

Supporting Information for

**Silver-Mediated Radical Coupling Reaction of Isocyanides and
Alcohols/Phenols in the Presence of Water: Unprecedented
Hydration and Radical Coupling Reaction Sequence**

Lin Zhang,^a Pin Xiao,^a Xiaoxue Guan,^a Zhouliang Huang,^a Jingping Zhang^{*a} and Xihe Bi^{*a,b}

^a Jilin Province Key Laboratory of Organic Functional Molecular Design & Synthesis, Northeast Normal University, Changchun 130024, China. ^b State Key Laboratory of Elemento-Organic Chemistry, Nankai University, Tianjin 300071, China.

E-mail: bixh507@nenu.edu.cn

Contents

I. General information.....	S2
II. Crystallography.....	S2-S5
III. Optimization of the Reaction Conditions.....	S6
IV. Synthesis and analytical data of the compounds.....	S6-S15
V. DFT study of the mechanism.....	S15-S16
VI. NMR spectracopies.....	S17-S54

I. General information

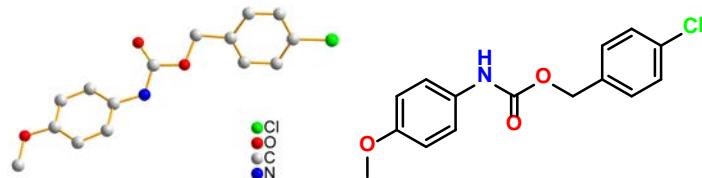
All reagents were purchased from commercial sources and used without treatment, unless otherwise indicated. The products were purified by column chromatography over silica gel. ^1H -NMR and ^{13}C -NMR spectra were recorded at 25 °C on a Varian 500 MHz and 125 MHz or on a Varian 400 MHz and 100 MHz respectively, and TMS was used as internal standard. Mass spectra were recorded on Bruker AutoflexIII Smartbeam MS-spectrometer. High resolution mass spectra (HRMS) were recorded on Bruck microTof by using ESI method.

II. Crystallography

Single-crystal X-ray diffraction data for the reported complex was recorded at a temperature of 273(2) K and 293(2) K on an Oxford Diffraction Gemini R Ultra diffractometer, using a ω scan technique with Mo-K α radiation ($\lambda = 0.71073 \text{ \AA}$). The structure was solved by Direct Method of SHELXS-97 and refined by full-matrix least-squares techniques using the SHELXL-97 program.¹ Non-hydrogen atoms were refined with anisotropic temperature parameters, and hydrogen atoms of the ligands were refined as rigid groups. Basic information pertaining to crystal parameters and structure refinement is summarized in Table S1-S3.

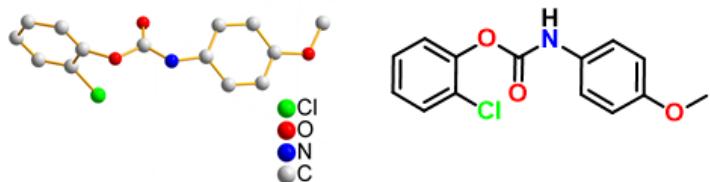
Ref: (a) G. M. Sheldrick, SHELXS-97, Program for Solution of Crystal Structures, University of Gottingen, Germany, 1997; (b) G. M. Sheldrick, SHELXL-97, Program for Refinement of Crystal Structures, University of Gottingen, Germany, 1997.

Table S1 Crystal data of **3a** and structure refinement



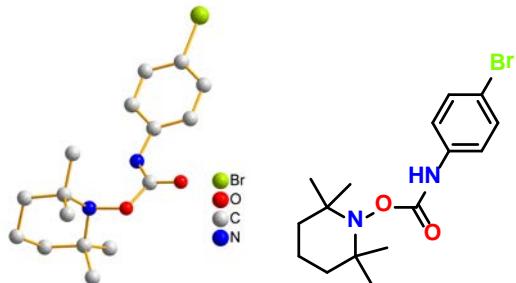
Empirical formula	C ₁₅ H ₁₄ ClNO ₃
Temperature	293(2)K
Wavelength	0.71073 Å
Unit cell dimensions	a = 5.407 Å alpha = 96.51 deg. b = 7.782 Å beta = 95.82 deg. c = 16.311 Å gamma = 90.74 deg.
Volume	678.2 Å ³
Z	2
Calculated density	0.714 Mg/m ³
Absorption coefficient	0.144 mm ⁻¹
F(000)	152
Crystal size	0.1 x 0.1x 0.1 mm
Theta range for data collection	2.53 to 28.25 deg.
Reflections collected / unique	4161 / 3028 [R(int) = 0.0183]
Data / restraints / parameters	3028 / 0 / 81
Goodness-of-fit on F ²	1.708
Final R indices [I>2sigma(I)]	R1 = 0.1178, wR2 = 0.3655
R indices (all data)	R1 = 0.1290, wR2 = 0.3964

Table S2 Crystal data of **5b** and structure refinement



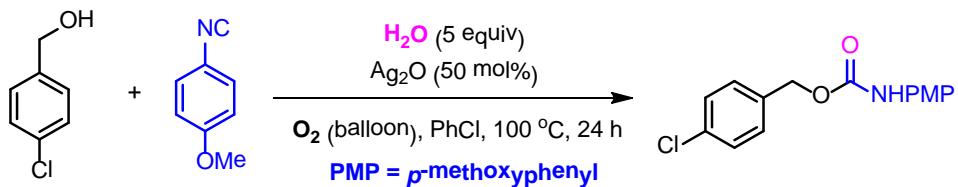
Empirical formula	C ₁₄ H ₁₂ ClNO ₃
Temperature	293(2)K
Wavelength	0.71073 Å
Unit cell dimensions	a = 9.5682(10) Å alpha = 88.829(2) deg. b = 9.6574(10) Å beta = 86.829(2) deg. c = 14.7650(15) Å gamma = 76.122(2) deg.
Volume	1322.5(2) Å ³
Z	17
Calculated density	1.675 Mg/m ³
Absorption coefficient	0.954 mm ⁻¹
F(000)	663
Crystal size	0.1 x 0.1x 0.1 mm
Theta range for data collection	2.17 to 28.29 deg.
Reflections collected / unique	7977 / 5892 [R(int) = 0.0205]
Data / restraints / parameters	5892 / 0 / 153
Goodness-of-fit on F ²	1.707
Final R indices [I>2sigma(I)]	R1 = 0.1430, wR2 = 0.3954
R indices (all data)	R1 = 0.1772, wR2 = 0.4520

Table S3 Crystal data of **10a** and structure refinement



Empirical formula	C ₁₆ H ₂₃ BrN ₂ O ₂
Temperature	273(2) K
Wavelength	0.71073 Å
Unit cell dimensions	a = 7.6713(19) Å alpha = 90 deg. b = 20.094(5) Å beta = 94.855(4) deg. c = 10.598(3) Å gamma = 90 deg.
Volume	1627.8(7) Å ³
Z	20
Calculated density	2.508 Mg/m ³
Absorption coefficient	12.366 mm ⁻¹
F(000)	1140
Crystal size	0.1 x 0.1x 0.1 mm
Theta range for data collection	2.03 to 28.31 deg.
Reflections collected / unique	11397 / 3837 [R(int) = 0.0536]
Data / restraints / parameters	3837 / 0 / 190
Goodness-of-fit on F ²	1.065
Final R indices [I>2sigma(I)]	R1 = 0.0641, wR2 = 0.1776
R indices (all data)	R1 = 0.0967, wR2 = 0.2014

III. Optimization of the Reaction Conditions^a



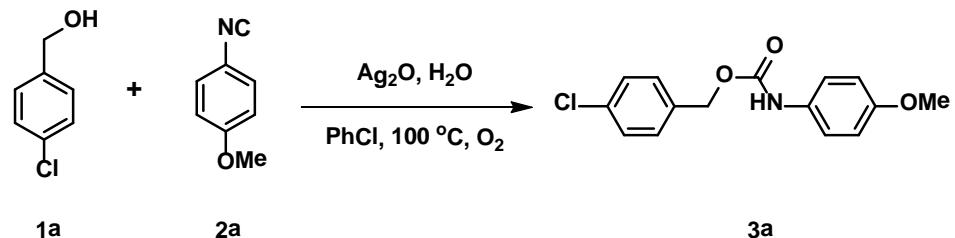
Entry	Variation from standard conditions	3a (%)^b
1	Co(acac) ₂ (50 mol%), instead of Ag ₂ O	23
2	Pd(OAc) ₂ (10 mol%), instead of Ag ₂ O	26
3	CuCl (50 mol%), instead of Ag ₂ O	0
4	Mn(OAc) ₃ (50 mol%), instead of Ag ₂ O	trace
5	AgOTf (50 mol%), instead of Ag ₂ O	trace
6	AgOAc (50 mol%), instead of Ag ₂ O	trace
7	Ag ₂ CO ₃ (50 mol%), instead of Ag ₂ O	52
8	Without Ag ₂ O	0
9	Without O ₂ , nitrogen protection	19
10	Without H ₂ O	26
11	CH ₃ CN, instead of PhCl	32
12	DCE, instead of PhCl	48
13	DCE, instead of PhCl	39
14	1,4-Dioxane, instead of PhCl	trace
15 ^c	DMSO, instead of PhCl	n.d.

^a Standard reaction conditions: **1a** (0.3 mmol), **2a** (0.45 mmol), Ag₂O (0.15 mmol), H₂O (1.5 mmol), in PhCl (1.5 mL) at 100 °C under oxygen atmosphere for 24 h. ^b Yield of isolated product.

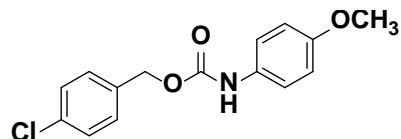
^c No **3a** was detected by ¹H-NMR.

IV. Synthesis and analytical data of the compounds

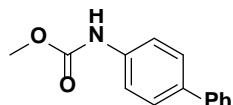
Typical synthetic procedure for compounds **3**, **5** and **6** (with **3a** as an example):



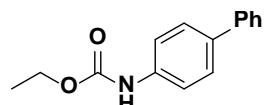
A mixture of **1a** (71 mg, 0.5 mmol), 4-methoxyphenyl isocyanide **2a** (100 mg, 0.75 mmol), Ag₂O (58 mg, 0.25 mmol) and H₂O (45 μL, 2.5 mmol) in chlorobenzene (2.0 mL) stirred at 100 °C under oxygen atmosphere. The mixture was then stirred until substrate **1a** consumed as indicated by TLC. The resulting mixture was concentrated and the residue was taken up in DCM. The organic layer was washed with brine, dried over MgSO₄ and concentrated. The resulted reaction product was purified by column chromatography to afford white solid **3a** in 77% yield.



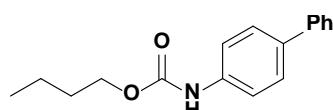
(3a) White solid, m.p. 130-131 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.33 (m, 4H), 7.28 (m, 2H), 6.84 (d, *J* = 9.0 Hz, 2H), 6.58 (s, 1H), 5.14 (s, 2H), 3.78 (s, 3H); **¹³C-NMR** (125 MHz, CDCl₃) δ 156.0, 153.5, 134.6, 134.1, 130.6, 129.6, 128.7, 120.7, 114.2, 66.0, 55.5; **HRMS** (ESI) m/z calculated for C₁₅H₁₅ClNO₃ [M+H]⁺ : 292.0735, found 292.0739.



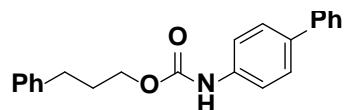
(3b) Yellow solid, m.p. 130-131 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.57-7.54 (m, 4H), 7.46-7.41 (m, 4H), 7.32 (t, *J* = 7.5 Hz, 1H), 6.73 (s, 1H), 3.80 (s, 3H); **¹³C-NMR** (125 MHz, CDCl₃) δ 154.0, 140.4, 137.1, 136.3, 128.7, 127.7, 127.0, 126.8, 118.9, 52.4; **HRMS** (ESI) m/z calculated for C₁₄H₁₄NO₂ [M+H]⁺ : 228.1019, found 228.1025.



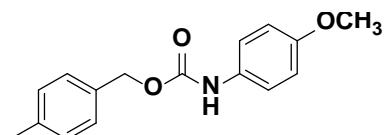
(3c) Yellow solid, m.p. 123-124 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.46-7.42 (m, 4H), 7.37-7.36 (m, 2H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.79 (s, 1H), 4.15 (q, *J* = 7.0 Hz, 2H), 1.21 (t, *J* = 7.0 Hz, 3H); **¹³C-NMR** (125 MHz, CDCl₃) δ 153.6, 140.4, 137.2, 136.1, 128.7, 127.5, 126.9, 126.7, 118.9, 61.2, 14.5; **HRMS** (ESI) m/z calculated for C₁₅H₁₆NO₂ [M+H]⁺ : 242.1176, found 242.1175.



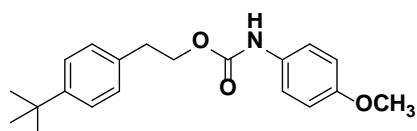
(3d) White solid, m.p. 111-112 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.56-7.53 (m, 4H), 7.46-7.40 (m, 4H), 7.33-7.24 (m, 1H), 6.74 (s, 1H), 4.18 (t, *J* = 7.0 Hz, 2H), 1.69-1.63 (m, 2H), 1.46-1.38 (m, 2H), 0.96 (t, *J* = 7.0 Hz, 3H); **¹³C-NMR** (125 MHz, CDCl₃) δ 153.7, 140.5, 137.2, 136.1, 128.7, 127.6, 126.9, 126.7, 118.8, 65.1, 30.9, 19.0, 13.7; **HRMS** (ESI) m/z calculated for C₁₇H₂₀NO₂ [M+Na]⁺ : 270.1489, found 270.1490.



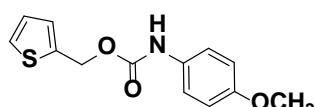
(3e) Yellow solid, m.p. 119-120 °C; **1H-NMR** (500 MHz, CDCl₃) δ 7.57-7.54 (m, 4H), 7.46-7.41 (m, 4H), 7.34-7.28 (m, 3H), 7.22 (m, 3H), 6.65 (s, 1H), 4.22 (t, *J* = 6.5 Hz, 2H), 2.74 (t, *J* = 7.5 Hz, 2H), 2.05-1.99 (m, 2H); **13C-NMR** (125 MHz, CDCl₃) δ 153.5, 141.2, 140.5, 137.2, 136.3, 128.7, 128.44, 128.40, 127.7, 127.0, 126.8, 126.0, 118.9, 64.7, 32.2, 30.5; **HRMS** (ESI) m/z calculated for C₂₂H₂₂NO₂ [M+H]⁺: 332.1645, found 332.1652.



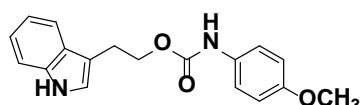
(3f) Yellow solid, m.p. 110-111 °C; **1H-NMR** (500 MHz, CDCl₃) δ 7.30-7.29 (m, 4H), 7.18 (d, *J* = 7.5 Hz, 2H), 6.83 (d, *J* = 9.0 Hz, 2H), 5.14 (s, 2H), 3.78 (s, 3H), 2.36 (s, 3H); **13C-NMR** (125 MHz, CDCl₃) δ 155.9, 153.7, 138.2, 133.1, 130.8, 129.3, 128.5, 120.6, 114.2, 66.9, 55.5, 21.2; **HRMS** (ESI) m/z calculated for C₁₆H₁₈NO₃ [M+H]⁺: 272.1281, found 272.1277.



(3g) White solid, m.p. 120-121 °C; **1H-NMR** (500 MHz, CDCl₃) δ 7.34 (d, *J* = 8.0 Hz, 2H), 7.27 (m, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.49 (s, 1H), 4.36 (t, *J* = 7.0 Hz, 2H), 3.78 (s, 3H), 2.95 (t, *J* = 7.5 Hz, 2H), 1.31 (s, 9H); **13C-NMR** (125 MHz, CDCl₃) δ 155.9, 153.8, 149.4, 134.7, 130.8, 128.5, 125.4, 120.6, 114.2, 65.5, 55.5, 34.8, 34.4, 31.4; **HRMS** (ESI) m/z calculated for C₂₀H₂₆NO₃ [M+H]⁺: 328.1907, found 328.1917.

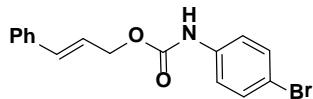


(3h) White solid, m.p. 91-92 °C; **1H-NMR** (400 MHz, CDCl₃) δ 7.33 (d, *J* = 5.2 Hz, 1H), 7.29-7.25 (m, 2H), 7.13 (d, *J* = 3.2 Hz, 1H), 7.00 (t, *J* = 4.0 Hz, 1H), 6.86-6.83 (m, 2H), 6.61 (s, 1H), 5.33 (s, 2H), 3.78 (s, 3H); **13C-NMR** (125 MHz, CDCl₃) δ 155.9, 153.4, 138.1, 130.6, 128.1, 126.78, 126.76, 120.6, 114.1, 60.9, 55.4; **HRMS** (ESI) m/z calculated for C₁₃H₁₃NNaO₃S [M+Na]⁺: 286.0508, found 286.0513.

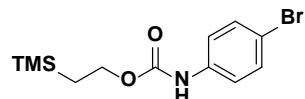


(3i) Gray solid, m.p. 126-127 °C; **1H-NMR** (500 MHz, CDCl₃) δ 8.04 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.29 (m, 2H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.06 (s, 1H), 6.83 (d, *J* = 8.5 Hz, 2H), 6.48 (s, 1H), 4.44 (t, *J* = 7.0 Hz, 2H), 3.78 (s, 3H), 3.14 (t, *J* = 7.0 Hz, 2H); **13C-NMR** (125 MHz, CDCl₃) δ 156.0, 154.0, 136.2, 130.9, 127.5, 122.1, 122.0,

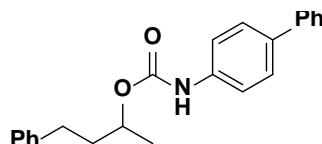
120.7, 119.4, 118.8, 114.2, 112.0, 111.2, 65.2, 55.5, 25.1; **HRMS** (ESI) m/z calculated for C₁₈H₁₈N₂NaO₃ [M+Na]⁺ : 333.1210, found 333.1205.



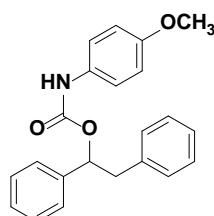
(3j) Yellow solid, m.p. 109-110 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.40 (t, *J* = 8.5 Hz, 4H), 7.34-7.26 (m, 5H), 6.70-6.67 (m, 2H), 6.35-6.29 (m, 1H), 4.81 (d, *J* = 6.0 Hz, 2H); **¹³C-NMR** (100 MHz, CDCl₃) δ 153.1, 136.9, 136.0, 134.5, 132.0, 128.6, 128.2, 126.6, 123.0, 120.2, 116.0, 66.0; **HRMS** (ESI) m/z calculated for C₁₆H₁₄BrNNaO₂ [M+Na]⁺ : 354.0100, found 354.0095.



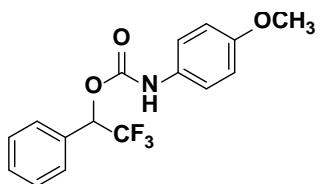
(3k) Yellow solid, m.p. 90-91 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.38 (m, 2H), 7.27 (m, 2H), 6.65 (s, 1H), 4.25 (t, *J* = 8.5 Hz, 2H), 1.04 (t, *J* = 8.5 Hz, 2H), 0.06 (s, 9H); **¹³C-NMR** (125 MHz, CDCl₃) δ 153.5, 137.1, 131.9, 120.2, 115.7, 63.8, 17.7, 1.0, -1.5; **HRMS** (ESI) m/z calculated for C₁₂H₁₈BrNNaO₂Si [M+Na]⁺ : 338.0182, found 338.0182.



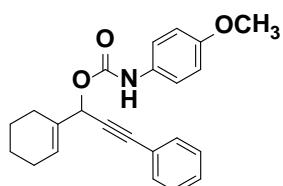
(3l) Yellow solid, m.p. 133-134 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.56 (t, *J* = 8.5 Hz, 4H), 7.47-7.41 (m, 4H), 7.34-7.28 (m, 3H), 7.21-7.18 (m, 3H), 6.59 (s, 1H), 5.00-4.96 (m, 1H), 2.78-2.66 (m, 2H), 2.03-1.84 (m, 2H), 1.33 (d, *J* = 6.0 Hz, 3H); **¹³C-NMR** (125 MHz, CDCl₃) δ 153.2, 141.6, 140.5, 137.3, 136.2, 128.7, 128.4, 128.3, 127.7, 127.0, 126.8, 125.9, 118.8, 71.8, 37.8, 31.9, 20.4; **HRMS** (ESI) m/z calculated for C₂₃H₂₄NO₂ [M+H]⁺ : 346.1802, found 346.1797.



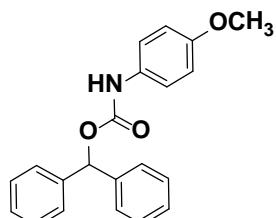
(3m) Gray solid, m.p. 81-82 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.23-7.18 (m, 5H), 7.17-7.08 (m, 5H), 7.02 (d, *J* = 7.0 Hz, 2H), 6.72 (d, *J* = 8.5 Hz, 2H), 6.48 (s, 1H), 5.87 (t, *J* = 7.5 Hz, 1H), 3.66 (s, 3H), 3.67 (q, *J* = 7.5, 13.5 Hz, 1H), 3.03 (q, *J* = 7.0, 13.5 Hz, 1H); **¹³C-NMR** (125 MHz, CDCl₃) δ 155.9, 153.0, 140.1, 136.9, 130.8, 129.5, 128.3, 128.2, 127.9, 126.52, 126.49, 120.5, 114.1, 77.4, 55.4, 43.0; **HRMS** (ESI) m/z calculated for C₂₂H₂₃NNaO₃ [M+Na]⁺ : 384.1570, found 384.1579.



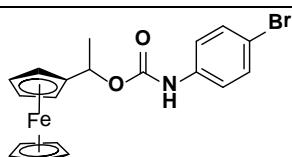
(3n) White solid, m.p. 107-108 °C; **1H-NMR** (500 MHz, CDCl₃) δ 7.47 (m, 2H), 7.40-7.39 (m, 3H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.90 (s, 1H), 6.82 (d, *J* = 8.5 Hz, 2H), 6.15 (q, *J* = 7.0, 1H), 3.76 (s, 3H); **13C-NMR** (125 MHz, CDCl₃) δ 156.4, 151.4, 131.4, 130.0, 129.8, 128.8, 128.7, 128.0, 126.7, 124.4, 122.2, 120.9, 114.3, 73.1, 72.9, 72.6, 55.4; **HRMS** (ESI) m/z calculated for C₁₆H₁₅F₃NO₃ [M+H]⁺: 326.0999, found 326.1003.



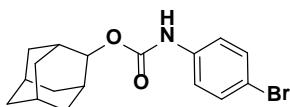
(3o) White solid, m.p. 145-146 °C; **1H-NMR** (500 MHz, CDCl₃) δ 7.44-7.42 (m, 2H), 7.31-7.29 (m, 5H), 6.87 (d, *J* = 9.0 Hz, 2H), 6.60 (s, 1H), 5.72 (s, 1H), 5.31 (dd, *J* = 4.0, 7.5 Hz, 2H), 3.78 (s, 3H), 2.85-2.83 (m, 1H), 2.38-2.33 (m, 1H), 2.01-1.97 (m, 1H), 1.83 (m, 1H), 1.71-1.68 (m, 2H), 1.62-1.55 (m, 2H); **13C-NMR** (125 MHz, CDCl₃) δ 156.0, 152.9, 151.5, 131.3, 130.8, 128.2, 127.9, 123.6, 120.6, 114.2, 102.5, 93.4, 86.2, 74.9, 55.5, 33.7, 29.8, 26.8, 23.1; **HRMS** (ESI) m/z calculated for C₂₃H₂₃NNaO₃ [M+Na]⁺: 384.1570, found 384.1579.



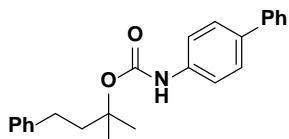
(3p) White solid, m.p. 143-144 °C; **1H-NMR** (500 MHz, CDCl₃) δ 7.29-7.21 (m, 8H), 7.21-7.16 (m, 4H), 6.80 (s, 1H), 6.75 (d, *J* = 9.0 Hz, 2H), 6.65 (s, 1H), 3.68 (s, 3H); **13C-NMR** (125 MHz, CDCl₃) δ 156.0, 152.9, 140.2, 130.8, 128.5, 127.9, 127.1, 120.5, 114.2, 77.7, 55.5; **HRMS** (ESI) m/z calculated for C₂₁H₁₉NNaO₃ [M+Na]⁺: 356.1257, found 356.1261.



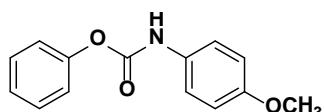
(3q) Brown solid, m.p. 90-91 °C; **1H-NMR** (500 MHz, CDCl₃) δ 7.25 (d, *J* = 8.5 Hz, 2H), 6.51 (d, *J* = 9.0 Hz, 2H), 4.28-4.21 (m, 1H), 4.18 (s, 5H), 4.16-4.13 (m, 3H), 3.93 (s, 1H), 1.48 (d, *J* = 6.5 Hz, 3H); **13C-NMR** (100 MHz, CDCl₃) δ 146.3, 132.0, 114.7, 108.5, 93.0, 68.4, 67.8, 67.6, 67.0, 66.0, 47.2, 20.7; **HRMS** (ESI) m/z calculated for C₁₉H₂₀BrFeNO₂ [M+H]⁺: 429.0021, found 429.0016.



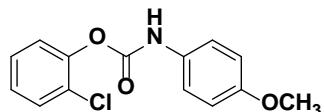
(3r) Yellow solid, m.p. 126-127 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.40 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.68 (s, 1H), 4.92 (s, 1H), 2.08 (s, 2H), 2.00-2.03 (m, 2H), 1.74-1.88(m, 8H), 1.57-1.62 (m, 3H); **¹³C-NMR** (125 MHz, CDCl₃) δ 153.0, 137.3, 131.9, 120.0, 115.6, 78.3, 37.3, 36.3, 32.0, 31.8, 27.2, 26.9; **HRMS** (ESI) m/z calculated for C₁₇H₂₀BrNNaO₂ [M+Na]⁺ : 372.0570, found 372.0572.



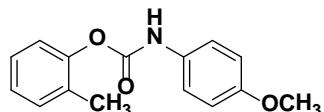
(3s) White solid, m.p. 127-128 °C; **¹H-NMR** (400 MHz, CDCl₃) δ 7.56-7.51 (m, 4H), 7.41 (t, *J* = 7.6 Hz, 4H), 7.31-7.28 (m, 3H), 7.22-7.16 (m, 3H), 6.50 (s, 1H), 2.73-2.69 (m, 2H), 2.16-2.12 (m, 2H), 1.58 (s, 6H); **¹³C-NMR** (100 MHz, CDCl₃) δ 152.5, 142.1, 140.6, 137.5, 135.9, 128.7, 128.4, 127.6, 126.9, 126.7, 125.8, 118.8, 82.3, 42.9, 30.4, 26.3; **HRMS** (ESI) m/z calculated for C₂₄H₂₆NO₂ [M+H]⁺ : 360.1958, found 360.1961.



(5a) White solid, m.p. 99-100 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.39-7.33 (m, 4H), 7.21 (m, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.96 (s, 1H), 6.84 (d, *J* = 8.5 Hz, 2H), 3.78 (s, 3H); **¹³C-NMR** (125 MHz, CDCl₃) δ 156.1, 151.9, 150.6, 130.4, 129.3, 125.6, 121.6, 120.6, 114.2, 55.4; **HRMS** (ESI) m/z calculated for C₁₄H₁₄NO₃ [M+H]⁺ : 244.0968, found 244.0964.

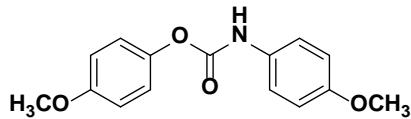


(5b) White solid, m.p. 110-111 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.45 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H), 7.30 (t, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 6.5 Hz, 1H), 7.00 (s, 1H), 6.87 (d, *J* = 9.0 Hz, 2H); **¹³C-NMR** (125 MHz, CDCl₃) δ 156.3, 150.8, 146.7, 130.3, 127.7, 127.3, 126.9, 124.1, 120.7, 114.3, 55.5; **HRMS** (ESI) m/z calculated for C₁₄H₁₃ClNO₃ [M+H]⁺ : 278.0578, found 278.0586.

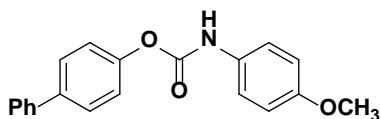


(5c) White solid, m.p. 125-126 °C; **¹H-NMR** (500 MHz, CDCl₃) δ 7.32 (d, *J* = 8.0 Hz, 2H), 7.22-7.18 (m, 2H), 7.14-7.10 (m, 3H), 6.80 (d, *J* = 8.5 Hz, 2H), 3.75 (s, 3H), 2.23 (s, 3H); **¹³C-NMR** (125 MHz, CDCl₃) δ 155.9, 151.8, 149.1, 131.0, 130.6, 130.5, 126.8, 125.8, 122.2, 120.4, 114.2, 55.4, 16.1; **HRMS** (ESI) m/z calculated for C₁₅H₁₅NNaO₃ [M+Na]⁺ : 280.0944,

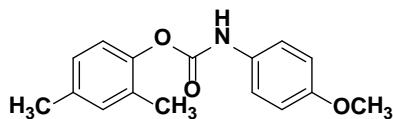
found 280.0954.



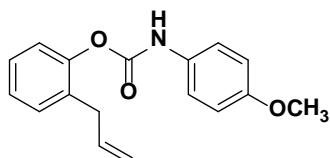
(5d) White solid, m.p. 162-163 °C; **1H-NMR** (500 MHz, DMSO) δ 9.97 (s, 1H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 3.75 (s, 3H), 3.71 (s, 3H); **13C-NMR** (125 MHz, DMSO) δ 157.1, 155.6, 152.7, 144.5, 132.2, 123.4, 120.5, 114.8, 114.6, 55.9, 55.7; **HRMS** (ESI) m/z calculated for C₁₅H₁₆NO₄ [M+H]⁺ : 274.1074, found 274.1065.



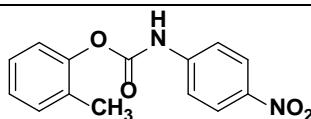
(5e) White solid, m.p. 164-165 °C; **1H-NMR** (500 MHz, CDCl₃) δ 7.60-7.55 (m, 4H), 7.43 (t, *J* = 7.5 Hz, 2H), 7.37-7.30 (m, 3H), 7.24 (d, *J* = 7.5 Hz, 2H), 6.95 (s, 1H), 6.86 (d, *J* = 8.5 Hz, 2H), 3.78 (s, 3H); **13C-NMR** (125 MHz, CDCl₃) δ 156.2, 151.9, 150.0, 140.4, 138.7, 130.3, 128.8, 128.1, 127.3, 127.1, 121.9, 120.6, 114.3, 55.5; **HRMS** (ESI) m/z calculated for C₂₀H₁₈NO₃ [M+H]⁺ : 320.1281, found 320.1296.



(5f) White solid, m.p. 144-145 °C; **1H-NMR** (400 MHz, CDCl₃) δ 7.30 (d, *J* = 8.0 Hz, 2H), 7.07 (s, 1H), 7.01 (d, *J* = 8.0 Hz, 2H), 6.98 (s, 1H), 6.79 (d, *J* = 8.4 Hz, 2H), 3.74 (s, 3H), 2.28 (s, 3H), 2.19 (s, 3H); **13C-NMR** (100 MHz, CDCl₃) δ 155.9, 152.0, 146.9, 135.4, 131.7, 130.7, 130.2, 127.3, 121.8, 120.4, 114.2, 55.4, 20.7, 16.0; **HRMS** (ESI) m/z calculated for C₁₆H₁₈NO₃ [M+H]⁺ : 272.1281, found 272.1281.

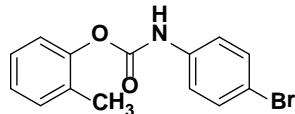


(5g) White solid, m.p. 85-86 °C; **1H-NMR** (500 MHz, CDCl₃) δ 7.28 (d, *J* = 8.5 Hz, 2H), 7.22-7.20 (m, 3H), 7.17-7.12 (m, 2H), 6.78 (d, *J* = 9.0 Hz, 2H), 5.92-5.85 (m, 1H), 5.06-5.02 (m, 2H), 3.71 (s, 3H), 3.34 (d, *J* = 6.5 Hz, 2H); **13C-NMR** (125 MHz, CDCl₃) δ 155.9, 151.9, 148.6, 135.8, 132.4, 130.5, 130.1, 127.3, 125.9, 122.5, 120.5, 116.1, 114.1, 55.3, 34.4; **HRMS** (ESI) m/z calculated for C₁₇H₁₇NNaO₃ [M+Na]⁺ : 306.1101, found 306.1092.

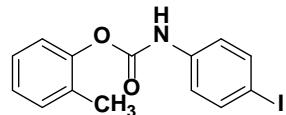


(5h) White solid, m.p. 149-150 °C; **1H-NMR** (400 MHz, CDCl₃) δ 8.14 (d, *J* = 9.2 Hz, 2H), 7.73

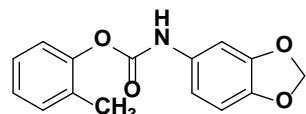
(s, 1H), 7.54 (d, J = 9.2 Hz, 2H), 7.27-7.18 (m, 3H), 7.12 (d, J = 8.0 Hz, 1H), 2.24 (s, 3H); **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3) δ 151.2, 148.5, 143.5, 143.1, 131.3, 130.4, 127.1, 126.5, 125.1, 121.9, 118.0, 16.0; **HRMS** (ESI) m/z calculated for $\text{C}_{14}\text{H}_{12}\text{N}_2\text{NaO}_4$ [$\text{M}+\text{Na}]^+$: 295.0689, found 295.0692.



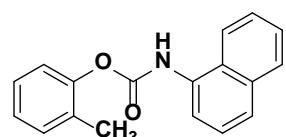
(5i) White solid, m.p. 145-146 °C; **$^1\text{H-NMR}$** (400 MHz, DMSO) δ 10.44 (s, 1H), 7.50 (m, 4H), 7.29 (d, J = 7.2 Hz, 1H), 7.22 (t, J = 8.4 Hz, 1H), 7.17 (t, J = 8.0 Hz, 2H), 2.19 (s, 3H); **$^{13}\text{C-NMR}$** (100 MHz, DMSO) δ 151.9, 149.4, 138.7, 132.2, 131.5, 130.8, 127.5, 126.3, 123.0, 120.8, 115.1, 16.2; **HRMS** (ESI) m/z calculated for $\text{C}_{14}\text{H}_{12}\text{BrNNaO}_2$ [$\text{M}+\text{Na}]^+$: 327.9944, found 327.9936.



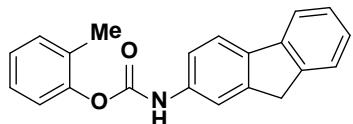
(5j) White solid, m.p. 156-157 °C; **$^1\text{H-NMR}$** (400 MHz, CDCl_3) δ 7.58 (d, J = 8.8 Hz, 2H), 7.24-7.15 (m, 5H), 7.09 (d, J = 8.0 Hz, 2H), 2.23 (s, 3H); **$^{13}\text{C-NMR}$** (100 MHz, CDCl_3) δ 151.3, 148.8, 137.9, 137.3, 131.2, 130.5, 126.9, 126.1, 122.0, 120.5, 86.8, 16.1; **HRMS** (ESI) m/z calculated for $\text{C}_{14}\text{H}_{12}\text{INNaO}_2$ [$\text{M}+\text{Na}]^+$: 375.9805, found 375.9802.



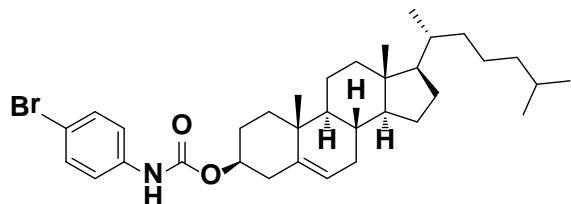
(5k) White solid, m.p. 109-110 °C; **$^1\text{H-NMR}$** (400 MHz, CDCl_3) δ 7.25-7.19 (m, 2H), 7.14-7.09 (m, 3H), 6.98 (s, 1H), 6.72 (s, 2H), 5.93 (s, 2H), 2.24 (s, 3H); **$^{13}\text{C-NMR}$** (125 MHz, CDCl_3) δ 151.7, 149.0, 147.8, 143.8, 131.7, 131.0, 130.6, 126.8, 125.9, 122.1, 111.9, 108.0, 101.6, 101.2, 16.0; **HRMS** (ESI) m/z calculated for $\text{C}_{15}\text{H}_{13}\text{NNaO}_4$ [$\text{M}+\text{Na}]^+$: 294.0737, found 294.0736.



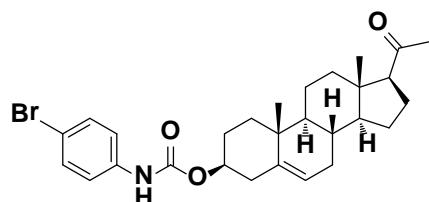
(5l) White solid, m.p. 136-137 °C; **$^1\text{H-NMR}$** (400 MHz, DMSO) δ 10.17 (s, 1H), 8.20 (d, J = 8.0 Hz, 1H), 7.96 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.62-7.50 (m, 3H), 7.32-7.17 (m, 4H), 2.27 (s, 3H); **$^{13}\text{C-NMR}$** (125 MHz, DMSO) δ 153.5, 149.8, 134.2, 133.8, 131.4, 130.9, 128.6, 127.4, 126.7, 126.6, 126.1, 126.0, 123.1, 123.0, 121.9, 16.3; **HRMS** (ESI) m/z calculated for $\text{C}_{18}\text{H}_{15}\text{NNaO}_2$ [$\text{M}+\text{Na}]^+$: 300.0995, found 300.0996.



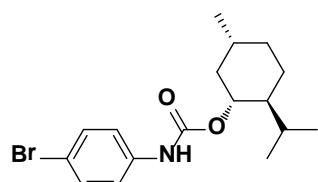
(5m) White solid, m.p. 151-152 °C; **¹H-NMR** (400 MHz, CDCl₃) δ 7.74-7.67 (m, 3H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.35-7.31 (m, 2H), 7.28-7.20 (m, 3H), 7.15 (m, 3H), 3.85 (s, 2H), 2.27 (s, 3H); **¹³C-NMR** (100 MHz, CDCl₃) δ 151.5, 149.0, 144.5, 143.0, 141.2, 137.7, 136.2, 131.1, 130.6, 126.9, 126.7, 126.3, 126.0, 124.9, 122.2, 120.2, 119.5, 117.5, 115.6, 37.0, 16.2; **HRMS** (ESI) m/z calculated for C₂₁H₁₇NNaO₂ [M+Na]⁺: 338.1151, found 338.1156.



(6a) White solid, m.p. 153-154 °C; **¹H-NMR** (400 MHz, CDCl₃) δ 7.39 (d, *J* = 8.8 Hz, 2H), 7.26 (d, *J* = 9.6 Hz, 2H), 6.56 (s, 1H), 5.40 (s, 1H), 4.60 (m, 1H), 2.45-2.29 (m, 2H), 2.03-1.83 (m, 5H), 1.62-0.86 (m, 33H), 0.68 (s, 3H); **¹³C-NMR** (100 MHz, CDCl₃) δ 152.8, 139.4, 137.1, 131.9, 122.8, 120.0, 115.6, 75.1, 56.6, 56.1, 49.9, 42.2, 39.6, 39.5, 38.4, 36.9, 36.5, 36.1, 35.8, 31.84, 31.78, 28.2, 28.0, 24.2, 23.8, 22.8, 22.6, 21.0, 19.3, 18.7, 11.8; **HRMS** (ESI) m/z calculated for C₃₄H₅₀BrNNaO₂ [M+Na]⁺: 606.2917, found 606.2921.

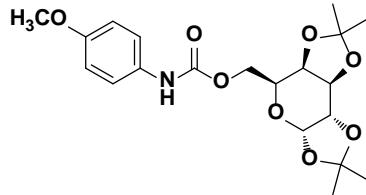


(6b) Yellow solid, m.p. 234-235 °C; **¹H-NMR** (400 MHz, CDCl₃) δ 7.39 (d, *J* = 7.2 Hz, 2H), 7.27 (d, *J* = 6.8 Hz, 2H), 6.61 (s, 1H), 5.39 (m, 1H), 4.62-4.58 (m, 1H), 2.54 (t, *J* = 7.2 Hz, 1H), 2.42 (t, *J* = 7.6 Hz, 1H), 2.33 (m, 1H), 2.18 (m, 1H), 2.13 (s, 3H), 2.07-1.15 (m, 16H), 1.03 (s, 3H), 0.64 (s, 3H); **¹³C-NMR** (125 MHz, CDCl₃) δ 209.6, 152.8, 139.5, 137.1, 131.9, 122.5, 120.1, 115.775.0, 63.7, 56.8, 49.8, 44.0, 38.8, 38.3, 36.9, 36.6, 31.8, 31.7, 31.6, 28.0, 24.5, 22.8, 21.0, 19.3, 13.2; **HRMS** (ESI) m/z calculated for C₂₈H₃₆BrNNaO₃ [M+Na]⁺: 536.1771, found 536.1775.

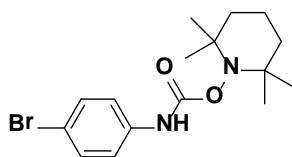


(6c) Yellow solid, m.p. 99-100 °C; **¹H-NMR** (400 MHz, CDCl₃) δ 7.39 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.60 (s, 1H), 4.68-4.62 (m, 1H), 2.08 (m, 1H), 1.97-1.92 (m, 1H), 1.70-1.62 (m, 2H), 1.51-1.49 (m, 1H), 1.39-1.33 (m, 1H), 1.12-0.85 (m, 9H), 0.80 (d, *J* = 6.8 Hz, 3H); **¹³C-NMR**

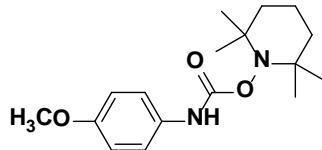
(100 MHz, CDCl₃) δ 153.1, 137.2, 131.9, 120.0, 115.6, 75.4, 47.2, 41.3, 34.2, 31.4, 26.2, 23.4, 22.0, 20.8, 16.4; **HRMS** (ESI) m/z calculated for C₁₇H₂₄BrNNaO₂ [M+Na]⁺: 376.0883, found 376.0878.



(6d) Yellow oil; **¹H-NMR** (500 MHz, CDCl₃) δ 7.28 (d, J = 9.0 Hz, 2H), 7.27 (d, J = 9.0 Hz, 2H), 6.73 (s, 1H), 5.57 (d, J = 5.0 Hz, 1H), 4.64-4.62 (m, 1H), 4.41-4.34 (m, 2H), 4.28-4.24 (m, 2H), 4.13-4.08 (m, 1H), 3.78 (s, 3H), 1.52 (s, 3H), 1.46 (s, 3H), 1.35 (s, 3H), 1.34 (s, 3H); **¹³C-NMR** (125 MHz, CDCl₃) δ 155.9, 153.5, 130.8, 120.5, 114.1, 109.6, 108.8, 96.30, 96.25, 71.0, 70.7, 70.3, 66.3, 64.1, 55.4, 26.0, 24.9, 24.4; **HRMS** (ESI) m/z calculated for C₂₀H₂₇NNaO₈ [M+Na]⁺: 432.1629, found 432.1622.



(10a) White solid, m.p. 127-128 °C; **¹H-NMR** (400 MHz, CDCl₃) δ 8.98 (s, 1H), 7.46-7.42 (m, 2H), 7.38-7.35 (m, 2H), 1.73-1.61 (m, 5H), 1.50-1.46 (m, 1H), 1.27 (s, 6H), 1.17 (s, 6H); **¹³C-NMR** (100 MHz, CDCl₃) δ 155.0, 136.2, 132.0, 120.6, 116.4, 61.1, 39.8, 31.7, 20.6, 16.6; **HRMS** (ESI) m/z calculated for C₁₆H₂₃BrNNaO₂ [M+Na]⁺: 377.0835, found 377.0831.



(10b) White solid, m.p. 107-108 °C; **¹H-NMR** (400 MHz, CDCl₃) δ 8.77 (s, 1H), 7.36-7.32 (m, 2H), 6.90-6.86 (m, 2H), 3.79 (s, 3H), 1.69-1.56 (m, 5H), 1.50-1.44 (m, 1H), 1.27 (s, 6H), 1.19 (s, 6H); **¹³C-NMR** (100 MHz, CDCl₃) δ 156.3, 155.6, 130.2, 121.2, 114.3, 60.9, 55.5, 39.8, 31.69, 31.65, 20.7, 20.6, 16.7; **HRMS** (ESI) m/z calculated for C₁₇H₂₆N₂NaO₃ [M+Na]⁺: 329.1836, found 329.1831.

V. DFT study of the mechanism

The density functional theory (DFT) study was performed using Gaussian 09 package, at the M06/SDD/6-311++G**/SMD (Chlorobenzene, 353.15 K)//B3LYP/LANL2DZ (f=1.611)/6-31G** calculation level.

Figure S1. DFT study on the generation of phenoxy radical from phenol

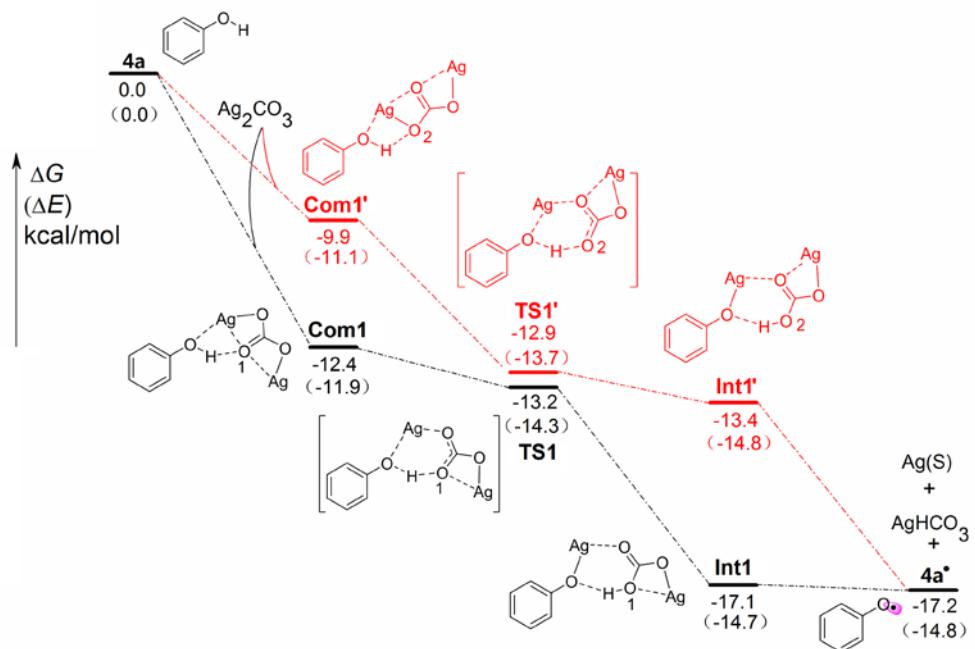
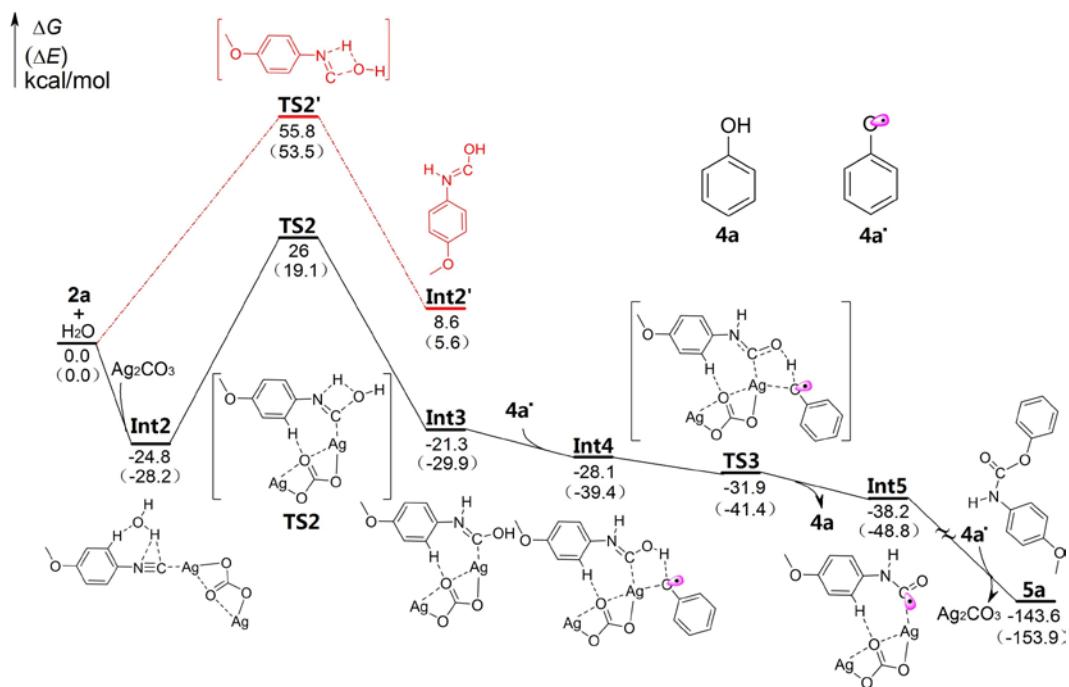
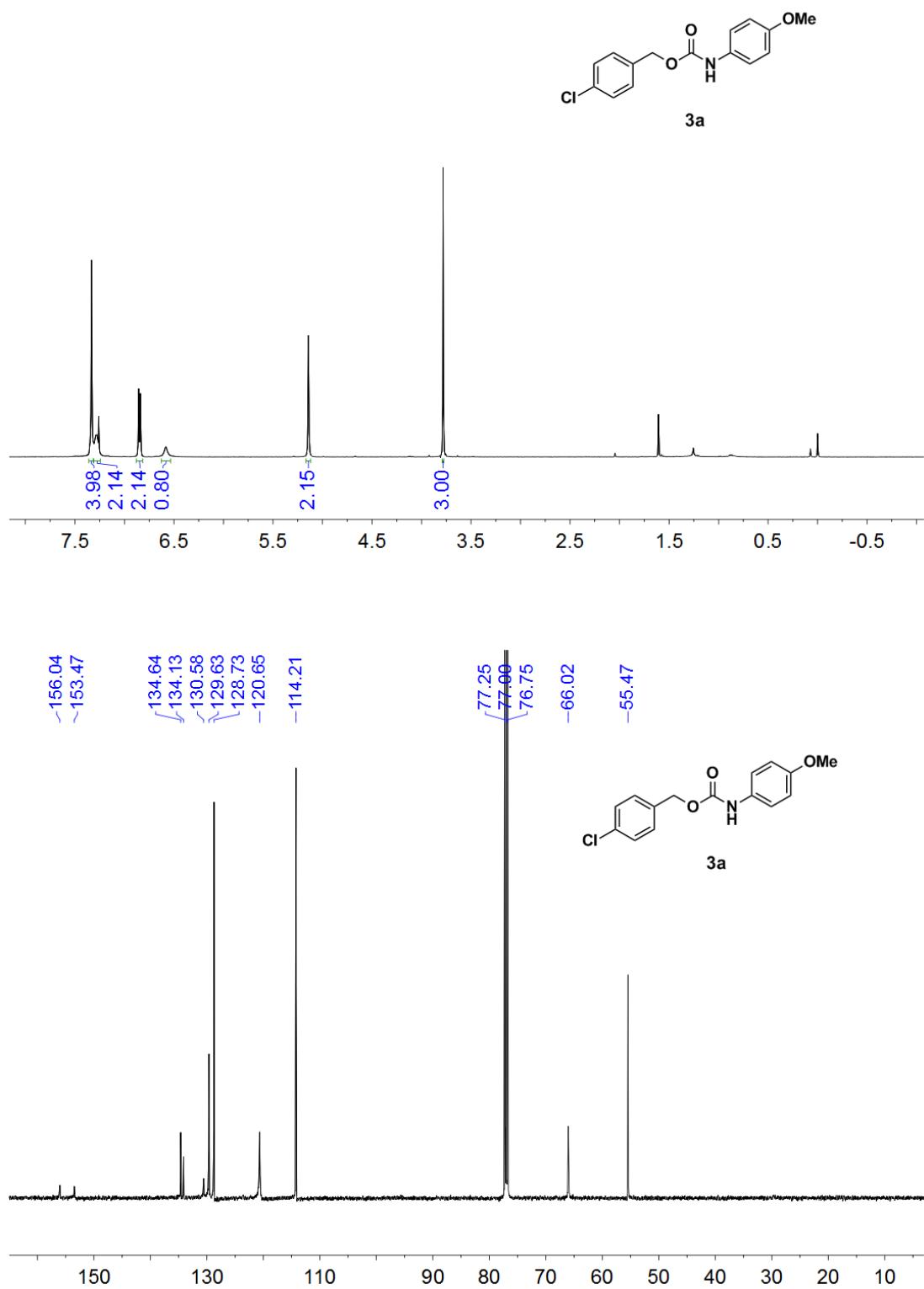
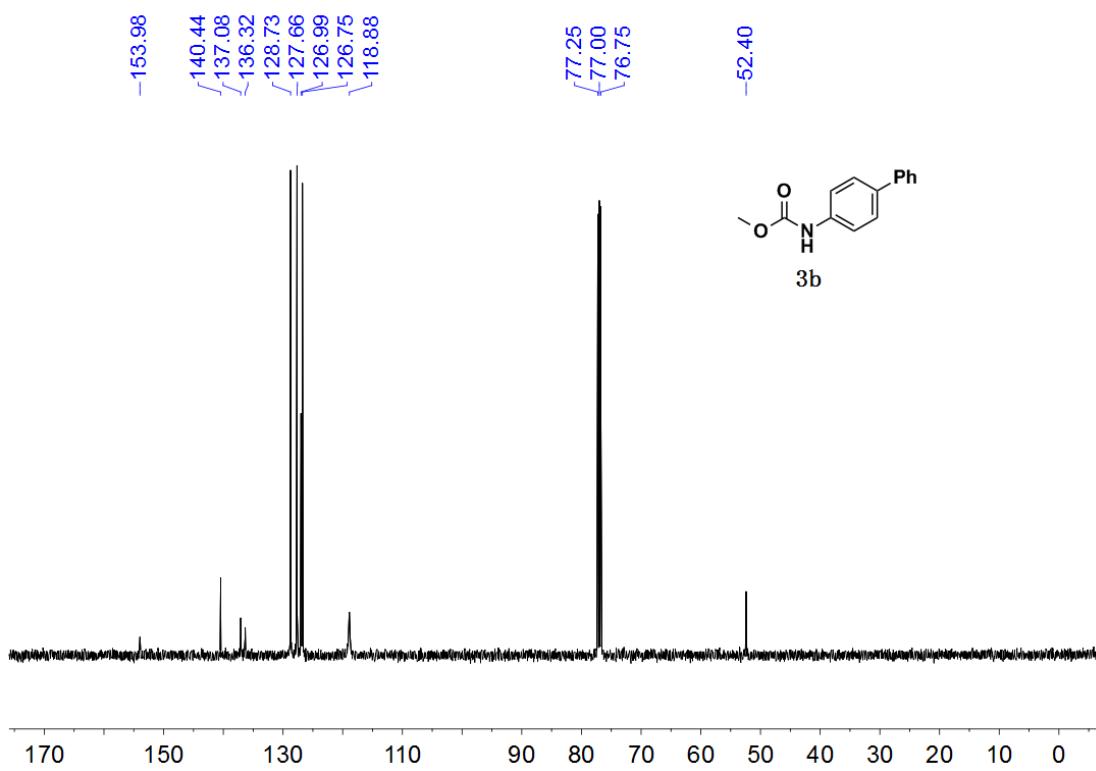
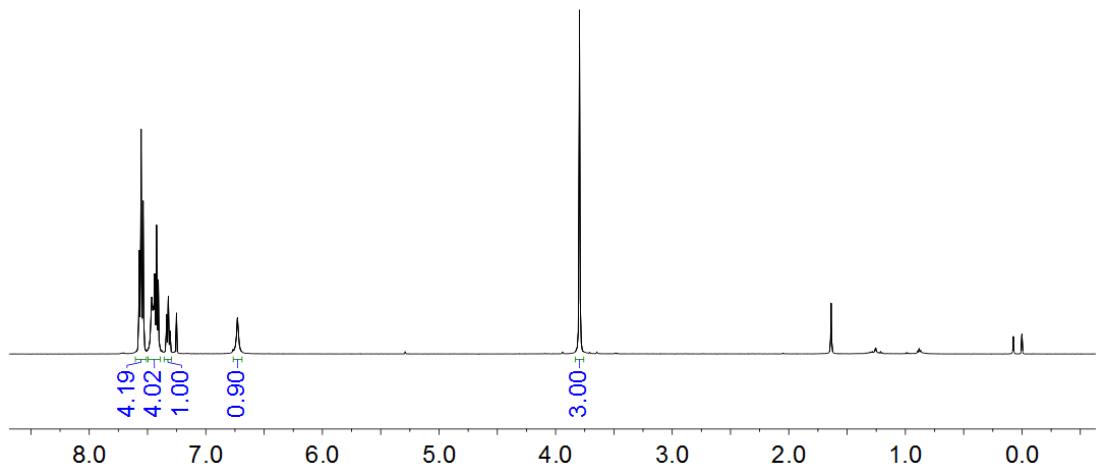
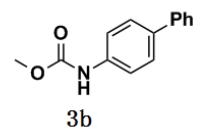


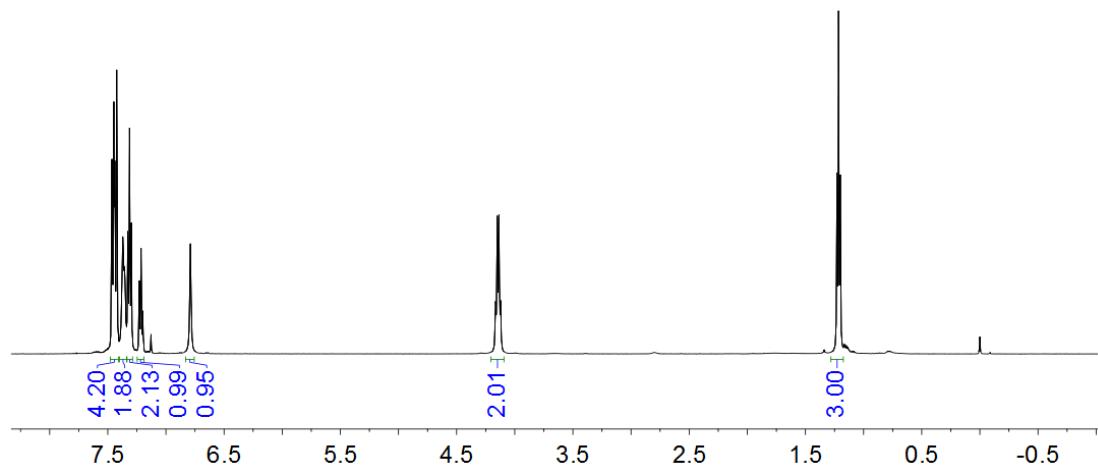
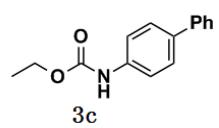
Figure S2. DFT study on the cross-coupling of isocyanide **2a and phenol **4a****



VI. NMR spectra copies



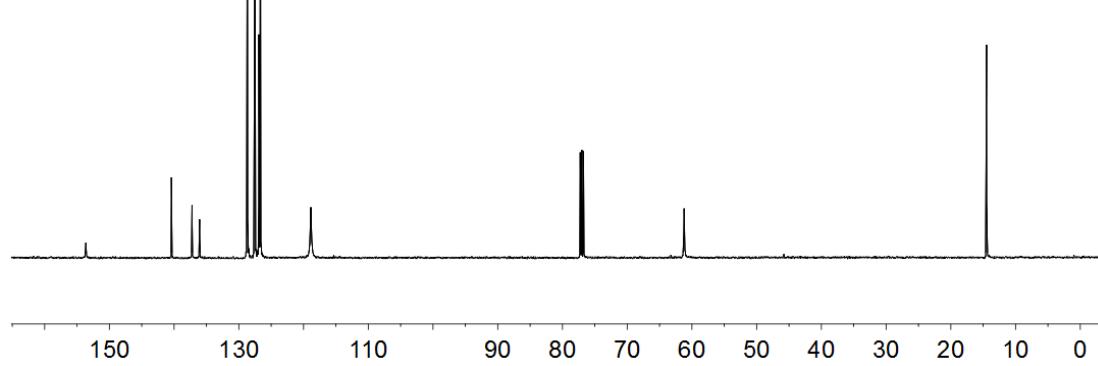
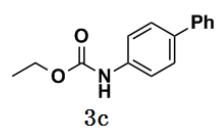


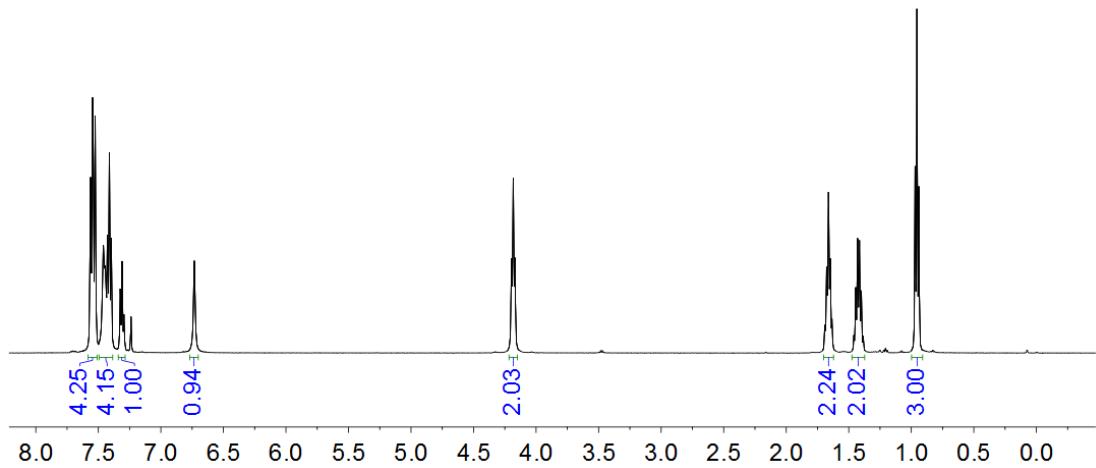
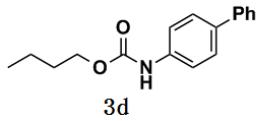


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 128.68
 127.53
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 \ 126.67
 -118.86

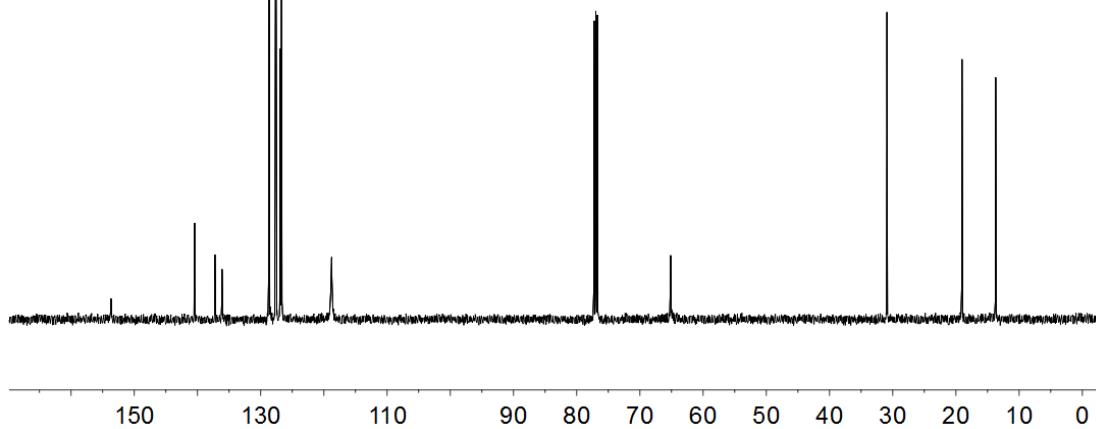
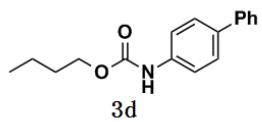
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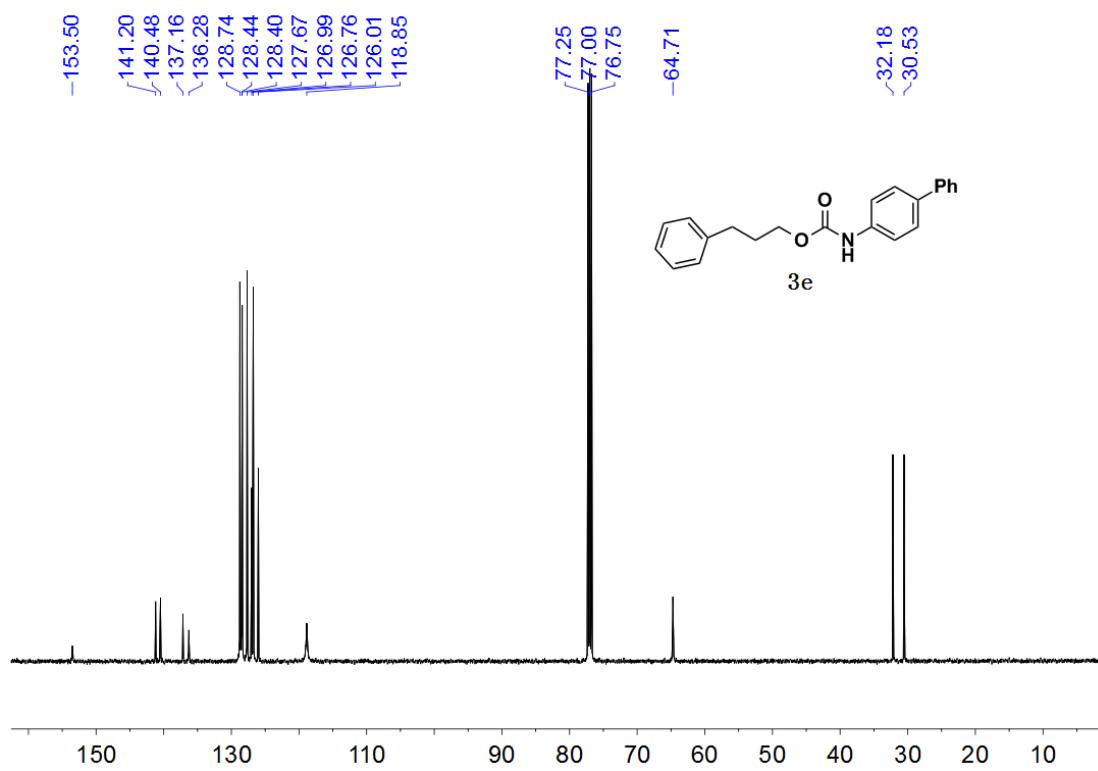
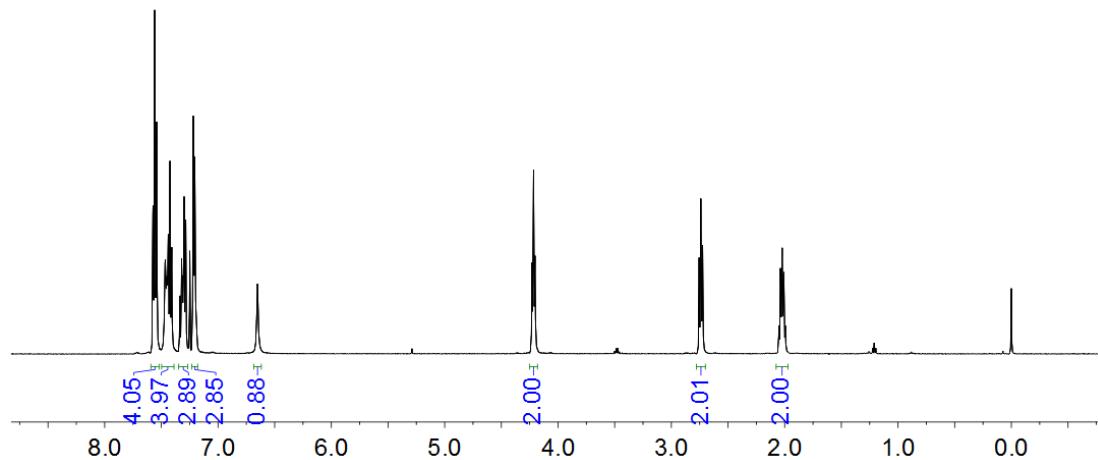
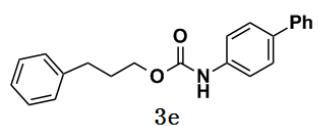
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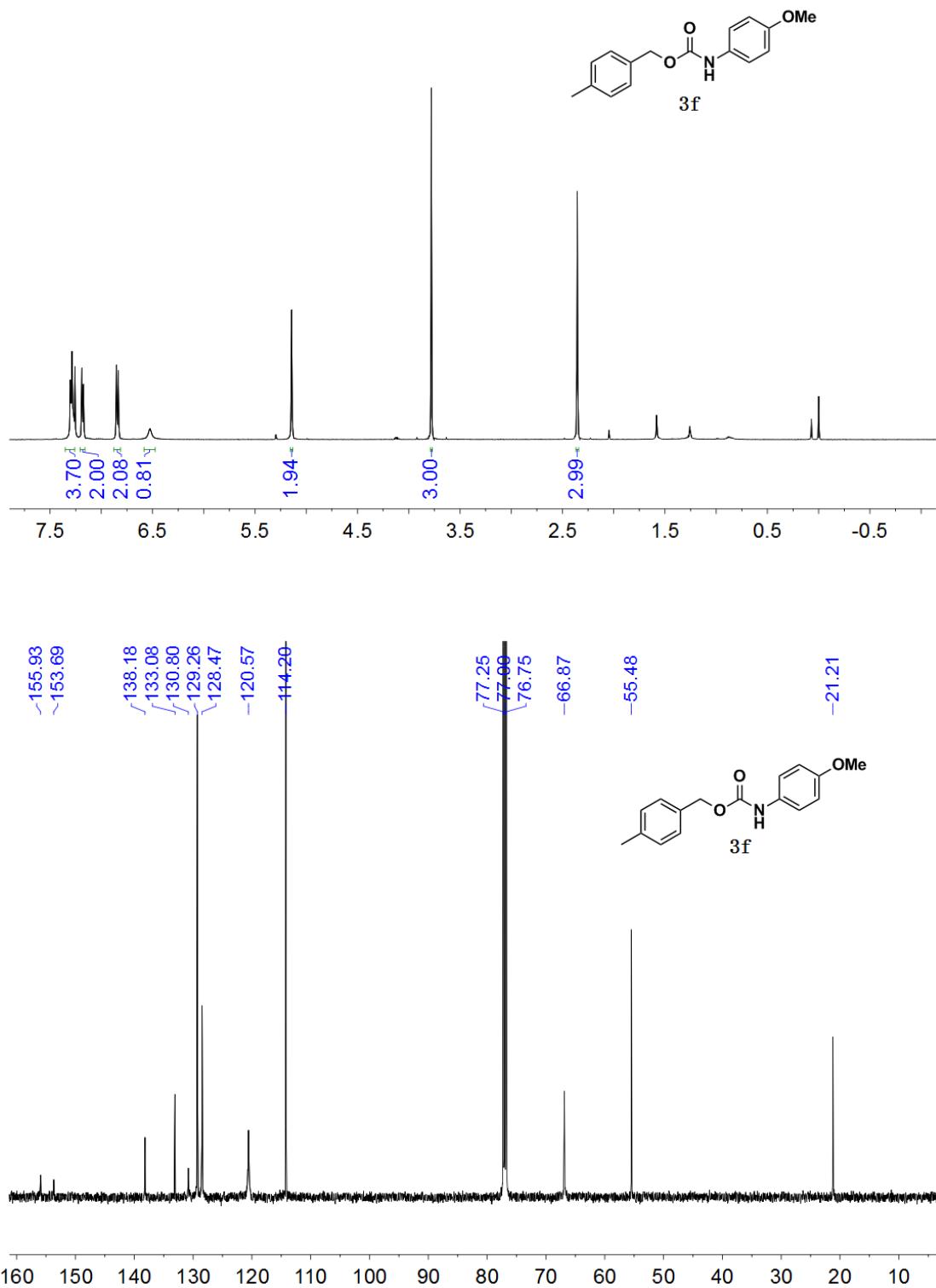


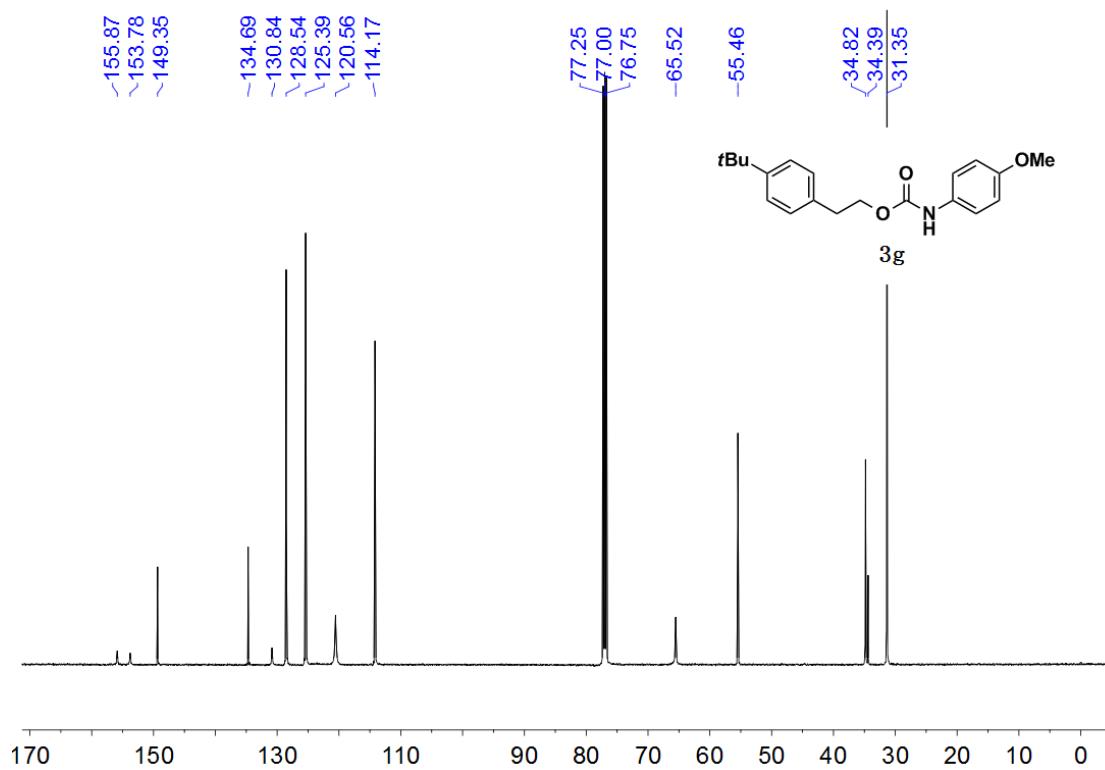
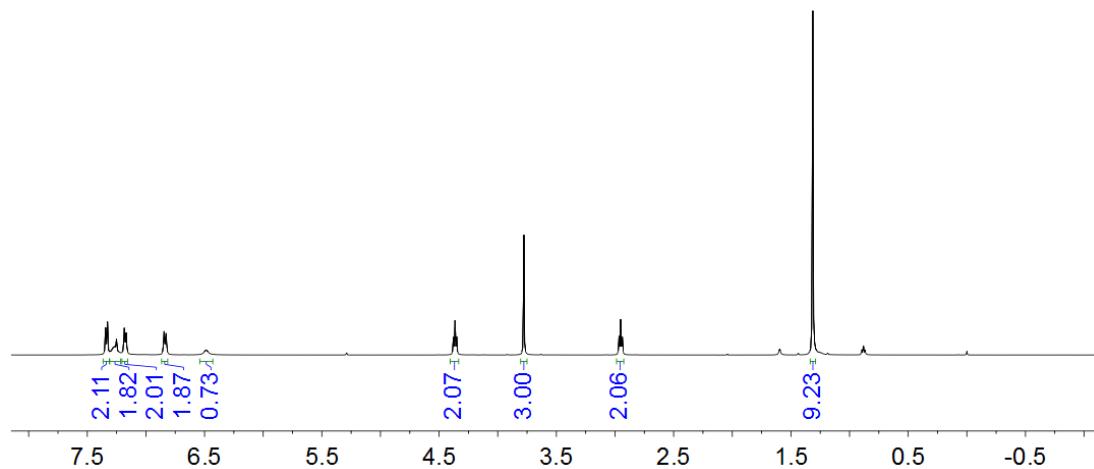
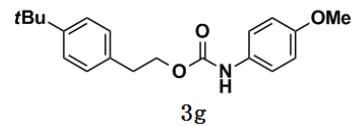


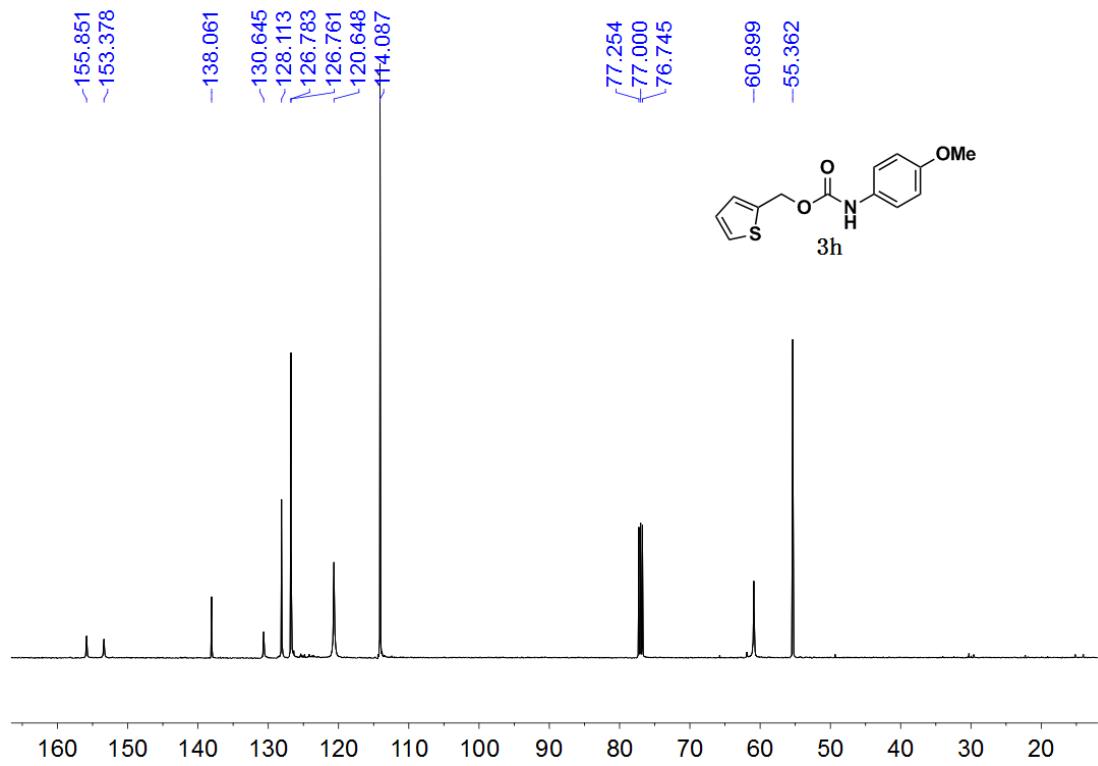
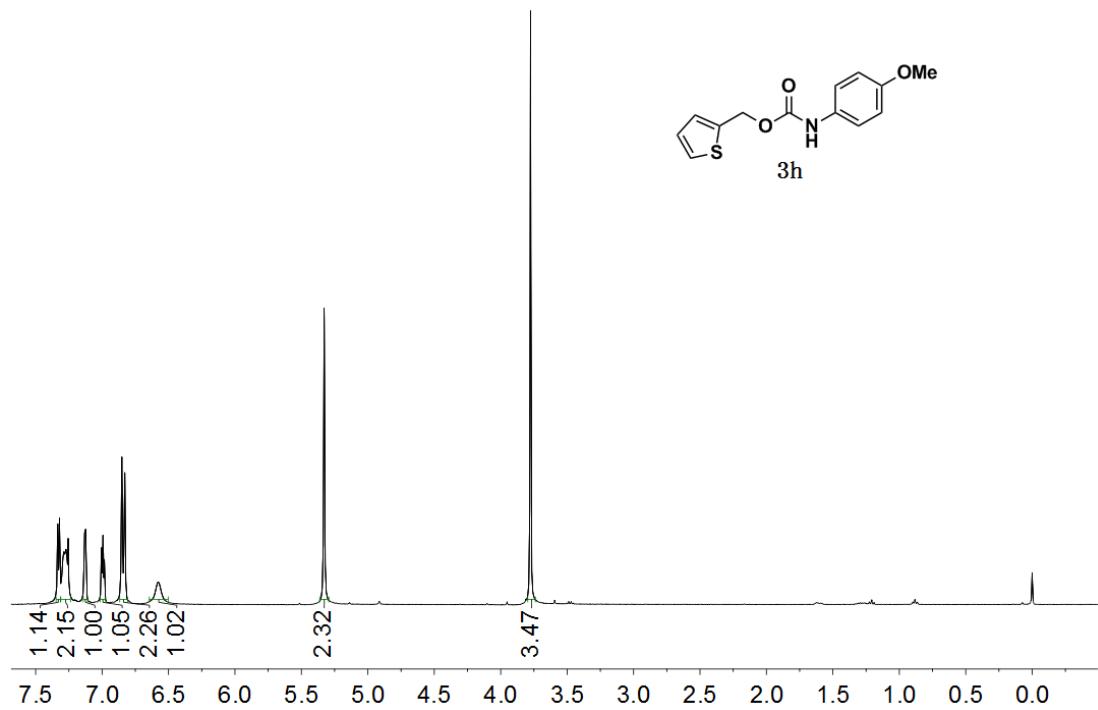
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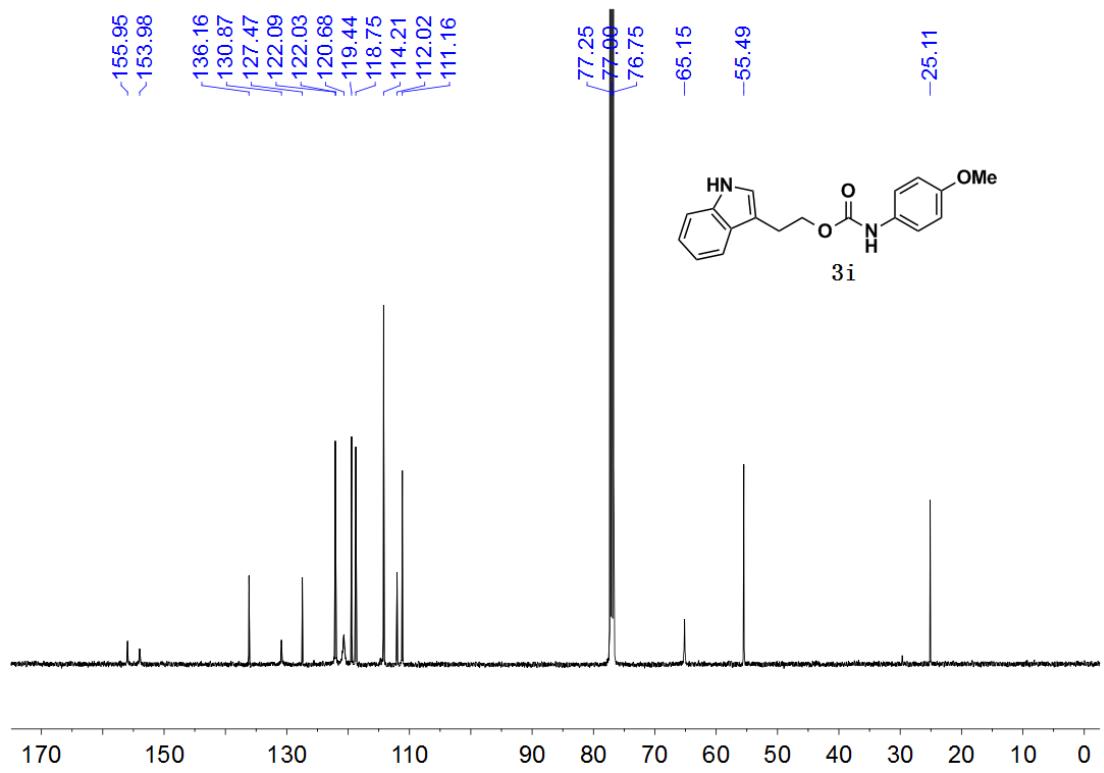
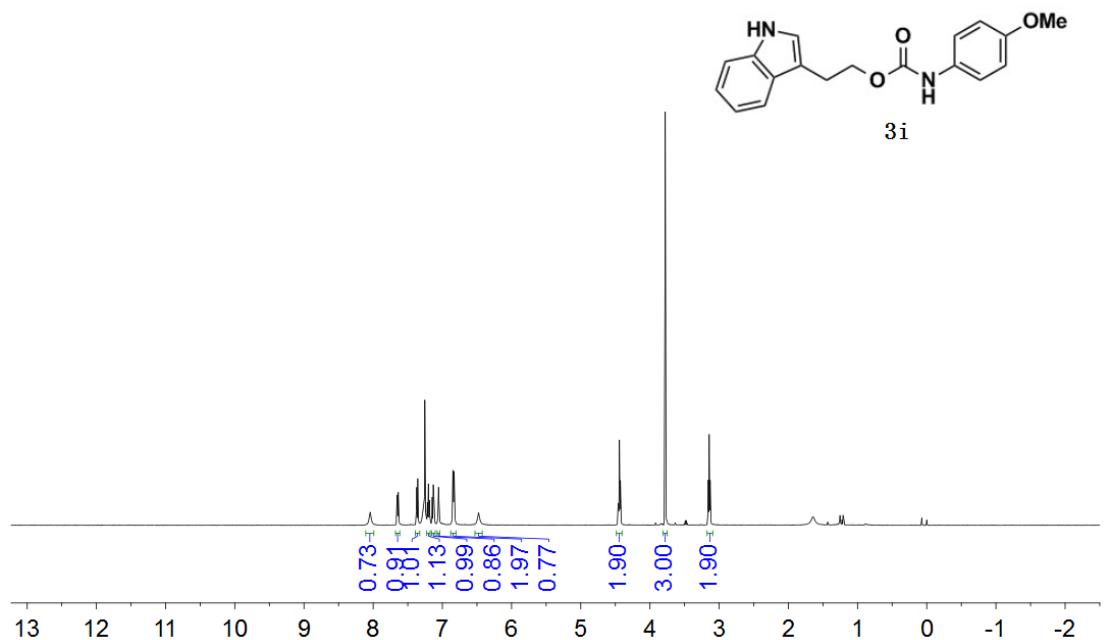


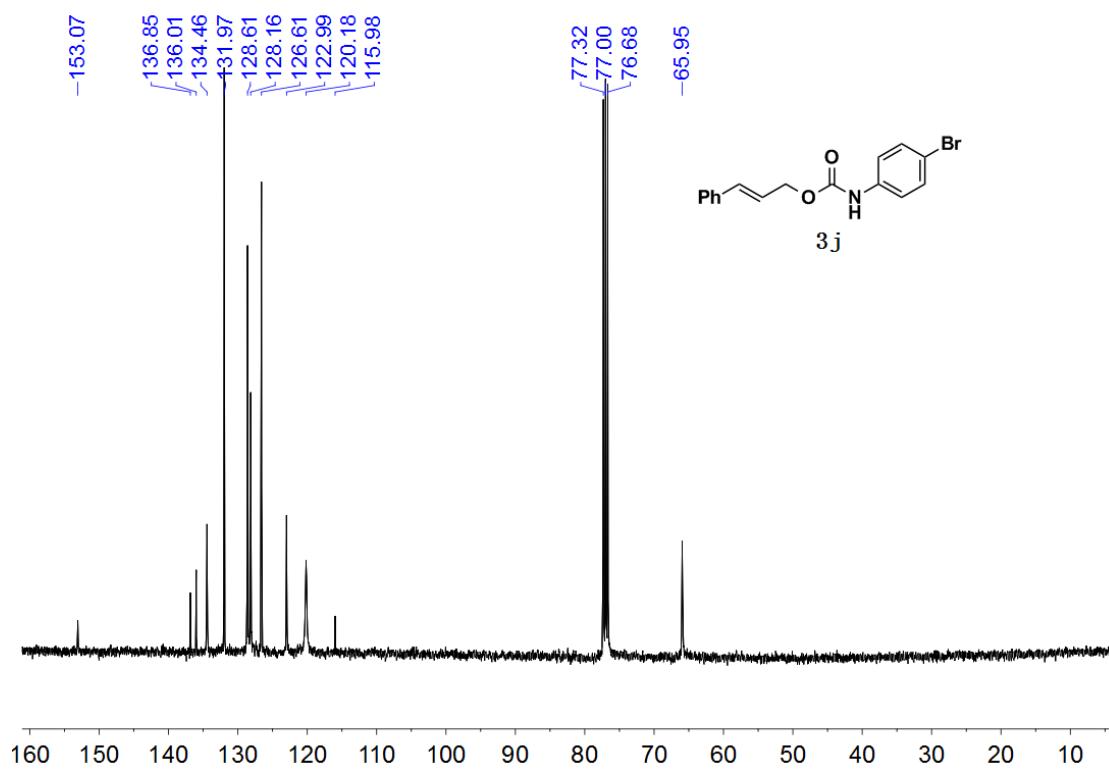
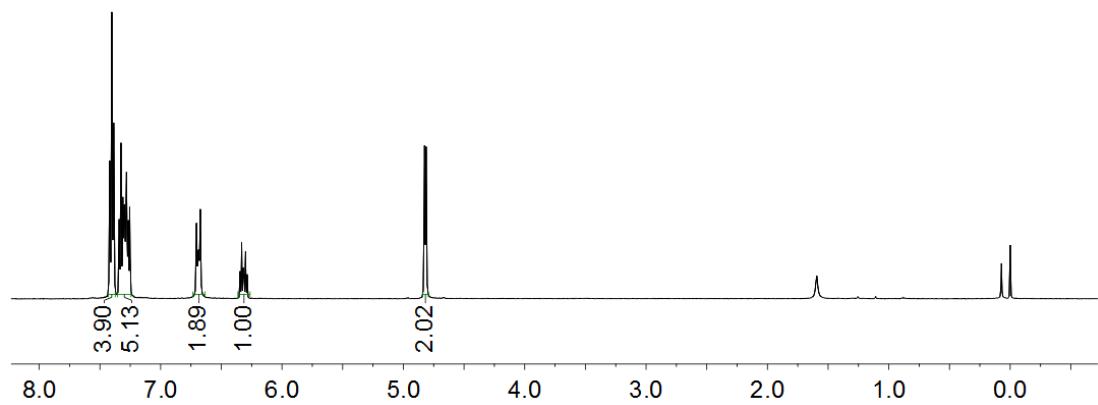
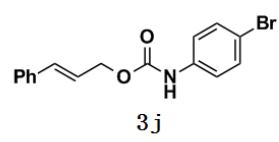


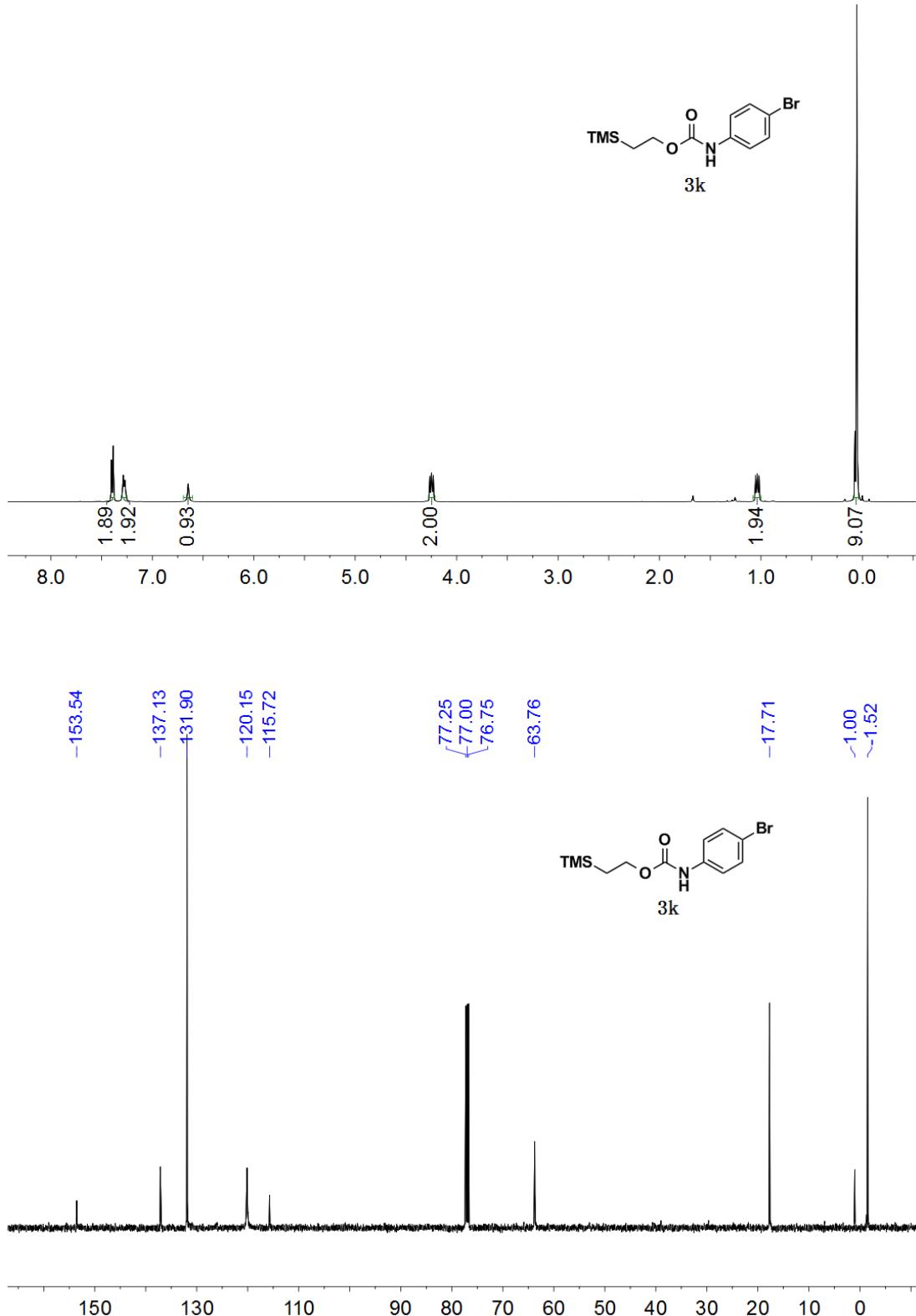


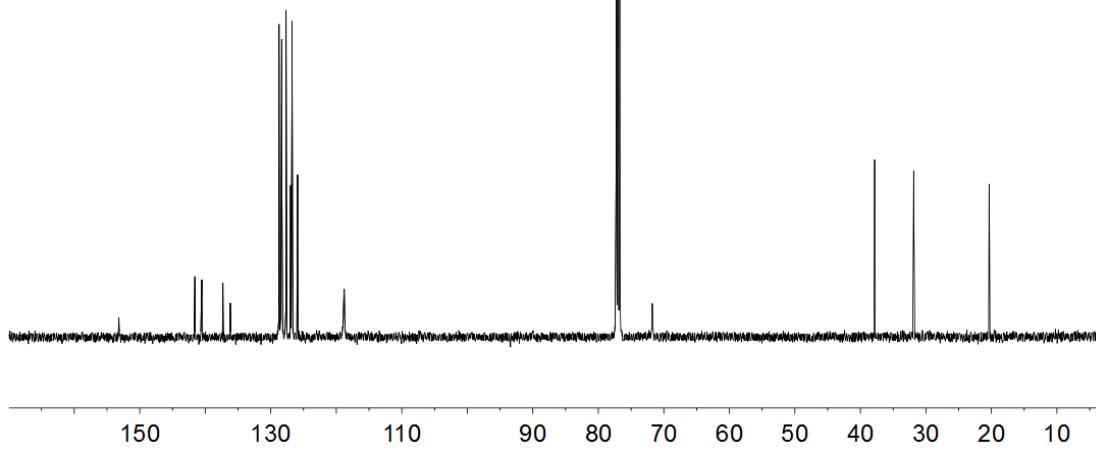
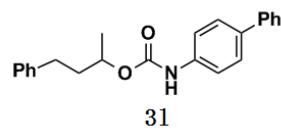
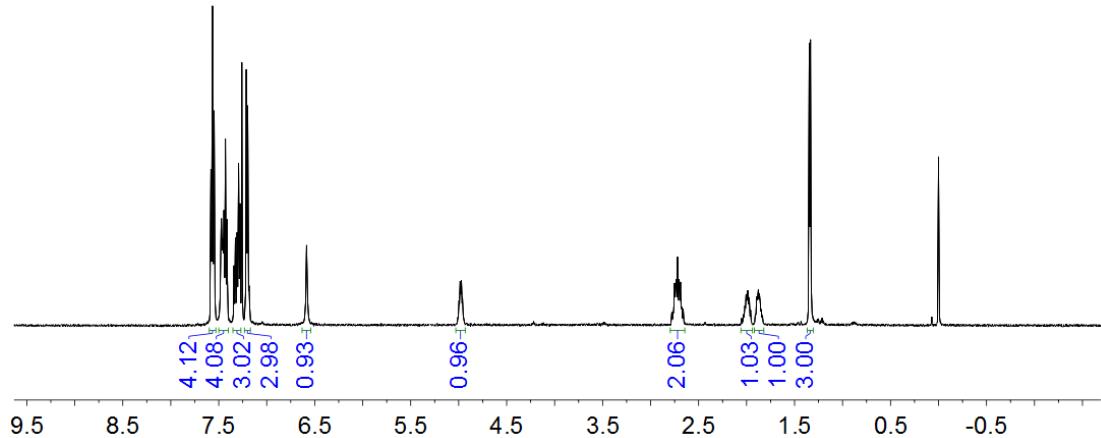
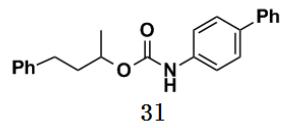


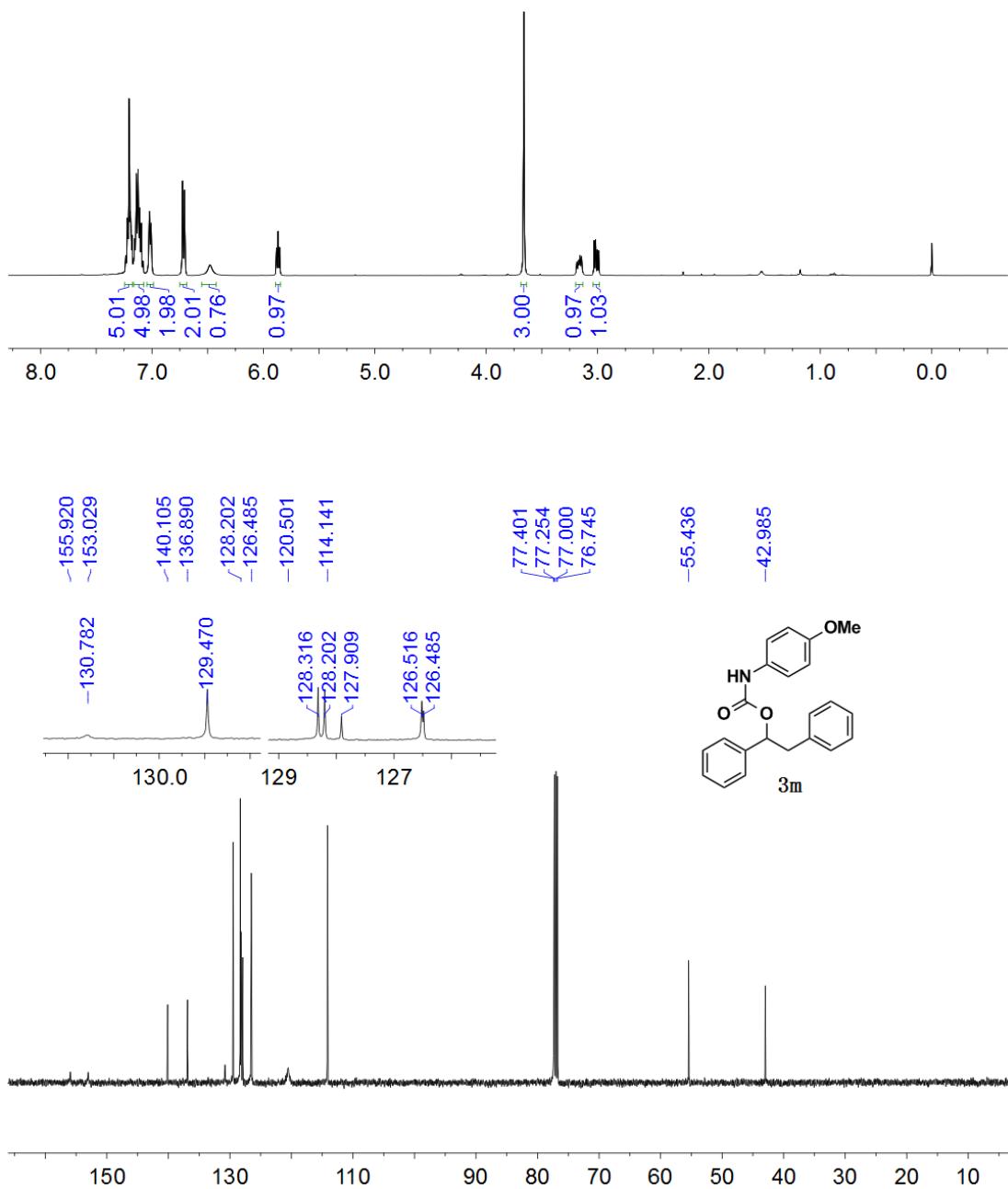
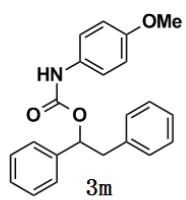


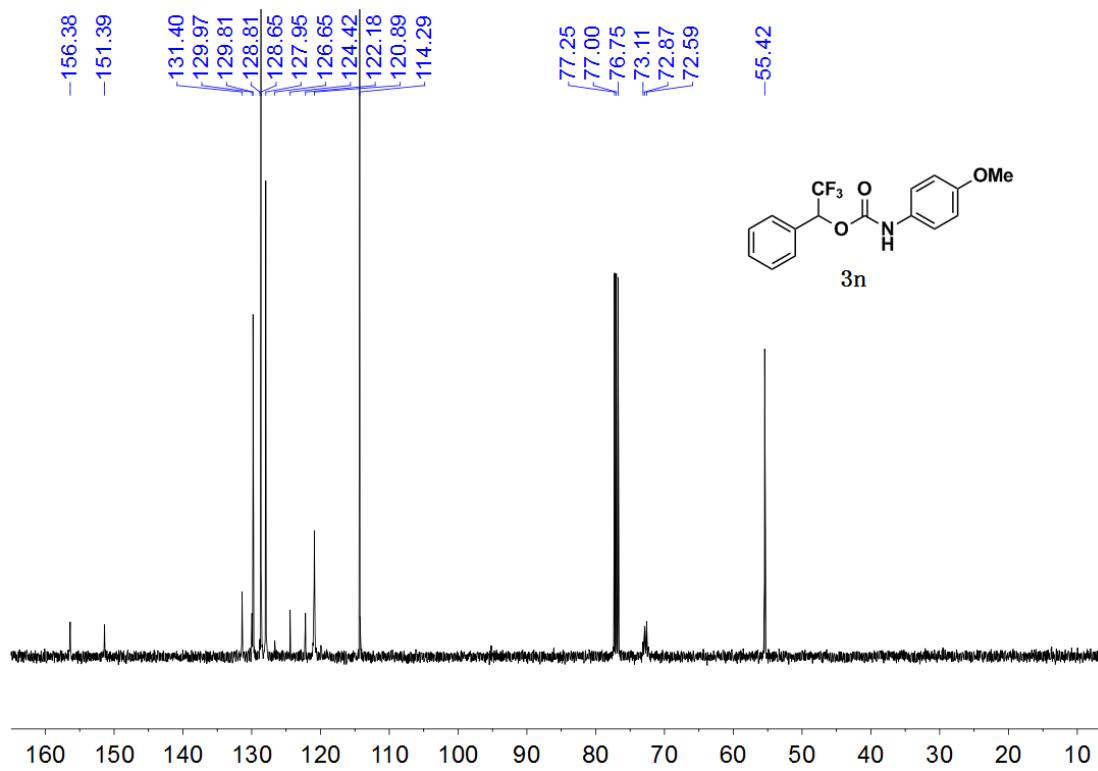
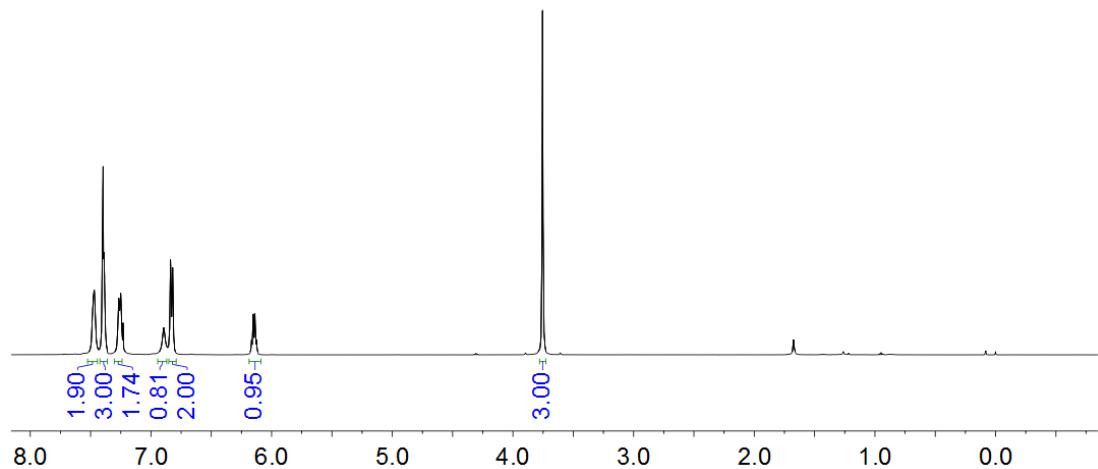
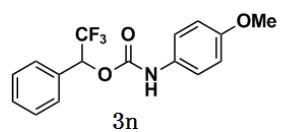


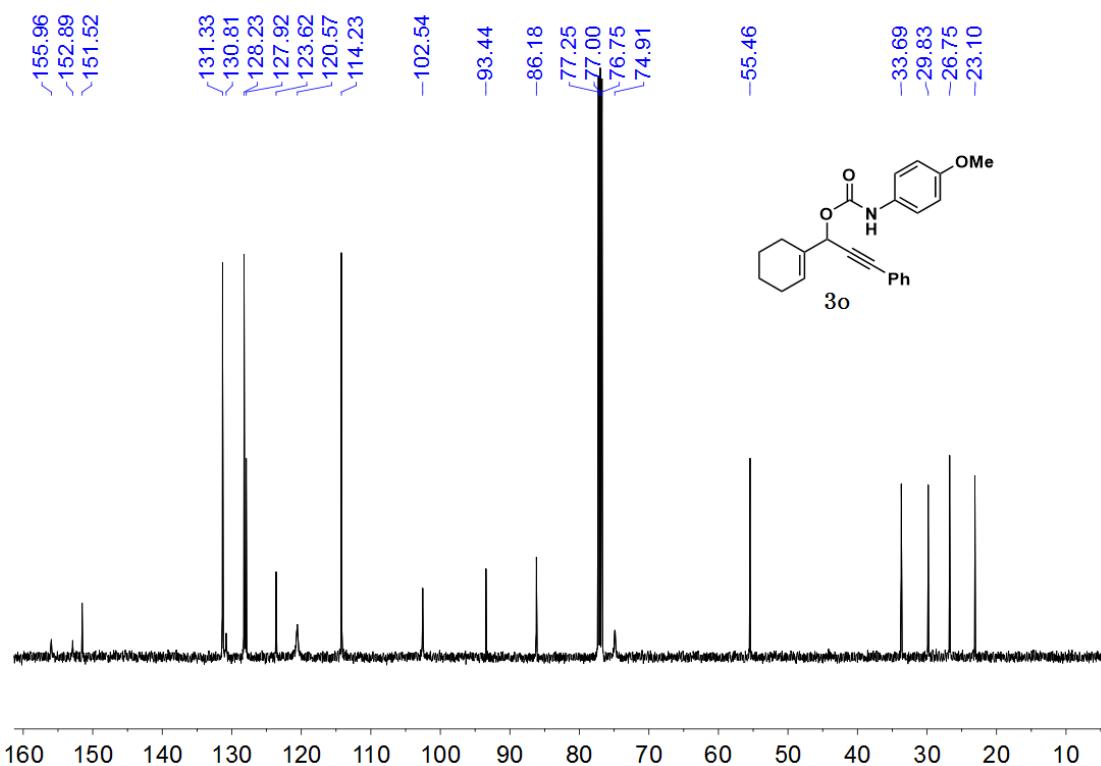
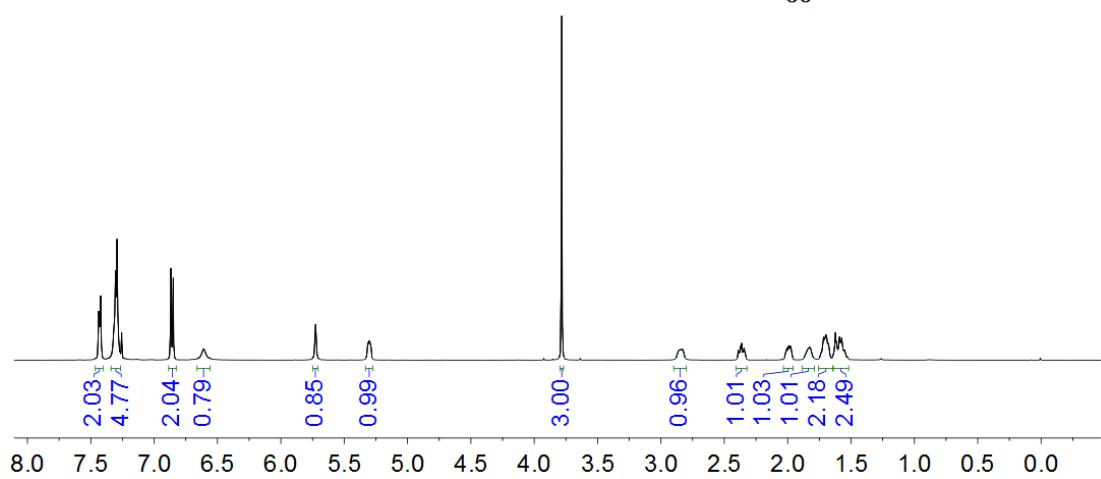
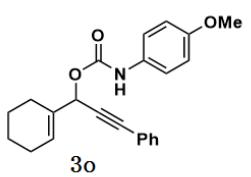


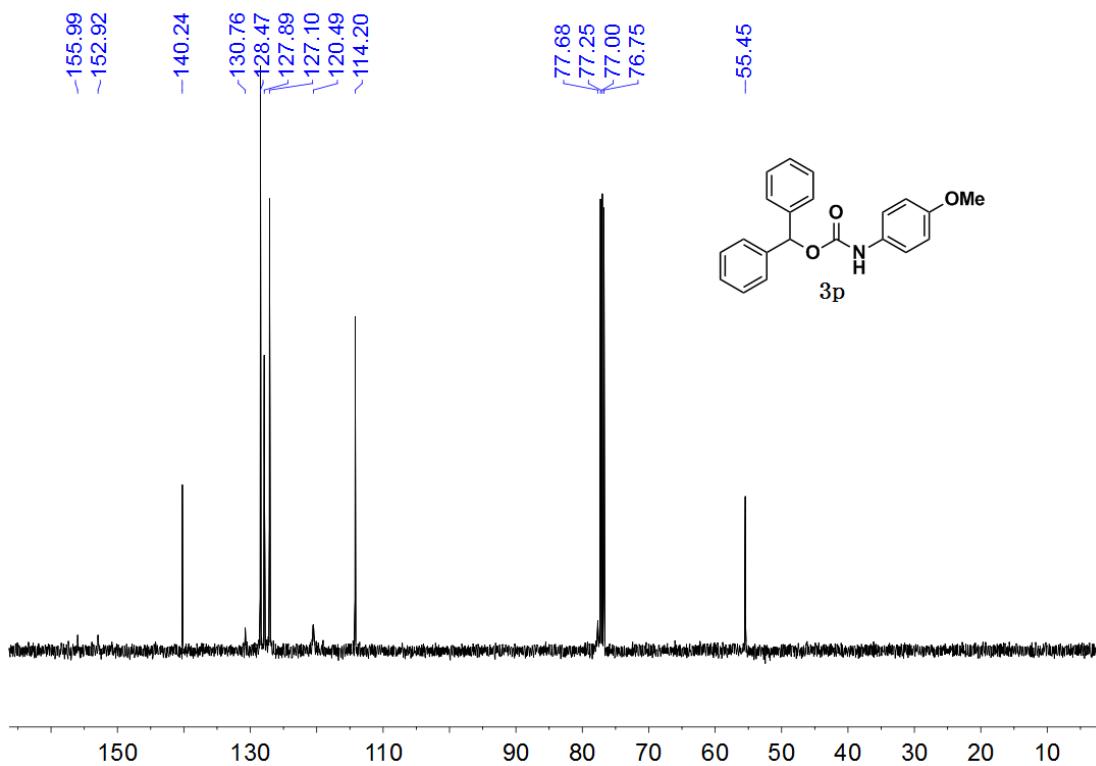
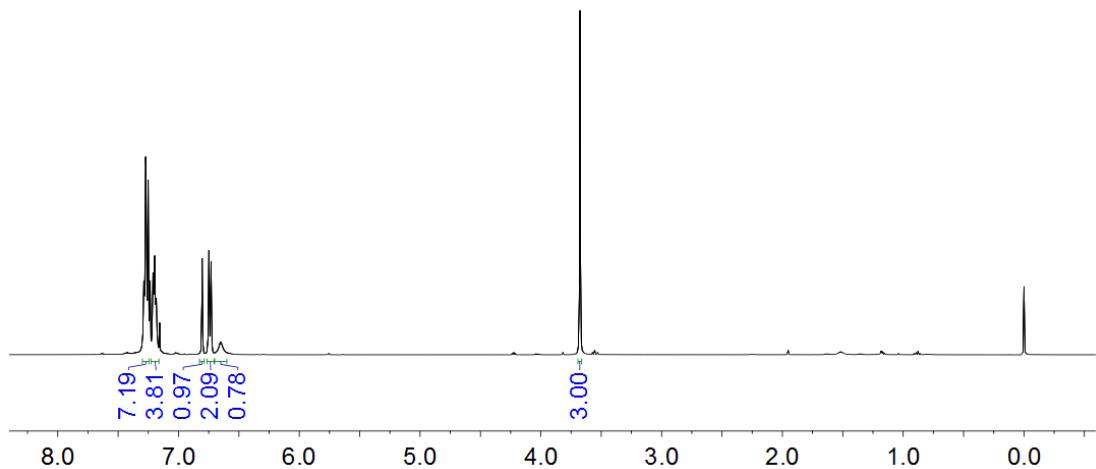
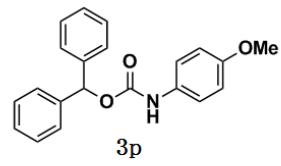


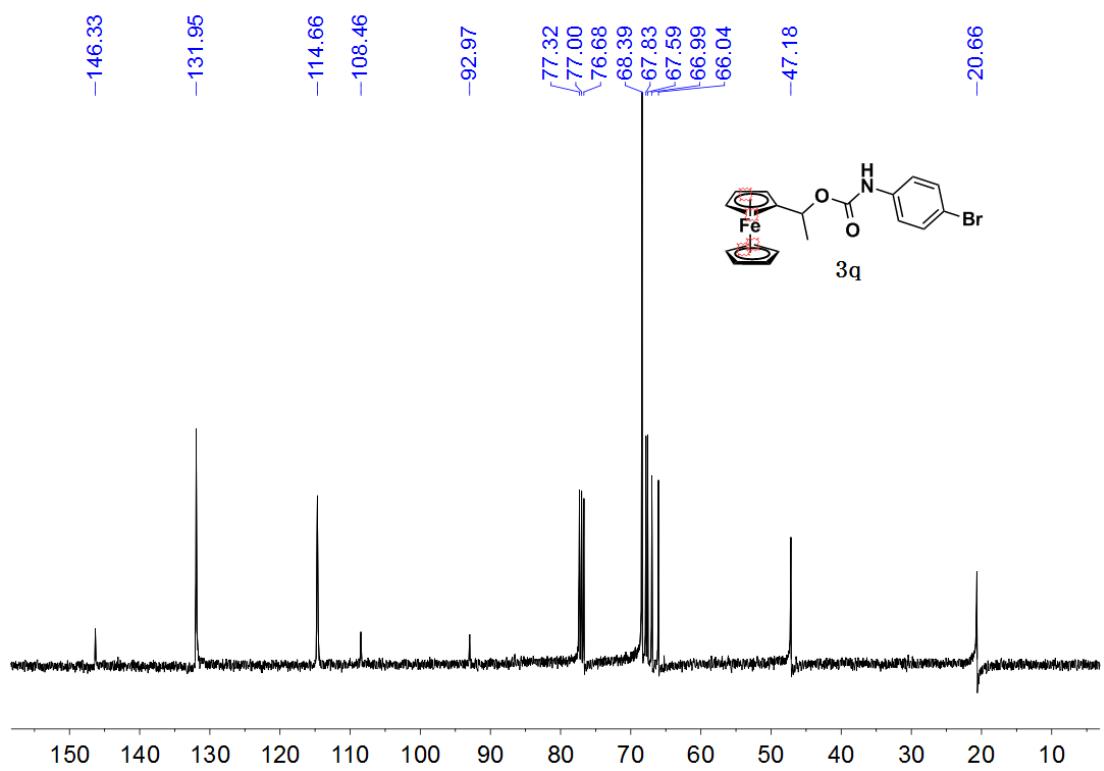
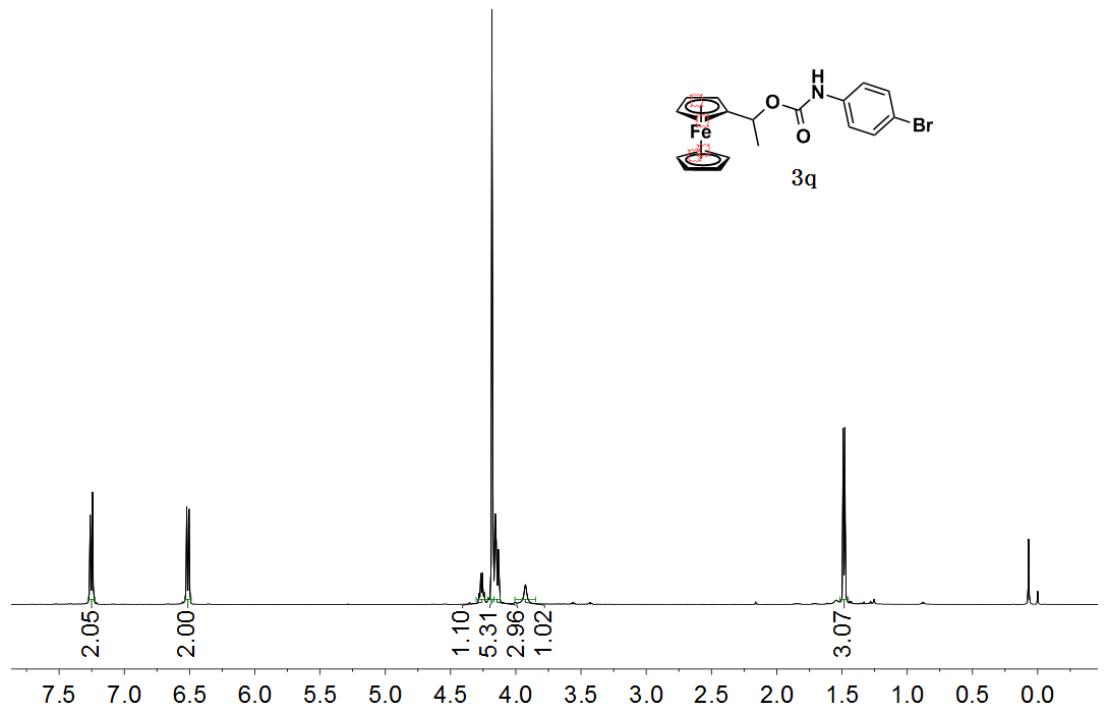


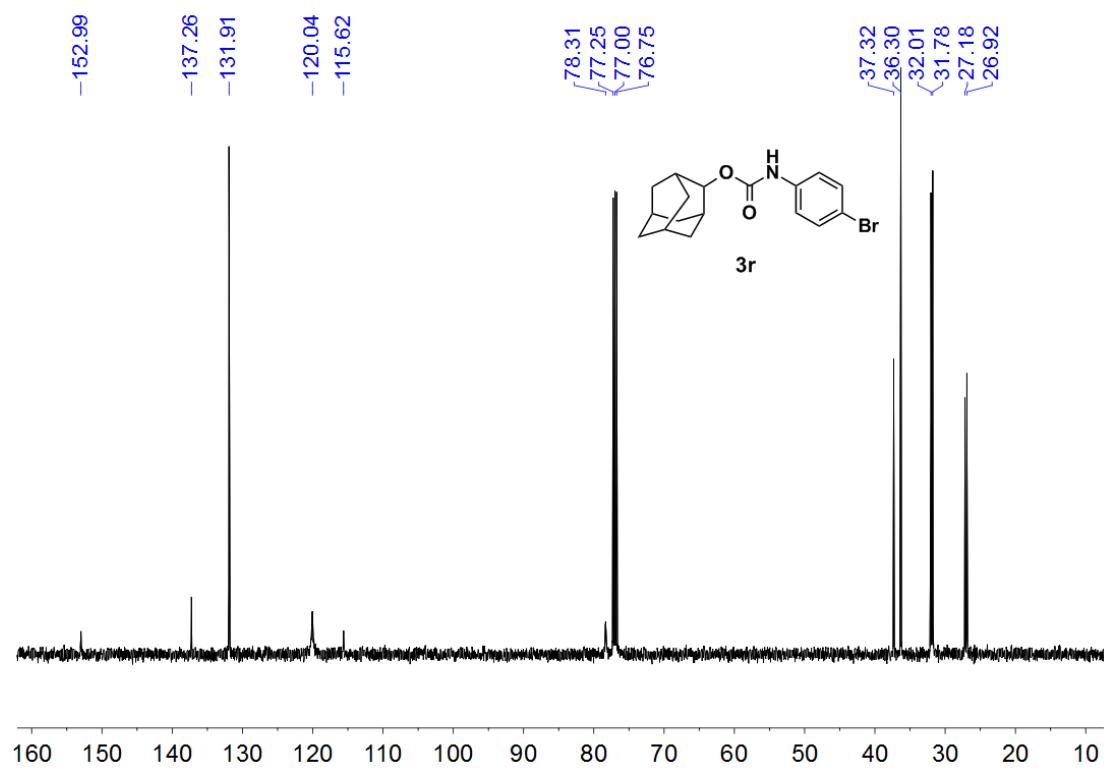
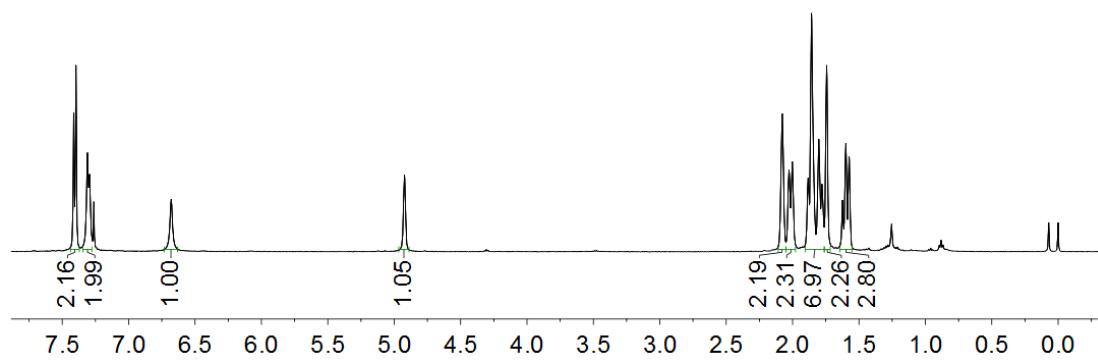
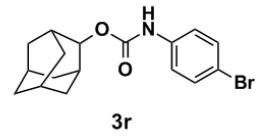


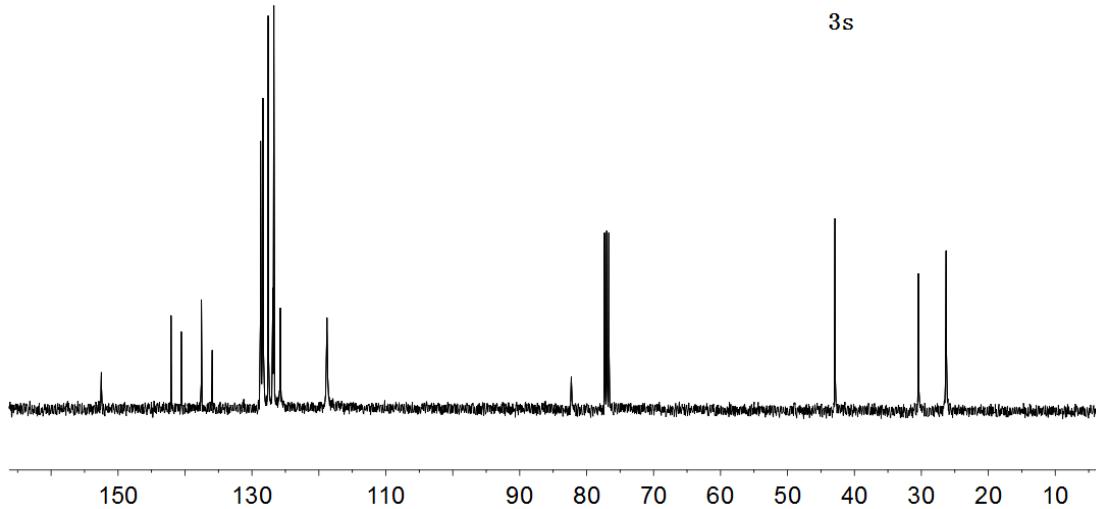
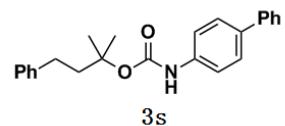
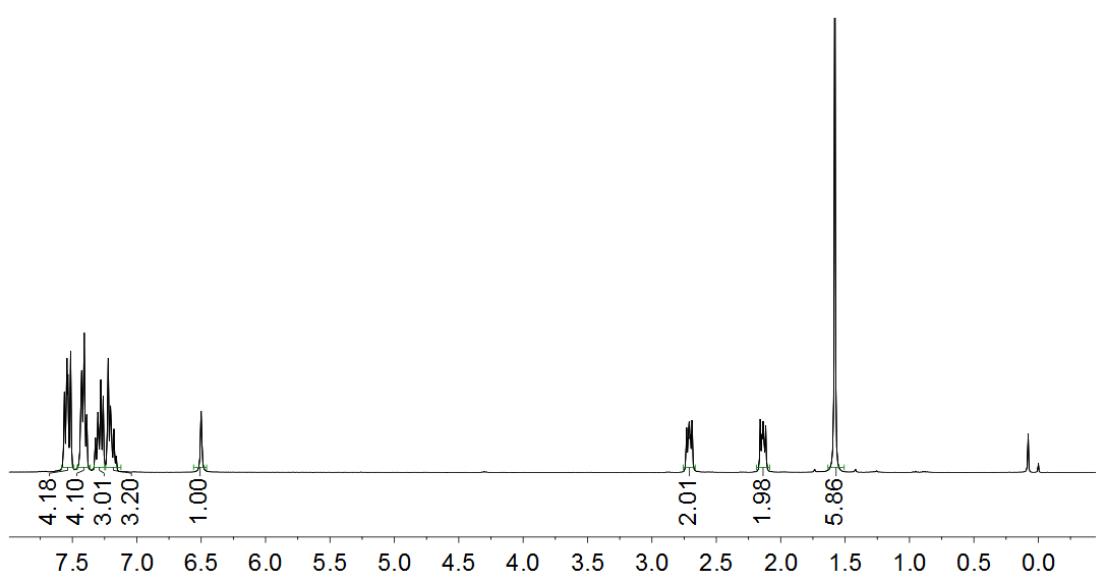
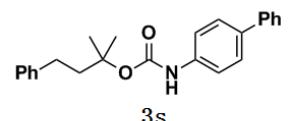


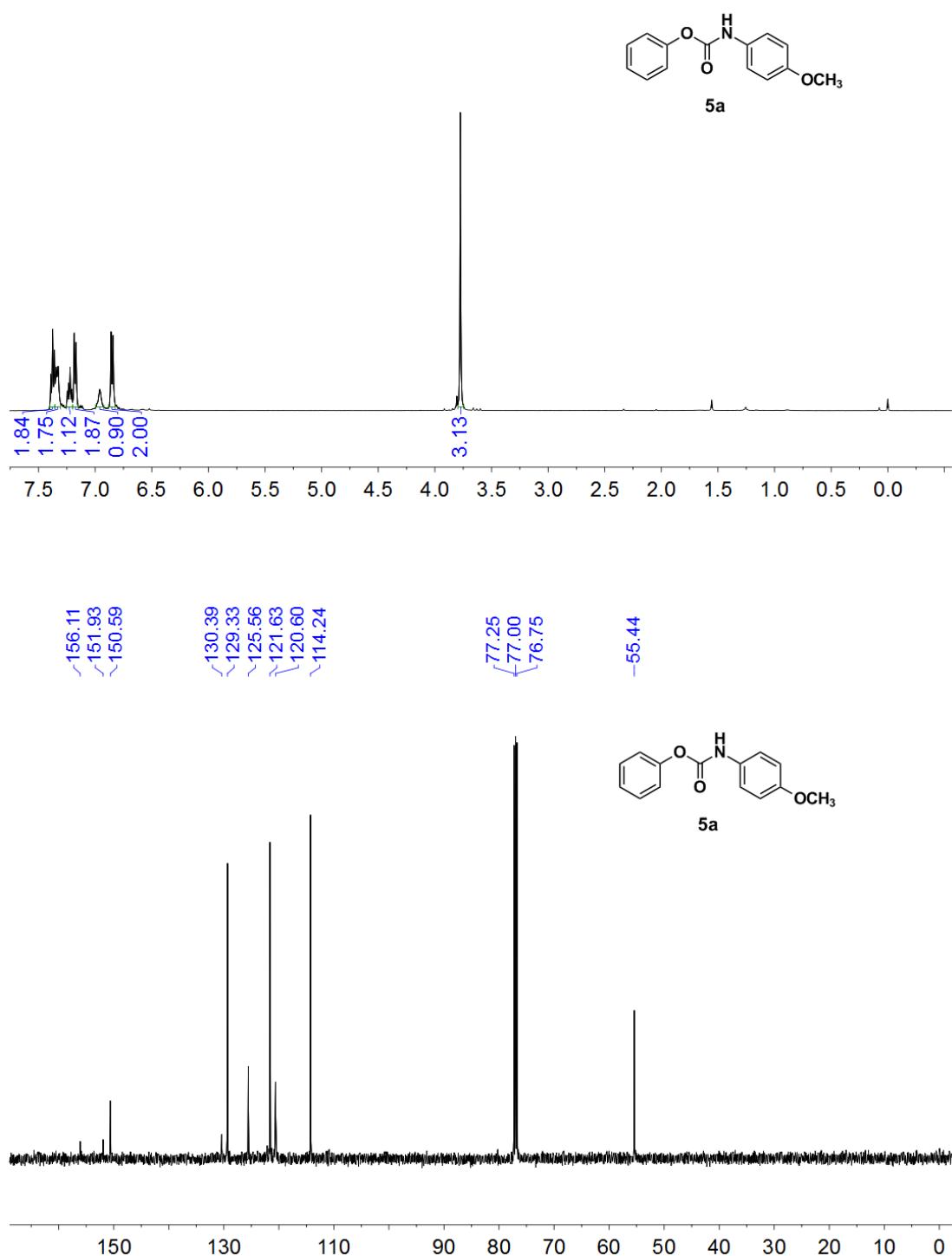


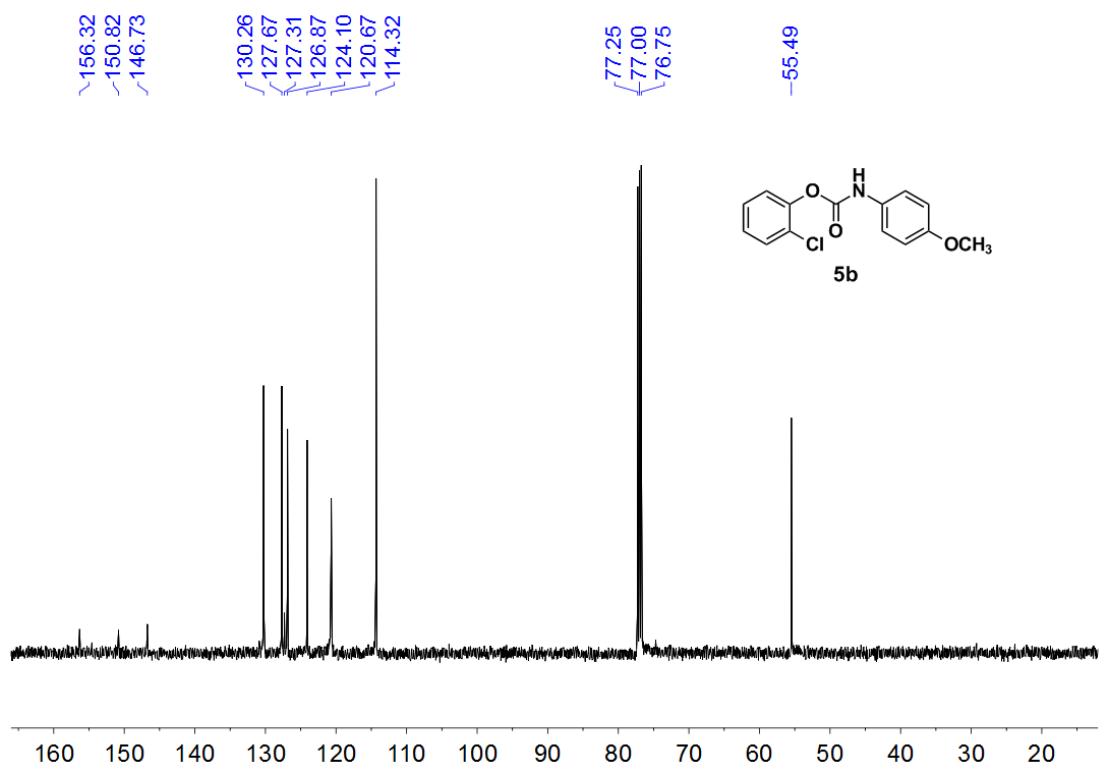
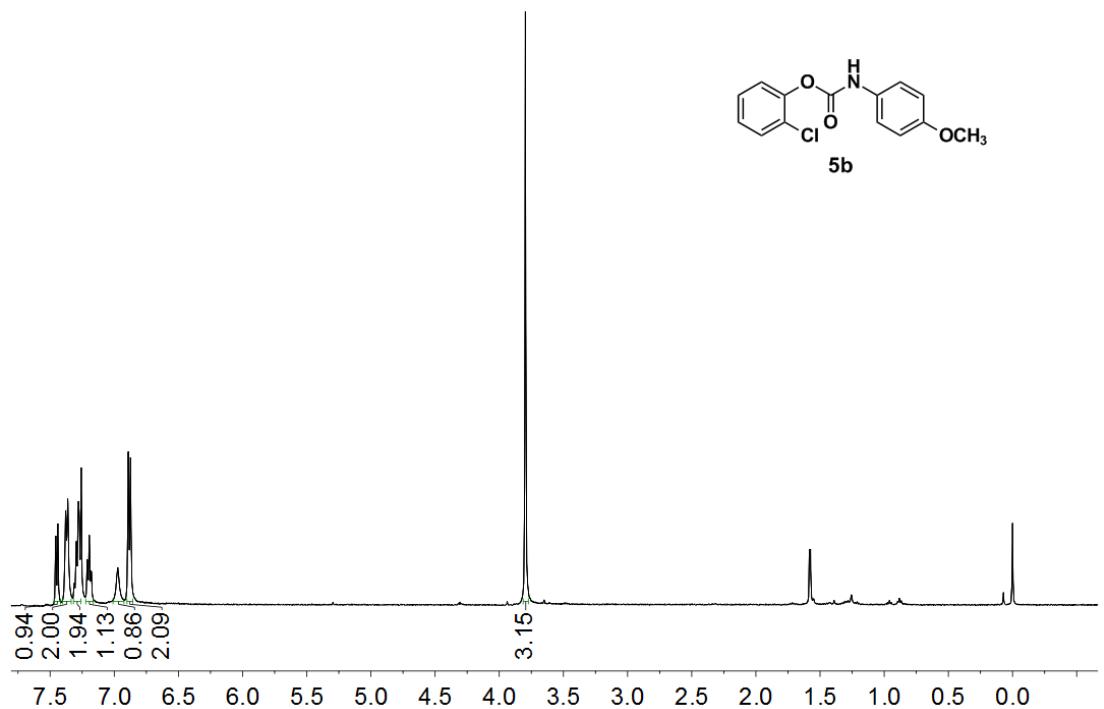


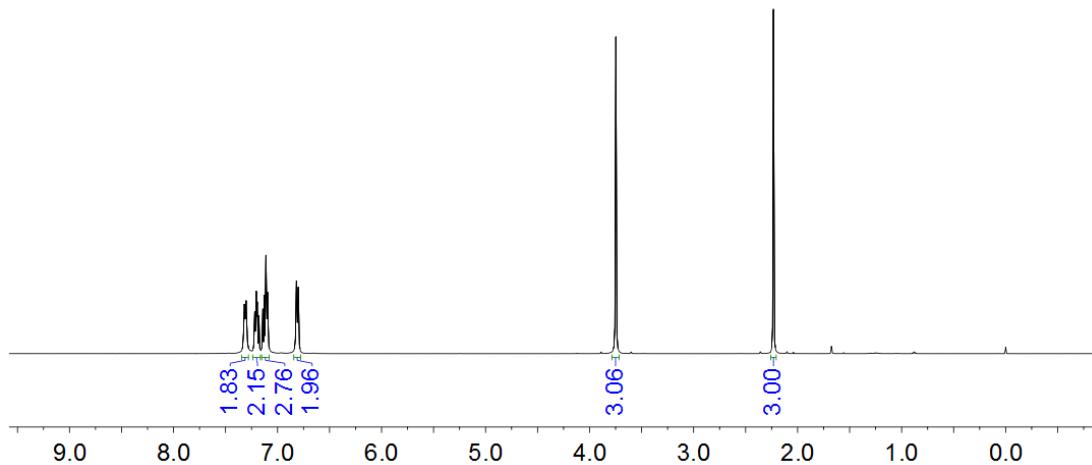
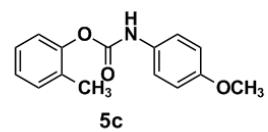






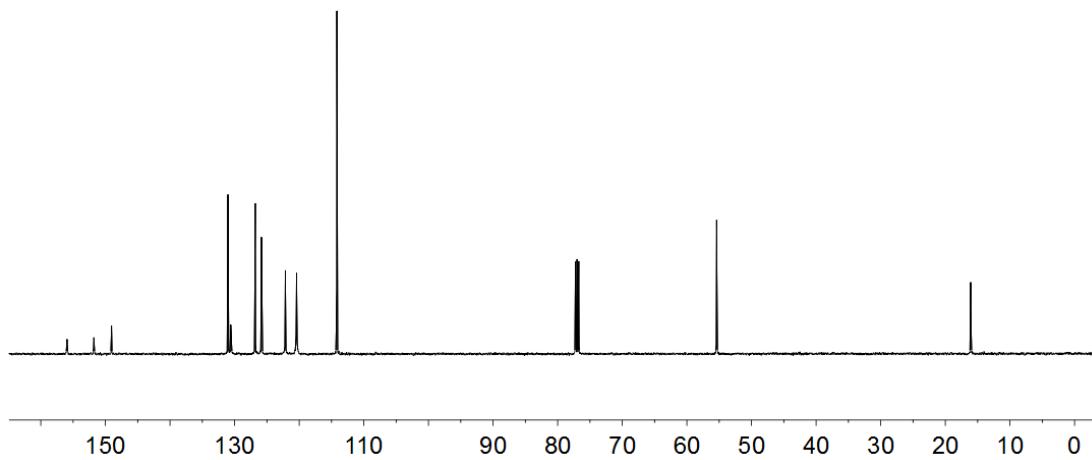
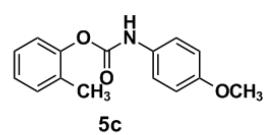


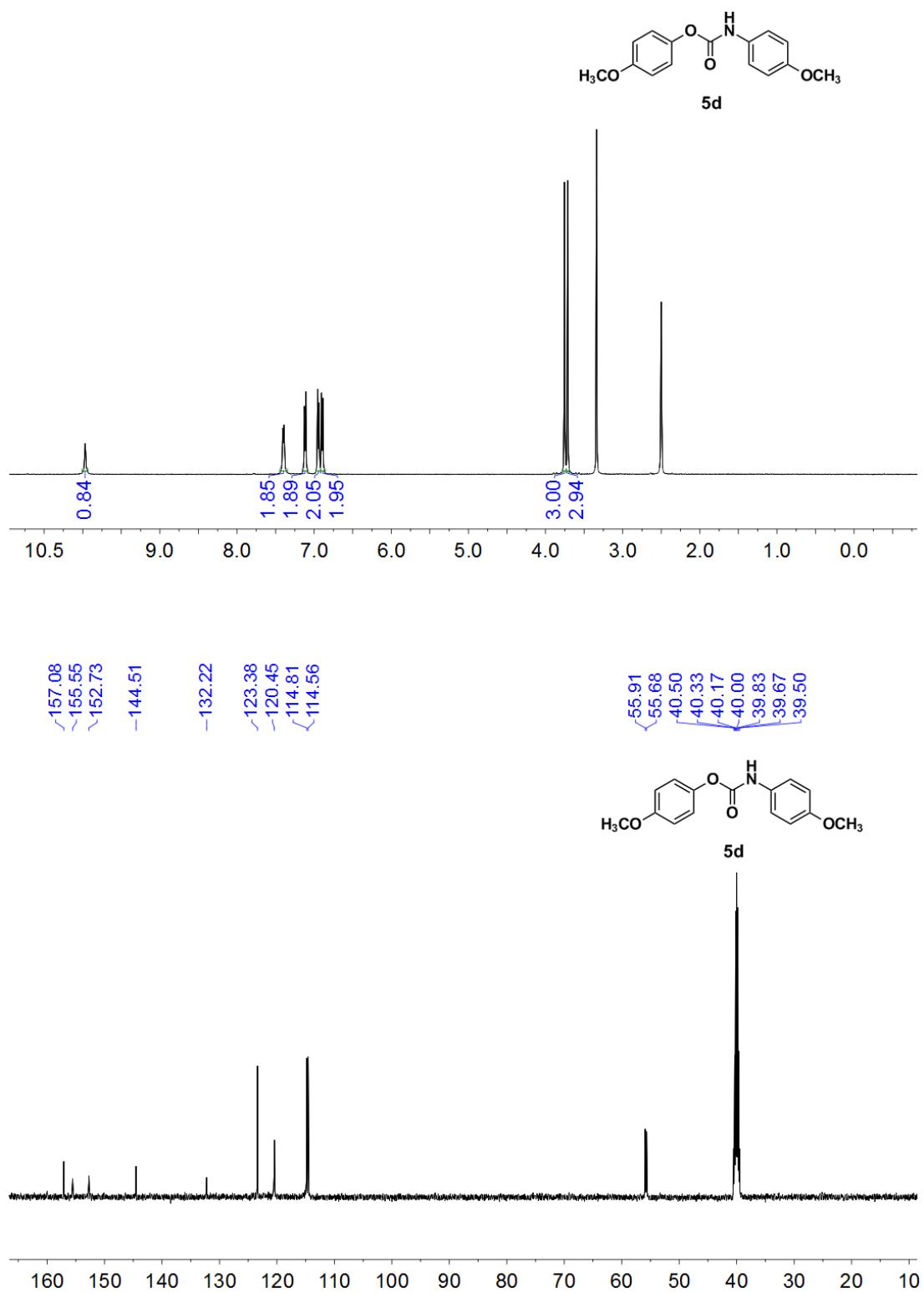


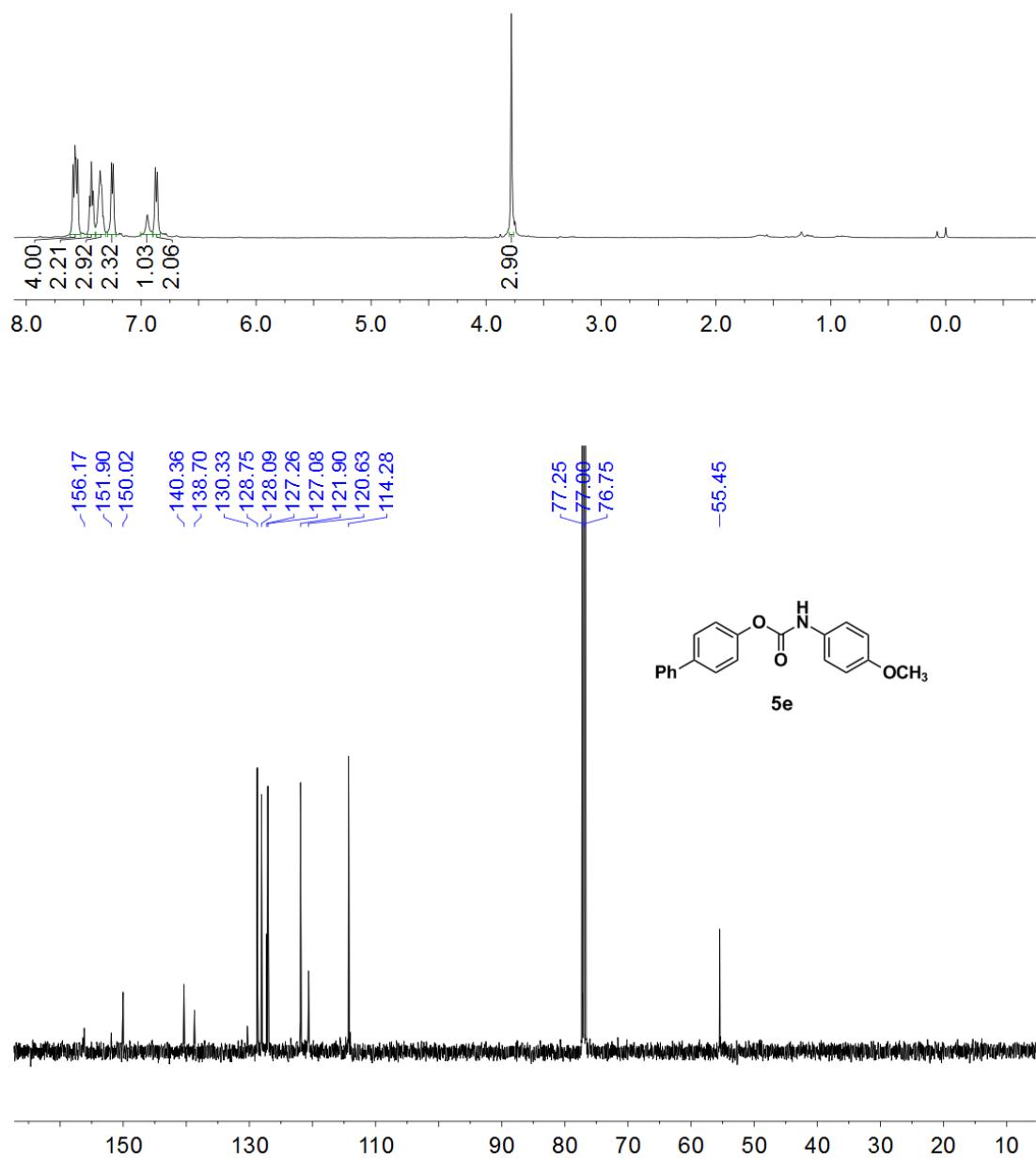
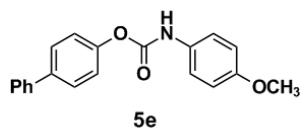


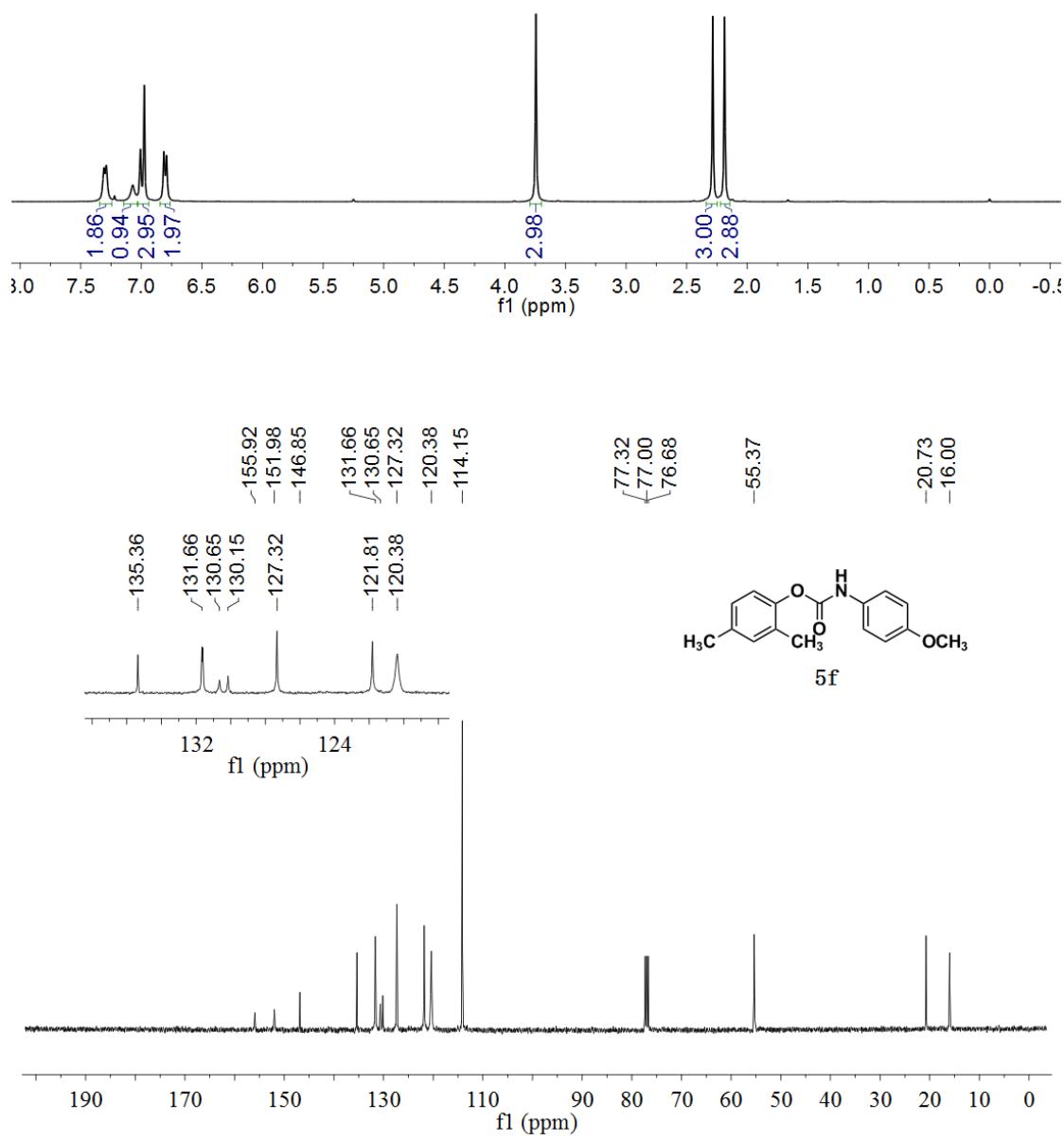
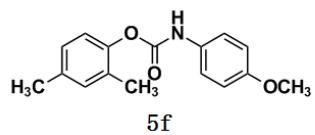
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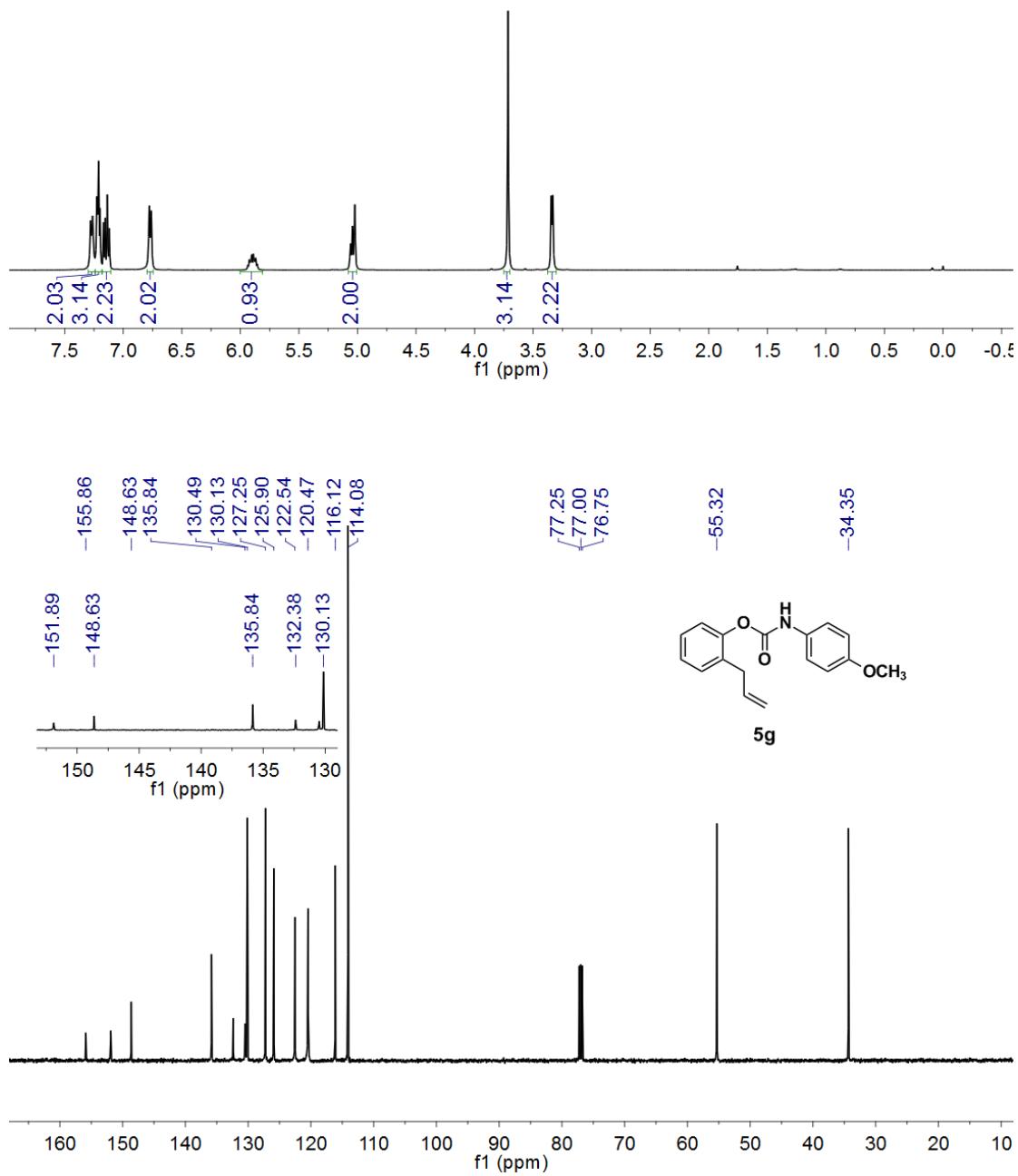
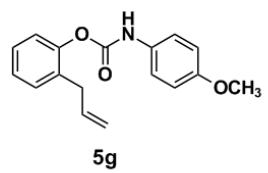
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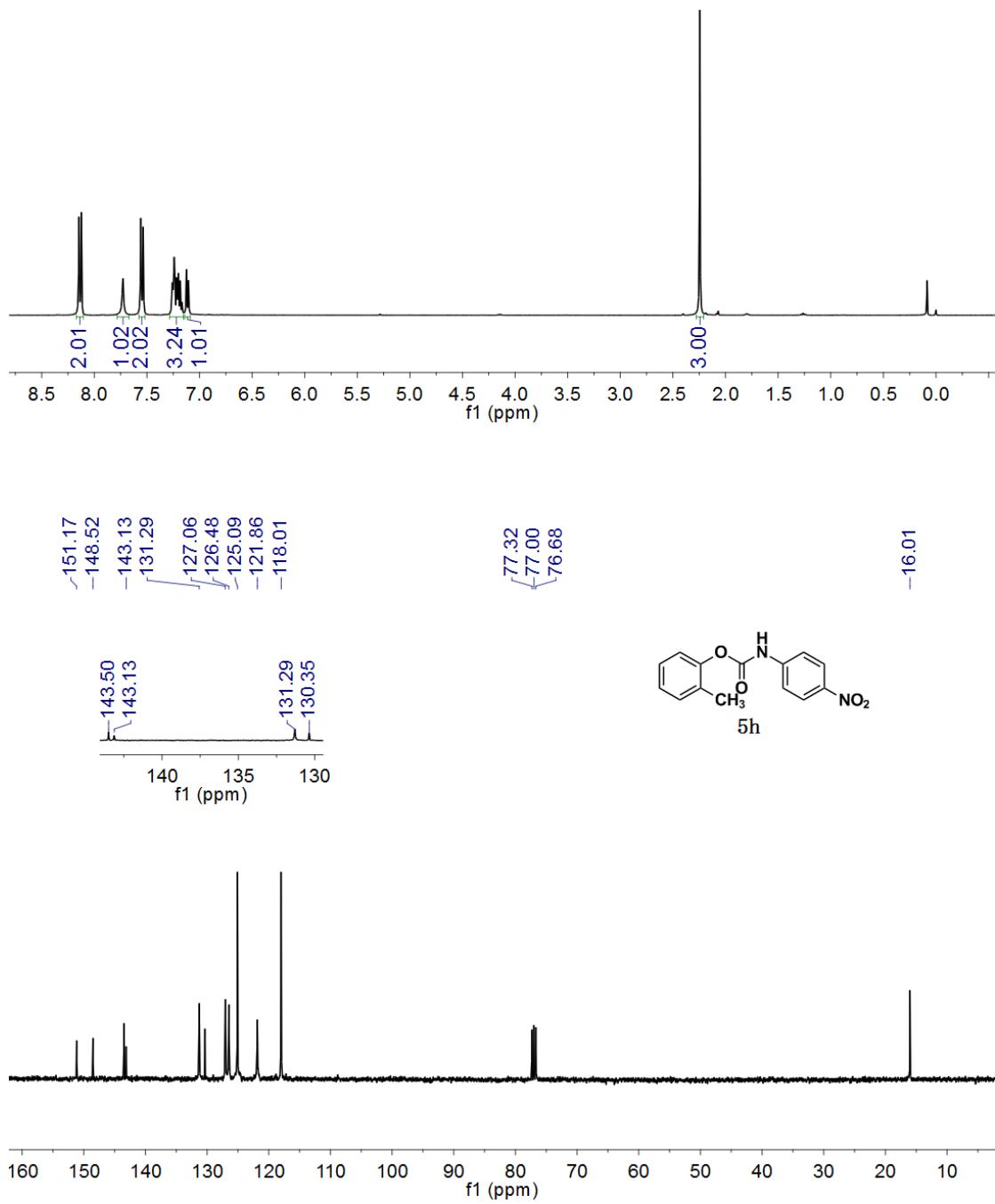
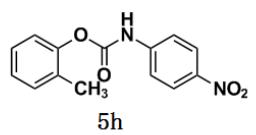


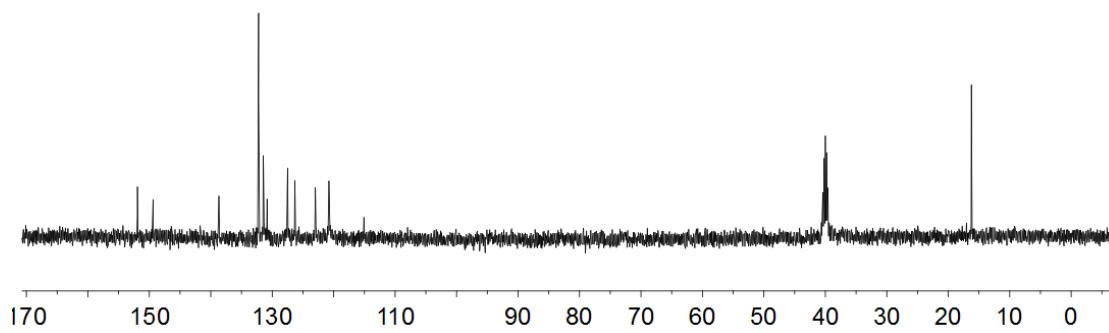
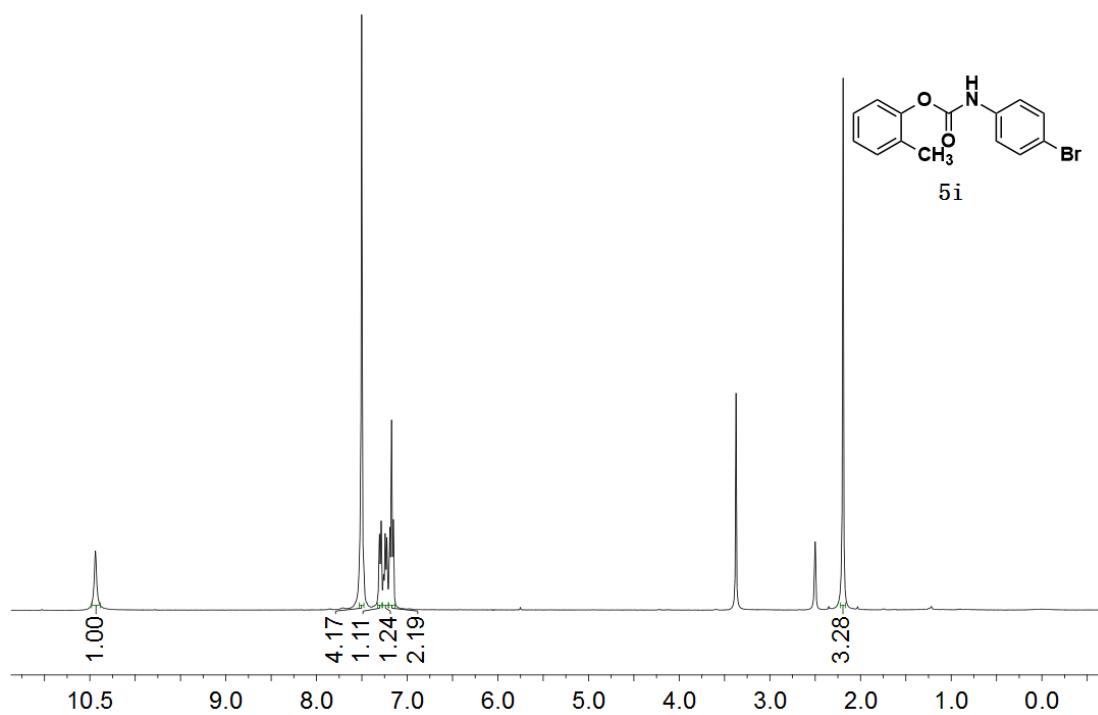


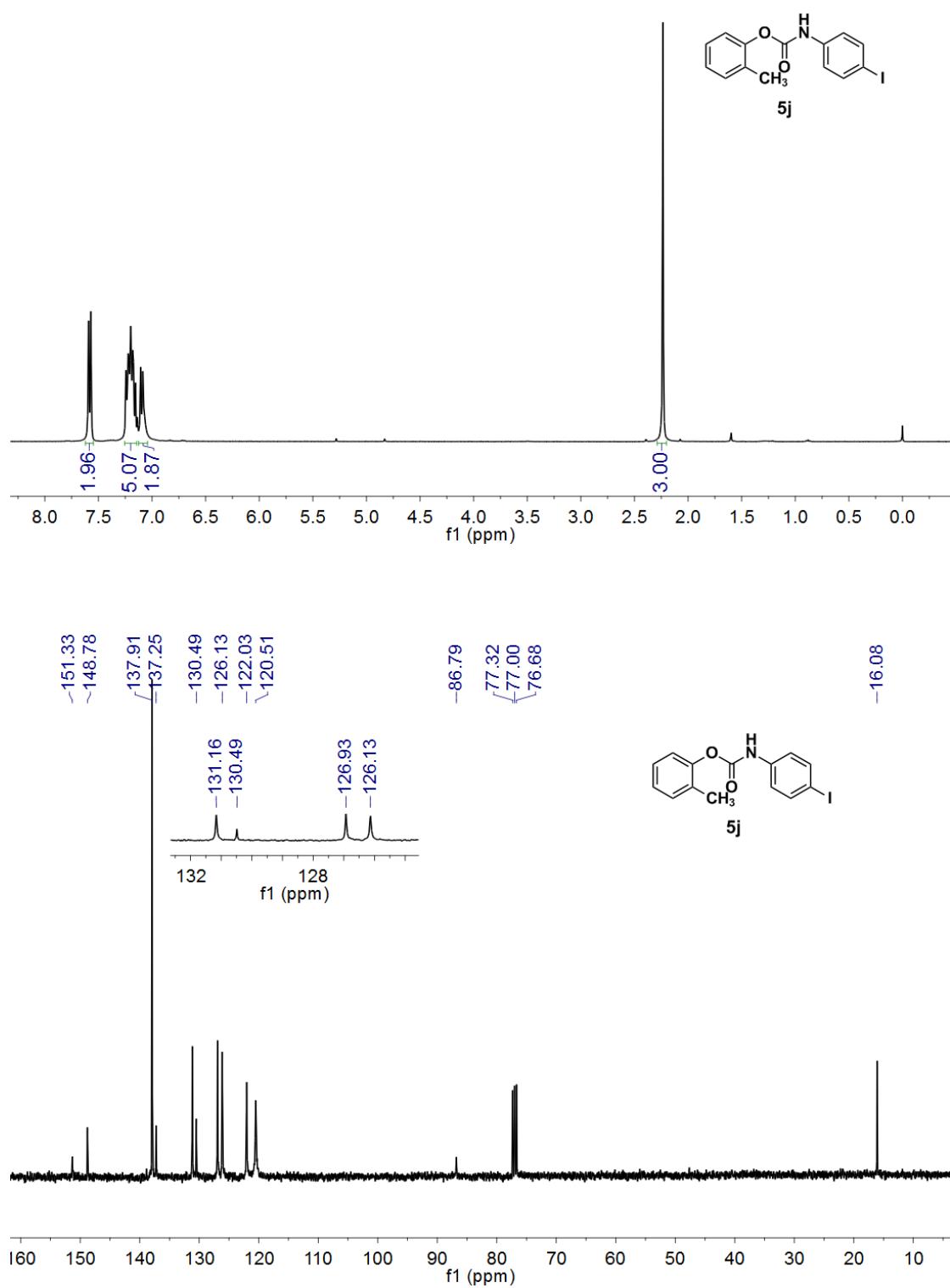


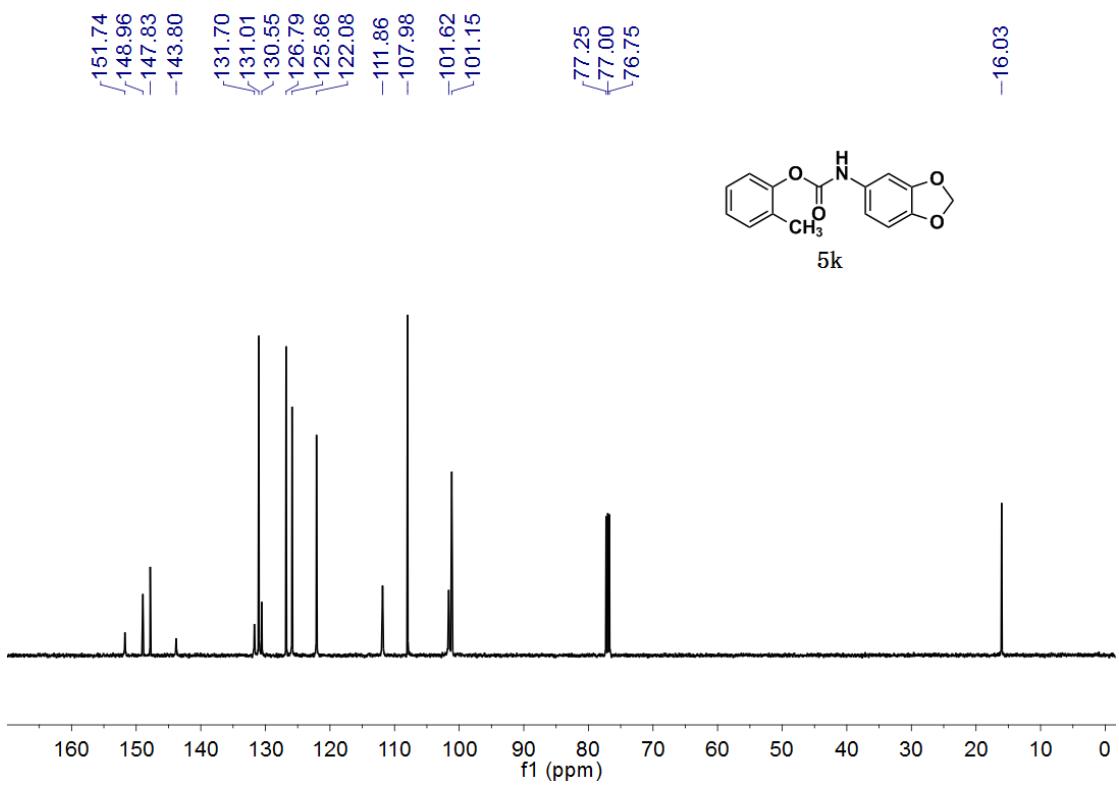
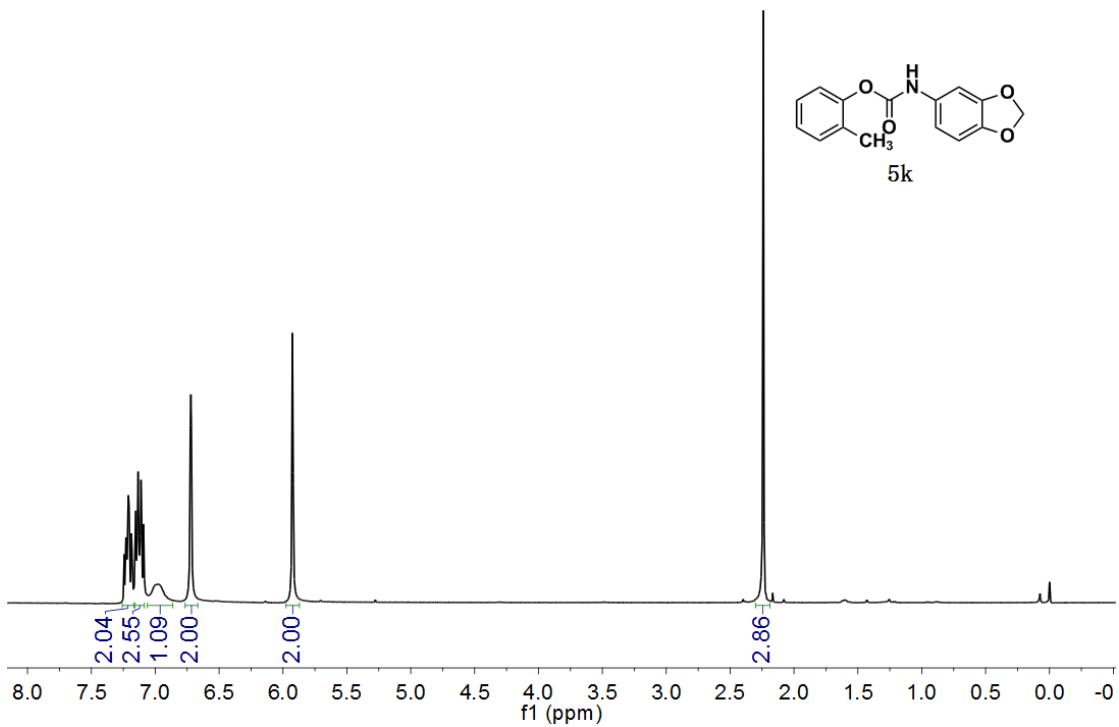


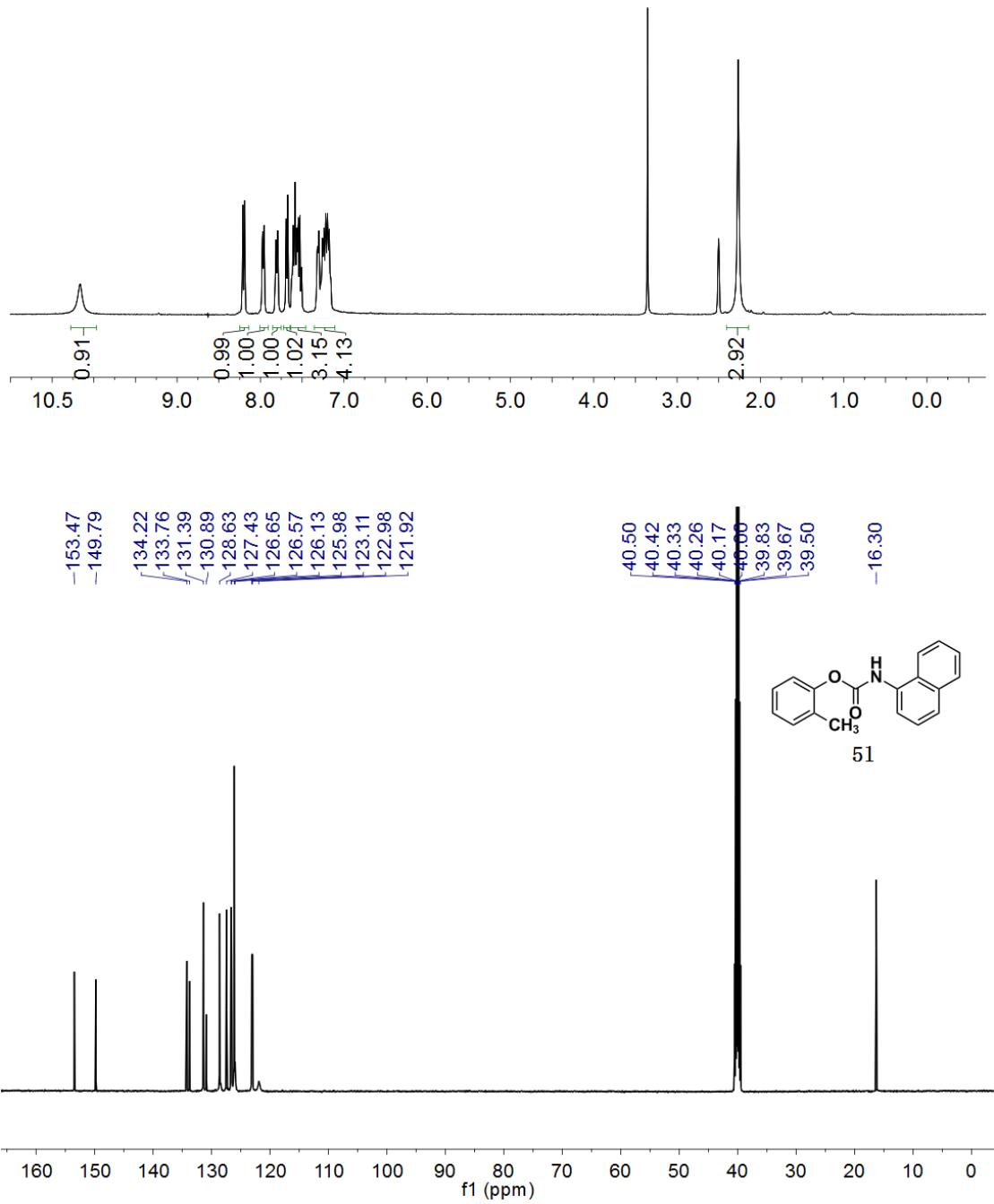
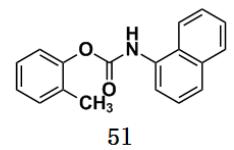


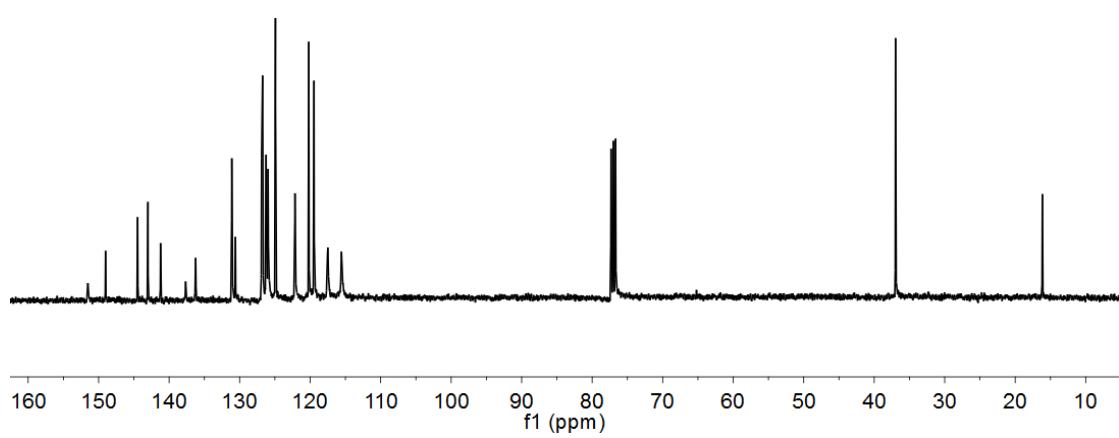
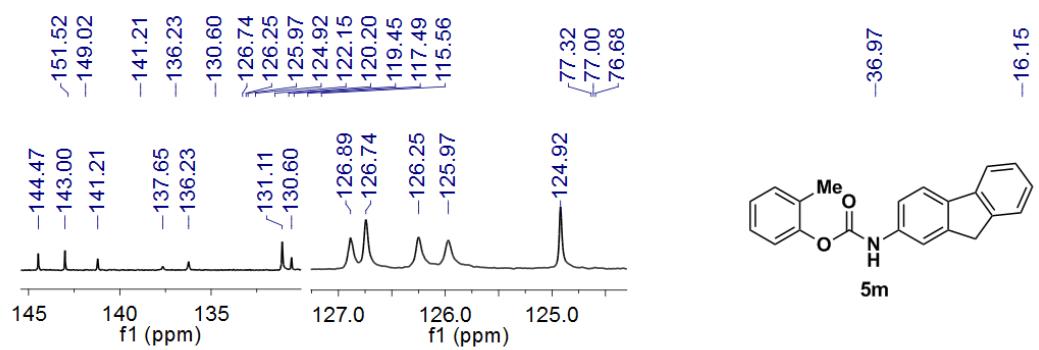
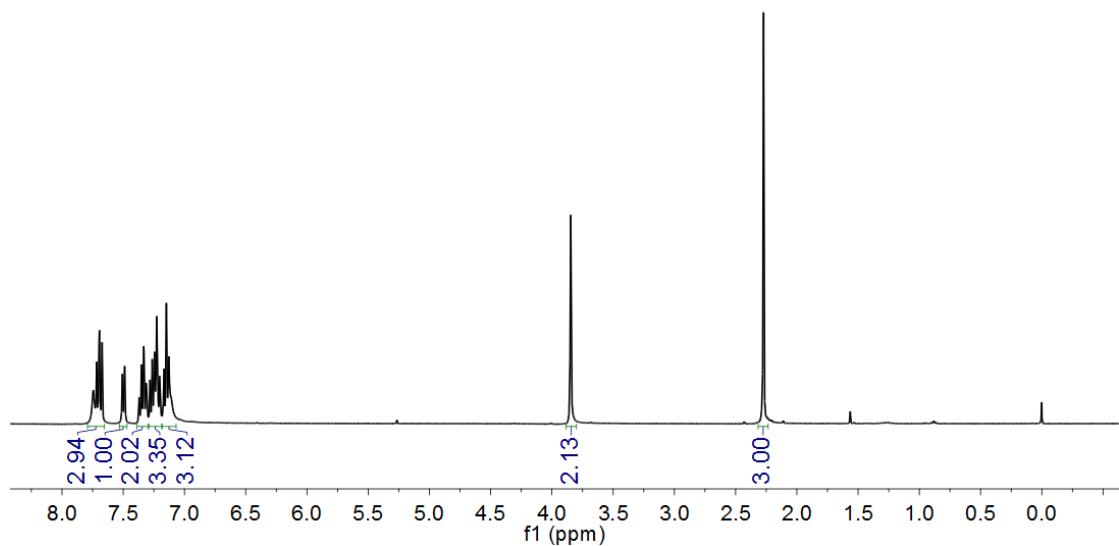
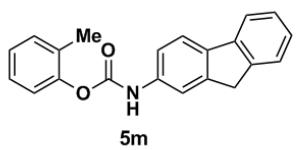


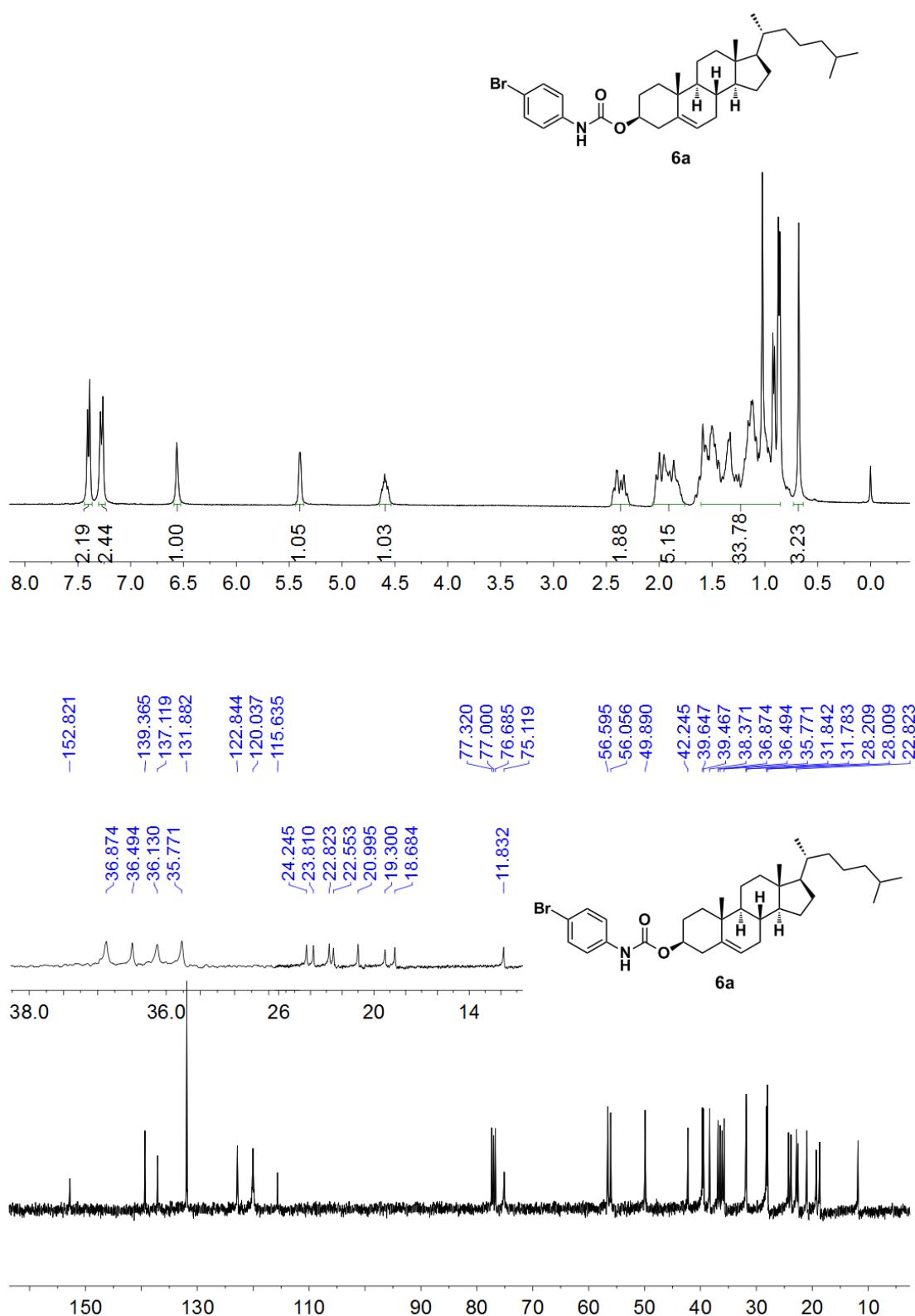


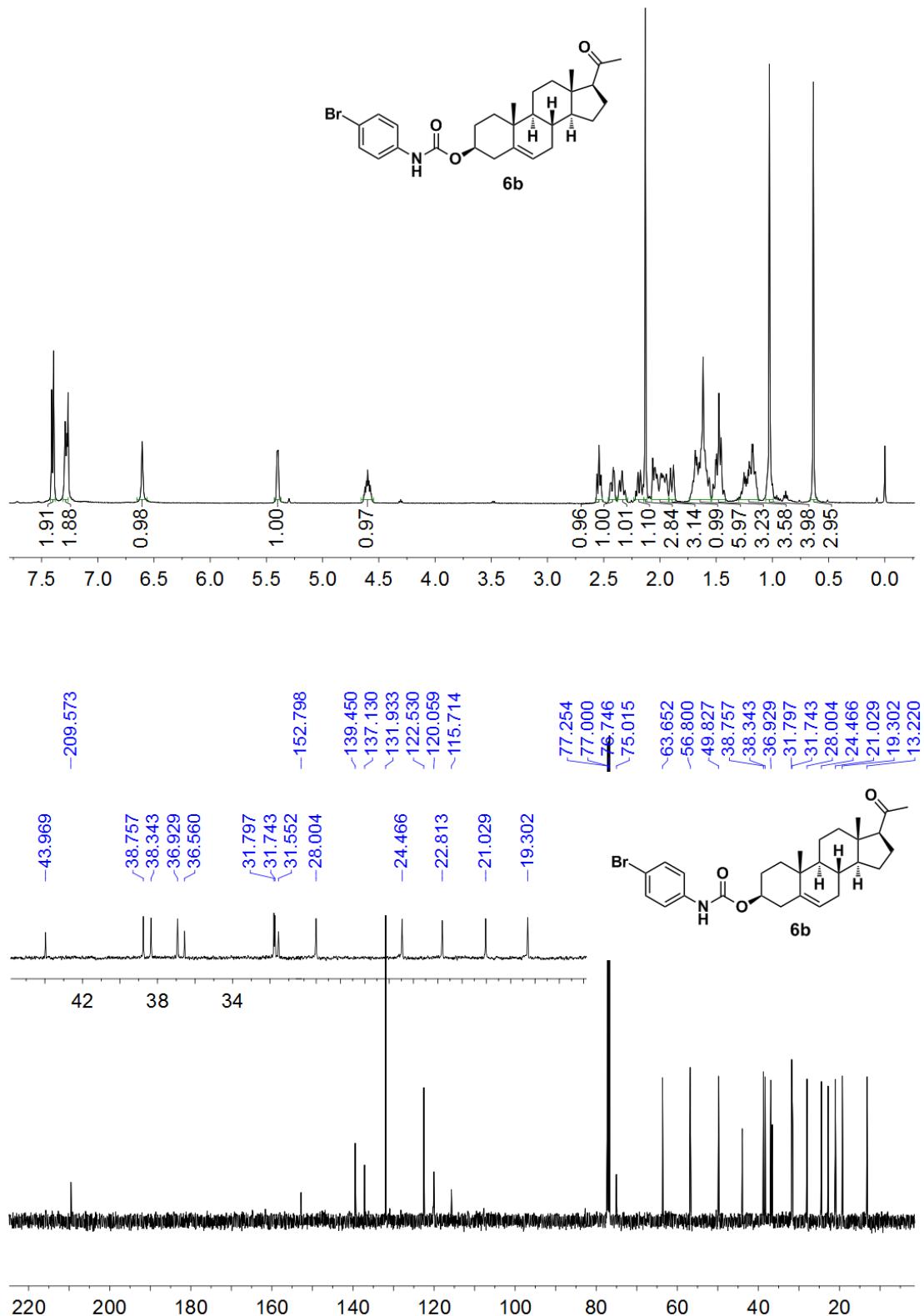


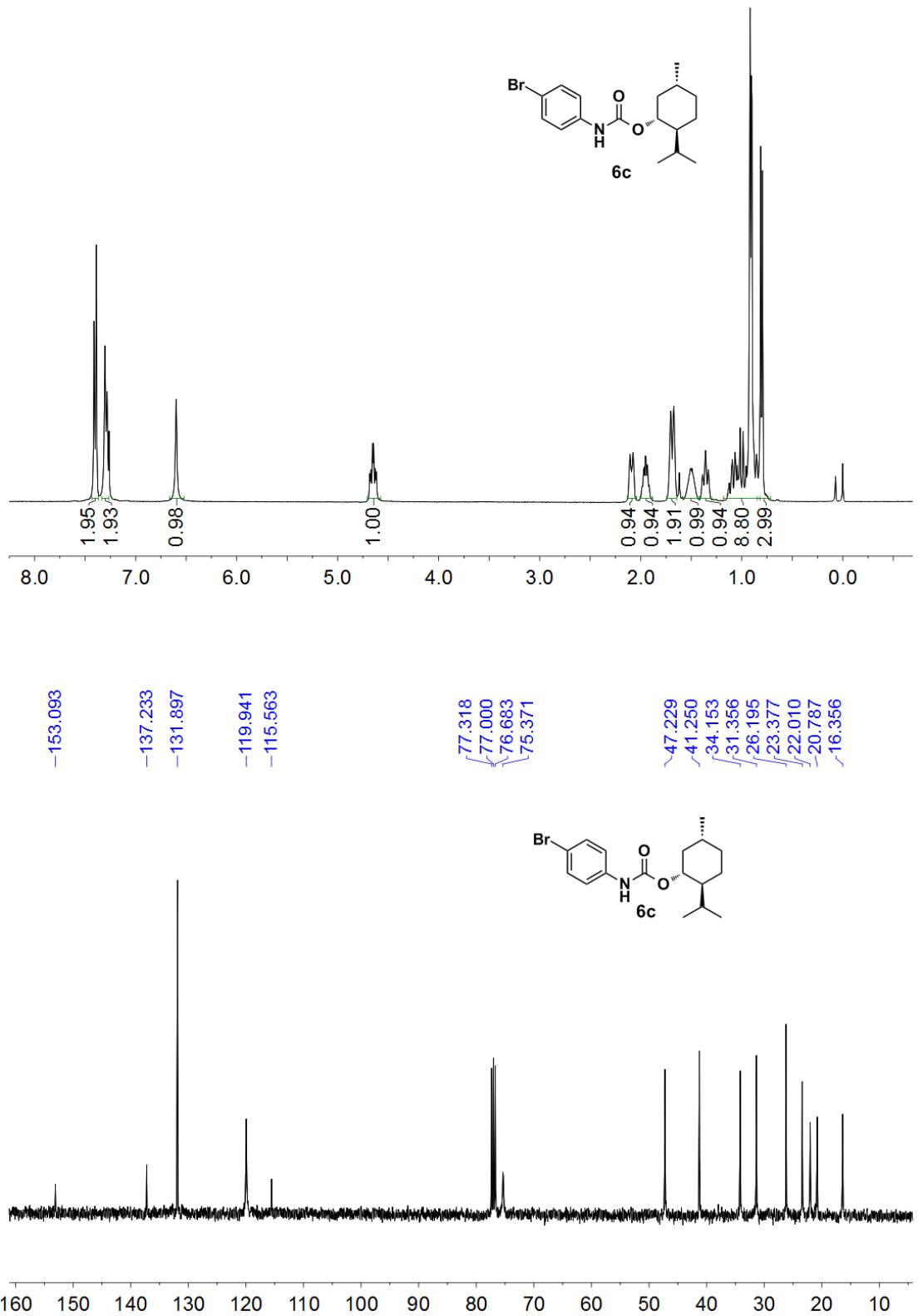


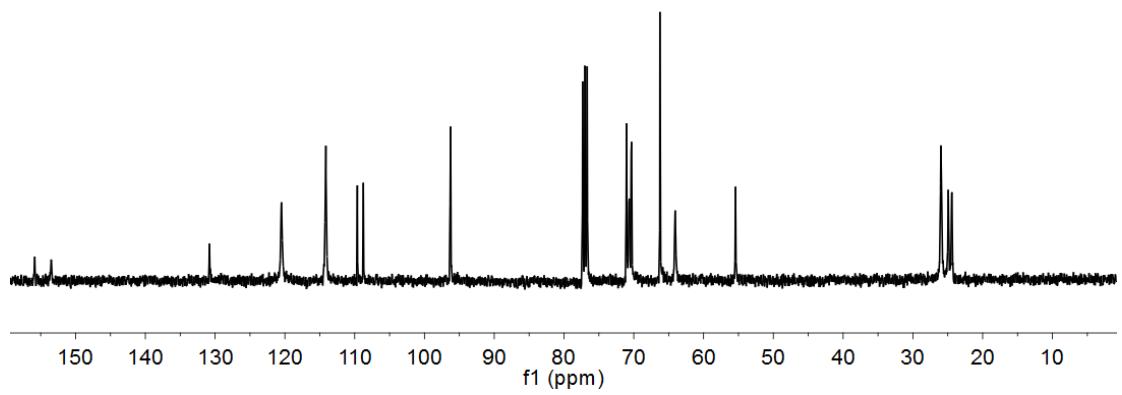
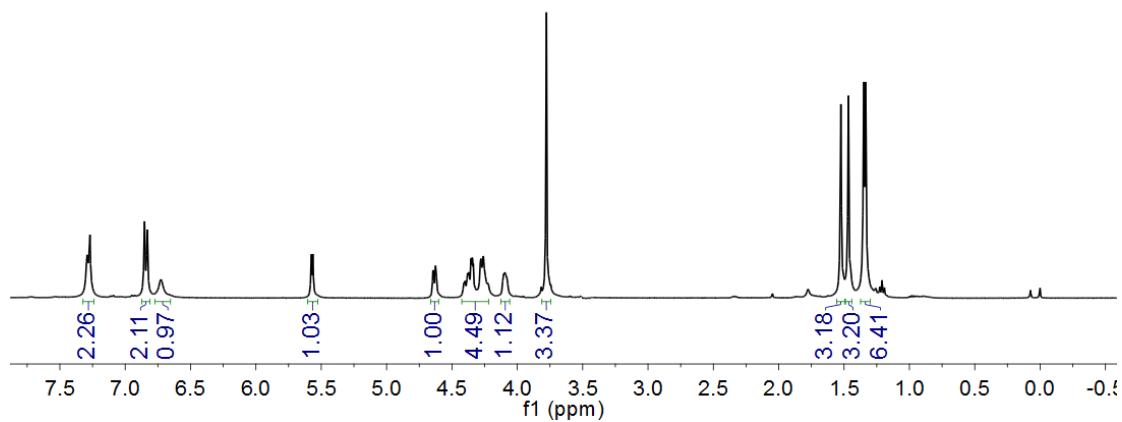
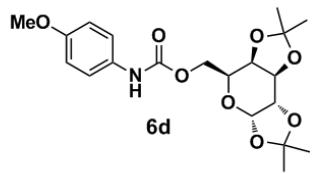


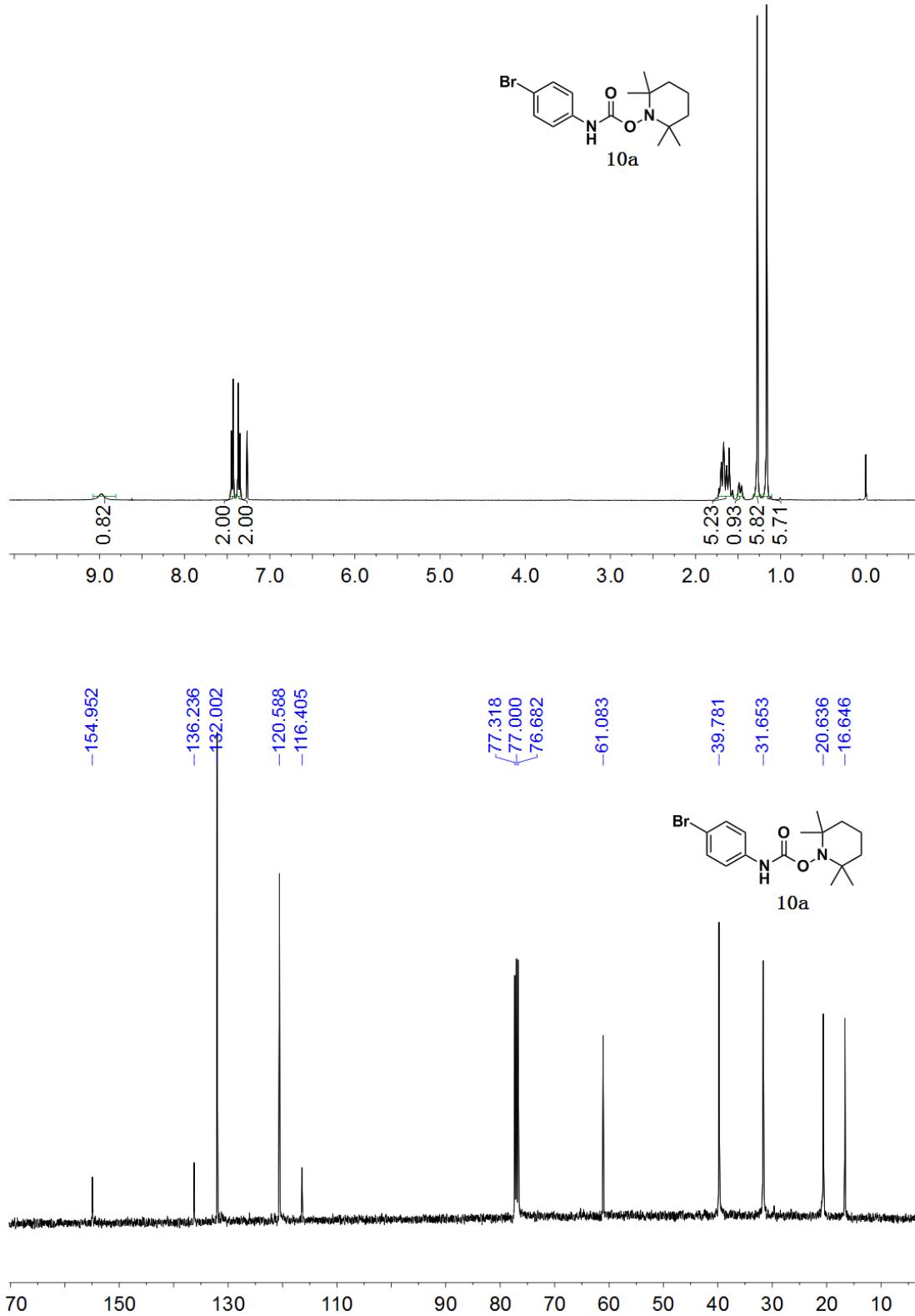


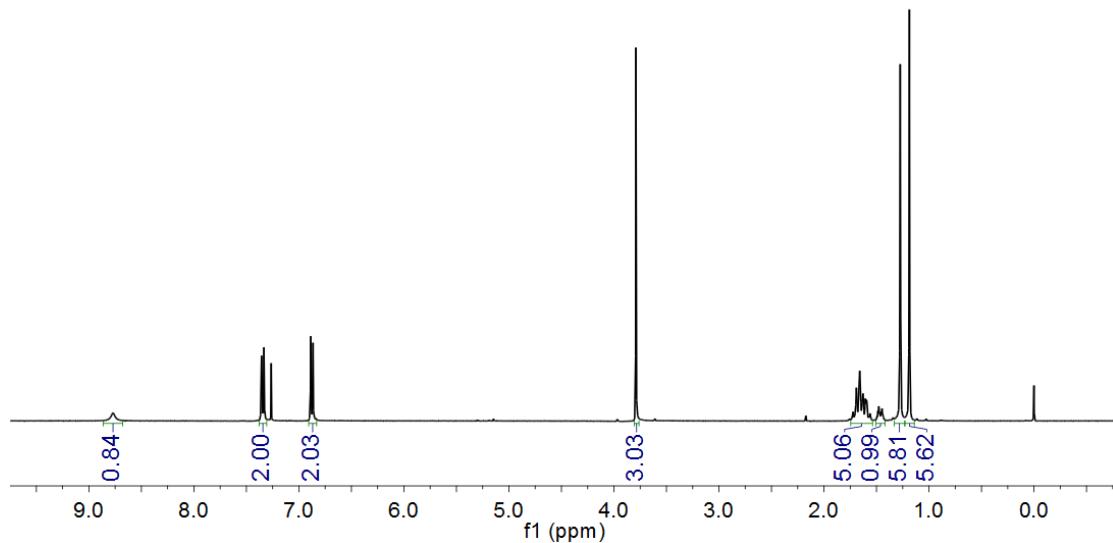
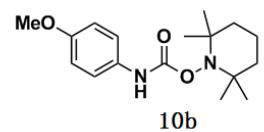












¹H NMR chemical shifts (δ , ppm):
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 156.28, 155.61, 130.21, 121.17, 114.27, 77.32, 77.00, 76.68, 60.94, 55.49, 39.79, 31.69, 31.65, 20.65, 20.60, 16.69

