Supplementary Information (SI) for Organic Chemistry Frontiers.
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Continuous 1,4/1,6- and 1,2-addition reactions combined with the skeletal rearrangement of 5a*H*,13*H*-chromeno[2,3-*b*]-quinolizin-13-ones with isocyanides to enable the synthesis of pyrido[2,3-*b*]indolizines

Bi-Na Shao, Jia-Ming Yang, Li Chen, Wei-Min Zhang, Long-Kun Chen, and Sheng-Jiao Yan*

Key Laboratory of Medicinal Chemistry for Natural Resources (Yunnan University), Ministry of Education, School of Chemical Science and Technology, Yunnan University, Kunming, 650091, P. R. China

Supporting Information

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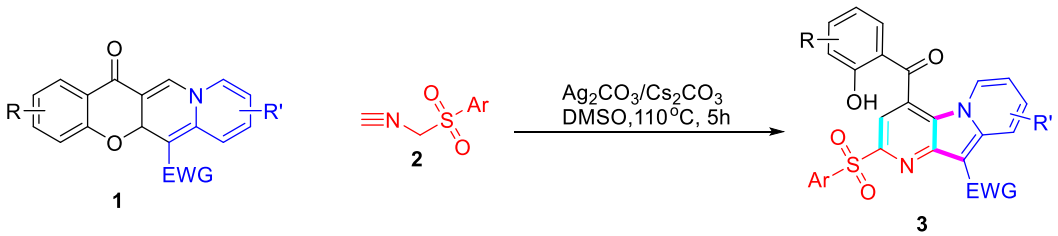
General Information

All compounds were fully characterised by spectroscopic data. The NMR spectra were recorded on a Bruker AVANCEIIIHD600 and DRX500. Chemical shifts (δ) are expressed in ppm, J values are given in Hz, DMSO-d_6 was used as solvent. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on a XT-4A melting point apparatus and are uncorrected.

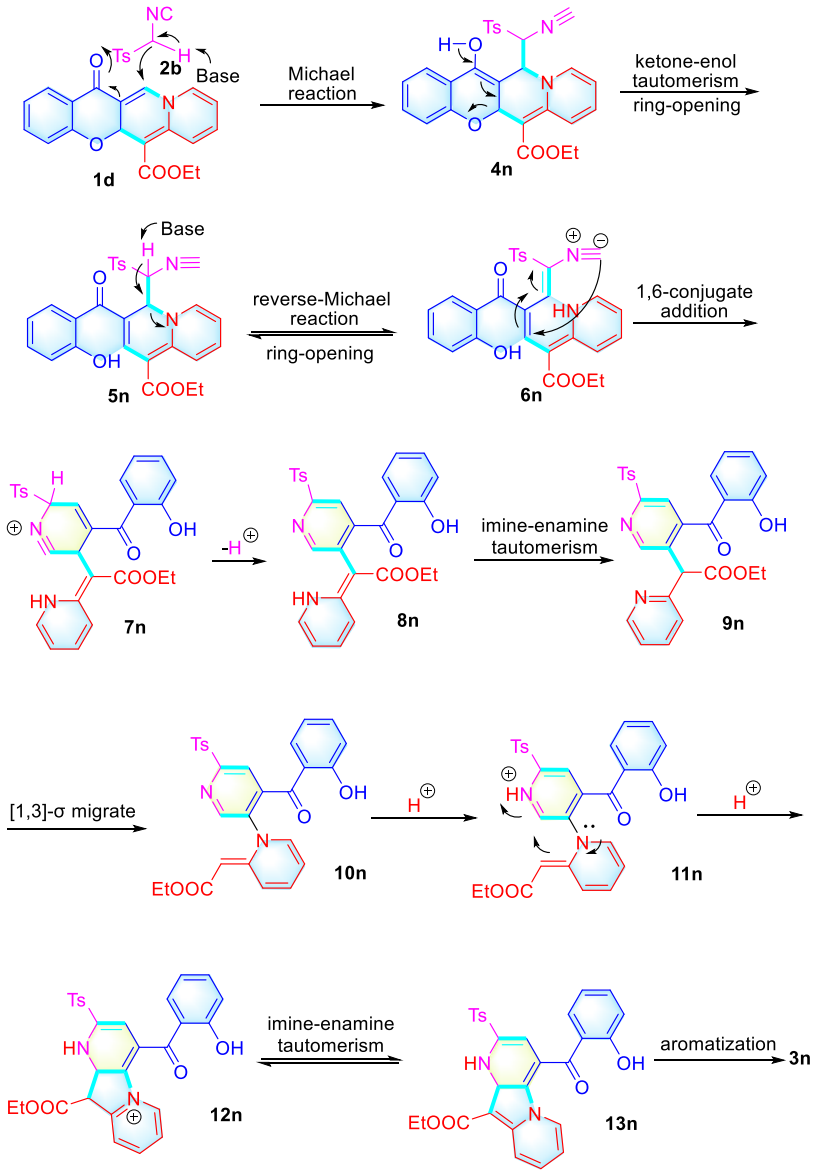
All reactions were carried out under air atmosphere. The substrates **1** were synthesized by known literature procedures.[1] The substrates **2** were synthesized by known literature procedures.[2] Other materials were purchased from Adamas-beta Corporation Limited. All chemicals and solvents were used as received without further purification unless otherwise stated. Two kinds of reagents which were used in the experiment were commercially available reagents.

General Procedure for the Synthesis of pyrido[2,3-*b*]indolizines



Chroman-4-one derivatives **1** (0.3 mmol) and isocyanides **2** (0.3 mmol) in a 25 mL round-bottom flask equipped with a magnetic stirrer. Next, add Cs_2CO_3 (0.6 mmol, 2.0 equivalents) and silver carbonate (0.09 mmol, 0.3 equivalents), followed by 2 mL of DMSO as a solvent. Stir the mixture and reflux it at 110 °C in air for 5 hours or until the reaction is complete. After cooling to room temperature, the mixture was extracted with ethyl acetate (3 × 15 mL) and saturated aqueous NaCl. The organic layer was washed with water and brine, dried over Na_2SO_4, filtered to remove the drying agent, and concentrated under reduced pressure using a rotary evaporator to obtain the crude product. Finally, the crude product was purified by column chromatography using a mixture of petroleum ether and ethyl acetate (5:1–4:1, v/v) as eluent to afford the desired products **3**.

The proposed mechanism of the cascade reaction



Scheme S1. The proposed mechanism of the cascade reaction.

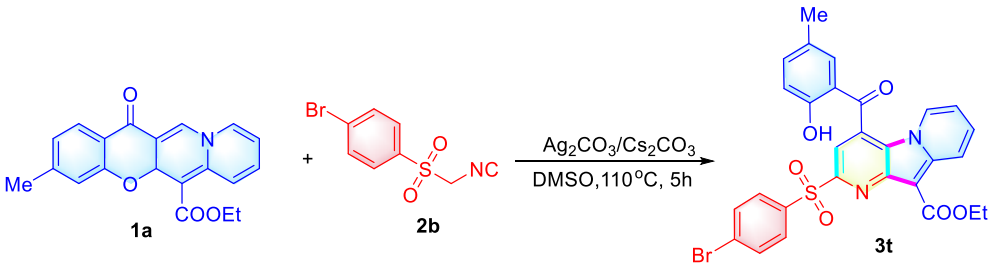
The proposed mechanism for the cascade reaction for the formation of compound **3n** is shown in Scheme S1. First, the active methylene of the isocyanide **2b** as the nucleophilic reagent attacked the double bond (C=C) of CMQZ **1d** *via* base-promoted (Cs_2CO_3) Michael reaction from the intermediate **4n**, which underwent a ketone–enol tautomerism accompanied by a ring-opening reaction to form the key intermediate **5n**. The intermediate **5n** formed the intermediate **6n** via a reverse-Michael reaction, which then further formed the intermediated **7n** through 1,6-conjugate addition. Then, **7n** lost one proton via base promotion (Cs_2CO_3) to produce the intermediate **8n**, which formed the intermediate **9n** by an imine–enamine tautomerism. This intermediate provided the

intermediate **10n** through a [1,3]-σ migrate reaction. Then, the nitrogen atom of pyridine formed a protonated intermediate **11n** after catalysis with an acid or Lewis acid (Ag_2CO_3). The α-C of enamine attacked the double bond (C=N) **12n** to obtain the key intermediate **13n** through another imine–enamine tautomerism. Finally, **13n** formed the final product **3n** through an aromatization reaction.

Mechanism verification

To verify the rationality of the mechanism, we packed chroman-4-one derivative (**1a**) (0.1 mmol) and p-Methylbenzenesulfonylmethyl isocyanide (**2b**) (0.1 mmol) into a round bottom flask, and then added cesium carbonate (0.2 mmol) and silver carbonate (0.03 mmol). The reaction was carried out in DMSO solvent at 110 ℃ for 1.5 hours, with continuous sampling. After the reaction, the obtained intermediate samples were detected by the high-pressure liquid chromatography-high-resolution mass spectrometry (HPLC-HRMS) system. HRMS (TOF ES^+): *m/z* calcd. for $C_{28}H_{25}N_2O_6S^+$ $[M+H]^+$, 517.1428; found, 517.1437; HRMS (TOF ES^+): *m/z* calcd. for $C_{28}H_{25}N_2O_6S^+$ $[M+H]^+$, 517.1428; found, 517.1434; HRMS (TOF ES^+): *m/z* calcd. for $C_{28}H_{25}N_2O_6S^+$ $[M+H]^+$, 517.1428; found, 517.1437; HRMS (TOF ES^+): *m/z* calcd. for $C_{28}H_{25}N_2O_6S^+$ $[M+H]^+$, 517.1428; found, 517.1437. There are the HRMS spectra of intermediate **8n-13n** and the target compound **3n** (SI, Figure S55–S58). In high-resolution mass spectrometry, the molecular ion peaks of intermediates **8n-13n** and the target compound were detected. Based on the experimental results, we believe that the proposed reaction mechanism is reasonable.

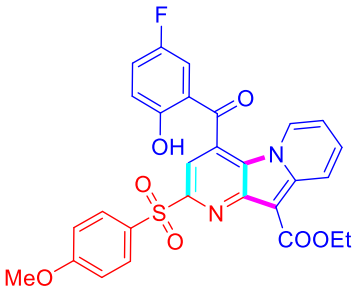
The gram-scale experiment



Ethyl 3-methyl-13-oxo-5a*H*,13*H*-chromeno[2,3-*b*]quinolizine-6-carboxylate **1a** (1.34g, 4.0 mmol) and 1-bromo-4-((isocyanomethyl)sulfonyl)benzene **2b** (1.04g, 4.0 mmol) were combined in a 50 mL round-bottom flask equipped with a magnetic stirring bar. Then, Cs_2CO_3 (2.61g, 8.0 mmol) and Ag_2CO_3 (0.33g, 1.2 mmol) was added followed by 25 mL of DMSO as solvent. The mixture was stirred and refluxed at 110 °C (on oil bath) in air for 5 h until the reaction was complete. After cooling to room temperature, the mixture was extracted with ethyl acetate (3 × 150 mL) and saturated aqueous NaCl. The organic layer was washed with water and brine, dried over Na_2SO_4, filtered to remove the drying agent, and concentrated under reduced pressure using a rotary evaporator to obtain the crude product. Finally, the crude product was purified by column chromatography using a mixture of petroleum ether and ethyl acetate (4:1, v/v) as eluent to afford the desired products **3t**, the yield is 63% (1.49 g).

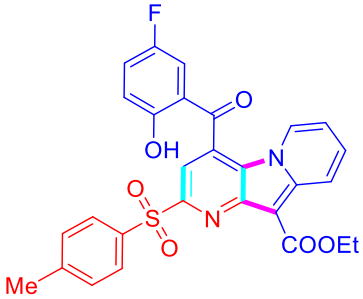
Spectroscopic Data of

Ethyl 4-(5-fluoro-2-hydroxybenzoyl)-2-((4-methoxyphenyl)sulfonyl)pyrido[2,3-b]-indolizine-10-carboxylate (3a)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 95 mg, 58%); Mp: 256.5–258.6 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.60 (s, 1H, OH), 8.47 (d, J = 9.3 Hz, 1H, ArH), 8.39 (d, J = 7.2 Hz, 1H, ArH), 8.05–8.01 (m, 2H, ArH), 7.96 (s, 1H, ArH), 7.72–7.63 (m, 1H, ArH), 7.59 (dd, J = 8.9, 3.3 Hz, 1H, ArH), 7.54–7.44 (m, 1H, ArH), 7.28–7.10 (m, 2H, ArH), 7.05 (td, J = 6.9, 1.4 Hz, 1H, ArH), 6.96 (dd, J = 9.1, 4.3 Hz, 1H, ArH), 4.37 (q, J = 7.1 Hz, 2H, CH_2), 3.85 (s, 3H, CH_3), 1.39 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) : δ = 193.21, 164.14, 163.58, 156.62, 155.65(d, J_1 = 246.00 Hz), 145.10(d, J_3 = 4.50 Hz), 136.59, 131.85, 131.68, 130.35, 129.21, 124.70(d, J_2 = 22.50 Hz), 123.32, 119.75(d, J_3 = 13.50 Hz), 116.91(d, J_2 = 24.00 Hz), 115.35, 115.08, 114.05, 110.35, 95.67, 59.83, 56.31, 14.98; ^{19}F NMR (564 MHz, DMSO-d_6) δ-124.28. HRMS (TOF ES$^+$): m/z calcd for $C_{28}H_{21}FN_2O_7S$ [M+Na]$^+$, 571.0946; found, 571.0950.

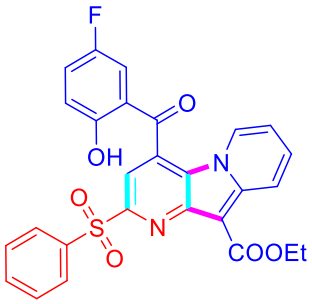
Ethyl 4-(5-fluoro-2-hydroxybenzoyl)-2-tosylpyrido[3,2-b]indolizine-5-carboxylate (3b)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 91 mg, 57%); Mp: 267.1–269.5 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.60 (s, 1H, OH), 8.49 (d, J = 9.4 Hz, 1H, ArH), 8.40 (d, J = 6.5 Hz, 1H, ArH), 8.02–8.00 (m, 3H, ArH), 7.68 (dd, J = 9.6, 6.0 Hz, 1H, ArH), 7.60 (dd, J = 8.9, 3.8 Hz, 1H, ArH), 7.48 (dd, J = 22.1, 5.6 Hz, 3H, ArH), 7.08-7.06 (m, 1H), 6.98–6.97 (m, 1H), 4.38 (q, J = 7.3,

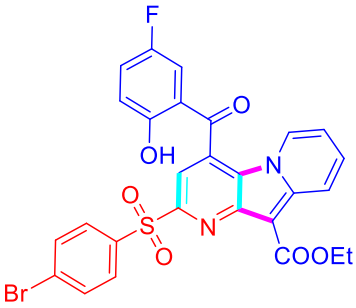
6.4 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3), 1.40 (s, 3H, CH_3); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) : δ = 193.16, 163.56, 156.50, 156.39, 156.27, 155.67(d, J_1 = 252.23 Hz), 145.38, 145.15(d, J_3 = 4.41 Hz), 136.61, 136.19, 131.88, 130.27, 129.39, 129.24, 124.71(d, J_2 = 23.81 Hz), 123.31, 123.27, 119.86, 119.86(d, J_3 = 7.8 Hz), 116.93(d, J_2 = 23.67 Hz), 114.07, 110.54, 95.67, 59.82, 21.57, 14.92;^{19}F NMR (470 MHz, DMSO-d_6):-124.3. HRMS (TOF ES$^+$): *m/z* calcd for $C_{28}H_{21}FN_2O_6S$ $[M+Na]^+$, 555.0997; found, 555.1001.

Ethyl 4-(5-fluoro-2-hydroxybenzoyl)-2-(phenylsulfonyl)pyrido[3,2-b]indolizine-5-carboxylate (3c)



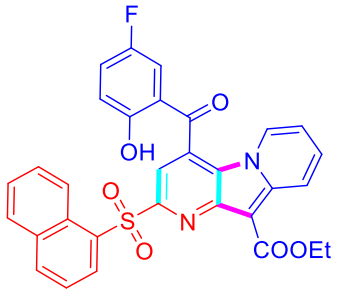
Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 87 mg, 56%); Mp: 251.6–253.1 °C; ^1H NMR (500 MHz, DMSO-d_6) : ^1H NMR (500 MHz, DMSO-d_6) δ 10.63 (s, 1H, ArH), 8.48 (d, *J* = 9.3 Hz, 1H, ArH), 8.39 (d, *J* = 7.1 Hz, 2H, ArH), 8.14-8.12 (m, 1H, ArH), 8.02 (s, 1H, ArH), 7.78-7.75 (m, 3H, ArH), 7.71-7.67 (m, 1H, ArH), 7.62 (m, 1H, ArH), 7.60 (dd, *J* = 8.9, 3.3 Hz, 1H, ArH), 7.50 (td, *J* = 8.5, 3.3 Hz, 1H, ArH), 6.94 (dd, *J* = 9.2, 4.3 Hz, 1H, ArH), 4.37 (q, *J* = 7.1 Hz, 2H, CH_2), 1.39 (t, J = 7.1 Hz, 3H, CH_3). $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) : δ = 193.10, 163.54, 159.70 (d, J_1 = 235.52 Hz), 156.38, 155.98, 145.19(d, J_3 = 7.40 Hz), 139.15, 136.68, 134.67, 131.96, 129.82, 129.33, 129.26, 124.82, 124.74(d, J_2=23.7 Hz), 124.66, 123.29, 123.24, 119.94, 119.89(d, J_3 = 7.14 Hz), 119.71, 116.92(d, J_2=23.58 Hz) 114.12, 110.69, 95.68, 59.82, 14.96.; ^{19}F NMR (564 MHz, DMSO-d_6):-124.3. HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{19}FN_2O_6S$ $[M+Na]^+$, 541.0841; found, 541.0837.

Ethyl 2-((4-bromophenyl)sulfonyl)-4-(5-fluoro-2-hydroxybenzoyl)pyrido[2,3-b]-indolizine-10-carboxylate (3d)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 106 mg, 60%); Mp: 197.5–198.6 °C; ^{1}H NMR (600 MHz, DMSO-d_6) : δ = 10.59 (s, 1H, OH), 8.48 (d, J = 9.3 Hz, 1H, ArH), 8.39 (d, J = 7.2 Hz, 1H, ArH), 8.03 (d, J = 7.5 Hz, 2H, ArH), 7.90 (d, J = 8.3 Hz, 1H, ArH), 7.80–7.46 (m, 2H, ArH), 7.07 (t, J = 7.0 Hz, 2H, ArH), 7.00–6.91 (m, 2H, ArH), 6.97 (d, J = 4.3 Hz, 1H, ArH), 4.36 (q, J = 7.1 Hz, 2H, CH_2), 1.36 (t, J = 7.1 Hz, 1H, CH_3);^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) : δ = 193.03, 164.50, 156.53, 155.61, 155.20(d, J_1 = 235.50 Hz), 145.08, 138.26, 136.74, 132.96, 132.03, 131.31, 129.26, 129.06, 124.78(d, J_2 = 24.00 Hz), 123.21, 120.01, 119.89(d, J_3 = 4.50 Hz), 119.72, 117.02, 116.87, 114.19, 110.61, 95.69, 79.64, 59.83, 14.98; ^{19}F NMR (564 MHz, DMSO-d_6) δ-124.28. HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{18}BrFN_2O_6S$ $[M+Na]^+$,618.9946; found, 618.9945.

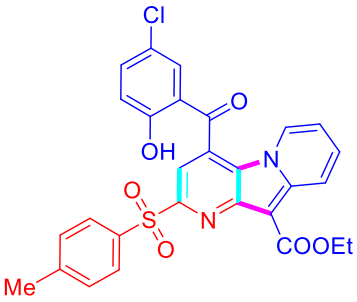
Ethyl 4-(5-fluoro-2-hydroxybenzoyl)-2-(naphthalen-1-ylsulfonyl)pyrido[2,3-*b*]-indolizine-10-carboxylate (3e)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 82 mg, 48%); Mp: 237.8–239.8 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.60 (s, 1H, OH), 8.79 (d, J = 1.8 Hz, 1H, ArH), 8.46 (d, J = 9.3 Hz, 1H, ArH), 8.42–8.33 (m, 1H, ArH), 8.24 (d, J = 8.2 Hz, 1H, ArH), 8.19 (d, J = 8.7 Hz, 1H, ArH), 8.12 (dd, J = 8.7, 1.9 Hz, 1H, ArH), 8.11–8.04 (m, 2H, ArH), 7.75 (ddd, J = 8.2, 6.8, 1.4 Hz, 1H, ArH), 7.72–7.64 (m, 2H, ArH), 7.61 (dd, J = 8.9, 3.3 Hz, 1H, ArH), 7.55–7.48 (m, 1H, ArH), 7.06 (td, J = 7.0, 1.4 Hz, 1H, ArH), 6.96 (dd, J = 9.1, 4.3 Hz, 1H, ArH), 4.28 (q, J = 7.2 Hz, 2H, CH_2), 1.25 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) : δ = 193.13, 163.51, 156.52, 156.13, 154.67, 145.17, 145.08,

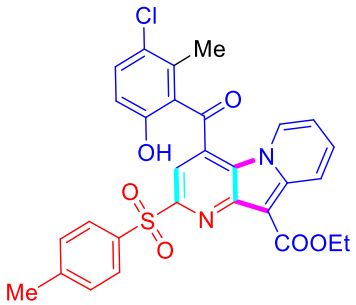
136.70, 136.13, 135.40, 132.12, 131.94, 130.84, 130.00, 129.78, 129.18(d, J_1 = 231.25 Hz), 128.38, 128.25, 124.74 (d, J_2 = 22.50 Hz), 124.33, 119.88 (d, J_3 = 7.5 Hz), 119.67, 117.04, 114.12, 110.66, 95.66, 79.65, 59.74, 14.86.; ^{19}F NMR (470 MHz, DMSO-d_6):-124.27. HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{21}FN_2O_6S$ $[M+Na]^+$, 591.0997; found, 591.0994.

Ethyl 4-(5-chloro-2-hydroxybenzoyl)-2-tosylpyrido[3,2-b]indolizine-5-carboxylate (3f)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 78 mg, 48%); Mp: 254.9–255.5 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.90 (s, 1H, OH), 8.54 (d, J = 9.3 Hz, 1H, ArH), 8.47 (d, J = 7.2 Hz, 1H, ArH), 8.06-8.04 (m, 3H, ArH), 7.87 (d, J = 2.8 Hz, 1H, ArH), 7.75-7.68 (m, 1H, ArH), 7.52 (dd, J = 8.9, 2.8 Hz, 1H, ArH), 7.12 (d, J = 8.1 Hz, 2H, ArH), 7.06 (td, J = 6.9, 1.4 Hz, 1H, ArH), 6.98 (d, J = 8.8 Hz, 1H, ArH), 4.42 (q, J = 7.1 Hz, 2H,CH_2), 2.46 (s, 3H,CH_3), 1.46 (t, J = 7.1 Hz, 3H,CH_3).; ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) : δ = 192.92, 163.56, 158.78, 156.25, 145.38, 145.17, 145.14, 136.77, 136.62, 136.21, 131.91, 130.92, 130.28, 129.36, 124.38, 123.78, 120.22, 119.87, 119.68, 114.07, 110.58, 95.65, 59.82, 21.58, 14.93; HRMS (TOF ES$^+$): *m/z* calcd for $C_{28}H_{21}ClN_2O_6S$ $[M+Na]^+$, 571.0702; found, 571.0707.

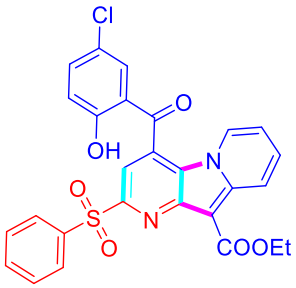
Ethyl 4-(3-chloro-6-hydroxy-2-methylbenzoyl)-2-tosylpyrido[3,2-b]indolizine-5-carboxylate (3g)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 72 mg, 43%); Mp: 230.1–231.2 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.33 (s, 1H, OH), 8.23 (s, 1H, ArH), 7.97-7.95 (m, 2H, ArH), 7.83-7.78 (m, 2H, ArH), 7.47-7.42 (m, 3H,

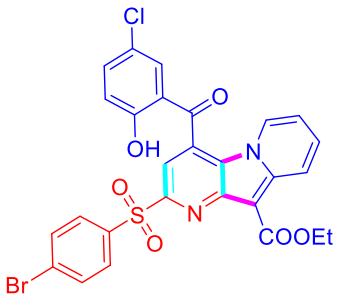
ArH), 7.17 (d, J = 8.9 Hz, 1H, ArH), 4.83-4.71 (m, 3H, CH_2), 4.42-4.41 (m, 1H, CH_2); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) : δ = 182.1, 154.3, 152.8, 137.4, 136.3, 134.0, 131.8, 131.8, 130.9, 129.4, 128.6, 128.6, 127.0, 126.7, 126.4, 124.2, 121.4, 119.2, 118.9, 60.5, 44.7; HRMS (TOF ES$^+$): m/z calcd for $C_{29}H_{23}ClN_2O_6S$ $[M+Na]^+$, 585.0858; found, 585.0856.

Ethyl 4-(5-chloro-2-hydroxybenzoyl)-2-(phenylsulfonyl)pyrido[3,2-b]indolizine-5-carboxylate (3h)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 85 mg, 53%); Mp: 255.1–256.9 °C; ^1H NMR (500 MHz, DMSO-d_6) δ = 10.90 (s, 1H, OH), 8.48 (d, J = 9.2 Hz, 1H, ArH), 8.42 (d, J = 7.2 Hz, 1H, ArH), 8.19-8.09 (m, 2H, ArH), 8.02 (s, 1H, ArH), 7.82 (d, J = 2.8 Hz, 1H, ArH), 7.78-7.75 (m, 1H, ArH), 7.70-7.63 (m, 4H, ArH), 7.08 (td, J = 6.9, 1.3 Hz, 1H, ArH), 6.98 (d, J = 8.8 Hz, 1H, ArH), 4.37 (d, J = 7.1 Hz, 2H, CH_2), 1.40 (t, J = 7.1 Hz, 3H, CH_3); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) : δ = 192.88, 163.53, 158.81, 155.94, 145.21, 145.18, 139.15, 136.79, 136.65, 134.67, 131.95, 130.93, 129.82, 129.34, 129.31, 124.35, 123.78, 120.22, 119.94, 119.67, 114.08, 110.74, 95.66, 59.82, 14.96. HRMS (TOF ES$^+$): m/z calcd for $C_{27}H_{19}ClN_2O_6S$ $[M+Na]^+$, 557.0545; found, 557.0544.

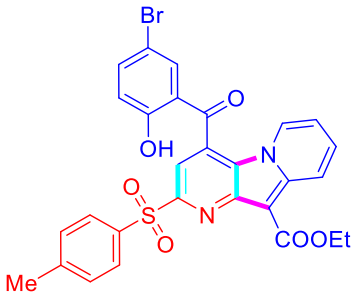
Ethyl 2-((4-bromophenyl)sulfonyl)-4-(5-chloro-2-hydroxybenzoyl)pyrido[2,3-b]-indolizine-10-carboxylate (3i)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 76 mg, 42%); Mp: 261.1–263.5 °C; IR (KBr): 3450, 1650, 1612, 1553, 1509, 1452, 1210, 1066, 892, 763, 650 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) : δ = 10.88 (s, 1H, OH), 8.47 (d, J

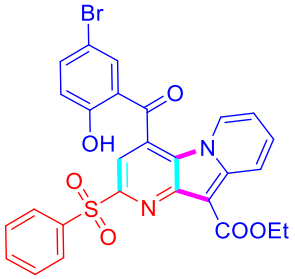
= 9.3 Hz, 1H, ArH), 8.41 (d, *J* = 7.2 Hz, 1H, ArH), 8.02 (d, *J* = 9.1 Hz, 3H, ArH), 7.90 (d, *J* = 8.3 Hz, 2H, ArH), 7.81 (d, *J* = 2.8 Hz, 1H, ArH), 7.73–7.65 (m, 1H, ArH), 7.64 (dd, *J* = 8.8, 2.8 Hz, 1H, ArH), 7.07 (t, *J* = 7.1 Hz, 1H, ArH), 6.97 (d, *J* = 8.9 Hz, 1H, ArH), 4.36 (q, *J* = 7.1 Hz, 2H, CH_2), 1.36 (t, *J* = 7.1 Hz, 3H, CH_3);$^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) : δ =192.82, 163.50, 158.71, 155.58, 145.26, 145.10, 138.25, 136.84, 136.71, 133.15, 132.97, 132.04, 131.29, 130.93, 129.32, 129.07, 124.31, 123.88, 120.21, 120.01, 119.70, 114.16, 110.66, 95.68, 59.84, 14.97; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{18}BrClN_2O_6S$ $[M+Na]^+$,634.9650; found, 634.9655.

ethyl 4-(5-bromo-2-hydroxybenzoyl)-2-tosylpyrido[3,2-b]indolizine-5-carboxylate (3j)



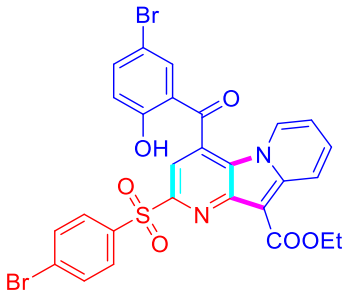
Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 99 mg, 56%); Mp: 274.1–278.4 °C; ^1H NMR (500 MHz, DMSO-d_6) : δ = 10.95 (s, 1H, OH), 8.48 (d, *J* = 9.2 Hz, 1H), 8.42 (d, *J* = 7.2 Hz, 1H, ArH), 8.00-7.99 (m, 2H, ArH), 7.93 (d, *J* = 2.6 Hz, 1H, ArH), 7.73-7.70 (m, 2H, ArH), 7.69-7.67 (m, 2H, ArH), 7.47 (d, *J* = 8.1 Hz, 1H, ArH), 7.07 (td, *J* = 7.0, 1.4 Hz, 1H, ArH), 6.89 (d, *J* = 8.8 Hz, 1H, ArH), 4.38 (q, *J* = 7.1 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3), 1.41 (t, *J* = 7.1 Hz, 3H, CH_3).; $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) : δ = 192.84, 163.55, 159.19, 156.23, 145.37, 145.16, 139.50, 136.62, 136.22, 133.85, 131.89, 130.27, 129.36, 129.17, 124.96, 120.59, 119.88, 119.67, 114.04, 111.11, 110.61, 95.64, 59.82, 21.58, 14.93.; HRMS (TOF ES$^+$): *m/z* calcd for $C_{28}H_{21}BrN_2O_6S$ $[M+Na]^+$, 615.0196; found, 615.0197.

Ethyl 4-(5-bromo-2-hydroxybenzoyl)-2-(phenylsulfonyl)pyrido[2,3-b]indolizine-10-carboxylate (3k)



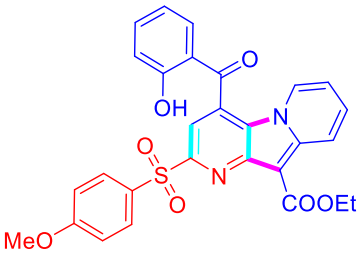
Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 88 mg, 51%); Mp: 259.1–263.4 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.89 (s, 1H, OH), 8.48 (d, J = 9.0 Hz, 2H, ArH), 8.42 (d, J = 7.1 Hz, 2H, ArH), 8.14-8.09 (m, 1H, ArH), 8.04 (s, 1H, ArH), 7.94 (d, J = 2.7 Hz, 1H, ArH), 7.75 (s, 1H, ArH), 7.81-7.71 (m, 1H, ArH), 7.68 (td, J = 7.2, 5.1 Hz, 2H, ArH), 7.06 (t, J = 6.9 Hz, 1H, ArH), 6.90 (d, J = 8.8 Hz, 1H, ArH), 4.36 (q, J = 7.1 Hz, 2H, CH_2), 1.39 (t, J = 7.1 Hz, 3H, CH_3).; ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) : δ = 192.79, 163.53, 159.12, 155.93, 145.21, 145.19, 139.53, 139.15, 136.63, 134.67, 133.88, 131.97, 129.83, 129.37, 129.30, 124.95, 120.58, 119.94, 119.67, 114.09, 111.16, 110.76, 95.65, 59.82, 14.96..; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{19}BrN_2O_6S$ $[M+Na]^+$, 601.0040; found, 601.0040.

Ethyl 4-(5-bromo-2-hydroxybenzoyl)-2-((4-bromophenyl)sulfonyl)pyrido[2,3-b]-indolizine-10-carboxylate (3l)



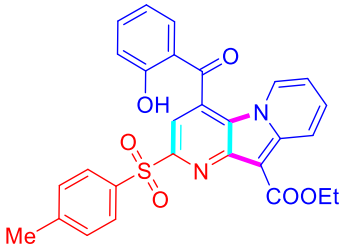
Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 92 mg, 46%); Mp: 252.2–253.3 °C; ^{1}H NMR (600 MHz, DMSO-d_6) : δ = 10.86 (s, 1H, OH), 8.49 (d, J = 9.3 Hz, 1H, ArH), 8.03 (d, J = 3.1 Hz, 1H, ArH), 8.02 (d, J = 2.0 Hz, 3H, ArH), 7.94 (d, J = 2.6 Hz, 3H, ArH), 7.91 (d, J = 2.0 Hz, 1H, ArH), 7.90 (d, J = 1.9 Hz, 1H, ArH), 7.75 (dd, J = 8.8, 2.6 Hz, 1H, ArH), 7.70 (ddd, J = 9.3, 6.7, 1.1 Hz, 1H, ArH), 4.36 (q, J = 7.1 Hz, 2H, CH_2), 1.36 (t, J = 7.1 Hz, 3H, CH_3).;^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) : δ = 192.71, 163.49, 159.08, 155.57, 145.26, 145.10,139.57, 138.27, 136.73, 133.88, 132.97, 132.05, 131.29, 129.37, 129.07, 124.92, 120.58, 120.02, 119.69, 114.16, 111.22, 110.67, 95.67, 59.83, 14.98; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{18}Br_2N_2O_6S$ $[M+Na]^+$,680.9125; found, 680.9122.

Ethyl 4-(2-hydroxybenzoyl)-2-((4-methoxyphenyl)sulfonyl)pyrido[2,3-b]indolizine-10-carboxylate (3m)



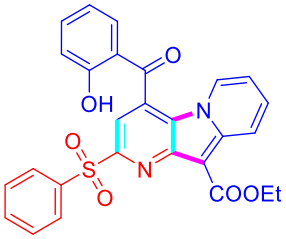
Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 95 mg, 60%); Mp: 241.2–243.0 °C; ^{1}H NMR (600 MHz, DMSO-d_6) : δ = 10.72 (s, 1H, OH), 8.48 (d, J = 9.3 Hz, 1H, ArH), 8.38 (d, J = 7.2 Hz, 1H, ArH), 8.04 (d, J = 8.9 Hz, 2H, ArH), 7.94 (s, 1H, ArH), 7.79–7.72 (m, 1H, ArH), 7.71–7.65 (m, 1H, ArH), 7.65–7.59 (m, 1H, ArH), 7.18 (d, J = 9.0 Hz, 2H , ArH), 7.10–7.01 (m, 2H, ArH), 6.98 (d, J = 8.3 Hz, 1H, ArH), 4.38 (q, J = 7.1 Hz, 2H, CH_2), 3.85 (s, 3H, CH_3), 1.40 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) : δ = ^{13}C NMR (151 MHz, DMSO-d_6) δ 194.67, 164.13, 163.58, 160.41, 156.63, 145.12, 145.10, 137.73, 136.60, 132.33, 131.83, 131.68, 130.38, 129.14, 122.67, 120.27, 119.79, 119.73, 118.24, 115.07, 114.06, 110.40, 95.68, 79.64, 59.81, 56.31, 14.98; HRMS (TOF ES$^+$): *m/z* calcd for $C_{28}H_{22}N_2O_7S$ $[M+Na]^+$, 553.1040; found, 553.1043.

Ethyl 4-(2-hydroxybenzoyl)-2-tosylpyrido[3,2-b]indolizine-5-carboxylate (3n)



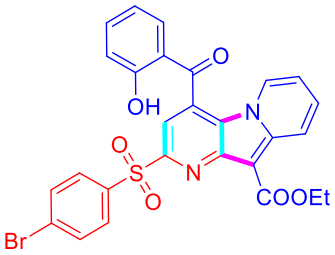
Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 86 mg, 56%); Mp: 204.1–205.2 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.74 (s, 1H, OH), 8.49 (d, J = 9.3 Hz, 1H, ArH), 8.38 (d, J = 7.3 Hz, 1H, ArH), 8.00 (d, J = 8.3 Hz, 2H, ArH), 7.96 (s, 1H, ArH), 7.75 (dd, J = 7.9, 1.7 Hz, 1H, ArH), 7.72-7.65 (m, 1H, ArH), 7.62 (ddd, J = 8.7, 7.1, 1.8 Hz, 1H, ArH), 7.47 (d, J = 8.1 Hz, 2H, ArH), 7.22-6.99 (m, 2H, ArH), 6.96 (d, J = 8.3 Hz, 1H, ArH), 4.37 (q, J = 7.1 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3), 1.41 (t, J = 7.1 Hz, 3H, CH_3). ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) : δ = 194.58, 163.57, 160.47, 156.27, 145.39, 145.18, 145.12, 137.74, 136.68, 136.20, 132.32, 131.90, 130.28, 129.39, 129.16, 122.67, 120.24, 119.87, 119.73, 118.27, 114.11, 110.57, 95.68, 59.82, 21.59, 14.93.; HRMS (TOF ES$^+$): *m/z* calcd for $C_{28}H_{22}N_2O_6S$ $[M+Na]^+$, 537.1091; found, 537.1093.

Ethyl 4-(2-hydroxybenzoyl)-2-(phenylsulfonyl)pyrido[3,2-b]indolizine-5-carboxyl-ate(3o)



Yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 99 mg, 66%); Mp: 258.2–259.5 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.75 (s, 1H, OH), 8.50(d, 1H, ArH), 8.48 (d, 1H, ArH), 8.40-8.38 (d, , 2H, ArH), 8.14-8.13 (d, 1H, ArH), 8.00 (s, 1H, ArH), 7.78-7.75 (m, 3H, ArH), 7.70-7.61 (m, 1H, ArH), 7.08-6.97 (m, 3H, ArH), 4.40-4.35 (m, 2H, CH_2), 1.41-1.39 (m, 3H, CH_3); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) : δ = 195.5, 163.6, 160.5, 156.0, 145.2, 145.2, 139.1, 137.8, 136.7, 134.7, 132.4, 132.0, 129.8, 129.3, 129.2, 122.7, 120.3, 119.9, 119.8, 118.3, 114.1, 110.7, 95.69, 59.82, 14.96; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{20}N_2O_6S$ $[M+Na]^+$,523.0935; found, 523.0937.

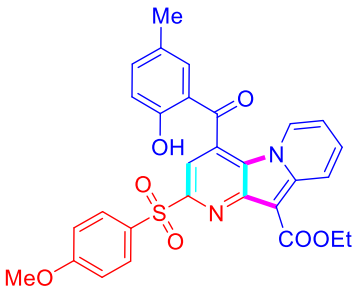
ethyl 2-((4-bromophenyl)sulfonyl)-4-(2-hydroxybenzoyl)pyrido[2,3-b]indolizine-10-carboxylate (3p)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 116 mg, 65%); Mp: 265.5–268.6 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.73 (s, 1H, OH), 8.48 (d, *J* = 9.3 Hz, 1H, ArH), 8.38 (d, *J* = 7.2 Hz, 1H, ArH), 8.03 (d, J = 8.6 Hz, 2H, ArH), 8.00 (s, 1H, ArH), 7.90 (d, *J* = 8.6 Hz, 2H, ArH), 7.75 (dd, *J* = 7.9, 1.8 Hz, 1H, ArH), 7.71–7.66 (m, 1H, ArH), 7.65–7.59 (m, 1H, ArH), 7.10–7.04 (m, 1H, ArH), 7.03 (t, *J* = 7.6 Hz, 1H, ArH), 6.98 (d, *J* = 8.3 Hz, 1H, ArH), 4.36 (q, *J* = 7.1 Hz, 2H,CH_2), 1.37 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) : δ = 194.47, 163.50, 160.43, 155.59, 145.26, 145.08, 138.25, 137.79, 136.73, 132.95, 132.37, 132.01, 131.32, 129.16, 129.05, 122.60, 120.30, 120.01, 119.73, 118.25, 114.18, 110.67, 95.70, 79.64, 59.82, 14.98.; HRMS (TOF ES$^+$): *m/z* calcd for

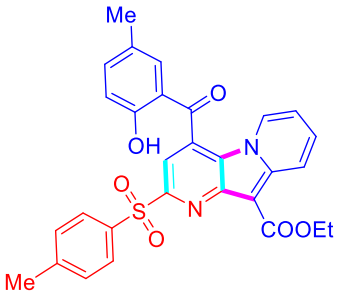
$C_{27}H_{19}BrN_2O_6S$ [M+Na]$^+$, 601.0040; found, 601.0040.

Ethyl 4-(2-hydroxy-5-methylbenzoyl)-2-((4-methoxyphenyl)sulfonyl)pyrido[2,3-b]-indolizine-10-carboxylate (3q)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ =4:1, R_f = 0.2, 110 mg, 68%); Mp: 268.0–269.3 °C; ^{1}H NMR (600 MHz, DMSO-d_6) : δ = 10.49 (s, 1H, OH), 8.48 (d, J = 9.3 Hz, 1H, ArH), 8.35 (d, J = 7.2 Hz, 1H, ArH), 8.04 (d, J = 9.0 Hz, 2H, ArH), 7.92 (s, 1H, ArH), 7.75–7.65 (m, 1H, ArH), 7.57–7.50 (m, 1H, ArH), 7.44 (dd, J = 8.5, 2.3 Hz, 1H, ArH), 7.18 (d, J = 9.0 Hz, 2H, ArH), 7.11–7.02 (m, 1H, ArH), 6.88 (d, J = 8.4 Hz, 1H, ArH), 4.38 (q, J = 7.1 Hz, 2H, CH_2), 3.85 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 1.40 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) : δ = 194.62, 164.14, 163.60, 158.47, 156.60, 145.11, 145.09, 138.73, 136.77, 131.83, 131.72, 131.68, 130.42, 129.14, 129.06, 122.24, 119.81, 119.75, 118.20, 115.09, 114.10, 110.36, 95.68, 59.81, 56.32, 20.24, 14.99; HRMS (TOF ES$^+$): *m/z* calcd for $C_{29}H_{24}N_2O_7S$ [M+Na]$^+$, 567.1197; found, 567.1197.

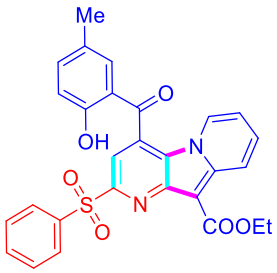
Ethyl 4-(2-hydroxy-5-methylbenzoyl)-2-tosylpyrido[3,2-b]indolizine-5-carboxylate (3r)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 103 mg, 65%); Mp: 208.7–210.5 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.54 (s, 1H, OH), 8.49 (d, J = 9.3 Hz, 1H, ArH), 8.36 (d, J = 7.3 Hz, 1H, ArH), 7.96 (d, J = 8.3 Hz, 2H, ArH), 7.93 (s, 1H, ArH), 7.69 (ddd, J = 9.3, 6.7, 1.1 Hz, 1H, ArH), 7.56-7.52 (m, 1H, ArH), 7.49-7.40 (m, 3H, ArH), 7.06 (td, J = 6.9, 1.3 Hz, 1H, ArH), 6.89 (d, J = 8.4 Hz, 1H, ArH), 4.37 (q, J = 7.1 Hz, 2H, CH_2), 2.40 (s, 3H, CH_3), 2.26 (s, 3H,

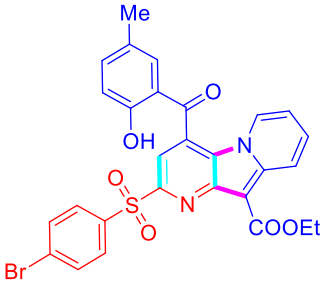
CH_3), 1.40 (t, J = 7.1 Hz, 3H, CH_3).$^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) : δ = 194.54, 163.59, 158.69, 156.24, 145.38, 145.15, 145.12, 138.73, 136.81, 136.24, 131.87, 131.71, 130.28, 129.38, 129.08, 122.23, 119.88, 119.74, 118.22, 114.12, 110.54, 95.68, 59.81, 21.58, 20.24, 14.93; HRMS (TOF ES^+): *m/z* calcd for $C_{29}H_{24}N_2O_6S$ $[M+Na]^+$, 551.1248; found, 551.1249.

Ethyl 4-(2-hydroxy-5-methylbenzoyl)-2-(phenylsulfonyl)pyrido[3,2-b]indolizine-5-carboxylate (3s)



Orange red solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 97 mg, 63%); Mp: 238.1–239.5 °C; ^1H NMR (500 MHz, DMSO-d_6) : δ = 10.52 (s, 1H, OH), 8.48 (d, J = 9.3 Hz, 1H, ArH),, 8.36 (s, 1H, ArH), 8.12 (d, J = 7.1 Hz, 2H, ArH), 7.98 (s, 1H, ArH), 7.76 (t, J = 7.5 Hz, 1H, ArH), 7.78-7.75 (m, 3H, ArH), 7.56 (d, J = 2.3 Hz, 1H, ArH), 7.44 (dd, J = 8.5, 2.3 Hz, 1H, ArH), 7.06 (td, J = 6.9, 1.3 Hz, 1H, ArH), 6.88 (d, J = 8.4 Hz, 1H, ArH), 4.38 (q, J = 7.1 Hz, 2H, CH_2), 2.26 (s, 3H, CH_3); 1.42-1.39 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ 163.6, 158.6, 155.9, 145.2, 145.2, 139.2, 138.7, 136.8, 134.7, 131.9, 131.7, 129.8, 129.3, 129.1, 122.2, 120.0, 119.7, 118.2, 114.1, 110.7, 95.7, 59.8, 20.20, 15.00; HRMS (TOF ES^+): *m/z* calcd for $C_{28}H_{22}N_2O_6S$ $[M+Na]^+$, 537.1091; found,537.1093.

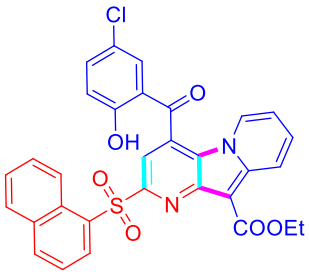
Ethyl 2-((4-bromophenyl)sulfonyl)-4-(2-hydroxy-5-methylbenzoyl)pyrido[2,3-b]-indolizine-10-carboxylate (3t)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 130 mg, 73%); Mp: 239.7–241.8 °C; ^1H NMR (600 MHz, DMSO-d_6) : δ = 10.50 (s, 1H, OH), 8.49 (d, J = 9.3 Hz, 1H, ArH), 8.36 (d, J = 7.2 Hz, 1H, ArH), 8.06–8.02 (m, 2H, ArH),

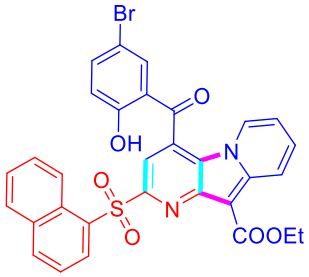
7.92–7.89 (m, 2H, ArH), 7.69 (ddd, *J* = 9.3, 6.7, 1.1 Hz, 2H, ArH), 7.57–7.55 (m, 1H, ArH), 7.44 (dd, *J* = 8.5, 2.3 Hz, 2H, ArH), 7.08 (td, *J* = 6.9, 1.3 Hz, 1H, ArH), 6.88 (d, *J* = 8.4 Hz, 1H, ArH), 4.37 (q, *J* = 7.1 Hz, 2H, CH_2), 1.37 (t, *J* = 7.1 Hz, 3H, CH_3); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-*d*$_6$) : δ = 194.40, 175.27, 163.53, 155.58, 153.94, 145.24, 145.07, 138.79, 138.30, 137.06, 132.97, 132.01, 131.74, 131.32, 129.09, 129.05, 122.18, 120.03, 119.76, 118.23, 114.23, 110.62, 108.03, 95.70, 59.82, 20.25, 14.99.; HRMS (TOF ES$^+$): *m/z* calcd for $C_{28}H_{21}BrN_2O_6S$ $[M+Na]^+$, 615.0196; found, 615.0200.

Ethyl 4-(5-chloro-2-hydroxybenzoyl)-2-(naphthalen-1-ylsulfonyl)pyrido[2,3-b]-indolizine-10-carboxylate (3u)



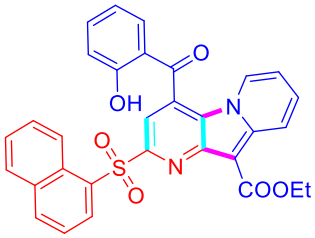
Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 75 mg, 43%); Mp: 238.8–240.0 °C; ^1H NMR (500 MHz, DMSO-*d*$_6$) : δ = 10.99 (s, 1H, OH), 8.78 (d, *J* = 1.8 Hz, 1H, ArH), 8.46 (d, *J* = 9.3 Hz, 1H, ArH), 8.41 (d, *J* = 7.2 Hz, 1H, ArH), 8.26–8.23 (m, 1H, ArH), 8.19 (d, *J* = 8.7 Hz, 1H, ArH), 8.14–8.04 (m, 3H, ArH), 7.82 (d, *J* = 2.8 Hz, 1H, ArH), 7.75 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 1H, ArH), 7.72–7.64 (m, 2H, ArH), 7.62 (dd, *J* = 8.8, 2.8 Hz, 2H, ArH), 7.06 (td, *J* = 7.0, 1.4 Hz, 1H, ArH), 4.28 (q, *J* = 7.1 Hz, 2H, CH_2), 1.25 (t, *J* = 7.1 Hz, 3H, CH_3); $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-*d*$_6$) : δ = 192.81, 163.51, 156.10, 145.16, 145.09, 136.73, 136.16, 135.40, 132.13, 131.94, 130.81, 130.09, 130.01, 129.80, 129.33, 128.39, 128.25, 124.36, 124.30, 120.37, 119.93, 119.65, 114.10, 110.69, 95.64, 59.74, 26.81, 14.85; HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{21}ClN_2O_6S$ $[M+Na]^+$, 607.0701; found, 607.0699.

Ethyl 4-(5-bromo-2-hydroxybenzoyl)-2-(naphthalen-1-ylsulfonyl)pyrido[2,3-b]-indolizine-10-carboxylate (3v)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 77 mg, 41%); Mp: 238.1–239.5 °C; ^{1}H NMR (500 MHz, DMSO-d_6) : δ = 10.87 (s, 1H, OH), 8.78 (d, J = 1.9 Hz, 1H, ArH), 8.46 (d, J = 9.3 Hz, 2H, ArH), 8.42 (d, J = 7.2 Hz, 1H, ArH), 8.23 (d, J = 8.9 Hz, 1H, ArH), 8.19 (d, J = 8.8 Hz, 1H, ArH), 8.15–8.06 (m, 2H, ArH), 7.95 (d, J = 2.6 Hz, 1H, ArH), 7.80–7.72 (m, 2H, ArH), 7.71–7.66 (m, 2H, ArH), 7.06 (td, J = 6.9, 1.4 Hz, 1H, ArH), 6.92 (d, J = 8.8 Hz, 1H, ArH), 4.28 (q, J = 7.1 Hz, 2H, CH_2), 1.25 (t, J = 7.1 Hz, 1H, CH_3).; ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) : δ = 192.82, 163.50, 159.09, 156.09, 145.18, 145.11, 139.54, 136.66, 136.15, 135.40, 133.88, 132.12, 131.95, 130.81, 130.10, 131.00, 129.80, 129.36, 128.38, 128.26, 124.97, 124.29, 120.59, 119.93, 119.65, 114.09, 111.20, 110.75, 95.65, 79.65, 59.74, 14.86.; HRMS (TOF ES$^+$): m/z calcd for $C_{31}H_{21}BrN_2O_6S$ $[M+Na]^+$, 651.0196; found, 651.0200.

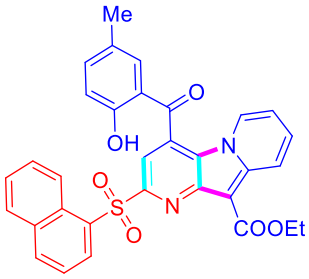
Ethyl 4-(2-hydroxybenzoyl)-2-(naphthalen-1-ylsulfonyl)pyrido[2,3-b]indolizine-10-carboxylate (3w)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 84 mg, 51%); Mp: 265.1–268.2 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.74 (s, 1H, OH), 8.78 (d, J = 1.8 Hz, 1H, ArH), 8.45 (d, J = 9.3 Hz, 1H, ArH), 8.37 (d, J = 7.2 Hz, 1H, ArH), 8.26–8.20 (m, 1H, ArH), 8.18 (d, J = 8.7 Hz, 1H, ArH), 8.12 (dd, J = 8.7, 1.8 Hz, 1H, ArH), 8.06 (d, J = 13.2 Hz, 2H, ArH), 7.80–7.72 (m, 2H, ArH), 7.71–7.67 (m, 1H, ArH), 7.66–7.60 (m, 2H, ArH), 7.19–6.99 (m, 1H, ArH), 6.98 (dd, J = 8.4, 0.9 Hz, 1H, ArH), 4.28 (q, J = 7.1 Hz, 2H, CH_2), 1.25 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) : δ = 194.58, 163.52, 160.42, 156.12, 145.19, 145.10, 137.78, 136.70, 136.13, 135.39, 132.36, 132.11, 131.91, 130.85, 130.09, 130.00, 129.78, 129.14, 128.37, 128.25, 124.34, 122.66, 120.31, 119.91, 119.70, 118.25, 114.12, 110.73, 95.68,

59.75, 14.85; HRMS (TOF ES$^+$): *m/z* calcd for $C_{31}H_{22}N_2O_6S$ $[M+Na]^+$, 573.1091; found, 573.1094.

Ethyl 4-(2-hydroxy-5-methylbenzoyl)-2-(naphthalen-1-ylsulfonyl)pyrido[2,3-b] indolizine-10-carboxylate (3x)



Orange yellow solid ($V_{Petroleum\ ether}/V_{Ethyl\ acetate}$ = 4:1, R_f = 0.2, 91 mg, 54%); Mp: 268.3–269.4 °C; ^{1}H NMR (600 MHz, DMSO-*d*$_6$) : δ = 10.55 (s, 1H, OH), 8.78 (d, *J* = 1.9 Hz, 1H, ArH), 8.45 (d, *J* = 9.3 Hz, 1H, ArH), 8.35 (d, *J* = 7.3 Hz, 1H, ArH), 8.24 (d, *J* = 8.2 Hz, 1H, ArH), 8.19 (d, *J* = 8.8 Hz, 1H, ArH), 8.12 (d, *J* = 8.7 Hz, 1H, ArH), 8.08 (d, *J* = 8.1 Hz, 1H, ArH), 8.02 (s, 1H, ArH), 7.78–7.72 (m, 1H, ArH), 7.72–7.64 (m, 2H, ArH), 7.56 (s, 1H, ArH), 7.45 (d, *J* = 8.4 Hz, 1H, ArH), 7.06 (t, *J* = 7.0 Hz, 1H, ArH), 6.92 (d, *J* = 8.4 Hz, 1H, ArH), 4.29 (q, *J* = 7.1 Hz, 2H, CH_2), 2.25 (s, 3H, CH_3), 1.26 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C{^{1}H} NMR (150 MHz, DMSO-*d*$_6$) : δ = 194.47, 163.52, 158.52, 156.08, 145.14, 145.07, 138.71, 136.90, 136.18, 135.39, 132.12, 131.88, 131.69, 130.82, 130.08, 129.99, 129.77, 129.10, 129.05, 128.37, 128.24, 124.32, 122.22, 119.92, 119.70, 118.23, 114.13, 110.69, 95.67, 79.66, 59.72, 20.24, 14.85.; HRMS (TOF ES$^+$): *m/z* calcd for $C_{32}H_{24}N_2O_6S$ $[M+Na]^+$, 587.1248; found, 587.1247.

X-ray Structure and Dataof 3b[3]

Single crystal culture and confirmation: First, Compound **3b** is added to the bottle and dissolved by adding ethyl acetate (EA), dichloromethane (DCM), and petroleum ether (PE) in a volume ratio of VEA:VDCM:VPE = 1:1:2. Then, place the sample bottle into a 50 mL conical flask containing an appropriate amount of petroleum ether, seal it with a stopper, and leave it at room temperature until crystals grow (for 5 days). Some crystals appeared, and for single crystal parsing, crystals were selected with sizes of 0.32 mm x 0.18 mm x 0.15 mm. The Bruker D8 VENTURE dual wavelength Mo/Cu was used to

obtain single crystal diffraction at 100 K with the use of three-circle diffractometer Mo K (lambda = 0.71073 A) for diffraction intensity data collection, using Φ and omega scanning. Multi-scan correction was performed for all intensity data. The crystal structure was solved by the atomic method using the SHELXL 2018/3 (Sheldrick, 2015) program (Supporting Information, Figure S1, CCDC 2396367).

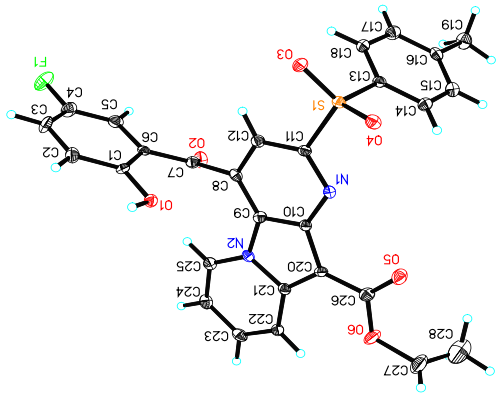


Figure S1. X-Ray crystal structure of **3b**

Table S1. Crystal data and structure refinement for **3b**

Identification code	mo_240806A
Empirical formula	$C_{28}H_{22}FN_2O_7S$
Formula weight	549.53 g/mol
Temperature	100 K
Crystal system	monoclinic
Space group	P 1 21/c 1
Unit cell dimensions	a = 14.5461(14) Å α = 90°. b = 22.704(2) Å β = 100.169(3)°. c = 8.0550(7) Å γ = 90°.
Volume	2618.4 (4) $Å^3$
Z	4
Density (calculated)	1.394 g/cm^3
Absorption coefficient	0.181 mm^{-1}
F(000)	1140
Theta range for data collection	2.29 to 26.77°.
Reflections collected	5578
Independent reflections	5578 [R(int) = 0.0601]
Max. and min. transmission	0.7454 and 0.6687
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5578 / 0 / 357
Goodness-of-fit on F^2	1.075
Final R indexes [I>2sigma(I)]	R_1 = 0.1108, wR_2 = 0.2411

Final R indexes (all data)	R_1 = 0.1574, wR_2 = 0.2606
Largest diff. peak and hole	1.368 and-0.552e.Å^{-3}

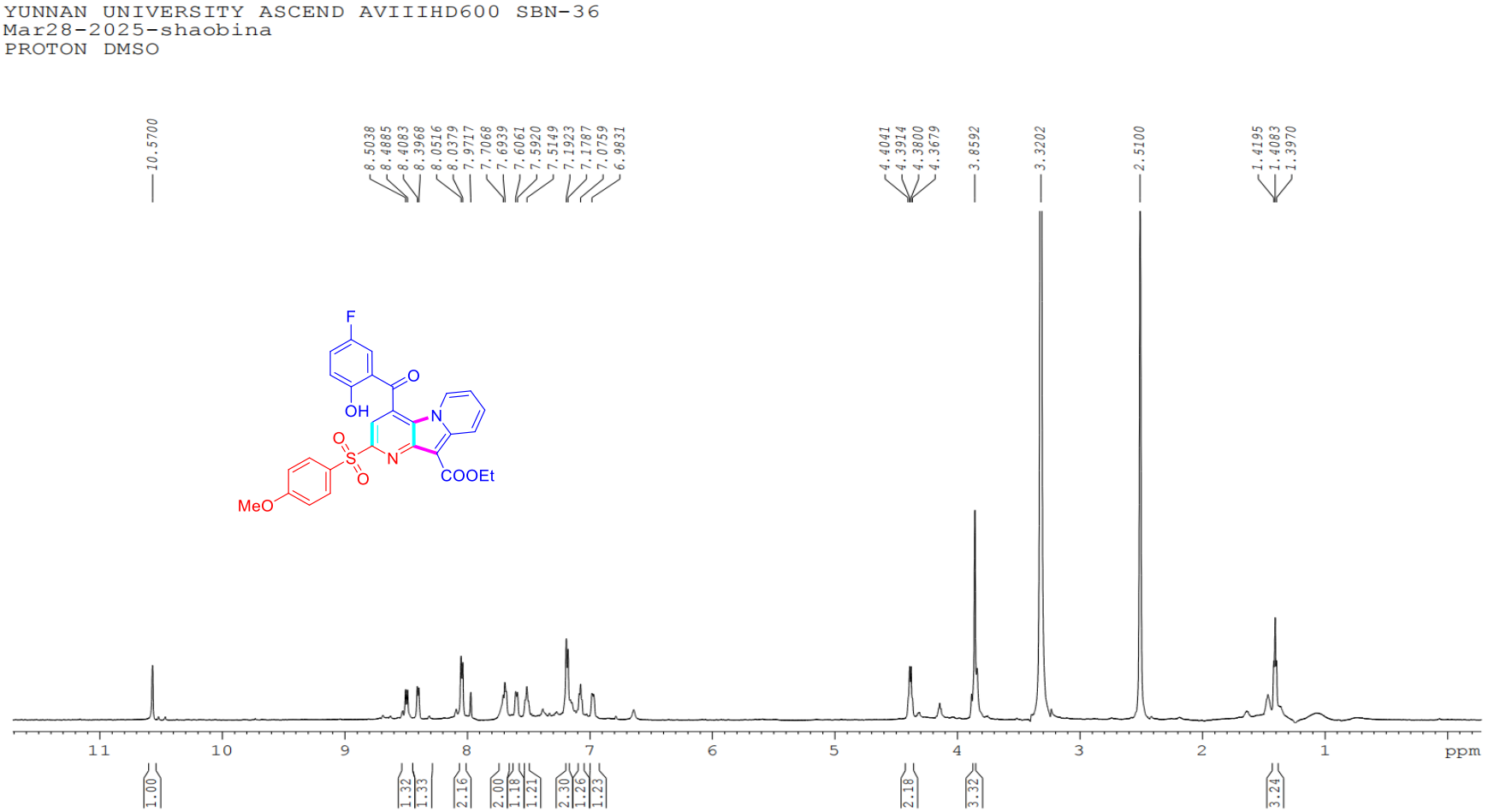


Figure S2. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3a**

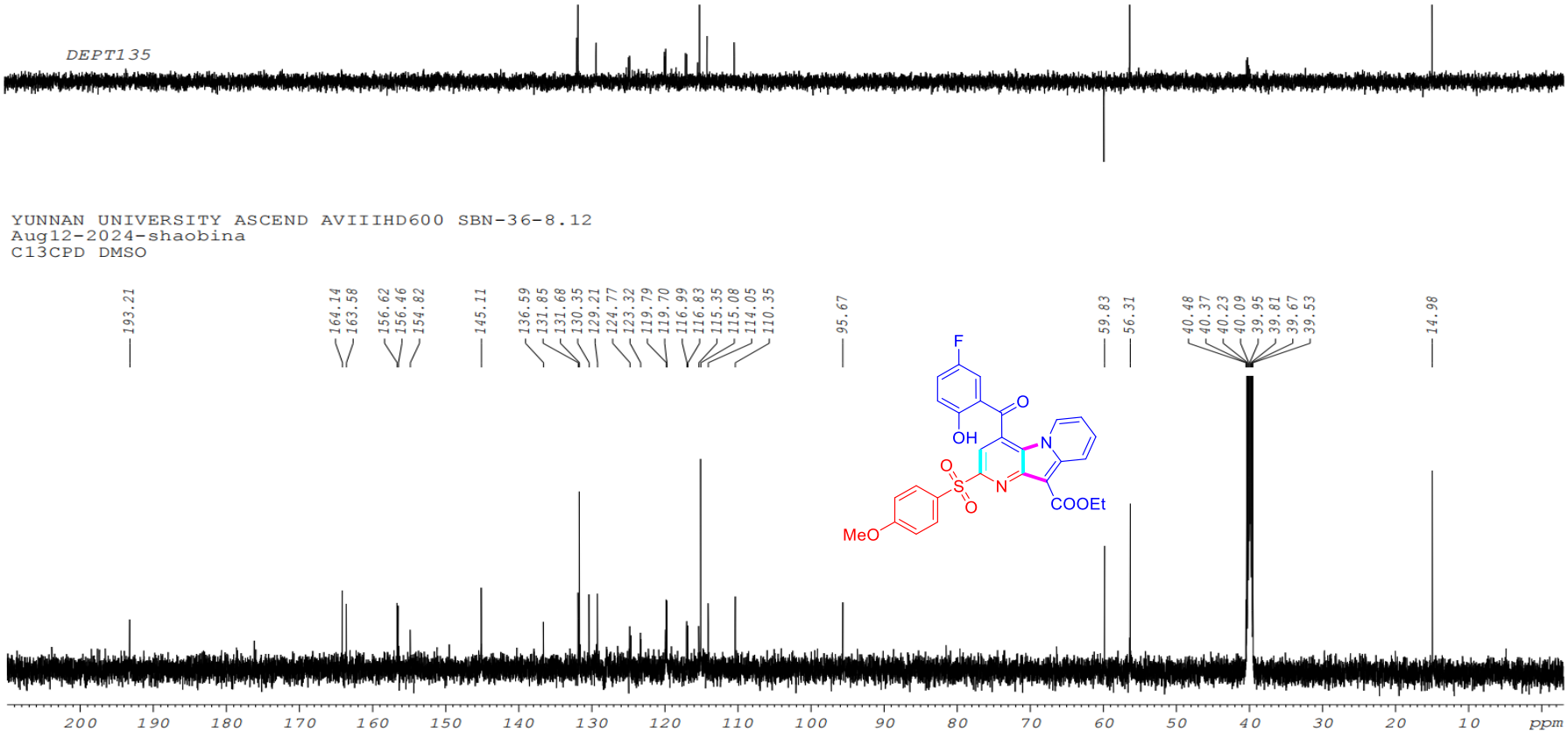


Figure S3. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3a**

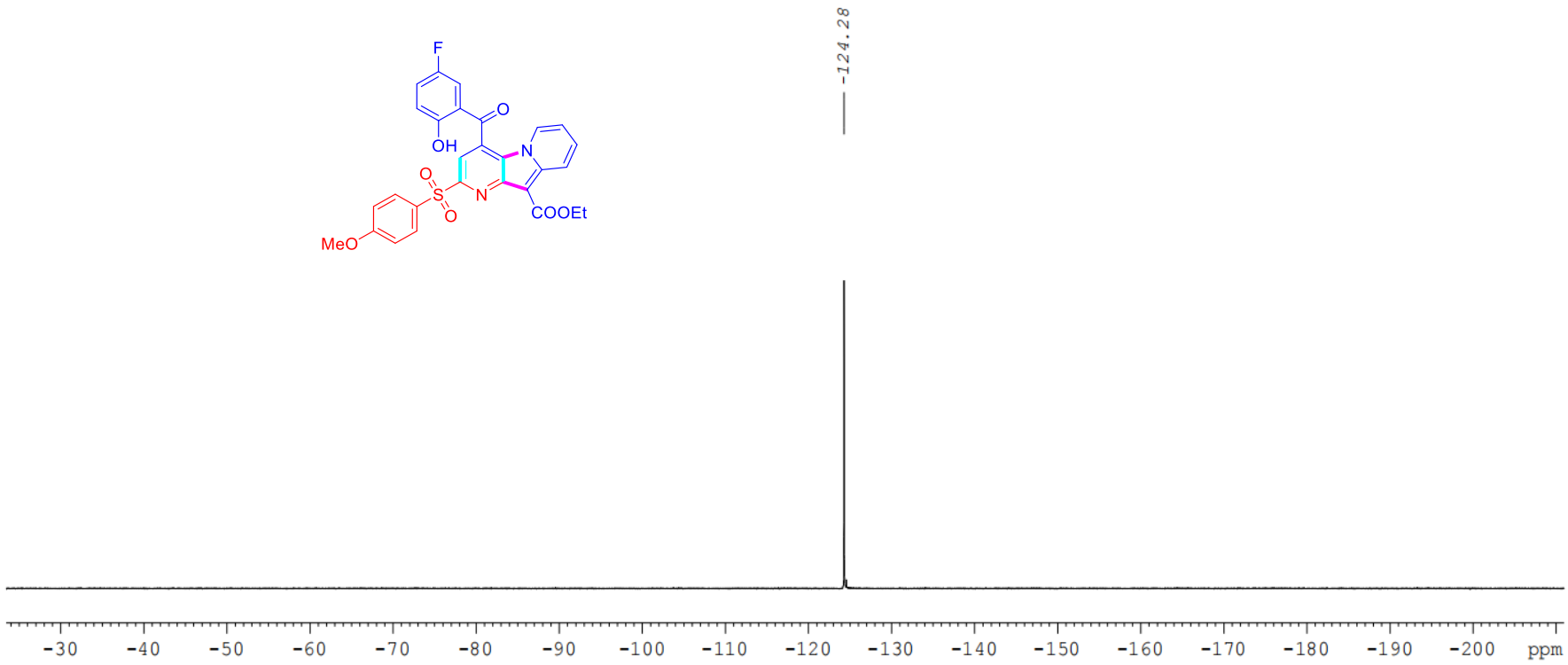


Figure S4. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound 3a

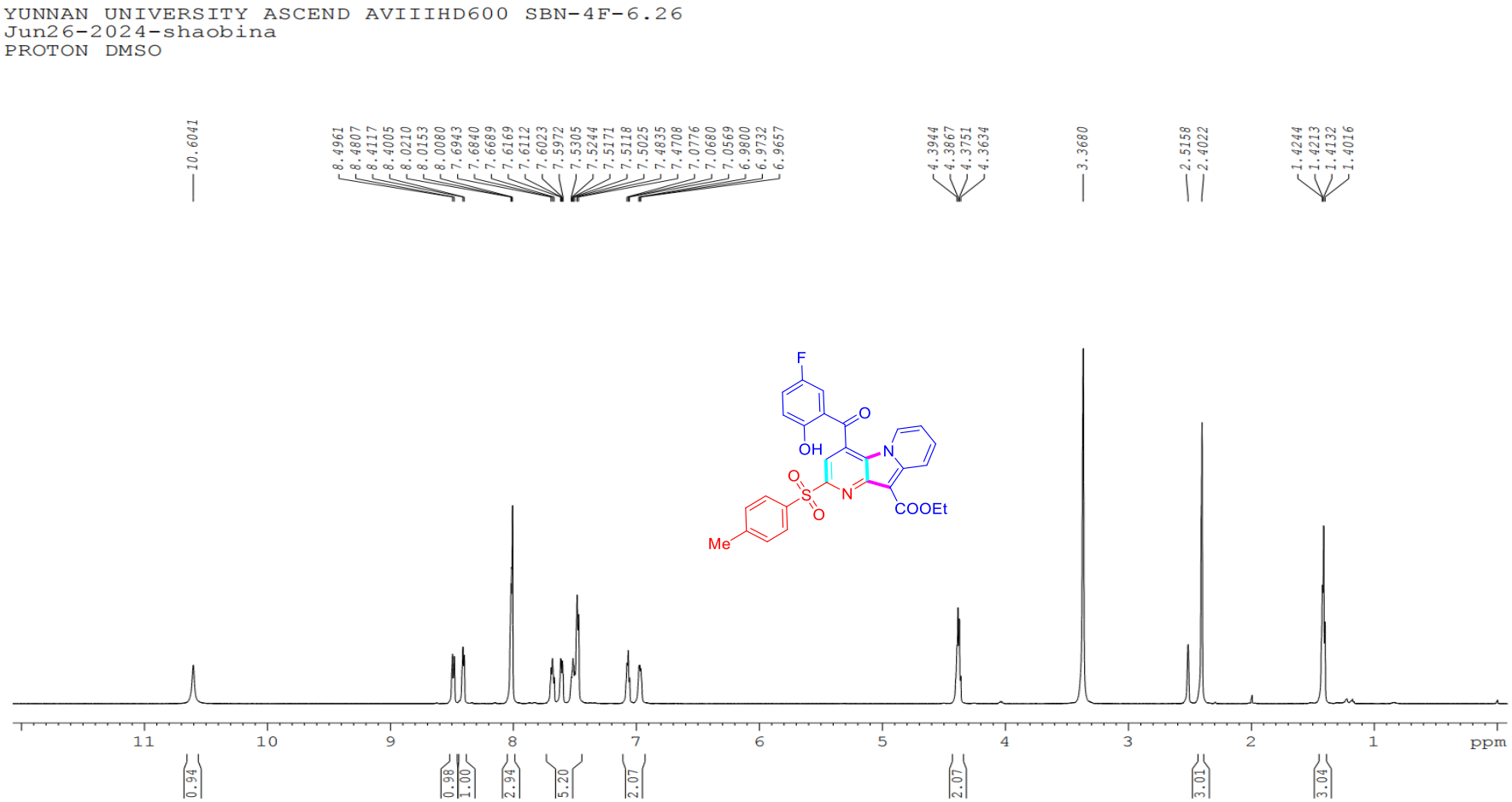


Figure S5. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3b**

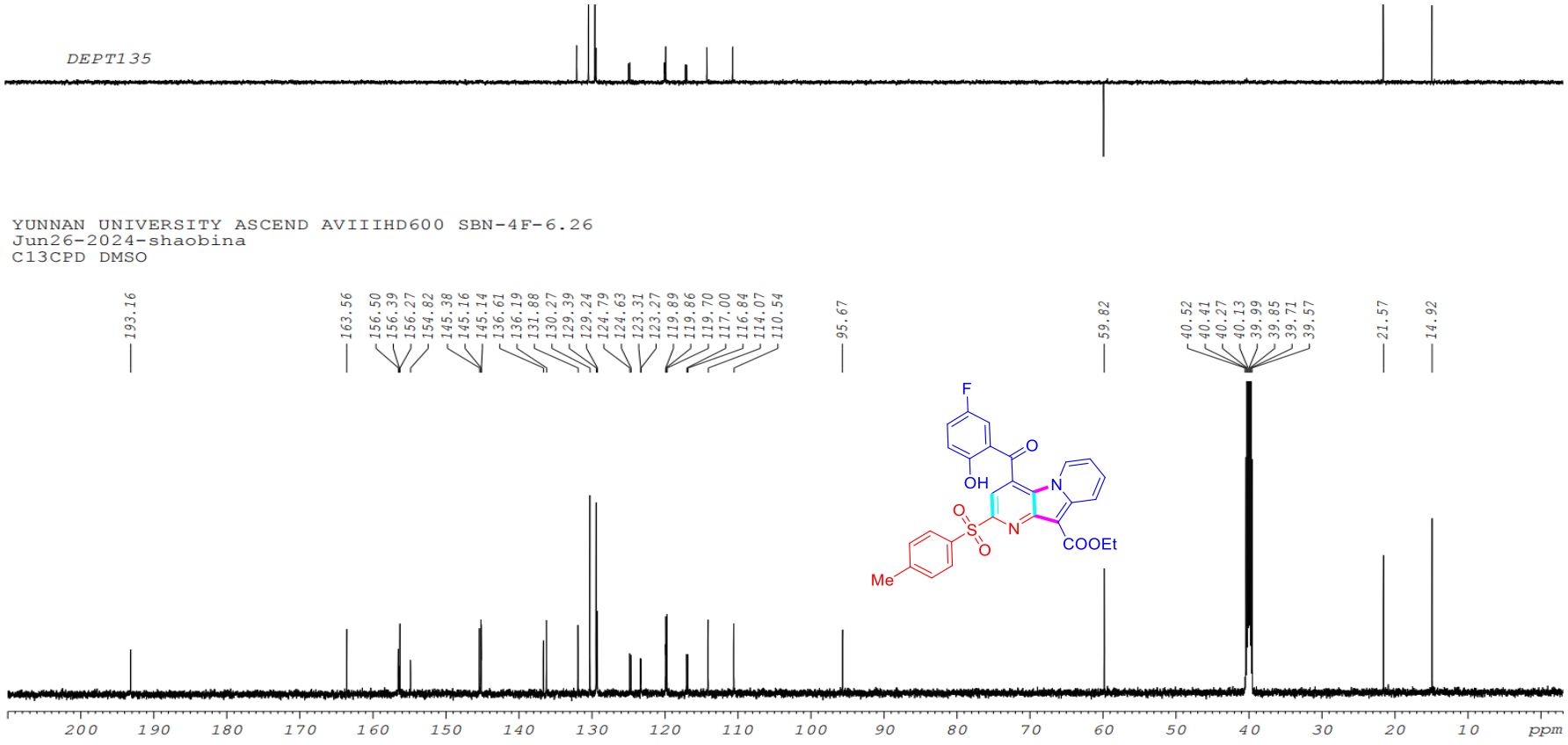


Figure S6. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3b**

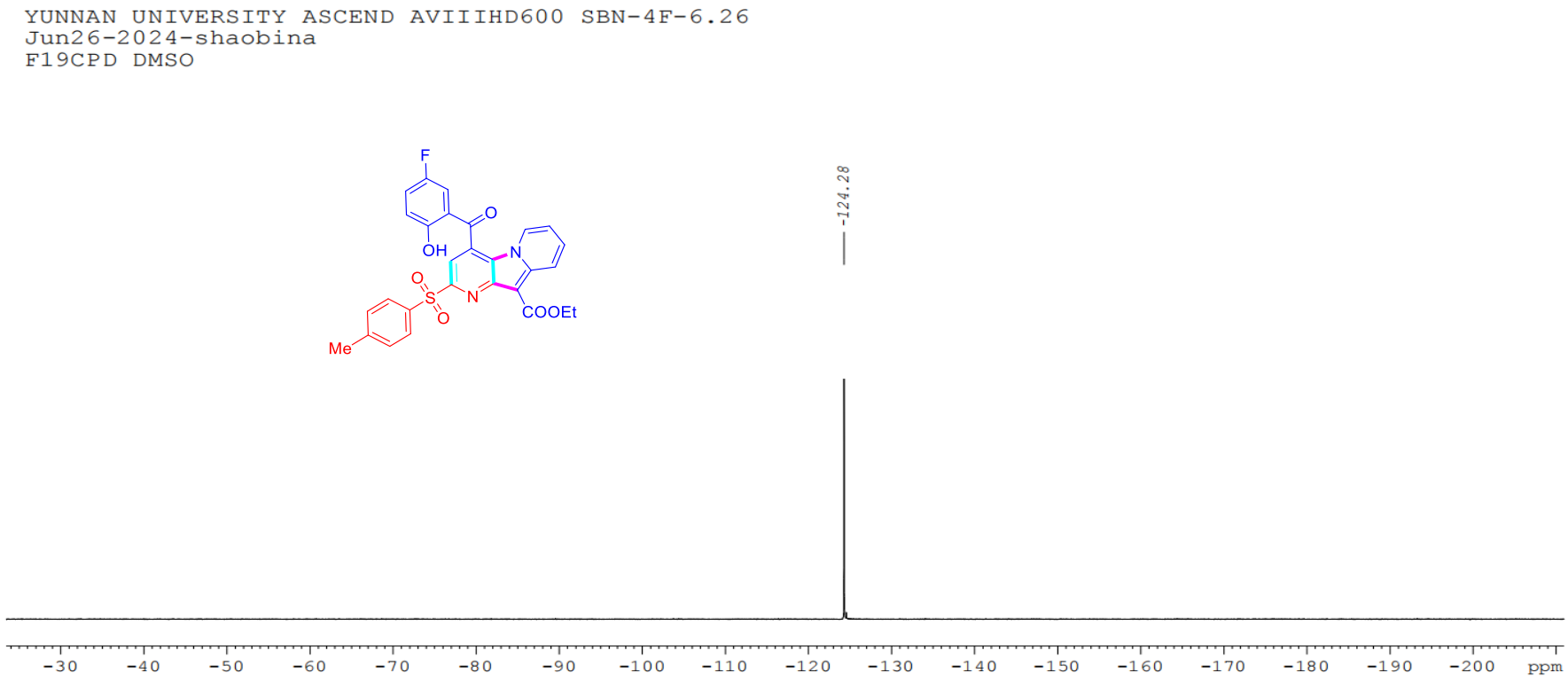


Figure S7. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **3b**

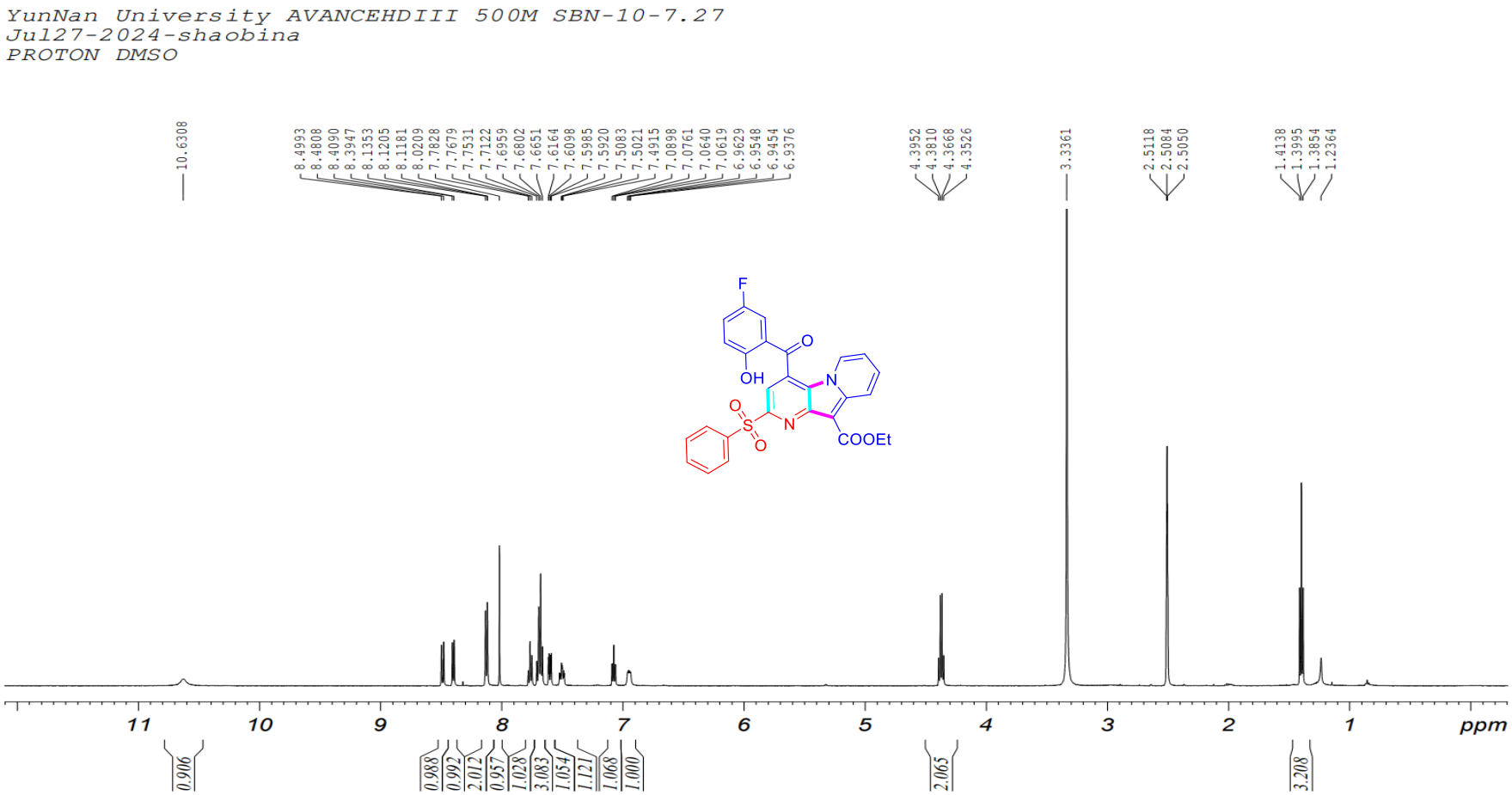


Figure S8. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3c**

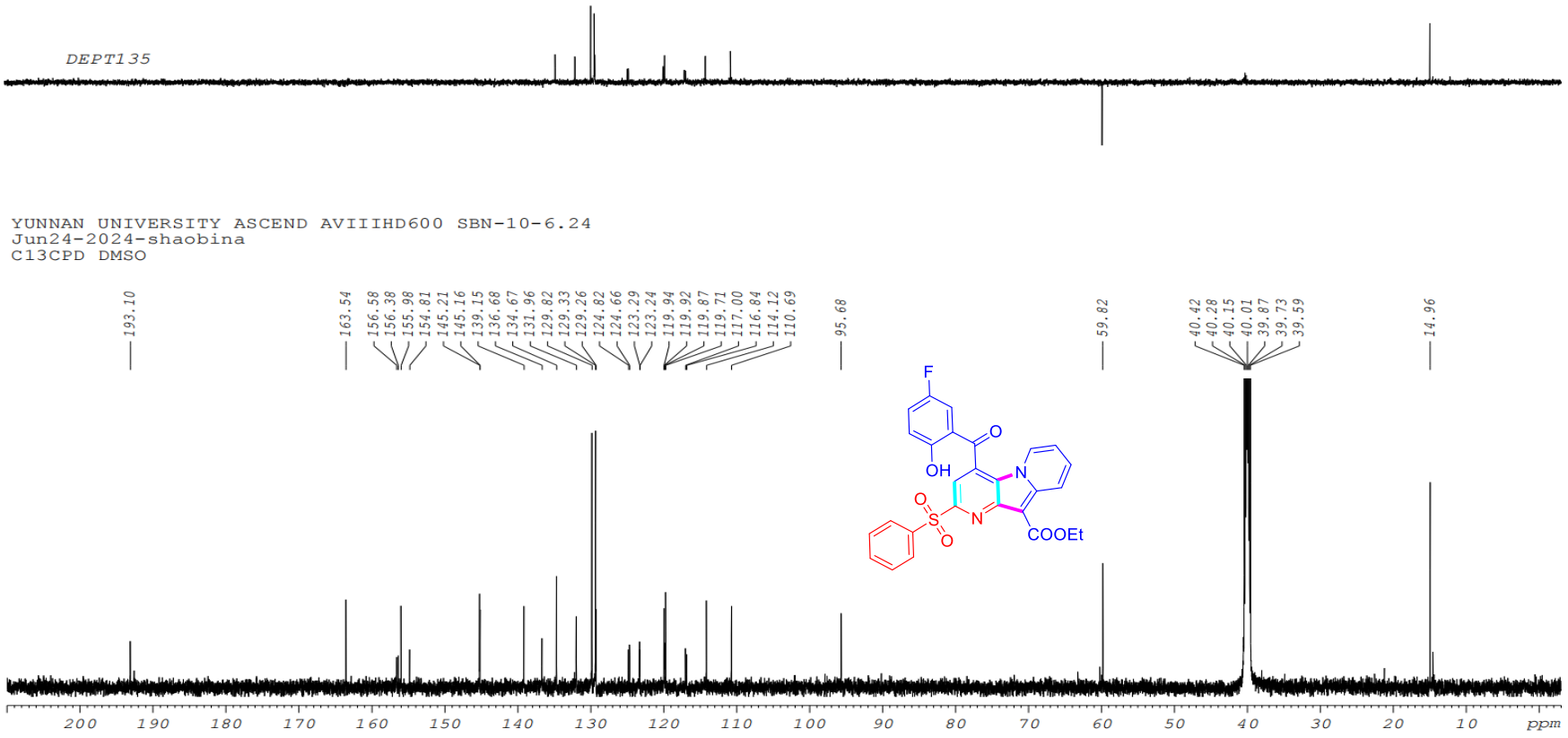


Figure S9. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3c**

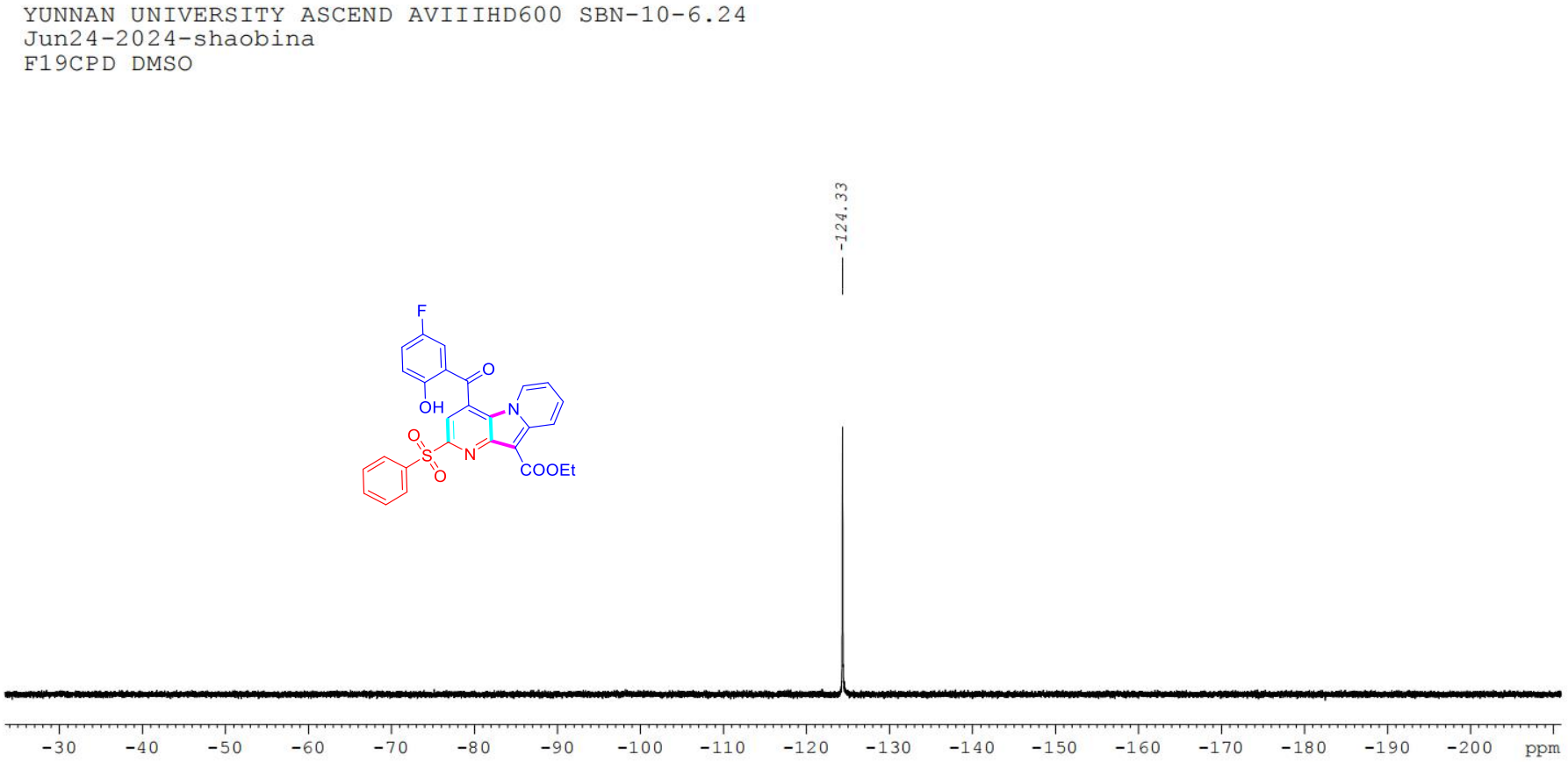


Figure S10. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **3c**

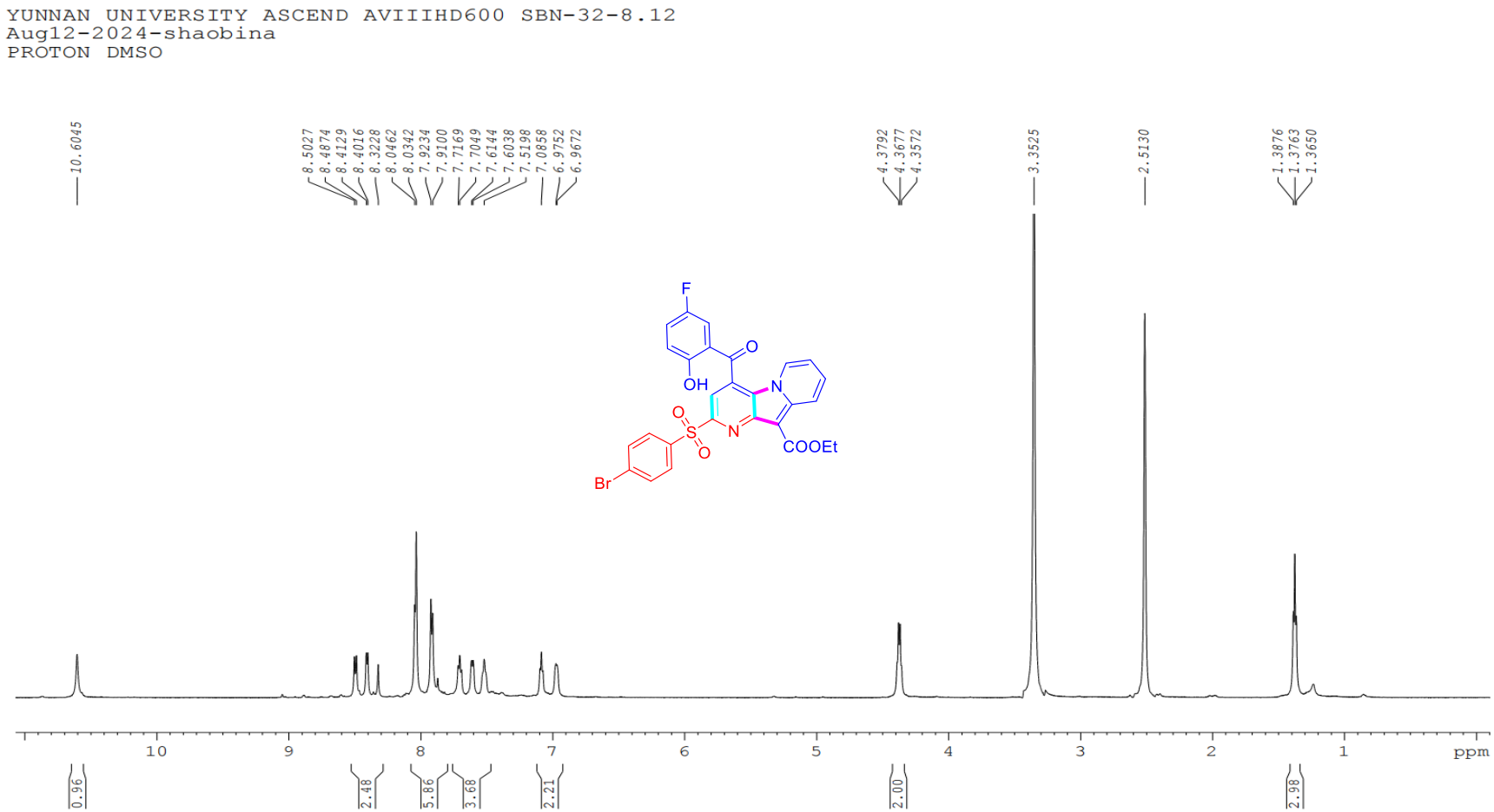


Figure S11. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3d**

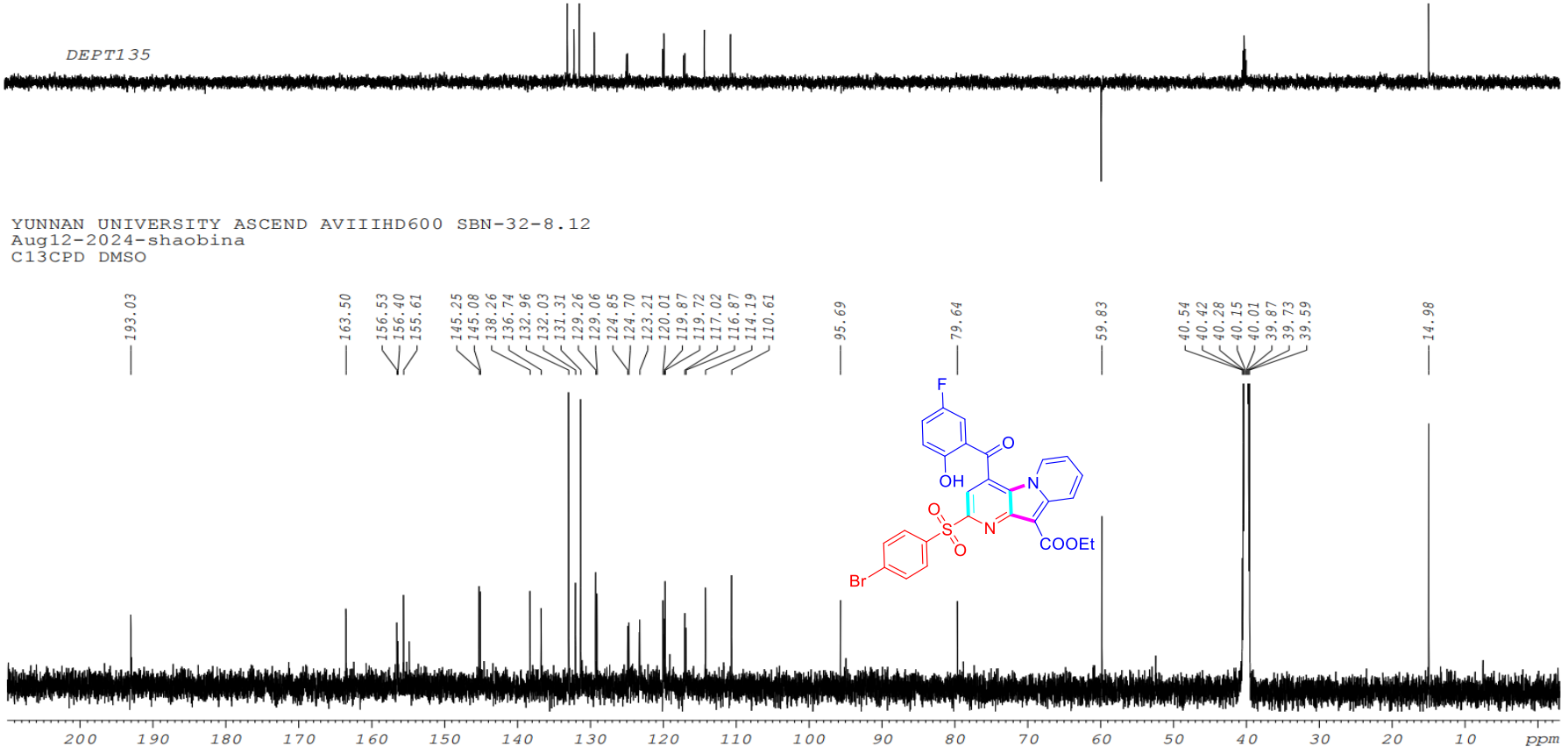


Figure S12. $^{13}C\{^{1}H\}$ NMR (150 MHz,DMSO-d_6) spectra of compound **3d**

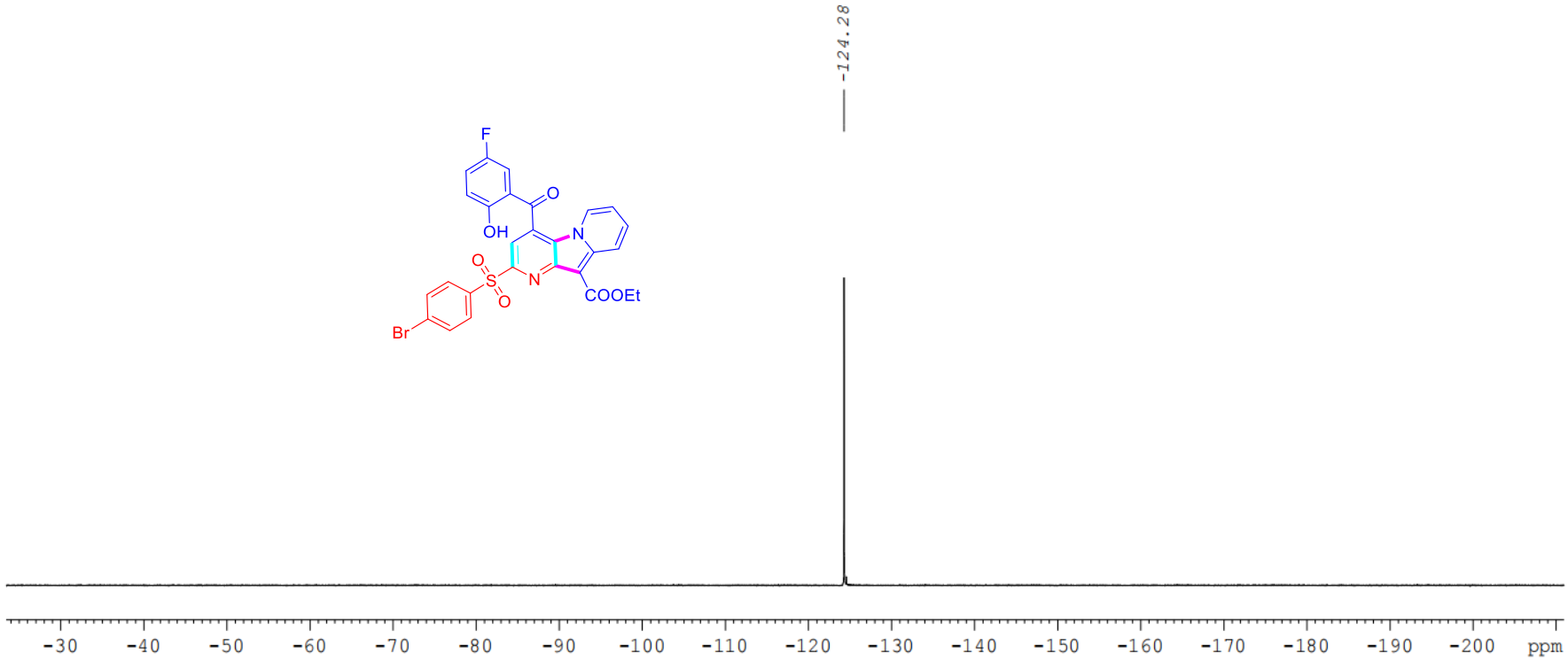


Figure S12. ^{19}F NMR (574 MHz, DMSO-d_6) spectra of compound **3d**

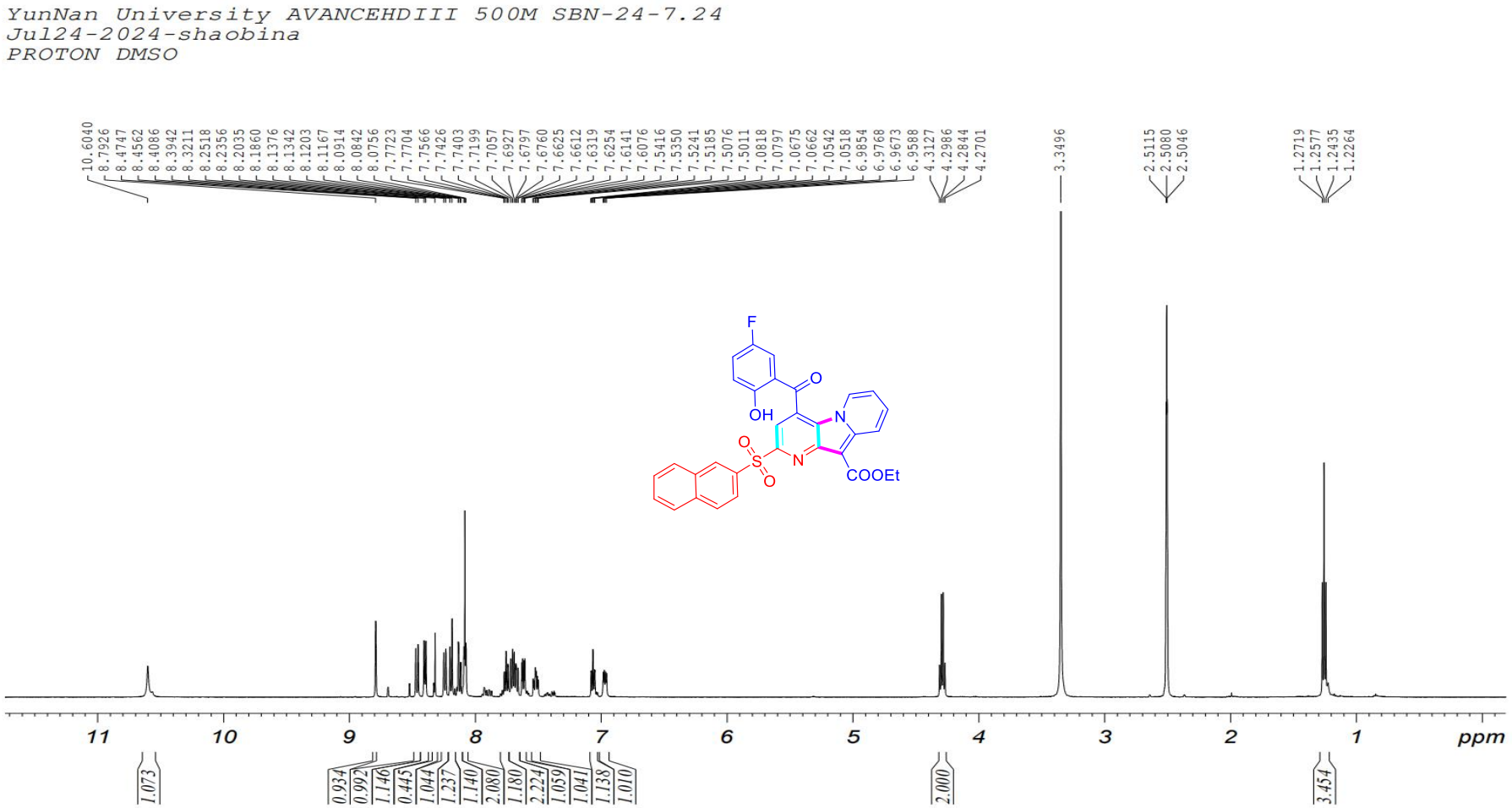


Figure S13. ^{1}H NMR (500 MHz, DMSO-d_6 spectra of compound **3e**

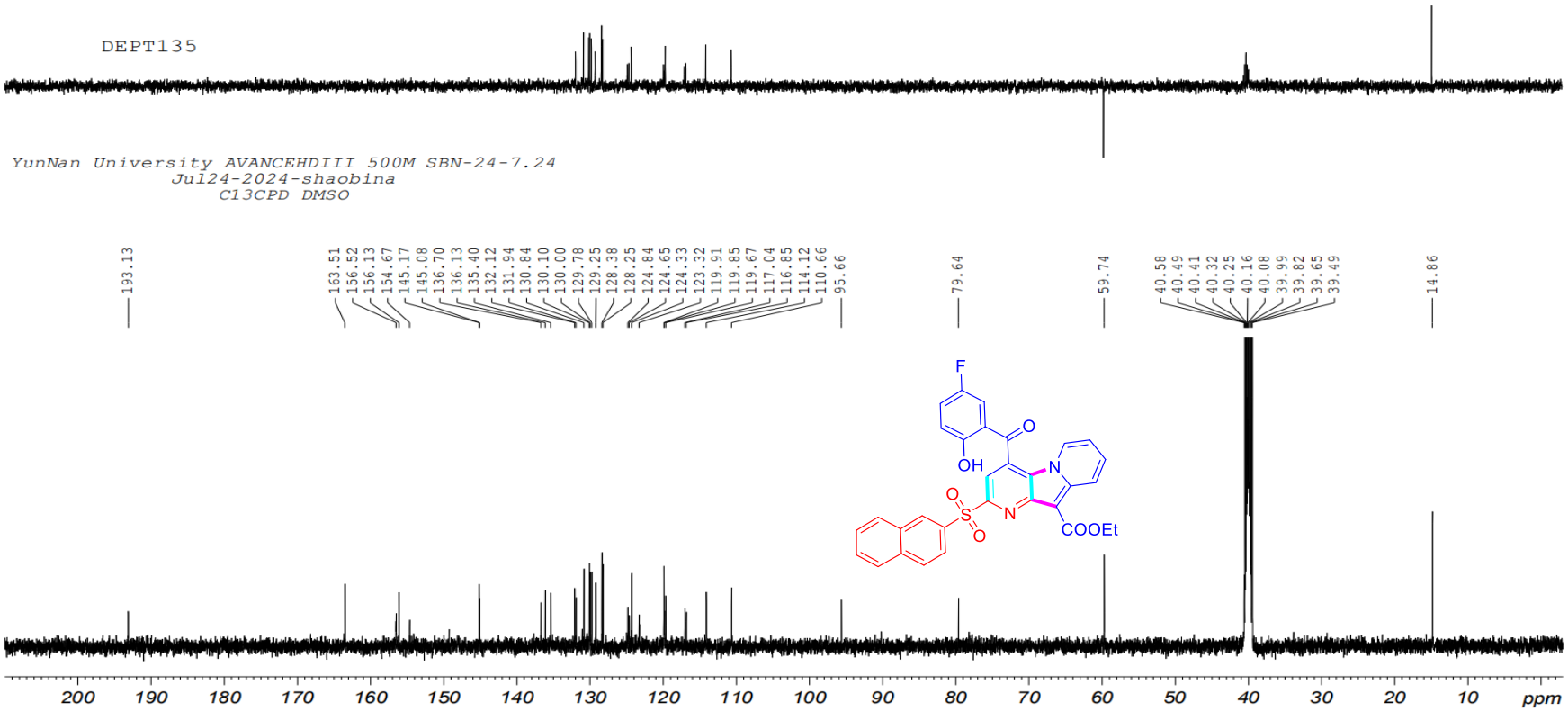


Figure S14. $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-d_6) spectra of compound **3e**

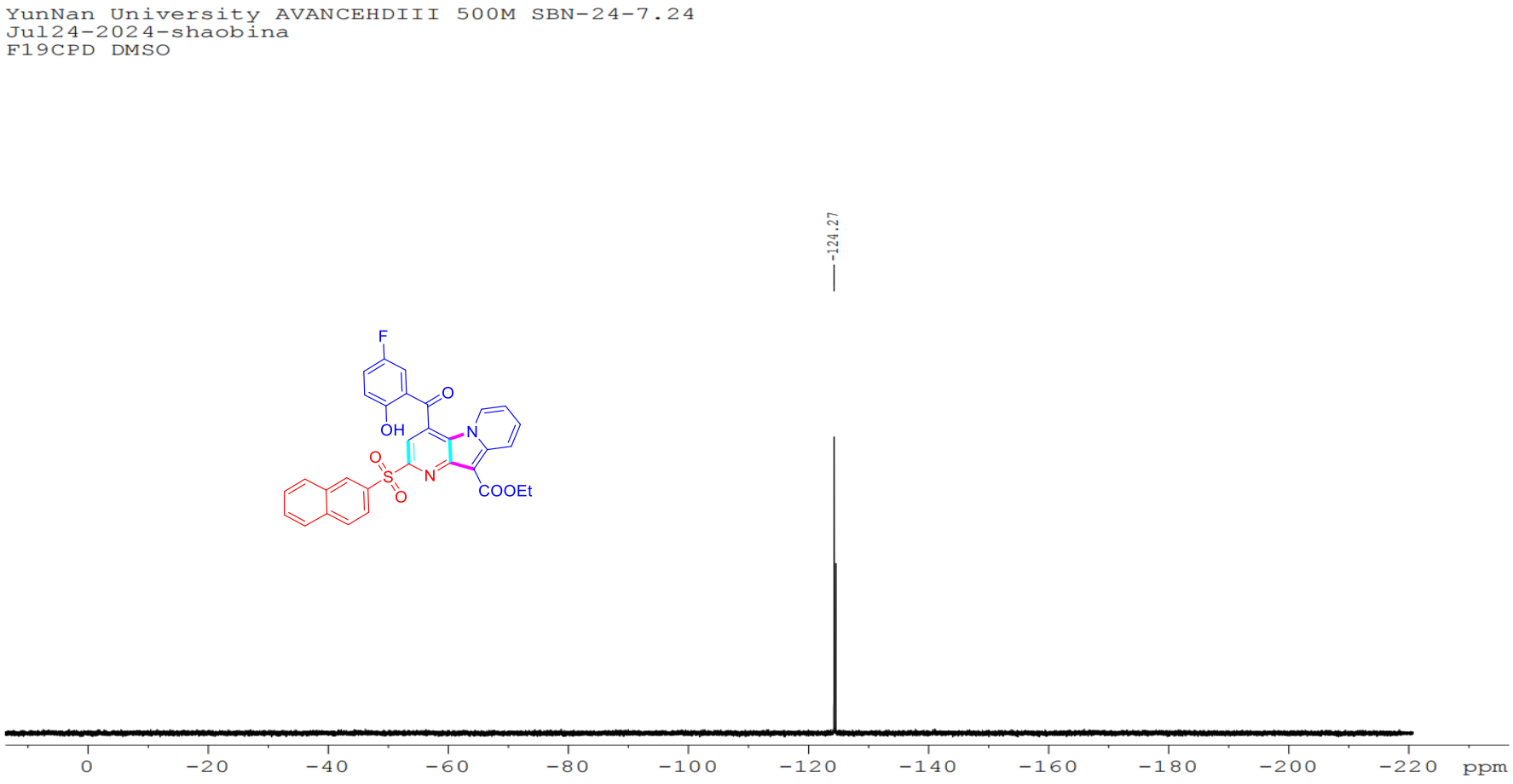


Figure S15. ^{19}F NMR (470 MHz, DMSO-d_6) spectra of compound **3e**

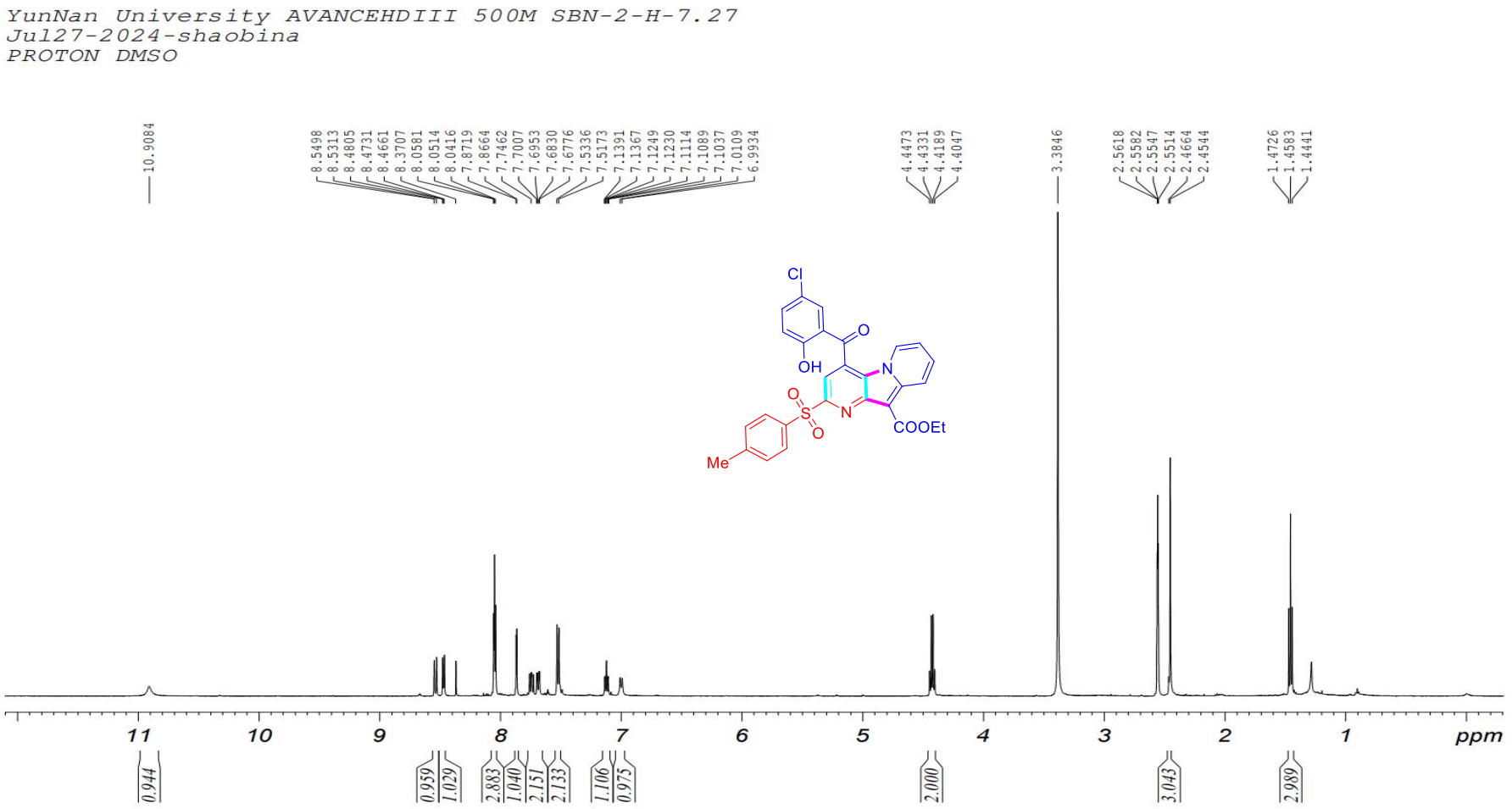


Figure S16. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3f**

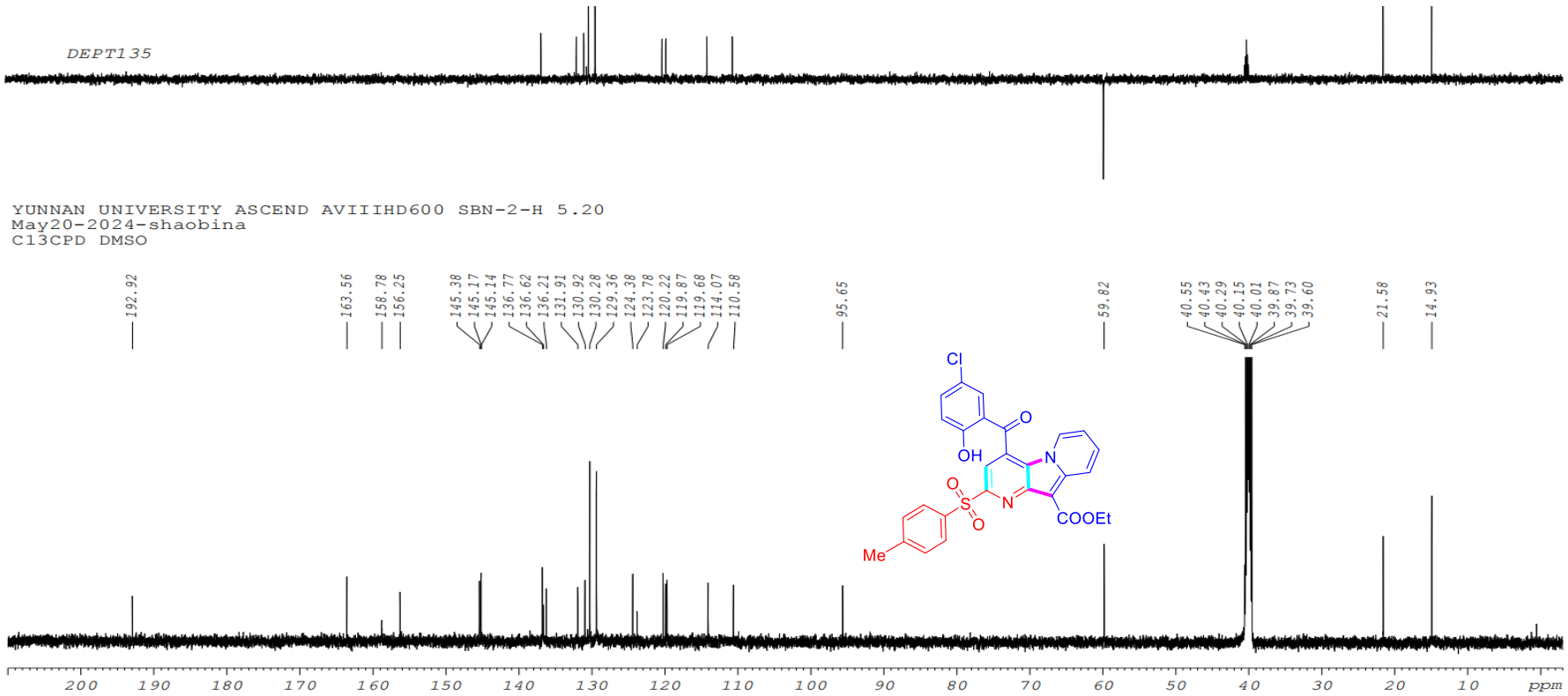


Figure S17. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3f**

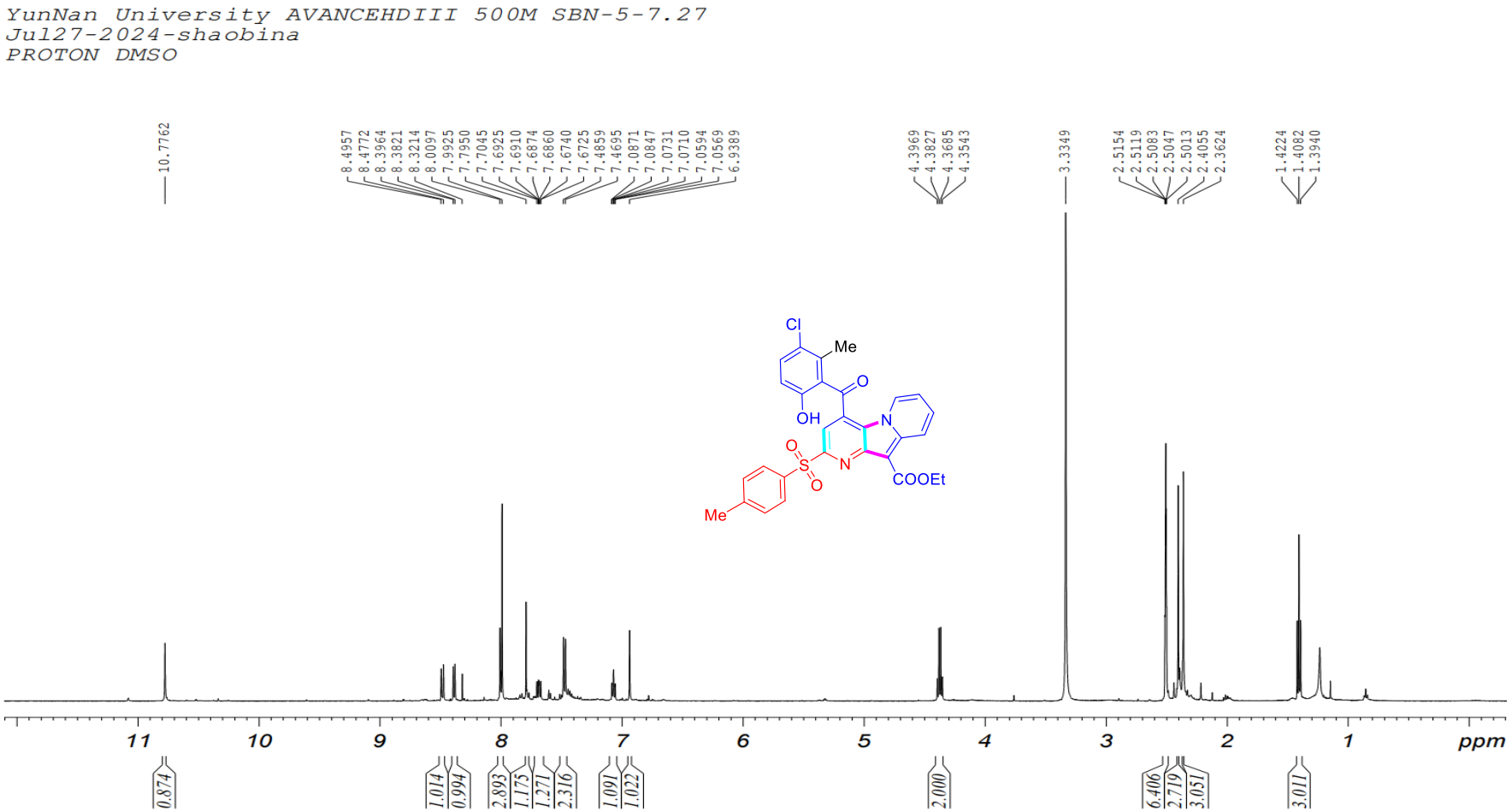


Figure S18. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3g**

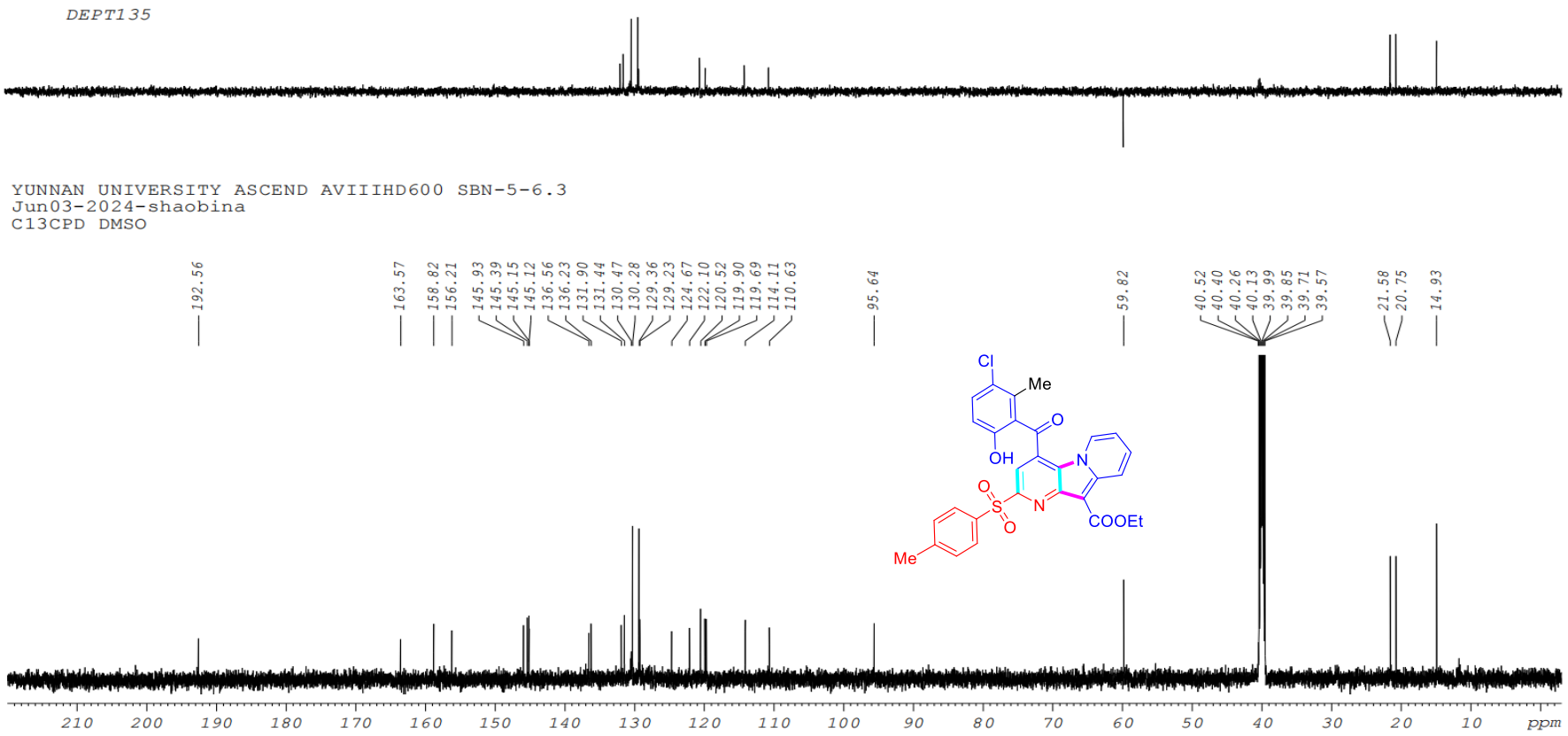


Figure S19. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3g**

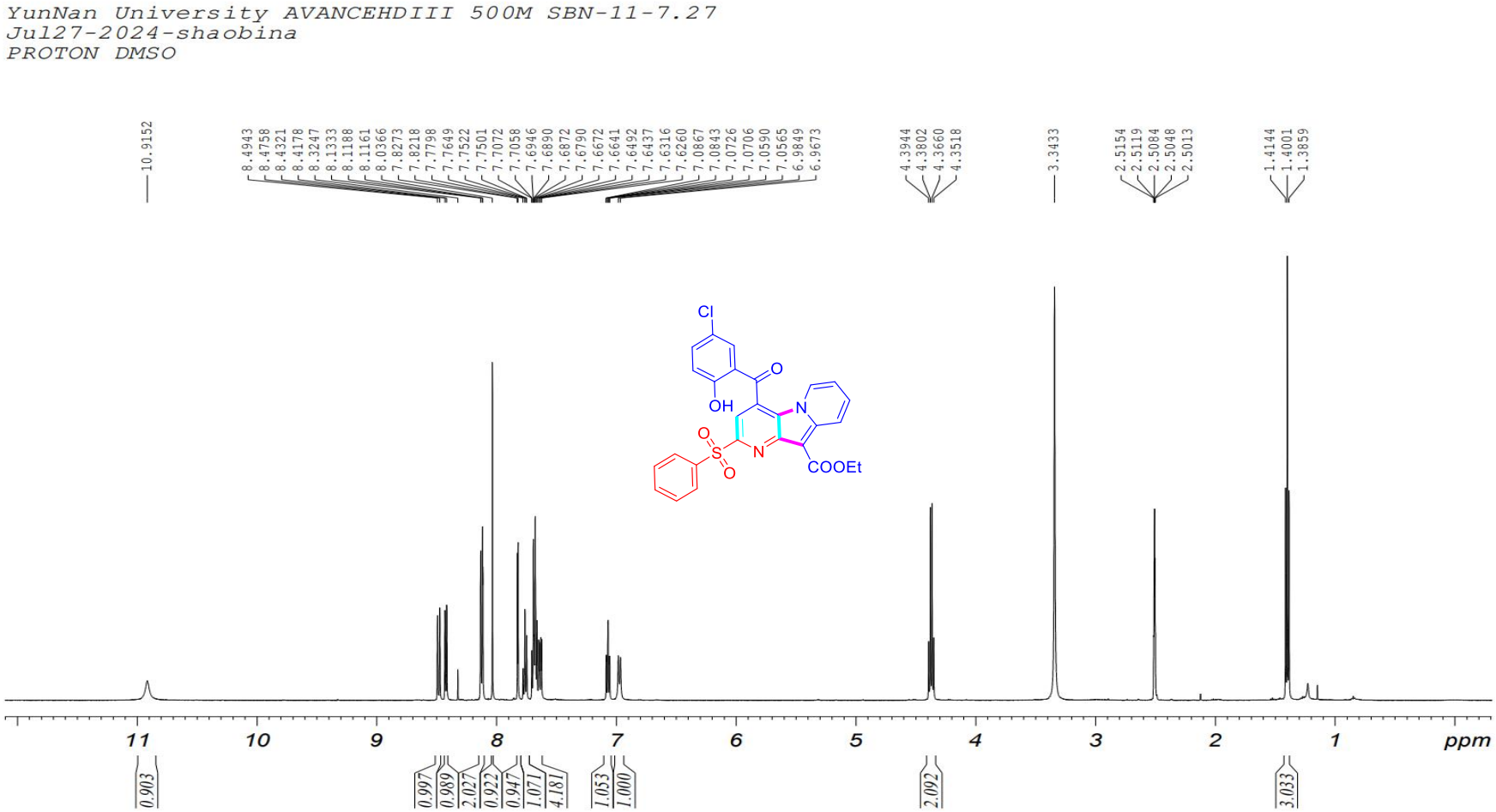


Figure S20. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3h**

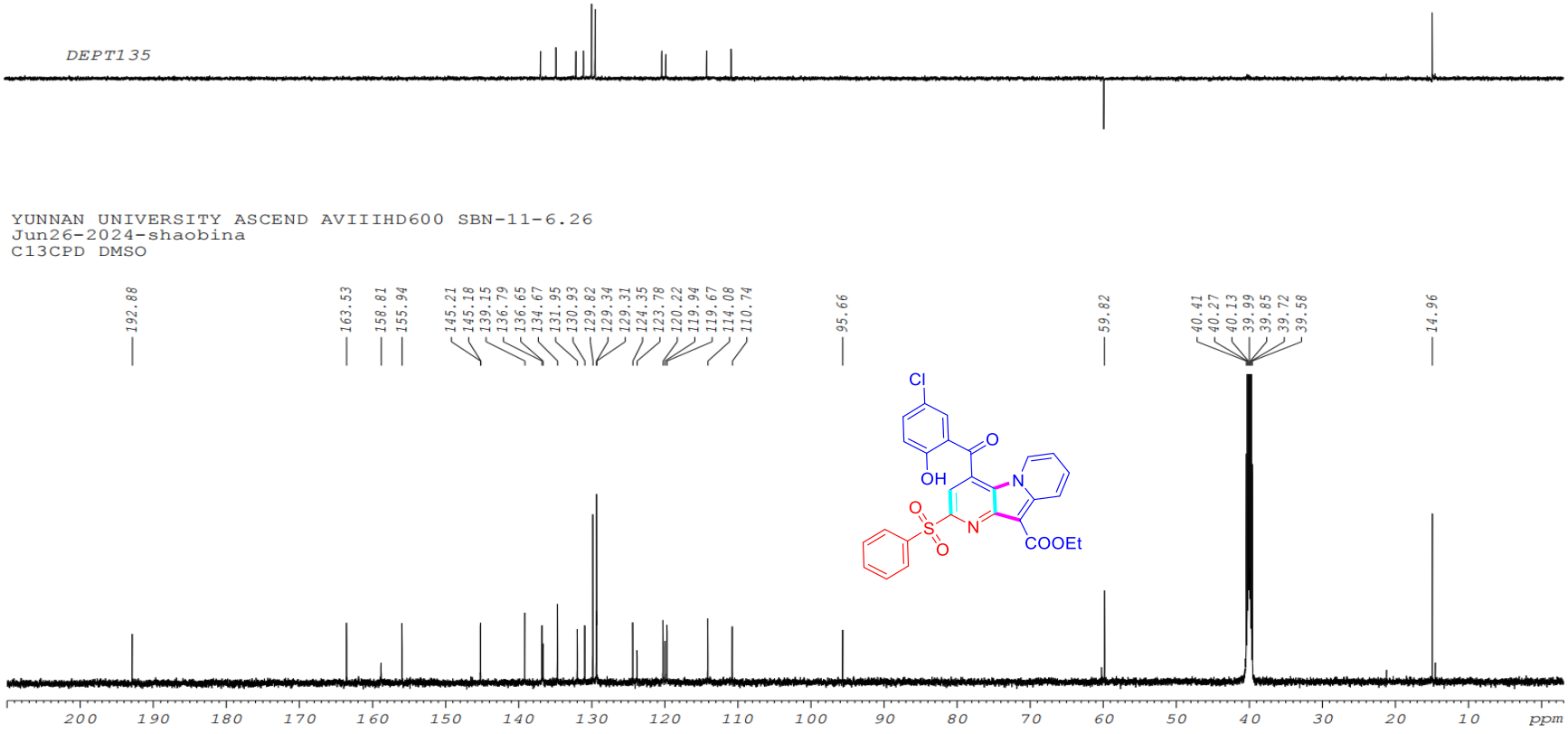


Figure S21. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3h**

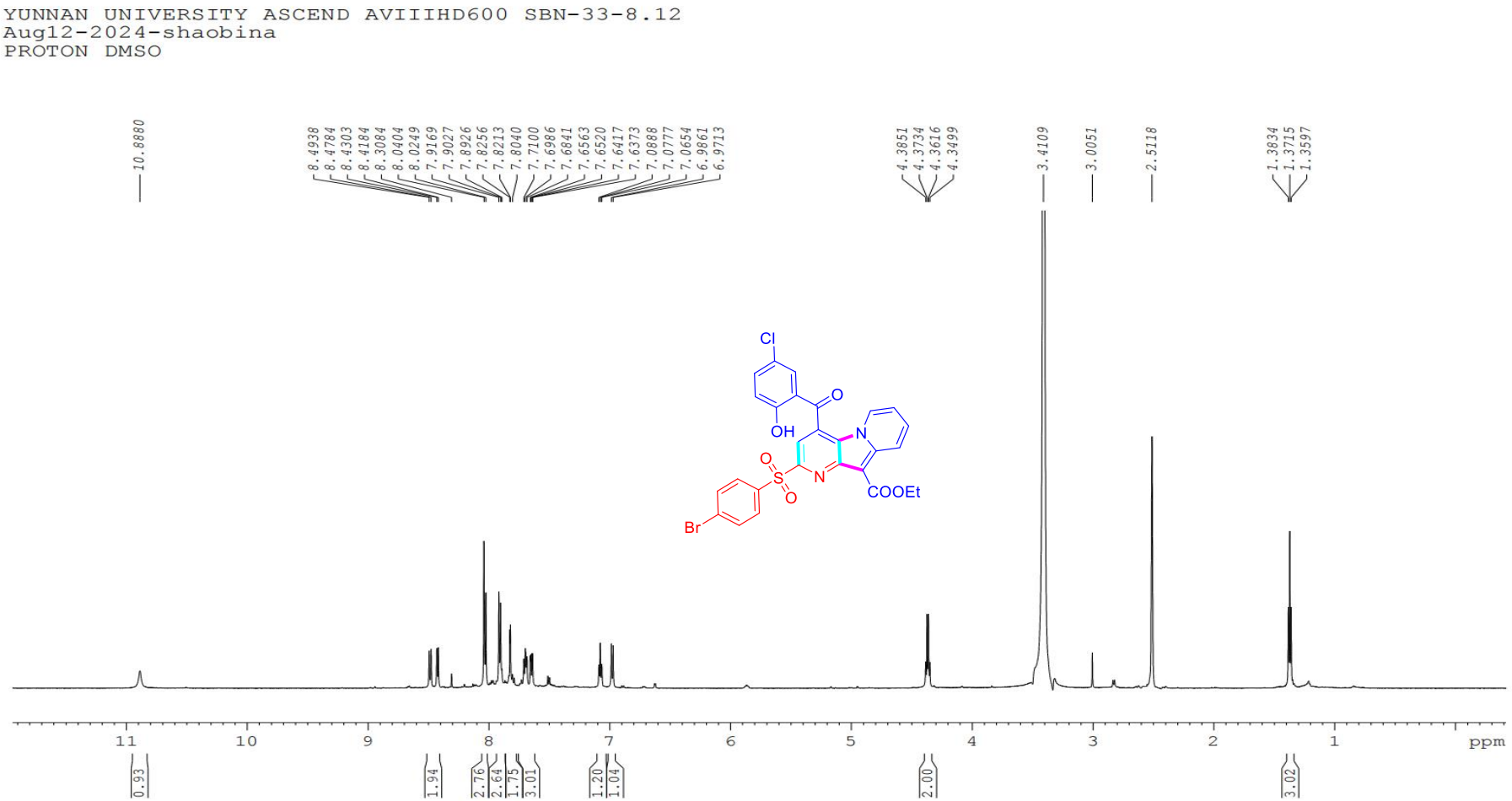


Figure S22. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3i**

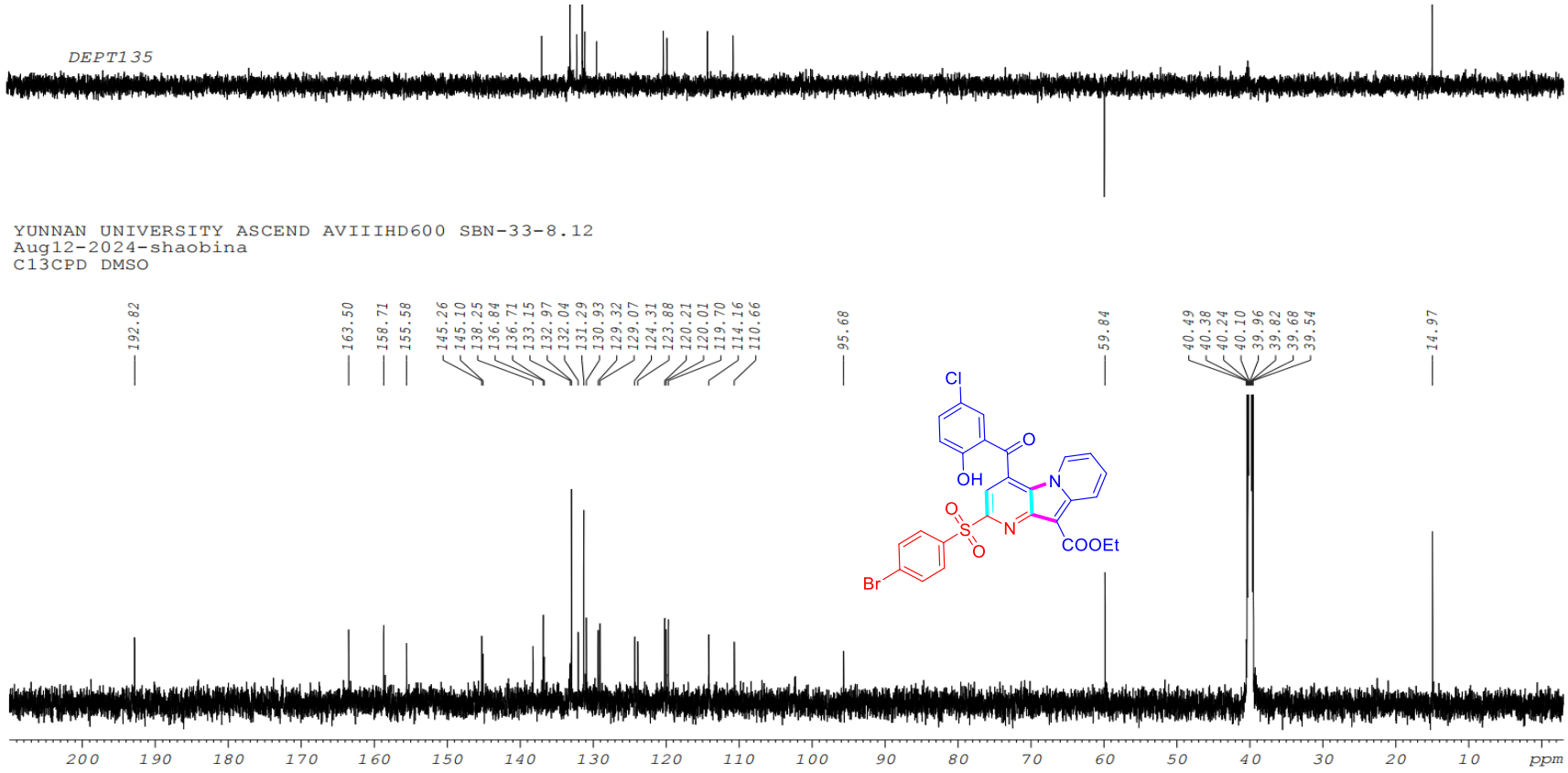


Figure S23. $^{13}C\{^{1}H\}$ NMR (150 MHz,DMSO-d_6) spectra of compound **3i**

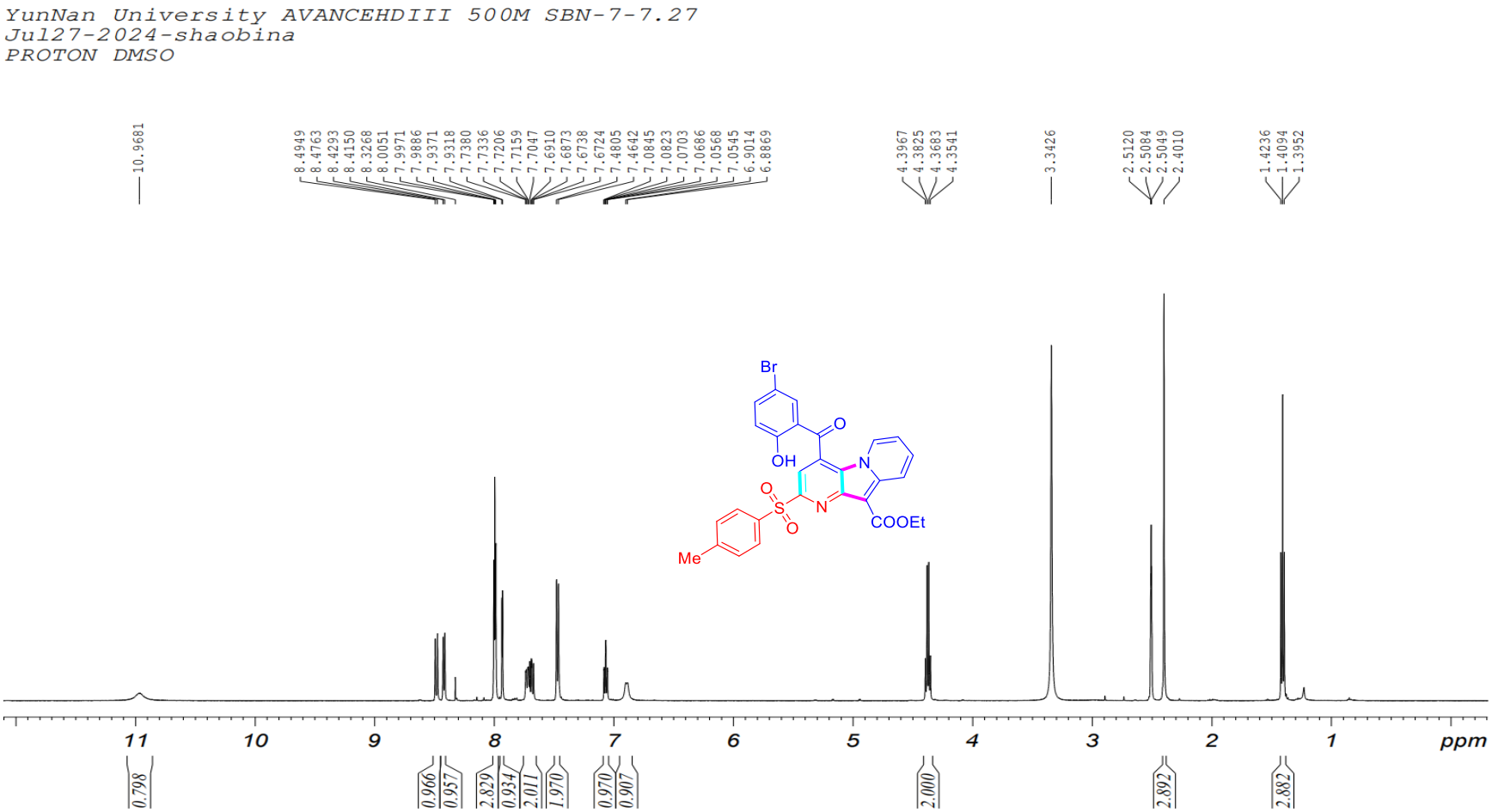


Figure S24. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3j**

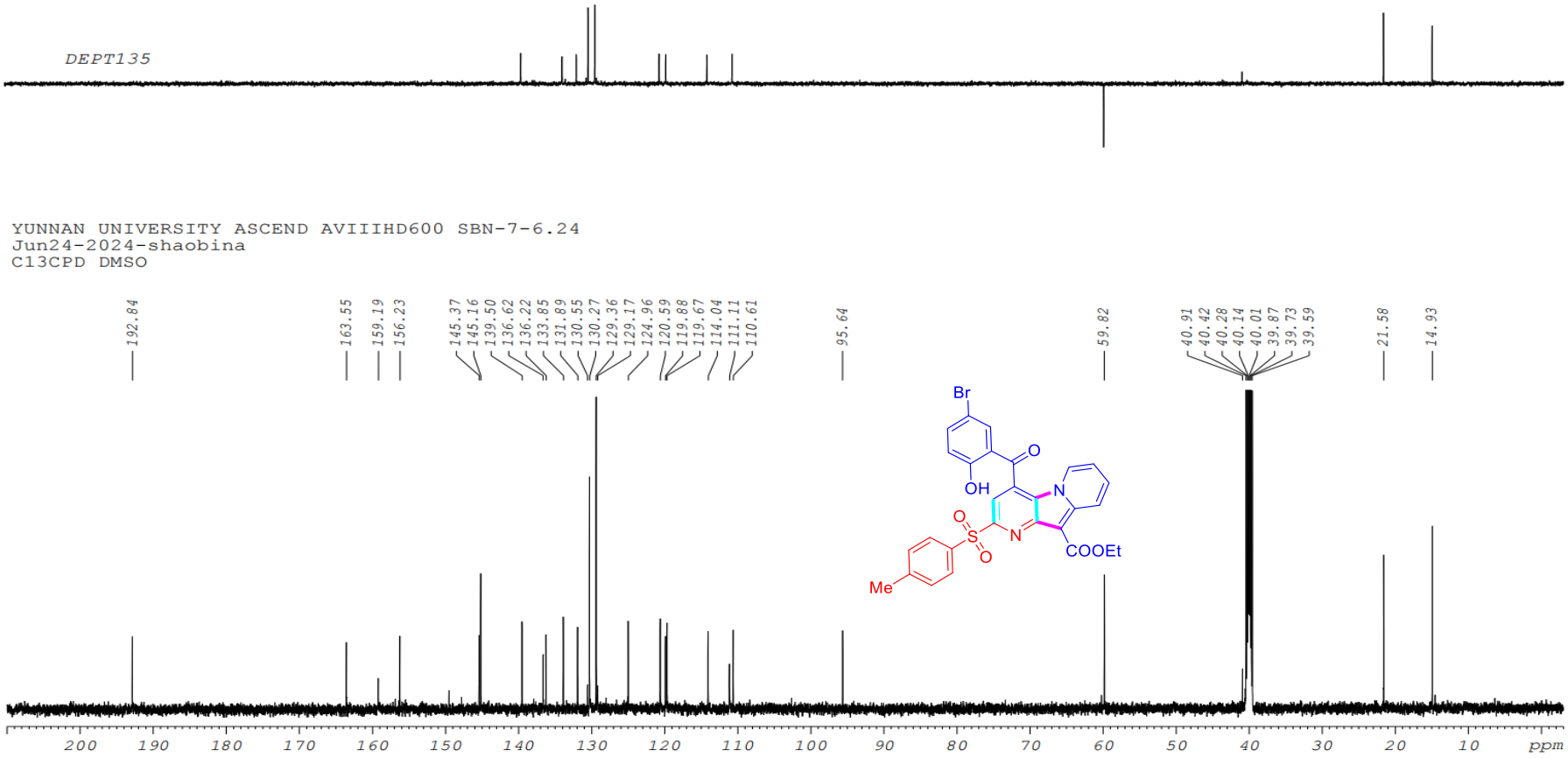


Figure S25. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3j**

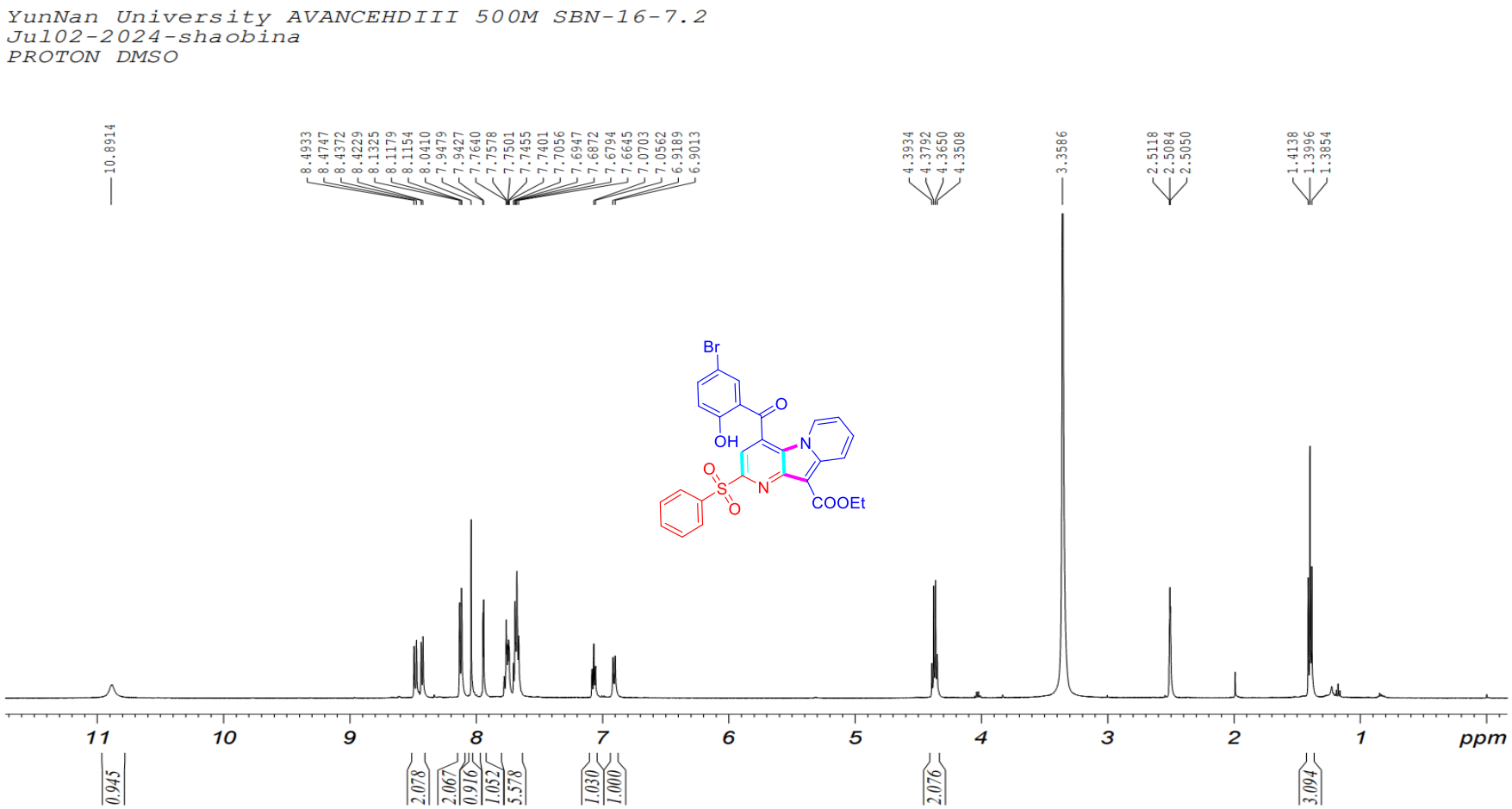


Figure S26. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3k**

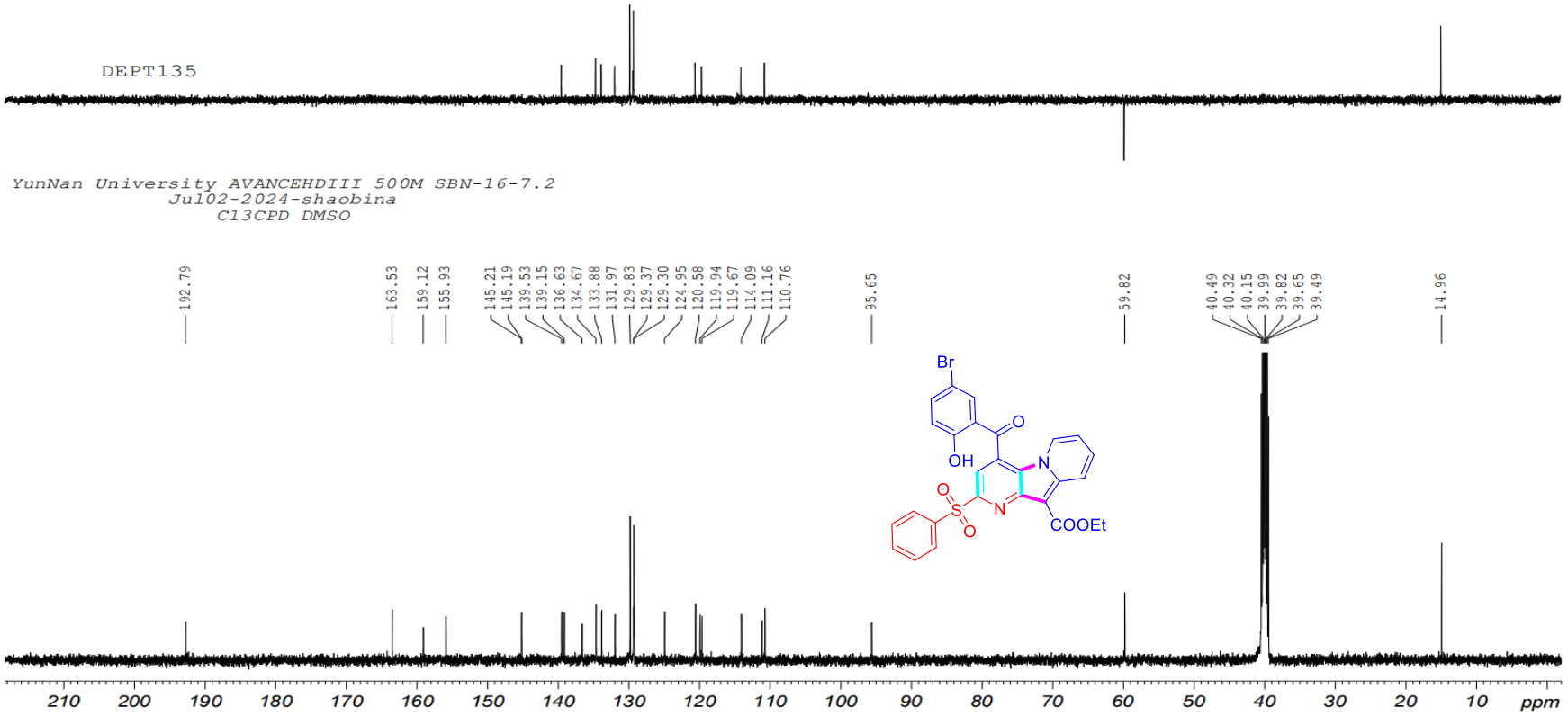


Figure S27. $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-d_6) spectra of compound **3k**

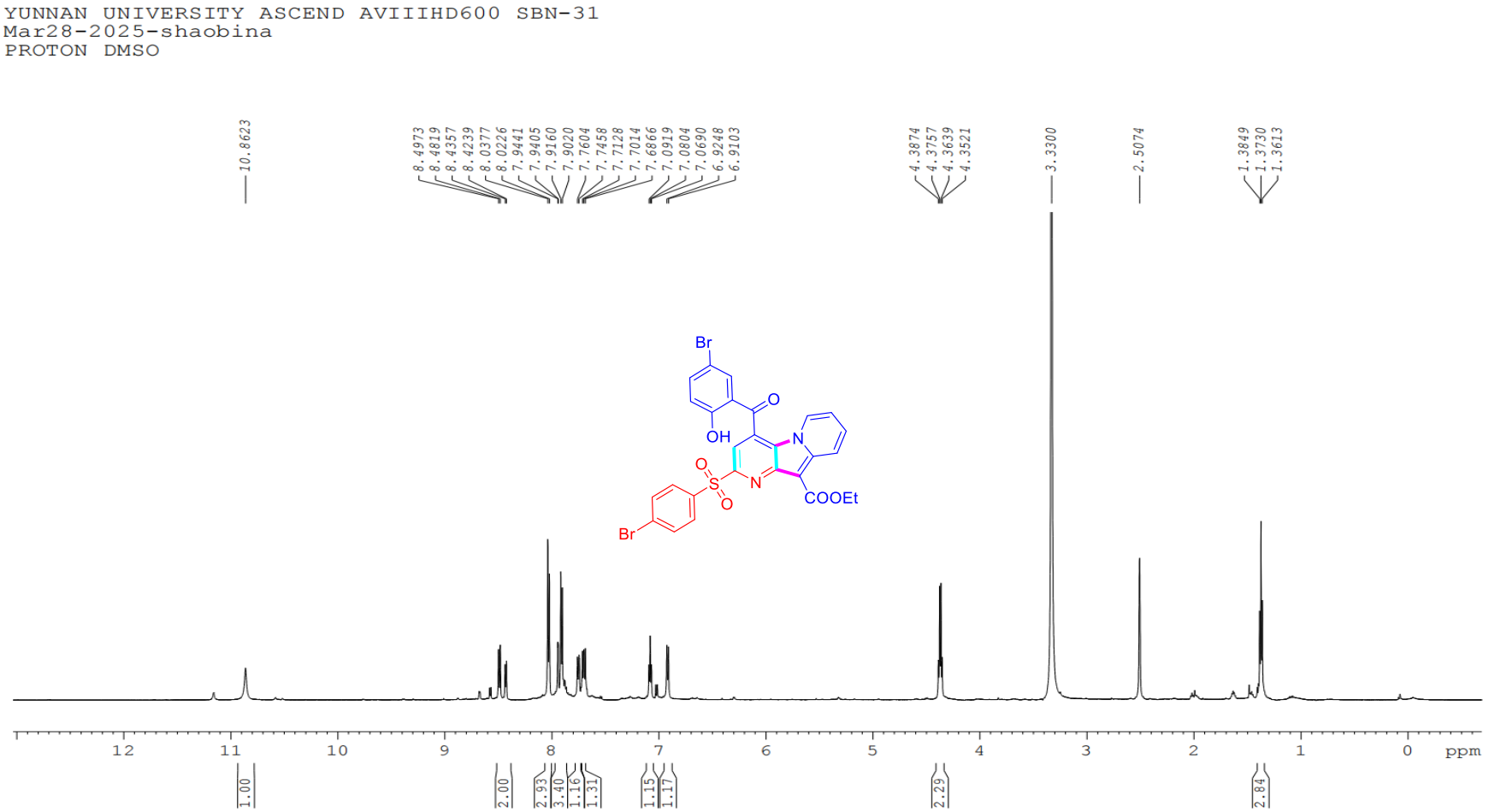


Figure S28. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3l**

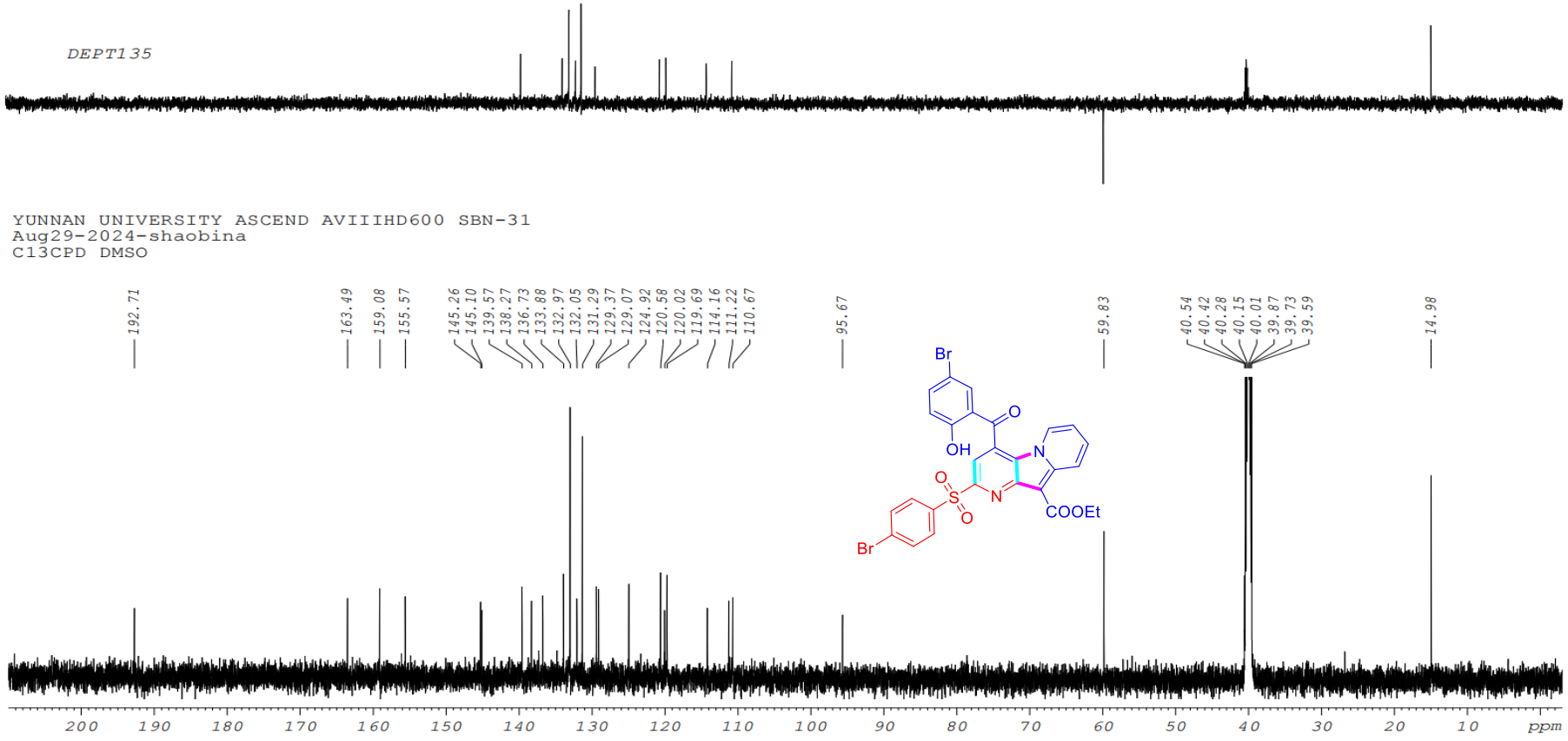


Figure S29. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3l**

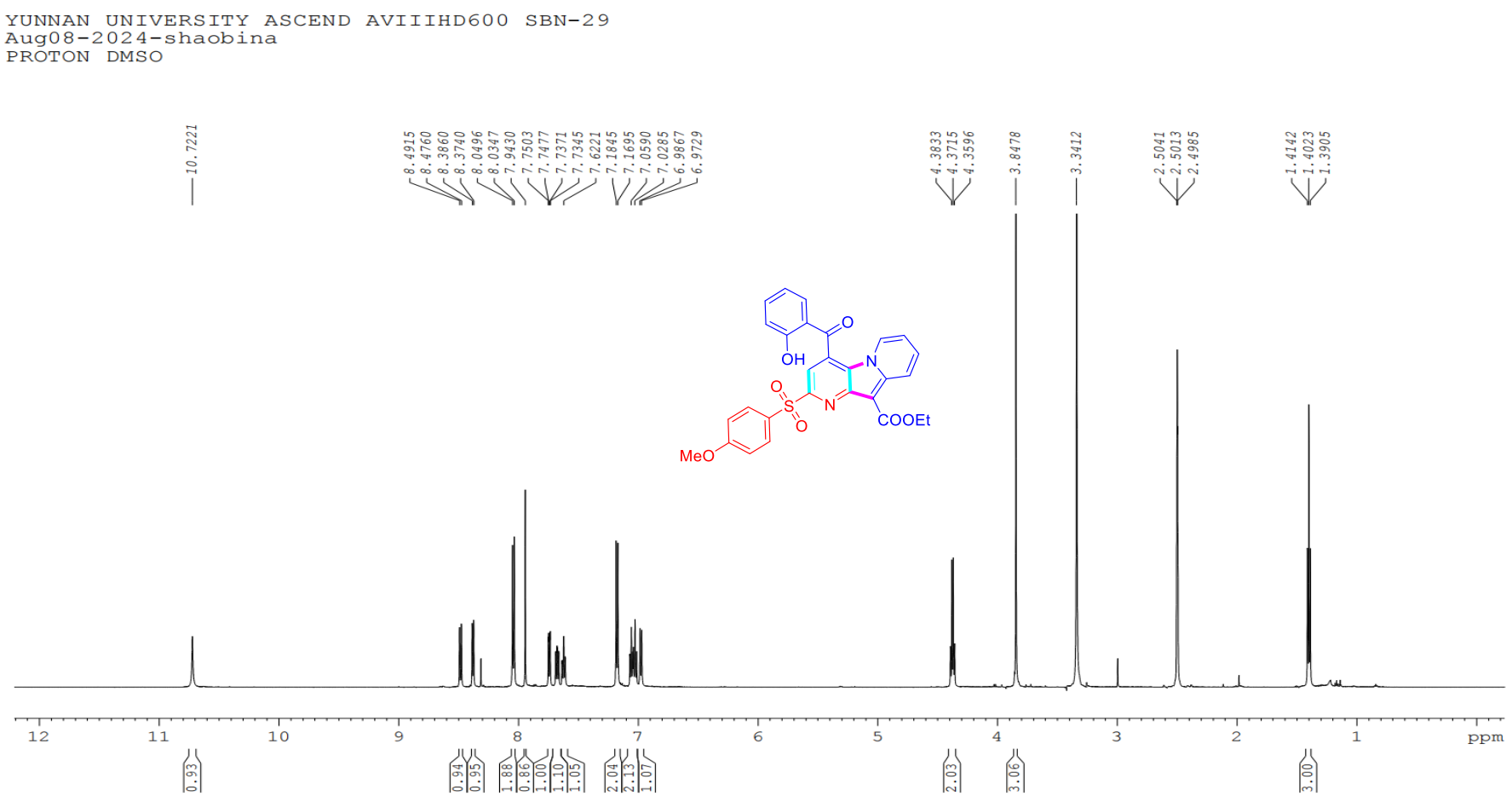


Figure S30. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3m**

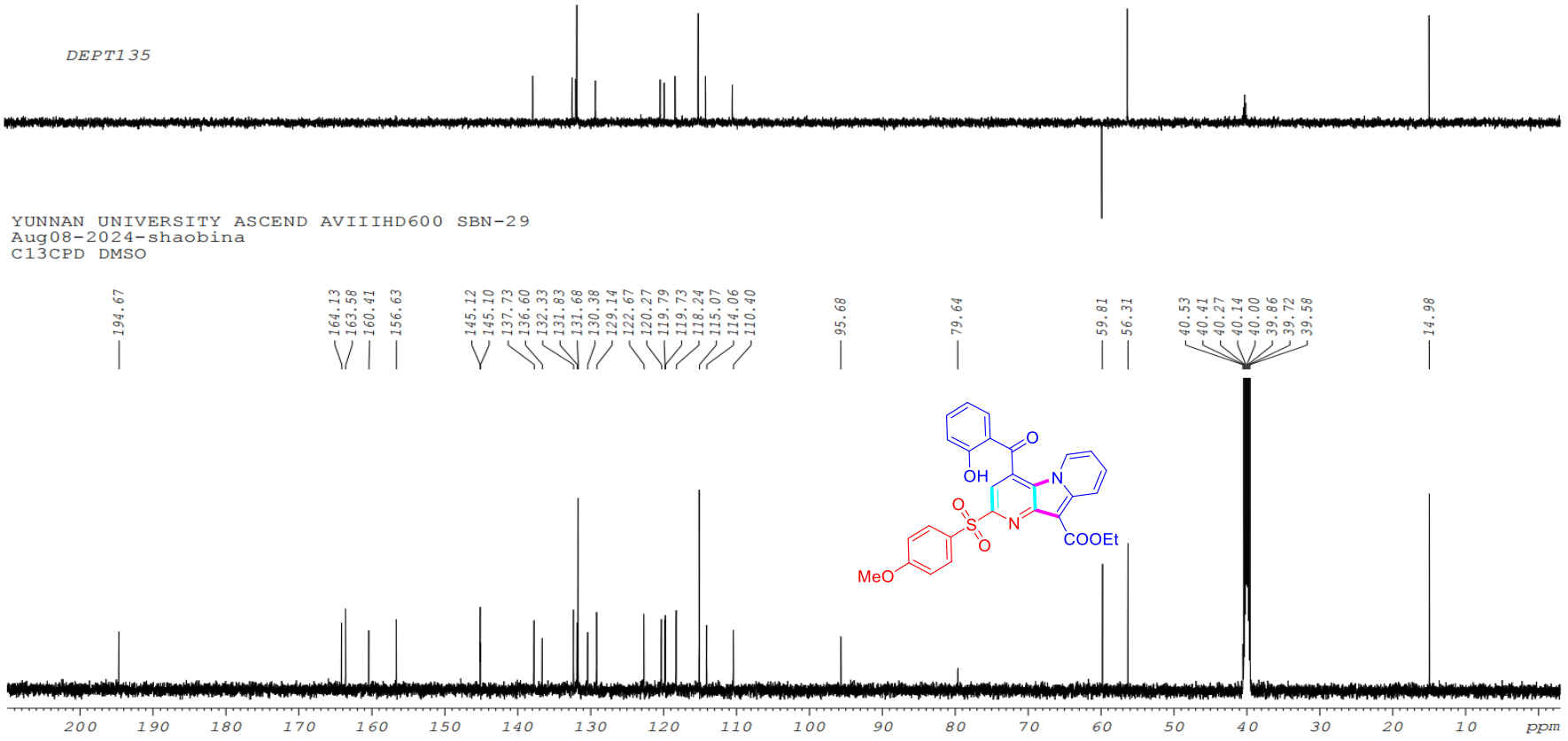


Figure S31. $^{13}C\{^{1}H\}$ NMR (150 MHz,DMSO-d_6) spectra of compound **3m**

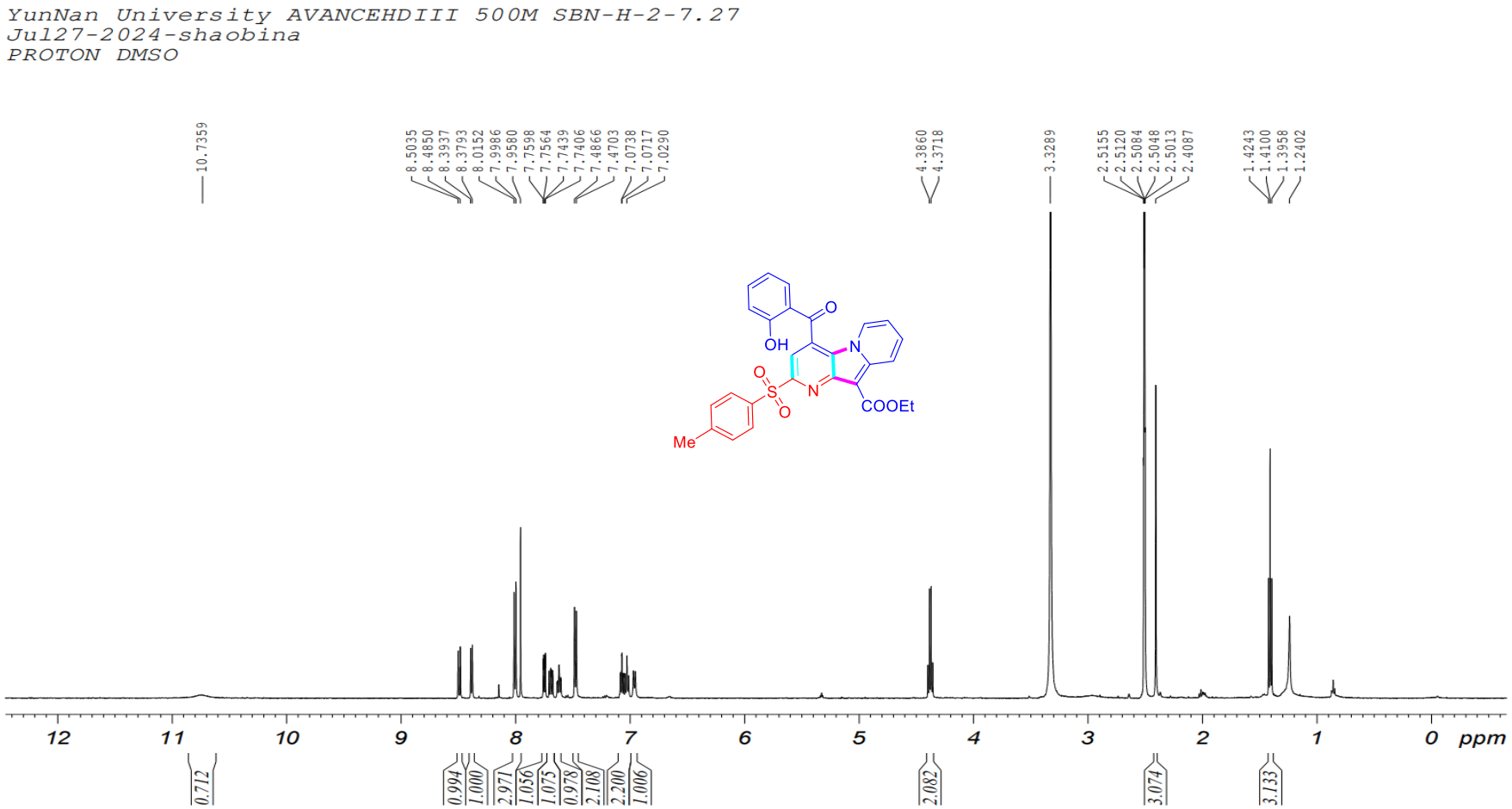


Figure S32. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3n**

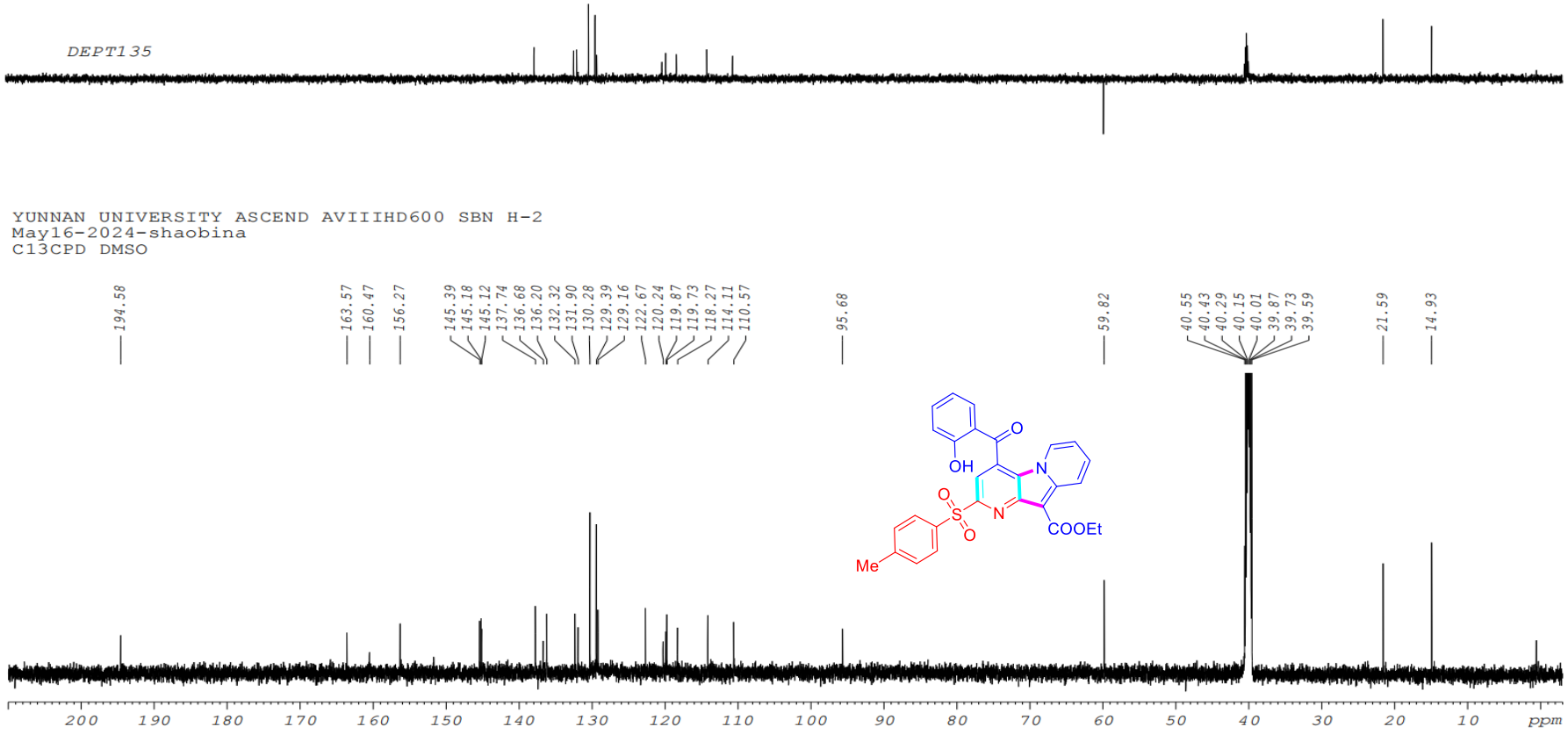


Figure S33. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3n**

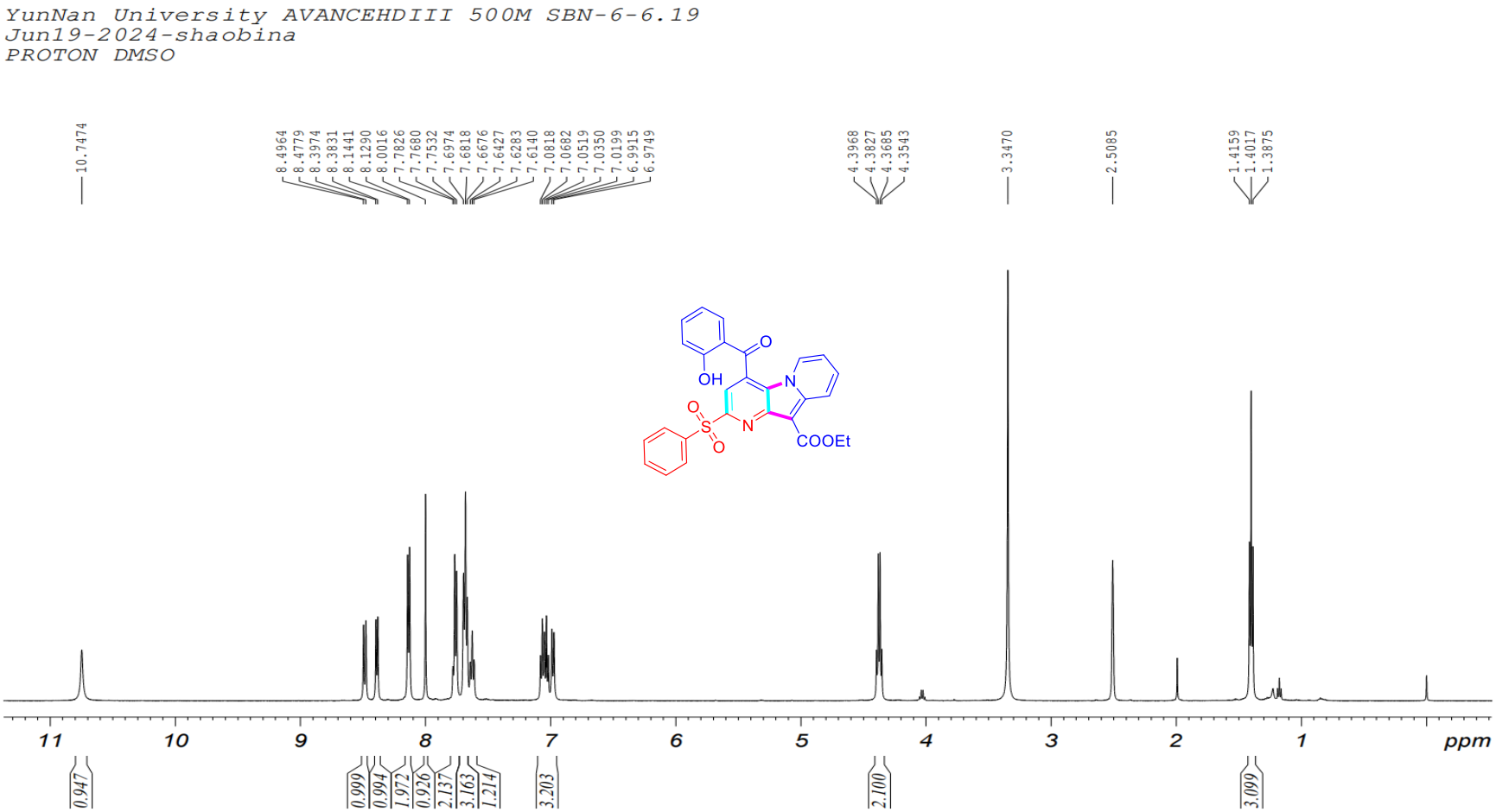


Figure S34. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3o**

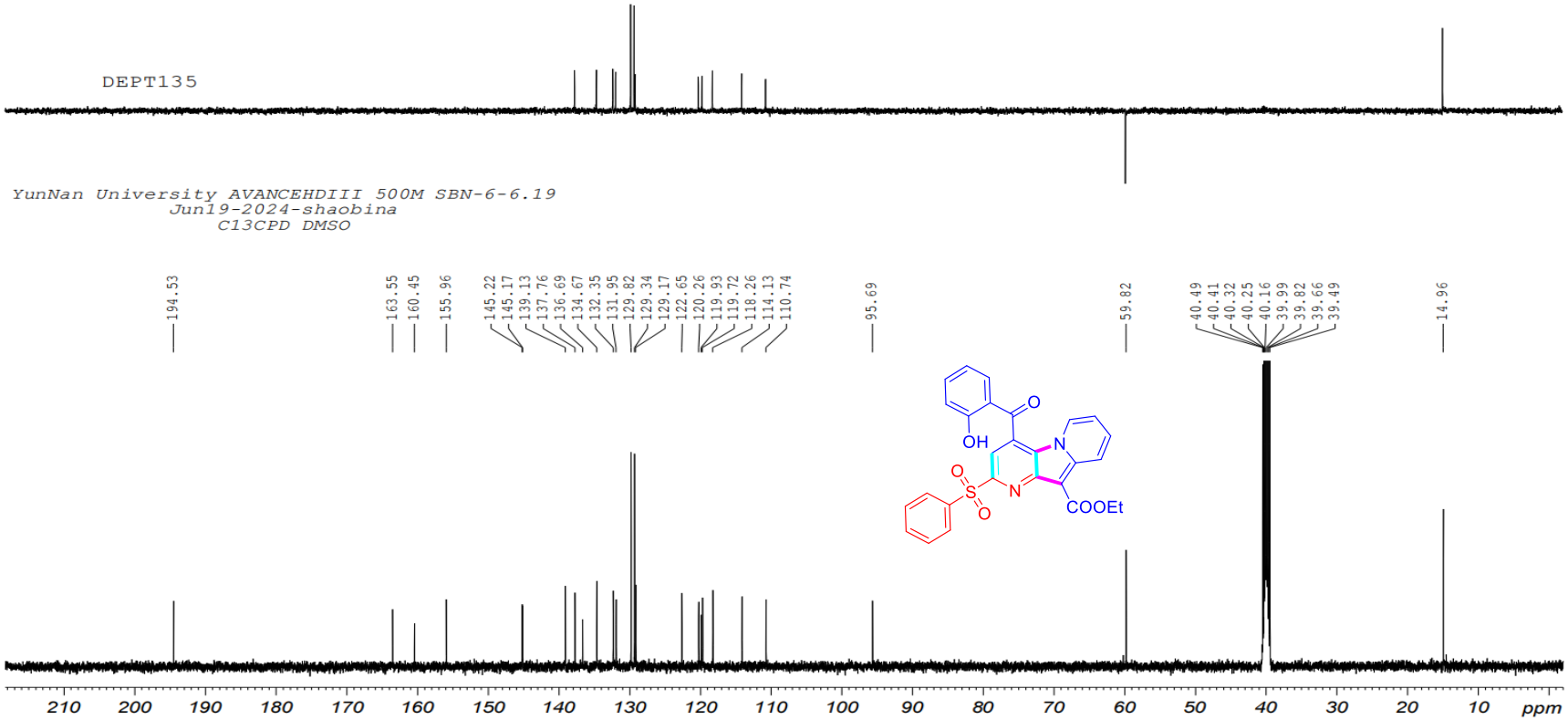


Figure S35. $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-d_6) spectra of compound **3o**

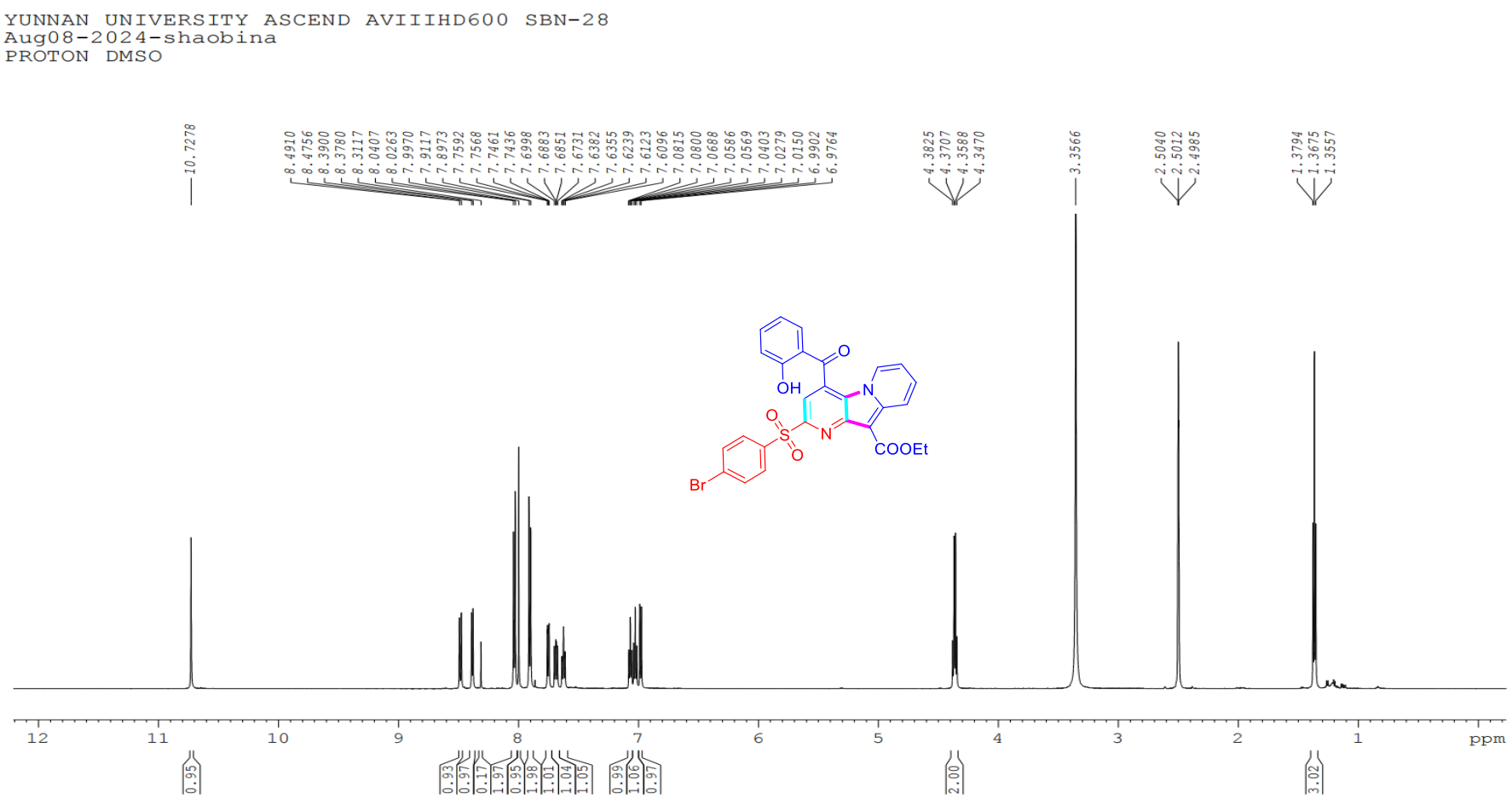


Figure S36. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3p**

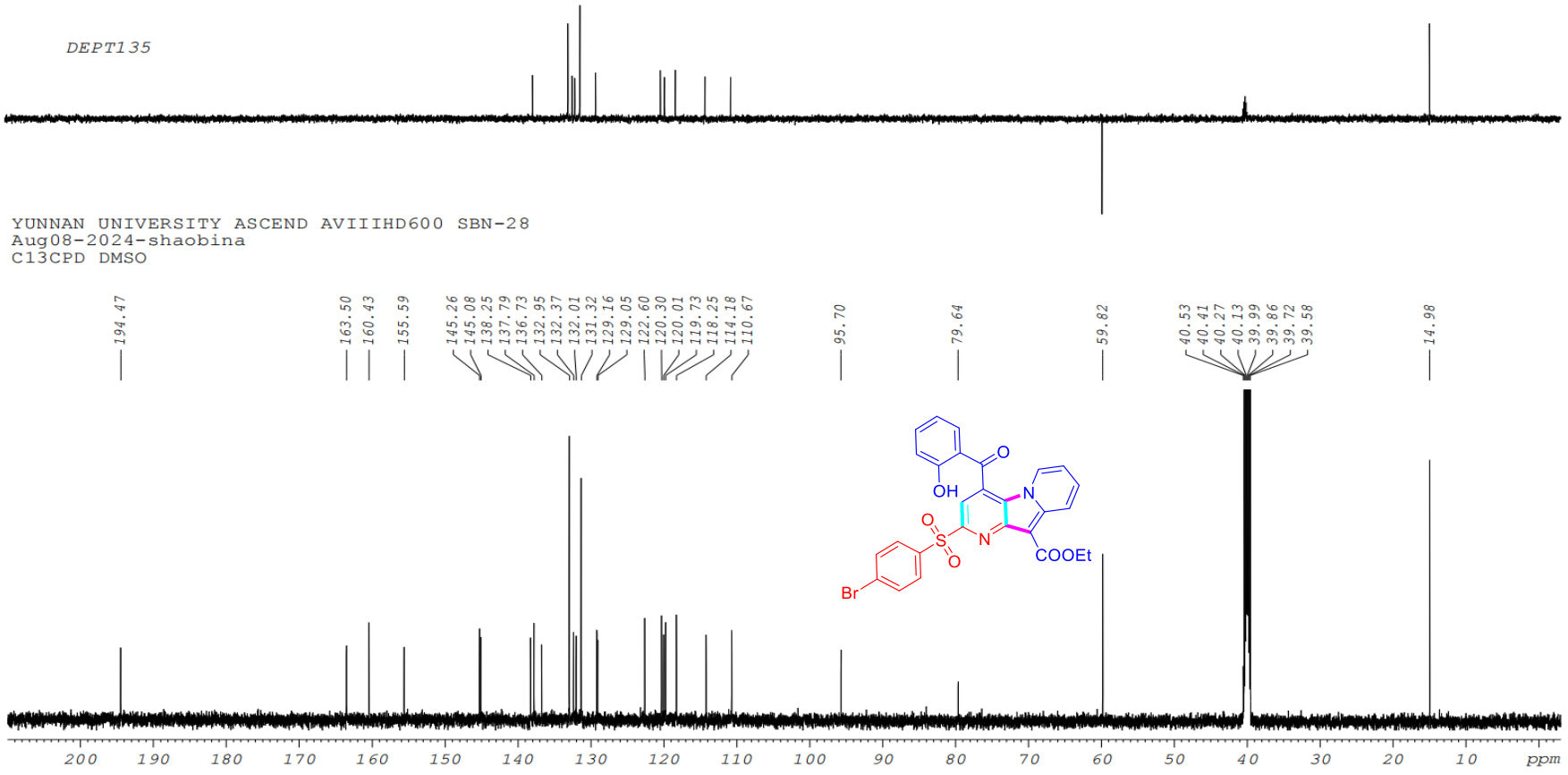


Figure S37. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3p**

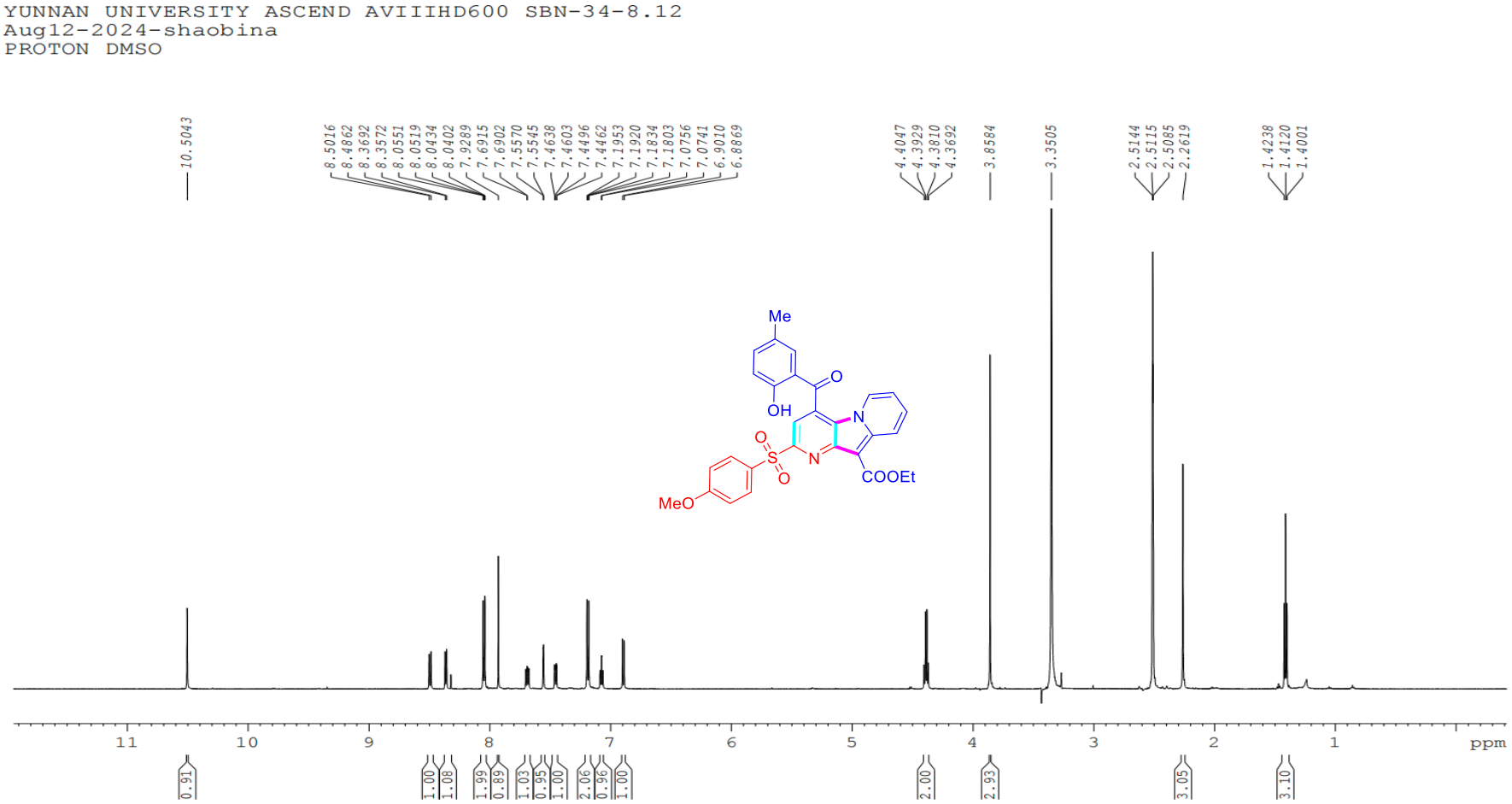


Figure S38. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3q**

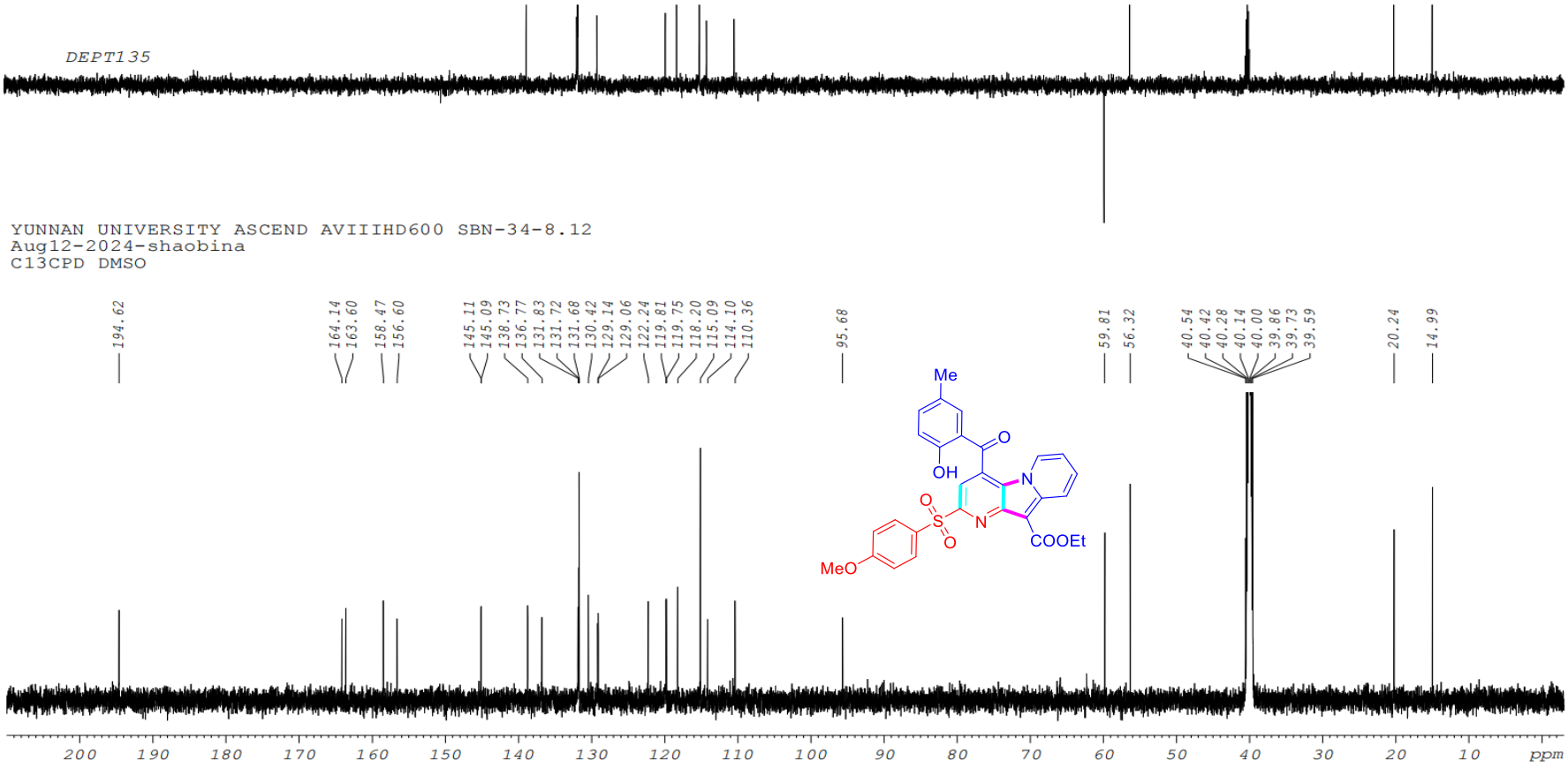


Figure S39. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3q**

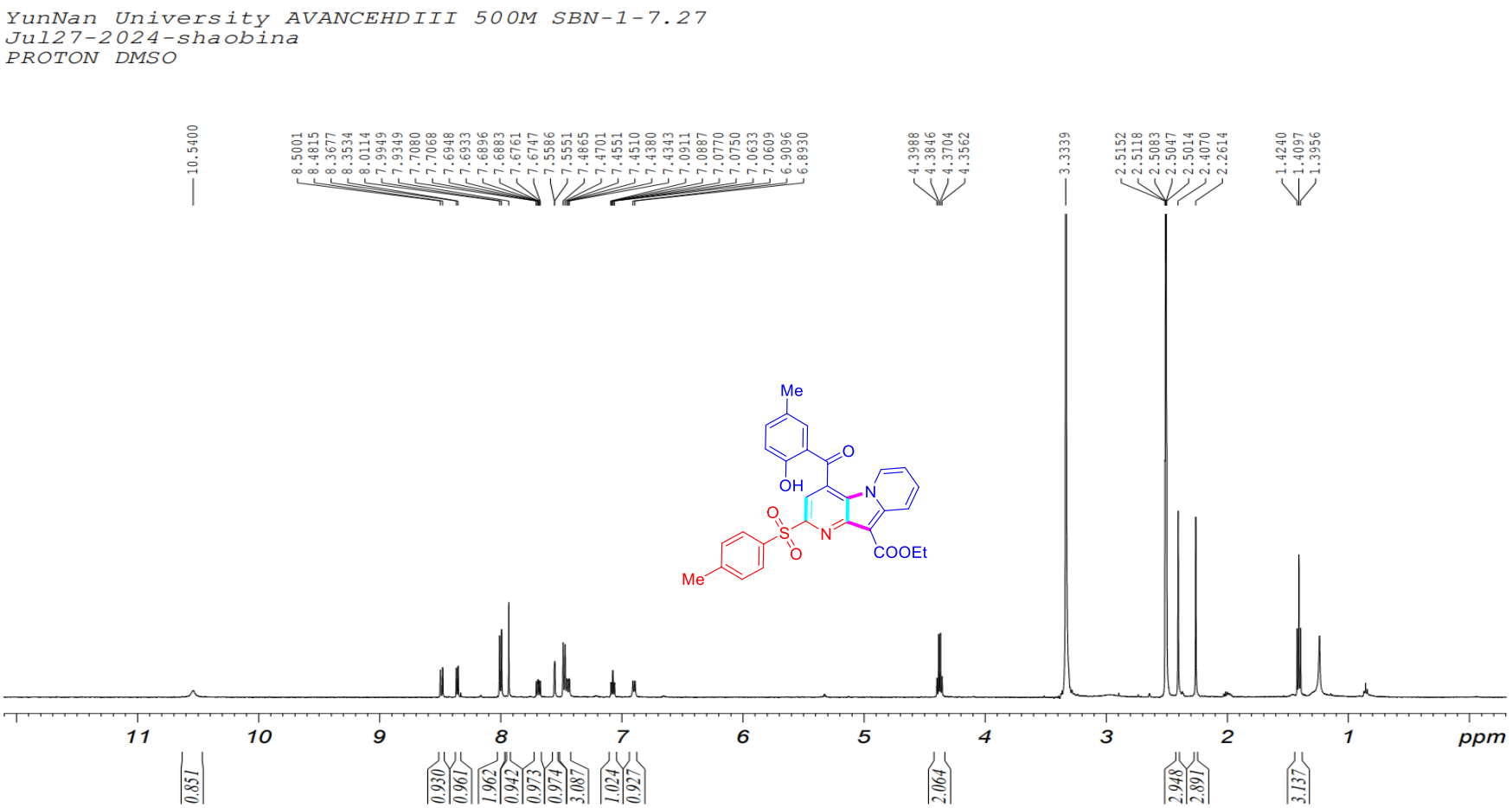


Figure S40. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3r**

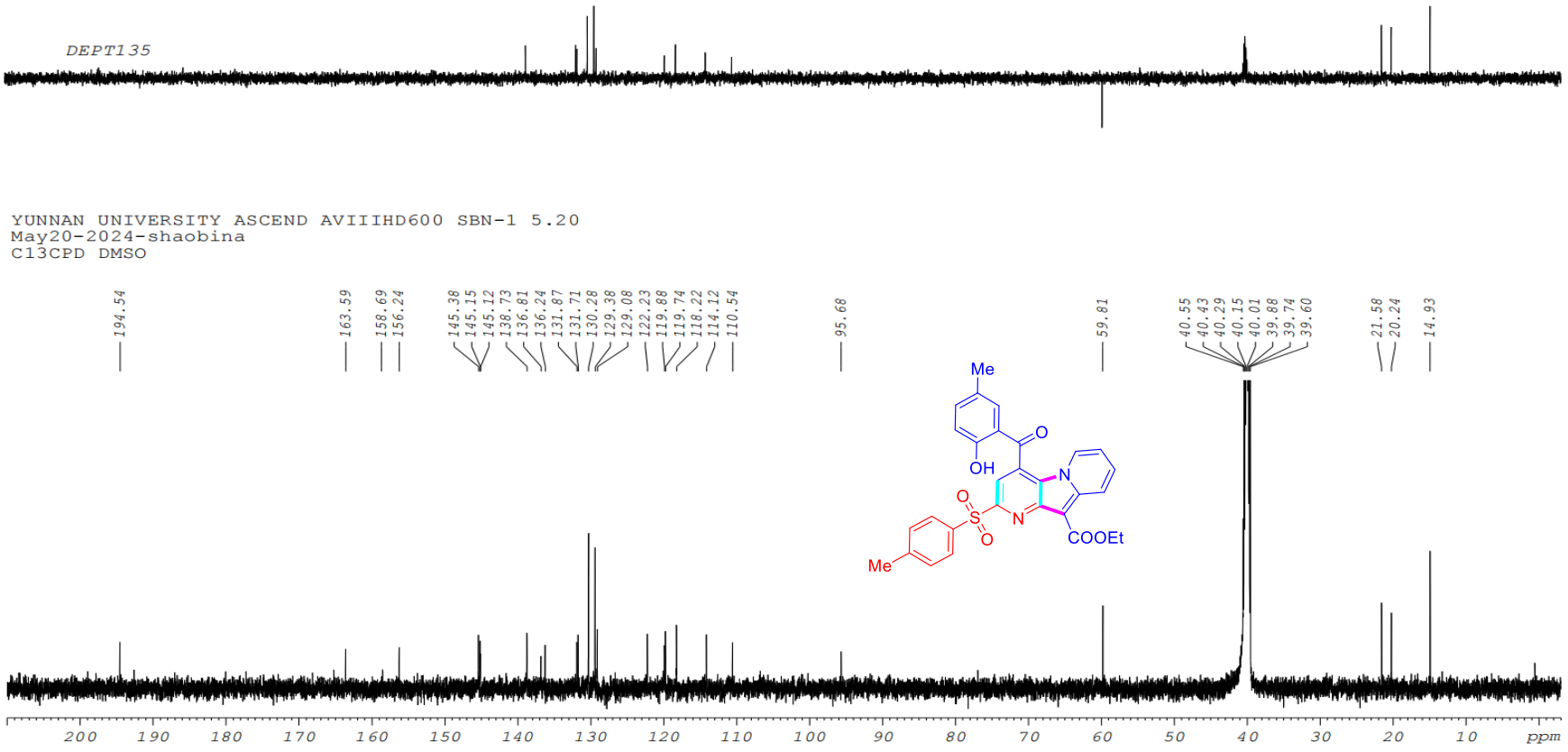


Figure S41. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3r**

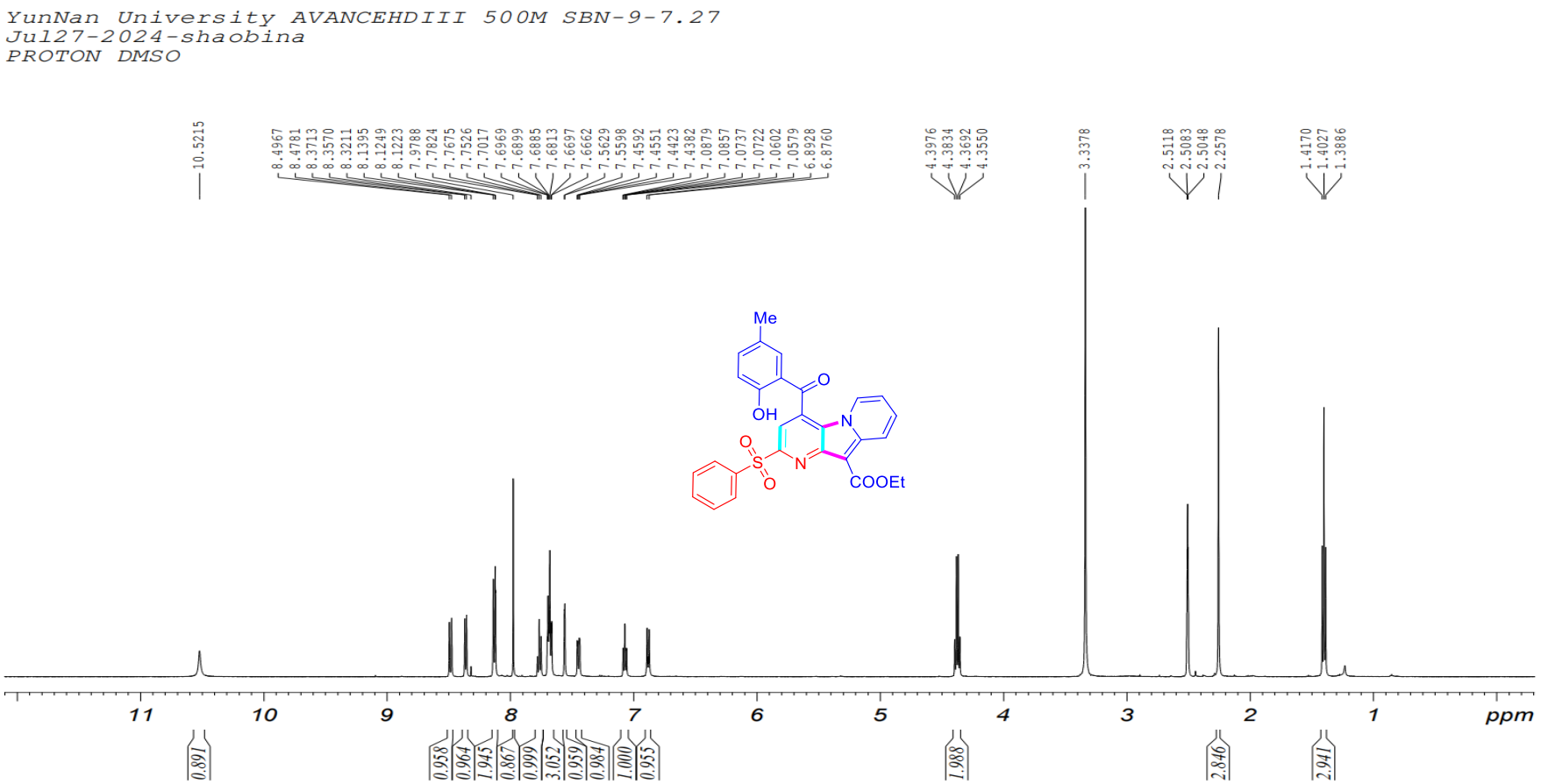


Figure S42. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3s**

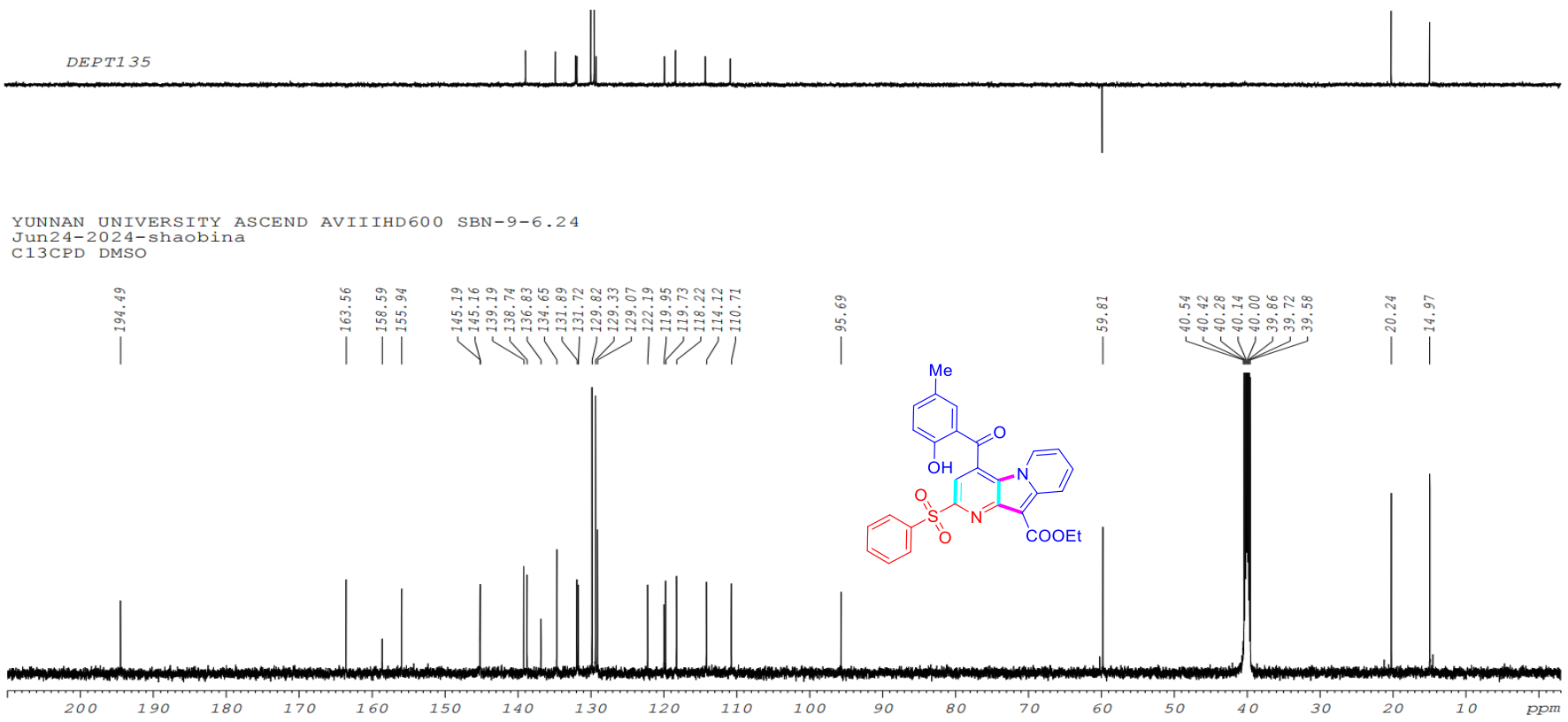


Figure S43. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3s**

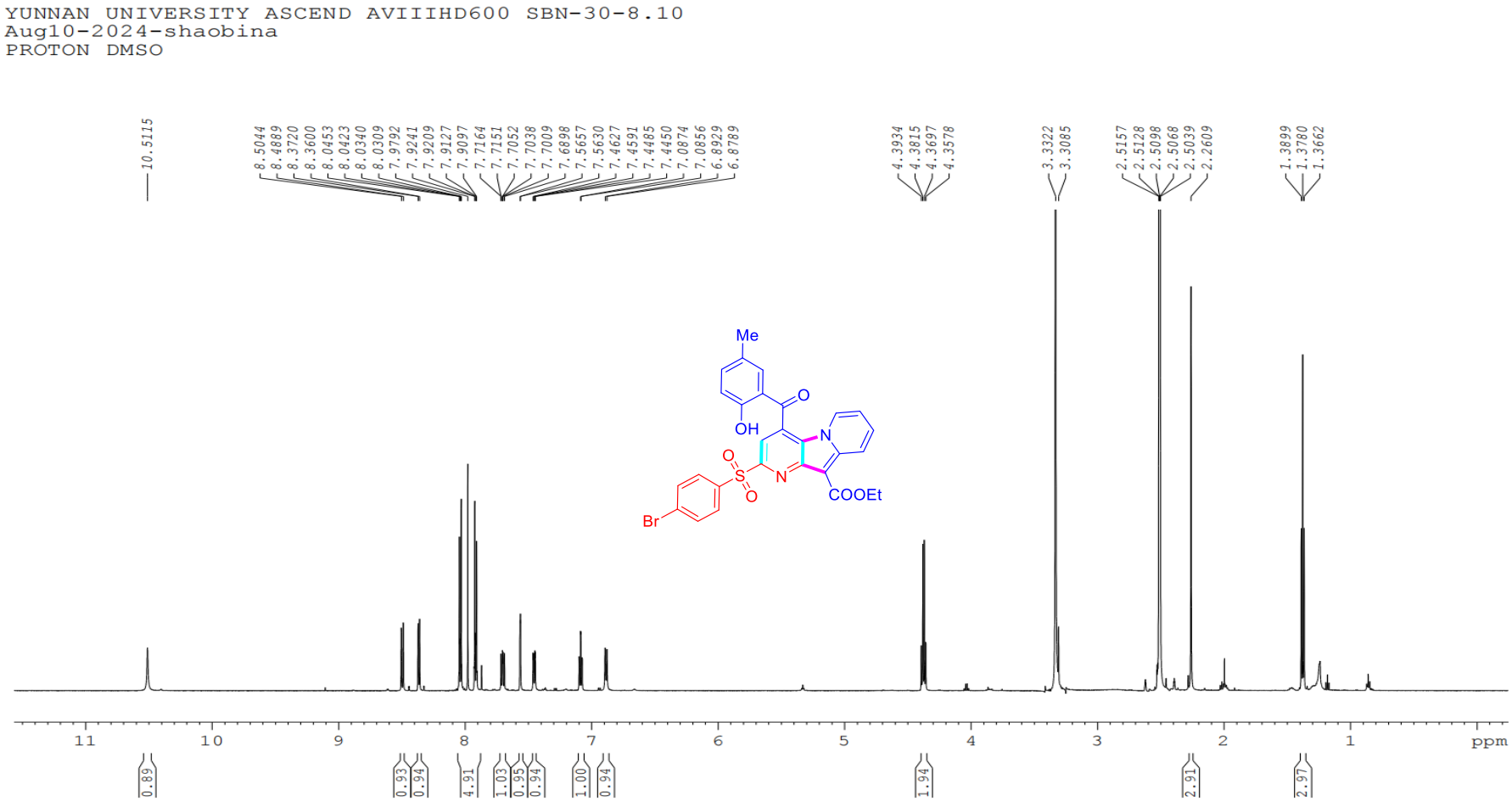


Figure S44. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3t**

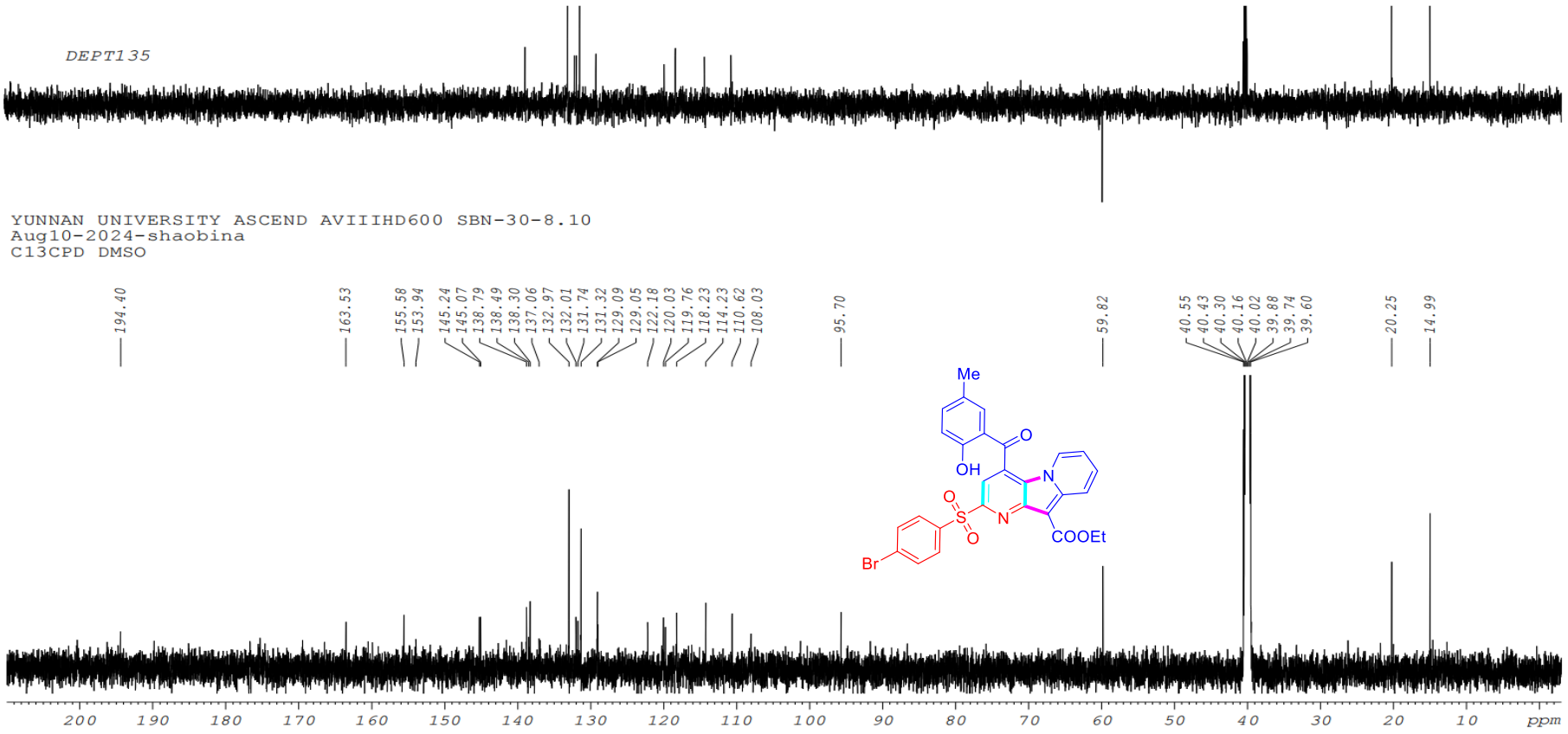


Figure S45. $^{13}C\{^{1}H\}$ NMR (150 MHz,DMSO-d_6) spectra of compound **3t**

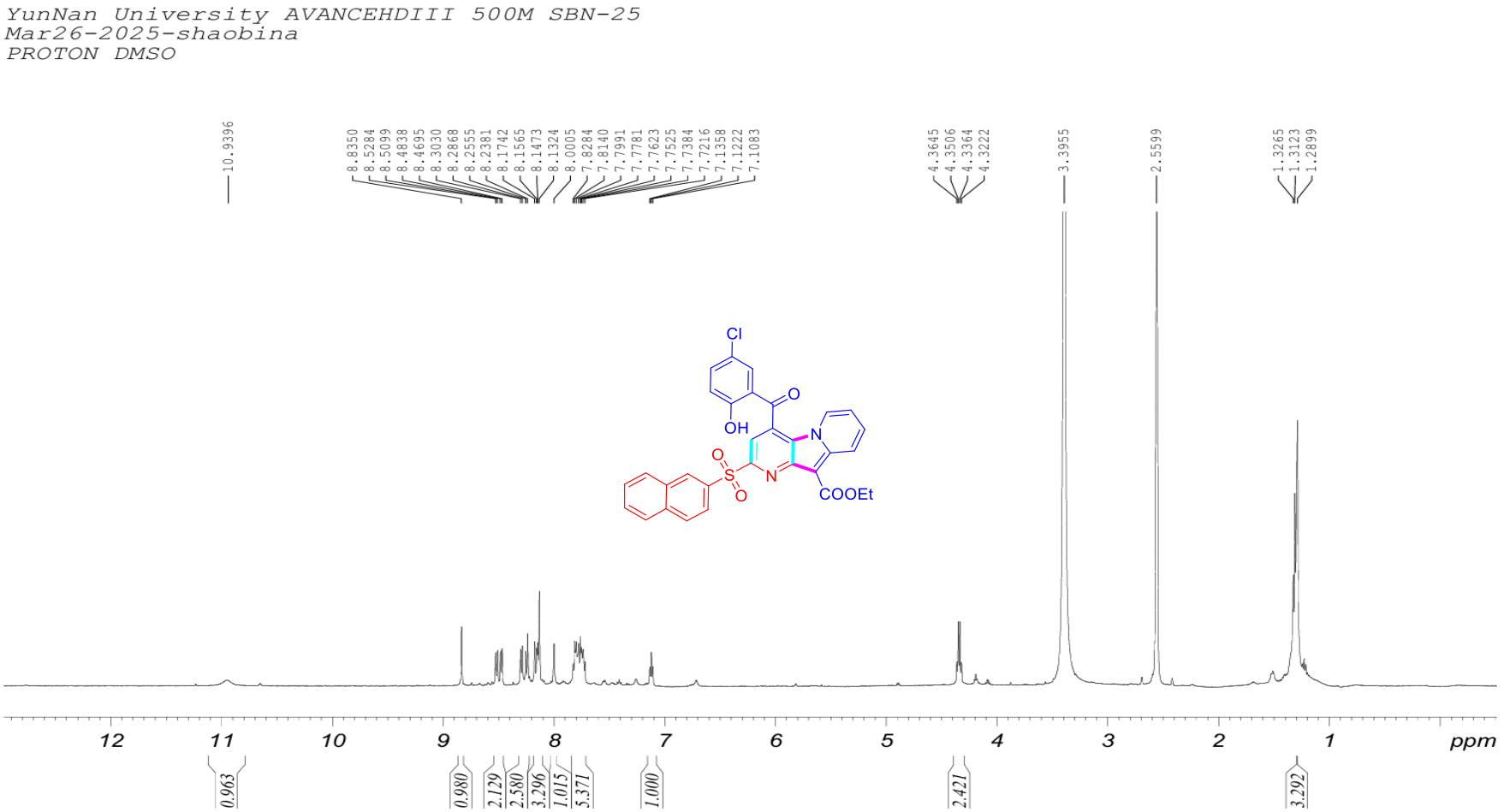


Figure S46. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3u**

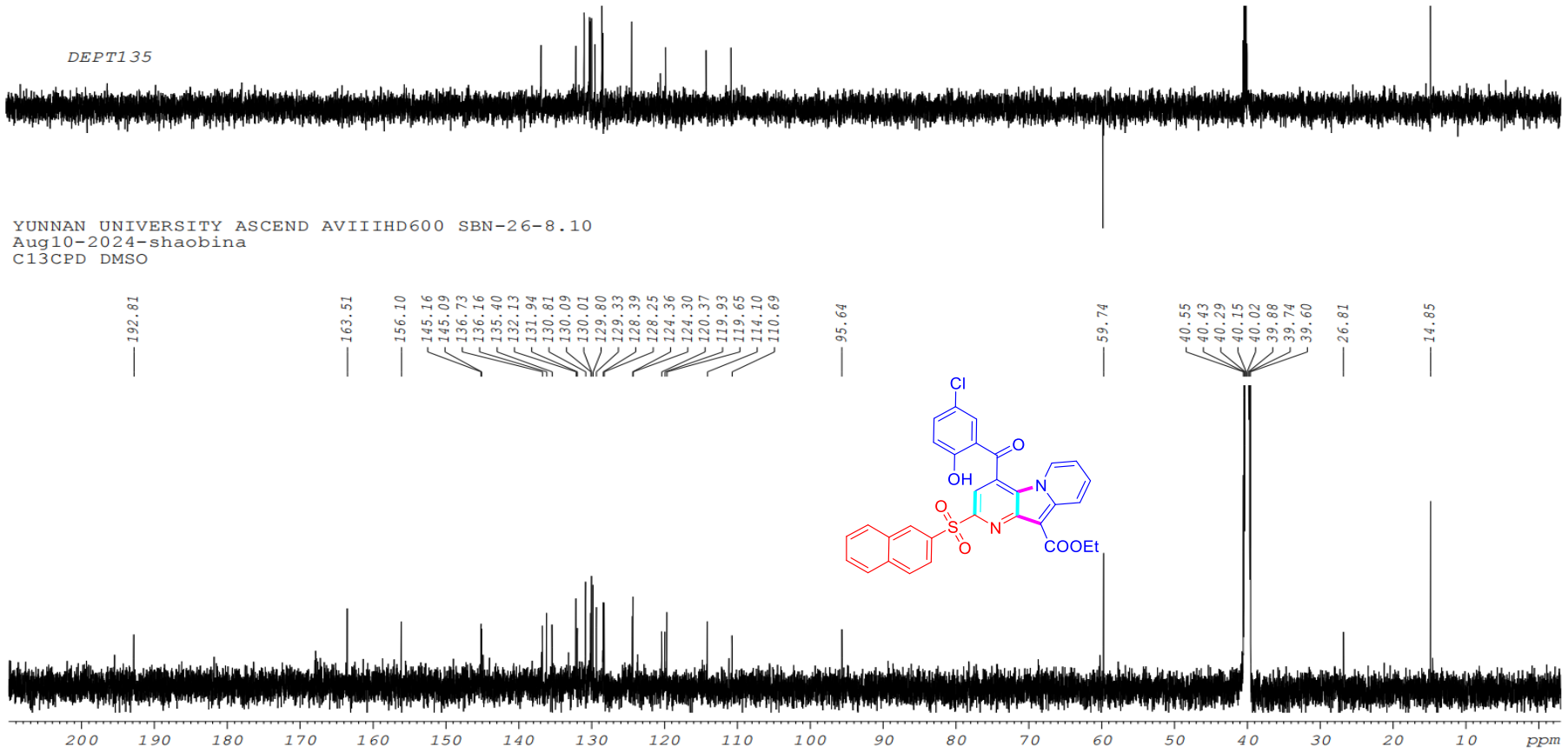


Figure S47. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3u**

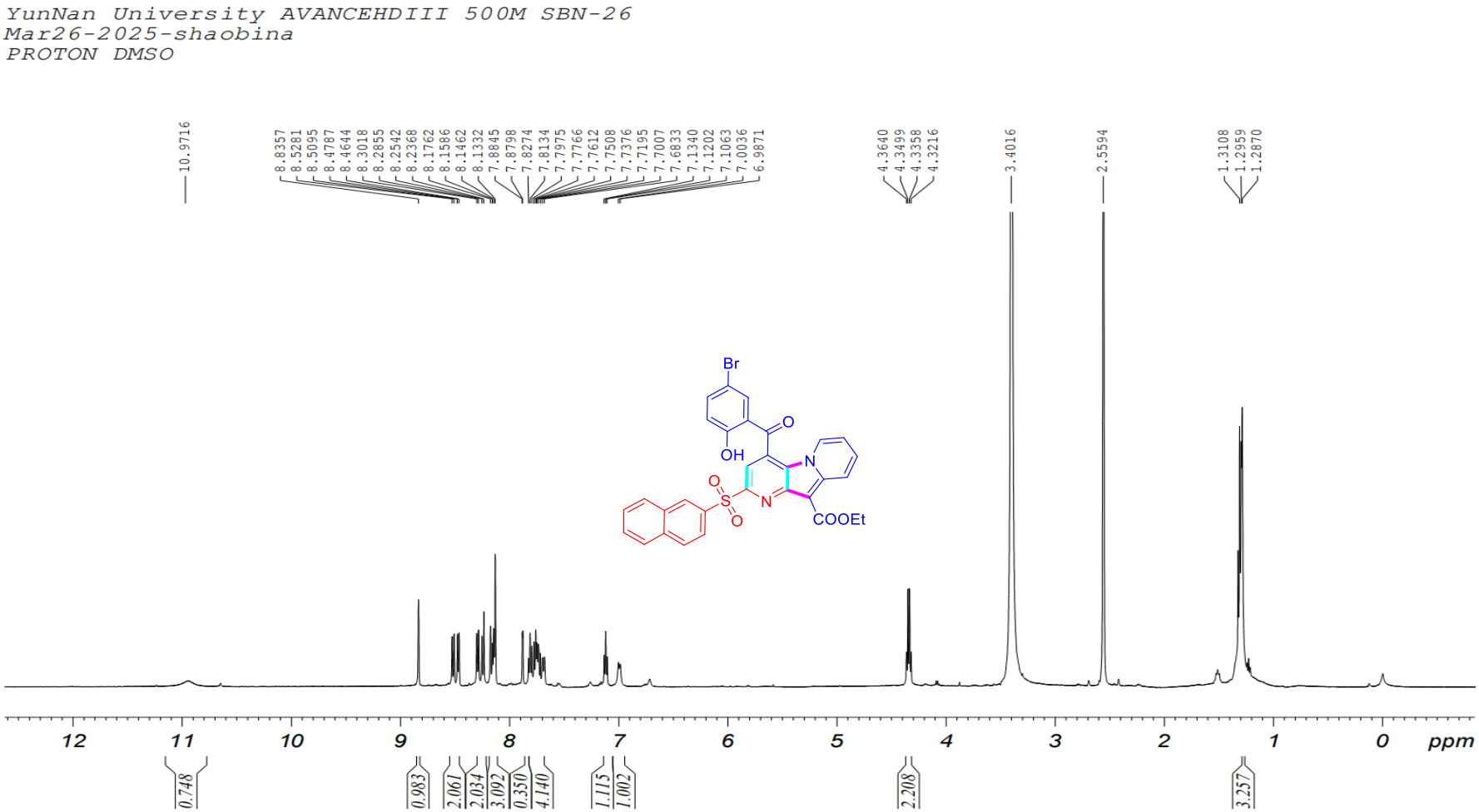


Figure S48. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3v**

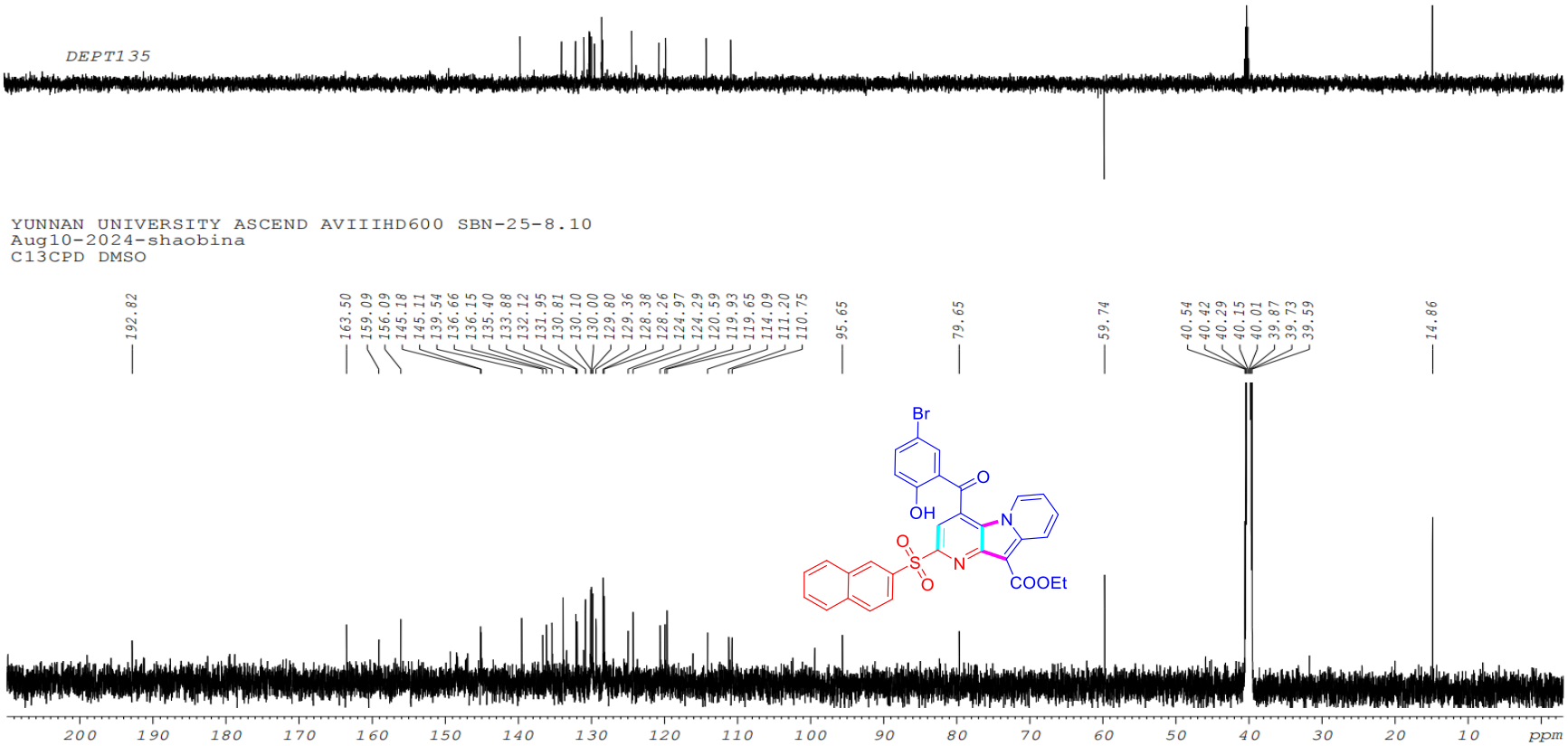


Figure S49. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3v**

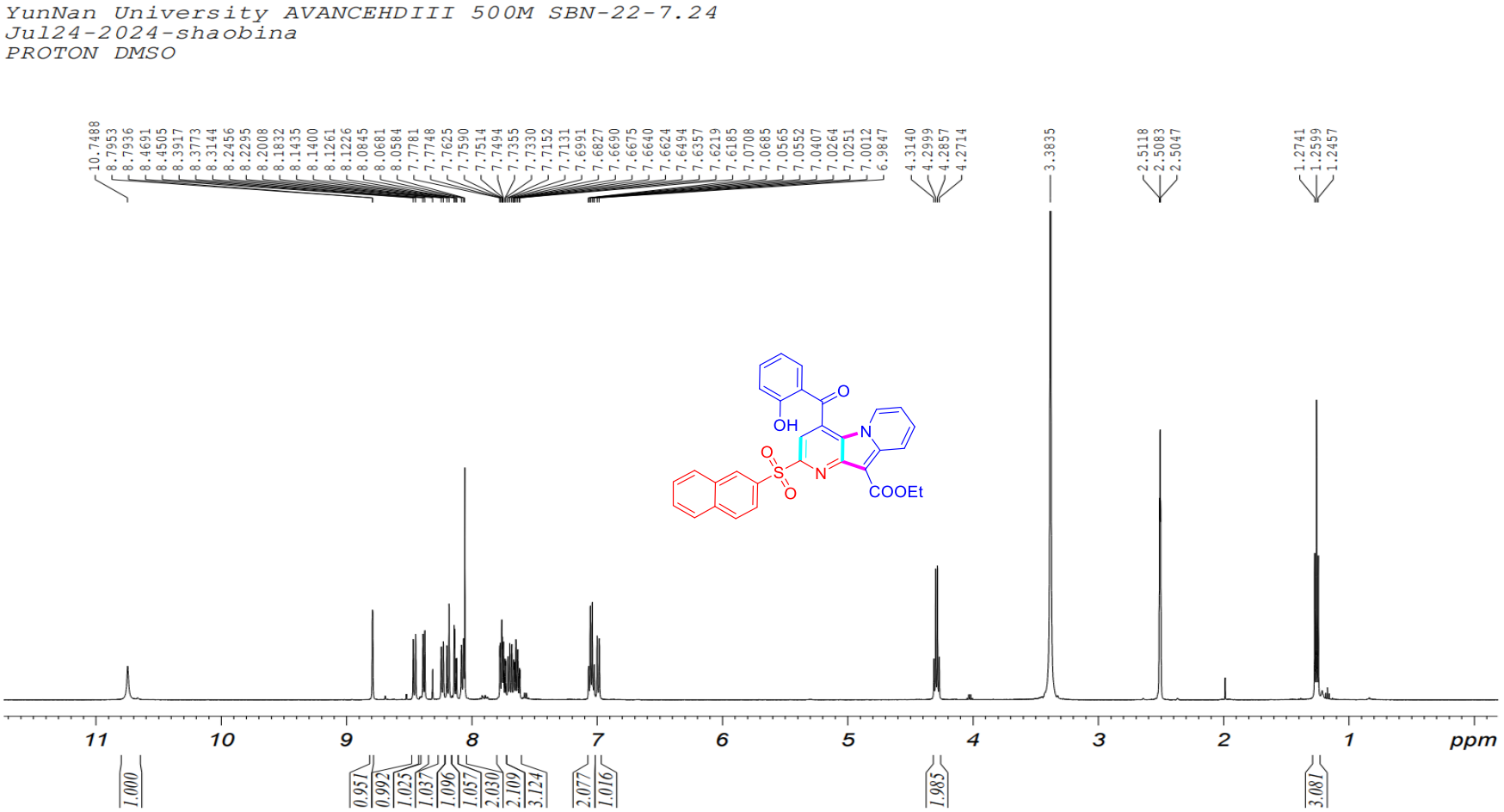


Figure S50. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3w**

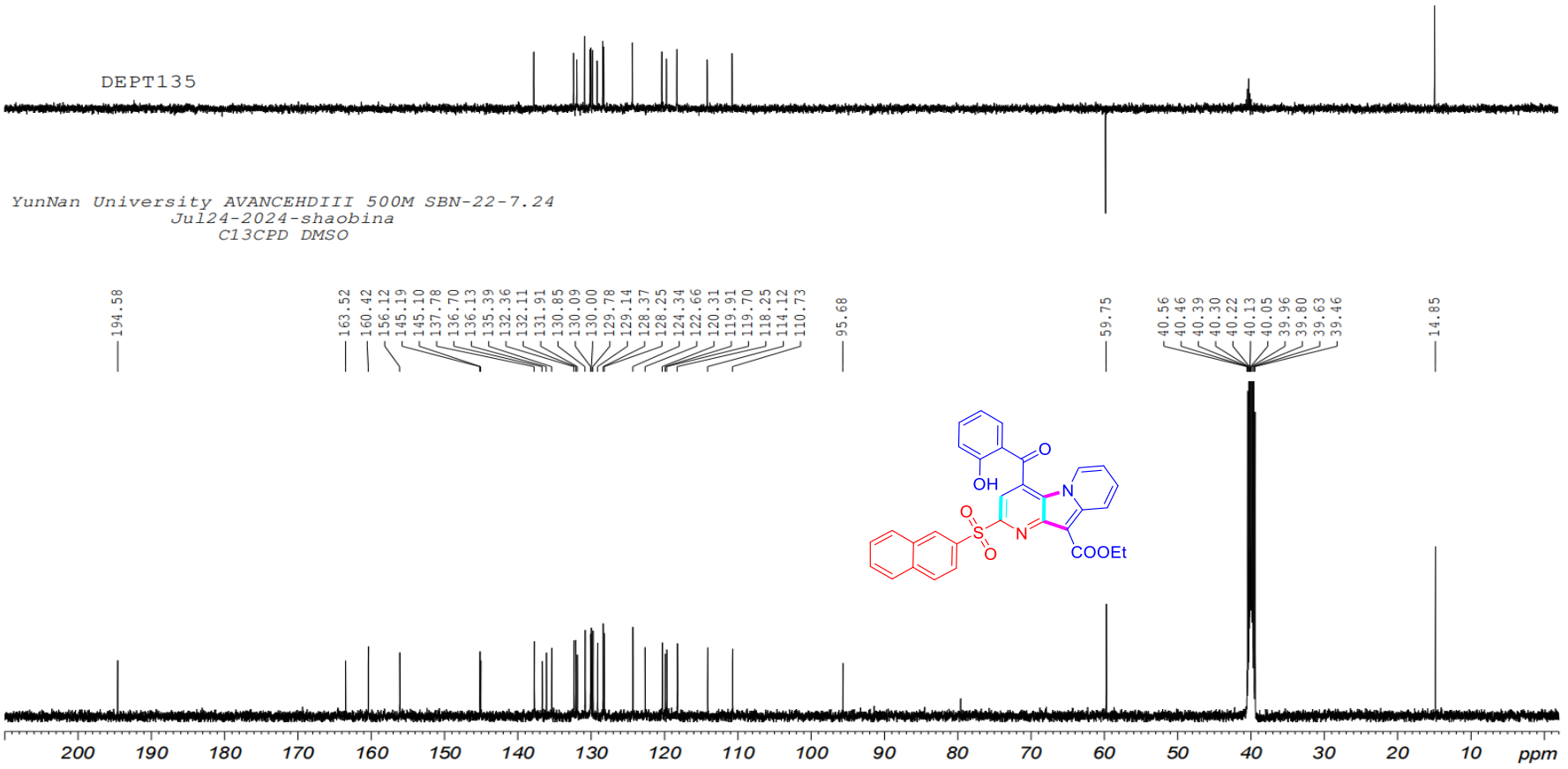


Figure S51. $^{13}C\{^{1}H\}$ NMR (125 MHz, DMSO-d_6) spectra of compound **3w**

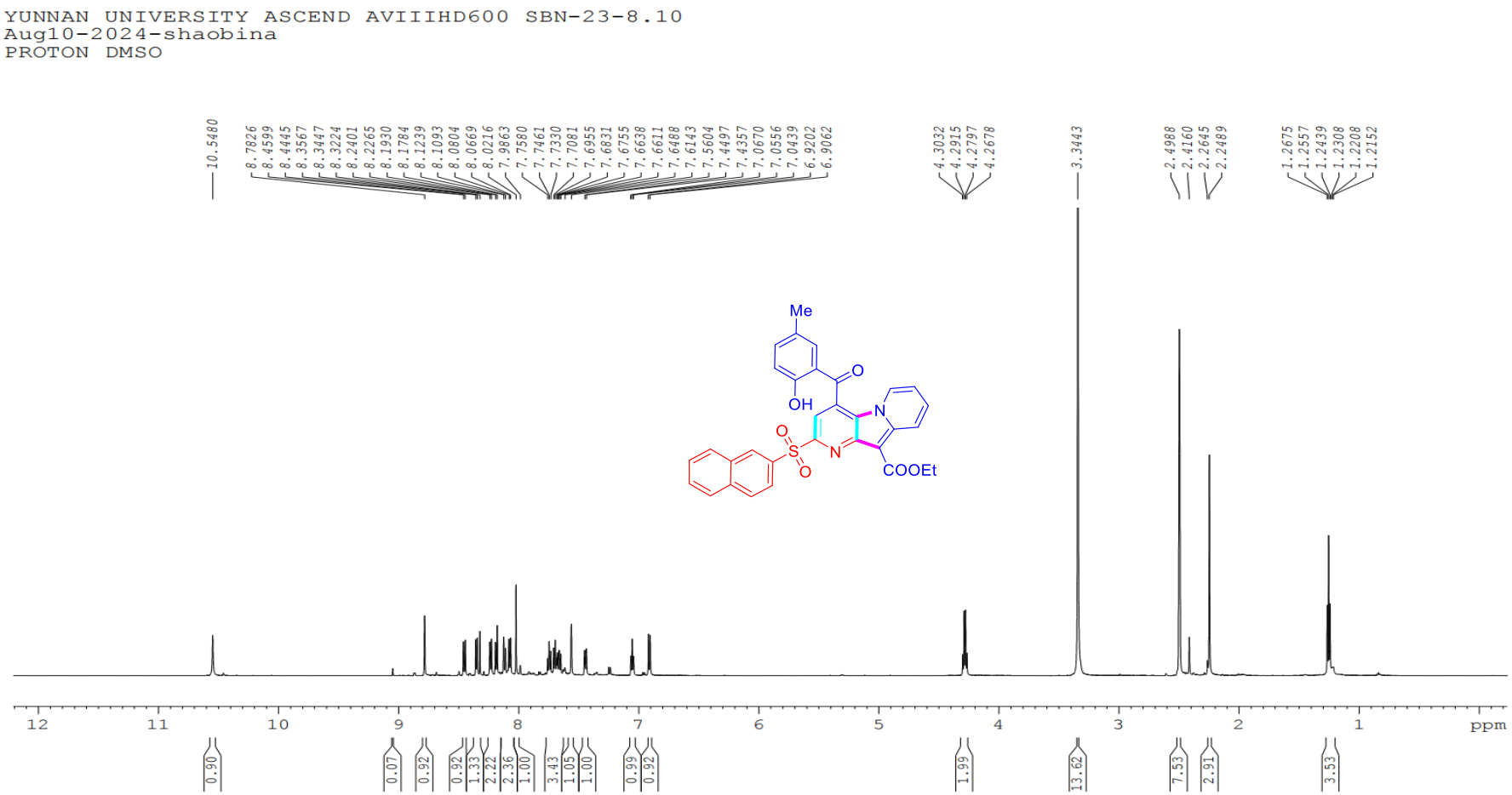


Figure S52. ^{1}H NMR (600 MHz, DMSO-d_6 spectra of compound **3x**

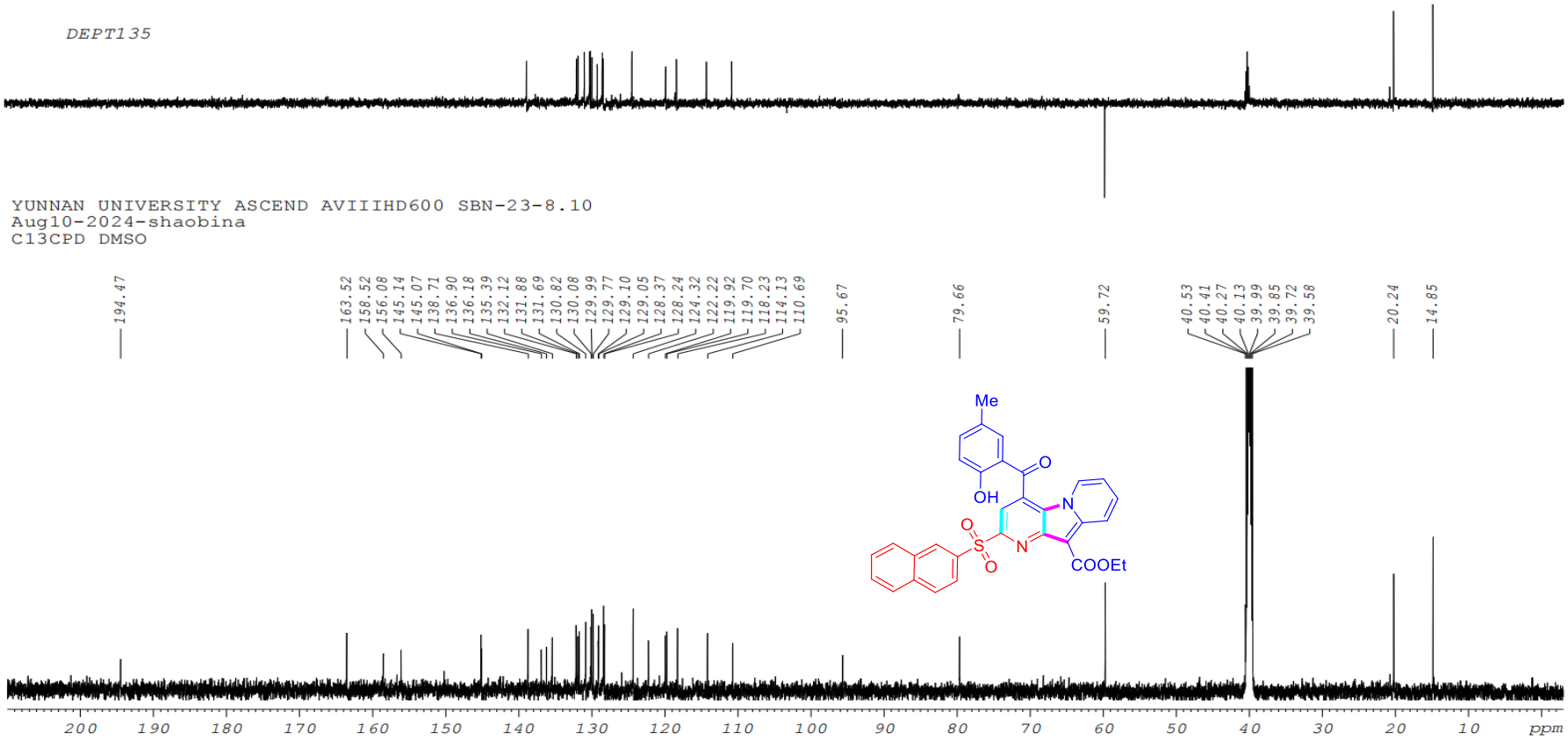


Figure S53. $^{13}C\{^{1}H\}$ NMR (150 MHz, DMSO-d_6) spectra of compound **3x**

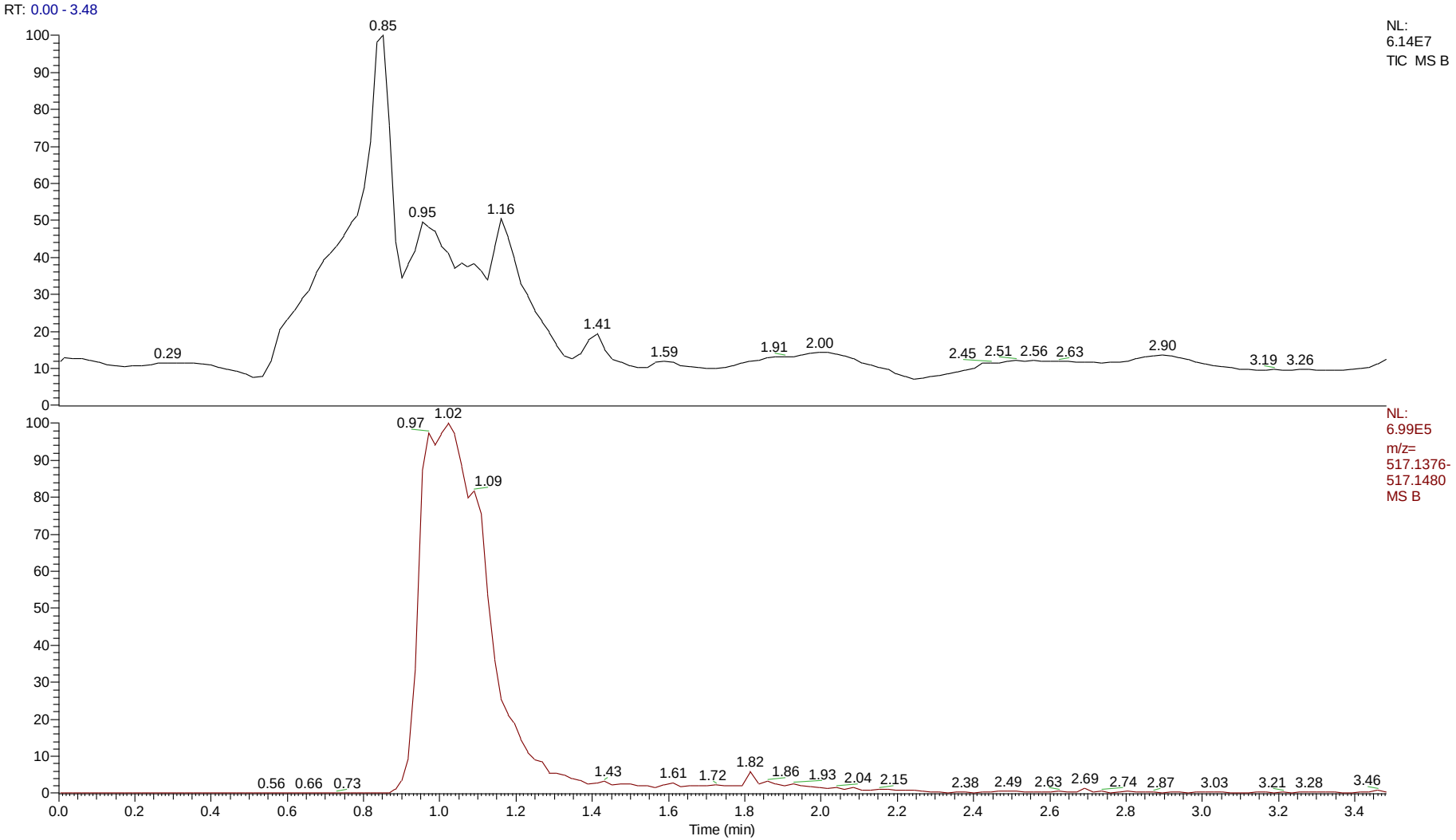


Figure S54. HPLC extracted ion flow diagrams for the synthesis of pyrido[2,3-*b*]indolizines

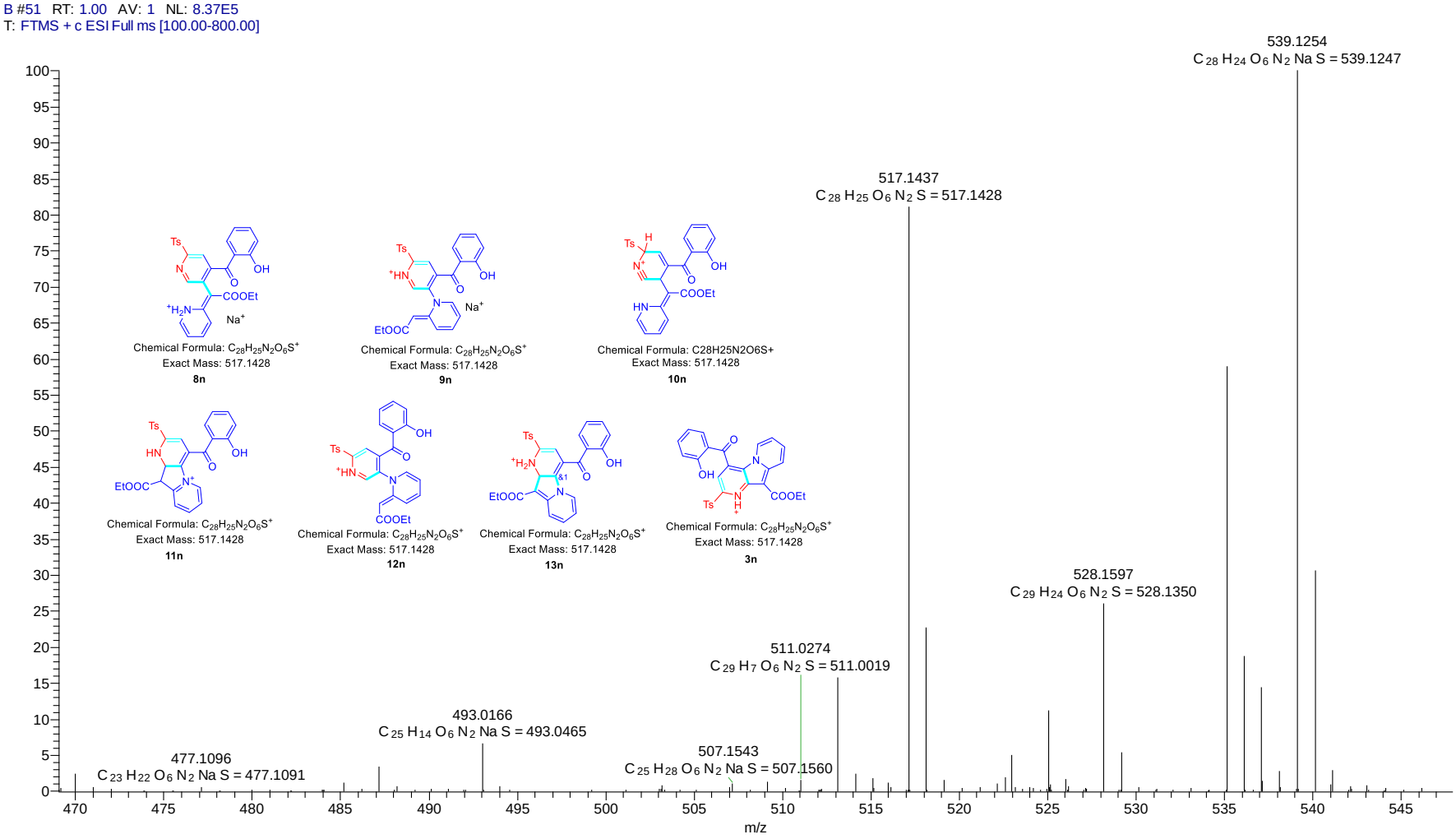


Figure S55. HRMs spectra of intermediates **8n/9n/10n/11n/12n/13n** and target compound **3n**

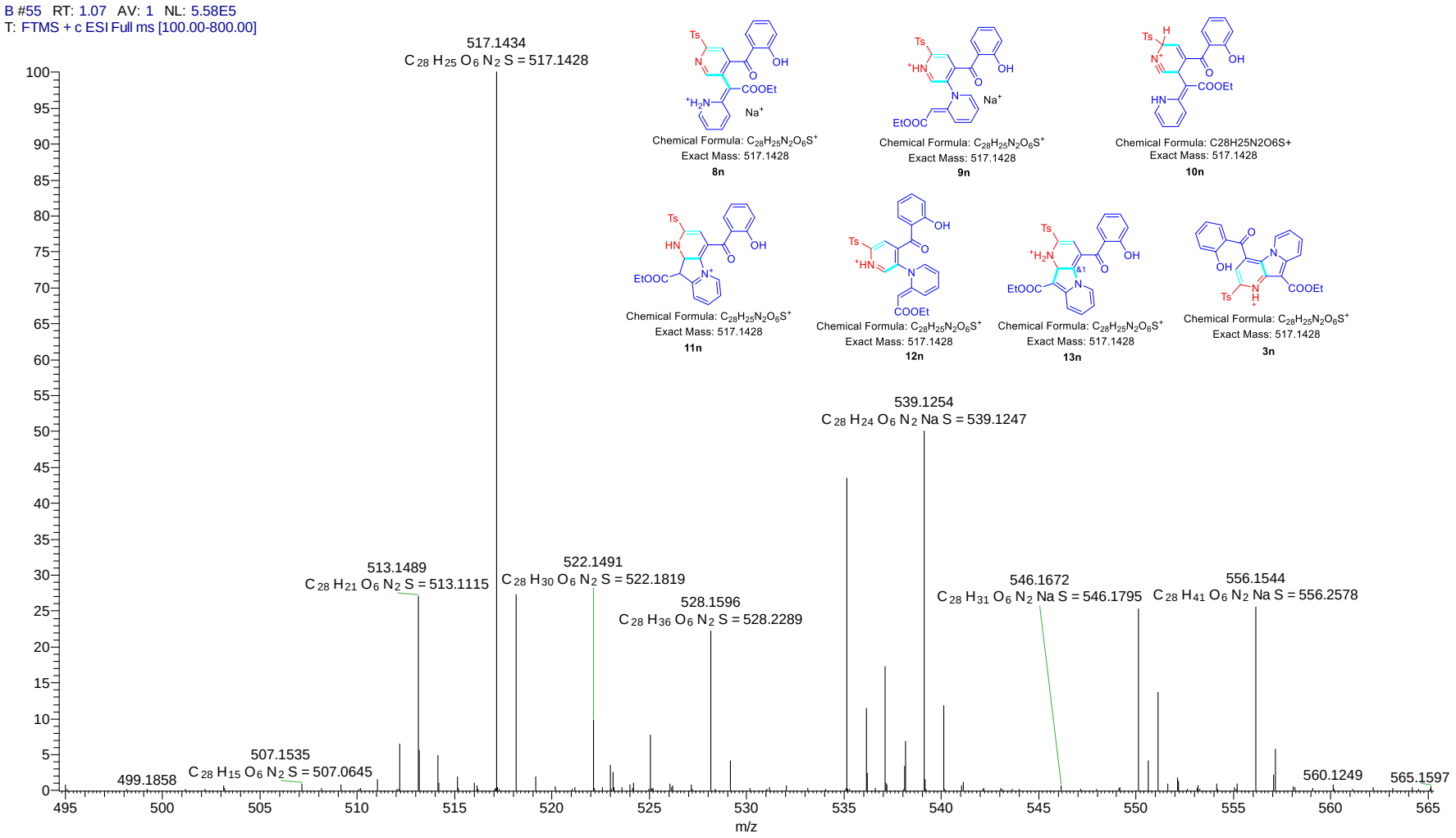


Figure S56. HRMs spectra of intermediates **8n/9n/10n/11n/12n/13n** and target compound **3n**

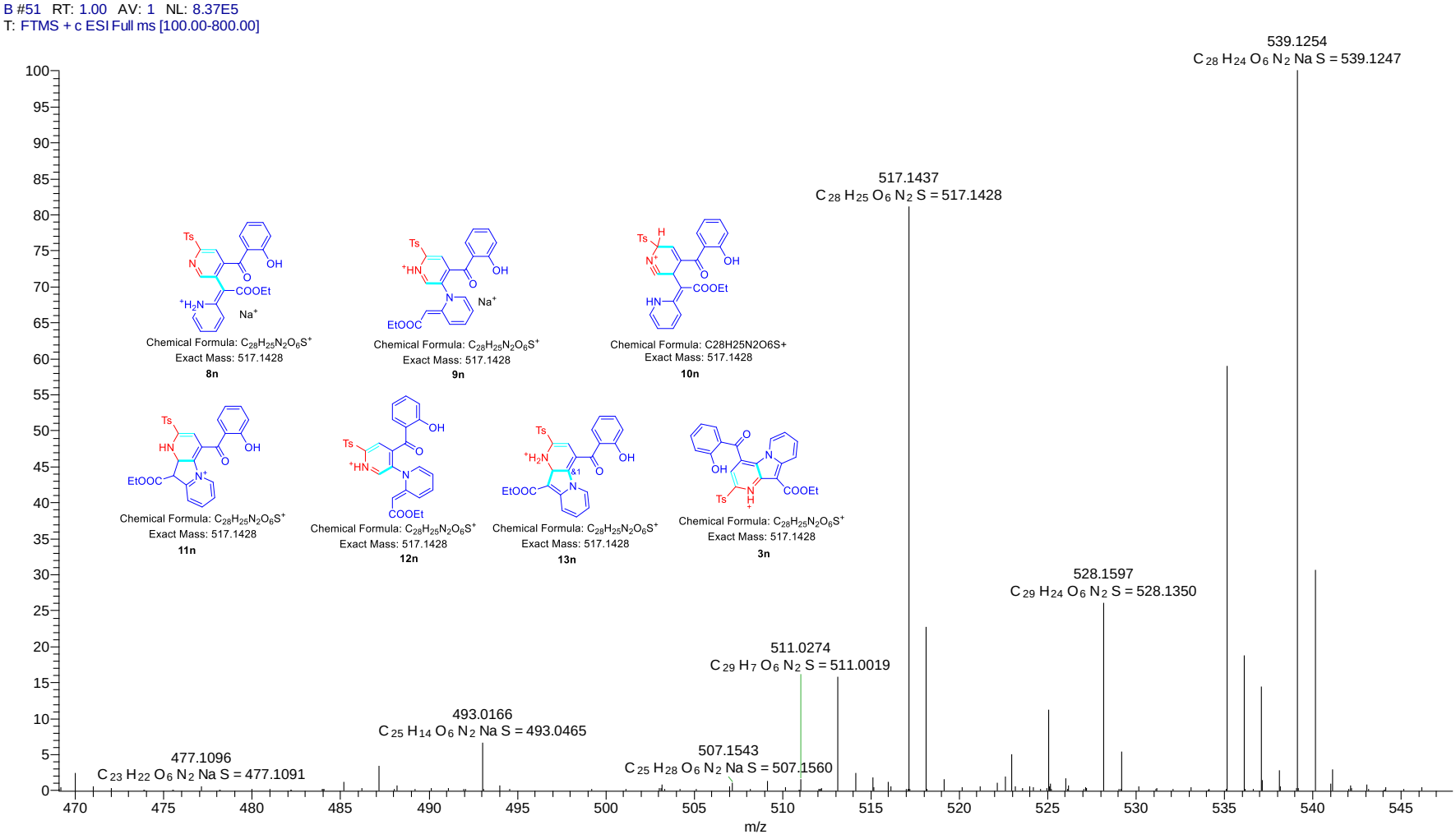


Figure S57. HRMs spectra of intermediates **8n/9n/10n/11n/12n/13n** and target compound **3n**

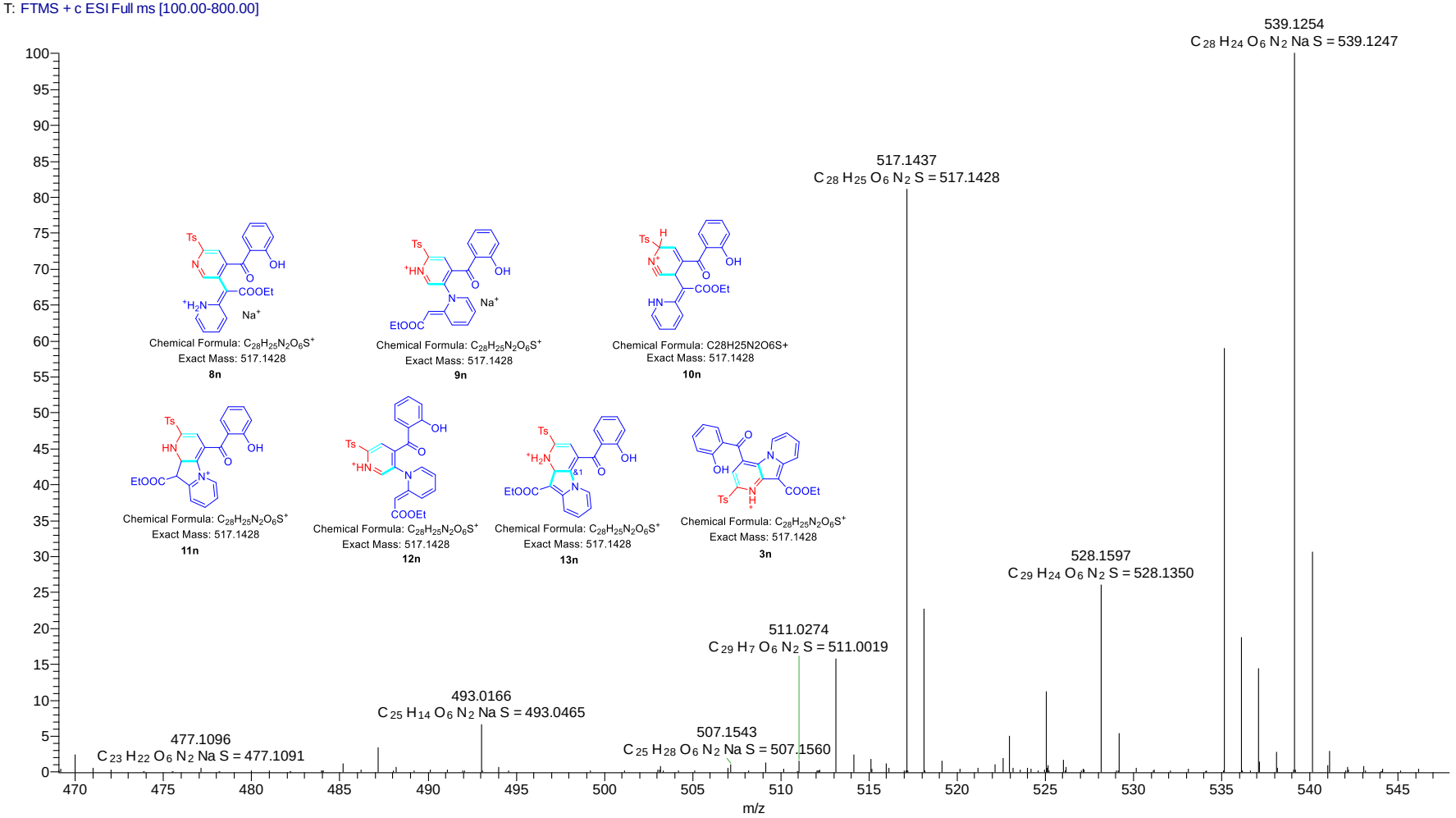


Figure S58. HRMs spectra of intermediates **8n/9n/10n/11n/12n/13n** and target compound **3n**

References and Notes

1. L. Chen, R. Huang, K. Li, X.-H. Yun, C.-L. Yang and S.-J. Yan, An environmentally benign cascade reaction of chromone-3-carboxaldehydes with ethyl 2-(pyridine-2-yl)acetate derivatives for highly site-selective synthesis of quinolizines and quinolizinium salts in water, *Green Chem.*, 2020, **22**, 6943–6953.

2. M. A. Abozeid, H. Y. Kim, K. Oh, Silver-Catalyzed Asymmetric Desymmetrization of Cyclohexadienones via Van Leusen Pyrrole Synthesis, *Org. Lett.*, 2022, **24**, 1812-1816.

3. CCDC2396367 contain the supplementary crystallographic data for compound **3b**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif