Supporting Information

Enantioselective synthesis of spirooxindole-pyran derivatives via remote Inverse-Electron-Demand Diels–Alder reaction of β,γ-unsaturated amides

Yuzhen Chen,[a] Jiajia Chen,[b] Lin Zhong,[b] Yili Zhang,[b] Ruoting Zhan,[b] Huicai Huang*[b] and Yongbo Xue*[a]

[a]School of Pharmaceutical Sciences (Shenzhen), Shenzhen Campus of Sun Yat-sen University, Shenzhen 518107, People's Republic of China.
Email: xueyb@mail.sysu.edu.cn
[b]Key Laboratory of Chinese Medicinal Resource from Lingnan, Ministry of Education, School of Pharmaceutical Sciences, Guangzhou University of Chinese Medicine, Guangzhou 510006, People's Republic of China.
Email: huanghc@gzucm.edu.cn

Table of Contents

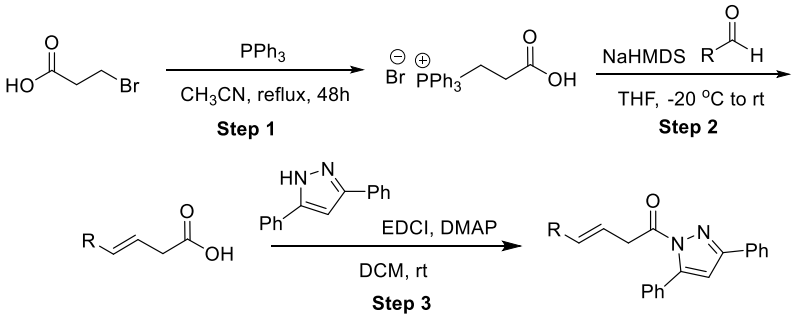
I. General information.

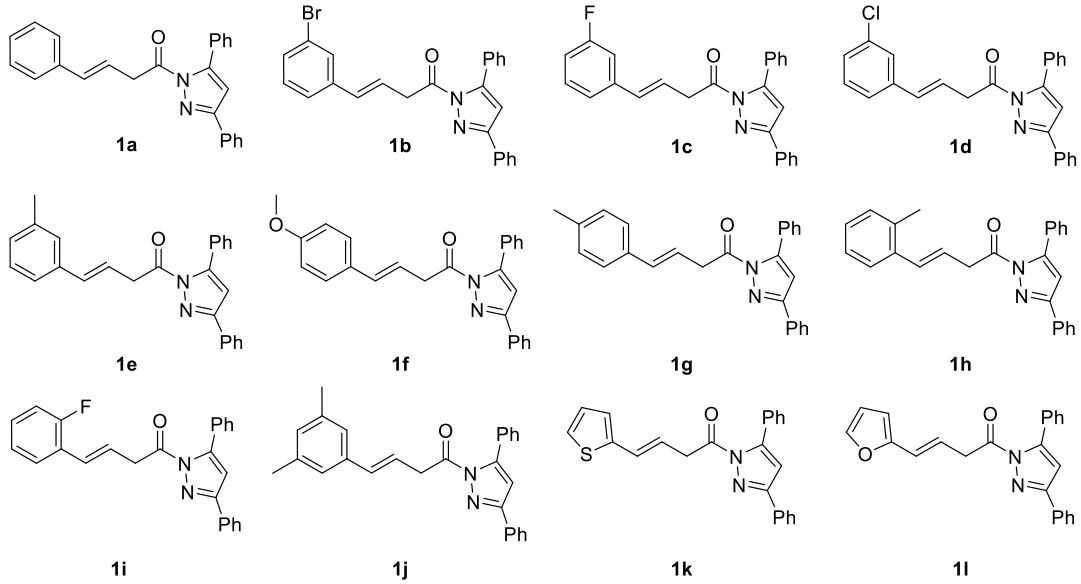
Proton nuclear magnetic resonance (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Bruker AV-400 spectrometer (400 MHz and 100 MHz). Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CDCl_3$: 7.26). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$: 77.16). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants in Hertz (Hz). High resolution mass spectra (EI) were measured on a Waters Micromass GCT spectrometer. High resolution mass spectrometry (ESI) were carried out using a Waters Quatro Macro triple quadrupole mass spectrometer. Optical rotations were measured on an Autopol III automatic polarimeter (Rudolph Research analytical). High performance liquid chromatography (HPLC) was performed on an Agilent 1200 Series chromatographs using chiral columns (DAICEL CHIRALPAK) as noted. All solvents and reagents were purchased from commercial sources (Adamas-beta) and used without purification unless otherwise noted.

II. Preparation of substrates.

1. β,γ-unsaturated pyrazolamide **1** were synthesized follow literature procedure.[1,2]

2. N-protect isatin-derived oxodiene **2** were synthesized by the combination of literature procedure. [3]





Step 1: To an oven-dried 50 mL Schlenk flask equipped with a stir bar and Graham condenser was added PPh_3 (2.62 g, 10 mmol). The flask was evacuated and back-filled with nitrogen. Next, bromide (10 mmol) and anhydrous MeCN (10 mL) was subsequently added via syringe. The homogeneous mixture was stirred at reflux for 36 h. The resulting colorless solution was cooled to room temperature and then Et_2O (30 mL) as added. After keeping at -20 ℃ for 4 h, the formed precipitate was filtered, washed with Et_2O (20 mL × 3), and dried *in vacuo* to afford the triphenylphosphonium bromide as a white solid.

Step 2: To an oven-dried 50 mL Schlenk flask with a stir bar was charged with triphenylphosphonium bromide (10 mmol). The flask was evacuated and back-filled with nitrogen. Then, 20 mL anhydrous THF was added via syringe and the suspension was cooled to -20 ℃. To the colorless suspension was added NaHMDS (2.5 M in THF) (8.8 mL, 22 mmol) dropwise via syringe over 5 min. The resulting orange solution was stirred at -20 ℃ for 30 min and became homogeneous gradually. Then a solution

of phenylpropyl aldehyde (1.19 mL, 9 mmol) in 2 mL anhydrous THF was added via syringe at -20 ℃. The resulting mixture was allowed to warm to room temperature and stirred overnight, after which the heterogeneous mixture was quenched with H_2O (50 mL) and washed with DCM (50 mL × 2). The aqueous phase was acidified to pH = 1 by aqueous 1M HCl solution, and then extracted with EtOAc (60 mL × 3). The organic extracts were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by silica gel column chromatography to afford the desired alkenoic acid. The trans-styrylacetic acid is commercially available.

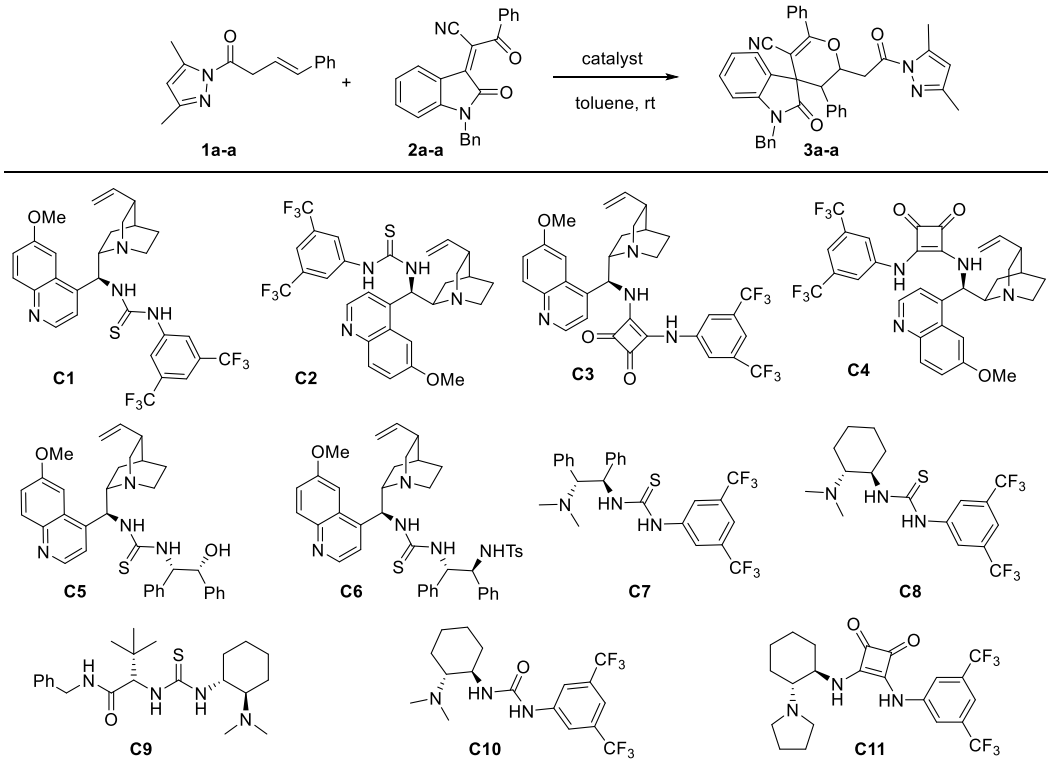
Step 3: To the mixture of carboxylic acid (10.0 mmol, 1.0 equiv.) and 3,5-diphenylpyrazole (2.19 g, 10 mmol, 1.0 equiv) in 20 mL dry Dichloromethane was added EDCI (2.11g, 11 mmol, 1.1 equiv.) and a small amount of DMAP at rt. Then the mixture was stirred at rt for 1 h. After removal of solvent under reduced pressure, the crude was purified by silica gel column chromatography (hexane/ethyl acetate = 50/1) to afford desired *N*-acylpyrazole.

References

1. Liu, X.; An, R.; Zhang, X.; Luo, J.; Zhao, X. *Angew. Chem. Int. Ed.* **2016**, *55*, 5846.
2. Zhang, H.-J.; Shi, C.-Y.; Zhong, F.; Yin, L. *J. Am. Chem. Soc.* **2017**, *139*, 2196.
3. He, X.-L.; Zhao, H.-R.; Duan, C.-Q.; Du, W.; Chen, Y.-C. *Org. Lett*. **2018**, *20*, 804.

III. Reaction conditions optimization

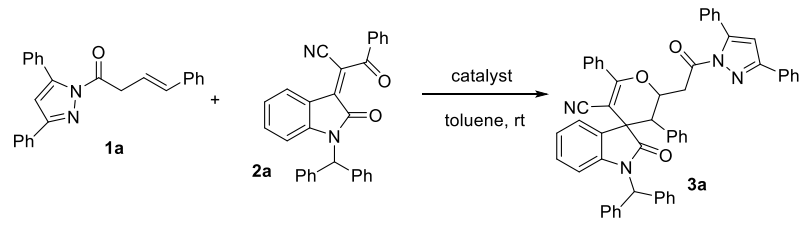
Table S1. Screening data of Diels−Alder Reaction.

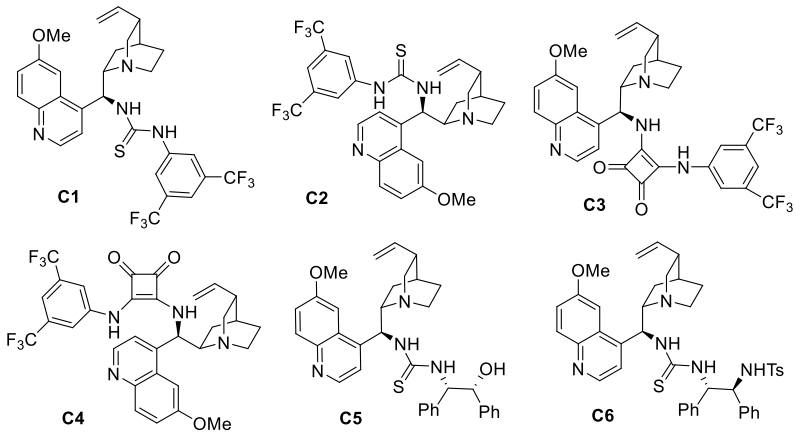


entry	catalyst	solvent	t (h)	yield (%)[b]	d.r.[c]	ee (%) [d]
1	**C1**	Toluene	24	99	>20:1	19
2	**C2**	Toluene	24	80	>20:1	-41
3	**C3**	Toluene	24	23	>20:1	70
4	**C4**	Toluene	24	99	>20:1	-47
5	**C5**	Toluene	24	60	>20:1	77
6	**C6**	Toluene	48	26	>20:1	67
7	**C7**	Toluene	24	83	>20:1	-13
8	**C8**	Toluene	24	58	>20:1	-11
9	**C9**	Toluene	24	37	>20:1	-41
10	**C10**	Toluene	24	59	>20:1	-38
11	**C11**	Toluene	24	38	>20:1	-17
12	**C5**	CH_2Cl_2	24	40	>20:1	57
13	**C5**	$CHCl_3$	24	54	>20:1	65
14	**C5**	EtOAc	24	80	>20:1	65
15	**C5**	cyclohexane	24	52	>20:1	33
16	**C5**	PhCl	24	61	>20:1	74
17	**C5**	$PhCF_3$	24	86	>20:1	65
18	**C5**	THF	24	No reaction	/	/
19[e]	**C5**	Toluene	60	80	>20:1	75
20[f]	**C5**	Toluene	72	84	>20:1	75

[a]Unless otherwise noted, the reactions were performed with 1.0 equiv of **1a-a** (0.06 mmol), 1.2 equiv of **2a-a** (0.05 mmol), catalyst **C** (10 mol %) in 1.0 mL solvent at rt. [b]Yield of the isolated product. [c]The dr was determined by ^{1}H NMR analysis of the crude product. [d]Determined by chiral HPLC analysis. [e]The reaction was performed at 10 ℃. [f]Catalyst **C5** (15 mol%) was used in the reaction and performed at 10 ℃. [e] The reaction was performed at 0 ℃. [f] The reaction was performed at -10 ℃.

Table S2. The screening conditions of Diels−Alder Reaction[a]

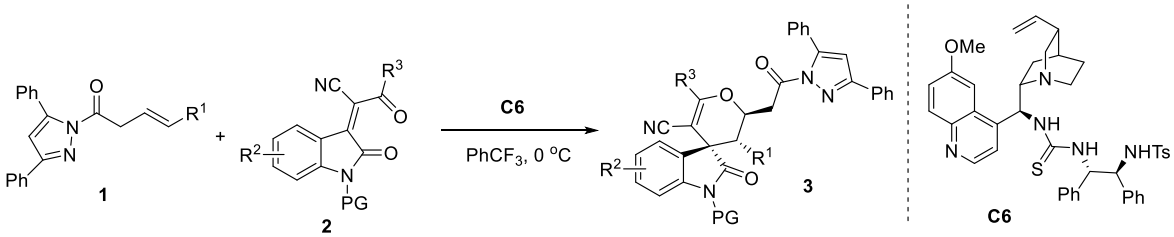




entry	catalyst	temp	solvent	t (h)	yield (%)[b]	d.r.[c]	ee (%) [d]
1	**C1**	rt	Toluene	12	76	>20:1	-20
2	**C2**	rt	Toluene	12	79	>20:1	-9
3	**C3**	rt	Toluene	12	32	>20:1	83
4	**C4**	rt	Toluene	12	trace	/	/
5	**C5**	rt	Toluene	24	61	>20:1	85
6	**C6**	rt	Toluene	24	60	>20:1	84
7	**C6**	rt	CH_2Cl_2	48	35	>20:1	81
8	**C6**	rt	$CHCl_3$	48	trace	/	/
9	**C6**	rt	THF	48	No reaction	/	/
9	**C6**	rt	Et_2O	48	65	>20:1	79
9	**C6**	rt	PhCl	48	52	>20:1	85
10	**C6**	rt	$PhCF_3$	48	81	>20:1	86
11	**C6**	10 ℃	$PhCF_3$	12	93	>20:1	87
12	**C6**	0 ℃	$PhCF_3$	36	98	>20:1	93
13	**C6**	-10 ℃	$PhCF_3$	48	96	>20:1	92
14	**C6**	-20 ℃	$PhCF_3$	96	53	>20:1	96

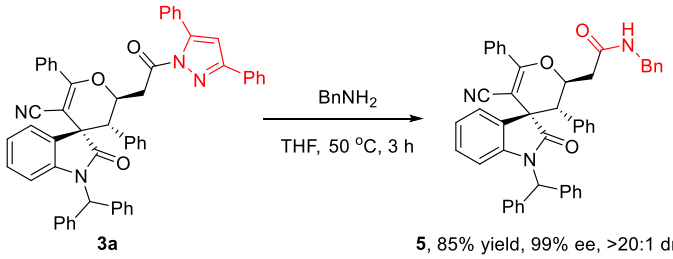
[a]Unless otherwise noted, the reactions were performed with 1.0 equiv of **1a** (0.06 mmol), 1.2 equiv of **2a** (0.05 mmol), catalyst **C** (10 mol %) in 1.0 mL solvent at rt. [b]Yield of the isolated product. [c]The dr was determined by ^{1}H NMR analysis of the crude product. [d]Determined by chiral HPLC analysis.

IV. General procedure and the derivatizations of product.

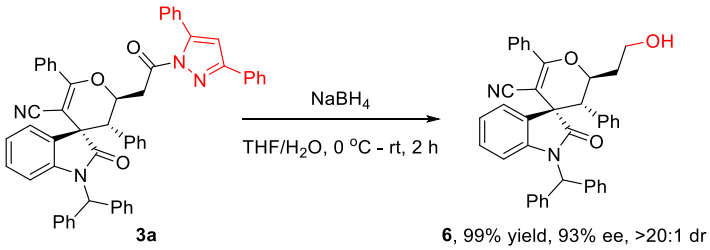


Step 1: $PhCF_3$ (2.0 mL) was added to a mixture of isatin-derived oxodiene **2** (0.10 mmol, 1.0 equiv), β,γ-unsaturated amides **1** (0.12 mmol, 1.2 equiv) and catalyst **C6** (7.3 mg, 0.010 mmol) at 0 ℃ and the reaction was stirred for 72h. Then mixture was directly loaded onto the flash column chromatography and was purified with CH_2Cl_2-hexane (1:1) to afford **3** as white solids.

Procedures for the derivatizations of product.



3a (80.5 mg, 0.10 mmol) in THF (2.0 mL), then $BnNH_2$ (21.4 mg, 0.2 mmol) was added and the mixture was stirred at 50 ℃ (bath oil) for 3 h. Then the solvent was removed under reduced pressure and the residue was purified by flash chromatography to give the product **5** (58.9 mg, white solids, 85% yield).



3a (80.5 mg, 0.10 mmol) in THF/H_2O (1.54 mL/0.42 mL), then $NaBH_4$ (30.26 mg, 0.8 mmol) was added in the 0 ℃ and the resulting mixture was stirred at rt for 2 h. Then the mixture was quenched by 1N HCl (10 mL), extracted with DCM (20 mL). The solvent was removed under reduced pressure and the residue was purified by flash chromatography to give the product **6** (58.5 mg, white solids, 99% yield).

V. X-ray crystallographic analysis of 4h.

The single crystal of compound **4j** was prepared from its solution in Dichloromethane/ n-hexane (1:10) by slow evaporation of the solvent (Figure S and Table 1).

CCDC 2074766 (**4j**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Centre viawww.ccdc.cam.ac.uk/data_request/cif.

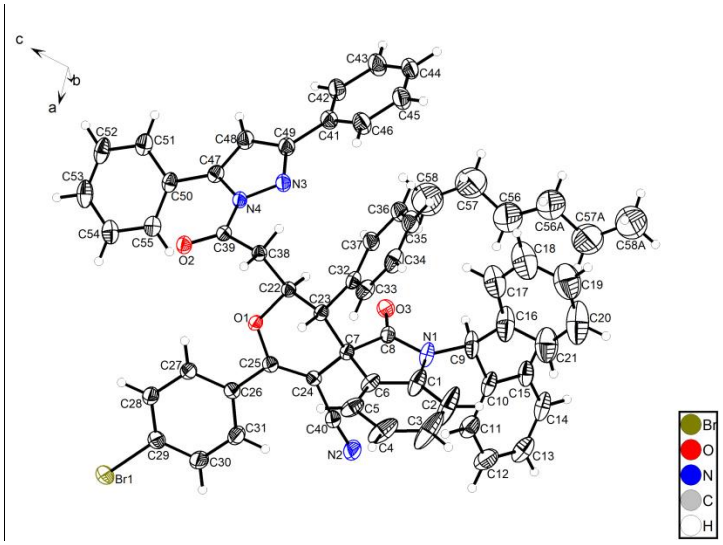


Figure S1 ORTEP of **4j** (at 50% level).

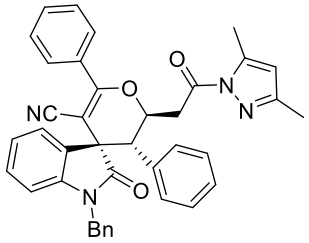
Table 1 Crystal data and structure refinement for YZ0644-1.

Identification code	YZ0644-1
Empirical formula	$C_{58}H_{46}BrN_4O_3$
Formula weight	926.90
Temperature/K	100.00(10)
Crystal system	triclinic
Space group	P-1
a/Å	11.2020(2)
b/Å	11.3554(2)
c/Å	18.8713(4)
α/°	103.7952(18)
β/°	102.2696(18)
γ/°	93.4841(16)
Volume/Å^3	2262.21(8)
Z	2
ρ_{calc}g/cm^3	1.361
μ/mm^{-1}	1.649
F(000)	962.0
Crystal size/mm^3	0.05 × 0.04 × 0.03
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	4.96 to 154.146
Index ranges	-14 ≤ h ≤14, -14 ≤ k ≤ 14, -22 ≤ l ≤23
Reflections collected	30212

Independent reflections	9179 [Rint = 0.0476, Rsigma = 0.0468]
Data/restraints/parameters	9179/18/596
Goodness-of-fit on F^2	1.065
Final R indexes [I>=2σ (I)]	R_1 = 0.0733, wR_2 =0.2054
Final R indexes [all data]	R_1 = 0.0798, wR_2 = 0.2130
Largest diff. peak/hole / e $Å^{-3}$	1.96/-0.85

VI. Characterization data.

3a-a:(2'S,3R,3'R)-1-benzyl-2'-(2-(3,5-dimethyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 50.7 mg, 84% yield (hexanes/Dichloromethane, v:v = 2:1), Mp 218-220 ℃. $[\alpha]_D^{rt}$ = + 29.5 (*c* 0.302, DCM), 93% ee, >20:1 d.r..

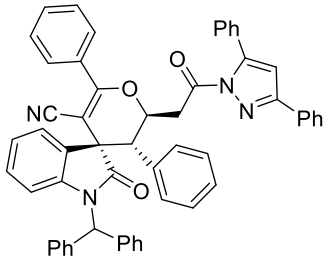
^{1}H NMR (500 MHz, chloroform-*d*) δ 7.84 – 7.71 (m, 2H), 7.48 – 7.46 (m, 1H), 7.45 – 7.43 (d, *J* = 7.0 Hz, 1H), 7.42 – 7.32 (m, 3H), 7.20 – 7.17 (m, 2H), 7.6 (s, 2H), 7.14 – 7.11 (m, 3H), 7.01 – 6.86 (m, 2H), 6.71 (dd, *J* = 7.3, 1.8 Hz, 2H), 6.37 (d, *J* = 7.5 Hz, 1H,), 6.29 (ddd, *J* = 11.6, 8.9, 3.1 Hz, 1H), 5.94 (s, 1H), 4.81 (d, *J* = 14.1 Hz, 1H), 4.62 (d, *J* = 14.1 Hz, 1H), 3.57 (d, *J* = 11.1 Hz, 1H), 3.44 (dd, *J* = 14.7, 8.9 Hz, 1H), 3.37 (dd, *J* = 14.7, 3.1 Hz, 1H), 2.56 (s, 3H), 2.18 (s, 3H).

^{13}C NMR (125 MHz, chloroform-*d*) δ 175.0, 169.9, 167.1, 152.2, 144.1, 143.0, 134.8, 133.7, 132.6, 1312, 129.4, 129.0, 128.6, 128.5, 128.3, 128.0, 127.2, 126.6, 123.4, 123.3, 117.5, 111.4, 109.8, 85.6, 73.5, 54.0, 50.1, 44.0, 38.9, 29.7, 14.5, 13.8.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{39}H_{32}N_4O_3$ 605.2547. Found 605.2556.

HPLC analysis: (IB column, Hexane: 2-propanol = 85:15, flow rate = 1.0 mL/min, wavelength = 254 nm): Rt_1 = 20.741, Rt_2 = 23.349.

3a:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 78.8 mg, 98% yield (hexanes/Dichloromethane, v:v = 1:1), Mp 183-185 ℃. $[\alpha]_D^{rt}$ = + 36.5 (*c* 0.564, DCM), 93% ee, >20:1 d.r..

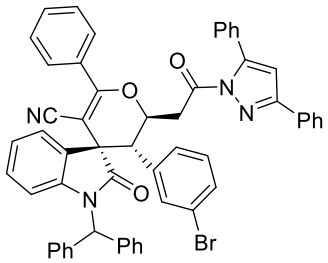
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.86 (d, *J* =1.7 Hz, 1H), 7.84 (d, *J* = 1.3 Hz, 1H), 7.81 (d, *J* = 1.5 Hz, 1H), 7.79 (d, *J* = 1.5 Hz, 1H), 7.47 – 7.45 (m, 2H), 7.44 (d, *J* = 2.8 Hz, 1H), 7.43 (d, *J* = 1.6 Hz, 1H), 7.42 (s, 1H), 7.41 – 7.40 (m, 4H), 7.40 – 7.39 (m, 2H), 7.38 – 7.36 (m, 1H), 7.26 (s, 2H), 7.25 – 7.22 (m, 3H), 7.21 – 7.19 (m, 4H), 7.12 (d, *J* = 7.8 Hz, 2H), 7.09 – 7.04 (m, 3H), 6.94 (td, *J* = 7.9, 1.2 Hz, 1H), 6.82 (s, 1H), 6.71 (s, 1H), 6.52 (d, *J* = 8.0 Hz, 2H), 6.40-6.36 (m, 1H), 6.08 (d, *J* = 7.9 Hz, 1H), 3.64 – 3.58 (m, 2H), 3.51 – 3.45 (m, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.3, 169.2, 166.9, 153.8, 147.4, 142.8, 137.0, 136.8, 133.7, 132.5, 131.6, 131.2, 130.8, 129.4, 129.2, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.3, 126.4, 123.4, 123.0, 117.5, 112.5, 110.1, 86.0, 73.8, 58.6, 53.4, 50.0, 39.6.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{55}H_{40}N_4O_3$ 805.3173. Found 805.3177.

HPLC analysis: (IA column, Hexane: 2-propanol = 96:4, flow rate = 0.6 mL/min, wavelength = 254 nm): Rt_1 = 29.457, Rt_2 = 37.508.

3b:(2'S,3R,3'R)-1-benzhydryl-3'-(3-bromophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 81.0 mg, 92% yield (hexanes/Dichloromethane, v:v = 1:1), Mp 189-191 ℃. $[\alpha]_D^{rt}$ = + 47.5 (*c* 0.764, DCM), 92% ee, >20:1 d.r..

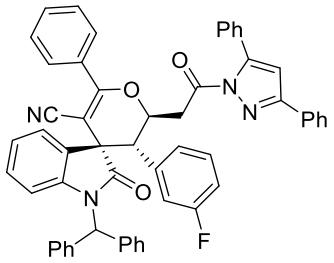
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.87 (d, *J* = 0.8 Hz, 2H), 7.81 (s, 1H), 7.79 (d, *J* = 1.7 Hz, 1H), 7.64 – 7.46 (m, 2H), 7.45 – 7.42 (m, 4H), 7.41 (d, *J* = 3.6 Hz, 4H), 7.40 – 7.38 (m, 2H), 7.37 – 7.31 (m, 1H), 7.28 – 7.25 (m, 3H), 7.23 (d, *J* = 3.2 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 7.16 (d, *J* = 7.2 Hz, 2H), 7.12 – 7.07 (m, 1H), 7.01 – 6.75 (m, 4H), 6.72 (s, 1H), 6.64 (s, 1H), 6.62 (s, 1H), 6.32 (s, 1H), 6.15 (d, *J* = 8.0 Hz, 1H), 3.78 – 3.55 (m, 2H), 3.50 – 3.34 (m, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 174.9, 168.9, 166.8, 154.0, 147.4, 136.9, 136.8, 132.3, 131.5, 131.3, 130.7, 129.4, 129.2, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.0, 127.9, 127.8, 127.5, 126.4, 123.3, 117.3, 112.7, 110.2, 85.9, 73.4, 58.6, 53.3, 49.6, 26.9.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{55}H_{39}BrN_4O_3$ 883.2278. Found 883.2274.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt$_1$ = 11.944, Rt$_2$ = 22.649.

3c:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(3-fluorophenyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 71.9 mg, 87% yield (hexanes/Dichloromethane, v:v = 1:1), Mp 200-202 ℃. $[\alpha]_D^{rt}$ = + 61.6 (*c* 0.631, DCM), 92% ee, >20:1 d.r..

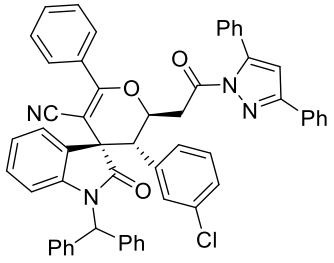
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.79 (d, *J* = 1.8 Hz, 1H), 7.77 (d, *J* = 1.5 Hz, 1H), 7.74 (d, *J* = 1.2 Hz, 1H), 7.72 (d, *J* = 1.6 Hz, 1H), 7.38 (d, *J* = 1.7 Hz, 1H), 7.36 (d, *J* = 1.6 Hz, 2H), 7.36 – 7.35 (m, 2H), 7.34 (s, 3H), 7.32 (d, *J* = 2.0 Hz, 2H), 7.18 – 7.17 (m, 5H), 7.16 (d, *J* = 2.4 Hz, 2H), 7.14 – 7.12 (m, 2H), 7.10 (d, *J* = 1.5 Hz, 1H), 7.08 (d, *J* = 1.2 Hz, 1H), 7.07 – 7.05 (m, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.89 (td, *J* = 7.8, 1.3 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 6.4 Hz, 1H), 6.77 (s, 1H), 6.65 (s, 1H), 6.59 (d, *J* = 7.6 Hz, 2H), 6.28 – 6.22 (m, 1H), 6.08 (d, *J* = 8.0 Hz, 1H), 3.54 (d, *J* = 10.7 Hz, 2H), 3.36 (s, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.1, 168.9, 166.8, 153.9, 147.4, 142.7, 136.9, 136.2, 132.4, 131.5, 131.2, 130.7, 129.3, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.3, 128.1, 128.0, 127.8, 127.5, 126.4, 123.3, 123.1, 117.3, 112.6, 110.1, 85.9, 73.5, 58.7, 53.2, 49.7, 26.9.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{55}H_{39}FN_4O_3$ 823.3079. Found 823.3077.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt$_1$ = 13.204, Rt$_2$ = 29.894.

3d:(2'S,3R,3'R)-1-benzhydryl-3'-(3-chlorophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 84.2 mg, 99% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 187-189 ℃. $[\alpha]_D^{rt}$ = + 66.5 (*c* 0.793, DCM), 90% ee, >20:1 d.r..

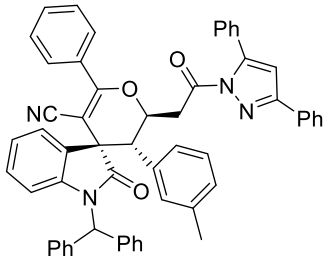
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.77 (d, *J* = 1.9 Hz, 1H), 7.76 (d, *J* = 1.5 Hz, 1H), 7.74 (d, *J* = 1.1 Hz, 1H), 7.72 (d, *J* = 1.6 Hz, 1H), 7.36 – 7.39 (m, 4H), 7.35 (d, *J* = 1.7 Hz, 2H), 7.34 (s, 4H), 7.30 – 7.32(m, 3H), 7.20 – 7.21 (m, 1H), 7.18 (s, 4H), 7.15 (d, *J* = 2.8 Hz, 3H), 7.13 – 7.14 (m, 1H), 7.10 (d, *J* = 2.0 Hz, 1H), 7.09 (s, 1H), 7.01 – 7.05 (m,1H), 6.89 (d, *J* = 0.8 Hz, 1H), 6.75 (s, 1H), 6.64 (s, 1H), 6.57 (s, 1H), 6.55 (s, 1H), 6.24 (ddd, *J* = 11.6, 9.0, 2.9 Hz, 1H), 6.06 (d, *J* = 7.9 Hz, 1H), 3.49 – 3.54 (m, 2H), 3.38 (dd, *J* = 15.2, 9.0 Hz, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.04, 168.91, 166.86, 153.89, 147.43, 142.70, 136.85, 136.71, 134.18, 132.35, 132.10, 131.54, 130.67, 129.36, 129.10, 128.99, 128.88, 128.84, 128.65, 128.56, 128.47, 128.45, 128.39, 128.35, 127.82, 127.58, 126.35, 123.31, 123.04, 117.32, 112.64, 110.16, 85.81, 73.48, 58.75, 53.27, 49.39, 39.40.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{55}H_{39}ClN_4O_3$ 839.2783. Found 839.2788.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 22.700, Rt_2 = 28.976.

3e:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(m-tolyl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 75.6 mg, 92% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 201-203 ℃. $[\alpha]_D^{rt}$ = + 19.7 (*c* 0.378, DCM), 95% ee, >20:1 d.r..

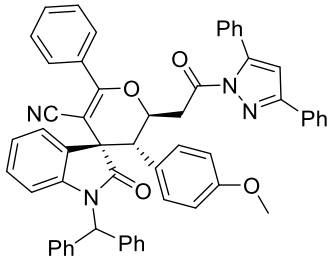
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.79 (d, *J* = 1.9 Hz, 1H), 7.77 (d, *J* = 1.5 Hz, 1H), 7.74 (d, *J* = 1.4 Hz, 1H), 7.72 (d, *J* = 1.7 Hz, 1H), 7.37 (dd, *J* = 7.2, 1.6 Hz, 2H), 7.34 (d, *J* = 3.2 Hz, 2H), 7.33– 7.22 (m, 5H), 7.31 – 7.30 (m, 2H), 7.30 – 7.28 (m, 1H), 7.18 – 7.16 (m, 1H), 7.15 – 7.14 (m, 3H), 7.12 – 7.10 (m, 3H), 7.03 (d, *J* = 7.9 Hz, 2H), 7.00 (d, *J* = 2.0 Hz, 1H), 6.98 – 6.90 (m, 2H), 6.83 (t, *J* = 7.6 Hz, 2H), 6.63 (s, 1H), 6.45 (s, 1H), 6.43 (s, 1H), 6.31 – 6.21 (m, 2H), 5.99 (d, *J* = 8.0 Hz, 1H), 3.59 – 3.36 (m, 2H), 3.41 – 3.34 (m 1H), 1.34 (s, 3H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.3, 169.3, 166.9, 153.8, 147.4, 142.8, 136.8, 133.6, 132.6, 131.6, 131.2, 130.8, 129.3, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.0, 127.8, 127.3, 126.4, 123.4, 122.9, 117.5, 112.5, 110.1, 86.0, 73.9, 53.4, 50.1, 39.7, 34.7, 27.0.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{56}H_{42}N_4O_3$ 819.3330. Found 819.3336.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 11.546, Rt_2 = 23.421

3f:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(4-methoxyphenyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



Colorless solid, 79.9 mg, 96% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 211-213 ℃. $[\alpha]_D^{rt}$ = + 55.6 (*c* 0.681, DCM), 98% ee, >20:1 d.r..

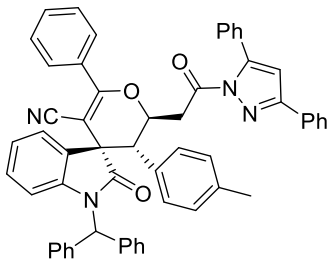
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.86 (t, *J* = 1.9 Hz, 1H), 7.85 (t, *J* = 1.6 Hz, 1H), 7.82 (t, *J* = 1.4 Hz, 1H), 7.80 (t, *J* = 1.6 Hz, 1H), 7.46 – 7.34 (m, 4H), 7.43 – 7.42 (m, 3H), 7.41 (s, 2H), 7.41 – 7.36 (m, 4H), 7.27 – 7.24 (m, 2H), 7.22 (d, *J* = 2.4 Hz, 2H), 7.21 – 7.19 (m, 3H), 7.14 – 7.11 (m, 2H), 7.08 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.94 (td, *J* = 7.8, 1.3 Hz, 1H), 6.84 (s, 1H), 6.71 (s, 1H), 6.57 (d, *J* = 1.6 Hz, 2H), 6.55 (d, *J* = 1.6 Hz, 2H), 6.30 (ddd, *J* = 11.1, 9.2, 2.9 Hz, 1H), 6.11 (d, *J* = 7.9 Hz, 1H), 3.71 (s, 3H), 3.62 (dd, *J* = 14.6, 2.9 Hz, 1H), 3.54 (d, *J* = 11.2 Hz, 1H), 3.52 – 3.46 (m, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.3, 169.3, 166.8, 159.3, 153.7, 147.4, 142.8, 137.0, 136.7, 132.5, 131.6, 131.1, 130.7, 129.3, 129.2, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.3, 126.3, 125.4, 123.3, 122.9, 117.5, 114.0, 112.5, 110.0, 85.9, 73.9, 58.4, 55.0, 53.5, 49.2, 39.6.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{56}H_{42}N_4O_4$ 835.3279. Found 835.3279.

HPLC analysis: (IC column, Hexane: 2-propanol = 85:15, flow rate = 1.0 mL/min, wavelength = 254 nm): Rt_1 = 13.918, Rt_2 = 15.763.

3g:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(p-tolyl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 59.8 mg, 73% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 180-182 ℃. $[\alpha]_D^{rt}$ = + 42.0 (*c* 0.544, DCM), 96% ee, >20:1 d.r..

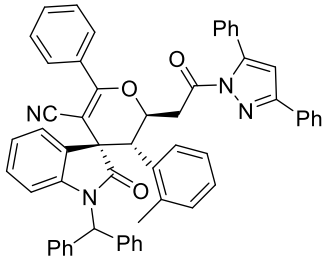
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.79 (t, *J* = 2.0 Hz, 1H), 7.77 (t, *J* = 1.6 Hz, 1H), 7.74 (t, *J* = 1.6 Hz, 1H), 7.72 (t, *J* = 2.4 Hz, 1H), 7.38 (d, *J* = 0.8 Hz, 1H), 7.36 (d, *J* = 2.0 Hz, 2H), 7.35 – 7.34 (m, 2H), 7.34 – 7.33 (m, 3H), 7.33 – 7.31 (m, 2H), 7.31 – 7.30 (m, 1H), 7.20 – 7.17 (m, 4H), 7.15 (d, *J* = 2.1 Hz, 2H), 7.13 (d, *J* = 2.2 Hz, 2H), 7.11 – 7.09 (m, 1H), 7.04 (d, *J* = 7.5 Hz, 2H), 7.01 (s, 1H), 6.86 (td, *J* = 7.8, 1.3 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 2H), 6.75 (s, 1H), 6.63 (s, 1H), 6.49 (d, *J* = 8.2 Hz, 2H), 6.27 (td, *J* = 8.8, 4.2 Hz, 1H), 6.01 (s, 1H), 3.52 (dd, *J* = 16.3, 2.9 Hz, 1H), 3.47 (d, *J* = 11.1 Hz, 1H), 3.40 (dd, *J* = 16.3, 9.3 Hz, 1H), 2.19 (s, 3H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.3, 169.2, 166.8, 153.7, 147.4, 142.8, 137.6, 137.1, 136.8, 132.6, 131.6, 131.1, 130.8, 130.6, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.8, 127.2, 126.4, 123.4, 122.9, 117.5, 112.5, 110.0, 86.0, 73.9, 58.9, 53.4, 49.6, 39.6, 21.2.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{56}H_{42}N_4O_3$ 819.3330. Found 819.3328.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 19.092, Rt_2 = 25.534.

3h:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(o-tolyl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 57.5 mg, 70% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 168-188 ℃. $[\alpha]_D^{rt}$ = + 37.9 (*c* 0.544, DCM), 90% ee, >20:1 d.r..

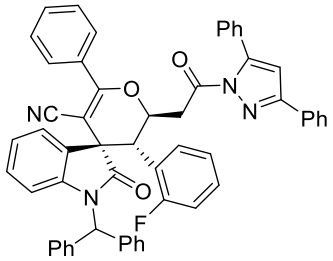
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.84 (d, *J* = 1.8 Hz, 1H), 7.82 (d, *J* = 1.4 Hz, 2H), 7.80 (d, *J* = 1.6 Hz, 1H), 7.48 – 7.47 (m, 1H), 7.46 – 7.44 (m, 1H), 7.43 (d, *J* = 1.6 Hz, 2H), 7.42 (s, 1H), 7.41 – 7.40 (m, 2H), 7.39 – 7.38 (m, 3H), 7.38 – 7.37 (m, 1H), 7.26 – 7.24 (m, 2H),7.23 (s, 2H), 7.22 (d, *J* = 3.2 Hz, 2H), 7.21 – 7.19 (m, 1H), 7.12 (d, *J* = 1.6 Hz, 2H), 7.11 – 7.04 (m, 2H), 7.02 (dd, *J* = 7.2, 0.8 Hz, 1H), 6.98 (d, *J* = 7.2 Hz, 1H), 6.92 (dd, *J* = 7.9, 1.3 Hz, 1H), 6.90 (s, 1H), 6.86 (t, *J* = 7.6 Hz, 1H), 6.69 (s, 1H), 6.65 (s, 1H), 6.63 (s, 1H), 6.25 (ddd, *J* = 10.8, 8.7, 3.3 Hz, 1H), 6.09 (d, *J* = 7.8 Hz, 1H), 4.06 (d, *J* = 10.8 Hz, 1H), 3.49 (dd, *J* = 15.2, 3.3 Hz, 1H), 3.37 (dd, *J* = 15.2, 8.7 Hz, 1H), 2.05 (s, 3H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.9, 169.1, 167.1, 153.7, 147.3, 142.8, 137.5, 137.0, 136.8, 132.6, 132.5, 131.6, 131.2, 131.0, 130.7, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.3, 127.0, 126.3, 124.3, 122.5, 117.4, 112.4, 110.0, 86.6, 74.9, 58.7, 53.8, 44.6, 39.1, 20.2.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{56}H_{42}N_4O_3$ 819.3330. Found 819.3324.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 11.015, Rt_2 = 26.167.

3i:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(2-fluorophenyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 65.8 mg, 80% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 183-185 ℃. $[\alpha]_D^{rt}$ = + 48.9 (*c* 0.629, DCM), 90% ee, >20:1 d.r..

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.78 (d, *J* = 1.9 Hz, 1H), 7.76 (d, *J* = 1.5 Hz, 1H), 7.75 (d, *J* = 1.2 Hz, 1H), 7.73 (d, *J* = 1.7 Hz, 1H), 7.42 (d, *J* = 7.7 Hz, 1H), 7.38 (t, *J* = 2.8 Hz, 1H), 7.37 – 7.35 (m, 2H), 7.34 (d, *J* = 1.6 Hz, 2H), 7.33 – 7.32 (m, 4H), 7.32 (s, 1H), 7.31 – 7.30 (m, 1H), 7.22 – 7.18 (m, 1H), 7.18 (s, 1H), 7.17 (s, 2H), 7.15 (d, *J* = 4.0 Hz, 1H), 7.14 (s, 1H), 7.12 – 7.11 (m, 1H), 7.08 – 7.04 (m, 3H), 7.00 (td, *J* = 7.6, 1.0 Hz, 1H), 6.86 (td, *J* = 7.9, 1.3 Hz, 1H), 6.80 (s, 1H), 6.75 (ddd, *J* = 9.7, 8.3, 1.2 Hz, 1H), 6.69 (td, *J* = 7.7, 1.2 Hz, 1H), 6.65 (s, 1H), 6.63 (d, *J* = 3.6 Hz, 2H), 6.31 (ddt, *J* = 11.9, 8.8, 2.2 Hz, 1H), 6.05 (d, *J* = 7.9 Hz, 1H), 4.08 (d, *J* = 11.1 Hz, 1H), 3.48 – 3.42 (m, 1H), 3.38 – 3.33 (m, 1H).

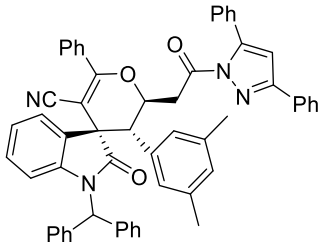
^{13}C NMR (100 MHz, chloroform-*d*) δ 175. 5, 168.2, 166.9, 153.8, 147.4, 142.4, 137.0, 136.9, 132.5, 131.6, 131.2, 130.7, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0,

127.9, 127.8, 127.4, 126.4, 125.0, 124.3, 123.0, 121.3, 117.2, 115. 7, 115.5, 112.1, 110.1, 86.3, 73.6, 58.8, 52.9, 40.6, 39.6.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{55}H_{39}FN_4O_3$ 823.3079. Found 823.3085.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 13.411, Rt_2 = 31.323.

3j:(2'S,3R,3'R)-1-benzhydryl-3'-(3,5-dimethylphenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxo ethyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 45.8 mg, 55% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 215-217 ℃. $[\alpha]_D^{rt}$ = + 81.5 (*c* 0.694, DCM), 91% ee, >20:1 d.r..

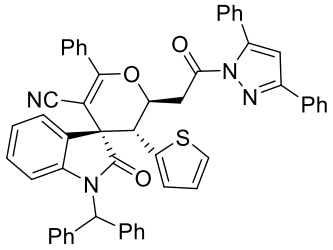
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.84 (d, *J* = 1.8 Hz, 1H), 7.82 – 7.83 (m, 2H), 7.80 (d, *J* = 1.6 Hz, 1H), 7.44 – 7.48 (m, 3H), 7.43 (dd, *J* = 3.2 Hz, 1.2 Hz, 2H), 7.40 – 7.42 (m, 2H), 7.39 (s, 4H), 7.37 – 7.38 (m, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.26 (s, 1H), 7.24 – 7.25 (m, 1H),7.23 (s, 1H), 7.22 (d, *J* = 1.6 Hz, 1H), 7.21 (s, 1H), 7.19 – 7.20 (m, 1H), 7.12 (t, *J* = 7.6 Hz, 2H), 7.03 (td, *J* = 7.5, 1.0 Hz, 1H), 6.92 (dd, *J* = 7.9, 1.4 Hz, 1H), 6.70 (s, 1H), 6.79 (s, 1H), 6.69 (s, 1H), 6.66 (s, 1H), 6.63 (d, *J* = 6.4 Hz, 2H), 6.21 (ddd, *J* = 10.8, 8.6, 3.3 Hz, 1H), 6.08 (d, *J* = 7.9 Hz, 1H), 4.00 (d, *J* = 10.8 Hz, 1H), 3.49 (dd, *J* = 16.0, 3.3 Hz, 1H), 3.38 (dd, *J* = 16.0, 8.7 Hz, 1H), 2.20 (s, 3H), 1.99 (s, 3H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.9, 169.2, 167.1, 153.6, 147.3, 142.8, 137.2, 137.1, 136.8, 132.5, 131.7, 131.6, 131.1, 130.8, 129.4, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.3, 127.2, 126.3, 124.3, 122.4, 117.5, 112.4, 110.0, 86.5, 74.9, 58.8, 53.8, 44.3, 39.0, 21.0, 20.1.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{57}H_{44}N_4O_3$ 833.3486. Found 833.3489.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 13.204, Rt_2 = 26.562.

3k:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(thiophen-2-yl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 77.4 mg, 96% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 226-228 ℃. $[\alpha]_D^{rt}$ = + 84.6 (*c* 0.731, DCM), 96% ee, >20:1 d.r..

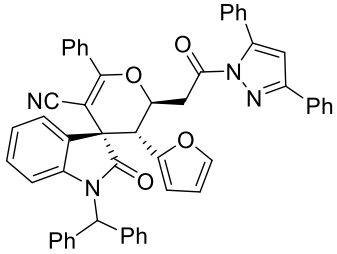
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.87 (t, *J* = 2.0 Hz, 1H), 7.86 (t, *J* = 1.6 Hz, 1H), 7.79 (d, *J* = 1.2 Hz, 1H), 7.77 (d, *J* = 1.6 Hz, 1H), 7.44 - 7.46 (m, 2H), 7.42 – 7.43 (m, 3H), 7.41 (d, *J* = 0.8 Hz, 4H), 7.39 – 7.40 (m, 2H), 7.37 – 7.38 (d, *J* = 2.8 Hz, 1H), 7.31 – 7.35 (m, 1H), 7.25 (d, *J* = 0.8 Hz, 2H), 7.24 (s, 2H), 7.22 – 7.23 (d, *J* = 3.2 Hz, 1H), 7.19 – 7.20 (m, 1H), 7.17 – 7.18 (m, 1H)，7.11 (t, *J* = 7.6 Hz, 1H), 7.03 (dd, *J* = 4.8, 0.4 Hz, 1H), 6.98 (td, *J* = 7.8, 1.3 Hz, 1H), 6.87 (s, 1H), 6.84 (dd, *J* = 3.6, 1.0 Hz, 1H), 6.75 (t, *J* = 2.6 Hz, 2H), 6.73 (t, *J* = 1.7 Hz, 1H), 6.71 (s, 1H), 6.28 (ddd, *J* = 11.4, 8.7, 3.0 Hz, 1H), 6.18 (d, *J* = 7.9 Hz, 1H), 3.92 (d, *J* = 10.9 Hz, 1H), 3.71 – 3.75 (m, 1H), 3.56 (dd, *J* = 16.5, 8.7 Hz, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.4, 169.4, 166.8, 153.8, 147.4, 143.0, 137.0, 136.9, 134.9, 132.4, 131.6, 131.2, 130.7, 129.3, 129.2, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.32, 128.2, 128.0, 127.8, 127.6, 127.5, 127.4, 127.1, 126.6, 126.4, 125.2, 123.3, 123.1, 117.3, 112.5, 110.08, 85.6, 73.9, 58.7, 53.2, 45.2, 39.3.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{53}H_{38}N_4O_3S$ 811.2737. Found 811.2729.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 20.116, Rt_2 = 42.101.

3l:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(furan-2-yl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 70.7 mg, 89% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 219-221 ℃. $[\alpha]_D^{rt}$ = + 81.5 (*c* 0.694, DCM), 85% ee, >20:1 d.r..

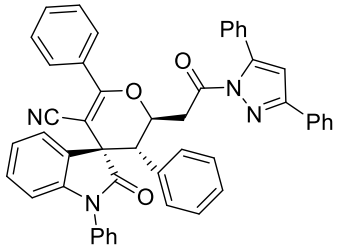
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.78 (d, *J* = 1.9 Hz, 1H), 7.76 (d, *J* = 1.6 Hz, 1H), 7.71 (d, *J* = 2.0 Hz, 1H), 7.69 (d, *J* = 1.7 Hz, 1H), 7.34 – 7.36 (m, 2H), 7.32 (s, 3H), 7.31 – 7.32 (m, 3H), 7.30 (s, 2H), 7.28 (d, *J* = 1.2 Hz, 2H), 7.17 (s, 2H), 7.17 (s, 4H), 7.14 - 7.16 (m, 2H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.93 (s, 1H), 6.92 (d, *J* = 0.8 Hz, 2H), 6.89 (s, 1H), 6.86 (s, 1H), 6.62 (s, 1H), 6.18 – 6.13 (m, 2H), 5.97 (dd, *J* = 3.3, 1.8 Hz, 1H), 5.82 (d, *J* = 3.2 Hz, 1H), 3.78 (d, *J* = 10.9 Hz, 1H), 3.48 (s, 1H), 3.47 (s, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.4, 168.8, 167.0, 153.7, 147.7, 147.4, 142.8, 137.1, 137.0, 132.4, 131.6, 131.2, 130.7, 129.3, 129.2, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.0, 127.8, 127.6, 126.3, 123.3, 123.1, 117.3, 112.4, 110.4, 110.1, 110.0, 85.6, 72.7, 58.9, 51.8, 44.1, 38.8.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{53}H_{38}N_4O_4$ 795.2966. Found 795.2958.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 19.662, Rt_2 = 62.790.

4a:(2'S,3R,3'R)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-1,3',6'-triphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 70.9 mg, 99% yield (hexanes/Dichloromethane, v:v = 1:4), Mp 200-202 ℃. $[\alpha]_D^{rt}$ = + 31.5 (*c* 0.379, DCM), 69% ee, >20:1 d.r..

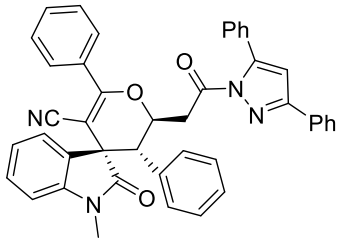
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (d, *J* = 2.0 Hz, 2H), 7.83 (d, *J* = 1.6 Hz, 2H), 7.52 (dd, *J* = 7.1, 1.5 Hz, 1H), 7.49 – 7.46 (m, 1H), 7.46 – 7.43 (m, 2H), 7.42 – 7.41 (m, 6H), 7.40 – 7.39 (m, 3H), 7.39 – 7.28 (m, 3H), 7.25 (s, 1H), 7.23 – 7.22 (m, 1H), 7.21 (d, *J* = 0.8 Hz, 1H), 7.19 (dd, *J* = 2.8, 1.6 Hz, 1H), 7.16 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.01 – 6.98 (m, 1H), 6.89 (d, *J* = 7.2 Hz, 2H), 6.71 (s, 1H), 6.44 (dd, *J* = 7.5, 1.3 Hz, 1H), 6.31 (ddd, *J* = 11.6, 9.1, 2.9 Hz, 1H), 3.65 (dd, *J* = 16.4, 2.9 Hz, 1H), 3.59 (d, *J* = 11.1 Hz, 1H), 3.51 (dd, *J* = 16.4, 9.1 Hz, 1H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 169.1, 167.5, 153.8, 147.4, 143.9, 133.8, 133.5, 132.5, 131.6, 131.2, 130.7, 129.5, 129.41, 129.3, 129.0, 128.9, 128.8, 128.7, 128.5, 128.4, 128.3, 128.2, 128.0, 126.7, 126.4, 123.7, 123.6, 117.5, 114.1, 110.1, 109.7, 85.0, 73.4, 54.2, 50.9, 39.4, 29.7.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{48}H_{34}N_4O_3$ 715.2704. Found 715.2708.

HPLC analysis: (IA column, Hexane: 2-propanol = 75:25, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 30.940, Rt_2 = 34.639.

4b:(2'S,3R,3'R)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-1-methyl-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 54.4 mg, 84% yield (hexanes/Dichloromethane, v:v = 1:4), Mp 216-218 ℃. $[\alpha]_D^{rt}$ = + 80.0 (*c* 0.528, DCM), 75% ee, >20:1 d.r..

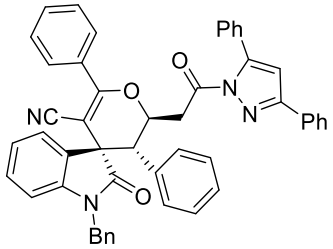
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.79 (d, *J* = 1.7 Hz, 1H), 7.77 (d, *J* = 1.3 Hz, 1H), 7.75 (d, *J* = 1.1 Hz, 1H), 7.73 (d, *J* = 1.7 Hz, 1H), 7.40 – 7.38 (m, 3H), 7.36 (d, *J* = 1.6 Hz, 2H), 7.35 – 7.34 (m, 5H), 7.33 – 7.31 (m, 3H), 7.18 (s, 3H), 7.15 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.10 (d, *J* = 7.2 Hz, 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 6.64 (s, 1H), 6.45 (d, *J* = 7.7 Hz, 1H), 6.23 (ddd, *J* = 11.6, 9.3, 2.9 Hz, 1H), 3.54 – 3.49 (m, 1H), 3.42 – 3.35 (m, 2H), 2.80 (s, 3H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 174.8, 169.1, 167.4, 153.8, 147.4, 143.6, 133.4, 132.6, 131.6, 131.2, 130.7, 129.5, 129.3, 129.1, 129.0, 128.9, 128.8, 128.5, 128.3, 128.1, 1280, 126.4, 123.4, 123.2, 117.5, 110.1, 108.4, 84.7, 73.4, 54.0, 50.8, 39.6, 26.2.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{43}H_{32}N_4O_3$ 653.2574. Found 653.2569.

HPLC analysis: (IA column, Hexane: 2-propanol = 75:25, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 12.944, Rt_2 = 16.351.

4c:(2'S,3R,3'R)-1-benzyl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 72.8 mg, 99% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 230-232 ℃. $[\alpha]_D^{rt}$ = + 63.8 (*c* 0.694, DCM), 84% ee, >20:1 d.r..

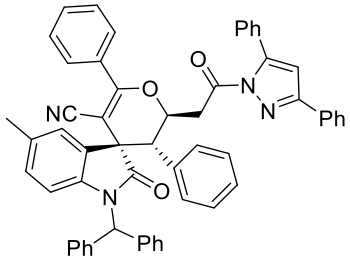
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.79 (d, *J* = 1.9 Hz, 1H), 7.78 (d, *J* = 1.4 Hz, 1H), 7.75 (d, *J* = 1.2 Hz, 1H), 7.73 (d, *J* = 1.6 Hz, 1H), 7.48 – 7.41 (m, 1H), 7.40 – 7.39 (m, 1H), 7.38 (d, *J* = 2.8 Hz, 1H), 7.37 (s, 1H), 7.36 – 7.35 (m, 1H), 7.35 – 7.34 (m, 5H), 7.33 (d, *J* = 2.0 Hz, 1H), 7.32 (s, 1H), 7.31 – 7.28 (m, 1H), 7.17 (s, 2H), 7.05 – 7.01 (m, 2H), 7.08 (d, *J* = 2.1 Hz, 2H), 7.06 (d, *J* = 2.8 Hz, 1H), 7.05 – 7.03 (m, 1H), 6.67 – 6.65 (m, 1H), 6.42 (s, 1H), 6.63 – 6.62 (m, 1H), 6.33 – 6.27 (m, 2H), 4.75 – 4.71 (m, 1H), 4.55 – 4.51 (m, 1H), 3.58 – 3.53 (m, 1H), 3.51 (d, *J* = 11.2 Hz, 1H), 3.41 (dd, *J* = 15.2, 9.3 Hz, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 174.9, 169.2, 167.1, 153.8, 147.4, 143.0, 134.7, 133.7, 132.5, 131.6, 131.2, 130.8, 129.5, 129.3, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.1, 128.0, 127.3, 126.7, 126.4, 123.5, 123.3, 117.4, 110.1, 109.9, 85.7, 73.8, 53.9, 50.0, 44.0, 39.7.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{49}H_{36}N_4O_3$ 729.2860. Found 729.2864.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 29.564, Rt_2 = 34.927.

4d:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-5-methyl-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 74.4 mg, 91% yield (hexanes/Dichloromethane, v:v = 1:1), Mp 150-152 ℃. $[\alpha]_D^{rt}$ = + 50.8 (*c* 0.680, DCM), 94% ee, >20:1 d.r..

^{1}H NMR (400 MHz, chloroform-*d*) δ 7.85 (s, 1H), 7.84 (s, 1H), 7.82 (s, 1H), 7.80 (d, *J* = 1.7 Hz, 1H), 7.46 – 7.43 (m, 3H), 7.42 (s, 1H), 7.40 (d, *J* = 2.3 Hz, 5H), 7.38 (s, 2H), 7.36 – 7.34 (m, 1H), 7.27 –

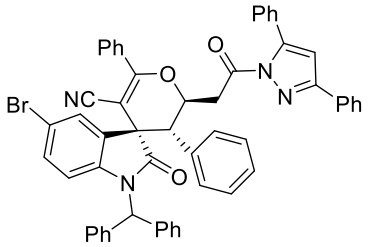
7.23 (m, 3H), 7.22 (s, 1H), 7.21 – 7.18 (m, 5H), 7.09 (t, *J* = 5.2 Hz, 2H), 7.06 (t, *J* = 7.6 Hz, 2H), 6.80 (s, 1H), 6.71 (d, *J* = 7.6 Hz, 1H), 6.70 (s, 1H), 6.50 (d, *J* = 7.6 Hz, 2H), 6.36 (ddd, *J* = 11.6, 9.2, 2.9 Hz, 1H), 5.96 (d, *J* = 8.1 Hz, 1H), 3.64 – 3.57 (m, 2H), 3.50 – 3.44 (m, 1H), 2.33 (s, 3H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.8, 169.2, 166.5, 153.7, 147.3, 138.2, 138.0, 134.7, 133.9, 132.8, 132.6, 131.7, 131.0, 130.7, 130.2, 130.1, 129.0, 129.9, 128.8, 128.5, 128.3, 128.2, 128.0, 127.4, 127.1, 126.4, 122.2, 117.9, 110.0, 86.6, 73.9, 52.9, 50.0, 39.7, 30.2, 20.9.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{56}H_{42}N_4O_3$ 819.3330. Found 819.3329.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 14.208, Rt_2 = 23.789.

4e:(2'S,3R,3'R)-1-benzhydryl-5-bromo-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3', 6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 76.4 mg, 86% yield (hexanes/Dichloromethane, v:v = 1:1), Mp 213-215 ℃. $[\alpha]_D^{rt}$ = + 31.0 (*c* 0.686, DCM), 86% ee, >20:1 d.r..

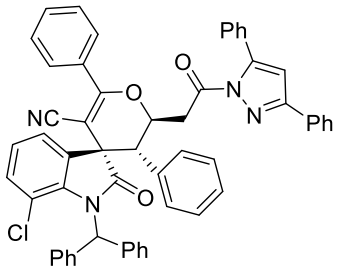
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.86 (d, *J* = 1.8 Hz, 1H), 7.84 (s, 1H), 7.82 (s, 1H), 7.79 (d, *J* = 1.7 Hz, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.47 (d, *J* = 7.2 Hz ,1H), 7.45 (s, 1H), 7.44 (s, 1H), 7.42 (s, 6H), 7.40 (d, *J* = 1.2 Hz, 2H), 7.38 (s, 1H), 7.25 – 7.28 (d, *J* = 6.8 Hz, 2H), 7.24 (s, 2H), 7.21 (d, *J* = 7.2 Hz, 2H), 7.18 (d, *J* = 2.2 Hz, 1H), 7.16 (s, 1H), 7.13 (s, 1H), 7.11 (s, 1H), 7.11 (s, 1H), 7.08 – 7.09 (m, 1H), 7.05 (dd, *J* = 8.6, 2.0 Hz, 1H), 6.80 (s, 1H), 6.71 (s, 1H), 6.47 (s, 1H), 6.45 (s, 1H), 6.32 (ddd, *J* = 11.5, 8.7, 3.2 Hz, 1H), 5.95 (d, *J* = 8.5 Hz, 1H), 3.57 - 3.61 (m, 2H), 3.51 (dd, *J* = 6.8 Hz, 15.0Hz, 8.8 Hz, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 174.8, 169.0, 167.2, 153.8, 147.4, 141.8, 136.6, 136.3, 133.3, 132.3, 131. 9, 131.5, 131.3, 131.2, 130.7, 129.3, 129.0, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.0, 127.9, 127.5, 126.5, 126.3, 117.3, 115.8, 113.9, 110.1, 85.3, 73.7, 58.6, 53.5, 49.9, 39.3.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{55}H_{39}BrN_4O_3$ 883.2278. Found 883.2270.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 15.225, Rt_2 = 19.427.

4f:(2'S,3R,3'R)-1-benzhydryl-7-chloro-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3', 6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



Colorless solid, 71.1 mg, 85% yield (hexanes/Dichloromethane, v:v = 1:1), Mp 176-178 ℃. $[\alpha]_D^{rt}$ = + 46.8 (*c* 0.687, DCM), 94% ee, >20:1 d.r..

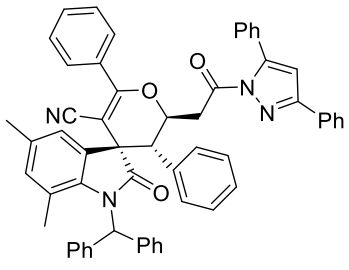
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.75 (d, *J* = 2.4 Hz, 1H), 7.73 (d, *J* = 1.7 Hz, 1H), 7.69 (s, 1H), 7.67 (d, *J* = 1.7 Hz, 1H), 7.38 – 7.37 (m, 1H), 7.36 – 7.35 (m, 2H), 7.33 – 7.31 (m, 4H), 7.30 (s, 1H), 7.29 – 7.28 (m, 4H), 7.26 – 7.23 (m, 1H), 7.20 – 7.18 (m, 4H), 7.16 – 7.13 (m, 5H), 7.10 (d, *J* = 8.4 Hz, 2H), 7.07 (s, 1H), 7.05 (d, *J* = 8.0 Hz, 2H), 7.03 – 6.95 (m, 3H), 6.61 (s, 1H), 6.17 (t, *J* = 10.3 Hz, 1H), 3.51 (dd, *J* = 15.2, 2.8 Hz, 1H), 3.43 (d, *J* = 11.0 Hz, 1H), 3.29 – 3.29 (m, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.3, 169.0, 167.1, 153.8, 147.4, 139.9, 137.9, 133.1, 132.8, 132.4, 131.6, 131.3, 130.6, 129.3, 128.9, 128.8, 128.5, 128.3, 128.2, 128.1, 128.0, 128.0, 127.4, 126.4, 124.1, 122.5, 117.6, 110.1, 85.5, 73.8, 53.0, 49.9, 39.6, 31.5.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{55}H_{39}ClN_4O_3$ 839.2783. Found 839.2789.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 10.884, Rt_2 = 16.461.

4g:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-5,7-dimethyl-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 42.1 mg, 51% yield (hexanes/Dichloromethane, v:v = 1:1), Mp 195-197 ℃. $[\alpha]_D^{rt}$ = +11.7 (*c* 0.381, DCM), 95% ee, >20:1 d.r..

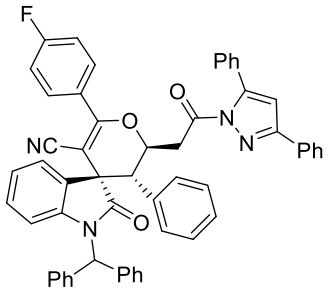
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 (d, *J* = 2.1 Hz, 1H), 7.82 (d, *J* = 1.6 Hz, 1H), 7.79 (d, *J* = 1.2 Hz, 1H), 7.77 (d, *J* = 1.7 Hz, 1H), 7.46 – 7.44 (m, 1H), 7.42 (d, *J* = 1.6 Hz, 1H), 7.41 (d, *J* = 1.6 Hz, 1H), 7.41 – 7.40 (m, 3H), 7.39 – 7.37 (m, 5H), 7.36 (s, 1H), 7.26 – 7.25 (m, 2H),7.24 (d, *J* = 2.0 Hz, 2H), 7.23 – 7.19 (m, 2H), 7.18 (s, 1H), 7.17 – 7.16 (m, 2H), 7.23 – 6.99 (m, 5H), 6.91 – 6.79 (m, 2H), 6.73 (s, 1H), 6.69 (s, 1H), 6.30 (t, *J* = 6.4 Hz, 1H), 3.61 (dd, *J* = 16.0, 2.8 Hz, 1H), 3.55 (d, *J* = 11.1 Hz, 1H), 3.38 (dd, *J* = 16.0, 9.3 Hz, 1H), 2.37 (s, 3H), 1.57 (s, 3H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 169.2, 166.5, 153.7, 147.3, 138.2, 138.0, 134.7, 133.9, 132.8, 132.6, 131.6, 131.0, 130.7, 130.2, 129.2, 129.0, 128.9, 128.8, 128.4, 128.3, 128.2, 128.0, 127.3, 127.1, 126.4, 122.2, 117.9, 110.0, 86.6, 73.9, 52.9, 50.0, 39.7, 29.7, 26.9, 20.9.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{57}H_{44}N_4O_3$ 833.3486. Found 833.3490.

HPLC analysis: (IB column, Hexane: 2-propanol = 85:15, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 12.588, Rt_2 = 14.470.

4h:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-6'-(4-fluorophenyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 67.4 mg, 82% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 188-190 ℃. $[\alpha]_D^{rt}$ = + 60.1 (*c* 0.651, DCM), 90% ee, >20:1 d.r..

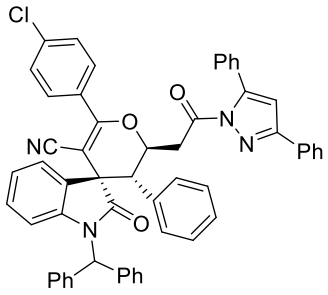
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 (d, *J* = 1.9 Hz, 1H), 7.84 – 7.85 (m, 1H), 7.82 – 7.83 (m, 1H), 7.79 – 7.81 (m, 1H), 7.46 (d, *J* = 1.4 Hz, 1H), 7.44 (s, 1H), 7.42 (s, 4H), 7.40 – 7.41 (m, 1H), 7.25 (s, 1H), 7.22 – 7.23 (m, 3H), 7.21 (s, 1H), 7.20 (s, 1H), 7.19 (s, 1H), 7.18 (s, 1H), 7.13 (s, 1H), 7.11 (s, 1H), 7.08 – 7.10 (m, 3H), 7.06 (s, 2H), 7.04 (d, *J* = 2.0 Hz), 6.94 (td, *J* = 7.8, 1.3 Hz, 1H), 6.81 (s, 1H), 6.72 (s, 1H), 6.53 (s, 1H), 6.51 (s, 1H), 6.36 (ddd, *J* = 11.7, 9.2, 2.9 Hz, 1H), 6.09 (d, *J* = 7.9 Hz, 1H), 3.59 – 3.63 (m, 1H) , 3.57 (d, *J* = 7.2 Hz, 1H), 3.48 (dd, *J* = 15.2Hz, 1H).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 175.2, 169.1, 165.7, 153.8, 147.4, 142.7, 137.1, 136.7, 133.6, 131.6, 130.7, 130.6, 129.3, 129.1, 129.0, 128.9, 128.8, 128.6, 128.5, 128.3, 128.2, 128.1 128.0, 127.8, 127.3, 126.3, 123.4, 122.9, 117.4, 115.6, 115.4, 112.5, 110.1, 85.9, 73.8, 58.7, 53.3, 49.9, 39.5.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{55}H_{39}FN_4O_3$ 823.3079. Found 823.3077.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt$_1$ = 16.495, Rt$_2$ = 54.563.

4i:(2'S,3R,3'R)-1-benzhydryl-6'-(4-chlorophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 79.1 mg, 94% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 218-220 ℃. $[\alpha]_D^{rt}$ = + 60.2 (*c* 0.751, DCM), 84% ee, >20:1 d.r..

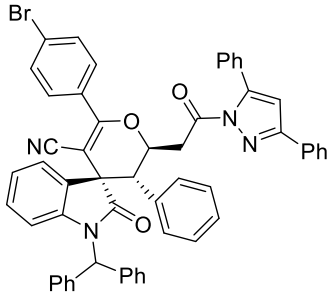
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.86 (d, *J* = 1.9 Hz, 1H), 7.84 (s, 1H), 7.76 (s, 1H), 7.73 (s, 1H), 7.45 (s, 1H), 7.44 (s, 2H), 7.42 (s, 4H), 7.41 (s, 2H), 7.34 - 7.36 (m, 3H), 7.25 (s, 1H), 7.23 (s, 2H), 7.21 (s, 1H), 7.20 (d, *J* = 2.1 Hz, 2H), 7.18 (s, 1H), 7.12 (d, *J* = 7.4 Hz, 2H), 7.04 – 7.09 (m, 4H), 6.94 (t, *J* = 7.8 Hz, 1H), 6.81 (s, 1H), 6.72 (s, 1H), 6.53 (s, 1H), 6.51 (s, 1H), 6.35 (ddd, *J* = 11.4, 9.2, 2.9 Hz, 1H), 6.09 (d, *J* = 8.0 Hz, 1H), 3.63 – 3.56 (m, 2H), 3.48 (dd, *J* =15.2, 9.2 Hz, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.1, 169.1, 165.6, 153.8, 147.4, 142.7, 137.2, 136.9, 136.7, 133.5, 131.5, 130.9, 130.7, 129.7, 129.3, 129.1, 129.0, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.3, 126.3, 123.4, 123.0, 117.2, 112.5, 110.1, 86.4, 73.9, 58.7, 53.3, 49.8, 39.4.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{55}H_{39}ClN_4O_3$ 839.2783. Found 839.2788.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt$_1$ = 16.017, Rt$_2$ = 77.164.

4j:(2'S,3R,3'R)-1-benzhydryl-6'-(4-bromophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 87.5 mg, 99% yield (hexanes/Dichloromethane, v:v = 1:1), Mp 194-196 ℃. $[\alpha]_D^{rt}$ = + 62.0 (*c* 0.864, DCM), 89% ee, >20:1 d.r..

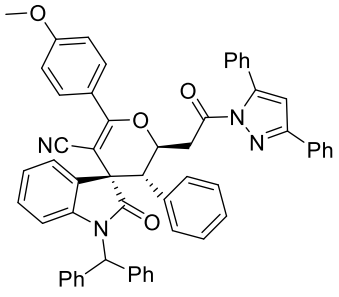
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.77 (s, 1H), 7.75 (s, 1H), 7.60 (s, 1H), 7.58 (s, 1H), 7.42 (s, 1H), 7.40 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 4H), 7.32 (d, *J* = 8.5 Hz, 5H), 7.29 – 7.28 (m, 1H), 7.18 – 7.16 (m, 1H), 7.13 (d, *J* = 7.7 Hz, 3H), 7.11 – 7.09 (m, 4H), 7.03 (d, *J* = 7.8 Hz, 2H), 7.00 (s, 1H), 6.96 (t, *J* = 6.4 Hz, 2H), 6.84 (t, *J* = 7.8 Hz, 1H), 6.72 (s, 1H), 6.62 (s, 1H), 6.43 (d, *J* = 7.6 Hz, 2H), 6.27 (ddd, *J* = 11.5, 9.1, 2.9 Hz, 1H), 6.00 (d, *J* = 8.0 Hz, 1H), 3.53 – 3.48 (m, 2H), 3.40 (dd, *J* = 15.2, 9.1 Hz, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.1, 169.1, 165.6, 153.8, 147.4, 142.7, 136.9, 136.7, 133.5, 132.2, 131.56, 131.4, 130.7, 129.9, 129.5, 129.3, 129.0, 128.9, 128.7, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 128.0, 127.8, 127.3, 127.0, 126.3, 125.7, 123.4, 123.0, 117.1, 112.5, 110.1, 86.4, 73.9, 58.7, 53.3, 49.8, 39.4.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{55}H_{39}BrN_4O_3$ 883.2278. Found 883.2281.

HPLC analysis: (IC column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 9.764, Rt_2 = 16.967.

4k:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-6'-(4-methoxyphenyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 76.2 mg, 91% yield (hexanes/Dichloromethane, v:v = 1:2), Mp 211-213 ℃. $[\alpha]_D^{rt}$ = + 56.7 (*c* 0.565, DCM), 93% ee, >20:1 d.r..

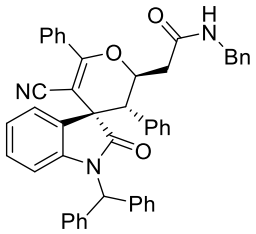
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.79 (d, *J* = 1.8 Hz, 1H), 7.77 (t, *J* = 1.7 Hz, 1H), 7.71 (d, *J* = 2.0 Hz, 1H), 7.69 (d, *J* = 2.1 Hz, 1H), 7.39 (s, 1H), 7.36 – 7.37 (m, 2H), 7.35 (s, 3H), 7.34 (s, 1H), 7.18 (s, 5H), 7.15 (d, *J* = 1.7 Hz, 2H), 7.14 (s, 2H), 7.11 (d, *J* = 7.2 Hz, 2H), 7.04 (d, *J* = 7.6 Hz, 2H), 7.02 (s, 1H), 6.98 (t, *J* = 7.6 Hz, 2H), 6.85 (td, *J* = 7.8, 1.2 Hz, 1H), 6.81 (s, 1H), 6.79 (s, 1H), 6.74 (s, 1H), 6.64 (s, 1H), 6.46 (s, 1H), 6.45 (s, 1H), 6.25 – 6.30 (m, 1H), 6.01 (d, *J* = 7.9 Hz, 1H), 3.75 (s, 3H), 3.48 – 3.56 (m, 2H), 3.38 (dd, *J* = 15.2, 9.3 Hz, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.4, 169.2, 166.4, 161.8, 153.8, 147.4, 142.7, 137.0, 136.8, 133.8, 131.6, 130.8, 130.1, 129.3, 129.2, 129.0, 128.9, 128.8, 128.6, 128.5, 128.3, 128.1, 128.0, 127.8, 127.2, 126.4, 124.8, 123.8, 122.9, 117.9, 113.6, 112.4, 110.1, 84.5, 73.6, 58.6, 55.4, 53.4, 50.1, 39.6.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{56}H_{42}N_4O_4$ 835.3279. Found 835.3270.

HPLC analysis: (IC column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt_1 = 19.145, Rt_2 = 28.956.

5:2-((2'S,3R,3'R)-1-benzhydryl-5'-cyano-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-2'-yl)-N-benzylacetamide



White solid, 58.9 mg, 85% yield (hexanes/ ethyl acetate, v:v = 2:1), Mp 206-208 ℃. $[\alpha]_D^{rt}$ = + 37.2 (*c* 0.574, DCM), 99% ee, >20:1 d.r..

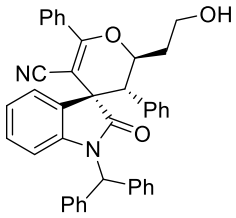
^{1}H NMR (400 MHz, chloroform-*d*) δ 7.66 (d, *J* = 7.6 Hz, 2H), 7.38 – 7.27 (m, 4H), 7.17 (s, 2H), 7.16 – 7.15 (m, 2H), 7.15 (d, *J* = 2.0 Hz, 1H), 7.14 (s, 1H), 7.14 – 7.13 (m, 2H), 7.12 – 7.11 (m, 3H), 7.10 – 7.10 (m, 2H), 7.03 (d, *J* = 7.6 Hz, 2H), 6.99 (d, *J* = 6.4 Hz,1H), 6.97 – 6.91 (m, 2H) 6.83 (td, *J* = 7.8, 1.2 Hz, 1H), 6.73 (s, 1H), 6.43 (d, *J* = 7.7 Hz, 2H), 6.05 – 5.96 (m, 2H), 5.92 (t, *J* = 5.8 Hz, 1H), 4.38 – 4.28 (m, 2H), 3.42 (d, *J* = 11.0 Hz, 1H), 2.55 (dd, *J* = 15.1, 3.1 Hz, 1H), 2.27 (dd, *J* = 15.1, 8.2 Hz, 1H).

^{13}C NMR (100 MHz, chloroform-*d*) δ 175.4, 168.6, 166.8, 142.7, 137.9, 136.9, 136.7, 133.7, 132.5, 131.2, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.1, 128.0, 127.8, 127.6, 127.3, 123.3, 122.9, 117.3, 112.5, 86.4, 74.1, 58.7, 53.3, 49.8, 43.7, 39.8.

HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{47}H_{37}N_3O_3$ 692.2908. Found 692.2900.

HPLC analysis: (IC column, Hexane: 2-propanol = 85:15, flow rate = 0.6 mL/min, wavelength = 254 nm): Rt$_1$ = 33.406, Rt$_2$ = 38.946.

6.(2'S,3R,3'R)-1-benzhydryl-2'-(2-hydroxyethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



White solid, 58.5 mg, 99% yield (hexanes/ ethyl acetate, v:v = 3:1), Mp 190-192 ℃. $[\alpha]_D^{rt}$ = + 59.3 (*c* 0.582, DCM), 93% ee, >20:1 d.r..

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.75 (d, *J* = 1.6 Hz, 1H), 7.74 (d, *J* = 1.9 Hz, 1H), 7.38 – 7.36 (m, 1H), 7.35 (d, *J* = 2.0 Hz, 1H), 7.32 – 7.34 (m, 2H), 7.18 – 7.16 (m, 2H), 7.14 – 7.13 (m, 2H), 7.12 (d, *J* = 2.0 Hz, 2H), 7.11 – 7.06 (m, 3H), 7.04 – 7.01 (m, 2H), 6.99 (d, *J* = 2.0 Hz, 1H), 6.93 (t, *J* = 7.6 Hz, 2H), 6.82 (td, *J* = 7.8, 1.3 Hz, 1H), 6.73 (s, 1H), 6.43 (d, *J* = 7.4 Hz, 2H), 5.98 (d, *J* = 7.9 Hz, 1H), 5.74 (ddd, *J* = 11.5, 9.7, 2.3 Hz, 1H), 3.80 (ddt, *J* = 14.6, 10.8, 5.3 Hz, 2H), 3.25 (d, *J* = 11.0 Hz, 1H), 2.06 – 1.97 (m, 1H), 1.84 (dtd, *J* = 14.4, 7.7, 7.1, 2.4 Hz, 1H), 1.62 (ddt, *J* = 14.9, 10.3, 5.4 Hz, 1H).

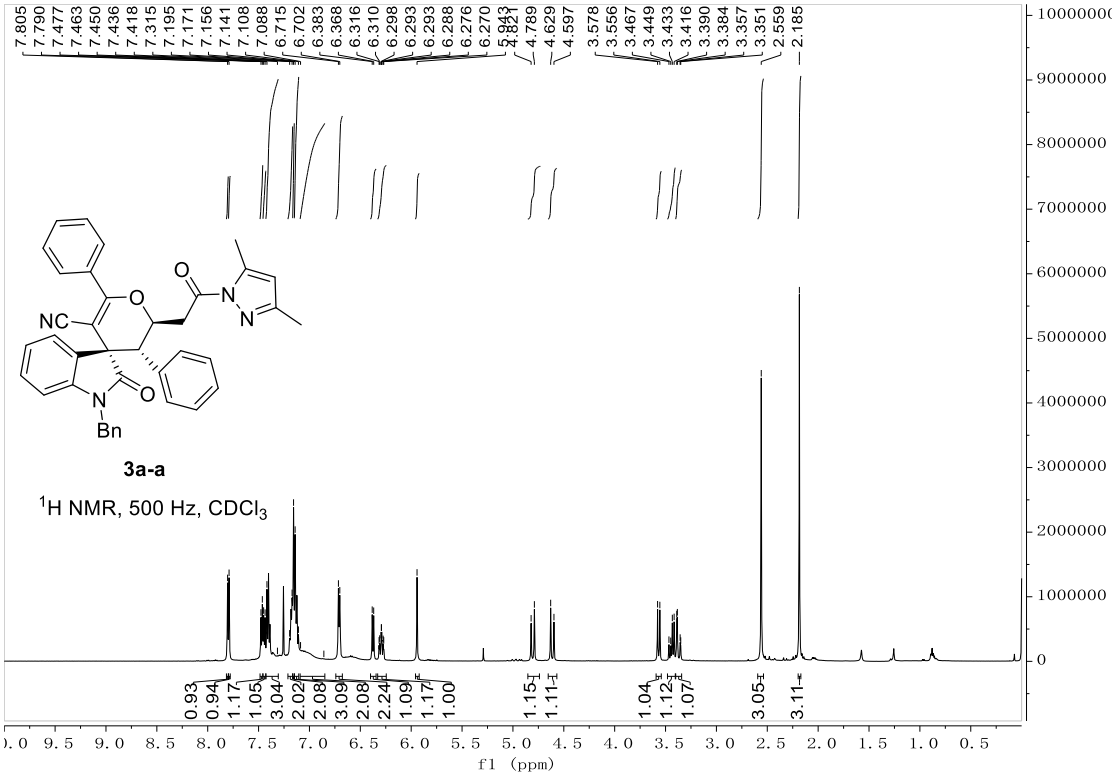
^{13}C NMR (100 MHz, Chloroform-*d*) δ 174.6, 166.0, 141.6, 135.9, 135.6, 133.1, 131.7, 130.2, 128.1, 127.8, 127.5, 127.4, 127.3, 127.2, 127.0, 126.8, 126.7, 126.3, 122.2, 121.9, 116.5, 111.5, 84.9, 73.7, 58.1, 57.6, 52.4, 49.6, 34.2.

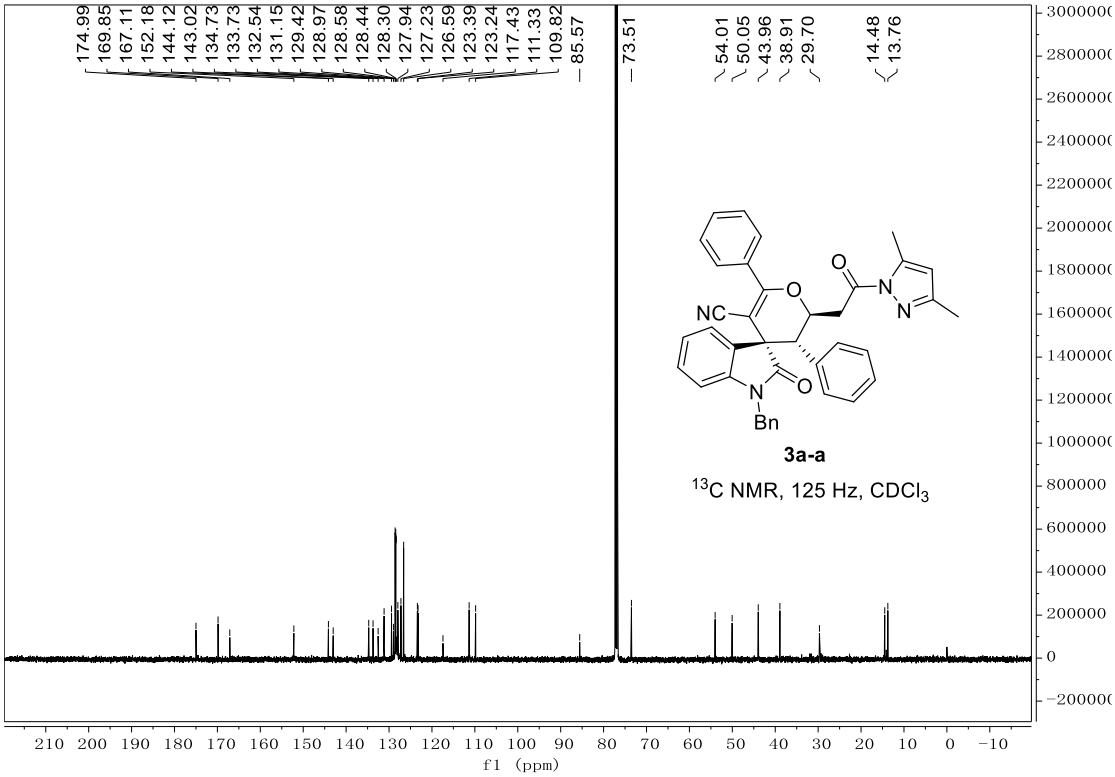
HRMS (ESI+TOF): $[M+H]^+$ Calcd for $C_{40}H_{32}N_2O_3$ 589.2486. Found 589.2489.

HPLC analysis: (IA column, Hexane: 2-propanol = 80:20, flow rate = 0.8 mL/min, wavelength = 254 nm): Rt$_1$ = 8.790, Rt$_2$ = 42.218.

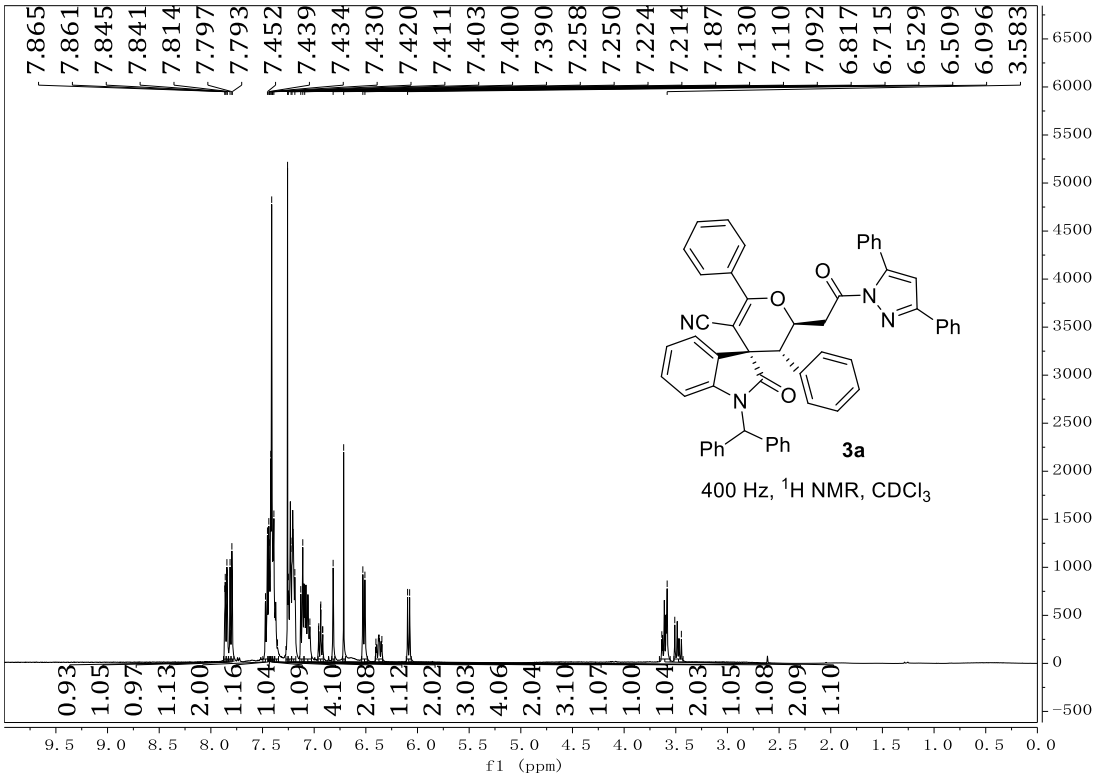
VII. ^{1}H NMR and ^{13}C NMR spectra.

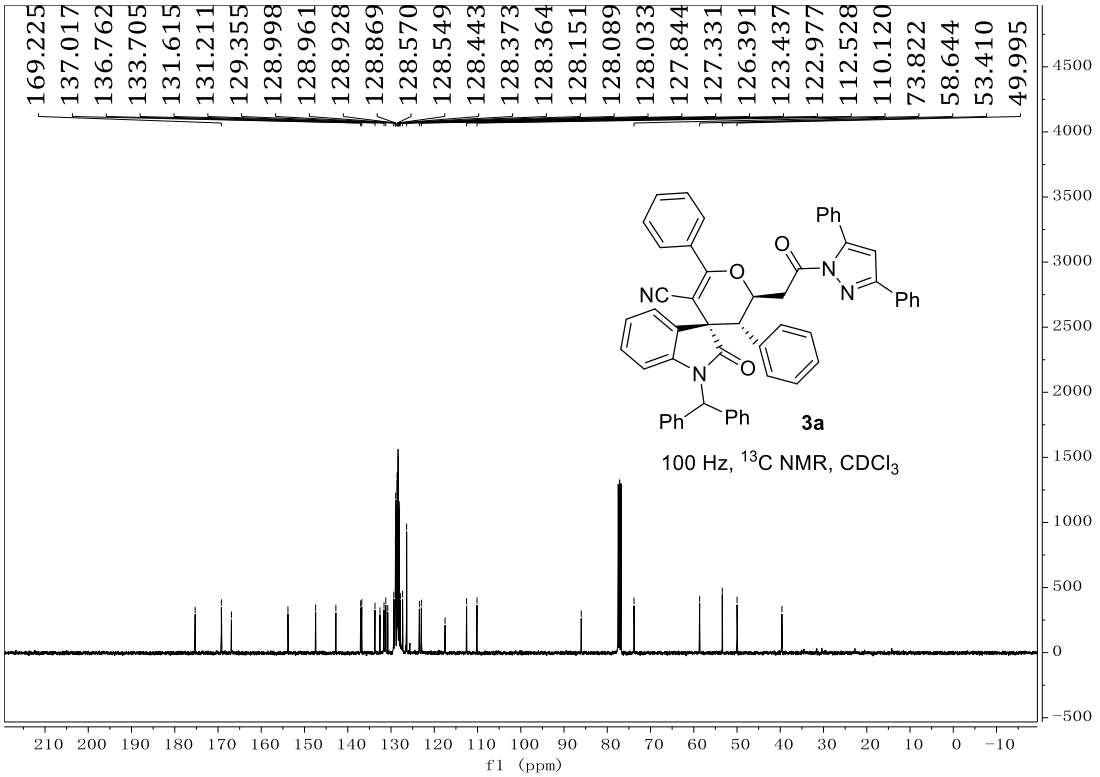
3a-a:(2'S,3R,3'R)-1-benzyl-2'-(2-(3,5-dimethyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



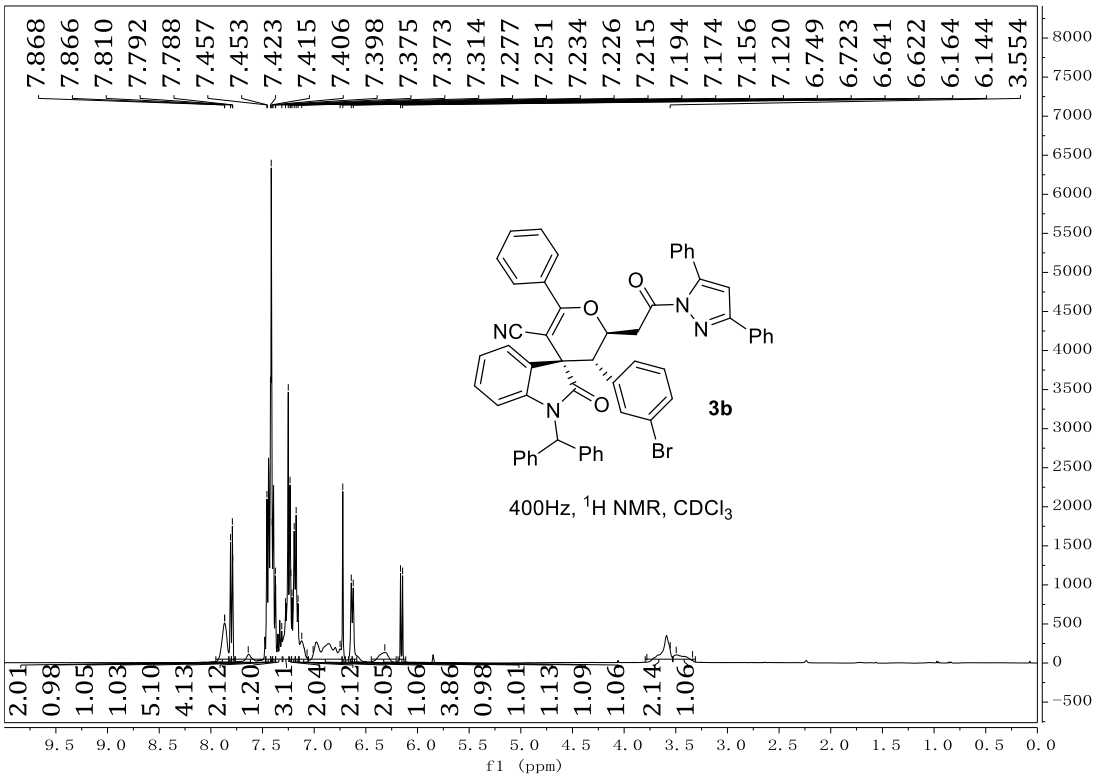


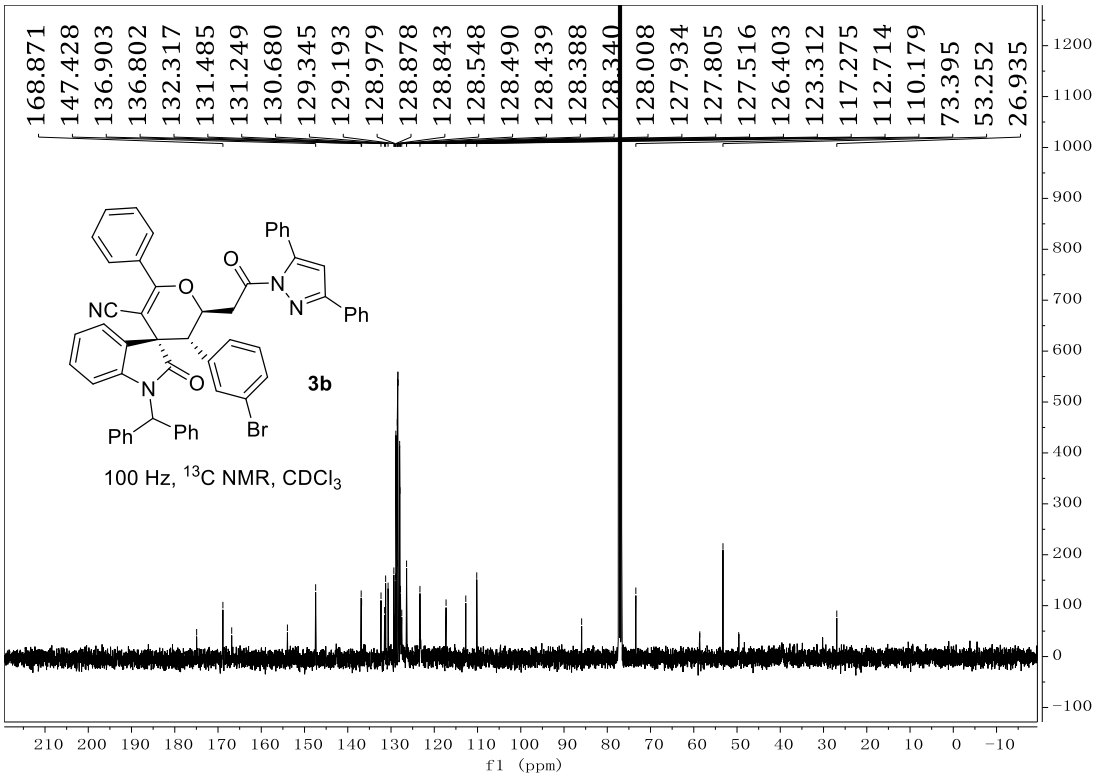
3a:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



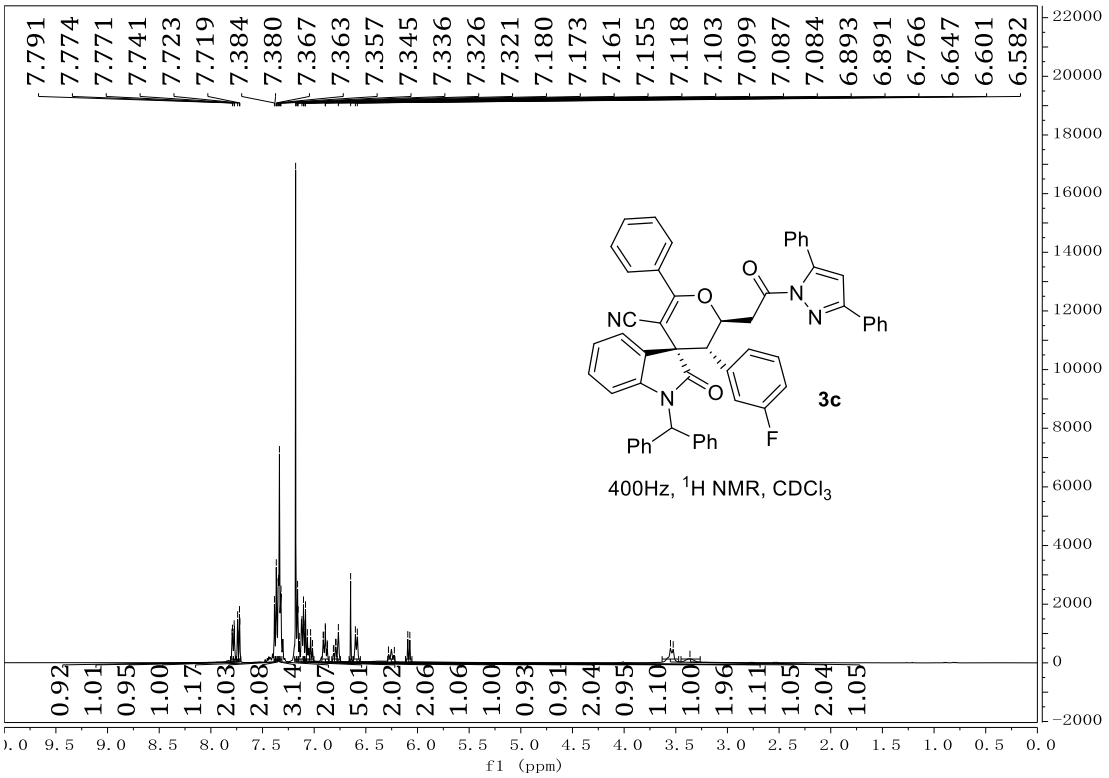


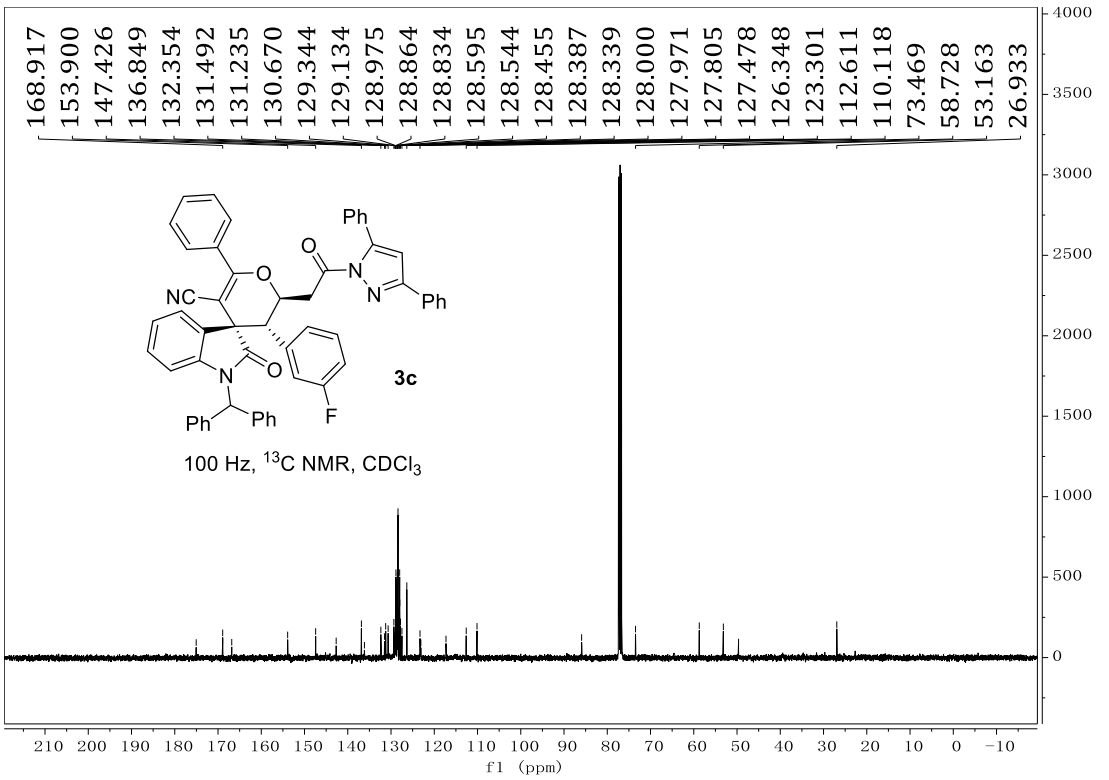
3b:(2'S,3R,3'R)-1-benzhydryl-3'-(3-bromophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

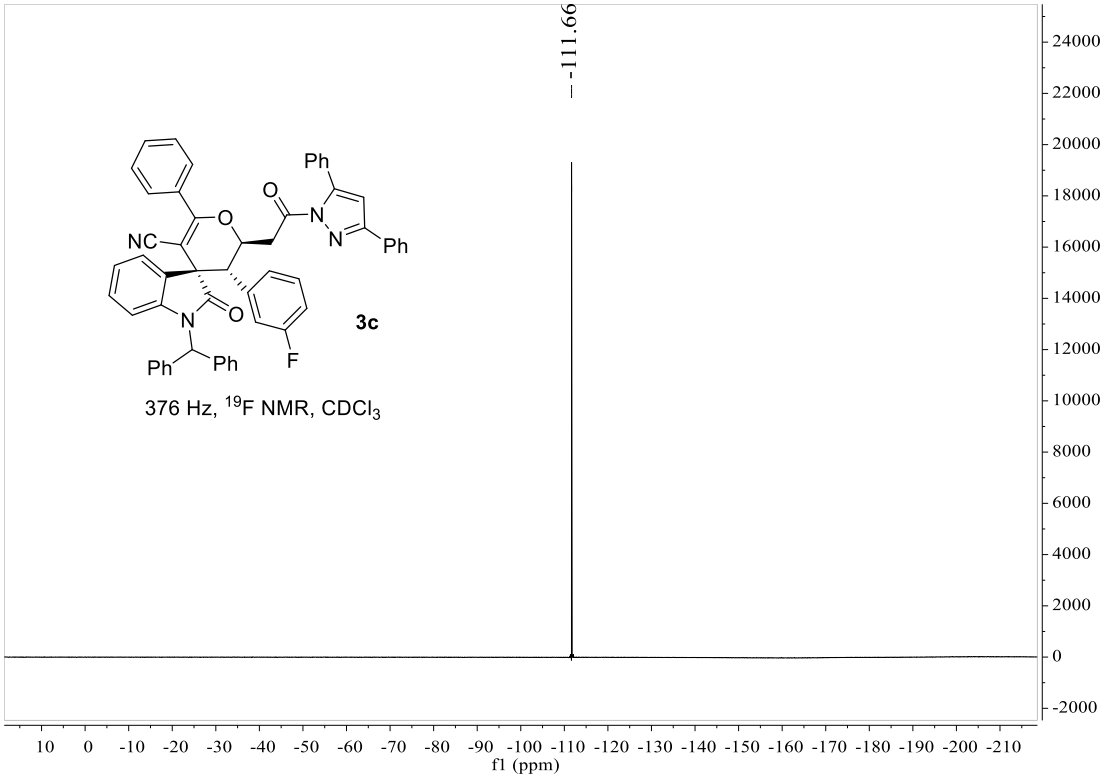

7.868
7.866
7.810
7.792
7.788
7.457
7.453
7.423
7.415
7.406
7.398
7.375
7.373
7.314
7.277
7.251
7.234
7.226
7.215
7.194
7.174
7.156
7.120
6.749
6.723
6.641
6.622
6.164
6.144
3.554
2.01
0.98
1.05
1.03
5.10
4.13
2.12
1.20
3.11
2.04
2.12
2.05
1.06
3.86
0.98
1.01
1.13
1.09
1.06
2.14
1.06
Ph
O
N
N
Ph
NC
O
N
O
Ph
Ph
Br
3b
400Hz, ^{1}H NMR, CDCl$_3$
f1 (ppm)


168.871
147.428
136.903
136.802
132.317
131.485
131.249
130.680
129.345
129.193
128.979
128.878
128.843
128.548
128.490
128.439
128.388
128.340
128.008
127.934
127.805
127.516
126.403
123.312
117.275
112.714
110.179
73.395
53.252
26.935
Ph
O
N
N
Ph
NC
O
N
O
Ph
Ph
Br
3b
100 Hz, ^{13}C NMR, CDCl$_3$
f1 (ppm)

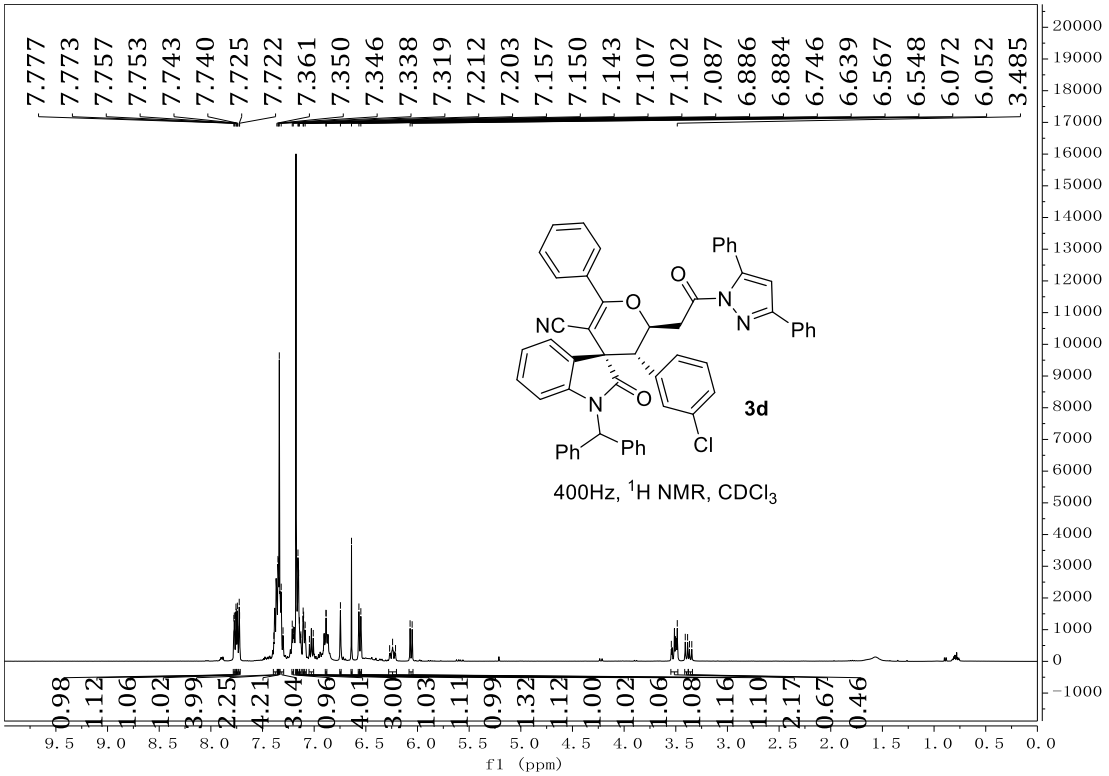
3c:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(3-fluorophenyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

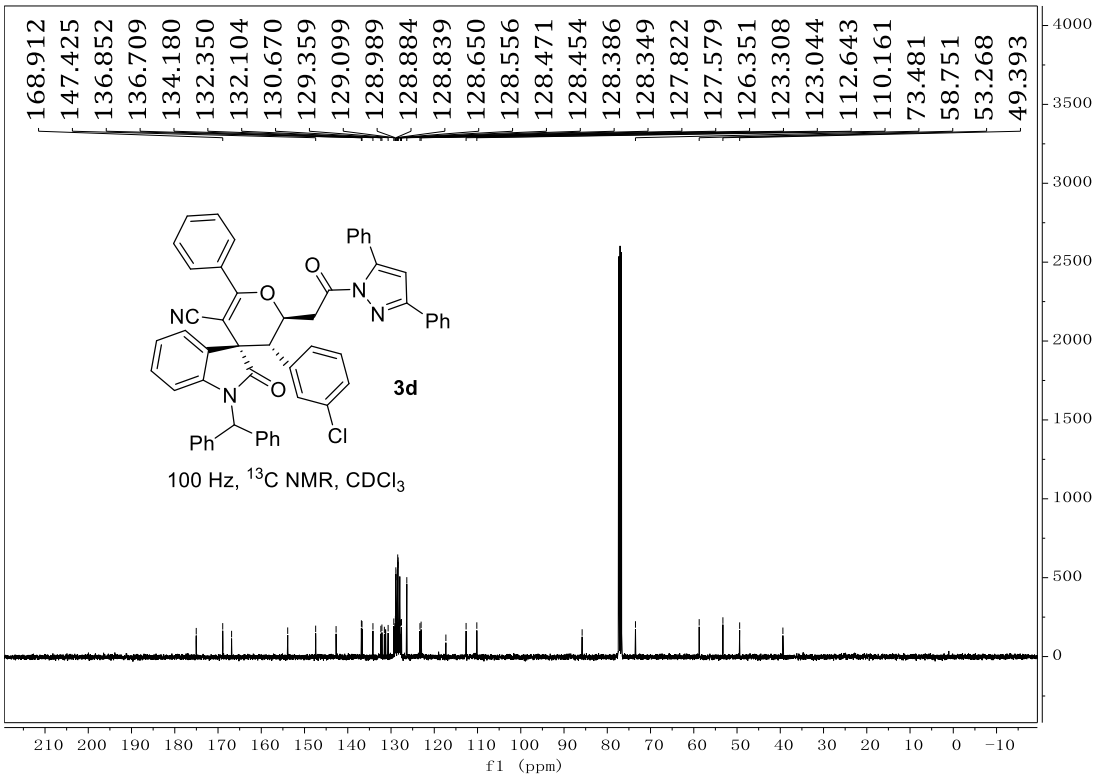




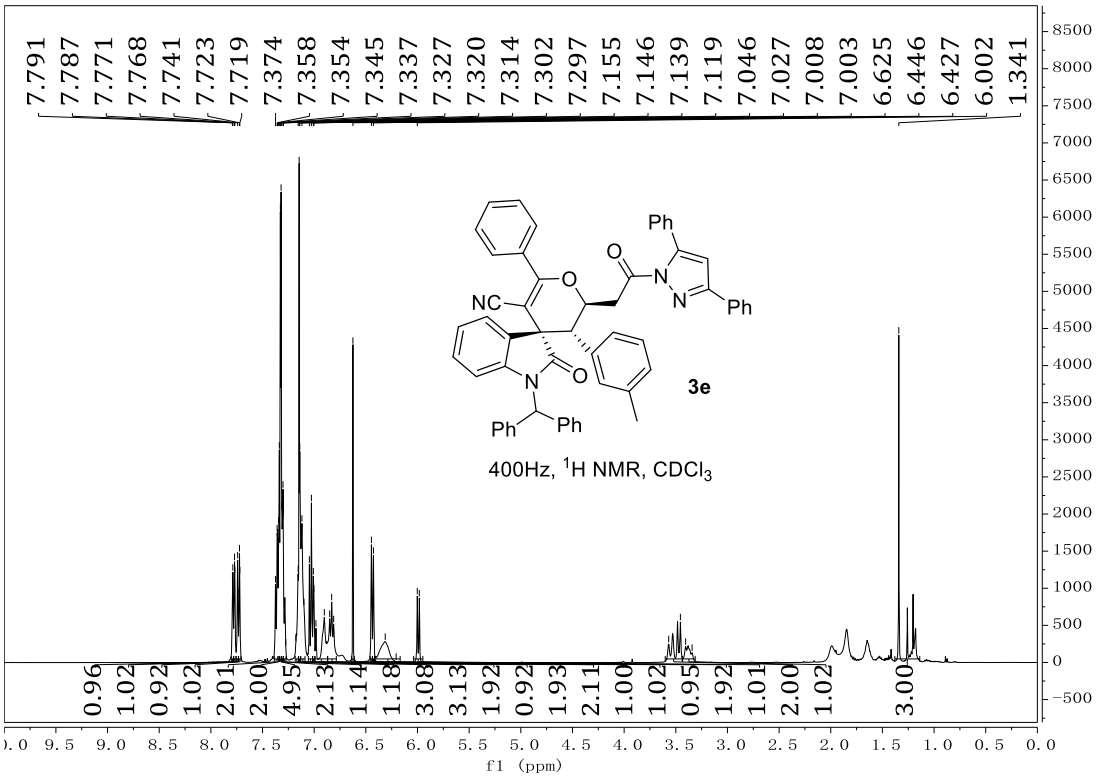


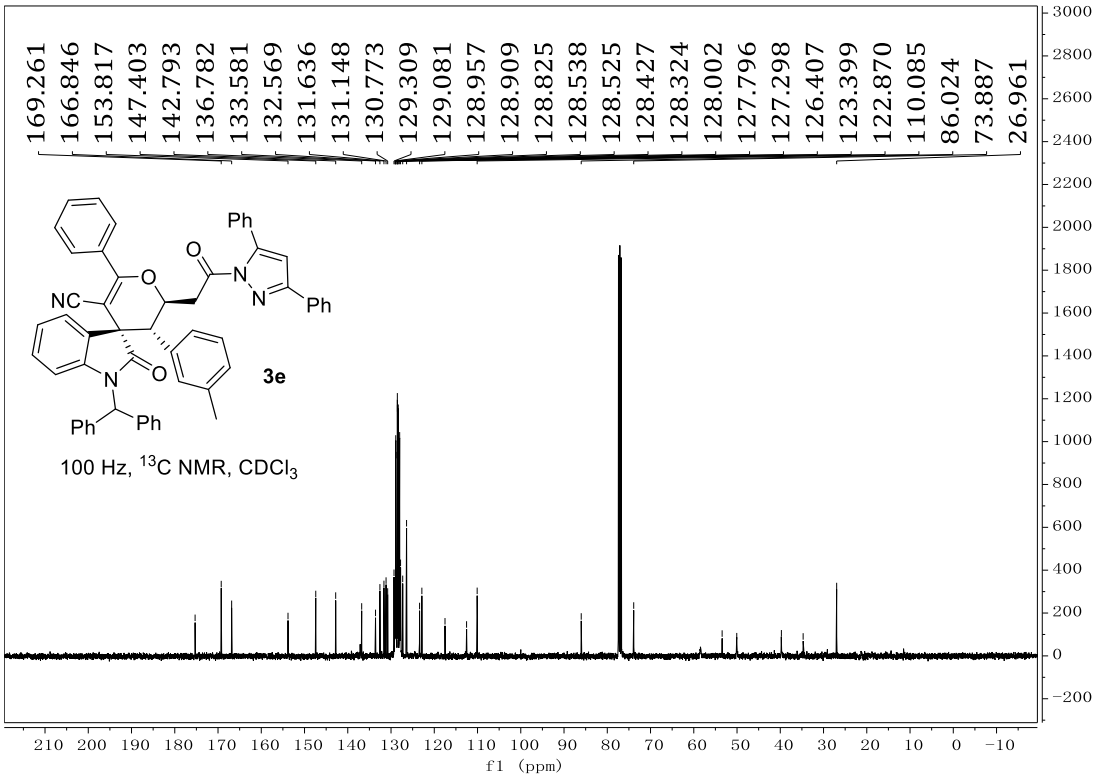
3d:(2'S,3R,3'R)-1-benzhydryl-3'-(3-chlorophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



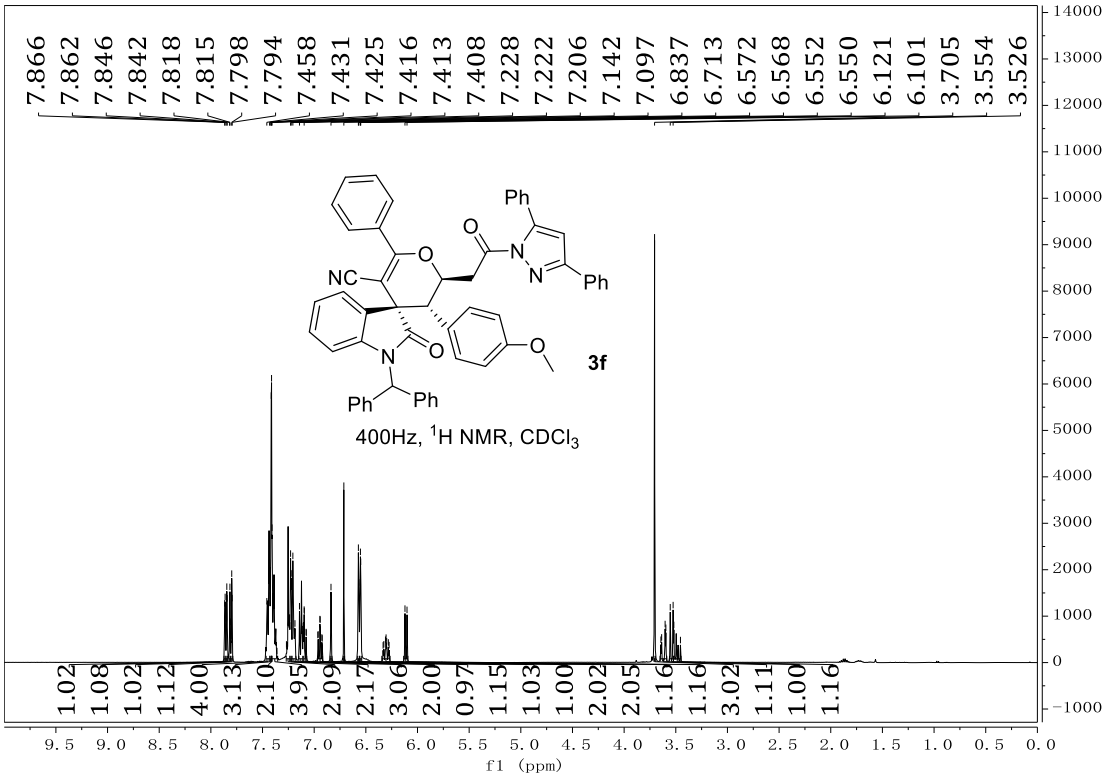


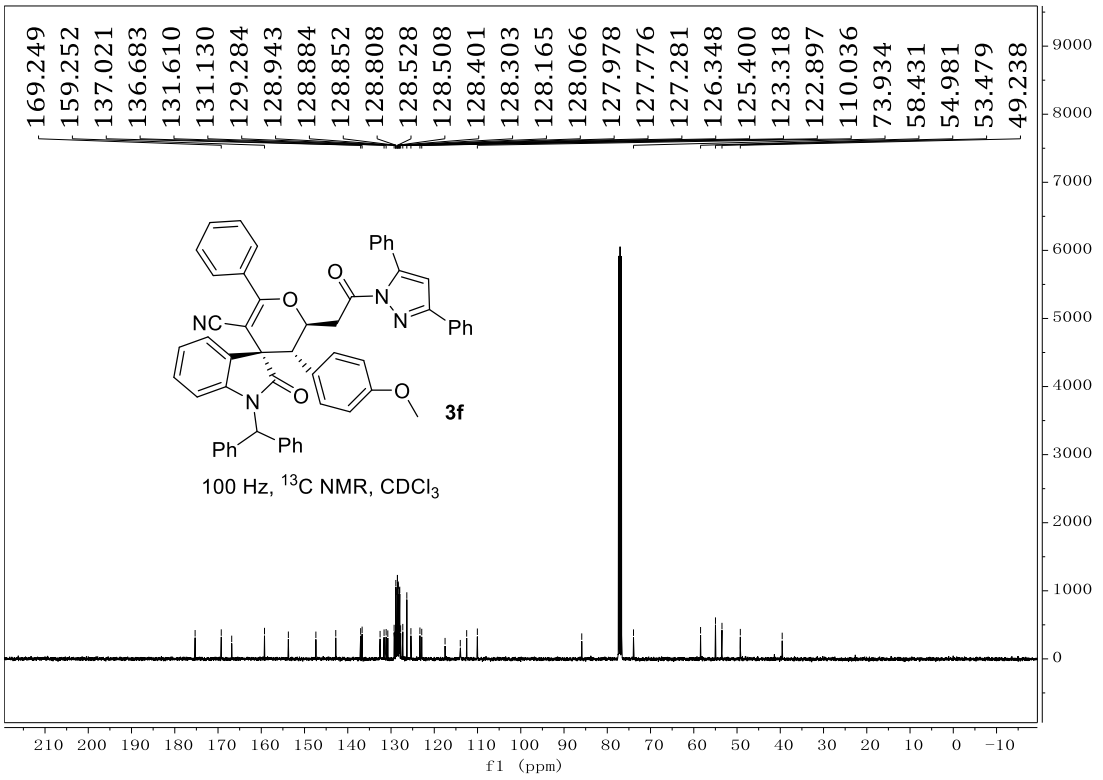
3e:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(m-tolyl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



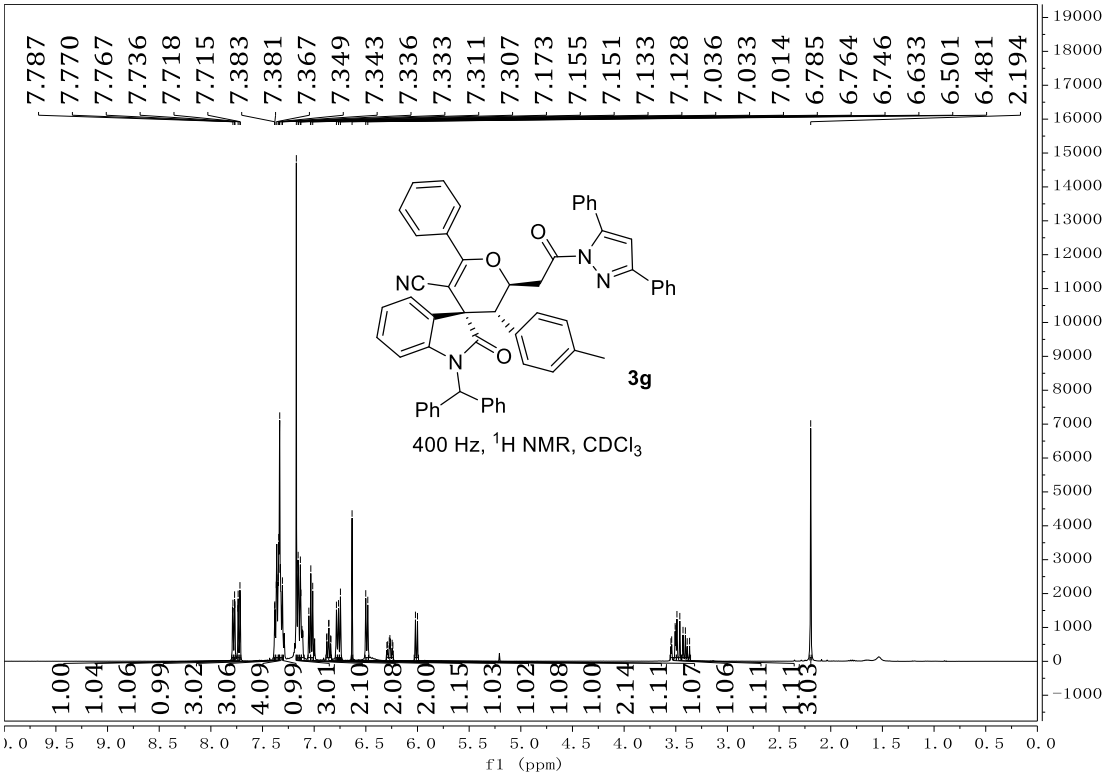


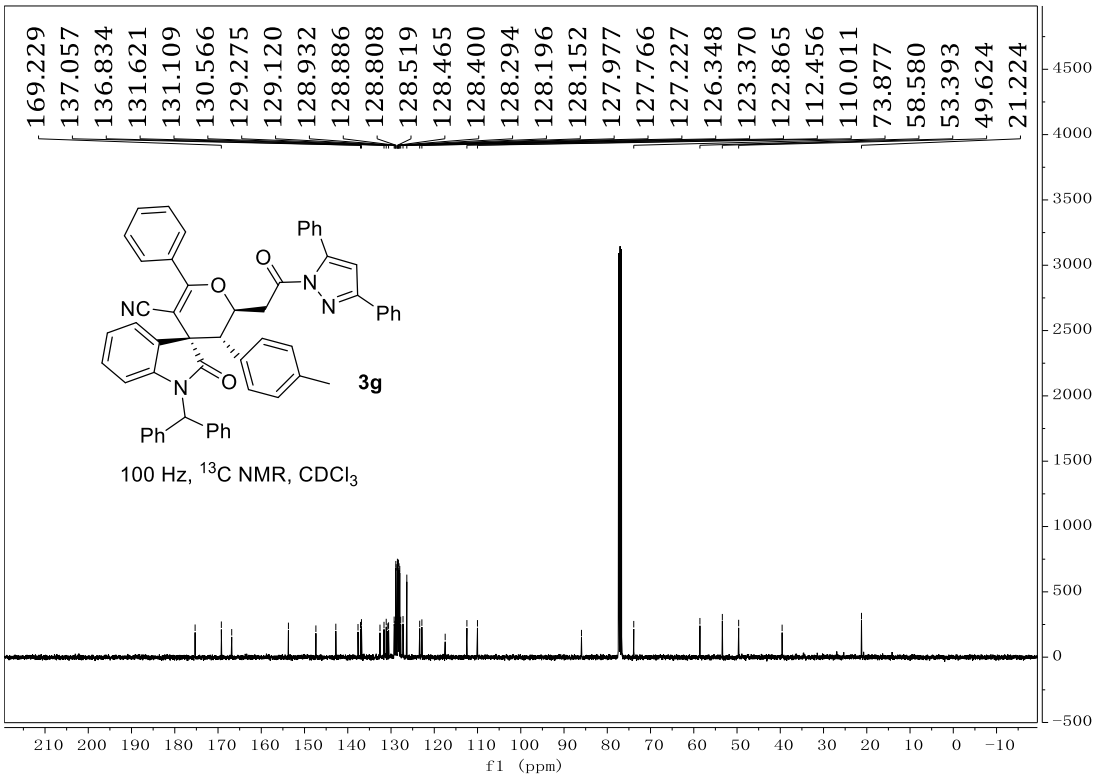
3f:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(4-methoxyphenyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



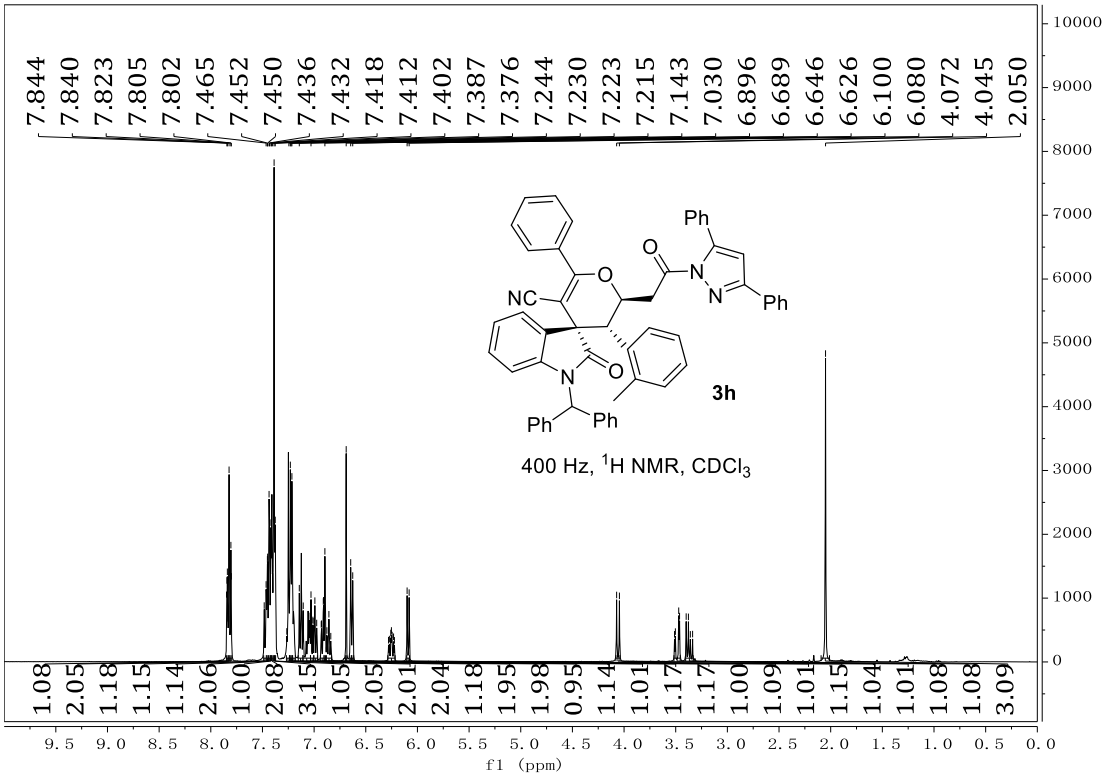


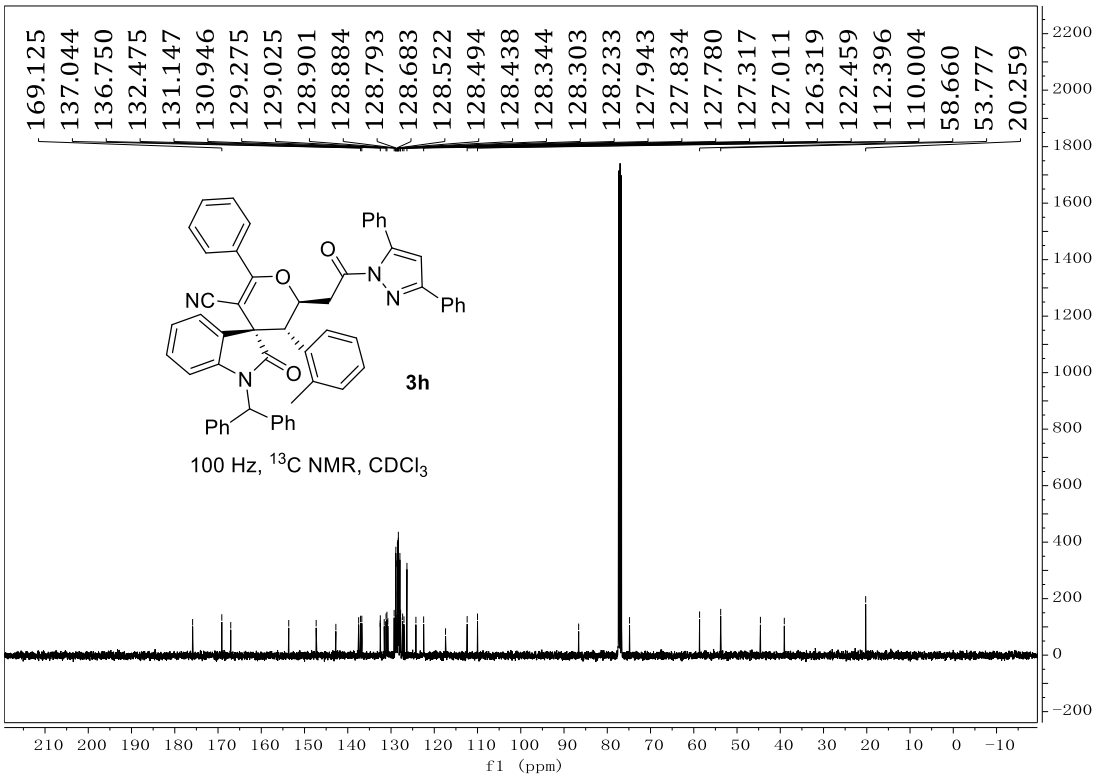
3g:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(p-tolyl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



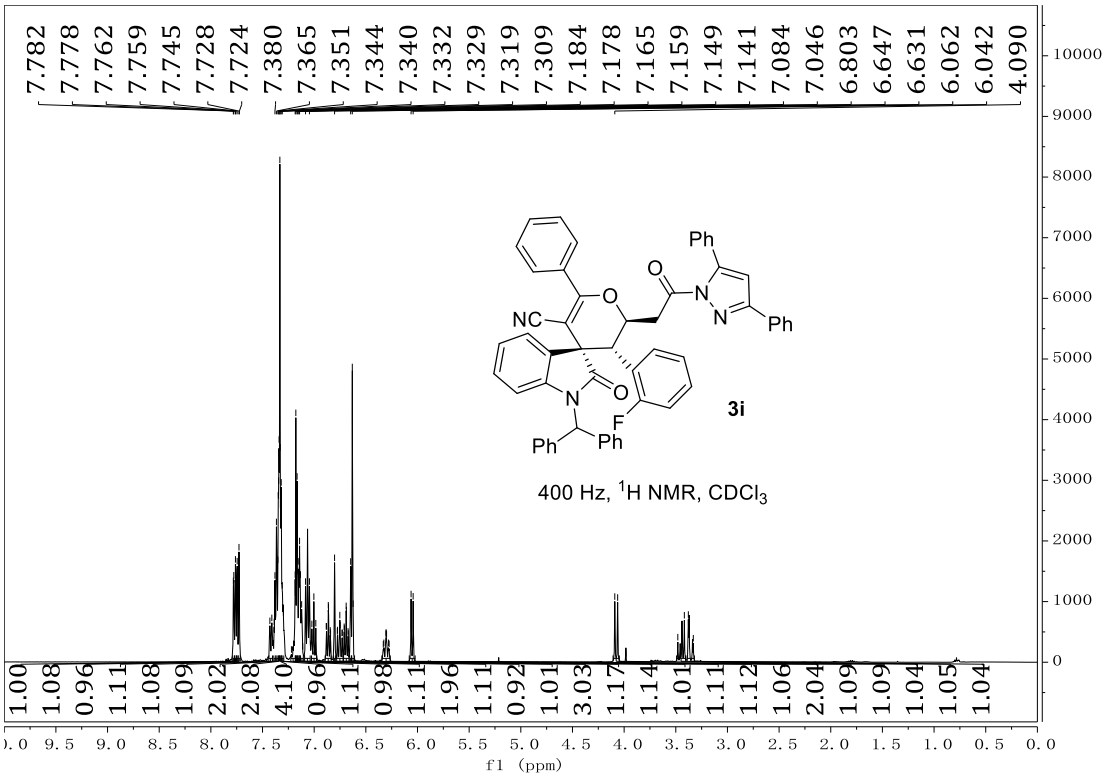


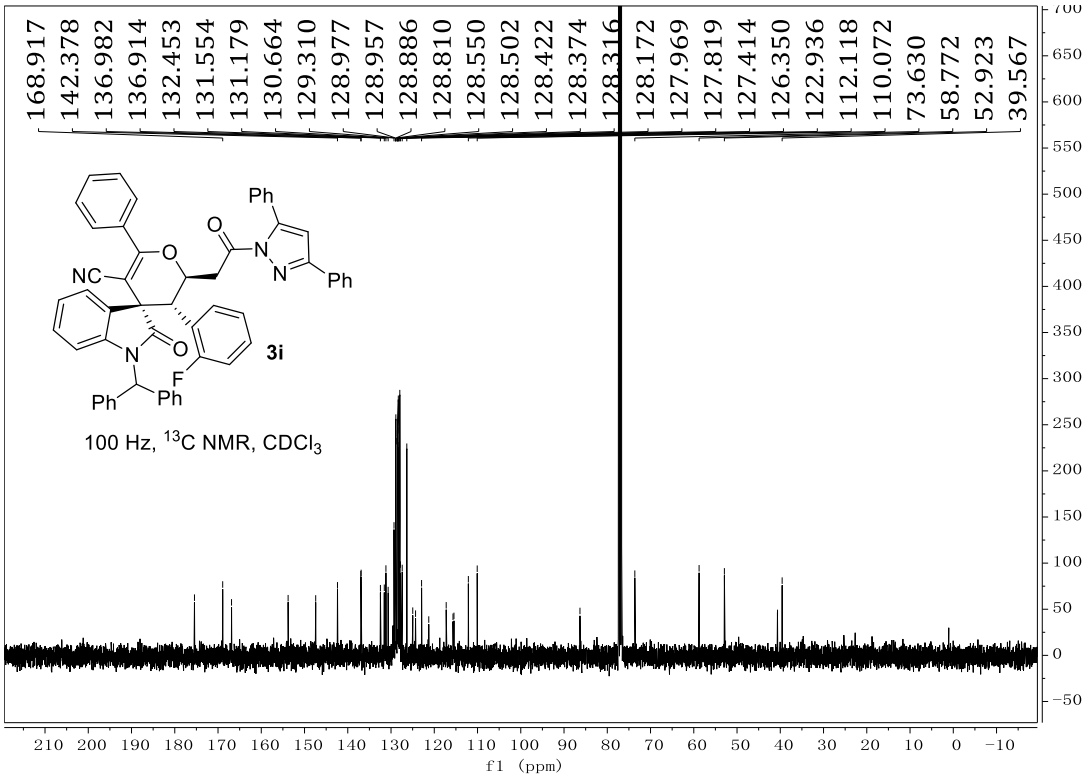
3h:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(o-tolyl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

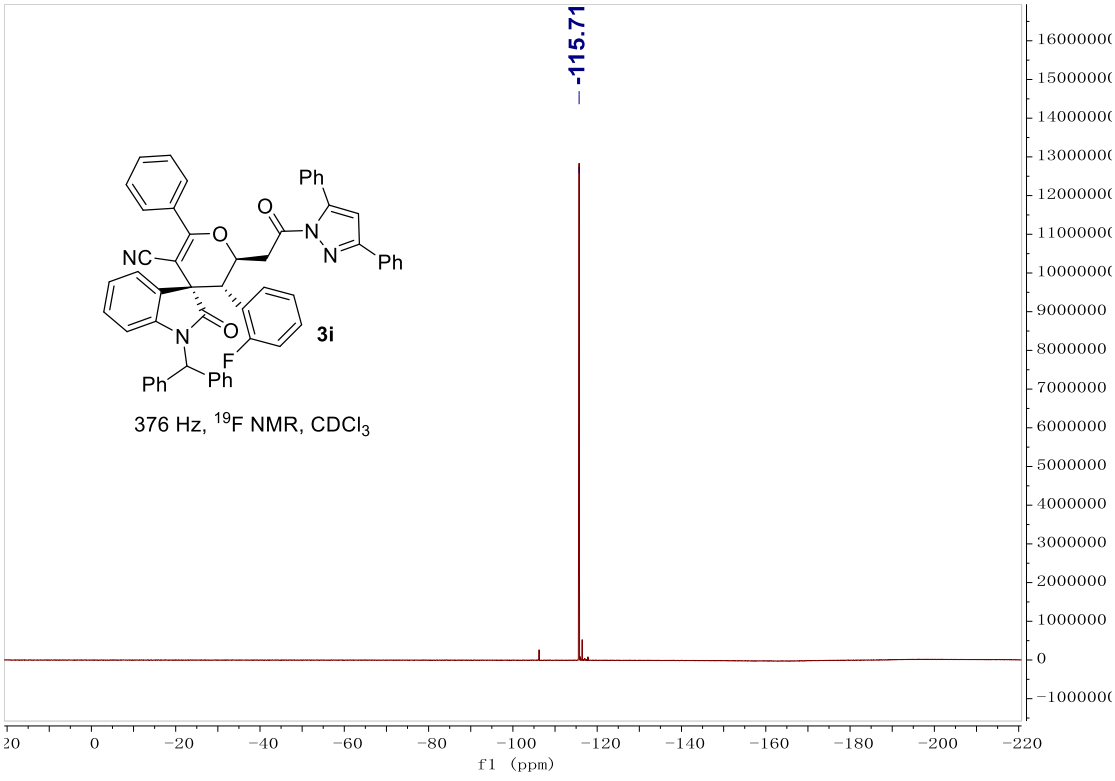




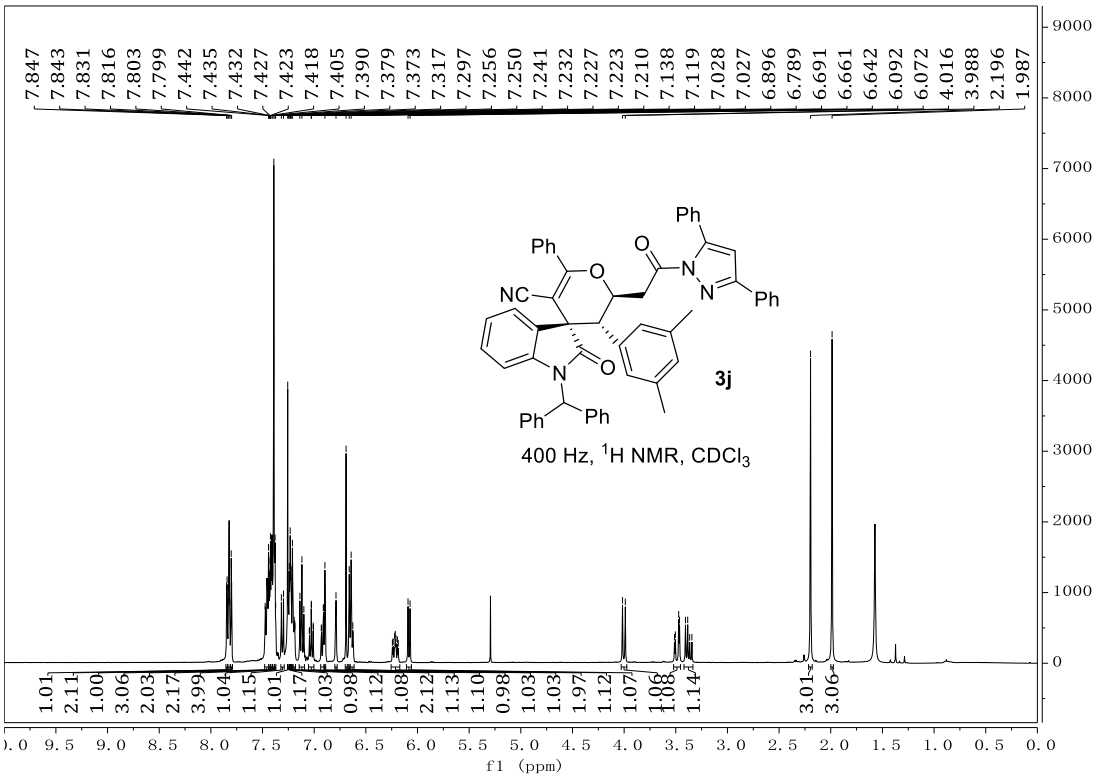
3i:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(2-fluorophenyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

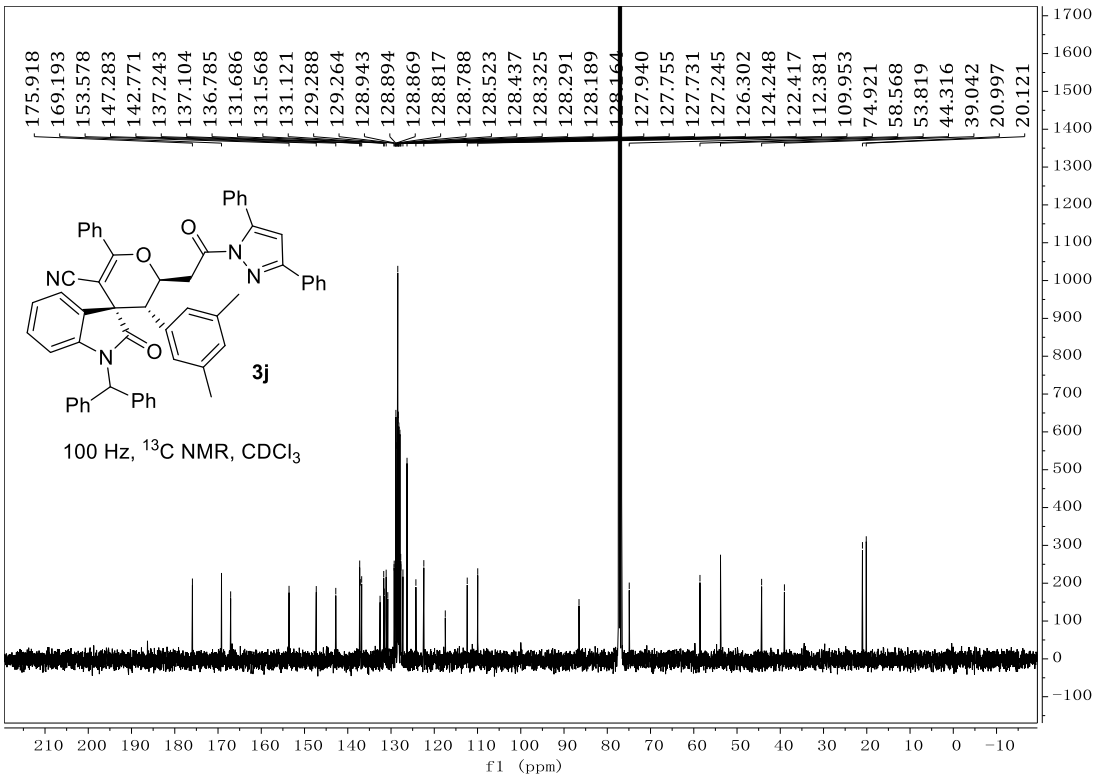




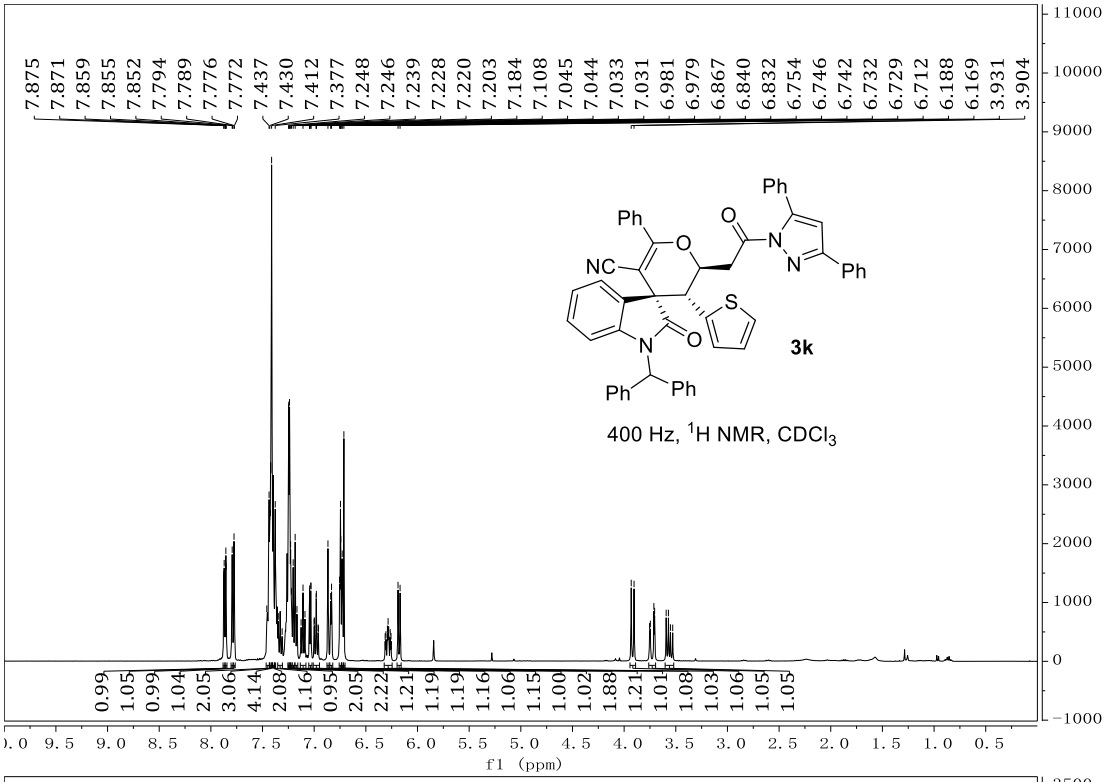


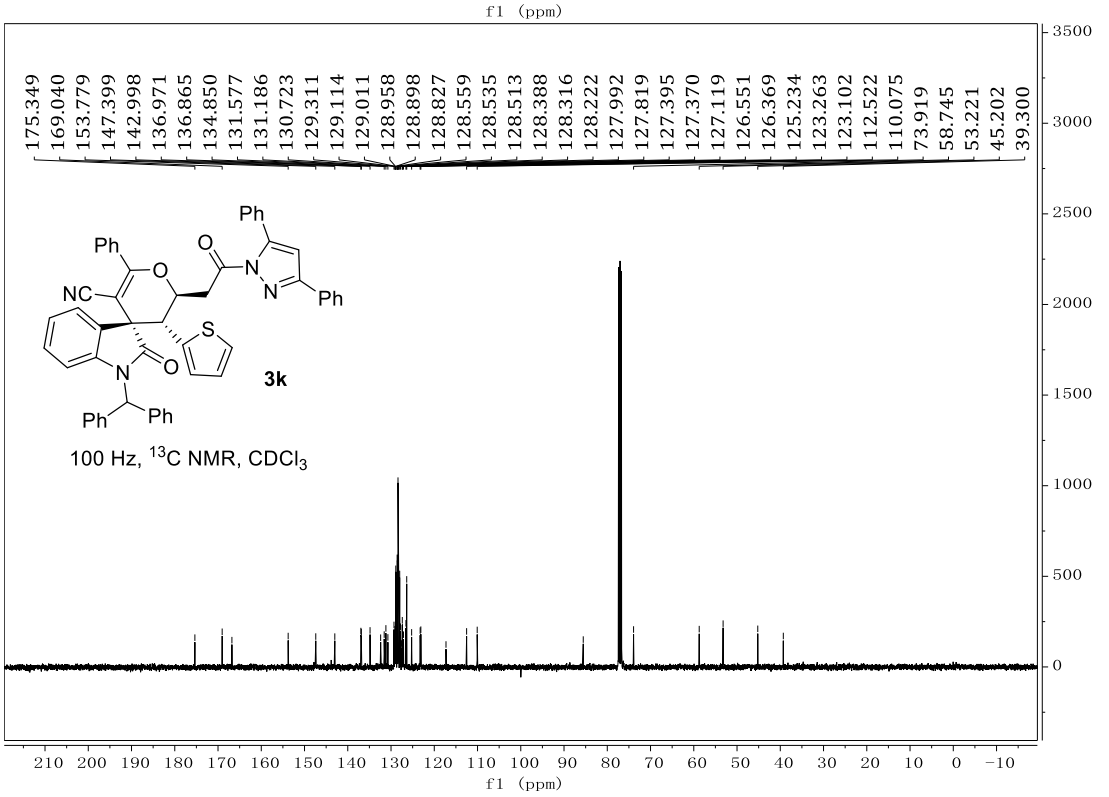
3j:(2'S,3R,3'R)-1-benzhydryl-3'-(3,5-dimethylphenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxo ethyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



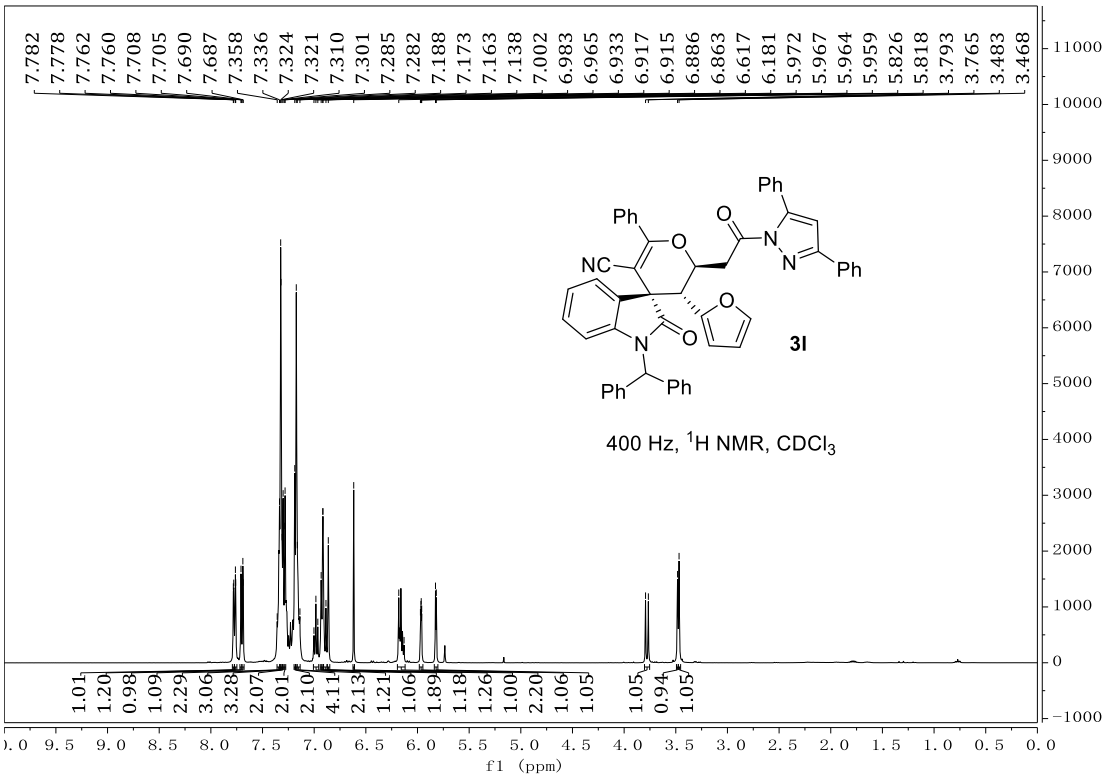


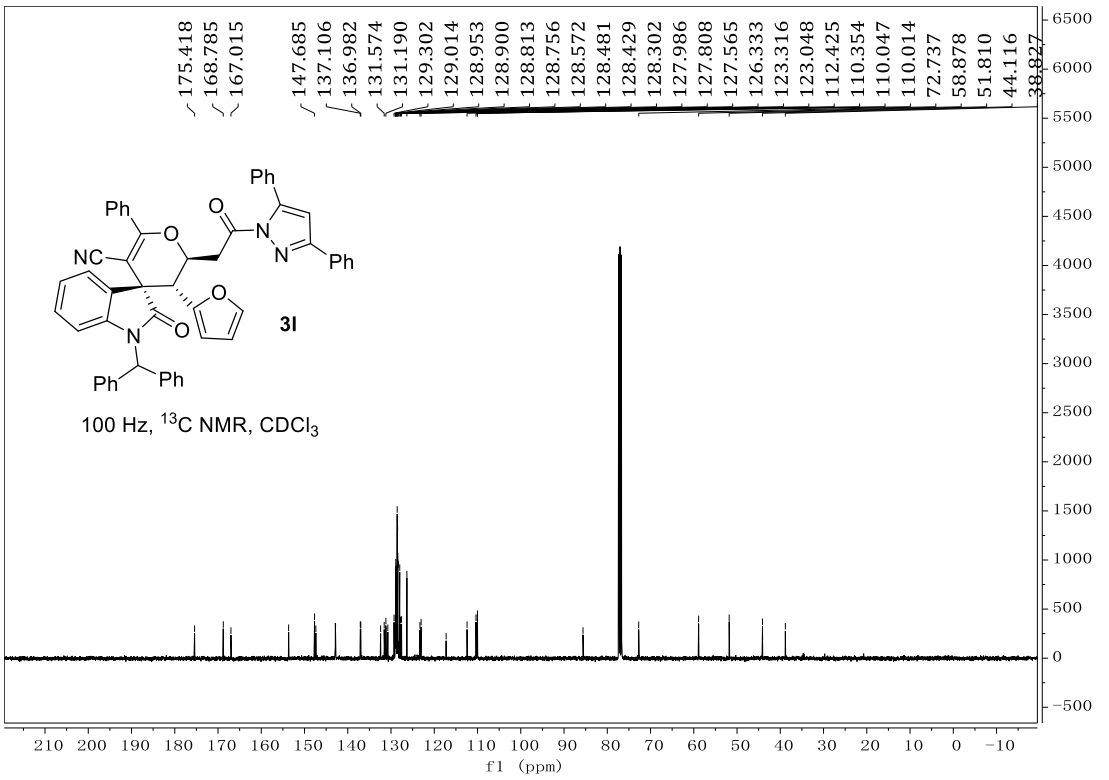
3k:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(thiophen-2-yl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



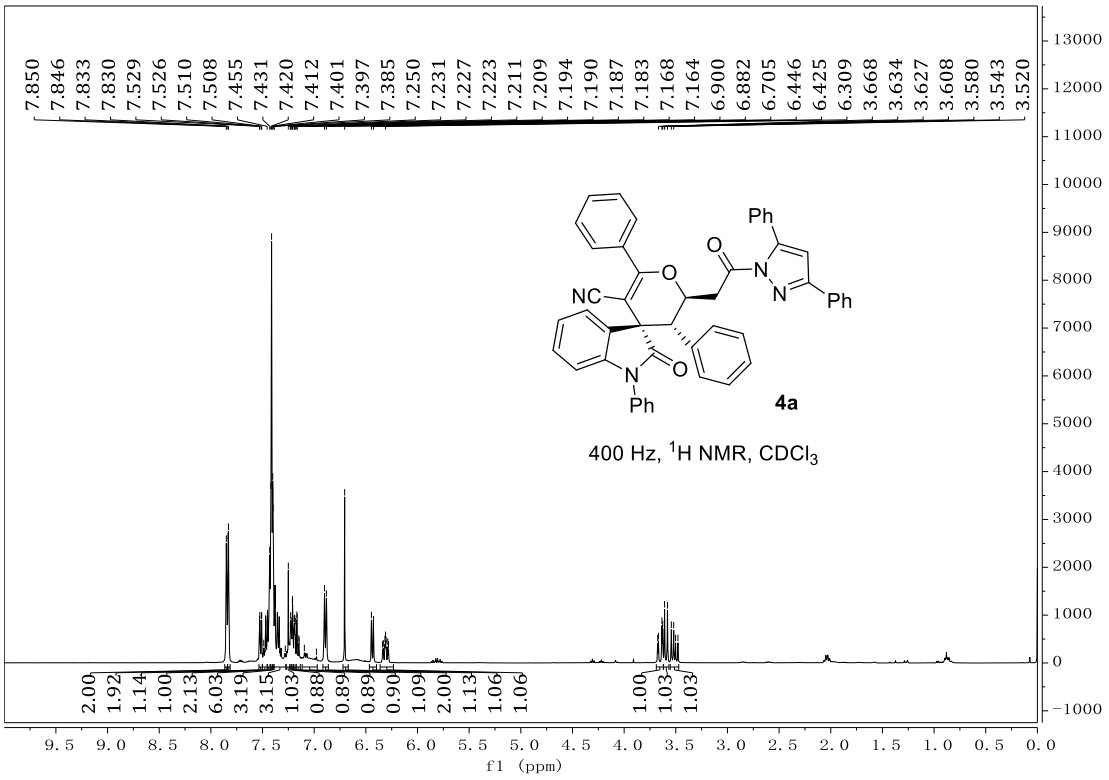


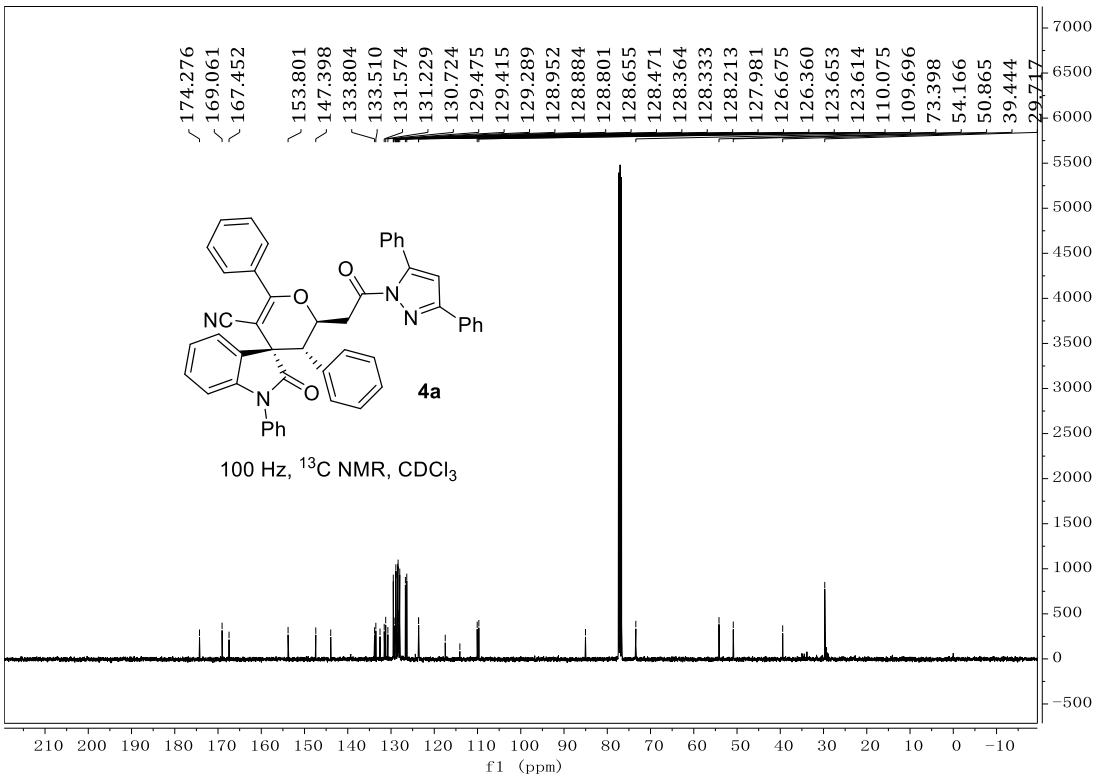
3l:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(furan-2-yl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



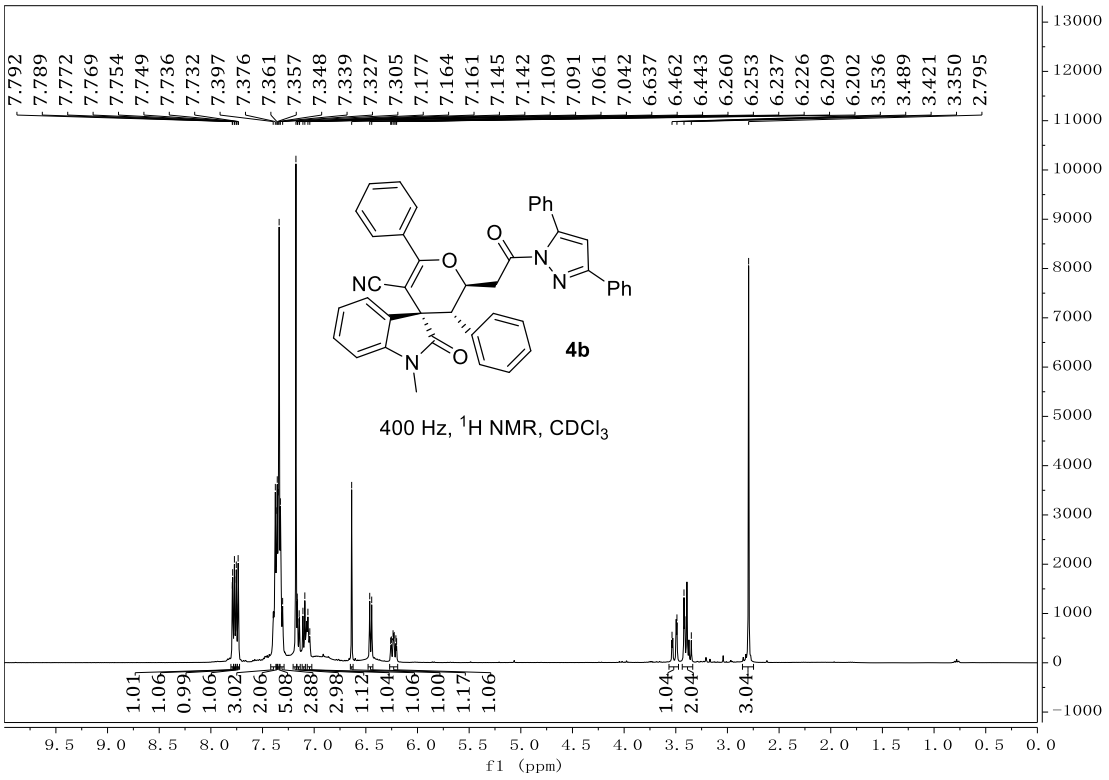


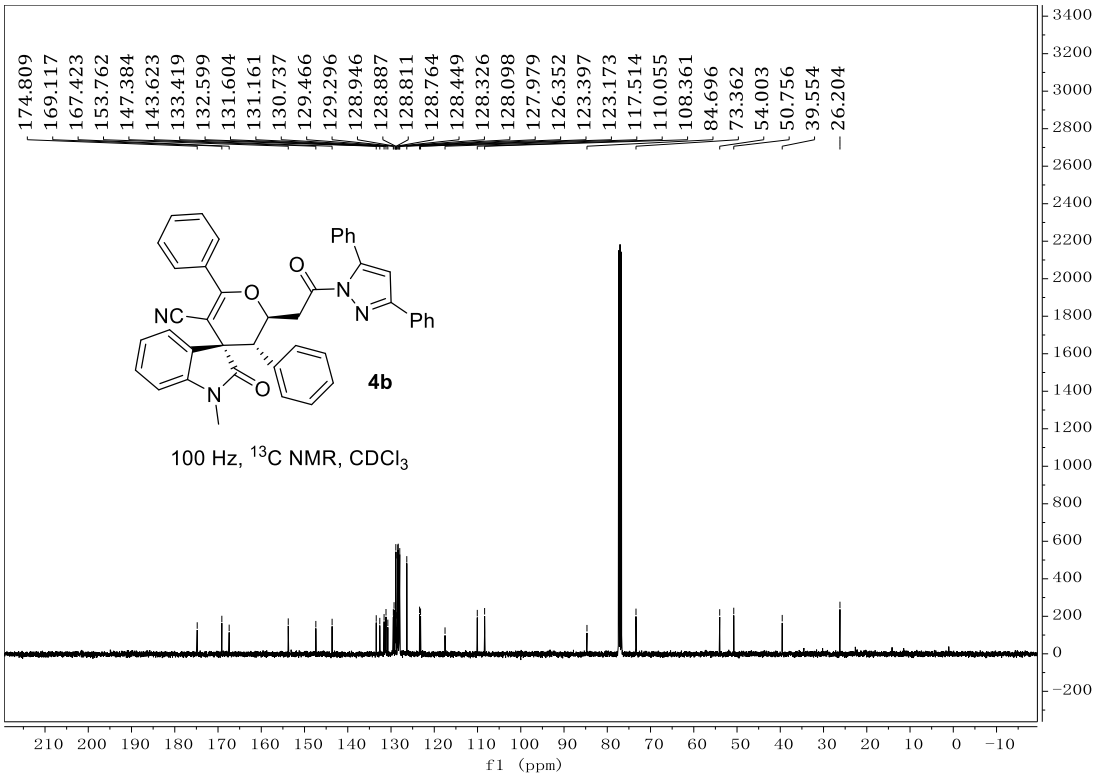
4a:(2'S,3R,3'R)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-1,3',6'-triphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile


7.850
7.846
7.833
7.830
7.529
7.526
7.510
7.508
7.455
7.431
7.420
7.412
7.401
7.397
7.385
7.250
7.231
7.227
7.223
7.211
7.209
7.194
7.190
7.187
7.183
7.168
7.164
6.900
6.882
6.705
6.446
6.425
6.309
3.668
3.634
3.627
3.608
3.580
3.543
3.520
2.00
1.92
1.14
1.00
2.13
6.03
3.19
3.15
1.03
0.88
0.89
0.89
0.90
1.09
2.00
1.13
1.06
1.06
1.00
1.03
1.03
Ph
O
N
N
Ph
NC
O
O
N
Ph
4a
400 Hz, ^{1}H NMR, CDCl$_3$
f1 (ppm)

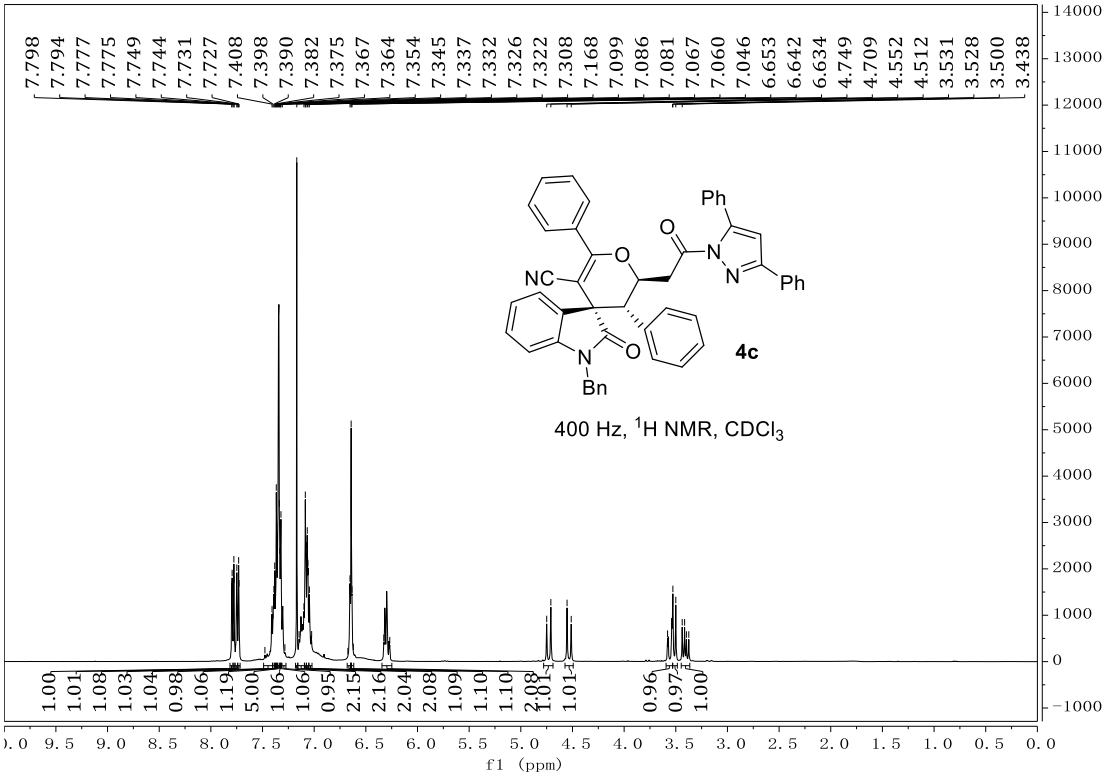

174.276
169.061
167.452
153.801
147.398
133.804
133.510
131.574
131.229
130.724
129.475
129.415
129.289
128.952
128.884
128.801
128.655
128.471
128.364
128.333
128.213
127.981
126.675
126.360
123.653
123.614
110.075
109.696
73.398
54.166
50.865
39.444
29.717
Ph
O
N
N
Ph
NC
O
O
N
Ph
4a
100 Hz, ^{13}C NMR, CDCl$_3$
f1 (ppm)

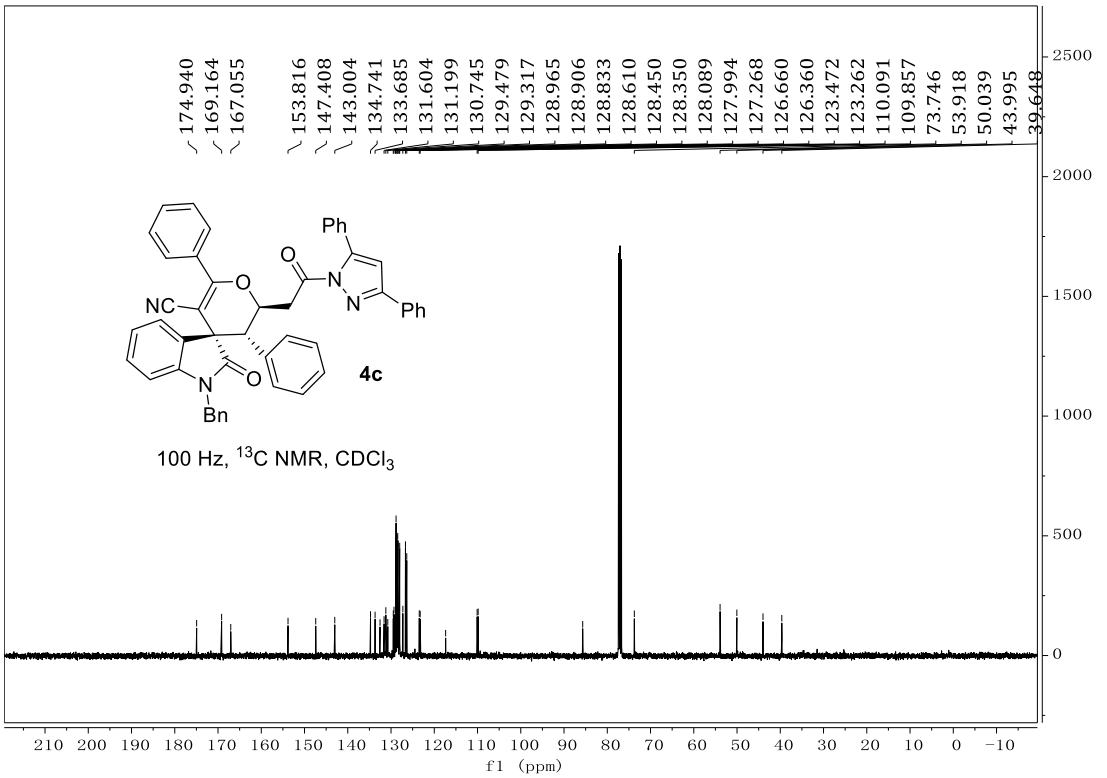
4b:(2'S,3R,3'R)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-1-methyl-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



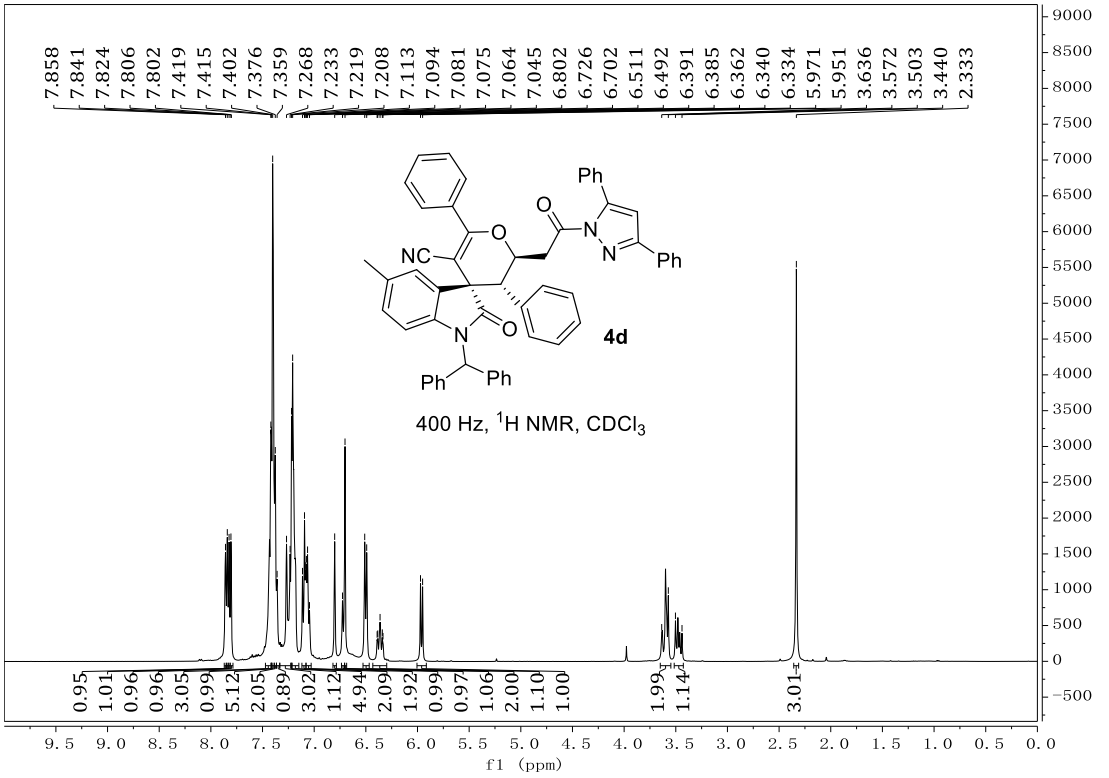


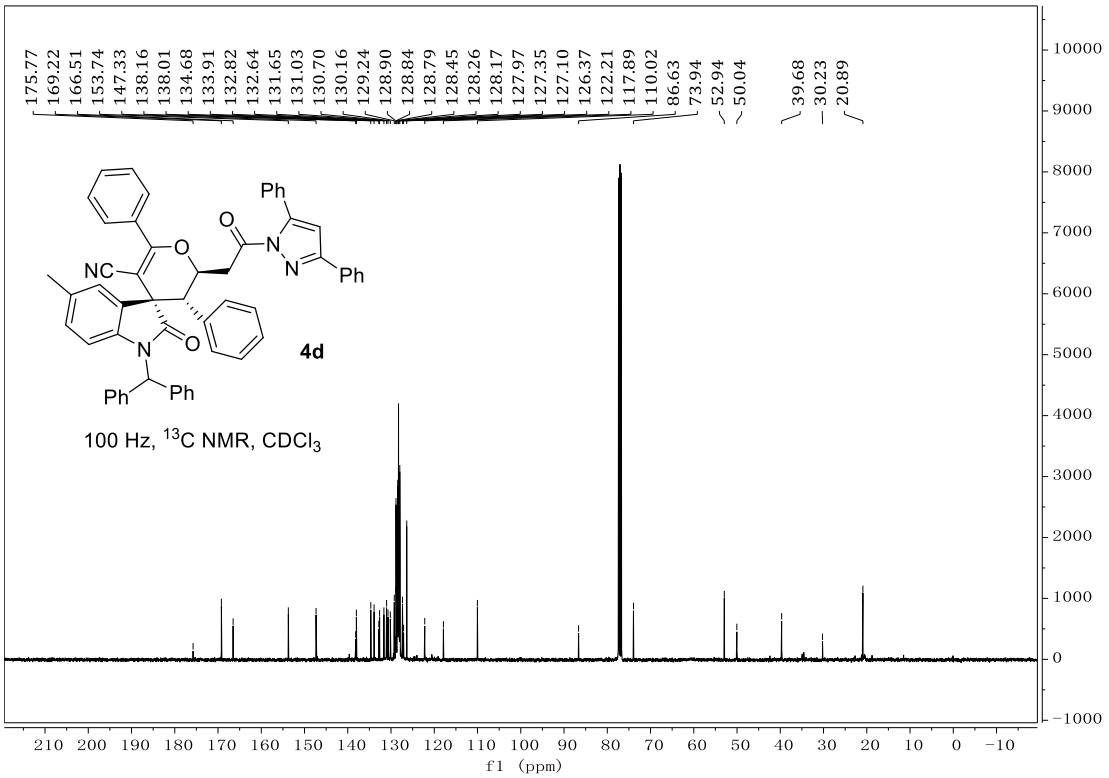
4c:(2'S,3R,3'R)-1-benzyl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



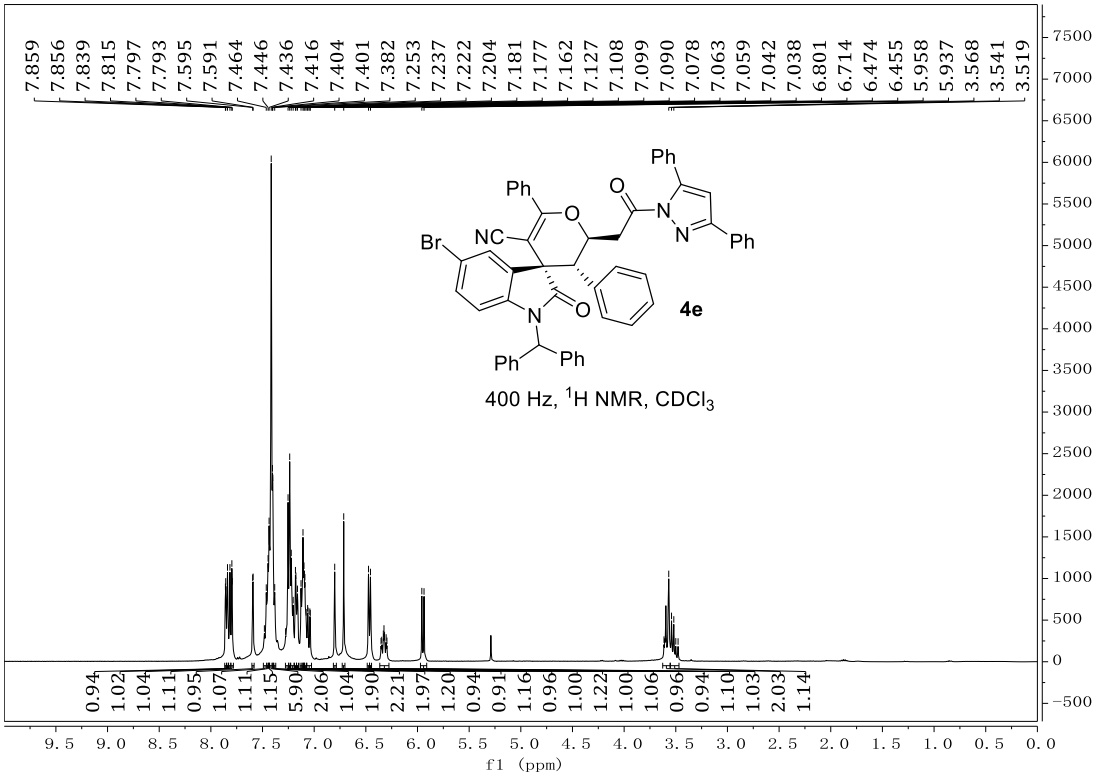


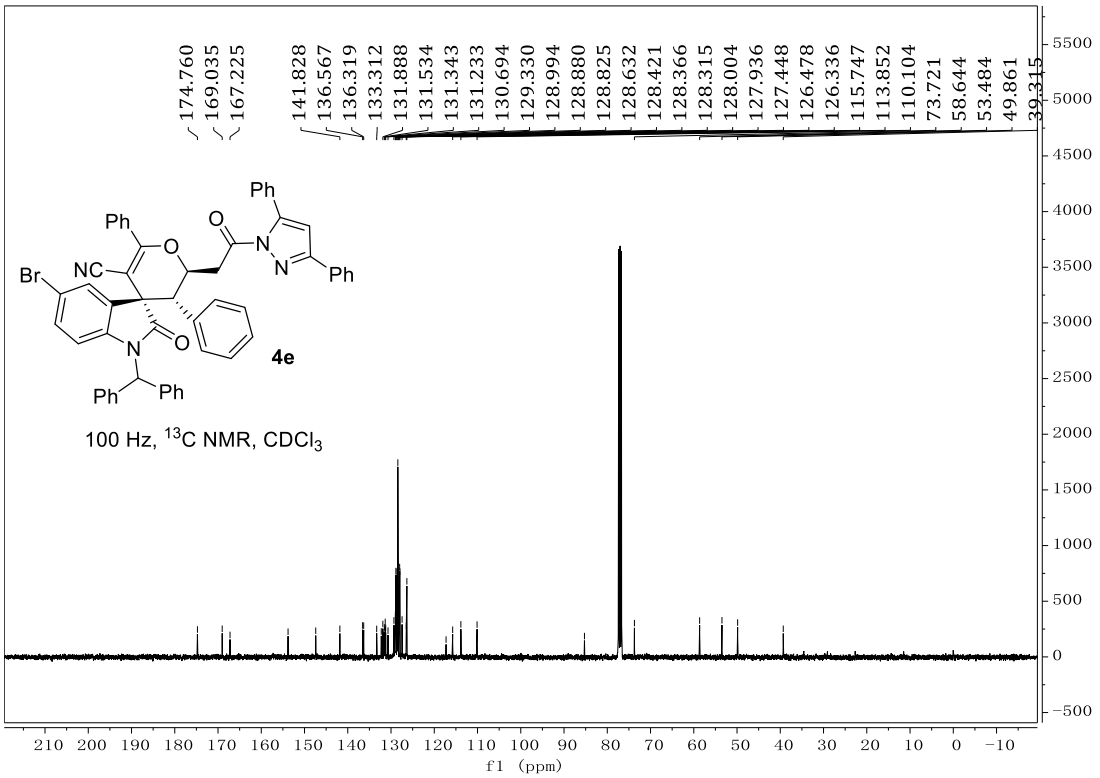
4d:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-5-methyl-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



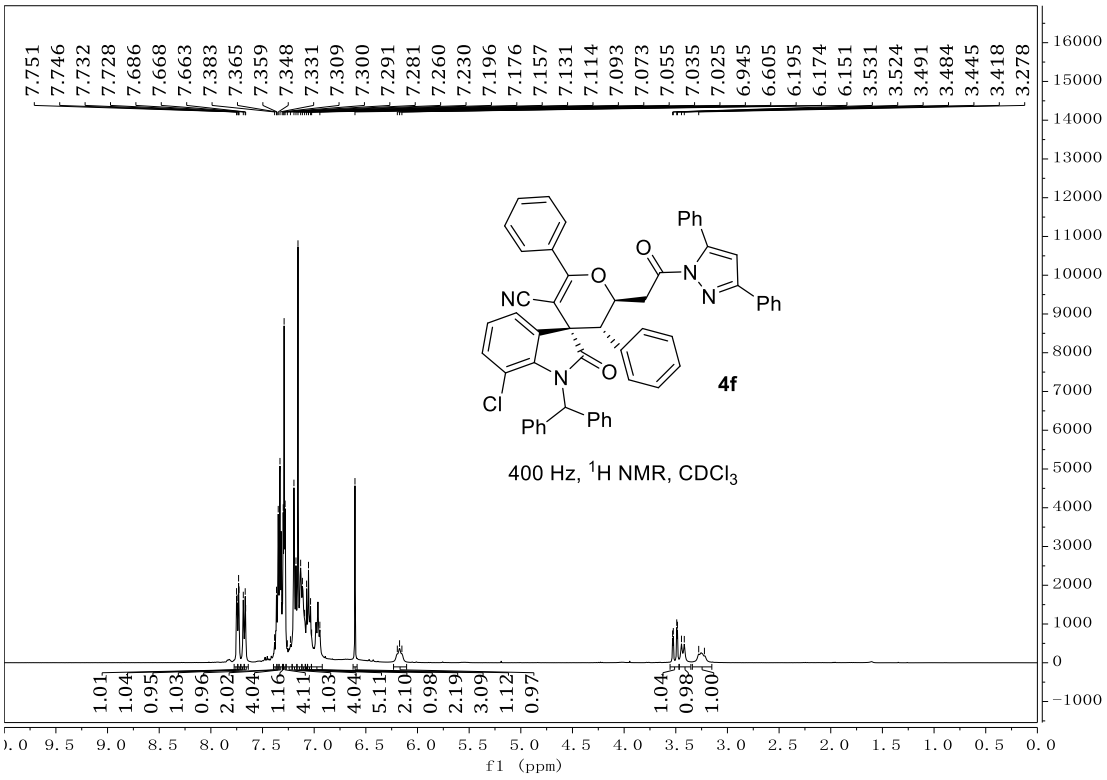


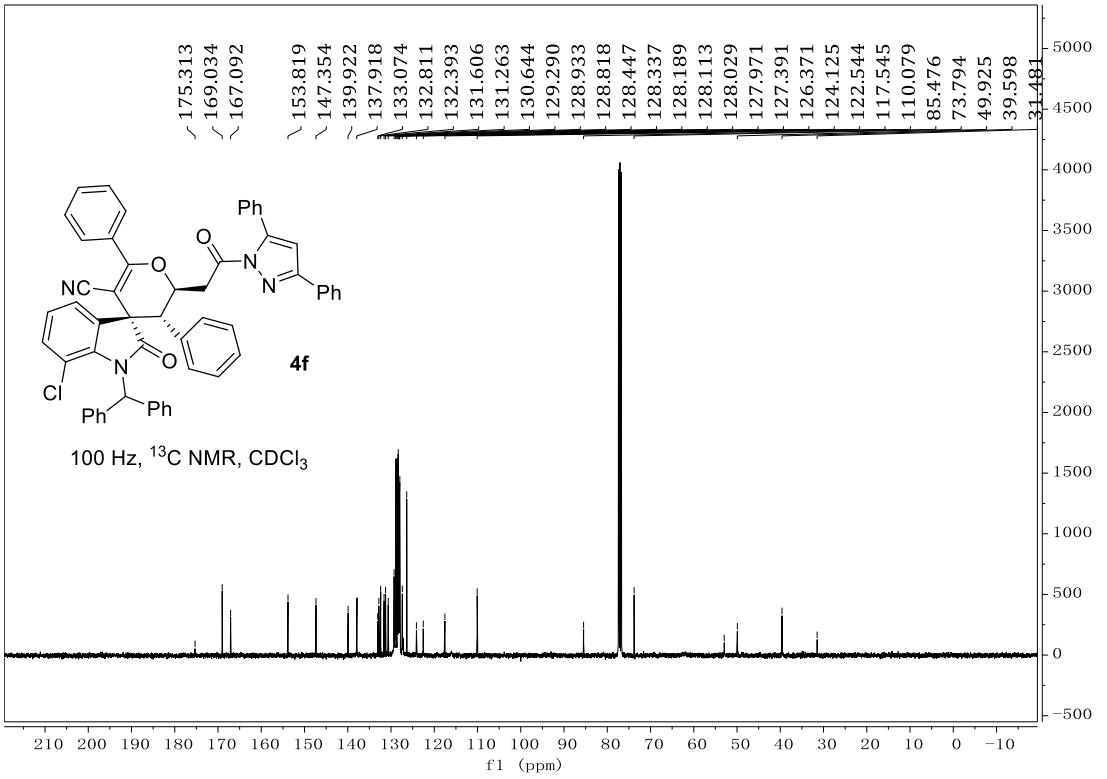
4e:(2'S,3R,3'R)-1-benzhydryl-5-bromo-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3', 6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



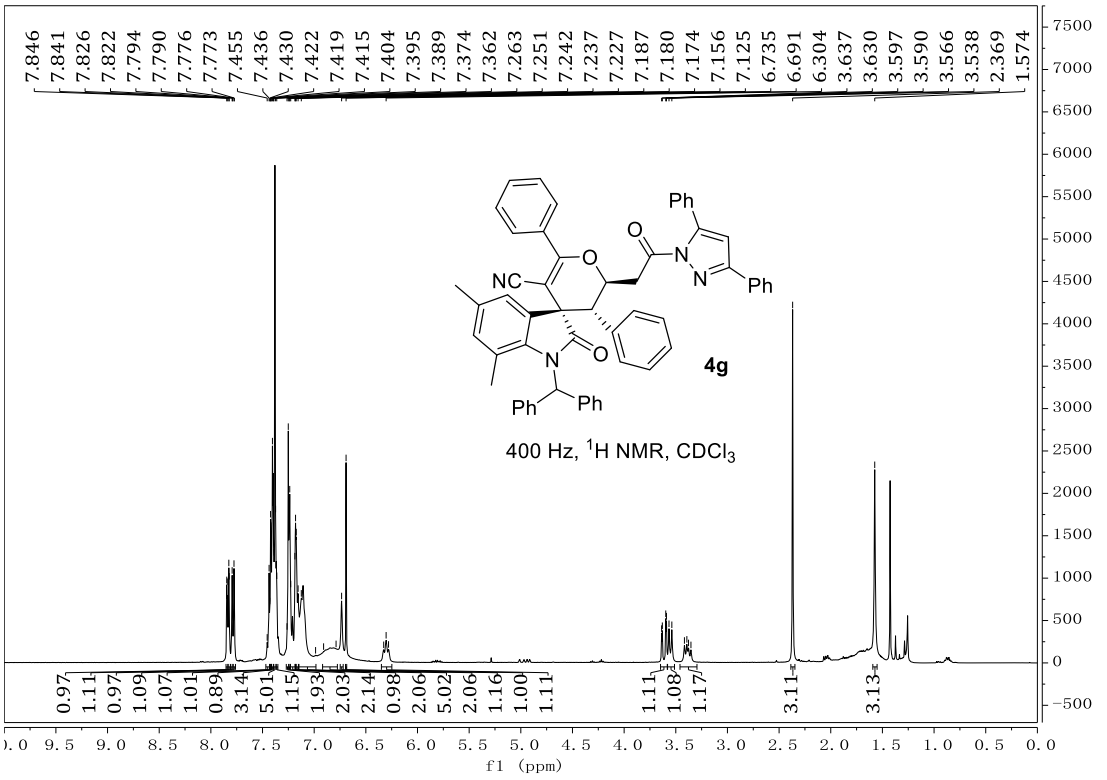


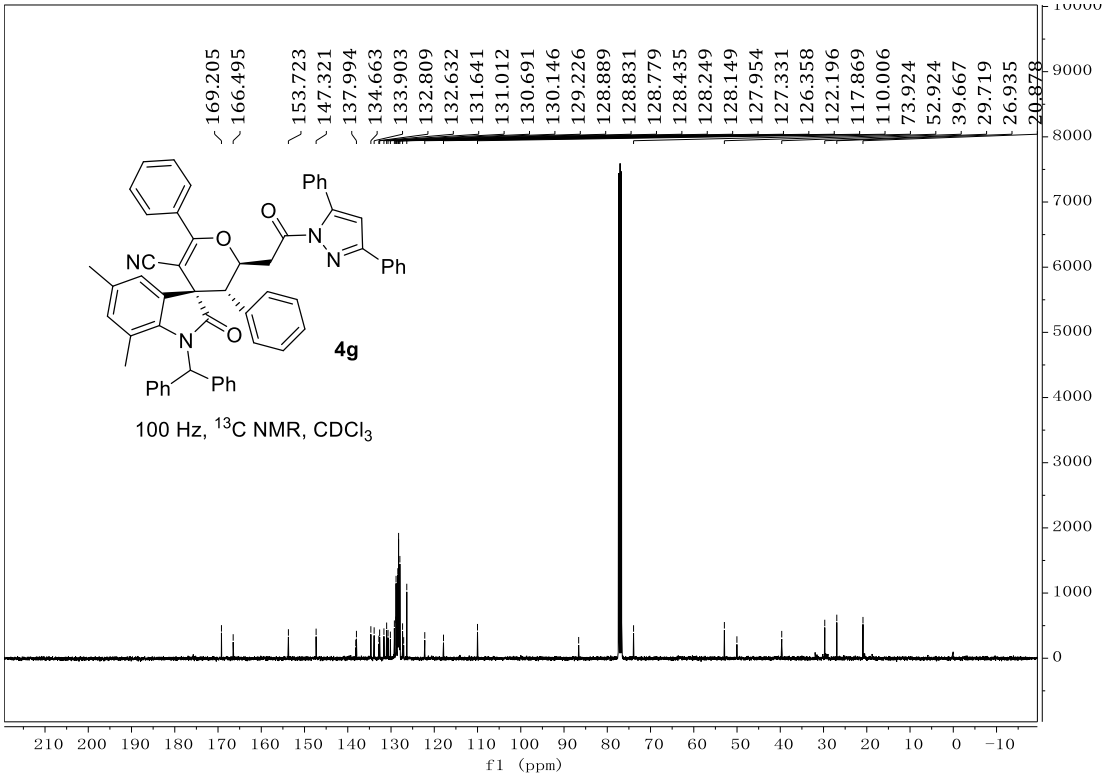
4f:(2'S,3R,3'R)-1-benzhydryl-7-chloro-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3', 6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



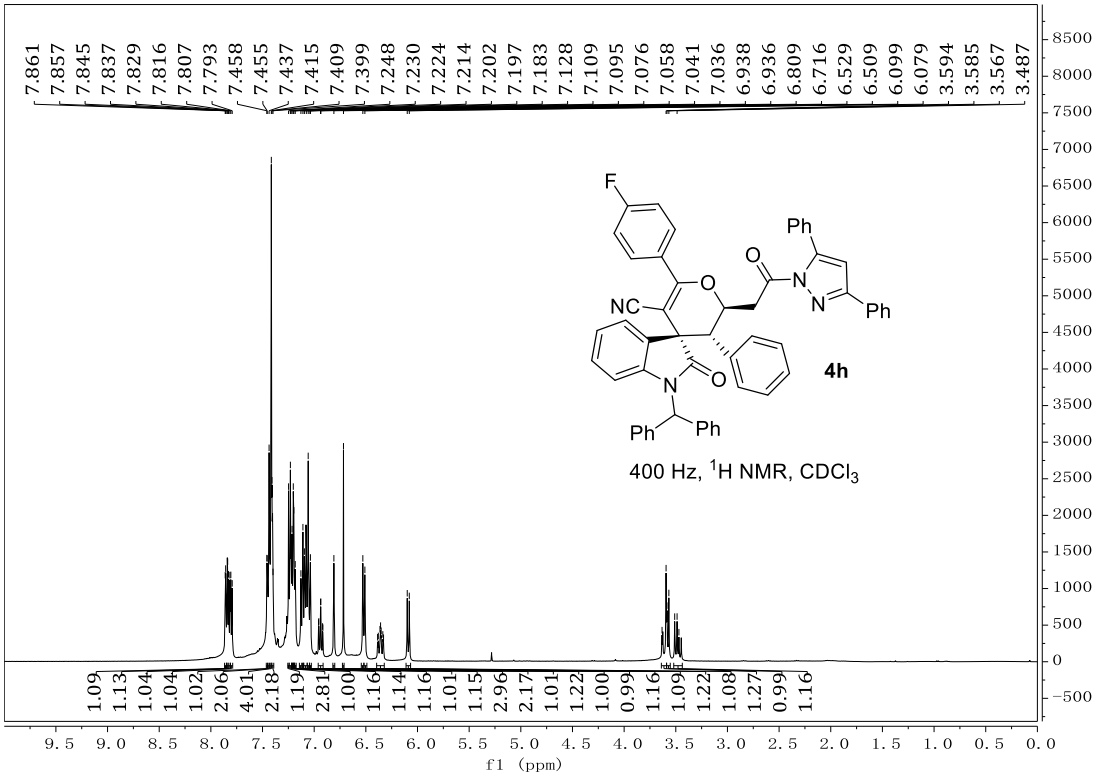


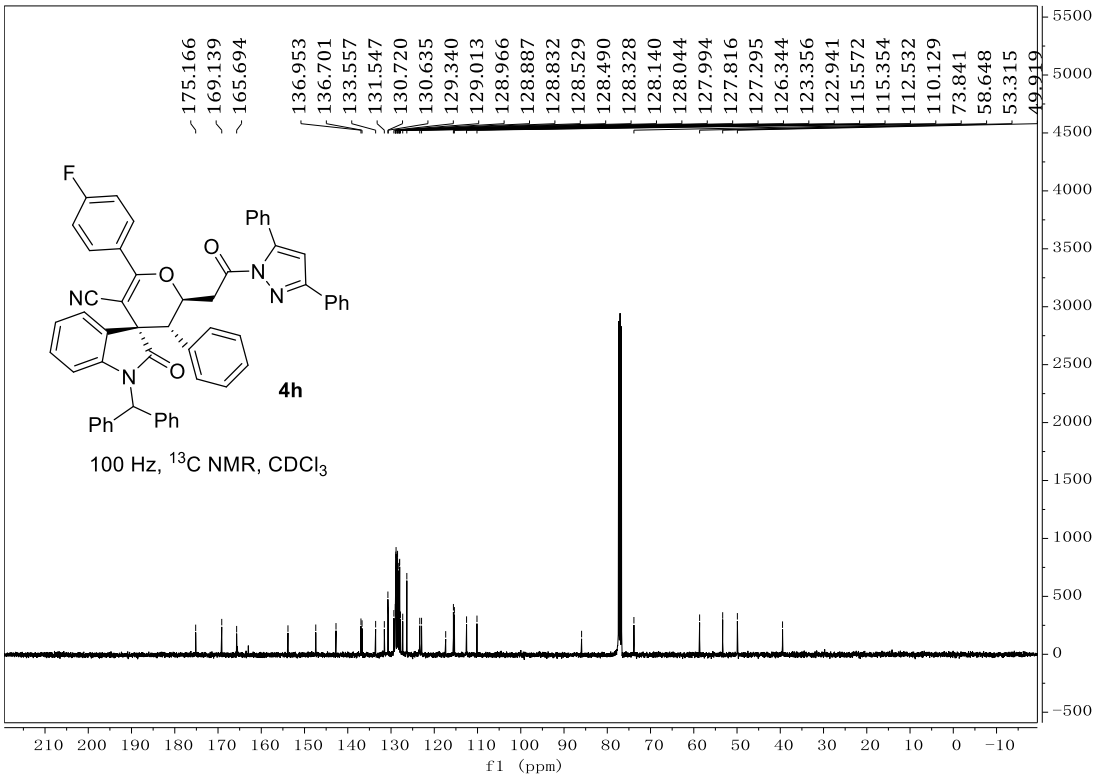
4g:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-5,7-dimethyl-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

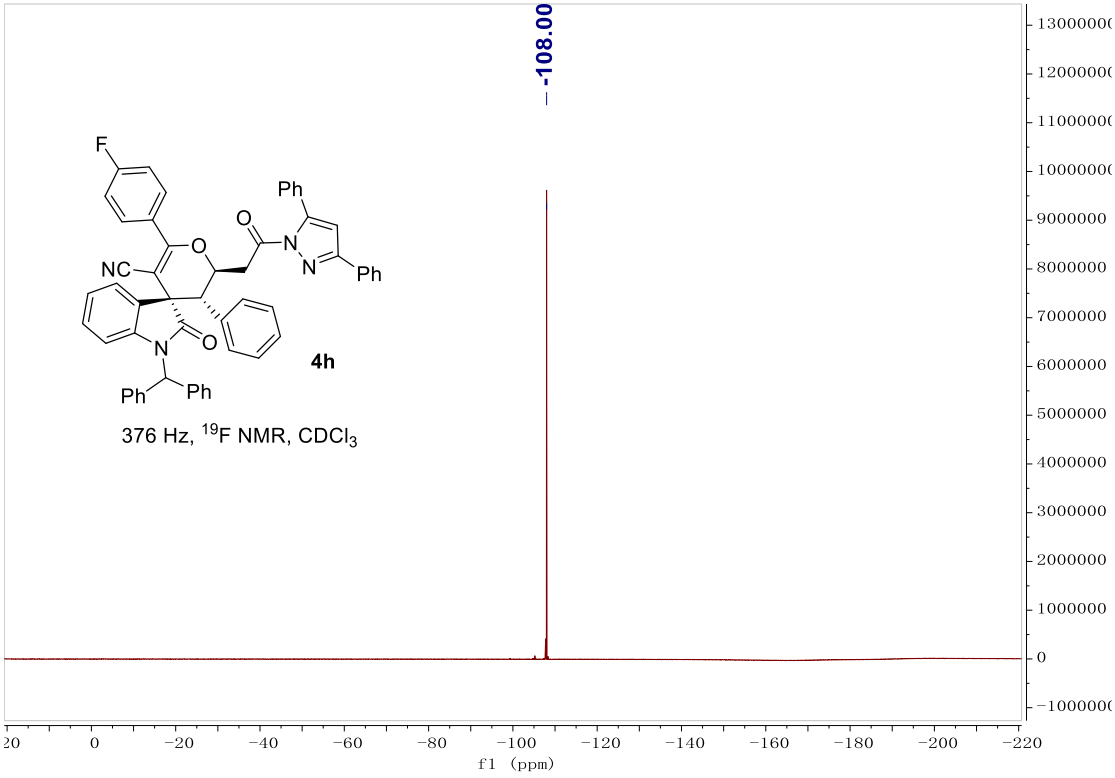




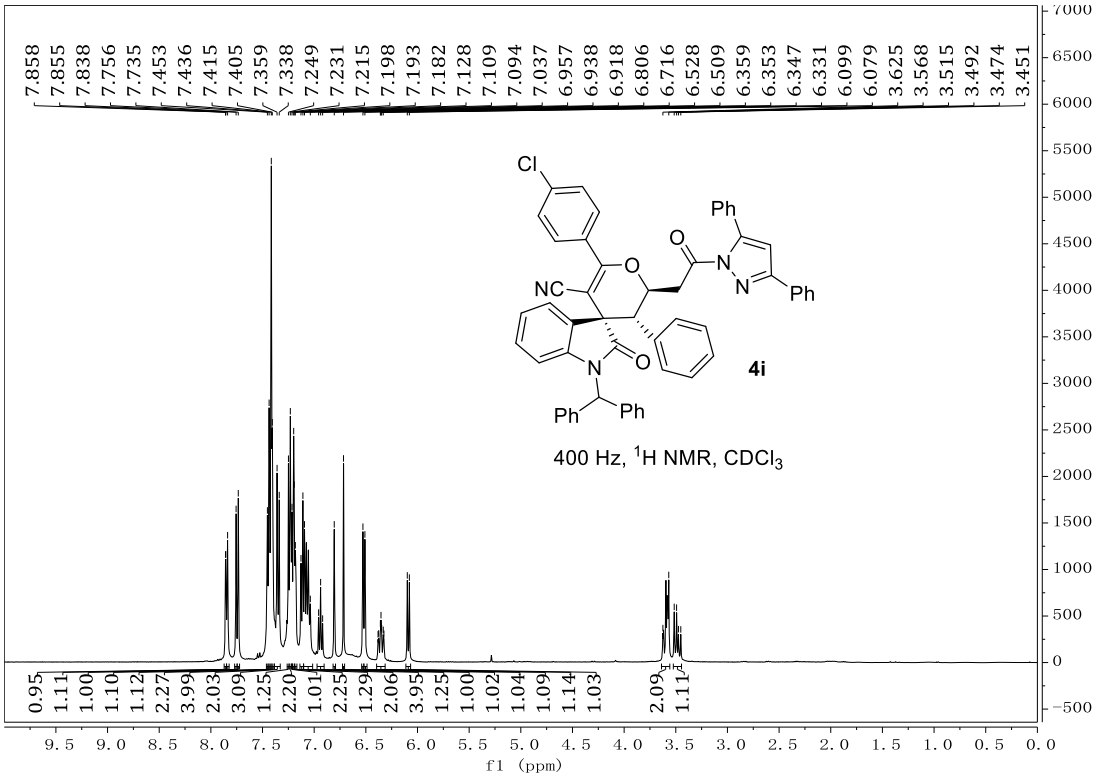
4h:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-6'-(4-fluorophenyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

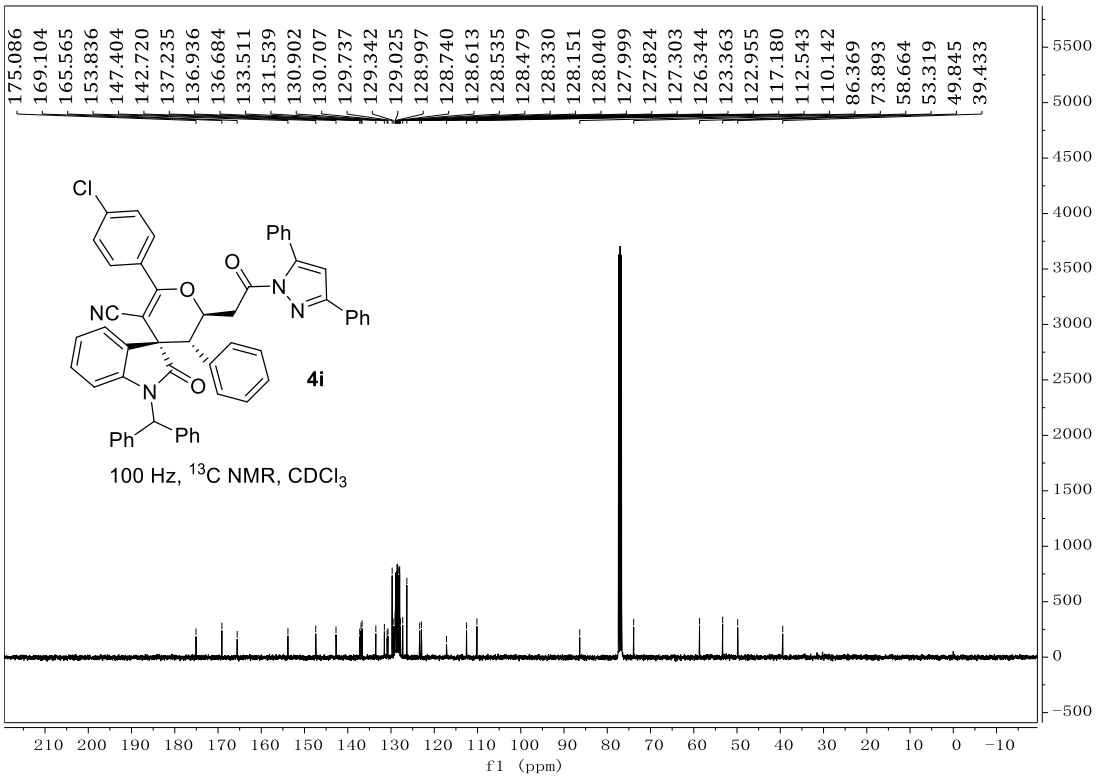




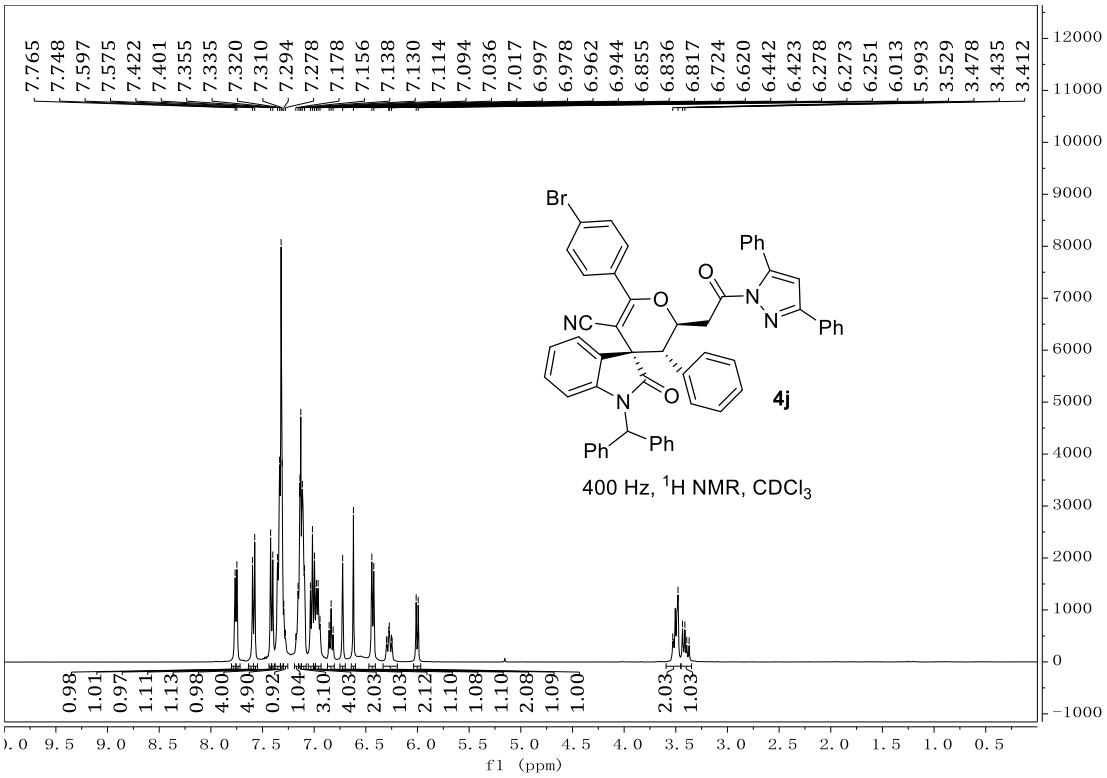


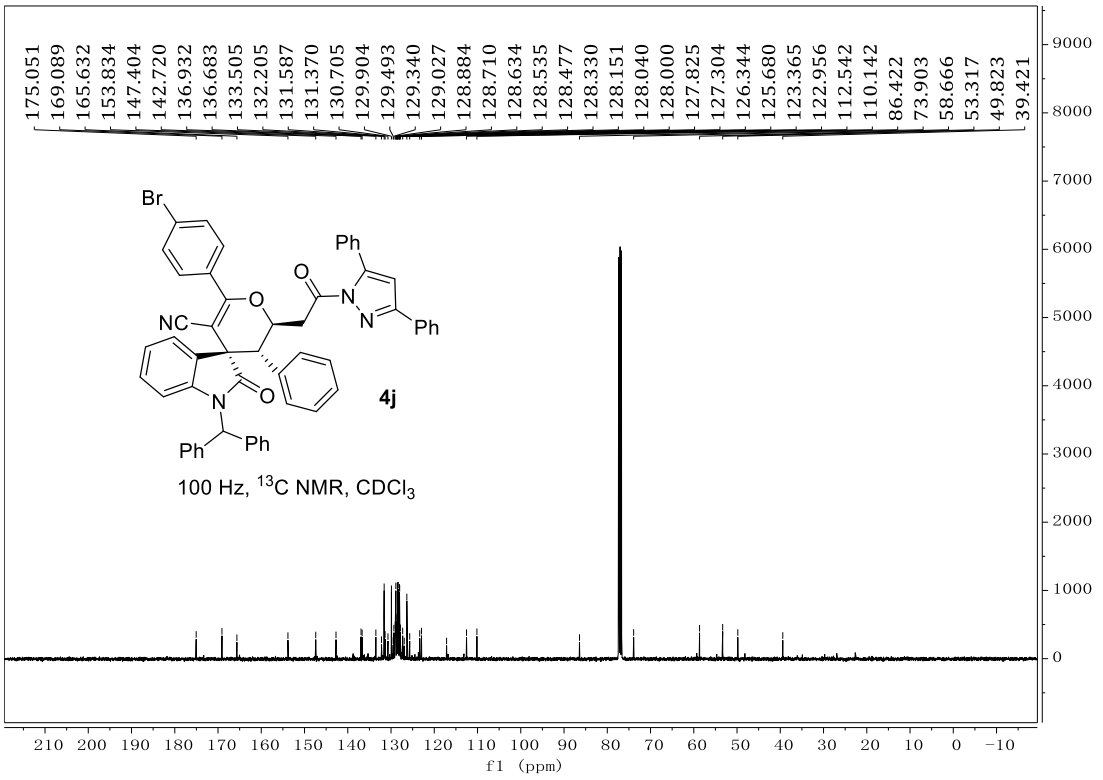
4i:(2'S,3R,3'R)-1-benzhydryl-6'-(4-chlorophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



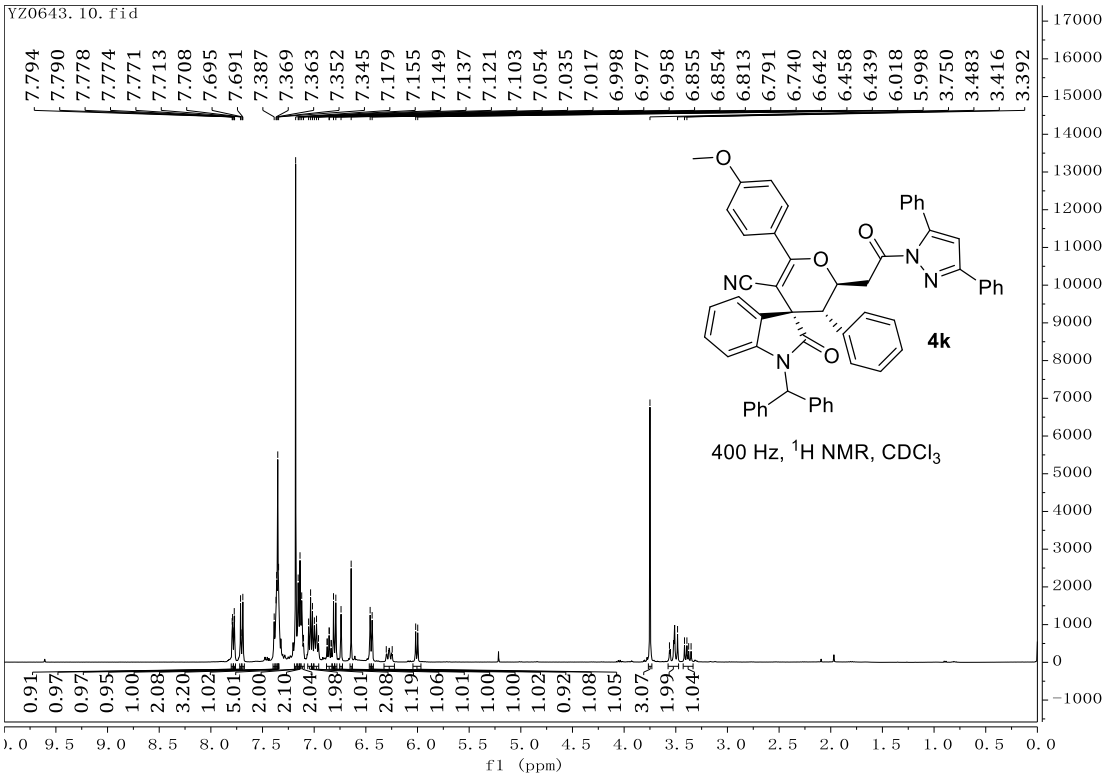


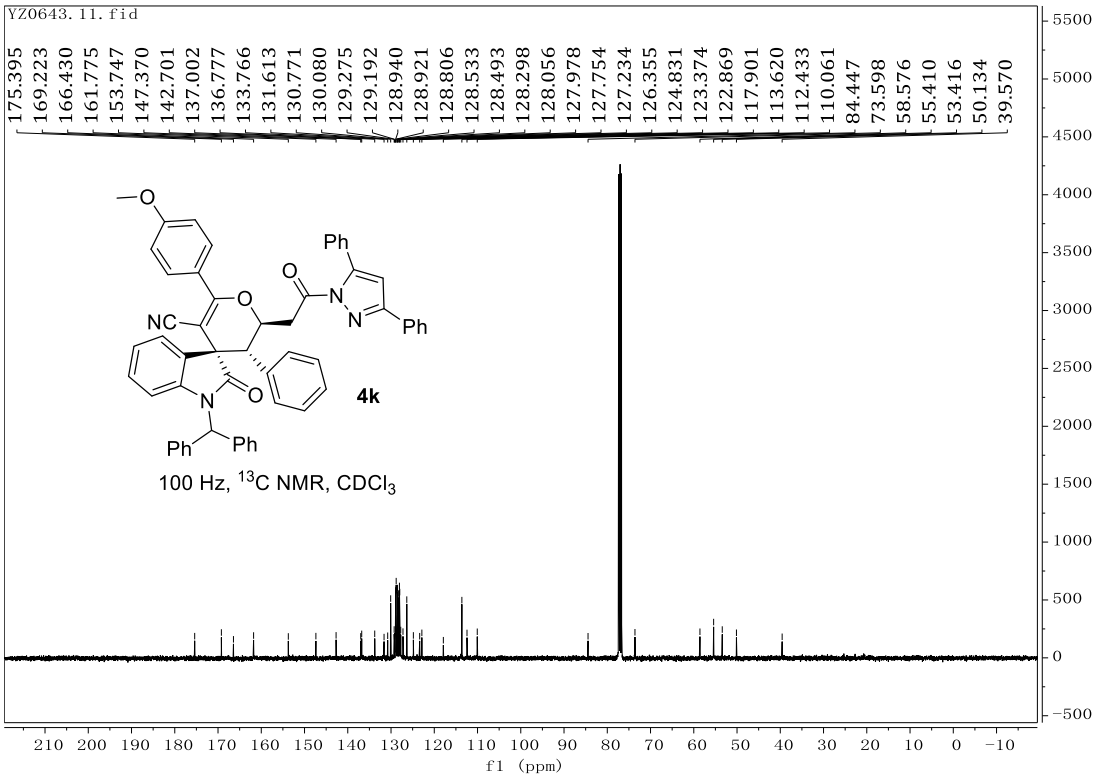
4j:(2'S,3R,3'R)-1-benzhydryl-6'-(4-bromophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



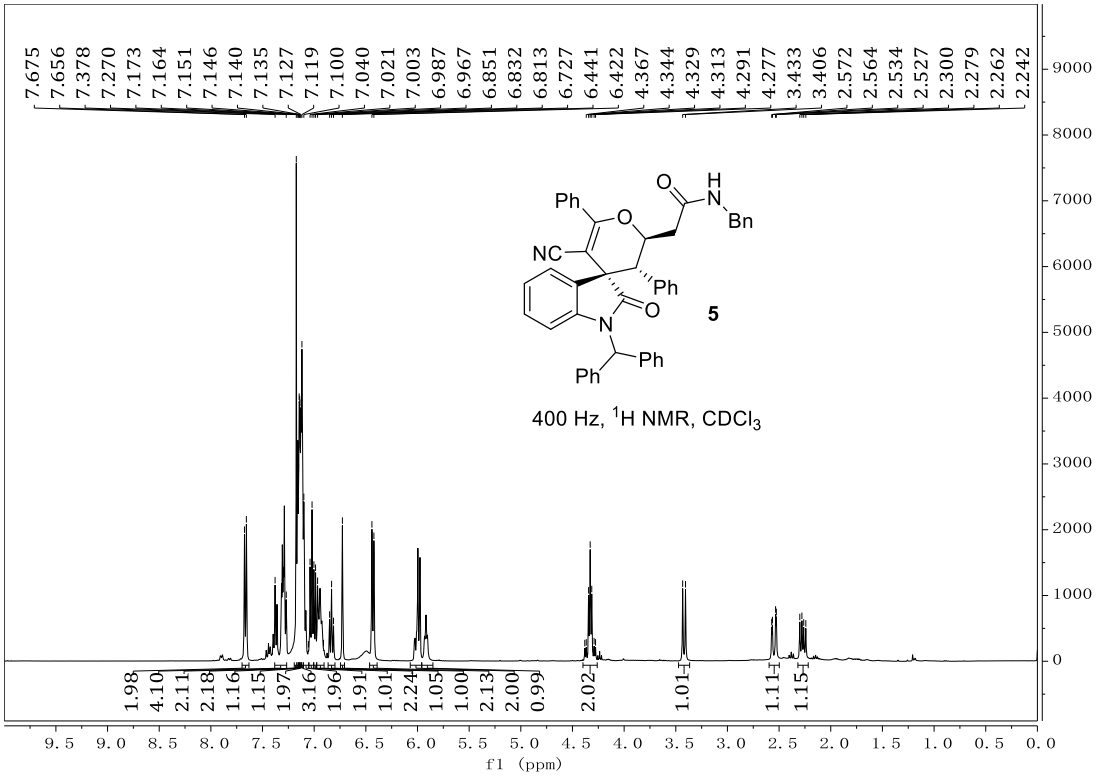


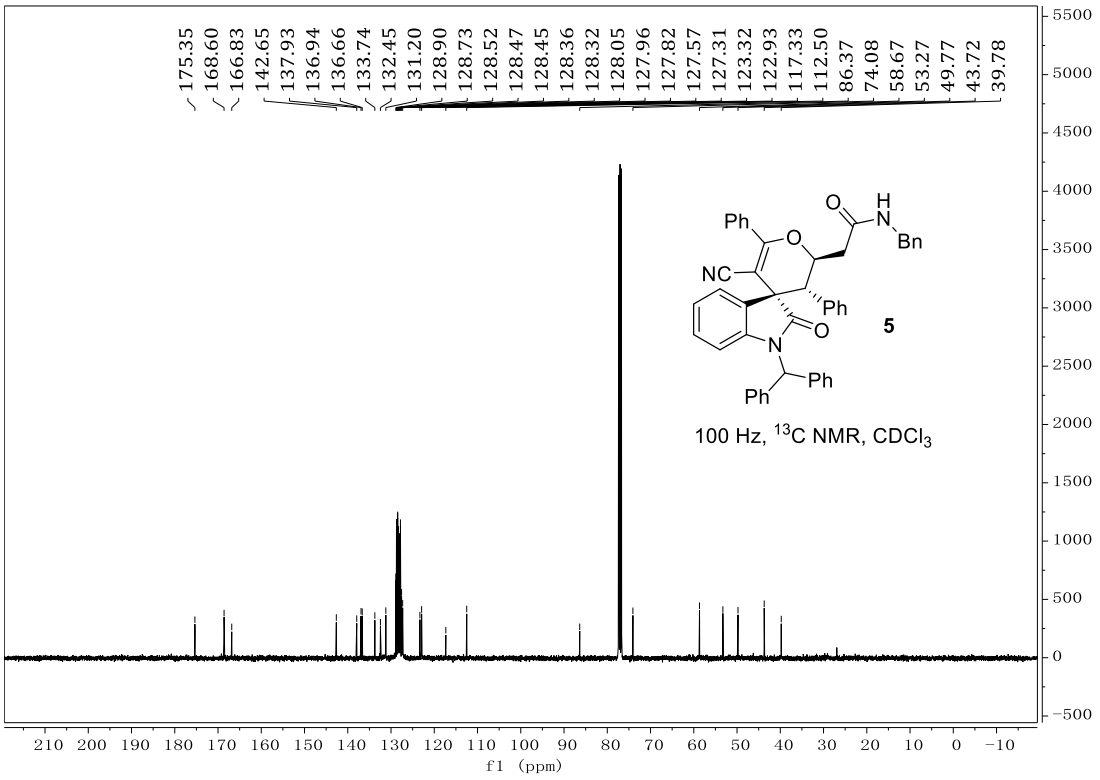
4k:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-6'-(4-methoxyphenyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



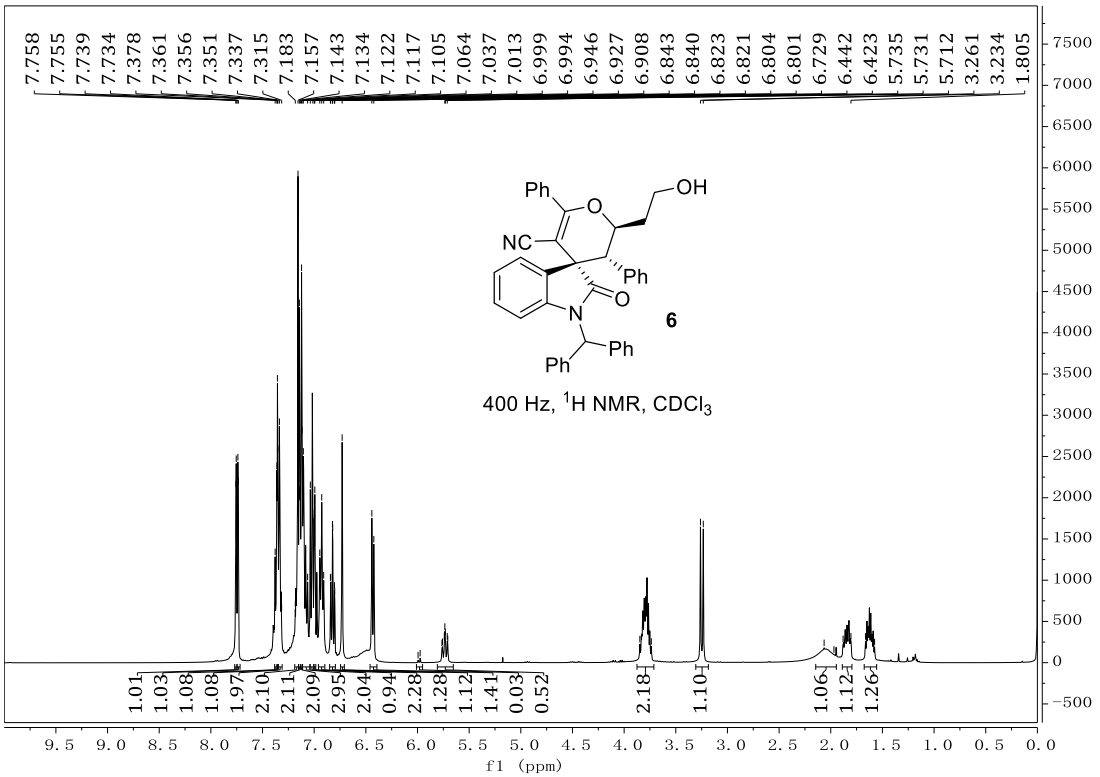


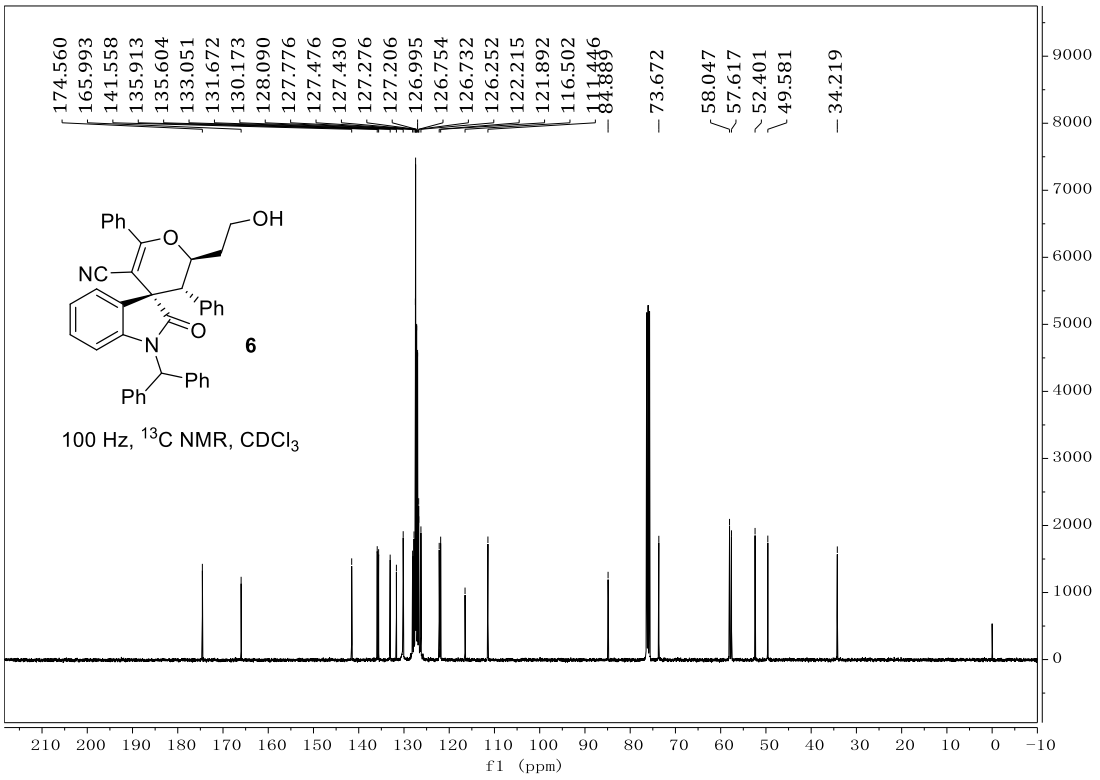
5:2-((2'S,3R,3'R)-1-benzhydryl-5'-cyano-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-2'-yl)-N-benzylacetamide





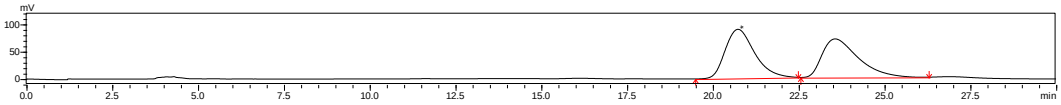
6:(2'S,3R,3'R)-1-benzhydryl-2'-(2-hydroxyethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



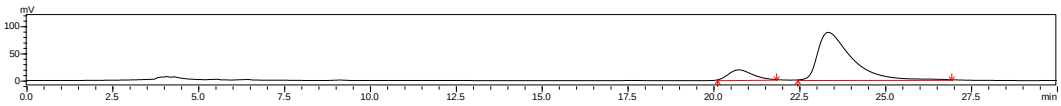

174.560
165.993
141.558
135.913
135.604
133.051
131.672
130.173
128.090
127.776
127.476
127.430
127.276
127.206
126.995
126.754
126.732
126.252
122.215
121.892
116.502
111.446
84.889
73.672
58.047
57.617
52.401
49.581
34.219
Ph
O
OH
NC
Ph
O
N
Ph
Ph
6
100 Hz, 13C NMR, CDCl3
f1 (ppm)

Ⅷ. HPLC Charts of products

3a-a:(2'S,3R,3'R)-1-benzyl-2'-(2-(3,5-dimethyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

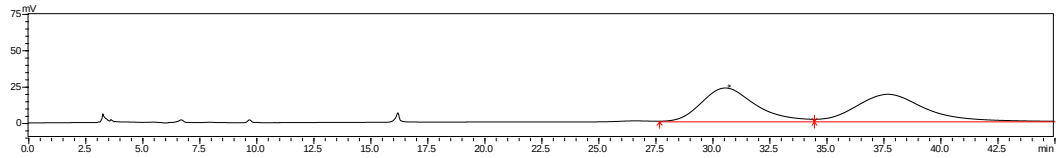


	Retention	Area	High	Area%
1	20.741	866053	18321	12.461
2	23.349	5867890	87338	87.639

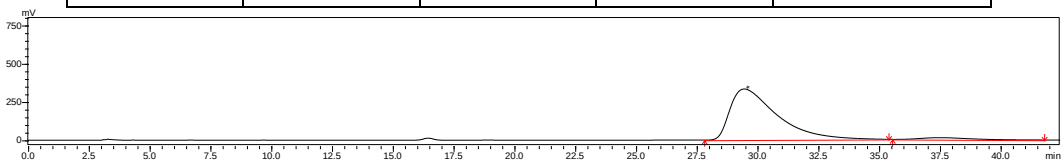


	Retention	Area	High	Area%
1	30.574	3716848	22837	49.315
2	37.706	3820166	18516	50.685

3a:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

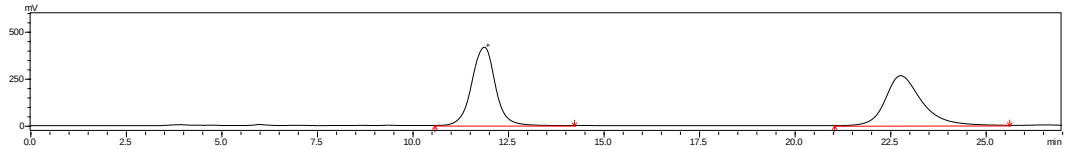


	Retention	Area	High	Area%
1	30.574	3716848	22837	49.315
2	37.706	3820166	18516	50.685

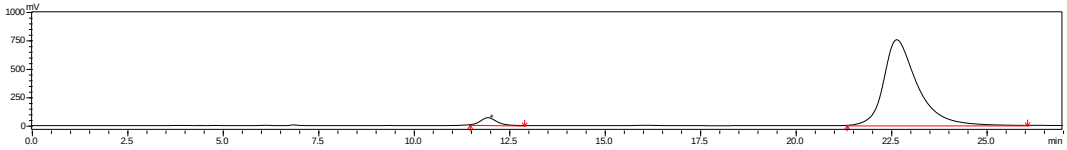


	Retention	Area	High	Area%
1	29.457	44566365	332898	96.449
2	37.508	1640995	12333	3.551

3b:(2'S,3R,3'R)-1-benzhydryl-3'-(3-bromophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

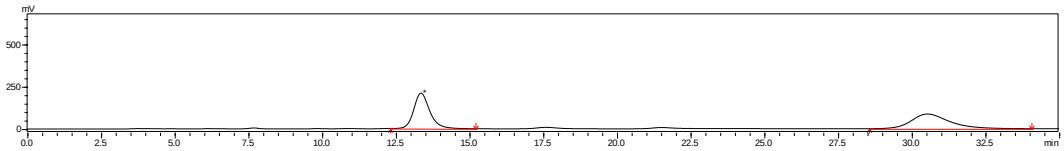


	Retention	Area	High	Area%
1	11.884	17905664	416885	50.568
2	22.780	17503526	265315	49.432

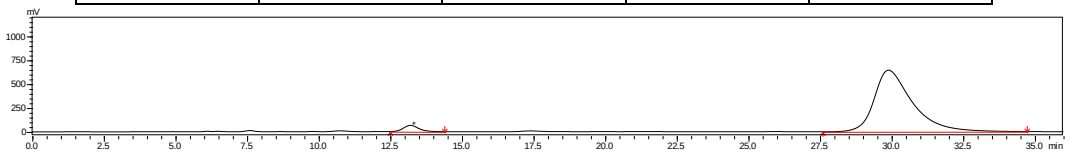


	Retention	Area	High	Area%
1	11.944	1811169	64081	3.791
2	22.649	45966931	752698	96.209

3c:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(3-fluorophenyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

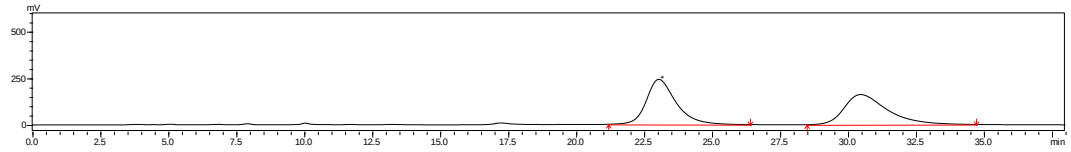


	Retention	Area	High	Area%
1	13.356	7878701	209452	50.012
2	30.536	7874885	86956	49.988

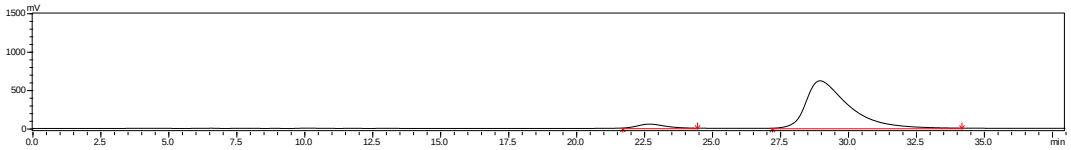


	Retention	Area	High	Area%
1	13.204	2442841	65702	3.923
2	29.894	59827147	645117	96.077

3d:(2'S,3R,3'R)-1-benzhydryl-3'-(3-chlorophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

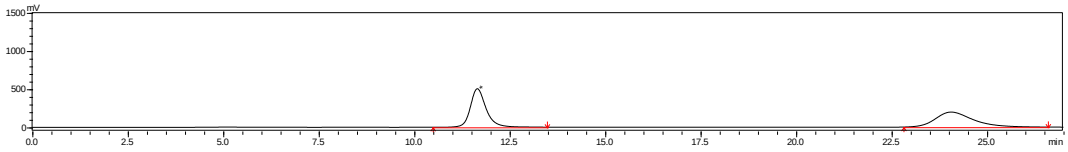


	Retention	Area	High	Area%
1	23.045	18324782	241784	50.621
2	30.472	17875244	161532	49.379

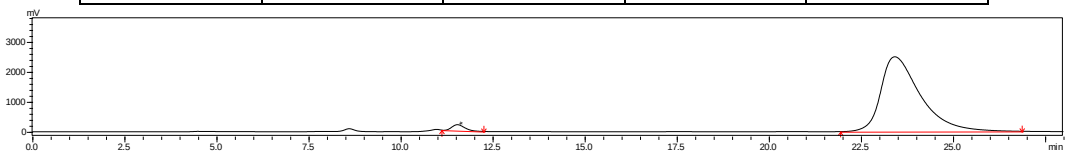


	Retention	Area	High	Area%
1	22.700	3484731	51510	4.957
2	28.976	66810541	616543	95.043

3e:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(m-tolyl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

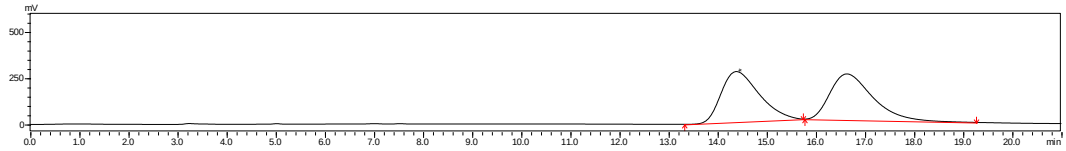


	Retention	Area	High	Area%
1	11.655	14486245	504436	51.764
2	24.062	13498876	196453	48.236

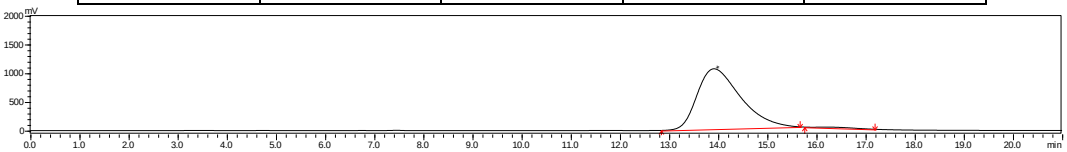


	Retention	Area	High	Area%
1	11.546	4564582	196554	2.399
2	23.421	185673647	2495254	97.601

3f:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(4-methoxyphenyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

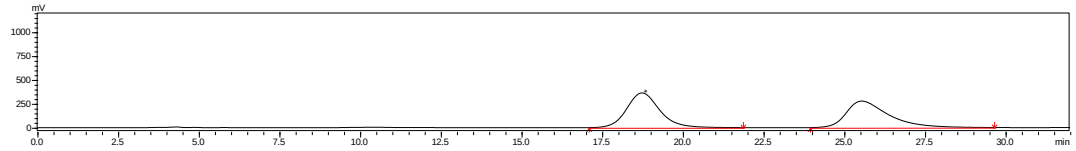


	Retention	Area	High	Area%
1	14.383	14607890	272964	49.399
2	16.632	14963226	248903	50.601

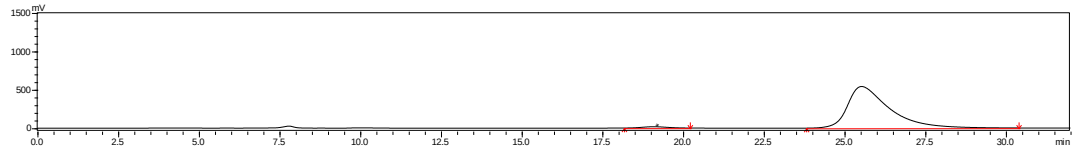


	Retention	Area	High	Area%
1	13.918	64046786	1048453	99.059
2	15.763	608537	73	0.941

3g:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(p-tolyl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

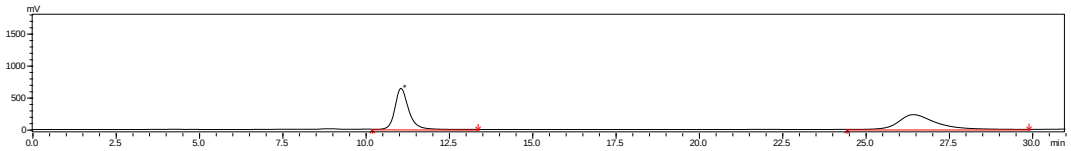


	Retention	Area	High	Area%
1	18.737	25888253	363846	50.478
2	25.542	25397453	278004	49.522

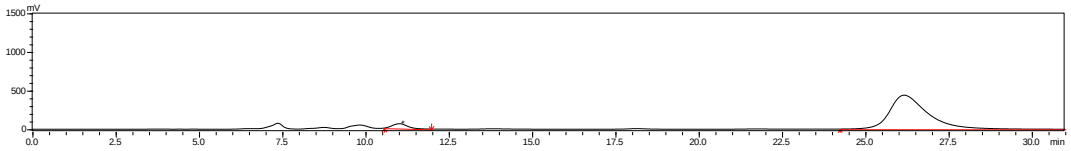


	Retention	Area	High	Area%
1	19.092	901280	16759	1.816
2	25.534	48722065	541247	98.184

3h:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(o-tolyl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

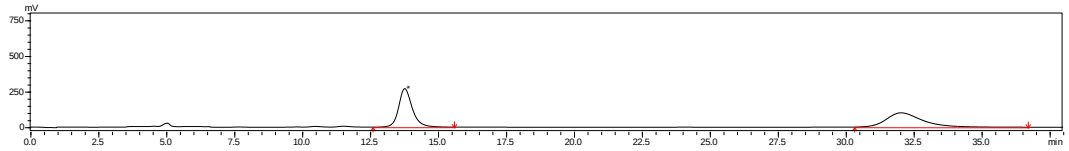


	Retention	Area	High	Area%
1	11.062	18063225	639513	50.641
2	26.439	17605640	230787	49.359

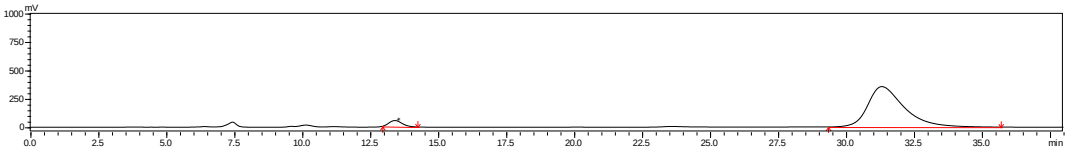


	Retention	Area	High	Area%
1	11.015	1836273	60458	5.063
2	26.167	34432186	438707	94.937

3i:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(2-fluorophenyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

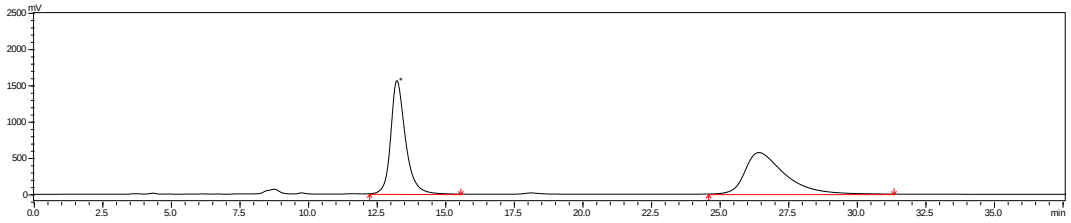


	Retention	Area	High	Area%
1	13.778	9436392	270296	50.584
2	32.041	9218539	100235	49.416

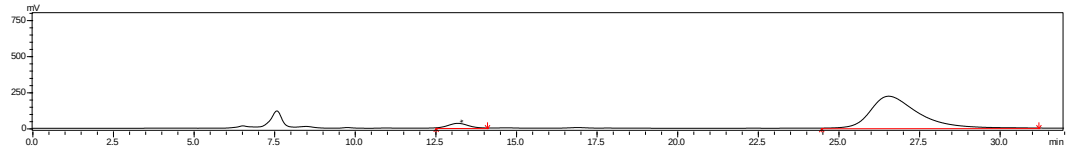


	Retention	Area	High	Area%
1	13.411	1761212	53152	5.067
2	31.323	32998287	354754	94.933

3j:(2'S,3R,3'R)-1-benzhydryl-3'-(3,5-dimethylphenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxo ethyl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

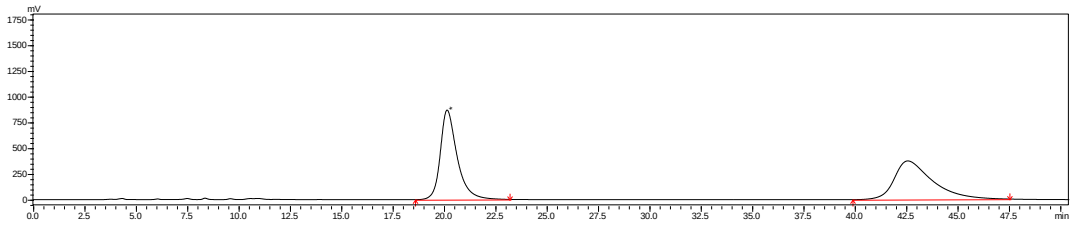


	Retention	Area	High	Area%
1	13.240	58102472	1559318	50.366
2	26.438	57257959	571594	49.634

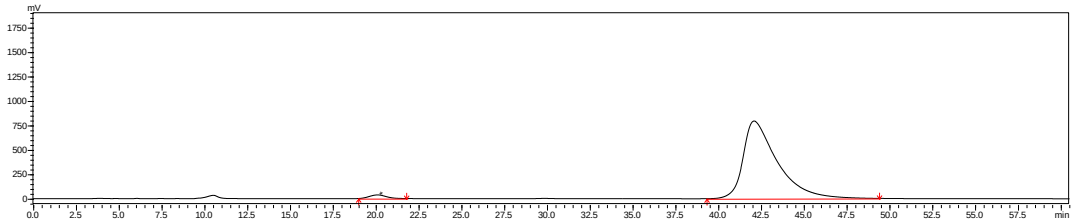


	Retention	Area	High	Area%
1	13.204	1301748	31545	5.491
2	26.562	22404168	220871	94.509

3k:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-6'-phenyl-3'-(thiophen-2-yl)-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

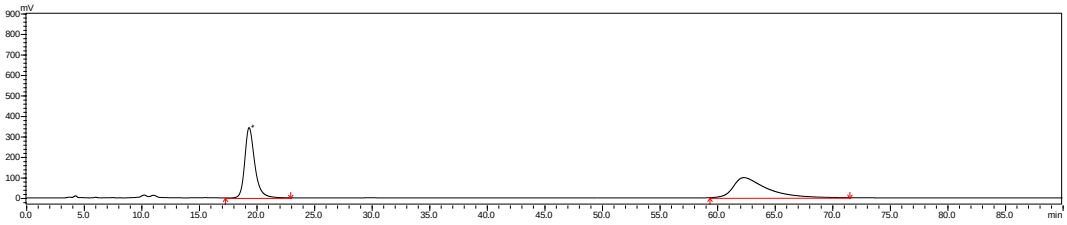


	Retention	Area	High	Area%
1	20.155	49493384	868445	50.659
2	42.583	48206086	373985	49.341

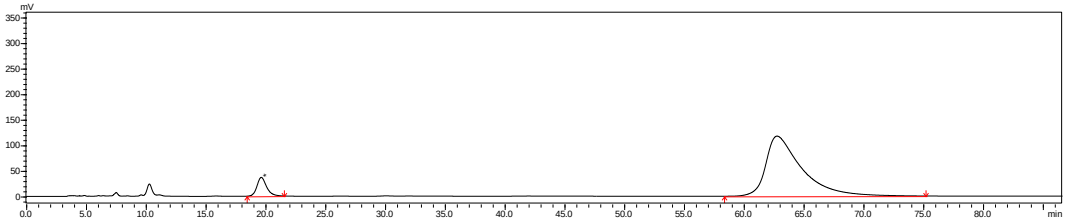


	Retention	Area	High	Area%
1	20.116	2513926	36925	2.233
2	42.101	110059122	793441	97.767

3l:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-3'-(furan-2-yl)-2-oxo-6'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

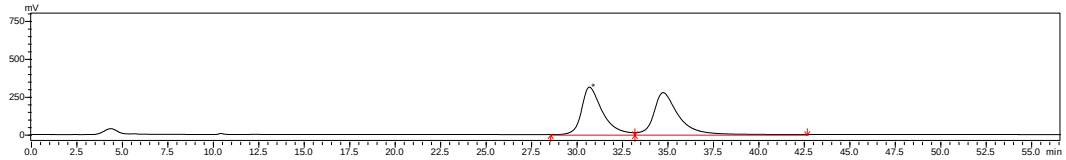


	Retention	Area	High	Area%
1	19.367	20586298	342704	51.135
2	62.339	19672588	97922	48.865

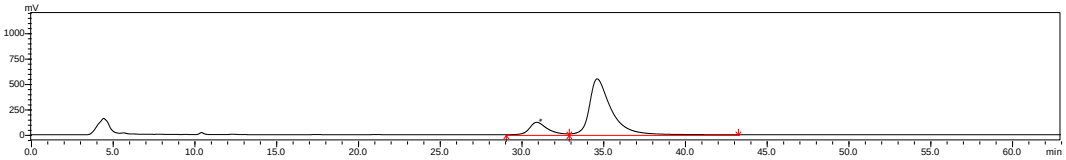


	Retention	Area	High	Area%
1	19.662	2043814	36709	7.691
2	62.790	24530109	117473	92.309

4a:(2'S,3R,3'R)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-1,3',6'-triphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

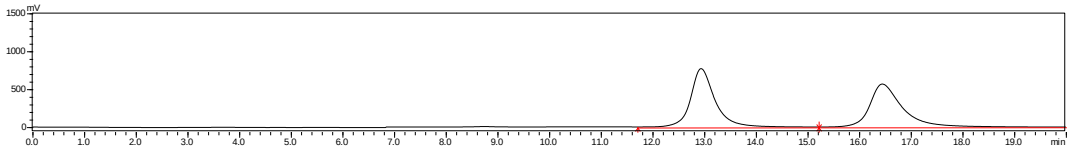


	Retention	Area	High	Area%
1	30.718	24925969	312388	49.058
2	34.771	25883104	276427	50.942

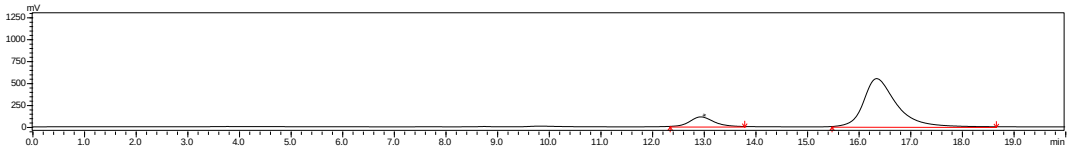


	Retention	Area	High	Area%
1	30.940	9328310	122380	15.588
2	34.639	50514612	549528	84.412

4b:(2'S,3R,3'R)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-1-methyl-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

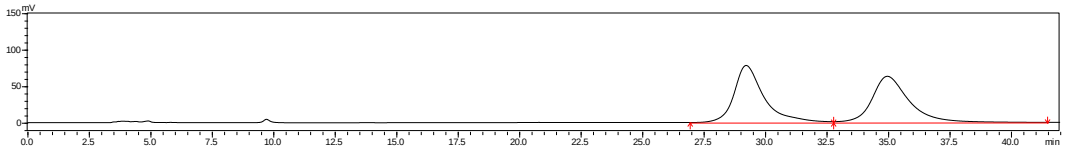


	Retention	Area	High	Area%
1	12.942	26155028	774178	50.616
2	16.451	25518525	569088	49.384

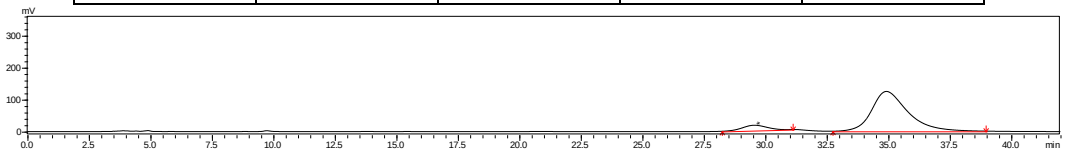


	Retention	Area	High	Area%
1	12.944	3410076	108766	12.482
2	16.351	23910326	547223	87.518

4c:(2'S,3R,3'R)-1-benzyl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3',6'-diphenyl-2', 3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

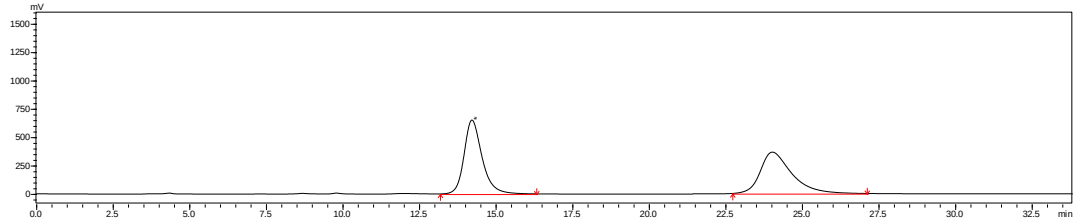


	Retention	Area	High	Area%
1	29.233	6636547	78097	50.058
2	34.975	6621073	63192	49.942

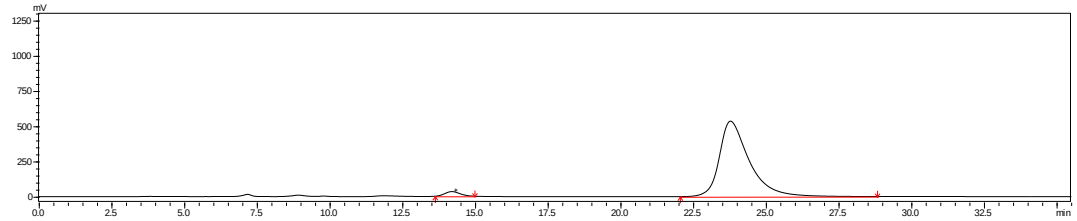


	Retention	Area	High	Area%
1	29.564	1116007	16325	8.100
2	34.927	12661454	124242	91.900

4d:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-5-methyl-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

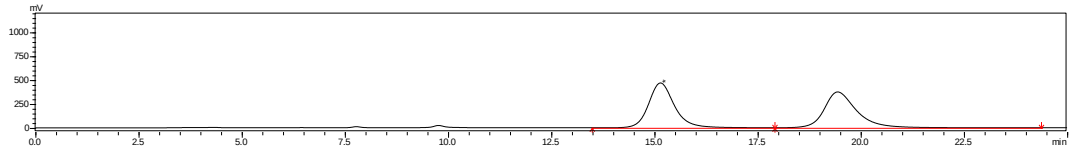


	Retention	Area	High	Area%
1	14.229	26663200	651158	50.693
2	24.038	25934418	364584	49.307

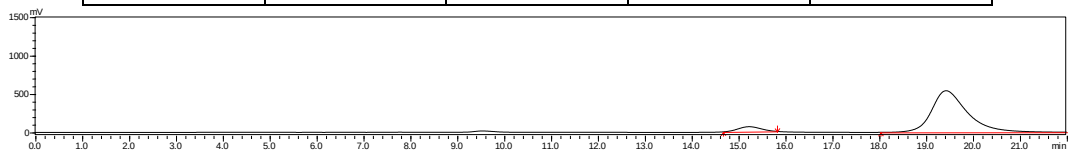


	Retention	Area	High	Area%
1	14.208	1191222	32911	3.020
2	23.789	38258521	535395	96.980

4e:(2'S,3R,3'R)-1-benzhydryl-5-bromo-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3', 6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

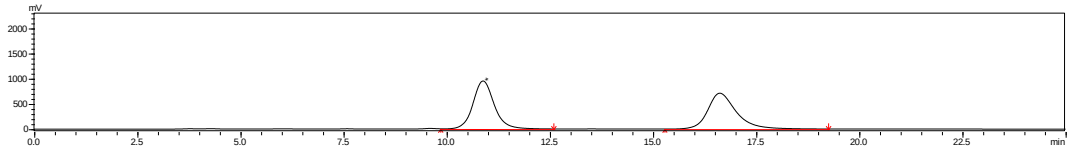


	Retention	Area	High	Area%
1	15.149	20542941	469758	49.996
2	19.443	20546140	375548	50.004

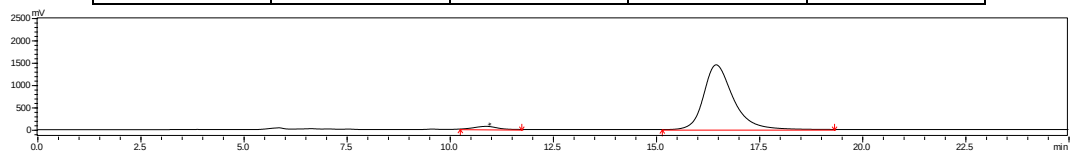


	Retention	Area	High	Area%
1	15.225	2156490	64398	6.978
2	19.427	28746517	541617	93.022

4f:(2'S,3R,3'R)-1-benzhydryl-7-chloro-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3', 6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

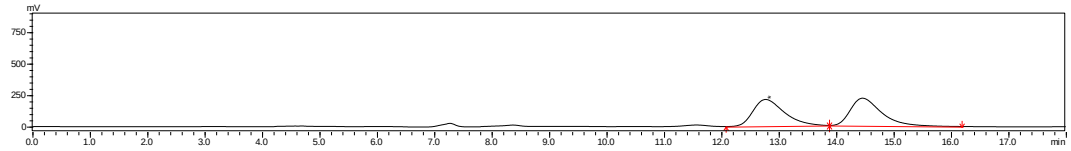


	Retention	Area	High	Area%
1	10.881	33932631	950622	49.804
2	16.621	34199813	711114	50.196

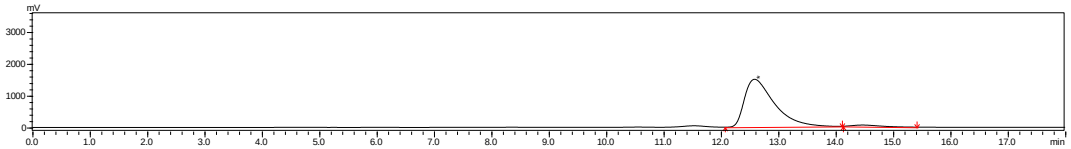


	Retention	Area	High	Area%
1	10.884	2330347	63866	3.134
2	16.461	72020781	1449493	96.866

4g:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-5,7-dimethyl-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

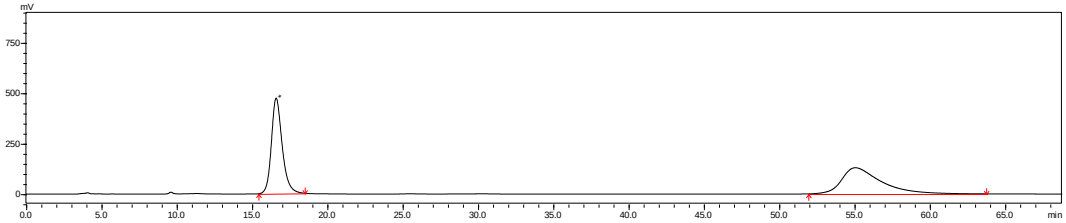


	Retention	Area	High	Area%
1	12.773	7972650	211721	49.409
2	14.461	8163483	218487	50.591

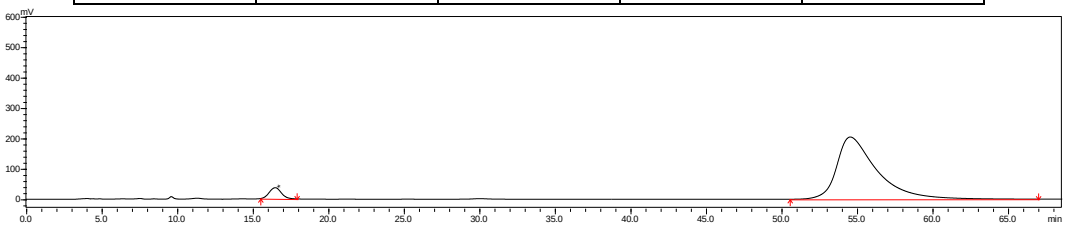


	Retention	Area	High	Area%
1	12.588	53935039	1499736	97.528
2	14.470	1366914	45051	2.472

4h:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-6'-(4-fluorophenyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

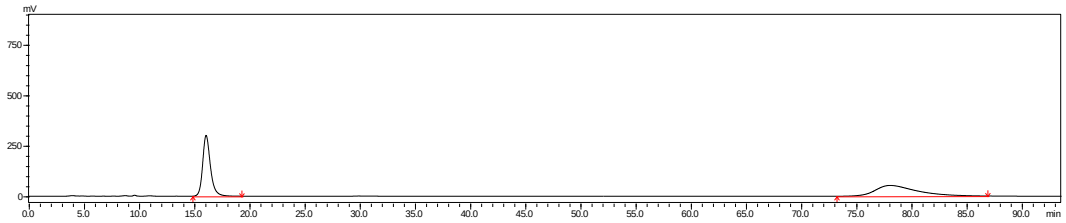


	Retention	Area	High	Area%
1	16.603	23574287	473385	50.015
2	55.060	23560082	129728	49.985

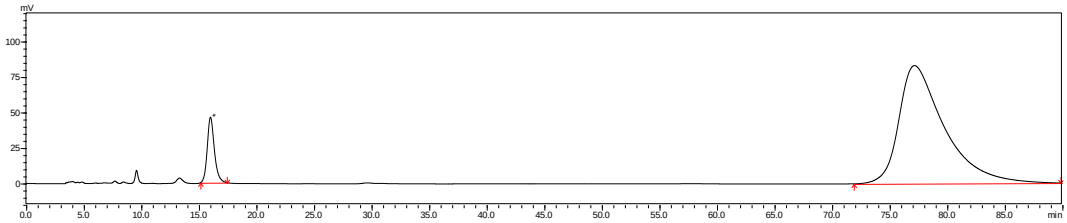


	Retention	Area	High	Area%
1	16.495	2003571	36269	5.042
2	54.563	37732782	204430	94.958

4i:(2'S,3R,3'R)-1-benzhydryl-6'-(4-chlorophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

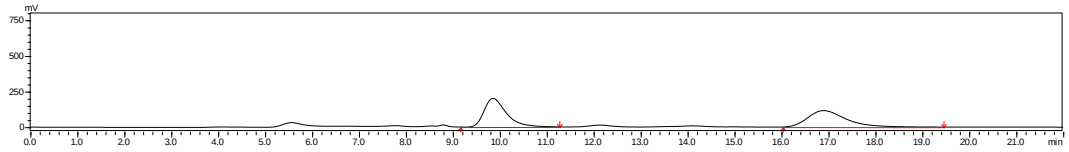


	Retention	Area	High	Area%
1	16.078	14809720	301111	51.608
2	78.083	13886865	53120	48.392

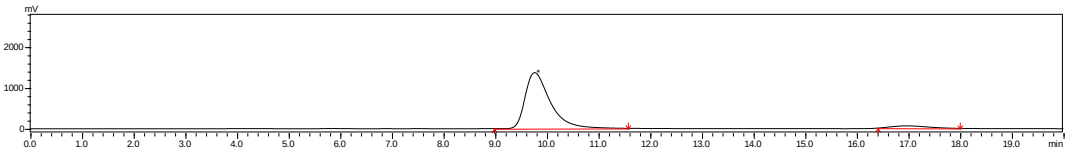


	Retention	Area	High	Area%
1	16.017	1979595	46199	7.990
2	77.164	22797634	83129	92.010

4j:(2'S,3R,3'R)-1-benzhydryl-6'-(4-bromophenyl)-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

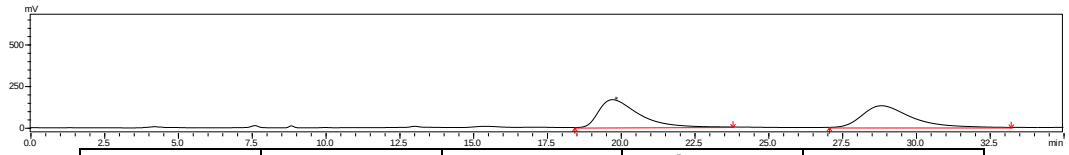


	Retention	Area	High	Area%
1	9.857	6582026	200260	50.322
2	16.900	6497820	115142	49.678

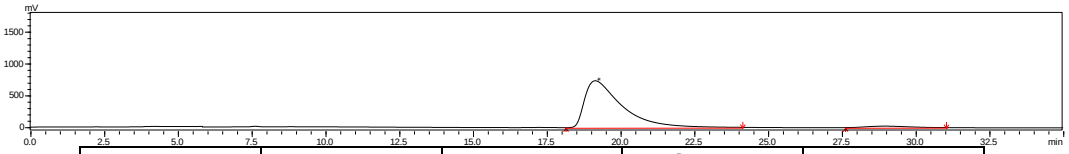


	Retention	Area	High	Area%
1	9.764	46016997	1370728	94.483
2	16.967	2686995	56682	5.517

4k:(2'S,3R,3'R)-1-benzhydryl-2'-(2-(3,5-diphenyl-1H-pyrazol-1-yl)-2-oxoethyl)-6'-(4-methoxyphenyl)-2-oxo-3'-phenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile

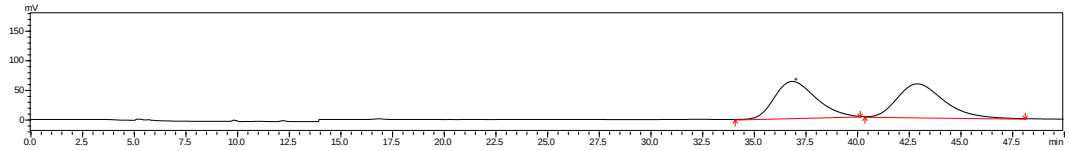


	Retention	Area	High	Area%
1	19.723	15440271	166439	51.298
2	28.837	14659117	129701	48.702

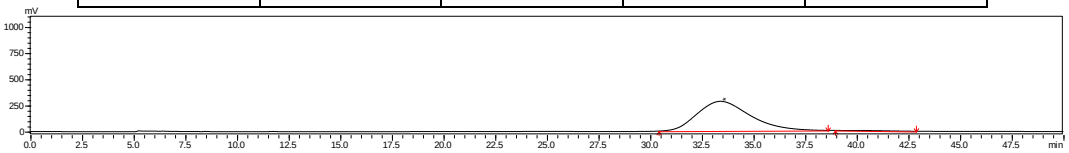


	Retention	Area	High	Area%
1	19.145	64104388	736362	96.615
2	28.956	2246298	23236	3.385

5:2-((2'S,3R,3'R)-1-benzhydryl-5'-cyano-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-2'-yl)-N-benzylacetamide

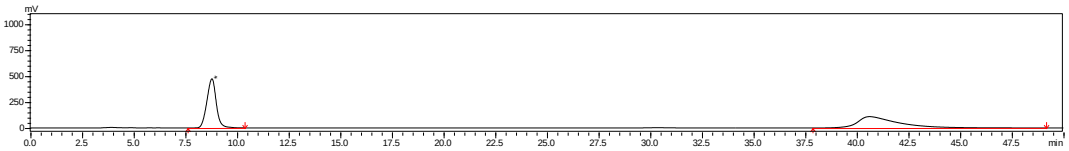


	Retention	Area	High	Area%
1	36.866	8535198	61886	49.373
2	42.912	8752144	56580	50.627

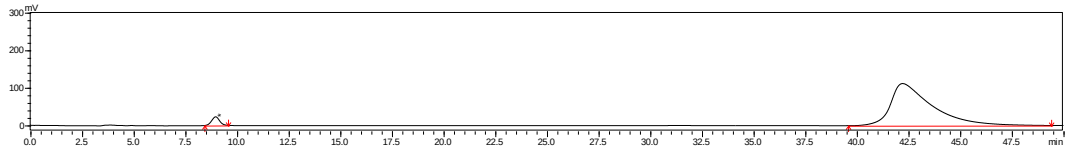


	Retention	Area	High	Area%
1	33.406	49987784	281625	99.596
2	38.946	202530	8	0.404

6:(2'S,3R,3'R)-1-benzhydryl-2'-(2-hydroxyethyl)-2-oxo-3',6'-diphenyl-2',3'-dihydrospiro[indoline-3,4'-pyran]-5'-carbonitrile



	Retention	Area	High	Area%
1	8.790	14954825	473677	50.171
2	40.621	14852918	109155	49.829



	Retention	Area	High	Area%
1	8.790	609198	22991	3.744
2	42.218	15661874	111958	96.256