Electronic Supplementary Information (ESI)

Highly diastereo- and enantioselective synthesis of spirooxindole-cyclohexaneamides through *N*,*N*′-dioxide/Ni(II)-catalyzed Diels–Alder reactions

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CONTENTS:

(A) General information

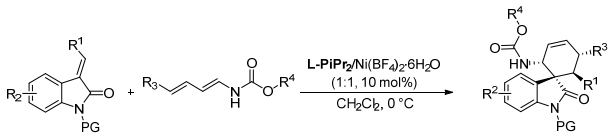
Reactions were carried out using commercial available reagents in oven-dried apparatus. CH_2Cl_2 was dried over powdered K_2CO_3 and distilled under nitrogen just before use. ^1H NMR spectra were recorded at 400 MHz. The chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets, td = triplet of doublets, dt = doublet of triplets, ddd = doublet of doublet of doublets), coupling constants (Hz), integration. ^{13}C NMR data were collected at 100 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard. Metal catalysts obtained from commercial sources were used without further purification. Enantiomeric excesses were determined by chiral HPLC analysis on Daicel Chiralcel IA/IB/IC/ID/IE/AD-H in comparison with the authentic racemates. Optical rotations were reported as follows: $[\alpha]_D^T$ = (c: g/100 mL, in solvent). HRMS was recorded on a commercial apparatus (ESI Source, TOF). Chiral *N*,*N*′-dioxide ligands, methyleneindolinones, 1,3-dienylcarbamates and 1,2-dihydropyridines were prepared according to previously reported method.[1-4]

(B) General procedure for asymmetric DA reactions

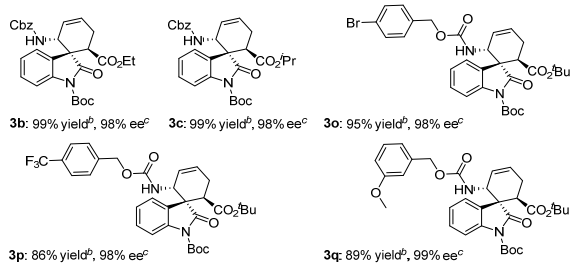
1. Representative experimental procedure for DA reaction of 1,3-dienylcarbamates and 1,2-dihydropyridines with methyleneindolinones

A mixture of methyleneindolinone **1a** (30.3 mg, 0.1 mmol), $Ni(BF_4)_2{\cdot}6H_2O$ (3.4 mg, 0.01 mmol, 10 mol%) and *N,N′*-dioxide ligand **L-PiPr$_2$** (6.5 mg, 0.01 mmol, 10 mol%) was weighted into a test tube under an inert atmosphere. Anhydrous CH_2Cl_2 (1.0 mL) was added and the solution was stirred at 30 ºC for 0.5 h and then stirred at 0 ºC for 5 min. Subsequently, 1,3-dienylcarbamate **2a** (22.3 mg, 0.11 mmol) was added at 0 ºC, and the reaction mixture was stirred for an additional 4 h. The product **3a** was purified by flash chromatography (Pet/EtOAc = 3:1).

Table 2 Scope of other substrates for the asymmetric D–A reaction of methyleneindolinones **1** with 1,3-Dienylcarbamates **2**[a]

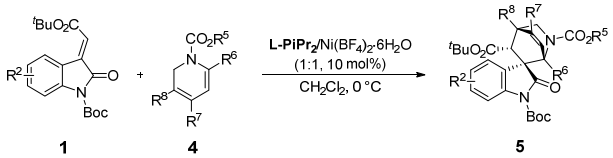


1 2 3

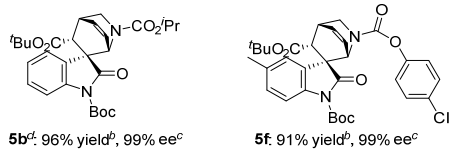


[a] Unless otherwise noted, the reaction was carried out with **1** (0.1 mmol), **2** (0.11 mmol), **L-PiPr$_2$**/$Ni(BF_4)_2{\cdot}6H_2O$ (1:1, 10 mol%) in CH_2Cl_2 (1.0 mL) at 0 ºC for 3-24 h and the dr >95:5 was determined by ^{1}H NMR analysis. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis.

Table 3 Scope of other substrates for the asymmetric D–A reaction of methyleneindolinones **1** with 1,2-dihydropyridines **4**[a]



1 4 5



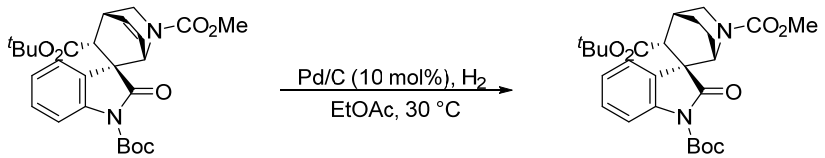
[a] Unless otherwise noted, the reaction was carried out with **1** (0.1 mmol), **4** (0.11 mmol), **L-PiPr$_2$**/Ni(BF$_4$)$_2$·6H$_2$O (1:1, 10 mol%) in CH_2Cl_2 (1.0 mL) at 0 °C for 24-36 h and the dr >95:5 was determined by ^{1}H NMR analysis. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] **4** (1.5 equiv, 0.15 mmol) was used.

2. General experimental procedure for the scale-up reaction

A mixture of Ni(BF$_4$)$_2$·6H$_2$O (85.1 mg, 0.25 mmol, 10 mol%) and *N,N′*-dioxide ligand **L-PiPr$_2$** (162.2 mg, 0.25 mmol, 10 mol%) was weighted into a round-bottomed flask. Then 10.0 mL anhydrous THF was added and the mixture was stirred at 30 °C for 30 min. After the solvent was removed under vacuo, methyleneindolinone **1a** (0.76 g, 2.5 mmol) were weighed into it followed by adding anhydrous CH_2Cl_2 (25 mL). The mixture was stirred at 0 °C for for 5 min. Subsequently, 1,3-dienylcarbamate **2a** (0.56 g, 2.75 mmol) was added under 0 °C and the reaction mixture was stirred for an additional 3 h. The residue was purified by flash chromatography on silica gel (Pet/EtOAc = 3:1) to afford the desired product **3a**.

3. General experimental procedure for hydrogenation of 3r and 5a

To a solution of **3r** (51.4 mg, 0.1 mmol, 1.0 equiv) in EtOAc (2.0 mL) was added Pd/C [21.3 mg (5%), 0.01 mmol, 0.1 equiv]. Under the H_2 atmosphere, the mixture was allowed to stir for 4 h at 30 °C. Then, filtration followed by removal of solvent under reduced pressure and silica gel flash column flash chromatography (Pet/EtOAc = 4:1) afford **6a** (51.6 mg, 99% yield, >95:5 dr and 99% ee).



5a
>95:5 dr, 99% ee

6b
94% yield, >95:5 dr, 99% ee

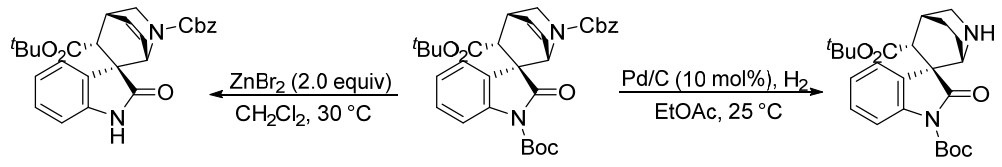
To a solution of **5a** (88.3 mg, 0.18 mmol, 1.0 equiv) in EtOAc (2.0 mL) was added Pd/C [38.2 mg (5%), 0.018 mmol, 0.1 equiv]. Under the H_2 atmosphere, the mixture was allowed to stir for 4 h at 30 °C. Then, filtration followed by removal of solvent

under reduced pressure and silica gel flash column flash chromatography (Pet/EtOAc = 4:1) afford **6b** (82.3 mg, 94% yield, >95:5 dr and 99% ee).

3. General experimental procedure for deprotection of 3d and 5d

To a solution of **3d** (104.5 mg, 0.19 mmol, 1.0 equiv) in CH_2Cl_2 (2.0 mL) was added $ZnBr_2$ (85.5 mg, 0.38 mmol, 2.0 equiv). Under the N_2 atmosphere, the mixture was allowed to stir for 40 min at 30 °C. Then, silica gel flash column flash chromatography (Pet/EtOAc = 1:1) afford **6c** (84.4 mg, 99% yield, >95:5 dr and 98% ee).

To a solution of **3d** (54.8 mg, 0.1 mmol, 1.0 equiv) in EtOAc (2.0 mL) was added Pd/C [21.3 mg (5%), 0.01 mmol, 0.1 equiv]. Under the H_2 atmosphere, the mixture was allowed to stir for 4 h at 25 °C. Then, filtration followed by removal of solvent under reduced pressure and silica gel flash column flash chromatography (Pet/acetone = 4:1) afford **6d** (36.9 mg, 89% yield, 73:27 dr and 99% ee).



6e
99% yield, >95:5 dr, 99% ee

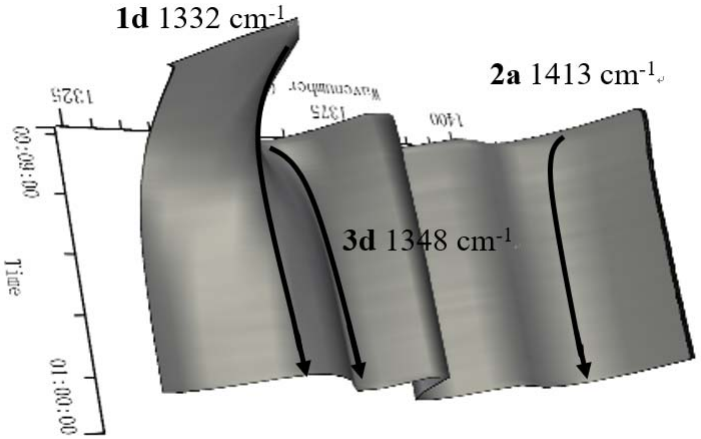
5d
>95:5 dr, 99% ee

6f
unstable

To a solution of **5d** (101.9 mg, 0.18 mmol, 1.0 equiv) in CH_2Cl_2 (2.0 mL) was added $ZnBr_2$ (81.1 mg, 0.36 mmol, 2.0 equiv). Under the N_2 atmosphere, the mixture was allowed to stir for 40 min at 30 °C. Then, silica gel flash column flash chromatography (Pet/EtOAc = 1:1) afford **6e** (82.1 mg, 99% yield, >95:5 dr and 99% ee).

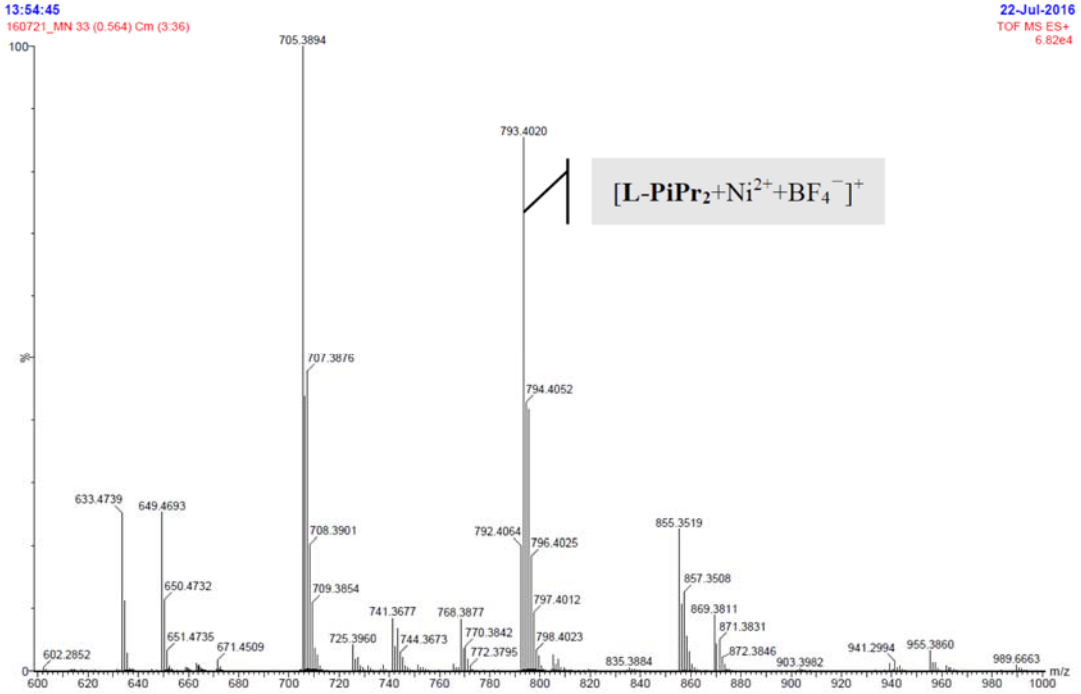
To a solution of **5d** (107.5 mg, 0.19 mmol, 1.0 equiv) in EtOAc (3.0 mL) was added Pd/C [40.7 mg (5%), 0.01 mmol, 0.1 equiv]. Under the H_2 atmosphere, the mixture was allowed to stir for 4 h at 25 °C. Then, filtration followed by removal of solvent under reduced pressure and silica gel flash column flash chromatography (EtOAc) afford **6f**. Regretfully, **6f** is very unstable and characterization data for **6f** can't be collected.

(C) Operando IR experiments

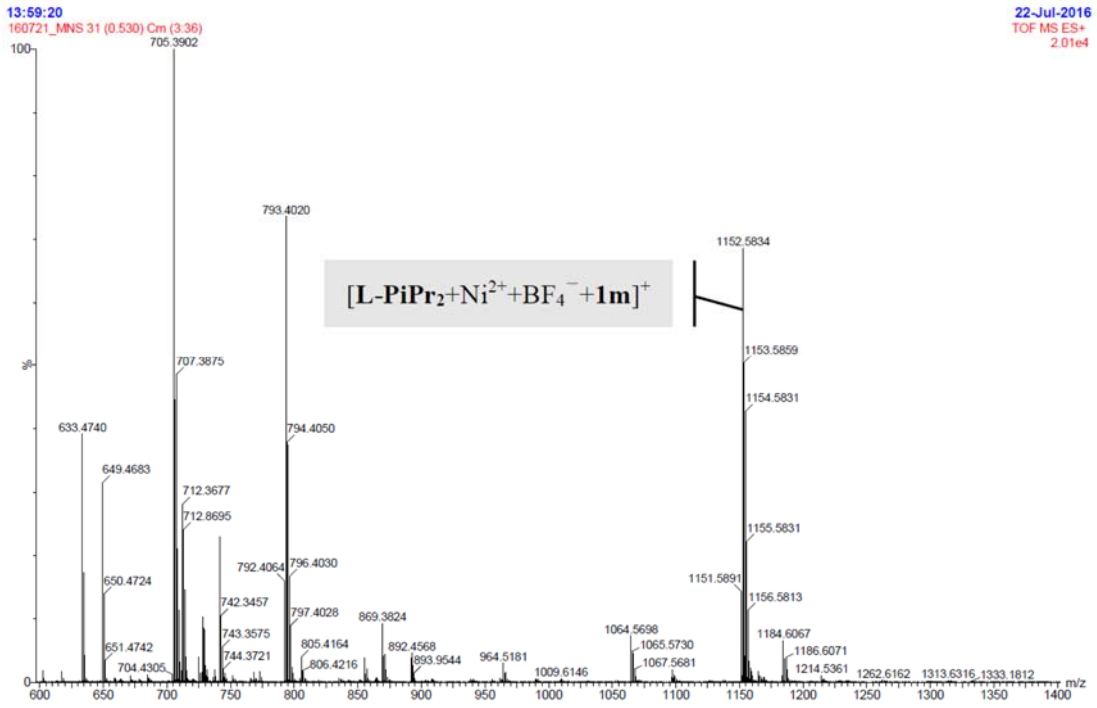


The 3D ATR-FTIR profile of the reaction.

(D) ESI-MS analysis of the solution of catalyst/substrate.



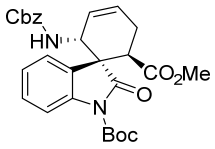
ESI-MS spectrum of a solution of $Ni(BF_4)_2 \cdot 6H_2O$ and **L-PiPr₂** in a 1:1 ratio



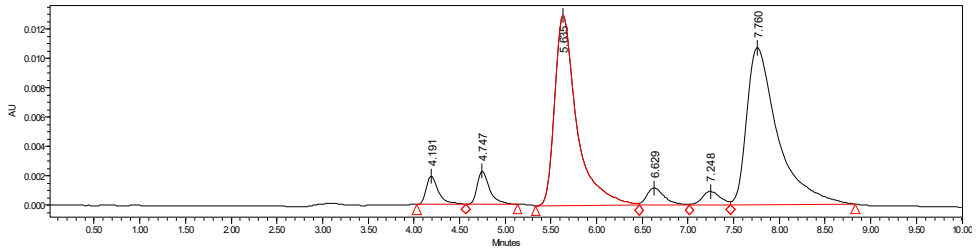
ESI-MS spectrum of a solution of **1m**, $Ni(BF_4)_2 \cdot 6H_2O$ and **L-PiPr₂** in a 1:1:1 ratio

(E) Spectral characterization data for the products

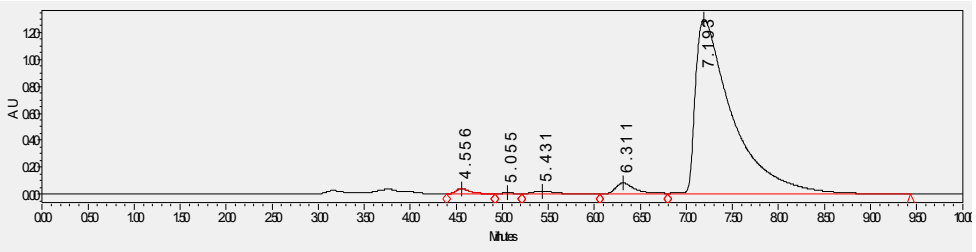
1'-(tert-butyl) 6-methyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3a)**



($C_{28}H_{30}N_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 98% ee. $[\alpha]_D^{16}$ = −90.8 (c = 1.00, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{minor1\text{-}major}$ = 4.56 min, $t_{minor1\text{-}minor}$ = 5.06 min, $t_{major\text{-}minor}$ = 5.43 min, $t_{minor2\text{-}major}$ = 6.31 min, $t_{major\text{-}major}$ = 7.19 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.40–7.24 (m, 6H), 7.17–7.02 (m, 2H), 6.31–6.04 (m, 1H), 6.01–5.78 (m, 1H), 5.34–4.82 (m, 3H), 4.19 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.52 (s, 3H), 3.38–3.14 (m, 1H), 2.92–2.46 (m, 2H), 1.67–1.57 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 172.0, 155.6, 149.2, 140.0, 136.4, 129.2, 128.6, 128.5, 128.1, 128.1, 125.3, 123.9, 123.7, 115.3, 83.8, 66.9, 52.1, 51.6, 50.9, 41.1, 28.1, 25.5. ESI-HRMS: calcd for $C_{28}H_{30}N_2O_7Na^+$ [M+Na$^+$] 529.1945, found 529.1948.



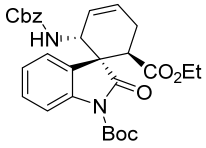
	Retention Time	Area	% Area
1	4.191	17921	3.36
2	4.747	20863	3.91
3	5.635	216722	40.58
4	6.629	15792	2.96
5	7.248	12483	2.34
6	7.760	250274	46.86



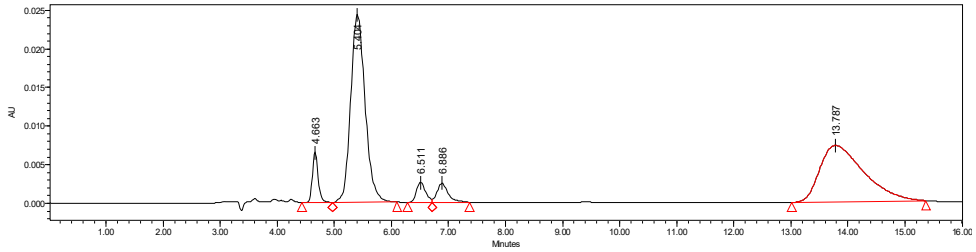
	Retention Time	Area	% Area
1	4.556	459775	1.19
2	5.055	92701	0.24
3	5.431	395924	1.03

4	6.311	1231359	3.20
5	7.193	36303200	94.34

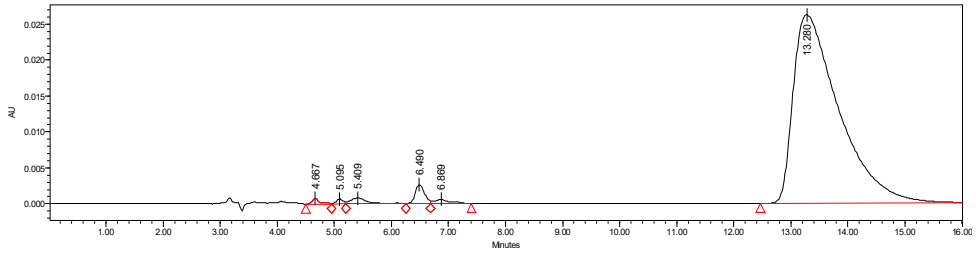
1'-(tert-butyl) 6-ethyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3b)**



($C_{29}H_{32}N_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 98% ee. $[\alpha]_D^{16}$ = −85.4 (c = 0.94, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{minor1\text{-}major}$ = 4.67 min, $t_{minor1\text{-}minor}$ = 5.10 min, $t_{major\text{-}minor}$ = 5.41 min, $t_{minor2\text{-}major}$ = 6.49 min, $t_{minor2\text{-}minor}$ = 6.87 min, $t_{major\text{-}major}$ = 13.28 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.47–7.25 (m, 6H), 7.15–7.03 (m, 2H), 6.25–6.01 (m, 1H), 5.92–5.66 (m, 1H), 5.33–4.86 (m, 3H), 4.17 (dd, *J* = 9.0, 5.0 Hz, 1H), 3.93 (q, *J* = 7.0 Hz, 2H), 3.30 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.93–2.53 (m, 2H), 1.68–1.47 (m, 9H), 1.04 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 171.6, 155.6, 149.3, 140.0, 136.4, 129.3, 128.7, 128.5, 128.5, 128.1, 128.1, 125.1, 123.9, 123.7, 115.2, 83.7, 66.9, 61.1, 51.6, 50.9, 40.9, 28.2, 25.5, 13.7. ESI-HRMS: calcd for $C_{29}H_{32}N_2O_7Na^+$ [M+Na$^+$] 543.2102, found 543.2105.



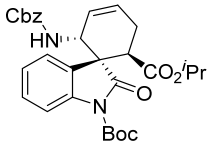
	Retention Time	Area	% Area
1	4.663	45099	4.86
2	5.404	426708	46.02
3	6.511	29602	3.19
4	6.886	33317	3.59
5	13.787	392577	42.34



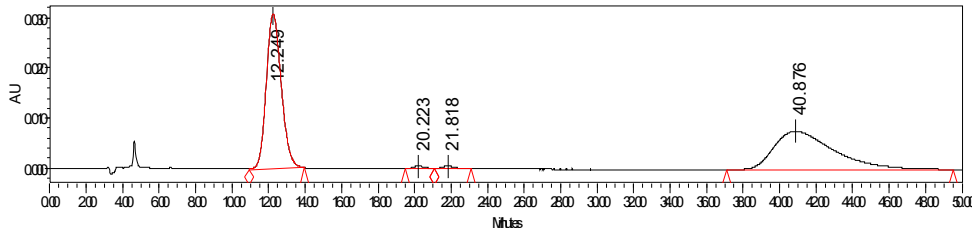
	Retention Time	Area	% Area
1	4.667	6670	0.44

2	5.095	5559	0.36
3	5.409	16502	1.08
4	6.490	30253	1.98
5	6.869	11151	0.73
6	13.280	1459518	95.41

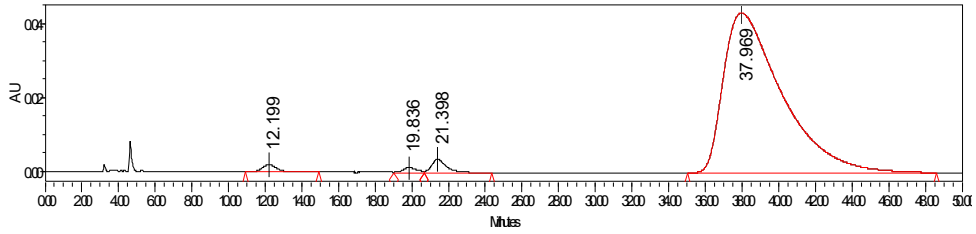
1'-(tert-butyl) 6-isopropyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3c)**



($C_{30}H_{34}N_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 98% ee. $[\alpha]_D^{20}$ = −79.2 (c = 1.07, in CH_2Cl_2), HPLC DAICEL CHIRALCEL ID, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{major\text{-}minor}$ = 12.20 min, $t_{minor\text{-}minor}$ = 19.84 min, $t_{minor\text{-}major}$ = 21.40 min, $t_{major\text{-}major}$ = 37.97 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.42–7.24 (m, 6H), 7.15–7.02 (m, 2H), 6.25–6.05 (m, 1H), 5.93–5.72 (m, 1H), 5.34–4.84 (m, 3H), 4.82–4.74 (m, 1H), 4.16 (dd, *J* = 9.0, 5.0 Hz, 1H), 3.27 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.88–2.50 (m, 2H), 1.68–1.47 (m, 9H), 1.05 (d, *J* = 6.0 Hz, 3H), 0.87 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 171.0, 155.6, 149.3, 139.9, 136.4, 129.4, 128.8, 128.5, 128.1, 128.0, 125.0, 123.9, 123.7, 115.0, 83.7, 68.6, 66.9, 51.5, 50.8, 40.8, 28.2, 25.5, 21.3, 21.2. ESI-HRMS: calcd for $C_{30}H_{34}N_2O_7Na^+$ [M+Na$^+$] 557.2258, found 557.2261.



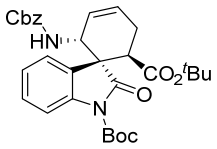
	Retention Time	Area	% Area
1	12.249	1764476	49.55
2	20.223	26290	0.74
3	21.818	28368	0.80
4	40.876	1742084	48.92



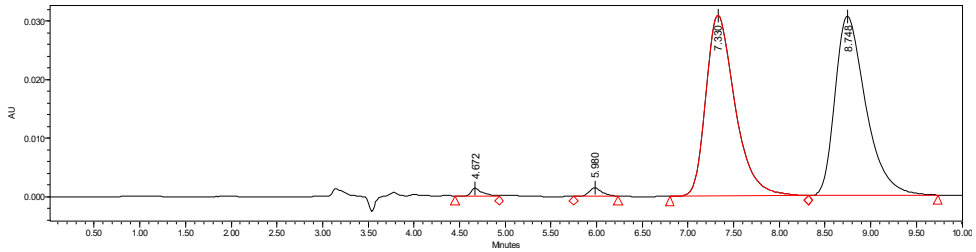
	Retention Time	Area	% Area
1	12.199	111668	1.12

2	19.836	62364	0.63
3	21.398	189212	1.90
4	37.969	9579905	96.35

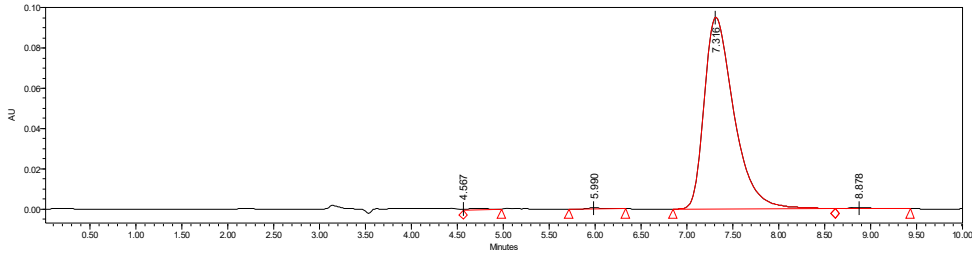
di-tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3d)**



($C_{31}H_{36}N_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 99% ee. $[\alpha]_D^{16}$ = −89.8 (c = 1.08, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{minor\text{-}major}$ = 4.57 min, $t_{minor\text{-}minor}$ = 5.99 min, $t_{major\text{-}major}$ = 7.32 min, $t_{major\text{-}minor}$ = 8.88 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.37–7.26 (m, 6H), 7.15–7.03 (m, 2H), 6.18–6.08 (m, 1H), 5.88–5.78 (m, 1H), 5.22–4.77 (m, 3H), 4.15 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.21 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.78–2.55 (m, 2H), 1.66–1.48 (m, 9H), 1.15 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 170.7, 155.6, 149.3, 139.8, 136.4, 129.5, 128.9, 128.5, 128.1, 128.0, 124.7, 123.9, 123.7, 115.0, 83.7, 81.9, 66.9, 51.5, 51.1, 41.1, 28.1, 27.5, 25.4. ESI-HRMS: calcd for $C_{31}H_{36}N_2O_7Na^+$ [M+Na^+] 571.2415, found 571.2420.



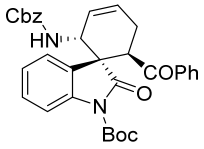
	Retention Time	Area	% Area
1	4.672	11552	0.82
2	5.980	13178	0.93
3	7.330	680110	48.06
4	8.748	710380	50.20



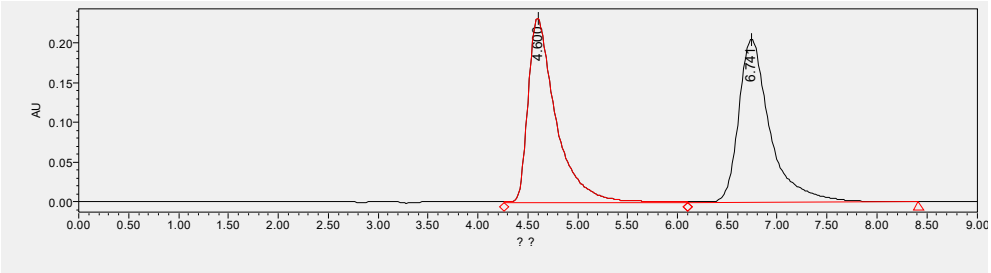
	Retention Time	Area	% Area
1	4.567	7818	0.36
2	5.990	6908	0.32
3	7.316	2149966	98.73

4	8.878	12890	0.59

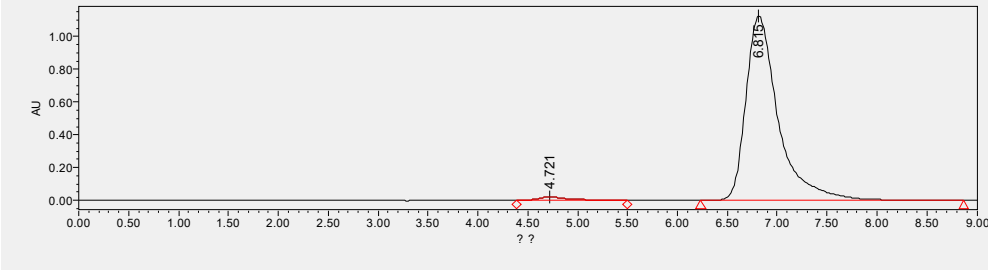
tert-butyl (1R,2R,6R)-6-benzoyl-2-(((benzyloxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1'-carboxylate **(3e)**



($C_{33}H_{32}N_2O_6$) white amorphous solid; 99% yield, >95:5 dr, 96% ee. $[\alpha]_D^{21}$ = −76.5 (c = 0.87, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 4.72 min, t_{major} = 6.82 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.54–7.48 (m, 1H), 7.43–7.24 (m, 8H), 7.18–7.02 (m, 2H), 6.22–6.03 (m, 1H), 5.99–5.79 (m, 1H), 5.29 (d, *J* = 9.0 Hz, 1H), 5.17–4.84 (m, 2H), 4.43–4.13 (m, 2H), 2.93–2.68 (m, 1H), 2.54–2.32 (m, 1H), 1.66–1.36 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 175.5, 155.6, 149.2, 139.8, 136.4, 136.0, 133.2, 129.6, 129.2, 128.6, 128.6, 128.5, 128.2, 128.1, 126.0, 123.9, 123.8, 115.3, 83.8, 67.0, 52.1, 51.5, 44.5, 28.1, 27.1. ESI-HRMS: calcd for $C_{33}H_{32}N_2O_6Na^+$ [M+Na^+] 575.2153, found 575.2156.

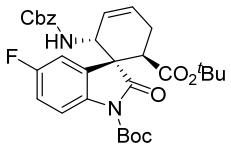


	Retention Time	Area	% Area
1	4.600	4555700	50.33
2	6.741	4496544	49.67

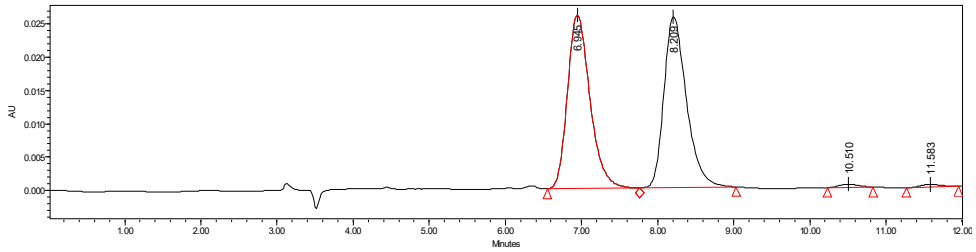


	Retention Time	Area	% Area
1	4.721	456812	1.77
2	6.815	25330384	98.23

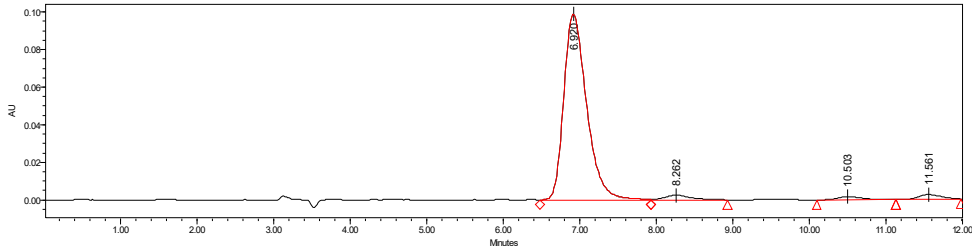
di-tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-5'-fluoro-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3f)**



($C_{31}H_{35}FN_2O_7$) white amorphous solid; 91% yield, >95:5 dr, 95% ee. $[\alpha]_D^{19}$ = −75.7 (c = 1.03, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{major\text{-}major}$ = 6.92 min, $t_{major\text{-}minor}$ = 8.26 min, $t_{minor\text{-}minor}$ = 10.50 min, $t_{minor\text{-}major}$ = 11.56 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 9.0 Hz, 5.0 Hz, 1H), 7.47–7.26 (m, 5H), 7.01 (td, *J* = 9.0 Hz, 3.0 Hz, 1H), 6.87 (dd, *J* = 8.0 Hz, 3.0 Hz, 1H), 6.23–6.10 (m, 1H), 5.88–5.76 (m, 1H), 5.24–4.74 (m, 3H), 4.12 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.22 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.82–2.49 (m, 2H), 1.66–1.46 (m, 9H), 1.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 170.5, 160.7, 158.3, 155.6, 149.3, 136.3, 135.9, 130.6 (d, *J* = 8.0 Hz), 129.7, 128.5, 128.2, 128.1, 124.6, 116.2 (d, *J* = 8.0 Hz), 114.7 (d, *J* = 22.0 Hz), 111.5 (d, *J* = 25 Hz), 83.8, 82.1, 67.0, 51.5, 51.3 (d, *J* = 2.0 Hz), 41.2, 28.1, 27.5, 25.4. ESI-HRMS: calcd for $C_{31}H_{35}FN_2O_7Na^+$ [M+Na$^+$] 589.2321, found 589.2311.

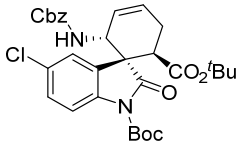


	Retention Time	Area	% Area
1	6.945	534619	49.50
2	8.209	529336	49.01
3	10.510	8102	0.75
4	11.583	8012	0.74

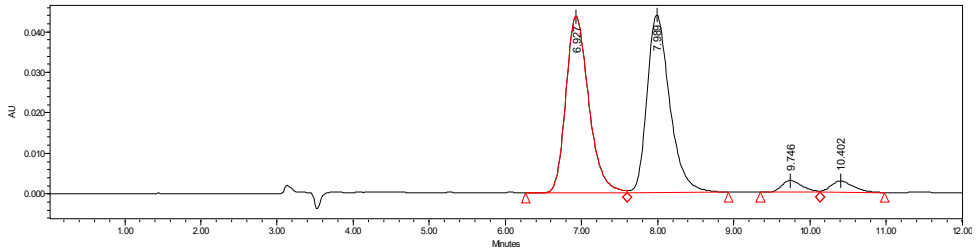


	Retention Time	Area	% Area
1	6.920	2052987	93.17
2	8.262	58300	2.65
3	10.503	38027	1.73
4	11.561	54093	2.45

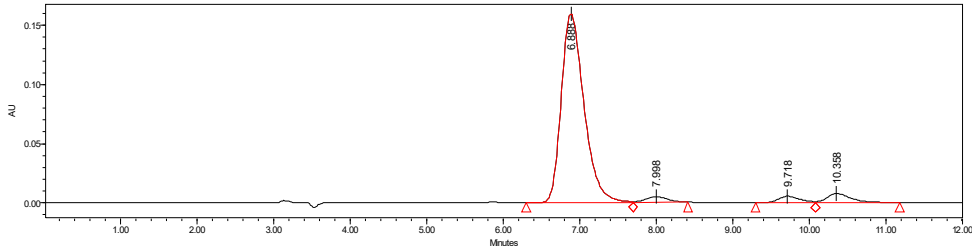
di-tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-5'-chloro-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3g)**



($C_{31}H_{35}ClN_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 94% ee. $[\alpha]_D^{20}$ = −72.1 (c = 1.17, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{major\text{-}major}$ = 6.89 min, $t_{major\text{-}minor}$ = 8.00 min, $t_{minor\text{-}minor}$ = 9.72, $t_{minor\text{-}major}$ = 10.36 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 1H), 7.40–7.26 (m, 6H), 7.08 (d, *J* = 2.0 Hz, 1H), 6.23–6.11 (m, 1H), 5.89–5.78 (m, 1H), 5.20–4.72 (m, 3H), 4.11 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.21 (dd, *J* = 12.0, 7.0 Hz, 1H), 2.81–2.49 (m, 2H), 1.66–1.46 (m, 9H), 1.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 170.5, 155.6, 149.2, 138.5, 136.3, 130.7, 129.8, 129.2, 128.5, 128.4, 128.2, 128.1, 124.5, 123.9, 116.2, 84.0, 82.1, 67.0, 51.5, 51.2, 41.2, 28.1, 27.6, 25.5. ESI-HRMS: calcd for $C_{31}H_{35}{}^{34.9689}ClN_2O_7Na^+$ [M+Na$^+$] 605.2025, found 605.2025; ESI-HRMS: calcd for $C_{31}H_{35}{}^{36.9659}ClN_2O_7Na^+$ [M+Na$^+$] 607.1995, found 607.2026.

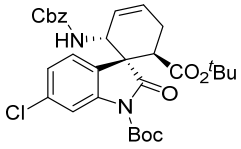


	Retention Time	Area	% Area
1	6.927	907789	47.11
2	7.989	904489	46.93
3	9.746	55342	2.87
4	10.402	59504	3.09

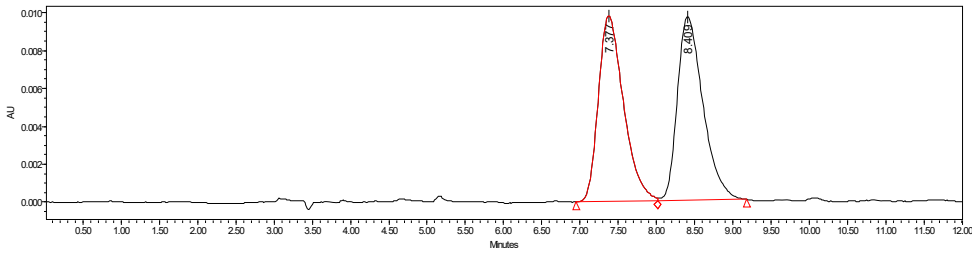


	Retention Time	Area	% Area
1	6.888	3279032	90.10
2	7.998	95686	2.63
3	9.718	101157	2.78
4	10.358	163646	4.50

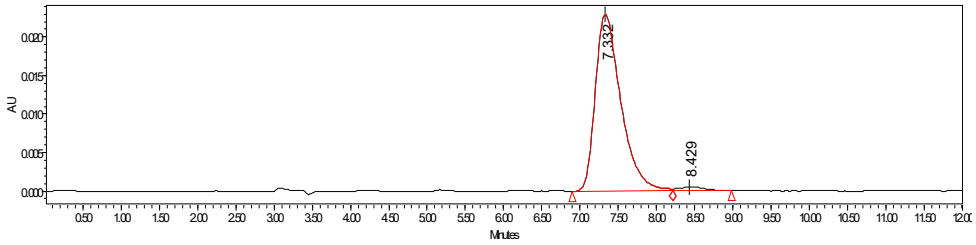
di-tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-6'-chloro-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3h)**



($C_{31}H_{35}ClN_2O_7$) white amorphous solid; 92% yield, >95:5 dr, 96% ee. $[\alpha]_D^{20}$ = −85.0 (c = 1.08, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 7.33 min, t_{minor} = 8.43 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.38–7.26 (m, 5H), 7.04 (d, *J* = 1.0 Hz, 2H), 6.19–6.10 (m, 1H), 5.86–5.75 (m, 1H), 5.29–4.81 (m, 3H), 4.12 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.20 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.80–2.49 (m, 2H), 1.65–1.47 (m, 9H), 1.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 170.5, 155.6, 149.1, 140.8, 136.3, 134.2, 129.7, 128.5, 128.2, 128.1, 127.4, 124.6, 124.6, 123.9, 115.7, 84.2, 82.1, 67.0, 51.6, 51.0, 41.2, 28.1, 27.6, 25.5. ESI-HRMS: calcd for $C_{31}H_{35}{}^{34.9689}ClN_2O_7Na^+$ [M+Na$^+$] 605.2025, found 605.2036; ESI-HRMS: calcd for $C_{31}H_{35}{}^{36.9659}ClN_2O_7Na^+$ [M+Na$^+$] 607.1995, found 607.2025.

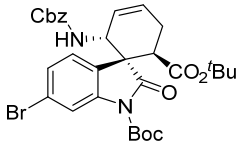


	Retention Time	Area	% Area
1	7.377	226201	50.11
2	8.409	225220	49.89

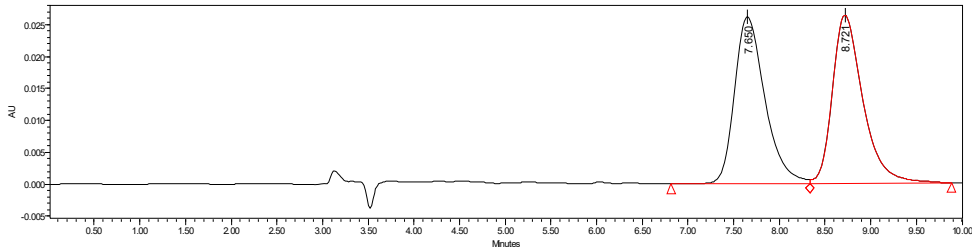


	Retention Time	Area	% Area
1	7.332	538195	97.77
2	8.429	12268	2.23

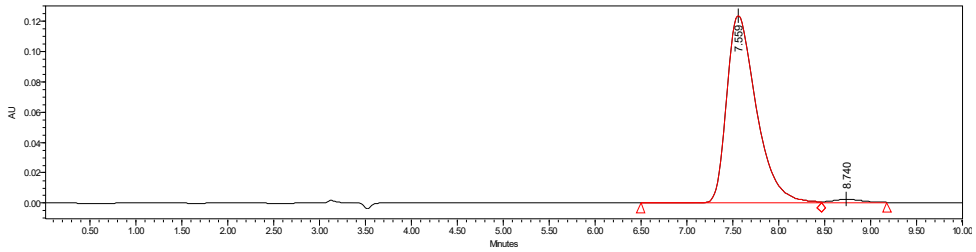
di-tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-6'-bromo-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3i)**



($C_{31}H_{35}BrN_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 97% ee. $[\alpha]_D^{21}$ = −79.7 (c = 1.25, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 7.56 min, t_{minor} = 8.74 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 2.0 Hz, 1H), 7.40–7.26 (m, 5H), 7.20 (dd, *J* = 8.0 Hz, 2.0 Hz, 1H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.17–6.10 (m, 1H), 5.84–5.77 (m, 1H), 5.15–4.75 (m, 3H), 4.12 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.20 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.80–2.48 (m, 2H), 1.66–1.50 (m, 9H), 1.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 170.5, 155.6, 149.1, 141.0, 136.3, 129.7, 128.5, 128.2, 128.1, 127.9, 126.8, 124.9, 124.6, 122.2, 118.5, 84.2, 82.1, 67.0, 51.5, 51.0, 41.2, 28.1, 27.6, 25.5. ESI-HRMS: calcd for $C_{31}H_{35}{}^{78.9183}BrN_2O_7Na^+$ [M+Na$^+$] 649.1520, found 649.1528; ESI-HRMS: calcd for $C_{31}H_{35}{}^{80.9163}BrN_2O_7Na^+$ [M+Na$^+$] 651.1500, found 651.1516.

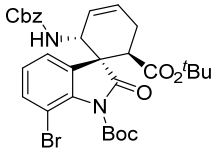


	Retention Time	Area	% Area
1	7.650	601547	49.72
2	8.721	608315	50.28

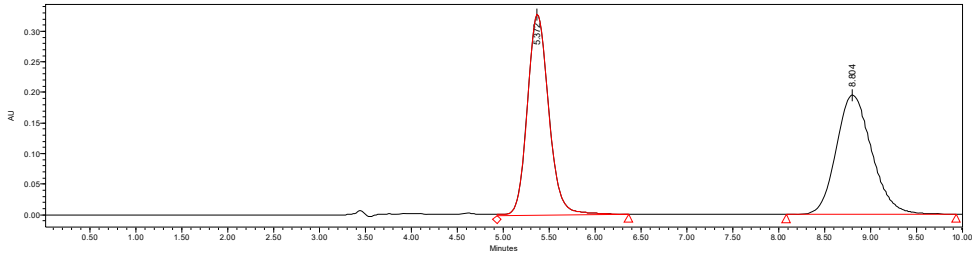


	Retention Time	Area	% Area
1	7.559	2768968	98.34
2	8.740	46780	1.66

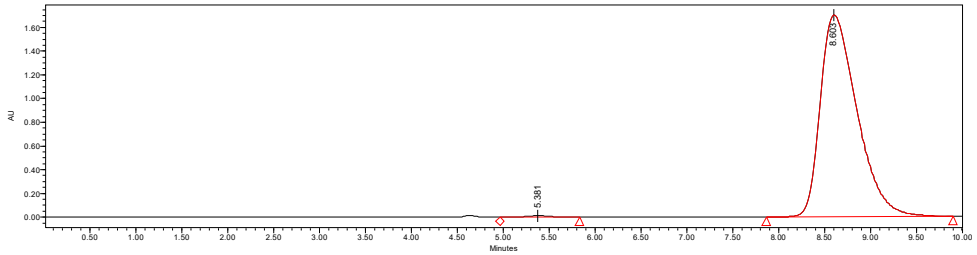
di-tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-7'-bromo-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3j)**



($C_{31}H_{35}BrN_2O_7$) white powder, mp 124.0−126.0 °C; 90% yield, >95:5 dr, 99% ee. $[\alpha]_D^{33}$ = −63.9 (c = 0.87, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 5.38 min, t_{major} = 8.60 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.0 Hz, 1H), 7.38–7.26 (m, 5H), 7.11 (d, *J* = 4.0 Hz, 1H), 6.93 (t, *J* = 8.0 Hz, 1H), 6.26–5.97 (m, 1H), 5.91–5.51 (m, 1H), 5.31–4.70 (m, 3H), 4.25 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.19 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.81–2.48 (m, 2H), 1.74–1.46 (m, 9H), 1.30–1.13 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 170.4, 155.6, 147.5, 138.9, 136.4, 133.3, 132.4, 129.6, 128.5, 128.1, 128.0, 124.9, 124.7, 122.9, 107.2, 84.7, 82.3, 66.9, 52.1, 51.4, 41.3, 27.8, 27.5, 25.4. ESI-HRMS: calcd for $C_{31}H_{35}{}^{78.9183}BrN_2O_7Na^+$ [M+Na$^+$] 649.1520, found 649.1532; ESI-HRMS: calcd for $C_{31}H_{35}{}^{80.9163}BrN_2O_7Na^+$ [M+Na$^+$] 651.1500, found 651.1520.

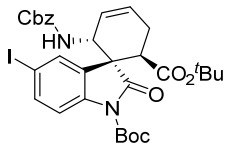


	Retention Time	Area	% Area
1	5.372	5327949	50.29
2	8.804	5265858	49.71

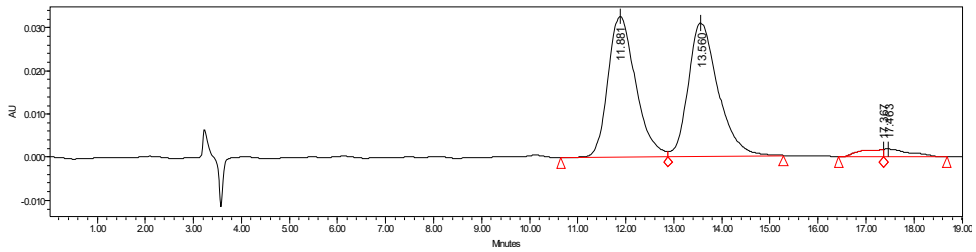


	Retention Time	Area	% Area
1	5.381	188902	0.40
2	8.603	47493328	99.60

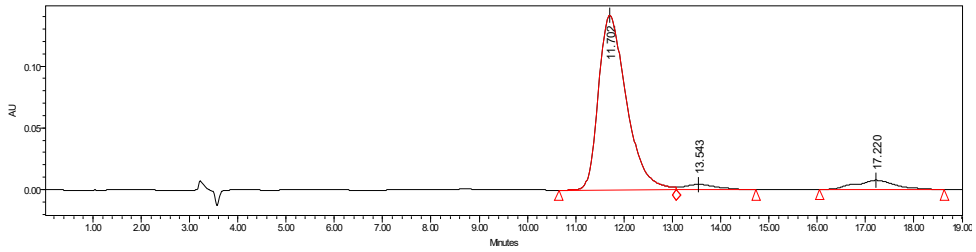
di-tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-5'-iodo-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3k)**



($C_{31}H_{35}IN_2O_7$) white amorphous solid; 99% yield, 93:7 dr, 93% ee. $[\alpha]_D^{20}$ = −69.3 (c = 1.35, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{major\text{-}major}$ = 11.70 min, $t_{major\text{-}minor}$ = 13.54 min, $t_{minor\text{-}major\&minor}$ = 17.22 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.57 (m, 2H), 7.47–7.26 (m, 6H), 6.25–5.99 (m, 1H), 5.90–5.58 (m, 1H), 5.29–4.75 (m, 3H), 4.24–4.03 (m, 1H), 3.20 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.86–2.44 (m, 2H), 1.66–1.42 (m, 9H), 1.19 (s, 8.37H), 1.18 (s, 0.63H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 170.5, 155.6, 149.1, 139.7, 137.3, 136.3, 132.3, 131.5, 129.8, 128.5, 128.2, 128.1, 124.6, 117.1, 87.3, 84.0, 82.1, 67.0, 51.5, 51.1, 41.2, 28.1, 27.6, 25.4. ESI-HRMS: calcd for $C_{31}H_{35}IN_2O_7Na^+$ [M+Na$^+$] 697.1381, found 697.1390.

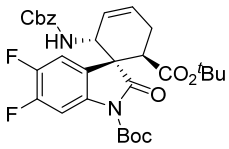


	Retention Time	Area	% Area
1	11.881	1306807	47.21
2	13.560	1329172	48.02
3	17.367	60581	2.19
4	17.463	71594	2.59

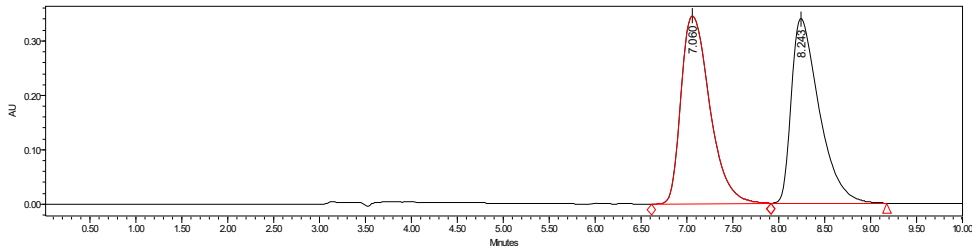


	Retention Time	Area	% Area
1	11.702	5702585	89.78
2	13.543	209794	3.30
3	17.220	439032	6.91

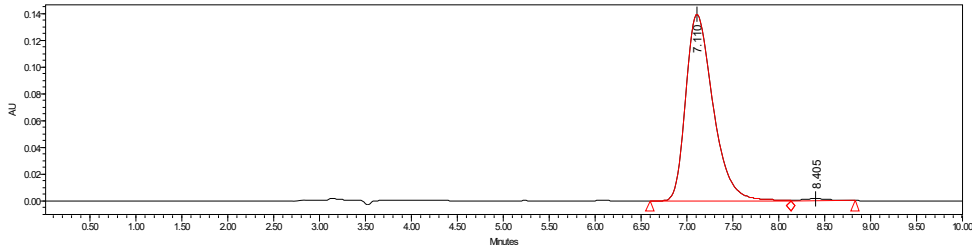
di-tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-5',6'-difluoro-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3l)**



($C_{31}H_{34}F_2N_2O_7$) light yellow amorphous solid; 99% yield, >95:5 dr, 98% ee. $[\alpha]_D^{20}$ = −81.2 (c = 1.17, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 7.11 min, t_{minor} = 8.40 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (dd, *J* = 12.0 Hz, 7.0 Hz, 1H), 7.38–7.26 (m, 5H), 6.96 (dd, *J* = 10.0 Hz, 8.0 Hz, 1H), 6.23–6.11 (m, 1H), 5.89–5.75 (m, 1H), 5.22–4.70 (m, 3H), 4.10 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.19 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.83–2.45 (m, 2H), 1.64–1.46 (m, 9H), 1.21 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 170.4, 155.6, 149.0, 136.2, 136.0, 129.8, 128.5, 128.2, 128.1, 124.6, 113.1 (d, *J* = 21 Hz), 105.7 (d, *J* = 24 Hz), 84.3, 82.2, 67.1, 51.6, 51.0, 41.2, 29.1, 27.6, 25.4. ESI-HRMS: calcd for $C_{31}H_{34}F_2N_2O_7Na^+$ [M+Na$^+$] 607.2226, found 607.2231.

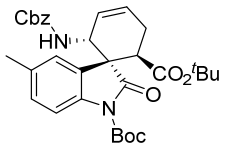


	Retention Time	Area	% Area
1	7.060	7577353	51.39
2	8.243	7167569	48.61

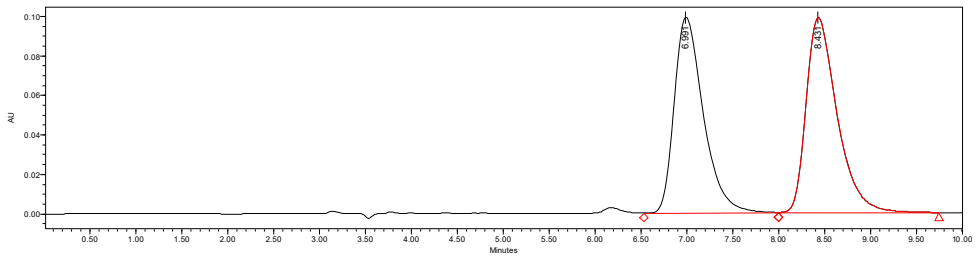


	Retention Time	Area	% Area
1	7.110	2894690	98.95
2	8.405	30660	1.05

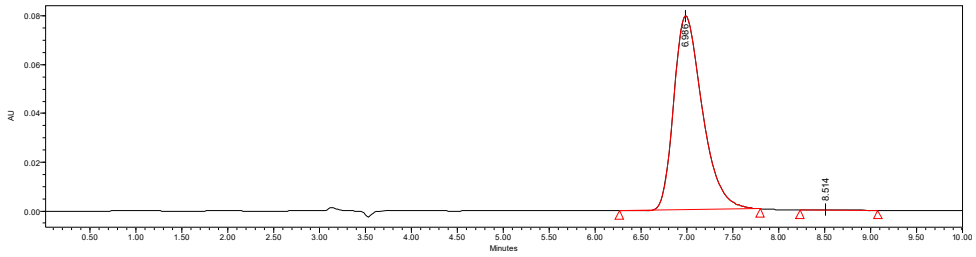
di-tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-5'-methyl-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3m)**



($C_{32}H_{38}N_2O_7$) white powder, mp 165.0−167.0 °C; 97% yield, >95:5 dr, 99% ee. $[\alpha]_D^{18}$ = −81.3 (c = 1.09, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 6.99 min, t_{minor} = 8.51 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.0 Hz, 1H), 7.40–7.24 (m, 5H), 7.10 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.92 (s, 1H), 6.24–6.06 (m, 1H), 5.95–5.77 (m, 1H), 5.35–4.77 (m, 3H), 4.14 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.19 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.83–2.53 (m, 2H), 2.29 (s, 3H), 1.67–1.44 (m, 9H), 1.16 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 170.7, 155.6, 149.3, 137.4, 136.4, 133.4, 129.3, 128.9, 128.4, 128.1, 128.0, 124.8, 124.3, 114.7, 83.5, 81.9, 66.9, 51.5, 51.1, 41.2, 28.2, 27.5, 25.3, 21.3. ESI-HRMS: calcd for $C_{32}H_{38}N_2O_7Na^+$ [M+Na$^+$] 585.2571, found 585.2577.

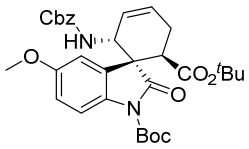


	Retention Time	Area	% Area
1	6.991	2200051	48.61
2	8.431	2325432	51.39

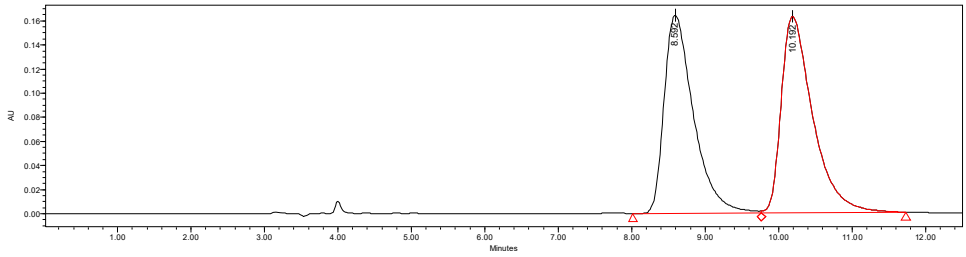


	Retention Time	Area	% Area
1	6.986	1723490	99.71
2	8.514	5063	0.29

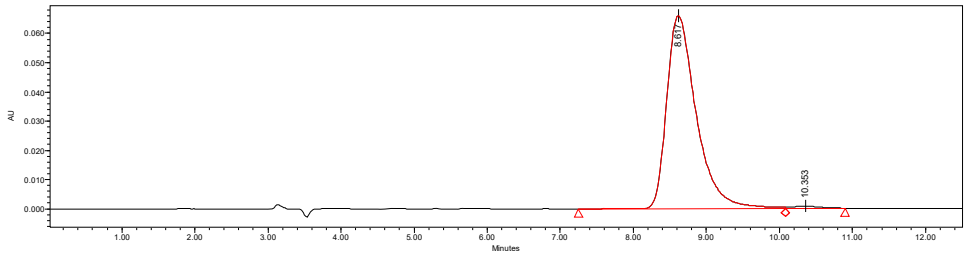
di-tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-5'-methoxy-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3n)**



($C_{32}H_{38}N_2O_8$) white amorphous solid; 87% yield, >95:5 dr, 98% ee. $[\alpha]_D^{19}$ = −78.6 (c = 1.00, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 8.62 min, t_{minor} = 10.35 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.0 Hz, 1H), 7.40–7.26 (m, 5H), 6.82 (dd, *J* = 9.0, 2.0 Hz, 1H), 6.74 (d, *J* = 3.0 Hz, 1H), 6.13 (dd, *J* = 13.0, 4.0 Hz, 1H), 5.89–5.72 (m, 1H), 5.33–4.78 (m, 3H), 4.21–4.09 (m, 1H), 3.76 (s, 3H), 3.20 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.79–2.48 (m, 2H), 1.66–1.45 (m, 9H), 1.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 170.6, 156.3, 155.6, 149.4, 136.4, 133.3, 130.3, 129.4, 128.5, 128.1, 128.0, 124.8, 115.6, 111.9, 111.4, 83.5, 81.9, 66.9, 55.6, 51.5, 51.2, 41.2, 28.2, 27.5, 25.4. ESI-HRMS: calcd for $C_{32}H_{38}N_2O_8Na^+$ [M+Na$^+$] 601.2520, found 601.2530.

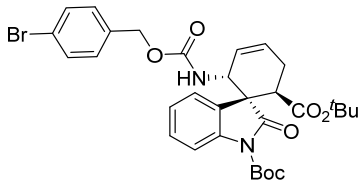


	Retention Time	Area	% Area
1	8.592	4569116	48.58
2	10.192	4836519	51.42

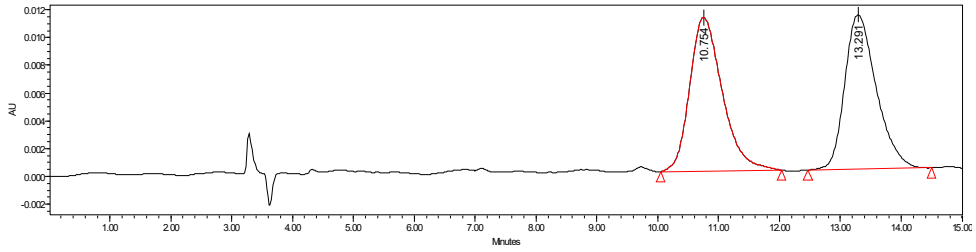


	Retention Time	Area	% Area
1	8.617	1854271	98.92
2	10.353	20179	1.08

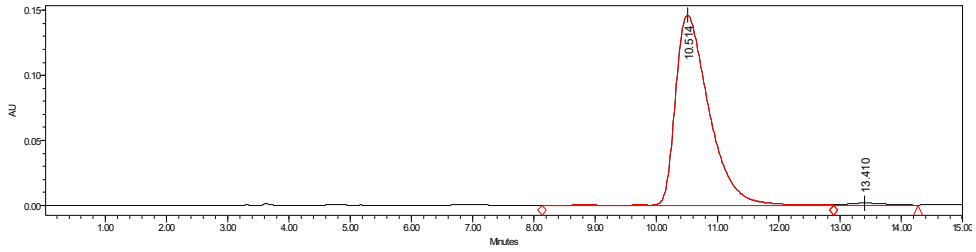
di-tert-butyl (1R,2R,6R)-2-((((4-bromobenzyl)oxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3o)**



($C_{31}H_{35}BrN_2O_7$) white amorphous solid; 95% yield, >95:5 dr, 98% ee. $[\alpha]_D^{33}$ = −75.3 (c = 1.15, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 10.51 min, t_{minor} = 13.41 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 2H), 7.34–7.27 (m, 1H), 7.26–7.01 (m, 4H), 6.26–6.04 (m, 1H), 5.94–5.64 (m, 1H), 5.23–4.77 (m, 3H), 4.13 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.21 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.88–2.48 (m, 2H), 1.68–1.45 (m, 9H), 1.15 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 170.6, 155.4, 149.2, 139.7, 135.5, 131.6, 129.7, 129.6, 128.9, 128.5, 124.6, 123.9, 123.7, 122.0, 115.0, 83.7, 81.9, 66.0, 51.5, 51.1, 41.1, 28.1, 27.5, 25.4. ESI-HRMS: calcd for $C_{31}H_{35}{}^{78.9183}BrN_2O_7Na^+$ [M+Na$^+$] 649.1520, found 649.1525; ESI-HRMS: calcd for $C_{31}H_{35}{}^{80.9163}BrN_2O_7Na^+$ [M+Na$^+$] 651.1500, found 651.1512.

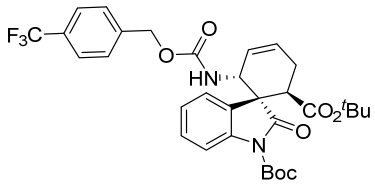


	Retention Time	Area	% Area
1	10.754	412349	50.71
2	13.291	400820	49.29

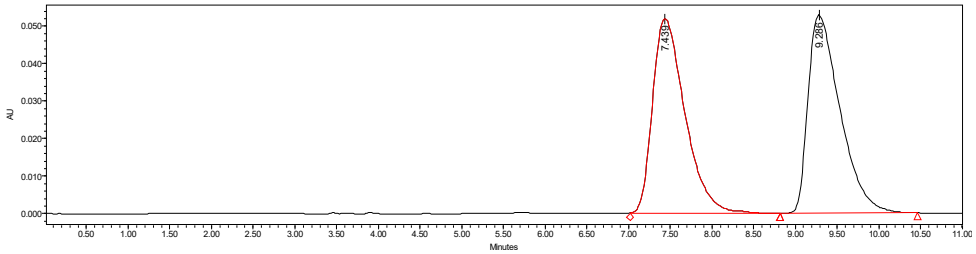


	Retention Time	Area	% Area
1	10.514	5530236	98.93
2	13.410	59738	1.07

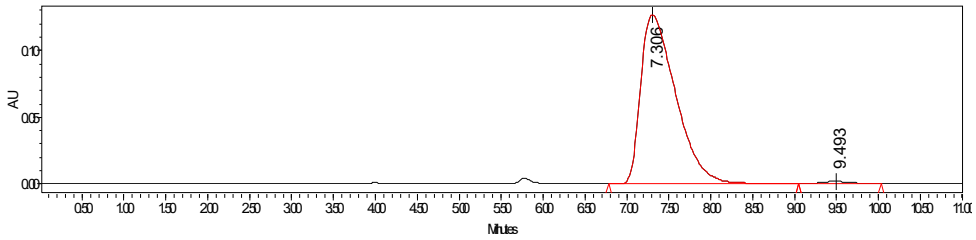
di-tert-butyl (1R,2R,6R)-2'-oxo-2-((((4-(trifluoromethyl)benzyl)oxy)carbonyl)amino)spiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3p)**



($C_{32}H_{35}F_3N_2O_7$) light yellow amorphous solid; 86% yield, >95:5 dr, 98% ee. $[\alpha]_D^{33} = -67.3$ (c = 1.04, in CH_2Cl_2), HPLC DAICEL CHIRALCEL ID, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 7.31 min, t_{minor} = 9.49 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 1H), 7.77–7.38 (m, 4H), 7.31 (td, *J* = 8.0, 2.0 Hz, 1H), 7.20–7.00 (m, 2H), 6.25–6.10 (m, 1H), 5.92–5.74 (m, 1H), 5.32–4.87 (m, 3H), 4.15 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.23 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.82–2.52 (m, 2H), 1.67–1.45 (m, 9H), 1.16 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 170.6, 155.4, 149.2, 140.6, 139.7, 129.7, 128.8, 128.5, 127.8, 125.4 (d, *J* = 12 Hz), 125.4 (d, *J* = 4 Hz), 124.6, 124.0, 123.8, 115.0, 83.7, 82.0, 65.8, 51.5, 51.0, 41.1, 28.1, 27.5, 25.4. ESI-HRMS: calcd for $C_{32}H_{35}F_3N_2O_7Na^+$ [M+Na$^+$] 639.2289, found 639.2290.

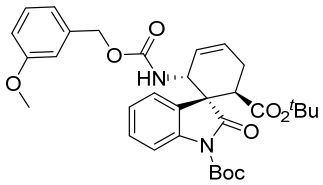


	Retention Time	Area	% Area
1	7.439	1409993	50.01
2	9.286	1409237	49.99

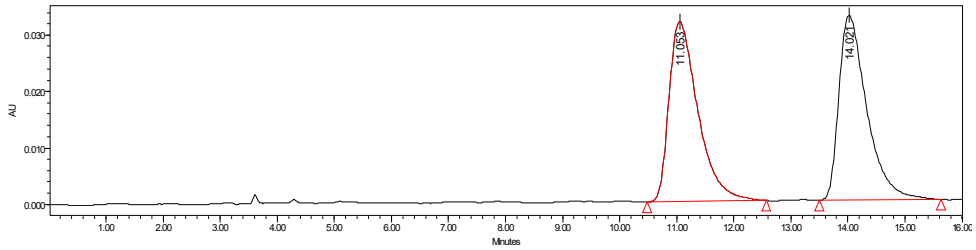


	Retention Time	Area	% Area
1	7.306	3681700	98.82
2	9.493	43899	1.18

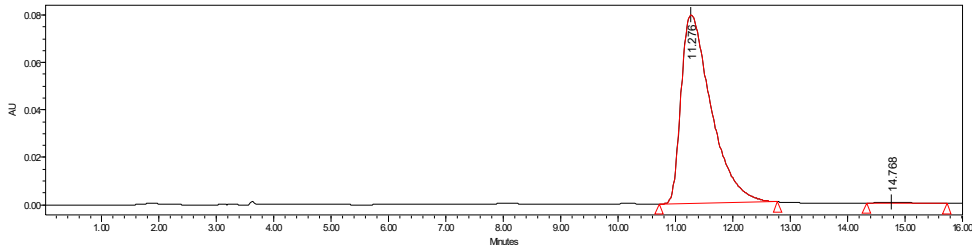
di-tert-butyl (1R,2R,6R)-2-((((3-methoxybenzyl)oxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3q)**



($C_{32}H_{38}N_2O_8$) white amorphous solid; 89% yield, >95:5 dr, 99% ee. $[\alpha]_D^{33}$ = −69.5 (c = 0.92, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 11.28 min, t_{minor} = 14.77 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.33–7.24 (m, 2H), 7.15–7.03 (m, 2H), 7.00–6.65 (m, 3H), 6.21–6.04 (m, 1H), 5.90–5.72 (m, 1H), 5.28–4.76 (m, 3H), 4.15 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.81 (s, 3H), 3.22 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.81–2.54 (m, 2H), 1.67–1.49 (m, 9H), 1.15 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 170.7, 159.7, 155.6, 149.3, 139.8, 137.9, 129.5, 128.9, 128.4, 124.7, 123.9, 123.7, 120.3, 115.0, 113.8, 113.3, 83.7, 81.9, 66.8, 55.3, 51.5, 51.1, 41.1, 28.1, 27.5, 25.4. ESI-HRMS: calcd for $C_{32}H_{38}N_2O_8Na^+$ [M+Na^+] 601.2520, found 601.2527.

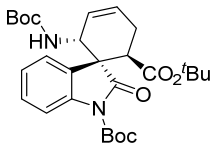


	Retention Time	Area	% Area
1	11.053	1124360	50.29
2	14.021	1111189	49.71

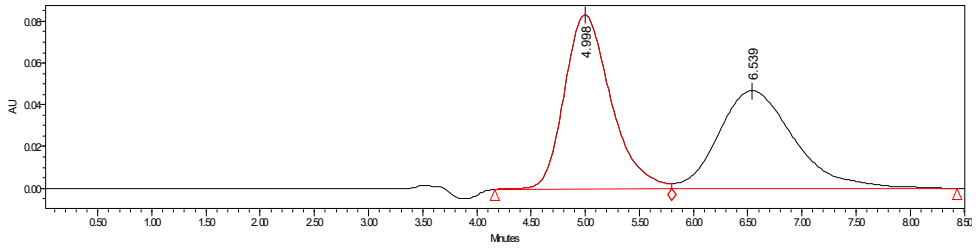


	Retention Time	Area	% Area
1	11.276	2903862	99.40
2	14.768	17491	0.60

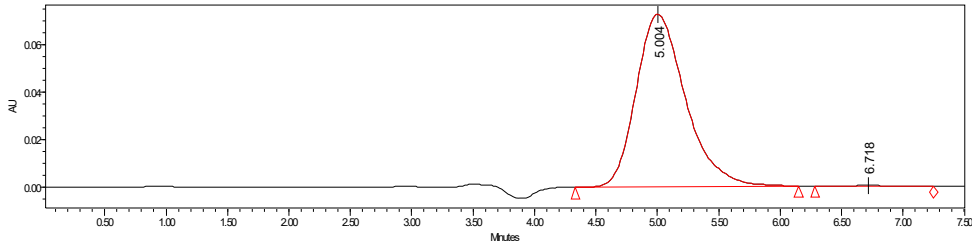
di-tert-butyl (1R,2R,6R)-2-((tert-butoxycarbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3r)**



($C_{28}H_{38}N_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 99% ee. $[\alpha]_D^{21}$ = −52.5 (c = 1.03, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 5.00 min, t_{minor} = 6.72 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.0 Hz, 1H), 7.33–7.27 (m, 1H), 7.15–6.98 (m, 2H), 6.23–6.08 (m, 1H), 5.87–5.75 (m, 1H), 4.78 (d, *J* = 10.0 Hz, 1H), 4.05 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.20 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.77–2.52 (m, 2H), 1.61 (s, 9H), 1.47–1.36 (m, 9H), 1.13 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 170.8, 154.9, 149.5, 139.8, 129.3, 129.2, 128.2, 124.9, 123.8, 123.5, 115.2, 83.5, 81.8, 79.8, 51.3, 51.2, 41.2, 28.4, 28.1, 27.4, 25.5. ESI-HRMS: calcd for $C_{28}H_{38}N_2O_7Na^+$ [M+Na$^+$] 537.2571, found 537.2574.

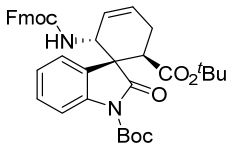


	Retention Time	Area	% Area
1	4.998	2505034	52.33
2	6.539	2281789	47.67

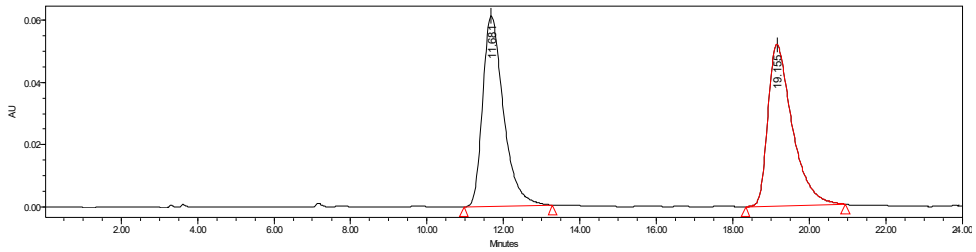


	Retention Time	Area	% Area
1	5.004	2037184	99.69
2	6.718	6361	0.31

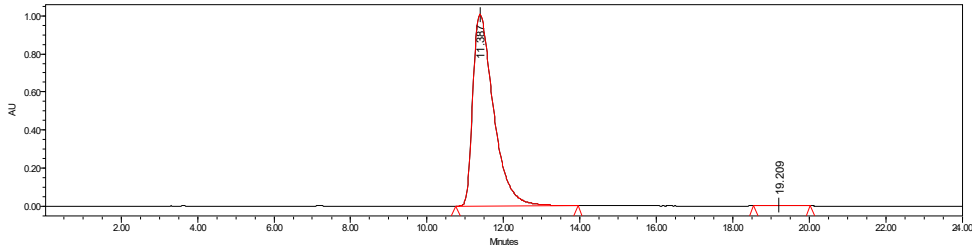
di-tert-butyl (1R,2R,6R)-2-((((9H-fluoren-9-yl)methoxy)carbonyl)amino)-2'-oxospiro [cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3s)**



($C_{38}H_{40}N_2O_7$) white amorphous solid; 95% yield, >95:5 dr, 99% ee. $[\alpha]_D^{33}$ = −63.2 (c = 1.03, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 11.39 min, t_{minor} = 19.21 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.0 Hz, 1H), 7.86–7.42 (m, 4H), 7.41–7.26 (m, 5H), 7.17–7.04 (m, 2H), 6.29–6.02 (m, 1H), 5.96–5.60 (m, 1H), 5.20 (d, *J* = 10.0 Hz, 1H), 4.58–4.04 (m, 4H), 3.27 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.91–2.42 (m, 2H), 1.64–1.34 (m, 9H), 1.15 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 170.7, 155.6, 149.4, 144.5, 143.6, 141.3, 141.1, 139.8, 129.5, 129.0, 128.5, 127.6, 127.6, 127.1, 127.0, 125.6, 125.1, 124.8, 124.0, 123.7, 119.9, 119.9, 115.1, 83.7, 82.0, 67.3, 51.5, 51.1, 47.2, 41.2, 28.1, 27.5, 25.5. ESI-HRMS: calcd for $C_{38}H_{40}N_2O_7Na^+$ [M+Na^+] 659.2728, found 659.2737.

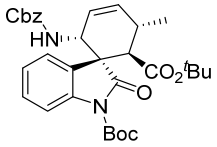


	Retention Time	Area	% Area
1	11.681	2307605	50.24
2	19.155	2285509	49.76

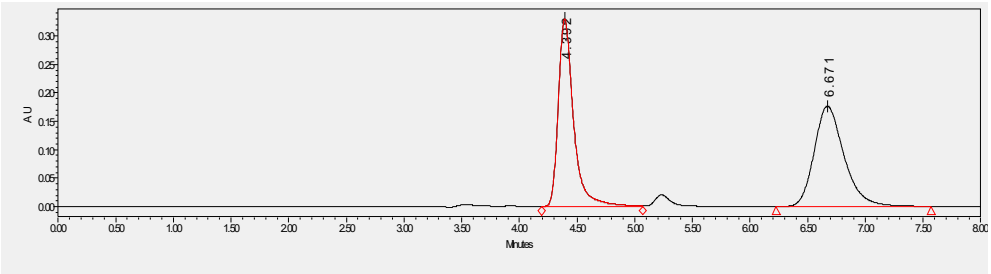


	Retention Time	Area	% Area
1	11.387	37893079	99.63
2	19.209	141882	0.37

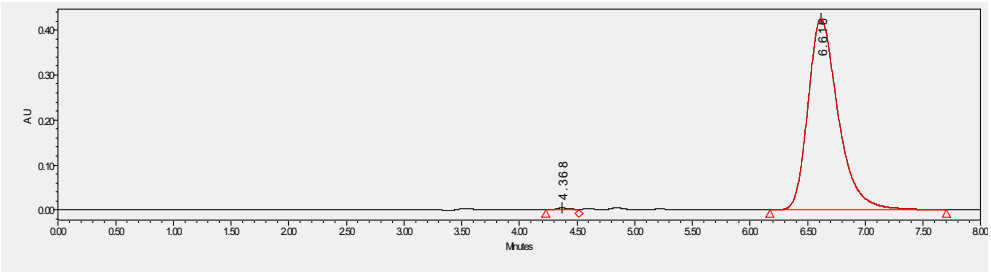
di-tert-butyl (1R,2R,5S,6R)-2-(((benzyloxy)carbonyl)amino)-5-methyl-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3t)**



($C_{32}H_{38}N_2O_7$) white amorphous solid; 94% yield, >95:5 dr, 99% ee. $[\alpha]_D^{33}$ = −22.9 (c = 0.85, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 4.37 min, t_{major} = 6.62 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.0 Hz, 1H), 7.45–7.26 (m, 6H), 7.18 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.06 (td, *J* = 8.0, 1.0 Hz, 1H), 6.06–5.90 (m, 1H), 5.87–5.70 (m, 1H), 5.29–4.84 (m, 3H), 4.08 (dd, *J* = 9.0, 6.0 Hz, 1H), 3.12–2.64 (m, 2H), 1.65–1.47 (m, 9H), 1.25–1.18 (m, 3H), 1.13 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 170.0, 155.6, 149.2, 139.5, 136.4, 136.2, 128.8, 128.5, 128.5, 128.2, 128.0, 124.1, 124.0, 123.1, 114.9, 83.8, 81.6, 67.0, 52.0, 51.1, 48.8, 30.2, 28.1, 27.4, 20.8. ESI-HRMS: calcd for $C_{32}H_{38}N_2O_7Na^+$ [M+Na^+] 585.2571, found 585.2571.

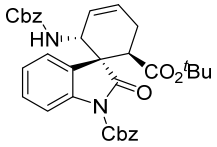


	Retention Time	Area	% Area
1	4.392	3073772	49.05
2	6.671	3192975	50.95

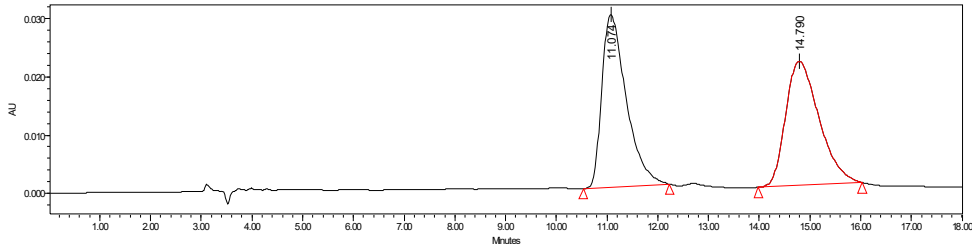


	Retention Time	Area	% Area
1	4.368	33064	0.43
2	6.616	7711224	99.57

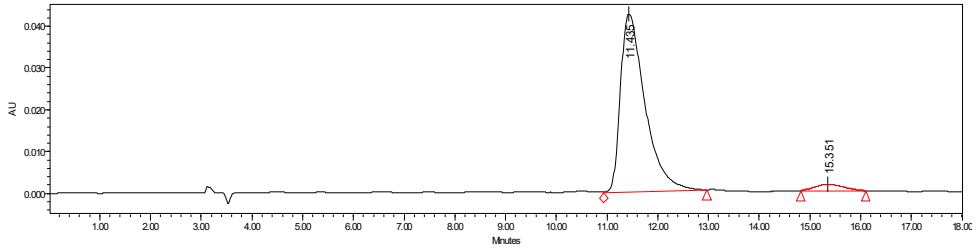
1'-benzyl 6-(tert-butyl) (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(3u)**



($C_{34}H_{34}N_2O_7$) white amorphous solid; 97% yield, >95:5 dr, 92% ee. $[\alpha]_D^{18}$ = −66.7 (c = 1.13, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 11.44 min, t_{minor} = 15.35 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.0 Hz, 1H), 7.60–7.47 (m, 2H), 7.41–7.24 (m, 9H), 7.14–7.05 (m, 2H), 6.21–6.11 (m, 1H), 5.85–5.76 (m, 1H), 5.45 (s, 2H), 5.13–4.76 (m, 3H), 4.20–4.10 (m, 1H), 3.26 (dd, *J* = 11.0, 7.0 Hz, 1H), 2.84–2.56 (m, 2H), 1.10 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 170.6, 155.7, 151.0, 139.4, 136.4, 135.4, 129.8, 129.1, 128.6, 128.5, 128.4, 128.1, 128.1, 128.0, 127.8, 124.5, 124.3, 123.7, 115.2, 82.0, 68.2, 67.0, 51.7, 51.3, 41.1, 27.5, 25.5. ESI-HRMS: calcd for $C_{34}H_{34}N_2O_7Na^+$ [M+Na^+] 605.2258, found 605.2266.

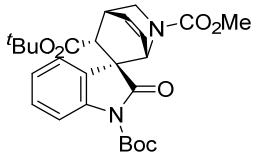


	Retention Time	Area	% Area
1	11.074	990574	50.42
2	14.790	973973	49.58

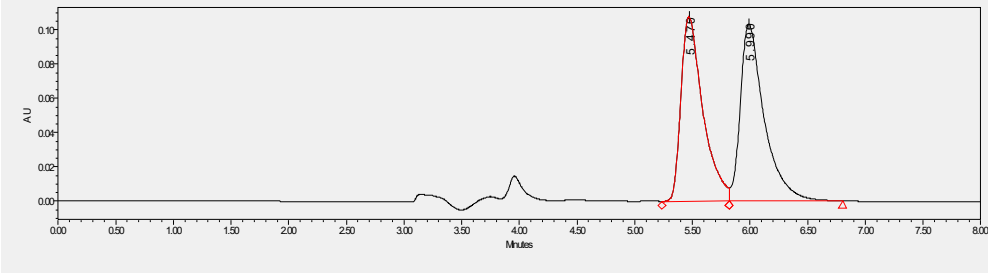


	Retention Time	Area	% Area
1	11.435	1430197	96.17
2	15.351	56931	3.83

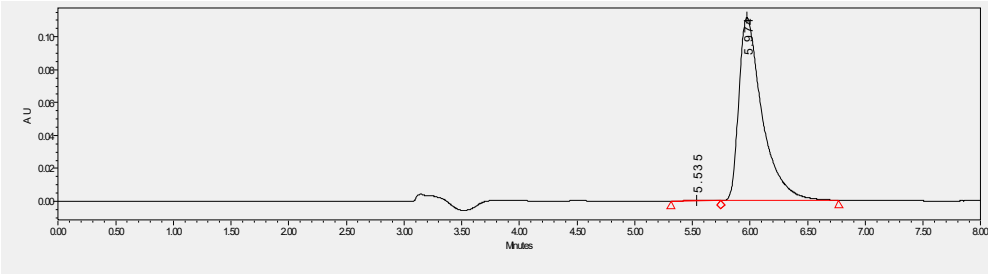
1',3-di-tert-butyl 6-methyl (1S,2R,3R,4R)-2'-oxo-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indolin]-7-ene-1',3,6-tricarboxylate **(5a)**



($C_{26}H_{32}N_2O_7$) white amorphous solid; 87% yield, >95:5 dr, 99% ee. $[\alpha]_D^{34}$ = 26.8 (c = 0.70, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 5.54 min, t_{major} = 5.97 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 7.89 (dd, *J* = 11.0, 8.0 Hz, 1H), 7.36–7.30 (m, 1H), 7.16–7.08 (m, 1H), 6.95 (t, *J* = 8.0 Hz, 1H), 6.76–6.66 (m, 1H), 6.58–6.48 (m, 1H), 4.58+4.40 (dd, *J* = 6.0, 1.0 Hz, 1H), 4.06–3.95 (m, 1H), 3.64+3.39 (s, 3H), 3.33–3.24 (m, 1H), 3.21–3.12 (m, 1H), 2.99–2.90 (m, 1H), 1.64 (s, 9H), 0.91+0.90 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 175.3+175.1, 169.6+169.3, 155.9+155.3, 149.1+149.0, 139.9+139.7, 135.2+134.7, 131.5+130.8, 128.8+128.7, 127.4+127.1, 124.8+124.4, 124.4+124.3, 114.9+114.7, 84.6+84.5, 81.2, 54.6+54.3, 52.7+52.4, 52.3+51.9, 48.2+48.1, 42.3+42.1, 32.3+32.0, 28.1, 27.3. ESI-HRMS: calcd for $C_{26}H_{32}N_2O_7Na^+$ [M+Na$^+$] 507.2102, found 507.2110.

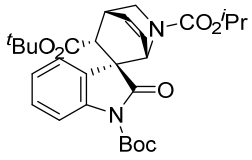


	Retention Time	Area	% Area
1	5.470	1427239	48.87
2	5.990	1493246	51.13

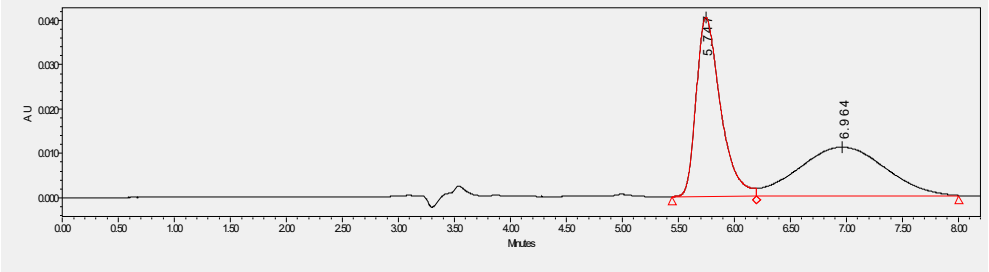


	Retention Time	Area	% Area
1	5.535	4459	0.28
2	5.974	1565621	99.72

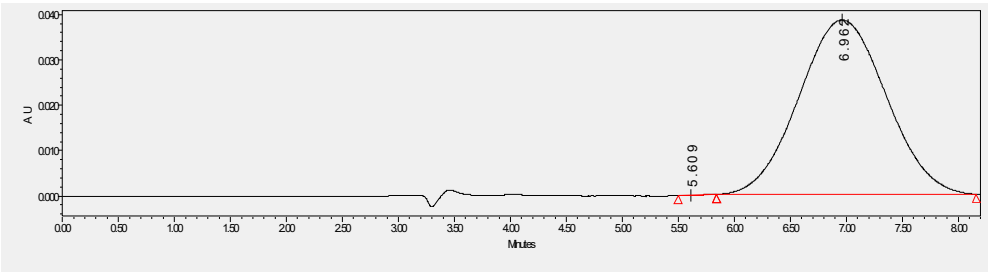
1',3-di-tert-butyl 6-isopropyl (1S,2R,3R,4R)-2'-oxo-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indolin]-7-ene-1',3,6-tricarboxylate **(5b)**



($C_{28}H_{36}N_2O_7$) white amorphous solid; 96% yield, >95:5 dr, 99% ee. $[\alpha]_D^{34}$ = 24.3 (c = 0.83, in CH_2Cl_2), HPLC DAICEL CHIRALCEL AD-H, 2-propanol/*n*-hexane = 20/80, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 5.61 min, t_{major} = 6.96 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 7.96–7.80 (m, 1H), 7.32 (tt, *J* = 8.0, 1.0 Hz, 1H), 7.14–7.03 (m, 1H), 6.99–6.89 (m, 1H), 6.76–6.65 (m, 1H), 6.59–6.47 (m, 1H), 4.85–4.66 (m, 1H), 4.58+4.41 (dd, *J* = 6.0, 1.0 Hz, 1H), 3.99 (td, *J* = 11.0, 2.0 Hz, 1H), 3.19–3.09 (m, 1H), 2.95 (dt, *J* = 6.0, 2.0 Hz, 1H), 1.64+1.63 (s, 9H), 1.22 (dd, *J* = 11.0, 6.0 Hz, 3H), 1.06–0.69 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 175.3+175.2, 169.8+169.3, 154.9+154.4, 149.2+149.0, 139.9+139.6, 135.2+134.7, 131.6+130.8, 128.8+128.5, 127.6+127.2, 124.9+124.5, 124.5+124.3, 114.9+114.6, 84.6+84.5, 81.2+81.2, 68.5+68.5, 54.7+54.5, 52.3+51.6, 48.3+48.3, 42.1+42.1, 32.3+32.1, 28.1, 27.3, 22.4+22.1, 22.0+21.8. ESI-HRMS: calcd for $C_{28}H_{36}N_2O_7Na^+$ [M+Na$^+$] 535.2415, found 535.2421.

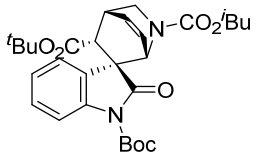


	Retention Time	Area	% Area
1	5.747	610339	50.80
2	6.964	591210	49.20

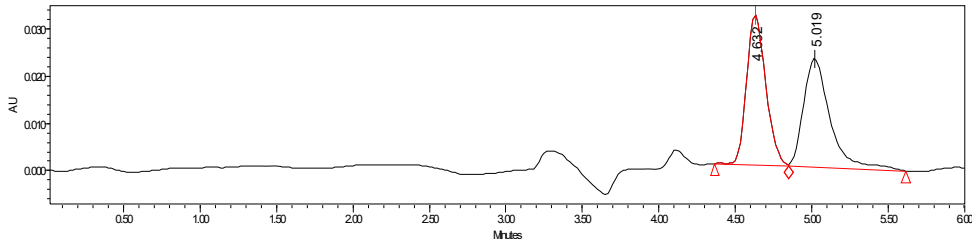


	Retention Time	Area	% Area
1	5.609	668	0.03
2	6.962	2086436	99.97

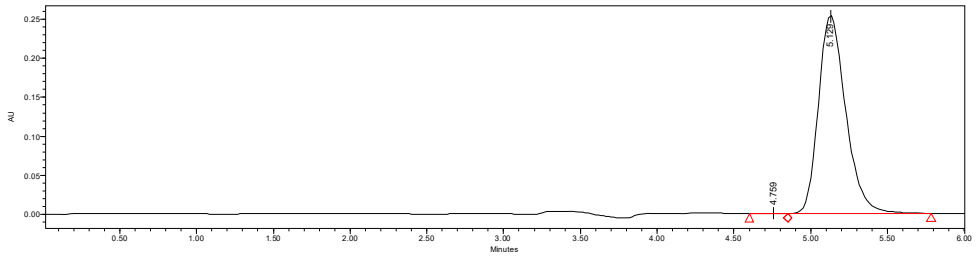
1',3-di-tert-butyl 6-isobutyl (1S,2R,3R,4R)-2'-oxo-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indolin]-7-ene-1',3,6-tricarboxylate **(5c)**



($C_{29}H_{38}N_2O_7$) white amorphous solid; 96% yield, >95:5 dr, 99% ee. $[\alpha]_D^{34}$ = 34.1 (c = 0.92, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 4.76 min, t_{major} = 5.13 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 7.97–7.80 (m, 1H), 7.32 (tt, *J* = 8.0, 2.0 Hz, 1H), 7.14–7.05 (m, 1H), 6.99–6.93 (m, 1H), 6.76–6.67 (m, 1H), 6.59–6.50 (m, 1H), 4.58+4.44 (dd, *J* = 6.0, 1.0 Hz, 1H), 4.07–3.95 (m, 1H), 3.87+3.71 (dd, *J* = 10.0, 6.0 Hz, 1H), 3.63+3.54 (dd, *J* = 10.0, 7.0 Hz, 1H), 3.34–3.25 (m, 1H), 3.21–3.13 (m, 1H), 2.99–2.92 (m, 1H), 1.91–1.62 (m, 10H), 0.97–0.89 (m, 12H), 0.56+0.54 (d, *J* = 6.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 175.3+175.3, 169.7+169.3, 155.5+154.9, 149.1+149.0, 139.9+139.7, 135.2+134.7, 131.6+130.8, 128.8+128.7, 127.5+127.2, 124.9+124.3, 124.5, 114.9+114.7, 100.0, 84.6+84.5, 81.2+81.2, 71.5+71.4, 54.6+54.4, 52.4+51.7, 48.3+48.2, 42.2+42.1, 32.3+32.1, 28.1, 28.0+27.6, 27.3+27.3, 19.1+19.0, 18.7+18.7. ESI-HRMS: calcd for $C_{29}H_{38}N_2O_7Na^+$ [M+Na^+] 549.2571, found 549.2573.

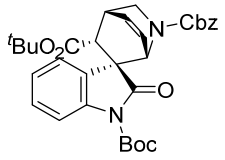


	Retention Time	Area	% Area
1	4.632	278094	49.83
2	5.019	279955	50.17

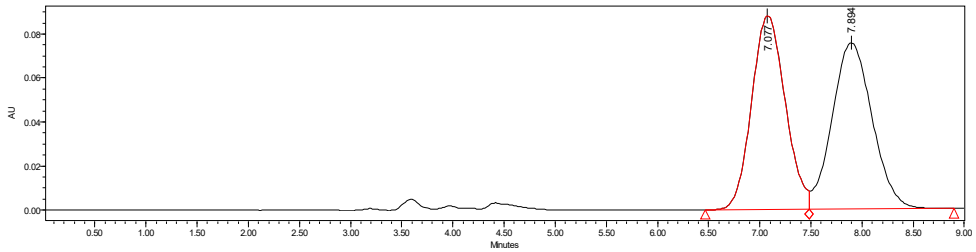


	Retention Time	Area	% Area
1	4.759	4190	0.13
2	5.129	3126767	99.87

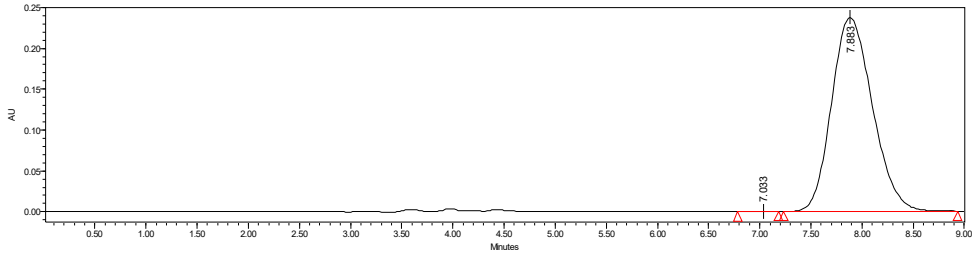
6-benzyl 1',3-di-tert-butyl (1S,2R,3R,4R)-2'-oxo-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indolin]-7-ene-1',3,6-tricarboxylate **(5d)**



($C_{32}H_{36}N_2O_7$) white amorphous solid; 91% yield, >95:5 dr, 99% ee. $[\alpha]_D^{34}$ = 49.8 (c = 0.95, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 7.03 min, t_{major} = 7.88 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 7.93+7.86 (d, *J* = 8.0 Hz, 1H), 7.38–7.20 (m, 5H), 7.11–6.96 (m, 1H), 6.92–6.79 (m, 2H), 6.76–6.67 (m, 1H), 6.60–6.46 (m, 1H), 5.16+4.96 (d, *J* = 12.0 Hz, 1H), 4.90+4.80 (d, *J* = 12.0 Hz, 1H), 4.59+4.48 (dd, *J* = 6.0, 1.0 Hz, 1H), 4.09–3.98 (m, 1H), 3.35–3.25 (m, 1H), 3.24–3.14 (m, 1H), 2.97+2.94 (t, *J* = 2.0 Hz, 1H), 1.63 (s, 9H), 0.92+0.88 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 175.3+175.1, 169.6+169.3, 155.2+154.6, 149.1+149.0, 139.9+139.7, 136.7+136.2, 135.3+134.8, 131.5+130.8, 128.7+128.7, 128.5+128.3, 128.1+127.6, 128.1+127.8, 127.5+127.0, 124.8+124.5, 124.4+124.4, 114.9+114.7, 84.6+84.6, 81.3+81.3, 67.0+66.8, 54.6+54.3, 52.5+51.9, 48.2+48.1, 42.4+42.2, 32.3+32.0, 28.1, 27.3+27.3. ESI-HRMS: calcd for $C_{32}H_{36}N_2O_7Na^+$ [M+Na$^+$] 583.2415, found 583.2425.

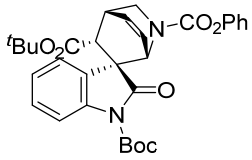


	Retention Time	Area	% Area
1	7.077	2012984	49.51
2	7.894	2052935	50.49

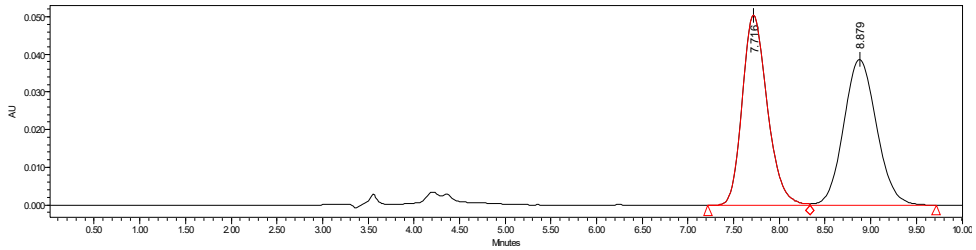


	Retention Time	Area	% Area
1	7.033	576	0.01
2	7.883	6581197	99.99

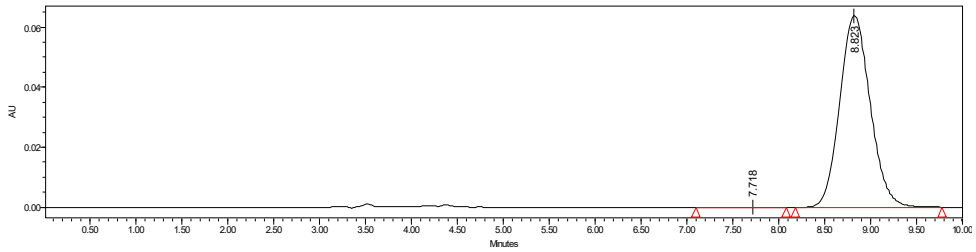
1',3-di-tert-butyl 6-phenyl (1S,2R,3R,4R)-2'-oxo-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indolin]-7-ene-1',3,6-tricarboxylate **(5e)**



($C_{31}H_{34}N_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 99% ee. $[\alpha]_D^{33}$ = 128.2 (c = 0.56, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 7.72 min, t_{major} = 8.82 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 7.90+7.96 (d, *J* = 8.0 Hz, 1H), 7.46–7.29 (m, 2H), 7.25–7.04 (m, 5H), 6.83–6.74 (m, 1H), 6.66–6.58 (m, 2H), 4.75–4.59 (m, 1H), 4.08+4.26 (dd, *J* = 11.0, 2.0 Hz, 1H), 3.42–3.23 (m, 2H), 3.03+3.01 (t, *J* = 2.0 Hz, 1H), 1.64 (s, 9H), 0.94+0.93 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 175.1+175.0, 169.6+169.3, 153.6+152.9, 151.1+150.6, 149.1+149.0, 140.0+139.9, 135.6+135.0, 131.4+130.6, 129.2+129.1, 128.9, 127.5+127.0, 125.4+125.3, 124.9+124.6, 124.4, 121.7+121.5, 115.1+115.0, 84.7+84.7, 81.4, 54.7+54.2, 53.0+52.1, 48.1+48.0, 42.7+42.6, 32.3+32.0, 28.1, 27.3. ESI-HRMS: calcd for $C_{31}H_{34}N_2O_7Na^+$ [M+Na$^+$] 569.2258, found 569.2264.

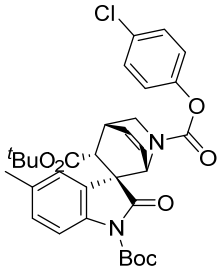


	Retention Time	Area	% Area
1	7.716	959997	49.87
2	8.879	965055	50.13

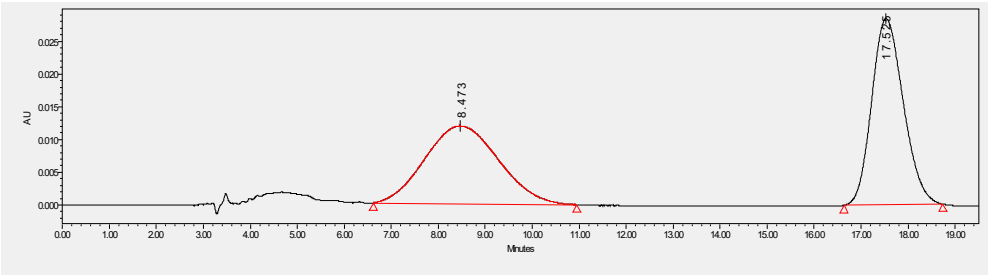


	Retention Time	Area	% Area
1	7.718	1556	0.10
2	8.823	1487993	99.90

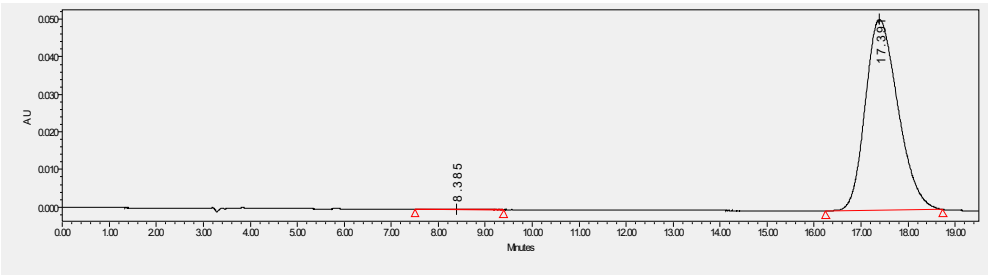
1',3-di-tert-butyl 6-(4-chlorophenyl) (1S,2R,3R,4R)-5'-methyl-2'-oxo-6-azaspiro[bicyclo[2.2.2] octane-2,3'-indolin]-7-ene-1',3,6-tricarboxylate **(5f)**



($C_{32}H_{35}ClN_2O_7$) white powder, mp 154.0−156.0 °C; 91% yield, >95:5 dr, 99% ee. $[\alpha]_D^{22}$ = 98.9 (c = 1.41, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 8.38 min, t_{major} = 17.39 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 7.84+7.78 (d, *J* = 8.0 Hz, 1H), 7.31–7.27 (m, 1H), 7.22–7.12 (m, 2H), 7.06–6.93 (m, 1H), 6.87–6.73 (m, 2H), 6.61–6.50 (m, 2H), 4.69–4.53 (m, 1H), 4.26+4.09 (dd, *J* = 12.0, 2.0 Hz, 1H), 3.40–3.20 (m, 2H), 3.02+2.99 (t, *J* = 2.0 Hz, 1H), 2.31+2.28 (s, 3H), 1.64+1.63 (s, 9H), 0.94+0.93 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 175.2+175.0, 169.6+169.3, 153.1+152.6, 151.1+150.6, 149.6+149.1+149.1+149.0 (2C), 137.6+137.4, 135.6+135.0, 134.1+133.7, 131.3+130.7+130.5+130.4 (2C), 129.4+129.1, 129.2+129.1, 127.5+127.0, 125.4+124.8, 123.0+122.7, 115.0+114.9, 84.6+84.5, 81.4, 54.9+54.2, 53.1+52.2, 47.9+47.8, 42.7, 32.3+31.9, 28.1, 27.3+27.2. ESI-HRMS: calcd for $C_{32}H_{35}{}^{34.9689}ClN_2O_7Na^+$ [M+Na^+] 617.2025, found 617.2018; ESI-HRMS: calcd for $C_{32}H_{35}{}^{36.9659}ClN_2O_7Na^+$ [M+Na^+] 619.1996, found 619.2021.

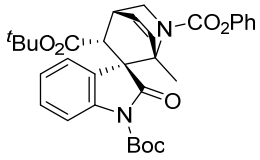


	Retention Time	Area	% Area
1	8.473	1299637	49.36
2	17.525	1333212	50.64

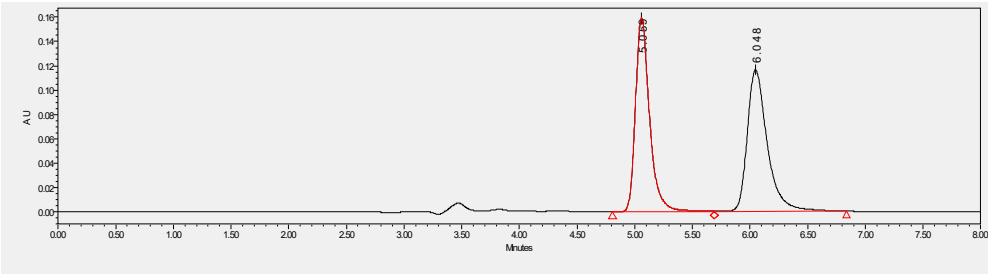


	Retention Time	Area	% Area
1	8.385	1753	0.07
2	17.391	2450985	99.93

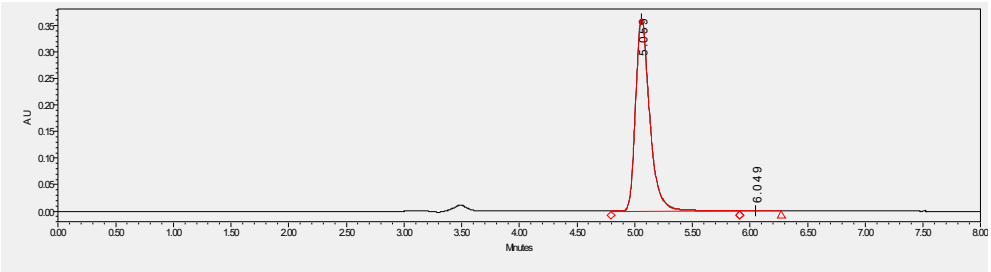
1',3-di-tert-butyl 6-phenyl (1S,2R,3R,4R)-1-methyl-2'-oxo-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indolin]-7-ene-1',3,6-tricarboxylate **(5g)**



($C_{32}H_{36}N_2O_7$) white amorphous solid; 95% yield, >95:5 dr, 99% ee. $[\alpha]_D^{34}$ = 80.2 (c = 0.70, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 5.06 min, t_{minor} = 6.05 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.0 Hz, 1H), 7.43–7.28 (m, 3H), 7.26–7.13 (m, 3H), 7.11–6.80 (m, 2H), 6.75 (t, *J* = 8.0 Hz, 1H), 6.30 (dd, *J* = 8.0, 1.0 Hz, 1H), 4.27 (d, *J* = 12.0 Hz, 1H), 3.44 (d, *J* = 12.0 Hz, 1H), 3.29–3.19 (m, 1H), 3.09 (t, *J* = 2.0 Hz, 1H), 1.63 (s, 9H), 1.50 (s, 3H), 0.91 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 169.6, 150.9, 148.9, 141.3, 137.1, 134.2, 129.2, 129.1, 126.5, 125.2, 124.9, 124.7, 121.8, 114.6, 84.6, 81.2, 60.9, 59.3, 50.5, 45.9, 31.4, 28.1, 27.2, 19.5. ESI-HRMS: calcd for $C_{32}H_{36}N_2O_7Na^+$ [M+Na$^+$] 583.2415, found 583.2420.

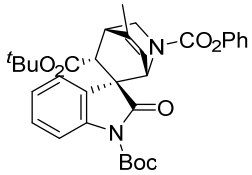


	Retention Time	Area	% Area
1	5.059	1349237	49.01
2	6.048	1403579	50.99

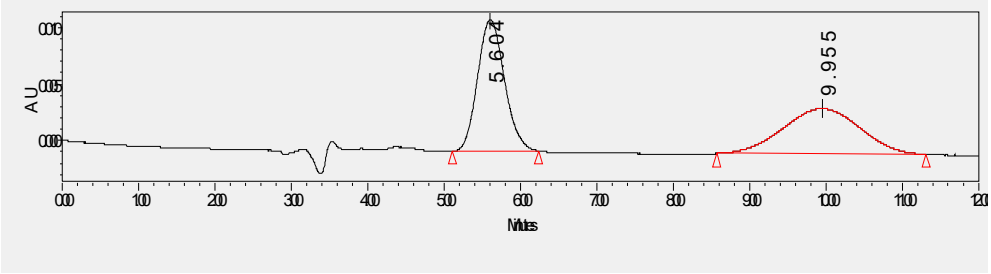


	Retention Time	Area	% Area
1	5.059	3140488	99.66
2	6.049	10701	0.34

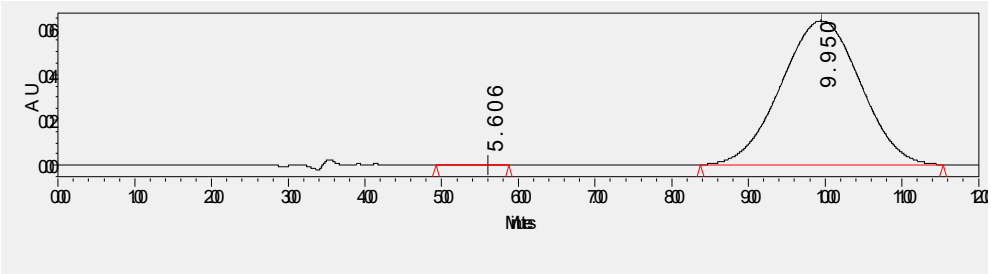
1',3-di-tert-butyl 6-phenyl (1S,2R,3R,4S)-8-methyl-2'-oxo-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indolin]-7-ene-1',3,6-tricarboxylate **(5h)**



($C_{32}H_{36}N_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 99% ee. $[\alpha]_D^{34}$ = 75.5 (c = 1.02, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 5.61 min, t_{major} = 9.95 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 7.89+7.95 (d, *J* = 8.0 Hz, 1H), 7.48–7.29 (m, 2H), 7.25–7.03 (m, 5H), 6.64–6.61 (m, 1H), 6.23–6.12 (m, 1H), 4.57+4.54 (d, *J* = 6.0 Hz, 1H), 4.21+4.03 (dd, *J* = 11.0, 2.0 Hz, 1H), 3.45–3.24 (m, 1H), 3.15–3.08 (m, 1H), 3.01+2.98 (t, *J* = 2.0 Hz, 1H), 2.06 (t, *J* = 2.0 Hz, 3H), 1.64 (s, 9H), 0.94+0.93 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 175.0+174.9, 169.8+169.5, 153.4+152.8, 151.1+150.6, 149.1+149.0, 145.2+144.6, 140.0+139.8, 129.2+129.0, 129.0+128.8, 127.9+127.4, 125.3+125.2, 124.9+124.5, 124.4+124.3, 124.0+123.3, 121.7+121.5, 115.0+114.9, 84.6+84.6, 81.4, 55.5+55.0, 54.0+53.1, 47.9+47.8, 42.3+42.3, 37.8+37.5, 28.1, 27.3, 19.5+19.4. ESI-HRMS: calcd for $C_{32}H_{36}N_2O_7Na^+$ [M+Na$^+$] 583.2415, found 583.2422.

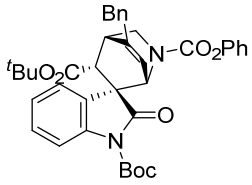


	Retention Time	Area	% Area
1	5.604	285435	50.43
2	9.955	280523	49.57

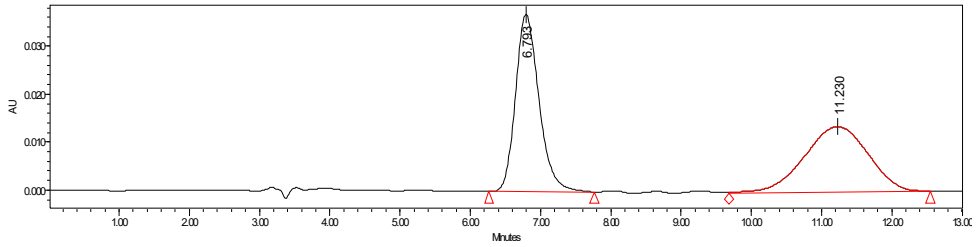


	Retention Time	Area	% Area
1	5.606	1280	0.03
2	9.950	4561376	99.97

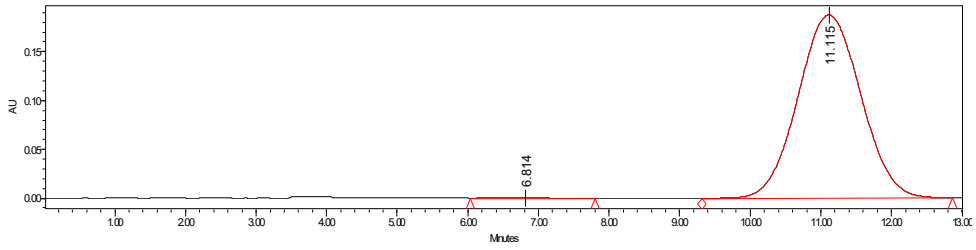
1',3-di-tert-butyl 6-phenyl (1S,2R,3R,4S)-8-benzyl-2'-oxo-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indolin]-7-ene-1',3,6-tricarboxylate **(5i)**



($C_{38}H_{40}N_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 99% ee. $[\alpha]_D^{34}$ = 60.8 (c = 1.28, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 6.81 min, t_{major} = 11.12 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 7.90+7.85 (d, *J* = 8.0 Hz, 1H), 7.43–7.27 (m, 6H), 7.26–7.02 (m, 6H), 6.64–6.60 (m, 1H), 6.34–6.10 (m, 1H), 4.60+4.58 (d, *J* = 6.0 Hz, 1H), 4.16+3.99 (dd, *J* = 11.0, 2.0 Hz, 1H), 3.77–3.49 (m, 2H), 3.27–3.05 (m, 2H), 2.98+2.95 (t, *J* = 2.0 Hz, 1H), 1.66+1.65 (s, 9H), 0.91+0.90 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 175.2+175.0, 169.7+169.4, 153.4+152.8, 151.1+150.6, 149.0+148.9, 147.9+147.2, 139.9+139.8, 137.4+137.3, 129.4, 129.2+129.0, 129.0+128.8, 128.7+128.7, 127.8+127.3, 126.7+126.7, 125.4+125.2, 124.9, 124.5+124.2, 124.4+124.3, 121.8+121.5, 115.1+114.9, 84.8+84.7, 81.4, 55.6+55.1, 54.1+53.3, 48.1+48.1, 43.0+42.9, 40.3+40.2, 36.3+36.0, 28.1, 27.3. ESI-HRMS: calcd for $C_{38}H_{40}N_2O_7Na^+$ [M+Na^+] 659.2728, found 659.2734.

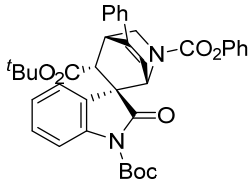


	Retention Time	Area	% Area
1	6.793	859759	49.69
2	11.230	870533	50.31

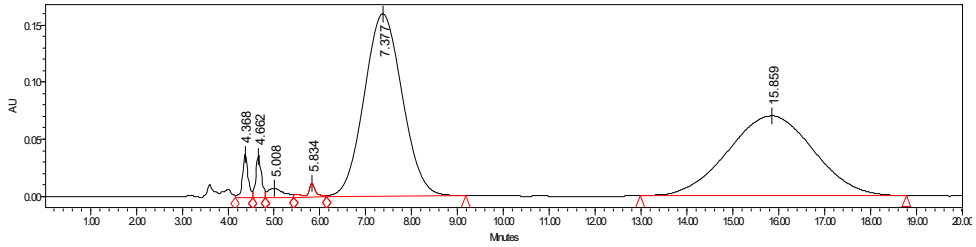


	Retention Time	Area	% Area
1	6.814	8981	0.08
2	11.115	11575445	99.92

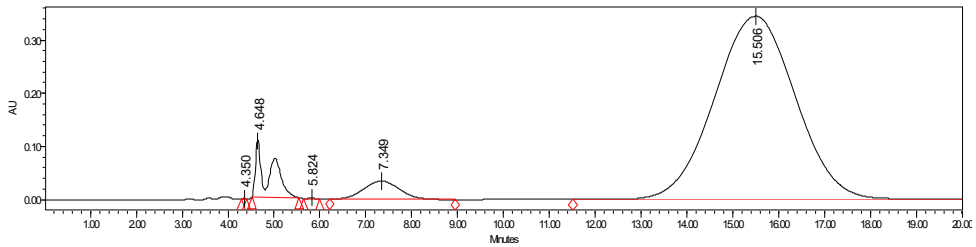
1',3-di-tert-butyl 6-phenyl (1S,2R,3R,4S)-2'-oxo-8-phenyl-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indolin]-7-ene-1',3,6-tricarboxylate **(5j)**



($C_{37}H_{38}N_2O_7$) white amorphous solid; 95% yield, >95:5 dr, 92% ee. $[\alpha]_D^{34}$ = 82.0 (c = 1.04, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{minor1\text{-}minor}$ = 4.35 min, $t_{minor1\text{-}major\&minor2\text{-}major}$ = 4.65 min, $t_{minor2\text{-}minor}$ = 5.82 min, $t_{major\text{-}minor}$ = 7.35 min, $t_{major\text{-}major}$ = 15.51 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 7.95+7.90 (d, *J* = 8.0 Hz, 1H), 7.67–7.52 (m, 2H), 7.45–7.30 (m, 5H), 7.25–7.03 (m, 5H), 6.81–6.75 (m, 1H), 6.69–6.62 (m, 1H), 4.79 (dd, *J* = 11.0, 6.0 Hz, 1H), 4.39+4.22 (dd, *J* = 11.0, 2.0 Hz, 1H), 3.89 (s, 1H), 3.61–3.40 (m, 1H), 3.13+3.11 (t, *J* = 2.0 Hz, 1H), 1.64 (s, 9H), 0.94+0.93 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 175.0+174.9, 169.7+169.4, 153.5+152.9, 151.1+150.6, 149.0+148.9, 146.7+146.1, 140.1+140.0, 136.1+136.0, 129.3+129.1, 129.1+128.9, 128.8, 128.5+128.5, 127.5+127.1, 125.7+125.6, 125.4+125.3, 125.0+124.6, 124.4+124.4, 124.3+123.6, 121.7+121.5, 115.2+115.0, 84.8+84.7, 81.5+81.5, 55.3+54.9, 54.1+53.3, 48.5+48.4, 43.0+43.0, 35.3+35.1, 28.1, 27.3. ESI-HRMS: calcd for $C_{37}H_{38}N_2O_7Na^+$ [M+Na^+] 645.2571, found 645.2578.

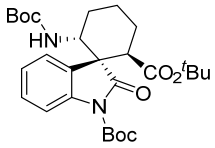


	Retention Time	Area	% Area
1	4.368	321733	1.66
2	4.662	312471	1.62
3	5.008	192700	1.00
4	5.834	148003	0.77
5	7.377	9242740	47.80
6	15.859	9120226	47.16

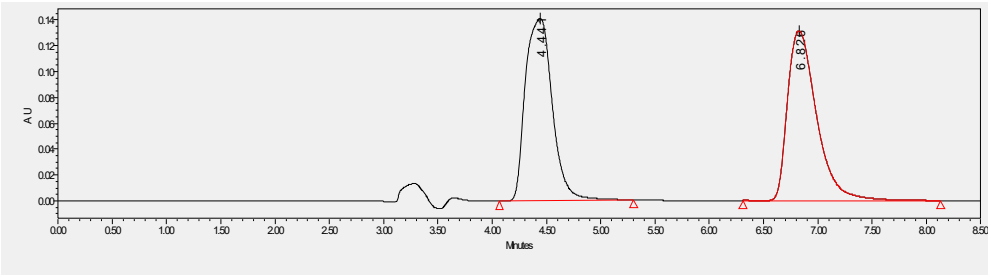


	Retention Time	Area	% Area
1	4.350	2237	0.00
2	4.648	2187107	4.73
3	5.824	14823	0.03
4	7.349	1776659	3.85
5	15.506	42215082	91.38

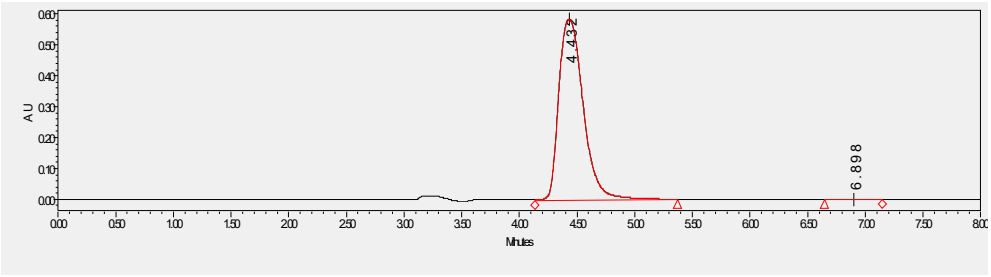
di-tert-butyl (1R,2R,6R)-2-((tert-butoxycarbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indoline]-1',6-dicarboxylate **(6a)**



($C_{28}H_{40}N_2O_7$) white amorphous solid; 99% yield, >95:5 dr, 99% ee. $[\alpha]_D^{34}$ = −29.5 (c = 0.73, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 5/95, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{major} = 4.43 min, t_{minor} = 6.90 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.34–7.28 (m, 1H), 7.09 (td, *J* = 8.0, 1.0 Hz, 1H), 5.15 (d, *J* = 9.0 Hz, 1H), 3.90 (s, 1H), 3.05 (dd, *J* = 12.0, 5.0 Hz, 1H), 2.29–2.20 (m, 1H), 2.00–1.88 (m, 4H), 1.62 (s, 9H), 1.39 (s, 9H), 1.05 (s, 9H), 0.90–0.85 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 170.7, 155.0, 149.4, 139.8, 129.8, 128.4, 124.6, 123.7, 115.0, 83.9, 81.5, 79.4, 52.5, 51.0, 43.7, 28.3, 28.1, 27.3, 25.5, 23.1, 18.7. ESI-HRMS: calcd for $C_{28}H_{40}N_2O_7Na^+$ [M+Na$^+$] 539.2728, found 539.2755.

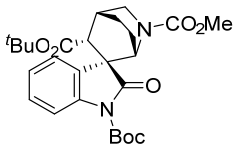


	Retention Time	Area	% Area
1	4.441	2427462	50.02
2	6.826	2425924	49.98

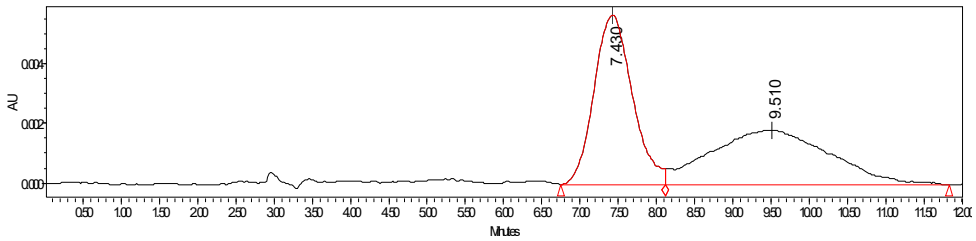


	Retention Time	Area	% Area
1	4.432	8675541	99.85
2	6.898	12648	0.15

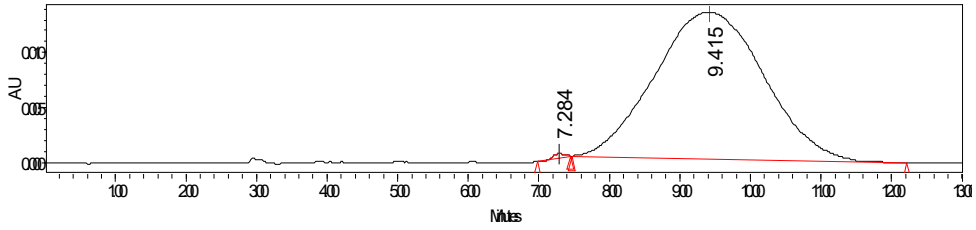
1',3-di-tert-butyl 6-methyl (1S,2R,3R,4R)-2'-oxo-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indoline]-1',3,6-tricarboxylate **(6b)**



($C_{26}H_{34}N_2O_7$) white powder, mp 124.0−126.0 °C; 94% yield, >95:5 dr, 99% ee. $[\alpha]_D^{21}$ = 12.8 (c = 0.51, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 7.28 min, t_{major} = 9.42 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 7.86 (t, *J* = 9.0 Hz, 1H), 7.39–7.29 (m, 1H), 7.13–7.03 (m, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 3.98–3.76 (m, 2H), 3.68–3.36 (m, 4H), 3.24 (s, 1H), 2.64–2.45 (m, 2H), 1.96–1.76 (m, 3H), 1.65 (s, 9H), 0.89 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 175.9+175.8, 169.6+169.3, 156.1+155.9, 149.1+149.0, 139.5+139.3, 128.6+128.5, 128.6+128.3, 124.8+124.3, 124.3, 114.8+114.5, 84.6+84.5, 80.9, 54.6+54.5, 52.7+52.3, 50.7+50.1, 47.8+47.7, 45.9+45.8, 28.1, 27.2, 27.1+26.9, 25.2+25.1, 20.4+20.1. ESI-HRMS: calcd for $C_{26}H_{34}N_2O_7Na^+$ [M+Na$^+$] 509.2258, found 509.2267.

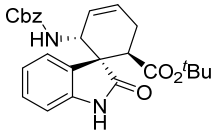


	Retention Time	Area	% Area
1	7.430	199080	49.88
2	9.510	200041	50.12

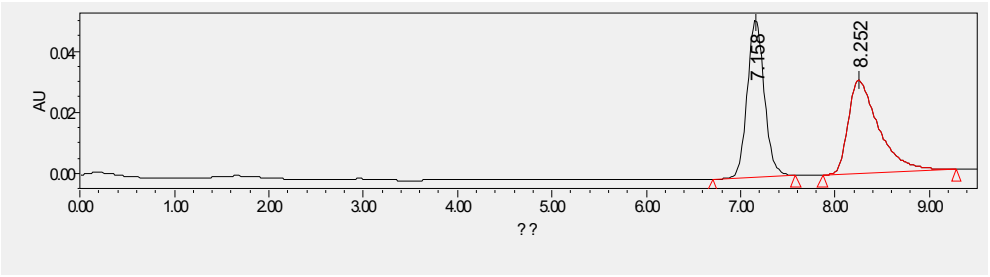


	Retention Time	Area	% Area
1	7.284	4194	0.29
2	9.415	1437899	99.71

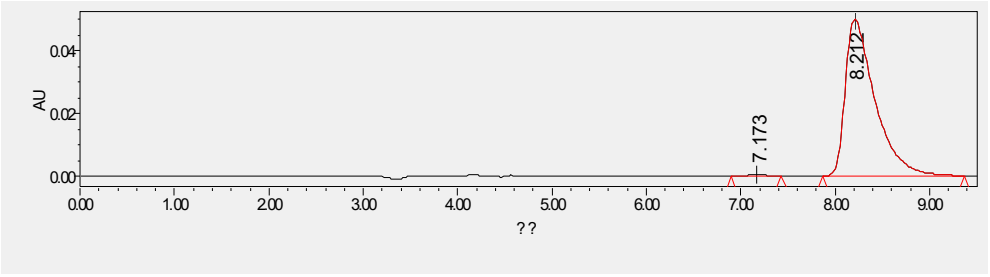
tert-butyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-6-carboxylate **(6c)**



($C_{26}H_{28}N_2O_5$) white amorphous solid; 99% yield, >95:5 dr, 98% ee. $[\alpha]_D^{17}$ = −100.4 (c = 1.02, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 7.17 min, t_{major} = 8.21 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H), 7.40–7.26 (m, 5H), 7.19–7.08 (m, 2H), 6.98–6.77 (m, 2H), 6.20–5.82 (m, 2H), 5.54 (d, *J* = 8.0 Hz, 1H), 5.16 (d, *J* = 12.0 Hz, 1H), 5.00 (d, *J* = 12.0 Hz, 1H), 4.19 (dd, *J* = 9.0, 5.0 Hz, 1H), 3.20 (dd, *J* = 10.0, 6.0 Hz, 1H), 2.86–2.51 (m, 2H), 1.20 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 171.0, 156.0, 141.2, 136.5, 130.2, 129.3, 128.4, 128.2, 128.0, 127.9, 125.3, 124.5, 121.9, 110.1, 81.4, 66.9, 51.3, 50.9, 41.0, 27.6, 25.7. ESI-HRMS: calcd for $C_{26}H_{28}N_2O_5Na^+$ [M+Na$^+$] 471.1890, found 471.1891.

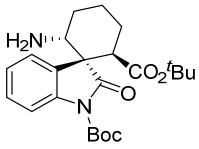


	Retention Time	Area	% Area
1	7.158	642270	48.31
2	8.252	687158	51.69

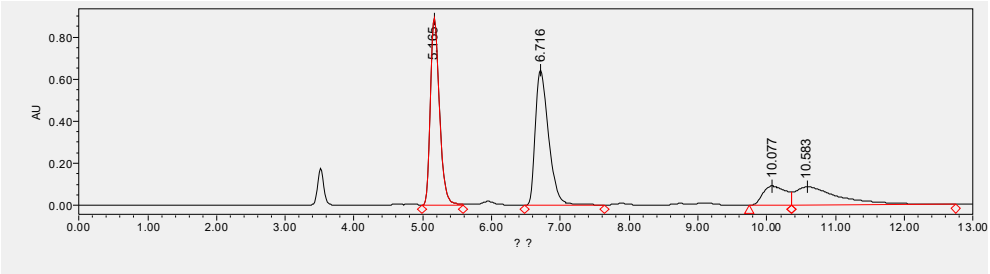


	Retention Time	Area	% Area
1	7.173	9050	0.82
2	8.212	1098305	99.18

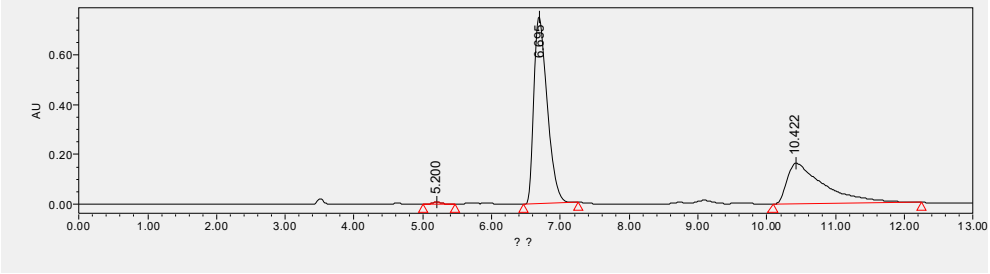
di-tert-butyl (1R,2R,6R)-2-amino-2'-oxospiro[cyclohexane-1,3'-indoline]-1',6-dicarboxylate **(6d)**



($C_{23}H_{32}N_2O_5$) white amorphous solid; 89% yield, 73:27 dr, 99% ee. HPLC DAICEL CHIRALCEL IE, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{major\text{-}minor}$ = 5.20 min, $t_{major\text{-}major}$ = 6.70 min, $t_{minor\text{-}major}$ = 10.42 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99–7.72 (m, 1H), 7.49–7.32 (m, 1H), 7.30–7.21 (m, 1H), 7.12–6.99 (m, 1H), 3.25–2.79 (m, 2H), 2.28–1.63 (m, 6H), 1.57 (s, 9H), 1.51–1.35 (m, 2H), 1.01 (s, 6.57H), 0.96 (s, 2.43H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 171.5, 149.4, 139.8, 130.5, 128.2, 124.8, 123.8, 114.7, 84.2, 81.2, 54.3, 52.3, 43.1, 28.1, 27.4, 26.7, 22.9, 17.9. ESI-HRMS: calcd for $C_{23}H_{32}N_2O_5Na^+$ [M+Na$^+$] 439.2203, found 439.2208.

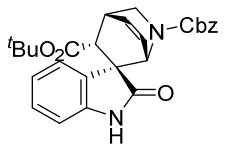


	Retention Time	Area	% Area
1	5.165	8214295	36.01
2	6.716	8675522	38.03
3	10.077	2007035	8.80
4	10.583	3912518	17.15

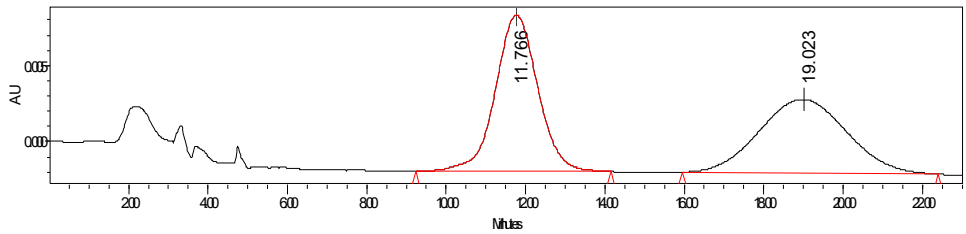


	Retention Time	Area	% Area
1	5.200	68141	0.41
2	6.695	10211367	62.11
3	10.422	6161608	37.48

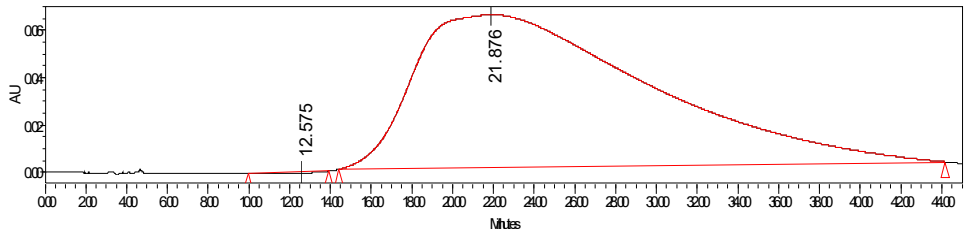
6-benzyl 3-(tert-butyl) (1S,2R,3R,4R)-2'-oxo-6-azaspiro[bicyclo[2.2.2]octane-2,3'-indolin]-7-ene-3,6-dicarboxylate **(6e)**



($C_{27}H_{28}N_2O_5$) white amorphous solid; 99% yield, >95:5 dr, 99% ee. $[\alpha]_D^{17}$ = 64.2 (c = 1.27, in CH_2Cl_2), HPLC DAICEL CHIRALCEL IC, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: t_{minor} = 12.58 min, t_{major} = 21.88 min. ^{1}H NMR (400 MHz, $CDCl_3$) mixture of rotamers δ 8.83+8.72 (s, 1H), 7.39–7.17 (m, 5H), 7.05–6.65 (m, 5H), 6.63–6.42 (m, 1H), 5.25–4.76 (m, 2H), 4.58+4.46 (dd, *J* = 6.0, 2.0 Hz, 1H), 4.14–4.03 (m, 1H), 3.42–3.12 (m, 2H), 2.94+2.90 (t, *J* = 2.0 Hz, 1H), 0.94+0.90 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) mixture of rotamers δ 178.7+178.6, 170.1+169.7, 155.3+154.7, 141.1+141.0, 136.8+136.3, 135.2+134.7, 131.7+131.0, 129.0+128.6, 128.5, 128.3, 128.0, 127.7+127.5, 125.4+124.9, 122.7+122.5, 109.9+109.7, 81.1+81.1, 67.0+66.8, 54.8+54.3, 52.3+51.7, 47.1+46.9, 42.4+42.2, 32.4+32.2, 27.4+27.4. ESI-HRMS: calcd for $C_{27}H_{28}N_2O_5Na^+$ [M+Na$^+$] 483.1890, found 483.1889.



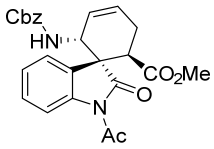
	Retention Time	Area	% Area
1	11.766	766328	50.55
2	19.023	749720	49.45



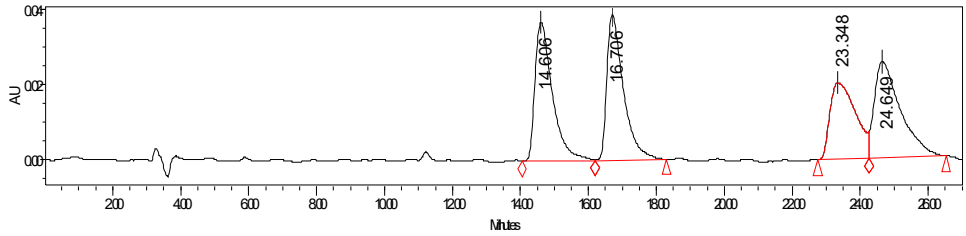
	Retention Time	Area	% Area
1	12.575	72235	0.14
2	21.876	51424886	99.86

(F) Control experiments

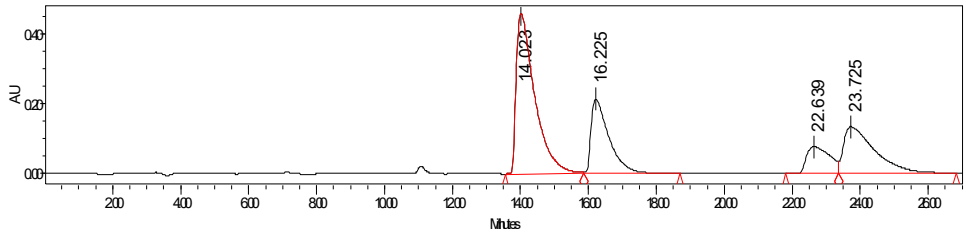
methyl (1R,2R,6R)-1'-acetyl-2-(((benzyloxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-6-carboxylate **(7d)**



($C_{25}H_{24}N_2O_6$) white amorphous solid; 84% yield, 67:33 dr, 38/40% ee. HPLC DAICEL CHIRALCEL IB, 2-propanol/*n*-hexane = 10/90, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{major\text{-}major}$ = 14.02 min, $t_{major\text{-}minor}$ = 16.23 min, $t_{minor\text{-}minor}$ = 22.64 min, $t_{minor\text{-}major}$ = 23.73 min. ESI-HRMS: calcd for $C_{25}H_{24}N_2O_6Na^+$ [M+Na^+] 471.1527, found 471.1529.

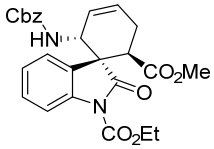


	Retention Time	Area	% Area
1	14.606	1309080	26.06
2	16.706	1297630	25.84
3	23.348	1066016	21.22
4	24.649	1349984	26.88

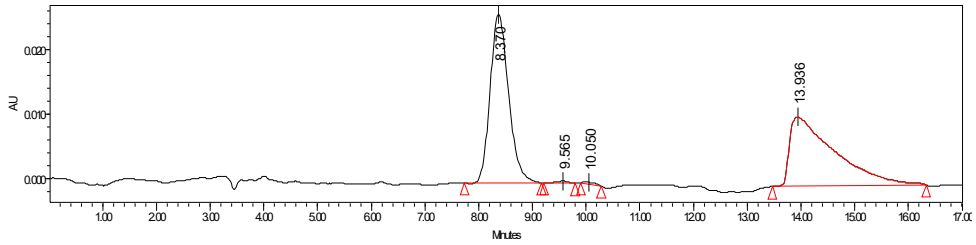


	Retention Time	Area	% Area
1	14.023	17433410	46.43
2	16.225	7839662	20.88
3	22.639	3685106	9.81
4	23.725	8588001	22.87

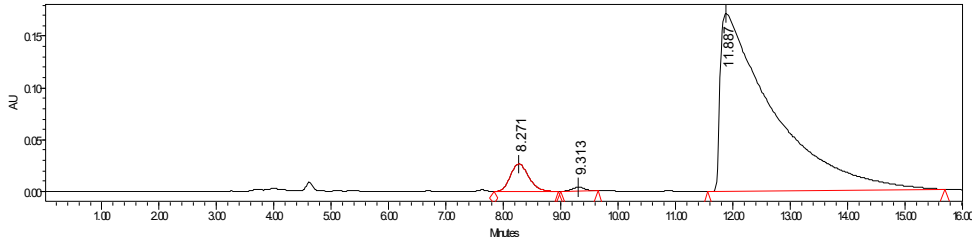
1'-ethyl 6-methyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)amino)-2'-oxospiro[cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(7e)**



($C_{26}H_{26}N_2O_7$) white amorphous solid; 87% yield, 99:1 dr, 90% ee. HPLC DAICEL CHIRALCEL IA, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{major\text{-}minor}$ = 8.27 min, $t_{minor\text{-}major}$ = 9.31 min, $t_{major\text{-}major}$ = 11.89 min. ESI-HRMS: calcd for $C_{26}H_{26}N_2O_7Na^+$ [M+Na^+] 501.1632, found 501.1640.

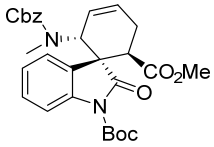


	Retention Time	Area	% Area
1	8.370	626686	49.61
2	9.565	5257	0.42
3	10.050	4648	0.37
4	13.936	626607	49.60

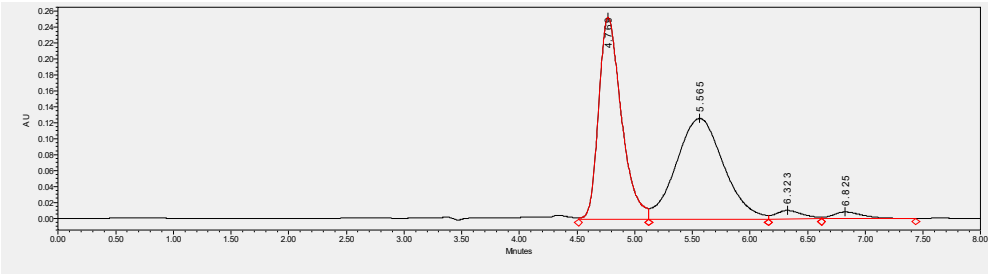


	Retention Time	Area	% Area
1	8.271	600899	5.16
2	9.313	59212	0.51
3	11.887	10977234	94.33

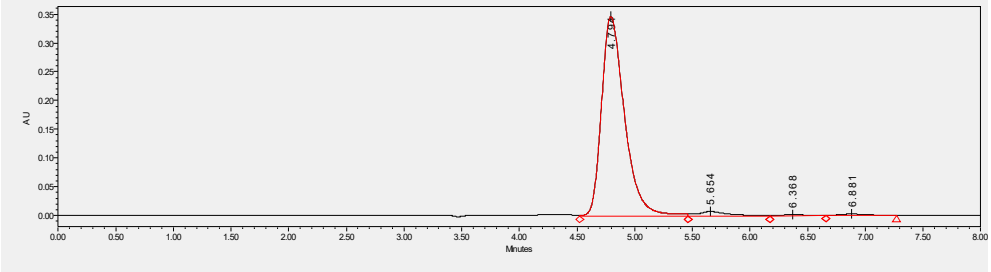
1'-(tert-butyl) 6-methyl (1R,2R,6R)-2-(((benzyloxy)carbonyl)(methyl)amino)-2'-oxospiro [cyclohexane-1,3'-indolin]-3-ene-1',6-dicarboxylate **(7f)**



($C_{29}H_{32}N_2O_7$) white amorphous solid; 91% yield, 98:2 dr, 94% ee. HPLC DAICEL CHIRALCEL AD-H, 2-propanol/*n*-hexane = 30/70, flow rate = 1.0 mL/min, λ = 254 nm, retention time: $t_{major\text{-}major}$ = 4.79 min, $t_{major\text{-}minor}$ = 5.65 min, $t_{minor\text{-}minor}$ = 6.37 min, $t_{minor\text{-}major}$ = 6.88 min. ESI-HRMS: calcd for $C_{29}H_{32}N_2O_7Na^+$ [M+Na^+] 543.2102, found 543.2110.



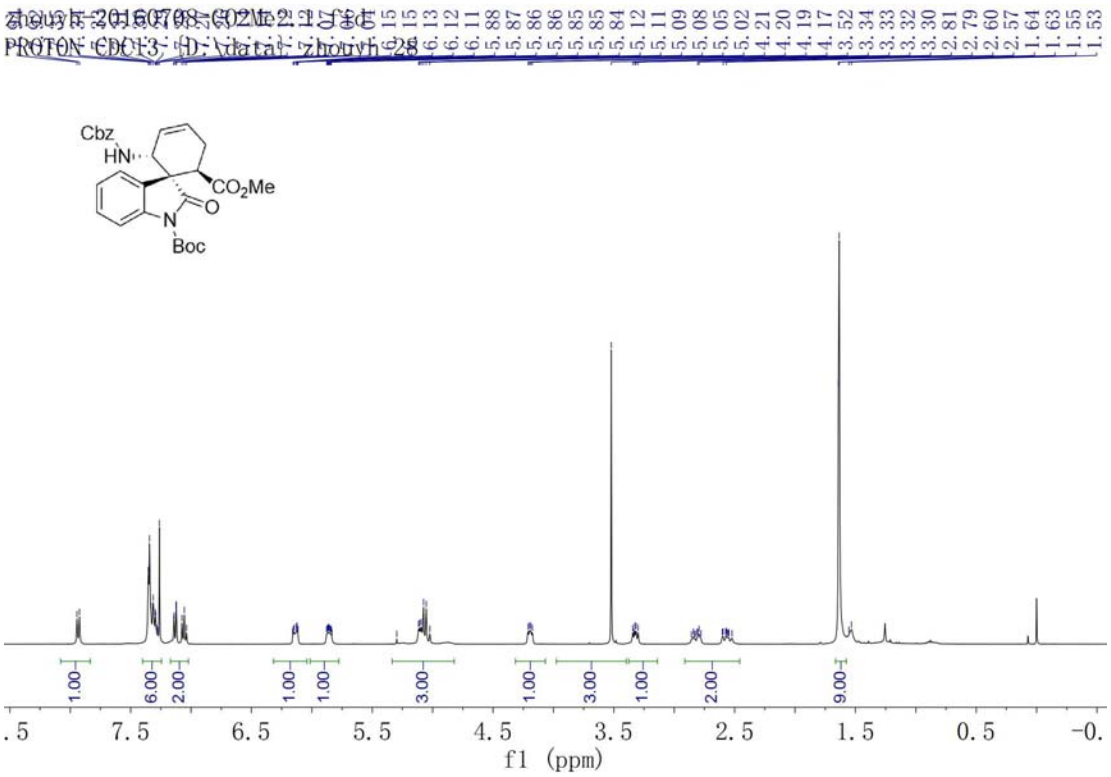
	Retention Time	Area	% Area
1	4.769	3484152	46.87
2	5.565	3612385	48.60
3	6.323	176992	2.38
4	6.825	160026	2.15

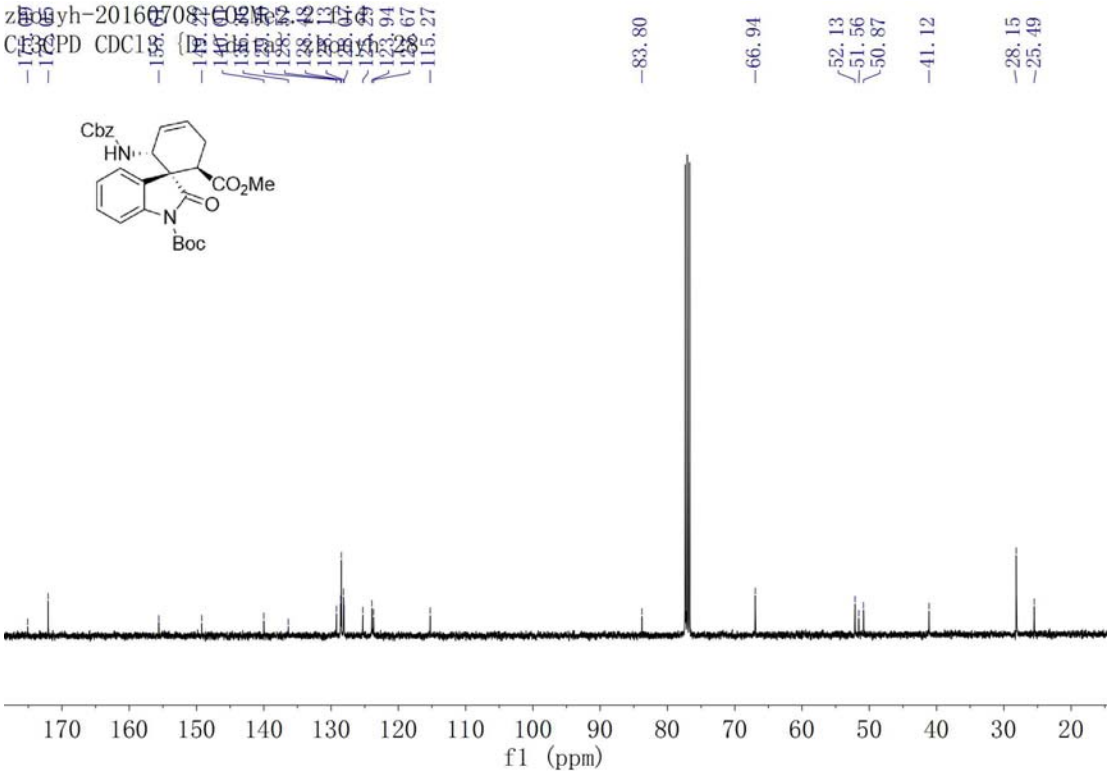


	Retention Time	Area	% Area
1	4.794	4843398	95.60
2	5.654	145926	2.88
3	6.368	31824	0.63
4	6.881	45281	0.89

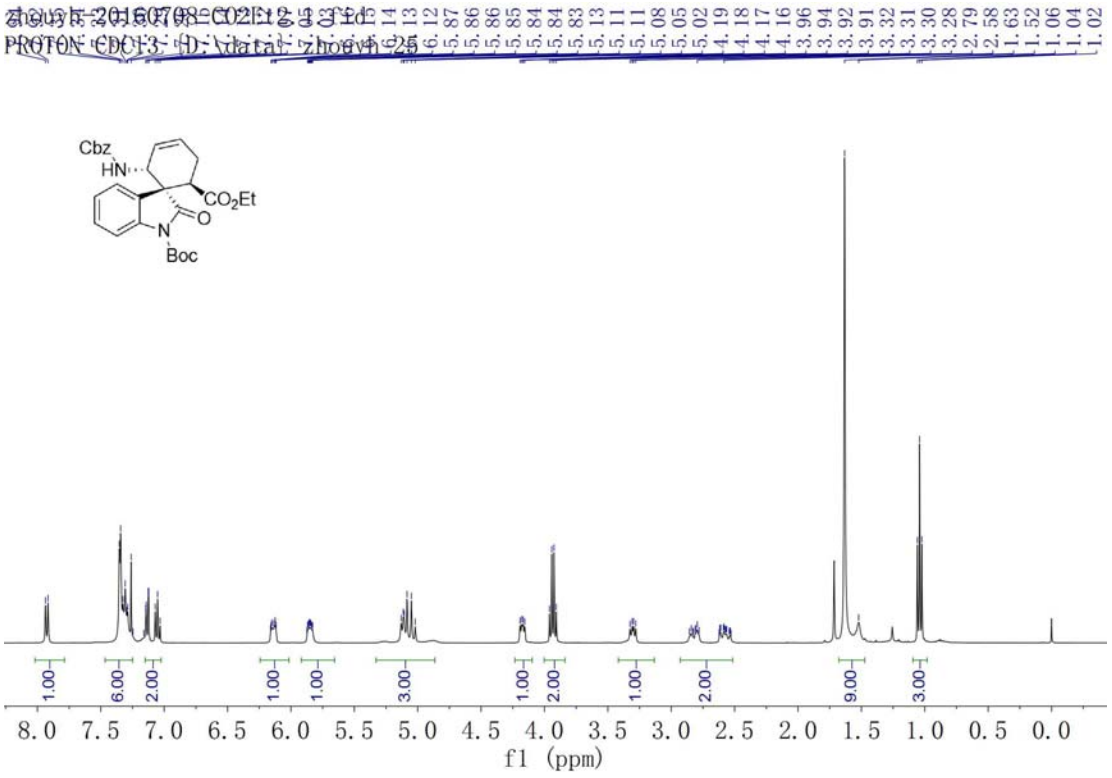
(G) Copies of NMR spectra for the products

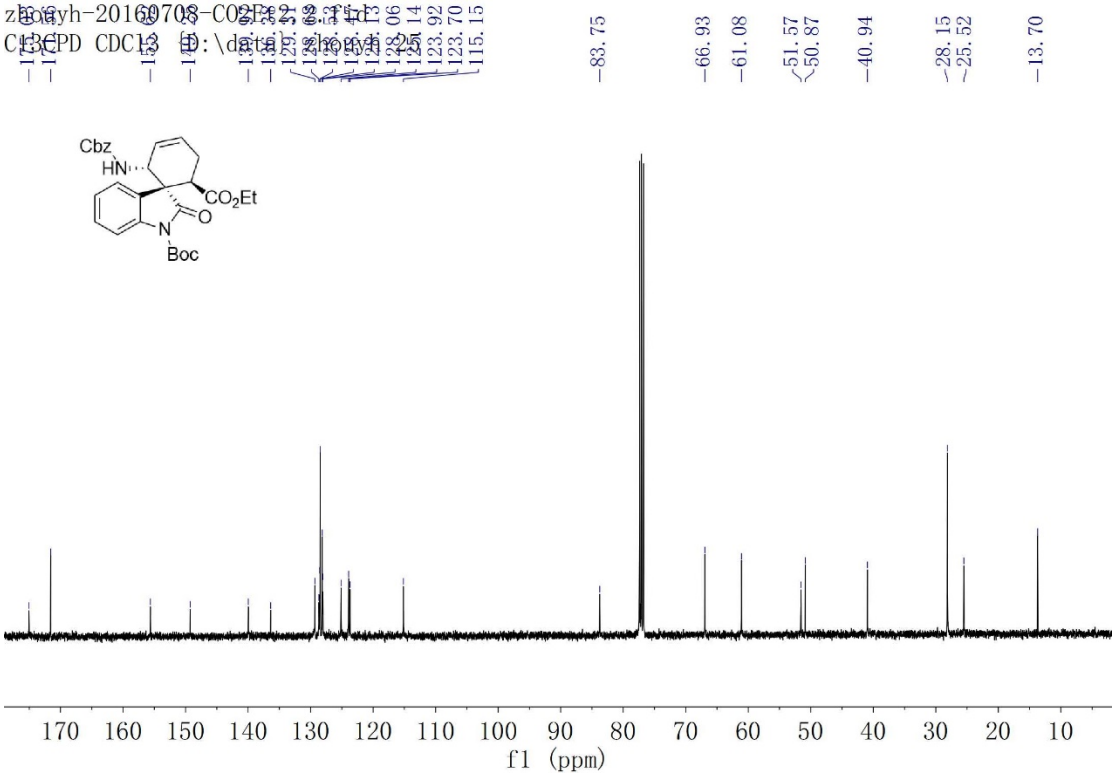
3a





3b


Cbz
HN
CO2Et
O
N
Boc
1.00
6.00
2.00
1.00
1.00
3.00
1.00
2.00
1.00
2.00
9.00
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Cbz
HN
CO2Et
O
N
Boc
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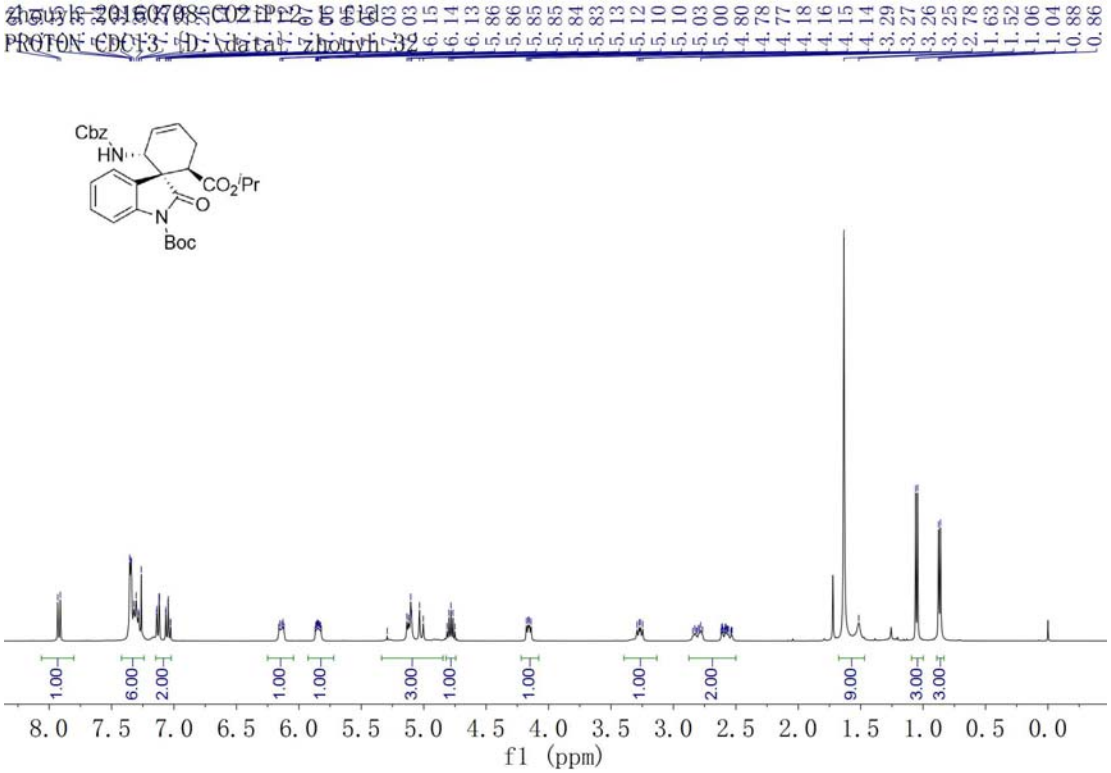
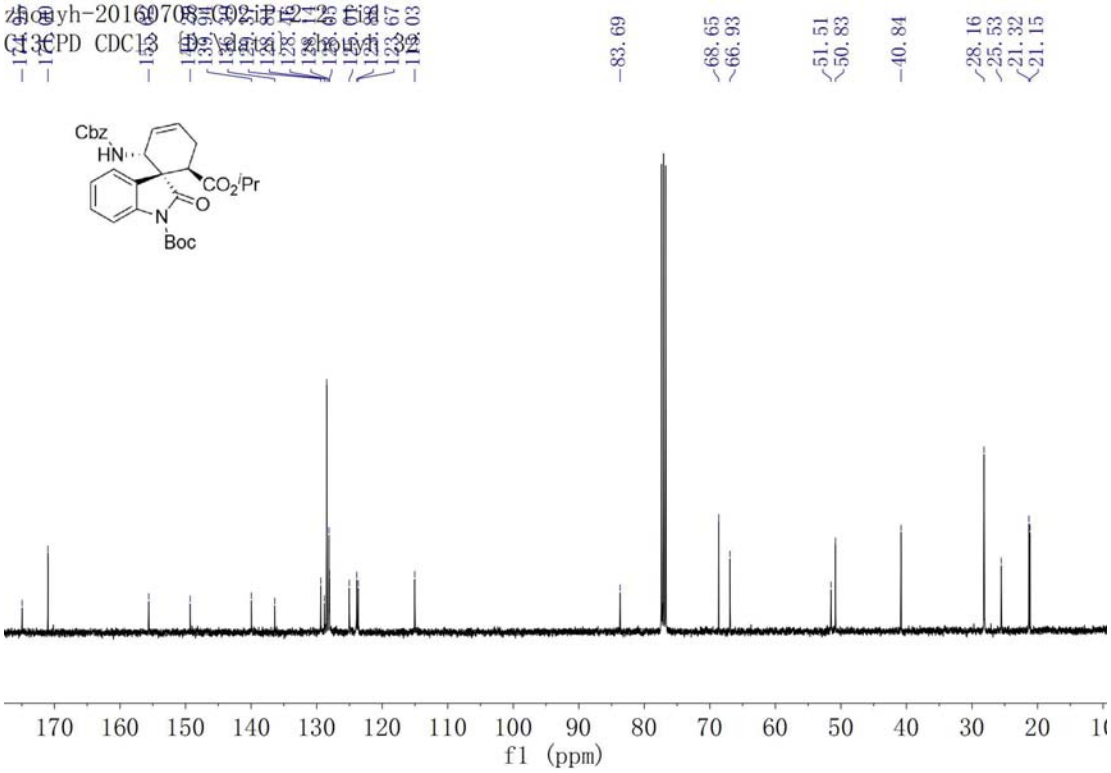
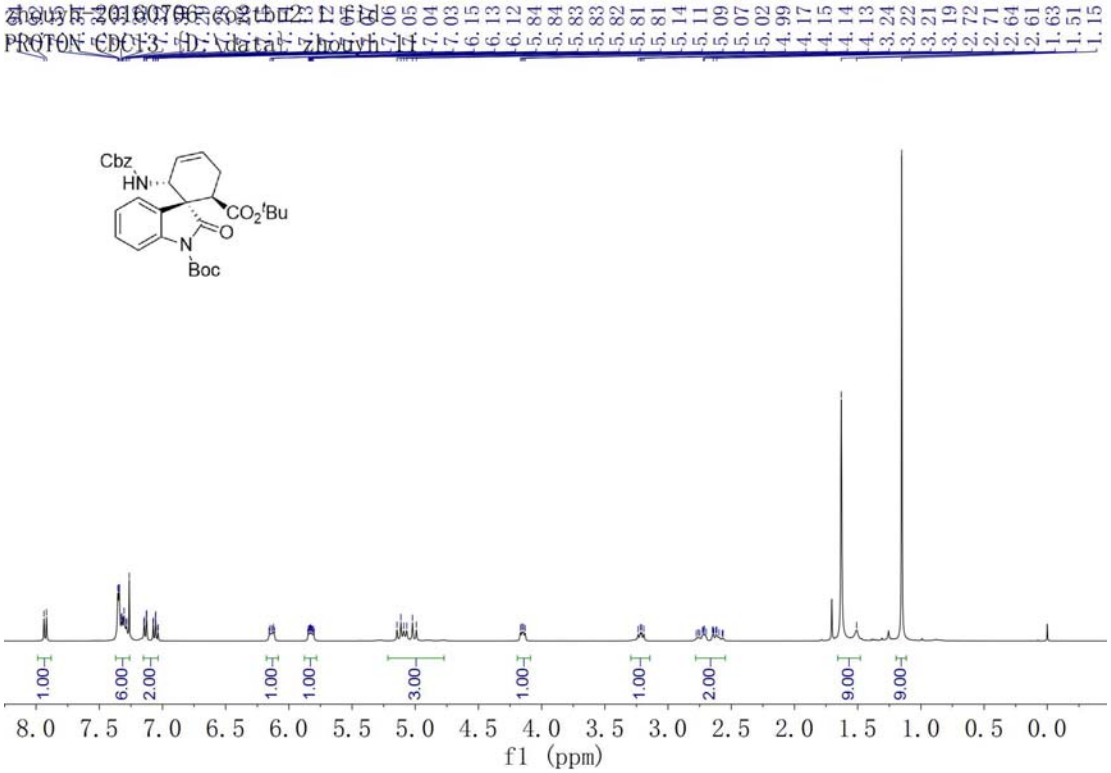
66.93
61.08
51.57
50.87
40.94
28.15
25.52
13.70
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

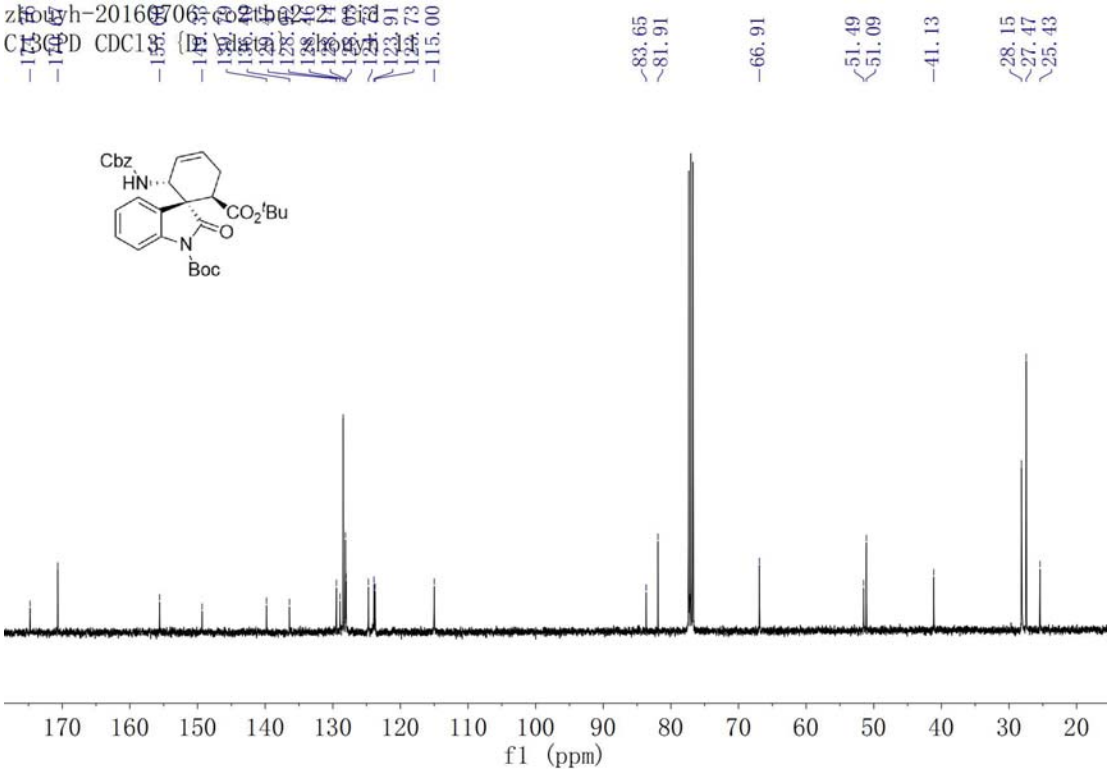
3c


Cbz
HN
CO2iPr
O
N
Boc
1.00
6.00
2.00
1.00
1.00
3.00
1.00
1.00
1.00
2.00
9.00
3.00
3.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

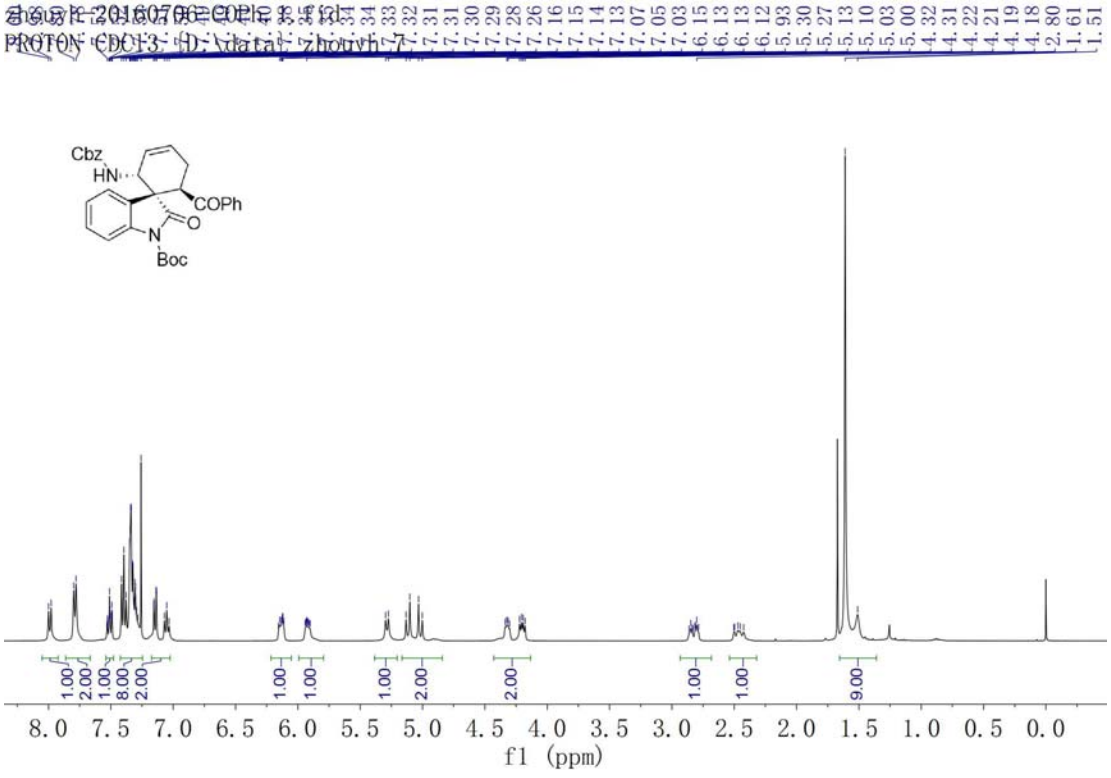

Cbz
HN
CO2iPr
O
N
Boc
83.69
68.65
66.93
51.51
50.83
40.84
28.16
25.53
21.32
21.15
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

3d


Cbz
HN
CO2tBu
O
N
Boc
1.00
6.00
2.00
1.00
1.00
3.00
1.00
1.00
2.00
9.00
9.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


83.65
81.91
66.91
51.49
51.09
41.13
28.15
27.47
25.43
Cbz
HN
CO2tBu
O
N
Boc
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

3e


Cbz
HN
COPh
O
N
Boc
1.00
2.00
1.00
8.00
2.00
1.00
1.00
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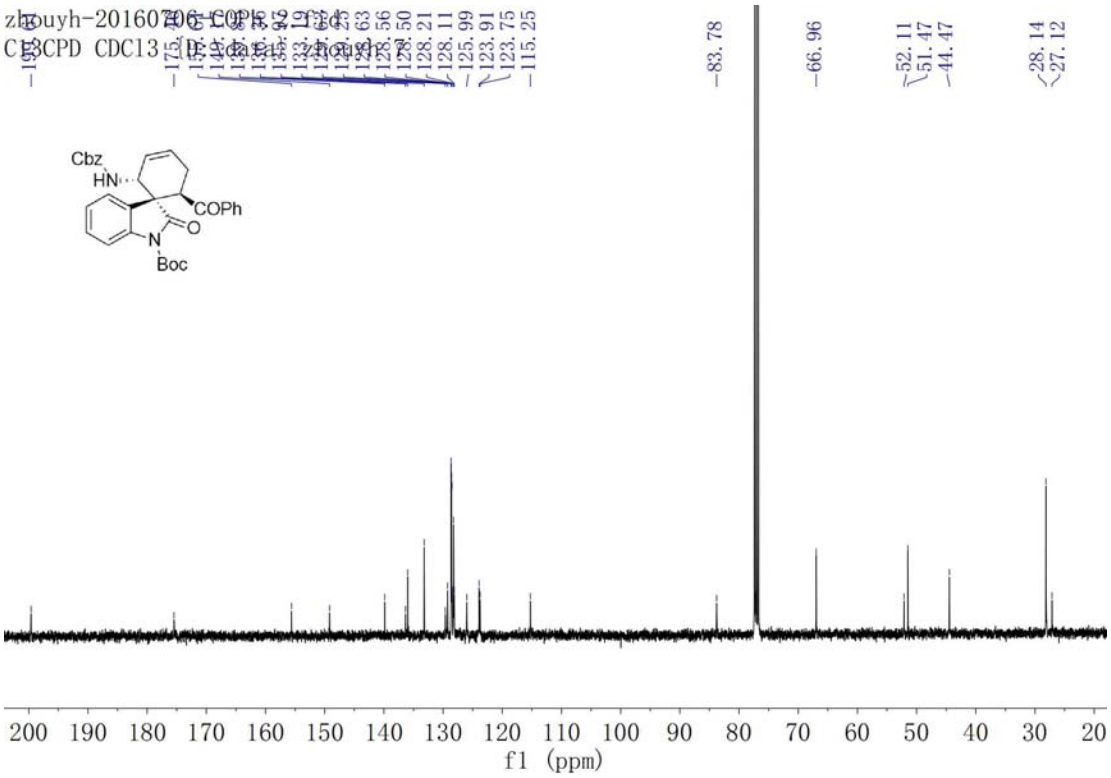
2.00
2.00
1.00
1.00
9.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Cbz
HN
COPh
O
N
Boc
83.78
66.96
52.11
51.47
44.47
28.14
27.12
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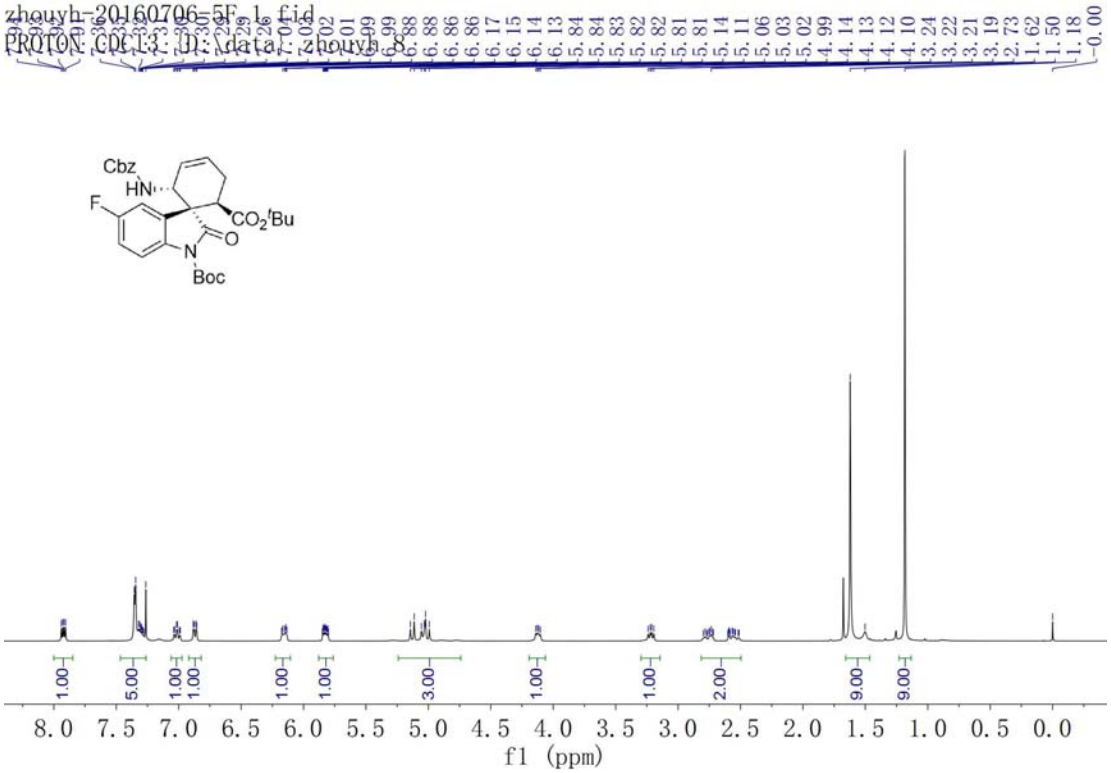
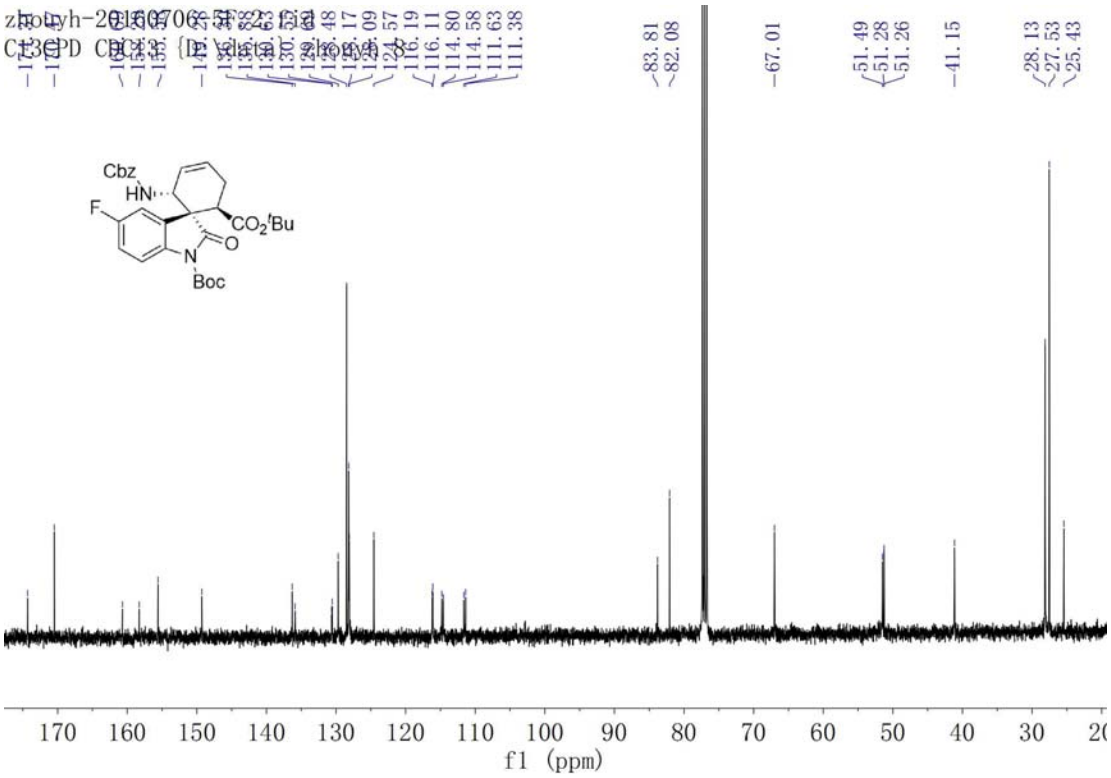
f1 (ppm)

3f


zhouyh-20160706-5F-1.fid
PROTON CDCl3 D:\data\zhouyh_8
Cbz
HN
F
CO2tBu
O
N
Boc
1.00
5.00
1.00
1.00
1.00
1.00
3.00
1.00
1.00
2.00
9.00
9.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


zhouyh-20160706-5F-2.fid
CDCl3 D:\data\zhouyh_8
Cbz
HN
F
CO2tBu
O
N
Boc
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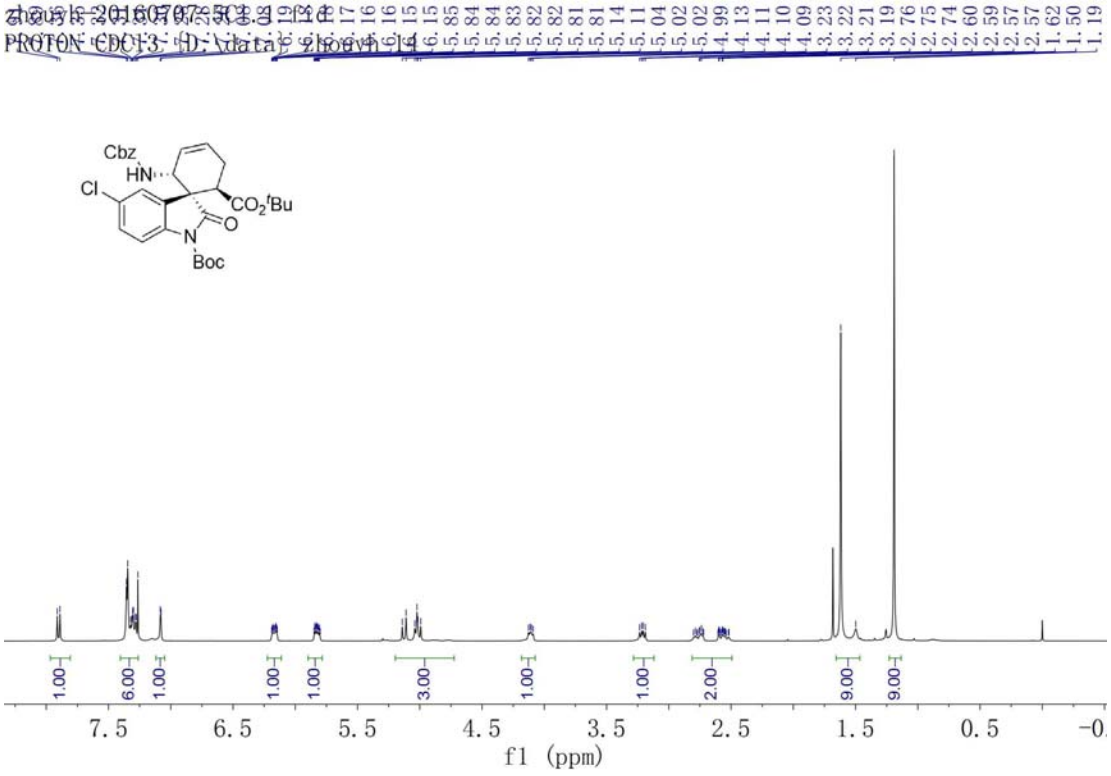
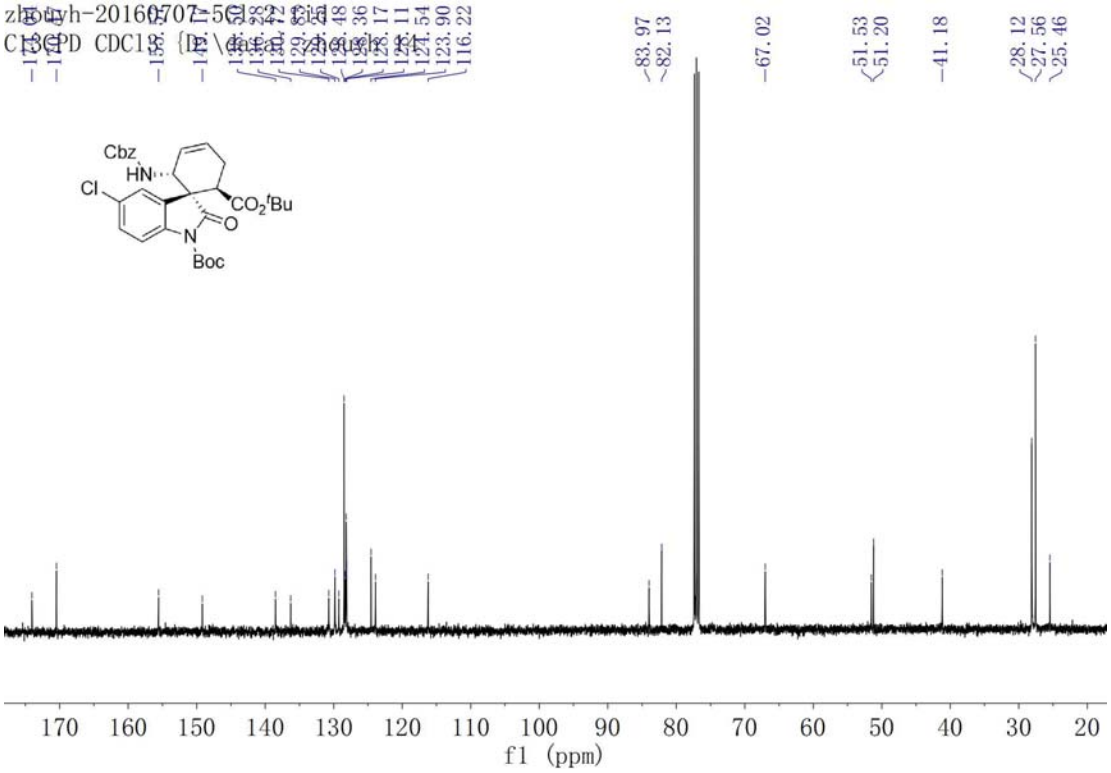
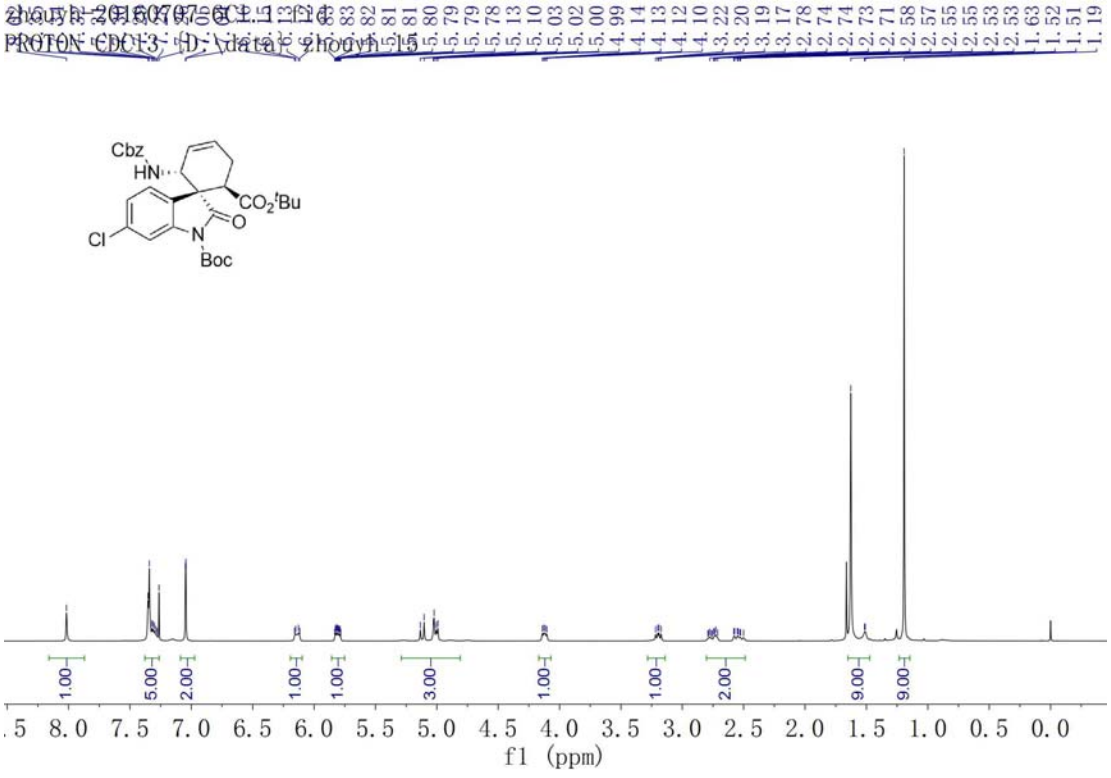
67.01
51.49
51.28
51.26
41.15
28.13
27.53
25.43
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30
f1 (ppm)

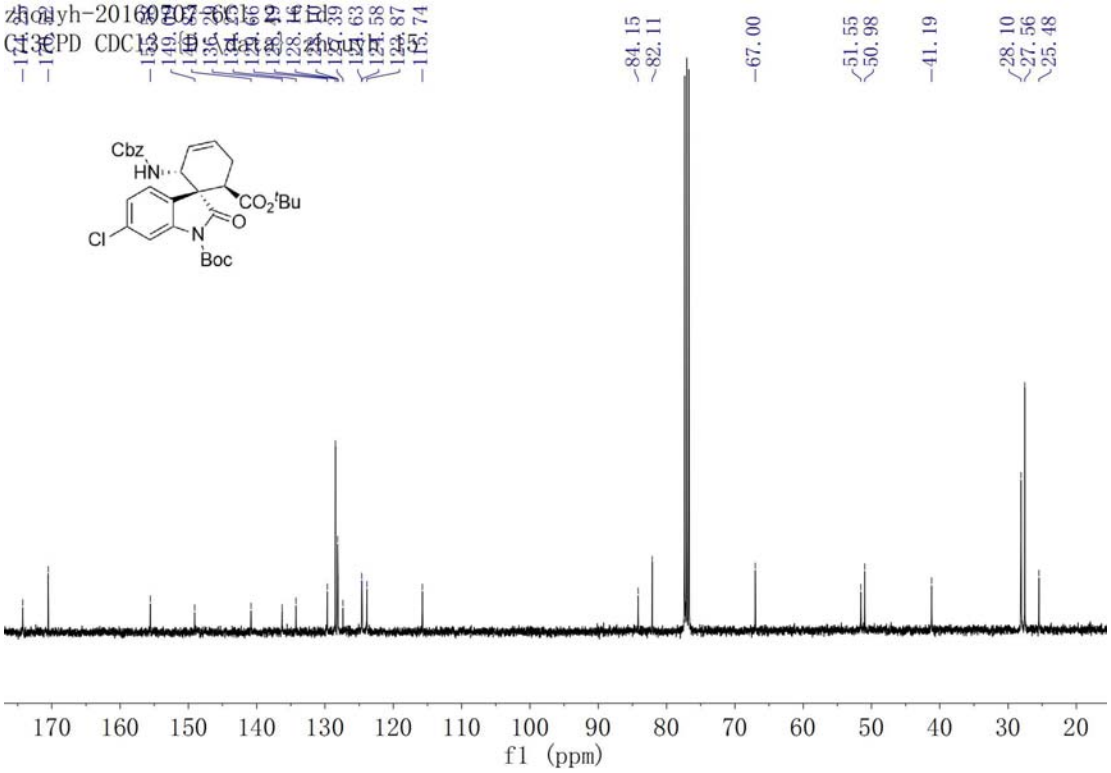
3g


Cbz
HN
Cl
CO2tBu
O
N
Boc
1.00
6.00
1.00
1.00
1.00
3.00
1.00
1.00
2.00
9.00
9.00
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

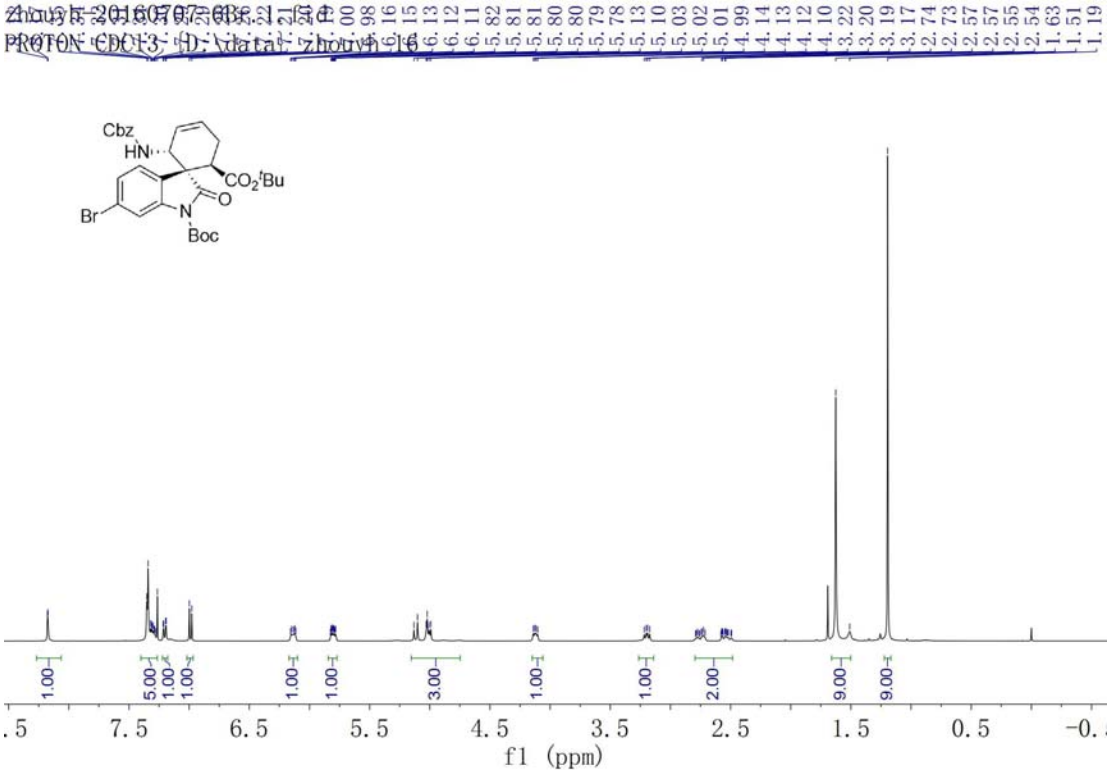

Cbz
HN
Cl
CO2tBu
O
N
Boc
83.97
82.13
67.02
51.53
51.20
41.18
28.12
27.56
25.46
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

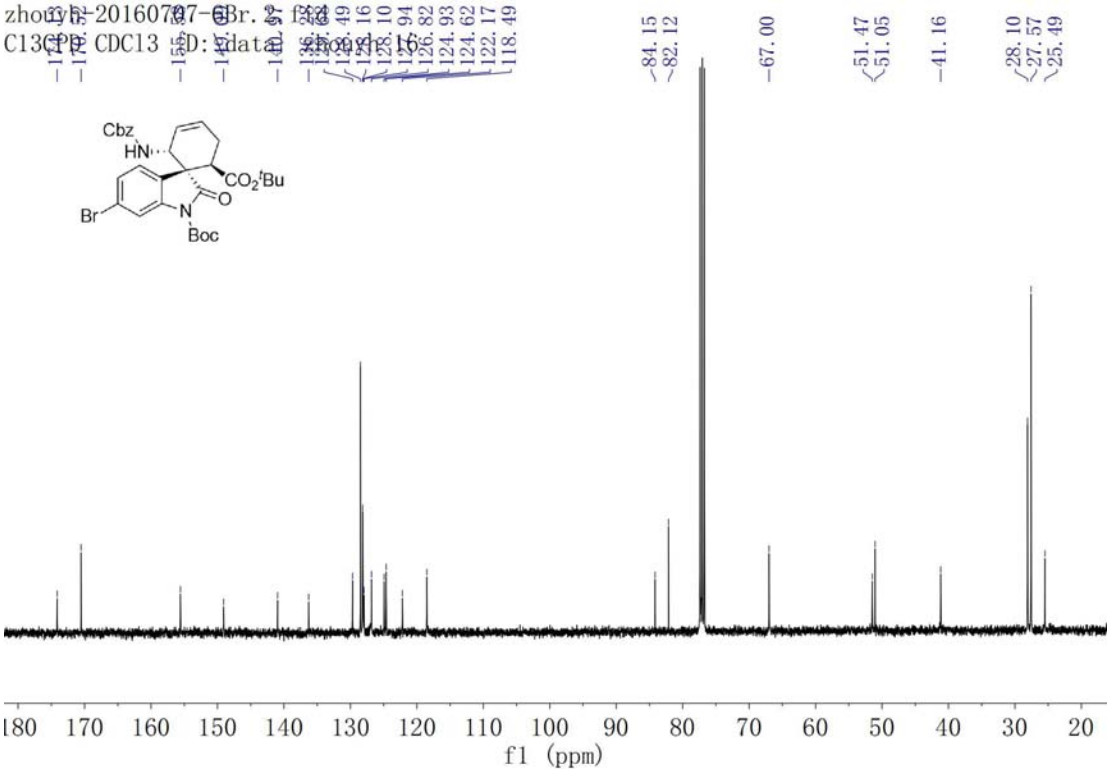
3h


Cbz
HN
CO2tBu
Cl
O
N
Boc
1.00
5.00
2.00
1.00
1.00
3.00
1.00
1.00
2.00
9.00
9.00
f1 (ppm)

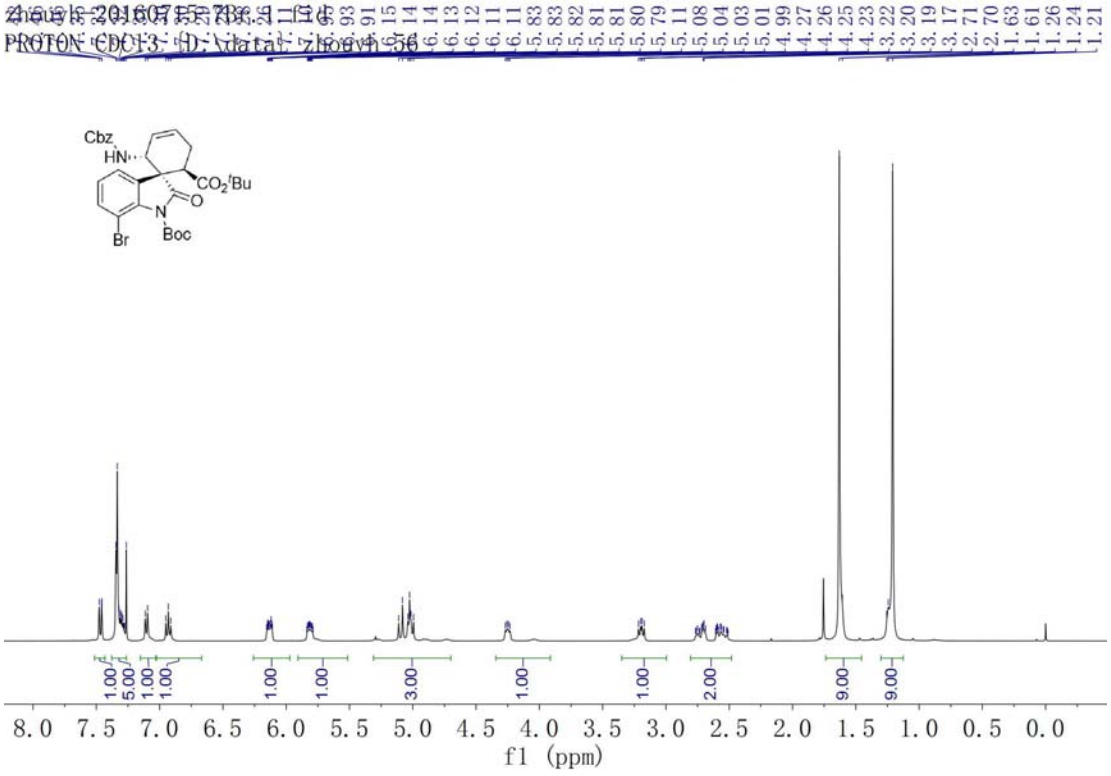

Cbz
HN
CO2tBu
Cl
O
N
Boc
84.15
82.11
67.00
51.55
50.98
41.19
28.10
27.56
25.48
f1 (ppm)

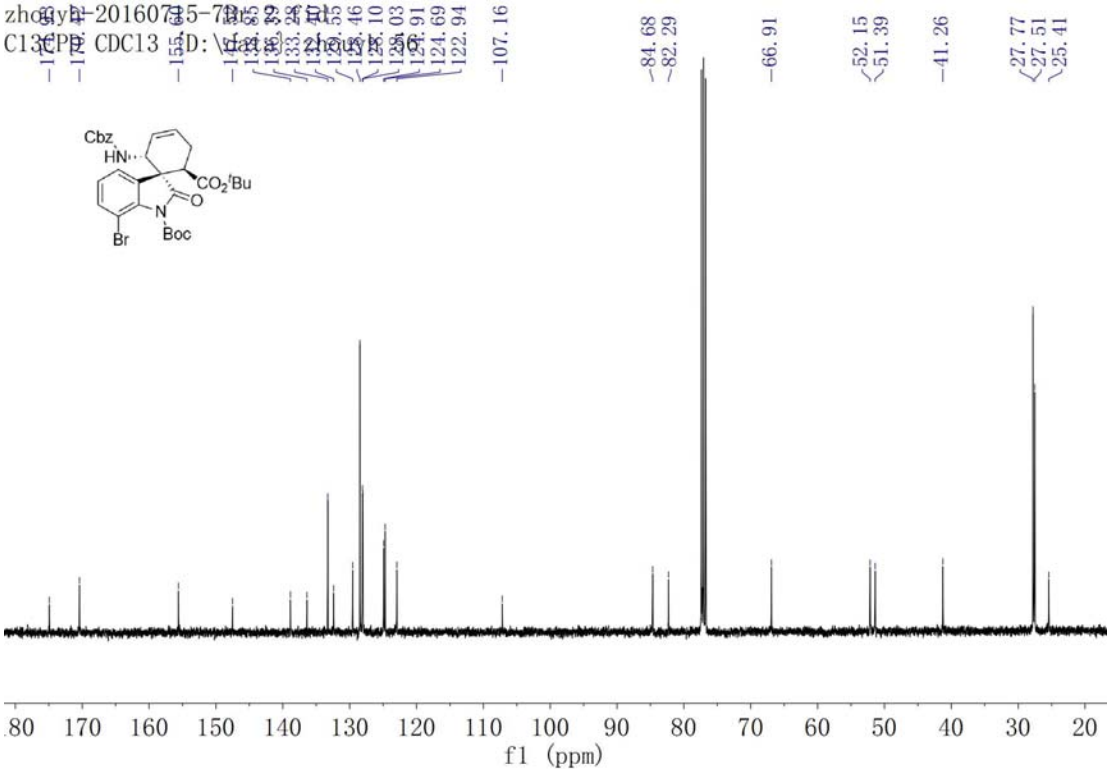
3i


Cbz
HN
CO2tBu
O
Br
N
Boc
1.00
5.00
1.00
1.00
1.00
1.00
3.00
1.00
1.00
2.00
9.00
9.00
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

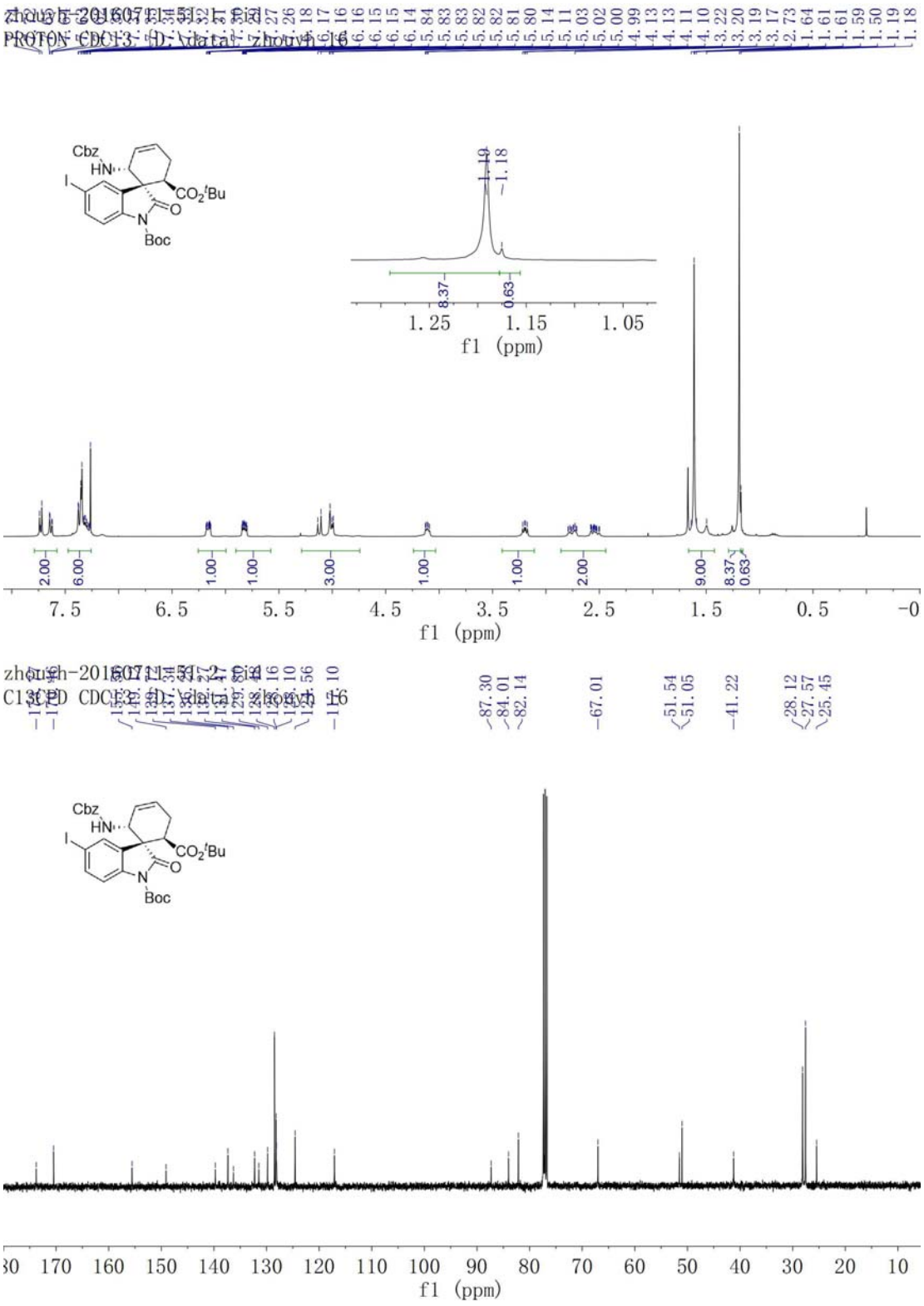

Cbz
HN
CO2tBu
O
Br
N
Boc
84.15
82.12
67.00
51.47
51.05
41.16
28.10
27.57
25.49
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

3j

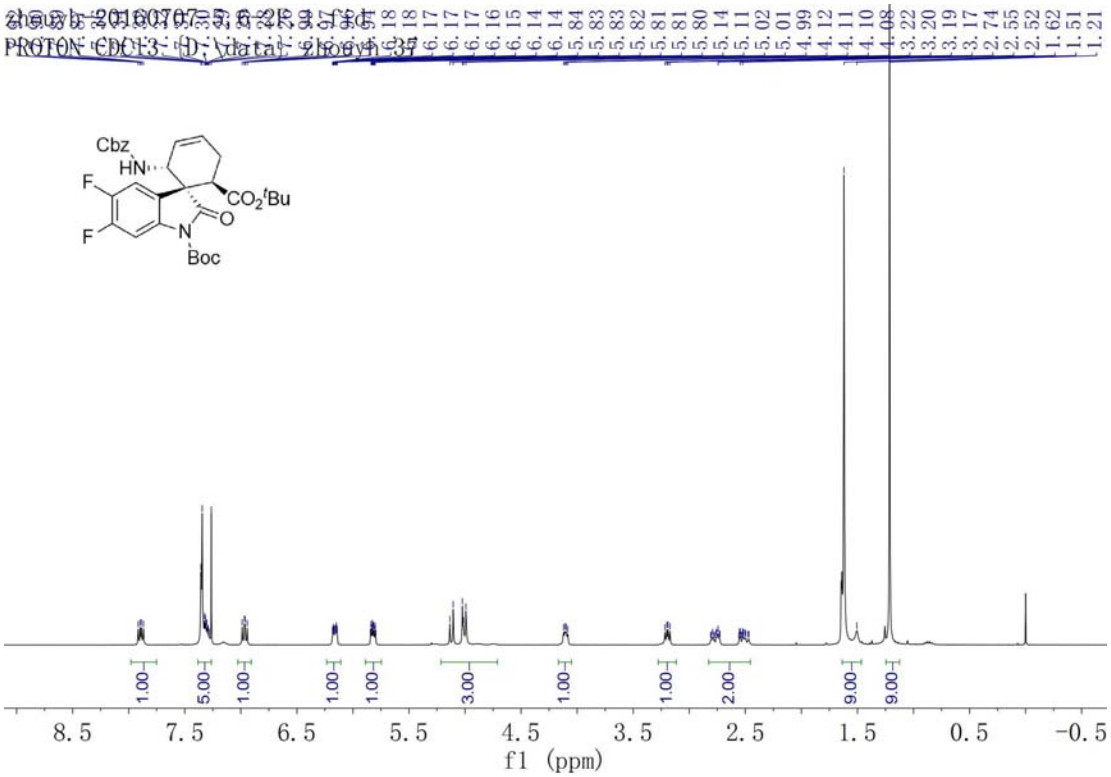

Cbz
HN
CO2tBu
O
N
Boc
Br
1.00
5.00
1.00
1.00
1.00
1.00
3.00
1.00
1.00
2.00
9.00
9.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

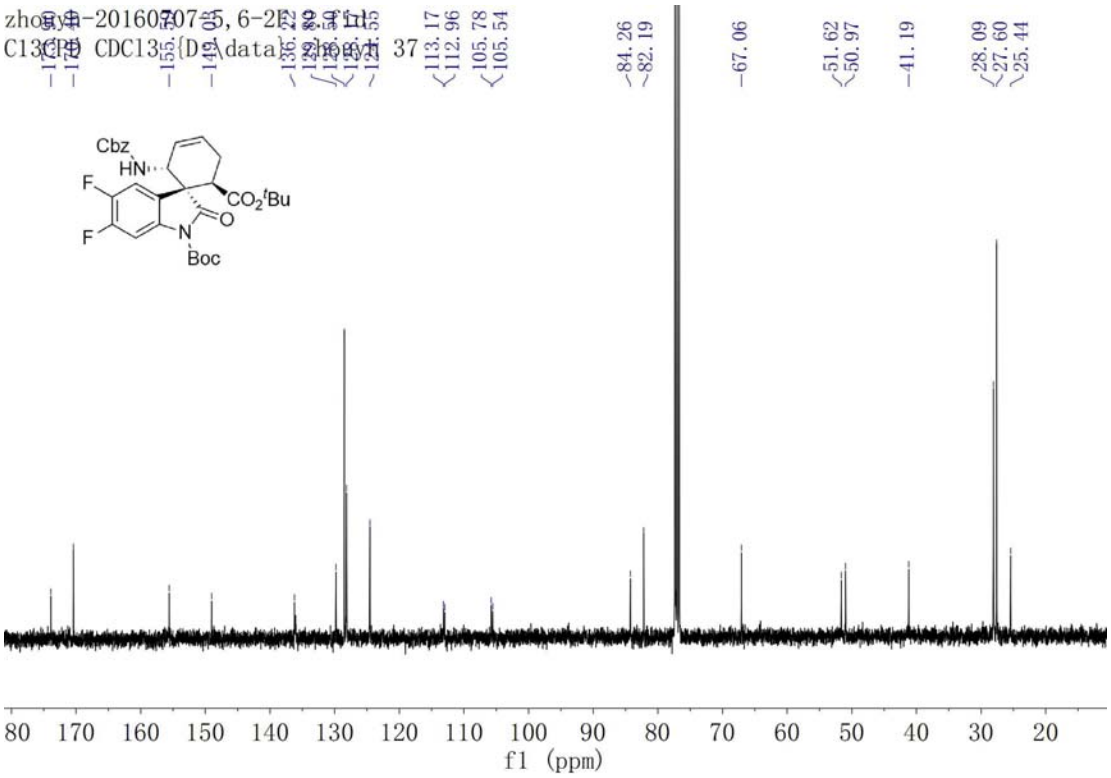

Cbz
HN
CO2tBu
O
N
Boc
Br
84.68
82.29
66.91
52.15
51.39
41.26
27.77
27.51
25.41
107.16
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

3k

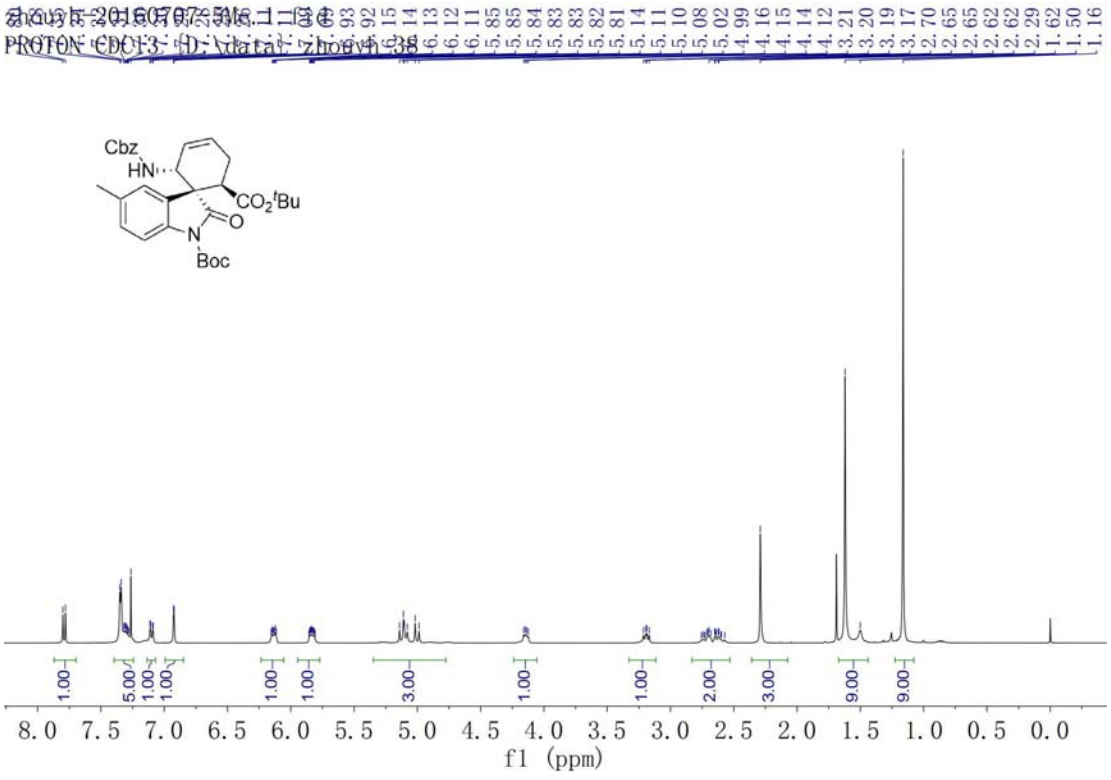

Cbz
HN
I
CO2tBu
O
N
Boc
1.19
1.18
8.37
0.63
1.25
1.15
1.05
f1 (ppm)
2.00
6.00
1.00
1.00
3.00
1.00
1.00
2.00
9.00
8.37
0.63
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)
87.30
84.01
82.14
67.01
51.54
51.05
41.22
28.12
27.57
25.45
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

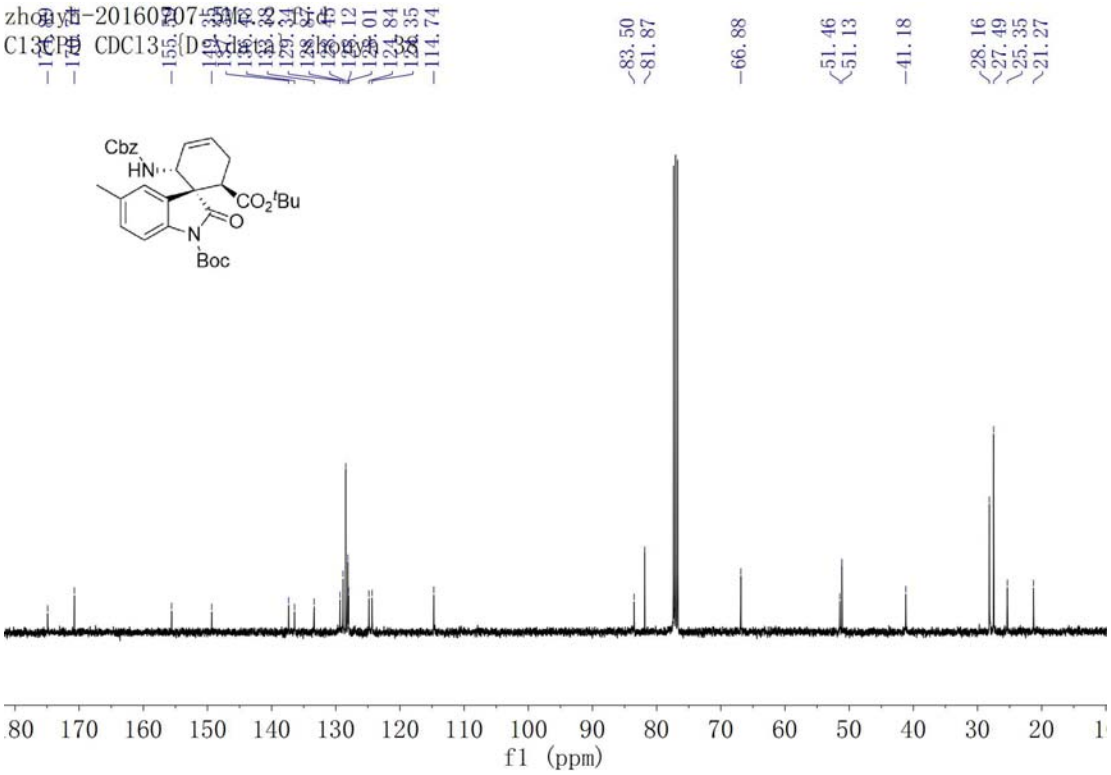
3l


Cbz
HN
F
F
CO2tBu
O
N
Boc
1.00
5.00
1.00
1.00
1.00
3.00
1.00
1.00
2.00
9.00
9.00
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

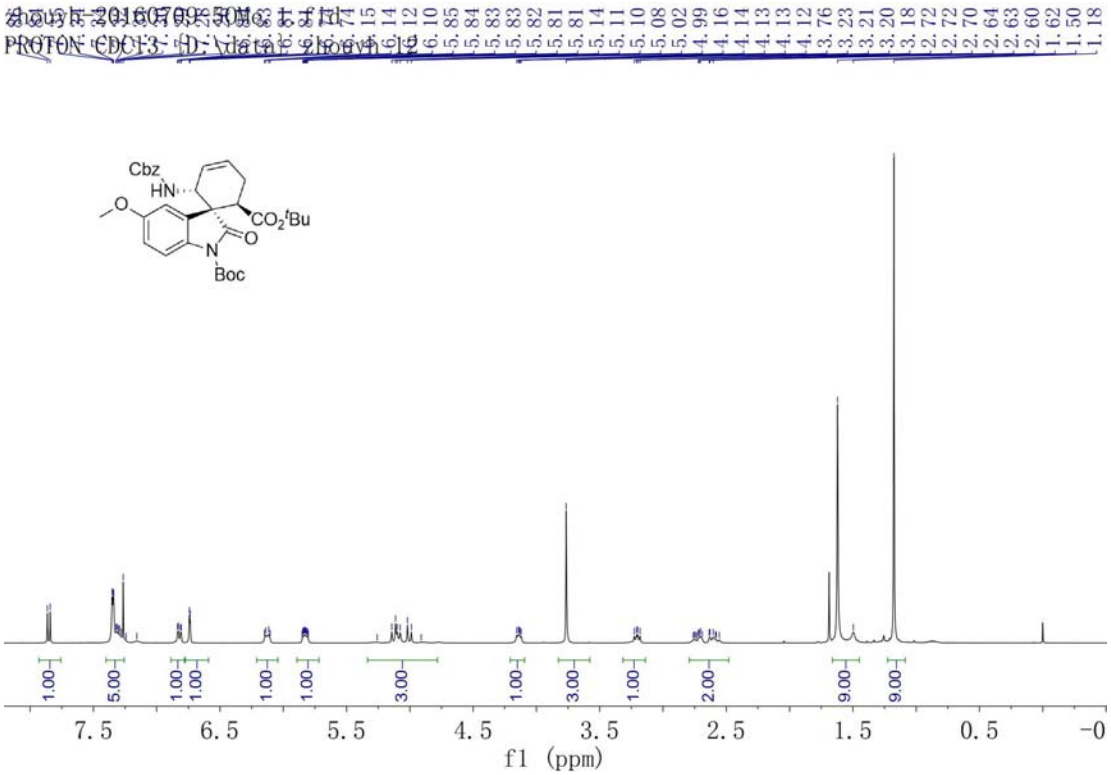

Cbz
HN
F
F
CO2tBu
O
N
Boc
84.26
82.19
67.06
51.62
50.97
41.19
28.09
27.60
25.44
113.17
112.96
105.78
105.54
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

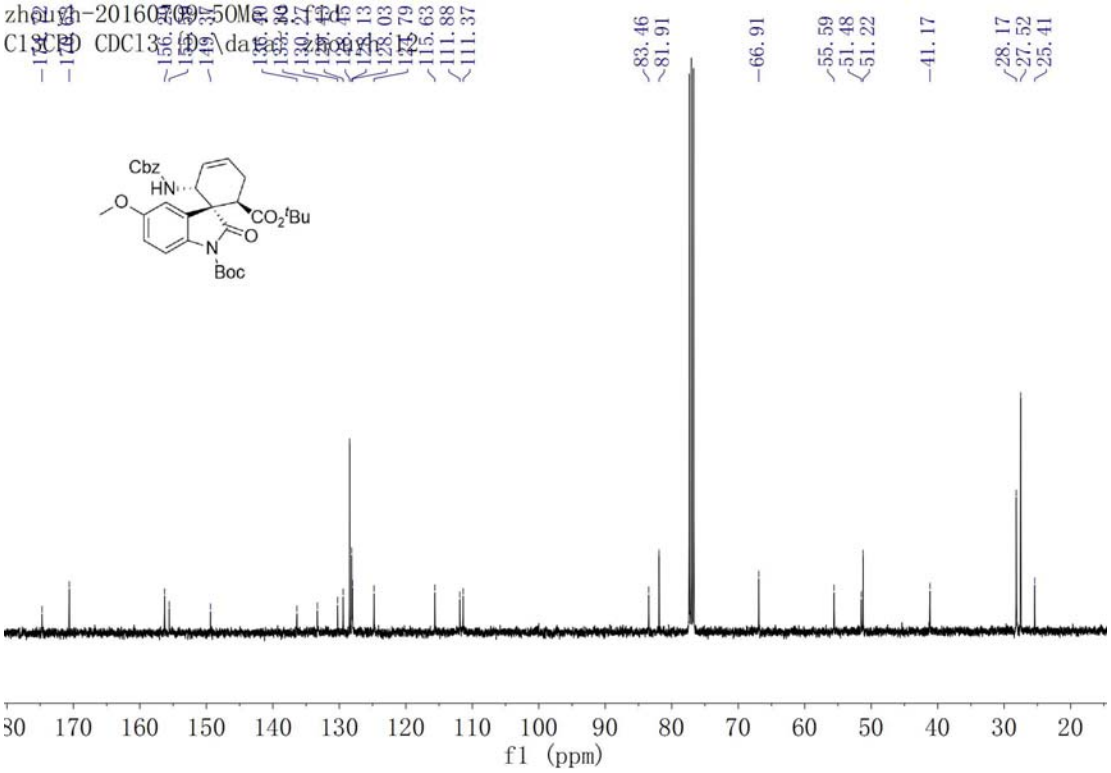
3m


Cbz
HN
CO2tBu
O
N
Boc
1.00
5.00
1.00
1.00
1.00
1.00
3.00
1.00
1.00
2.00
3.00
9.00
9.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

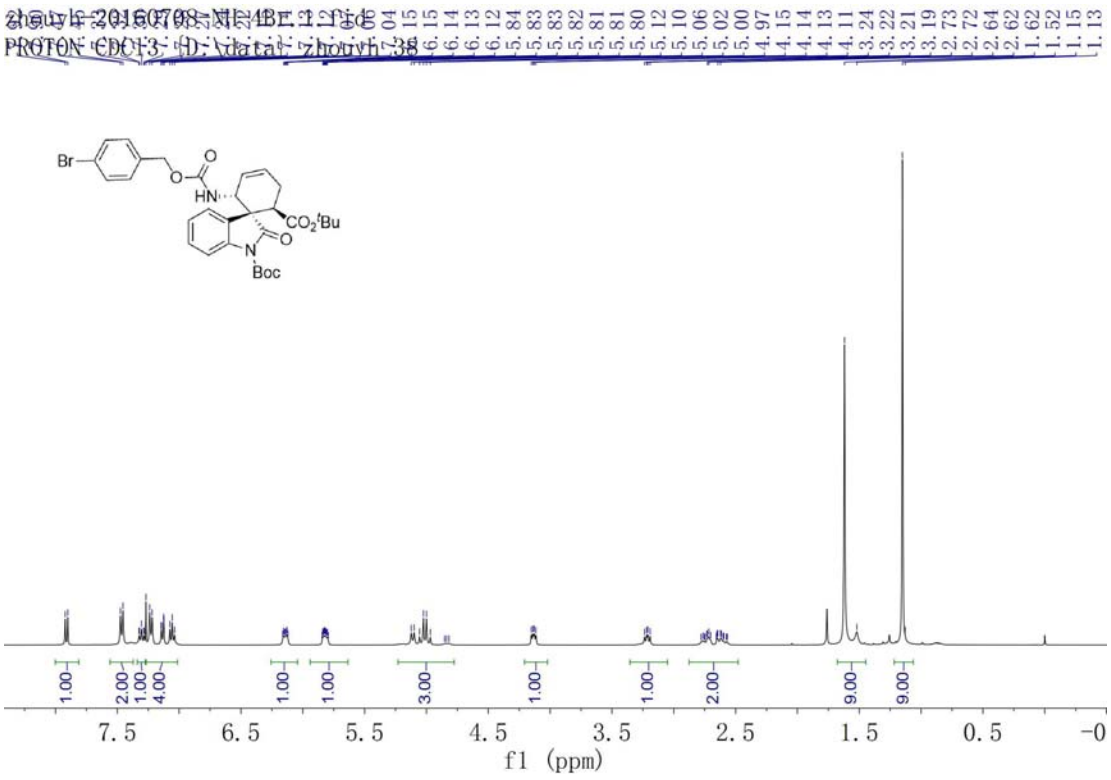

Cbz
HN
CO2tBu
O
N
Boc
83.50
81.87
66.88
51.46
51.13
41.18
28.16
27.49
25.35
21.27
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 1
f1 (ppm)

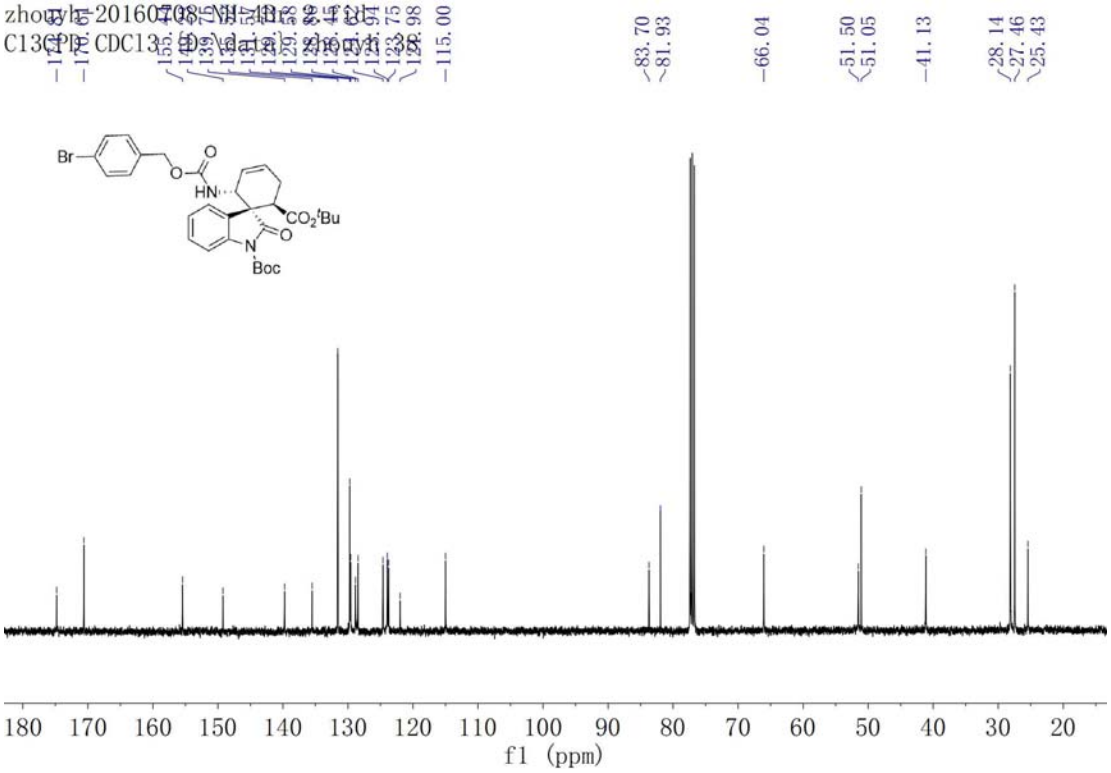
3n


Cbz
HN
O
CO2tBu
O
N
Boc
1.00
5.00
1.00
1.00
1.00
1.00
3.00
1.00
3.00
1.00
2.00
9.00
9.00
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

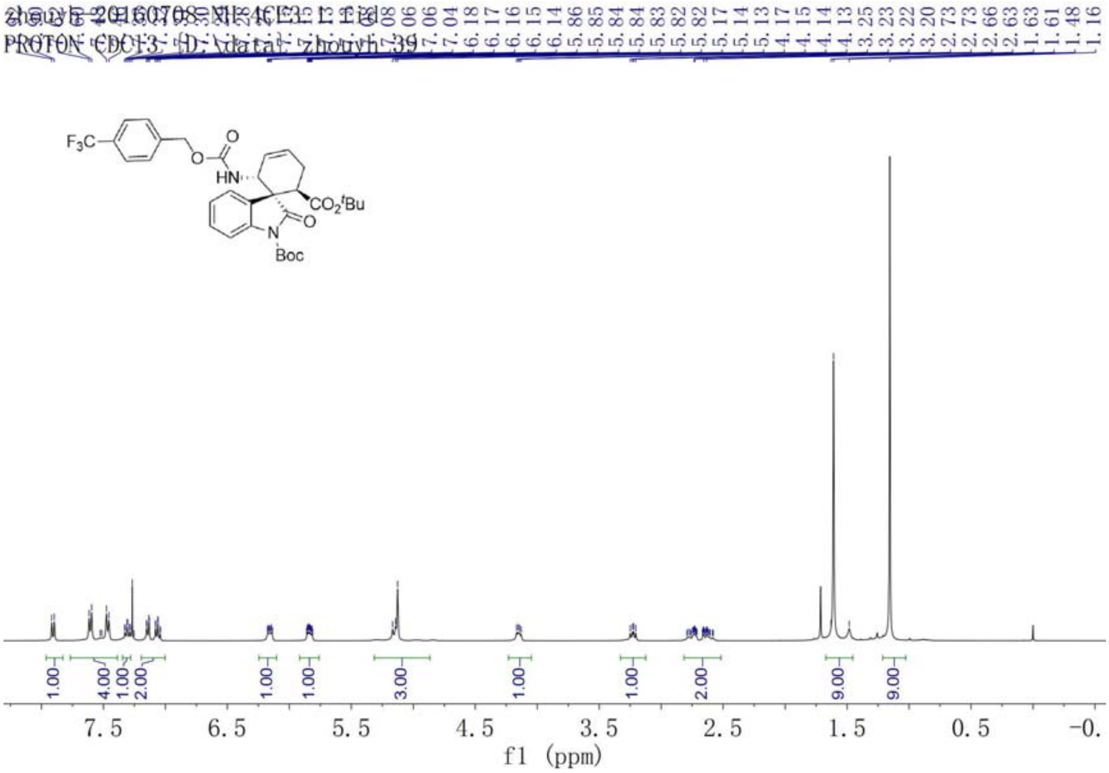

83.46
81.91
66.91
55.59
51.48
51.22
41.17
28.17
27.52
25.41
Cbz
HN
O
CO2tBu
O
N
Boc
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

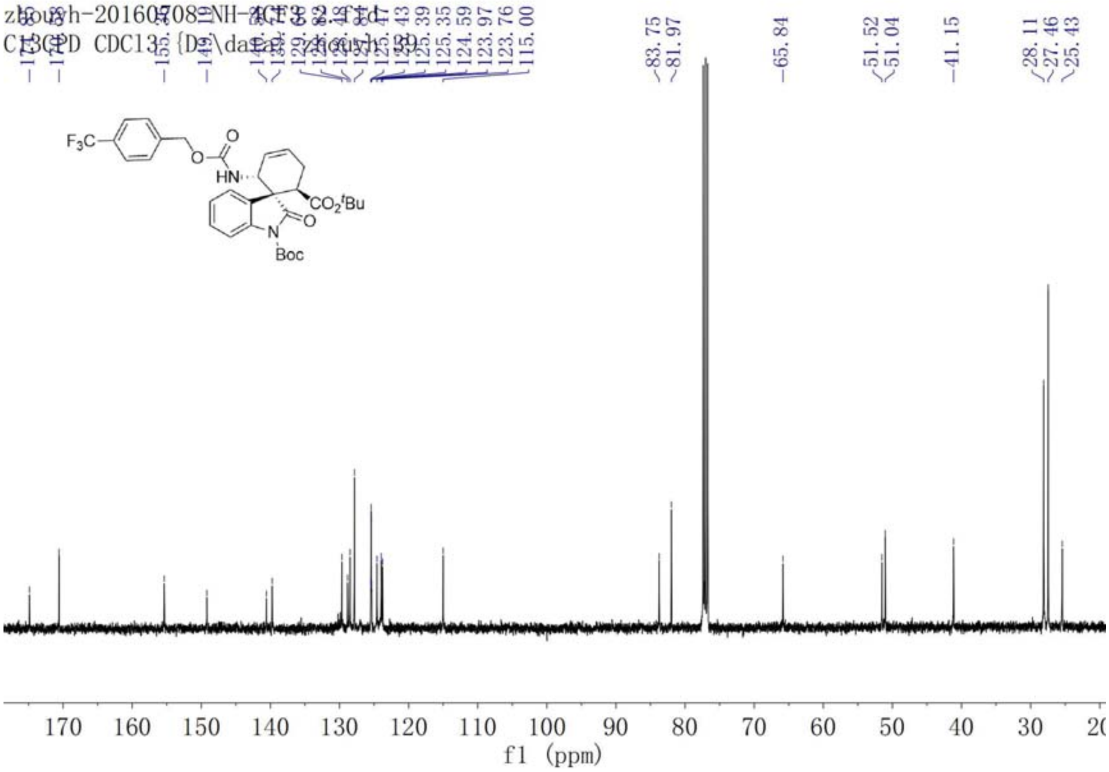
3o


Br
O
HN
CO2tBu
O
N
Boc
1.00
2.00
1.00
4.00
1.00
1.00
3.00
1.00
1.00
2.00
9.00
9.00
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

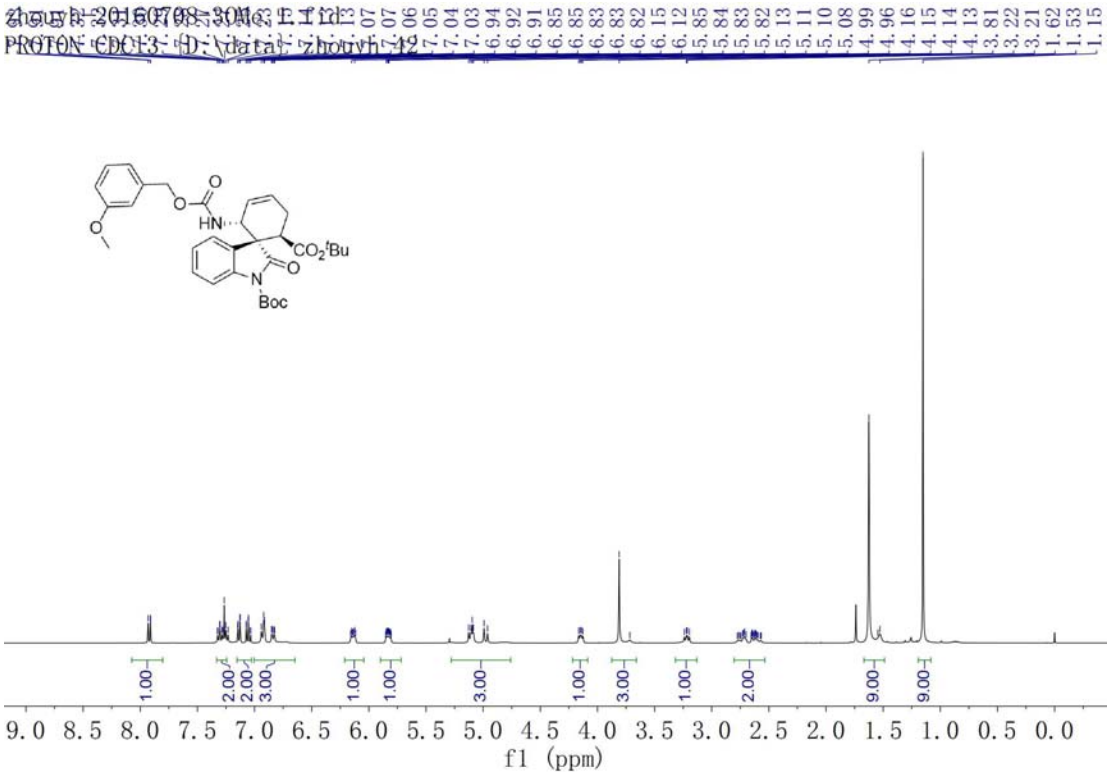

Br
O
HN
CO2tBu
O
N
Boc
83.70
81.93
66.04
51.50
51.05
41.13
28.14
27.46
25.43
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

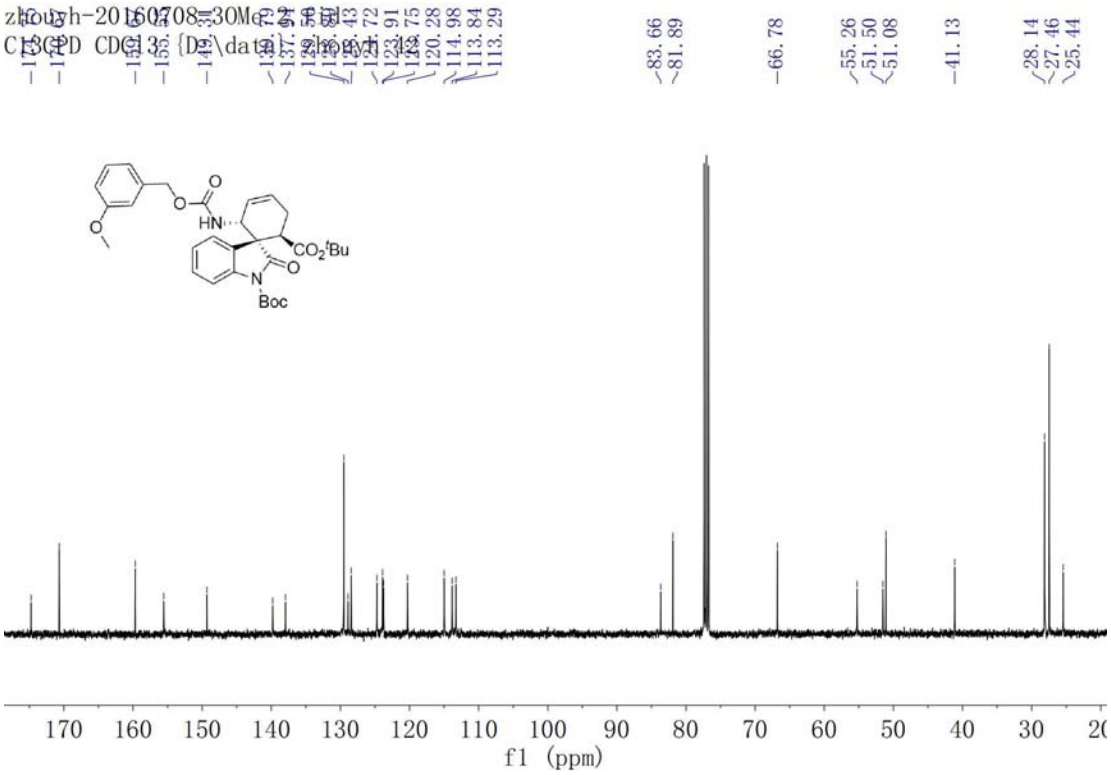
3p



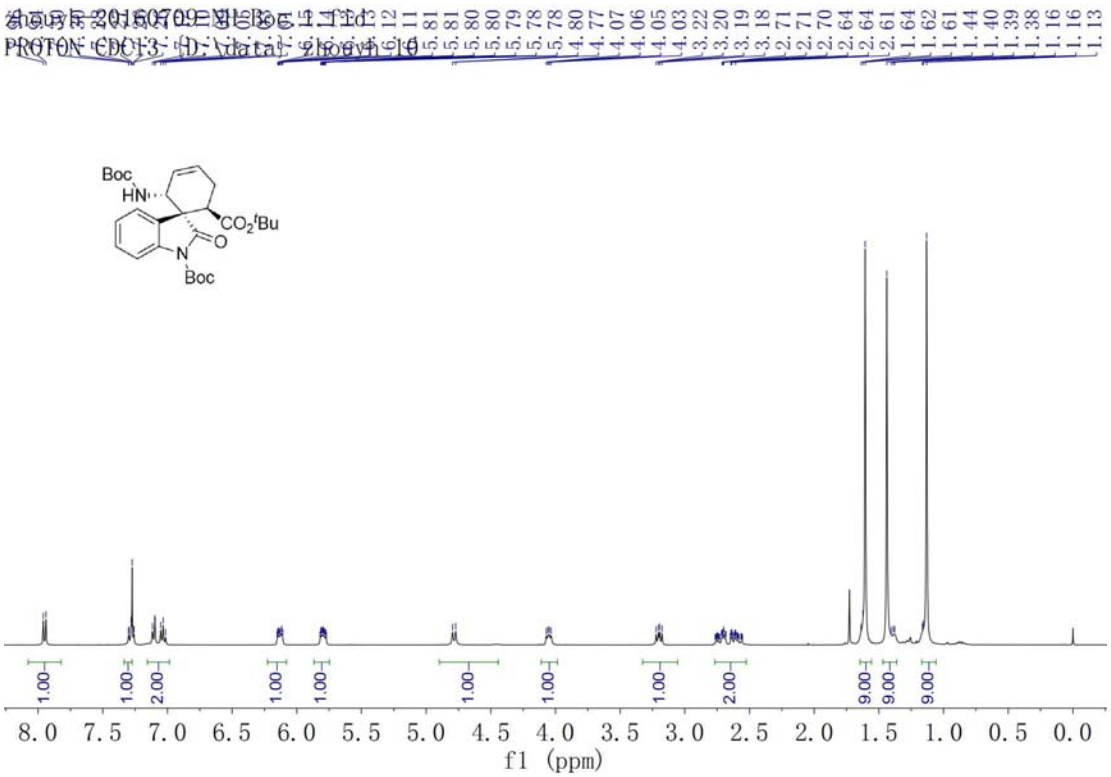


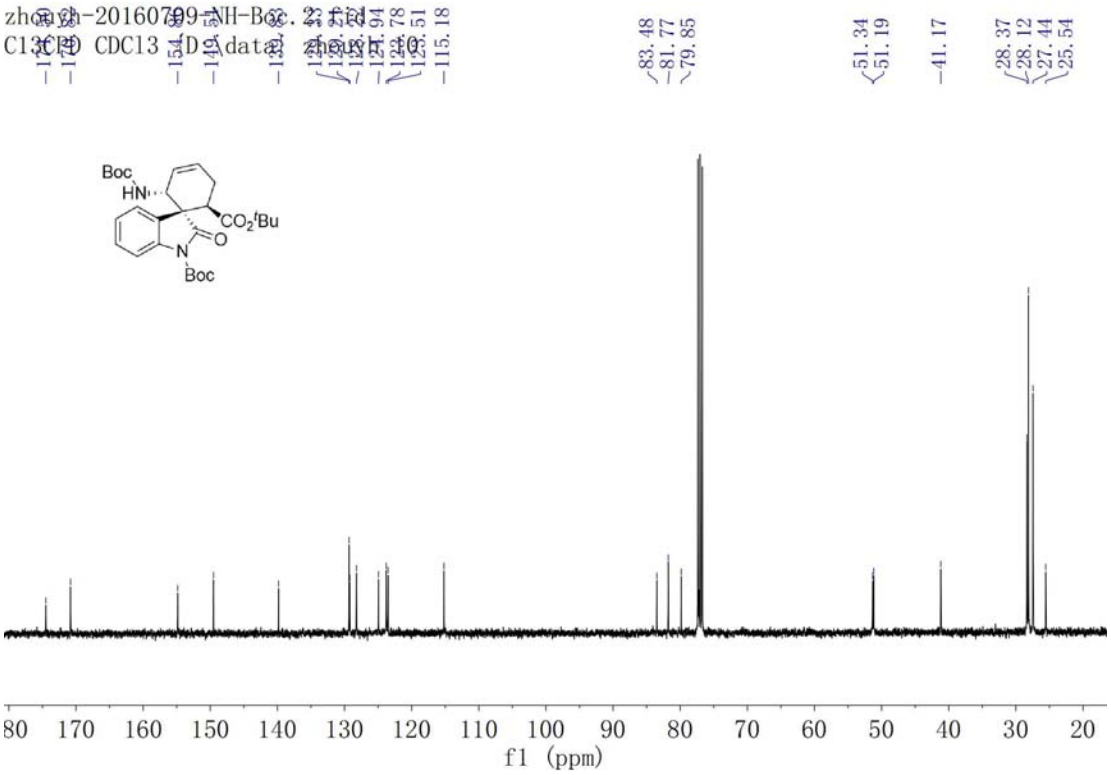
3q


HN
O
CO2tBu
N
Boc
1.00
2.00
2.00
3.00
1.00
1.00
3.00
1.00
3.00
1.00
2.00
9.00
9.00
f1 (ppm)

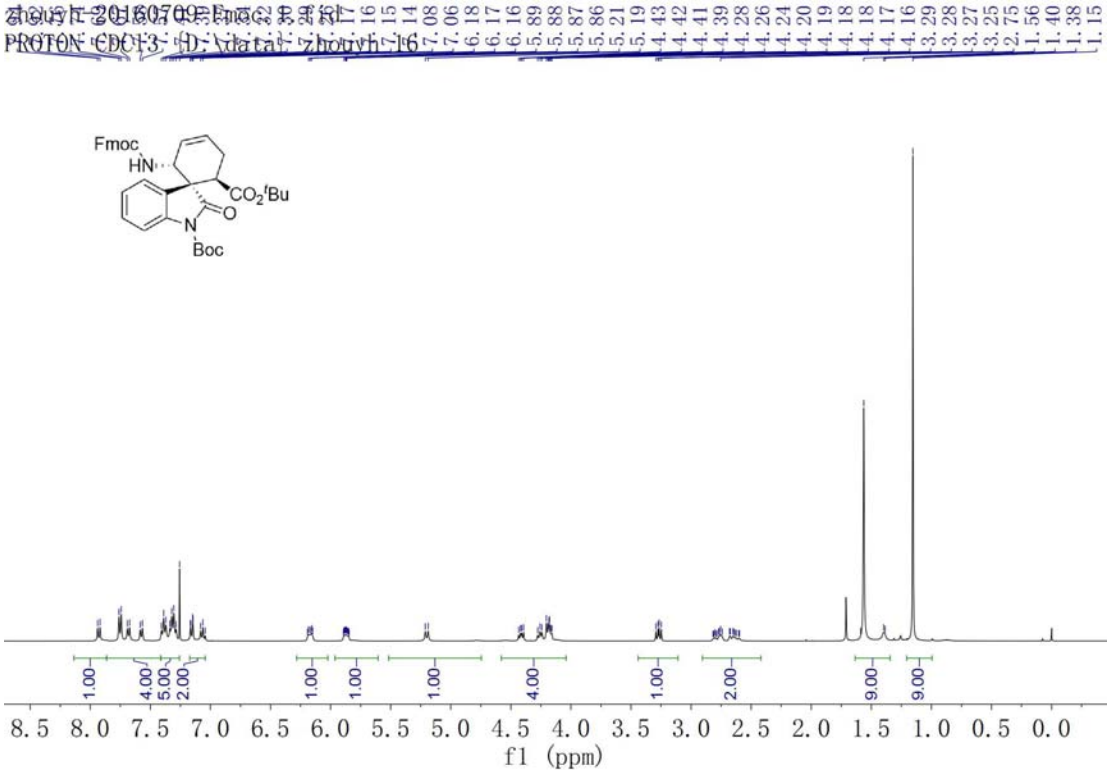

HN
O
CO2tBu
N
Boc
83.66
81.89
66.78
55.26
51.50
51.08
41.13
28.14
27.46
25.44
f1 (ppm)

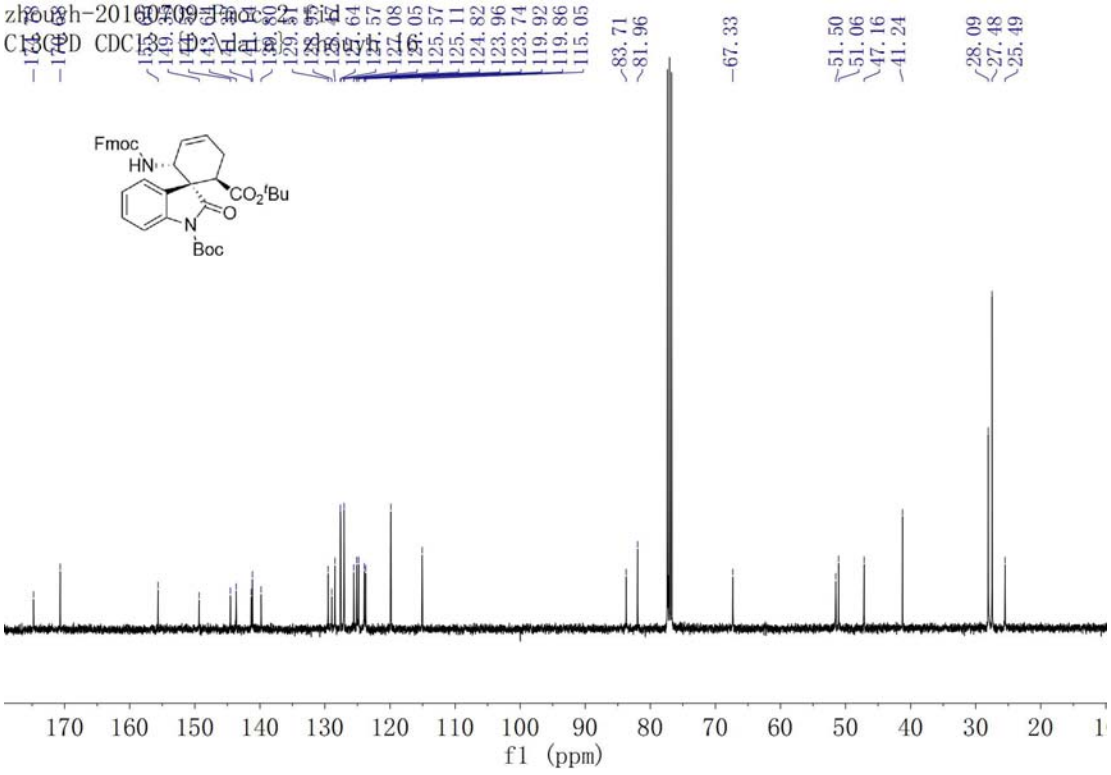
3r


Boc
HN
CO2tBu
O
N
Boc
1.00
1.00
2.00
1.00
1.00
1.00
1.00
1.00
2.00
9.00
9.00
9.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

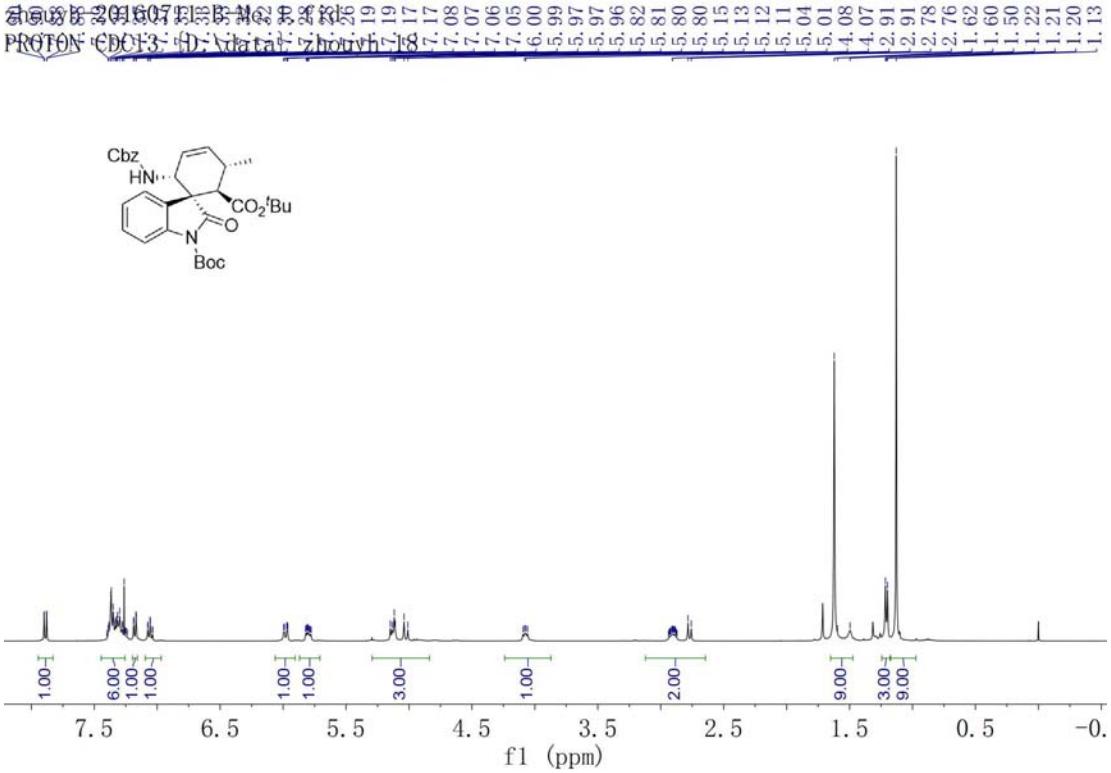

83.48
81.77
79.85
51.34
51.19
41.17
28.37
28.12
27.44
25.54
Boc
HN
CO2tBu
O
N
Boc
80 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

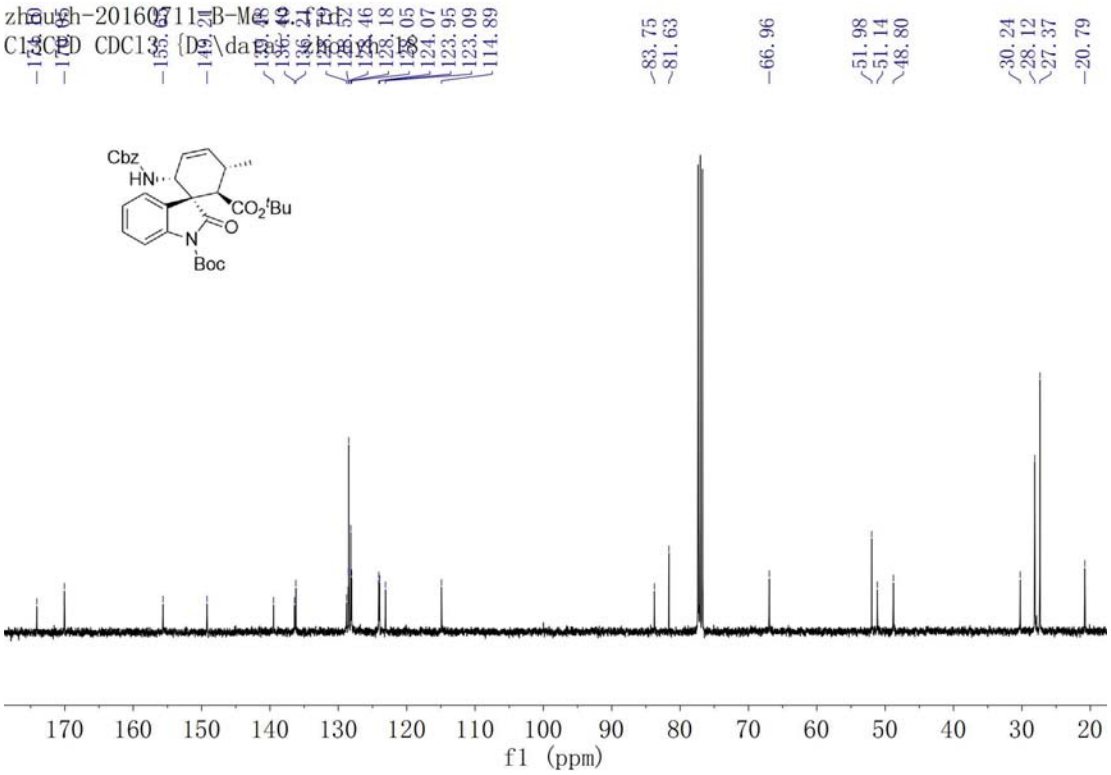
3s


Fmoc
HN
CO2tBu
O
N
Boc
1.00
4.00
5.00
2.00
1.00
1.00
1.00
4.00
1.00
2.00
9.00
9.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

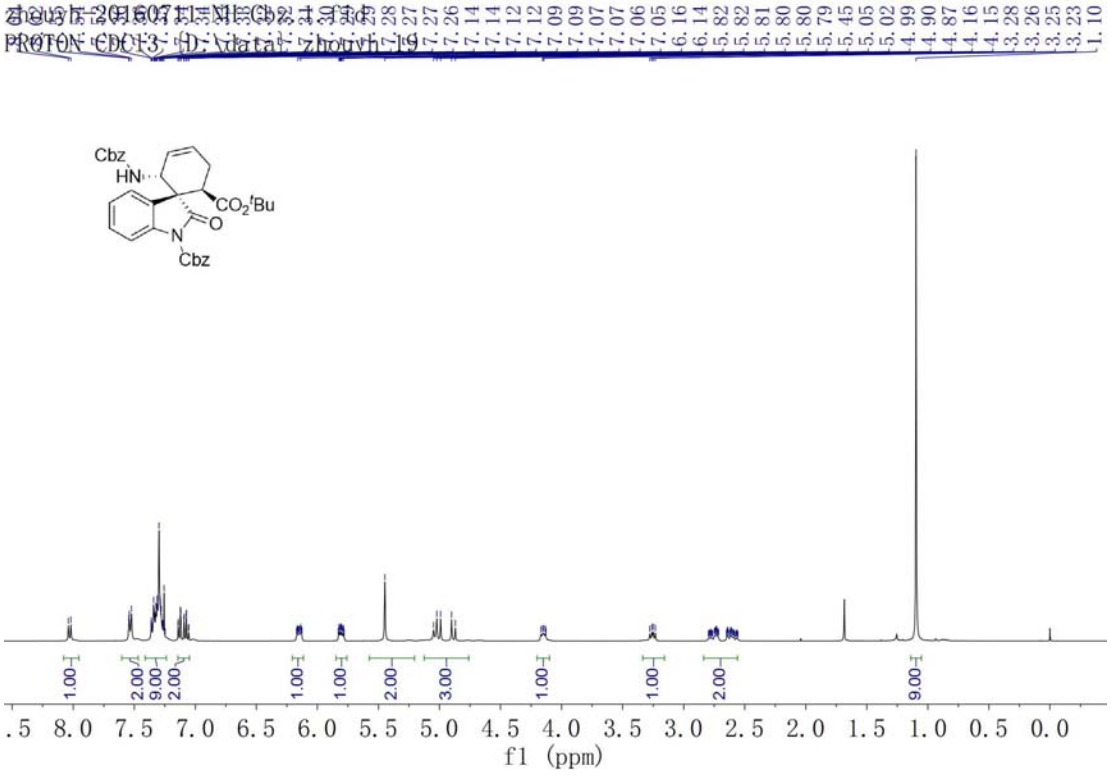

Fmoc
HN
CO2tBu
O
N
Boc
83.71
81.96
67.33
51.50
51.06
47.16
41.24
28.09
27.48
25.49
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 1
f1 (ppm)

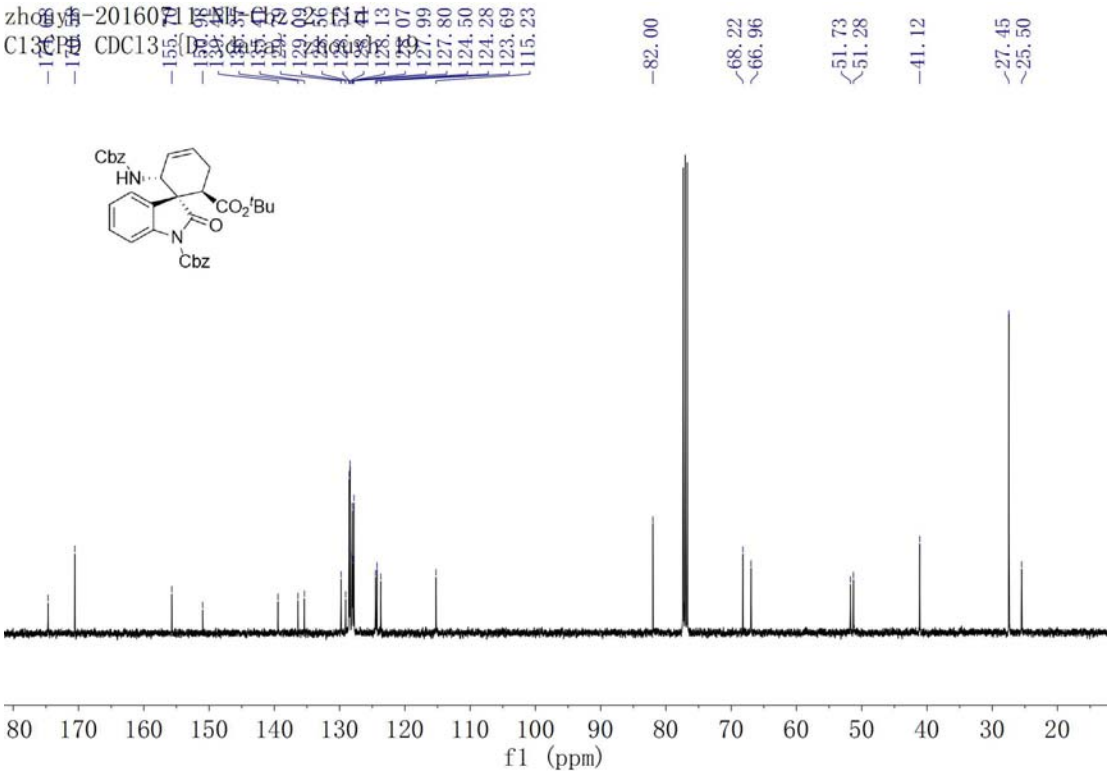
3t


Cbz
HN
CO2tBu
O
N
Boc
1.00
6.00
1.00
1.00
1.00
3.00
1.00
2.00
9.00
3.00
9.00
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

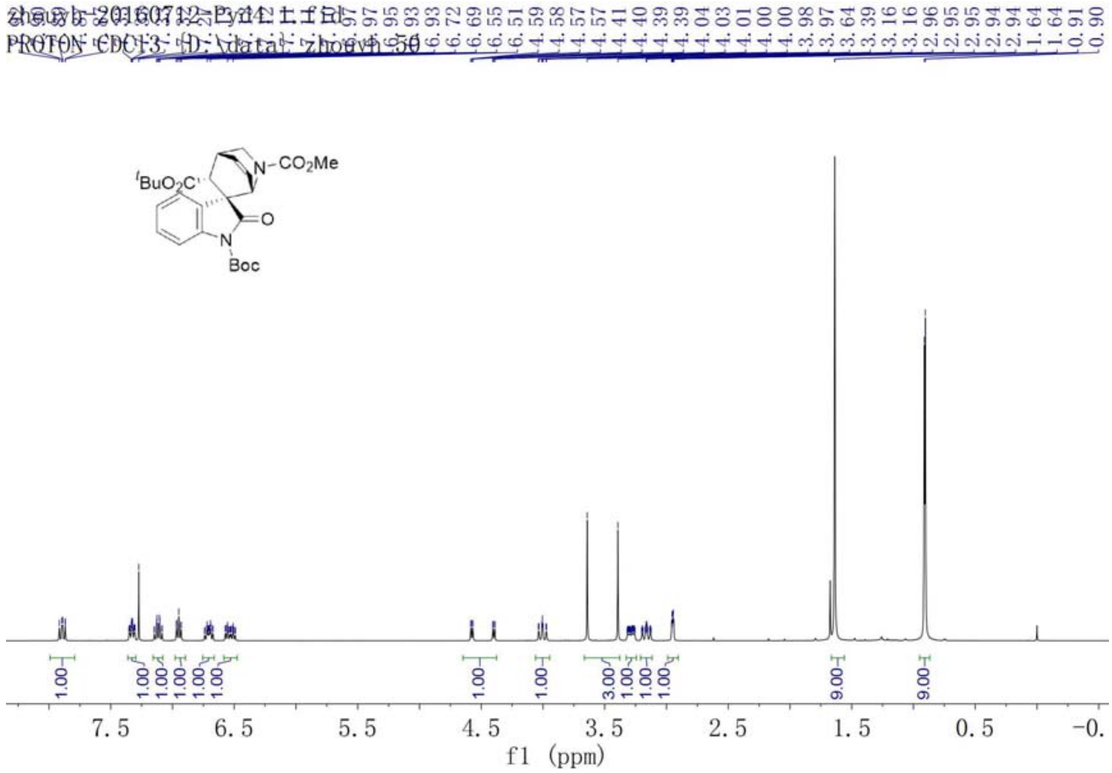

Cbz
HN
CO2tBu
O
N
Boc
83.75
81.63
66.96
51.98
51.14
48.80
30.24
28.12
27.37
20.79
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

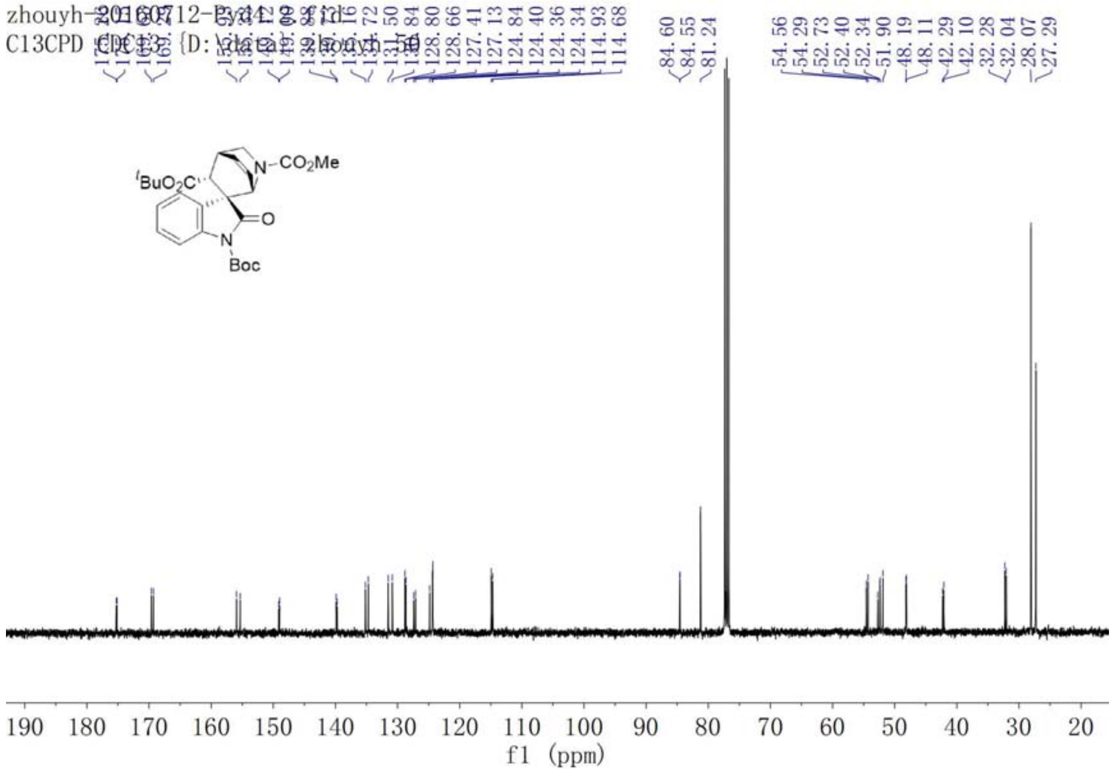
3u


Cbz
HN
CO2tBu
O
N
Cbz
1.00
2.00
9.00
2.00
1.00
1.00
2.00
3.00
1.00
1.00
2.00
9.00
f1 (ppm)

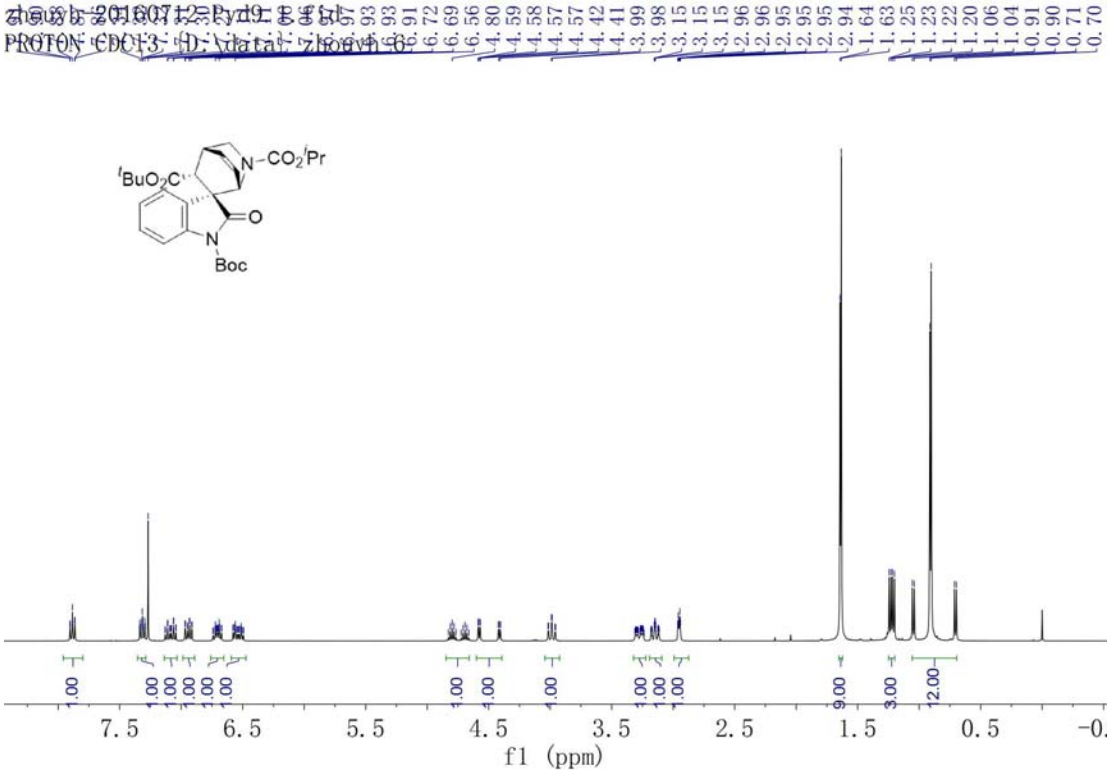

Cbz
HN
CO2tBu
O
N
Cbz
82.00
68.22
66.96
51.73
51.28
41.12
27.45
25.50
f1 (ppm)

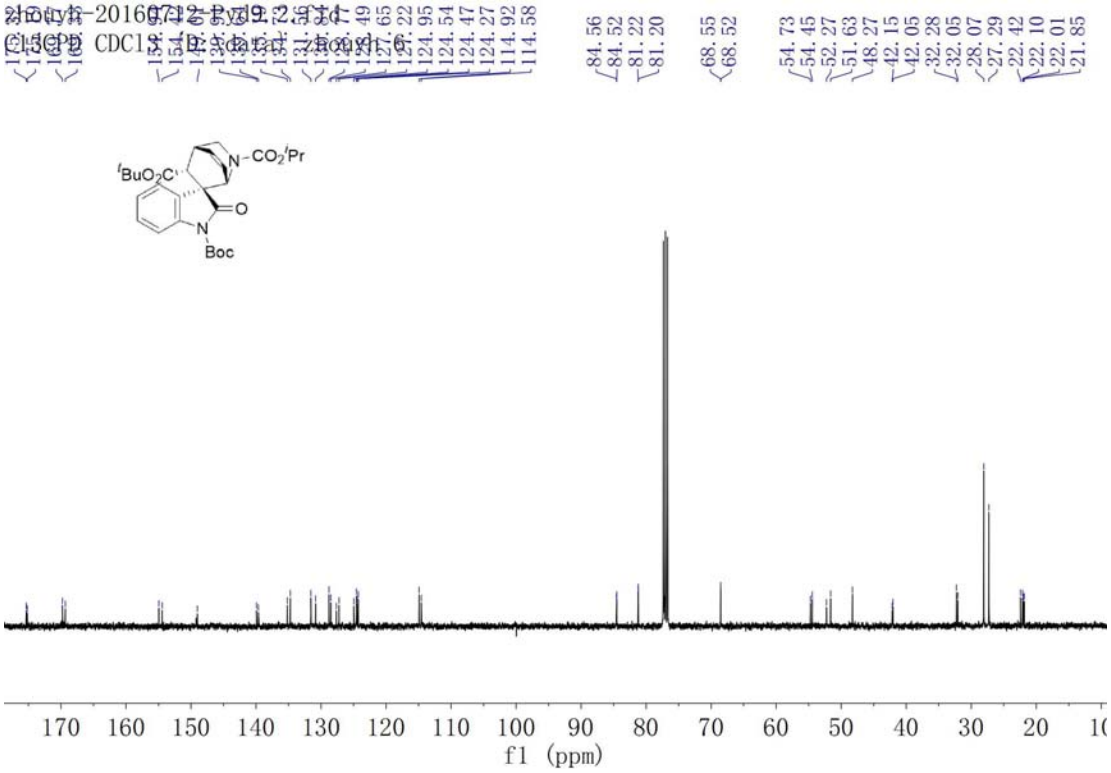
5a


PROTON CDCl3
6.93
6.72
6.69
6.55
6.51
4.59
4.58
4.57
4.41
4.40
4.39
4.04
4.03
4.01
4.00
3.98
3.97
3.64
3.39
3.16
2.96
2.95
2.95
2.94
1.64
1.64
0.91
0.90
N-CO2Me
tBuO2C
O
N
Boc
1.00
3.00
9.00
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

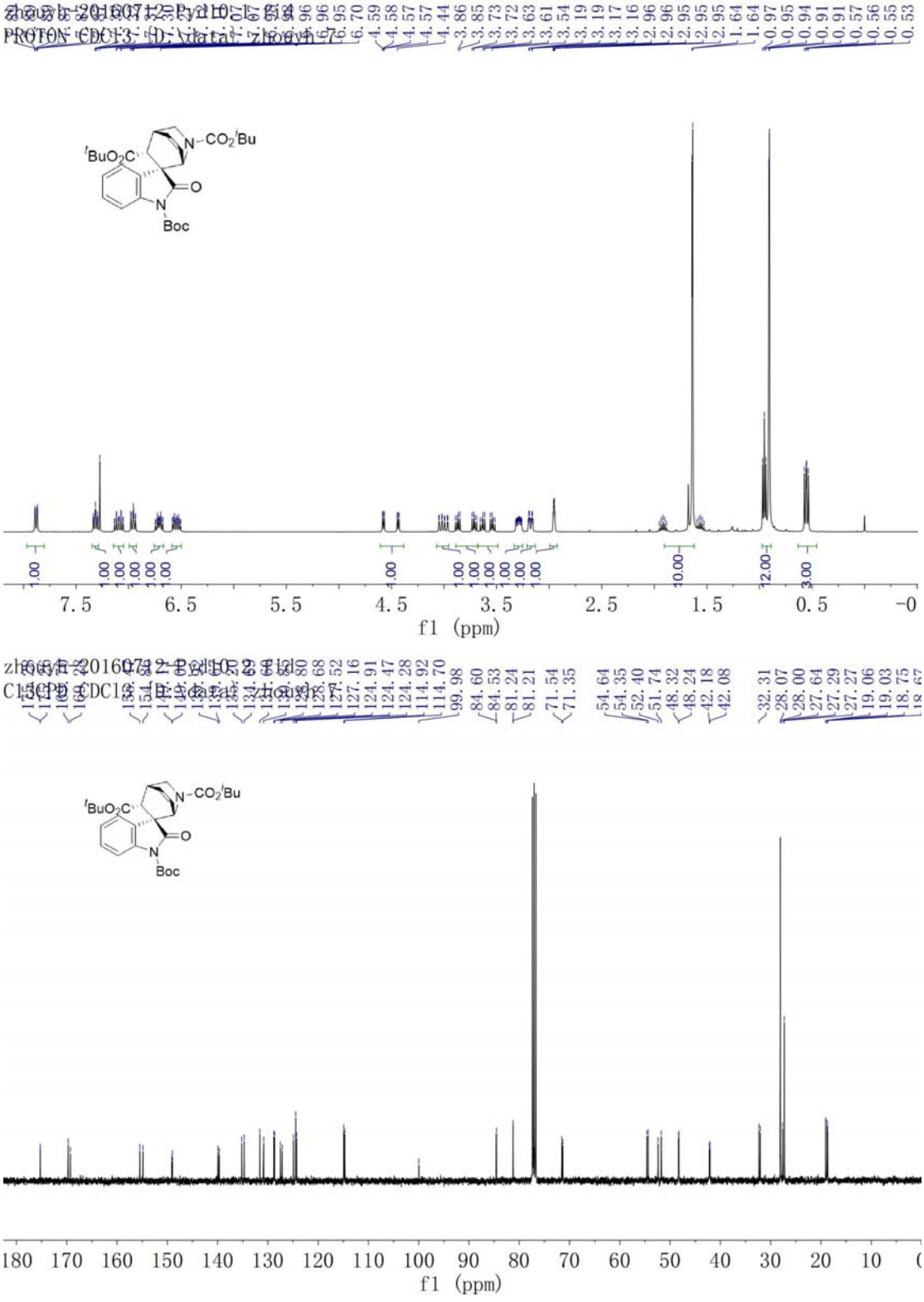

C13CPD CDCl3
128.80
128.66
127.41
127.13
124.84
124.40
124.36
124.34
114.93
114.68
84.60
84.55
81.24
54.56
54.29
52.73
52.40
52.34
51.90
48.19
48.11
42.29
42.10
32.28
32.04
28.07
27.29
N-CO2Me
tBuO2C
O
N
Boc
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

5b



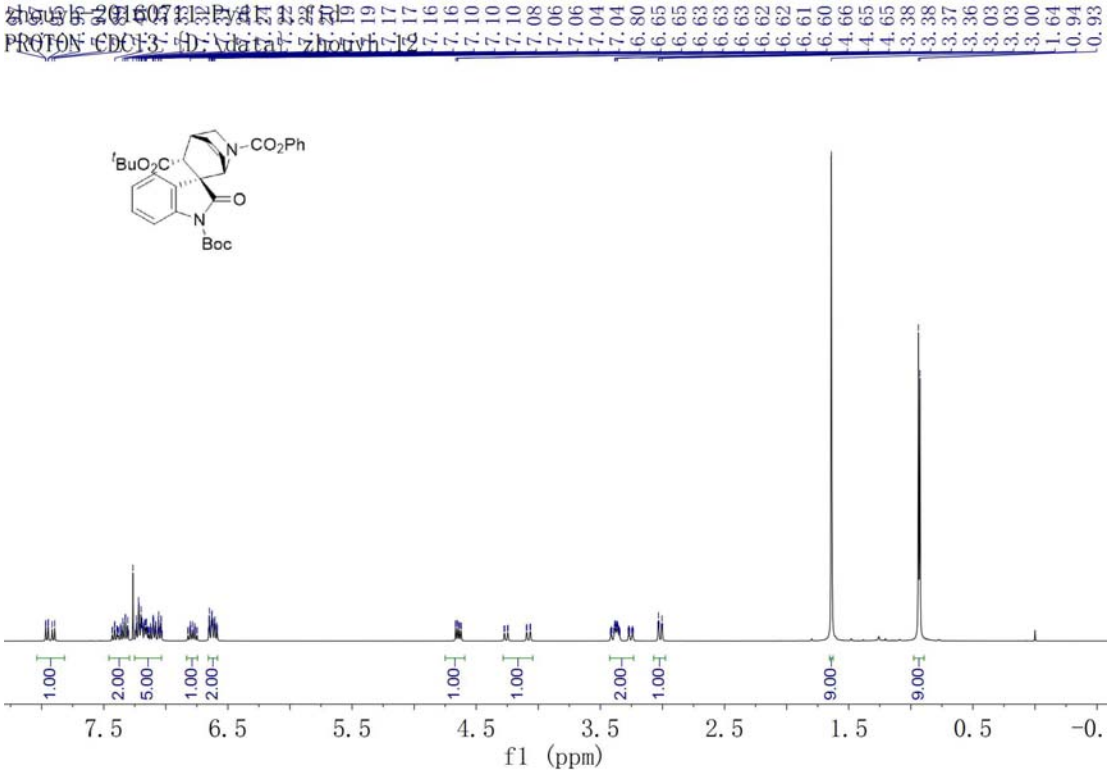


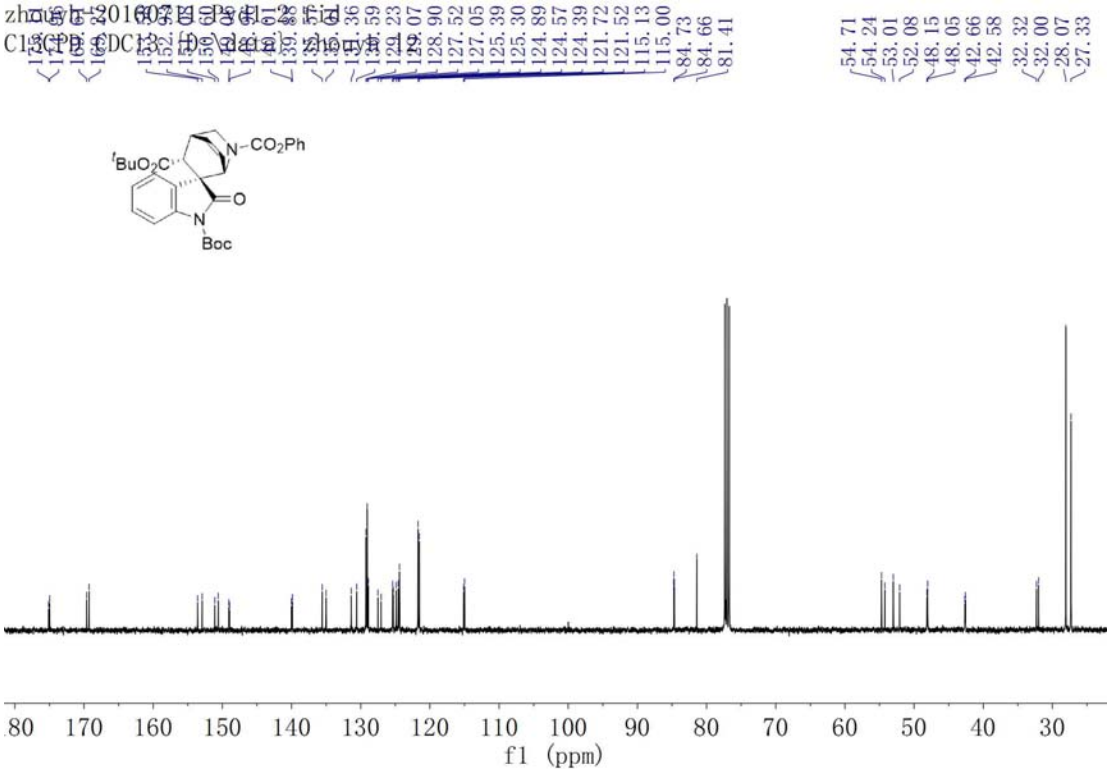
5c



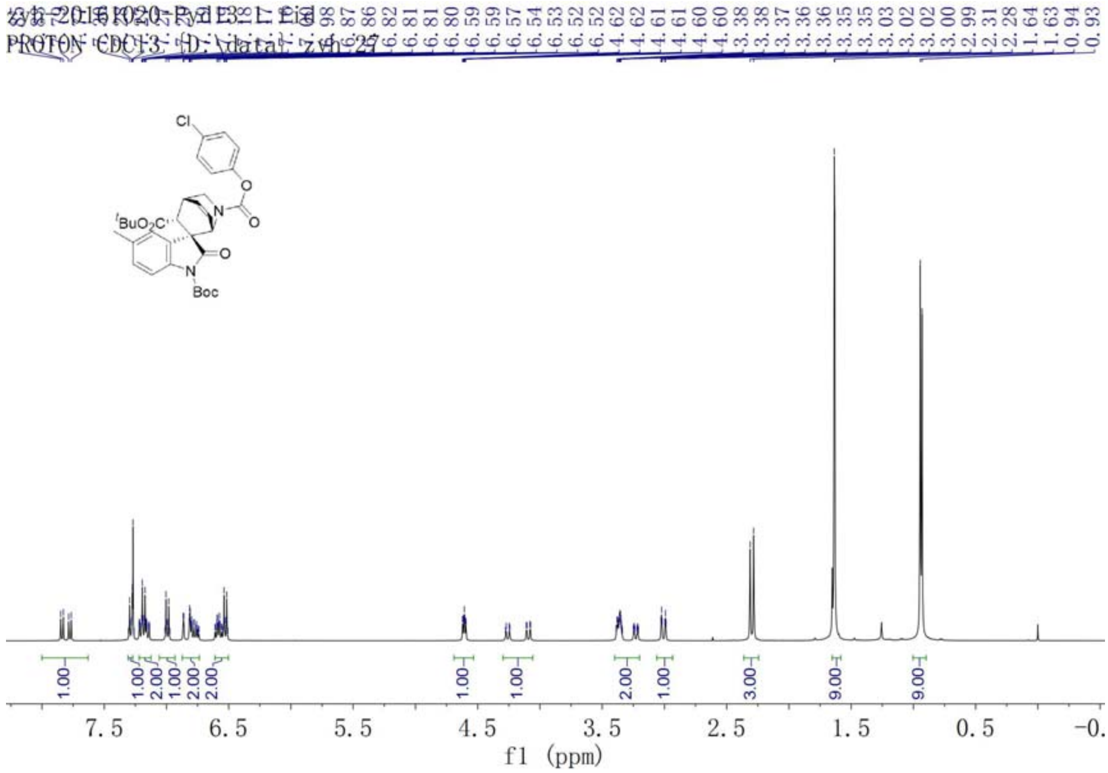
5d

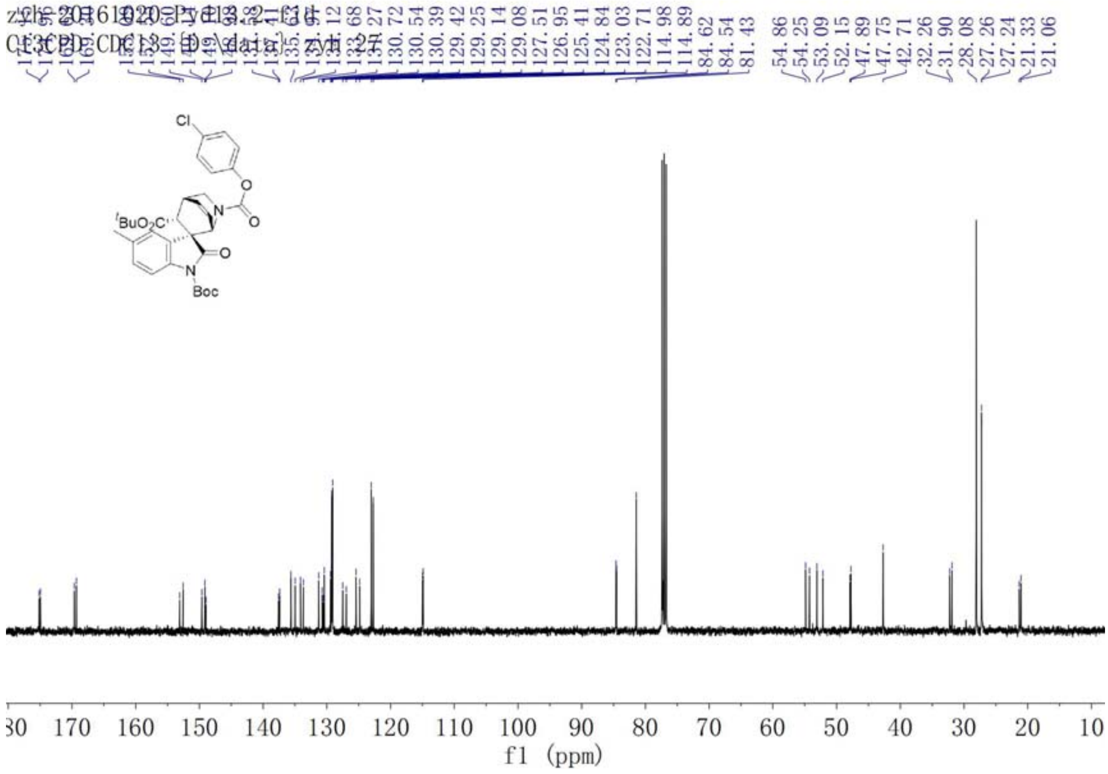
5e


PROTON CDCl3 5D zhouyh 1-2
tBuO2C
N
CO2Ph
O
N
Boc
1.00
2.00
5.00
1.00
2.00
1.00
1.00
2.00
1.00
9.00
9.00
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

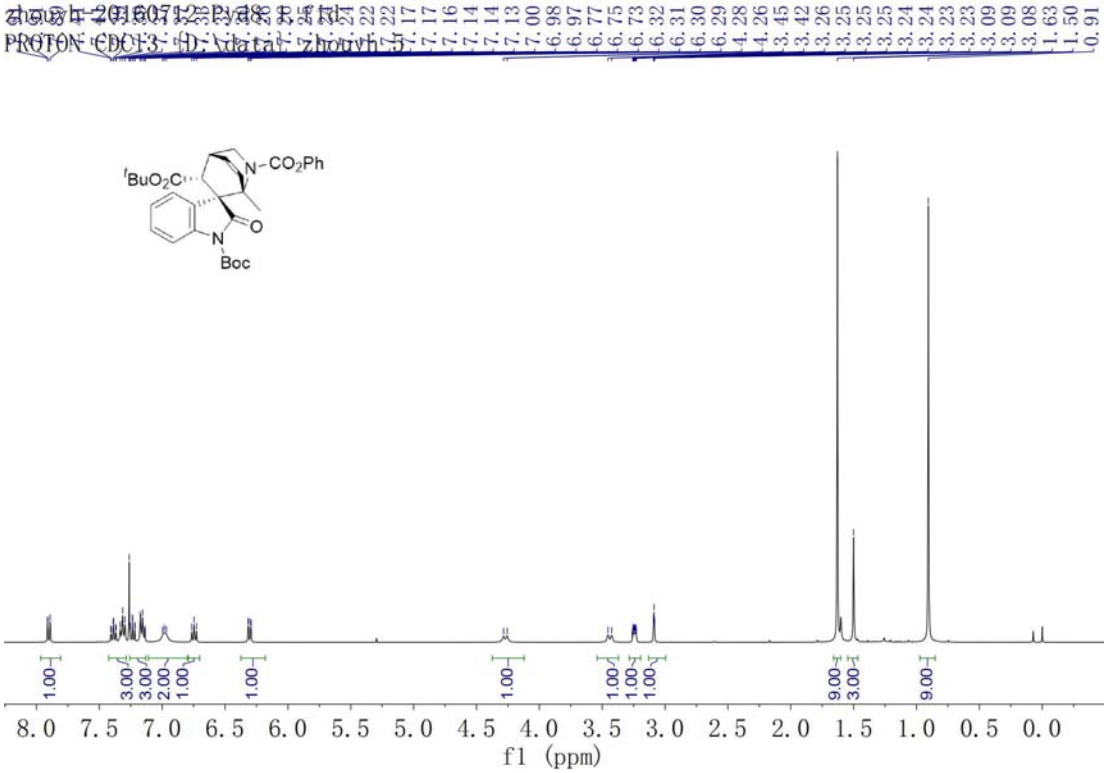

C13CPD CDCl3 1D zhouyh 1-2
84.73
84.66
81.41
54.71
54.24
53.01
52.08
48.15
48.05
42.66
42.58
32.32
32.00
28.07
27.33
tBuO2C
N
CO2Ph
O
N
Boc
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
f1 (ppm)

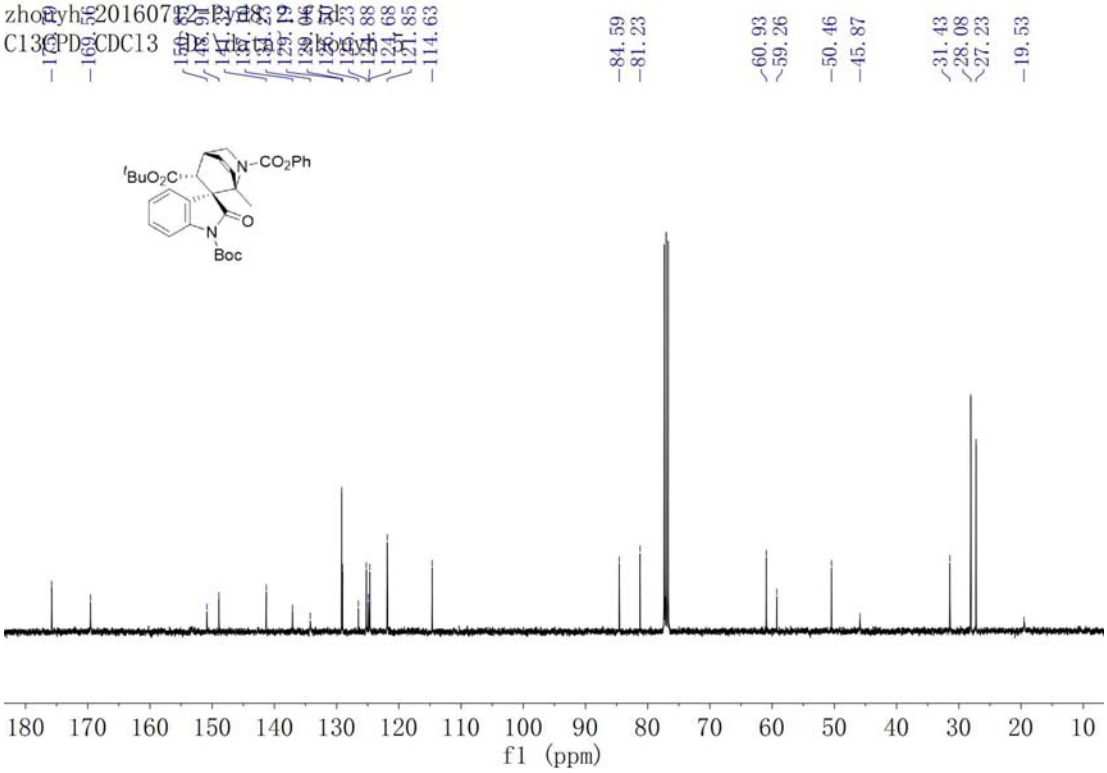
5f


PROTON CDCl3
Cl
O
N
O
^{t}BuO$_2$C
O
N
Boc
1.00
1.00
2.00
1.00
2.00
2.00
1.00
1.00
2.00
1.00
3.00
9.00
9.00
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

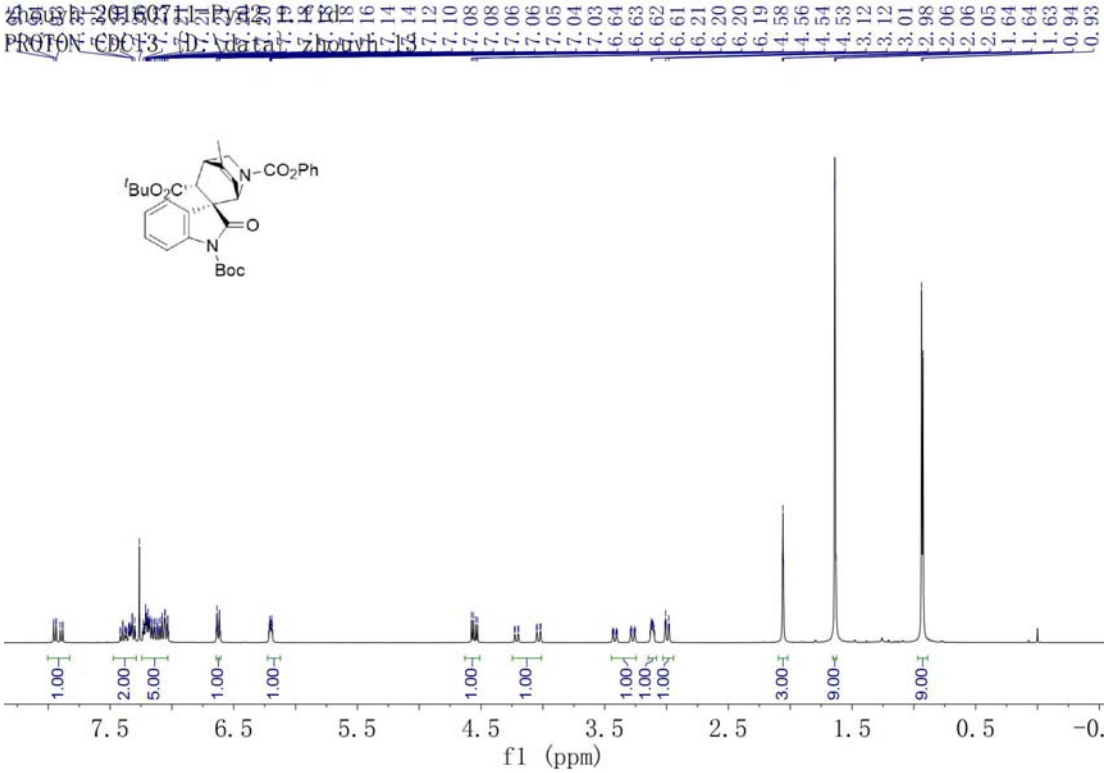

Cl
O
N
O
^{t}BuO$_2$C
O
N
Boc
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

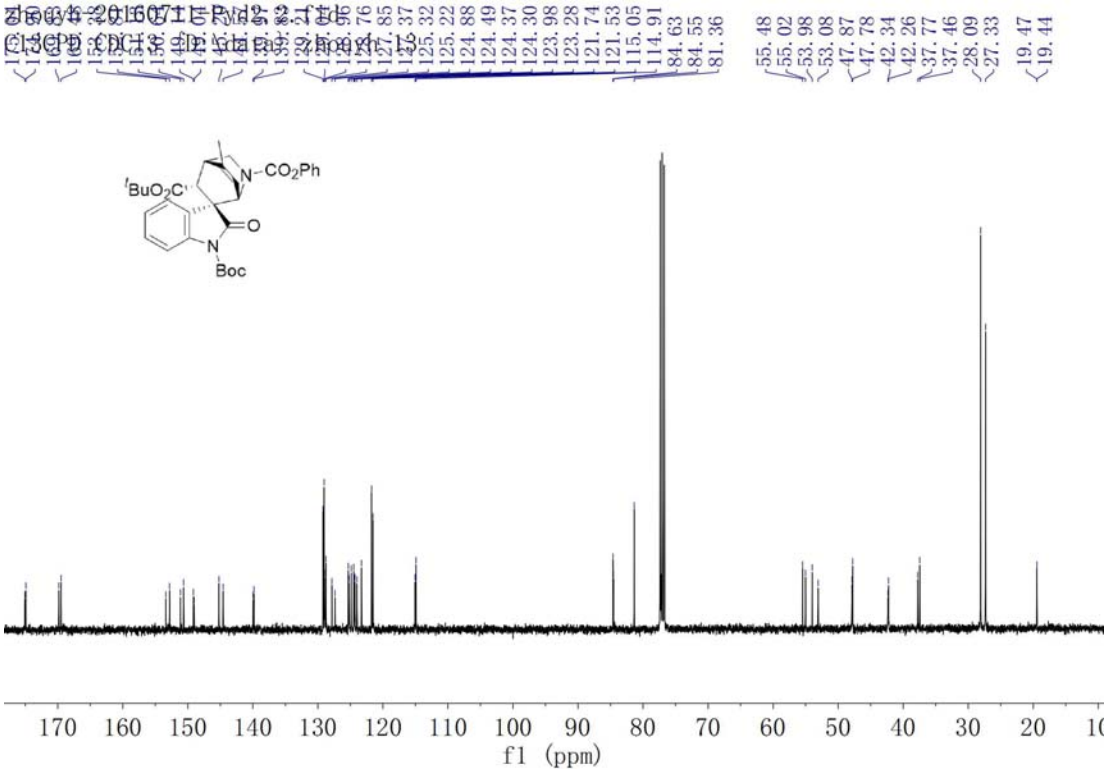
5g


1.00
3.00
3.00
2.00
1.00
1.00
1.00
1.00
1.00
9.00
3.00
9.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

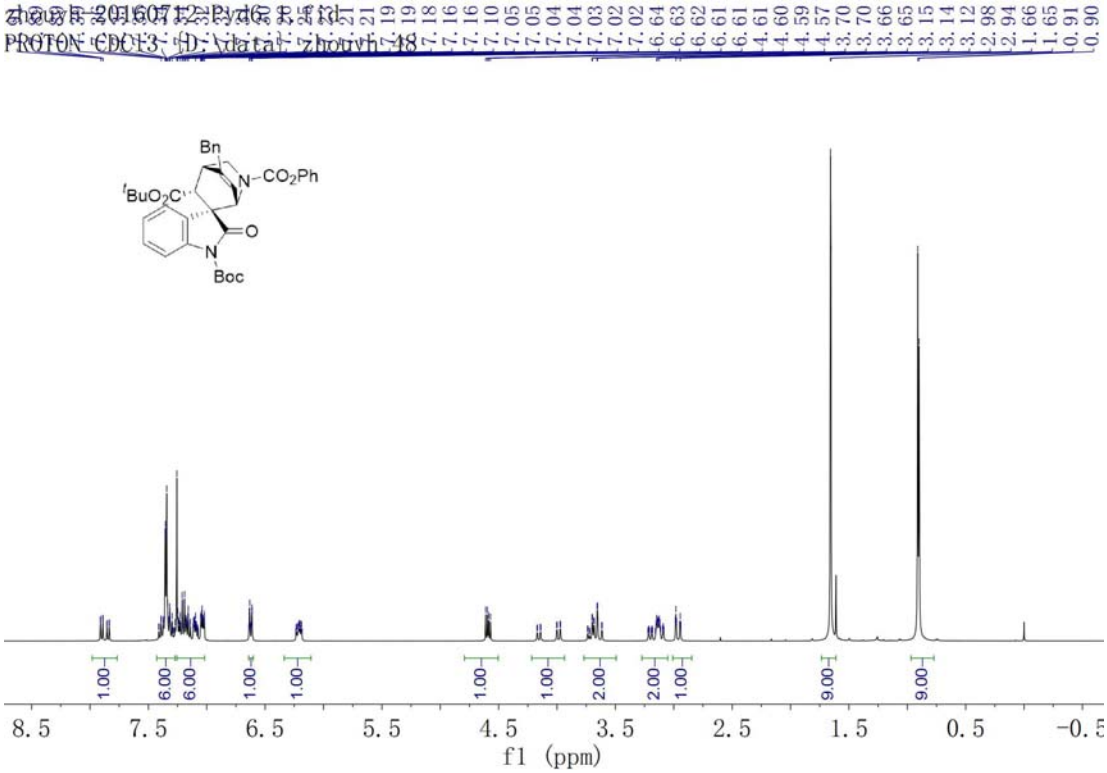

84.59
81.23
60.93
59.26
50.46
45.87
31.43
28.08
27.23
19.53
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

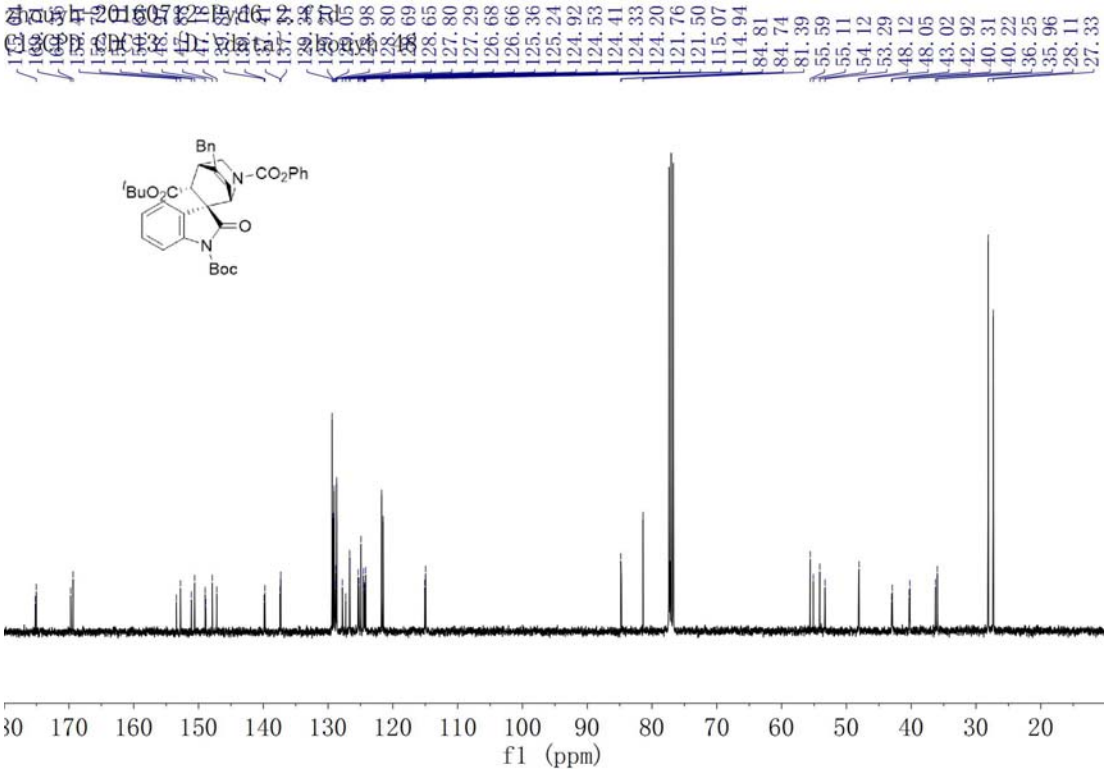
5h


N–CO2Ph
tBuO2C
O
N
Boc
1.00
2.00
5.00
1.00
1.00
1.00
1.00
1.00
1.00
3.00
9.00
9.00
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

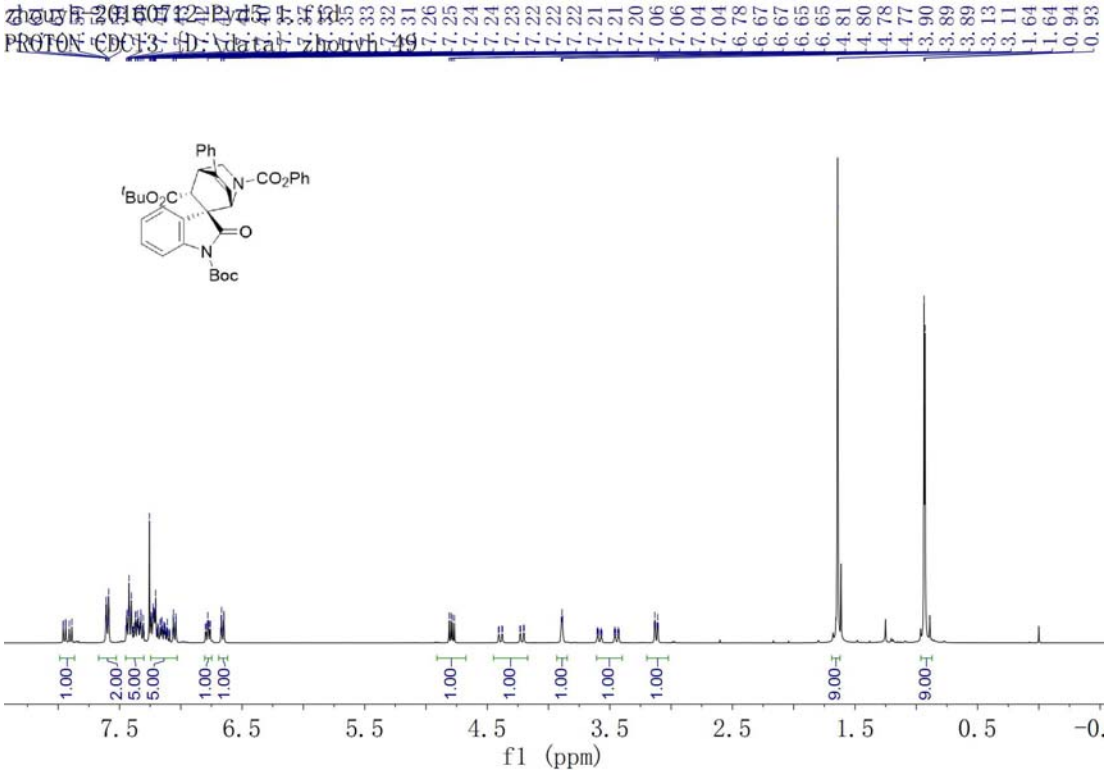

N–CO2Ph
tBuO2C
O
N
Boc
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

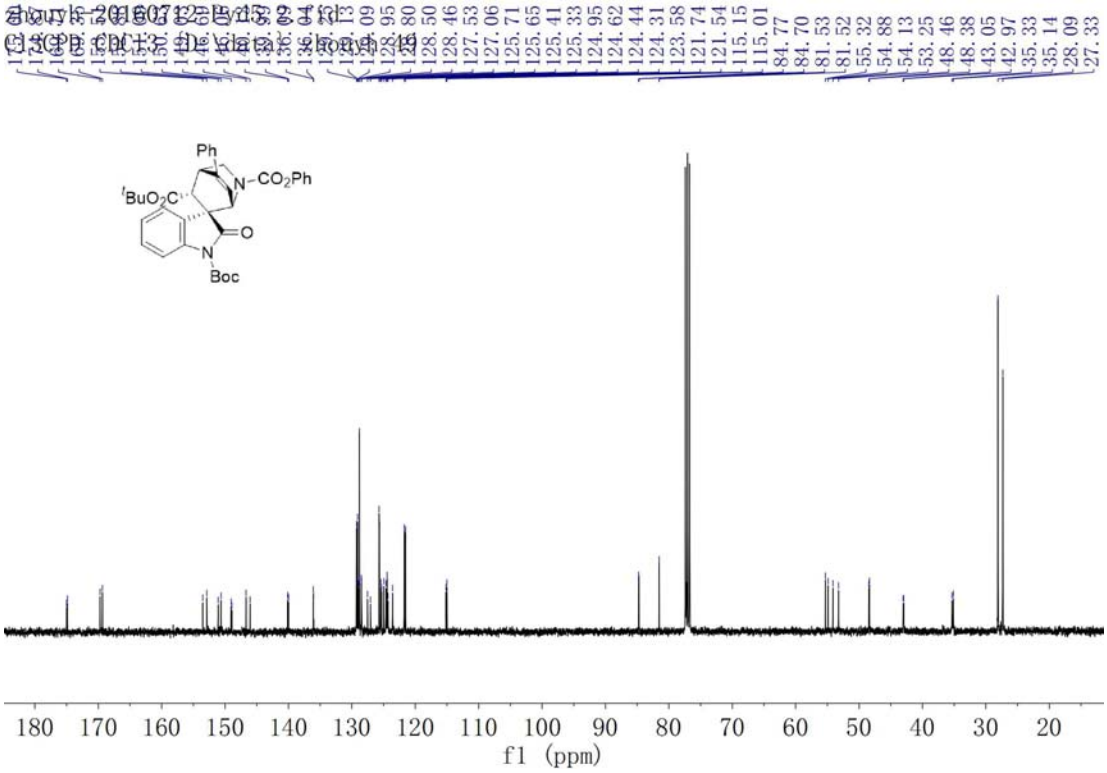
5i


Bn
N–CO2Ph
tBuO2C
O
N
Boc
1.00
6.00
6.00
1.00
1.00
1.00
1.00
2.00
2.00
1.00
9.00
9.00
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
−0.5
f1 (ppm)

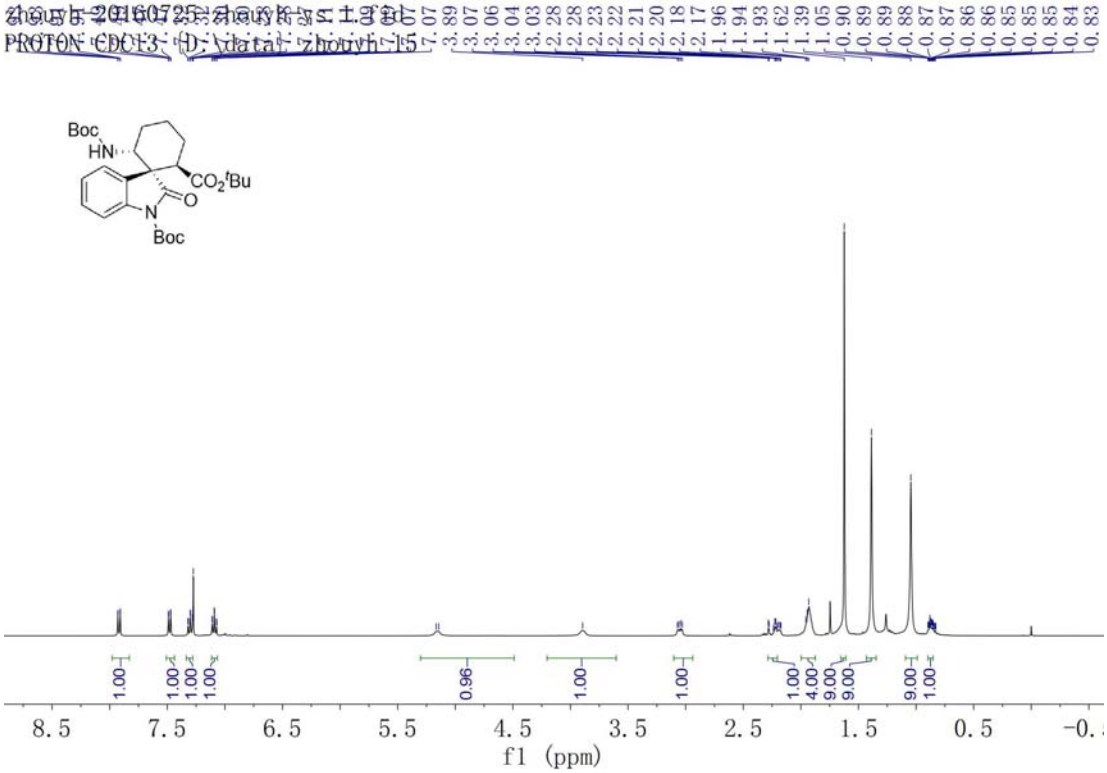

Bn
N–CO2Ph
tBuO2C
O
N
Boc
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

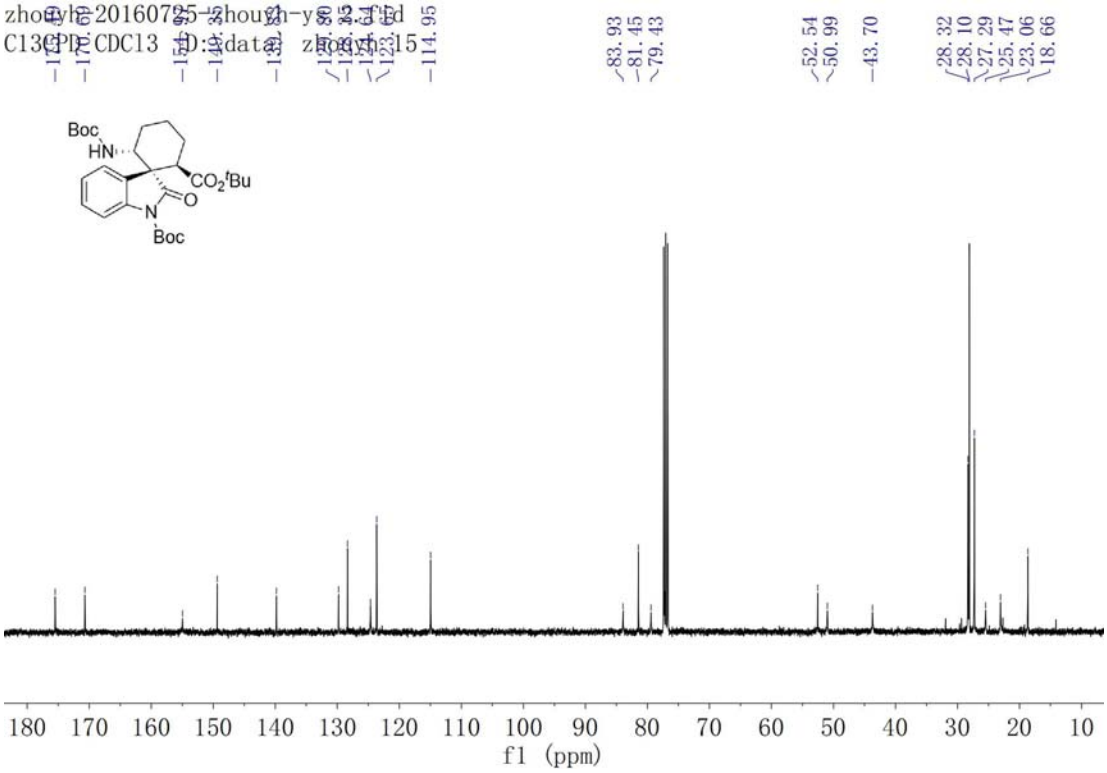
5j


Ph
N–CO2Ph
tBuO2C
O
N
Boc
1.00
2.00
5.00
1.00
1.00
1.00
1.00
1.00
1.00
9.00
9.00
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

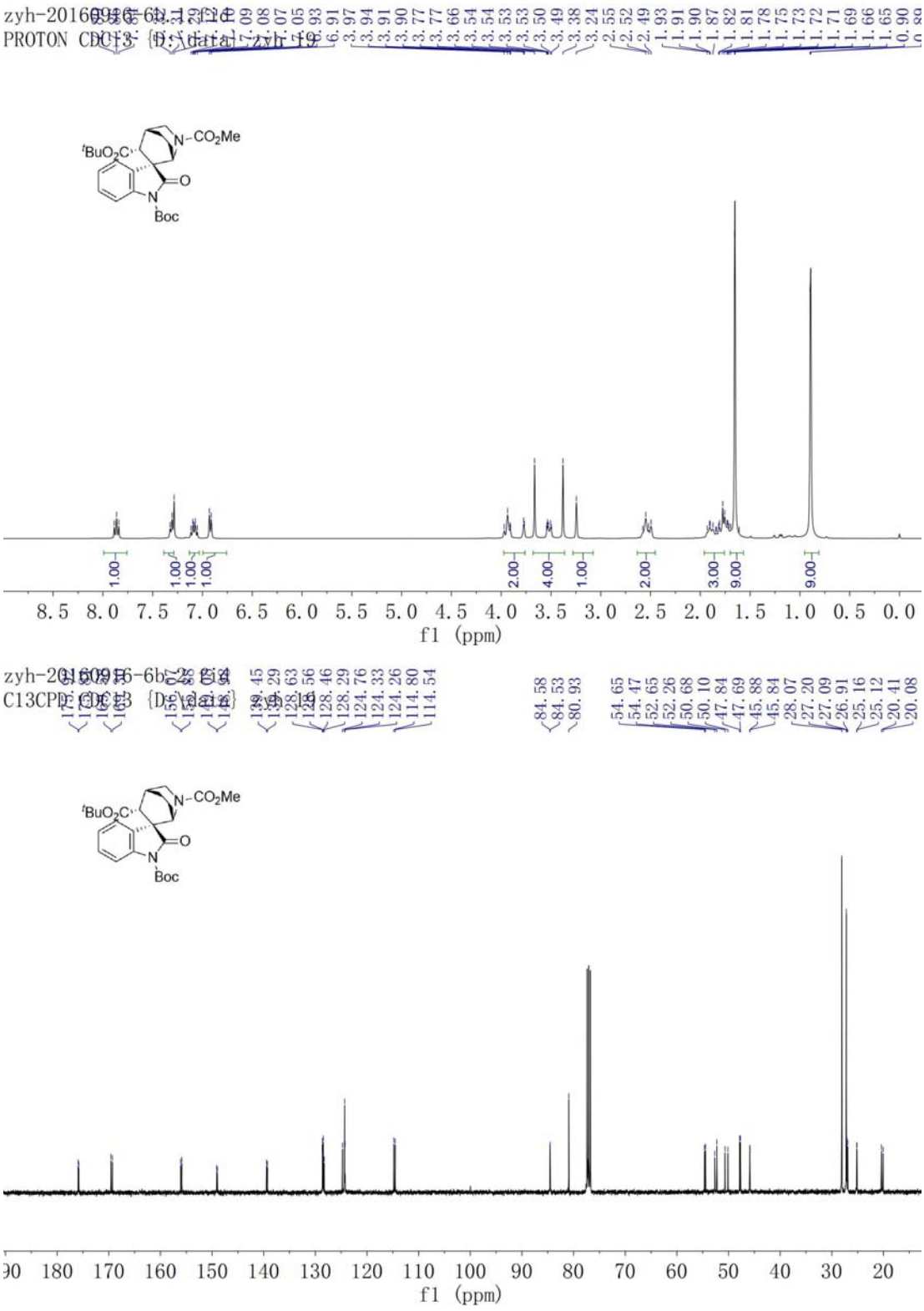

Ph
N–CO2Ph
tBuO2C
O
N
Boc
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

6a

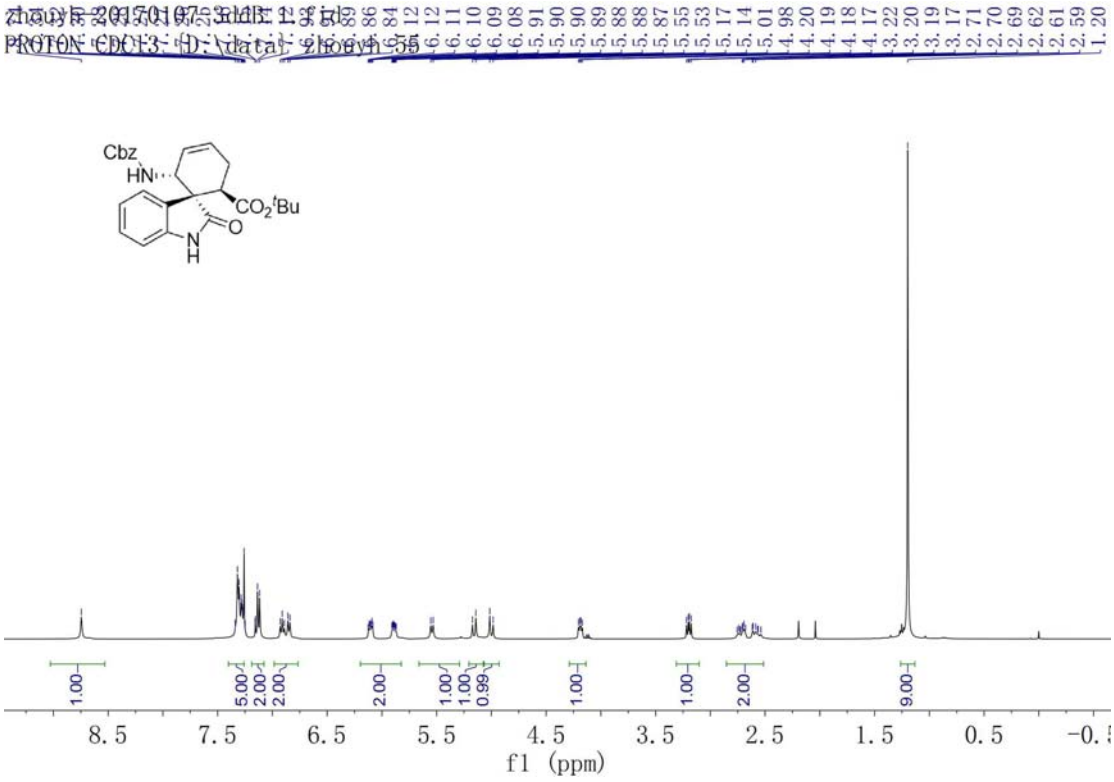

Boc
HN
CO2tBu
O
N
Boc
1.00
1.00
1.00
0.96
1.00
1.00
1.00
4.00
9.00
9.00
1.00
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

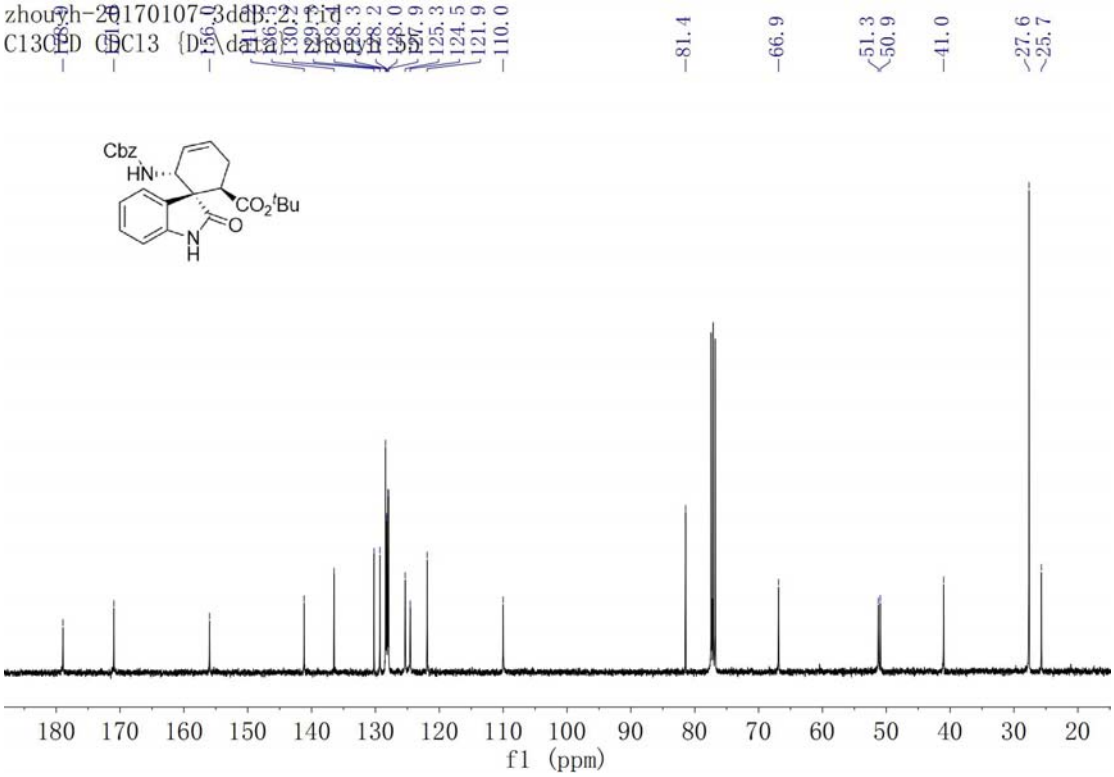

Boc
HN
CO2tBu
O
N
Boc
83.93
81.45
79.43
52.54
50.99
43.70
28.32
28.10
27.29
25.47
23.06
18.66
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

6b

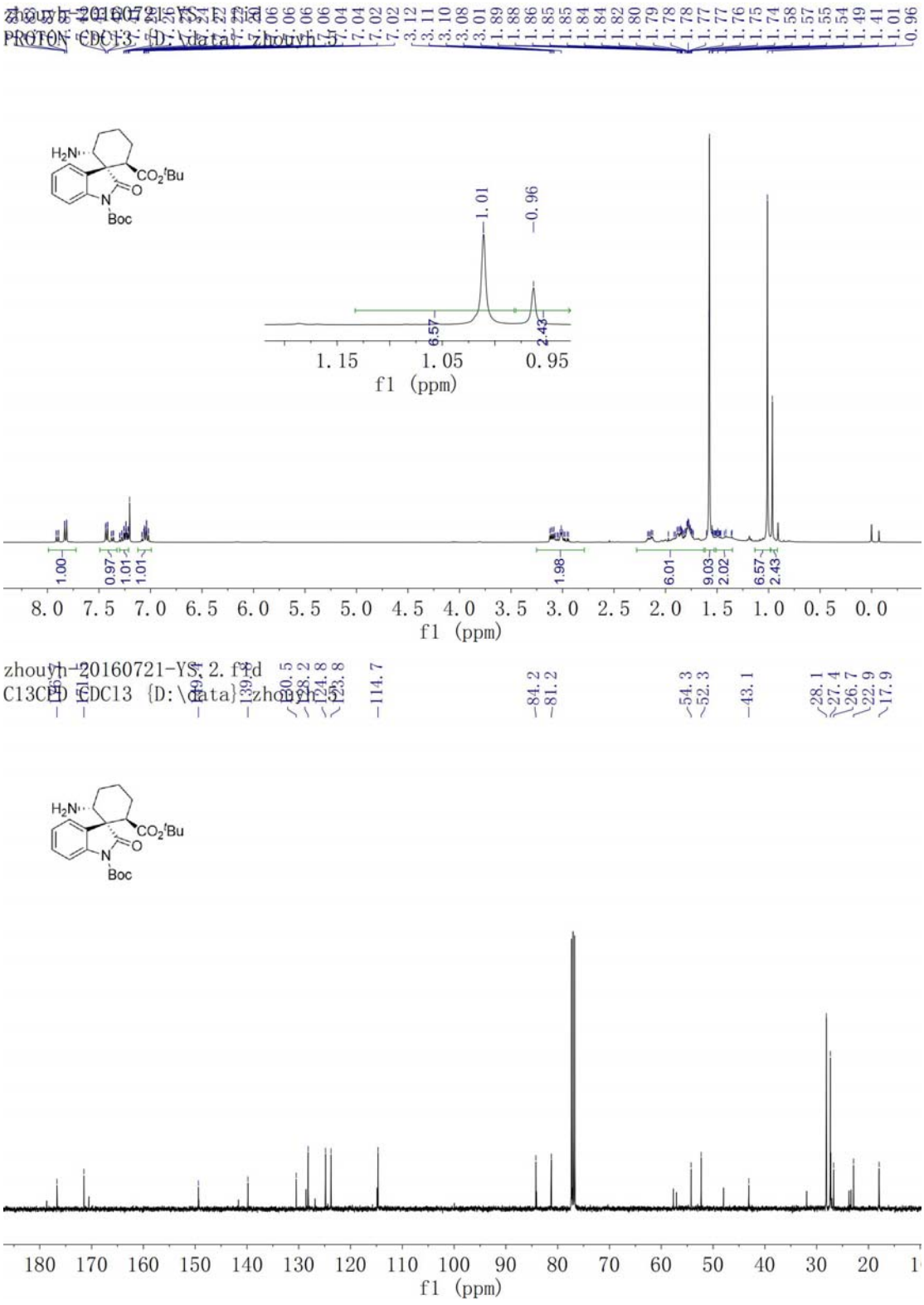

zyh-20160916-6b
PROTON CDCl3
N-CO2Me
tBuO2C
O
N
Boc
1.00
1.00
1.00
1.00
2.00
4.00
1.00
2.00
3.00
9.00
9.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
zyh-20160916-6b
C13CPD
CDCl3
84.58
84.53
80.93
54.65
54.47
52.65
52.26
50.68
50.10
47.84
47.69
45.88
45.84
28.07
27.20
27.09
26.91
25.16
25.12
20.41
20.08
N-CO2Me
tBuO2C
O
N
Boc
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

6c

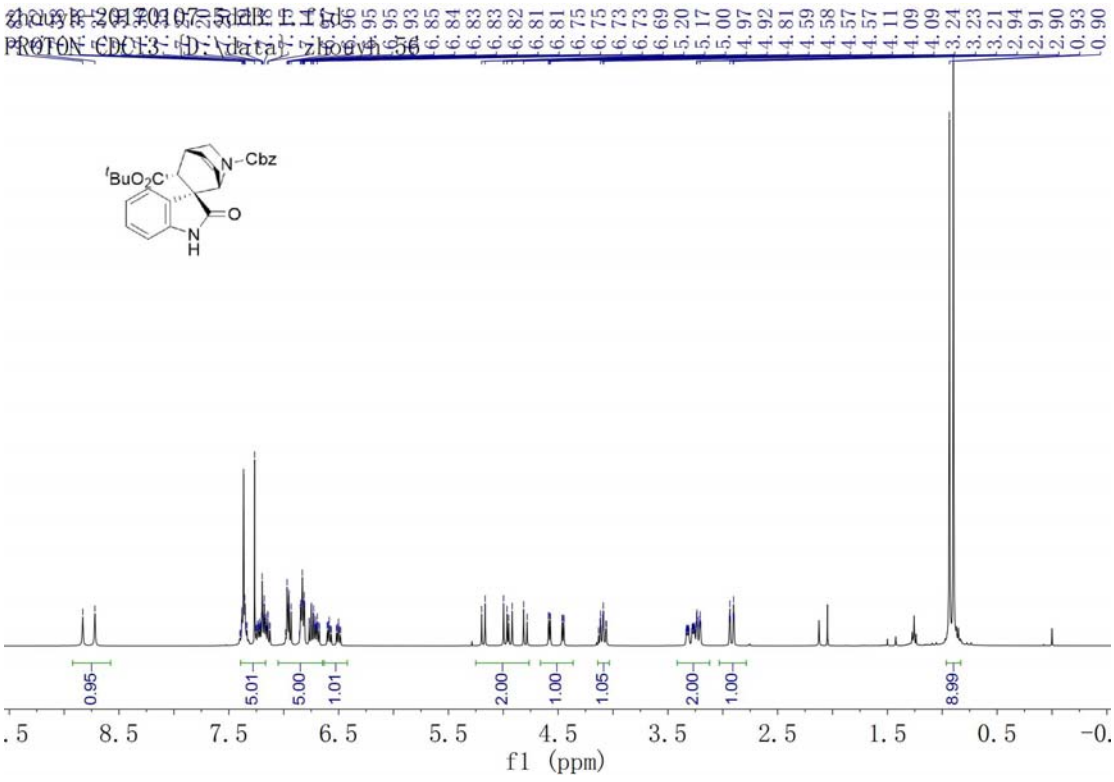

Cbz
HN
CO2tBu
O
N
H
1.00
5.00
2.00
2.00
2.00
1.00
1.00
0.99
1.00
1.00
2.00
9.00
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
f1 (ppm)

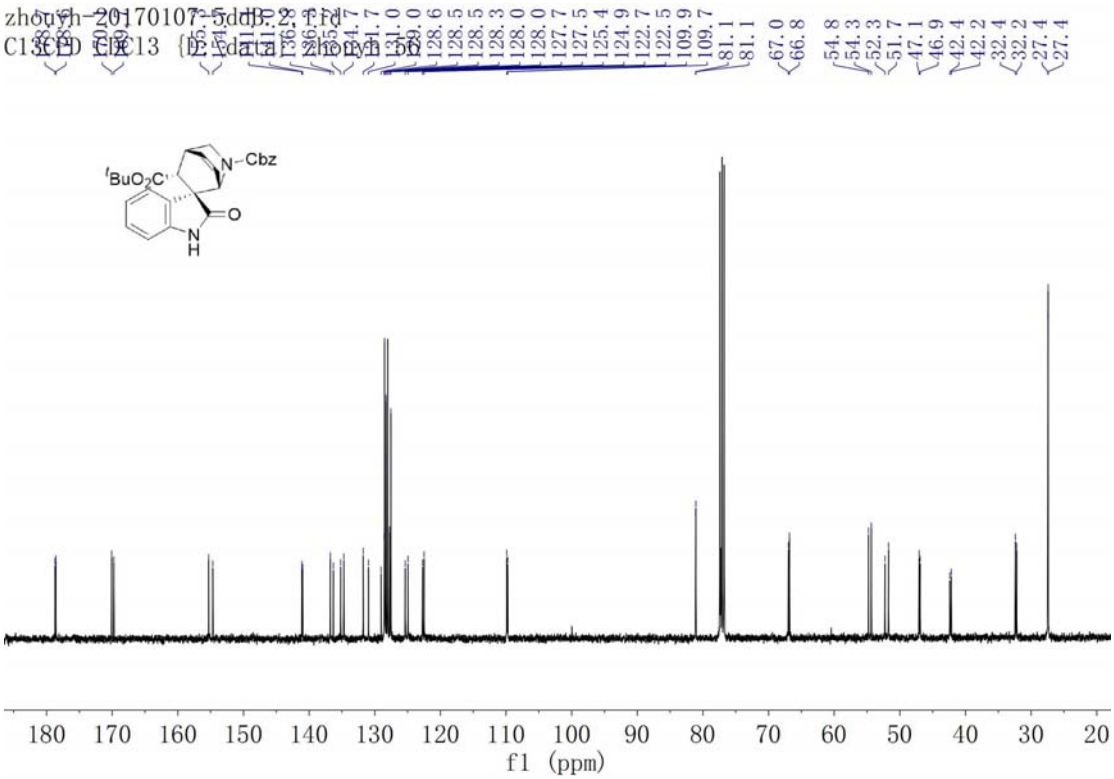

Cbz
HN
CO2tBu
O
N
H
-81.4
-66.9
51.3
50.9
-41.0
-27.6
-25.7
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

6d


zhouyh-20160721-YS-1.fid
PROTON CDCl3 {D:\data\zhouyh\1}
zhouyh-20160721-YS-2.fid
C13CPD CDCl3 {D:\data\zhouyh\2}
f1 (ppm)

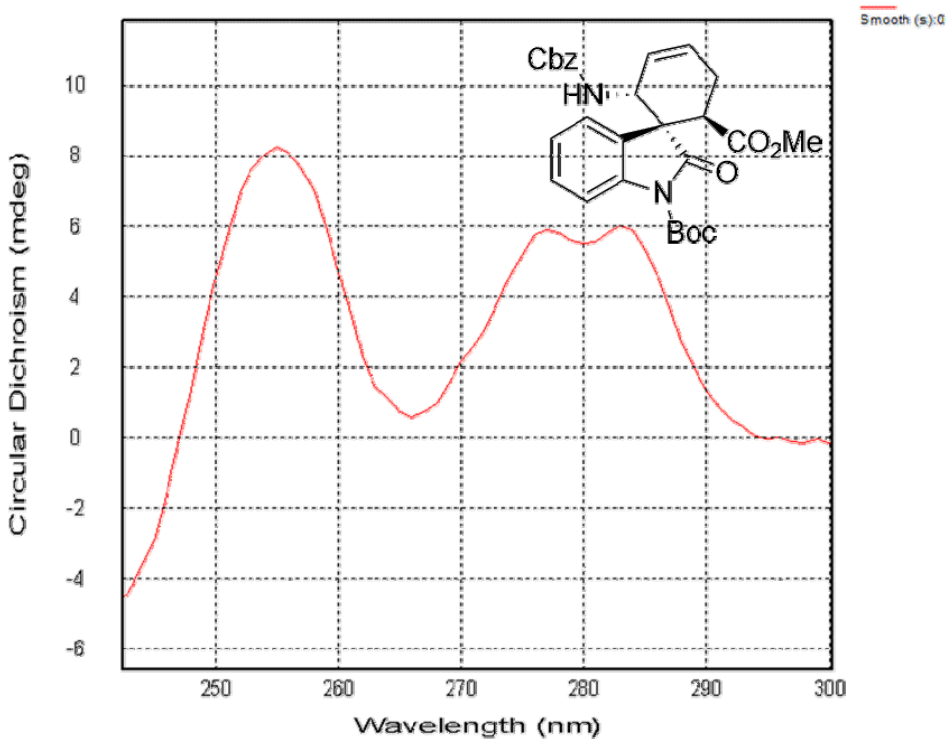
6e


Cbz
O
N
H
0.95
5.01
5.00
1.01
2.00
1.00
1.05
2.00
1.00
8.99
f1 (ppm)

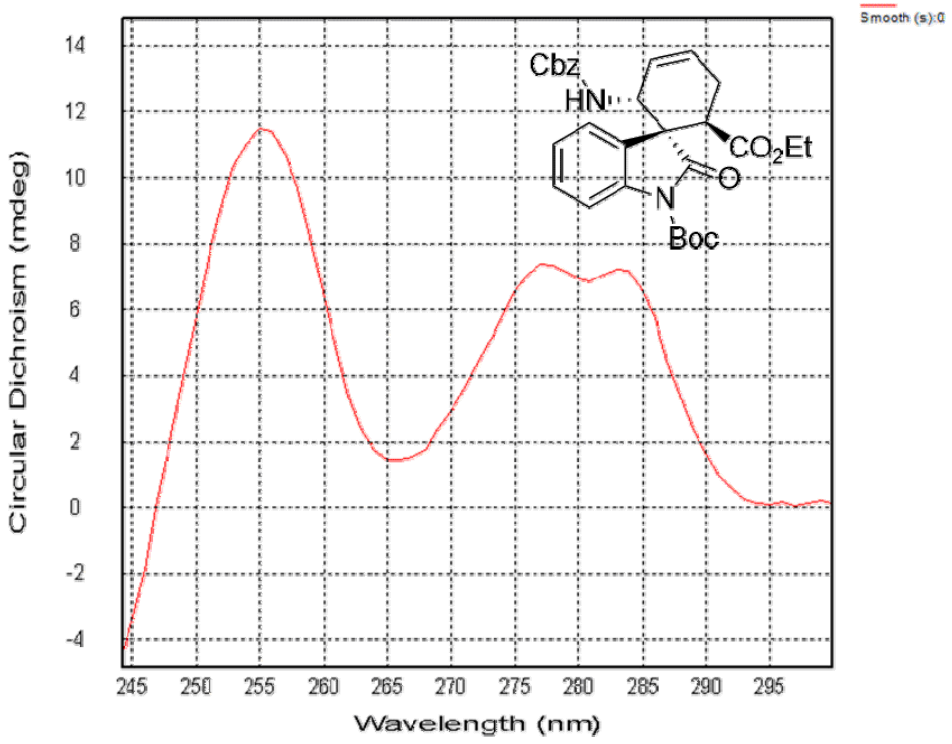

Cbz
O
N
H
f1 (ppm)

(H) Copies of CD spectra in CH_2Cl_2

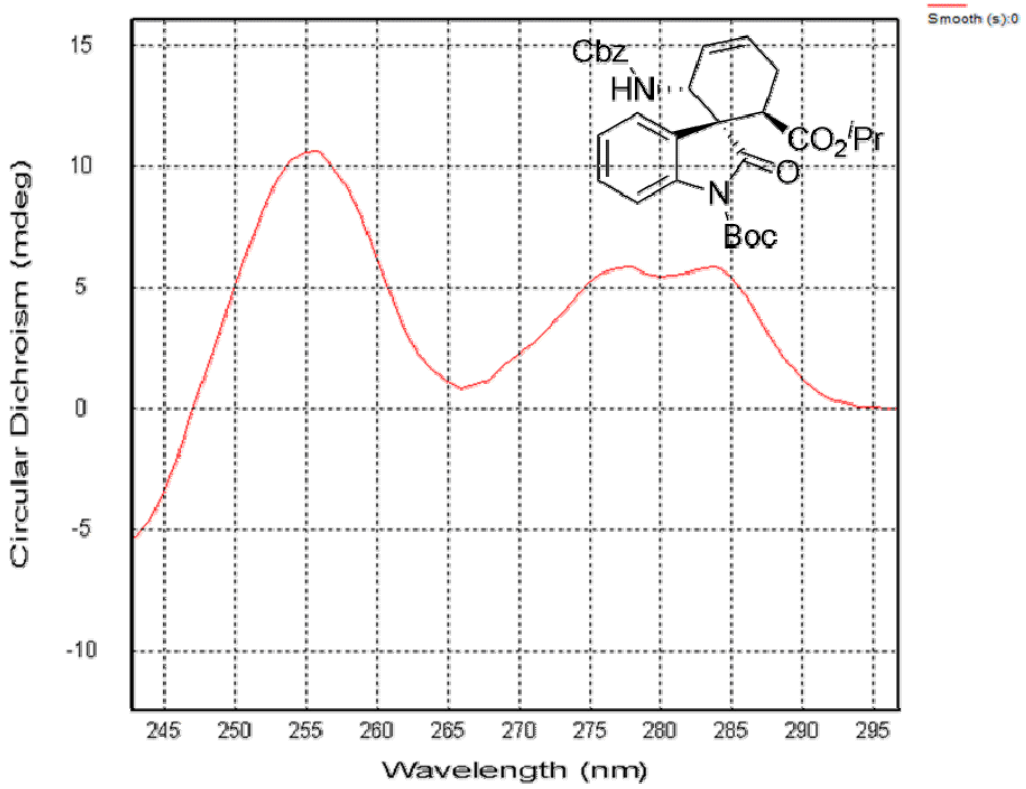
3a



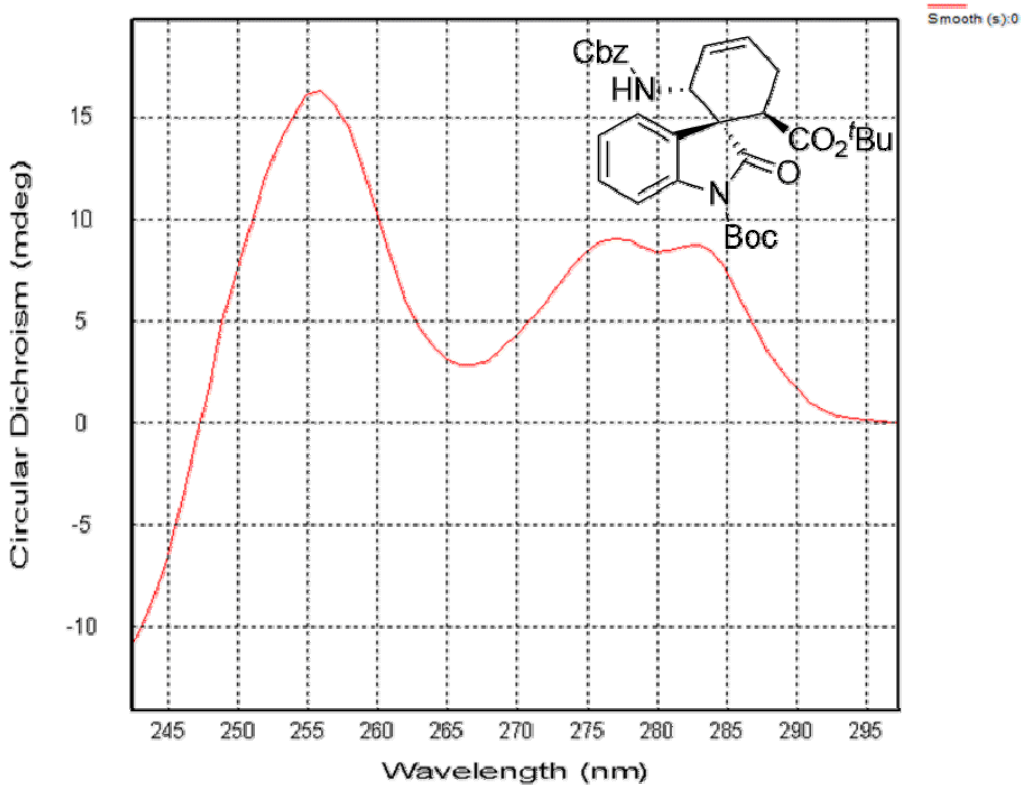
3b



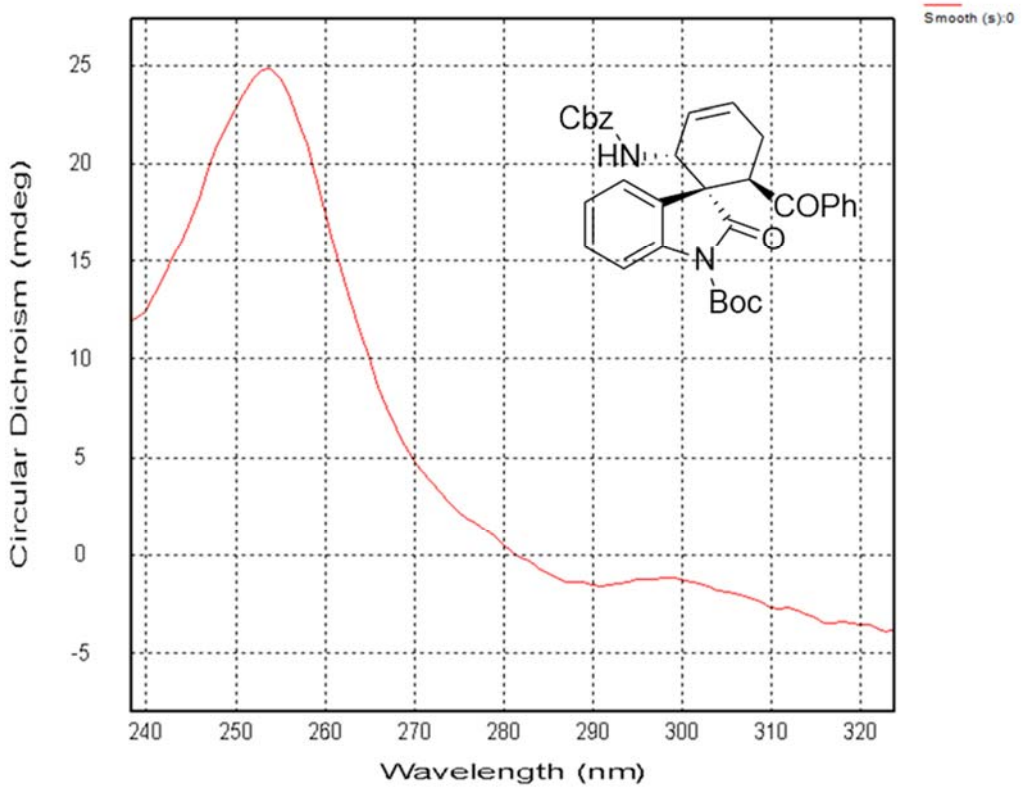
3c


Smooth (s):0
Cbz
HN
CO2iPr
O
N
Boc
Circular Dichroism (mdeg)
15
10
5
0
-5
-10
245
250
255
260
265
270
275
280
285
290
295
Wavelength (nm)

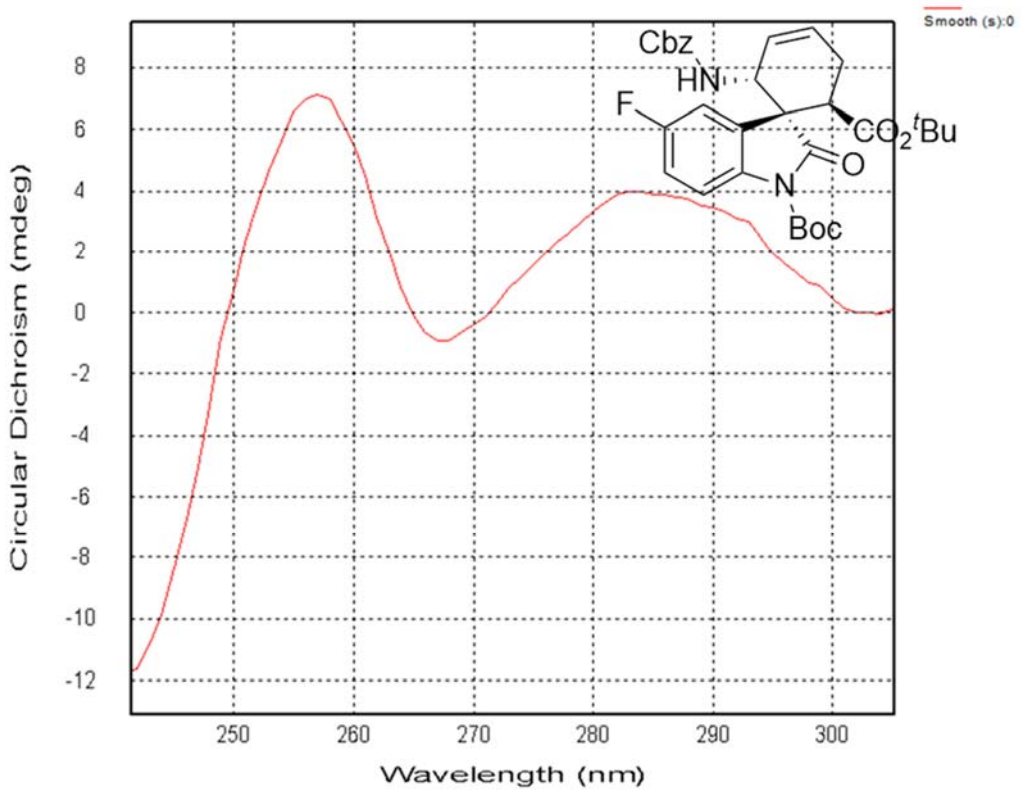
3d


Smooth (s):0
Cbz
HN
CO2tBu
O
N
Boc
Circular Dichroism (mdeg)
15
10
5
0
-5
-10
245
250
255
260
265
270
275
280
285
290
295
Wavelength (nm)

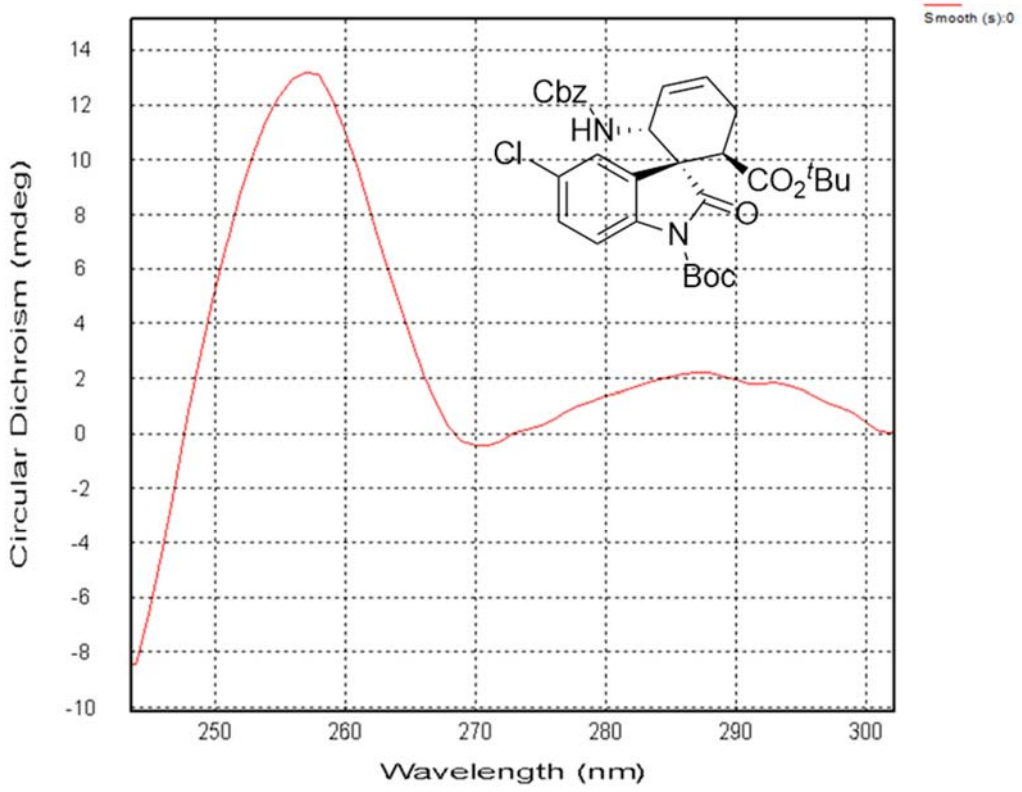
3e


Smooth (s):0
Circular Dichroism (mdeg)
25
20
15
10
5
0
-5
240
250
260
270
280
290
300
310
320
Wavelength (nm)
Cbz
HN
COPh
O
N
Boc

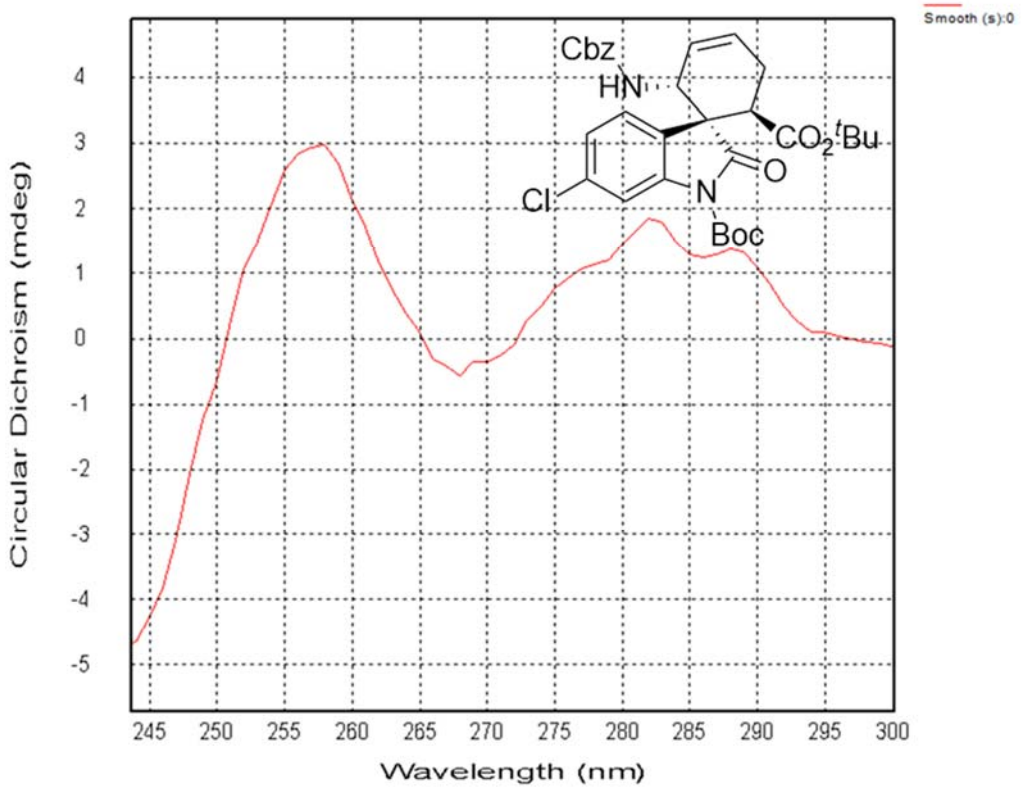
3f


Smooth (s):0
Circular Dichroism (mdeg)
8
6
4
2
0
-2
-4
-6
-8
-10
-12
250
260
270
280
290
300
Wavelength (nm)
Cbz
HN
F
CO2tBu
O
N
Boc

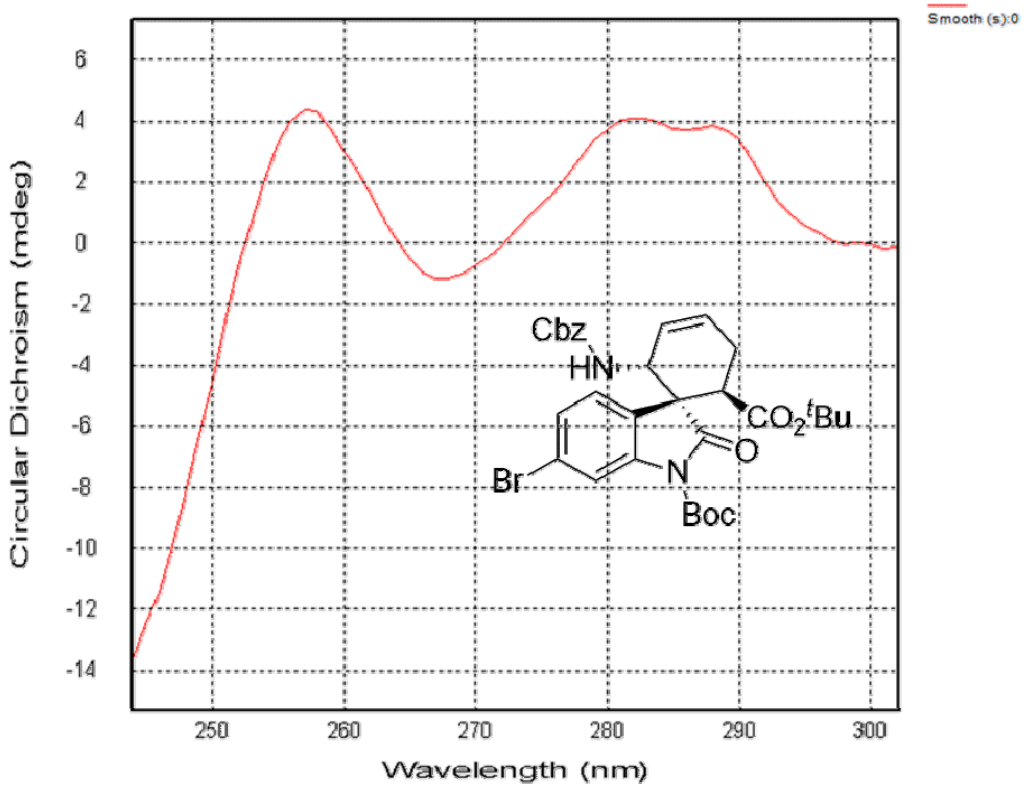
3g


Smooth (s):0
Circular Dichroism (mdeg)
14
12
10
8
6
4
2
0
-2
-4
-6
-8
-10
250
260
270
280
290
300
Wavelength (nm)
Cbz
HN
Cl
CO2tBu
O
N
Boc

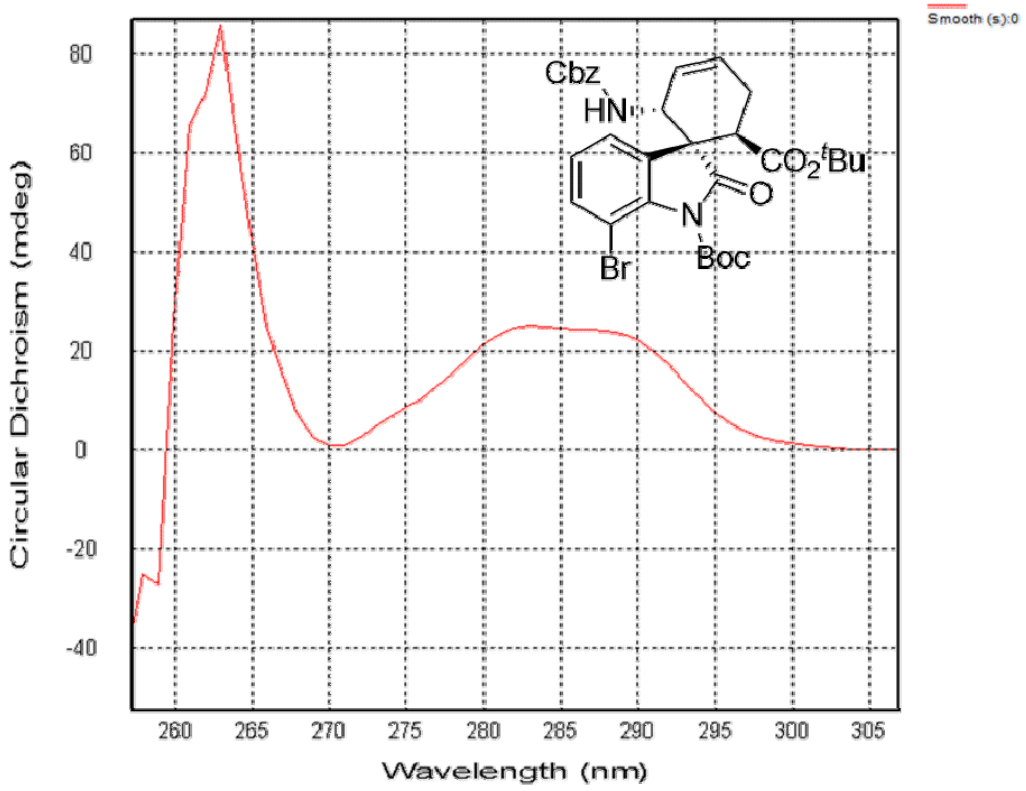
3h


Smooth (s):0
Circular Dichroism (mdeg)
4
3
2
1
0
-1
-2
-3
-4
-5
245
250
255
260
265
270
275
280
285
290
295
300
Wavelength (nm)
Cbz
HN
CO2tBu
O
Cl
N
Boc

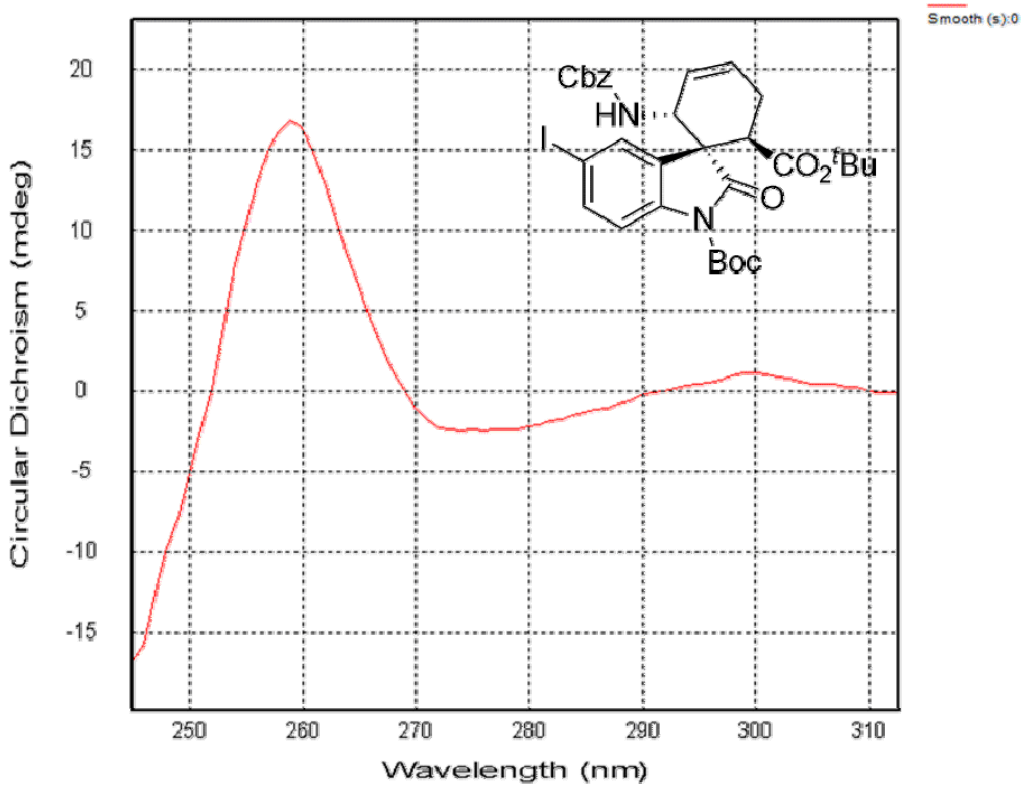
3i


Smooth (s):0
Circular Dichroism (mdeg)
6
4
2
0
-2
-4
-6
-8
-10
-12
-14
250
260
270
280
290
300
Wavelength (nm)
Cbz
HN
CO2tBu
O
N
Br
Boc

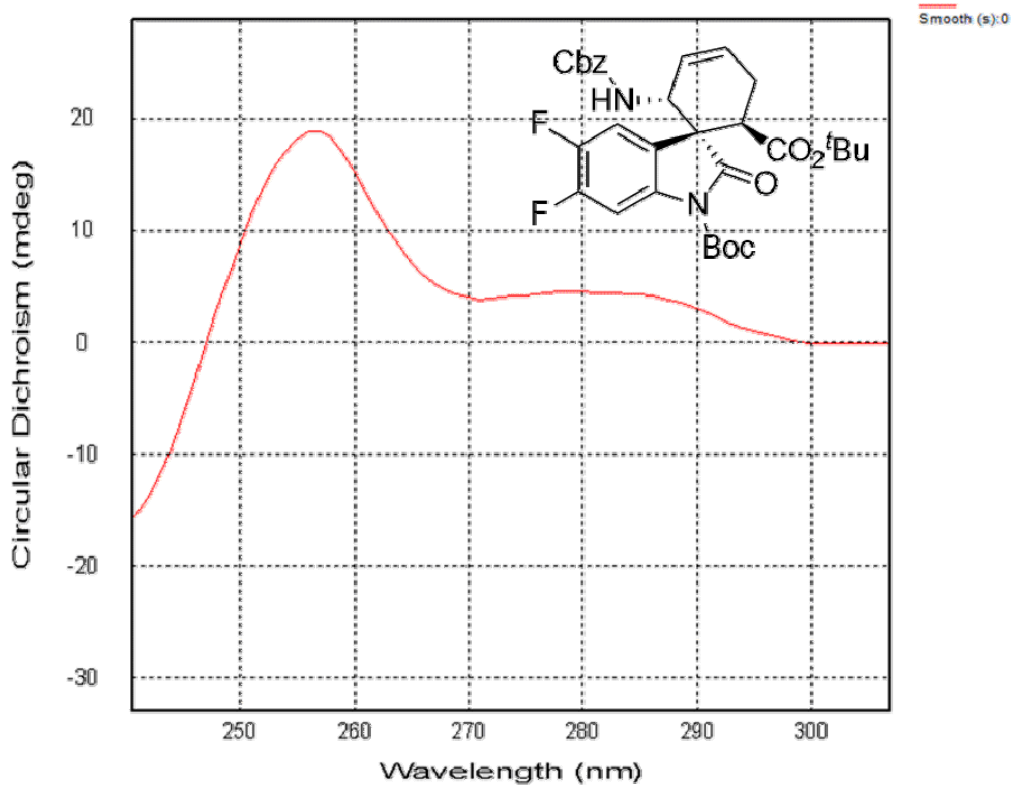
3j


Smooth (s):0
Circular Dichroism (mdeg)
80
60
40
20
0
-20
-40
260
265
270
275
280
285
290
295
300
305
Wavelength (nm)
Cbz
HN
CO2tBu
O
N
Br
Boc

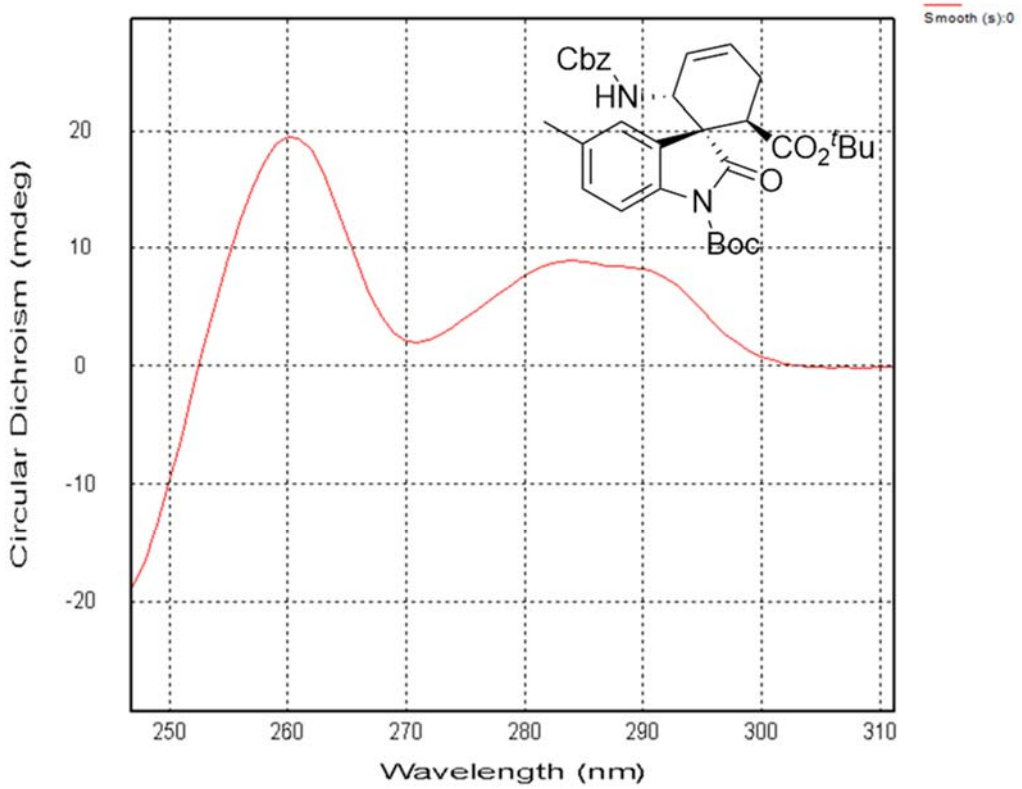
3k


Smooth (s):0
Cbz
HN
I
CO2tBu
O
N
Boc
Circular Dichroism (mdeg)
20
15
10
5
0
-5
-10
-15
250
260
270
280
290
300
310
Wavelength (nm)

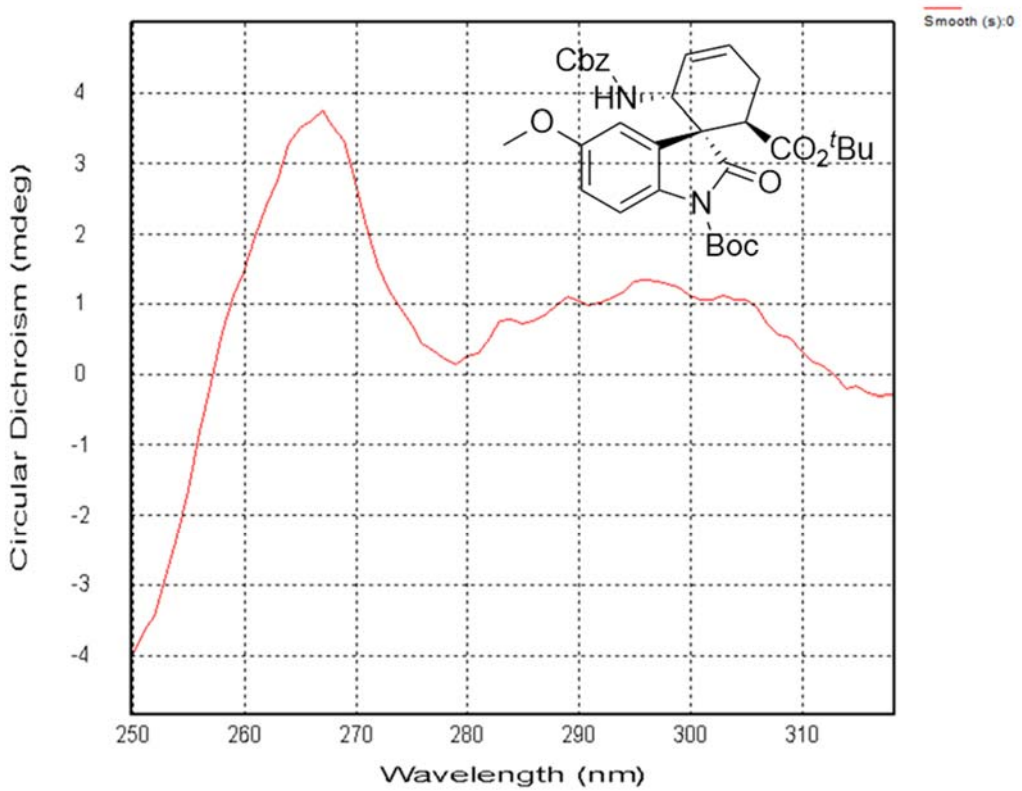
3l


Smooth (s):0
Cbz
HN
F
F
CO2tBu
O
N
Boc
Circular Dichroism (mdeg)
20
10
0
-10
-20
-30
250
260
270
280
290
300
Wavelength (nm)

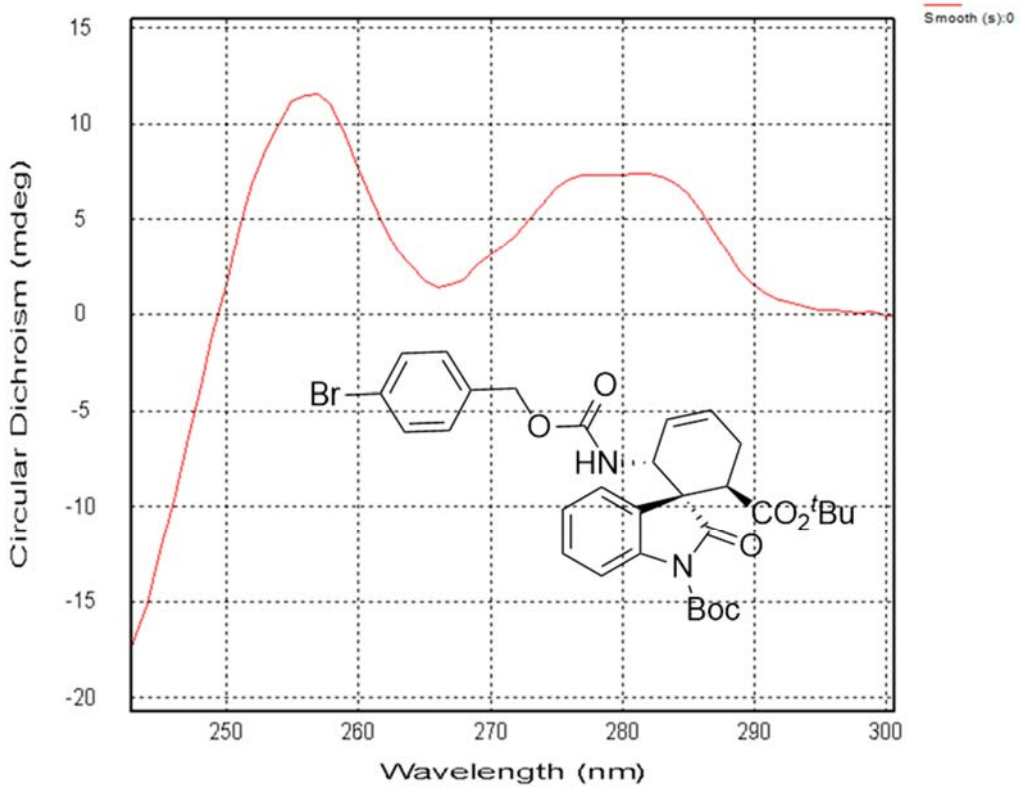
3m


Smooth (s):0
Cbz
HN
CO2tBu
O
N
Boc
Circular Dichroism (mdeg)
20
10
0
-10
-20
250
260
270
280
290
300
310
Wavelength (nm)

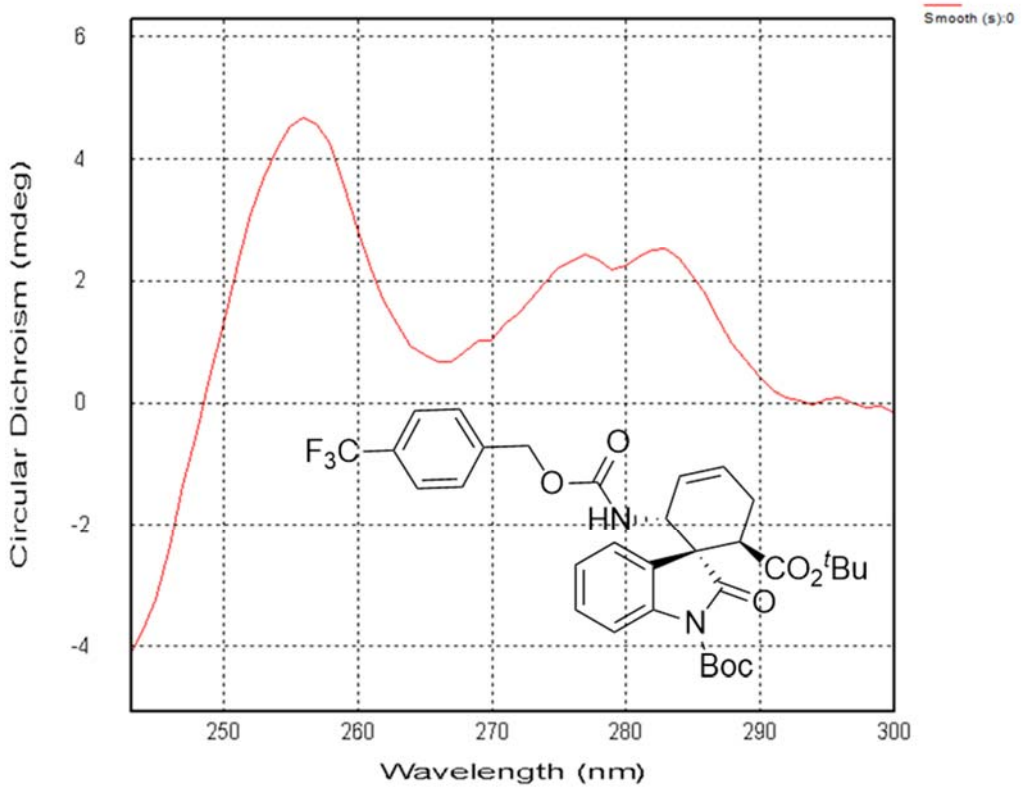
3n


Smooth (s):0
Cbz
HN
O
CO2tBu
O
N
Boc
Circular Dichroism (mdeg)
4
3
2
1
0
-1
-2
-3
-4
250
260
270
280
290
300
310
Wavelength (nm)

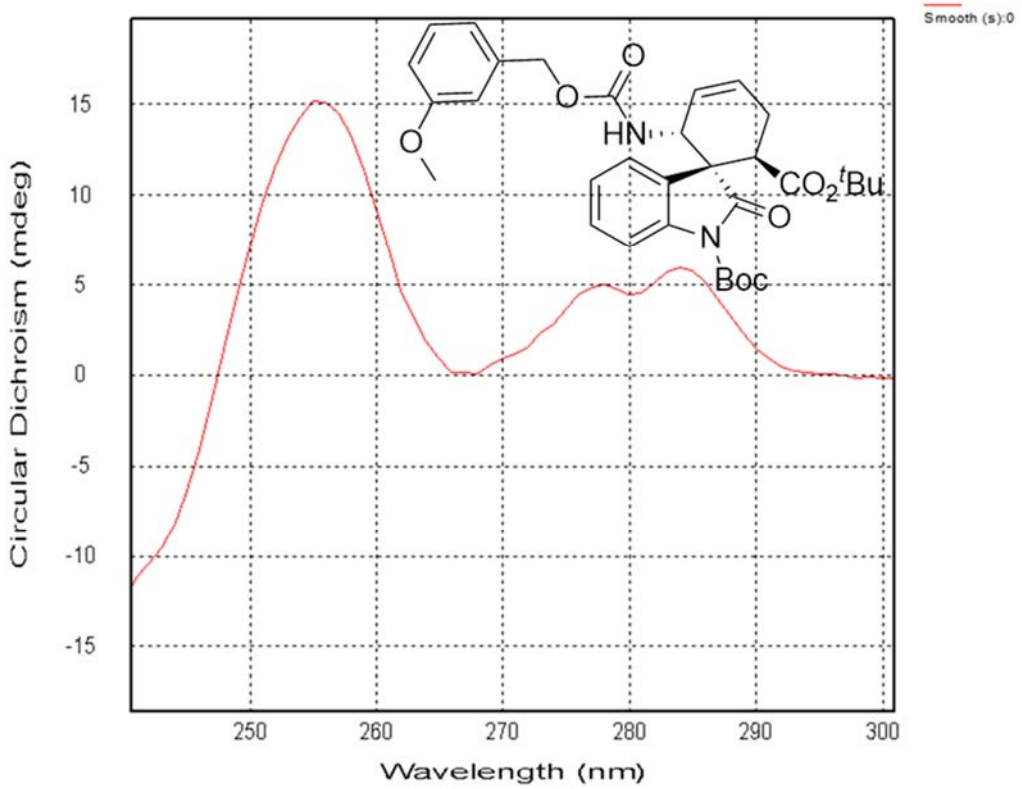
3o


Smooth (s):0
Circular Dichroism (mdeg)
15
10
5
0
-5
-10
-15
-20
250
260
270
280
290
300
Wavelength (nm)
Br
O
O
HN
CO2tBu
O
N
Boc

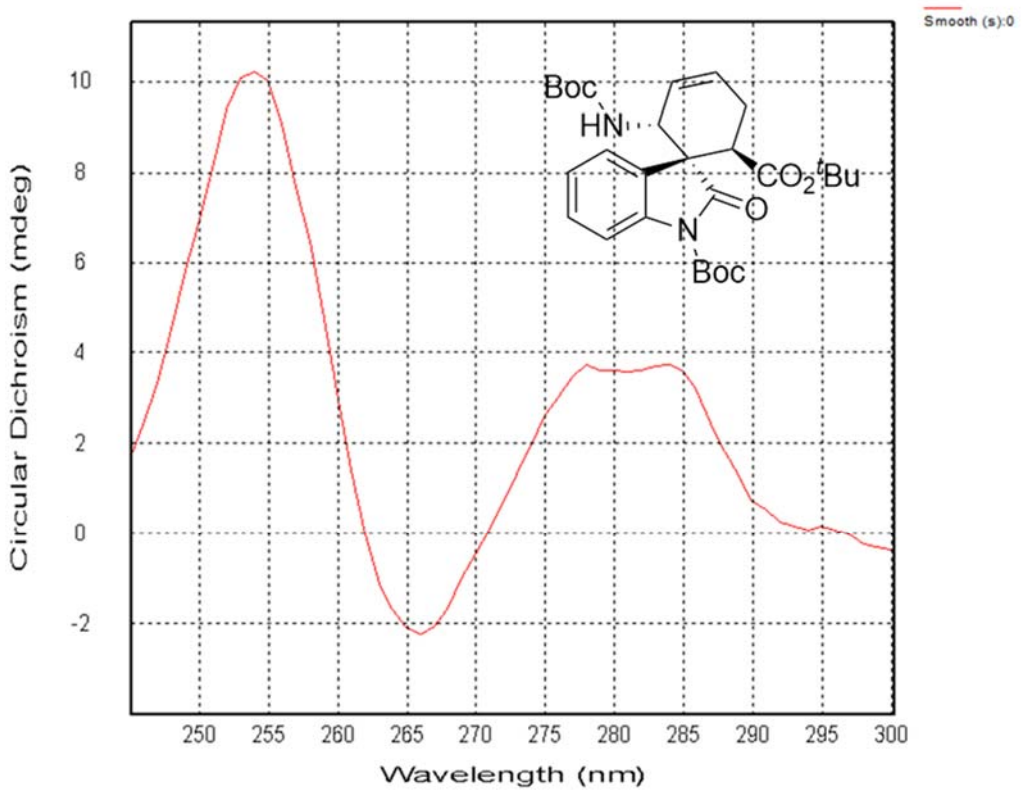
3p


Smooth (s):0
Circular Dichroism (mdeg)
6
4
2
0
-2
-4
250
260
270
280
290
300
Wavelength (nm)
F3C
O
O
HN
CO2tBu
O
N
Boc

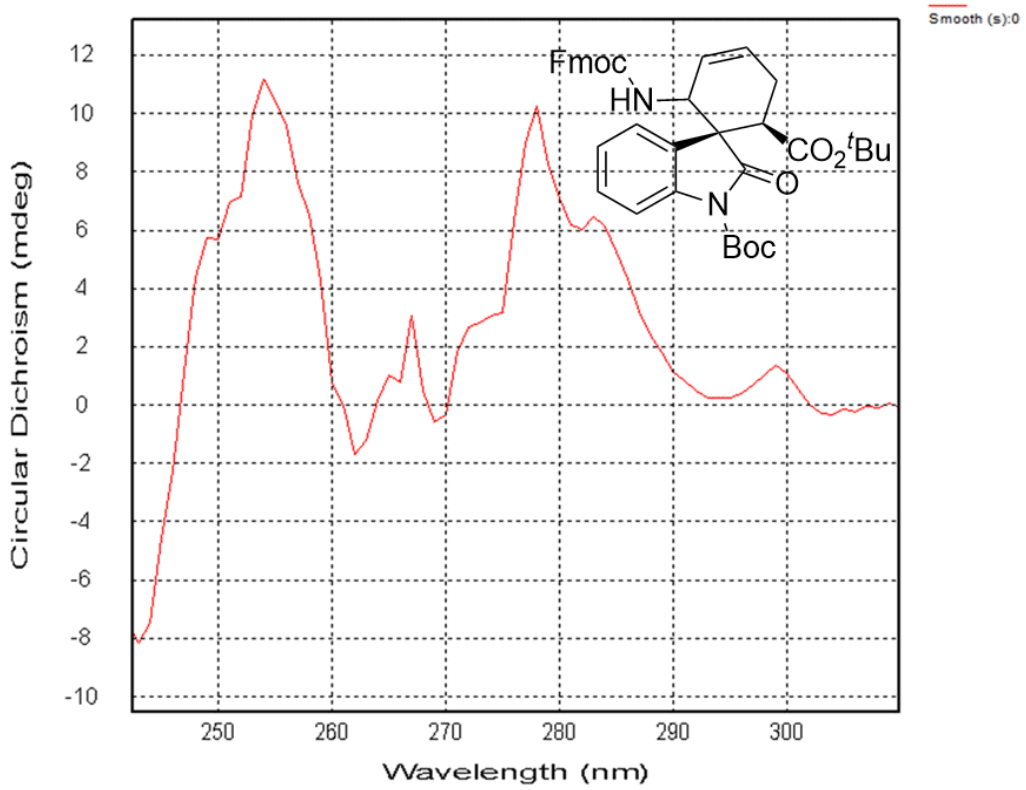
3q


Smooth (s):0
Circular Dichroism (mdeg)
15
10
5
0
-5
-10
-15
250
260
270
280
290
300
Wavelength (nm)
O
O
HN
O
CO2tBu
O
N
Boc
O

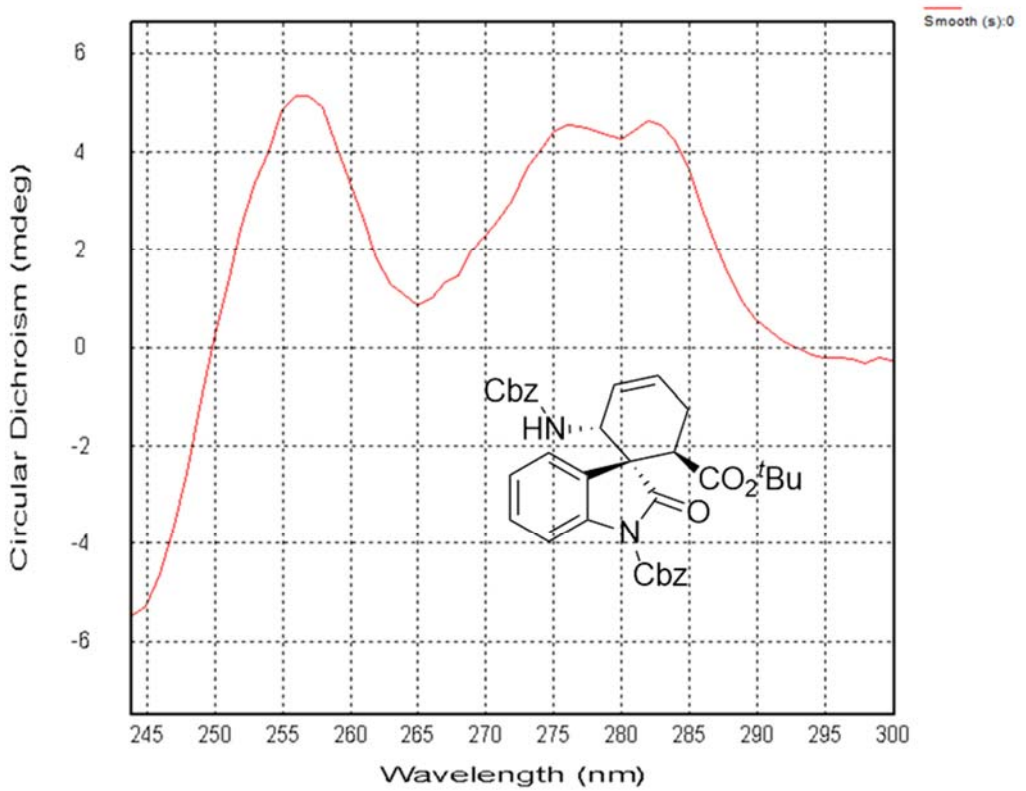
3r


Smooth (s):0
Circular Dichroism (mdeg)
10
8
6
4
2
0
-2
250
255
260
265
270
275
280
285
290
295
300
Wavelength (nm)
Boc
HN
CO2tBu
O
N
Boc

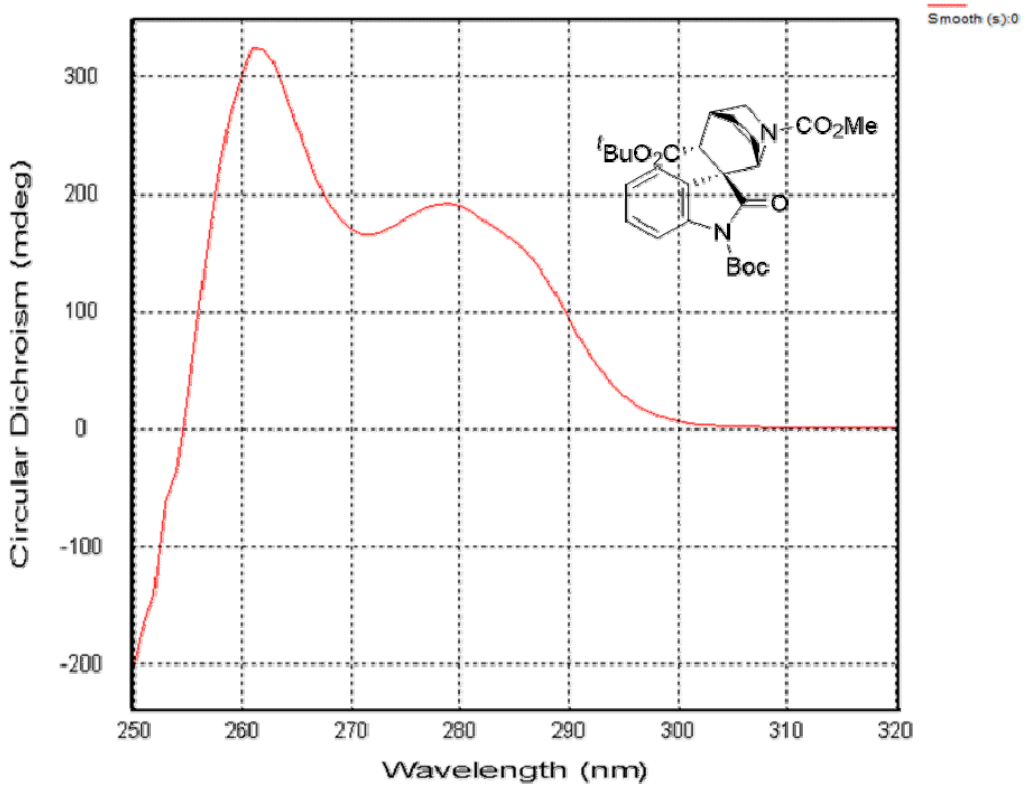
3s


Smooth (s):0
Fmoc
HN
$CO_2{}^tBu$
O
N
Boc
Circular Dichroism (mdeg)
12
10
8
6
4
2
0
-2
-4
-6
-8
-10
250
260
270
280
290
300
Wavelength (nm)

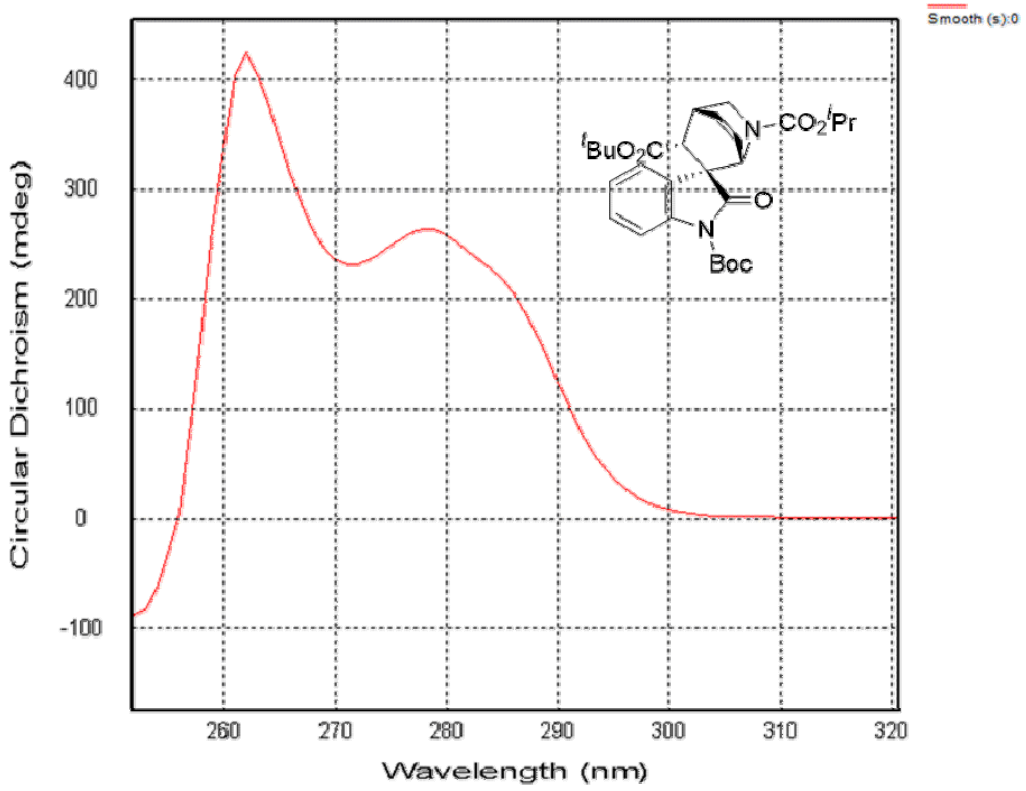
3u


Smooth (s):0
Cbz
HN
$CO_2{}^tBu$
O
N
Cbz
Circular Dichroism (mdeg)
6
4
2
0
-2
-4
-6
245
250
255
260
265
270
275
280
285
290
295
300
Wavelength (nm)

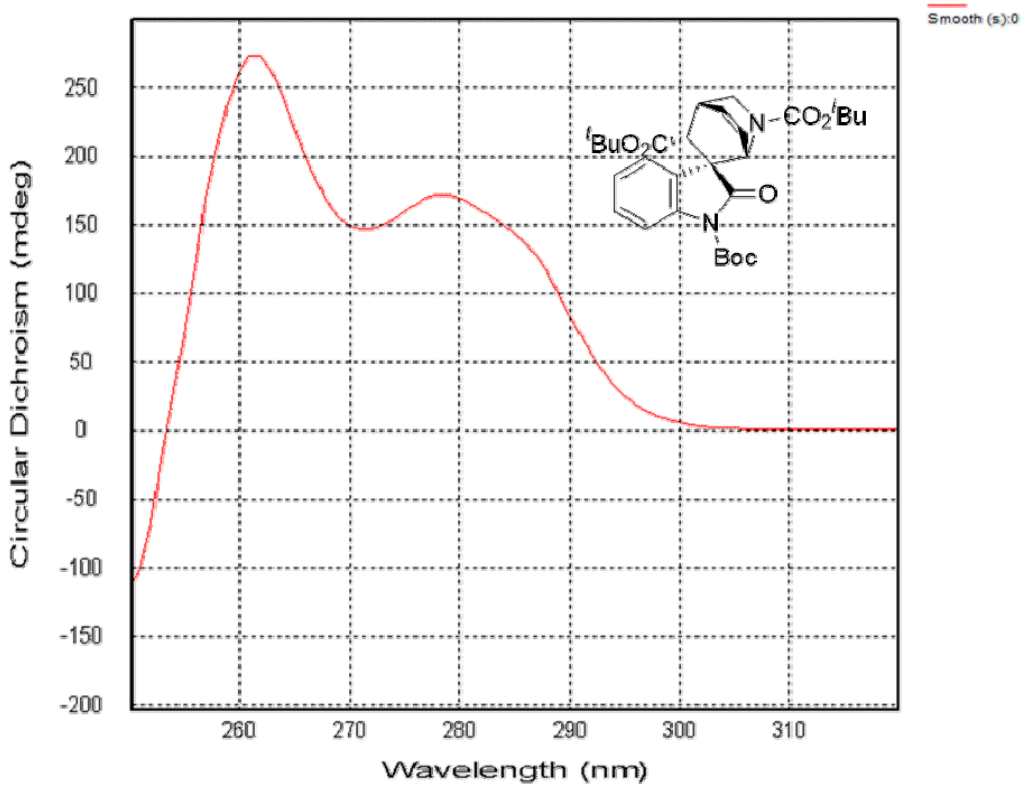
5a


Smooth (s):0
Circular Dichroism (mdeg)
300
200
100
0
-100
-200
250
260
270
280
290
300
310
320
Wavelength (nm)
tBuO2C
N
CO2Me
O
N
Boc

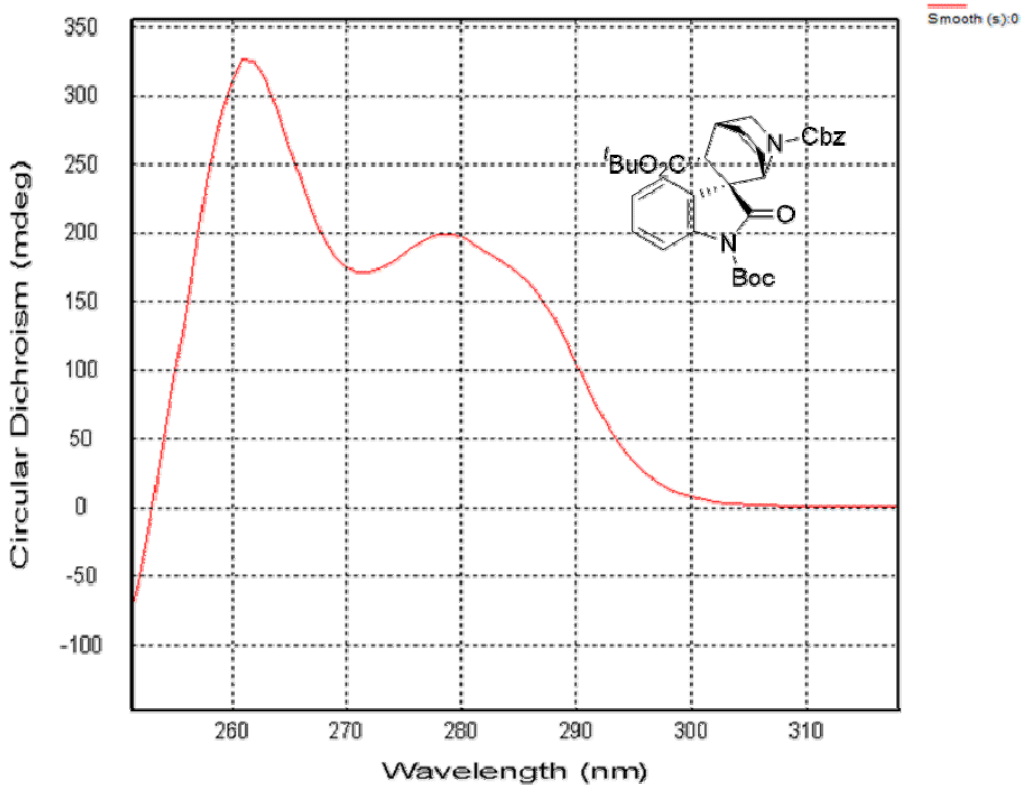
5b


Smooth (s):0
Circular Dichroism (mdeg)
400
300
200
100
0
-100
260
270
280
290
300
310
320
Wavelength (nm)
tBuO2C
N
CO2iPr
O
N
Boc

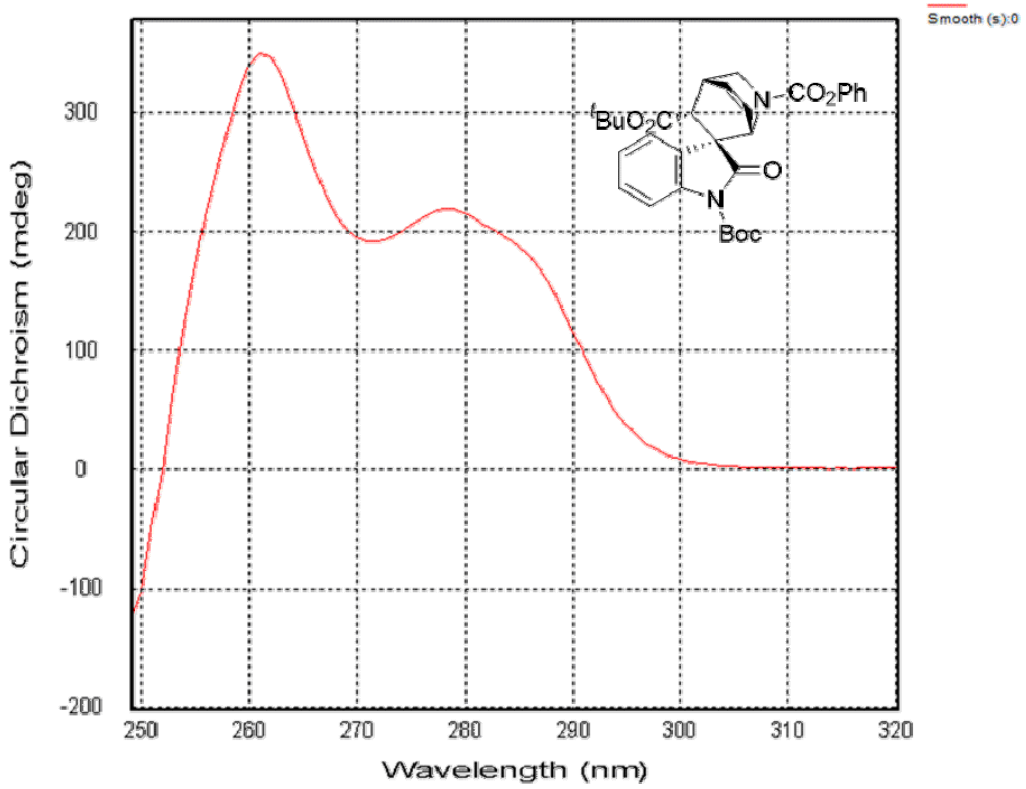
5c


Smooth (s):0
Circular Dichroism (mdeg)
250
200
150
100
50
0
-50
-100
-150
-200
260
270
280
290
300
310
Wavelength (nm)
tBuO2C
N-CO2tBu
O
N
Boc

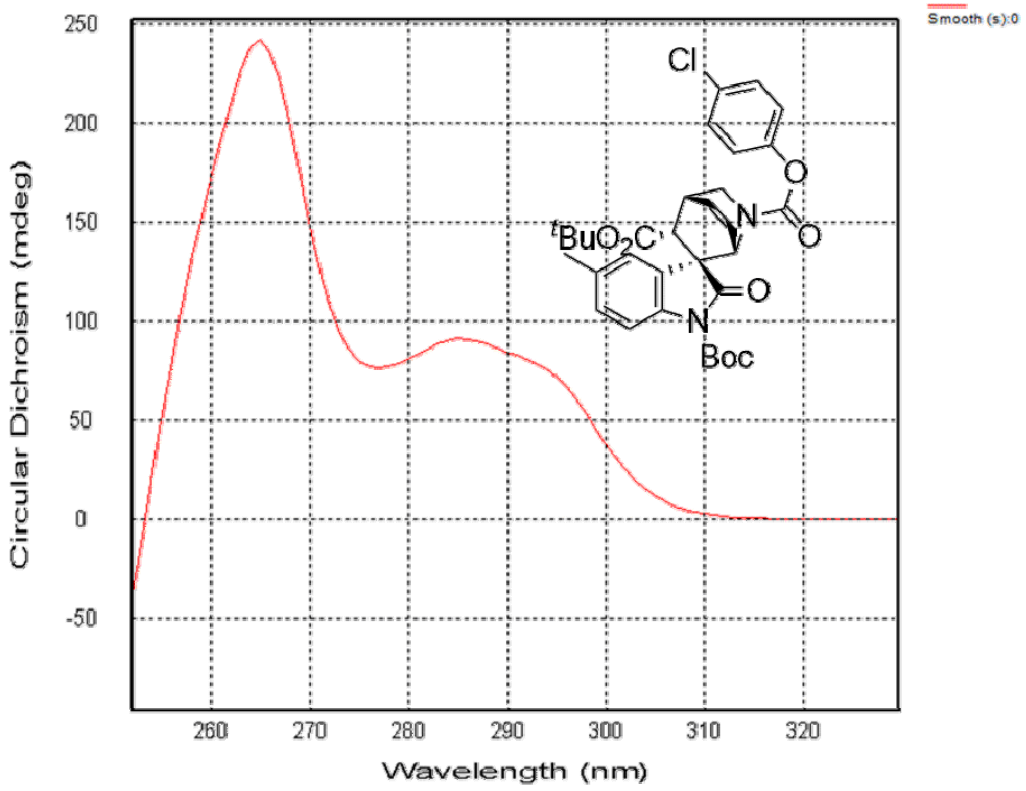
5d


Smooth (s):0
Circular Dichroism (mdeg)
350
300
250
200
150
100
50
0
-50
-100
260
270
280
290
300
310
Wavelength (nm)
tBuO2C
N-Cbz
O
N
Boc

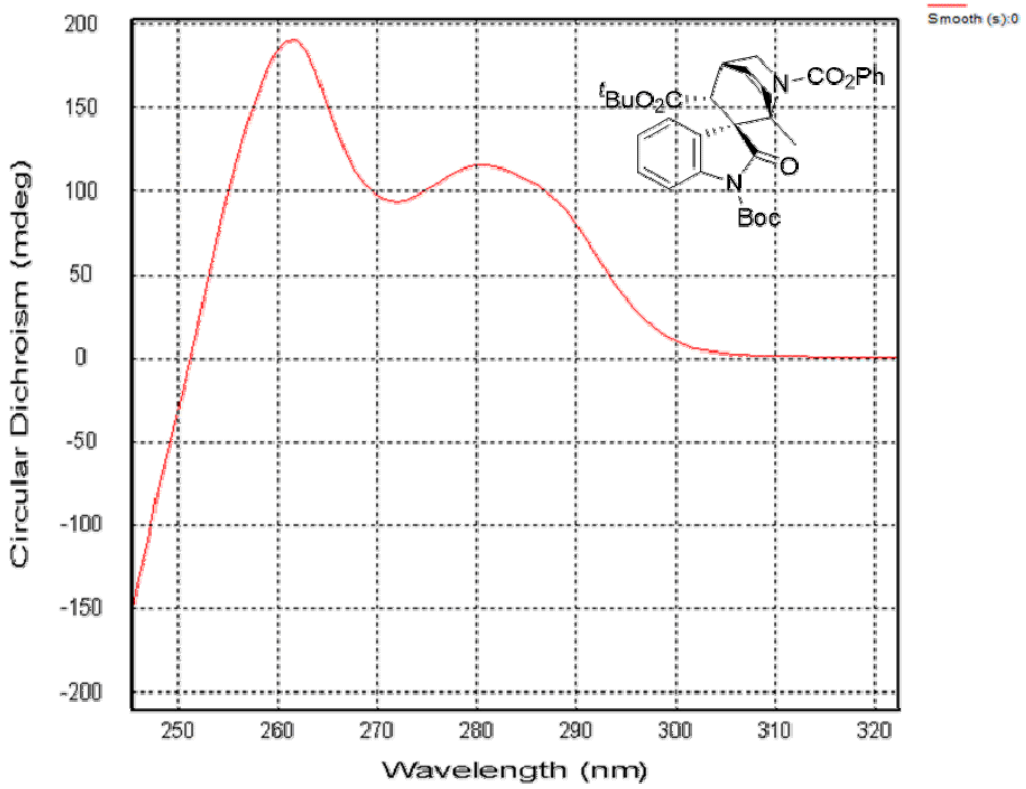
5e


Smooth (s):0
Circular Dichroism (mdeg)
300
200
100
0
-100
-200
250
260
270
280
290
300
310
320
Wavelength (nm)
tBuO2C
N
CO2Ph
O
N
Boc

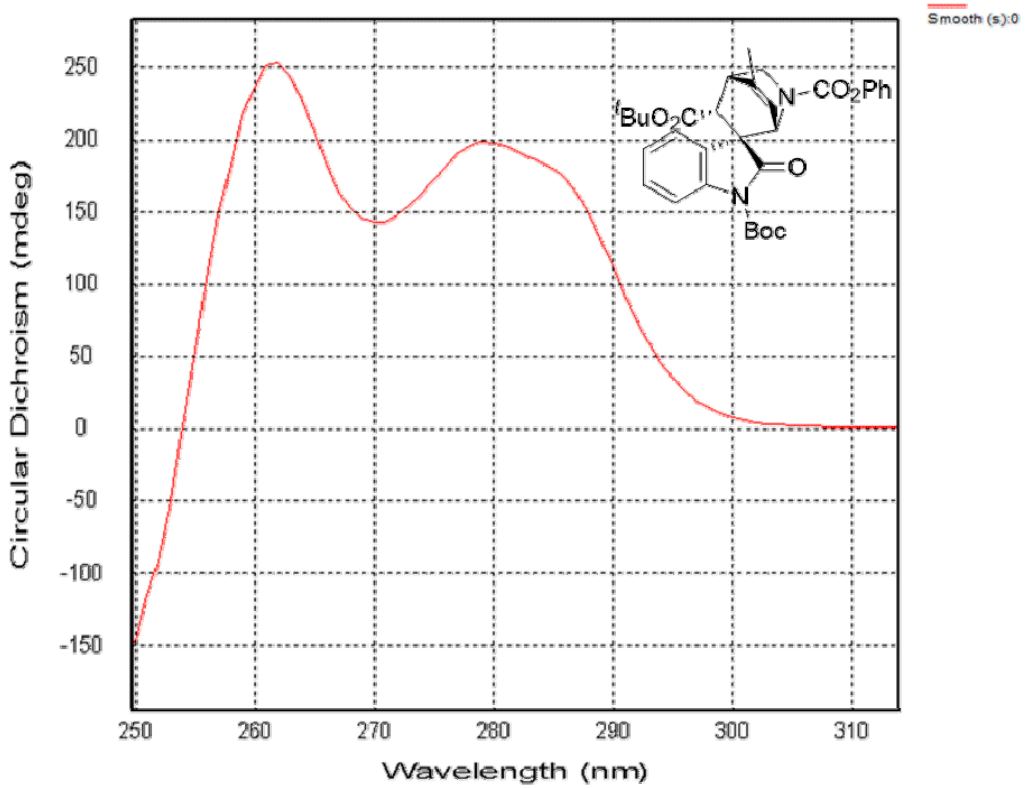
5f


Smooth (s):0
Circular Dichroism (mdeg)
250
200
150
100
50
0
-50
260
270
280
290
300
310
320
Wavelength (nm)
Cl
O
N
O
tBuO2C
O
N
Boc

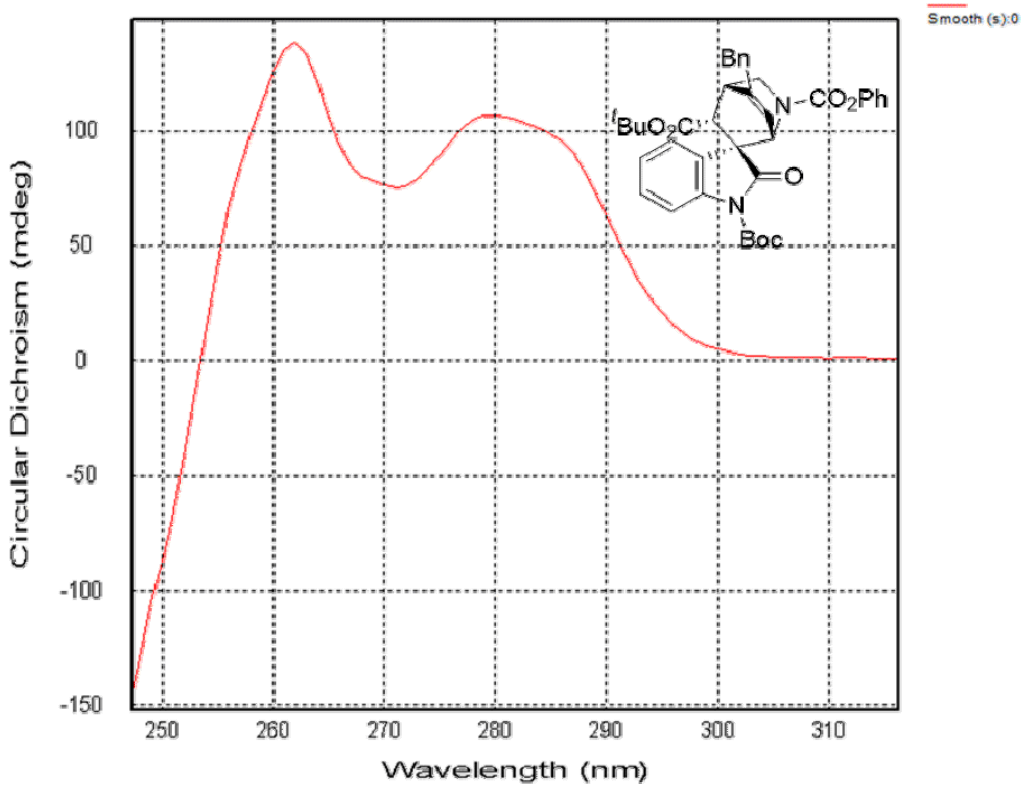
5g


Smooth (s):0
Circular Dichroism (mdeg)
200
150
100
50
0
-50
-100
-150
-200
250
260
270
280
290
300
310
320
Wavelength (nm)
^{t}BuO$_2$C
N-CO$_2$Ph
O
N
Boc

5h


Smooth (s):0
Circular Dichroism (mdeg)
250
200
150
100
50
0
-50
-100
-150
250
260
270
280
290
300
310
Wavelength (nm)
^{t}BuO$_2$C
N-CO$_2$Ph
O
N
Boc

5i


Smooth (s):0
Circular Dichroism (mdeg)
100
50
0
-50
-100
-150
250
260
270
280
290
300
310
Wavelength (nm)
Bn
N
CO2Ph
tBuO2C
O
N
Boc

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