SUPPORTING INFORMATION

Synthesis of Functionalized Tetrahydroquinoline Containing Indole Scaffold via Chemoselective Annulation of Aza-ortho-quinone Methide Precursor

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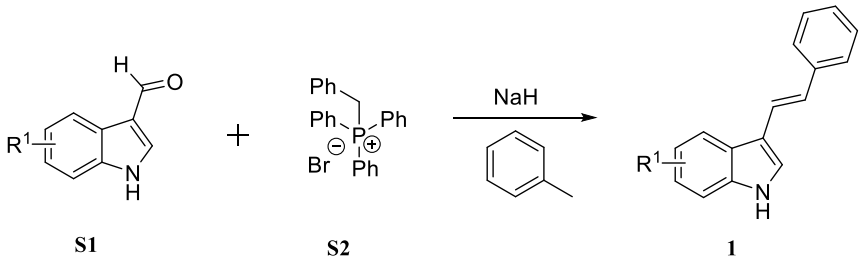
1) General information

All reactions were carried out in the air. All reagents were purchased from commercial suppliers and used without further purification unless otherwise noted. Thin-layer chromatography was performed using silica gel GF254 precoated plates (0.20–0.25 mm thickness) with a fluorescent indicator. Visualization on TLC was achieved by UV light (254 nm). Column chromatography was performed on silica gel 90, 200-300 mesh. ^{1}H and ^{13}C NMR (400 and 100 MHz, respectively) spectra were recorded on a Bruker Avance 400 spectrometer. ^{1}H NMR chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$, δ 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$, δ 77.16). High resolution mass spectra (HRMS) were obtained using a fourier transfer ion cyclotron resonance (FTICR) mass spectrometer and electrospray ionization (ESI).

2) General procedure for substrates 1[1]

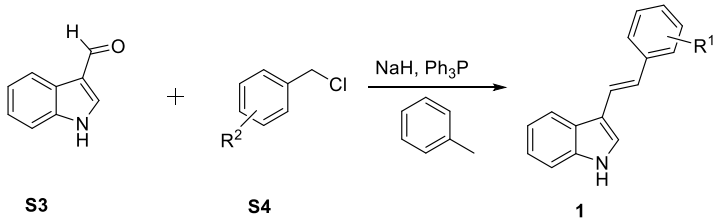


S1 **S2** **1**

Scheme S1. The synthesis of 1

Sodium hydride in mineral oil (540 mg, 60%, 22 mmol) was added to the suspension of $BnPh_3PBr$ (10.0 g, 23 mmol) in toluene (80 mL) at -5 ℃. The mixture was stirred at room temperature for 40 min followed by the addition of indole 3-carboxaldehyde (12 mmol) in toluene (20 mL). Then the mixture was heated to 80 ℃ for 4 h monitored by TLC and quenched by saturated solution of

NH_4Cl at room temperature. The extracts with ethyl acetate were dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. The crude product was purified by column chromatography petroleum ether/EtOAc 20:1) to give **1a-e** (50−75 % yields).



Scheme S2. The synthesis of 1

To the solution of Ph_3P (22 mmol) in toluene benzyl chloride **S4** (11 mmol) was added at rt, and then refluxed overnight providing $BnPh_3PCl$. NaH in mineral oil (270 mg, 60%, 11 mmol) was added to the suspension of $BnPh_3PCl$ (4.8 g, 11 mmol) in toluene (40 mL) at room temperature. The mixture was stirred at room temperature for 30 min followed by the addition of indole 3-carboxaldehyde (5.57 mmol) in toluene (10 mL). Then the mixture was heated to 80 ℃ for 2 h monitored by TLC and quenched by saturated solution of NH_4Cl at room temperature. The extracts with ethyl acetate were dried over anhydrous sodium sulfate and the solvent was removed under reduced pressure. The crude product was purified by column chromatography petroleum /EtOAc 20:1 to give **1f-l** (65−80 % yields).

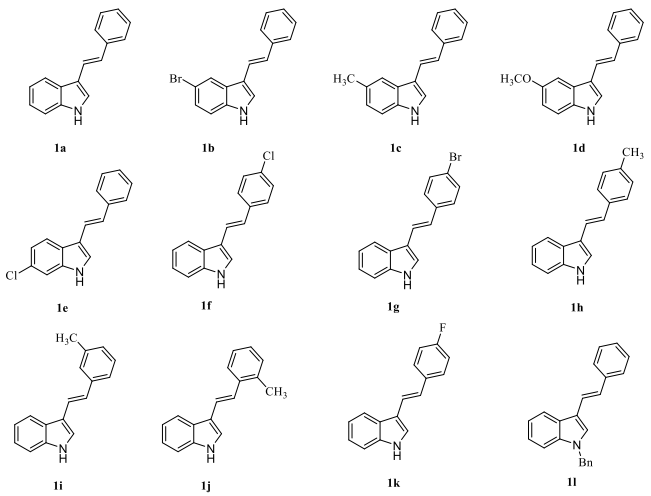
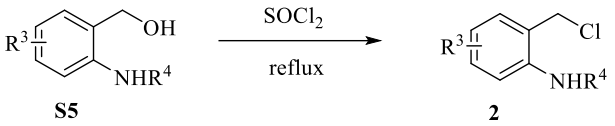


Figure S1. The structure of 1

3) General procedure for substrates 2 [2]



Scheme S3. The synthesis of 2

To a solution of thionyl chloride (13.93 mmol) in $CHCl_3$ (5 mL), was added a solution of **S5** (5.8 mmol) in $CHCl_3$ (20 mL) over 5 min. The mixture was heated to 40 °C for overnight. After the reaction cooled to room temperature, then poured into ice water (10 mL). The aqueous layer was extracted with $CHCl_3$ (100 mL). The combined organic layers were washed with brine (30 mL), and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure and the crude product was purified by flash chromatogray afforded **2**.

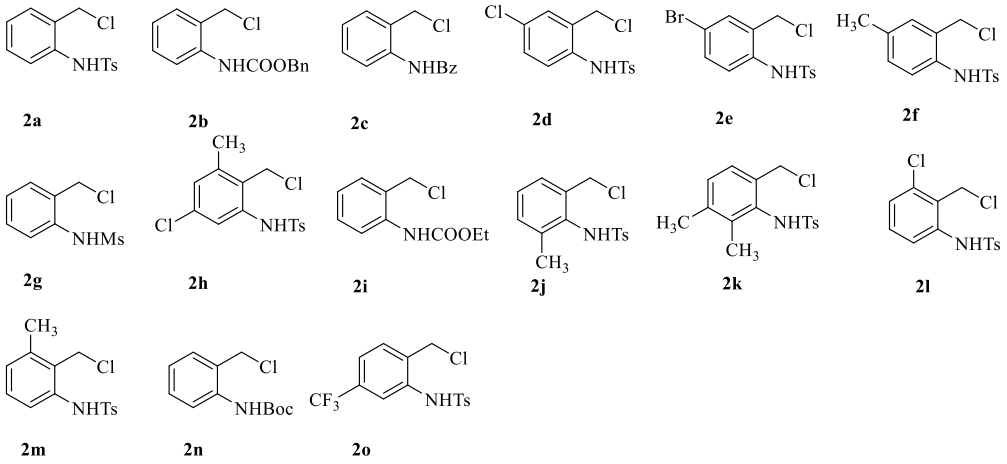
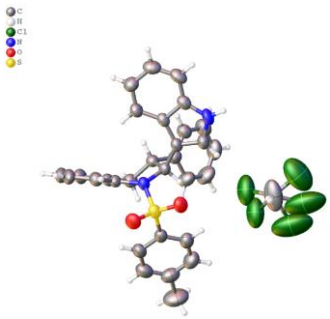
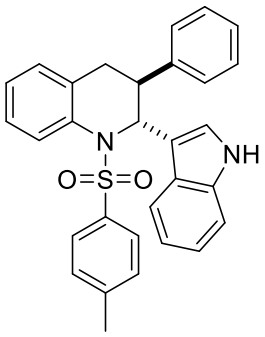


Figure S2. The structure of 2

4) The x-ray data of 3a





Single crystal of **3a** [$C_{30}H_{26}N_2O_2S$] was obtained from the $CDCl_3$. CCDC 2205697 containing the supplementary crystallographic data can be obtained free of charge from The Cambrige Crystallographic Data Centere via www.ccdc.cam.ac.uk/data_request/cif

Identification code **3a**

Empirical formula $C_{31}H_{27}Cl_3N_2O_2S$

Formula weight 597.95

Temperature/K 293.15

Crystal system monoclinic

Space groupP21/n

a/Å10.4332(6)

b/Å 13.1692(7)

c/Å20.7935(14)

α /° 90

β /° 90.877(5)

γ /° 90

Volume/Å3 2856.6(3)

Z 4

ρ calcg/cm3 1.390

μ /mm-1 0.426

F(000) 1240.0

Crystal size/mm3 0.35 × 0.3 × 0.25

Radiation MoKα (λ = 0.71073)

2Θ range for data collection/° 6.188 to 52.744

Index ranges -13 ≤ h ≤ 13, -16 ≤ k ≤ 14, -22 ≤ l ≤ 25

Reflections collected 13843

Independent reflections 5824 [Rint = 0.0305, Rsigma = 0.0585]

Data/restraints/parameters 5824/2/360

Goodness-of-fit on F2 1.029

Final R indexes [I>=2σ (I)] R1 = 0.0802, wR2 = 0.2101

Final R indexes [all data] R1 = 0.1347, wR2 = 0.2486

Largest diff. peak/hole / e Å-3 0.39/-0.74

5) References

[1] Guan, X. K.; Liu, G. F.; An, D.; Zhang, H.; Zhang, S. Q. Chiral Imidodiphosphoric Acid-Catalyzed Highly Diastereo- and Enantioselective Synthesis of Poly-Substituted 3,4-Dihydro-2H-pyrans: [4 + 2] Cycloadditions of β,γ-Unsaturated α-Ketoesters and 3-Vinylindoles. *Org. Lett.* **2019**, *21*, 14, 5438.

[2] (a)Wagner, A. M.; knezevic, C. E. K.; Wall, J. L.; Sun, V. L.; Buss, J. A.; Allen, L. T.; Wenzel, A. G. Green synthesis of novel chalcone and coumarin derivatives via Suzuki coupling reaction. *Tetrahedron. Lett.* **2012**, *53*, 833. (b) Yang, Q. Q.; Xiao, C.; Lu, L. Q.; An, J.; Tan, F.; Li, B. J.; Xiao, W. J. Synthesis of Indoles through Highly Efficient Cascade Reactions of Sulfur Ylides and N-(ortho-Chloromethyl) aryl Amides. *Angew. Chem. Int. Ed.* **2012**, *51*, 9137.

6) NMR spectra

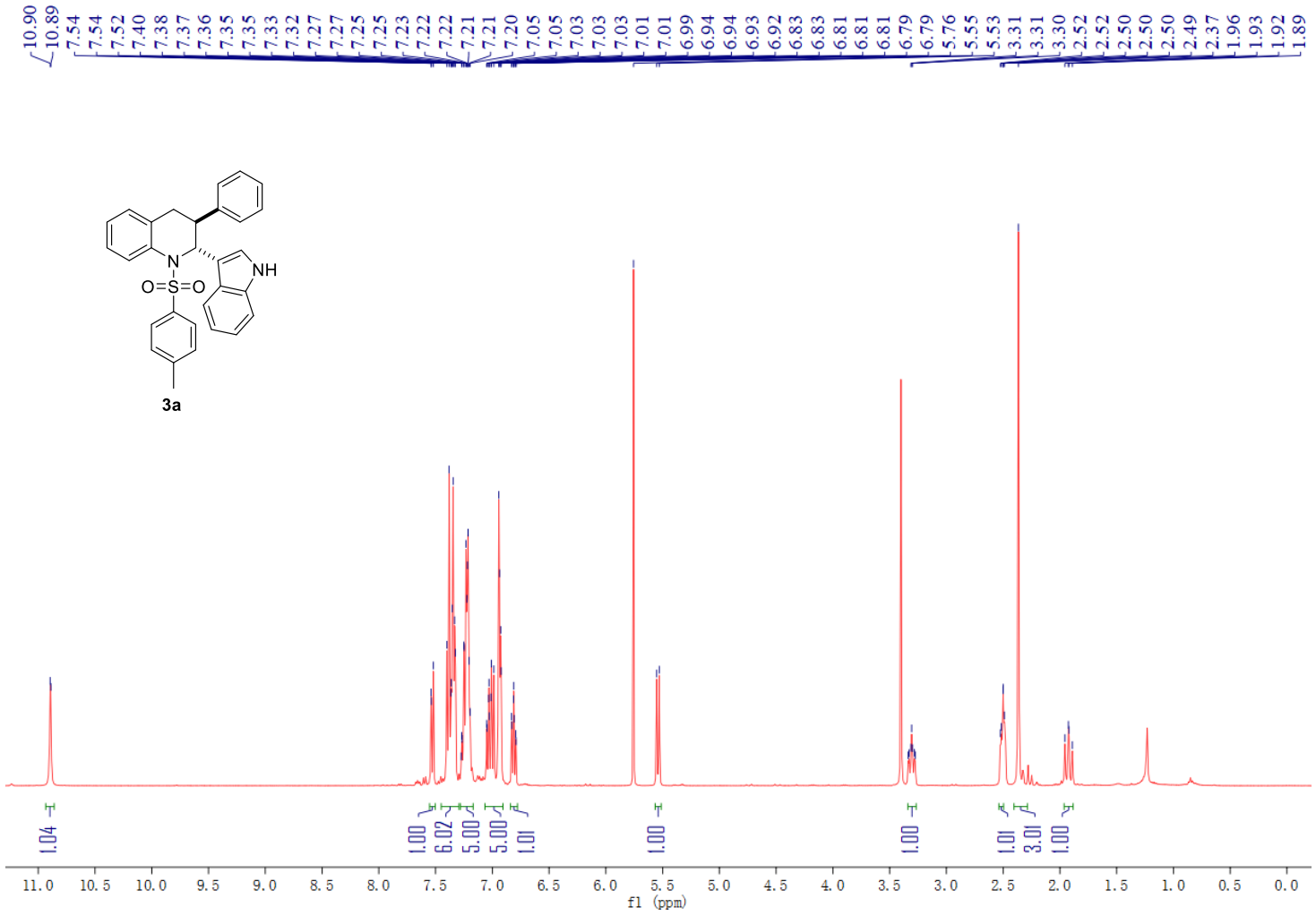


Figure S3. The ^{1}H NMR of 3a

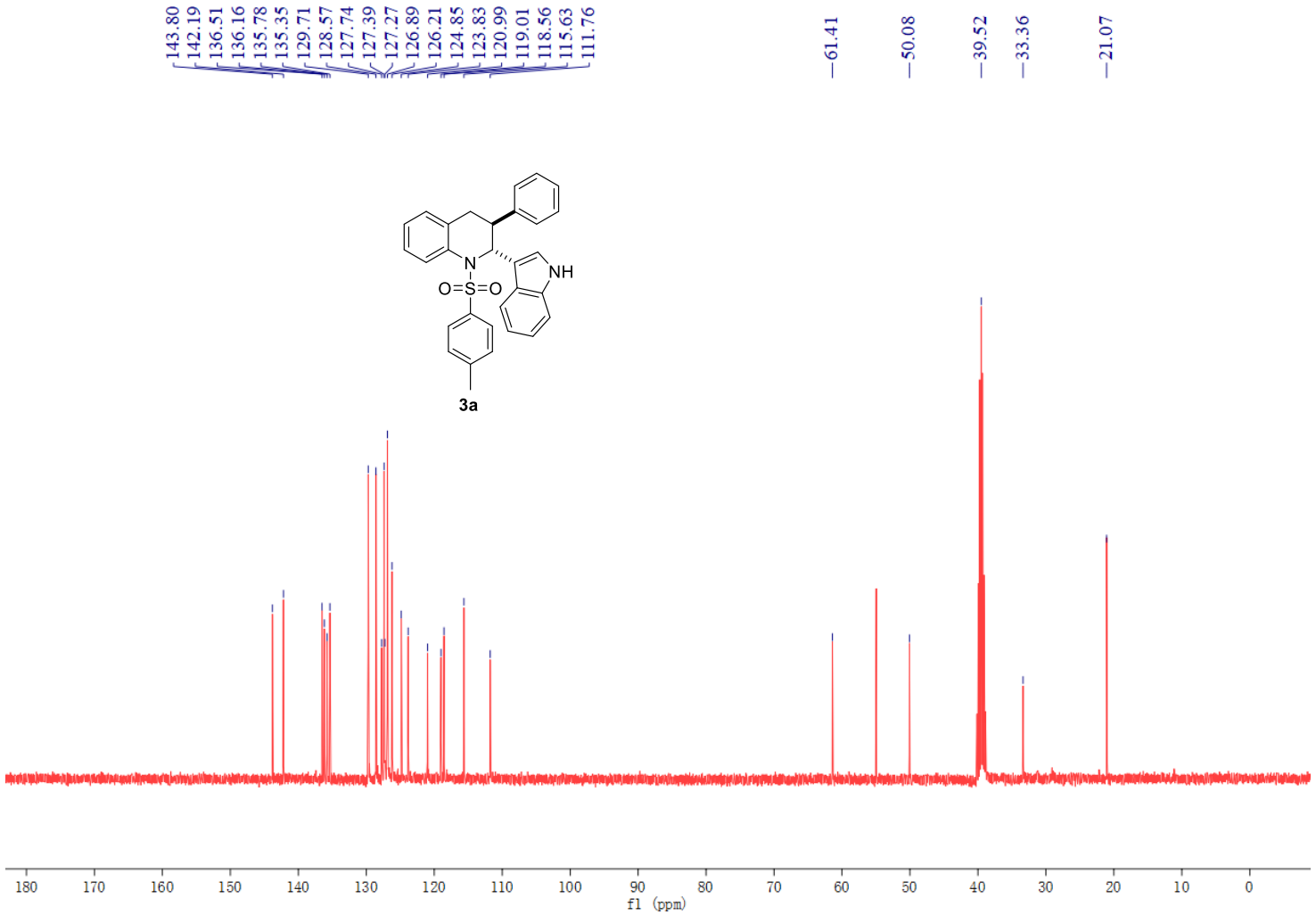


Figure S4. The ^{13}C NMR of 3a

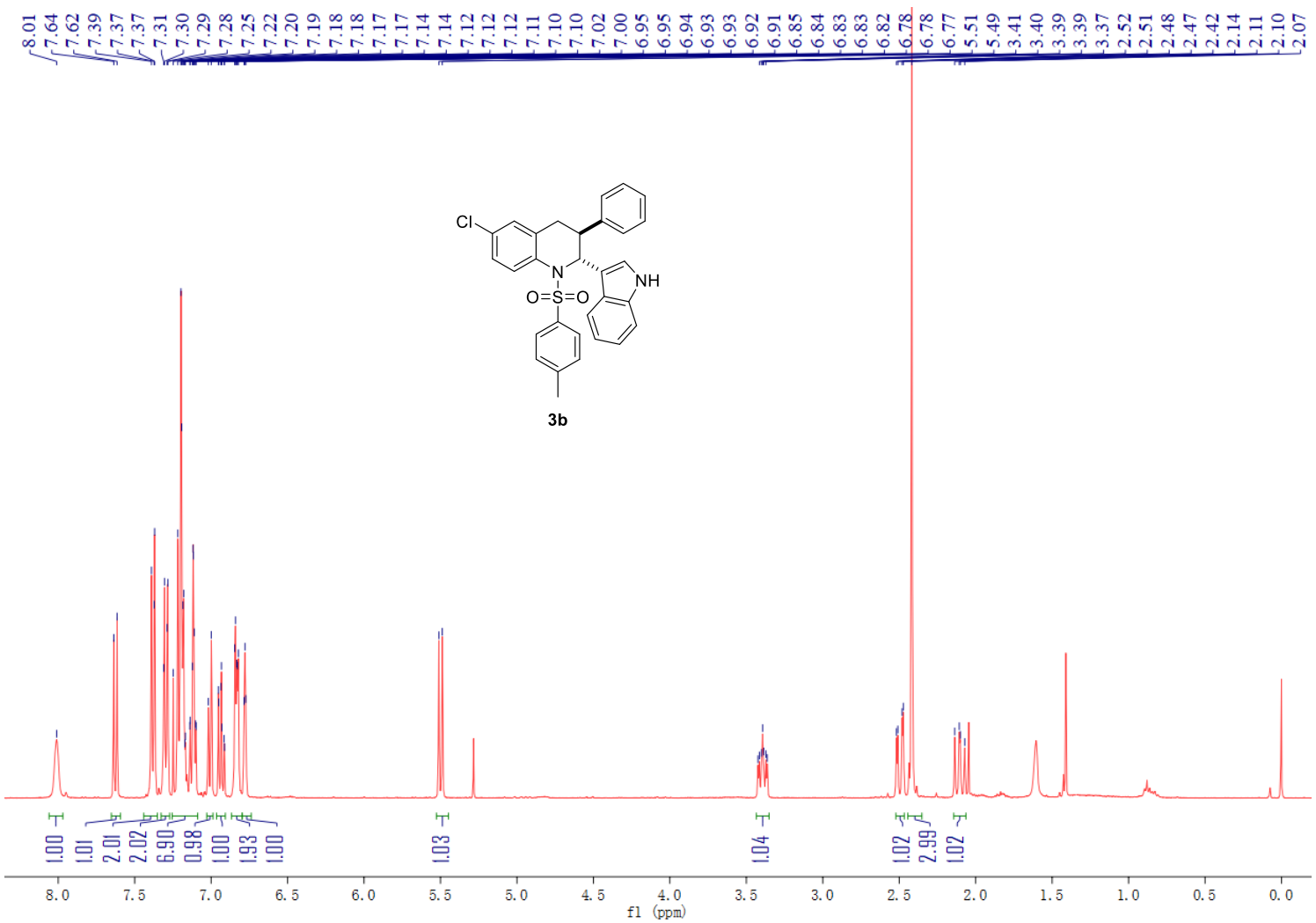


Figure S5. The ^{1}H NMR of 3b

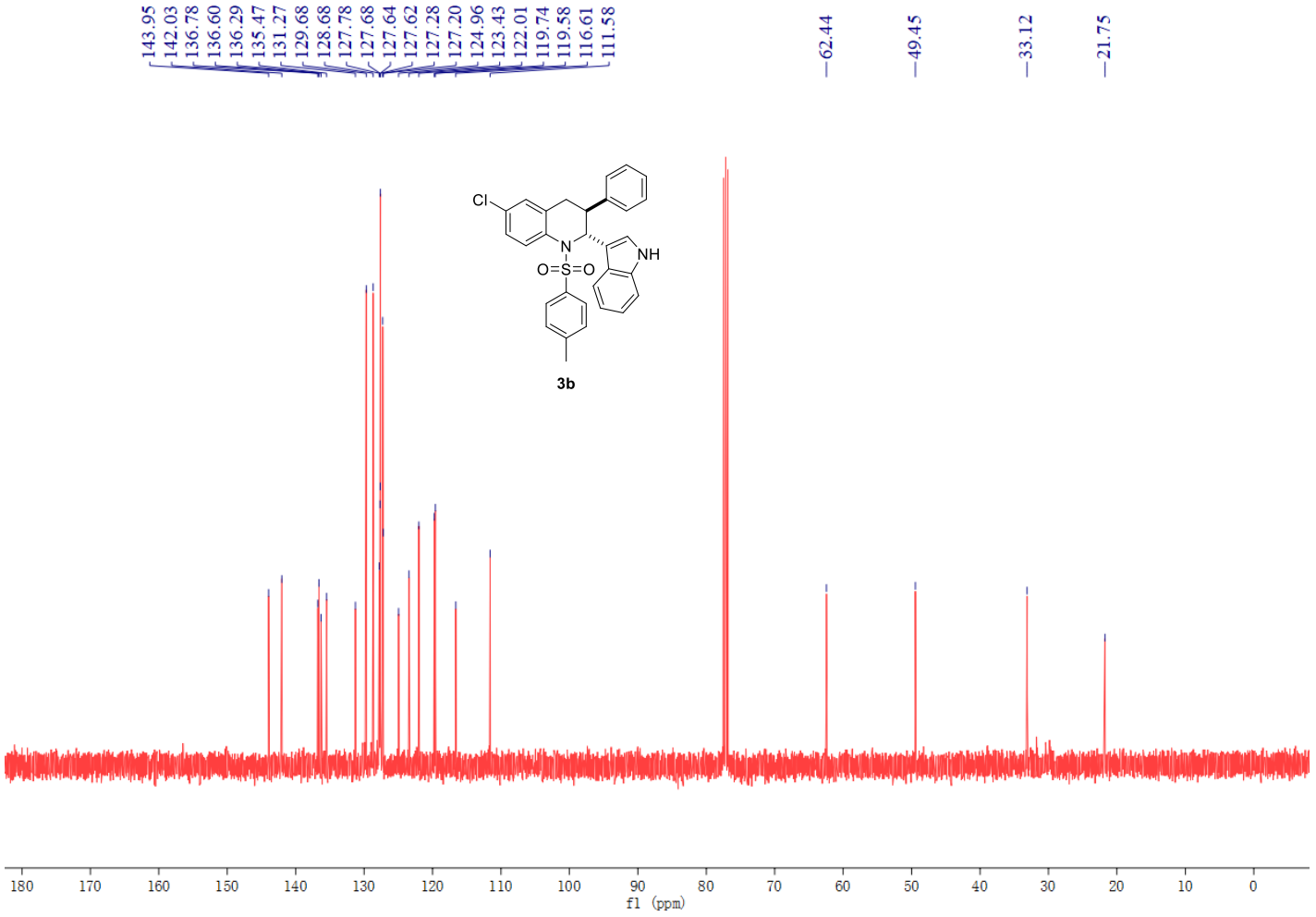


Figure S6. The ^{13}C NMR of 3b

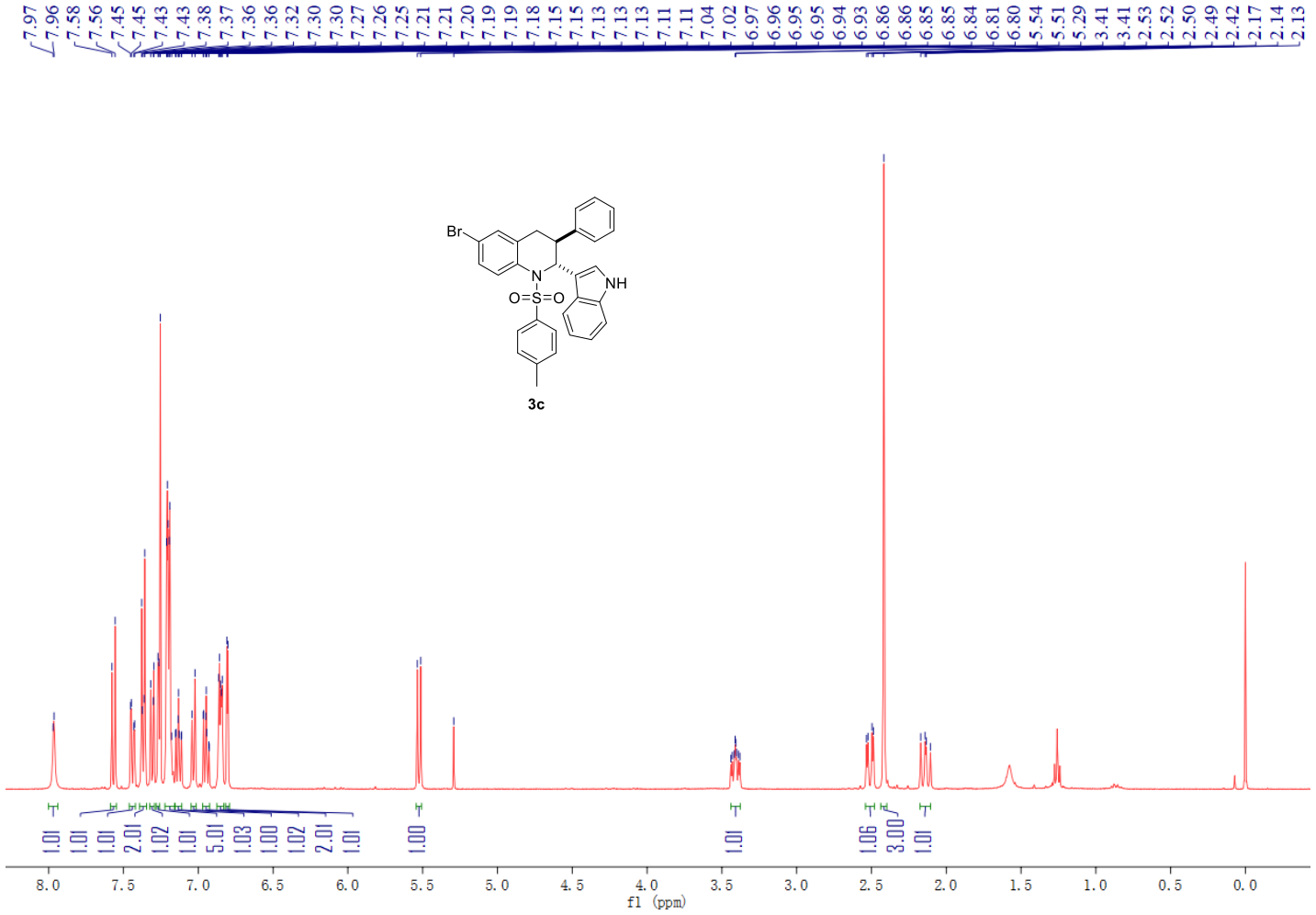


Figure S7. The ^{1}H NMR of 3c

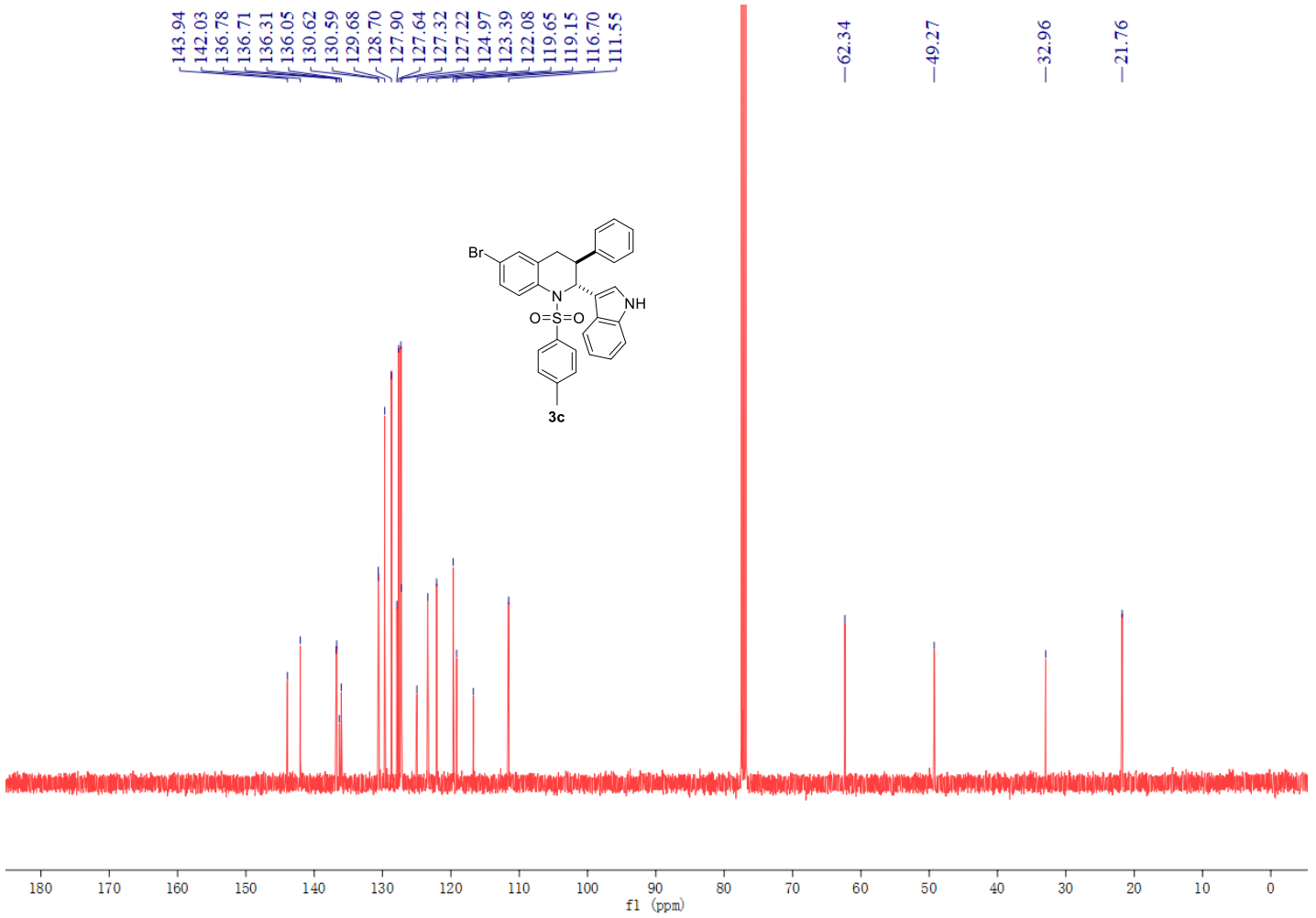


Figure S8. The ^{13}C NMR of 3c

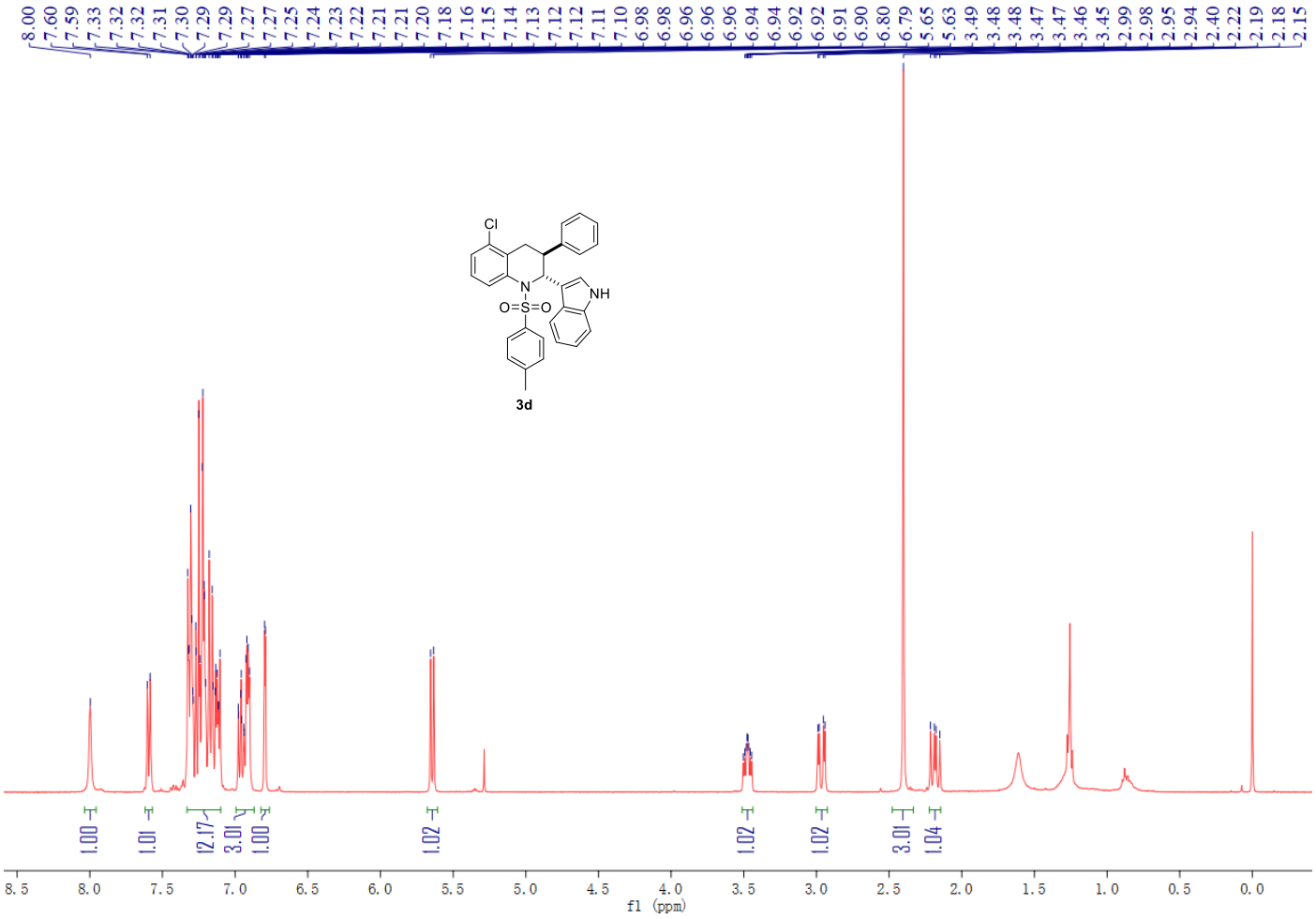
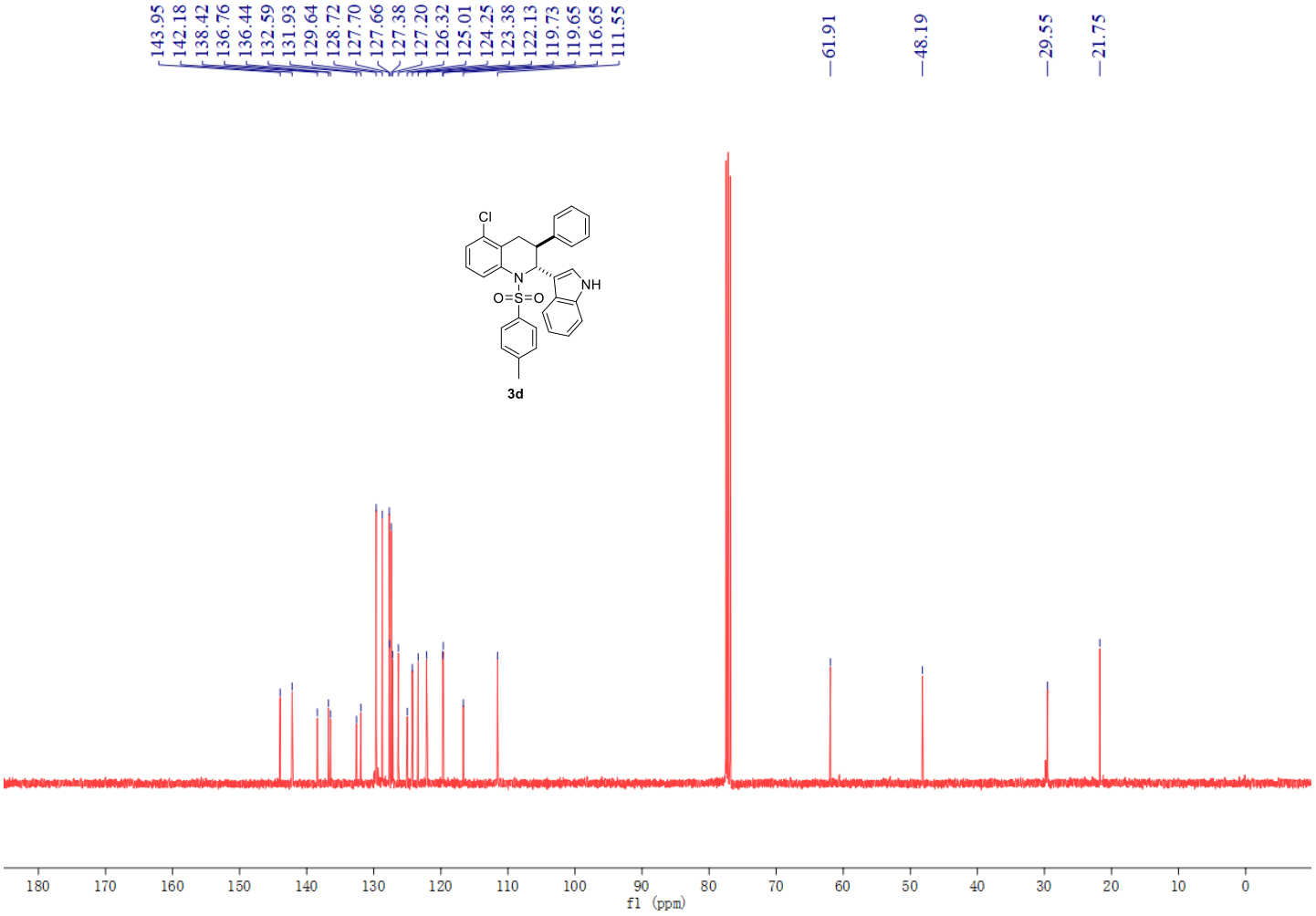


Figure S9. The ^{1}H NMR of 3d



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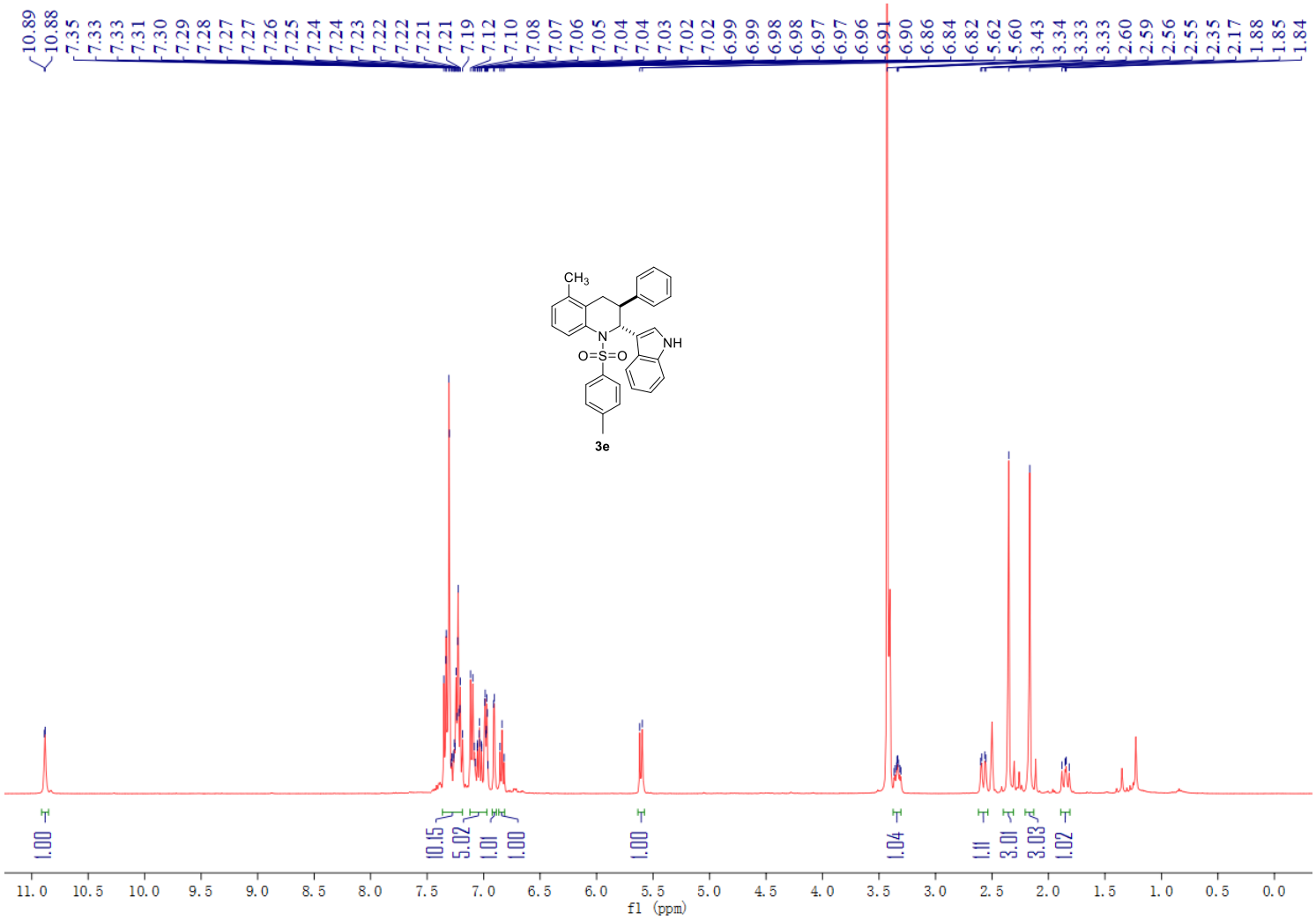


Figure S11. The ^{1}H NMR of 3e

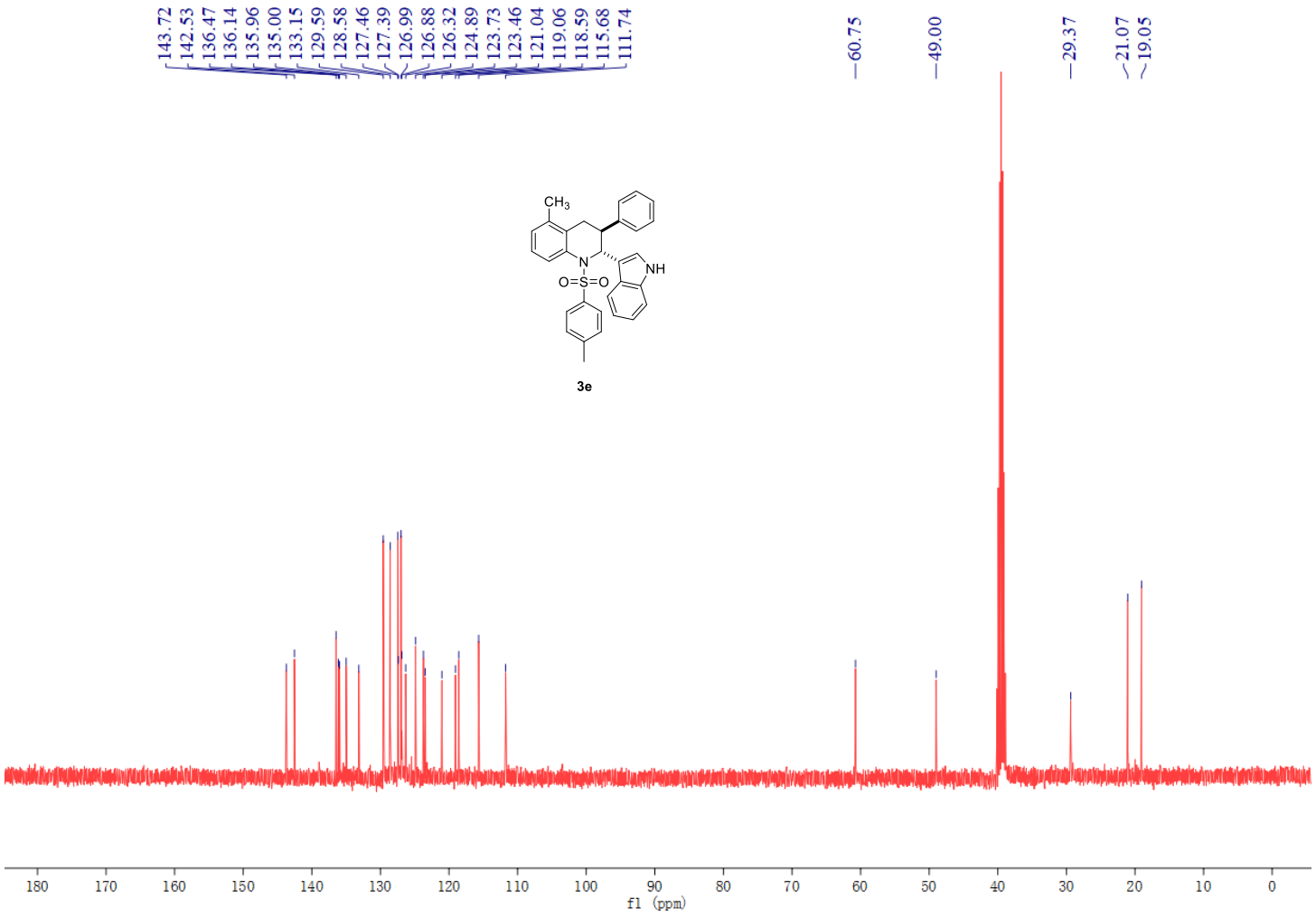


Figure S12. The ^{13}C NMR of 3e

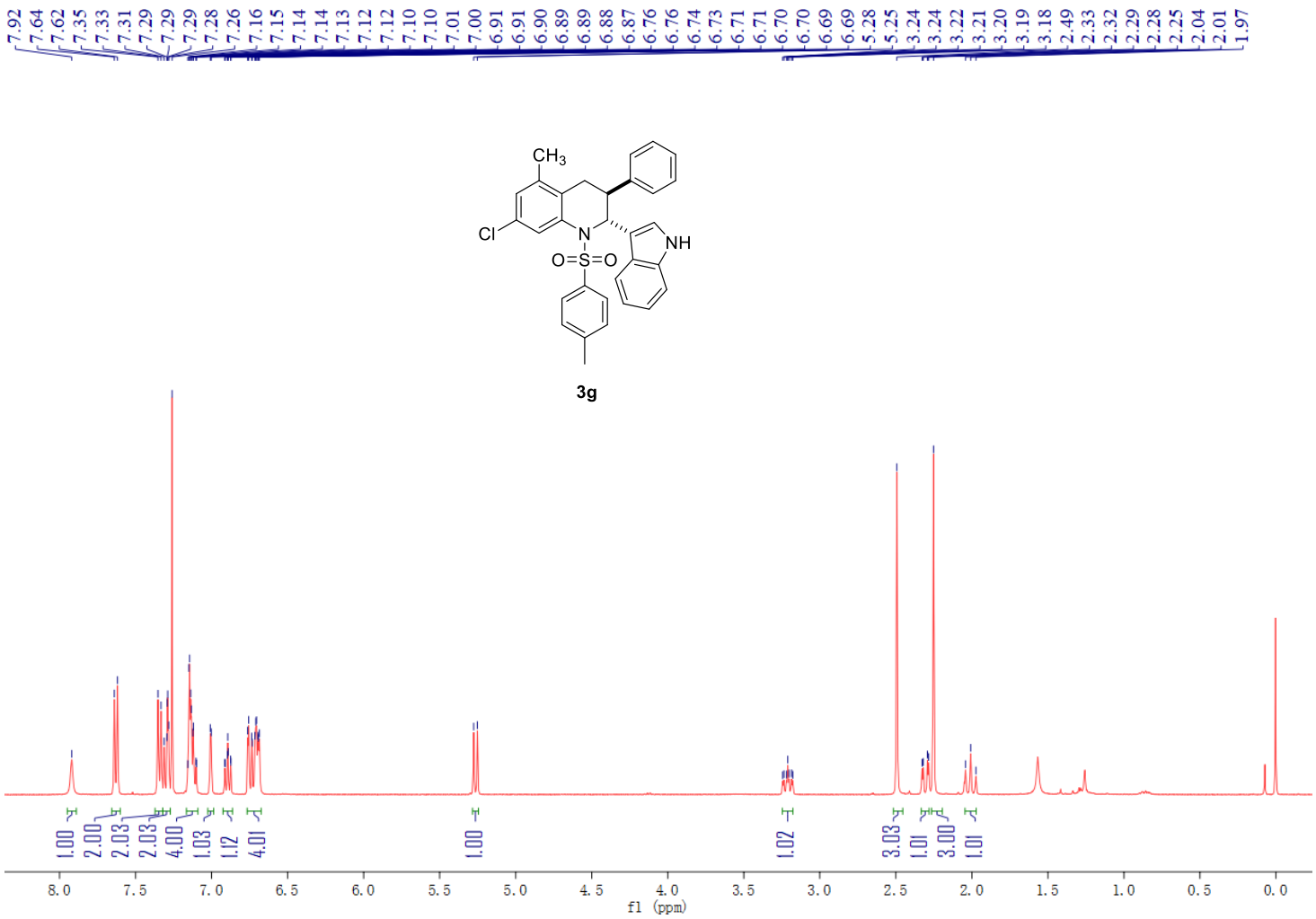


Figure S13. The ^{1}H NMR of 3g

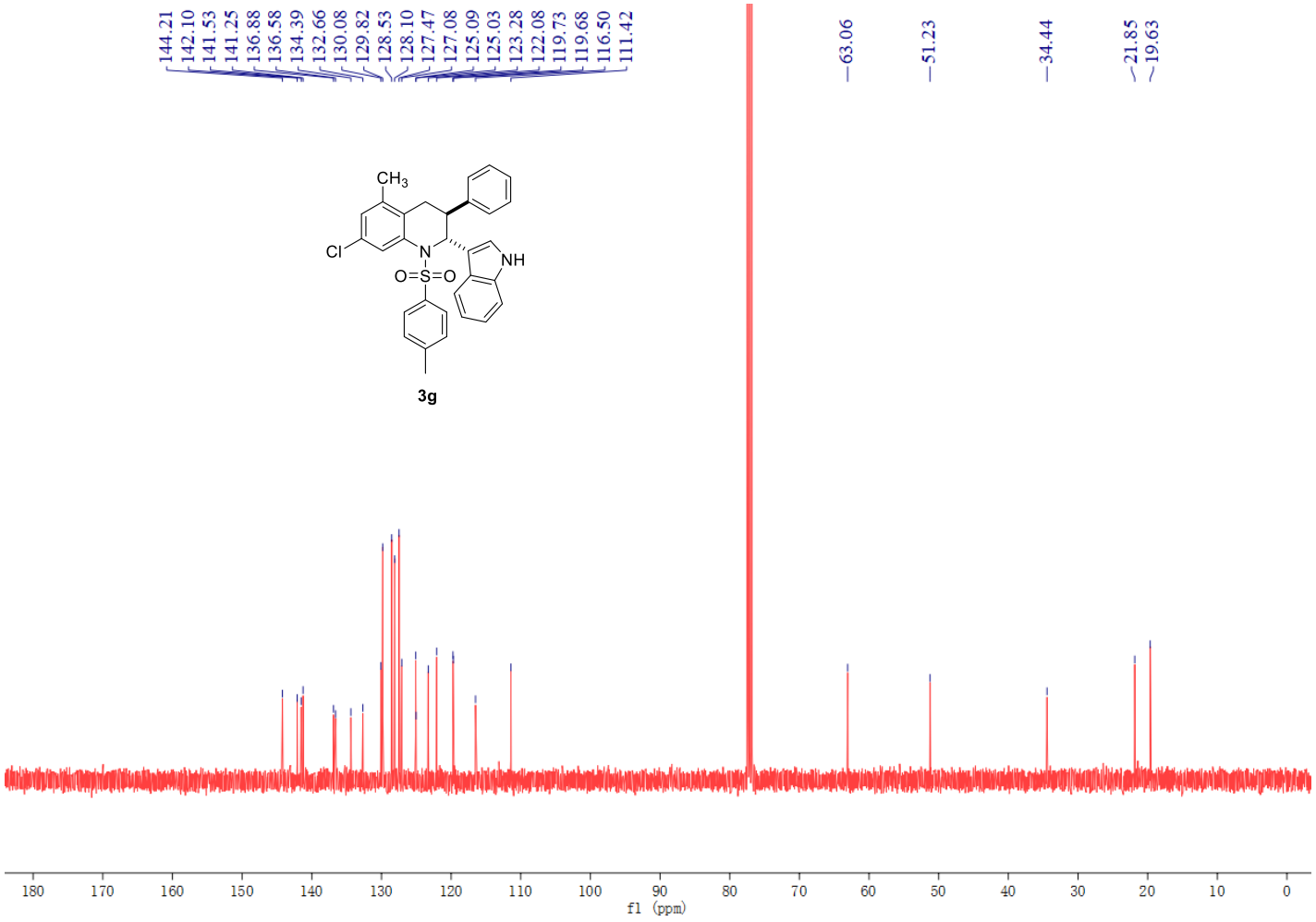


Figure S14. The ^{13}C NMR of 3g

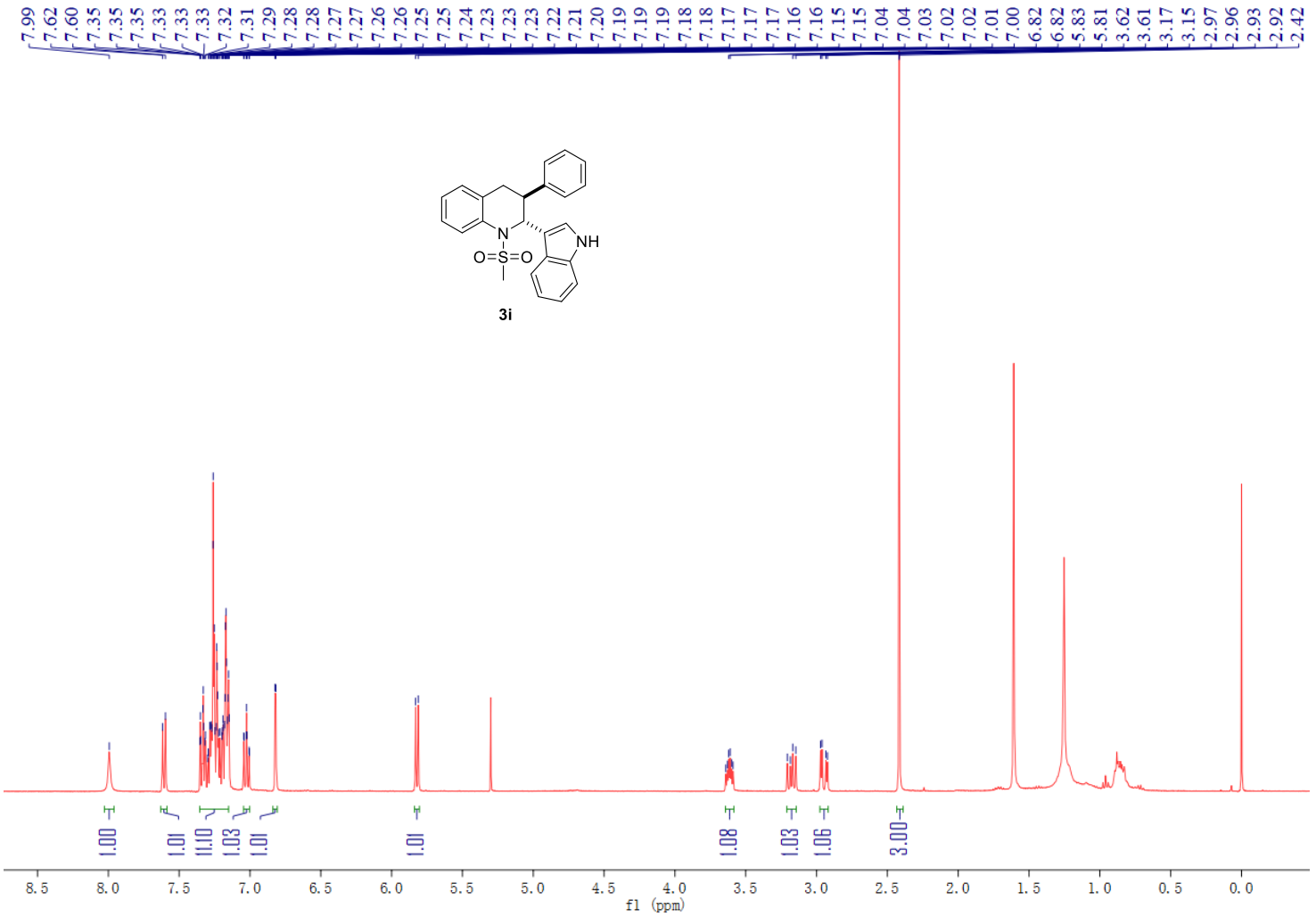


Figure S15. The ^{1}H NMR of 3i

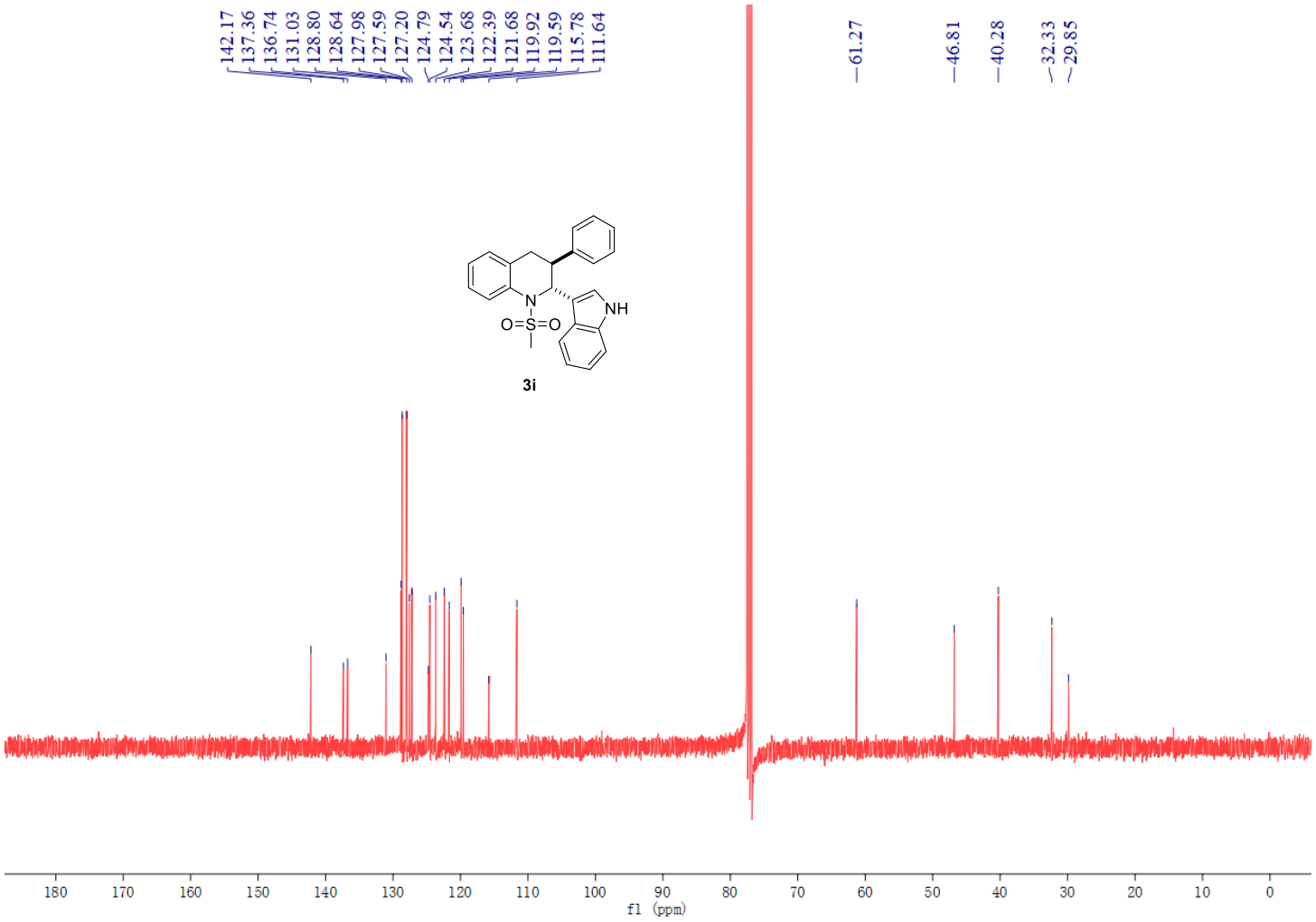


Figure S16. The ^{13}C NMR of 3i

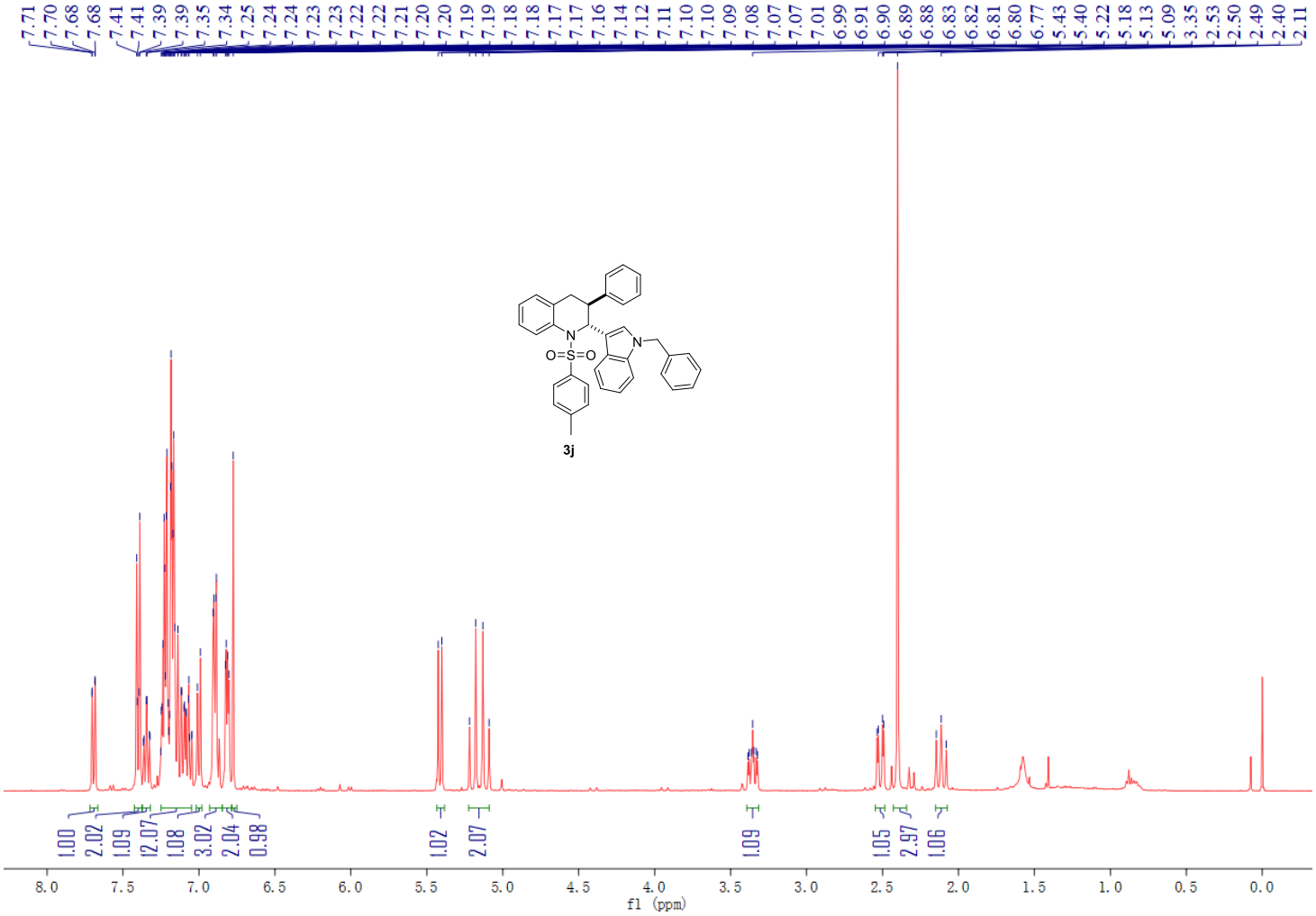


Figure S17. The ^{1}H NMR of 3j

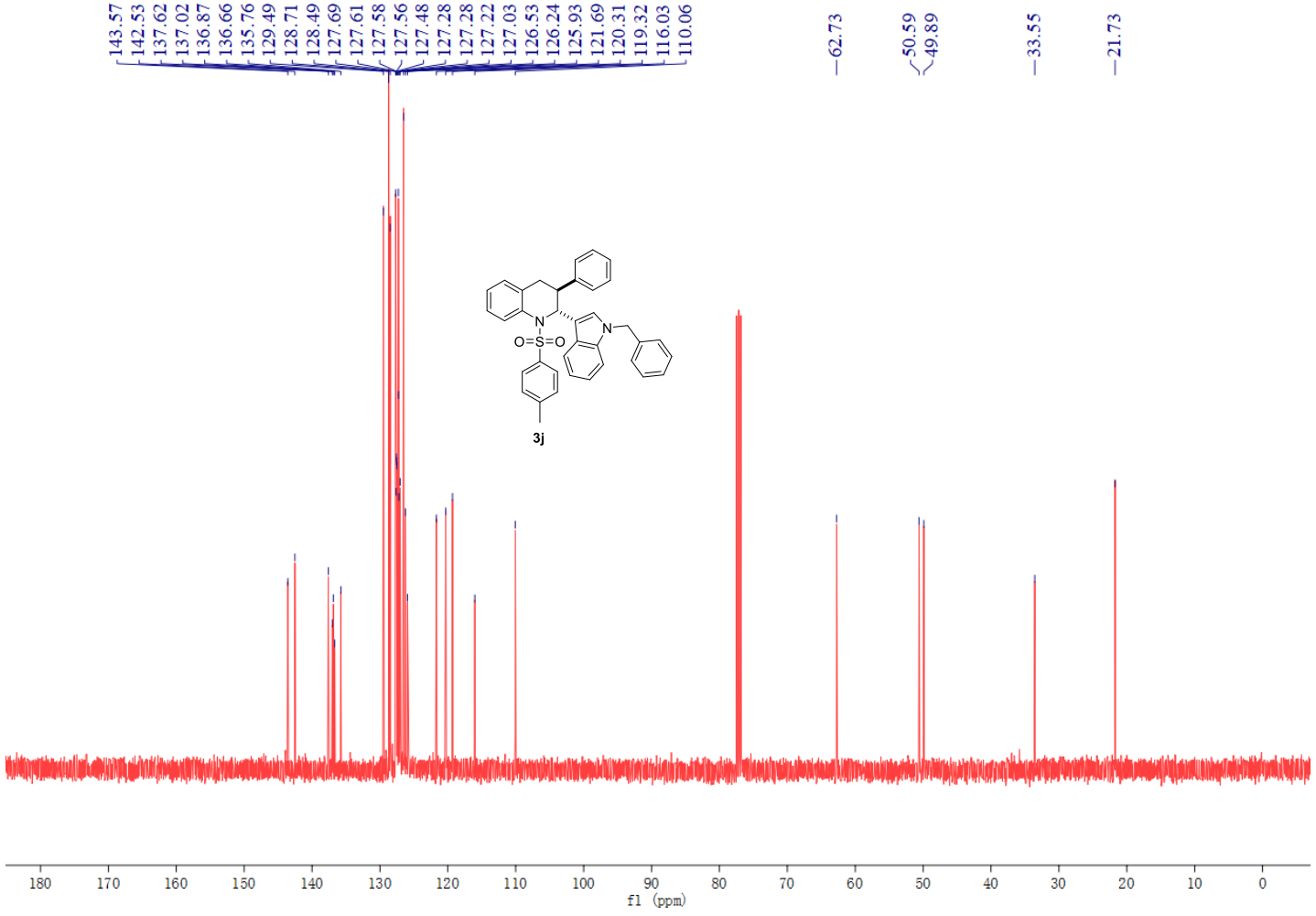


Figure S18. The ^{13}C NMR of 3j

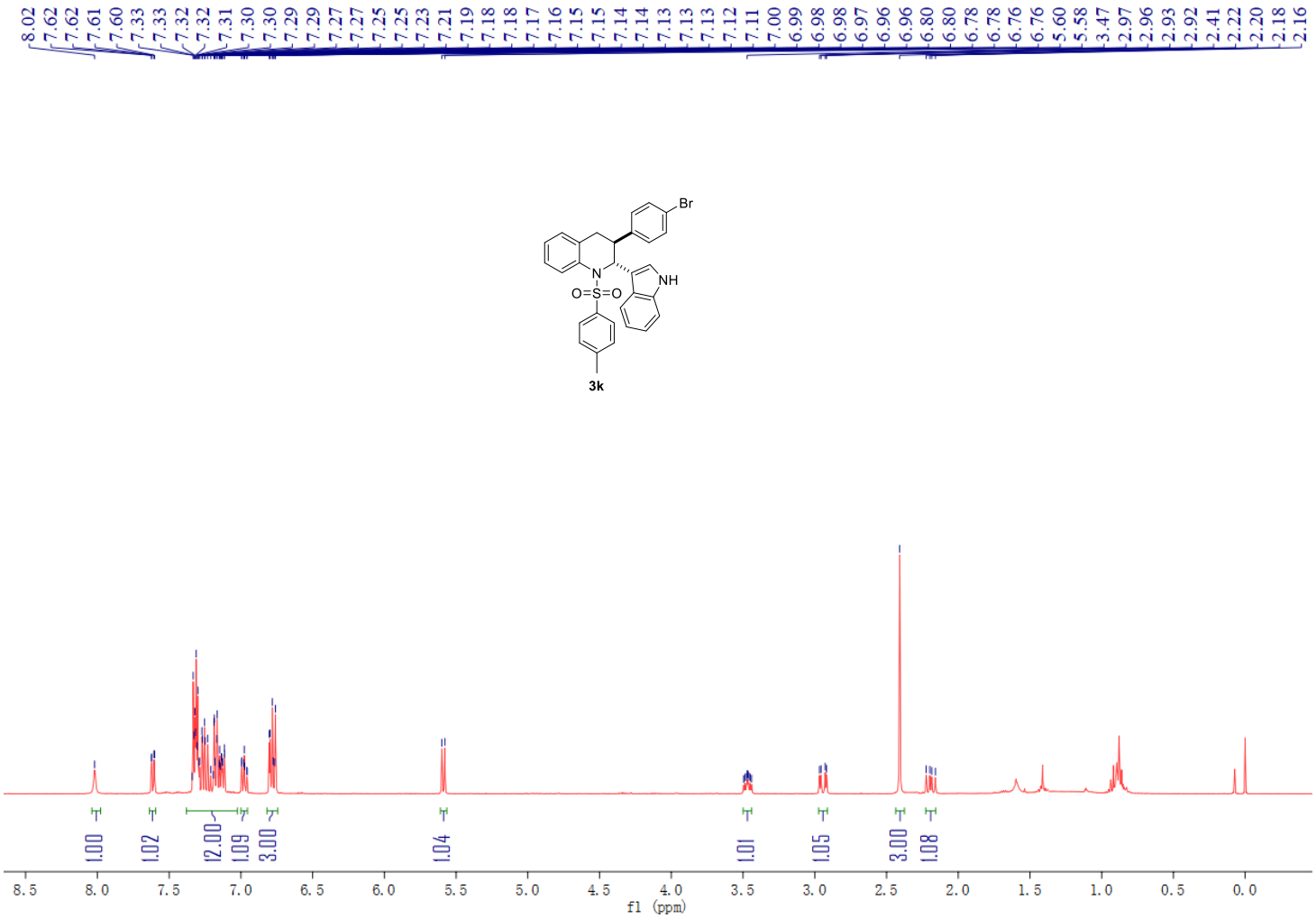
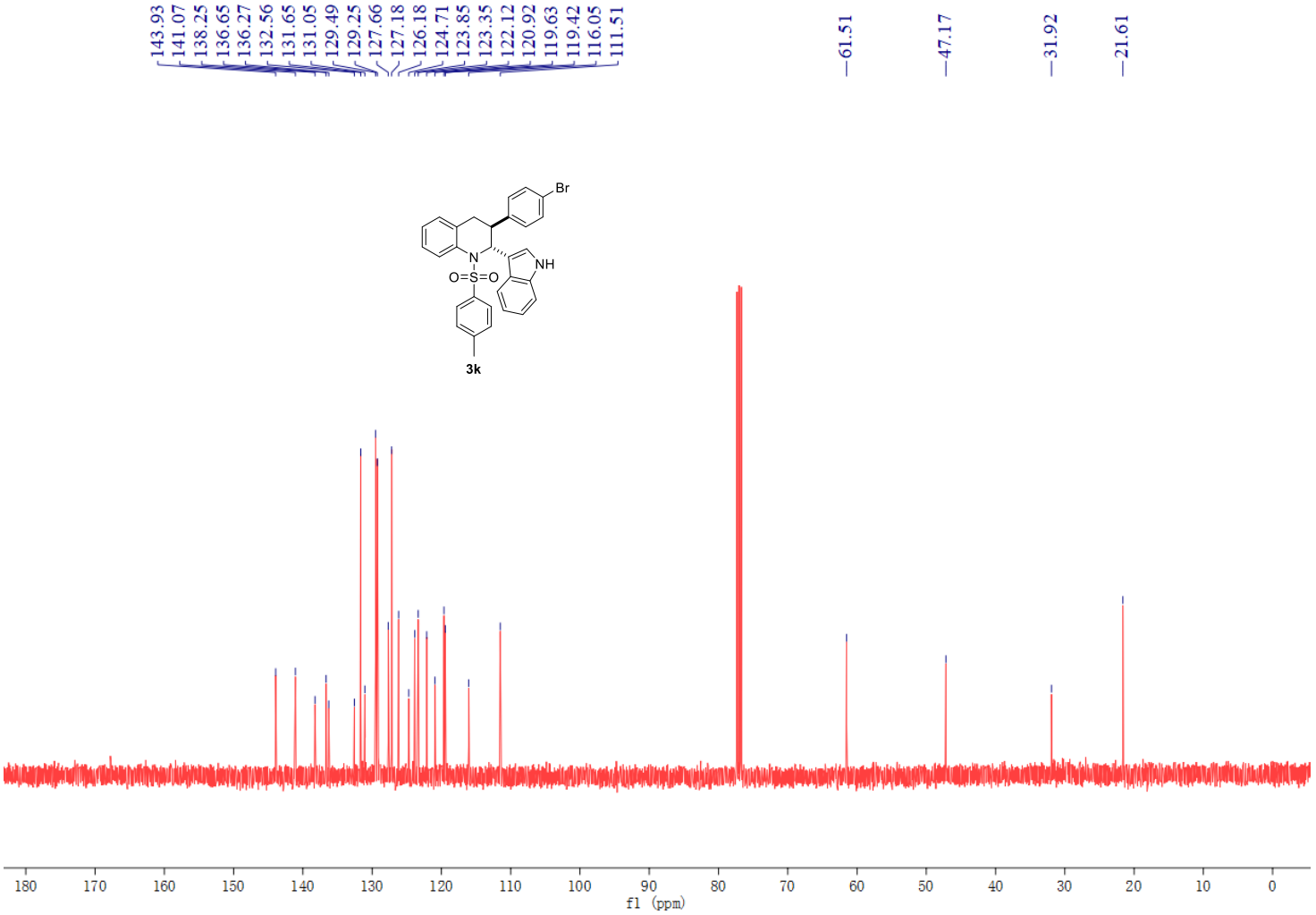


Figure S19. The ^{1}H NMR of 3k



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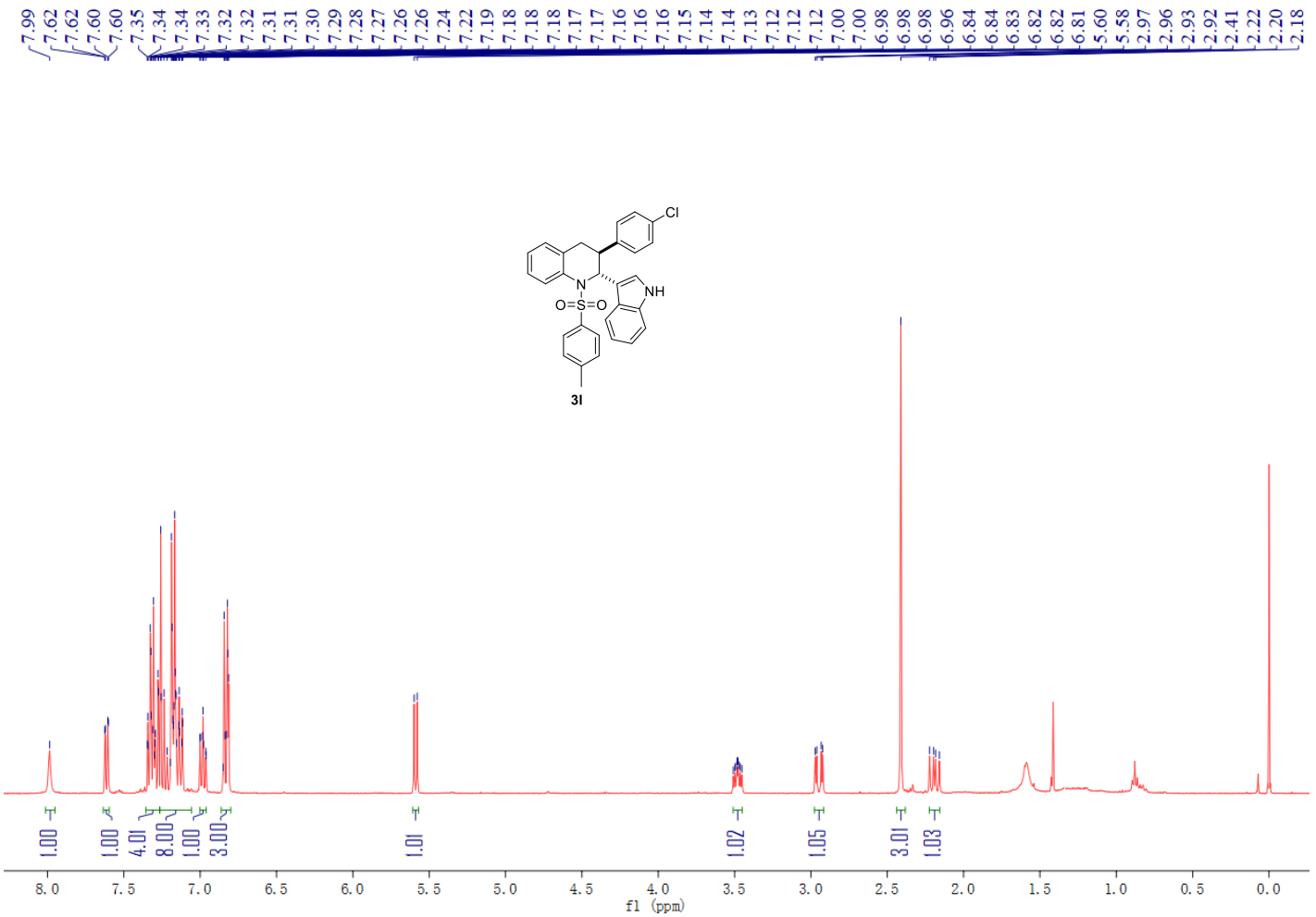
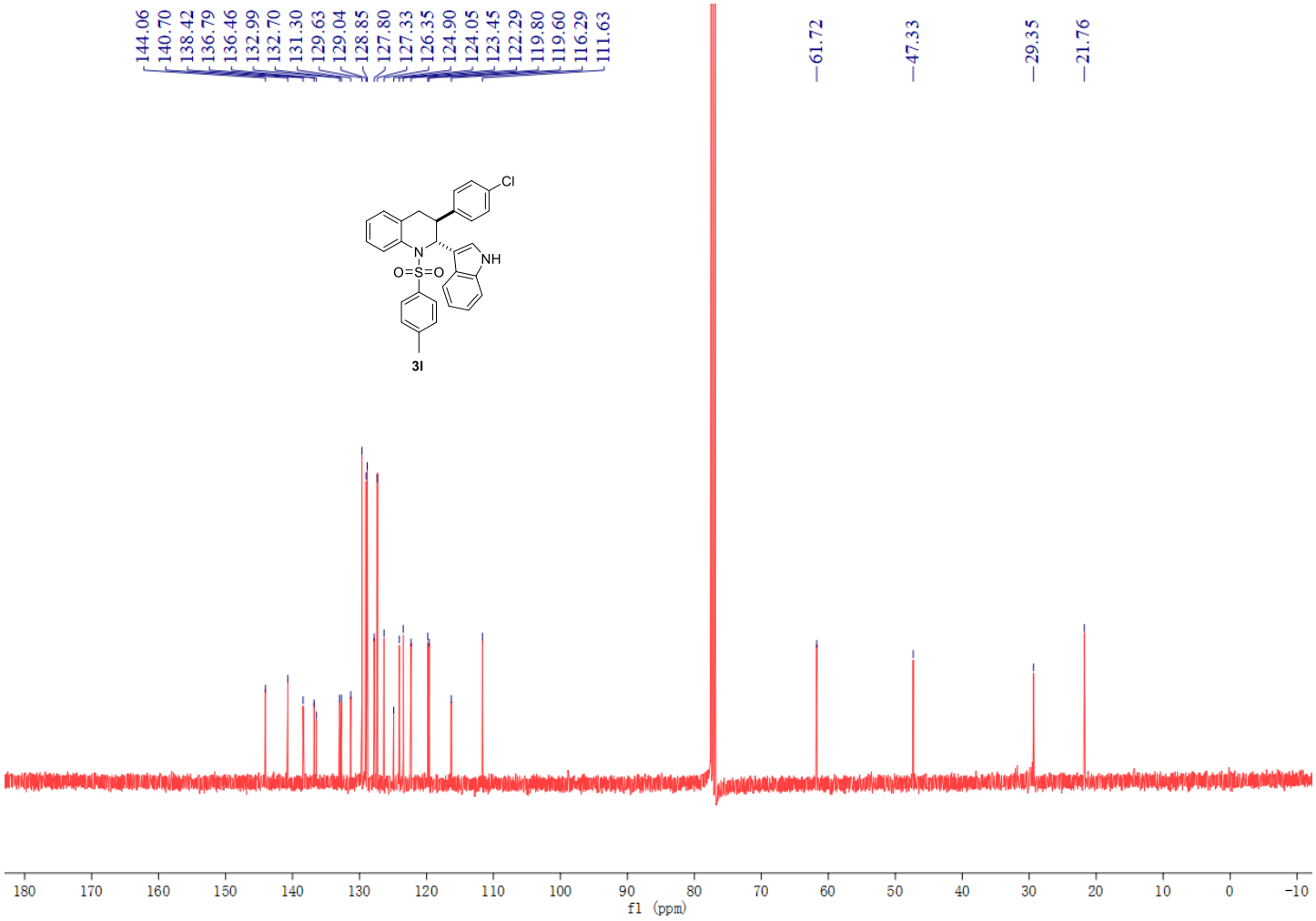


Figure S21. The ^{1}H NMR of 3l



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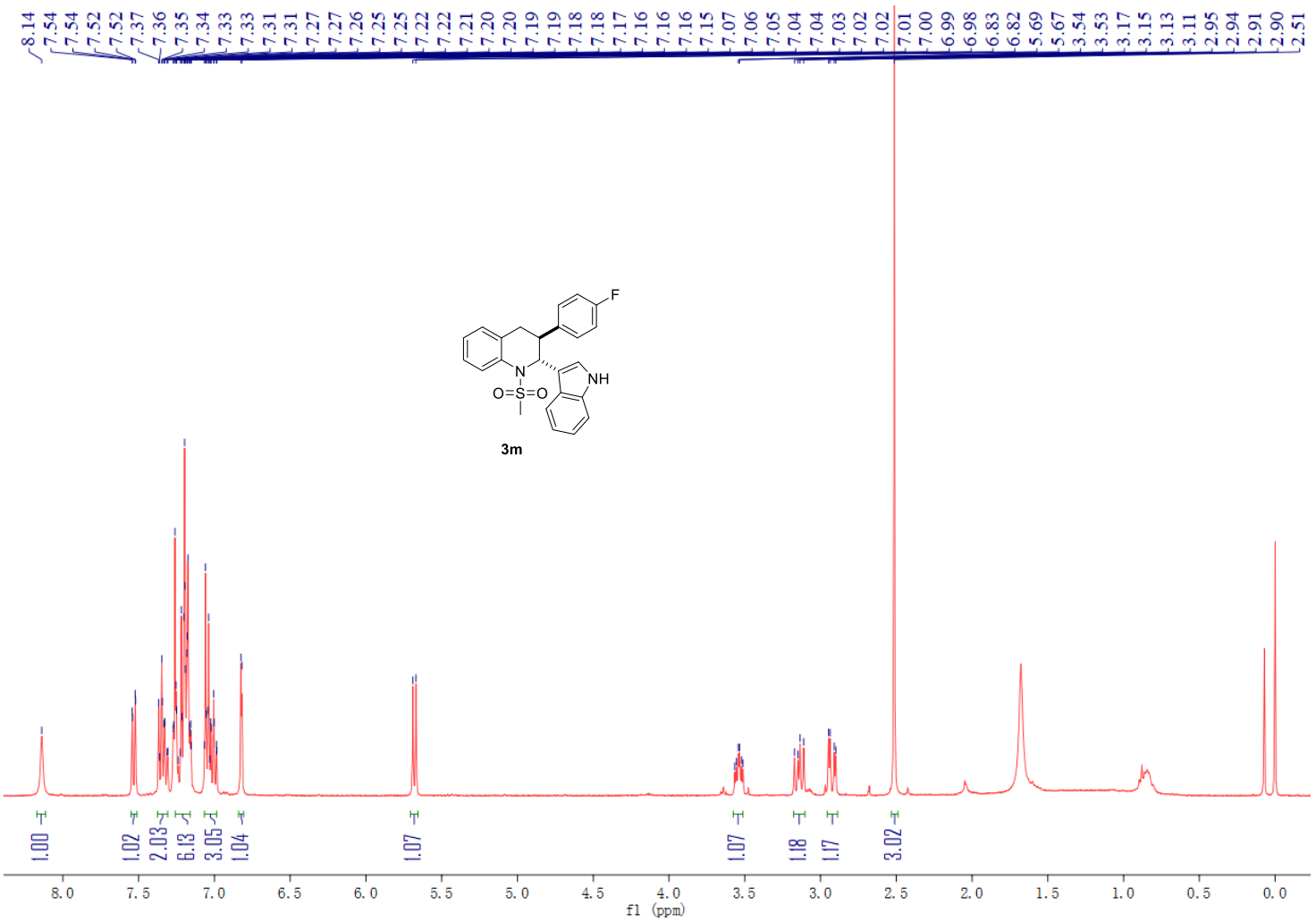

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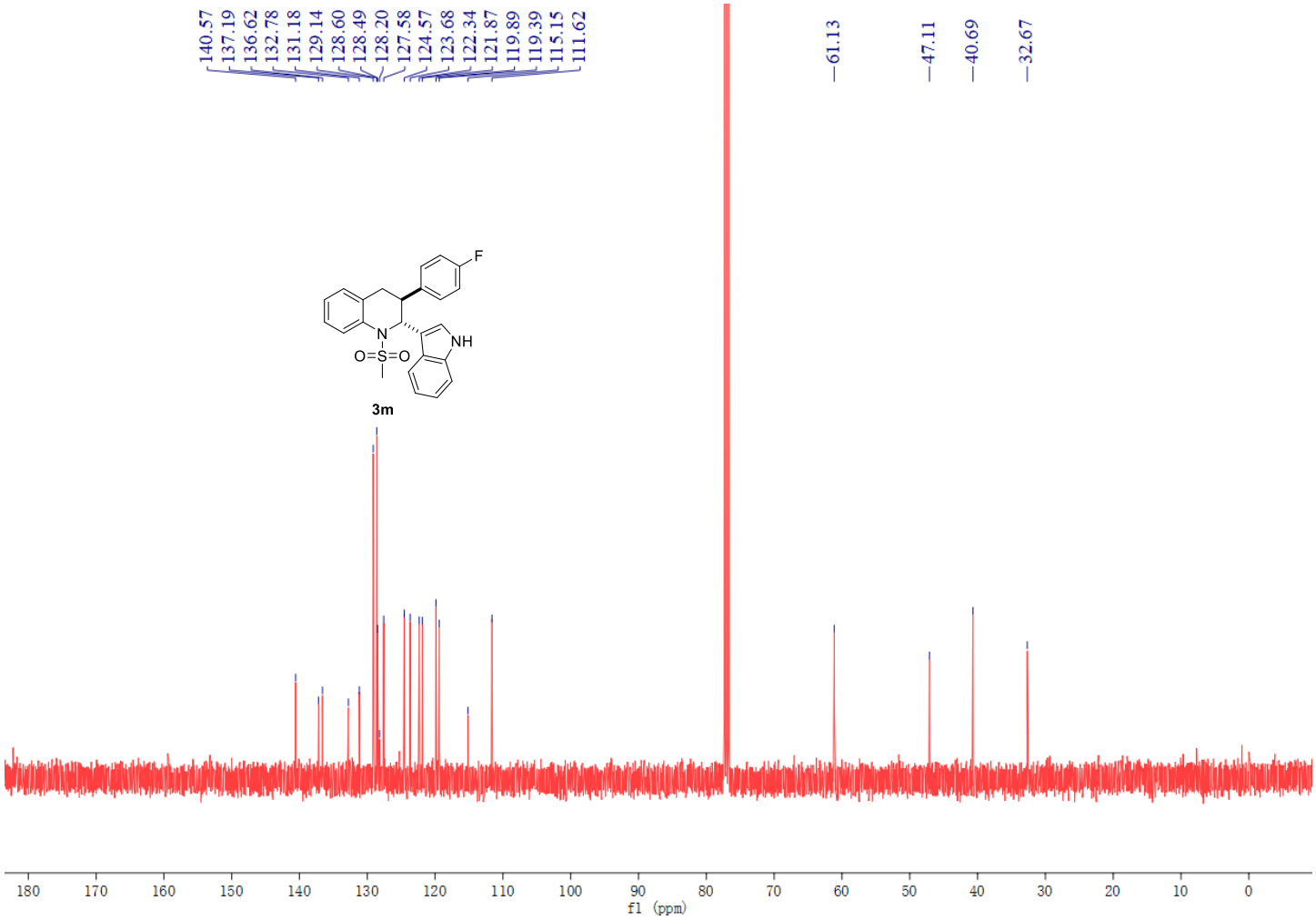

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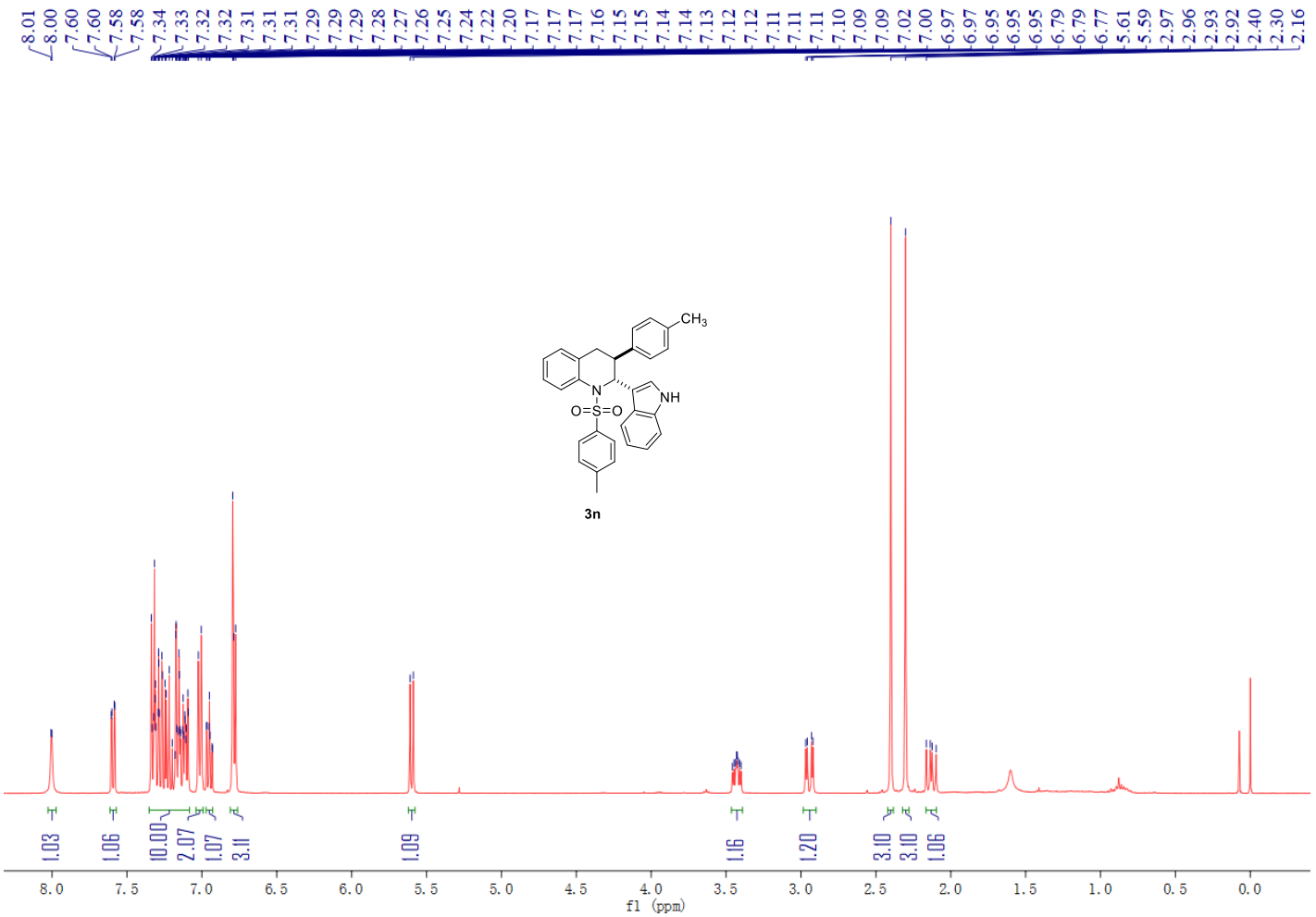

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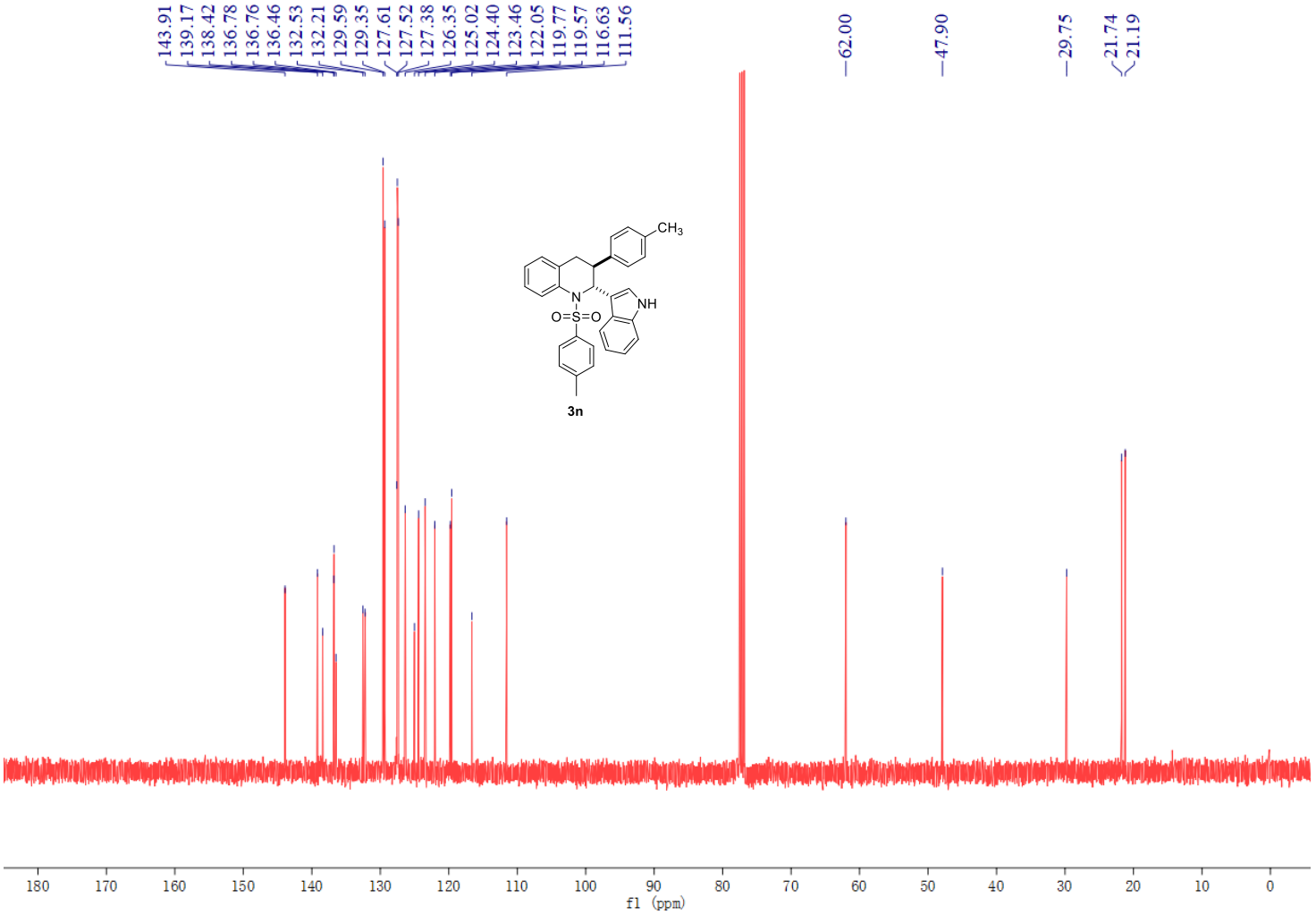
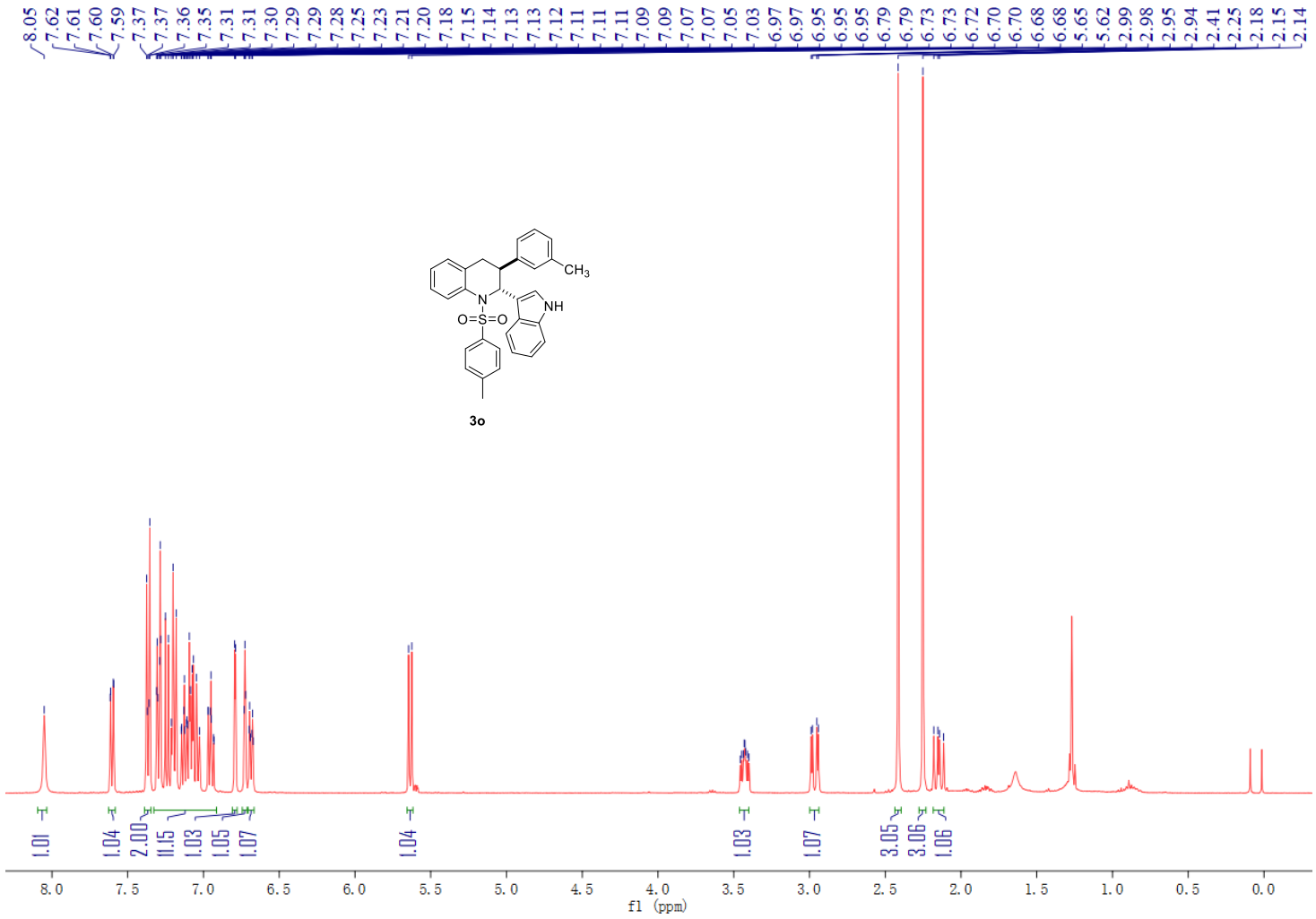


Figure S26. The ^{13}C NMR of 3n



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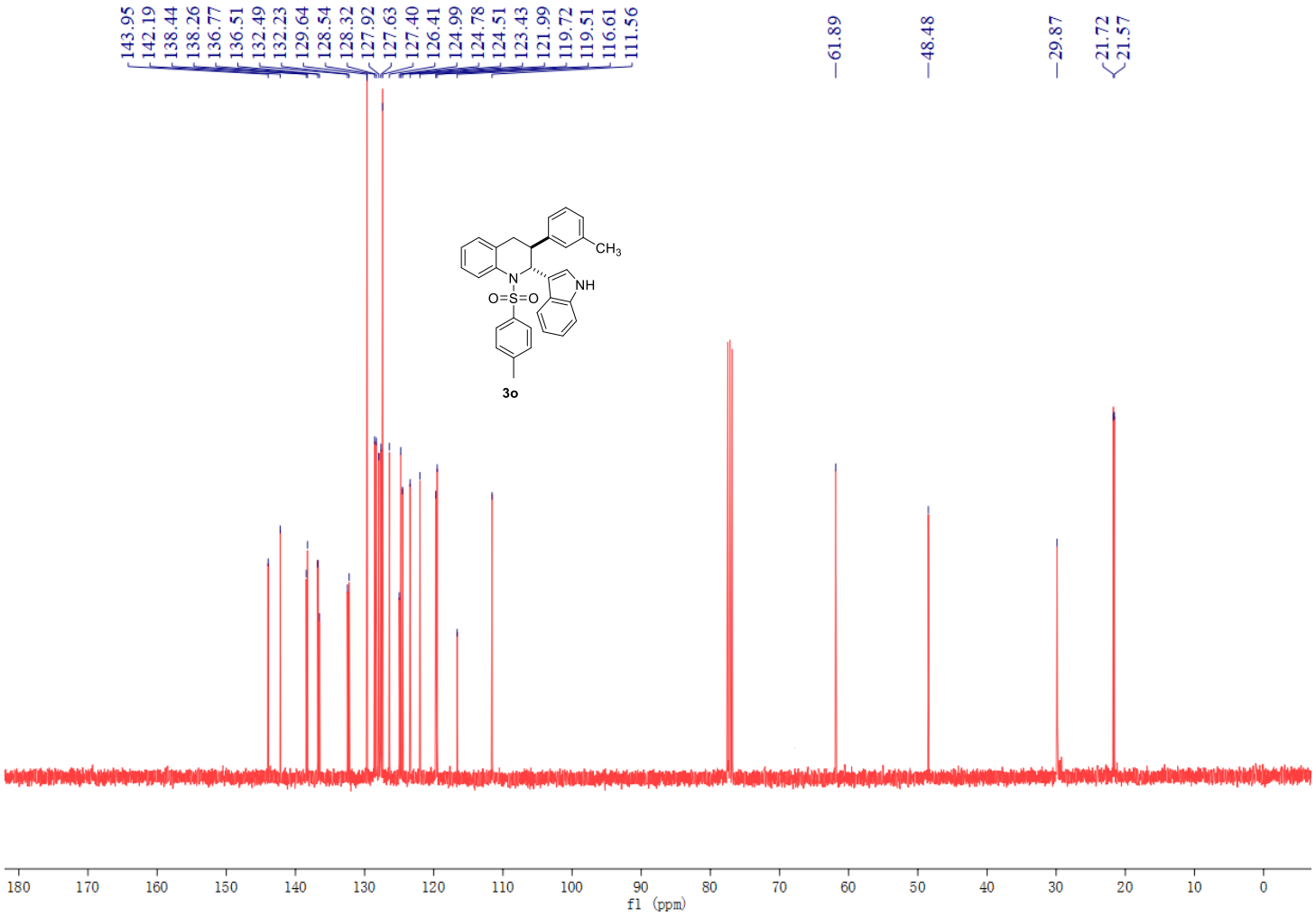

Figure S28. The ^{13}C NMR of 3o

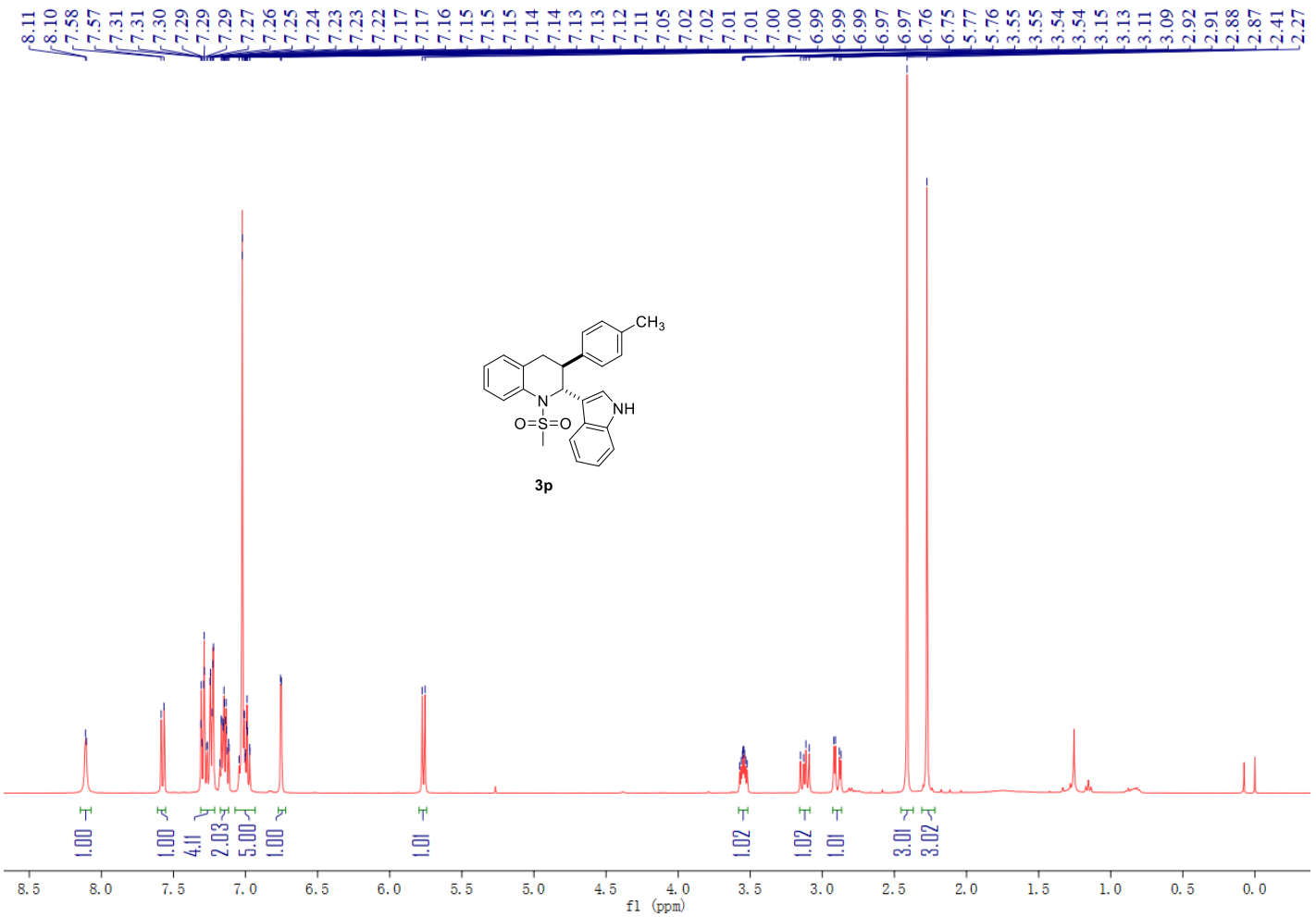

Figure S29. The ^{1}H NMR of 3p

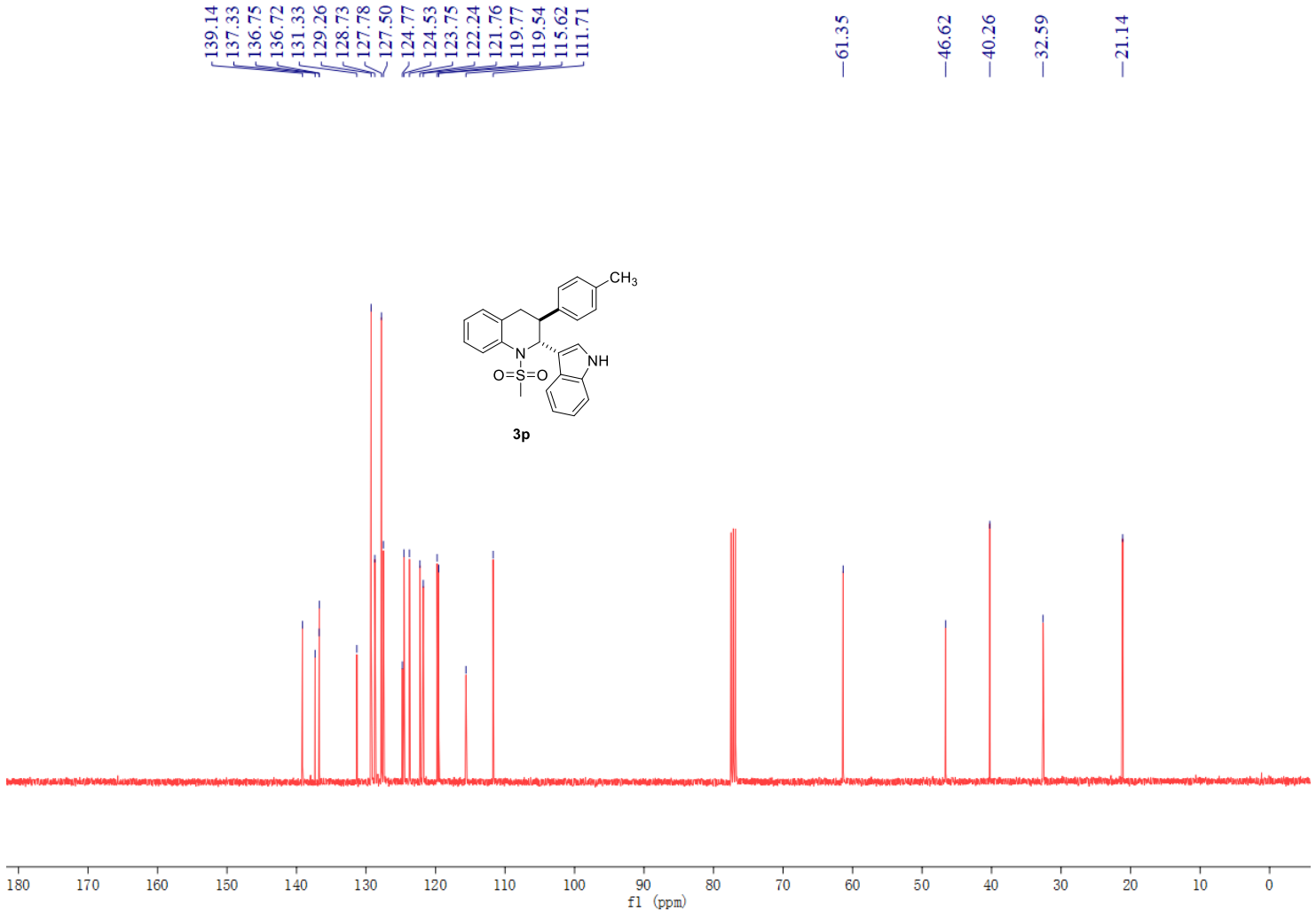

Figure S30. The ^{13}C NMR of 3p

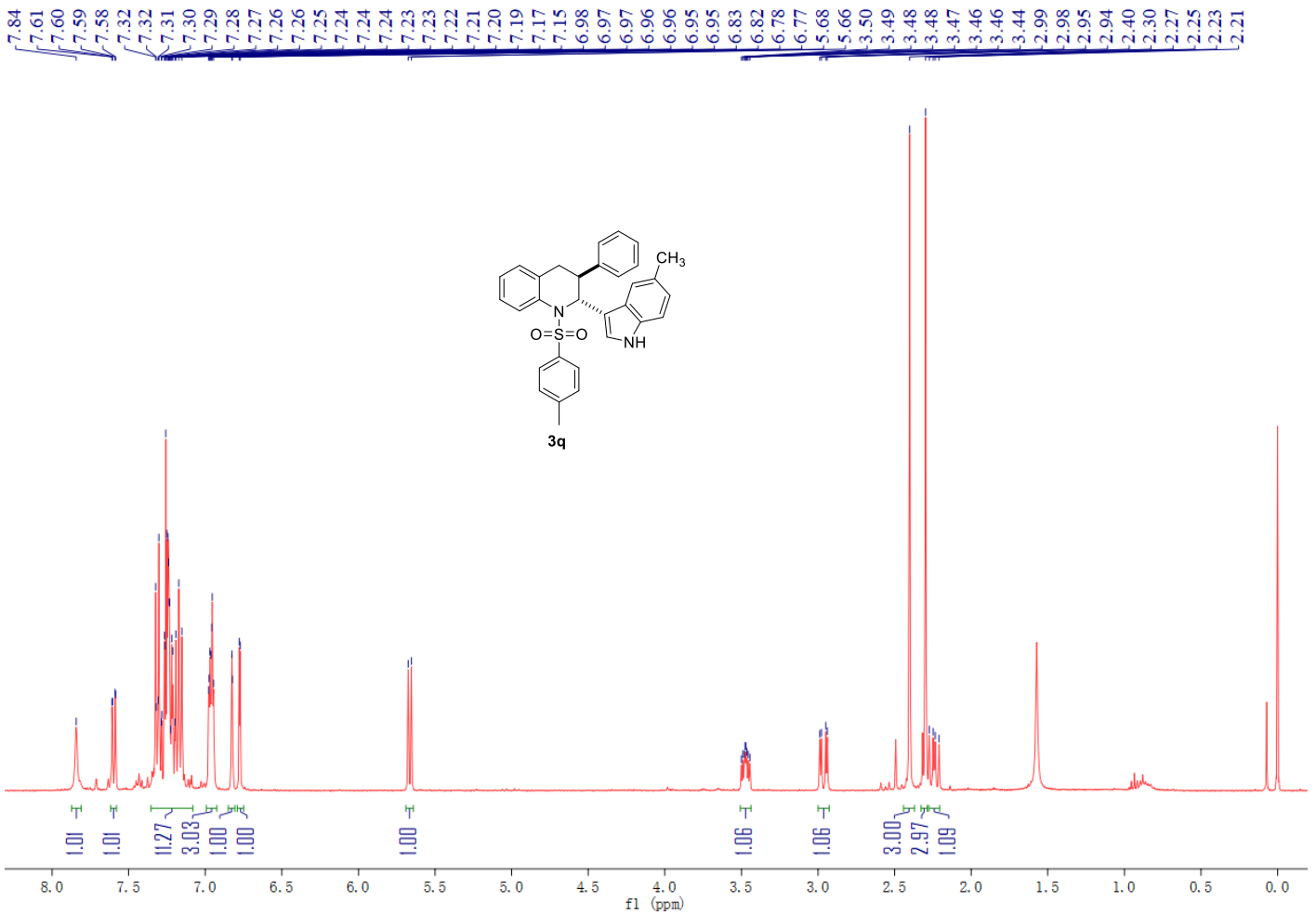

Figure S31. The ^{1}H NMR of 3q

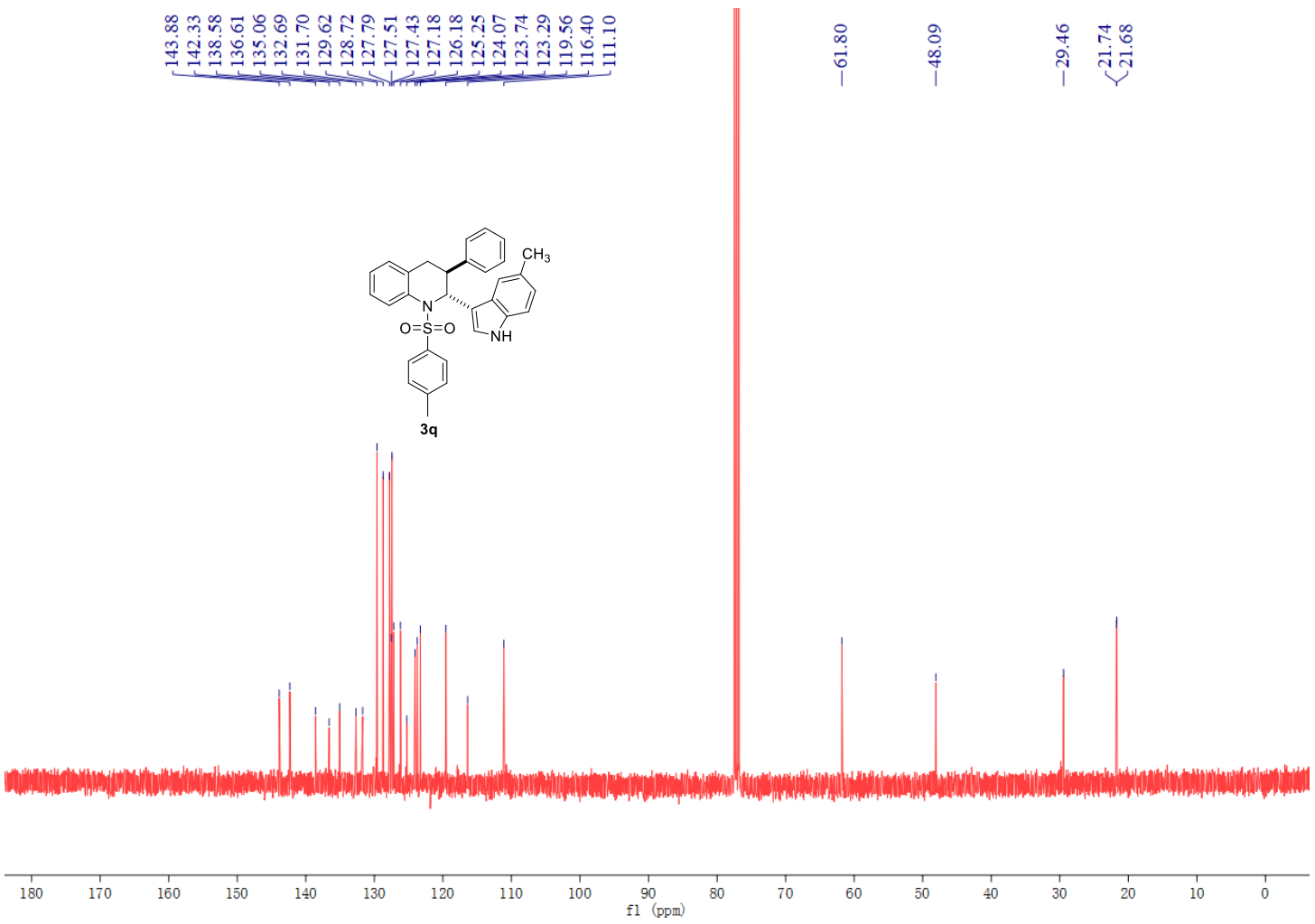

Figure S32. The ^{13}C NMR of 3q

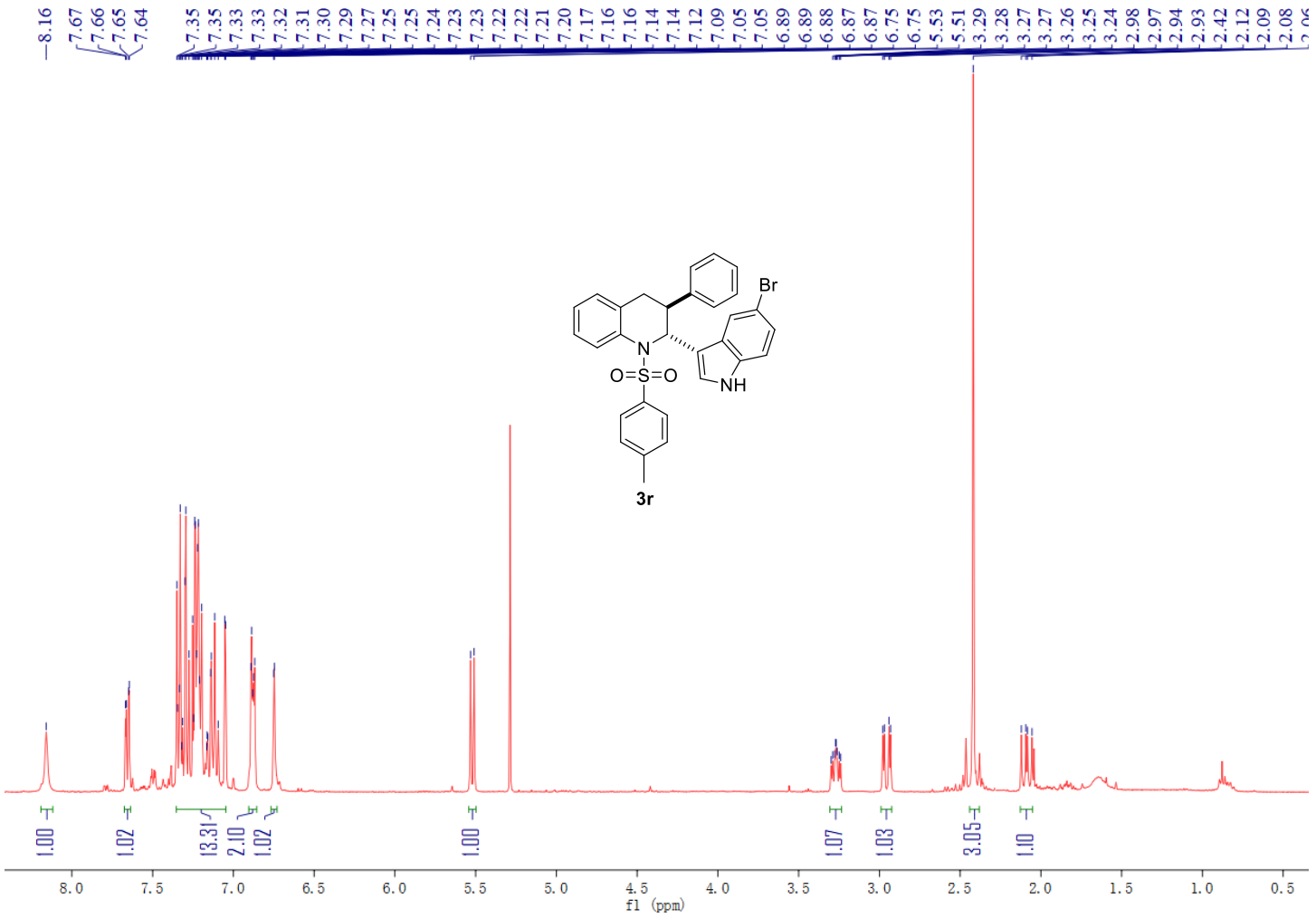

Figure S33. The ^{1}H NMR of 3r

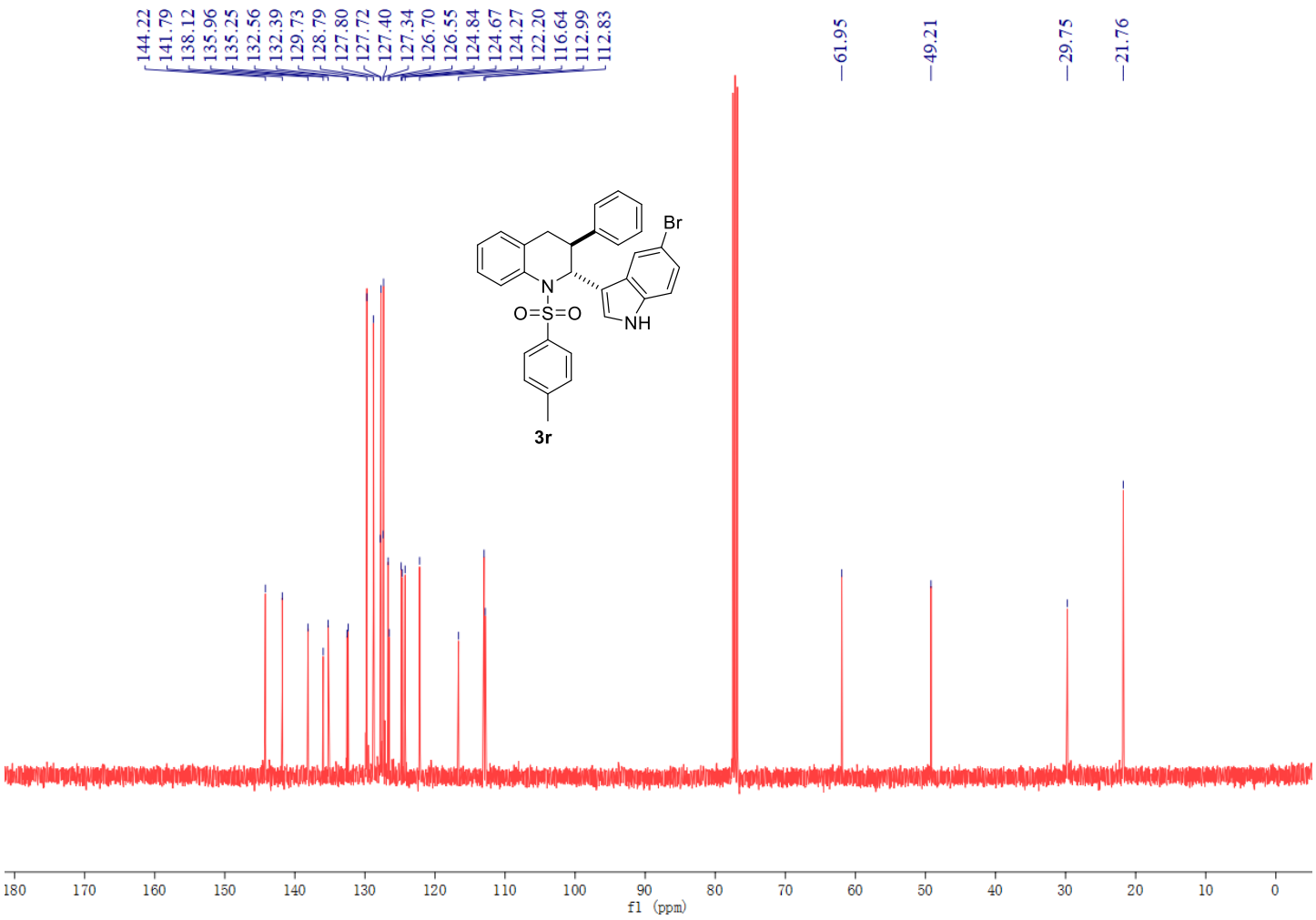

Figure S34. The ^{13}C NMR of 3r

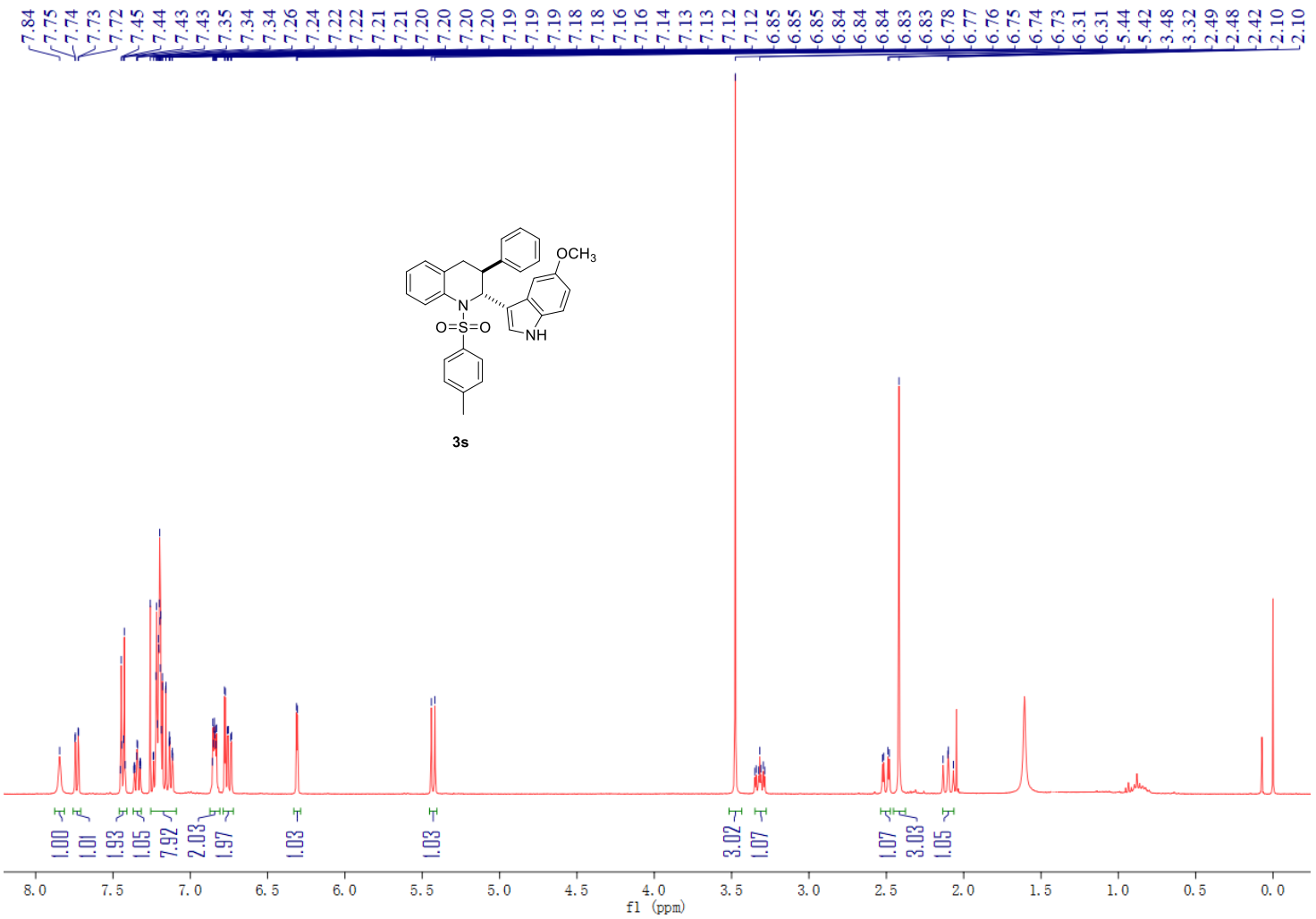

Figure S35. The ^{1}H NMR of 3s

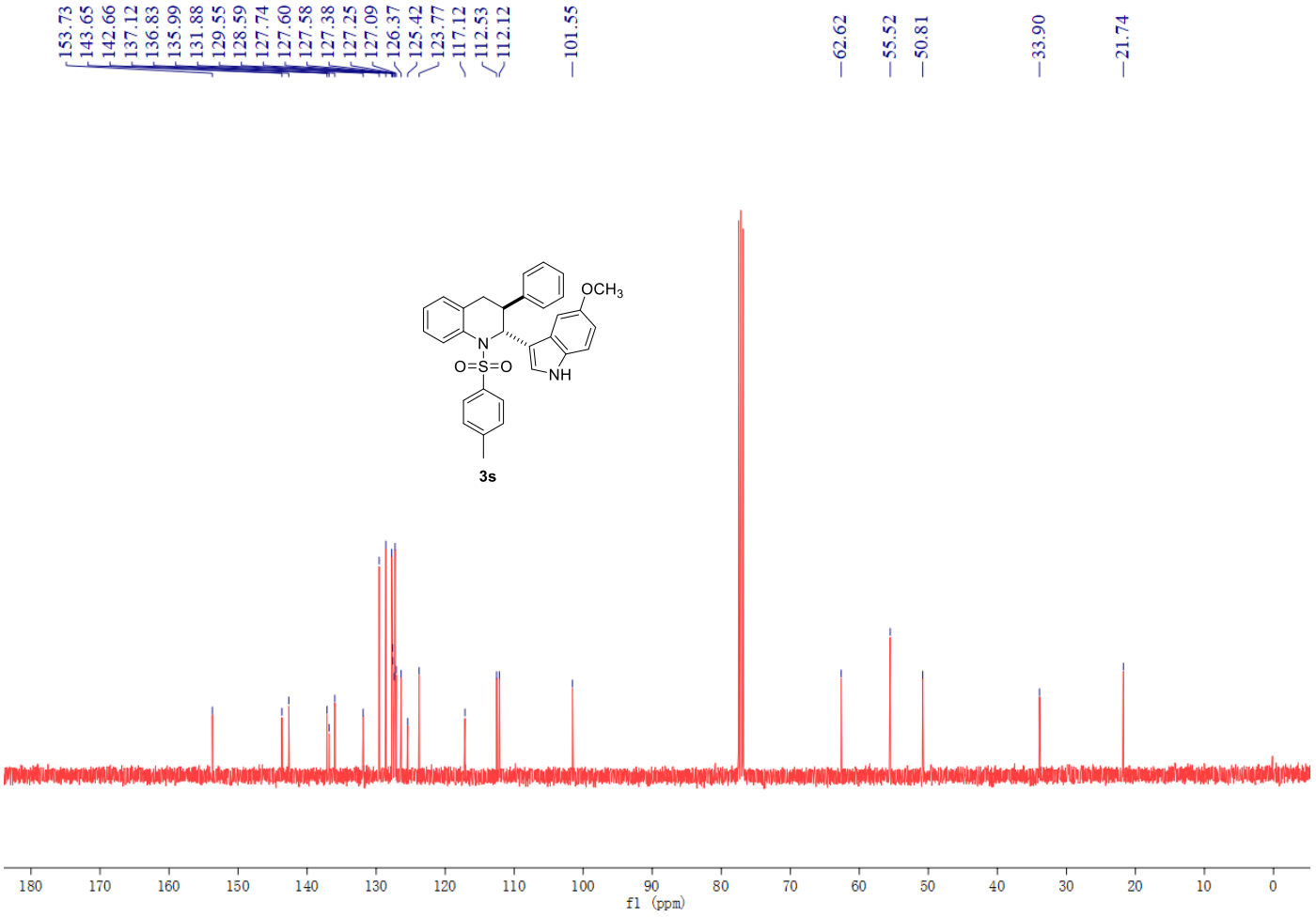

Figure S36. The ^{13}C NMR of 3s

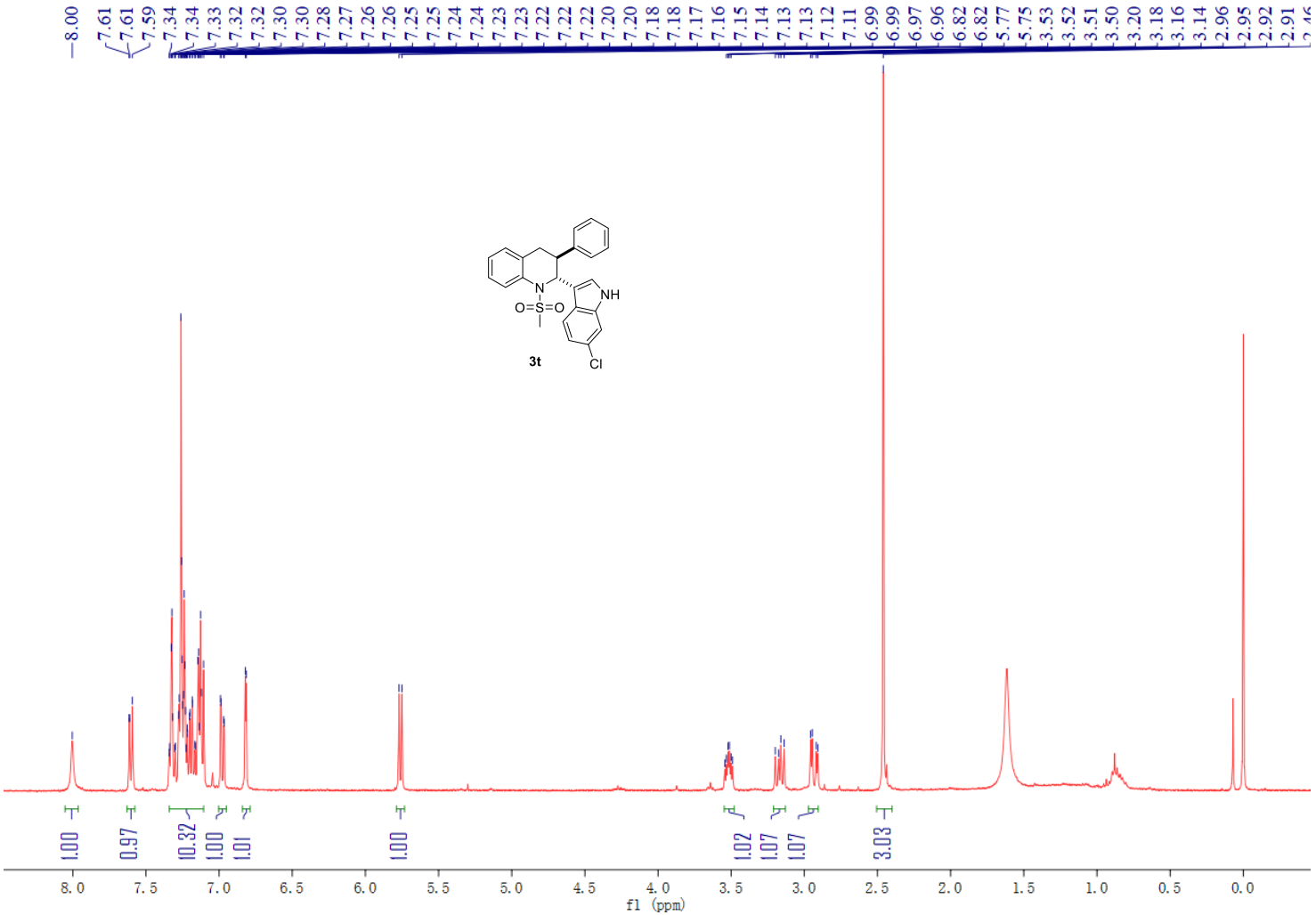

Figure S37. The ^{1}H NMR of 3t

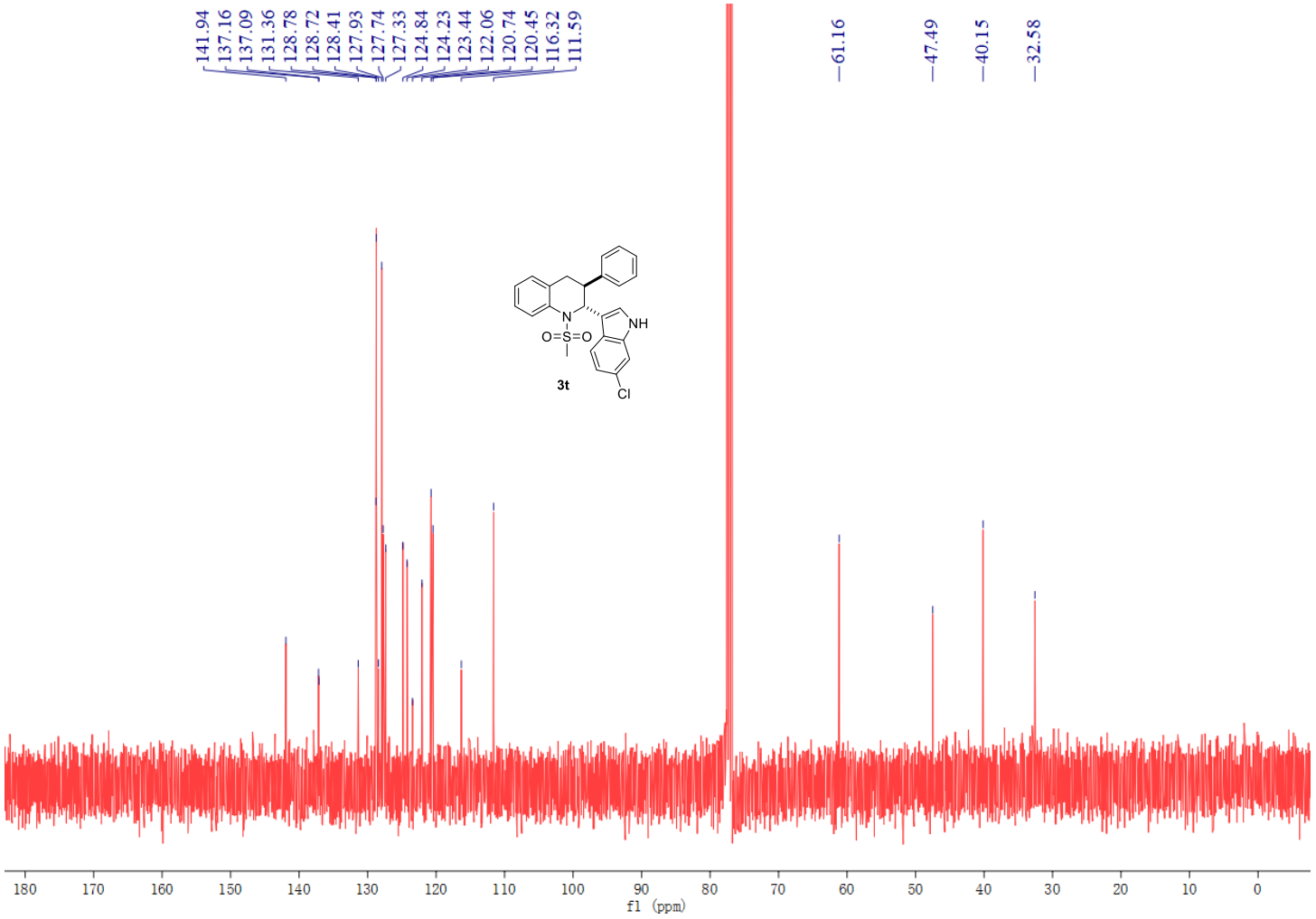

Figure S38. The ^{13}C NMR of 3t

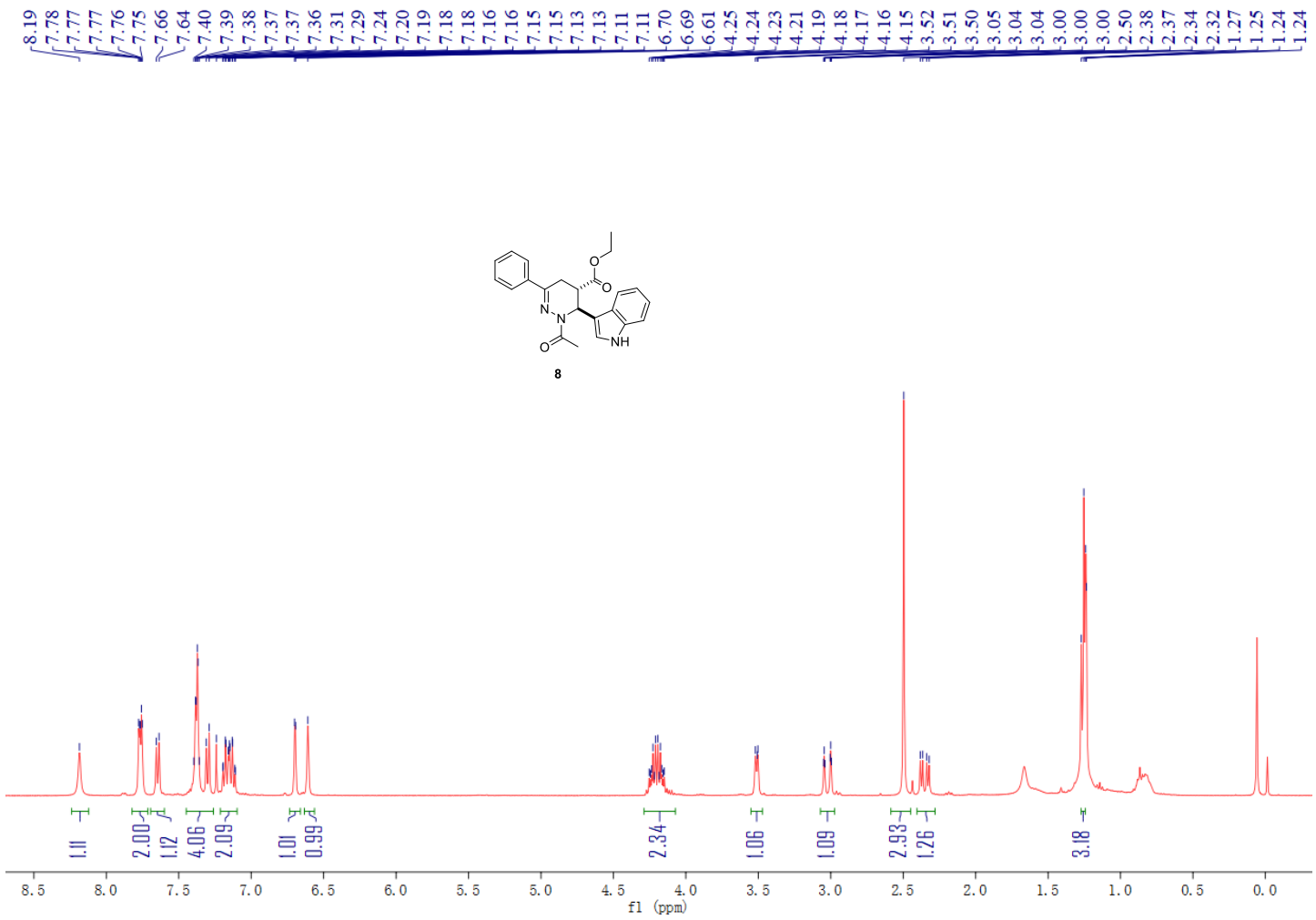

Figure S39. The ^{1}H NMR of 8

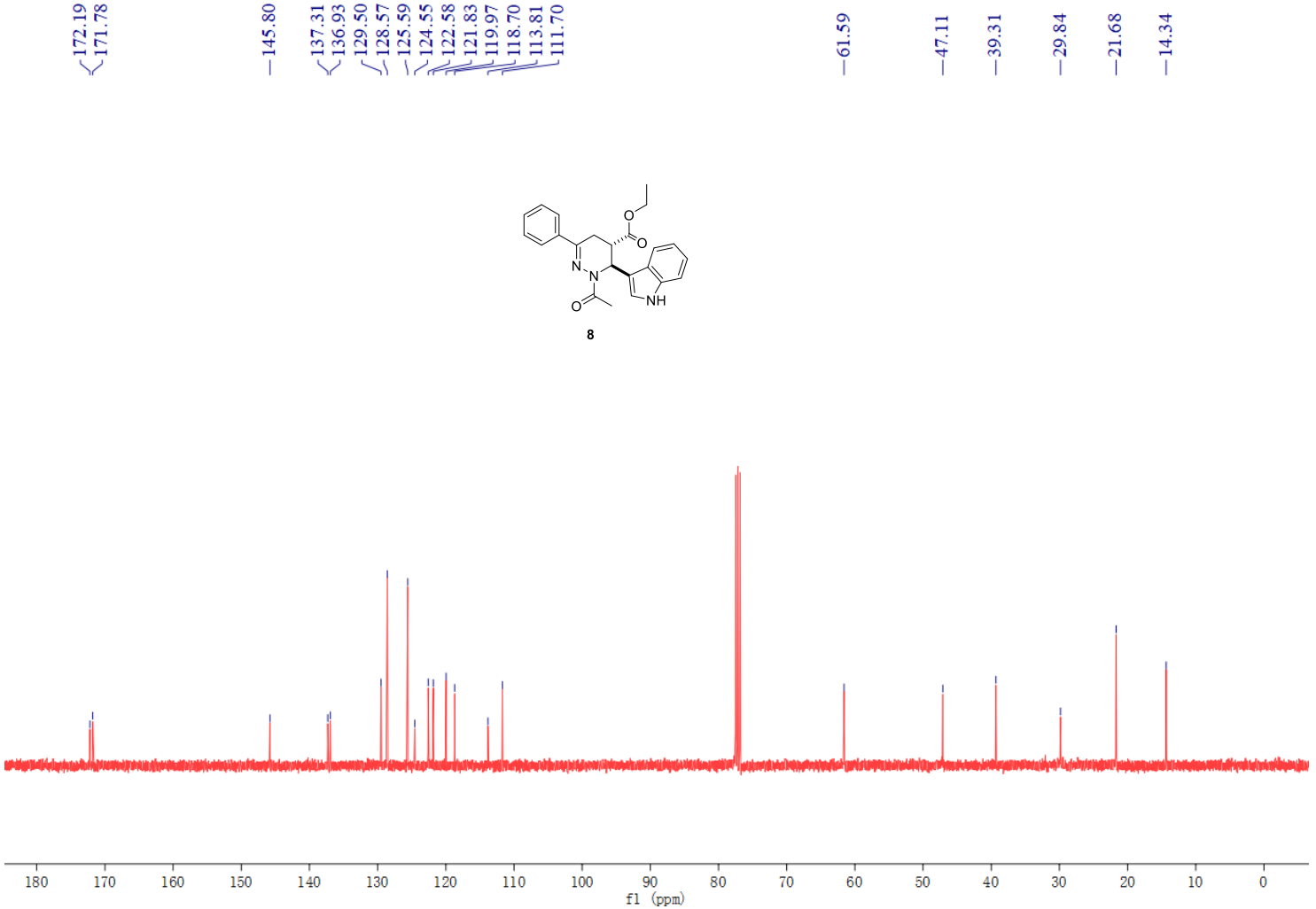

Figure S40. The ^{13}C NMR of 8

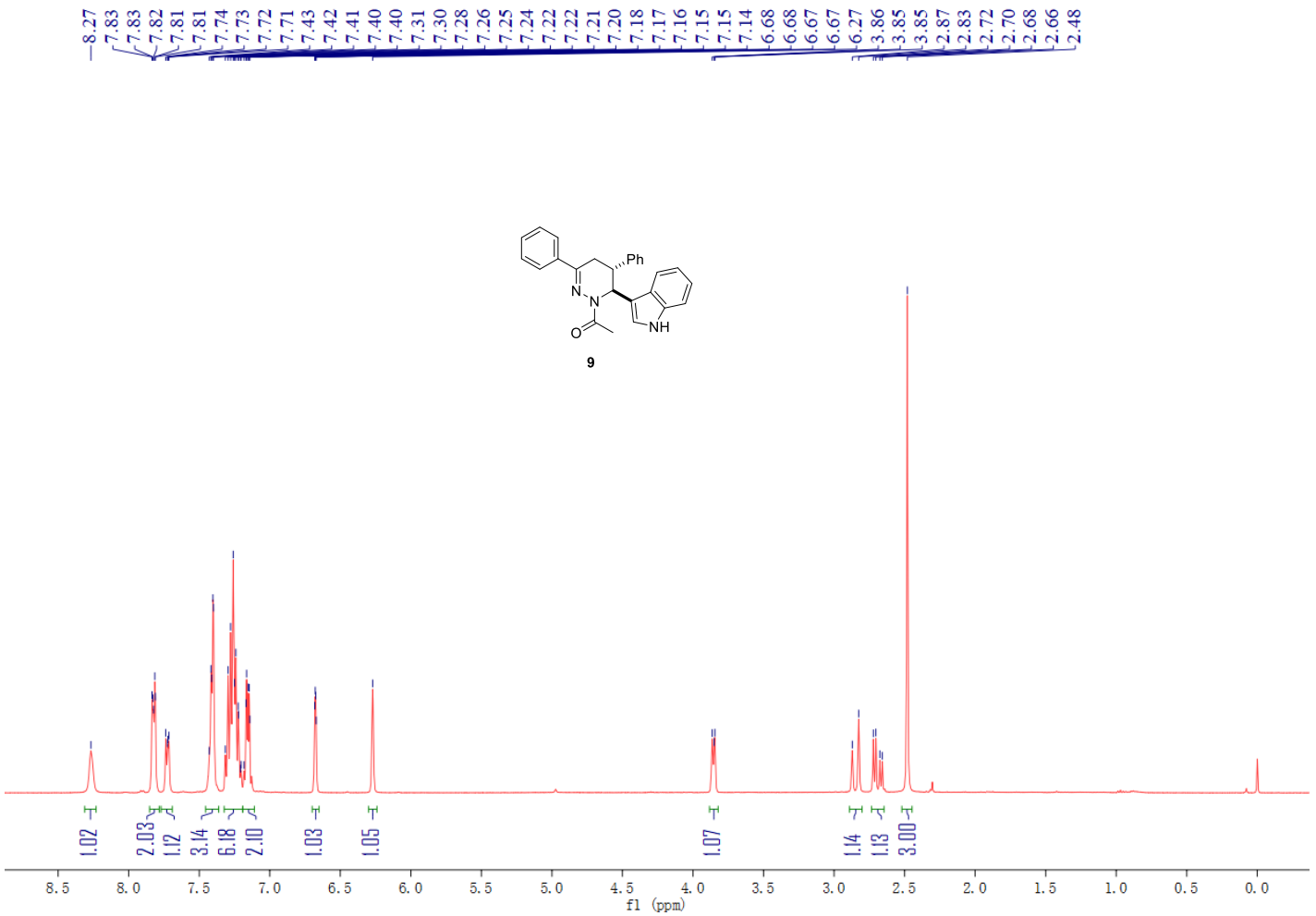

Figure S41. The ^{1}H NMR of 9

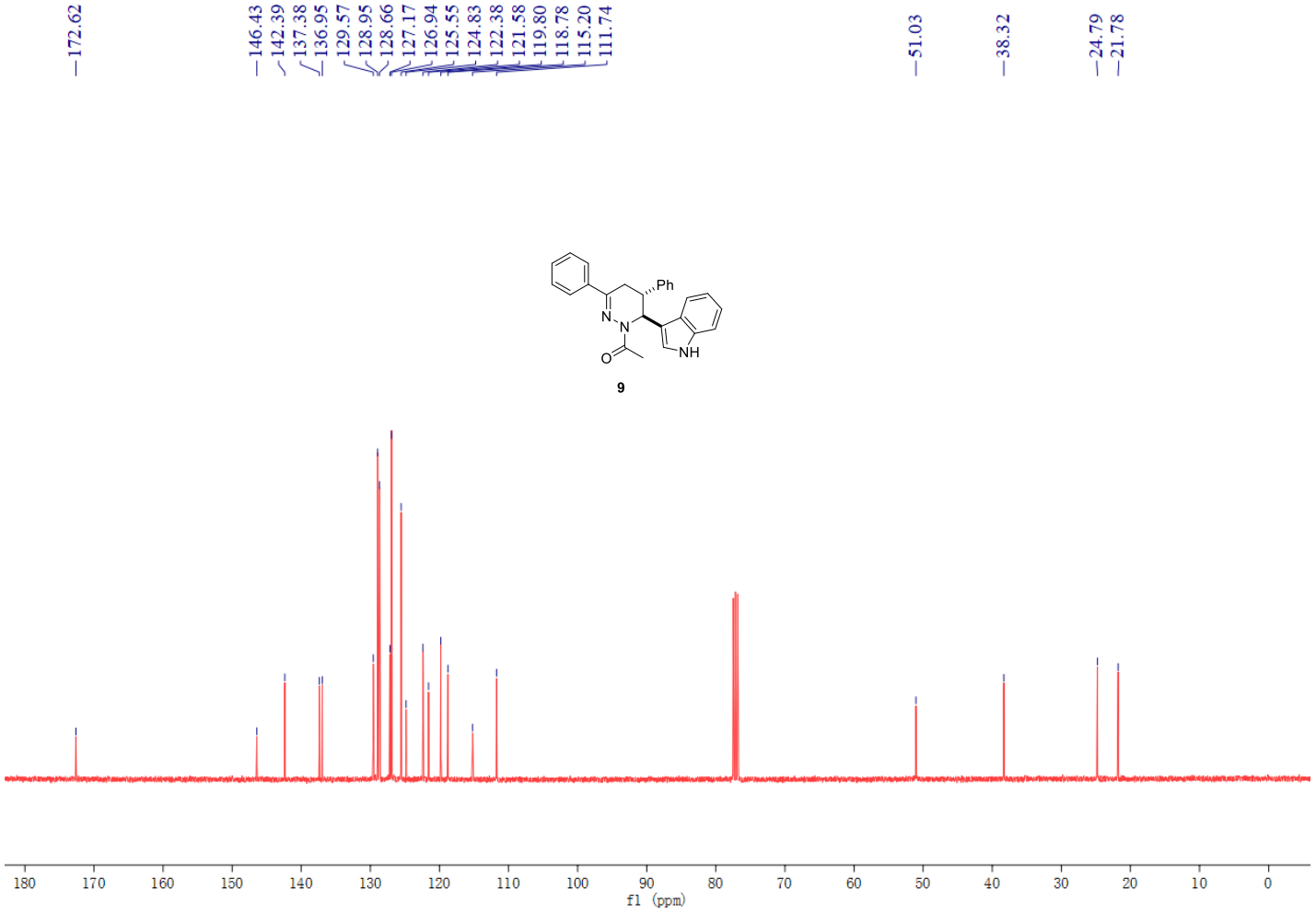

Figure S42. The ^{13}C NMR of 9