Supporting Information

Synergistic Photo-Copper Catalyzed Hydroxylation of (Hetero) Aryl Halides with Molecular Oxygen

Xin Zhang,[†] Ge Wu,[*,‡] Wenxia Gao,[†] Jinchang Ding,[†] Xiaobo Huang,[†] Miaochang Liu,[*,†] and Huayue Wu[†]

†*College of Chemistry and Materials Engineering, Wenzhou University, Wenzhou 325035, P. R. China.*

‡*School of Pharmacy, Wenzhou Medical University, Wenzhou, Zhejiang 325035, P. R. China.*

*[†]***E-mail:** mcl@wzu.edu.cn **[*‡]E-mail:** wuge@wmu.edu.cn

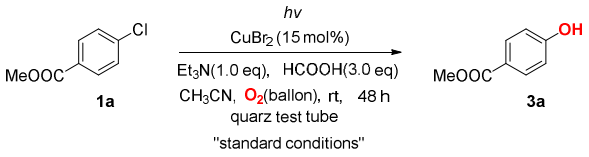
Table of Contents

1. General Information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. All the solvents were treated according to general methods. Melting points are uncorrected and recorded on Digital Melting Point Apparatus WRS-1B. ^{1}H NMR and ^{13}C NMR spectra were measured on a 500 MHz Bruker spectrometer (500 MHz for ^{1}H and 125 MHz for ^{13}C) or 400 MHz Zhongke-Niujin spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C), using DMSO-d_6 or $CDCl_3$ as the solvent with tetramethylsilane (TMS) as the internal standard at room temperature. Chemical shifts are given in δ relative to TMS, the coupling constants J are given in Hz. IR spectra were recorded on an AVATAR 370 FI-Infrared Spectrophotometer. High-resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometer. Column chromatography was performed using EM silica gel 60 (300-400 mesh). A 500 W super high pressure mercury lamp was used for photoirradiation.

2. Experimental Section

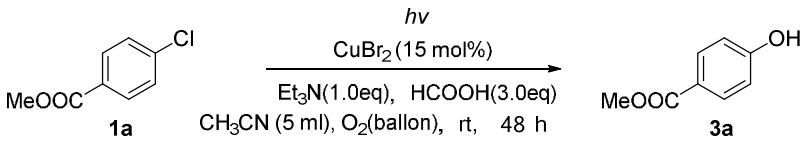
2.1 Optimization of Reaction Conditions[a]



Entry	Variation from the "standard conditions"	Yield[%][b]
1	none	73
2	CuF_2 , instead of $CuBr_2$	53
3	$CuCl_2$, instead of $CuBr_2$	68
4	CuI , instead of $CuBr_2$	46
5	CuO , instead of $CuBr_2$	23
6	$Cu(OH)_2$, instead of $CuBr_2$	37
7[c]	NaO*t*-Bu , instead of Et_3N	6
8[c]	KO*t*-Bu , instead of Et_3N	3
9[c]	$C_{S2}CO_3$, instead of Et_3N	<1
10	CH_3OH , instead of CH_3CN	trace
11	DMF , instead ofCH_3CN	0
12	DMSO , instead of CH_3CN	0
13	toluene , instead of CH_3CN	0
14	H_2O , instead of CH_3CN	0
15	TFE , instead ofCH_3CN	0
16	n-Hexane , instead of CH_3CN	0
17	$CHCl_3$, instead of CH_3CN	0
18	500-watt Metal Halide Lamp , instead of Hg lamp	trace
19	Blue LED , instead of Hg lamp	0
20	Green LED , instead of Hg lamp	0
21	Write LED , instead of Hg lamp	0
22	p-Touenesulfonic acid, instead of HCOOH	trace
23	TfOH , instead of HCOOH	0
24	Acetic acid , instead of HCOOH	trace
25	Diphenylphosphinic acid(20mol%), instead of HCOOH	23
26	L-Glutamic acid, instead of HCOOH	18
27	bpy , instead of HCOOH	0
28	1,10-phenanthroline , instead of HCOOH	0
29	10 mol% $CuBr_2$	62
30	5 mol% $CuBr_2$	47
31	36 h	68
32	24 h	61
33	borosilicate, instead of quartz, test tube	trace

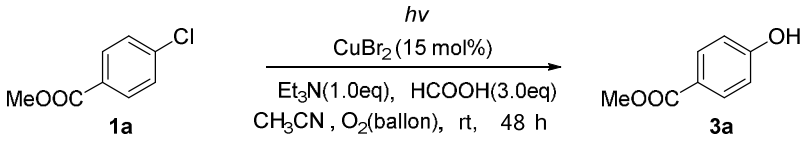
[a]Reaction conditions: **1a** (0.25 mmol, 1.0 equiv), $CuBr_2$ (15 mol%), Et_3N (1.0 equiv), HCOOH (3.0 equiv), CH_3CN (5 mL), 500 W super high pressure mercury lamp irradiation, and O_2 for 48 h. [b]Yield of isolated product.[c]Yield obtained via calibrated GC analysis with the aid of an internal standard.

2.2 General Procedure for the Visible-Light Photoredox Synthesis of Phenols



An oven-dried 10 mL quarz test tube equipped with a magnetic stir bar was charged with Methyl 4-chlorobenzoate (42.6 mg, 0.25 mmol, 1.0 equiv) and $CuBr_2$ (8.3 mg, 15 mol %)，and the quartz test tube was evacuated and backfilled with O_2 (3 cycles). Et_3N (34 μl, 0.25 mmol), HCOOH (47 μl, 0.75 mmol) and CH_3CN (5 ml) were added in turn via syringe. The resulting mixture was stirred for 5 minutes, and then the tube transferred to photoreactor. The tube was placed approximately 2 cm from a 500 W super high pressure mercury lamp. This mixture was irradiated for 48 h. After the indicated time period, the crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 5:1) directly to give the desired product **3a** in 73% yield as a white solid.

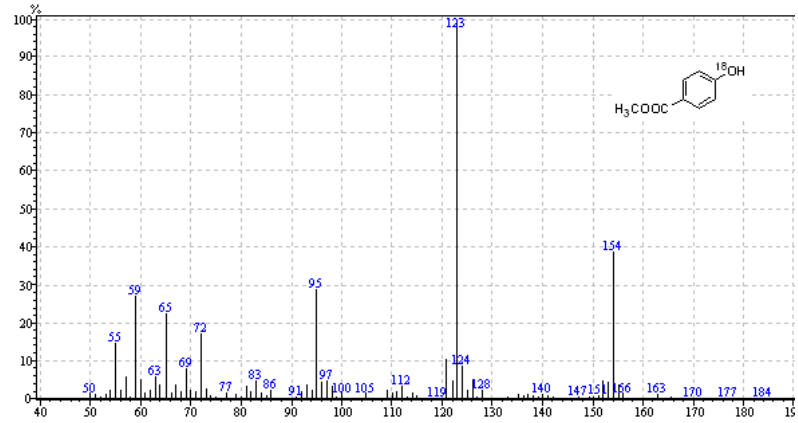
1mmol Scale Reaction Synthesis:

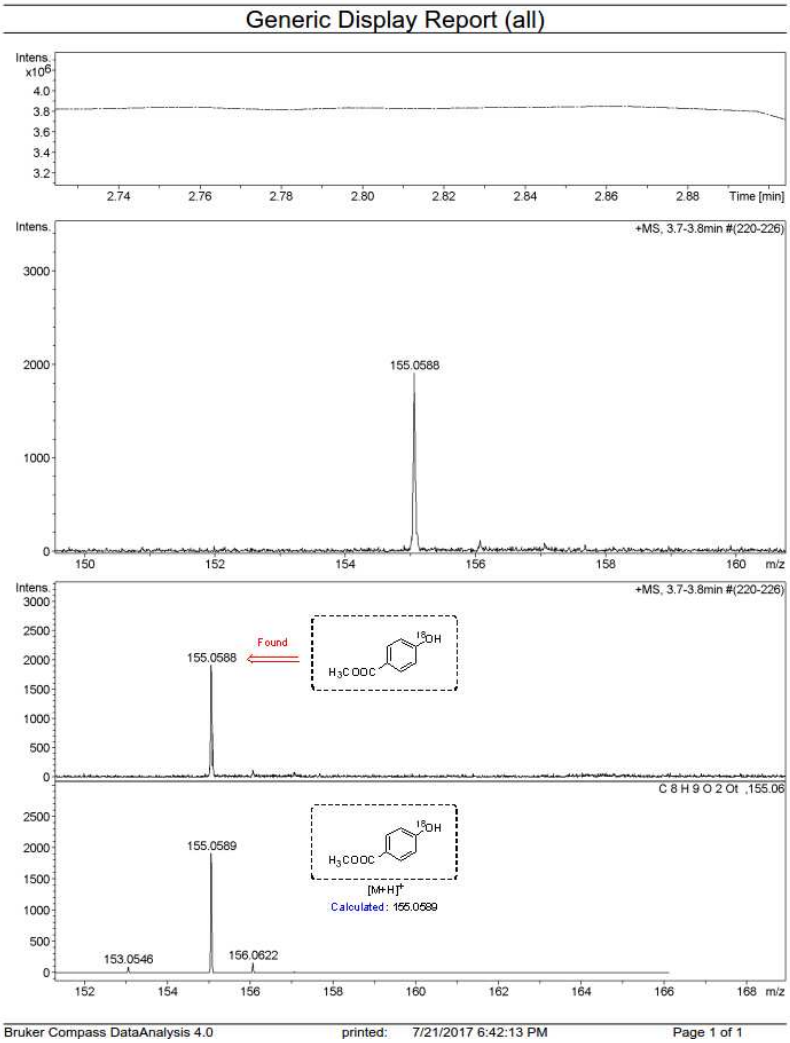


An oven-dried 50 mL quarz test tube equipped with a magnetic stir bar was charged with Methyl 4-chlorobenzoate (170.4 mg, 1.0 mmol, 1.0 equiv) and $CuBr_2$ (33.2 mg, 15 mol %)，and the quartz test tube was evacuated and backfilled with O_2 (3 cycles). Et_3N (136 μl, 1.0 mmol), HCOOH (188 μl, 3.0 mmol) and CH_3CN (20 ml) were added in turn via syringe. The resulting mixture was stirred for 5 minutes, and then the tube transferred to photoreactor. The tube was placed approximately 2 cm from a 500 W super high pressure mercury lamp. This mixture was irradiated for 48 h. After the indicated time period, the crude product was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate 5:1) directly to give the desired product **3a** in 61% yield as a white solid.

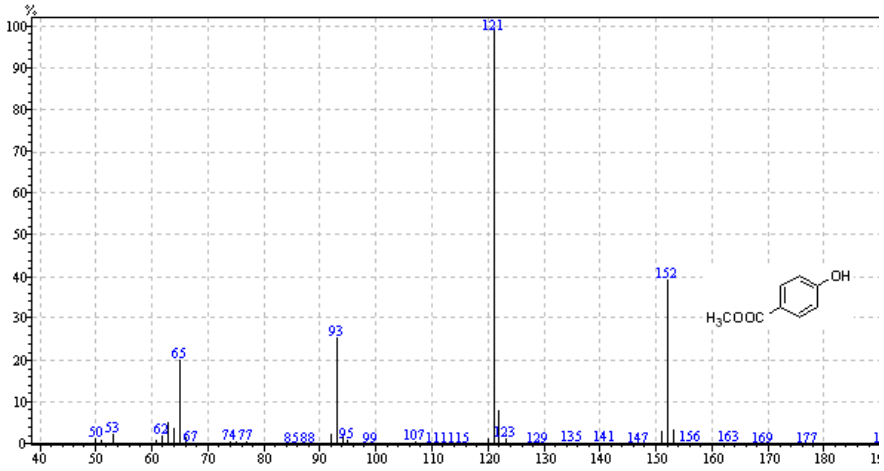
3. ^{18}O Labeling Experiments

3.1 The MS and HRMS data of 3a for the reaction in the presence of $^{18}O_2$

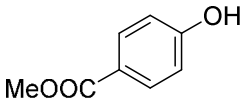




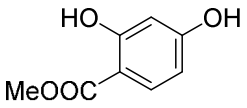
3.2 The MS data of 2a for the reaction in the presence of $H_2{}^{18}O$



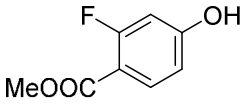
4. Analytical Data for All Products



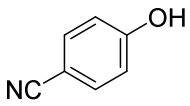
*methyl 4-hydroxybenzoate (**3a**)*: White solid (27.7 mg, 73%), mp 127-128 °C (lit.[1] 128 °C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.32 (s, 1H), 7.81 (d, J = 8.0 Hz, 2H), 6.84 (d, J = 8.0 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 166.0, 161.9, 131.3, 120.3, 115.3, 51.5.



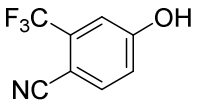
*methyl 2,4-dihydroxybenzoate (**3b**)*: White solid (34.0 mg, 81%), mp 114-115 °C (lit.[2] 112-114 °C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.71 (s, 1H), 10.44 (s, 1H), 7.63 (d, J = 9.0 Hz, 1H), 6.37 (dd, J = 2.5, 9.0 Hz, 1H), 6.30 (d, J = 2.0 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 169.5, 164.2, 162.7, 131.5, 108.3, 104.0, 102.5, 51.9.



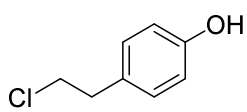
*methyl 2-fluoro-4-hydroxybenzoate (**3c**)*: White solid (28.5 mg, 67%), mp 85-86 °C (lit.[3] not reported). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.80 (s, 1H), 7.75 (t, J = 9.0 Hz, 1H), 6.69 (d, J = 9.0 Hz, 1H), 6.62 (d, J = 13.5 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 163.8 (t, $J_{C\text{-}F}$ = 5.0 Hz), 163.4 (d, $J_{C\text{-}F}$ = 12.5 Hz), 161.7, 133.3 (d, $J_{C\text{-}F}$ = 2.5 Hz), 111.9 (d, $J_{C\text{-}F}$ = 2.5 Hz), 108.5 (d, $J_{C\text{-}F}$ = 10.0 Hz), 103.4 (d, $J_{C\text{-}F}$ = 23.8 Hz), 51.7.



*4-hydroxybenzonitrile (**3d**)*: White solid (15.2 mg, 51%), mp 111-112 °C (lit.[4] 111-113 °C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.60 (s, 1H), 7.62 (d, J = 7.5 Hz, 2H), 6.90 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.6, 134.2, 119.4, 116.4, 101.0.

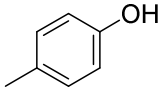


*4-hydroxy-2-(trifluoromethyl)benzonitrile (**3e**)*: White solid (24.3 mg, 52%), mp 117-118 °C (lit.[5] 119-120 °C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.42 (s, 1H), 7.94 (d, J = 8.5 Hz, 1H), 7.26 (s, 1H), 7.17 (d, J = 9.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.8, 137.3, 132.8 (q, $J_{C\text{-}F}$ = 31.2 Hz), 122.4 (q, $J_{C\text{-}F}$ = 271.2 Hz), 119.5, 116.1, 114.2 (q, $J_{C\text{-}F}$ = 5.0 Hz), 97.8 (d, $J_{C\text{-}F}$ = 1.2 Hz)

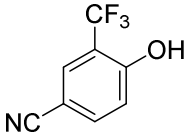


*4-(2-chloroethyl)phenol (**3f**)*[19]: yellow oil (15.2 mg, 39%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.27 (s, 1H), 7.06 (d, J = 7.6 Hz, 2H), 6.69 (d, J = 7.2 Hz, 2H), 3.75 (t, J = 6.8 Hz, 2H),

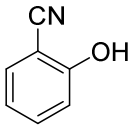
2.89 (t, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.5, 130.3, 128.7, 115.5, 46.2, 38.0.



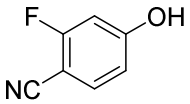
p-cresol (***3g***)[4]: colorless oil (11.3 mg, 42%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.07(s, 1H), 6.95 (d, J = 8.0 Hz, 2H), 6.64 (d, J = 8.5 Hz, 2H), 2.17 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.0, 129.6, 127.1, 115.0, 20.0.



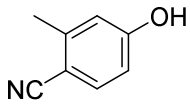
4-hydroxy-3-(trifluoromethyl)benzonitrile (***3h***)[20]: White solid (22.4 mg, 48%), mp 174-175 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.86 (s, 1H), 8.02 (s, 1H), 7.90 (dd, J = 2.0, 9.0 Hz, 1H), 7.15 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 159.8 (d, $J_{C\text{-}F}$ = 1.2 Hz), 137.8, 131.6 (q, $J_{C\text{-}F}$ = 5.0 Hz), 122.9 (q, $J_{C\text{-}F}$ = 270.0 Hz), 118.2, 118.1, 116.6 (q, $J_{C\text{-}F}$ = 30.0 Hz), 101.2.



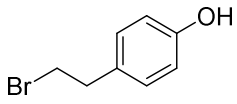
2-hydroxybenzonitrile (***3i***): White solid (18.1 mg, 61%), mp 97-98 °C (lit.[6] 99-100 °C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.04 (s, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.01 (d, J = 8.5 Hz, 1H), 6.92 (t, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.1, 134.6, 133.2, 119.5, 116.9, 116.1, 98.9.



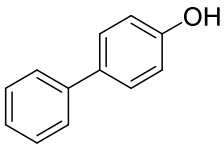
2-fluoro-4-hydroxybenzonitrile (***3j***): White solid (28.1 mg, 82%), mp 124-125 °C (lit.[7] not reported). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.19 (s, 1H), 7.69 (t, J = 8.5 Hz, 1H), 6.80 (d, J = 12.0 Hz, 1H), 6.76 (d, J = 8.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 164.0 (d, $J_{C\text{-}F}$ = 252.5 Hz), 163.9 (d, $J_{C\text{-}F}$ = 11.2 Hz), 134.7 (d, $J_{C\text{-}F}$ = 2.5 Hz), 114.7, 113.1 (d, $J_{C\text{-}F}$ = 1.2 Hz), 103.4 (d, $J_{C\text{-}F}$ = 21.2 Hz), 89.8 (d, $J_{C\text{-}F}$ = 15.0 Hz).



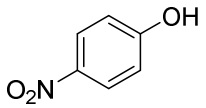
4-hydroxy-2-methylbenzonitrile (***3k***): White solid (17.6 mg, 53%), mp 95-96 °C (lit.[8] not reported). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.47 (s, 1H), 7.54 (d, J = 8.5 Hz, 1H), 6.78 (s, 1H), 6.72 (d, J = 8.5 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.4, 143.6, 134.3, 118.6, 117.1, 113.9, 101.6, 19.9.



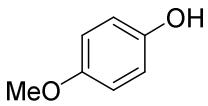
*4-(2-bromoethyl)phenol (**3l**)*[21]: yellow oil (16.5 mg, 33%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.28 (s, 1H), 7.05 (d, J = 8.0 Hz, 2H), 6.69 (d, J = 7.0 Hz, 2H), 3.63 (t, J = 7.0 Hz, 2H), 2.99 (t, J = 7.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.1, 129.6, 129.0, 115.1, 37.8, 34.8.



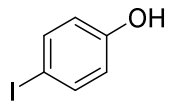
*[1,1'-biphenyl]-4-ol (**3m**)*: White solid (25.9 mg, 61%).mp 167-168 ^{o}C (lit.[9] 165 ^{o}C) ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.54 (s, 1H), 7.56 (d, J = 7.5 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.27 (t, J = 7.5 Hz, 1H), 6.85 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.1, 140.2, 130.9, 128.7, 127.7, 126.3, 125.9, 115.7.



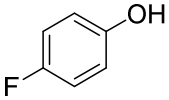
*4-nitrophenol (**3n**)*: yellow solid (15.6 mg, 45%), mp 110-111 ^{o}C (lit.[10] 113-114 ^{o}C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.04 (s, 1H), 8.11 (d, J = 9.0 Hz, 2H), 6.93 (d, J = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 163.9, 139.6, 126.1, 115.8.



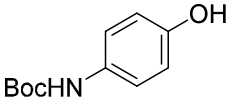
*4-methoxyphenol (**3o**)*[12]: yellow oil (22.3 mg, 72%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.86 (s, 1H), 6.74-6.68 (m, 4H), 3.65 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.1, 151.1, 115.7, 114.6, 55.3.



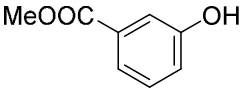
*4-iodophenol (**3p**)*[14]: Pale-yellow solid (39.0 mg, 81%), mp 89-90 ^{o}C (lit.[4] 66 ^{o}C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.68 (s, 1H), 7.45 (d, J = 8.5 Hz, 2H), 6.61 (d, J = 9.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.3, 137.8, 118.2, 80.6.



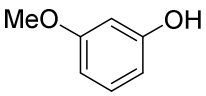
*4-fluorophenol (**3q**)*[14]: yellow oil (10.9 mg, 39%), ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.37 (s, 1H), 6.96 (t, J = 7.2 Hz, 2H), 6.76 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 156.0 (d, J_F = 232.0 Hz), 154.1, 116.5 (d, J_F = 8.0 Hz), 116.0 (d, J_F = 23.0 Hz).



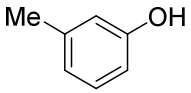
*tert-butyl (4-hydroxyphenyl)carbamate (**3r**)*: Yellow solid (31.9 mg, 61%), mp 146-147 ^{o}C (lit.[11] 146 ^{o}C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.02 (s, 1H), 8.96 (s, 1H), 7.20 (s, 2H), 6.65-6.63 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.0, 152.5, 131.0, 120.0, 115.0, 78.4, 28.2.



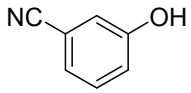
*methyl 3-hydroxybenzoate (**3s**)*[22]: Yellow oil (29.6 mg, 78%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.82 (s, 1H), 7.38 (d, J= 7.5Hz, 1H), 7.34 (s, 1H), 7.31 (t, J = 8.0 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 166.2, 157, 10.8, 129.8, 120.3, 119.8, 115.6, 52.0.



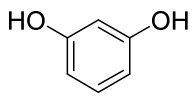
*3-methoxyphenol (**3t**)*[12]: yellow oil (22.9 mg, 74%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.37 (s, 1H), 7.04 (t, J = 8.0 Hz, 1H), 6.34 (t, J = 8.0 Hz, 3H), 3.68 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 160.5, 158.5, 129.8, 107.8, 104.6, 101.2, 54.8.



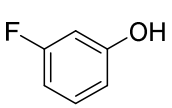
*m-cresol (**3u**)*[4]: colorless oil (17.0 mg, 63%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.19(s, 1H), 7.02 (t, J = 8.0 Hz, 1H), 6.58-6.53 (m, 3H), 2.20 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.2, 138.6, 129.0, 119.5, 115.8, 112.3, 21.0.



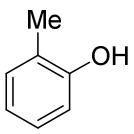
*3-hydroxybenzonitrile (**3v**)*: White solid (20.8 mg, 70%), mp 78-80 ^{o}C (lit.[12] 79-81 ^{o}C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.21 (s, 1H), 7.37 (t, J = 8.0 Hz, 1H), 7.22 (d, J = 7.5 Hz, 1H), 7.11-7.09 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 157.8, 130.8, 122.8, 120.7, 118.8, 118.2, 112.0.



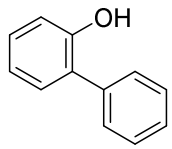
*Resorcinol (**3w**)*: White solid (24.7 mg, 90%), mp 109-110 ^{o}C (lit.[10] 111-112 ^{o}C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.14 (s, 2H), 6.91 (t, J = 8.0 Hz, 1H), 6.18 (d, J = 9.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.4, 129.6, 106.2, 102.5.



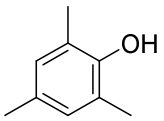
*3-fluorophenol (**3x**)*[10]: yellow oil (13.2 mg, 47%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.85 (s, 1H), 7.18 (q, J = 8.0 Hz, 1H), 6.61-6.52 (m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 163.0 (d, $J_{C\text{-}F}$ = 241.2 Hz), 159.0 (d, $J_{C\text{-}F}$ = 11.2 Hz), 130.5 (d, $J_{C\text{-}F}$ = 10.0 Hz), 111.5 (d, $J_{C\text{-}F}$ = 2.5 Hz), 105.4 (d, $J_{C\text{-}F}$ = 21.2 Hz), 102.4 (d, $J_{C\text{-}F}$ = 22.5 Hz).



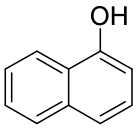
*o-cresol (**3y**)*[10]: colorless oil (13.7 mg, 51%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.20 (s, 1H), 7.03 (d, J = 7.5 Hz, 1H), 6.97 (t, J = 8.0 Hz, 1H), 6.75 (d, J = 8.0 Hz, 1H), 6.67 (t, J = 7.0 Hz, 1H), 2.10 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 155.3, 130.5, 126.6, 123.7, 118.7, 114.5, 15.9.



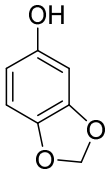
*[1,1'-biphenyl]-2-ol (**3z**)*: White solid (25.1 mg, 59%), mp 56-57 °C (lit.[13] 56-58 °C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.50 (s, 1H), 7.54 (d, J = 7.0 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.5 Hz, 1H), 7.25 (t, J = 1.5 Hz, 1H), 7.16 (t, J = 8.0 Hz, 1H), 6.95 (d, J = 8.0 Hz, 1H), 6.87 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 154.2, 138.6, 130.3, 129.0, 128.4, 127.9, 127.7, 126.4, 119.4, 116.0.



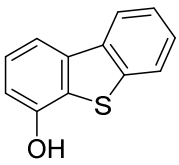
*2,4,6-trimethylphenol (**3aa**)*: White solid (17.3 mg, 51%), mp 70-72 °C (lit.[12] 70-73 °C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.88 (s, 1H), 6.69 (s, 2H), 2.11 (d, J = 7.0 Hz, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 150.7, 128.6, 127.3, 124.0, 20.0, 16.4.



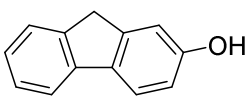
*naphthalen-1-ol (**3ab**)*: White solid (21.9 mg, 61%), mp 92-93 °C (lit.[14] 91-93 °C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.08 (s, 1H), 8.13 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H), 7.48-7.41 (m, 2H), 7.34-7.28 (m, 2H), 6.88-6.86 (m, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.1, 134.4, 127.3, 126.4, 126.0, 124.6, 124.5, 121.9, 118.3, 108.0.



*benzo[d][1,3]dioxol-5-ol (**3ac**)*: White solid (17.9 mg, 52%), mp 66-67 °C (lit.[15] 64-66 °C). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.10 (s, 1H), 6.68 (d, J = 8.5 Hz, 1H), 6.37 (d, J = 2.0 Hz, 1H), 6.18 (dd, J = 2.0, 8.0 Hz, 1H), 5.88 (s, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 152.5, 147.6, 139.6, 108.1, 106.2, 100.5, 97.8.

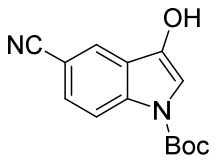


*tert-butyl (4-hydroxyphenyl)carbamate (**3ad**)*: White solid (36.5 mg, 73%), mp 158-159 °C (lit.[14] 158-160°C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (s, 1H), 8.27 (d, J = 6.4 Hz, 1H), 8.00 (d, J = 7.2 Hz, 1H), 7.80 (d, J = 7.6 Hz, 1H), 7.51-7.46 (m, 2H), 7.34 (t, J = 7.6 Hz, 1H), 6.95 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.8, 139.2, 137.4, 136.1, 127.4, 126.6, 126.0, 125.0, 123.6, 122.6, 113.4, 111.9.

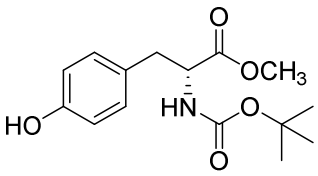


*9H-fluoren-2-ol (**3ae**)*: White solid (22.3 mg, 49%), mp 168-169 °C (lit.[16] 170-170.5 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.49 (s, 1H), 7.71 (d, J = 6.4 Hz, 1H), 7.66 (d, J = 7.6 Hz, 1H), 7.48 (d, J = 6.0 Hz, 1H), 7.30 (t, J = 6.8 Hz, 1H), 7.19 (d, J = 6.4 Hz, 1H), 6.98 (s, 1H), 6.79 (d,

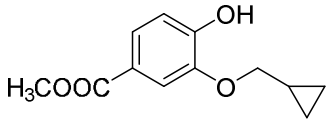
J = 6.8 Hz, 1H), 3.81 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.5, 145.4, 142.6, 142.0, 132.9, 127.0, 125.6, 125.3, 121.2, 119.2, 114.5, 112.5, 36.8.



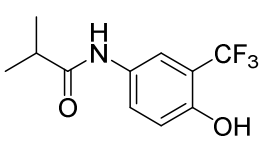
tert-butyl 5-cyano-3-hydroxy-1H-indole-1-carboxylate ***(3af)***: White solid (26.4 mg, 41%), mp 125-126 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 7.2 Hz, 1H), 7.87 (s, 1H), 7.69 (s, 1H), 7.53 (d, J = 8.0 Hz, 1H), 6.61 (s, 1H), 1.67 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.0, 137.0, 130.5, 128.1, 127.3, 125.8, 119.8, 116.0, 106.9, 106.0, 84.9, 28.1. IR (KBr): 3013, 2916, 2224, 1739, 1603, 1573, 1543, 1461, 1362, 1437, 1280, 1214, 1160, 1118, 1081, 886, 815, 761, 726, 637 cm^{-1}. HRMS (ESI) calcd for $C_{14}H1_4N_2O_3$ $[M+H]^+$: 259.1077 , found 259.1075.



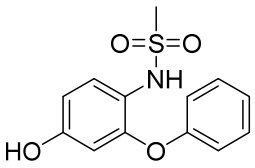
methyl (tert-butoxycarbonyl)-D-tyrosinate ***(4a)***[23]: yellow oil (62.6 mg, 85%), ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.23 (s, 1H), 7.21 (d, J = 7.2 Hz, 1H), 7.01 (d, J = 7.2 Hz, 2H), 6.66 (d, J = 6.8 Hz, 2H), 4.08 (d, J = 4.4 Hz, 1H), 3.59 (s, 3H), 2.85 (d, J = 13.6 Hz, 1H), 2.73 (t, J = 11.6 Hz, 1H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.2, 156.4, 155.9, 130.4, 128.0, 115.4, 78.7, 56.0, 52.1, 36.2, 28.6.



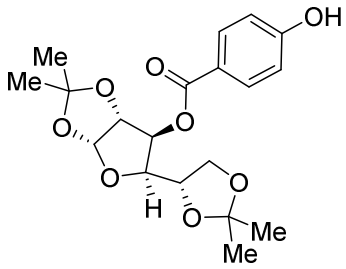
methyl 3-(cyclopropylmethoxy)-4-hydroxybenzoate ***(4b)***[24]: colorless oil (49.4 mg, 89%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.95 (s, 1H), 7.45 (dd, J = 2.0, 8.5 Hz, 1H), 7.40 (d, J = 1.5 Hz, 1H), 6.88 (d, J = 8.5 Hz, 1H), 3.83 (d, J = 7.0 Hz, 2H), 3.78 (s, 3H), 1.25-1.19 (m, 1H), 0.57-0.54 (m, 2H), 0.34-0.32, (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 166.0, 151.8, 146.6, 123.4, 120.4, 115.3, 114.3, 73.0, 51.6, 10.1, 3.1.



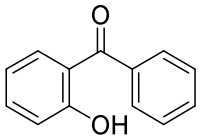
N-(4-hydroxy-3-(trifluoromethyl)phenyl)isobutyramide ***(4c)***: brown solid (37.7 mg, 61%), mp 145-148 ^{o}C(lit.[17] not reported). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.24 (s, 1H), 9.79 (s, 1H)，7.86 (d, J = 2.0 Hz, 1H), 7.58 (d, J = 9.0 Hz, 1H), 6.94 (d, J = 8.5 Hz, 1H), 2.57-2.52 (m, 1H), 1.08 (d, J = 6.5 Hz, 6H) ; ^{13}C NMR (125 MHz, DMSO-d_6) δ 174.9, 151.2, 130.9, 124.8, 123.9 (q, $J_{C\text{-}F}$ = 270.0 Hz), 117.4 (q, $J_{C\text{-}F}$ = 6.2 Hz), 117.1, 114.9 (q, $J_{C\text{-}F}$ = 28.8 Hz), 34.8, 19.4.



N-(4-hydroxy-2-phenoxyphenyl)methanesulfonamide ***(4d)***: brown solid (44.6 mg, 64%), mp 166-167 °C (lit.[18] not reported). ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.60 (s, 1H), 8.97 (s, 1H), 7.42 (t, J = 8.0 Hz, 2H), 7.18 (t, J = 7.0 Hz, 1H), 7.15 (d, J = 8.5 Hz, 1H), 7.07 (d, J = 8.0 Hz, 2H), 6.50 (dd, J = 2.5, 8.5 Hz, 1H), 6.20 (d, J = 2.5 Hz, 1H), 2.90 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 156.9, 155.8, 152.8, 130.0, 123.9, 119.4, 118.4, 110.3, 104.8, 40.2.



(3aR,5R,6S,6aR)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl) -2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-6-yl 4-hydroxybenzoate ***(4e)***: white solid (99.3 mg, 81%), mp 150-151 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.46 (s, 1H), 7.82 (d, J = 6.4 Hz, 2H), 6.88 (d, J = 6.4 Hz, 2H), 5.95 (s, 1H), 5.20 (s, 1H), 4.64 (s, 1H), 4.34 (s, 1H), 4.22 (s, 1H), 4.04 (s, 1H), 3.94 (s, 1H), 1.45 (s, 3H), 1.33 (s, 3H), 1.25 (s, 3H), 1.20 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.0, 162.9, 132.2, 120.0, 116.0, 111.8, 108.9, 105.1, 83.2, 79.5, 76.3, 72.6, 66.7, 27.1, 26.9, 26.4, 25.5. IR (KBr): 3356, 2983, 2874, 2357, 1715, 1606, 1591, 1446, 1383, 1314, 1268, 1229, 1160, 1090, 889, 857, 776, 616, 591 cm^{-1}. HRMS (ESI) calcd for $C_{19}H_{24}O_8$ $[M+H]^+$: 381.1544 , found 381.1536.



(2-hydroxyphenyl)(phenyl)methanone ***(5a)***[25]: colorless oil (39.6 mg, 80%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.48 (s, 1H), 7.72 (s, 1H), 7.70 (d, J = 1.0 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 7.5 Hz, 2H), 7.47-7.43 (m, 1H), 7.35 (dd, J = 1.5, 8.0 Hz, 1H), 6.99 (d, J = 8.0 Hz, 1H), 6.94 (t, J = 7.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 197.8, 157.4, 137.4, 133.5, 132.7, 130.6, 129.1, 128.4, 124.1, 119.0, 116.8.

Reference

[1] Dieskau, A. P.; Plietker, B. *Org. Lett.* **2011**, *13*, 5544.

[2] Ploypradith, P.; Cheryklin, P.; Niyomtham, N.; Bertoni, D. R.; Ruchirawat, S. *Org. Lett.* **2007**, *9*, 2637.

[3] Han, C.; Yang, L.; Raghunath, P.; Lin, M.; Kumara, R.; Lin, H. *Rsc Adv.* **2016**, *6*,

110482.

[4] Inamoto, K.; Nozawa, K.; Yonemoto, M.; Kondo, Y. *Chem. Commun*. **2011**, *47*, 11775.

[5] Hauptschein, M.; Nodiff, E. A.; Saggiomo, A. J. *J. Am. Chem. Soc*. **1954**, *76*, 1051.

[6] Johns, I. B.; Dipietro, H. R. *J. Org. Chem*. **1962**, *27*, 592.

[7] Lepore, S. D.; Wiley, M. R. *Org. Lett*. **2003**, *5*, 7.

[8] Shu, Z.; Ji, W.; Wang, X.; Zhou, Y.; Zhang, Y.; Wang, J. *Angew.Chem., Int. Ed*., **2014**, *53*, 2186.

[9] Syper, L. *Synthesis.* **1989**, 167.

[10] Xu, J.; Wang, X.; Shao, C.; Su, D.; Cheng, G.; Hu, Y. *Org. Lett.* **2010**, *12*, 1964.

[11] Chankeshwara, S. V.; Chakraborti, A. K. *Org. Lett.* **2006**, *8*, 3259.

[12] Anderson, K. W.; Ikawa, T.; Tundel, R. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 10694.

[13] Wei, J.; Jiao, J.; Feng, J.; Lv, J.; Zhang, X.; Shi, X.; Chen, Z. *J. Org. Chem*. **2009**, *74*, 6283.

[14] Molander, G. A.; Cavalcanti, L. N. *J. Org. Chem*. **2011**, *76*, 623.

[15] Bezerra-Netto, H. J. C.; Lacerda, D. I.; Miranda, A. L. P.; Alves, H. M.; Barreiro, E. J.; Fraga, C. A. M. *Bioorg. Med. Chem.* **2006**, *14*, 7924.

[16] Kreiter, V. P.; Bonner. W. A.; Eastman. R. H.; *J. Am. Chem. Soc*. **1954**, *76*, 5770.

[17] Udagawa, C.; Fukuyoshi, S.; Morimoto, S.; Tanimoto, Y.; Nakagaki, R.; *J. Photochem. Photobiol*. A, **2011**, *226*, 57.

[18] Macpherson, D. *J. Drug Metab. Toxicol*. **2012**, *4*, 140.

[19] Spivey, A. C.; Tseng, C. C.; Jons, T. C.; Kohler, A. D.; Ellames, G. J. *Org. Lett*. **2009**, *17*, 4760.

[20] Cusack, K. P.; Breinlinger, E. C.; Fix, S. S. R.; Stoffel, R. H.; Woller, K. R., WO2011071570A1, 2010.

[21] Moriya, T.; Yoneda, S.; Kawana, K.; Ikeda, R.; Konakahara, T.; SaKai, N. *Org. Lett*. **2012**, *14*, 4842.

[22] Segal, M.; Avinery, R.; Buzhor, M.; Shaharabani, R.; Harnoy, A. J.; Tirosh, E.; Beck, R.; Amir, R. J. *J. Am. Chem. Soc*. **2017**, *139* , 803.

[23] Betts, H. M.; Sephton, S. M.; Tong, C.; Awais, R. O.; Hill, P. J.; Perkins, A. C.; Aigbirhio, F. I. *J. Med. Chem.* **2016**, *59*, 9422.

[24] Feng, N.; Li, J. *Synthesis*. **2012**, *44*, 3598.

[25] Mo, F.; Trzepkowski, L. J.; Dong, G. *Angew.Chem., Int. Ed*., **2012**, *51*, 13075.

5. NMR Spectra for All Products

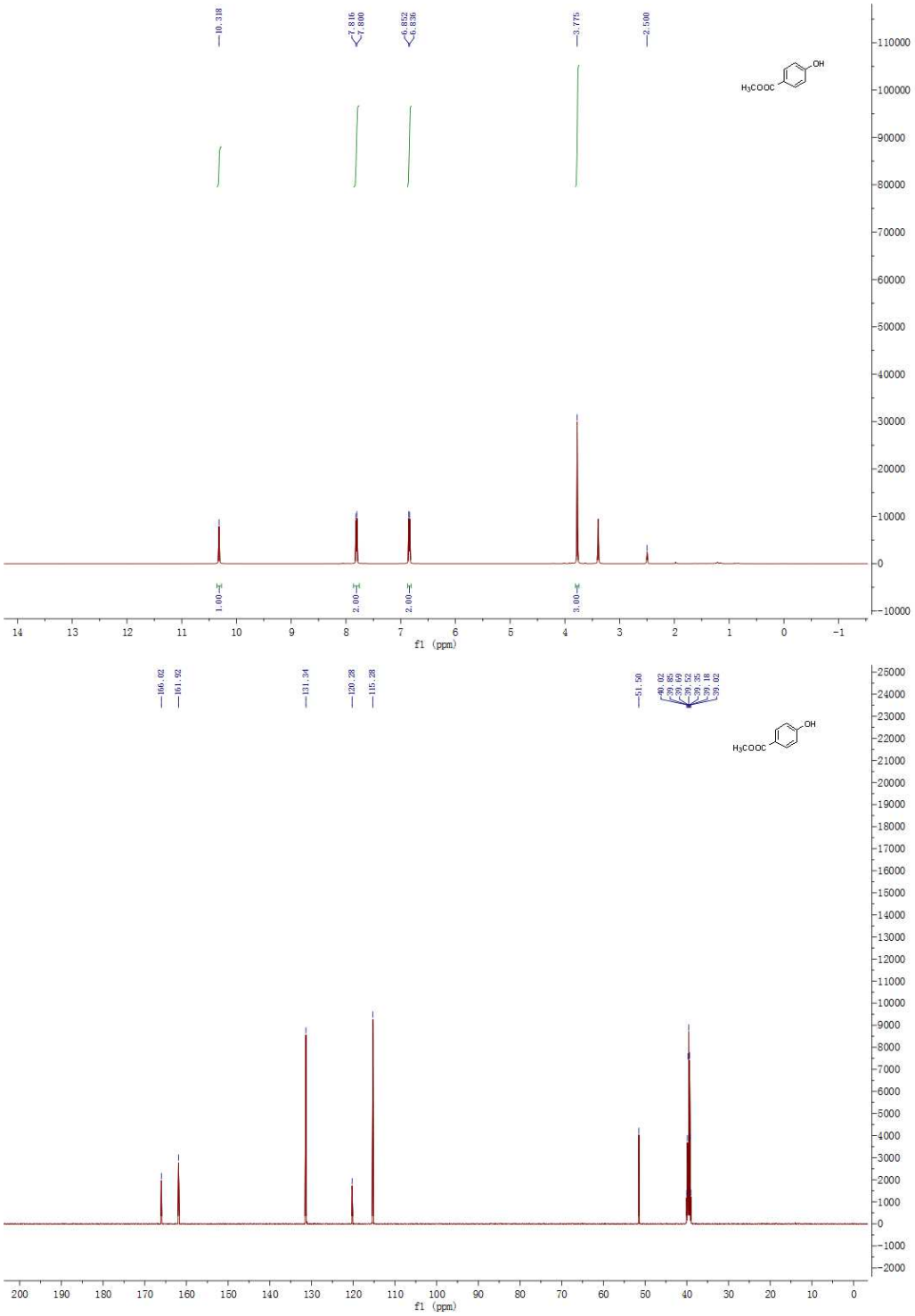


Figure S1. ^{1}H NMR of **3a** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3a** (125 MHz, DMSO-d_6)

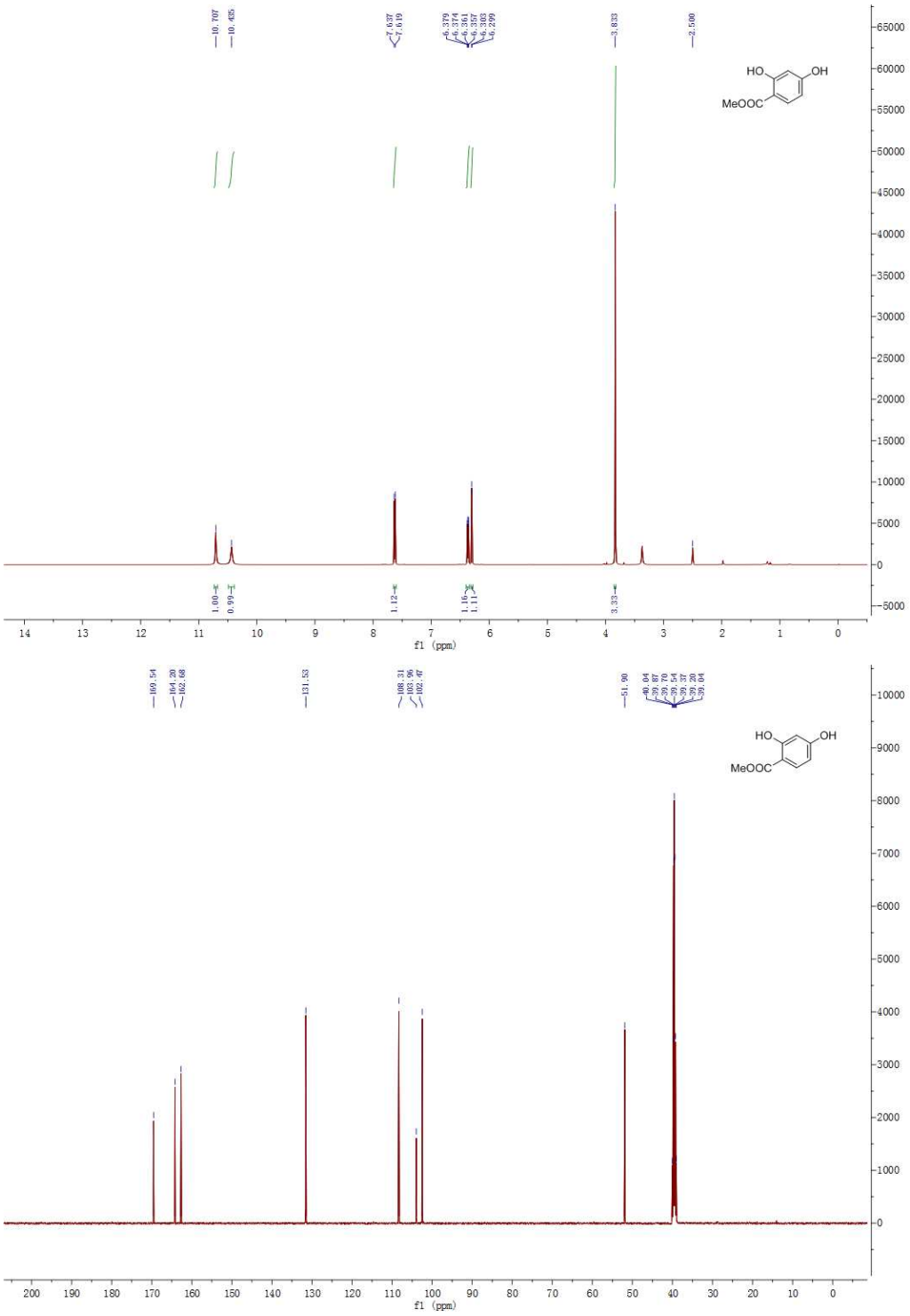


Figure S2. ^{1}H NMR of **3b** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3b** (125 MHz, DMSO-d_6)

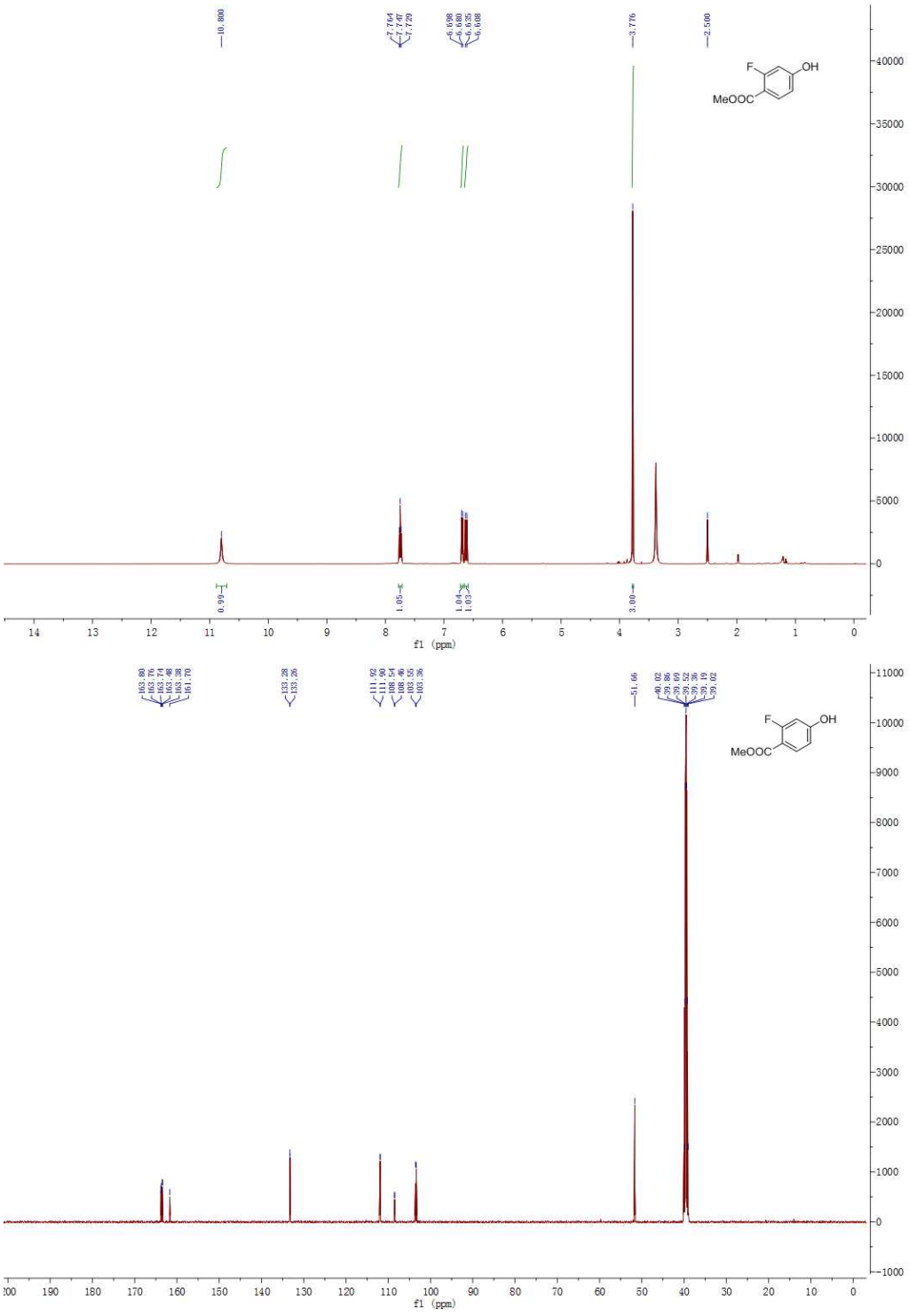


Figure S3. ^{1}H NMR of **3c** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3c** (125 MHz, DMSO-d_6)

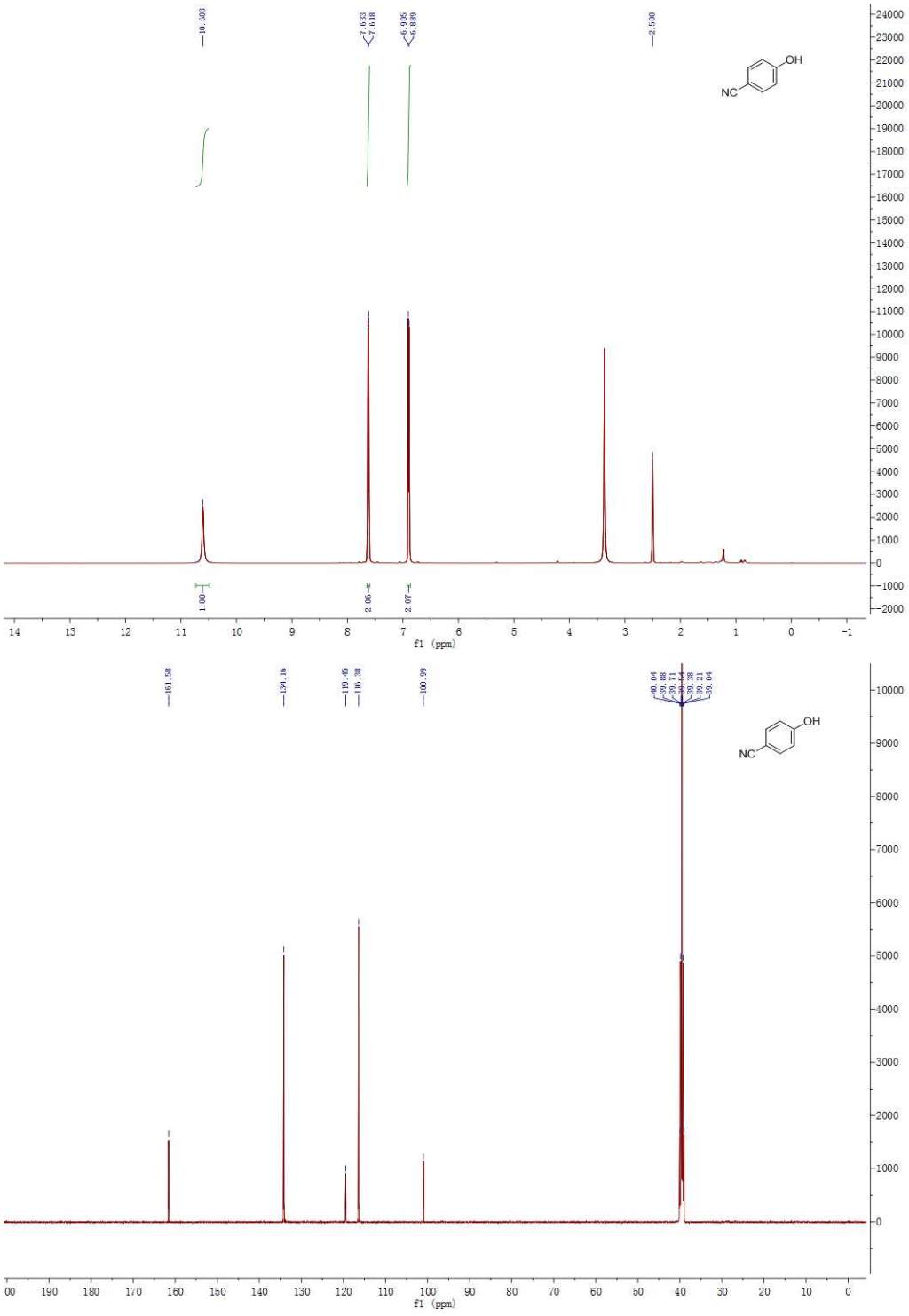


Figure S4. ^{1}H NMR of **3d** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3d** (125 MHz, DMSO-d_6)

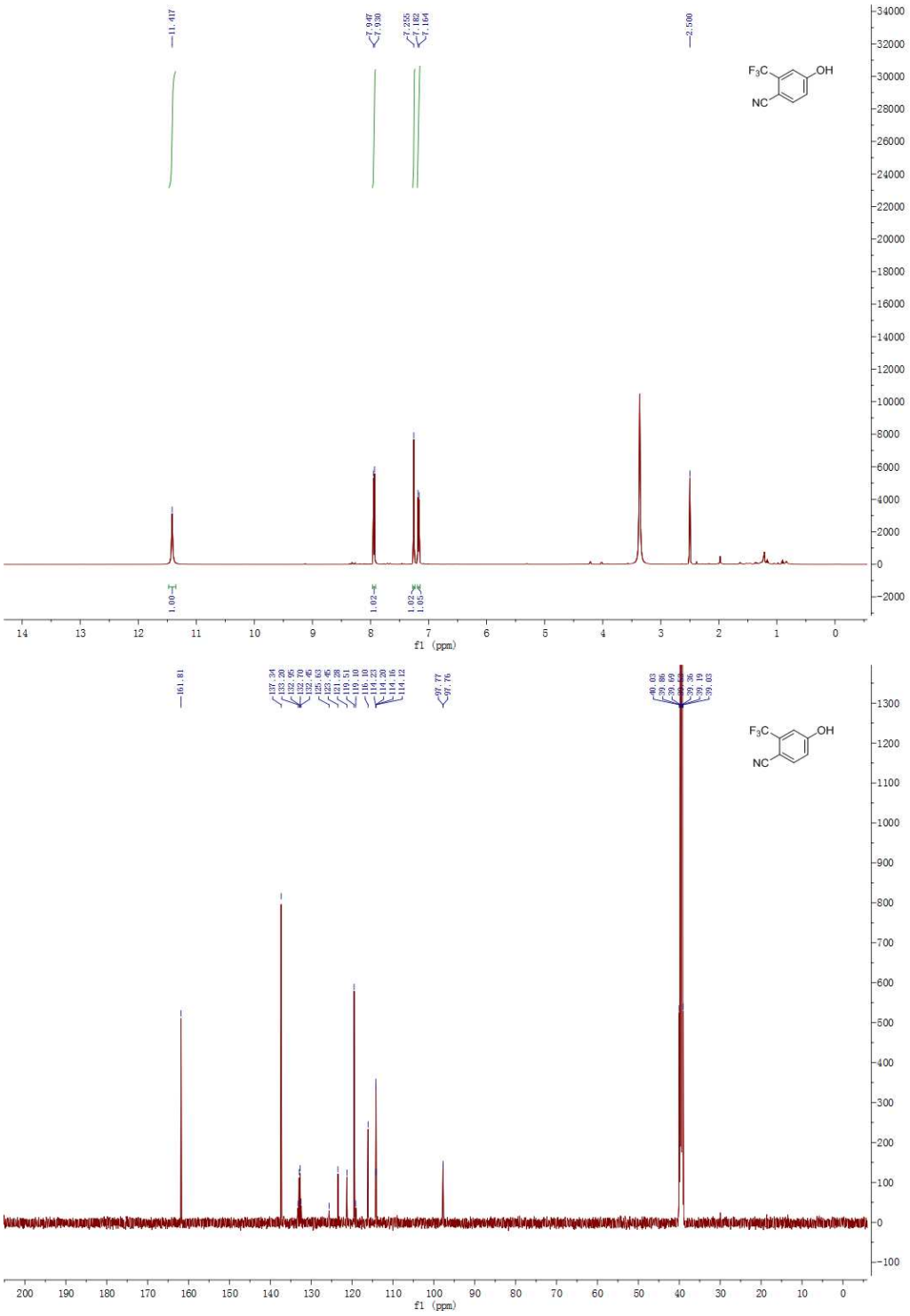


Figure S5. ^{1}H NMR of **3e** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3e** (125 MHz, DMSO-d_6)

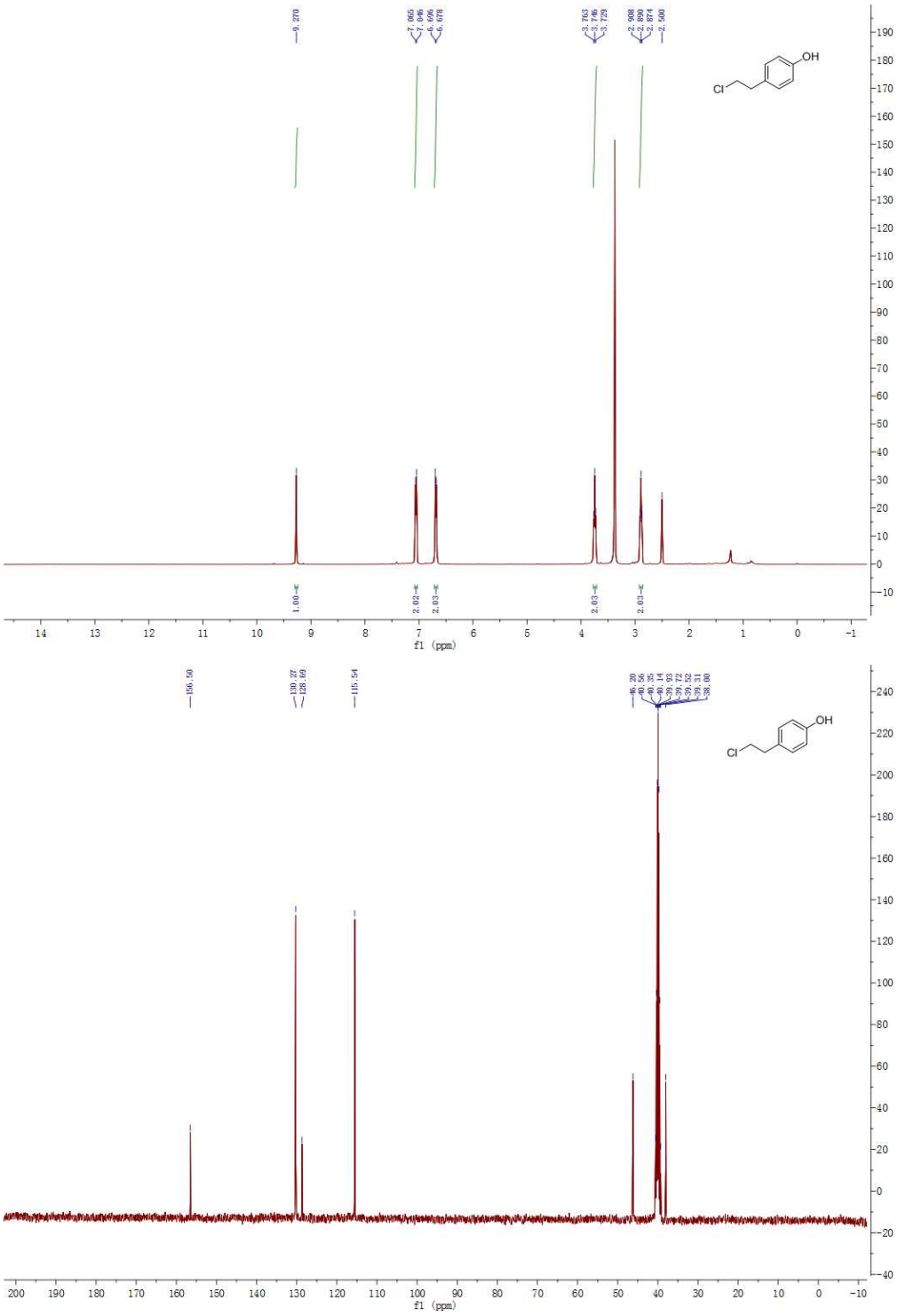


Figure S6. ^{1}H NMR of **3f** (400 MHz, DMSO-d_6) and ^{13}C NMR of **3f** (100 MHz, DMSO-d_6)

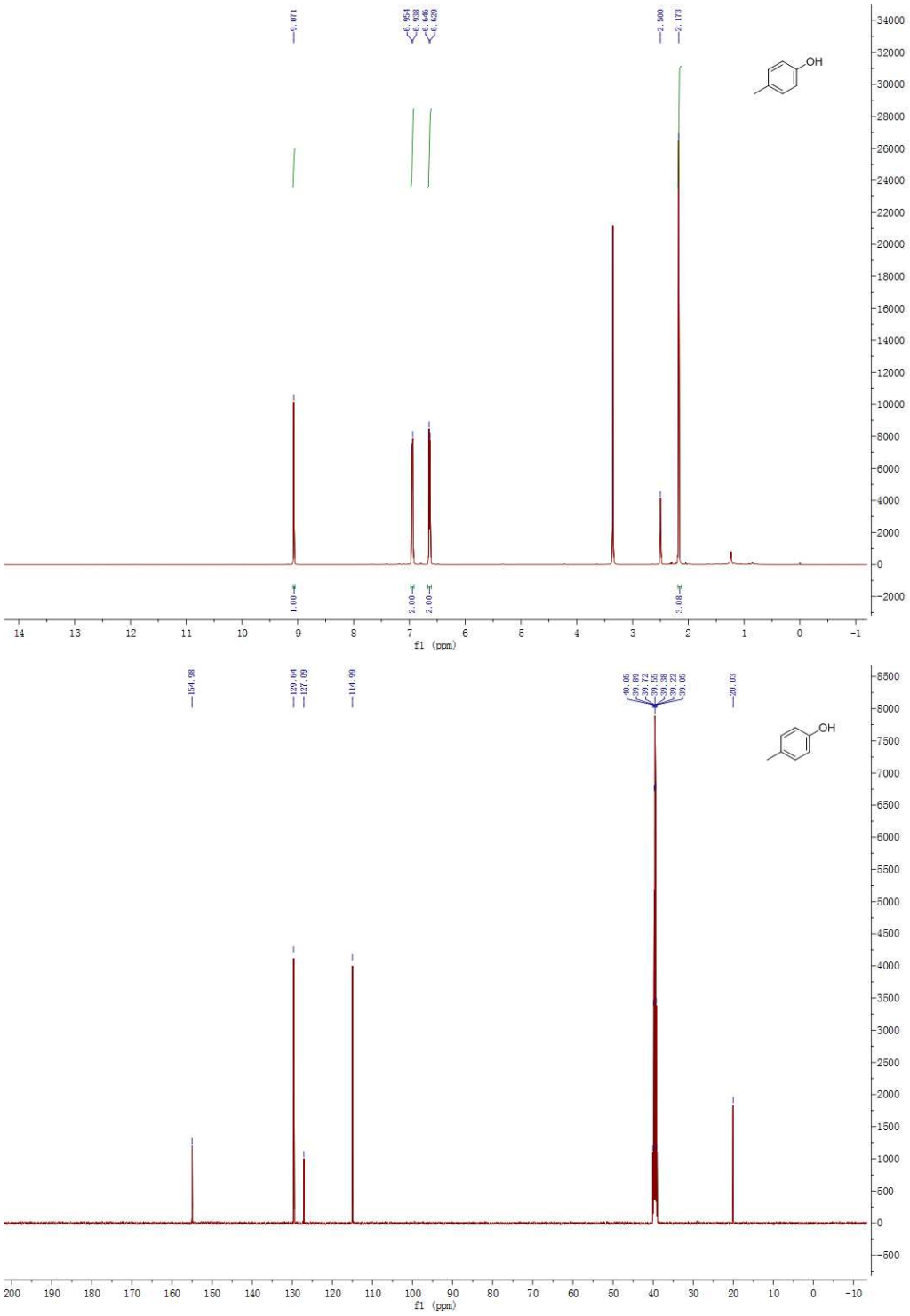


Figure S7. ^{1}H NMR of **3g** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3g** (125 MHz, DMSO-d_6)

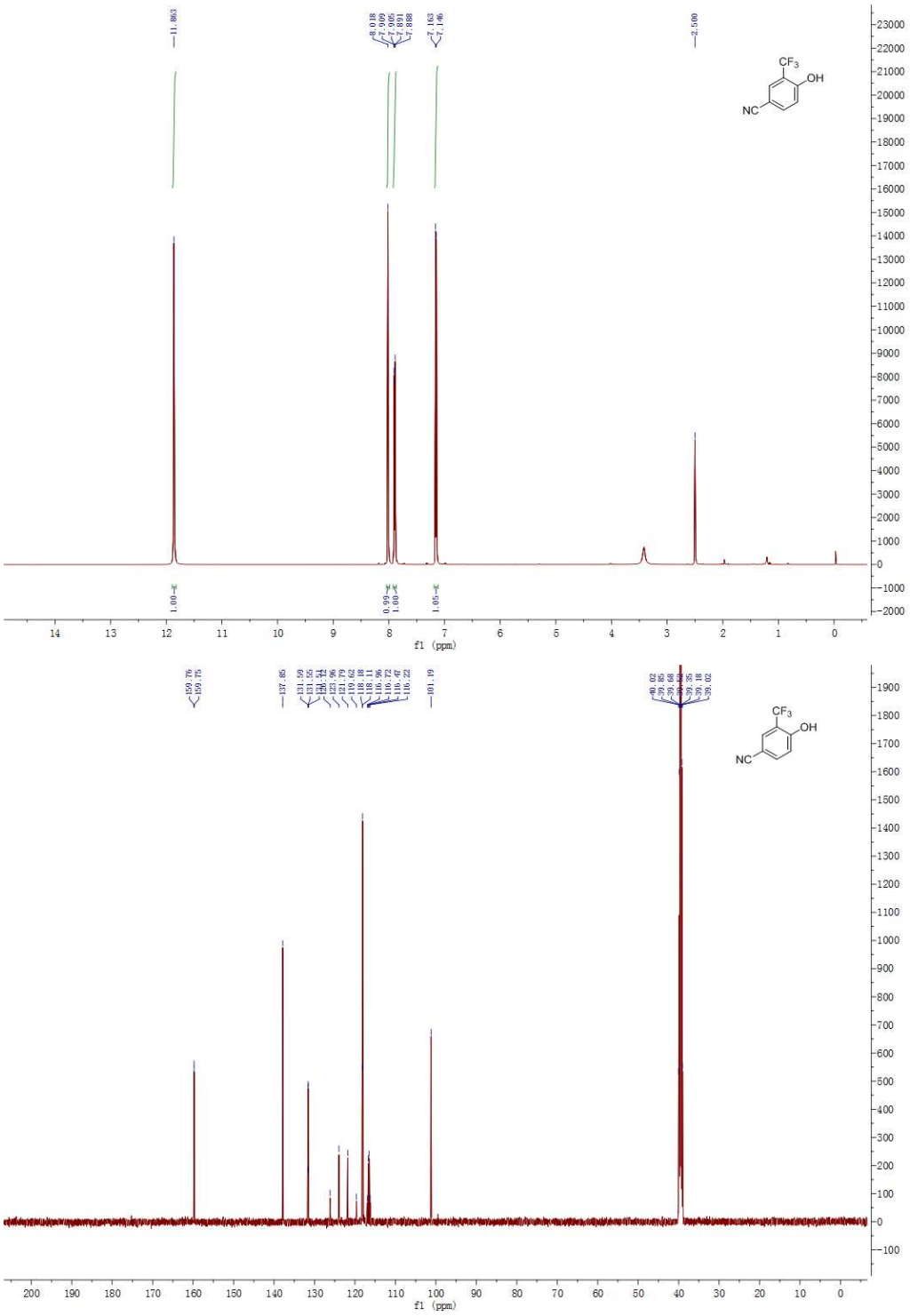


Figure S8. ^{1}H NMR of **3h** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3h** (125 MHz, DMSO-d_6)

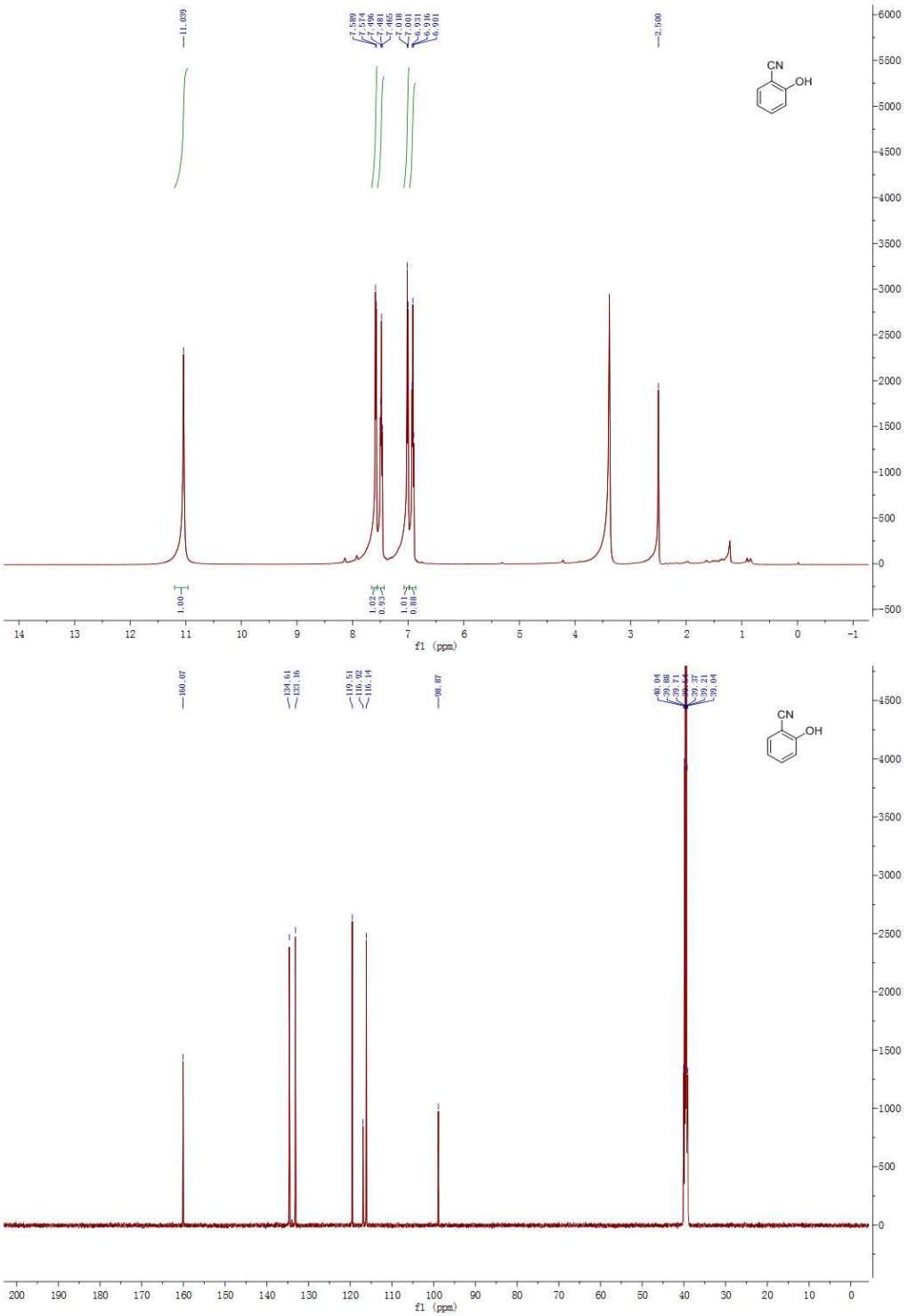


Figure S9. ^{1}H NMR of **3i** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3i** (125 MHz, DMSO-d_6)

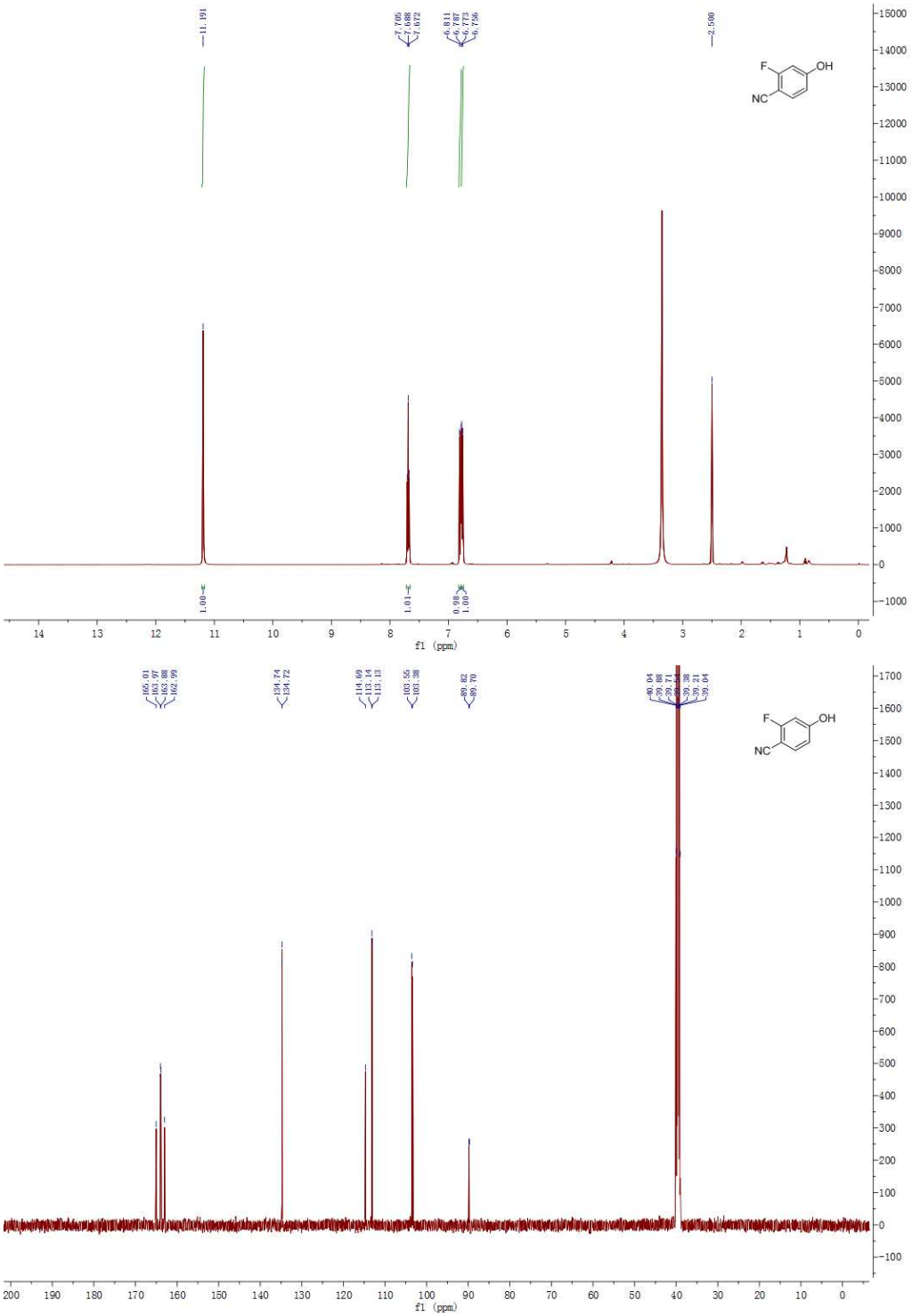


Figure S10. ^{1}H NMR of **3j** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3j** (125 MHz, DMSO-d_6)

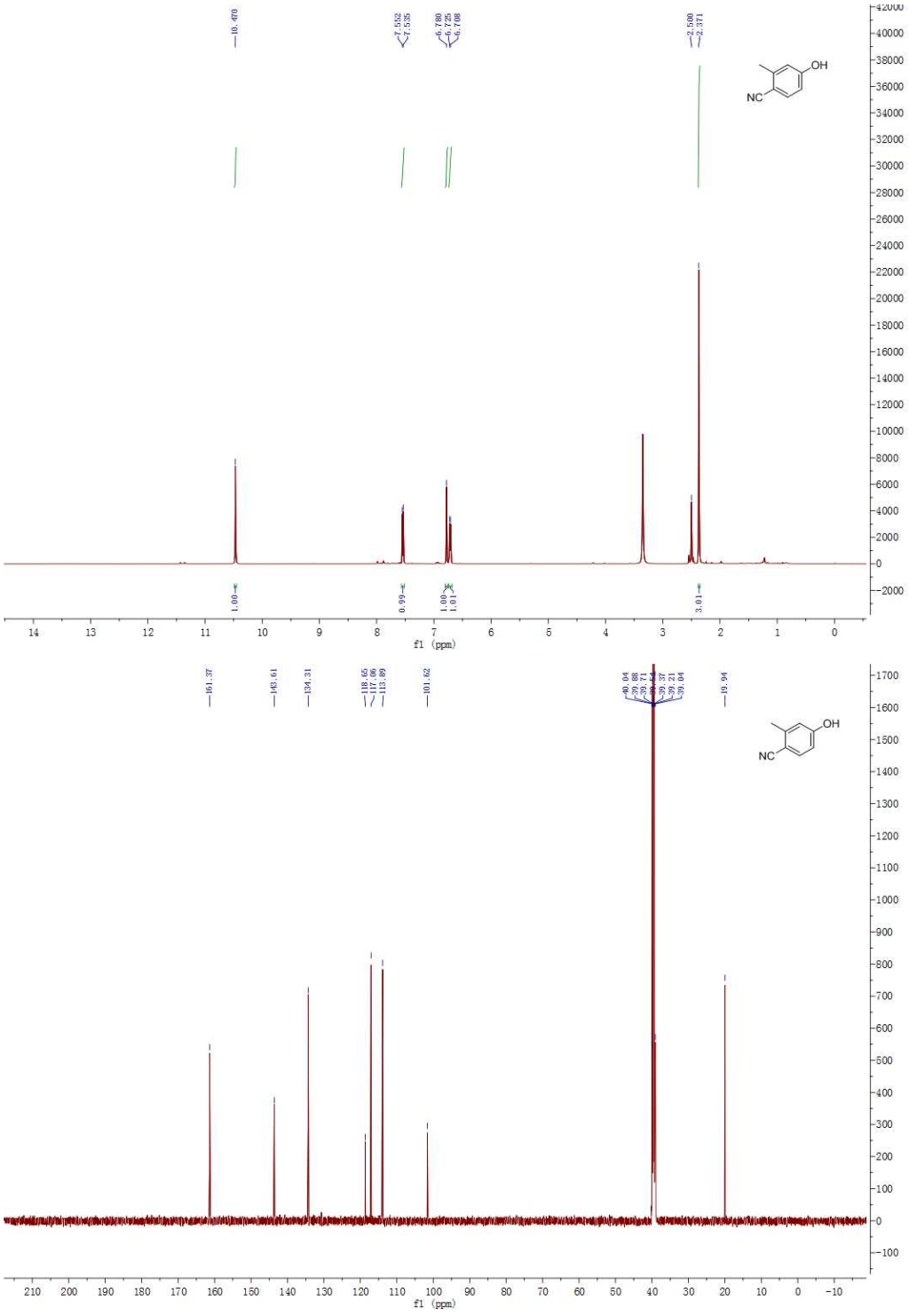


Figure S11. ^{1}H NMR of **3k** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3k** (125 MHz, DMSO-d_6)

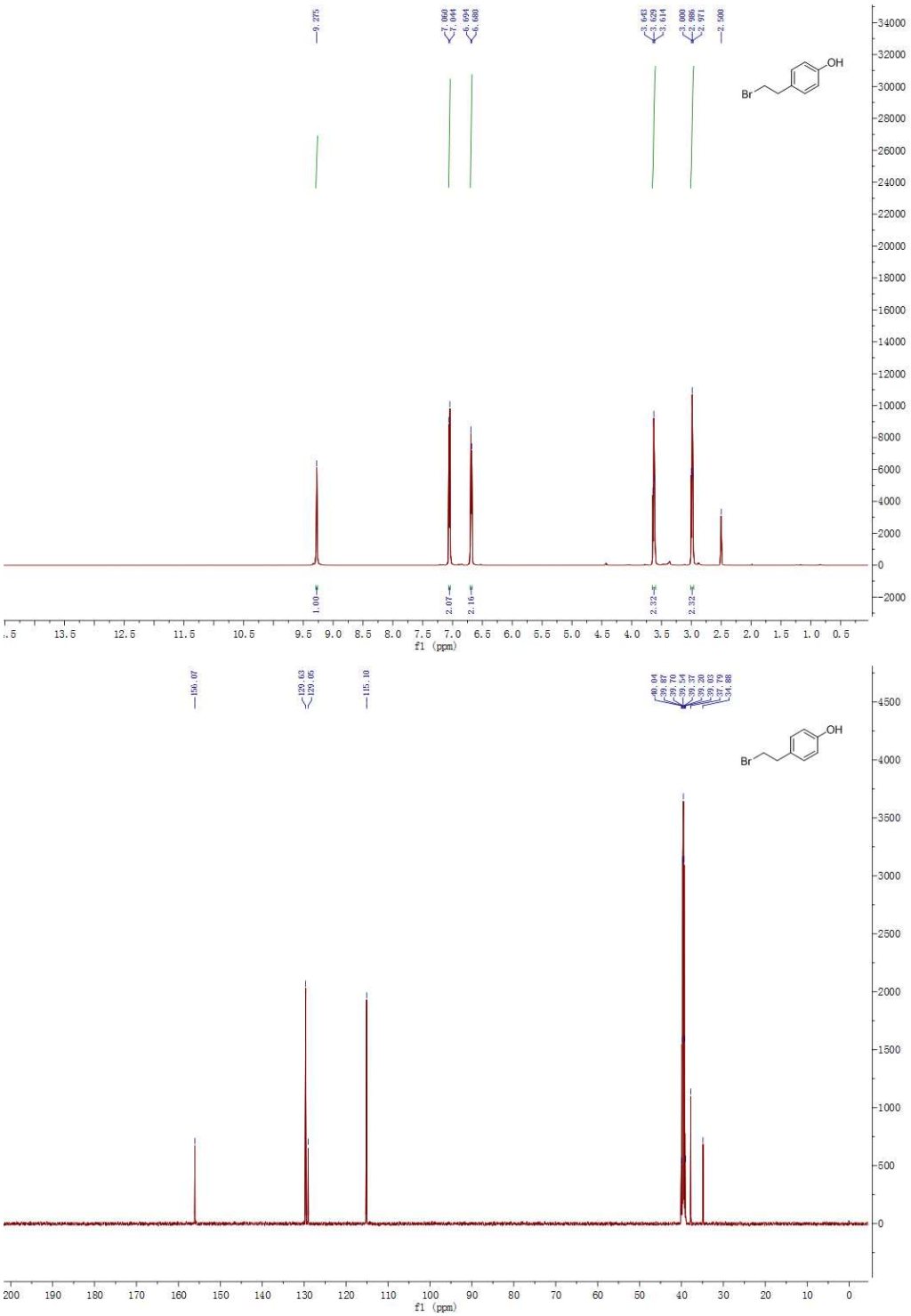


Figure S12. ^{1}H NMR of **3l** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3l** (125 MHz, DMSO-d_6)

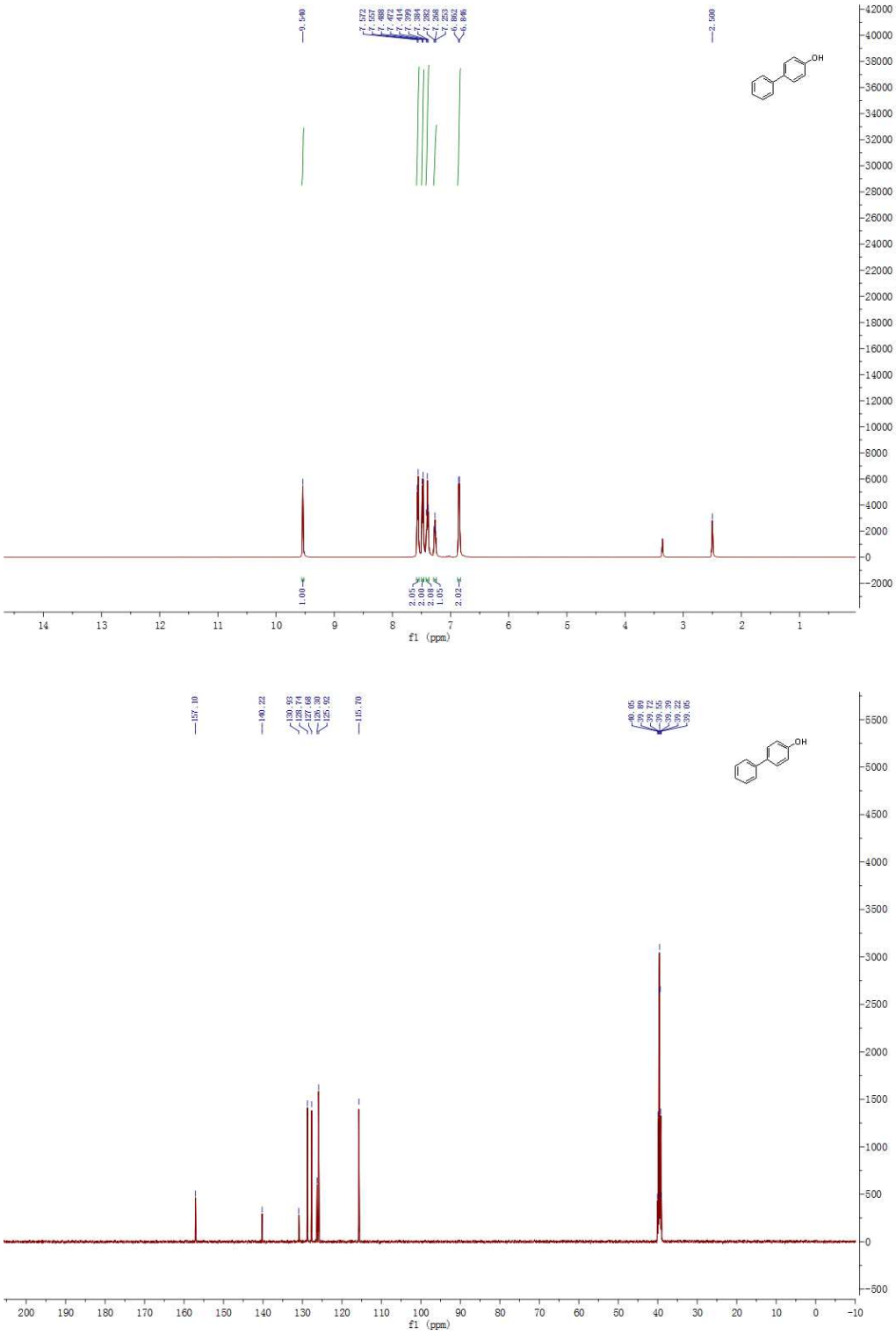


Figure S13. ^{1}H NMR of **3m** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3m** (125 MHz, DMSO-d_6)

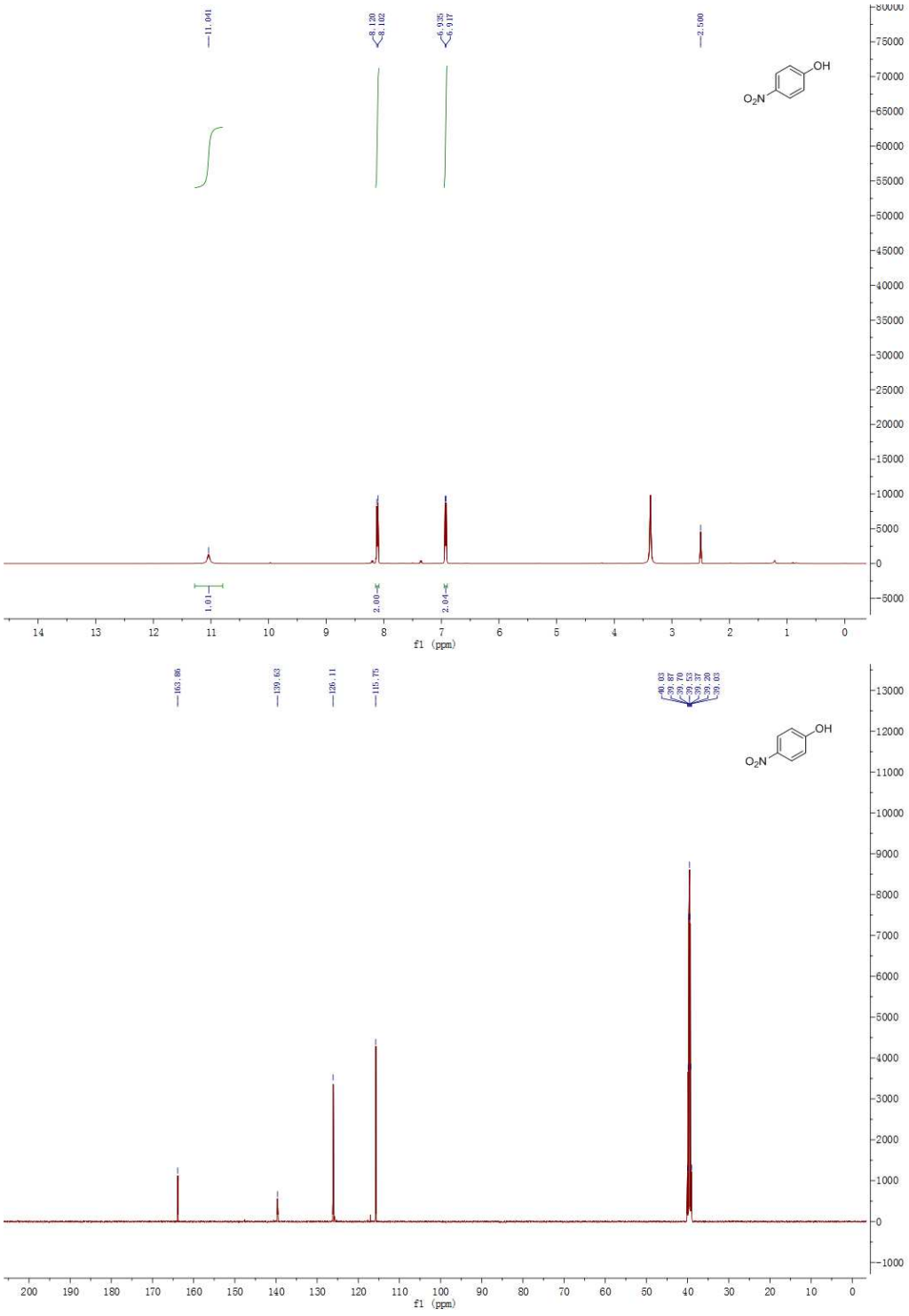


Figure S14. ^{1}H NMR of **3n** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3n** (125 MHz, DMSO-d_6)

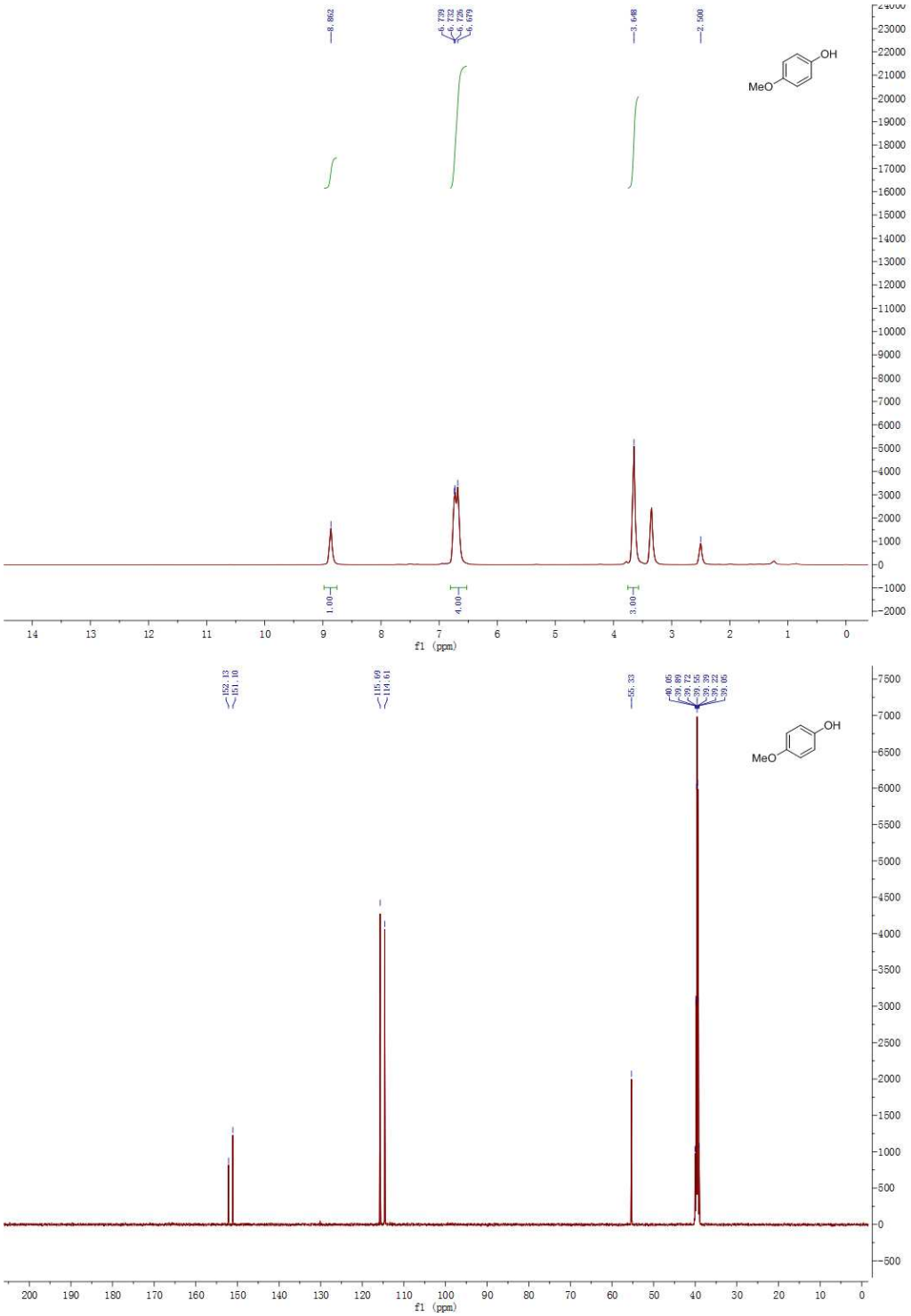


Figure S15. ^{1}H NMR of **3o** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3o** (125 MHz, DMSO-d_6)

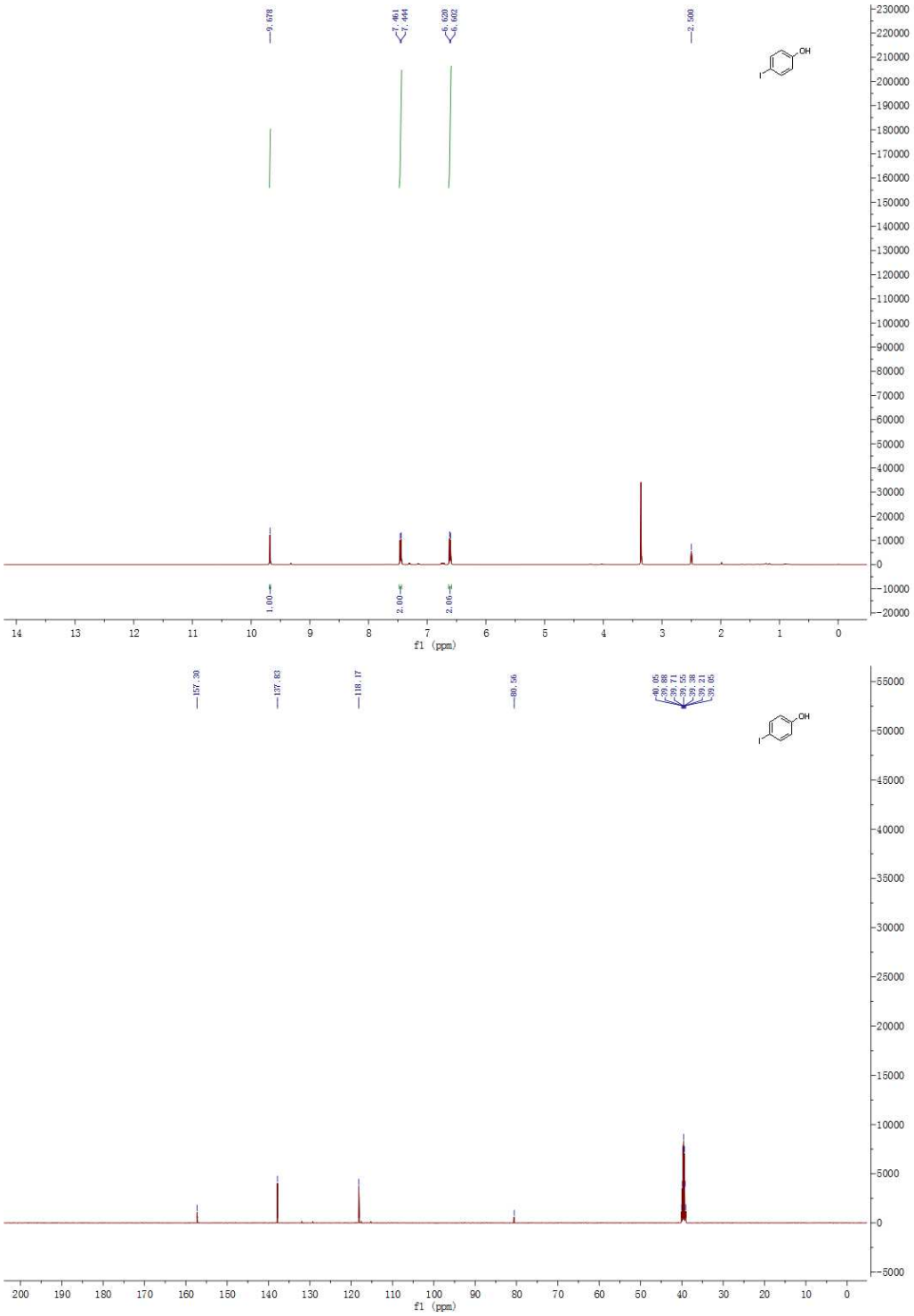


Figure S16. ^{1}H NMR of **3p** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3p** (125 MHz, DMSO-d_6)

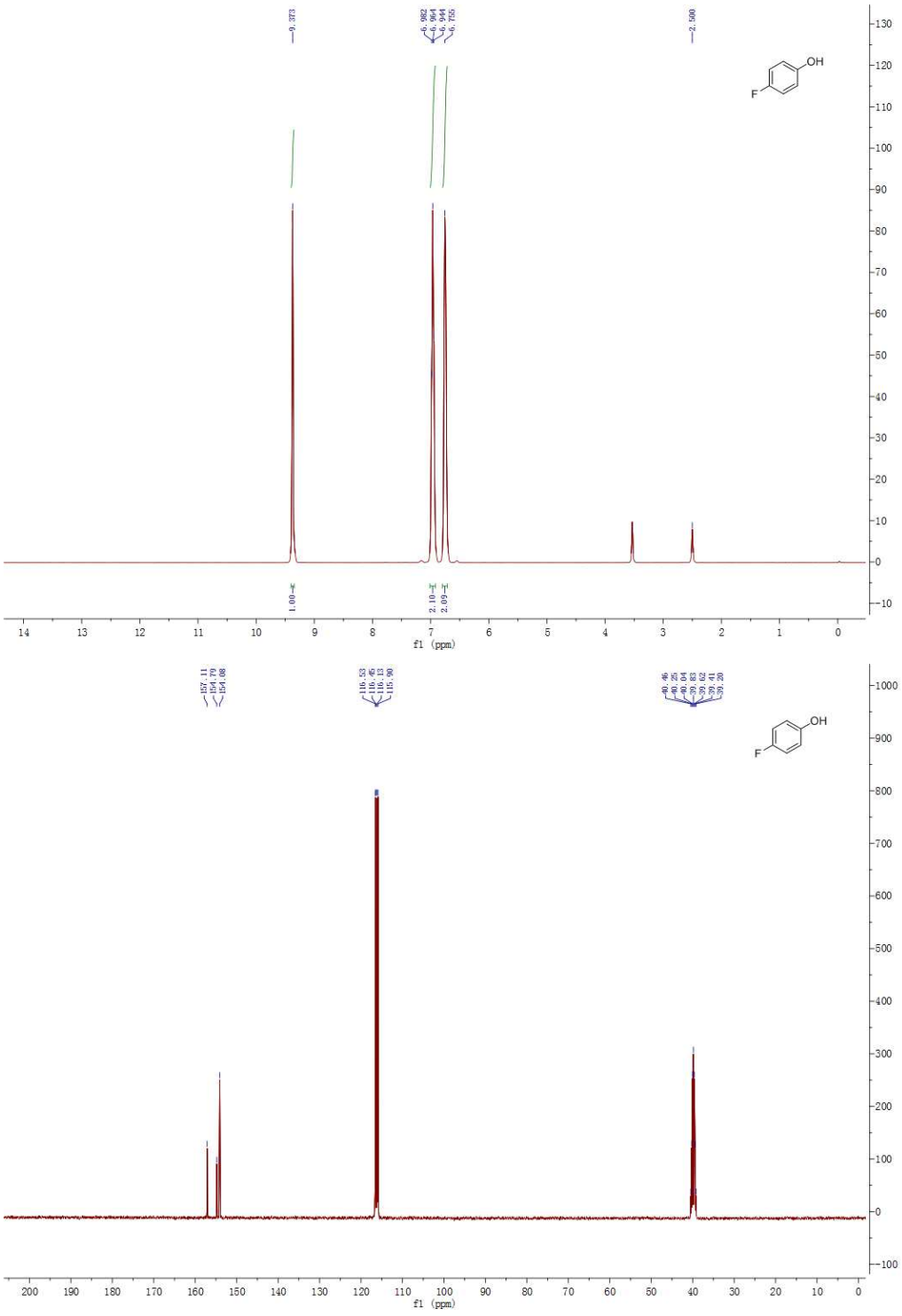


Figure S17. ^{1}H NMR of **3q** (400 MHz, DMSO-d_6) and ^{13}C NMR of **3q** (100 MHz, DMSO-d_6)

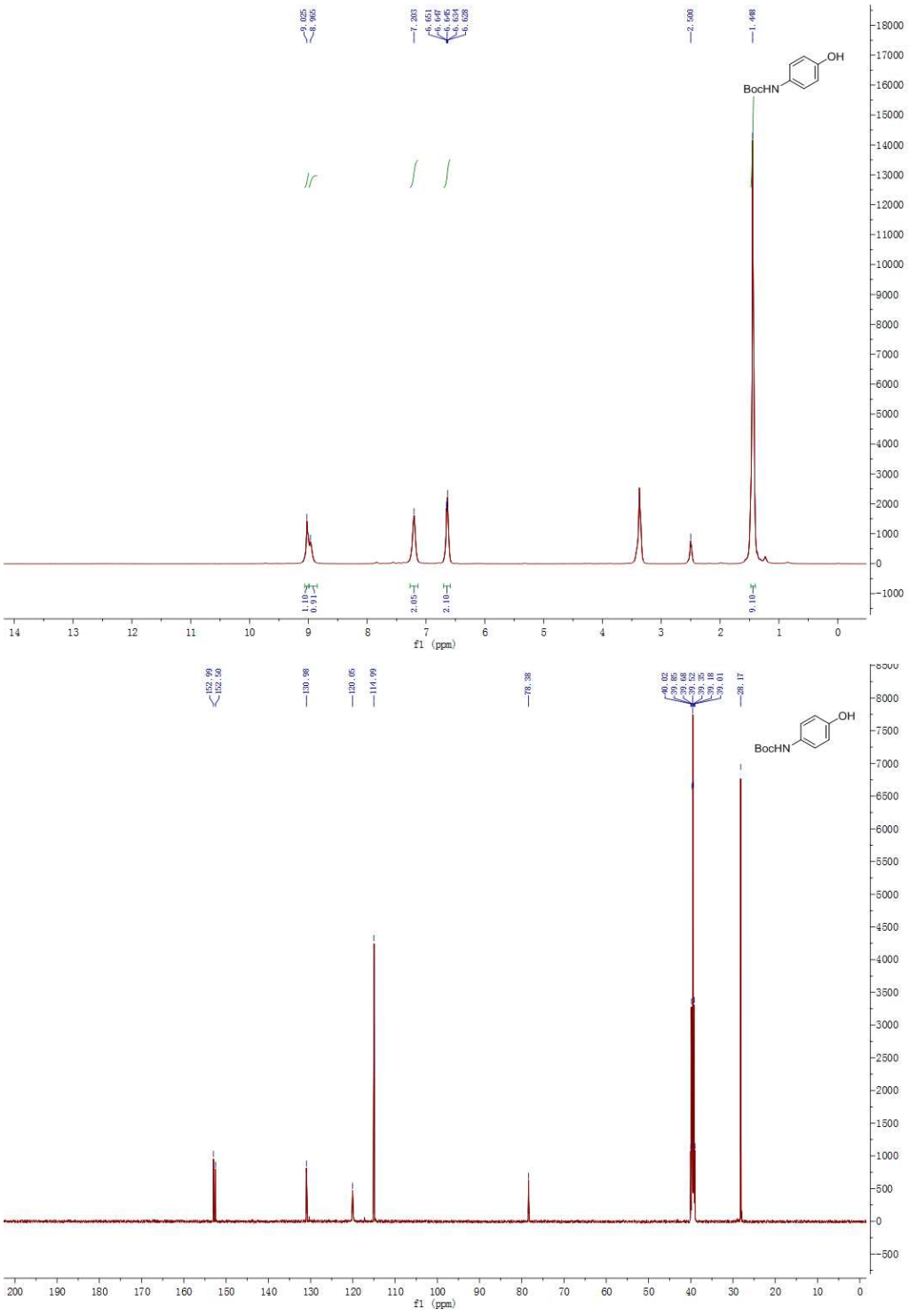


Figure S18. ^{1}H NMR of **3r** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3r** (125 MHz, DMSO-d_6)

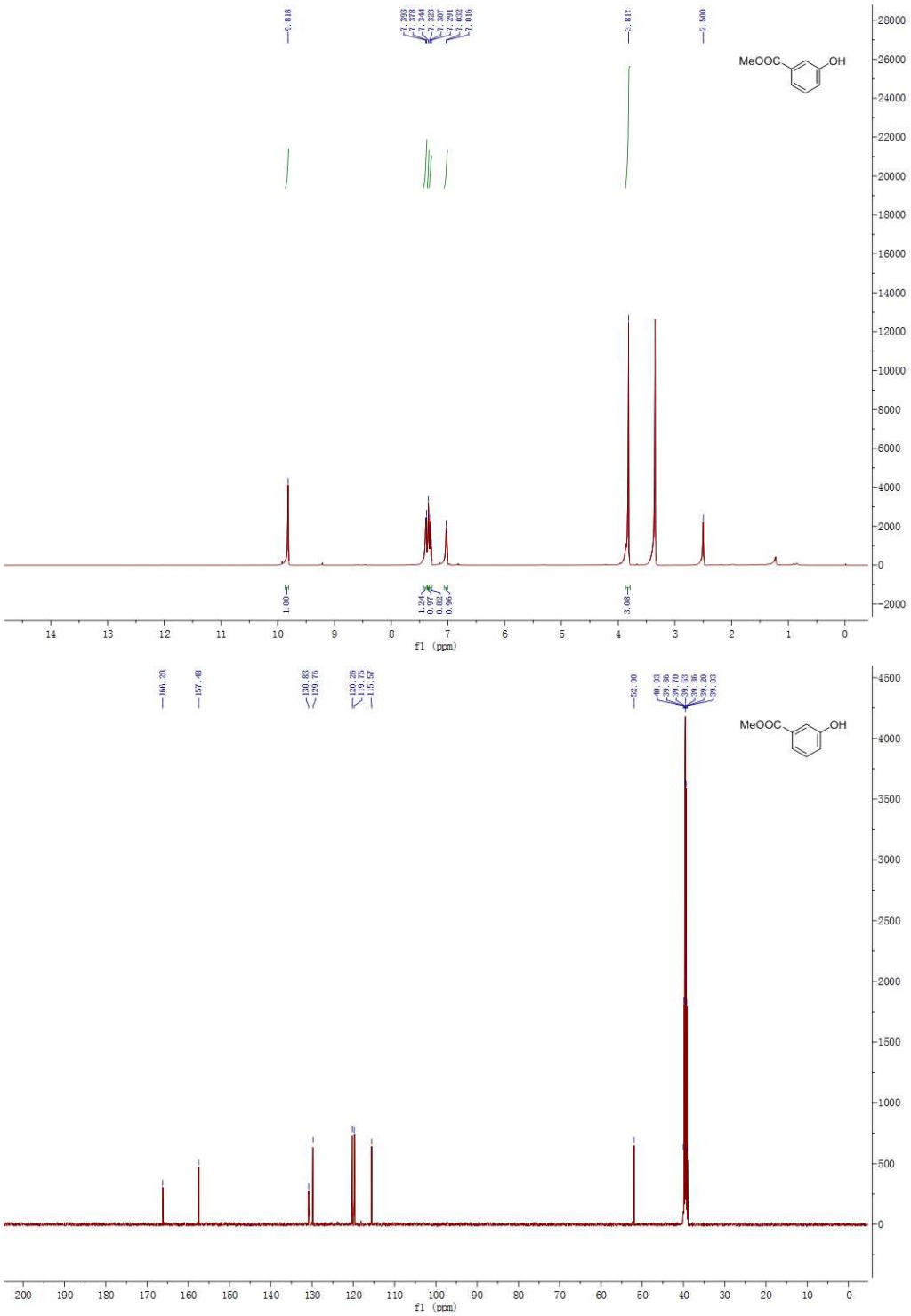


Figure S19. ^{1}H NMR of **3s** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3s** (125 MHz, DMSO-d_6)

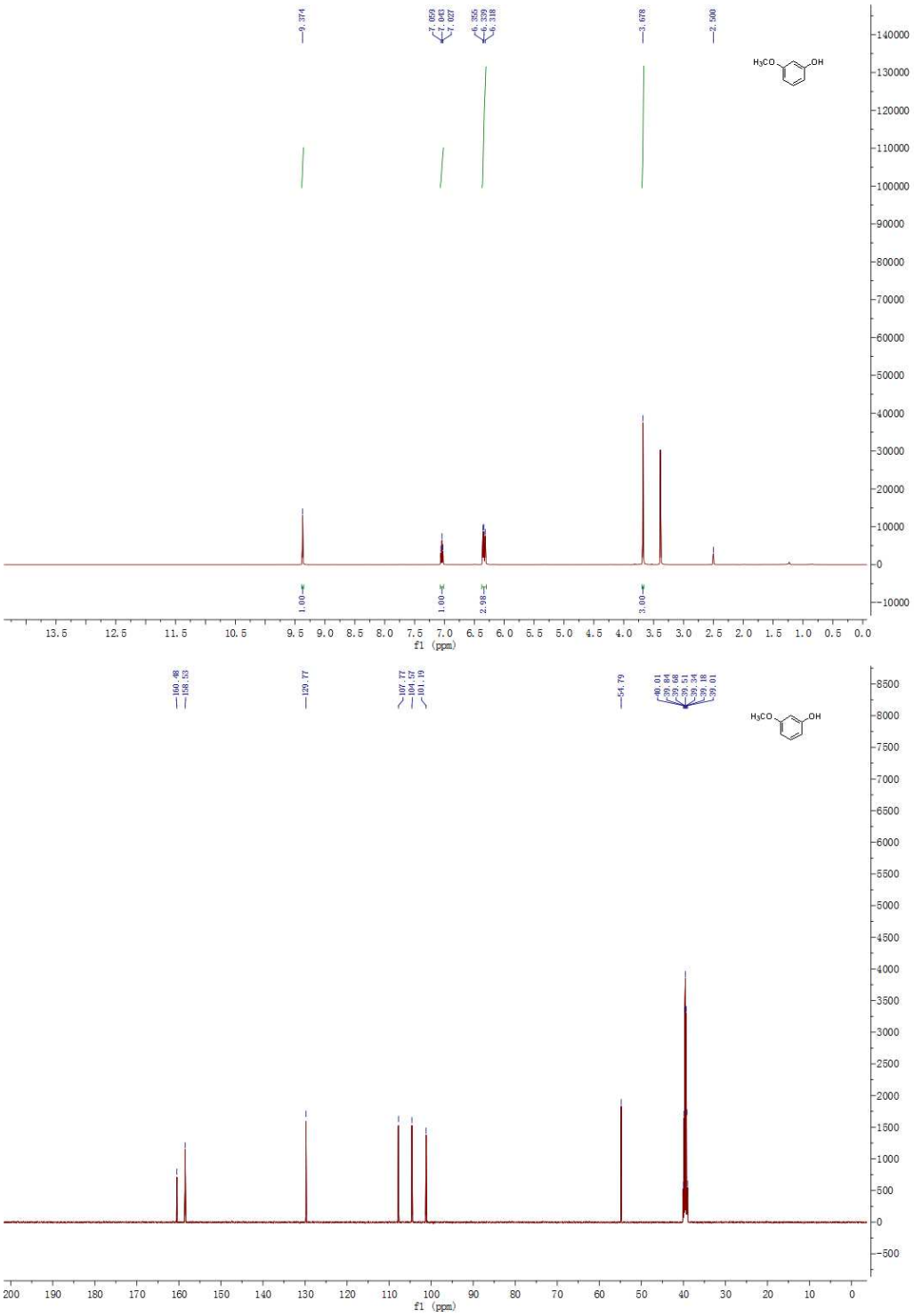


Figure S19. ^{1}H NMR of **3t** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3t** (500 MHz, DMSO-d_6)

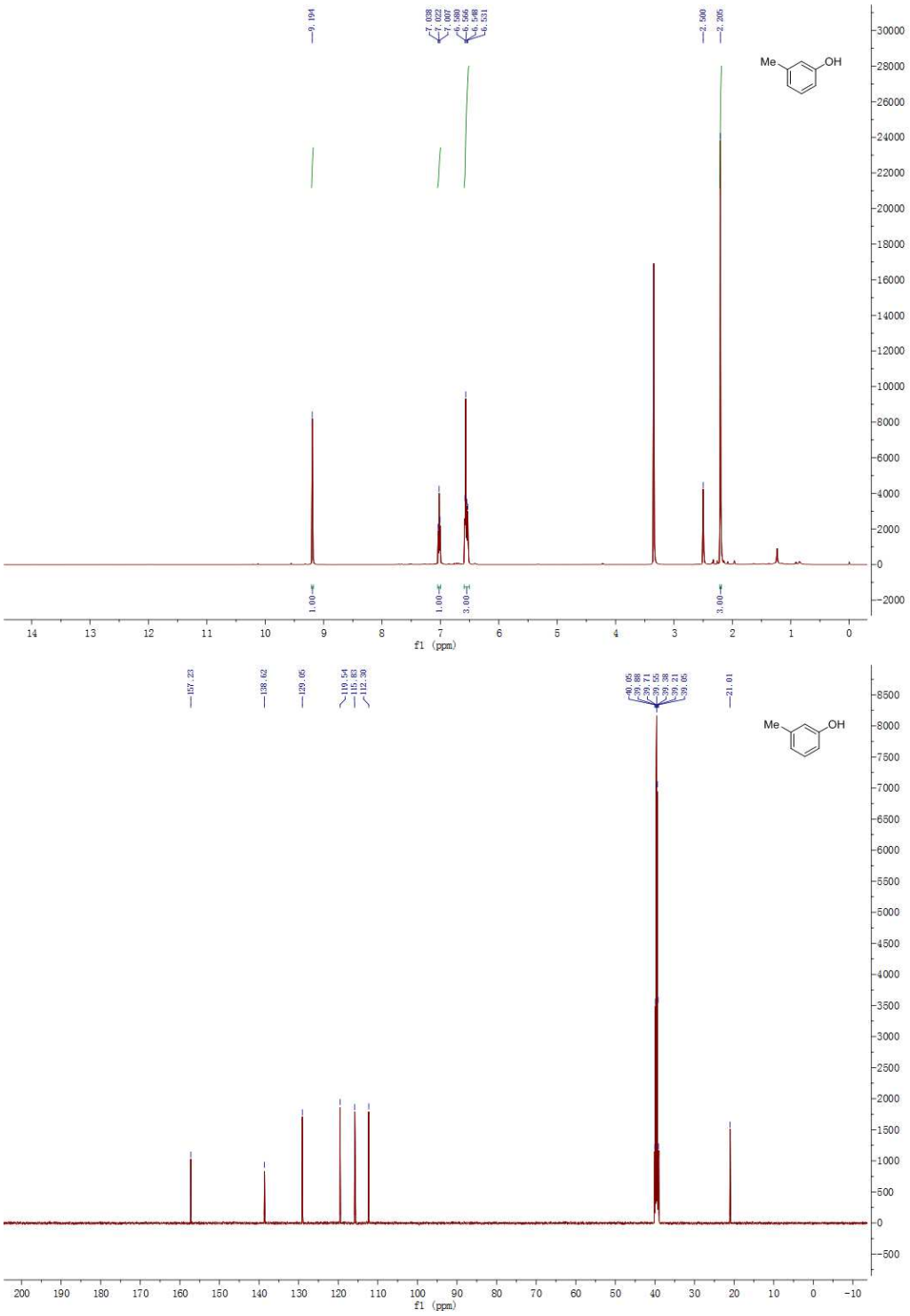


Figure S20. ^{1}H NMR of **3u** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3u** (125 MHz, DMSO-d_6)

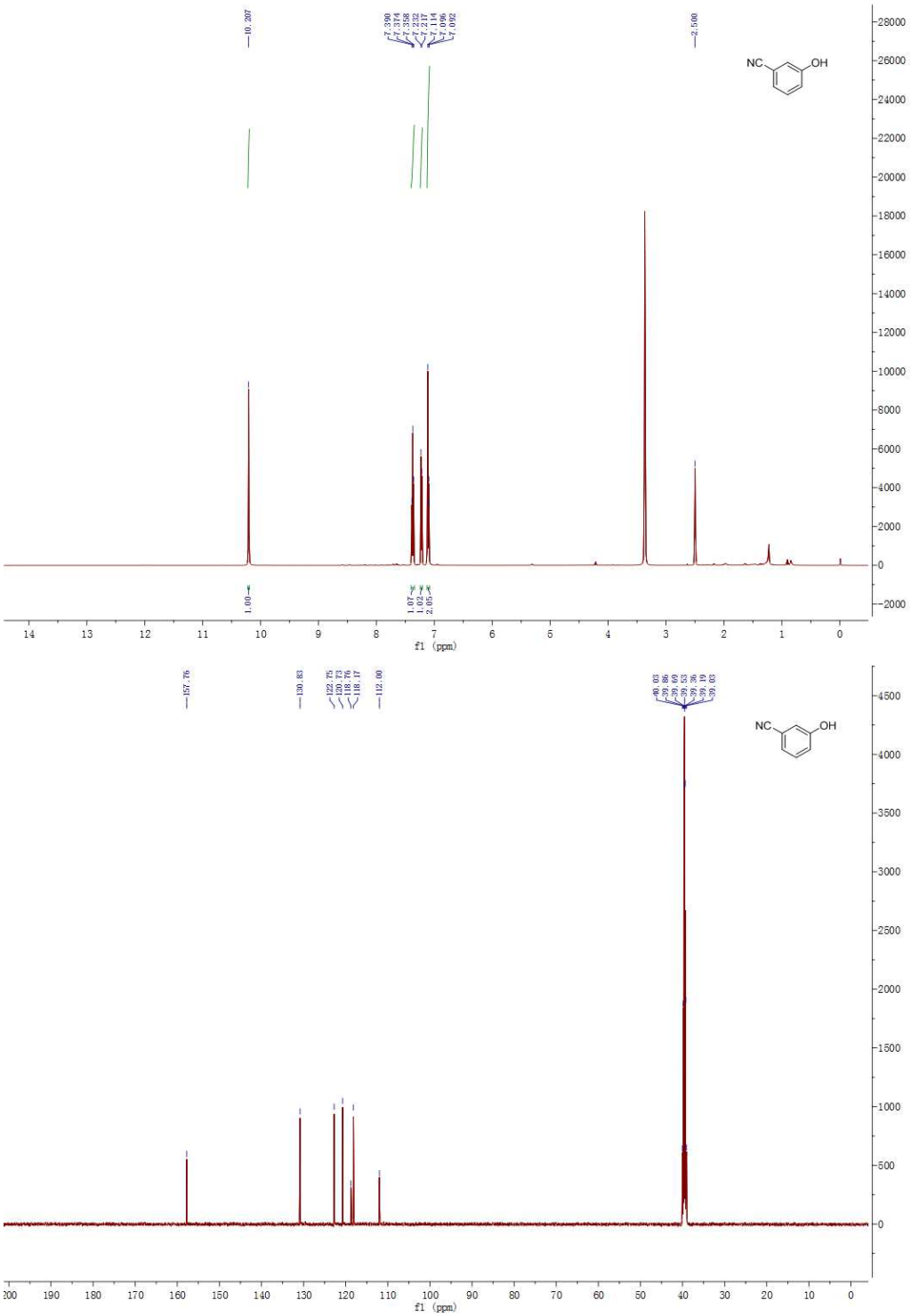


Figure S21. ^{1}H NMR of **3v** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3v** (125 MHz, DMSO-d_6)

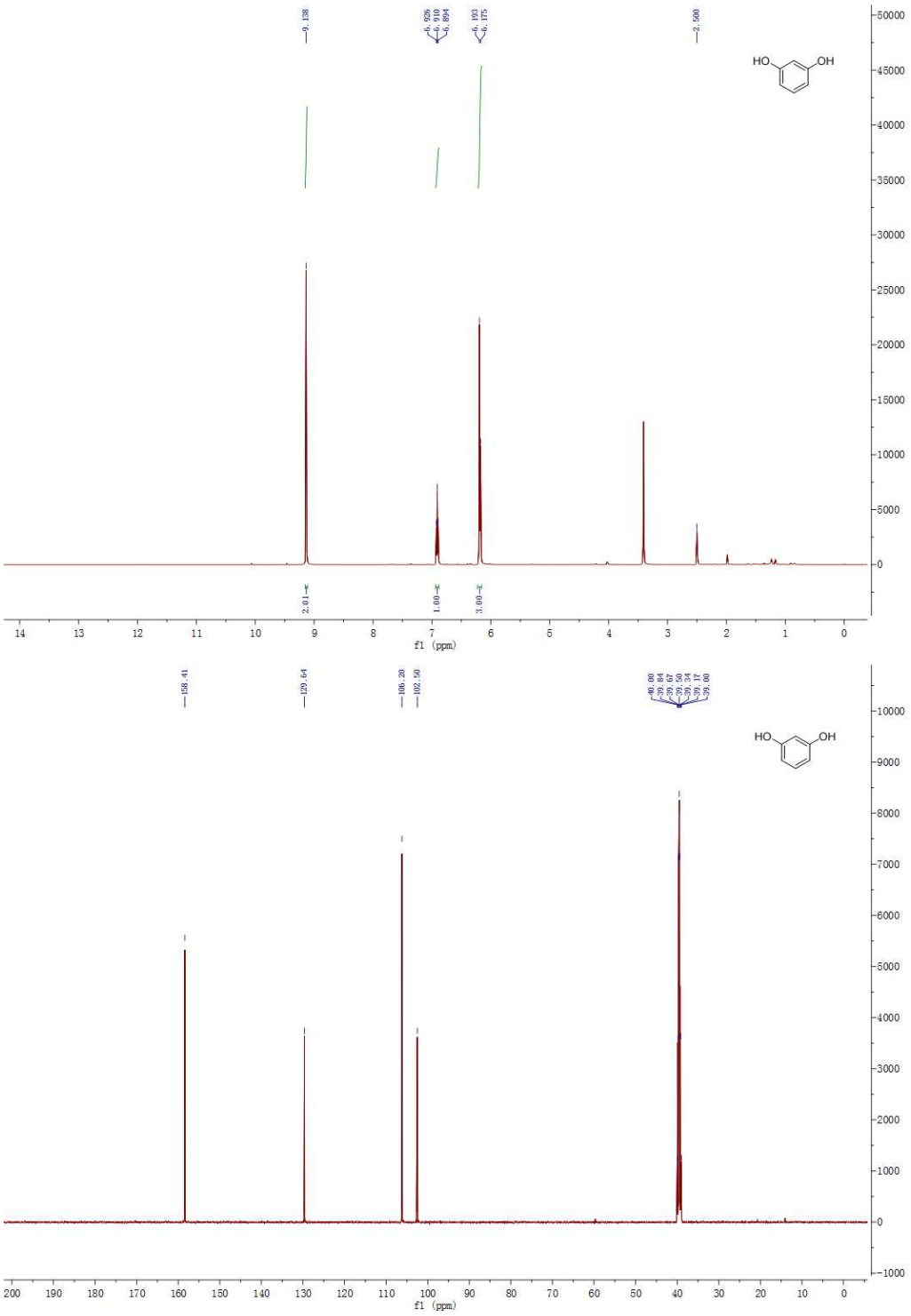


Figure S22. ^{1}H NMR of **3w** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3w** (125 MHz, DMSO-d_6)

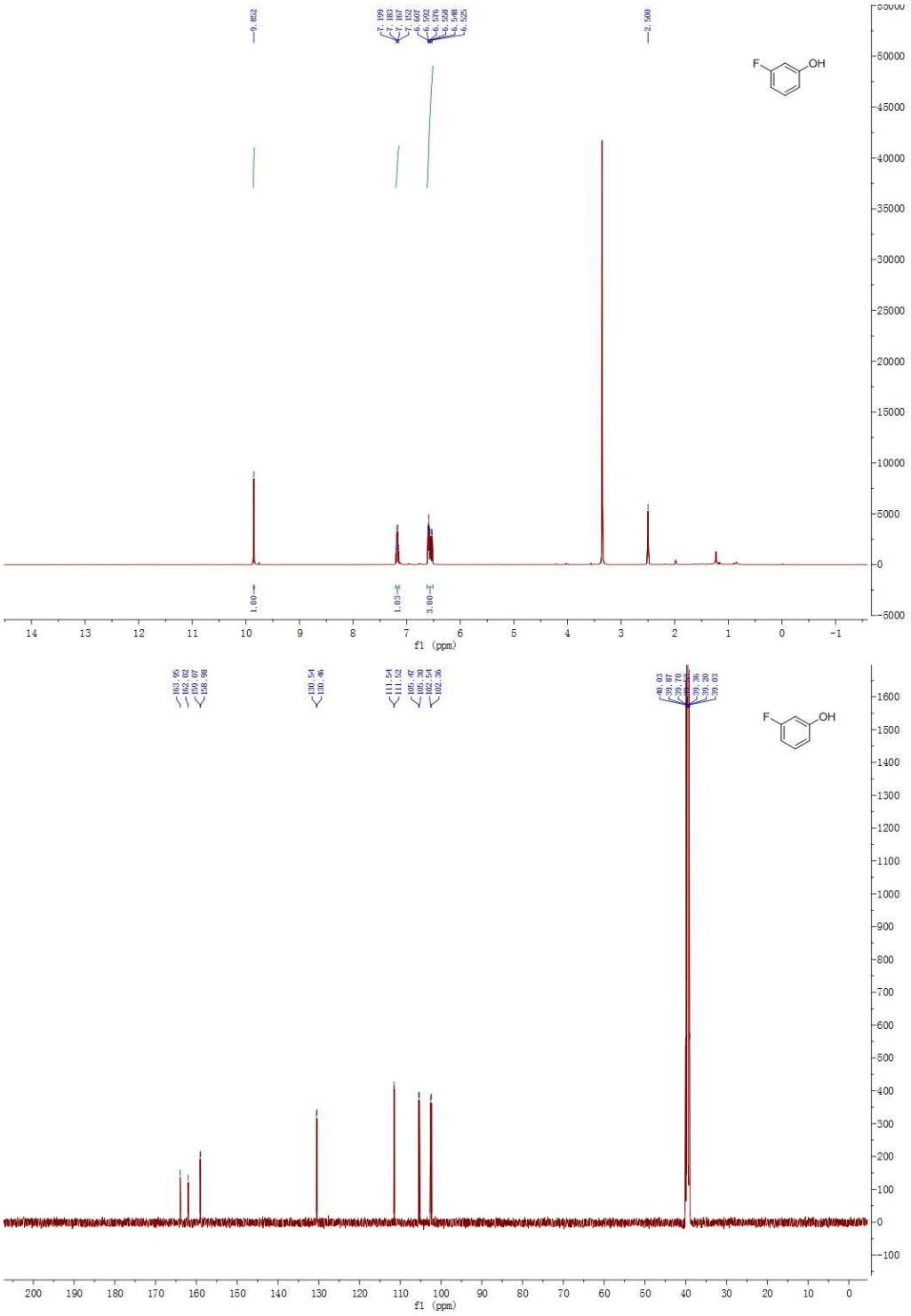


Figure S23. ^{1}H NMR of **3x** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3x** (125 MHz, DMSO-d_6)

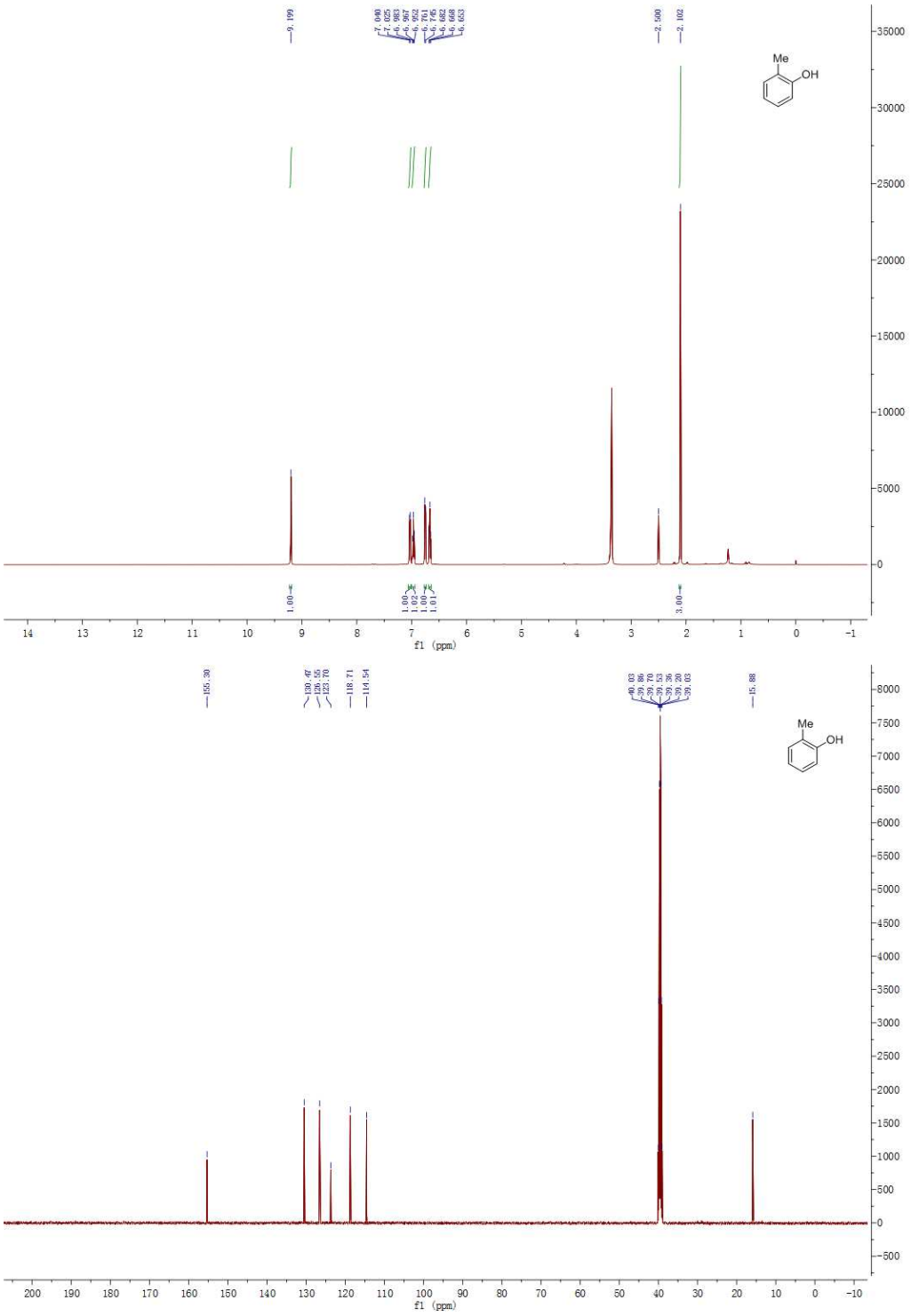


Figure S24. ^{1}H NMR of **3y** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3y** (125 MHz, DMSO-d_6)

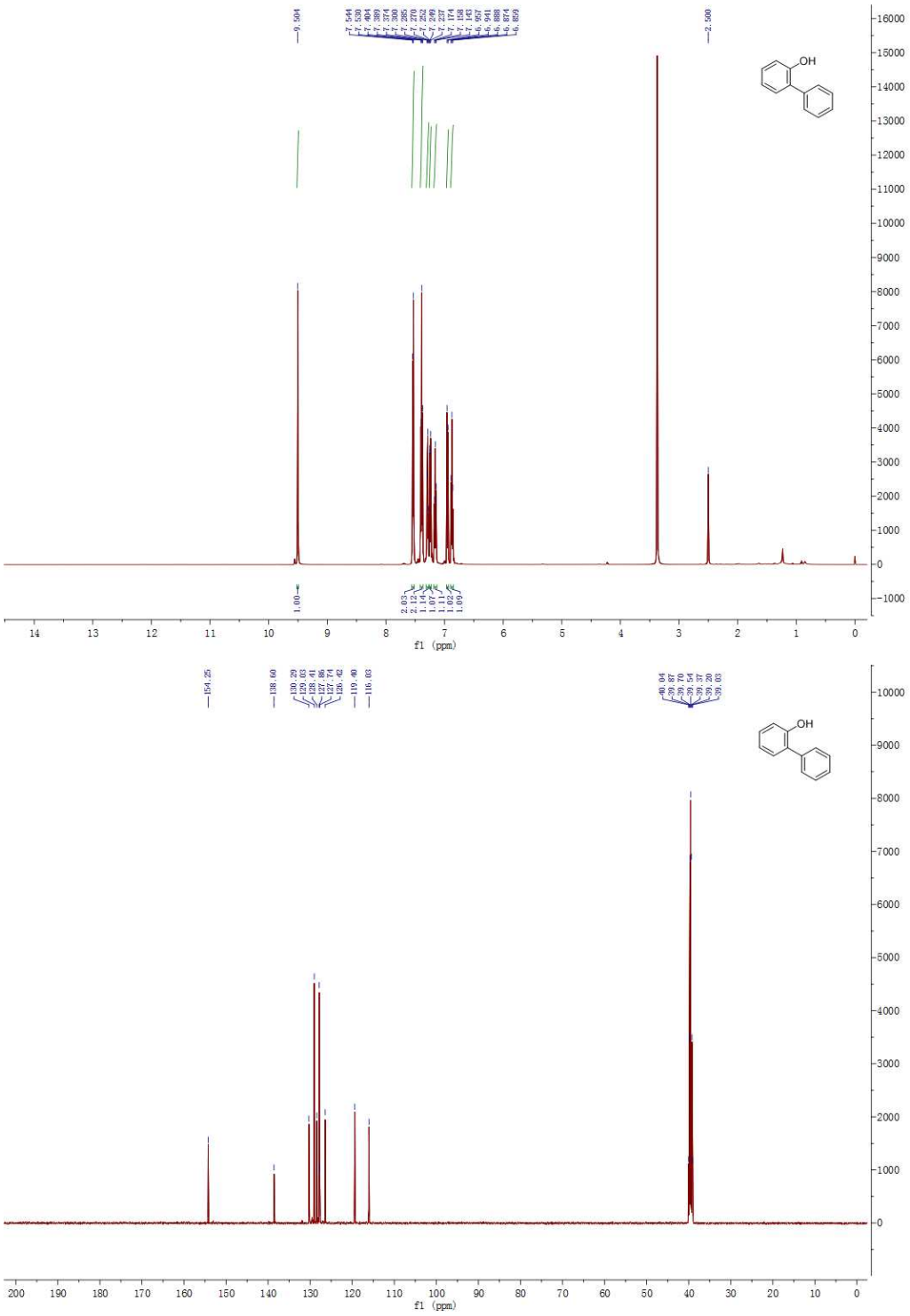


Figure S25. ^{1}H NMR of **3z** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3z** (125 MHz, DMSO-d_6)

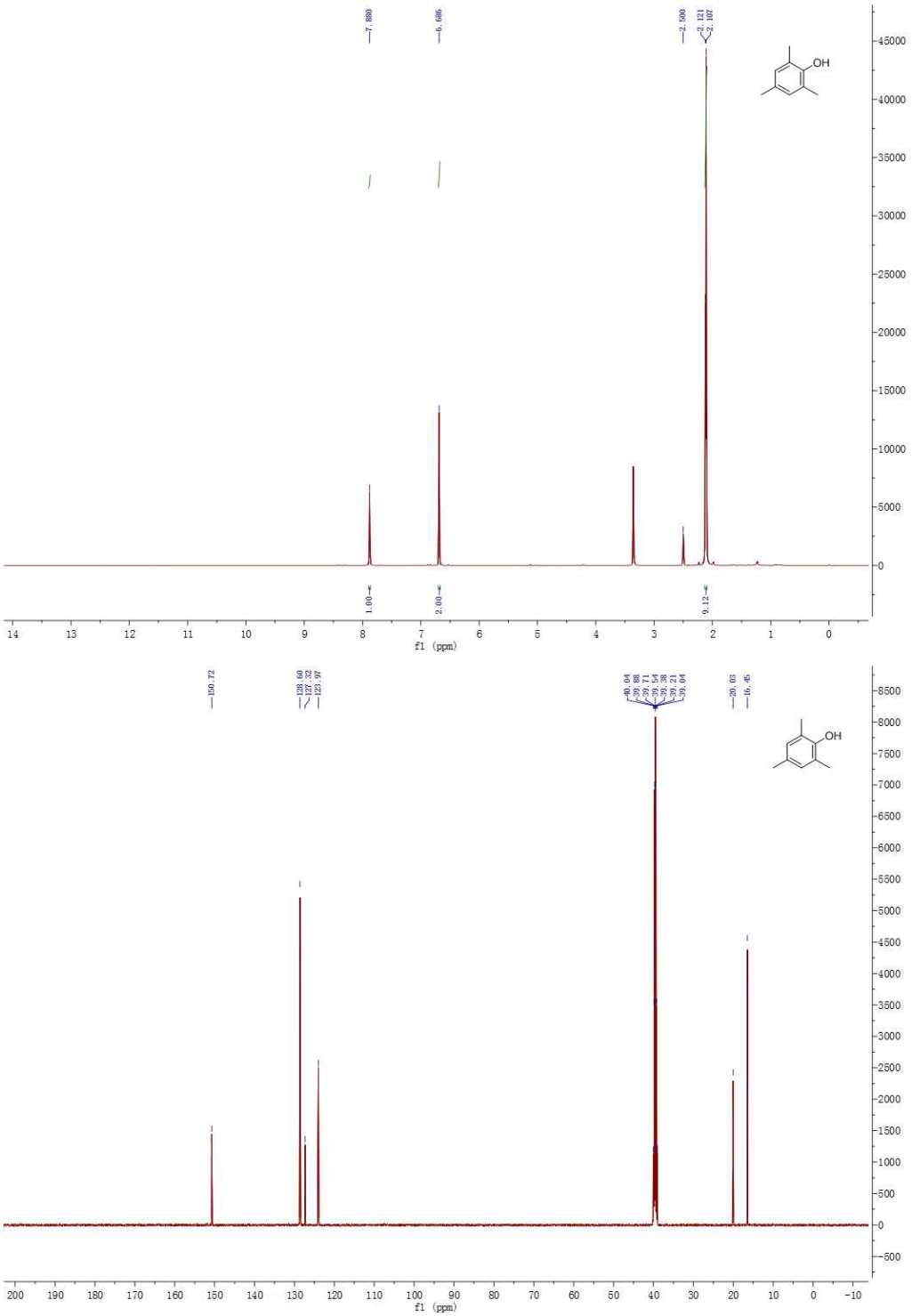


Figure S26. ^{1}H NMR of **3aa** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3aa** (125 MHz, DMSO-d_6)

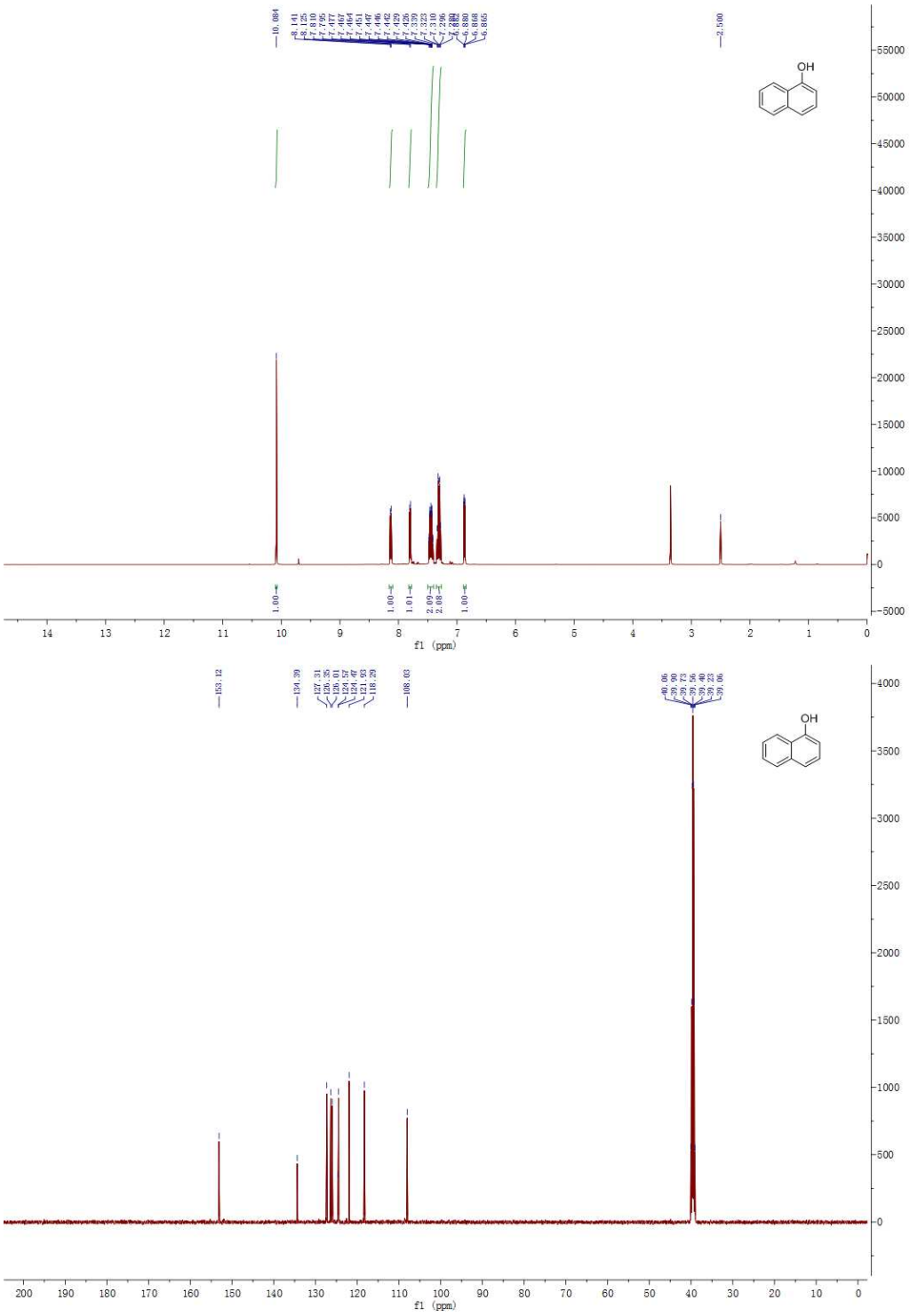


Figure S27. ^{1}H NMR of **3ab** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3ab** (500 MHz, DMSO-d_6)

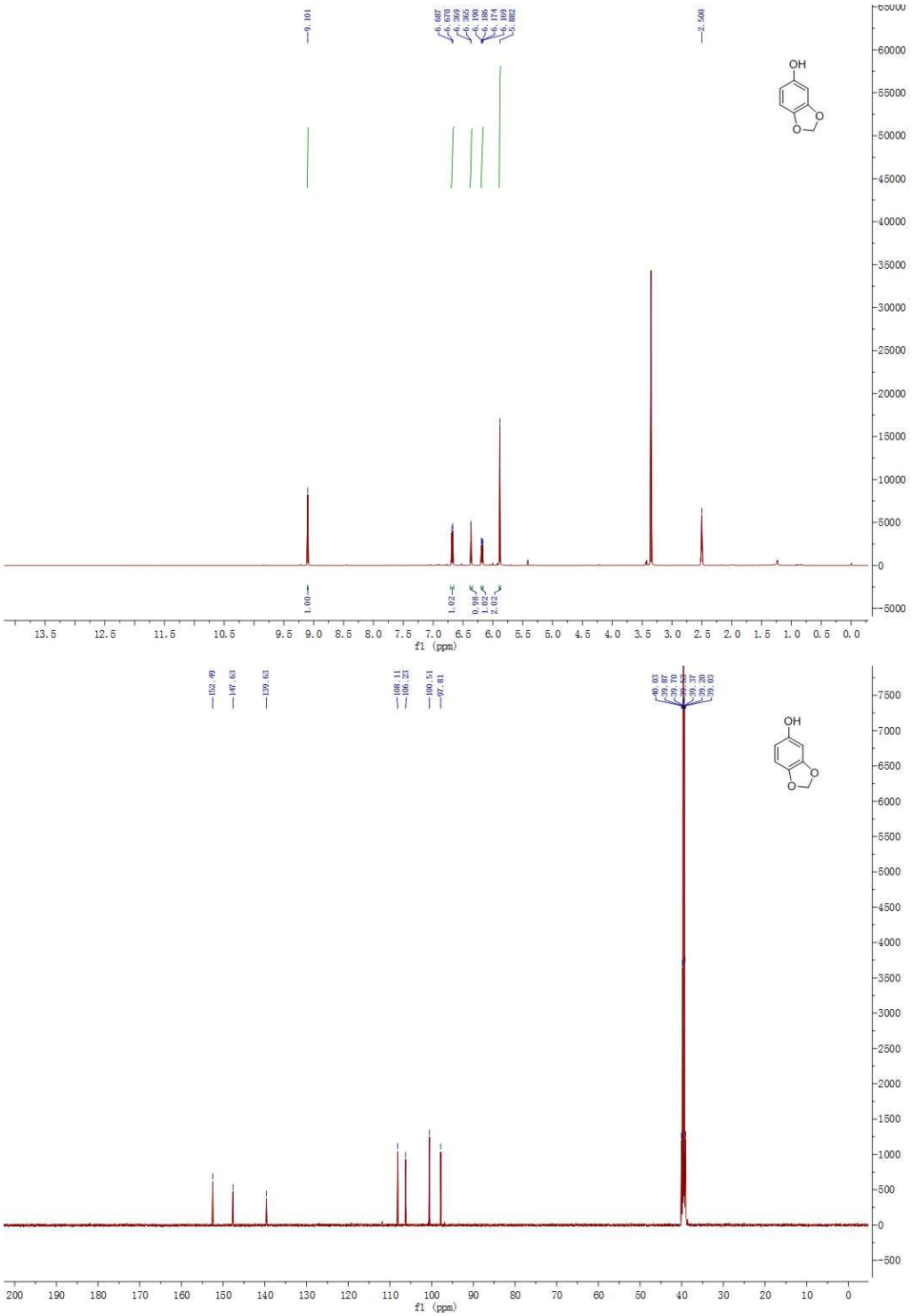


Figure S28. ^{1}H NMR of **3ac** (500 MHz, DMSO-d_6) and ^{13}C NMR of **3ac** (500 MHz, DMSO-d_6)

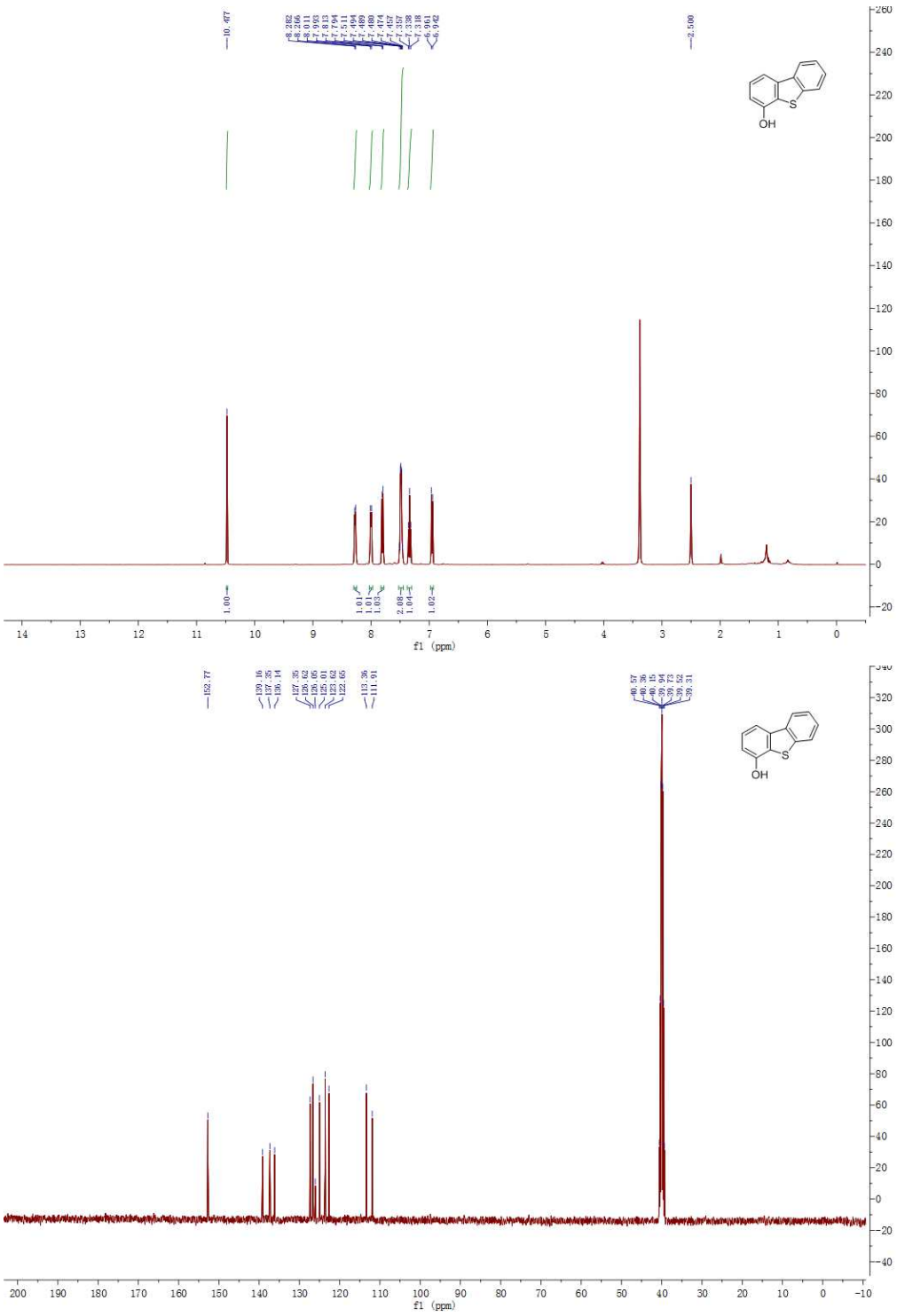


Figure S29. ^{1}H NMR of **3ad** (400 MHz, DMSO-d_6) and ^{13}C NMR of **3ad** (100 MHz, DMSO-d_6)

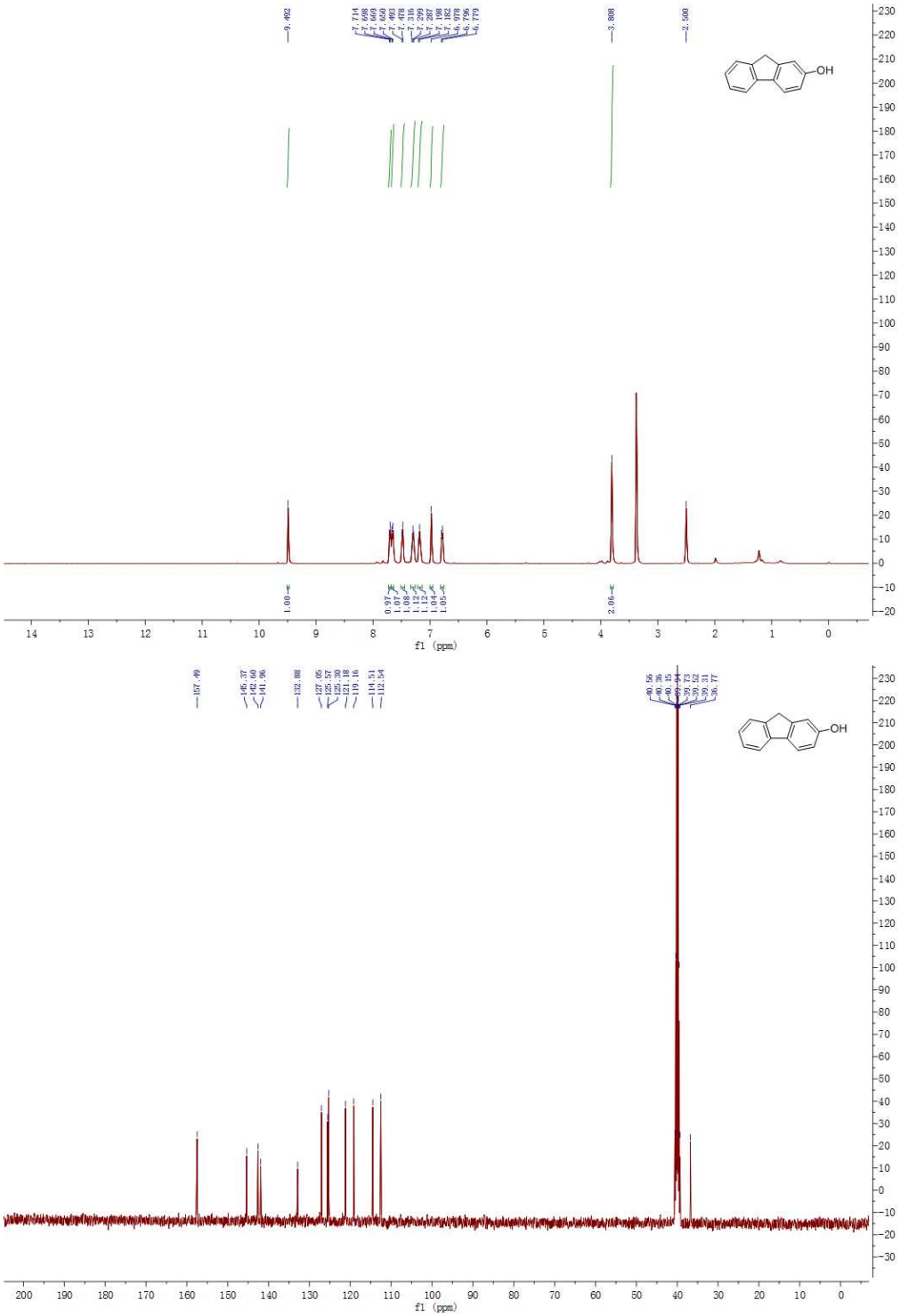


Figure S30. ^{1}H NMR of **3ae** (400 MHz, DMSO-d_6) and ^{13}C NMR of **3ae** (100 MHz, DMSO-d_6)

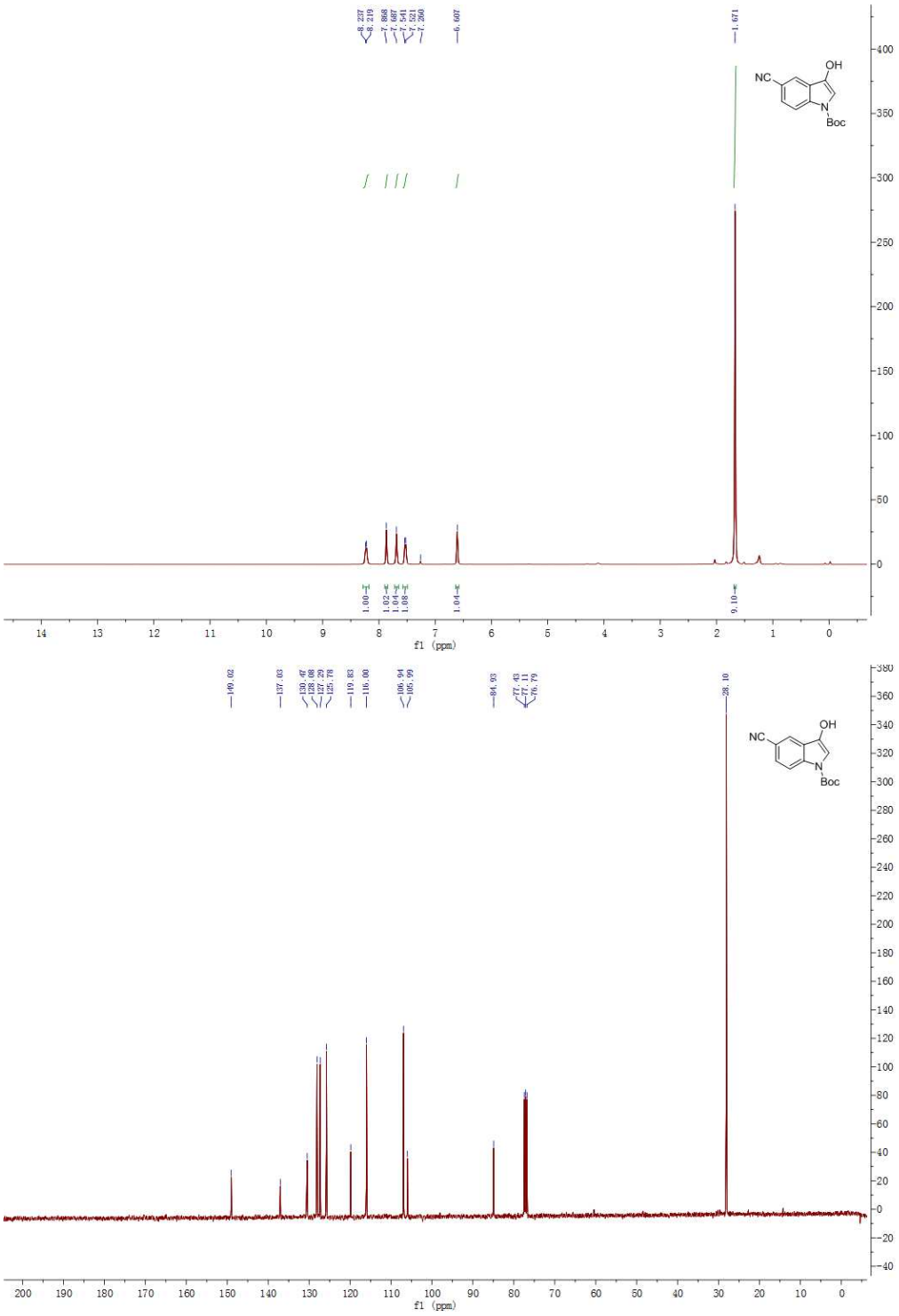


Figure S31. ^{1}H NMR of **3af** (400 MHz, $CDCl_3$) and ^{13}C NMR of **3af** (100 MHz, $CDCl_3$)

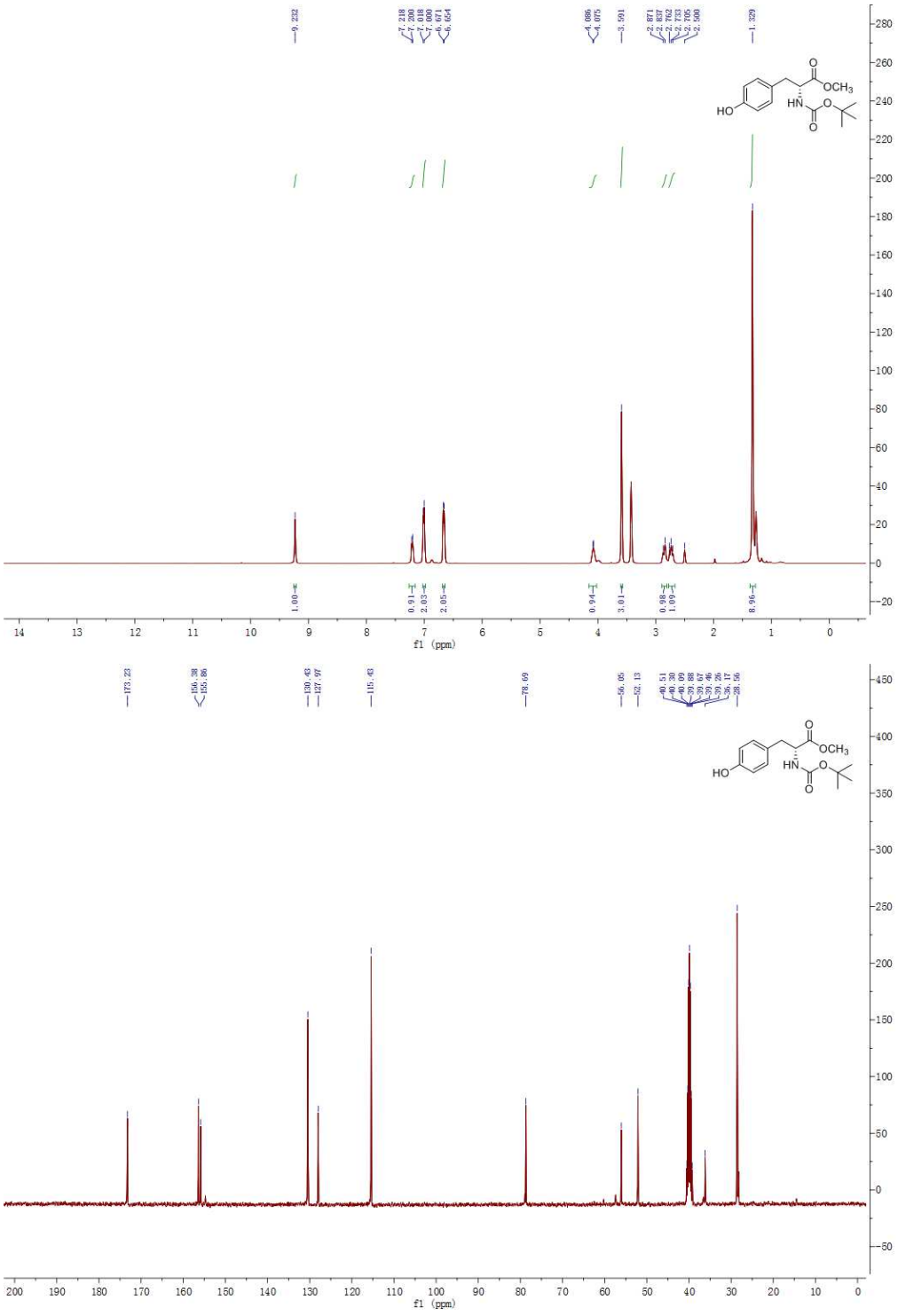


Figure S32. ^{1}H NMR of **4a** (400 MHz, DMSO-d_6) and ^{13}C NMR of **4a** (100 MHz, DMSO-d_6)

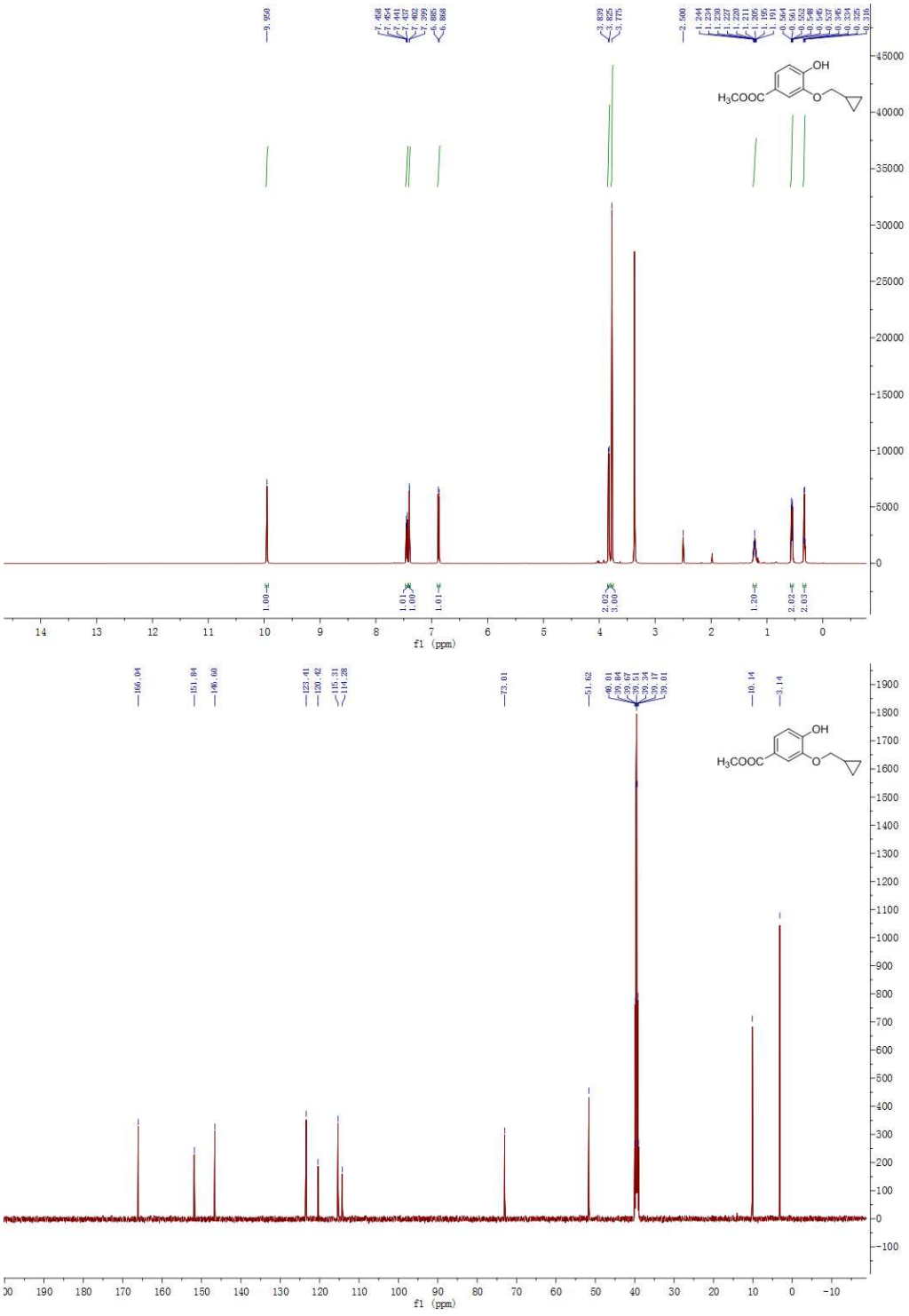


Figure S33. ^{1}H NMR of **4b** (500 MHz, DMSO-d_6) and ^{13}C NMR of **4b** (125 MHz, DMSO-d_6)

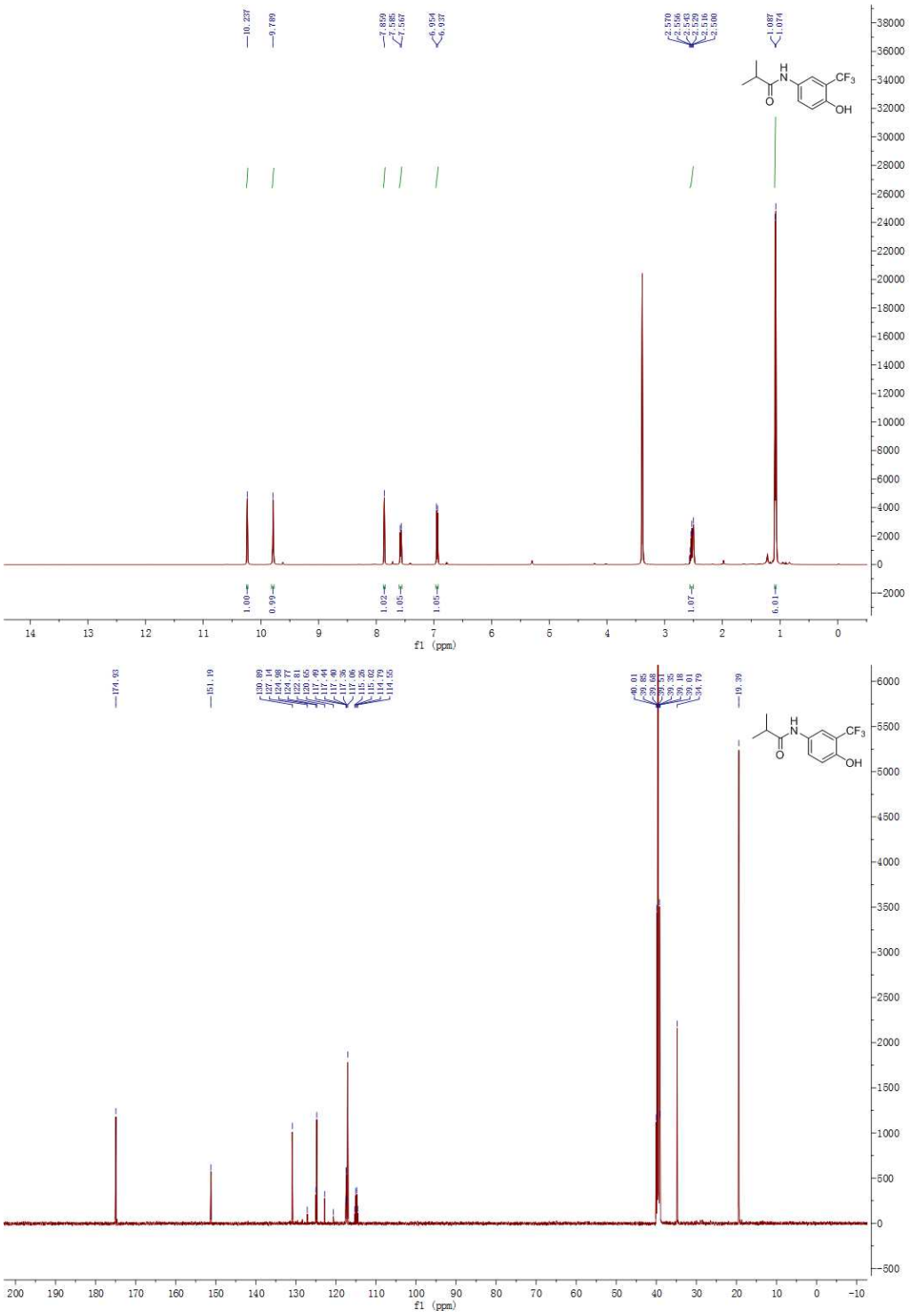


Figure S34. ^{1}H NMR of **4c** (500 MHz, DMSO-d_6) and ^{13}C NMR of **4c** (125 MHz, DMSO-d_6)

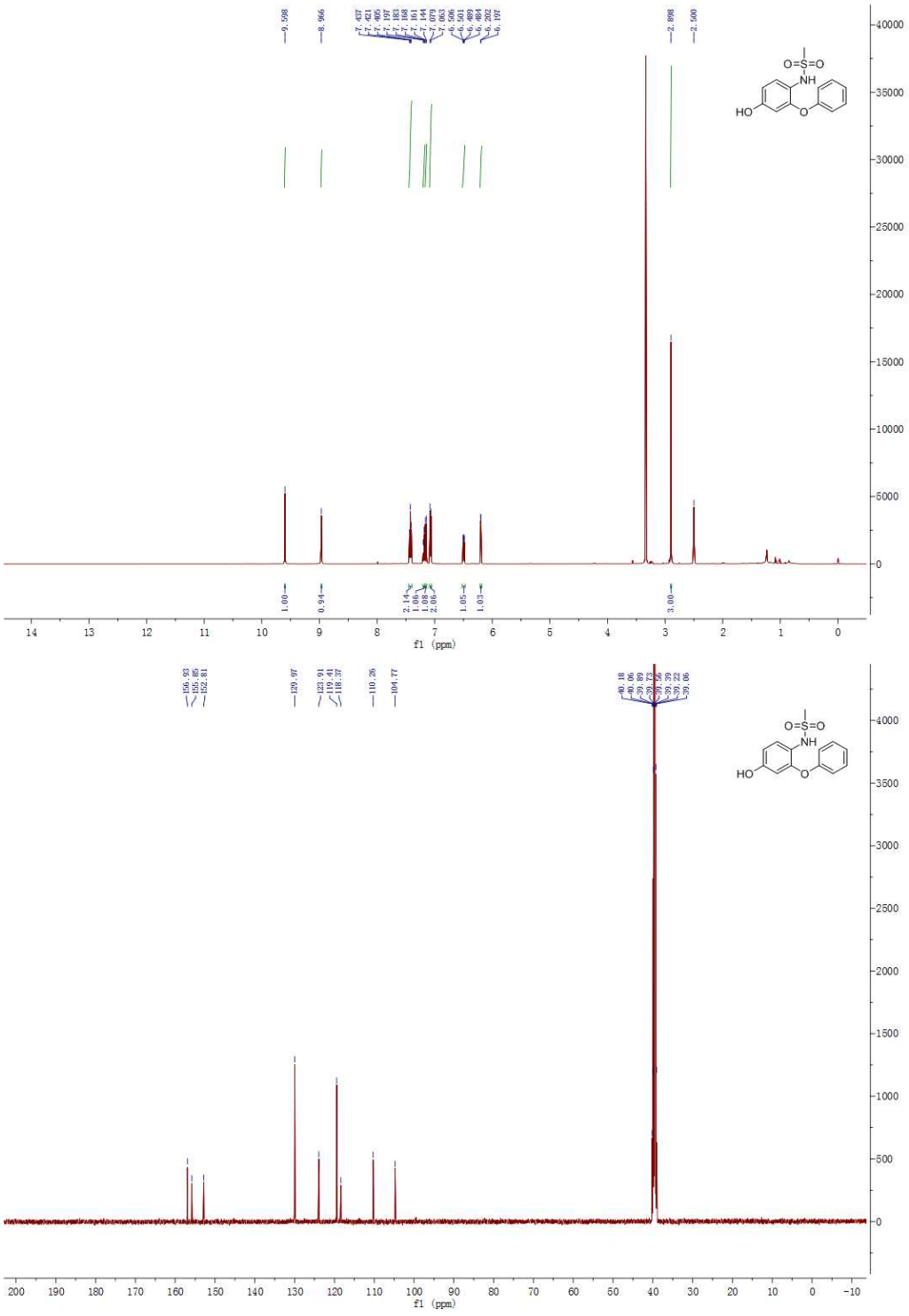


Figure S35. ^{1}H NMR of **4d** (500 MHz, DMSO-d_6) and ^{13}C NMR of **4d** (125 MHz, DMSO-d_6)

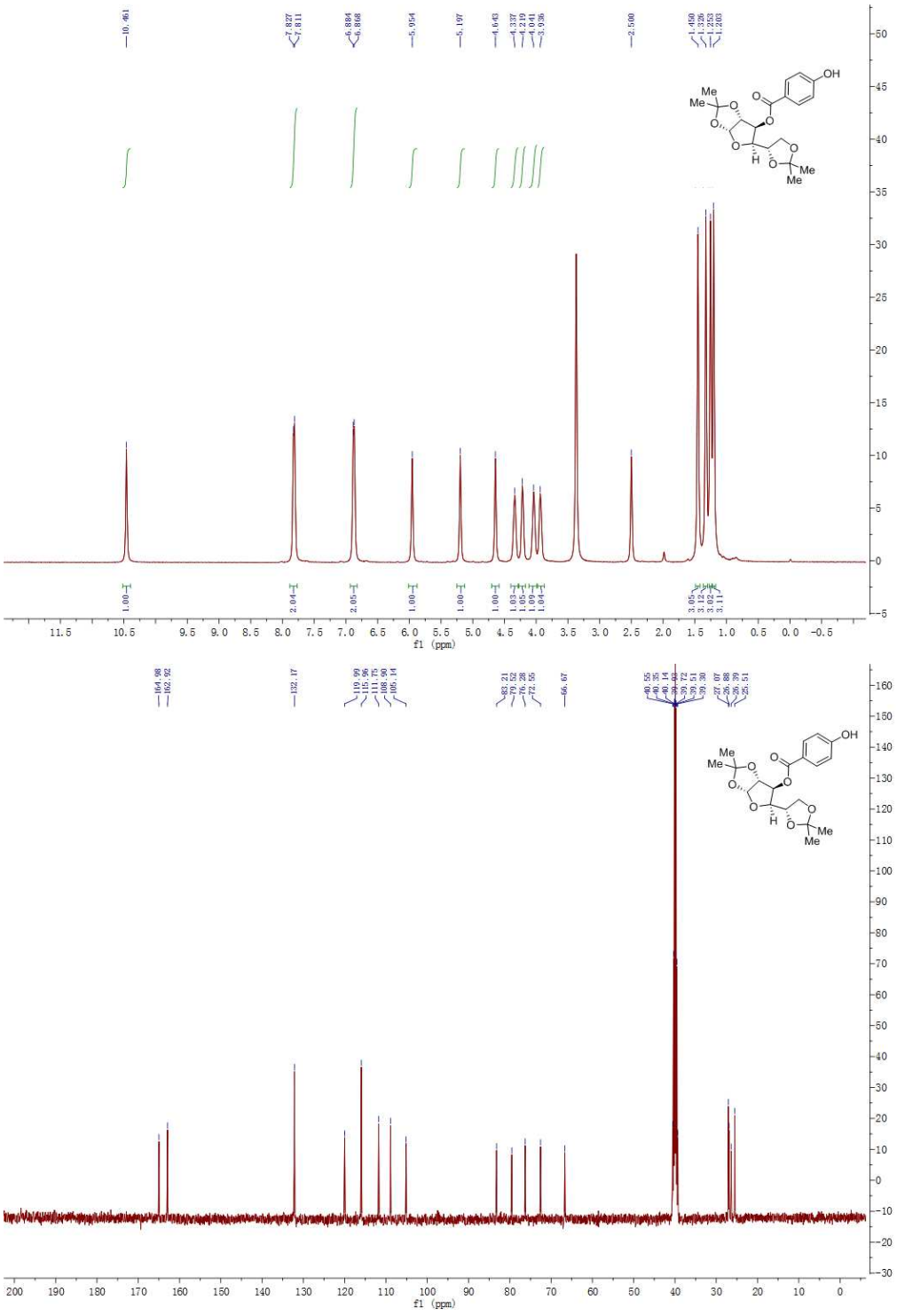


Figure S36. ^{1}H NMR of **4e** (400 MHz, DMSO-d_6) and ^{13}C NMR of **4e** (100 MHz, DMSO-d_6)

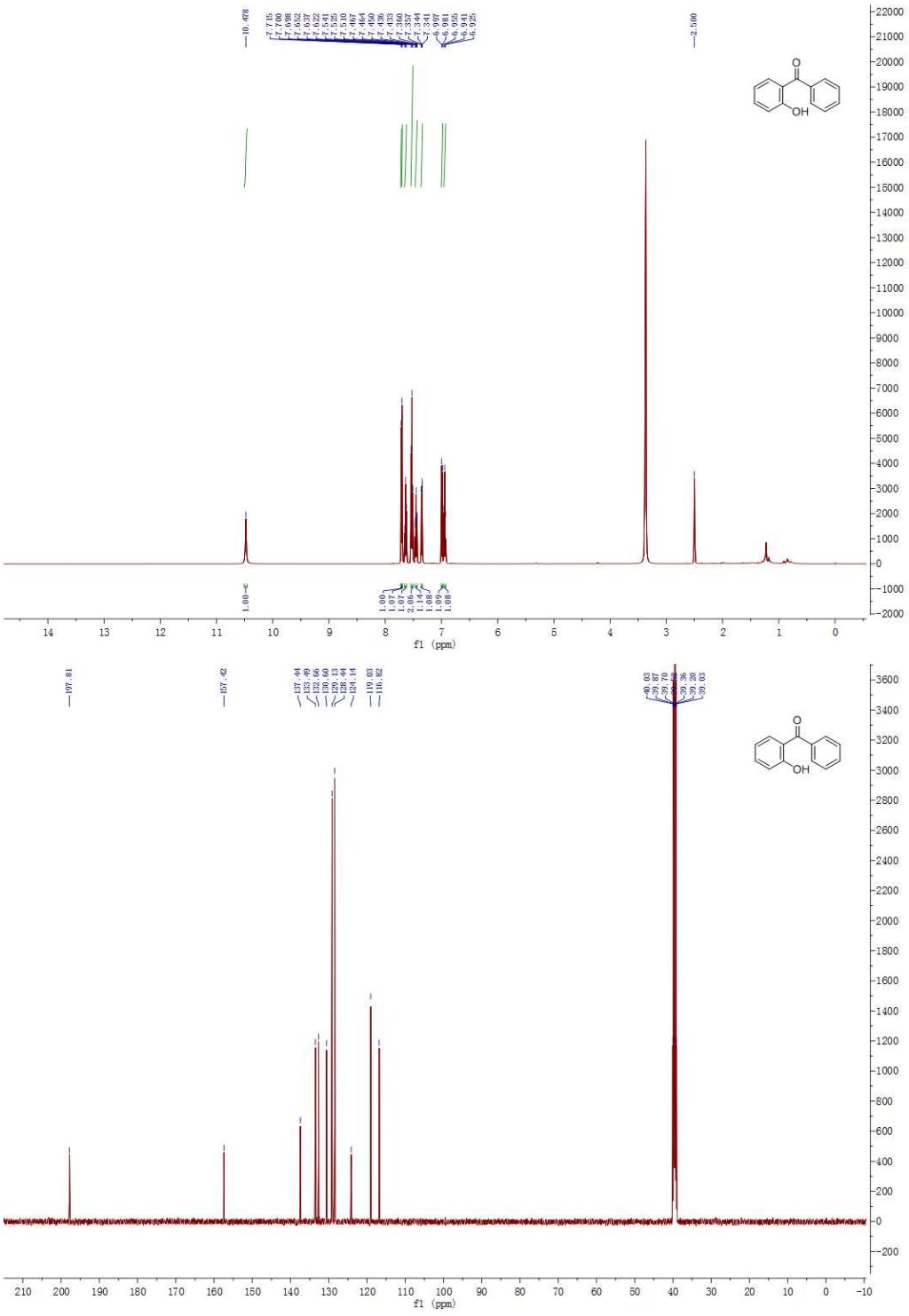


Figure S37 . ^{1}H NMR of 5**a** (500 MHz, DMSO-d_6) and ^{13}C NMR of 5**a** (125 MHz, DMSO-d_6)