

Supporting Information

Synthesis of Substituted Pyridines from Cascade [1+5] Cycloaddition of Isonitriles to N-Formylmethyl-substituted Enamides, Aerobic Oxidative Aromatization and Acyl Transfer Reaction

Chuan-Hu Lei,[†] De-Xian Wang,[†] Liang Zhao,[‡] Jieping Zhu,[§] and Mei-Xiang Wang^{†,*}

[†]Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China

[‡]Key Laboratory of Bioorganic Phosphorous and Chemical Biology (Ministry of Education), Tsinghua University, Beijing 100184 China

[§]Ecole Polytechnique Fédérale de Lausanne, EPFL-SB-ISIC-LSPN, BCH 5304, 1015 Lausanne, Switzerland

E-mail: wangmx@mail.tsinghua.edu.cn

Table of Contents

1. General Information.....	S2
2. Preparation of Substrates	S3
3. ¹ H NMR Spectroscopic Study of 2a, 2e and 2f Associated with Zinc Ion.....	S10
4. Scope of the Reactions.....	S12
5. Mechanistic Studies	S24
6. Crystallographic Data	S28
7. References.....	S31
8. Copies of ¹ H and ¹³ C NMR Spectra.....	S31

1. General Information

Unless otherwise noted, all reactions were carried out in oven dried glasswares. Anhydrous solvents were purified and dried following standard procedures. All commercially available reagents were used as received. TLC analysis was performed on pre-coated, glass-backed silica gel plates and visualized with UV light. Flash column chromatography was performed on silica gel (200-300 mesh).

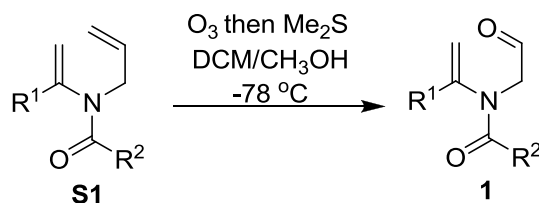
Melting points were uncorrected. The ^1H NMR and ^{13}C NMR spectra were recorded on a JEOL ECX-400 400 MHz spectrometers or ECX-300 300 MHz spectrometers. ^1H NMR chemical shifts were reported relative to residual CDCl_3 (7.26 ppm) or acetone- d_6 (2.05 ppm). ^{13}C NMR chemical shifts were reported relative to the central line of CDCl_3 (77.2 ppm) or acetone- d_6 (29.8 ppm, 206.2 ppm). Abbreviations are used in the description of NMR data as follows: chemical shift (δ , ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet), coupling constant (J , Hz). Low-resolution mass spectra (MS) were recorded on a shimadzu GC-MS QP 2010 Plus spectrometer. The high resolution mass spectra (HRMS) were recorded on a GCT-MS Micromass UK spectrometer or a micrOTOF-Q spectrometer. Infrared spectra were recorded using a PerkinElmer Spectrum 100 FT-IR spectrometer with KBr pellets in the 4000-400 cm^{-1} region.

2. Preparation of Substrates

The compounds **S1** were prepared according to a slightly modified published procedure^[1].

2.1 General Procedure for the Synthesis of Substrates 1.

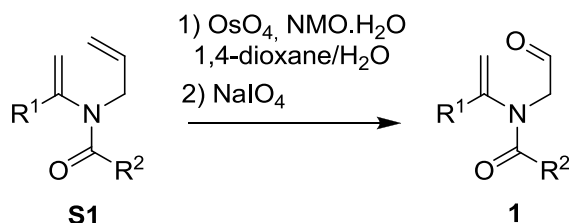
Method A:



Scheme S1 Synthesis of substrates **1**

S1 (5 mmol) was dissolved in $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (v:v = 5:1) (48 mL). After cooling to $-78\text{ }^\circ\text{C}$, ozone and oxygen gas were bubbled into the solution, After 2 h, the ozone was evacuated with nitrogen for 15 min at $-78\text{ }^\circ\text{C}$, and dimethyl sulfide (5.0 mL) was added. The resulting solution was allowed to warm to rt over 1 h. The clear solution was concentrated *in vacuo* and then purified by flash column chromatography on silica gel (petroleum ether/EtOAc, 5:1) to afford substrate **1**

Method B:

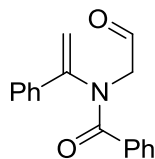


Scheme S2 Synthesis of substrates **2**

To a mixture of **S1** (5 mmol) and aqueous NMO (50%) solution (15 mmol) in $1,4\text{-dioxane}/\text{H}_2\text{O}$ (2:1) (60 mL) at rt was added OsO_4 (0.075 M in water) (0.67 mL, 0.05 mmol). After the mixture was stirred at rt overnight, NaIO_4 (10 mmol, 2.14 g) was added. Upon stirring at rt for another 2 h, the reaction mixture was quenched with water, extracted with EtOAc ($3 \times 20\text{ mL}$), washed with water and brine, dried over MgSO_4 , filtered, concentrated and purified by flash column chromatography on silica gel (petroleum ether/EtOAc) to give compound **1**.

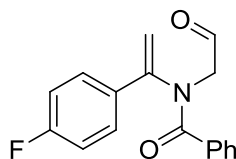
2.2 Characterization of substrates

N-(2-oxoethyl)-N-(1-phenylvinyl)benzamide (1a)



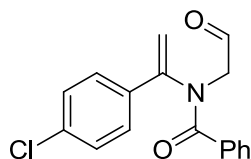
Following method A. White solid (782 mg, yield: 59%). **m.p.** 98-99 °C. **¹H NMR** (300 MHz, CDCl₃) δ 9.70 (s, 1H), 7.59-7.22 (m, 10H), 5.41 (s, 1H), 4.98 (s, 1H), 4.30 (s, 2H). **¹³C NMR** (75 MHz, CDCl₃) δ 196.5, 171.8, 148.0, 135.6, 134.6, 130.7, 129.5, 129.2, 128.1, 128.0, 126.4, 113.9, 57.8. **IR** (KBr, cm⁻¹) ν 2814, 1736, 1643, 1615, 1368. **MS** (CI) 266 [M+1]⁺ (10), 265 [M]⁺ (12), 146 (33), 105 (100). **HRMS** (EI) calcd. for C₁₇H₁₅NO₂ [M] 265.1103, found 265.1106.

N-(1-(4-fluorophenyl)vinyl)-N-(2-oxoethyl)benzamide (1b)



Following method B. White solid (835 mg, yield: 59%). **m.p.** 88-89 °C. **¹H NMR** (400 MHz, CDCl₃) δ 9.71 (s, 1H), 7.53 (dd, *J* = 8.2, 1.2, 2H), 7.48-7.45 (m, 2H), 7.34(t, *J* = 7.5 1H), 7.26-7.22 (m, 2H), 7.05 (t, *J* = 8.6, 2H), 5.33 (s, 1H), 4.98 (s, 1H), 4.34 (s, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ 196.1, 171.6, 164.5, 162.0, 147.2, 134.5, 131.9, 130.7, 128.2 (d, *J* = 8.2), 128.0 (d, *J* = 6.6), 116.2, 115.9, 113.2, 57.8. **IR** (KBr, cm⁻¹) ν 2848, 1647, 1601, 1505, 1365. **MS** (CI) 284 [M+1]⁺ (26), 283 [M]⁺ (16), 164 (27), 105 (100). **HRMS** (EI) calcd. for C₁₇H₁₄NO₂F [M] 283.1009, found 283.1013.

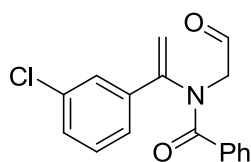
N-(1-(4-chlorophenyl)vinyl)-N-(2-oxoethyl)benzamide (1c)



Following method A. White solid (945 mg, yield: 63%). **m.p.** 102-104 °C. **¹H NMR** (400 MHz, CDCl₃) δ 9.70 (s, 1H), 7.52 (dd, *J* = 5.3, 3.3, 2H), 7.45-7.42 (m, 2H),

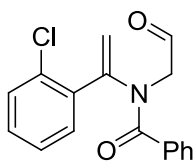
7.37-7.33 (m, 3H), 7.27-7.23 (m, 2H), 5.38 (d, $J = 1.0$, 1H), 5.02 (d, $J = 0.7$, 1H), 4.33 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 196.0, 171.6, 147.1, 135.3, 134.4, 134.3, 130.7, 129.2, 128.0, 127.9, 127.6, 113.9, 57.8. IR (KBr, cm^{-1}) ν 2930, 2829, 1733, 1637, 1376. MS (CI) 301 $[\text{M}+2]^+$ (4), 300 $[\text{M}+1]^+$ (9), 299 $[\text{M}]^+$ (10), 180 (17), 105 (100). HRMS (EI) calcd. for $\text{C}_{17}\text{H}_{14}\text{NO}_2\text{Cl}$ $[\text{M}]$ 299.0713, found 299.0717.

N-(1-(3-chlorophenyl)vinyl)-N-(2-oxoethyl)benzamide (1d)

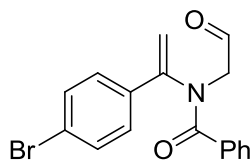


Following method A. White solid (1.169 g, yield: 78%). m.p. 78-79 °C. ^1H NMR (400 MHz, CDCl_3) δ 9.70 (s, 1H), 7.53-7.51 (m, 2H), 7.44 (d, $J = 1.8$, 1H), 7.38-7.23 (m, 6H), 5.41 (d, $J = 0.7$, 1H), 5.04 (s, 1H), 4.34 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 196.1, 171.7, 147.0, 137.9, 135.2, 134.4, 130.8, 130.4, 129.5, 128.2, 128.1, 126.6, 124.5, 114.7, 58.0. IR (KBr, cm^{-1}) ν 2808, 1756, 1639, 1381. MS (CI) 301 $[\text{M}+2]^+$ (14), 300 $[\text{M}+1]^+$ (38), 299 $[\text{M}]^+$ (22), 180 (20), 105 (100). HRMS (EI) calcd. for $\text{C}_{17}\text{H}_{14}\text{NO}_2\text{Cl}$ $[\text{M}]$ 299.0713, found 299.0716.

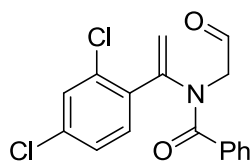
N-(1-(2-chlorophenyl)vinyl)-N-(2-oxoethyl)benzamide (1e)



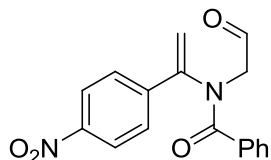
Following method A. White solid (688 mg, yield: 46%). Yellow oil. ^1H NMR (400 MHz, CDCl_3) δ 9.75 (s, 1H), 7.38-7.36 (m, 2H), 7.23-7.11 (m, 4H), 7.05-7.01 (m, 1H), 6.92-6.90 (m, 2H), 5.18 (s, 1H), 5.09 (s, 1H), 4.63 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 197.0, 171.1, 147.4, 136.4, 136.0, 131.6, 131.4, 130.3, 130.1, 129.6, 128.0, 127.5, 126.8, 113.1, 60.9. IR (KBr, cm^{-1}) ν 2924, 1732, 1653, 1618, 1360. MS (CI) 301 $[\text{M}+2]^+$ (2), 300 $[\text{M}+1]^+$ (2), 299 $[\text{M}]^+$ (3), 180 (12), 105 (100). HRMS (EI) calcd. for $\text{C}_{17}\text{H}_{14}\text{NO}_2\text{Cl}$ $[\text{M}]$ 299.0713, found 299.0717.

N-(1-(4-bromophenyl)vinyl)-N-(2-oxoethyl)benzamide (1f)

Following method A. White solid (583 mg, yield: 34%). **m.p.** 126-128 °C. **¹H NMR** (400 MHz, CDCl₃) δ 9.70 (s, 1H), 7.53-7.49 (m, 4H), 7.38-7.33 (m, 3H), 7.27– 7.23 (m, 2H), 5.40 (d, *J* = 0.7, 1H), 5.02 (d, *J* = 0.6, 1H), 4.33 (s, 2H). **¹³C NMR** (100 MHz, CDCl₃) δ 196.1, 171.7, 147.3, 134.9, 134.5, 132.3, 130.9, 128.2, 128.1, 128.0, 123.7, 114.2, 57.9. **IR** (KBr, cm⁻¹) ν 2830, 1734, 1638, 1377. **MS** (CI) 345 [M+2]⁺ (27), 344 [M+1]⁺ (34), 343 [M]⁺ (23), 105 (100). HRMS calcd. for C₁₇H₁₄NO₂⁷⁹Br, C₁₇H₁₄NO₂⁸¹Br [M] 343.0208, [M+2] 345.0187 found 343.0212, 345.0193.

N-(1-(2,4-dichlorophenyl)vinyl)-N-(2-oxoethyl)benzamide (1g)

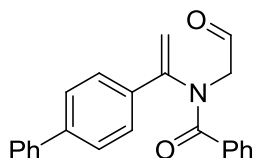
Following method A. Yellow solid (1.200 g, yield: 72%). **m.p.** 86-88 °C. **¹H NMR** (300 MHz, CDCl₃) δ 9.81 (s, 1H), 7.37 (dd, *J* = 8.3, 1.3, 2H), 7.32-7.28 (m, 1H), 7.24-7.18 (m, 3H), 6.95-6.84 (m, 2H), 5.22 (d, *J* = 1.1, 1H), 5.12 (d, *J* = 1.1, 1H), 4.68 (s, 2H). **¹³C NMR** (150 MHz, CDCl₃) δ 196.6, 171.0, 146.8, 136.0, 135.2, 134.8, 132.6, 132.1, 130.5, 130.0, 128.2, 127.6, 127.1, 113.2, 61.0. **IR** (KBr, cm⁻¹) ν 3076, 2842, 1731, 1651, 1615, 1359. **MS** (CI) 334 [M+1]⁺ (5), 333 [M]⁺ (7), 214 (14), 105 (100). **HRMS** (EI) calcd. for C₁₇H₁₃NO₂Cl₂ [M] 333.0323, found 333.0327.

N-(1-(4-nitrophenyl)vinyl)-N-(2-oxoethyl)benzamide (1h)

Following method A. Yellow solid (837 mg, yield: 54%). **m.p.** 146-147 °C. **¹H NMR** (300 MHz, CDCl₃) δ 9.73 (s, 1H), 8.16 (d, *J* = 8.8, 2H), 7.61 (d, *J* = 8.8, 2H), 7.47-7.44 (dd, *J* = 5.2, 3.3, 2H), 7.34-7.19 (m, 3H), 5.52 (d, *J* = 1.3, 1H), 5.25 (d, *J* =

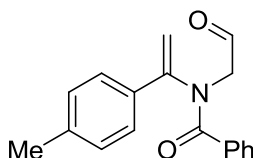
1.3, 1H), 4.47 (s, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 195.6, 171.4, 148.0, 147.0, 142.8, 134.4, 131.0, 128.2, 128.0, 127.2, 124.2, 116.0, 58.6. IR (KBr, cm^{-1}) ν 2840, 1727, 1638, 1513, 1369. MS (CI) 311 $[\text{M}+1]^+$ (6), 310 $[\text{M}]^+$ (7), 191 (7), 105 (100). HRMS (EI) calcd. for $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_4$ [M] 310.0954, found 310.0957.

N-(1-(biphenyl-4-yl)vinyl)-N-(2-oxoethyl)benzamide (1i)



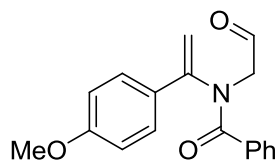
Following method B. White solid (1.108 g, yield: 65%). m.p. 115-116 °C. ^1H NMR (400 MHz, CDCl_3) δ 9.73 (s, 1H), 7.65-7.58 (m, 8H), 7.47 (t, J = 7.5, 2H), 7.41-7.34 (m, 2H), 7.29-7.26 (m, 5H), 5.47 (s, 1H), 5.01 (s, 1H), 4.35 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 196.5, 171.9, 147.7, 142.4, 140.2, 134.54, 134.47, 130.8, 129.1, 128.2, 128.1, 128.0, 127.9, 127.2, 126.9, 114.0, 57.8. IR (KBr, cm^{-1}) ν 1753, 1724, 1640, 1385, 1373. MS (CI) 342 $[\text{M}+1]^+$ (37), 341 $[\text{M}]^+$ (35), 222 (38), 105 (100). HRMS (EI) calcd. for $\text{C}_{23}\text{H}_{19}\text{NO}_2$ [M] 341.1416, found 341.1421.

N-(2-oxoethyl)-N-(1-p-tolylvinyl)benzamide (1j)



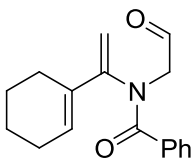
Following method B. White solid (781 mg, yield: 56%). m.p. 101-102 °C. ^1H NMR (400 MHz, CDCl_3) δ 9.69 (s, 1H), 7.60-7.58 (m, 2H), 7.43-7.41 (m, 2H), 7.35-7.33 (m, 1H), 7.28-7.20 (m, 4H), 5.37 (d, J = 0.6, 1H), 4.92 (s, 1H), 4.27 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 196.7, 171.9, 147.8, 139.7, 134.5, 132.7, 130.7, 129.9, 128.2, 128.1, 126.4, 113.4, 57.6, 21.4. IR (KBr, cm^{-1}) ν 2931, 2821, 1732, 1639, 1375. MS (CI) 280 $[\text{M}+1]^+$ (31), 280 $[\text{M}]^+$ (22), 160 (39), 105 (100). HRMS (EI) calcd. for $\text{C}_{18}\text{H}_{17}\text{NO}_2$ [M] 279.1259, found 279.1263.

N-(1-(4-methoxyphenyl)vinyl)-N-(2-oxoethyl)benzamide (1k)



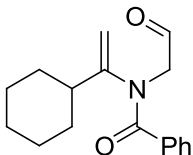
Following method B. White solid (1.018 g, yield: 69%). **m.p.** 67-69 °C. **¹H NMR** (400 MHz, CDCl₃) δ 9.69 (s, 1H), 7.58 (d, *J* = 7.6, 2H), 7.45 (d, *J* = 8.7, 2H), 7.35 (t, *J* = 7.4, 1H), 7.26 (t, *J* = 7.6, 3H), 6.92 (d, *J* = 8.7, 2H), 5.30 (s, 1H), 4.87 (s, 1H), 4.28 (s, 2H), 3.84 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 196.7, 171.8, 160.7, 147.5, 134.6, 130.7, 128.13, 128.06, 128.0, 127.8, 114.6, 112.3, 57.7, 55.5. **IR** (KBr, cm⁻¹) ν 2840, 2816, 1732, 1634, 1511, 1374. **MS** (CI) 296 [M+1]⁺ (4), 295 [M]⁺ (16), 176 (30), 105 (100). **HRMS** (EI) calcd. for C₁₈H₁₇NO₃ [M] 295.1208, found 295.1212.

N-(1-cyclohexenylvinyl)-N-(2-oxoethyl)benzamide (1l)



Following method B. Colorless oil (740 mg, yield: 55%). **¹H NMR** (400 MHz, CDCl₃) δ 9.68 (s, 1H), 7.54-7.56 (m, 2H), 7.39-7.35 (m, 1H), 7.31-7.27 (m, 2H), 6.13 (t, *J* = 4.0, 1H), 5.04 (s, 1H), 4.88 (s, 1H), 4.26 (s, 2H), 2.18-2.16 (m, 2H), 2.01-1.99 (m, 2H), 1.58 (ddt, *J* = 10.5, 8.6, 2.9, 4H). **¹³C NMR** (100 MHz, CDCl₃) δ 197.4, 171.7, 149.6, 135.1, 132.9, 130.5, 128.6, 127.9, 127.8, 112.4, 58.7, 25.8, 25.6, 22.5, 22.0. **IR** (KBr, cm⁻¹) ν 2929, 1732, 1638, 1372. **MS** (CI) 270 [M+1]⁺ (7), 269 [M]⁺ (10), 240 (22), 105 (100). **HRMS** (ESI) calcd. for C₁₇H₁₉NO₂ [M+H] 270.1489, found 270.1487

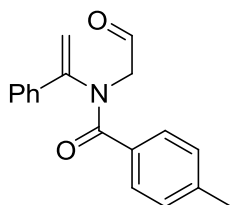
N-(1-cyclohexylvinyl)-N-(2-oxoethyl)benzamide (1m)



Following method B. Colorless oil (772 mg, yield: 57%). **¹H NMR** (400 MHz, CDCl₃) δ 9.70 (s, 1H), 7.60-7.58 (m, 2H), 7.40-7.32 (m, 3H), 5.00 (s, 1H), 4.91 (s, 1H), 4.38 (s, 2H), 1.67–1.57 (m, 6H), 1.04-0.97 (m, 5H). **¹³C NMR** (100 MHz, CDCl₃) δ 197.3,

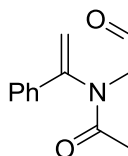
170.6, 156.0, 135.8, 130.5, 128.2, 128.1, 110.6, 60.9, 44.1, 32.0, 26.4, 26.1. **IR** (KBr, cm^{-1}) ν 2928, 2853, 1734, 1630, 1367. **MS** (ESI) 272 [M+H]. **HRMS** (ESI) calcd. for $\text{C}_{17}\text{H}_{21}\text{NO}_2$ [M+H] 272.1645, found 272.1645.

4-methyl-N-(2-oxoethyl)-N-(1-phenylvinyl)benzamide (1n)



Following method A. Light yellow oil (279 mg, yield: 20%). **^1H NMR** (400 MHz, CDCl_3) δ 9.69 (s, 1H), 7.54-7.48 (m, 4H), 7.41-7.39 (m 3H), 7.26 (s, 2H), 7.06 (d, J = 7.9, 2H), 5.42 (d, J = 0.7, 1H), 4.97 (d, J = 0.6, 1H), 4.26 (s, 2H), 2.31 (s, 3H). **^{13}C NMR** (100 MHz, CDCl_3) δ 196.8, 171.9, 148.1, 141.2, 135.6, 131.5, 129.5, 129.2, 128.8, 128.4, 126.5, 114.0, 57.7, 21.6. **IR** (KBr, cm^{-1}) ν 2923, 1732, 1645, 1370. **MS** (CI) 280 [M+1] $^+$ (7), 279 [M] $^+$ (10), 146 (22), 105 (100). **HRMS** (ESI) calcd. for $\text{C}_{18}\text{H}_{17}\text{NO}_2$ [M+H] 280.1332, found 280.1337.

N-(2-oxoethyl)-N-(1-phenylvinyl)acetamide (1o)



Following method B. Colorless Oil (578 mg, yield: 57%). **^1H NMR** (400 MHz, CDCl_3) δ 9.61 (s, 1H), 7.43-7.39 (m, 5H), 5.75 (s, 1H), 5.41 (s, 1H), 4.18 (s, 2H), 2.12 (s, 3H). **^{13}C NMR** (100 MHz, CDCl_3) δ 196.7, 171.6, 147.6, 135.2, 129.7, 129.2, 125.9, 114.2, 57.4, 21.5. **IR** (KBr, cm^{-1}) ν 2921, 1734, 1660, 1630, 1379. **MS** (CI) 204 [M+1] $^+$ (14), 203 [M] $^+$ (17), 105 (100). **HRMS** (ESI) calcd. for $\text{C}_{12}\text{H}_{13}\text{NO}_2$ [M+H] 204.1019, found 204.1019.

3. ^1H NMR Spectroscopic Study of **2a**, **2e** and **2f** Associated with Zinc Ion.

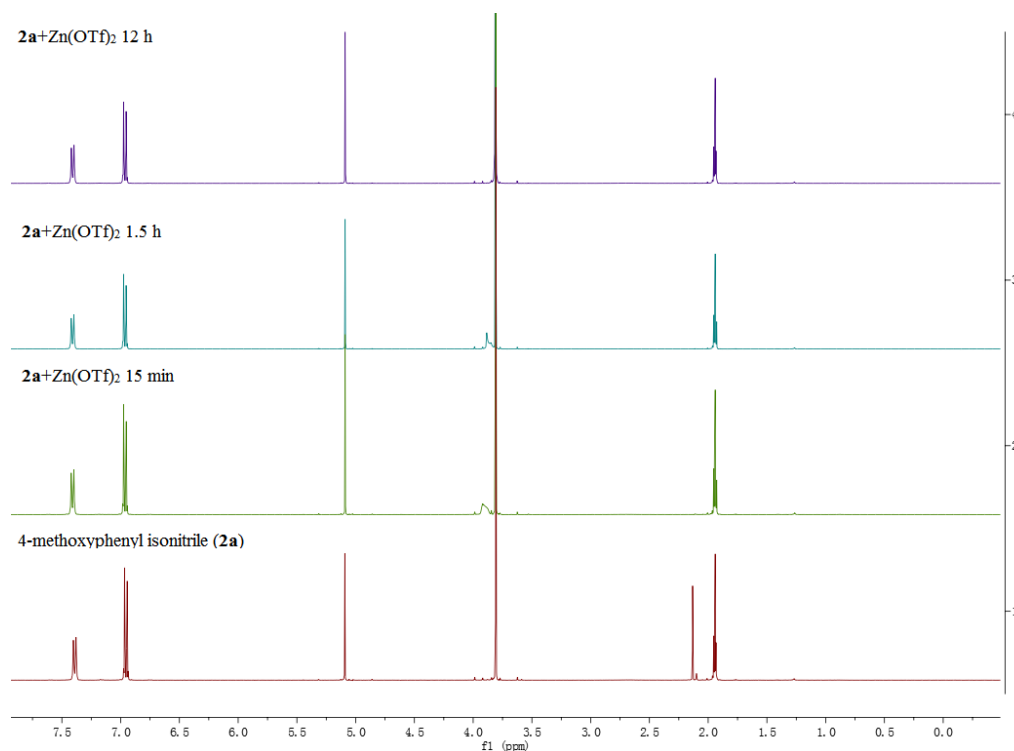


Figure S1. ^1H NMR spectra of **2a** in CD_3CN with the addition of $\text{Zn}(\text{OTf})_2$ at different time.

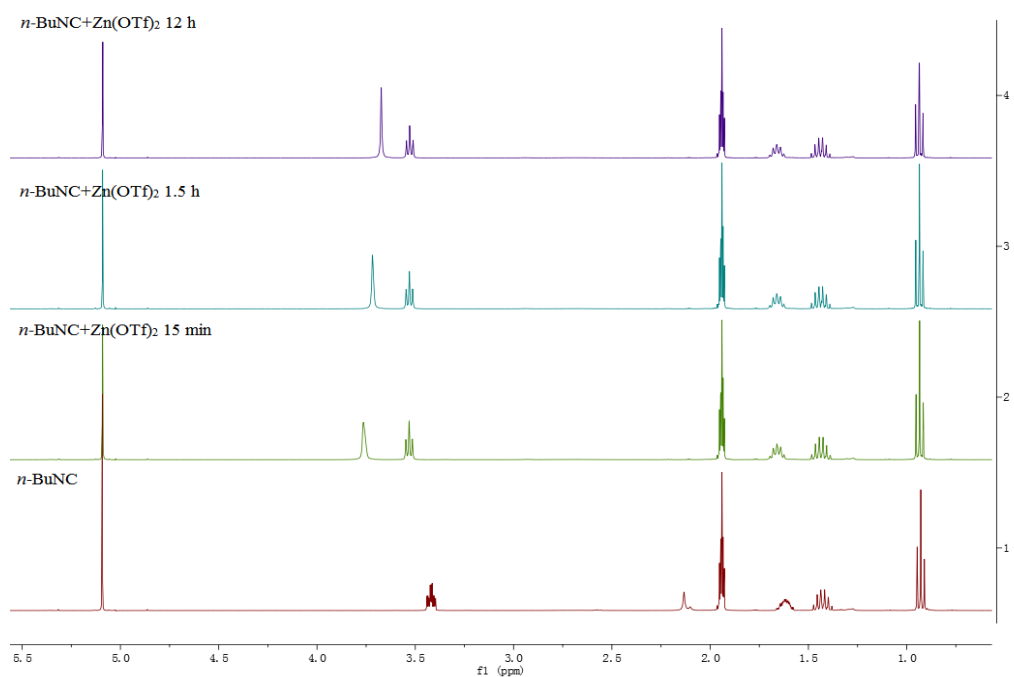


Figure S2. ^1H NMR spectra of *n*-BuNC (**2e**) in CD_3CN with the addition of $\text{Zn}(\text{OTf})_2$ at different time.

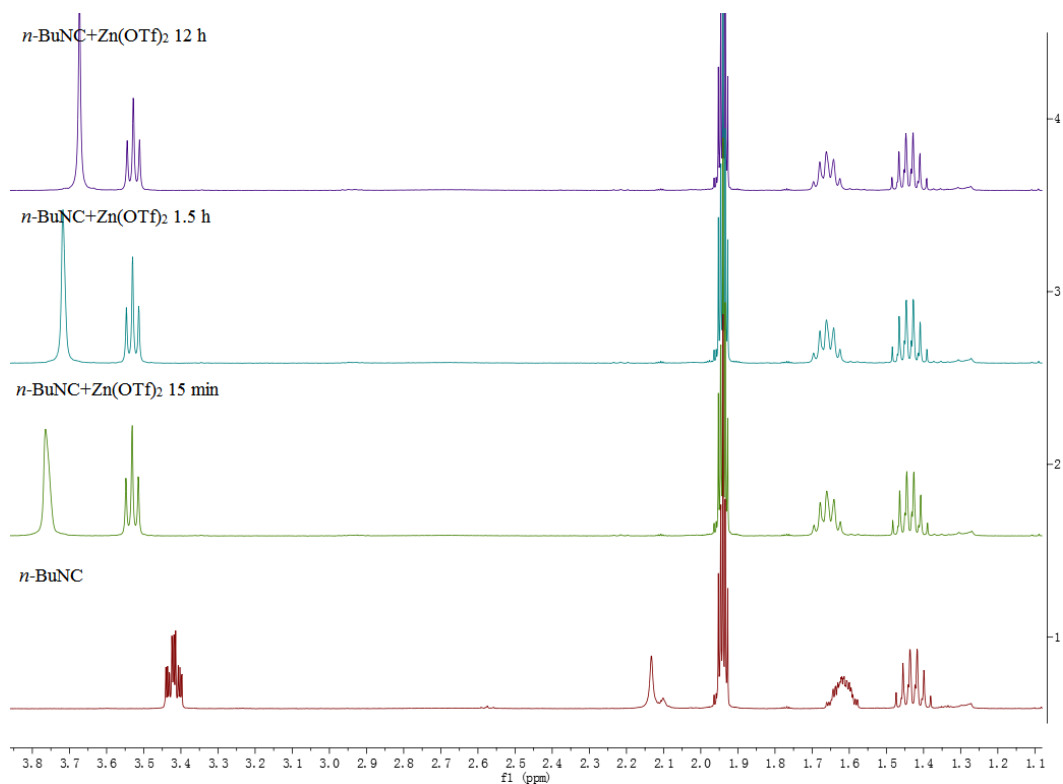


Figure S3. Partial view for the ^1H NMR spectra of *n*-BuNC (**2e**) in CD_3CN with the addition of $\text{Zn}(\text{OTf})_2$ at different time.

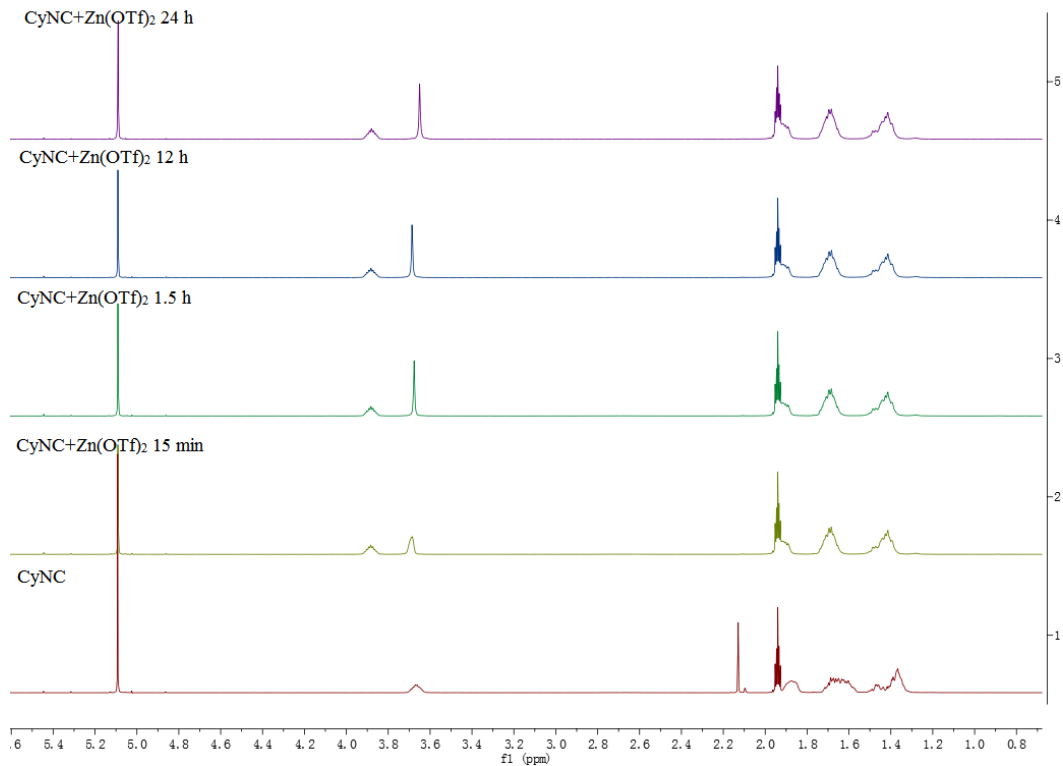


Figure S4. ^1H NMR spectra of CyNC (**2f**) in CD_3CN with the addition of $\text{Zn}(\text{OTf})_2$ at different time.

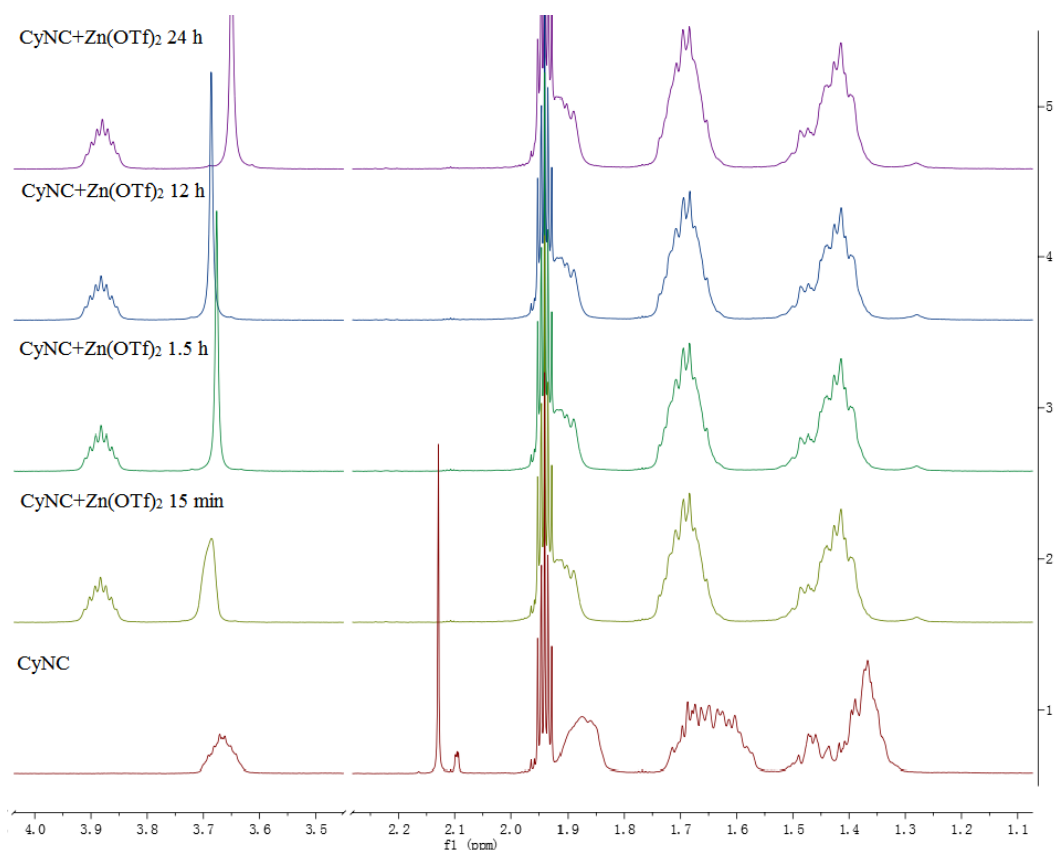
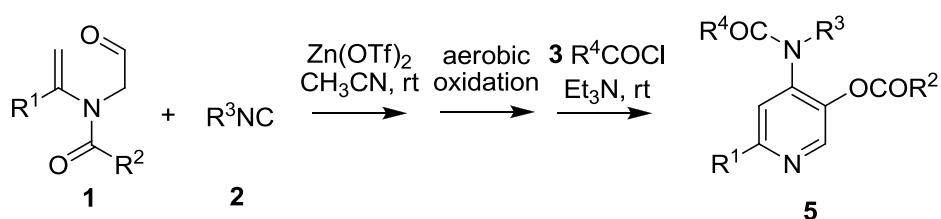


Figure S5. Partial view for the ^1H NMR spectra of CyNC (**2f**) in CD_3CN with the addition of $\text{Zn}(\text{OTf})_2$ at different time.

4. Scope of the Reactions



Scheme S3. Reaction scope

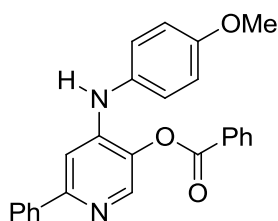
4.1 General Procedure for the Synthesis of Substituted Pyridine Derivatives

To a solution of **2** (0.36 mmol) in acetonitrile (15 mL) was added **1** (0.3 mmol), 4 Å molecular sieves (300 mg) and $\text{Zn}(\text{OTf})_2$ (0.3 mmol, 109.1 mg). The reaction mixture

was stirred at ambient temperature until the disappearance of **1** (monitored by TLC), then quenched with saturated aqueous NaHCO₃ (5 mL), filtrated through a pad of Celite and extracted with CH₂Cl₂ (3×15 mL). The combined organic extracts were washed with brine, dried over MgSO₄. The dried organic extracts were left under atmospheric conditions overnight. Et₃N (1.2 mmol) and acyl chloride (1.2 mmol) were added, and resulting mixture was stirred for 2 hours. After filtration and concentration *in vacuo*, the residue was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate/dichloromethane) to give the product **5**.

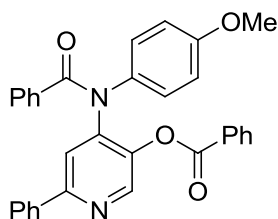
4.2 Characterization of Products

4-(4-Methoxyphenylamino)-6-phenylpyridin-3-yl benzoate (**4a**)



White solid (75 mg, yield: 63%). **m.p.** 130-131 °C. **¹H NMR** (400 MHz, acetone-*d*₆) δ 8.32 (s, 1H), 8.25-8.17 (m, 2H), 7.95-7.91 (m, 2H), 7.82 (s, 1H), 7.77-7.70 (m, 1H), 7.64-7.57 (m, 2H), 7.45-7.35 (m, 4H), 7.30-7.23 (m, 2H), 7.02-6.95 (m, 2H), 3.81 (s, 3H). **¹³C NMR** (100 MHz, acetone-*d*₆) δ 164.6, 157.2, 155.1, 145.6, 143.7, 139.7, 134.7, 133.8, 132.4, 130.3, 129.5, 128.7, 128.5, 128.5, 126.6, 125.7, 114.7, 104.0, 54.9. **IR** (KBr, cm⁻¹) ν 3384, 1732, 1598, 1519, 1246. **MS** (ESI) 397 [M+H]⁺ **HRMS** (EI) calcd. for C₂₅H₂₀N₂O₃ [M] 396.1474, found 396.1479.

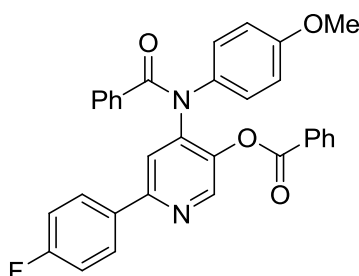
4-(N-(4-methoxyphenyl)benzamido)-6-phenylpyridin-3-yl benzoate (**5a**)



White solid (136 mg, yield: 91%). **m.p.** 125-126 °C. **¹H NMR** (400 MHz, CDCl₃) δ

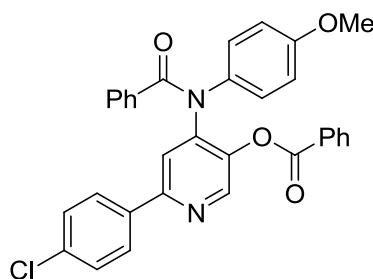
8.64 (s, 1H), 8.08-7.97 (m, 2H), 7.84-7.73 (m, 2H), 7.62-7.49 (m, 1H), 7.48-7.32 (m, 8H), 7.31-7.21 (m, 1H), 7.14 (t, $J = 7.7$, 2H), 7.10-7.02 (m, 2H), 6.76-6.67 (m, 2H), 3.72 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.2, 164.6, 158.3, 156.4, 145.6, 144.6, 141.2, 138.3, 135.1, 134.6, 134.0, 130.9, 130.4, 129.2, 129.1, 128.7, 128.6, 128.5, 128.2, 128.0, 126.9, 119.6, 114.6, 55.4. IR (KBr, cm^{-1}) ν 1735, 1681, 1509, 1227. MS (ESI) 501 $[\text{M}+1]^+$. HRMS (EI) calcd. for $\text{C}_{32}\text{H}_{24}\text{N}_2\text{O}_4$ $[\text{M}]$ 500.1736, found 500.1743.

6-(4-Fluorophenyl)-4-(N-(4-methoxyphenyl)benzamido)pyridin-3-yl benzoate (5b)



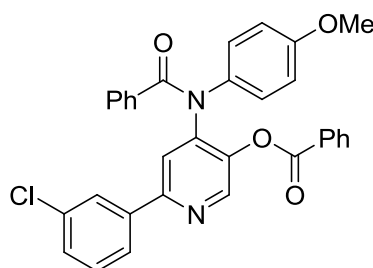
Foam-like solid (132 mg, yield: 85%). ^1H NMR (400 MHz, CDCl_3) δ 8.62 (s, 1H), 8.03 (d, $J = 7.3$, 2H), 7.77 (dd, $J = 8.7$, 5.4, 2H), 7.54 (m, 1H), 7.44-7.31 (m, 5H), 7.17-7.01 (m, 6H), 6.71 (m, 2H), 3.72 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.1, 164.8, 164.6, 162.3, 158.3, 155.4, 145.6, 144.7, 141.1, 135.1, 134.5, 134.5, 134.0, 130.9, 130.4, 129.2, 128.8, 128.8, 128.6, 128.5, 128.1, 128.0, 119.2, 115.8, 115.6, 114.6, 55.4. IR (KBr, cm^{-1}) ν 1743, 1671, 1509, 1249. MS (CI) 519 $[\text{M}+1]^+$ (26), 518 $[\text{M}]^+$ (54), 397 (16), 105 (100). HRMS (EI) calcd. for $\text{C}_{32}\text{H}_{23}\text{N}_2\text{O}_4\text{F}$ $[\text{M}]$ 518.1642, found 518.1647.

6-(4-Chlorophenyl)-4-(N-(4-methoxyphenyl)benzamido)pyridin-3-yl benzoate (5c)



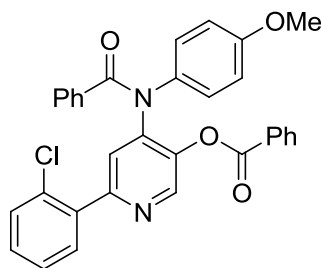
White solid (120 mg, yield: 91%). **m.p.** 142-144 °C. **¹H NMR** (400 MHz, CDCl₃) δ 8.62 (s, 1H), 8.02 (dd, *J* = 8.3, 1.1, 2H), 7.74 (d, *J* = 8.5, 2H), 7.59 - 7.50 (m, 1H), 7.46-7.31 (m, 7H), 7.14 (t, *J* = 7.6, 2H), 7.05 (d, *J* = 8.9, 2H), 6.71 (d, *J* = 8.9, 2H), 3.73 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.1, 164.6, 158.3, 155.1, 145.7, 144.7, 141.3, 136.8, 135.4, 135.1, 134.6, 134.1, 131.0, 130.5, 129.3, 129.0, 128.7, 128.6, 128.3, 128.2, 128.1, 119.3, 114.7, 55.4. **IR** (KBr, cm⁻¹) ν 1744, 1672, 1510, 1248. **MS** (CI) 536 [M+2]⁺ (6), 534 [M]⁺ (14), 413 (5), 105 (100). **HRMS** (EI) calcd. for C₃₂H₂₃ClN₂O₄ [M] 534.1346, found 534.1352.

6-(3-Chlorophenyl)-4-(N-(4-methoxyphenyl)benzamido)pyridin-3-yl benzoate (5d)



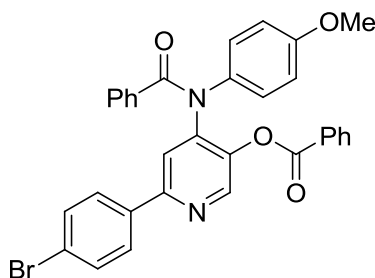
White solid (144 mg, yield: 90%). **m.p.** 151-152 °C. **¹H NMR** (400 MHz, CDCl₃) δ 8.64 (s, 1H), 8.03 (d, *J* = 8.0, 2H), 7.81 (s, 1H), 7.72-7.61 (m, 1H), 7.55 (t, *J* = 7.5, 1H), 7.46-7.32 (m, 7H), 7.31-7.21 (m, 3H), 7.15 (t, *J* = 7.7, 2H), 7.06 (d, *J* = 8.9, 2H), 6.72 (d, *J* = 8.9, 2H), 3.73 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.1, 164.5, 158.3, 154.9, 145.8, 144.7, 141.6, 140.1, 135.0, 134.8, 134.5, 134.0, 131.0, 130.4, 130.0, 129.2, 129.1, 128.6, 128.5, 128.1, 128.0, 127.1, 125.0, 119.6, 114.7, 55.4. **IR** (KBr, cm⁻¹) ν 1738, 1674, 1510, 1247. **MS** (CI) 536 [M+2]⁺ (13), 535 [M+1]⁺ (14), 534 [M]⁺ (33), 413 (8), 105 (100). **HRMS** (EI) calcd. for C₃₂H₂₃N₂O₄Cl [M] 534.1346, found 534.1354.

6-(2-Chlorophenyl)-4-(N-(4-methoxyphenyl)benzamido)pyridin-3-yl benzoate (5e)



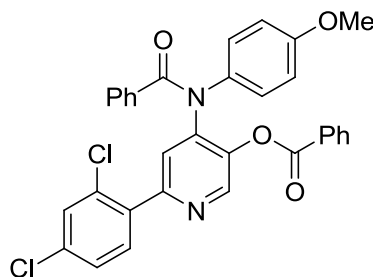
White solid (131 mg, yield: 82%). **m.p.** 169-171 °C. **¹H NMR** (400 MHz, CDCl₃) δ 8.66 (s, 1H), 8.08-7.97 (m, 2H), 7.62-7.53 (m, 2H), 7.46 (d, J = 7.5, 2H), 7.42-7.36 (m, 4H), 7.35-7.26 (m, 3H), 7.16 (t, J = 7.7, 2H), 7.06 (d, J = 8.8, 2H), 6.71 (d, J = 8.8, 2H), 3.72 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.1, 164.4, 158.3, 155.1, 145.5, 143.7, 141.1, 137.9, 135.0, 134.6, 134.0, 132.1, 131.6, 131.0, 130.4, 130.1, 129.9, 129.4, 128.6, 128.5, 128.1, 128.0, 127.0, 124.1, 114.6, 55.4. **IR** (KBr, cm⁻¹) ν 1738, 1672, 1510, 1250. **MS** (CI) 536 [M+2]⁺ (20), 535 [M+1]⁺ (20), 534 [M]⁺ (46), 413 (9), 105 (100). **HRMS** (EI) calcd. for C₃₂H₂₃N₂O₄Cl [M] 534.1346, found 534.1355.

6-(4-Bromophenyl)-4-(N-(4-methoxyphenyl)benzamido)pyridin-3-yl benzoate (5f)



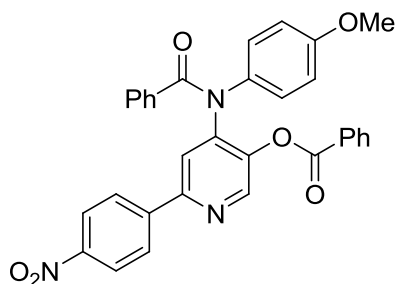
White solid (158 mg, yield: 91%). **m.p.** 161-163 °C. **¹H NMR** (400 MHz, CDCl₃) δ 8.63 (s, 1H), 8.06-7.96 (m, 2H), 7.67 (d, J = 8.4, 2H), 7.58-7.51 (m, 3H), 7.44-7.32 (m, 5H), 7.14 (t, J = 7.6, 2H), 7.08-7.02 (m, 2H), 6.77-6.64 (m, 2H), 3.73 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.1, 164.6, 158.3, 155.1, 145.7, 144.7, 141.4, 137.1, 135.0, 134.5, 134.0, 131.9, 131.0, 130.4, 129.2, 128.6, 128.5, 128.1, 128.0, 123.7, 119.3, 114.7, 55.4. **IR** (KBr, cm⁻¹) ν 1741, 1681, 1509, 1476, 1228. **MS** (CI) 580 [M+2]⁺ (20), 579 [M+1]⁺ (8), 578 [M]⁺ (20), 105 (100). **HRMS** (EI) calcd. for C₃₂H₂₃N₂O₄⁷⁹Br [M] C₃₂H₂₃N₂O₄⁸¹Br [M+2] 578.0841, 580.0821, found 578.0849, 580.0828.

6-(2,4-Dichlorophenyl)-4-(N-(4-methoxyphenyl)benzamido)pyridin-3-yl benzoate (5g)



White solid (149 mg, yield: 87%). **m.p.** 164-165 °C. **¹H NMR** (400 MHz, CDCl₃) δ 8.65 (s, 1H), 8.02 (dd, *J* = 8.4, 1.3, 2H), 7.60-7.52 (m, 2H), 7.49-7.43 (m, 2H), 7.41 (d, *J* = 2.0, 1H), 7.40-7.34 (m, 3H), 7.32 (dd, *J* = 8.4, 2.1, 1H), 7.28 (s, 1H), 7.16 (t, *J* = 7.7, 2H), 7.04 (d, *J* = 9.0, 2H), 6.71 (d, *J* = 9.0, 2H), 3.72 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.1, 164.4, 158.3, 153.9, 145.7, 143.8, 141.2, 136.3, 135.2, 135.0, 134.4, 134.1, 132.8, 132.5, 131.0, 130.4, 129.8, 129.4, 128.6, 128.5, 128.1, 127.4, 124.0, 114.6, 55.4. **IR** (KBr, cm⁻¹) ν 1743, 1664, 1508, 1245. **MS** (CI) 570 [M+2]⁺ (24), 569 [M+1]⁺ (16), 568 [M]⁺ (34), 447 (5), 105 (100). **HRMS** (EI) calcd. for C₃₂H₂₂N₂O₄Cl₂ [M] 568.0957, found 568.0963.

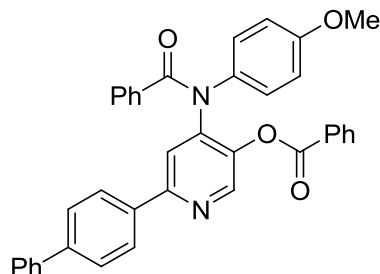
4-(N-(4-methoxyphenyl)benzamido)-6-(4-nitrophenyl)pyridin-3-yl benzoate (5h)



Yellow solid (105 mg, yield: 64%). **m.p.** 173-174 °C. **¹H NMR** (400 MHz, CDCl₃) δ 8.71 (s, 1H), 8.28 (d, *J* = 8.8, 2H), 8.08-7.96 (m, 4H), 7.58-7.52 (m, 1H), 7.46 (s, 1H), 7.44-7.34 (m, 4H), 7.32-7.27 (m, 1H), 7.15 (t, *J* = 7.7, 2H), 7.06 (d, *J* = 8.9, 2H), 6.73 (d, *J* = 8.9, 2H), 3.73 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.1, 164.4, 158.5, 153.4, 148.2, 145.9, 145.2, 143.7, 142.2, 134.8, 134.2, 131.1, 130.4, 129.3, 128.6, 128.5, 128.1, 127.9, 127.8, 124.0, 120.2, 114.8, 55.4. **IR** (KBr, cm⁻¹) ν 1748, 1682,

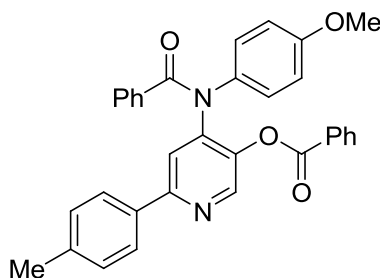
1519, 1226. **MS** (CI) 546 $[M+1]^+$ (18), 545 $[M]^+$ (29), 439 (29), 105 (100). **HRMS** (EI) calcd. for $C_{32}H_{23}N_3O_6$ $[M]$ 545.1587, found 545.1594.

6-(Biphenyl-4-yl)-4-(N-(4-methoxyphenyl)benzamido)pyridin-3-yl benzoate (5i)



White solid (142 mg, yield: 82%). **m.p.** 186-187 °C. ^1H **NMR** (400 MHz, CDCl_3) δ 8.66 (s, 1H), 8.04 (d, $J = 8.3$, 2H), 7.88 (d, $J = 8.3$, 2H), 7.69-7.60 (m, 4H), 7.59-7.52 (m, 1H), 7.50-7.41 (m, 5H), 7.41-7.34 (m, 3H), 7.31 - 7.25 (m, 1H), 7.15 (t, $J = 7.7$, 2H), 7.08 (d, $J = 8.9$, 2H), 6.73 (d, $J = 8.9$, 2H), 3.73 (s, 3H). ^{13}C **NMR** (100 MHz, CDCl_3) δ 170.2, 164.6, 158.3, 155.9, 145.6, 144.7, 142.0, 141.2, 140.4, 137.1, 135.1, 134.6, 134.0, 130.9, 130.4, 129.3, 128.8, 128.6, 128.5, 128.2, 128.0, 127.6, 127.4, 127.4, 127.1, 119.4, 114.7, 55.4. **IR** (KBr, cm^{-1}) ν 1748, 1662, 1510, 1248. **MS** (CI) 577 $[M+1]^+$ (27), 576 $[M]^+$ (58), 455 (29), 105 (100). **HRMS** (EI) calcd. for $C_{38}H_{28}N_2O_4$ $[M]$ 576.2049, found 576.2056.

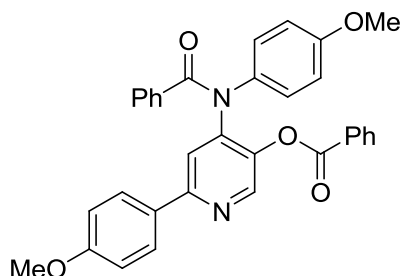
4-(N-(4-methoxyphenyl)benzamido)-6-p-tolylpyridin-3-yl benzoate (5j)



White solid (130 mg, yield: 84%). **m.p.** 130-131 °C. ^1H **NMR** (400 MHz, CDCl_3) δ 8.62 (s, 1H), 8.06-7.98 (m, 2H), 7.69 (d, $J = 8.1$, 2H), 7.54 (t, $J = 7.5$, 1H), 7.43 (d, $J = 7.3$, 2H), 7.40-7.33 (m, 3H), 7.30-7.20 (m, 3H), 7.14 (t, $J = 7.7$, 2H), 7.06 (d, $J = 8.8$, 2H), 6.71 (d, $J = 8.8$, 2H), 3.73 (s, 3H), 2.38 (s, 3H). ^{13}C **NMR** (100 MHz, CDCl_3) δ 170.2, 164.6, 158.2, 156.4, 145.4, 144.5, 140.9, 139.2, 135.5, 135.1, 134.6, 133.9,

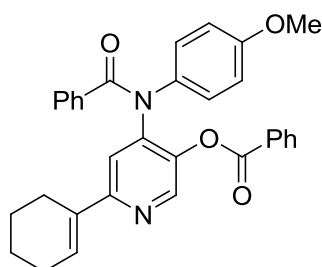
130.9, 130.4, 129.4, 129.2, 128.5, 128.5, 128.2, 128.0, 126.8, 119.3, 114.6, 55.4, 21.3. **IR** (KBr, cm^{-1}) ν 1751, 1659, 1511, 1250. **MS** (CI) 515 $[\text{M}+1]^+$ (35), 514 $[\text{M}]^+$ (65), 393 (30), 105 (100). **HRMS** (EI) calcd. for $\text{C}_{33}\text{H}_{26}\text{N}_2\text{O}_4$ $[\text{M}]$ 514.1893, found 514.1898.

6-(4-Methoxyphenyl)-4-(N-(4-methoxyphenyl)benzamido)pyridin-3-yl benzoate (5k)



White solid (123 mg, yield: 77%). **m.p.** 129-130 °C. **^1H NMR** (400 MHz, CDCl_3) δ 8.58 (s, 1H), 8.08-7.98 (m, 2H), 7.74 (d, J = 8.8, 2H), 7.54 (t, J = 7.5, 1H), 7.42 (d, J = 7.2, 2H), 7.37 (t, J = 7.8, 2H), 7.31 (s, 1H), 7.29-7.23 (m, 1H), 7.14 (t, J = 7.6, 2H), 7.06 (d, J = 8.9, 2H), 6.93 (d, J = 8.9, 2H), 6.71 (d, J = 8.9, 2H), 3.84 (s, 3H), 3.72 (s, 3H). **^{13}C NMR** (100 MHz, CDCl_3) δ 170.2, 164.6, 160.6, 158.2, 156.1, 145.4, 144.5, 140.6, 135.2, 134.7, 133.9, 131.0, 130.9, 130.4, 129.2, 128.5, 128.4, 128.2, 128.0, 118.8, 114.6, 114.1, 55.4. **IR** (KBr, cm^{-1}) ν 1732, 1679, 1479, 1228. **MS** (CI) 531 $[\text{M}+1]^+$ (23), 530 $[\text{M}]^+$ (34), 409 (27), 105 (100). **HRMS** (EI) calcd. for $\text{C}_{33}\text{H}_{26}\text{N}_2\text{O}_5$ $[\text{M}]$ 530.1842, found 530.1848.

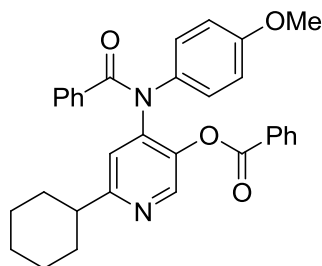
6-Cyclohexenyl-4-(N-(4-methoxyphenyl)benzamido)pyridin-3-yl benzoate (5l)



White solid (91 mg, yield: 60%). **m.p.** 153-155 °C. **^1H NMR** (400 MHz, CDCl_3) δ 8.47 (s, 1H), 8.00-7.98 (m, 2H), 7.55-7.52 (m, 1H), 7.41-7.36 (m, 4H), 7.28-7.23 (m, 1H), 7.13 (t, J = 7.7, 2H), 7.04-7.00 (m, 3H), 6.70 (d, J = 8.9, 2H), 6.51 (br, 1H), 3.72

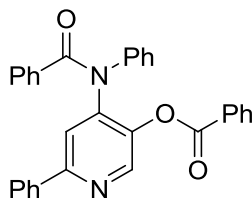
(s, 3H), 2.34 (d, $J = 1.7$, 2H), 2.20 (dt, $J = 5.8, 3.7$, 2H), 1.75-1.72 (m, 2H), 1.65-1.61 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.3, 164.7, 158.3, 158.1, 144.7, 144.1, 140.6, 135.7, 135.3, 134.9, 134.0, 130.9, 130.5, 129.5, 129.3, 128.6, 128.4, 128.1, 118.1, 114.6, 55.5, 26.0, 22.8, 22.1. IR (KBr, cm^{-1}) ν 2930, 1736, 1668, 1510, 1322, 1249. MS (CI). 505 $[\text{M}+1]^+$ (11), 504 $[\text{M}]^+$ (17), 105 (60). HRMS (ESI) calcd. for $\text{C}_{32}\text{H}_{28}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]$ 505.2122, found 505.2122.

6-Cyclohexyl-4-(N-(4-methoxyphenyl)benzamido)pyridin-3-yl benzoate (5m)



Sticky Oil (106 mg, yield:70%). ^1H NMR (400 MHz, $\text{acetone-}d_6$) δ 8.51 (s, 1H), 8.02 (dd, $J = 8.2, 1.2$, 2H), 7.65-7.61 (m, 1H), 7.48-7.41 (m, 4H), 7.31-7.27 (m, J , 1H), 7.18 (t, $J = 7.6$, 2H), 7.11 (d, $J = 8.9$, 2H), 7.00 (s, 1H), 6.78 (d, $J = 9.0$, 2H), 3.72 (s, 3H), 2.63 (tt, $J = 1.7, 3.2$, 1H), 1.53 (m, 10H). ^{13}C NMR (100 MHz, $\text{acetone-}d_6$) δ 170.4, 165.8, 165.2, 159.4, 145.8, 145.1, 141.5, 136.6, 136.4, 134.9, 131.5, 131.1, 130.0, 129.8, 129.7, 129.6, 128.8, 121.1, 115.3, 55.8, 33.5, 27.2, 26.8, 19.5. IR (KBr, cm^{-1}) ν 2927, 1740, 1670, 1509, 1248. MS (CI). 507 $[\text{M}+1]^+$ (59), 506 $[\text{M}]^+$ (71), 105 (100). HRMS (ESI) calcd. for $\text{C}_{32}\text{H}_{30}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]$ 507.2278, found 507.2278..

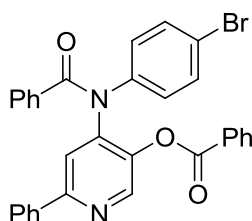
6-Phenyl-4-(N-phenylbenzamido)pyridin-3-yl benzoate (5n)



White solid (109 mg, yield: 77%). m.p. 149-150 $^\circ\text{C}$. ^1H NMR (400 MHz, CDCl_3) δ 8.65 (s, 1H), 8.03-7.95 (m, 2H), 7.84-7.73 (m, 2H), 7.59-7.49 (m, 1H), 7.47-7.33 (m, 8H), 7.31-7.26 (m, 1H), 7.23-7.11 (m, 7H). ^{13}C NMR (100 MHz, CDCl_3) δ 170.2, 164.5, 156.4, 145.6, 144.5, 142.3, 141.3, 138.2, 134.5, 134.0, 131.1, 130.4, 129.4,

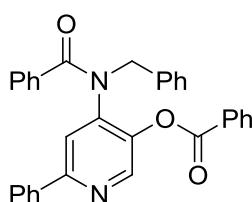
129.3, 129.2, 128.8, 128.5, 128.1, 128.0, 127.2, 127.0, 119.9. **IR** (KBr, cm^{-1}) ν 1750, 1664, 1589, 1483, 1226. **MS** (CI) 471 $[\text{M}+1]^+$ (23), 470 $[\text{M}]^+$ (32), 349 (33), 105 (100). **HRMS** (ESI) calcd. for $\text{C}_{31}\text{H}_{22}\text{N}_2\text{O}_3$ $[\text{M}+\text{H}]$ 471.1703, found 471.1703.

4-(N-(4-bromophenyl)benzamido)-6-phenylpyridin-3-yl benzoate (5o)



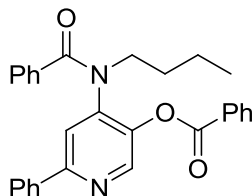
Foam-like Solid (73 mg, yield: 44%). **^1H NMR** (400 MHz, CDCl_3) δ 8.63 (s, 1H), 8.02-7.92 (m, 2H), 7.76 (dd, $J = 7.8, 1.6$, 2H), 7.66-7.53 (m, 1H), 7.53-7.36 (m, 8H), 7.35-7.29 (m, 3H), 7.19 (t, $J = 7.7$, 2H), 7.01 (d, $J = 8.8$, 2H). **^{13}C NMR** (100 MHz, CDCl_3) δ 170.1, 164.5, 156.6, 145.8, 144.0, 141.3, 141.1, 138.0, 134.1, 134.1, 132.5, 131.4, 130.3, 129.3, 128.8, 128.5, 128.2, 127.9, 126.9, 120.5, 119.8. **IR** (KBr, cm^{-1}) ν 1743, 1674, 1593, 1486, 1258. **MS** (CI) 550 $[\text{M}+2]^+$ (3), 548 $[\text{M}]^+$ (3), 430 (5), 432 (5), 105 (100). **HRMS** (EI) calcd. for $\text{C}_{31}\text{H}_{21}\text{N}_2\text{O}_3^{79}\text{Br}$ $[\text{M}]$, $\text{C}_{31}\text{H}_{213}\text{N}_2\text{O}_3^{81}\text{Br}$ $[\text{M}+2]$ 548.0736, 550.0715, found 548.0745, 550.0720.

4-(N-benzylbenzamido)-6-phenylpyridin-3-yl benzoate (5p)



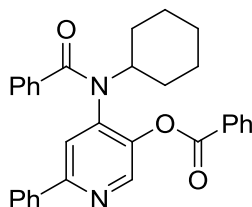
White solid (102 mg, yield: 70%). **m.p.** 149-150 $^\circ\text{C}$. **^1H NMR** (400 MHz, CDCl_3) δ 8.51 (s, 1H), 8.08-8.00 (m, 2H), 7.78-7.62 (m, 3H), 7.52 (m 2H), 7.44-7.21 (m, 12H), 7.21-7.15 (m, 2H), 5.12 (s, 2H). **^{13}C NMR** (100 MHz, CDCl_3) δ 170.4, 163.7, 155.8, 145.7, 143.8, 141.7, 138.0, 137.0, 134.8, 134.2, 130.9, 130.4, 129.5, 128.81, 128.76, 128.7, 128.4, 128.0, 127.9, 126.9, 120.3, 53.0. **IR** (KBr, cm^{-1}) ν 3063, 3032, 1748, 1658, 1591, 1479, 1258. **MS** (CI) 485 $[\text{M}+1]^+$ (21), 484 $[\text{M}]^+$ (9), 363 (43), 105 (100). **HRMS** (EI) calcd. for $\text{C}_{32}\text{H}_{24}\text{N}_2\text{O}_3$ $[\text{M}]$ 484.1787, found 484.1792.

4-(N-butylbenzamido)-6-phenylpyridin-3-yl benzoate (5q)



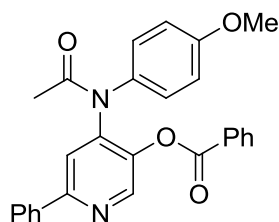
White solid (80 mg, yield: 60%). **m.p.** 118-119 °C. **¹H NMR** (400 MHz, CDCl₃) δ 8.57 (s, 1H), 8.14 (d, *J* = 7.8, 2H), 7.88-7.78 (m, 2H), 7.70 (t, *J* = 7.4, 1H), 7.56 (t, *J* = 7.7, 2H), 7.52 (s, 1H), 7.50-7.41 (m, 3H), 7.38 (d, *J* = 7.5, 2H), 7.32 (t, *J* = 7.3, 1H), 7.20 (t, *J* = 7.6, 2H), 3.91 (t, *J* = 7.8, 2H), 1.72-1.58 (m, 2H), 1.42-1.28 (m, 2H), 0.88 (t, *J* = 7.3, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.4, 163.8, 155.9, 145.8, 144.1, 141.6, 137.9, 134.9, 134.4, 130.7, 130.4, 129.4, 128.9, 128.6, 128.2, 128.0, 126.9, 120.4, 49.9, 30.0, 20.2, 13.7. **IR** (KBr, cm⁻¹) ν 2961, 1745, 1648, 1259, 1229. **MS** (CI) 451 [M+1]⁺ (7), 450 [M]⁺ (5), 329 (50), 105 (100). **HRMS** (EI) calcd. for C₂₉H₂₆N₂O₃ [M] 450.1943, found 450.1949.

4-(N-cyclohexylbenzamido)-6-phenylpyridin-3-yl benzoate (5r)



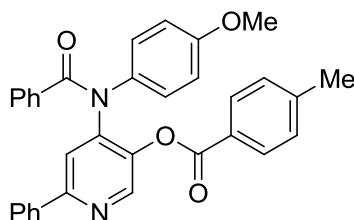
Yellow oil (59 mg, yield: 41%). **¹H NMR** (400 MHz, CDCl₃) δ 8.62 (s, 1H), 8.20-8.09 (m, 2H), 7.94 (d, *J* = 7.2, 2H), 7.69 (t, *J* = 7.4, 1H), 7.63 (s, 1H), 7.56 (t, *J* = 7.7, 2H), 7.51-7.43 (m, 3H), 7.34-7.29 (m, 2H), 7.26-7.19 (m, 1H), 7.13 (t, *J* = 7.6, 2H), 4.53 (tt, *J* = 8.4, 3.6, 1H), 2.07-1.94 (m, 2H), 1.85-1.74 (m, 2H), 1.63-1.31 (m, 6H), 1.15-1.01 (m, 1H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.5, 163.6, 155.0, 145.8, 143.3, 141.4, 138.2, 136.0, 134.2, 130.4, 130.3, 129.4, 128.9, 128.8, 128.3, 127.9, 127.0, 122.2, 58.5, 31.5, 26.1, 25.4. **IR** (KBr, cm⁻¹) ν 2930, 1748, 1660, 1258. **MS** (CI) 477 [M+1]⁺ (5), 476 [M]⁺ (2), 355 (42), 105 (100). **HRMS** (ESI) calcd. for C₃₁H₂₈N₂O₃ [M+H] 477.2173, found 477.2175.

4-(N-(4-methoxyphenyl)acetamido)-6-phenylpyridin-3-yl benzoate (5s)



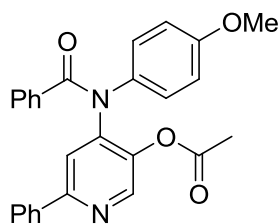
White solid (87 mg, yield: 66%). **m.p.** 149-150 °C. **¹H NMR** (400 MHz, CDCl₃) δ 8.51 (s, 1H), 7.75 (dd, *J* = 7.8, 1.5, 2H), 7.58-7.51 (m, 2H), 7.38 (dd, *J* = 14.1, 7.5, 4H), 7.33-7.27 (m, 3H), 7.08 (d, *J* = 8.9, 2H), 6.80 (d, *J* = 8.9, 2H), 3.77 (s, 3H), 2.16 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 169.9, 168.7, 158.4, 156.4, 145.3, 144.5, 140.8, 138.2, 135.2, 134.7, 131.2, 129.3, 129.2, 128.7, 128.6, 128.2, 126.9, 119.3, 114.7, 55.4, 20.6. **IR** (KBr, cm⁻¹) ν 1764, 1670, 1509, 1248. **MS** (CI): 439 [M+1]⁺ (18), 438 [M]⁺ (41), 396 (43), 105 (100). **HRMS** (EI) calcd. for C₂₇H₂₂N₂O₄ [M] 438.1580, found 438.1585.

4-(N-(4-methoxyphenyl)benzamido)-6-phenylpyridin-3-yl 4-methylbenzoate (5t)



White solid (131 mg, yield: 85%). **m.p.** 79-81 °C. **¹H NMR** (400 MHz, CDCl₃) δ 8.62 (s, 1H), 8.03-8.01 (m, 2H), 7.79 (dd, *J* = 8.0, 1.4, 2H), 7.54 (t, *J* = 7.5, 1H), 7.44-7.31 (m, 11H), 7.06 (d, *J* = 8.9, 2H), 6.93 (d, *J* = 8.0, 2H), 6.71 (d, *J* = 8.9, 2H), 3.72 (s, 3H), 2.24 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.2, 164.6, 158.2, 156.3, 145.5, 144.9, 141.4, 141.2, 138.3, 135.4, 133.9, 130.4, 129.4, 129.1, 128.72, 128.66, 128.6, 128.5, 128.3, 127.0, 119.6, 114.6, 55.4, 21.4. **IR** (KBr, cm⁻¹) ν 1741, 1669, 1508, 1248. **MS** (CI) 515 [M+1]⁺ (45), 514 [M]⁺ (62), 119 (100), 105 (42). **HRMS** (ESI) calcd. for C₃₃H₂₆N₂O₄ [M+H] 515.1965, found 515.1964.

4-(N-(4-methoxyphenyl)benzamido)-6-phenylpyridin-3-yl acetate (5u)

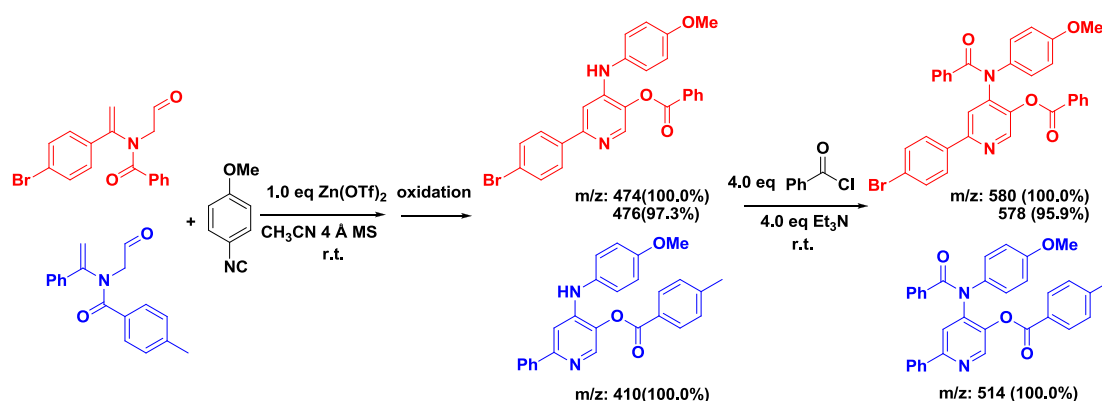


White solid (40 mg, yield: 30%). **m.p.** 159-160. °C. **¹H NMR** (400 MHz, CDCl₃) δ 8.65 (s, 1H), 8.14 (d, *J* = 7.7, 2H), 7.90 (d, *J* = 7.4, 2H), 7.65 (t, *J* = 7.4, 1H), 7.62-7.30 (m, 6H), 7.17 (d, *J* = 8.8, 2H), 6.82 (d, *J* = 8.8, 2H), 3.77 (s, 3H), 2.04 (s, 3H). **¹³C NMR** (100 MHz, CDCl₃) δ 170.1, 164.3, 159.2, 156.4, 145.9, 143.5, 141.8, 138.4, 134.4, 134.1, 130.5, 129.3, 129.0, 128.81, 128.77, 127.0, 119.9, 115.0, 55.6, 23.0. **IR** (KBr, cm⁻¹) ν 1730, 1682, 1509, 1251. **MS** (CI) 439 [M+1]⁺ (31), 438 [M]⁺ (58), 396 (45), 105 (100). **HRMS** (ESI) *m/z* calcd. for C₂₇H₂₂N₂O₄ [M+H]⁺ 439.1652, found 439.1653.

5. Mechanistic Studies

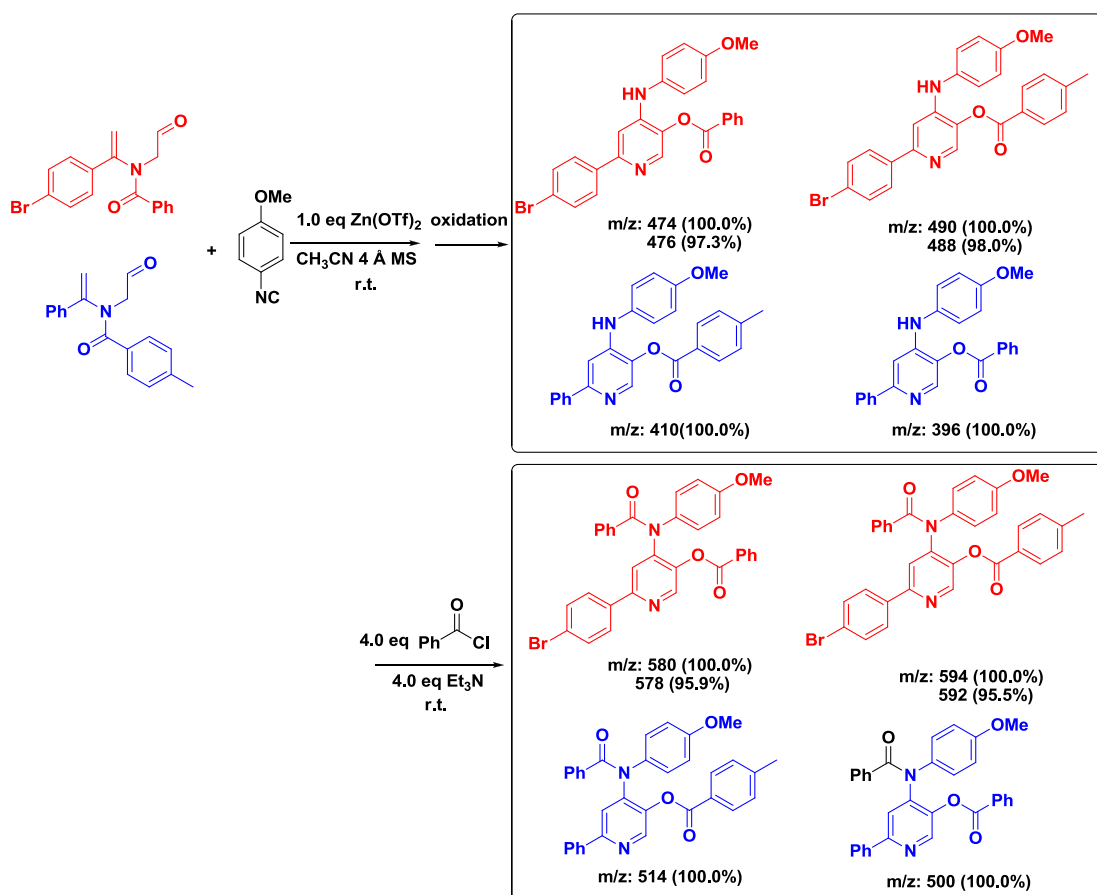
5.1 HPLC-MS analysis of products from a crossover experiment

If the acyl transfer from nitrogen of enamide to hydroxyl oxygen of pyridine occurs in an intramolecular manner, two pyridine products would be detected.



Scheme S4 Intramolecular acyl transfer

If reaction proceeded in an intermolecular manner, two pairs of constitutional isomers would be resulted.



Scheme S5 Intermolecular acyl transfer

As indicated clearly by HPLC-MS analysis, treatment of an equimolar amount of enamides **1f** and **1n** with isonitrile **2a**, followed by auto-oxidation and reaction with benzoyl chloride **3a** led to the formation of a mixture of four pyridine products. The outcomes are in agreement with intermolecular acyl transfer mechanism.

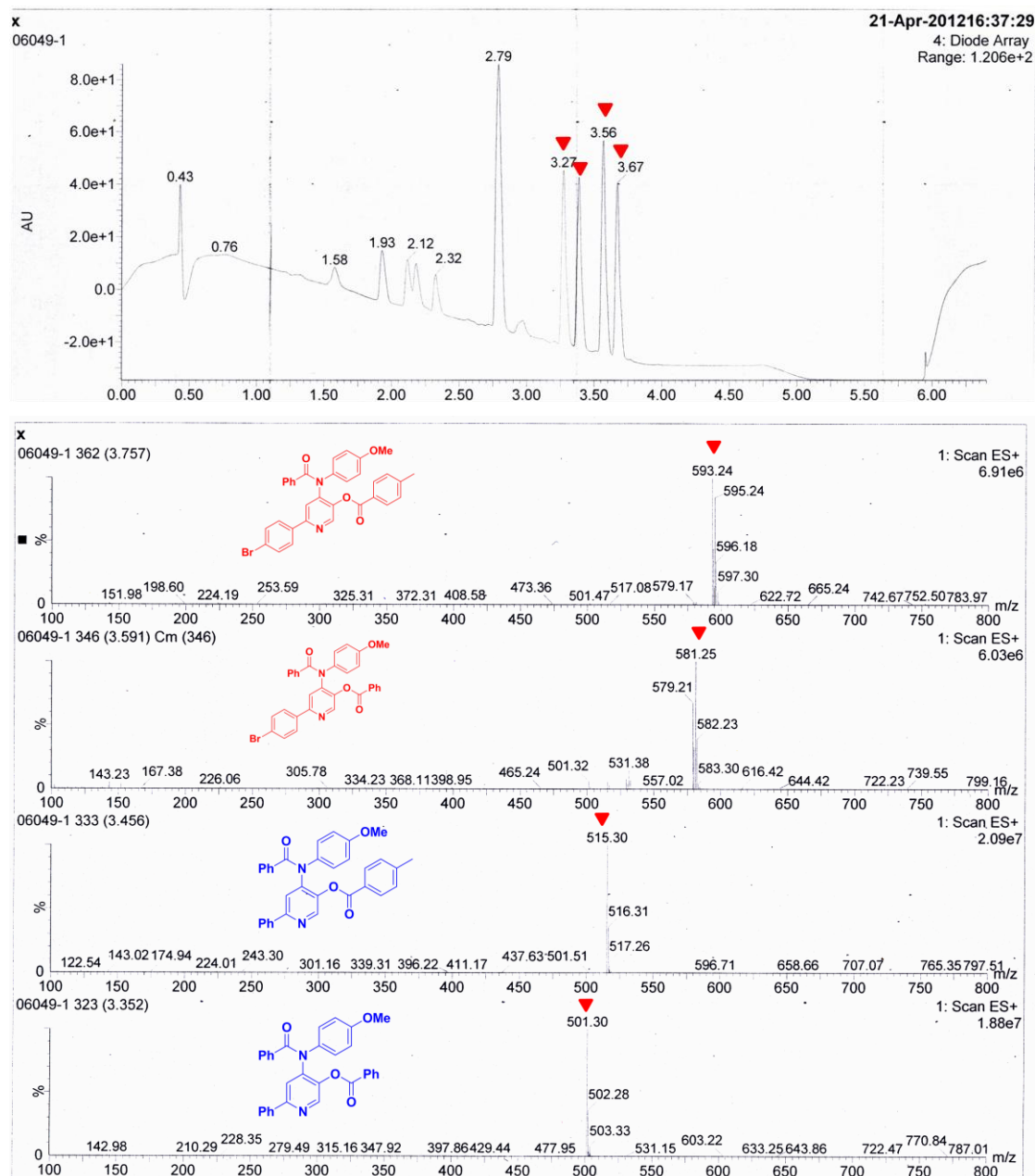
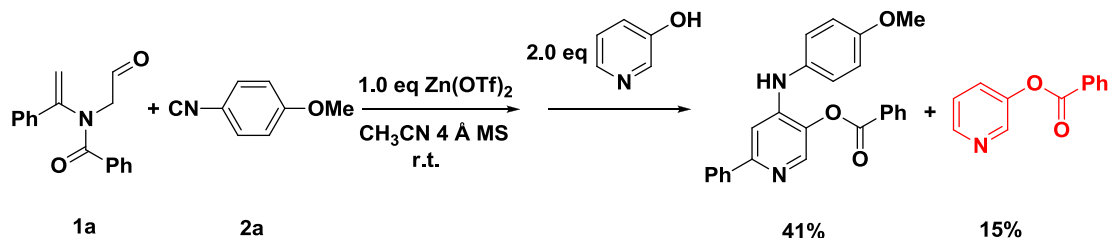


Figure S6 HPLC-MS spectra of crossover experiment

5.2 HPLC-MS Spectra and HPLC Spectra for the Benzoylation of 3-hydroxypyridine

To study the mechanism in more detail, we conducted this control experiment. To a solution of **2a** (0.36 mmol, 47.9 mg) in acetonitrile (15 mL) was added **1** (0.3 mmol, 79.6mg), 4 Å molecular sieves (300 mg) and Zn(OTf)₂ (0.3 mmol, 109.1 mg). The reaction mixture was stirred at ambient temperature until the disappearance of **1a** (monitored by TLC), 3-hydroxypyridine was added, then quenched with saturated aqueous NaHCO₃ (5 mL), filtrated through a pad of Celite and extracted with CH₂Cl₂

(3×15 mL). The combined organic extracts were washed with brine, dried over MgSO₄. The dried organic extracts were left under atmospheric conditions overnight. The residue was subjected to HPLC-MS analysis or HPLC analysis.



Scheme S6 Benzoylation of external 3-hydroxypyridine.

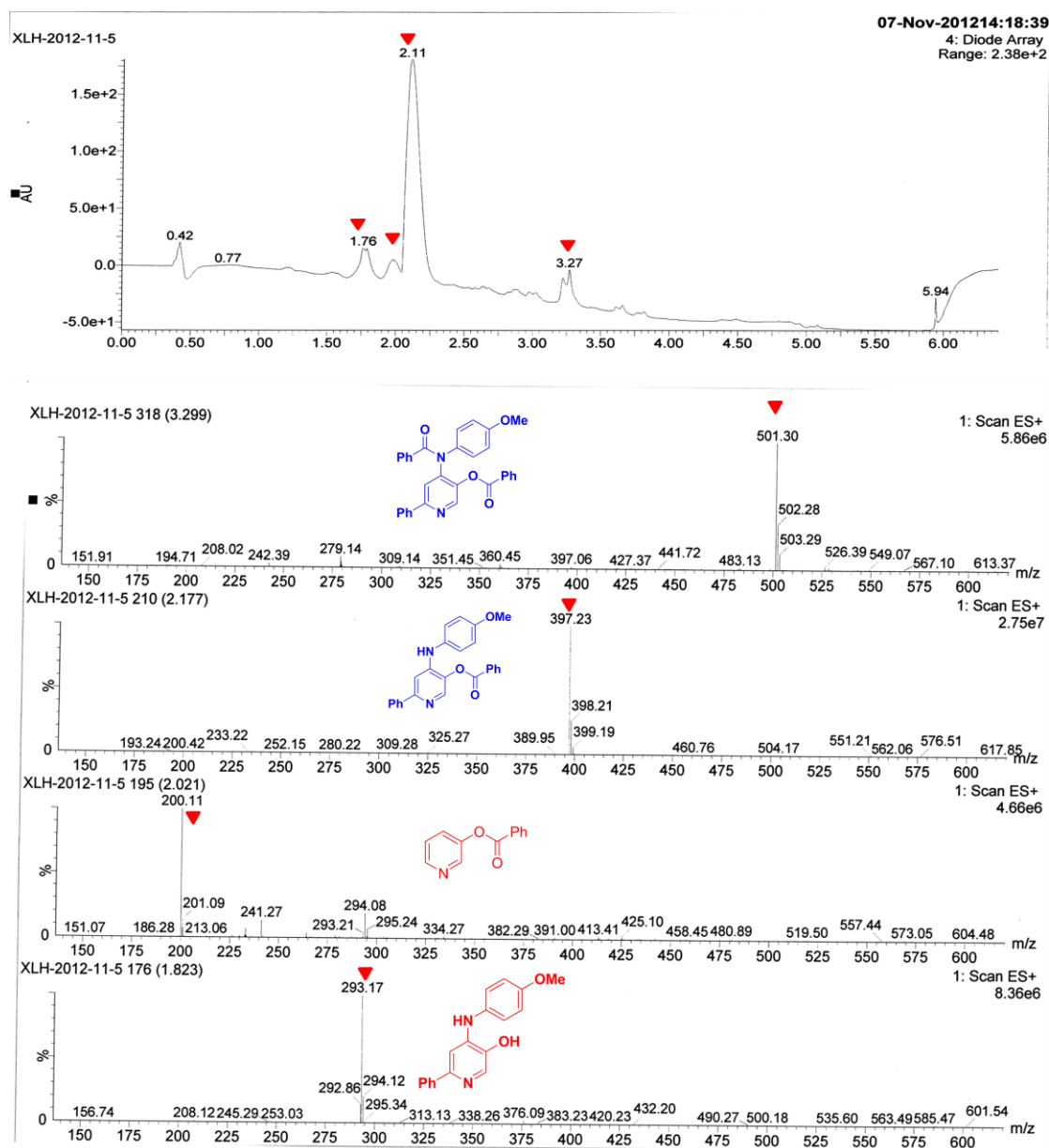


Figure S7 HPLC-MS spectra of experiment by adding external 3-hydroxypyridine into the reaction mixture of **1a** and **2a**.

After crude flash column chromatography on silica gel, A Shimadzu LC-10AVP HPLC system was also used to analyze the mixtures. Chiral columns (ADH) were purchased from DAICEL Chemical Industries, LTD. A mixture of hexane and 2-propanol (2:1) was used as mobile phase with a flow rate of 0.5 ml/min. The temperature of the column chamber was set to 25 °C. 3-Hydroxypyridine produced in the system has the same retention time and UV-spectrum with the standard sample. see Figure S8.

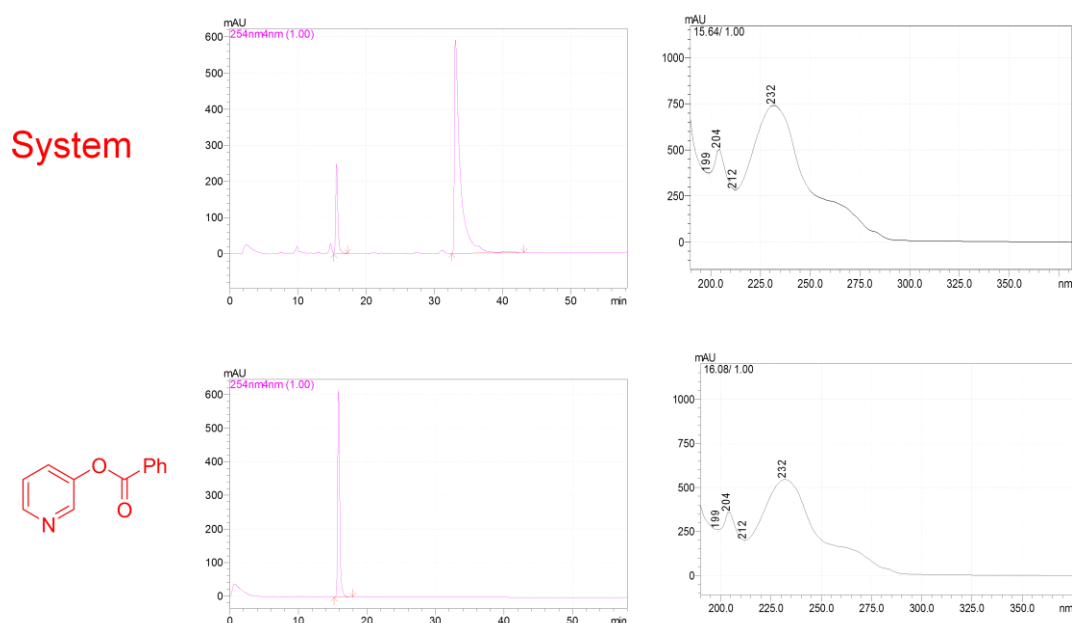


Figure S8 HPLC spectra of experiment by adding external 3-hydroxypyridine into the reaction mixture of **1a** and **2a** after crude column chromatography.

6. Crystallographic Data

Crystal data and structure refinement for **4a**

Identification code	4a
Empirical formula	C ₂₅ H ₂₀ N ₂ O ₃
Formula weight	396.43
Temperature	173(2) K
Wavelength	0.71073 Å

Crystal system	Triclinic
Space group	<i>P</i> -1
Unit cell dimensions	$a = 7.3246(15) \text{ \AA}$ $\alpha = 82.46(3)^\circ$ $b = 8.8640(18) \text{ \AA}$ $\beta = 84.33(3)^\circ$ $c = 15.446(3) \text{ \AA}$ $\gamma = 74.63(3)^\circ$
Volume	$956.5(3) \text{ \AA}^3$
Z	2
Calculated density	1.376 Mg/m^3
Absorption coefficient	0.091 mm^{-1}
F(000)	416
Crystal size	$0.23 \times 0.20 \times 0.14 \text{ mm}$
Theta range for data collection	2.87 to 27.48°
Limiting indices	$-9 \leq h \leq 9$, $-11 \leq k \leq 11$, $19 \leq l \leq 20$
Reflections collected/unique	8533/4346 [$R(\text{int}) = 0.0322$]
Completeness to $\theta = 27.48^\circ$	98.7%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.6831
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	4346/0/272
Goodness-of-fit on F^2	1.123
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0580$, $wR2 = 0.1292$
R indices (all data)	$R1 = 0.0648$, $wR2 = 0.1338$
Largest diff. peak and hole	0.242 and $-0.184 \text{ e.\AA}^{-3}$

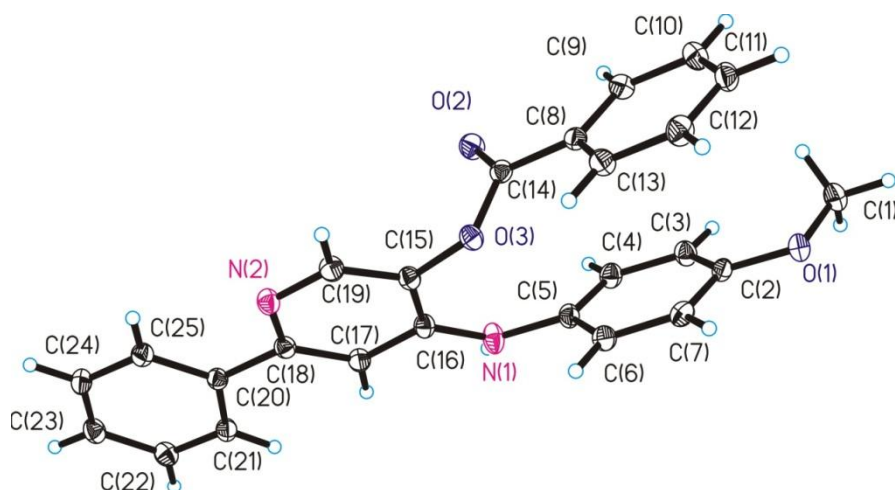


Figure S9 ORTEP presentation of **4a**

Crystal data and structure refinement for **5c**

Identification code	5c
Empirical formula	$C_{32}H_{23}ClN_2O_4$
Formula weight	534.97
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	<i>P</i> -1
Unit cell dimensions	$a = 10.985(2)$ Å $\alpha = 77.49(3)^\circ$ $b = 11.022(2)$ Å $\beta = 76.30(3)^\circ$ $c = 11.542(2)$ Å $\gamma = 82.60(3)^\circ$
Volume	$1321.0(5)$ Å ³
Z	2
Calculated density	1.345 Mg/m ³
Absorption coefficient	0.186 mm ⁻¹
F(000)	556
Crystal size	0.24 × 0.23 × 0.21 mm
Theta range for data collection	1.85 to 27.46°

Limiting indices	-14<=h<=14, -14<=k<=14, -14<=l<=14
Reflections collected/unique	17913/6028 [R(int) = 0.0566]
Completeness to theta = 27.48°	99.8%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.7817
Refinement method	Full-matrix least-squares on F ²
Data/restraints/parameters	6028/0/353
Goodness-of-fit on F ²	1.123
Final R indices [I>2sigma(I)]	R1 = 0.0615, wR2 = 0.1276
R indices (all data)	R1 = 0.0751, wR2 = 0.1350
Largest diff. peak and hole	0.283 and -0.460 e.Å ⁻³

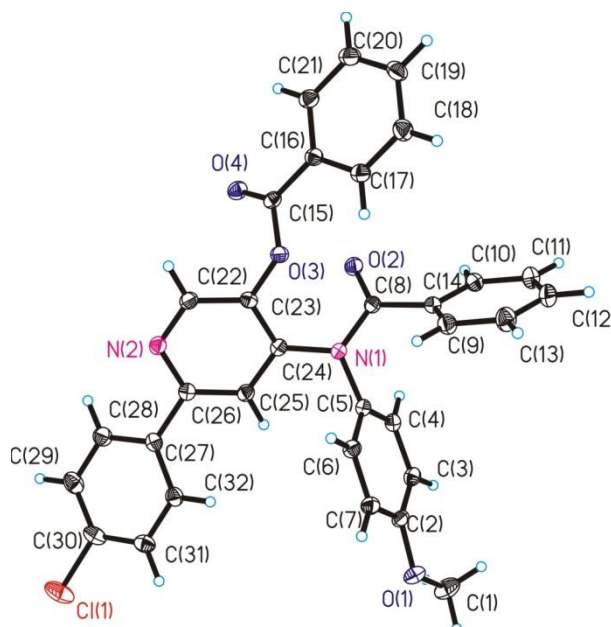
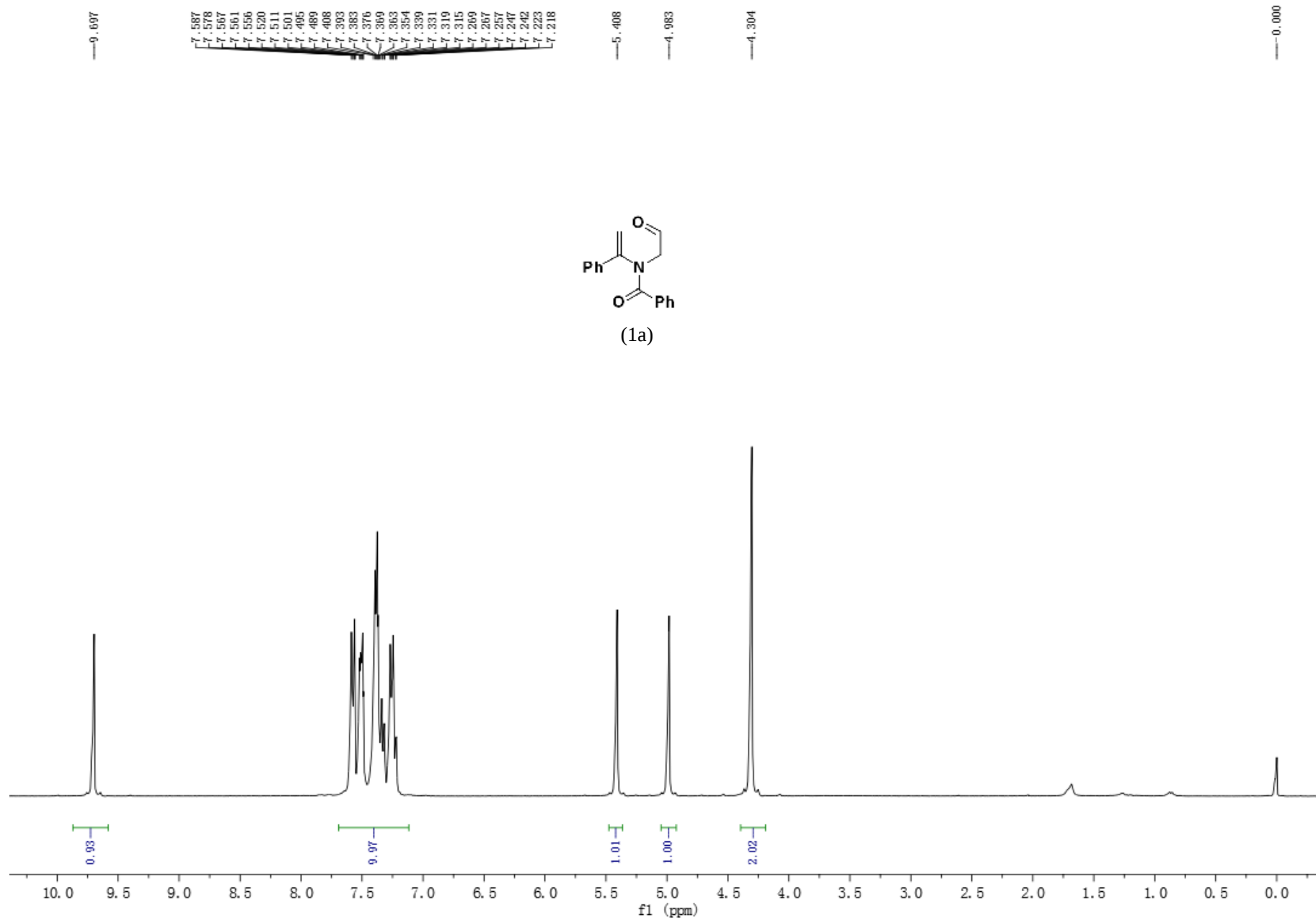


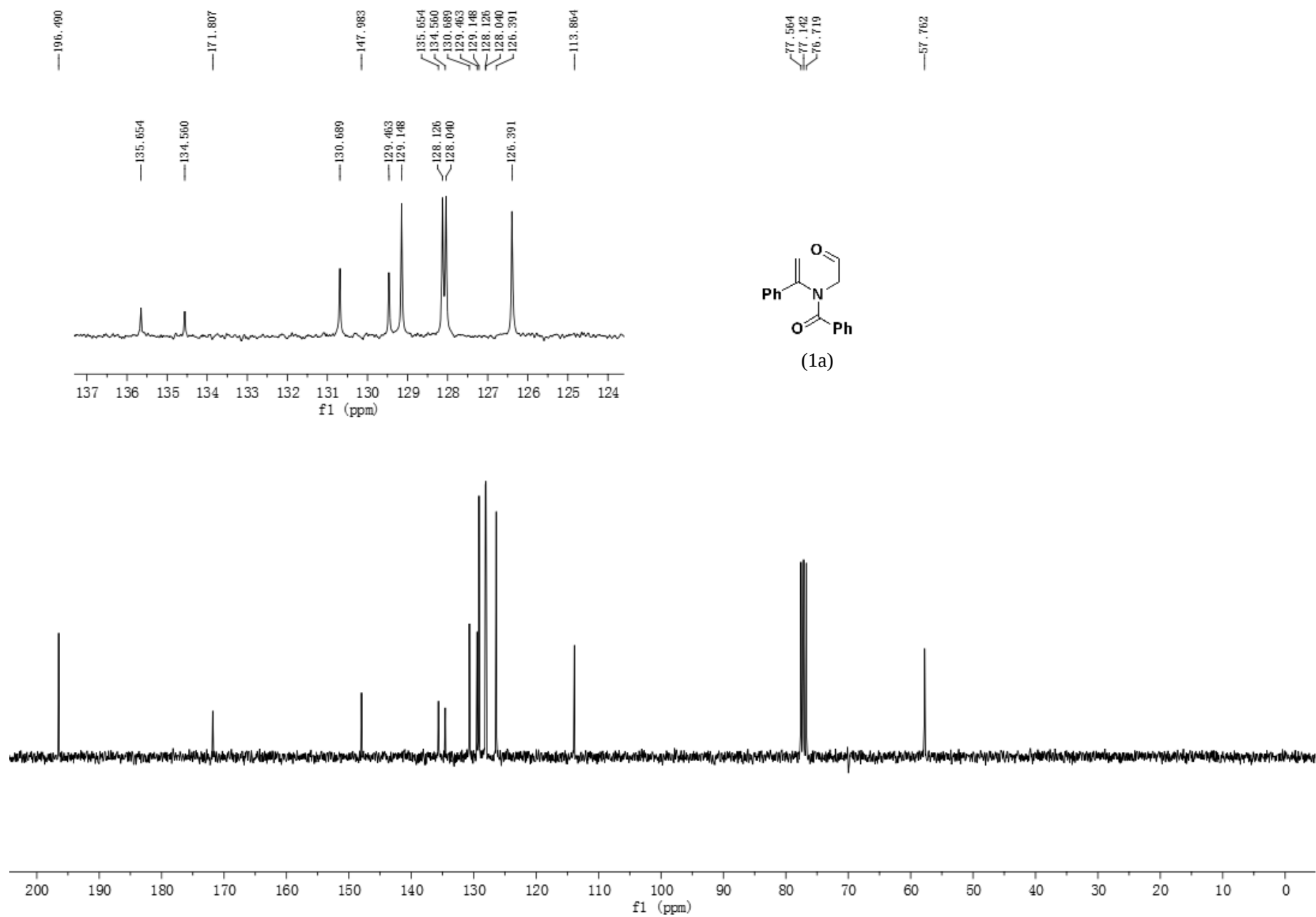
Figure S10 ORTEP presentation of **5c**

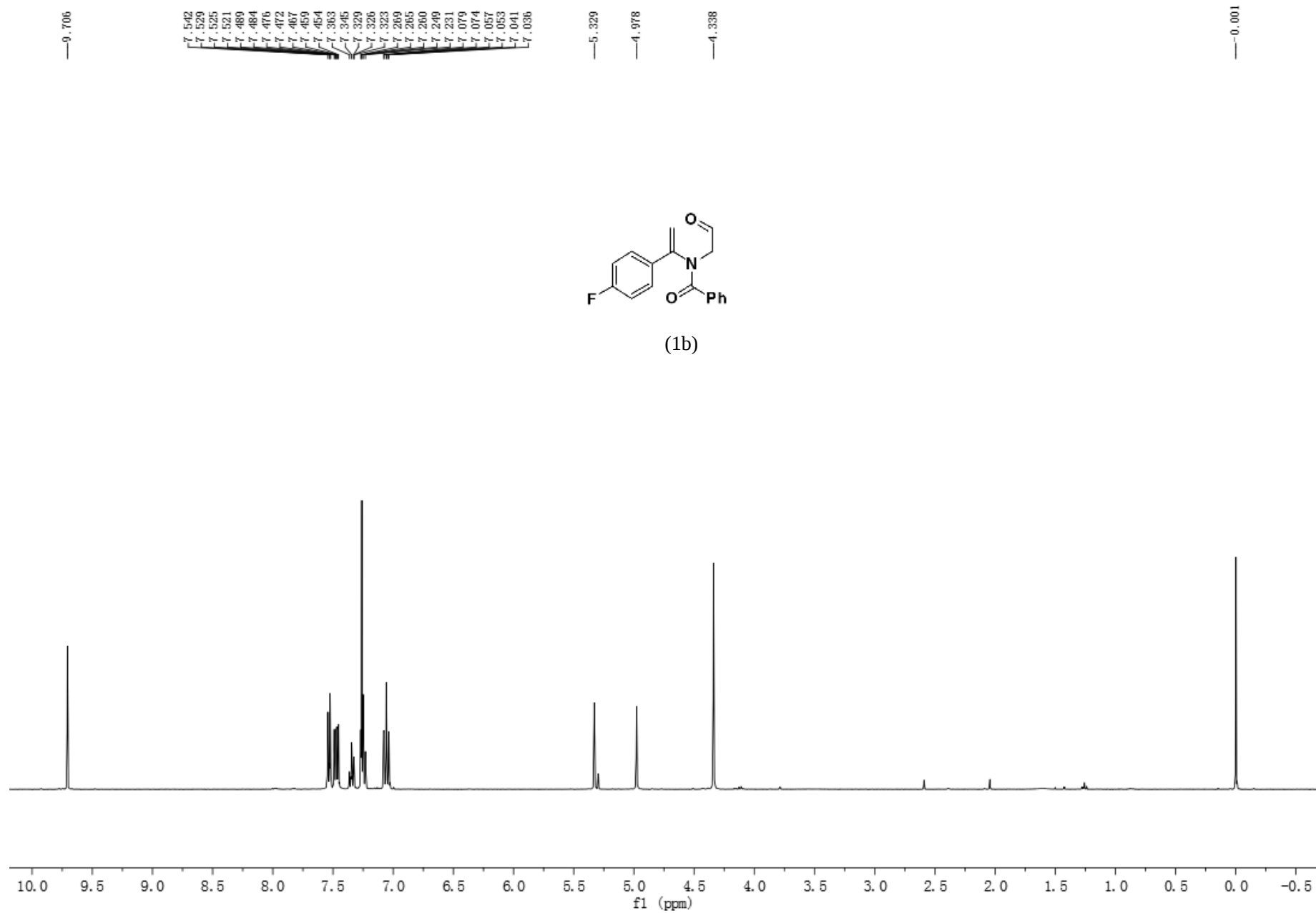
7. References

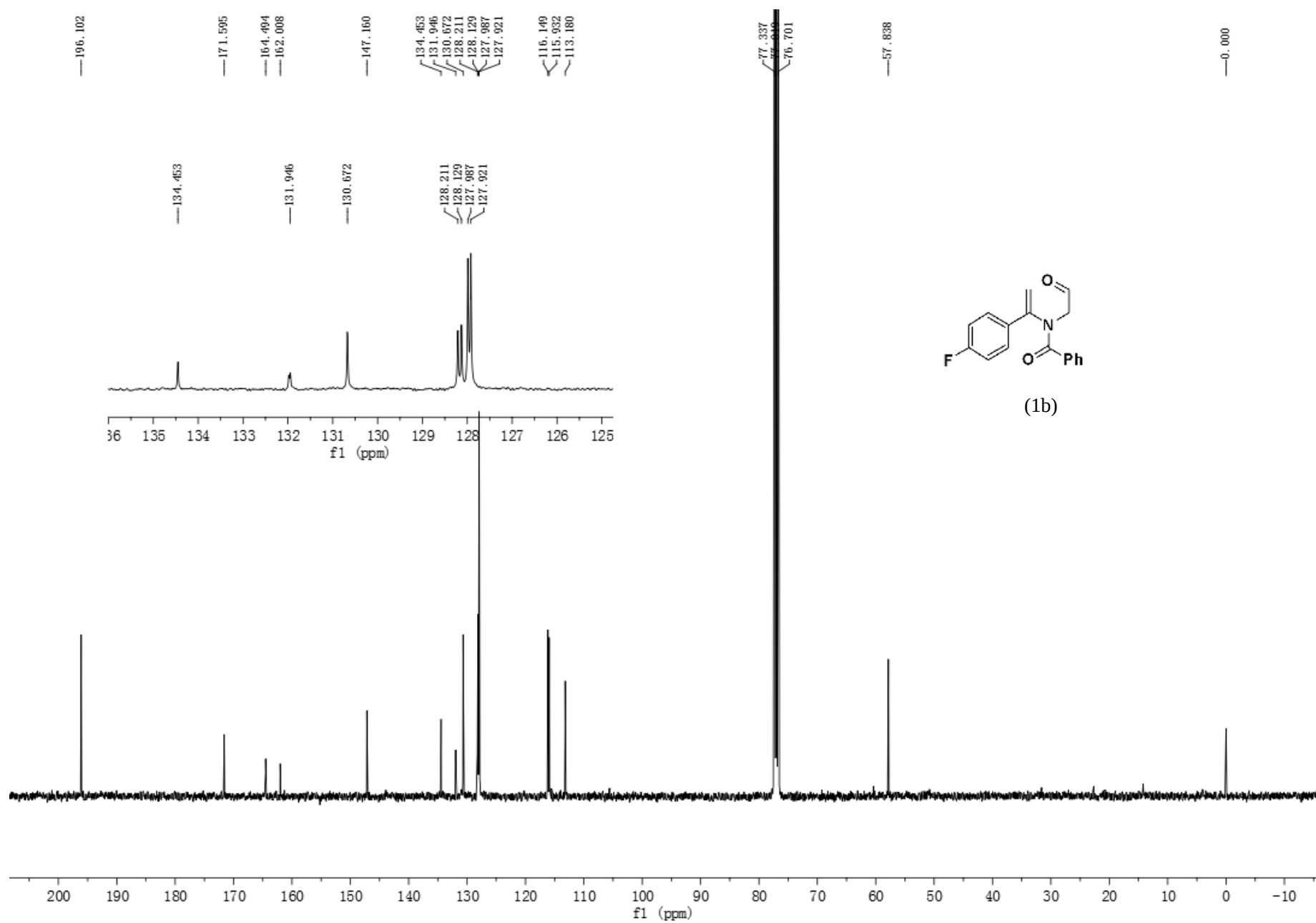
- [1] (a) Yang, L., Wang, D.- X.; Huang, Z.- T.; Wang, M.- X. *J. Am. Chem. Soc.* **2009**, *131*, 10390-10391. (b) Yang, L.; Lei, C.- H.; Wang, D.- X.; Huang, Z.- T.; Wang, M.- X. *Org. Lett.* **2010**, *12*, 3918-3921.

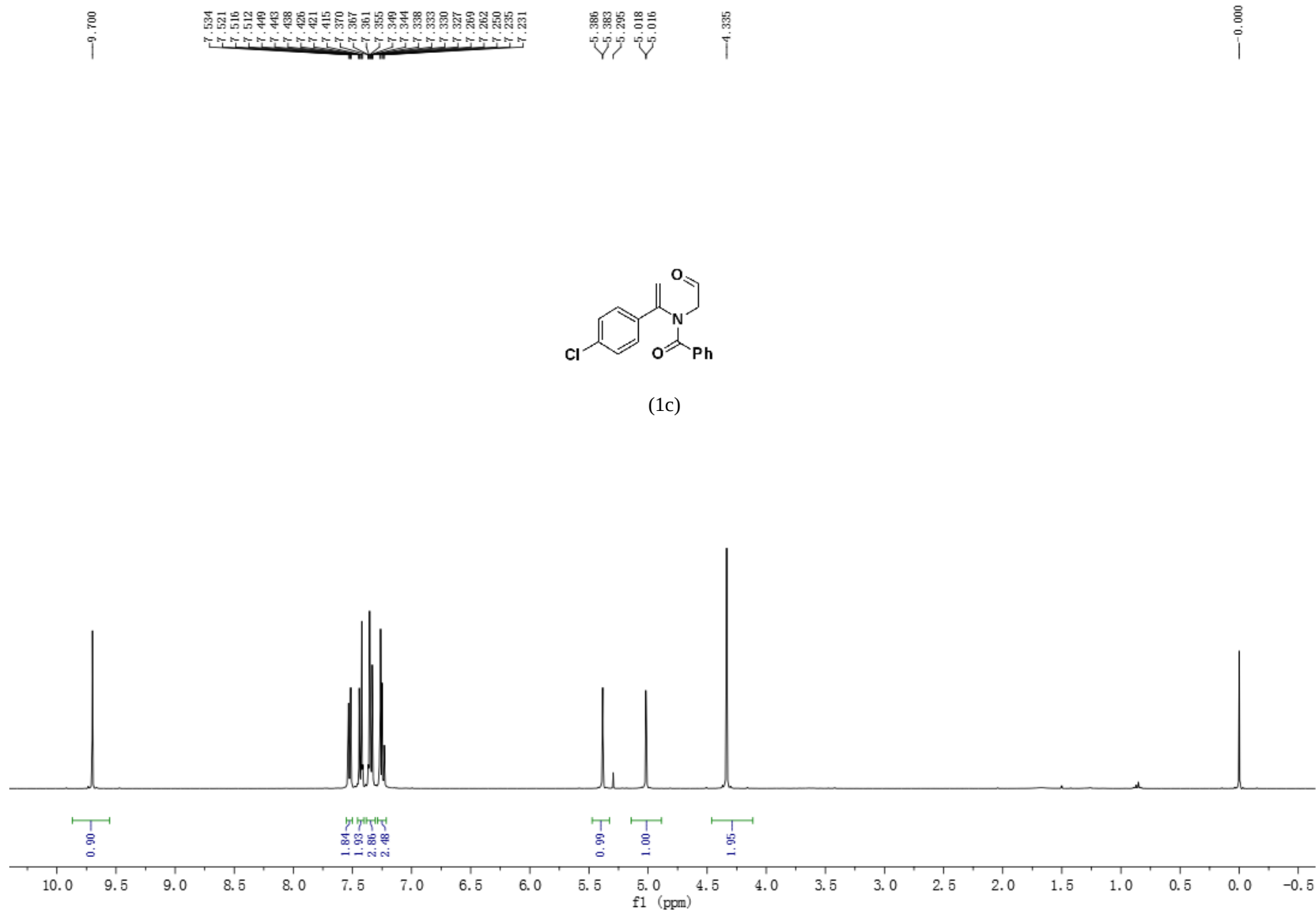
8. Copies of ¹H and ¹³C NMR Spectra

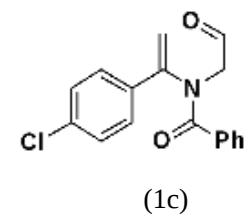
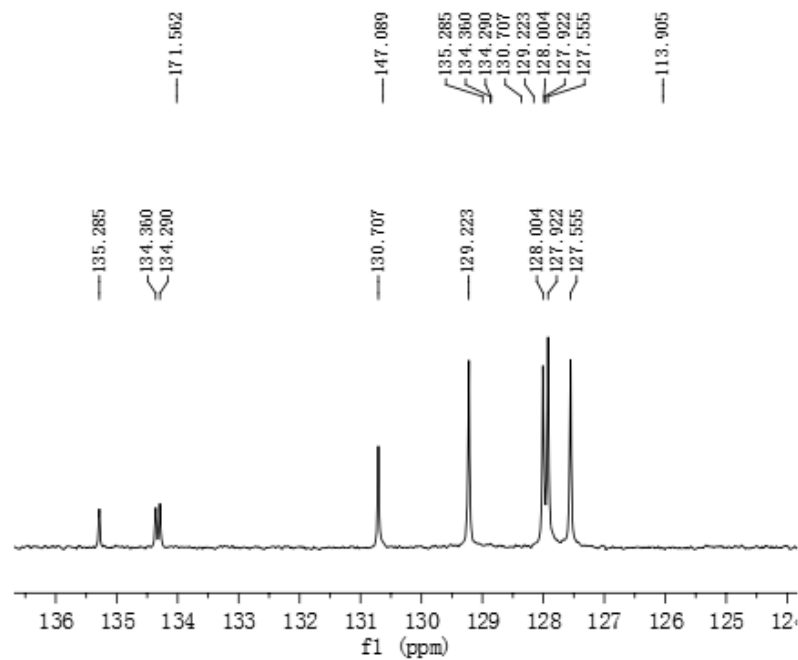
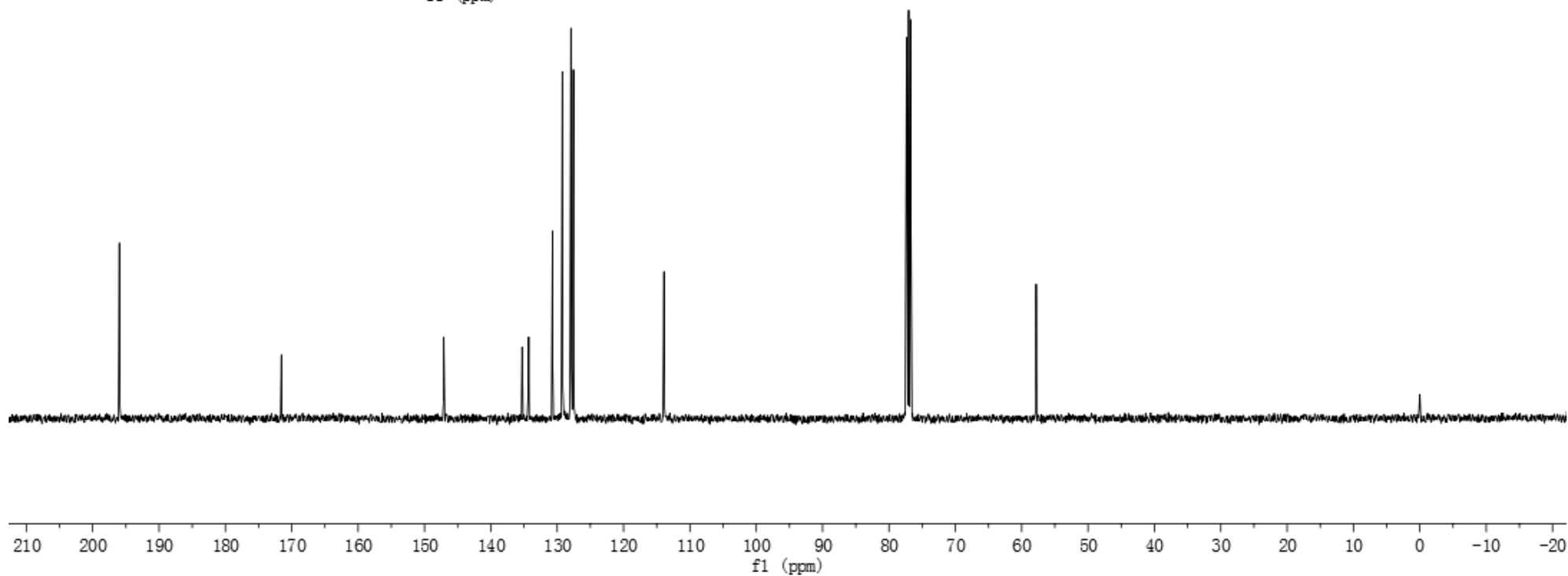


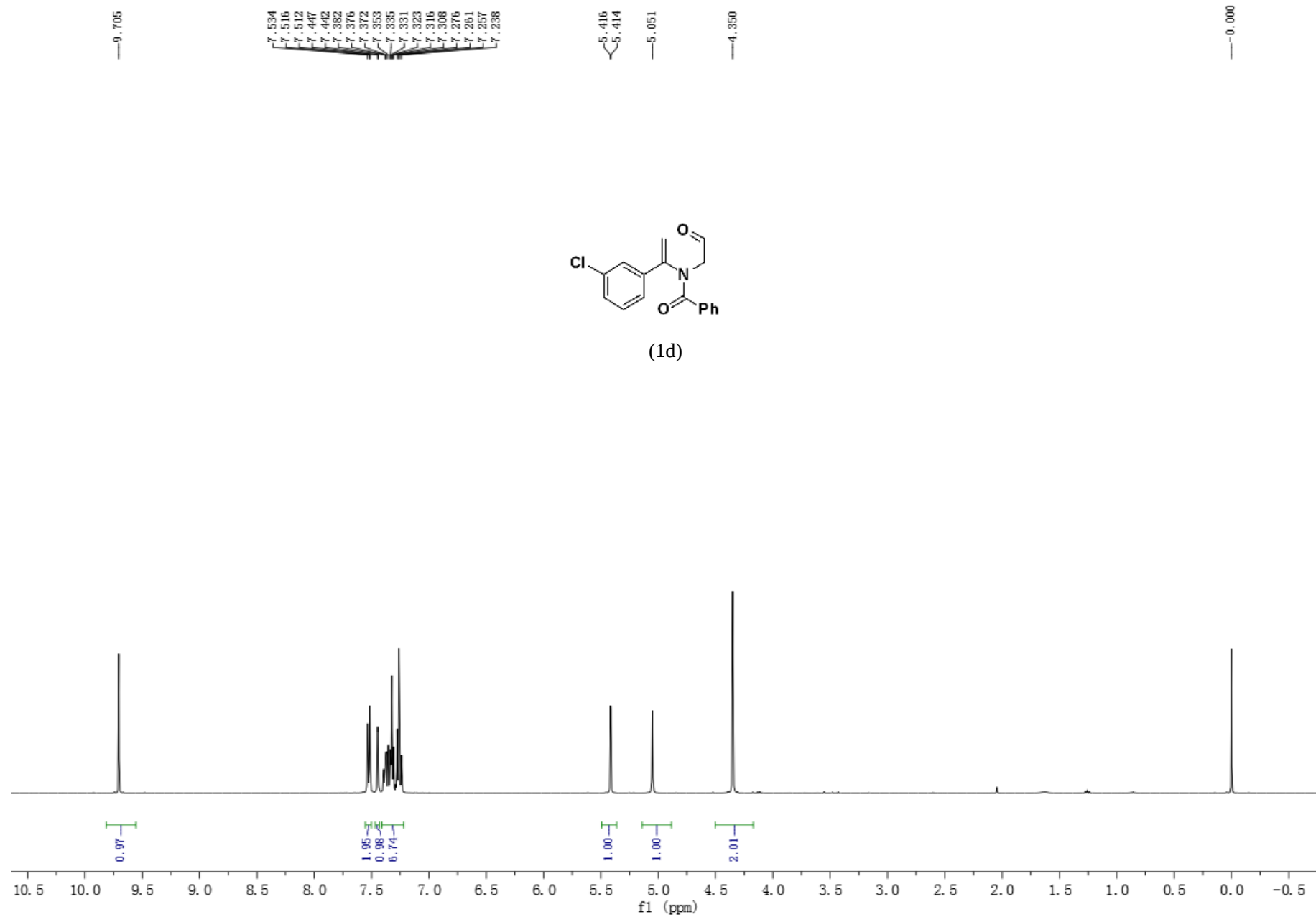


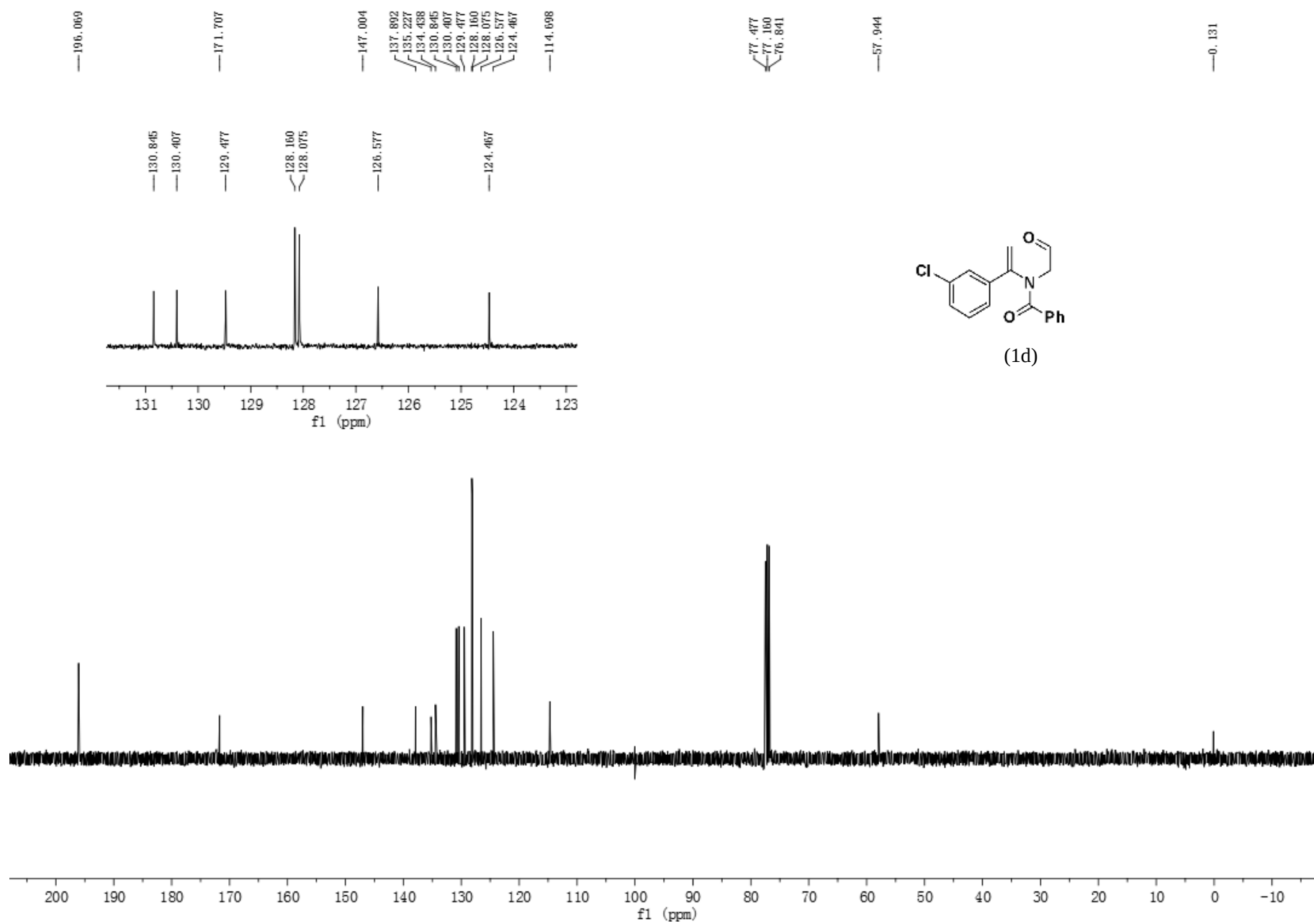


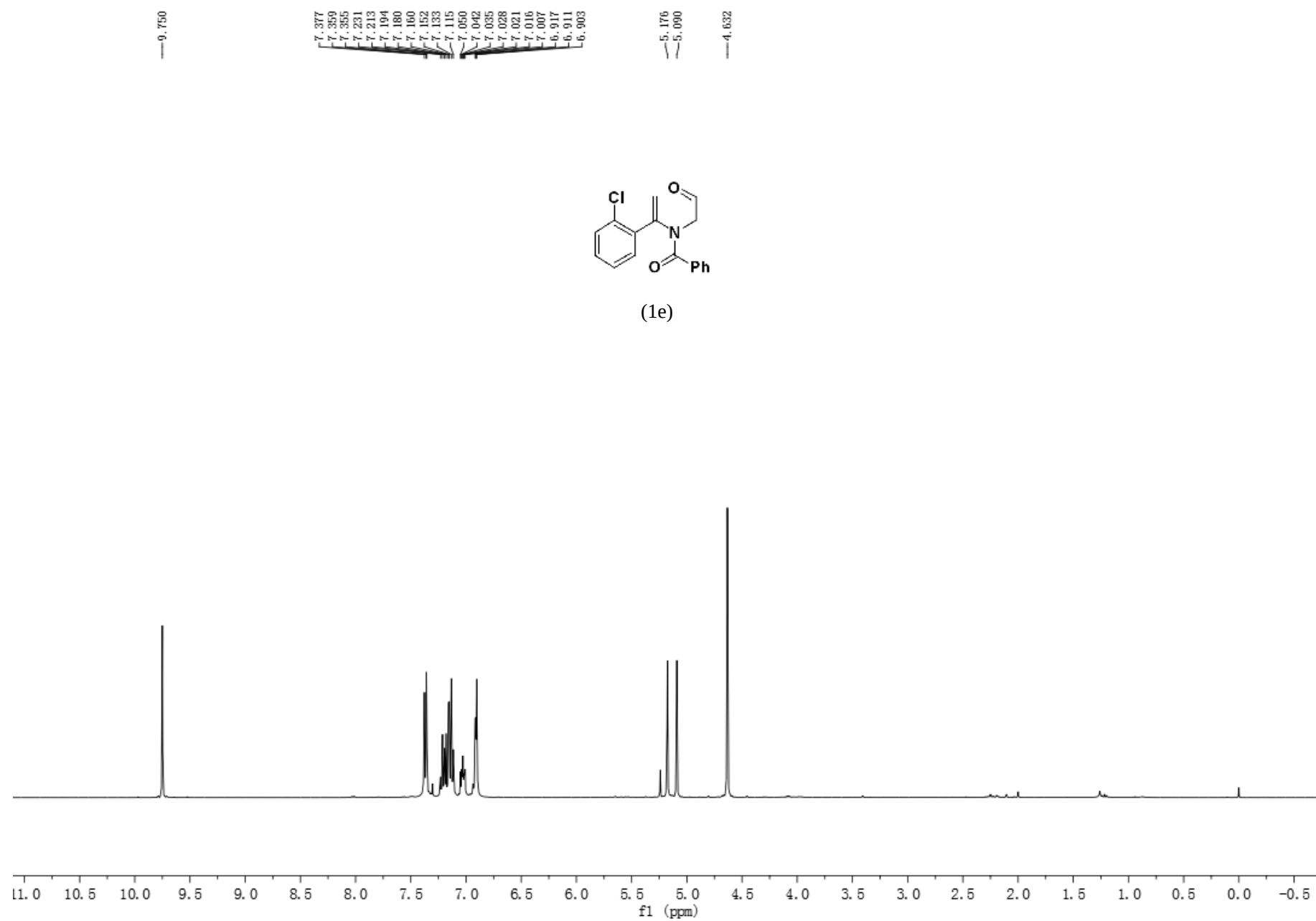


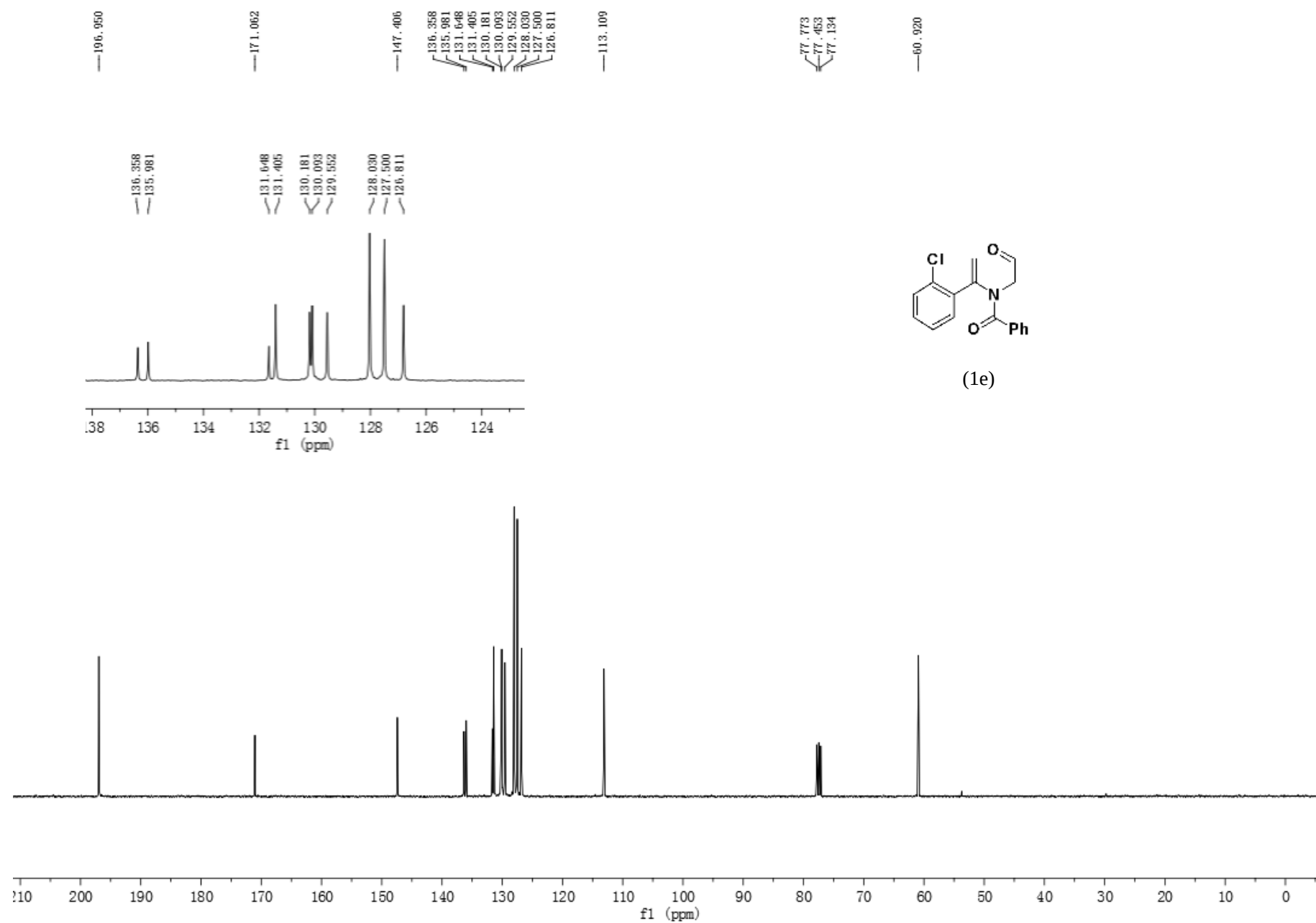


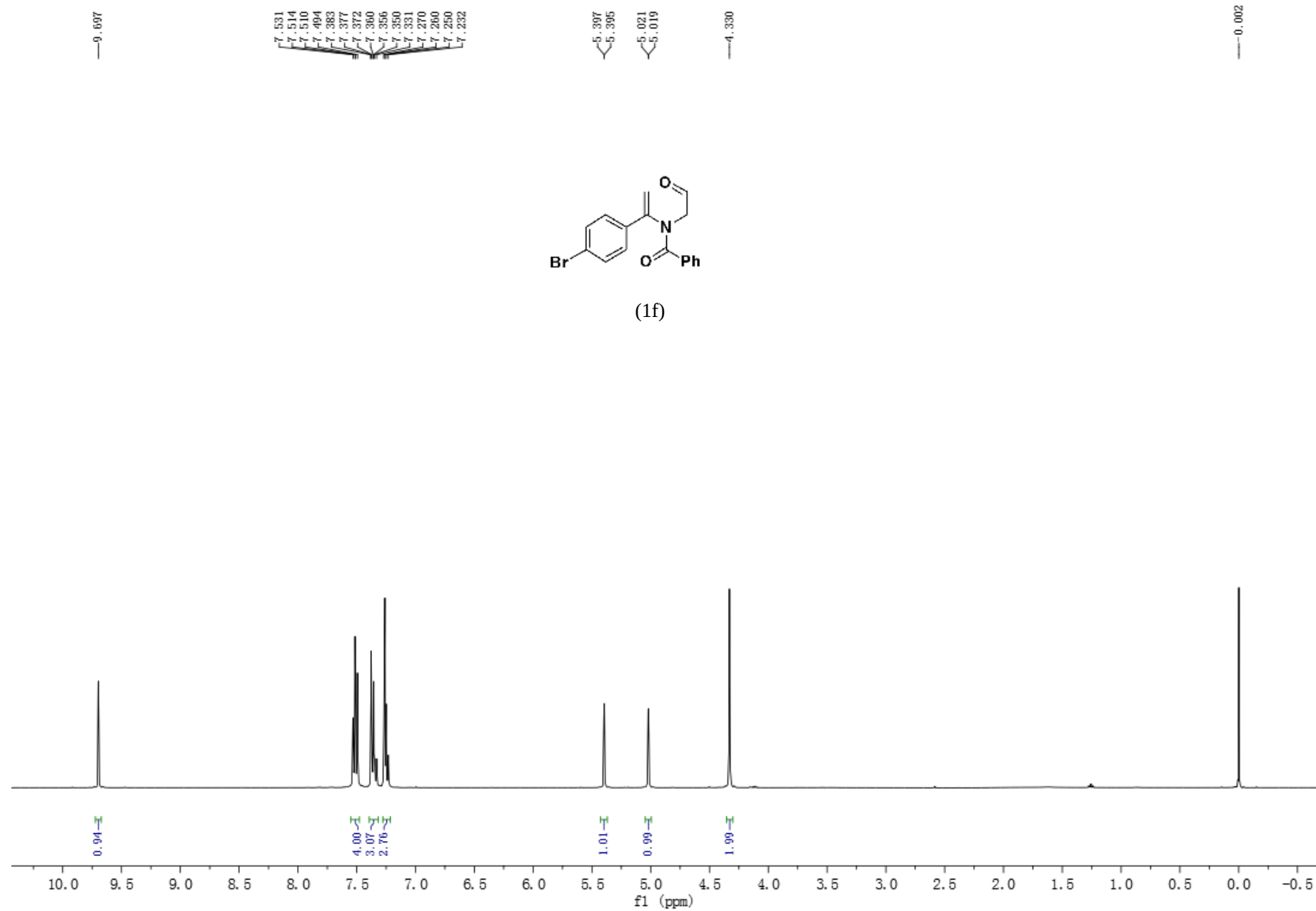


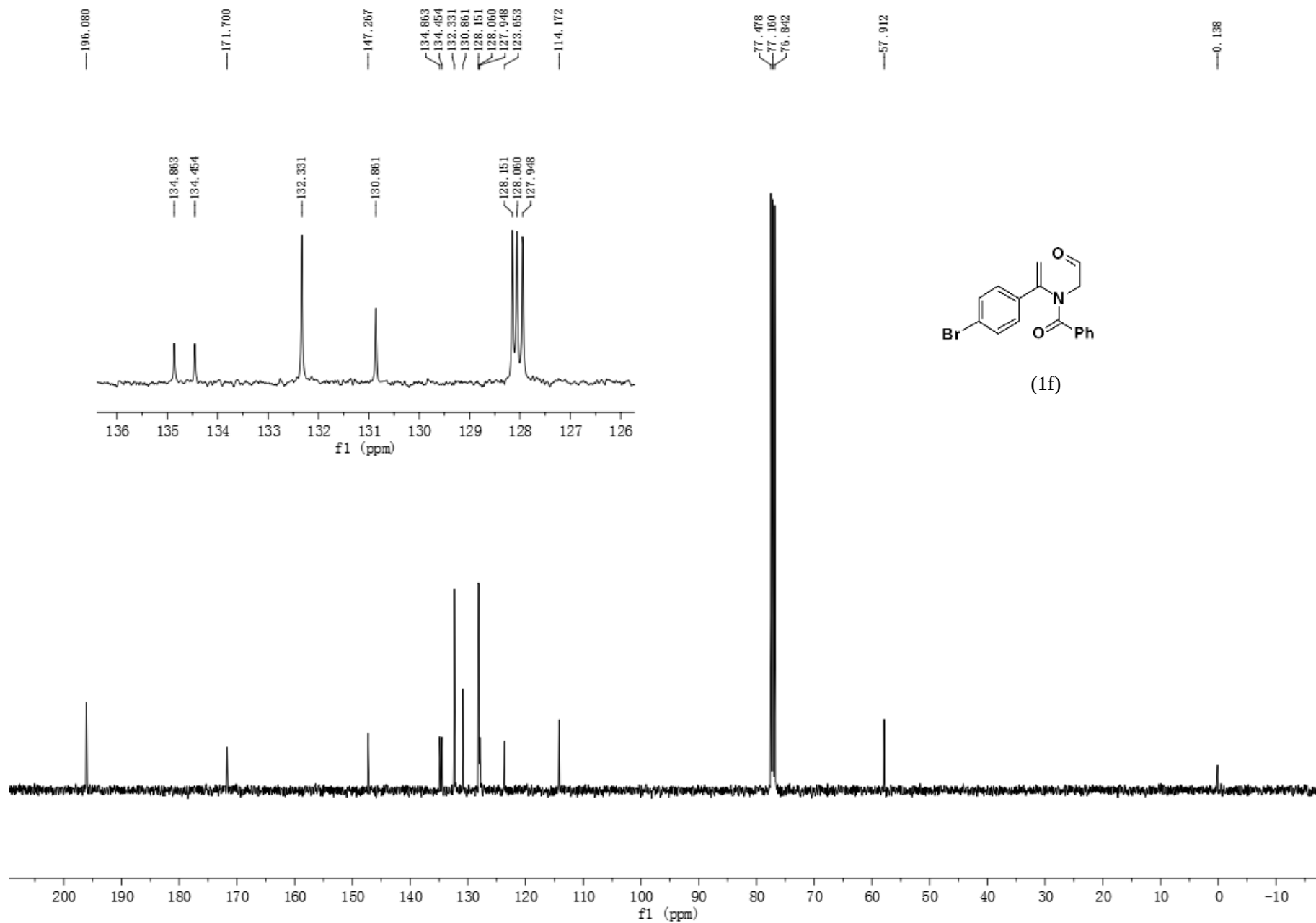


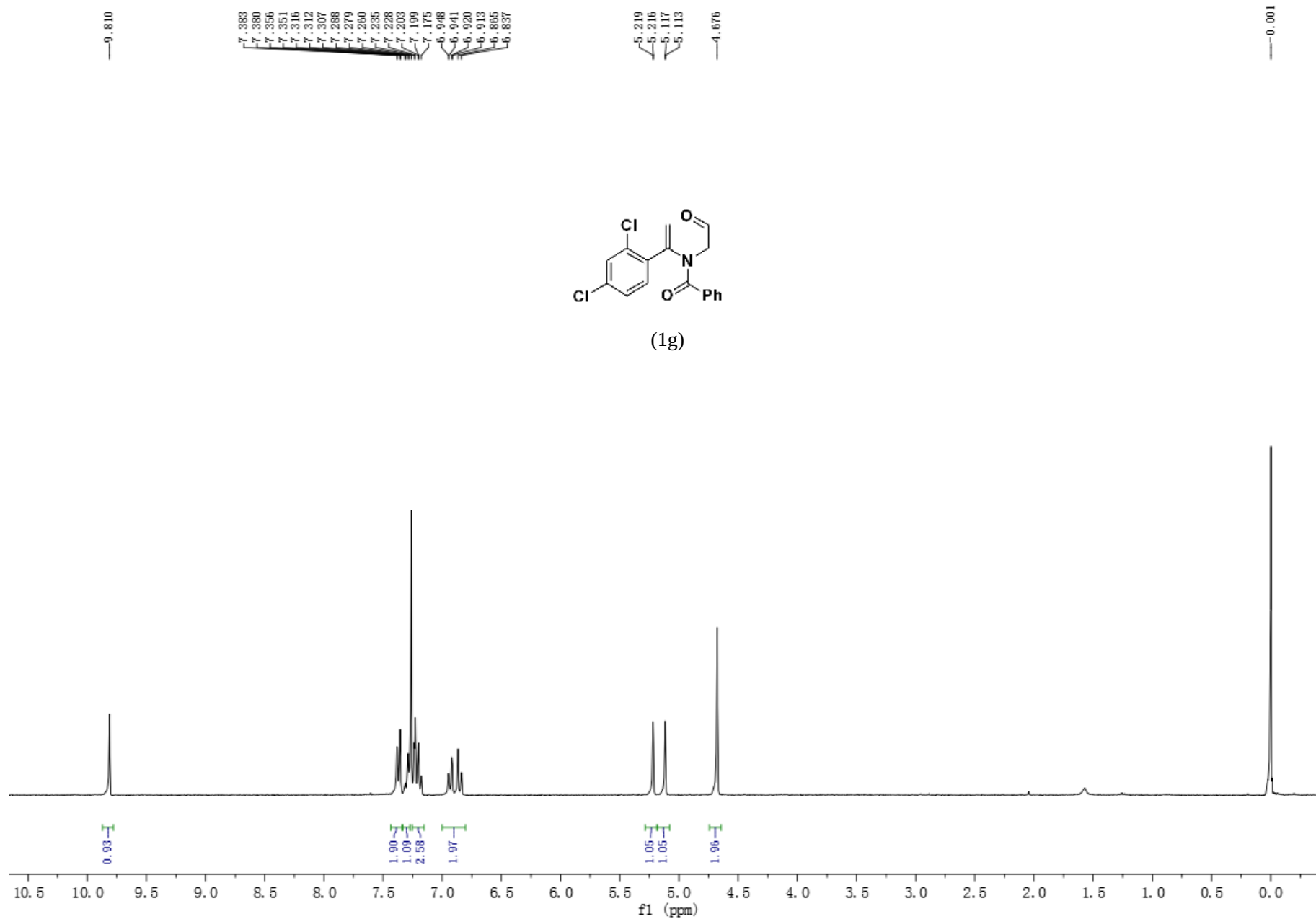


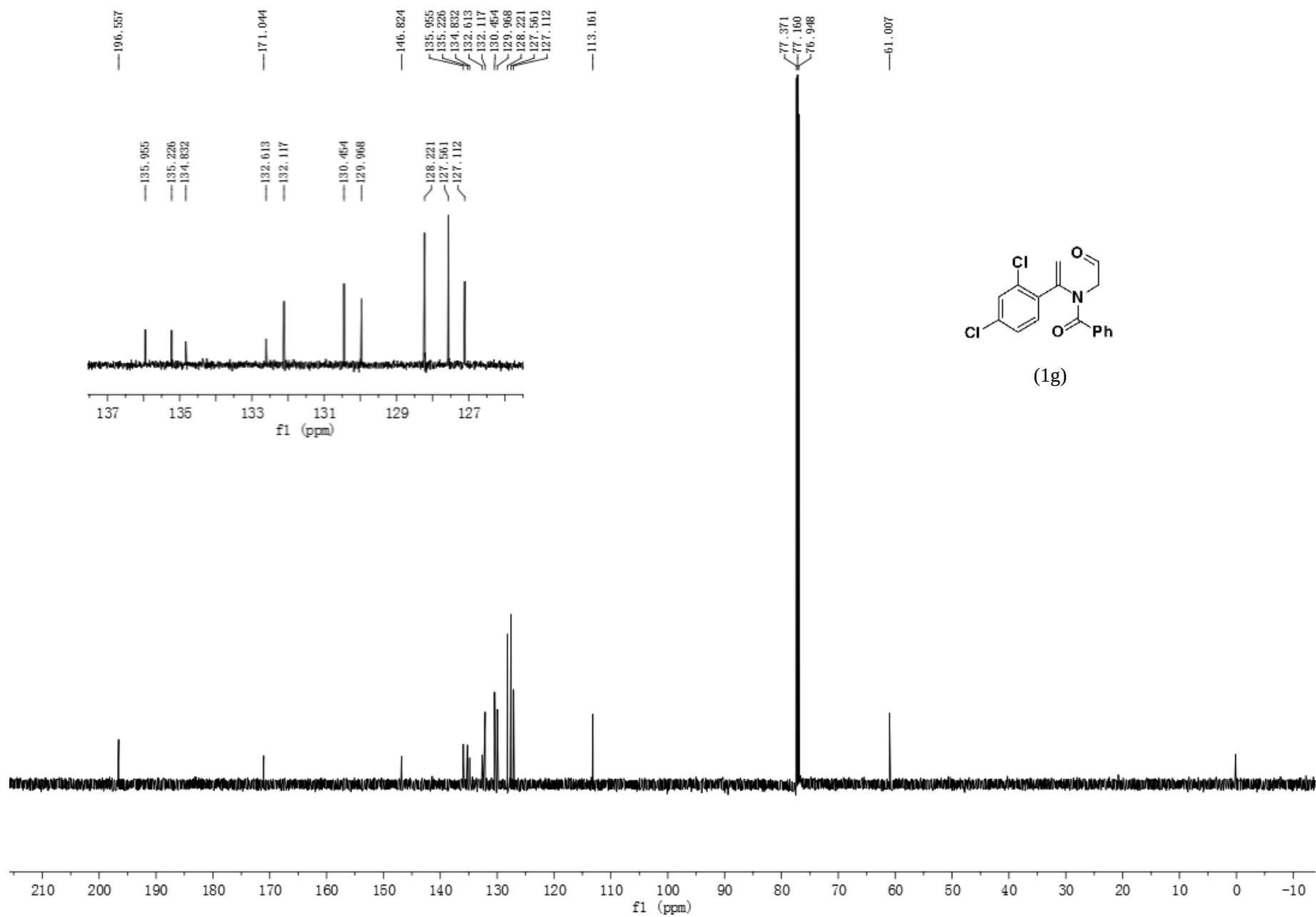


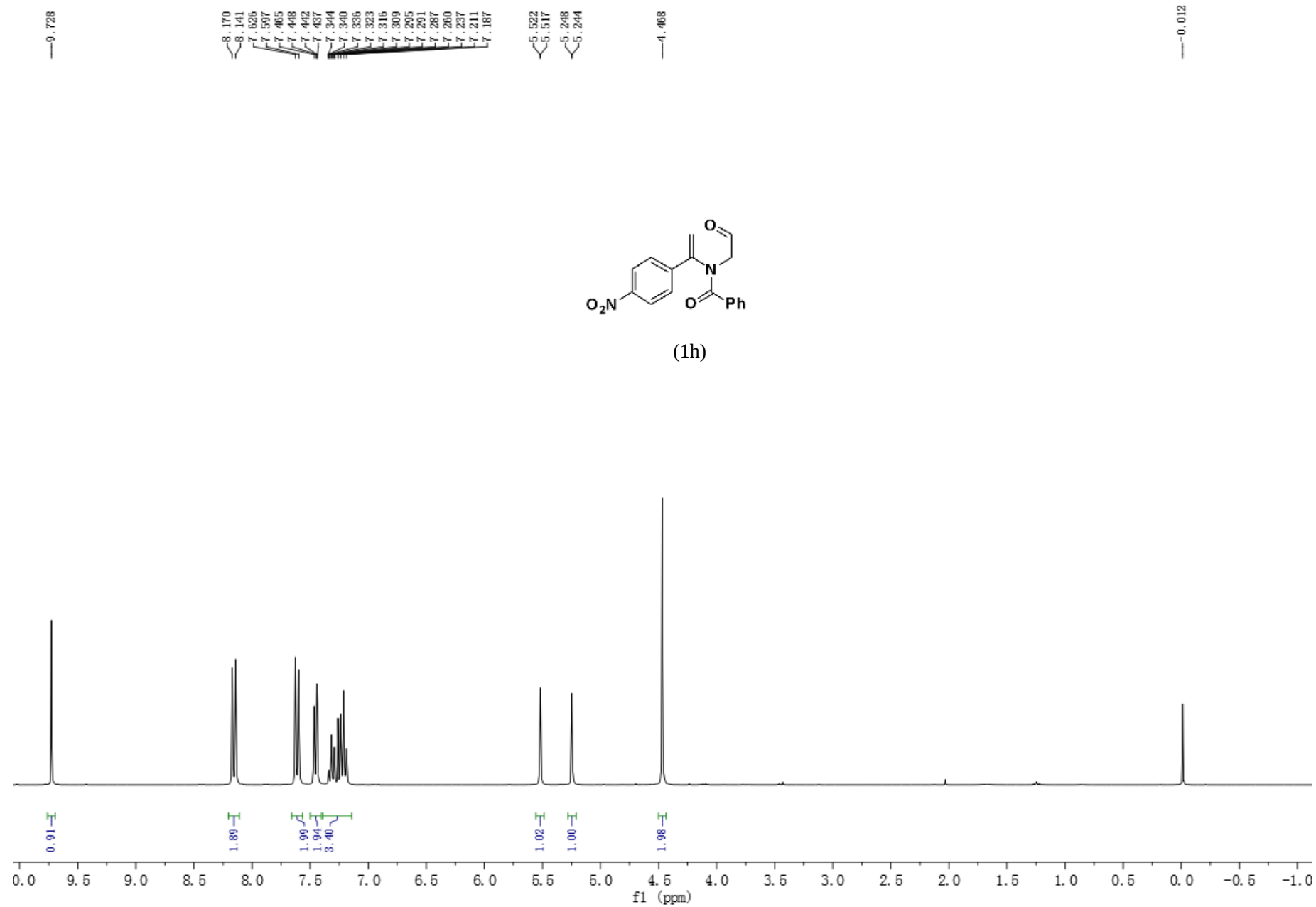


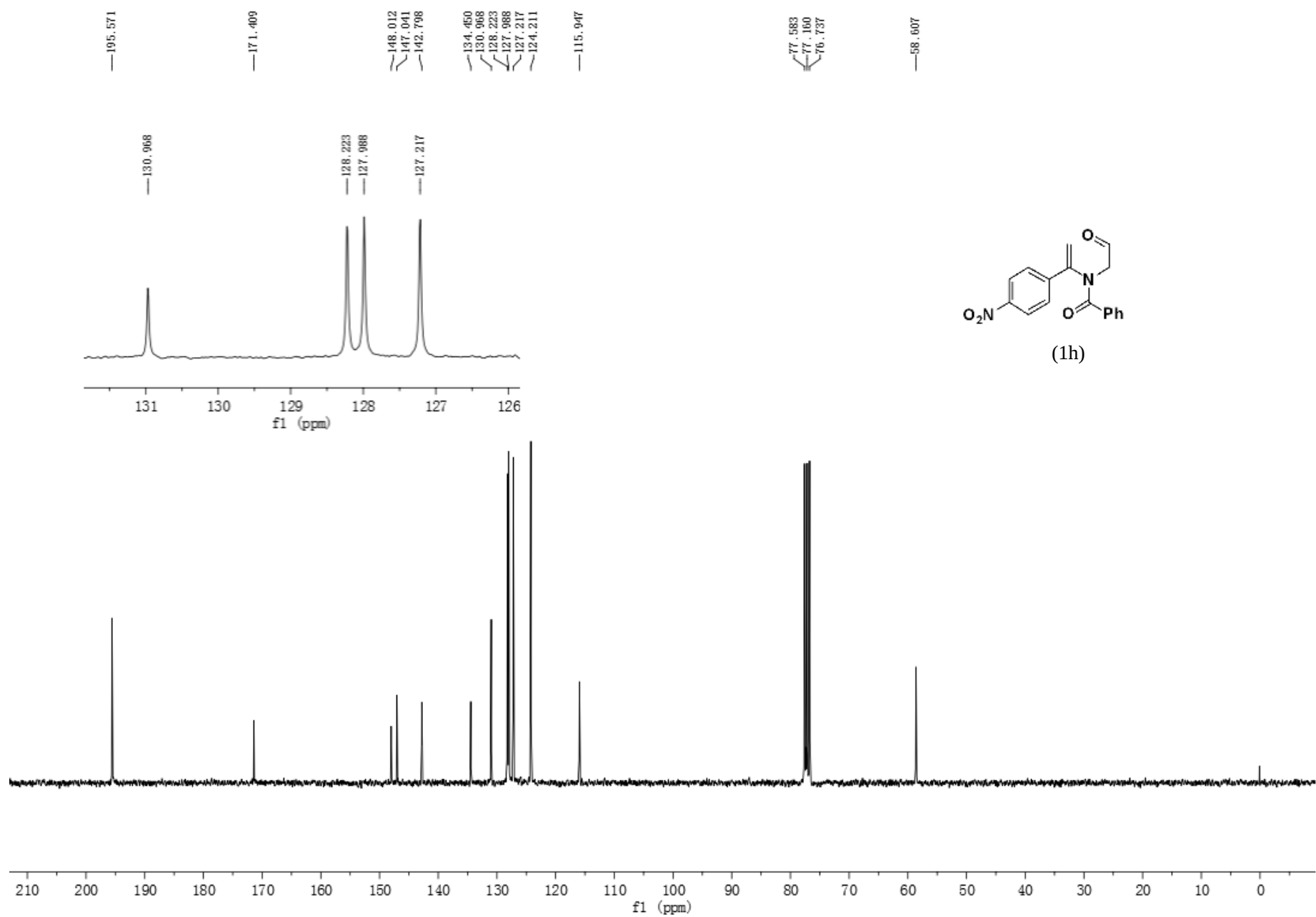


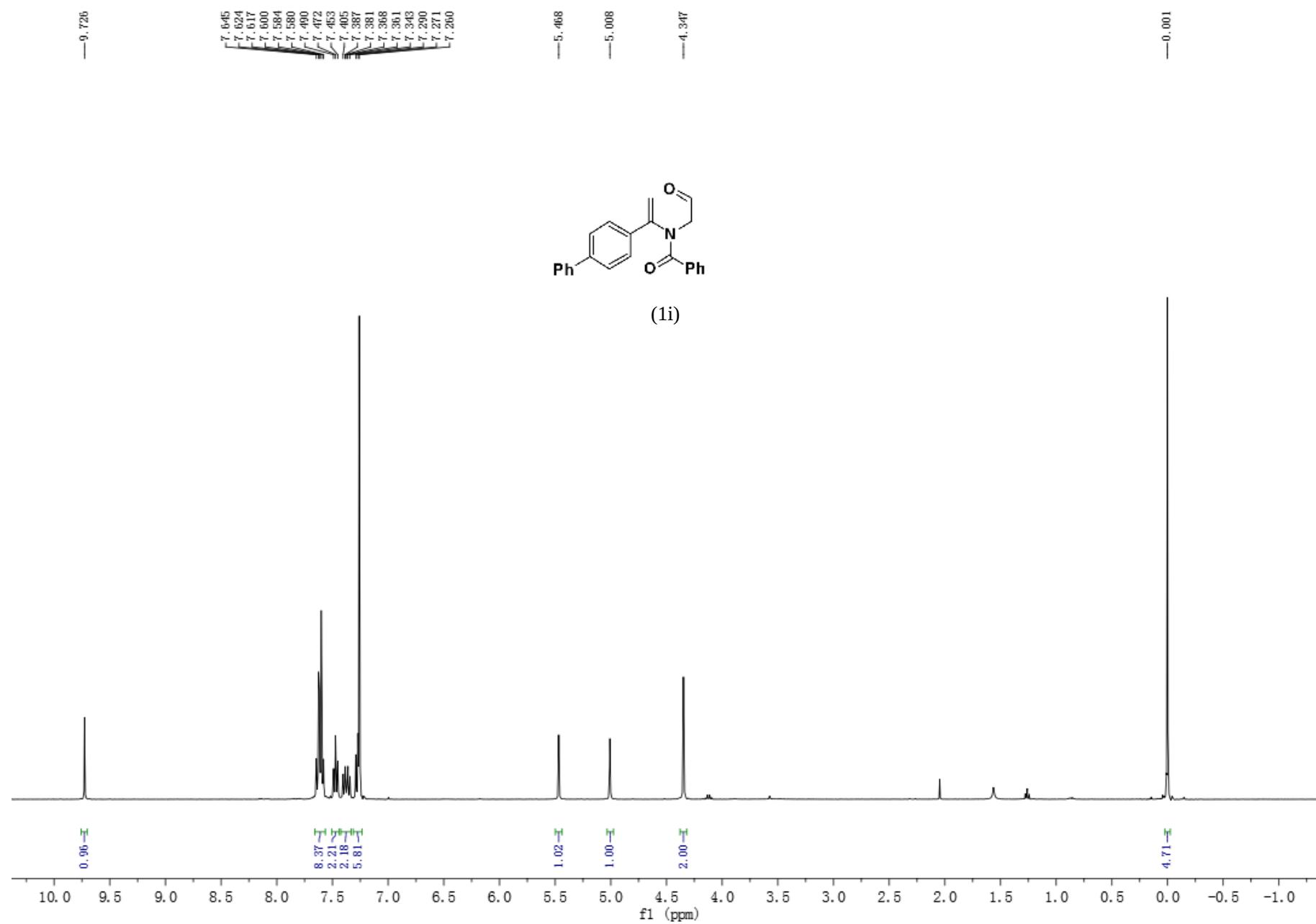


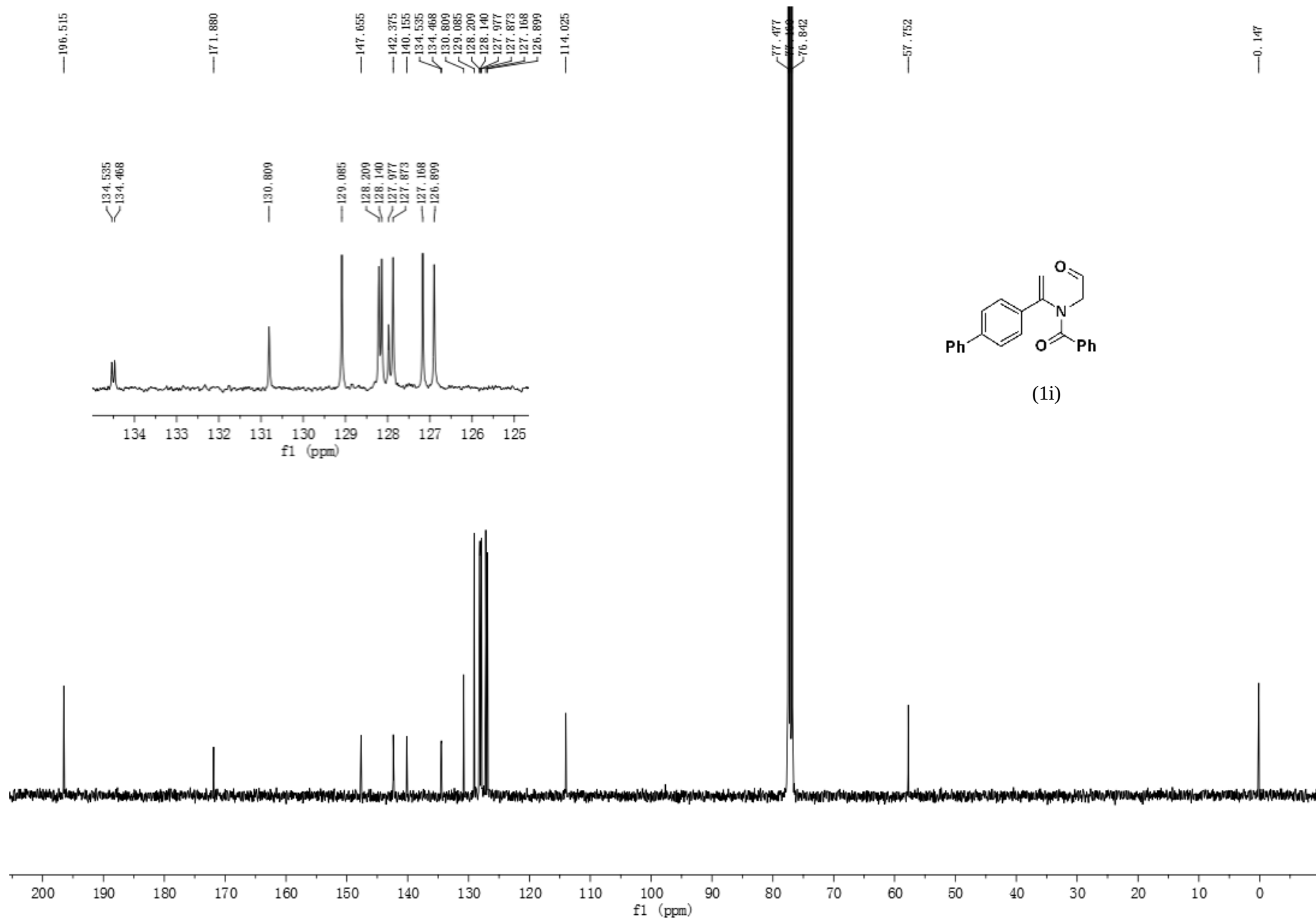


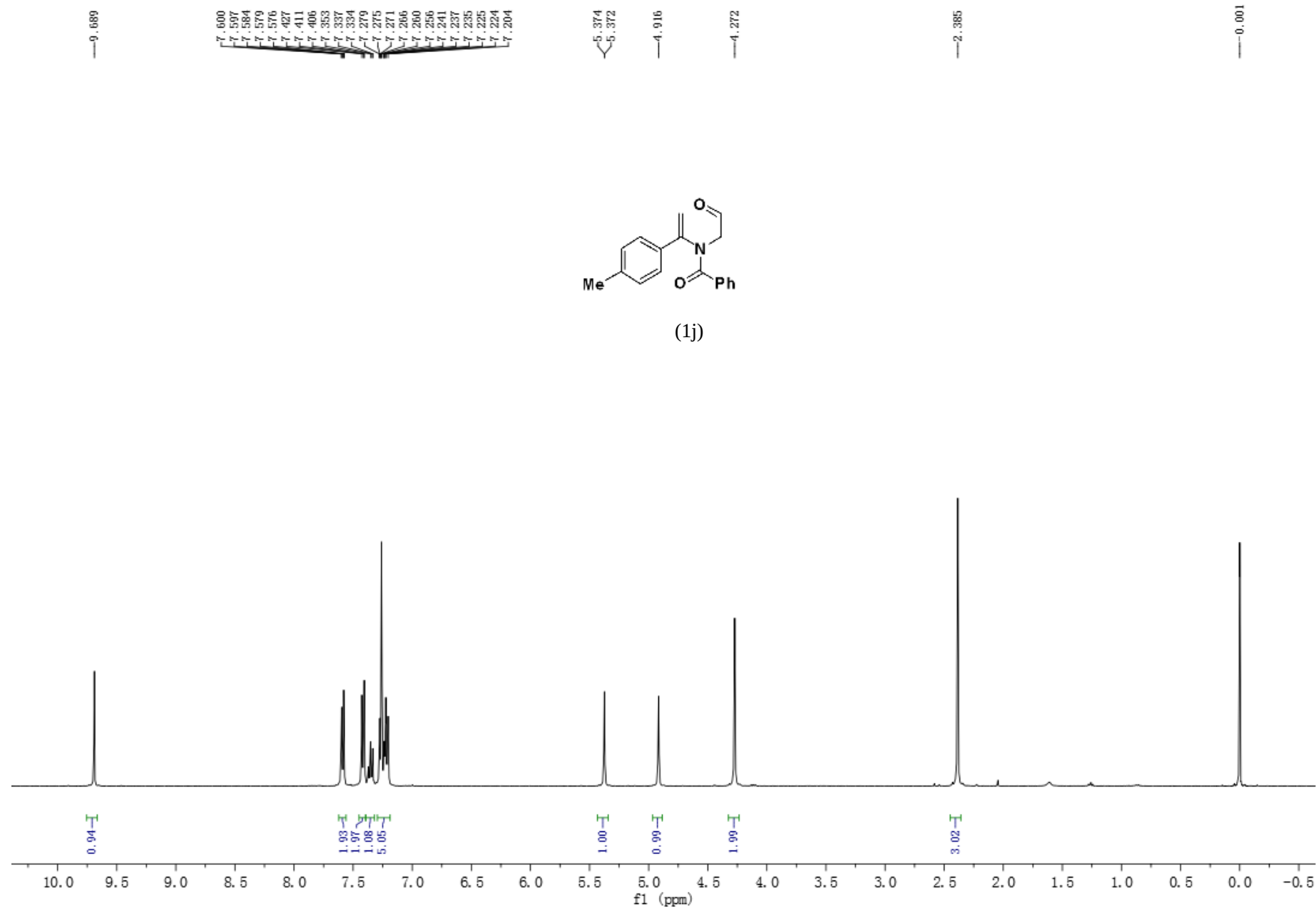


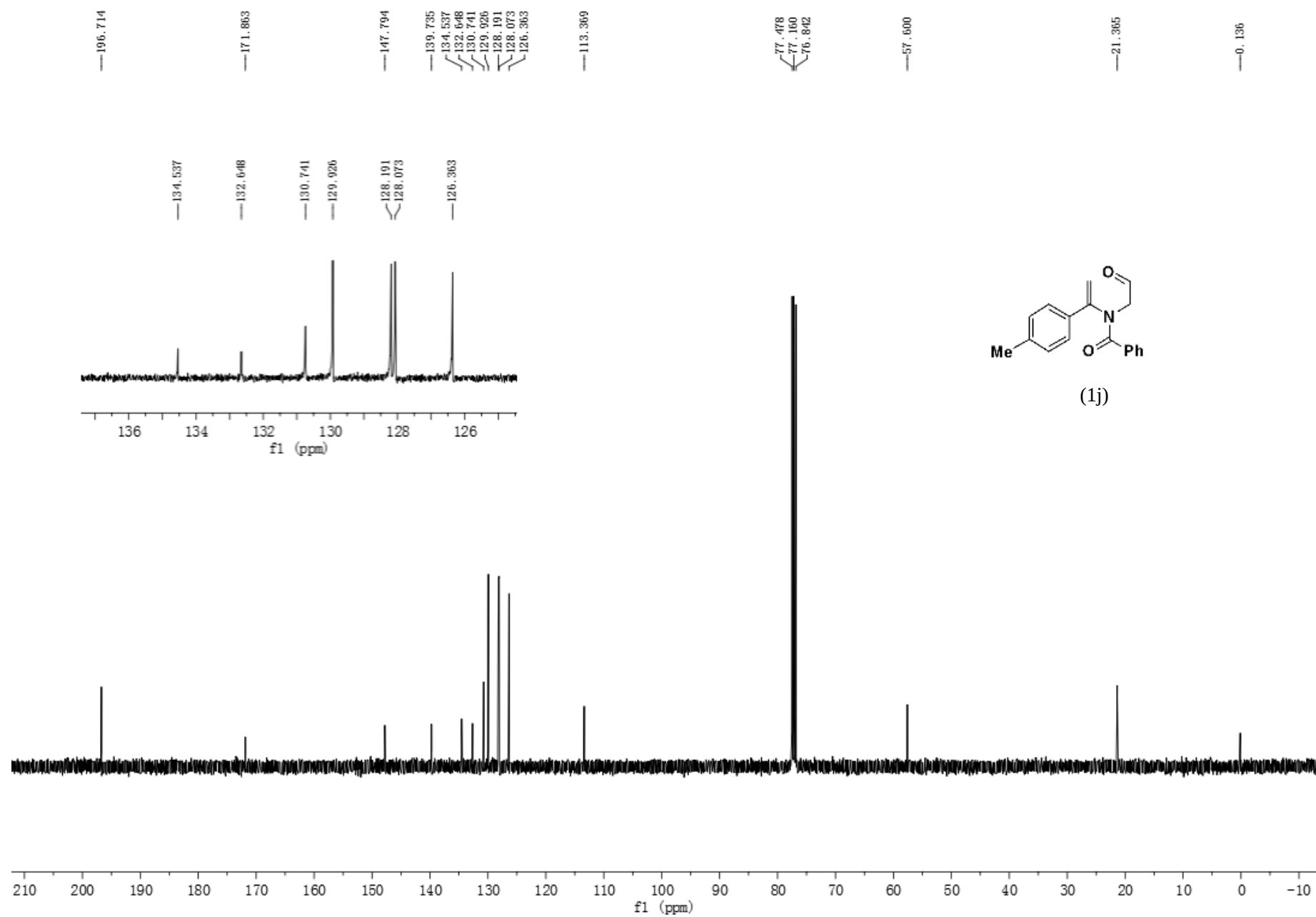


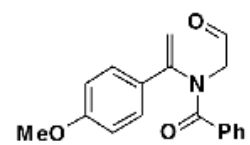












(1k)

