Supporting Information

Platinum-Catalyzed Double Acylation of 2-Aryloxypyridines via Direct C–H Activation

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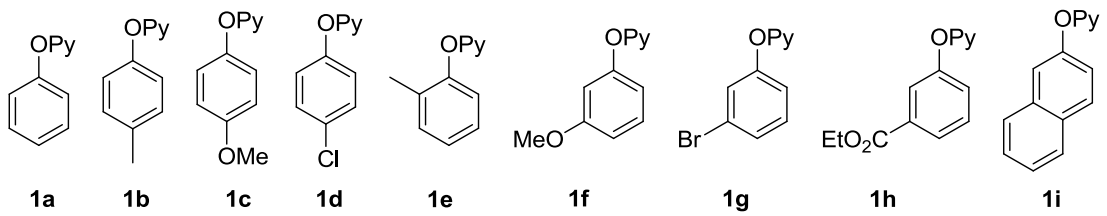
Contents **Page**

General experimental information

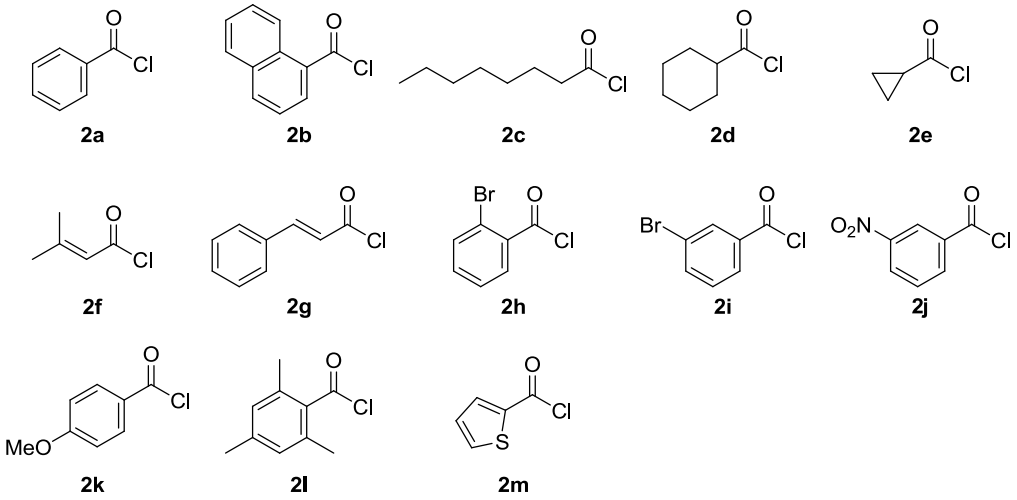
All reactions involving moisture- and/or oxygen-sensitive compounds were carried out under argon atmosphere and anhydrous conditions. All anhydrous solvents were purchased from Aldrich Chemical Co. and were used as received. $(PhCN)_2PtCl_2$,[1] $(DMSO)_2PtCl_2$,[2] and $(PPh_3)_2PtCl_2$[3] was prepared according to literature procedures. All starting materials and other reagents were purchased from chemical companies and were used as received. Gas chromatography was performed on a Shimadzu GC-2010 AFC equipped with FID detector. ^1H and ^{13}C NMR spectra were measured on a Bruker 400 spectrometer using $CDCl_3$ as the solvent and tetramethylsilane (TMS, δ 0.00 ppm) or the solvent peak ($CDCl_3$, δ 7.24 ppm for ^1H NMR and 77.0 ppm for ^{13}C NMR) as standard. Coupling constants (*J*) are reported in Hz. Mass spectra were measured on a Waters UPLC/Micromass Quadrupole-ToF mass spectrometer. IR spectra of neat samples were recorded on a Nicolet 6700 FT-IR spectrometer equipped with an ATR accessory. Melting points were measured on a Mel-temp apparatus and were uncorrected. 2-Aryloxypyrdines **1a**-**1i** (**Chart S1**) were prepared according to literature procedures.[4-9] A general procedure was described for the synthesis and characterization of compounds **1g**, **1h**, and **1i**. In the literature, compound **1h** was prepared with a different method.[10] Acyl chlorides **2a**-**2m** were purchased from commercial vendors and used as received (Chart S1).

Chart S1. Structures of 2-aryloxypyridines (**1a**-**1i**) and acyl chlorides (**2a**-**2m**) studied in the Pt-catalyzed acylation reaction



1a **1b** **1c** **1d** **1e** **1f** **1g** **1h** **1i**

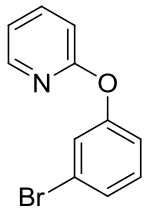
Structures of substrates 2-Aryloxypyridines **1a-i** (Py = pyridyl)



2a **2b** **2c** **2d** **2e** **2f** **2g** **2h** **2i** **2j** **2k** **2l** **2m**

Structures of acyl chlorides **2a-m**)

Synthesis and characterization of 2-aryloxypyridines 1g, 1h, and 1i

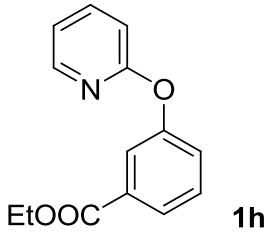


1g

Synthesis of 2-(3-bromophenoxy)pyridine[5] (**1g**). **General procedure A**.[4] Under argon atmosphere, to an oven-dried, 100 mL round-bottom flask were charged 2-bromopyridine (3.16 g, 20 mmol), 3-bromophenol (4.15 g, 24 mmol), CuI (0.038 g, 2 mmol), picolinic acid (0.492 g, 4 mmol), K_3PO_4 (8.49 g, 40 mmol), and anhydrous DMSO (40 mL). The mixture was stirred at 90 ^oC for 24 h, TLC and GC showed the complete consumption of 2-bromopyridine. After cooling to room temperature, water (100 mL) was added and the mixture was extracted with tert-butylmethyl ether

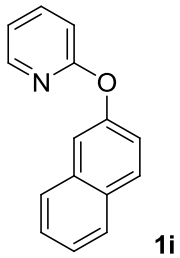
(3 × 50 mL). The combined organic solution was washed with water (2 × 100 mL), 3 M NaOH (20 mL), water (100 mL), brine (100 mL), and dried over anhydrous Na_2SO_4. After evaporation of the solvents, the crude product was purified by recrystallization from hexanes. White fine needles were obtained, 3.60 g, 72% yield. Melting point: 48-50°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (ddd, J = 4.8 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.66 (ddd, J = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.32-7.28 (m, 2H), 7.22 (t, J = 8.4 Hz, 1H), 7.09-7.05 (m, 1H), 6.99 (ddd, J = 7.2 Hz, 4.8 Hz, 0.8 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.89(C), 154.71(C), 147.51(CH), 139.46(CH), 130.50(CH), 127.49(CH), 124.31(CH), 122.43(C), 119.74(CH), 118.83(CH), 111.68(CH). MS Calcd for $C_{11}H_9BrNO$ ($M+H^+$): 249.99; Found: 249.91.

The following compounds were synthesized using the General Procedure A.



1h

ethyl 3-(pyridin-2-yloxy)benzoate[10] (**1h**): Purified by column chromatography (hexanes-ethyl acetate: v/v = 7:2). Colorless oil, 3.25 g, 67% yield. IR (C=O): 1712.7 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.16 (dd, J = 5.2 Hz, 2.0 Hz, 1H), 7.89 (dt, J = 7.6 Hz, 1.6 Hz, 1H), 7.82 (t, J = 2.0 Hz, 1H), 7.68 (ddd, J = 8.0 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.45 (t, J = 8.0 Hz, 1H), 7.34 (ddd, J = 8.2 Hz, 2.4 Hz, 1.2 Hz, 1H), 6.99 (dd, J = 7.2 Hz, 5.2 Hz, 1H), 6.93 (d, J = 8.4 Hz, 1H), 4.35 (quartet, J = 7.2 Hz, 2H), 1.36 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.67(C), 163.10(C), 153.92(C), 147.40(CH), 139.39(CH), 131.96(C), 129.34(CH), 125.62(CH), 125.53(CH), 122.08(CH), 118.59(CH), 111.54(CH), 60.88(CH_2), 14.07(CH_3). MS Calcd for $C_{14}H_{14}NO_3$ ($M+H^+$): 244.10; Found: 244.10.



1i

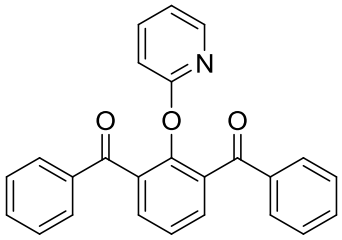
2-(Naphthalen-2-yloxy)pyridine[9] (**1i**): Purified by recrystallization from hexanes. Light yellow needles. Melting point: 50-52°C. 2.72 g, 62% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (ddd, J = 4.8 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.82 (d, J = 8.8 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.59 (ddd, J = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.55 (d, J = 2.4 Hz, 1H), 7.44-7.35 (m, 2H), 7.27 (dd, J = 8.8 Hz, 2.4 Hz, 1H), 6.94-6.88 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.65(C), 151.69(C), 147.62(CH), 139.29(CH), 134.10(C), 130.81(C), 129.47(CH), 127.63(CH), 127.28(CH), 126.26(CH), 125.02(CH), 121.26(CH), 118.41(CH), 117.29(CH), 111.45(CH). MS Calcd for $C_{15}H_{12}NO$ ($M+H^+$): 222.09; Found: 221.08.

Table S1. Optimization of conditions for the reactions of **1a** and **1g** with benzoyl chloride.[a]

Entry	Substrate	Catalyst (%)	Solvent (mL)	T (°C)	t (h)	Remark	Yield (%)[b]	
							3aa	**4aa**
1	**1a**	K_2PtCl_4 (10)	MeCN (2)	reflux	12	NR[c]	-	-
2	**1a**	K_2PtCl_4 (10)	AcOH (2)	reflux	12	NR	-	-
3	**1a**	K_2PtCl_4 (10)	PhCN (2)	150	24	-	46	10
4	**1a**	Na_2PdCl_4 (10)	PhCN (2)	150	12	NR	-	-
5	**1a**	$PdCl_2$ (10)	PhCN (2)	150	12	NR	-	-
6	**1a**	$Pd(OAc)_2$ (10)	PhCN (2)	150	12	NR	-	-
7	**1a**	$(MeCN)_2PdCl_2$ (10)	PhCN (2)	150	12	NR	-	-
8	**1a**	Cu(I)Br (10)	PhCN (2)	150	12	NR	-	-
9	**1a**	Cu(II)Cl_2 (10)	PhCN (2)	150	12	NR	-	-
10	**1a**	$NiCl_2$ (10)	PhCN (2)	150	12	NR	-	-
11	**1a**	K_2PtCl_4 (10)[d]	DCB (2)	150	12	NR	-	-
12	**1a**	$(PhCN)_2PtCl_2$ (10)	DCB (2)	140	24	-	54	7
13	**1a**	$(DMSO)_2PtCl_2$ 10)	DCB (2)	150	24	Low conversion	-	-
14	**1a**	$(PPh_3)_2PtCl_2$ (10)	DCB (2)	150	24	NR	-	-
15	**1a**	$(PhCN)_2PtCl_2$ (10)	*m*-xylene (3)	reflux	48	-	-	66
16	**1a**	$PtCl_2$ (10)	*m*-xylene (3)	reflux	48	-	-	62
17	**1a**	$(PhCN)_2PtCl_2$ (10)	PhCl (3)	reflux	48	-	-	72
18	**1a**	$(PhCN)_2PtCl_2$ (5)	PhCl (3)	reflux	48	Lower conversion	-	-
19[e]	**1a**	$(PhCN)_2PtCl_2$ (10)	PhCl (3)	reflux	48	Lower conversion	-	-
							Yield of **3ga** (%)	
20	**1g**	$(PhCN)_2PtCl_2$ (10)	PhCl (3)	reflux	24	-	69	
21[f]	**1g**	$(PhCN)_2PtCl_2$ (10)	PhCl (3)	reflux	24	-	70	
22	**1g**	$(PhCN)_2PtCl_2$ (10)	PhCl (1 mL)	reflux	48	-	61	
23	**1g**	$(PhCN)_2PtCl_2$ (10)	PhCl (2 mL)	reflux	41	-	83	
24	**1g**	$(PhCN)_2PtCl_2$ (10)	PhCl (3 mL)	reflux	41	-	84	
25	**1g**	$(PhCN)_2PtCl_2$ (10)	PhCl (4 mL)	reflux	41	-	82	

[a] General conditions: Substrate (1 mmol), benzoyl chloride (5 mmol), solvent (2-3 mL). MeCN = acetonitrile; AcOH = acetic acid; PhCN = benzonitrile; DCB = 1,2-dichlorobenezene; PhCl = chlorobenzene. [b]Isolated yield. [c]NR = no *ortho* acylation reaction. [d]K_2PtCl_4 did not dissolve in DCB. [e]Three equivalents of benzoyl chloride was used. [f]The reaction was run under argon.

General Procedure for the Pt-catalyzed acylation reaction.



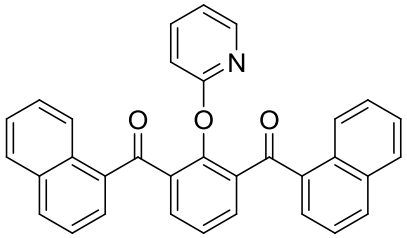
4aa

Preparation of (2-(pyridin-2-yloxy)-1,3-phenylene)bis(phenylmethanone)[11] (**4aa**): **General Procedure B**. Under argon flushing, a 25 mL round-bottom flask equipped with a magnetic stirring bar and a condenser was dried with a heat-gun. A drying tube was placed on the top of the condenser. To the flask were placed 2-phenoxypyridine (**1a**) (171 mg, 1 mmol), $(PhCN)_2PtCl_2$ (47 mg, 0.1 mmol), benzoyl chloride (700 mg, 5 mmol), and anhydrous chlorobenzene (3 mL). The mixture was stirred under reflux for 41 h and TLC showed the completion of the reaction. The temperature was lowered to 100 ^oC and 2 mL of 6 M NaOH was added. The mixture was stirred for 30 min and cooled to room temperature. Water (20 mL) was added, and the mixture was extracted with dichloromethane (3 × 15 mL). The combined organic layers was dried over anhydrous Na_2SO_4. After filtration and removal of the solvents, the crude product was purified by column chromatography with hexanes-ethyl acetate (v/v = 5:1) as the eluting solvent. A small amount of dichloromethane was used to dissolve the crude product for introducing it onto the column. The fractions containing the product were combined and evaporated to yield an off-white solid, 273 mg, 72% yield. Melting point: 121-122°C. IR (C=O): 1656.1 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (ddd, J = 4.8 Hz, 1.8 Hz, 0.4 Hz, 1H), 7.74-7.69 (m, 6H), 7.41-7.45 (m, 3H), 7.27 (t, J = 7.8 Hz, 4H), 7.23 (ddd, J = 7.8 Hz, 1.8 Hz, 0.8 Hz, 1H), 6.69 (ddd, J = 6.8 Hz, 4.8 Hz, 0.8 Hz, 1H), 6.12 (d, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.65(2C), 161.95(C), 148.67(C), 145.95(CH), 139.04(CH), 137.04(2C), 133.55(2C), 132.82(2CH), 132.38(2H),

129.63(4CH), 127.93(4CH), 124.70(CH), 118.32(CH), 110.67(CH). MS Calcd for $C_{25}H_{18}NO_3$ ($M+H^+$): 380.13; Found: 380.13. Anal. Calcd for $C_{25}H_{17}NO_3$: C, 79.14; H, 4.52; N, 3.69. Found C, 78.90; H, 4.62; N, 3.73.

When the reaction was carried out in m-xylene at reflux for 48 h, **4aa** was isolated in 66% yield. When the reaction was carried out in 1,2-dichlorobenzene at 140 ^oC for 24 h, **3aa** was isolated in 54% yield as the major product, and its NMR spectrum is consistent with that reported in literature.[7] Diacylated product **4aa** was obtained in 7% yield. The separation of **3aa** and **4aa** was achieved by column chromatography on silica gel with hexanes-ethyl acetate (v/v = 5:1) as the eluting solvent. When benzonitrile was used as the solvent and K_2PtCl_4 as the catalyst, **3aa** was isolated in 46% yield and **4aa** in 10% yield.

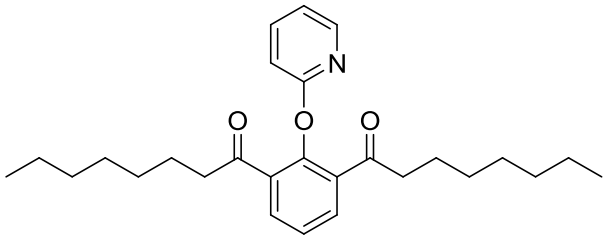
The following compounds were synthesized using the General Procedure B.



4ab

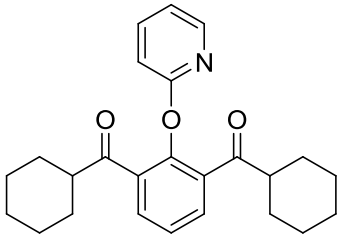
(2-(Pyridin-2-yloxy)-1,3-phenylene)bis(naphthalen-1-ylmethanone) (**4ab**). Purified by column chromatography (hexane-ethyl acetate: v/v = 10:1) and recrystallization (hexanes and dichloromethane). Off-white solid, 342 mg, 71% yield. Melting point: 136-137°C. IR (C=O): 1647.8 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.37 (ddd, J = 8.2 Hz, 1.0 Hz, 2H), 7.90 (d, J = 7.6 Hz, 2H), 7.79-7.68 (m, 5H), 7.59 (dd, J = 7.2 Hz, 1.2 Hz, 2H), 7.47-7.37 (m, 5H), 7.19 (dd, J = 8.0 Hz, 7.2 Hz, 2H), 6.72 (ddd, J = 8.4 Hz, 6.6 Hz, 1.8 Hz, 1H), 6.43 (ddd, J = 7.2 Hz, 5.2 Hz, 0.8 Hz, 1H), 5.39 (d, J = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.00(2C), 161.66(C),

149.72(C), 145.79(CH), 138.34(CH), 135.19(2C), 135.09(2C), 133.93(2CH), 133.33(2C), 132.31(2CH), 130.18(2C), 129.92(2CH), 127.96(2CH), 127.44(2CH) 126.07(2CH), 125.43(2CH), 125.07(CH), 123.81(2CH), 118.05(CH), 109.86(CH). MS Calcd for $C_{33}H_{22}NO_3$ ($M+H^+$): 480.16; Found: 480.17. Anal. Calcd for $C_{33}H_{21}NO_3$: C, 82.66; H, 4.41; N, 2.92. Found C, 82.83; H, 4.35; N, 2.92.



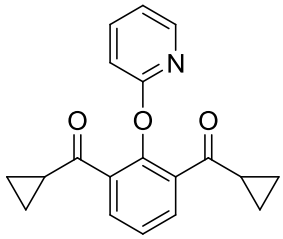
4ac

1,1'-(2-(pyridin-2-yloxy)-1,3-phenylene)dioctan-1-one (**4ac**). Purified by column chromatography (hexane-ethyl acetate: v/v = 8:1). Colorless oil, 293 mg, 69% yield. IR (C=O): 1658.1 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (dd, J = 4.8 Hz, 1.2 Hz, 1H), 7.78 (d, J = 7.6 Hz, 2H), 7.71 (ddd, J = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.36 (t, J = 7.6 Hz, 1H), 7.00-6.95 (m, 2H), 2.79 (t, J = 7.6 Hz, 4H), 1.51 (quintet, J = 7.2 Hz, 4H), 1.29-1.10 (m, 16H), 0.85 (t, J = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.87(2C), 162.81(C), 148.67(C), 147.21(CH), 139.80(CH), 134.64(2C), 132.15(2CH), 125.36(CH), 118.70(CH), 111.20(CH), 42.45($2CH_2$), 31.54($2CH_2$), 28.97($2CH_2$), 28.90($2CH_2$), 23.88($2CH_2$), 22.49($2CH_2$), 13.97($2CH_3$). MS Calcd for $C_{27}H_{38}NO_3$ ($M+H^+$): 424.29; Found: 424.30. Anal. Calcd for $C_{27}H_{37}NO_3$: C, 76.56; H, 8.80; N, 3.31. Found C, 76.49; H, 8.79; N, 3.37.



4ad

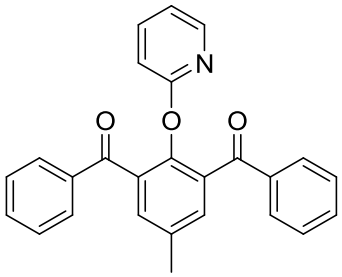
(2-(pyridin-2-yloxy)-1,3-phenylene)bis(cyclohexylmethanone) (**4ad**). Purified by column chromatography (hexane-ethyl acetate: v/v = 8:1). White solid, 211 mg, 54% yield. Melting point: 104-105°C. IR (C=O): 1680.9 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 3.6 Hz, 1H), 7.74-7.63 (m, 3H), 7.35 (t, J = 7.6 Hz, 1H), 7.0-6.92 (m, 2H), 2.95 (tt, J = 11.2 Hz, 2.8 Hz, 2H), 1.72-1.54 (m, 10H), 1.31-1.03 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.74(2C), 162.96(C), 148.20(C), 147.26(CH), 139.74(CH), 134.59(2C), 131.89(2CH), 125.41(CH), 118.75(CH), 110.93(CH), 49.47(2CH), 28.73($4CH_2$), 25.73($2CH_2$), 25.62($4CH_2$). MS Calcd for $C_{25}H_{30}NO_3$ ($M+H^+$): 392.22; Found: 392.24. Anal. Calcd for $C_{25}H_{29}NO_3$: C, 76.70; H, 7.47; N, 3.58. Found C, 76.47; H, 7.52; N, 3.53.



4ae

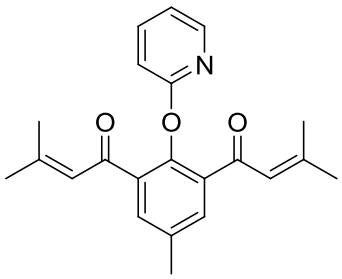
(2-(pyridin-2-yloxy)-1,3-phenylene)bis(cyclopropylmethanone) (**4ae**). Purified by column chromatography (hexane-ethyl acetate: v/v = 4:1). Light yellow oil, 174 mg, 57% yield. IR (C=O): 1668.2 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (ddd, J = 5.0 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.80 (d, J = 8.0 Hz, 2H), 7.69 (ddd, J = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.39 (t, J = 7.6 Hz, 1H), 6.99-6.92 (m, 2H), 2.46 (tt, J = 7.6 Hz, 4.8 Hz, 2H), 1.02 (m, 4H), 0.85-0.79 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.16(2C), 163.11(C), 148.85(C), 147.28(CH), 139.60(CH), 135.30(2C),

132.13(2CH), 125.45(CH), 118.62(CH), 110.99(CH), 21.38(2CH), 12.33($4CH_2$). MS Calcd for $C_{19}H_{18}NO_3$ ($M+H^+$): 308.13; Found: 308.11. Anal. Calcd for $C_{19}H_{17}NO_3$: C, 74.25; H, 5.58; N, 4.56. Found C, 74.14; H, 5.71; N, 4.53.



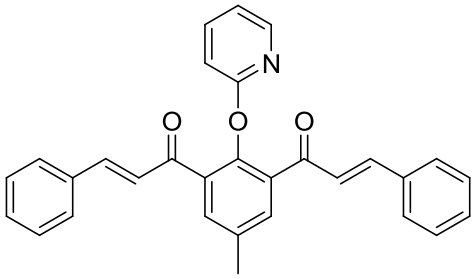
4ba

(5-methyl-2-(pyridin-2-yloxy)-1,3-phenylene)bis(phenylmethanone) (**4ba**). Purified by column chromatography (hexane-ethyl acetate v/v = 6:1). White solid, 323 mg, 82% yield. Melting point: 106-107°C. IR (C=O): 1651.9 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.79 (ddd, J = 4.8 Hz, 1.8 Hz, 0.8 Hz, 1H), 7.73-7.68 (m, 4H), 7.53 (d, J = 0.8 Hz, 2H), 7.42 (tt, J = 7.6 Hz, 1.2 Hz, 2H), 7.30-7.24 (m, 4H), 7.20 (ddd, J = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H), 6.69 (ddd, J = 7.2 Hz, 5.2 Hz, 0.8 Hz, 1H), 6.05 (d, J = 8.0 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.93(2C), 162.13(C), 146.41(C), 146.00(CH), 138.96(CH), 137.19(2C) 134.83(C), 133.33(2C), 132.87(2CH), 132.77(2CH), 129.62(4CH), 127.91(4CH), 118.19(CH), 110.61(CH), 20.73(CH_3). MS Calcd for $C_{26}H_{20}NO_3$ ($M+H^+$): 394.14; Found: 394.15. Anal. Calcd for $C_{26}H_{19}NO_3$: C, 79.37; H, 4.87; N, 3.56. Found C, 79.28; H, 4.98; N, 3.48.



4bf

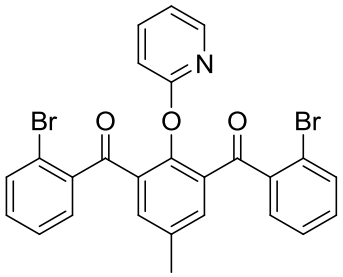
1,1'-(5-methyl-2-(pyridin-2-yloxy)-1,3-phenylene)bis(3-methylbut-2-en-1-one) **(4bf**). Purified by column chromatography (hexane-ethyl acetate, v/v = 6:1). Light orange viscous oil, 190 mg, 54% yield. IR (C=O): 1660.2 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (ddd, J = 4.8 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.63 (ddd, J = 11.6 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.56 (d, J = 0.4 Hz, 2H), 6.89 (ddd, J = 7.2 Hz, 4.8 Hz, 0.8 Hz, 1H), 6.81 (d, J = 7.6 Hz, 1H), 6.34 (t, J = 1.2 Hz, 2H), 2.41 (s, 3H), 1.95 (d, J = 1.2 Hz, 6H), 1.75 (d, J = 0.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.78(2C), 163.41(C), 155.42(2C), 147.21(CH), 146.36(C), 139.16(CH), 135.53(2C), 135.30(C), 132.83(2CH), 124.88(2CH), 118.02(CH), 110.78(CH), 27.45($2CH_3$), 20.74($2CH_3$), 20.69(CH_3). MS Calcd for $C_{22}H_{24}NO_3$ ($M+H^+$): 350.18; Found: 350.17. Anal. Calcd for $C_{22}H_{23}NO_3$: C, 75.62; H, 6.63; N, 4.01. Found C, 75.44; H, 6.57; N, 3.88.



4bg

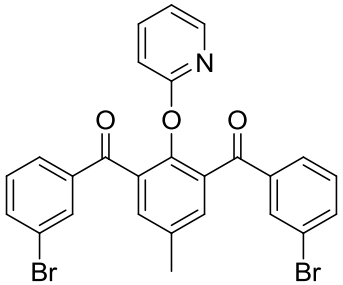
(2E,2'E)-1,1'-(5-methyl-2-(pyridin-2-yloxy)-1,3-phenylene)bis(3-phenylprop-2-en-1-one) (**4bg**). Purified by column chromatography (hexane-ethyl acetate, v/v = 4:1). Off-white solid, 352 mg, 79% yield. Melting point: 133-134°C. IR (C=O): 1643.7 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (ddd, J = 4.8 Hz, 1.8 Hz, 0.8 Hz, 1H), 7.64 (d, J = 0.4 Hz, 2H), 7.48 (d, J = 16.0 Hz, 2H), 7.43 (ddd, J = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.40-7.35 (m, 4H), 7.34-7.27 (m, 6H), 7.10 (d, J = 16.0 Hz, 2H), 6.82-6.76 (m, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.02(2C), 162.93(C), 146.89(CH), 146.75(C), 144.68(2CH), 139.41(CH), 135.39(C), 134.38(2C), 134.28(2C), 132.91(2CH), 130.37(2CH), 128.68(4CH), 128.16(4CH), 125.69(2CH), 118.46(CH),

111.09(CH), 20.64(CH_3). MS Calcd for $C_{30}H_{24}NO_3$ ($M+H^+$): 446.18; Found: 446.18. Anal. Calcd for $C_{30}H_{23}NO_3$: C, 80.88; H, 5.20; N, 3.14. Found C, 80.65; H, 5.36; N, 3.10.



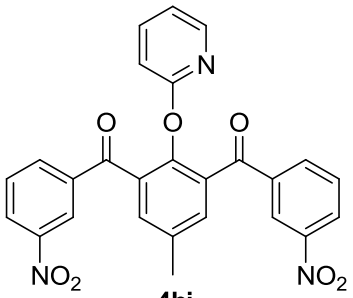
4bh

(5-methyl-2-(pyridin-2-yloxy)-1,3-phenylene)bis((2-bromophenyl)methanone) (**4bh**). Purified by column chromatography (hexanes-ethyl acetate-dichloromethane: v/v/v = 5:1:1) and recrystallization from hexanes-dichloromethane. Off-white crystals, 304 mg, 55% yield. Melting point: 118-119°C. IR (C=O): 1663.8, 1646.0 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (dd, J = 5.2 Hz, 2.0 Hz, 1H), 7.80 (s, 2H), 7.41 (dd, J = 8.0 Hz, 1.2 Hz, 2H), 7.20 (ddd, J = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.15-7.03 (m, 6H), 6.73 (dd, J = 7.2 Hz, 5.2 Hz, 1H), 5.84 (d, J = 8.4 Hz, 1H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.64(2C), 162.17(C), 148.38(C), 146.06(CH), 140.36(CH), 138.75(2C), 135.71(2CH), 135.47(C), 133.01(2CH), 132.65(2C), 131.32(2CH), 129.78(2CH), 126.48(2CH), 119.70(2C), 118.08(CH), 109.95(CH), 20.65(CH_3). MS Calcd for $C_{26}H_{18}Br_2NO_3$ ($M+H^+$): 551.96; Found: 551.95. Anal. Calcd for $C_{26}H_{17}Br_2NO_3$: C, 56.65; H, 3.11; N, 2.54. Found C, 56.36; H, 3.26; N, 2.41.



4bi

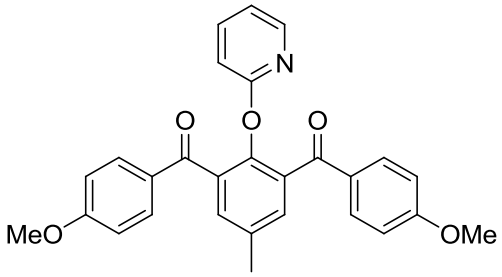
(5-methyl-2-(pyridin-2-yloxy)-1,3-phenylene)bis((3-bromophenyl)methanone) (**4bi**). Purified by column chromatography (hexane-ethyl acetate-dichloromethane: v/v/v = 6:1:1.5) and recrystallization (hexanes-dichloromethane). White fine needles, 421 mg, 76% yield. Melting point: 172-173°C. IR (C=O): 1672.7 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.84 (ddd, J = 5.0 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.77 (t, J = 1.6 Hz, 2H), 7.62 (dt, J = 8.0 Hz, 0.8 Hz, 2H), 7.56 (d, J = 0.8 Hz, 2H), 7.53 (ddd, J = 8.0 Hz, 2.0 Hz, 1.2 Hz, 2H), 7.27 (ddd, J = 8.2 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.15 (t, J = 7.8 Hz, 2H) 6.76 (ddd, J = 7.0 Hz, 5.0 Hz, 1.2 Hz, 1H), 6.05 (d, J = 8.0 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.46(2C), 161.78(C), 146.50(C), 146.24(CH), 139.27(CH), 139.03(2C), 135.52(2CH), 135.25(C), 133.30(2CH), 132.64(2C), 132.18(2CH), 129.52(2CH) 127.99(2CH), 122.21(2C), 118.61(CH), 110.37(CH), 20.72(CH_3). MS Calcd for $C_{26}H_{18}Br_2NO_3$ ($M+H^+$): 551.96; Found: 551.96. Anal. Calcd for $C_{26}H_{17}Br_2NO_3$: C, 56.65; H, 3.11; N, 2.54. Found C, 56.48; H, 3.24; N, 2.55.



4bj

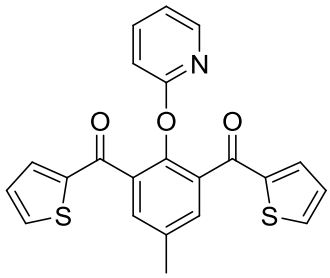
(5-methyl-2-(pyridin-2-yloxy)-1,3-phenylene)bis((3-nitrophenyl)methanone) (**4bj**). Purified by column chromatography (hexane-ethyl acetate-dichloromethane: v/v/v = 4:1:1). White solid, 374 mg, 77% yield. Melting point: 187-188°C. IR (C=O): 1664.4 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.44 (t, J = 1.8 Hz, 2H), 8.25 (ddd, J = 8.0 Hz, 2.4 Hz, 1.2 Hz, 2H), 8.02 (dt, J = 7.8 Hz, 1.2 Hz, 2H), 7.76 (ddd, J = 5.2 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.64 (d, J = 0.8 Hz, 2H), 7.49 (t, J = 8.0 Hz, 2H), 7.20 (ddd, J = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H), 6.71 (ddd, J = 7.2 Hz, 5.0 Hz, 0.8 Hz, 1H), 5.91 (d, J

= 8.4 Hz, 1H), 2.52 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.47(2C), 161.43(C), 147.85(2C), 146.62(C), 146.30(CH), 139.55(CH), 138.72(2C), 135.98(C), 134.82(2CH), 133.90(2CH), 132.26(2C), 129.77(2CH), 126.95(2CH), 124.05(2CH), 118.97(CH), 110.01(CH), 20.79(CH_3). MS Calcd for $C_{26}H_{18}N_3O_7$ ($M+H^+$): 484.11; Found: 484.13. Anal. Calcd for $C_{26}H_{17}N_3O_7$: C, 64.60; H, 3.54; N, 8.69. Found C, 64.37; H, 3.45; N, 8.62.



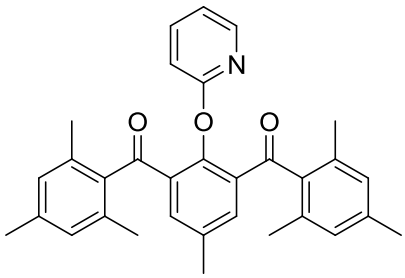
4bk

(5-methyl-2-(pyridin-2-yloxy)-1,3-phenylene)bis((4-methoxyphenyl)methanone) (**4bk**). Purified by column chromatography (hexane-ethyl acetate-dichloromethane: v/v/v = 4:1:1). White crystals, 235 mg, 52% yield. Melting point: 152-153°C. IR (C=O): 1650.4 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (ddd, J = 5.2 Hz, 1.8 Hz, 0.4 Hz, 1H), 7.74-7.70 (m, 4H), 7.45 (s, 2H), 7.25 (ddd, J = 8.0 Hz, 6.8 Hz, 2.0 Hz, 1H), 6.79-6.74 (m, 4H), 6.69 (ddd, J = 7.2 Hz, 4.8 Hz, 0.8 Hz, 1H), 6.18 (d, J = 8.4 Hz, 1H), 3.79 (s, 6h), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.48(2C), 163.39(2C), 162.35(C), 146.15(CH), 145.90(C), 138.83(CH), 134.63(C), 133.69(2C), 132.15(4CH), 132.11(2CH), 129.94(2C), 118.05(CH), 113.14(4CH), 110.71(CH), 55.32($2OCH_3$), 20.68(CH_3). MS Calcd for $C_{28}H_{24}NO_5$ ($M+H^+$): 454.16; Found: 454.18. Anal. Calcd for $C_{28}H_{23}NO_5$: C, 74.16; H, 5.11; N, 3.09. Found C, 73.90; H, 5.16; N, 3.04.



4bl

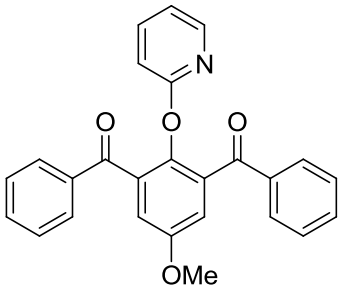
(5-methyl-2-(pyridin-2-yloxy)-1,3-phenylene)bis(thiophen-2-ylmethanone) (**4bl**). Purified by column chromatography (hexane-ethyl acetate: v/v = 3:1). Pale yellow solid, 210 mg, 52% yield. Melting point: 134-135°C. IR (C=O): 1628.2 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (ddd, J = 5.2 Hz, 1.6 Hz, 0.4 Hz, 1H), 7.61 (dd, J = 5.0 Hz, 1.2 Hz, 2H), 7.56 (dd, J = 4.0 Hz, 1.2 Hz, 2H), 7.54 (d, J = 0.4 Hz, 2H) 7.37 (ddd, J = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H) 7.00 (dd, J = 5.0 Hz, 4.0 Hz, 2H), 6.75 (ddd, J = 7.2 Hz, 5.2 Hz, 0.8 Hz, 1H), 6.43 (d, J = 8.4 Hz, 1H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.30(2C), 162.39(C), 146.28(CH), 145.67(C), 143.53(2C), 139.04(CH), 135.44(2CH), 134.61(2CH), 133.38(3C), 131.95(2CH), 127.72(2CH), 118.26(CH), 110.83(CH), 20.63(CH_3). MS Calcd for $C_{22}H_{16}NO_3S_2$ ($M+H^+$): 406.06; Found: 406.06. Anal. Calcd for $C_{22}H_{15}NO_3S_2$: C, 65.16; H, 3.73; N, 3.45. Found C, 64.96; H, 3.74; N, 3.45.



4bm

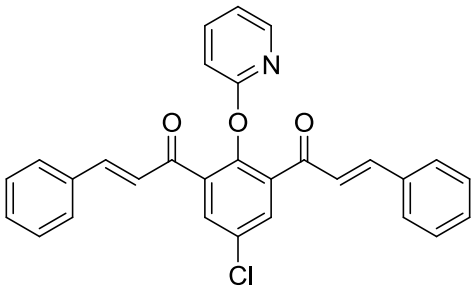
(5-methyl-2-(pyridin-2-yloxy)-1,3-phenylene)bis(mesitylmethanone) (**4bm**). Purified by column chromatography (hexane-ethyl acetate: v/v = 7:1) and recrystallization (hexane-ethyl acetate). Off-white fine needles, 352 mg, 74% yield. Melting point: 171-172°C. IR (C=O): 1676.8 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 0.4 Hz, 2H), 7.78 (ddd, J = 5.2 Hz, 1.8 Hz, 0.4 Hz,

1H), 7.25 (ddd, *J* = 8.2 Hz, 4.8 Hz, 2.0 Hz, 1H), 6.73 (ddd, *J* = 7.0 Hz, 5.0 Hz, 1.2 Hz, 1H), 6.60 (s, 4h), 6.02 (d, *J* = 8.4 Hz, 1H), 2.41 (s, 3H), 2.16 (s, 6H), 1.98 (s, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.29(2C), 162.96(C), 150.07(C), 145.45(CH), 138.33(CH), 137.94(2C), 137.87(2C), 136.75(4C), 135.72(C), 134.33(2CH), 133.33(2C), 128.21(4CH), 117.61(CH), 110.38(CH), 20.95($2CH_3$), 20.83(CH_3), 19.61($4CH_3$). MS Calcd for $C_{32}H_{32}NO_3$ ($M+H^+$): 478.24; Found: 478.26. Anal. Calcd for $C_{32}H_{31}NO_3$: C, 80.47; H, 6.54; N, 2.93. Found C, 80.45; H, 6.65; N, 2.92.



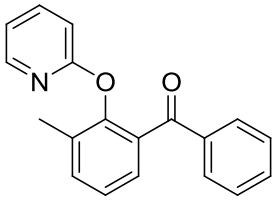
4ca

(5-methoxy-2-(pyridin-2-yloxy)-1,3-phenylene)bis(phenylmethanone) (**4ca**). Purified by column chromatography (hexanes-ethyl acetate: v/v = 5:1). Light yellow solid, 310 mg, 76% yield. Melting point: 83-84°C. IR (C=O): 1660.2 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (ddd, *J* = 4.8 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.74-7.69 (m, 4H), 7.42 (tt, *J* = 7.6 Hz, 1.2 Hz, 2H), 7.29-7.23 (m, 6H), 7.18 (ddd, *J* = 8.0 Hz, 6.8 Hz, 2.0 Hz, 1H), 6.67 (ddd, *J* = 7.2 Hz, 4.8 Hz, 0.8 Hz, 1H), 6.03 (d, *J* = 8.4 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.38(2C), 162.13(C), 156.03(C), 145.89(CH), 141.78(C), 138.86(CH), 136.85(2C), 134.39(2C), 132.81(2CH), 129.57(4CH), 127.86(4CH), 118.06(CH), 117.33(2CH), 110.42(CH), 55.86(OCH_3). MS Calcd for $C_{26}H_{20}NO_4$ ($M+H^+$): 410.14; Found: 410.15. Anal. Calcd for $C_{26}H_{19}NO_4$: C, 76.27; H, 4.68; N, 3.42. Found C, 76.27; H, 4.82; N, 3.36.



4dg

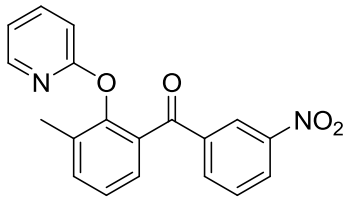
(2E,2'E)-1,1'-(5-chloro-2-(pyridin-2-yloxy)-1,3-phenylene)bis(3-phenylprop-2-en-1-one) (**4dg**). Purified by column chromatography (4:1 hexanes-ethyl acetate-dichloromethane: v/v/v = 4:1:0.25). Light yellow fine needles, 304 mg, 64% yield. Melting point: 116-117°C. IR (C=O): 1668.5 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (dd, J = 4.8 Hz, 2.0 Hz, 1H), 7.78 (s, 2H), 7.52-7.44 (m, 3H), 7.42-7.30 (m, 10H), 7.06 (d, J = 16.0 Hz, 2H), 6.83 (ddd, J = 7.2 Hz, 5.2 Hz, 0.8 Hz, 1H), 6.80 (d, J = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.60(2C), 162.60(C), 147.39(C), 146.89(CH), 145.73(2CH), 139.73(CH), 136.08(2C), 134.22(2C), 132.00(2CH), 131.19(C), 130.76(2CH), 128.85(4CH), 128.36(4CH), 125.16(2CH), 118.97(CH), 111.25(CH). MS Calcd for $C_{29}H_{21}ClNO_3$ ($M+H^+$): 466.12; Found: 466.14. Anal. Calcd for $C_{29}H_{20}ClNO_3$: C, 74.76; H, 4.33; N, 3.01. Found C, 74.71; H, 4.36; N, 2.90.



3ea

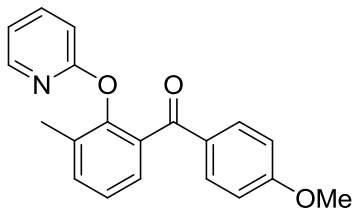
(3-methyl-2-(pyridin-2-yloxy)phenyl)(phenyl)methanone[7] (**3ea**). Purified by column chromatography (hexanes-ethyl acetate: v/v = 5:1). Pale yellow oil, 237 mg, 82% yield. IR (C=O): 1663.8cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (ddd, J = 5.0 Hz, 2.0 Hz, 0.8 Hz, 1 H), 7.74-7.70 (m, 2H), 7.51-7.42 (m, 3H), 7.35-7.29 (m, 3H), 7.22 (t, J = 7.4 Hz, 1H), 6.79 (ddd, J = 7.2 Hz, 5.0

Hz, 0.8 Hz, 1H), 6.61 (dt, J = 8.4 Hz, 0.8 Hz, 1H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.39(C), 162.83(C), 149.44(C), 146.92(CH), 139.10(CH), 137.41(C), 133.69(CH), 132.87(C), 132.60(CH), 132.38(C), 129.82(2CH), 127.83(2CH), 127.66(CH), 124.72(CH), 117.83(CH), 110.48(CH), 16.55(CH_3). MS Calcd for $C_{19}H_{16}NO_2$ ($M+H^+$): 290.12; Found: 290.08.



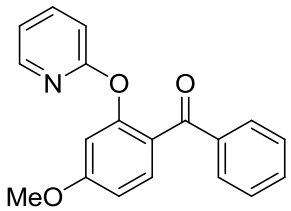
3ej

(3-methyl-2-(pyridin-2-yloxy)phenyl)(3-nitrophenyl)methanone (**3ej**). Purified by column chromatography (hexanes-ethyl acetate: v/v/v = 3:1:0.1). Off-white solid, 231 mg, 69% yield. Melting point: 72-74°C. IR (C=O): 1659.3 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (t, J = 1.8 Hz, 1H), 8.30 (ddd, J = 8.4 Hz, 2.2 Hz, 0.8 Hz, 1H), 8.03 (dt, J = 7.6 Hz, 1.2 Hz, 1H), 7.92 (dd, J = 4.8 Hz, 1.2 Hz, 1 H), 7.55-7.46 (m, 3H), 7.40 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 7.29 (t, J = 7.6 Hz, 1H), 6.82 (ddd, J = 7.0 Hz, 4.8 Hz, 0.8 Hz, 1H), 6.56 (d, J = 8.4 Hz, 1H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.38(C), 162.41(C), 149.49(C), 147.76(C), 146.90(CH), 139.38(CH), 139.17(C), 135.04(CH), 134.83(CH), 132.71(C), 131.73(C), 129.07(CH), 127.65(CH), 126.68(CH), 125.19(CH), 124.35(CH), 118.19(CH), 110.30(CH), 16.57(CH_3). MS Calcd for $C_{19}H_{15}N_2O_4$ ($M+H^+$): 335.10; Found: 335.10. Anal. Calcd for $C_{19}H_{14}N_2O_4$: C, 68.26; H, 4.22; N, 8.38. Found C, 68.28; H, 4.19; N, 8.41.



3ek

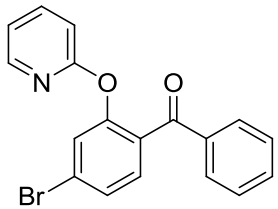
(4-methoxyphenyl)(3-methyl-2-(pyridin-2-yloxy)phenyl)methanone (**3ek**). Purified by column chromatography (hexanes-ethyl acetate-dichloromethane: v/v/v = 2:1:0.3). Off-white solid, 239 mg, 75% yield. Melting point: 72-74°C. IR (C=O): 1654.9 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (ddd, *J* = 4.8 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.75-7.71 (m, 2H), 7.50 (ddd, *J* = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.41 (ddd, *J* = 7.4 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.29 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 1H), 6.83-6.78 (m, 3H), 6.65 (dt, *J* = 8.4 Hz, 0.8 Hz, 1H), 3.82 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.01(C), 163.32(C), 162.95(C) 149.21(C), 147.02(CH), 139.10(CH), 133.36(C), 133.22(CH), 132.34(2CH, 1C?), 130.21(C), 127.33(CH), 124.74(CH), 117.81(CH), 113.13(2CH), 110.51(CH), 55.33(OCH_3), 16.58(CH_3); one quaternary carbon is missing and may overlap with the CH signal at 132.34 ppm. MS Calcd for $C_{20}H_{18}NO_3$ ($M+H^+$): 320.13; Found: 320.11. Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.22; H, 5.37; N, 4.39. Found C, 75.23; H, 5.33; N, 4.48.



3fa

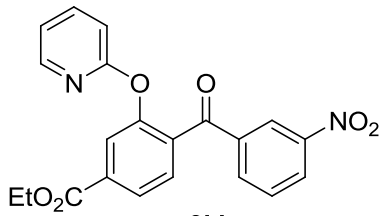
(4-methoxy-2-(pyridin-2-yloxy)phenyl)(phenyl)methanone[7] (**3fa**). Purified by column chromatography (hexanes-ethyl acetate: v/v = 4:1). Light yellow oil, 143 mg, 47% yield. IR (C=O): 1654.9cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 4.8 Hz, 1.6 Hz, 1H), 7.70-7.65 (m, 2H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.47 (ddd, *J* = 8.4 Hz, 6.8 Hz, 2.0 Hz, 1H), 7.42 (tt, *J* = 7.6 Hz, 1.2 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 2H), 6.86-6.81 (m, 2H), 6.78 (d, *J* = 2.4 Hz, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.39(C), 163.00(C), 162.75(C), 153.47(C), 146.81(CH), 139.16(CH) 138.23(C), 132.26(CH), 132.09(CH), 129.38(2CH), 127.71(2CH),

124.40(C), 118.30(CH), 111.25(CH), 110.39(CH), 108.15(CH), 55.46(OCH_3). MS Calcd for $C_{19}H_{16}NO_3$ ($M+H^+$): 306.11; Found: 306.12.



3ga

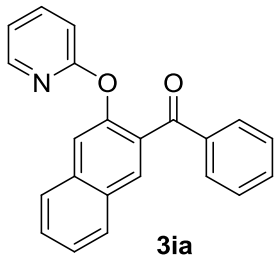
(4-bromo-2-(pyridin-2-yloxy)phenyl)(phenyl)methanone[5] (**3ga**). Purified by column chromatography (hexanes-ethyl acetate: v/v = 7:1). White solid, 297 mg, 84% yield. Melting point: 91-93 °C. IR (C=O): 1659.3 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (ddd, J = 4.8 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.74-7.70 (m, 2H), 7.52-7.41 (m, 5H), 7.31 (t, J = 8.0 Hz, 2H), 6.87 (ddd, J = 7.2 Hz, 4.8 Hz, 0.8 Hz, 1H), 6.57 (dt, J = 8.4 Hz, 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.13(C), 162.20(C), 152.05(C), 146.79(CH), 139.38(CH), 137.06(C), 132.83(CH), 131.2(CH), 130.92(C), 129.53(2CH), 127.96(2CH), 127.72(CH), 125.86(CH), 125.36(C), 118.84(CH), 111.40(CH). MS Calcd for $C_{18}H_{13}BrNO_2$ ($M+H^+$): 354.01; Found: 354.01.



3hj

ethyl 4-(3-nitrobenzoyl)-3-(pyridin-2-yloxy)benzoate (**3hj**). In this case, the reaction mixture was quenched with water at room temperature and neutralized with $NaHCO_3$. The crude product was purified by column chromatography (hexanes-ethyl acetate: v/v = 4:1). Light yellow oil, 124 mg, 32% yield. IR (C=O): 1714.1 cm^{-1}, 1678.8 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.54 (t, J = 1.8 Hz, 1H), 8.31 (ddd, J = 8.4 Hz, 2.2 Hz, 0.8 Hz, 1H), 8.09 (dt, J = 7.6 Hz, 1.2 Hz, 1H), 8.03 (dd, J

=8.0 Hz, 1.6 Hz, 1H), 7.99 (ddd, *J* = 4.8 Hz, 2.0 Hz, 0.8 Hz, 1H), 7.93 (d, *J* = 1.2 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 2H), 6.92 (ddd, *J* = 7.2 Hz, 4.8 Hz, 0.8 Hz, 1H), 6.61 (dt, *J* = 7.6 Hz, 0.8 Hz, 1H), 4.41 (quartet, *J* = 7.2 Hz, 2H), 1.41 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.45(C), 165.06(C), 162.07(C), 151.57(C), 147.95(C), 146.96(CH), 139.70(CH), 138.49(C), 134.94(CH), 134.79(C), 134.60(C), 130.01(CH), 129.31(CH), 127.12(CH), 125.90(CH), 124.31(CH), 124.06(CH), 119.16(CH), 111.33(CH), 61.58(CH_2), 14.23(CH_3). MS Calcd for $C_{21}H_{17}N_2O_6$ ($M+H^+$): 393.11; Found: 393.12. Anal. Calcd for $C_{21}H_{16}N_2O_6$: C, 64.28; H, 4.11; N, 7.14. Found C, 64.33; H, 4.19; N, 7.12.

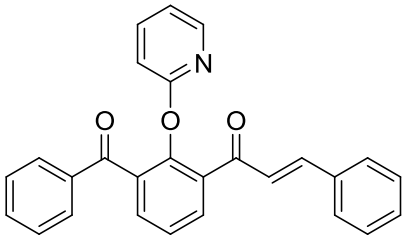


3ia

Phenyl(3-(pyridin-2-yloxy)naphthalen-2-yl)methanone[11] (**3ia**). Purified by column chromatography (hexanes to ethyl acetate: v/v = 6:1). Yellow viscous oil, 267 mg, 82% yield. IR (C=O): 1656.1 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (s, 1H), 7.94 (ddd, *J* = 5.0 Hz, 1.8 Hz, 0.4 Hz, 1H), 7.87-7.76 (m, 4H), 7.68 (s, 1H), 7.56-7.44 (m, 4H), 7.37-7.31 (m, 2H), 6.82 (ddd, *J* = 7.0 Hz, 5.2 Hz, 0.8 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.80(C), 163.09(C), 148.67(C), 146.81(CH), 139.24(CH), 137.48(C), 135.12(C), 132.69(CH), 132.00(C), 131.08(CH), 130.03(C), 129.90(2CH), 128.53(CH), 127.94(2CH), 127.88(CH), 127.25(CH), 125.96(CH), 119.36(CH), 118.37(CH), 111.37(CH). MS Calcd for $C_{22}H_{16}NO_2$ ($M+H^+$): 326.12; Found: 326.10.

Pt-catalyzed acylation reaction of 3aa.

Synthesis of **4aa**. Under argon flushing, a 25 mL round-bottom flask equipped with a magnetic stirring bar and a condenser was dried with a heat-gun. A drying tube was placed on the top of the condenser. To the flask were placed phenyl(2-(pyridin-2-yloxy)phenyl)methanone (**3aa**) (143 mg, 0.5 mmol), $(PhCN)_2PtCl_2$ (24 mg, 0.05 mmol), benzoyl chloride (0.35 g, 2.5 mmol), and anhydrous chlorobenzene (2 mL). The mixture was stirred under reflux for 48 h, and TLC showed that a small amount of starting material still remained. The temperature was lowered to 100 ^oC and 1.5 mL of 6 M NaOH was added. The mixture was stirred for 30 min and cooled to room temperature. Water (20 mL) was added, and the mixture was extracted with dichloromethane (3 × 15 mL). The combined organic layers was dried over anhydrous Na_2SO_4. After filtration and removal of the solvents, the crude product was purified by column chromatography with hexanes-ethyl acetate (v/v = 5:1) as the eluting solvent. The fractions containing the product were combined and evaporated to yield **4aa** as an off-white solid, 125 mg, 65% yield.



5

Synthesis of (E)-1-(3-benzoyl-2-(pyridin-2-yloxy)phenyl)-3-phenylprop-2-en-1-one (**5**). Under argon flushing, a 25 mL round-bottom flask equipped with a magnetic stirring bar and a condenser was dried with a heat-gun. A drying tube was placed on the top of the condenser. To the flask were placed phenyl(2-(pyridin-2-yloxy)phenyl)methanone (**3aa**) (142 mg, 0.5 mmol), $(PhCN)_2PtCl_2$ (24 mg, 0.05 mmol), cinnamoyl chloride (250 mg, 1.5 mmol), and anhydrous chlorobenzene (2 mL). The mixture was stirred under reflux for 3 h, and TLC showed that the reaction was complete. The temperature was lowered to 100 ^oC and 2 mL of 6 M NaOH was added. The mixture was

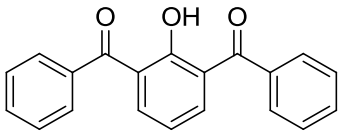
stirred for 30 min and cooled to room temperature. Water (20 mL) was added, and the mixture was extracted with dichloromethane (3 × 15 mL). The combined organic layers was dried over anhydrous Na_2SO_4. After filtration and removal of the solvents, the crude product was purified by column chromatography with hexanes-ethyl acetate (v/v = 4:1) as the eluting solvent. The fractions containing the product were combined and evaporated to yield **5** as an off-white solid, 156 mg, 75% yield. Melting point: 104-106°C. IR (C=O): 1668.2, 1628.2 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.90-7.84 (m, 2H), 7.73-7.70 (m, 2H), 7.68 (dd, *J* = 7.6 Hz, 1.6 Hz, 1H), 7.50 (d, *J* = 16.0 Hz, 1H), 7.48-7.41 (m, 2H), 7.37-7.25 (m, 8H), 7.10 (d, *J* = 16.0 Hz, 1H), 6.76 (ddd, *J* = 7.2 Hz, 5.0 Hz, 1.2 Hz, 1H), 6.47 (dt, *J* = 8.4 Hz, 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.58(C), 191.95(C), 162.40(C), 148.89(C), 146.46(CH), 144.68(CH), 139.30(CH), 136.95(CH), 134.48(C), 134.41(C), 133.64(C), 132.91(CH), 132.70(CH), 132.24(CH), 130.38(CH), 129.67(2CH), 128.70(2CH), 128.17(2CH), 127.96(2CH), 125.74(CH), 125.05(CH), 118.50(CH), 110.97(CH). MS Calcd for $C_{27}H_{20}NO_3$ ($M+H^+$): 406.14; Found: 406.15. Anal. Calcd for $C_{27}H_{19}NO_3$: C, 79.98; H, 4.72; N, 3.45. Found C, 79.67; H, 4.87; N, 3.38.

Competing acylation of 1e with 2j and 2k.

Under argon flushing, a 25 mL round-bottom flask equipped with a magnetic stirring bar and a condenser was dried with a heat-gun. A drying tube was placed on the top of the condenser. To the flask were placed 2-(2-methylphenoxy)pyridine (**1e**) (186 mg, 1 mmol), $(PhCN)_2PtCl_2$ (47 mg, 0.1 mmol), 3-nitrobenzoyl chloride (**2j**) (370 mg, 2 mmol), 4-methoxybenzoyl chloride (**2k**) (340 mg, 2 mmol) and anhydrous chlorobenzene (3 mL). The mixture was stirred under reflux for 3 h. The temperature was lowered to 100 °C and 3 mL of 6 M NaOH was added. The mixture was stirred for 30 min and cooled to room temperature. Water (20 mL) was added, and the mixture was extracted with dichloromethane (3 × 15 mL). The combined organic layers was dried over

anhydrous Na_2SO_4. After filtration and removal of the solvents, the crude mixture was examined by ^1H NMR, which showed that the ratio of products **3ej** and **3ek** was 9:1 and the ratio of the products (**3ej** + **3ek**) and the starting material (**1e**) is 2.2:1. After column chromatography with hexanes-ethyl acetate-dichloromethane (v/v = 2:1:) as the eluting solvent, the fractions containing the product were combined and evaporated to yield an off-white solid, 185 mg. The ^1H NMR spectrum of the isolated product showed the ratio of **3ej** and **3ek** to be 9:1, which suggests a combined yield of 56%.

Removal of the directing pyridyl group



6

Synthesis of (2-hydroxy-1,3-phenylene)bis(phenylmethanone) (**6**). **General procedure** (modified from the literature procedures[6,7]): To a solution of (2-(pyridin-2-yloxy)-1,3-phenylene)bis(phenylmethanone) (**4aa**, 379 mg, 1.0 mmol) in anhydrous toluene (40 mL) was added MeOTf (0.2 mL, 1.76 mmol). The mixture was stirred under argon at 100 ^oC for 2 h, and then cooled to room temperature. The solvent was removed by rotary evaporation. The residue was dissolved in methanol (10 mL) and combined with a solution prepared from Na (601 mg, 26 mmol) and methanol (30 mL). The mixture was refluxed for 30 min. After cooling to room temperature, the reaction mixture was neutralized by treating with 3 M HCl (9 mL). Most of methanol was removed by rotary evaporation, and the product was extracted by ethyl acetate (3 × 20 mL). The combined organic solution was washed with brine and dried over anhydrous Na_2SO_4. After filtration and removal of the solvents, the residue was purified by column chromatography

(silica gel, dichloromethane) and recrystallization from hexane-dichloromethane to give **6** as light yellow needles, 259 mg, 86% yield. Melting point: 125-127 °C. IR (C=O): 1646.0 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 12.40 (s, 1H), 7.81-7.77 (m, 4H), 7.73 (d, J = 8.0 Hz, 2H), 7.61 (tt, J = 7.2, 1.2 Hz, 2H), 7.52-7.46 (m, 4 H), 7.00 (t, J = 7.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.29 (2C), 160.91 (C), 137.35 (2C), 136.28 (2CH), 132.76 (2CH), 129.46 (4CH), 128.39 (4CH), 124.33 (2 C), 118.33 (CH). MS Calcd for $C_{20}H_{13}O_3$ ($M-H^+$) 301.09; Found: 301.37. Anal. Calcd for $C_{20}H_{14}O_3$: C, 79.46; H, 4.67. Found C, 79.22; H, 4.80.

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Figure 1. ^{1}H and ^{13}C NMR spectra of **1g.**

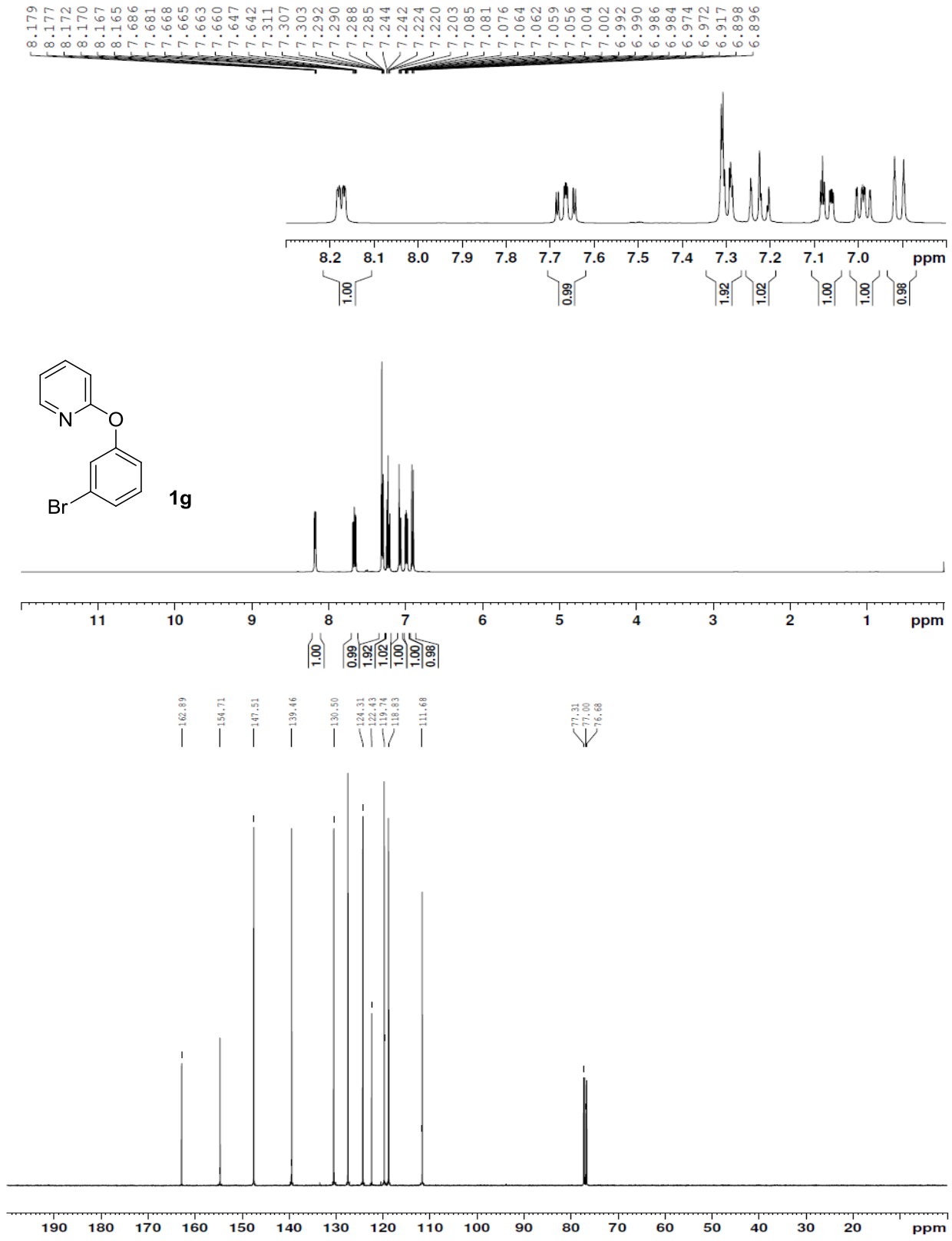

Figure 2. ^{1}H and ^{13}C NMR spectra of **1h.**

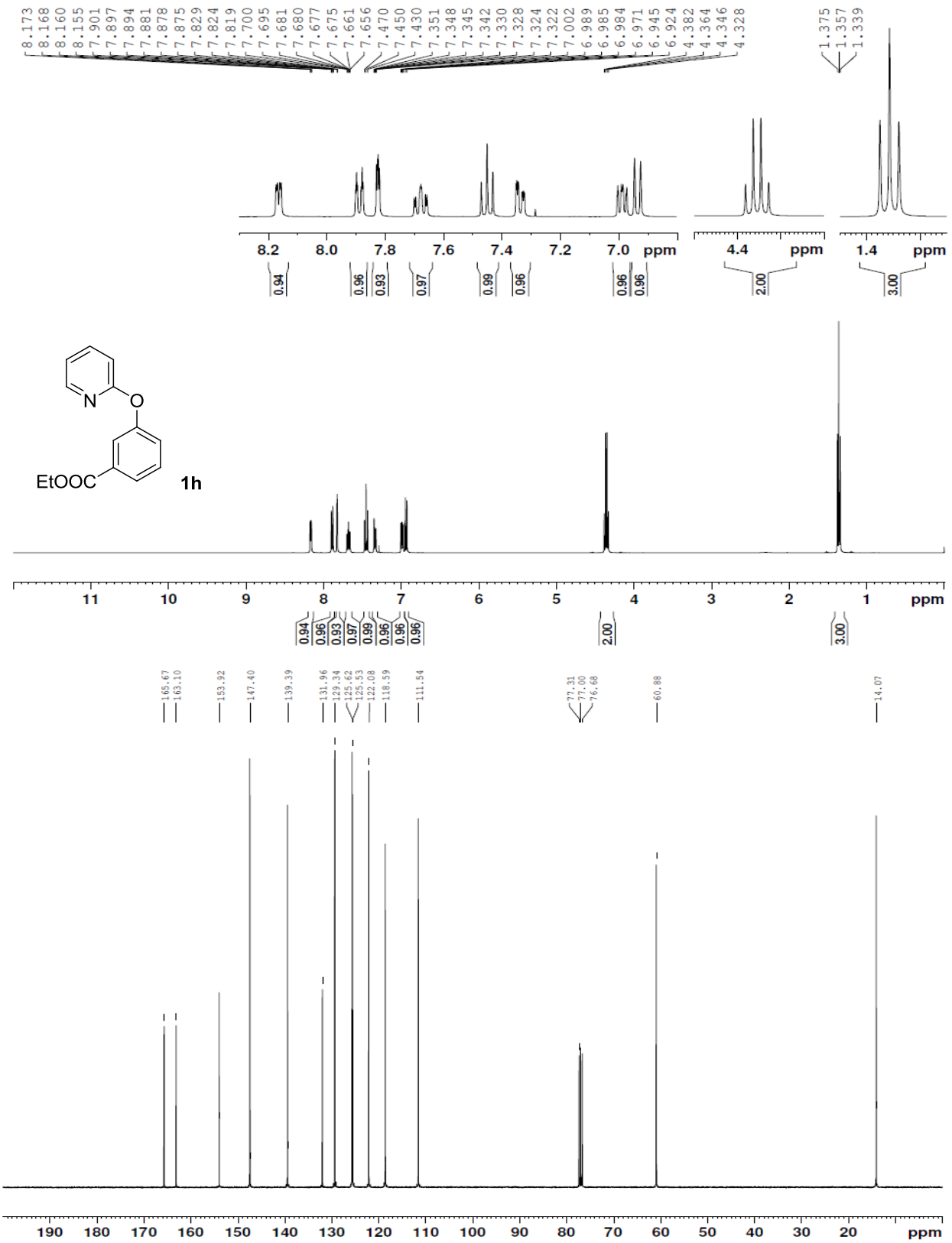

Figure 3. ^{1}H and ^{13}C NMR spectra of **1i.**

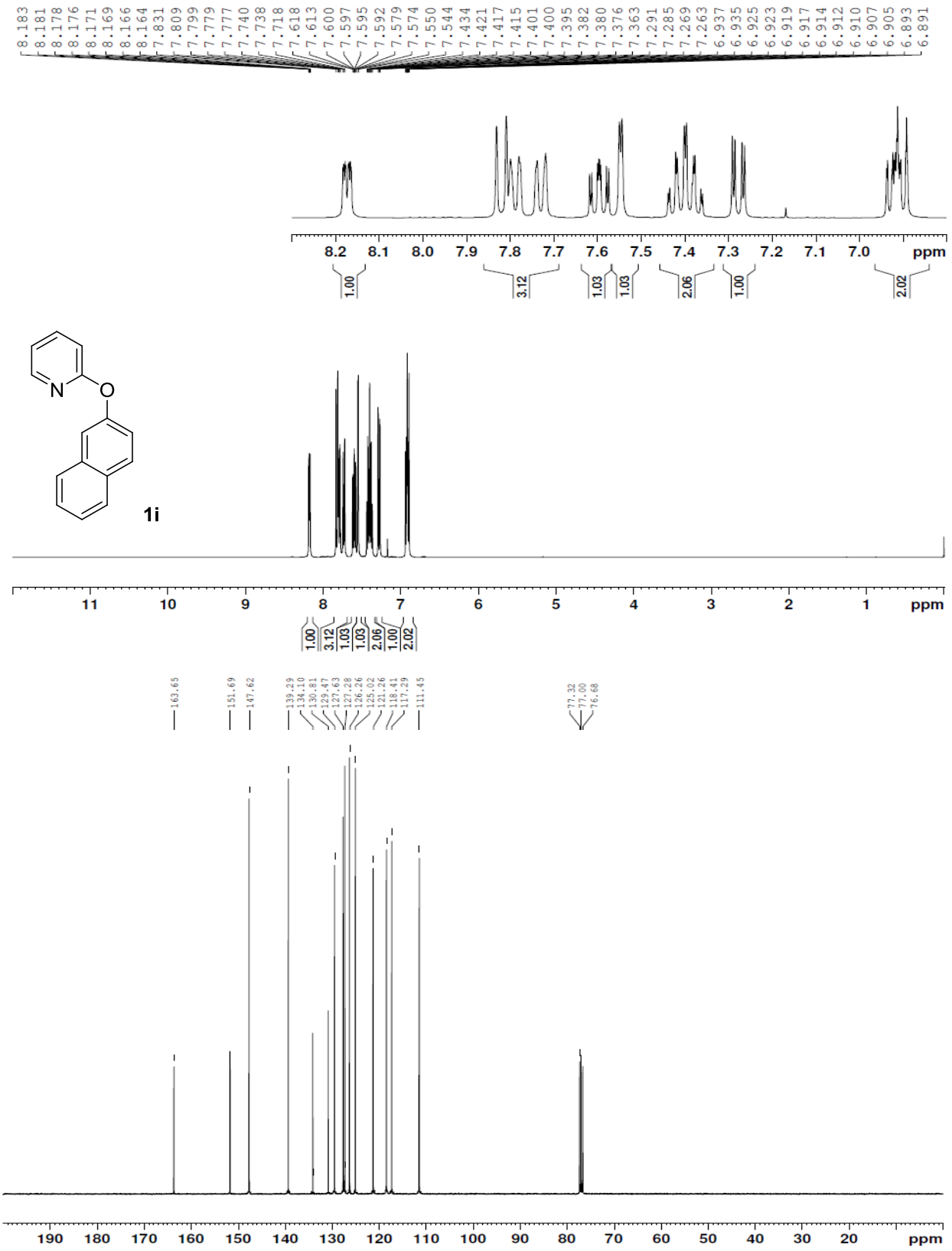

Figure 4. ^{1}H and ^{13}C NMR spectra of **4aa.**

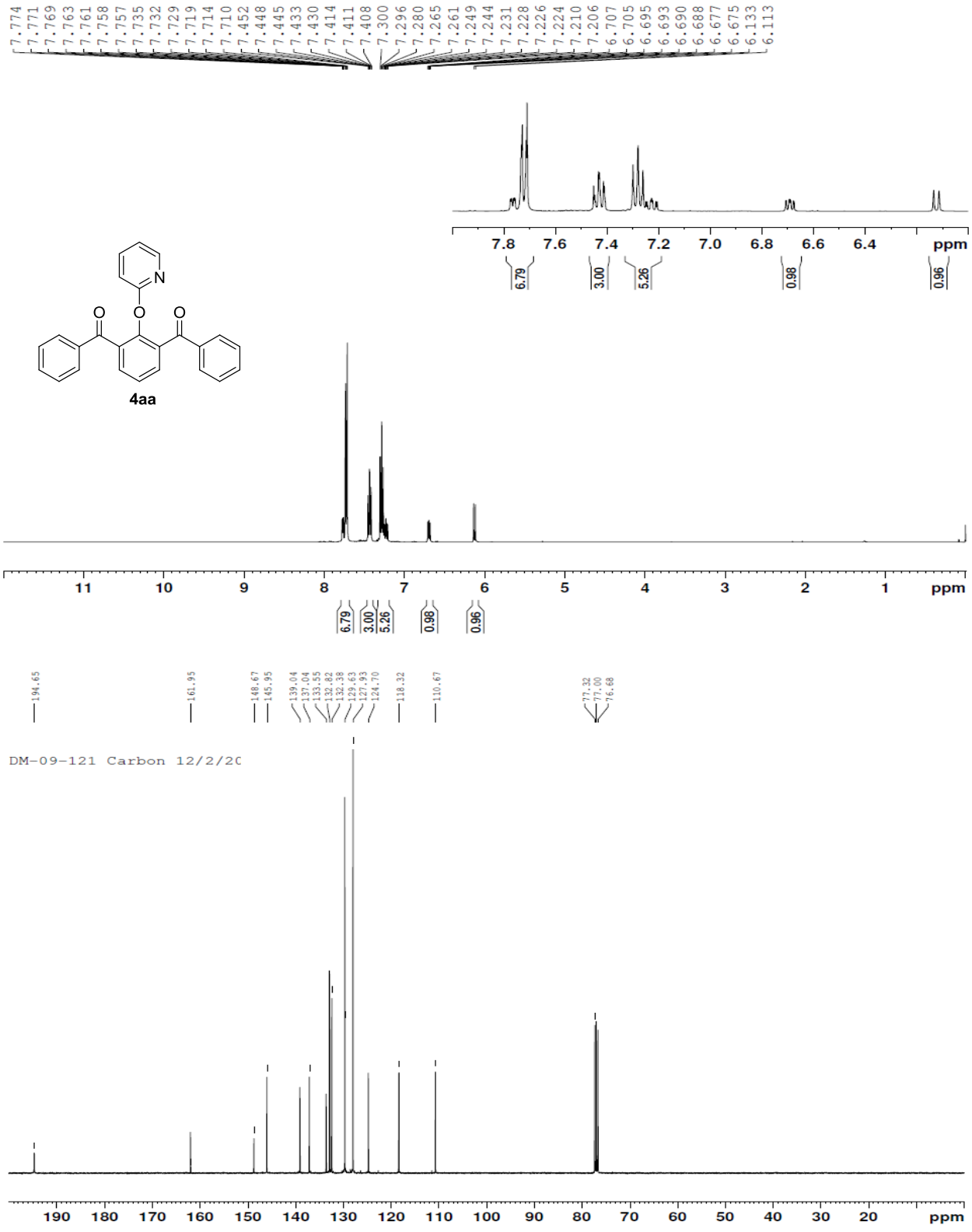

Figure 5. ^{1}H and ^{13}C NMR spectra of **4ab**

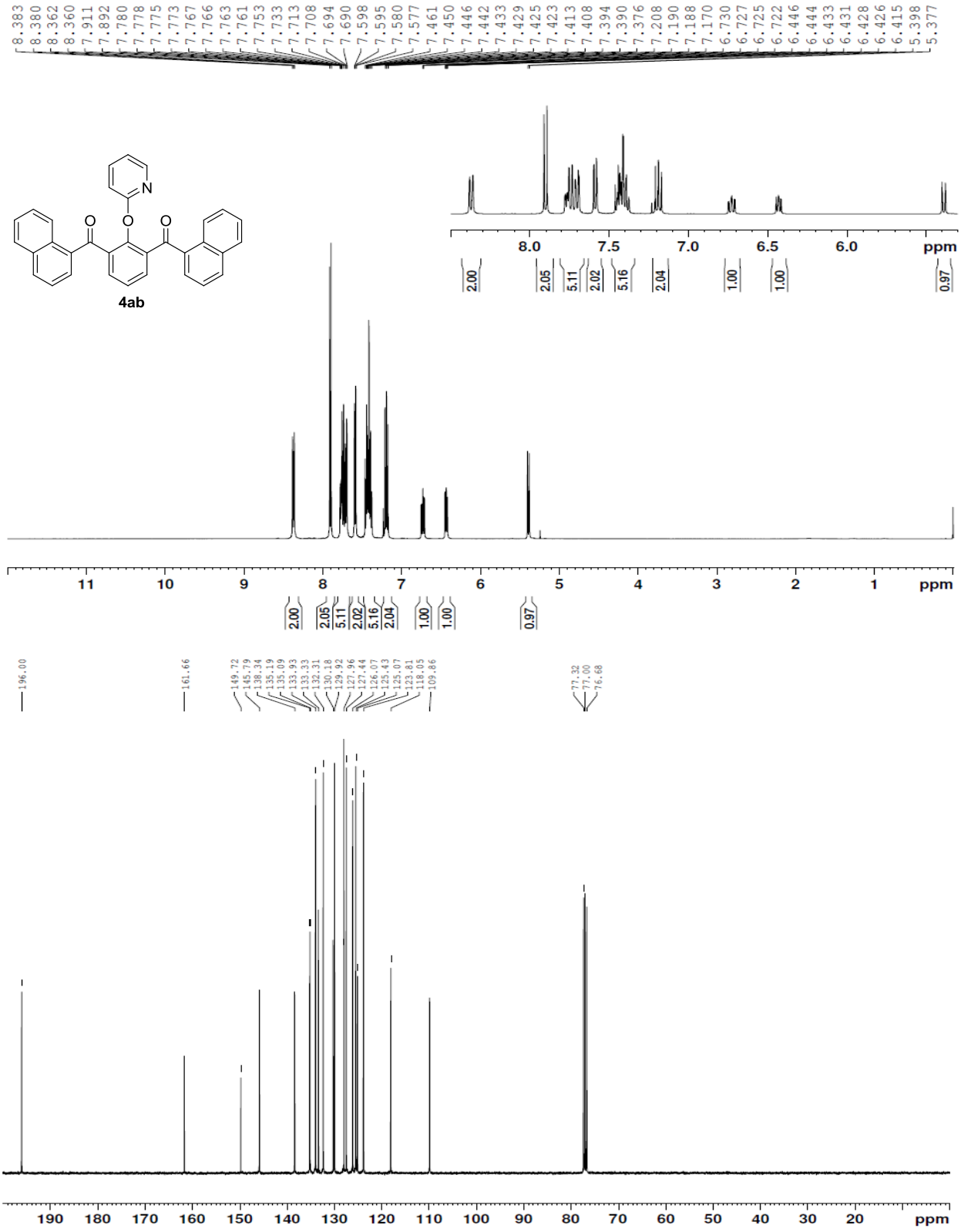

Figure 6. ^{1}H and ^{13}C NMR spectra of **4ac**

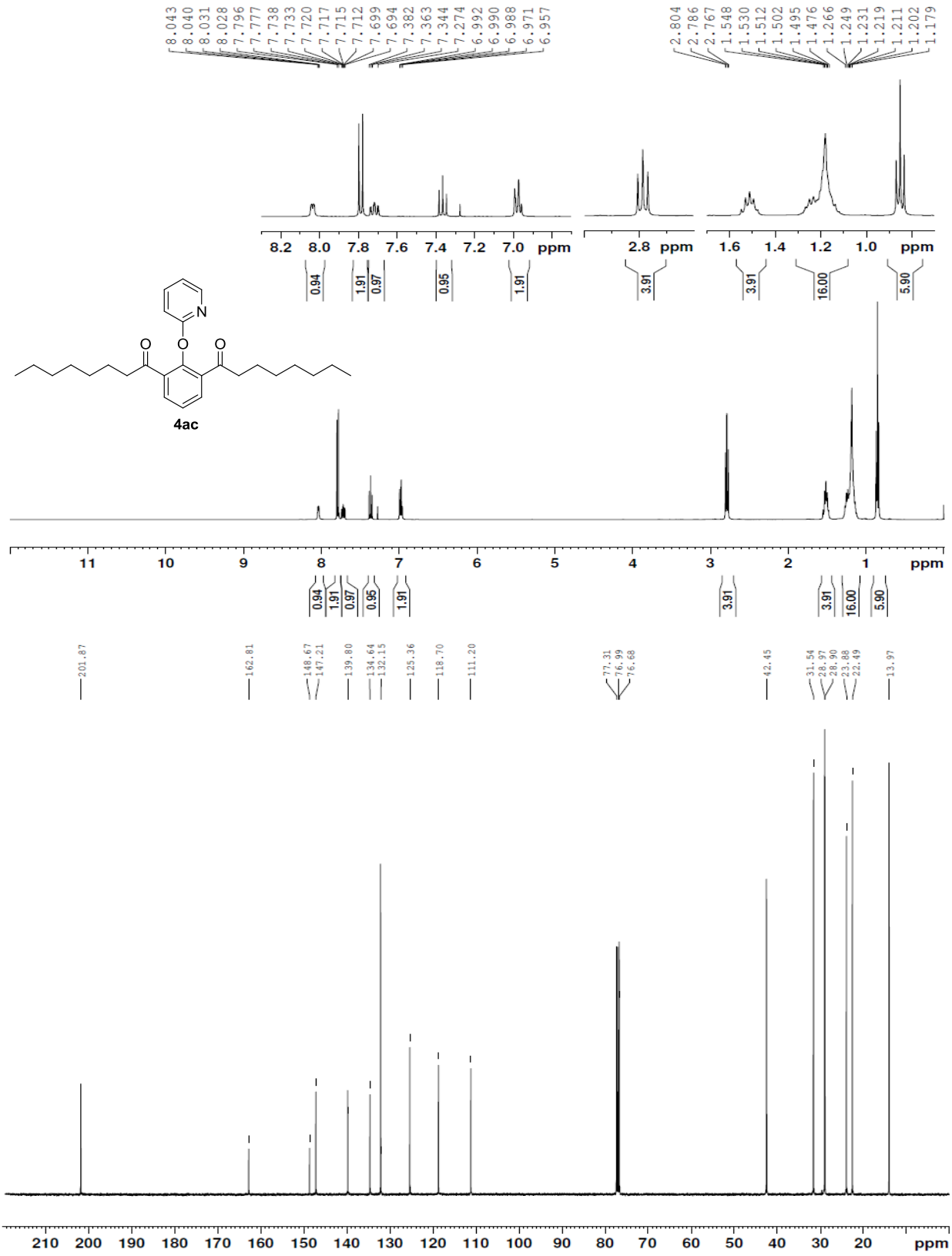

Figure 7. ^{1}H and ^{13}C NMR spectra of **4ad**

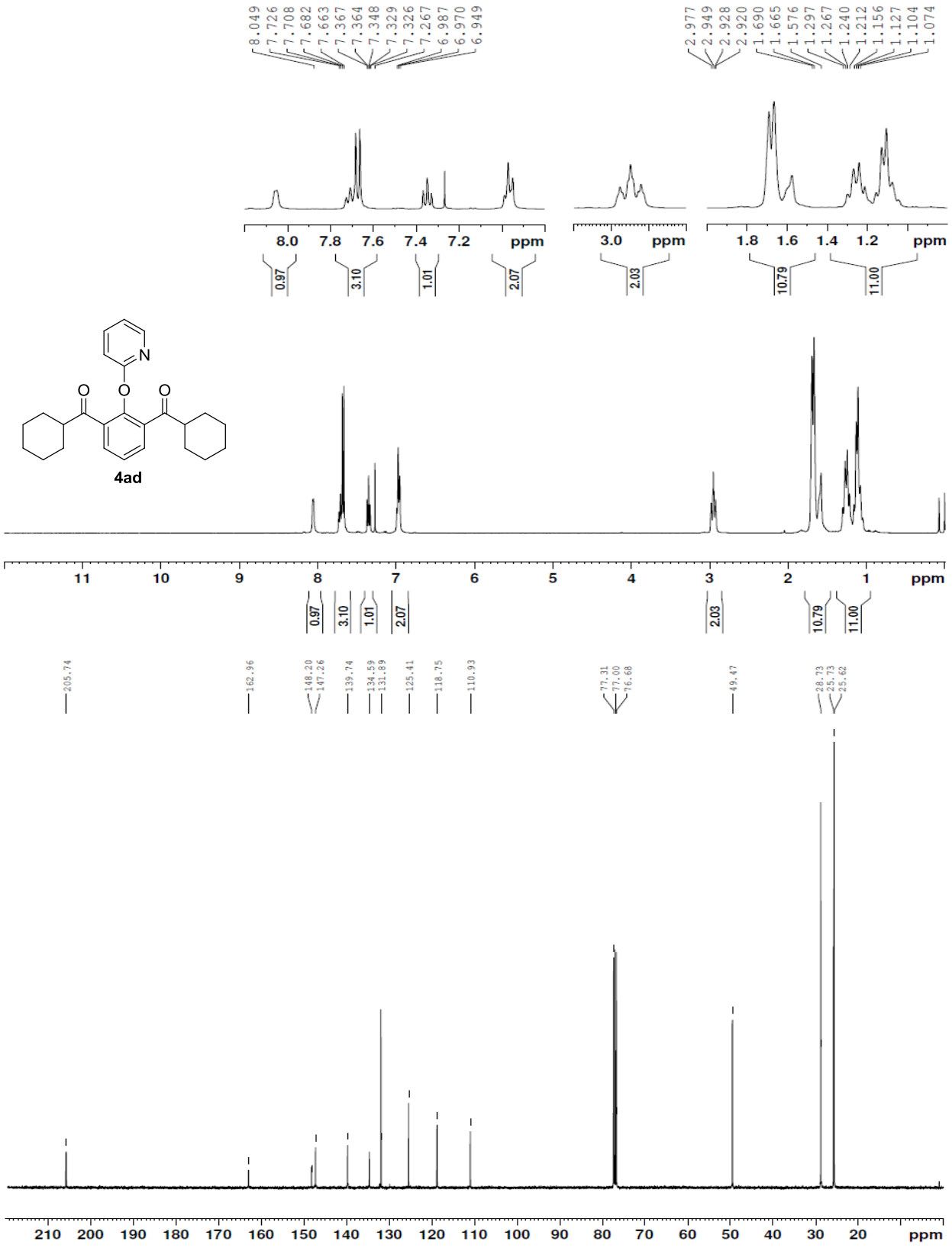

Figure 8. ^{1}H and ^{13}C NMR spectra of **4ae**

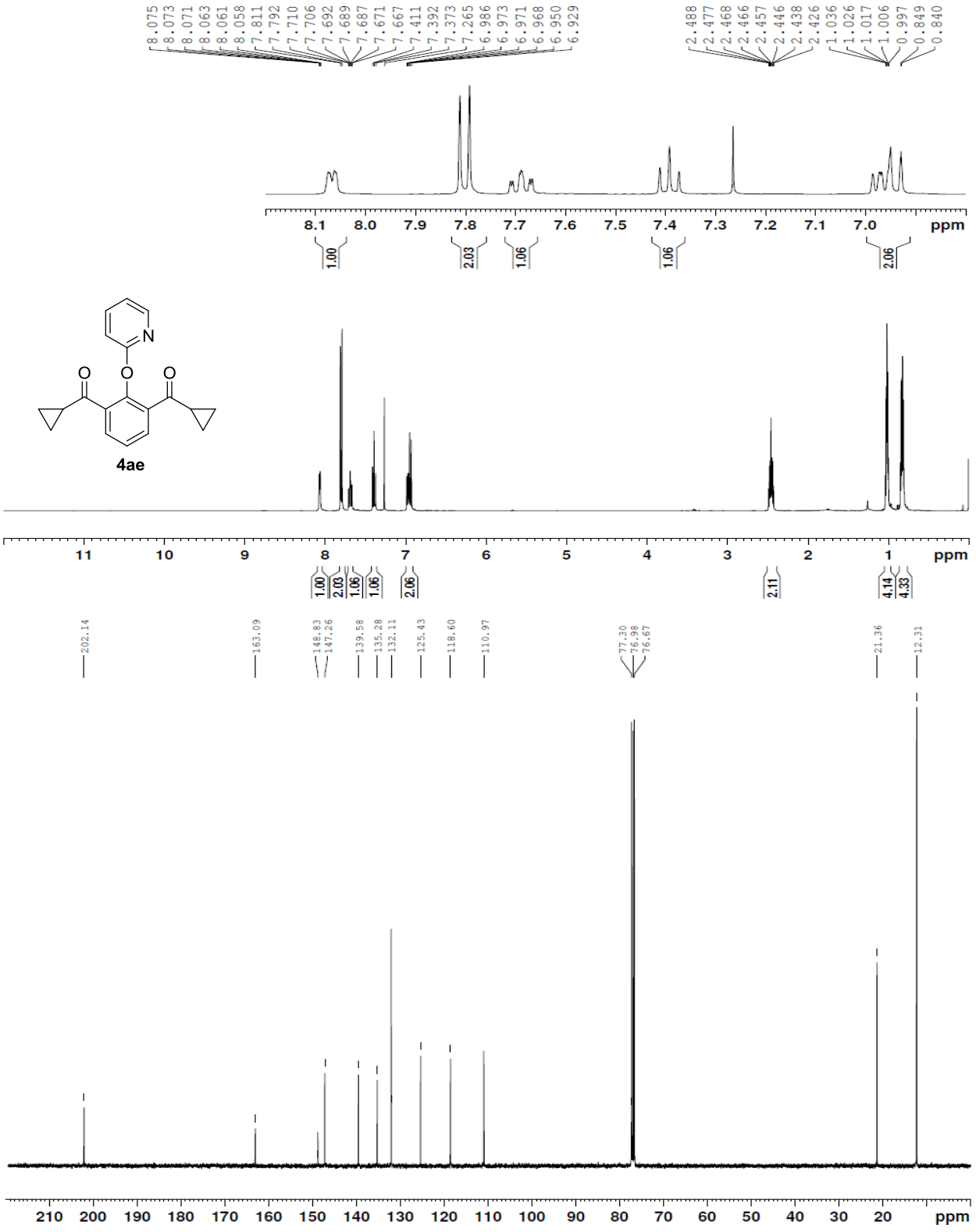

Figure 9. ^{1}H and ^{13}C NMR spectra of **4ba**

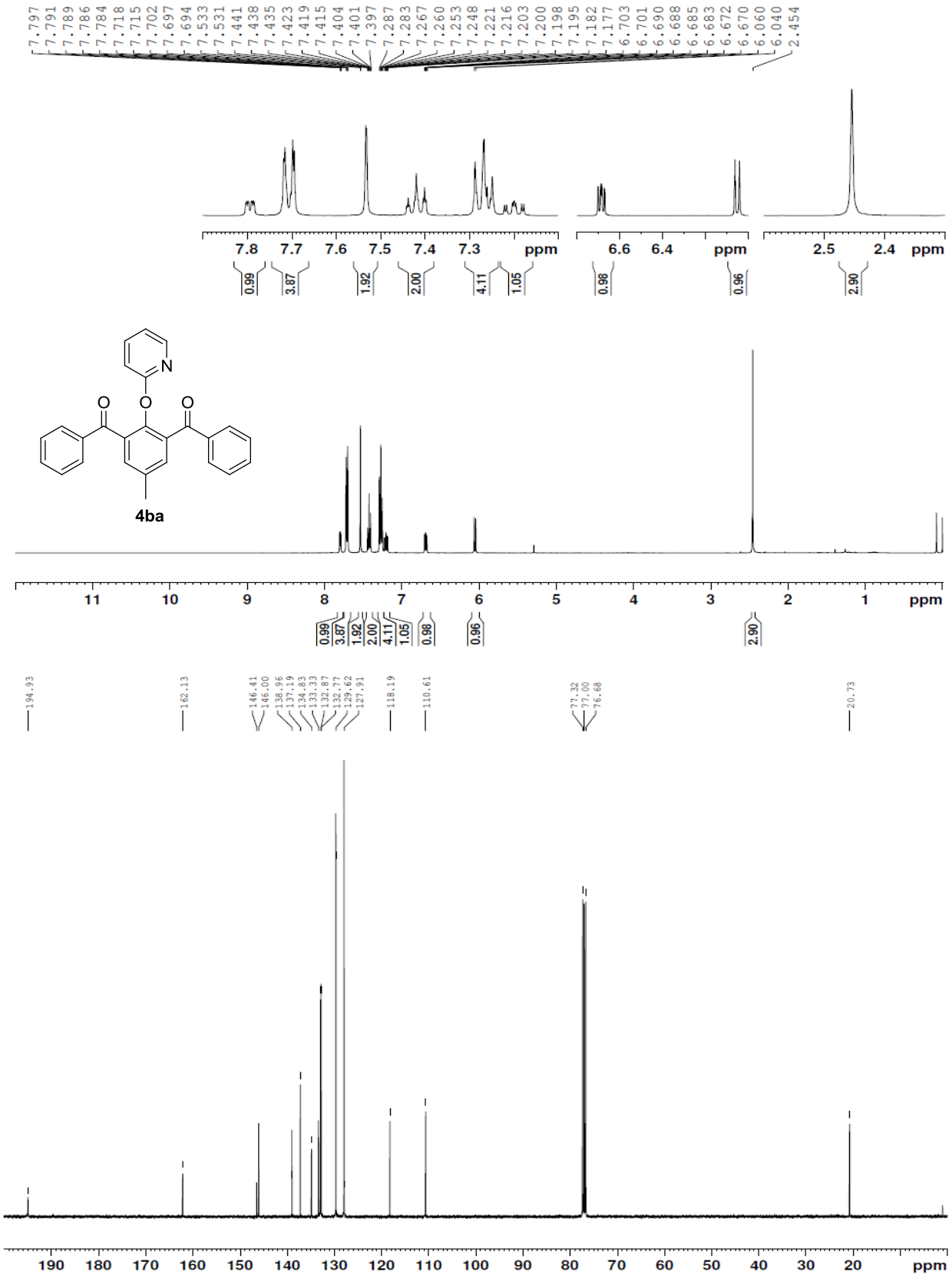

Figure 10. ^{1}H and ^{13}C NMR spectra of **4bf**

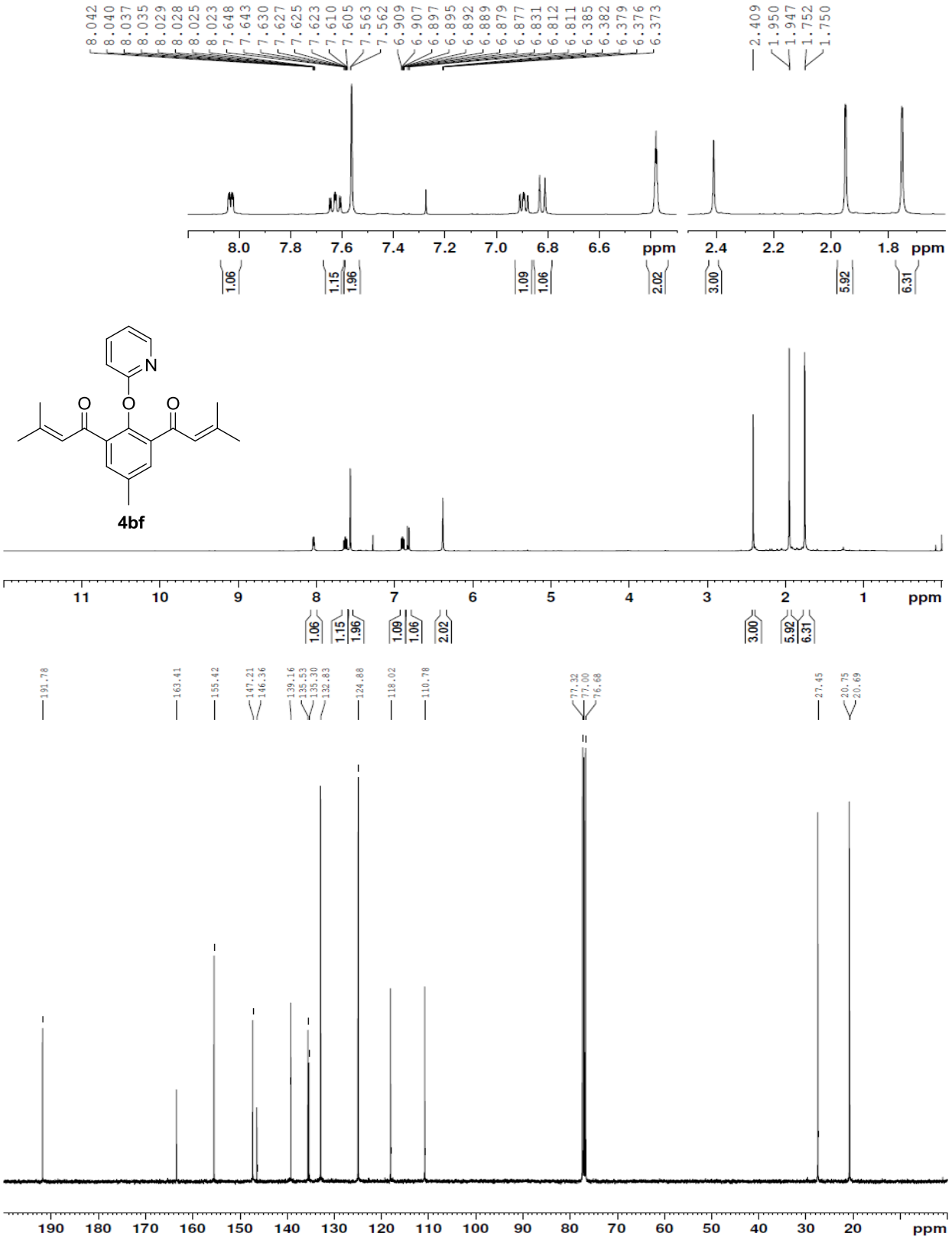

Figure 11. ^{1}H and ^{13}C NMR spectra of **4bg**

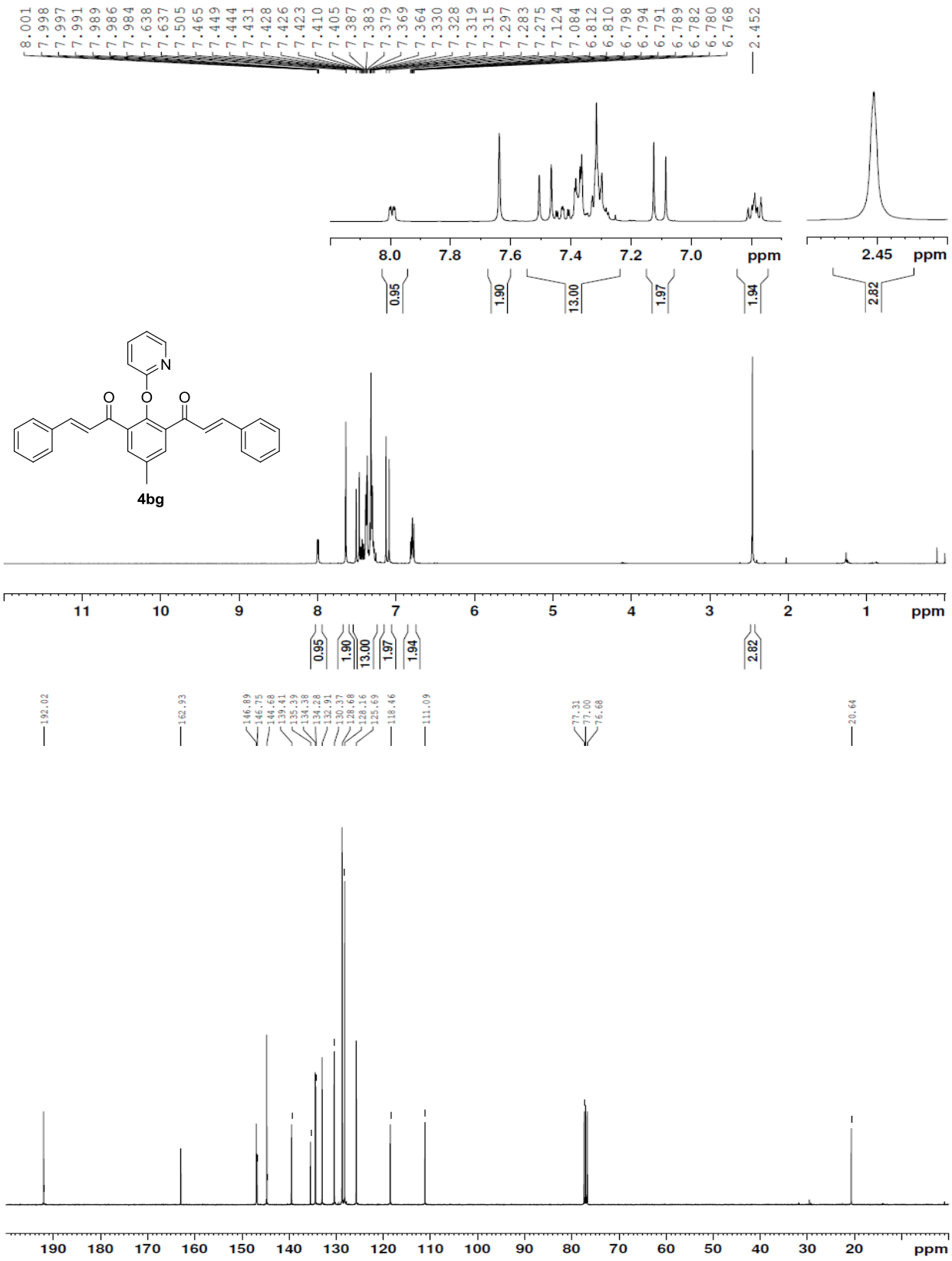

Figure 12. ^{1}H and ^{13}C NMR spectra of **4bh**

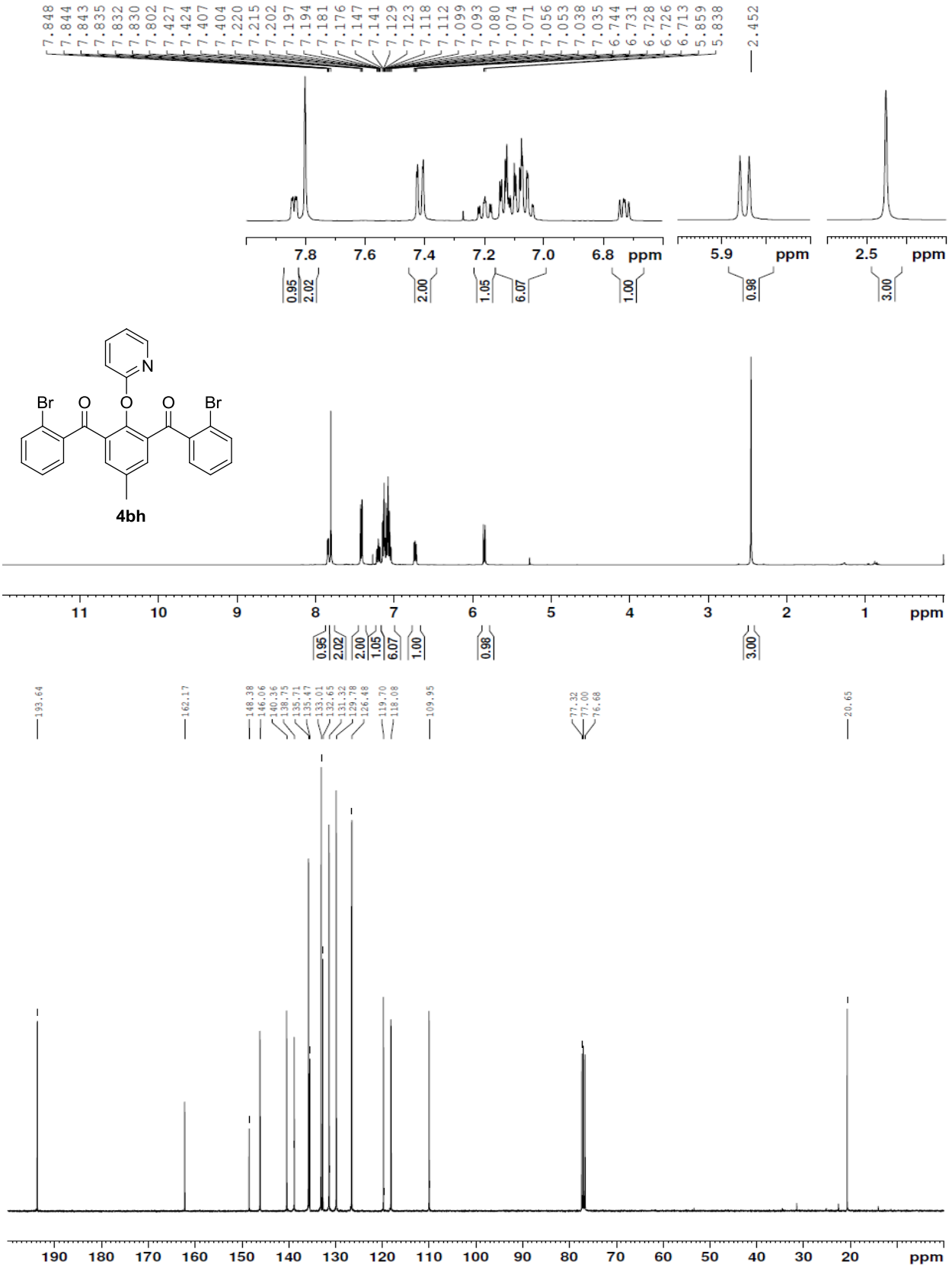

Figure 13. ^{1}H and ^{13}C NMR spectra of **4bi**

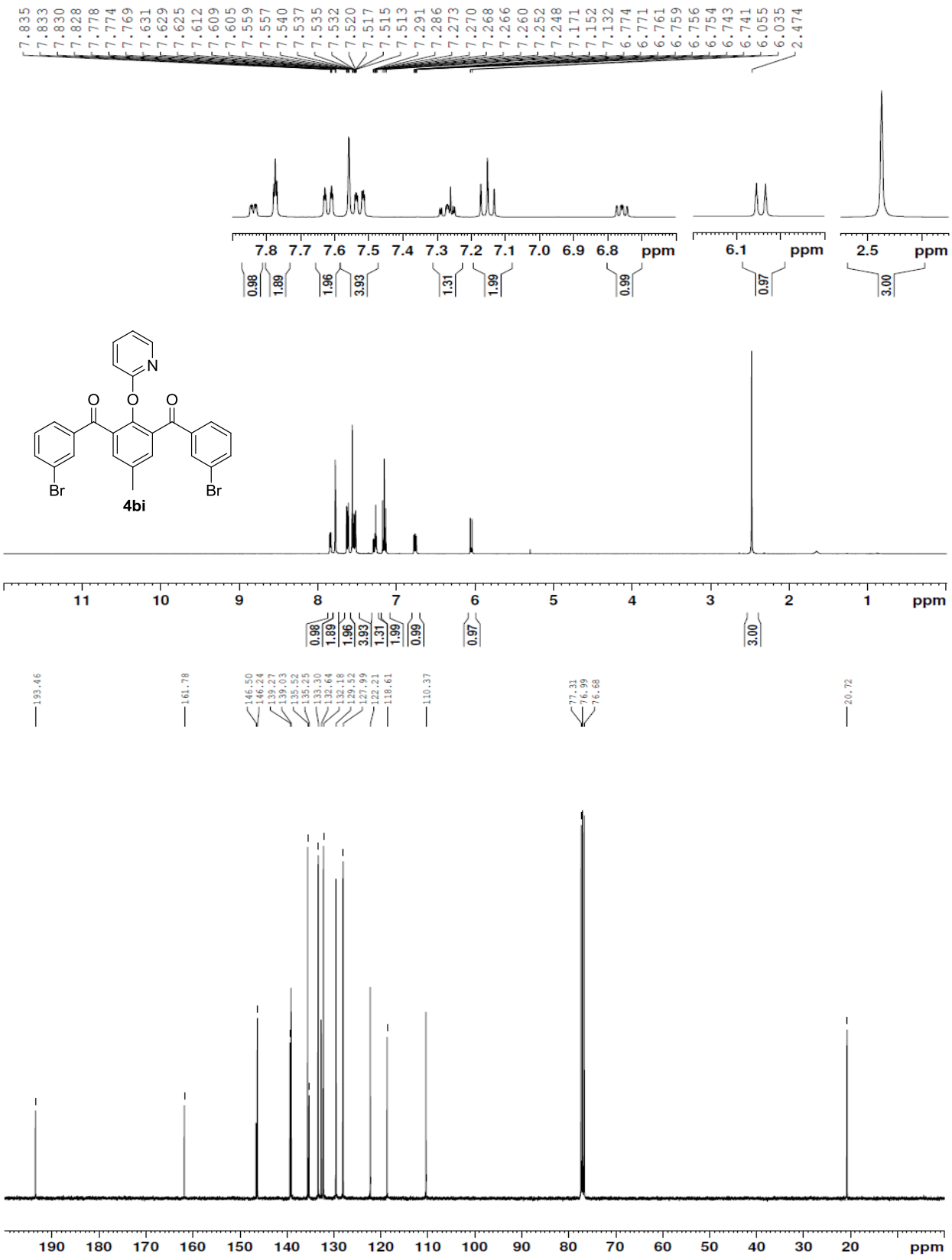

Figure 14. ^{1}H and ^{13}C NMR spectra of **4bj**

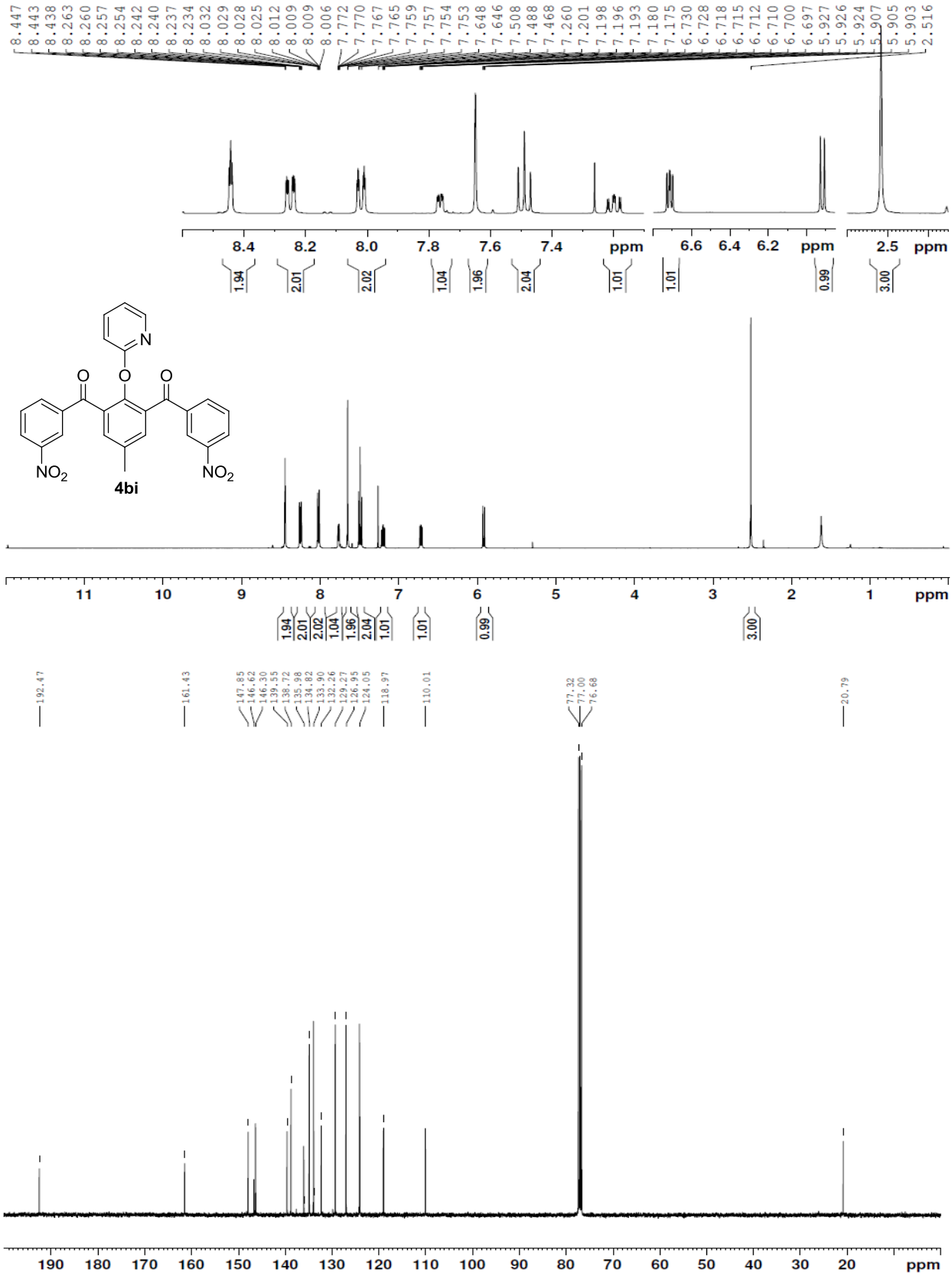

Figure 15. ^{1}H and ^{13}C NMR spectra of **4bk**

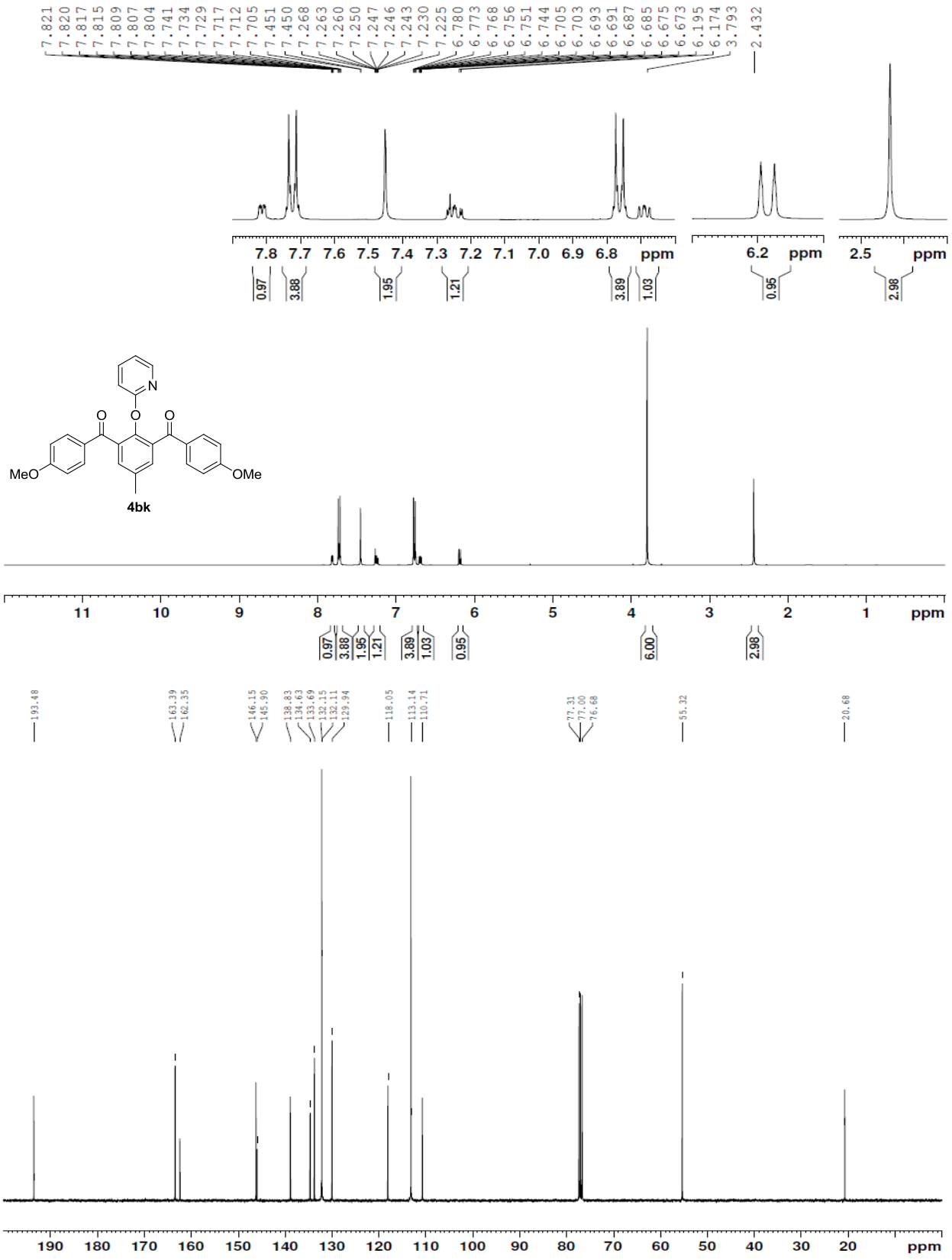

Figure 16. ^{1}H and ^{13}C NMR spectra of **4bl**

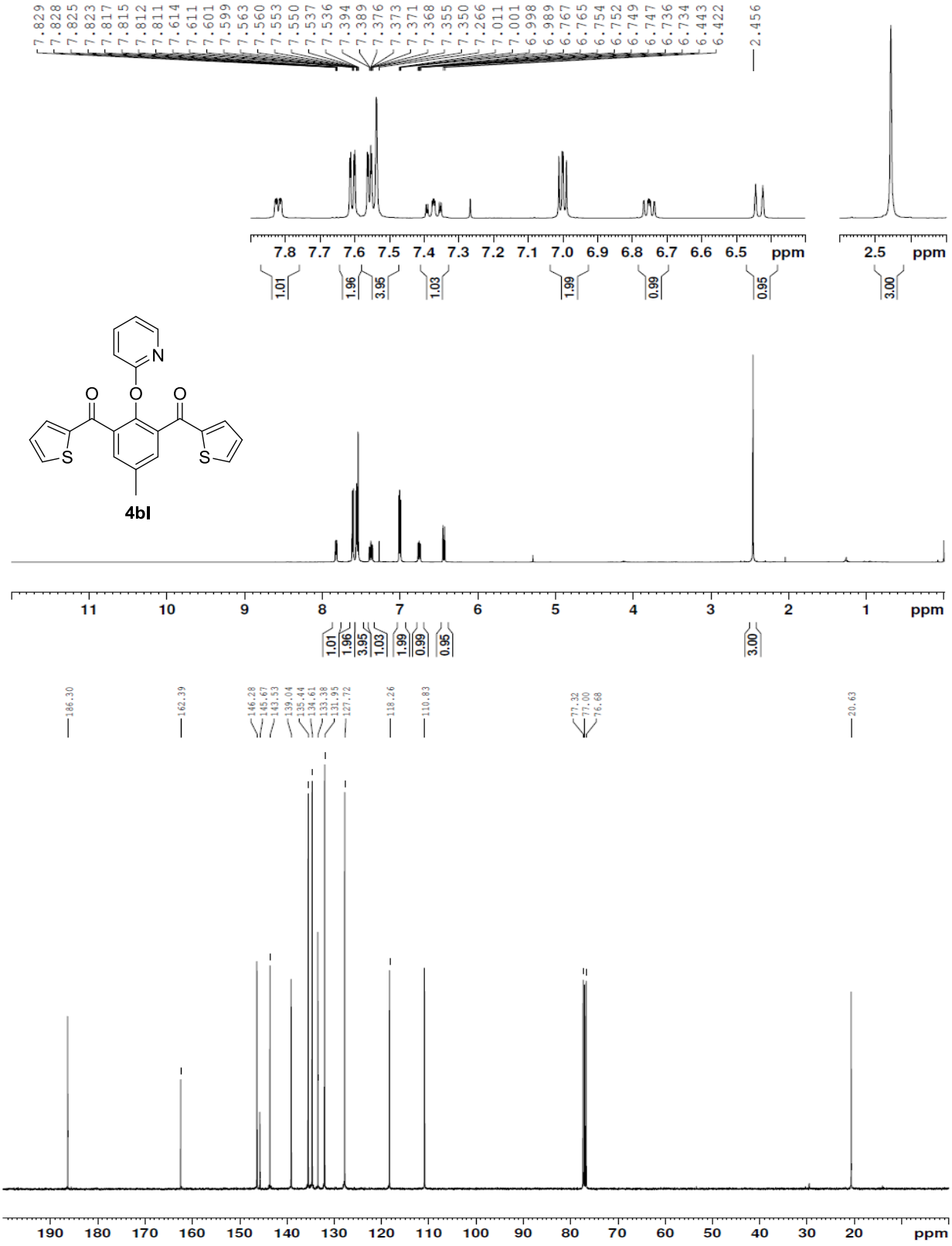

Figure 17. ^{1}H and ^{13}C NMR spectra of **4bm**.

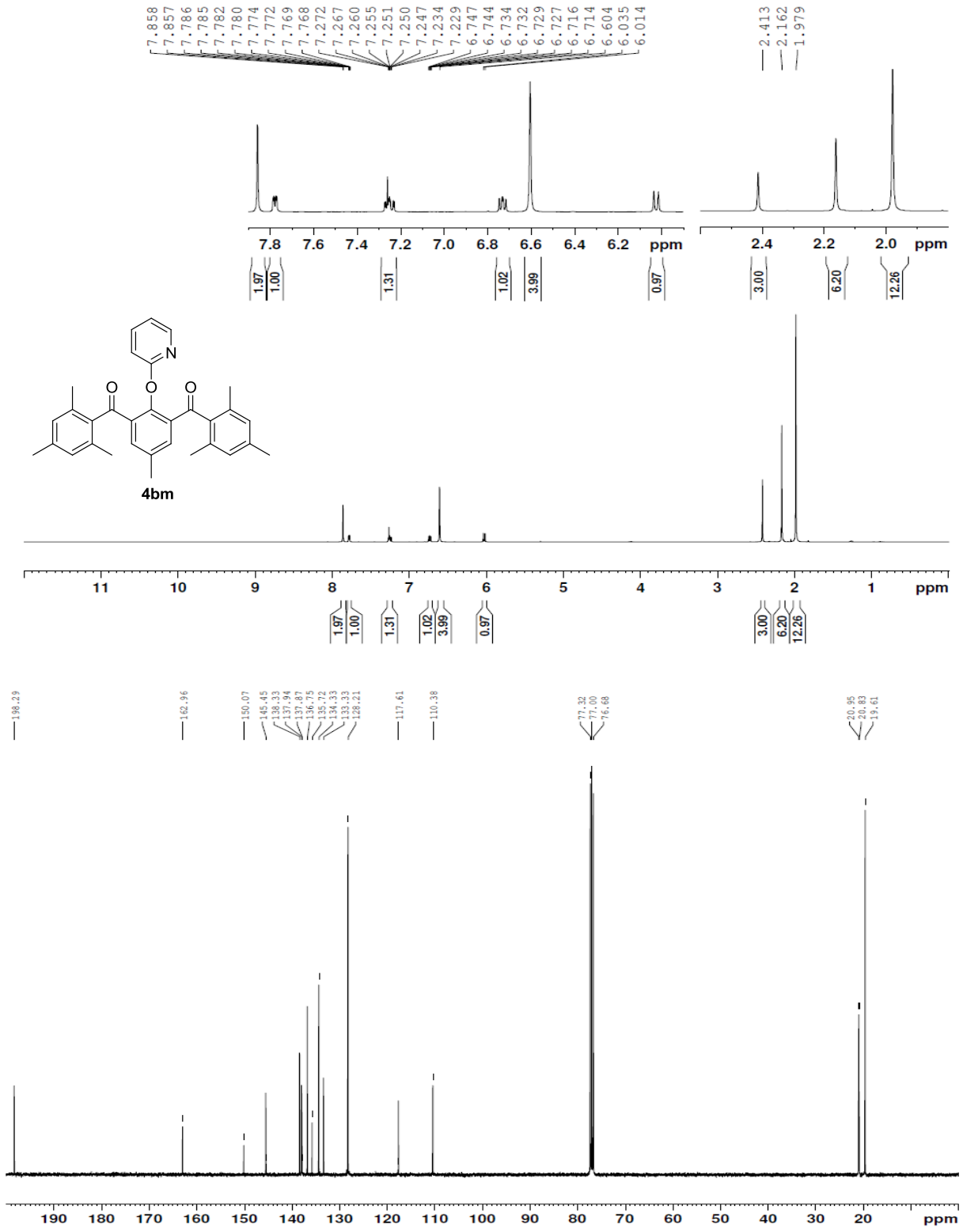

Figure 18. ^{1}H and ^{13}C NMR spectra of **4ca**.

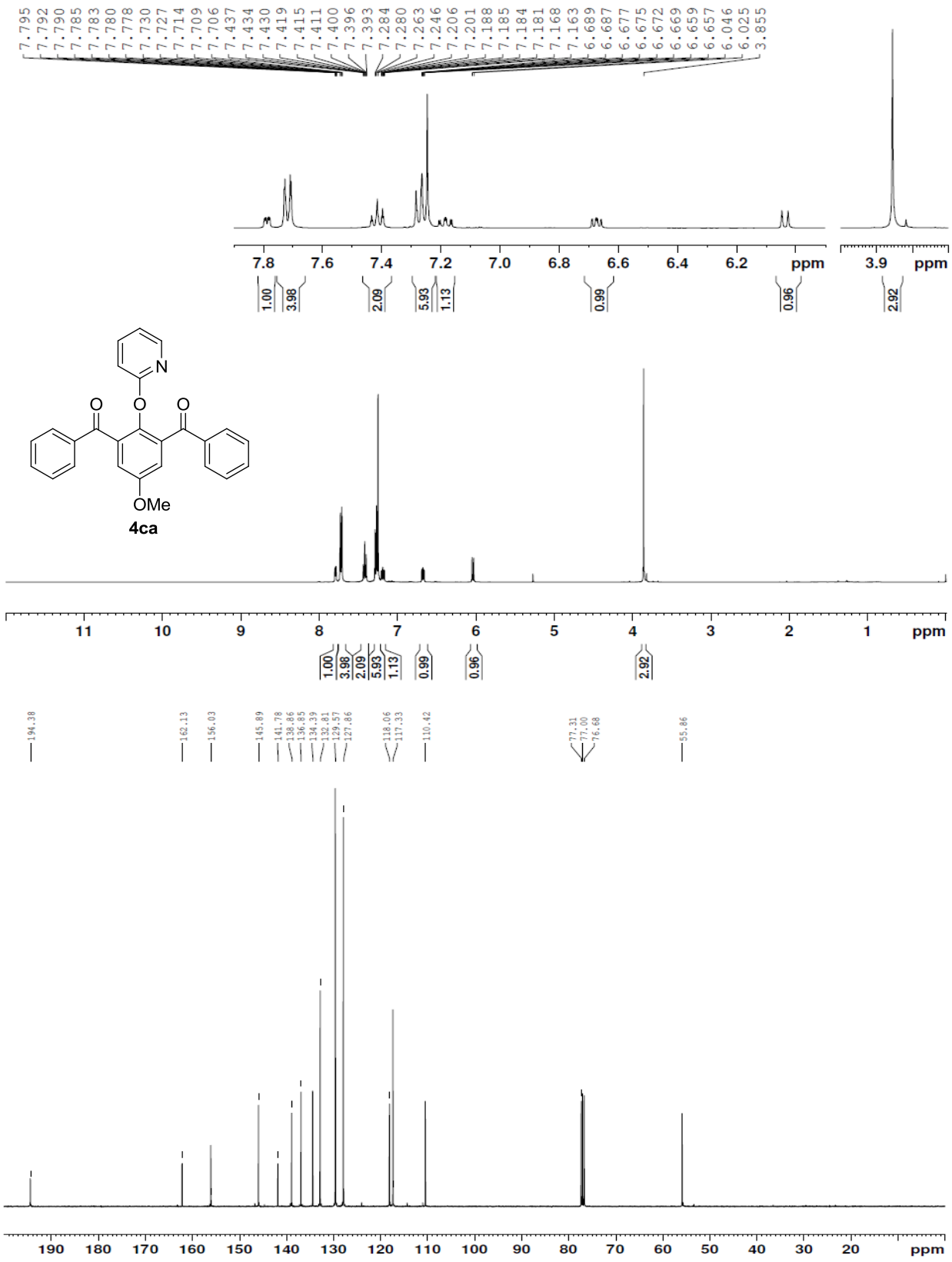

Figure 19. ^{1}H and ^{13}C NMR spectra of **4dg**

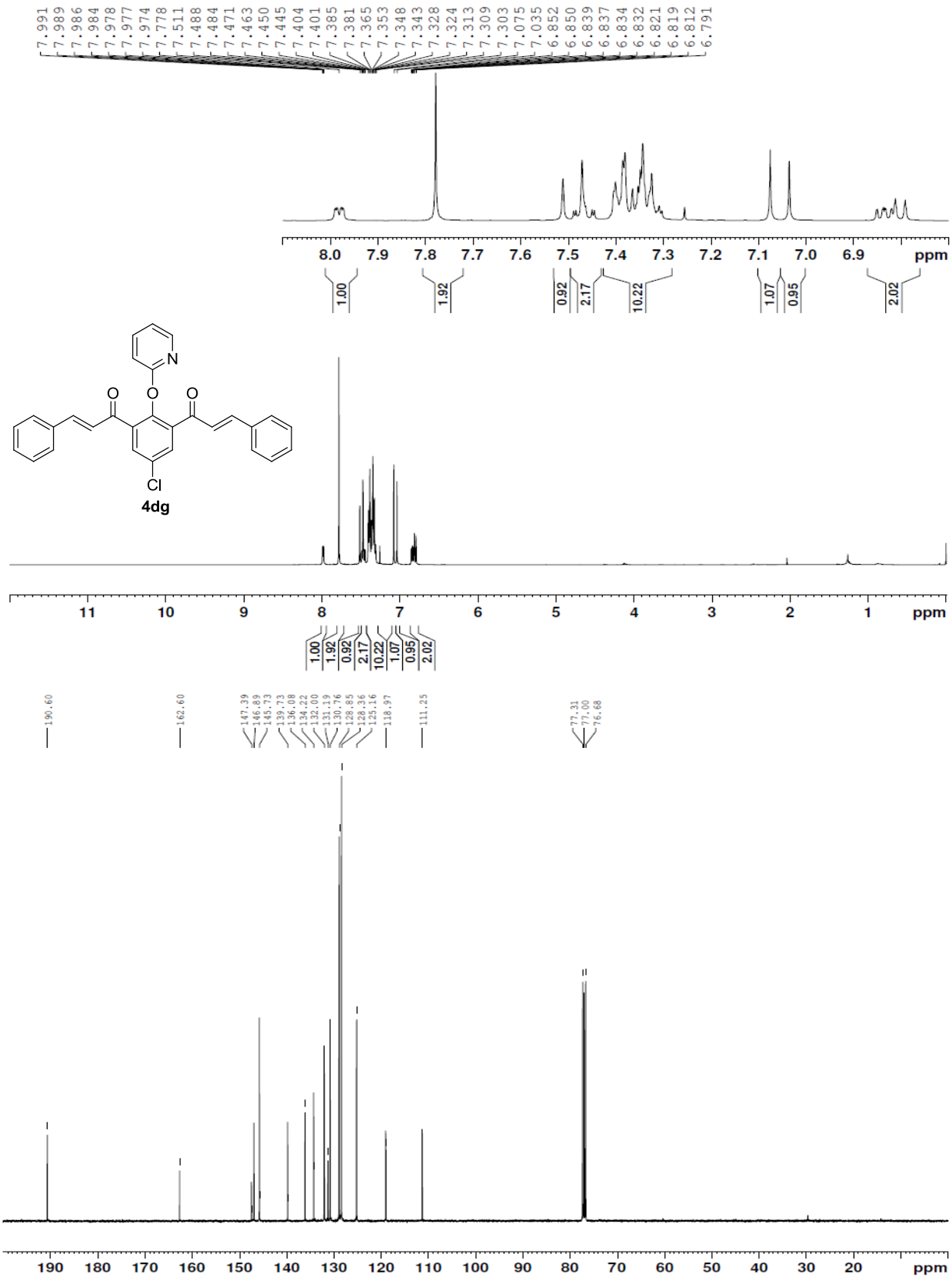

Figure 20. ^{1}H and ^{13}C NMR spectra of **3ea**

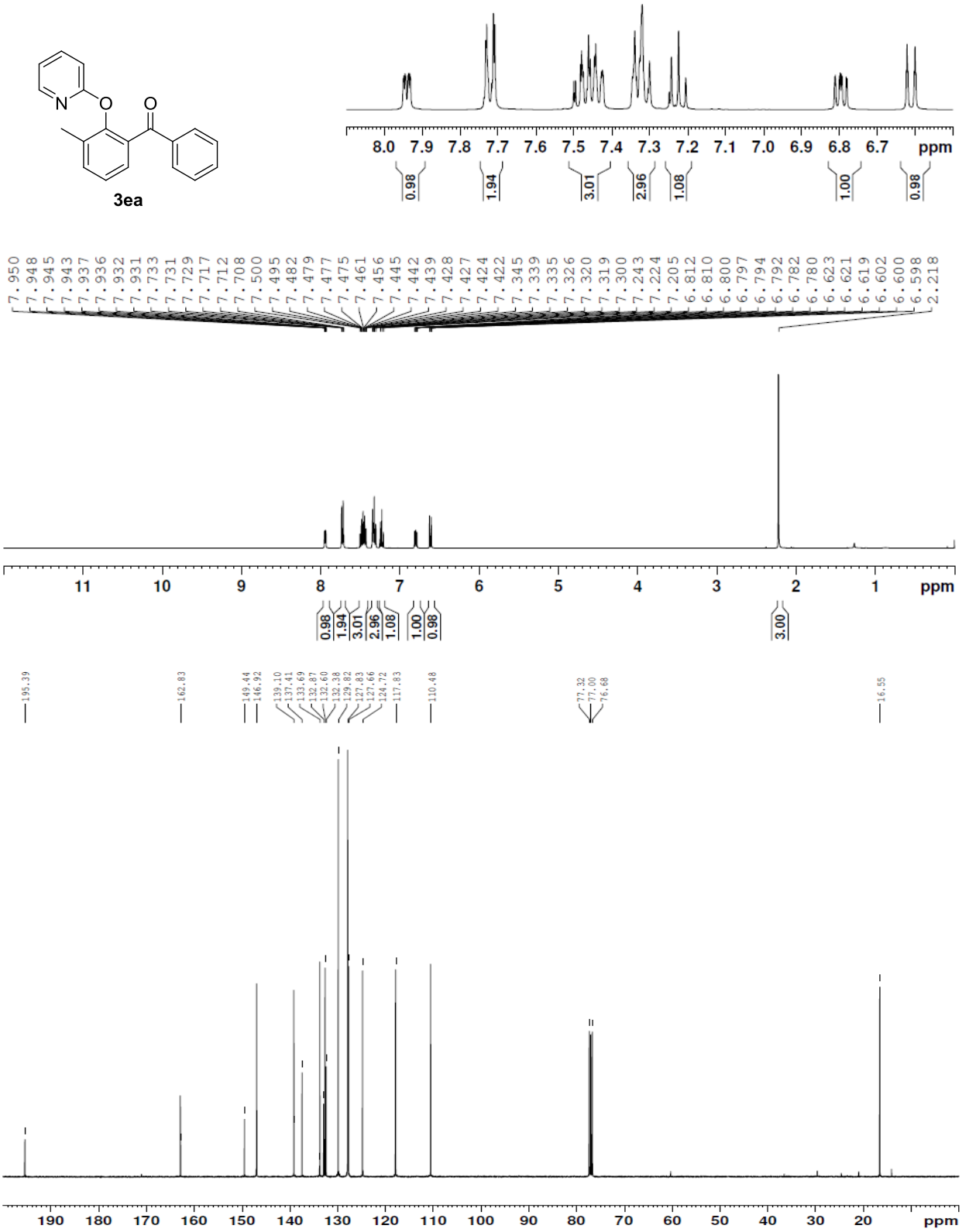

Figure 21. ^{1}H and ^{13}C NMR spectra of **3ej**

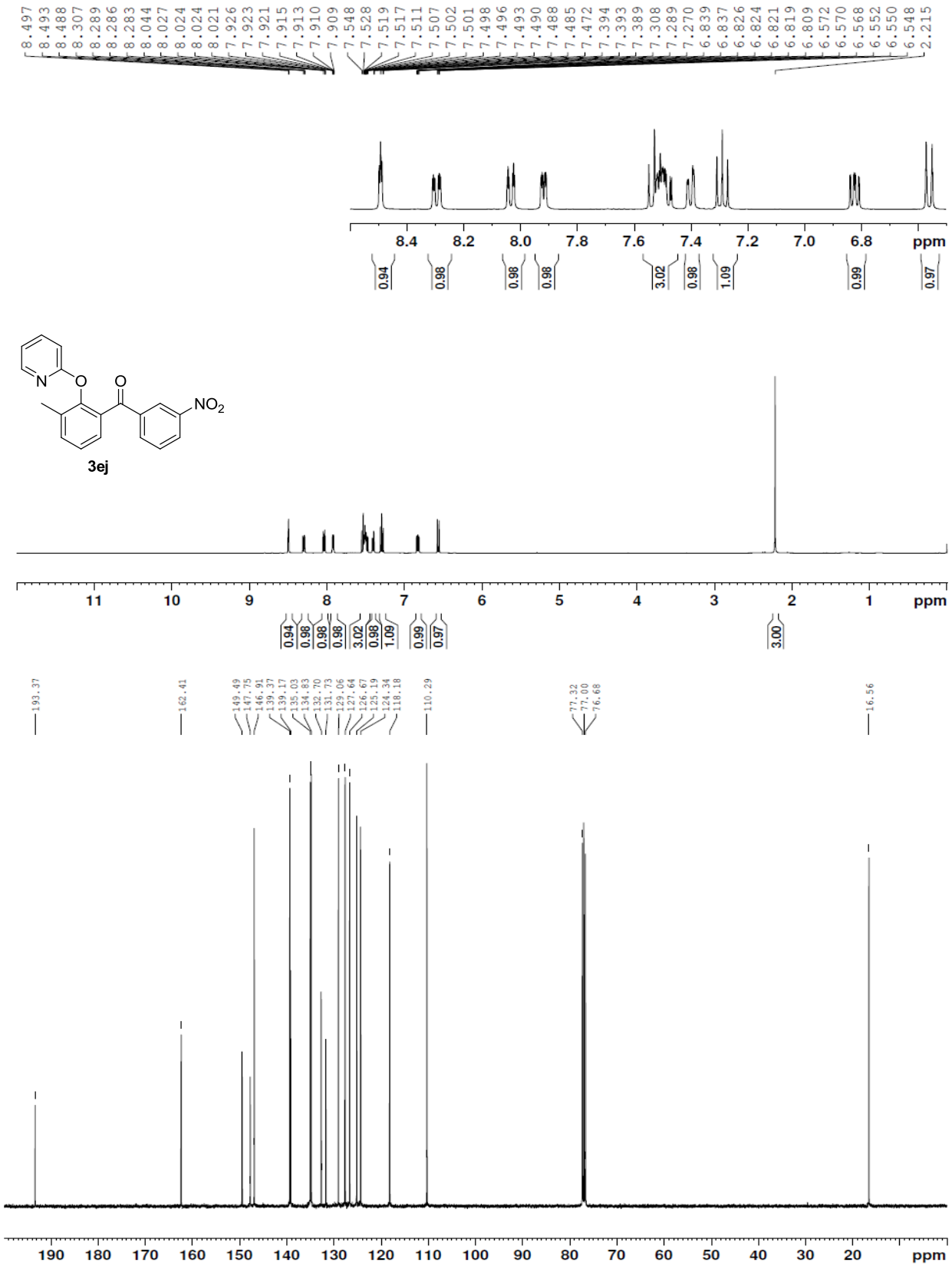

Figure 22. ^{1}H and ^{13}C NMR spectra of **3ek**

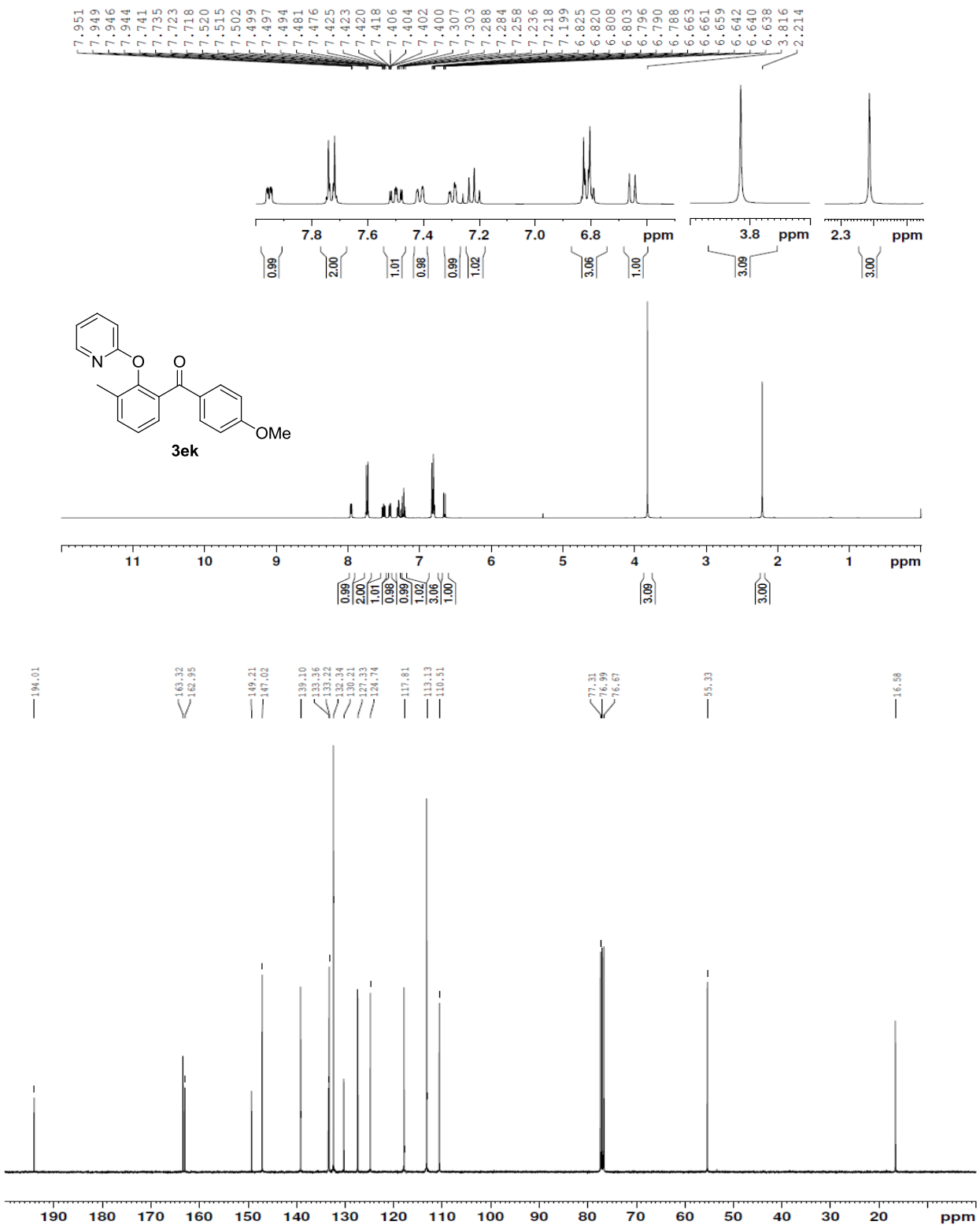

Figure 23. ^{1}H and ^{13}C NMR spectra of **3fa**

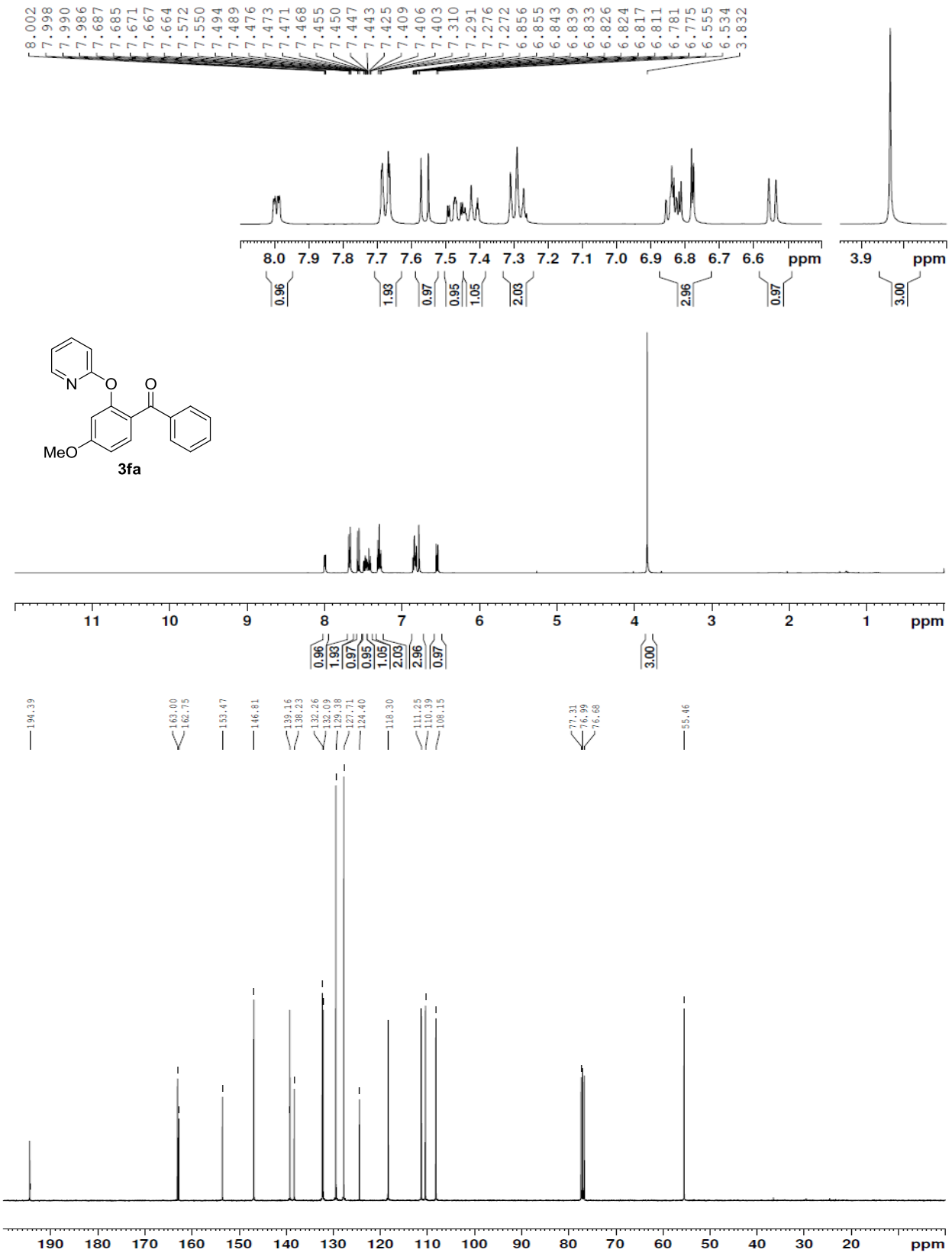

Figure 24. ^{1}H and ^{13}C NMR spectra of **3ga**

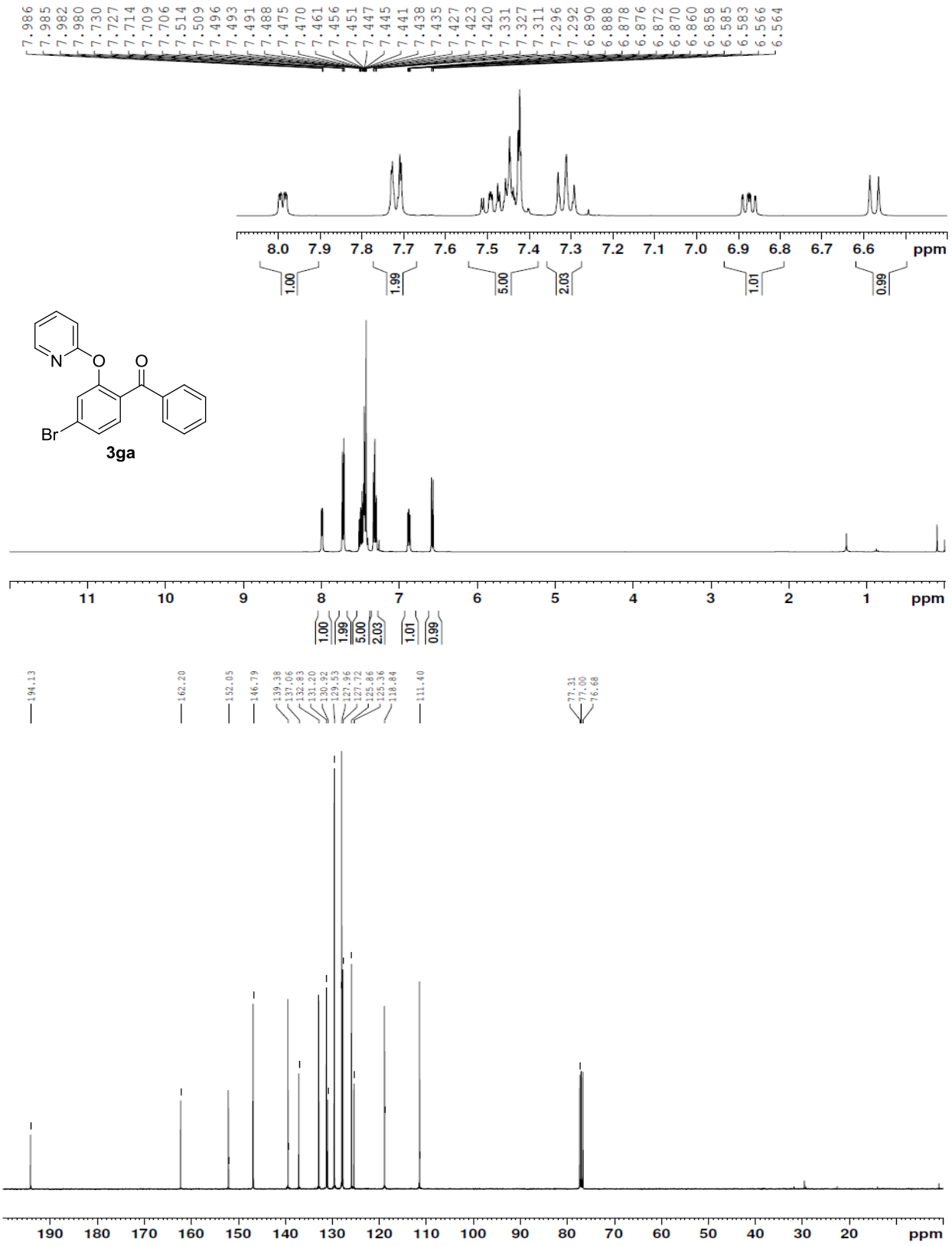

Figure 25. ^{1}H and ^{13}C NMR spectra of **3hj**

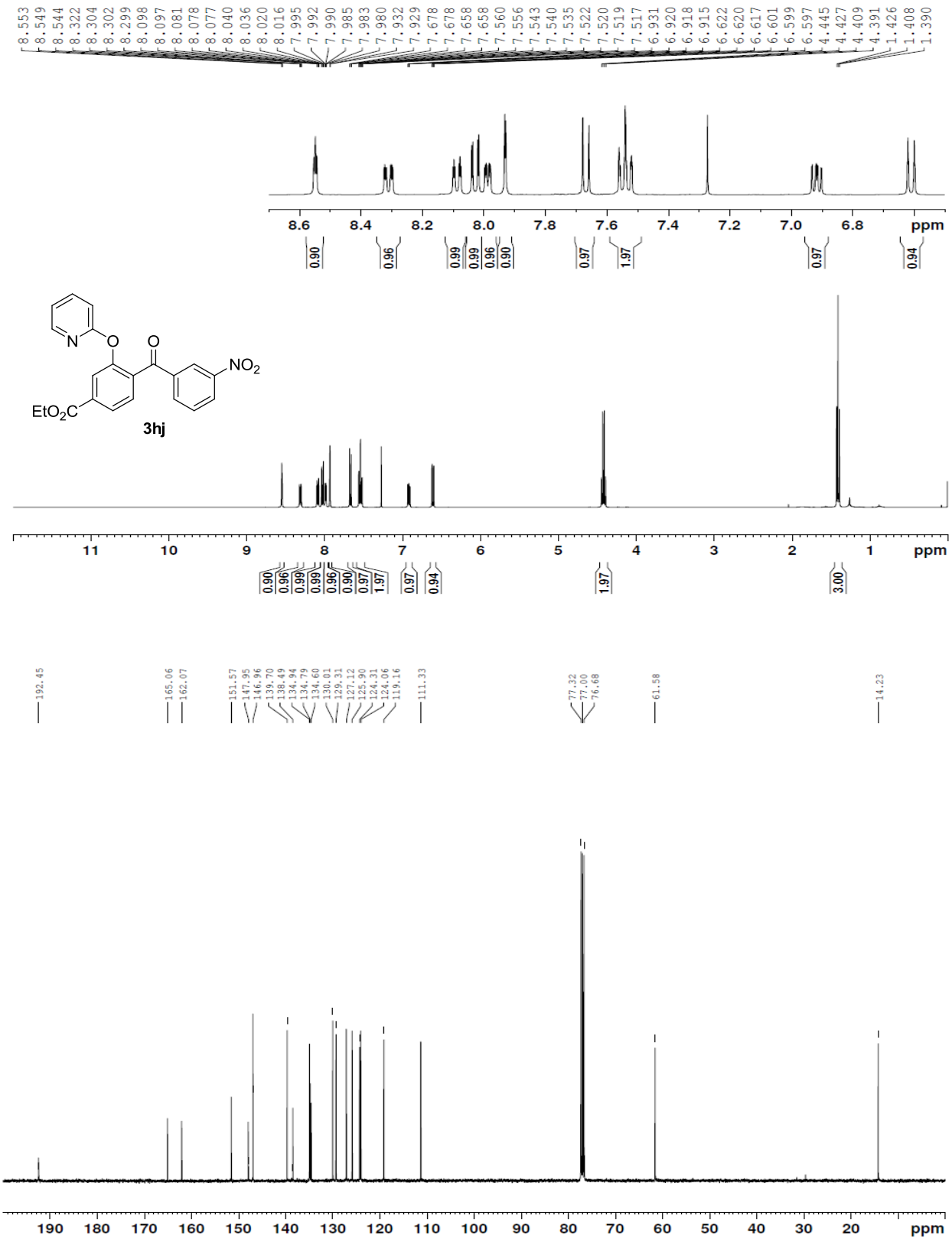

Figure 26. ^{1}H and ^{13}C NMR spectra of **3ia**

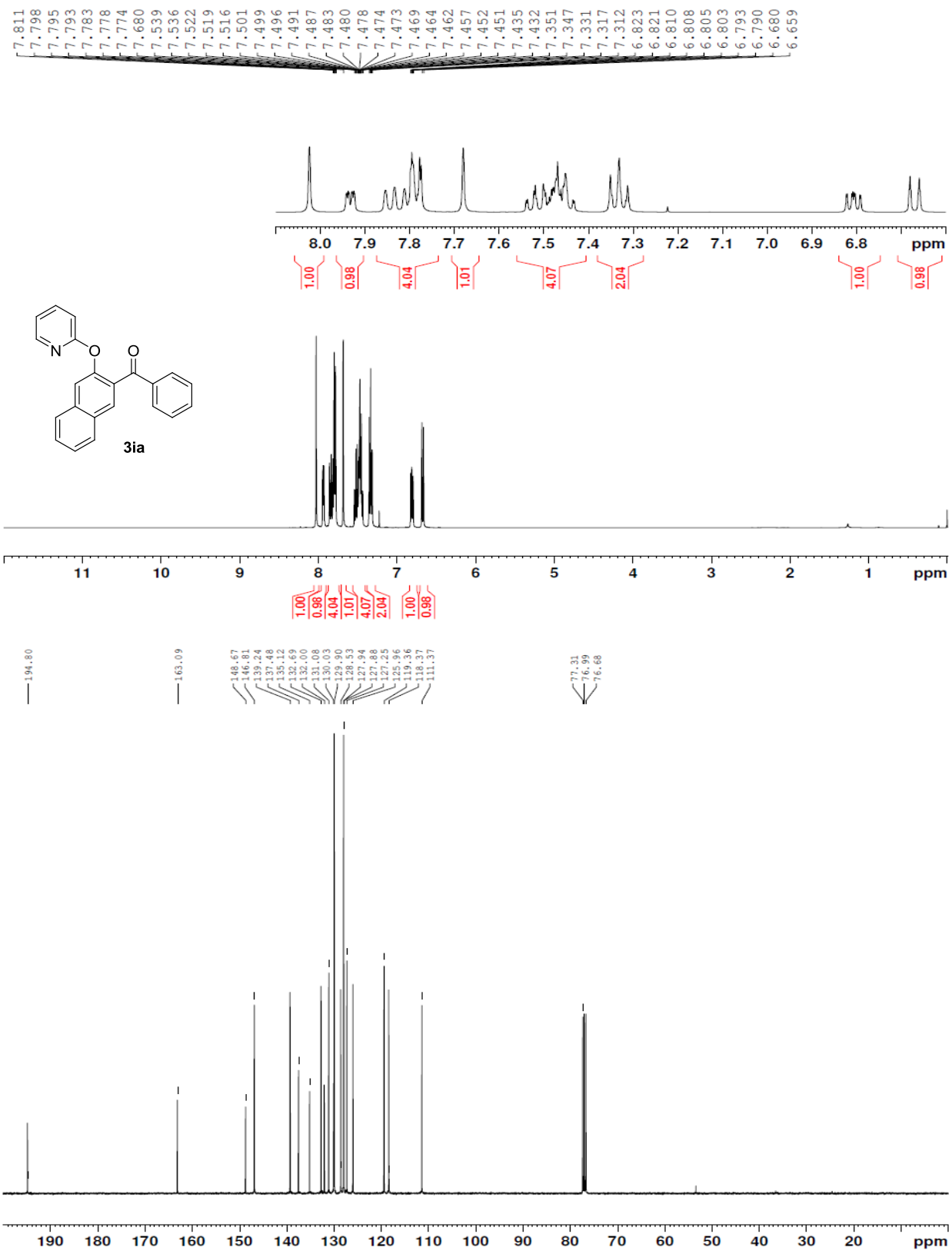

Figure 27. ^{1}H and ^{13}C NMR spectra of **5.**

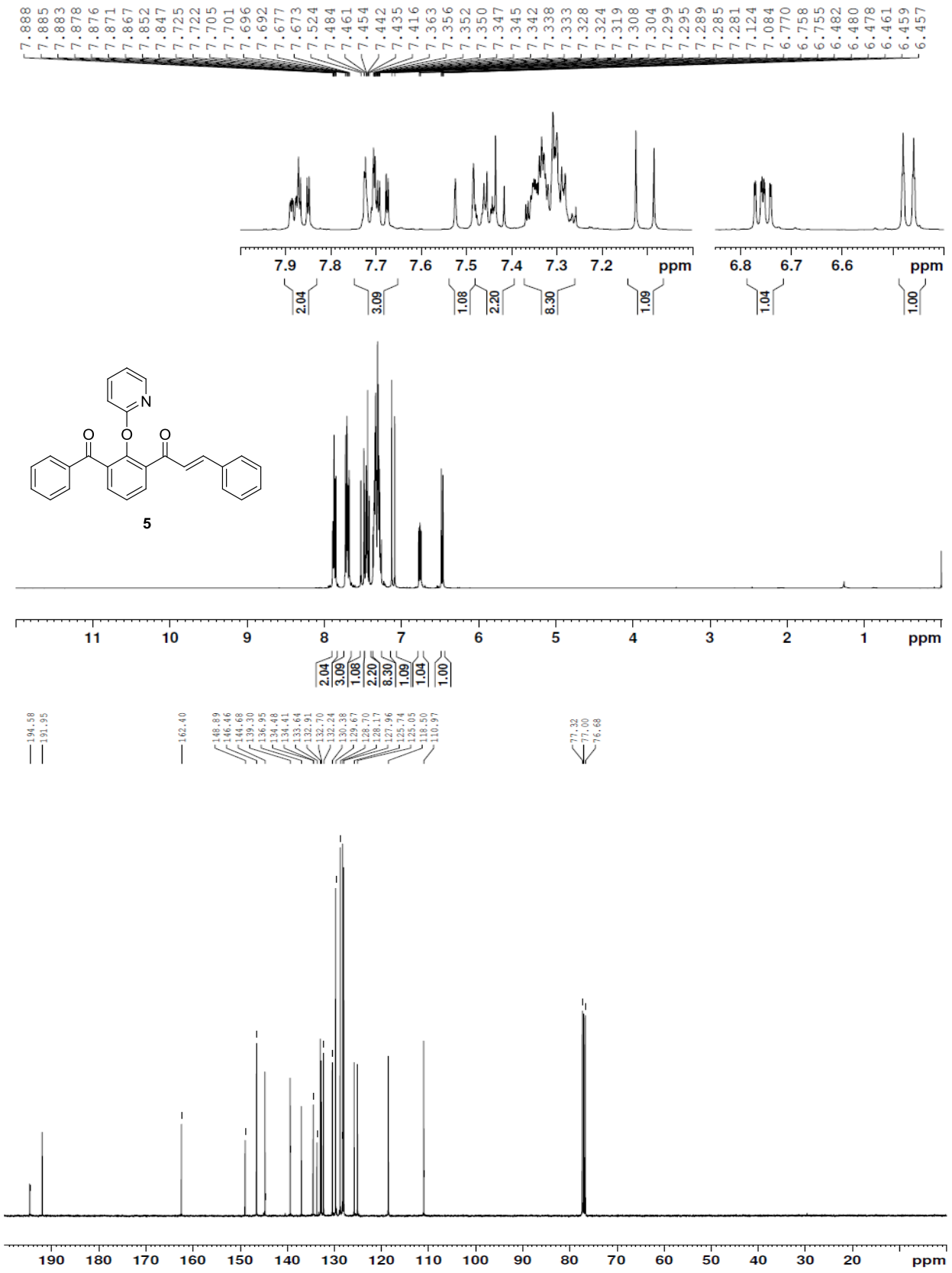

Figure 28. ^{1}H NMR of crude reaction mixture from competing acylation reaction of **1e** with **2j** and **2k**.

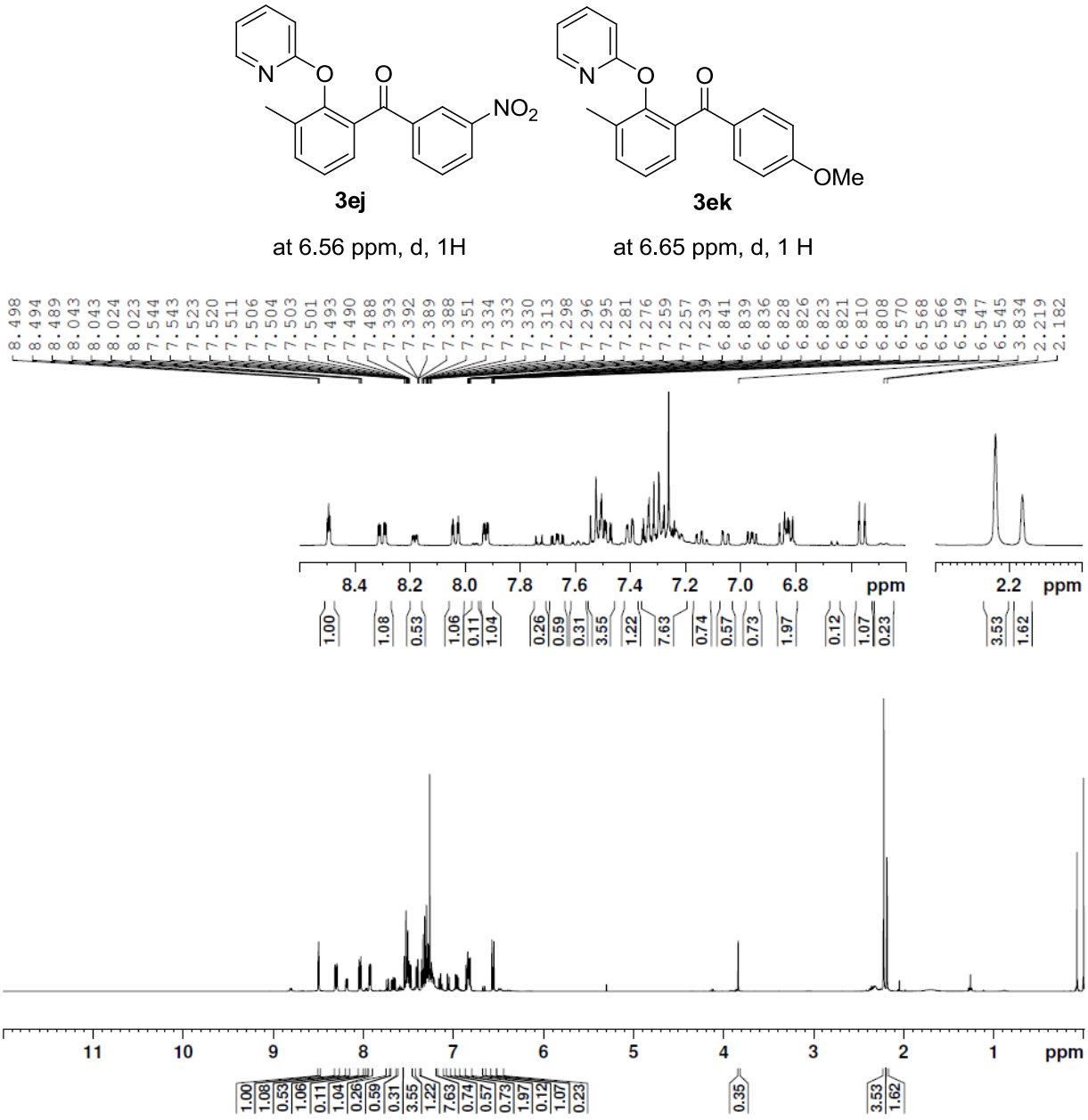

Figure 29. ^{1}H NMR of isolated product (mixture of **3ej** and **3ek)** from the competing acylation reaction of **1e** with **2j** and **2k**.

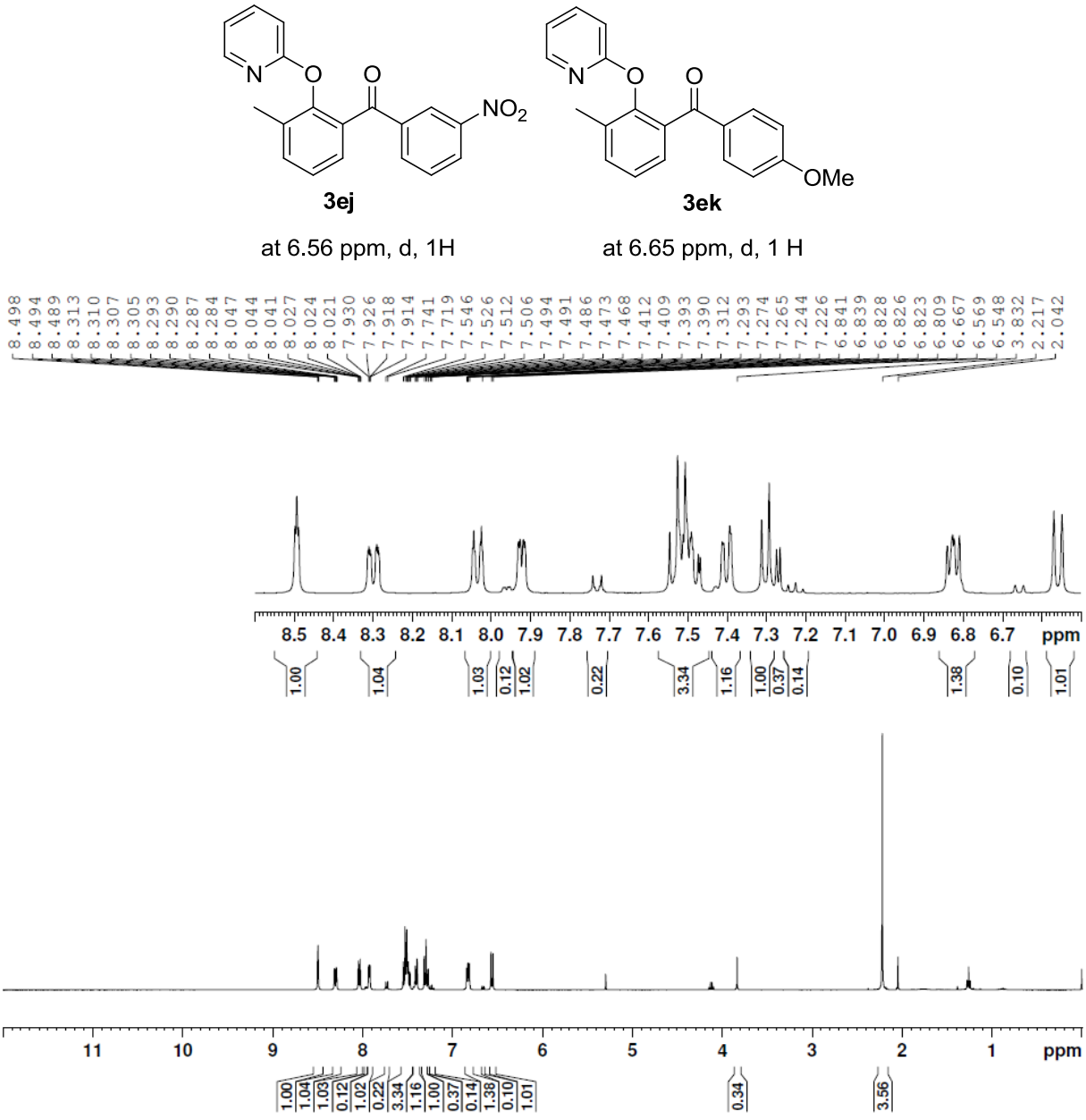

Figure 30. ^{1}H and ^{13}C NMR spectra of **6**.