

MeOTf-mediated De-arylmethylation of N-carboxamides via Retro-Mannich Reaction Induced by Dearomatization/Aromatization in Aqueous Medium

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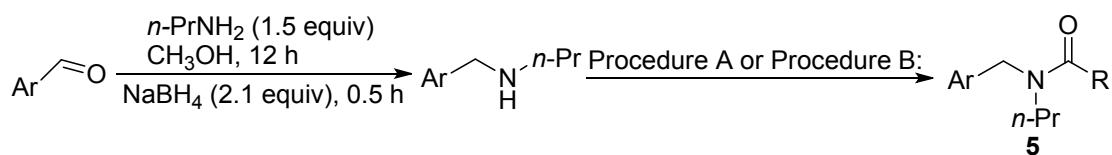
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General information

All reactions were carried out in air. Unless otherwise noted, all reagents and starting materials were purchased from commercial suppliers and used as received. FT-IR spectra were obtained with thin film samples or KBr pellets on a Bruker Vector 22 spectrometer, and data are expressed in cm^{-1} . ^1H and ^{13}C NMR spectra were recorded on a Bruker AVANCE III 400 (400 MHz for ^1H ; 100MHz for ^{13}C), ^1H (400 MHz) and ^{13}C (101 MHz) NMR spectra were recorded in CDCl_3 as a solvent. Chemical shifts are reported in ppm downfield from tetramethylsilane. MS were performed on Bruker Agilent1100/Esquire HCT PLUS mass spectrometer. The HRMS measurements were recorded on a TOF analyzer using an ESI source in the positive mode. Column chromatography was performed on silica gel (100–200 mesh) with mixtures of petroleum ether and ethyl acetate as the eluent.

Experimental procedure

General procedure for the preparation of 5



A solution of aromatic aldehydes (2 mmol, 1.0 equiv), propanamines, (3 mmol, 1.5 equiv) was stirred in CH_3OH (10 mL) at room temperature for 12 h. To the mixture was added NaBH_4 (4.2 mmol, 159 mg, 2.1 equiv) in portion at 0 °C. The reaction was warmed to room temperature. After stirring at the same temperature for 0.5 h, the solvent was removed after reduced pressure and obtain the crude products.

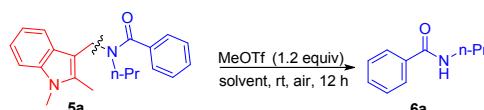
Procedure A: To the solution of the above crude product in DCM (2 mmol, 5 mL) was added the acid (2.4 mmol, 1.2 equiv) at 0 °C, then a mixture of DCC (0.618 g, 3 mmol) and DMAP (0.024 g, 0.2 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The mixture was stirred for 12 h at room temperature and filtered through a short plug of silica gel, which was rinsed with EtOAc . The residue was purified by a silica gel column chromatography (petroleum ether/ EtOAc = 5:1) to give the products.

Procedure B: To the solution of the above crude product and Et_3N (1.5 eq) in dichloromethane (2

mL/mmol), acyl chloride (1.0 equiv) was added in dropwise at 0 °C. The reaction mixture was stirred overnight at room temperature. The solution, diluted with dichloromethane, was washed with 1N HCl, dried over Na₂SO₄ and concentrated under reduced. The residue was purified by a silica gel column chromatography (petroleum ether/EtOAc = 5:1) to give the products.

Optimization of the reaction condition

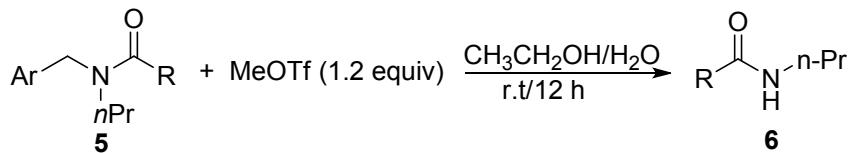
Table s1 Optimization of conditions for deindoylmethylation ^a



Entry	Electrophile	Solvent	Yield (%) ^b
1	MeOTf	DCM	86
2	MeOTf	Ethyl acetate	96
3	MeOTf	THF	ND
4	MeOTf	1,4-Dioxane	96
5	MeOTf	Acetone	94
6	MeOTf	MeCN	71
7	MeOTf	DMF	99
8	MeOTf	MeOH	99
9	MeOTf	EtOH	99
10	MeOTf	Ethylene glycol	89
11	MeOTf	Glycerol	95
12 ^c	MeOTf	H ₂ O	93
13	MeOTf	1:1 (v/v) EtOH/H ₂ O	99
14	MeOTf	2:1 (v/v) EtOH/H ₂ O	99
15	MeOTf	1:2 (v/v) EtOH/H ₂ O	91
16 ^d	MeOTf	1:1 (v/v) EtOH/H ₂ O	95
17 ^e	MeOTf	1:1 (v/v) EtOH/H ₂ O	97
18	EtOTf	1:1 (v/v) EtOH/H ₂ O	97
19	Methyl methanesulfonate	1:1 (v/v) EtOH/H ₂ O	96
20	NBS	1:1 (v/v) EtOH/H ₂ O	66
21	NCS	1:1 (v/v) EtOH/H ₂ O	59
22	Selectflour	1:1 (v/v) EtOH/H ₂ O	77
23	NFSI	1:1 (v/v) EtOH/H ₂ O	70

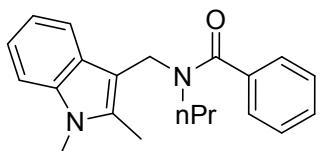
^aReaction conditions: **5a** (0.3 mmol), 2 mL of solvent. ^bIsolated yields are given. ND = not detected. ^cTime = 18 h. ^dTemp = 40 °C, Time = 6 h. ^eMeOTf (1 equiv).

General procedure for the preparation of 6

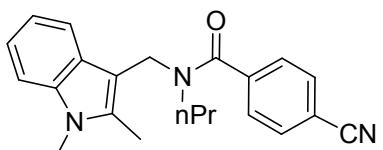


To a solution of **5** (0.3 mmol, 1.0 equiv) in the mixture of solvent (2 mL, EtOH/H₂O = 1/1, v/v) was added the methyl trifluoromethanesulfonate (0.36 mmol, 1.2 equiv) at room temperature. The mixture was stirred at room temperature for 12 hours. Then, the crude mixture was filtered and concentrated. The residue was purified by a silica gel column chromatography (petroleum ether/EtOAc = 5:1) to give the desired products.

Characterization Data for 5

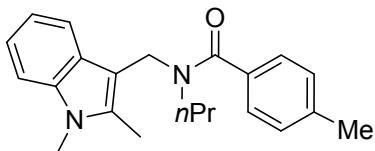


N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylbenzamide (5a): Prepared by the general procedure B in 62% yield as white solid; m.p 59 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.75 – 7.07 (m, 9H), 4.97 (s, 1.5H), 4.66 (s, 0.5H), 3.59 (s, 3H), 3.35 (s, 0.5H), 2.98 (s, 1.5H), 2.42 (br, 2.25H), 2.22 (br, 0.75H), 1.72 – 1.44 (m, 2H), 0.89(br, 0.75H), 0.66 (br, 2.25H); ¹³C NMR (101 MHz, CDCl₃) δ 171.71, 137.48, 136.74, 135.70, 129.07, 128.47, 127.83, 126.51, 121.08, 119.59, 118.45, 108.83, 106.82, 48.38, 37.00, 29.62, 21.49, 11.21, 10.41. HRMS (ESI) *m/z* calcd for C₂₁H₂₄N₂NaO [M+Na]⁺ 343.1786, Found 343.1781.

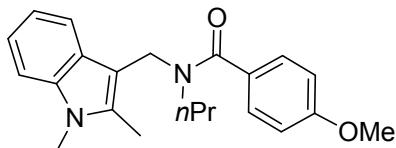


4-Cyano-N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylbenzamide (5b): Prepared by the general procedure A in 45% yield as yellow solid; m.p 57 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.62 (d, *J* = 6.3 Hz, 3H), 7.55 – 7.03 (m, 5H), 4.95 (s, 1.5H), 4.59 (s, 0.5H), 3.65 (s, 3H), 3.37 (br, 0.5H), 2.92 (br, 1.5H), 2.45 (s, 2.25H), 2.24 (s, 0.7H), 1.66 – 1.44(m, 2H), 0.89 (br, 0.75H), 0.69 (br, 2.25H); ¹³C NMR (101 MHz, CDCl₃) δ 169.57, 141.76, 136.75, 135.86, 132.41, 127.62, 127.23, 121.23, 119.71,

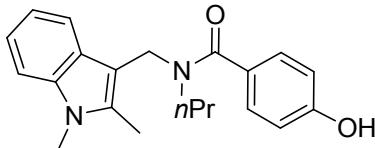
118.30, 118.20, 112.86, 108.92, 106.29, 48.34, 37.17, 29.67, 21.49, 11.15, 10.40. HRMS (ESI) m/z calcd for $C_{22}H_{23}N_3NaO$ [M+Na]⁺ 368.1739, Found 368.1733.



N-((1,2-dimethyl-1H-indol-3-yl)methyl)-4-methyl-N-propylbenzamide (5c) Prepared by the general procedure B in 60% yield as yellow syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.85 – 7.13 (m, 8H), 5.06 (s, 1.33H), 4.79 (s, 0.67H), 3.66 (s, 3H), 3.44 (br, 0.67H), 3.11 (s, 1.33H), 2.51 (s, 2H), 2.41 (s, 4H), 1.62 (br, 2H), 0.98 (br, 1H), 0.78 (br, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 171.86, 139.02, 136.74, 135.65, 134.58, 129.08, 127.81, 126.62, 121.06, 119.55, 118.46, 108.84, 106.89, 48.46, 37.03, 33.96, 29.58, 21.44, 11.26, 10.39. HRMS (ESI) m/z calcd for $C_{22}H_{27}N_2O$ [M+H]⁺ 335.2123, Found 335.2118.

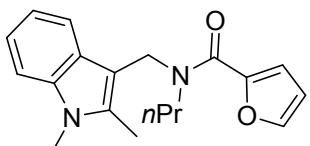


N-((1,2-dimethyl-1H-indol-3-yl)methyl)-4-methoxy-N-propylbenzamide (5d): Prepared by the general procedure A in 50% yield as yellow syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.62 (br, 1H), 7.36 (br, 2H), 7.24 (d, J = 8.2 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.08 (t, J = 7.4 Hz, 1H), 6.87 (d, J = 7.7 Hz, 2H), 4.91 (s, 2H), 3.77 (s, 3H), 3.62 (s, 3H), 3.09 (br, 2H), 2.40 (br, 3H), 1.55 (br, 2H), 0.73 (br, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 171.53, 160.29, 136.70, 135.35, 129.64, 128.58, 127.71, 121.02, 119.53, 118.32, 113.70, 108.76, 55.34, 33.95, 29.59, 25.10, 21.30, 11.27, 10.37. HRMS (ESI) m/z calcd for $C_{22}H_{27}N_2O_2$ [M+H]⁺ 351.2073, Found 351.2067.

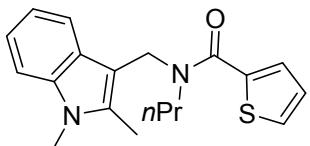


N-((1,2-dimethyl-1H-indol-3-yl)methyl)-4-hydroxy-N-propylbenzamide (5e): Prepared by the general procedure A in 43% yield as white solid; m.p 140 °C; ¹H NMR (400 MHz, DMSO) δ 9.87 (br, 1H), 7.68 – 7.15 (m, 4H), 7.09 (t, J = 7.2 Hz, 1H), 7.01 (t, J = 7.0 Hz, 1H), 6.85 (d, J = 6.0 Hz, 2H), 4.81 (s, 2H), 3.64 (s, 3H), 3.02 (br, 2H), 2.38 (s, 3H), 1.59 – 1.40 (m, 2H), 0.68 (br, 3H); ¹³C NMR (101 MHz, DMSO) δ 170.94, 158.77, 136.83, 136.20, 128.90, 128.16, 127.61, 120.97, 119.43, 118.16,

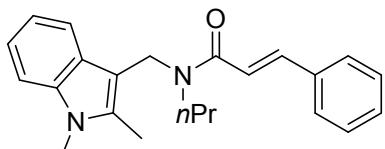
115.44, 109.62, 106.60, 29.79, 21.11, 21.05, 11.58, 10.30. HRMS (ESI) m/z calcd for C₂₁H₂₄N₂NaO₂ [M+Na]⁺ 359.1735, Found 359.1730.



N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylfuran-2-carboxamide (5f): Prepared by the general procedure B in 55% yield as yellow syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.60 (br, 1H), 7.44 (s, 1H), 7.26 – 7.19 (m, 1H), 7.15 (t, J = 7.5 Hz, 1H), 7.10 – 6.96 (m, 2H), 6.44 (br, 1H), 4.96 (s, 2H), 3.61 (s, 3H), 3.41 – 3.30 (m, 2H), 2.40 (s, 3H), 1.68 – 1.55 (m, 2H), 0.83 (t, J = 7.4 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 160.0, 148.8, 143.5, 136.7, 127.8, 121.0, 119.5, 118.4, 116.0, 111.2, 108.7, 77.6, 77.2, 76.9, 34.0, 29.6, 25.8, 25.1, 11.4, 10.4. HRMS (ESI) m/z calcd for C₁₉H₂₂N₂NaO₂ [M+Na]⁺ 333.1579, Found 333.1573.

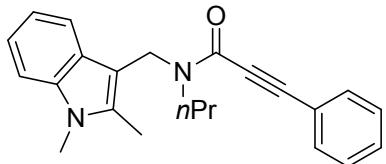


N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylthiophene-2-carboxamide (5g): Prepared by the general procedure B in 50% yield as yellow syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (br, 1H), 7.38 – 7.25 (m, 2H), 7.20 (t, J = 6.7 Hz, 1H), 7.14 (t, J = 7.3 Hz, 1H), 7.07 (t, J = 6.9 Hz, 1H), 6.96 (s, 1H), 4.95 (s, 2H), 3.57 (s, 3H), 3.29 (t, J = 7.0 Hz, 2H), 2.36 (s, 3H), 1.68 – 1.55 (m, 2H), 0.80 (t, J = 6.7 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 164.33, 138.57, 136.72, 135.57, 128.37, 127.65, 126.79, 121.11, 119.62, 118.36, 108.85, 106.36, 34.02, 29.63, 25.20, 21.49, 11.34, 10.43. HRMS (ESI) m/z calcd for C₁₉H₂₂N₂NaOS [M+Na]⁺ 349.1351, Found 349.1345.



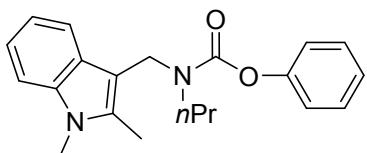
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylcinnamamide (5h): Prepared by the general procedure A in 59% yield as yellow solid; m.p 95–98 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.79 (d, J = 15.3 Hz, 1H), 7.63 (d, J = 7.7 Hz, 1H), 7.50 (d, J = 7.0 Hz, 2H), 7.33 (t, J = 7.3 Hz, 3H), 7.24 (d, J = 8.4 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.09 (t, J = 7.2 Hz, 1H), 6.85 (d, J = 15.4 Hz, 1H), 4.93 (s, 2H),

3.64 (s, 3H), 3.24 (t, $J = 7.5$ Hz, 2H), 2.44 (s, 3H), 1.55-1.68 (m, 2H), 0.89 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 166.09, 142.42, 136.65, 135.75, 135.64, 129.45, 128.81, 127.91, 127.78, 121.00, 119.53, 118.41, 118.16, 108.65, 107.22, 47.45, 38.40, 29.60, 22.53, 11.56, 10.42. HRMS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{26}\text{N}_2\text{NaO} [\text{M}+\text{Na}]^+$ 369.1943, Found 369.1937.

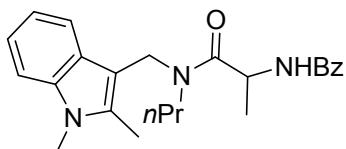


N-((1,2-dimethyl-1H-indol-3-yl)methyl)-3-phenyl-N-propylpropiolamide (5i):

Prepared by the general procedure A in 52% yield as yellow syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.70 – 7.48 (m, 3H), 7.40 – 7.10 (m, 6H), 5.08 (s, 0.75H), 4.87 (s, 1.25H), 3.68 (d, $J = 5.1$ Hz, 3H), 3.42 (t, $J = 7.5$ Hz, 1.25H), 3.22 (t, $J = 7.5$ Hz, 0.75H), 2.45 (s, 3H), 1.73 – 1.66 (m 1.25H), 1.57 – 1.51 (m, 0.75H), 0.94 (t, $J = 7.4$ Hz, 1.88H), 0.84 (t, $J = 7.4$ Hz, 1.12H); ^{13}C NMR (101 MHz, CDCl_3) δ 154.47 (153.92), 136.69 (136.59), 135.93 (135.47), 132.36 (132.31), 129.96 (129.85), 128.56 (128.51), 127.75 (127.50), 121.24 (121.10), 120.89, 119.78 (119.63), 118.32 (118.13), 108.85 (108.68), 106.33, 105.51, 100.00, 89.51, 82.63 (82.19), 48.65, 44.34 (43.52), 36.79 (33.99), 29.63, 24.98, 21.77 (20.17), 11.46 (10.44). HRMS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{24}\text{N}_2\text{NaO} [\text{M}+\text{Na}]^+$ 367.1786, Found 367.1781

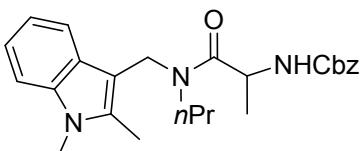


Phenyl ((1,2-dimethyl-1H-indol-3-yl)methyl)(propyl)carbamate (5j): Prepared by the general procedure B in 43% yield as white syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.67 (d, $J = 6.6$ Hz, 1H), 7.34 (br, 2H), 7.23 (d, $J = 7.9$ Hz, 1H), 7.17 - 7.08 (m, 5H), 4.79 (s, 2H), 3.60 (s, 3H), 3.26 - 3.16 (m 2H), 2.41 (s, 3H), 1.70 – 1.57 (m, 2H), 0.92 – 0.83 (m, 3H); ^1H NMR (400 MHz, CDCl_3) δ 7.68, 7.66, 7.34, 7.24, 7.22, 7.18, 7.17, 7.15, 7.12, 7.10, 7.09, 4.82, 4.75, 3.60, 3.22, 3.21, 2.41, 1.65, 1.63, 0.90, 0.88. HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{24}\text{N}_2\text{NaO}_2 [\text{M}+\text{Na}]^+$ 359.1735, Found 359.1730.



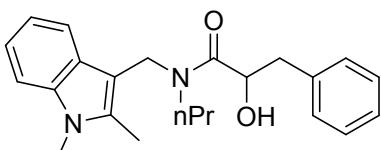
N-((1,2-dimethyl-1H-indol-3-yl)methyl)(propyl)amino)-1-oxopropan-2-yl)benzamide (5k):

Prepared by the general procedure A in 50% yield as syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.85 (d, $J = 7.7$ Hz, 2H), 7.51 (dd, $J = 11.4, 7.5$ Hz, 2H), 7.43 (t, $J = 7.4$ Hz, 3H), 7.26 (d, $J = 7.3$ Hz, 1H), 7.17 (t, $J = 7.5$ Hz, 1H), 7.08 (t, $J = 7.4$ Hz, 1H), 5.49 – 5.39 (m, 0.17H), 5.32 (d, $J = 15.2$ Hz, 0.83H), 5.14 – 5.04 (m, 0.83H), 4.86 (d, $J = 15.2$ Hz, 0.17H), 4.66 (d, $J = 15.2$ Hz, 0.17H), 4.39 (d, $J = 15.2$ Hz, 0.83H), 3.67 (s, 3H), 3.26 – 2.97 (m, 2H), 2.41 (s, 3H), 1.76 – 1.60 (m, 2H), 1.52 (d, $J = 6.7$ Hz, 0.5H), 1.42 (d, $J = 6.6$ Hz, 2.5H), 0.91 (t, $J = 7.4$ Hz, 2.5H), 0.81 (t, $J = 7.4$ Hz, 0.5H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.17, 166.29, 136.64, 135.65, 134.26, 131.55, 128.52, 127.64, 127.11, 121.15, 119.60, 118.06, 108.76, 106.47, 46.62, 46.08, 37.75, 29.61, 21.82, 19.53, 11.32, 10.26. HRMS (ESI) m/z calcd for $\text{C}_{24}\text{H}_{29}\text{N}_3\text{NaO}_2$ [M+Na] $^+$ 414.2157, Found 414.2152



Benzyl (1-((1,2-dimethyl-1H-indol-3-yl)methyl)(propyl)amino)-1-oxopropan-2-yl)carbamate (5l):

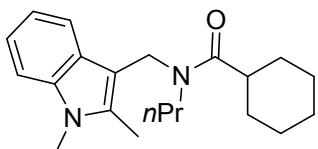
Prepared by the general procedure A in 47% yield as white solid; m.p 76–78°C; ^1H NMR (400 MHz, CDCl_3) δ 7.49 (d, $J = 7.8$ Hz, 1H), 7.39 – 7.28 (m, 5H), 7.25 (t, $J = 4.0$ Hz, 1H), 7.17 (t, $J = 7.5$ Hz, 1H), 7.07 (t, $J = 7.4$ Hz, 1H), 5.86 (d, $J = 7.7$ Hz, 1H), 5.25 (d, $J = 14.9$ Hz, 1H), 5.16 – 5.06 (m, 2H), 4.73 – 4.56 (m, 1H), 4.38 (d, $J = 14.9$ Hz, 1H), 3.66 (s, 3H), 3.15 – 2.97 (m, 2H), 2.39 (s, 3H), 1.69 – 1.61 (m, 2H), 1.40 (d, $J = 6.6$ Hz, 0.6H), 1.31 (d, $J = 6.7$ Hz, 2.4H), 0.88 (t, $J = 7.3$ Hz, 2.4H), 0.79 (t, $J = 7.4$ Hz, 0.6H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.08, 155.61, 136.60, 135.65, 128.50, 128.03, 127.94, 127.68, 121.09, 119.56, 118.09, 108.70, 106.58, 66.66, 47.18, 46.68, 37.75, 29.60, 21.85, 19.66, 11.33, 10.24. HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{32}\text{N}_3\text{O}_3$ [M+H] $^+$ 422.2444, Found 422.2438.



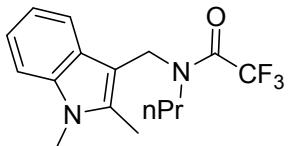
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-2-hydroxy-3-phenyl-N-propylpropanamide (5m):

Prepared by the general procedure B in 63% yield as white solid; m.p 84°C; ^1H NMR (400 MHz, CDCl_3) δ 7.55 (br, 0.5H), 7.34 – 7.08 (m, 8.5H), 5.26 (d, $J = 15.0$ Hz, 0.75H), 4.98 (s, 0.25H), 4.61 (d, $J = 15.0$ Hz, 0.25H), 4.50 (s, 0.75H), 4.41 (d, $J = 15.0$ Hz, 0.75H), 4.09 (d, $J = 15.0$ Hz, 0.25H), 3.87

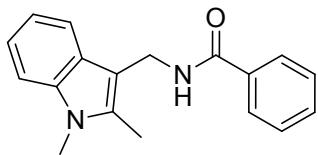
(s, 0.75H), 3.62 (s, 2.25H), 3.59 (s, 0.75H), 3.14 – 2.72 (m, 4H), 2.38 (s, 2.25H), 2.29 (s, 0.75H), 1.66 – 1.49 (m, 2H), 0.91– 0.75 (m, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 173.51 (173.38), 137.44 (137.24), 136.71, 135.90 (135.09), (129.85) 129.64, 129.40, (128.55) 128.41, 127.76 (127.08), 126.86 (126.66), (121.38) 121.22, (119.92) 119.68, 118.29 (117.84), (109.04) 108.83, 106.37, 104.71, 69.63, 46.16 (46.06), 42.61 (42.37), 38.04, 29.68, 21.61 (20.43), 11.66 (11.40), 10.45 (10.34). HRMS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{28}\text{N}_2\text{NaO}_2$ [M+Na] $^+$ 387.2048, Found 387.2043.



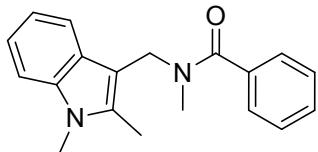
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylcyclohexanecarboxamide (5n): Prepared by the general procedure B in 43% yield as white syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.53 (d, $J = 7.7$ Hz, 0.85H), 7.39 (d, $J = 7.8$ Hz, 0.15H), 7.22 (d, $J = 8.8$ Hz, 1H), 7.14 (t, $J = 7.5$ Hz, 1H), 7.06 (t, $J = 7.3$ Hz, 1H), 4.81 (s, 1.66H), 4.68 (s, 0.34H), 3.62 (s, 3H), 3.21 (t, $J = 7.1$ Hz, 0.34H), 3.04 (t, $J = 7.4$ Hz, 1.66H), 2.38 (s, 3H), 1.89 – 1.52 (m, 9H), 1.50 – 1.18 (m, 4H), 0.86 (t, $J = 7.3$ Hz, 2.5H), 0.79 (t, $J = 7.2$ Hz, 0.5H); ^{13}C NMR (101 MHz, CDCl_3) δ 175.90, 136.58, 135.49, 127.84, 120.89, 119.36, 118.42, 108.58, 107.47, 46.78, 41.12, 37.33, 29.74, 29.55, 25.98, 25.90, 22.26, 11.47, 10.28. HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{31}\text{N}_2\text{O}$ [M+H] $^+$ 327.2436, Found 327.2431.



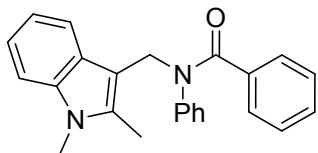
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-2,2,2-trifluoro-N-propylacetamide (5o): Prepared by the general procedure A in 33% yield as white solid; m.p 84–86°C; ^1H NMR (400 MHz, DMSO) δ 7.47–7.34 (m, 2H), 7.16–7.08 (m, 1H), 7.06–6.98 (m, 1H), 4.84 (s, 1.6H), 4.80 (s, 0.4H), 3.68 (s, 0.6H), 3.67 (s, 2.4H), 3.08 (t, $J = 7.5$ Hz, 2H), 2.43 (s, 2.4H), 2.40 (s, 0.6H), 1.70–1.57 (m, 2H), 0.81 (t, $J = 7.4$ Hz, 2.4H), 0.68 (t, $J = 7.4$ Hz, 0.6H); ^{13}C NMR (101 MHz, DMSO) δ 156.00 (156.32), 155.65 (155.31), 137.37 (137.16), 136.85 (136.89), 127.36 (127.17), 121.22, 119.68, 117.88, 109.77 (109.95), 104.86 (103.15), 46.59 (46.23), 31.97 (33.83), 29.85 (30.20), 21.37 (19.71), 11.15 (11.43), 10.27 (10.12); HRMS (ESI) m/z calcd for $\text{C}_{16}\text{H}_{19}\text{F}_3\text{N}_2\text{NaO}$ [M+Na] $^+$ 335.1347, Found 335.1342.



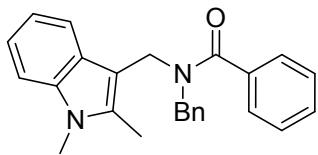
N-((1,2-dimethyl-1H-indol-3-yl)methyl)benzamide (5p): Prepared by the general procedure B in 60% yield as white syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.71 (d, *J* = 7.4 Hz, 2H), 7.58 (d, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 7.2 Hz, 1H), 7.35 – 7.31 (m, 2H), 7.24 (s, 1H), 7.17 (t, *J* = 7.3 Hz, 1H), 7.09 (t, *J* = 7.3 Hz, 1H), 6.28 (br, 1H), 4.75 (d, *J* = 4.3 Hz, 2H), 3.62 (s, 3H), 2.41 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.32, 136.70, 135.27, 134.65, 131.34, 128.51, 127.20, 126.97, 121.21, 119.61, 117.85, 108.91, 107.21, 34.90, 29.61, 10.33; HRMS (ESI) *m/z* calcd for C₁₈H₁₈N₂NaO⁺ [M+Na]⁺ 301.1311, Found 301.1312



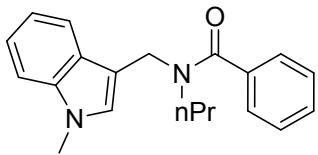
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-methylbenzamide (5q): Prepared by the general procedure B in 80 % yield as white syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.75 – 7.53 (m, 1H), 7.51 – 7.22 (m, 5H), 7.20 – 7.04 (m, 3H), 4.90 (s, 1.5H), 4.63 (s, 0.5H), 3.52 (s, 3H), 2.87 (s, 0.75H), 2.68 (s, 2.25H), 2.38 (s, 2.25H), 2.16 (s, 0.75H); ¹³C NMR (101 MHz, CDCl₃) δ 171.05, 137.03, 136.76, 135.90, 129.42, 128.43, 127.83, 126.97, 121.11, 119.60, 118.52, 108.87, 106.57, 40.61, 36.25, 29.58, 10.36; HRMS (ESI) *m/z* calcd for C₁₉H₂₀N₂NaO⁺ [M+Na]⁺ 315.1468, Found 315.1467.



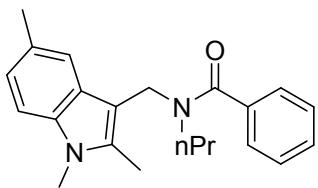
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-phenylbenzamide (5r): Prepared by the general procedure B in 40 % yield as white syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.58 (d, *J* = 7.8 Hz, 1H), 7.22 (s, 1H), 7.20 – 6.96 (m, 10H), 6.77 – 6.73 (m, 2H), 5.27 (s, 2H), 3.49 (s, 3H), 2.01 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 170.24, 142.91, 136.73, 136.68, 136.22, 129.15, 129.03, 128.76, 128.50, 127.67, 127.60, 126.88, 120.87, 119.39, 119.24, 108.45, 107.13, 43.83, 29.53, 9.93; HRMS (ESI) *m/z* calcd for C₂₄H₂₂N₂NaO⁺ [M+Na]⁺ 377.1624, Found 377.1625.



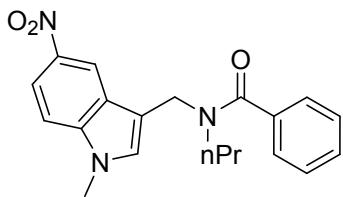
N-benzyl-N-((1,2-dimethyl-1H-indol-3-yl)methyl)benzamide (5s): Prepared by the general procedure B in 83% yield as white syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.59 (s, 1H), 7.48 – 7.40 (m, 2H), 7.38 – 7.22 (m, 8H), 7.21 – 7.15 (m, 1H), 7.10 (d, J = 5.4 Hz, 2H), 4.62 (dd, J = 127.1, 121.4 Hz, 4H), 3.61 (s, 3H), 2.10 (s, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.16, 137.17, 136.87, 136.20, 129.50, 128.78, 128.59, 127.89, 127.45, 126.78, 126.69, 121.19, 119.62, 118.72, 108.82, 106.21, 50.69, 37.34, 29.60, 10.21; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{24}\text{N}_2\text{NaO} [\text{M}+\text{Na}]^+$ 391.1781, Found 391.1783.



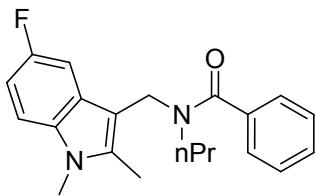
N-((1-methyl-1H-indol-3-yl)methyl)-N-propylbenzamide (5aa): Prepared by the general procedure B in 60% yield as yellow syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.65 (d, J = 103.7 Hz, 1H), 7.41 – 6.86 (m, 9H), 4.93 (s, 1.2H), 4.65 (s, 0.8H), 3.70 (s, 3H), 3.50 (s, 0.8H), 3.07 (s, 1.2H), 1.69 (br, 0.8H), 1.54 (br, 1.2H), 0.93 (br, 1.2H), 0.70 (br, 1.8H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.82, 137.22, 129.17, 128.93, 128.47, 127.64, 126.92, 126.58, 121.99, 119.51, 118.80, 110.51, 109.47, 48.99, 38.30, 32.83, 21.42 (20.55), 11.57 (11.14). HRMS (ESI) m/z calcd for $\text{C}_{20}\text{H}_{22}\text{N}_2\text{NaO} [\text{M}+\text{Na}]^+$ 329.1630, Found 329.1624.



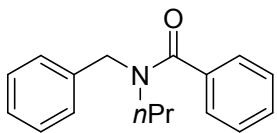
N-propyl-N-((1,2,5-trimethyl-1H-indol-3-yl)methyl)benzamide (5ab): Prepared by the general procedure B in 57% yield as yellow syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.65 – 7.25 (m, 6H), 7.16 – 6.97 (m, 2H), 4.95 (s, 1.5H), 4.65 (s, 0.5H), 3.61 (s, 3H), 3.36 (br, 0.5H), 2.99 (br, 1.5H), 2.44 (s, 4.5H), 2.23 (s, 1.5H), 1.65 – 1.46 (m, 2H), 0.95 – 0.85 (m, 0.75H), 0.68 (br, 2.25H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.66, 137.51, 135.70, 135.14, 129.01, 128.71, 128.43, 128.06, 127.02, 126.48, 122.55, 118.11, 108.48, 106.25, 48.30, 36.99, 29.62, 22.98, 21.61, 11.14, 10.38. HRMS (ESI) m/z calcd for $\text{C}_{22}\text{H}_{26}\text{N}_2\text{NaO} [\text{M}+\text{Na}]^+$ 357.1943, Found 357.1937



N-((1,2-dimethyl-5-nitro-1H-indol-3-yl)methyl)-N-propylbenzamide (5ac): Prepared by the general procedure B in 35% yield as yellow solid; m.p 101°C; ¹H NMR (400 MHz, CDCl₃) δ 8.48 (d, *J* = 181.4 Hz, 1H), 8.07 (s, 1H), 7.60 – 7.10 (m, 7H), 4.93 (s, 1.3H), 4.70 (s, 0.7H), 3.82 (s, 3H), 3.49 (s, 0.7H), 3.12 (br, 1.3H), 1.79 – 1.51 (m, 2H), 0.95 (br, 1.1H), 0.74 (br, 1.9H); ¹³C NMR (101 MHz, CDCl₃) δ 171.95, 141.43, 139.81, 136.80, 131.85, 129.32, 128.49, 126.46, 117.41, 116.61, 113.61, 109.49, 49.51, 38.38, 33.28, 21.52, 11.03. HRMS (ESI) *m/z* calcd for C₂₀H₂₂N₃O₃ [M+H]⁺ 352.1661, Found 352.1656.

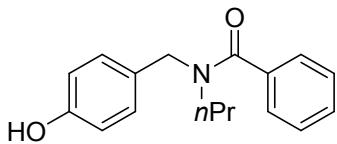


N-((5-fluoro-1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylbenzamide (5ad): Prepared by the general procedure B in 43% yield as yellow solid; m.p 105–108°C; ¹H NMR (400 MHz, CDCl₃) δ 7.62 – 7.23 (m, 6H), 7.15 (d, *J* = 4.6 Hz, 1H), 6.90 (t, *J* = 8.8 Hz, 1H), 4.92 (s, 1.5 H), 4.64 (s, 0.5H), 3.65 (s, 3H), 3.33 (br, 0.5H), 3.00 (br, 1.5H), 2.46 (br, 2.25H), 2.27 (br, 0.75H), 1.81 – 1.58 (m, 0.5H), 1.58 – 1.47 (s, 1.5H), 0.88 (br, 0.75H), 0.69 (br, 2.25H); ¹³C NMR (101 MHz, CDCl₃) δ 171.69, 159.21, 156.87, 137.27, 133.24, 129.08, 128.43, 126.46, 109.30, 109.20, 108.94, 107.10, 103.35, 48.47, 36.99, 29.82, 21.44, 11.12, 10.52. HRMS (ESI) *m/z* calcd for C₂₁H₂₃FN₂NaO [M+Na]⁺ 361.1692, Found 361.1687.

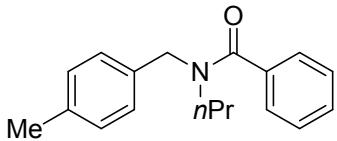


N-benzyl-N-propylbenzamide (5ae): Prepared by the general procedure B in 60% yield as white syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.46 – 7.09 (m, 10H), 4.78 (s, 1H), 4.49 (s, 1H), 3.42 (br, 1H), 3.10 (br, 1H), 1.66 (br, 1H), 1.50 (br, 1H), 0.93 (br, 1.5H), 0.68 (br, 1.5H); ¹³C NMR (101 MHz, CDCl₃) δ 172.13, 137.52, 136.82, 129.37, 128.74, 128.48, 128.06, 127.45, 126.83, 126.59, 52.59 (49.86), 47.2, (46.30), 21.45 (20.28), 11.42 (11.05). HRMS (ESI) *m/z* calcd for C₁₇H₂₀NO [M+H]⁺

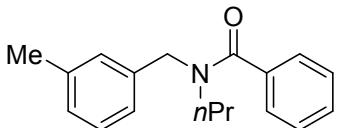
254.1545, Found 254.1539.



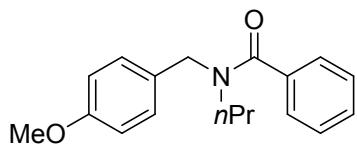
N-(4-hydroxybenzyl)-N-propylbenzamide (5af): Prepared by the general procedure B in 62% yield as white syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.85 (br, 1H), 7.47 – 7.33 (m, 5H), 7.19 (d, J = 7.3 Hz, 1H), 6.98 – 6.79 (m, 3H), 4.73 (s, 1H), 4.43 (s, 1H), 3.46 (br, 1H), 3.12 (br, 1H), 1.68 (br, 1H), 1.51 (br, 1H), 0.95 (br, 1.5H), 0.70 (br, 1.5H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.40, 156.40, 135.99, 135.89, 129.39, 129.13, 128.31, 127.91, 127.39, 126.54, 126.30 (126.16), 115.69, 52.10 (49.44), 46.78 (46.01), 21.05 (19.97), 11.12 (10.70). HRMS (ESI) m/z calcd for $\text{C}_{17}\text{H}_{19}\text{NNaO}_2$ [M+Na] $^+$ 292.1313, Found 292.1308.



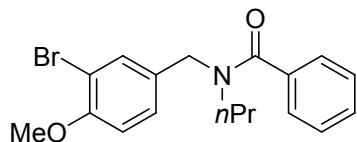
N-(4-methylbenzyl)-N-propylbenzamide (5ag): Prepared by the general procedure B in 65% yield as white syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.46 – 6.99 (m, 9H), 4.73 (s, 1H), 4.44 (s, 1H), 3.41 (br, 1H), 3.08 (br, 1H), 2.30 (s, 3H), 1.65 (br, 1H), 1.48 (br, 1H), 0.91 (br, 1.5H), 0.66 (br, 1.5H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.01, 136.96, 134.50, 133.94, 129.41, 128.45, 128.11, 126.81, 126.60, 52.28 (49.67), 46.94 (46.15), 21.44 (20.27), 21.13, 11.43 (11.02). HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{21}\text{NNaO}$ [M+Na] $^+$ 290.1521, Found 290.1515.



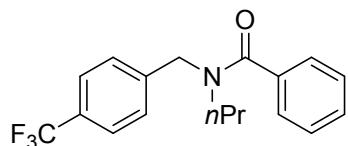
N-(3-methylbenzyl)-N-propylbenzamide (5ah): Prepared by the general procedure B in 62% yield as white syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.43 – 7.32 (m, 5H), 7.25 (br, 1H), 7.18 – 7.01 (m, 3H), 4.73 (s, 1H), 4.46 (s, 1H), 3.41 (br, 1H), 3.09 (br, 1H), 2.33 (s, 3H), 1.66 (br, 1H), 1.51 (br, 1H), 0.93 (br, 1.5H), 0.69 (br, 1.5H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.11, 136.88, 129.41, 128.45, 128.11, 127.40, 126.92, 126.78, 126.60, 65.08, 52.30 (49.67), 46.94 (46.15), 21.40 (21.12), 11.41 (11.00). HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{22}\text{NO}$ [M+H] $^+$ 268.1701, Found 268.1696.



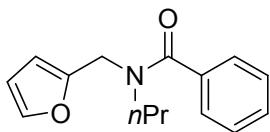
N-(4-methoxybenzyl)-N-propylbenzamide (5ai): Prepared by the general procedure B in 63% yield as white syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.44 – 7.26 (m, 6H), 7.06 (s, 1H), 6.87 (br, 2H), 4.71 (s, 1H), 4.42 (s, 1H), 3.76 (s, 3H), 3.40 (br, 1H), 3.08 (br, 1H), 1.65 (br, 1H), 1.50 (br, 1H), 0.92 (s, 1.5H), 0.68 (s, 1.5H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.98, 159.03, 136.92, 129.29, 128.44, 128.13, 126.56, 114.10, 55.24, 51.97 (49.59), 46.62 (46.02), 21.41 (20.25), 11.33 (11.01). HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{22}\text{NO}_2$ [M+H] $^+$ 284.1651, Found 284.1645.



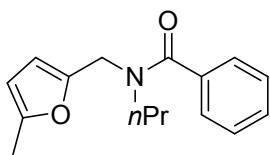
N-(3-bromo-4-methoxybenzyl)-N-propylbenzamide (5aj): Prepared by the general procedure B in 59% yield as white solid; m.p 70°C; ^1H NMR (400 MHz, CDCl_3) δ 7.56 – 7.23 (m, 7H), 6.88 (d, $J = 8.0$ Hz, 1H), 4.68 (s, 1H), 4.42 (s, 1H), 3.89 (s, 3H), 3.40 (br, 1H), 3.11 (br, 1H), 1.67 (br, 1H), 1.52 (br, 1H), 0.94 (br, 1.5H), 0.72 (br, 1.5H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.05, 155.28, 136.63, 132.97, 131.84, 129.43, 128.50, 126.53, 112.08, 100.00, 56.32, 51.48 (49.87), 46.29 (46.18), 21.51 (20.27), 11.42 (11.02). HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{20}\text{BrNNaO}_2$ [M+Na] $^+$ 384.0575, Found 384.0570.



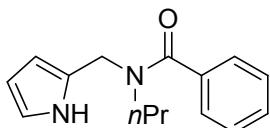
N-propyl-N-(4-(trifluoromethyl)benzyl)benzamide (5ak): Prepared by the general procedure B in 57% yield as white syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.61 (d, $J = 7.8$ Hz, 2H), 7.51 – 7.25 (m, 7H), 4.81 (s, 1.2H), 4.57 (s, 0.8H), 3.42 (br, 0.8H), 3.15 (br, 1.2H), 1.67 (br, 0.8H), 1.53 (br, 1.2H), 0.95 (br, 1.2H), 0.72 (br, 1.8H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.26, 141.83, 141.37, 136.41, 129.56, 128.54, 128.16, 127.08, 126.52, 125.66, 52.16, 50.39, 47.28, 46.57, 21.60, 20.33, 11.26, 10.93. HRMS (ESI) m/z calcd for $\text{C}_{18}\text{H}_{18}\text{F}_3\text{NNaO}$ [M+Na] $^+$ 344.1238, Found 344.1233.



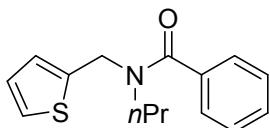
N-(furan-2-ylmethyl)-N-propylbenzamide (5al): Prepared by the general procedure B in 62% yield as yellow syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.64 – 7.19 (m, 6H), 6.47 – 6.10 (m, 2H), 4.74 (s, 1H), 4.38 (s, 1H), 3.45 (br, 1H), 3.16 (br, 1H), 1.66 – 1.46 (m, 2H), 0.92 (s, 1.5H), 0.71 (s, 1.5H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.80, 151.00 (150.37), 142.56 (142.08), 136.63, 129.38, 128.41, 126.86, 110.42, 108.49, 50.24 (46.44), 46.19 (40.63), 21.46 (20.26), 11.29 (10.99); HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{17}\text{NNaO}_2$ [M+H] $^+$ 266.1157, Found 266.1151.



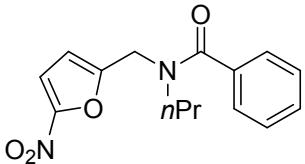
N-((5-methylfuran-2-yl)methyl)-N-propylbenzamide (5am): Prepared by the general procedure B in 62% yield as brown syrup; ^1H NMR (400 MHz, CDCl_3) δ 7.45 – 7.17 (m, 5H), 6.17 – 5.75 (m, 2H), 4.60 (s, 1H), 4.23 (s, 1H), 3.36 (br, 1H), 3.08 (br, 1H), 2.18 (s, 3H), 1.51 (br, 2H), 0.84 (br, 1.5H), 0.63 (br, 1.5 H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.7, 152.3, 148.4, 136.8, 129.3, 128.4, 126.9, 109.3, 106.2, 50.0, 46.3, 40.7, 13.6, 11.1. HRMS (ESI) m/z calcd for $\text{C}_{16}\text{H}_{20}\text{NO}_2$ [M+H] $^+$ 258.1494, Found 258.1489.



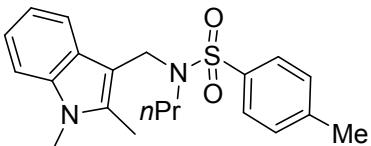
N-((1H-pyrrol-2-yl)methyl)-N-propylbenzamide (5an): Prepared by the general procedure B in 32% yield as yellow syrup; ^1H NMR (400 MHz, CDCl_3) δ 9.01 (br, 0.6H), 8.84 (br, 0.4H), 7.52–7.34 (m, 5H), 6.8–6.48 (m, 2H), 6.25 (br, 0.4H), 6.04 (br, 0.6H), 4.67 (s, 0.8H), 4.36 (s, 1.2H), 3.49 (s, 1.2H), 3.15 (s, 0.8H), 1.76–1.61 (m, 1.2H), 1.61–1.48 (m, 0.8H), 0.97 (s, 1.8H), 0.74 (s, 1.2H); ^{13}C NMR (101 MHz, CDCl_3) δ 171.82, 137.19, 129.21, 128.40, 126.71, 126.51, 119.05, 118.57, 117.21, 116.25, 108.66, 107.49, 49.38 (46.24), 45.89 (40.49), 21.47 (20.34), 11.44 (11.07). HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_{19}\text{N}_2\text{O}$ [M+H] $^+$ 243.1497, Found 243.1492.



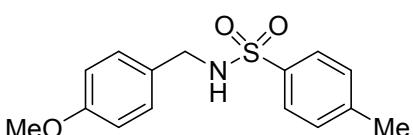
N-propyl-N-(thiophen-2-ylmethyl)benzamide (5ao): Prepared by the general procedure B in 52% yield as yellow syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.51– 7.30 (m, 5H), 7.20 (s, 1H), 7.08 – 6.74 (m, 2H), 4.87 (br, 1.2H), 4.58 (br, 0.8H), 3.45 (br, 0.8H), 3.14 (br, 1.2H), 1.73 – 1.43 (m, 2H), 0.91 (br, 1.2H), 0.70 (br, 1.8H); ¹³C NMR (101 MHz, CDCl₃) δ 171.68, 140.21, 136.61, 129.42, 128.46, 126.61, 125.44, 49.83, 42.60, 21.57, 11.06. HRMS (ESI) *m/z* calcd for C₁₅H₁₇NNaOS [M+Na]⁺ 282.0929, Found 282.0923.



N-((5-nitrofuran-2-yl)methyl)-N-propylbenzamide (5ap): Prepared by the general procedure B in 31% yield as yellow syrup; ¹H NMR (400 MHz, CDCl₃) δ 7.41 (s, 5H), 7.29 (d, *J* = 1.9 Hz, 1H), 6.61 (br, 1H), 4.74 (br, 2H), 3.32 (br, 2H), 1.70 - 1.55 (m, 2H), 0.79 (br, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 172.21, 155.19, 135.63, 129.91, 128.62, 126.85, 126.62, 112.73, 111.83, 51.65, 41.84, 21.92, 10.84. HRMS (ESI) *m/z* calcd for C₁₅H₁₆N₂NaO₄ [M+Na]⁺ 311.1008, Found 311.1002.



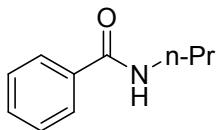
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-4-methyl-N-propylbenzenesulfonamide (7a): Prepared by the general procedure B in 52% yield as yellow solid; m.p 104-106°C; ¹H NMR (400 MHz, CDCl₃) δ 7.72 (d, *J* = 7.9 Hz, 2H), 7.55 – 7.49 (m, 1H), 7.26 (d, *J* = 7.7 Hz, 2H), 7.20 (d, *J* = 5.7 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.03 (t, *J* = 7.3 Hz, 1H), 4.45 (s, 2H), 3.58 (s, 3H), 2.95 (t, *J* = 7.4 Hz, 2H), 2.40 (s, 3H), 2.34 (s, 3H), 1.32-1.21 (m, 2H), 0.58 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 143.00, 137.13, 136.60, 136.02, 129.67, 127.78, 127.25, 120.99, 119.49, 118.21, 108.72, 105.03, 49.13, 42.92, 29.59, 21.73, 21.58, 11.31, 10.31. HRMS (ESI) *m/z* calcd for C₂₁H₂₆N₂NaO₂S [M+Na]⁺ 393.1613, Found 393.1607.



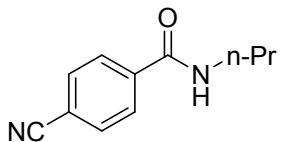
N-(4-methoxybenzyl)-4-methylbenzenesulfonamide (7b): Prepared by the general procedure B in

20% yield as white solid; m.p 6.8 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.73 (d, *J* = 7.9 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 6.76 (d, *J* = 8.1 Hz, 2H), 4.99 (br, 1H), 4.02 (d, *J* = 6.1 Hz, 2H), 3.74 (s, 3H), 2.42 (s, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 159.24, 143.42, 136.95, 129.72, 129.28, 128.42, 127.19, 114.03, 55.30, 46.74, 21.55. HRMS (ESI) *m/z* calcd for C₁₅H₁₇NNaO₃S [M+Na]⁺ 314.0827, Found 314.0821.

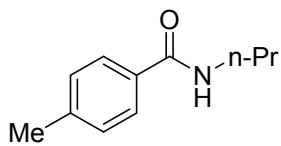
Characterization Data for 6



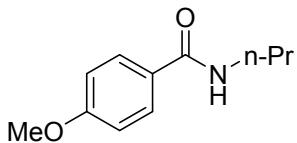
N-propylbenzamide (6a):¹ White solid was obtained in 99% (49 mg) isolated yield; ¹H NMR (400 MHz, CDCl₃) δ 7.80 – 7.74 (m, 2H), 7.48 – 7.42 (m, 1H), 7.42 – 7.34 (m, 2H), 6.63 (br, 1H), 3.38 (q, *J* = 6.6 Hz, 2H), 1.67 – 1.56 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.74, 134.88, 131.22, 128.44, 126.92, 41.79, 22.87, 11.40.



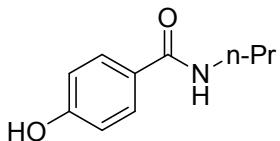
4-Cyano-N-propylbenzamide (6b): White solid was obtained in 99% (56.5 mg) isolated yield; mp 63 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 7.0 Hz, 2H), 6.52 (br, 1H), 3.42 (q, *J* = 6.0 Hz, 2H), 1.71 – 1.58 (m, 2H), 0.98 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 165.84, 138.81, 132.38, 127.67, 118.05, 114.85, 42.04, 22.77, 11.41. HRMS (ESI) *m/z* calcd for C₁₁H₁₃N₂O [M+H]⁺ 189.1028, Found 189.1022.



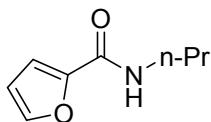
4-Methyl-N-propylbenzamide (6c):² Yellow solid was obtained in 99% (53.1 mg) isolated yield. ¹H NMR (400 MHz, CDCl₃) δ 7.68 (d, *J* = 7.3 Hz, 2H), 7.22 (d, *J* = 7.5 Hz, 2H), 6.33 (br, 1H), 3.41 (q, *J* = 6.6 Hz, 2H), 2.40 (s, 3H), 1.71 – 1.58 (m, 2H), 0.98 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.55, 141.61, 132.04, 129.15, 126.86, 41.71, 22.95, 21.38, 11.43.



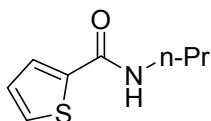
4-Methoxy-N-propylbenzamide (6d):² Yellowish liquid was obtained in 99% (58 mg) isolated yield; ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, *J* = 8.1 Hz, 2H), 6.86 (d, *J* = 8.2 Hz, 2H), 6.73 (br, 1H), 3.80 (s, 3H), 3.35 (q, *J* = 6.6 Hz, 2H), 1.67 - 1.51 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 167.29, 161.97, 128.75, 127.15, 113.60, 55.32, 41.74, 22.92, 11.43.



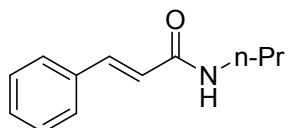
4-Hydroxy-N-propylbenzamide (6e):³ Brown syrup was obtained in 83% (44.6 mg) isolated yield. ¹H NMR (400 MHz, CD₃OD) δ 7.73 – 7.67 (m, 2H), 6.86 – 6.80 (m, 2H), 4.88 (s, 2H), 3.33 – 3.28 (m, 2H), 1.68 – 1.56 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (101 MHz, CD₃OD) δ 168.74, 160.51, 128.78, 125.33, 114.69, 41.32, 22.42, 10.39. HRMS (ESI) *m/z* calcd for C₁₀H₁₃NNaO₂ [M+Na]⁺ 202.0844, Found 202.0838.



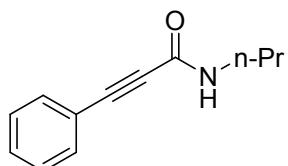
N-propylfuran-2-carboxamide (6f):⁴ Yellow syrup was obtained in 94% (43.2 mg) isolated yield. ¹H NMR (400 MHz, CDCl₃) δ 7.42 (s, 1H), 7.10 (d, *J* = 2.8 Hz, 1H), 6.58 – 6.41 (m, 2H), 3.39 (q, *J* = 6.6 Hz, 2H), 1.69 – 1.56 (m, 2H), 0.97 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 158.47, 148.19, 143.68, 113.87, 112.06, 40.83, 22.93, 11.36;



N-propylthiophene-2-carboxamide (6g): Yellow solid was obtained in 99% (50.2 mg) isolated yield; m.p 58-59°C; ¹H NMR (400 MHz, CDCl₃) δ 7.56 (d, *J* = 3.1 Hz, 1H), 7.44 (d, *J* = 4.8 Hz, 1H), 7.05 (t, *J* = 3.8 Hz, 1H), 6.54 (s, 1H), 3.38 (q, *J* = 6.6 Hz, 2H), 1.69 – 1.56 (m, 2H), 0.95 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 162.11, 139.38, 129.67, 127.87, 127.57, 41.74, 22.93, 11.40. HRMS (ESI) *m/z* calcd for C₈H₁₁NNaOS [M+Na]⁺ 192.0459, Found 192.0454.

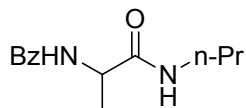


N-propylcinnamamide (6h):⁵ White syrup was obtained in 90 % (52.2 mg) isolated yield; ¹H NMR (400 MHz, CDCl₃) δ 7.62 (d, *J* = 15.6 Hz, 1H), 7.46 (s, 2H), 7.30 (s, 3H), 6.51 (d, *J* = 15.6 Hz, 1H), 6.43 (br, 1H), 3.34 (q, *J* = 6.7 Hz, 2H), 1.65 – 1.54 (m, 2H), 0.94 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 166.21, 140.55, 134.98, 129.51, 128.76, 127.73, 121.18, 41.54, 22.91, 11.45.

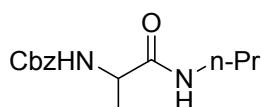


3-Phenyl-N-propylpropiolamide (6i): Yellow syrup was obtained in 96 % (53.9 mg) isolated yield;

¹H NMR (400 MHz, CDCl₃) δ 7.56 – 7.49 (m, 2H), 7.42 – 7.28 (m, 3H), 3.31 (q, *J* = 6.5 Hz, 2H), 1.64 – 1.53 (m, 2H), 0.95 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 153.62, 132.45, 129.96, 128.48, 120.34, 84.51, 83.21, 41.70, 22.60, 11.34. HRMS (ESI) *m/z* calcd for C₁₂H₁₃NNaO [M+Na]⁺ 210.0895, Found 210.0889.

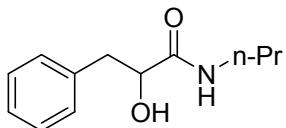


N-(1-oxo-1-(propylamino)propan-2-yl)benzamide (6k): White syrup was obtained in 90 % (63.2 mg) isolated yield; ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, *J* = 7.6 Hz, 2H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.3 Hz, 1H), 7.45 – 7.35 (m, 3H), 4.85 (p, *J* = 6.9 Hz, 1H), 3.30 – 3.12 (m, 2H), 1.58 – 1.49 (m, 2H), 1.47 (d, *J* = 6.9 Hz, 3H), 0.90 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 172.74, 167.26, 133.85, 131.67, 128.46, 127.21, 49.29, 41.29, 22.63, 18.75, 11.35. HRMS (ESI) *m/z* calcd for C₁₃H₁₈N₂NaO₂ [M+Na]⁺ 257.1266, Found 257.1260.

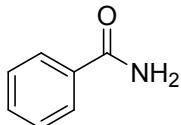


Benzyl (1-oxo-1-(propylamino)propan-2-yl)carbamate (6l): White solid was obtained in 90 % (71.3 mg) isolated yield; m.p 93-95°C; ¹H NMR (400 MHz, CDCl₃) δ 7.38 – 7.23(m, 5H), 6.67 (s,

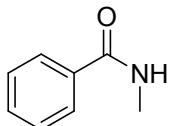
1H), 5.86 (s, 1H), 5.08 (s, 2H), 4.33 – 4.15 (m, 1H), 3.16 (br, 2H), 1.54 – 1.40 (m, 2H), 1.34 (d, J = 7.0 Hz, 3H), 0.88 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 172.55, 156.12, 136.28, 128.51, 128.16, 127.94, 66.88, 50.60, 41.21, 22.65, 18.80, 11.28. HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{20}\text{N}_2\text{NaO}_3$ [M+Na] $^+$ 287.1372, Found 287.1366.



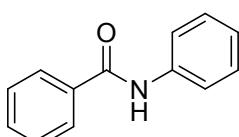
2-Hydroxy-3-phenyl-N-propylpropanamide (6m): Brown syrup was obtained in 55% (34.2 mg) isolated yield; ^1H NMR (400 MHz, CDCl_3) δ 7.35 -7.18 (m, 5H), 6.65 (br, 1H), 4.24 (br, 1H), 3.55 (br, 1H), 3.25 -3.06 (m, 3H), 2.91-2.81 (m, 1H), 1.52-1.38 (m, 2H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 173.11, 137.15, 129.61, 128.55, 126.82, 72.77, 40.91, 40.77, 22.67, 11.32. HRMS (ESI) m/z calcd for $\text{C}_{12}\text{H}_{17}\text{NNaO}_2$ [M+Na] $^+$ 230.1157, Found 230.1151.



Benzamide (6p):⁶ White solid was obtained in 93% (33.7 mg) isolated yield; ^1H NMR (400 MHz, DMSO) δ 8.03 (s, 1H), 7.92 (d, J = 7.6 Hz, 2H), 7.56 – 7.49 (m, 1H), 7.49 – 7.38 (m, 3H); ^{13}C NMR (101 MHz, DMSO) δ 168.50, 134.72, 131.70, 128.68, 127.95.

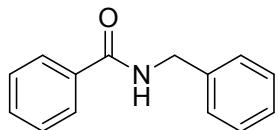


N-methylbenzamide (6q):⁷ White solid was obtained in 70% (28 mg) isolated yield; ^1H NMR (400 MHz, CDCl_3) δ 7.78 (d, J = 7.4 Hz, 2H), 7.44 (t, J = 7.2 Hz, 1H), 7.36 (t, J = 7.5 Hz, 2H), 7.00 (br, 1H), 2.94 (d, J = 4.5 Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3) δ 168.54, 134.57, 131.28, 128.44, 126.97, 26.81.

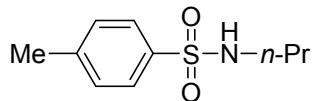


N-phenylbenzamide (6r):⁸ White solid was obtained in 99% (58.5 mg) isolated yield; ^1H NMR (400

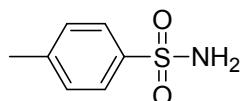
MHz, DMSO) δ 10.27 (br, 1H), 7.98 (d, *J* = 7.3 Hz, 2H), 7.82 (d, *J* = 7.8 Hz, 2H), 7.63-7.51 (m, 3H), 7.37 (t, *J* = 7.8 Hz, 2H), 7.12 (t, *J* = 7.1 Hz, 1H); ¹³C NMR (101 MHz, DMSO) δ 166.06, 139.67, 135.49, 132.00, 129.07, 128.84, 128.13, 124.13, 120.86;



N-benzylbenzamide (6s):⁹ White solid was obtained in 99% (63 mg) isolated yield; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.45 (t, *J* = 7.3 Hz, 1H), 7.36 (t, *J* = 7.3 Hz, 2H), 7.32 – 7.22 (m, 5H), 6.84 (s, 1H), 4.57 (d, *J* = 5.5 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃) δ 167.53, 138.36, 134.43, 131.51, 128.73, 128.55, 127.85, 127.52, 127.08, 44.06;



4-Methyl-N-propylbenzenesulfonamide (8a):¹⁰ Yellow solid was obtained in 99% (63.3 mg) isolated yield; ¹H NMR (400 MHz, CDCl₃) δ 7.77 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 5.05 (s, 1H), 2.88 (q, *J* = 6.9 Hz, 2H), 2.42 (s, 3H), 1.52 – 1.42 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (101 MHz, CDCl₃) δ 143.26, 137.10, 129.66, 127.09, 44.95, 22.86, 21.47, 11.09.



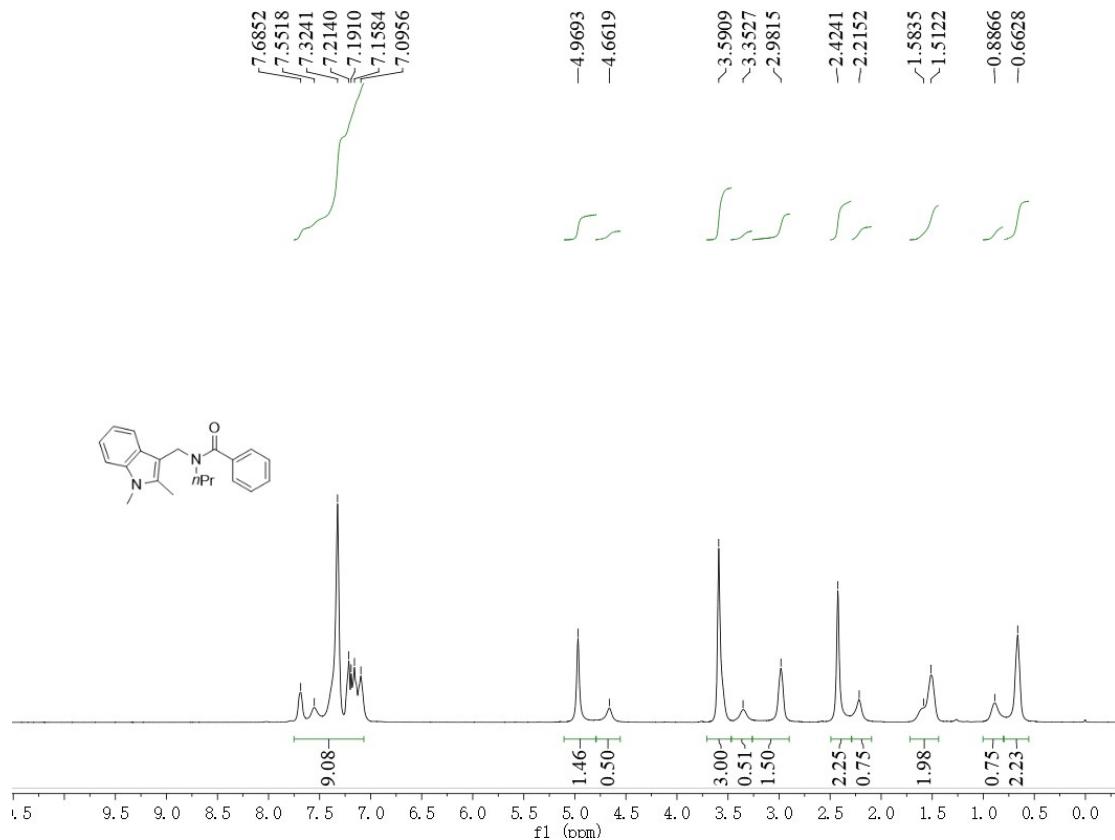
4-Methylbenzenesulfonamide (8b):¹¹ White solid was obtained in 87% (44.6 mg) isolated yield; ¹H NMR (400 MHz, CD₃OD) δ 7.80 (d, *J* = 7.9 Hz, 2H), 7.35 (d, *J* = 7.9 Hz, 2H), 4.82 (s, 2H), 2.42 (s, 3H); ¹³C NMR (101 MHz, CD₃OD) δ 142.80, 140.67, 129.17, 125.79.

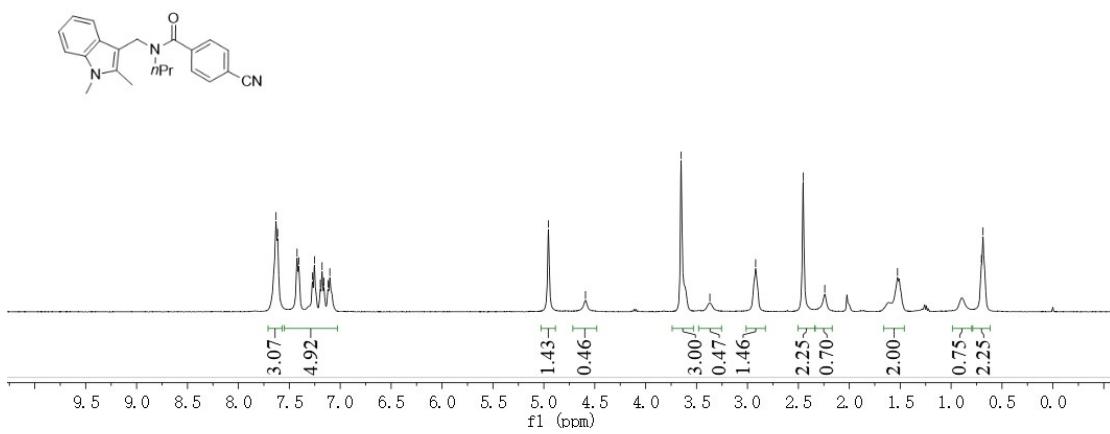
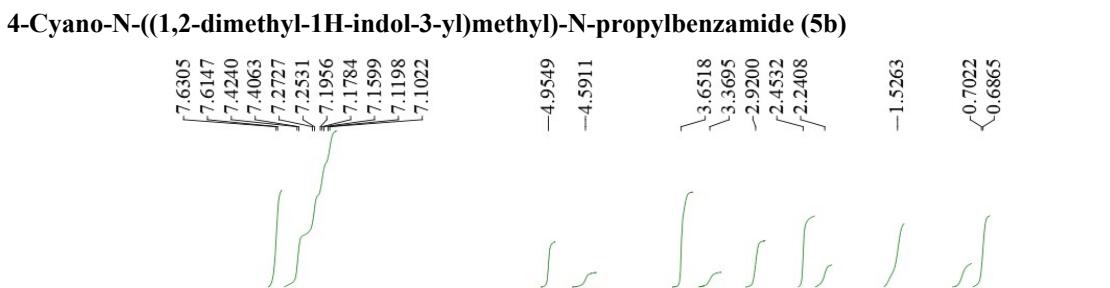
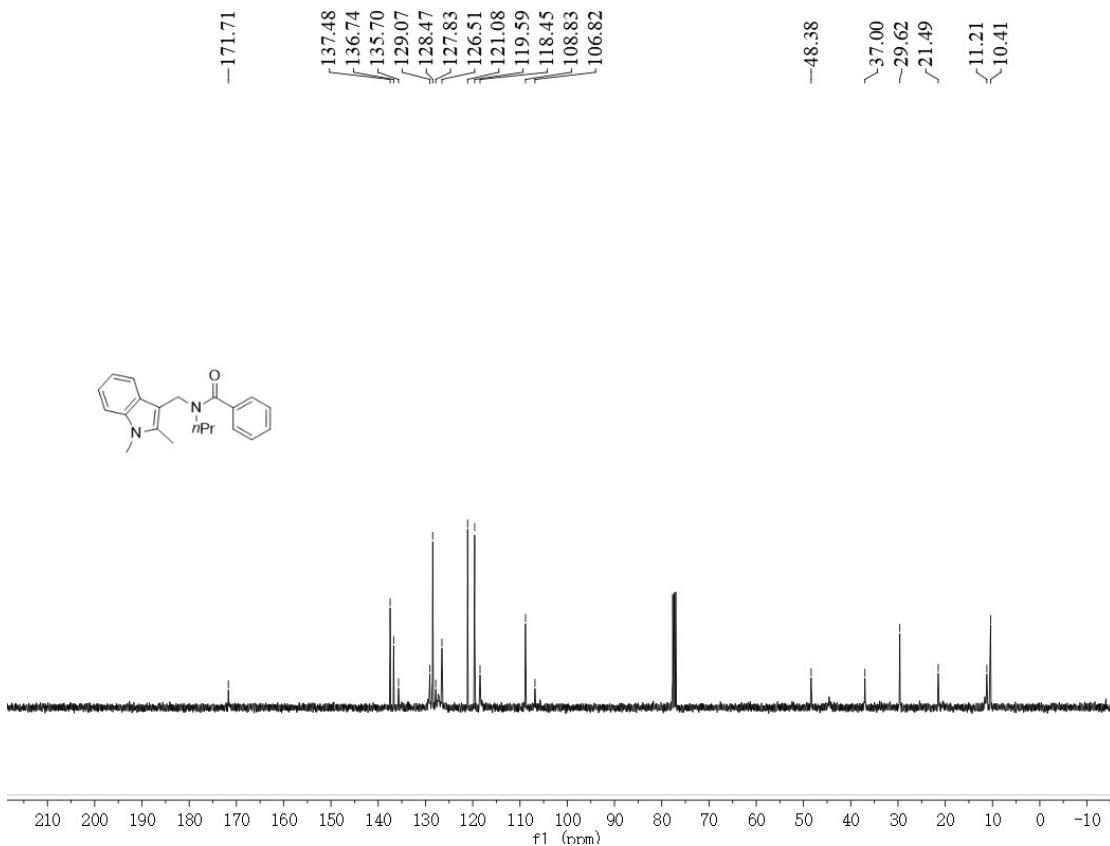
References

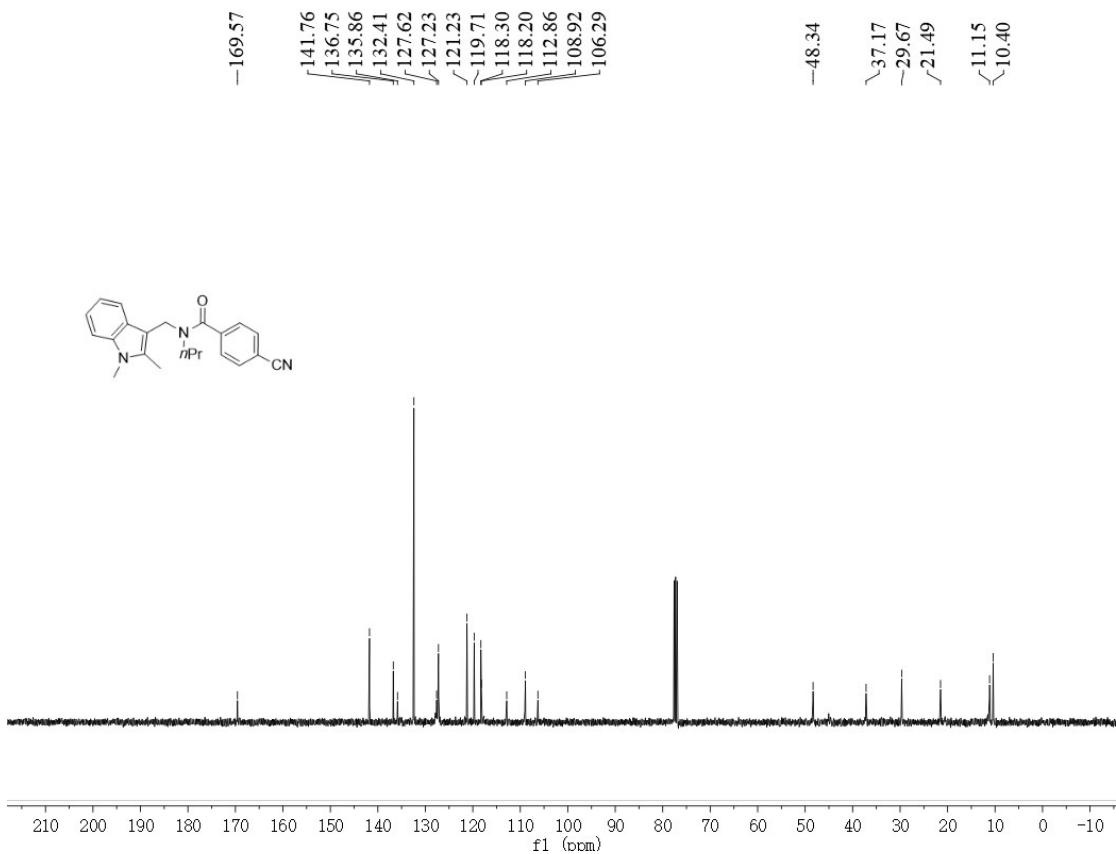
1. D. P. Ojha, K. Gadde, and K. R. Prabhu, *Org. Lett.*, 2016, **18**, 5062.
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¹H and ¹³C NMR spectra of all products

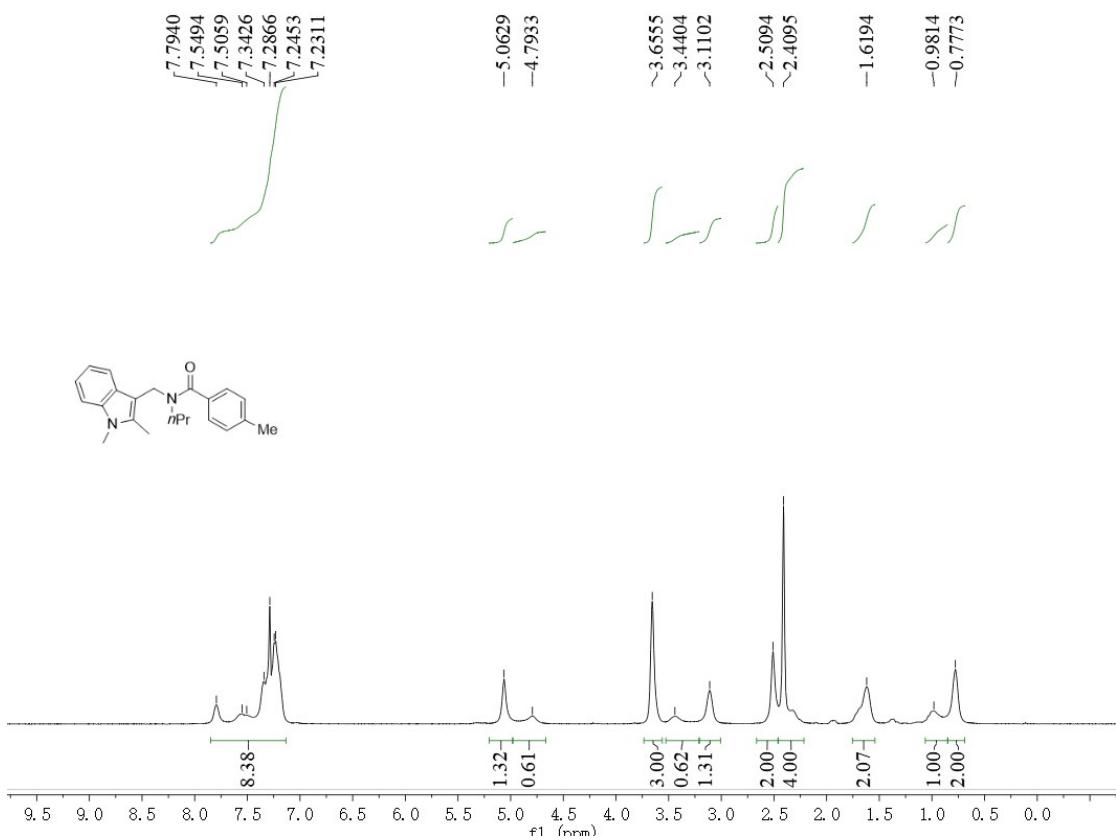
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylbenzamide (5a)

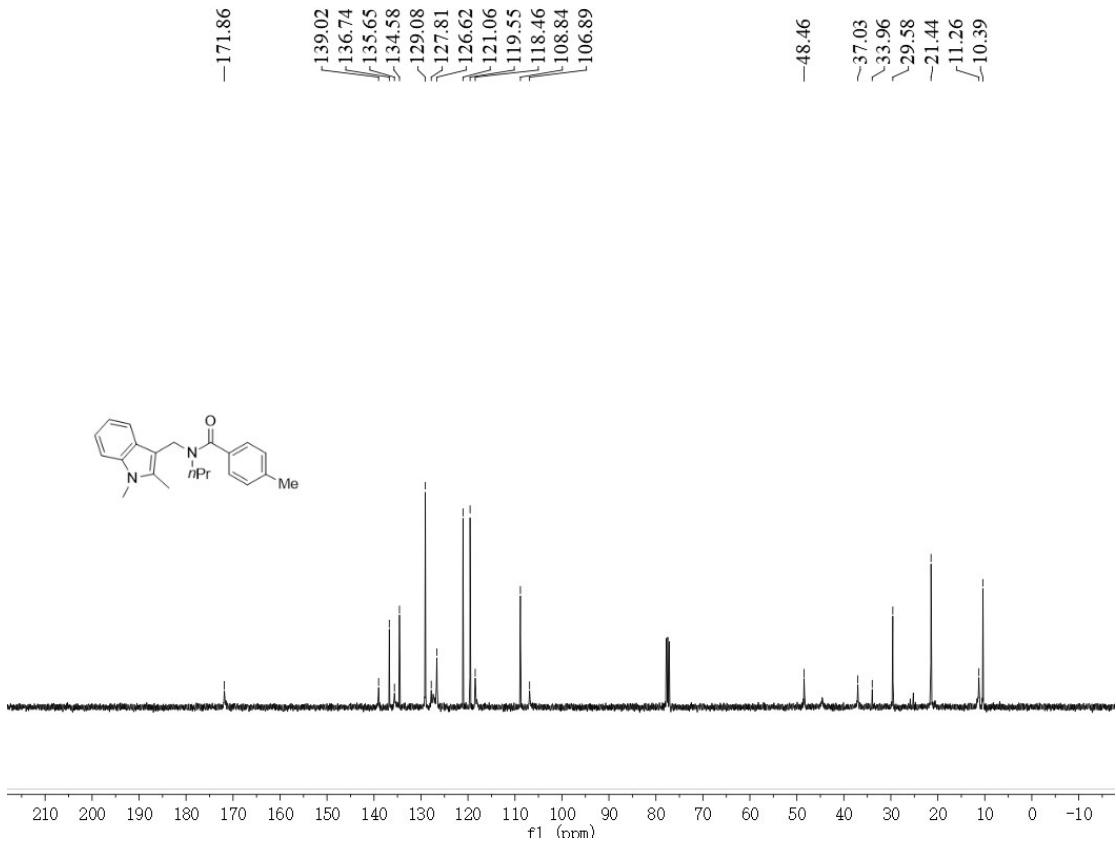




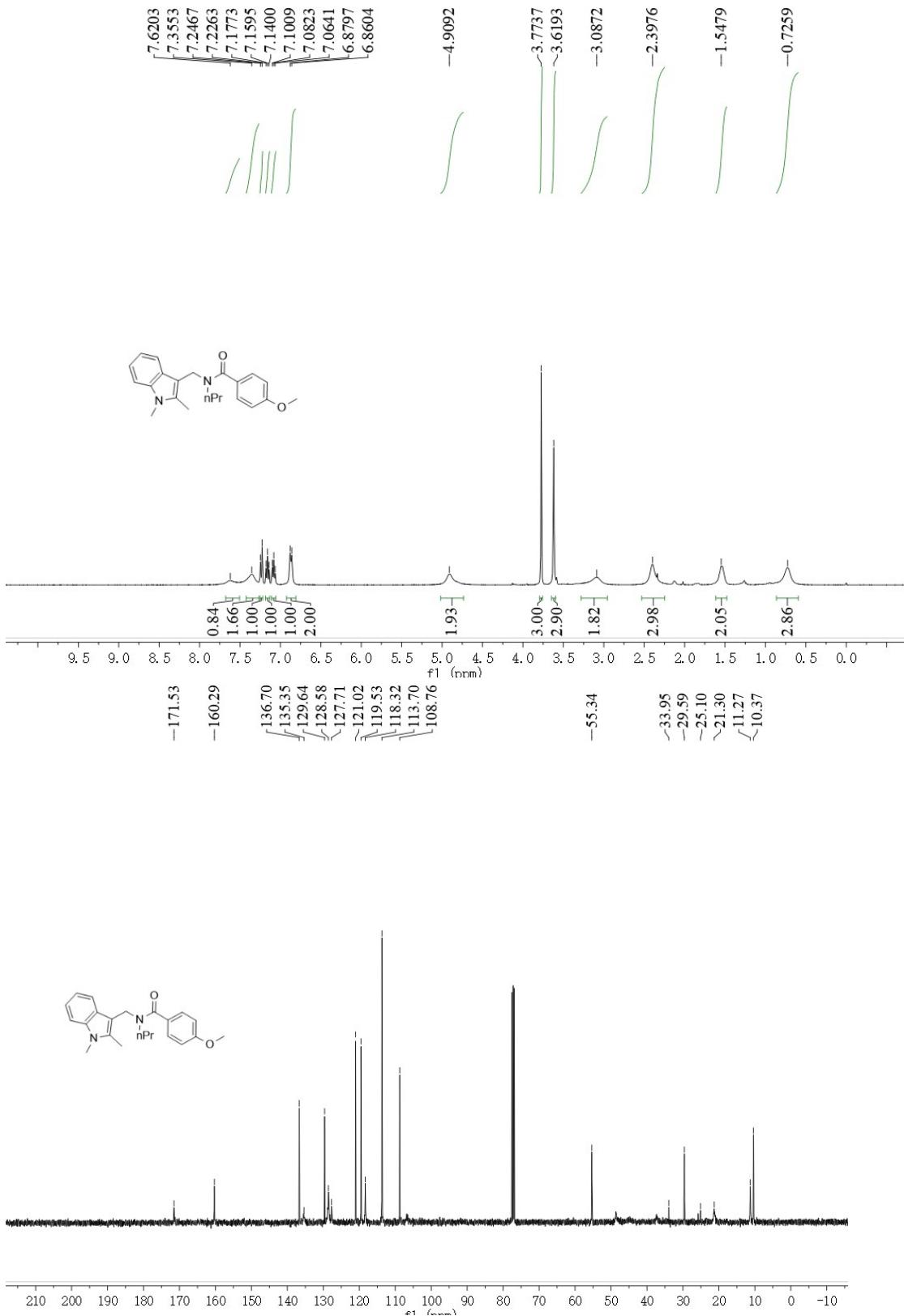


N-((1,2-dimethyl-1H-indol-3-yl)methyl)-4-methyl-N-propylbenzamide (5c)

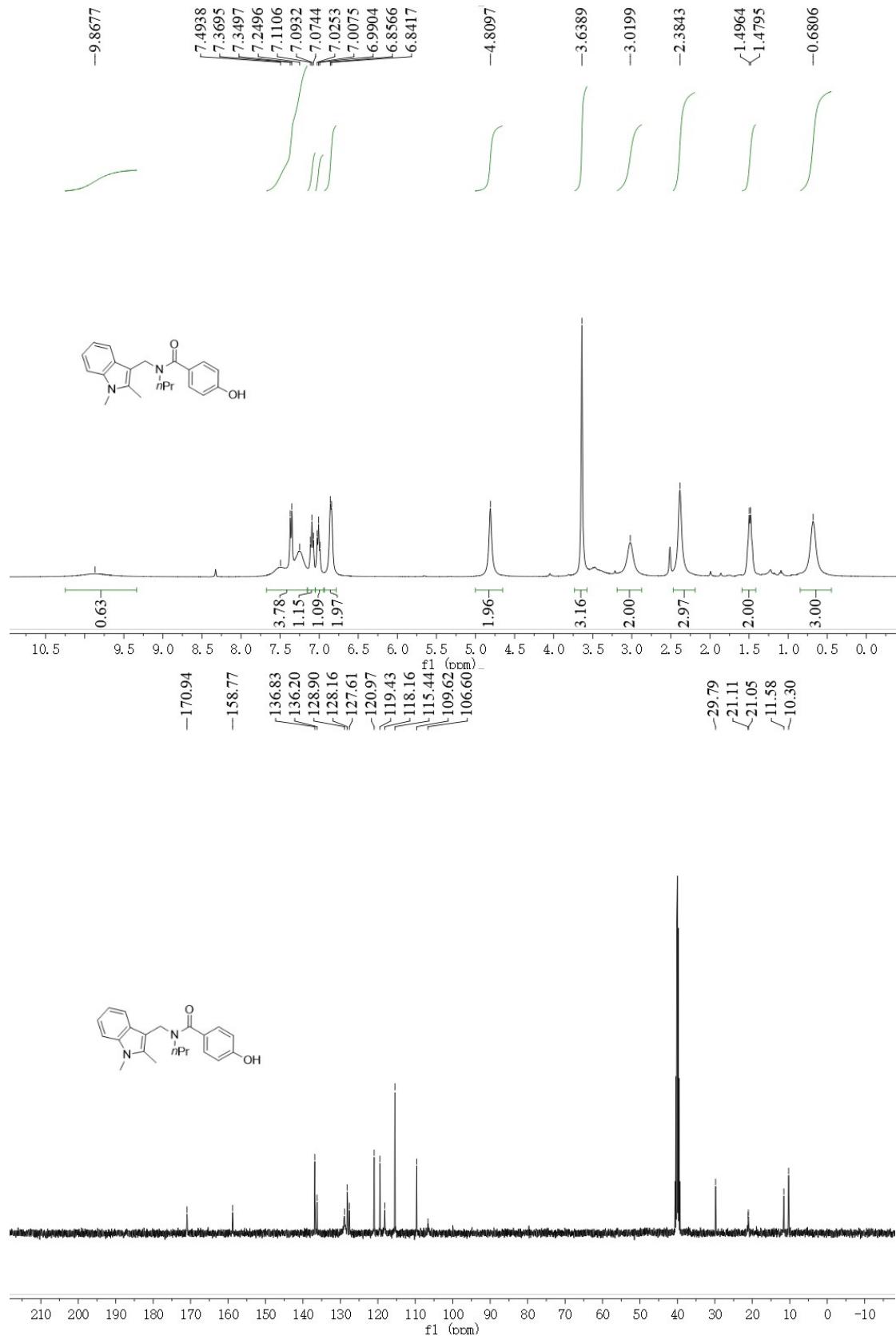




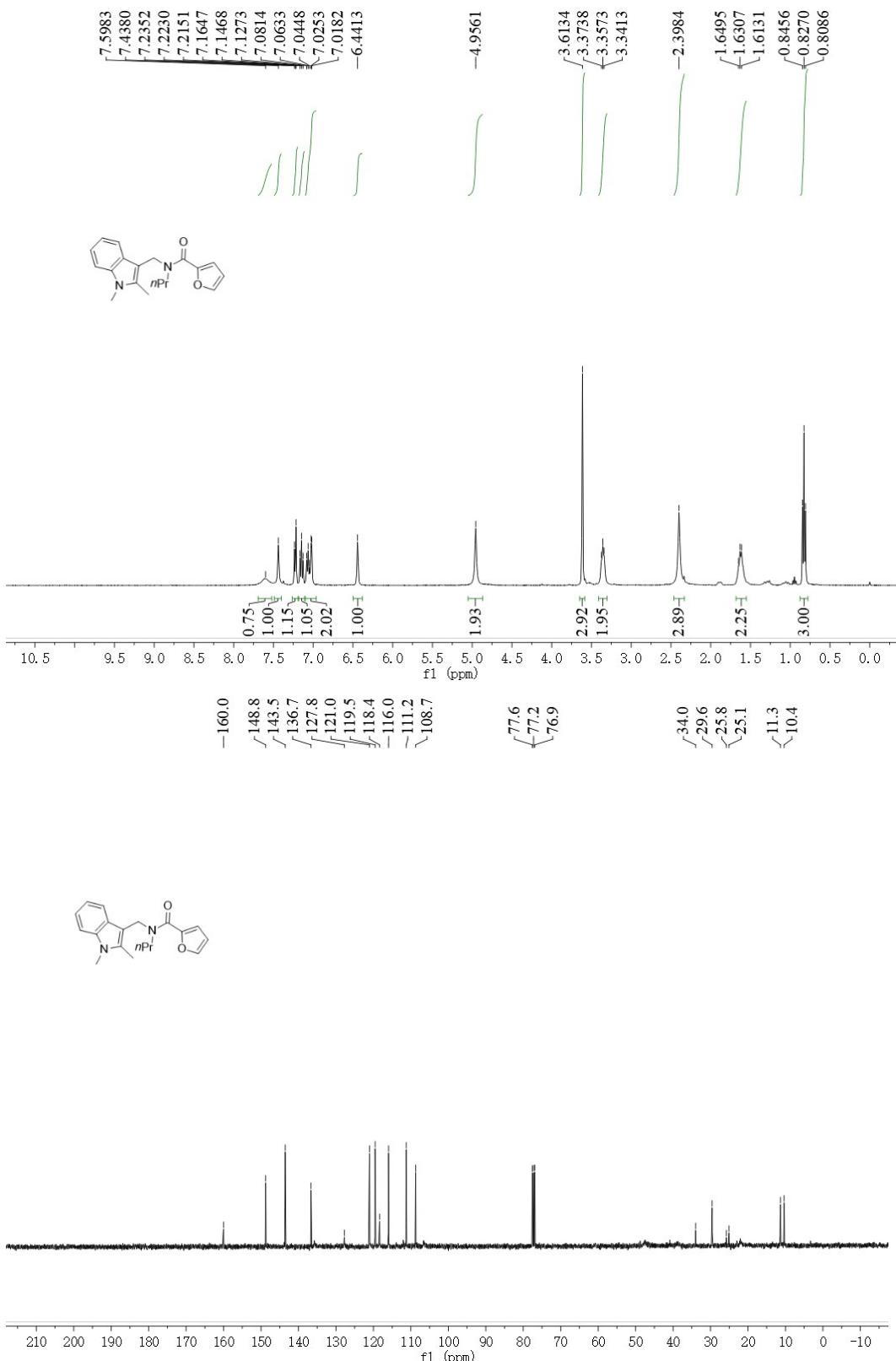
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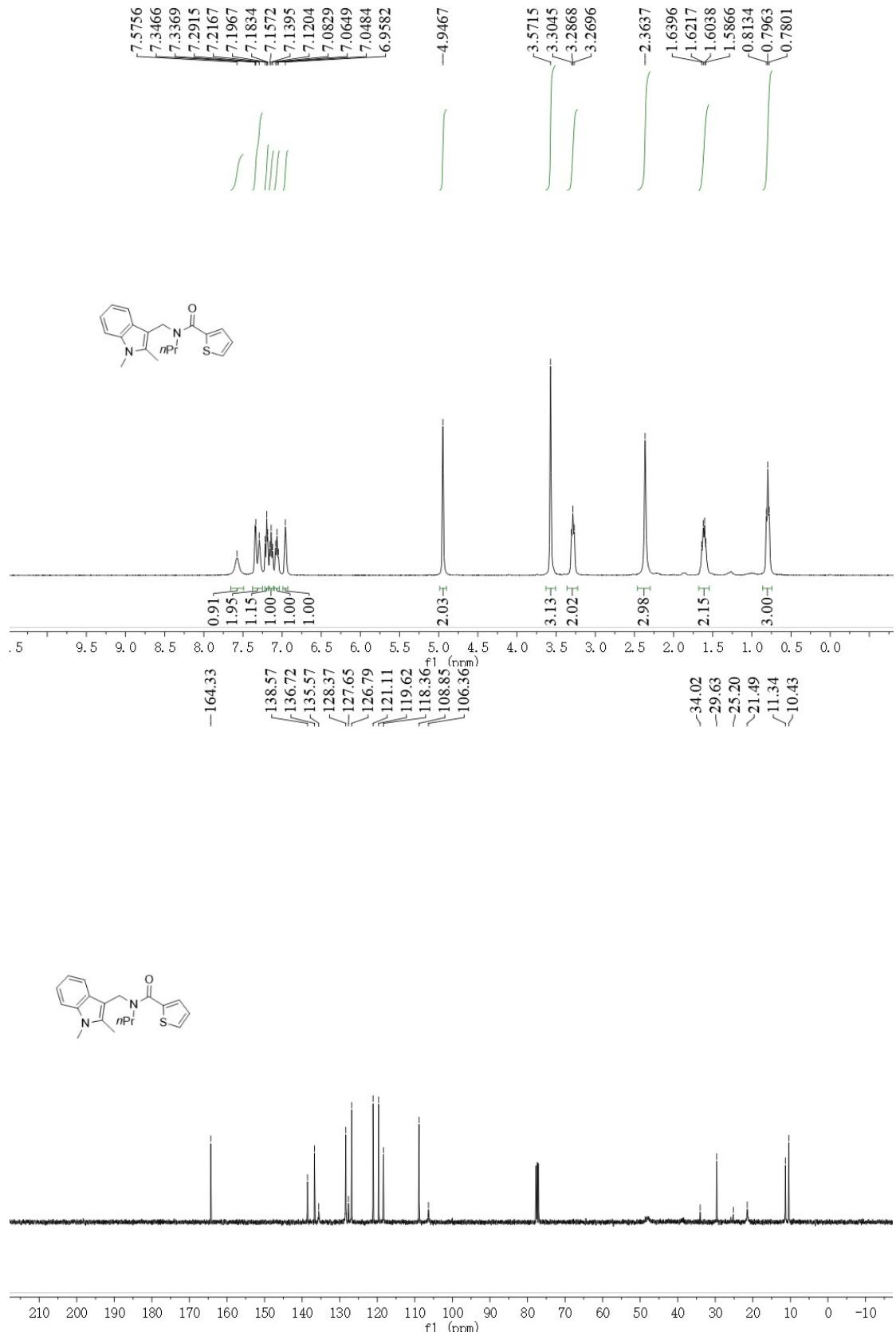
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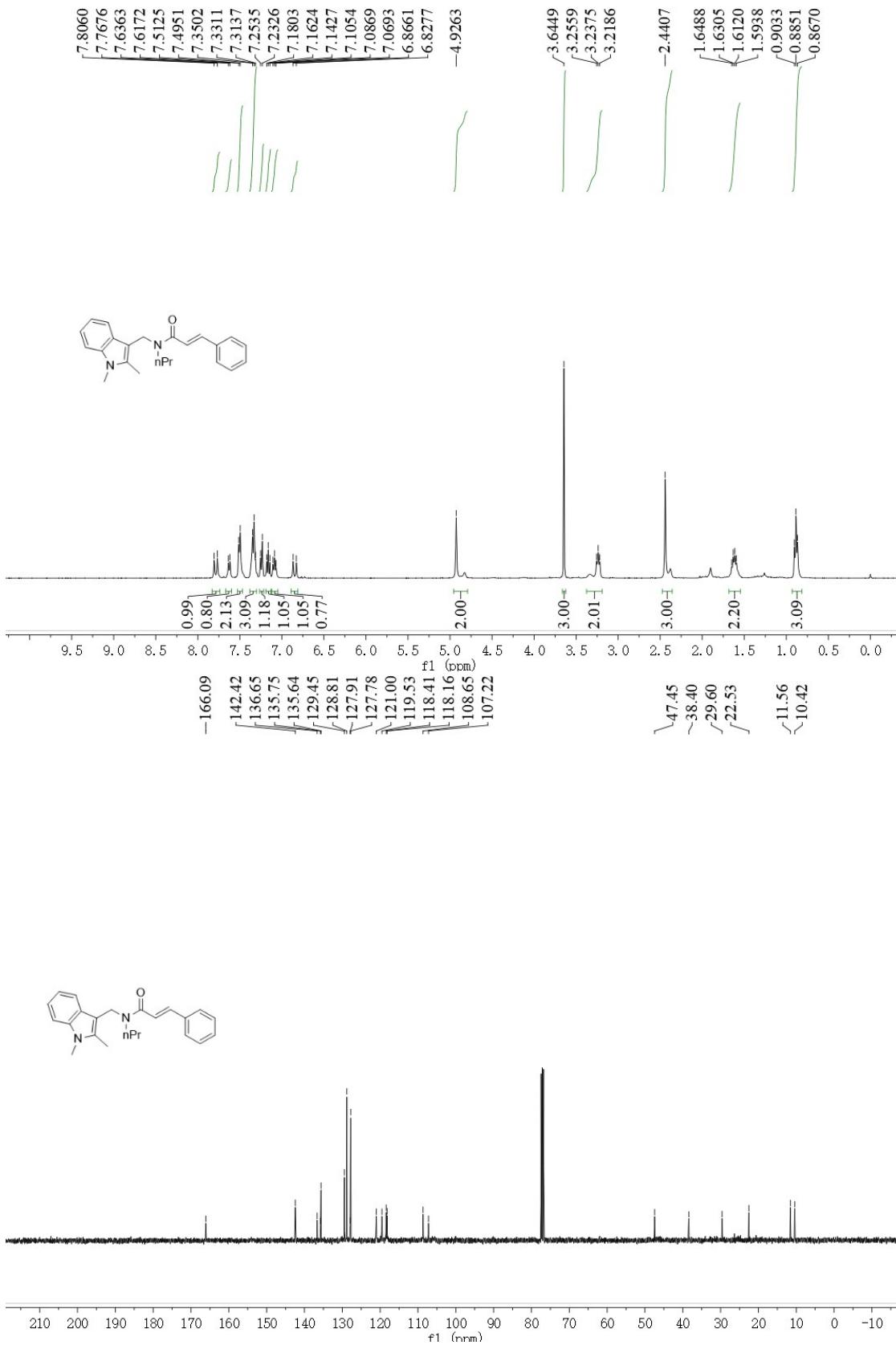


N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylfuran-2-carboxamide (**5f**)

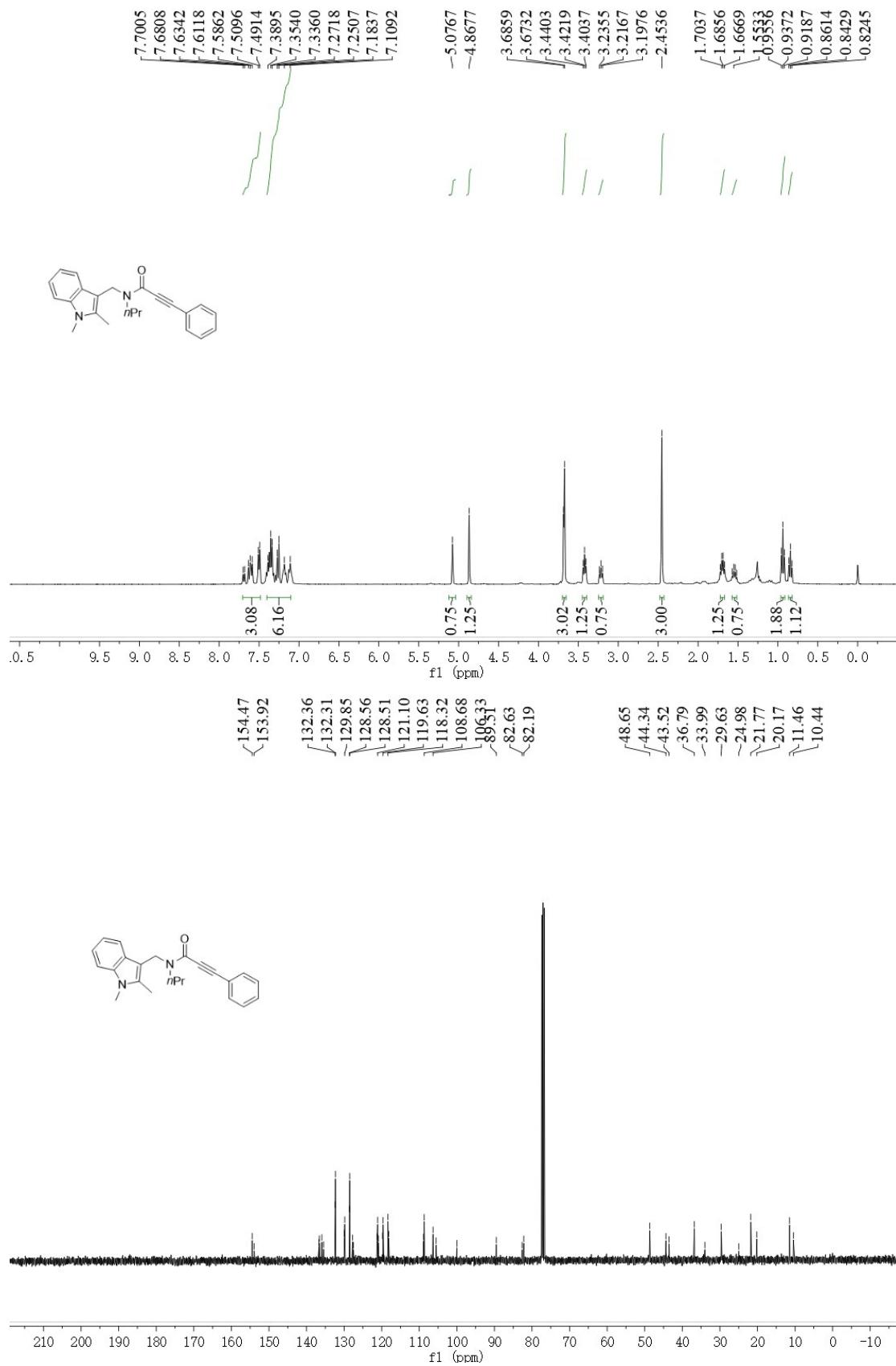


N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylthiophene-2-carboxamide (5g)

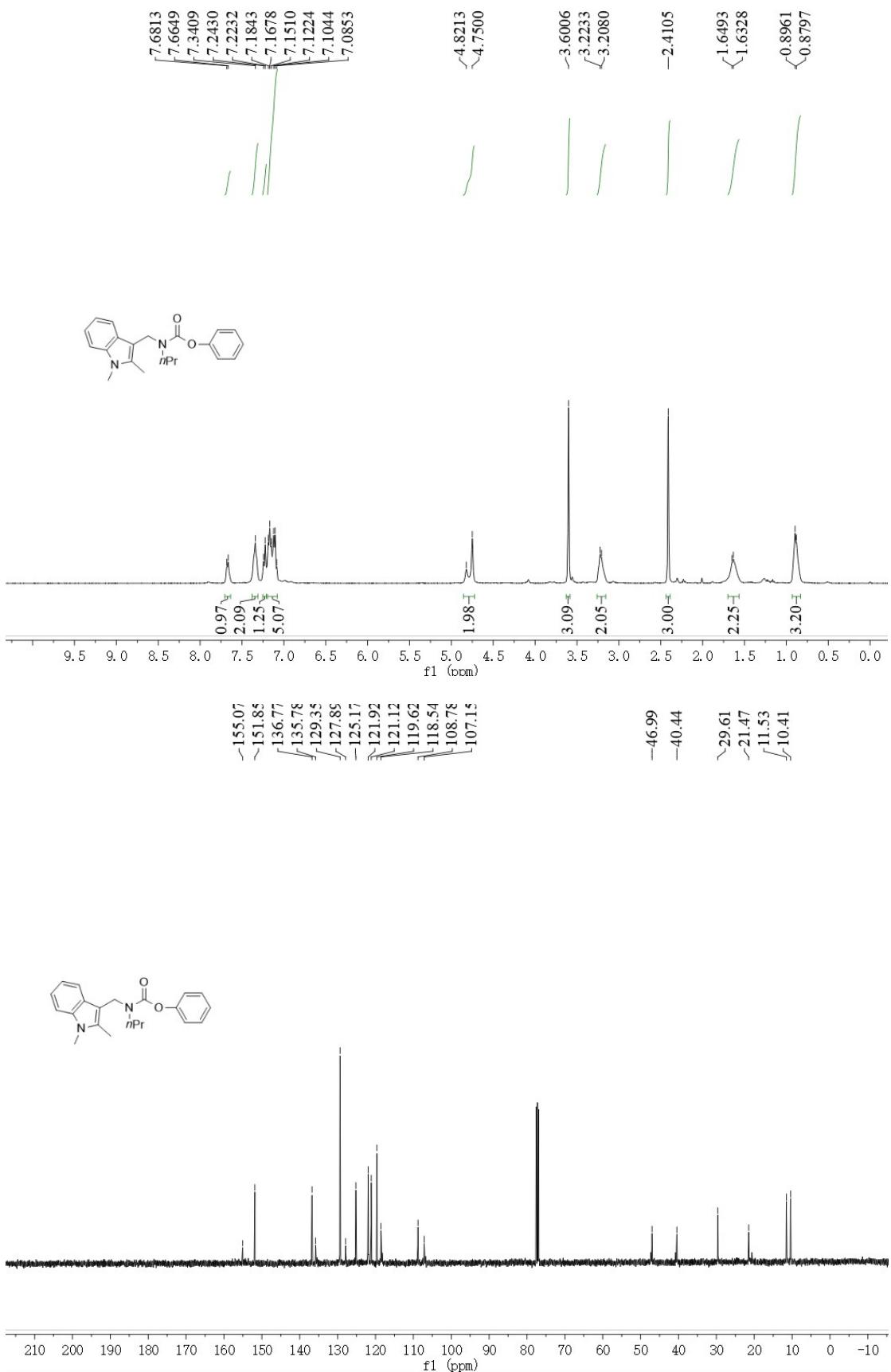




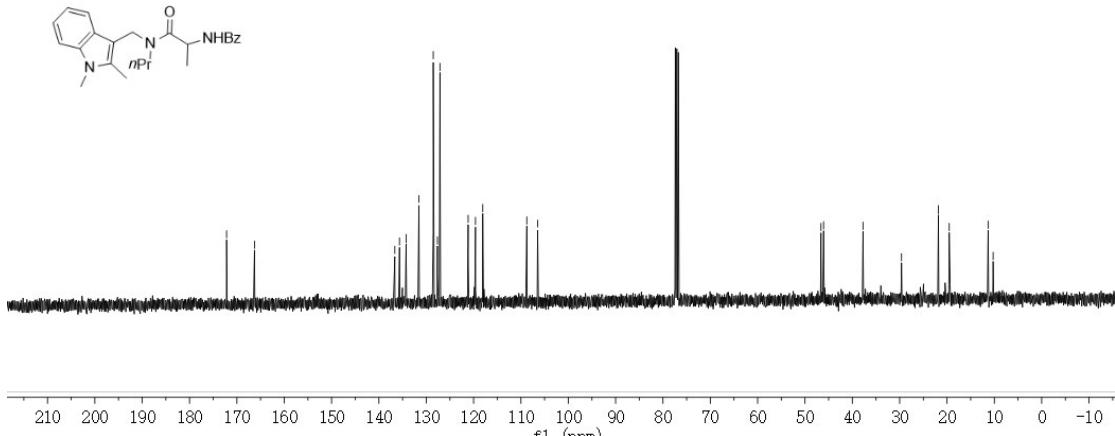
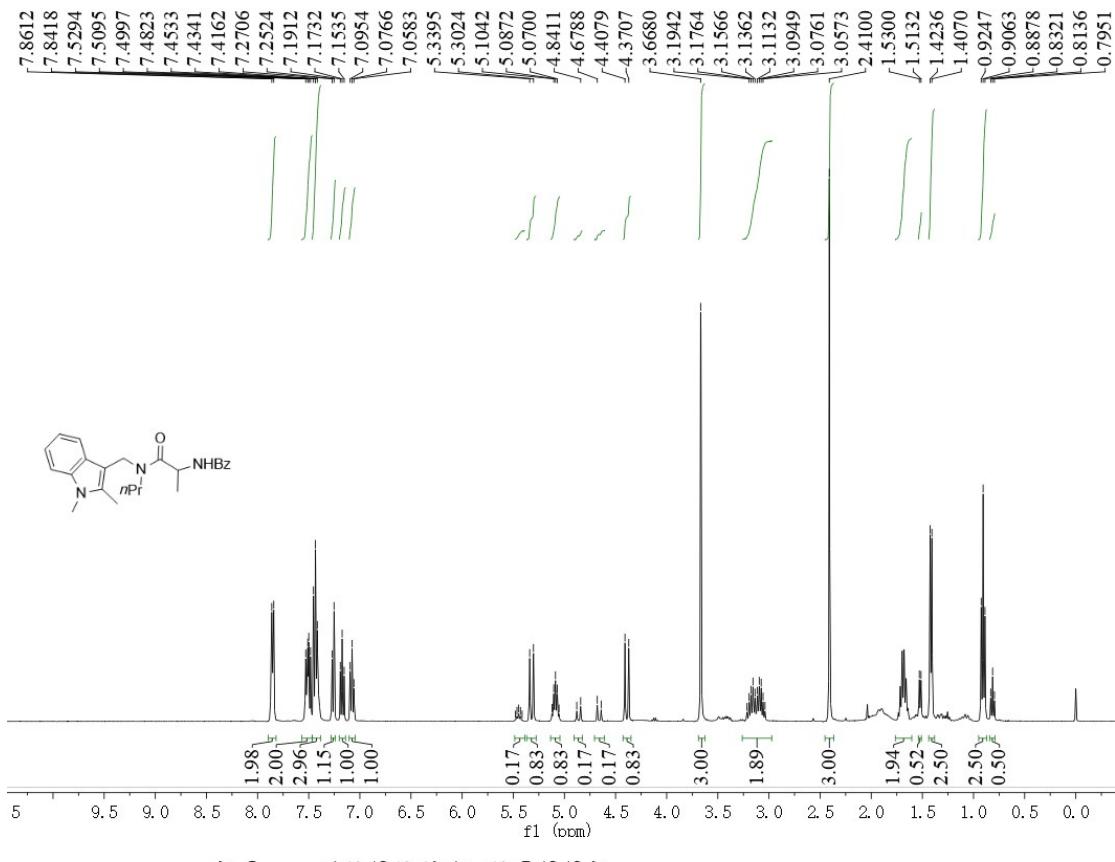
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-3-phenyl-N-propylpropiolamide (5i)



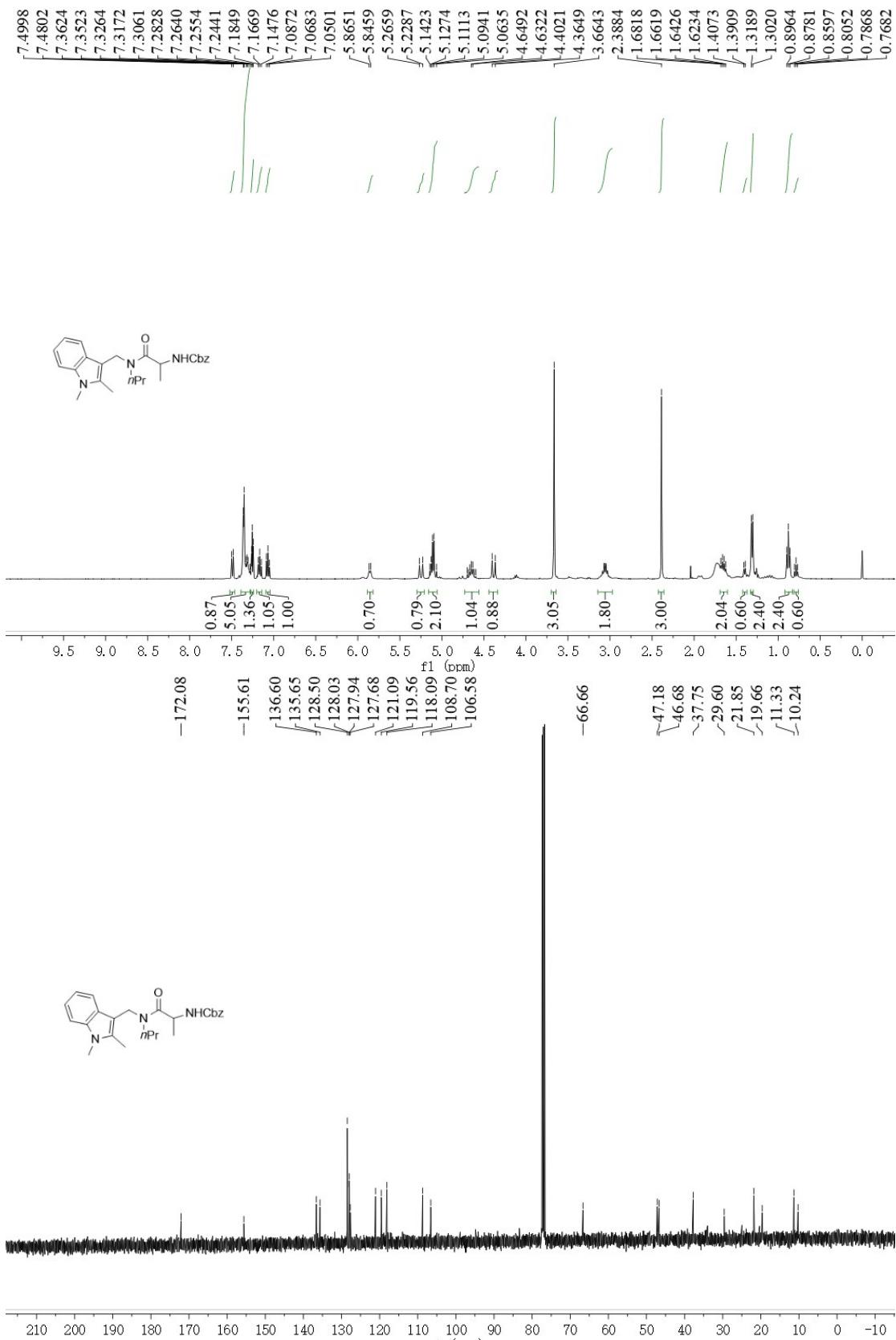
Phenyl ((1,2-dimethyl-1H-indol-3-yl)methyl)(propyl)carbamate (5j)



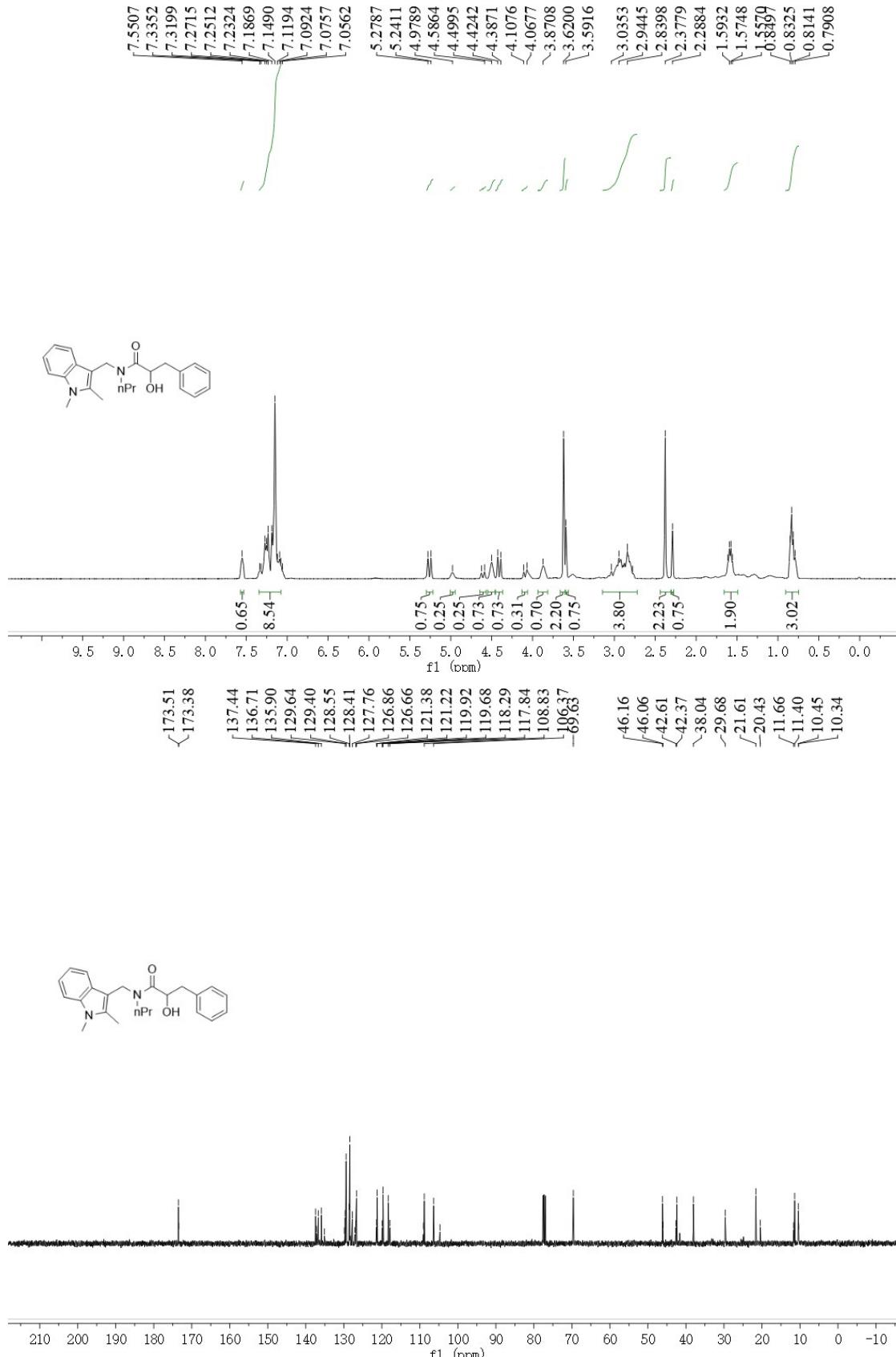
N-((1-((1,2-dimethyl-1H-indol-3-yl)methyl)(propyl)amino)-1-oxopropan-2-yl)benzamide (5k)



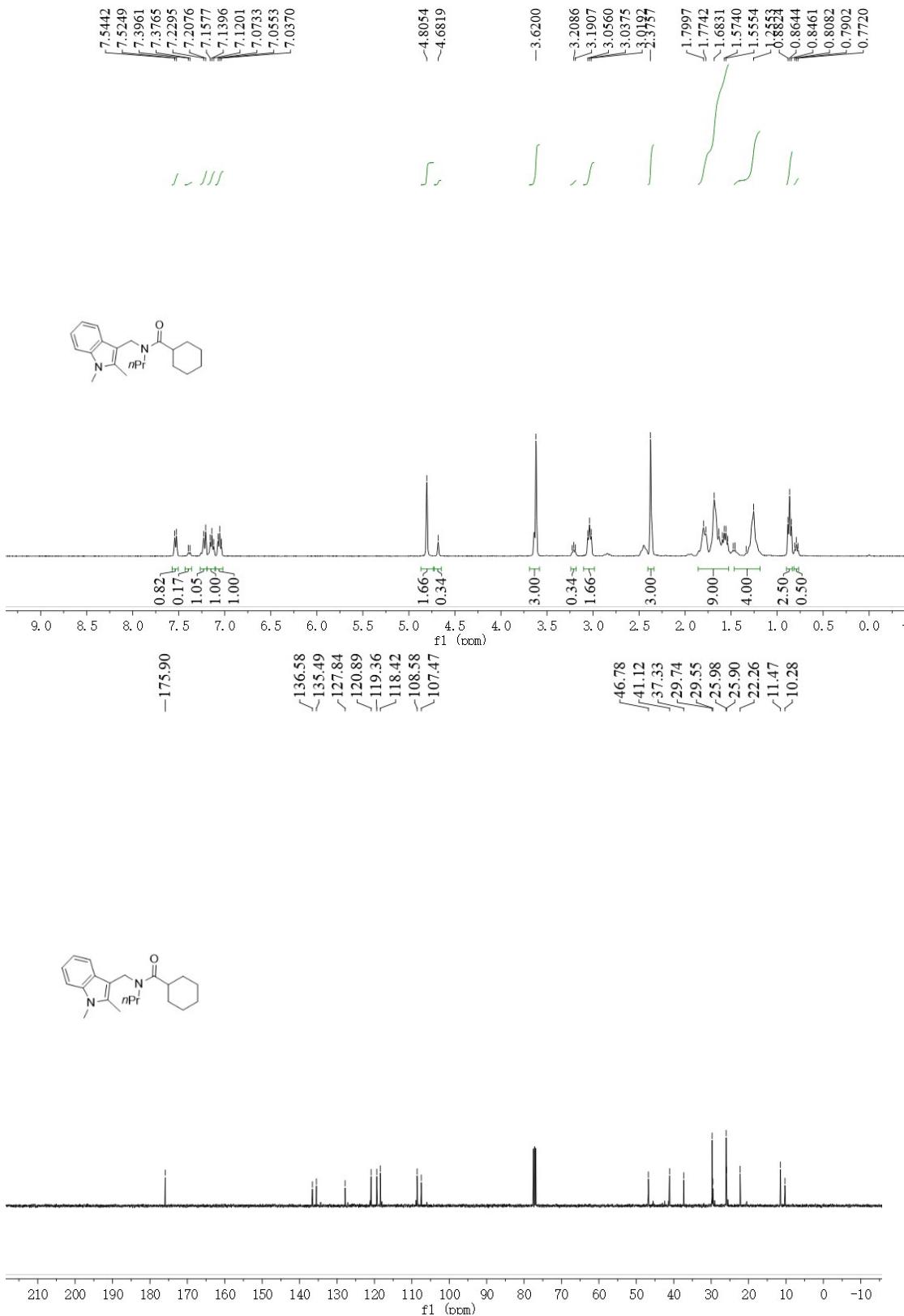
Benzyl ((1,2-dimethyl-1H-indol-3-yl)methyl)(propyl)amino-1-oxopropan-2-yl carbamate (5l)



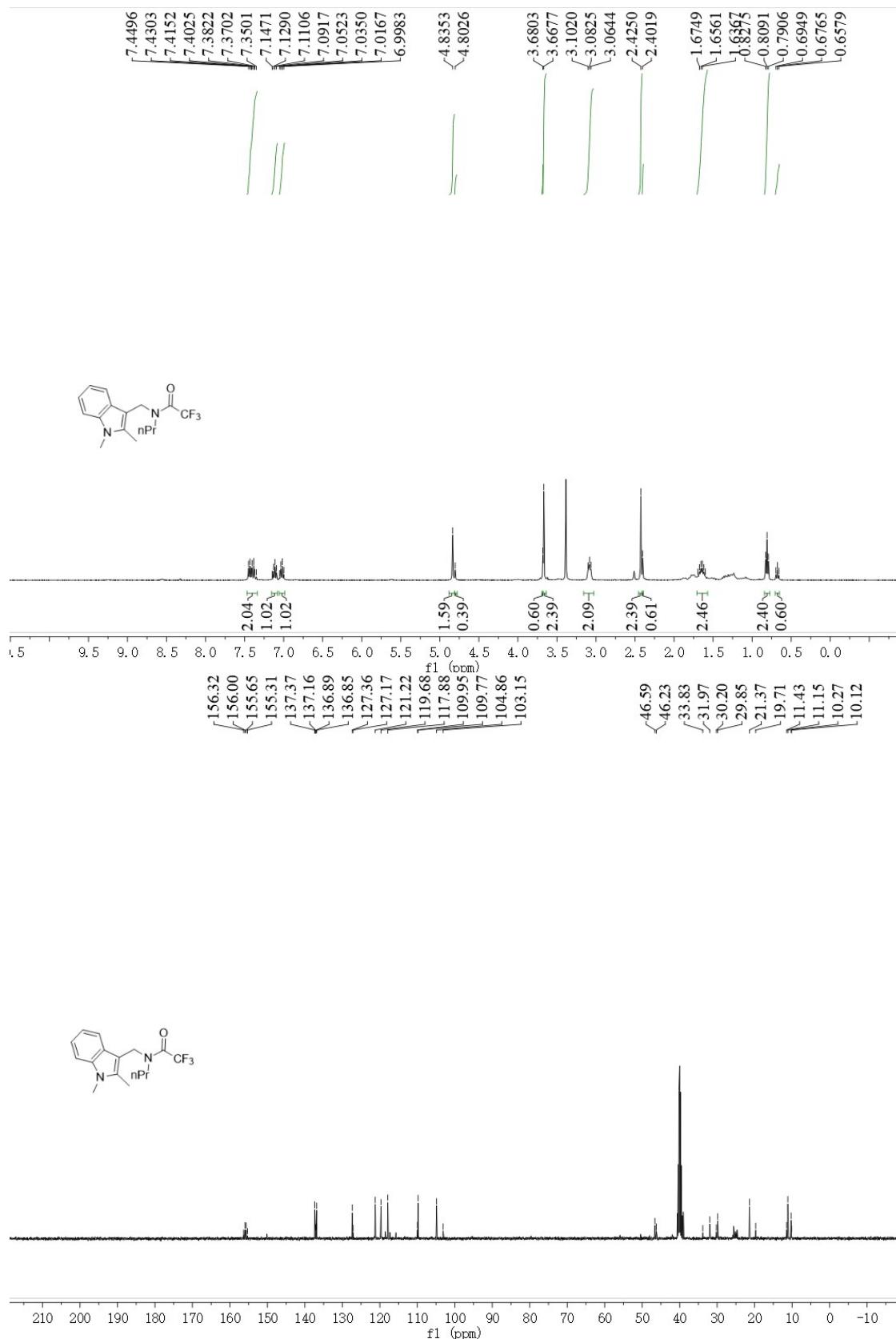
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-2-hydroxy-3-phenyl-N-propylpropanamide (5m)

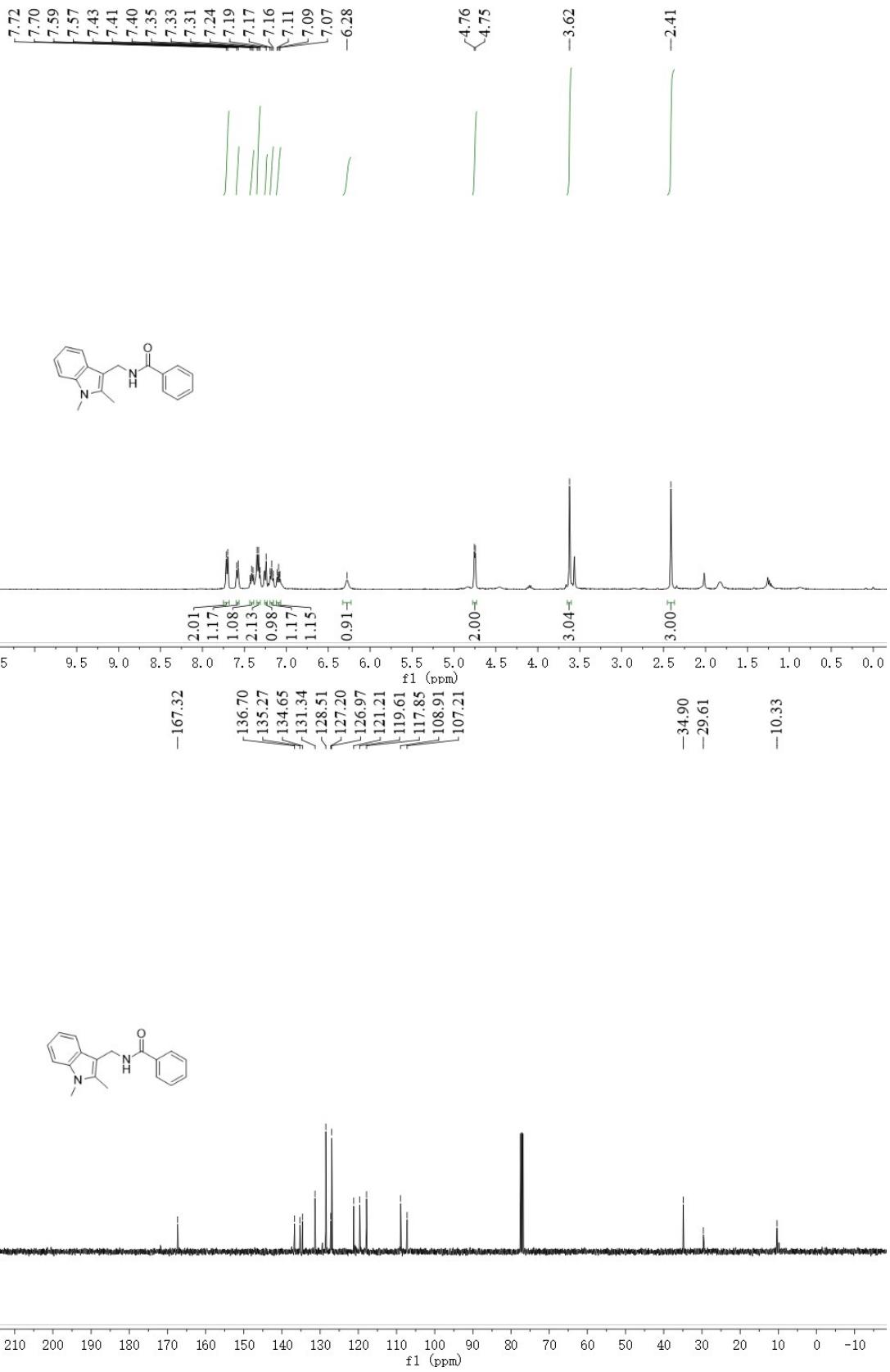


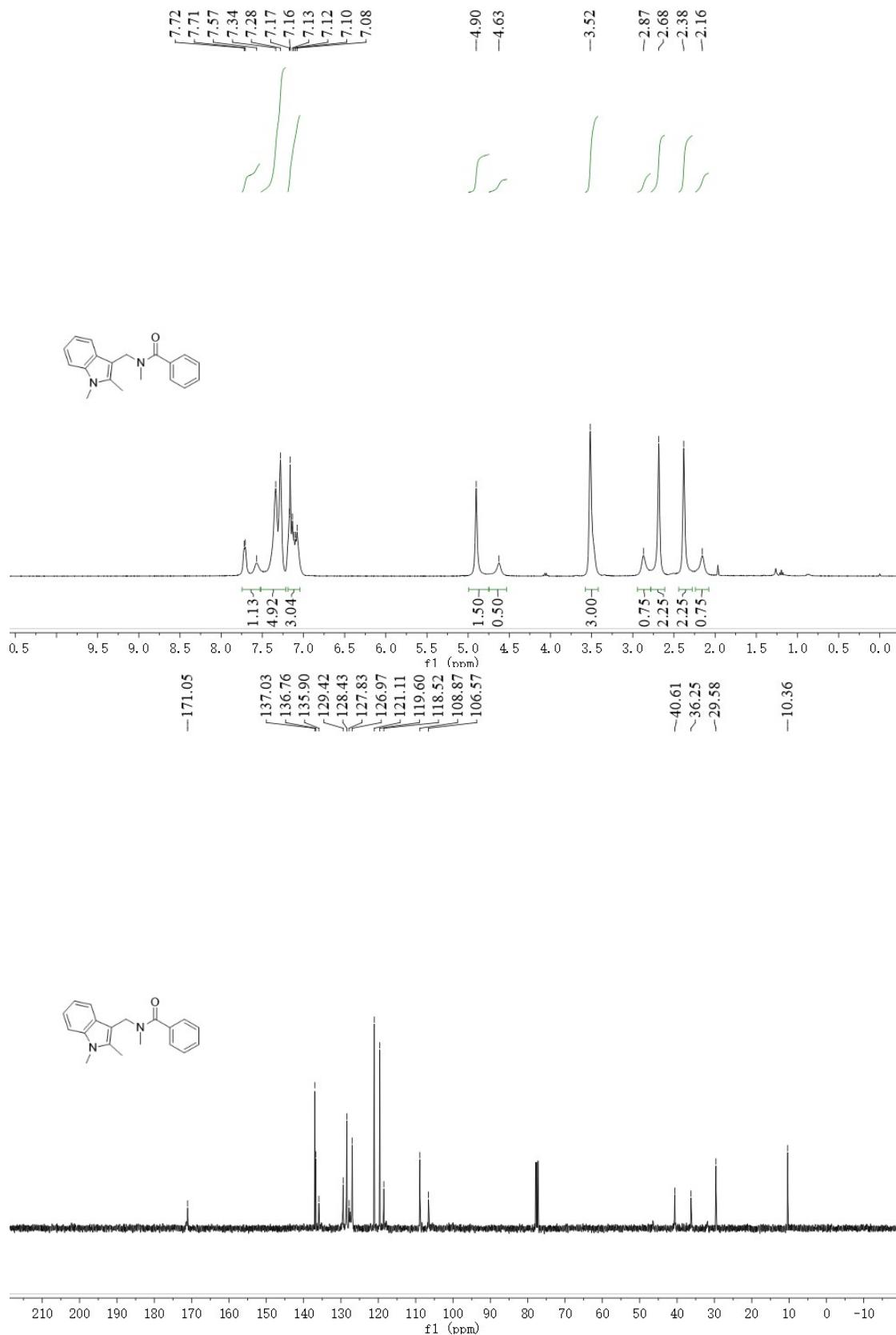
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylcyclohexanecarboxamide (5n)



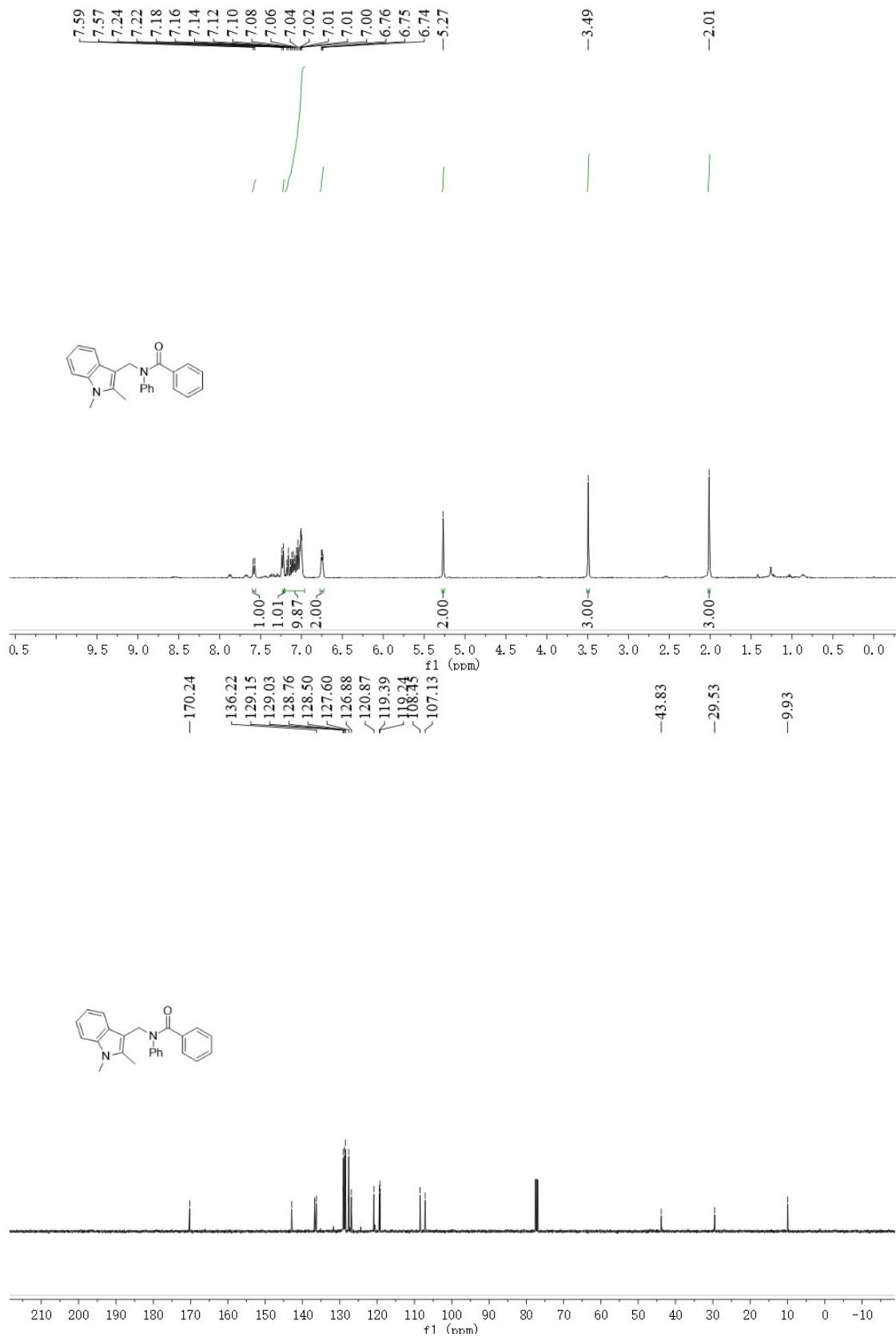
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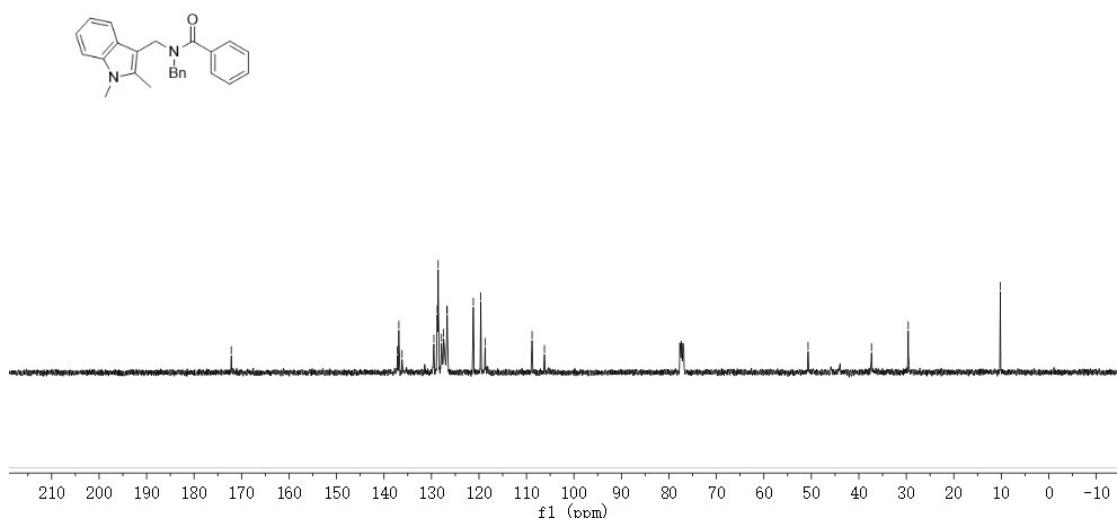
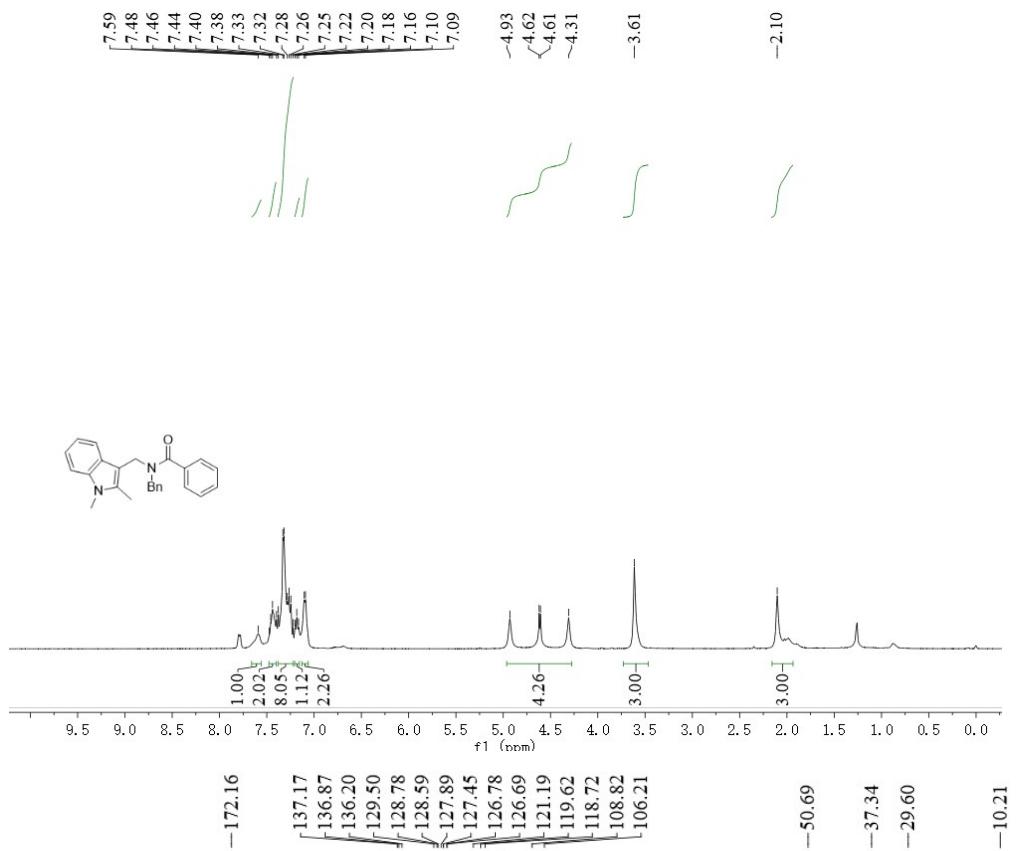




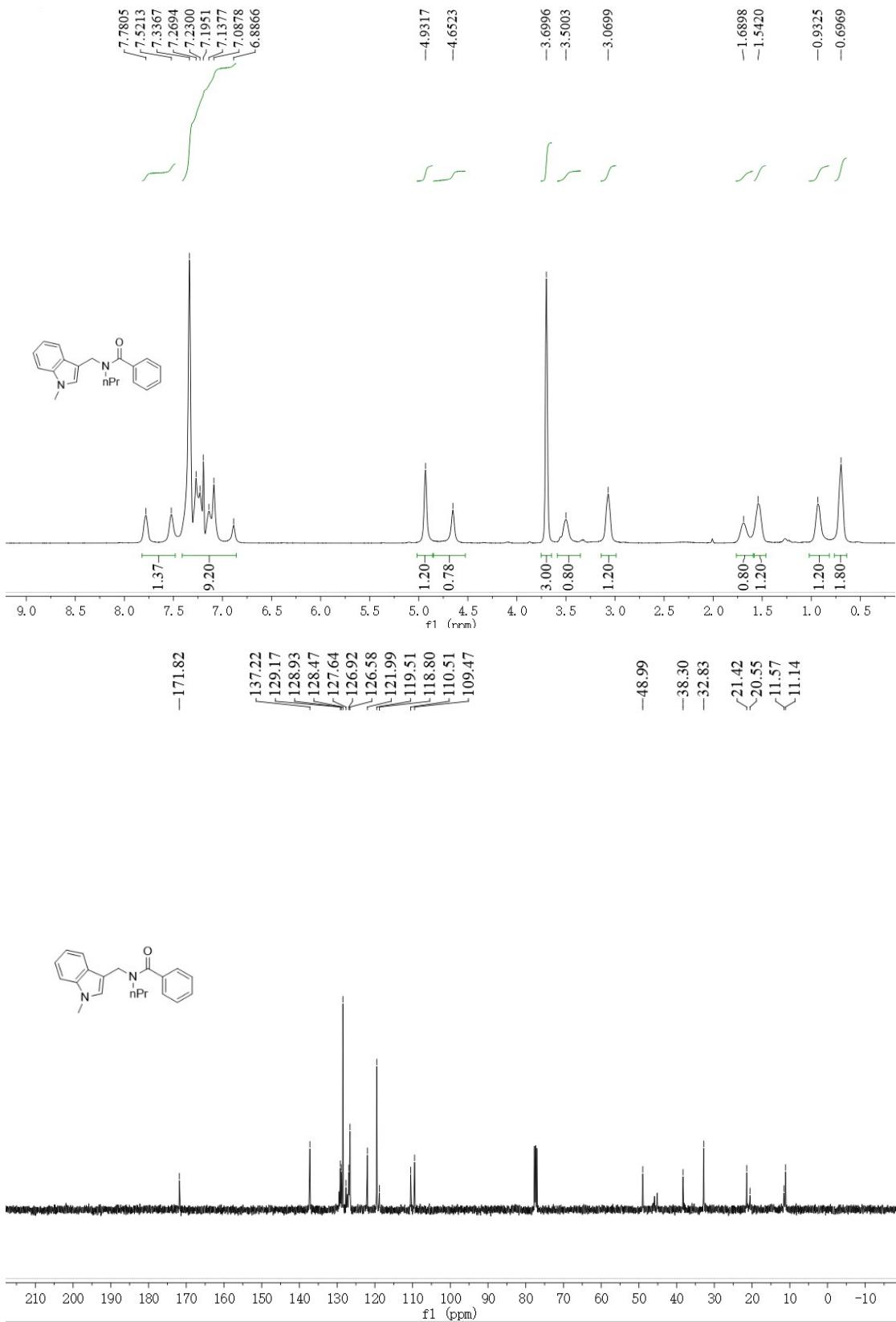
N-((1,2-dimethyl-1H-indol-3-yl)methyl)-N-phenylbenzamide (5r)



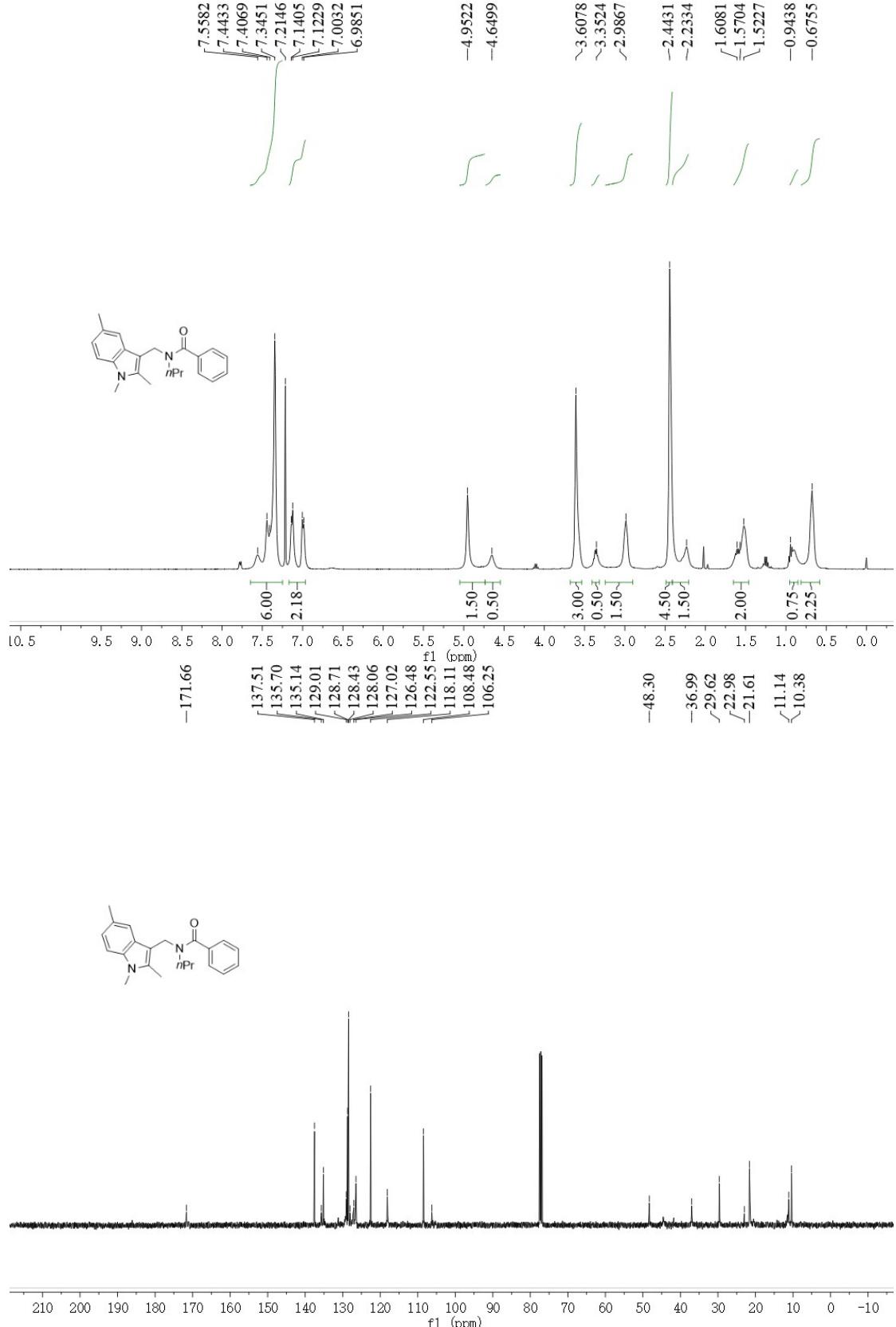
N-benzyl-N-((1,2-dimethyl-1H-indol-3-yl)methyl)benzamide (5s)



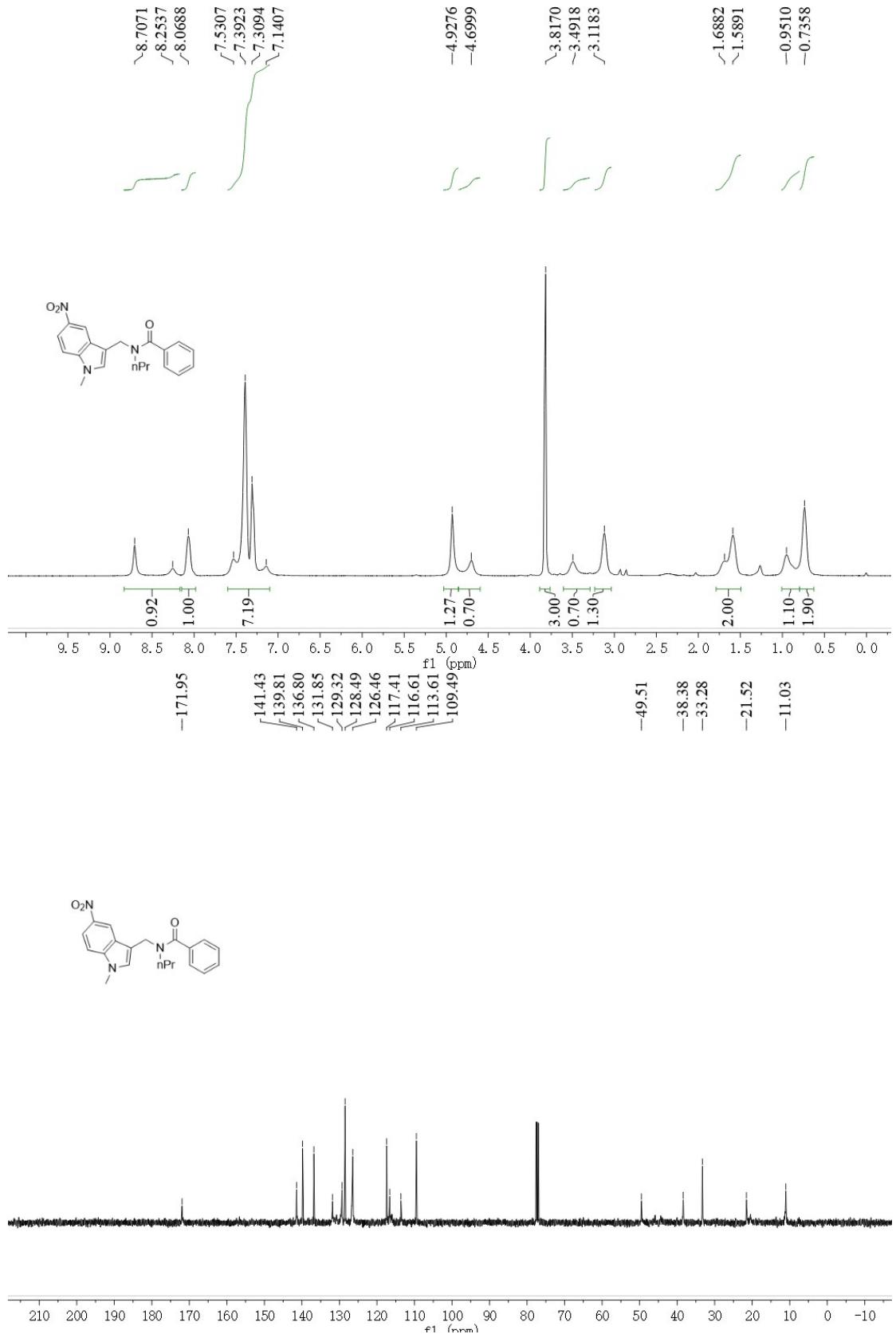
N-((1-methyl-1H-indol-3-yl)methyl)-N-propylbenzamide (5aa)



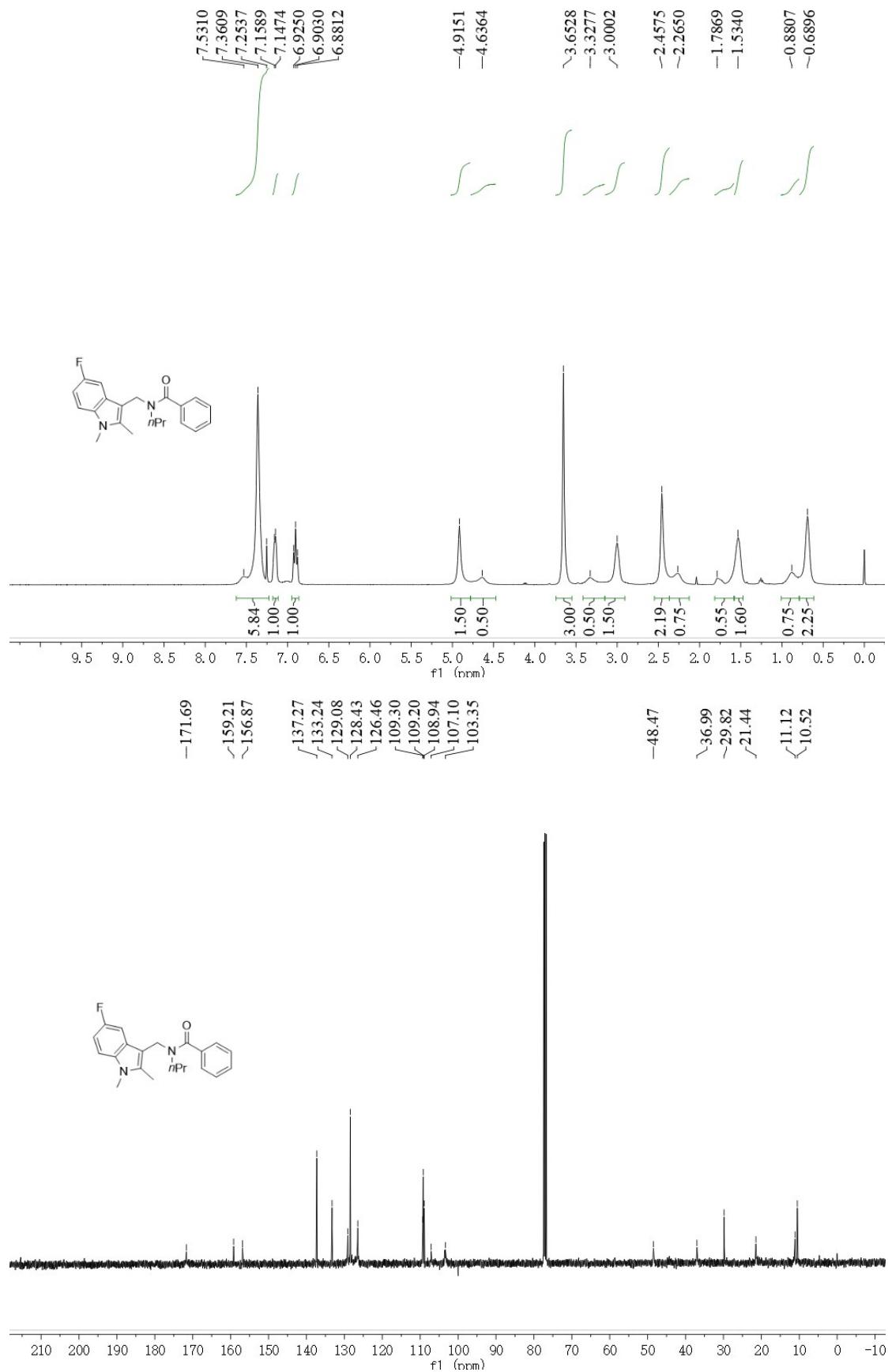
N-propyl-N-((1,2,5-trimethyl-1H-indol-3-yl)methyl)benzamide (5ab)



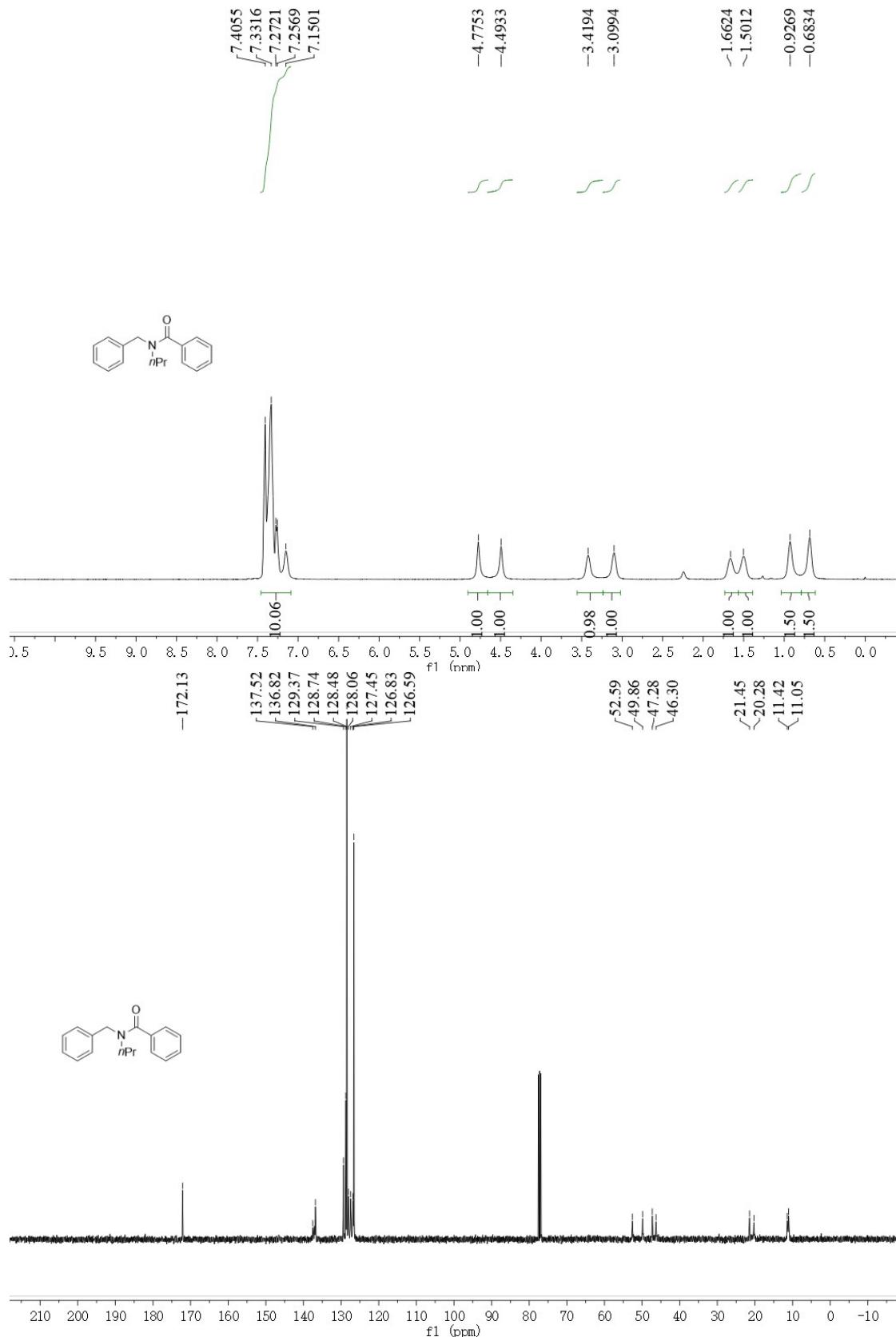
N-((1,2-dimethyl-5-nitro-1H-indol-3-yl)methyl)-N-propylbenzamide (**5ac**)

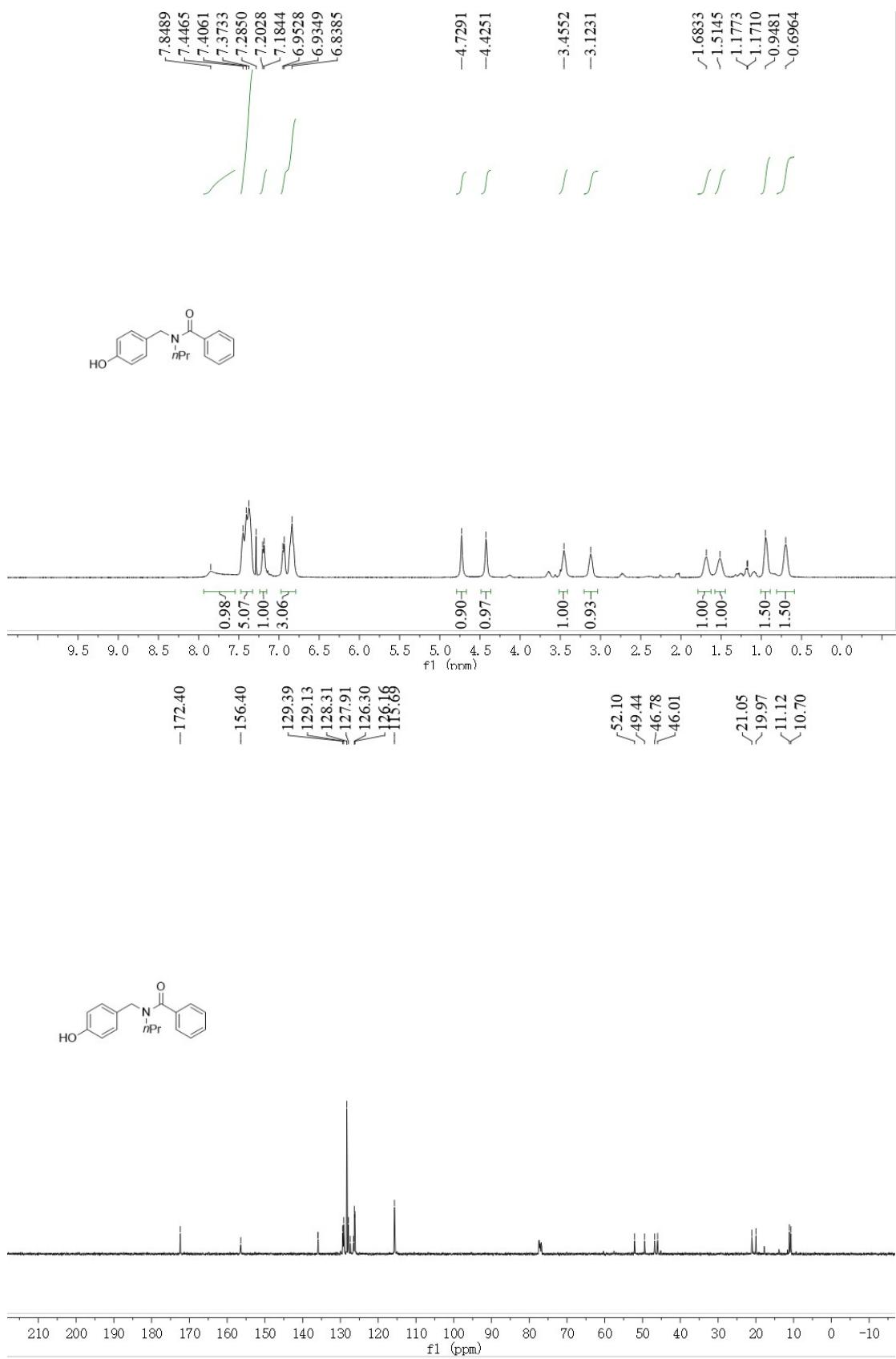


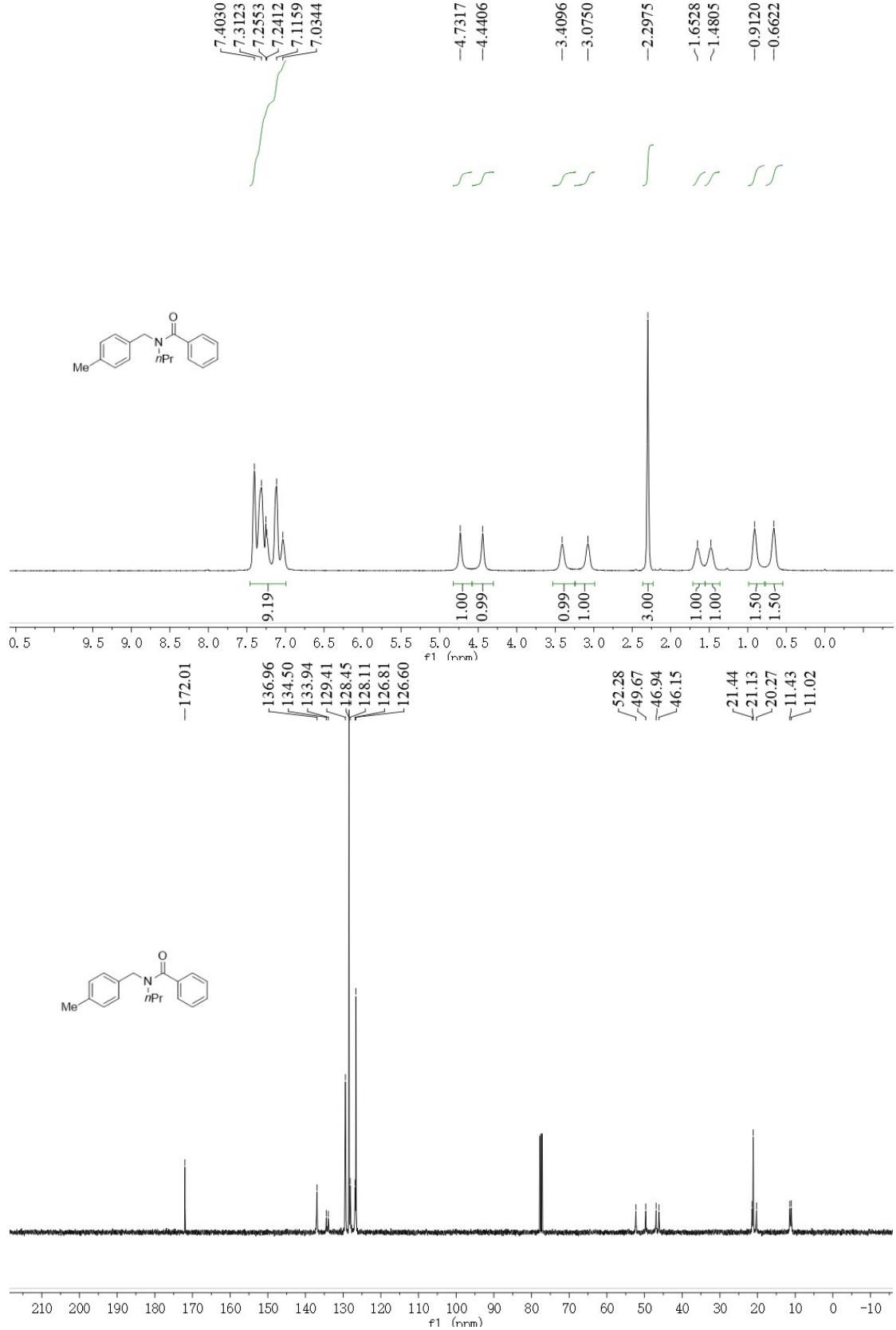
N-((5-fluoro-1,2-dimethyl-1H-indol-3-yl)methyl)-N-propylbenzamide (5ad)



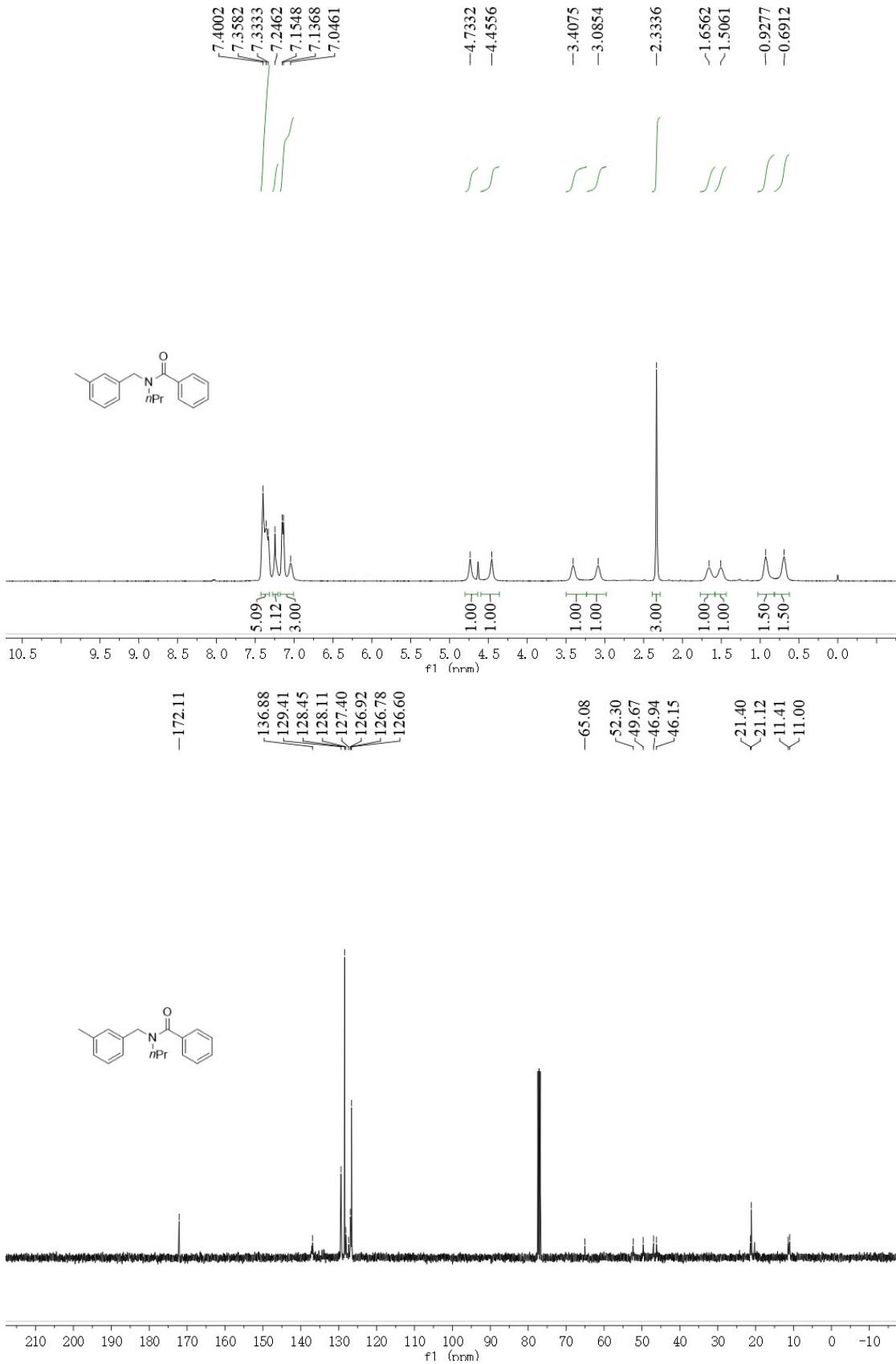
N-benzyl-N-propylbenzamide (5ae)



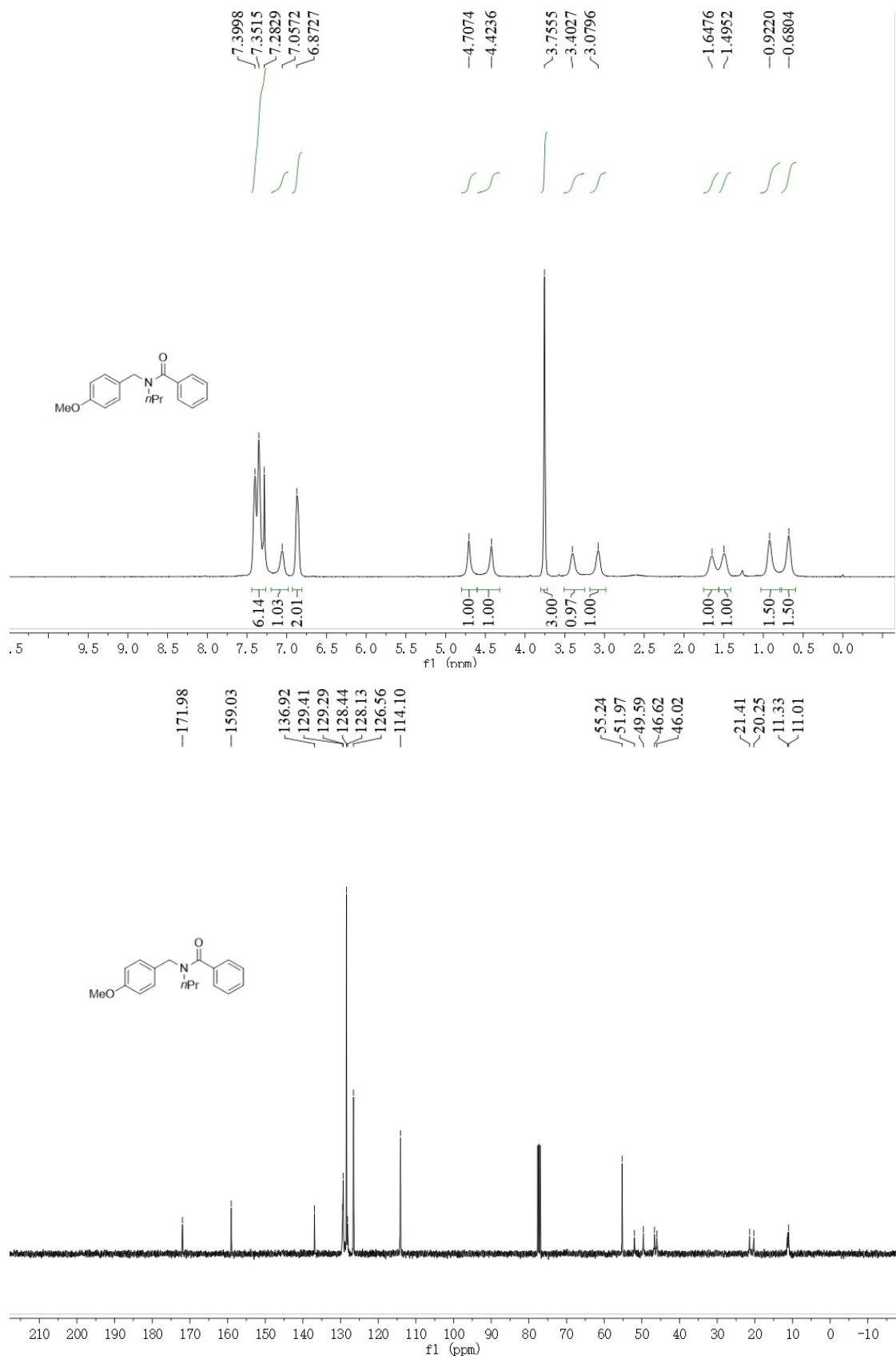




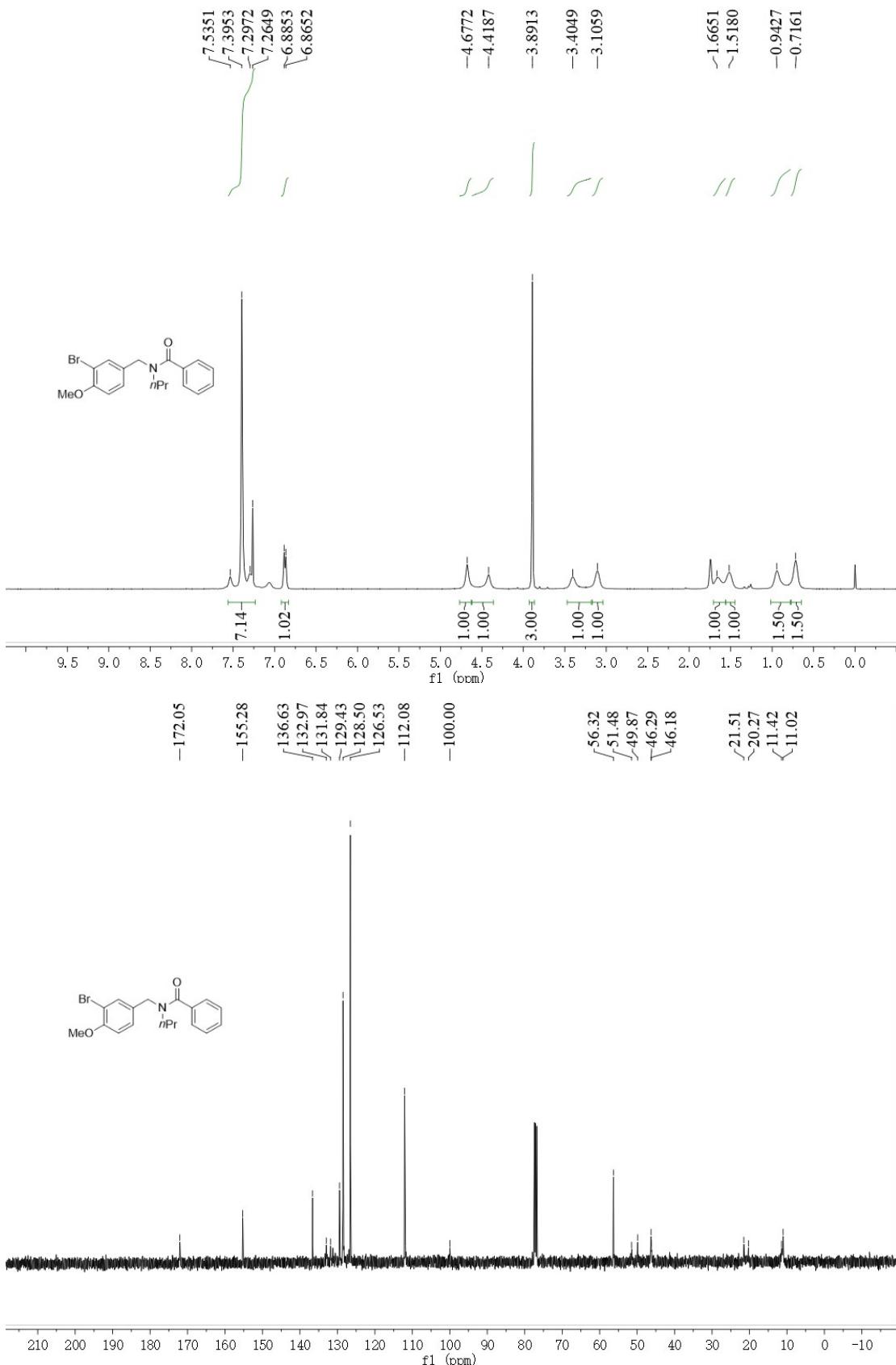
N-(3-methylbenzyl)-N-propylbenzamide (5ah)



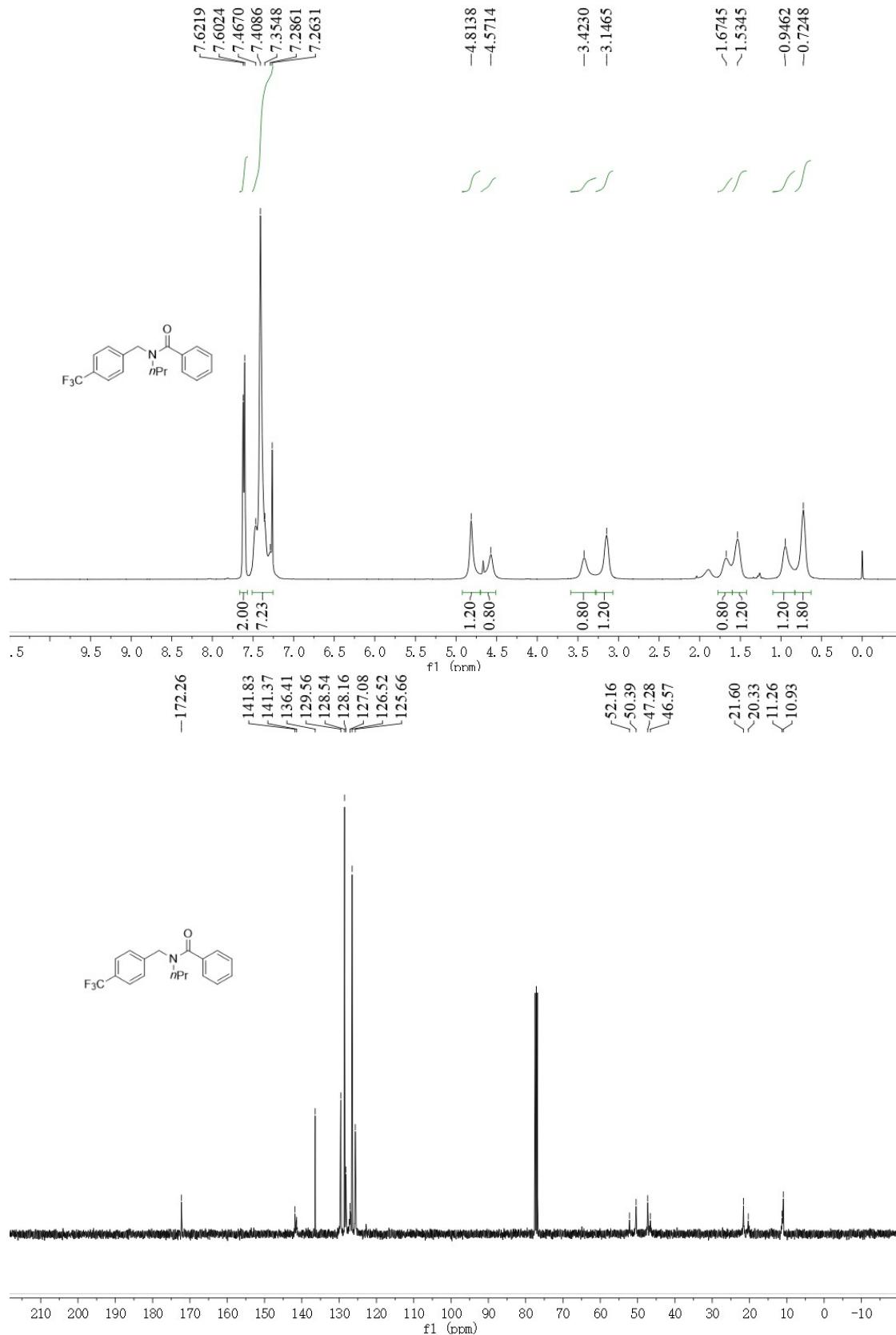
N-(4-methoxybenzyl)-N-propylbenzamide (5ai)



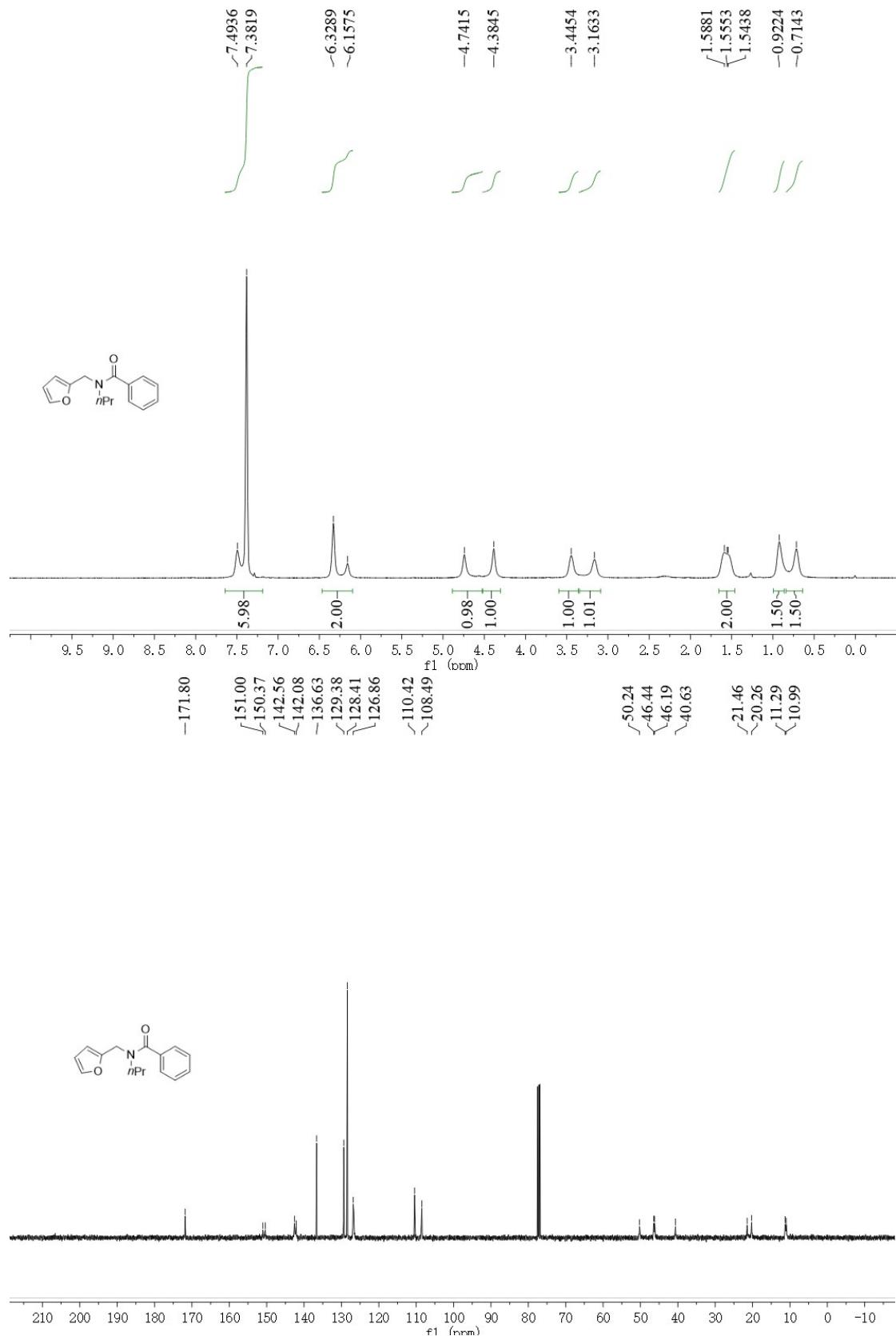
N-(3-bromo-4-methoxybenzyl)-N-propylbenzamide (5aj)



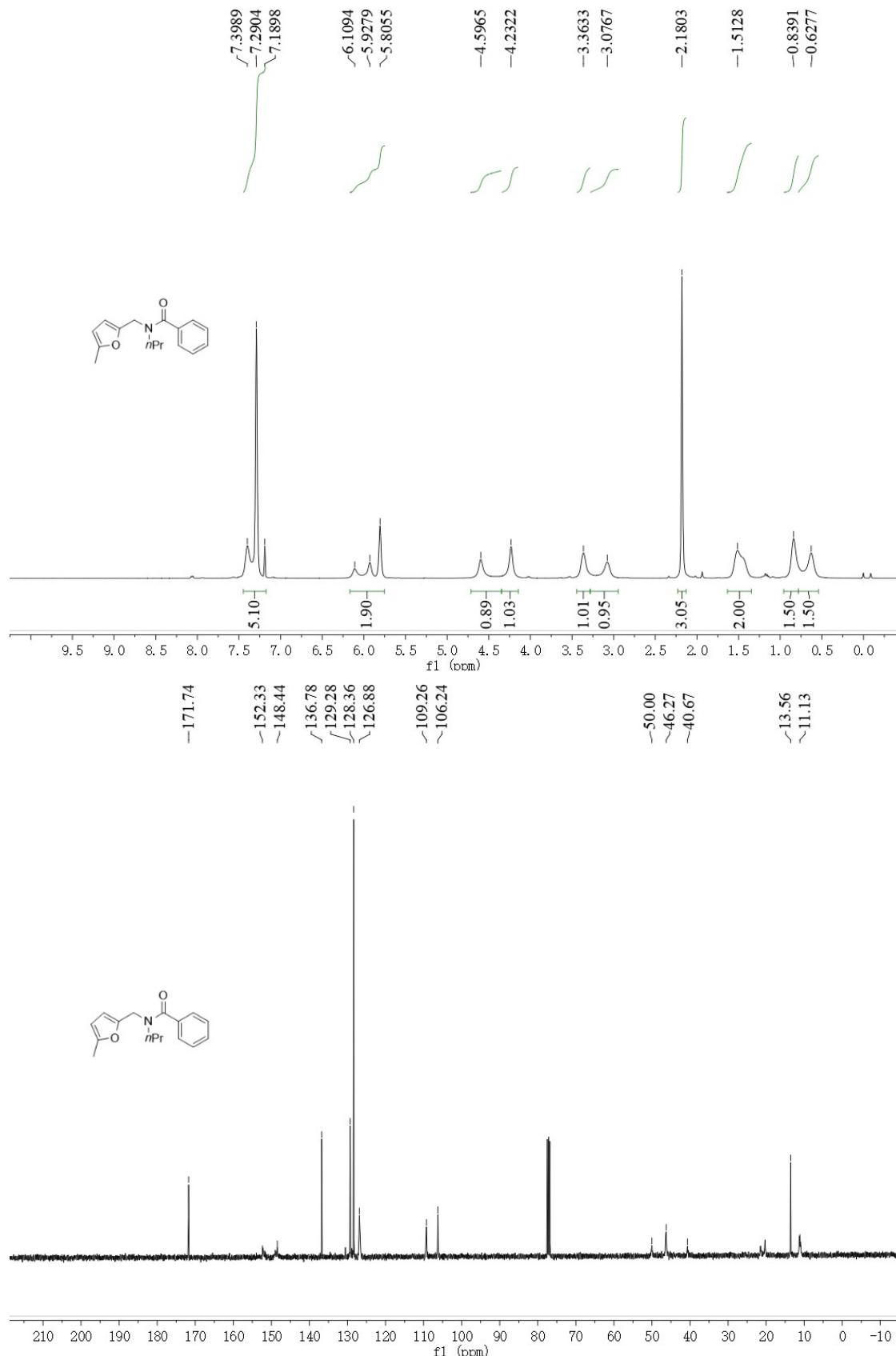
N-propyl-N-(4-(trifluoromethyl)benzyl)benzamide (5ak)



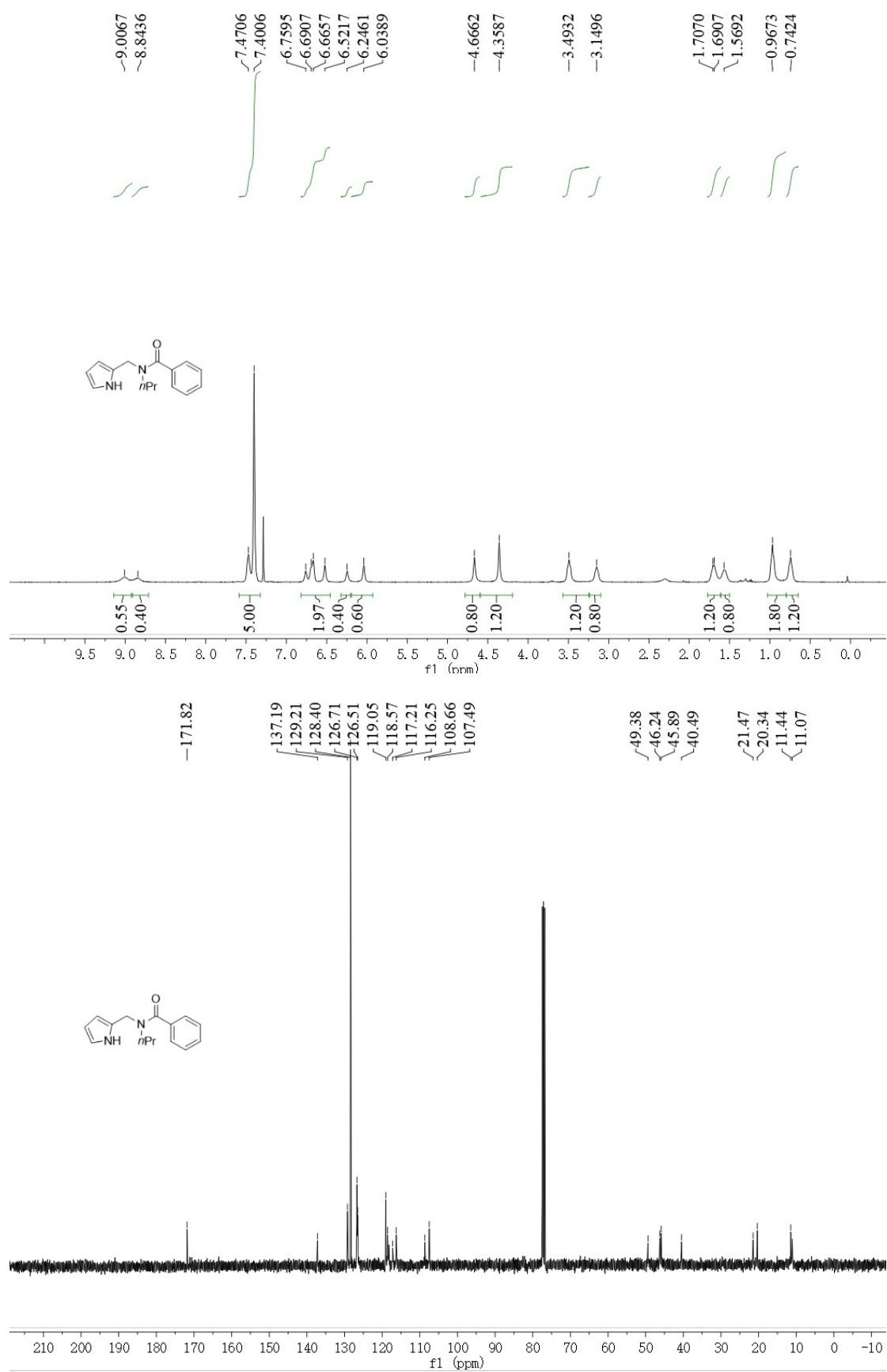
N-(furan-2-ylmethyl)-N-propylbenzamide (5al)



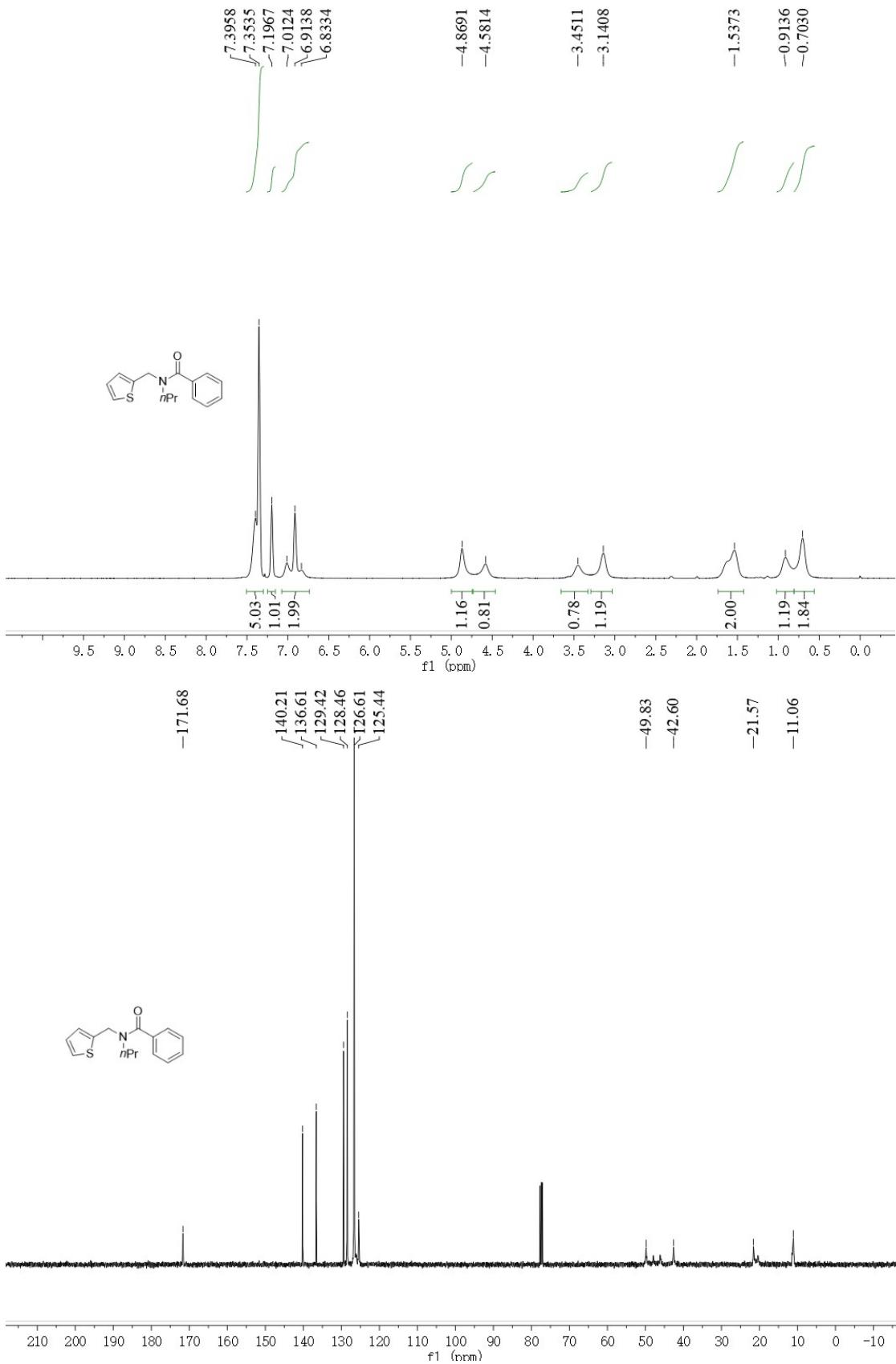
N-((5-methylfuran-2-yl)methyl)-N-propylbenzamide (5am)



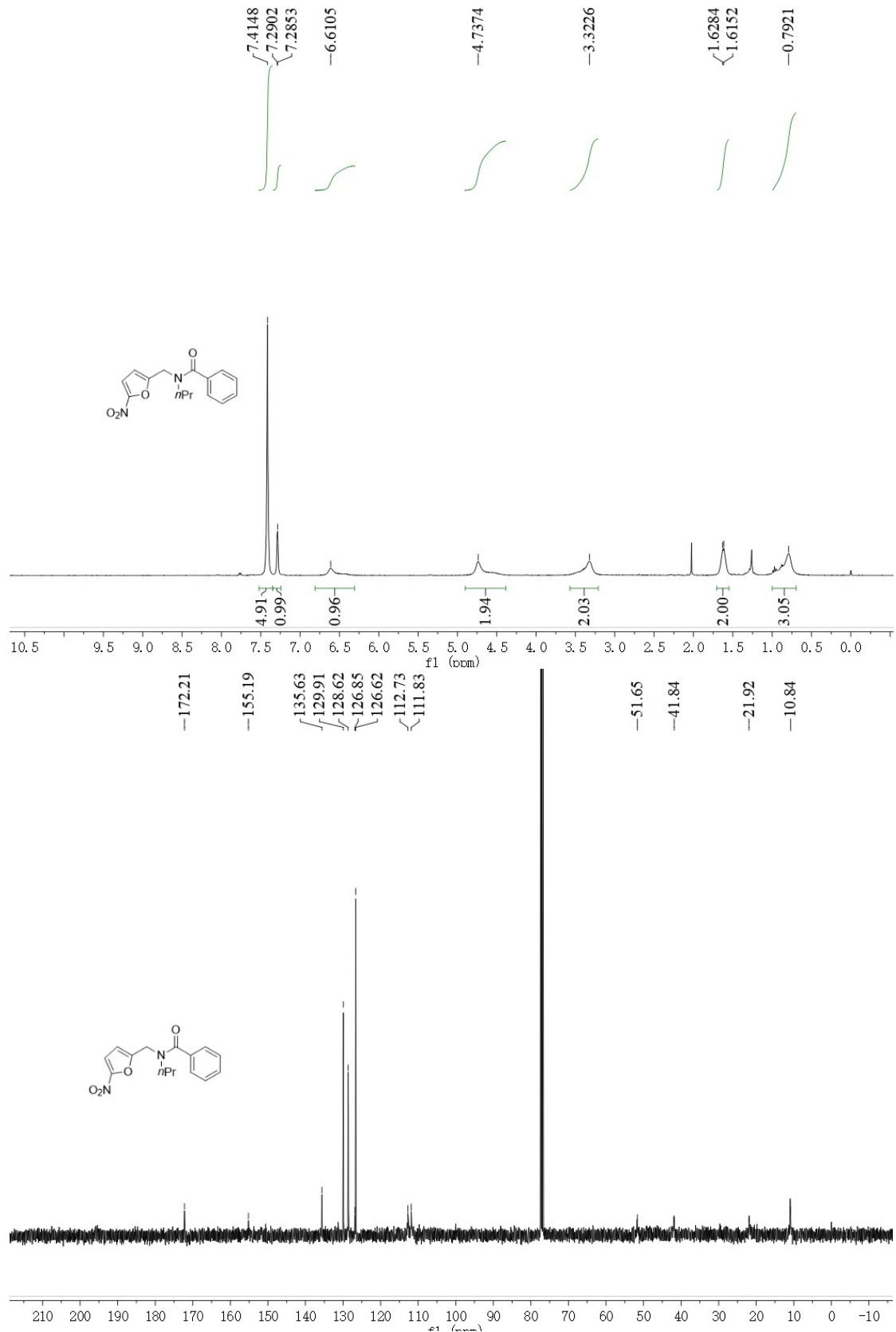
N-((1H-pyrrol-2-yl)methyl)-N-propylbenzamide (5an)



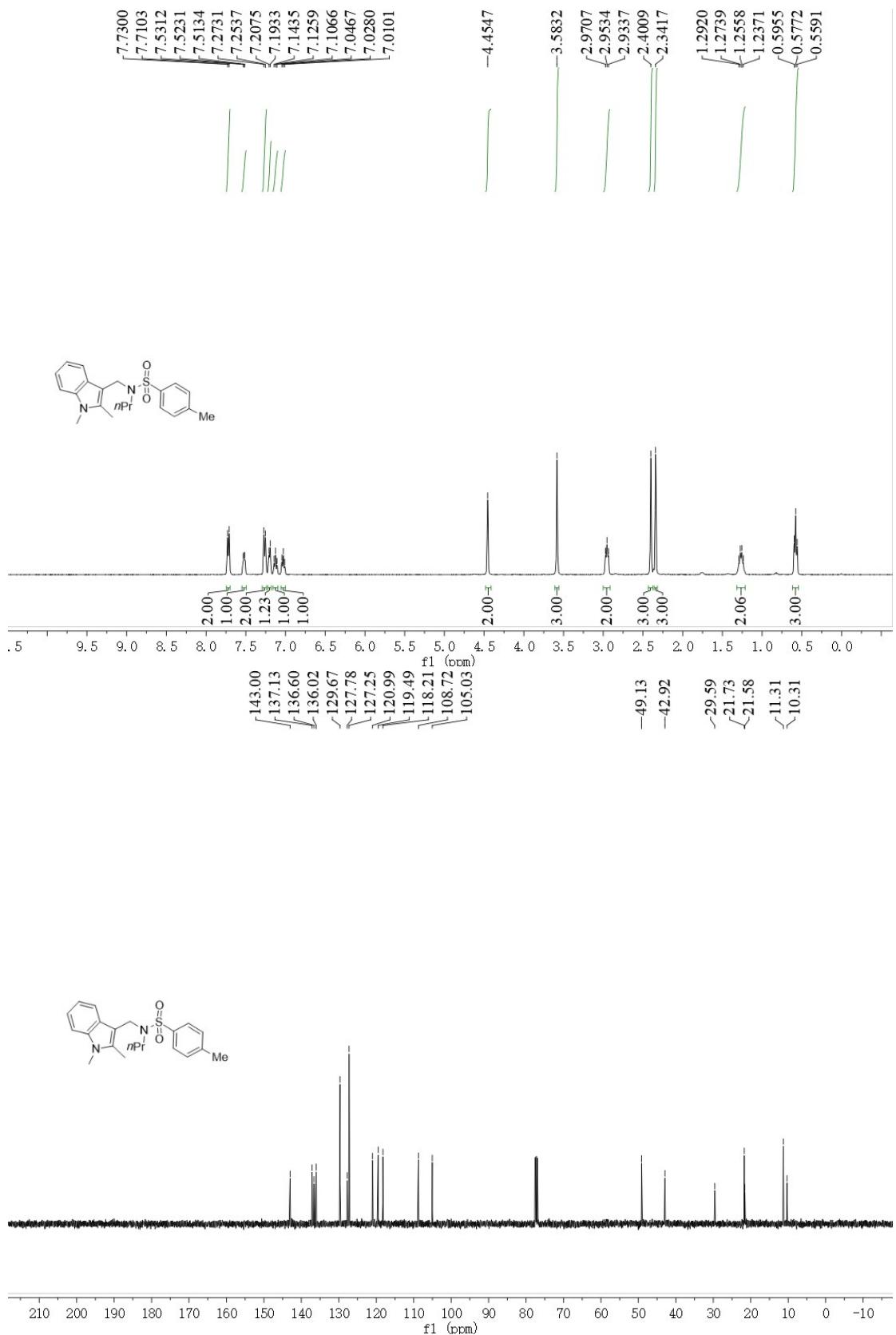
N-propyl-N-(thiophen-2-ylmethyl)benzamide (5ao)



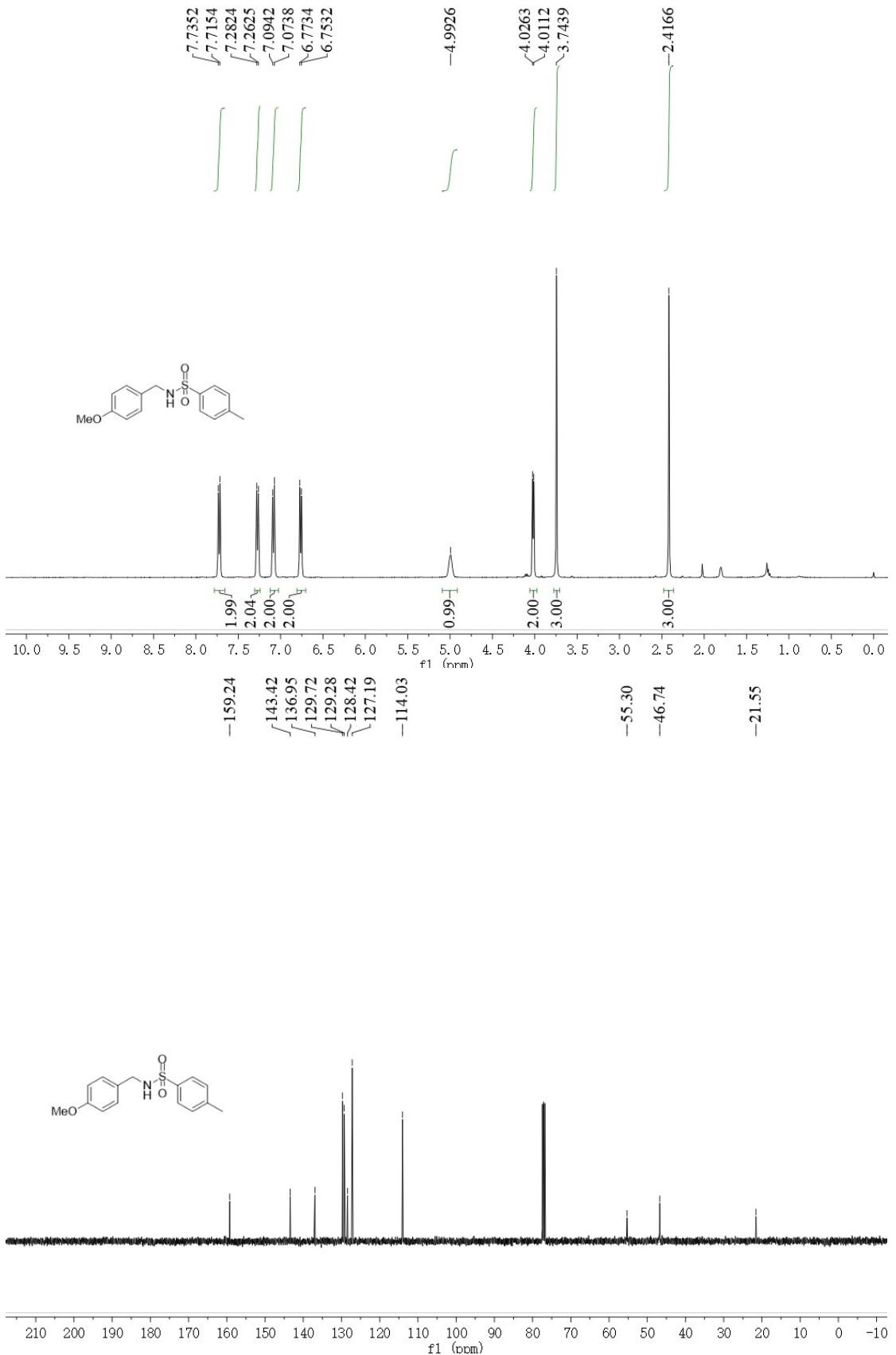
N-((5-nitrofuran-2-yl)methyl)-N-propylbenzamide (5ap)

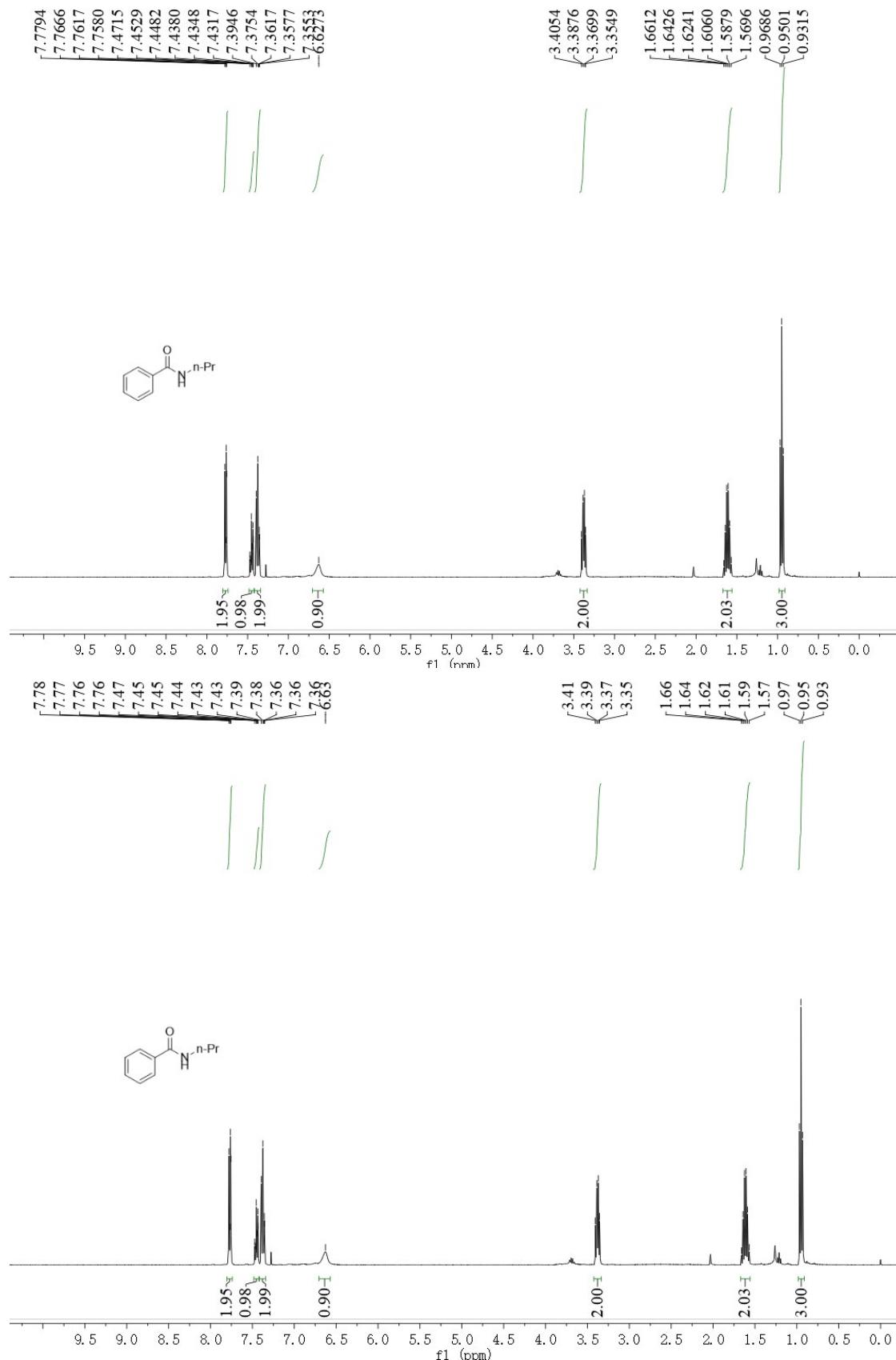


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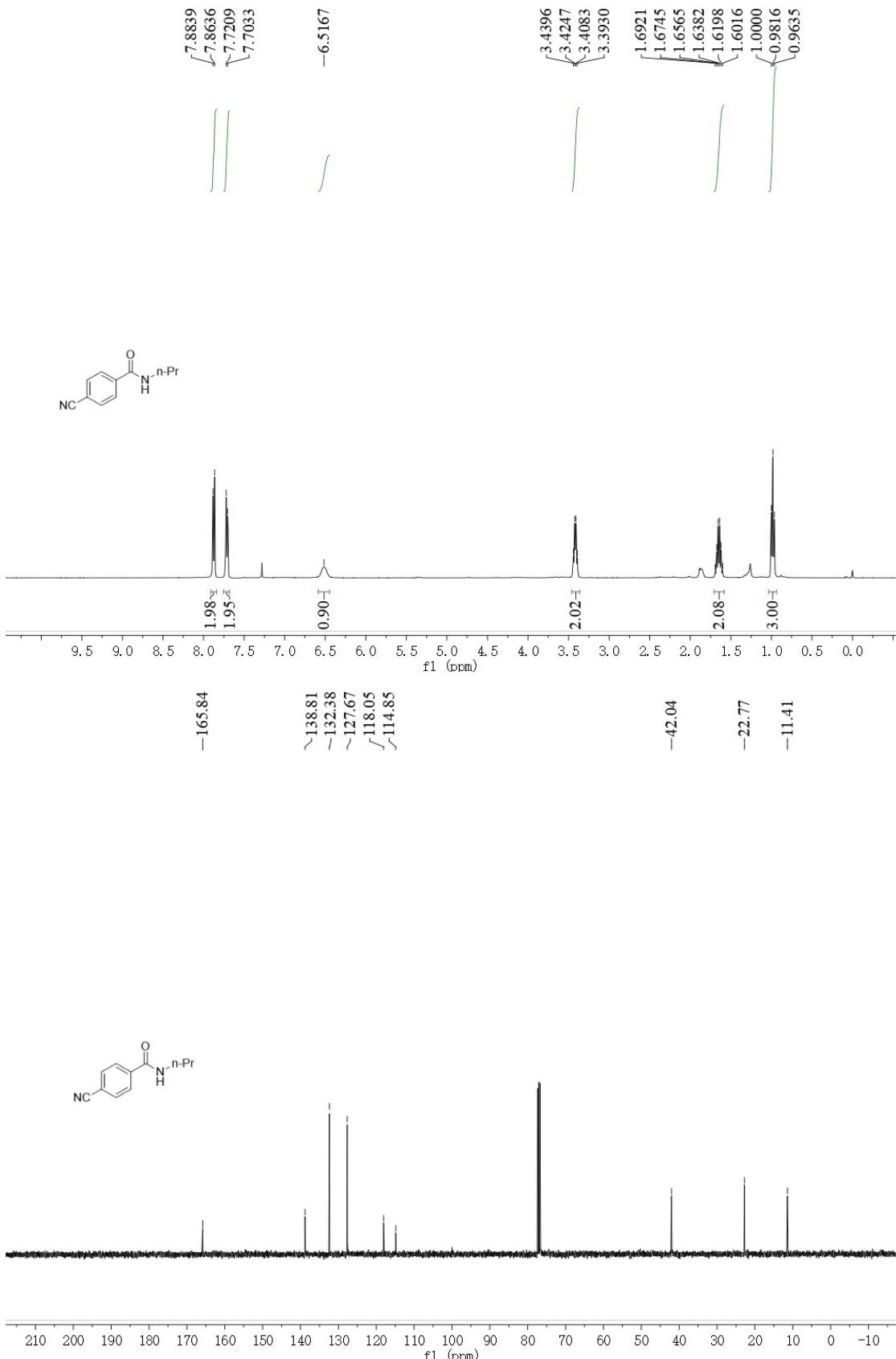


N-(4-methoxybenzyl)-4-methylbenzenesulfonamide (7b)

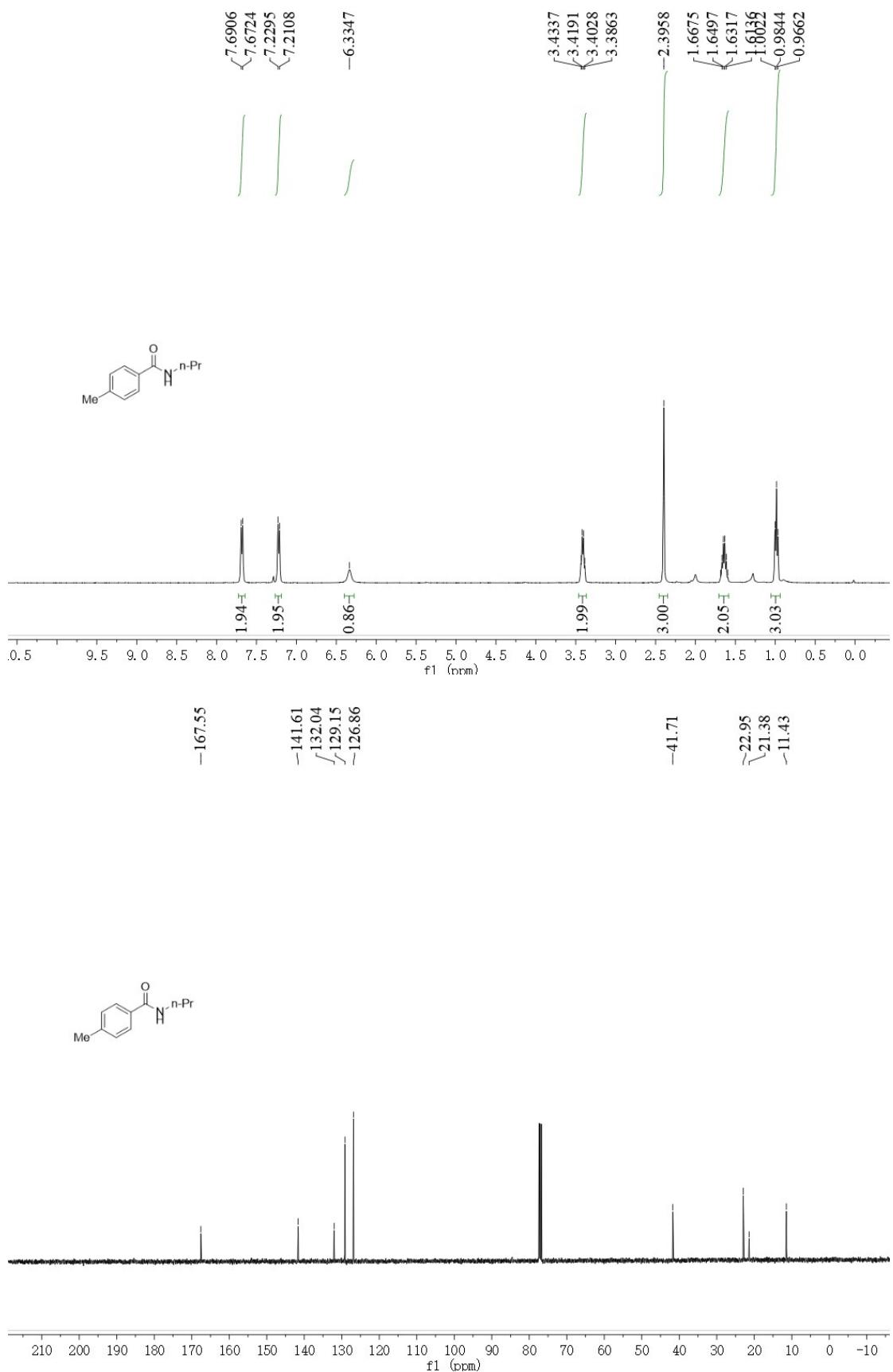




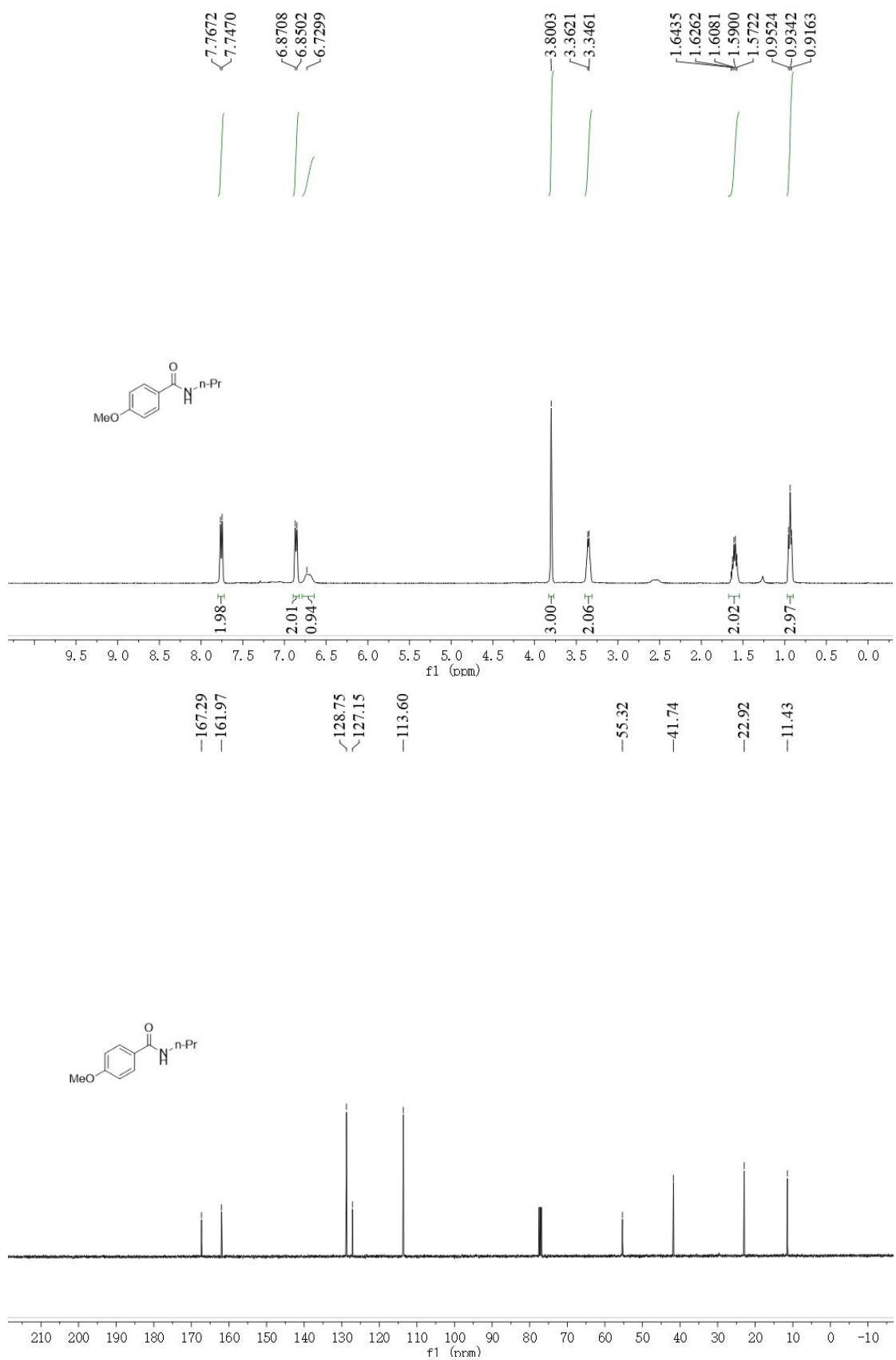
4-Cyano-N-propylbenzamide (6b)



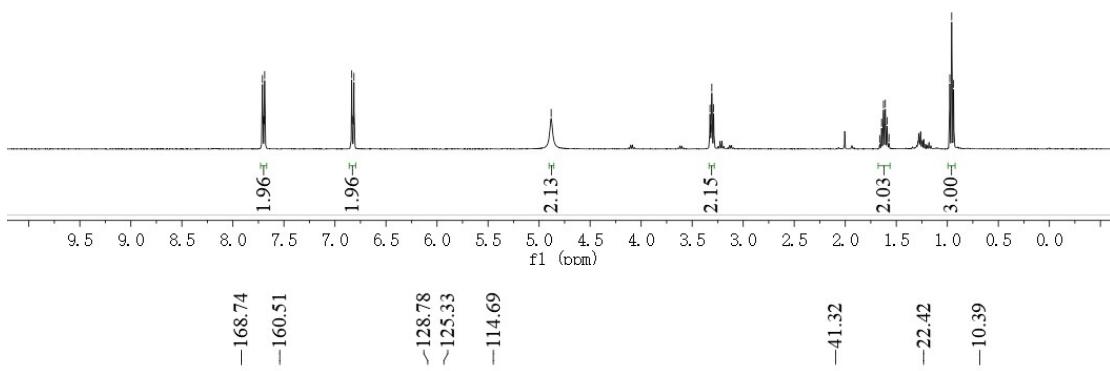
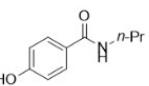
4-Methyl-N-propylbenzamide (6c)



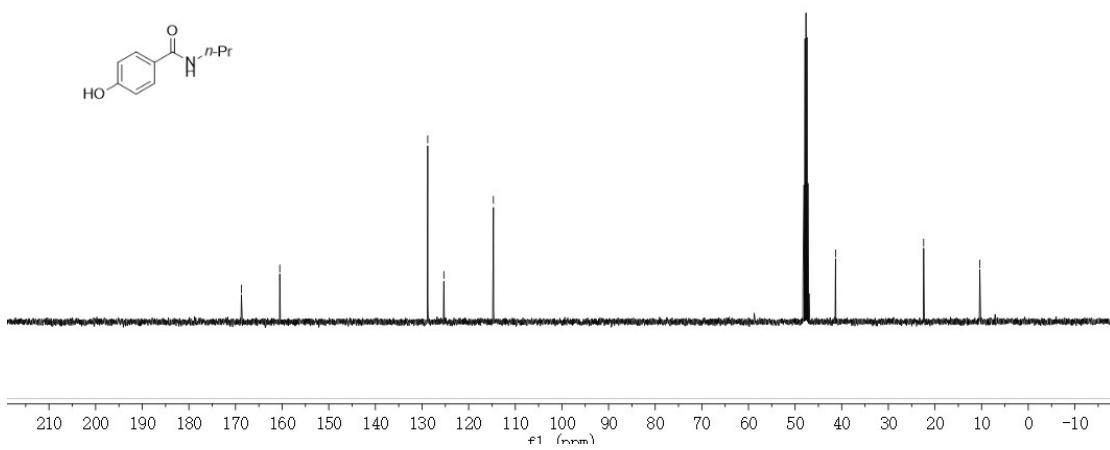
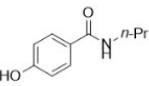
4-Methoxy-N-propylbenzamide (6d)



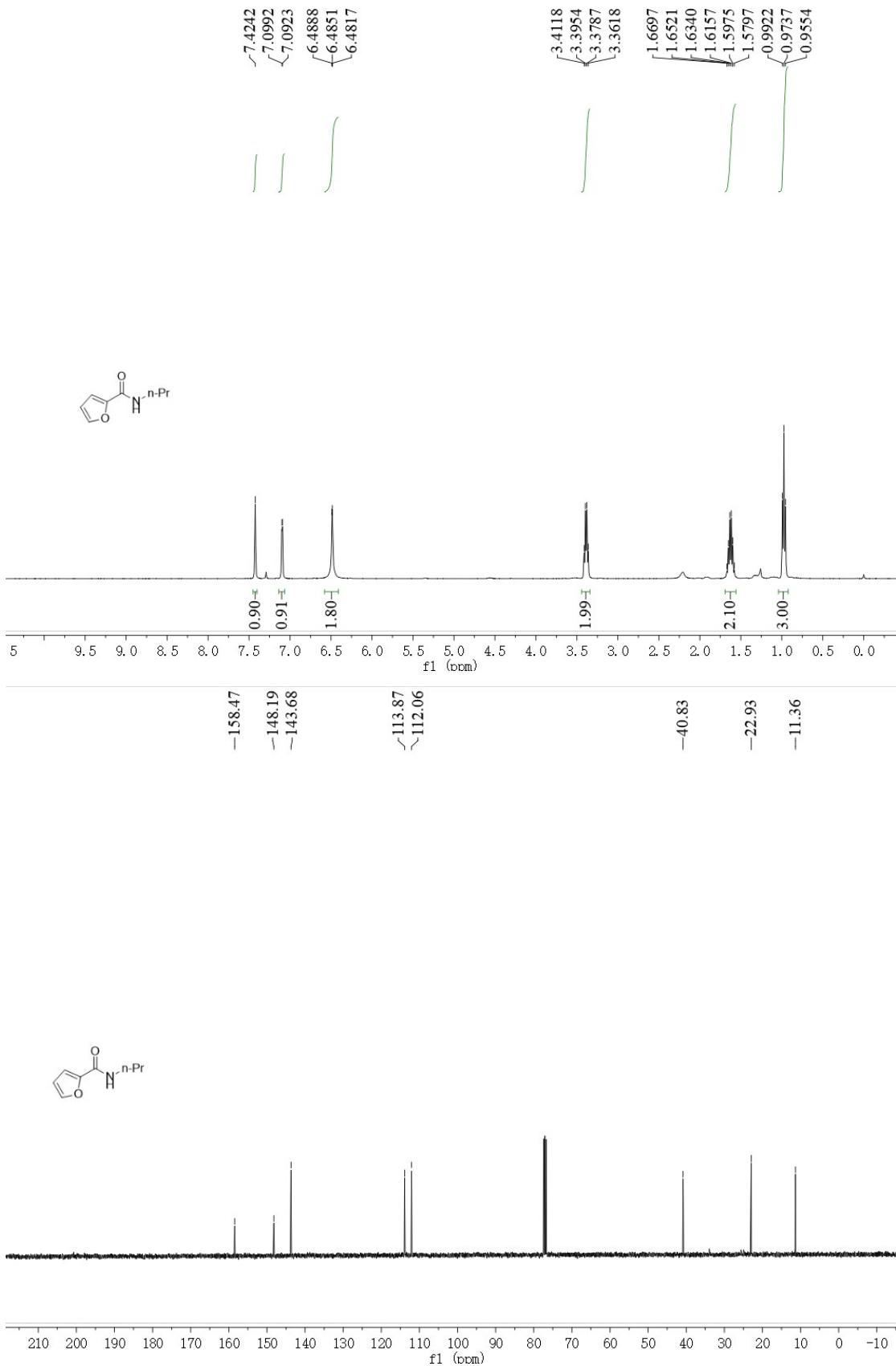
4-Hydroxy-N-propylbenzamide (6e)



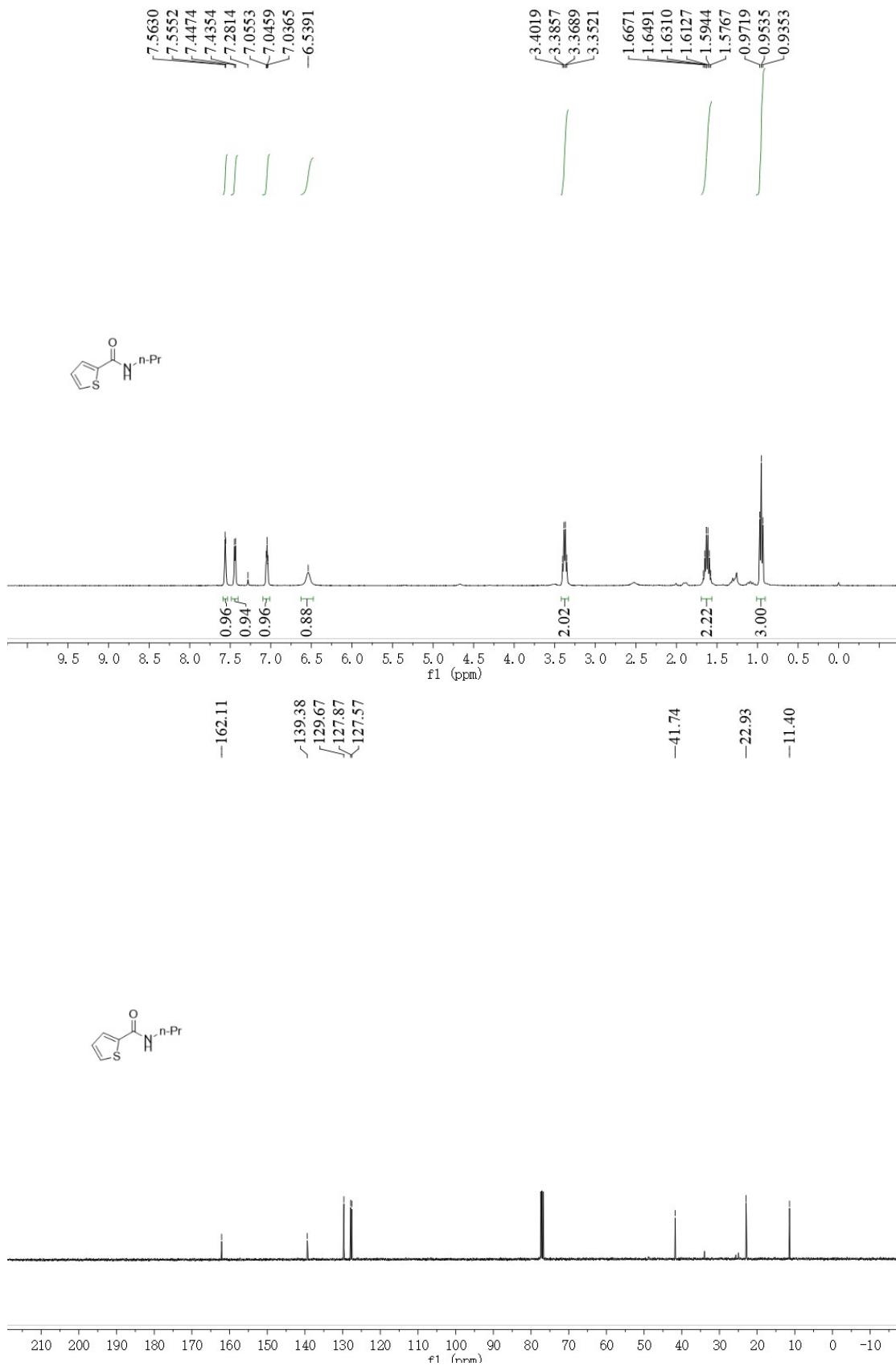
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-160.51
-128.78
~125.33
-114.69
2.13^t
2.15^t
3.00^t
4.13^t
4.88^t
5.33^t
6.81^t
7.05^t
7.10^t
7.69^t
7.68^t
8.00^t
8.50^t



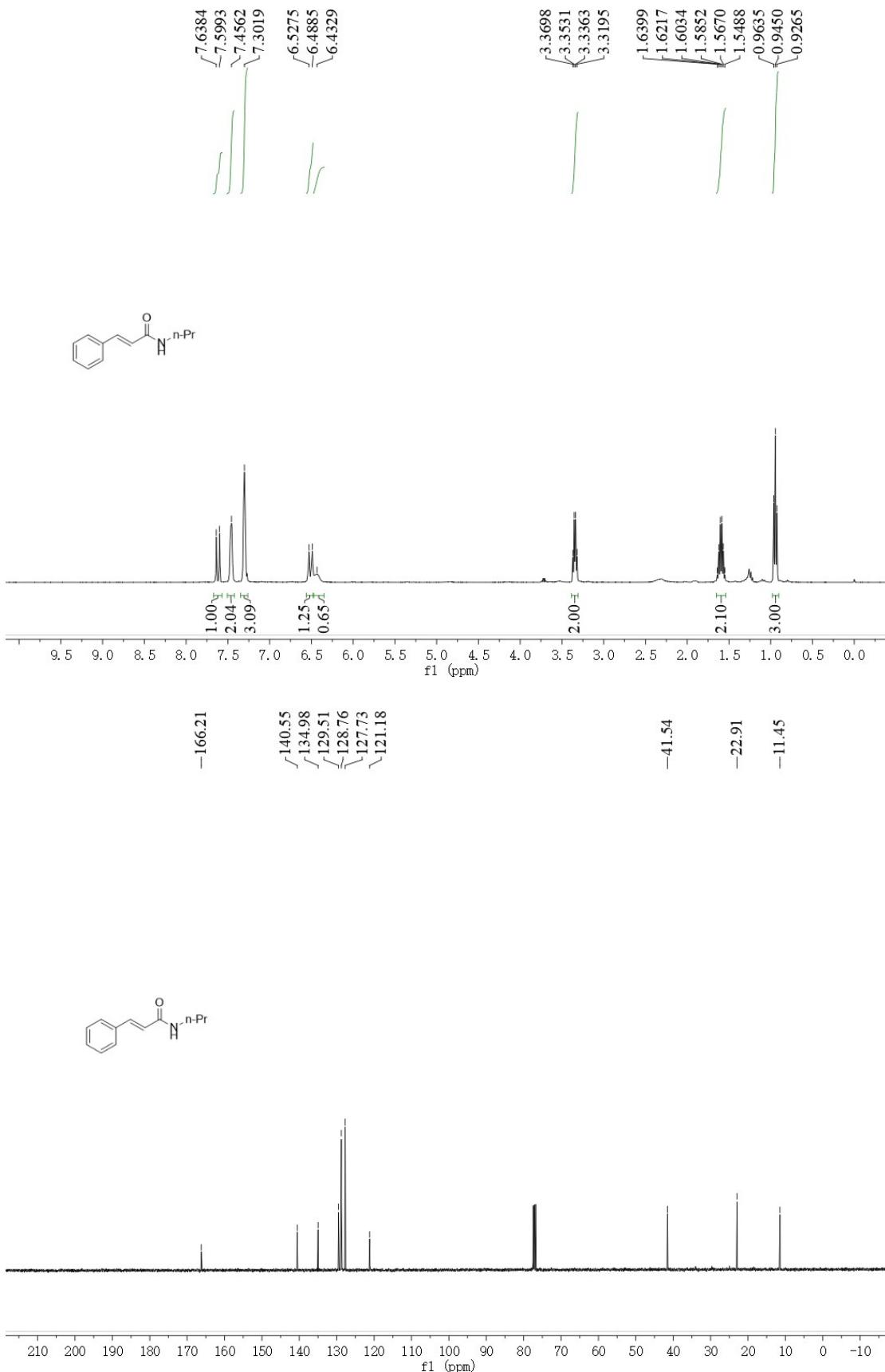
N-propylfuran-2-carboxamide (6f)



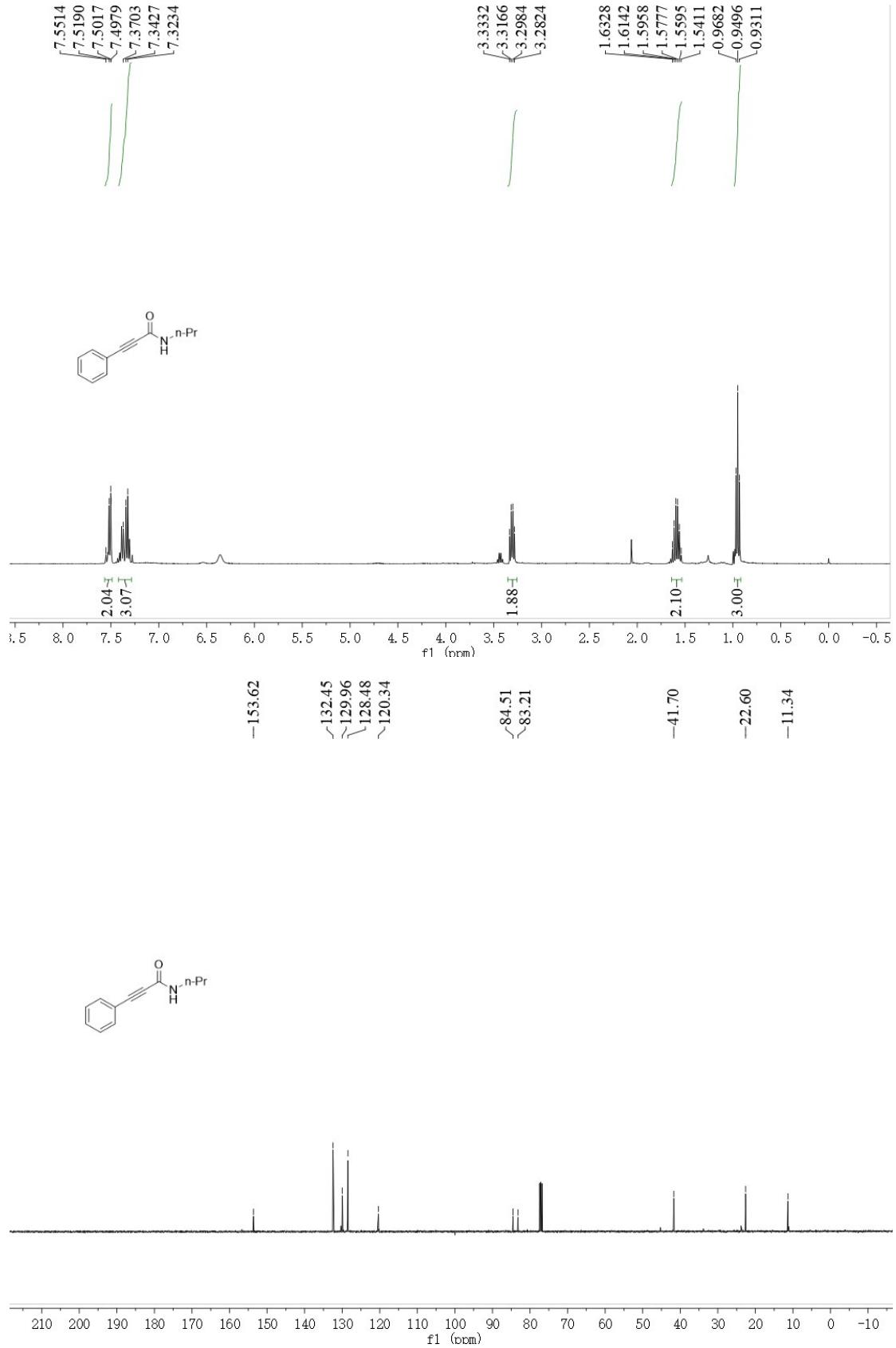
N-propylthiophene-2-carboxamide (6g)



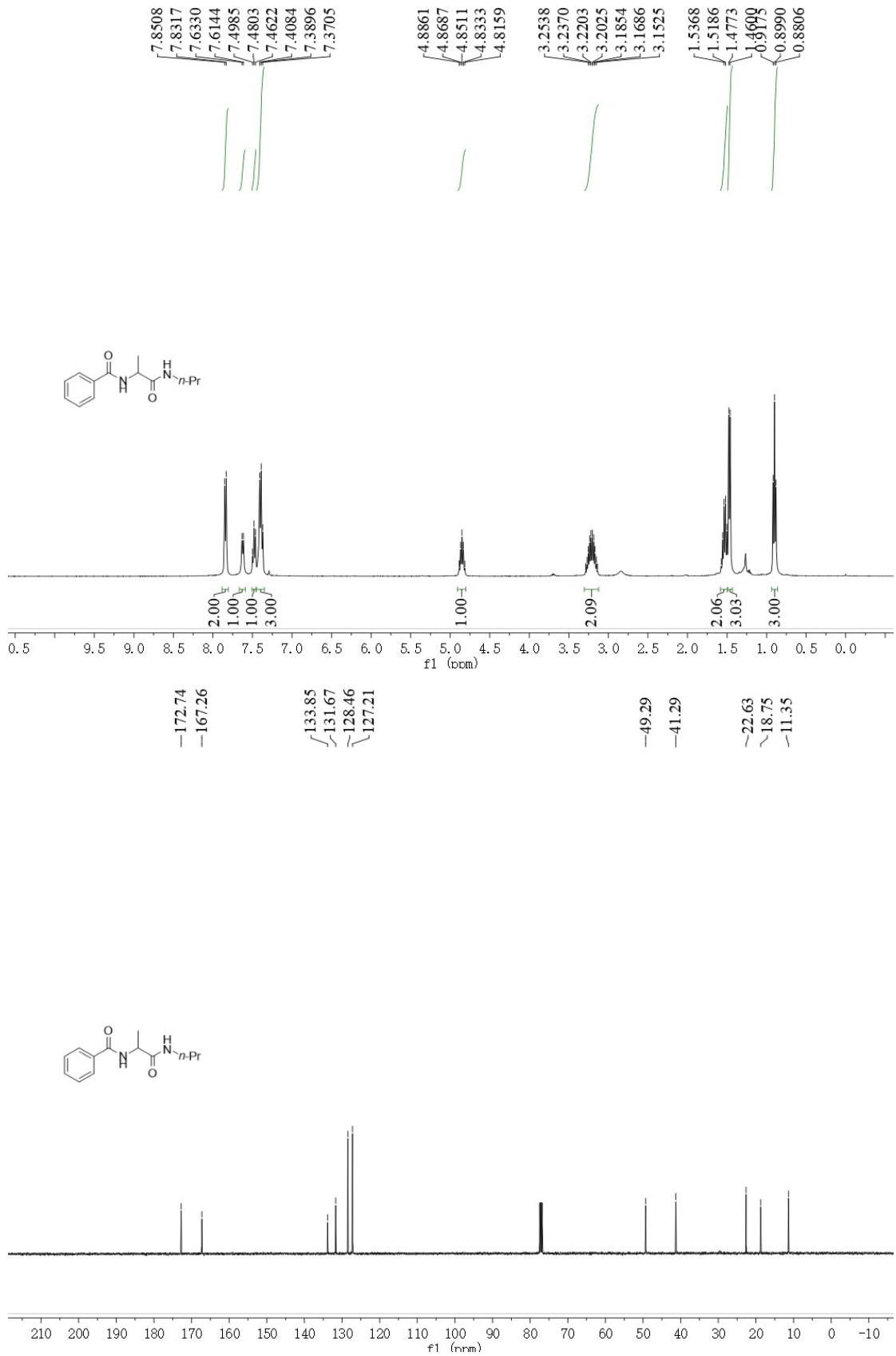
N-propylcinnamamide (6h)



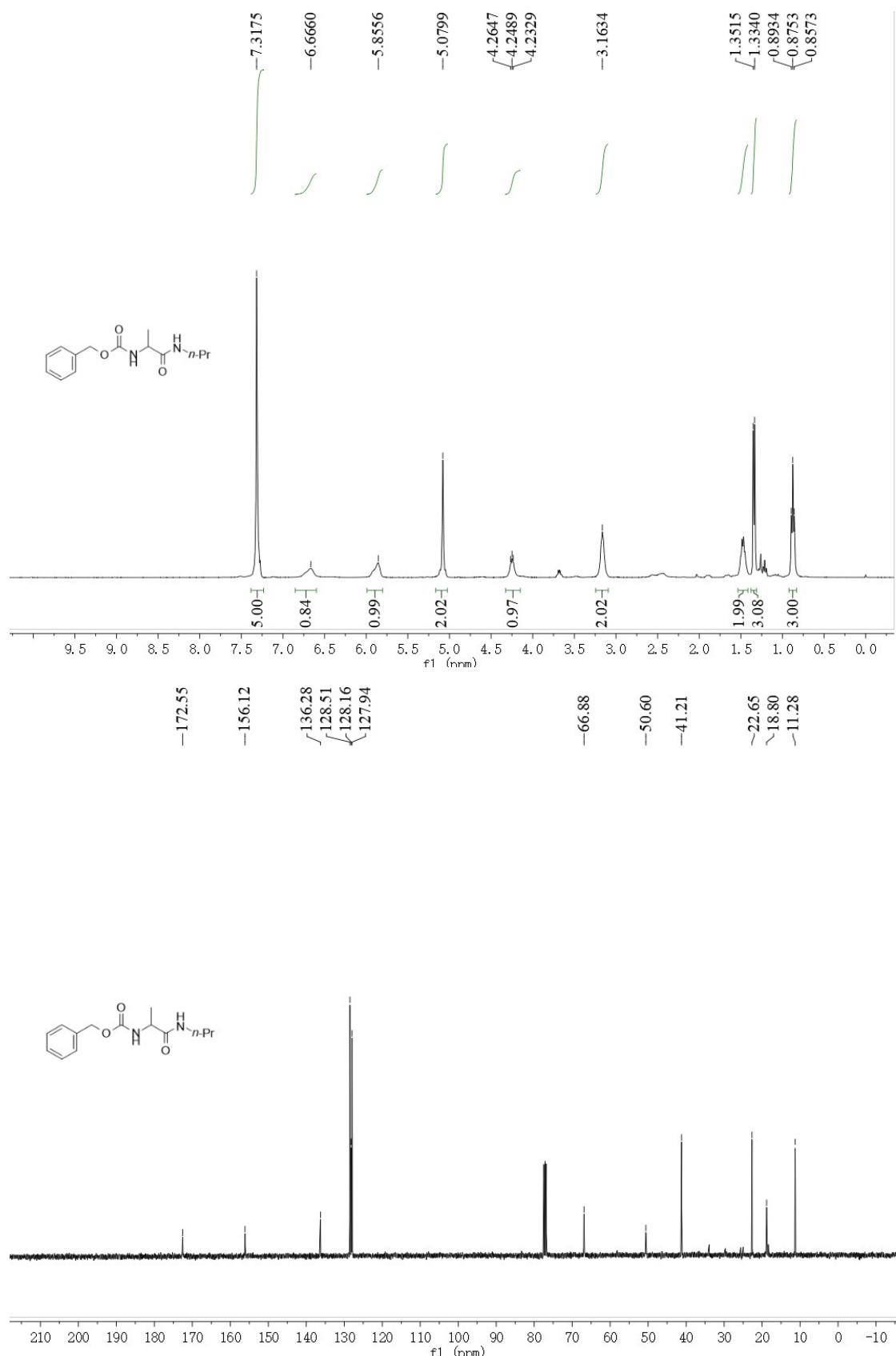
3-Phenyl-N-propylpropiolamide (6i)



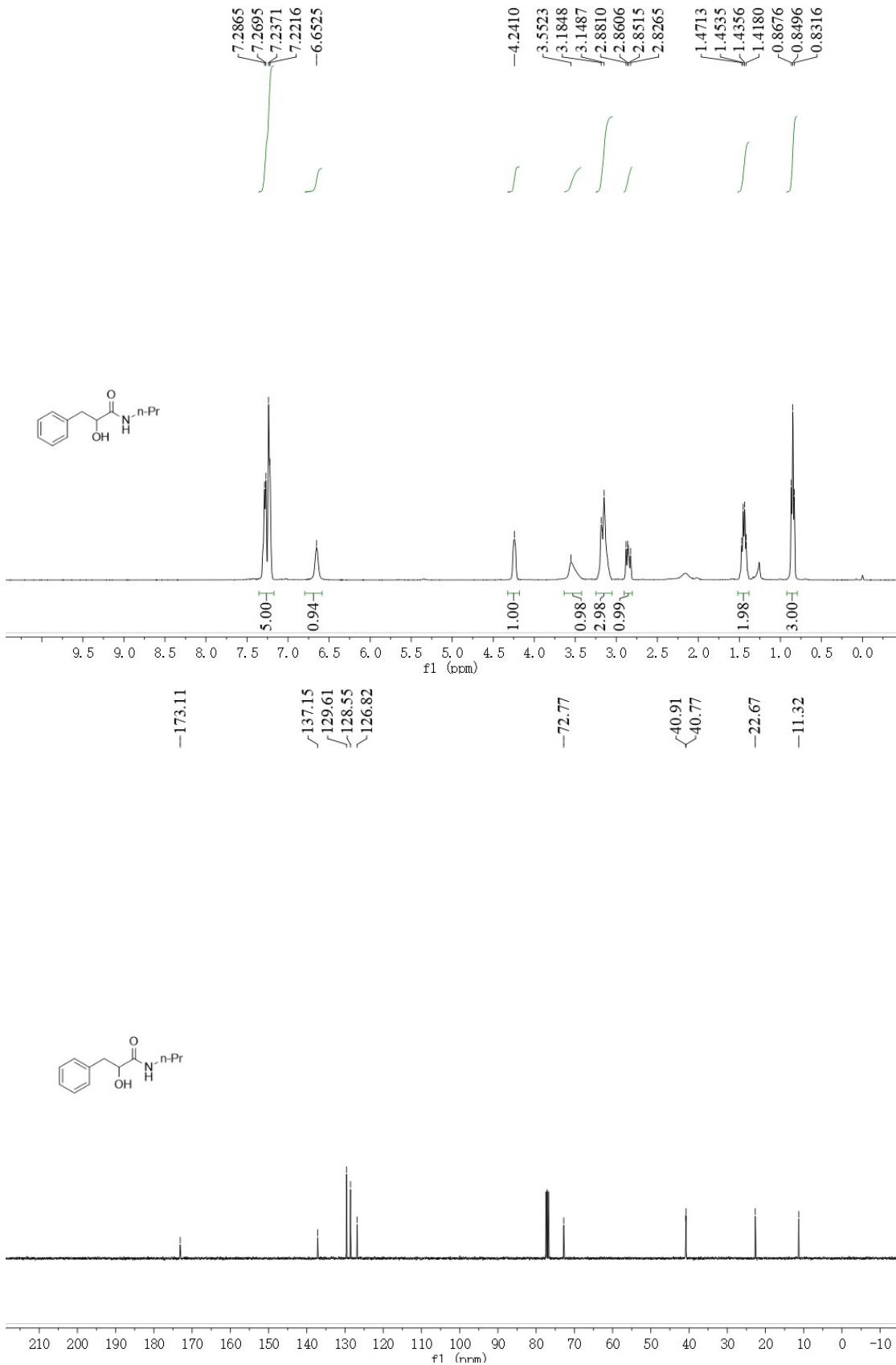
N-(1-oxo-1-(propylamino)propan-2-yl)benzamide (6k)



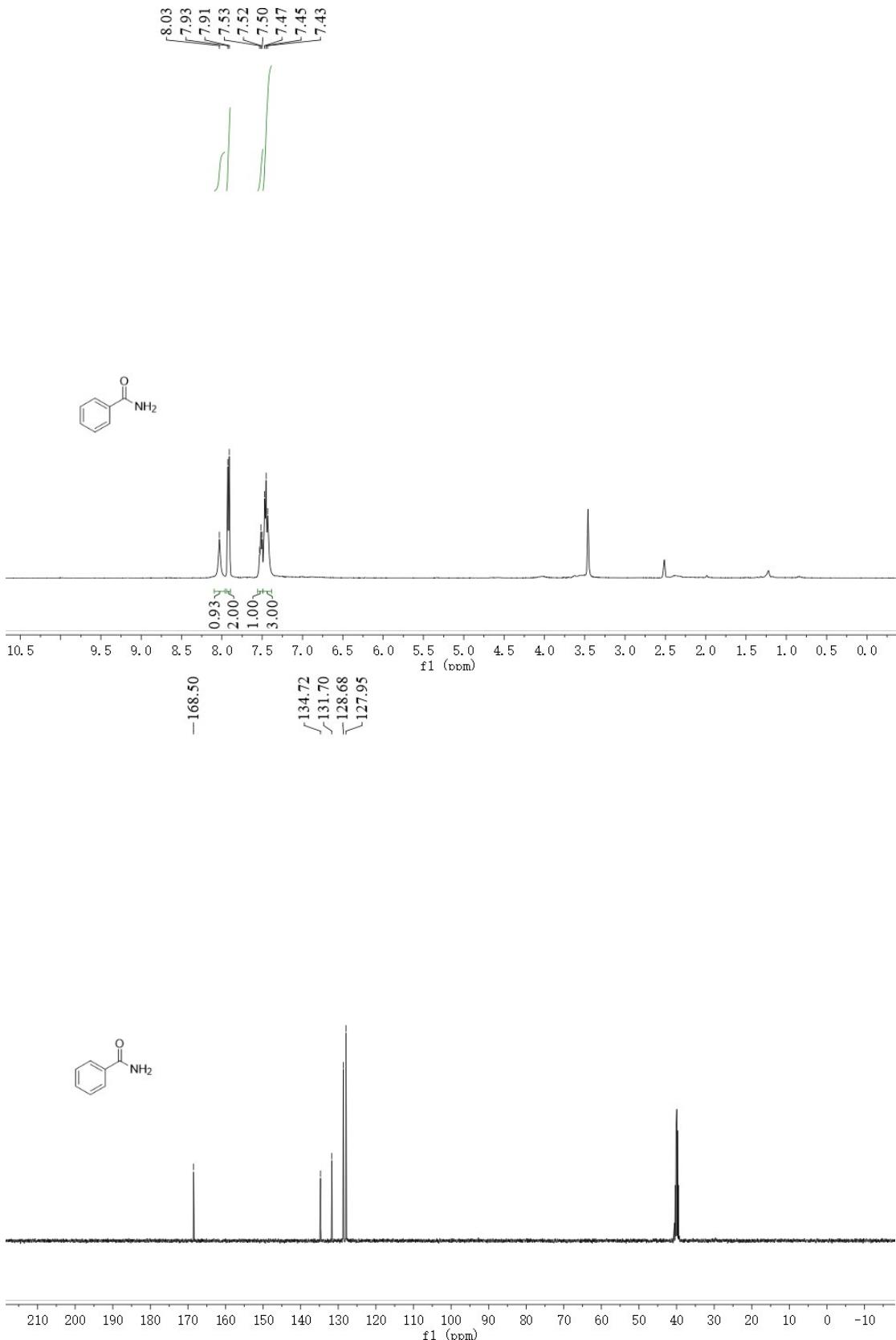
Benzyl (1-oxo-1-(propylamino)propan-2-yl)carbamate (6l)



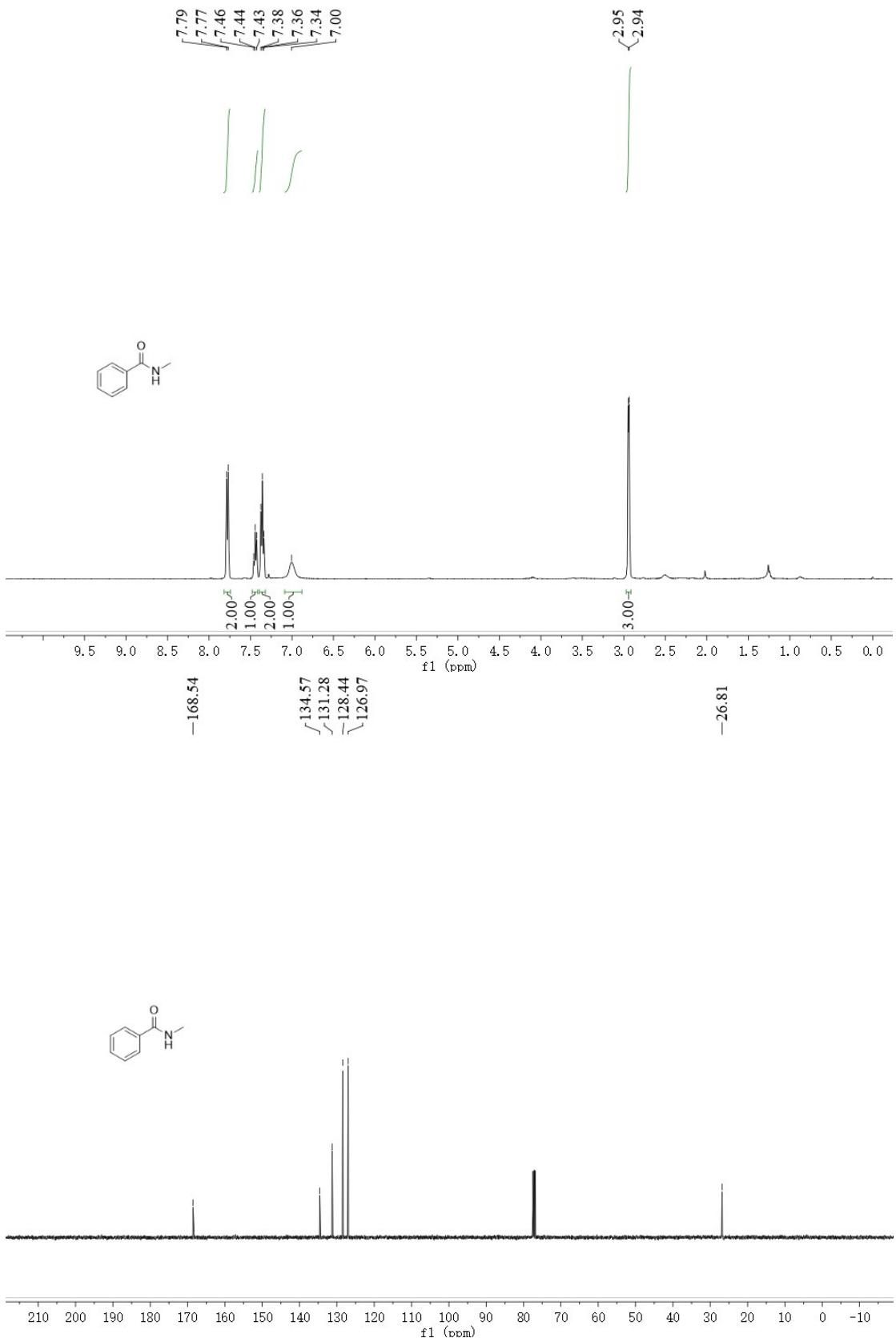
2-Hydroxy-3-phenyl-N-propylpropanamide (6m)



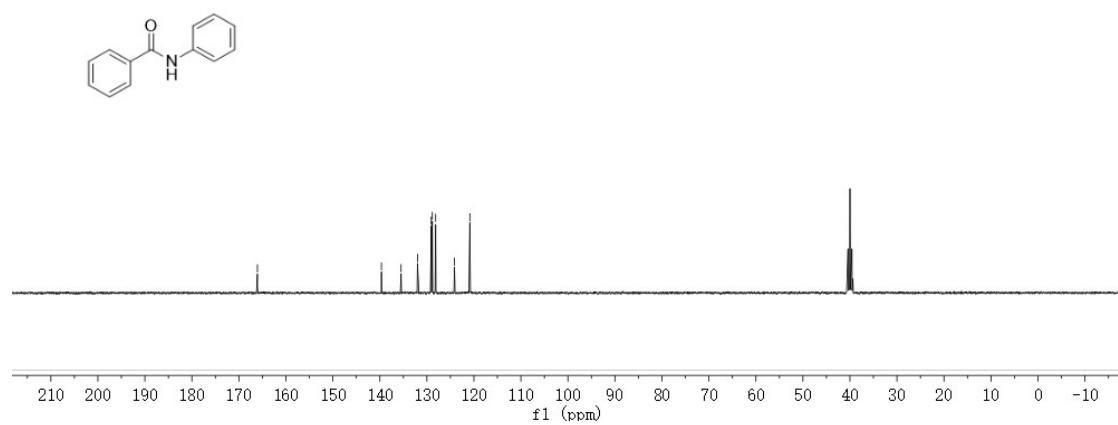
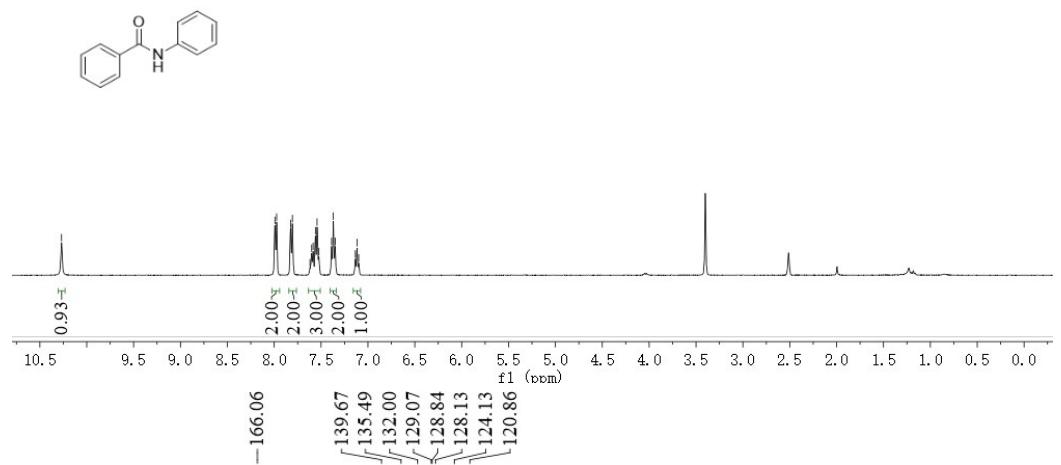
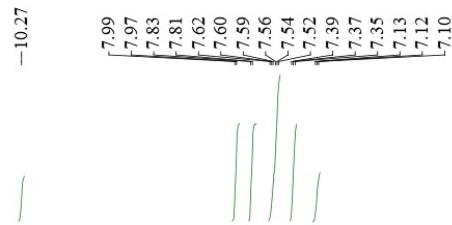
Benzamide (6p)



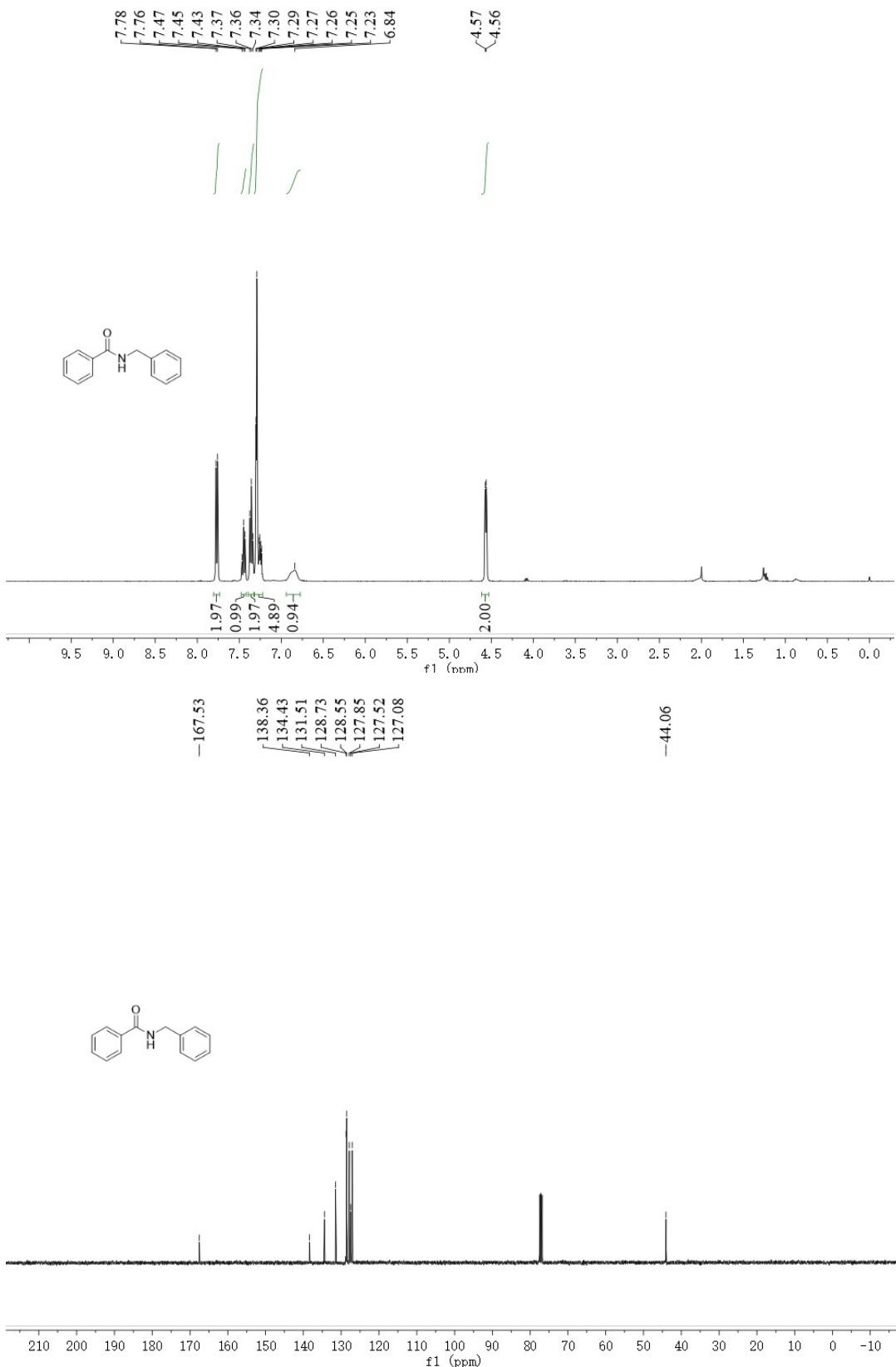
N-methylbenzamide (6q)



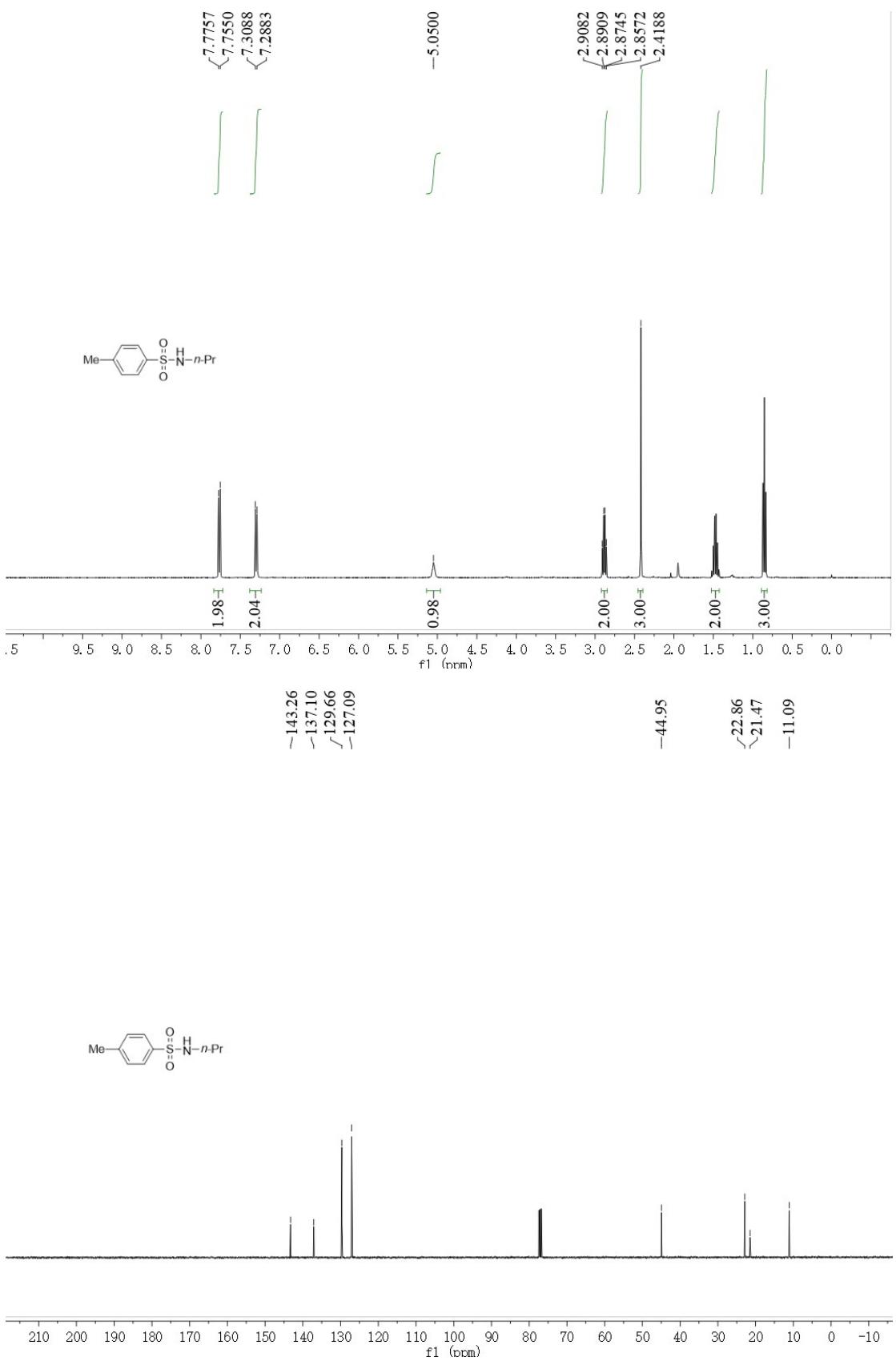
N-phenylbenzamide (6r)



N-benzylbenzamide (6s)



4-Methyl-N-propylbenzenesulfonamide (8a)



4-Methylbenzenesulfonamide (8b)

