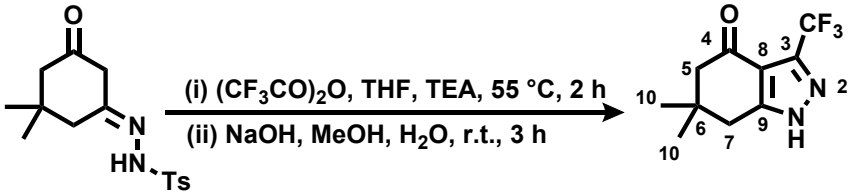
Rationally modified SNX-class Hsp90 inhibitors disrupt extracellular fibronectin assembly without intracellular Hsp90 activity

Supplementary data

Chemistry

General experimental procedures

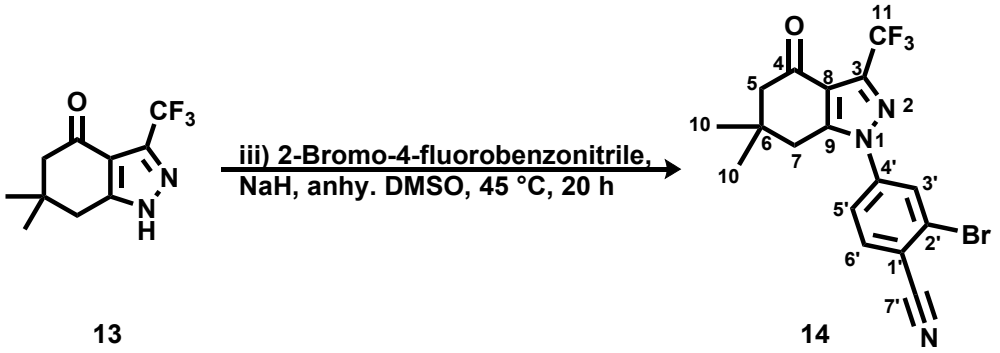
Solvents and commercially available reagents used for this project were purchased from Honeywell or Sigma-Aldrich and used without further purification. All reactions that included the use of air and/or moisture sensitive reagents were carried out under an inert atmosphere of nitrogen using oven-dried glassware and anhydrous solvents. Infrared (IR) spectral data was obtained using an Alpha II FTIR spectrometer and the IR data is reported as absorption frequency (cm^{-1}). All nuclear magnetic resonance (NMR) spectra were recorded either on a Bruker 400 MHz or 500 MHz UltraShield NMR spectrometer. ^{1}H and ^{13}C NMR chemical shifts are listed in ppm referenced against the NMR solvent as the internal standard ($CDCl_3$: δ 7.26, 77.16; CD_3OD: δ 3.31, 49.00; $(CD_3)_2SO$: δ 2.50, 39.52; $(CD_3)_2CO$: δ 2.05, 29.84). NMR spectral data is reported as: chemical shift, integration, multiplicity (b = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constants (*J*) in Hertz (Hz). High resolution mass spectrometric (HRMS) data was obtained using a Waters Synapt G2 TOF instrument with an ESI source. All data were reported in m/z values.



12 **13**

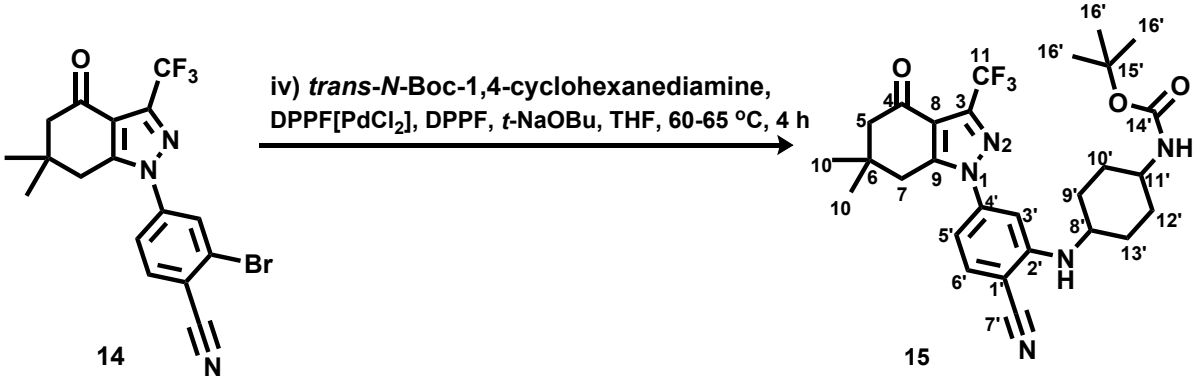
Trifluoroacetic anhydride (0.220 mL, 1.59 mmol, 1.0 eq.) was added to a suspension of **12** (500 mg, 1.59 mmol, 1.0 eq.) and TEA (2.88 mL, 20.7 mmol, 13.0 eq.) in THF (9 mL). The reaction mixture was heated to 55 ˚C to give an orange solution which was stirred for 2 hours. After cooling to room temperature, the mixture was quenched with sat. NH_4Cl (20 mL) and extracted with EtOAc (3 x 20 mL). The combined organic fractions were washed with sat. brine (20 mL), dried over anhydrous $MgSO_4$, concentrated in *vacuo* to yield an orange-brown oil which was purified with silica gel chromatography to yield **13** as an orange-yellow solid.

6,6-Dimethyl-3-(trifluoromethyl)-1,5,6,7-tetrahydro-*4H*-indazol-4-one (**13**): orange-yellow solid (166 mg, 45% yield over two step); IR (ν_{max} cm^{-1}) 3230, 3124, 2961, 1665, 1511, 1482; ^{1}H NMR (DMSO, 500 MHz): δ_H 13.86 (1H, s, NH-1), 2.80 (2H, s, H-6), 2.37 (2H, s, H-4), 1.04 (6H, s, H-7); ^{13}C NMR (DMSO, 125 MHz): δ_C 190.0 (CO, C-3), 152.0 (q_c, C-1), 138.9 (q_c, q, J = 38.7 Hz, C-10), 120.9 (CF_3, q, J = 269.5 Hz, C-11), 113.5 (q_c, C-2), 52.1 (CH_2, C-4), 35.3 (q_c, C-5), 33.7 (CH_2, C-6), 27.6 (CH_3, C-7) ppm.



A solution of **13** (349 mg, 1.50 mmol, 1.0 eq.) in anhydrous DMSO (7 mL) was treated with NaH (60.0 mg, 1.50 mmol, 1.0 eq.) and stirred for 15 minutes. Thereafter, 2-bromo-4-fluorobenzonitrile (480 mg, 2.40 mmol, 1.6 eq.) was added and the reaction mixture was stirred at 45 °C for 20 hours. Thereafter, the reaction mixture was cooled to room temperature, quenched with sat. NH_4Cl, diluted with water and washed with EtOAc (x 3). The combined organic layers were washed with sat. brine, dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to give a brown crude material which was purified using silica gel chromatography to give **14** as an orange-yellow solid (353 mg, 0.856 mmol, 57% yield).

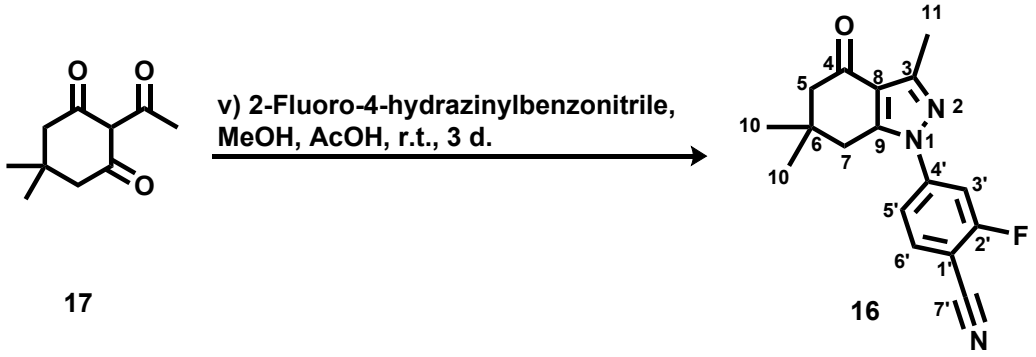
2'-Bromo-4'-(6,6-dimethyl-4-oxo-3-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-indazol-1-yl) benzonitrile (**14**): orange-yellow solid (57% yield); IR (ν_{max} cm^{-1}) 2963, 2951, 2925, 2870, 2854, 2233, 1682, 1593; ^1H NMR (DMSO, 400 MHz): δ_H 8.21 – 8.18 (2H, m, H-6', H-3'), 7.92 – 7.89 (1H, dd, *J* = 8.5, 2.1 Hz, H-5'), 3.05 (2H, s, H-7), 2.45 (2H, s, H-5), 1.05 (6H, s, 2 x CH_3); ^{13}C NMR (DMSO, 100 MHz): δ_C 190.1 (q_C, C-4) , 152.9 (q_C, C-9), 141.4 (q_C, C-4'), 139.4 (q_C, q, *J* = 39.1 Hz, C-3) , 136.0 (CH, C-6'), 128.3 (CH, C-3'), 125.5 (q_C, C-2'), 123.8 (CH, C-5'), 120.4 (q_C, q, *J* = 270.7 Hz, C-11) , 116.6 (q_C, C-8), 115.9 (CN, C-7'), 114.8 (q_C, C-1'), 51.6 (CH_2, C-5), 35.5 (q_C, C-6), 35.3 (CH_2, C-7), 27.5 (2 x CH_3, C-10).



DPPF[$PdCl_2$] (5 mol%) and DPPF (10 mol%) were consecutively added to a solution of **14** (333 mg, 0.809 mmol, 1.0 eq.) and Na^{t}OBu (155 mg, 1.62 mmol, 2.0 eq.) in anhydrous THF (4.5 mL) to give a reddish-brown suspension. Thereafter, *trans-N*-Boc-1,4-cyclohexanediamine (520 mg, 2.43 mmol, 3.0 eq.) was added and the reaction mixture was stirred between 60 – 65 °C. After 30 min TLC analysis indicated only the presence of a spot with an R_f value similar to the starting material, however, it was fluorescent purple spot under UV. The reaction was stopped, filtered through a flash silica plug, concentrated *in vacuo*. The resulting suspension was purified using silica gel chromatography to obtain **15** as an off-white solid.

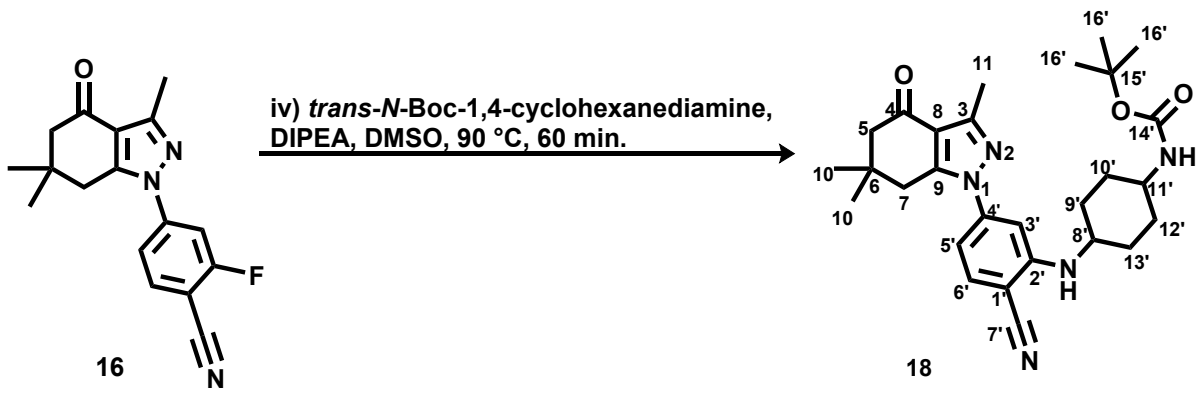
***tert*-Butyl(4-((2-cyano-5-(6,6-dimethyl-4-oxo-3-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)phenyl)amino)cyclohexyl)carbamate** (**15**): off-white solid (287 mg, 65% yield); ^1H NMR ($CDCl_3$, 400 MHz): δ_H 7.51 (1H, d, *J* = 8.3 Hz, H-6'), 6.81 (1H, d, *J* = 1.8 Hz, H-3'), 6.70-6.67 (1H, dd, *J* = 8.3, 1.9 Hz, H-5'), 4.66

(1H, d, *J* = 7.7 Hz, NH), 4.43 – 4.39 (2H, m, NH), 3.54 – 3.46 (1H, 3, H-11'), 3.40 – 3.32 (2H, m, H-8'), 2.83 (2H, s, H-7), 2.47 (2H, s, H-5), 2.17 – 2.10 (4H, m), 2.00 – 1.99 (2H, m), 1.43 (18H, 2 x s, H-16'), 1.38 – 1.15 (6H, m), 1.13 (6H, s, H-10); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 189.8 (CO, C-4), 155.4 (CO, C-14'), 150.7 (q_C, C-8), 150.3 (q_C, C-2'), 142.6 (q_C, C-4'), 141.1 (q_c, q, *J* = 39.3 Hz, C-3), 134.3 (CH, C-6'), 120.4 (CF_3, q, *J* = 270.1 Hz, C-11), 116.8 (q_C, C-9), 116.7 (CN, C-7'), 111.1 (CH, C-5'), 106.6 (CH, C-3'), 96.5 (q_C, C-1'), 79.3 (q_C, C-15'), 52.4 (CH_2, C-5), 51.4 (CH, C-8'), 49.1 (CH, C-11'), 37.5 (CH_2, C-7), 35.8 (q_C, C-6), 32.2 (2 x CH_2), 31.6 (2 x CH_2), 28.5 (3 x CH_3, C-16'), 28.4 (2 x CH_3, C-10) ppm.



An orange solution of **17** (503 mg, 2.76 mmol, 1.0 eq.) and 2-fluoro-4-hydrazinylbenzonitrile (417 mg, 2.76 mmol, 1.0 eq.) in MeOH (1.70 mL) was treated with acetic acid (40.0 µL, 0.690 mmol, 0.25 eq.) and stirred at room temperature for 5 days. Thereafter, the reaction mixture was concentrated *in vacuo* and purified using silica gel chromatography to get the desired product **16** as an off-white solid.

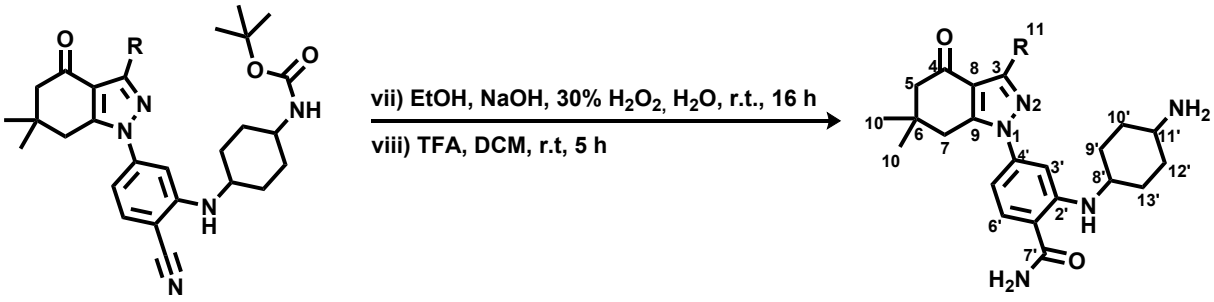
2'-Fluoro-4'-(3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)-benzonitrile (**16**): off-white solid (279 mg, 67% yield); IR (ν_{max} cm^{-1}) 2962, 2937, 2873, 2229, 1669, 1617; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.76 – 7.73 (1H, dd, *J* = 8.5, 7.0 Hz, H-6'), 7.52 – 7.45 (2H, m, H-3' and H-5'), 2.87 (2H, s, H-7), 2.53 (3H, s, H-11), 2.42 (2H, s, H-5), 1.13 (6H, s, H-10); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 193.2 (CO, C-4), 163.6 (CF, d, *J* = 260.7 Hz, C-2'), 151.5 (CH, C-3), 149.4 (q_C, C-9), 144.1 (q_C, d, *J* = 10.6 Hz, C-4'), 134.4 (CH, d, *J* = 1.6 Hz, C-6'), 118.6 (q_c, C-8), 118.5 (CH, C-5'), 113.3 (CN, C-7'), 111.1 (CH, d, *J* = 23.7 Hz, C-3'), 100.1 (q_C, d, *J* = 15.7 Hz, C-1'), 52.3 (CH_2, C-5), 38.0 (CH_2, C-7), 36.1 (q_C, C-6), 28.5 (2 x CH_3, C-10), 13.5 (CH_3, C-11) ppm.



16 (79.0 mg, 0.225 mmol, 1.0 eq.) and *trans*-*N*-Boc-1,4-cyclohexanediamine (193 mg, 0.900 mmol, 4.0 eq.) were dissolved in DMSO (1 mL) and treated with DIPEA (120 µL, 0.675 mmol, 3.0 eq.). The reaction mixture was

heated to 90 °C and stirred for 1 hour to give a black reaction mixture. The crude reaction mixture was purified using silica gel chromatography to obtain **18** as an off-white solid.

***tert*-Butyl(4-((2-cyano-5-(3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)phenyl)amino)cyclohexyl)carbamate (18)**: Off-white solid (82 mg, 74% yield); IR (ν_{max} cm^{-1}) 3399, 3296, 2933, 2861, 2206, 1707, 1661; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 7.47 (1H, d, *J* = 8.4 Hz, H-6'), 6.84 (1H, d, *J* = 1.8 Hz, H-3'), 6.69-6.69 – 6.66 (1H, dd, *J* = 8.3, 1.8 Hz, H-5'), 4.57 (1H, d, *J* = 7.7 Hz, NH), 4.40 (1H, bs, NH), 3.48 (1H, bs, H-8'), 3.43 – 3.34 (1H, m, H-11'), 2.80 (2H, s, H-7), 2.54 (3H, s, H-11), 2.40 (2H, s, H-5), 2.18 – 2.11 (4H, m, H-10', H-12'), 1.45 (9H, s, H-16'), 1.40-1.23 (4H, m, H-9', H-13'), 1.11 (6H, s, H-10); ^{13}C NMR ($CDCl_3$, 100 MHz): δ_C 193.4 (CO, C-4), 155.3 (CO, C-14'), 150.6 (q_C, C-3), 150.3 (q_C, C-4'), 149.2 (q_C, C-9), 143.7 (q_C, C-2'), 134.1 (CH, C-6'), 117.8 (q_C, C-8), 117.3 (CN, C-7'), 110.7 (CH, C-5'), 105.8 (CH, C-3'), 95.1 (q_C, C-1'), 79.7 (q_C, C-15'), 52.5 (CH_2, C-5), 51.3 (CH, C-11'), 49.2 (CH, C-8'), 37.9 (CH_2, C-7), 36.0 (q_C, C-6), 32.0 (2 x CH_2, C-9', C-13'), 31.7 (2 x CH_2, C-10', C-12'), 28.6 (5 x CH_3, C-10, C-16'), 13.5 (CH_3, C-11) ppm.



15. R = CF_3
18. R = Me

19. R = CF_3
20. R = Me

General procedure for the nitrile hydrolysis of 15 and 18: The nitrile (1.0 eq.) and K_2CO_3 (2.2 eq.) were suspended in DMSO. The reaction mixture was then treated with 30% H_2O_2 and stirred at room temperature. After 2 – 3 hours the crude reaction mixture was poured into ice-water and filtered; the precipitate was recrystallized from ethyl acetate to obtain the desired products.

Amide analogue of 15 was synthesised following the general procedure using **15** (506 mg, 0.927 mmol, 1.00 eq.), K_2CO_3 (282 mg, 2.04 mmol, 2.20 eq.) and 30% H_2O_2 (150 µL) in DMSO (3 mL) to obtain **the amide** as a white solid.

***tert*-Butyl(4-((2-carbamoyl-5-(6,6-dimethyl-4-oxo-3-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)phenyl)amino)cyclohexyl)carbamate**: White solid (381 mg, 73% yield); IR (ν_{max} cm^{-1}) 3336, 2933, 1677, 1586, 1511, 1451; ^{13}C NMR (DMSO, 125 MHz): δ_C 190.1 (CO, C-4), 170.7 (CO, C-7'), 154.8 (q_C, C-14'), 151.9 (q_c, C-9), 149.5 (q_c, C-4'), 140.6 (q_c, C-2'), 130.6 (CH, C-6'), 120.6 (CF_3, q, *J* = 274.8 Hz, C-11), 115.3 (q_c, C-8), 114.0 (q_c, C-1'), 108.9 (CH, C-5'), 106.9 (CH, C-3'), 51.7 (CH_2, C-5), 49.6 (CH, C-8'), 40.4 (CH, C-11'), 36.0 (CH_2, C-7), 35.1 (q_c, C-6), 31.3 (2 x CH_2, C-10', C-12'), 31.1 (2 x CH_2, C-9', C-13'), 28.2 (3 x CH_3, C-16'), 27.5 (2 x CH_3, C-10) ppm.

Amide analogue of 18 was synthesised following the general procedure using **18** (80.0 mg, 0.163 mmol, 1.00 eq.), K_2CO_3 (49.0 mg, 0.358 mmol, 2.20 eq.) and 30% H_2O_2 (25.0 µL) in DMSO (0.5 mL) to obtain the product as a white fluffy solid.

***tert*-Butyl(4-((2-carbamoyl-5-(3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)phenyl)amino)cyclohexyl)carbamate**: White fluffy solid (50 mg, 60% yield); IR (ν_{max} cm^{-1}) 3358, 3174, 2922,

1698, 1675, 1649, 1626; ^{1}H NMR ($CDCl_3$, 500 MHz): δ_H 8.05 (1H, d, *J* = 7.5 Hz, NH), 7.46 (1H, d, *J* = 8.4 Hz, H-6'), 6.76 (1H, d, *J* = 1.9 Hz, H-3'), 6.60-6.58 (1H, dd, *J* = 8.4, 2.0 Hz, H-5'), 5.77 (2H, bs, NH_2), 4.42 (1H, s, NH), 3.48 (1H, s, H-8'), 3.34-3.26 (1H, m, H-11'), 2.80 (2H, s, H-7), 2.54 (3H, s, H-11), 2.39 (2H, s, H-5), 2.15-2.03 (4H, m, H-10', H-12'), 1.44 (9H, s, H-16'), 1.41-1.21 (4H, m, H-9', H-13'), 1.10 (6H, s, H-10); ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 193.5 (CO, C-4), 171.1 (CO, C-7'), 155.4 (CO, C-14'), 151.2 (q_C, C-3), 150.3 (q_C, C-4'), 149.3 (q_C, C-9), 142.9 (q_C, C-2'), 129.9 (CH, C-6'), 117.5 (q_C, C-8), 113.8 (q_C, C-1'), 110.5 (CH, C-5'), 108.2 (CH, C-3'), 79.5 (q_C, C-15'), 52.5 (CH_2, C-5), 52.0 (CH, C-11'), 49.2 (CH, C-8'), 37.9 (CH_2, C-7), 36.0 (q_C, C-6), 31.9 (2 x CH_2, C-9', C-13'), 31.1 (2 x CH_2, C-10', C-12'), 28.6 (5 x CH_3, C-10, C-16'), 13.6 (CH_3, C-11) ppm.

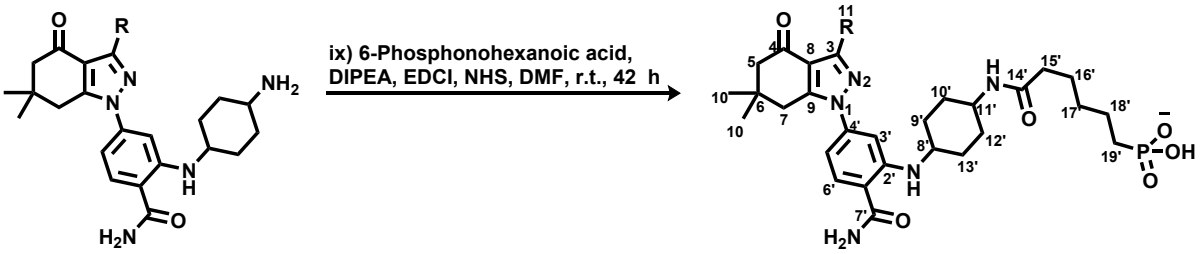
General procedure for the removal of the Boc protecting group: The Boc protected compounds were dissolved in a 4:1 DCM: TFA solution and stirred at room temperature. After 5 – 7 hours, the reaction mixture was concentrated in *vacuo* and the crude material was purified by silica gel chromatography (DCM: MeOH: NH_3, 20:1:0.1-5:1:0.1) to afford the desired product either as a TFA salt or free amine.

19 was synthesised following the general procedure using **15** (500 mg, 0.887 mmol, 1.0 eq.) in a 15.0 mL solution of DCM: TFA (4:1) to afford **19** as an off-white solid.

2-((4-Aminocyclohexyl)amino)-4-(6,6-dimethyl-4-oxo-3-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)benzamide (**19**, **isolated as a free amine**): Off-white solid (170 mg, 41% yield); IR (ν_{max} cm^{-1}) 3421, 2931, 2865, 1654, 1620, 1579, 1507; ^{1}H NMR (DMSO, 400 MHz): δ_H 8.35 (1H, d, *J* = 7.6 Hz, NH), 7.96 (1H, bs, NH_2), 7.78 (1H, d, *J* = 8.4 Hz, H-6'), 7.30 (1H, bs, NH_2), 6.87 (1H, d, *J* = 2.0 Hz, H-3'), 6.72-6.70 (1H, dd, *J* = 8.4, 2.1 Hz, H-5'), 3.31 (1H, bs, H-8'), 2.97 (2H, s, H-7), 2.66 (1H, bs, H-11'), 2.45 (2H, s, H-5), 2.05-1.97 (2H, m), 1.84-1.75 (2H, m), 1.21 (4H, quin., *J* = 11.5, 9.7 Hz,), 1.04 (6H, s, H-10); ^{13}C NMR (DMSO, 100 MHz): δ_C 190.1 (CO, C-4), 170.7 (CO, C-7'), 151.9 (q_c, C-9), 149.5 (q_c, C-4'), 140.6 (q_c, C-2'), 138.3 (q_c, q, *J* = 39.1 Hz, C-3), 130.6 (CH, C-6'), 120.6 (CF_3, q, *J* = 270.1 Hz, C-11), 115.3 (q_c, C-8), 113.9 (q_c, C-1'), 108.8 (CH, C-5'), 106.8 (CH, C-3'), 51.7 (CH_2, C-5), 49.8 (CH, C-8'), 49.5 (CH, C-11'), 36.0 (CH_2, C-7), 35.1 (q_c, C-6), 33.9 (2 x CH_2, C-10', C-12'), 31.0 (2 x CH_2, C-9', C-13'), 27.5 (2 x CH_3, C-10) ppm.

20 was synthesised following the general procedure using **18** (218 mg, 0.428 mmol, 1.0 eq.) in a 7.5 mL solution of DCM: TFA (4:1) to afford **20** as an off-white solid.

2-((4-Aminocyclohexyl)amino)-4-(3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)benzamide (**20**,**isolated as a free amine**): off-white solid (139 mg, 64% yield); IR (ν_{max} cm^{-1}) 3300, 2926, 2864, 1653, 1617; ^{1}H NMR (DMSO, 400 MHz): δ_H 8.34 (1H, d, *J* = 7.7 Hz, NH), 7.88 (1H, bs, NH_2), 7.73 (1H, d, *J* = 8.5 Hz, H-6'), 7.20 (1H, bs, NH_2), 6.77 (1H, d, *J* = 1.8 Hz, H-3'), 6.68 – 6.66 (1H, dd, *J* = 8.4, 1.8 Hz, H-5'), 3.29 (1H, bs, H-8'), 2.93 (2H, s, H-7), 2.69 – 2.60 (1H, m, H-11'), 2.40 (3H, s, H-11), 2.33 (2H, s, H-5), 2.05 – 1.97 (2H, m, H-9', H-13'), 1.84 – 1.74 (2H, m, H-10'), 1.26 – 1.15 (4H, m,H-12', H-13'),1.02 (6H, s, H-10); ^{13}C NMR (DMSO, 100 MHz): δ_C 192.8 (CO, C-4), 170.9 (CO, C-7'), 149.5 (q_c, C-9), 149.4 (q_c, C-4'), 148.2 (q_c, C-3), 141.6 (q_c, C-2'), 130.5 (CH, C-6'), 116.3 (q_c, C-8), 112.6 (q_c, C-1'), 108.0 (CH, C-5'), 105.5 (CH, C-3'), 51.7 (CH_2, C-5), 49.8 (CH, C-8'), 49.6 (CH, C-11'), 36.6 (CH_2, C-7), 35.2 (q_c, C-6), 34.1 (2 x CH_2, C-9', C-13'), 31.1 (2 x CH_2, C-10', C-12'), 27.7 (2 x CH_3, C-10), 13.1 (CH_3, C-11) ppm.



19. R = CF_3
20. R = Me

8. R= CF_3
9. R = Me

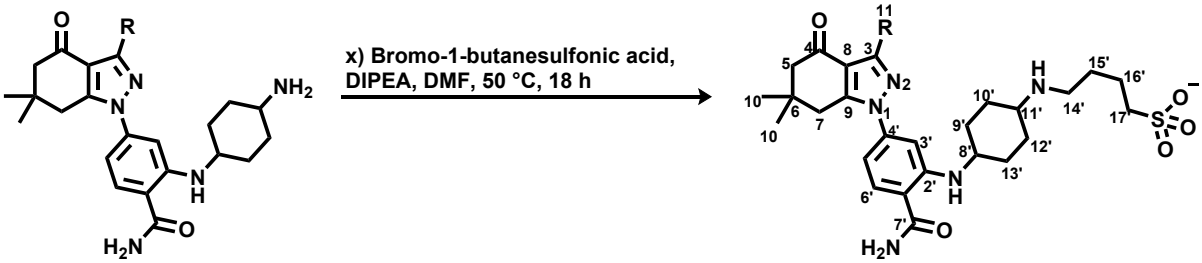
General procedure for the amide coupling reaction to yield 8 and 9: The amine was added to a round bottomed flask containing a solution of DIPEA in DMF, the resulting mixture was stirred at room temperature for 1 hour. Thereafter, a solution of carboxylic acid, EDCI and NHS in DMF was added to the reaction mixture and continued stirring at room temperature for 3 days. The solvent was removed in vacuo, and the crude material was directly loaded onto normal phase silica gel chromatography and purified using DCM:MeOH:NH_3 (5:1:0.1) as a mobile phase.

8: The general procedure was followed using **19** (55 mg, 1.0 eq., 0.12 mmol), DIPEA (0.28 mL, 13 eq., 1.5 mmol) in DMF (0.50 mL); and carboxylic acid (35 mg, 1.5 eq., 0.18 mmol), EDCI (34 mg, 1.5 eq., 0.18 mmol), NHS (16 mg, 1.2 eq., 0.14 mmol) in DMF (0.50 mL) to yield **8** as an off-white solid.

(6-((4-((2-Carbamoyl-5-(6,6-dimethyl-4-oxo-3-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)phenyl)amino)cyclohexyl)amino)-6-oxohexyl)phosphonic acid (**8**): Off-white solid (40 mg, 52% yield, 98% purity); IR (ν_{max} cm^{-1}) 3232, 3125, 2936, 2873, 1665, 1576, 1509, 1482; ^{1}H NMR (DMSO, 400 MHz): δ_H 8.36 (1H, d, *J* = 7.6 Hz, NH), 7.96 (1H, s, NH), 7.78 (1H, d, *J* = 8.5 Hz, H-6'), 7.72 (1H, d, *J* = 7.6 Hz, NH), 7.30 (1H, bs, NH), 6.89 (1H, d, *J* = 1.7 Hz, H-3'), 6.72-6.70 (1H, dd, *J* = 8.4, 1.7 Hz, H-5'), 3.60 – 3.51 (m, H-11'), 3.38 – 3.28 (m, H-8'), 2.97 (2H, s, H-5), 2.44 (2H, s, H-7), 2.29 – 2.16 (1H, m), 2.05-1.97 (4H, m), 1.82 – 1.79 (2H, m), 1.52 – 1.19 (17H, m), 1.04 (6H, s, H-10); ^{13}C NMR (DMSO, 100 MHz): δ_C 190.2 (CO, C-4), 171.4 (CO, C-14'), 170.7 (CO, C-7'), 151.9 (q_C, C-9), 149.5 (q_C, C-4'), 140.6 (q_C, C-2'), 138.3 (q_C, q, *J* = 39.0 Hz, C-3), 130.7 (CH, C-6'), 120.6 (q_C, q, *J* = 270.5 Hz, C-11), 115.3 (q_C, C-8), 113.9 (q_C, C-1'), 108.9 (CH, C-5'), 106.8 (CH, C-3'), 51.7 (CH_2, C-5), 49.6 (CH, C-8'), 47.0 (CH, C-11'), 36.0 (CH_2, C-7), 35.4 (CH_2, C-15'), 35.1 (q_C, C-6), 31.1 (2 x CH_2), 30.7 (2 x CH_2), 29.5 (? X CH_2), 28.1 (CH_2), 27.5 (2 x CH_3, C-10), 25.2 (CH_2), 23.3 (2 x CH_2) ppm. ESI-MS *m/z* 642.2668 (calculated for $[M+H]^+$ $C_{29}H_{40}N_5O_6PF_3$ 642.2668).

9: The general procedure was followed using **20** (68 mg, 1.0 eq., 0.17 mmol), DIPEA (0.38 mL, 13 eq., 2.2 mmol) in DMF (0.60 mL); and carboxylic acid (49 mg, 1.5 eq., 0.25 mmol), EDCI (48 mg, 1.5 eq., 0.25 mmol), NHS (23 mg, 1.2 eq., 0.20 mmol) in DMF (0.60 mL) to yield **9** as an off-white solid.

(6-((4-((2-Carbamoyl-5-(3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)phenyl)amino)cyclohexyl)amino)-6-oxohexyl)phosphonic acid (**9**): Off-white solid (38 mg, 39% yield 97% purity); ^{1}H NMR (DMSO, 500 MHz): δ_H 8.34 (1H, d, *J* = 7.9 Hz, NH), 7.89 (1H, bs, NH), 7.75 – 7.71 (2H, m, H-6'), 7.21 (1H, bs), 6.79 (1H, d, *J* = 1.9 Hz, H-3'), 6.68 – 6.66 (1H, dd, *J* = 8.5, 1.9 Hz, H-5'), 6.63 (1H, bs), 3.60 – 3.50 (2 x CH, m, H-11'), *3.37 – 3.28 (1H, m, H-8'), 2.93 (2H, m, H-7), 2.40 (3H, s, H-11), 2.33 (2H, s, H-5), 2.06 – 1.99 (6H, m), 1.85 – 1.78 (2H, m), 1.53 – 1.18 (24H, m), 1.01 (6H, s, H-10); ^{13}C NMR (DMSO, 125 MHz): δ_C 192.8 (CO, C-4), 171.4 (CO, C-14'), 170.9 (CO, C-7'), 149.49 (q_C,), 149.47 (q_C), 148.2 (q_C, C-3), 141.6 (q_C, C-2'), 130.5 (CH, C-6'), 116.4 (q_C, C-8), 112.7 (q_C, C-1'), 108.1 (CH, C-5'), 105.6 (CH, C-3'), 51.7 (CH_2, C-5), 49.6 (CH, C-8'), 47.1 (CH, C-11'), 36.7 (CH_2, C-7), 35.4 (q_C, C-6), 35.2 (2 x CH_2), 34.2 (2 x CH_2), 31.1 (2 x CH_2), 30.7 (2 x CH_2), 27.7 (2 x CH_3, C-10), 25.3 (CH_2), 23.4 (CH_2), 13.1 (CH_3, C-11) ppm. ESI-MS *m/z* 588.2947 (calculated for $[M+H]^+$ $C_{29}H_{43}N_5O_6P$ 588.2951).*resolved by HSQC



19. R = CF_3
20. R = Me

10. R= Me
11. R = CF_3

General procedure for bromine displacement to yield 10 and 11: The reactants were suspended in DMF and stirred 50 °C. After 18 hours the reaction mixture was concentrated *in vacuo* and purified using silica gel chromatography using DCM:MeOH:NH_3 (5:1:0.1) solvent mixture as the mobile phase.

10 was synthesised following the general procedure using **20** (110 mg, 0.269 mmol, 1.00 eq.), 4-bromobutane-1-sulfonic acid (64.0 mg, 0.269 mmol, 1.00 eq.) and DIPEA (140 µL, 0.806 mmol, 3.00 eq.) in DMF (1.00 mL) to afford the desired product as a white fluffy solid.

4-((4-((2-Carbamoyl-5-(3,6,6-trimethyl-4-oxo-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)phenyl)amino)cyclohexyl)amino)butane-1-sulfonic acid (**10**): White fluffy solid (94 mg, 62% yield, 97% purity); IR (ν_{max} cm^{-1}) 3358, 2938, 1651, 1621, 1581, 1551; ^{1}H NMR (DMSO, 500 MHz): δ_H 8.36 (1H, d, *J* = 7.7 Hz, NH), 7.93 (1H, bs, NH), 7.75 (1H, d, *J* = 8.6 Hz, H-6'), 7.71 – 7.44 (6H, m), 7.23 (1H, bs, NH), 6.83 (1H, d, *J* = 1.91 Hz, H-3'), 6.69 – 6.67 (1H, dd, *J* = 8.4, 1.9 Hz, H-5'), *3.36 (bs, H-8'), 3.06 – 3.02 (1H, m, H-11'), 2.92 – 2.89 (4H, m, H-7), *2.50 – 2.46 (2H, m), 2.40 (3H, s, H-11), 2.33 (2H, s, H-5), 2.11 (4H, d, *J* = 10.6 Hz), 1.76 – 1.62 (4H, m), 1.59 – 1.45 (2H, m), 1.28 – 1.21 (2H, m), 1.02 (6H, s, H-10); ^{13}C NMR (DMSO, 125 MHz): δ_C 192.8 (CO, C-4), 170.9 (CO, C-7'), 149.5 (q_C), 149.4 (q_C), 148.2 (q_C, C-3), 141.6 (q_C, C-2'), 130.5 (CH, C-6'), 116.3 (q_C, C-8), 112.8 (q_C, C-1'), 108.4 (CH, C-5'), 105.7 (CH, C-3'), 55.2 (CH, C-11'), 51.8 (CH_2, C-5), 50.6 (CH_2), 49.2 (CH, C-8'), 44.0 (CH_2), 36.6 (CH_2, C-7), 35.3 (q_C, C-6), 30.3 (2 x CH_2), 27.8 (2 x CH_3, C-10), 27.1 (2 x CH_2), 25.0 (CH_2), 22.4 (CH_2), 13.1 (CH_3, C-11) ppm. ESI-MS *m/z* 546.2756 (calculated for $[M+H]^+$ $C_{27}H_{40}N_5O_5S$ 546.2750). *resolved by HSQC

11 was synthesised following the general procedure using **19** (100 mg, 0.216 mmol, 1.00 eq.), 4-bromo-1-butanesulfonic acid (52.0 mg, 0.216 mmol, 1.00 eq.), DIPEA (120 µL, 0.647 mmol, 3.00 eq.) in DMF (1.00 mL) to afford the desired product as a white powder.

4-((4-((2-carbamoyl-5-(6,6-dimethyl-4-oxo-3-(trifluoromethyl)-4,5,6,7-tetrahydro-1*H*-indazol-1-yl)phenyl)amino)cyclohexyl)amino)butane-1-sulfonic acid (**11**): White powder (71 mg, 53% yield, 95% purity); IR (ν_{max} cm^{-1}) 3410, 3349, 3215, 2950, 2857, 1660, 1627, 1579, 1509; ^{1}H NMR (DMSO, 400 MHz): δ_H 8.37 (1H, d, *J* = 7.7 Hz, NH), 7.99 (1H, bs, NH), 7.79 (1H, d, *J* = 8.5 Hz, H-6'), 7.76 – 7.41 (3H, m), 7.33 (1H, bs, NH), 6.93 (1H, d, *J* = 1.9 Hz, H-3'), 6.74 – 6.71 (1H, dd, *J* = 8.4, 1.9 Hz, H-5'), *3.37 – 3.29 (H-8'), 3.10 – 2.98 (1H, m, H-11'), 2.97 (2H, s, H-7), 2.93 (2H, t, *J* = 7.0 Hz, H-17'), *2.50 – 2.38 (4H, m, H-5, H-14'), 2.18 – 2.03 (4H, m, H-9', H-10'), 1.76 – 1.62 (4H, m, H-15', H-16'), 1.56 – 1.41 (2H, m, H-12'), 1.32 – 1.18 (2H, m, H-13'), 1.04 (6H, s, H-10); ^{13}C NMR (DMSO, 100 MHz): δ_C 190.2 (CO, C-4), 170.7 (CO, C-7'), 152.0 (q_C, C-9), 149.4 (q_C, C-4'), 140.6 (q_C, C-2'), 138.4 (q_C, q, *J* = 39.0 Hz, C-3), 130.7 (CH, C-6'), 120.6 (q_C, q, *J* = 270.5 Hz, C-11), 115.3 (q_C, C-8), 114.1 (q_C, C-1'), 109.2 (CH, C-5'), 107.0 (CH, C-3'), 55.3 (CH, C-11'), 51.7 (CH_2, C-5), 50.5 (CH_2, C-14'), 49.2 (CH, C-8'), 44.1 (CH_2, C-17'), 36.0 (CH_2, C-7), 35.1 (q_C, C-6), 30.2 (2 x CH_2), 27.5 (2 x CH_3, C-10), 27.2 (2 x CH_2), 25.0 (CH_2), 22.3 (CH_2) ppm. ESI-MS *m/z* 600.2469 (calculated for $[M+H]^+$ $C_{27}H_{37}N_5O_5SF_3$ 600.2467). *resolved by HSQC

Biological assay

Cytotoxicity assay

Cells were seeded at a dilution of $1x10^5$cells/ml in triplicate in 96well plate in 50 µl in DMEM supplemented with 10% [v/v] Foetal Bovine Serum (Capricorn) and 1% [v/v] Penicillin-Streptomycin-Amptotericin (Gibco). The next day, cells were treated with an range of concentrations for 72 hrs. Following this, resazurin solution (0.54 mM) was added to the cells, incubated at 37°C for 4 h and fluorescence (Ex 560 nm, Em 590 nm) was read. Graph Pad Prism software was used to determine the half-maximal inhibitory concentration (IC_{50}) by non-linear regression.

Recombinant protein production and purification

Purification of recombinant proteins (human Hsp90α, wild type FUD and mutant FUD) was conducted as previously described.[1]

ATPase activity assay

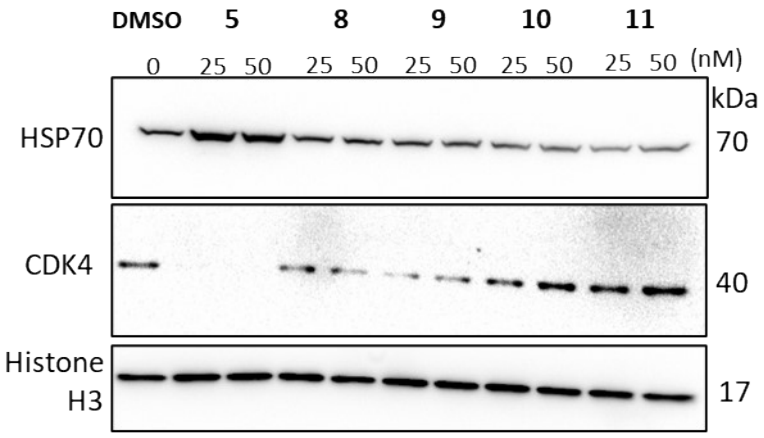
ATPase activity assay was performed using a Kinase-Glo® Luminescent kinase kit (Promega, V6072) according to the manufacturer's instructions with modifications. In this assay, the luciferase activity is proportional to the remaining ATP after hydrolysis in the presence of Hsp90. Therefore, inhibition of Hsp90 is indicated by an increase in luciferase activity relative to the DMSO control. Hsp90α (18 µM) was incubated with the compounds (20 µM) or controls at 37 °C with rotation for at least 6 h in ATPase buffer (40 mM HEPES, 150 mM KCl, 5 mM MgCl2,1mM ATP, pH 7.5.). Next, 100 µM of ATP was added and the reactions incubated for another 6 h. The ATPase reaction was stopped by transferring the samples to ice. The reactions were mixed with a 50 µL volume of reaction mixture in triplicate, transferred to a white opaque 96-well plate and mixed with 50 µl of Kinase-Glo working solution. Luminescence endpoint readings were recorded after 10 min incubation at RT using the Promega Glomax plate reader at 25 ºC with an integration time of 2 s. Data were normalized to reactions with DMSO (taken as 1). Controls lacking Hsp90 were conducted to confirm that the compounds did not inhibit luciferase activity.

Western blot analysis

Cells were lysed in RIPA buffer (Sigma Aldrich) supplemented with Protease Inhibitory Cocktail (Roche). Equal amounts of protein were loaded and analyzed by using the modified standard Laemelli SDS-PAGE method.[2] The gel was transferred to nitrocellulose membrane and blocked in 1% (w/v) Blotto (Santa Cruz) in TBS for 1 h at room temperature. Primary antibodies (Table S1) for Cdk4 and Histone were incubated overnight whereas HSP/HSC70 was incubated for 1 h at room temperature. Species specific HRP conjugated secondary antibodies (Table S1) were incubated for 1 h at room temperature. The visualization of protein was done by addition of ECL substrate (Bio-Rad) and detection using the Bio-Rad Chemi-doc. The band intensity was quantified using Image J software, normalized to the control and statistical analysis was done using the software Graph Pad.

Table S1: Antibodies used for western blot analysis

Type	Name	Supplier	Catalogue number	Dilution
Primary	Cdk4	Abcam	ab137675	1:1000
	HSP70/HSC70	Santa Cruz Biotechnology	sc-24	1:10,000
	Histone H3	Abcam	ab1791	1:2500
Secondary	Donkey Anti-Rabbit	Abcam	ab97064	1:5000
	Goat Anti-Mouse	Abcam	ab97023	1:5000



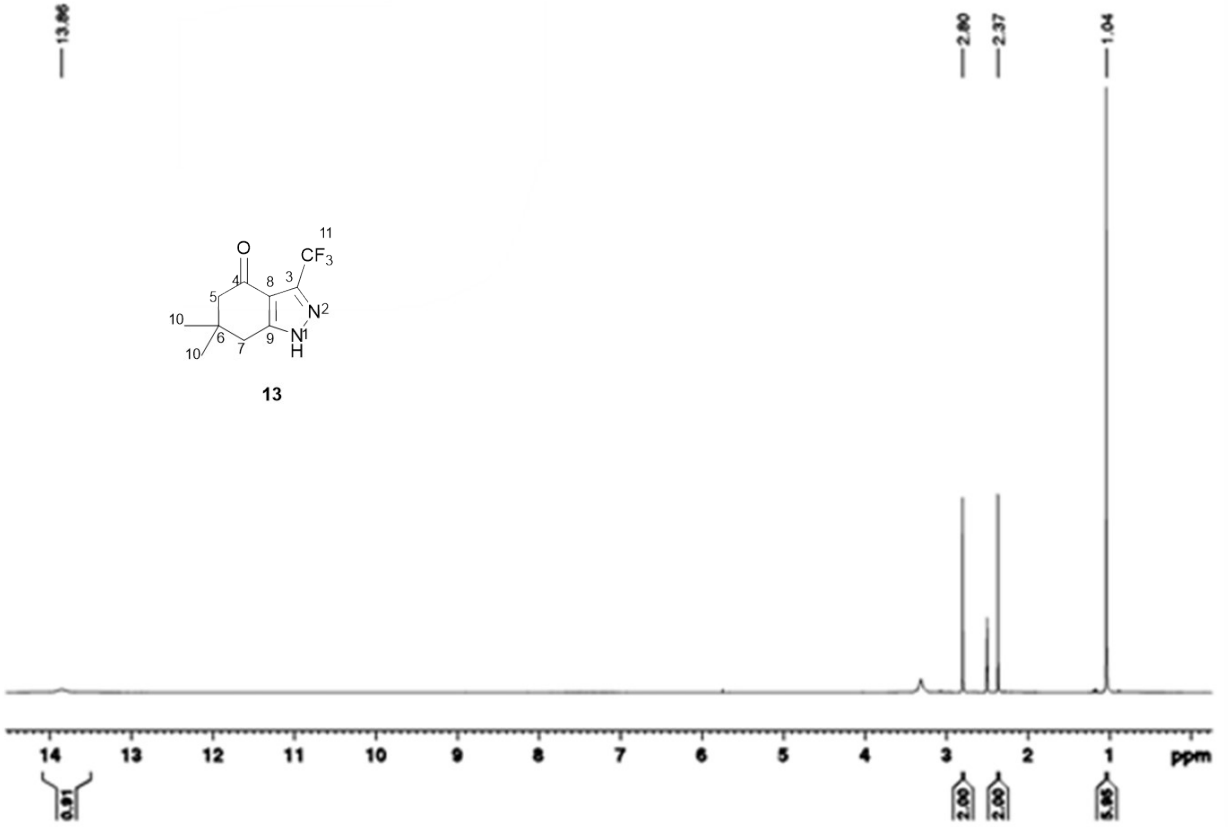
Decellularization assay

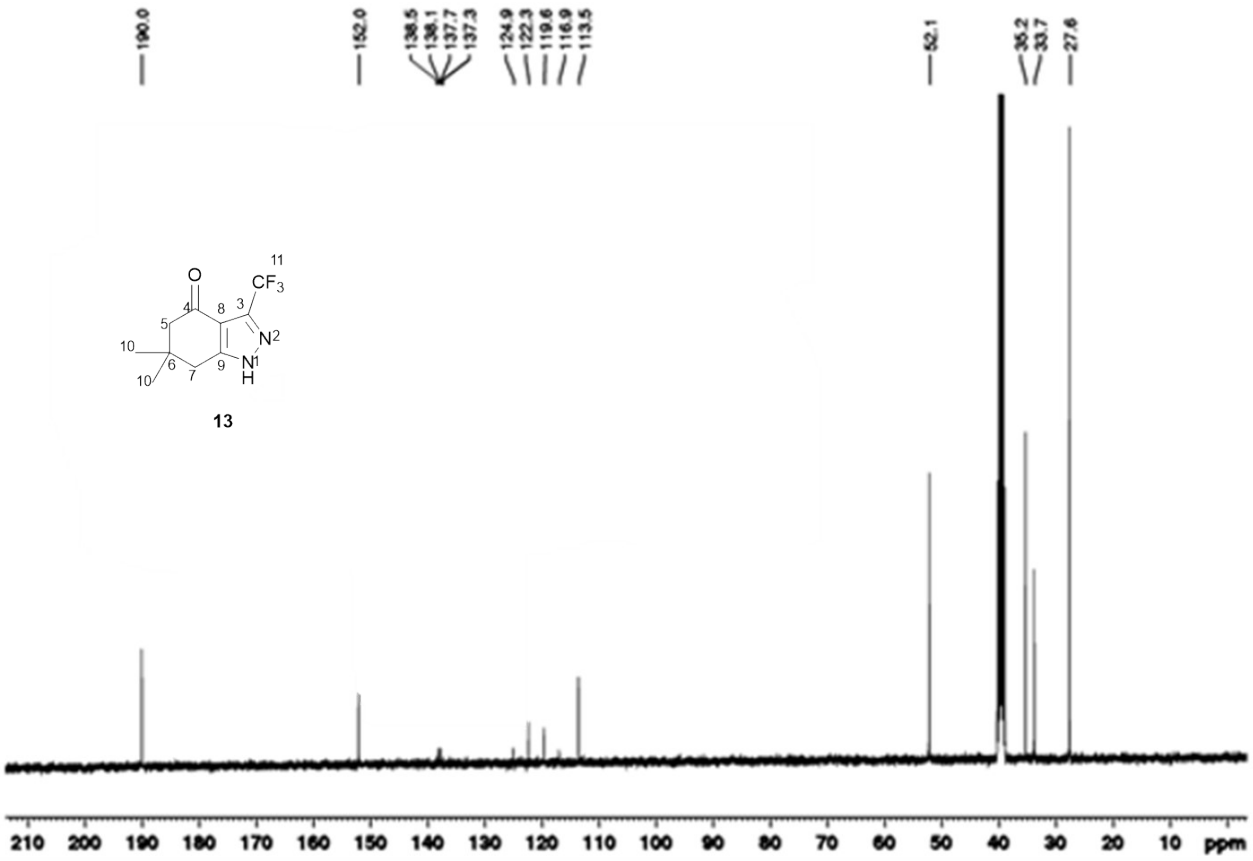
Preparation of the decellularized extracellular matrix (ECM) from Hs578T breast carcinoma cells was adapted from previously published method.[1] Briefly, coverslips were incubated with 0.2% [w/v] sterile gelatin for 1 h at 37 °C before crosslinking with 1% [v/v] sterile glutaraldehyde in PBS for 30 min at room temperature. Coverslips were washed with PBS, quenched with 1 M sterile ethanolamine, and washed again with PBS. Hs578T cells were seeded onto the prepared coverslips in 12-well plates at high cell density. Upon confluency, the medium was replaced with 50 µg/ml ascorbic acid-containing medium, which was changed every second day thereafter. After 6 days of culture, cells were treated for 24 h with compounds (5 nM) or controls. The following day, the cells were incubated with 50 mM EDTA for 10 min at 37 °C before cell denuding with extraction buffer (20 mM NH_4OH and 0.5% [v/v] Triton-X in PBS). Without removing the extraction buffer, PBS was added to each of the wells and placed at 4°C overnight to improve the stability of the newly extracted matrices. To remove DNA, wells were incubated with 10 µg/mL of DNase I (Roche, Basel, Switzerland) for 30 min at 37 °C. Fresh ECM were fixed with 3.7% [w/v] paraformaldehyde solution. Fixed cell matrices were blocked with 1% [w/v] BSA/PBS followed by overnight incubation with rabbit anti- human fibronectin (FN) primary antibody in 1% [w/v] BSA/TBS at 4 °C. The following day, samples were washed twice with 1% [w/v] BSA/TBS-T (TBS containing 0.1% [w/v] Tween-20) followed by 1 h incubation with species-specific fluorescently tagged secondary antibodies (donkey anti-mouse Alexa Fluor 555). Nuclei were stained with Hoechst 33342 dye (1 µg/ml in distilled water). Images were captured using the Olympus Fluorescence BX50 microscope and analysed using Image J.

1 A. Chakraborty, R. Tonui and A. L. Edkins, *Cell Stress Chaperones*, 2023, **28**, 697–707.

2 M. C. Hunter, K. L. O'Hagan, A. Kenyon, K. C. H. Dhanani, E. Prinsloo and A. L. Edkins, *PLoS One*, 2014, **9**, e86842.

^{1}H and ^{13}C NMR spectra

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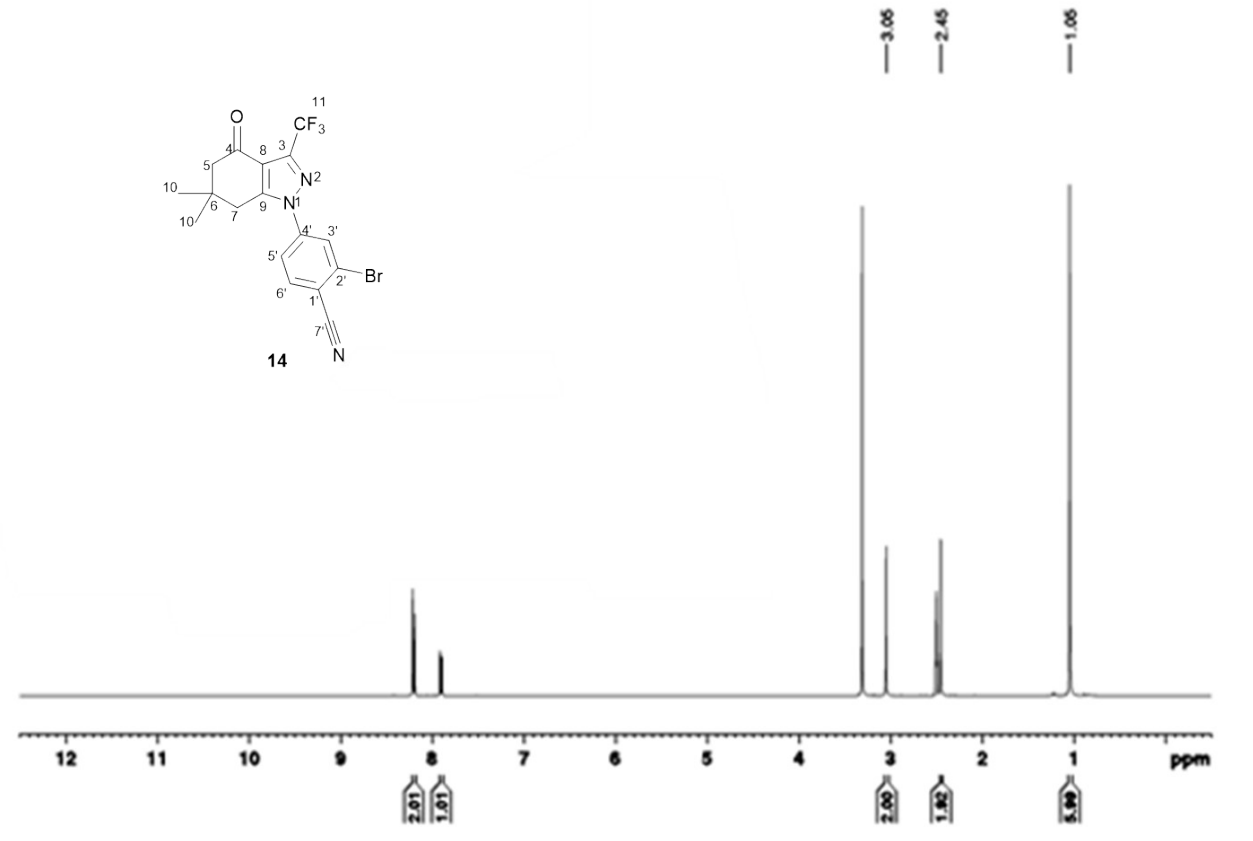
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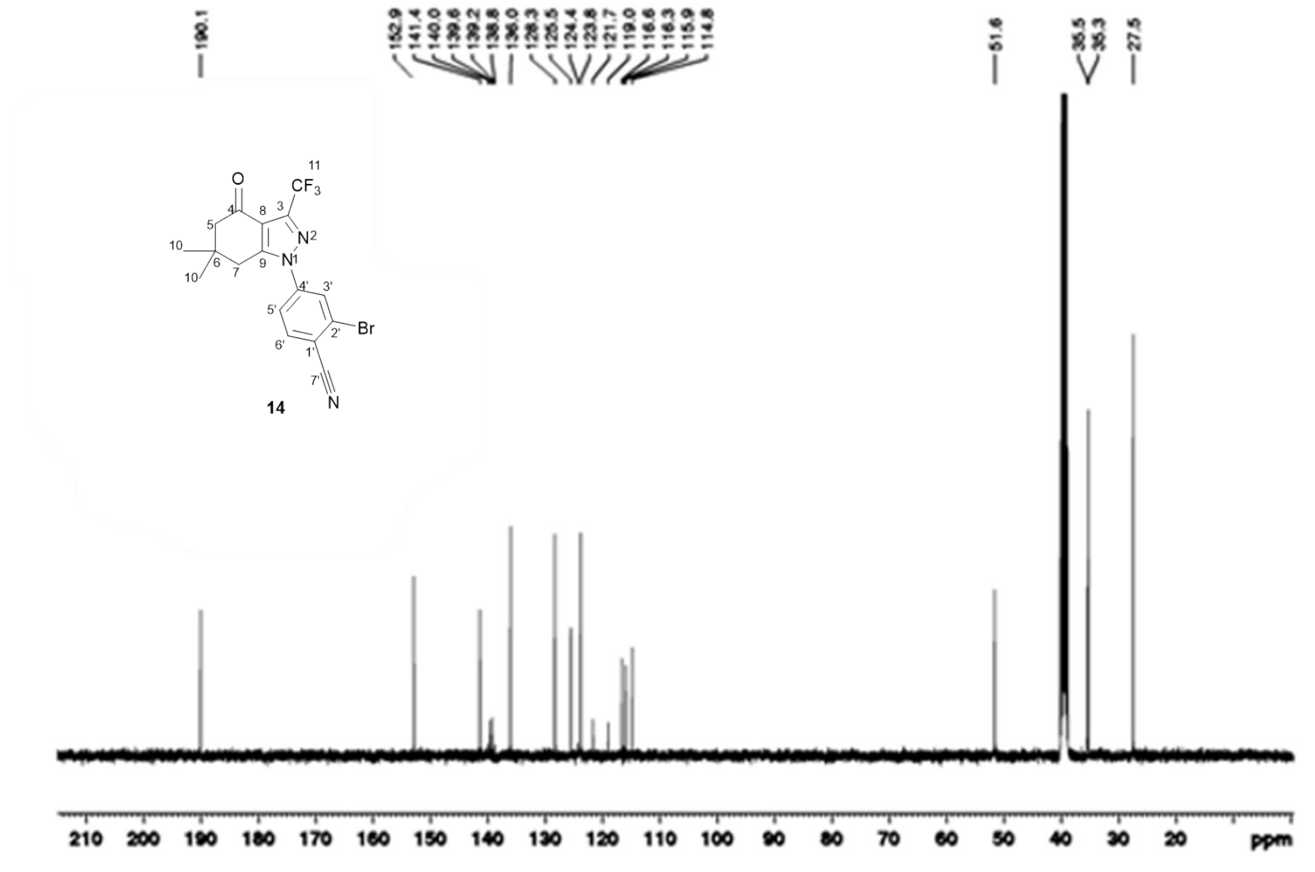
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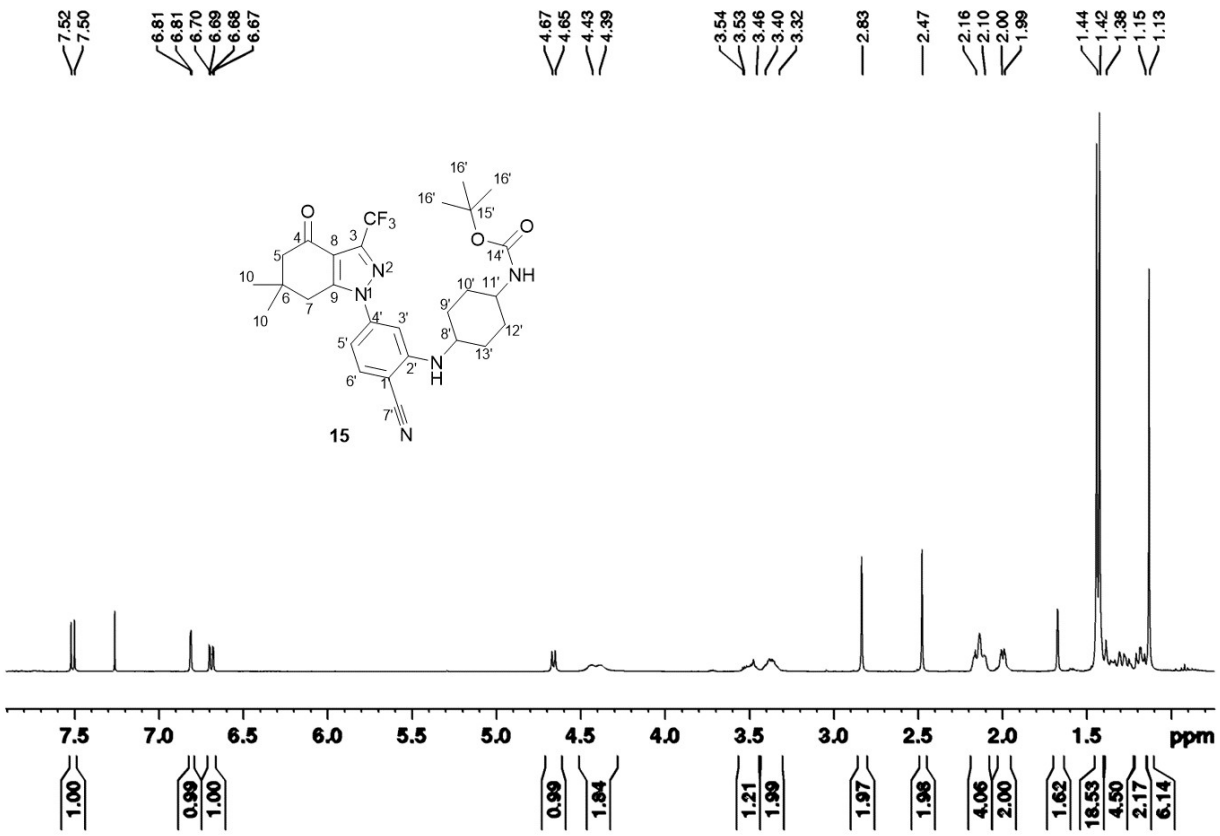
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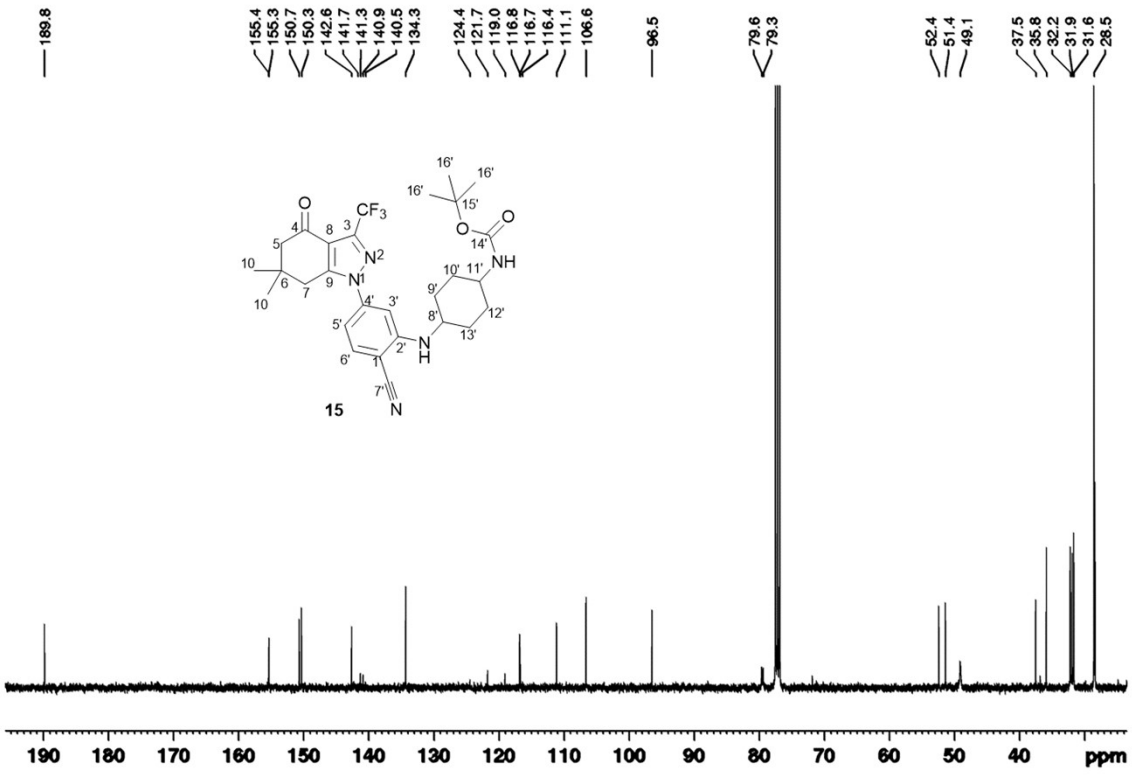
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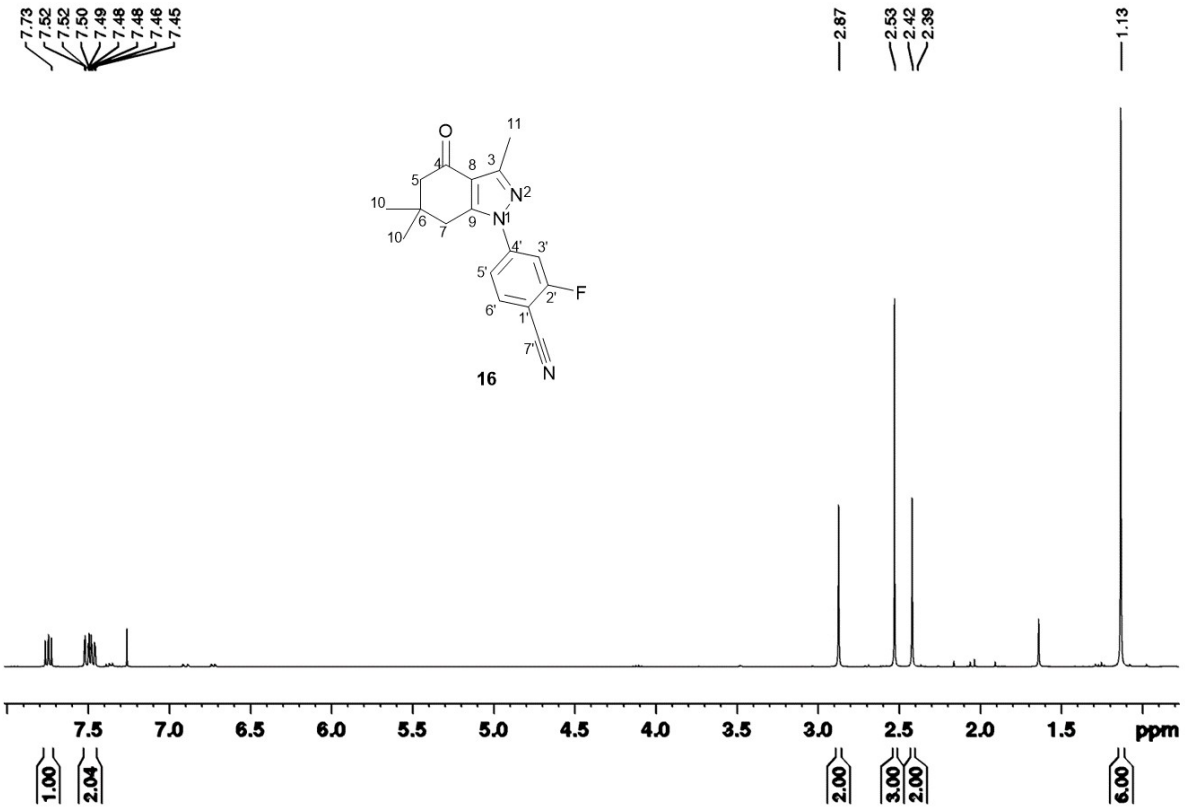
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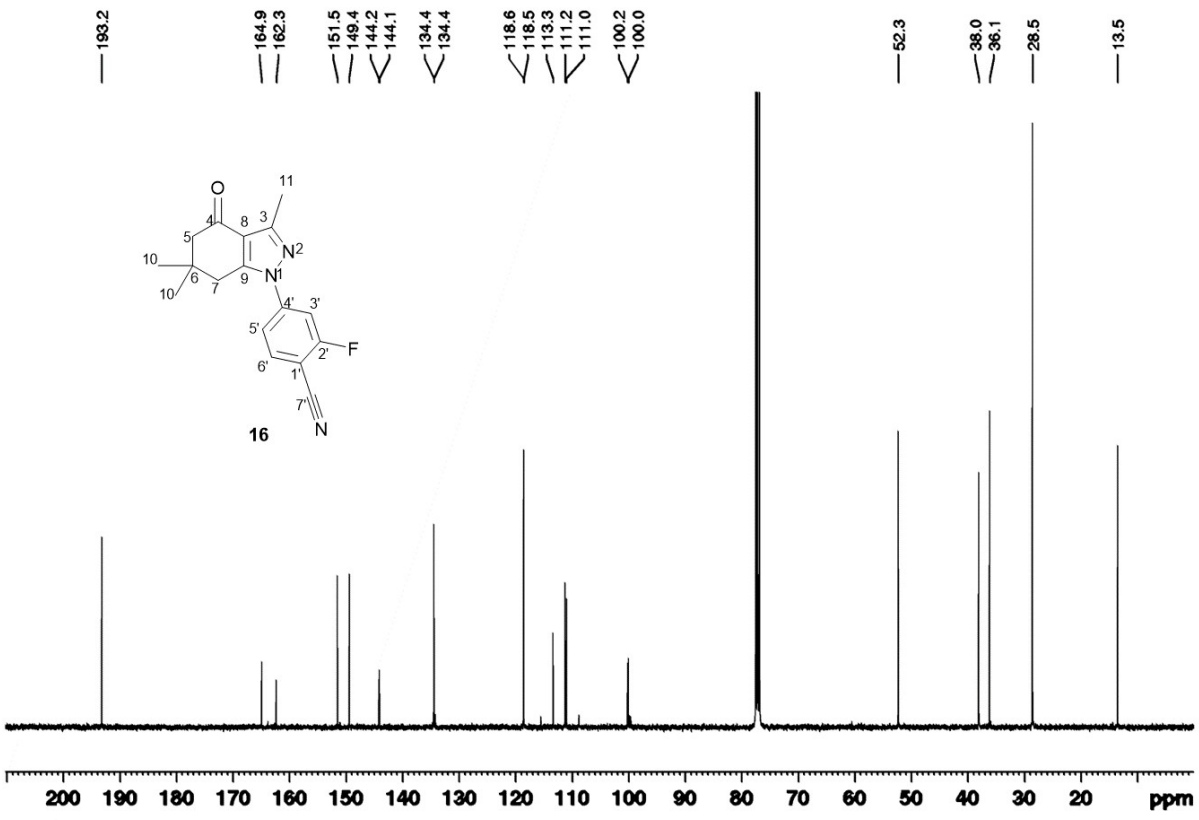
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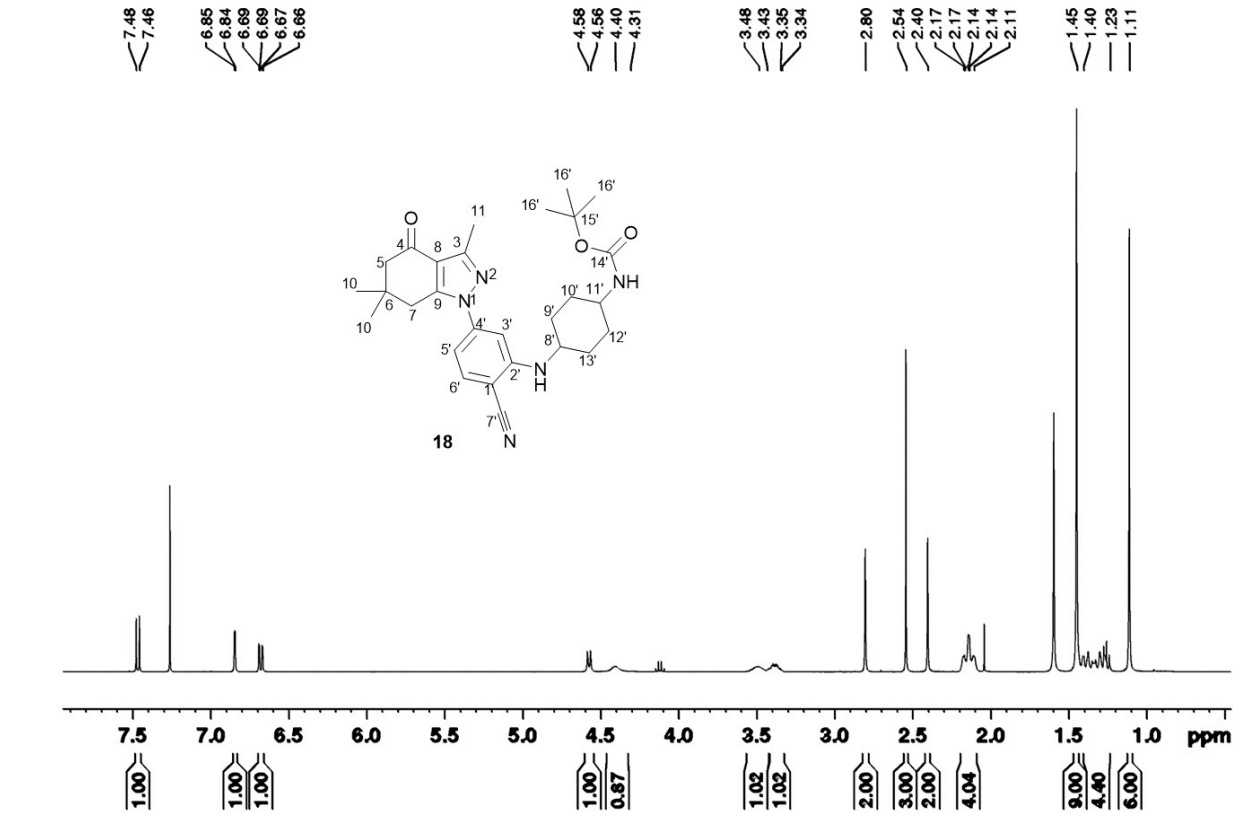
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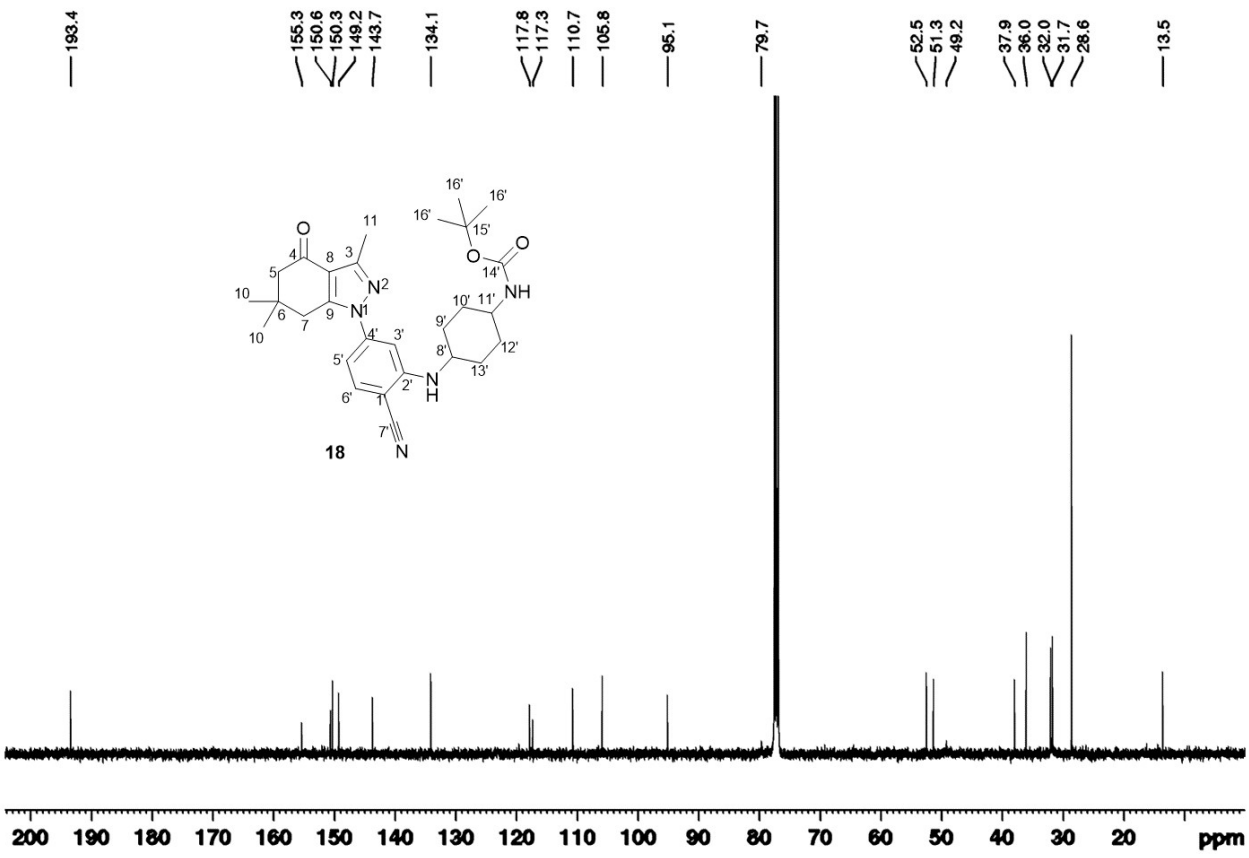
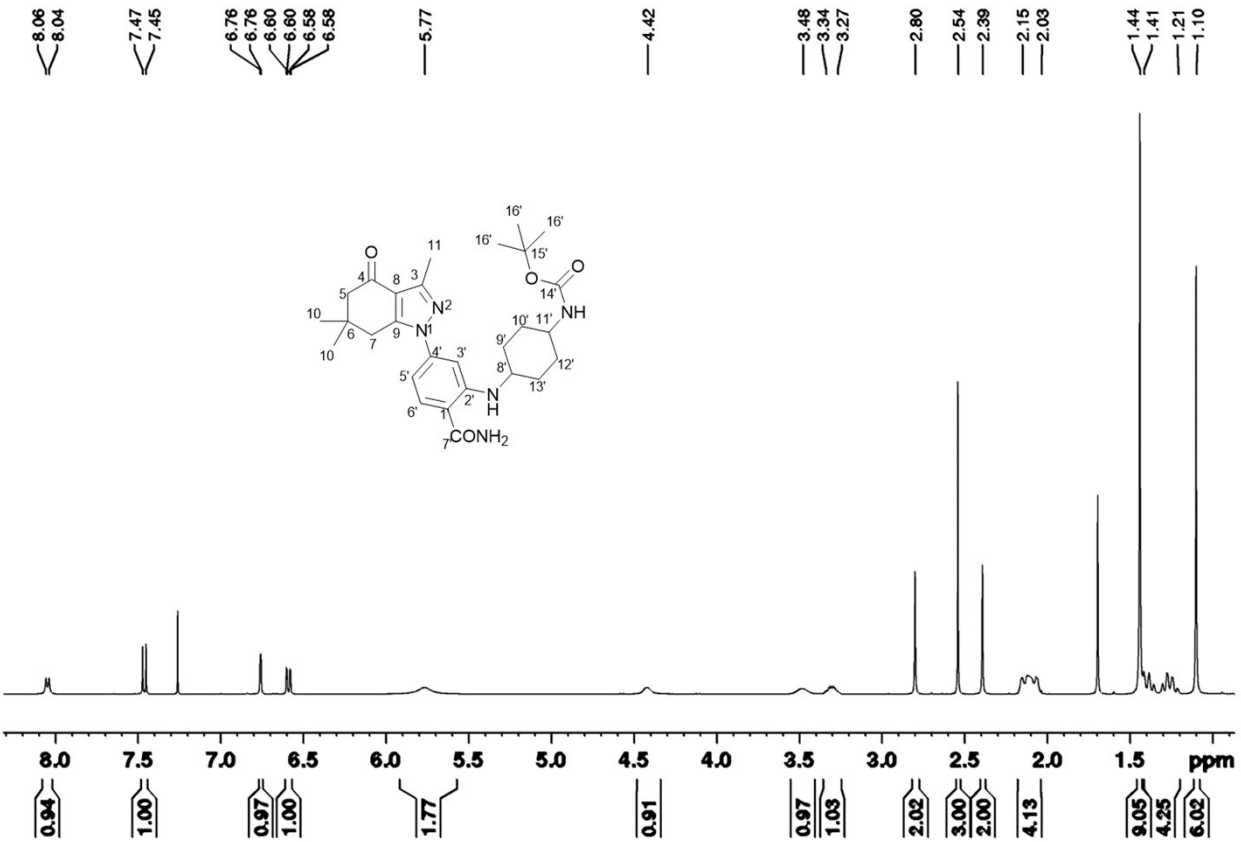
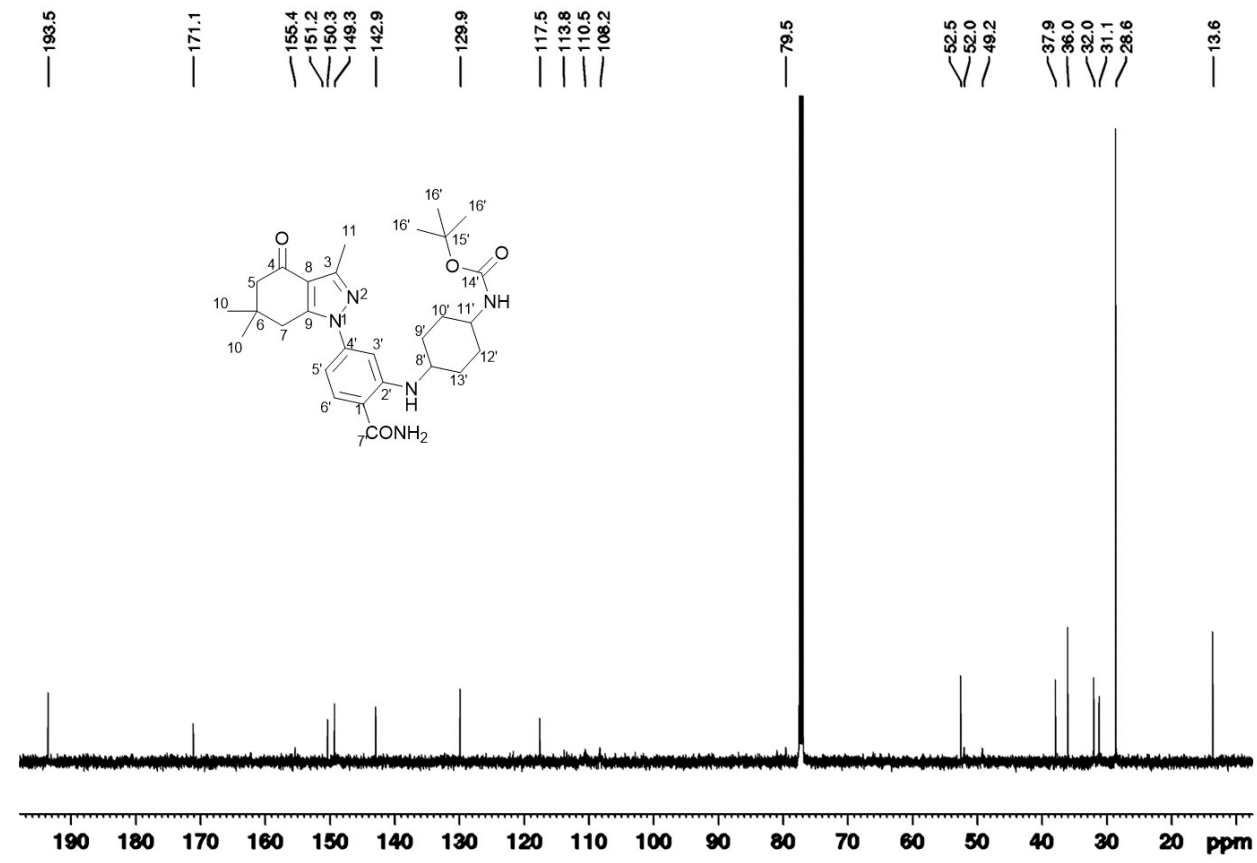
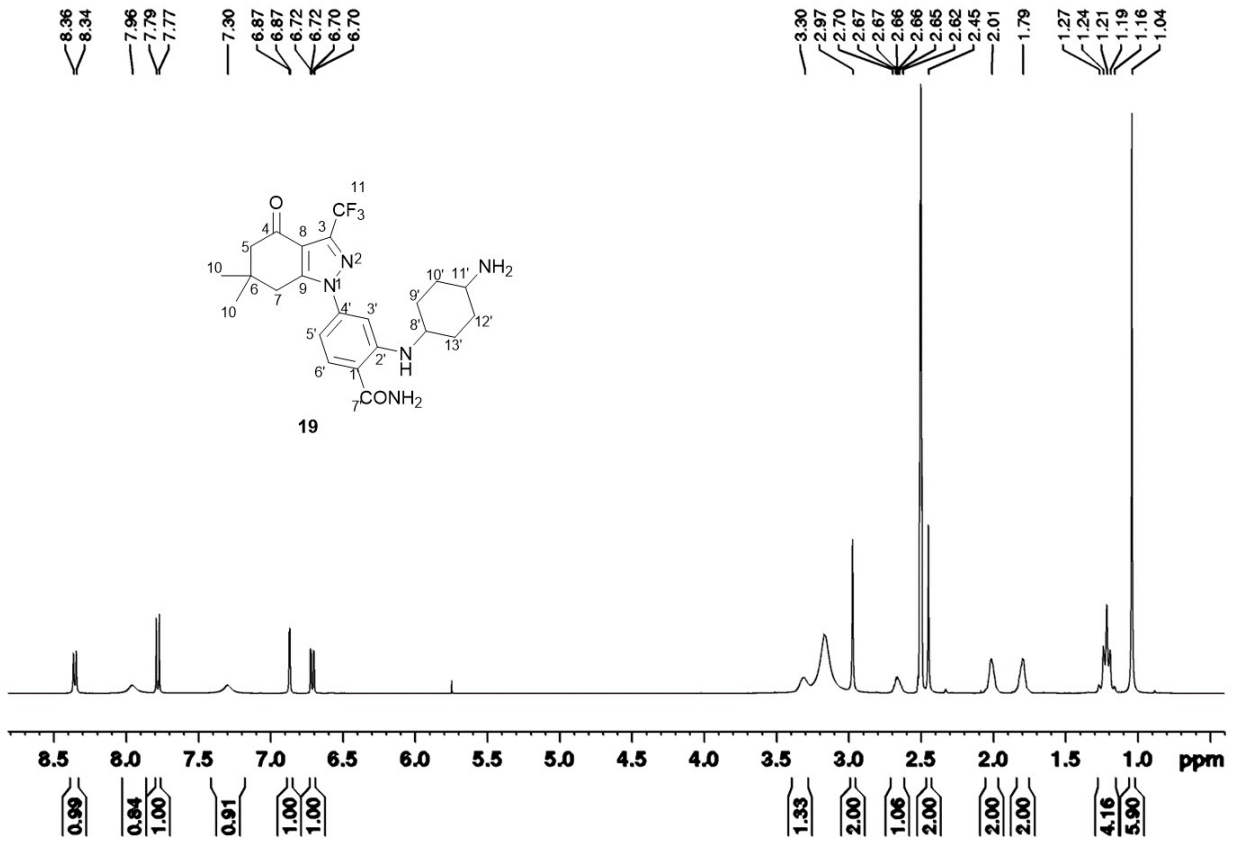
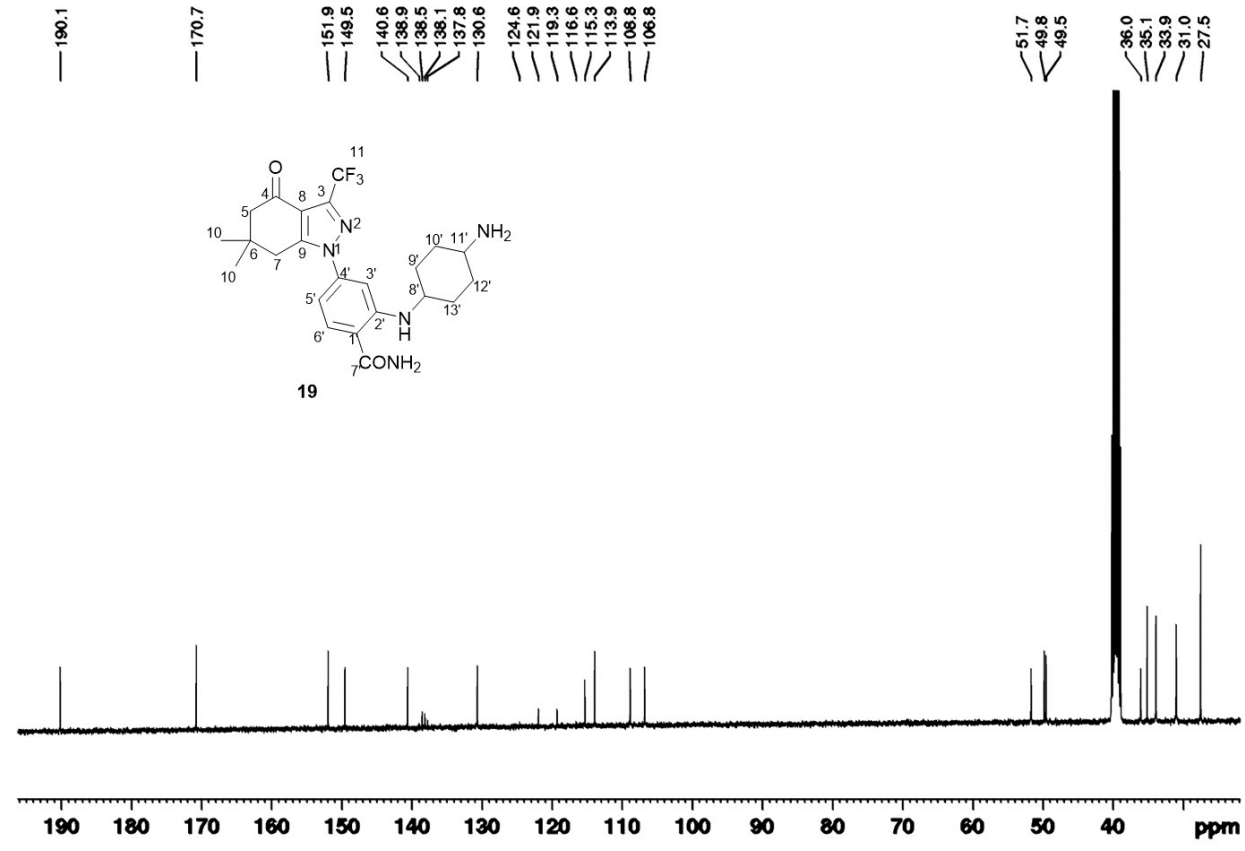
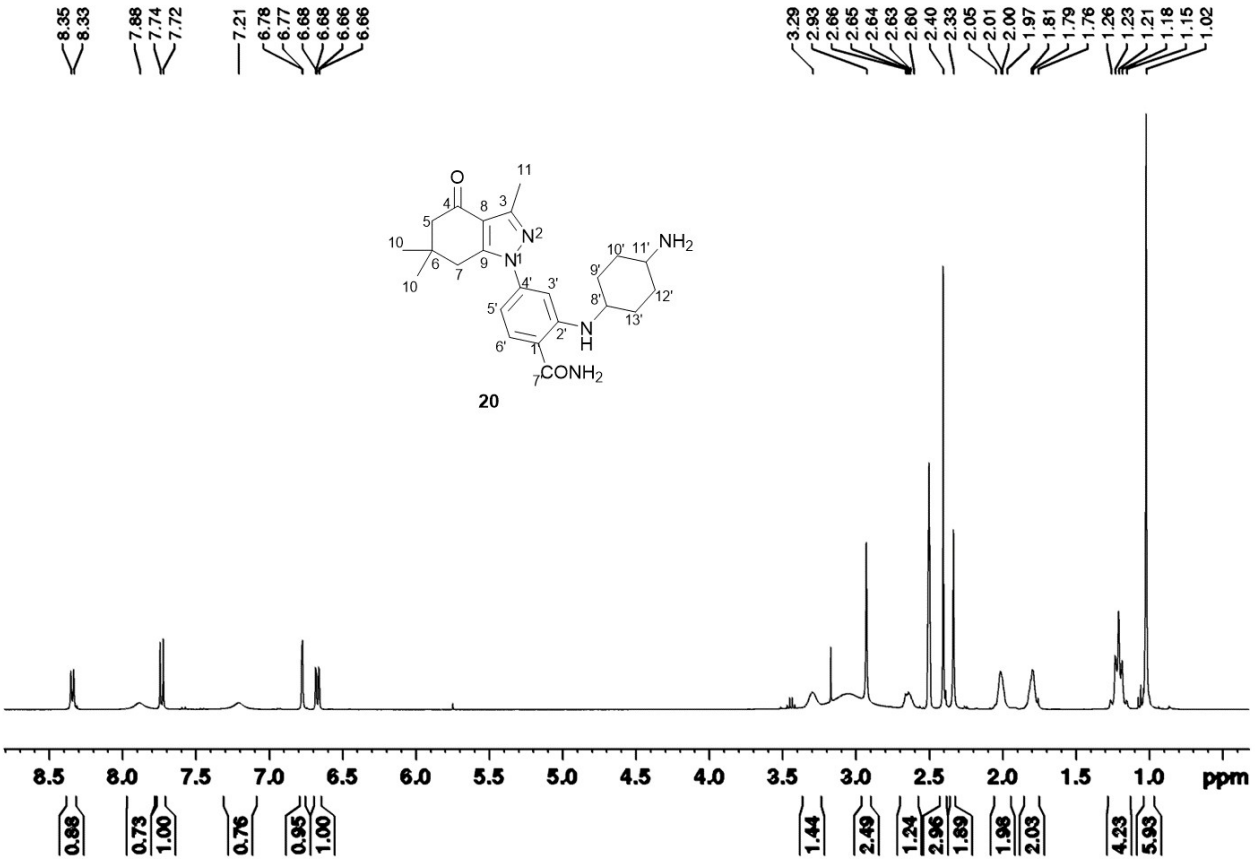

193.4
155.3
150.6
150.3
149.2
143.7
134.1
117.8
117.3
110.7
105.8
95.1
79.7
52.5
51.3
49.2
37.9
36.0
32.0
31.7
28.6
13.5
18
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

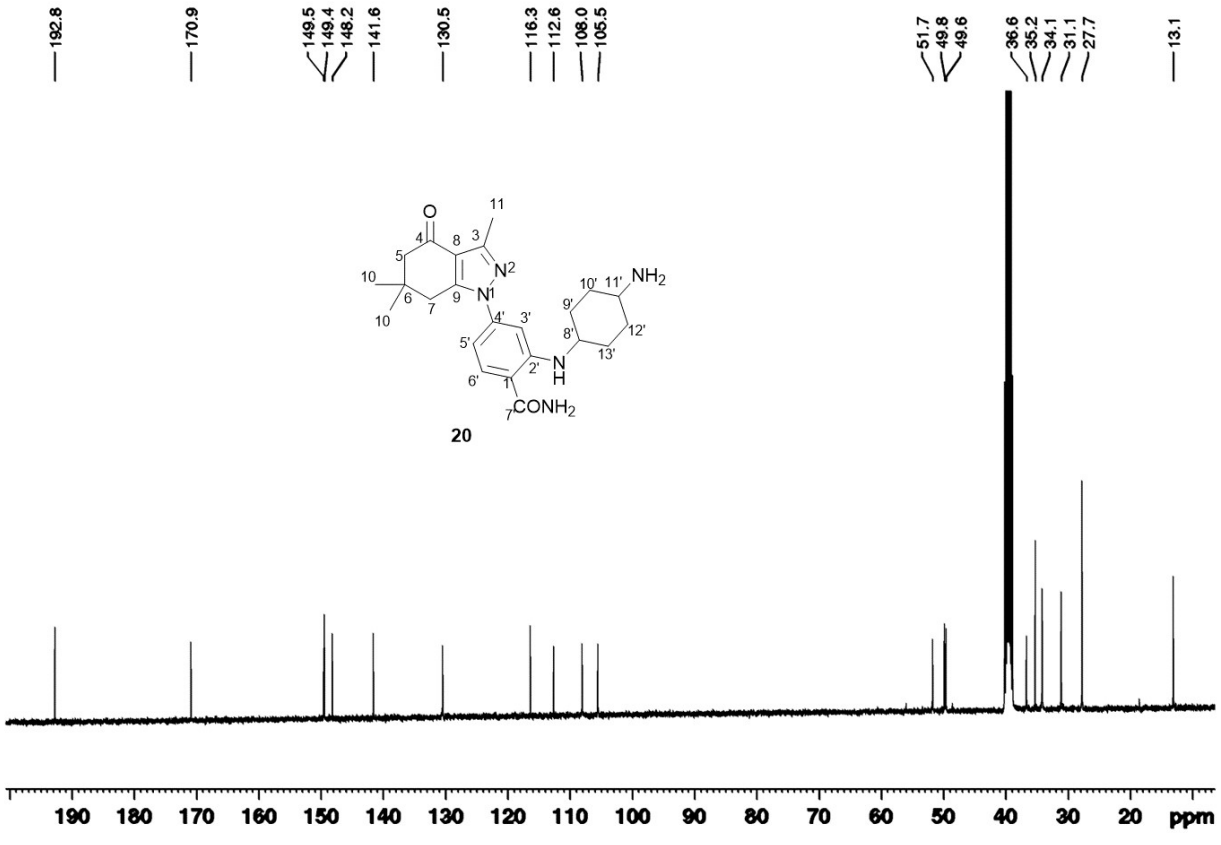

8.06
8.04
7.47
7.45
6.76
6.76
6.60
6.60
6.58
6.58
5.77
4.42
3.48
3.34
3.27
2.80
2.54
2.39
2.15
2.03
1.44
1.41
1.21
1.10
CONH2
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
0.94
1.00
0.97
1.00
1.77
0.91
0.97
1.03
2.02
3.00
2.00
4.13
9.05
4.25
6.02

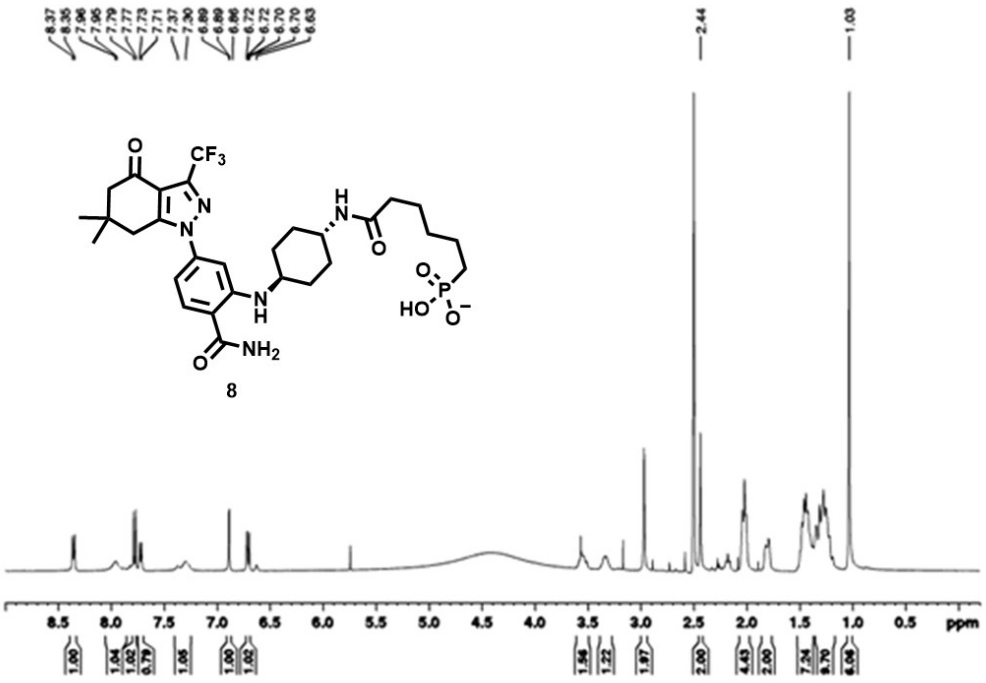

193.5
171.1
155.4
151.2
150.3
149.3
142.9
129.9
117.5
113.8
110.5
108.2
79.5
52.5
52.0
49.2
37.9
36.0
32.0
31.1
28.6
13.6
CONH2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

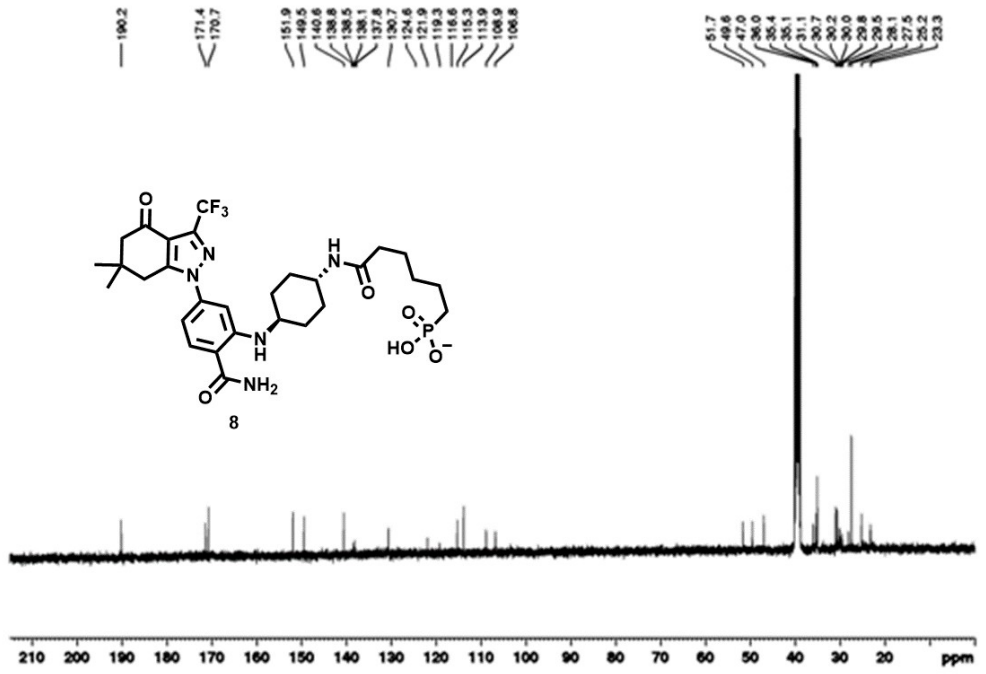

8.36
8.34
7.96
7.79
7.77
7.30
6.87
6.87
6.72
6.72
6.70
6.70
3.30
2.97
2.70
2.67
2.67
2.66
2.66
2.65
2.62
2.45
2.01
1.79
1.27
1.24
1.21
1.19
1.16
1.04
19
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.99
0.84
1.00
0.91
1.00
1.00
1.33
2.00
1.06
2.00
2.00
2.00
4.16
5.90

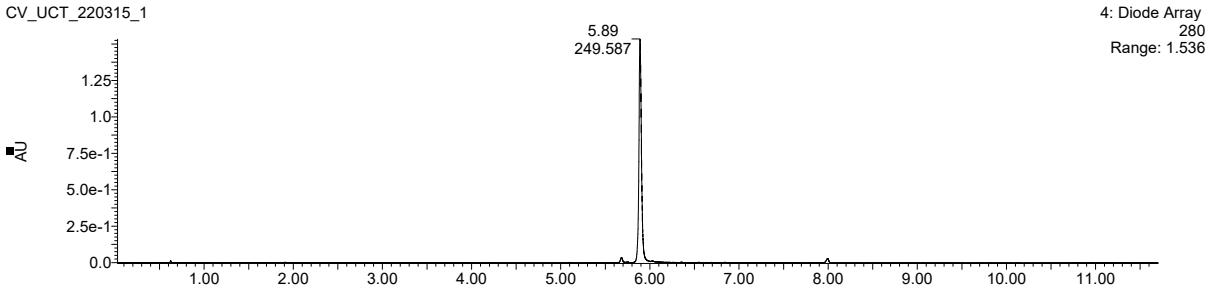

190.1
170.7
151.9
149.5
140.6
138.9
138.5
138.1
137.8
130.6
124.6
121.9
119.3
116.6
115.3
113.9
108.8
106.8
51.7
49.8
49.5
36.0
35.1
33.9
31.0
27.5
19
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
ppm

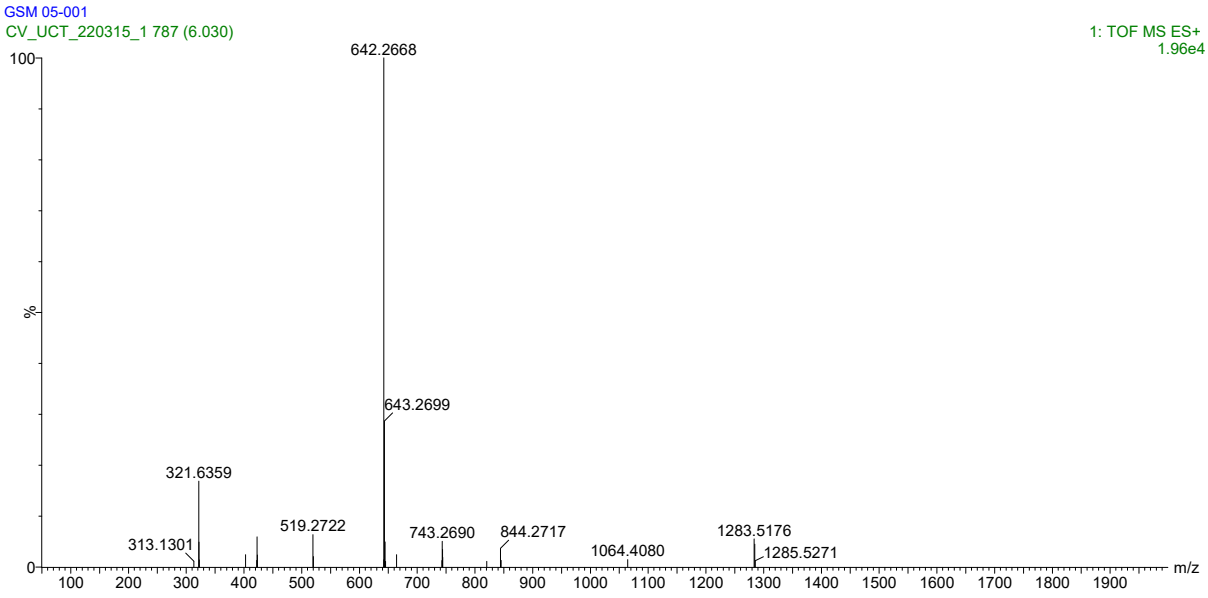

8.35
8.33
7.88
7.74
7.72
7.21
6.78
6.77
6.68
6.68
6.66
6.66
3.29
2.93
2.66
2.65
2.64
2.63
2.60
2.40
2.33
2.05
2.01
2.00
1.97
1.81
1.79
1.76
1.26
1.23
1.21
1.18
1.15
1.02
O
11
4
3
8
5
N2
10
6
9
N1
7
10
4'
3'
5'
2'
NH
6'
1
7CONH2
10'
11'
NH2
9'
8'
12'
13'
20
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.88
0.73
1.00
0.76
0.95
1.00
1.44
2.49
1.24
2.96
1.89
1.98
2.03
4.23
5.93

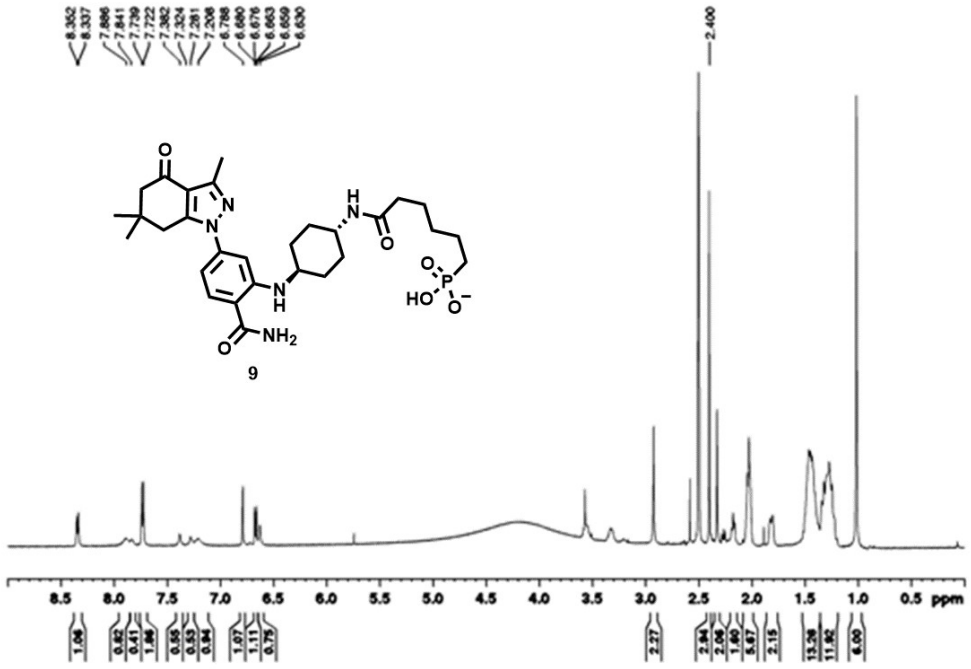

192.8
170.9
149.5
149.4
148.2
141.6
130.5
116.3
112.6
108.0
105.5
51.7
49.8
49.6
36.6
35.2
34.1
31.1
27.7
13.1
O
11
4
3
8
5
N2
10
6
9
N1
7
10
4'
3'
5'
2'
NH
6'
1
7CONH2
10'
11'
NH2
9'
8'
12'
13'
20
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

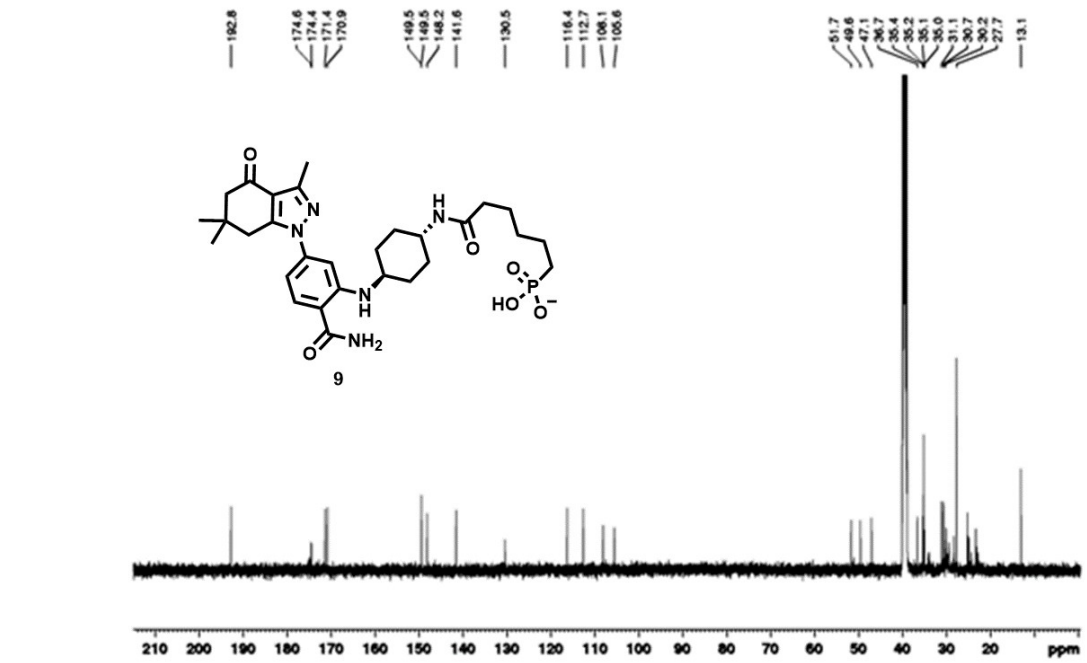

8.37
8.35
7.96
7.95
7.79
7.77
7.73
7.71
7.37
7.30
6.89
6.86
6.72
6.70
6.70
6.63
2.44
1.03
O
CF3
N
N
H
N
O
O
P
HO
O−
N
H
O
NH2
8
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.04
1.02
0.79
1.06
1.00
1.02
1.56
1.22
1.97
2.00
4.43
2.00
7.24
4.70
6.06

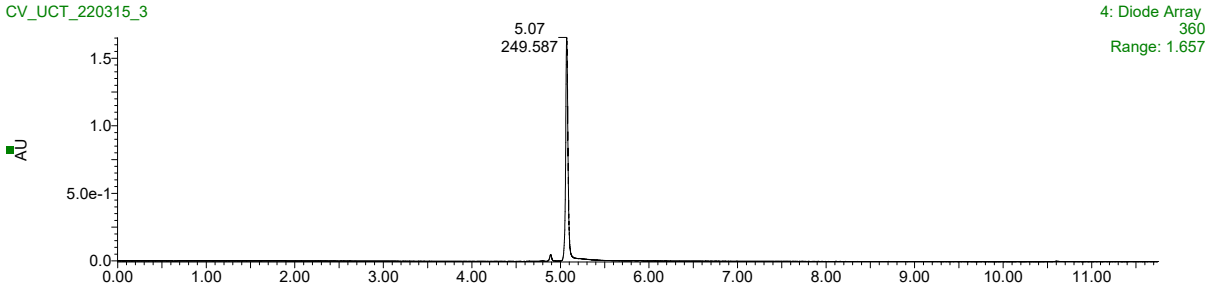

190.2
171.4
170.7
151.9
149.5
140.6
138.8
138.5
138.1
137.8
130.7
124.6
121.9
119.3
116.6
115.3
113.9
108.9
106.8
51.7
49.6
47.0
36.0
35.4
35.1
31.1
30.7
30.2
30.0
29.8
29.5
28.1
27.5
25.2
23.3
O
CF3
N
N
H
N
O
O
P
HO
O−
N
H
O
NH2
8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

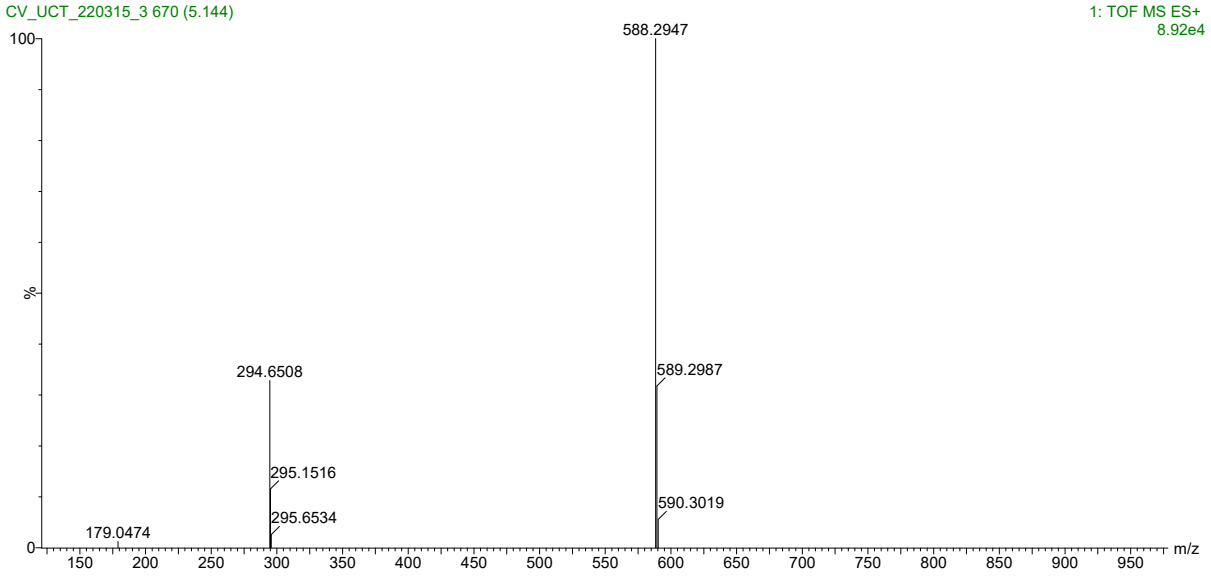

CV_UCT_220315_1
4: Diode Array
280
Range: 1.536
5.89
249.587
AU
1.25
1.0
7.5e-1
5.0e-1
2.5e-1
0.0
1.00
2.00
3.00
4.00
5.00
6.00
7.00
8.00
9.00
10.00
11.00

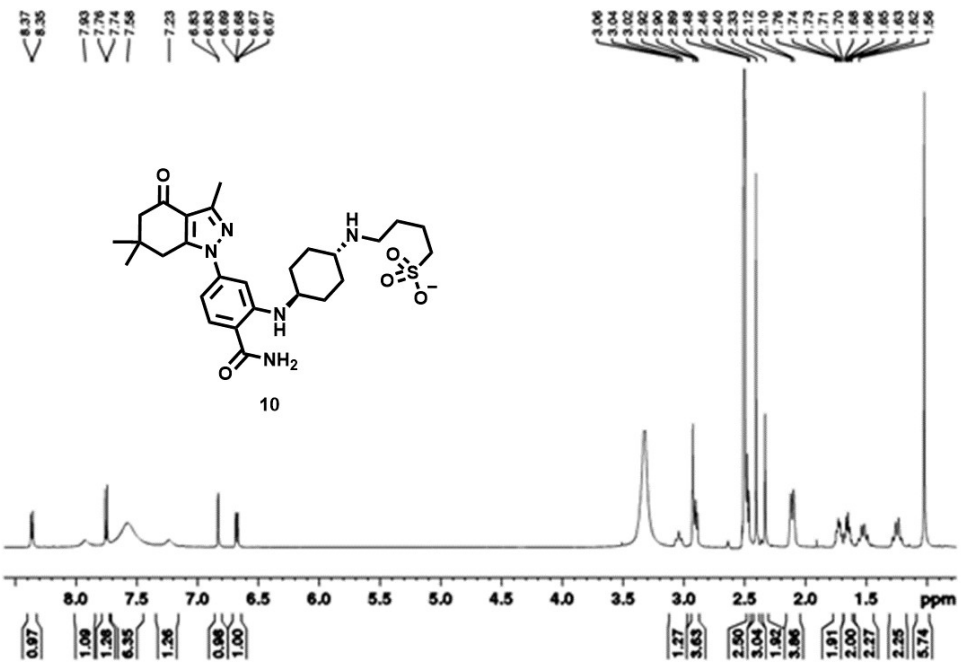

GSM 05-001
CV_UCT_220315_1 787 (6.030)
1: TOF MS ES+
1.96e4
100
%
0
642.2668
643.2699
321.6359
519.2722
313.1301
743.2690
844.2717
1064.4080
1283.5176
1285.5271
m/z
100 200 300 400 500 600 700 800 900 1000 1100 1200 1300 1400 1500 1600 1700 1800 1900

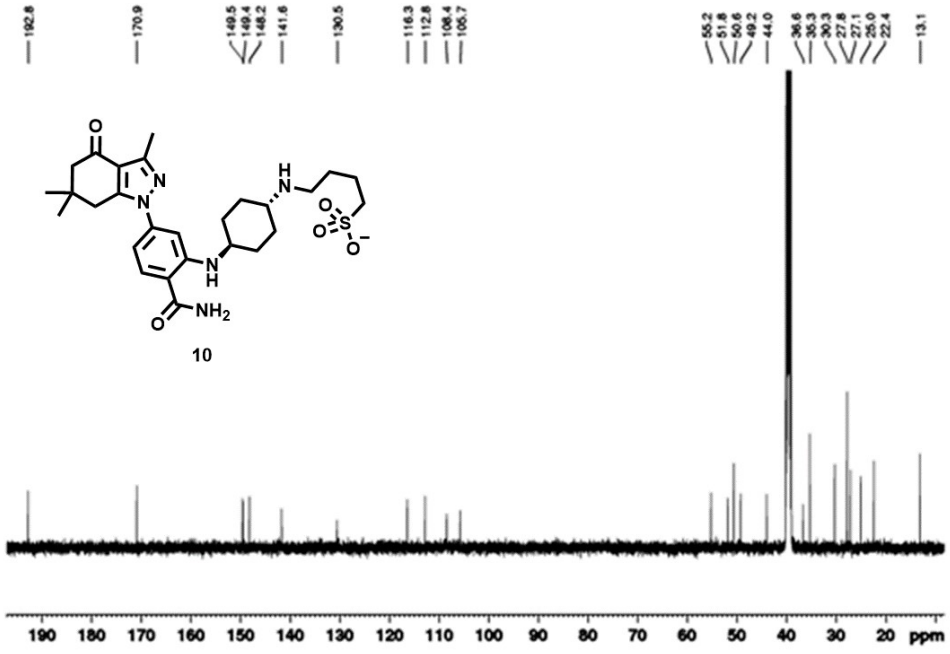

2.400
9
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

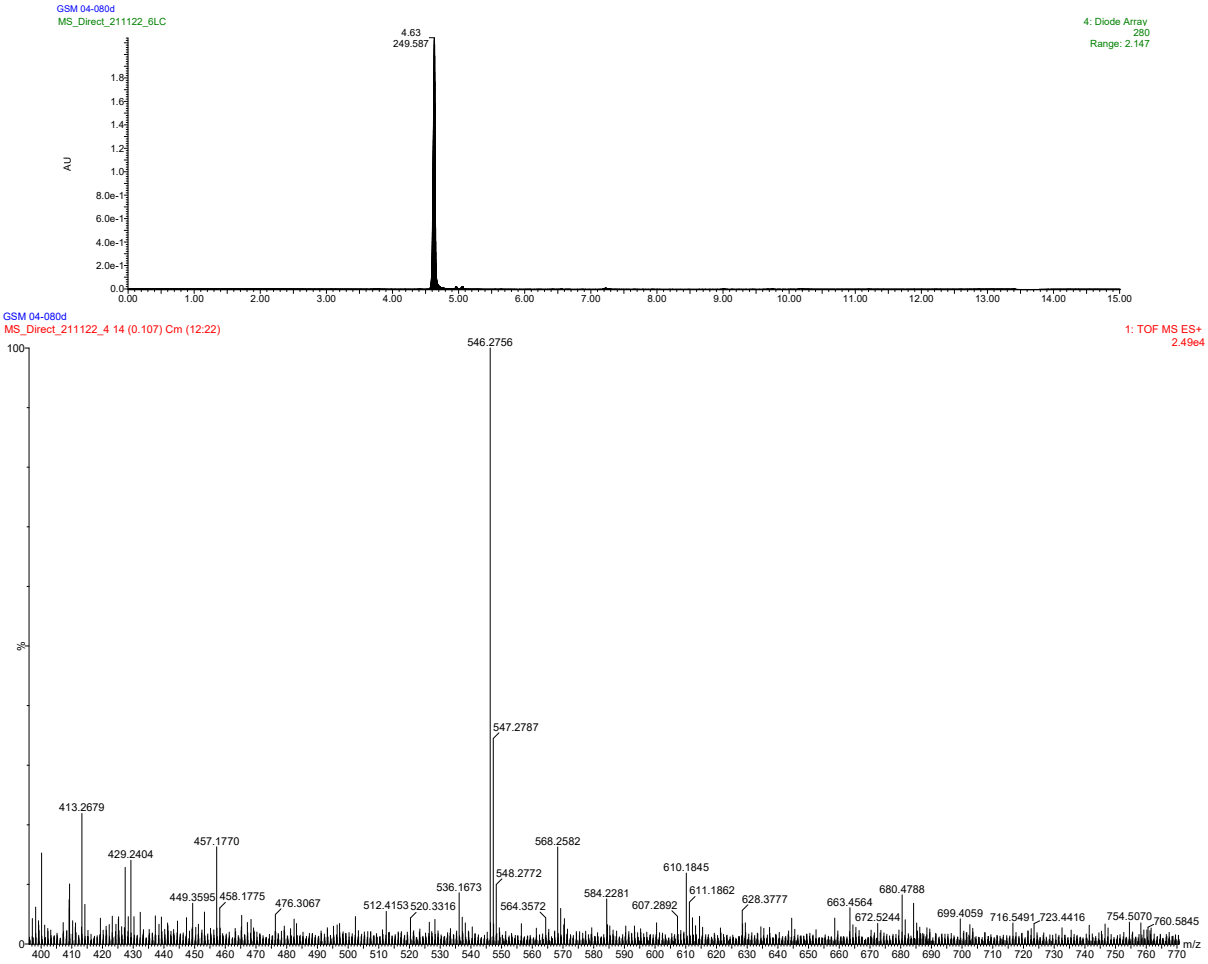

192.8
174.6
174.4
171.4
170.9
149.5
149.5
148.2
141.6
130.5
116.4
112.7
106.1
105.6
51.7
49.6
47.1
36.7
35.4
35.2
35.1
35.0
31.1
30.7
30.2
27.7
13.1
9
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

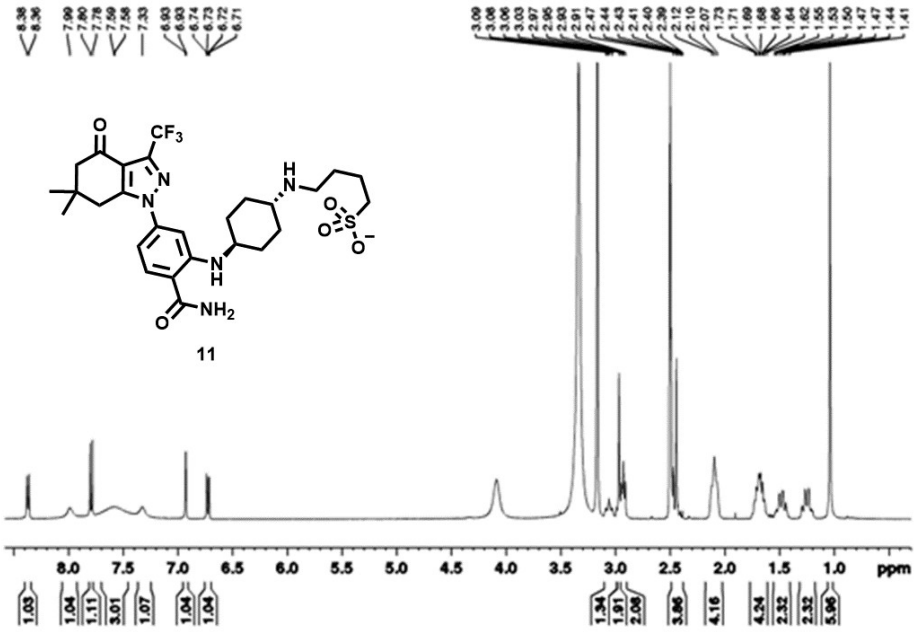

CV_UCT_220315_3
4: Diode Array
360
Range: 1.657
5.07
249.587
AU
1.5
1.0
5.0e-1
0.0
0.00 1.00 2.00 3.00 4.00 5.00 6.00 7.00 8.00 9.00 10.00 11.00

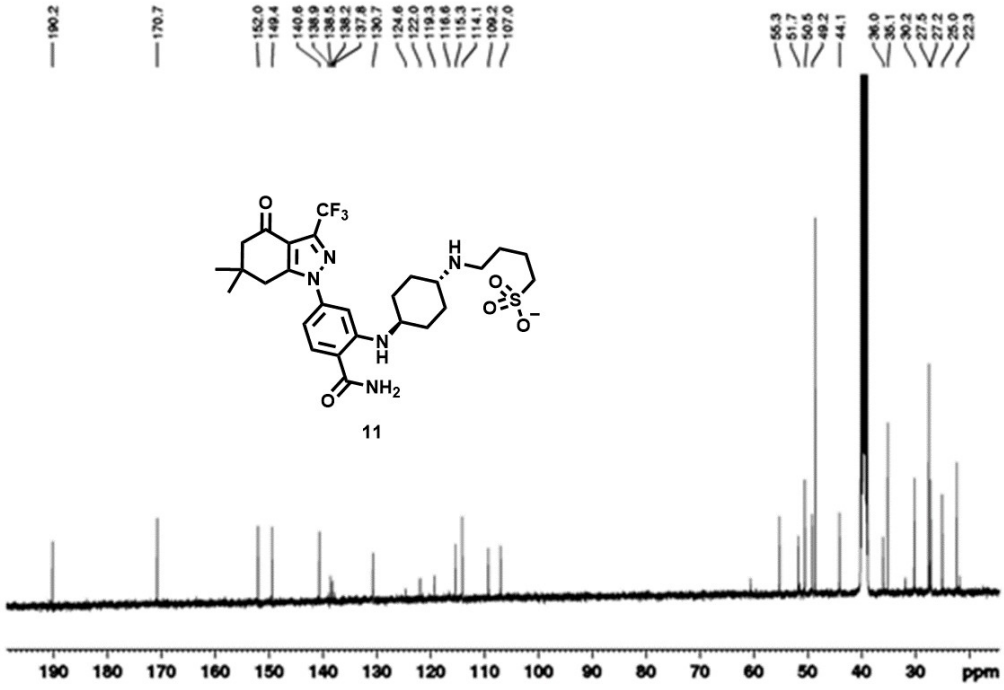

GSM 05-005
CV_UCT_220315_3 670 (5.144)
1: TOF MS ES+
8.92e4
100
%
588.2947
294.6508
589.2987
295.1516
590.3019
295.6534
179.0474
0
150 200 250 300 350 400 450 500 550 600 650 700 750 800 850 900 950
m/z

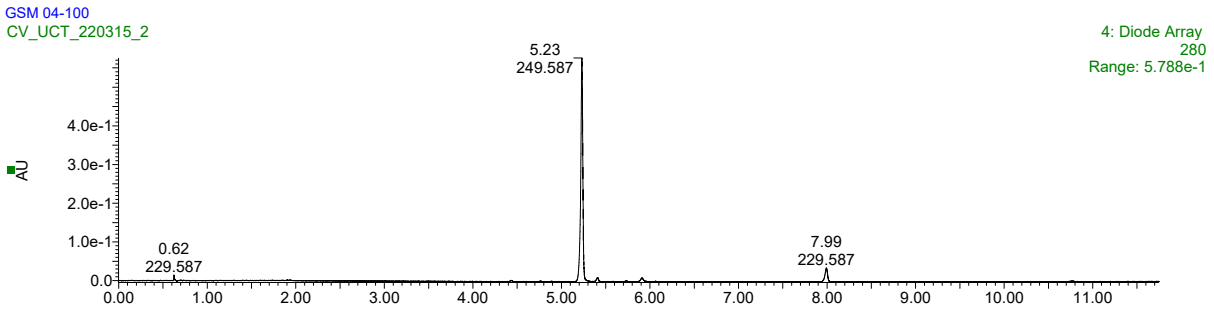

8.37
8.35
7.80
7.76
7.74
7.58
7.23
6.83
6.83
6.69
6.68
6.67
6.67
3.06
3.04
3.02
2.92
2.90
2.89
2.48
2.46
2.40
2.33
2.12
2.10
1.76
1.74
1.73
1.71
1.70
1.68
1.66
1.65
1.63
1.62
1.56
O
N
N
H
N
H
O
S
O
O
NH2
O
10
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
0.97
1.09
1.28
6.35
1.26
0.98
1.00
1.27
3.63
2.50
3.04
1.92
3.86
1.91
2.00
2.27
2.25
5.74

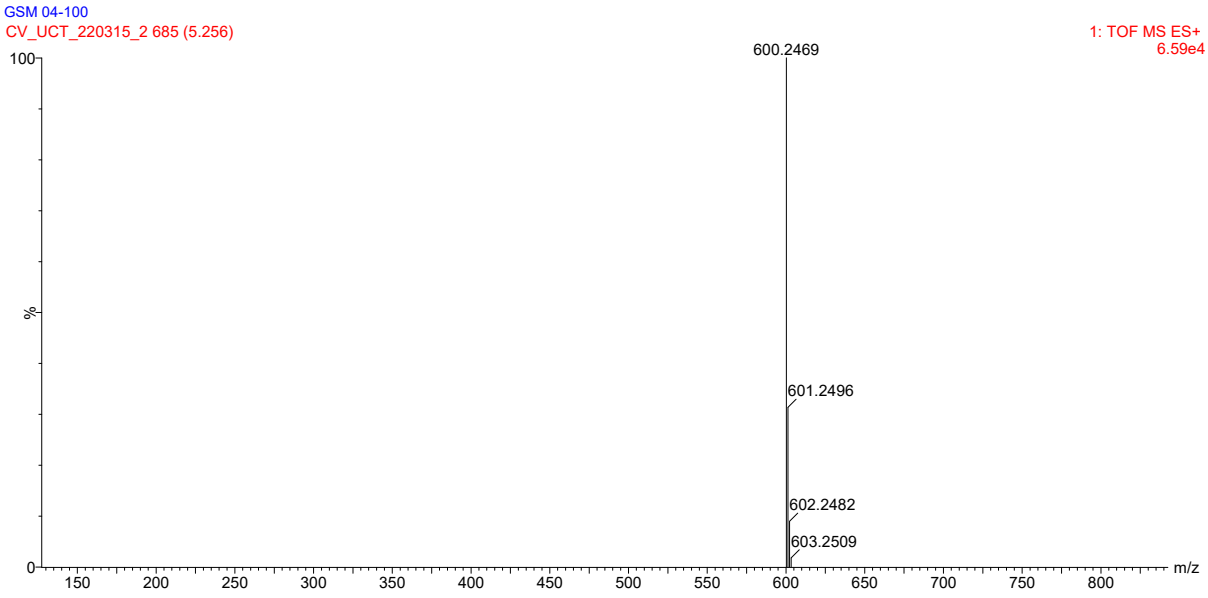

192.8
170.9
149.5
149.4
148.2
141.6
130.5
116.3
112.8
106.4
105.7
55.2
51.8
50.6
49.2
44.0
36.6
35.3
30.3
27.8
27.1
25.0
22.4
13.1
O
N
N
H
N
H
O
S
O
O
NH2
O
10
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm


GSM 04-080d
MS_Direct_211122_6LC
4: Diode Array
280
Range: 2.147
4.63
249.587
AU
GSM 04-080d
MS_Direct_211122_4 14 (0.107) Cm (12:22)
1: TOF MS ES+
2.49e4
546.2756
547.2787
413.2679
429.2404
457.1770
458.1775
449.3595
476.3067
512.4153
520.3316
536.1673
548.2772
564.3572
568.2582
584.2281
607.2892
610.1845
611.1862
628.3777
663.4564
672.5244
680.4788
699.4059
716.5491
723.4416
754.5070
760.5845
%
m/z


11


11


GSM 04-100
CV_UCT_220315_2
4: Diode Array
280
Range: 5.788e-1
5.23
249.587
0.62
229.587
7.99
229.587
AU


GSM 04-100
CV_UCT_220315_2 685 (5.256)
1: TOF MS ES+
6.59e4
100
%
0
600.2469
601.2496
602.2482
603.2509
150
200
250
300
350
400
450
500
550
600
650
700
750
800
m/z