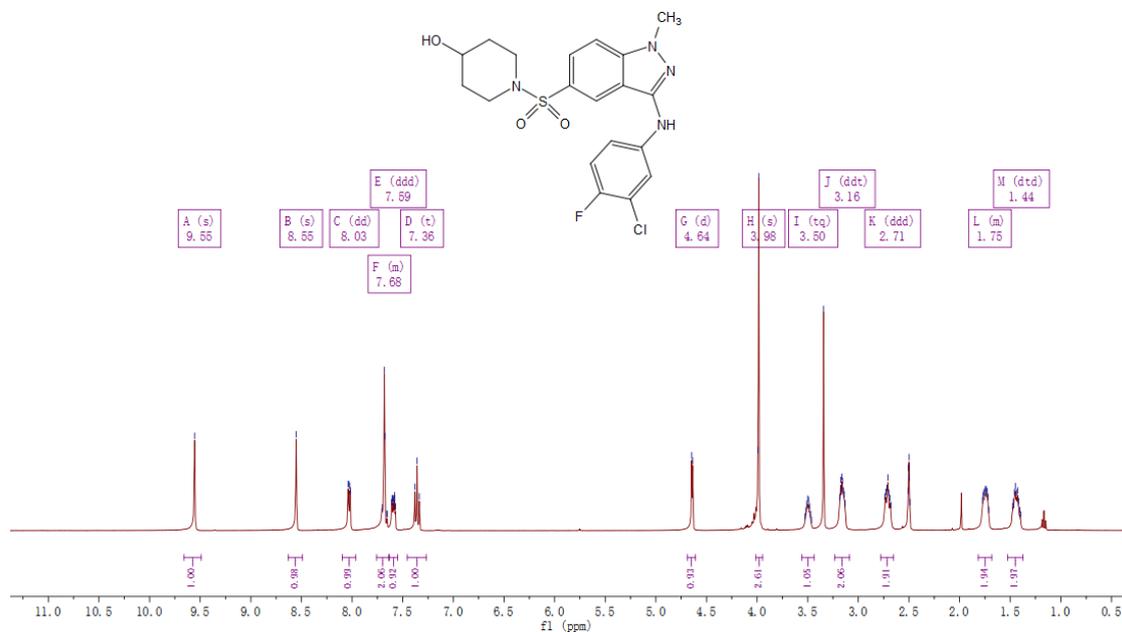
20190306-wet-1095-1-C/10
C13CPD DMSO [D:\NMR_DATA] LG 16



Compound 2.

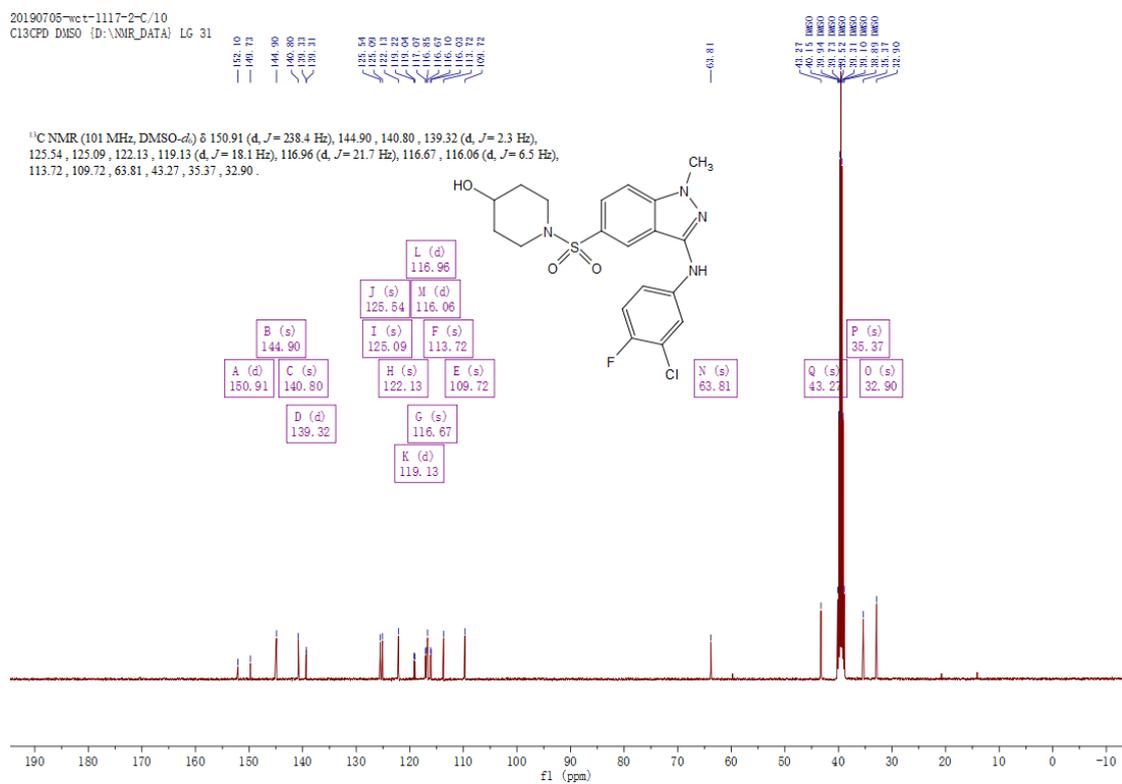
20190705-wet-1117-2-H/10
 PROTON DMSO [D:\NMR_DATA] LG 33

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.55 (s, 1H), 8.55 (s, 1H), 8.03 (dd, *J* = 6.6, 2.7 Hz, 1H), 7.76–7.64 (m, 2H), 7.59 (ddd, *J* = 9.1, 4.1, 2.7 Hz, 1H), 7.36 (t, *J* = 9.1 Hz, 1H), 4.64 (d, *J* = 3.8 Hz, 1H), 3.98 (s, 3H), 3.50 (tq, *J* = 7.6, 3.5 Hz, 1H), 3.16 (ddt, *J* = 10.7, 6.7, 3.5 Hz, 2H), 2.71 (ddd, *J* = 11.9, 8.5, 3.5 Hz, 2H), 1.81–1.68 (m, 2H), 1.44 (dtd, *J* = 12.2, 7.9, 3.5 Hz, 2H).



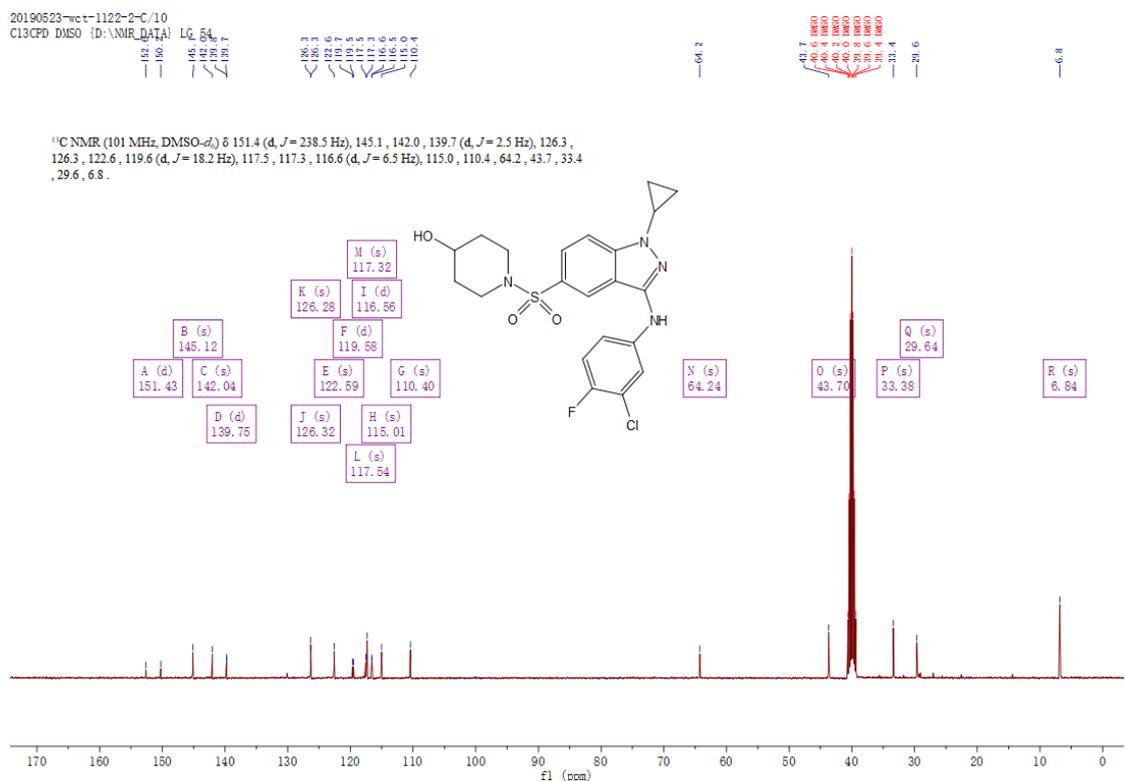
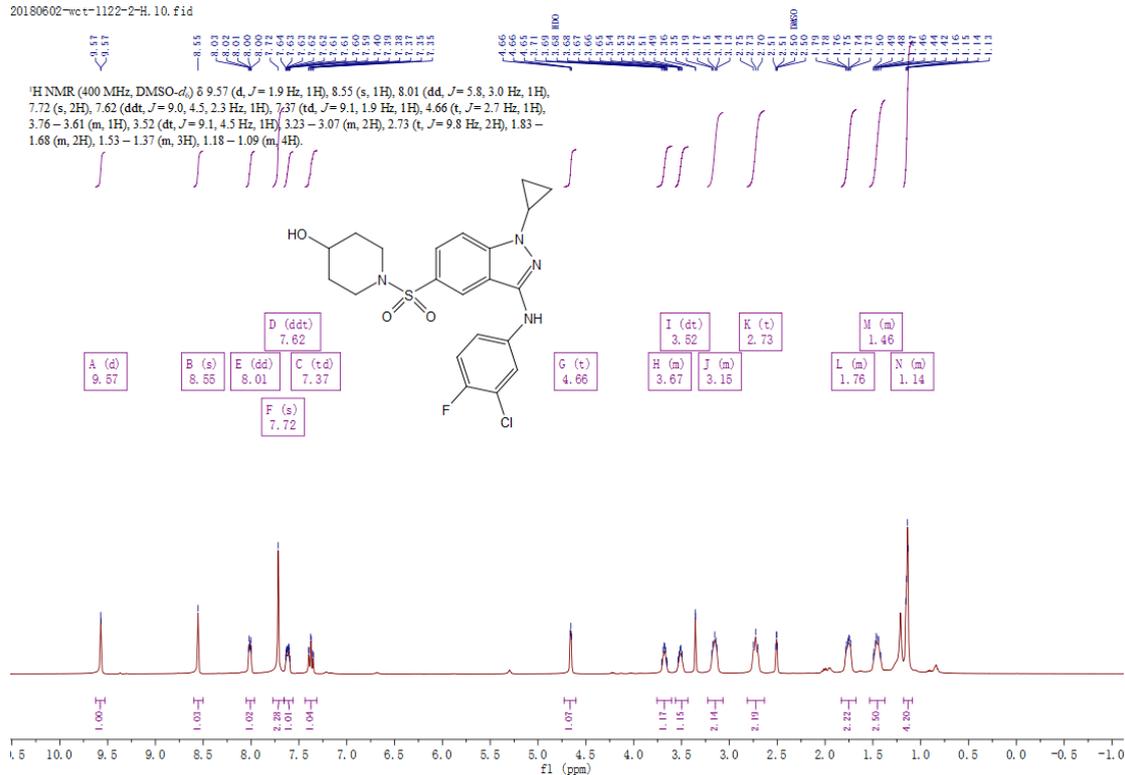
20190705-wet-1117-2-C/10
 C13CPD DMSO [D:\NMR_DATA] LG 31

¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.91 (d, *J* = 238.4 Hz), 144.90, 140.80, 139.32 (d, *J* = 2.3 Hz), 125.54, 125.09, 122.13, 119.13 (d, *J* = 18.1 Hz), 116.96 (d, *J* = 21.7 Hz), 116.67, 116.06 (d, *J* = 6.5 Hz), 113.72, 109.72, 63.81, 43.27, 35.37, 32.90.



Compound 3.

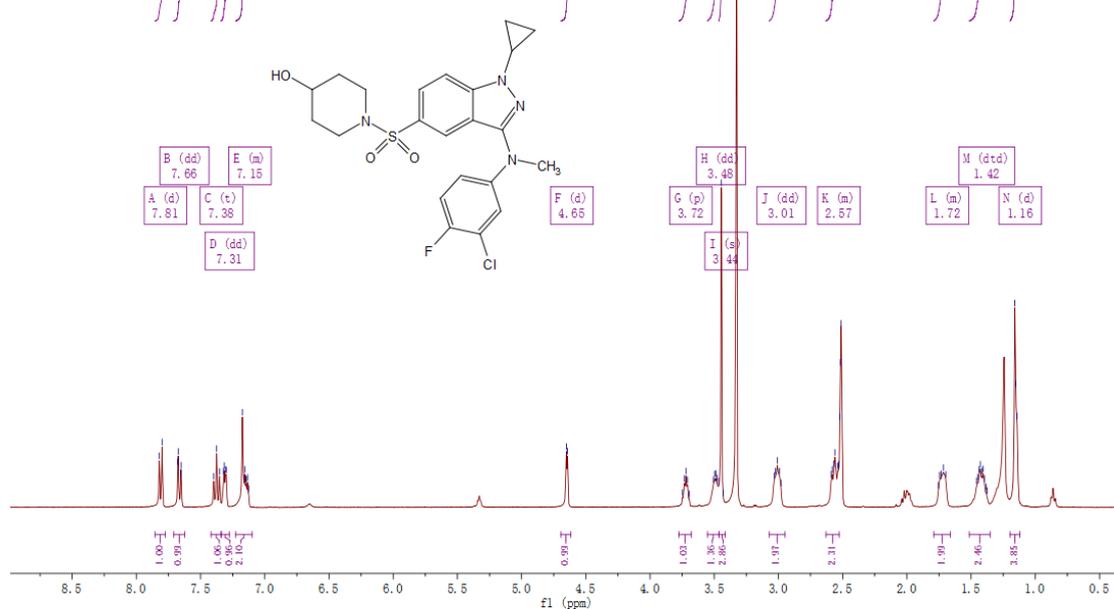
20180602-wet-1122-2-H.10.fid



Compound 4.

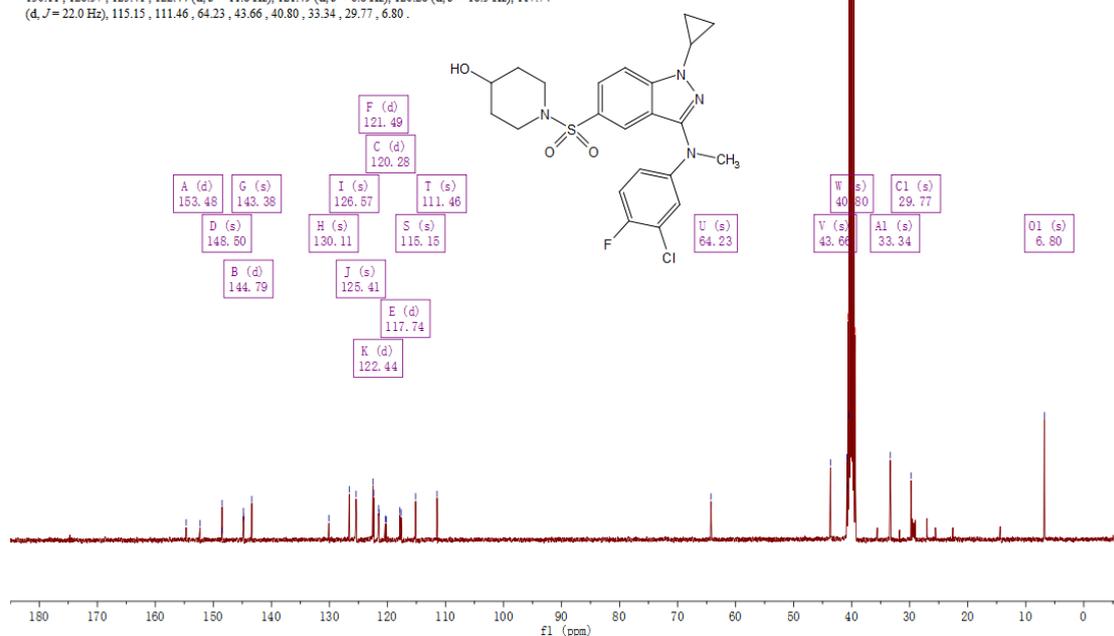
20190525-wct-1135-1-H/10
 PROTON DMSO (D:\NMR_DATA\LG_31)

¹H NMR (400 MHz, DMSO-*d*₆) δ 7.81 (d, *J* = 8.9 Hz, 1H), 7.66 (dd, *J* = 8.9, 1.6 Hz, 1H), 7.38 (t, *J* = 9.0 Hz, 1H), 7.31 (dd, *J* = 6.6, 2.8 Hz, 1H), 7.23 – 7.10 (m, 2H), 4.65 (d, *J* = 3.8 Hz, 1H), 3.72 (p, *J* = 6.0 Hz, 1H), 3.48 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.44 (s, 3H), 3.01 (dd, *J* = 11.2, 5.3 Hz, 2H), 2.63 – 2.53 (m, 2H), 1.79 – 1.66 (m, 2H), 1.42 (dtd, *J* = 11.9, 8.0, 3.5 Hz, 2H), 1.16 (d, *J* = 3.3 Hz, 4H).



20190528-wct-1135-1-C/10
 C13CPD DMSO (D:\NMR_DATA\LG_31)

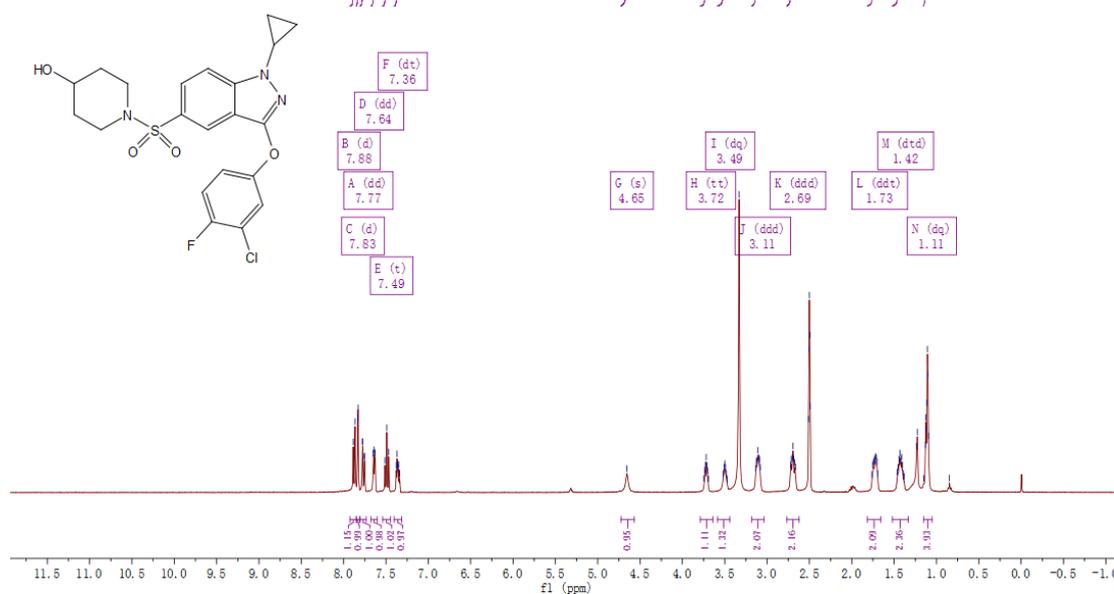
¹³C NMR (101 MHz, DMSO-*d*₆) δ 153.48 (d, *J* = 242.0 Hz), 148.50, 144.79 (d, *J* = 2.9 Hz), 143.38, 130.11, 126.57, 125.41, 122.44 (d, *J* = 11.8 Hz), 121.49 (d, *J* = 6.8 Hz), 120.28 (d, *J* = 18.5 Hz), 117.74 (d, *J* = 22.0 Hz), 115.15, 111.46, 64.23, 43.66, 40.80, 33.34, 29.77, 6.80.



Compound 5.

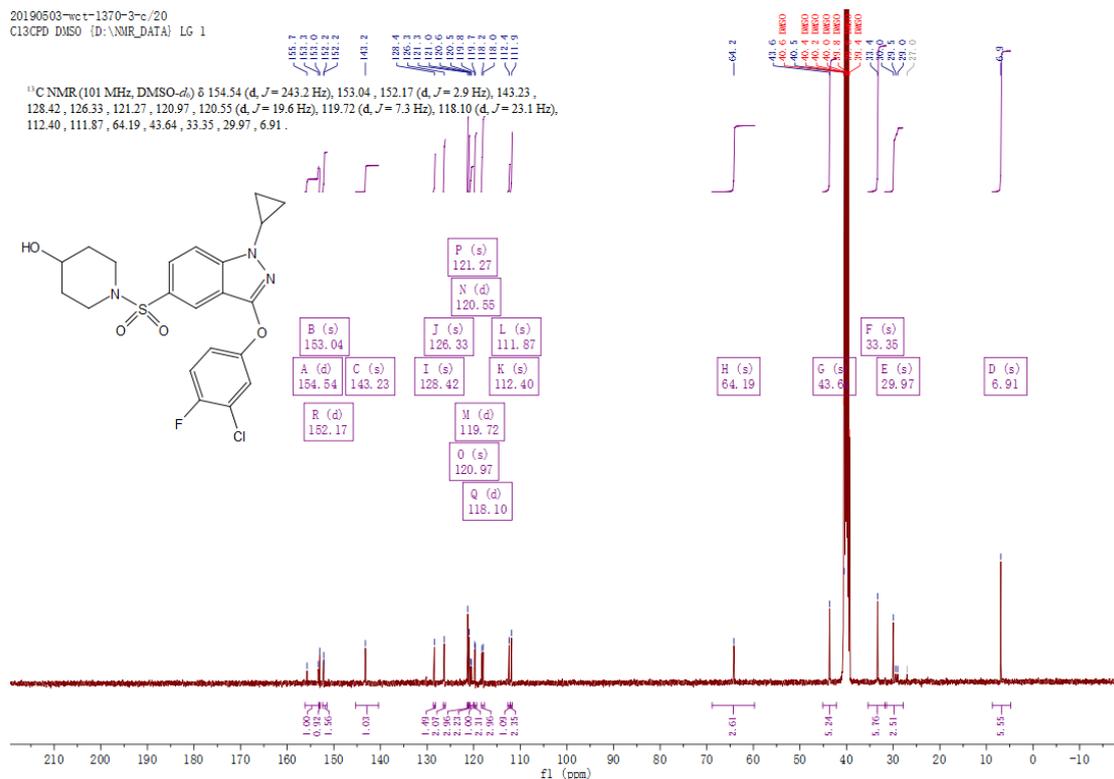
20190503-wct-1370-3-H/10
 PROTON DMSO [D:\NMR_DATA] LG 1

¹H NMR (400 MHz, DMSO-*d*₆) δ 7.88 (d, *J* = 8.9 Hz, 1H), 7.83 (d, *J* = 1.5 Hz, 1H), 7.77 (dd, *J* = 8.9, 1.7 Hz, 1H), 7.64 (dd, *J* = 6.2, 3.0 Hz, 1H), 7.49 (t, *J* = 9.0 Hz, 1H), 7.36 (dt, *J* = 9.1, 3.5 Hz, 1H), 4.65 (s, 1H), 3.72 (tt, *J* = 6.8, 4.1 Hz, 1H), 3.49 (dq, *J* = 7.7, 4.0 Hz, 1H), 3.11 (ddd, *J* = 11.2, 7.1, 3.7 Hz, 2H), 2.69 (ddd, *J* = 11.7, 8.3, 3.4 Hz, 2H), 1.73 (ddt, *J* = 13.9, 7.2, 3.5 Hz, 2H), 1.42 (dtd, *J* = 12.2, 8.1, 3.7 Hz, 2H), 1.11 (dq, *J* = 7.7, 2.5 Hz, 4H).



20190503-wct-1370-3-c/20
 C13CPD DMSO [D:\NMR_DATA] LG 1

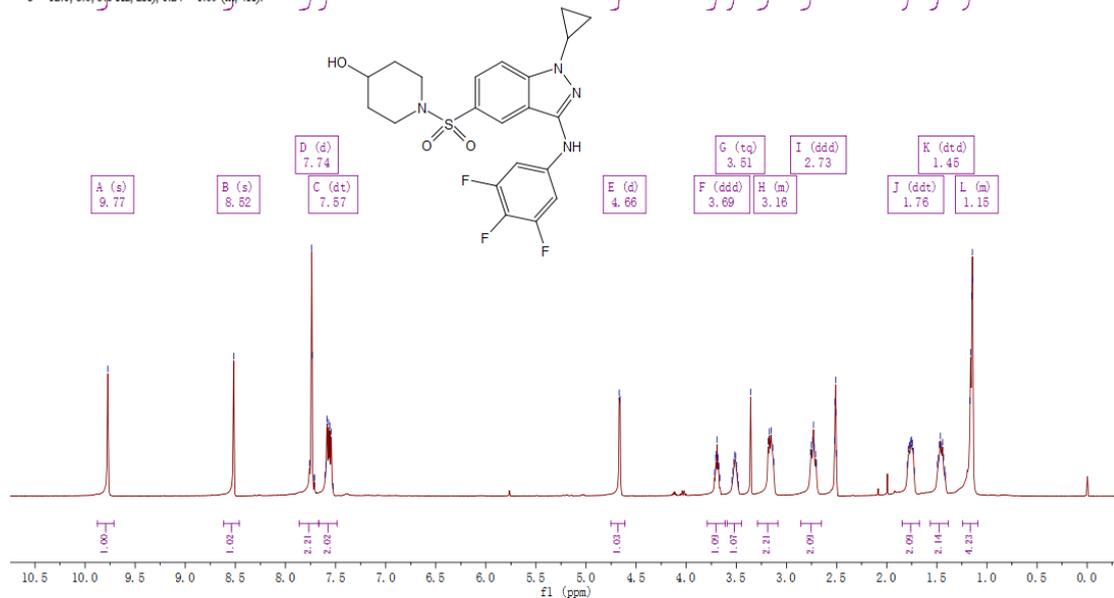
¹³C NMR (101 MHz, DMSO-*d*₆) δ 154.54 (d, *J* = 243.2 Hz), 153.04, 152.17 (d, *J* = 2.9 Hz), 143.23, 128.42, 126.33, 121.27, 120.97, 120.55 (d, *J* = 19.6 Hz), 119.72 (d, *J* = 7.3 Hz), 118.10 (d, *J* = 23.1 Hz), 112.40, 111.87, 64.19, 43.64, 33.35, 29.97, 6.91.



Compound 6.

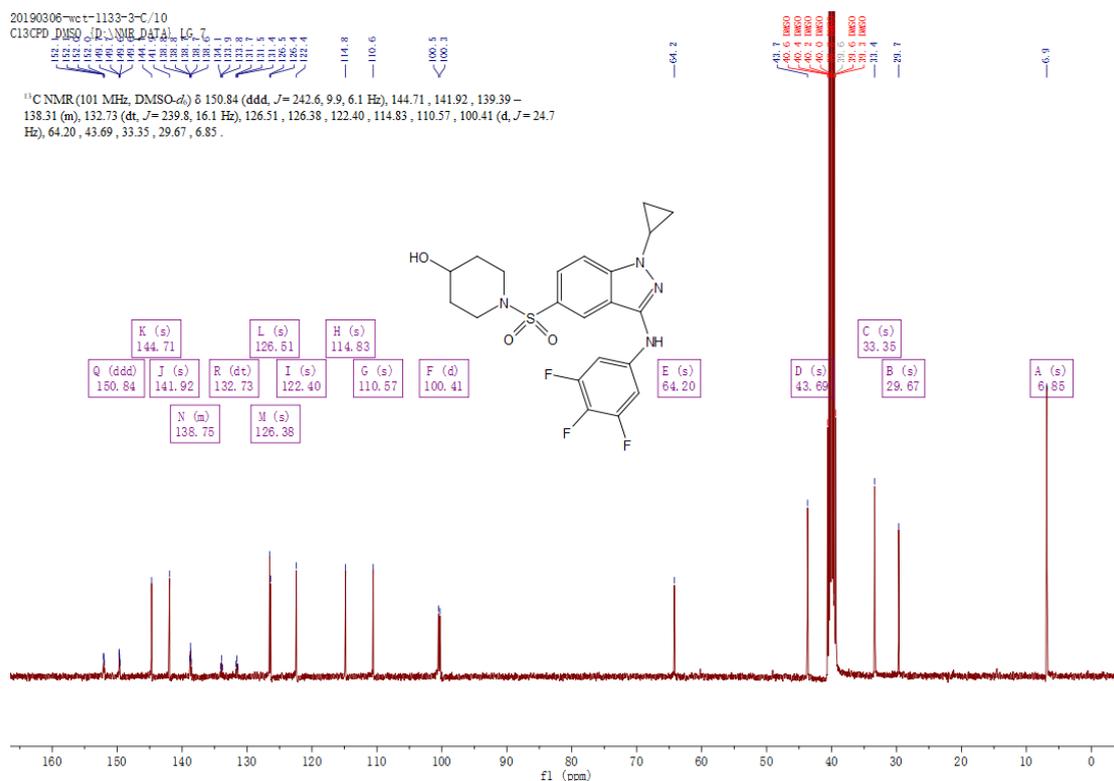
20190306-wet-1133-3-H/10
 PROTON DMSO (D₂O-NMR_DATA) LG 17

¹H NMR (400 MHz, DMSO-d₆) δ 9.77 (s, 1H), 8.52 (s, 1H), 7.74 (d, J = 1.8 Hz, 2H), 7.57 (dt, J = 10.9, 5.0 Hz, 2H), 4.66 (d, J = 3.9 Hz, 1H), 3.69 (ddd, J = 10.6, 6.9, 4.3 Hz, 1H), 3.51 (tq, J = 7.5, 3.7 Hz, 1H), 3.29–3.09 (m, 2H), 2.73 (ddd, J = 11.6/8.4, 3.4 Hz, 2H), 1.76 (ddt, J = 13.9, 7.2, 3.6 Hz, 2H), 1.45 (ddt, J = 12.0, 8.0, 3.6 Hz, 2H), 1.24–1.09 (m, 4H).



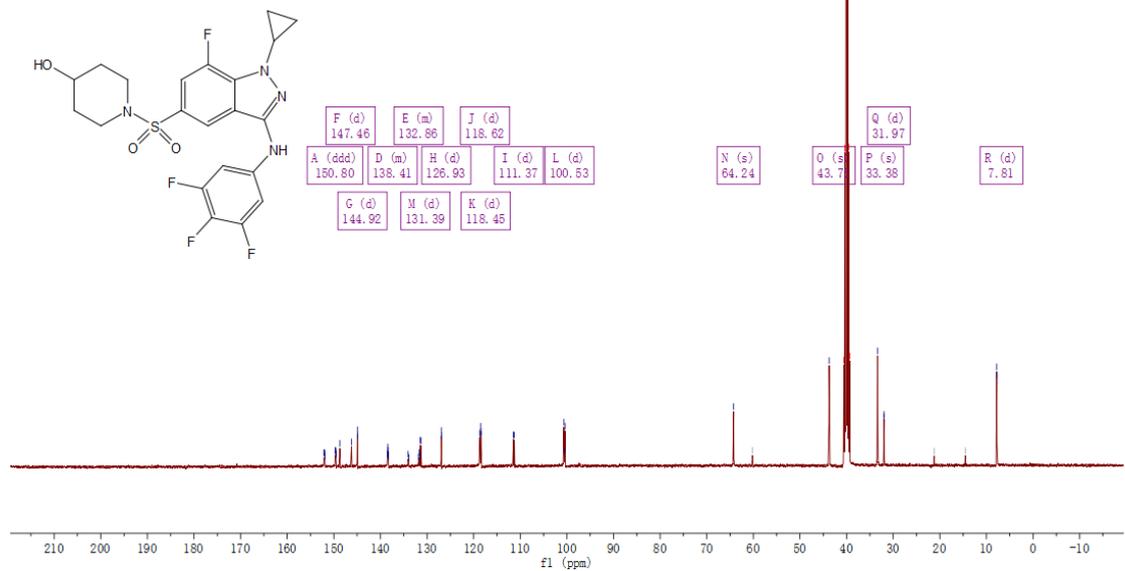
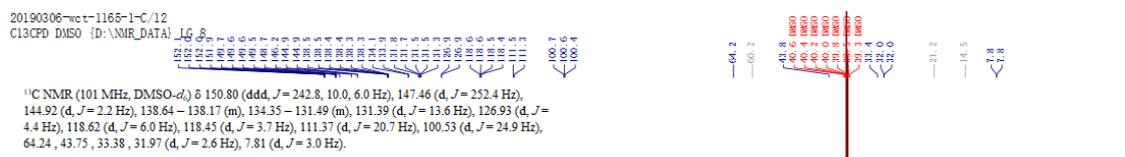
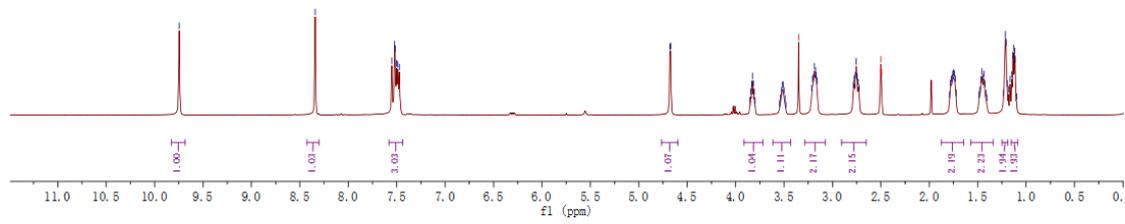
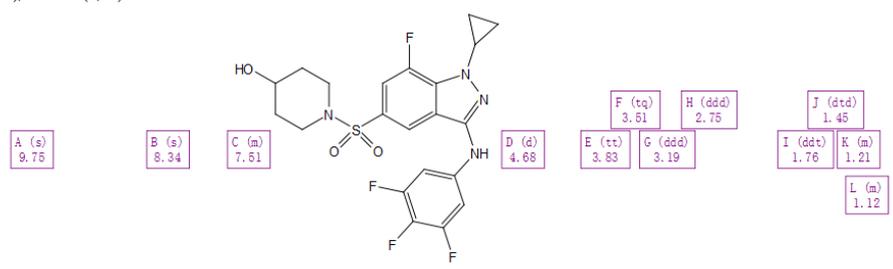
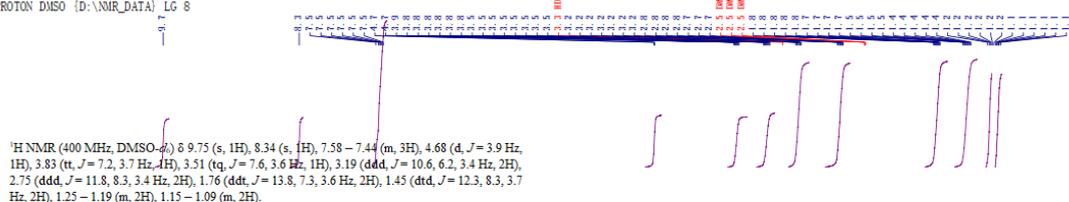
20190306-wet-1133-3-C/10
 C13CPD DMSO (D₂O-NMR_DATA) LG 17

¹³C NMR (101 MHz, DMSO-d₆) δ 150.84 (ddd, J = 242.6, 9.9, 6.1 Hz), 144.71, 141.92, 139.39–138.31 (m), 132.73 (dt, J = 239.8, 16.1 Hz), 126.51, 126.38, 122.40, 114.83, 110.57, 100.41 (d, J = 24.7 Hz), 64.20, 43.69, 33.35, 29.67, 6.85.



Compound 7

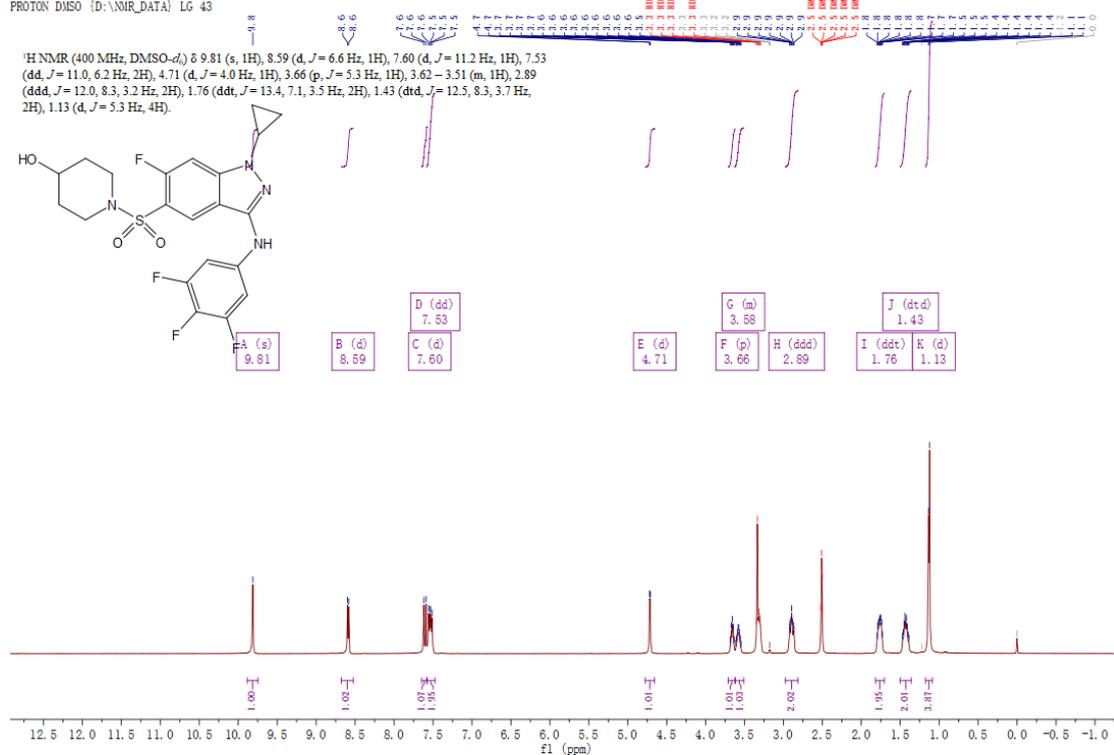
20190306-wct-1165-1-H/10
 PROTON DMSO [D:\NMR_DATA] LG 8



Compound 8.

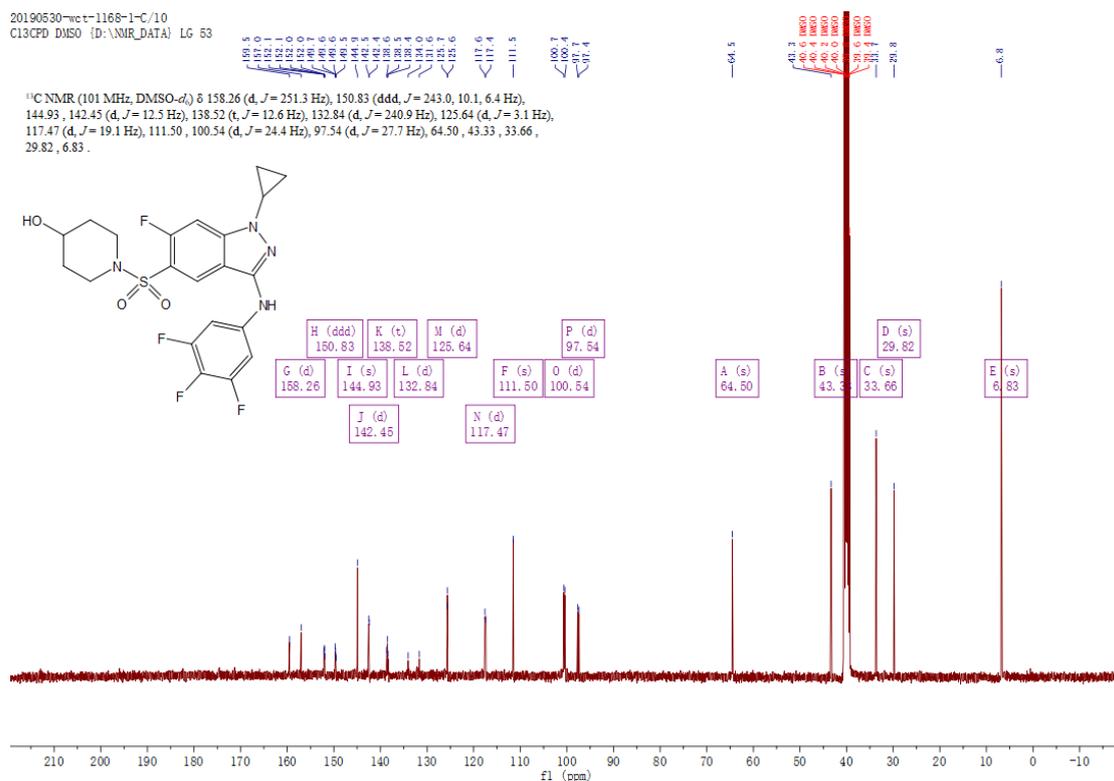
20190530-wet-1168-1-H/10
 PROTON DMSO [D:\NMR_DATA] LG 43

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.81 (s, 1H), 8.59 (d, *J* = 6.6 Hz, 1H), 7.60 (d, *J* = 11.2 Hz, 1H), 7.53 (dd, *J* = 11.0, 6.2 Hz, 2H), 4.71 (d, *J* = 4.0 Hz, 1H), 3.66 (p, *J* = 5.3 Hz, 1H), 3.62–3.51 (m, 1H), 2.89 (ddd, *J* = 12.0, 8.3, 3.2 Hz, 2H), 1.76 (ddt, *J* = 13.4, 7.1, 3.5 Hz, 2H), 1.43 (dtd, *J* = 12.5, 8.3, 3.7 Hz, 2H), 1.13 (d, *J* = 5.3 Hz, 4H).



20190530-wet-1168-1-C/10
 C13CPD DMSO [D:\NMR_DATA] LG 53

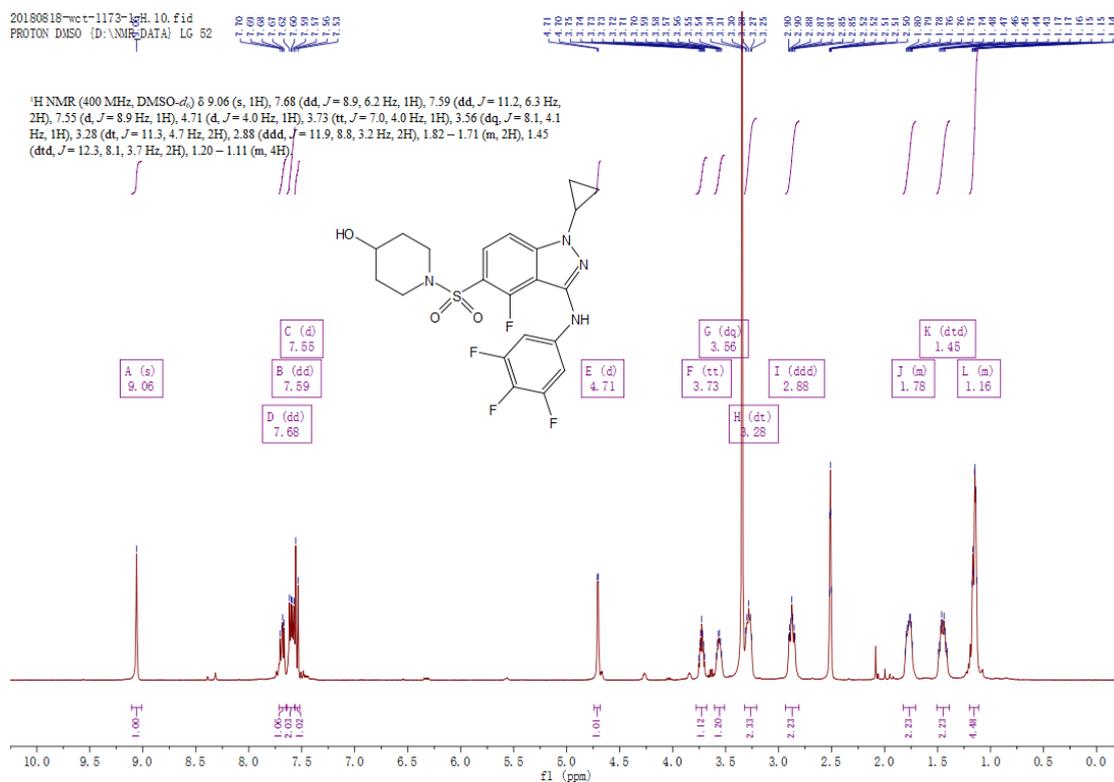
¹³C NMR (101 MHz, DMSO-*d*₆) δ 158.26 (d, *J* = 251.3 Hz), 150.83 (ddd, *J* = 243.0, 10.1, 6.4 Hz), 144.93, 142.45 (d, *J* = 12.5 Hz), 138.52 (t, *J* = 12.6 Hz), 132.84 (d, *J* = 240.9 Hz), 125.64 (d, *J* = 3.1 Hz), 117.47 (d, *J* = 19.1 Hz), 111.50, 100.54 (d, *J* = 24.4 Hz), 97.54 (d, *J* = 27.7 Hz), 64.50, 43.33, 33.66, 29.82, 6.83.



Compound 9.

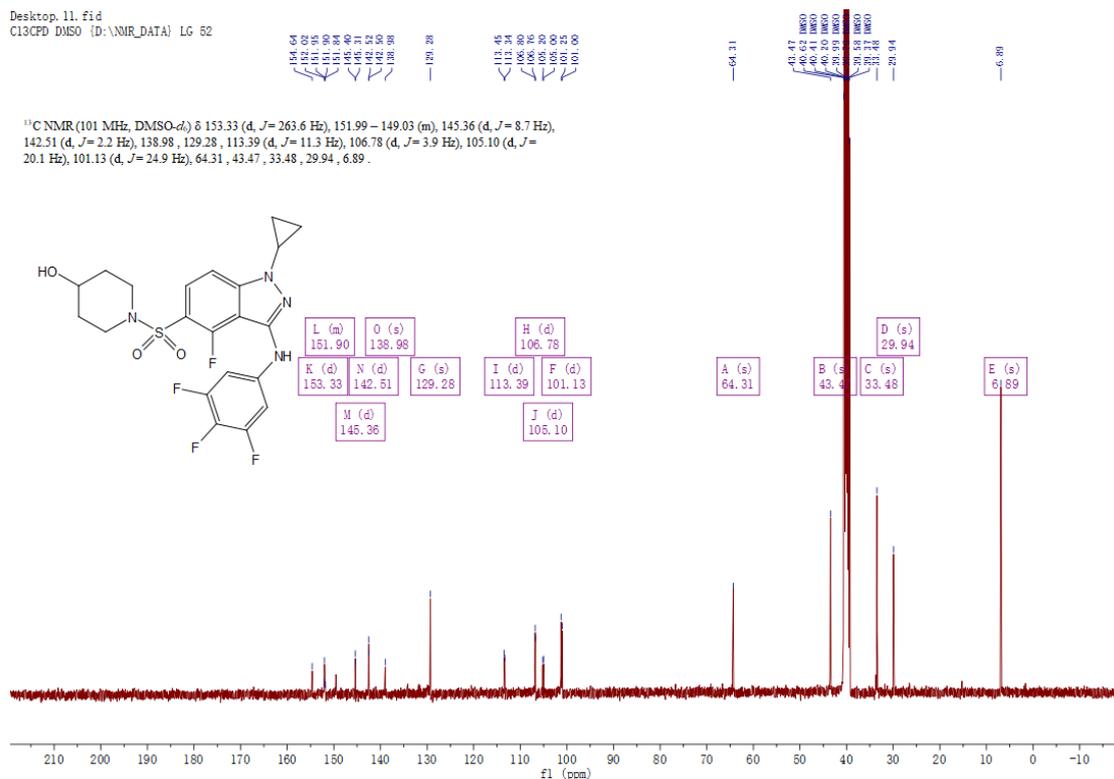
20180818-wct-1173-1gH.10.fid
 PROTON DMSO [D:\NMR\DATA] LG 52

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.06 (s, 1H), 7.68 (dd, *J* = 8.9, 6.2 Hz, 1H), 7.59 (dd, *J* = 11.2, 6.3 Hz, 2H), 7.55 (d, *J* = 8.9 Hz, 1H), 4.71 (d, *J* = 4.0 Hz, 1H), 3.73 (tt, *J* = 7.0, 4.0 Hz, 1H), 3.56 (dq, *J* = 8.1, 4.1 Hz, 1H), 3.28 (dt, *J* = 11.3, 4.7 Hz, 2H), 2.88 (ddd, *J* = 11.9, 8.8, 3.2 Hz, 2H), 1.82 – 1.71 (m, 2H), 1.45 (dtd, *J* = 12.3, 8.1, 3.7 Hz, 2H), 1.20 – 1.11 (m, 4H)



Desktop. 11.fid
 C13CPD DMSO [D:\NMR\DATA] LG 52

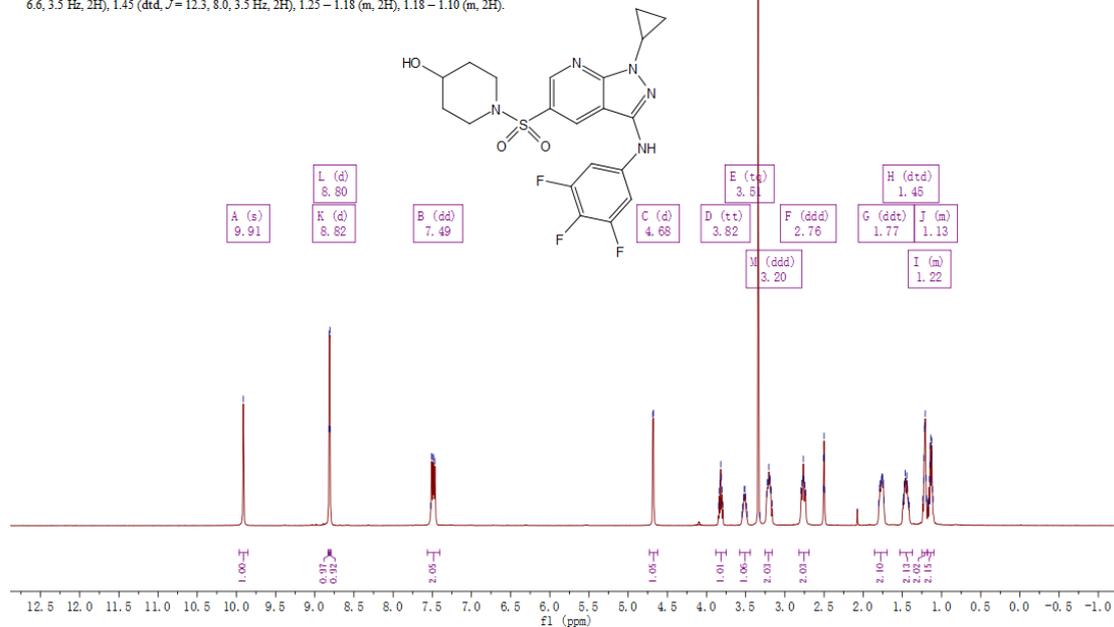
¹³C NMR (101 MHz, DMSO-*d*₆) δ 153.33 (d, *J* = 263.6 Hz), 151.99 – 149.03 (m), 145.36 (d, *J* = 8.7 Hz), 142.51 (d, *J* = 2.2 Hz), 138.98, 129.28, 113.39 (d, *J* = 11.3 Hz), 106.78 (d, *J* = 3.9 Hz), 105.10 (d, *J* = 20.1 Hz), 101.13 (d, *J* = 24.9 Hz), 64.31, 43.47, 33.48, 29.94, 6.89.



Compound 10.

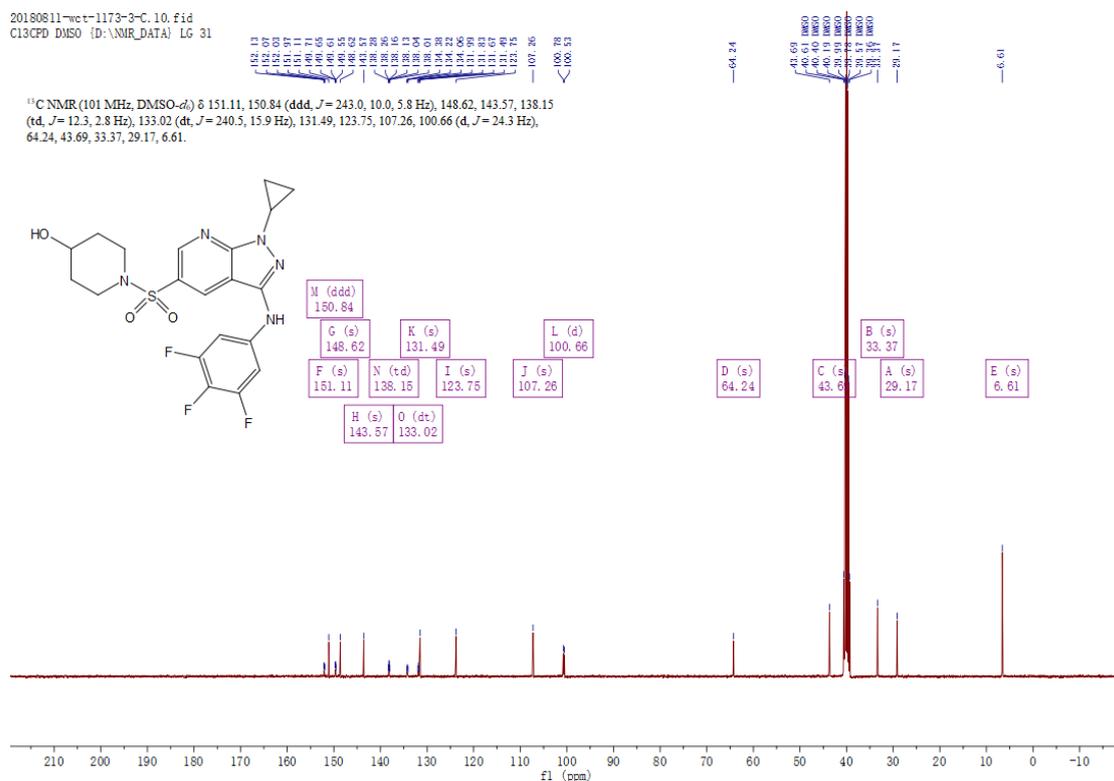
20180811-wet-1171-3-H.10.fid
 PROTON DMSO [D:\NMR_DATA] LG 31

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.91 (s, 1H), 8.82 (d, *J* = 2.1 Hz, 1H), 8.80 (d, *J* = 2.1 Hz, 1H), 7.49 (dd, *J* = 10.8, 6.2 Hz, 2H), 4.68 (d, *J* = 4.0 Hz, 1H), 3.82 (tt, *J* = 7.3, 3.7 Hz, 1H), 3.51 (tq, *J* = 7.5, 3.6 Hz, 1H), 3.20 (ddd, *J* = 13.1, 6.1, 3.0 Hz, 2H), 2.76 (ddd, *J* = 11.8, 8.6, 3.3 Hz, 2H), 1.77 (ddt, *J* = 13.5, 6.6, 3.5 Hz, 2H), 1.45 (dtd, *J* = 12.3, 8.0, 3.5 Hz, 2H), 1.25–1.18 (m, 2H), 1.18–1.10 (m, 2H).



20180811-wet-1173-3-C.10.fid
 C13CPD DMSO [D:\NMR_DATA] LG 31

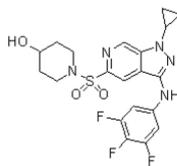
¹³C NMR (101 MHz, DMSO-*d*₆) δ 151.11, 150.84 (ddd, *J* = 243.0, 10.0, 5.8 Hz), 148.62, 143.57, 138.15 (td, *J* = 12.3, 2.8 Hz), 133.02 (dt, *J* = 240.5, 15.9 Hz), 131.49, 123.75, 107.26, 100.66 (d, *J* = 24.3 Hz), 64.24, 43.69, 33.37, 29.17, 6.61.



Compound 11.

20180903-wet-1190g2-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 35

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.86 (s, 1H), 9.15 (s, 1H), 8.62 (s, 1H), 7.48 (dd, *J* = 10.9, 6.1 Hz, 2H), 4.69 (d, *J* = 3.9 Hz, 1H), 3.84 (dq, *J* = 6.9, 3.5, 3.0 Hz, 1H), 3.63–3.48 (m, 2H), 3.41 (dt, *J* = 11.4, 4.5 Hz, 2H), 2.94 (ddd, *J* = 12.2, 8.8, 3.4 Hz, 2H), 1.83–1.67 (m, 2H), 1.52–1.33 (m, 2H), 1.23–1.16 (m, 4H).



A (s) 9.86
 B (s) 9.15
 C (s) 8.62

D (dd) 7.48

E (d) 4.69

F (dq) 3.84

G (m) 3.55

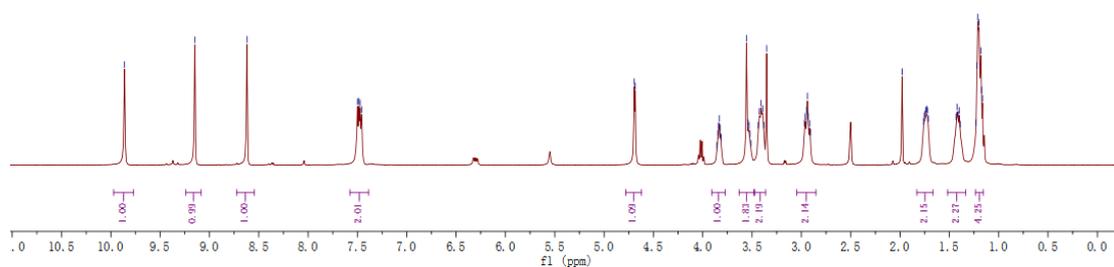
H (dt) 3.41

I (ddd) 2.94

J (m) 1.74

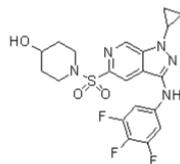
K (m) 1.41

L (m) 1.20



20180903-wet-1190-2-C.12.fid
 C13CPD DMSO (D:\NMR_DATA) LG 35

¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.83 (ddd, *J* = 242.6, 10.0, 5.8 Hz), 144.60, 143.90, 138.94–137.93 (m), 137.46, 134.84, 132.90 (d, *J* = 240.7 Hz), 118.74, 116.43, 100.48 (d, *J* = 24.7 Hz), 64.77, 44.16, 33.76, 30.30, 6.94.



L (ddd) 150.83
 N (m) 138.31
 I (s) 137.46
 J (s) 143.90
 H (s) 134.84
 K (s) 144.60
 M (d) 132.90

G (s) 118.74
 F (s) 116.43

O (d) 100.48

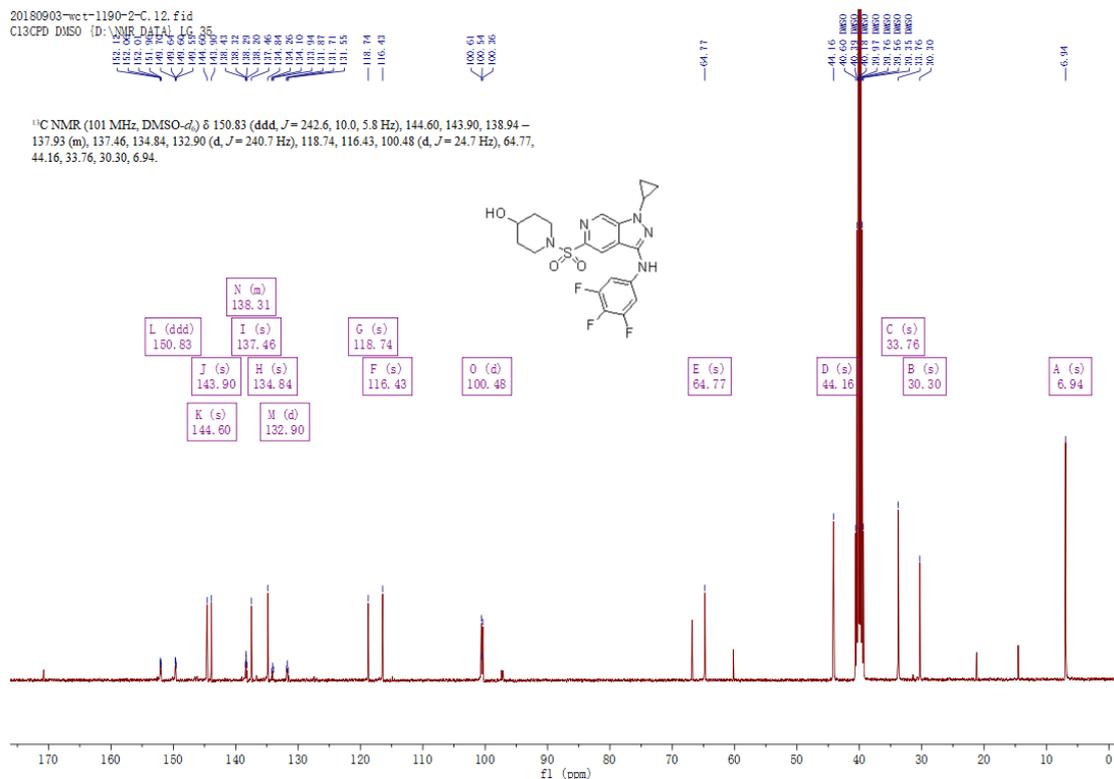
E (s) 64.77

D (s) 44.16

C (s) 33.76

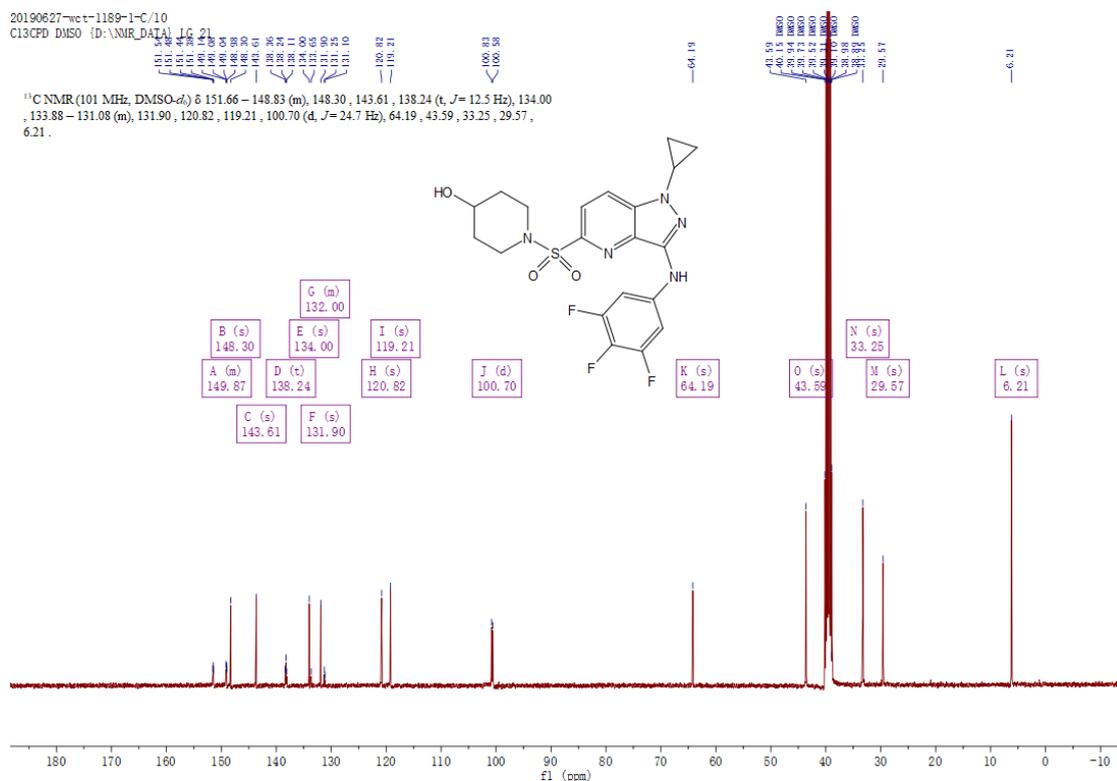
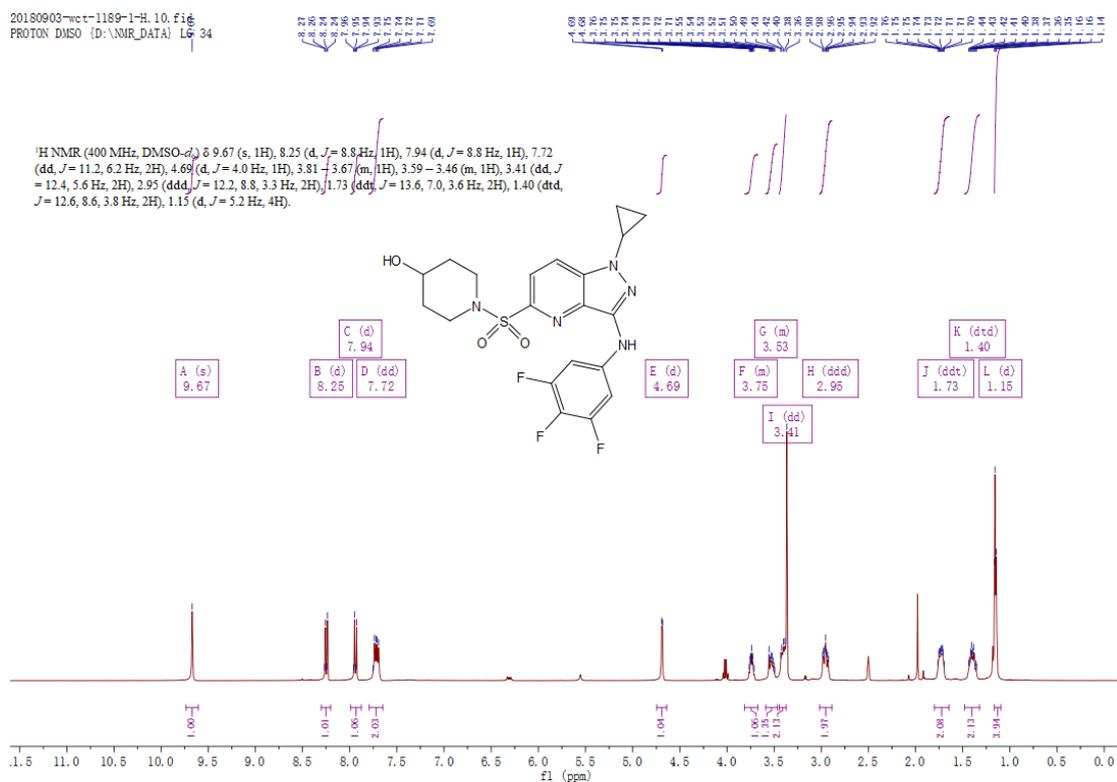
B (s) 30.30

A (s) 6.94



Compound 12.

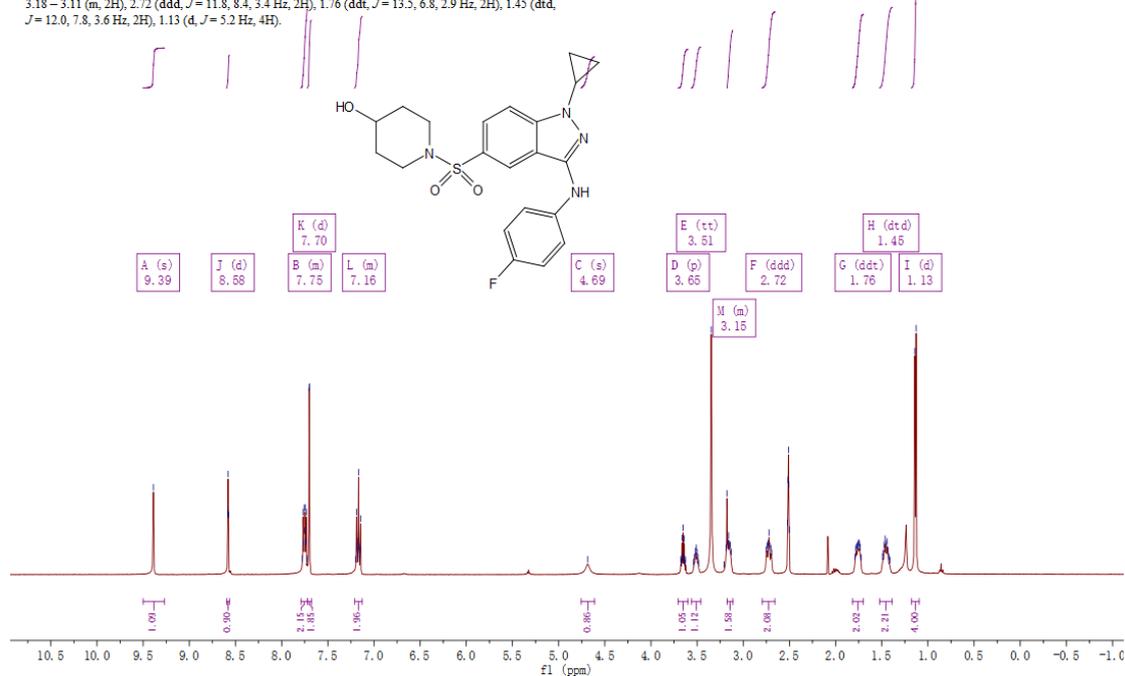
20180903-wct-1189-1-H.10. fig
 PROTON DMSO (D:\NMR_DATA) LG 34



Compound 13.

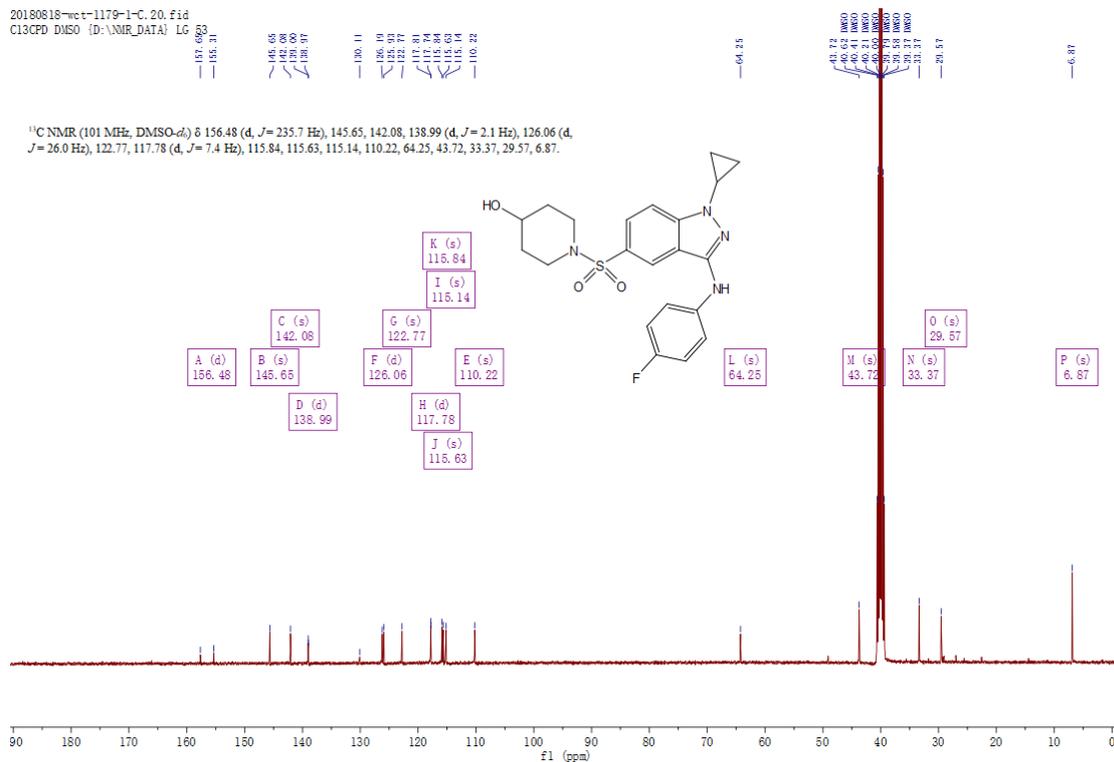
20180818-wet-1179-1-H₂O.fid
 PROTON DMSO (D:\NMR_DATA) L659

¹H NMR (400 MHz, DMSO-d₆) δ 9.39 (s, 1H), 8.58 (d, *J* = 1.3 Hz, 1H), 7.79 – 7.72 (m, 2H), 7.70 (d, *J* = 1.2 Hz, 2H), 7.21 – 7.13 (m, 2H), 4.69 (s, 1H), 3.65 (p, *J* = 5.3 Hz, 1H), 3.51 (tt, *J* = 7.6, 3.6 Hz, 1H), 3.18 – 3.11 (m, 2H), 2.72 (ddd, *J* = 11.8, 8.4, 3.4 Hz, 2H), 1.76 (ddt, *J* = 13.5, 6.8, 2.9 Hz, 2H), 1.45 (dtd, *J* = 12.0, 7.8, 3.6 Hz, 2H), 1.13 (d, *J* = 5.2 Hz, 4H).



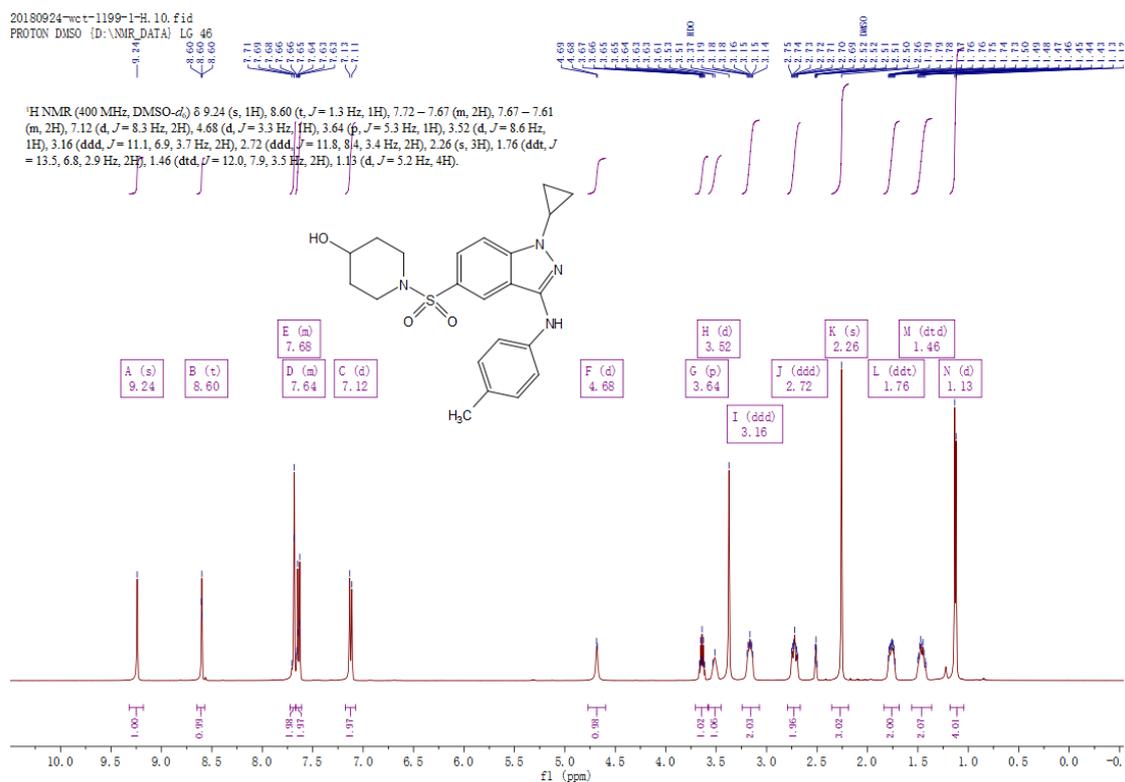
20180818-wet-1179-1-C.20.fid
 C13CPD DMSO (D:\NMR_DATA) L6

¹³C NMR (101 MHz, DMSO-d₆) δ 156.48 (d, *J* = 235.7 Hz), 145.65, 142.08, 138.99 (d, *J* = 2.1 Hz), 126.06 (d, *J* = 26.0 Hz), 122.77, 117.78 (d, *J* = 7.4 Hz), 115.84, 115.63, 115.14, 110.22, 64.25, 43.72, 33.37, 29.57, 6.87.

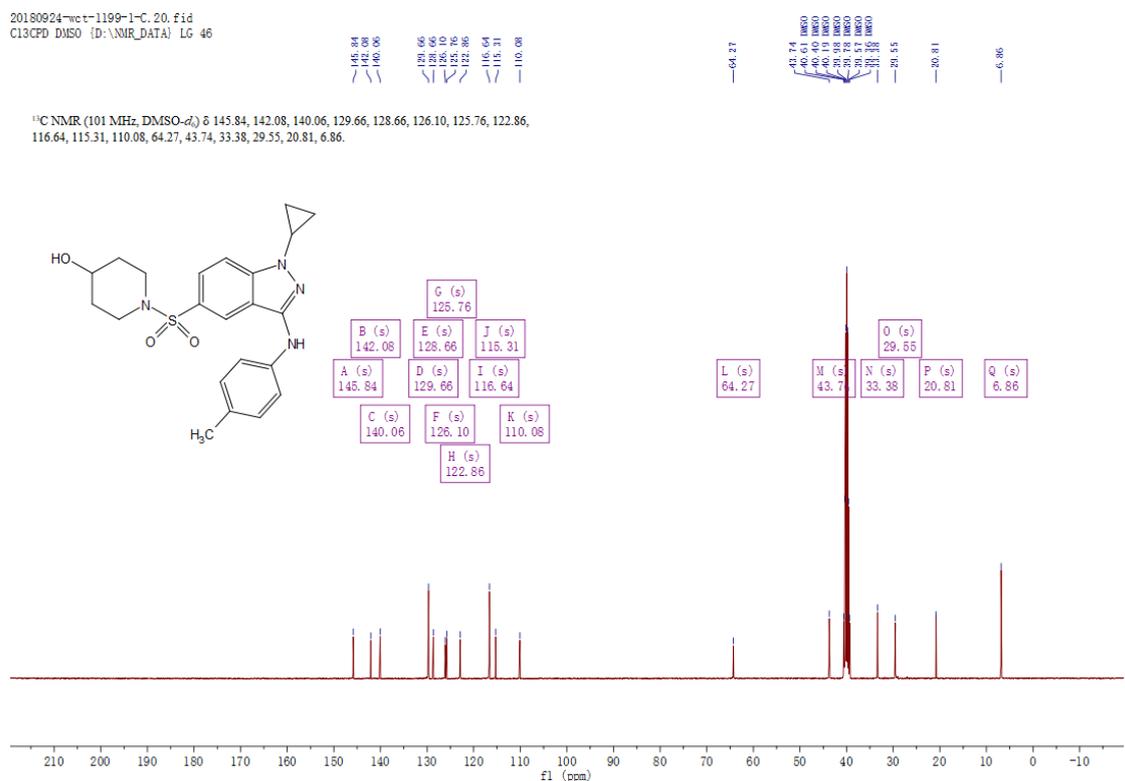


Compound 14.

20180924-wct-1199-1-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 46

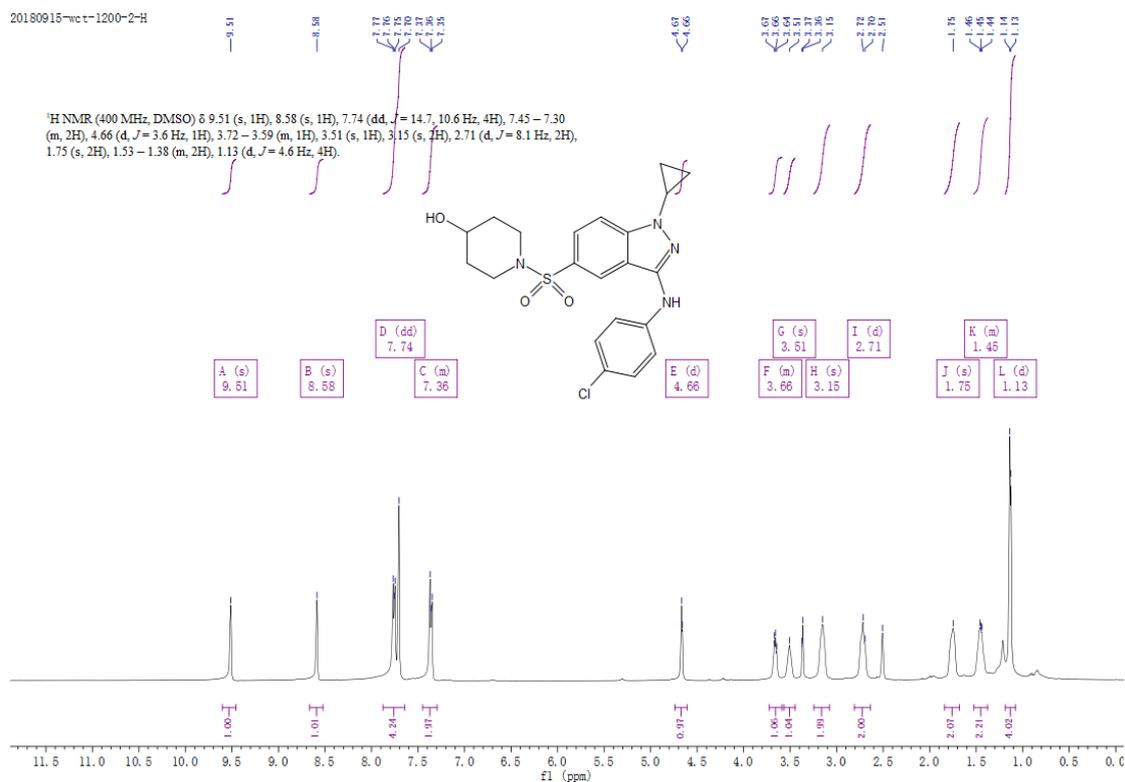


20180924-wct-1199-1-C.20.fid
 C13CPD DMSO (D:\NMR_DATA) LG 46

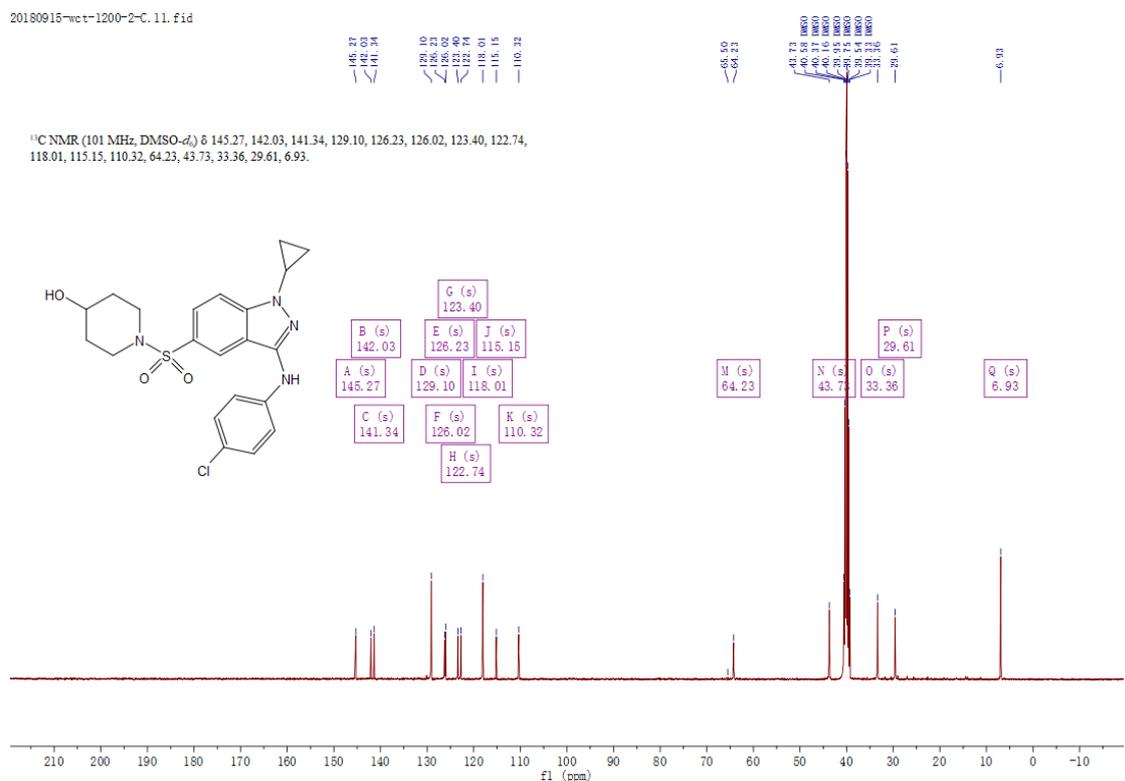


Compound 15.

20180915-wct-1200-2-H



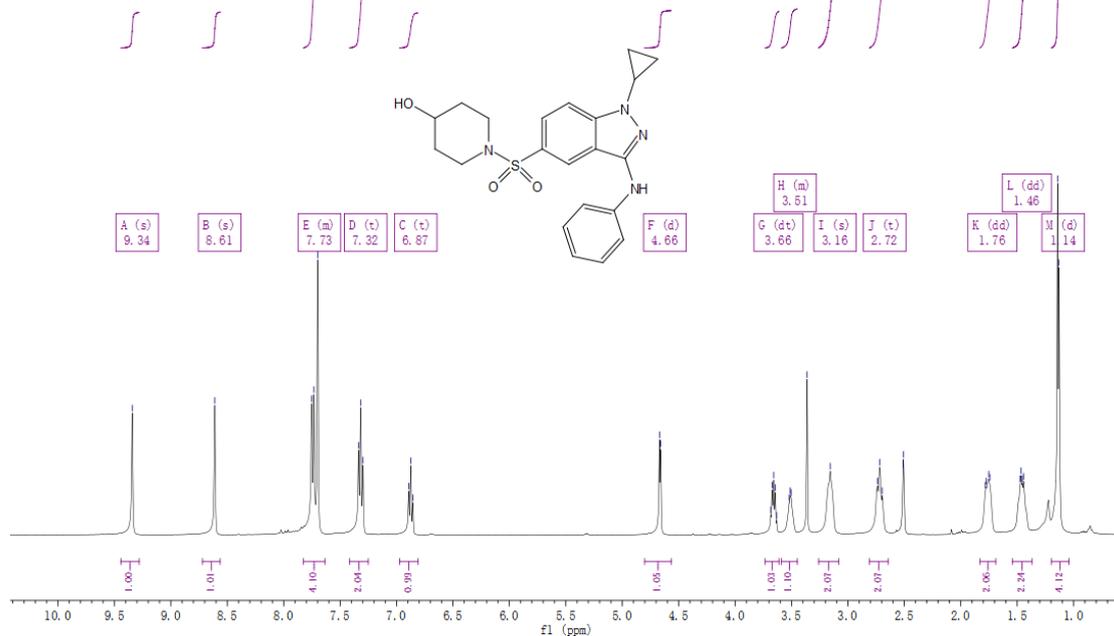
20180915-wct-1200-2-C.11.fid



Compound 16.

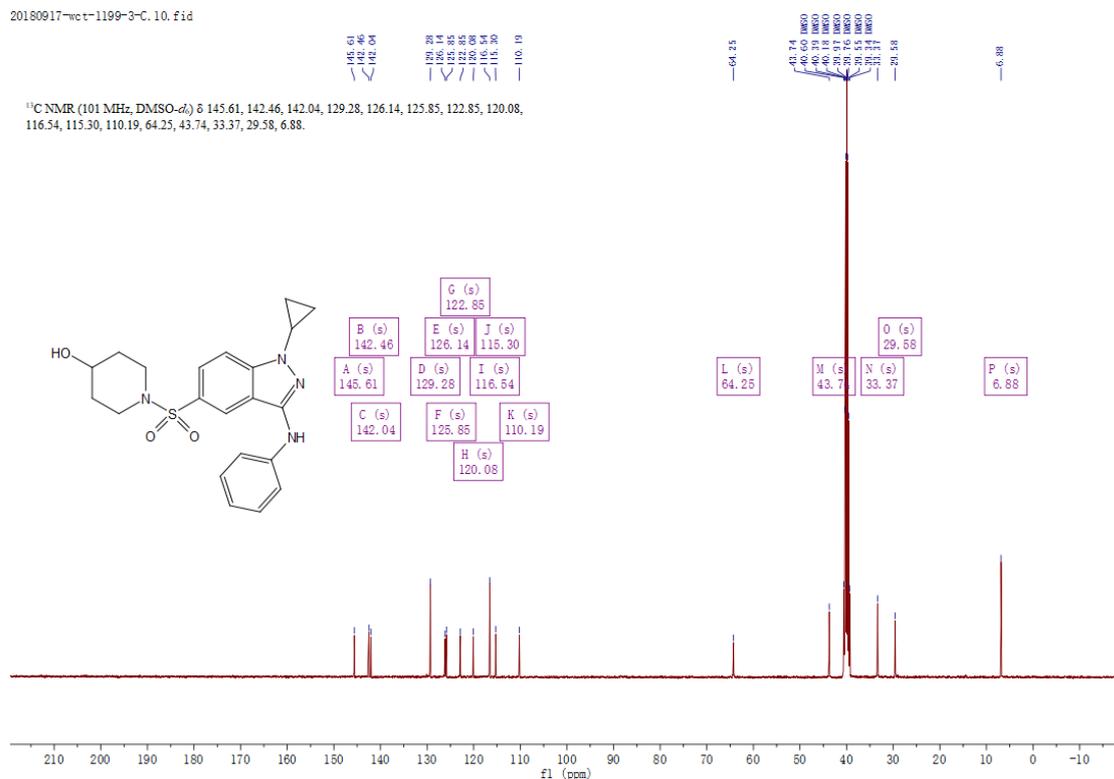
20180915-wet-1199-3-H

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.34 (s, 1H), 8.61 (s, 1H), 7.83–7.64 (m, 4H), 7.32 (t, *J* = 7.9 Hz, 2H), 6.87 (t, *J* = 7.3 Hz, 1H), 4.66 (d, *J* = 3.8 Hz, 1H), 3.66 (dt, *J* = 10.4, 5.3 Hz, 1H), 3.59–3.45 (m, 1H), 3.16 (s, 2H), 2.72 (t, *J* = 8.3 Hz, 2H), 1.76 (dd, *J* = 12.3, 3.4 Hz, 2H), 1.46 (dd, *J* = 8.2, 3.8 Hz, 2H), 1.14 (d, *J* = 5.2 Hz, 4H).



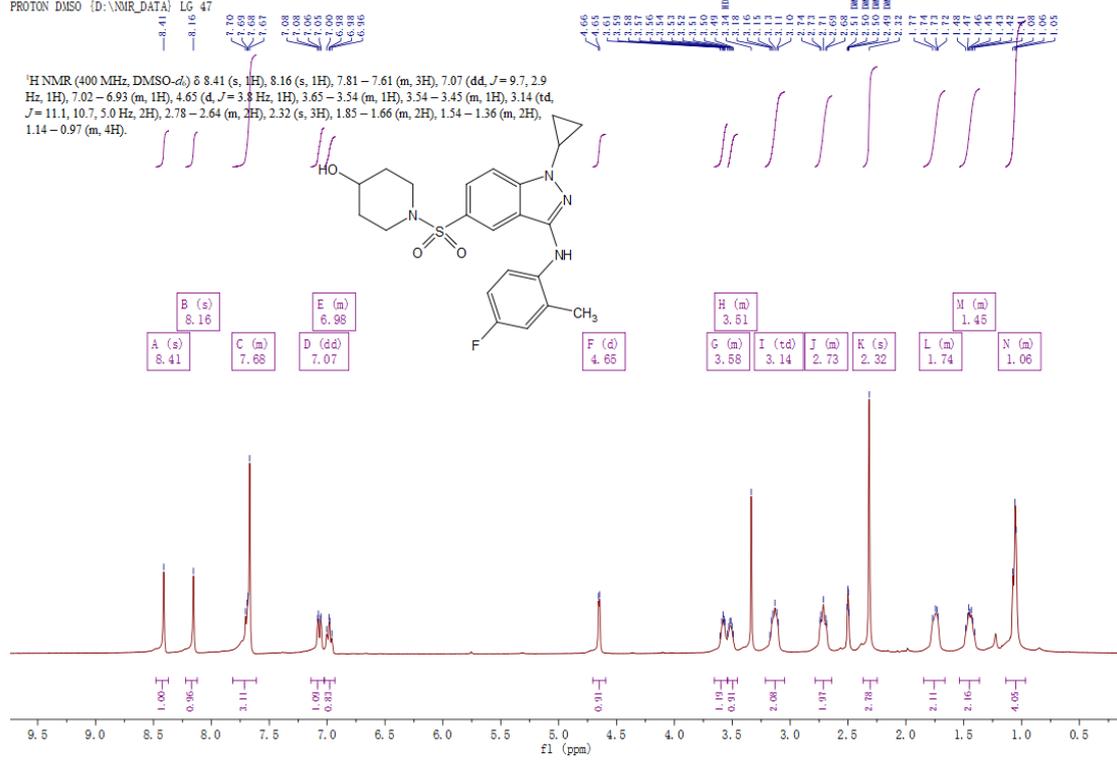
20180917-wet-1199-3-C.10.fid

¹³C NMR (101 MHz, DMSO-*d*₆) δ 145.61, 142.46, 142.04, 129.28, 126.14, 125.85, 122.85, 120.08, 116.54, 115.30, 110.19, 64.25, 43.74, 33.37, 29.58, 6.88.

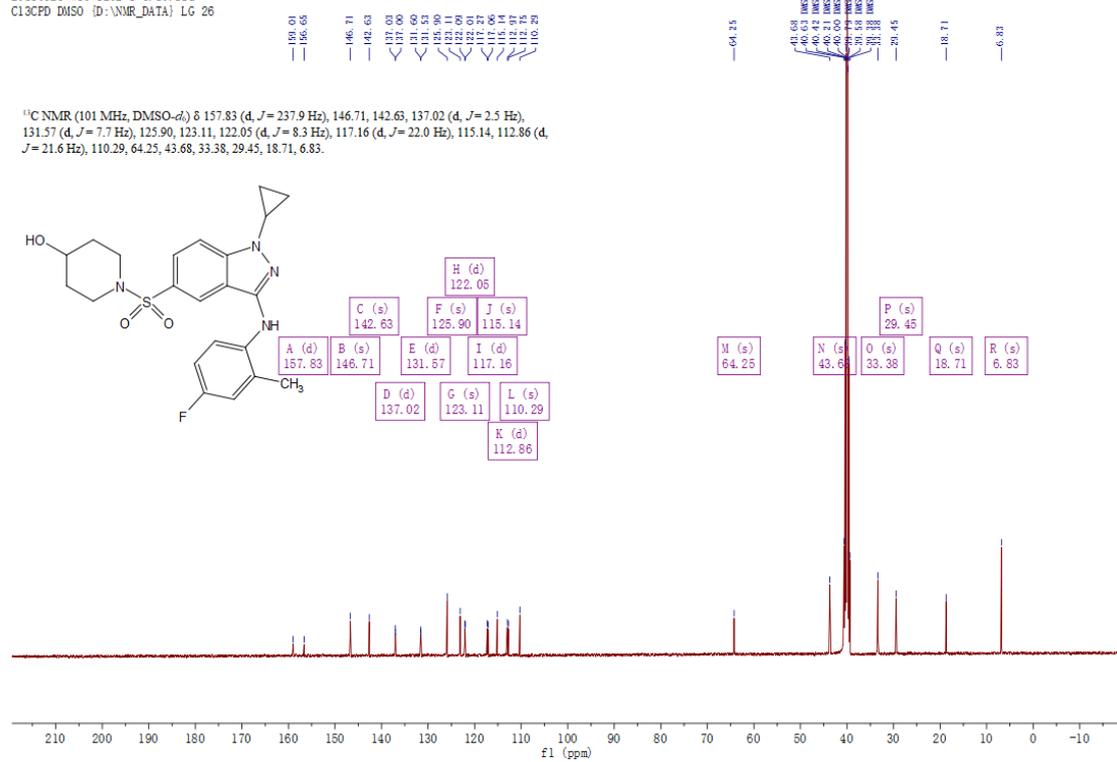


Compound 17.

20180924-wet-1202-1-H.10.fid
 PROTON DMSO [D:\NMR_DATA] LG 47

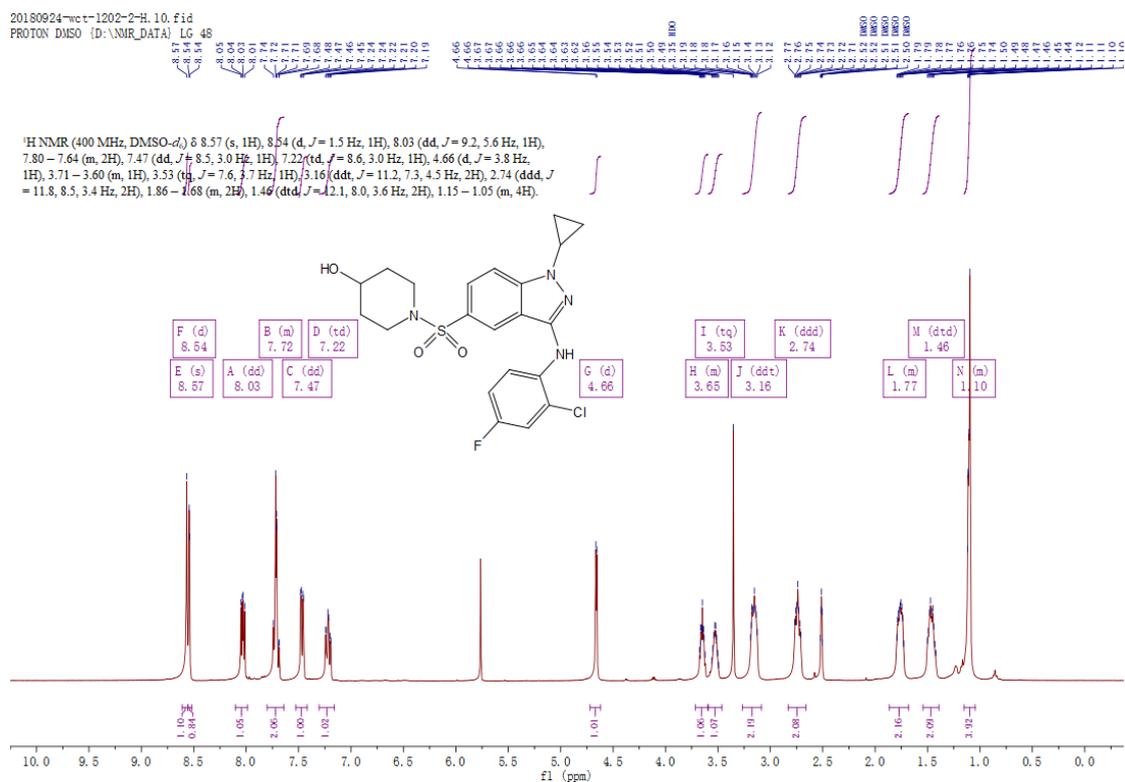


20180925-wet-1202-1-C.10.fid
 C13CPD DMSO [D:\NMR_DATA] LG 26

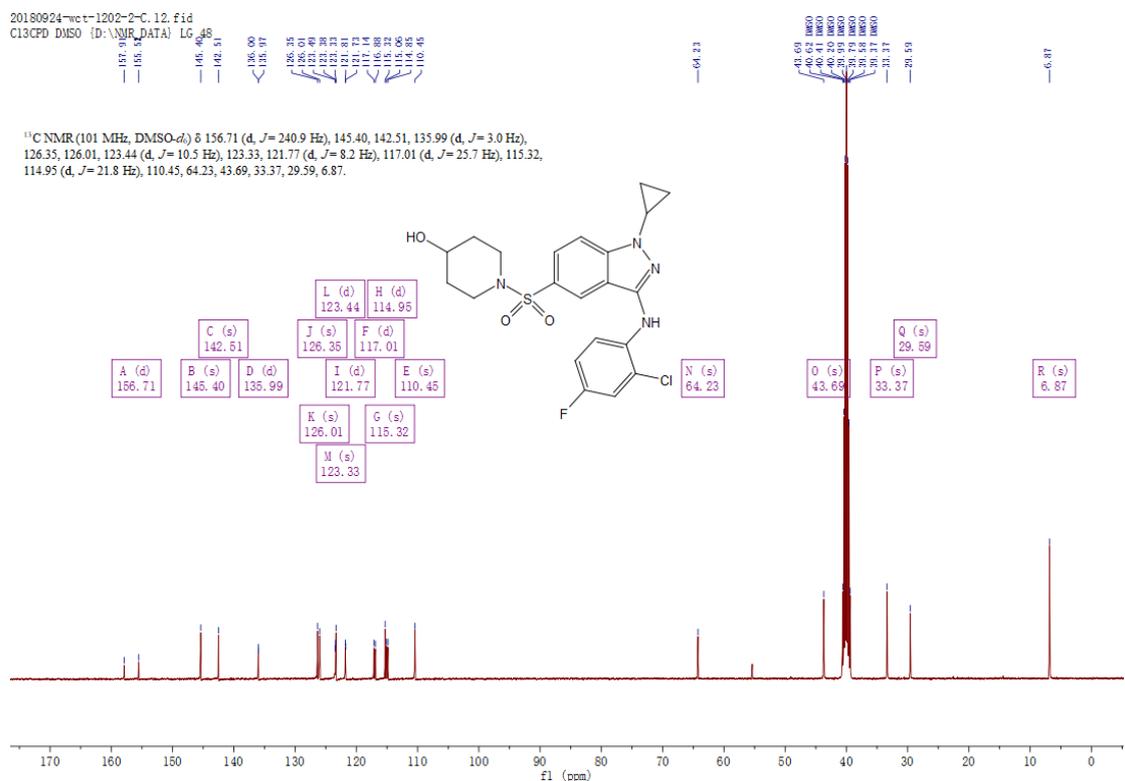


Compound 18.

20180924-wct-1202-2-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 48

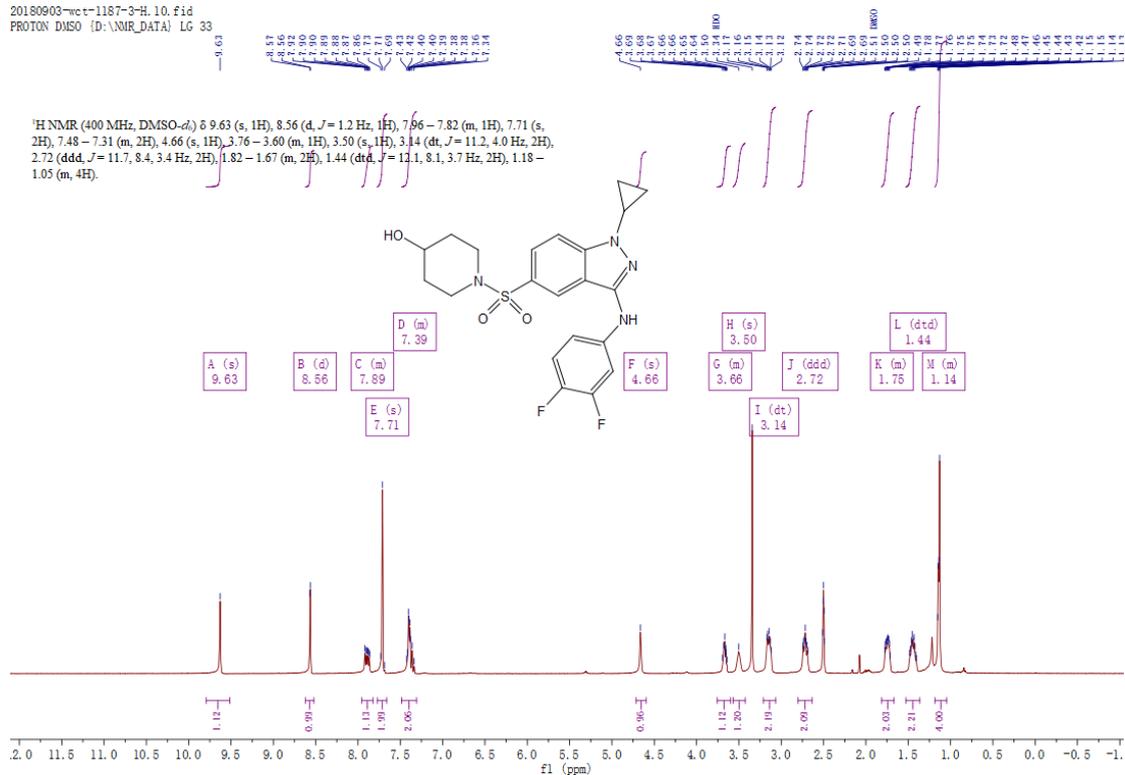


20180924-wct-1202-2-C.12.fid
 C13CPD DMSO (D:\NMR_DATA) LG 48

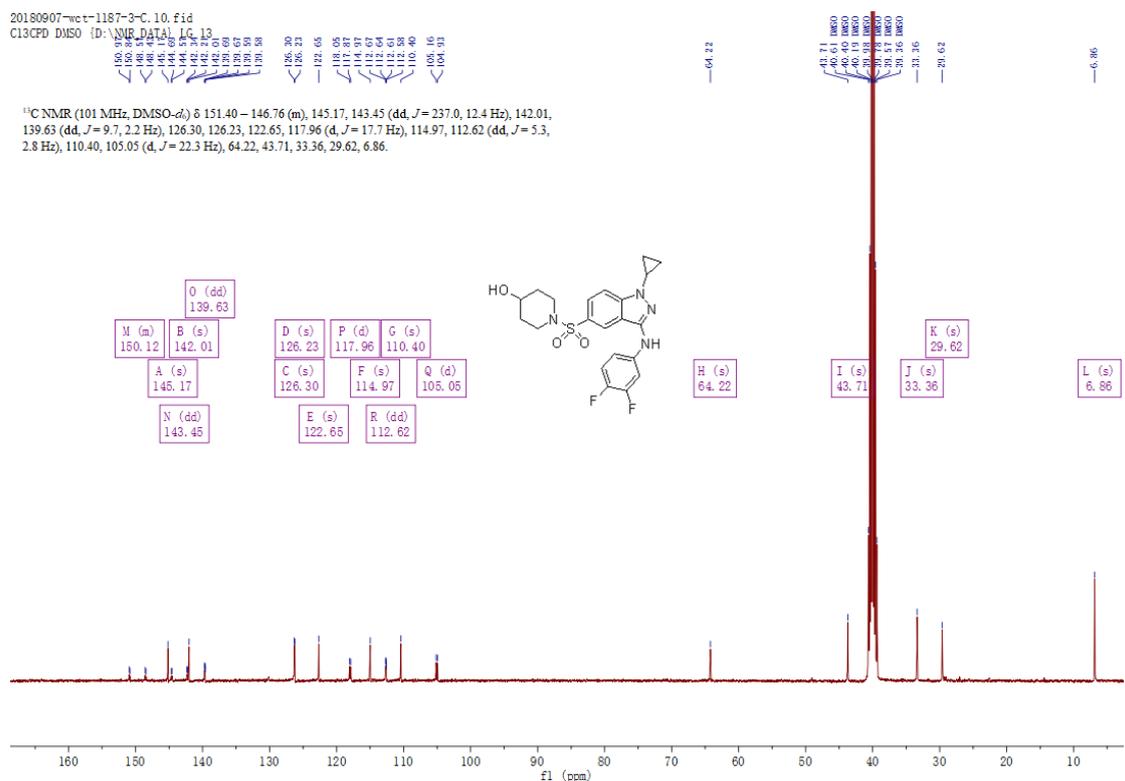


Compound 19.

20180903-wet-1187-3-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 33



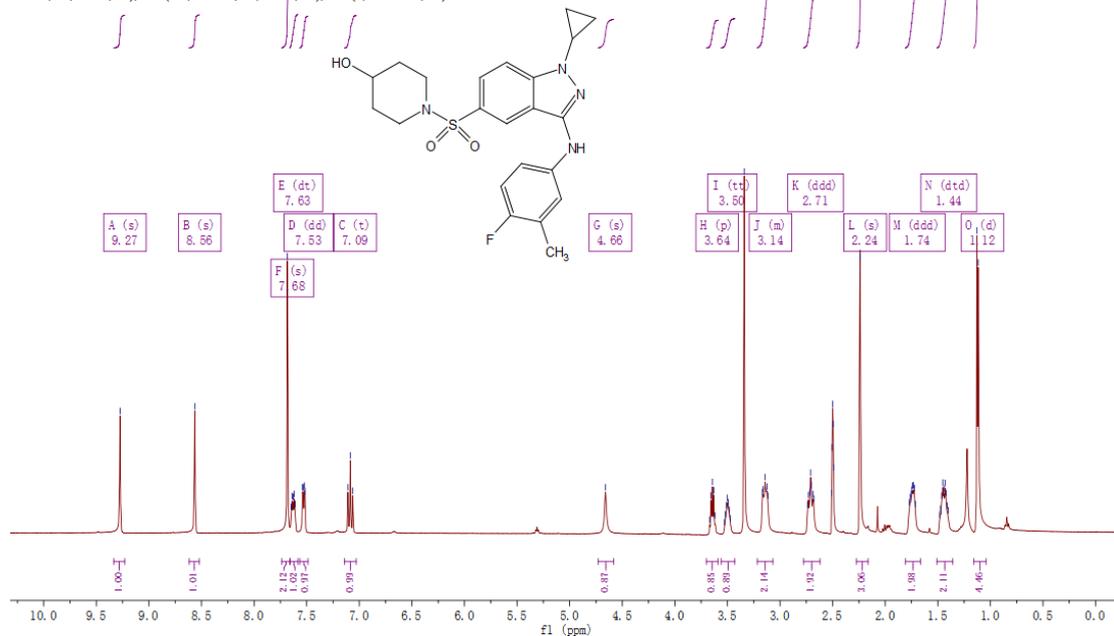
20180907-wet-1187-3-C.10.fid
 C13CPD DMSO (D:\NMR_DATA) LG 13



Compound 20.

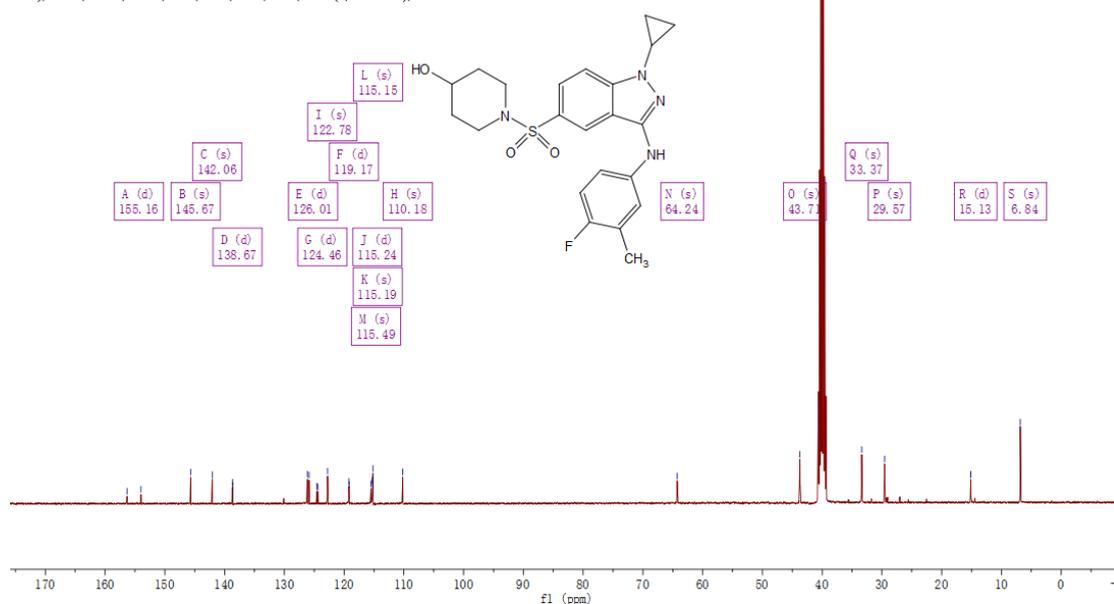
20180903-wct-1182-3-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG:31

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.27 (s, 1H), 8.56 (s, 1H), 7.68 (s, 2H), 7.63 (dt, *J* = 8.2, 3.6 Hz, 1H), 7.53 (dd, *J* = 6.9, 2.8 Hz, 1H), 7.09 (t, *J* = 9.2 Hz, 1H), 4.66 (s, 1H), 3.64 (p, *J* = 5.3 Hz, 1H), 3.50 (tt, *J* = 7.9, 3.6 Hz, 1H), 3.22–3.07 (m, 2H), 2.71 (ddd, *J* = 11.9, 8.6, 3.5 Hz, 2H), 2.24 (s, 3H), 1.74 (ddd, *J* = 13.9, 7.3, 3.6 Hz, 2H), 1.44 (dtd, *J* = 12.3, 8.2, 3.6 Hz, 2H), 1.12 (d, *J* = 5.2 Hz, 4H).



20180905-wct-1182-3-H.10.fid
 C13CPD DMSO (D:\NMR_DATA) LG:34

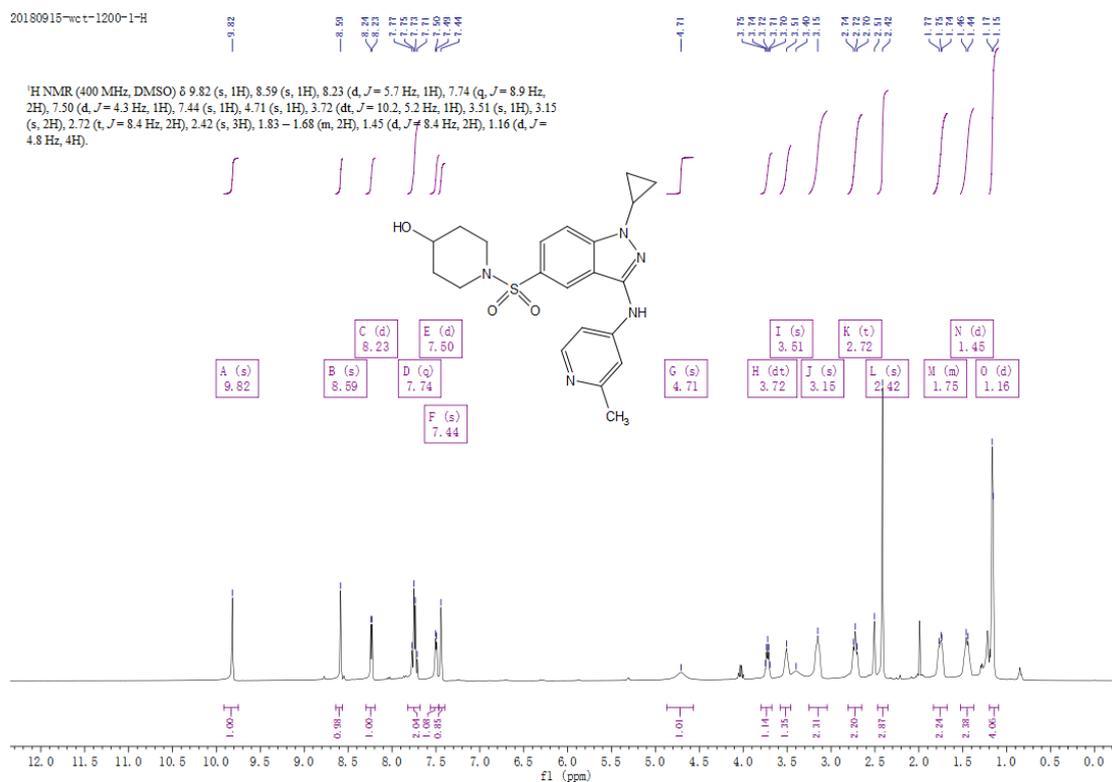
¹³C NMR (101 MHz, DMSO-*d*₆) δ 155.16 (d, *J* = 234.8 Hz), 145.67, 142.06, 138.67 (d, *J* = 2.2 Hz), 126.01 (d, *J* = 29.0 Hz), 124.46 (d, *J* = 18.0 Hz), 122.78, 119.17 (d, *J* = 4.0 Hz), 115.49, 115.24 (d, *J* = 4.1 Hz), 115.19, 115.15, 110.18, 64.24, 43.71, 33.37, 29.57, 15.13 (d, *J* = 2.9 Hz), 6.84.



Compound 21.

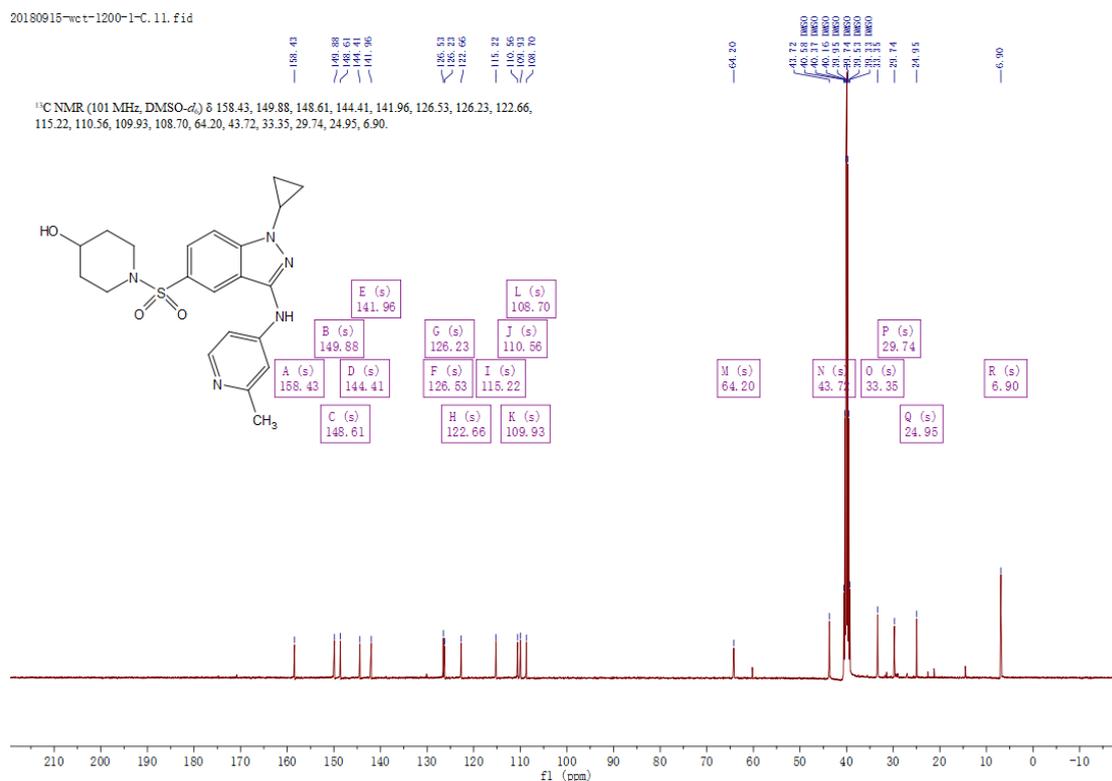
20180915-wet-1200-1-H

¹H NMR (400 MHz, DMSO) δ 9.82 (s, 1H), 8.59 (s, 1H), 8.23 (d, *J* = 5.7 Hz, 1H), 7.74 (q, *J* = 8.9 Hz, 2H), 7.50 (d, *J* = 4.3 Hz, 1H), 7.44 (s, 1H), 4.71 (s, 1H), 3.72 (dt, *J* = 10.2, 5.2 Hz, 1H), 3.51 (s, 1H), 3.15 (s, 2H), 2.72 (t, *J* = 8.4 Hz, 2H), 2.42 (s, 3H), 1.83–1.68 (m, 2H), 1.45 (d, *J* = 8.4 Hz, 2H), 1.16 (d, *J* = 4.8 Hz, 4H).



20180915-wet-1200-1-C.11.fid

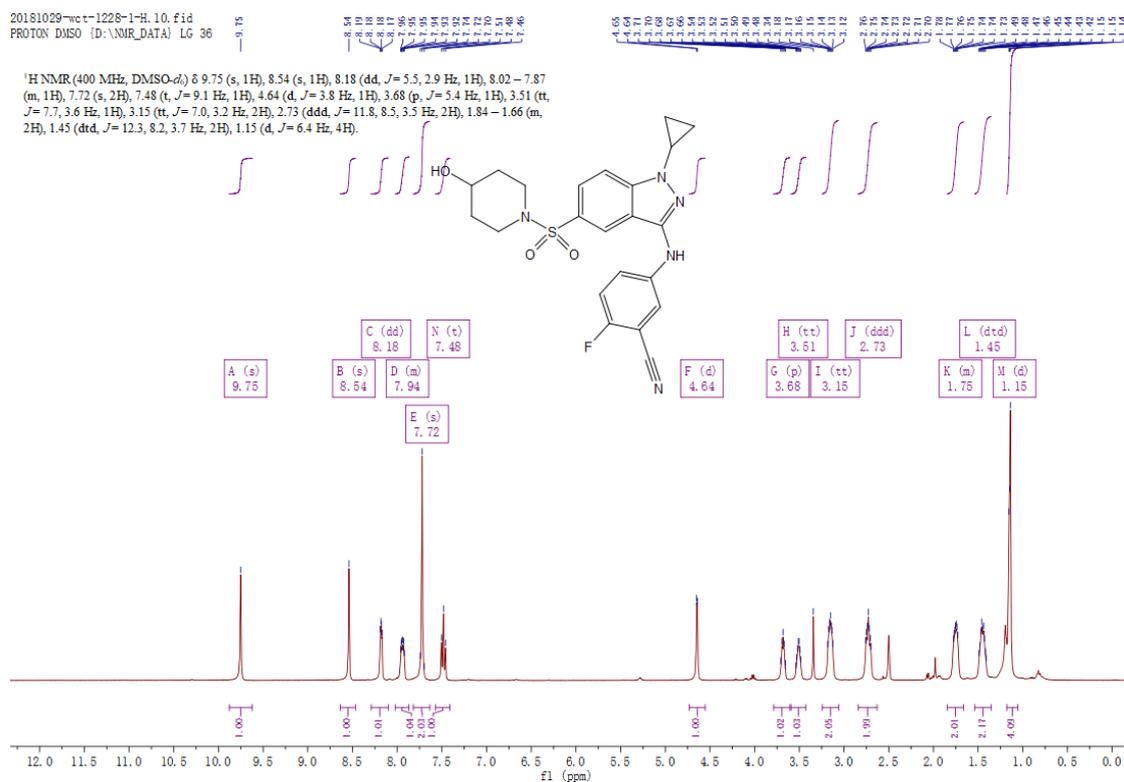
¹³C NMR (101 MHz, DMSO-*d*₆) δ 158.43, 149.88, 148.61, 144.41, 141.96, 126.53, 126.23, 122.66, 115.22, 110.56, 109.93, 108.70, 64.20, 43.72, 33.35, 29.74, 24.95, 6.90.



Compound 22.

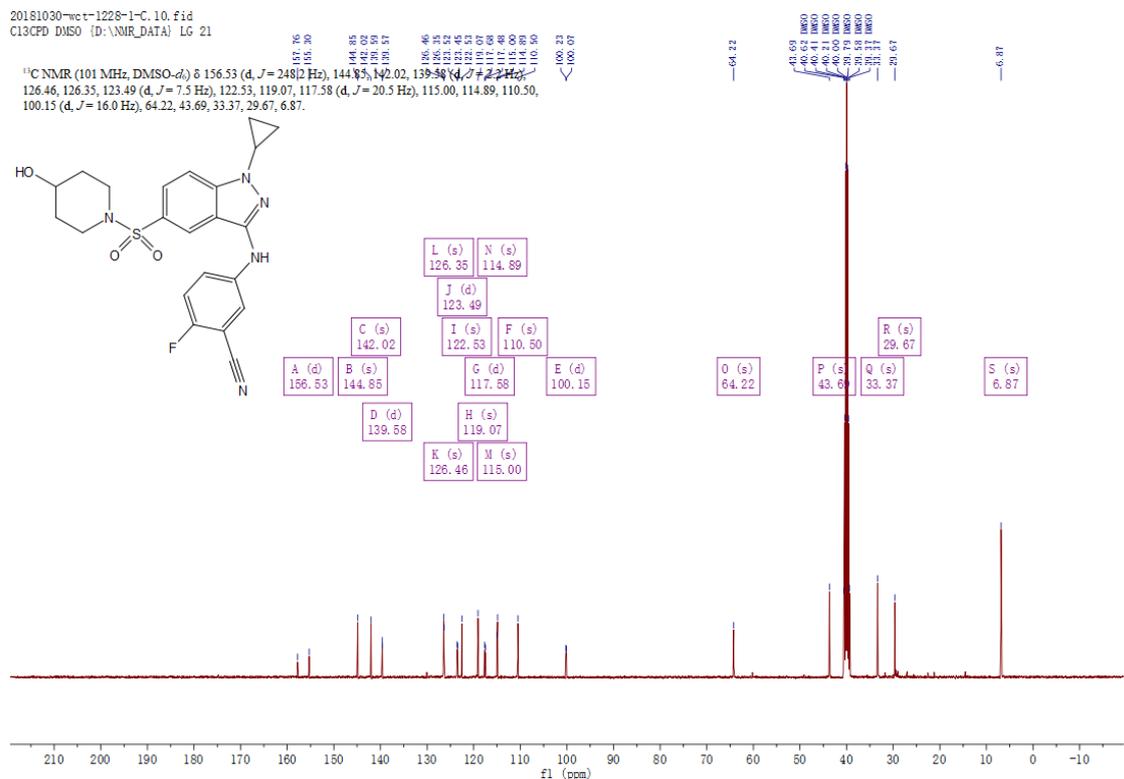
20181029-wct-1228-1-H.10.fid
 PROTON DMSO [D:\NMR_DATA] LG 36

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.75 (s, 1H), 8.54 (s, 1H), 8.18 (dd, *J* = 5.5, 2.9 Hz, 1H), 8.02 – 7.87 (m, 1H), 7.72 (s, 2H), 7.48 (t, *J* = 9.1 Hz, 1H), 4.64 (d, *J* = 3.8 Hz, 1H), 3.68 (p, *J* = 5.4 Hz, 1H), 3.51 (tt, *J* = 7.7, 3.6 Hz, 1H), 3.15 (tt, *J* = 7.0, 3.2 Hz, 2H), 2.73 (ddd, *J* = 11.8, 8.5, 3.5 Hz, 2H), 1.84 – 1.66 (m, 2H), 1.45 (dtd, *J* = 12.3, 8.2, 3.7 Hz, 2H), 1.15 (d, *J* = 6.4 Hz, 4H).



20181030-wct-1228-1-C.10.fid
 C13CPD DMSO [D:\NMR_DATA] LG 21

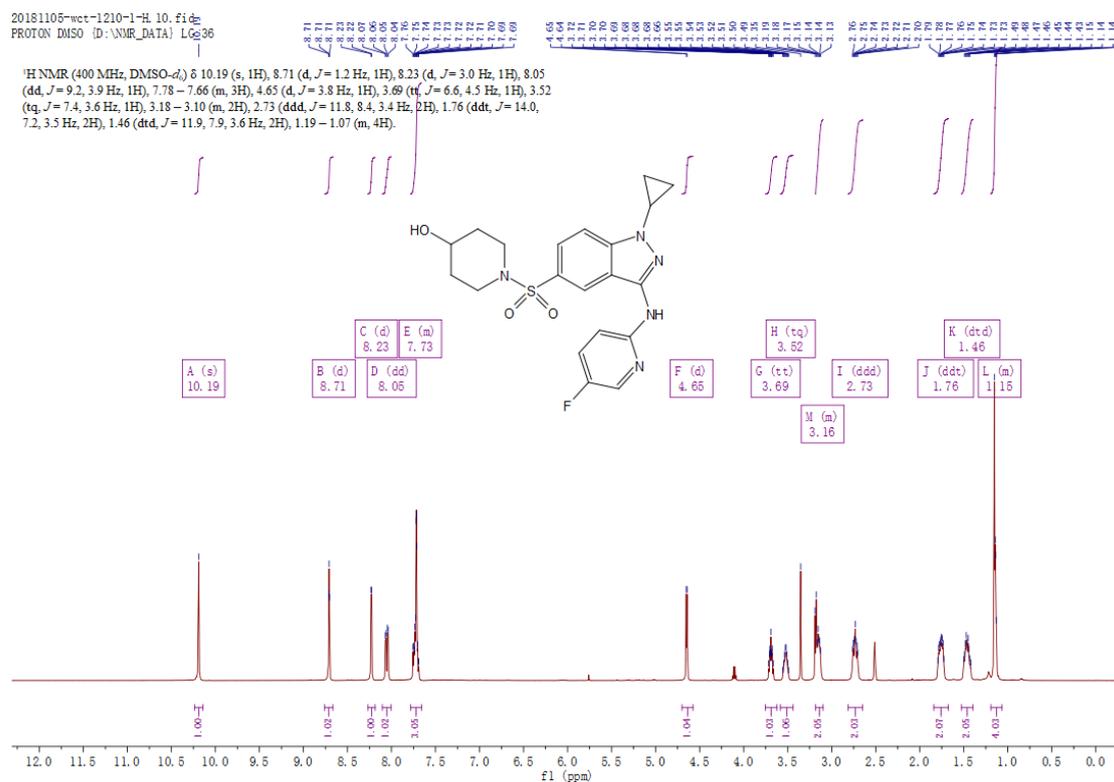
¹³C NMR (101 MHz, DMSO-*d*₆) δ 156.53 (d, *J* = 248 Hz), 144.85, 142.02, 139.58 (d, *J* = 2.2 Hz), 126.46, 126.35, 123.49 (d, *J* = 7.5 Hz), 122.53, 119.07, 117.58 (d, *J* = 20.5 Hz), 115.00, 114.89, 110.50, 100.15 (d, *J* = 16.0 Hz), 64.22, 43.69, 33.37, 29.67, 6.87.



Compound 23.

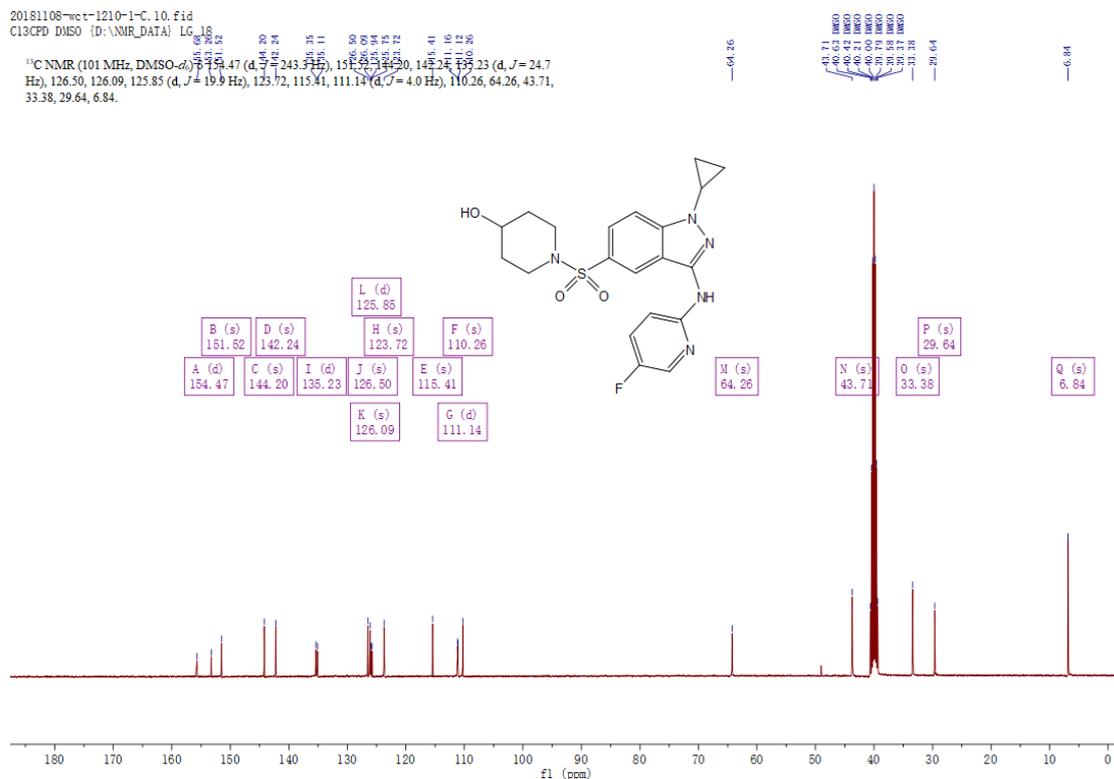
20181105-wet-1210-1-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG36

¹H NMR (400 MHz, DMSO-d₆) δ 10.19 (s, 1H), 8.71 (d, J = 1.2 Hz, 1H), 8.23 (d, J = 3.0 Hz, 1H), 8.05 (dd, J = 9.2, 3.9 Hz, 1H), 7.78–7.66 (m, 3H), 4.65 (d, J = 3.8 Hz, 1H), 3.69 (t, J = 6.6, 4.5 Hz, 1H), 3.52 (tq, J = 7.4, 3.6 Hz, 1H), 3.18–3.10 (m, 2H), 2.73 (ddd, J = 11.8, 8.4, 3.4 Hz, 2H), 1.76 (ddt, J = 14.0, 7.2, 3.5 Hz, 2H), 1.46 (dtd, J = 11.9, 7.9, 3.6 Hz, 2H), 1.19–1.07 (m, 4H).



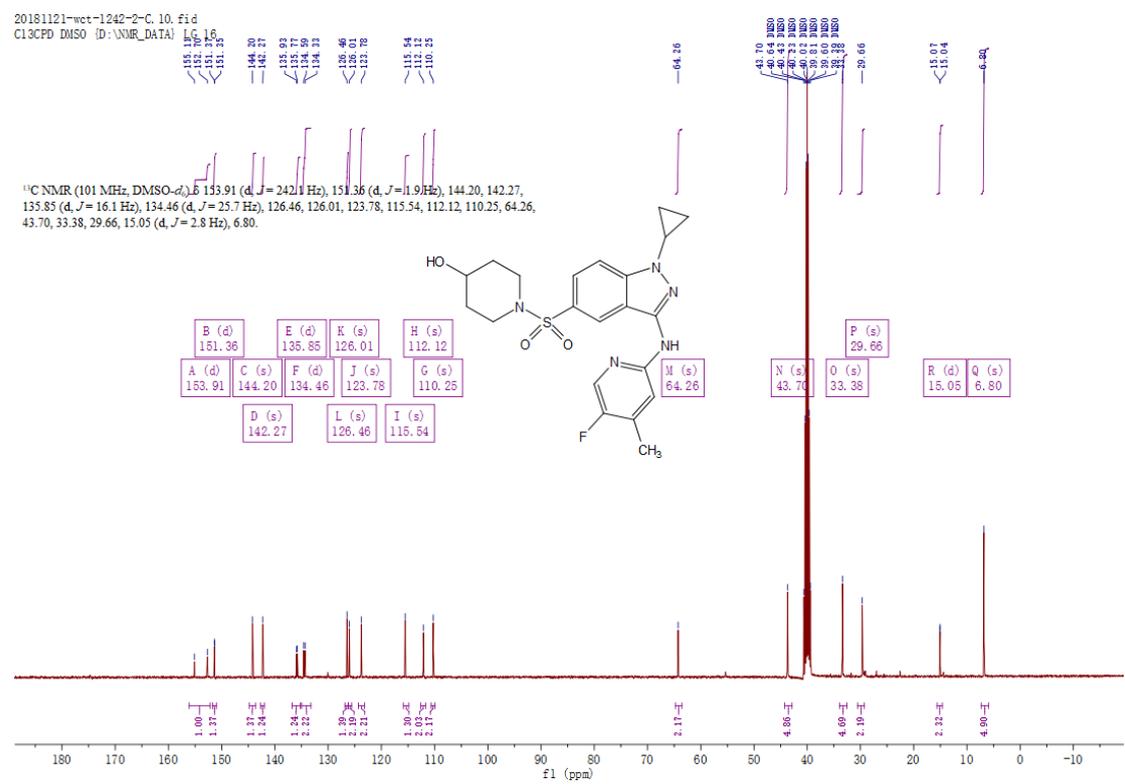
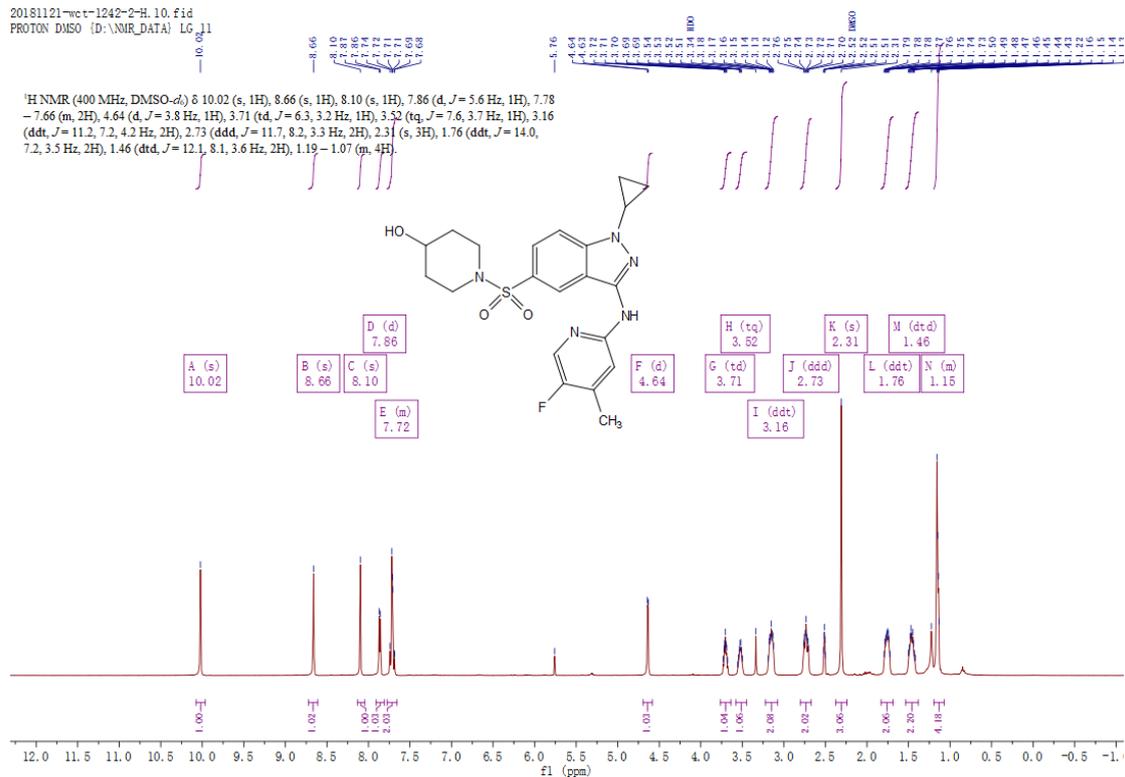
20181108-wet-1210-1-C.10.fid
 13CPD DMSO (D:\NMR_DATA) LG 18

¹³C NMR (101 MHz, DMSO-d₆) δ 154.47 (d), 144.20 (s), 142.24 (s), 135.23 (d), 126.50 (s), 125.85 (d, J = 19.9 Hz), 123.72, 115.41, 111.14 (d, J = 4.0 Hz), 110.26, 64.26, 43.71, 33.38, 29.64, 6.84.



Compound 24.

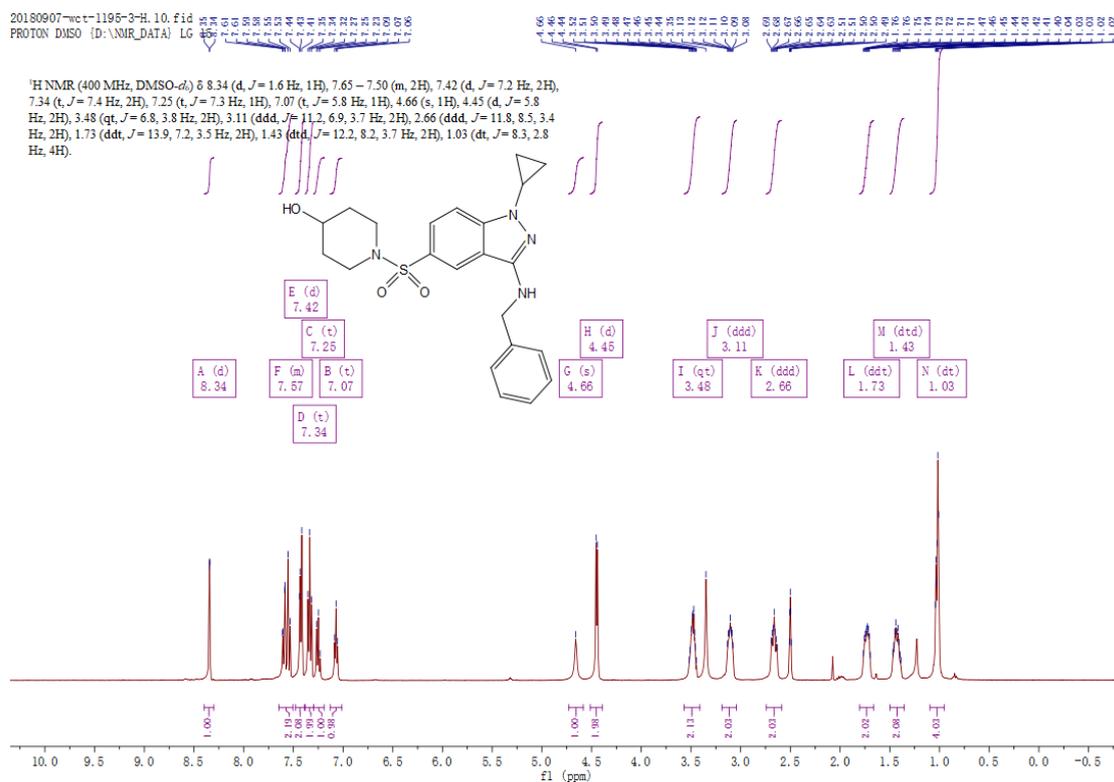
20181121-wet-1242-2-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG_11



Compound 25.

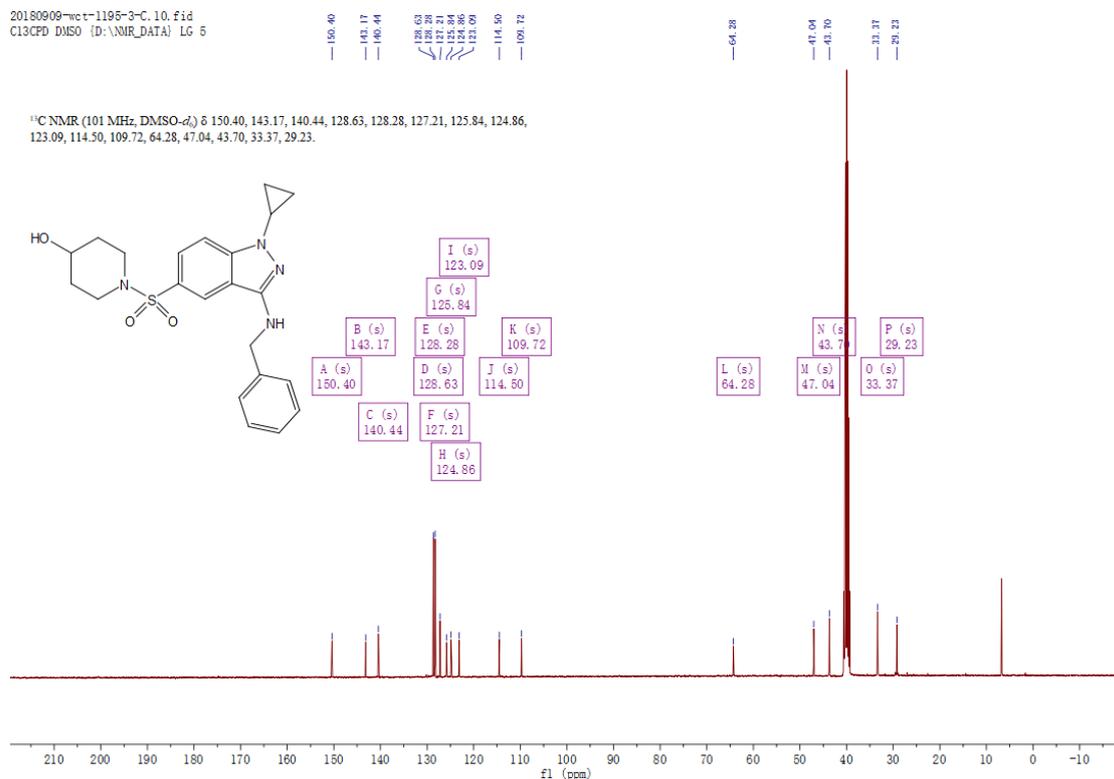
20180907-wct-1195-3-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG

¹H NMR (400 MHz, DMSO-*d*₆) δ 8.34 (d, *J* = 1.6 Hz, 1H), 7.65 – 7.50 (m, 2H), 7.42 (d, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.25 (t, *J* = 7.3 Hz, 1H), 7.07 (t, *J* = 5.8 Hz, 1H), 4.66 (s, 1H), 4.45 (d, *J* = 5.8 Hz, 2H), 3.48 (qt, *J* = 6.8, 3.8 Hz, 2H), 3.11 (ddd, *J* = 11.2, 6.9, 3.7 Hz, 2H), 2.66 (ddd, *J* = 11.8, 8.5, 3.4 Hz, 2H), 1.73 (ddt, *J* = 13.9, 7.2, 3.5 Hz, 2H), 1.43 (ddd, *J* = 12.2, 8.2, 3.7 Hz, 2H), 1.03 (dt, *J* = 8.3, 2.8 Hz, 4H).



20180909-wct-1195-3-C.10.fid
 C13CPD DMSO (D:\NMR_DATA) LG 5

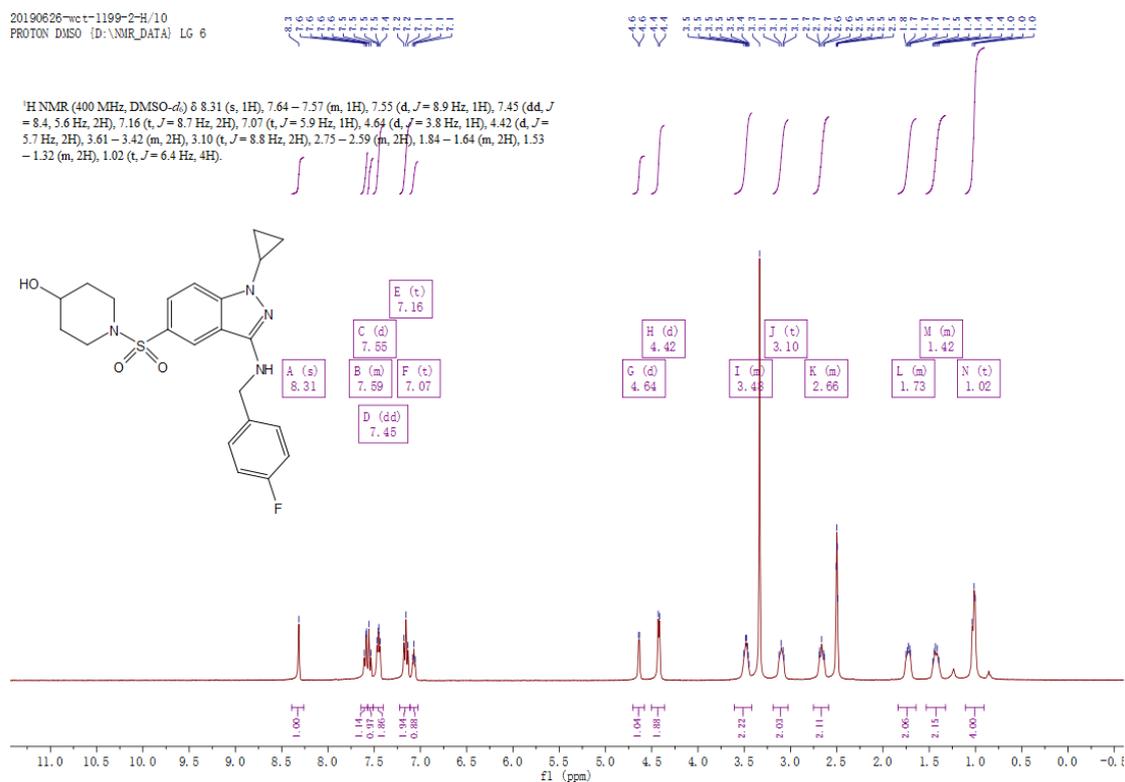
¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.40, 143.17, 140.44, 128.63, 128.28, 127.21, 125.84, 124.86, 123.09, 114.50, 109.72, 64.28, 47.04, 43.70, 33.37, 29.23.



Compound 26.

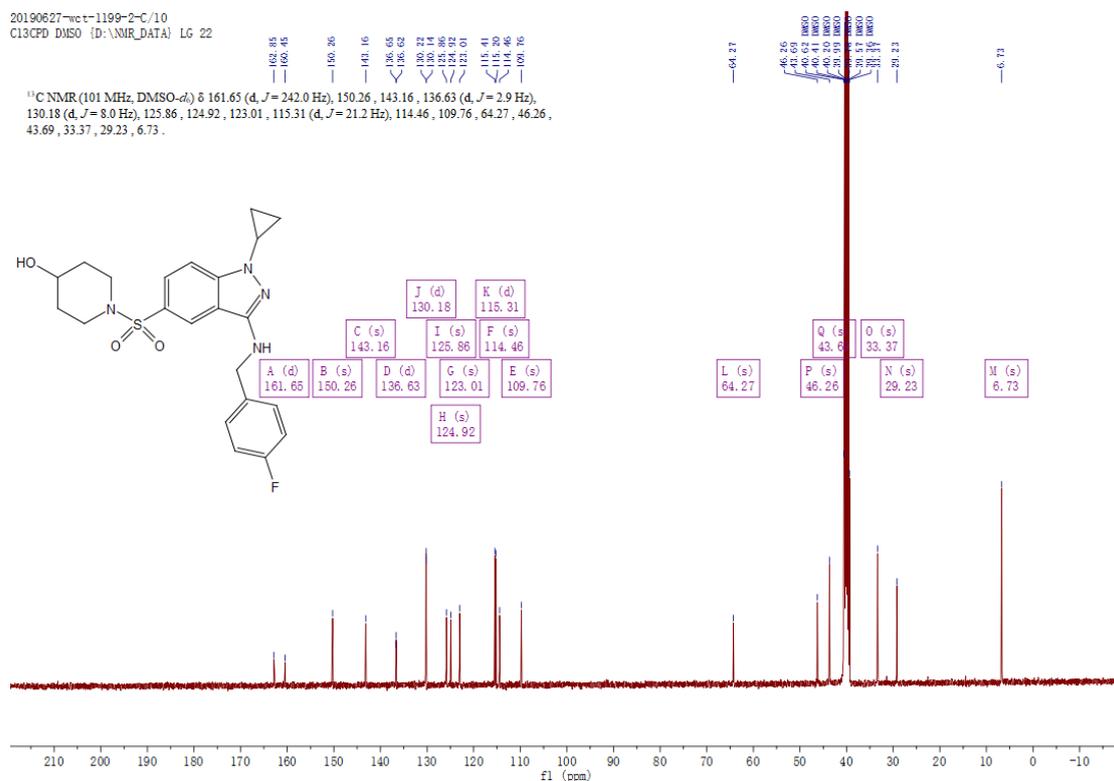
20190626-wct-1199-2-H/10
 PROTON DMSO [D:\NMR_DATA] LG 6

¹H NMR (400 MHz, DMSO-*d*₆) δ 8.31 (s, 1H), 7.64 – 7.57 (m, 1H), 7.55 (d, *J* = 8.9 Hz, 1H), 7.45 (dd, *J* = 8.4, 3.6 Hz, 2H), 7.16 (t, *J* = 8.7 Hz, 2H), 7.07 (t, *J* = 5.9 Hz, 1H), 4.64 (d, *J* = 3.8 Hz, 1H), 4.42 (d, *J* = 3.7 Hz, 2H), 3.61 – 3.42 (m, 2H), 3.10 (t, *J* = 8.8 Hz, 2H), 2.75 – 2.59 (m, 2H), 1.84 – 1.64 (m, 2H), 1.53 – 1.32 (m, 2H), 1.02 (t, *J* = 6.4 Hz, 4H).



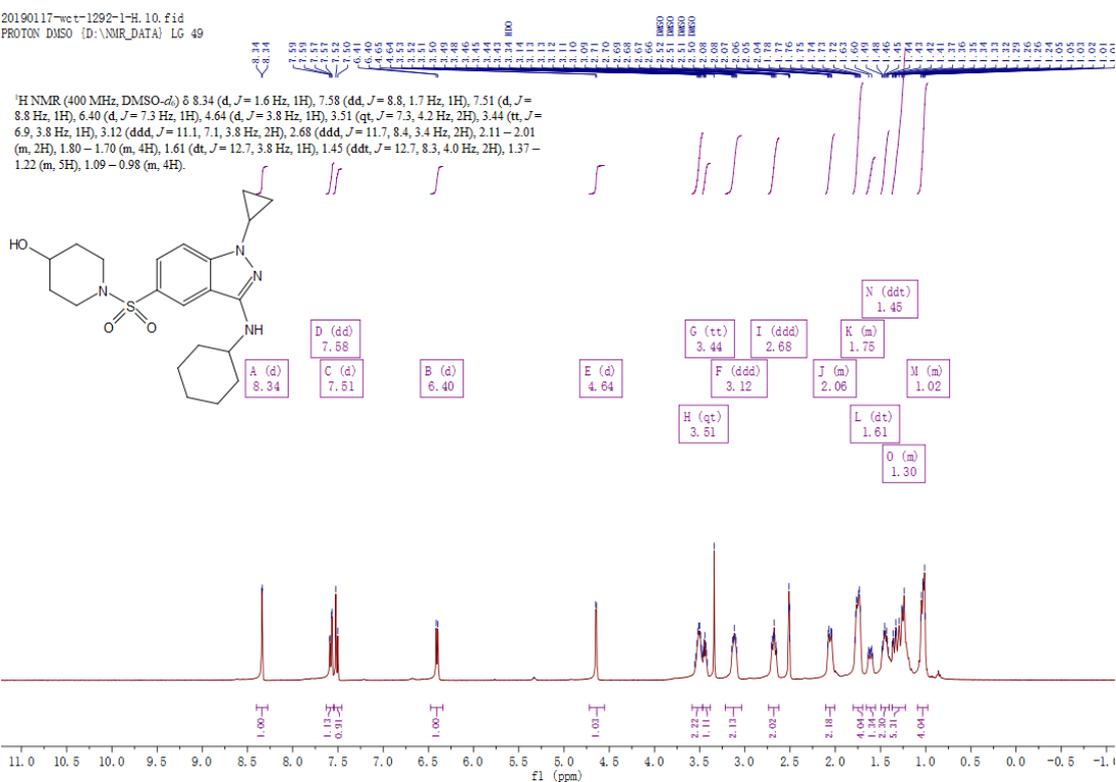
20190627-wct-1199-2-C/10
 C13CPD DMSO [D:\NMR_DATA] LG 22

¹³C NMR (101 MHz, DMSO-*d*₆) δ 161.65 (d, *J* = 242.0 Hz), 150.26, 143.16, 136.63 (d, *J* = 2.9 Hz), 130.18 (d, *J* = 8.0 Hz), 125.86, 124.92, 123.01, 115.31 (d, *J* = 21.2 Hz), 114.46, 109.76, 64.27, 46.26, 43.69, 33.37, 29.23, 6.73.

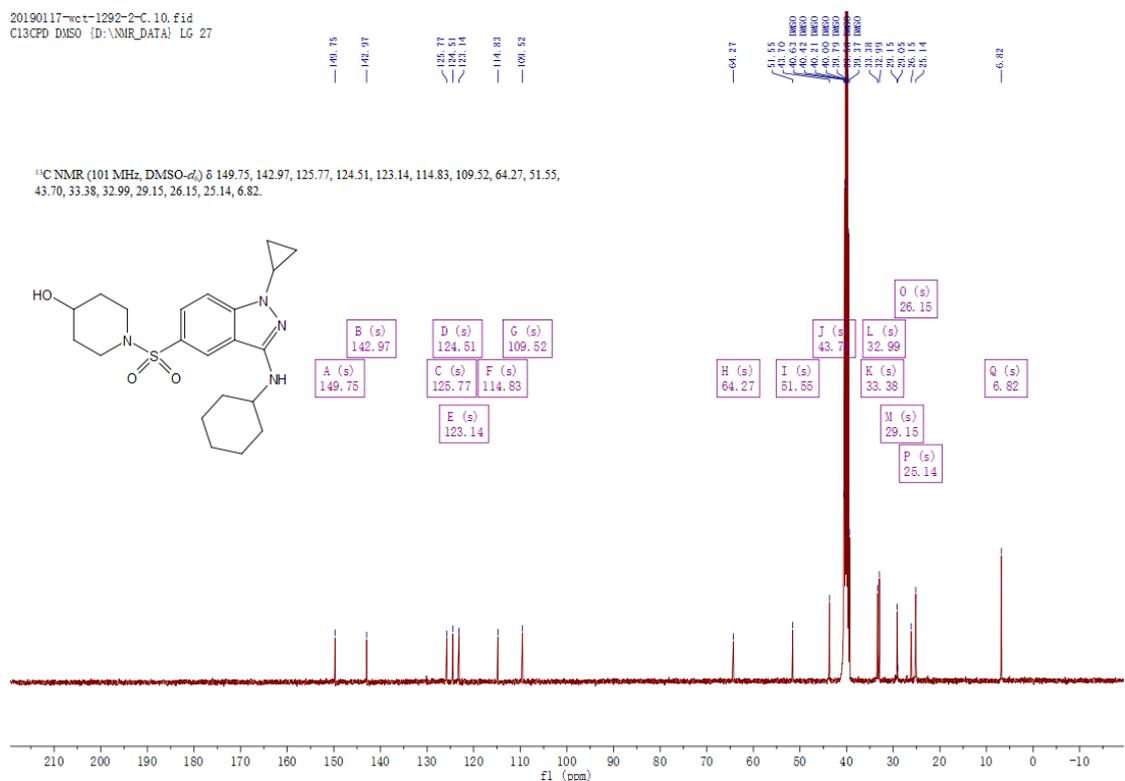


Compound 27.

20190117-wet-1292-1-H.10.fid
 PROTON DMSO [D:\NMR_DATA] LG 49



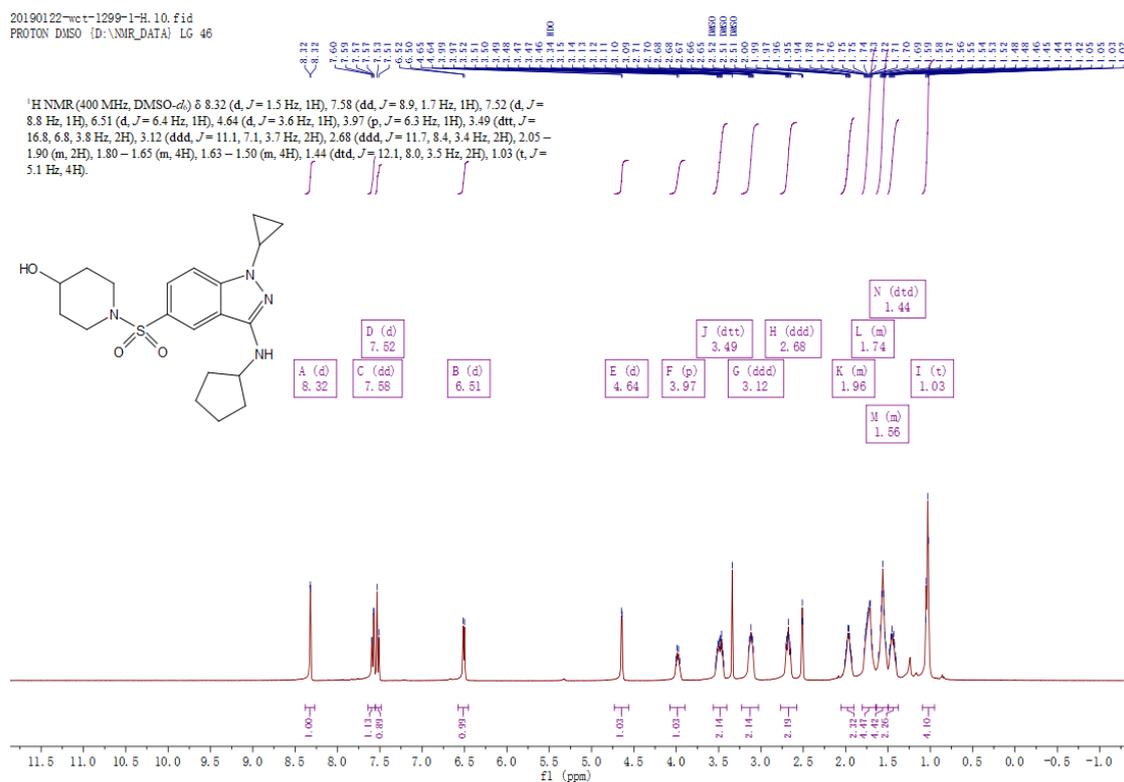
20190117-wet-1292-2-C.10.fid
 C13CPD DMSO [D:\NMR_DATA] LG 27



Compound 28.

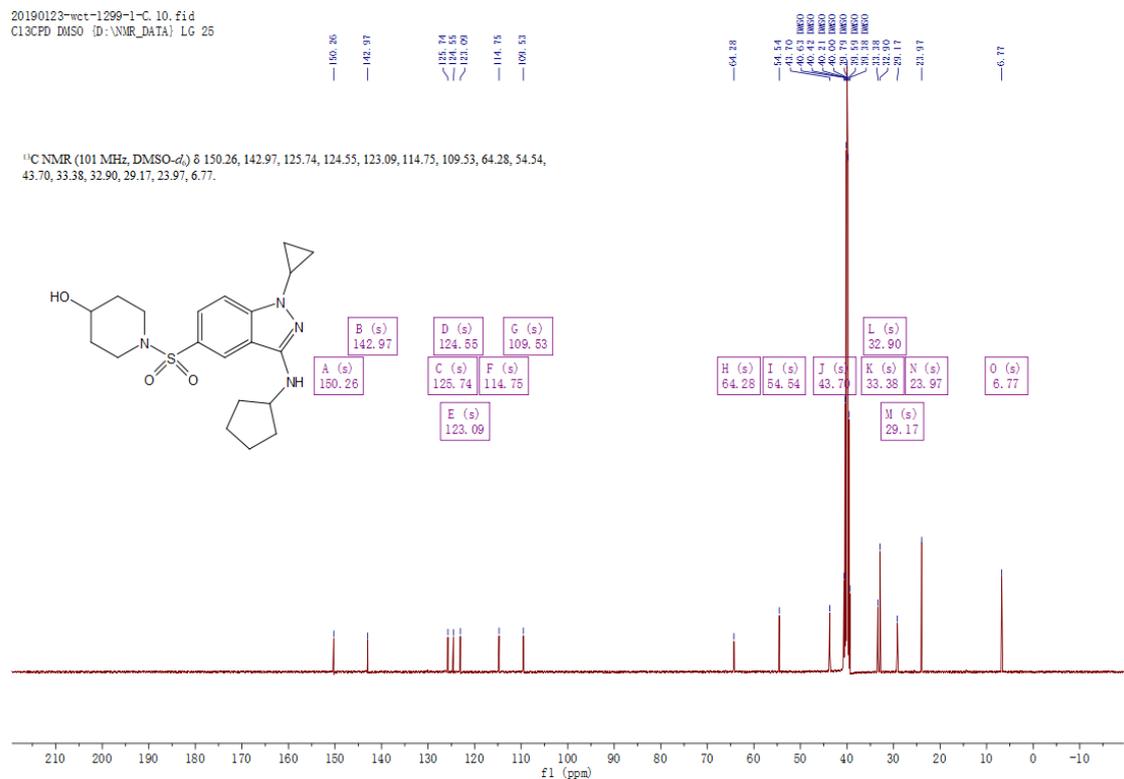
20190122-wet-1299-1-H.10.fid
 PROTON DMSO [D:\NMR_DATA] LG 46

¹H NMR (400 MHz, DMSO-*d*₆) δ 8.32 (d, *J* = 1.5 Hz, 1H), 7.58 (dd, *J* = 8.9, 1.7 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 6.51 (d, *J* = 6.4 Hz, 1H), 4.64 (d, *J* = 3.6 Hz, 1H), 3.97 (p, *J* = 6.3 Hz, 1H), 3.49 (dt, *J* = 16.8, 6.8, 3.8 Hz, 2H), 3.12 (ddd, *J* = 11.1, 7.1, 3.7 Hz, 2H), 2.68 (ddd, *J* = 11.7, 8.4, 3.4 Hz, 2H), 2.05–1.90 (m, 2H), 1.80–1.65 (m, 4H), 1.63–1.50 (m, 4H), 1.44 (dtd, *J* = 12.1, 8.0, 3.5 Hz, 2H), 1.03 (t, *J* = 5.1 Hz, 4H).



20190123-wet-1299-1-C.10.fid
 C13CPD DMSO [D:\NMR_DATA] LG 25

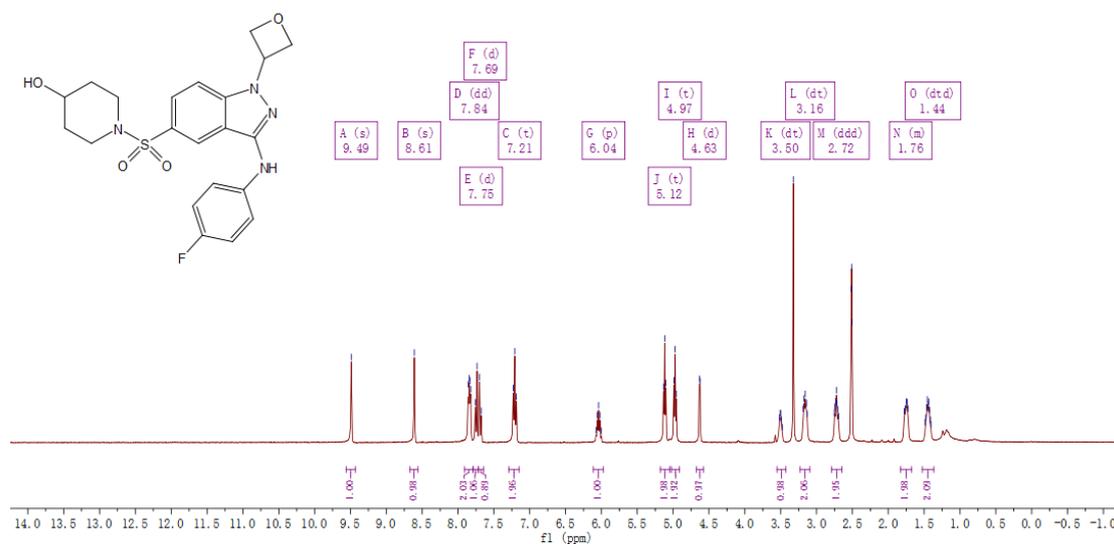
¹³C NMR (101 MHz, DMSO-*d*₆) δ 150.26, 142.97, 125.74, 124.55, 123.09, 114.75, 109.53, 64.28, 54.54, 43.70, 33.38, 32.90, 29.17, 23.97, 6.77.



Compound 29.

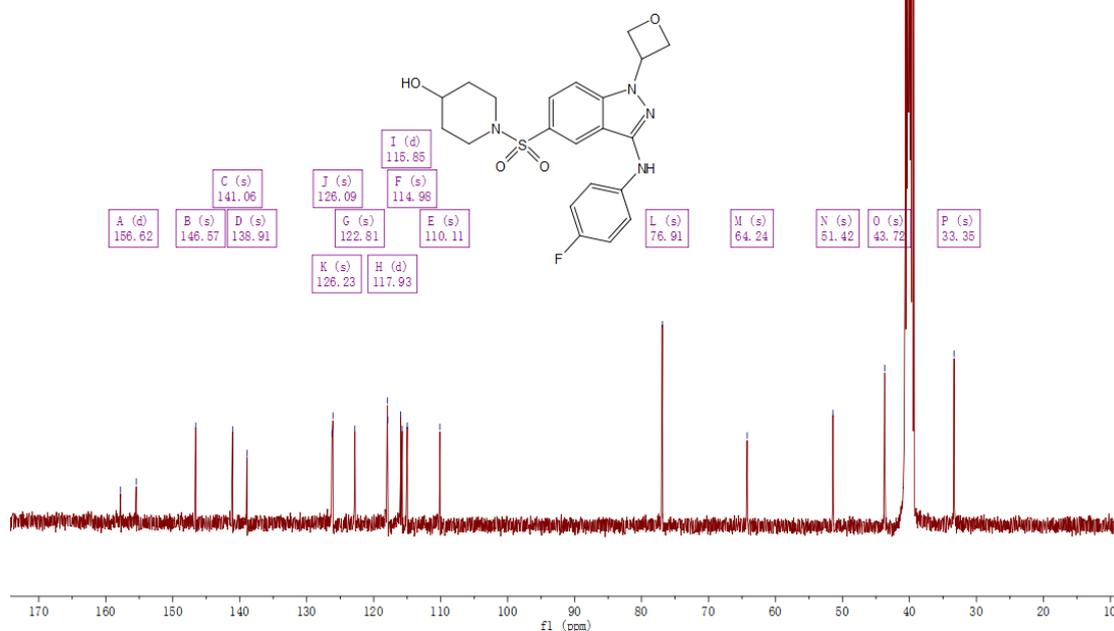
20181122-wct-1257-2-h.10.fid
 PROTON DMSO [D:\NMR_DATA] LG 13

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.49 (s, 1H), 8.61 (s, 1H), 7.84 (dd, *J* = 8.9, 4.8 Hz, 2H), 7.75 (d, *J* = 8.9 Hz, 1H), 7.69 (d, *J* = 9.0 Hz, 1H), 7.21 (t, *J* = 8.7 Hz, 2H), 6.04 (p, *J* = 7.2 Hz, 1H), 5.12 (t, *J* = 6.4 Hz, 2H), 4.97 (t, *J* = 7.0 Hz, 2H), 4.63 (d, *J* = 3.8 Hz, 1H), 3.50 (dt, *J* = 8.2, 3.9 Hz, 1H), 3.16 (dt, *J* = 11.2, 4.6 Hz, 2H), 2.72 (ddd, *J* = 12.0, 8.9, 3.3 Hz, 2H), 1.83–1.67 (m, 2H), 1.44 (ddd, *J* = 12.5, 8.4, 3.7 Hz, 2H).



20181123-wct-1257-2-c.10.fid

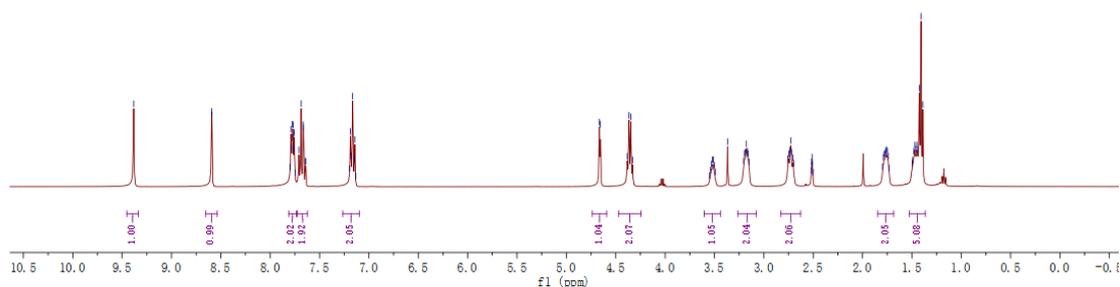
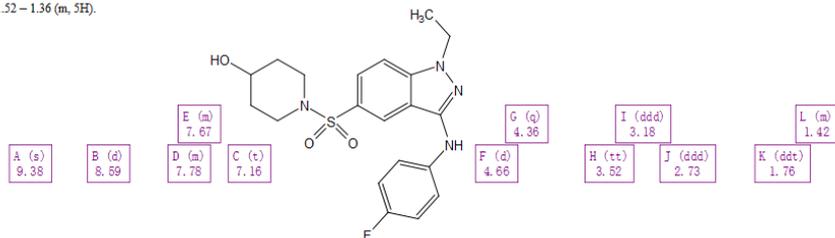
¹³C NMR (101 MHz, DMSO-*d*₆) δ 156.62 (d, *J* = 236.2 Hz), 146.57, 141.06, 138.91, 126.23, 126.09, 122.81, 117.93 (d, *J* = 7.3 Hz), 115.85 (d, *J* = 22.1 Hz), 114.98, 110.11, 76.91, 64.24, 51.42, 43.72, 33.35.



Compound 30.

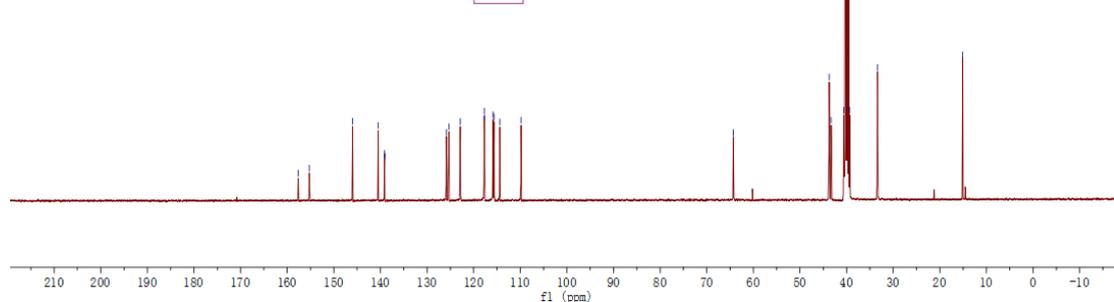
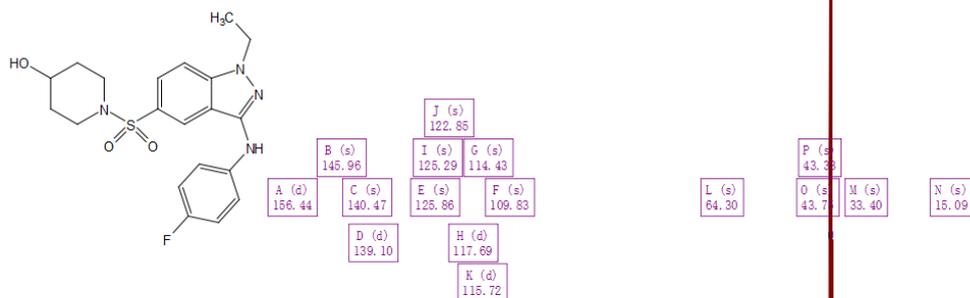
20181006-wet-1210-2r-Hz-10-52-2
 PROTON DMSO (D:\NMR_DATA\LG 52)

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.38 (s, 1H), 8.59 (d, *J* = 1.6 Hz, 1H), 7.81–7.73 (m, 2H), 7.72–7.62 (m, 2H), 7.16 (t, *J* = 8.9 Hz, 2H), 4.66 (d, *J* = 3.9 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.52 (tt, *J* = 7.8, 3.9 Hz, 1H), 3.18 (ddd, *J* = 11.1, 7.0, 3.7 Hz, 2H), 2.73 (ddd, *J* = 11.8, 8.6, 3.4 Hz, 2H), 1.76 (ddt, *J* = 14.0, 7.3, 3.6 Hz, 2H), 1.52–1.36 (m, 5H).



20181006-wet-1210-3-C.20.fid
 C13CPD DMSO (D:\NMR_DATA\LG 52)

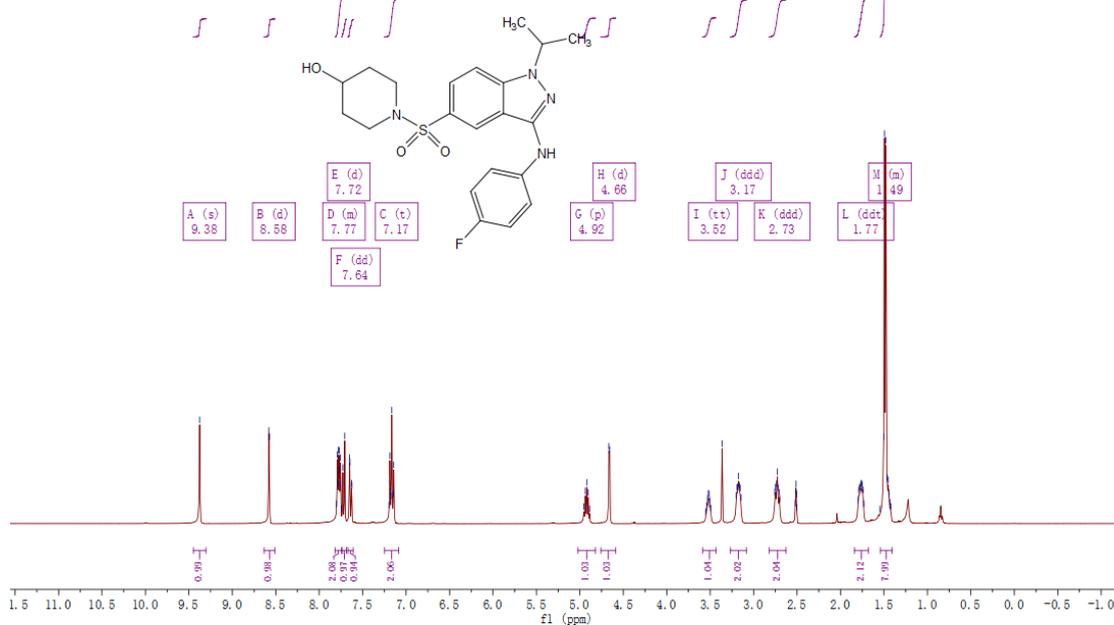
¹³C NMR (101 MHz, DMSO-*d*₆) δ 156.44 (d, *J* = 235.7 Hz), 145.96, 140.47, 139.10 (d, *J* = 2.2 Hz), 125.86, 125.29, 122.85, 117.69 (d, *J* = 7.3 Hz), 115.72 (d, *J* = 22.0 Hz), 114.43, 109.83, 64.30, 43.75, 43.33, 33.40, 15.09.



Compound 31.

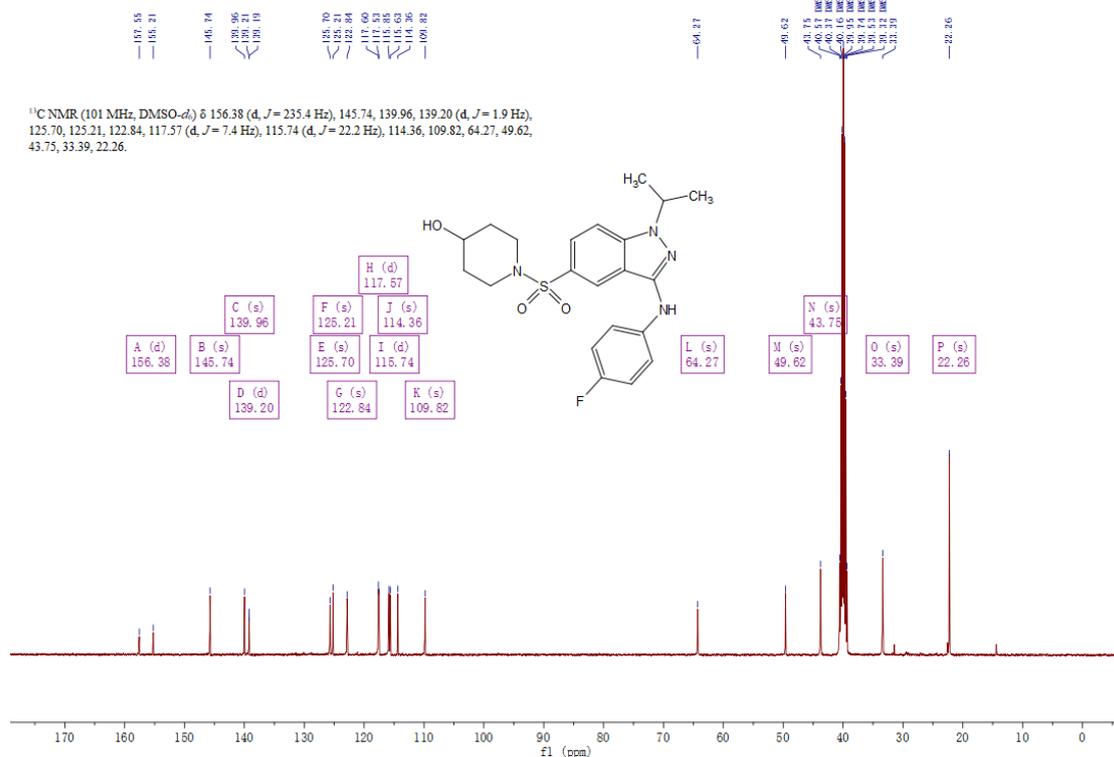
20181006-wet-1211-1-H.10.fid
 PROTON DMSO [D:\NMR_DATA] LG=66

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.38 (s, 1H), 8.58 (d, *J* = 1.6 Hz, 1H), 7.82 – 7.74 (m, 2H), 7.72 (d, *J* = 9.0 Hz, 1H), 7.64 (dd, *J* = 8.9, 1.7 Hz, 1H), 7.17 (t, *J* = 8.9 Hz, 2H), 4.92 (p, *J* = 6.5 Hz, 1H), 4.66 (d, *J* = 3.9 Hz, 1H), 3.52 (tt, *J* = 7.6, 3.7 Hz, 1H), 3.17 (ddd, *J* = 11.1, 7.0, 3.8 Hz, 2H), 2.73 (ddd, *J* = 11.7, 8.5, 3.4 Hz, 2H), 1.77 (ddt, *J* = 13.7, 7.1, 3.2 Hz, 2H), 1.54 – 1.41 (m, 8H).



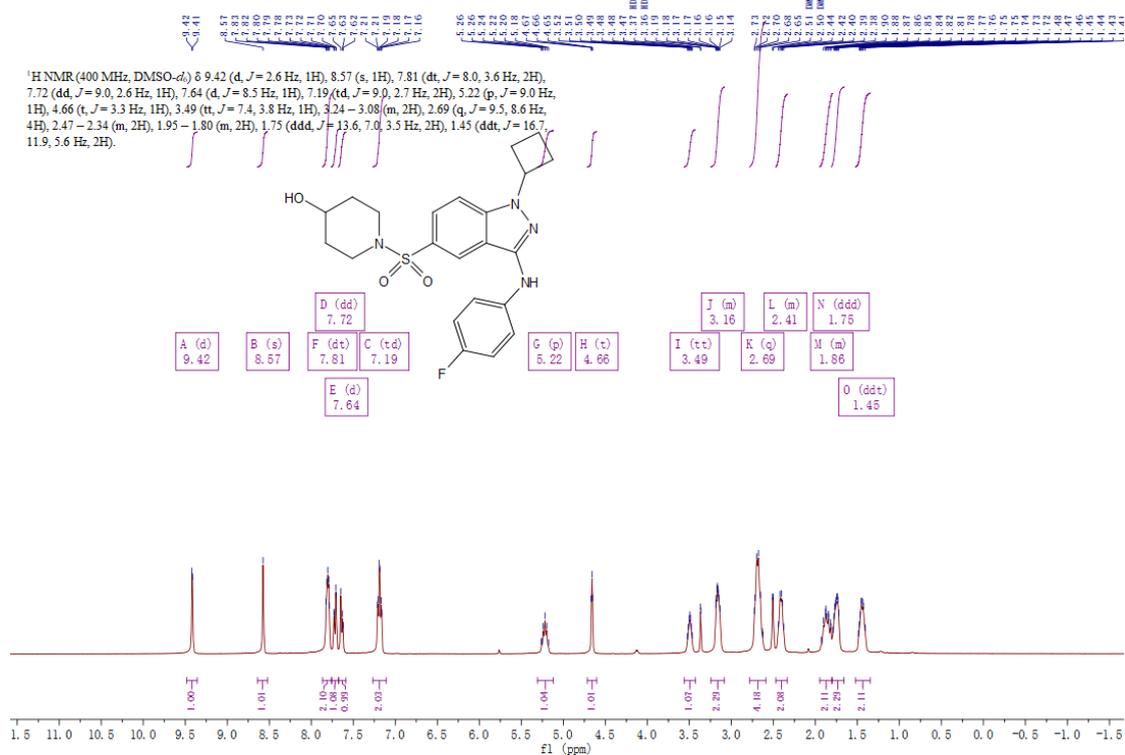
20181006-wet-1211-1-C.10.fid

¹³C NMR (101 MHz, DMSO-*d*₆) δ 156.38 (d, *J* = 235.4 Hz), 145.74, 139.96, 139.20 (d, *J* = 1.9 Hz), 125.70, 125.21, 122.84, 117.57 (d, *J* = 7.4 Hz), 115.74 (d, *J* = 22.2 Hz), 114.36, 109.82, 64.27, 49.62, 43.75, 33.39, 22.26.

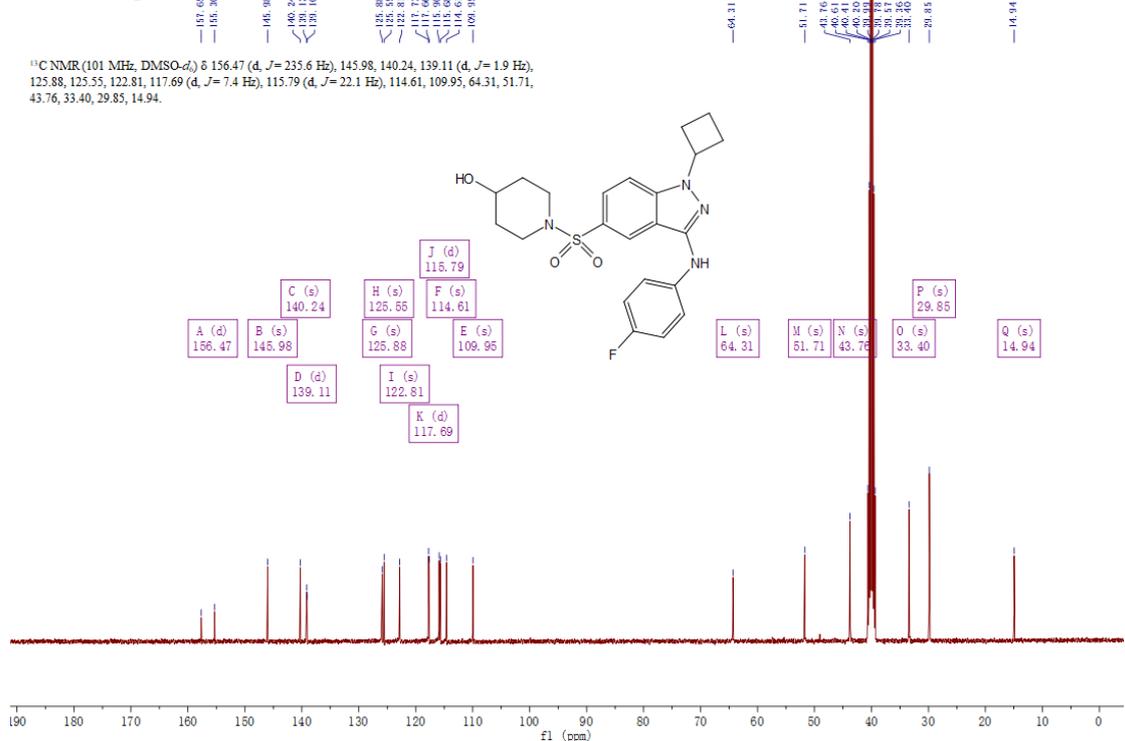


Compound 32.

20190104-wet-1290-1-H.10.fid



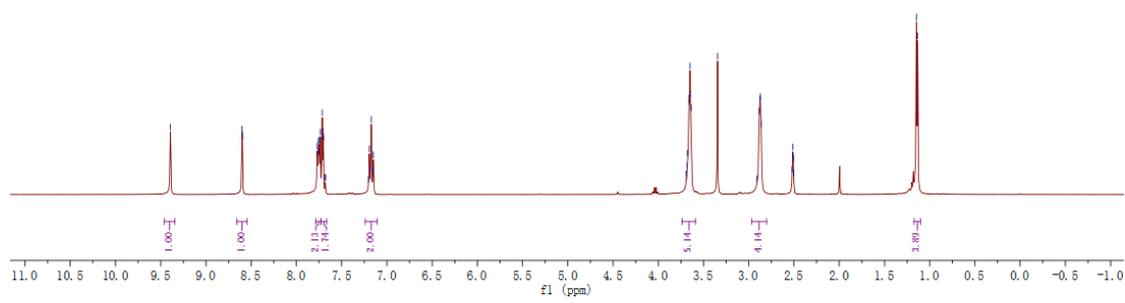
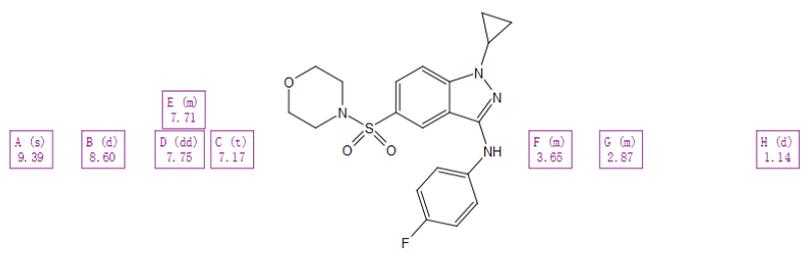
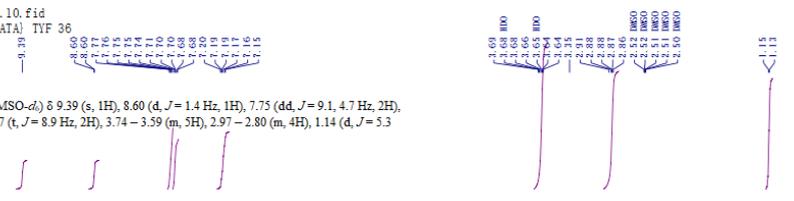
20190104-wet-1290-1-C.10.fid
C13CPD DMSO (D:\NMR_DATA) LG 34



Compound 33.

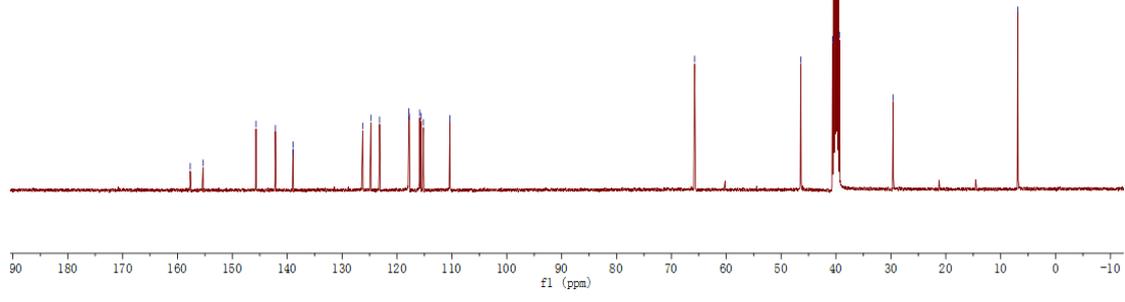
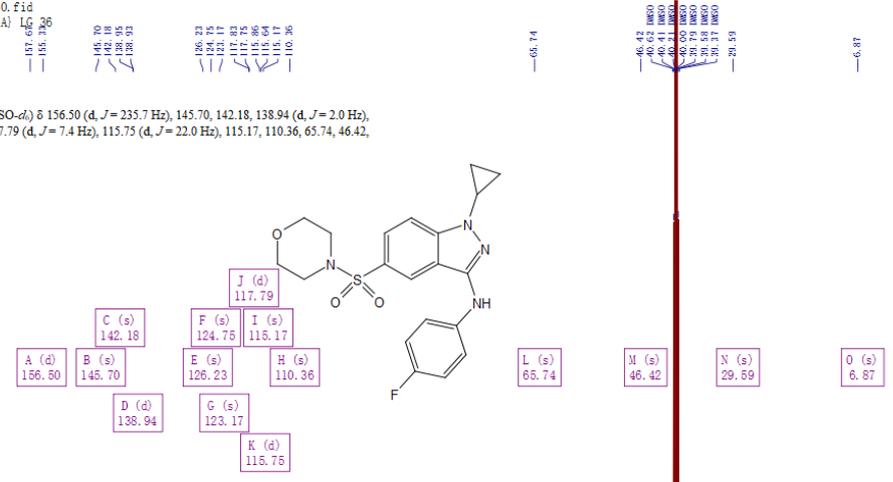
20180928-wct-1206-1-H.10.fid
 PROTON DMSO (D:\NMR_DATA) TYF 36

¹H NMR (400 MHz, DMSO-d₆) δ 9.39 (s, 1H), 8.60 (d, *J* = 1.4 Hz, 1H), 7.75 (dd, *J* = 9.1, 4.7 Hz, 2H), 7.73 - 7.67 (m, 2H), 7.17 (t, *J* = 8.9 Hz, 2H), 3.74 - 3.59 (m, 5H), 2.97 - 2.80 (m, 4H), 1.14 (d, *J* = 5.3 Hz, 4H).



20180928-wct-1206-1-C.10.fid
 C13CPD DMSO (D:\NMR_DATA) LG

¹³C NMR (101 MHz, DMSO-d₆) δ 156.50 (d, *J* = 235.7 Hz), 145.70, 142.18, 138.94 (d, *J* = 2.0 Hz), 126.23, 124.75, 123.17, 117.79 (d, *J* = 7.4 Hz), 115.75 (d, *J* = 22.0 Hz), 115.17, 110.36, 65.74, 46.42, 29.59, 6.87.

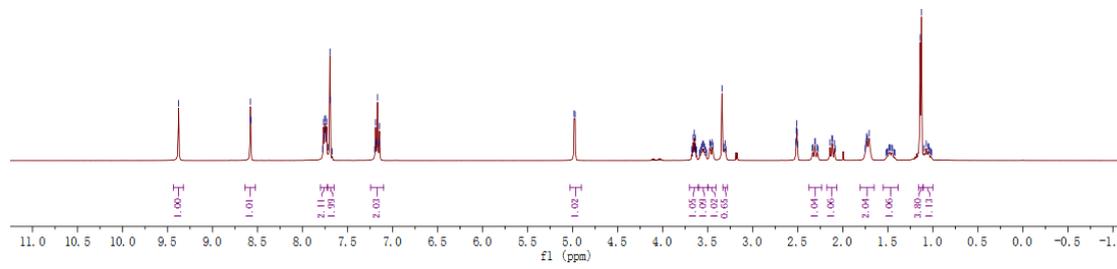
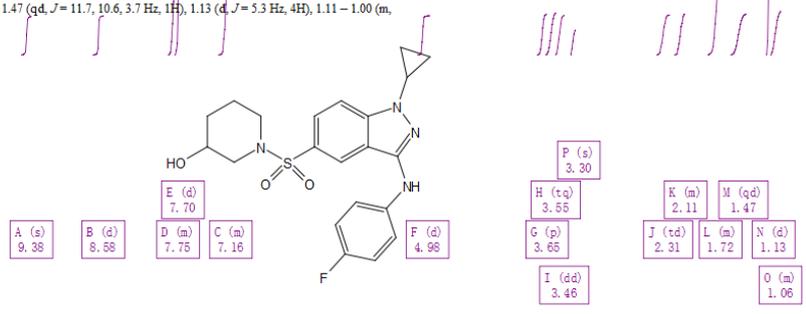


Compound 34.

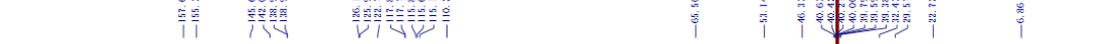
20181030-wet-1230-2-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 22



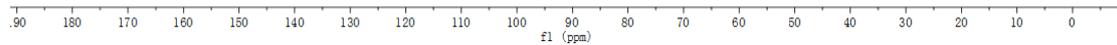
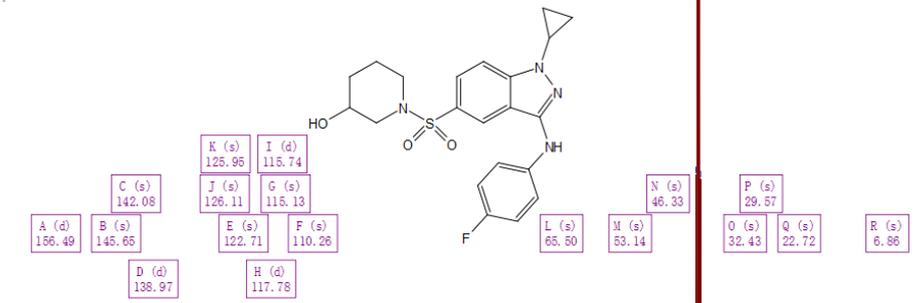
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.38 (s, 1H), 8.58 (d, *J* = 1.2 Hz, 1H), 7.80 – 7.72 (m, 2H), 7.70 (d, *J* = 1.7 Hz, 2H), 7.24 – 7.10 (m, 2H), 4.98 (d, *J* = 4.8 Hz, 1H), 3.65 (p, *J* = 5.3 Hz, 1H), 3.55 (tq, *J* = 8.8, 4.1 Hz, 1H), 3.46 (dd, *J* = 10.9, 4.2 Hz, 1H), 3.30 (s, 1H), 2.81 (td, *J* = 11.1, 2.5 Hz, 1H), 2.18 – 2.07 (m, 1H), 1.81 – 1.65 (m, 2H), 1.47 (qd, *J* = 11.7, 10.6, 3.7 Hz, 1H), 1.13 (d, *J* = 5.3 Hz, 4H), 1.11 – 1.00 (m, 1H).



20181030-wet-1230-2-C.12.fid
 C13CPD DMSO (D:\NMR_DATA) LG 22

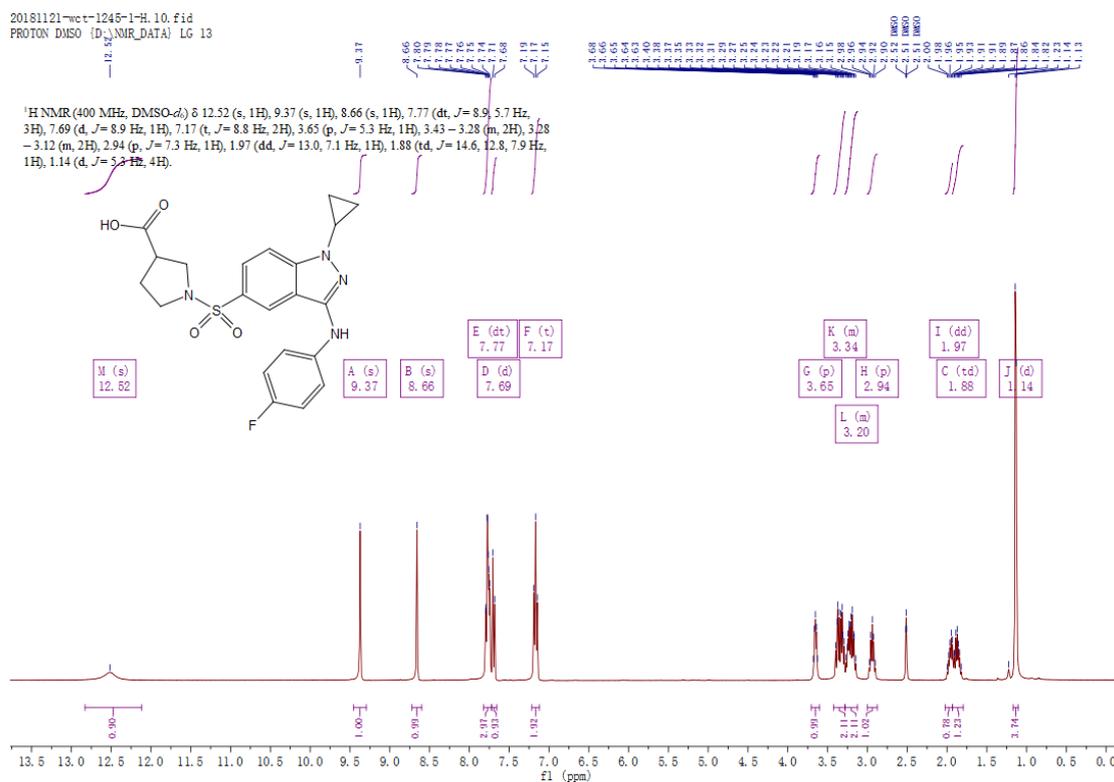


¹³C NMR (101 MHz, DMSO-*d*₆) δ 156.49 (d, *J* = 235.5 Hz), 145.65, 142.08, 138.97 (d, *J* = 2.0 Hz), 126.11, 125.95, 122.71, 117.78 (d, *J* = 7.3 Hz), 115.74 (d, *J* = 22.1 Hz), 115.13, 110.26, 65.50, 53.14, 46.33, 32.43, 29.57, 22.72, 6.86.

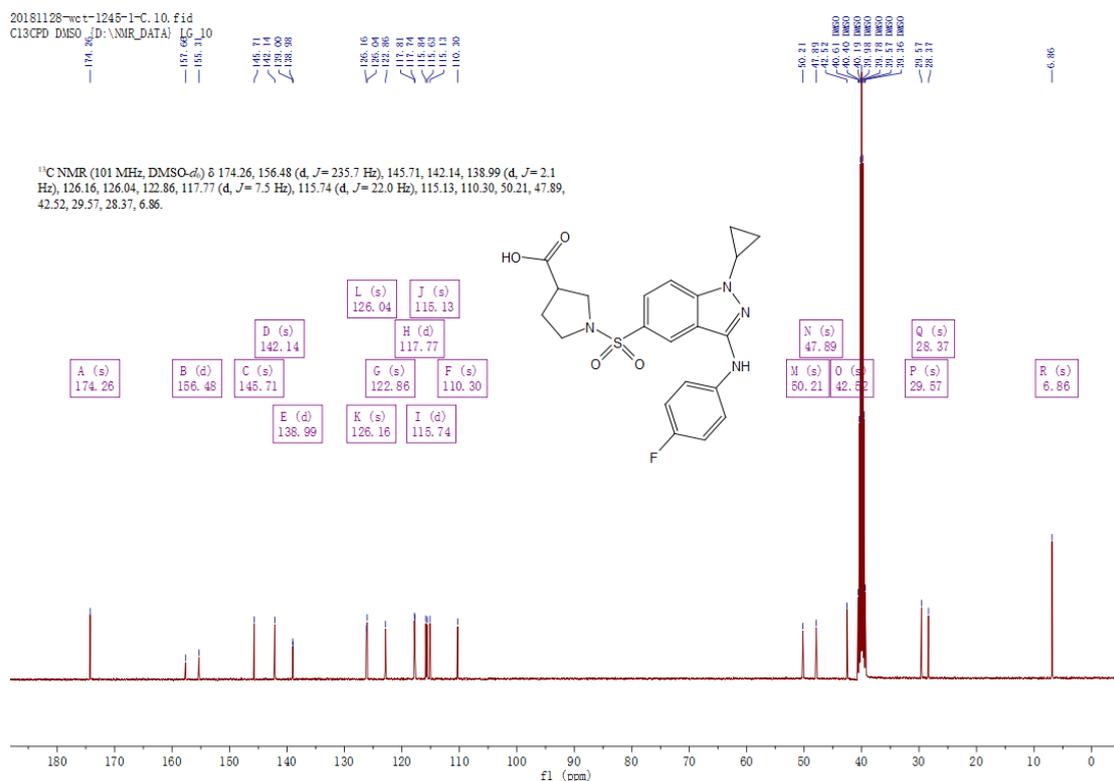


Compound 35.

20181121-wet-1245-1-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 13

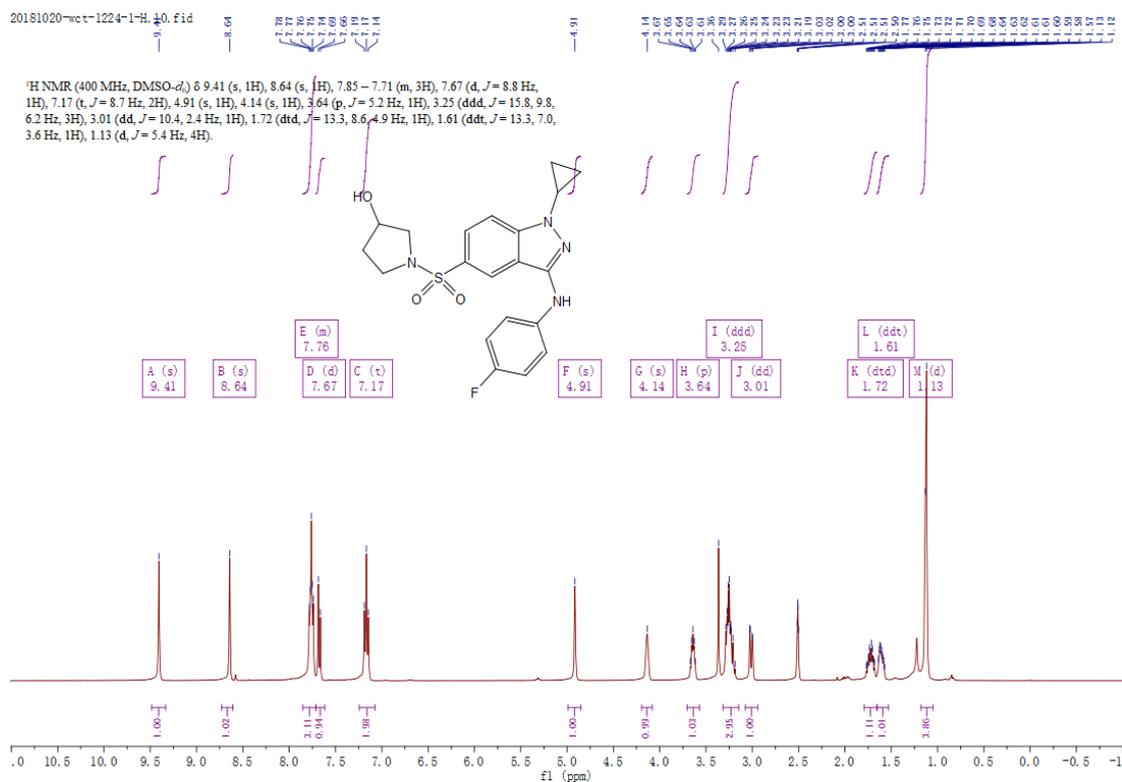


20181128-wet-1245-1-C.10.fid
 C13CPD DMSO (D:\NMR_DATA) LG 10



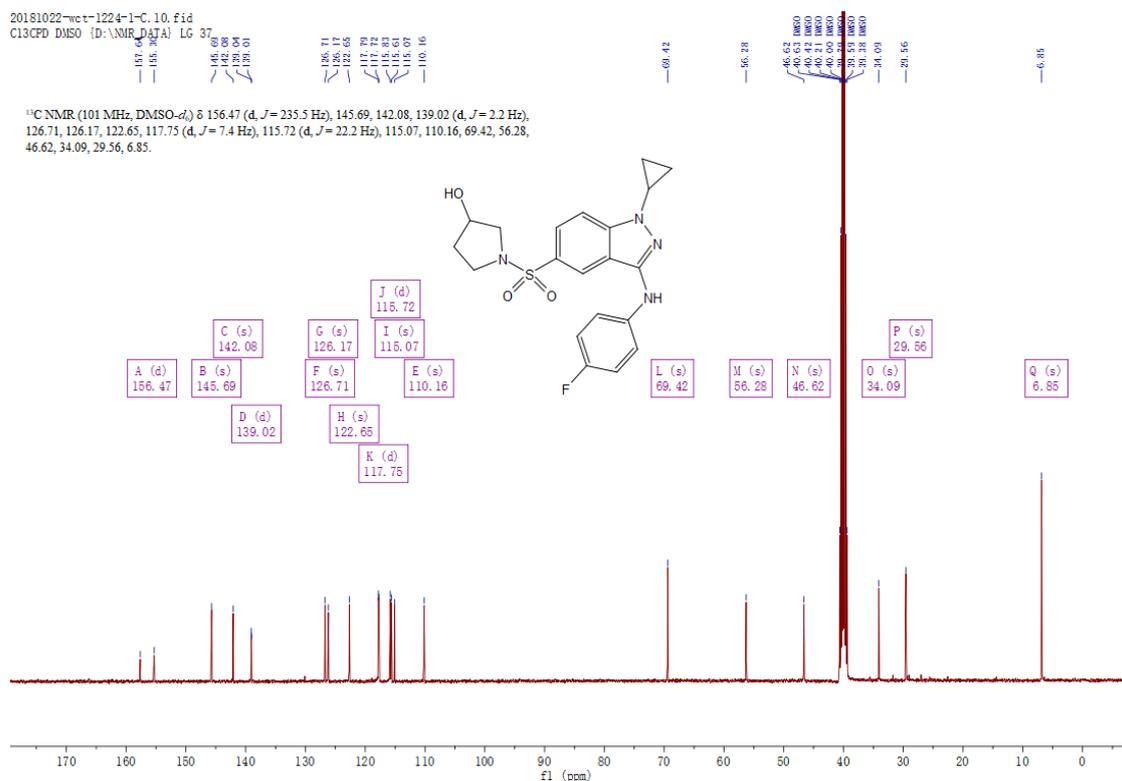
Compound 36.

20181020-wet-1224-1-H.40.fid



20181022-wet-1224-1-C.10.fid

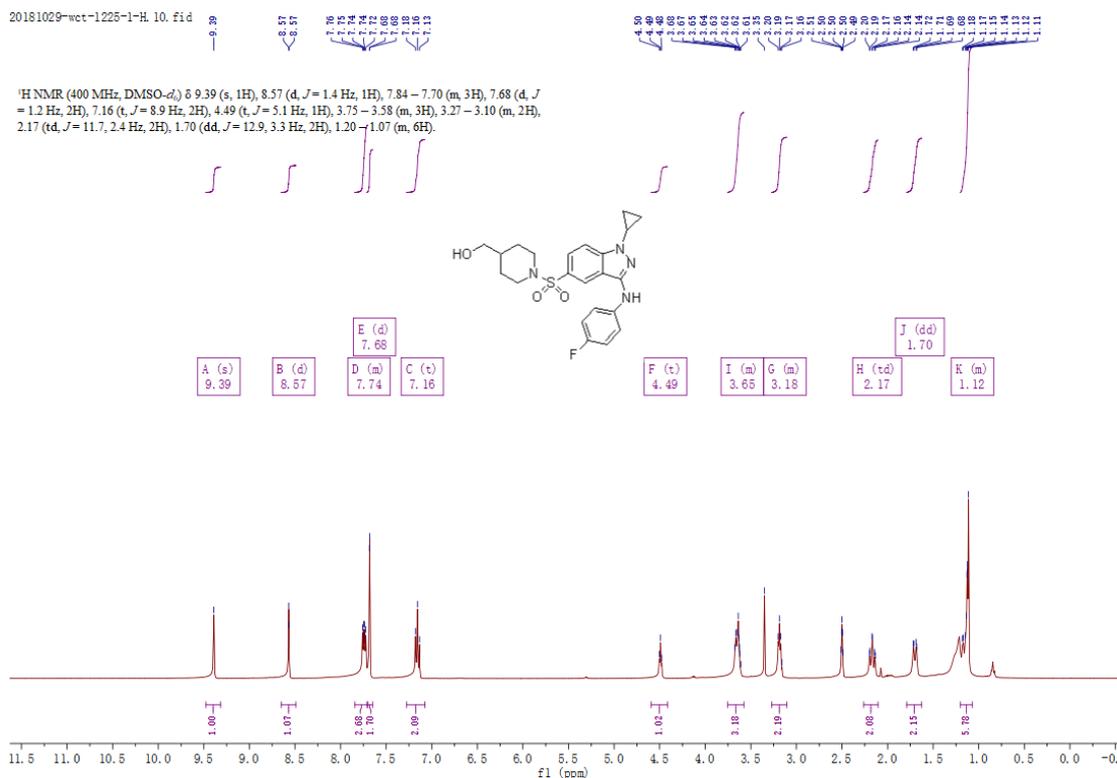
C13CPD DMSO {D:\NMR_DATA} LG 37



Compound 37.

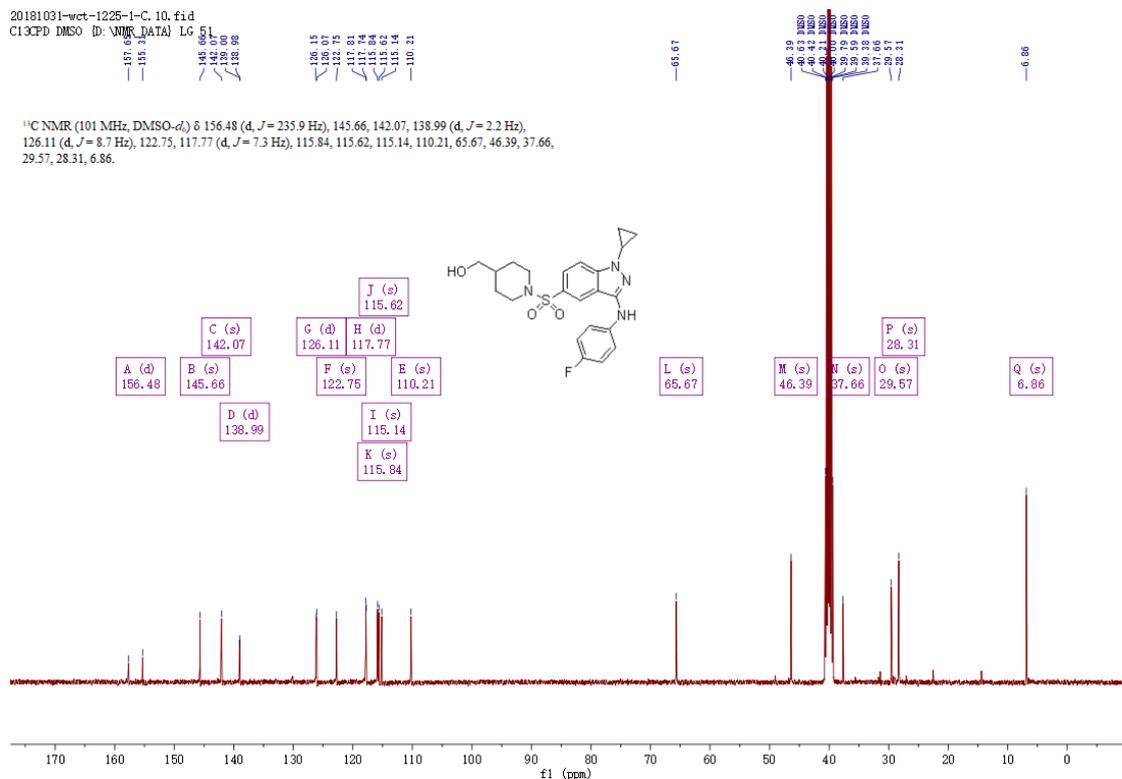
20181029-wet-1225-1-H. 10. fid

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.39 (s, 1H), 8.57 (d, *J* = 1.4 Hz, 1H), 7.84 – 7.70 (m, 3H), 7.68 (d, *J* = 1.2 Hz, 2H), 7.16 (t, *J* = 8.9 Hz, 2H), 4.49 (t, *J* = 5.1 Hz, 1H), 3.75 – 3.58 (m, 3H), 3.27 – 3.10 (m, 2H), 2.17 (td, *J* = 11.7, 2.4 Hz, 2H), 1.70 (dd, *J* = 12.9, 3.3 Hz, 2H), 1.20 – 1.07 (m, 6H).



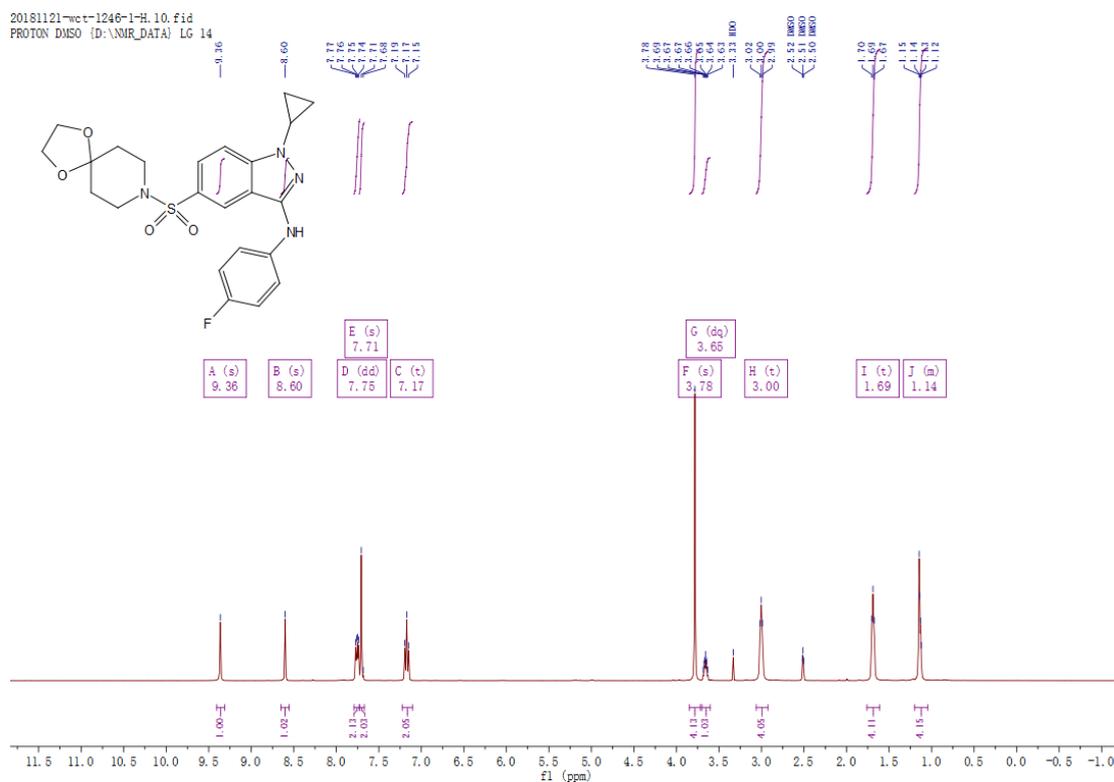
20181031-wet-1225-1-C. 10. fid
C13CPD DMSO (D:\NMR\DATA) LG 51

¹³C NMR (101 MHz, DMSO-*d*₆) δ 156.48 (d, *J* = 235.9 Hz), 145.66, 142.07, 138.99 (d, *J* = 2.2 Hz), 126.11 (d, *J* = 8.7 Hz), 122.75, 117.77 (d, *J* = 7.3 Hz), 115.84, 115.62, 115.14, 110.21, 65.67, 46.39, 37.66, 29.57, 28.31, 6.86.



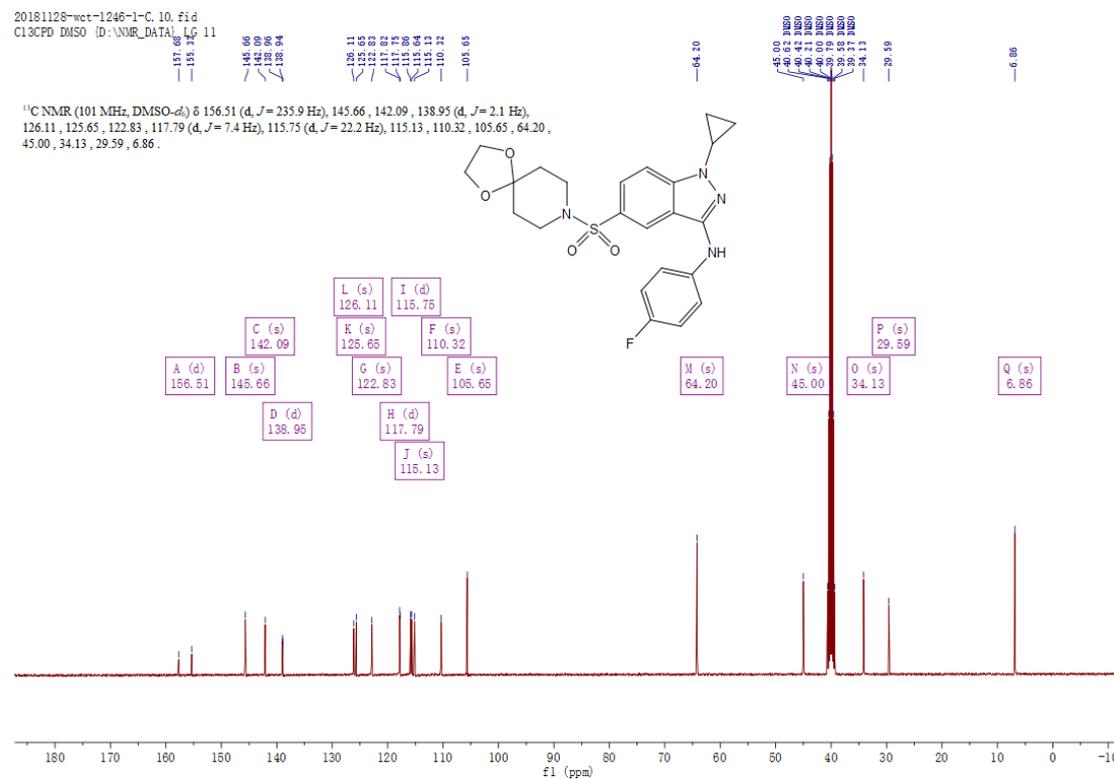
Compound 38.

20181121-wet-1246-1-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 14



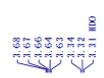
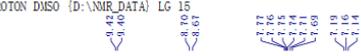
20181128-wet-1246-1-C.10.fid
 C13CPD DMSO (D:\NMR_DATA) LG 11

¹³C NMR (101 MHz, DMSO-d₆) δ 156.51 (d, J=235.9 Hz), 145.66, 142.09, 138.95 (d, J=2.1 Hz), 126.11, 125.65, 122.83, 117.79 (d, J=7.4 Hz), 115.75 (d, J=22.2 Hz), 115.13, 110.32, 105.65, 64.20, 45.00, 34.13, 29.59, 6.86.

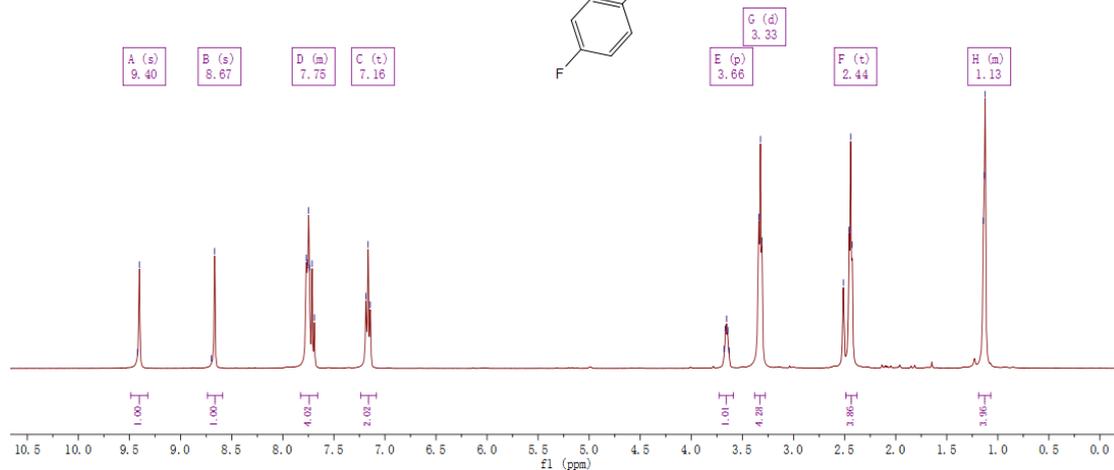
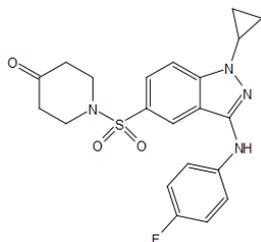


Compound 39.

20181121-wet-1247-1-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 15



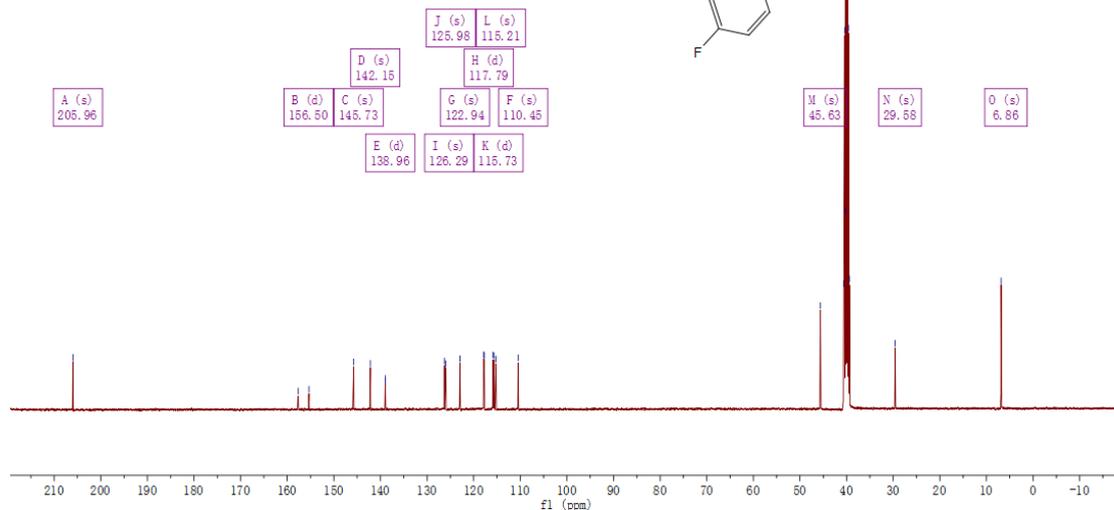
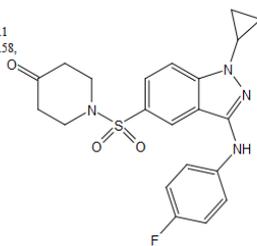
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.40 (s, 1H), 8.67 (s, 1H), 7.82–7.66 (m, 4H), 7.16 (t, *J* = 8.7 Hz, 2H), 3.66 (p, *J* = 5.4 Hz, 1H), 3.33 (d, *J* = 6.6 Hz, 4H), 2.44 (t, *J* = 6.1 Hz, 4H), 1.19–1.07 (m, 4H).



20181127-wet-1247-1-C.10.fid
 C13CPD DMSO (D:\NMR_DATA) LG 7



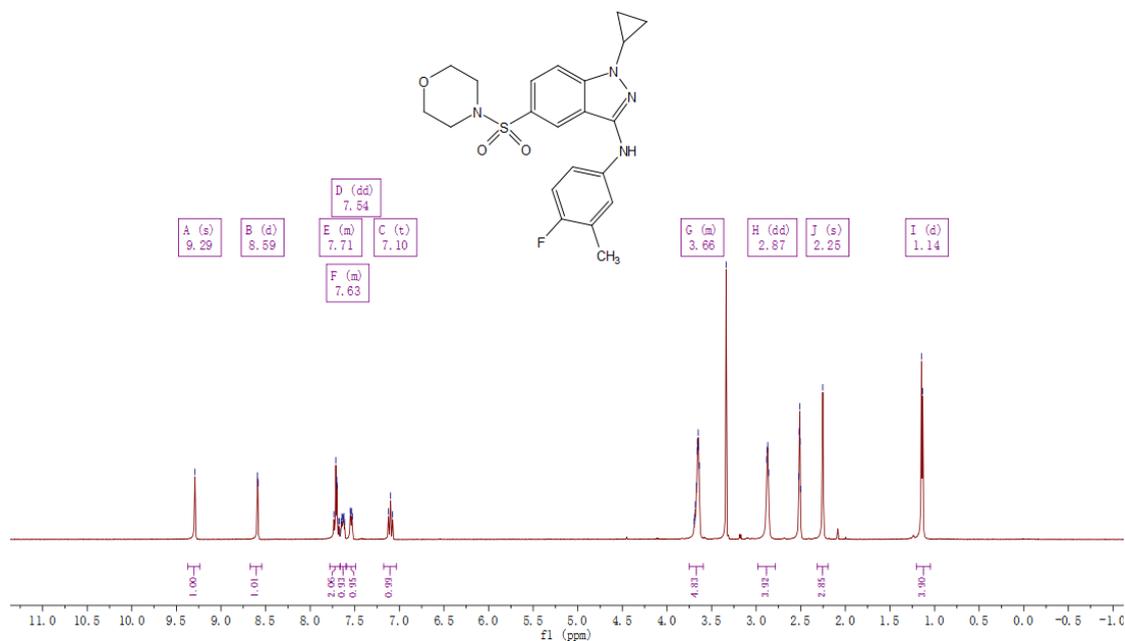
¹³C NMR (101 MHz, DMSO-*d*₆) δ 205.96, 156.50 (d, *J* = 235.6 Hz), 145.73, 142.15, 138.96 (d, *J* = 2.1 Hz), 126.29, 125.98, 122.94, 117.79 (d, *J* = 7.4 Hz), 115.73 (d, *J* = 22.2 Hz), 115.21, 110.45, 45.63, 29.58, 6.86.



Compound 40.

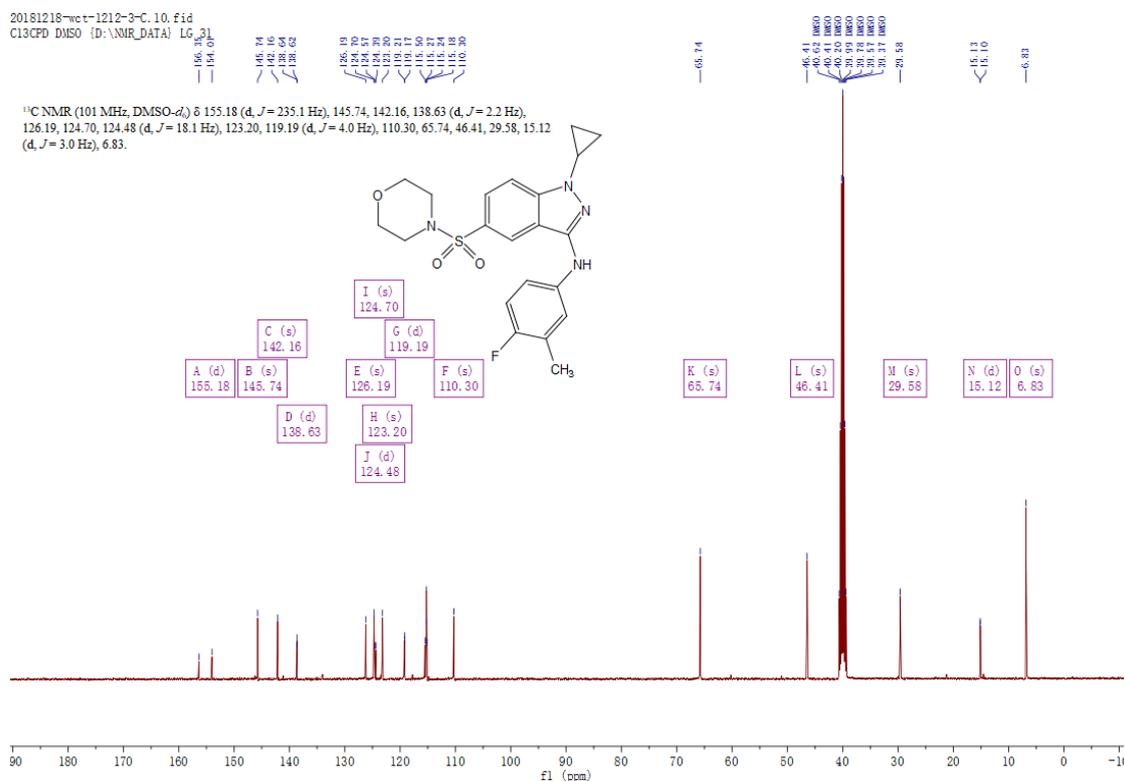
20181024-wct-1212-3-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG_33

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.29 (s, 1H), 8.59 (d, *J* = 1.5 Hz, 1H), 7.78 – 7.67 (m, 2H), 7.67 – 7.60 (m, 1H), 7.54 (dd, *J* = 6.9, 2.8 Hz, 1H), 7.10 (t, *J* = 9.2 Hz, 1H), 3.75 – 3.59 (m, 5H), 2.87 (dd, *J* = 5.6, 3.4 Hz, 4H), 2.25 (s, 3H), 1.14 (d, *J* = 5.3 Hz, 4H).



20181218-wct-1212-3-C.10.fid
 C13CPD DMSO (D:\NMR_DATA) LG_31

¹³C NMR (101 MHz, DMSO-*d*₆) δ 155.18 (d, *J* = 235.1 Hz), 145.74, 142.16, 138.63 (d, *J* = 2.2 Hz), 126.19, 124.70, 124.48 (d, *J* = 18.1 Hz), 123.20, 119.19 (d, *J* = 4.0 Hz), 110.30, 65.74, 46.41, 29.58, 15.12 (d, *J* = 3.0 Hz), 6.83.

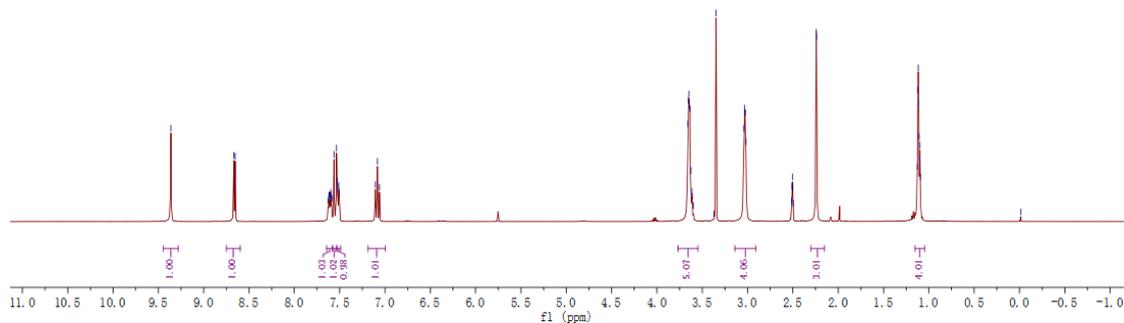
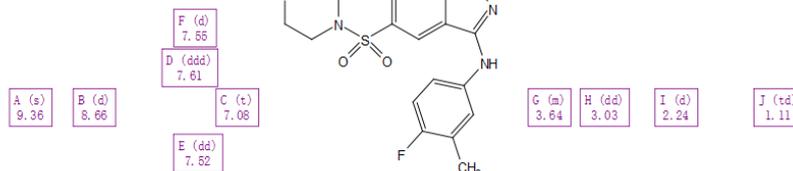
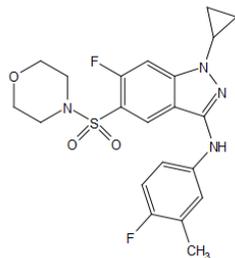


Compound 41.

20190717-wet-1419-1-H/10
 PROTON DMSO (D:\NMR_DATA) LG 16



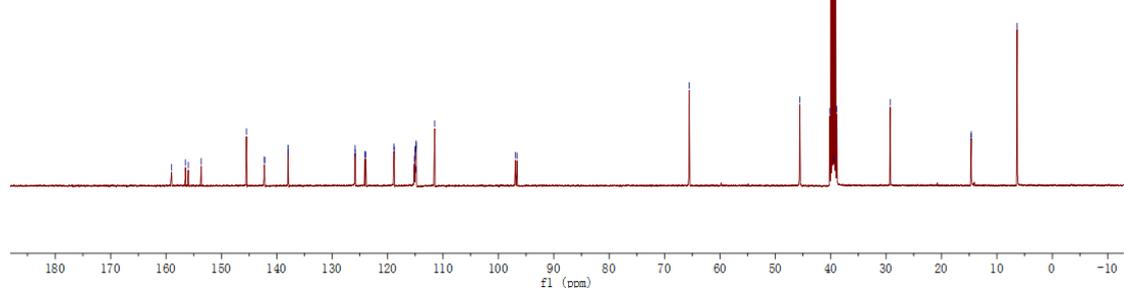
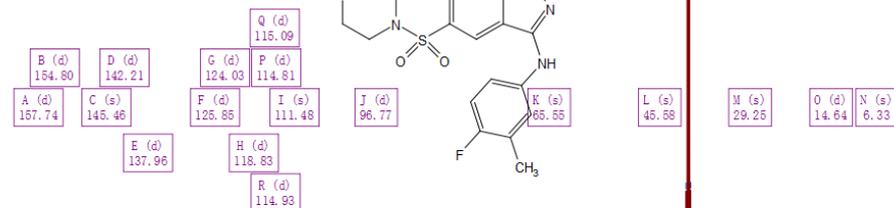
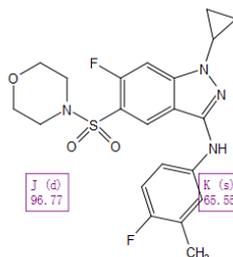
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.36 (s, 1H), 8.66 (d, *J* = 6.7 Hz, 1H), 7.61 (ddd, *J* = 8.9, 4.4, 2.9 Hz, 1H), 7.55 (d, *J* = 11.3 Hz, 1H), 7.52 (dd, *J* = 6.8, 2.8 Hz, 1H), 7.08 (t, *J* = 9.2 Hz, 1H), 3.77 – 3.55 (m, 3H), 3.03 (dd, *J* = 5.7, 3.5 Hz, 4H), 2.24 (d, *J* = 1.8 Hz, 3H), 1.11 (td, *J* = 5.2, 4.6, 3.1 Hz, 4H).



20190717-wet-1419-1-C/20
 C13CPD DMSO (D:\NMR_DATA) LG 16



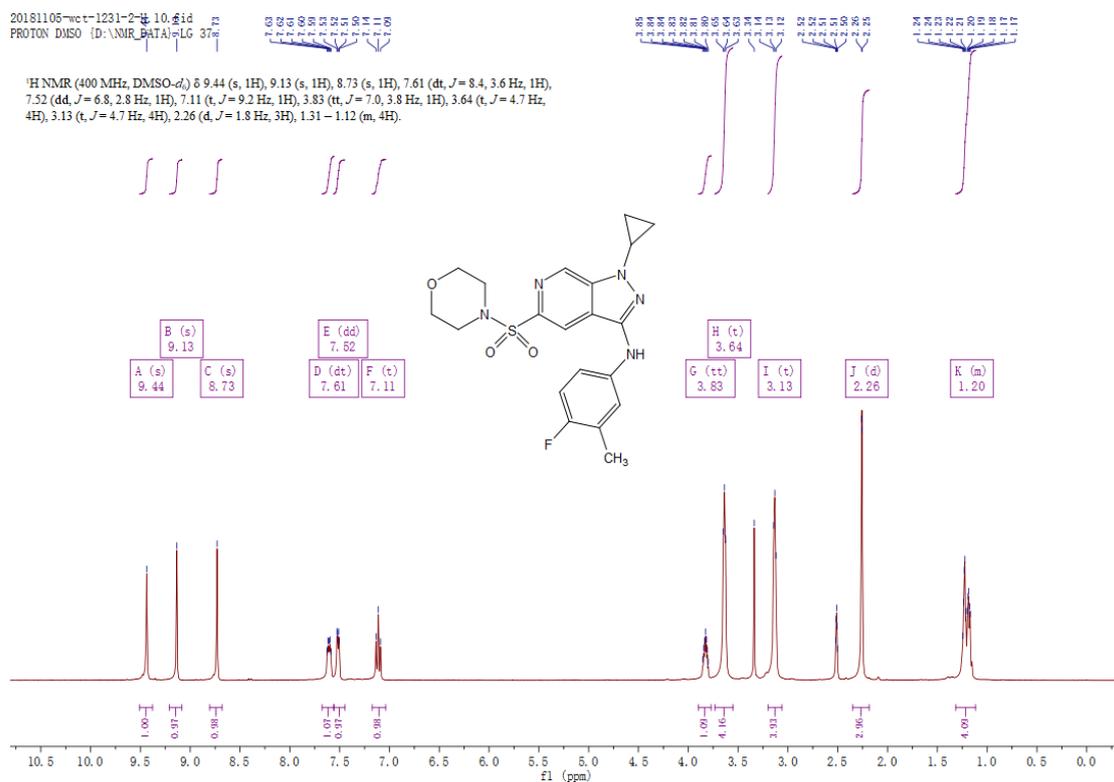
¹³C NMR (101 MHz, DMSO-*d*₆) δ 157.74 (d, *J* = 250.6 Hz), 154.80 (d, *J* = 235.3 Hz), 145.46, 142.21 (d, *J* = 12.5 Hz), 137.96 (d, *J* = 2.2 Hz), 125.85 (d, *J* = 3.2 Hz), 124.03 (d, *J* = 18.1 Hz), 118.83 (d, *J* = 4.0 Hz), 115.09 (d, *J* = 11.7 Hz), 114.93 (d, *J* = 6.2 Hz), 114.81 (d, *J* = 2.1 Hz), 111.48, 96.77 (d, *J* = 27.7 Hz), 65.55, 45.58, 29.25, 14.64 (d, *J* = 3.0 Hz), 6.33.



Compound 42.

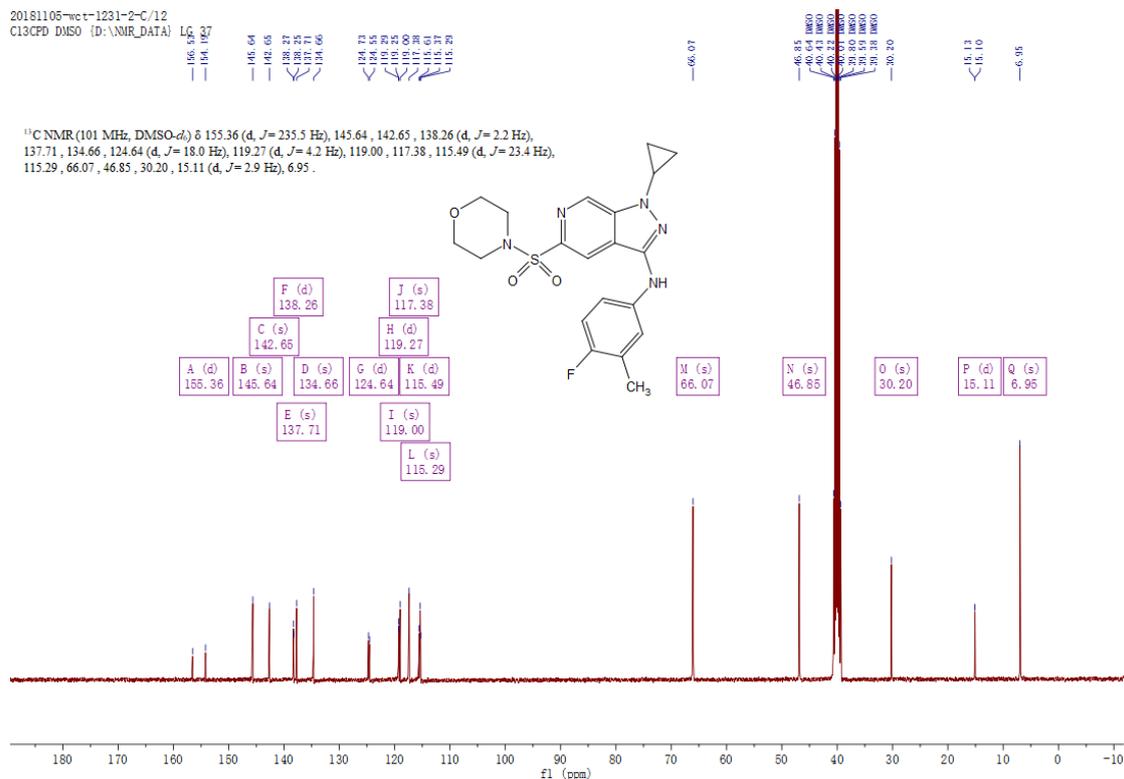
20181105-wet-1231-2-10.gid
 PROTON DMSO [D:\NMR_DATA] LG 37

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.44 (s, 1H), 9.13 (s, 1H), 8.73 (s, 1H), 7.61 (dt, *J* = 8.4, 3.6 Hz, 1H), 7.52 (dd, *J* = 6.8, 2.8 Hz, 1H), 7.11 (t, *J* = 9.2 Hz, 1H), 3.83 (tt, *J* = 7.0, 3.8 Hz, 1H), 3.64 (t, *J* = 4.7 Hz, 4H), 3.13 (t, *J* = 4.7 Hz, 4H), 2.26 (d, *J* = 1.8 Hz, 3H), 1.31–1.12 (m, 4H).



20181105-wet-1231-2-C/12
 C13CPD DMSO [D:\NMR_DATA] LG 37

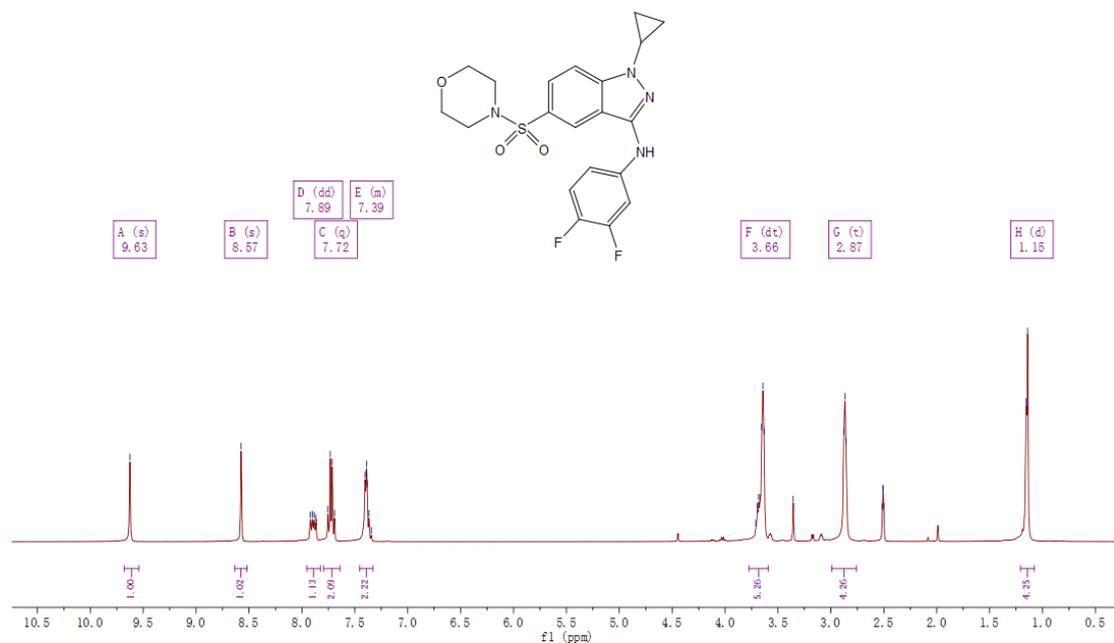
¹³C NMR (101 MHz, DMSO-*d*₆) δ 155.36 (d, *J* = 235.5 Hz), 145.64, 142.65, 138.26 (d, *J* = 2.2 Hz), 137.71, 134.66, 124.64 (d, *J* = 18.0 Hz), 119.27 (d, *J* = 4.2 Hz), 119.00, 117.38, 115.49 (d, *J* = 23.4 Hz), 115.29, 66.07, 46.85, 30.20, 15.11 (d, *J* = 2.9 Hz), 6.95.



Compound 43.

20190104-wet-1290-2-H. 10. fid

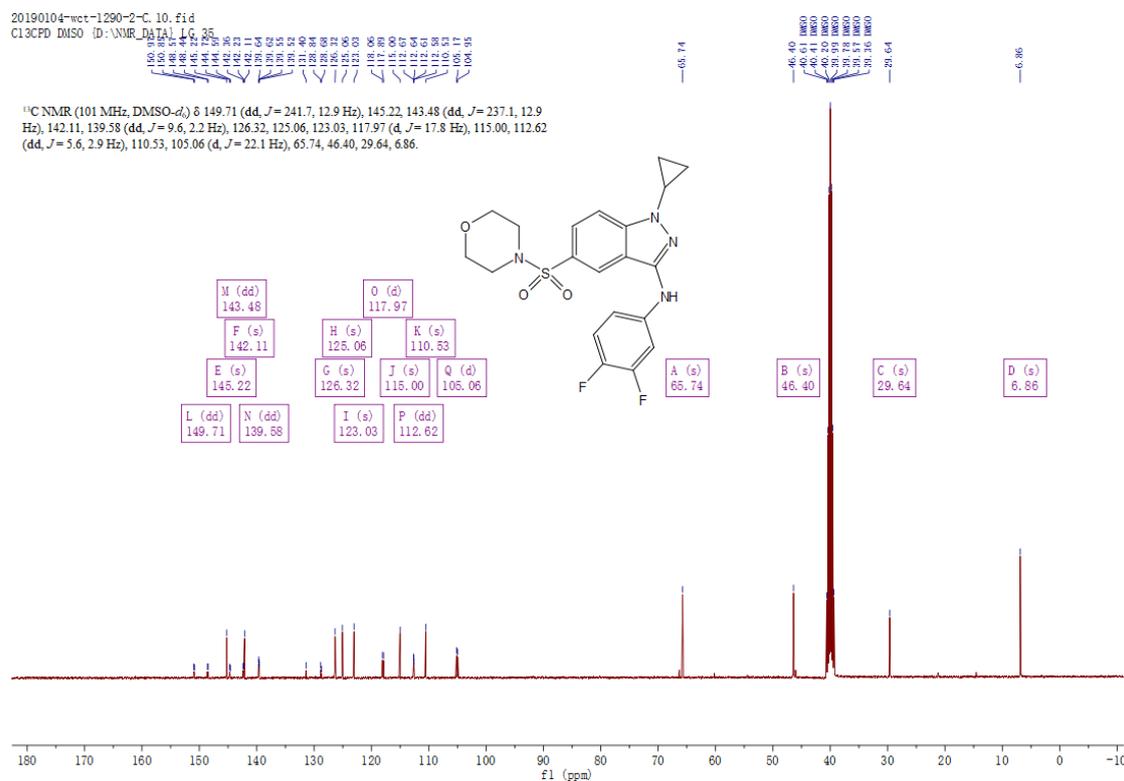
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.63 (s, 1H), 8.57 (s, 1H), 7.89 (dd, *J* = 13.8, 7.1 Hz, 1H), 7.72 (q, *J* = 8.9 Hz, 2H), 7.45 – 7.33 (m, 2H), 3.66 (dt, *J* = 15.6, 5.0 Hz, 5H), 2.87 (t, *J* = 4.5 Hz, 4H), 1.15 (d, *J* = 5.3 Hz, 4H).



20190104-wet-1290-2-C. 10. fid

C13CPD DMSO ID:\NMR_DATA\1 LG 35

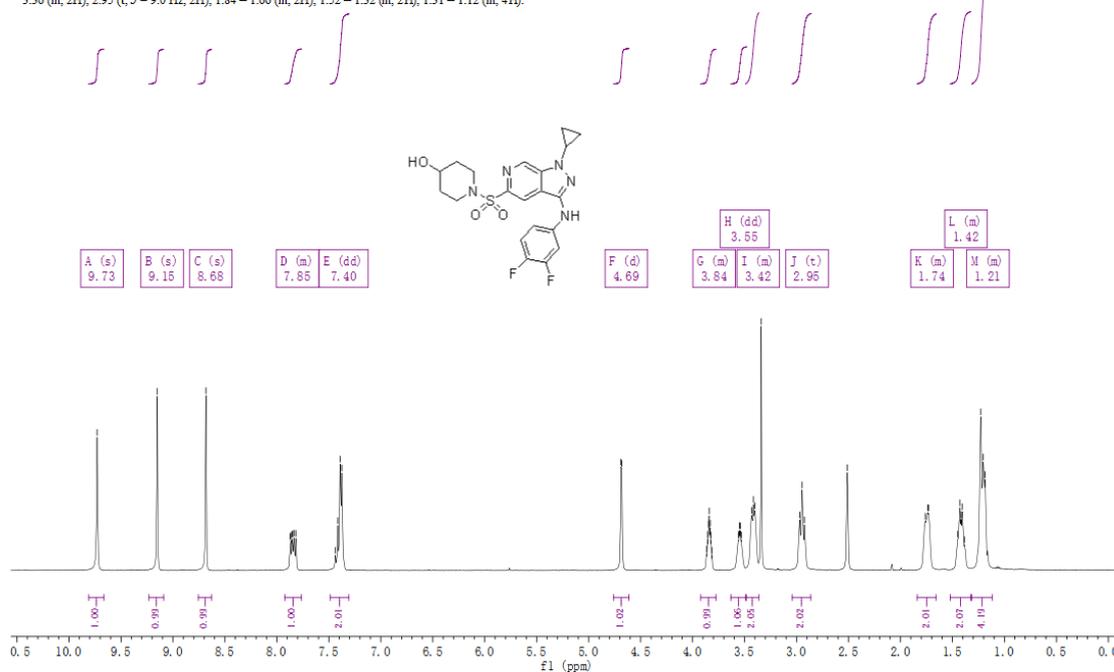
¹³C NMR (101 MHz, DMSO-*d*₆) δ 149.71 (dd, *J* = 241.7, 12.9 Hz), 145.22, 143.48 (dd, *J* = 237.1, 12.9 Hz), 142.11, 139.58 (dd, *J* = 9.6, 2.2 Hz), 126.32, 125.06, 123.03, 117.97 (d, *J* = 17.8 Hz), 115.00, 112.62 (dd, *J* = 5.6, 2.9 Hz), 110.53, 105.06 (d, *J* = 22.1 Hz), 65.74, 46.40, 29.64, 6.86.



Compound 44.

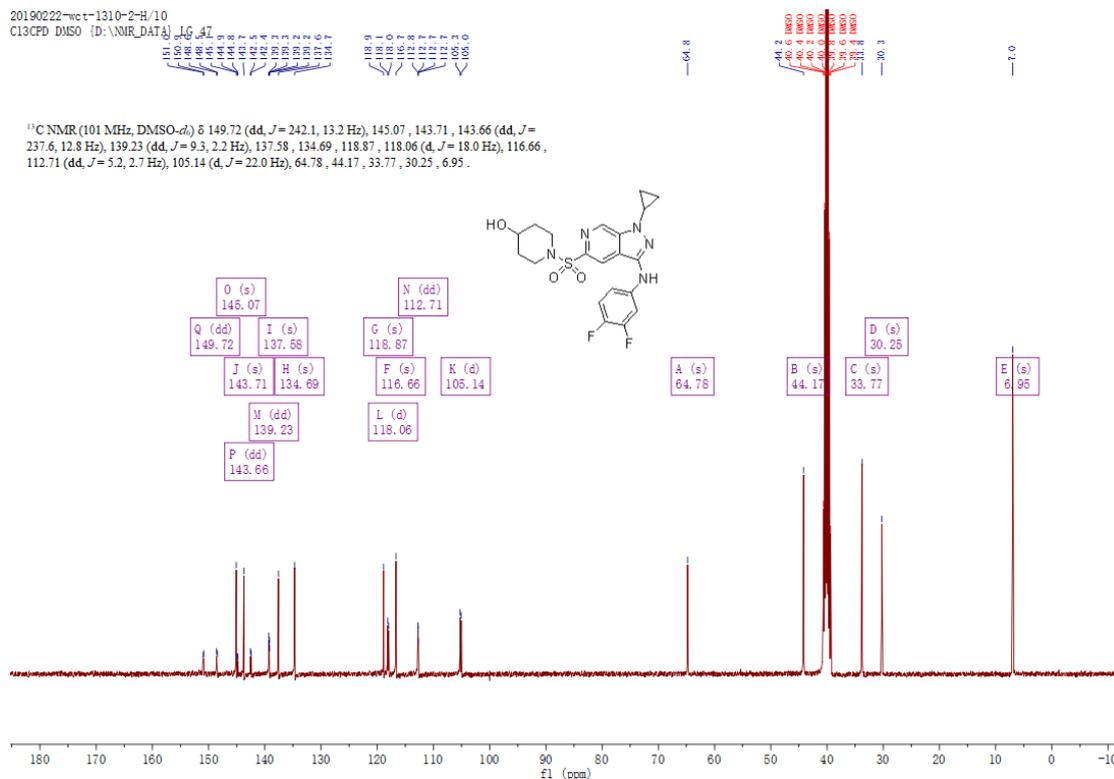
20190214-wet-1310-2-H/10
 PROTON DMSO (D:\NMR_DATA) LG 10

¹H NMR (400 MHz, DMSO-d₆) δ 9.73 (s, 1H), 9.15 (s, 1H), 8.68 (s, 1H), 7.92–7.76 (m, 1H), 7.40 (dd, J=16.9, 7.9 Hz, 2H), 4.69 (d, J=3.9 Hz, 1H), 3.92–3.77 (m, 1H), 3.55 (dd, J=7.4, 3.7 Hz, 1H), 3.49–3.36 (m, 2H), 2.95 (t, J=9.0 Hz, 2H), 1.84–1.66 (m, 2H), 1.52–1.32 (m, 2H), 1.31–1.12 (m, 4H).



20190222-wet-1310-2-H/10
 C13CPD DMSO (D:\NMR_DATA) LG 47

¹³C NMR (101 MHz, DMSO-d₆) δ 149.72 (dd, J=242.1, 13.2 Hz), 145.07, 143.71, 143.66 (dd, J=237.6, 12.8 Hz), 139.23 (dd, J=9.3, 2.2 Hz), 137.58, 134.69, 118.87, 118.06 (d, J=18.0 Hz), 116.66, 112.71 (dd, J=5.2, 2.7 Hz), 105.14 (d, J=22.0 Hz), 64.78, 44.17, 33.77, 30.25, 6.95.



Compound 45.

20190214-wet-1311-2-H₂

PROTON DMSO [D:\NMR_DATA] LG 14

8.709

7.877
7.841
7.822
7.485
7.400
7.394

3.891
3.636

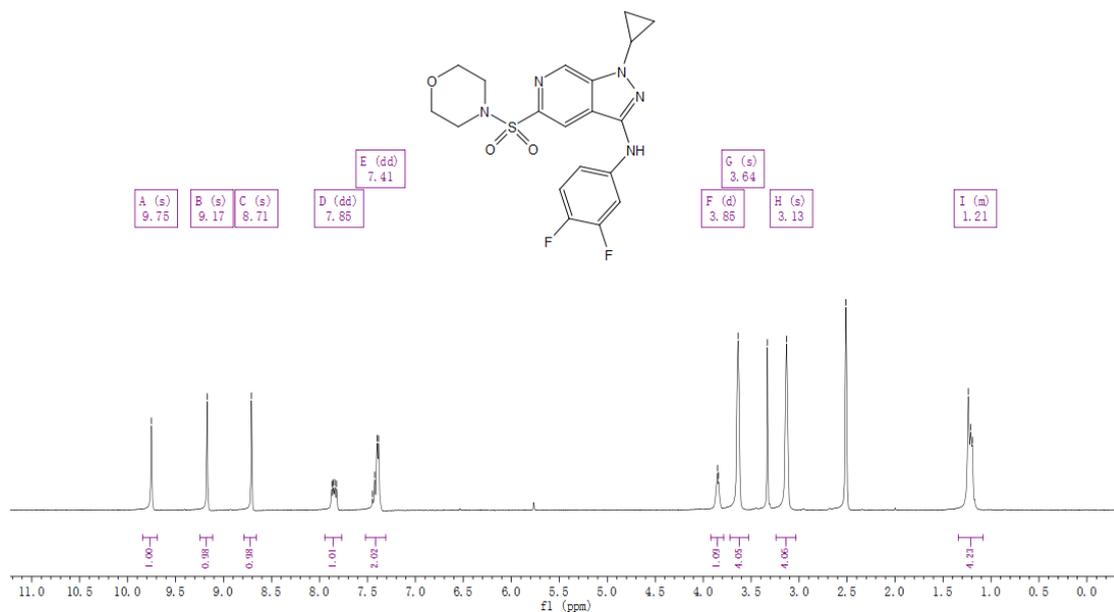
3.331

3.131

2.512

1.226
1.202
1.194

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.75 (s, 1H), 9.17 (s, 1H), 8.71 (s, 1H), 7.85 (dd, *J* = 12.8, 6.6 Hz, 1H), 7.41 (dd, *J* = 17.8, 7.7 Hz, 2H), 3.85 (d, *J* = 3.7 Hz, 1H), 3.64 (s, 4H), 3.13 (s, 4H), 1.34 – 1.08 (m, 4H).



20190226-wet-1311-2-C/10

C13CPD DMSO [D:\NMR_DATA] LG 26

150.826
148.588
148.588
144.965
144.838
142.547
139.231
139.115
137.633
134.888

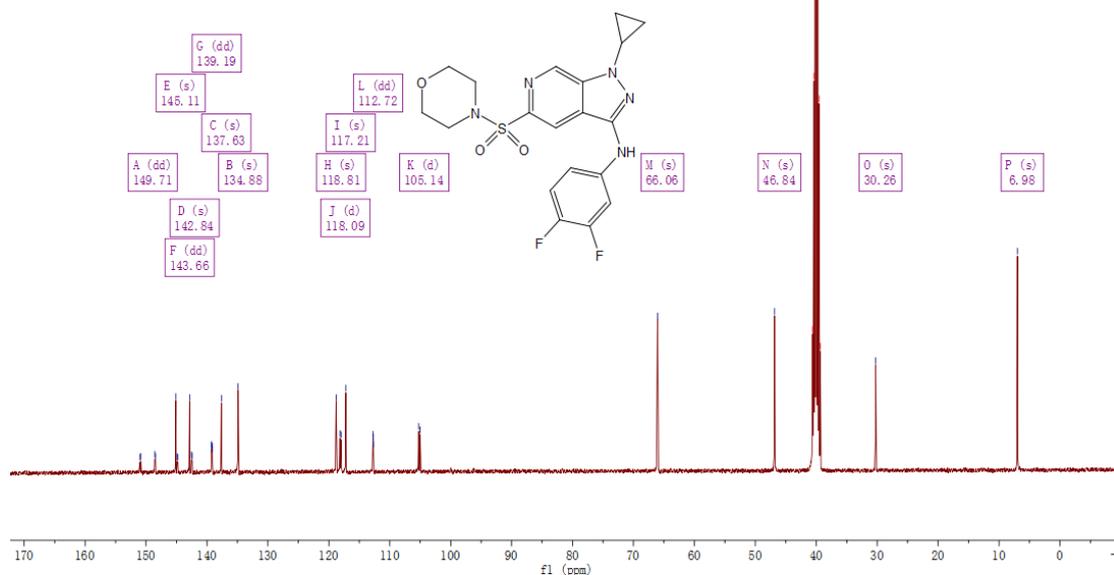
118.81
118.09
117.21
117.21
112.76
112.76
112.67
108.25
105.14

66.06

46.84
46.60
40.39
40.39
39.16
39.16
39.15
39.15

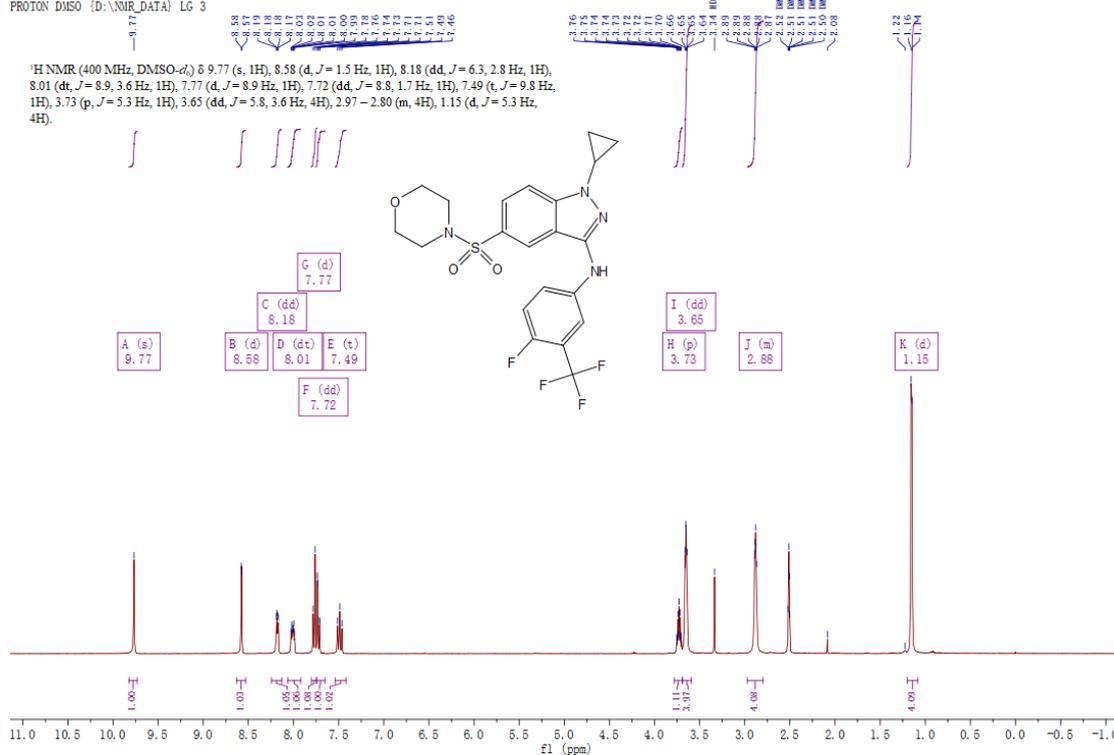
6.98

¹³C NMR (101 MHz, DMSO-*d*₆) δ 149.71 (dd, *J* = 242.0, 13.3 Hz), 145.11, 143.66 (dd, *J* = 237.7, 12.8 Hz), 142.84, 139.19 (dd, *J* = 9.5, 2.1 Hz), 137.63, 134.88, 118.81, 118.09 (d, *J* = 17.8 Hz), 117.21, 112.72 (dd, *J* = 5.7, 3.0 Hz), 105.14 (d, *J* = 22.2 Hz), 66.06, 46.84, 30.26, 6.98.

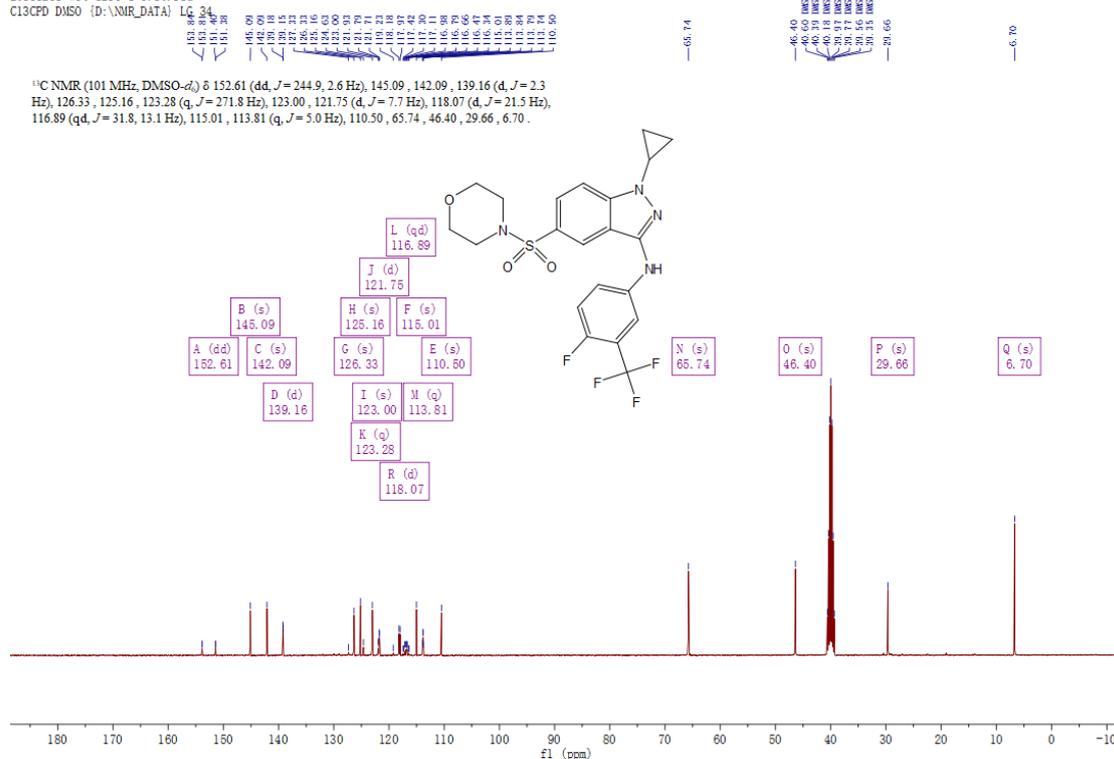


Compound 46.

20181229-wet-1286-1-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 3

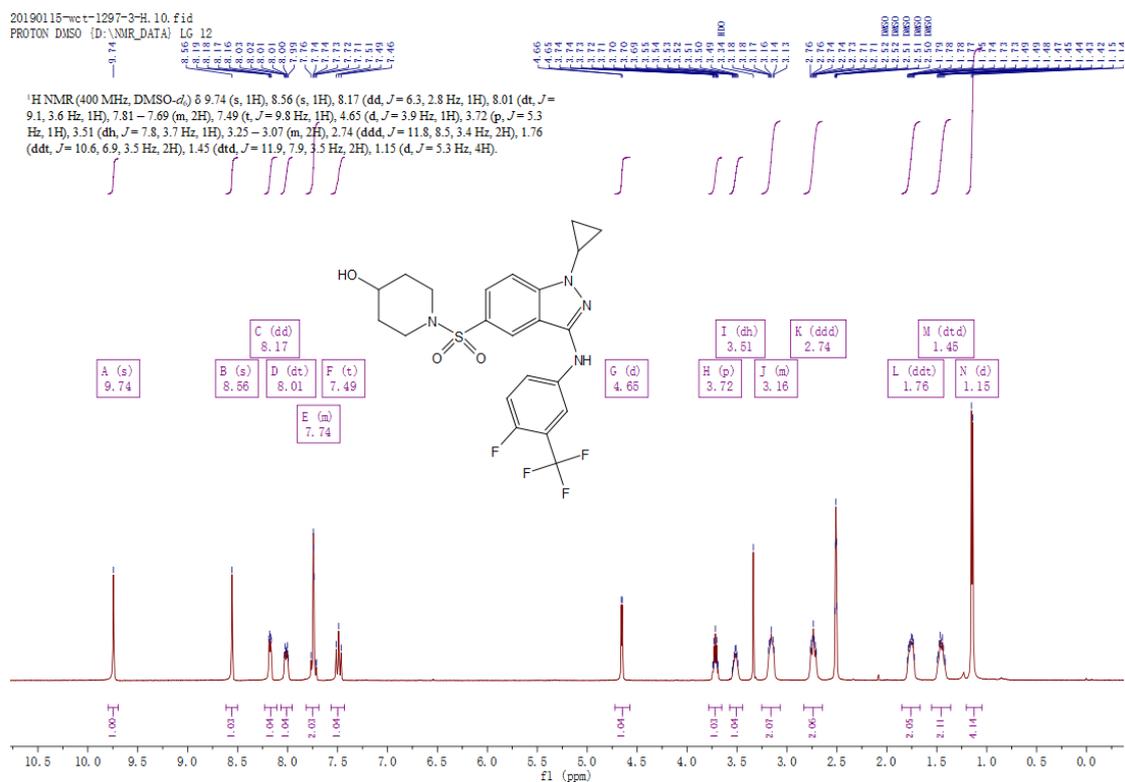


20181231-wet-1286-1-C.10.fid
 C13CPD DMSO (D:\NMR_DATA) LG 34

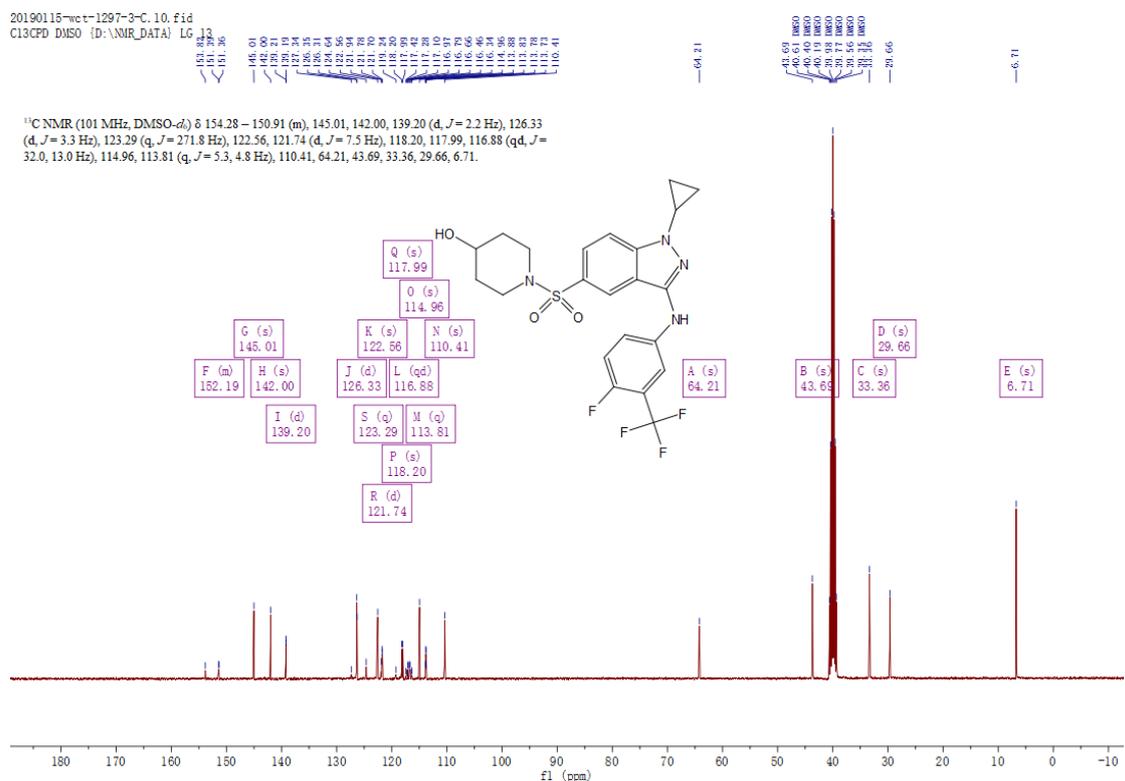


Compound 47.

20190115-wet-1297-3-H.10.fid
 PROTON DMSO [D:\NMR_DATA] LG 12



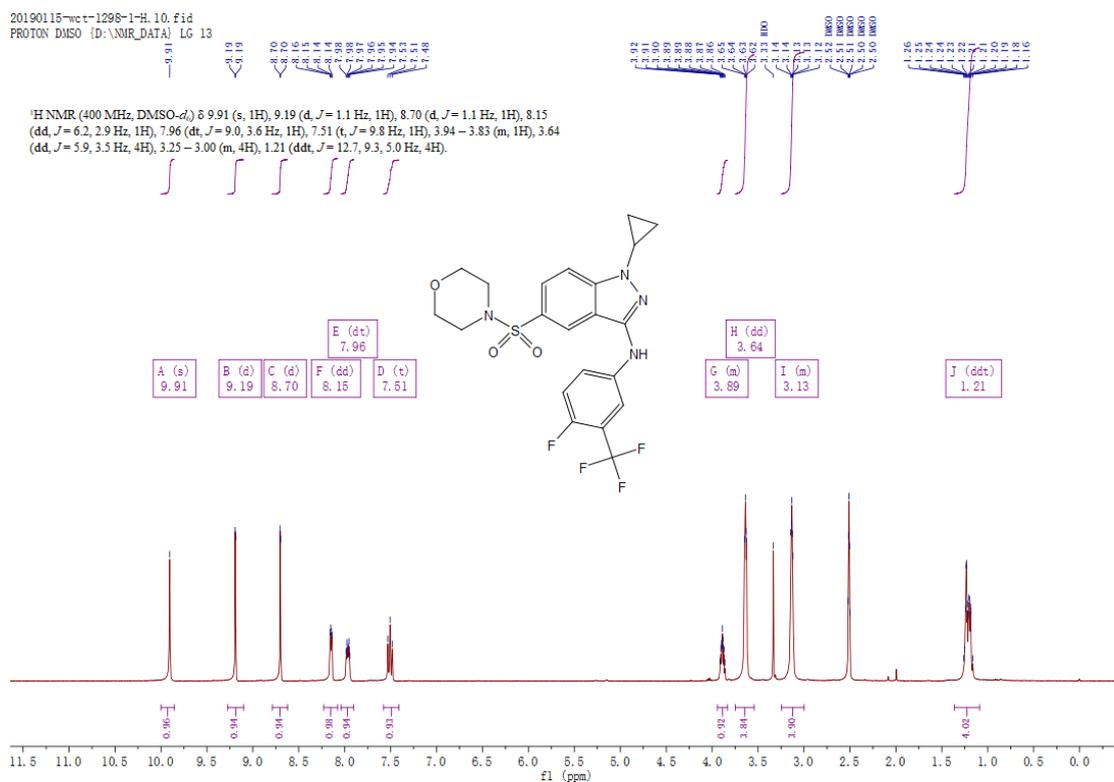
20190115-wet-1297-3-C.10.fid
 C13CPD DMSO [D:\NMR_DATA] LG 13



Compound 48.

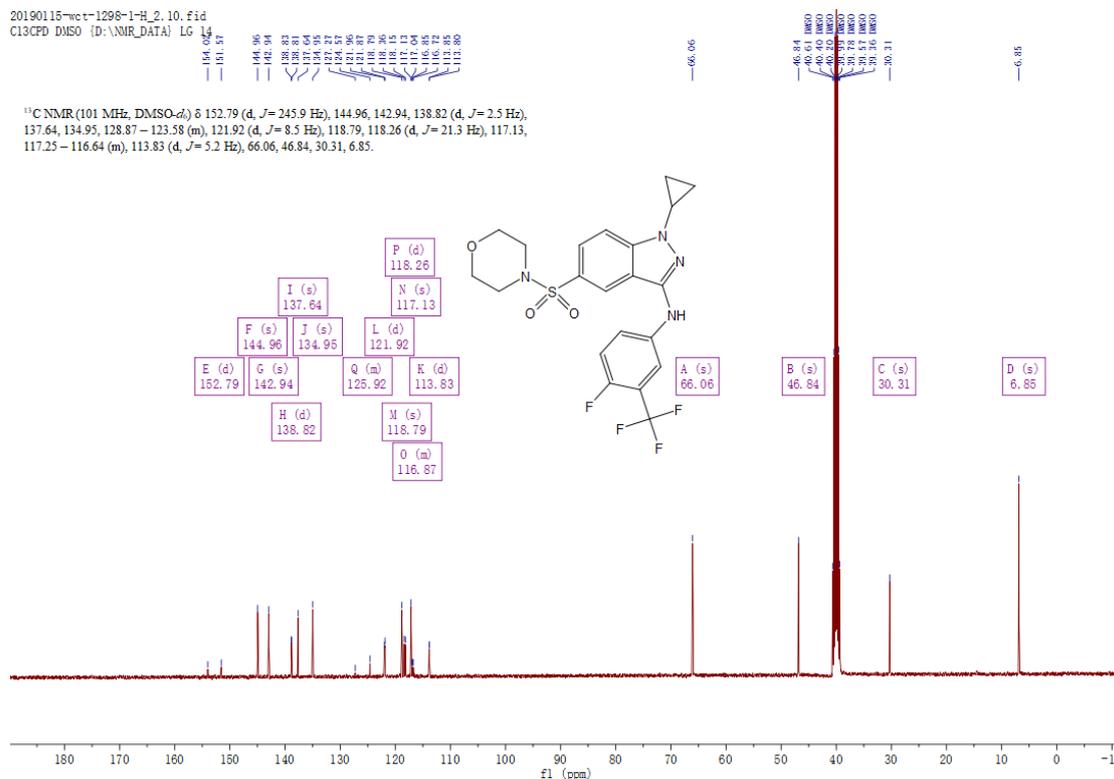
20190115-wet-1298-1-H_10.fid
 PROTON DMSO (D:\NMR_DATA) LG 13

¹H NMR (400 MHz, DMSO-d₆) δ 9.91 (s, 1H), 9.19 (d, J = 1.1 Hz, 1H), 8.70 (d, J = 1.1 Hz, 1H), 8.15 (dd, J = 6.2, 2.9 Hz, 1H), 7.96 (dt, J = 9.0, 3.6 Hz, 1H), 7.51 (t, J = 9.8 Hz, 1H), 3.94–3.83 (m, 1H), 3.64 (dd, J = 5.9, 3.5 Hz, 4H), 3.25–3.00 (m, 4H), 1.21 (ddt, J = 12.7, 9.3, 5.0 Hz, 4H).



20190115-wet-1298-1-H_2_10.fid
 C13CPD DMSO (D:\NMR_DATA) LG

¹³C NMR (101 MHz, DMSO-d₆) δ 152.79 (d, J = 245.9 Hz), 144.96, 142.94, 138.82 (d, J = 2.5 Hz), 137.64, 134.95, 128.87–123.58 (m), 121.92 (d, J = 8.5 Hz), 118.79, 118.26 (d, J = 21.3 Hz), 117.13, 117.25–116.64 (m), 113.83 (d, J = 5.2 Hz), 66.06, 46.84, 30.31, 6.85.

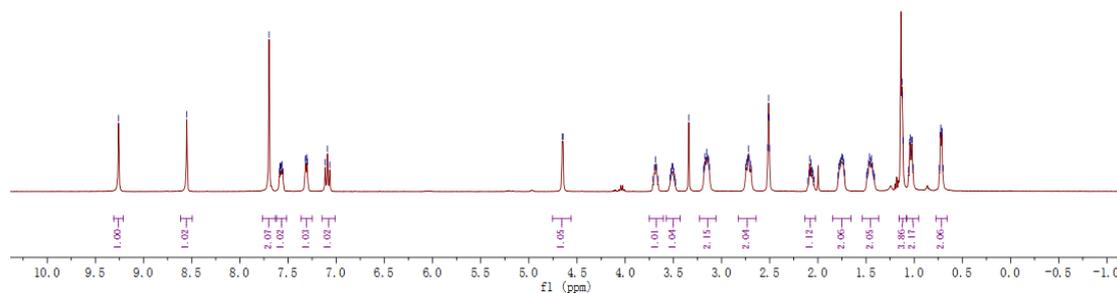
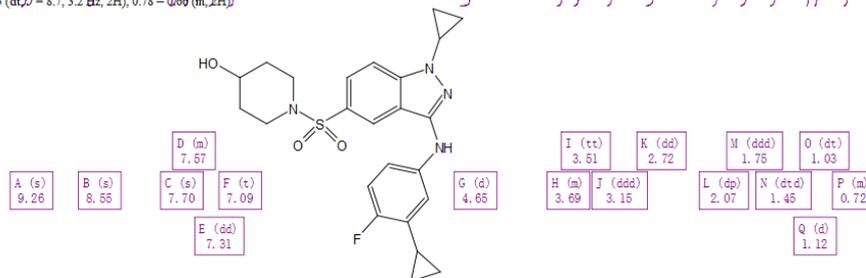


Compound 49.

20190108-wet-1294-1-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 23



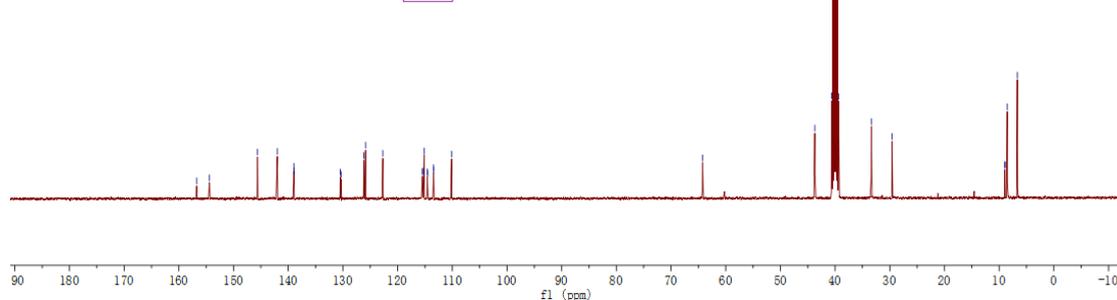
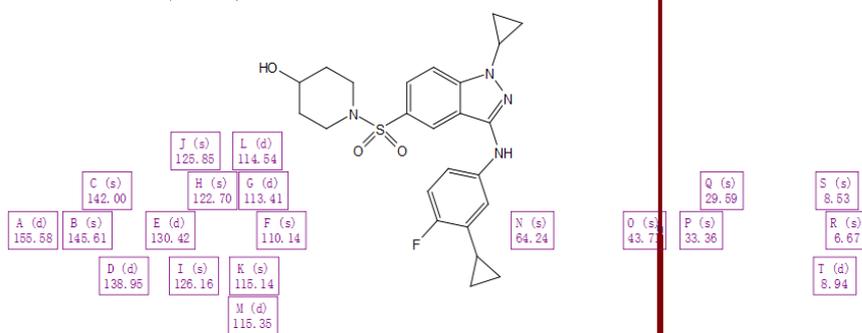
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.26 (s, 1H), 8.55 (s, 1H), 7.70 (s, 2H), 7.62–7.52 (m, 1H), 7.31 (dd, *J* = 6.8, 2.8 Hz, 1H), 7.09 (t, *J* = 9.5 Hz, 1H), 4.65 (d, *J* = 3.8 Hz, 1H), 3.75–3.61 (m, 1H), 3.51 (tt, *J* = 7.6, 3.9 Hz, 1H), 3.45 (ddd, *J* = 11.2, 6.7, 3.5 Hz, 2H), 2.72 (dd, *J* = 20.2, 3.4 Hz, 2H), 2.07 (dp, *J* = 8.5, 5.1 Hz, 1H), 1.75 (ddd, *J* = 11.4, 7.4, 3.6 Hz, 2H), 1.45 (dtd, *J* = 12.5, 8.2, 3.6 Hz, 2H), 1.12 (d, *J* = 2.3 Hz, 4H), 1.03 (dt, *J* = 8.7, 3.2 Hz, 2H), 0.78–0.69 (m, 2H)



20190111-wet-1294-1-C.10.fid
 C13CPD DMSO (D:\NMR_DATA) LG 27



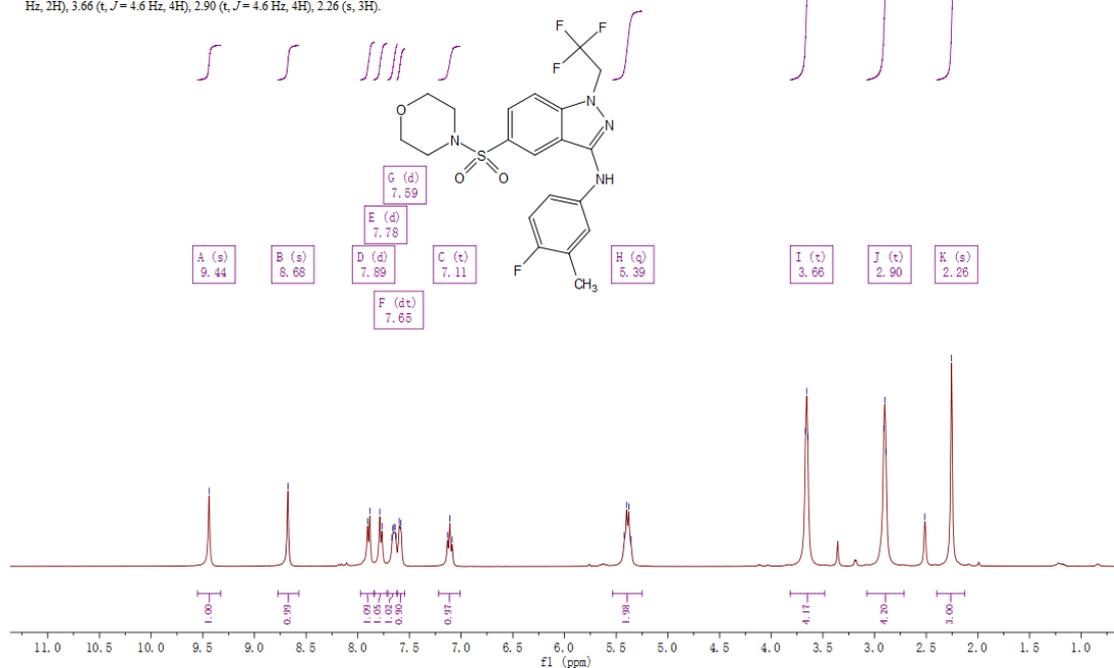
¹³C NMR (101 MHz, DMSO-*d*₆) δ 155.58 (d, *J* = 235.3 Hz), 145.61, 142.00, 138.95 (d, *J* = 2.0 Hz), 130.42 (d, *J* = 15.3 Hz), 126.16, 125.85, 122.70, 115.35 (d, *J* = 23.1 Hz), 115.14, 114.54 (d, *J* = 7.5 Hz), 113.41 (d, *J* = 3.4 Hz), 110.14, 64.24, 43.71, 33.36, 29.59, 8.94 (d, *J* = 4.7 Hz), 8.53, 6.67.



Compound 50.

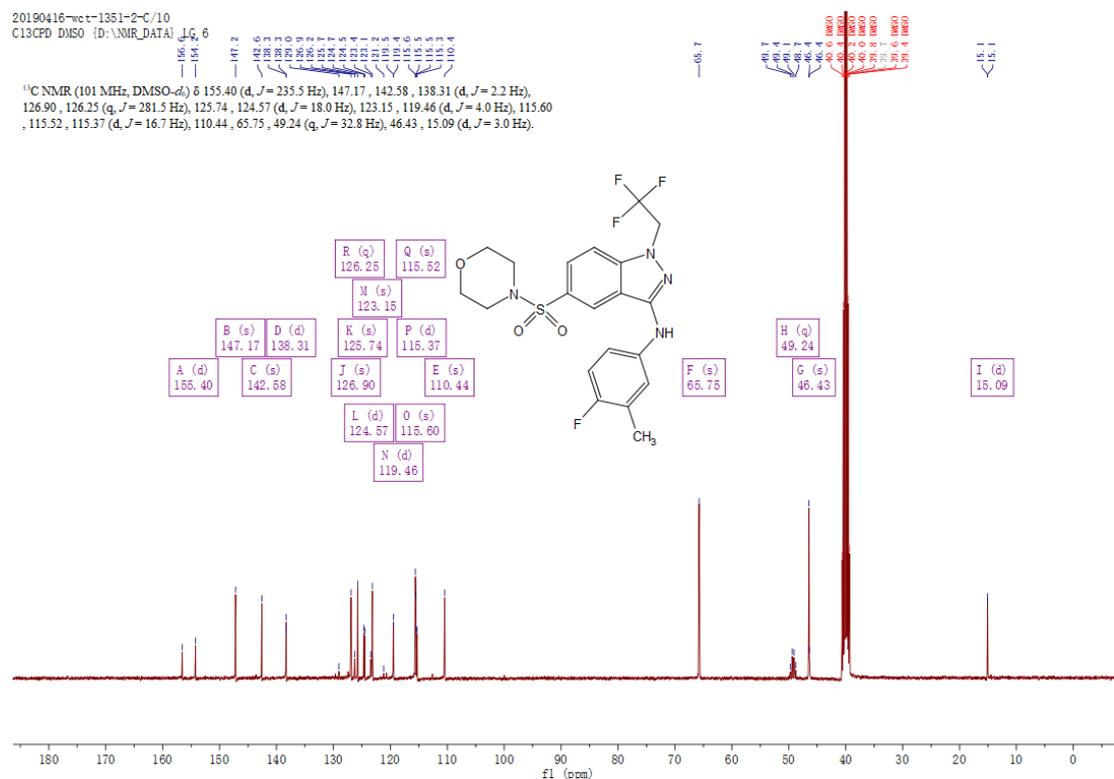
20190410-wct-1351-2-H/10
 PROTON DMSO [D:\NMR_DATA] LG

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.44 (s, 1H), 8.68 (s, 1H), 7.89 (d, *J* = 8.8 Hz, 1H), 7.78 (d, *J* = 9.0 Hz, 1H), 7.65 (dt, *J* = 8.2, 3.6 Hz, 1H), 7.59 (d, *J* = 6.9 Hz, 1H), 7.11 (t, *J* = 9.2 Hz, 1H), 5.39 (q, *J* = 9.0 Hz, 2H), 3.66 (t, *J* = 4.6 Hz, 4H), 2.90 (t, *J* = 4.6 Hz, 4H), 2.26 (s, 3H).



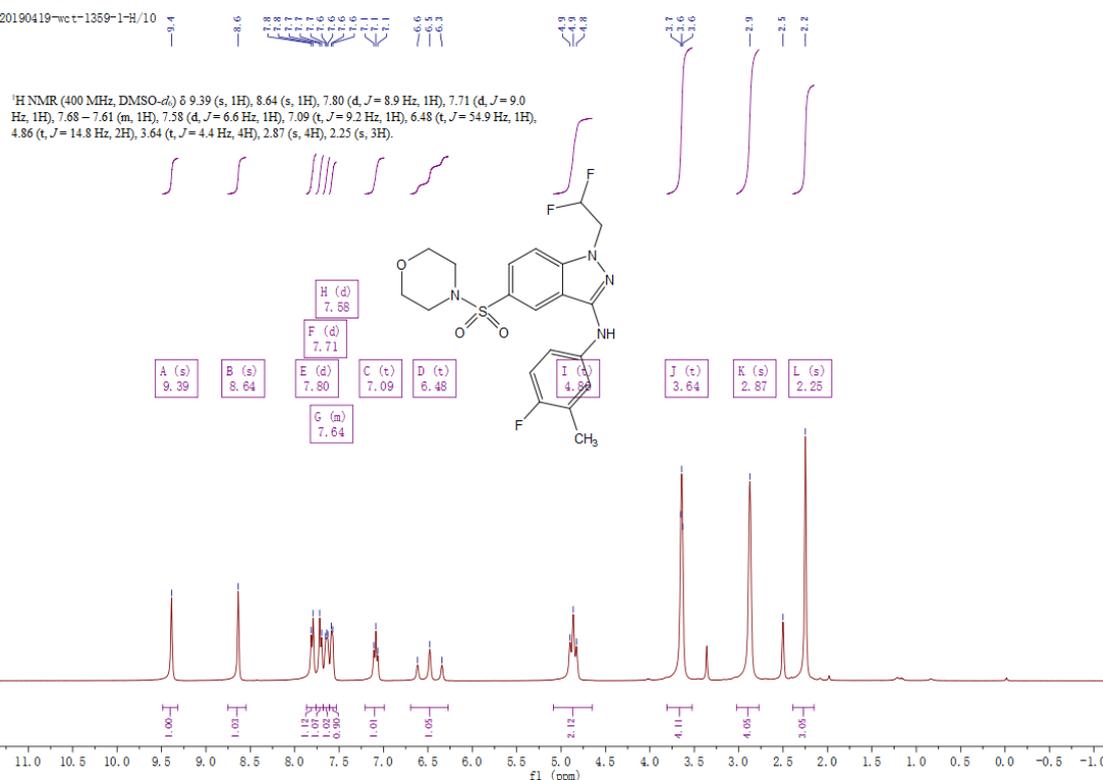
20190416-wct-1351-2-C/10
 C13CPD DMSO [D:\NMR_DATA] LG, 6

¹³C NMR (101 MHz, DMSO-*d*₆) δ 155.40 (d, *J* = 235.5 Hz), 147.17, 142.58, 138.31 (d, *J* = 2.2 Hz), 126.90, 126.25 (q, *J* = 281.5 Hz), 125.74, 124.57 (d, *J* = 18.0 Hz), 123.15, 119.46 (d, *J* = 4.0 Hz), 115.60, 115.52, 115.37 (d, *J* = 16.7 Hz), 110.44, 65.75, 49.24 (q, *J* = 32.8 Hz), 46.43, 15.09 (d, *J* = 3.0 Hz).



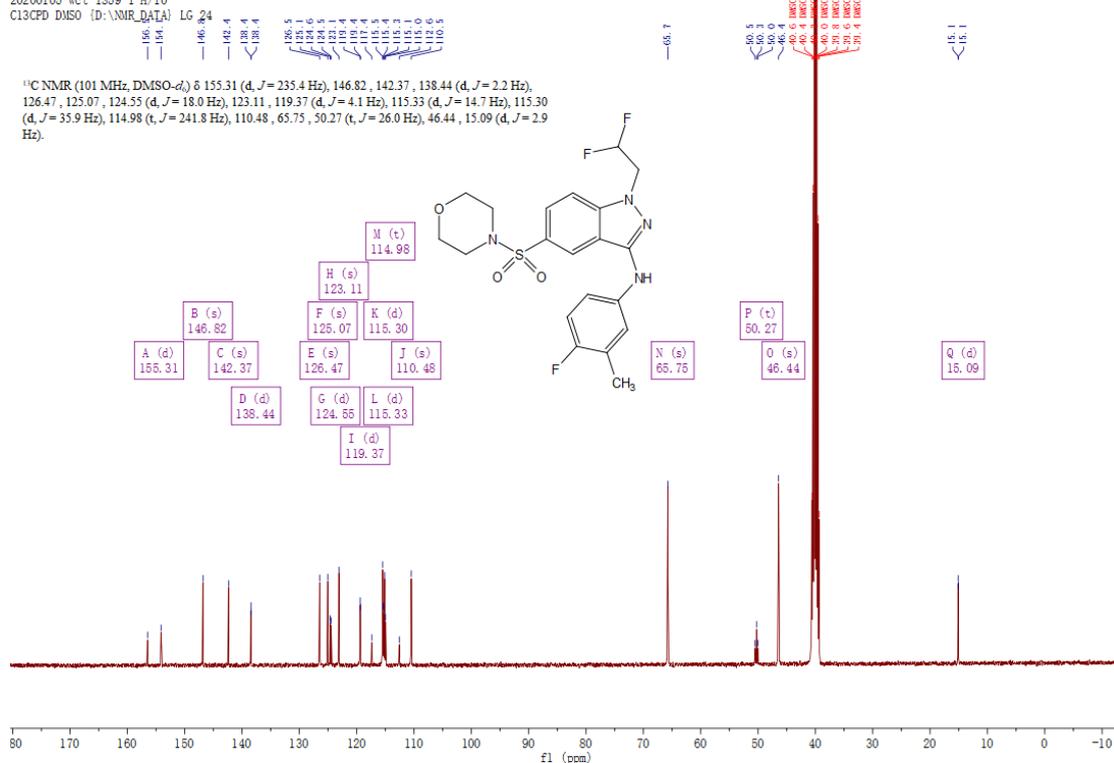
Compound 51.

20190419-wet-1389-1-H/10



20200105-wet-1389-1-H/10

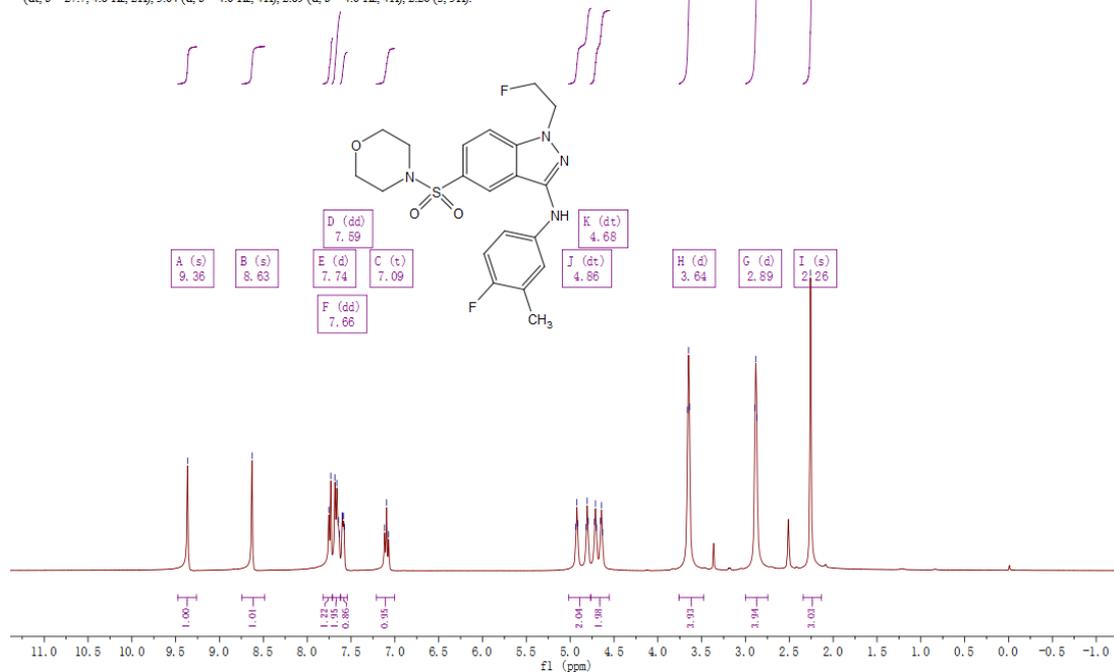
C13CPD DMSO {D:\NMR_DATA} LG_24



Compound 52.

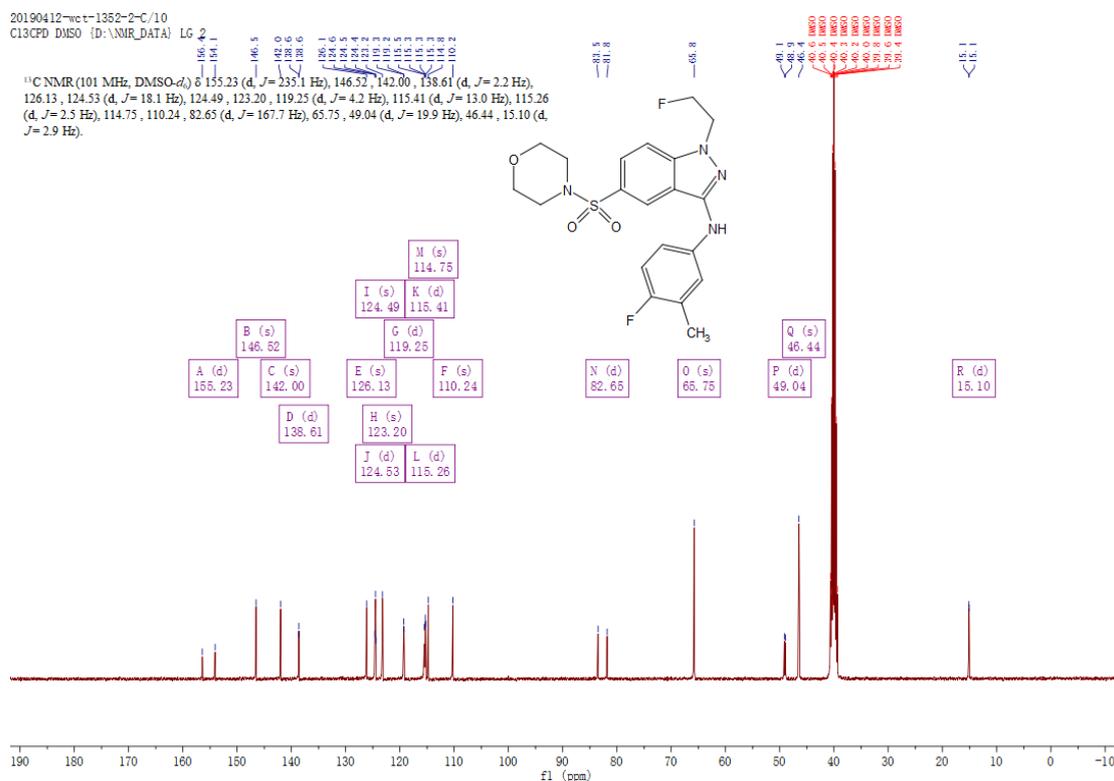
20190405-wet-1352-2-H/10
 PROTON DMSO (D:\NMR_DATA) LG_2

¹H NMR (400 MHz, DMSO-d₆) δ 9.36 (s, 1H), 8.63 (s, 1H), 7.74 (d, J = 8.9 Hz, 1H), 7.66 (dd, J = 14.4, 6.3 Hz, 2H), 7.59 (dd, J = 6.9, 2.7 Hz, 1H), 7.09 (t, J = 9.2 Hz, 1H), 4.86 (dt, J = 47.3, 4.7 Hz, 2H), 4.68 (dt, J = 27.7, 4.8 Hz, 2H), 3.64 (d, J = 4.6 Hz, 4H), 2.89 (d, J = 4.6 Hz, 4H), 2.26 (s, 3H).



20190412-wet-1352-2-C/10
 C13CPD DMSO (D:\NMR_DATA) LG_2

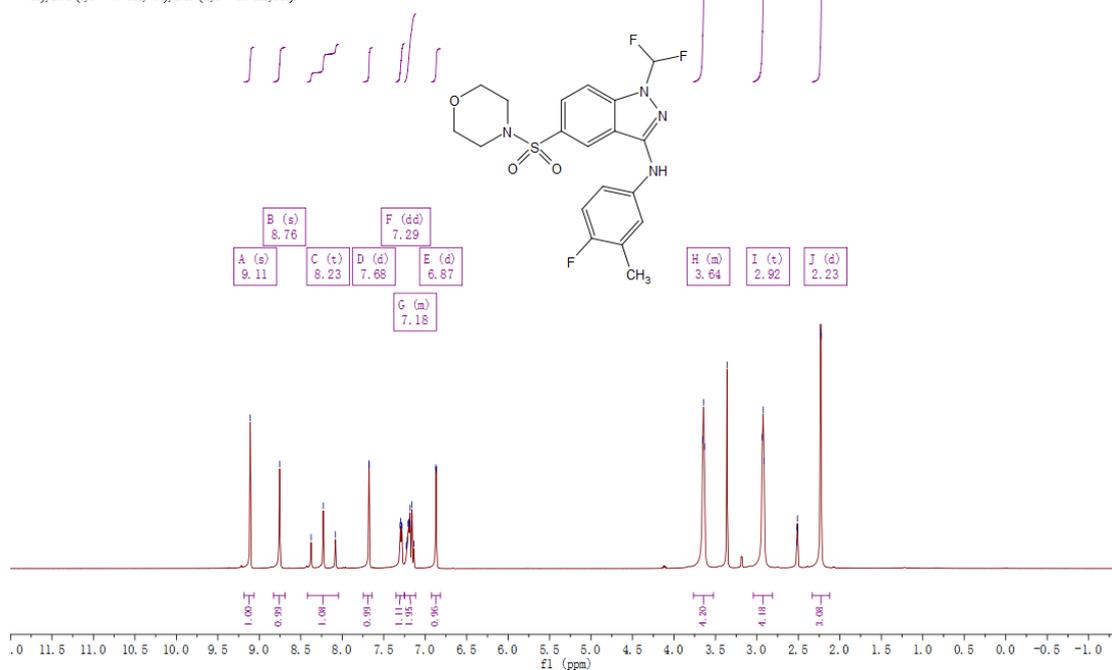
¹³C NMR (101 MHz, DMSO-d₆) δ 155.23 (d, J = 235.1 Hz), 146.52, 142.00, 138.61 (d, J = 2.2 Hz), 126.13, 124.53 (d, J = 18.1 Hz), 124.49, 123.20, 119.25 (d, J = 4.2 Hz), 115.41 (d, J = 13.0 Hz), 115.26 (d, J = 2.5 Hz), 114.75, 110.24, 82.65 (d, J = 167.7 Hz), 65.75, 49.04 (d, J = 19.9 Hz), 46.44, 15.10 (d, J = 2.9 Hz).



Compound 53.

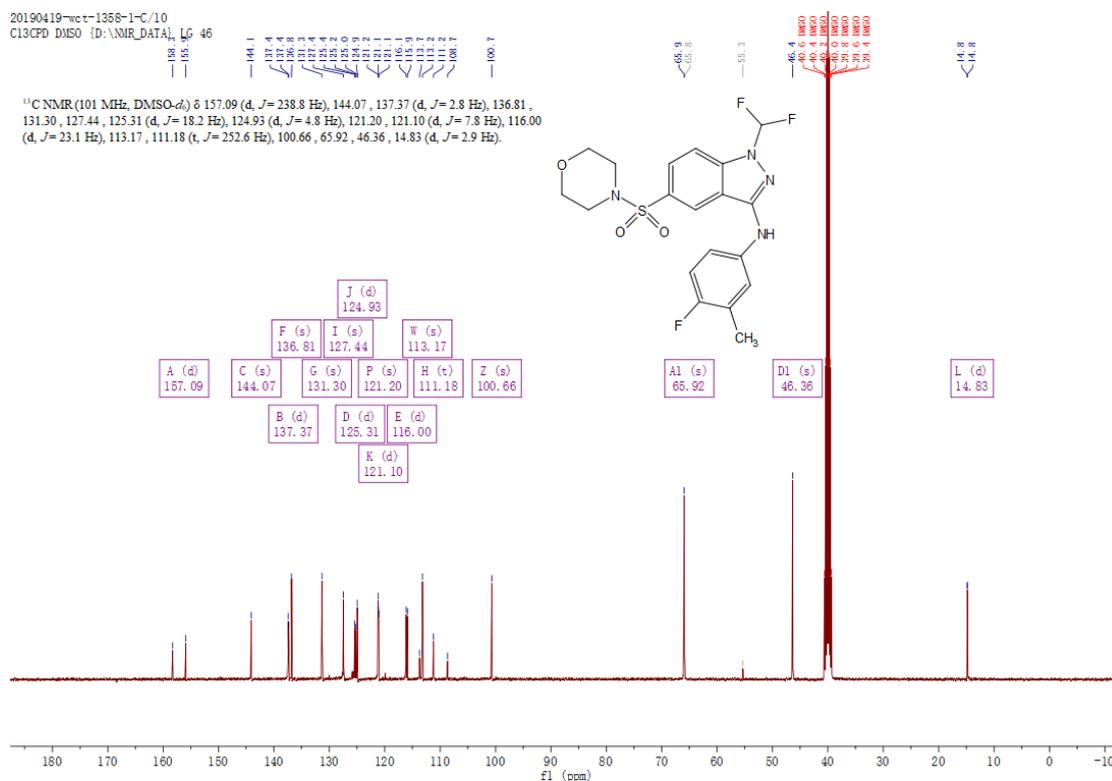
20190429-wct-1358-1-H/10
 PROTON DMSO [D:\NMR_DATA] LG 13

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.11 (s, 1H), 8.76 (s, 1H), 8.23 (t, *J* = 58.7 Hz, 1H), 7.68 (d, *J* = 1.4 Hz, 1H), 7.29 (dd, *J* = 7.0, 2.5 Hz, 1H), 7.25–7.12 (m, 2H), 6.87 (d, *J* = 1.4 Hz, 1H), 3.76–3.53 (m, 4H), 2.92 (t, *J* = 4.7 Hz, 4H), 2.23 (d, *J* = 1.9 Hz, 3H).



20190419-wct-1358-1-C/10
 C13CPD DMSO [D:\NMR_DATA] LG 46

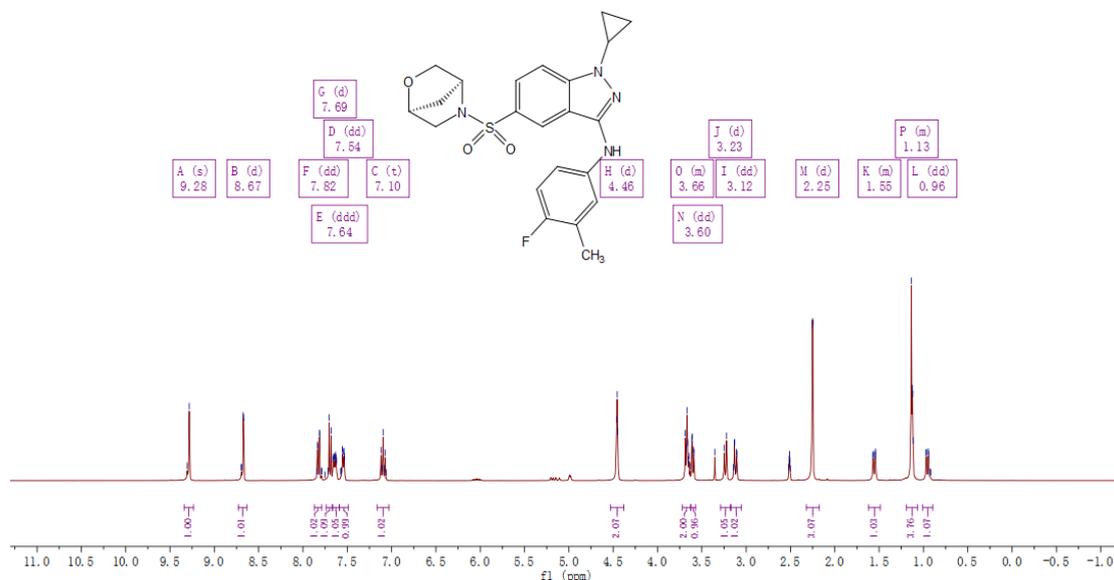
¹³C NMR (101 MHz, DMSO-*d*₆) δ 157.09 (d, *J* = 238.8 Hz), 144.07, 137.37 (d, *J* = 2.8 Hz), 136.81, 131.30, 127.44, 125.31 (d, *J* = 18.2 Hz), 124.93 (d, *J* = 4.8 Hz), 121.20, 121.10 (d, *J* = 7.8 Hz), 116.00 (d, *J* = 23.1 Hz), 113.17, 111.18 (t, *J* = 252.6 Hz), 100.66, 65.92, 46.36, 14.83 (d, *J* = 2.9 Hz).



Compound 54.

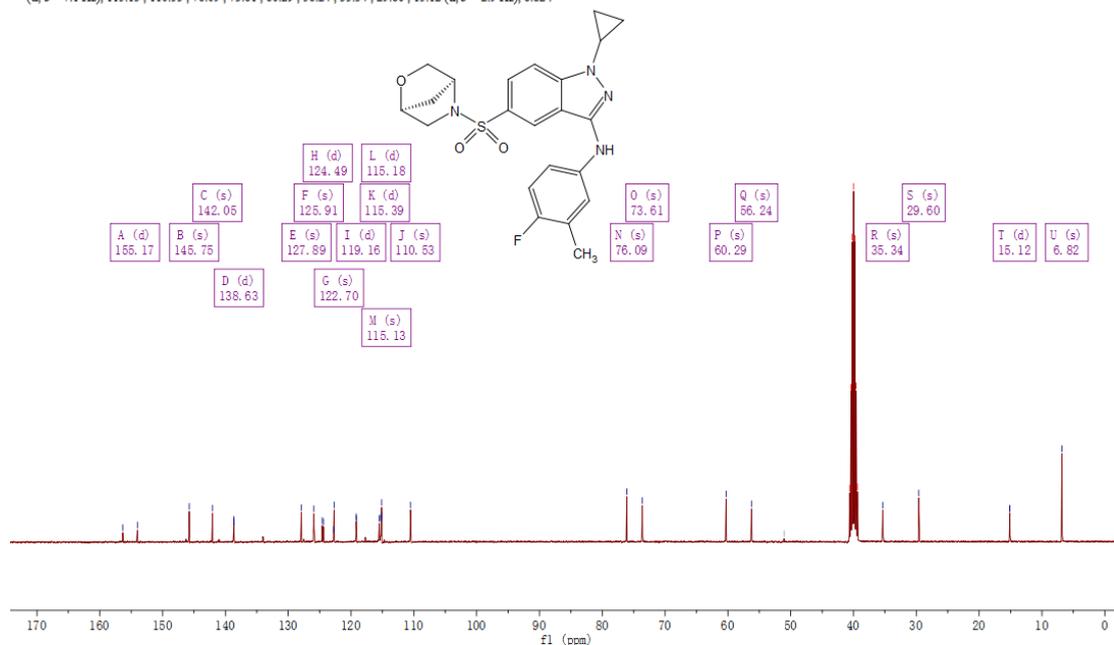
20181203-wet-1263-4-H.10.fid
 PROTON DMSO (D:\NMR_DATA) LG 56

¹H NMR (400 MHz, DMSO-d₆) δ 9.28 (s, 1H), 8.67 (d, J = 1.6 Hz, 1H), 7.82 (dd, J = 8.8, 1.7 Hz, 1H), 7.69 (d, J = 8.8 Hz, 1H), 7.64 (ddd, J = 8.9, 4.5, 3.0 Hz, 1H), 7.54 (dd, J = 6.9, 2.8 Hz, 1H), 7.10 (t, J = 9.2 Hz, 1H), 4.46 (d, J = 3.0 Hz, 2H), 3.72–3.63 (m, 2H), 3.60 (dd, J = 7.6, 1.8 Hz, 1H), 3.23 (d, J = 10.0 Hz, 1H), 3.12 (dd, J = 10.0, 4.6 Hz, 1H), 2.25 (d, J = 1.9 Hz, 3H), 1.62–1.49 (m, 1H), 1.19–1.07 (m, 4H), 0.96 (dd, J = 10.1, 2.3 Hz, 1H).



20191223-wet-1263-4-C/10
 C13CPD DMSO (D:\NMR_DATA) LG 30

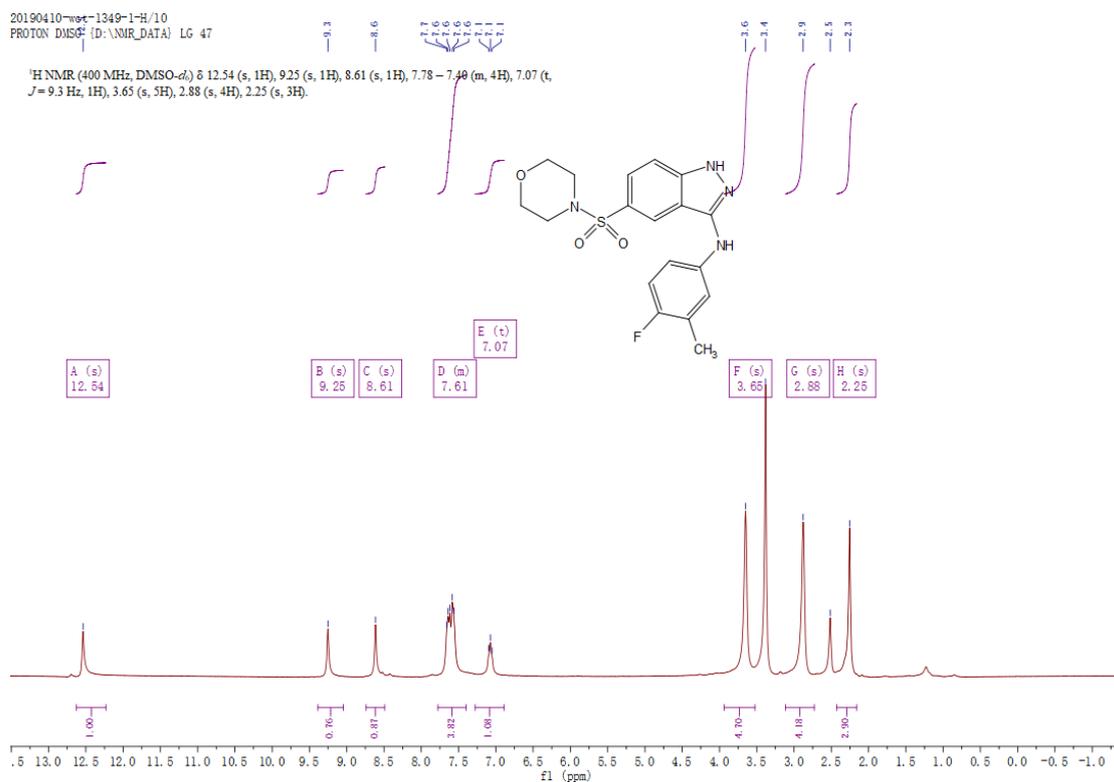
¹³C NMR (101 MHz, DMSO-d₆) δ 155.17 (d, J = 235.1 Hz), 145.75, 142.05, 138.63 (d, J = 2.4 Hz), 127.89, 125.91, 124.49 (d, J = 18.0 Hz), 122.70, 119.16 (d, J = 4.1 Hz), 115.39 (d, J = 22.9 Hz), 115.18 (d, J = 7.1 Hz), 115.13, 110.53, 76.09, 73.61, 60.29, 56.24, 35.34, 29.60, 15.12 (d, J = 2.9 Hz), 6.82.



Compound 55.

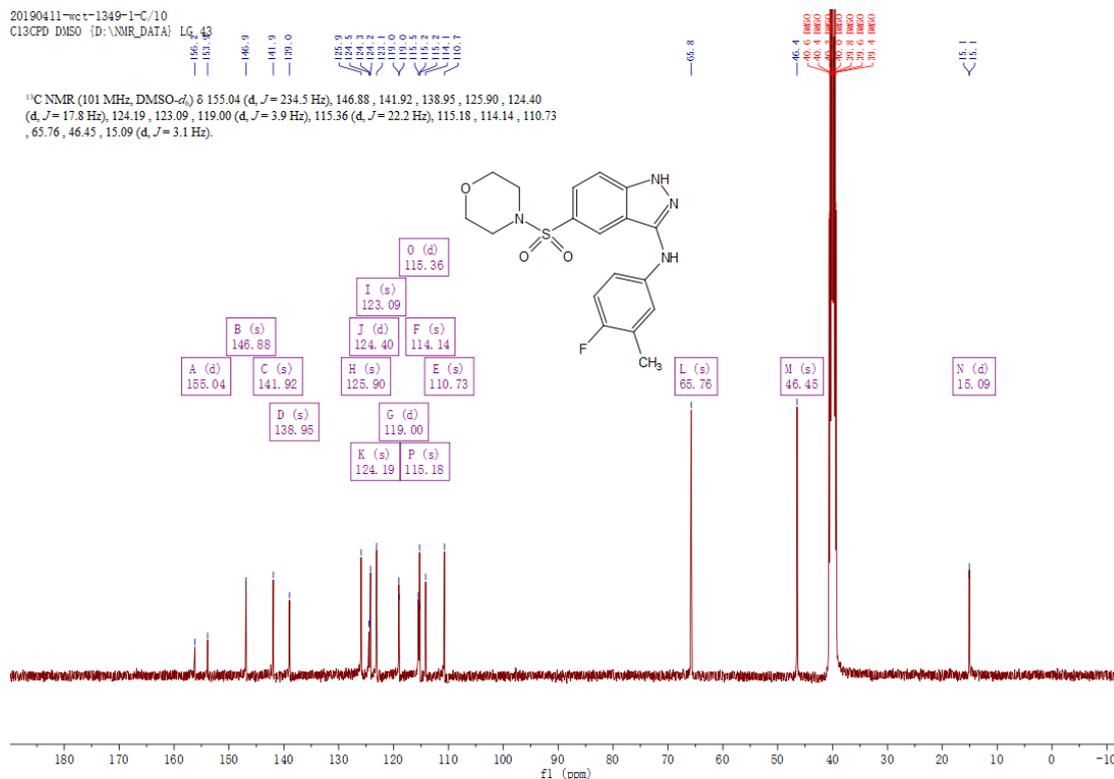
20190410-wet-1349-1-H/10
 PROTON DMSO-D6 (D:\NMR_DATA) LG 47

¹H NMR (400 MHz, DMSO-d₆) δ 12.54 (s, 1H), 9.25 (s, 1H), 8.61 (s, 1H), 7.78 – 7.49 (m, 4H), 7.07 (t, J = 9.3 Hz, 1H), 3.65 (s, 3H), 2.88 (s, 4H), 2.25 (s, 3H).

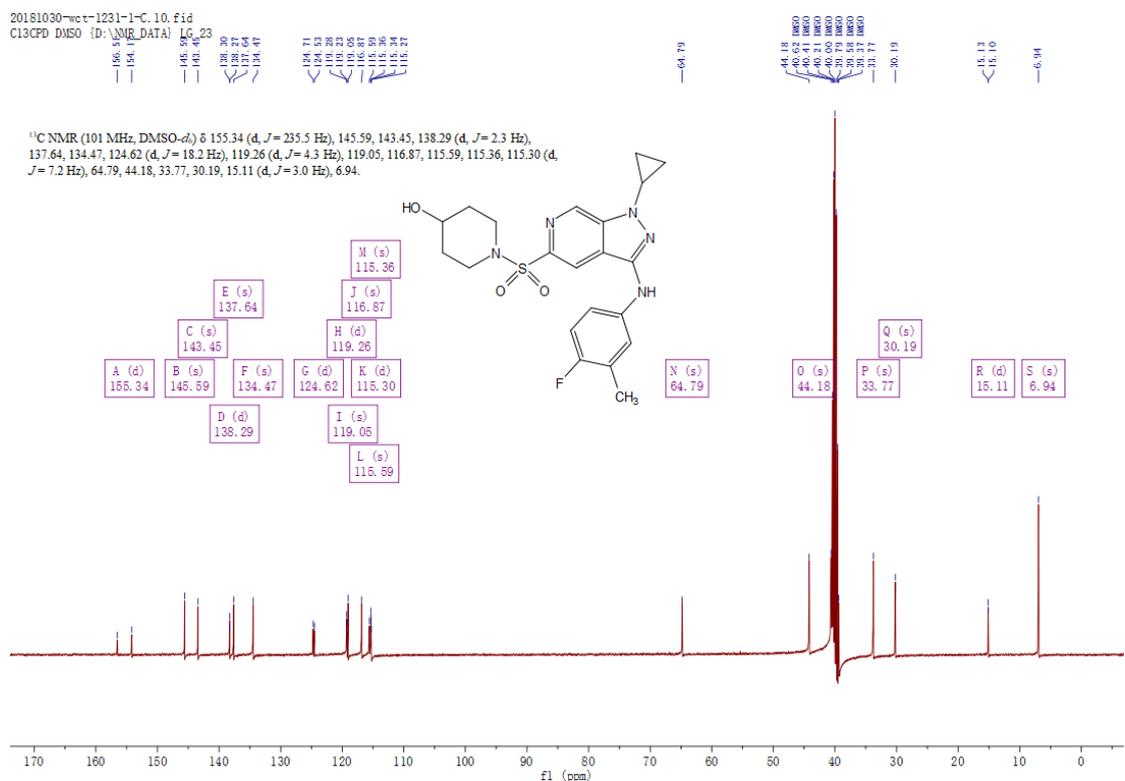
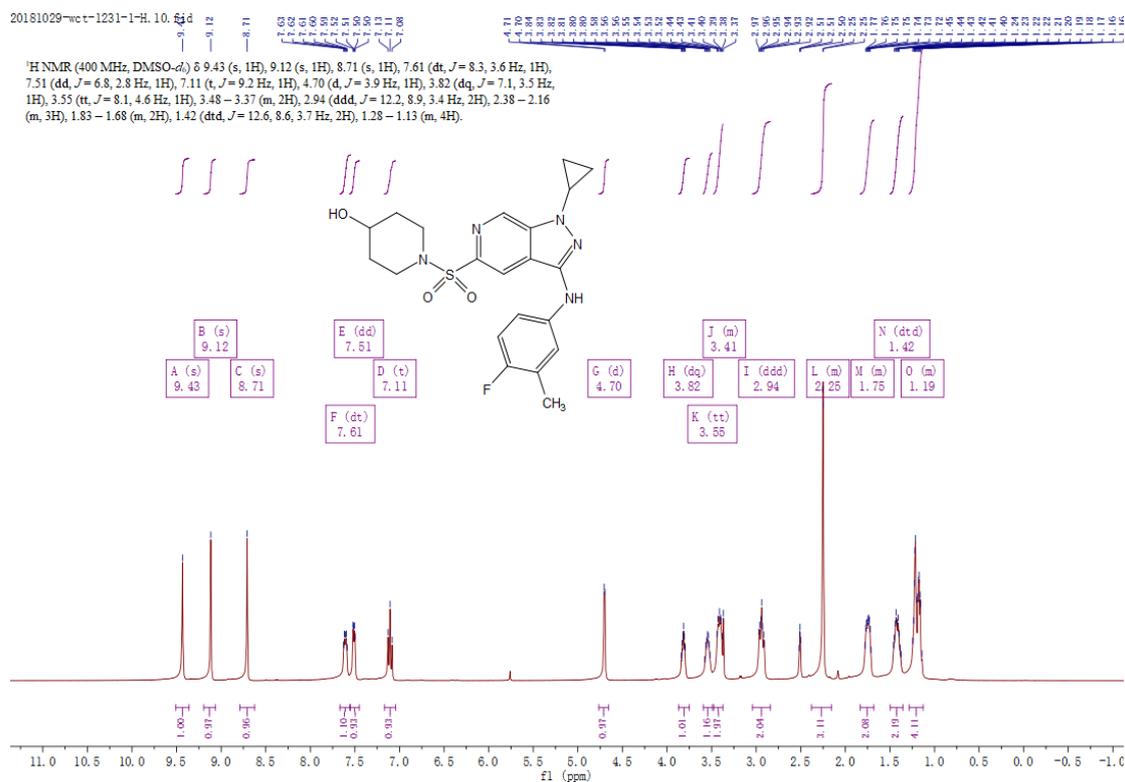


20190411-wet-1349-1-C/10
 C13CPD DMSO (D:\NMR_DATA) LG 43

¹³C NMR (101 MHz, DMSO-d₆) δ 155.04 (d, J = 234.5 Hz), 146.88, 141.92, 138.95, 124.40 (d, J = 17.8 Hz), 124.19, 123.09, 119.00 (d, J = 3.9 Hz), 115.36 (d, J = 22.2 Hz), 115.18, 114.14, 110.73, 65.76, 46.45, 15.09 (d, J = 3.1 Hz).

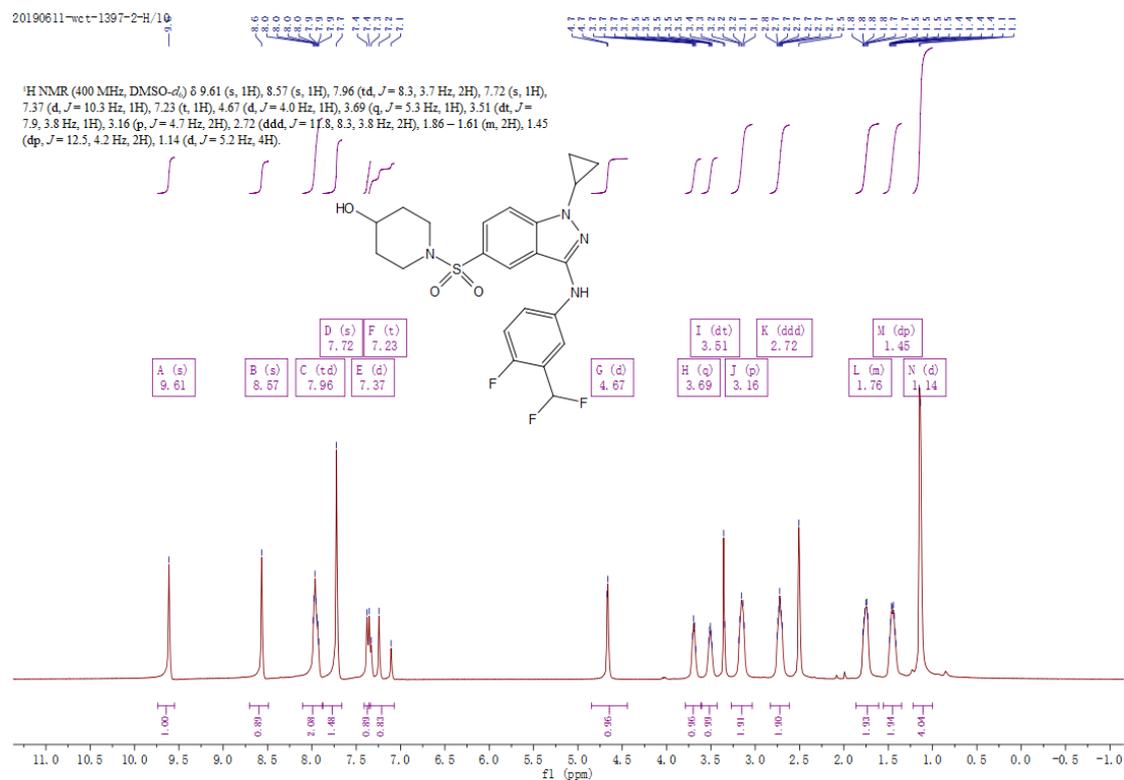


Compound 56.



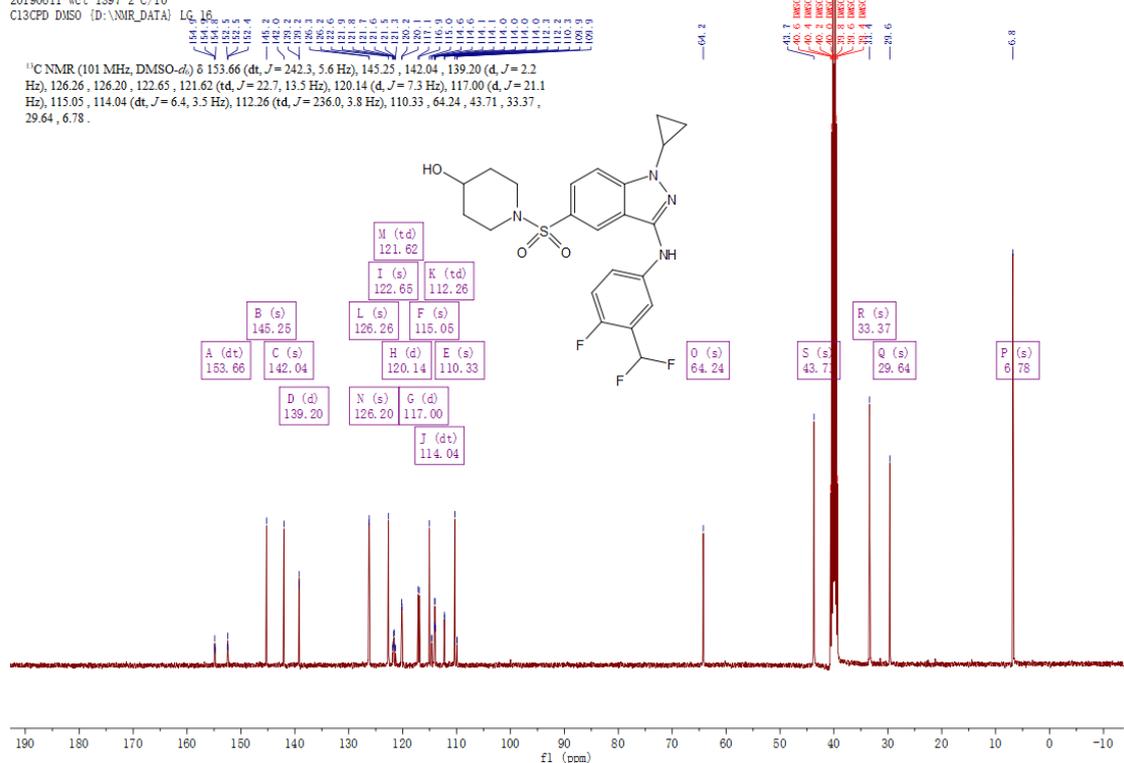
Compound 57.

20190611-wet-1397-2-H/10



20190611-wet-1397-2-C/10

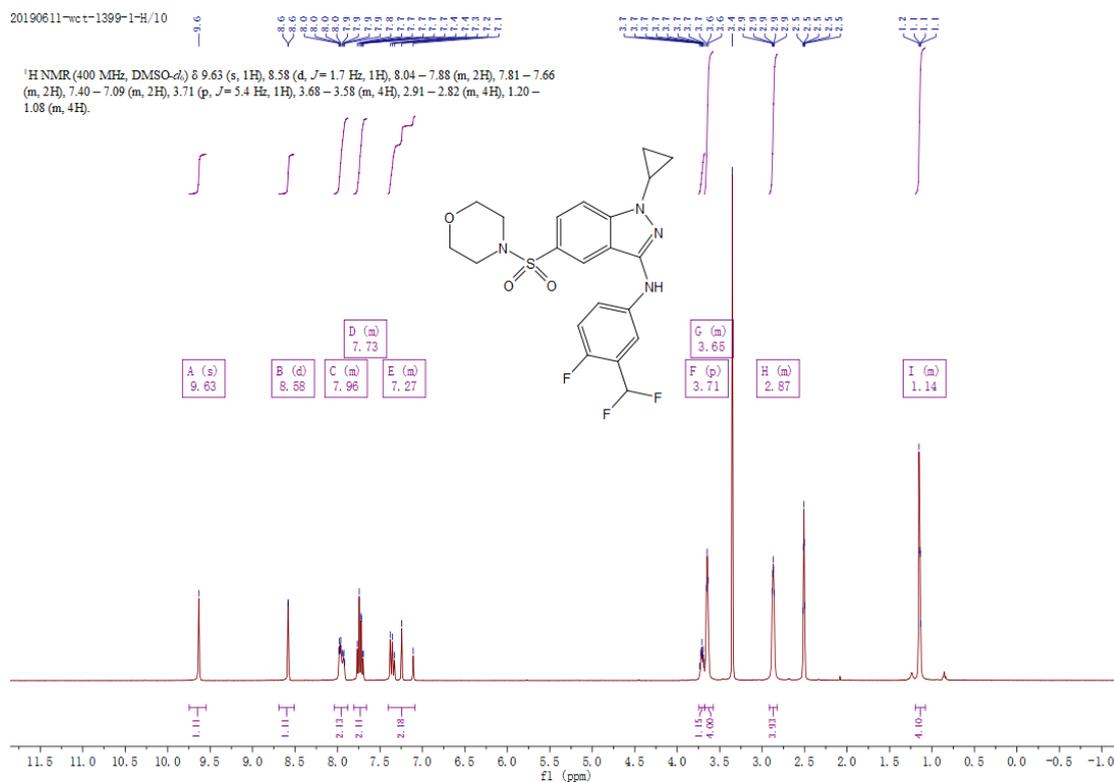
C13CPD DMSO (D:\NMR_DATA) LG_16



Compound 58.

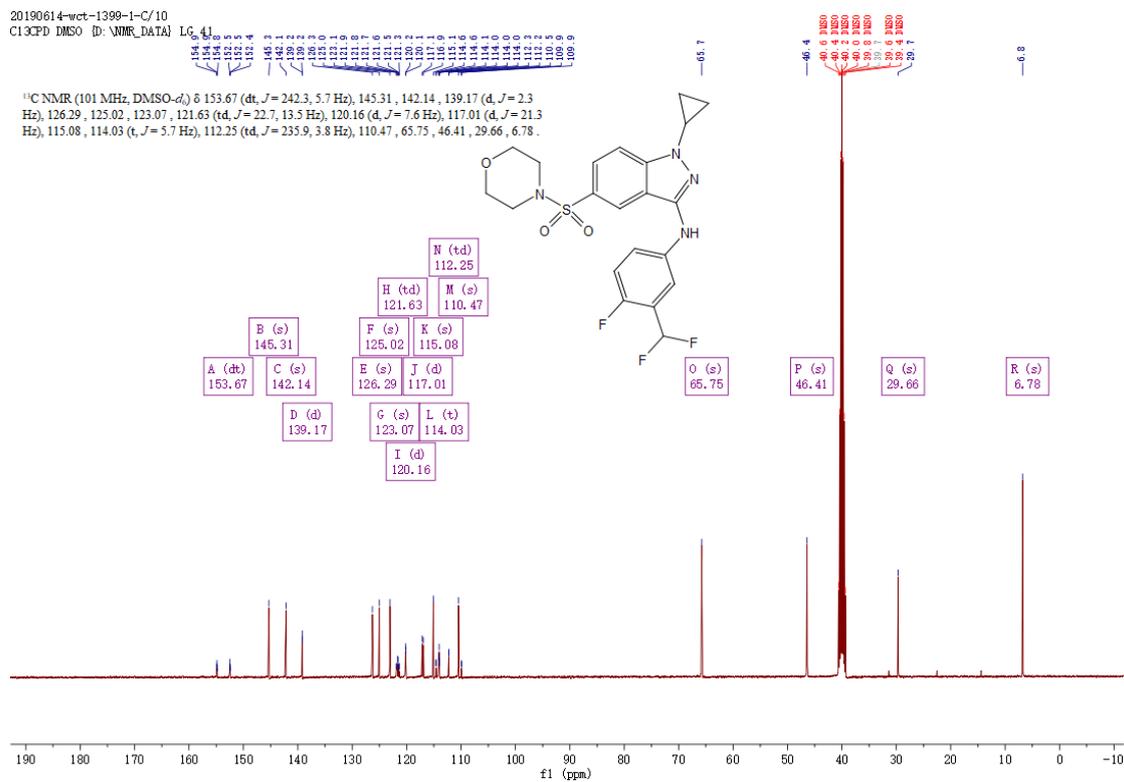
20190611-wct-1399-1-H/10

$^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 9.63 (s, 1H), 8.58 (d, $J=1.7$ Hz, 1H), 8.04–7.88 (m, 2H), 7.81–7.66 (m, 2H), 7.40–7.09 (m, 2H), 3.71 (p, $J=5.4$ Hz, 1H), 3.68–3.58 (m, 4H), 2.91–2.82 (m, 4H), 1.20–1.08 (m, 4H).



20190614-wct-1399-1-C/10
C13CPD DMSO (D:\NMR_DATA) LG_41

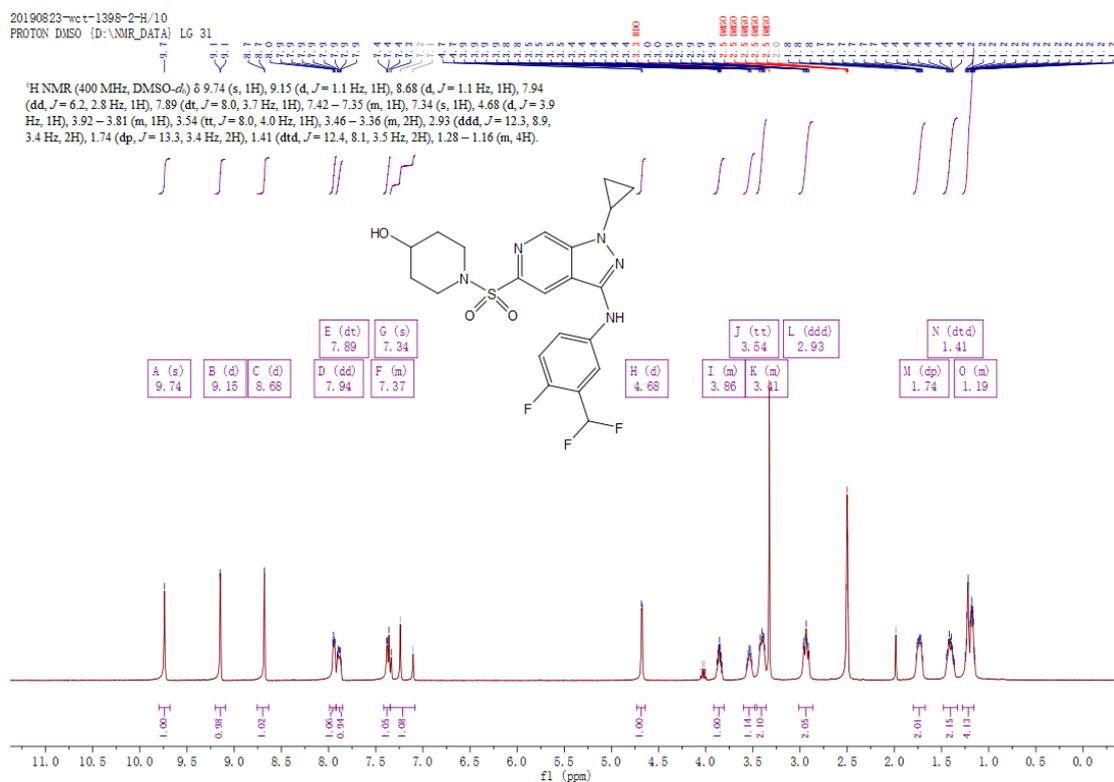
$^{13}\text{C NMR}$ (101 MHz, $\text{DMSO-}d_6$) δ 153.67 (dt, $J=242.3, 5.7$ Hz), 145.31, 142.14, 139.17 (d, $J=2.3$ Hz), 126.29, 125.02, 123.07, 121.63 (td, $J=22.7, 13.5$ Hz), 120.16 (d, $J=7.6$ Hz), 117.01 (d, $J=21.3$ Hz), 115.08, 114.03 (t, $J=5.7$ Hz), 112.25 (td, $J=235.9, 3.8$ Hz), 110.47, 65.75, 46.41, 29.66, 6.78.



Compound 59.

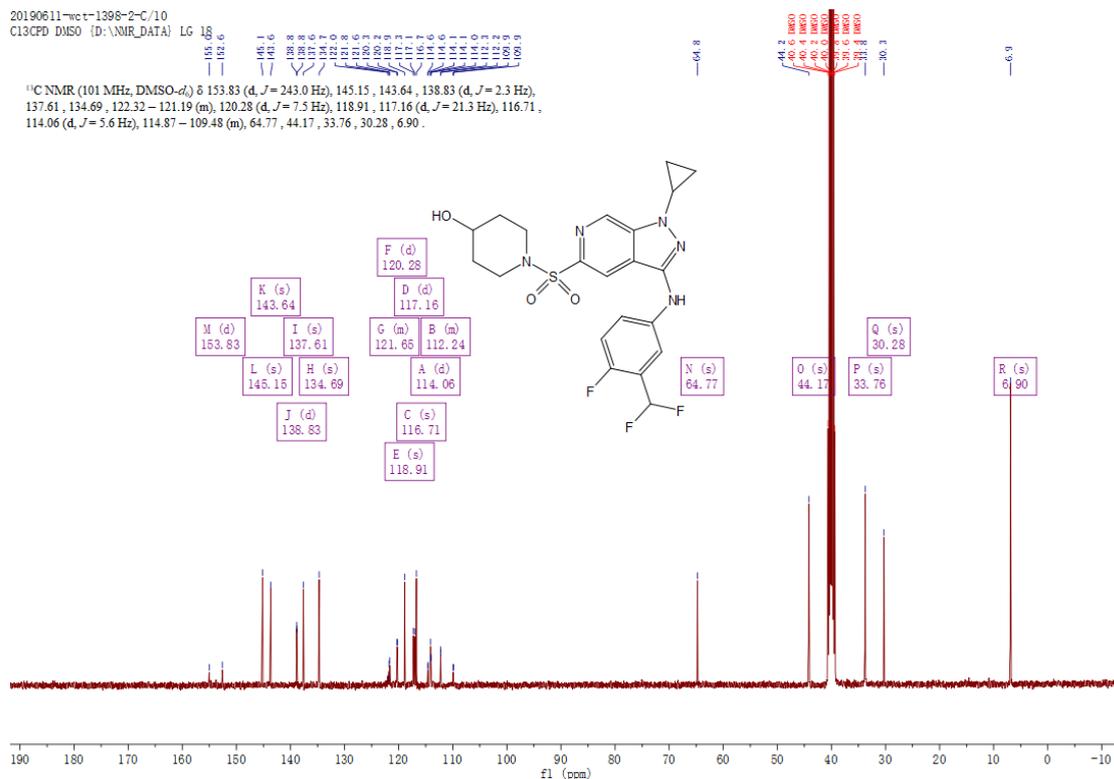
20190823-wet-1398-2-H/10
 PROTON DMSO (D:\NMR_DATA) LG 31

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.74 (s, 1H), 9.15 (d, *J* = 1.1 Hz, 1H), 8.68 (d, *J* = 1.1 Hz, 1H), 7.94 (dd, *J* = 6.2, 2.8 Hz, 1H), 7.89 (dt, *J* = 8.0, 3.7 Hz, 1H), 7.42–7.35 (m, 1H), 7.34 (s, 1H), 4.68 (d, *J* = 3.9 Hz, 1H), 3.92–3.81 (m, 1H), 3.54 (tt, *J* = 8.0, 4.0 Hz, 1H), 3.46–3.36 (m, 2H), 2.93 (ddd, *J* = 12.3, 8.9, 3.4 Hz, 2H), 1.74 (dp, *J* = 13.3, 3.4 Hz, 2H), 1.41 (dtd, *J* = 12.4, 8.1, 3.5 Hz, 2H), 1.28–1.16 (m, 4H).



20190811-wet-1398-2-C/10
 C13CPD DMSO (D:\NMR_DATA) LG 18

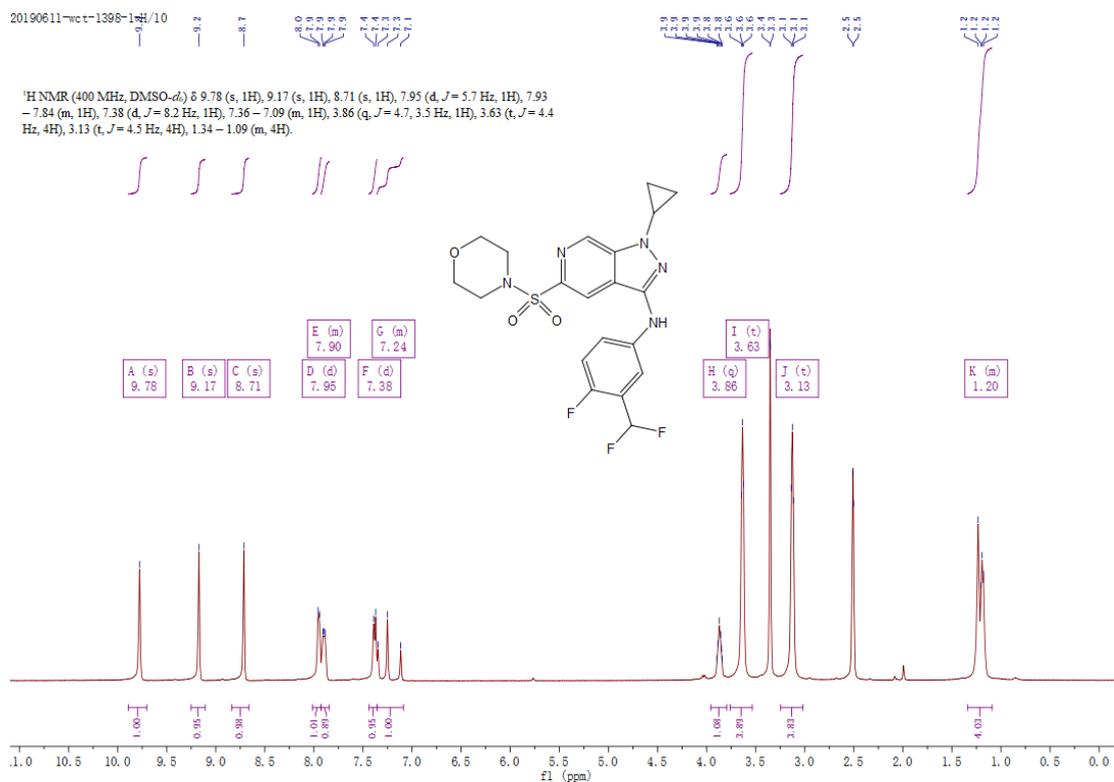
¹³C NMR (101 MHz, DMSO-*d*₆) δ 153.83 (d, *J* = 243.0 Hz), 145.15, 143.64, 138.83 (d, *J* = 2.3 Hz), 137.61, 134.69, 122.32–121.19 (m), 120.28 (d, *J* = 7.5 Hz), 118.91, 117.16 (d, *J* = 21.3 Hz), 116.71, 114.06 (d, *J* = 5.6 Hz), 114.87–109.48 (m), 64.77, 44.17, 33.76, 30.28, 6.90.



Compound 60.

20190611-wet-1398-1-H/10

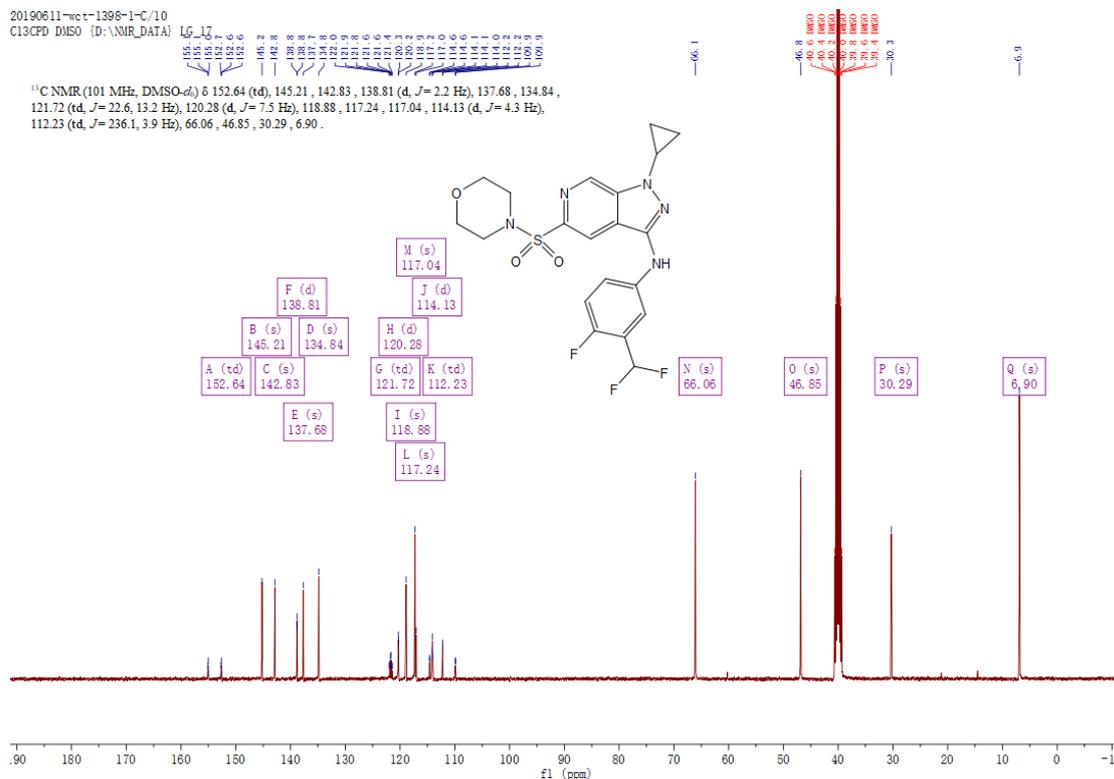
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.78 (s, 1H), 9.17 (s, 1H), 8.71 (s, 1H), 7.95 (d, *J* = 5.7 Hz, 1H), 7.93 - 7.84 (m, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.36 - 7.09 (m, 1H), 3.86 (q, *J* = 4.7, 3.5 Hz, 1H), 3.63 (t, *J* = 4.4 Hz, 4H), 3.13 (t, *J* = 4.5 Hz, 4H), 1.34 - 1.09 (m, 4H).



20190611-wet-1398-1-C/10

C13CPD DMSO (D:\NMR_DATA)

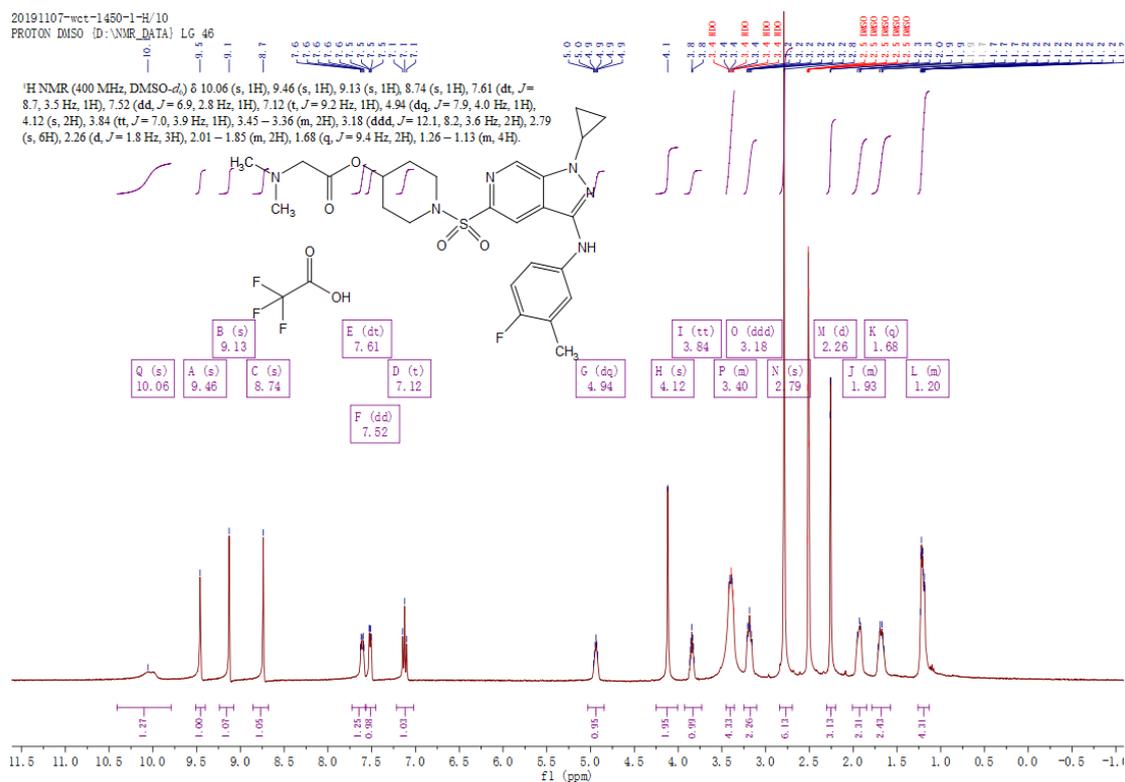
¹³C NMR (101 MHz, DMSO-*d*₆) δ 152.64 (td), 145.21, 142.83, 138.81 (d, *J* = 2.2 Hz), 137.68, 134.84, 121.72 (td, *J* = 22.6, 13.2 Hz), 120.28 (d, *J* = 7.5 Hz), 118.88, 117.24, 117.04, 114.13 (d, *J* = 4.3 Hz), 112.23 (td, *J* = 236.1, 3.9 Hz), 66.06, 46.85, 30.29, 6.90.



Compound 61.

20191107-wct-1450-1-H/10
 PROTON DMSO (D:\NMR_DATA) LG 46

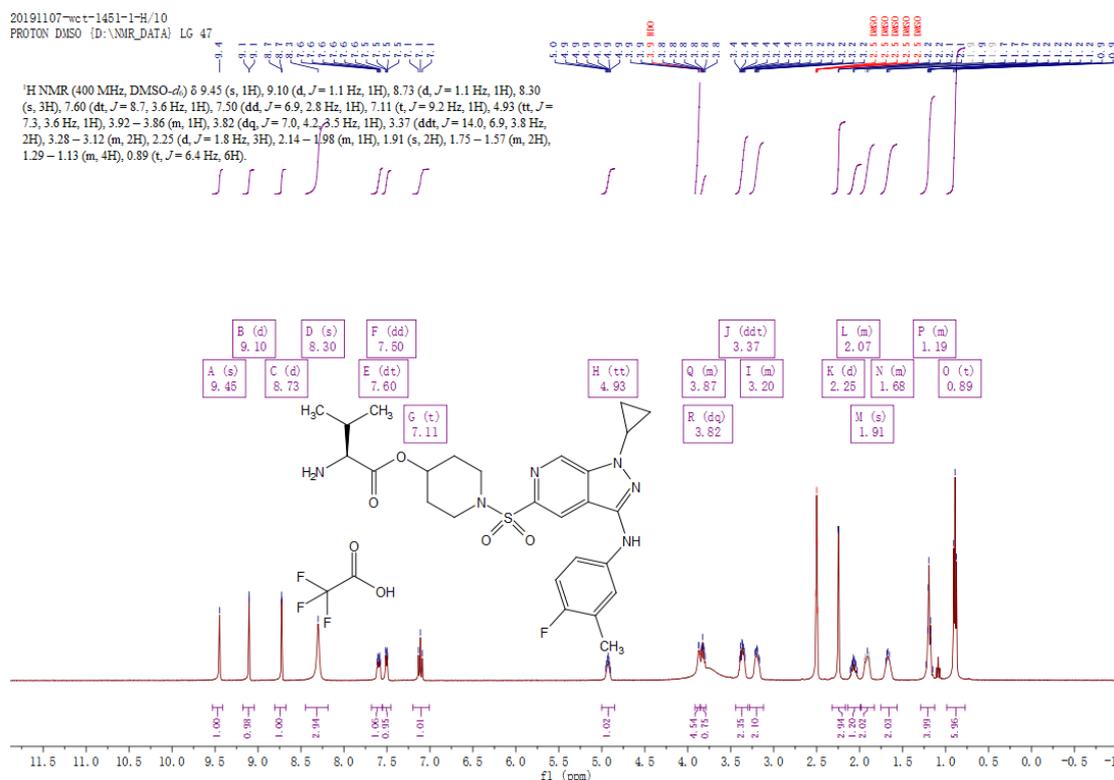
¹H NMR (400 MHz, DMSO-d₆) δ 10.06 (s, 1H), 9.46 (s, 1H), 9.13 (s, 1H), 8.74 (s, 1H), 7.61 (dt, J=8.7, 3.5 Hz, 1H), 7.52 (dd, J=6.9, 2.8 Hz, 1H), 7.12 (t, J=9.2 Hz, 1H), 4.94 (dq, J=7.9, 4.0 Hz, 1H), 4.12 (s, 2H), 3.84 (tt, J=7.0, 3.9 Hz, 1H), 3.45–3.36 (m, 2H), 3.18 (ddd, J=12.1, 8.2, 3.6 Hz, 2H), 2.79 (s, 6H), 2.26 (d, J=1.8 Hz, 3H), 2.01–1.85 (m, 2H), 1.68 (q, J=9.4 Hz, 2H), 1.26–1.13 (m, 4H).



Compound 62

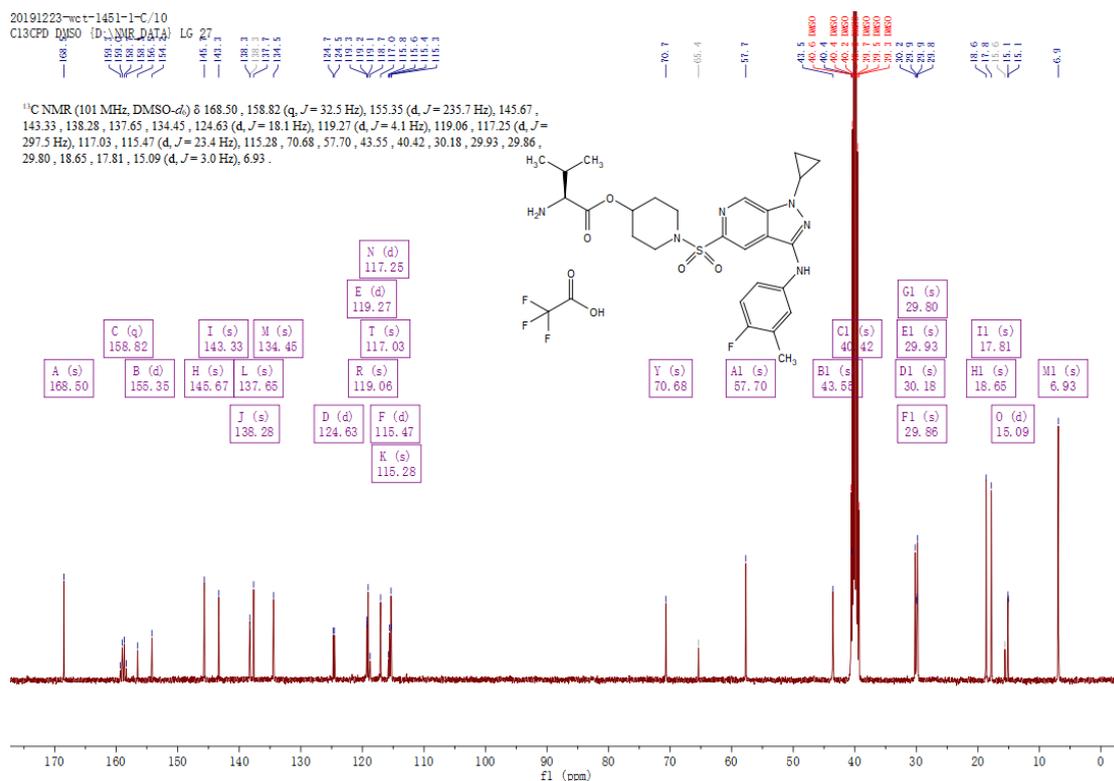
20191107-wet-1451-1-H/10
 PROTON DMSO [D:\NMR_DATA] LG 47

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.45 (s, 1H), 9.10 (d, *J* = 1.1 Hz, 1H), 8.73 (d, *J* = 1.1 Hz, 1H), 8.30 (s, 3H), 7.60 (dt, *J* = 8.7, 3.6 Hz, 1H), 7.50 (dd, *J* = 6.9, 2.8 Hz, 1H), 7.11 (t, *J* = 9.2 Hz, 1H), 4.93 (t, *J* = 7.3, 3.6 Hz, 1H), 3.92 – 3.86 (m, 1H), 3.82 (dq, *J* = 7.0, 4.2, 2.5 Hz, 1H), 3.37 (ddt, *J* = 14.0, 6.9, 3.8 Hz, 2H), 3.28 – 3.12 (m, 2H), 2.25 (d, *J* = 1.8 Hz, 3H), 2.14 – 1.98 (m, 1H), 1.91 (s, 2H), 1.75 – 1.57 (m, 2H), 1.29 – 1.13 (m, 4H), 0.89 (t, *J* = 6.4 Hz, 6H).



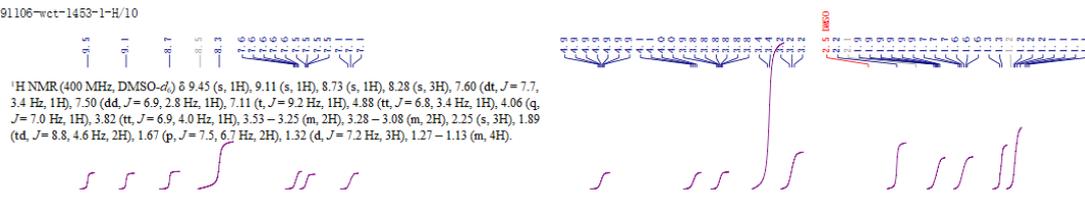
20191223-wet-1451-1-C/10
 C13CPD DMSO [D:\NMR_DATA] LG 27

¹³C NMR (101 MHz, DMSO-*d*₆) δ 168.50, 158.82 (q, *J* = 32.5 Hz), 155.35 (d, *J* = 235.7 Hz), 145.67, 143.33, 138.28, 137.65, 134.45, 124.63 (d, *J* = 18.1 Hz), 119.27 (d, *J* = 4.1 Hz), 119.06, 117.25 (d, *J* = 297.5 Hz), 117.03, 115.47 (d, *J* = 23.4 Hz), 115.28, 70.68, 57.70, 43.55, 40.42, 30.18, 29.93, 29.86, 29.80, 18.65, 17.81, 15.09 (d, *J* = 3.0 Hz), 6.93.

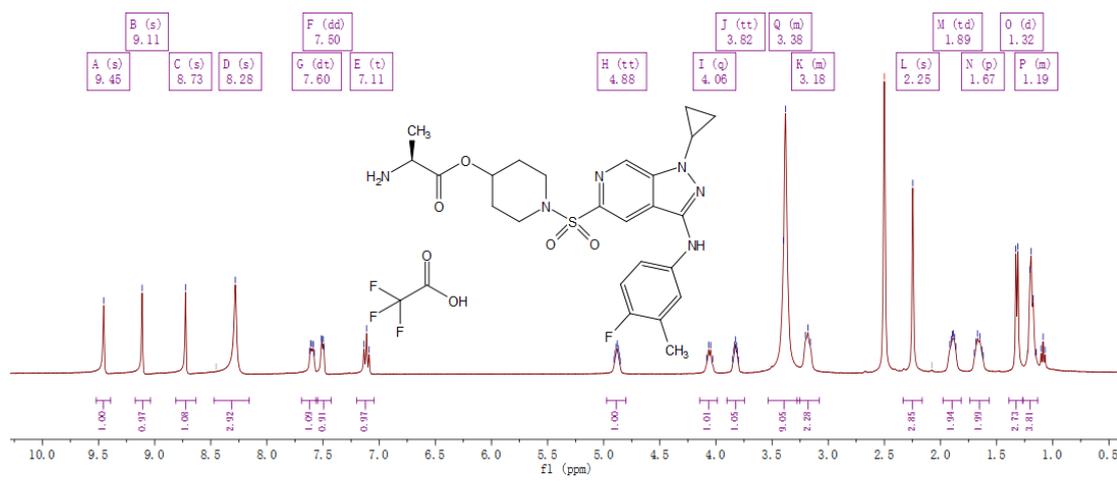


Compound 63.

191106-wet-1453-1-H/10

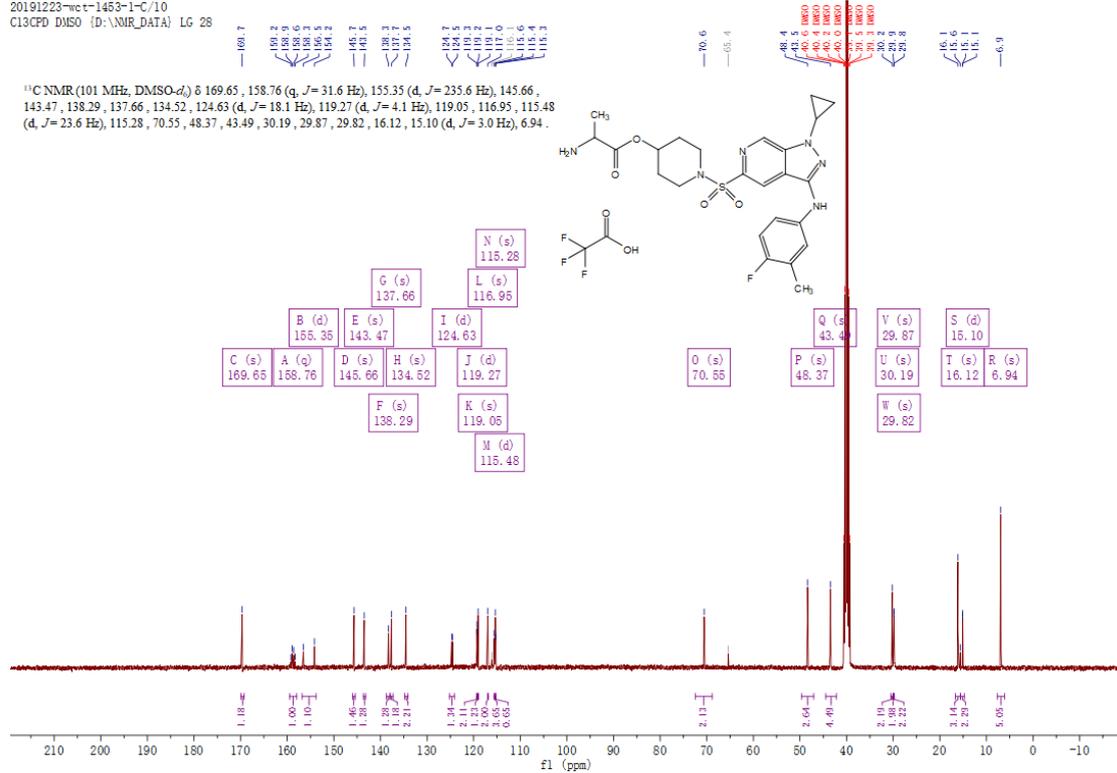


¹H NMR (400 MHz, DMSO-*d*₆) δ 9.45 (s, 1H), 9.11 (s, 1H), 8.73 (s, 1H), 8.28 (s, 3H), 7.60 (dt, *J* = 7.7, 3.4 Hz, 1H), 7.50 (dd, *J* = 6.9, 2.8 Hz, 1H), 7.11 (t, *J* = 9.2 Hz, 1H), 4.88 (tt, *J* = 6.8, 3.4 Hz, 1H), 4.06 (q, *J* = 7.0 Hz, 1H), 3.82 (tt, *J* = 6.9, 4.0 Hz, 1H), 3.53–3.25 (m, 2H), 3.28–3.08 (m, 2H), 2.25 (s, 3H), 1.89 (td, *J* = 8.8, 4.6 Hz, 2H), 1.67 (p, *J* = 7.5, 6.7 Hz, 2H), 1.32 (d, *J* = 7.2 Hz, 3H), 1.27–1.13 (m, 4H).



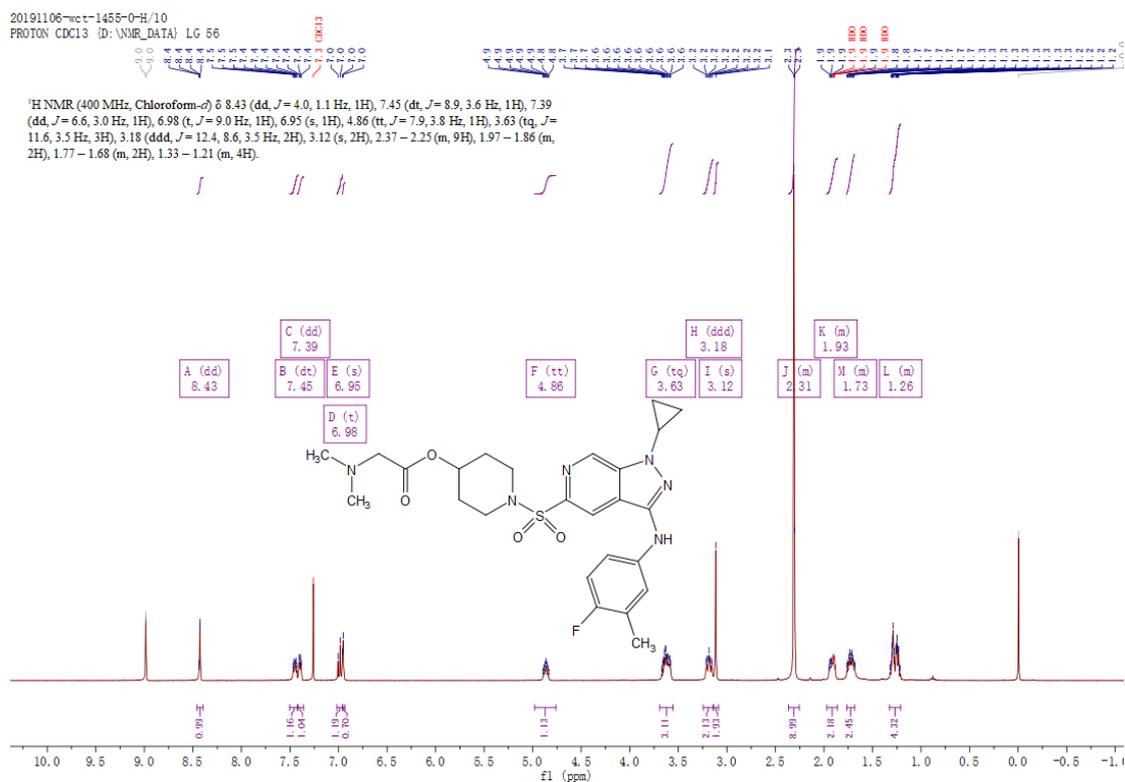
20191223-wet-1453-1-C/10
 C13CPD DMSO {D:\NMR_DATA} LG 28

¹³C NMR (101 MHz, DMSO-*d*₆) δ 169.65, 158.76 (q, *J* = 31.6 Hz), 155.35 (d, *J* = 235.6 Hz), 145.66, 143.47, 138.29, 137.66, 134.52, 124.63 (d, *J* = 18.1 Hz), 119.27 (d, *J* = 4.1 Hz), 119.05, 116.95, 115.48 (d, *J* = 23.6 Hz), 115.28, 70.55, 48.37, 43.49, 30.19, 29.87, 29.82, 16.12, 15.10 (d, *J* = 3.0 Hz), 6.94.

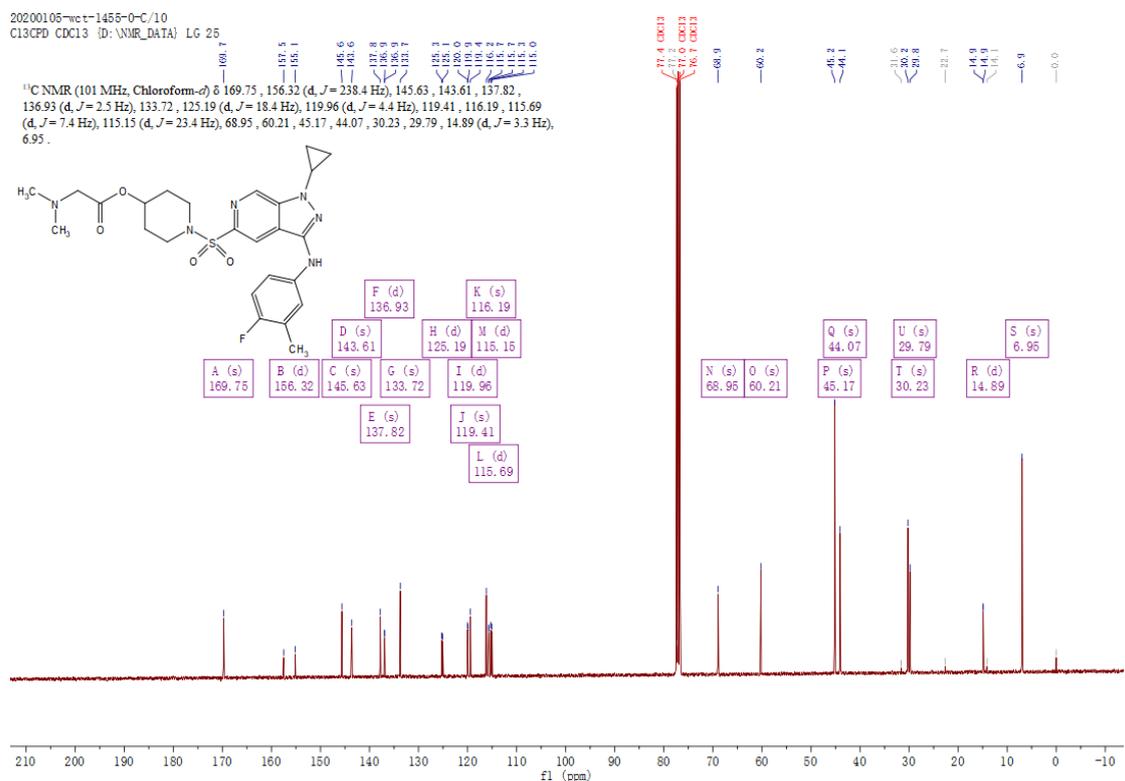


Compound 65.

20191106-wet-1458-0-H/10
 PROTON CDCl3 [D:\NMR_DATA] LG 56

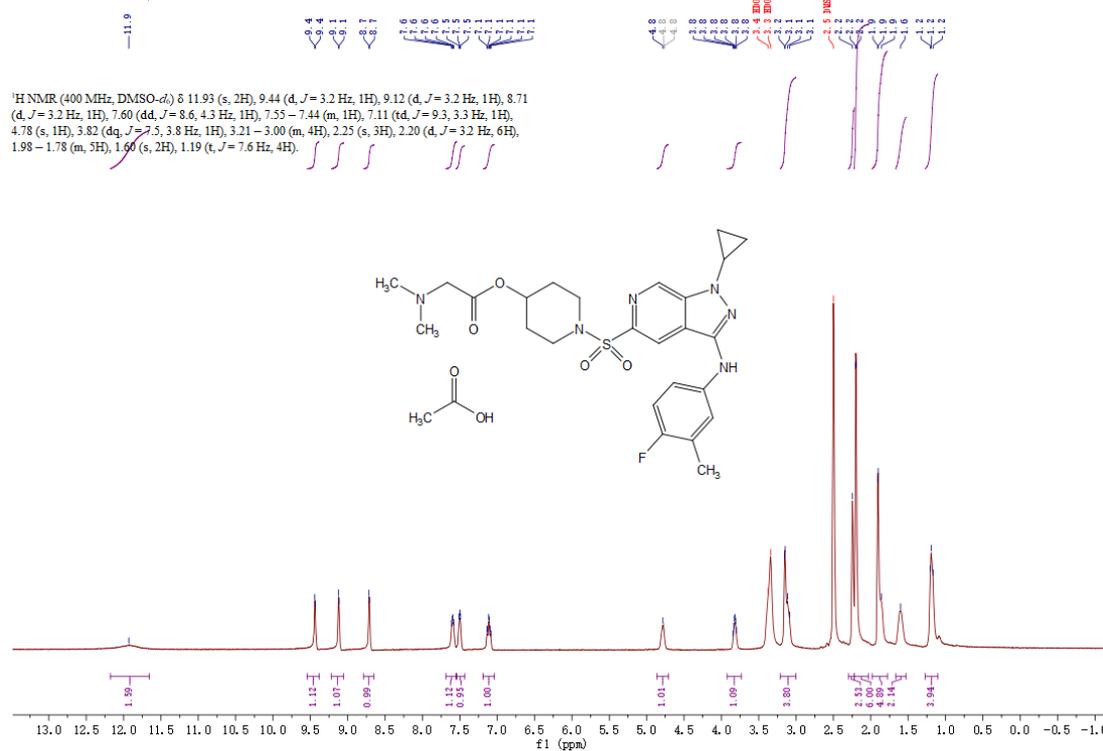


20200105-wet-1458-0-C/10
 C13CPD CDCl3 [D:\NMR_DATA] LG 25



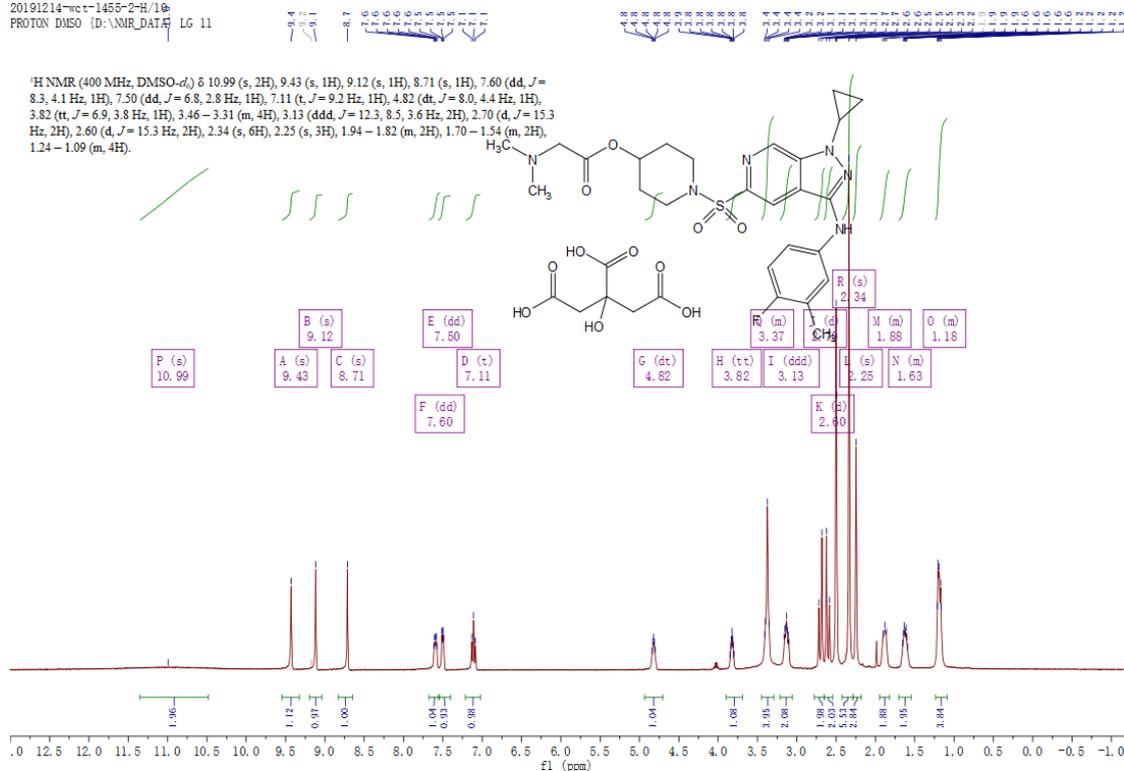
Compound 66.

20191016-wet-1455-1-H/10



Compound 67.

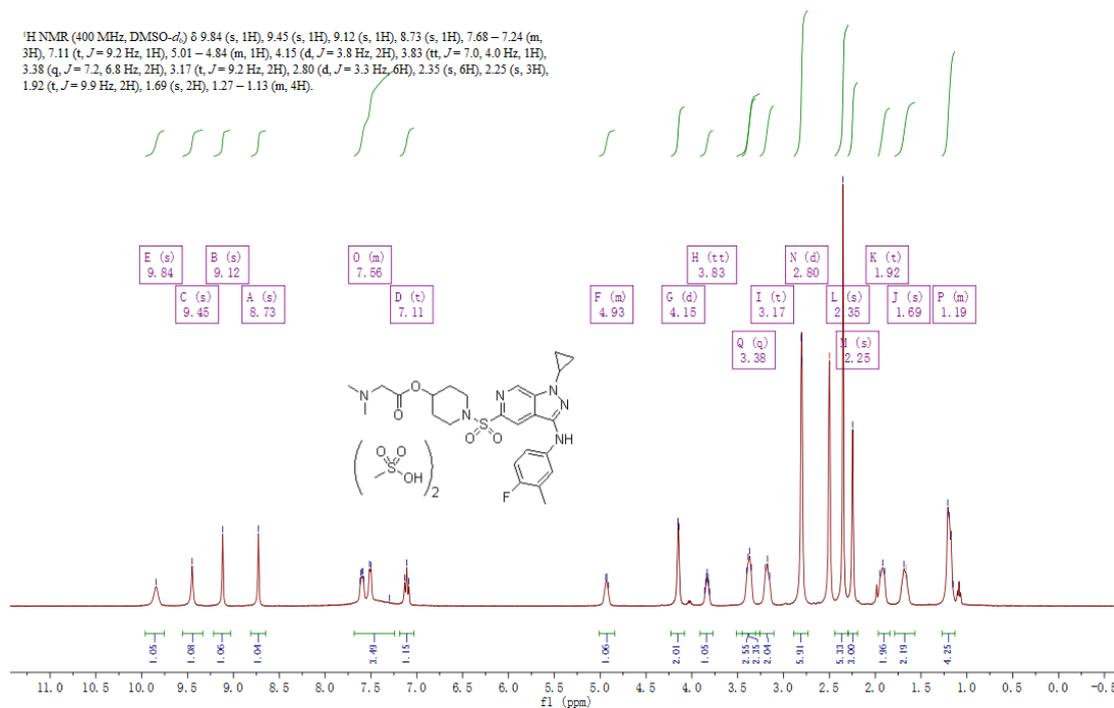
20191214-wet-1458-2-H/10
PROTON DMSO [D:\NMR_DATA\LG 11



Compound 68.

20200113-wct-1455-3-H/10
 PROTON DMSO [D:\NMR_DATA] LG 18

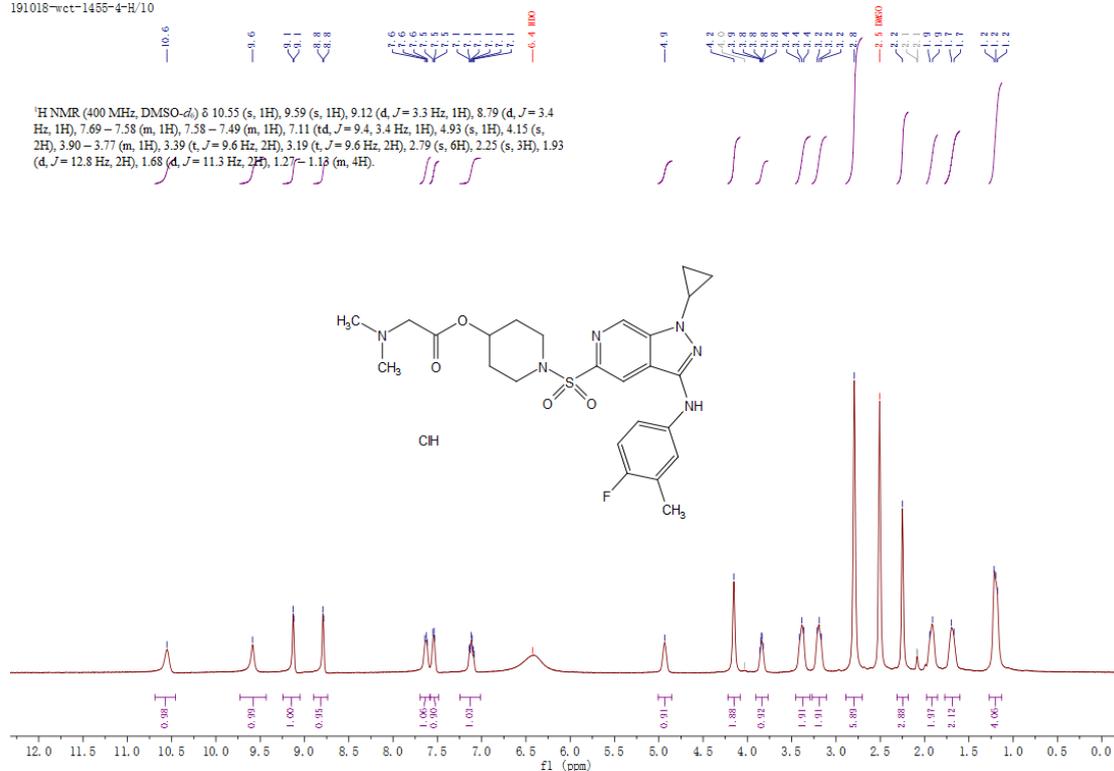
¹H NMR (400 MHz, DMSO-*d*₆) δ 9.84 (s, 1H), 9.45 (s, 1H), 9.12 (s, 1H), 8.73 (s, 1H), 7.68–7.24 (m, 3H), 7.11 (t, *J* = 9.2 Hz, 1H), 5.01–4.84 (m, 1H), 4.15 (d, *J* = 3.8 Hz, 2H), 3.83 (tt, *J* = 7.0, 4.0 Hz, 1H), 3.38 (q, *J* = 7.2, 6.8 Hz, 2H), 3.17 (t, *J* = 9.2 Hz, 2H), 2.80 (d, *J* = 3.3 Hz, 6H), 2.35 (s, 3H), 1.92 (t, *J* = 9.9 Hz, 2H), 1.69 (s, 2H), 1.27–1.13 (m, 4H).



Compound 69.

191018-wct-1455-4-H/10

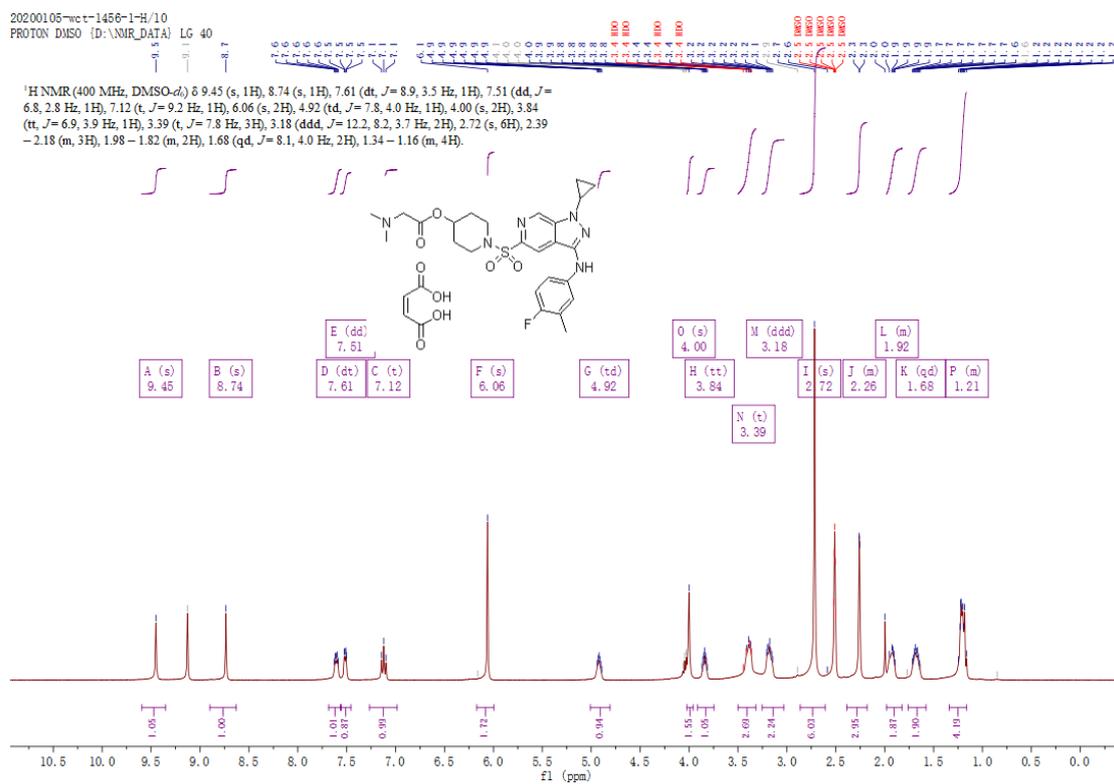
¹H NMR (400 MHz, DMSO-*d*₆) δ 10.55 (s, 1H), 9.59 (s, 1H), 9.12 (d, *J* = 3.3 Hz, 1H), 8.79 (d, *J* = 3.4 Hz, 1H), 7.69–7.58 (m, 1H), 7.58–7.49 (m, 1H), 7.11 (td, *J* = 9.4, 3.4 Hz, 1H), 4.93 (s, 1H), 4.15 (s, 2H), 3.90–3.77 (m, 1H), 3.39 (t, *J* = 9.6 Hz, 2H), 3.19 (t, *J* = 9.6 Hz, 2H), 2.79 (s, 6H), 2.25 (s, 3H), 1.93 (d, *J* = 12.8 Hz, 2H), 1.68 (d, *J* = 11.3 Hz, 2H), 1.27–1.13 (m, 4H).



Compound 70.

20200105-wct-1456-1-H/10
 PROTON DMSO [D:\NMR_DATA] LG 40

¹H NMR (400 MHz, DMSO-*d*₆) δ 9.45 (s, 1H), 8.74 (s, 1H), 7.61 (dt, *J* = 8.9, 3.5 Hz, 1H), 7.51 (dd, *J* = 6.8, 2.8 Hz, 1H), 7.12 (t, *J* = 9.2 Hz, 1H), 6.06 (s, 2H), 4.92 (td, *J* = 7.8, 4.0 Hz, 1H), 4.00 (s, 2H), 3.84 (tt, *J* = 6.9, 3.9 Hz, 1H), 3.39 (t, *J* = 7.8 Hz, 3H), 3.18 (ddd, *J* = 12.2, 8.2, 3.7 Hz, 2H), 2.72 (s, 6H), 2.39 - 2.18 (m, 3H), 1.98 - 1.82 (m, 2H), 1.68 (qd, *J* = 8.1, 4.0 Hz, 2H), 1.34 - 1.16 (m, 4H).

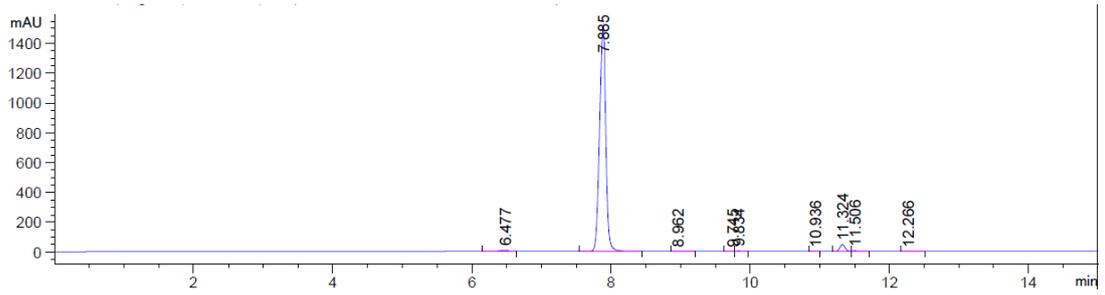


Supplementary Table S2: Purity of the tested compounds.

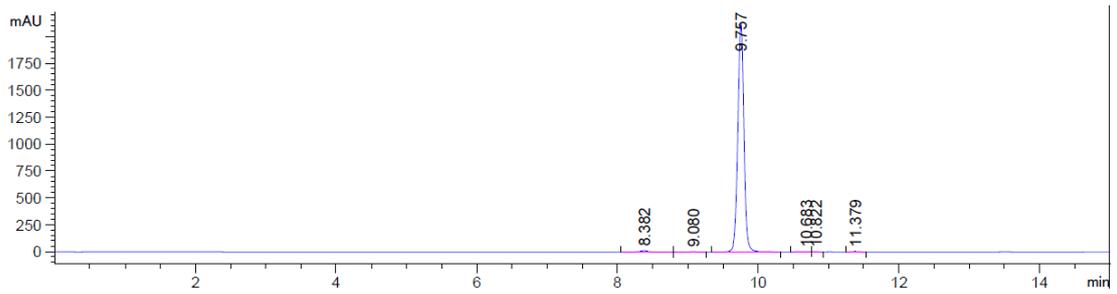
Compd.	t _R (min)	Purity (%)	Compd.	t _R (min)	Purity (%)
1	7.885	96.41	32	11.032	98.14
2	9.757	98.88	33	11.214	98.54
3	10.960	96.52	34	1230-2	97.86
4	9.828	99.89	35	9.681	98.07
5	10.163	99.62	36	9.396	98.85
6	11.062	96.08	37	9.993	98.37
7	12.032	97.96	38	11.826	96.76
8	11.422	98.94	39	10.760	95.88
9	11.098	95.55	40	11.94	95.13
10	11.564	98.14	41	12.233	99.58
11	9.805	95.58	42	10.896	98.36
12	10.306	95.90	43	11.796	98.81
13	10.311	99.79	44	8.983	98.39
14	10.133	100.00	45	10.684	98.56
15	10.758	99.77	46	12.745	98.22
16	9.321	99.28	47	11.349	98.99
17	9.221	98.90	48	11.762	90.66
18	10.180	99.40	49	11.226	96.39
19	10.241	99.00	50	11.483	98.73
20	10.338	97.76	51	10.846	97.80
21 ^a	1.55	95.85	52	11.519	98.26
22	9.553	98.20	53	10.189	98.09
23	7.600	98.72	54	11.297	97.18
24	7.773	99.24	55	13.265	97.60
25	8.264	97.99	56	9.158	98.97
26	8.502	98.44	57	10.058	98.94
27	9.272	99.00	58	11.538	97.48
28	8.299	97.99	59	8.875	98.85
29	7.650	97.98	60	10.414	97.95
30	9.326	97.99	67	7.240	99.60
31	10.290	98.32			

HPLC spectrum

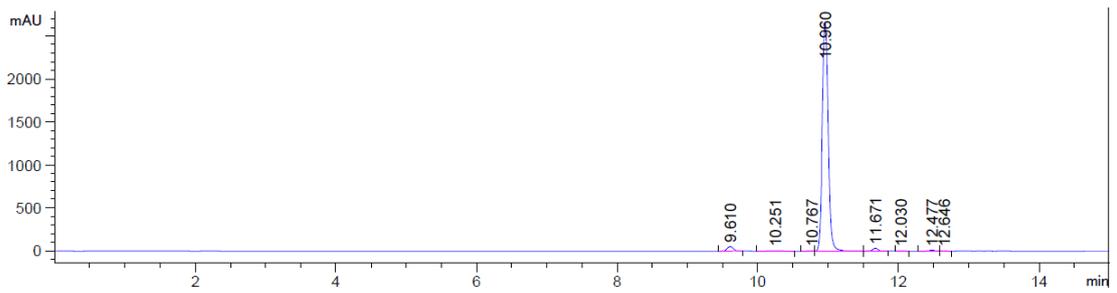
1



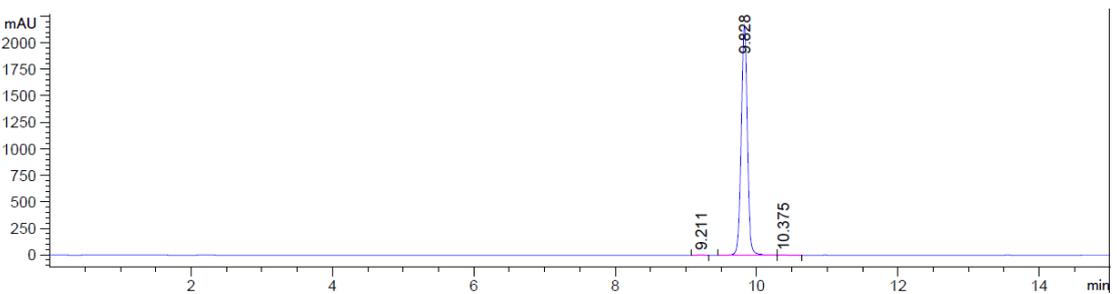
2



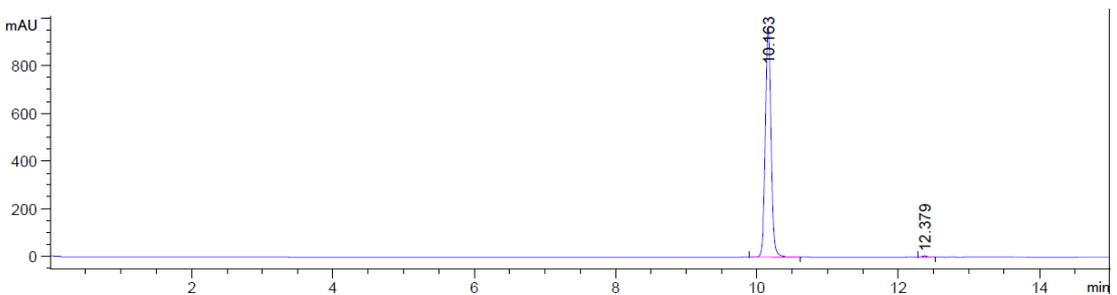
3

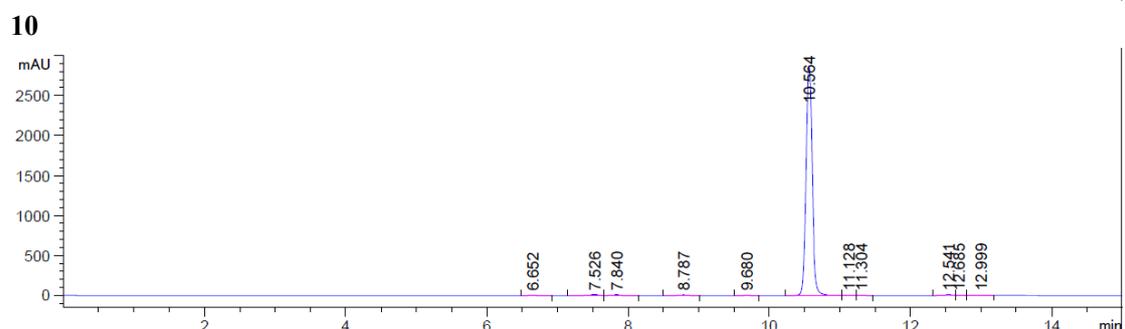
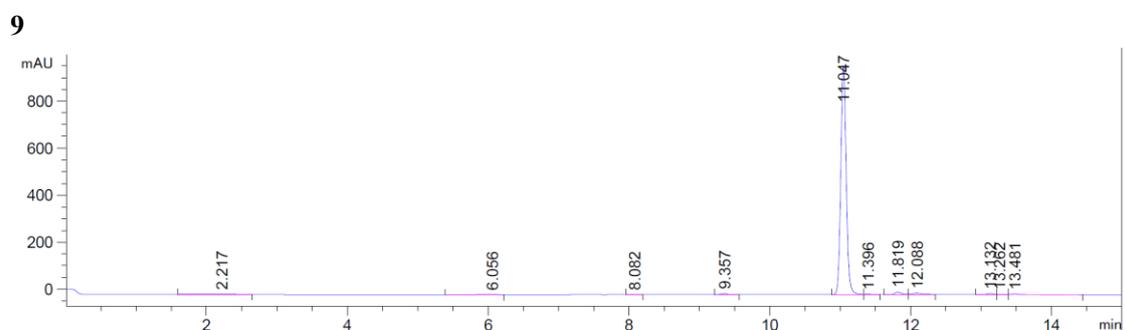
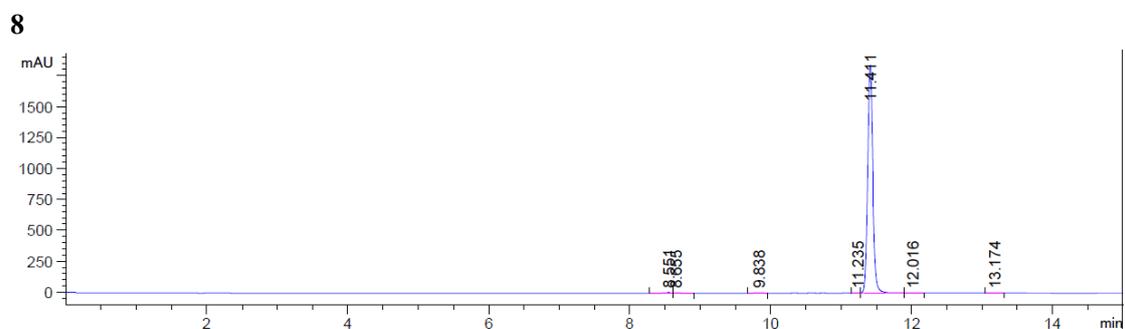
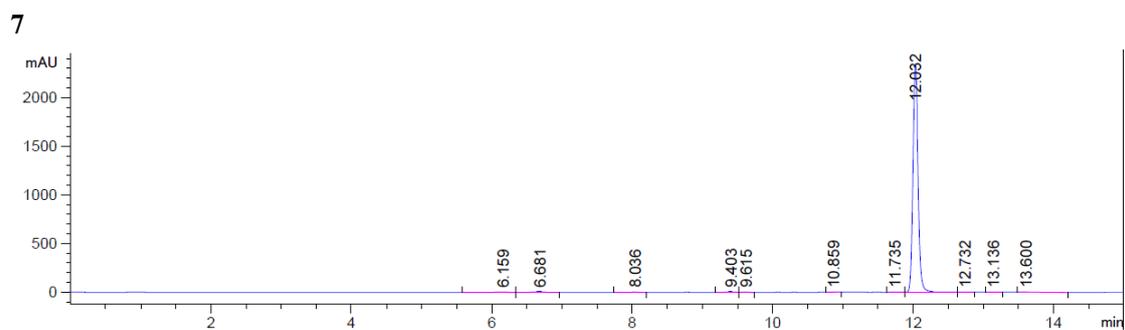
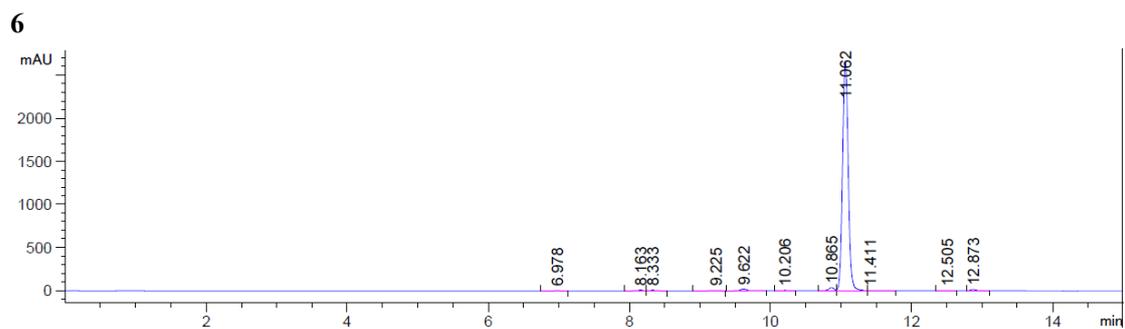


4

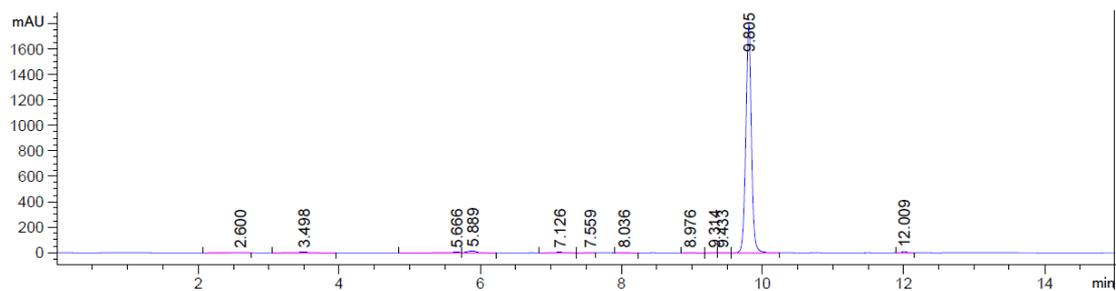


5

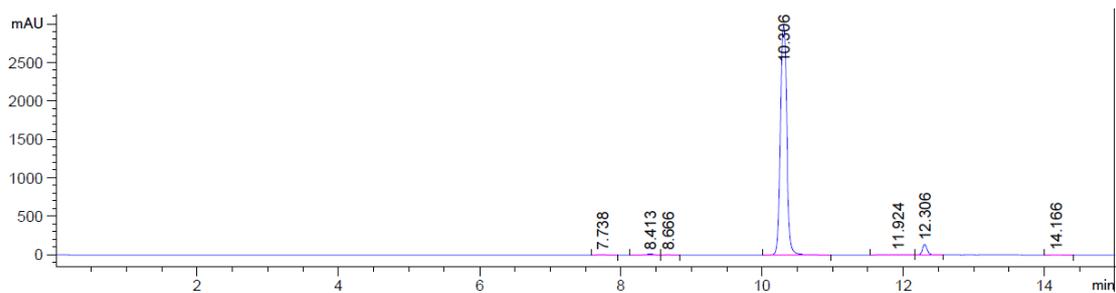




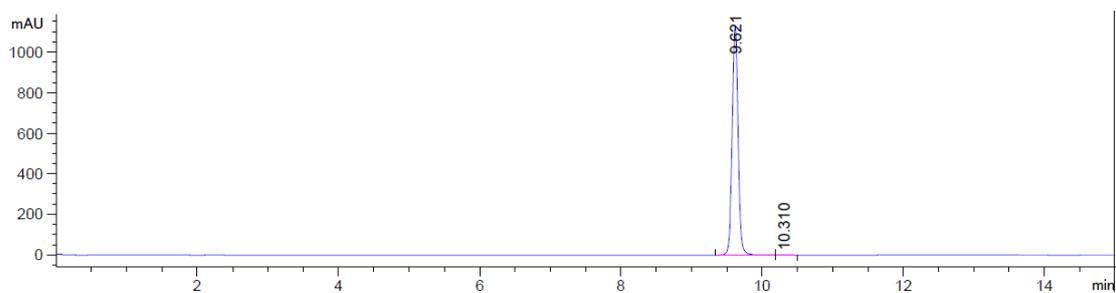
11



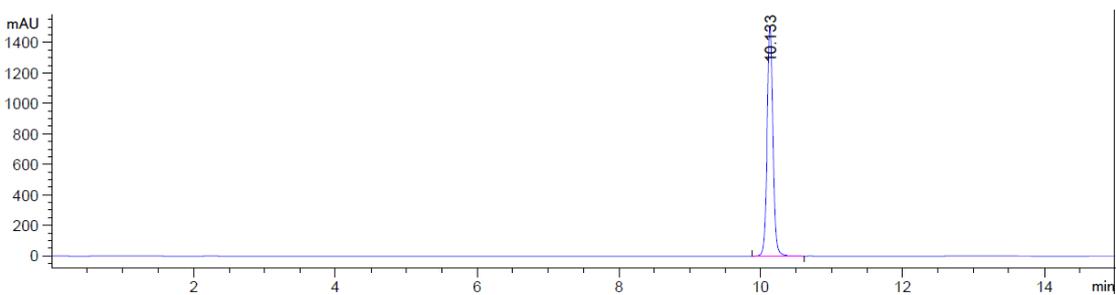
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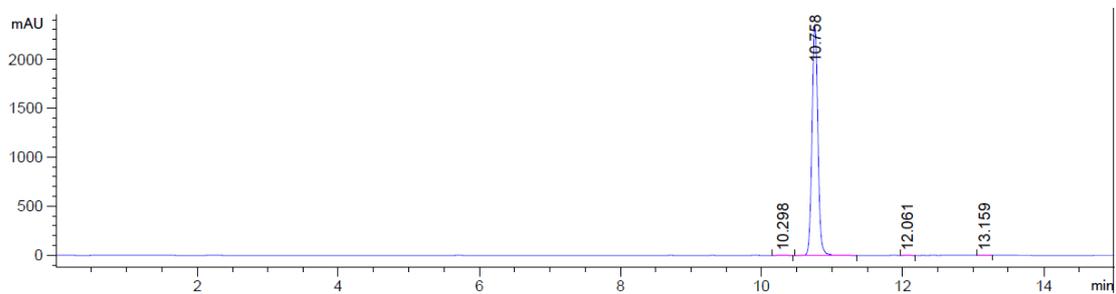
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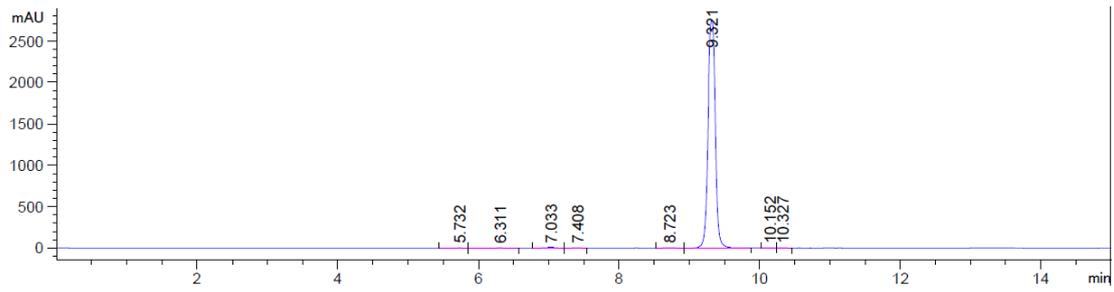
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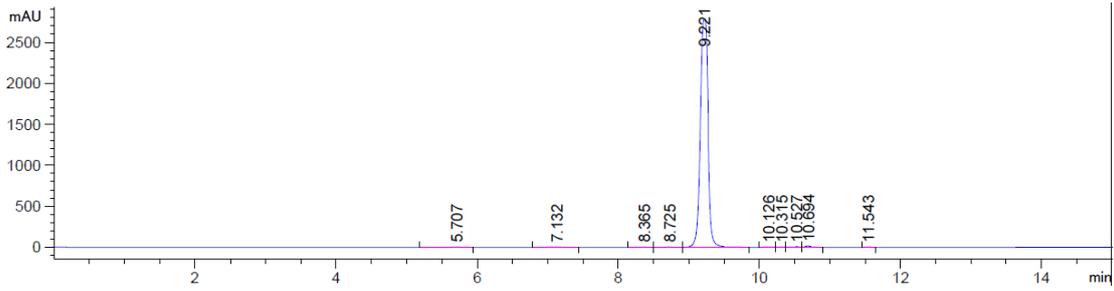
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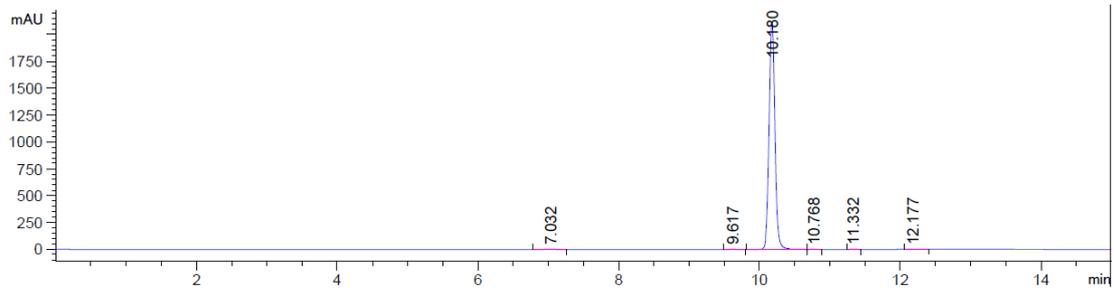
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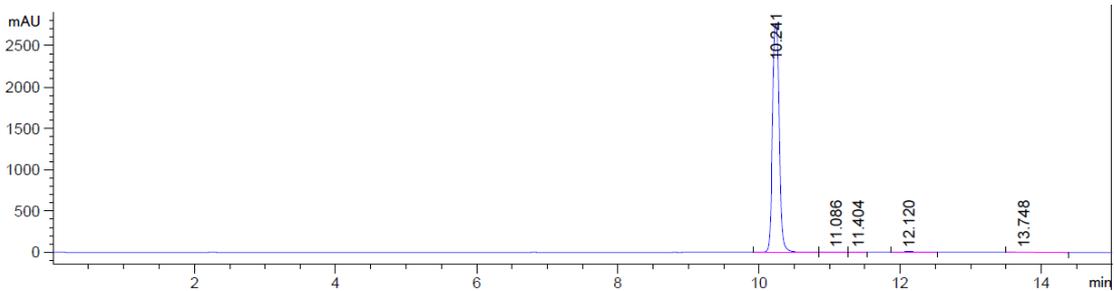
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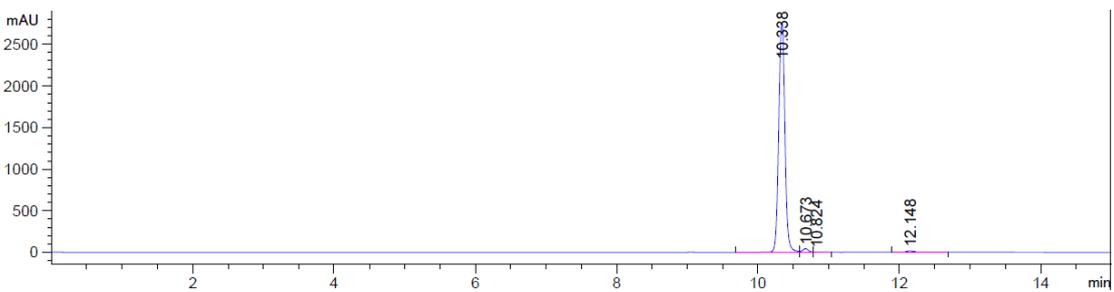
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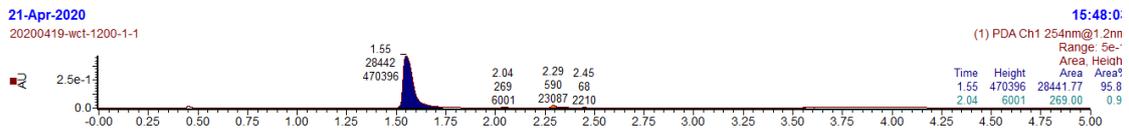
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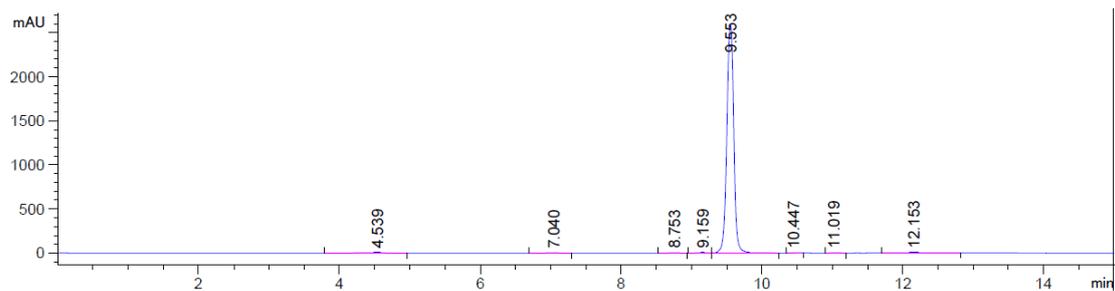
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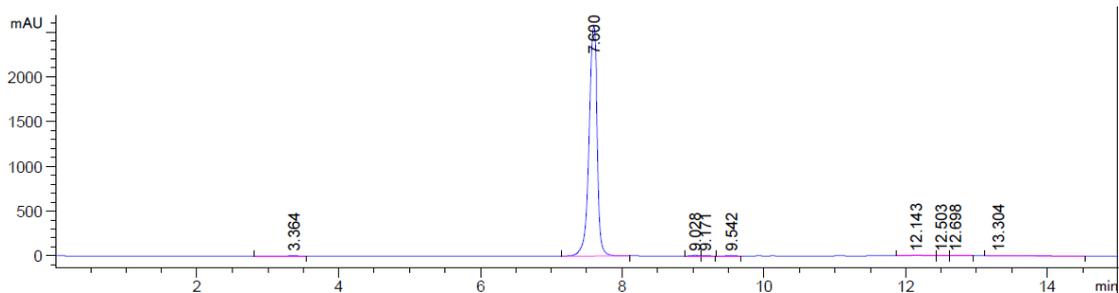
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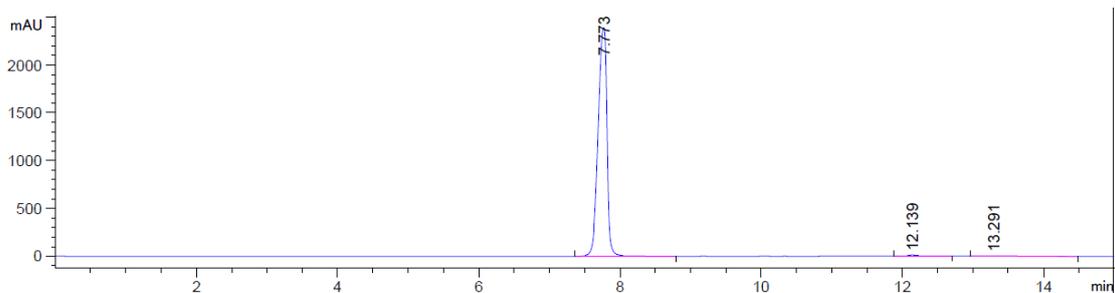
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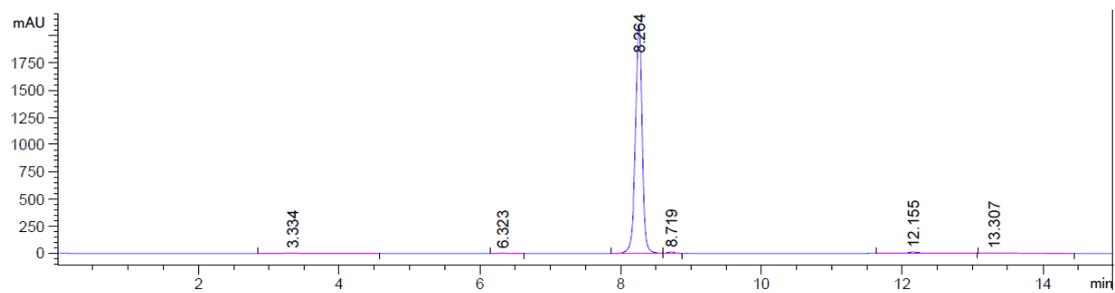
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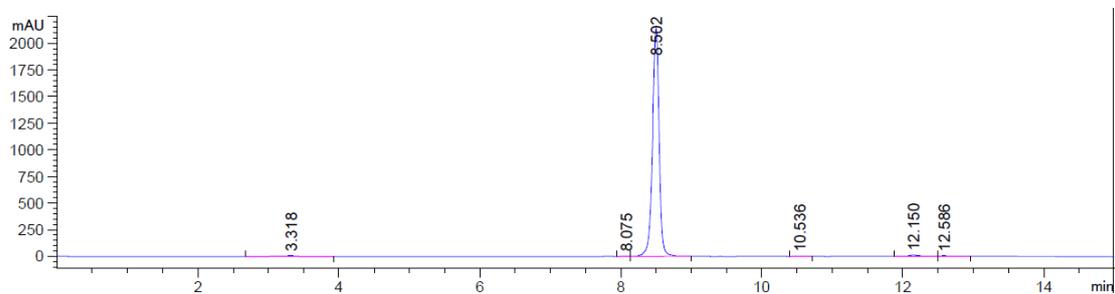
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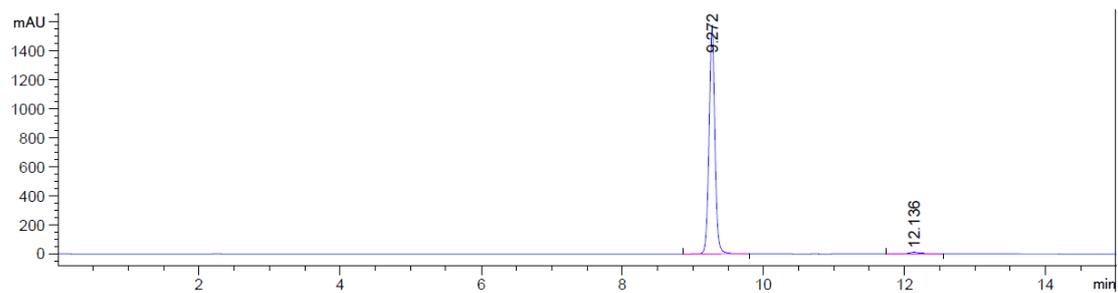
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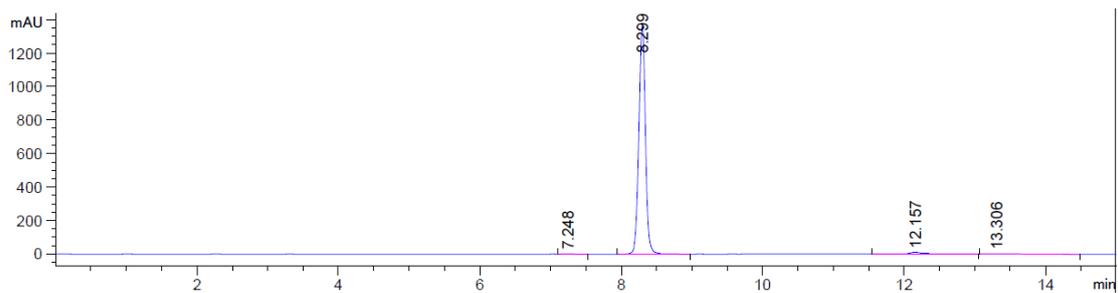
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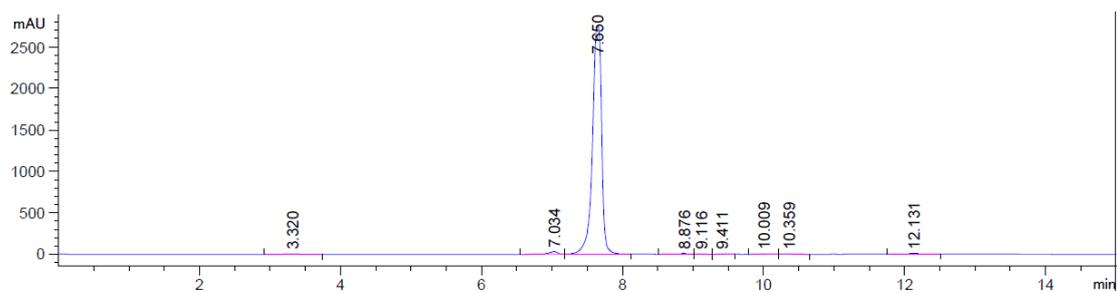
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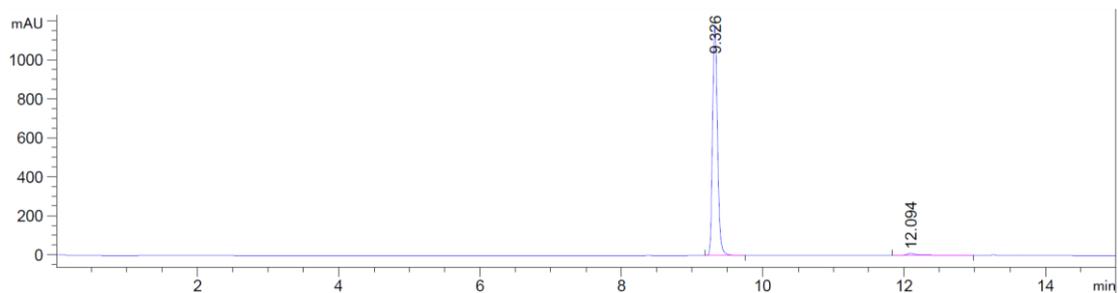
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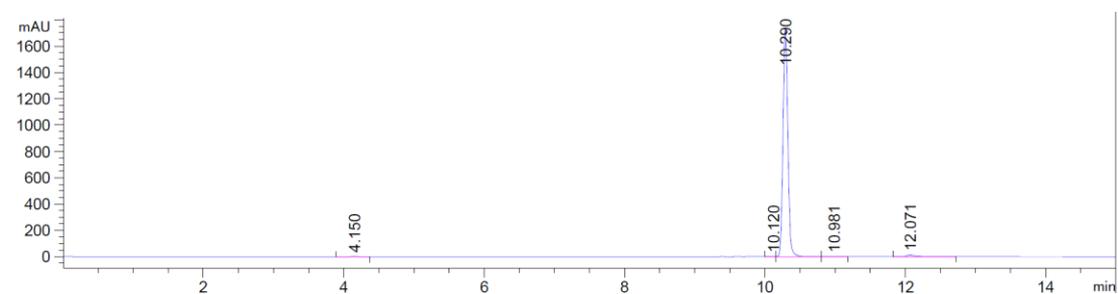
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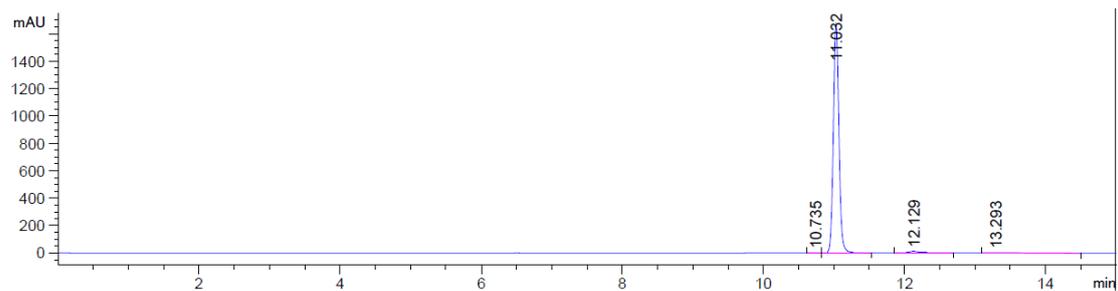
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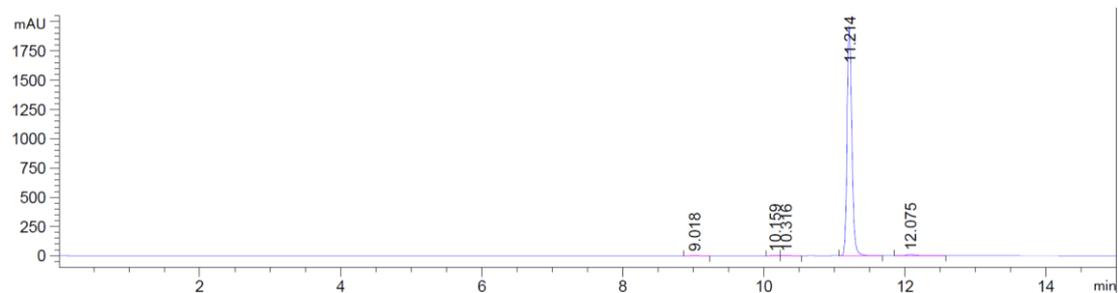
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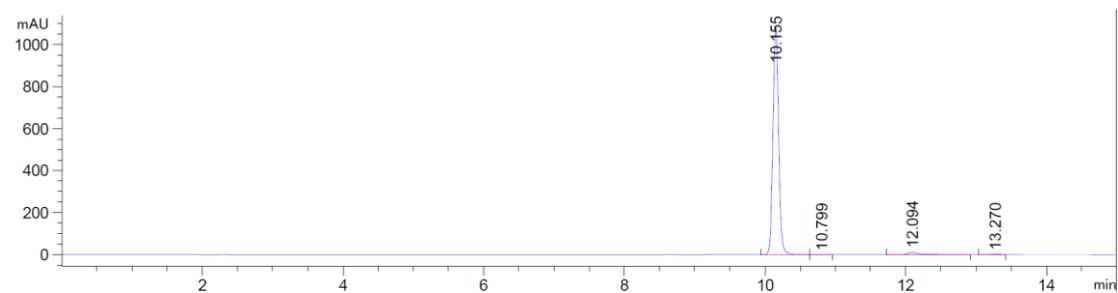
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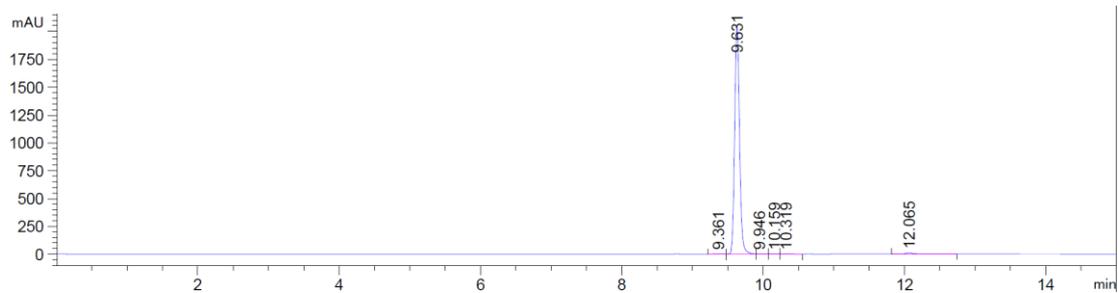
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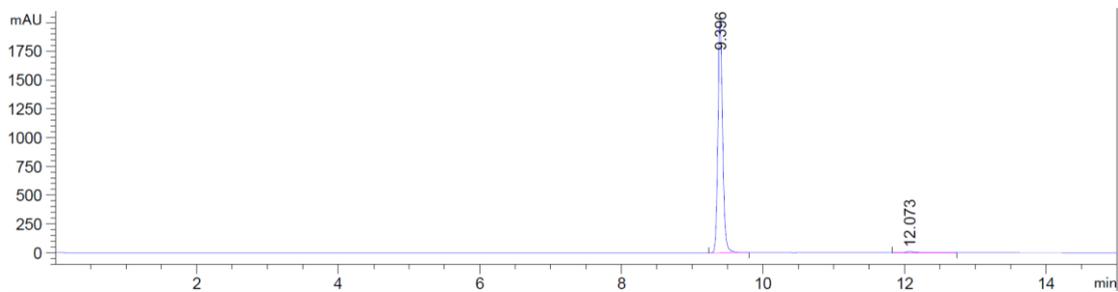
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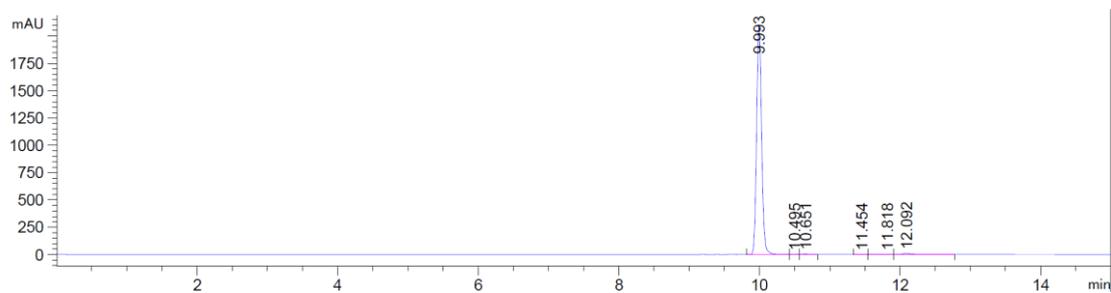
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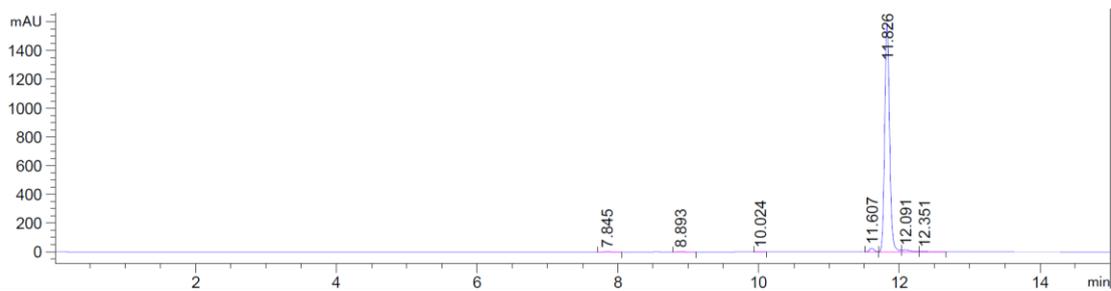
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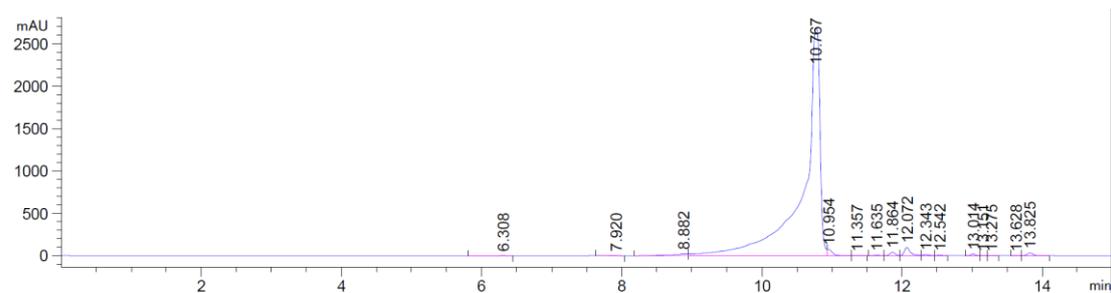
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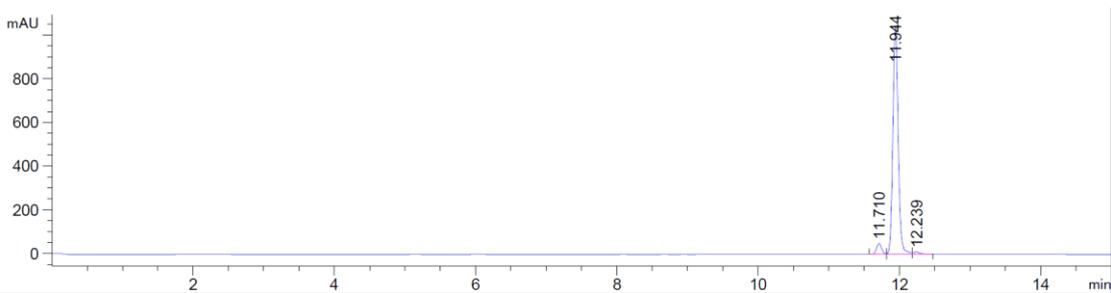
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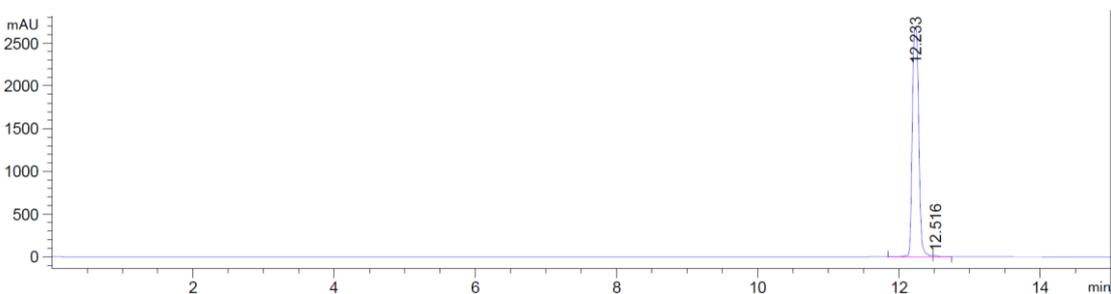
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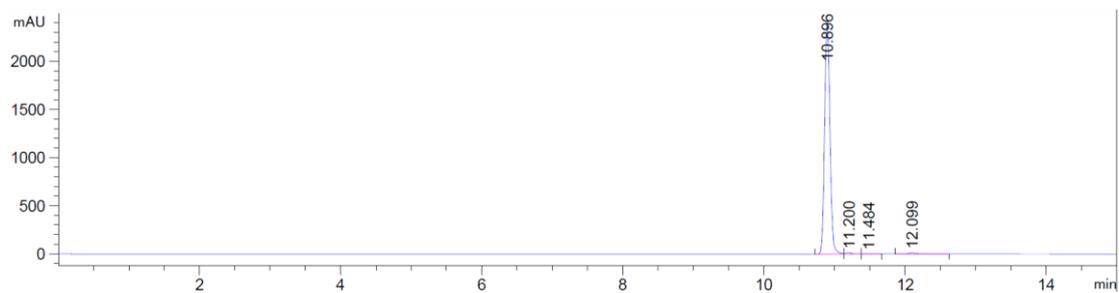
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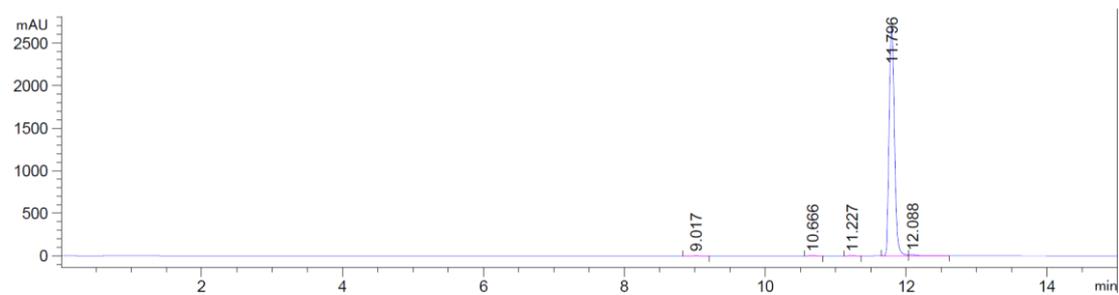
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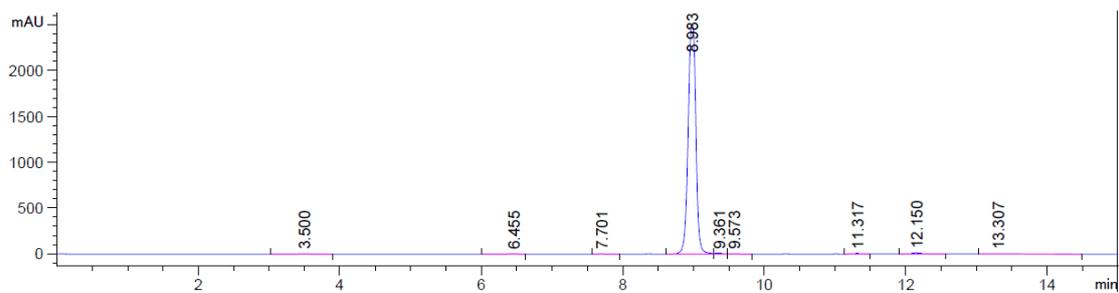
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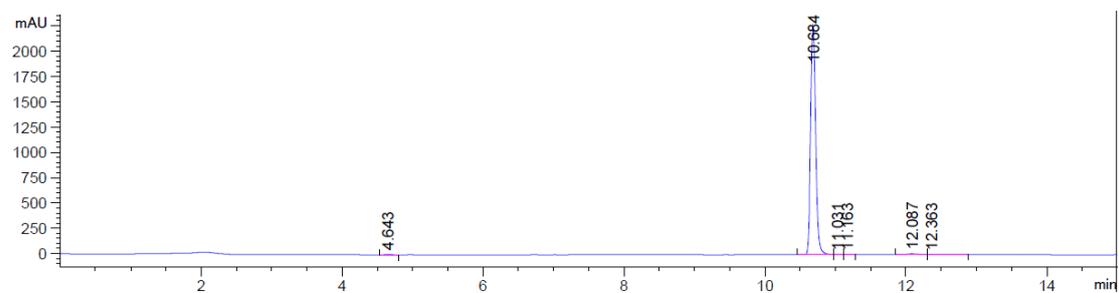
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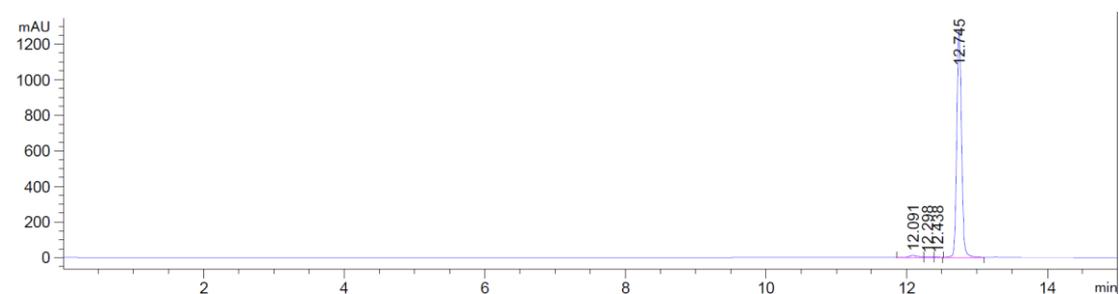
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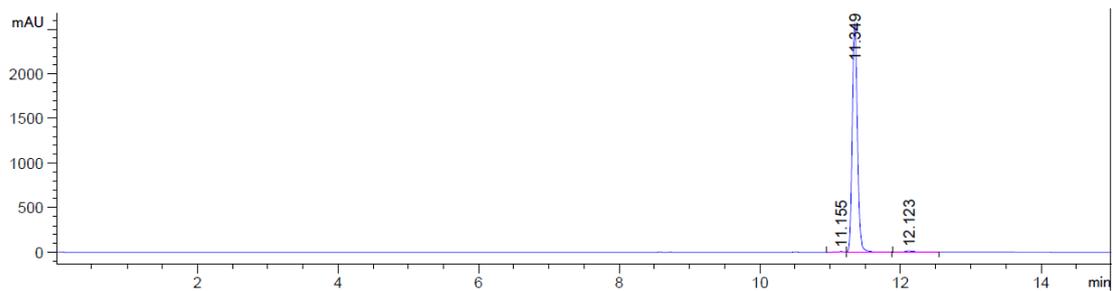
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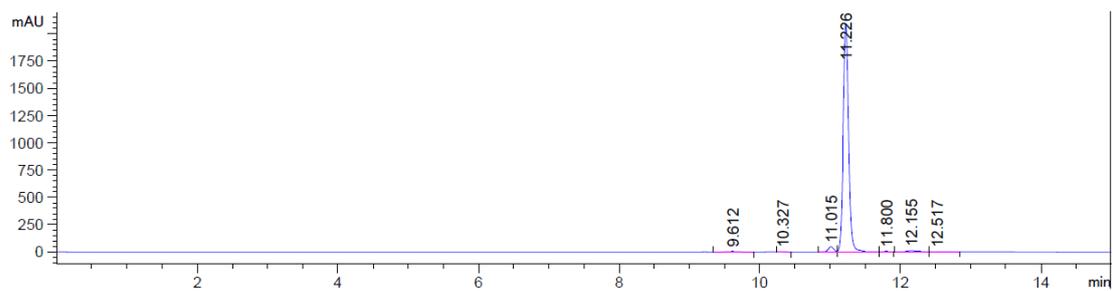
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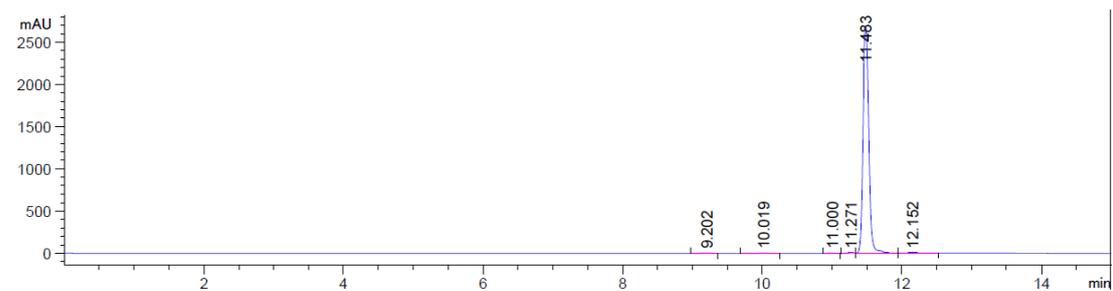
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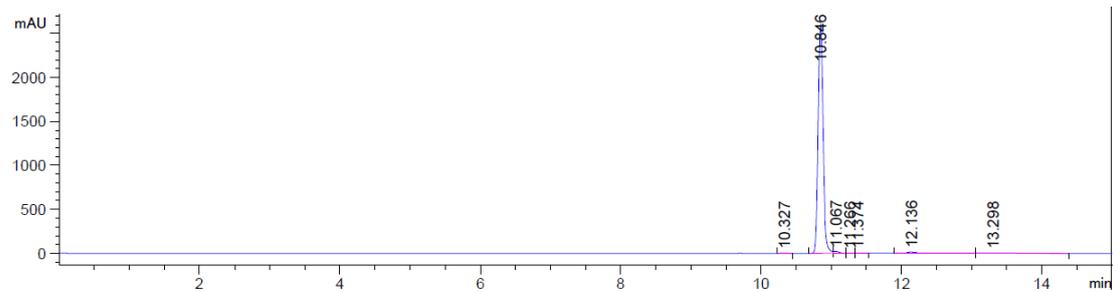
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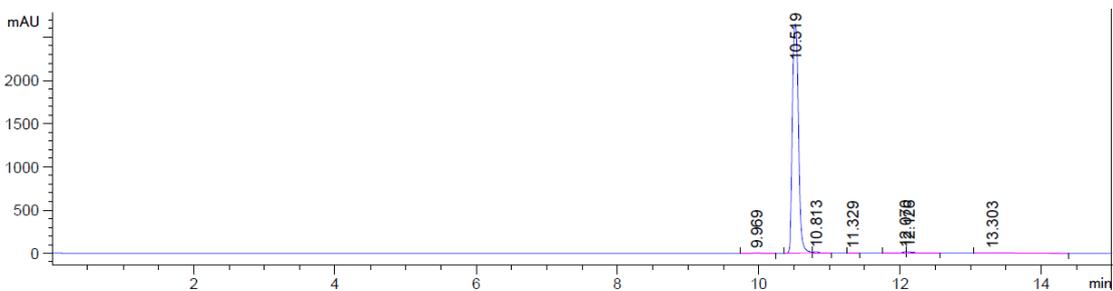
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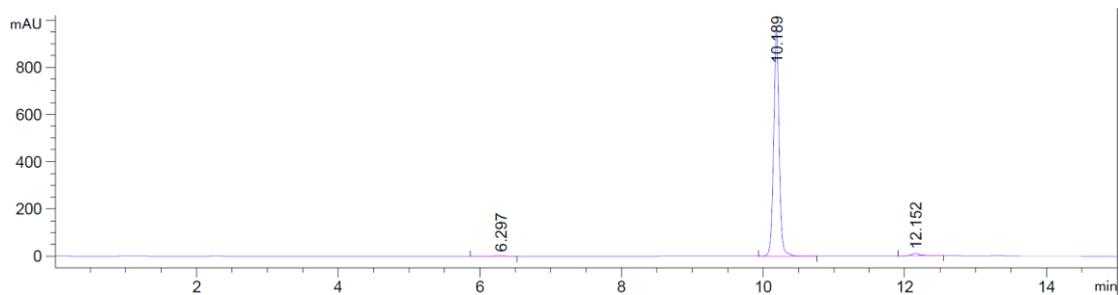
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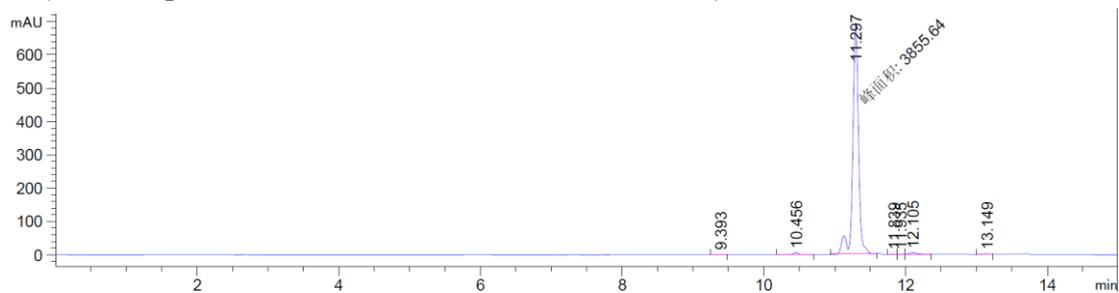
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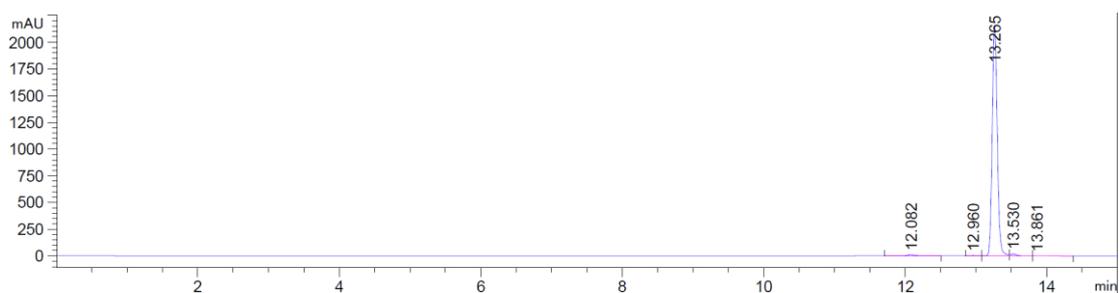
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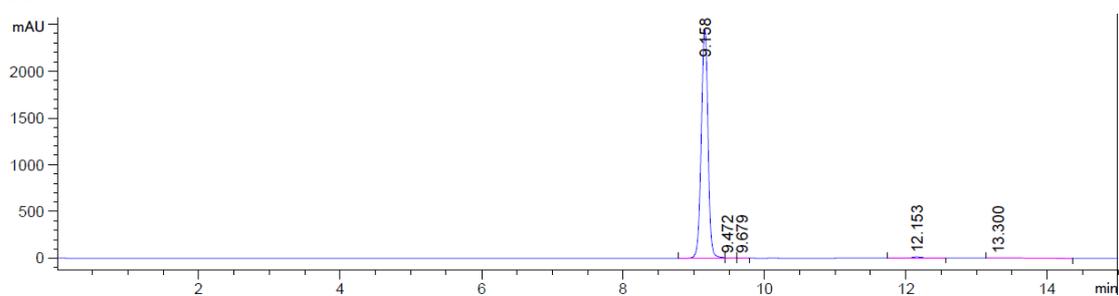
54 (containing an diastereomer as indicated in the ^1H NMR)



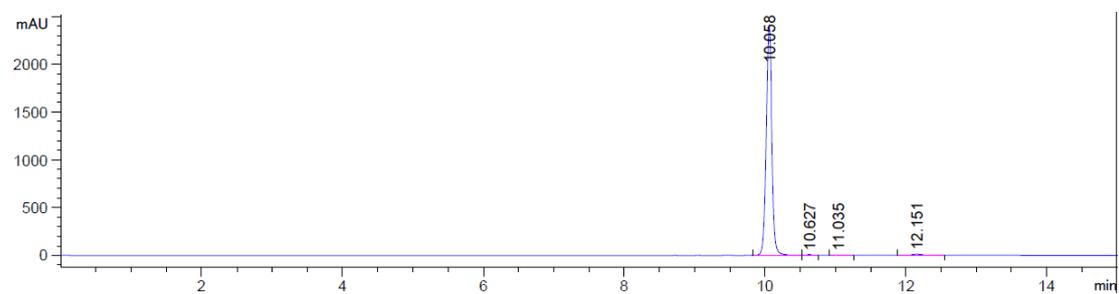
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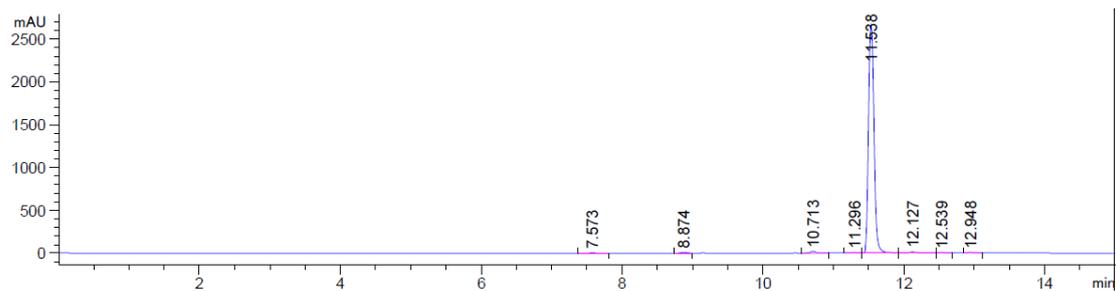
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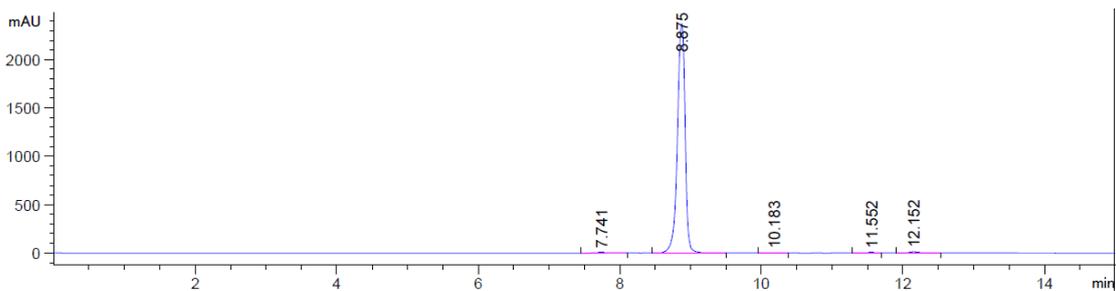
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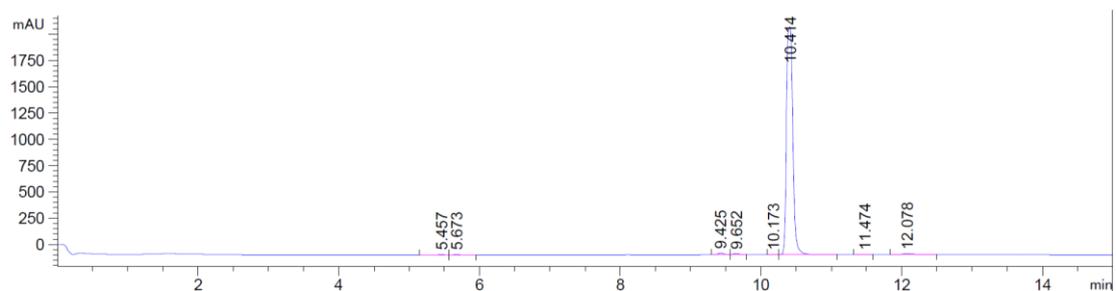
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59



60



67

