Supporting Information

Indium-catalysed amide allylation of α-iminoamide: highly enantioselective synthesis of amide functionalised α-methylene-γ-butyrolactams

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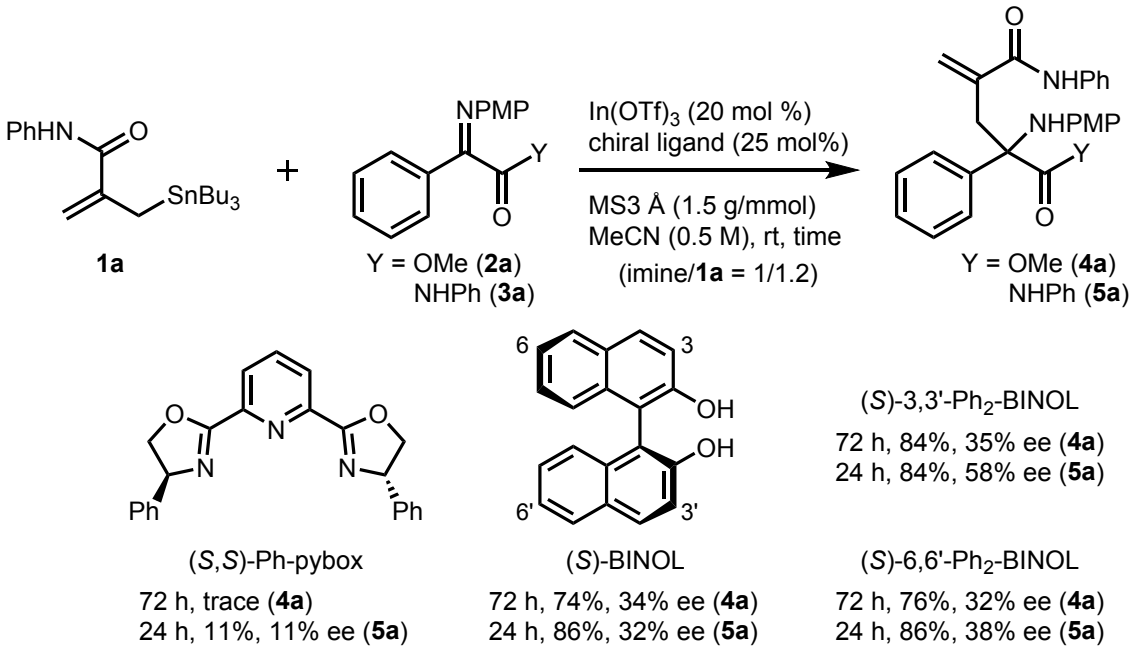
The following data are included in this material:

General methods:

All solvents and reagents were of reagent grade quality and used without further purification unless otherwise stated. Indium salts ($In(OTf)_3$ and $InCl_3$) and molecular sieves (MS3 Å and MS4 Å) were dried at 140 and 180 ˚C for 1 and 3 h under reduced pressure (ca. 1.0 Torr) prior to use, respectively. Acetonitrile (MeCN) was dried over MS3 Å and degassed by freeze–pump–thaw prior to use. β-Amido allylstannanes **1**[1] and α-iminoester **2**[2] were synthesized according to the literature. All new compounds were characterized by NMR, IR, and elemental analysis. The ^1H and ^{13}C NMR spectra operating at the frequencies of 300 and 75 MHz, respectively, on a JEOL JNM–AL300 spectrometer were recorded in chloroform–*d* ($CDCl_3$) unless otherwise noted. Chemical shifts are reported in parts per million (ppm) relative to TMS and the solvent used as internal standards, and the coupling constants are reported in hertz (Hz). Optical rotations were measured in 1 dm path length cell of 2 mL capacity using a JASCO Model DIP–1000 polarimeter at a wavelength of 589 nm. Reactions were monitored by thin layer chromatography using 0.25 mm Merck silica gel 60–F254 precoated silica gel plates by irradiation with UV light and/or by treatment with a solution of phosphomolybdic acid in EtOH followed by heating. Column chromatography was performed using silica gel 60N from Kanto Chemical Co. and eluting with the indicated solvent system. Melting points were measured with a Yanaco MP–S3 micro melting point apparatus. Fourier transform infrared (FTIR) spectra were recorded on a JASCO FT/IR–550 spectrometer. Elemental analyses were performed by JSL Model JM 10 instruments.

Preliminary investigations on enantioselective amide allylation of α-iminocarbonyl derivatives:



Scheme S1. Reaction of **2a**/**3a** with **1a** in the presence of various chiral catalysts. The ee values were determined by HPLC analysis using Daicel Chiralpak IE (for **4a**) and IC (for **5a**), respectively.

X-ray structure for 8:

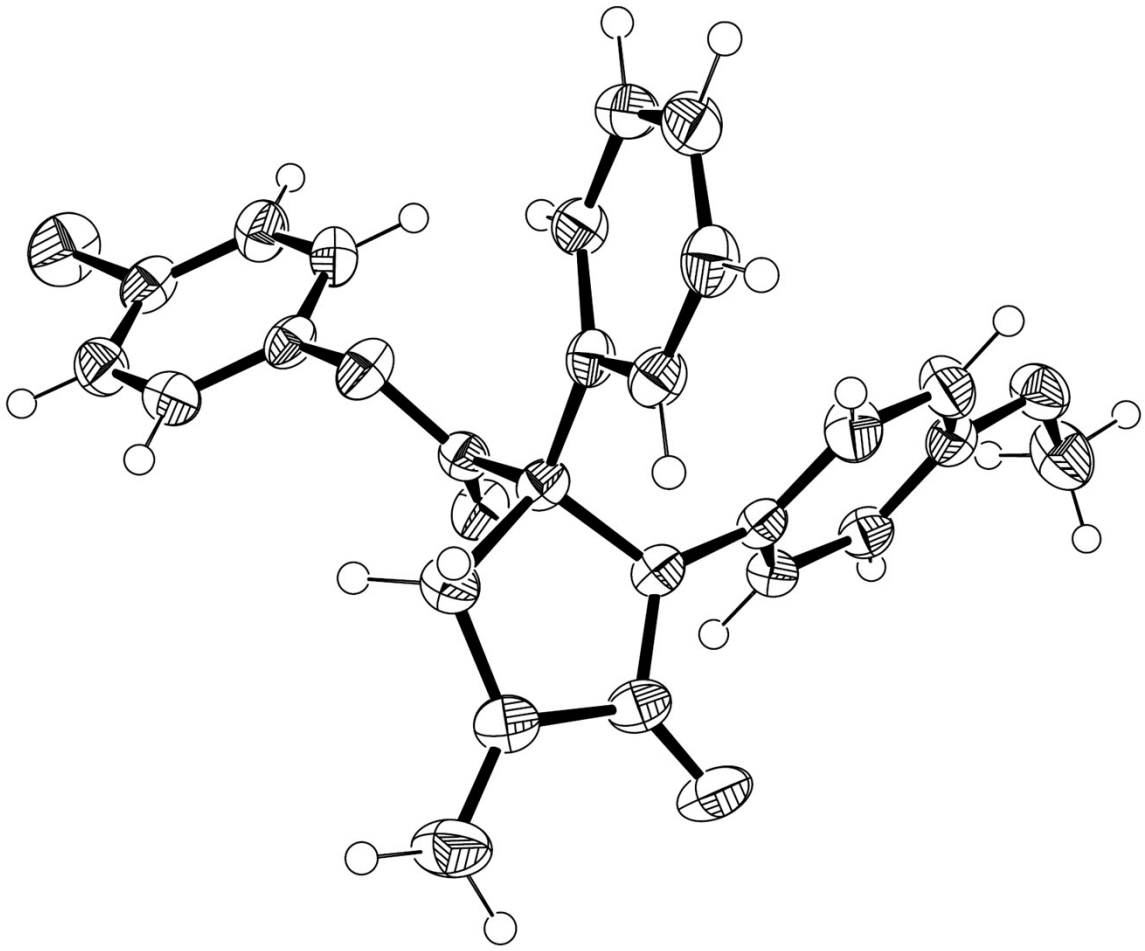


Figure S1. ORTEP diagram for X–ray structure of **8** (50% thermal ellipsoid probability).

^{1}H NMR spectra of indium complexes:

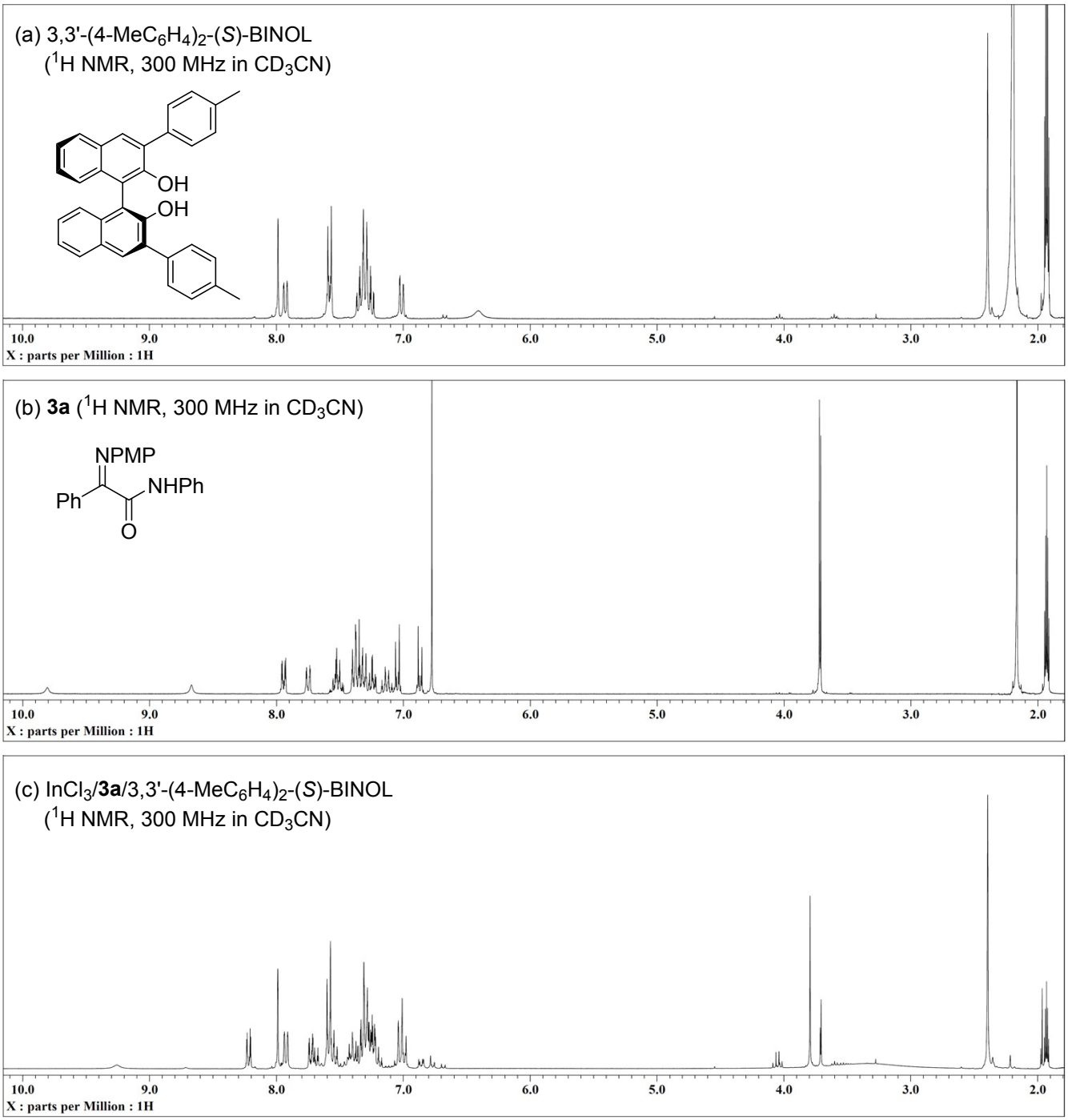


Figure S2. ^{1}H NMR spectra (300 MHz, CD_3CN) of (a) 3,3'-(4-MeC_6H_4)$_2$-(*S*)-BINOL, (b) **3a** and (c) $InCl_3$/**3a**/3,3'-(4-MeC_6H_4)$_2$-(*S*)-BINOL (1/1/1, stirred for 1 h at rt).

^{1}H NMR spectra of the samples prepared from 1a and metal salts ($InCl_3$ and/or $ZnCl_2$):

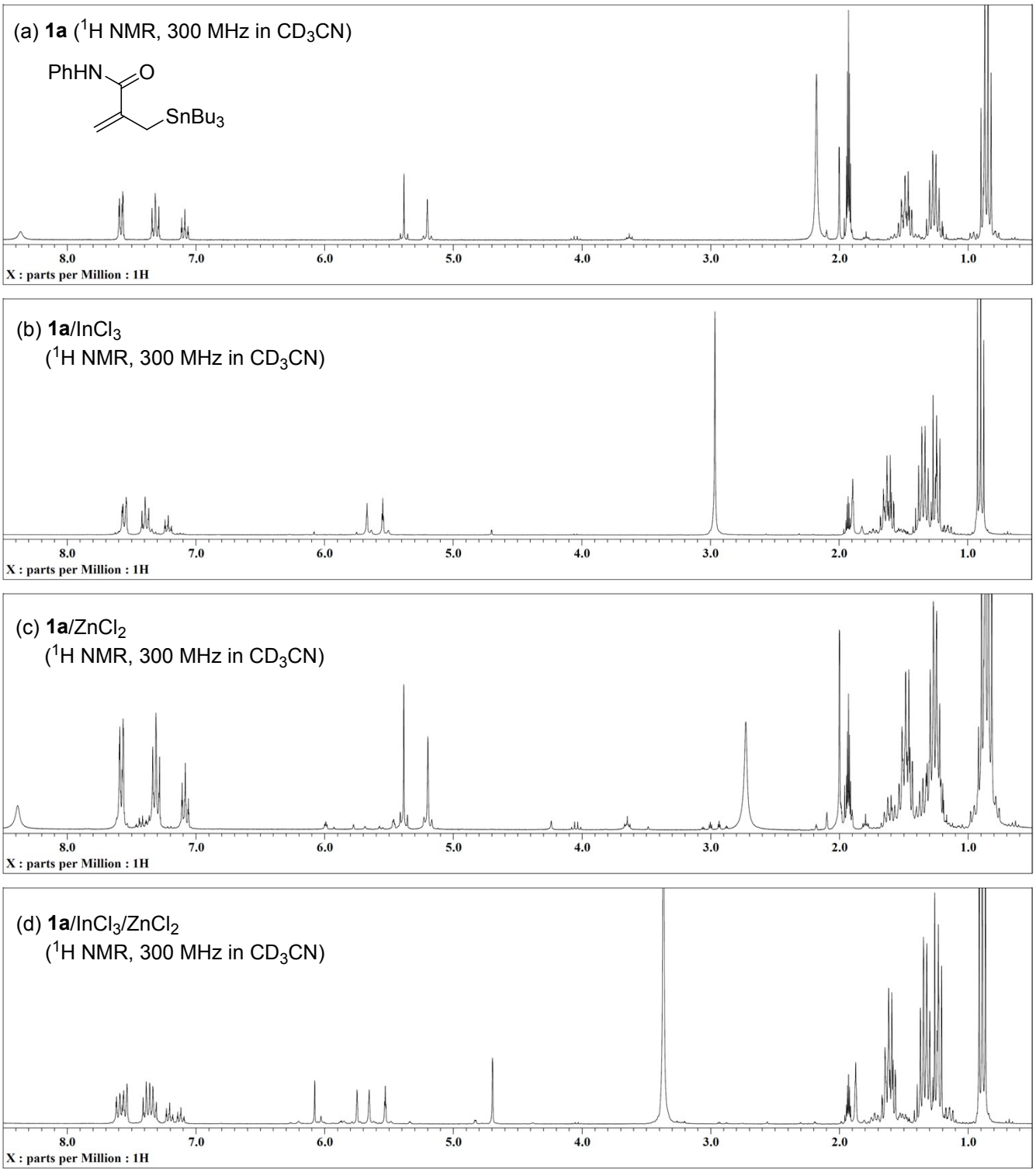


Figure S3. ^{1}H NMR spectra (300 MHz, CD_3CN) of (a) **1a**, (b) **1a**/$InCl_3$ (1/1, stirred for 30 min at rt), (c) **1a**/$ZnCl_2$ (1/1, stirred for 3 h at rt) and (d) **1a**/$InCl_3$/$ZnCl_2$ (1/1/1, stirred for 4 h at rt).

Experimental procedures and characterization data:

General procedure for preparation of ketimines

All the experiments for the the synthesis of ketimines were carried out as described in the following typical procedure. For example, the reaction of *N*-phenyl-2-oxo-2-phenylacetamide with *p*-anisidine for the synthesis of **3a** was exemplified as follows.

Synthesis and characterization of 3a

To a solution of *N*-phenyl-2-oxo-2-phenylacetamide (500 mg, 3.07 mmol) and *p*-toluenesulfonic acid monohydrate (60.9 mg, 0.320 mmol, 10 mol %) in toluene (3.3 mL) was added *p*-anisidine (479 mg, 3.89 mmol, 1.2 equiv.) at room temperature. After stirring the mixture at reflux for 19 h, the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 5/1) and recrystallization from EtOAc-hexane to give **3a** (548 mg, 54%) as a yellow solid: R_f = 0.57 (silica gel, hexane/EtOAc = 2/1); M.p. 155–157 °C; IR (KBr) 3279 (N–H), 1650 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.73 (brs, 1H, major isomer, N*H*), 8.02 (m, 2H, minor isomer, Ar*H*), 7.74 (m, 2H, major isomer, Ar*H*), 7.49 (m, 2H, minor isomer, Ar*H*), 7.40-7.23 (m, 7H, Ar*H*), 7.14 (m, 1H, major isomer, Ar*H*), 6.80-6.73 (m, 4H, Ar*H*), 3.77 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.5 (*C*), 159.9 (*C*), 157.7 (*C*), 140.3 (*C*), 137.6 (*C*), 131.8 (*C*), 129.5 (*C*H), 129.4 (*C*H), 129.0 (*C*H), 128.9 (*C*H), 128.6 (*C*H), 128.6 (*C*H), 128.2 (*C*H), 128.1 (*C*H), 124.2 (*C*H), 123.7 (*C*H), 121.9 (*C*H), 120.7 (*C*H), 119.4 (*C*H), 114.4 (*C*H), 114.0 (*C*H), 55.4 (*C*H_3), 55.3 (*C*H_3); Anal. Calcd for $C_{21}H_{18}N_2O_2$: C, 76.34; H, 5.49; N, 8.48. Found: C, 76.34; H, 5.52; N, 8.47.

Characterization for 3b

A solution of *N*-phenyl-2-oxo-2-(4-methoxyphenyl)acetamide, *p*-toluenesulfonic acid monohydrate and *p*-anisidine in toluene was stirred at reflux for 11 h, The crude product was purified by column

chromatography (silica gel, hexane/EtOAc = 5/1) and recrystallization from EtOAc-hexane to give **3b** (378 mg, 41%) as a yellow solid: R_f = 0.44 (silica gel, hexane/EtOAc = 2/1); M.p. 135–137 °C; IR (KBr) 3278 (N–H), 1668 (C=O), 1645 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.74 (brs, 1H, major isomer, N*H*), 7.94 (m, 2H, minor isomer, Ar*H*), 7.73 (dd, *J* = 1.5, 9.0 Hz, 2H, major isomer, Ar*H*), 7.36 (t, *J* = 8.0 Hz, 2H, major isomer, Ar*H*), 7.27-7.07 (m, 4H , Ar*H*), 6.94 (d, *J* = 9.0 Hz, 2H, minor isomer, Ar*H*), 6.84-6.74 (m, 5H, Ar*H*), 3.85 (s, 3H, minor isomer, CH_3), 3.78 (s, 3H, major isomer, CH_3), 3.76 (s, 3H, major isomer, CH_3), 3.74 (s, 3H, minor isomer, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.5 (*C*), 162.3 (*C*), 161.8 (*C*), 161.0 (*C*), 160.4 (*C*), 159.5 (*C*), 157.4 (*C*), 157.2 (*C*), 142.6 (*C*), 140.9 (*C*), 137.7 (*C*), 136.4 (*C*), 131.6 (*C*H), 130.0 (*C*H), 129.0 (*C*H), 128.9 (*C*H), 127.4 (*C*H), 125.2 (*C*H), 124.2 (*C*H), 123.6 (*C*H), 123.4 (*C*H), 121.8 (*C*H), 120.7 (*C*H), 119.4 (*C*H), 114.3 (*C*H), 114.1 (*C*H), 114.0 (*C*H), 113.5 (*C*H), 55.4 (*C*H_3), 55.3 (*C*H_3), 55.2 (*C*H_3). Anal. Calcd for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.23; H, 5.62; N, 7.79.

Characterization for 3c

A solution of *N*-phenyl-2-oxo-2-(4-trifluoromethylphenyl)acetamide, *p*-toluenesulfonic acid monohydrate and *p*-anisidine in toluene was stirred at reflux for 15 h. The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 5/1) and recrystallization from EtOAc-hexane to give **3c** (132 mg, 19%) as a yellow solid: R_f = 0.63 (silica gel, hexane/EtOAc = 2/1); M.p. 154–156 °C; IR (KBr) 3354 (N–H), 1683 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.69 (brs, 1H, major isomer, N*H*), 8.14 (d, *J* = 7.5 Hz, 2H, minor isomer, Ar*H*), 7.73 (d, *J* = 7.5 Hz, 2H, major isomer, Ar*H*), 7.60 (d, *J* = 8.1 Hz, 2H, major isomer, Ar*H*), 7.41-7.36 (m, 4H, major isomer, Ar*H*), 7.32-7.29 (m, 2H, minor isomer, Ar*H*), 7.16 (t, *J* = 7.2 Hz, 1H, major isomer, Ar*H*), 6.77 (s, 4H , Ar*H*), 3.78 (s, 3H, major isomer, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.0 (*C*), 158.4 (*C*), 158.1 (*C*), 157.9 (*C*), 139.7 (*C*), 137.4 (*C*), 135.7 (*C*), 130.0 (*CH*), 129.1 (*C*H), 125.1 (q, *J* = 3.7 Hz, *C*H), 124.5 (*C*H), 123.9 (*C*), 123.8

(*C*H), 119.5 (*C*H), 114.2 (*C*H), 55.4 (*C*H_3). Anal. Calcd for $C_{22}H_{17}F_3N_2O_2$: C, 66.33; H, 4.30; N, 7.03. Found: C, 66.28; H, 4.50; N, 7.08.

Characterization for 3d

A solution of *N*-phenyl-2-oxo-2-(1-naphthyl)acetamide (1.37 mg, 6.00 mmol), *p*-toluenesulfonic acid monohydrate (114 mg, 0.600 mmol, 10 mol %) and *p*-anisidine (887 mg, 7.20 mmol, 1.2 equiv.) in toluene (6.5 mL) was stirred at reflux for 24 h. The crude product was purified by column chromatography (silica gel, hexane/EtOAc = 5/1) and recrystallization from EtOAc-hexane to give **3d** (1.28 g, 56%) as a yellow solid: R_f = 0.57 (silica gel, hexane/EtOAc = 2/1); M.p. 146–148 °C; IR (KBr) 3288 (N–H), 1676 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.87 (brs, 1H, N*H*), 7.87 (t, *J* = 6.9 Hz, 2H, Ar*H*), 7.77 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.60 (d, *J* = 8.1 Hz, 1H, Ar*H*), 7.48-7.26 (m, 6H, Ar*H*), 7.14 (t, *J* = 7.5 Hz, 1H, Ar*H*), 6.79 (m, 2H, Ar*H*), 6.60 (m, 2H, Ar*H*), 3.68 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8 (*C*), 160.2 (*C*), 158.2 (*C*), 139.7 (*C*), 137.7 (*C*), 133.2 (*C*), 131.5 (*C*), 130.8 (*C*), 129.6 (*C*H), 129.2 (*C*H), 129.1 (*C*H), 128.6 (*C*H), 126.8 (*C*H), 126.2 (*C*H), 125.5 (*C*H), 125.1 (*C*H), 124.8 (*C*H), 124.23 (*C*H), 124.19 (*C*H), 119.8 (*C*H), 119.4 (*C*H), 113.9 (*C*H), 55.2 (*C*H_3). Anal. Calcd for : $C_{25}H_{20}N_2O_2$: C, 78.93; H, 5.30; N, 7.36. Found: C, 78.56; H, 5.21; N, 7.58.

General procedure for amide allylation of ketimines

All the experiments for amide allylation of ketimines were carried out as described in the following typical procedure. For example, the reaction of **3** with **1** for the synthesis of **5a** was exemplified as follows.

Synthesis and characterization of 5a

To a suspension of $InCl_3$ (9.6 mg, 0.0434 mmol, 0.2 equiv.) and MS3 Å (326 mg, 1.5 g/mmol) in

MeCN (0.43 mL) was added $ZnCl_2$ (3.0 mg, 0.0217 mmol, 0.1 equiv.) at room temperature under a nitrogen atmosphere, and the resulting mixture was stirred for 1 h. After addition of 3,3'-(4-MeC_6H_4)$_2$-(*S*)-BINOL (25.3 mg, 0.0543 mmol, 0.25 equiv.), the mixture was stirred at this temperature for 1 h, and then **3a** (71.7 mg, 0.217 mmol) was added. The resulting mixture was stirred for 1 h and cooled to 0 °C. After addition of **1a** (17.3 mg, 0.260 mmol, 1.2 equiv.), the reaction mixture was stirred at the same temperature for an additional 6 h. The reaction was then quenched by addition of saturated aqueous $NaHCO_3$ (10 mL), and the resulting mixture was extracted with EtOAc (50 mL), washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to give a crude material. This material was purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5a** (134 mg, 99%, 96% ee) as a colorless oil: R_f = 0.43 (silica gel, hexane/AcOEt = 2/1); $[\alpha]_D^{27}$ +42.9 (*c* 0.97, $CHCl_3$); IR (NaCl) 3016 (N–H), 2935 (C–H), 1671 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.78 (brs, 1H, N*H*), 7.76 (brs, 1H, N*H*), 7.70 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.47-7.04 (m, 13H, Ar*H*), 6.59 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.43 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.40 (brs, 1H, N*H*), 5.69 (s, 1H, CH_2), 5.34 (s, 1H, CH_2), 3.62 (s, 3H, CH_3), 3.34 (d, *J* = 14.1 Hz, 1H, CH_2), 3.31 (d, *J* = 14.1 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (*C*), 168.2 (*C*), 152.3 (*C*), 140.7 (*C*), 139.7 (*C*), 137.9 (*C*), 137.3 (*C*), 137.2 (*C*), 128.9 (*C*H), 128.8 (*C*H), 128.3 (*C*H), 127.7 (*C*H), 127.4 (*C*H), 124.7 (*C*H), 124.5 (*C*H), 123.1 (*C*H_2), 120.3 (*C*H), 120.1 (*C*H), 116.9 (*C*H), 114.4 (*C*H), 68.3 (*C*), 55.4 (*C*H_3), 42.3 (*C*H_2). Anal. Calcd for $C_{31}H_{29}N_3O_3$: C, 75.74; H, 5.95; N, 8.55. Found: C, 76.06; H, 5.91; N, 8.51. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IC column (hexane/EtOH = 96/4), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 35.2 min, t_R (minor) = 27.3 min.

Characterization for 5b

The reaction of **3a** with **1b** was performed at 0 °C for 6 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5b** (71.2 mg, 99%, 91% ee) as a colorless oil:

R_f = 0.54 (silica gel, hexane/AcOEt = 2/1); $[\alpha]_D^{28}$ +52.4 (*c* 0.95, $CHCl_3$); IR (NaCl) 3019 (N–H), 2931 (C–H), 1671 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.82 (brs, 1H, N*H*), 7.72 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.57 (brs, 1H, N*H*), 7.43 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.33-7.08 (m, 10H, Ar*H*), 6.59 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.47 (brs, 1H, N*H*), 6.43 (d, *J* = 8.7 Hz, 2H, Ar*H*), 5.69 (s, 1H, CH_2), 5.38 (s, 1H, CH_2), 3.64 (s, 3H, CH_3), 3.36 (d, *J* = 13.8 Hz, 1H, CH_2), 3.30 (d, *J* = 13.8 Hz, 1H, CH_2), 2.33 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (*C*), 168.2 (*C*), 152.3 (*C*), 140.9 (*C*), 139.8 (*C*), 138.0 (*C*), 137.3 (*C*), 134.7 (*C*), 134.5 (*C*), 129.5 (*C*H), 128.8 (*C*H), 128.3 (*C*H), 127.7 (*C*H), 127.3 (*C*H), 124.5 (*C*H), 122.9 (*C*H_2), 120.4 (*C*H), 120.1 (*C*H), 117.0 (*C*H), 114.4 (*C*H), 68.4 (*C*), 55.4 (*C*H_3), 42.9 (*C*H_2), 20.9 (*C*H_3). Anal. Calcd for $C_{32}H_{31}N_3O_3$: C, 76.02; H, 6.18; N, 8.31. Found: C, 76.27; H, 6.42; N, 8.44. The enantiomeric excess was determined by HPLC with a Daicel Chiralcel IE column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 22.1 min, t_R (minor) = 18.5 min.

Characterization for 5c

The reaction of **3a** with **1c** was performed at 0 °C for 6 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5c** (69.1 mg, 98%, 92% ee) as a colorless oil: R_f = 0.37 (silica gel, hexane/AcOEt = 2/1); $[\alpha]_D^{29}$ +52.6 (*c* 1.03, $CHCl_3$); IR (NaCl) 3018 (N–H), 2936 (C–H), 1672 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.82 (brs, 1H, N*H*), 7.72-7.67 (m, 3H, Ar*H*, N*H*), 7.43-7.18 (m, 9H, Ar*H*), 7.07 (m, 1H, Ar*H*), 6.84 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.59 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.51 (brs, 1H, N*H*), 6.43 (d, *J* = 9.0 Hz, 2H, Ar*H*), 5.68 (s, 1H, CH_2), 5.34 (s, 1H, CH_2), 3.78 (s, 3H, CH_3), 3.63 (s, 3H, CH_3), 3.35 (d, *J* = 13.5 Hz, 1H, CH_2), 3.28 (d, *J* = 13.5 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (*C*), 168.2 (*C*), 156.7 (*C*), 152.3 (*C*), 140.7 (*C*), 139.7 (*C*), 138.0 (*C*), 137.3 (*C*), 130.3 (*C*), 128.8 (*C*H), 128.3 (*C*H), 127.7 (*C*H), 127.3 (*C*H), 124.5 (*C*H), 122.9 (*C*H_2), 122.3 (*C*H), 120.1 (*C*H), 116.9 (*C*H), 114.4 (*C*H), 114.1 (*C*H), 68.4 (*C*), 55.4 (*C*H_3), 55.4 (*C*H_3), 42.7 (*C*H_2). Anal. Calcd for $C_{32}H_{31}N_3O_4$: C, 73.68; H, 5.99; N, 8.06. Found: C, 73.78; H, 6.12; N, 8.12. The

enantiomeric excess was determined by HPLC with a Daicel Chiralpak IE column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 26.0 min, t_R (minor) = 32.2 min.

Characterization for 5d

The reaction of **3a** with **1d** was performed at 0 °C for 6 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5d** (72.1 mg, 98%, 92% ee) as a colorless oil: R_f = 0.60 (silica gel, hexane/AcOEt = 2/1); $[\alpha]_D^{26}$ +56.2 (*c* 1.13, $CHCl_3$); IR (NaCl) 3019 (N–H), 2965 (C–H), 1665 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.82 (brs, 1H, N*H*), 7.74-7.71 (m, 2H, Ar*H*), 7.55 (brs, 1H, N*H*), 7.45-7.17 (m, 11H, Ar*H*), 7.08 (dt, *J* = 0.9, 7.2 Hz, 1H, Ar*H*), 6.60 (m, 2H, Ar*H*), 6.47 (brs, 1H, N*H*), 6.44 (m, 2H, Ar*H*), 5.70 (s, 1H, CH_2), 5.40 (s, 1H, CH_2), 3.65 (s, 3H, CH_3), 3.37 (d, *J* = 13.8 Hz, 1H, CH_2), 3.31 (d, *J* = 13.8 Hz, 1H, CH_2), 1.32 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (*C*), 168.2 (*C*), 152.3 (*C*), 147.9 (*C*), 141.0 (*C*), 139.8 (*C*), 138.0 (*C*), 137.3 (*C*), 134.6 (*C*), 129.0 (*C*H), 128.3 (*C*H), 127.8 (*C*H), 127.3 (*C*H), 125.8 (*C*H), 124.5 (*C*H), 122.9 (*C*H_2), 120.13 (*C*H), 120.07 (*C*H), 117.0 (*C*H), 114.3 (*C*H), 68.5 (*C*), 55.4 (*C*H_3), 43.0 (*C*H_2), 34.4 (*C*), 31.3 (*C*H_3). Anal. Calcd for $C_{35}H_{37}N_3O_3$: C, 76.75; H, 6.81; N, 7.67. Found: C, 76.80; H, 7.03; N, 8.05. The enantiomeric excess was determined by HPLC with a Daicel Chiralcel IE column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 18.2 min, t_R (minor) = 15.3 min.

Characterization for 5e

The reaction of **3a** with **1e** was performed at 0 °C for 6 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5e** (55.6 mg, 99%, 94% ee) as a white solid: R_f = 0.49 (silica gel, hexane/AcOEt = 2/1); $[\alpha]_D^{23}$ +33.7 (*c* 0.910, $CHCl_3$); IR (KBr) 3344 (N–H), 2948 (C–H), 1677 (C=O), 1624 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.79 (brs, 1H, N*H*), 7.94-7.71 (m, 7H, Ar*H*, N*H*), 7.53-7.04 (m, 11H, Ar*H*), 6.59 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.46-6.39 (m, 3H, Ar*H*, N*H*),

5.88 (s, 1H, CH_2), 5.48 (s, 1H, CH_2), 3.64 (s, 3H, CH_3), 3.45 (d, J = 13.8 Hz, 1H, CH_2), 3.40 (d, J = 13.8 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6 (*C*), 169.0 (*C*), 152.3 (*C*), 141.0 (*C*), 139.8 (*C*), 138.0 (*C*), 137.3 (*C*), 134.1 (*C*), 131.8 (*C*), 128.9 (*C*H), 128.7 (*C*H), 128.4 (*C*H), 127.7 (*C*H), 127.4 (*C*H), 126.5 (*C*H), 126.4 (*C*H), 126.1 (*C*H), 125.6 (*C*H), 124.5 (*C*H), 123.1 (*C*H_2), 121.4 (*C*H), 120.7 (*C*H), 120.1 (*C*H), 116.9 (*C*H), 114.4 (*C*H), 68.4 (*C*), 55.4 (*C*H), 42.5 (*C*H_2). Anal. Calcd for $C_{35}H_{31}N_3O_3$: C, 77.61; H, 5.77; N, 7.76. Found: C, 77.25; H, 5.94; N, 7.62. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IE column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 38.8 min, t_R (minor) = 28.9 min.

Characterization for 5f

The reaction of **3a** with **1f** was performed at 0 °C for 18 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5f** (67.2 mg, 96%, 90% ee) as a colorless oil: R_f = 0.45 (silica gel, hexane/AcOEt = 2/1); $[\alpha]_D^{24}$ +45.4 (*c* 1.05, $CHCl_3$); IR (NaCl) 3019 (N–H), 1646 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (brs, 1H, N*H*), 7.71 (d, J = 8.7 Hz, 2H, Ar*H*), 7.60 (brs, 1H, N*H*), 7.42-7.20 (m, 11H, Ar*H*), 7.08 (t, J = 7.2 Hz, 1H, Ar*H*), 6.62 (dt, J = 2.7, 9.0 Hz, 2H, Ar*H*), 6.44 (dd, J = 3.6, 9.0 Hz, 2H, Ar*H*), 6.12 (brs, 1H, N*H*), 5.73 (s, 1H, CH_2), 5.38 (s, 1H, CH_2), 3.66 (s, 3H, CH_3), 3.43 (d, J = 14.1 Hz, 1H, CH_2), 3.37 (d, J = 14.1 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (*C*), 167.9 (*C*), 152.5 (*C*), 140.8 (*C*), 139.7 (*C*), 137.8 (*C*), 137.2 (*C*), 136.0 (*C*), 129.7 (*C*), 129.0 (*C*H), 128.9 (*C*H), 128.5 (*C*H), 127.6 (*C*H), 127.5 (*C*H), 124.6 (*C*H), 123.4 (*C*H_2), 121.4 (*C*H), 120.1 (*C*H), 117.0 (*C*H), 114.5 (*C*H), 68.2 (*C*), 55.5 (*C*H_3), 41.3 (*C*H_2). Anal. Calcd for $C_{31}H_{28}ClN_3O_3$: C, 70.78; H, 5.37; Cl, 6.74; N, 7.99. Found: C, 71.00; H, 5.38; N, 8.22. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IC column (hexane/EtOH = 96/4), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 18.4 min, t_R (minor) = 21.9 min.

Characterization for 5g

The reaction of **3a** with **1g** was performed at 0 °C for 19 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5g** (82.1 mg, 92%, 82% ee) as a colorless oil: R_f = 0.45 (silica gel, hexane/AcOEt = 2/1); $[\alpha]_D^{26}$ +104 (*c* 1.05, $CHCl_3$); IR (NaCl) 3019 (N–H), 2933 (C–H), 1652 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.89 (brs, 1H, N*H*), 7.72 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.46 (d, *J* = 7.8 Hz, 2H, Ar*H*), 7.32-7.19 (m, 5H, Ar*H*), 7.09 (t, *J* = 7.2 Hz, 1H, Ar*H*), 6.76 (brs, 1H, N*H*), 6.59 (dt, *J* = 2.1, 9.0 Hz, 2H, Ar*H*), 6.43 (dt, *J* = 2.1, 9.0 Hz, 2H, Ar*H*), 5.88 (brs, 1H, N*H*), 5.52 (s, 1H, CH_2), 5.29 (s, 1H, CH_2), 3.65 (s, 3H, CH_3), 3.30-3.16 (m, 4H, CH_2), 1.50 (m, 2H, CH_2), 1.38-1.26 (m, 4H, CH_2), 0.90 (t, *J* = 6.9 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7 (*C*), 170.3 (*C*), 152.1 (*C*), 140.4 (*C*), 139.8 (*C*), 138.2 (*C*), 137.5 (*C*), 128.9 (*C*H), 128.1 (*C*H), 128.0 (*C*H), 127.1 (*C*H), 124.4 (*C*H), 122.1 (*C*H_2), 120.0 (*C*H), 116.8 (*C*H), 114.3 (*C*H), 68.5 (*C*), 55.4 (*C*H_3), 43.9 (*C*H_2), 40.0 (*C*H_2), 29.1 (*C*H_2), 22.3 (*C*H_2), 13.9 (*C*H_3). Anal. Calcd for $C_{30}H_{35}N_3O_3$: C, 74.20; H, 7.26; N, 8.65. Found: C, 74.02; H, 7.24; N, 8.68. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IC column (hexane/EtOH = 96/4), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 22.6 min, t_R (minor) = 31.7 min.

Characterization for 5h

The reaction of **3b** with **1a** was performed at 0 °C for 3 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5h** (70.2 mg, 96%, 93% ee) as a white solid: R_f = 0.38 (silica gel, hexane/EtOAc = 2/1); M.p. 195–197 °C; $[\alpha]_D^{29}$ +52.7 (*c* 0.96, $CHCl_3$); IR (KBr) 3321 (N–H), 1660 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.72 (brs, 1H, N*H*), 7.65-7.60 (m, 3H, N*H*, Ar*H*), 7.46-7.03 (m, 10H, Ar*H*), 6.79 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.61 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.45 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.25 (brs, 1H, N*H*), 5.69 (s, 1H, CH_2), 5.33 (s, 1H, CH_2), 3.71 (s, 3H, CH_3), 3.65 (s, 3H, CH_3), 3.36 (d, *J* = 14.7 Hz, 1H, CH_2), 3.31 (d, *J* = 14.7 Hz, 1H, CH_2); ^{13}C NMR (75 MHz,

$CDCl_3$) δ 171.0 (*C*), 168.2 (*C*), 158.6 (*C*), 152.3 (*C*), 141.0 (*C*), 138.0 (*C*), 137.4 (*C*), 137.3 (*C*), 131.6 (*C*), 128.9 (*C*H), 128.8 (*C*H), 124.7 (*C*H), 124.5 (*C*H), 123.0 (CH_2), 120.2 (*C*H), 120.1 (*C*H), 117.0 (*C*H), 114.4 (*C*H), 113.6 (*C*H), 67.7 (*C*), 55.4 (CH_3), 55.1 (CH_3), 42.0 (CH_2). Anal. Calcd for $C_{32}H_{31}N_3O_4$: C, 73.68; H, 5.99; N, 8.06. Found: C, 73.34; H, 6.15; N, 8.17. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IC column (hexane/EtOH = 96/4), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 39.7 min, t_R (minor) = 49.1 min.

Characterization for 5i

The reaction of **3c** with **1a** was performed at 0 °C for 5 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5i** (62.1 mg, 99%, 95% ee) as a colorless oil: R_f = 0.60 (silica gel, hexane/EtOAc = 2/1); $[\alpha]_D^{25}$ +45.5 (*c* 1.01, $CHCl_3$); IR (NaCl) 3019 (N–H), 1668 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.00 (brs, 1H, N*H*), 7.92 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.59 (brs, 1H, N*H*), 7.53-7.09 (m, 12H, Ar*H*), 6.85 (brs, 1H, N*H*), 6.61 (dt, *J* = 2.1, 9.0 Hz, 2H, Ar*H*), 6.41 (dt, *J* = 2.1, 8.7 Hz, 2H, Ar*H*), 5.74 (s, 1H, CH_2), 5.46 (s, 1H, CH_2), 3.66 (s, 3H, CH_3), 3.29 (d, *J* = 13.8 Hz, 1H, CH_2), 3.20 (d, *J* = 13.8 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1 (*C*), 168.3 (*C*), 152.5 (*C*), 143.9 (*C*), 140.4 (*C*), 137.5 (*C*), 137.2 (*C*), 137.1 (*C*), 129.2 (*C*H), 129.0 (*C*H), 128.6 (*C*H), 125.2 (*C*H), 125.0 (q, *J* = 3.7 Hz, *C*H), 124.7 (*C*H), 123.4 (CH_2), 120.3 (*C*H), 120.1 (*C*H), 116.8 (*C*H), 114.5 (*C*H), 68.4 (*C*), 55.4 (CH_3), 45.1 (CH_2). Anal. Calcd for $C_{32}H_{28}F_3N_3O_3$: C, 68.68; H, 5.04; N, 7.51. Found: C, 68.36; H, 5.12; N, 7.47. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IB column (hexane/EtOH = 96/4), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 24.8 min, t_R (minor) = 31.4 min.

Characterization for 5j

The reaction of **3d** with **1a** was performed at room temperature for 66 h. The crude material was

purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5j** (54.3 mg, 94%, 57% ee) as a colorless oil: R_f = 0.46 (silica gel, hexane/EtOAc = 2/1); $[\alpha]_D^{27}$ +99.9 (*c* 1.08, $CHCl_3$); IR (NaCl) 3019 (N–H), 1683 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 50.2 °C) δ 8.54 (brs, 1H, N*H*), 8.04 (d, *J* = 7.5 Hz, 1H, Ar*H*), 7.88-7.77 (m, 3H, Ar*H*), 7.54 (t, *J* = 7.8 Hz, 1H, Ar*H*), 7.40-6.91 (m, 12H, Ar*H*), 6.47 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.35 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.02 (brs, 1H, N*H*), 5.79 (s, 1H, CH_2), 5.37 (s, 1H, CH_2), 3.92 (d, *J* = 12.9 Hz, 1H, CH_2), 3.75 (d, *J* = 12.9 Hz, 1H, CH_2), 3.57 (s, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$, 50.2 °C) δ 171.8 (*C*), 167.7 (*C*), 152.3 (*C*), 141.9 (*C*), 138.5 (*C*), 137.9 (*C*), 136.6 (*C*), 136.3 (*C*), 134.8 (*C*), 131.6 (*C*), 130.4 (*C*H), 129.0 (*C*H), 128.8 (*C*H), 128.6 (*C*H), 126.7 (*C*H), 126.6 (*C*H), 126.1 (*C*H), 125.3 (*C*H), 124.9 (*C*H), 124.7 (*C*H), 124.2 (*C*H), 122.5 (*C*H_2), 121.0 (*C*H), 120.3 (*C*H), 116.5 (*C*H), 114.7 (*C*H), 67.3 (*C*), 55.6 (*C*H_3), 37.7 (*C*H_2). Anal. Calcd for $C_{35}H_{31}N_3O_3$: C, 77.61; H, 5.77; N, 7.76. Found: C, 77.27; H, 5.47; N, 8.12. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IC column (hexane/EtOH = 96/4), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 30.9 min, t_R (minor) = 26.5 min.

Characterization for 5k

The reaction of **3a** with **1h** was performed at 0 °C for 72 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 6/1) to give **5k** (21.1 mg, 18%, 22% ee) as a colorless oil: R_f = 0.45 (silica gel, hexane/EtOAc = 2/1); $[\alpha]_D^{27}$ +0.79 (*c* 0.94, $CHCl_3$); IR (NaCl) 3019 (N–H), 1642 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.81 (brs, 1H, N*H*), 7.68 (m, 2H, Ar*H*), 7.40 (m, 2H, Ar*H*), 7.35-7.20 (m, 8H, Ar*H*), 7.05 (m, 1H, Ar*H*), 6.93 (m, 8.4 Hz, 2H, Ar*H*), 6.68 (dt, *J* = 2.1, 9.0 Hz, 2H, Ar*H*), 6.54 (dt, *J* = 2.4, 9.0 Hz, 2H, Ar*H*), 6.27 (brs, 1H, N*H*), 4.98 (s, 1H, CH_2), 4.78 (s, 1H, CH_2), 3.70 (s, 3H, CH_3), 3.27 (d, *J* = 14.4 Hz, 1H, CH_2), 3.16 (s, 3H, CH_3), 2.95 (d, *J* = 14.4 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.0 (*C*), 171.2 (*C*), 152.6 (*C*), 143.8 (*C*), 139.9 (*C*), 138.8 (*C*), 138.4 (*C*), 137.7 (*C*), 129.2 (*C*H), 128.8 (*C*H), 128.3 (*C*H), 127.3 (*C*H), 127.1 (*C*H), 126.9 (*C*H), 126.7 (*C*H),

124.2 (*C*H, *C*H$_2$), 119.9 (*C*H), 117.4 (*C*H), 114.4 (*C*H), 67.5 (*C*), 55.5 (*C*H$_3$), 41.1 (*C*H$_2$), 37.7 (*C*H$_3$). Anal. Calcd for $C_{32}H_{31}N_3O_3$: C, 76.02; H, 6.18; N, 8.31. Found: C, 75.85; H, 6.49; N, 8.69. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IC column (hexane/EtOH = 90/10), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 18.8 min, t_R (minor) = 22.4 min.

General procedure for lactamization

The experiments for lactamization were carried out as described in the following typical procedure. For example, the reaction of **5a** with di-*tert*-butyl dicarbonate (Boc_2O) for the synthesis of **7a** was exemplified as follows.

Synthesis and characterization of 7a

To a solution of **5a** (65.1 mg, 0.132 mmol) in CH_2Cl_2 (0.26 mL) was added Boc_2O (115 mg, 0.528 mmol, 4.0 equiv.), triethylamine (Et_3N, 134 mg, 1.32 mmol, 10 equiv.) and *N*,*N*-dimethyl-4-aminopyridine (DMAP, 8.1 mg, 0.066 mmol, 0.5 equiv.) at room temperature under a nitrogen atmosphere. After stirring the solution at the same temperature for 24 h, the solvent was removed under reduced pressure. The crude residue was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 0/1) to give **7a** (63.1 mg, 96%, 94% ee) as a red oil: R_f = 0.53 (silica gel, hexane/EtOAc = 2/1); $[\alpha]_D^{27}$ +133 (*c* 1.04, $CHCl_3$); IR (NaCl) 3014 (C–H), 1747 (C=O), 1698 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.14 (m, 8H, Ar*H*), 7.04 (m, 2H, Ar*H*), 6.63 (s, 4H, Ar*H*), 6.21 (t, *J* = 2.4 Hz, 1H, C*H*$_2$), 5.58 (t, *J* = 2.4 Hz, 1H, C*H*$_2$), 4.14 (dt, *J* = 2.4, 18.3 Hz, 1H, C*H*$_2$), 3.77 (dt, *J* = 2.4, 18.3 Hz, 1H, C*H*$_2$), 3.73 (s, 3H, C*H*$_3$), 0.94 (s, 9H, C*H*$_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2 (*C*), 168.5 (*C*), 158.7 (*C*), 151.5 (*C*), 139.1 (*C*), 138.1 (*C*), 137.5 (*C*), 131.7 (*C*H), 129.5 (*C*), 129.1 (*C*H), 128.15 (*C*H), 128.06 (*C*H), 128.0 (*C*H), 127.7 (*C*H), 126.9 (*C*H), 116.9 (*C*H$_2$), 113.4 (*C*H), 83.4 (*C*), 75.3 (*C*), 55.2 (*C*H$_3$), 37.6 (*C*H$_2$), 27.1 (*C*H$_3$). Anal. Calcd for $C_{30}H_{30}N_2O_5$: C, 72.27; H, 6.07; N, 5.62. Found: C,

71.97; H, 6.02; N, 5.99. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IF column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 25.5 min, t_R (minor) = 32.5 min.

Specific rotation of 7a prepared from 5b

A solution of **5b**, Boc_2O, Et_3N, and DMAP in CH_2Cl_2 was stirred at room temperature for 24 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 0/1) to give **7a** (70.8 mg, 98%, 91% ee) as a red oil: $[\alpha]_D^{25}$ +126 (*c* 1.05, $CHCl_3$).

Specific rotation of 7a prepared from 5c

A solution of **5c**, Boc_2O, Et_3N, and DMAP in CH_2Cl_2 was stirred at room temperature for 24 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 0/1) to give **7a** (68.5 mg, 96%, 92% ee) as a red oil: $[\alpha]_D^{27}$ +128 (*c* 1.05, $CHCl_3$).

Specific rotation of 7a prepared from 5d

A solution of **5d**, Boc_2O, Et_3N, and DMAP in CH_2Cl_2 was stirred at room temperature for 24 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 0/1) to give **7a** (71.8 mg, 97%, 92% ee) as a red oil: $[\alpha]_D^{25}$ +126 (*c* 1.02, $CHCl_3$).

Specific rotation of 7a prepared from 5e

A solution of **5e**, Boc_2O, Et_3N, and DMAP in CH_2Cl_2 was stirred at room temperature for 24 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 0/1) to give **7a** (55.4 mg, 98%, 93% ee) as a red oil: $[\alpha]_D^{26}$ +128 (*c* 0.98, $CHCl_3$).

Specific rotation of 7a prepared from 5f

A solution of **5f**, Boc_2O, Et_3N, and DMAP in CH_2Cl_2 was stirred at room temperature for 24 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 0/1) to give **7a** (65.8mg, 90%, 90% ee) as a red oil: $[\alpha]_D^{27}$ +120 (*c* 0.98, $CHCl_3$).

Specific rotation of 7a prepared from 5g

A solution of **5g**, Boc_2O, Et_3N, and DMAP in CH_2Cl_2 was stirred at room temperature for 24 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 0/1) to give **7a** (80.9 mg, 95%, 80% ee) as a red oil: $[\alpha]_D^{26}$ +109 (*c* 0.96, $CHCl_3$).

Characterization for 7b

A solution of **5h**, Boc_2O, Et_3N, and DMAP in CH_2Cl_2 was stirred at room temperature for 24 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 1/1) to give **7b** (69.8 mg, 90%, 92% ee) as a colorless oil: R_f = 0.44 (silica gel, hexane/EtOAc = 2/1); $[\alpha]_D^{27}$ +102 (*c* 0.84, $CHCl_3$); IR (NaCl) 3019 (C–H), 1748 (C=O), 1696 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42-7.29 (m, 3H, Ar*H*), 7.09-7.01 (m, 4H, Ar*H*), 6.79 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.67 (s, 4H, ArH), 6.19 (t, *J* = 2.4 Hz, 1H, CH_2), 5.56 (t, *J* = 2.4 Hz, 1H, CH_2), 4.05 (dt, *J* = 2.4, 18.3 Hz, 1H, CH_2), 3.81-3.73 (m, 1H, CH_2), 3.78 (s, 3H, CH_3), 3.74 (s, 3H, CH_3), 0.97 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.5 (*C*), 168.5 (*C*), 159.3 (*C*), 158.7 (*C*), 151.5 (*C*), 139.1 (*C*), 137.5 (*C*), 131.7 (*C*H), 130.1 (*C*), 129.5 (*C*), 129.0 (*C*H), 128.3 (*C*H), 127.9 (*C*H), 127.6 (*C*H), 116.8 (*C*H_2), 113.5 (*C*H), 113.4 (*C*H), 83.3 (*C*), 74.8 (*C*), 55.3 (*C*H_3), 55.2 (*C*H_3), 37.7 (*C*H_2), 27.1 (*C*H_3). Anal. Calcd for $C_{31}H_{32}N_2O_6$: C, 70.44; H, 6.10; N, 5.30. Found: C, 70.09; H, 6.06; N, 5.35. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IF column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 38.8 min, t_R (minor) = 52.3 min.

Characterization for 7c

A solution of **5i**, Boc_2O, Et_3N, and DMAP in CH_2Cl_2 was stirred at room temperature for 24 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 1/1) to give **7c** (61.8 mg, 97%, 95% ee) as a white oil: R_f = 0.59 (silica gel, hexane/EtOAc = 2/1); $[\alpha]_D^{27}$ +76.1 (*c* 0.86, $CHCl_3$); IR (NaCl) 3018 (C–H), 1747 (C=O), 1700 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.44-7.27 (m, 5H, Ar*H*), 7.04-7.01 (m, 2H, Ar*H*), 6.67 (s, 4H, Ar*H*), 6.24 (t, *J* = 2.4 Hz, 1H, CH_2), 5.62 (t, *J* = 2.4 Hz, 1H, CH_2), 4.14 (dt, *J* = 2.4, 18.3 Hz, 1H, CH_2), 3.79 (dt, *J* = 2.4, 18.3 Hz, 1H, CH_2), 3.74 (s, 3H, CH_3), 0.94 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.7 (*C*), 168.5 (*C*), 159.0 (*C*), 151.5 (*C*), 142.1 (*C*), 138.7 (*C*), 136.7 (*C*), 131.6 (*C*), 129.2 (*C*H), 129.1 (*C*), 128.2 (*C*H), 127.5 (*C*H), 127.2 (*C*H), 125.0 (q, *J* = 3.8 Hz, *C*H), 117.5 (*C*H_2), 113.7 (*C*H), 83.7 (*C*), 74.8 (*C*), 55.3 (*C*H_3), 37.5 (*C*H_2), 27.0 (*C*H_3). Anal. Calcd for $C_{31}H_{29}F_3N_2O_5$: C, 65.72; H, 5.16; N, 4.94. Found: C, 65.93; H, 5.25; N, 5.18. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IE column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 43.0 min, t_R (minor) = 33.6 min.

Characterization for 7d

A solution of **5j**, Boc_2O, Et_3N, and DMAP in CH_2Cl_2 was stirred at room temperature for 24 h. The crude material was purified by column chromatography (silica gel, hexane/EtOAc = 3/1 to 1/1) to give **7d** (63.9 mg, 90%, 57% ee) as a colorless oil: R_f = 0.47 (silica gel, hexane/EtOAc = 1/1); $[\alpha]_D^{27}$ +87.6 (*c* 1.05, $CHCl_3$); IR (NaCl) 3019 (C–H), 1643 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 50 °C) δ 7.80-7.75 (m, 2H, Ar*H*), 7.59-7.25 (m, 8H, Ar*H*), 7.00 (d, *J* = 6.3 Hz, 2H, Ar*H*), 6.76 (d, *J* = 8.4 Hz, 2H, Ar*H*), 6.47 (d, *J* = 9.3 Hz, 2H, Ar*H*), 6.31 (s, 1H, CH_2), 5.61 (s, 1H, CH_2), 4.37 (d, *J* = 18.9 Hz, 1H, CH_2), 3.84 (d, *J* = 18.9 Hz, 1H, CH_2), 3.62 (s, 3H, CH_3), 0.82 (s, 9H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$,

50 °C) δ 174.2 (*C*), 168.6 (*C*), 158.8 (*C*), 151.1 (*C*), 139.2 (*C*), 137.6 (*C*), 134.5 (*C*), 130.8 (*C*H), 130.2 (*C*H), 129.4 (*C*H), 128.9 (*C*H), 128.0 (*C*H), 125.6 (*C*H), 125.3 (*C*H), 124.8 (*C*H), 117.3 (*C*), 113.5 (*C*H), 83.2 (*C*), 55.3 (*C*H_3), 39.9 (*C*H_2), 28.2 (*C*), 27.1 (*C*H_3). Anal. Calcd for $C_{34}H_{32}N_2O_5$: C, 74.43; H, 5.88; N, 5.11. Found: C, 74.56; H, 5.70; N, 5.36. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IE column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 52.9 min, t_R (minor) = 38.2 min.

Synthesis and characterization of 8

To a solution of **7a** (85.2 mg, 0.171 mmol) in THF/H_2O (4/1, 1.7 mL) was added LiOH (12.3 mg, 0.513 mmol, 3.0 equiv.) at room temperature. The resulting mixture was warmed to 60 °C and stirred for 24 h. The reaction was quenched by addition of saturated aqueous citric acid (10 mL). The resulting mixture was extracted with EtOAc (50 mL), washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo to give a crude material (51.6 mg). To a solution of this crude material in CH_2Cl_2 (0.90 mL) was added 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDCI·HCl, 39.3 mg, 0.205 mmol, 1.2 equiv.), *p*-chlorophenol (26.4 mg, 0.205 mmol, 1.2 equiv.) and DMAP (9.6 mg, 0.086 mmol, 0.5 equiv.) at room temperature under a nitrogen atmosphere. After stirring the solution at the same temperature for 72 h, the reaction mixture was diluted with EtOAc (50 mL), washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by column chromatography (silica gel, hexane/EtOAc = 4/1 to 2/1) to give **8** (28.9 mg, 52%, 95% ee) as a white solid: R_f = 0.43 (silica gel, hexane/EtOAc = 2/1); M.p. 127–129 °C; $[\alpha]_D^{27}$ +18.2 (*c* 1.08, $CHCl_3$); IR (KBr) 1757 (C=O), 1703 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42-7.26 (m, 7H, Ar*H*), 7.02 (d, *J* = 9.0, Hz, 2H, Ar*H*), 6.81 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.74 (d, *J* = 9.0 Hz, 2H, Ar*H*), 6.28 (s, 1H, CH_2), 5.57 (s, 1H, CH_2), 3.79-3.70 (m, 4H, , CH_3, CH_2), 3.50 (d, *J* = 16.8 Hz, 1H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2 (*C*), 167.7 (*C*), 158.2 (*C*), 148.6 (*C*), 138.4 (*C*),

136.5 (*C*), 131.8 (*C*), 129.7 (*C*), 129.6 (*C*H), 128.7 (*C*H), 128.6 (*C*H), 128.0 (*C*H), 127.2 (*C*H), 122.3 (*C*H), 118.3 (CH_2), 113.8 (*C*H), 71.9 (*C*), 55.3 (CH_3), 40.9 (CH_2). Anal. Calcd for $C_{25}H_{20}ClNO_4$: C, 69.21; H, 4.65; N, 3.23. Found: C, 69.15; H, 4.79; N, 3.46. The enantiomeric excess was determined by HPLC with a Daicel Chiralpak IF column (hexane/EtOH = 80/20), flow rate 0.5 mL/min, UV detection 274 nm, t_R (major) = 29.6 min, t_R (minor) = 32.8 min.

References

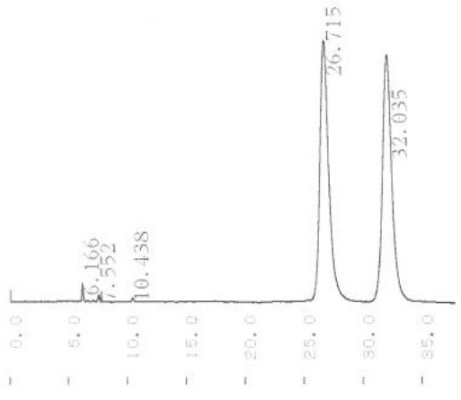
[1] (*a*) T. Suzuki, J. ichi Atsumi, T. Sengoku, M. Takahashi and H. Yoda, *J. Organomet. Chem.*, 2010, **695**, 128–136; (*b*) M. Takahashi, Y. Murata, M. Ishida, F. Yagishita, M. Sakamoto, T. Sengoku and H. Yoda, *Org. Biomol. Chem.*, 2014, **12**, 7686–7689.

[2] J. S. Dickstein, M. W. Fennie, A. L. Norman, B. J. Paulose and M. C. Kozlowski, *J. Am. Chem. Soc.*, 2008, **130**, 15794–15795.

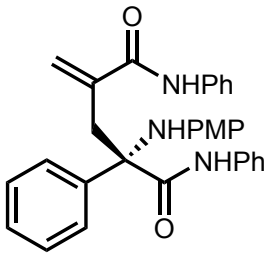
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IC (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 96/4; Flow rate: 0.5 mL/min; UV detection: 274 nm.

Racemate of **5a**

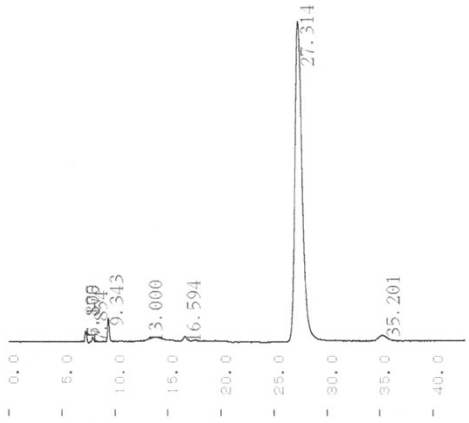


TIME	AREA	HEIGHT	MK	IDNO	CONC
6.166	1367	181			0.5104
7.552	644	65			0.2406
10.438	430	38			0.1606
26.715	130360	2515			48.6663
32.035	135063	2383			50.4221
TOTAL	267865	5183			100



(+)-**5a**

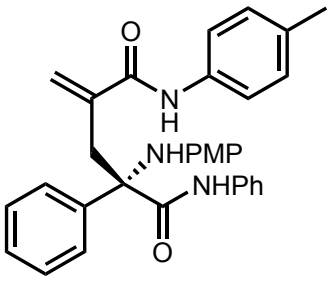
Enantiomerically enriched (+)–**5a** (96% ee)



TIME	AREA	HEIGHT	MK	IDNO	CONC
6.8	215	14			0.1254
7.175	1786	125	V		1.0405
7.854	761	55			0.4433
9.343	2809	254			1.6365
13	38	5			0.0223
16.594	1106	48			0.6446
27.314	161750	3461			94.2474
35.201	3158	59			1.8401
TOTAL	171622	4020			100

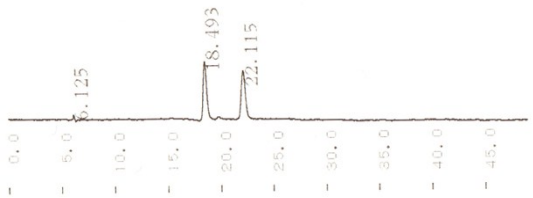
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IE (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.



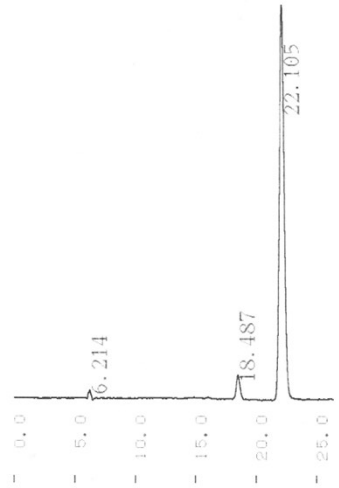
(+)-**5b**

Racemate of **5b**



TIME	AREA	HEIGHT	MK	IDNO	CONC
6.125	551	60			1.8816
18.493	14554	627			49.6807
22.115	14190	520			48.4378
TOTAL	29295	1206			100

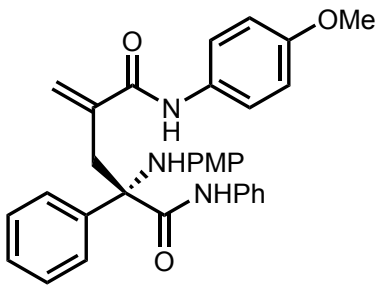
Enantiomerically enriched (+)–**5b** (96% ee)



TIME	AREA	HEIGHT	MK	IDNO	CONC
6.214	1331	96			1.2221
18.487	5030	231			4.619
22.105	102538	3725			94.159
TOTAL	108899	4051			100

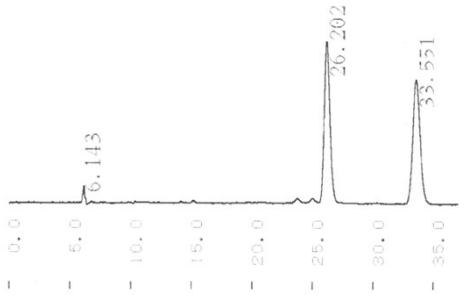
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IE (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.



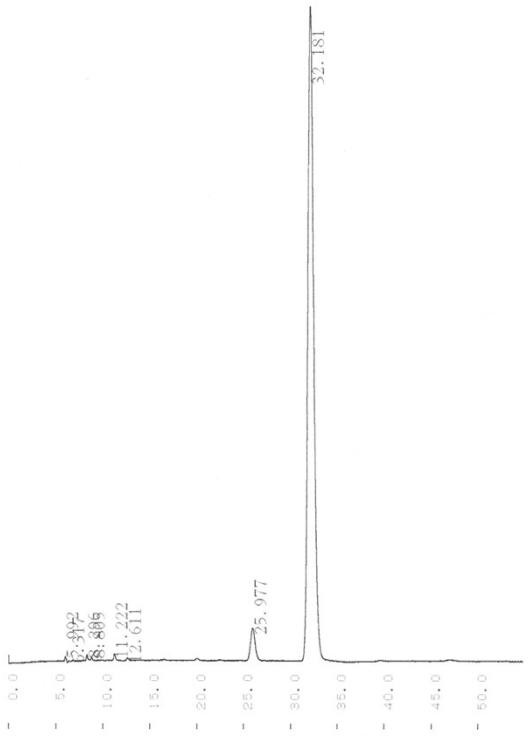
(+)-**5c**

Racemate of **5c**



TIME	AREA	HEIGHT	MK	IDNO	CONC
6.143	1894	167			1.8962
26.202	48632	1512			48.6996
33.551	49336	1165			49.4042
TOTAL	99862	2844			100

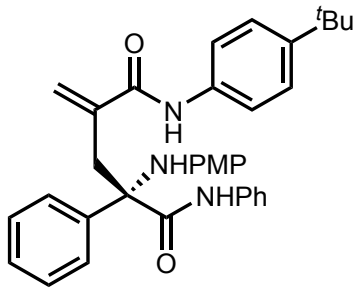
Enantiomerically enriched (+)–**5c** (96% ee)



TIME	AREA	HEIGHT	MK	IDNO	CONC
5.992	632	65			0.1759
6.317	257	19			0.0716
8.296	839	72			0.2334
8.805	489	36	V		0.1362
11.222	1037	80			0.2886
12.611	526	37			0.1463
25.977	13563	401			3.7751
32.181	341922	7965			95.1728
TOTAL	359264	8674			100

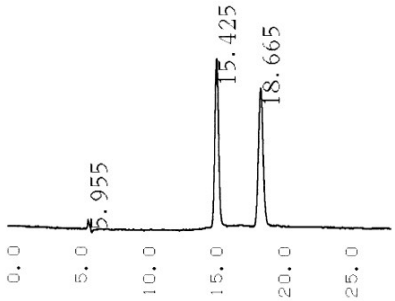
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IE (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.



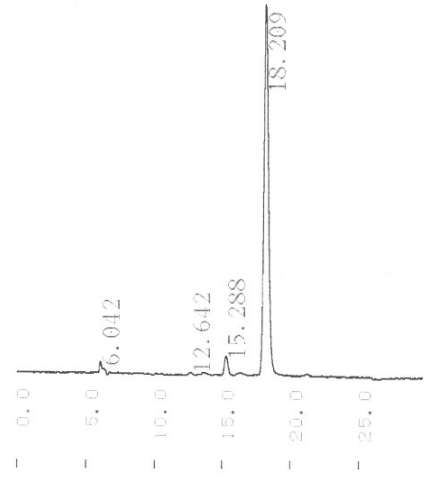
(+)-**5d**

Racemate of **5d**



TIME	AREA	HEIGHT	MK	IDNO	CONC
5.955	1074	94			1.9234
15.425	27501	1411			49.2588
18.665	27255	1152			48.8178
TOTAL	55829	2657			100

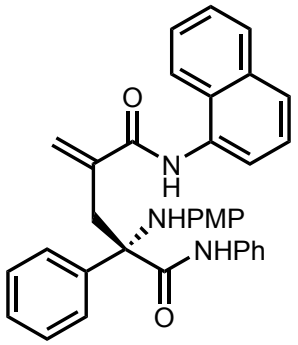
Enantiomerically enriched (+)–**5d** (96% ee)



TIME	AREA	HEIGHT	MK	IDNO	CONC
6.042	636	80			0.8273
12.642	326	25			0.4239
15.288	3091	166			4.0239
18.209	72766	3111			94.7249
TOTAL	76818	3382			100

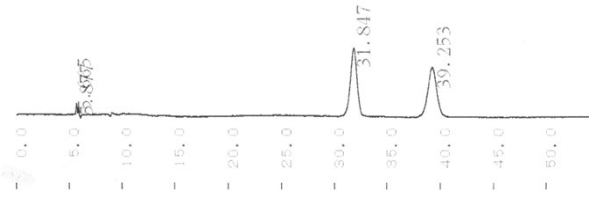
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IE (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.



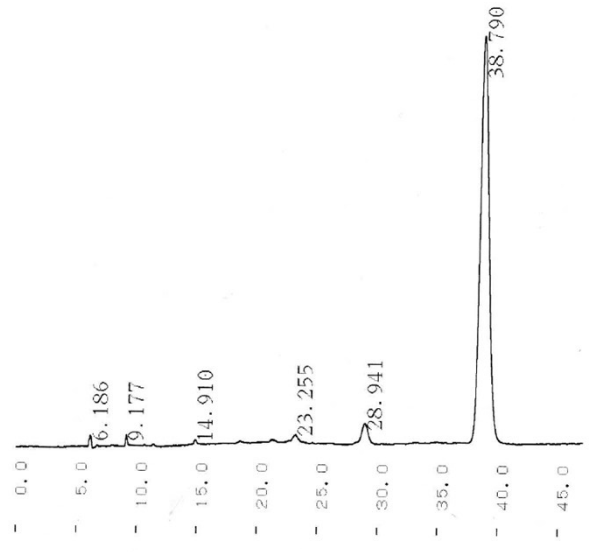
(+)-**5e**

Racemate of **5e**



TIME	AREA	HEIGHT	MK	IDNO	CONC
5.665	1211	135			1.8356
5.877	719	94	V		1.0899
31.847	32115	731			48.6763
39.253	31932	541			48.3981
TOTAL	65977	1502			100

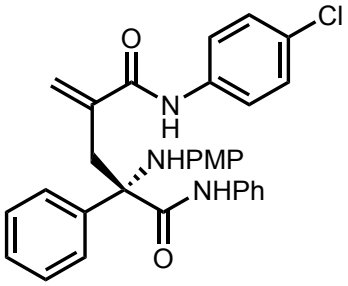
Enantiomerically enriched (+)–**5e** (94% ee)



TIME	AREA	HEIGHT	MK	IDNO	CONC
6.186	1621	118			0.7878
9.177	1105	107			0.5372
14.91	647	42			0.3144
23.255	1635	62			0.7948
28.941	6337	183			3.0803
38.79	194372	3826			94.4855
TOTAL	205717	4338			100

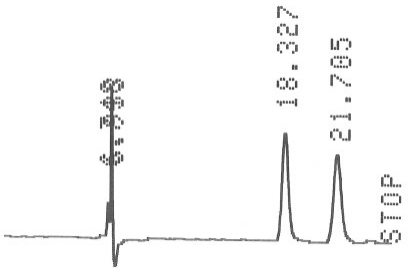
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IC (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 96/4; Flow rate: 0.5 mL/min; UV detection: 274 nm.



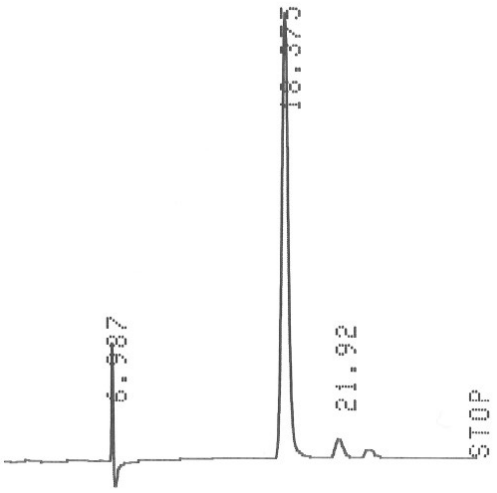
(+)-**5f**

Racemate of **5f**



TIME	AREA	MK	IDNO	CONC
6.748	3588			6.0209
6.933	8984	V		15.0783
18.327	23720			39.8086
21.705	23293			39.0922
TOTAL	59584			100

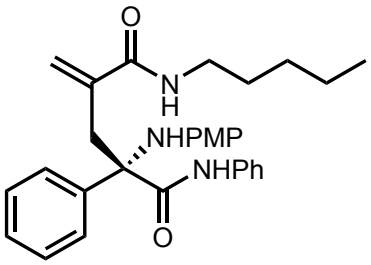
Enantiomerically enriched (+)–**5f** (90% ee)



TIME	AREA	MK	IDNO	CONC
6.987	6249			5.684
18.375	98517			89.6031
21.92	5182			4.713
TOTAL	109948			100

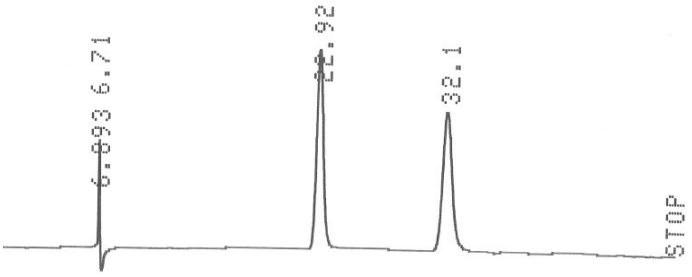
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IC (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 96/4; Flow rate: 0.5 mL/min; UV detection: 274 nm.



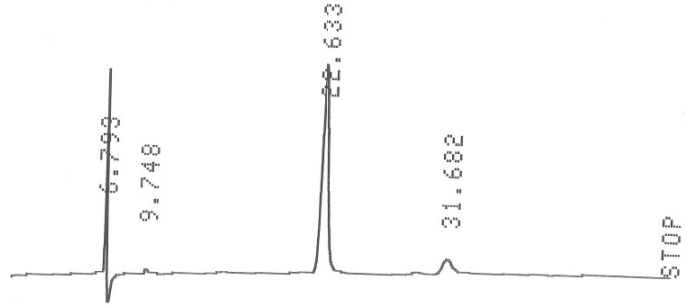
(+)-**5g**

Racemate of **5g**



TIME	AREA	MK	IDNO	CONC
6.71	652			0.5435
6.893	6668	V		5.5546
22.92	56351			46.9397
32.1	56378			46.9622
TOTAL	120050			100

Enantiomerically enriched (+)–**5g** (82% ee)

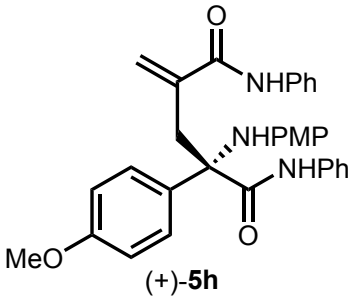


TIME	AREA	MK	IDNO	CONC
6.793	11647			15.134
9.748	467			0.6071
22.633	59080			76.769
31.682	5764			7.4899
TOTAL				

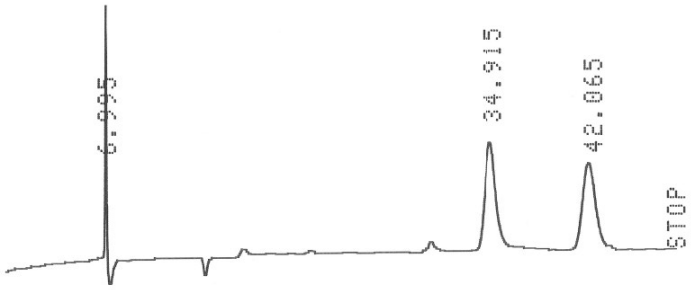
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IC (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 96/4; Flow rate: 0.5 mL/min; UV detection: 274 nm.

Racemate of **5h**

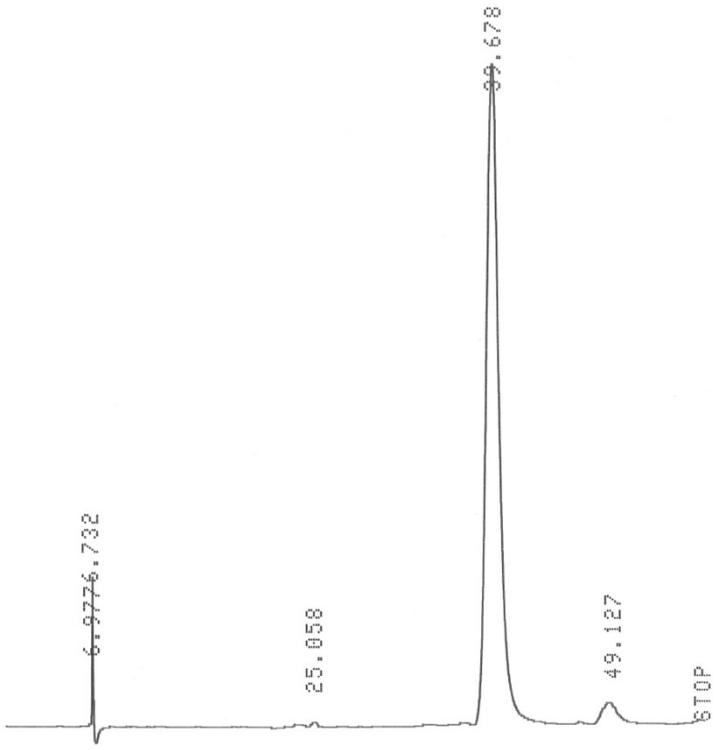


(+)-**5h**



TIME	AREA	MK	IDNO	CONC
6.995	14646			12.6099
34.915	51692			44.5068
42.065	49806			42.8833
TOTAL	116144			100

Enantiomerically enriched (+)–**5h** (93% ee)

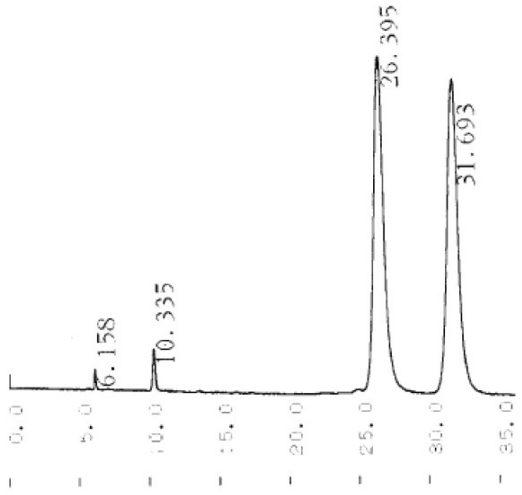


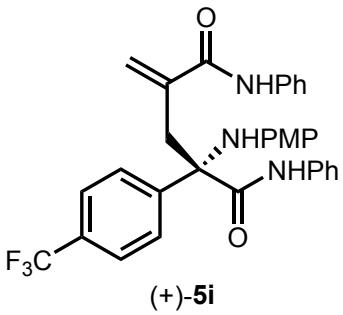
TIME	AREA	MK	IDNO	CONC
6.732	730			0.1508
6.977	9696	V		2.0026
25.058	1517			0.3134
39.678	455075			93.9845
49.127	17183			3.5487
TOTAL	484202			100

HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IB (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 96/4; Flow rate: 0.5 mL/min; UV detection: 274 nm.

Racemate of **5i**

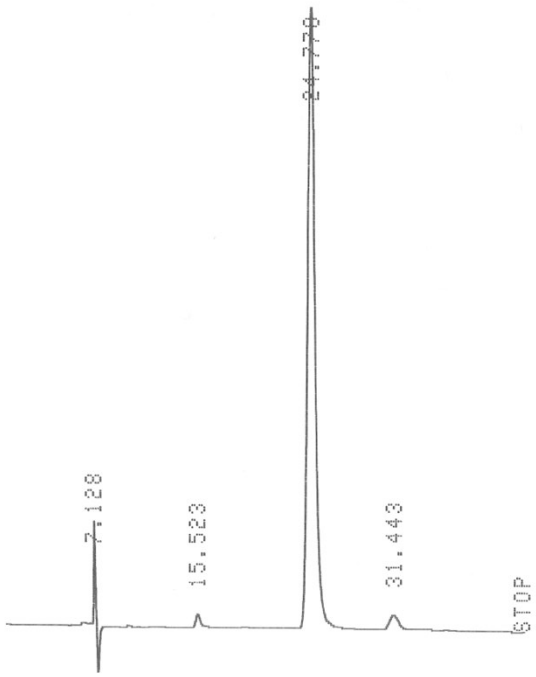




(+)-**5i**

TIME	AREA	HEIGHT	MK	IDNO	CONC
6.158	1360	176			0.4808
10.335	4538	346			1.6039
26.395	136304	2716			48.1735
31.693	140741	2545			49.7417
TOTAL	282943	5784			100

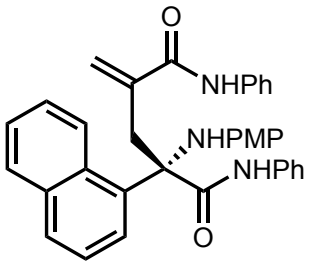
Enantiomerically enriched (+)–**5i** (95% ee)



TIME	AREA	MK	IDNO	CONC
7.128	11778			4.3935
15.523	2112			0.788
24.778	248071			92.5378
31.443	6114			2.2808
TOTAL	268075			100

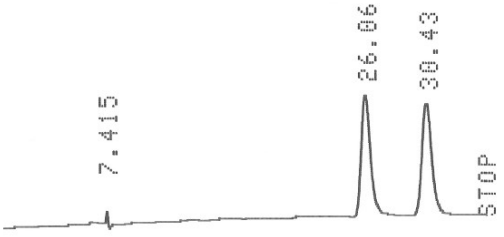
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IC (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 96/4; Flow rate: 0.5 mL/min; UV detection: 274 nm.



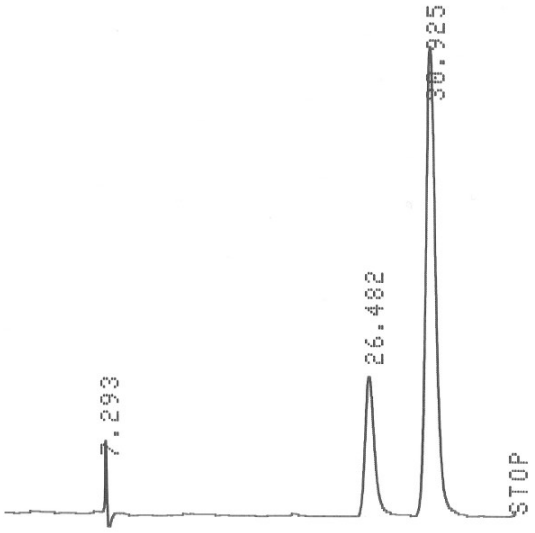
(+)-**5j**

Racemate of **5j**



TIME	AREA	MK	IDNO	CONC
7.415	918			0.9815
26.06	45745			48.9204
30.43	46846			50.0981
TOTAL	93509			100

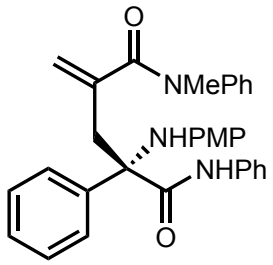
Enantiomerically enriched (+)–**5j** (57% ee)



TIME	AREA	MK	IDNO	CONC
7.293	4741			1.8371
26.482	54087			20.9586
30.925	199240			77.2043
TOTAL	258068			100

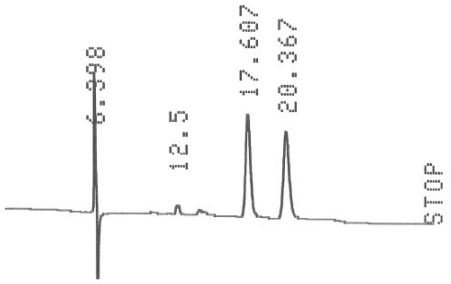
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IC (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 90/10; Flow rate: 0.5 mL/min; UV detection: 274 nm.



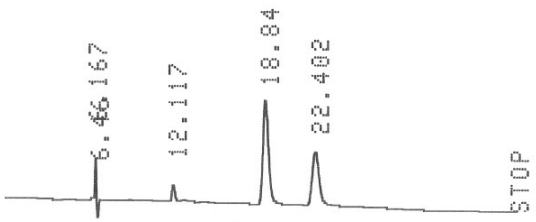
(+)-**5k**

Racemate of **5k**



TIME	AREA	MK	IDNO	CONC
6.398	12586			22.8342
12.5	1491			2.7058
17.607	20448			37.0986
20.367	20593			37.3615
TOTAL	55119			100

Enantiomerically enriched (+)–**5k** (22% ee)

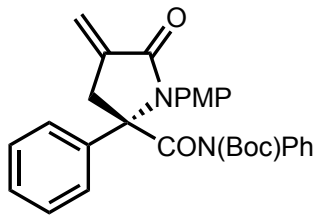


TIME	AREA	MK	IDNO	CONC
6.167	912			1.9769
6.46	3092	V		6.7054
12.117	2218			4.8095
18.84	24362			52.8339
22.402	15527			33.6744
TOTAL	46110			100

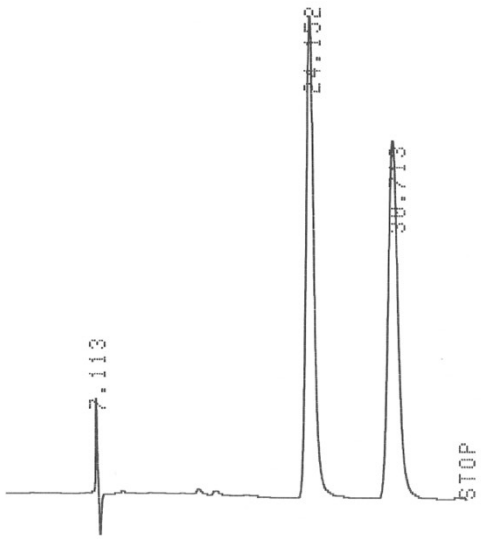
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IF (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.

Racemate of **7a**

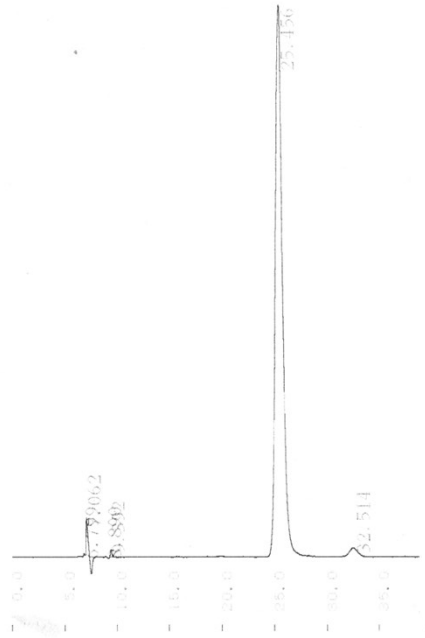


(+)-**7a**



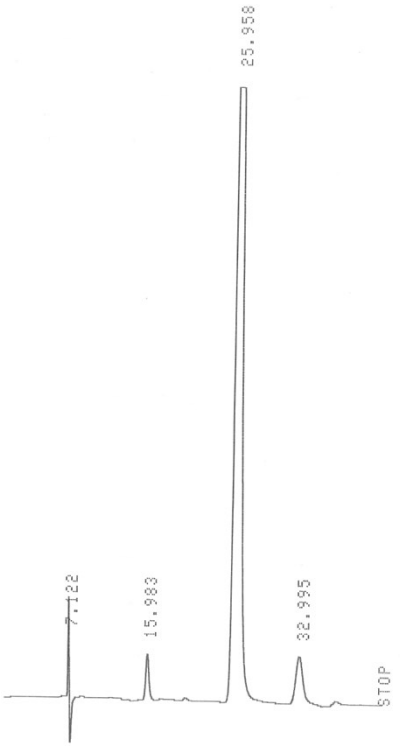
TIME	AREA	MK	IDNO	CONC
7.113	11547			2.9866
24.152	189561			49.0316
30.713	185502			47.9818
TOTAL	386609			100

Enantiomerically enriched (+)–**7a** (96% ee, from **5a**)



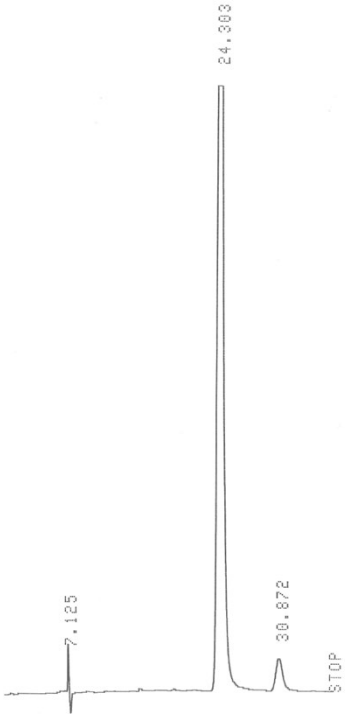
TIME	AREA	HEIGHT	MK	IDNO	CONC
6.799	672	59			0.2312
7.062	7934	515	V		2.728
8.89	243	19			0.0834
9.392	1119	97			0.3847
25.456	275874	5959			94.8548
32.514	4996	89			1.7179
TOTAL	290838	6738			100

Enantiomerically enriched (+)–**7a** (91% ee, from **5b**)



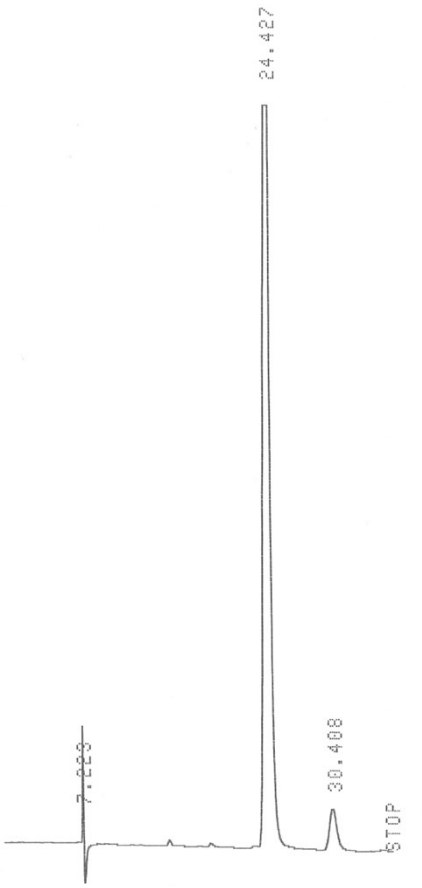
TIME	AREA	MK	IDNO	CONC
7.122	15742			1.9482
15.983	15045			1.8619
25.958	743442			92.0089
32.995	33782			4.1809
TOTAL	808011			100

Enantiomerically enriched (+)–**7a** (92% ee, from **5c**)



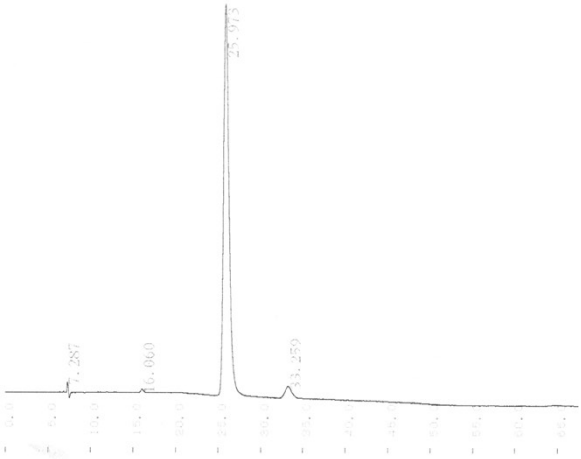
TIME	AREA	MK	IDNO	CONC
7.125	6873			1.1491
24.303	568186			95.0013
30.872	23023			3.8495
TOTAL	598082			100

Enantiomerically enriched (+)–**7a** (92% ee, from **5d**)



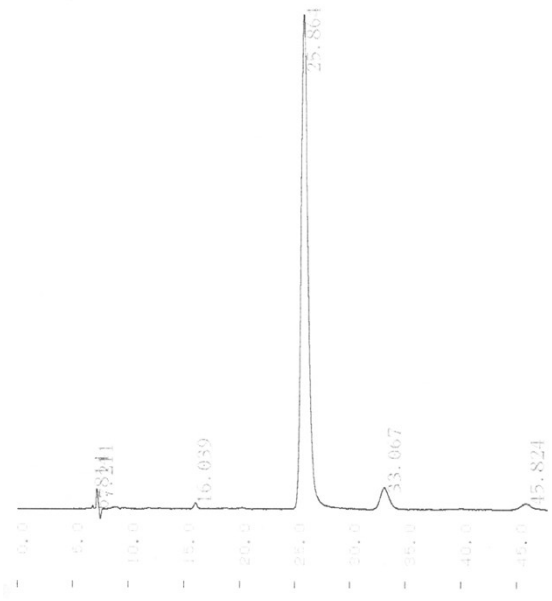
TIME	AREA	MK	IDNO	CONC
7.223	10556			2.1952
24.427	449443			93.4636
30.408	20876			4.3412
TOTAL	480875			100

Enantiomerically enriched (+)–**7a** (94% ee, from **5e**)



TIME	AREA	HEIGHT	MK	IDNO	CONC
7.287	1865	175			0.7678
16.06	1165	49			0.4796
25.973	230878	5220			95.0604
33.259	8967	161			3.6921
TOTAL	242874	5606			100

Enantiomerically enriched (+)–**7a** (90% ee, from **5f**)



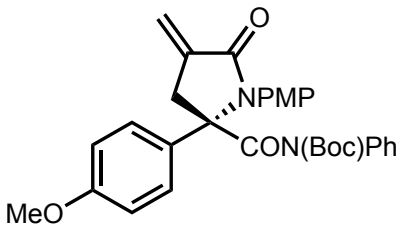
TIME	AREA	HEIGHT	MK	IDNO	CONC
6.814	766	48			0.3171
7.211	3872	278	V		1.604
16.039	1143	55			0.4735
25.864	220583	5036			91.3701
33.067	12131	222			5.0247
45.824	2922	52			1.2105
TOTAL	241417	5690			100

Enantiomerically enriched (+)–**7a** (82% ee, from **5g**)

TIME	AREA	HEIGHT	MK	IDNO	CONC
6.013	864	143			0.5655
20.96	135493	3895			88.6942
23.412	1428	48			0.9348
26.582	14979	246			9.8054
TOTAL	152764	4332			100

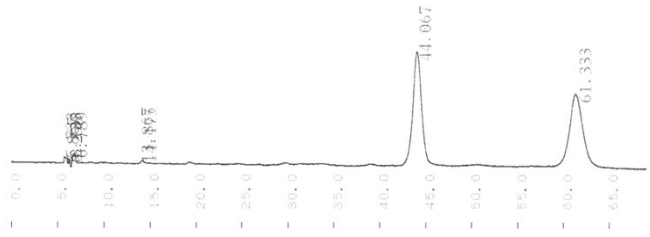
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IE (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.



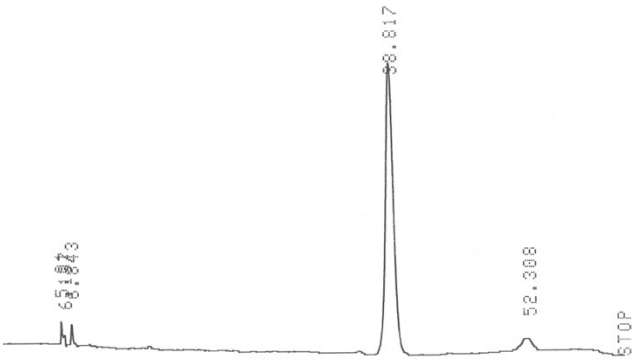
(+)-**7b**

Racemate of **7b**



TIME	AREA	HEIGHT	MK	IDNO	CONC
5.733	746	83			0.3978
5.867	703	74	V		0.375
6.133	146	32			0.0781
6.258	604	89	V		0.3219
6.789	3594	150			1.9163
13.867	71	9			0.038
14.175	864	43	V		0.4605
44.067	91807	1394			48.9506
61.333	89015	893			47.4618
TOTAL	187551	2766			100

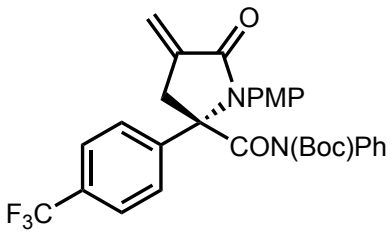
Enantiomerically enriched (+)–**7b** (92% ee)



TIME	AREA	MK	IDNO	CONC
5.81	2952			1.468
6.137	909	V		0.4521
6.843	2571			1.2782
38.817	187219			93.0955
52.308	7453			3.7062
TOTAL	201104			100

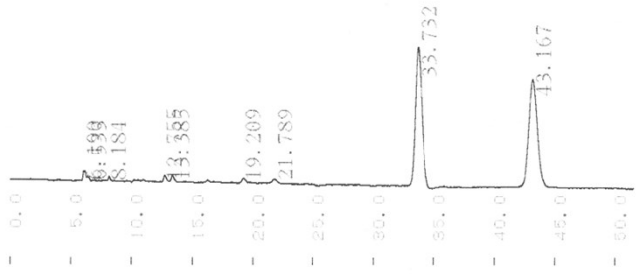
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IE (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.



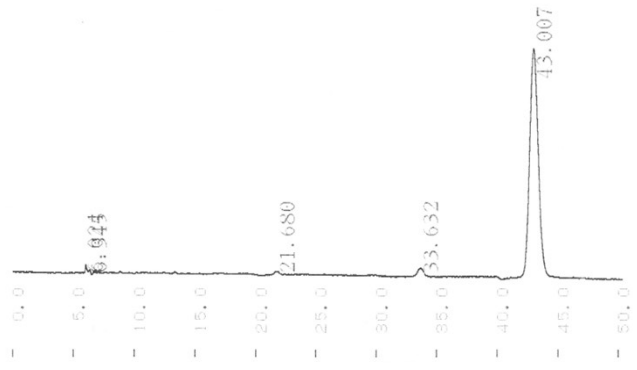
(+)-**7c**

Racemate of **7c**



TIME	AREA	HEIGHT	MK	IDNO	CONC
6.19	1692	100			1.5623
6.533	648	38	V		0.5981
8.184	495	46			0.4568
12.755	1140	69			1.0522
13.385	1183	67	V		1.092
19.209	999	48			0.9222
21.789	861	42			0.7953
33.732	51095	1324			47.1817
43.167	50182	1018			46.3393
TOTAL	108294	2750			100

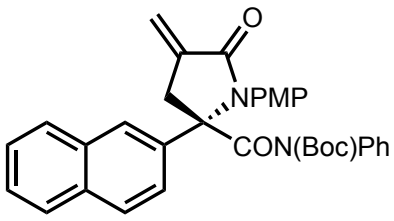
Enantiomerically enriched (+)–**7c** (95% ee)



TIME	AREA	HEIGHT	MK	IDNO	CONC
6.024	835	85			0.755
6.345	446	46	V		0.4037
21.68	699	31			0.6322
33.632	2508	76			2.2682
43.007	106077	2153			95.9408
TOTAL	110565	2390			100

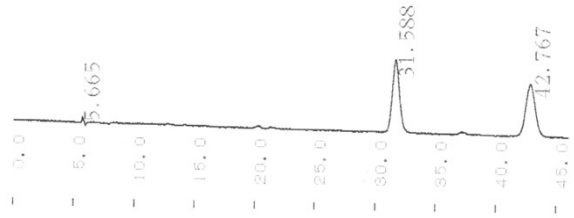
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IE (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.



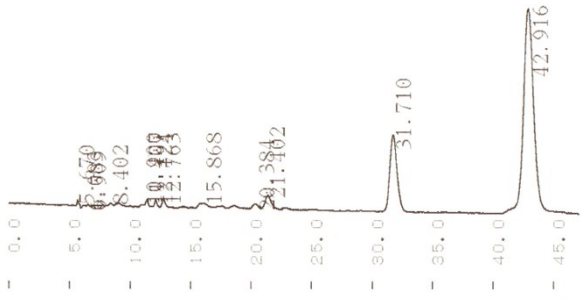
(+)-**7d**

Racemate of **7d**



TIME	AREA	HEIGHT	MK	IDNO	CONC
5.665	704	68			1.2612
31.588	27757	681			49.7472
42.767	27335	495			48.9916
TOTAL	55795	1244			100

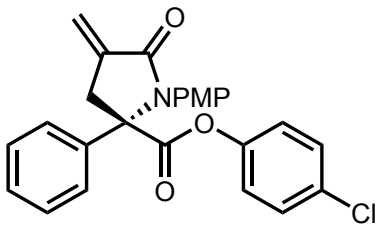
Enantiomerically enriched (+)–**7d** (57% ee)



TIME	AREA	HEIGHT	MK	IDNO	CONC
5.67	837	70			0.5365
6.083	396	18			0.2538
6.509	261	22	V		0.167
8.402	330	25			0.2117
10.9	425	16			0.2724
11.407	1064	73	V		0.6821
12.124	1039	71	V		0.6658
12.763	1493	87			0.9571
15.868	1520	39			0.9741
20.384	1073	40			0.6881
21.402	4081	126			2.6161
31.71	30129	727			19.313
42.916	113357	1921			72.6621
TOTAL	156006	3235			100

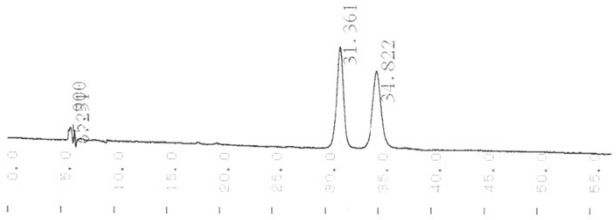
HPLC Chromatographic Conditions

Column: Daicel CHIRALPAK IE (ϕ 0.46 cm, L 25 cm); Eluent: *n*–hexane/EtOH = 80/20; Flow rate: 0.5 mL/min; UV detection: 274 nm.



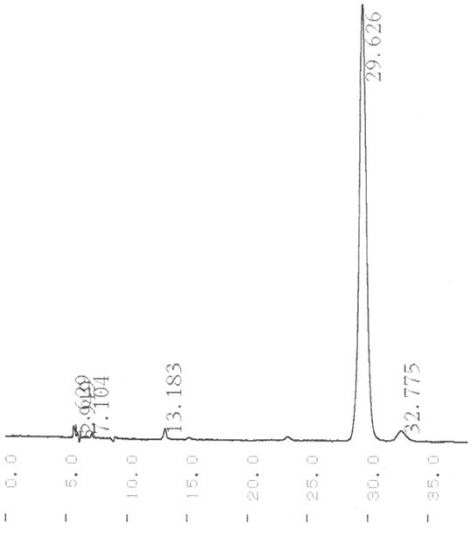
(+)-**8**

Racemate of **8**

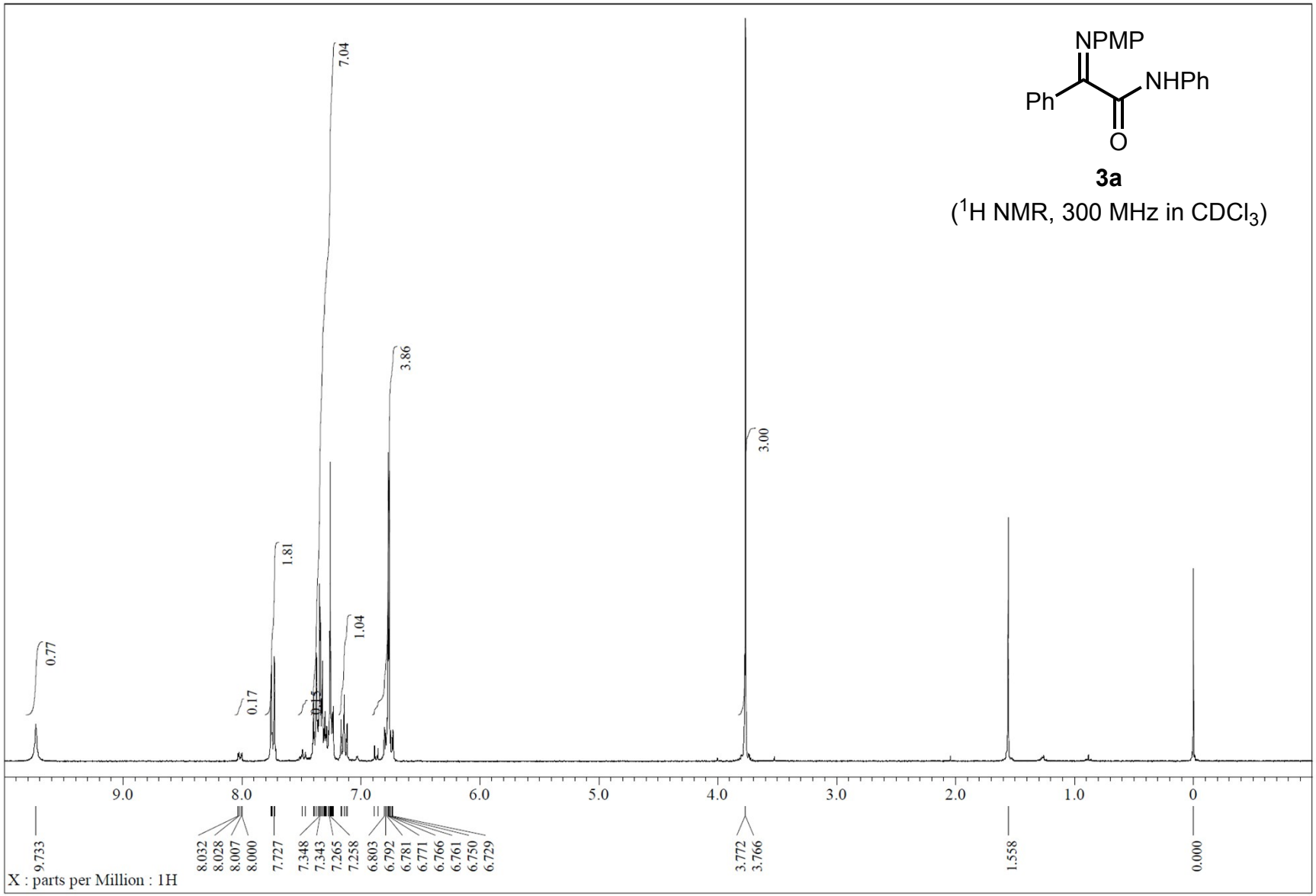


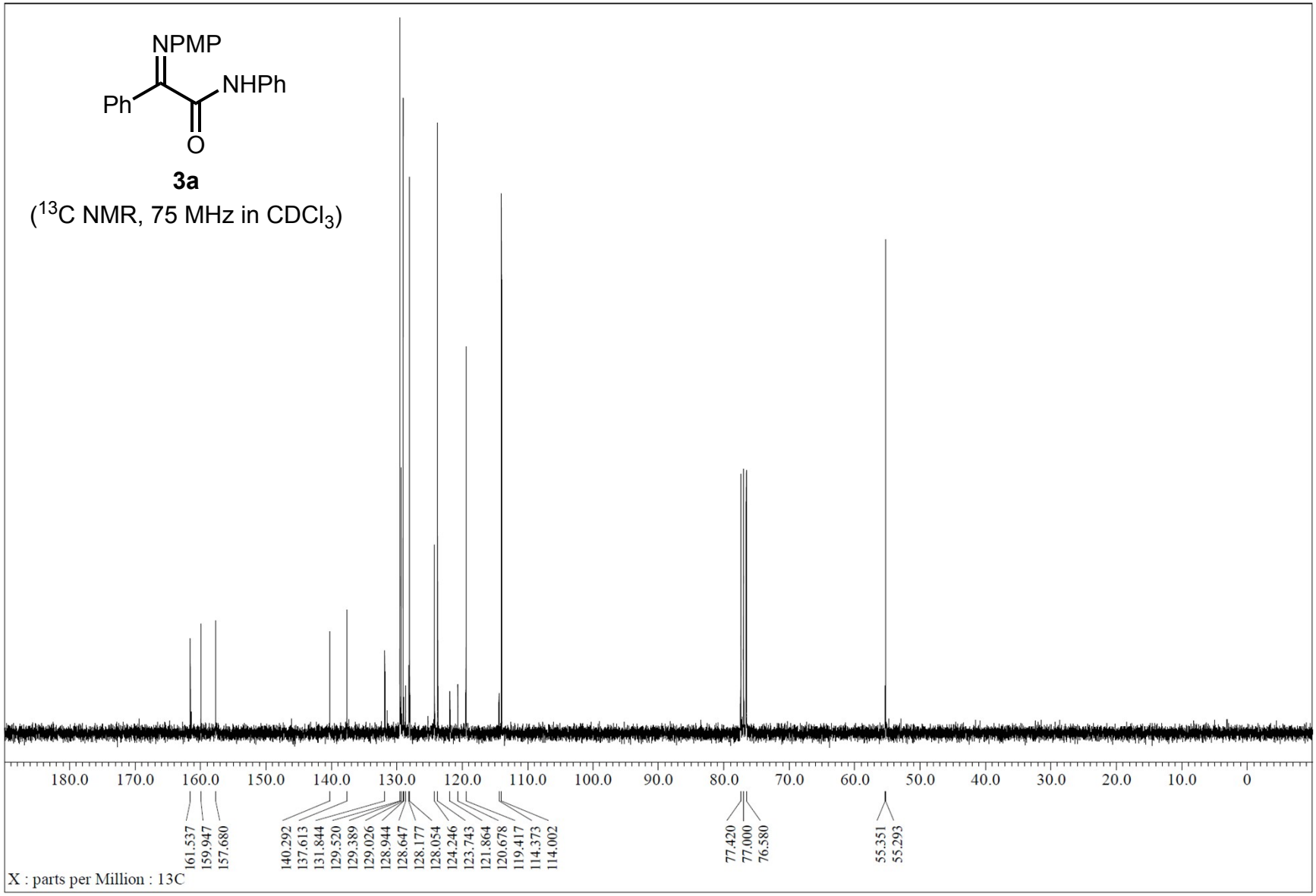
TIME	AREA	HEIGHT	MK	IDNO	CONC
5.9	2927	155			2.9223
6.251	1252	162			1.25
31.361	47426	1081			47.3492
34.822	48558	833			48.4785
TOTAL	100163	2231			100

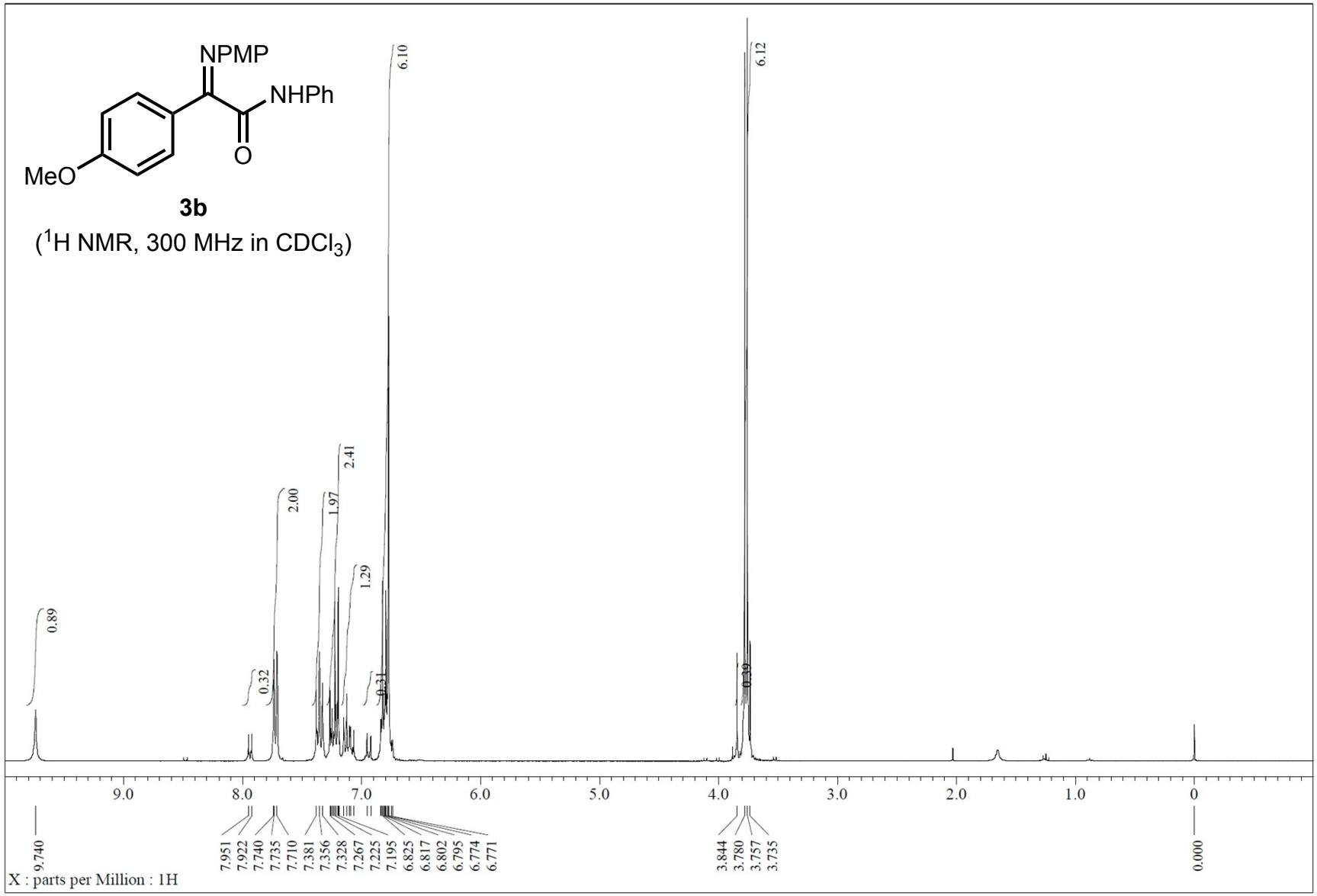
Enantiomerically enriched (+)–**8** (95% ee, from **7a**)

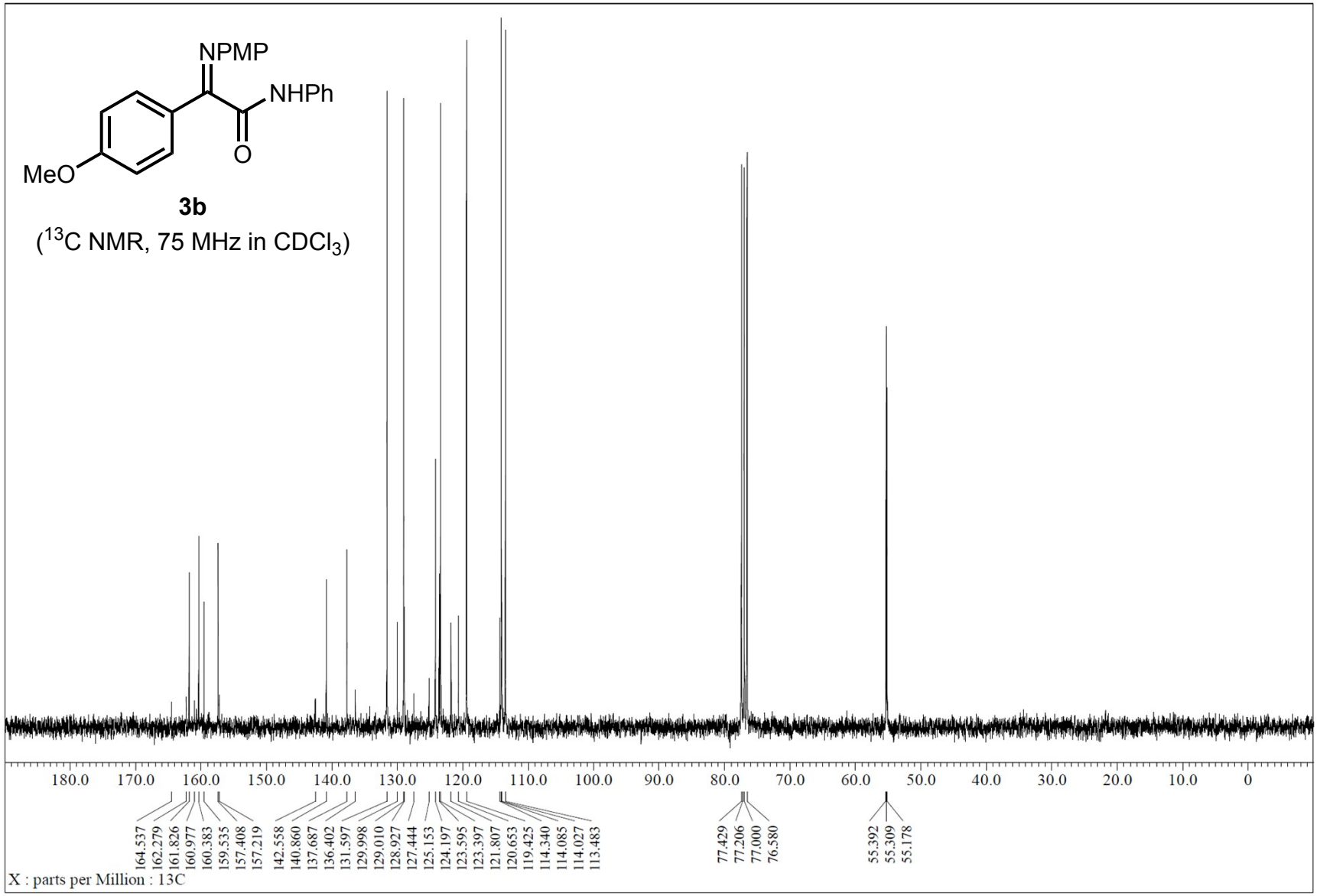


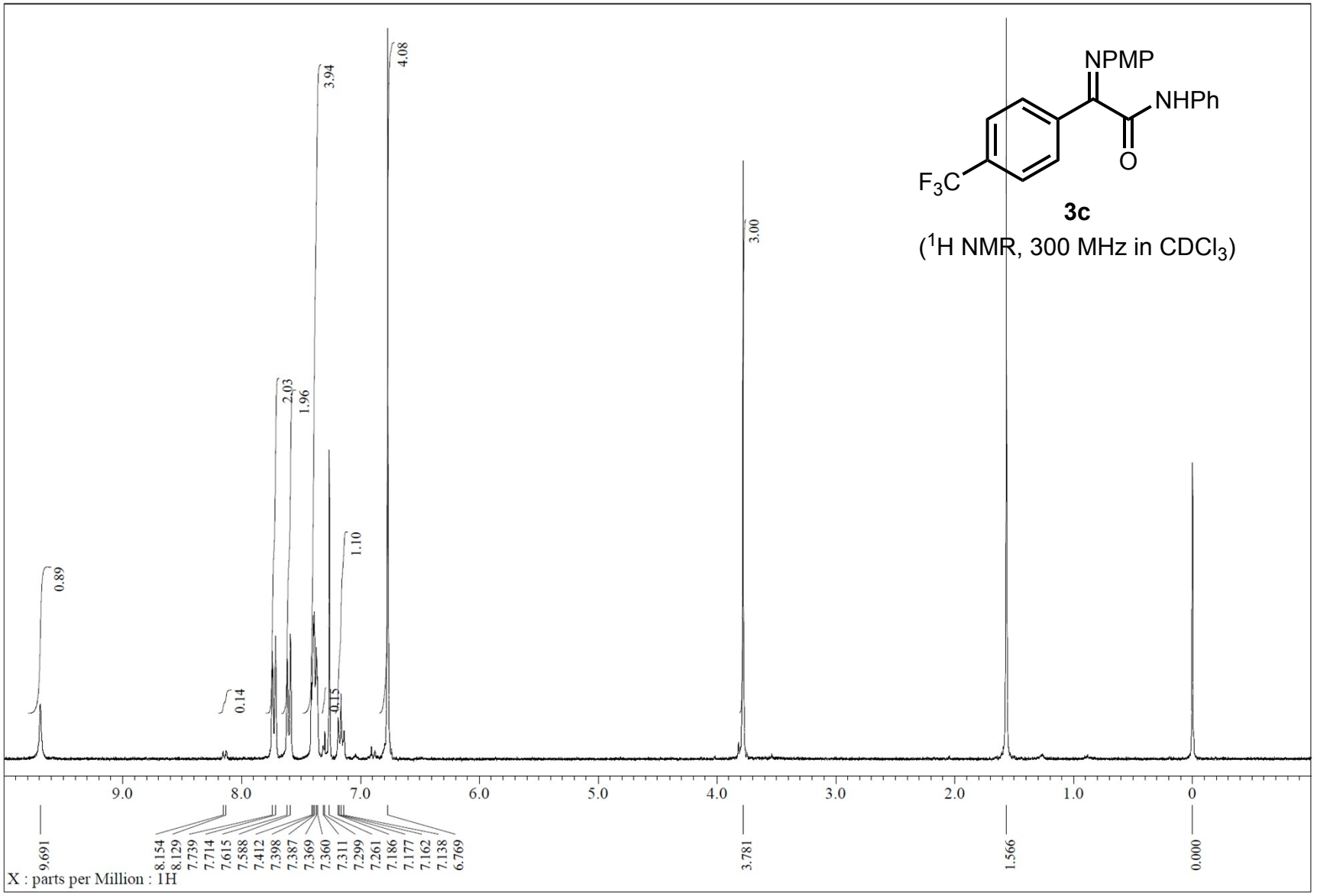
TIME	AREA	HEIGHT	MK	IDNO	CONC
5.629	1549	127			0.8596
5.949	735	88	V		0.4081
7.104	418	48			0.232
13.183	1712	101			0.9504
29.626	171171	4119			94.9999
32.775	4595	97			2.55
TOTAL	180180	4580			100

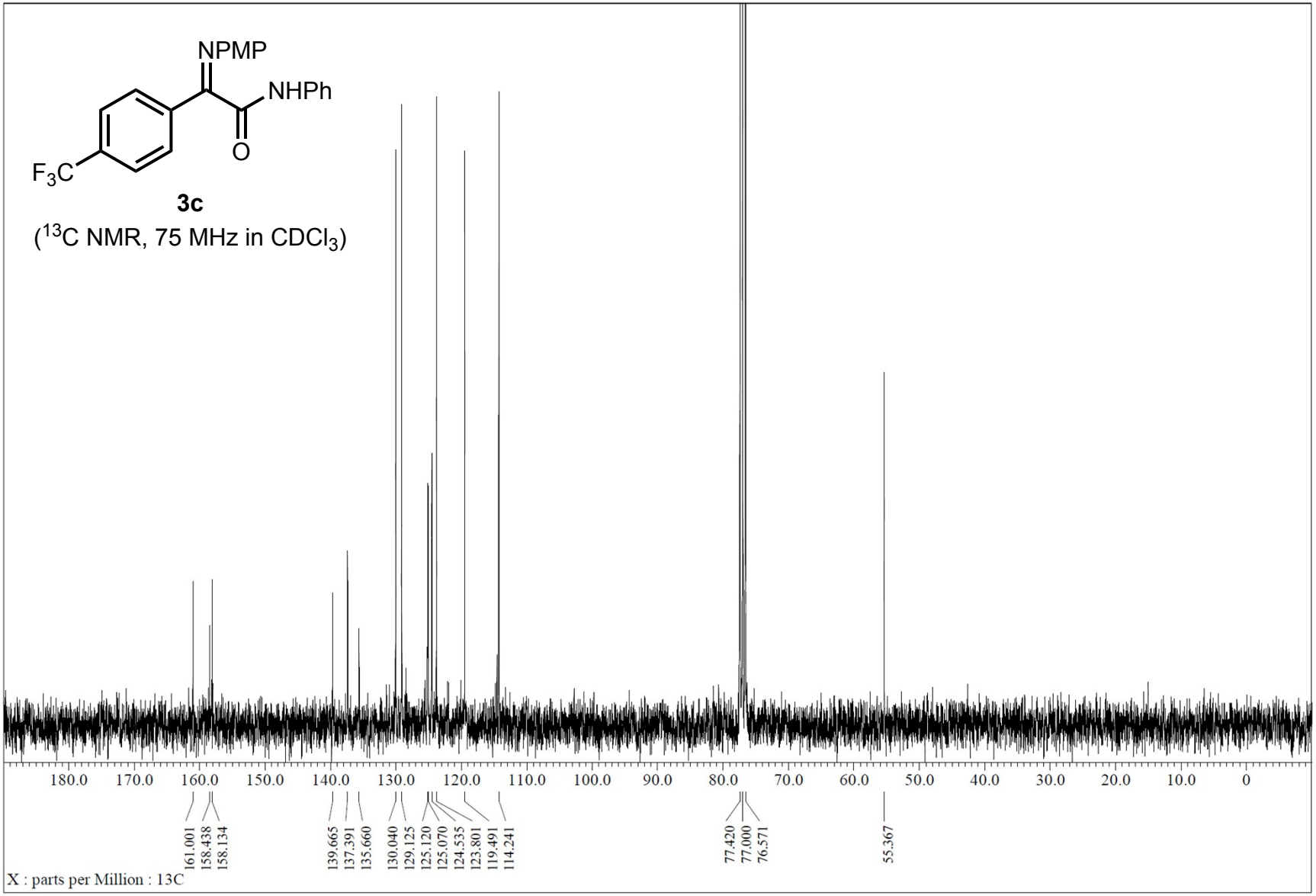

NPMP
NHPh
Ph
O
3a
(1H NMR, 300 MHz in CDCl3)
7.04
3.86
3.00
1.81
1.04
0.77
0.17
0.15
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.733
8.032
8.028
8.007
8.000
7.727
7.348
7.343
7.265
7.258
6.803
6.792
6.781
6.771
6.766
6.761
6.750
6.729
3.772
3.766
1.558
0.000
X : parts per Million : 1H

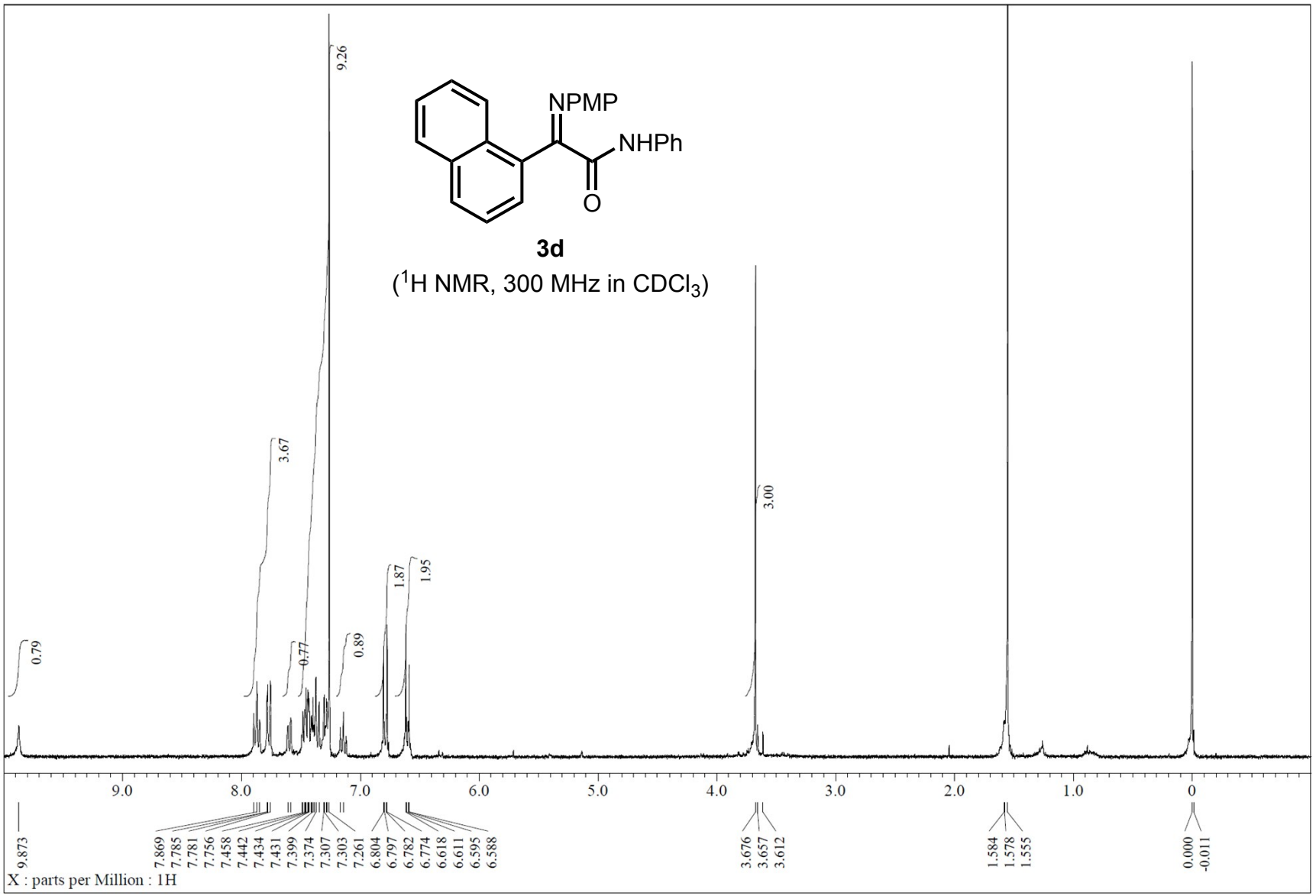

NPMP
NHPh
Ph
O
3a
(13C NMR, 75 MHz in CDCl3)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
161.537 159.947 157.680
140.292 137.613 131.844 129.520 129.389 129.026 128.944 128.647 128.177 128.054 124.246 123.743 121.864 120.678 119.417 114.373 114.002
77.420 77.000 76.580
55.351 55.293
X : parts per Million : 13C

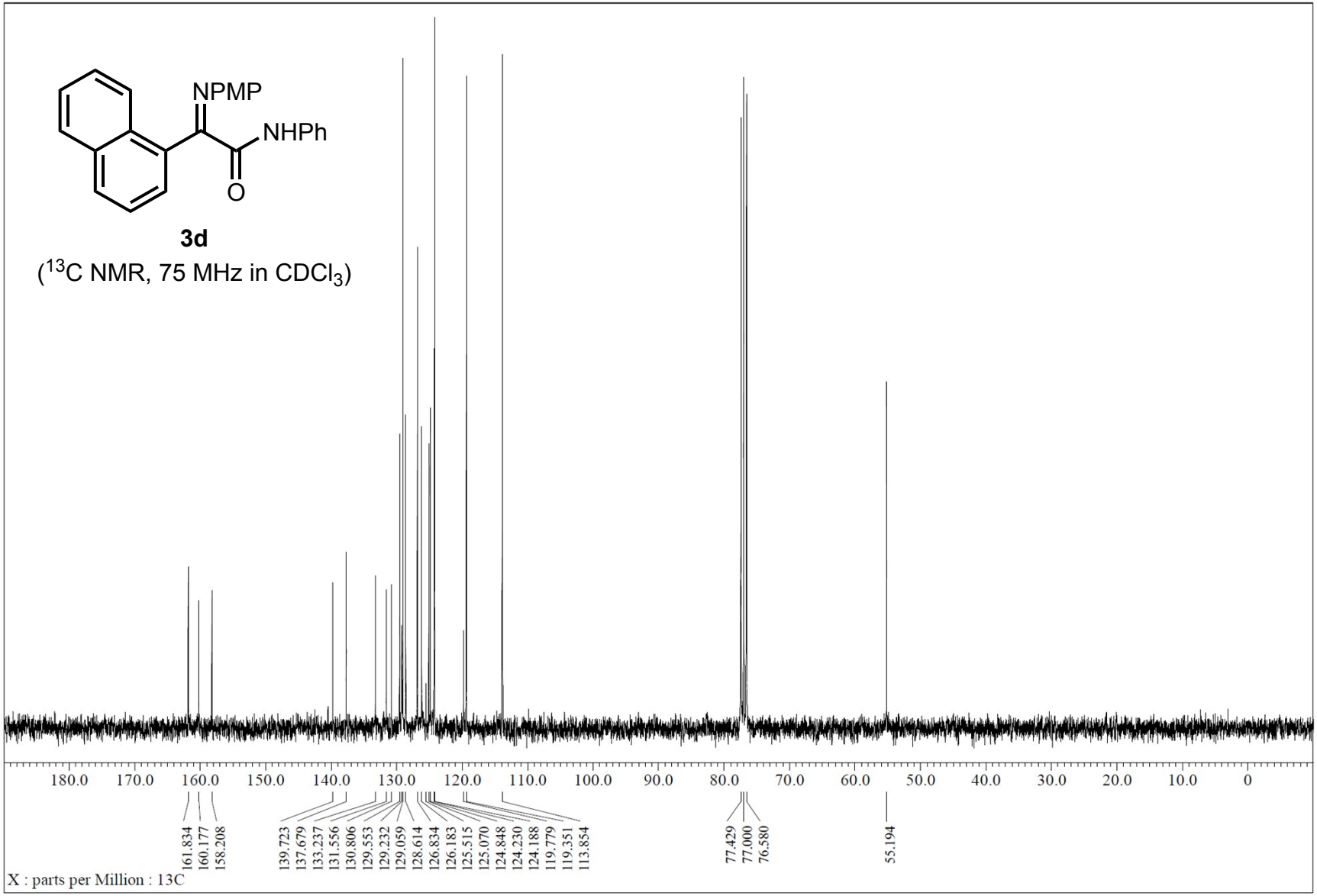

NPMP
NHPh
O
MeO
3b
(1H NMR, 300 MHz in CDCl3)
6.10
6.12
2.41
2.00
1.97
1.29
0.89
0.32
0.31
0.39
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.740
7.951
7.922
7.740
7.735
7.710
7.381
7.356
7.328
7.267
7.225
7.195
6.825
6.817
6.802
6.795
6.774
6.771
3.844
3.780
3.757
3.735
0.000
X : parts per Million : 1H

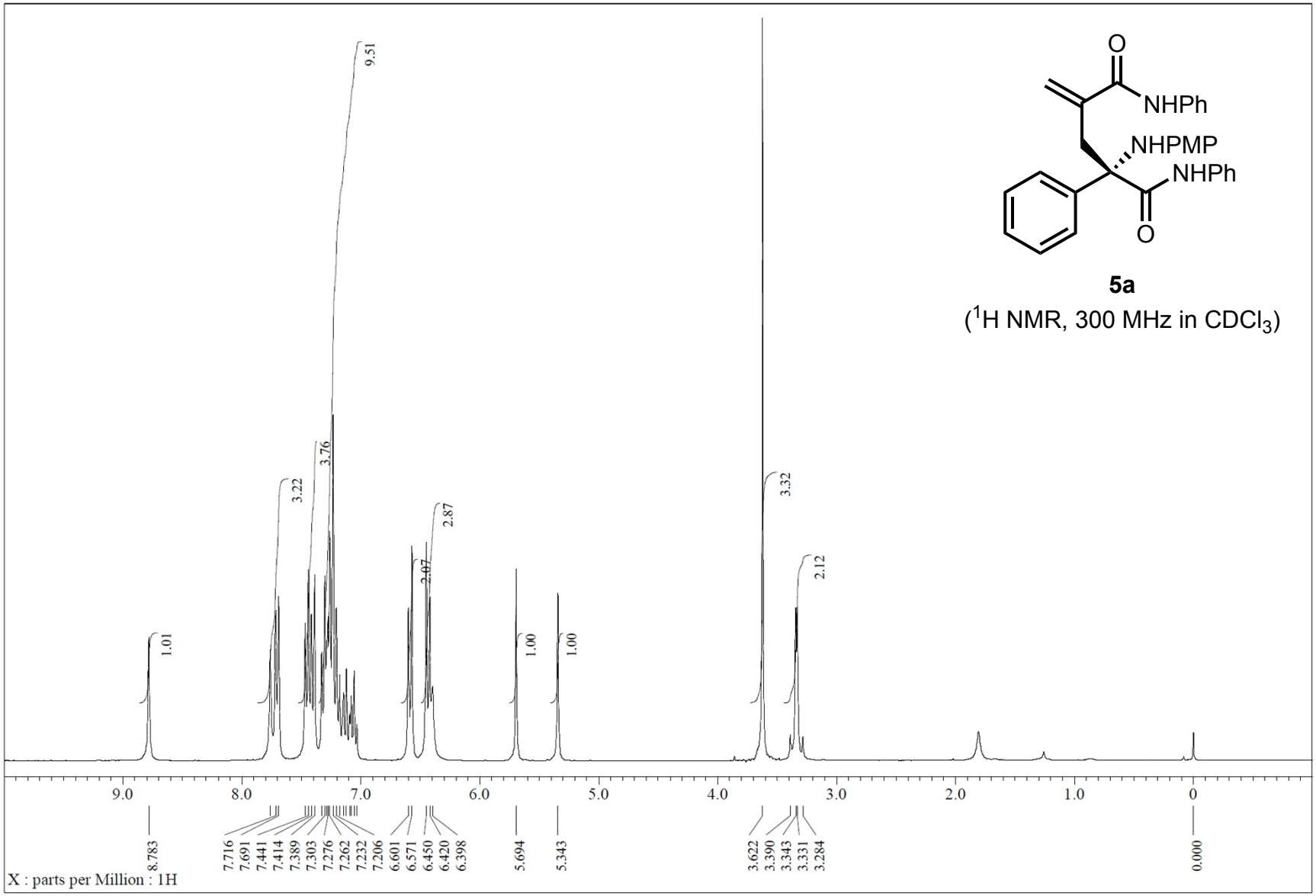

NPMP
NHPh
O
MeO
3b
(13C NMR, 75 MHz in CDCl3)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
164.537 162.279 161.826 160.977 160.383 159.535 157.408 157.219 142.558 140.860 137.687 136.402 131.597 129.998 129.010 128.927 127.444 125.153 124.197 123.595 123.397 121.807 120.653 119.425 114.340 114.085 114.027 113.483 77.429 77.206 77.000 76.580 55.392 55.309 55.178
X : parts per Million : 13C

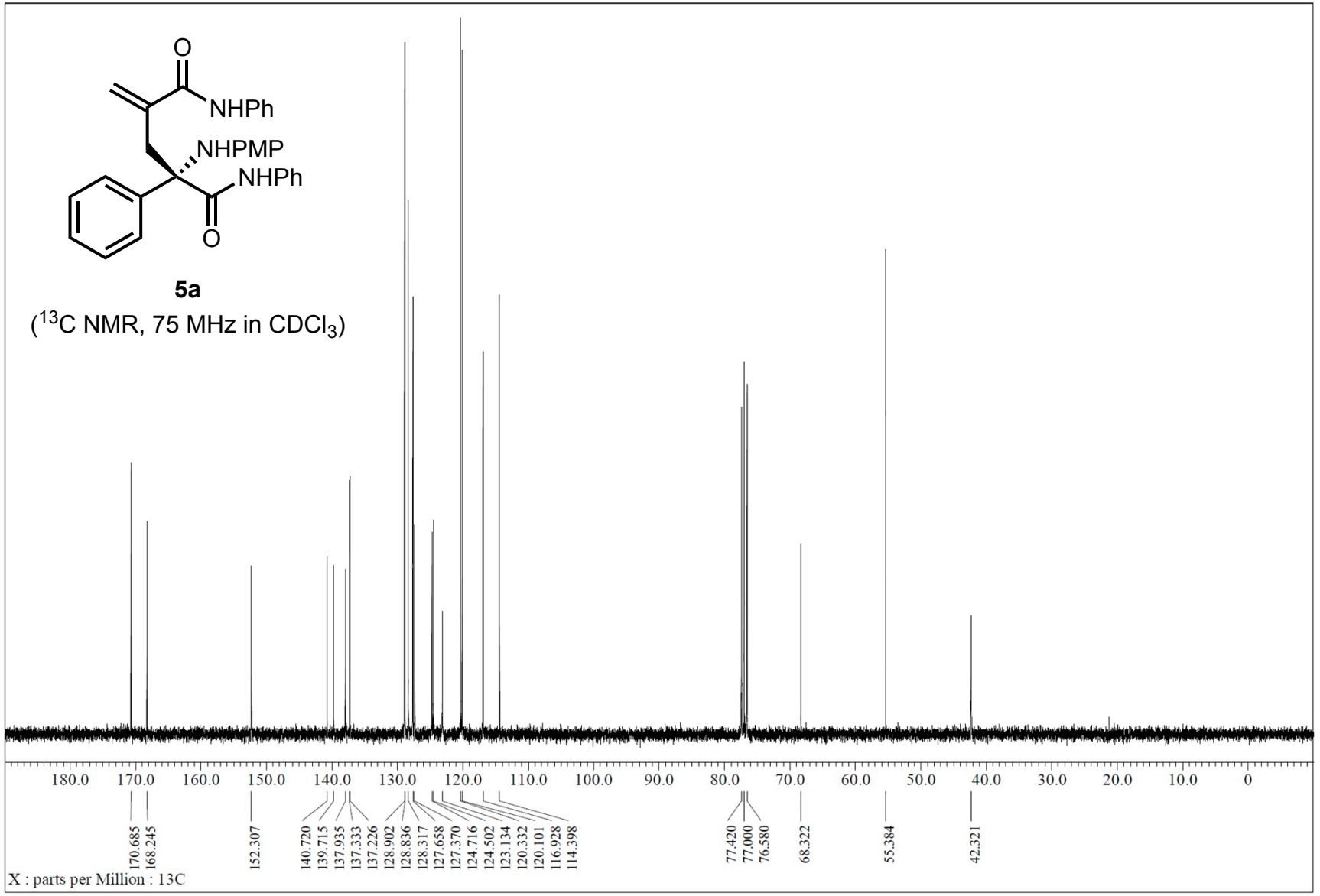

NPMP
NHPh
O
F3C
3c
(1H NMR, 300 MHz in CDCl3)
0.89
0.14
2.03
1.96
3.94
4.08
0.15
1.10
3.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.691
8.154
8.129
7.739
7.714
7.615
7.588
7.412
7.398
7.387
7.369
7.360
7.311
7.299
7.261
7.186
7.177
7.162
7.138
6.769
3.781
1.566
0.000
X : parts per Million : 1H

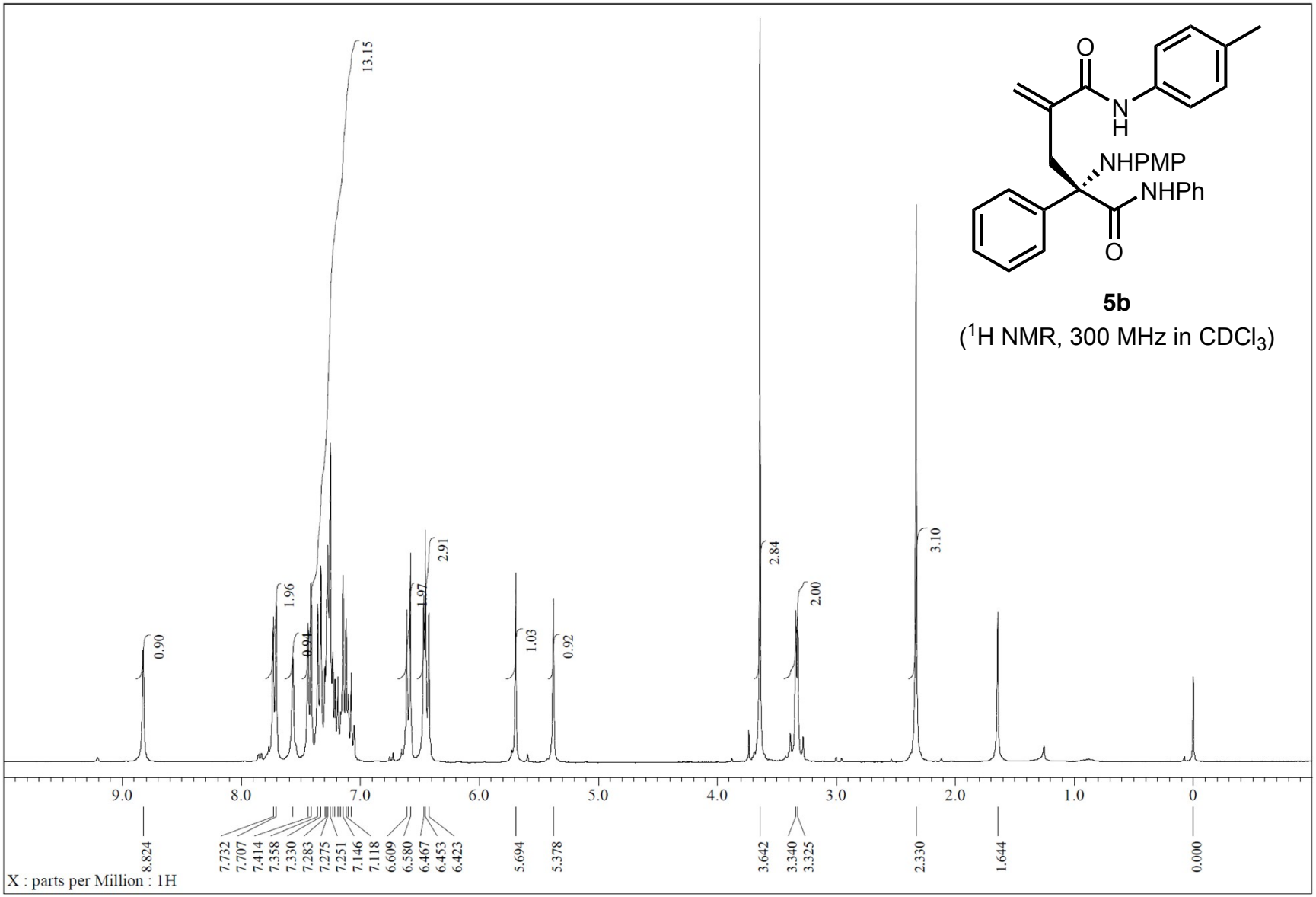

NPMP
NHPh
O
F3C
3c
(13C NMR, 75 MHz in CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
161.001
158.438
158.134
139.665
137.391
135.660
130.040
129.125
125.120
125.070
124.535
123.801
119.491
114.241
77.420
77.000
76.571
55.367
X : parts per Million : 13C


NPMP
NHPh
O
3d
(1H NMR, 300 MHz in CDCl3)
9.26
3.67
3.00
1.87
1.95
0.79
0.77
0.89
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.873
7.869
7.785
7.781
7.756
7.458
7.442
7.434
7.431
7.399
7.374
7.307
7.303
7.261
6.804
6.797
6.782
6.774
6.618
6.611
6.595
6.588
3.676
3.657
3.612
1.584
1.578
1.555
0.000
-0.011
X : parts per Million : 1H


NPMP
NHPh
O
3d
(^{13}C NMR, 75 MHz in $CDCl_3$)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
161.834
160.177
158.208
139.723
137.679
133.237
131.556
130.806
129.553
129.232
129.059
128.614
126.834
126.183
125.515
125.070
124.848
124.230
124.188
119.779
119.351
113.854
77.429
77.000
76.580
55.194
X : parts per Million : 13C

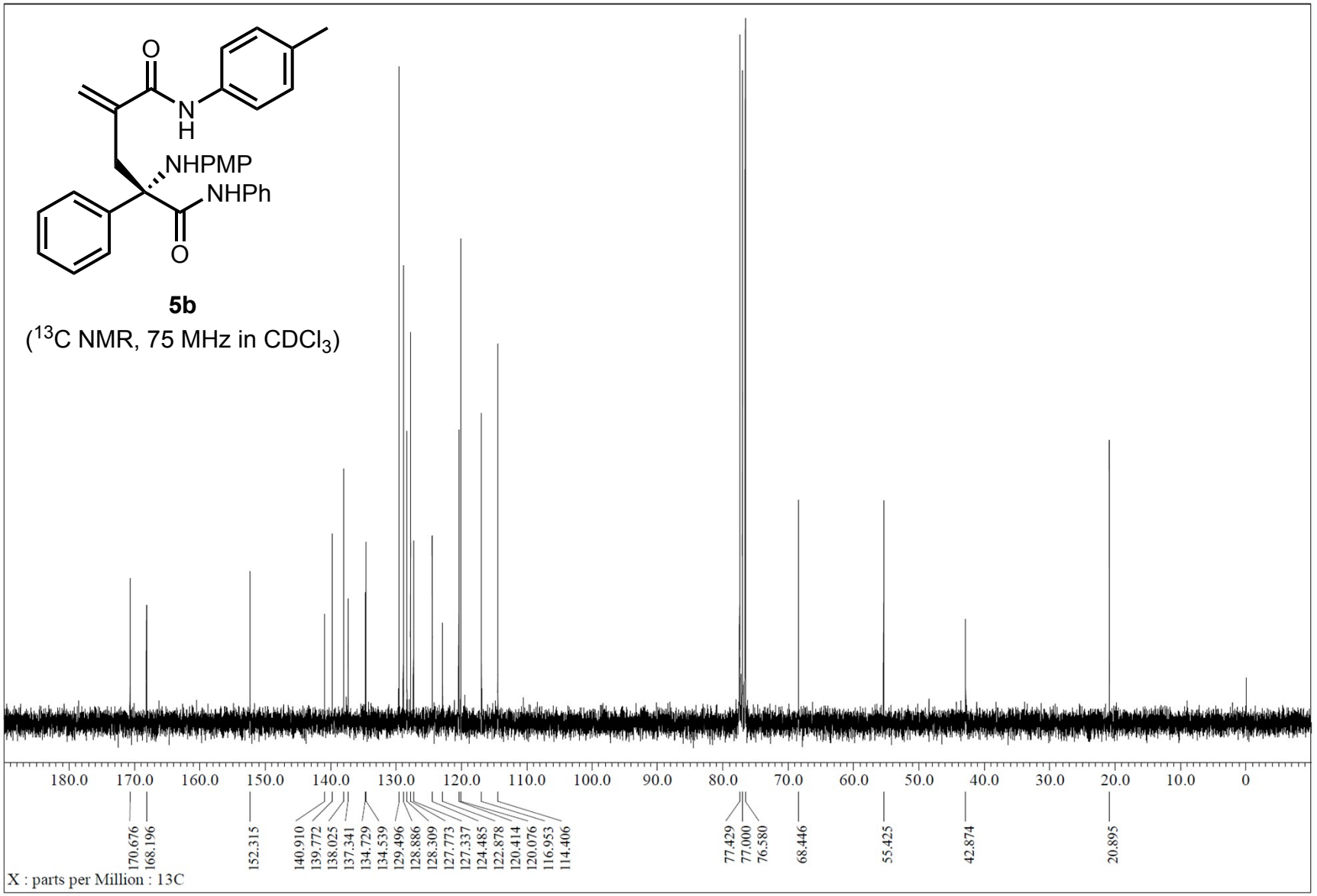

O
NHPh
NHPMP
NHPh
O
5a
(1H NMR, 300 MHz in CDCl3)
9.51
3.76
3.22
2.87
2.07
3.32
2.12
1.01
1.00
1.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.783
7.716
7.691
7.441
7.414
7.389
7.303
7.276
7.262
7.232
7.206
6.601
6.571
6.450
6.420
6.398
5.694
5.343
3.622
3.390
3.343
3.331
3.284
0.000
X : parts per Million : 1H

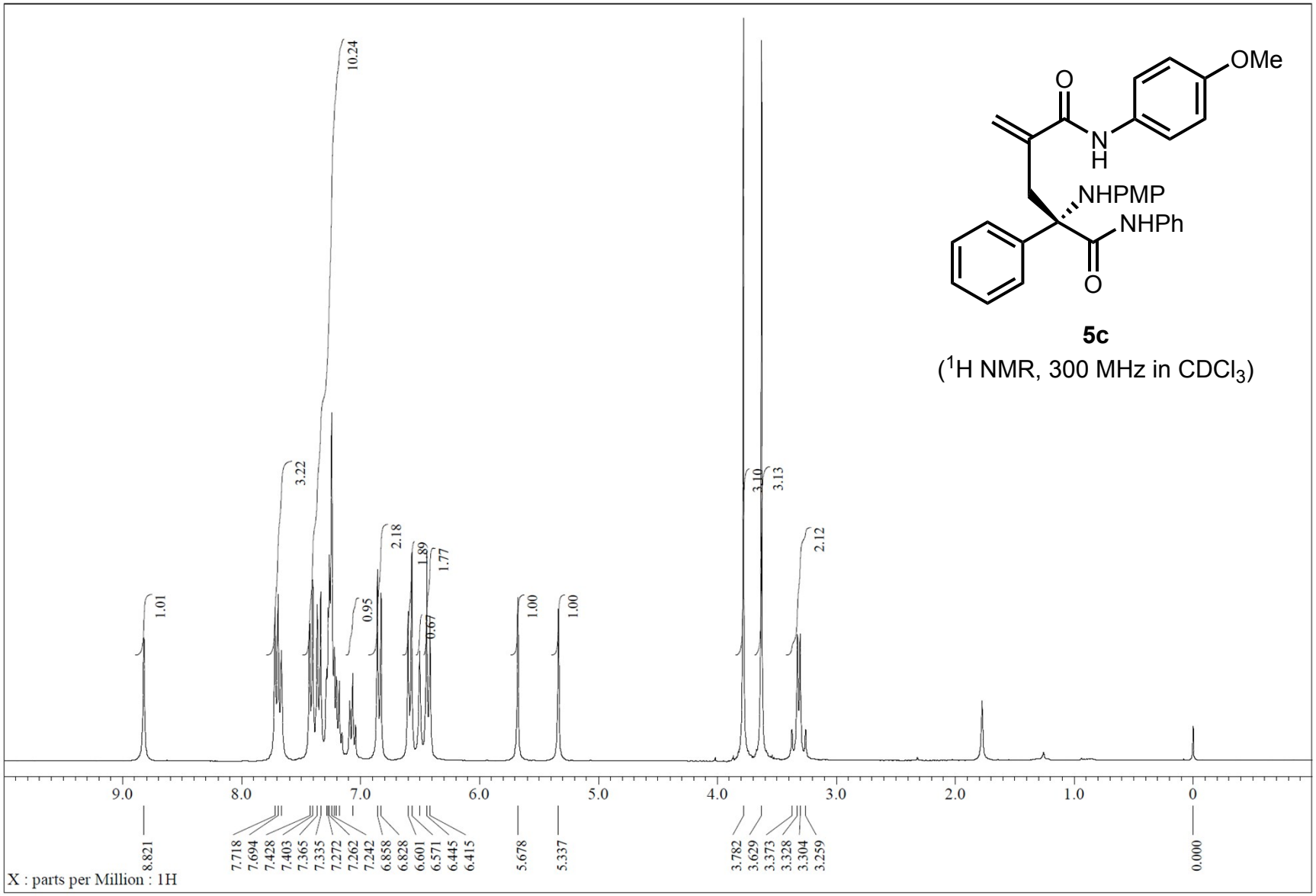

O
NHPh
NHPMP
NHPh
O
5a
(13C NMR, 75 MHz in CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
170.685
168.245
152.307
140.720
139.715
137.935
137.333
137.226
128.902
128.836
128.317
127.658
127.370
124.716
124.502
123.134
120.332
120.101
116.928
114.398
77.420
77.000
76.580
68.322
55.384
42.321
X : parts per Million : 13C

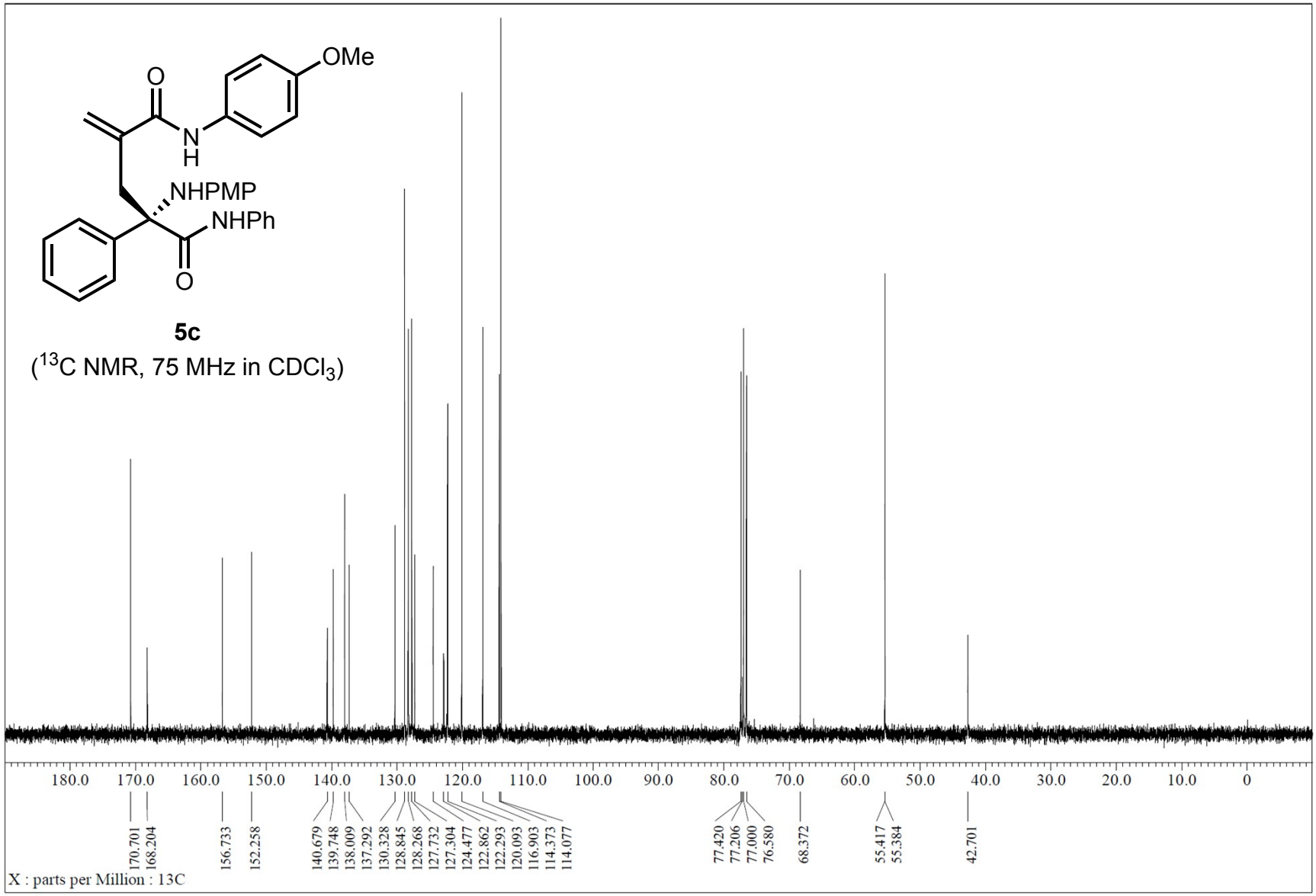


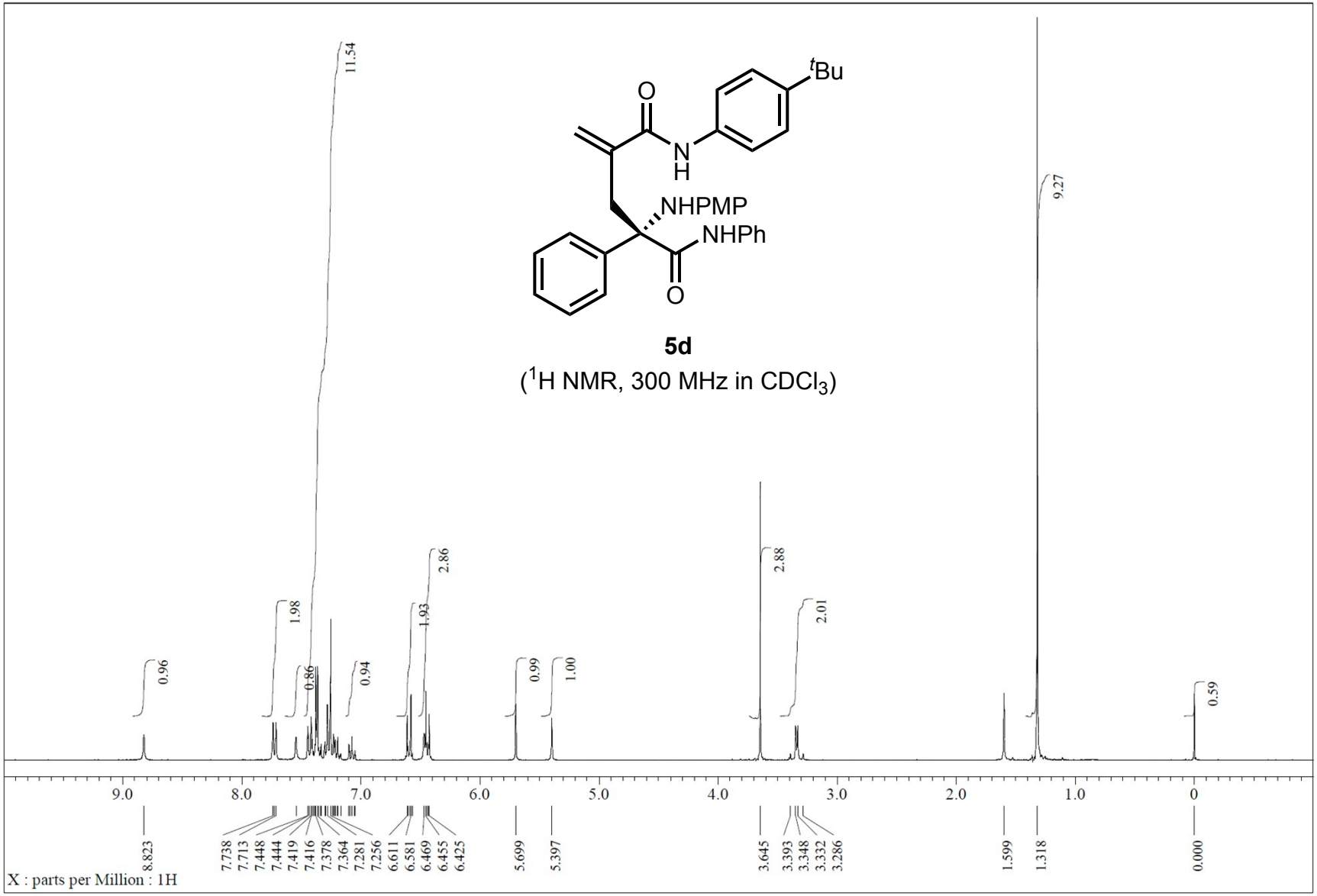
5b

(^{1}H NMR, 300 MHz in $CDCl_3$)


O
N
H
NHPMP
NHPh
O
5b
(13C NMR, 75 MHz in CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
170.676
168.196
152.315
140.910
139.772
138.025
137.341
134.729
134.539
129.496
128.886
128.309
127.773
127.337
124.485
122.878
120.414
120.076
116.953
114.406
77.429
77.000
76.580
68.446
55.425
42.874
20.895
X : parts per Million : 13C

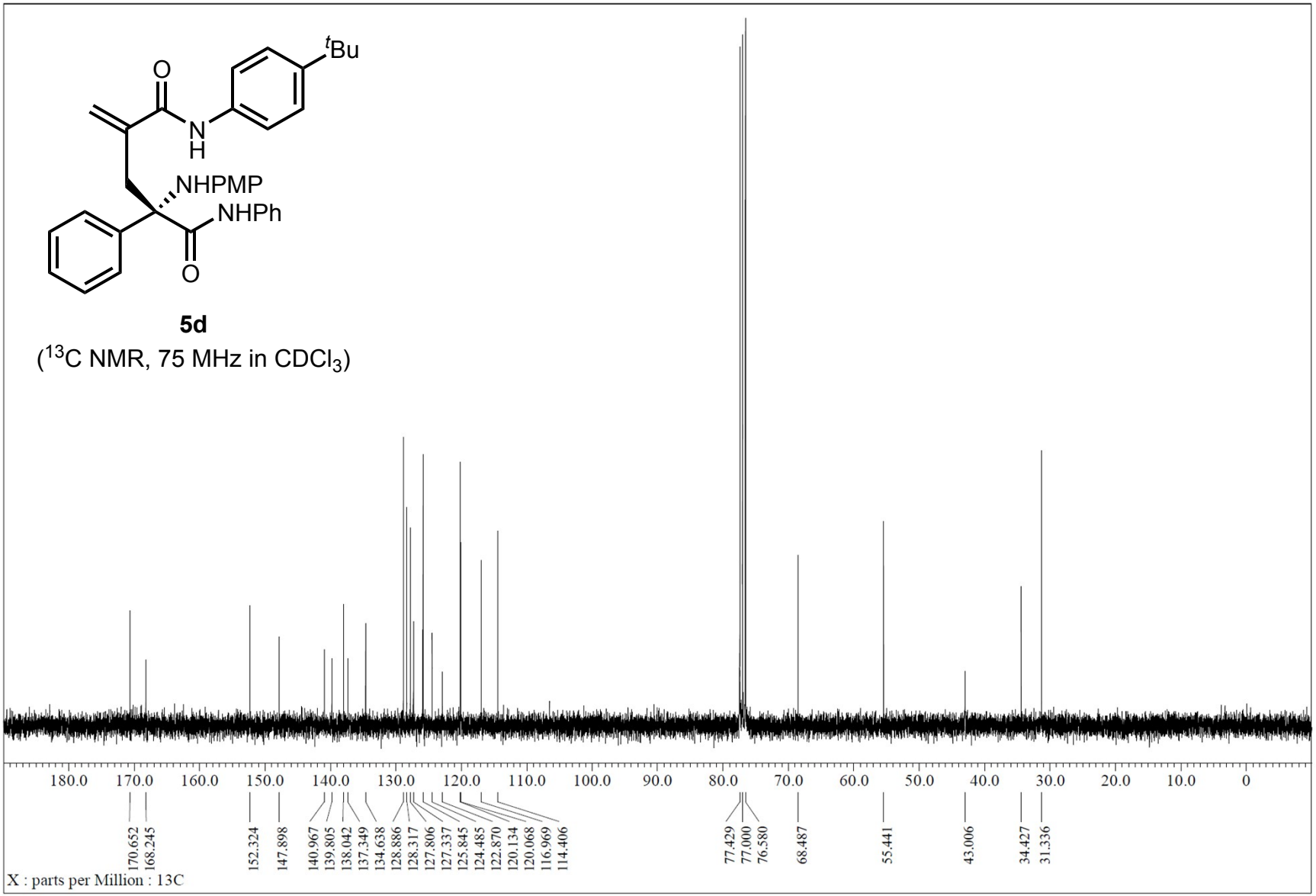

OMe
O
N
H
NHPMP
NHPh
O
5c
(1H NMR, 300 MHz in CDCl3)
10.24
3.22
2.18
1.89
1.77
0.95
0.67
1.01
1.00
1.00
3.10
3.13
2.12
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.821
7.718
7.694
7.428
7.403
7.365
7.335
7.272
7.262
7.242
6.858
6.828
6.601
6.571
6.445
6.415
5.678
5.337
3.782
3.629
3.373
3.328
3.304
3.259
0.000
X : parts per Million : 1H

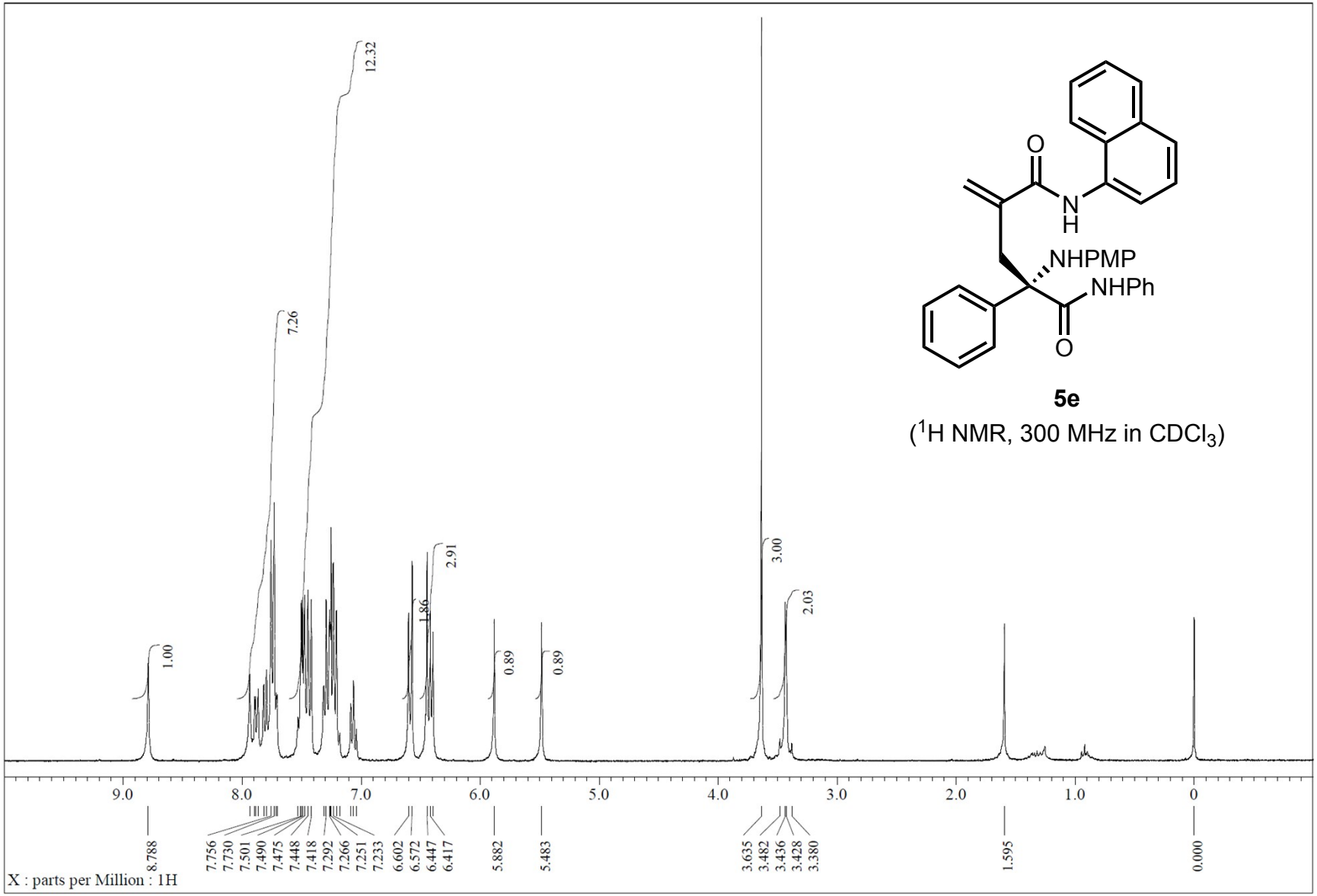

OMe
O
N
H
NHPMP
NHPh
O
5c
(13C NMR, 75 MHz in CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
170.701
168.204
156.733
152.258
140.679
139.748
138.009
137.292
130.328
128.845
128.268
127.732
127.304
124.477
122.862
122.293
120.093
116.903
114.373
114.077
77.420
77.206
77.000
76.580
68.372
55.417
55.384
42.701
X : parts per Million : 13C

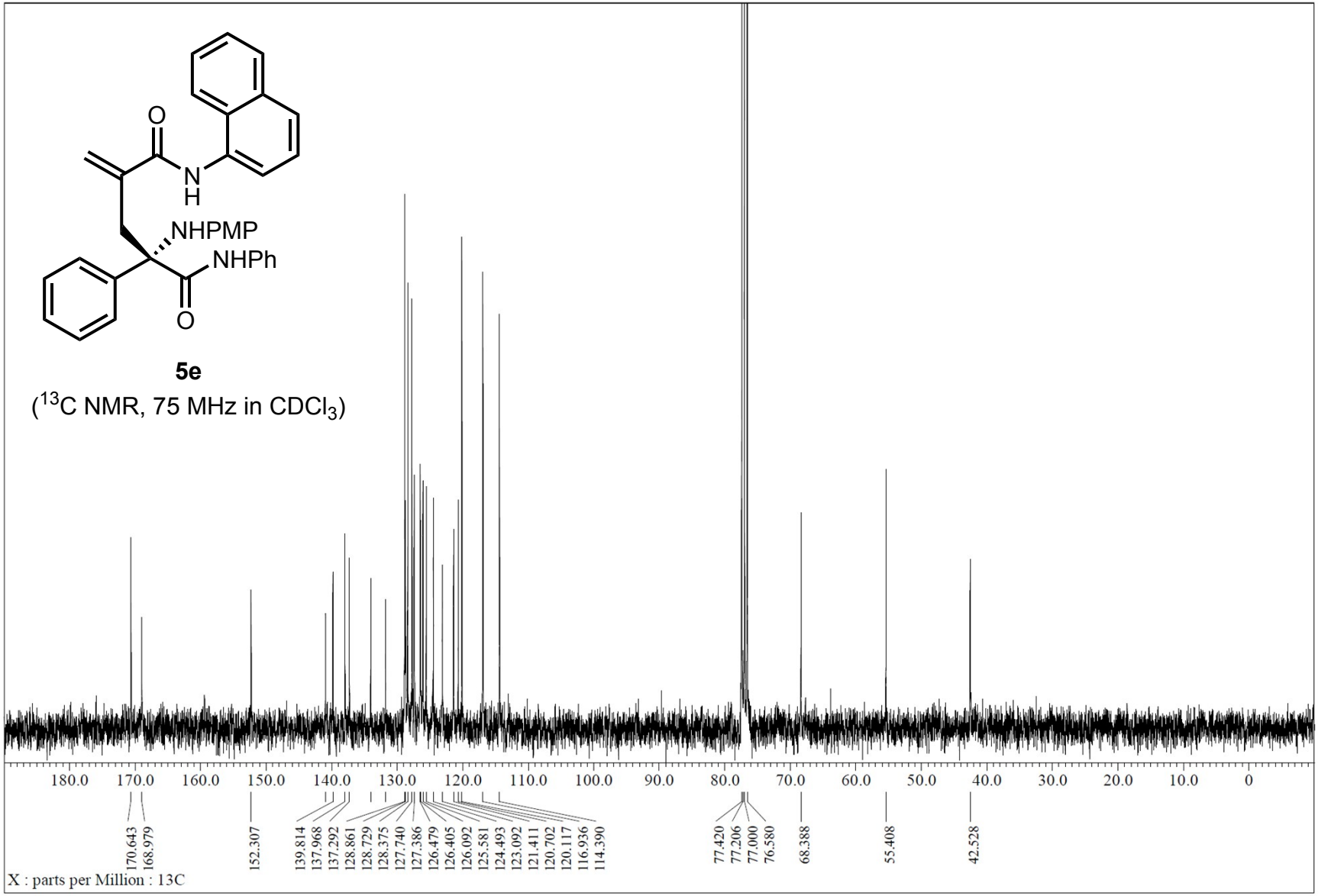


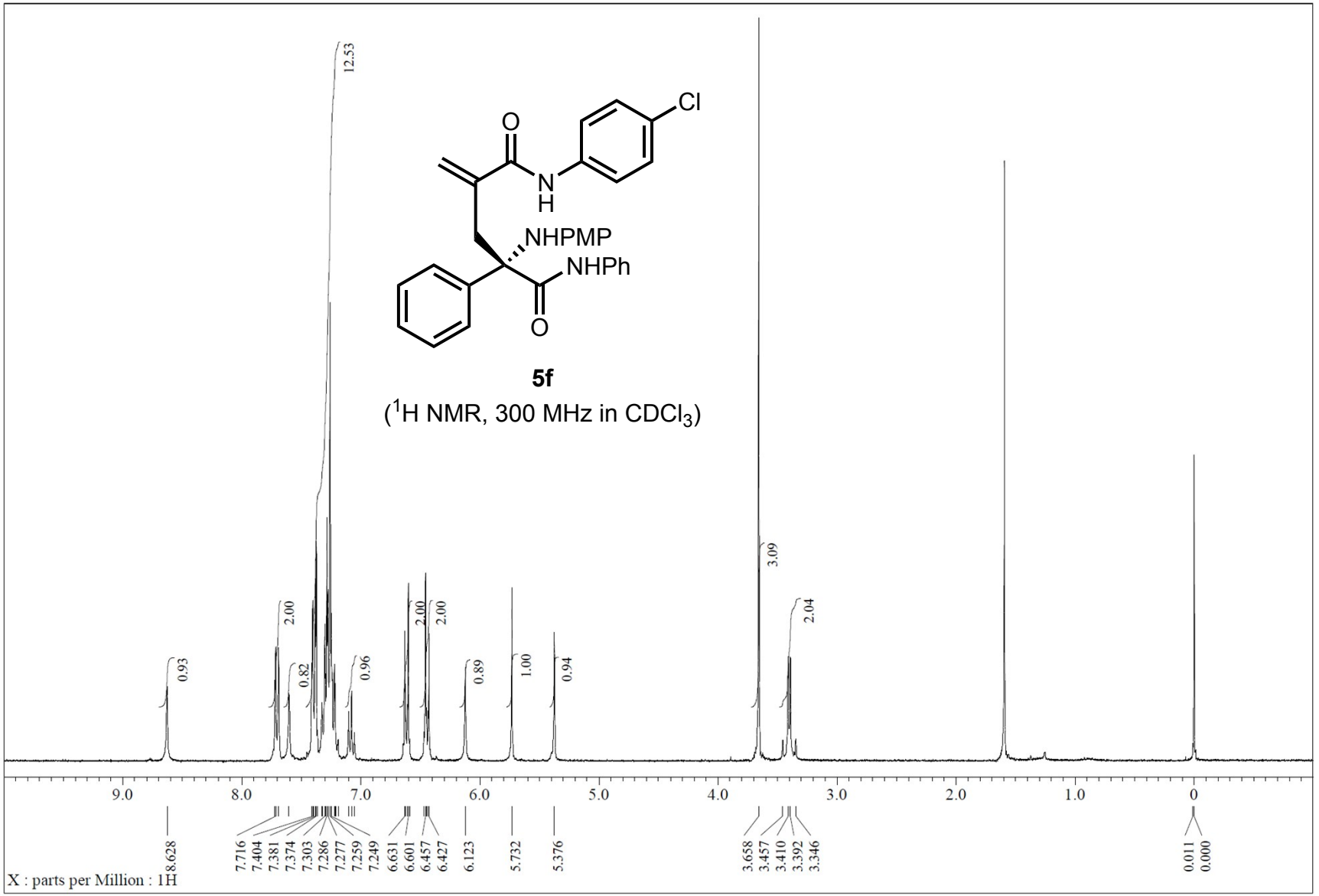
5d

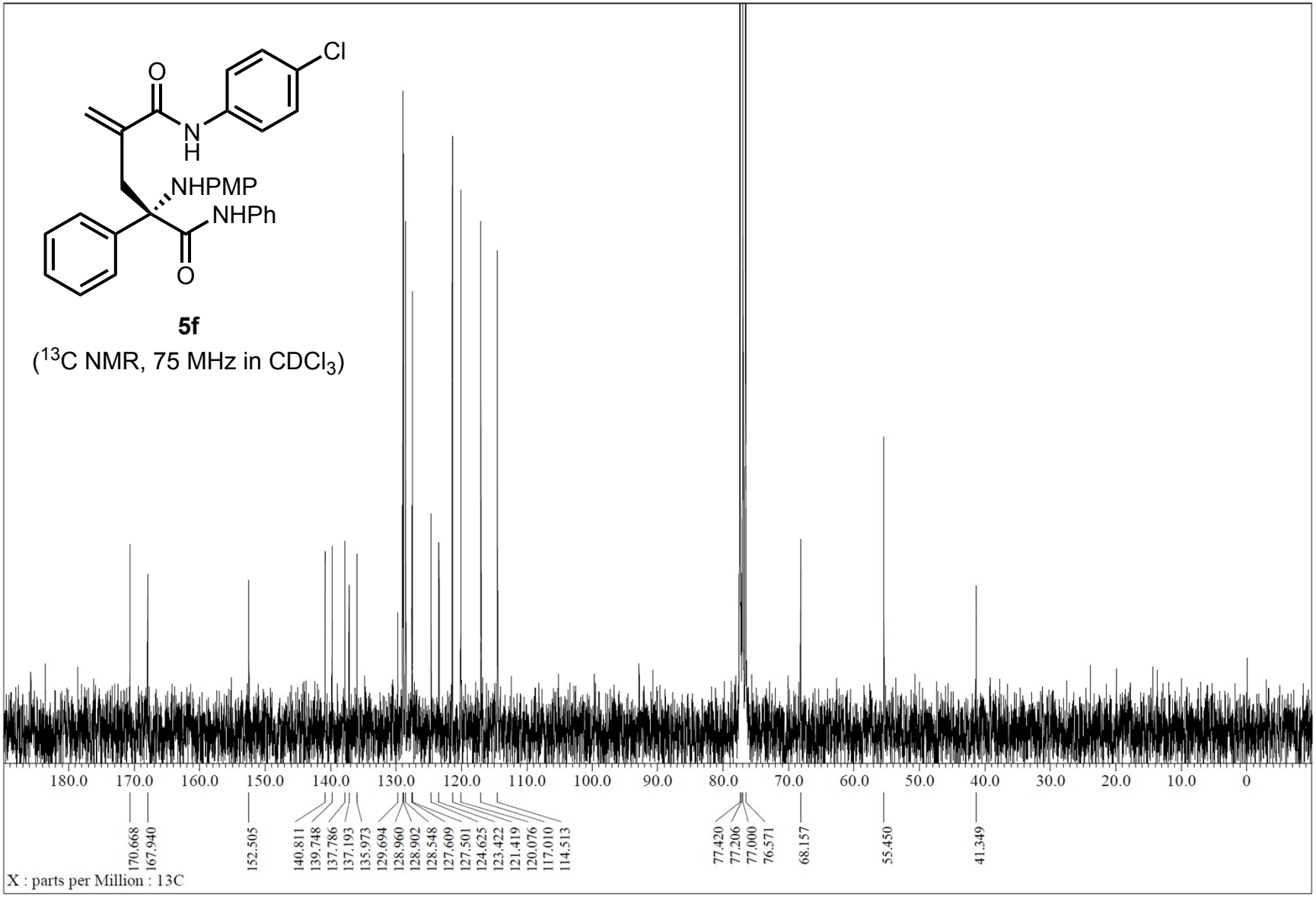
(^{1}H NMR, 300 MHz in $CDCl_3$)

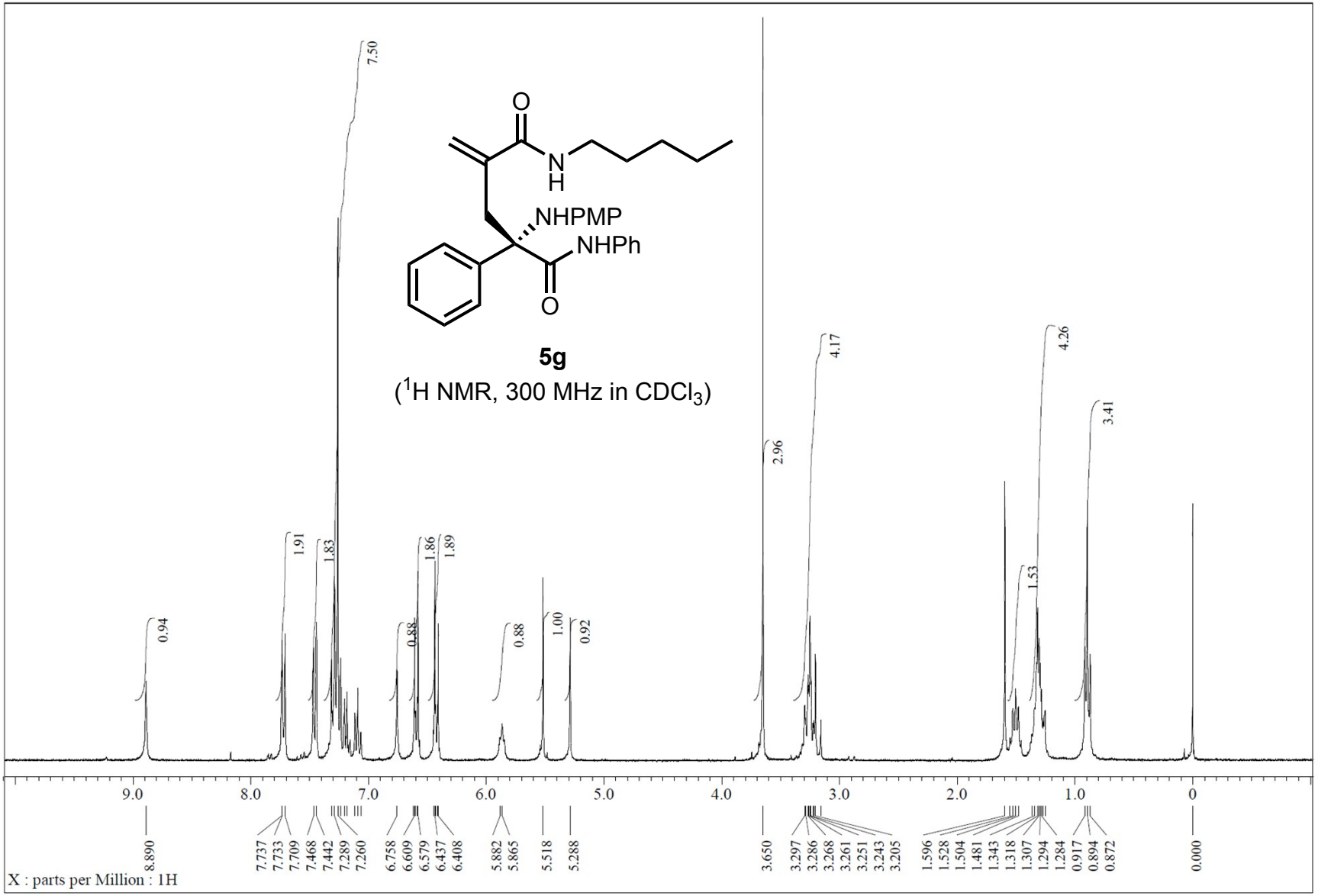

tBu
O
N
H
NHPMP
NHPh
O
5d
(13C NMR, 75 MHz in CDCl3)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
170.652
168.245
152.324
147.898
140.967
139.805
138.042
137.349
134.638
128.886
128.317
127.806
127.337
125.845
124.485
122.870
120.134
120.068
116.969
114.406
77.429
77.000
76.580
68.487
55.441
43.006
34.427
31.336
X : parts per Million : 13C

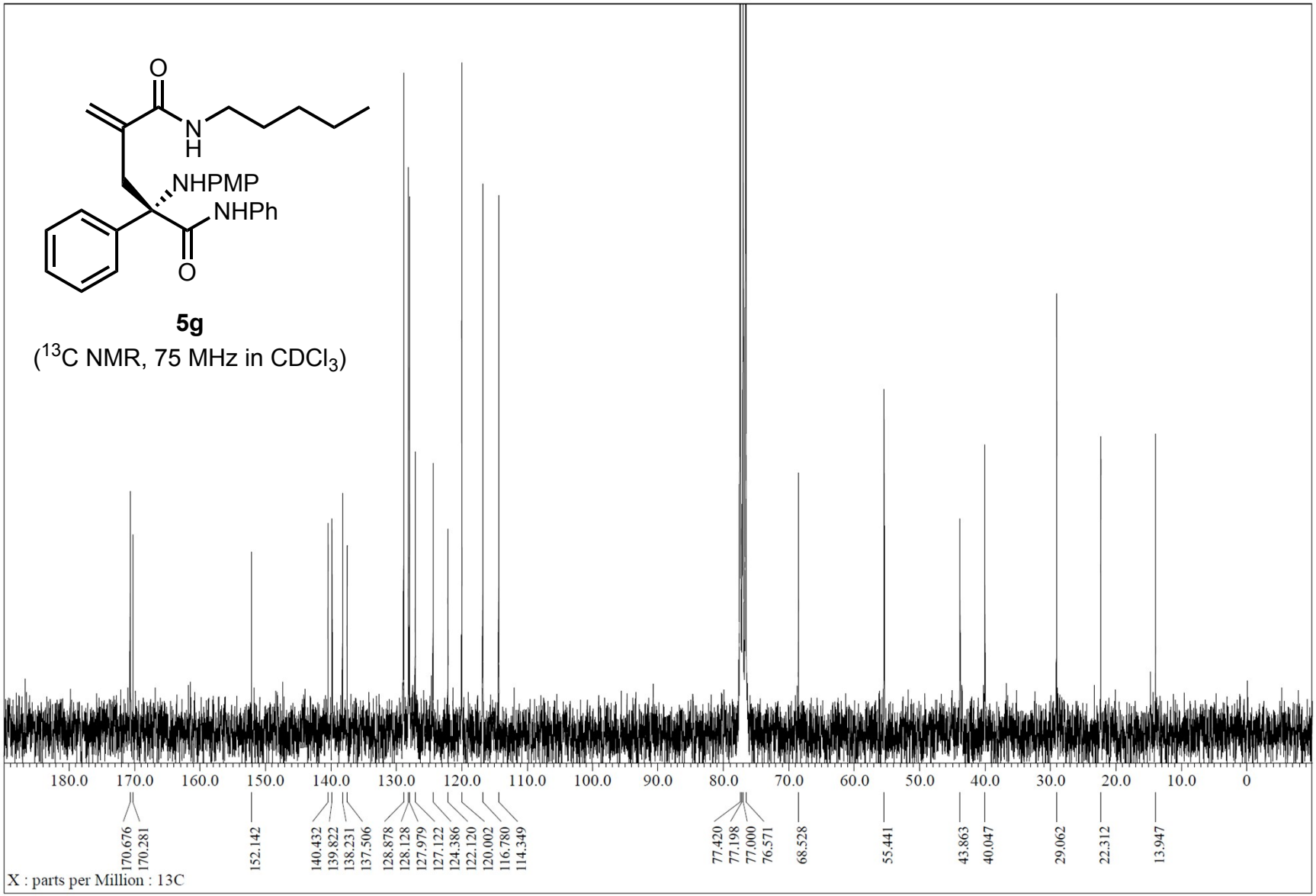

12.32
7.26
2.91
1.86
1.00
0.89
0.89
3.00
2.03
O
N
H
NHPMP
NHPh
O
5e
(1H NMR, 300 MHz in CDCl3)
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.788
7.756
7.730
7.501
7.490
7.475
7.448
7.418
7.292
7.266
7.251
7.233
6.602
6.572
6.447
6.417
5.882
5.483
3.635
3.482
3.436
3.428
3.380
1.595
0.000
X : parts per Million : 1H

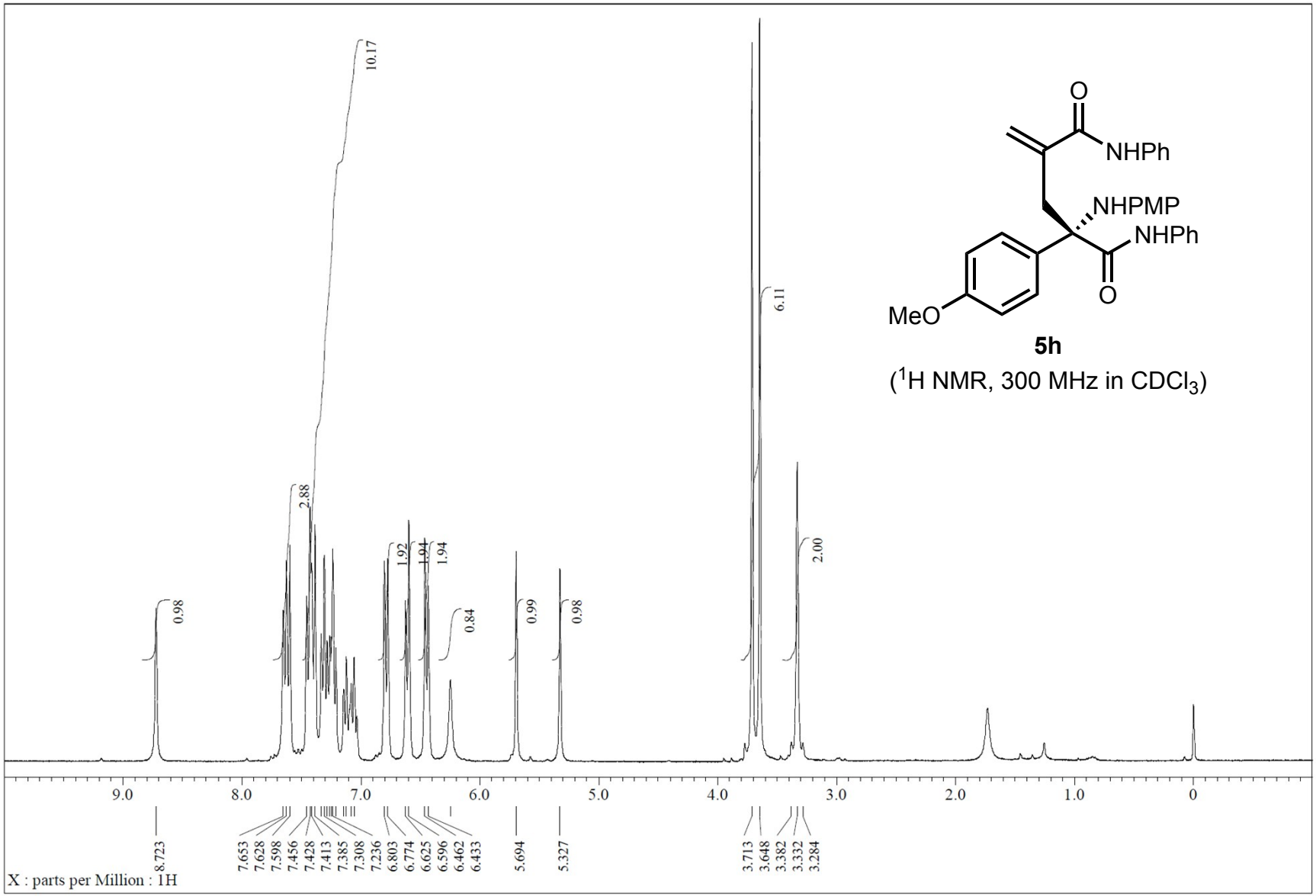

O
N
H
NHPMP
NHPh
O
5e
(13C NMR, 75 MHz in CDCl3)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
170.643
168.979
152.307
139.814
137.968
137.292
128.861
128.729
128.375
127.740
127.386
126.479
126.405
126.092
125.581
124.493
123.092
121.411
120.702
120.117
116.936
114.390
77.420
77.206
77.000
76.580
68.388
55.408
42.528
X : parts per Million : 13C

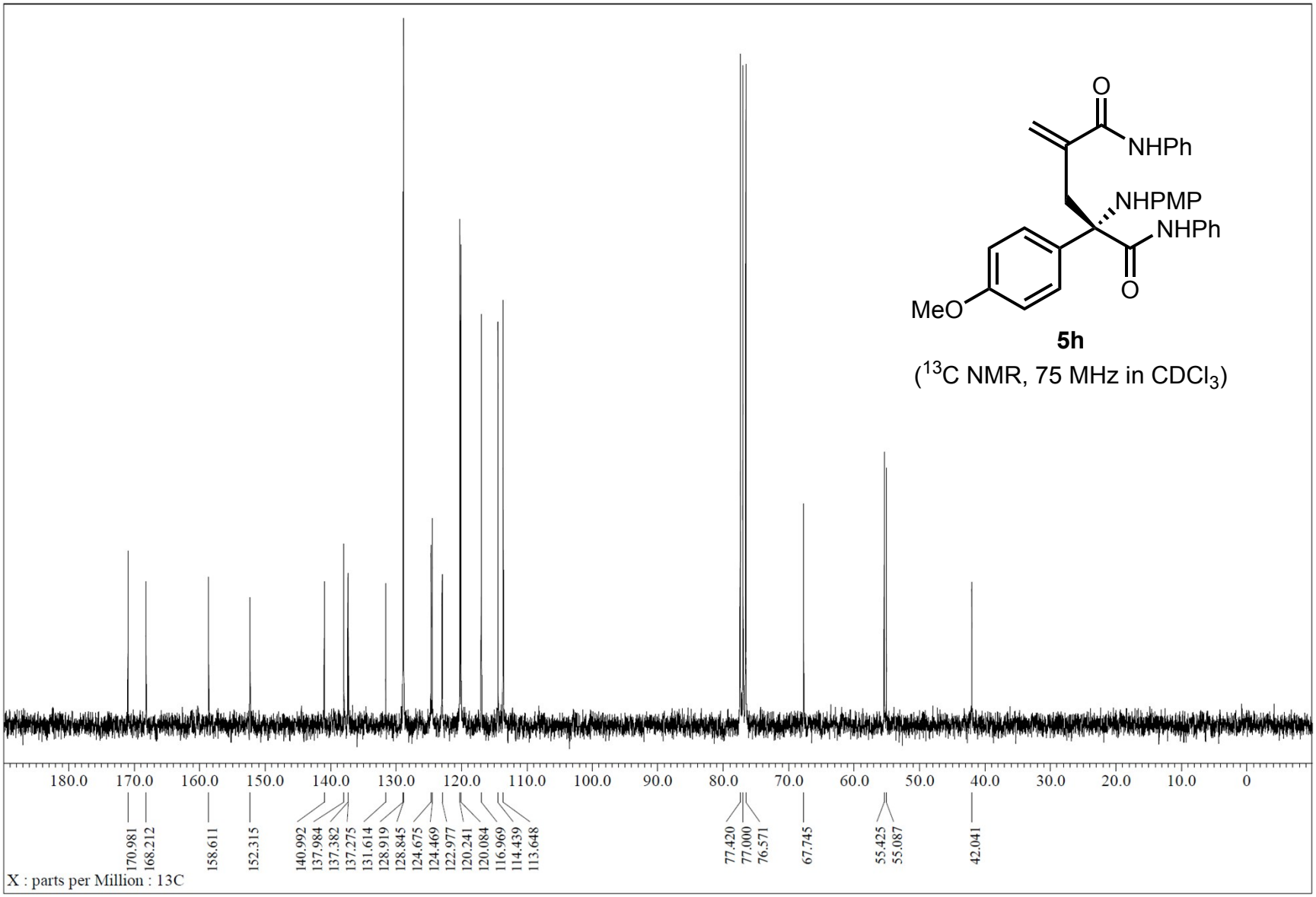

12.53
Cl
O
N
H
NHPMP
NHPh
O
5f
(1H NMR, 300 MHz in CDCl3)
0.93
2.00
0.82
0.96
2.00
2.00
0.89
1.00
0.94
3.09
2.04
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.628
7.716
7.404
7.381
7.374
7.303
7.286
7.277
7.259
7.249
6.631
6.601
6.457
6.427
6.123
5.732
5.376
3.658
3.457
3.410
3.392
3.346
0.011
0.000
X : parts per Million : 1H

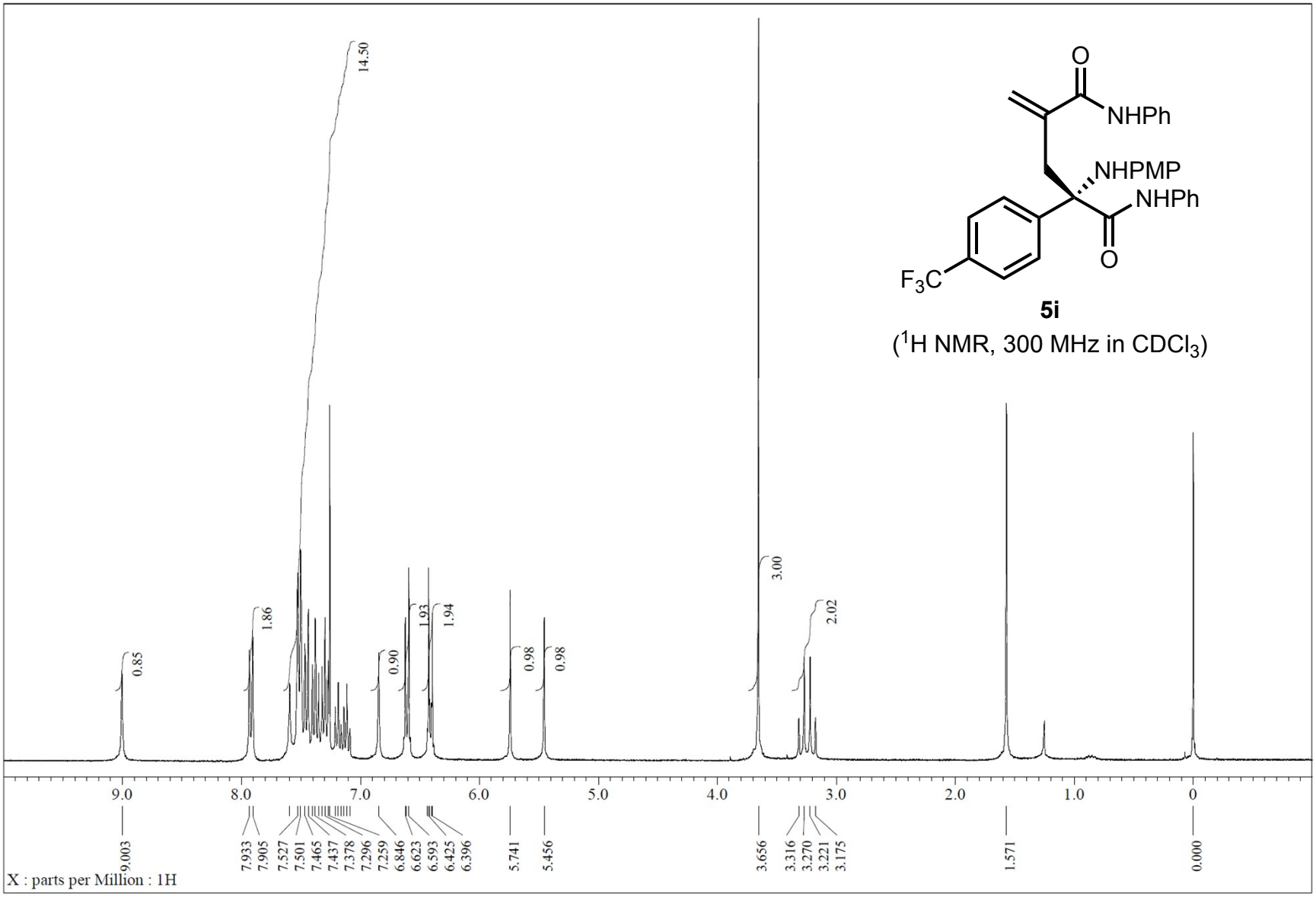

Cl
O
N
H
NHPMP
NHPh
O
5f
(^{13}C NMR, 75 MHz in $CDCl_3$)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
170.668
167.940
152.505
140.811
139.748
137.786
137.193
135.973
129.694
128.960
128.902
128.548
127.609
127.501
124.625
123.422
121.419
120.076
117.010
114.513
77.420
77.206
77.000
76.571
68.157
55.450
41.349
X : parts per Million : 13C

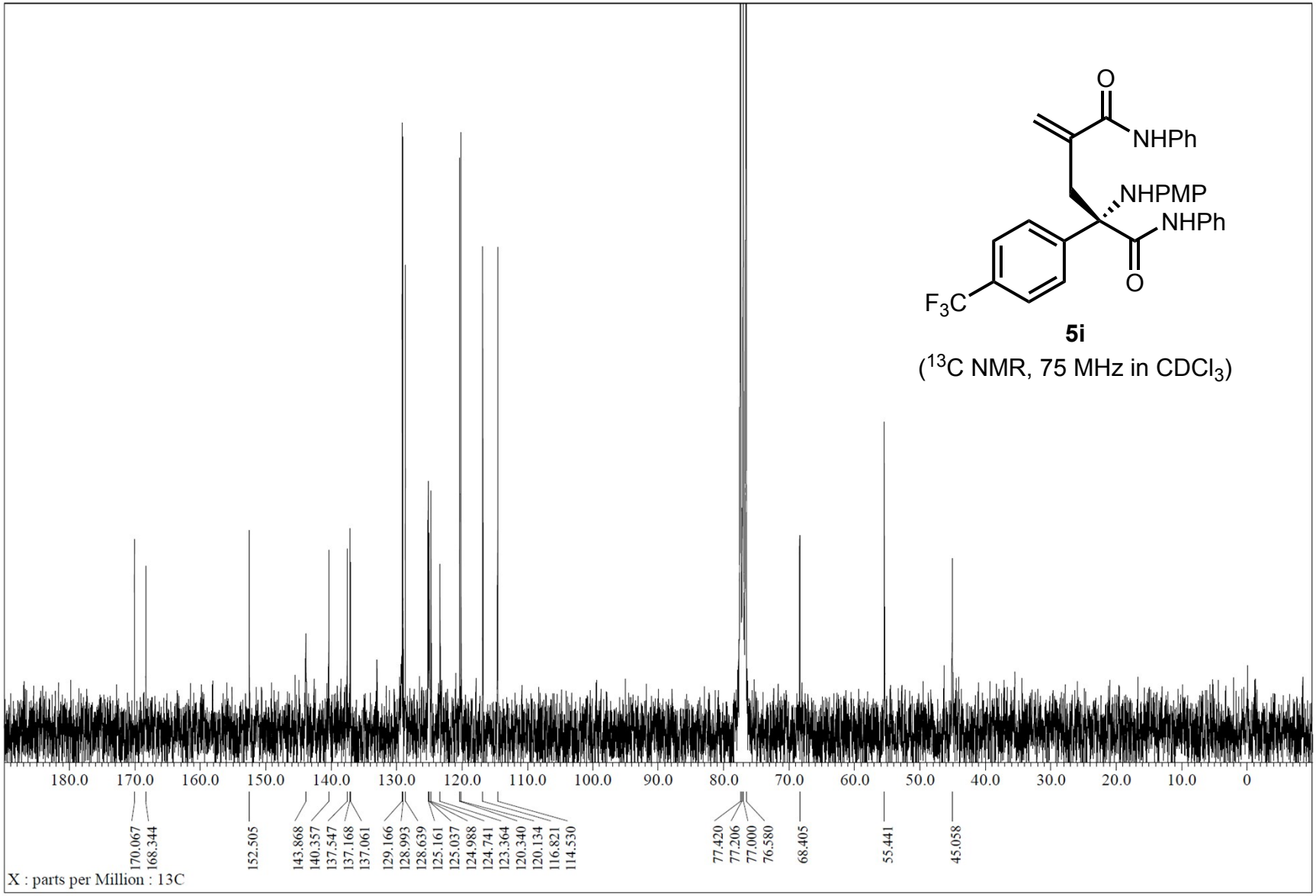

O
N
H
NHPMP
NHPh
O
5g
(1H NMR, 300 MHz in CDCl3)
7.50
4.17
4.26
3.41
2.96
1.91
1.83
1.86
1.89
1.53
0.94
0.88
0.88
1.00
0.92
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.890
7.737
7.733
7.709
7.468
7.442
7.289
7.260
6.758
6.609
6.579
6.437
6.408
5.882
5.865
5.518
5.288
3.650
3.297
3.286
3.268
3.261
3.251
3.243
3.205
1.596
1.528
1.504
1.481
1.343
1.318
1.307
1.294
1.284
0.917
0.894
0.872
0.000
X : parts per Million : 1H

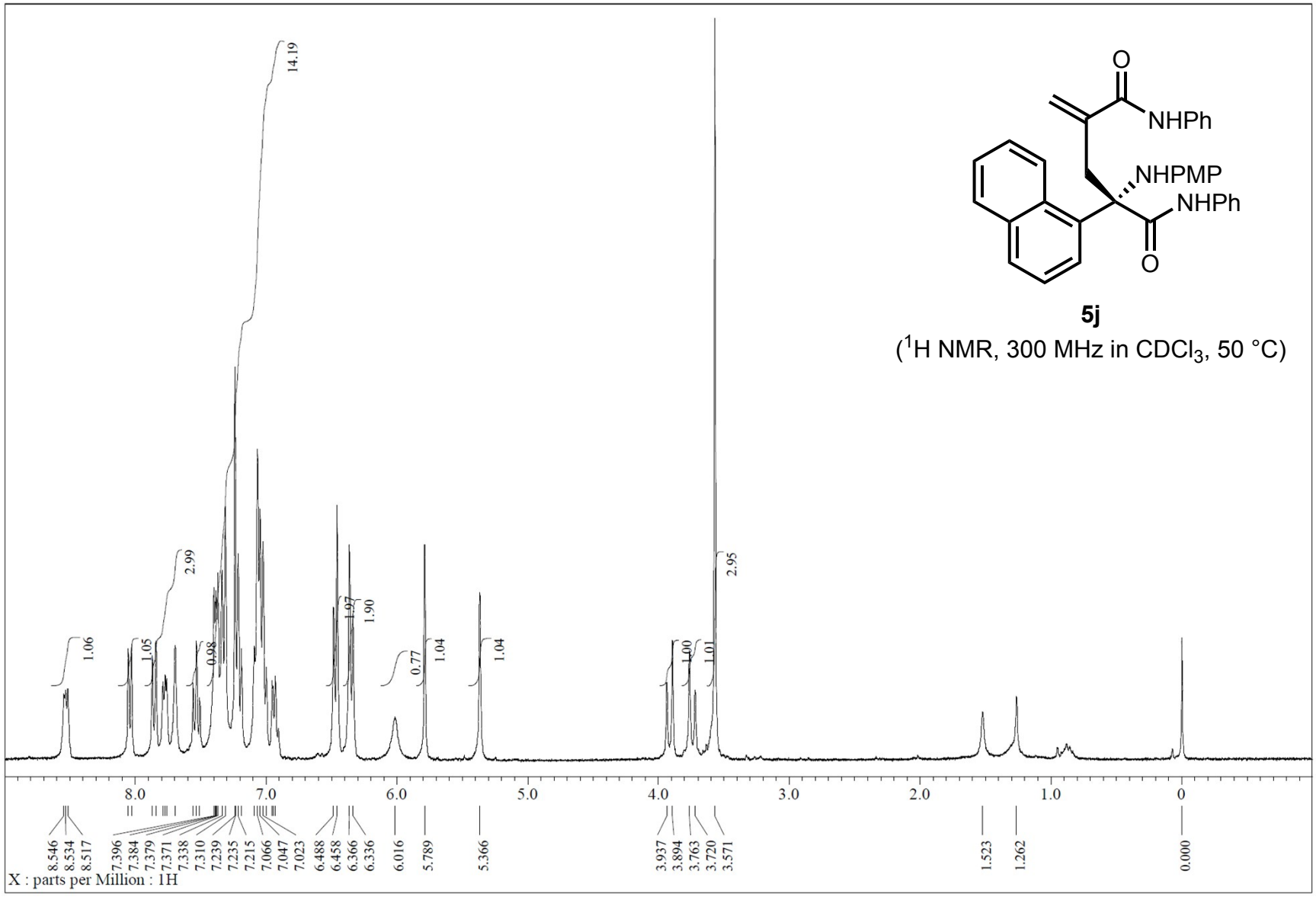

O
N
H
NHPMP
NHPh
O
5g
(13C NMR, 75 MHz in CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
170.676
170.281
152.142
140.432
139.822
138.231
137.506
128.878
128.128
127.979
127.122
124.386
122.120
120.002
116.780
114.349
77.420
77.198
77.000
76.571
68.528
55.441
43.863
40.047
29.062
22.312
13.947
X : parts per Million : 13C

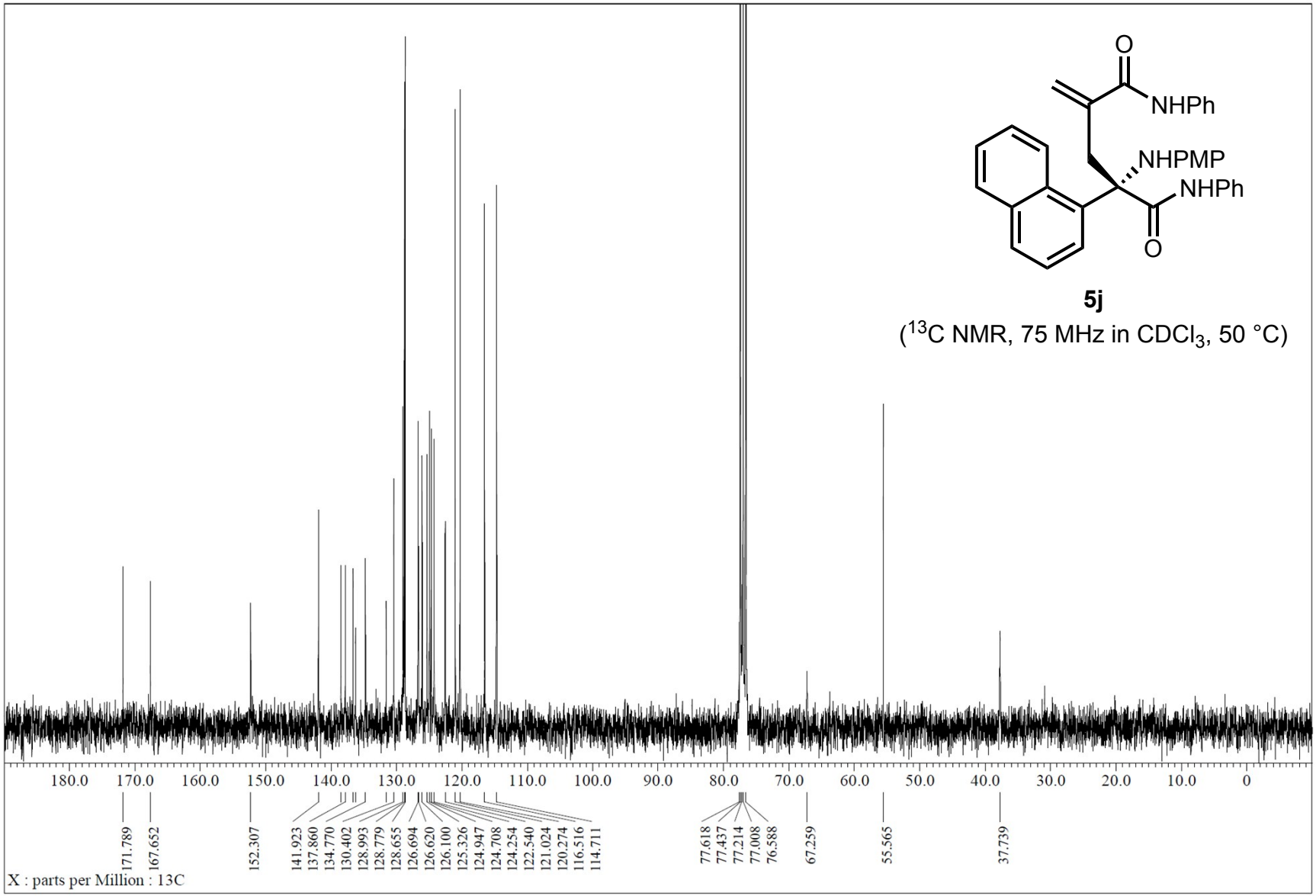

10.17
6.11
2.88
2.00
1.92
1.94
1.94
0.98
0.84
0.99
0.98
O
NHPh
NHPMP
NHPh
O
MeO
5h
(1H NMR, 300 MHz in CDCl3)
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.723
7.653
7.628
7.598
7.456
7.428
7.413
7.385
7.308
7.236
6.803
6.774
6.625
6.596
6.462
6.433
5.694
5.327
3.713
3.648
3.382
3.332
3.284
X : parts per Million : 1H

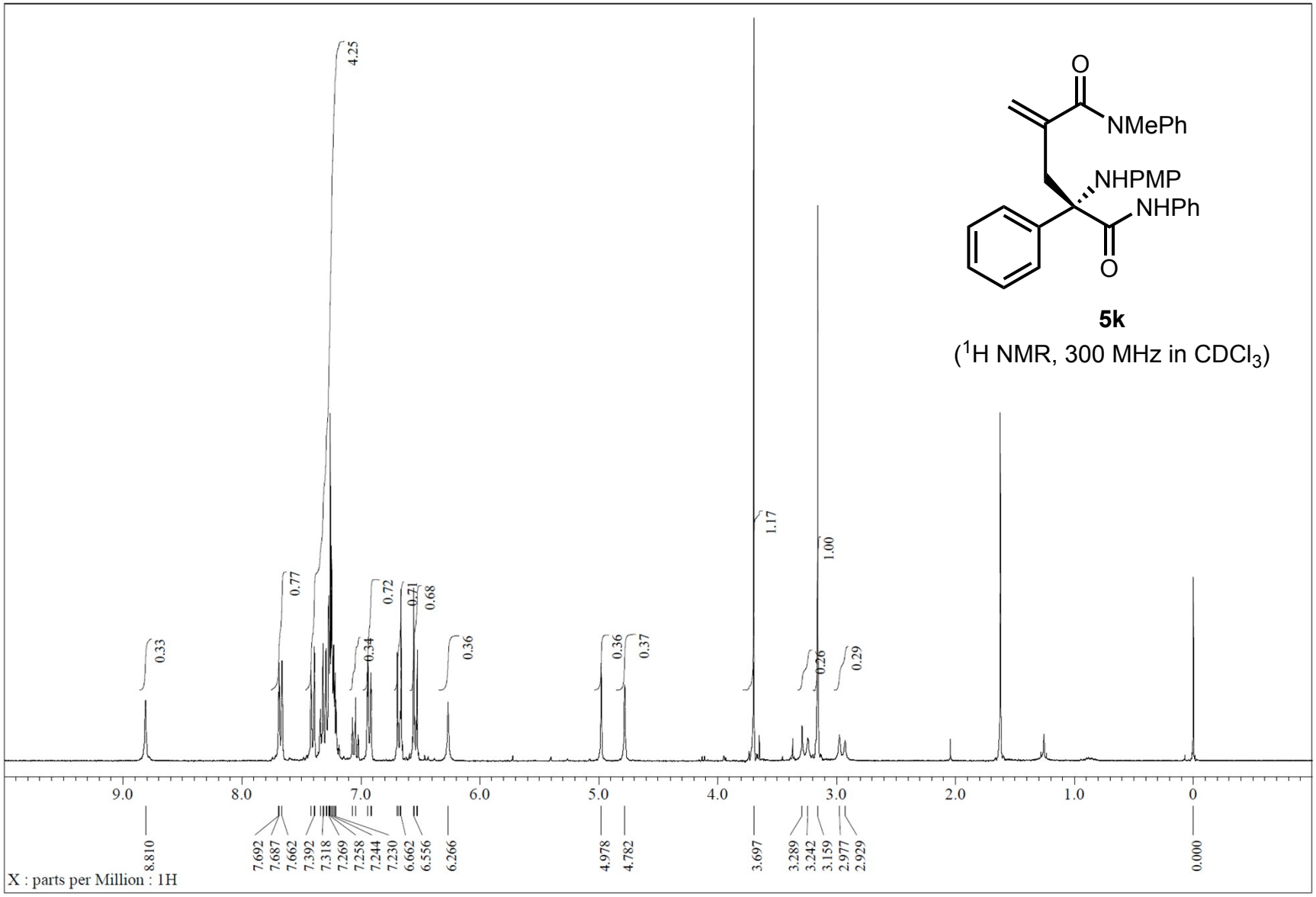

O
NHPh
NHPMP
NHPh
O
MeO
5h
(13C NMR, 75 MHz in CDCl3)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
170.981
168.212
158.611
152.315
140.992
137.984
137.382
137.275
131.614
128.919
128.845
124.675
124.469
122.977
120.241
120.084
116.969
114.439
113.648
77.420
77.000
76.571
67.745
55.425
55.087
42.041
X : parts per Million : 13C

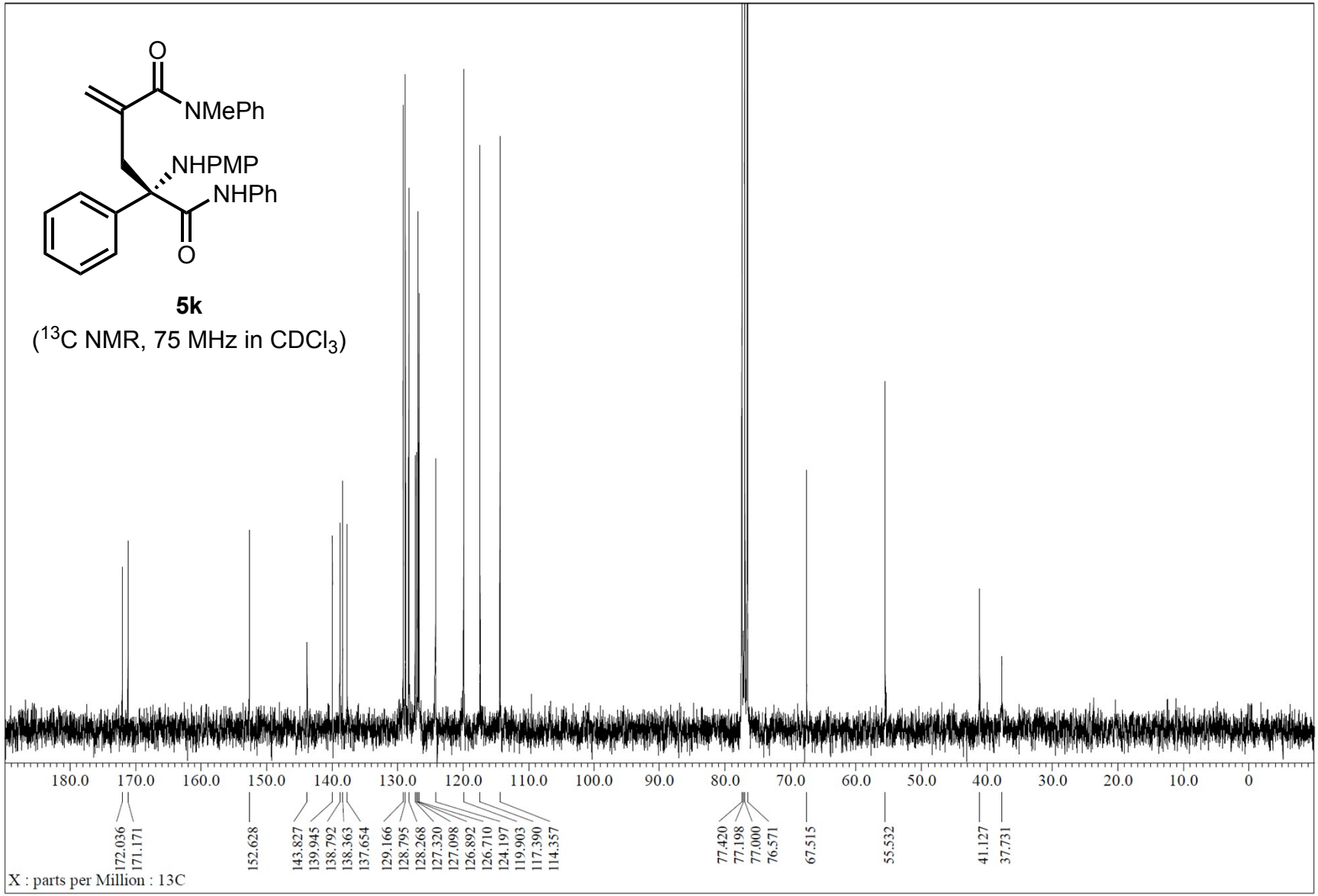

O
NHPh
NHPMP
NHPh
O
F3C
5i
(1H NMR, 300 MHz in CDCl3)
14.50
0.85
1.86
1.93
1.94
0.90
0.98
0.98
3.00
2.02
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.003
7.933
7.905
7.527
7.501
7.465
7.437
7.378
7.296
7.259
6.846
6.623
6.593
6.425
6.396
5.741
5.456
3.656
3.316
3.270
3.221
3.175
1.571
0.000
X : parts per Million : 1H

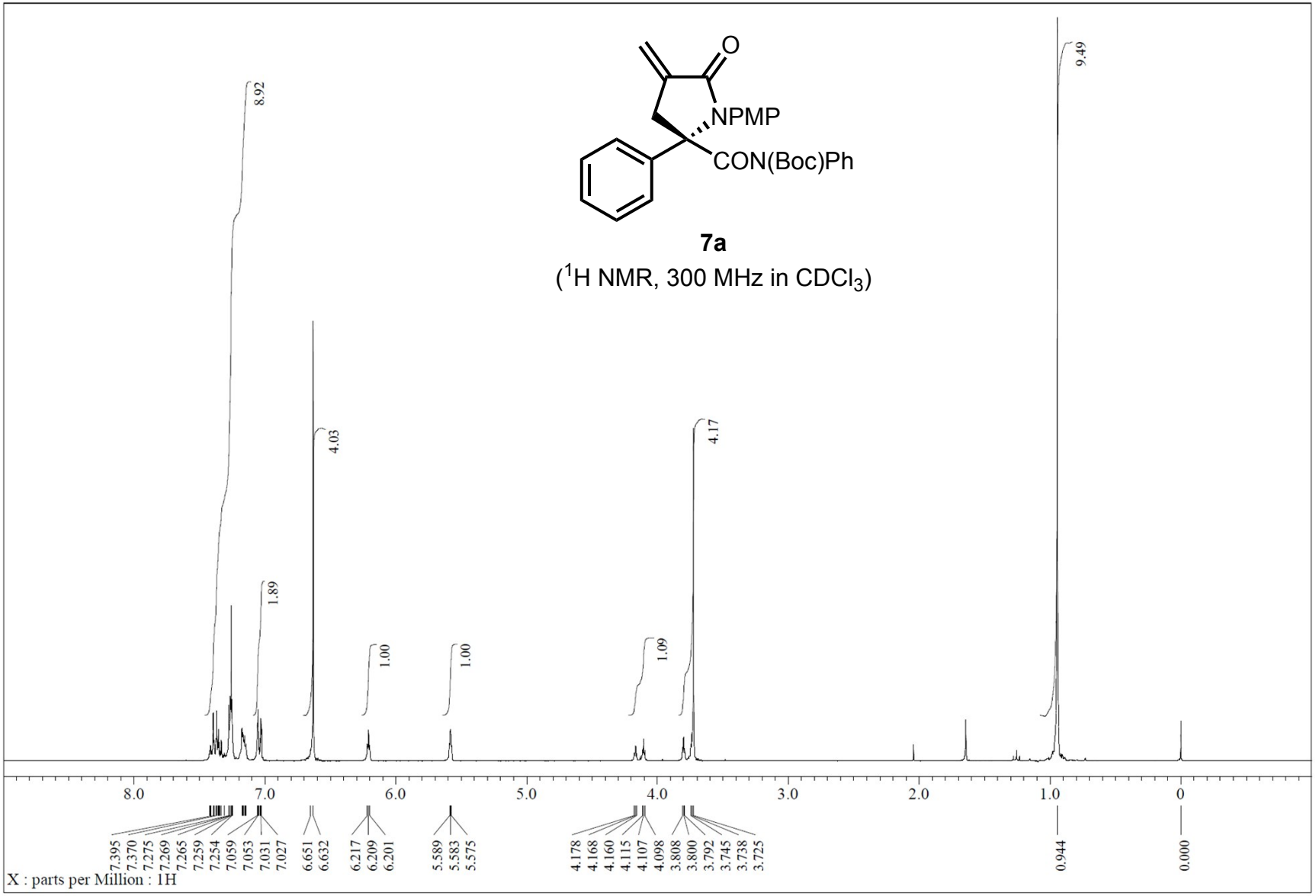

O
NHPh
NHPMP
NHPh
O
F3C
5i
(13C NMR, 75 MHz in CDCl3)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
170.067
168.344
152.505
143.868
140.357
137.547
137.168
137.061
129.166
128.993
128.639
125.161
125.037
124.988
124.741
123.364
120.340
120.134
116.821
114.530
77.420
77.206
77.000
76.580
68.405
55.441
45.058
X : parts per Million : 13C

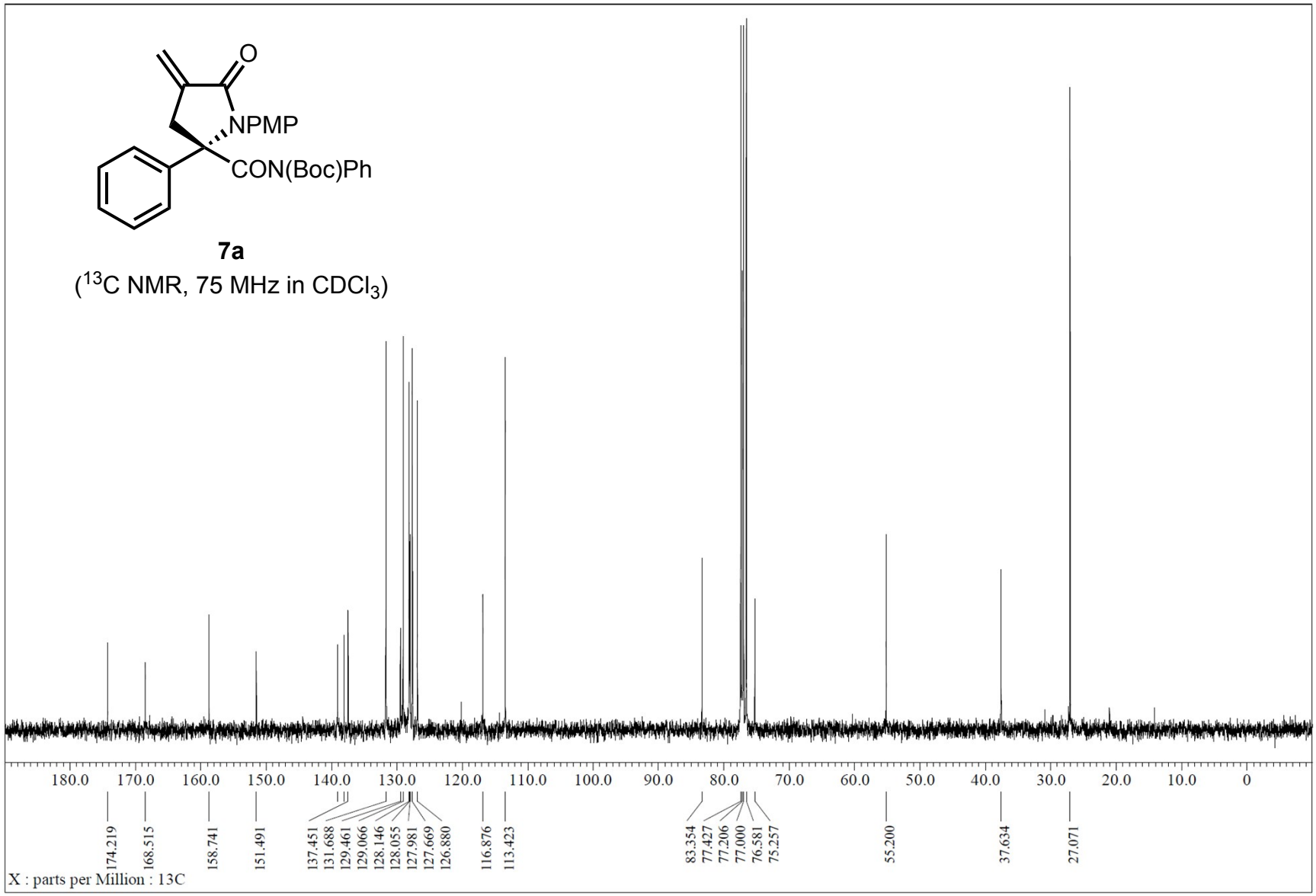

O
NHPh
NHPMP
NHPh
O
5j
(1H NMR, 300 MHz in CDCl3, 50 °C)
14.19
2.99
1.06
1.05
0.98
1.97
1.90
0.77
1.04
1.04
2.95
1.00
1.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.546
8.534
8.517
7.396
7.384
7.379
7.371
7.338
7.310
7.239
7.235
7.215
7.066
7.047
7.023
6.488
6.458
6.366
6.336
6.016
5.789
5.366
3.937
3.894
3.763
3.720
3.571
1.523
1.262
0.000
X : parts per Million : 1H

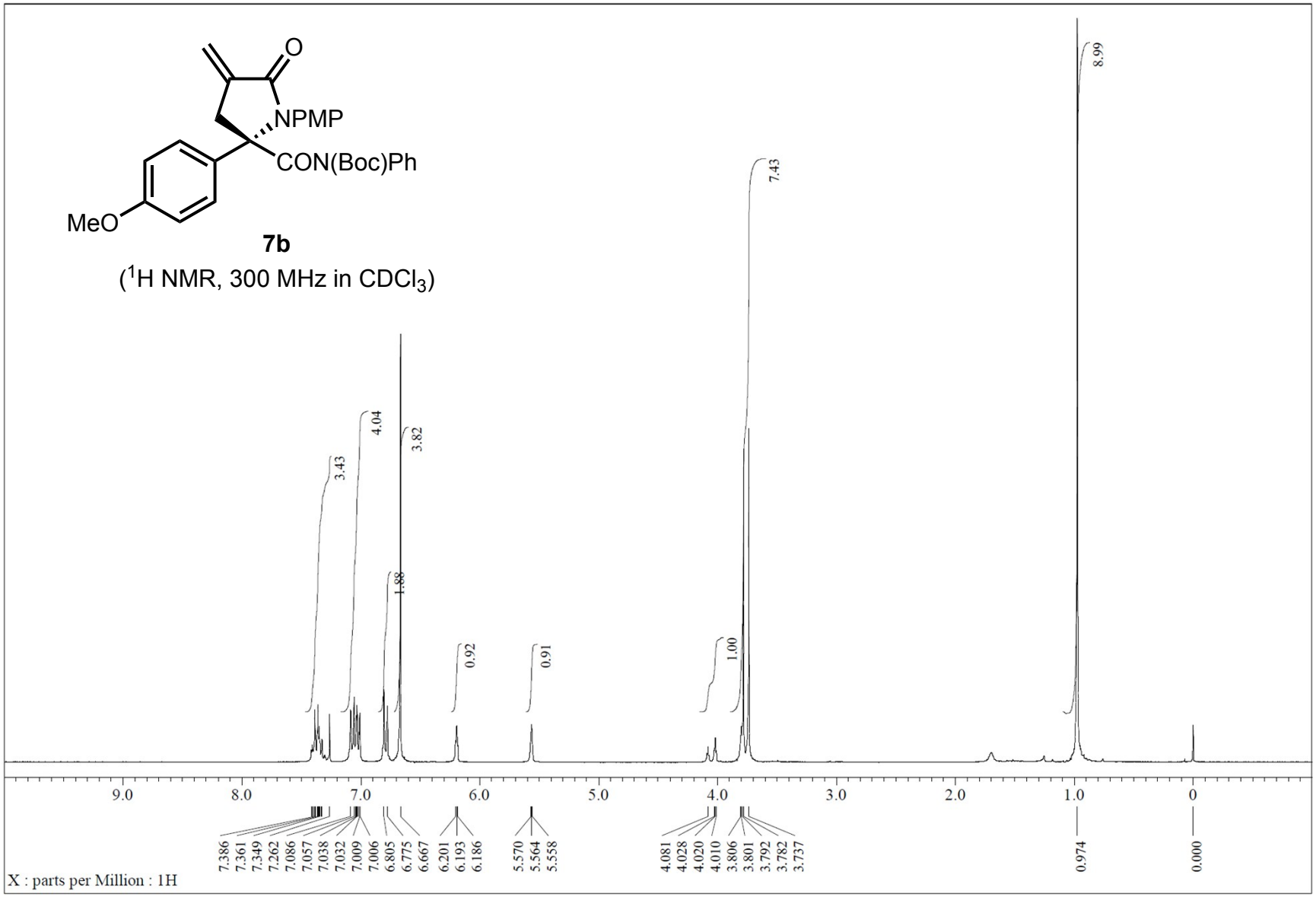

O
NHPh
NHPMP
NHPh
O
5j
(^{13}C NMR, 75 MHz in $CDCl_3$, 50 °C)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
171.789 167.652 152.307 141.923 137.860 134.770 130.402 128.993 128.779 128.655 126.694 126.620 126.100 125.326 124.947 124.708 124.254 122.540 121.024 120.274 116.516 114.711 77.618 77.437 77.214 77.008 76.588 67.259 55.565 37.739
X : parts per Million : 13C

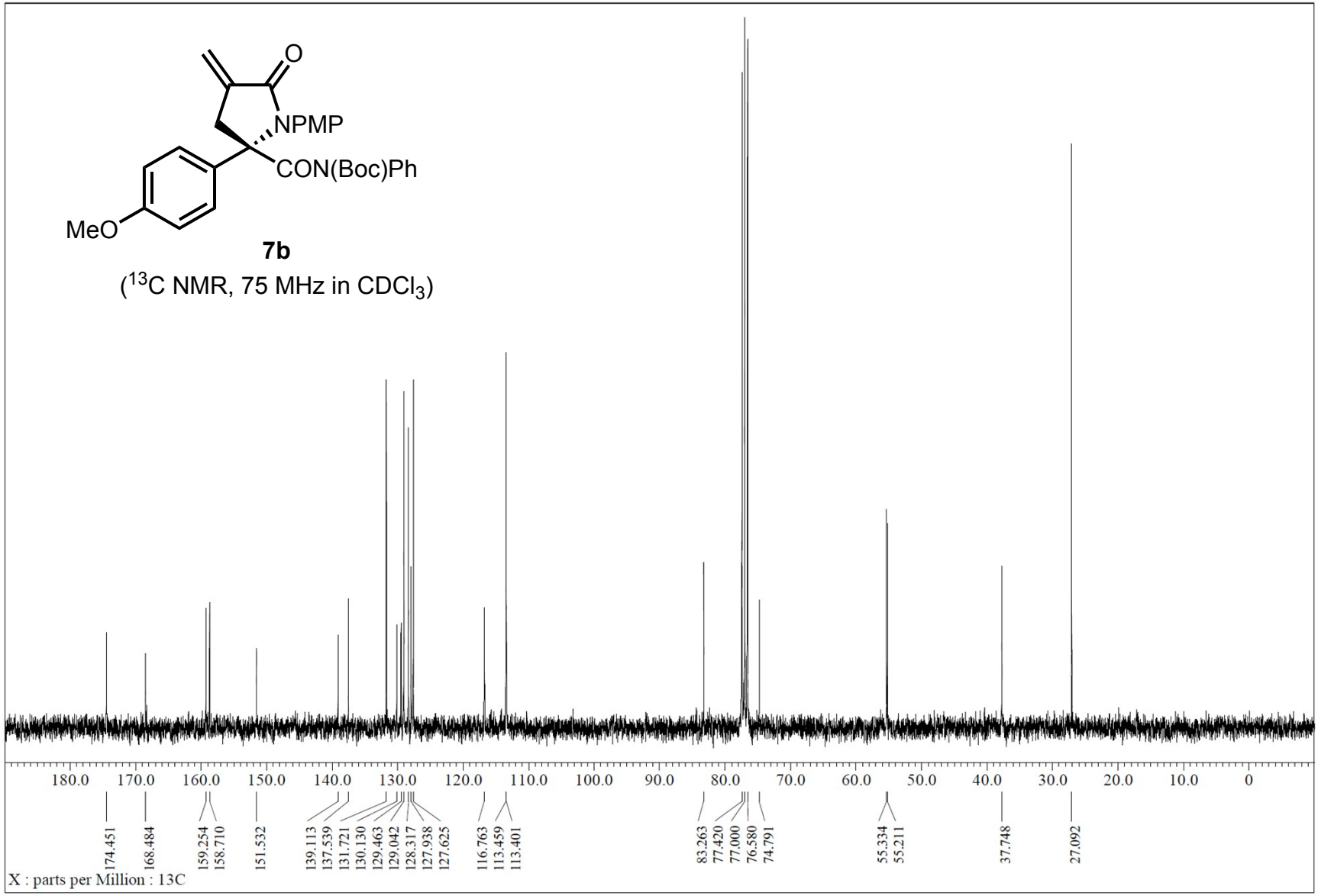

O
NMePh
NHPMP
NHPh
O
5k
(1H NMR, 300 MHz in CDCl3)
4.25
0.77
0.72
0.71
0.68
0.34
0.33
0.36
0.36
0.37
1.17
1.00
0.26
0.29
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.810
7.692
7.687
7.662
7.392
7.318
7.269
7.258
7.244
7.230
6.662
6.556
6.266
4.978
4.782
3.697
3.289
3.242
3.159
2.977
2.929
0.000
X : parts per Million : 1H

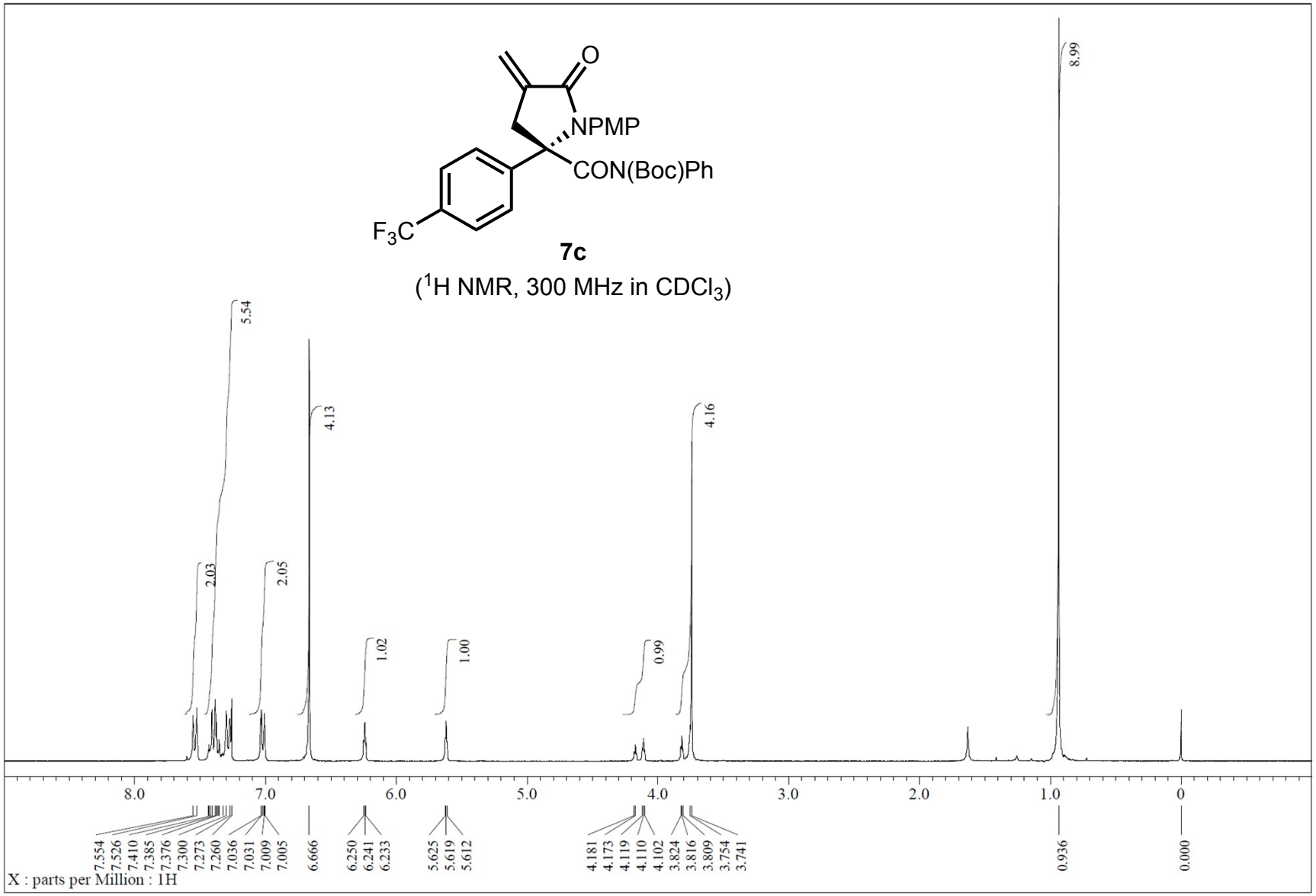

O
NMePh
NHPMP
NHPh
O
5k
(13C NMR, 75 MHz in CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
172.036
171.171
152.628
143.827
139.945
138.792
138.363
137.654
129.166
128.795
128.268
127.320
127.098
126.892
126.710
124.197
119.903
117.390
114.357
77.420
77.198
77.000
76.571
67.515
55.532
41.127
37.731
X : parts per Million : 13C

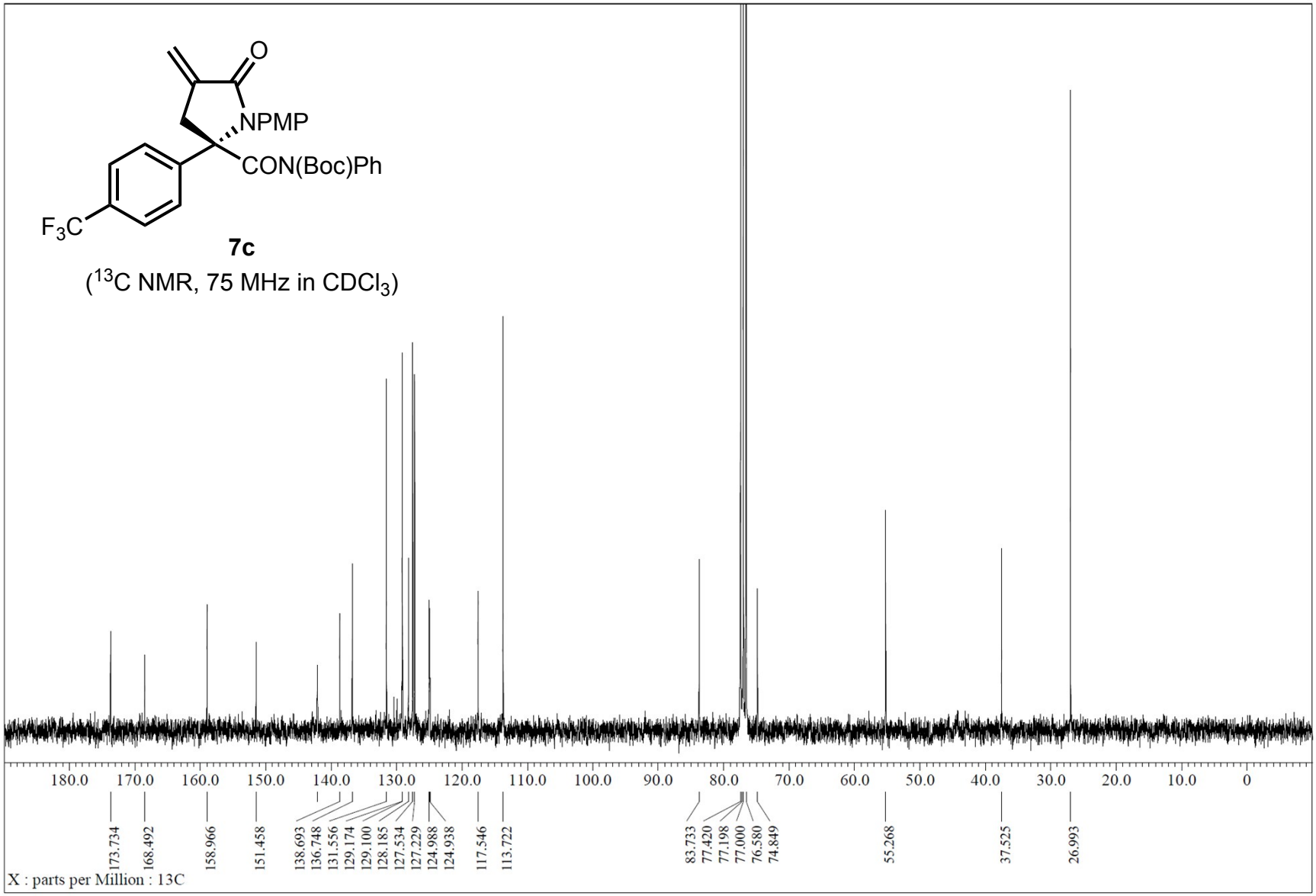

O
NPMP
CON(Boc)Ph
7a
(1H NMR, 300 MHz in CDCl3)
8.92
1.89
4.03
1.00
1.00
1.09
4.17
9.49
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.395
7.370
7.275
7.269
7.265
7.259
7.254
7.059
7.053
7.031
7.027
6.651
6.632
6.217
6.209
6.201
5.589
5.583
5.575
4.178
4.168
4.160
4.115
4.107
4.098
3.808
3.800
3.792
3.745
3.738
3.725
0.944
0.000
X : parts per Million : 1H

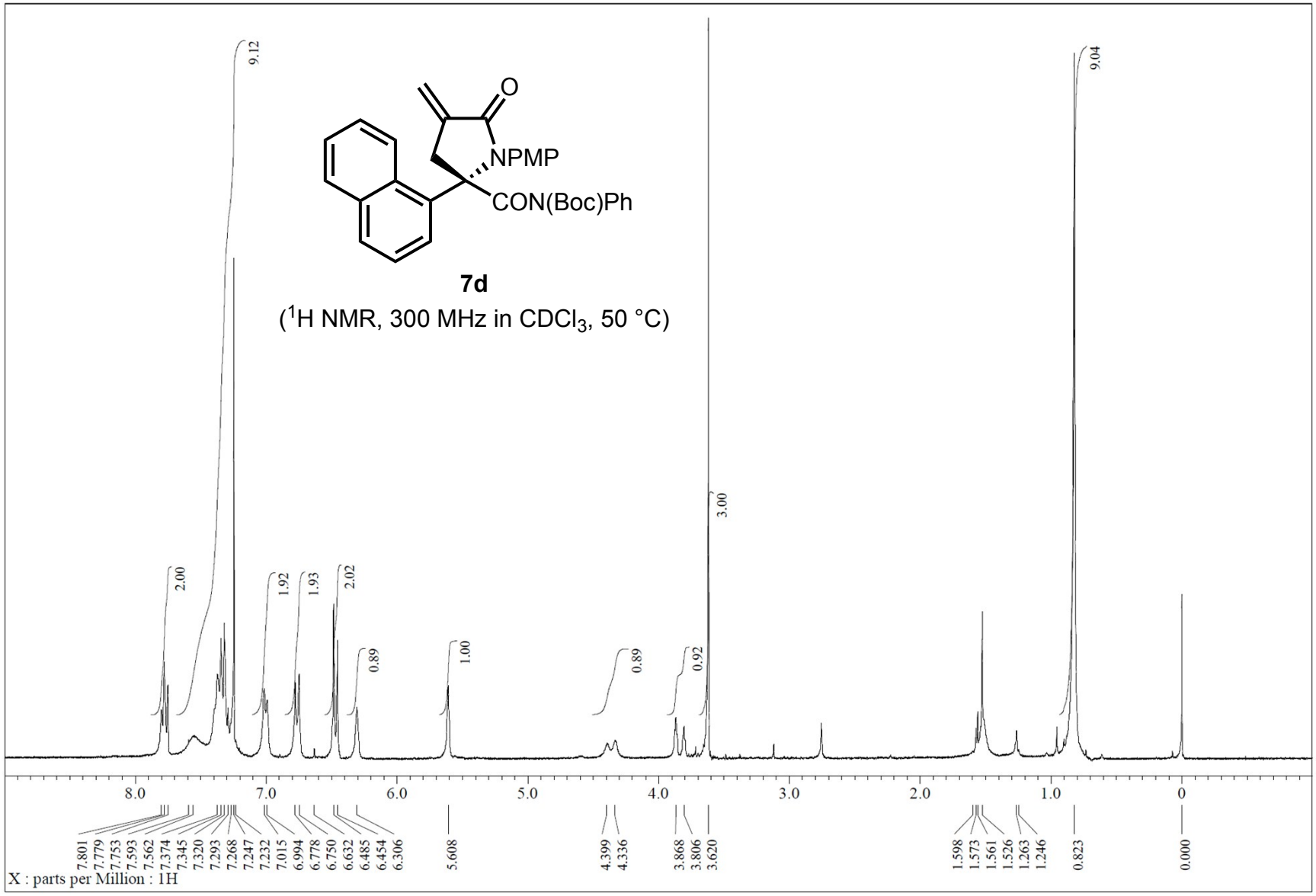

O
NPMP
CON(Boc)Ph
7a
(13C NMR, 75 MHz in CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
174.219
168.515
158.741
151.491
137.451
131.688
129.461
129.066
128.146
128.055
127.981
127.669
126.880
116.876
113.423
83.354
77.427
77.206
77.000
76.581
75.257
55.200
37.634
27.071
X : parts per Million : 13C


O
NPMP
CON(Boc)Ph
MeO
7b
(1H NMR, 300 MHz in CDCl3)
8.99
7.43
4.04
3.82
3.43
1.88
0.92
0.91
1.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.386
7.361
7.349
7.262
7.086
7.057
7.038
7.032
7.009
7.006
6.805
6.775
6.667
6.201
6.193
6.186
5.570
5.564
5.558
4.081
4.028
4.020
4.010
3.806
3.801
3.792
3.782
3.737
0.974
0.000
X : parts per Million : 1H


O
NPMP
CON(Boc)Ph
MeO
7b
(13C NMR, 75 MHz in CDCl3)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
174.451
168.484
159.254
158.710
151.532
139.113
137.539
131.721
130.130
129.463
129.042
128.317
127.938
127.625
116.763
113.459
113.401
83.263
77.420
77.000
76.580
74.791
55.334
55.211
37.748
27.092
X : parts per Million : 13C

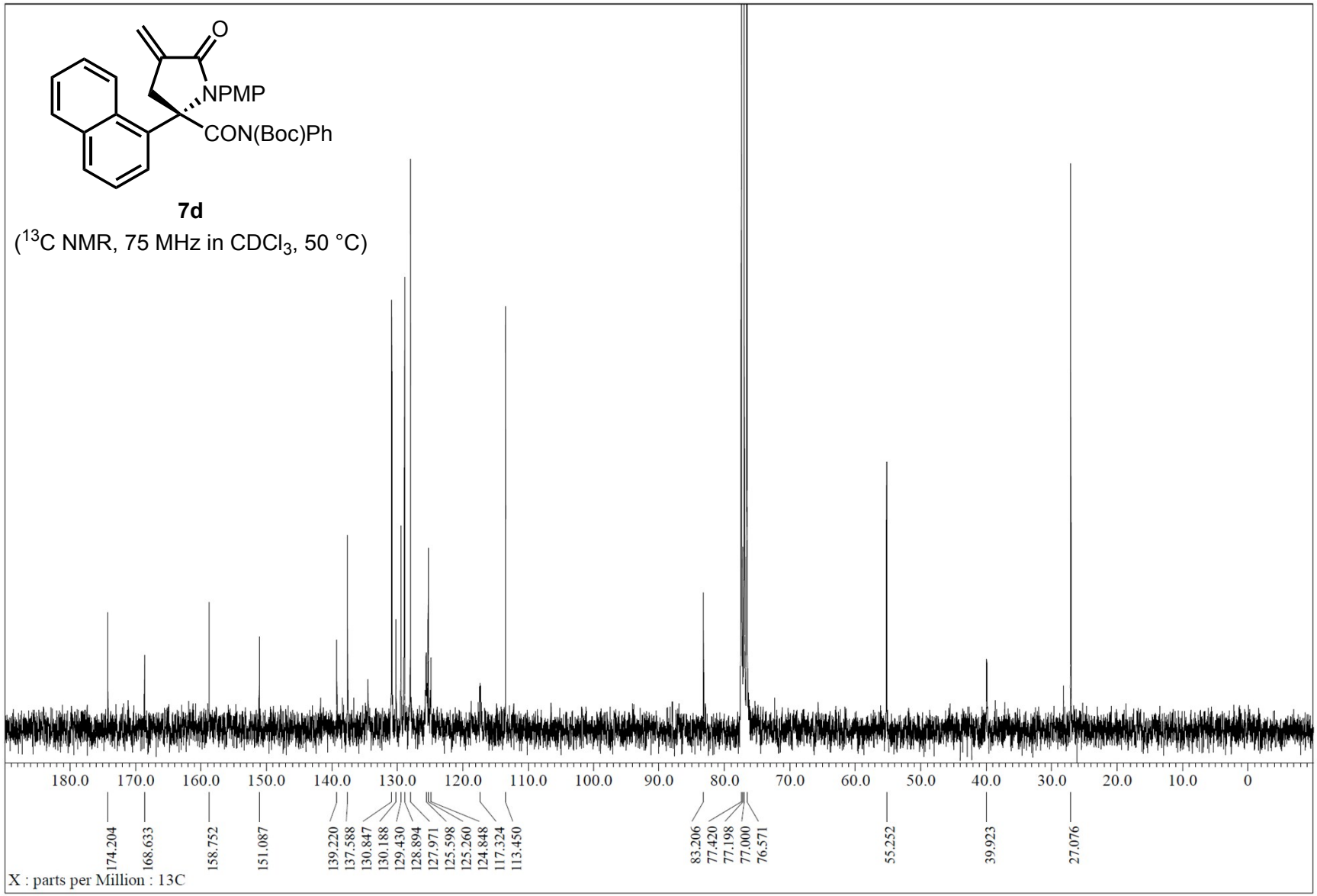

O
NPMP
CON(Boc)Ph
F3C
7c
(1H NMR, 300 MHz in CDCl3)
8.99
5.54
4.13
4.16
2.03
2.05
1.02
1.00
0.99
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.554
7.526
7.410
7.385
7.376
7.300
7.273
7.260
7.036
7.031
7.009
7.005
6.666
6.250
6.241
6.233
5.625
5.619
5.612
4.181
4.173
4.119
4.110
4.102
3.824
3.816
3.809
3.754
3.741
0.936
0.000
X : parts per Million : 1H

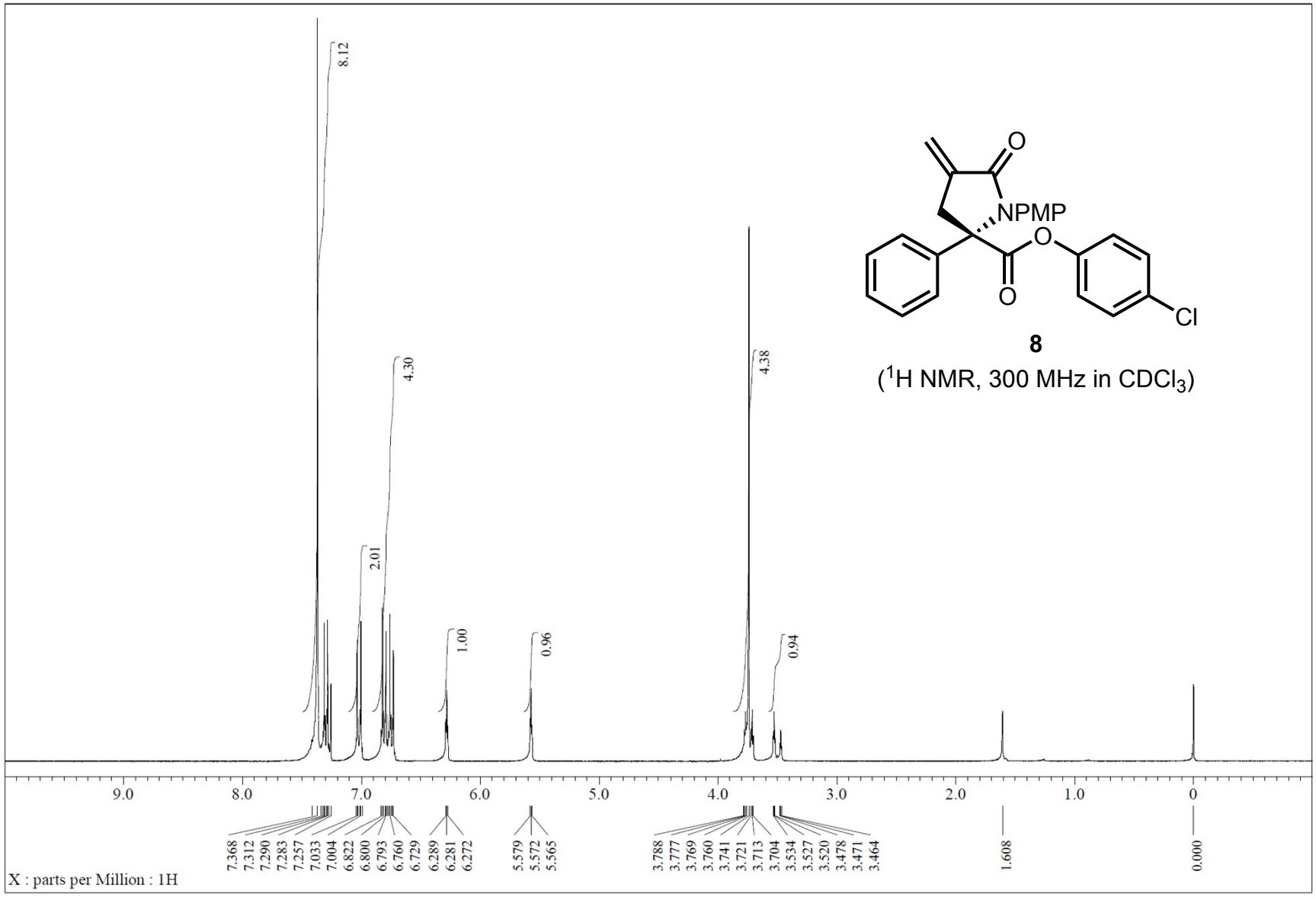

O
NPMP
CON(Boc)Ph
F3C
7c
(13C NMR, 75 MHz in CDCl3)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
173.734
168.492
158.966
151.458
138.693
136.748
131.556
129.174
129.100
128.185
127.534
127.229
124.988
124.938
117.546
113.722
83.733
77.420
77.198
77.000
76.580
74.849
55.268
37.525
26.993
X : parts per Million : 13C



7d

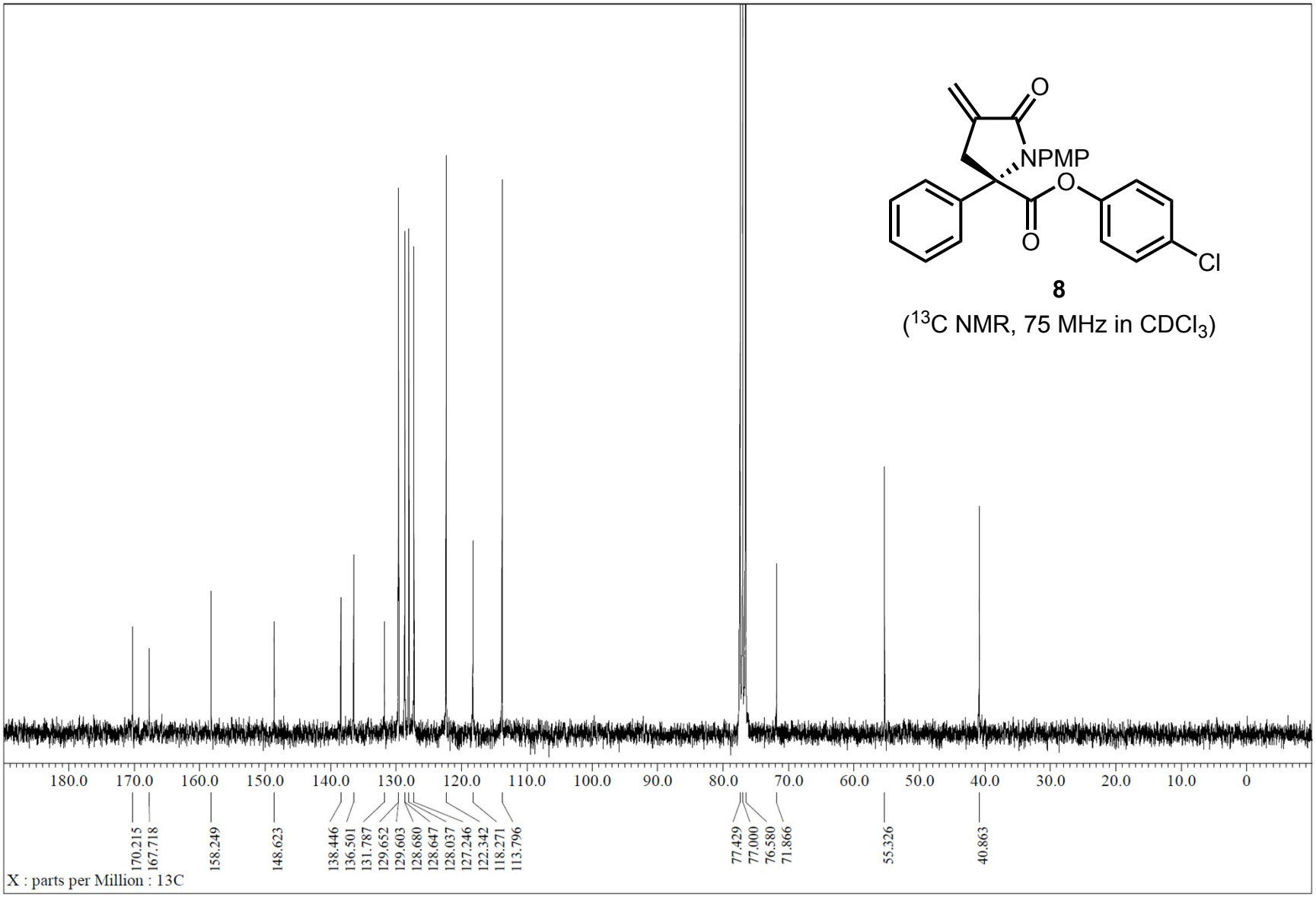
(^{1}H NMR, 300 MHz in $CDCl_3$, 50 °C)


O
NPMP
CON(Boc)Ph
7d
(^{13}C NMR, 75 MHz in $CDCl_3$, 50 °C)
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
174.204
168.633
158.752
151.087
139.220
137.588
130.847
130.188
129.430
128.894
127.971
125.598
125.260
124.848
117.324
113.450
83.206
77.420
77.198
77.000
76.571
55.252
39.923
27.076
X : parts per Million : 13C



8

(^{1}H NMR, 300 MHz in $CDCl_3$)


O
NPMP
O
O
Cl
8
(13C NMR, 75 MHz in CDCl3)
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
170.215
167.718
158.249
148.623
138.446
136.501
131.787
129.652
129.603
128.680
128.647
128.037
127.246
122.342
118.271
113.796
77.429
77.000
76.580
71.866
55.326
40.863
X : parts per Million : 13C