Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Nickel-Catalyzed Cyanation Reaction of Aryl/Alkenyl Halides with Alkyl Isocyanides

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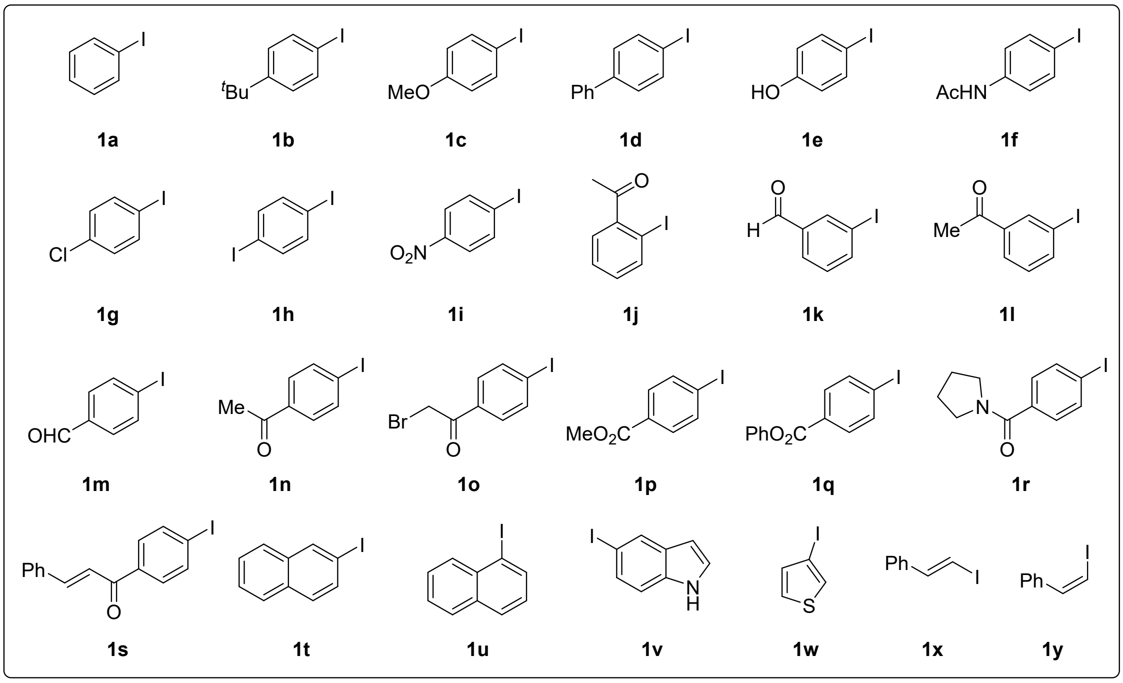
1. General Information

Unless otherwise noted, all reactions were carried out in flame-dried reaction vessels with Teflon screw caps under nitrogen. Solvents were purified and dried according to standard methods prior to use. All commercially available reagents were obtained from chemical suppliers and used after proper purification if necessary. Flash column chromatography was performed on silica gel (200-300 mesh) with the indicated solvent mixtures. TLC analysis was performed on pre-coated, glass-backed silica gel plates and visualized with UV light.

The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 or 500 or 600 AV spectrometers. Chemical shifts (δ) were reported as parts per million (ppm) downfield from tetramethylsilane and the following abbreviations were used to identify the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, br = broad and all combinations thereof can be explained by their integral parts. Coupling constant (*J*) was reported in hertz unit (Hz).

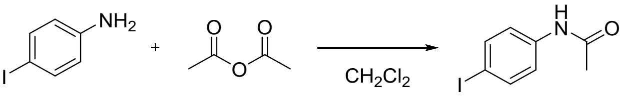
2. Preparation of Substrates

2.1 Preparation of aryl/alkenyl iodides



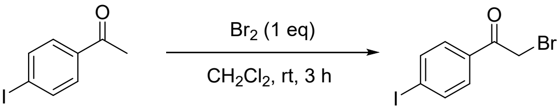
The substrates **1f**, **1o**, **1q**, **1r**, **1s**, **1x** and **1y** were prepared according to known literature.[1-7] The other aryl/alkenyl iodides and all bromides were purchased from chemical suppliers and used as received.

N-(4-iodophenyl)acetamide (1f)[1]



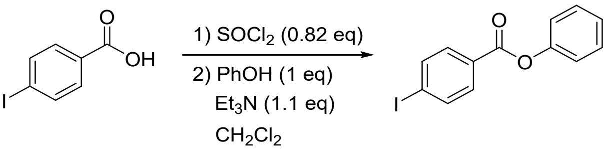
To a 100 mL Schlenk tube was added 4-iodoaniline (5.0 mmol, 1.1 g) and 20 mL dichloromethane under nitrogen atmosphere. Acetic anhydride (6.0 mmol, 1.2 eq) was then added dropwise and the mixture was stirred at room temperature for 12 hours. After the completion, it was quenched with brine and extracted with DCM (10 mL×3). The combined organic layer was dried over Na_2SO_4, and concentrated under reduced pressure to obtain the crude product. It could be further purified by flash chromatography using ethyl acetate/hexane and pure product was obtained in 88% yield.

2-bromo-1-(4-iodophenyl)ethan-1-one (1o)[2]



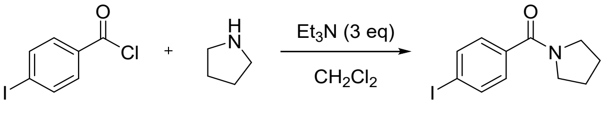
To a stirred solution of 4-iodoacetophenone (10.0 mmol, 2.48 g) in DCM (16 mL) was added Br_2 (10.0 mmol, 1.6 g) at room temperature. The reaction was conducted for 3 hours and water was added to quench the reaction. The mixture was extracted with DCM (10 mL×3). The combined organic phases was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The crude mixture was purified by flash chromatography using ethyl acetate/hexane to obtain the target product in 85% yield as a brown solid.

phenyl 4-iodobenzoate (1q)[3]



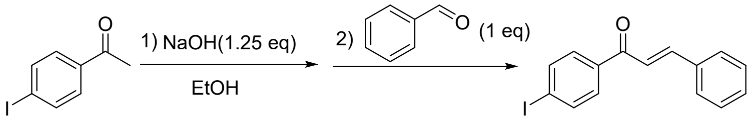
Under a nitrogen atmosphere, a mixed solution of 4-iodobenzoic acid (10 mmol, 2.48 g) and thionyl chloride (8.2 mmol, 0.97 g) was refluxed for 12 hours and concentrated under reduced pressure to remove volatiles. To the residue were added anhydrous dichloromethane (96 mL) and a solution of phenol (10 mmol, 1.08 g, in 3.5 mL anhydrous DCM) and Et_3N (11 mmol, 1.11 g) was then added dropwise. The mixture was stirred at room temperature for 3 hour. After the completion, the reaction was quenched with water, extracted with DCM, and the organic phases were combined. The organic phase was washed with 1M hydrochloric acid and saturated $NaHCO_3$, and dried over anhydrous $MgSO_4$. The product was obtained in 78% yield by recrystallization using ethyl acetate/hexane as mixed solvent.

(4-iodophenyl)(pyrrolidin-1-yl)methanone (1r)[4]



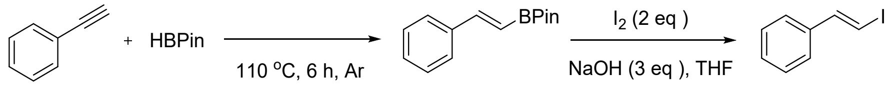
To a 100 mL Schlenk tube was added 4-iodobenzoyl chloride (1.5 equiv, 7.5 mmol, 1.99 g), triethylamine (3 eq, 15 mmol, 1.52 g) and DCM (10 mL). Pyrrolidine (5 mmol, 0.355 g) was then added dropwise at ice bath and the mixture was allowed to warm to rt and stirred for 3 hours. After the completion, the reaction was quenched with water and extracted with DCM (10 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude amide product was purified by flash chromatography in 82% yield.

(E)-1-(4-iodophenyl)-3-phenylprop-2-en-1-one (1s)[5]



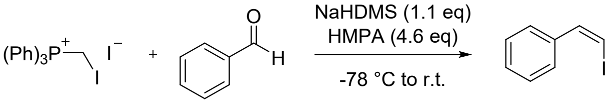
To 150 mL round flask was added 4-iodoacetophenone (10 mmol, 2.46 g), sodium hydroxide (12.5 mmol, 0.5 g) and 15 mL EtOH. The mixture was stirred at room temperature for 10 minutes. Benzaldehyde (10 mmol, 1.06 g) was then added and further stirred for 4 hours. After the reaction was completed, it was quenched with 20 mL of water, extracted with DCM (30 mL×2), washed with brine and dried over anhydrous $MgSO_4$. The product was obtained in 63% yield by flash chromatography using ethyl acetate/hexane as eluent.

(E)-(2-iodovinyl)benzene (1x)[6]

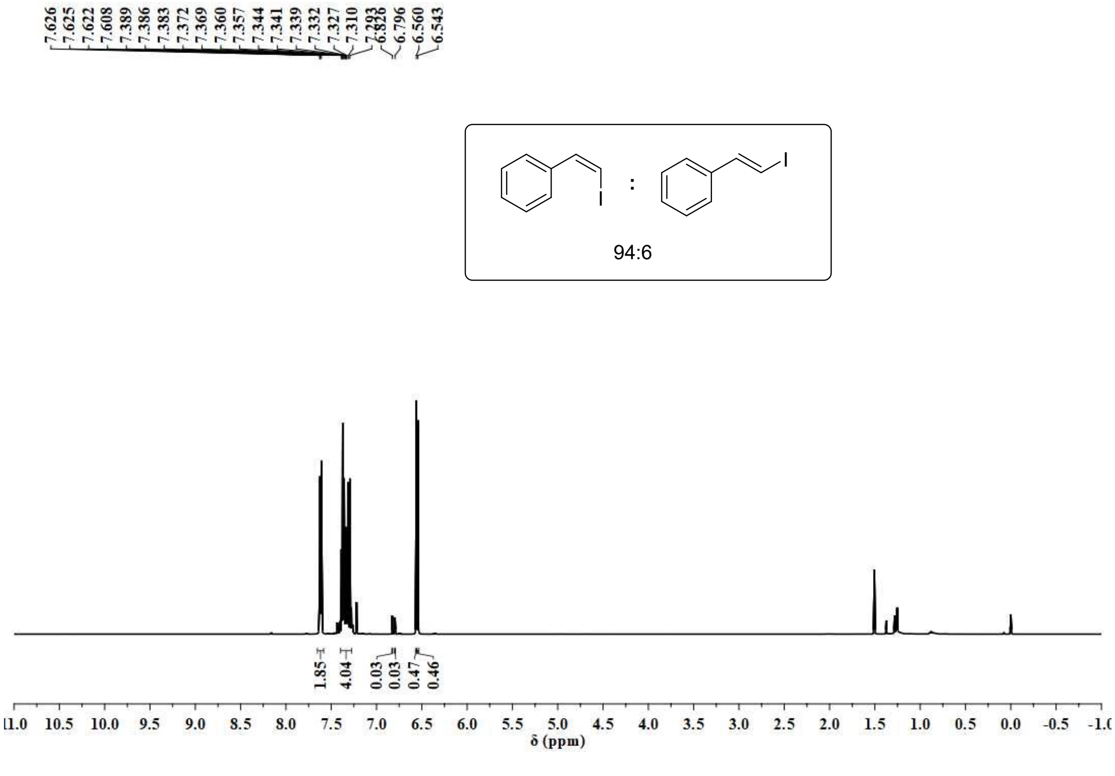


To a 50 mL Schlenk tube was added phenylacetylene (10 mmol, 1.02 g) and pinacol borane (20 mmol, 2.6 g). The mixture was stirred at 110°C for 6 hours. After the completion, the reaction mixture was cooled to room temperature and water (10 ml) was added to quench the unreacted substrate. The mixture was extracted with EtOAc (10 mL×3) and the combined organic layer was dried over anhydrous $MgSO_4$. After concentration under reduced pressure, the residual mixture was subjected to flash column chromatography to obtain the target product. It was then dissolved in THF (0.4 M). NaOH (3 eq, 1.2 g) was added at room temperature and stir the mixture for 10 minutes. I_2 (2 eq, 5.08 g, 0.2 M in THF) was next added and continued to stir for 2 hours. After the completion of the reaction, saturated $Na_2S_2O_3$ was added until the reaction mixture was observed to be decolorized. The crude product was extracted with ether (10 mL×3) and the combined organic layer was dried over anhydrous Na_2SO_4. The desired product was obtained in 82% yield by flash column chromatography using hexane as the eluent.

(Z)-(2-iodovinyl)benzene (1y)[7]



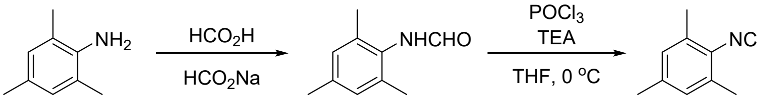
To a 50 mL Schlenk tube was added iodomethylenetriphenylphosphorane (1.1 mmol, 583 mg) and dry THF (2.5 mL) under nitrogen atmosphere. The tube was cooled to -60 °C and NaHMDS (0.55 mL, 2 M in THF) was added slowly. Then HMPA (4.6 mmol, 828 mg) was added and the solution was further cooled to -78°C. Benzaldehyde (1 mmol, 106 mg) was added, and the mixture was stirred at -78°C for 5 minutes. The reaction was then warmed to room temperature in 35 minutes. Et_2O (20 mL) was added and the mixture was filtered through celite. The crude product was isolated in 65% yield by flash chromatography using ethyl acetate/hexane as an eluent.



2.2 Preparation of isocyanides

The isocyanides **2a**, **2b**, **2c**, **2d** and **2e** were purchased from chemical suppliers and used as received. Isocyanide **2f** was prepared from the known procedure.[8]

2-isocyano-1,3,5-trimethylbenzene (2f)

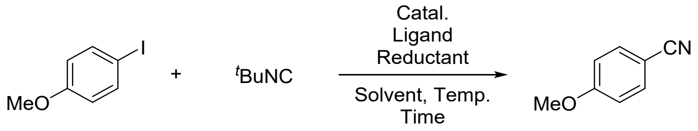


A mixture of aryl amine (10 mmol), formic acid (4.0 equiv) and sodium formate (0.2 equiv) in a round-bottom flask was stirred with a magnet at room temperature for 4 hours. Then EtOAc was added to the mixture, and the organic solvent was washed with water and saturated solution of $NaHCO_3$. After drying with Na_2SO_4 the solvent was removed under reduced pressure. The resulting residue was taken on to the next step without further purification.

To a solution of formamide 10mmol) and Et_3N (3.0 equiv) in anhydrous THF was added dropwise $POCl_3$ (1.2 equiv) in THF at 0 °C under nitrogen atmosphere over 30min. After keeping 0℃ for 1 hour the reaction mixture was poured into a saturated solution of K_2CO_3. Then the mixture was extracted by 2-methoxy-2-methylpropane and the organic phase was dried over Na_2SO_4 and concentrated in vacuum. The crude product was isolated in 78% yield by flash chromatography using PE/EA (80:1) as an eluent.

3. Ni-Catalyzed Cyanation of Aryl/Alkenyl Iodides with Isocyanides

3.1 Optimization of reaction conditions

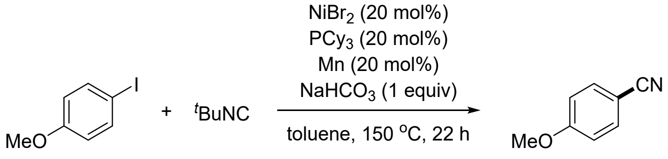


1c **2a** (0.2 mmol) **3c**

Entry	Catal./mol%	Ligand	Reductant	Base	**1c**:**2a**	Temp./°C	Time/h	Yield/%
1	$NiBr_2$/20	dppp	-	$NaHCO_3$	1:1	150	12	trace
2	$NiBr_2$/20	dppp	Zn	$NaHCO_3$	1:1	150	12	35
3	$NiBr_2$/20	dppp	Sn	$NaHCO_3$	1:1	150	12	trace
5	$NiBr_2$/20	dppp	Mn	$NaHCO_3$	1:1	150	12	50
6	$NiBr_2$/20	dppp	Mn	Na_2CO_3	1:1	150	12	30
7	$NiBr_2$/20	dppp	Mn	Cs_2CO_3	1:1	150	12	16
8	$NiBr_2$/20	dppp	Mn	NaOH	1:1	150	12	20
9	$NiBr_2$/20	dppp	Mn	Et_3N	1:1	150	12	17
10	$NiBr_2$/20	dppp	Mn	-	1:1	150	12	trace
11	$NiBr_2$/20	dppp	Mn	$NaHCO_3$	1:2	150	12	30
12	$NiBr_2$/20	dppp	Mn	$NaHCO_3$	1:3	150	12	27
13	$NiBr_2$/20	dppp	Mn	$NaHCO_3$	2:1	150	12	55

14	$NiBr_2$/20	dppp	Mn	$NaHCO_3$	3:1	150	12	53
15	$NiBr_2$/20	dppe	Mn	$NaHCO_3$	2:1	150	12	40
16	$NiBr_2$/20	dppb	Mn	$NaHCO_3$	2:1	150	12	45
17	$NiBr_2$/20	PCy_3	Mn	$NaHCO_3$	2:1	150	12	62
18	$NiBr_2$/20	PPh_3	Mn	$NaHCO_3$	2:1	150	12	35
19	$NiBr_2$/20	Bipy	Mn	$NaHCO_3$	2:1	150	12	20
20	$NiBr_2$/20	IMes	Mn	$NaHCO_3$	2:1	150	12	trace
21	$NiBr_2$/20	-	Mn	$NaHCO_3$	2:1	150	12	16
22	$NiBr_2$/20	PCy_3	Mn	$NaHCO_3$	2:1	150	22	87
23	$NiBr_2$/20	PCy_3	Mn	$NaHCO_3$	2:1	150	32	89
24	$NiCl_2$/20	PCy_3	Mn	$NaHCO_3$	2:1	150	22	41
25	$Ni(OAc)_2$/20	PCy_3	Mn	$NaHCO_3$	2:1	150	22	43
26	$Ni(acac)_2$/20	PCy_3	Mn	$NaHCO_3$	2:1	150	22	42
27	$Ni(cod)_2$/20	PCy_3	-	$NaHCO_3$	2:1	150	22	78
28	$NiBr_2$/10	PCy_3	Mn	$NaHCO_3$	2:1	150	22	72
29	-	PCy_3	Mn	$NaHCO_3$	2:1	150	22	0
30	$NiBr_2$/20	PCy_3	Mn	$NaHCO_3$	2:1	120	22	57
31	$NiBr_2$/20	PCy_3	Mn	$NaHCO_3$	2:1	100	22	35
32	$NiBr_2$/20	PCy_3	Mn	$NaHCO_3$	2:1	80	22	trace

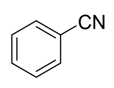
3.2 Experimental details and characterization of products



1c **2a** **3c**

To a 25 ml flame-dried Schlenk tube containing a stirring bar was added $NiBr_2$ (20 mol%, 0.04 mmol, 8.7 mg), Mn (0.04 mmol, 2.2 mg), PCy_3 (0.04 mmol, 11.2 mg), toluene (1 mL), ^{t}BuNC **2a** (0.2 mmol, 16.6 mg), 1-iodo-4-methoxybenzene **1c** (0.4 mmol, 93.6 mg), sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 22 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to provide the product **3c** in 87% yield.

benzonitrile (3a)[9]

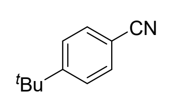


3a

Purified by silica gel column chromatography as a light brown liquid. Yield: 56% (11.5 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 – 7.66 (m, 2H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H). **^{13}C NMR (150 MHz, $CDCl_3$)** δ 132.90, 132.24, 129.25, 118.94, 112.55.

4-(tert-butyl) benzonitrile (3b)[10]

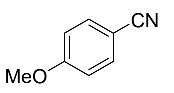


3b

Purified by silica gel column chromatography as a light brown liquid. Yield: 75% (23.9 mg).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.61 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H), 1.35 (s, 9H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 156.87, 132.18, 126.37, 119.36, 109.55, 35.48, 31.16.

4-methoxybenzonitrile (3c)[9]

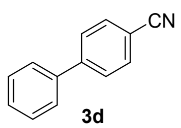


3c

Purified by silica gel column chromatography as a white solid. Yield: 87% (23.2 mg). Melting point: 58-59 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 7.61 (d, *J* = 8.8 Hz, 2H), 6.97 (d, *J* = 8.8 Hz, 2H), 3.87 (s, 3H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 163.12, 134.21, 119.37, 115.00, 104.33, 55.75.

[1,1'-biphenyl]-4-carbonitrile (3d)[9]

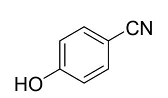


3d

Purified by silica gel column chromatography as a white solid. Yield: 82% (29.4 mg). Melting point: 85-87 °C.

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.72 (d, *J* = 8.5 Hz, 2H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.60 – 7.56 (m, 2H), 7.51 – 7.46 (m, 2H), 7.43 (d, *J* = 7.3 Hz, 1H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 145.84, 139.35, 132.73, 129.27, 128.83, 127.88, 127.38, 119.04, 111.14.

4-((trimethylsilyl)oxy)benzonitrile (3e)[11]

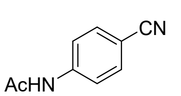


3e

Purified by silica gel column chromatography as a white solid. Yield: 71% (16.9 mg). Melting point: 110-113 °C.

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.63 (s, 1H), 7.64 (d, *J* = 6.3 Hz, 2H), 6.90 (d, *J* = 8.1 Hz, 2H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 160.43, 134.52, 119.46, 116.67, 103.33.

N-(4-cyanophenyl)acetamide (3f)[9]

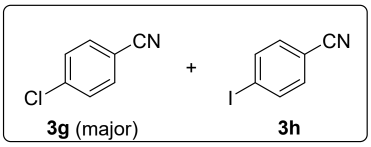


3f

Purified by silica gel column chromatography as a white solid. Yield: 65% (20.8 mg). Melting point: 206-208 °C.

^{1}H NMR (500 MHz, DMSO-d_6) δ 10.37 (s, 1H), 7.75 (s, 4H), 2.09 (s, 3H). **^{13}C NMR (150 MHz, DMSO-d_6)** δ 169.04, 143.38, 133.09, 118.96, 118.89, 104.66 , 24.06.

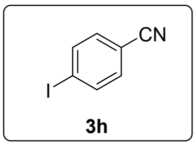
4-chlorobenzonitrile (3g)[9]



Purified by silica gel column chromatography as a white solid. Inseparable mixture of **3g** and **3h** was isolated. Total yield: 58% (15.8 mg, **3g** : **3h** = 3.1 : 1).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.85 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.6 Hz, 2H), 7.47 (d, *J* = 8.6 Hz, 2H), 7.37 (d, *J* = 8.4 Hz,2H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 139.76, 138.72, 133.58, 133.36, 129.90, 118.39, 118.15, 111.96, 111.00, 100.47.

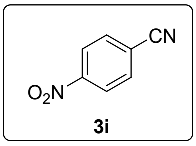
4-iodobenzonitrile (3h)[12]



Purified by silica gel column chromatography as a white solid. Yield: 45% (20.6 mg). Melting point: 124-128 °C.

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.85 (d, *J* = 8.3 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 138.66, 133.32, 118.34, 111.91, 100.45.

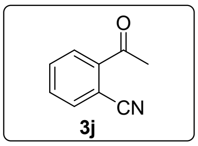
4-nitrobenzonitrile (3i)[9]



Purified by silica gel column chromatography as a yellow solid. Yield: 60% (17.7 mg). Melting point: 144-147 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.39 (d, *J* = 8.8 Hz, 2H), 7.92 (d, *J* = 8.8 Hz, 2H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 150.31, 133.67, 124.48, 118.58, 116.95.

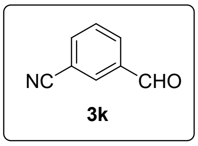
2-acetylbenzonitrile (3j)[13]



Purified by silica gel column chromatography as a white solid. Yield: 55% (15.9 mg). Melting point: 46-48 °C.

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.96 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.73 (t, *J* = 7.7 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 2.71 (s, 3H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 196.28, 140.18, 135.44, 132.80, 132.63, 130.04, 118.24, 111.27, 28.04.

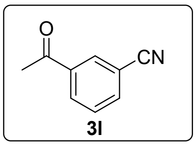
3-formylbenzonitrile (3k)[14]



Purified by silica gel column chromatography as a white solid. Yield: 55% (14.4 mg). Melting point: 75-78 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 10.07 (s, 1H), 8.20 (s, 1H), 8.15 (d, *J* = 7.8 Hz, 1H), 7.96 – 7.92 (m, 1H), 7.72 (t, *J* = 7.7 Hz, 1H). **^{13}C NMR (150 MHz, $CDCl_3$)** δ 190.09, 137.40, 137.10, 133.46, 133.34, 130.30, 117.72, 113.95.

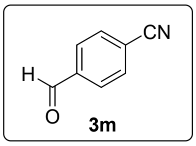
3-acetylbenzonitrile (3l)[15]


3l

Purified by silica gel column chromatography as a white solid. Yield: 63% (18.3 mg). Melting point: 98-100 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (t, *J* = 1.5 Hz, 1H), 8.21 – 8.18 (m, 1H), 7.89 – 7.83 (m, 1H), 7.64 (t, *J* = 7.8 Hz, 1H), 2.65 (s, 3H). **^{13}C NMR (150 MHz, $CDCl_3$)** δ 195.92, 138.05, 136.15, 132.36, 132.20, 129.87, 118.06, 113.46, 26.68.

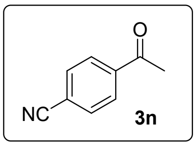
4-formylbenzonitrile (3m)[14]


3m

Purified by silica gel column chromatography as a yellow solid. Yield: 57% (15.0 mg).

1H NMR (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.93 (d, *J* = 8.5 Hz, 2H), 7.78 (d, *J* = 8.3 Hz, 2H). **^{13}C NMR (150 MHz, $CDCl_3$)** δ 190.70, 139.03, 133.11, 130.08, 117.88, 117.87.

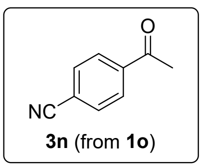
4-acetylbenzonitrile (3n)[15]


3n

Purified by silica gel column chromatography as a white solid. Yield: 67% (19.5 mg). Melting point: 56-59 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 2H), 2.68 (s, 3H). **^{13}C NMR (150 MHz, $CDCl_3$)** δ 196.64, 140.23, 132.73, 128.91, 118.08, 116.70, 26.90.

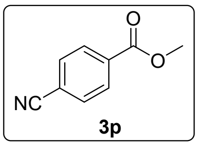
4-acetylbenzonitrile (3n)[15]


3n (from **1o**)

Purified by silica gel column chromatography as a white solid. Yield: 69% (20.0 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 2H), 2.58 (s, 3H).

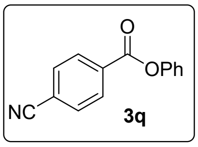
methyl 4-cyanobenzoate (3p)[9]


3p

Purified by silica gel column chromatography as a white solid. Yield: 65% (21.0 mg). Melting point: 65-67 °C.

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.16 (d, *J* = 8.4 Hz, 2H), 7.77 (d, *J* = 8.4 Hz, 2H), 3.98 (s, 3H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 165.63, 134.21, 132.42, 130.31, 118.12, 116.69, 52.88.

phenyl 4-cyanobenzoate (3q)[16]

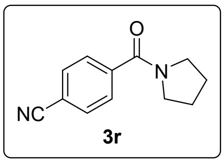


3q

Purified by silica gel column chromatography as a white solid. Yield: 70% (31.3 mg). Melting point: 165-166 ^{o}C.

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.32 (d, *J* = 8.5 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H), 7.50 – 7.44 (m, 2H), 7.35 – 7.30 (m, 1H), 7.25 – 7.21 (m, 2H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 163.68, 150.69, 133.54, 132.51, 130.73, 129.77, 126.46, 121.56, 117.96, 117.10.

4-(pyrrolidine-1-carbonyl)benzonitrile (3r)[17]

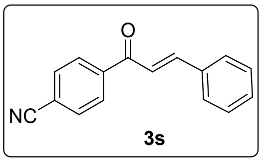


3r

Purified by silica gel column chromatography as a stick oil. Yield: 71% (28.4 mg).

^{1}H NMR (400 MHz, CDCl$_3$ δ 7.72 (d, *J* = 8.3 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 3.65 (t, *J* = 6.9 Hz, 2H), 3.38 (t, *J* = 6.5 Hz, 2H), 2.02 – 1.90 (m, 4H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 167.77, 141.55, 132.39, 127.94, 118.32, 113.68, 49.56, 46.48, 26.51, 24.49.

4-cinnamoylbenzonitrile (3s)[18]

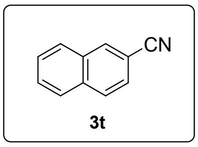


3s

Purified by silica gel column chromatography as a white solid. Yield: 75% (35.0 mg). Melting point: 112-114 ^{o}C.

^{1}H NMR (500 MHz, CDCl$_3$ δ 8.08 (d, *J* = 8.3 Hz, 2H), 7.87 – 7.76 (m, 3H), 7.68 – 7.61 (m, 2H), 7.52 – 7.38 (m, 4H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 189.31, 146.73, 141.64, 134.54, 132.66, 131.32, 129.26, 129.03, 128.84, 121.36, 118.19, 116.12.

2-naphthonitrile (3t)[9]

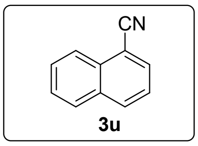


3t

Purified by silica gel column chromatography as a white solid. Yield: 73% (22.4 mg). Melting point: 63-66 ^{o}C.

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.22 (s, 1H), 7.93 – 7.87 (m, 3H), 7.68 – 7.59 (m, 3H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 134.82, 134.26, 132.43, 129.34, 129.18, 128.55, 128.20, 127.80, 126.48, 119.35, 109.58.

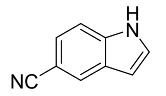
1-naphthonitrile (3u)[9]


3u

Purified by silica gel column chromatography as a colorless oil. Yield: 67% (20.5 mg).

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.22 (d, *J* = 8.5 Hz, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.93 – 7.87 (m, 2H), 7.70 – 7.64 (m, 1H), 7.63 – 7.57 (m, 1H), 7.52 – 7.48 (m, 1H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 133.44, 133.17, 132.79, 132.60, 128.82, 128.78, 127.74, 125.37, 125.11, 117.95, 110.47.

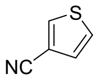
1H-indole-5-carbonitrile (3v)[19]


3v

Purified by silica gel column chromatography as a white solid. Yield: 35% (9.9 mg). Melting point: 106-108 °C.

^{1}H NMR (500 MHz, CDCl$_3$) δ 8.71 (s, 1H), 8.02 (s, 1H), 7.50 (d, *J* = 8.5 Hz, 1H), 7.47 – 7.43 (m, 1H), 7.39 – 7.36 (m, 1H), 6.68 – 6.64 (m, 1H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 137.66, 127.88, 126.65, 126.58, 125.18, 120.96, 112.15, 103.76, 103.23.

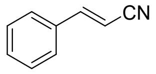
thiophene-3-carbonitrile (3w)[20]


3w

Purified by silica gel column chromatography as a light brown oil solid. Yield: 45% (9.8 mg).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.97 – 7.95 (m, 1H), 7.46 – 7.43 (m, 1H), 7.33 – 7.31 (m, 1H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 135.57, 128.97, 127.49, 115.32, 111.02.

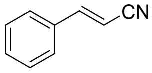
cinnamonitrile (3x)[20]


3x

Purified by silica gel column chromatography as a yellow liquid. Yield: 72% (18.6 mg).

^{1}H NMR (500 MHz, CDCl$_3$) δ 7.48 – 7.40 (m, 6H), 5.90 (d, *J* = 16.7 Hz, 1H). **^{13}C NMR (150 MHz, CDCl$_3$)** δ 150.80, 133.75, 131.42, 129.33, 127.56, 118.33, 96.58.

3-formylbenzonitrile (3x)[20]

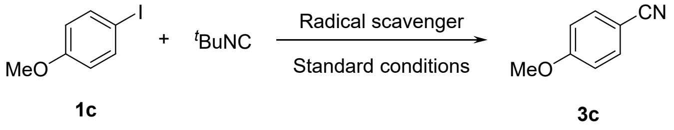

3x

Purified by silica gel column chromatography as a yellow liquid. Yield: 45% (11.7 mg).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 – 7.41 (m, 6H), 5.89 (d, *J* = 16.7 Hz, 1H).

4. Mechanistic Studies

4.1 Radical trapping experiments

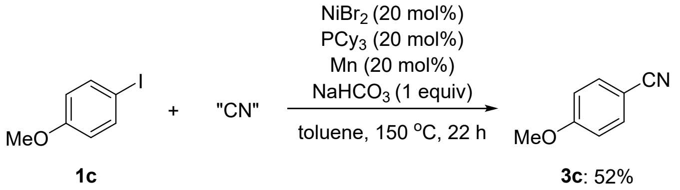


Radical scavenger	yield of **3c**
TEMPO	NR
BHT	66%
1,1'-diphenylethene	78%

Experimental procedure:

To a 25 ml flame-dried Schlenk tube containing a stirring bar was added $NiBr_2$ (20 mol%, 0.04 mmol, 8.7 mg), Mn (0.04 mmol, 2.2 mg), PCy_3 (11.2 mg), toluene (1 mL), *t*-BuNC (0.2 mmol, 16.6 mg), 1-iodo-4-methoxybenzene (0.4mmol, 93.6 mg), sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 22 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to provide the product **3c**.

4.2 Cyanation reaction using CuCN or TMSCN as cyano source



"CN" source	Yield/**3c**
CuCN	52%
TMSCN	76%

Experimental procedure:

To a 25 ml flame-dried Schlenk tube containing a stirring bar was added $NiBr_2$ (20 mol%, 0.04 mmol, 8.7 mg), Mn (0.04 mmol, 2.2 mg), PCy_3 (0.04 mmol, 11.2 mg), toluene (1 mL), CuCN (0.2 mmol, 18 mg) or TMSCN (0.2 mmol, 19.8 mg), 1-iodo-4-methoxybenzene (0.4 mmol, 93.6 mg) sequentially under nitrogen. The tube was sealed and stirred at 150 °C for 22 h. After completion, the reaction mixture was concentrated and purified by silica gel column chromatography to provide the product **3c** in 52% and 76% yield, respectively.

5. Reference

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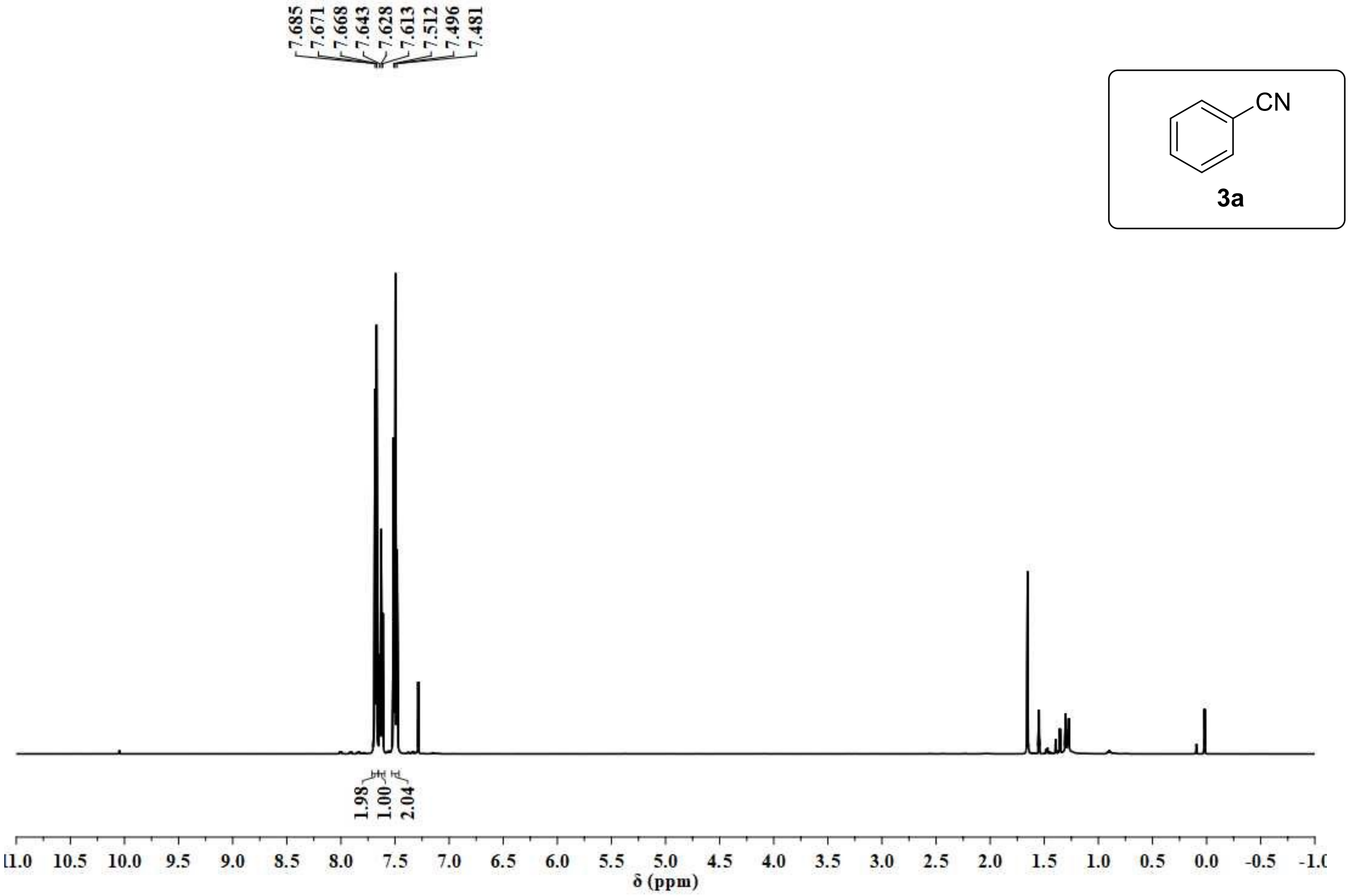
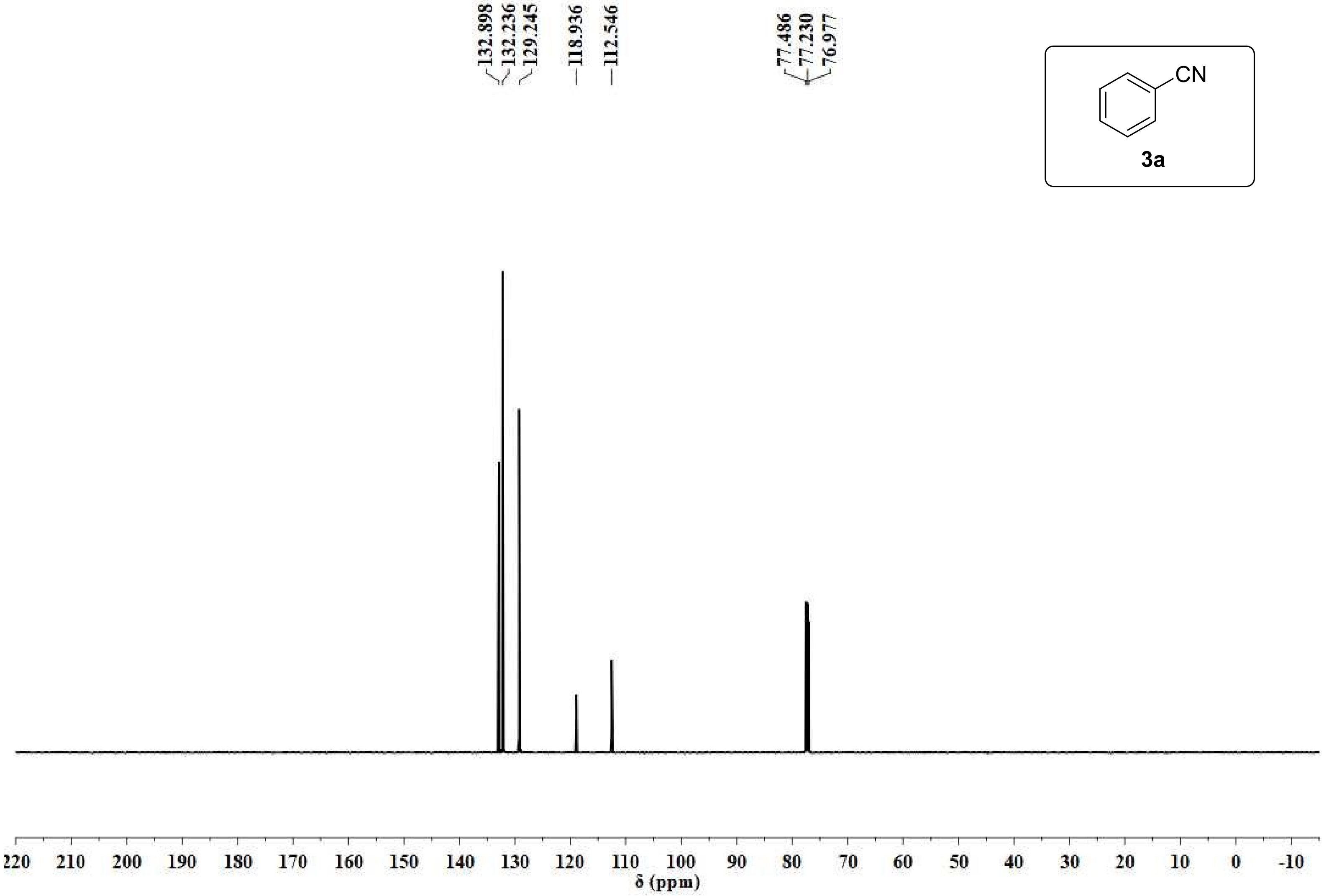
6. ^{1}H and ^{13}C NMR spectra

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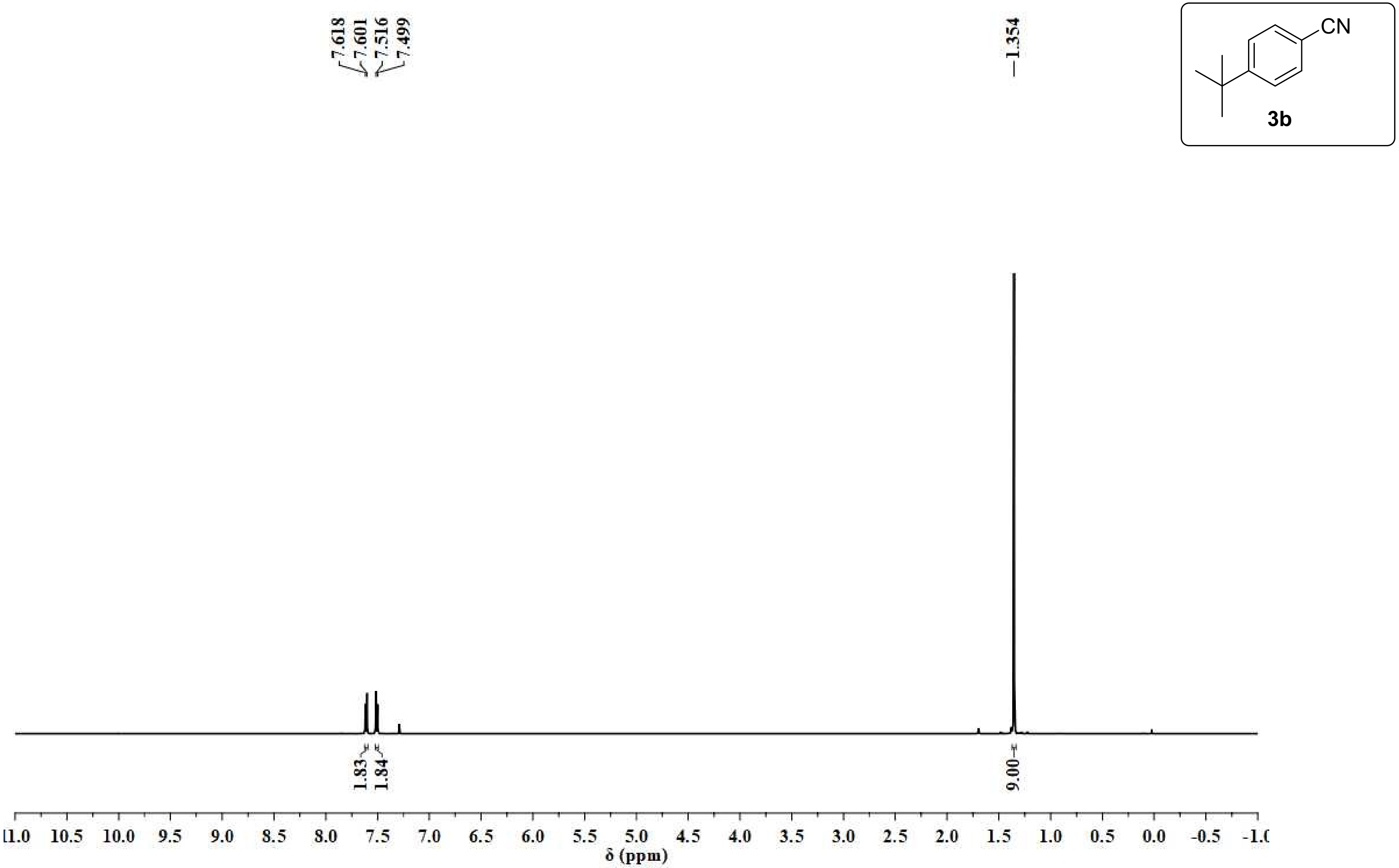
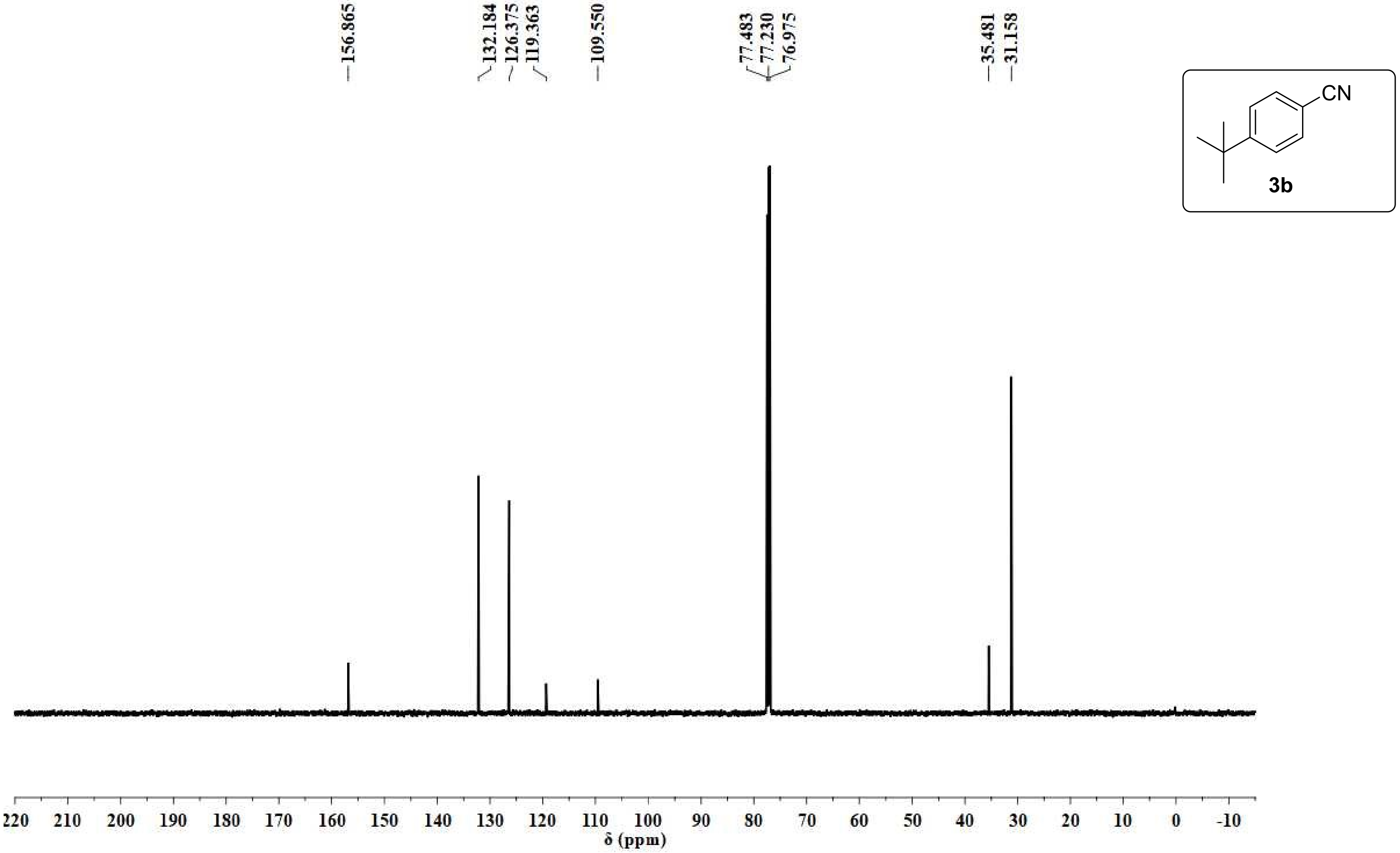
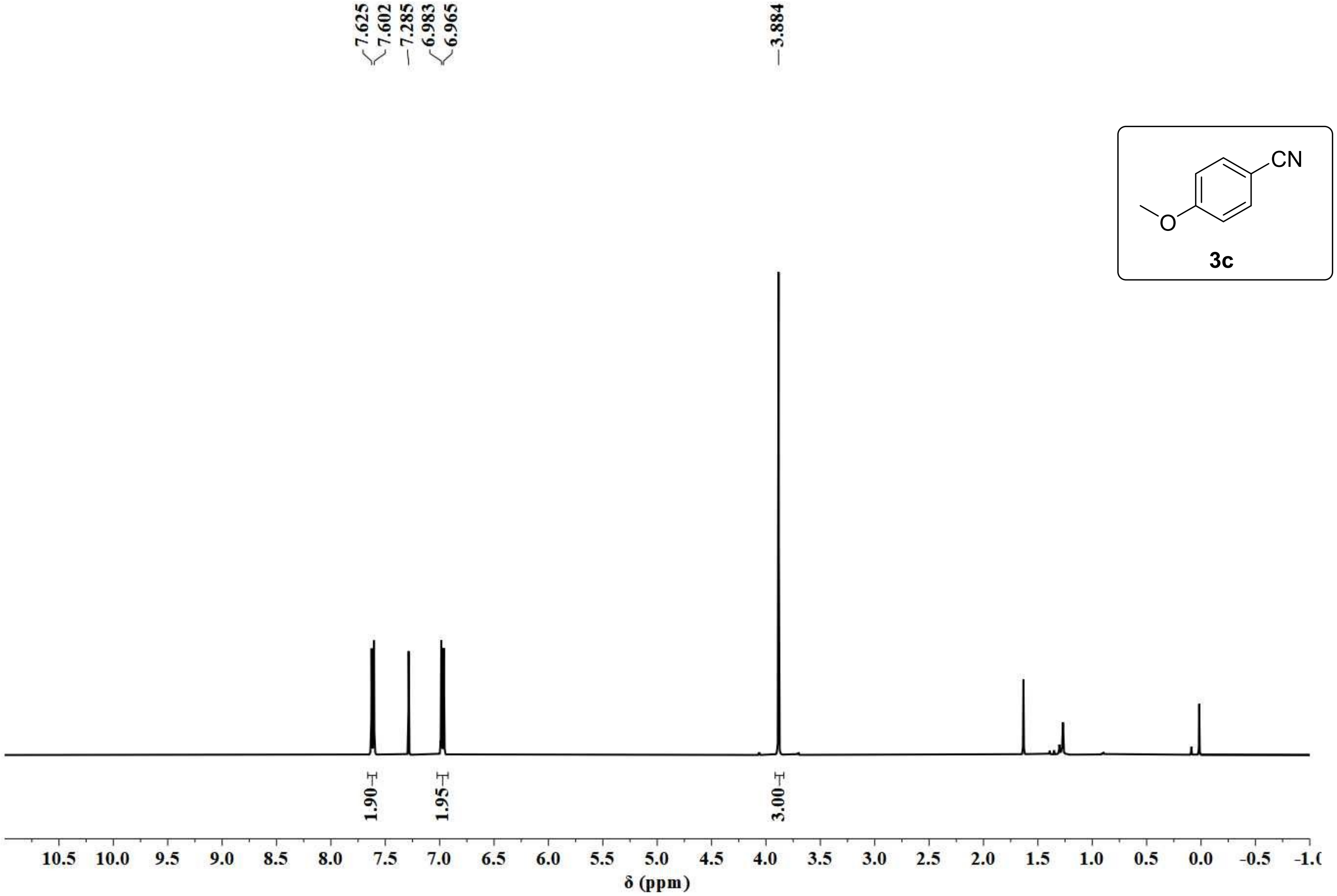
132.236
129.245
118.936
112.546
77.486
77.230
76.977
CN
3a
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)


7.618
7.601
7.516
7.499
1.354
CN
1.83
1.84
9.00
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.(
δ (ppm)

3b


156.865
132.184
126.375
119.363
109.550
77.483
77.230
76.975
35.481
31.158
CN
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)

3b


7.625
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6.965
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CN
O
3c
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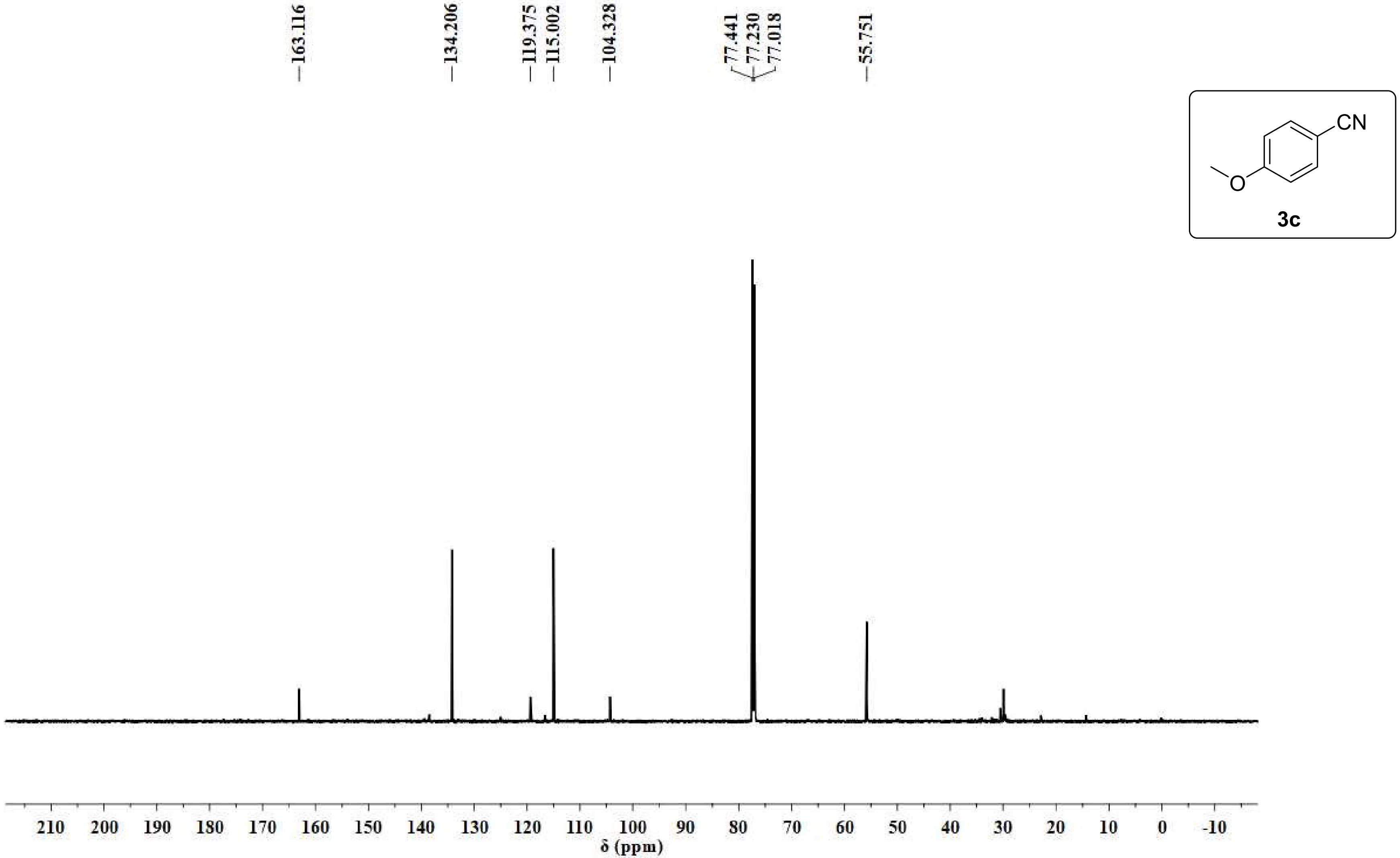
1.95
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.(
δ (ppm)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119.375
115.002
104.328
77.441
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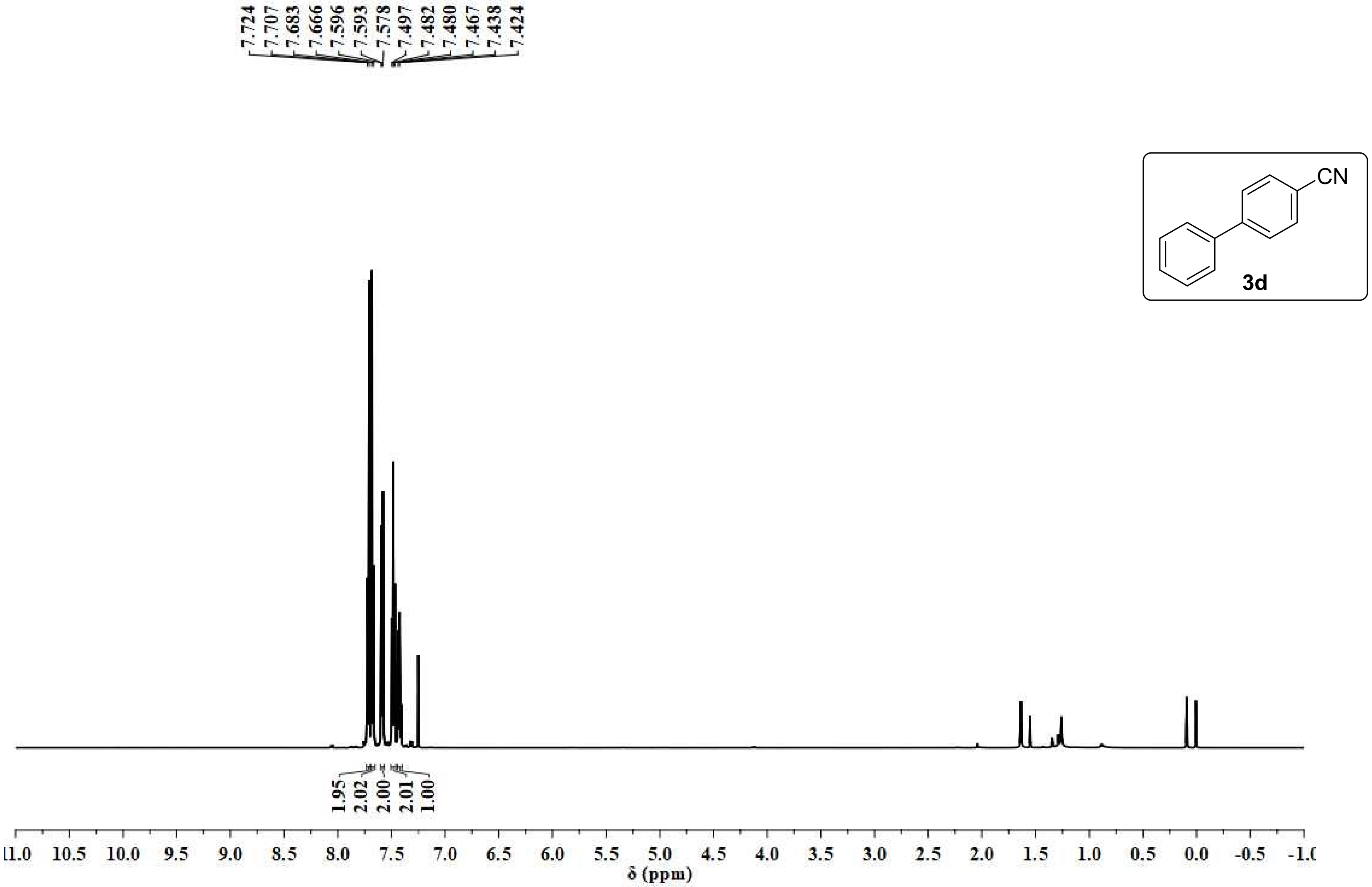
77.018
55.751
CN
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)

3c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7.593
7.578
7.497
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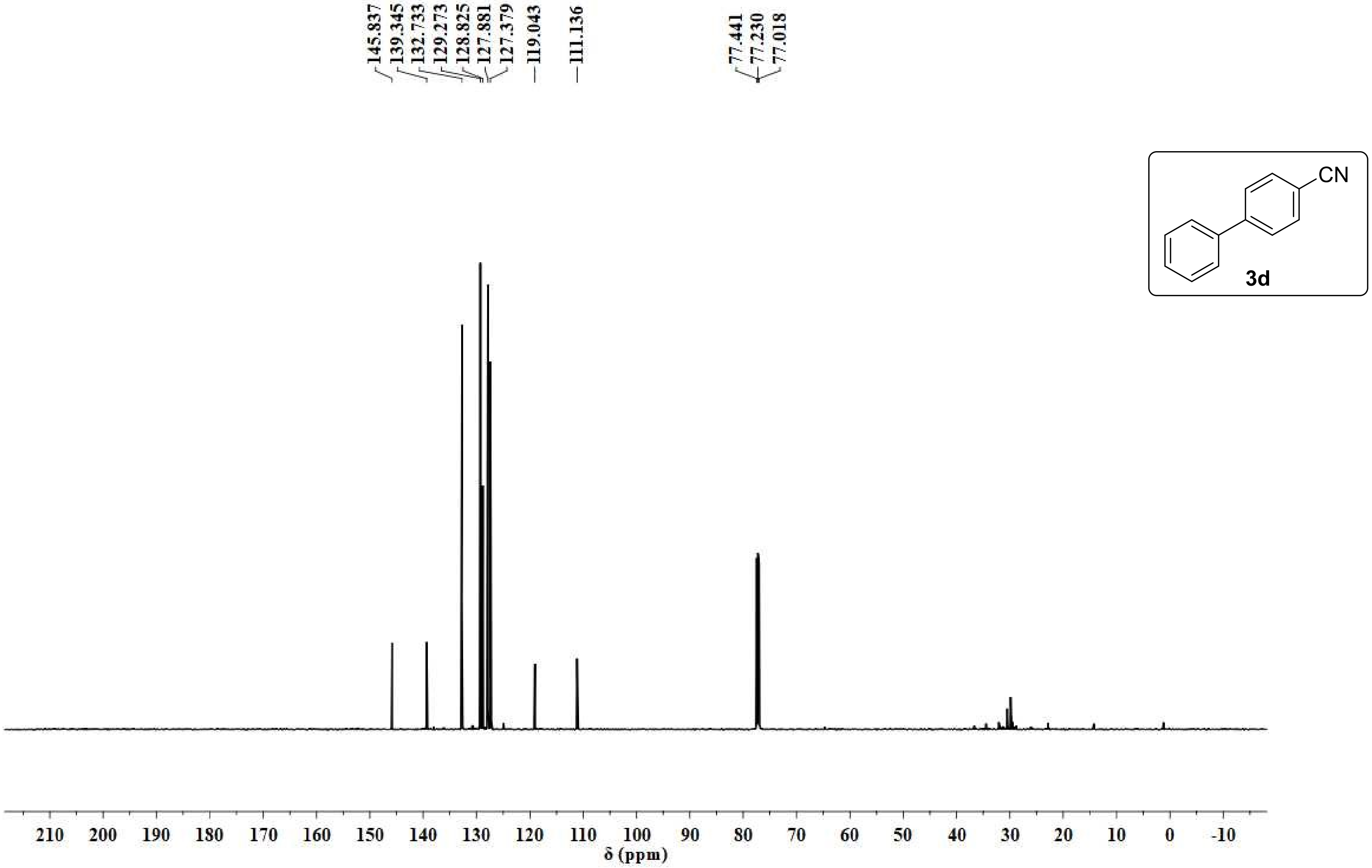
7.480
7.467
7.438
7.424
1.95
2.02
2.00
2.01
1.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
δ (ppm)
CN

3d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127.379
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77.441
77.230
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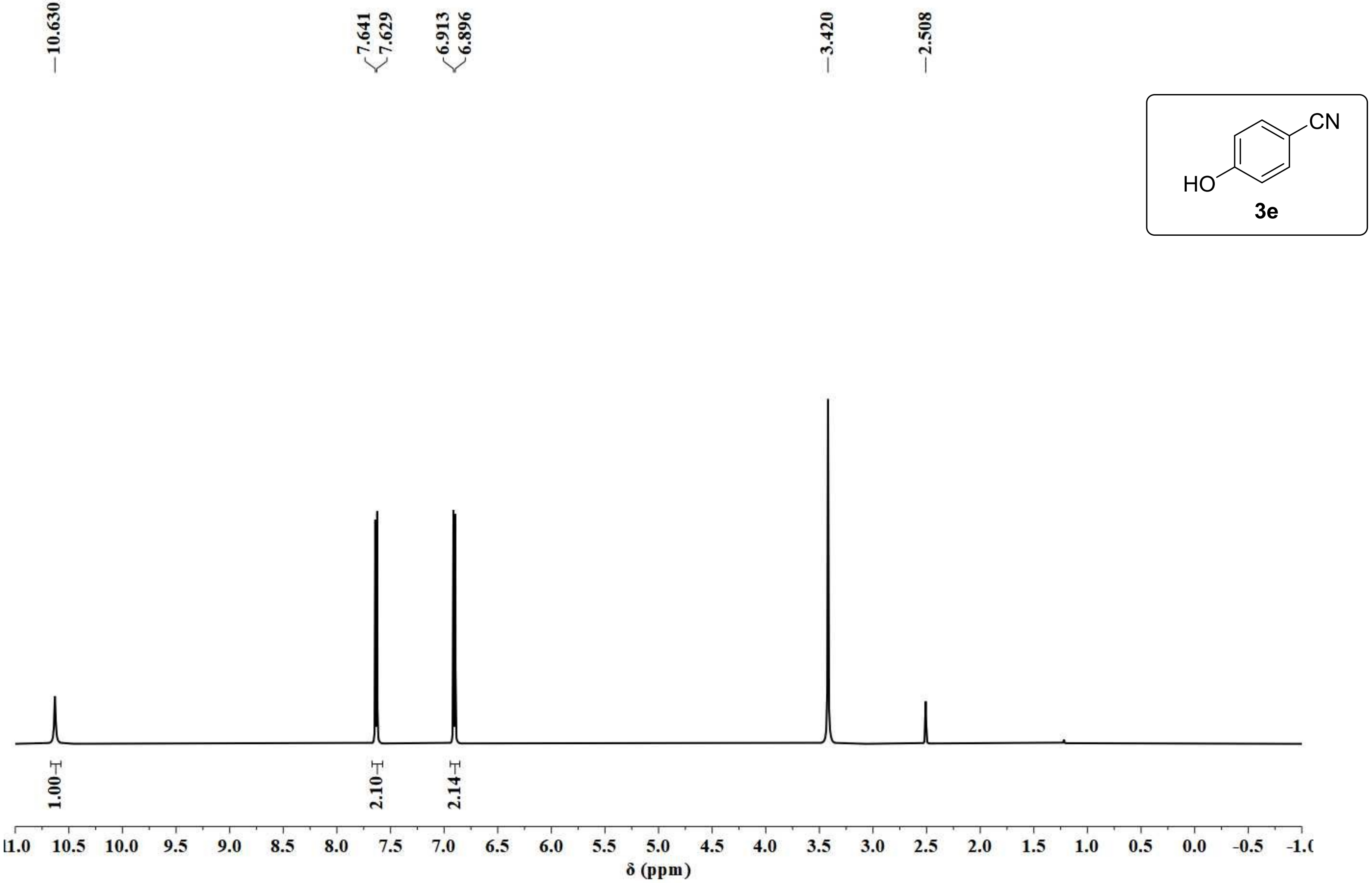
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)
CN

3d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6.896
3.420
2.508
CN
HO
1.00
2.10
2.14
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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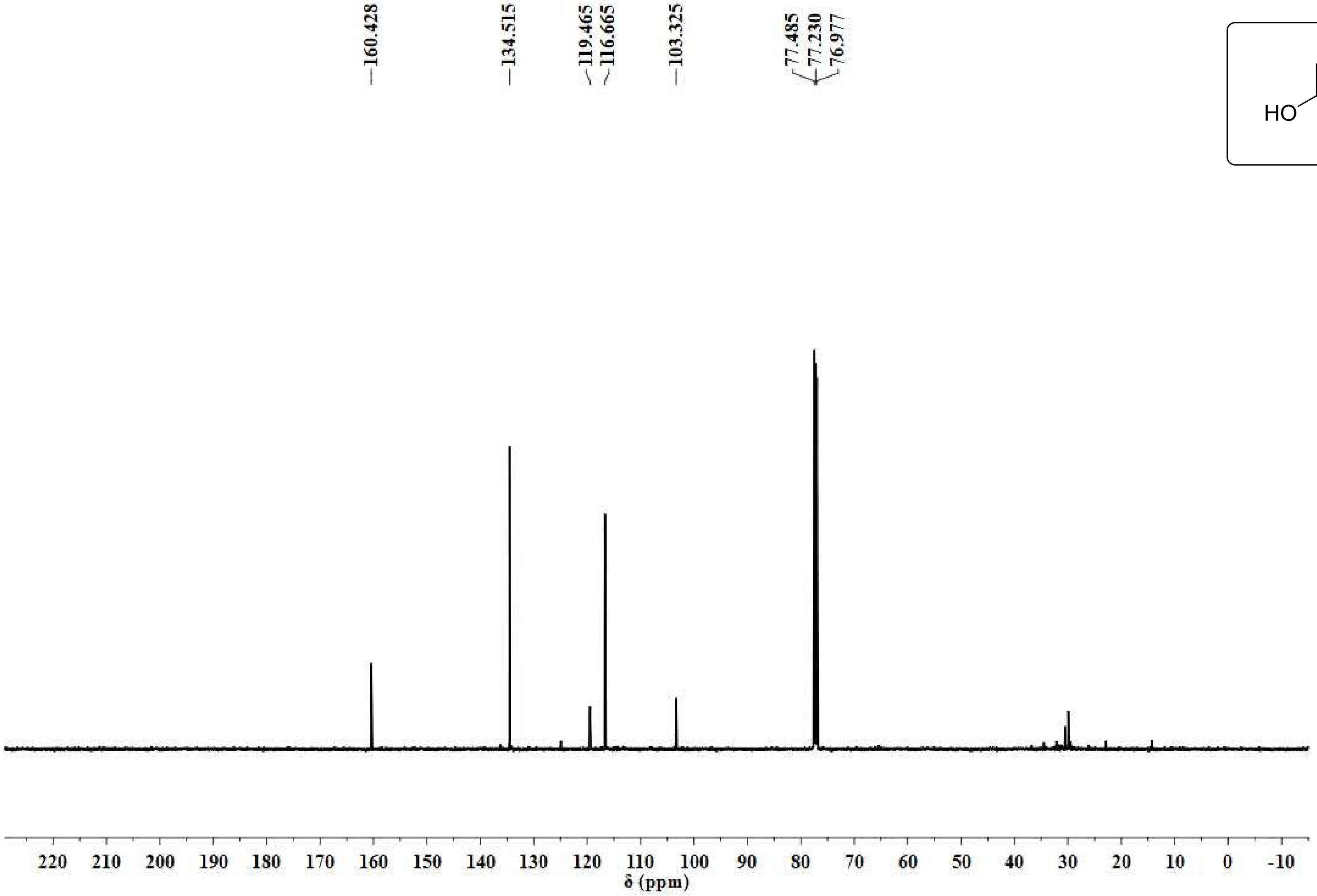
0.0
-0.5
-1.(
δ (ppm)

3e



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134.515
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77.485
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76.977
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210
200
190
180
170
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150
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130
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110
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90
80
70
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50
40
30
20
10
0
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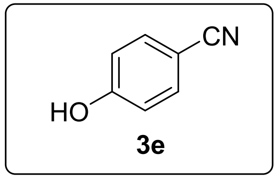
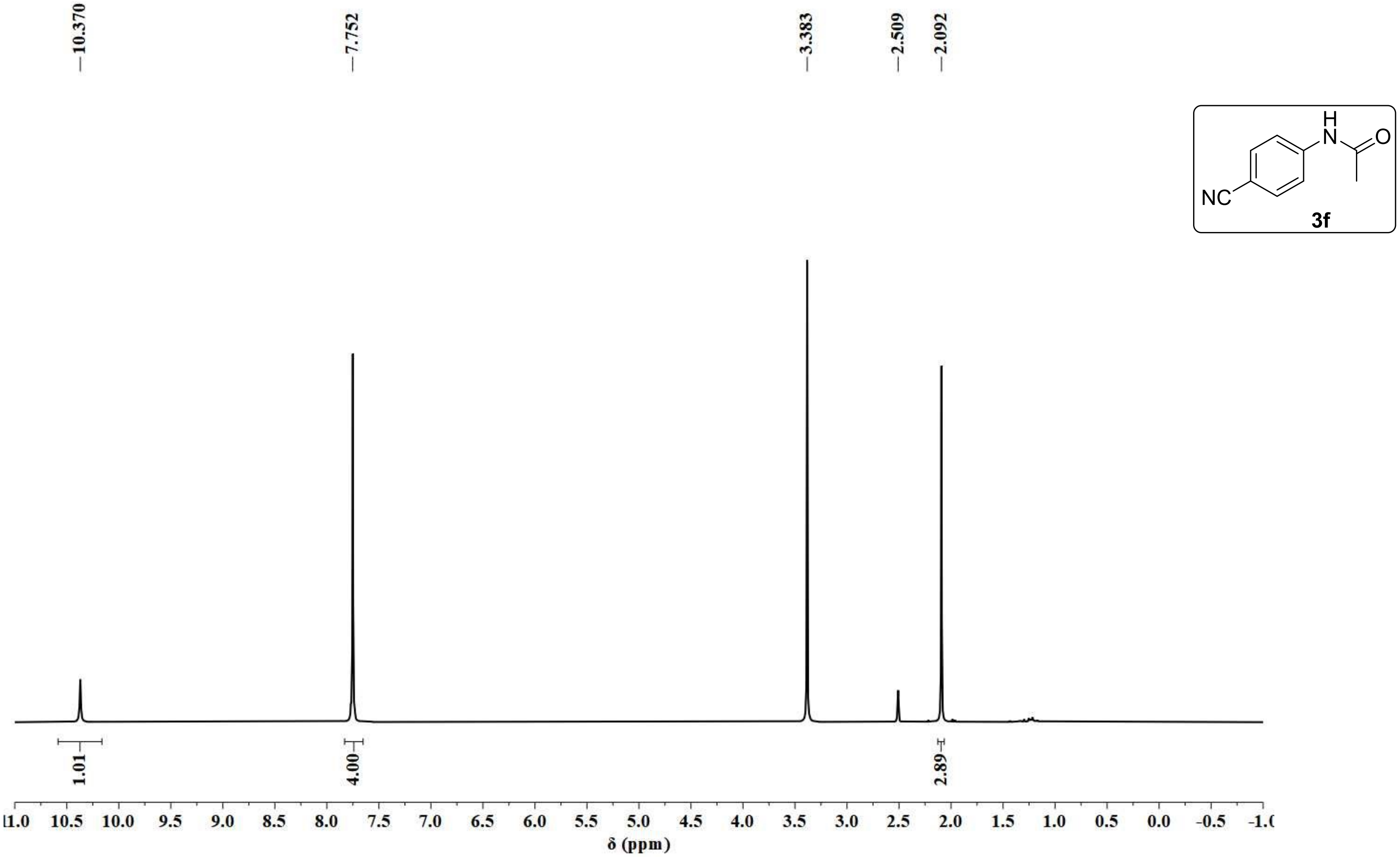
δ (ppm)



CN
HO

3e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10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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1.5
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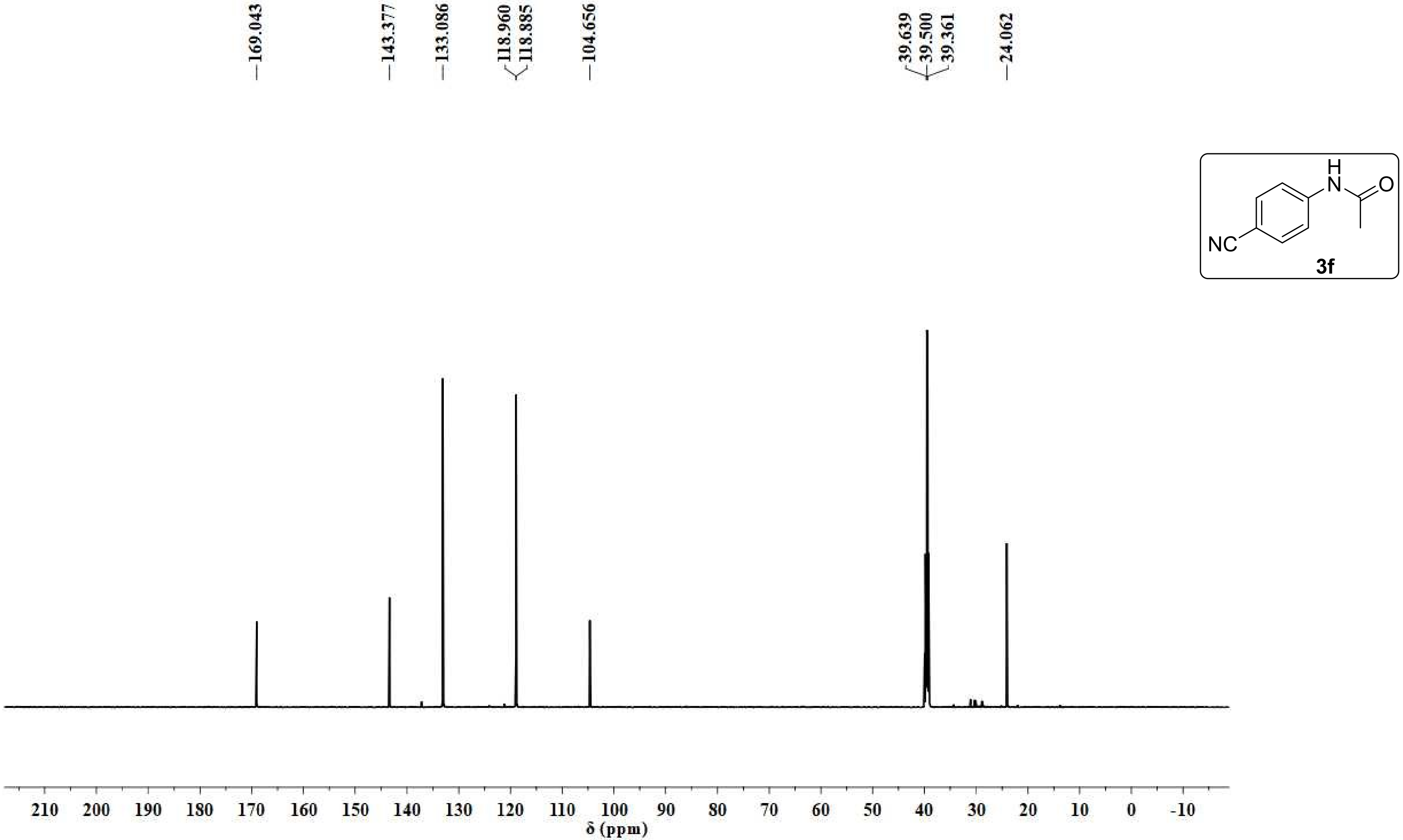
-1.
δ (ppm)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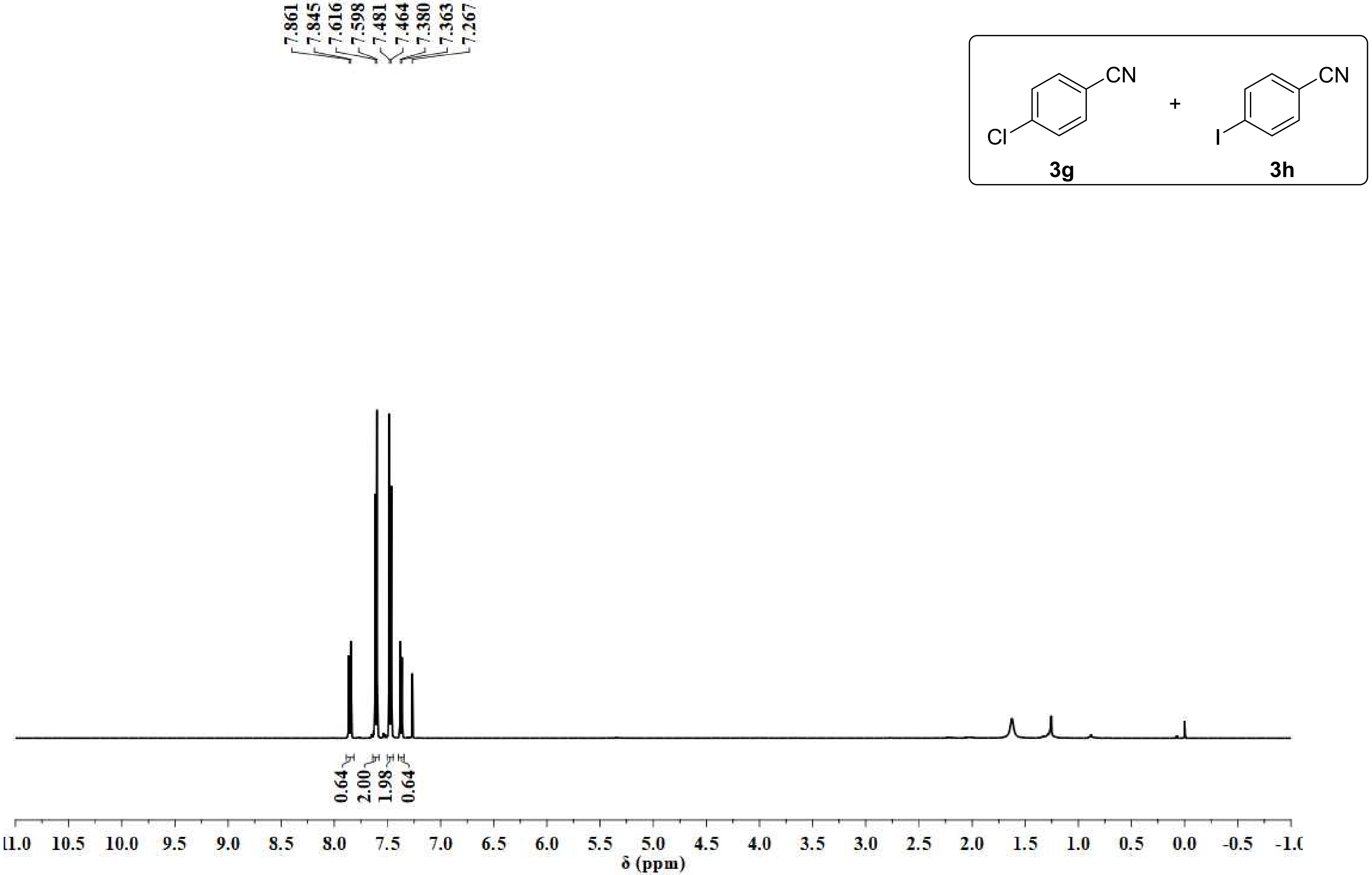
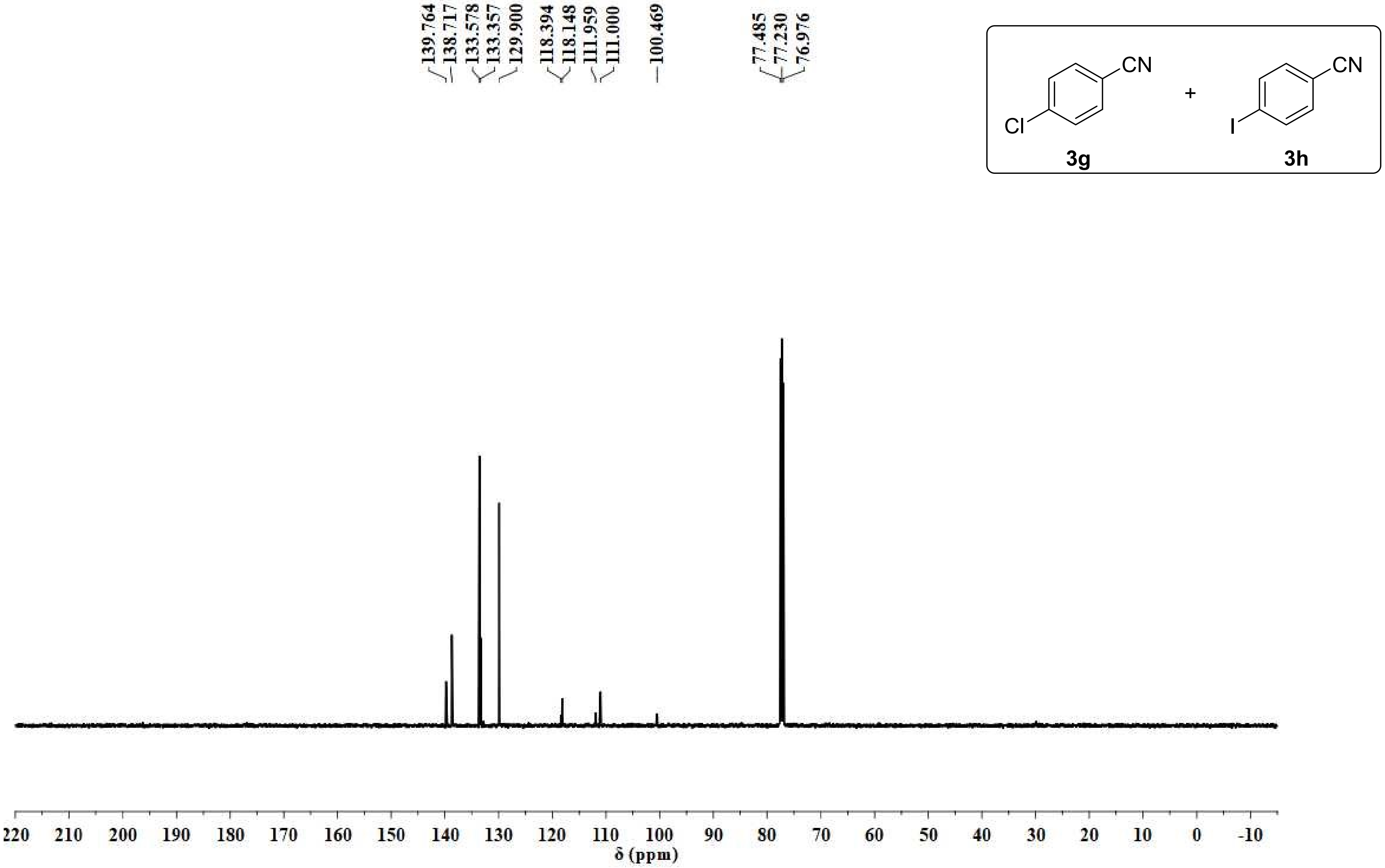
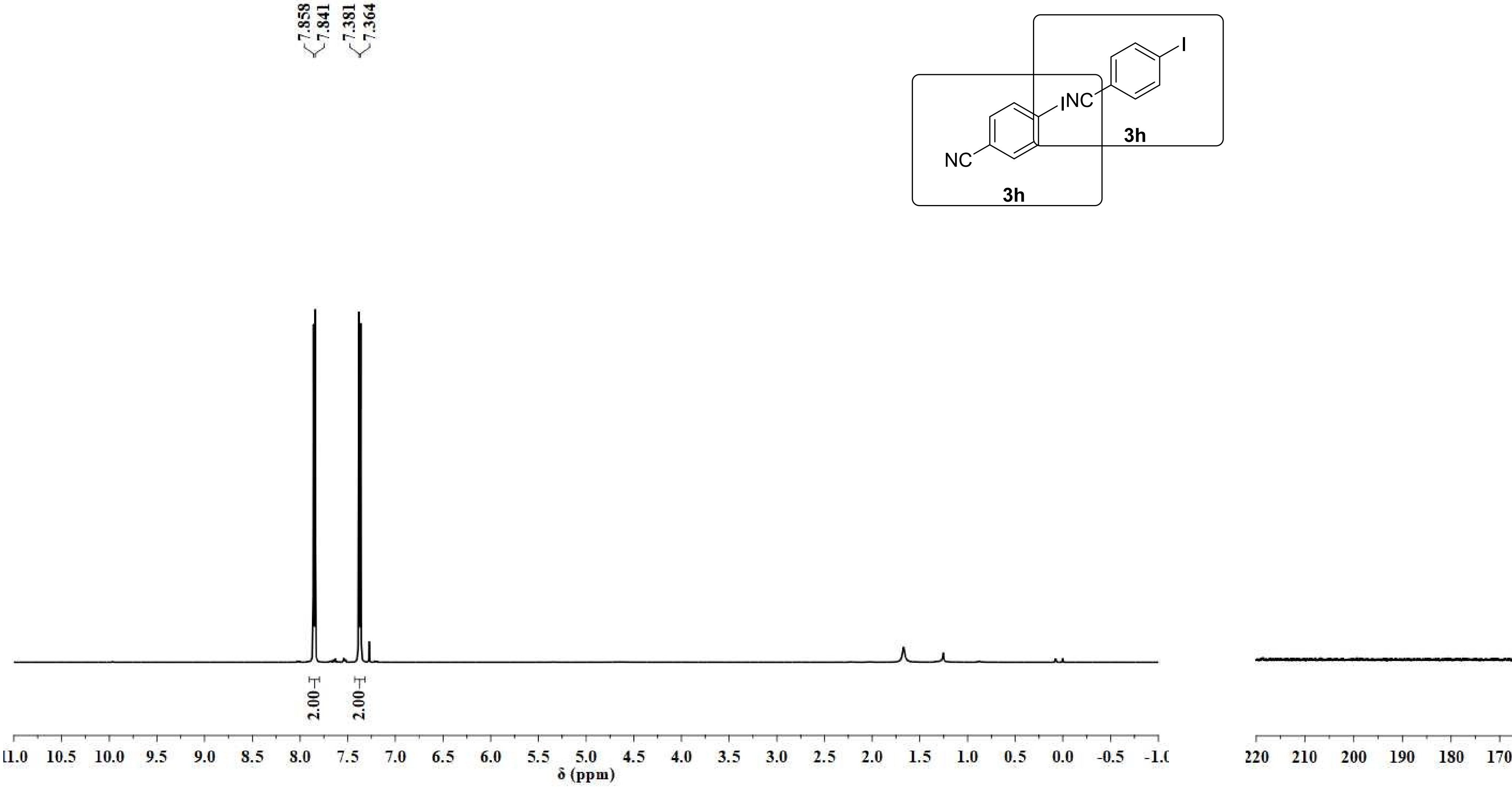
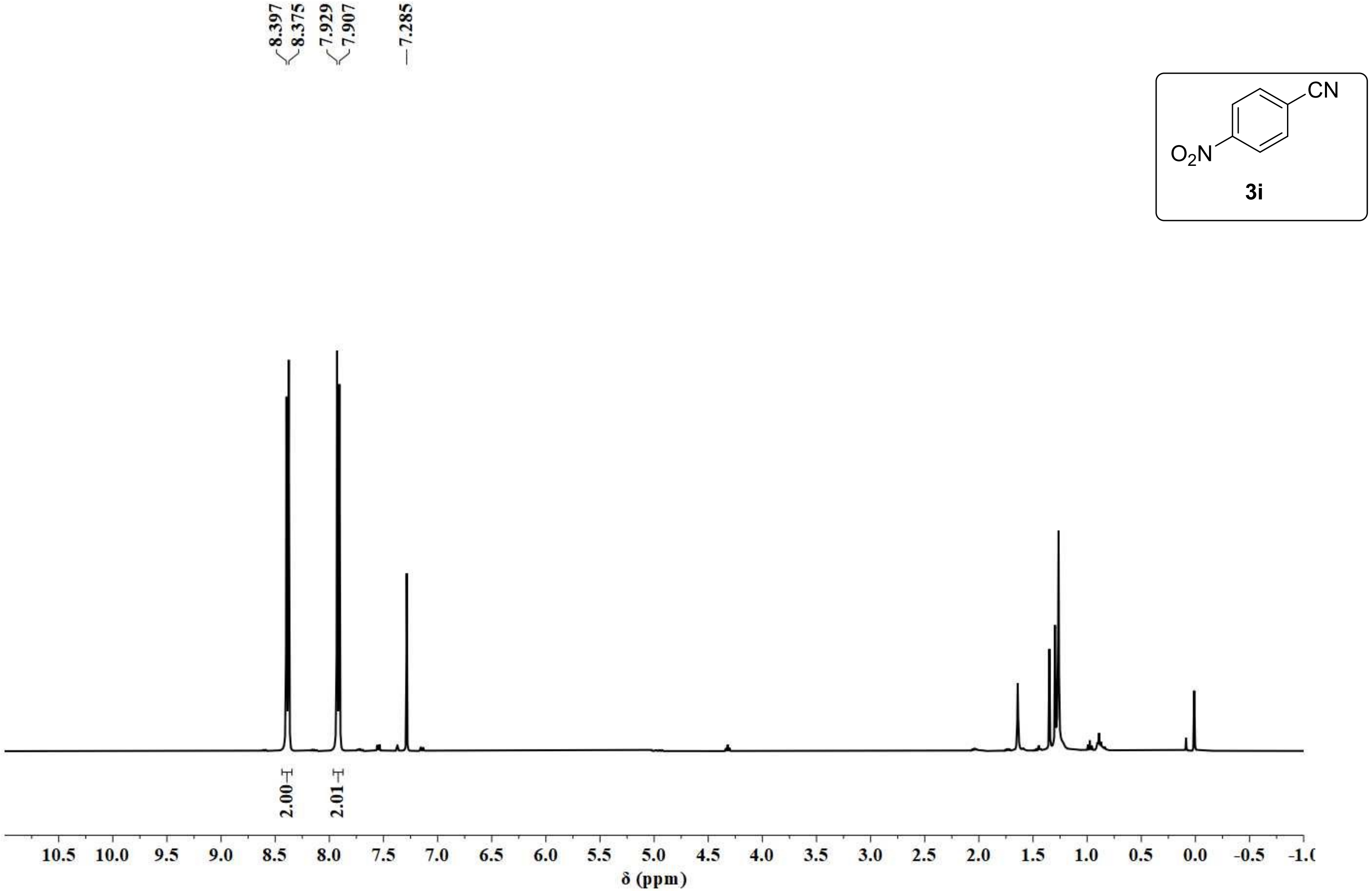
104.656
39.639
39.500
39.361
24.062
H
N
O
NC
3f
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)


3g + 3h

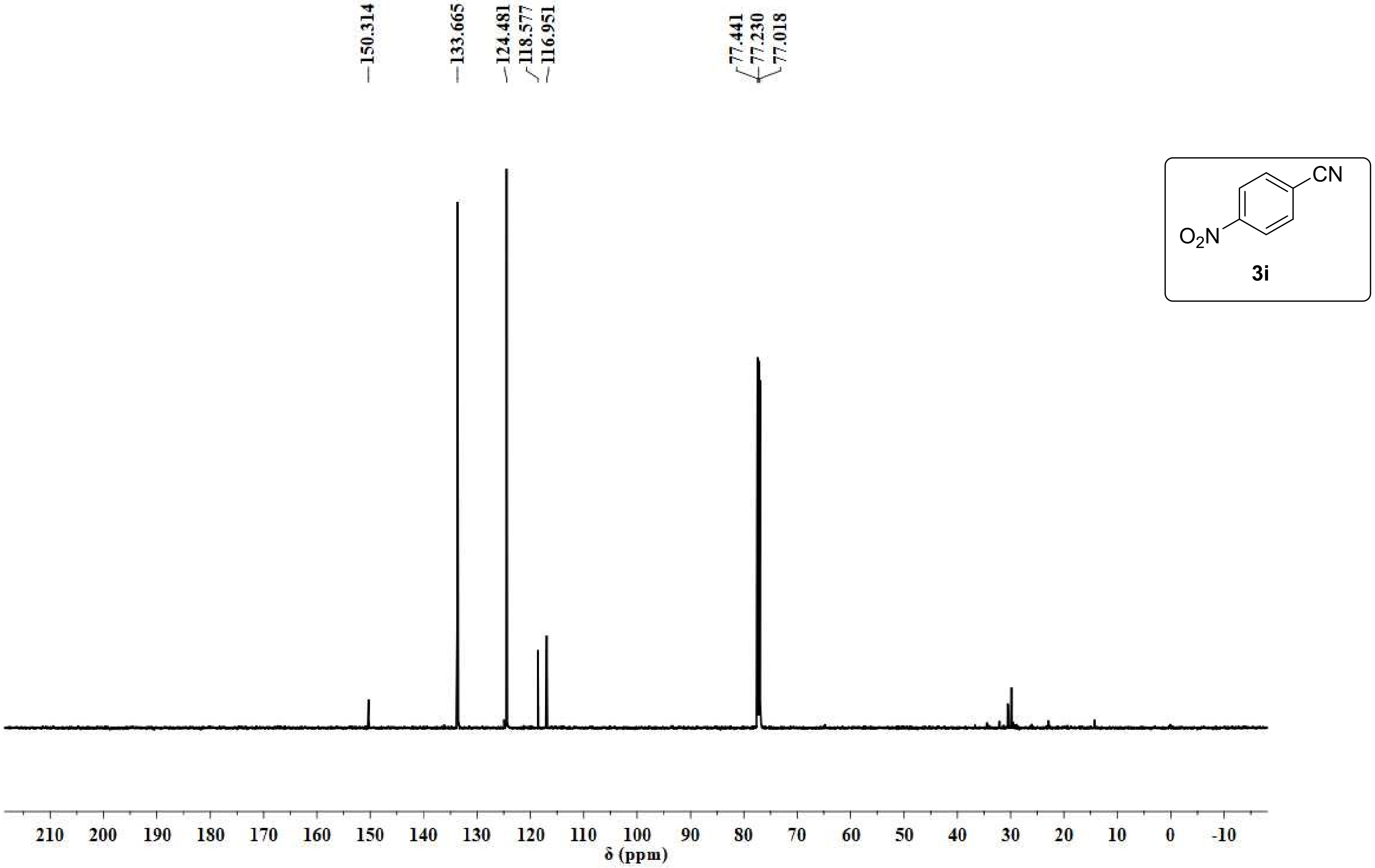
7.861
7.845
7.616
7.598
7.481
7.464
7.380
7.363
7.267
0.64
2.00
1.98
0.64
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.(
δ (ppm)

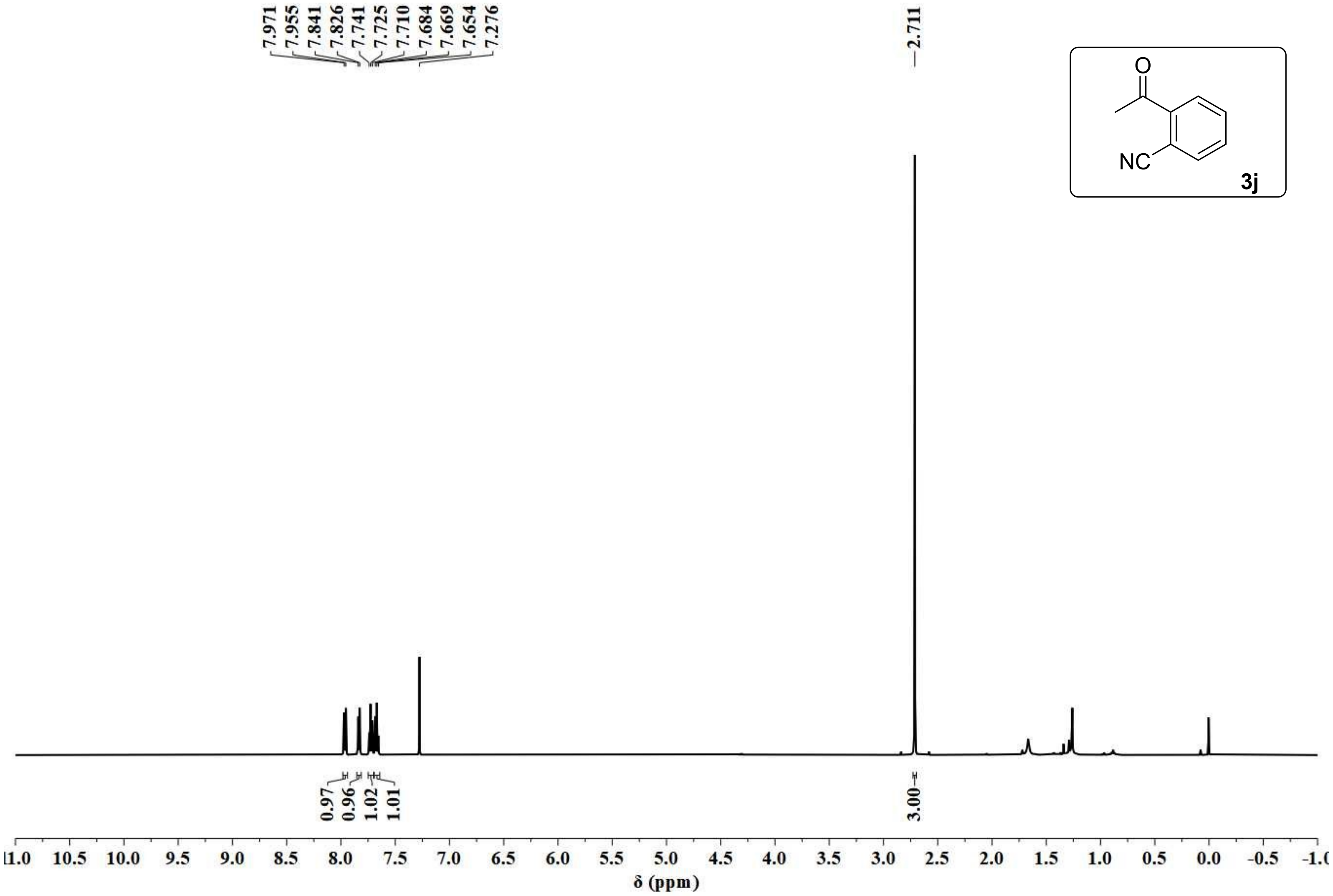

139.764
138.717
133.578
133.357
129.900
118.394
118.148
111.959
111.000
100.469
77.485
77.230
76.976
CN
Cl
+
CN
I
3g
3h
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)

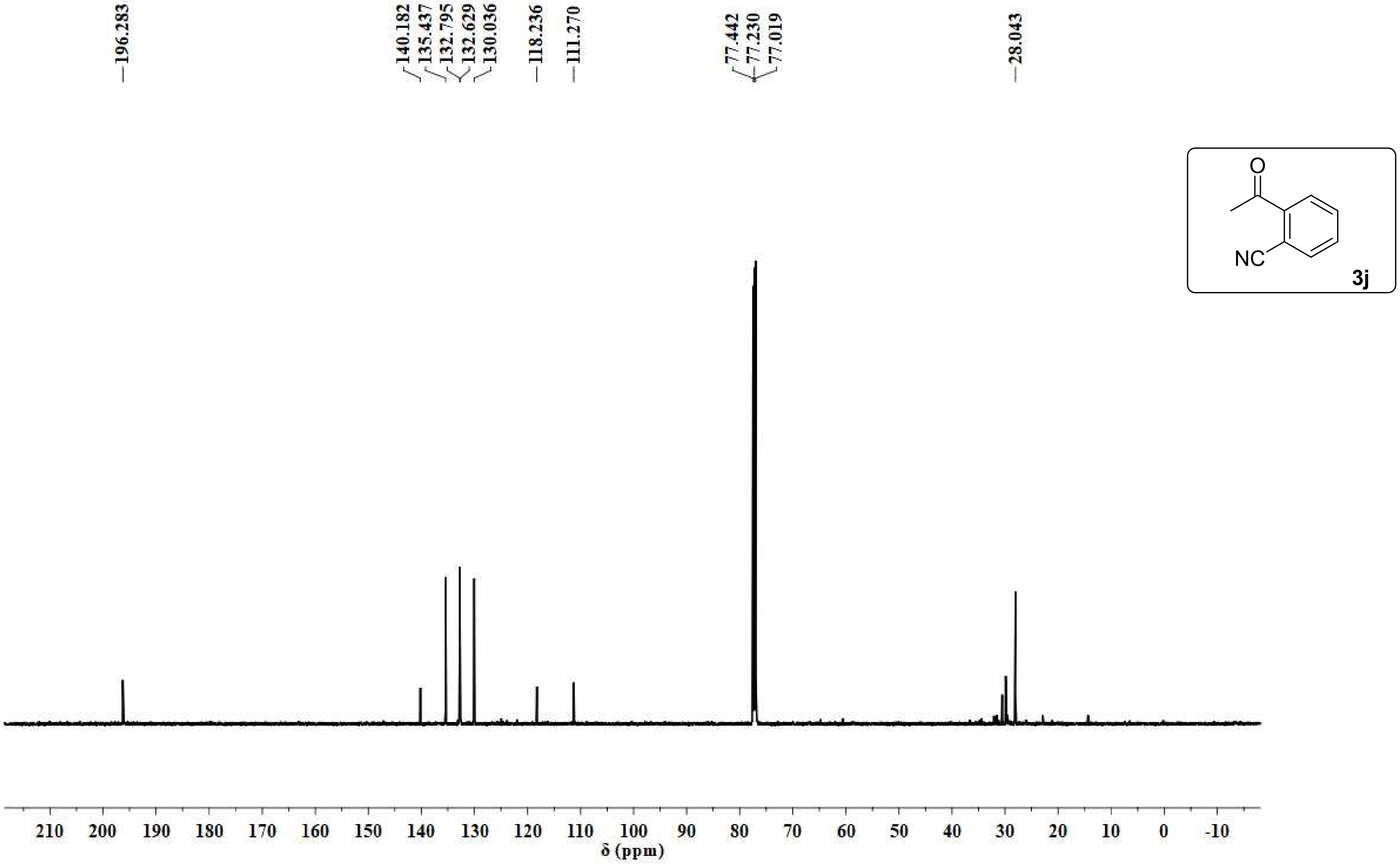

7.858
7.841
7.381
7.364
NC
I
NC
I
3h
3h
2.00
2.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
δ (ppm)
220
210
200
190
180
170

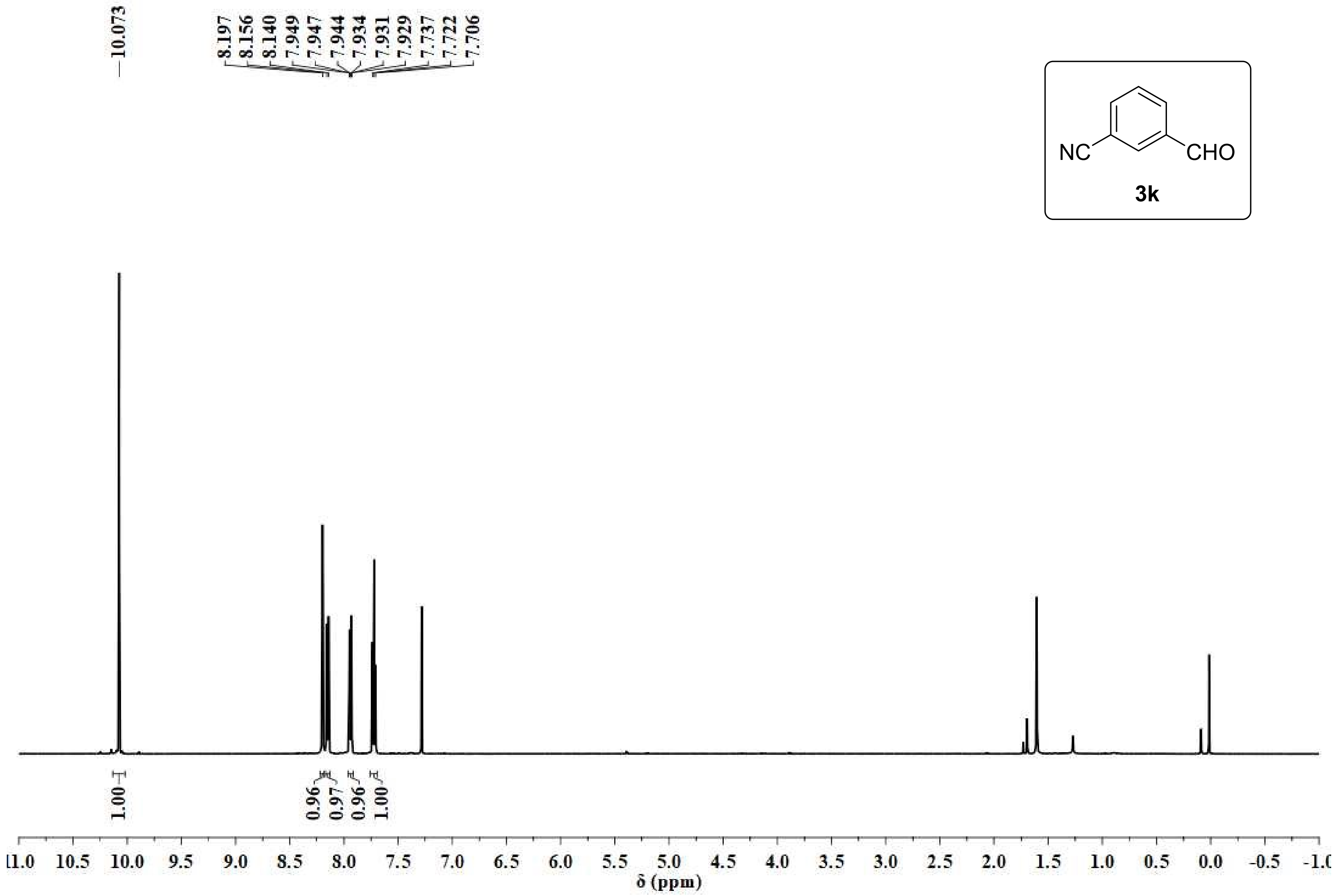

8.397
8.375
7.929
7.907
7.285
CN
O$_2$N
2.00
2.01
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
δ (ppm)

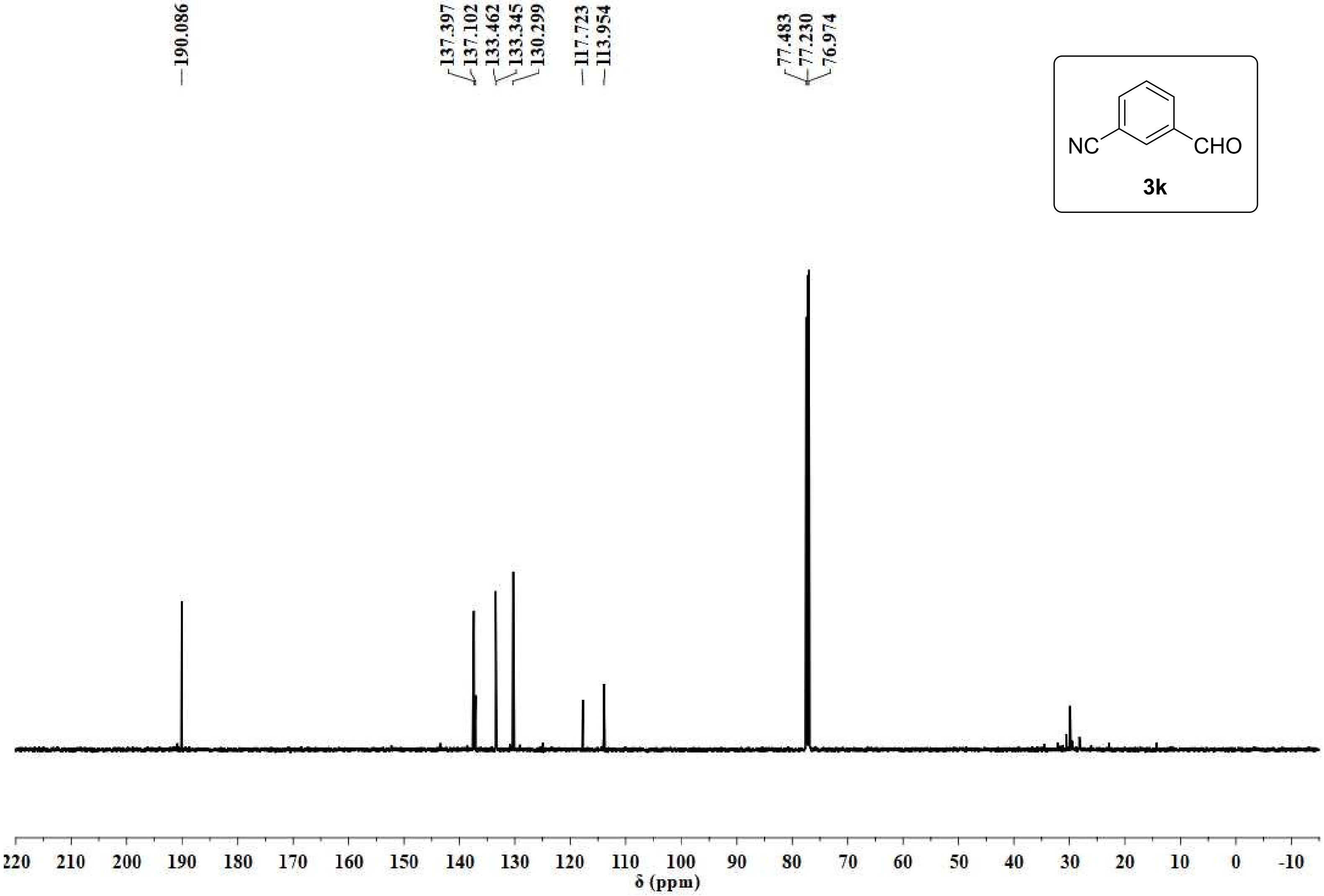
3i

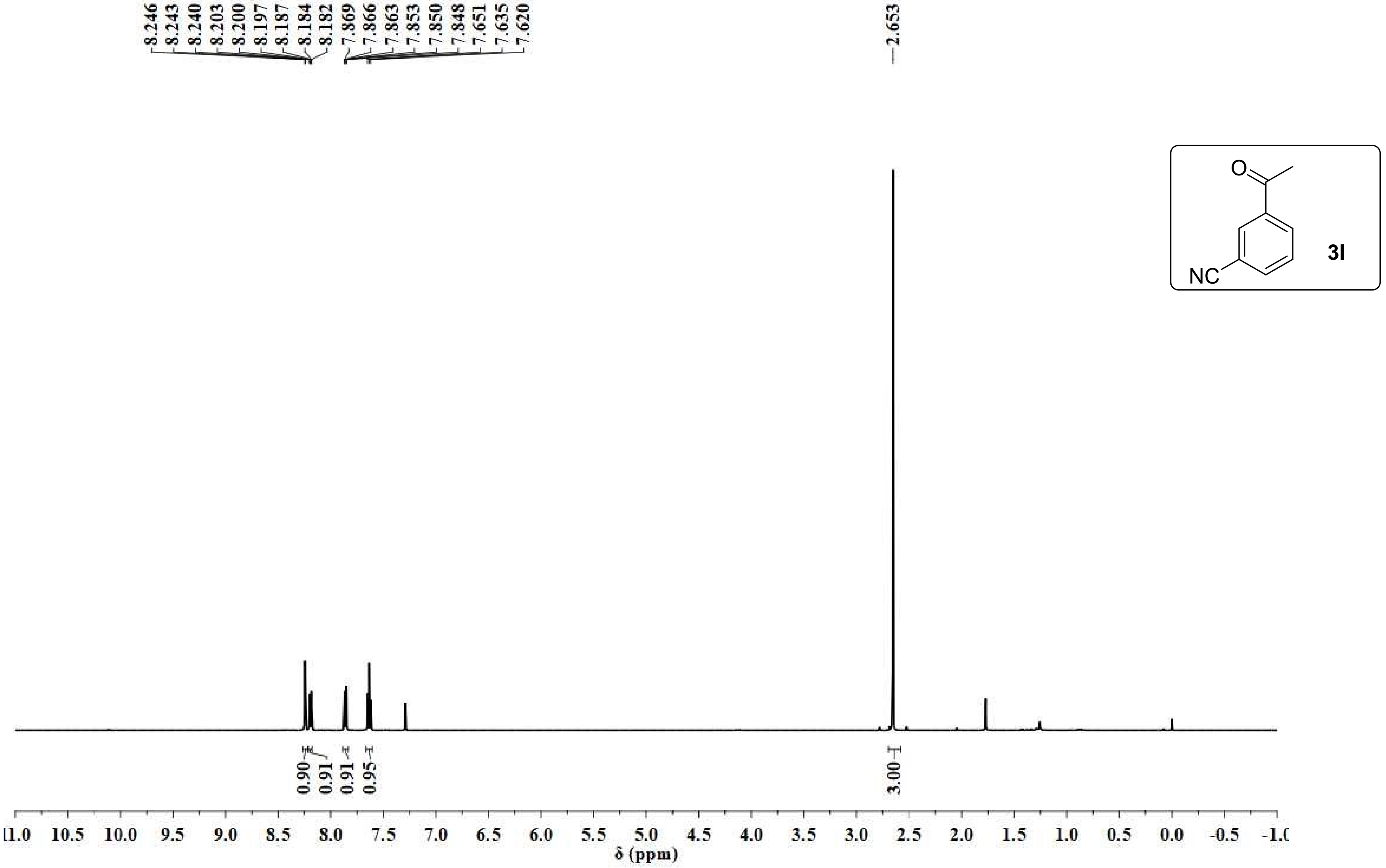

150.314
133.665
124.481
118.577
116.951
77.441
77.230
77.018
CN
O2N
3i
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)

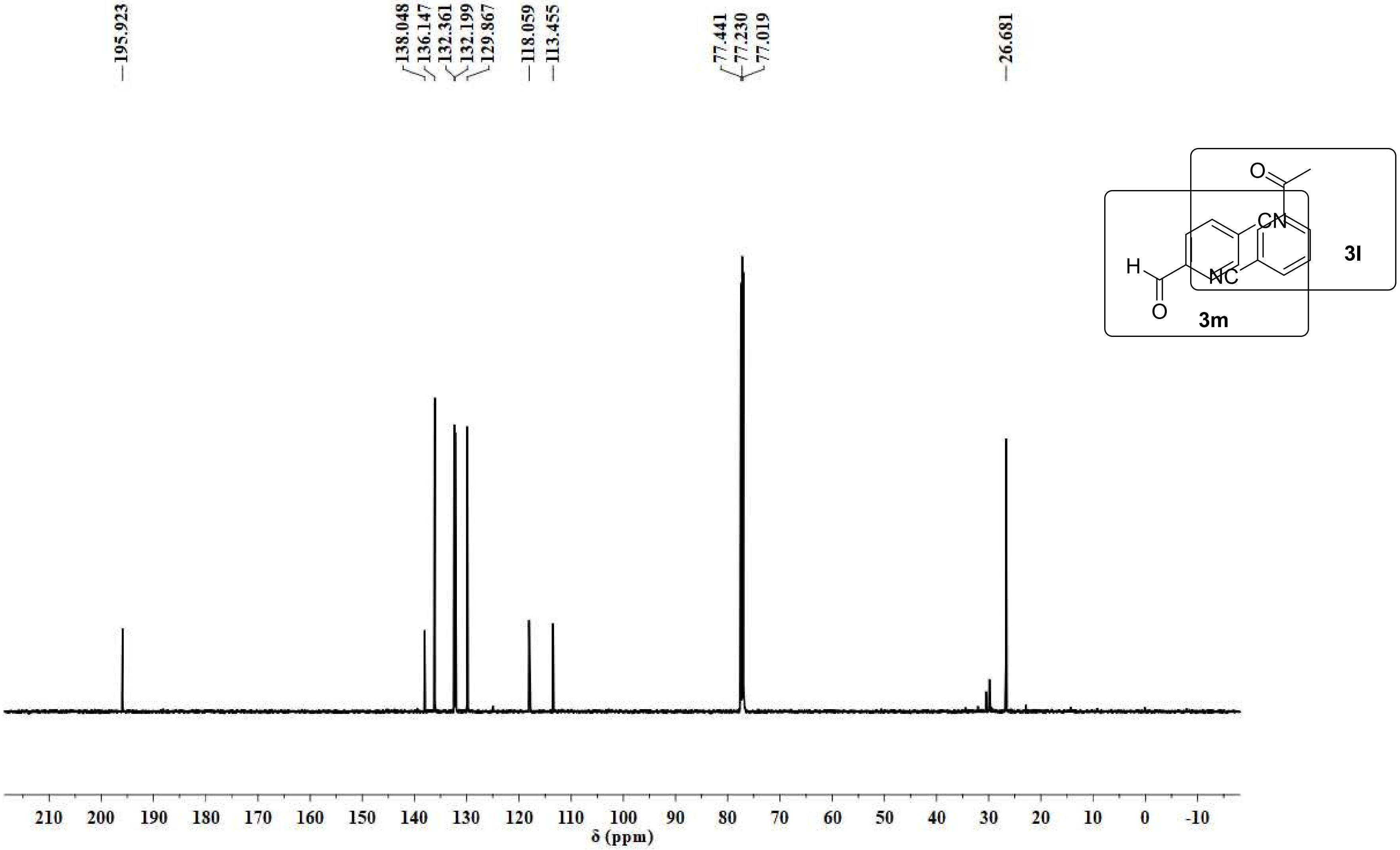

7.971
7.955
7.841
7.826
7.741
7.725
7.710
7.684
7.669
7.654
7.276
2.711
O
NC
3j
0.97
0.96
1.02
1.01
3.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
δ (ppm)


196.283
140.182
135.437
132.795
132.629
130.036
118.236
111.270
77.442
77.230
77.019
28.043
O
NC
3j
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)

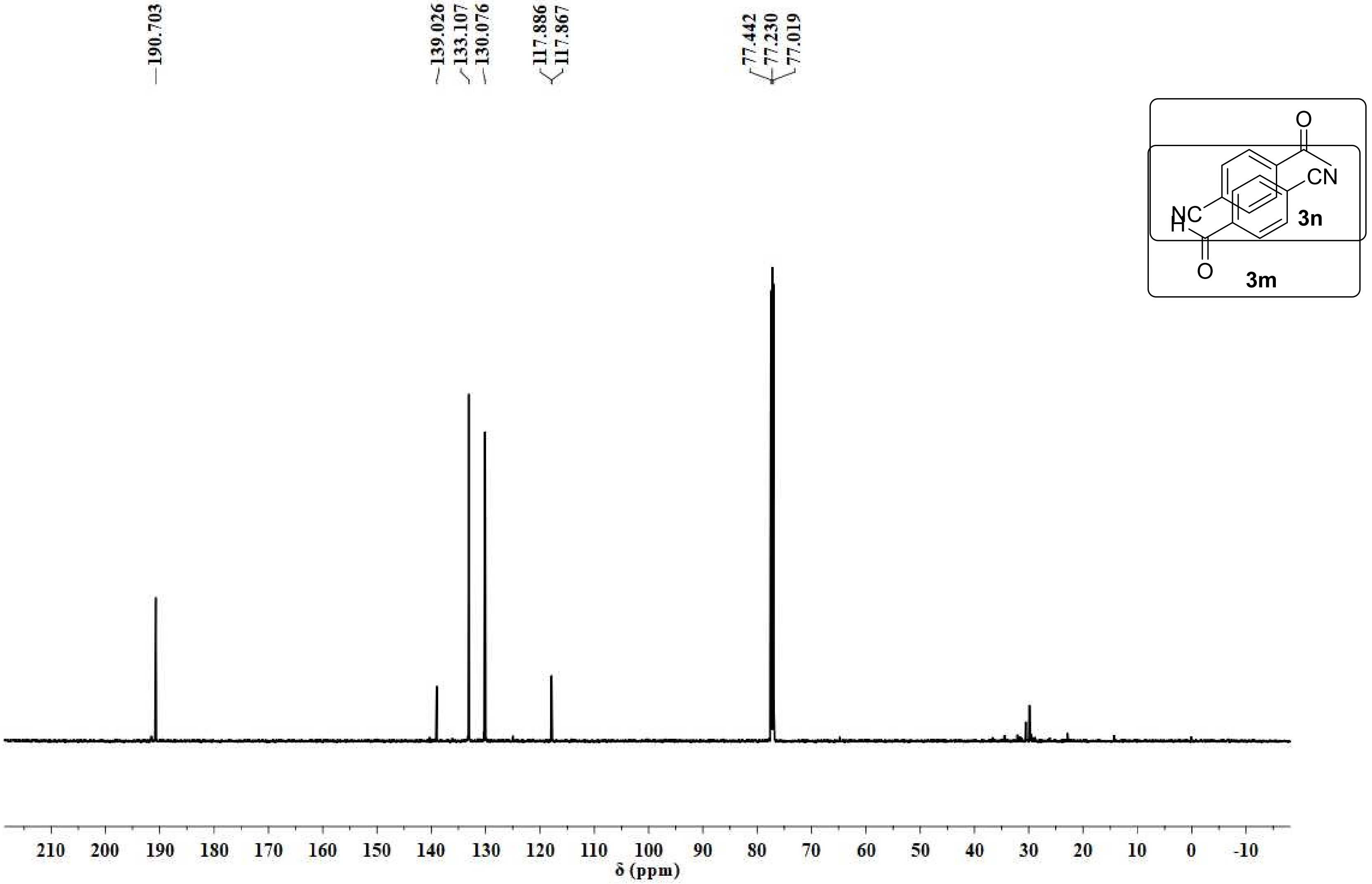

10.073
8.197
8.156
8.140
7.949
7.947
7.944
7.934
7.931
7.929
7.737
7.722
7.706
NC
CHO
3k
1.00
0.96
0.97
0.96
1.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
δ (ppm)

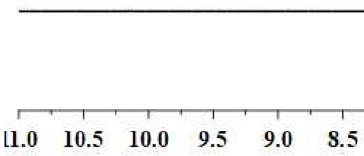

190.086
137.397
137.102
133.462
133.345
130.299
117.723
113.954
77.483
77.230
76.974
NC
CHO
3k
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)

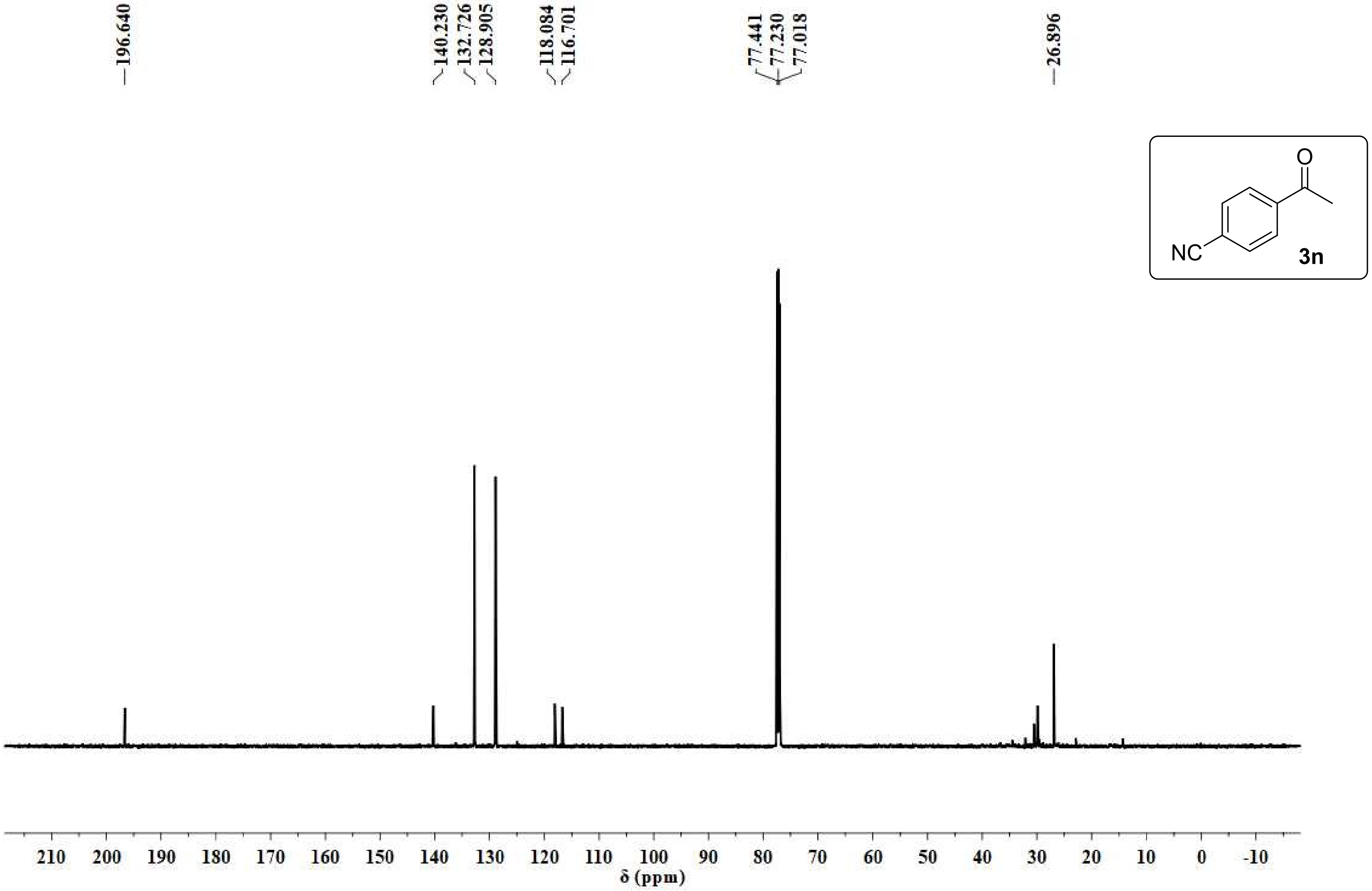

8.246
8.243
8.240
8.203
8.200
8.197
8.187
8.184
8.182
7.869
7.866
7.863
7.853
7.850
7.848
7.651
7.635
7.620
2.653
O
NC
3l
0.90
0.91
0.91
0.95
3.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
δ (ppm)

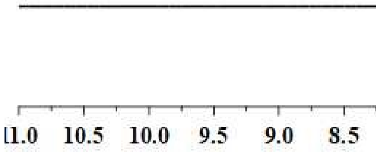

195.923
138.048
136.147
132.361
132.199
129.867
118.059
113.455
77.441
77.230
77.019
26.681
H
O
NC
CN
O
3m
3l
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)

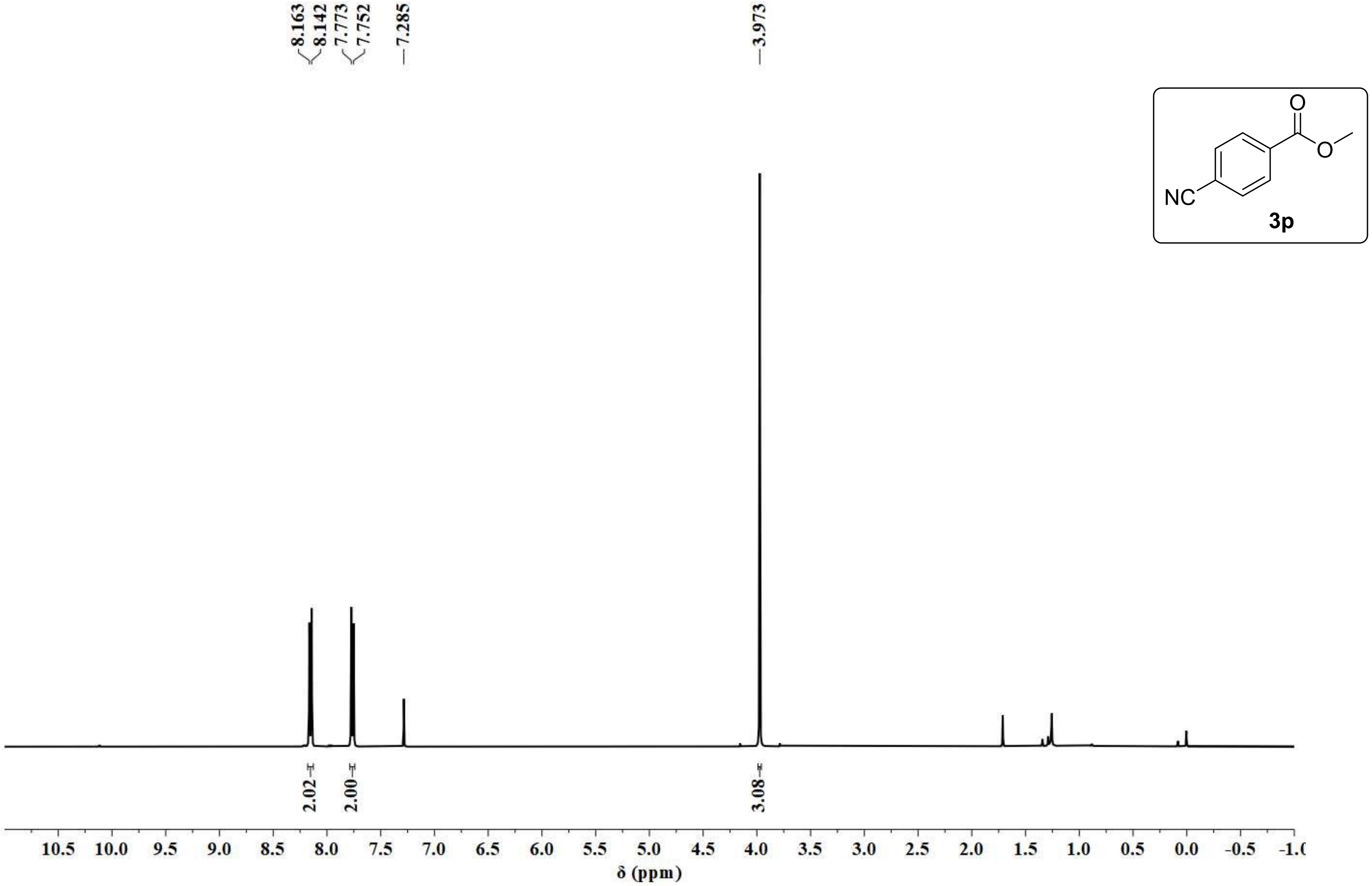

10.026
1.00
11.0 10.5 10.0 9.5

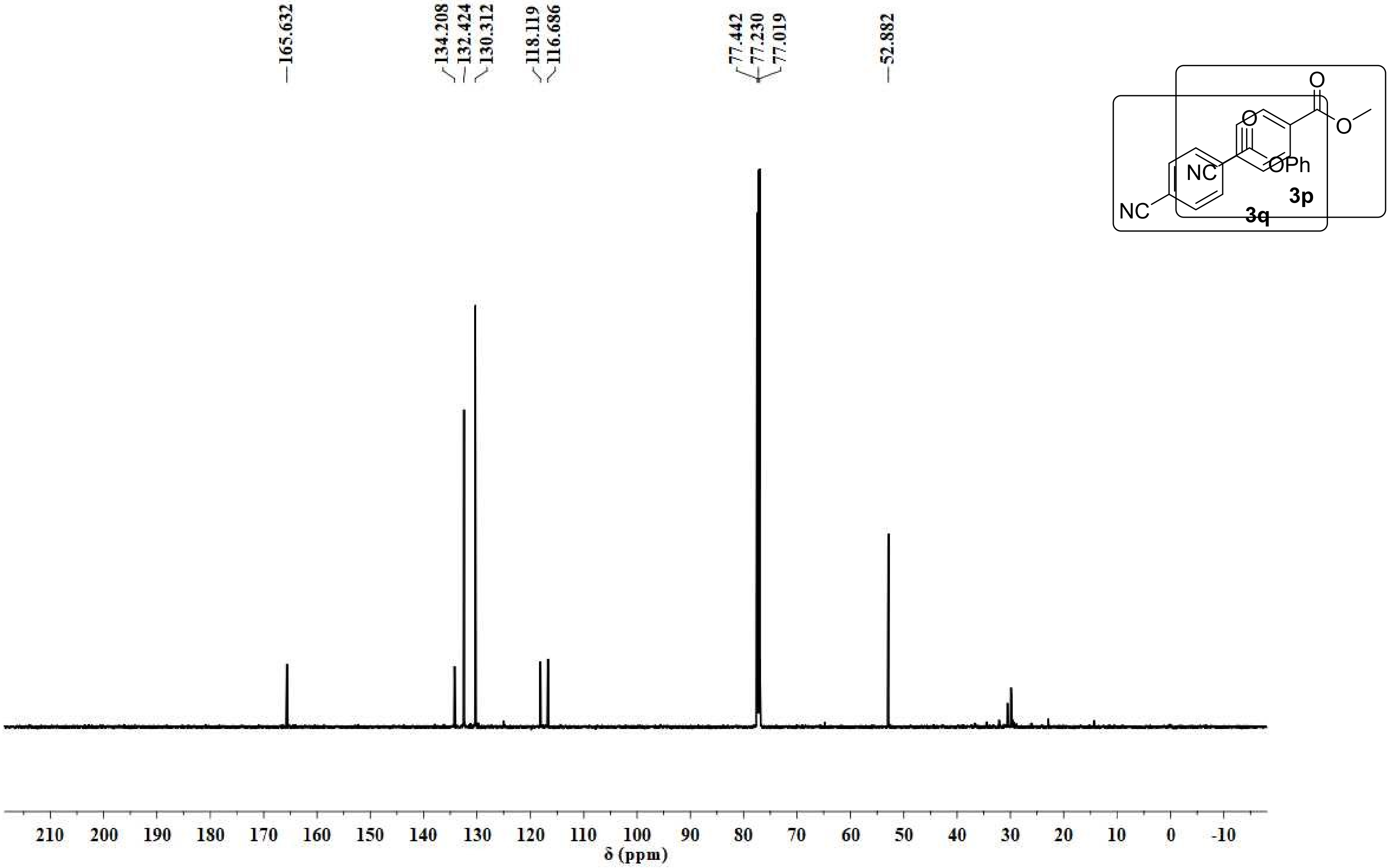

190.703
139.026
133.107
130.076
117.886
117.867
77.442
77.230
77.019
O
CN
NC
H
O
3n
3m
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)

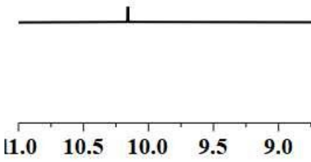

11.0 10.5 10.0 9.5 9.0 8.5

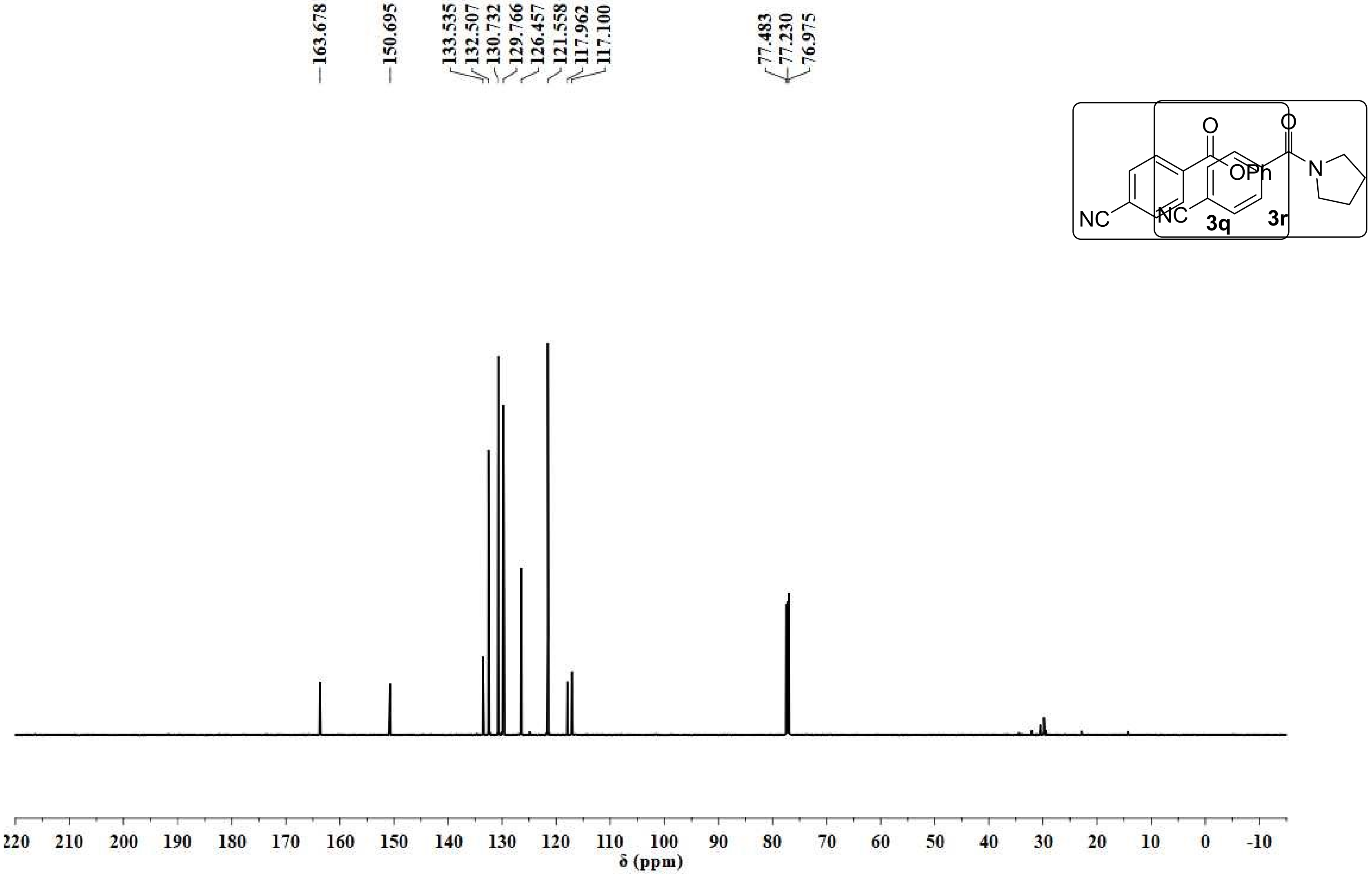

196.640
140.230
132.726
128.905
118.084
116.701
77.441
77.230
77.018
26.896
O
NC
3n
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)

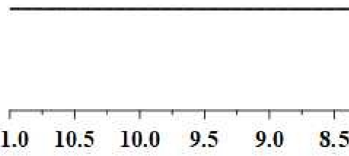

11.0
10.5
10.0
9.5
9.0
8.5

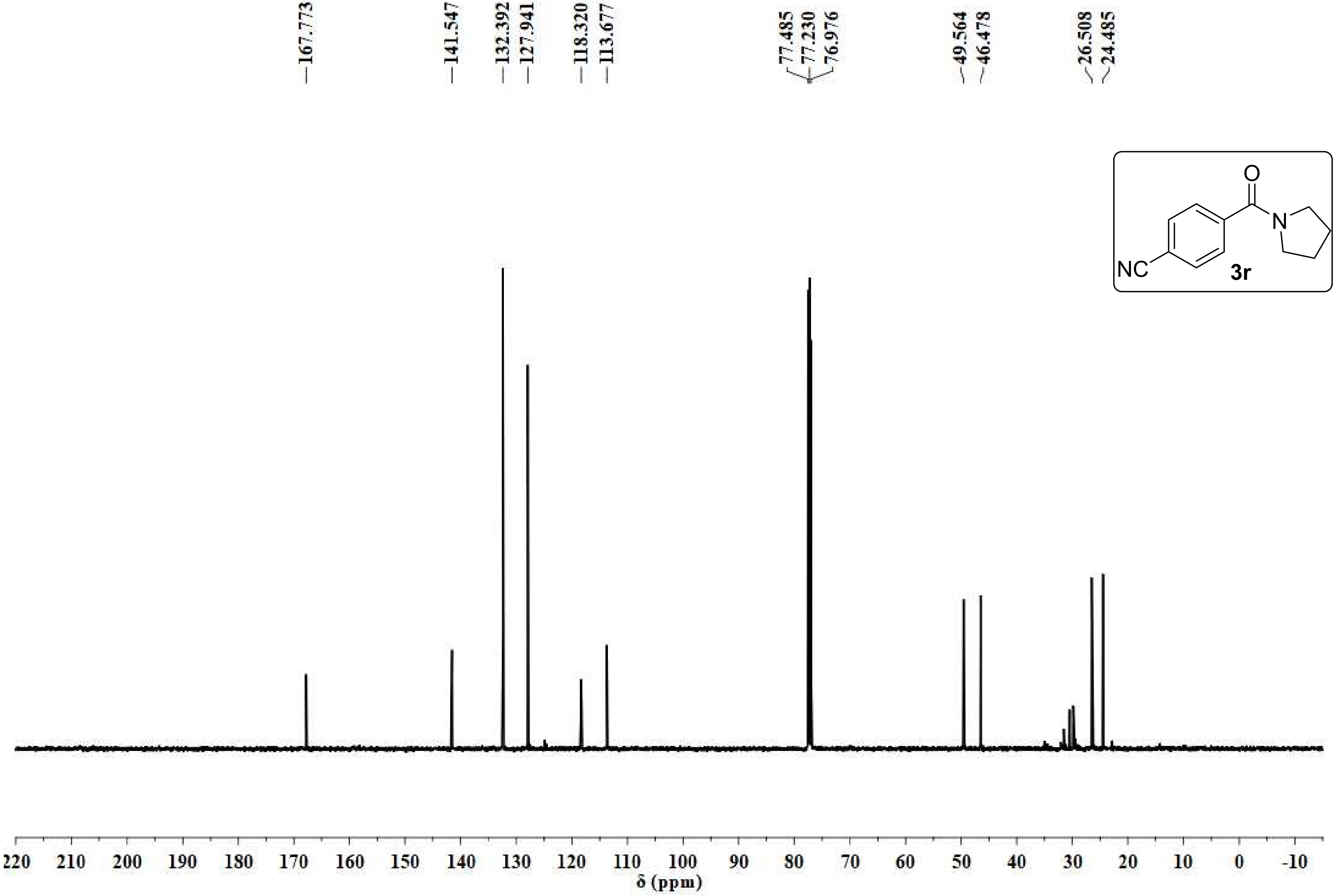

8.163
8.142
7.773
7.752
7.285
3.973
2.02
2.00
3.08
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.(
δ (ppm)
O
O
NC
3p

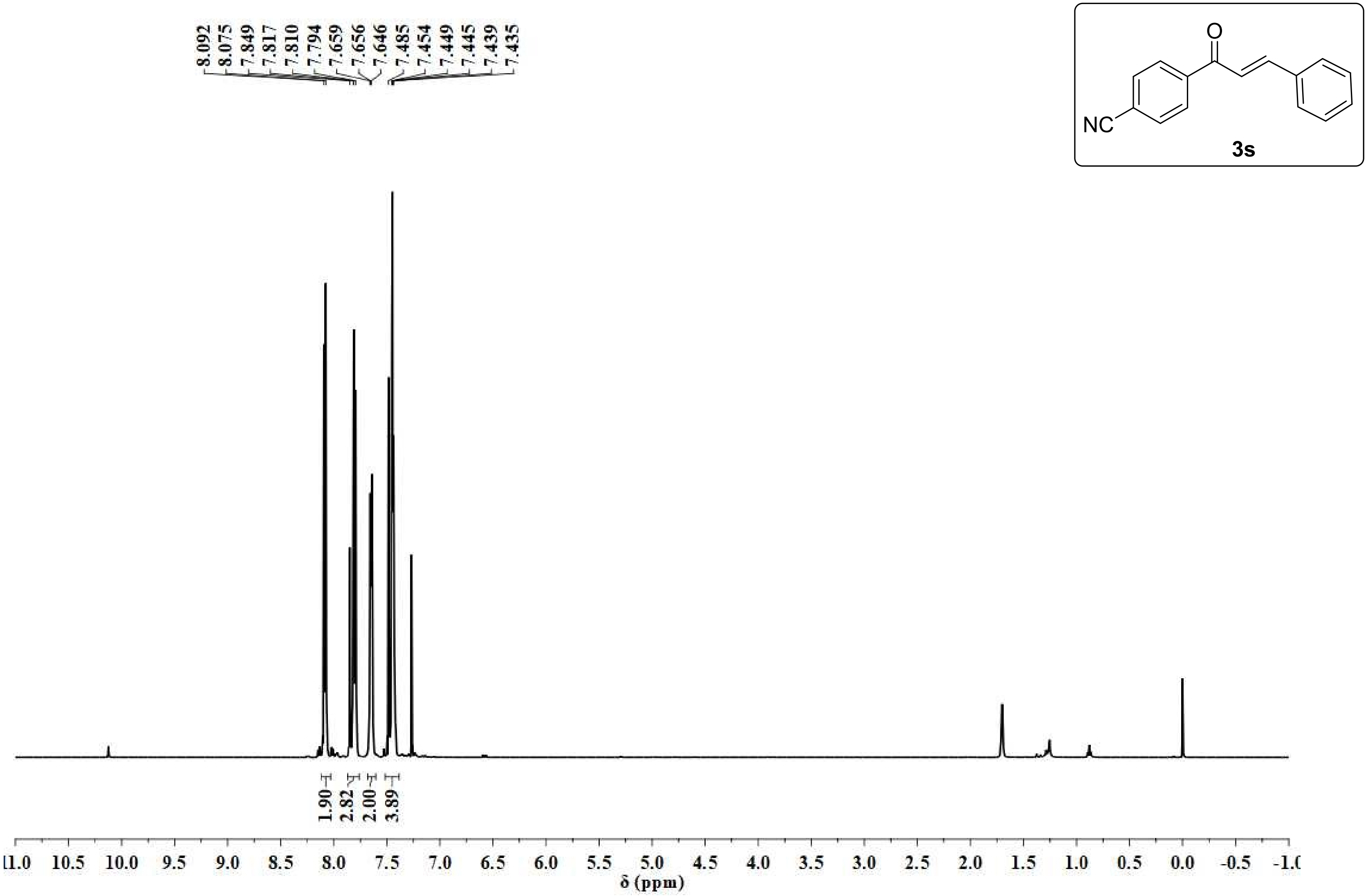

165.632
134.208
132.424
130.312
118.119
116.686
77.442
77.230
77.019
52.882
O
O
O
NC
OPh
NC
3p
3q
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)

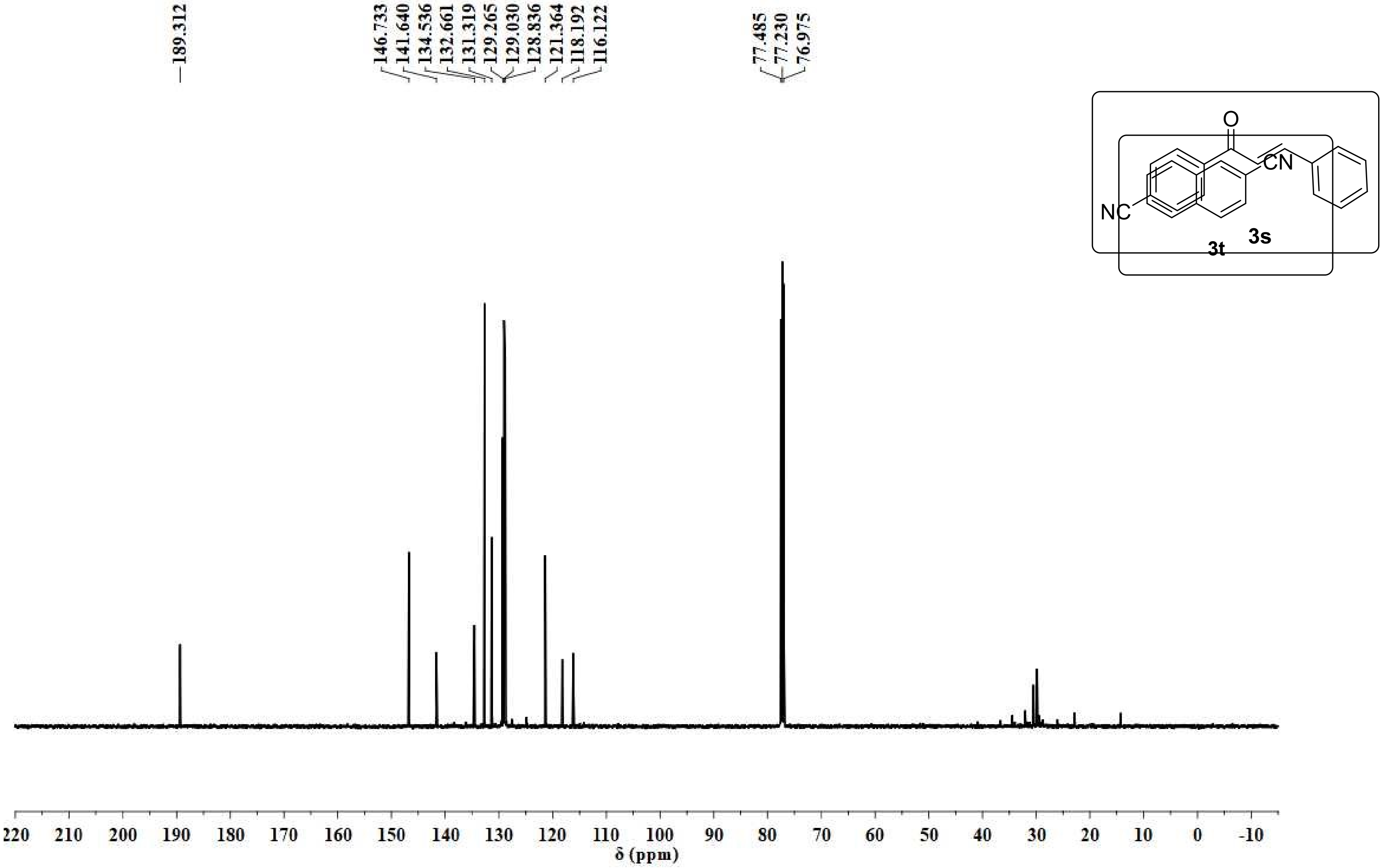

11.0 10.5 10.0 9.5 9.0


163.678
150.695
133.535
132.507
130.732
129.766
126.457
121.558
117.962
117.100
77.483
77.230
76.975
O
O
OPh
N
NC
NC
3q
3r
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)

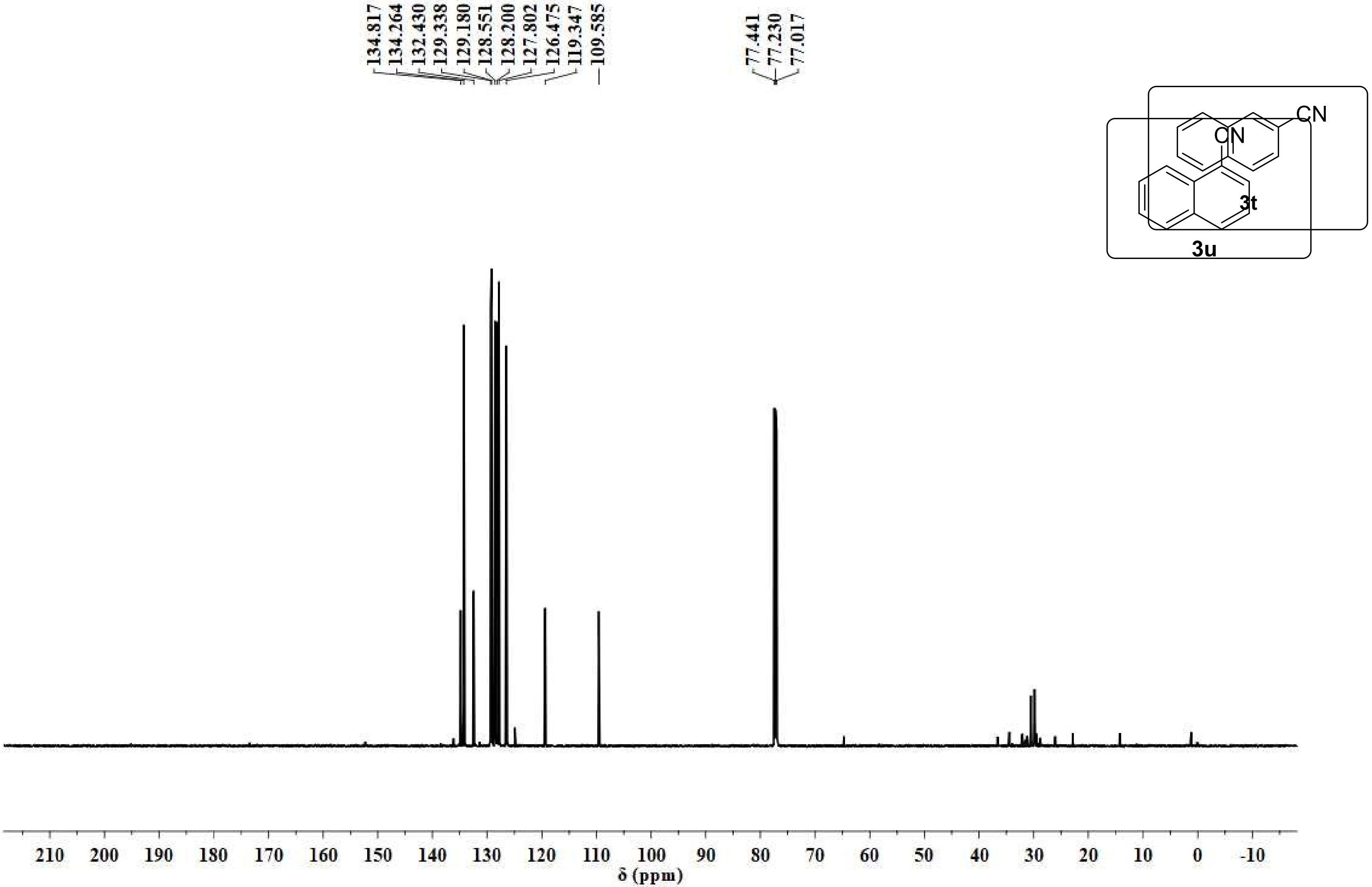

11.0
10.5
10.0
9.5
9.0
8.5


167.773
141.547
132.392
127.941
118.320
113.677
77.485
77.230
76.976
49.564
46.478
26.508
24.485
O
N
NC
3r
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)

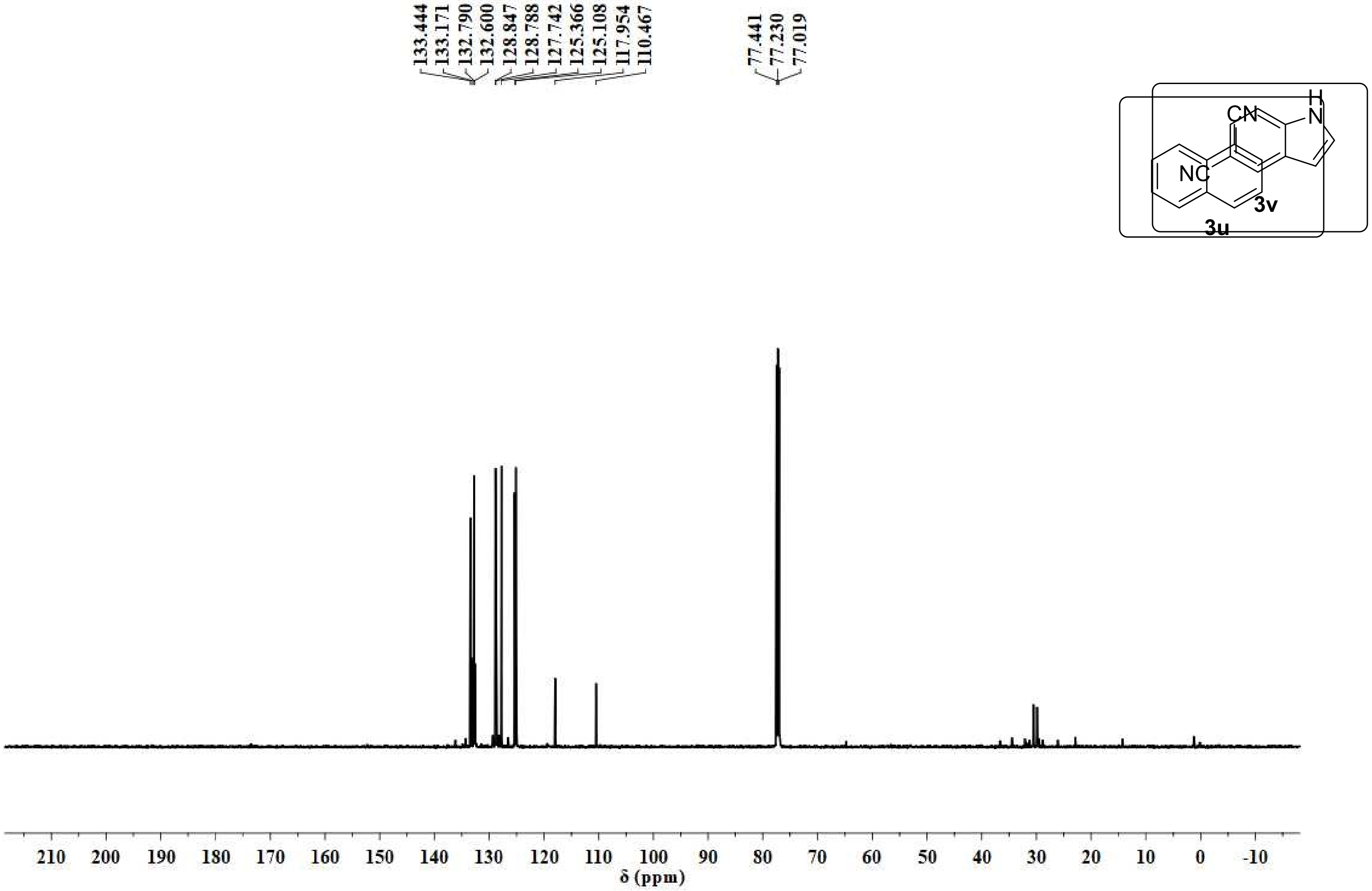

8.092
8.075
7.849
7.817
7.810
7.794
7.659
7.656
7.646
7.485
7.454
7.449
7.445
7.439
7.435
1.90
2.82
2.00
3.89
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
δ (ppm)
O
NC
3s


189.312
146.733
141.640
134.536
132.661
131.319
129.265
129.030
128.836
121.364
118.192
116.122
77.485
77.230
76.975
O
CN
NC
3s
3t
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)

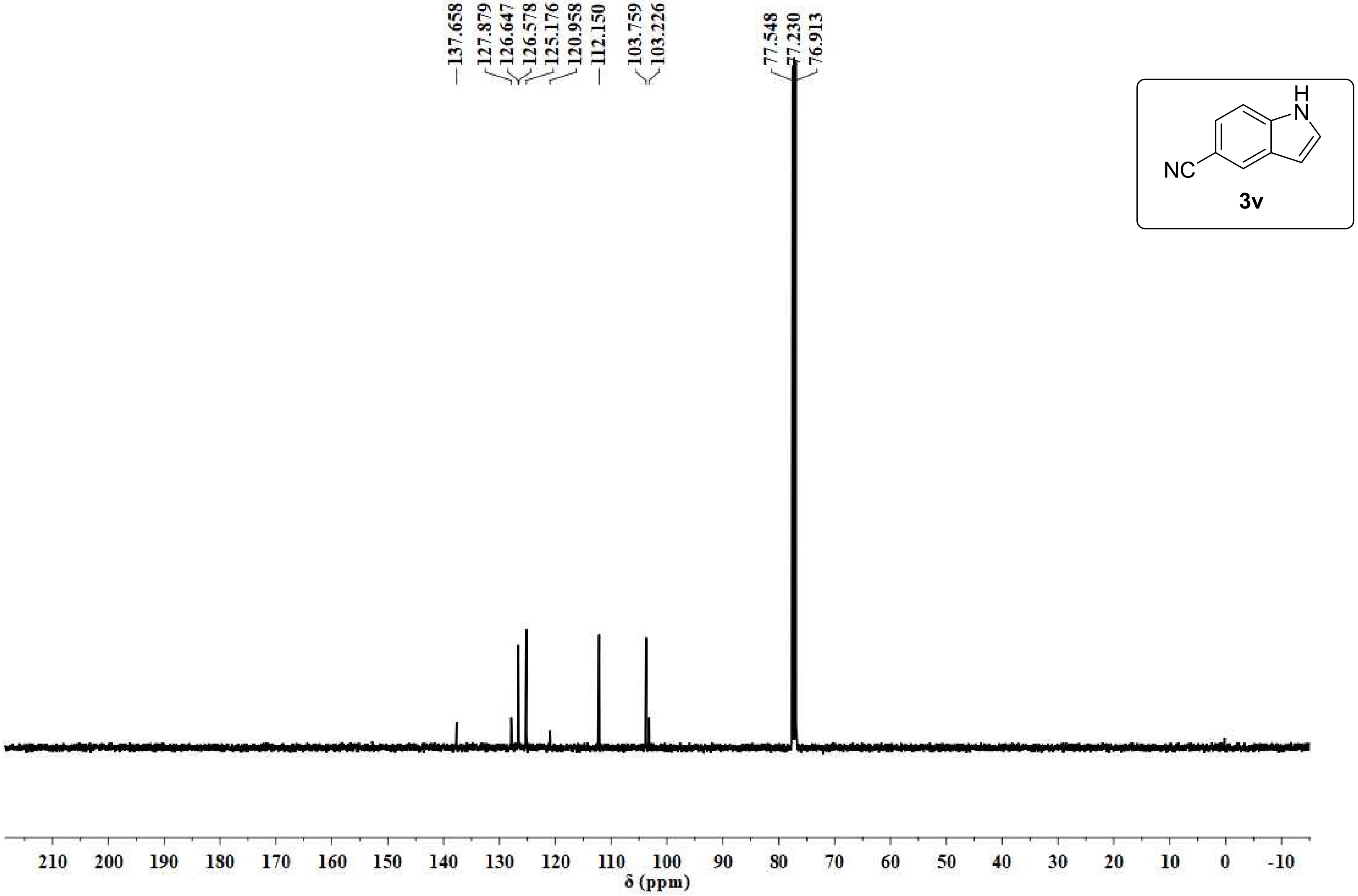

8.224
7.920
7.903
7.899
7.881
7.664
11.0 10.5 10.0 9.5 9.0


134.817
134.264
132.430
129.338
129.180
128.551
128.200
127.802
126.475
119.347
109.585
77.441
77.230
77.017
CN
CN
3t
3u
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)


8.224
8.207
8.064
8.047
7.911
7.895
7.893
7.881
7.878
7.689
7.687
1.00
11.0 10.5 10.0 9.5 9.0 8.5

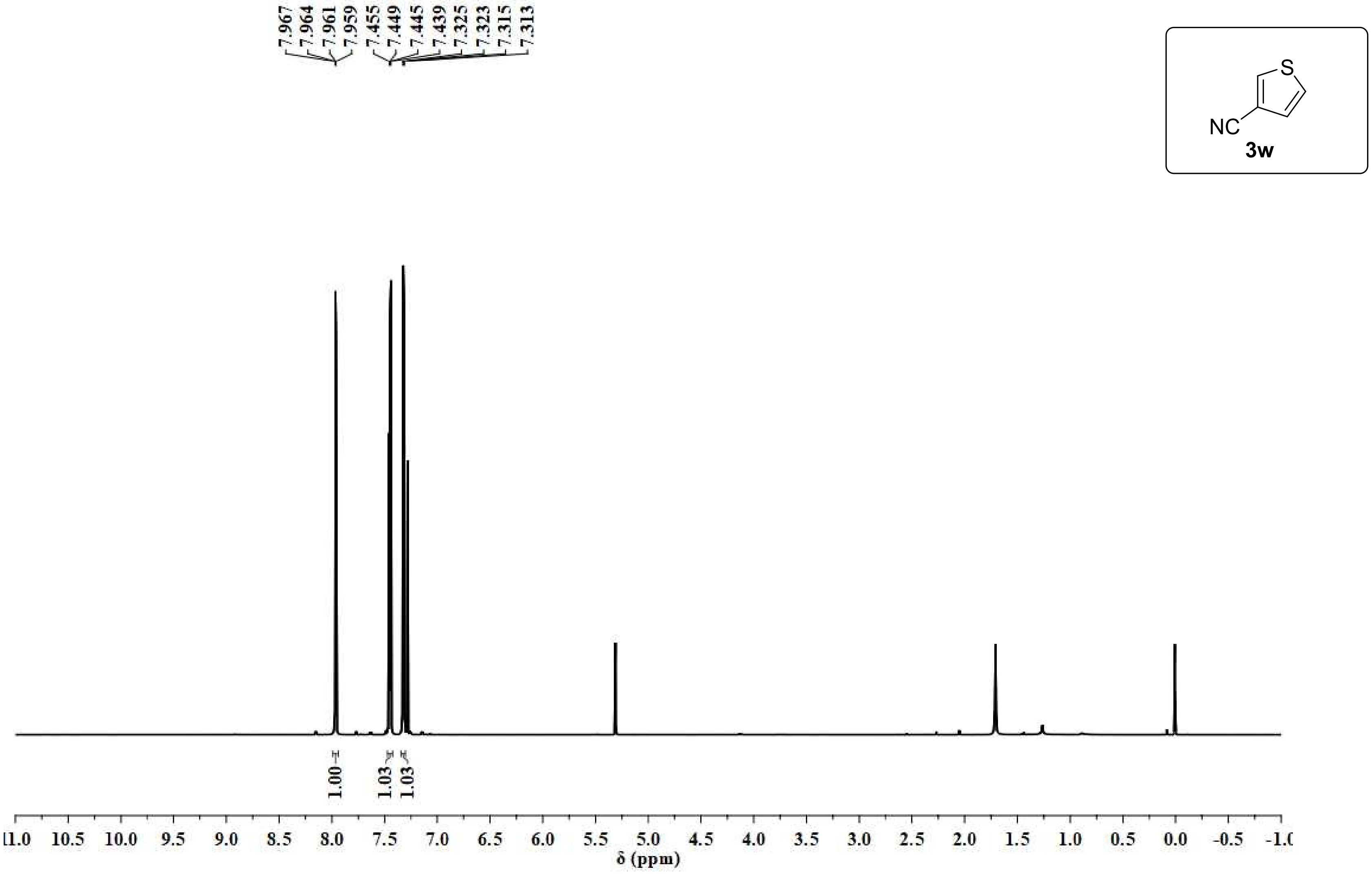

133.444
133.171
132.790
132.600
128.847
128.788
127.742
125.366
125.108
117.954
110.467
77.441
77.230
77.019
CN
H
N
NC
3v
3u
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
δ (ppm)


8.707
0.94
11.0 10.5 10.0 9.5 9.0 8.5

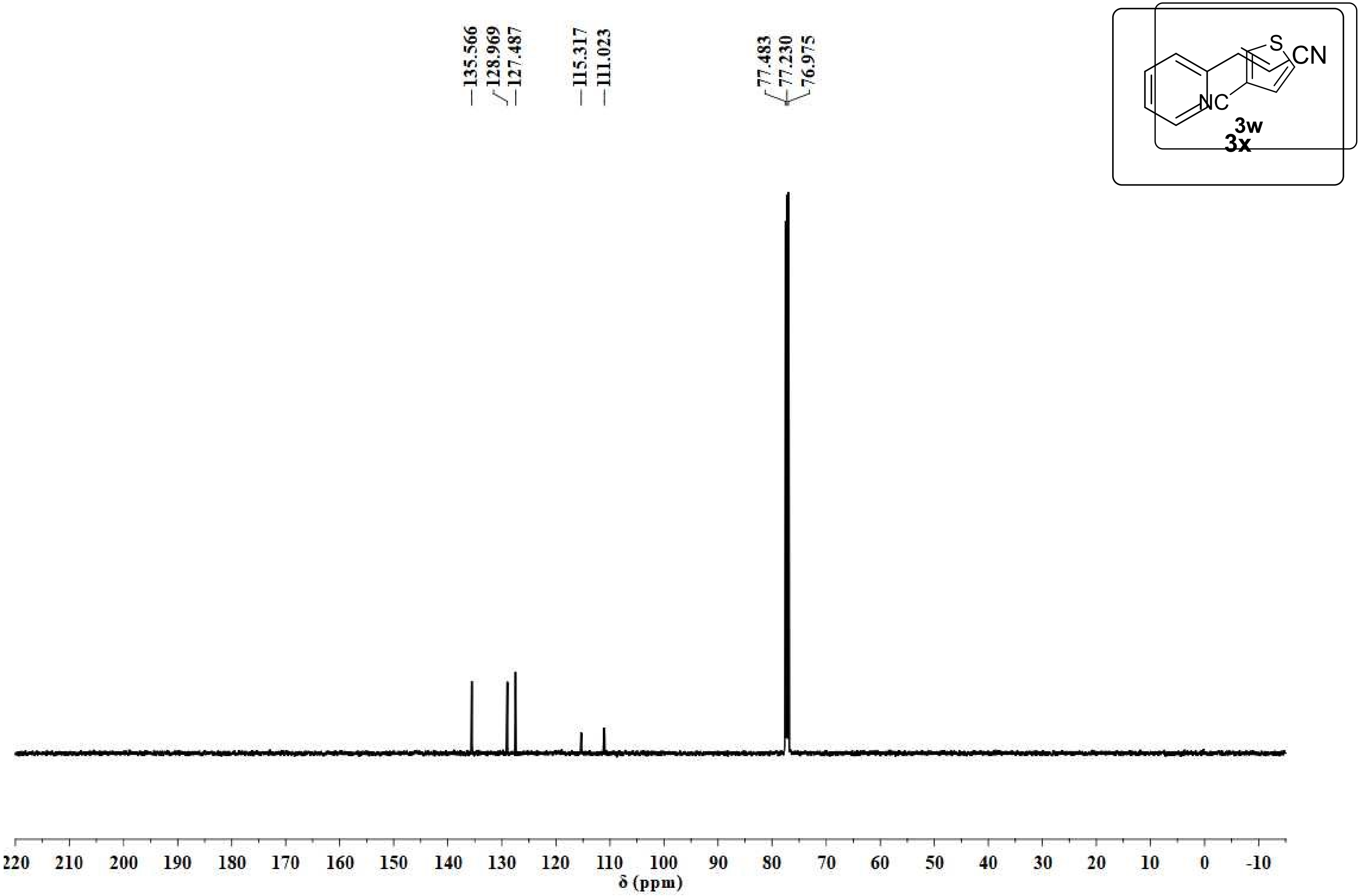

137.658
127.879
126.647
126.578
125.176
120.958
112.150
103.759
103.226
77.548
77.230
76.913
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)

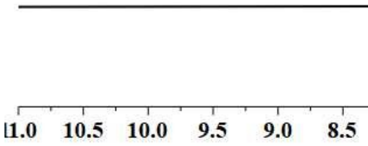
H
N
NC

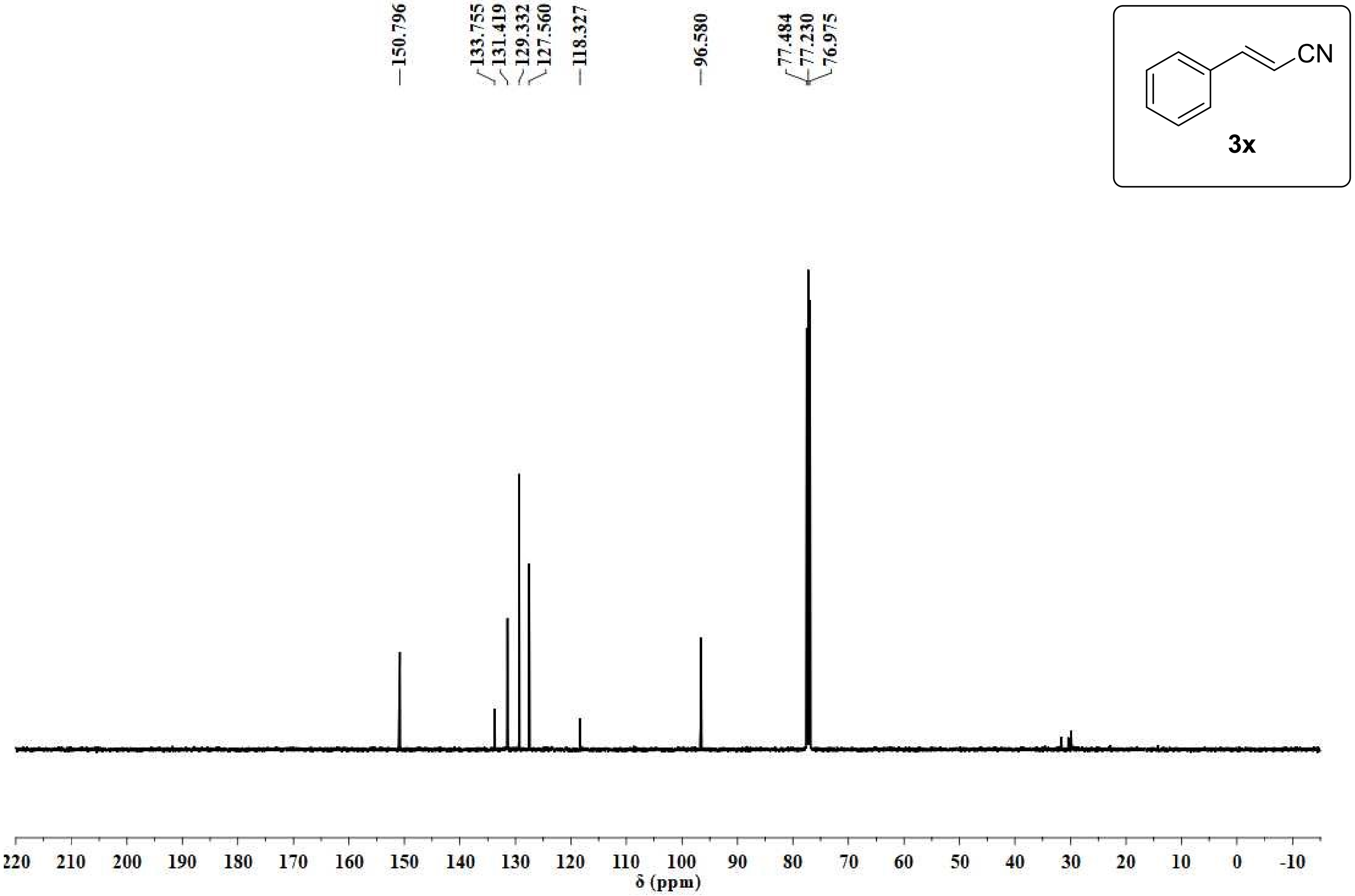
3v


7.967
7.964
7.961
7.959
7.455
7.449
7.445
7.439
7.325
7.323
7.315
7.313
1.00
1.03
1.03
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
δ (ppm)
S
NC

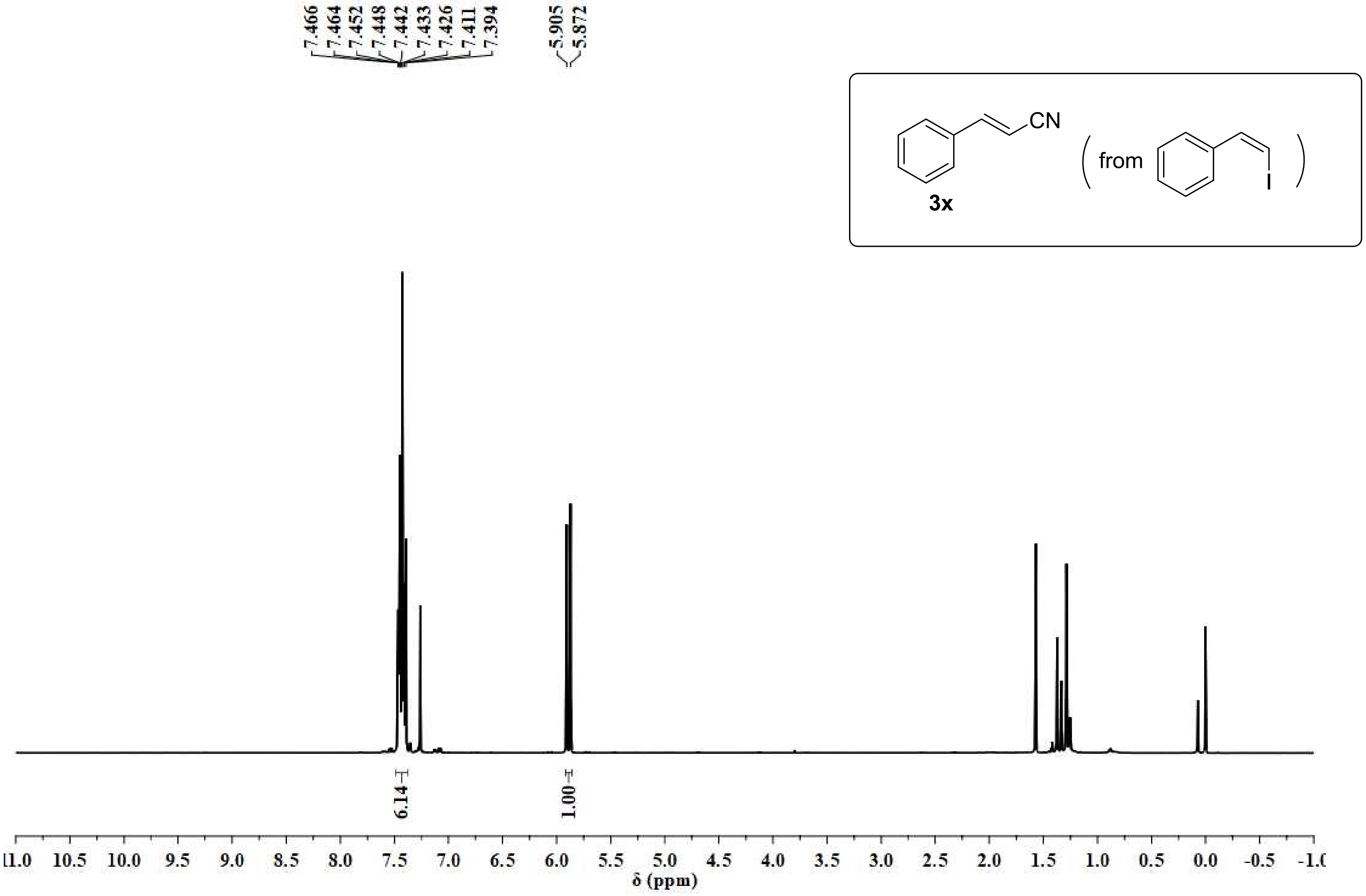
3w


135.566
128.969
127.487
115.317
111.023
77.483
77.230
76.975
S
CN
NC
3w
3x
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)


11.0
10.5
10.0
9.5
9.0
8.5


150.796
133.755
131.419
129.332
127.560
118.327
96.580
77.484
77.230
76.975
CN
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
δ (ppm)

3x


7.466
7.464
7.452
7.448
7.442
7.433
7.426
7.411
7.394
5.905
5.872
CN
3x
from
I
6.14
1.00
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
δ (ppm)