

Supporting Information

Solvent-Minimized, Chromatography-Free, Diastereoselective Synthesis of Oxazolidine-Dispirooxindoles via *oxa*-1, 3-Dipolar Cycloaddition of 3-Oxindole

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1. Studies on stability of product

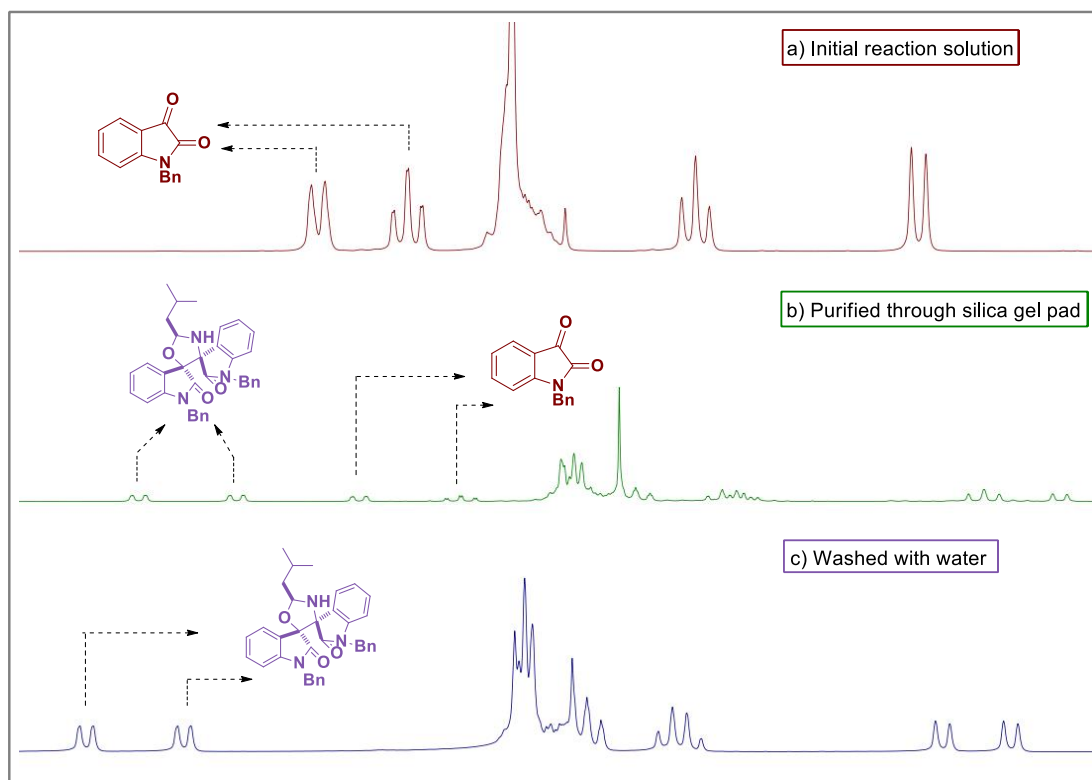
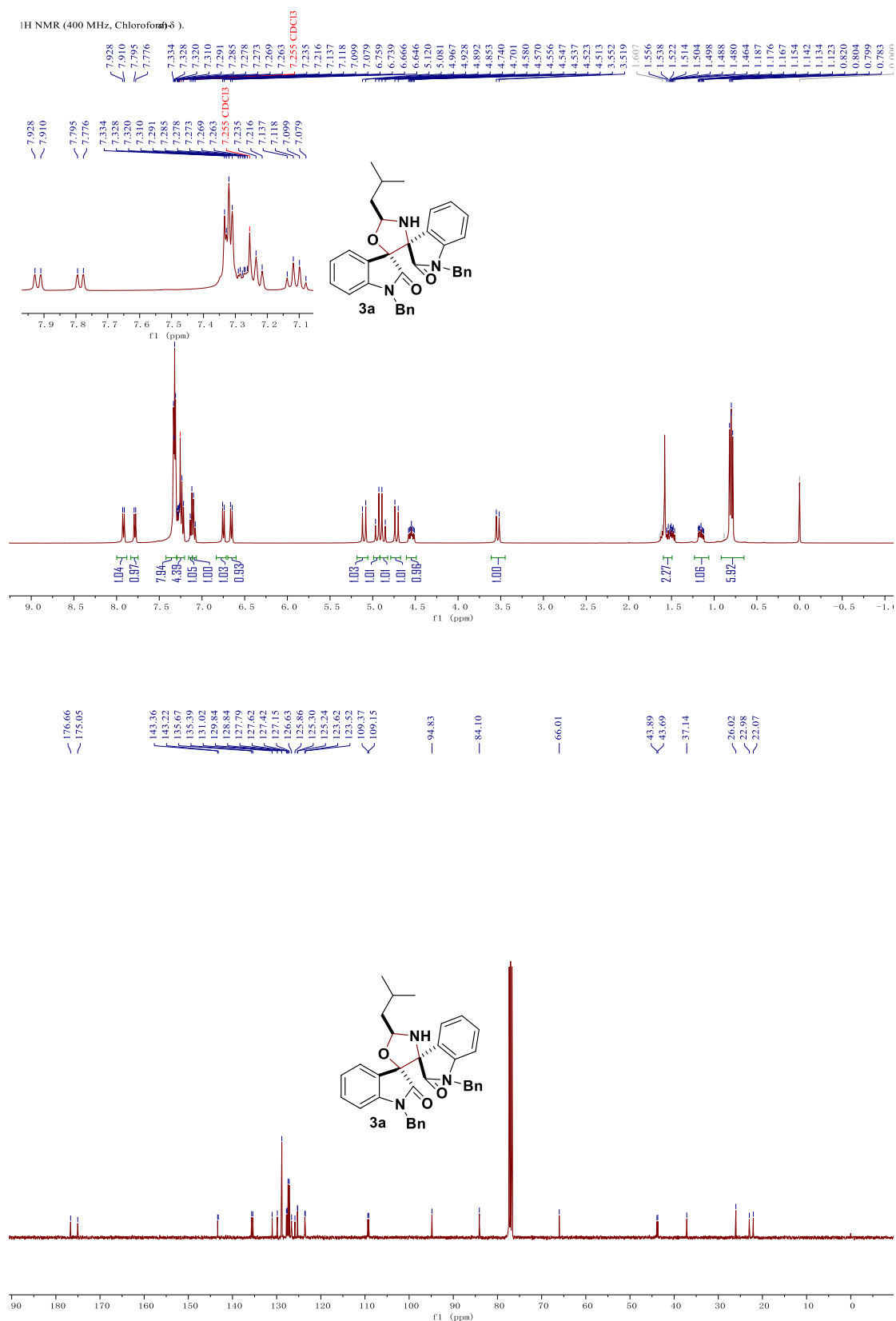


Figure S1 NMR spectra of (a) initial mixture of **1a** and **2a**; (b) reaction mixture purified through silica gel pad; (c) reaction mixture washed with water.

In order to better understand the inherent features of cycloadduct **3a**, different purification modes of **3a** were carried out and the results are presented in Figure S1. Once the reaction was complete, the reaction mixture was purified through a short silica gel pad. It was found that the resulting cycloadduct **3a** partially decomposed to give starting material **1a** (Fig. S1b), suggesting that **3a** is sensitive to acidic condition. On the other hand, the reaction mixture was subjected to washing with water, affording pure **3a** in excellent yield (Fig. S1c). Moreover, NMR spectrum of pure **3a** is still clean after being saved in air as solid for several days, suggesting that **3a** is quite stable as solid state.

2. NMR spectra of compound 3a-3g, 4a-4m



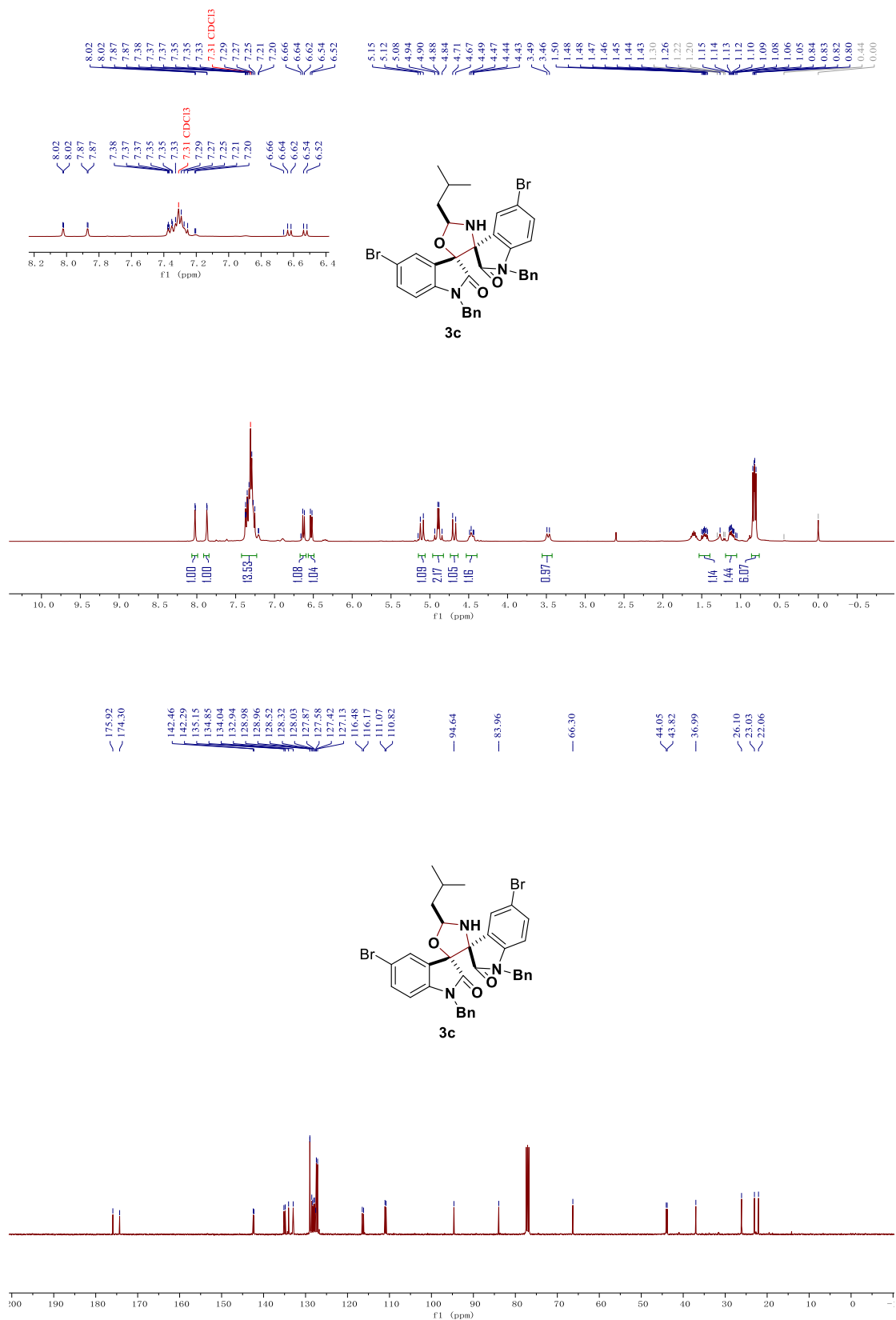
The figure displays the chemical structure of compound **3b** and its corresponding ¹H and ¹³C NMR spectra.

Chemical Structure of 3b: The structure shows a central benzene ring substituted with a 2-chlorophenyl group, a 2-chlorophenyl group, and a 2-chlorophenyl group. The central ring is also substituted with a 2-chlorophenyl group and a 2-chlorophenyl group. The structure is labeled **3b**.

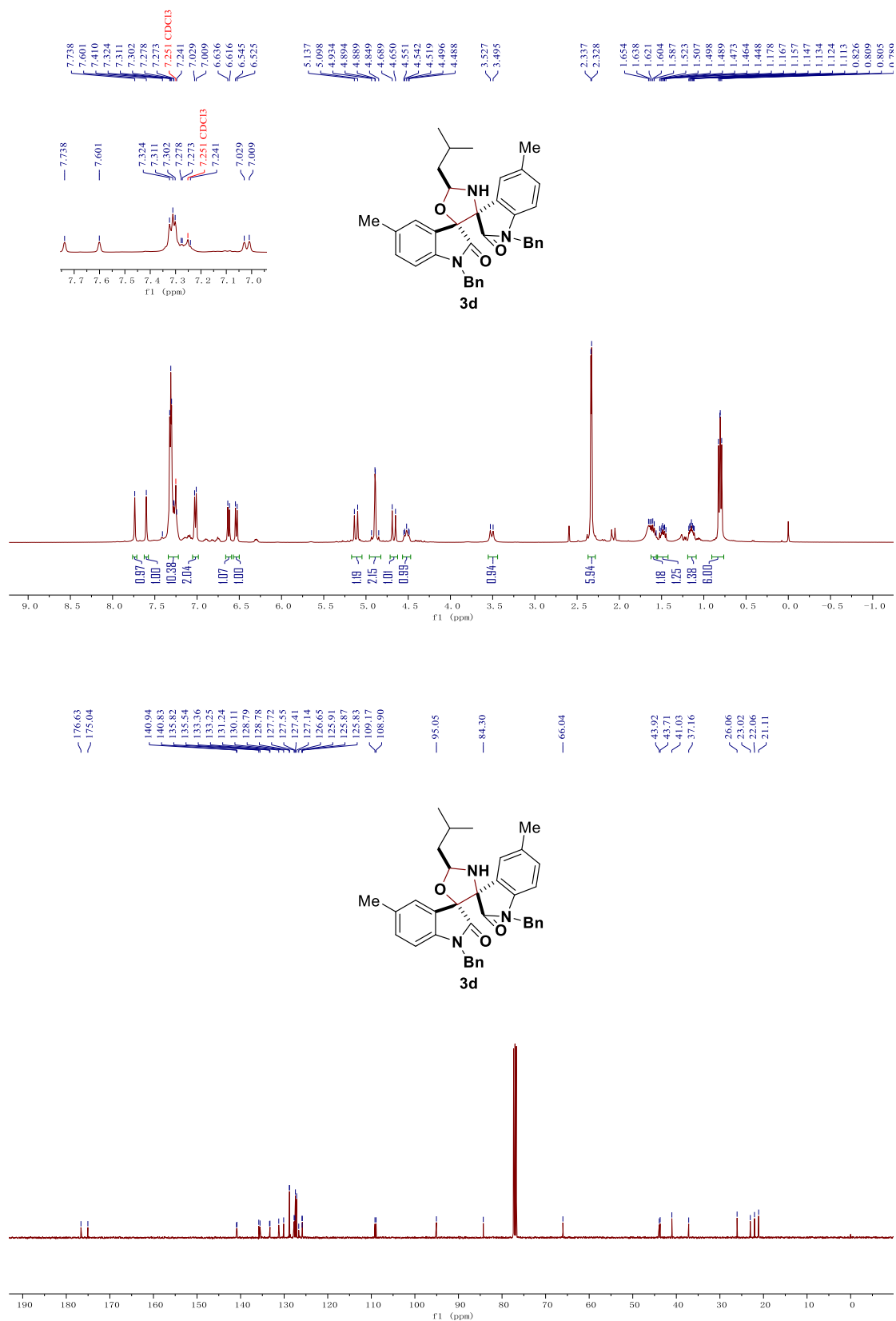
¹H NMR Spectrum (Top): The spectrum shows peaks in the aromatic region (6.6–7.9 ppm) and aliphatic region (1.0–3.5 ppm). Key peaks are labeled with their chemical shifts (ppm): 7.898, 7.892, 7.748, 7.743, 7.743, 7.351, 7.348, 7.330, 7.326, 7.317, 7.312, 7.296, 7.289, 7.286, 7.282, 7.266, 7.269, 7.256, 7.235, 7.205, 7.200, 7.216, 7.205, 7.200, 7.195, 6.683, 6.662, 6.587, 6.566, 5.117, 5.078, 4.946, 4.906, 4.886, 4.846, 4.722, 4.683, 4.507, 4.497, 4.482, 4.474, 4.465, 4.450, 4.439, 3.497, 3.464, 1.506, 1.491, 1.481, 1.472, 1.466, 1.456, 1.447, 1.447, 1.432, 1.150, 1.140, 1.130, 1.117, 1.106, 1.096, 1.086, 1.077, 1.062, 0.842, 0.826, 0.817, 0.801, and -0.000.

¹³C NMR Spectrum (Bottom): The spectrum shows peaks in the aromatic region (110–142 ppm) and aliphatic region (22–44 ppm). Key peaks are labeled with their chemical shifts (ppm): 176.06, 174.45, 141.93, 141.77, 135.18, 134.88, 131.10, 130.01, 129.18, 128.96, 128.95, 128.80, 128.62, 127.86, 127.42, 127.26, 127.12, 126.84, 125.77, 125.56, 110.60, 110.35, 94.69, 84.00, 66.29, 44.05, 43.82, 36.99, 26.07, 23.02, and 22.04.

^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)

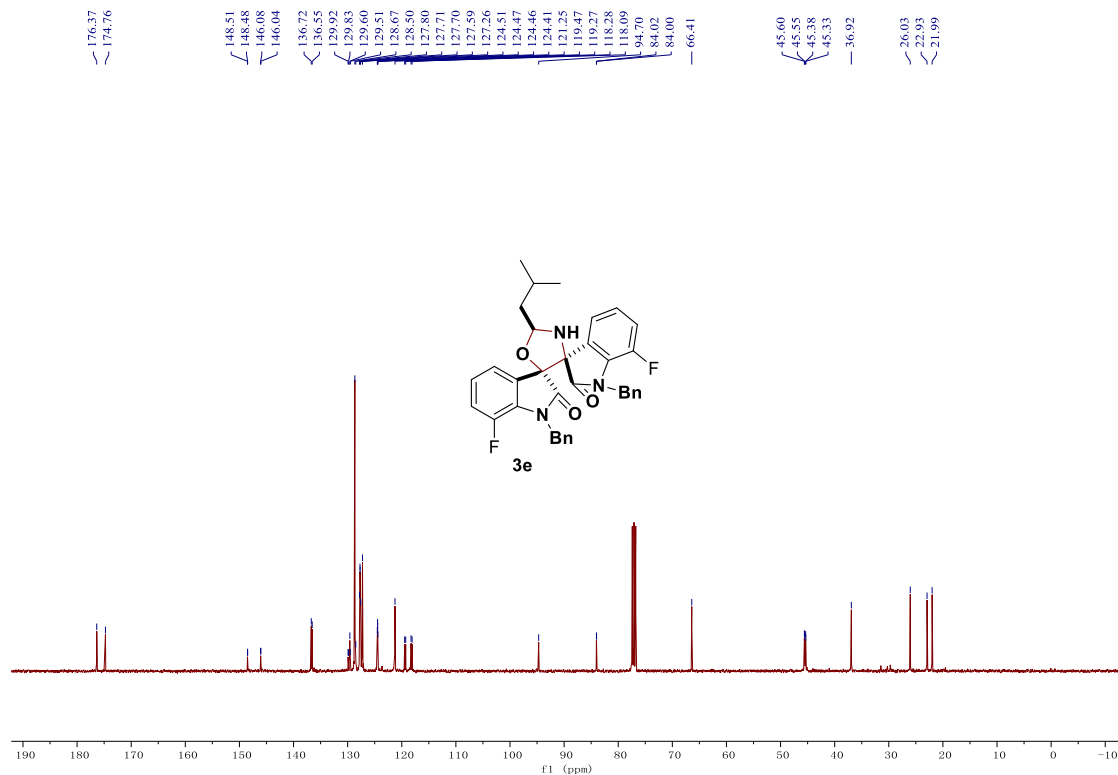


^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)

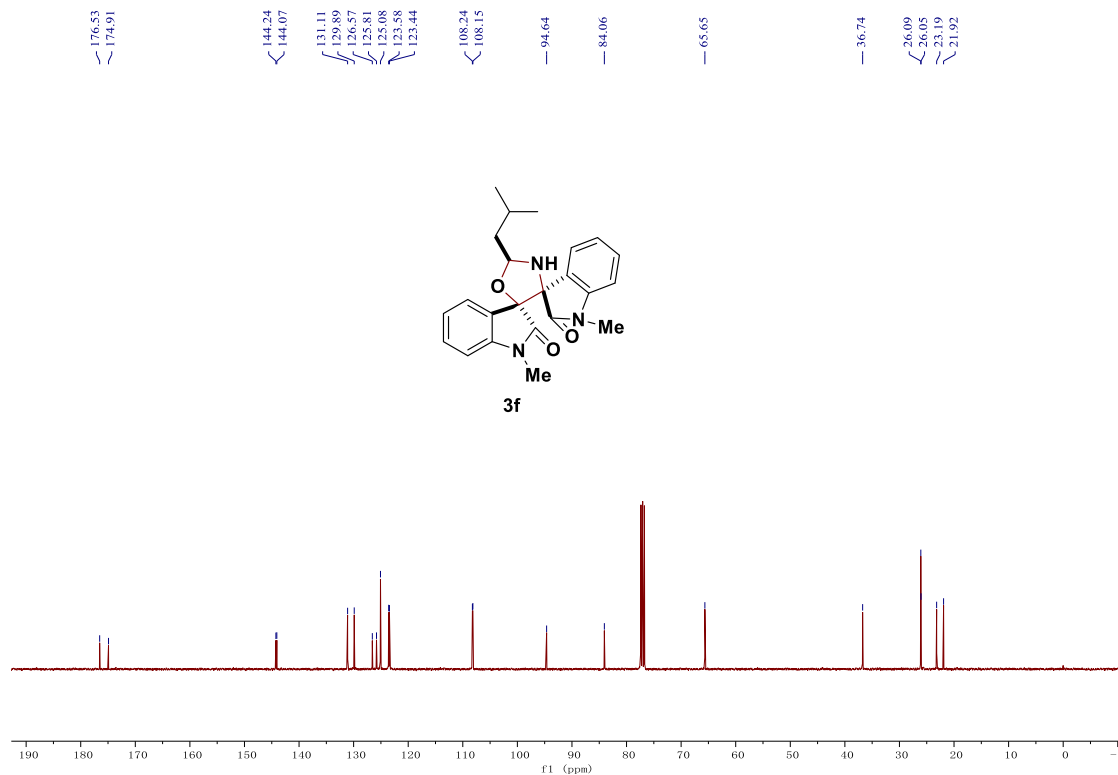
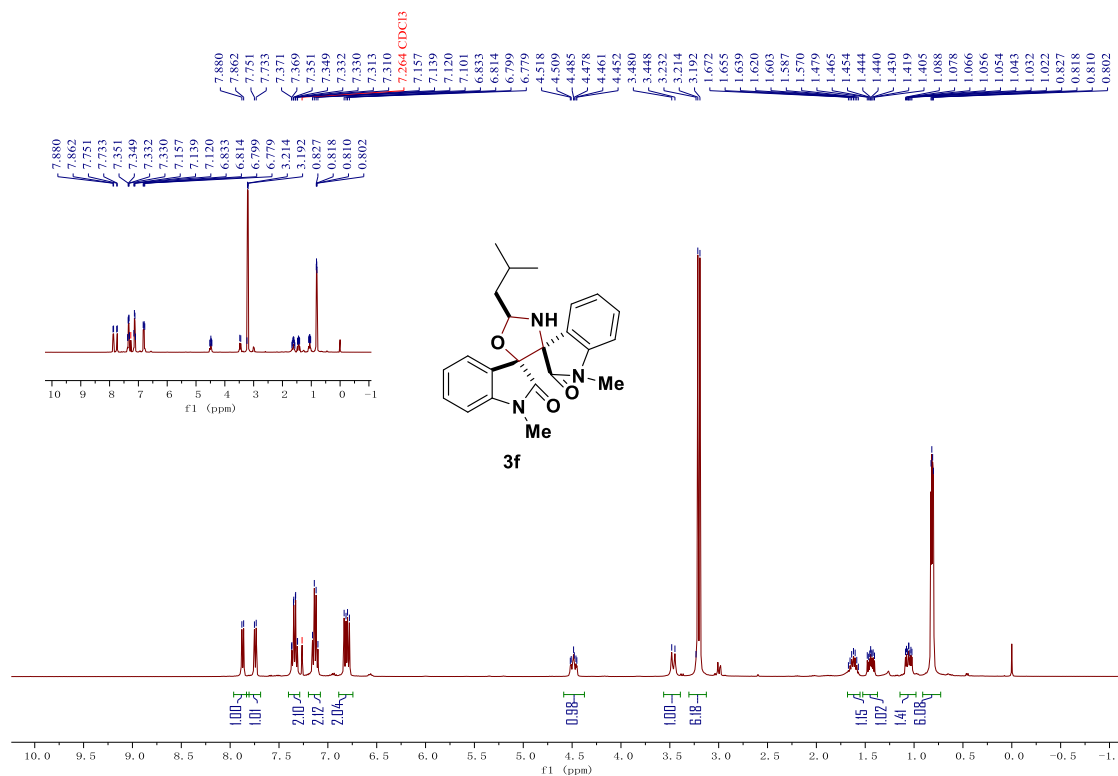


Chemical structure of **3e** is shown above the spectrum. The structure is a complex molecule featuring a benzene ring with a fluorine substituent, a benzyl group, and a chiral auxiliary (a 1,3-dioxolane ring with a benzyl group and a fluorine substituent).

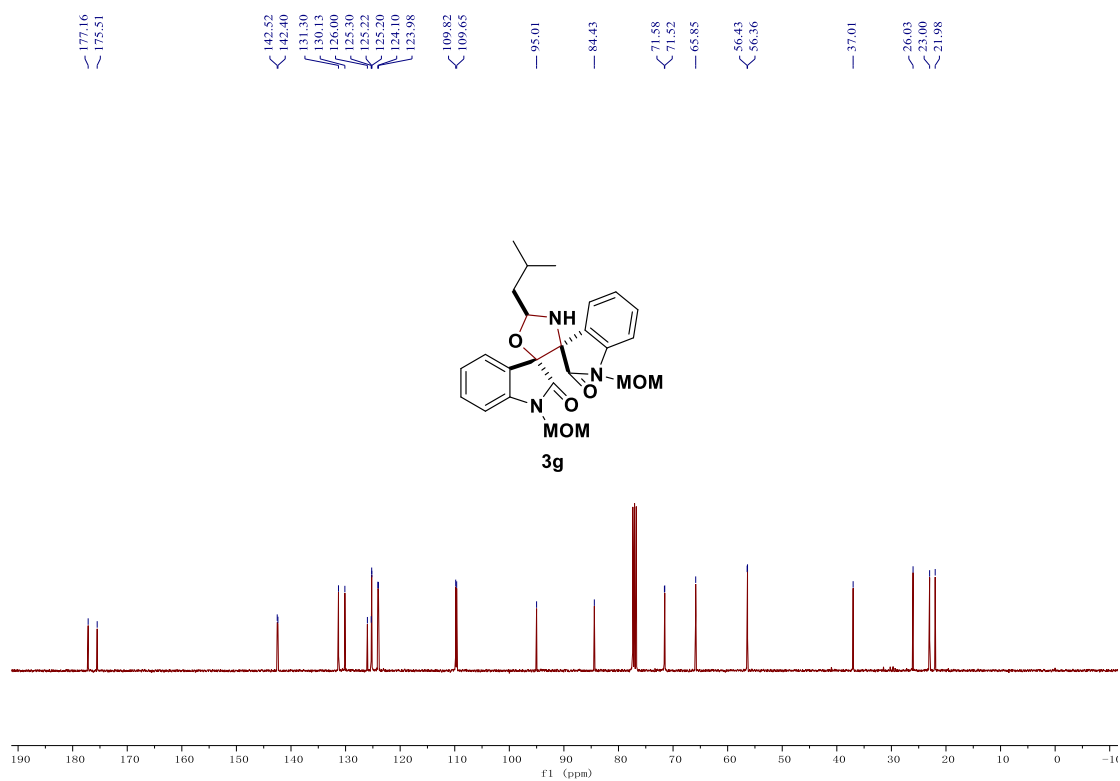
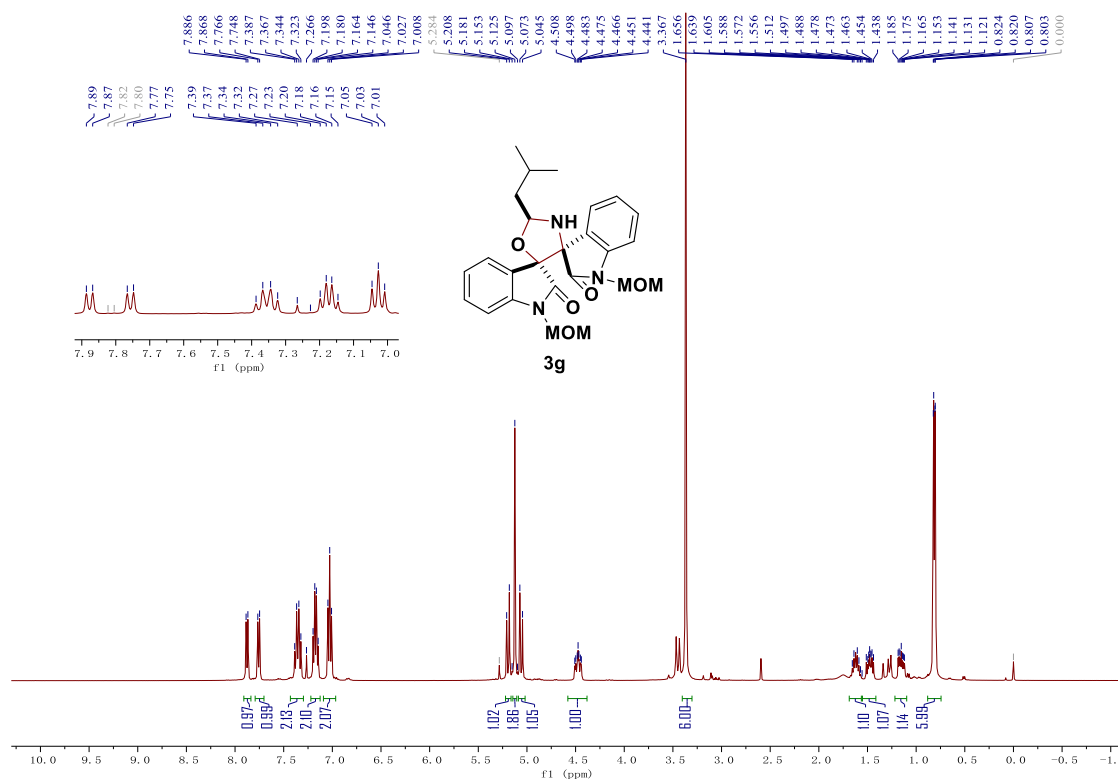
¹H NMR spectrum (CDCl₃) of compound **3e**. The spectrum shows peaks from 0 to 8 ppm. Integration values are provided below the peaks: 1.00, 1.02, 3.23, 5.07, 4.55, 1.05, 1.06, 1.20, 1.12, 1.00, and 6.14. A chemical structure of **3e** is shown above the spectrum.



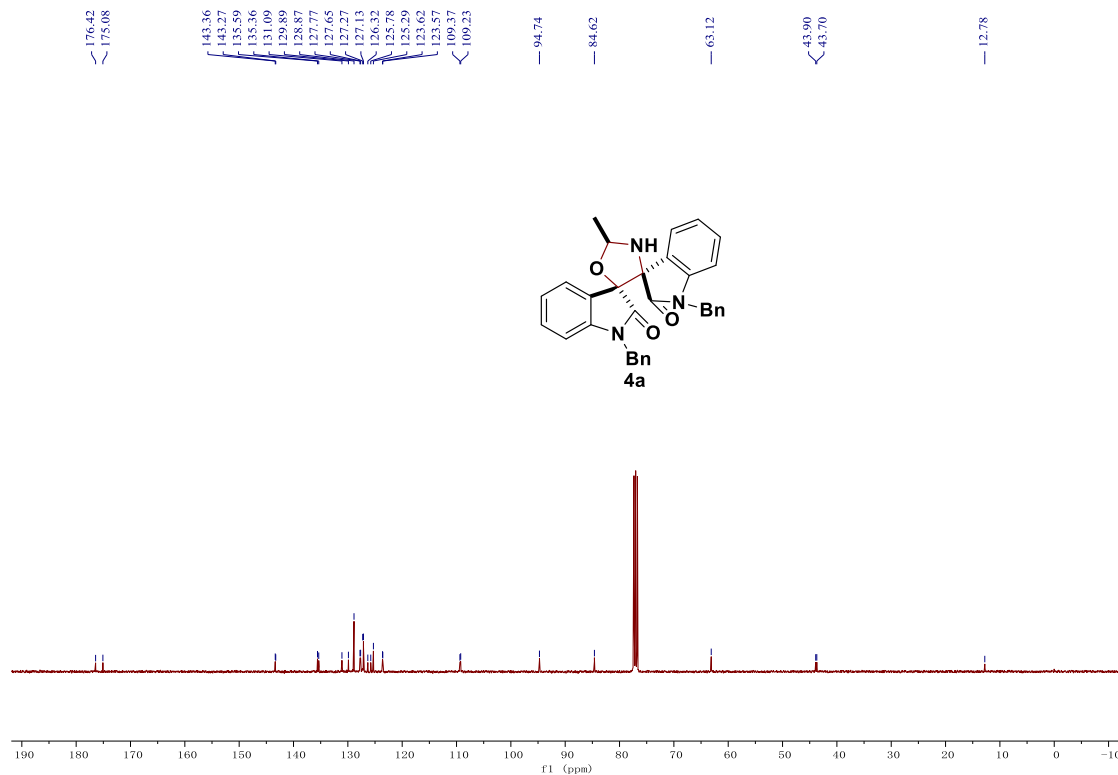
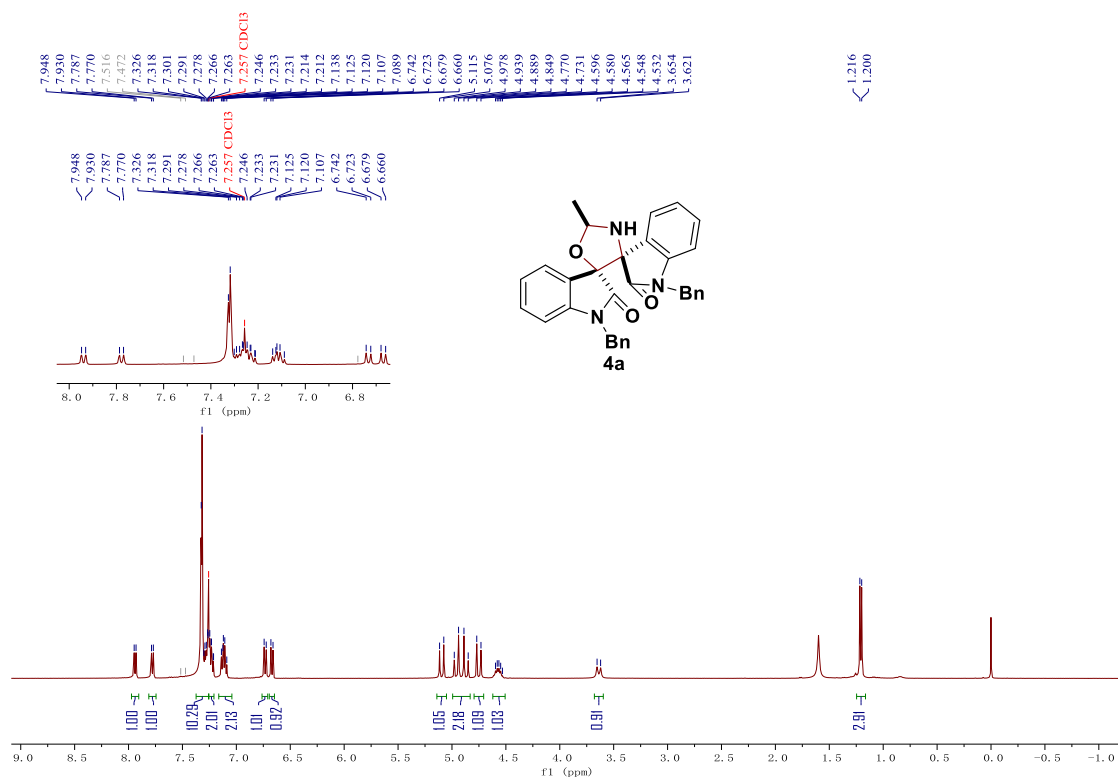
^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



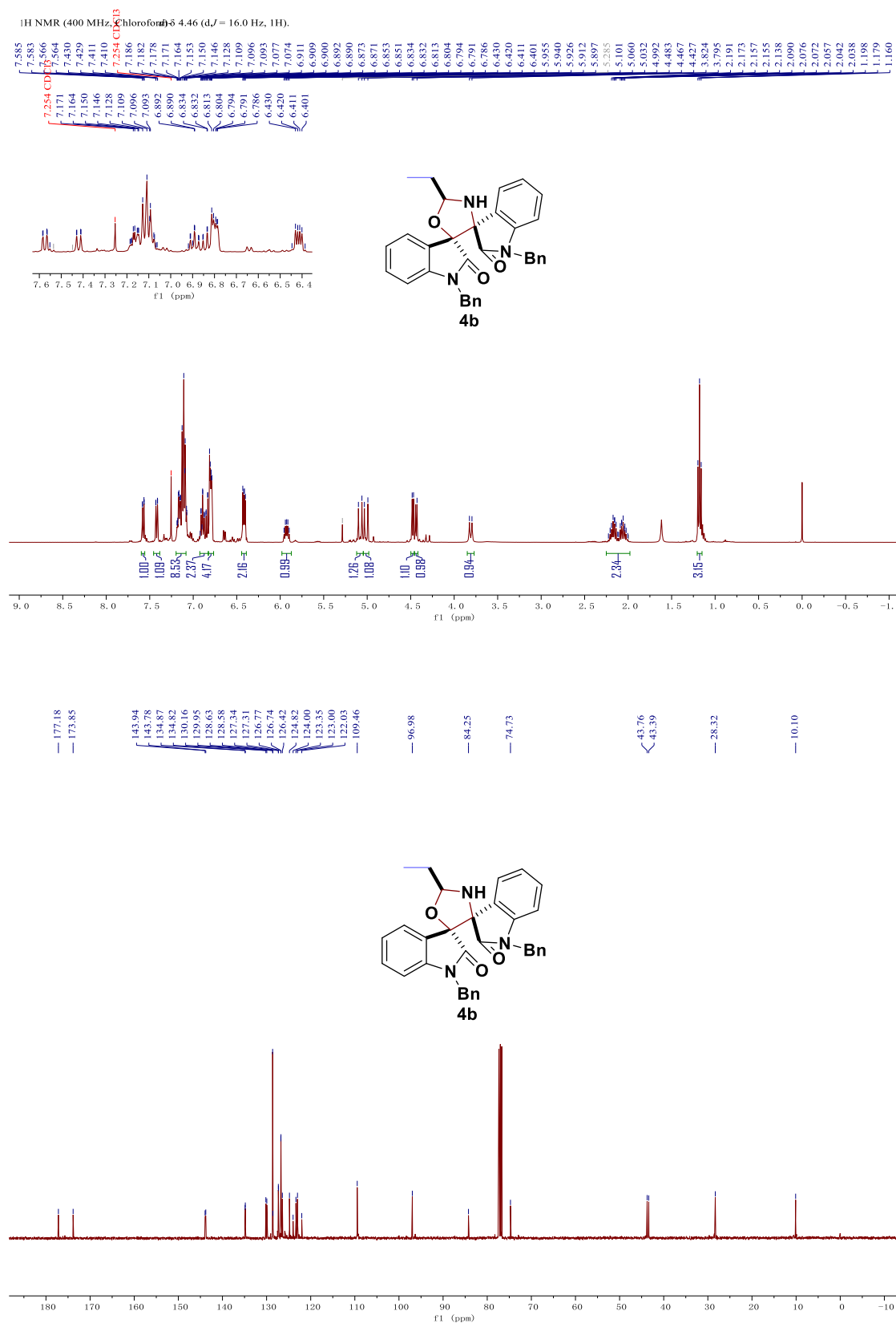
^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



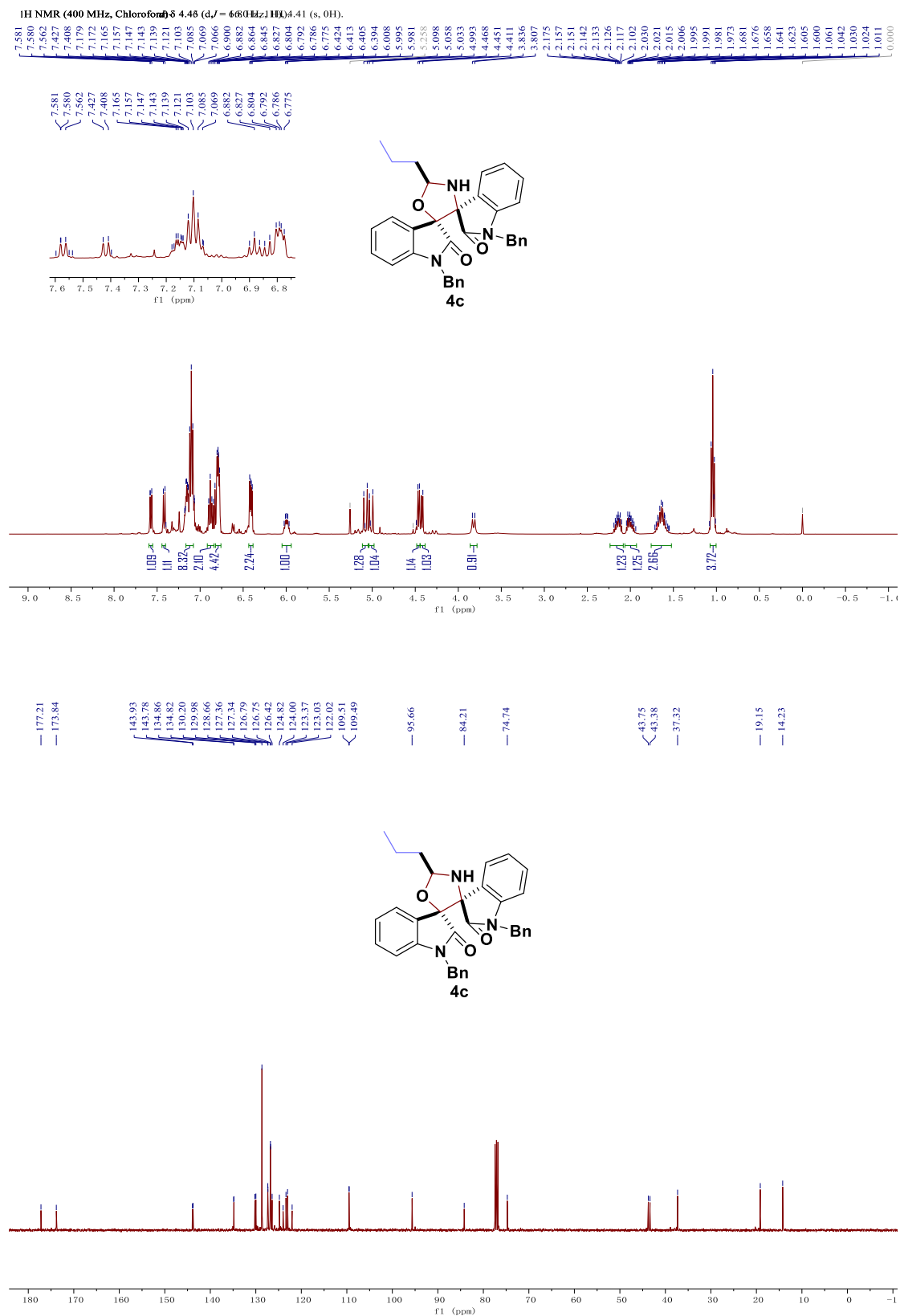
^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



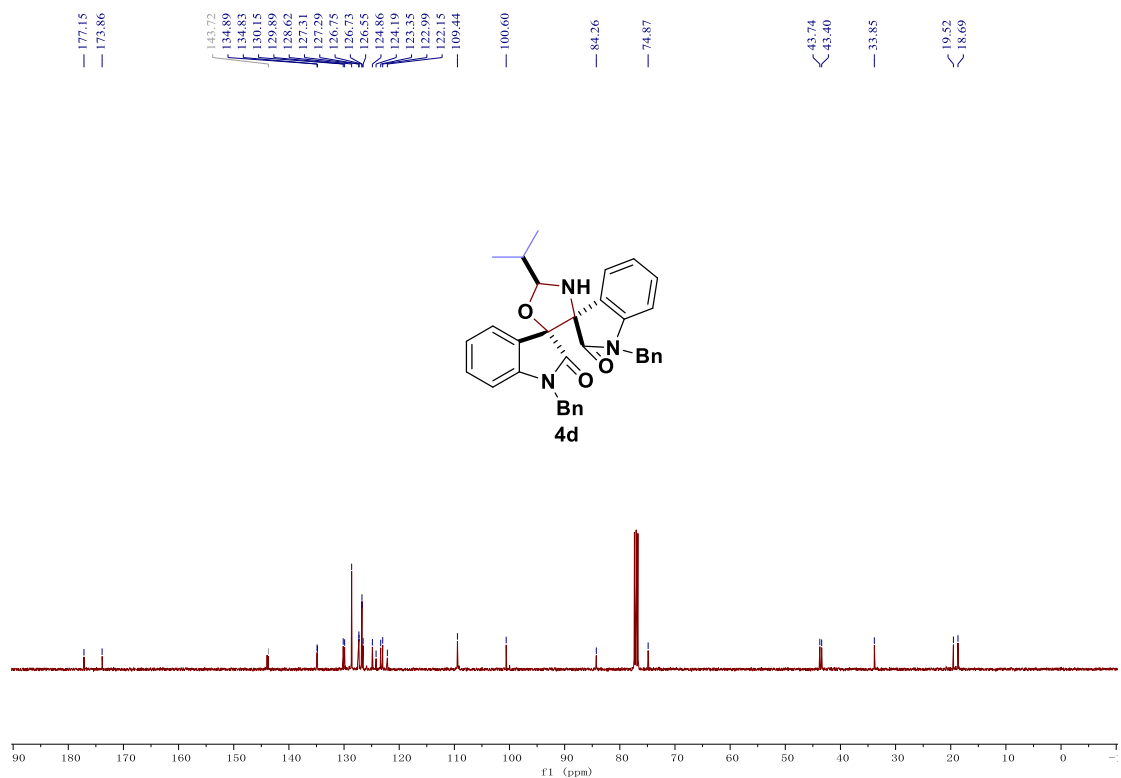
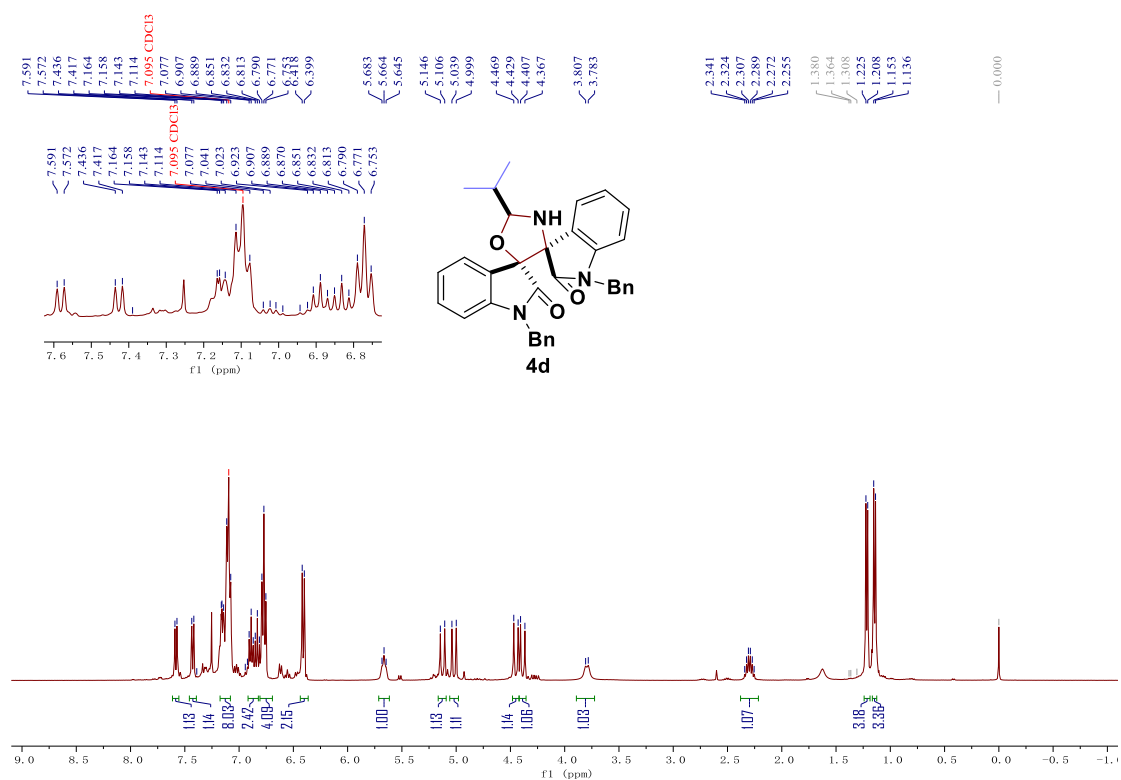
^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)

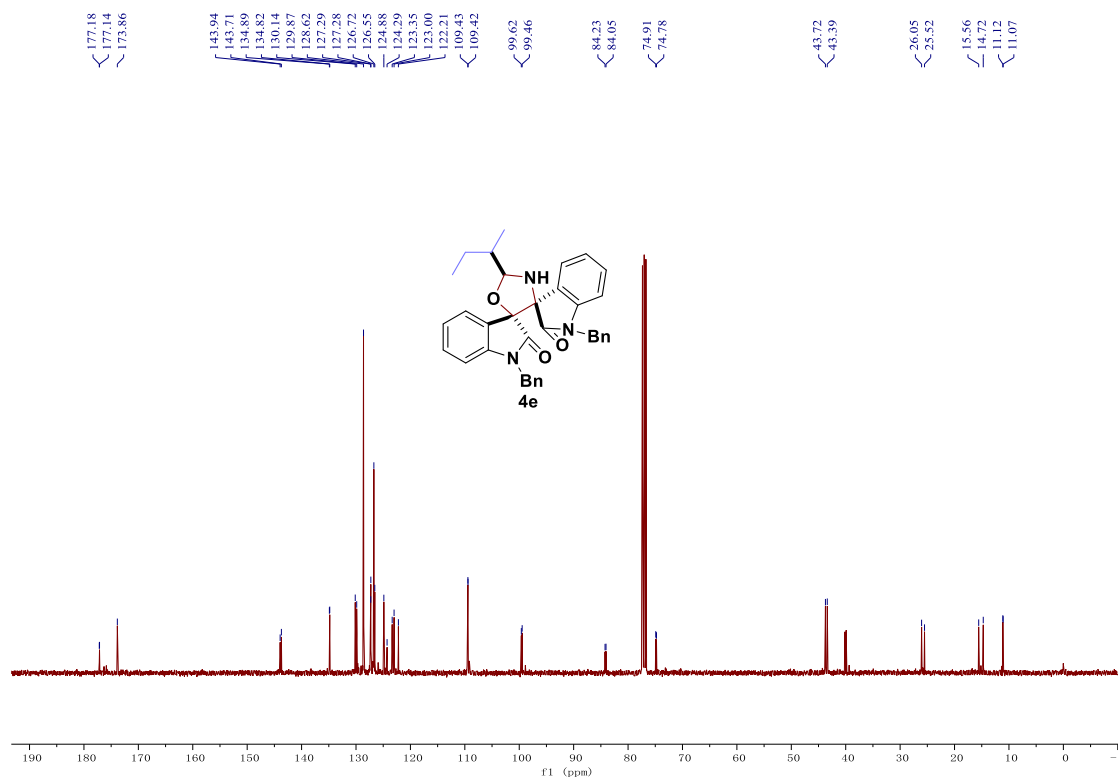
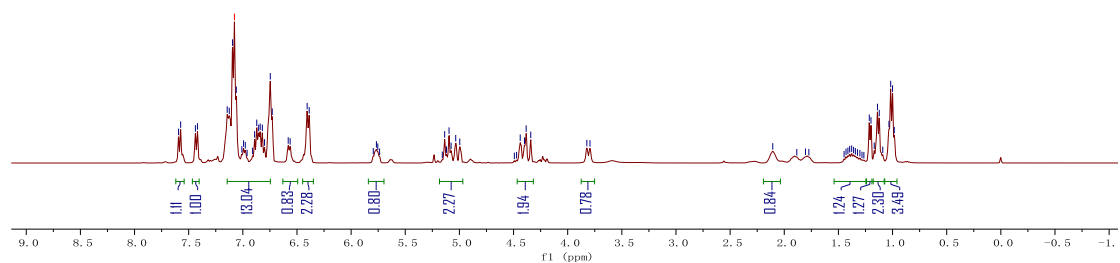


¹H NMR spectrum of compound 4e in CDCl₃.

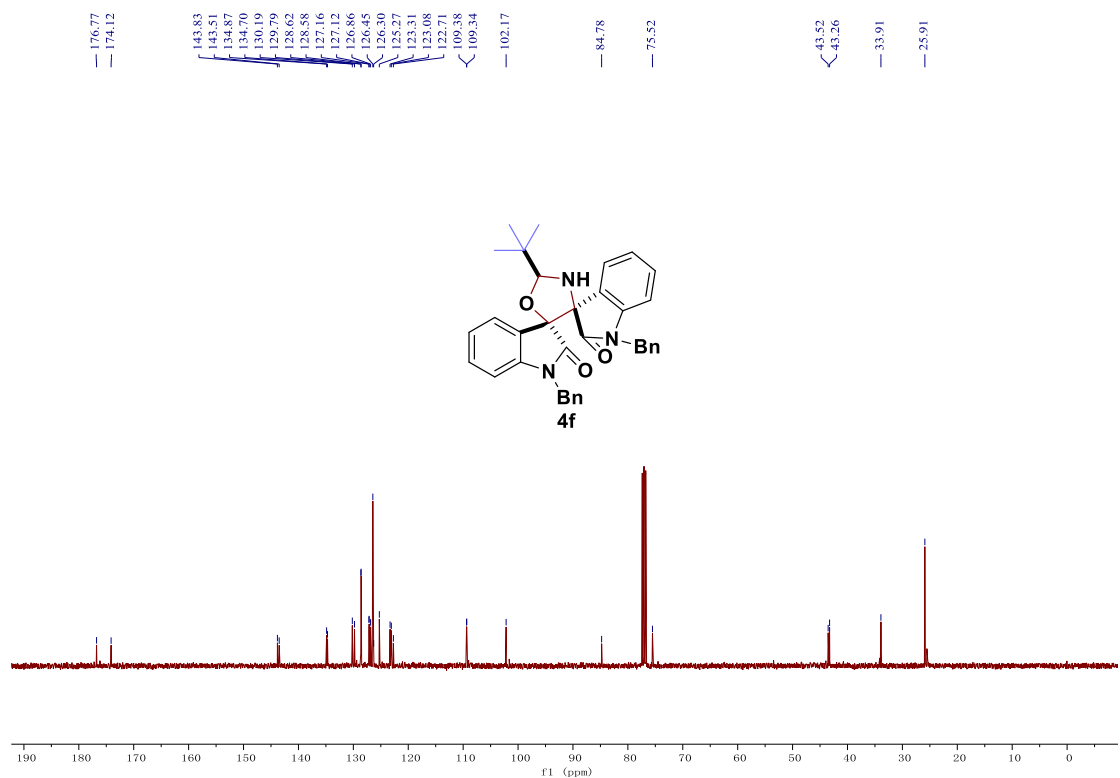
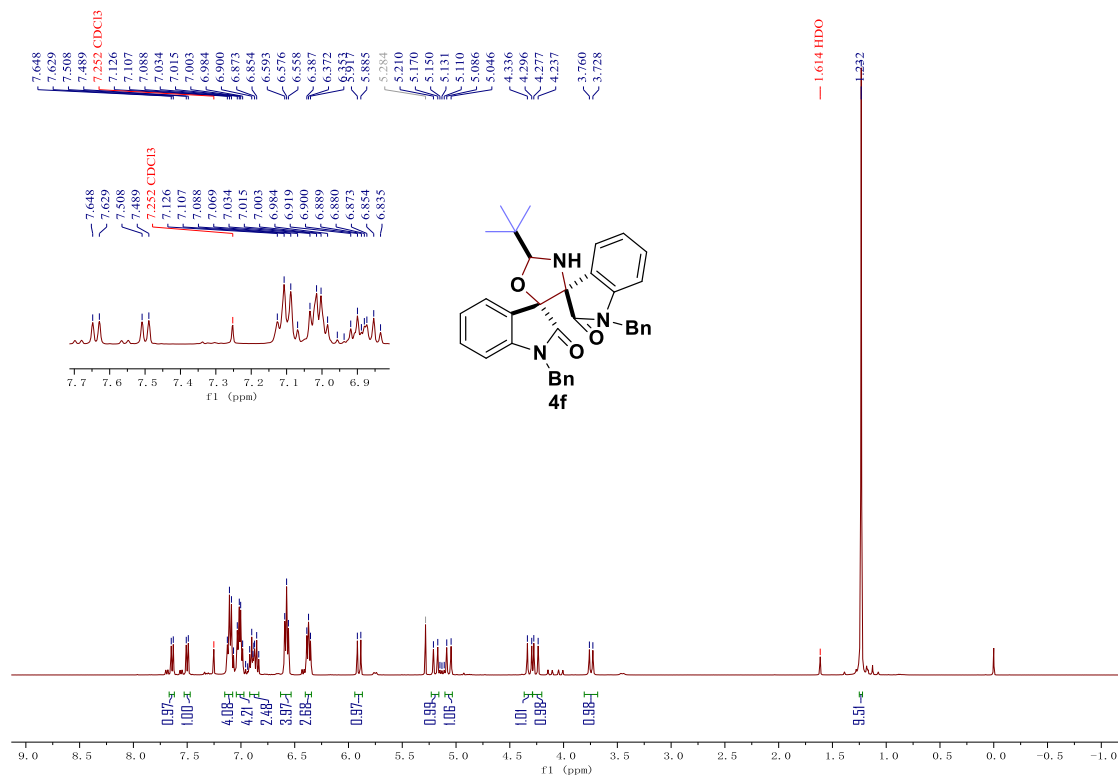
Chemical structure of 4e: C[C@H]1N[C@@H](c2ccccc2)[C@H](C(=O)Nc3ccccc3)O[C@H]1c4ccccc4

Peak list (ppm):

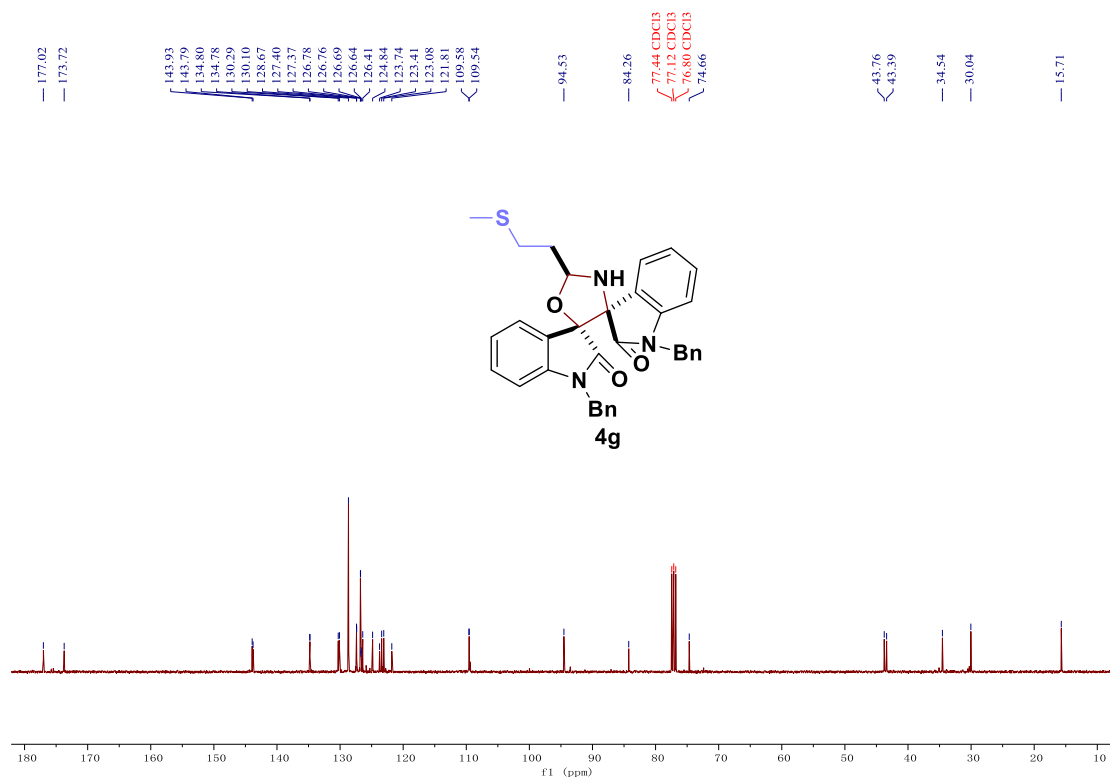
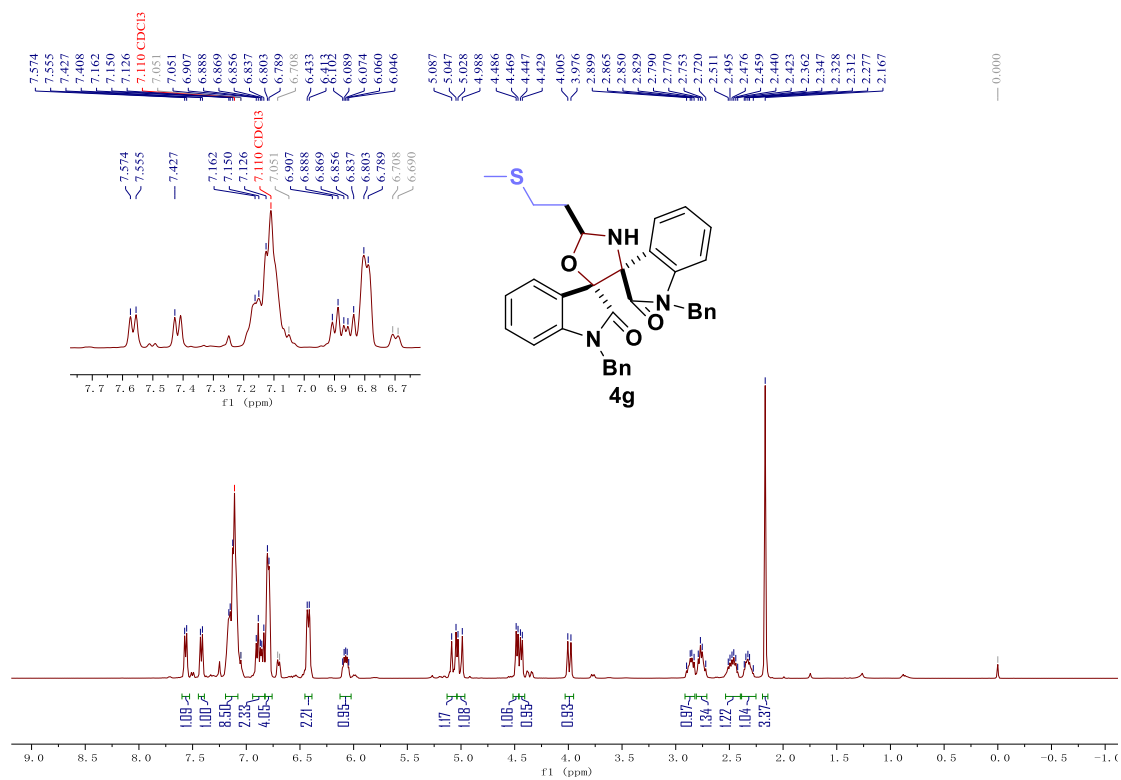
Peak (ppm)	Integration
7.593	0.98
7.574	0.98
7.438	0.98
7.419	0.98
7.144	0.98
7.125	0.98
7.095	0.98
7.060	0.98
6.891	0.98
6.871	0.98
6.854	0.98
6.871	0.98
6.854	0.98
6.820	0.98
6.800	0.98
6.747	0.98
6.728	0.98
6.581	0.98
6.563	0.98
6.406	0.98
6.382	0.98
6.367	0.98
5.754	0.98
5.737	0.98
5.158	0.98
5.136	0.98
5.119	0.98
5.096	0.98
5.077	0.98
5.034	0.98
4.997	0.98
4.493	0.98
4.472	0.98
4.438	0.98
4.399	0.98
4.384	0.98
4.341	0.98
4.323	0.98
4.169	0.98
4.152	0.98
4.132	0.98
4.100	0.98
4.033	0.98
4.017	0.98
4.000	0.98
3.984	0.98



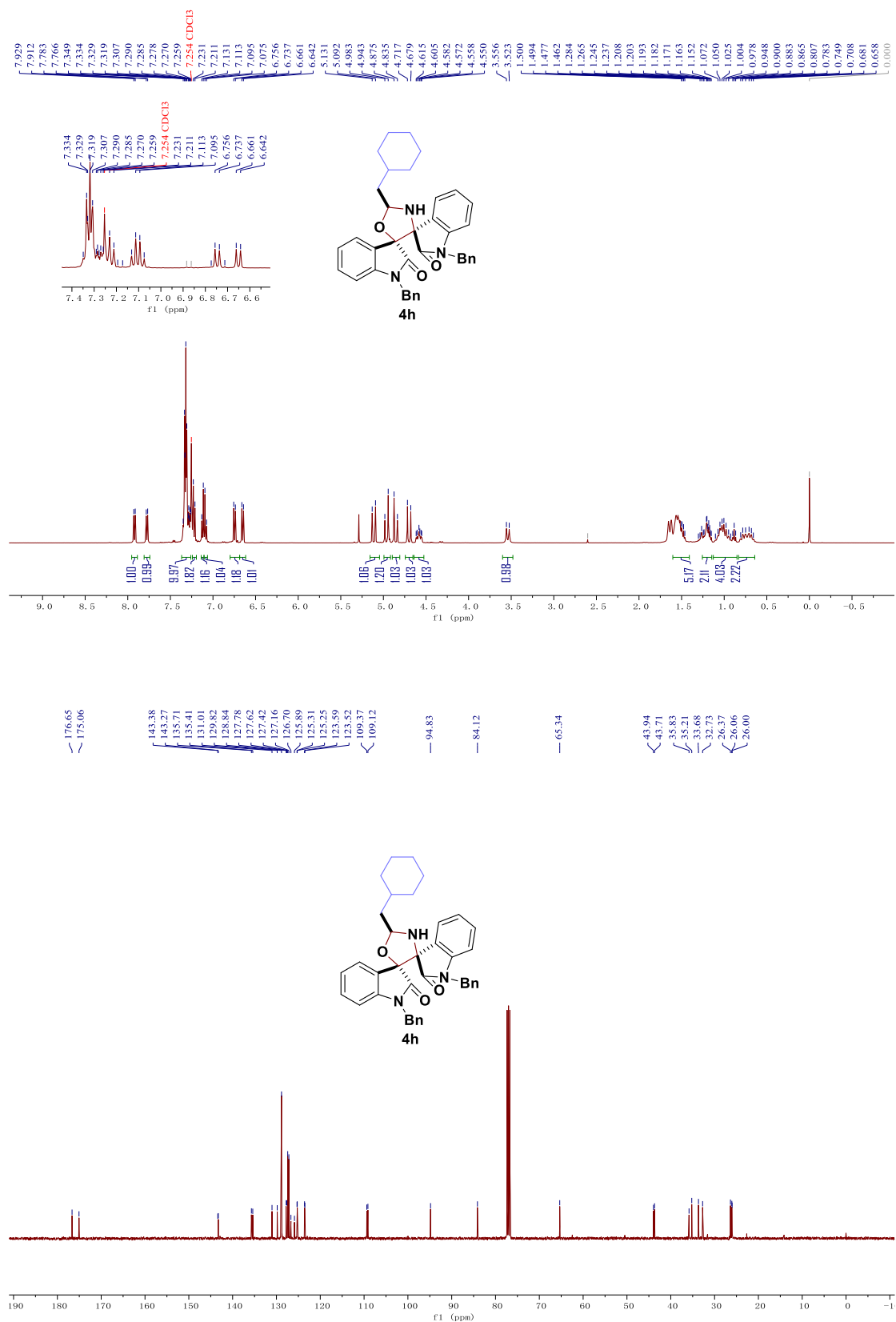
^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



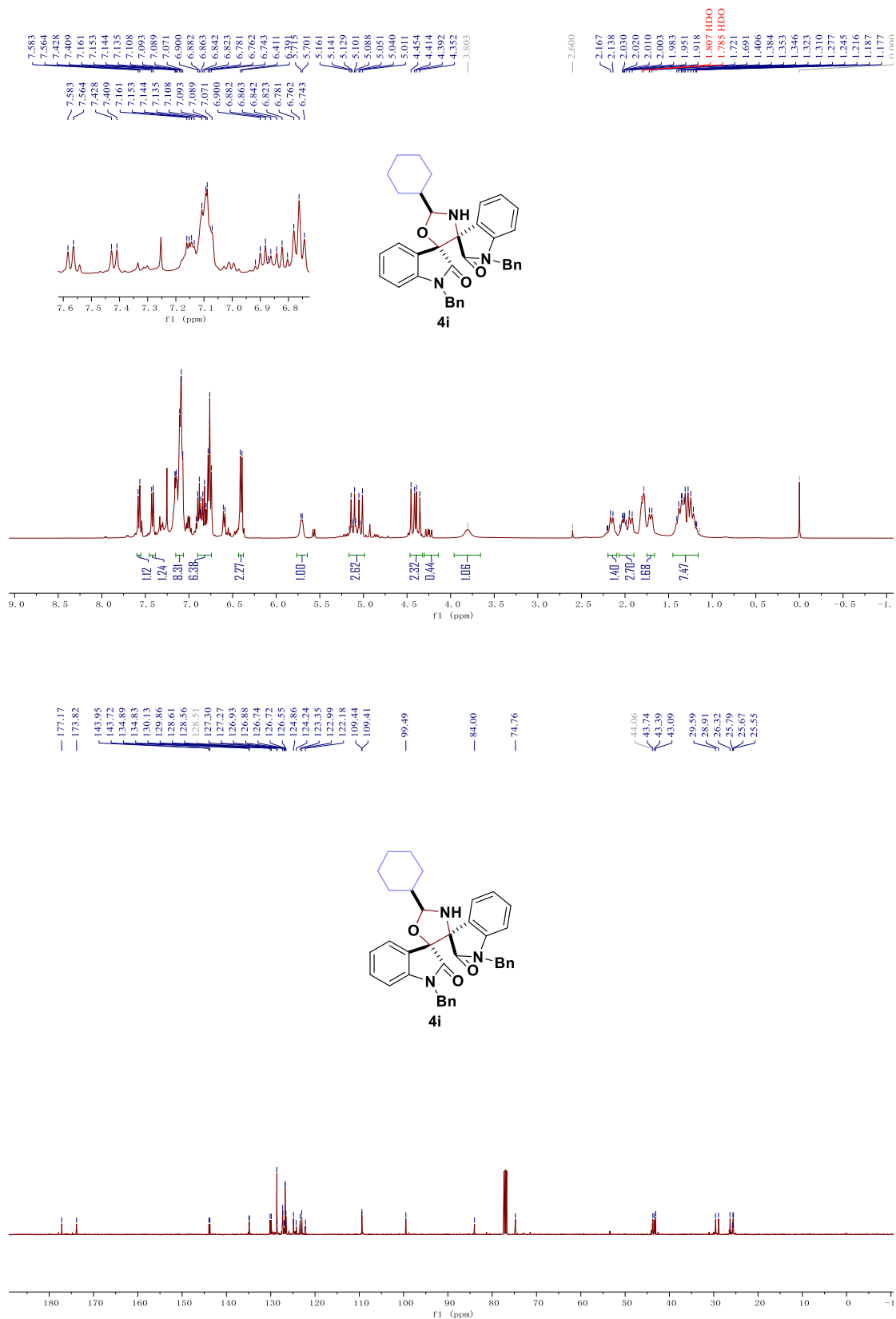
^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



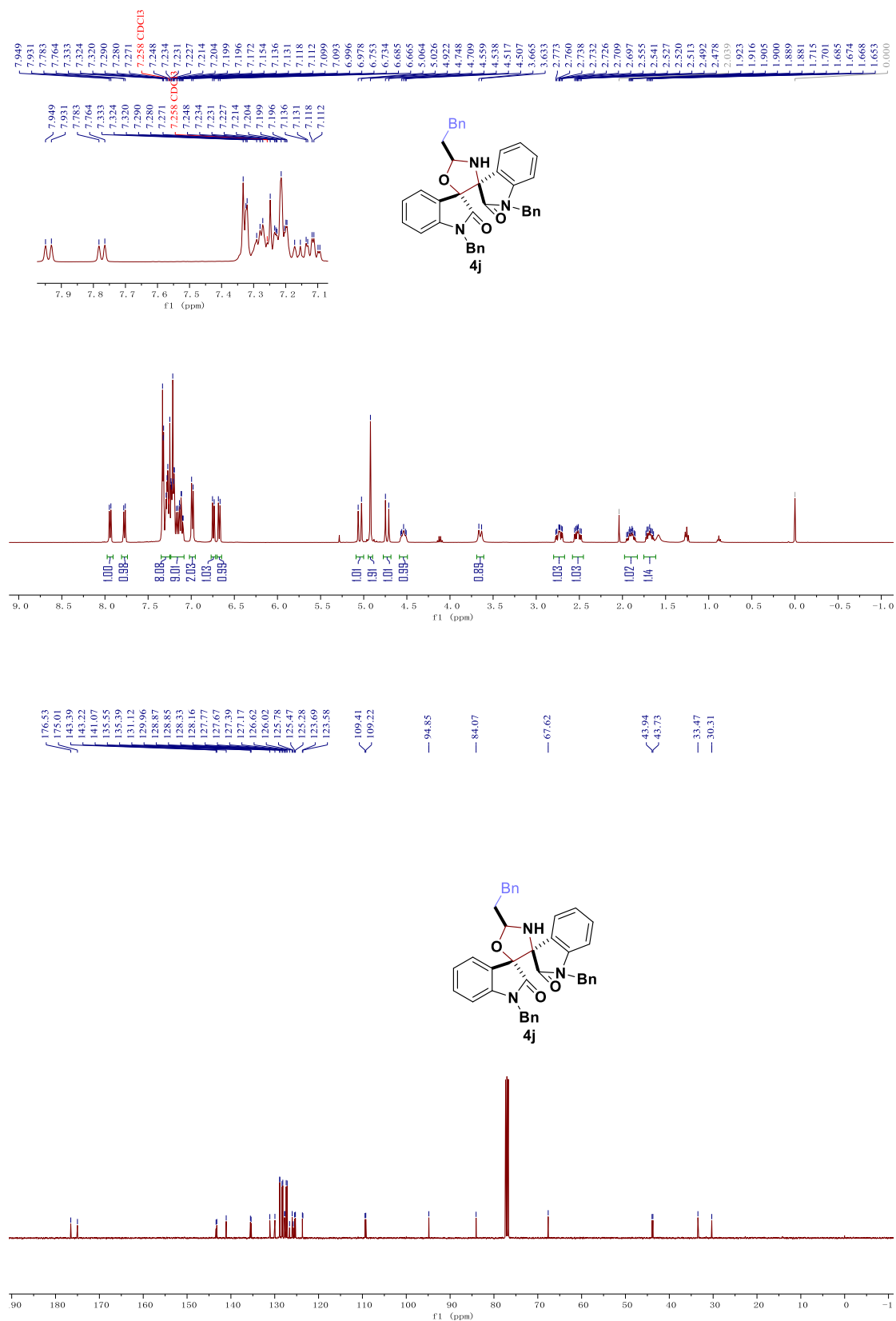
^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



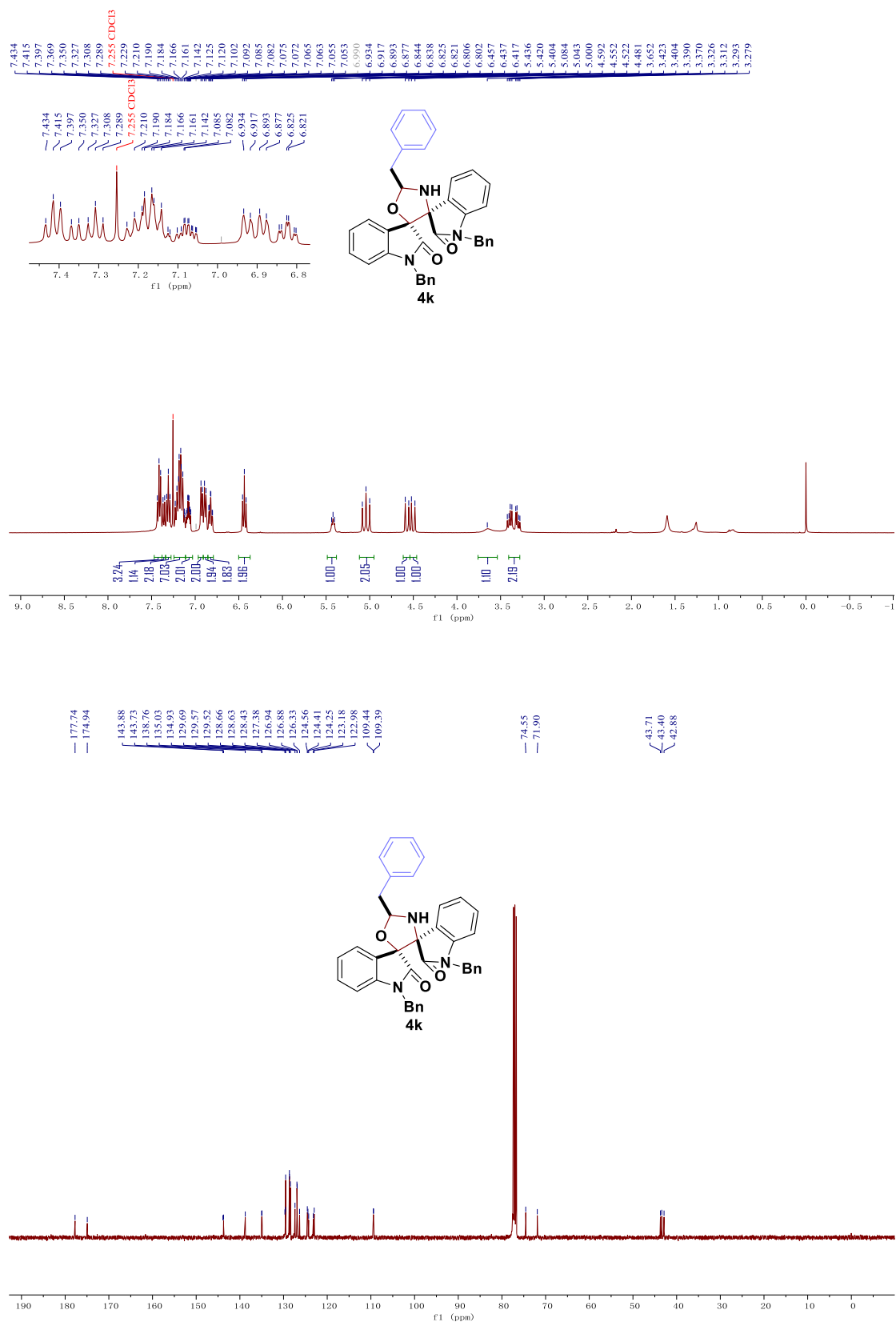
^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



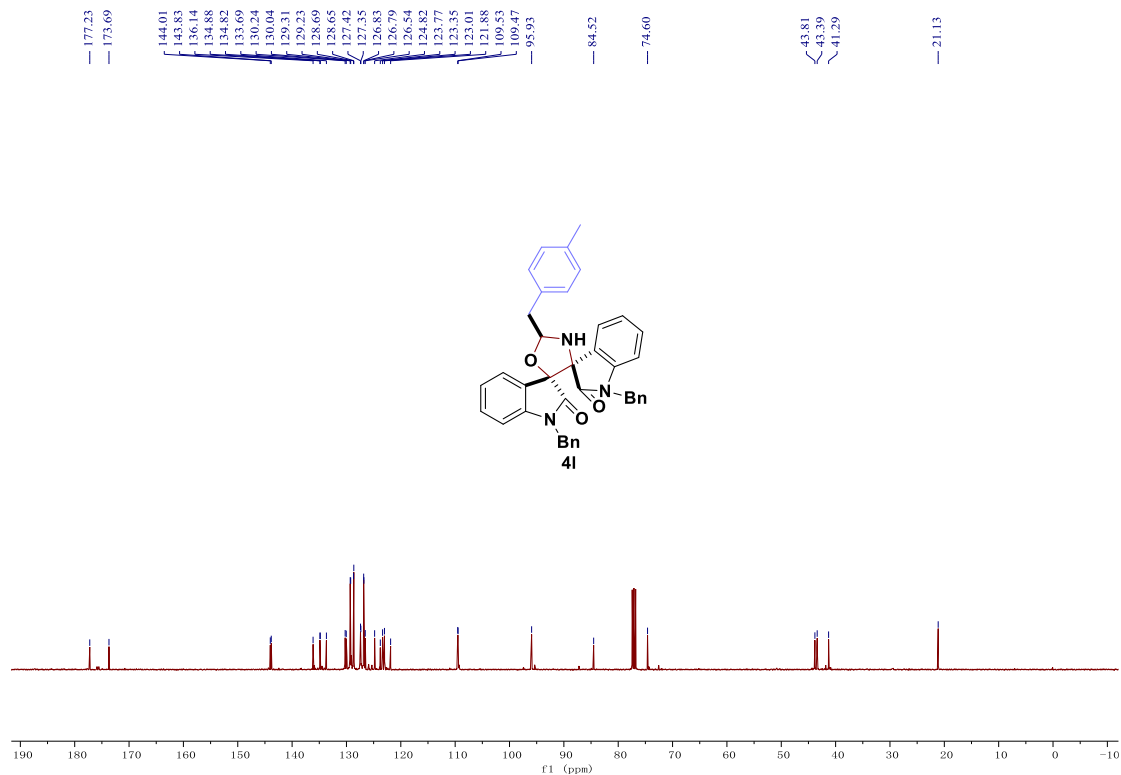
^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



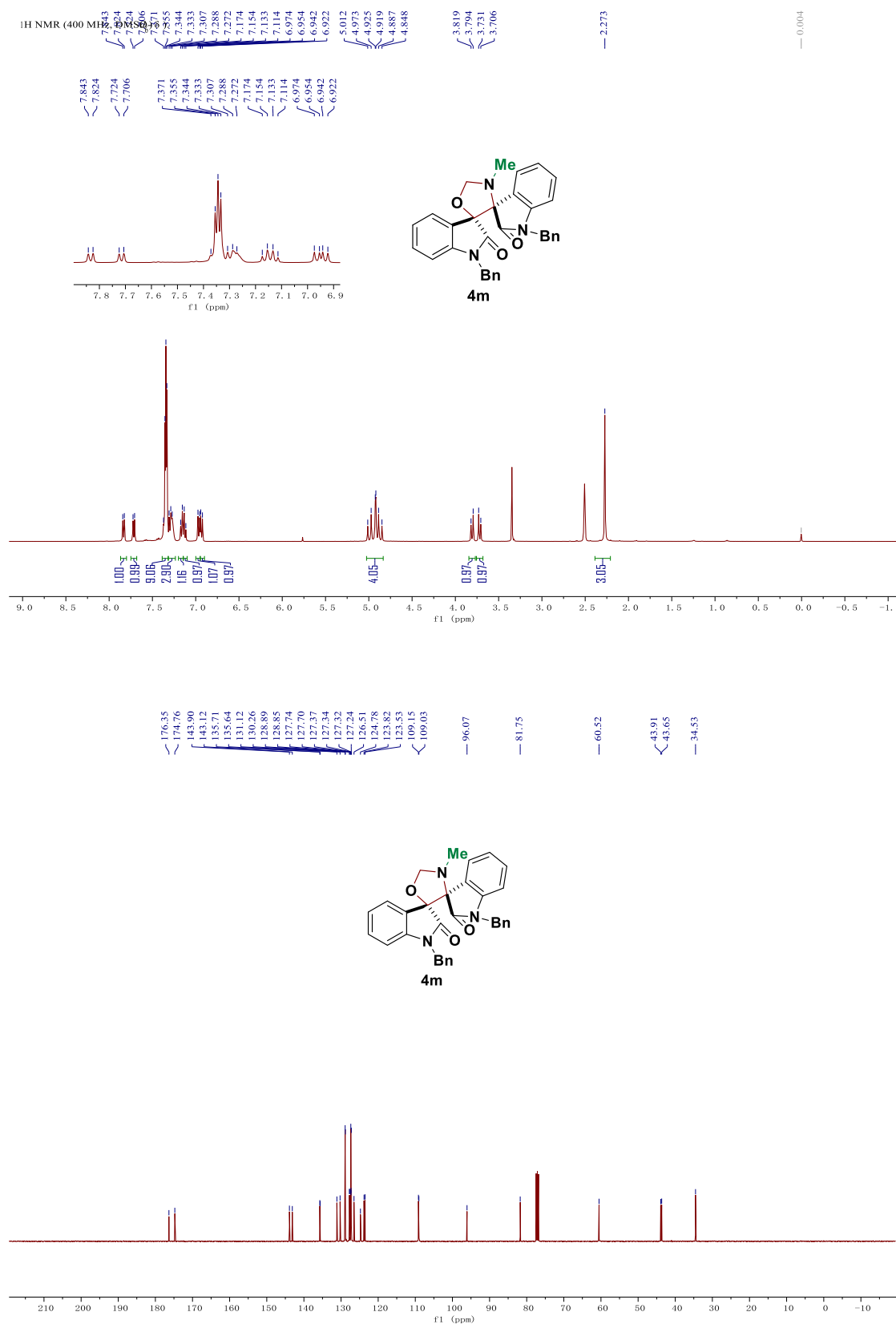
^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



Chemical structure of **4l** is shown. The ¹H NMR spectrum (CDCl₃) displays peaks corresponding to the structure, with integration values provided below the peaks.

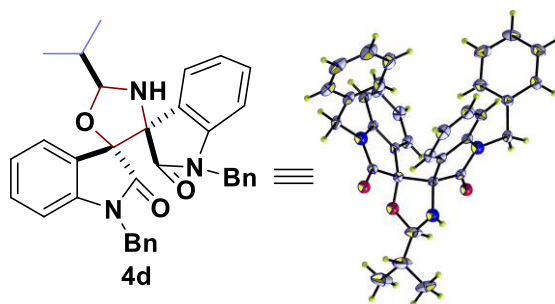


^1H NMR (CDCl_3 , 400 MHz), ^{13}C NMR (CDCl_3 , 100 MHz)



3. X-ray crystallographic data of compound 4d

X-Ray crystallographic analysis of dispirooxindole-piperazine **4d** (CCDC 1568850) showing the thermal ellipsoids at 30% probability level.



Bond precision: C-C = 0.0059 Å

Wavelength=0.71073

Cell: a=9.4793 (2) b=12.6384 (3) c=13.2202 (4)
alpha=98.616 (2) beta=92.833 (2) gamma=107.212 (1)
Temperature: 293 K

	Calculated	Reported
Volume	1488.43 (7)	1488.43 (7)
Space group	P -1	P-1
Hall group	-P 1	?
Moiety formula	C34 H31 N3 O3	?
Sum formula	C34 H31 N3 O3	C34 H31 N3 O3
Mr	529.62	529.62
Dx, g cm ⁻³	1.182	1.182
Z	2	2
Mu (mm ⁻¹)	0.076	0.076
F000	560.0	560.0
F000'	560.23	
h, k, lmax	11, 15, 15	11, 15, 15
Nref	5253	5224
Tmin, Tmax	0.982, 0.985	
Tmin'	0.977	

Correction method= Not given

Data completeness= 0.994

Theta(max)= 25.030

R(reflections)= 0.0813 (3917)

wR2(reflections)= 0.2718 (5224)

S = 1.063

Npar= 363