

Evidence for umpolung type of [2+2] cycloaddition of 2-carbamoyl ketenes.

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Supporting Information

CONTENTS

Page S2	General Information
Page S3-S7	Experimental Procedures and Characterization Data
Page S8-S56	¹ H and ¹³ C-NMR Spectra
Page S57	References

General Information

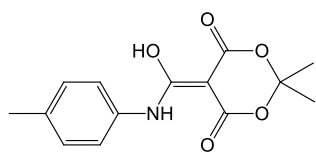
Commercially available reagents were purchased from Sigma-Aldrich or Acros. Chlorobenzene was distilled over P₄O₁₀ and stored over molecular sieves. Commercially unavailable reagents were prepared according to literature procedures:

5-[hydroxy((3-chlorophenyl)amino)methylene]-2,2-dimethyl-1,3-dioxo-4,6-dione	1a , ¹	5-
[hydroxy(phenylamino)methylene]-2,2-dimethyl-1,3-dioxo-4,6-dione	1b , ¹	5-[hydroxy((4-
metoxyphenyl)amino)methylene]-2,2-dimethyl-1,3-dioxo-4,6-dione	1d , ²	5-[hydroxy((4-
nitrophenyl)amino)methylene]-2,2-dimethyl-1,3-dioxo-4,6-dione	1e , ³	5-[hydroxy((ethyl)amino)methylene]-2,2-
dimethyl-1,3-dioxo-4,6-dione	1g , ¹	iminium salts 3'a-d . ⁴

Analytical TLC was performed on aluminum sheets of silica gel UV-254 Merck. Flash chromatography was performed using 40-63 microns of Zeochem silica gel. The ¹H, ¹³C were recorded on Bruker Avance III HD 400 MHz, chemical shifts (δ) in ppm rel. to internal Me₄Si; coupling constants *J* in Hz. High-resolution (HRMS) were recorded on *MicroMas Quattro LCT* mass spectrometer. Melting points were determined with *Warsztat Elektromechaniczny W-wa* apparatus and are not corrected.

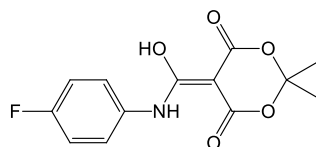
Experimental Procedures and Characterization Data

5-[Hydroxy((4-methylphenyl)amino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1c**).



To a cooled to 0°C solution of Meldrum's acid (0.72 g, 5 mmol) in dry DMF (5 ml) was added Et₃N (1.4 ml, 10 mmol). The mixture was stirred for 10 min and 4-methylphenylisocyanate (0.665 g, 5 mmol) was added. The stirring was continued for 15 min at 0°C and 1 h at R.T. The reaction mixture was poured into 2 M HCl ice cooled aqueous solution (30 ml). The solid precipitate was filtered and washed with cold water. Crystallization from AcOEt/Hexan gave 0.900 g 65% yield; mp 118-120 °C. ¹H NMR (400 MHz, CDCl₃): δ 15.65 (s, 1H) 11.10 (s, 1H), 7.36-7.34 (m, 2 H), 7.23-7.21 (m, 2 H), 2.83 (s, 3H) 1.79 (s, 6 H), ¹³C NMR (100 MHz, CDCl₃): δ 170.7, 168.9, 164.3, 136.5, 132.1, 129.8, 122.2, 105.0, 73.5, 26.3, 20.9. HRMS (ESI-): m/z calcd for C₁₄H₁₄NO₅Na [M-H]⁻ 276.0872, found. 276.0877.

5-[Hydroxy((4-fluorophenyl)amino)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1f**).

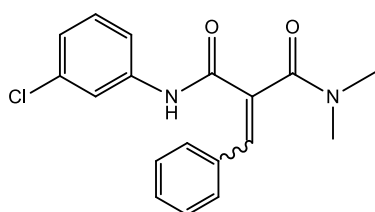


To a cooled to 0°C solution of Meldrum's acid (0.72 g, 5 mmol) in dry DMF (5 ml) was added Et₃N (1.4 ml, 10 mmol). The mixture was stirred for 10 min and 4-fluorophenylisocyanate (0.685 g, 5 mmol) was added. The stirring was continued for 15 min at 0°C and 1 h at R.T. The reaction mixture was poured into 2 M HCl ice cooled aqueous solution (30 ml). The solid precipitate was filtered and washed with cold water. Crystallization from AcOEt/Hexan gave 0.955g 68% yield; mp 134-137 °C. ¹H NMR (400 MHz, CDCl₃): δ 15.83 (s, 1H) 11.12 (s, 1H), 7.46-7.28 (m, 2 H), 7.14-7.10 (m, 2 H), 1.79 (s, 6 H). ¹³C NMR (100 MHz, CDCl₃): δ 170.8, 169.1, 164.3, 160.7 (d, ¹J_{CF} = 245 Hz), 130.7 (d, ⁴J_{CF} = 3 Hz), 124.1 (d, ³J_{CF} = 8 Hz), 116.2 (d, ²J_{CF} = 24 Hz), 105.2, 73.6, 26.3. HRMS (ESI-): m/z calcd for C₁₃H₁₁FNO₅Na [M-H]⁻ 280.0621, found. 280.0622.

Preparation of 2-arylidene malonoamides (**8aa/8aa'**- **8gc/8gc'**). General Procedure

To a solution of 5-[(N-aryl/alkylamino)(hydroxyl)methylene]-2,2-dimethyl-1,3-dioxane-4,6-dione (**1a-g**) (1 mmol) in dry chlorobenzene (10 ml) was added iminium salts **3'a-d** (2 mmol). The resulting mixture was stirred and heated to reflux for 2 h. After completion of the reaction, the solvent was removed under vacuum, and the residue was purified with flash chromatography as specified below.

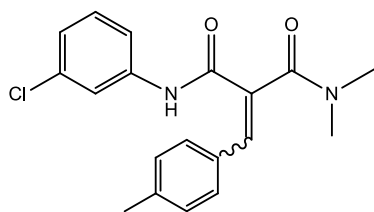
2-benzylidene-N¹-(3-chlorophenyl)-N³,N³-dimethylmalonamide (**8aa**) (**8aa'**)



Purification by flash column chromatography, (EtOAc/Hex, 1:2-1:1), brown oil;
(E)-isomer (**8aa**) 0.170 g, 51% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 9.36 (s, 1 H), 7.80 (s, 1 H), 7.79 (t, *J* = 2.0 Hz, 1 H), 7.46 (dq, *J* = 8.0 Hz, *J* = 0.8 Hz, 1 H), 7.40 (s, 5 H), 7.26 (t, *J* = 8.0 Hz, 1 H), 7.10 (dq, *J* = 8.0 Hz, *J* = 1.2 Hz, 1 H), 3.01 (s, 3 H), 2.64 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.0, 162.1, 139.6, 138.9, 134.5, 133.7, 130.1, 129.9, 129.3, 128.9, 128.7, 124.4, 120.2, 118.1, 37.8, 34.9; (Z)-isomer (**8aa'**) 0.144 g, 44% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 9.15 (s, 1 H), 7.70 (t, *J* = 2.0 Hz, 1 H), 7.54-7.51 (m, 2 H), 7.38-7.36 (m, 4 H), 7.24 (t, *J* = 8.0

H_z, 1 H), 7.10 (dq, *J* = 8.0 Hz, *J* = 0.8 Hz, 1 H), 6.77 (s, 1 H), 3.28 (s, 3 H), 3.09 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.1, 162.7, 138.8, 136.5, 134.5, 133.3, 131.3, 129.9, 129.6, 129.2, 128.6, 124.4, 120.0, 117.9, 39.6, 35.3, HRMS (ESI+): *m/z* [M + Na]⁺ calcd for C₁₈H₁₇ClN₂O₂Na: 351.0876; found: 351.0862. HRMS (ESI+): *m/z* [M + Na]⁺ calcd for C₁₈H₁₇ClN₂O₂Na: 351.0876; found: 351.0869

N¹-(3-chlorophenyl)-N³,N³-dimethyl-2-(4-methylbenzylidene)malonamide (8ab), (8ab')

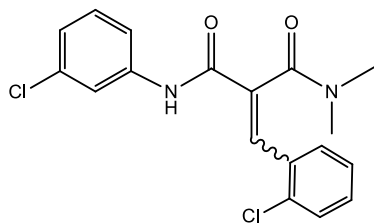


Purification by flash column chromatography, (EtOAc/Hex, 1:2-1:1), brown oil;

(E)-isomer (**8ab**) 0.189 g, 55% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 9.33 (s, 1 H), 7.79-7.78 (m, 2 H), 7.46 (dq, *J* = 8.0 Hz, *J* = 0.8 Hz, 1 H), 7.32-7.25 (m, 3 H), 7.22-7.20 (m, 1 H), 7.10 (dq, *J* = 8.0 Hz, *J* = 1.2 Hz, 1 H), 3.04 (s, 3 H), 2.68 (s, 3 H), 2.40 (s, 3 H) ¹³C NMR (CDCl₃, 100 MHz): δ = 169.3, 162.2, 140.6, 139.7, 139.0, 134.5, 130.9, 129.9, 129.7, 128.8, 128.1, 124.3, 120.1, 118.0, 37.8, 35.0, 21.5;

(Z)-isomer (**8ab'**) 0.145 g 42% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 9.22 (s, 1 H), 7.78 (t, *J* = 2.0 Hz, 1 H), 7.42 (d, *J* = 8.0 Hz, 2 H), 7.39 (dq, *J* = 8.4 Hz, *J* = 0.8 Hz, 1 H), 7.24 (t, *J* = 8.0 Hz, 1 H), 7.17 (d, *J* = 8.0 Hz, 2 H), 7.10 (dq, *J* = 8.0 Hz, *J* = 0.8 Hz, 1 H), 6.74 (s, 1 H), 3.27 (s, 3 H), 3.09 (s, 3 H), 2.36 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.4, 162.8, 140.0, 138.9, 137.0, 134.6, 131.3, 130.4, 130.0, 129.4, 129.3, 124.4, 120.0, 117.9, 39.7, 35.3, 21.4, HRMS (ESI+): *m/z* [M + Na]⁺ calcd for C₁₉H₁₉ClN₂O₂Na: 365.1033; found: 365.1045.

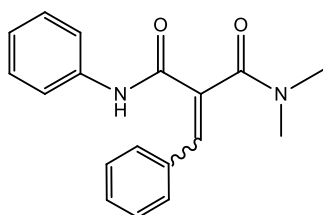
2-(2-chlorobenzylidene)-N¹-(3-chlorophenyl)-N³,N³-dimethylmalonamide (8ac, 8ac')



Purification by flash column chromatography, (EtOAc/Hex, 1:2), brown oil, 0.322 g, 89% yield; mixture of (Z) and (E) stereoisomers with ratio 1:1; ¹H NMR (CDCl₃, 400 MHz): δ = 9.72 (s, 0.5 H), 9.44 (s, 0.5 H), 8.02 (s, 0.5 H), 7.81 (t, *J* = 2.4 Hz, 0.5 H), 7.72 (t, *J* = 2.5 Hz, 0.5 H), 7.48-7.45 (m, 1.5H), 7.41 (dd, *J* = 8.0 Hz, *J* = 1.2 Hz, 0.5 H), 7.37-7.30 (m, 1.5 H), 7.29-7.17 (m, 2.5 H), 7.10 (dq, *J* = 8.0 Hz, *J* = 0.8 Hz, 0.5 H), 7.07-7.04 (m, 1H), 3.33 (s, 1.5

H), 3.09 (s, 1.5 H), 2.92 (s, 1.5 H), 2.61 (s, 1.5 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.0, 169.4, 161.6, 161.4, 138.9, 138.7, 136.8, 135.0, 134.6, 134.5, 134.4, 133.8, 132.6, 132.5, 132.1, 131.2, 131.1, 130.3, 130.0, 129.9, 129.8, 129.7, 129.4, 129.1, 126.9, 126.8, 124.4, 124.3, 120.2, 119.9, 118.0, 117.8, 39.9, 37.8, 35.3, 34.9, HRMS (ESI+): *m/z* [M + Na]⁺ calcd for C₁₈H₁₆Cl₂N₂O₂Na: 385.0487; found: 385.0495. Ratio of stereoisomers was determined based on integration of ¹H NMR spectra.

2-benzylidene-N¹,N¹-dimethyl-N³-phenylmalonamide (8ba), (8ba')

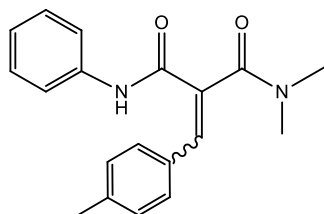


Purification by flash column chromatography, (EtOAc/Hex, 1:2-1:1), brown oil;

(E)-isomer (**8ba**) 0.115 g, 39% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 9.23 (s, 1 H), 7.81 (s, 1 H), 7.66-7.63 (m, 2 H), 7.43-7.34 (m, 7 H), 7.16-7.11 (m, 1 H), 3.02 (s, 3 H), 2.67 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.2, 161.9, 139.0, 133.9, 129.9, 129.7, 129.0, 128.9, 128.7, 124.4, 120.1, 37.8, 34.9; (Z)-isomer (**8ba'**) 0.121 g, 41% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 8.92 (s, 1 H), 7.59-7.53 (m, 4 H), 7.39-7.32 (m, 5 H), 7.15-7.11 (m, 1 H), 6.76 (s, 1 H), 3.29 (s, 3 H), 3.10 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ =

169.2, 162.6, 137.6, 135.9, 133.4, 131.7, 129.4, 129.3, 128.9, 128.6, 124.5, 119.9, 39.6, 35.3. HRMS (ESI+): m/z [M + Na]⁺ calcd for C₁₈H₁₈N₂O₂Na: 317.1266; found: 317.1260.

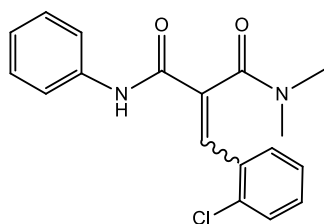
N¹,N¹-dimethyl-2-(4-methylbenzylidene)-N³-phenylmalonamide (**8bb**), (**8bb'**)



Purification by flash column chromatography, (EtOAc/Hex, 1:2-1:1), brown oil

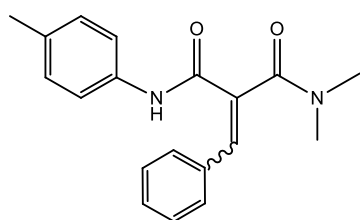
(E)-isomer (**8bb**) 0.110 g, 35% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 9.21 (s, 1 H), 7.78 (s, 1 H), 7.66-7.63 (m, 2 H), 7.38-7.30 (m, 4 H), 7.21-7.19 (m, 2 H), 7.15-7.11 (m, 1 H), 3.04 (s, 3 H), 2.69 (s, 3 H), 2.39 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.5, 162.1, 140.4, 139.2, 137.8, 131.0, 129.6, 128.9, 128.8, 128.6, 124.3, 120.1, 37.8, 34.9, 21.4; (Z)-isomer (**8bb'**) 0.155 g, 50% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 8.98 (s, 1 H), 7.60-7.58 (m, 2 H), 7.45-7.43 (m, 2 H), 7.35-7.18 (m, 2 H), 7.17-7.11 (m, 3 H), 6.72 (s, 1 H), 3.27 (s, 3 H), 3.08 (s, 3 H), 2.35 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.4, 162.8, 139.7, 137.7, 136.2, 130.7, 130.5, 129.4, 129.3, 128.9, 124.4, 119.9, 39.6, 35.3, 21.4; HRMS (ESI+): m/z [M + Na]⁺ calcd for C₁₉H₂₀N₂O₂Na: 331.1422; found: 331.1416.

2-(2-chlorobenzylidene)-N¹,N¹-dimethyl-N³-phenylmalonamide (**8bc**, **8bc'**)



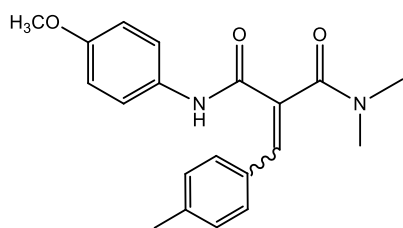
Purification by flash column chromatography, (EtOAc/Hex, 1:1), brown oil, 0.242 g, 74% yield; mixture of (Z) and (E) stereoisomers with ratio 1:1; ¹H NMR (CDCl₃, 400 MHz): δ = 9.45 (s, 0.5 H), 9.33 (s, 0.5 H), 8.10 (s, 0.5 H), 7.67-7.65 (m, 1 H), 7.57-7.55 (m, 1 H), 7.51 (dd, *J* = 7.6 Hz, *J* = 1.6 Hz, 0.5 H), 7.46 (dd, *J* = 8.0 Hz, *J* = 1.2 Hz, 0.5 H), 7.41 (dd, *J* = 8.0 Hz, *J* = 1.2 Hz, 0.5 H), 7.38-7.28 (m, 3.5 H), 7.27-7.19 (m, 1 H), 7.16-7.08 (m, 1 H), 7.04 (s, 0.5 H), 3.33 (s, 1.5 H), 3.11 (s, 1.5 H), 2.93 (s, 1.5 H), 2.63 (s, 1.5 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.2, 168.6, 161.4, 161.2, 137.7, 137.6, 136.6, 134.6, 134.3, 133.8, 132.7, 132.6, 132.6, 131.6, 130.9, 130.2, 129.9, 129.8, 129.4, 129.1, 129.0, 128.9, 126.9, 126.8, 124.5, 124.4, 120.0, 119.9, 39.8, 37.8, 35.3, 34.9, HRMS (ESI+): m/z [M + Na]⁺ calcd for C₁₈H₁₇ClN₂O₂Na: 351.0876; found: 351.0870. Ratio of stereoisomers was determined based on integration of ¹H NMR spectra.

2-benzylidene-N¹,N¹-dimethyl-N³-(p-tolyl)malonamide (**8ca**), (**8ca'**)



Purification by flash column chromatography, (EtOAc/Hex, 1:2-1:1), brown oil; (E)-isomer (**8ca**) 0.207 g, 67% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 9.14 (s, 1 H), 7.79 (s, 1 H), 7.53-7.50 (m, 2 H), 7.42-7.37 (m, 5 H), 7.15-7.13 (m, 2 H), 3.01 (s, 3 H), 2.65 (s, 3 H), 2.33 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.2, 161.7, 138.8, 135.2, 134.0, 133.9, 129.9, 129.8, 129.4, 128.8, 128.7, 120.1, 37.8, 34.9, 20.9 (Z)-isomer (**8ca'**) 0.085 g, 28% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 8.78 (s, 1 H), 7.54-7.51 (m, 2 H), 7.47-7.43 (m, 2 H), 7.38-7.33 (m, 3 H), 7.15-7.12 (m, 2 H), 6.74 (s, 1 H), 3.28 (s, 3 H), 3.09 (s, 3 H), 2.33 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.2, 162.5, 135.6, 135.0, 134.1, 133.5, 132.0, 129.5, 129.4, 129.3, 128.6, 119.9, 39.6, 35.2, 20.9; HRMS (ESI+): m/z [M + Na]⁺ calcd for C₁₉H₂₀N₂O₂Na: 331.1422; found: 331.1412.

N¹-(4-methoxyphenyl)-N³,N³-dimethyl-2-(4-methylbenzylidene)malonamide (8db), (8db')

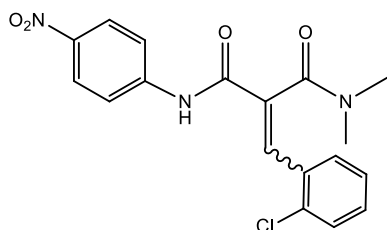


Purification by flash column chromatography, (EtOAc/Hex, 1:2-1:1), brown oil;

(E)-isomer (**8db**) 0.081 g, 24% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 9.06 (s, 1 H), 7.77 (s, 1 H), 7.57-7.53 (m, 2 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 7.20 (d, *J* = 8.0 Hz, 2 H), 6.91-6.87 (m, 2 H), 3.81 (s, 3 H), 3.03 (s, 3 H), 2.69 (s, 3 H), 2.39 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.5, 161.8, 156.4,

140.3, 138.8, 131.1, 131.0, 129.6, 128.7, 128.6, 121.7, 114.0, 55.4, 37.8, 34.9, 21.4; (Z)-isomer (**8db'**) 0.110 g, 33% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 8.82 (s, 1 H), 7.51-7.47 (m, 2 H), 7.43 (d, *J* = 8.0 Hz, 2 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 6.88-6.84 (m, 2 H), 6.70 (s, 1 H), 3.80 (s, 3 H), 3.27 (s, 3 H), 3.08 (s, 3 H), 2.35 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.5, 162.6, 156.4, 139.7, 135.8, 130.9, 130.8, 130.6, 129.3, 129.3, 121.6, 114.0, 55.4, 39.6, 35.3, 21.3; HRMS (ESI+): *m/z* [M + Na]⁺ calcd for C₂₀H₂₂N₂O₃Na: 361.1528; found: 361.1542.

2-(2-chlorobenzylidene)-N¹,N¹-dimethyl-N³-(4-nitrophenyl)malonamide (8ec, 8ec')

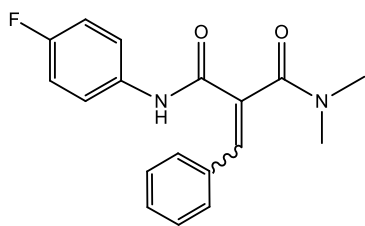


Purification by flash column chromatography, (EtOAc/Hex, 1:1), brown oil, 0.298 g, 80% yield; mixture of (Z) and (E) stereoisomers with ratio 0.37:0.63;

¹H NMR (CDCl₃, 400 MHz): δ = 10.22 (s, 0.37 H), 9.94 (s, 0.63 H), 8.27-8.23 (m, 1.26 H), 8.20-8.16 (m, 0.74 H), 8.13 (s, 0.63 H), 7.86-7.82 (m, 1.26 H), 7.75-7.71 (m, 0.74 H), 7.49 (dd, *J* = 8.0 Hz, *J* = 0.8 Hz, 0.63 H), 7.46-7.43 (m, 0.74 H), 7.40-7.22 (m, 2.63 H), 7.13 (s, 0.37 H), 3.37 (s, 1.11 H),

3.14 (s, 1.11 H), 2.94 (s, 1.89 H), 2.62 (s, 1.89 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.0, 168.3, 161.9, 161.8, 143.6, 143.6, 143.5, 143.4, 138.0, 136.8, 134.4, 133.8, 132.3, 131.3, 131.2, 130.6, 130.5, 129.9, 129.6, 129.5, 129.0, 127.0, 126.8, 125.0, 124.9, 119.6, 119.4, 40.0, 37.9, 35.5, 35.0, HRMS (ESI+): *m/z* [M + Na]⁺ calcd. for C₁₈H₁₆ClN₃O₄Na: 396.0727; found: 396.0735. Ratio of stereoisomers was determined based on integration of ¹H NMR spectra.

2-benzylidene-N¹-(4-fluorophenyl)-N³,N³-dimethylmalonamide (8fa), (8fa')

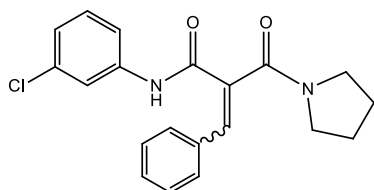


Purification by flash column chromatography, (EtOAc/Hex, 1:2-1:1), brown oil;

(E)-isomer (**8fa**) 0.165 g, 52% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 9.27 (s, 1 H), 7.80 (s, 1 H), 7.63-7.58 (m, 2 H), 7.40 (s, 5 H), 7.07-7.01 (m, 2 H), 3.01 (s, 3 H), 2.65 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.2, 161.9, 159.4 (d, *J*¹ = 242.1 Hz), 139.2, 133.8 (d, *J*¹ = 1.8 Hz), 130.0, 129.4, 128.9, 128.7, 121.8 (d, *J*³ = 7.8 Hz), 115.6 (d, *J*² = 22.3 Hz), 37.8, 34.9; (Z)-isomer (**8fa'**) 120 mg,

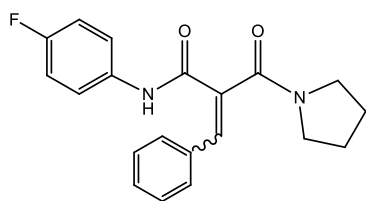
39% yield; ¹H NMR (CDCl₃, 400 MHz): δ = 9.05 (s, 1 H), 7.56-7.51 (m, 4 H), 7.40-7.34 (m, 3 H), 7.03-6.99 (m, 2 H), 6.75 (s, 1 H), 3.28 (s, 3 H), 3.08 (s, 3 H), ¹³C NMR (CDCl₃, 100 MHz): δ = 169.2, 162.6, 159.4 (d, *J*¹ = 242.1 Hz), 136.1, 133.7 (d, *J*¹ = 1.3 Hz), 133.4, 131.4, 129.5, 129.2, 128.6, 121.7 (d, *J*³ = 7.8 Hz), 115.6 (d, *J*² = 22.3 Hz), 39.6, 35.3; HRMS (ESI+): *m/z* [M + Na]⁺ calcd for C₁₈H₁₇FN₂O₂Na: 335.1172; found: 335.1161.

N-(3-chlorophenyl)-3-phenyl-2-(pyrrolidine-1-carbonyl)acrylamide (**8ad**), (**8ad'**)



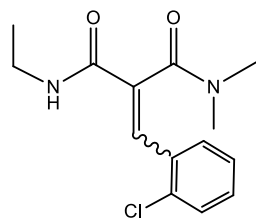
Purification by flash column chromatography, (EtOAc/Hex, 1:2-1:1), brown oil; (E)-isomer (**8ad**) 0.150 g, 42% yield; ^1H NMR (CDCl_3 , 400 MHz): δ = 9.50 (s, 1 H), 7.80 (t, J = 2.0 Hz, 1 H), 7.79 (s, 1 H), 7.48-7.44 (m, 3 H), 7.41-7.38 (m, 3 H), 7.26 (t, J = 8.0 Hz, 1 H), 7.10 (dq, J = 8.0 Hz, J = 0.8 Hz, 1 H), 3.55 (s, 2 H), 3.29-3.03 (m, 1 H), 2.91-2.46 (m, 1 H), 1.84-1.53 (m, 4 H), ^{13}C NMR (CDCl_3 , 100 MHz): δ = 167.3, 162.0, 139.4, 139.0, 134.6, 133.8, 130.5, 130.2, 129.9, 128.9, 128.7, 124.3, 120.1, 118.0, 47.4, 46.0, 25.5, 24.0; (Z)-isomer (**8ad'**) 0.091 g, 26% yield; ^1H NMR (CDCl_3 , 400 MHz): δ = 9.49 (s, 1 H), 7.80 (t, J = 2.0 Hz, 1 H), 7.54-7.51 (m, 2 H), 7.40 (dq, J = 8.0 Hz, J = 0.8 Hz, 1 H), 7.38-7.34 (m, 3 H), 7.24 (t, J = 8.0 Hz, 1 H), 7.10 (dq, J = 8.0 Hz, J = 1.2 Hz, 1 H), 6.93 (s, 1 H), 3.73 (t, J = 6.4 Hz, 2 H), 3.59 (t, J = 6.4 Hz, 2 H), 2.01-1.95 (m, 4 H), ^{13}C NMR (CDCl_3 , 100 MHz): δ = 167.4, 162.6, 138.9, 137.9, 134.6, 133.3, 132.0, 129.9, 129.6, 129.4, 128.6, 124.4, 120.0, 117.9, 49.5, 46.3, 26.0, 24.4; HRMS (ESI+): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{ClN}_2\text{O}_4\text{Na}$: 377.1033; found: 377.1025.

N-(4-fluorophenyl)-3-phenyl-2-(pyrrolidine-1-carbonyl)acrylamide (**8fd**), (**8fd'**)



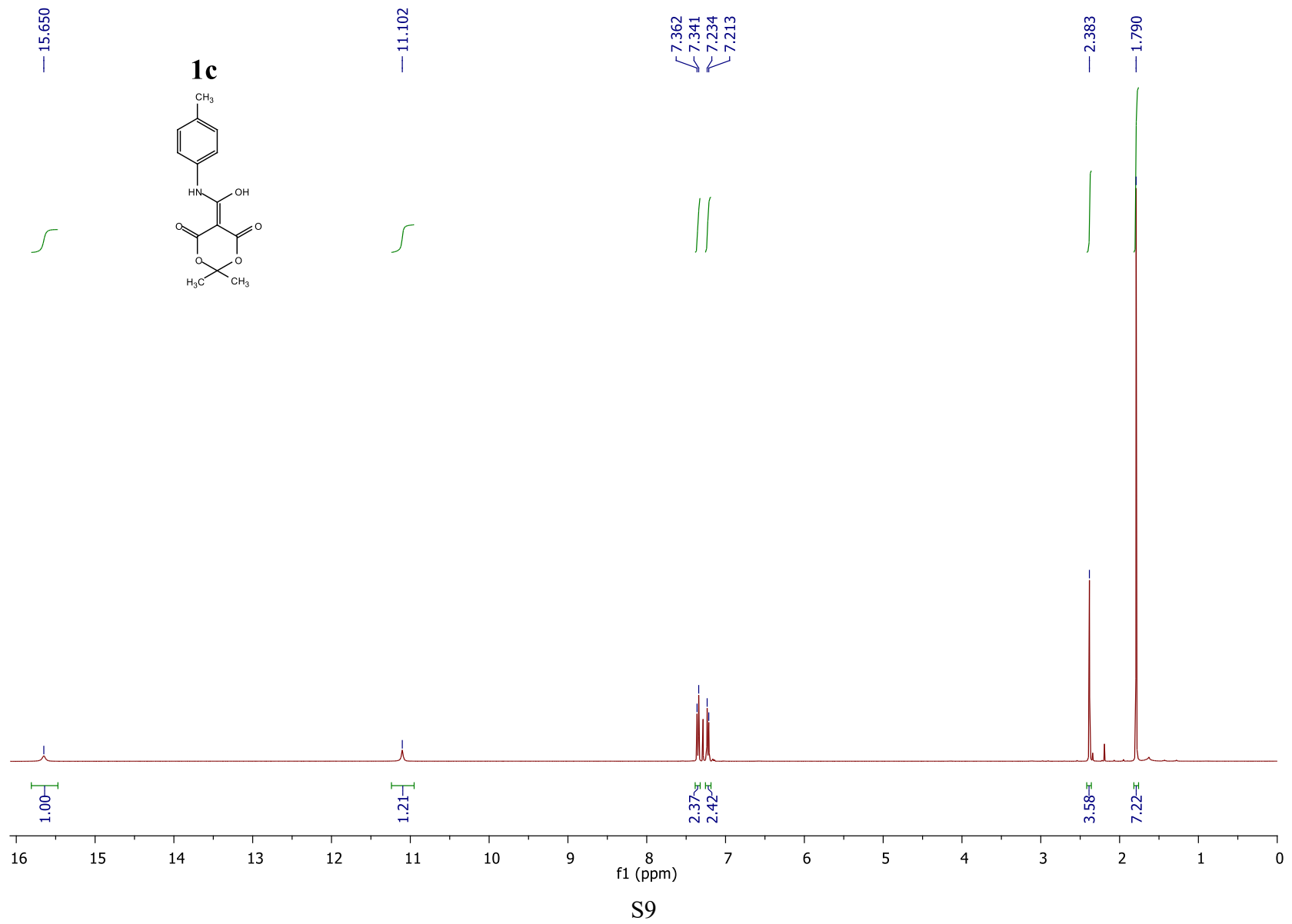
Purification by flash column chromatography, (EtOAc/Hex, 1:2-1:1), brown oil; (E)-isomer (**8fd**) 0.153 g, 45% yield; ^1H NMR (CDCl_3 , 400 MHz): δ = 9.40 (s, 1 H), 7.80 (s, 1 H), 7.64-7.60 (m, 2 H), 7.48-7.44 (m, 2 H), 7.42-7.36 (m, 3 H), 7.08-7.02 (m, 2 H), 3.63-3.50 (m, 2 H), 3.63-3.50 (m, 2 H), 3.34-3.10 (m, 1 H), 2.78-2.42 (m, 1 H), 1.88-1.55 (m, 4 H), ^{13}C NMR (CDCl_3 , 100 MHz): δ = 167.4, 161.8, 159.3 (d, J^1 = 242.0 Hz), 139.0, 133.9 (d, J^1 = 3.1 Hz), 130.7, 130.1, 128.8, 128.7, 121.8 (d, J^3 = 7.8 Hz), 115.6 (d, J^2 = 22.4 Hz), 47.3, 46.0, 25.5, 24.0; (Z)-isomer (**8fd'**) 0.106 g, 31% yield; ^1H NMR (CDCl_3 , 400 MHz): δ = 9.29 (s, 1 H), 7.59-7.52 (m, 4 H), 7.37-7.34 (m, 3 H), 7.05-7.00 (m, 2 H), 6.91 (s, 1 H), 3.74 (t, J = 6.4 Hz, 2 H), 3.59 (t, J = 6.4 Hz, 2 H), 2.02-1.95 (m, 4 H), ^{13}C NMR (CDCl_3 , 100 MHz): δ = 167.5, 162.5, 159.4 (d, J^1 = 242.1 Hz), 137.4, 133.8 (d, J^1 = 2.8 Hz), 133.4, 132.3, 129.5, 129.4, 128.5, 121.6 (d, J^3 = 7.8 Hz), 115.5 (d, J^2 = 22.3 Hz), 49.5, 46.2, 26.0, 24.4. HRMS (ESI+): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{20}\text{H}_{20}\text{FN}_2\text{O}_2\text{Na}$: 361.1328; found: 361.1320.

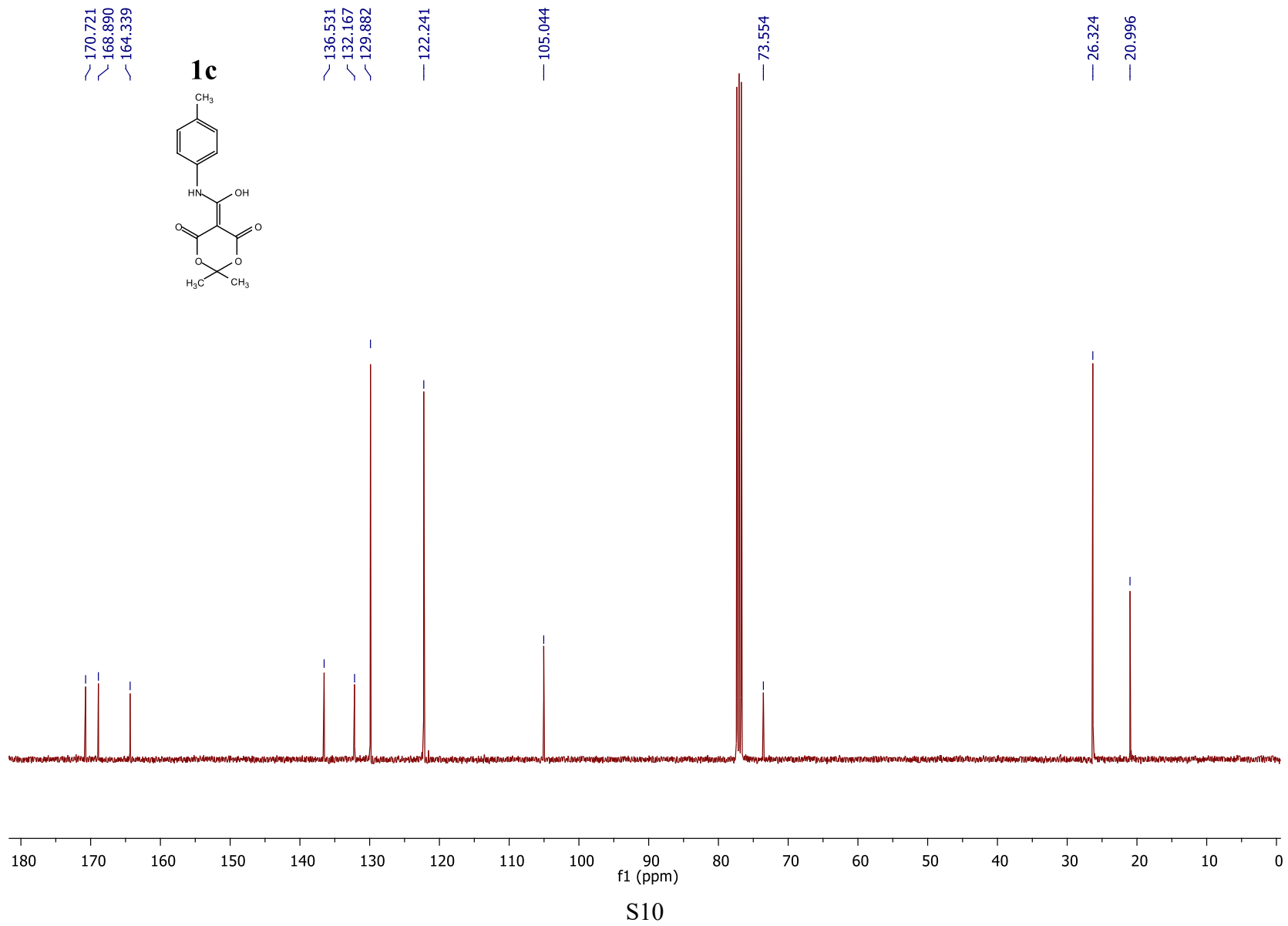
2-(2-chlorobenzylidene)-N¹-ethyl-N³,N³-dimethylmalonamide (**8gc**, **8gc'**)

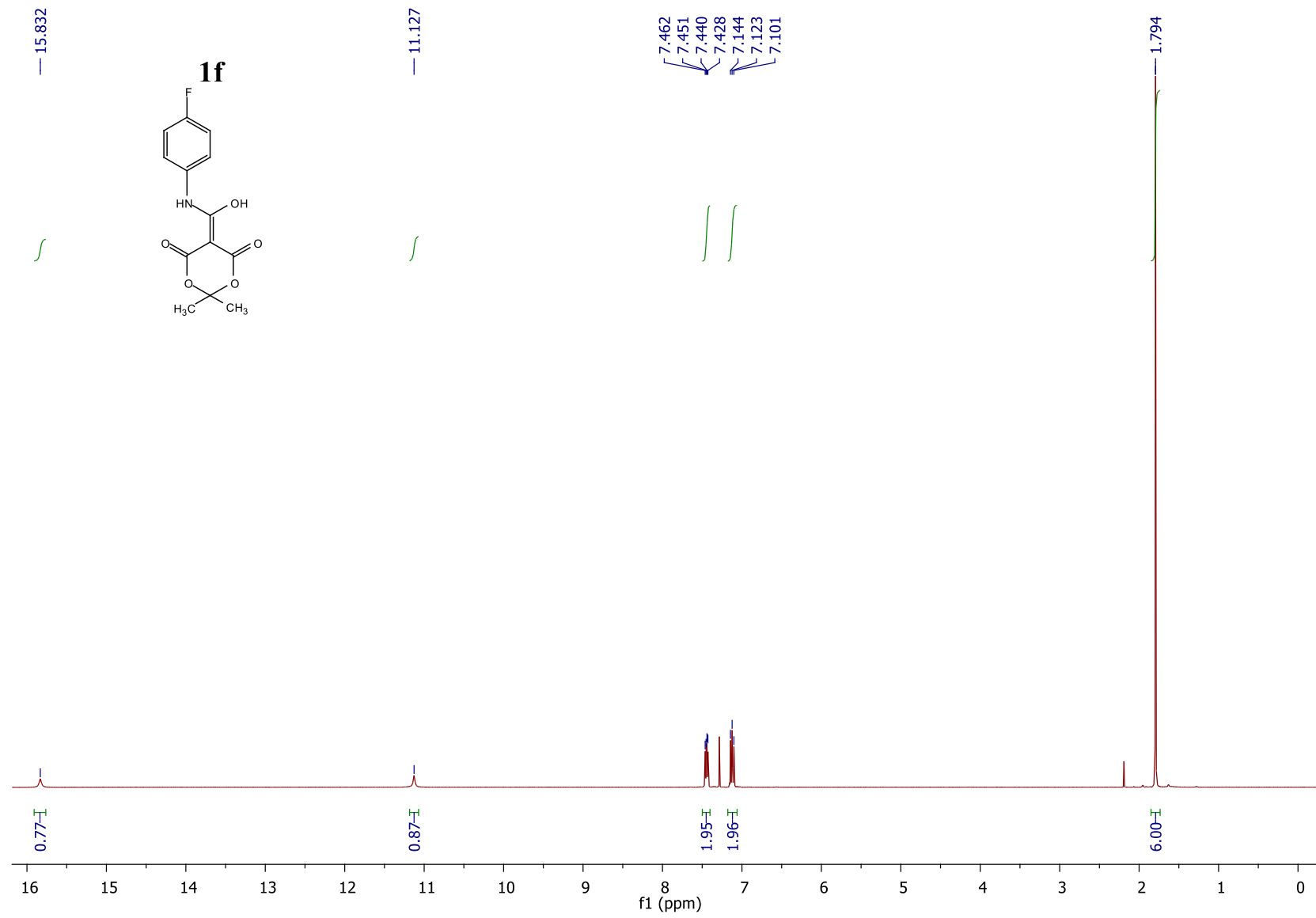


Purification by flash column chromatography, (EtOAc/Hex, 2:1), brown oil, 0.249 g, 89% yield; mixture of (E) and (Z) stereoisomers with ratio 3:1; ^1H NMR (CDCl_3 , 400 MHz): δ = 7.98 (s, 0.75 H), 7.49 (dd, J = 7.6 Hz, J = 2.0 Hz, 0.25 H), 7.42 (dd, J = 8.0 Hz, J = 1.2 Hz, 0.75 H), 7.38 (dd, J = 7.2 Hz, J = 1.6 Hz, 0.63 H), 7.34-7.20 (m, 2.75 H), 7.10 (brs, 0.75 H), 7.02 (brs, 0.25 H), 6.90 (s, 0.25 H), 3.39 (quint, J = 7.2 Hz, 1.5 H), 3.33-3.25 (m, 1.25 H), 3.07 (s, 0.75 H), 2.86 (s, 2.25 H), 2.60 (s, 2.25 H), 1.20 (t, J = 7.2 Hz, 2.25 H), 1.11 (t, J = 7.2 Hz, 0.75 H). ^{13}C NMR (CDCl_3 , 100 MHz): δ = 168.9, 168.6, 163.6, 163.0, 135.0, 134.2, 133.7, 133.4, 132.8, 132.7, 132.5, 131.6, 130.5, 130.0, 129.8, 129.7, 129.3, 129.1, 126.8, 126.6, 39.7, 37.7, 35.2, 34.8, 34.7, 34.4, 14.6, 14.4. HRMS (ESI+): m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{17}\text{ClN}_2\text{O}_2\text{Na}$: 303.0876; found: 303.0884. Ratio of stereoisomers was determined based on integration of ^1H NMR spectra.

^1H and ^{13}C -NMR Spectra



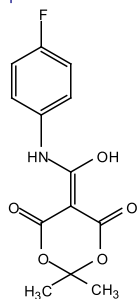




S11

170.848
169.127
164.300
161.989
159.533

1f

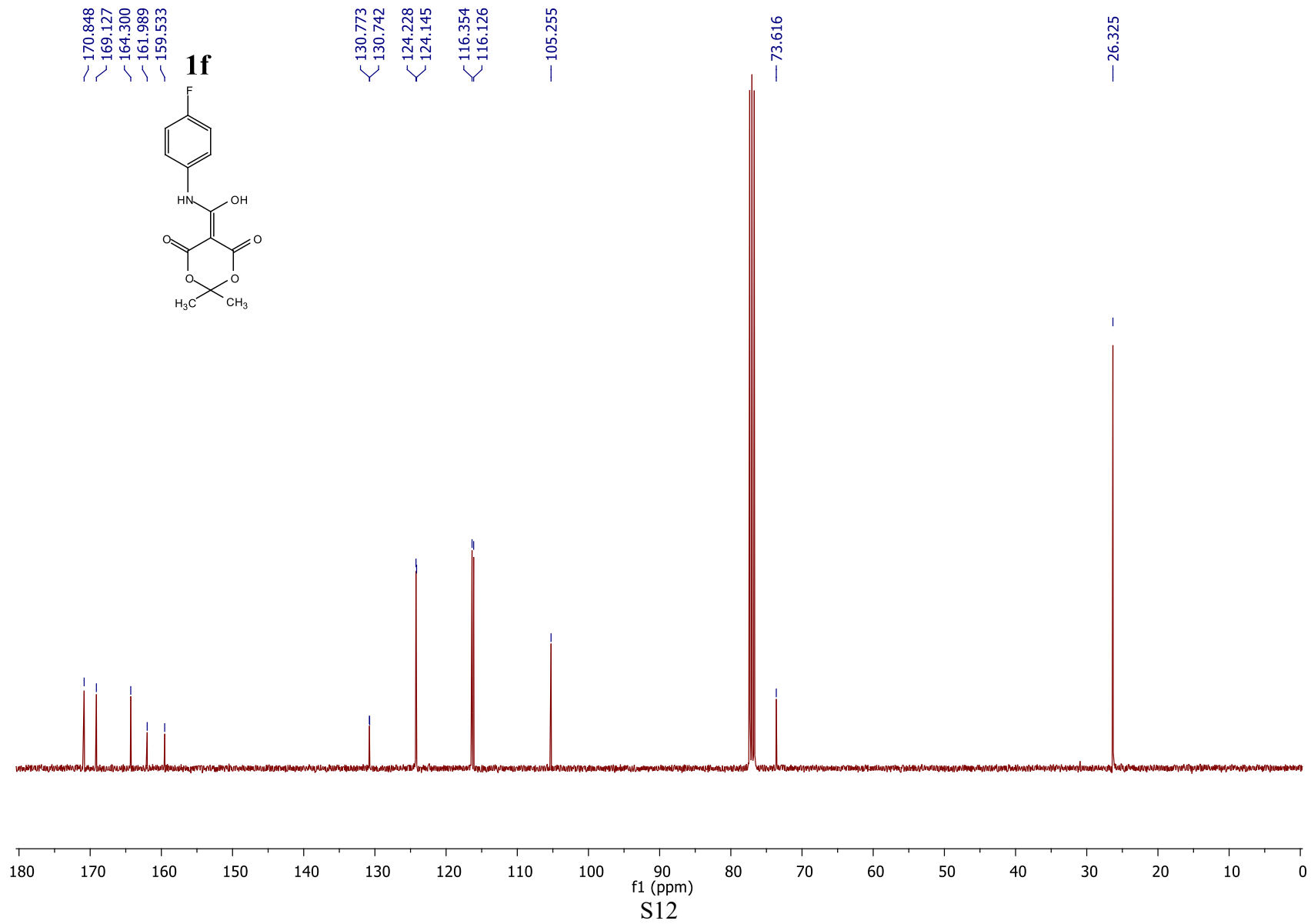


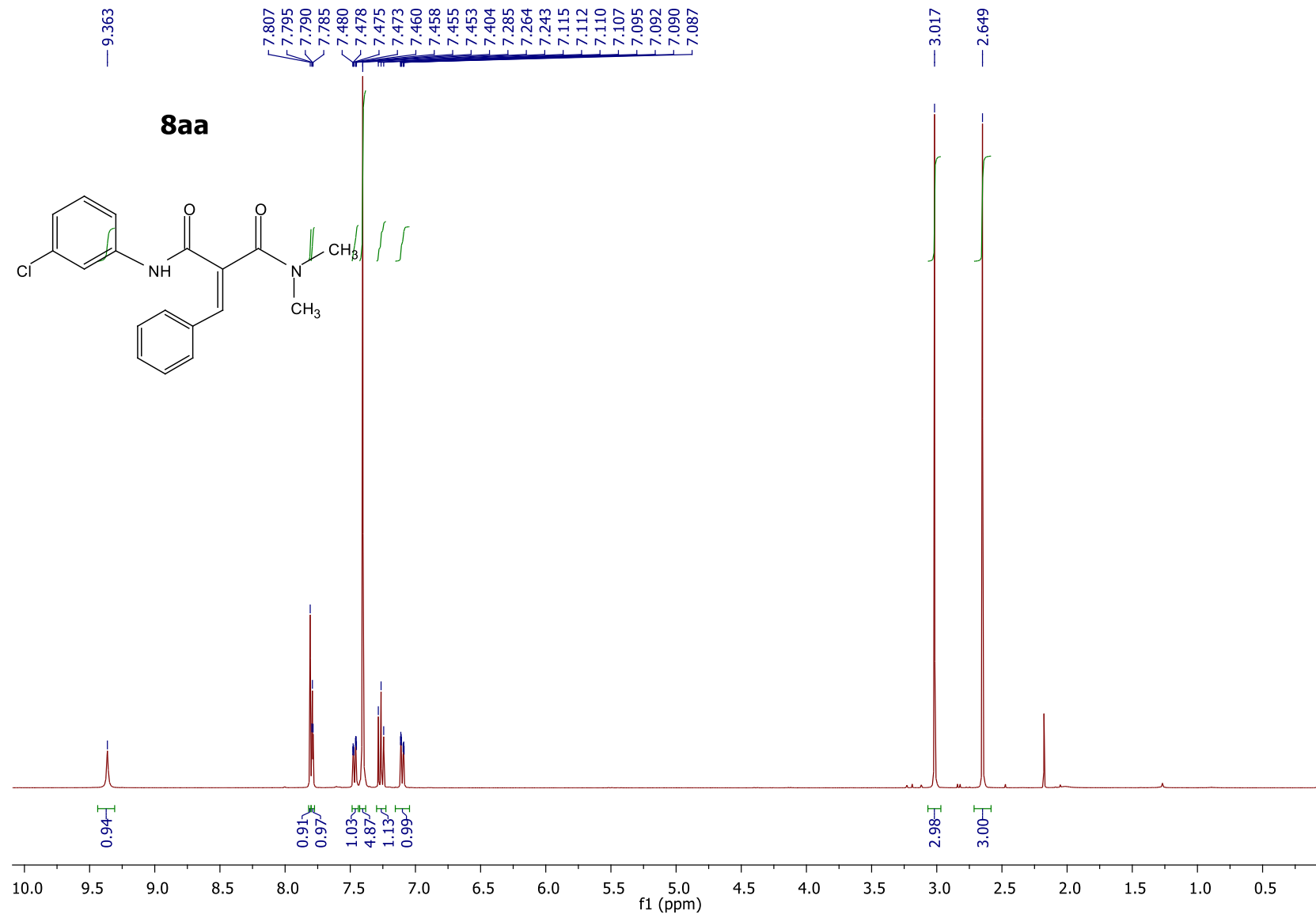
130.773
130.742
124.228
124.145
116.354
116.126

105.255

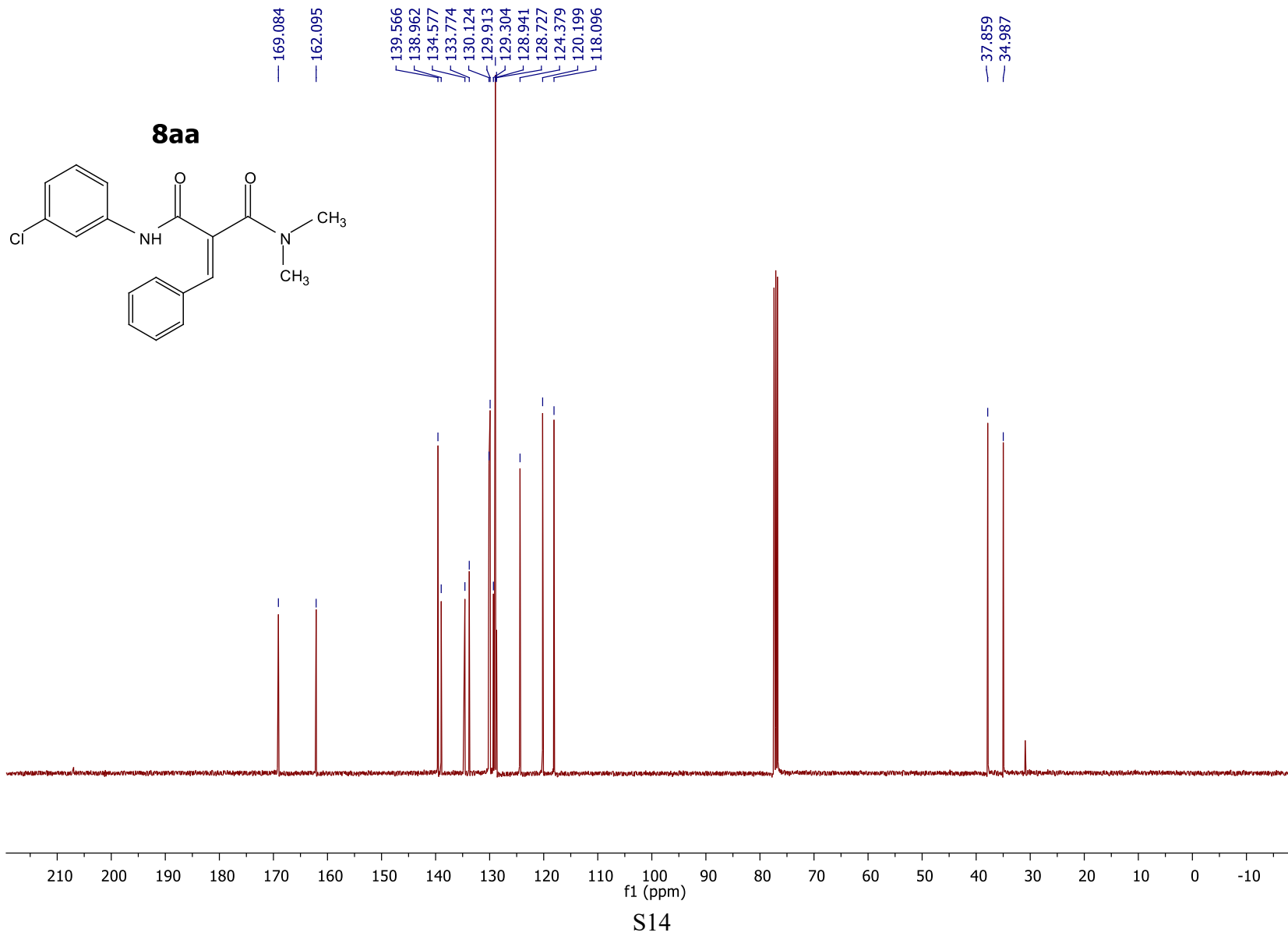
73.616

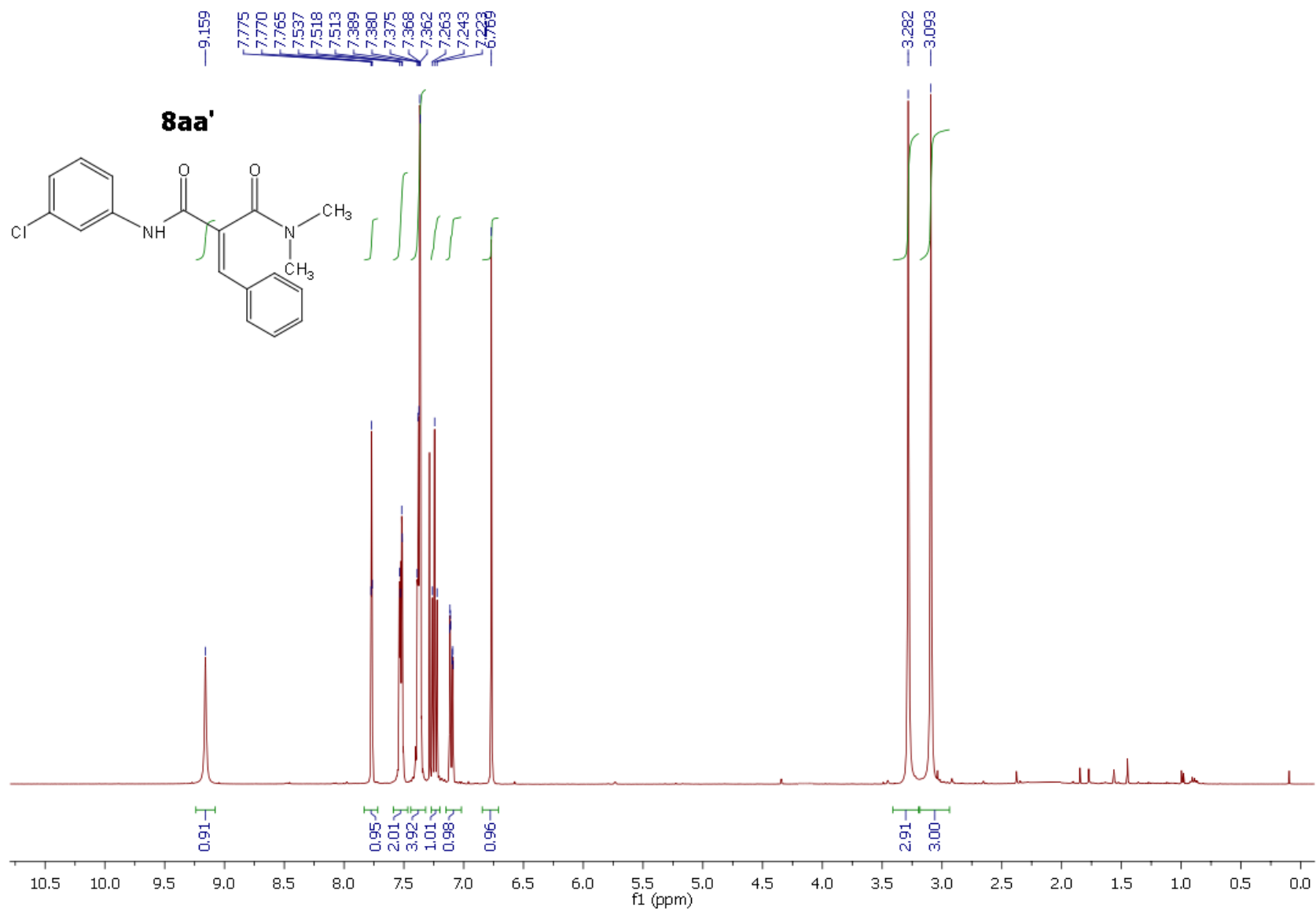
26.325



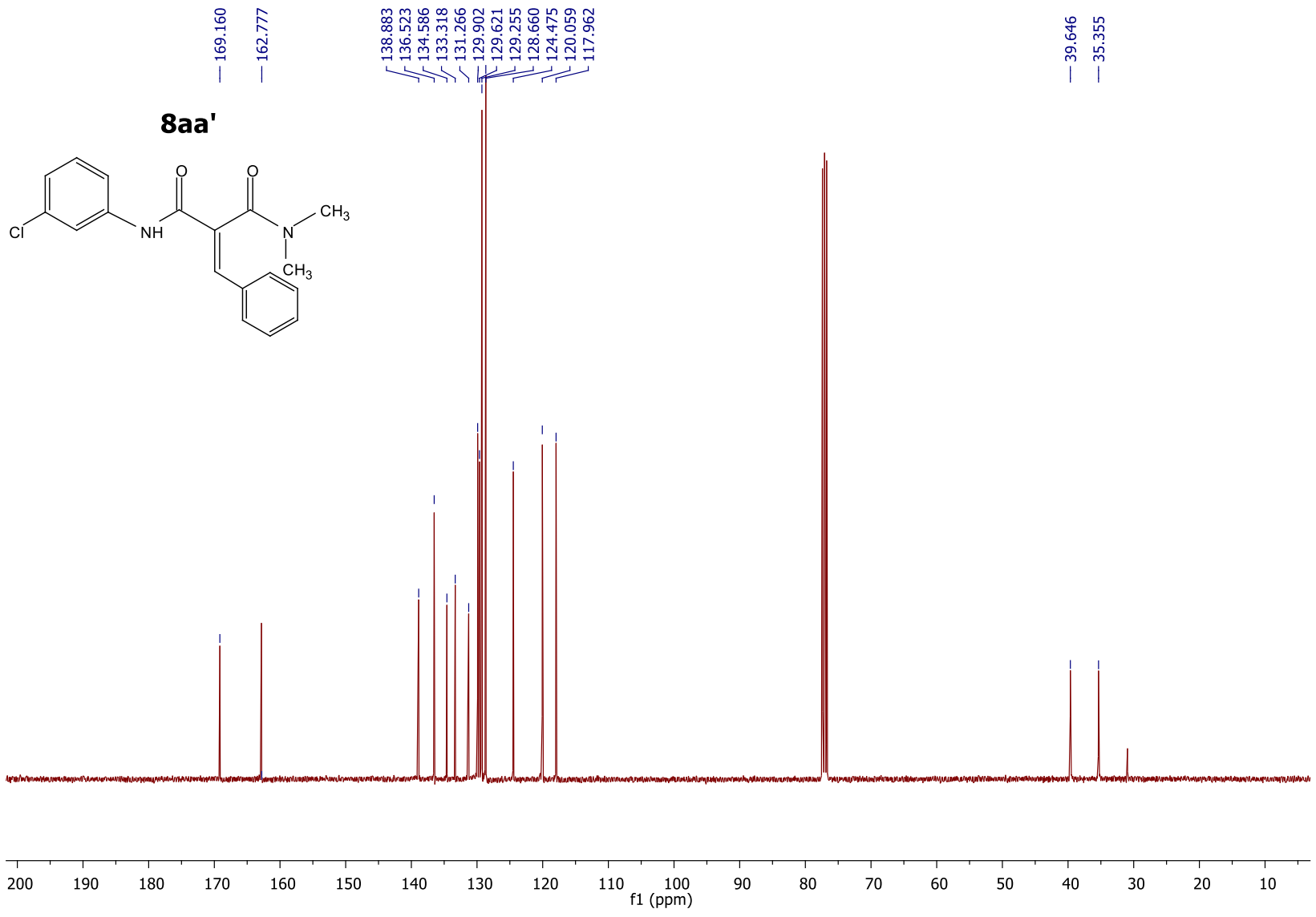


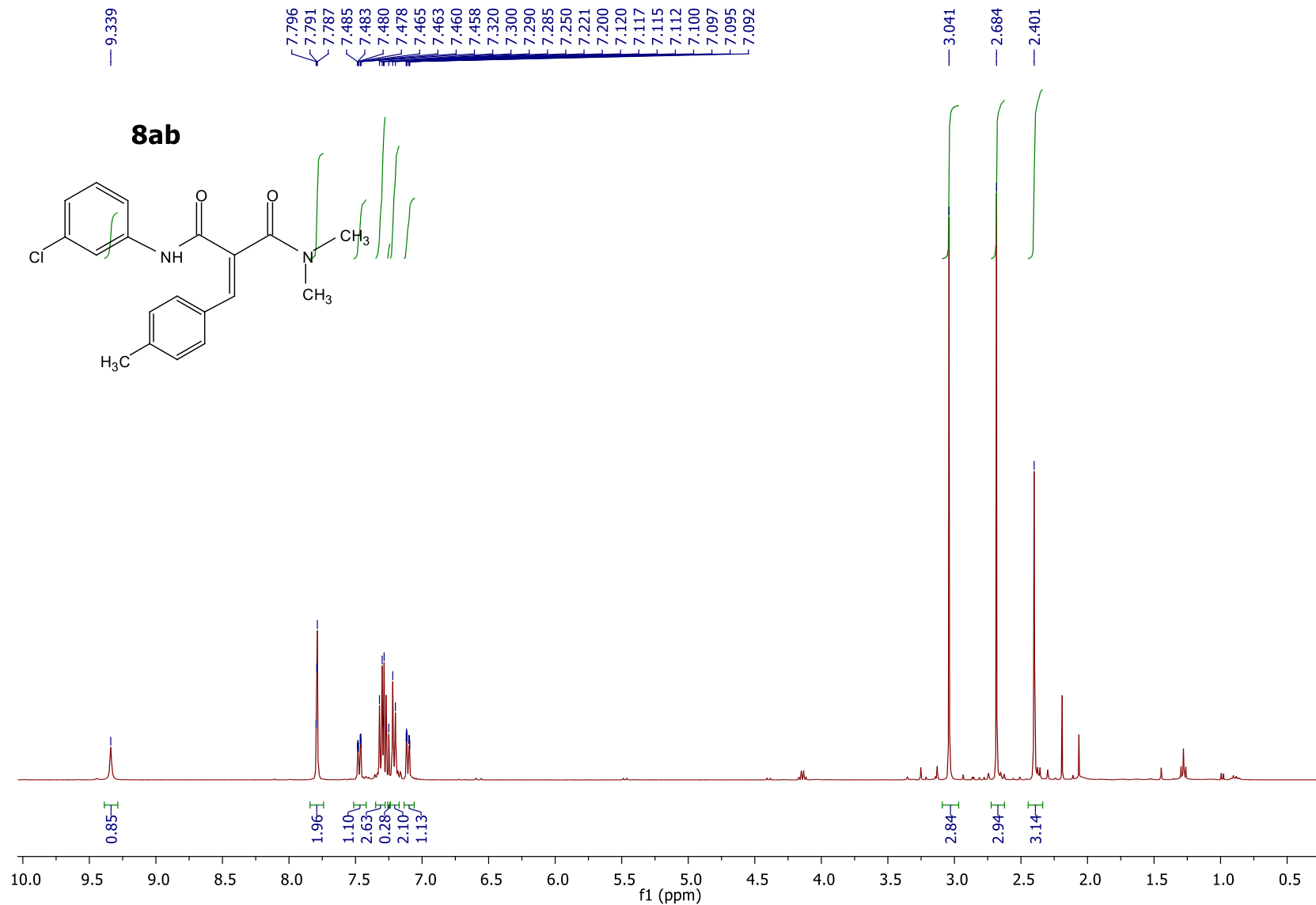
S13

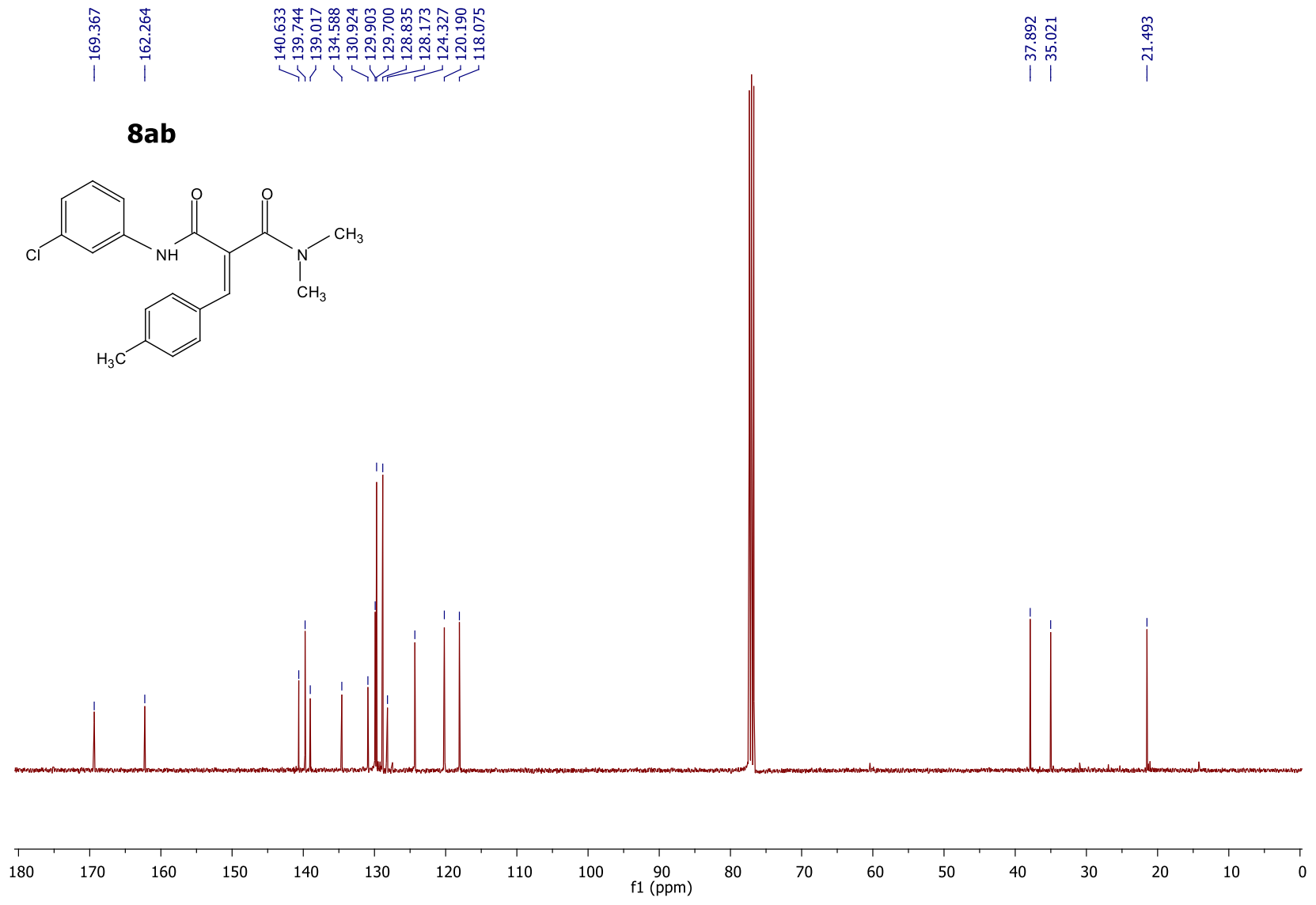




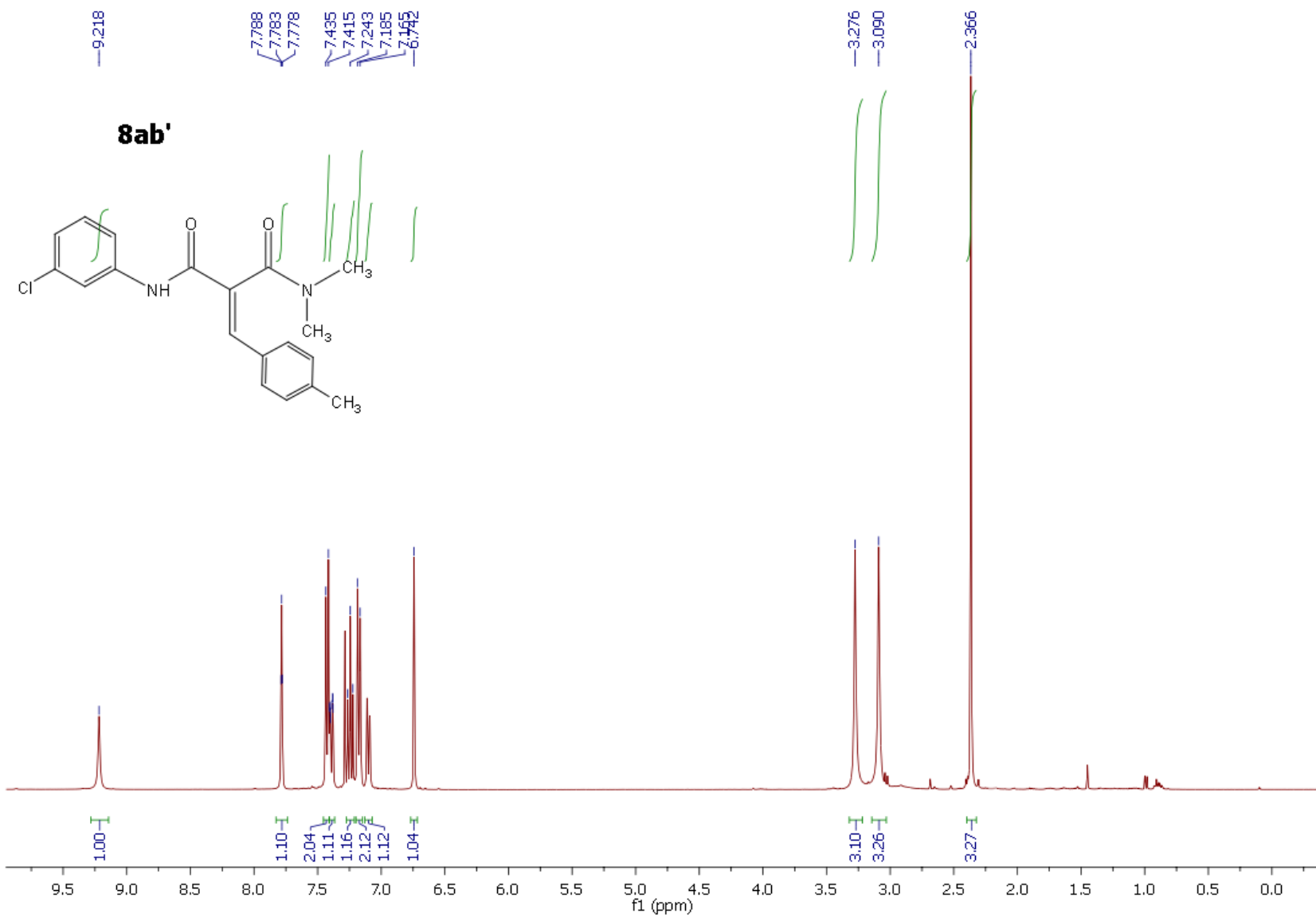
S15

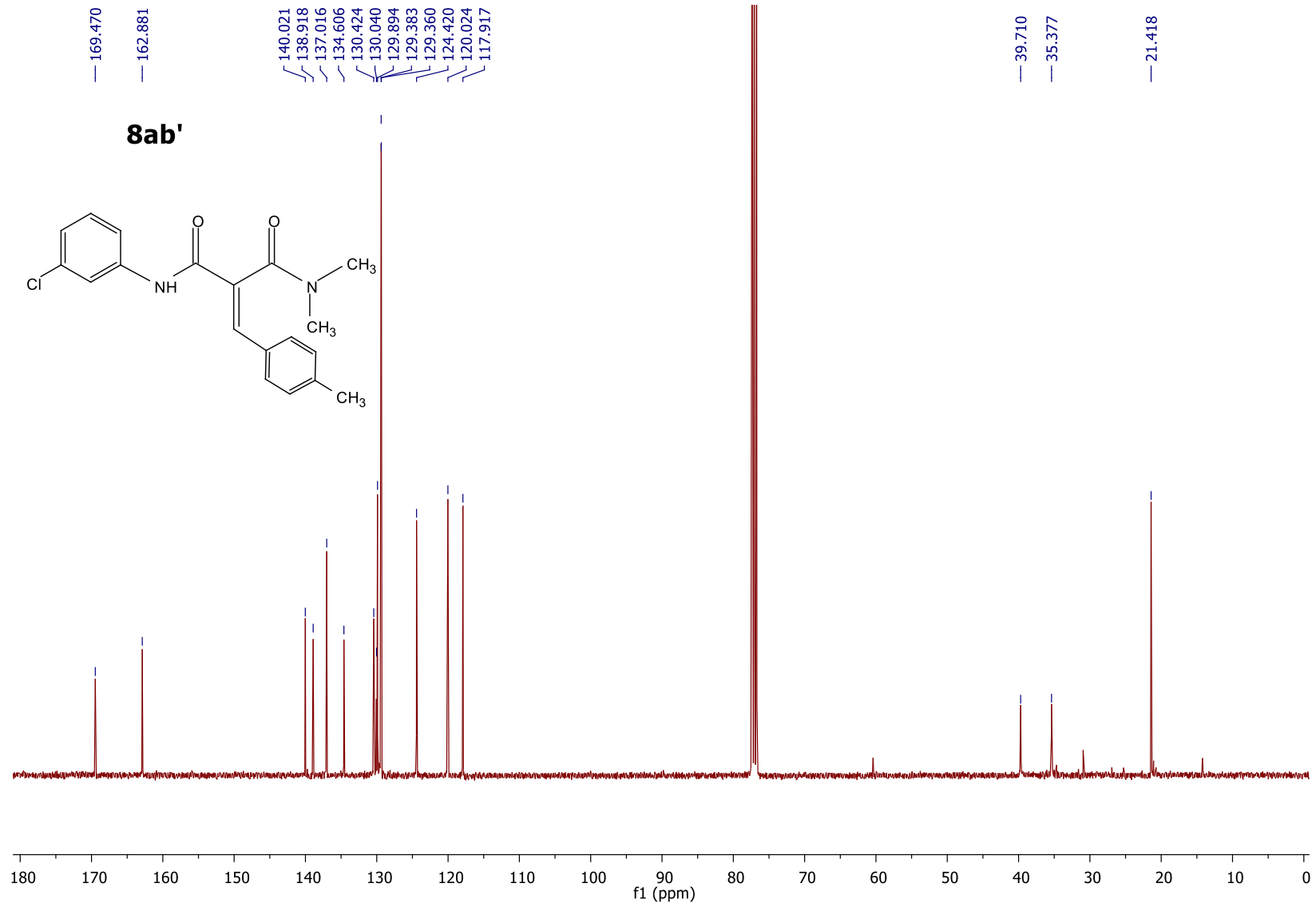




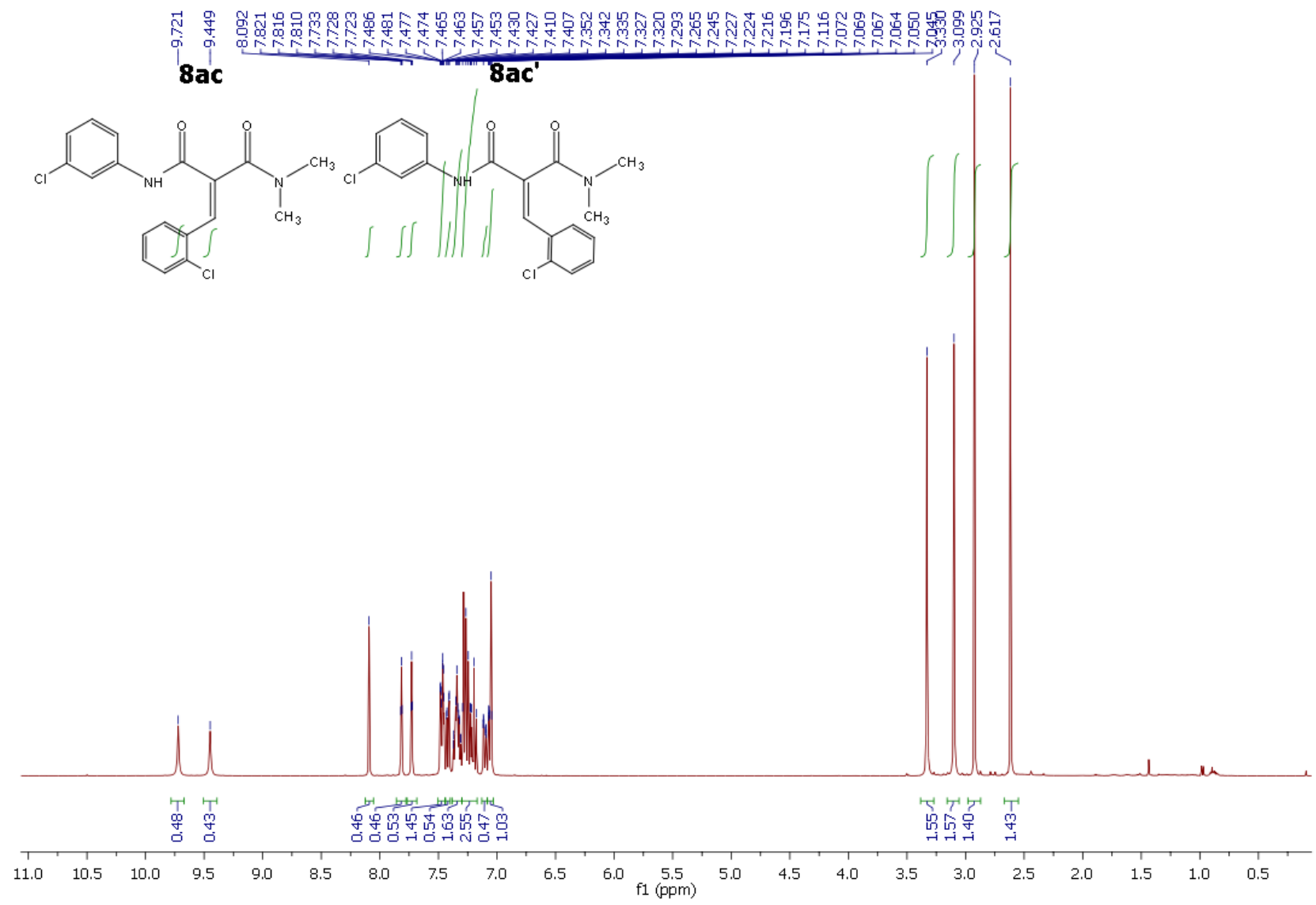


S18

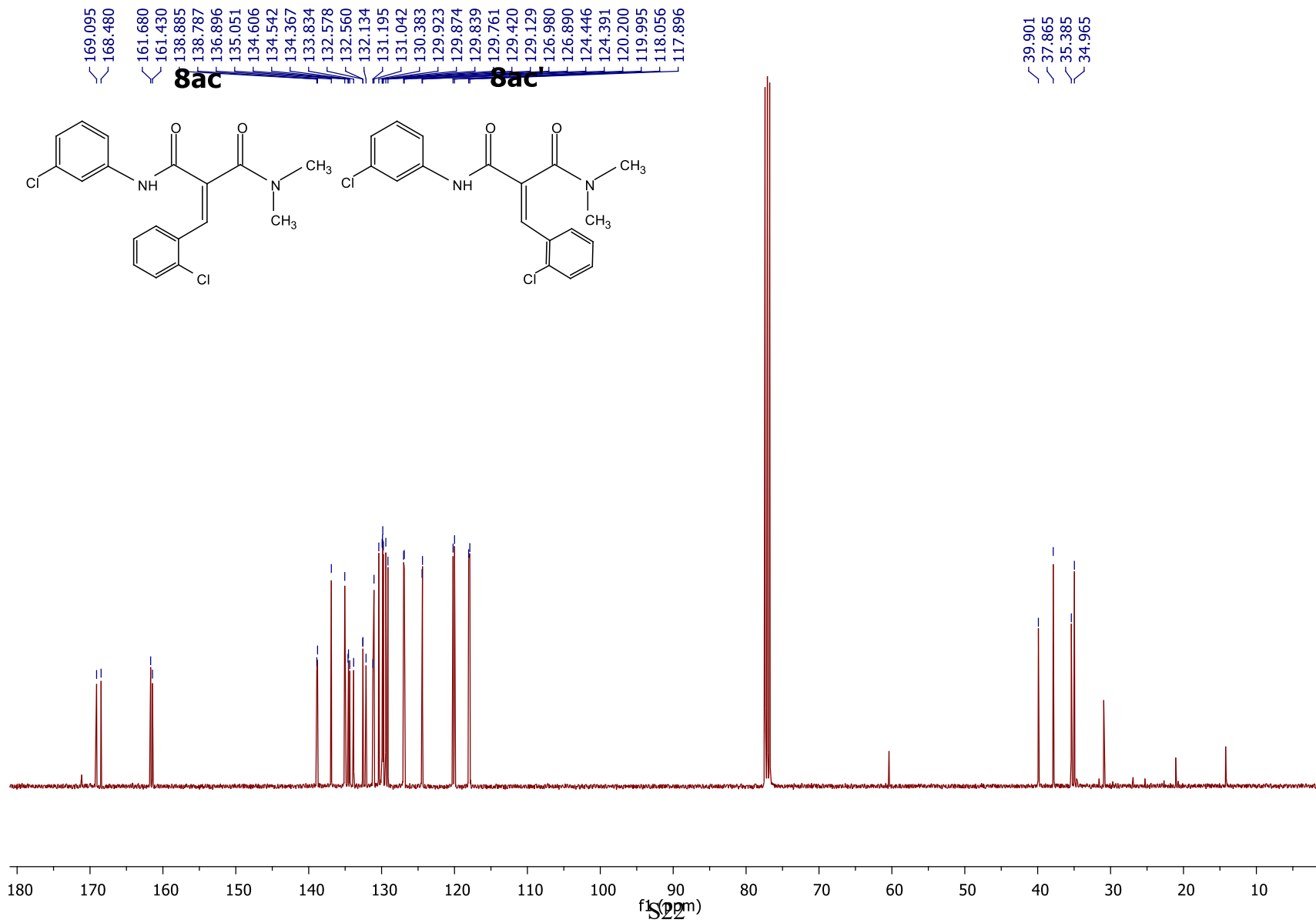


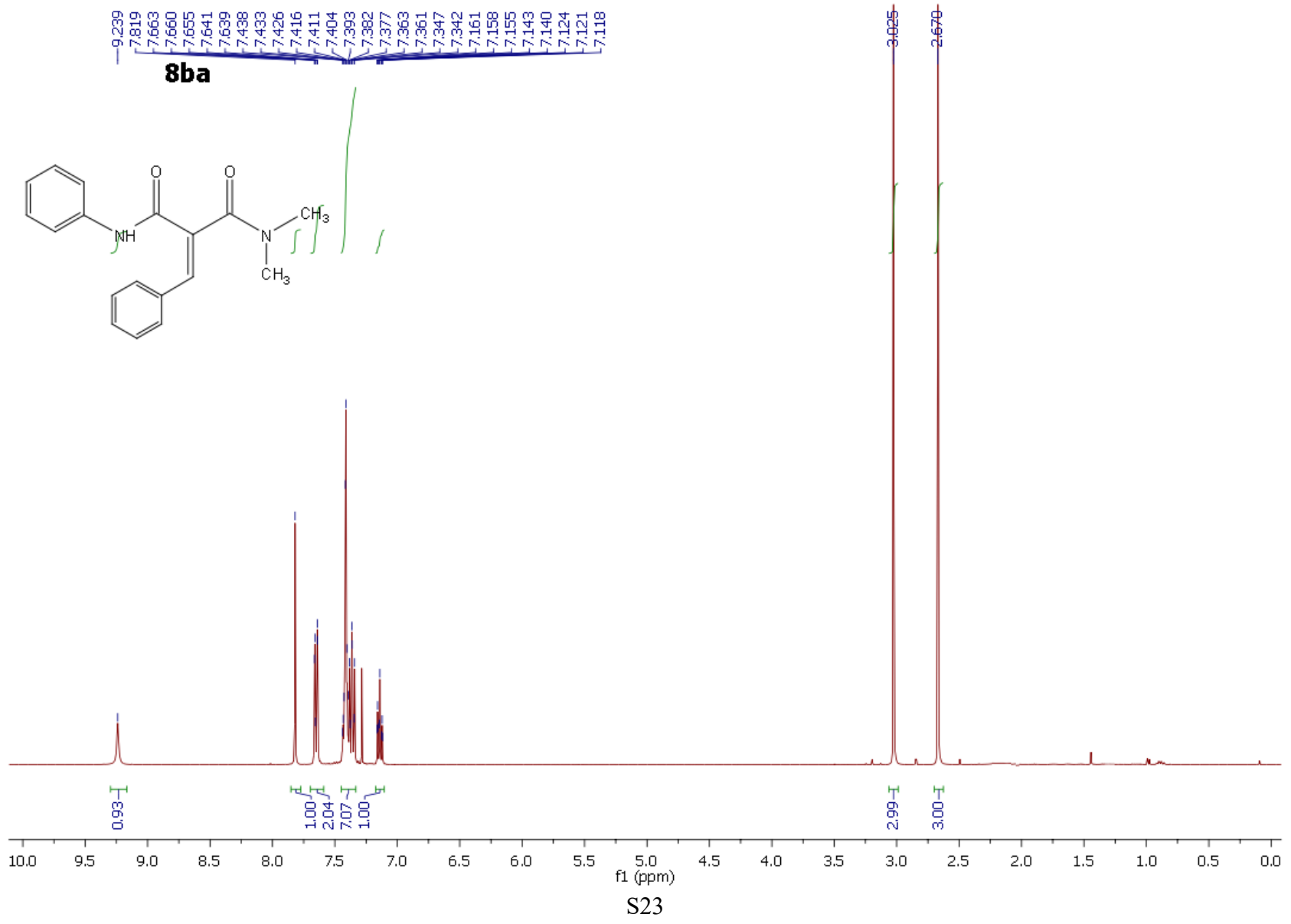


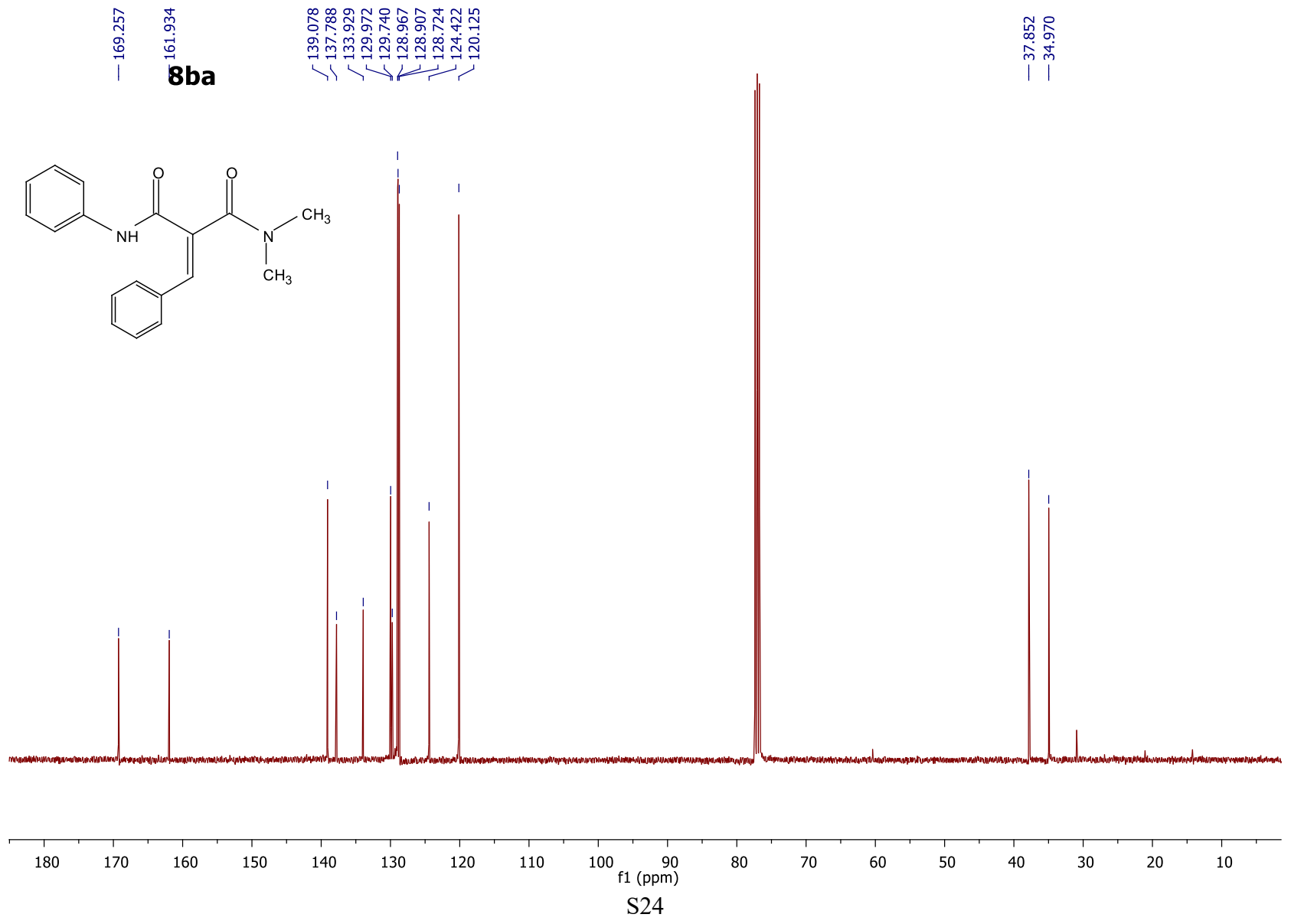
S20

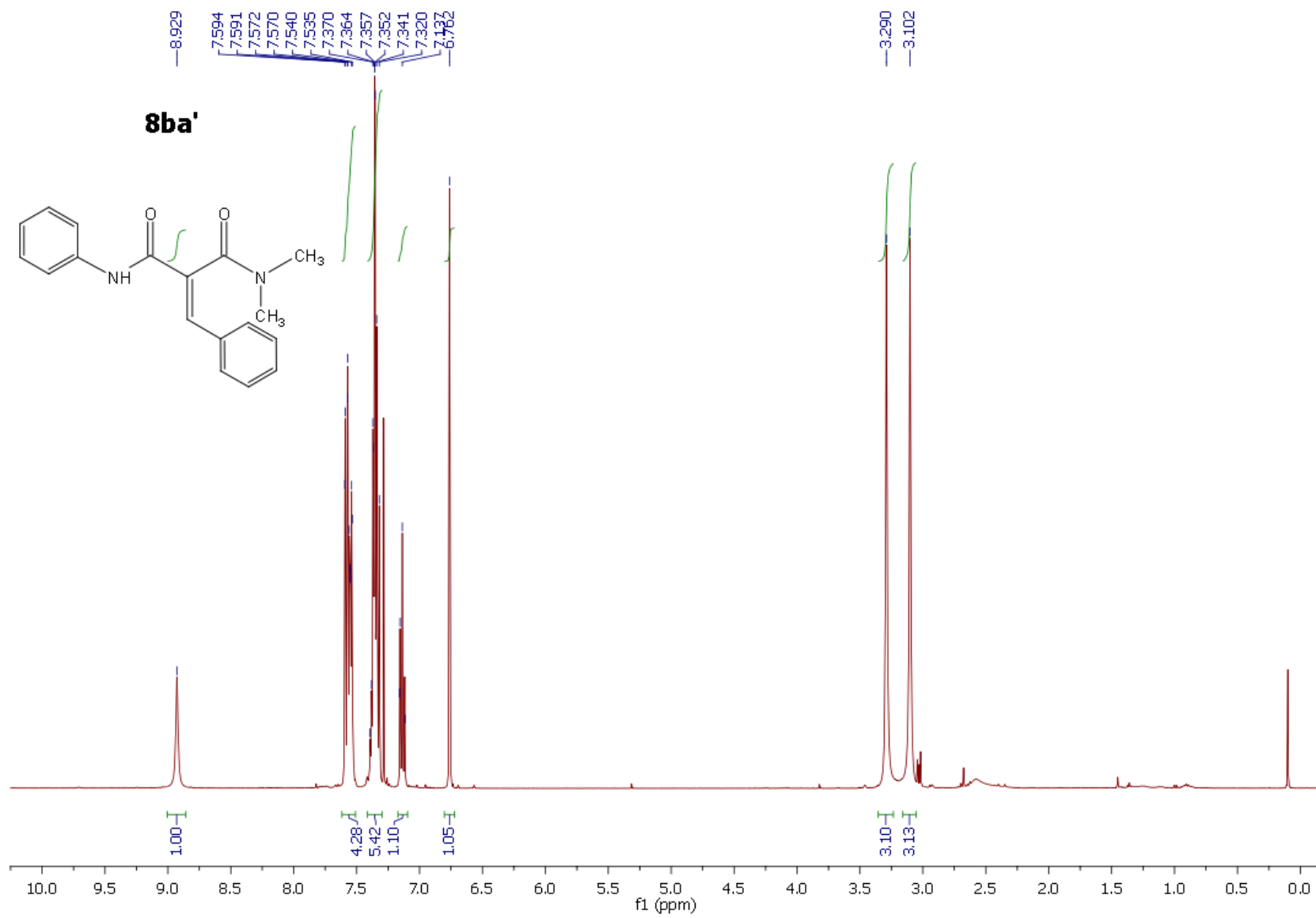


S21

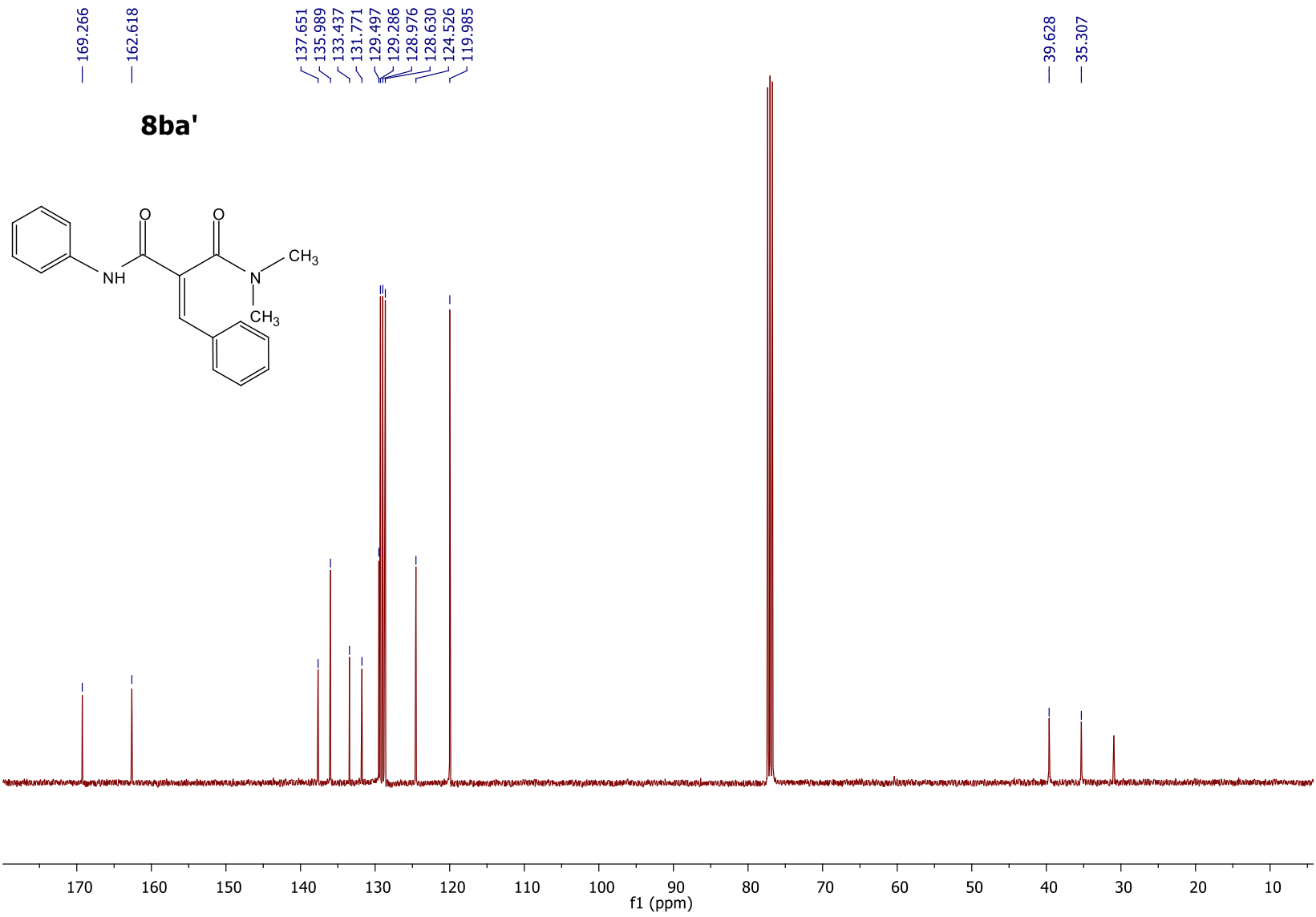


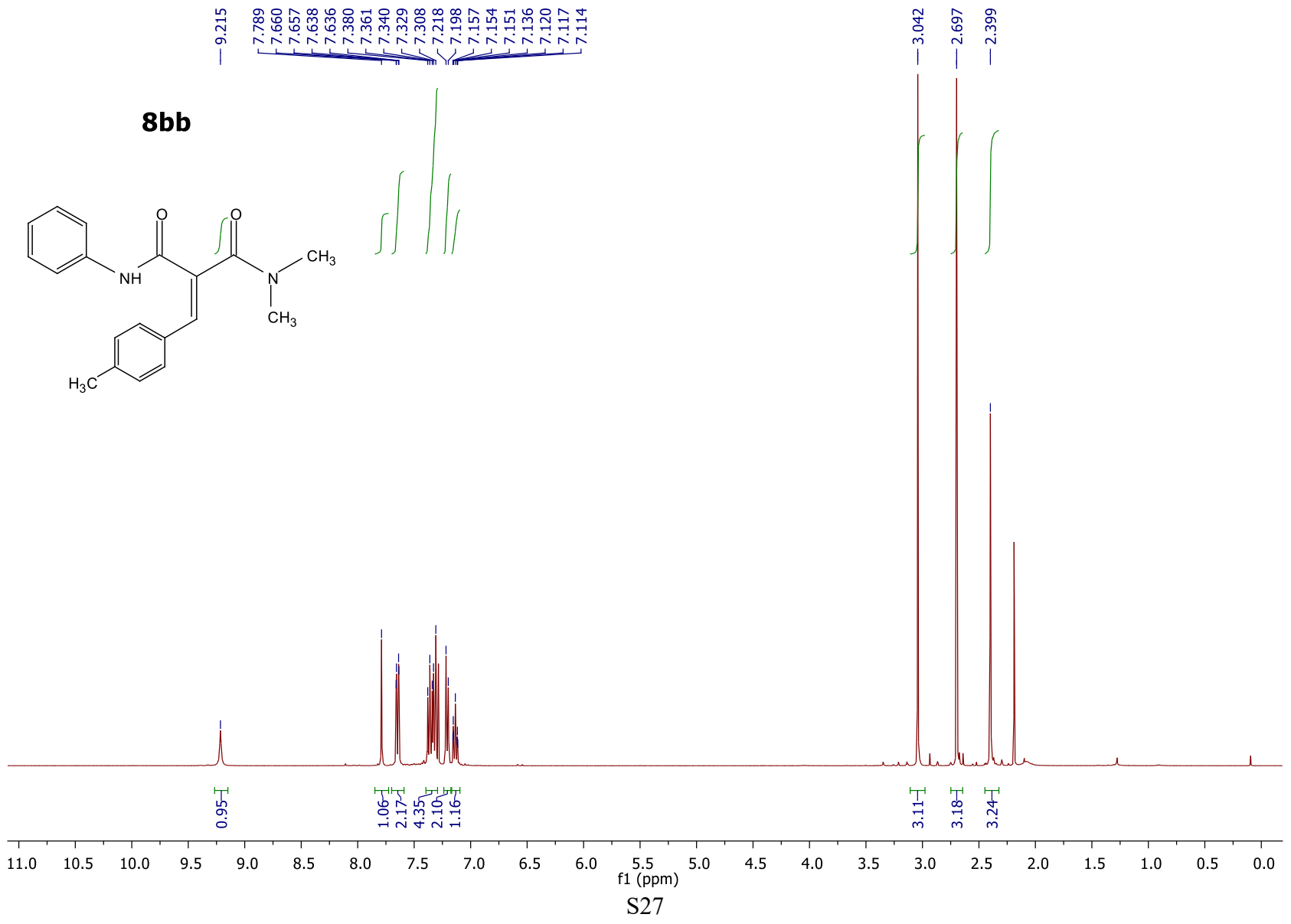






S25





— 169.499

— 162.117

— 140.431

— 139.192

— 137.854

— 131.059

— 129.662

— 128.951

— 128.815

— 128.625

— 124.348

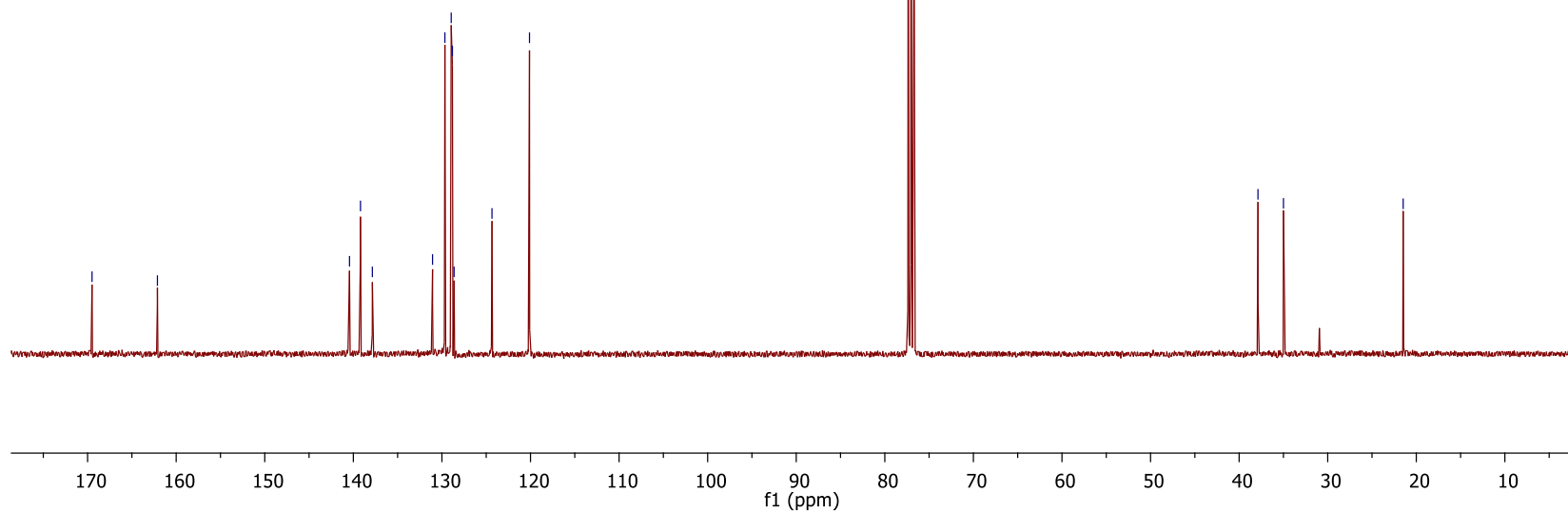
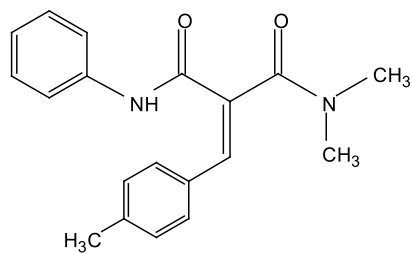
— 120.113

— 37.875

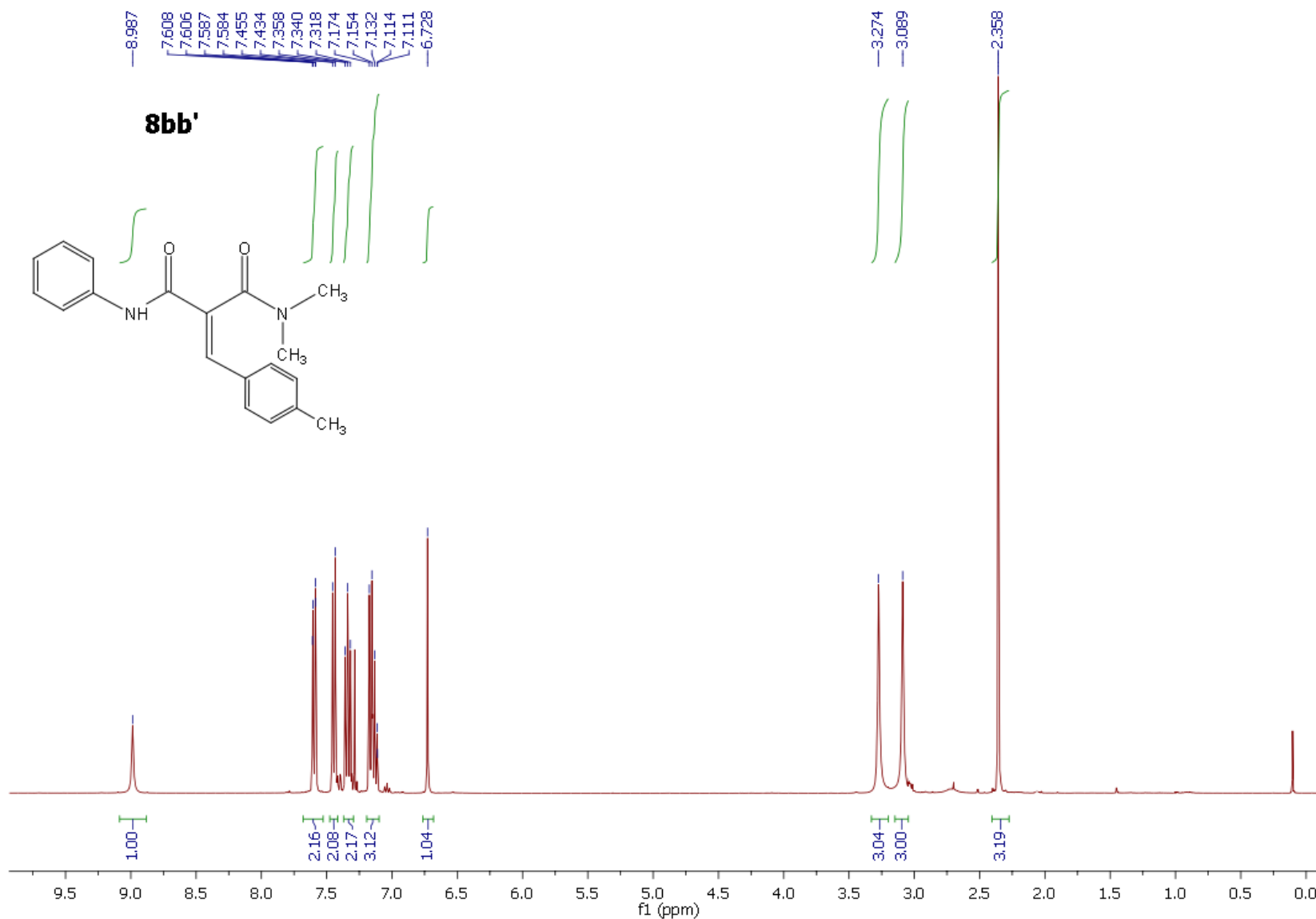
— 34.995

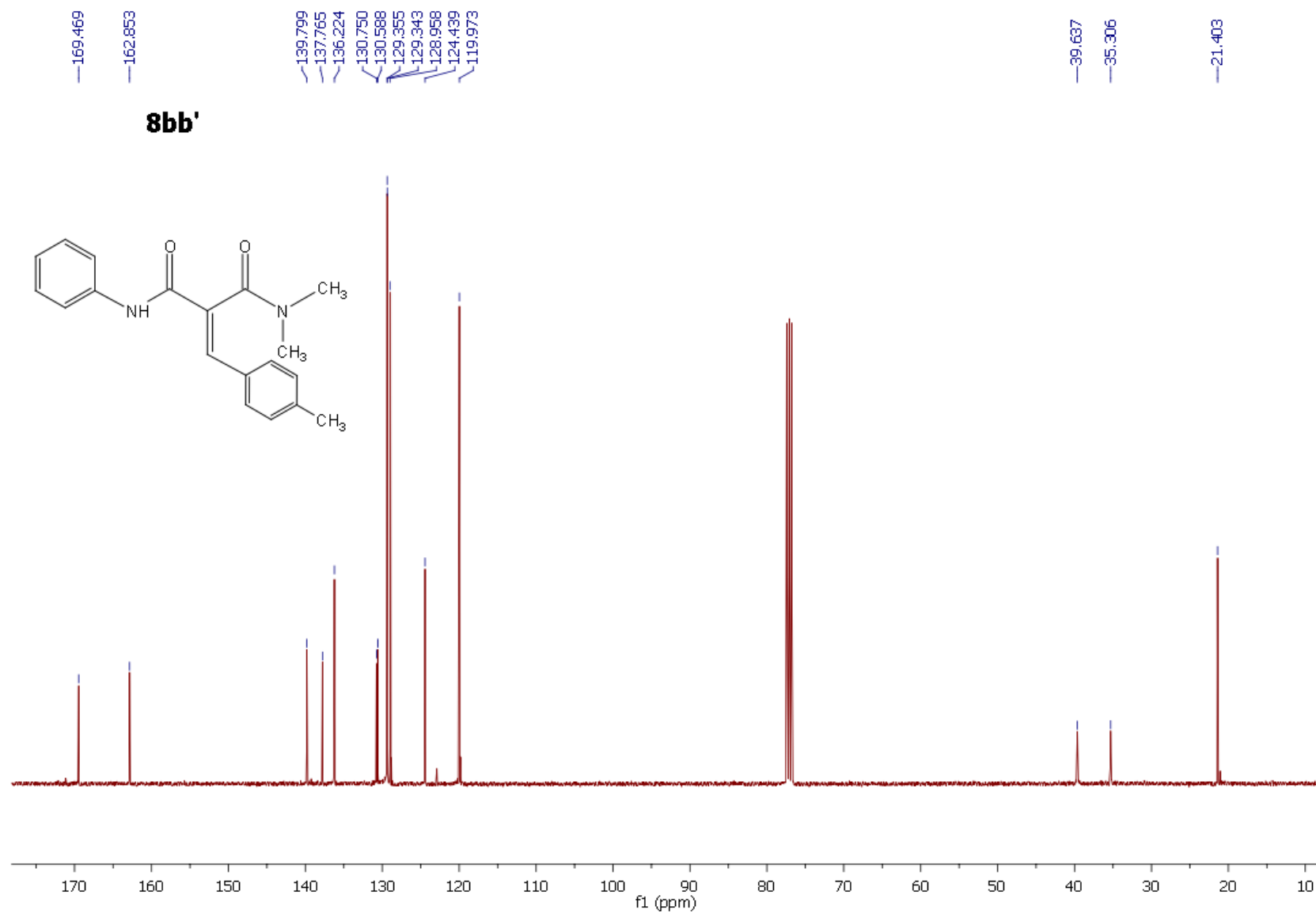
— 21.479

8bb

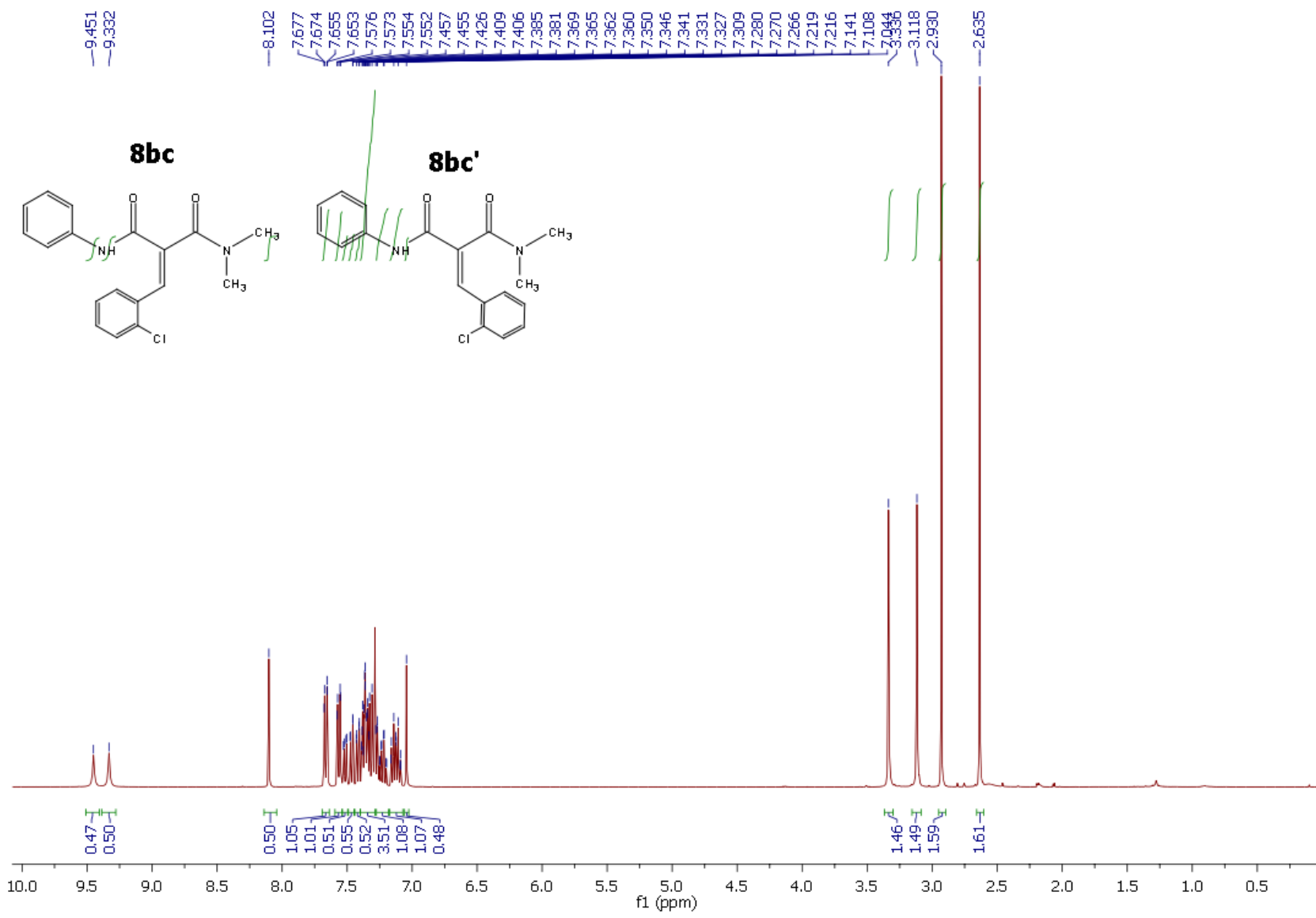


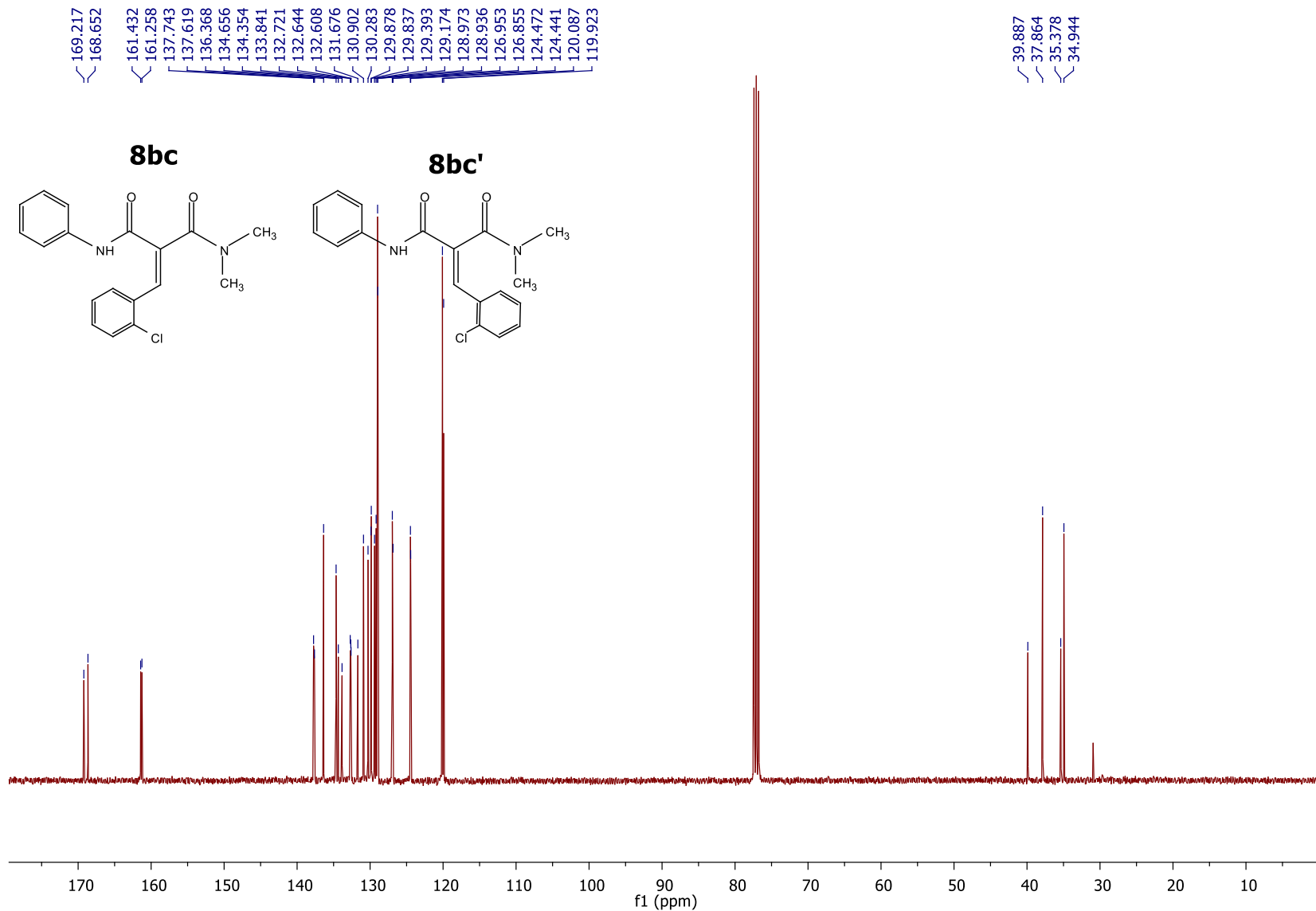
S28

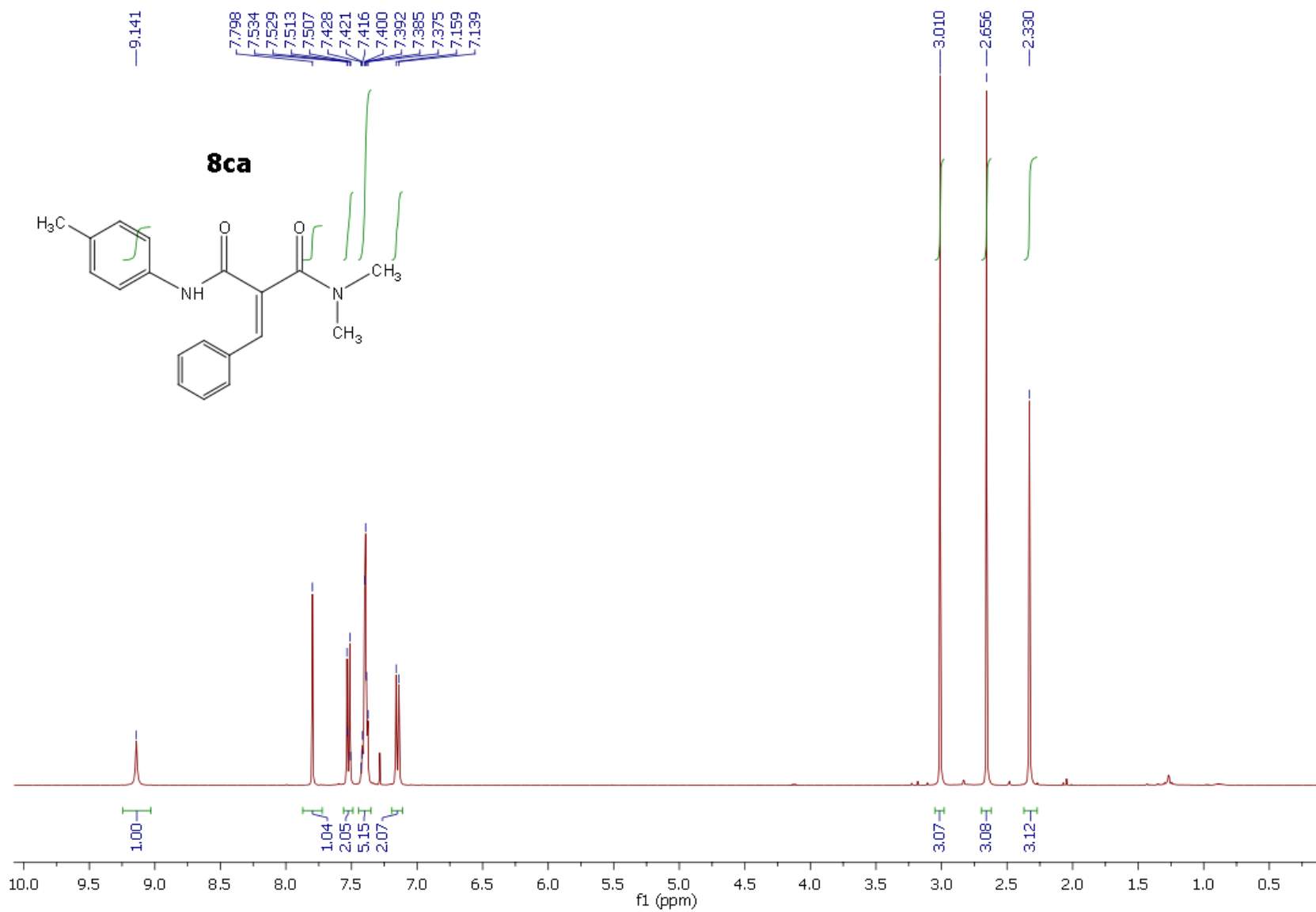


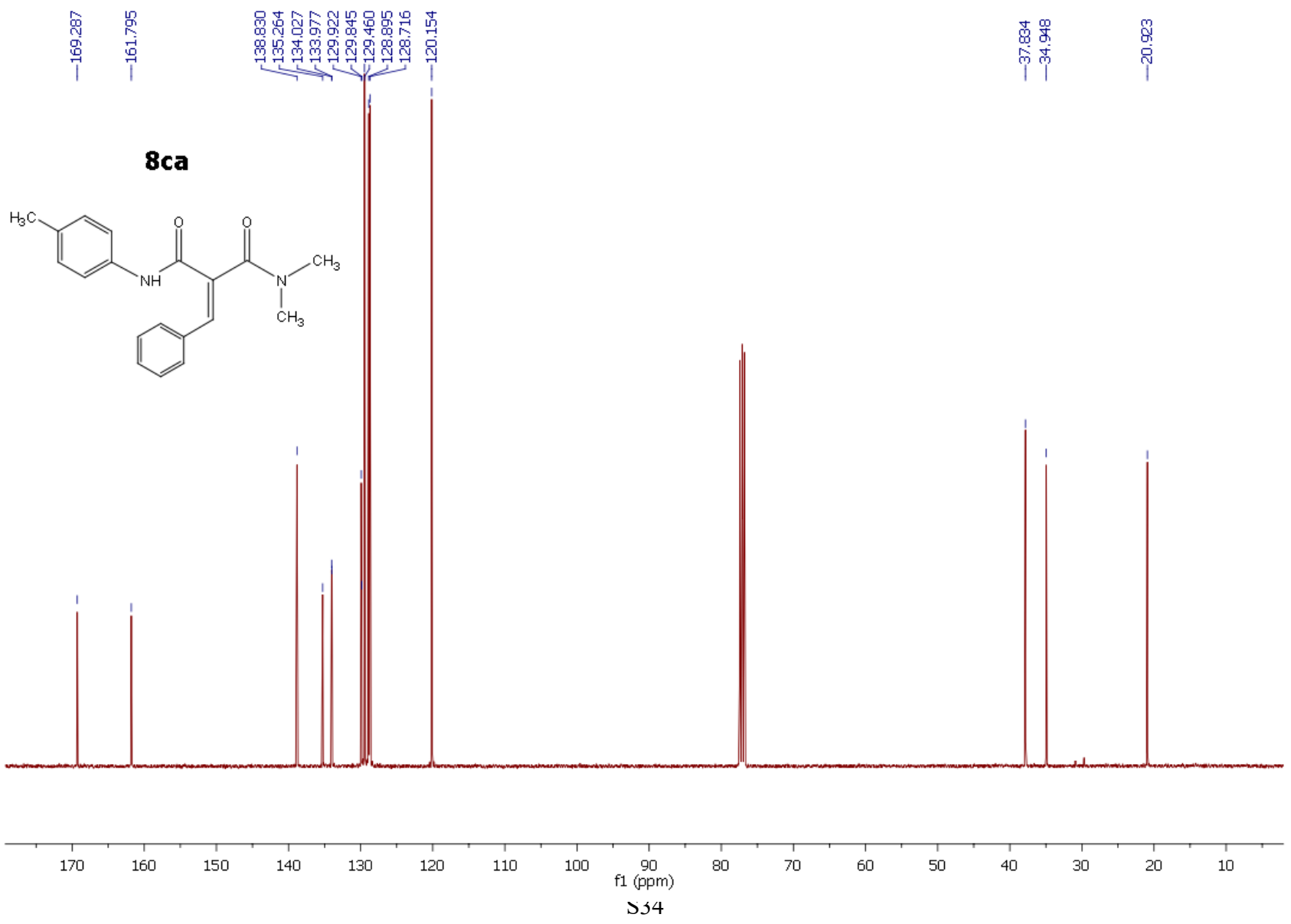


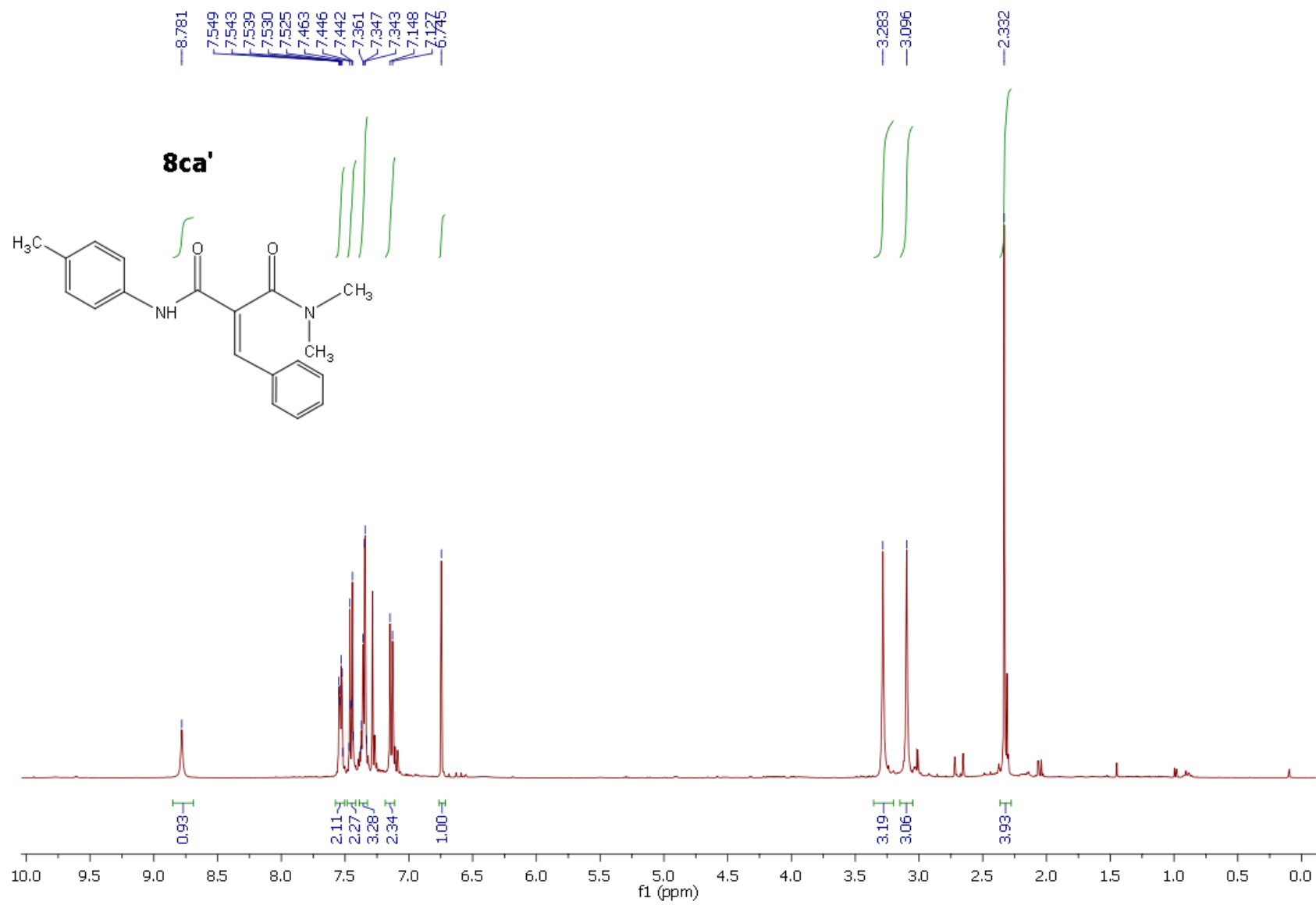
S30



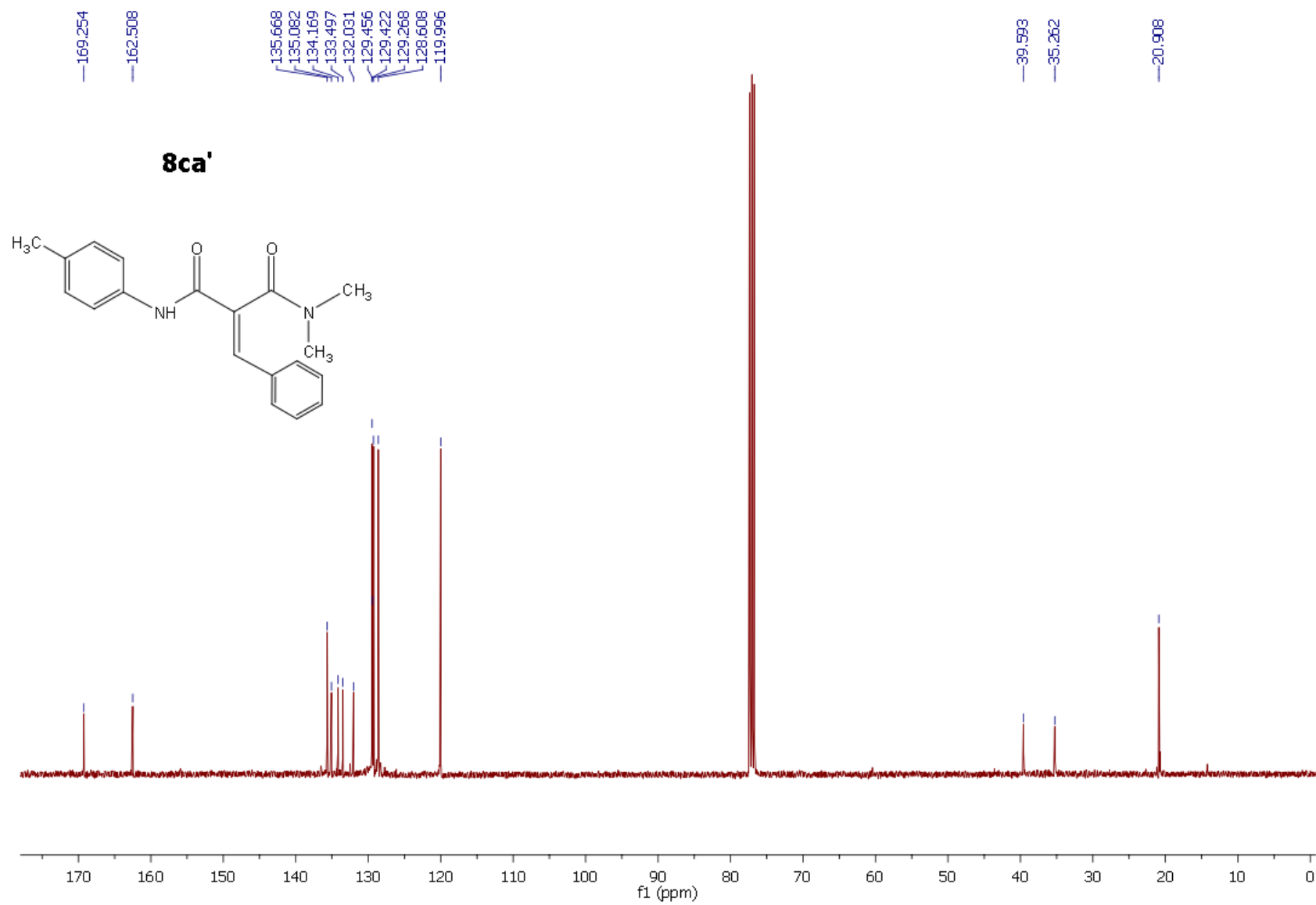




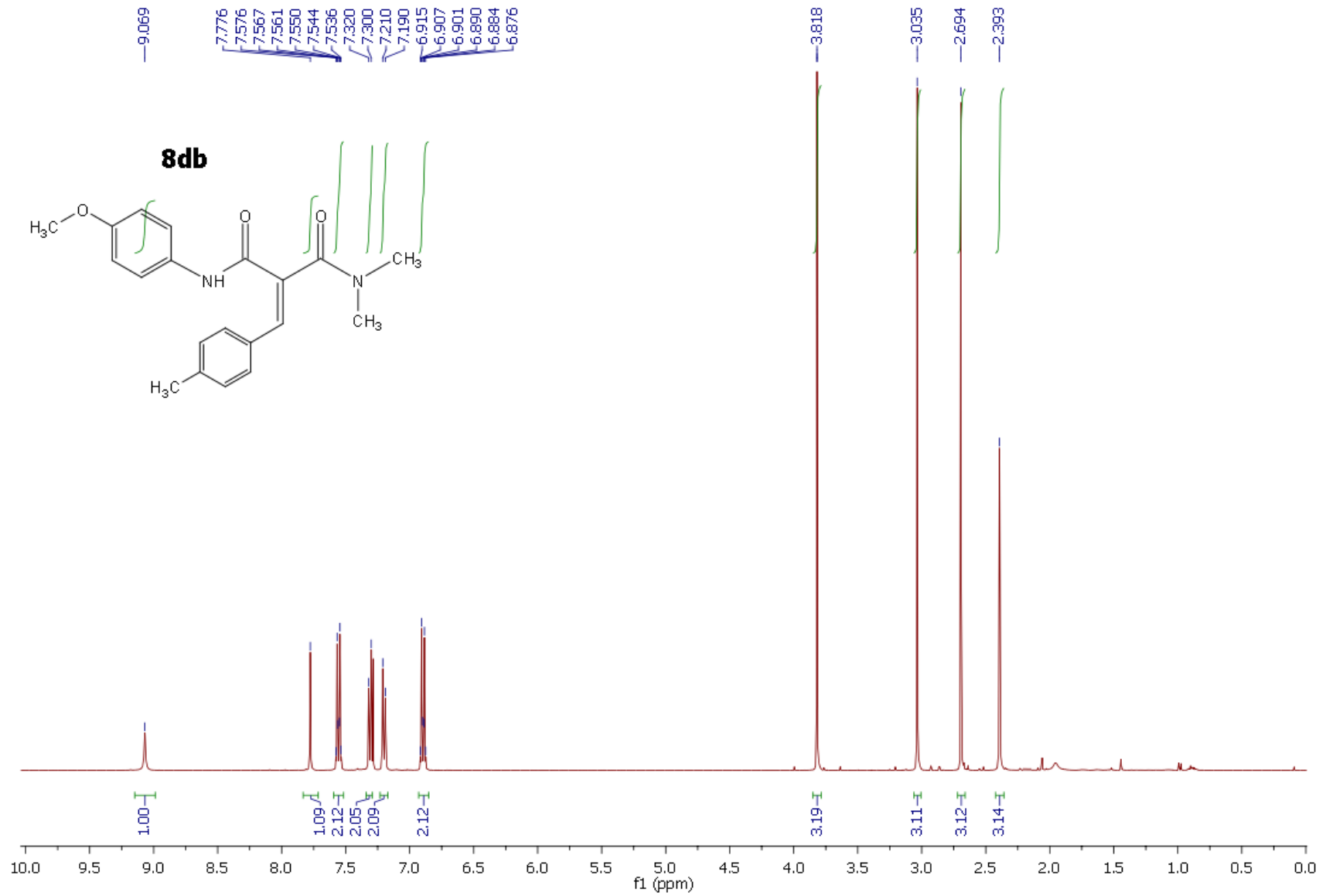




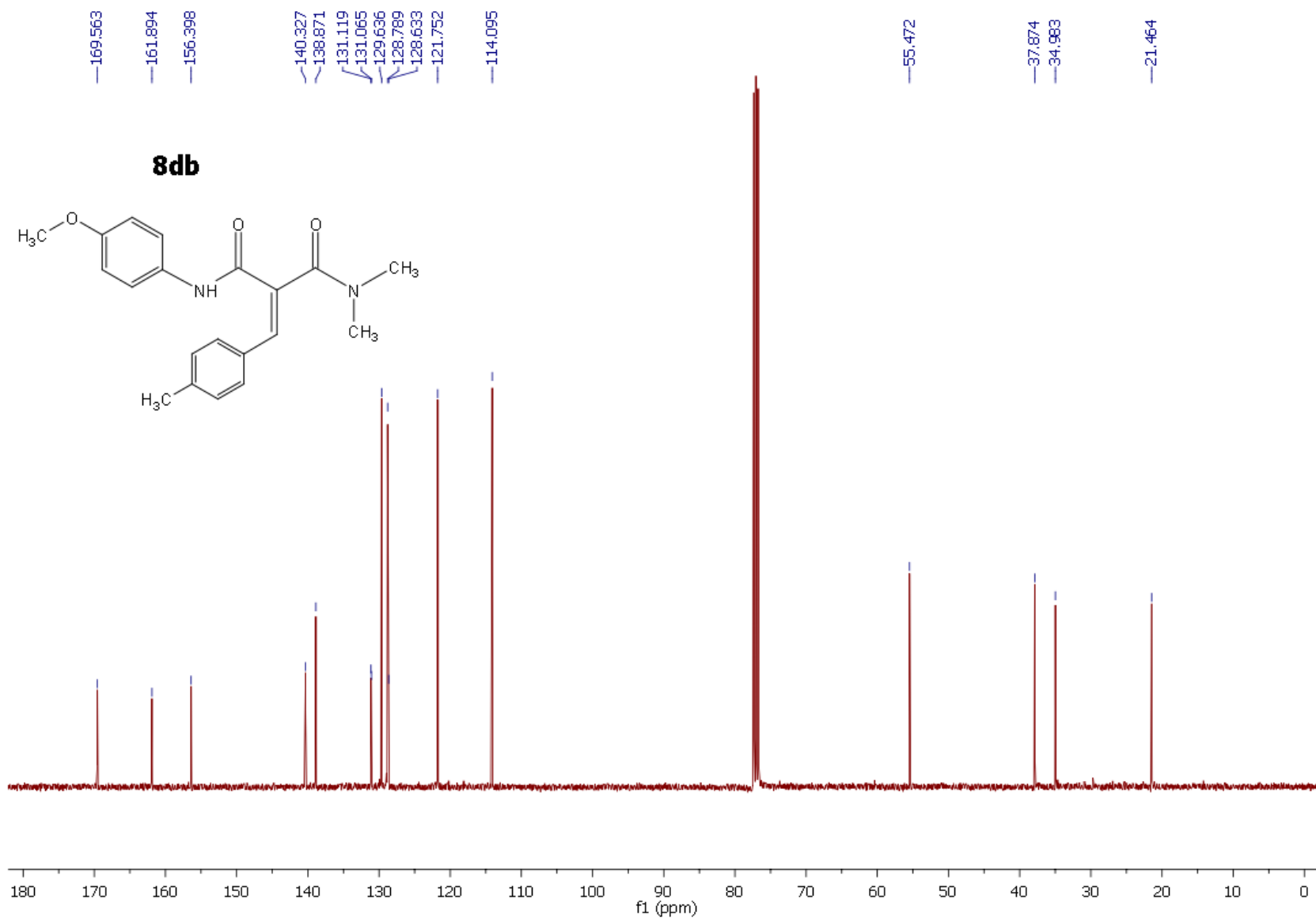
S35



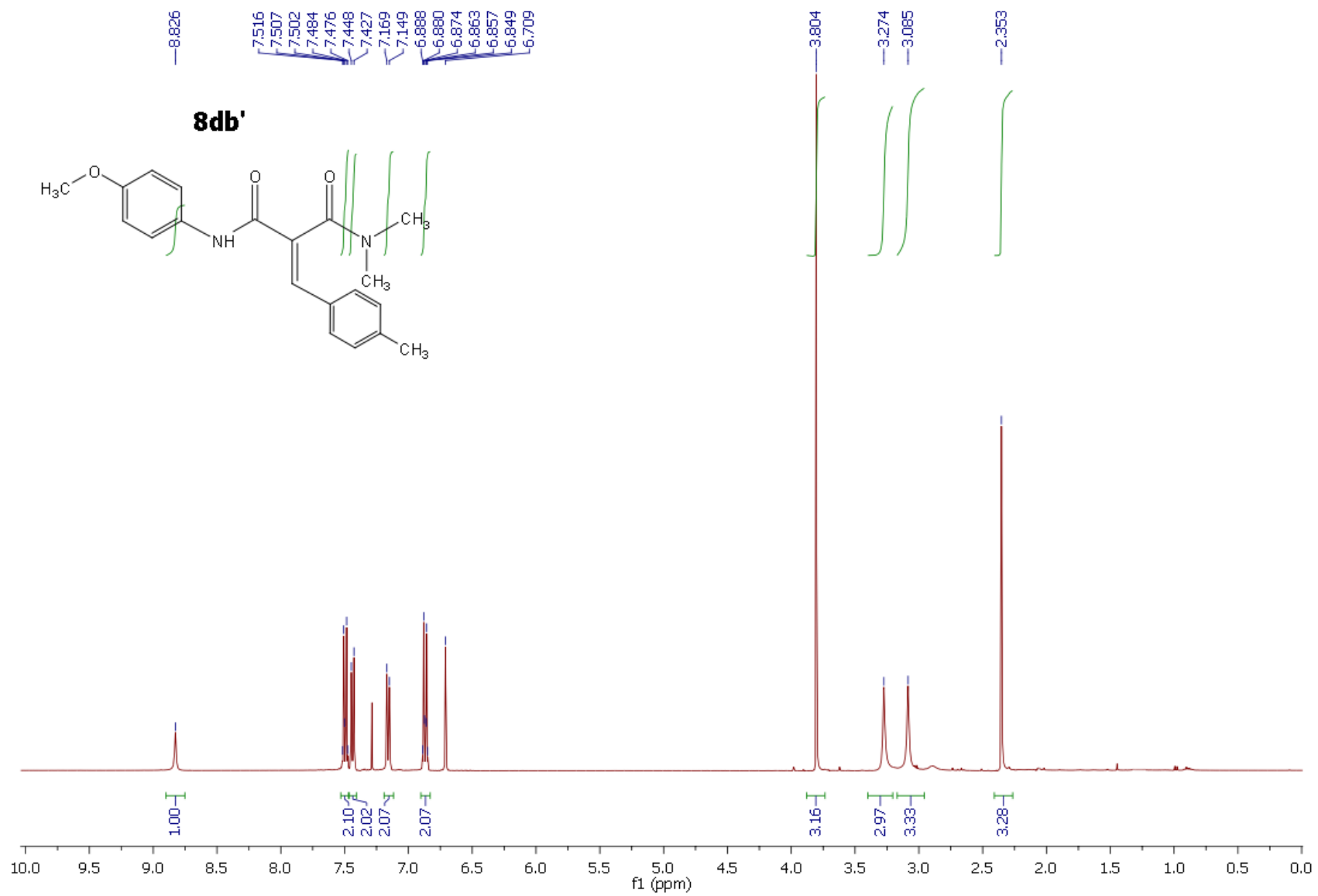
S36



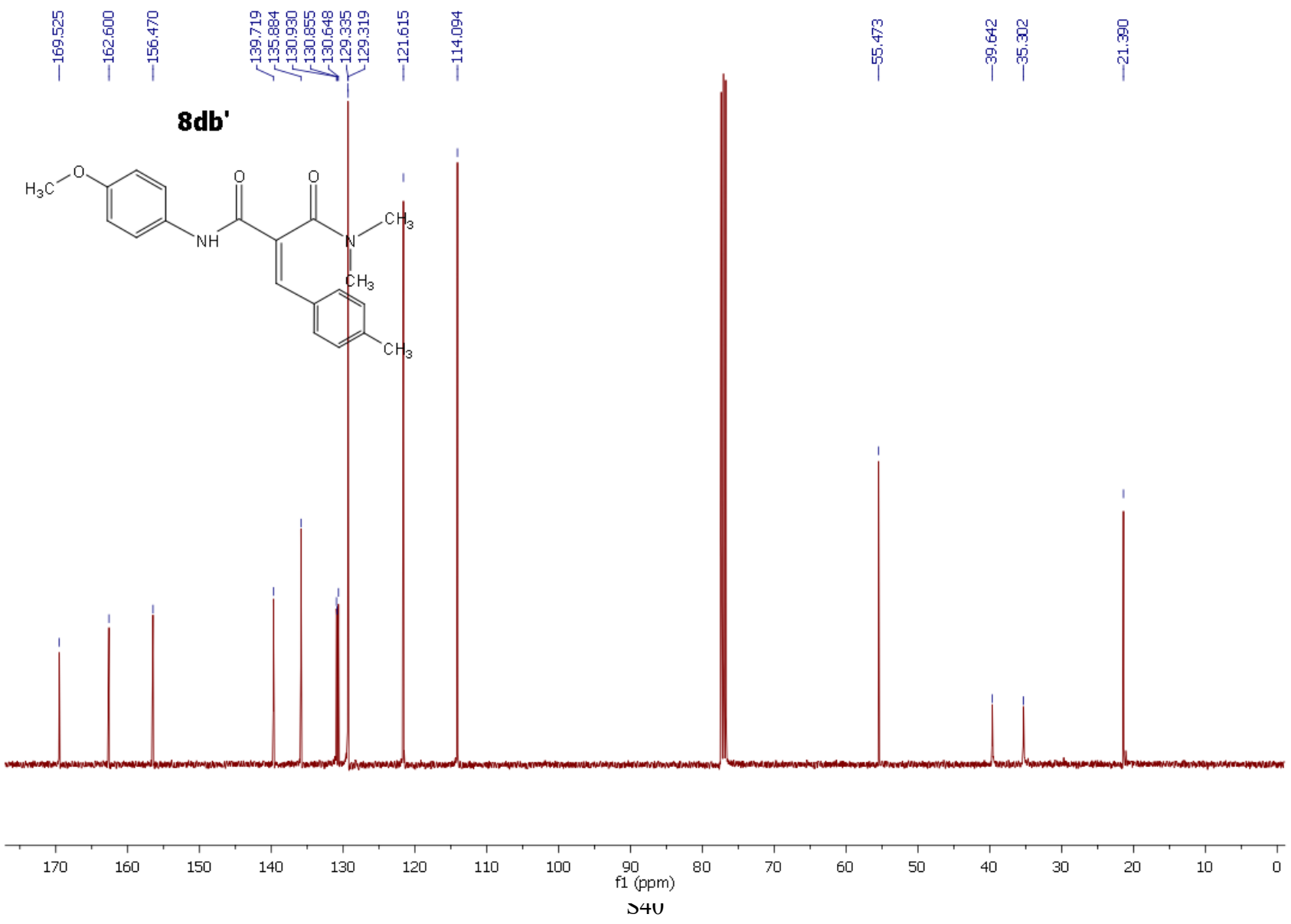
S37

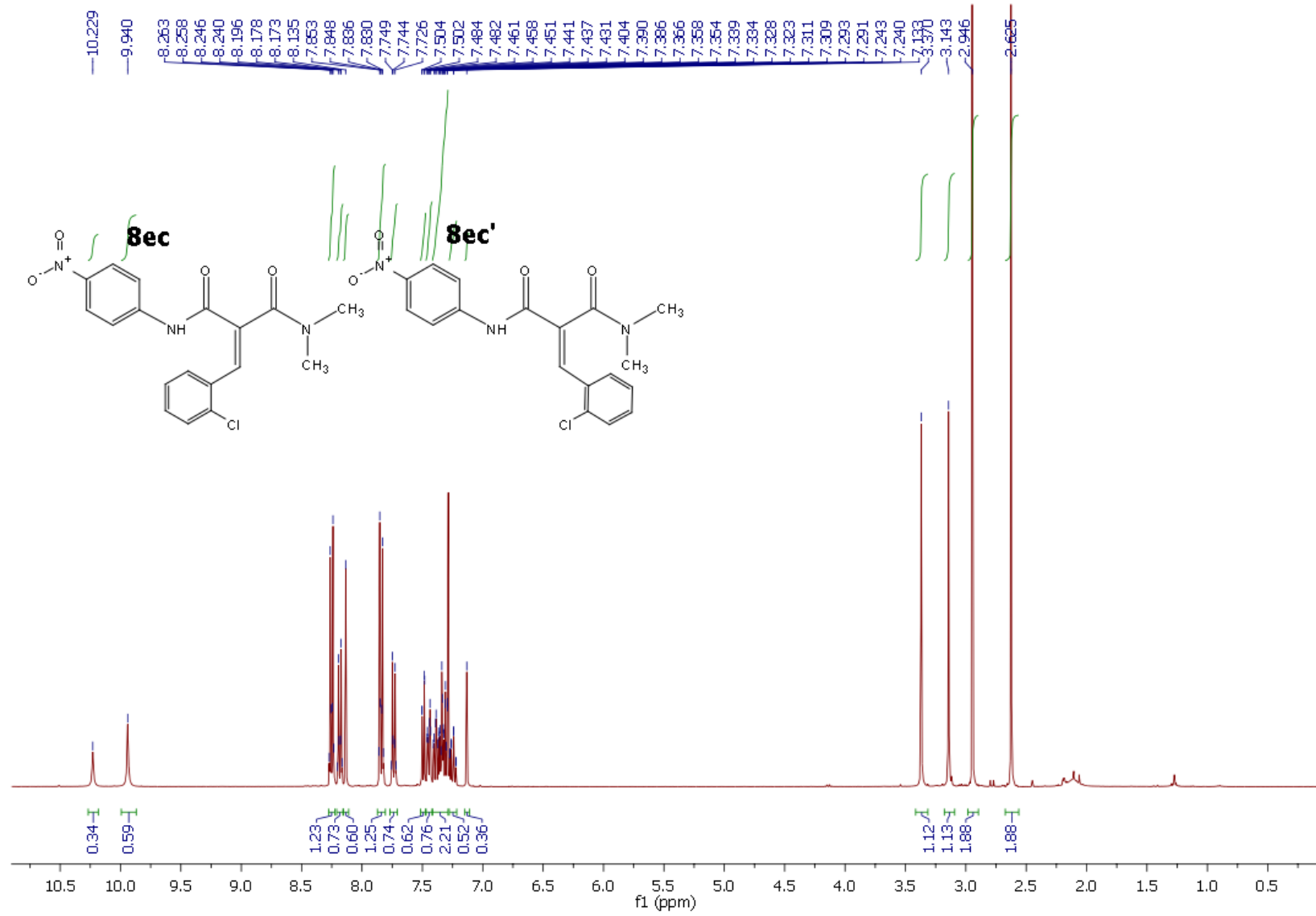


S38

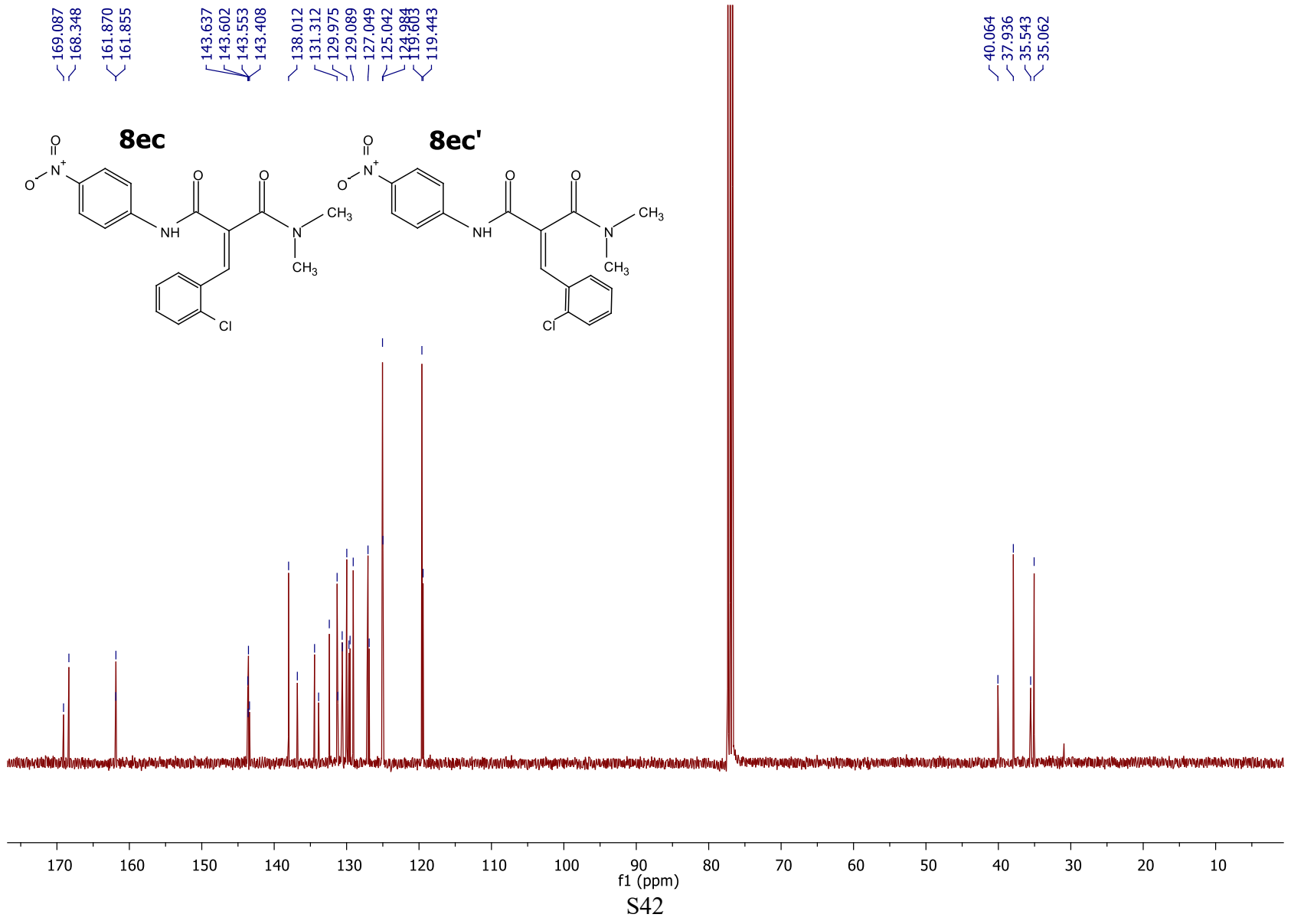


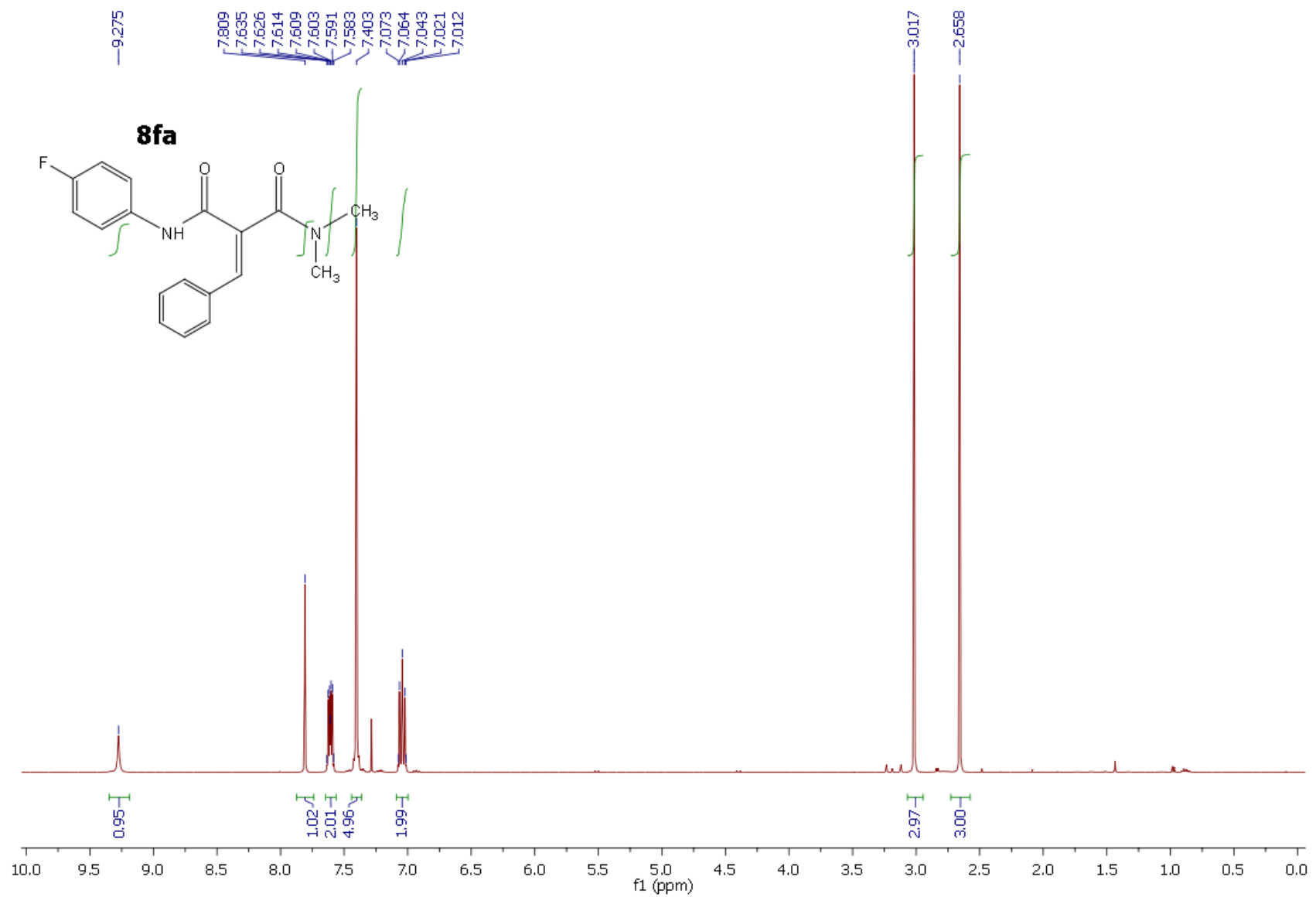
S39



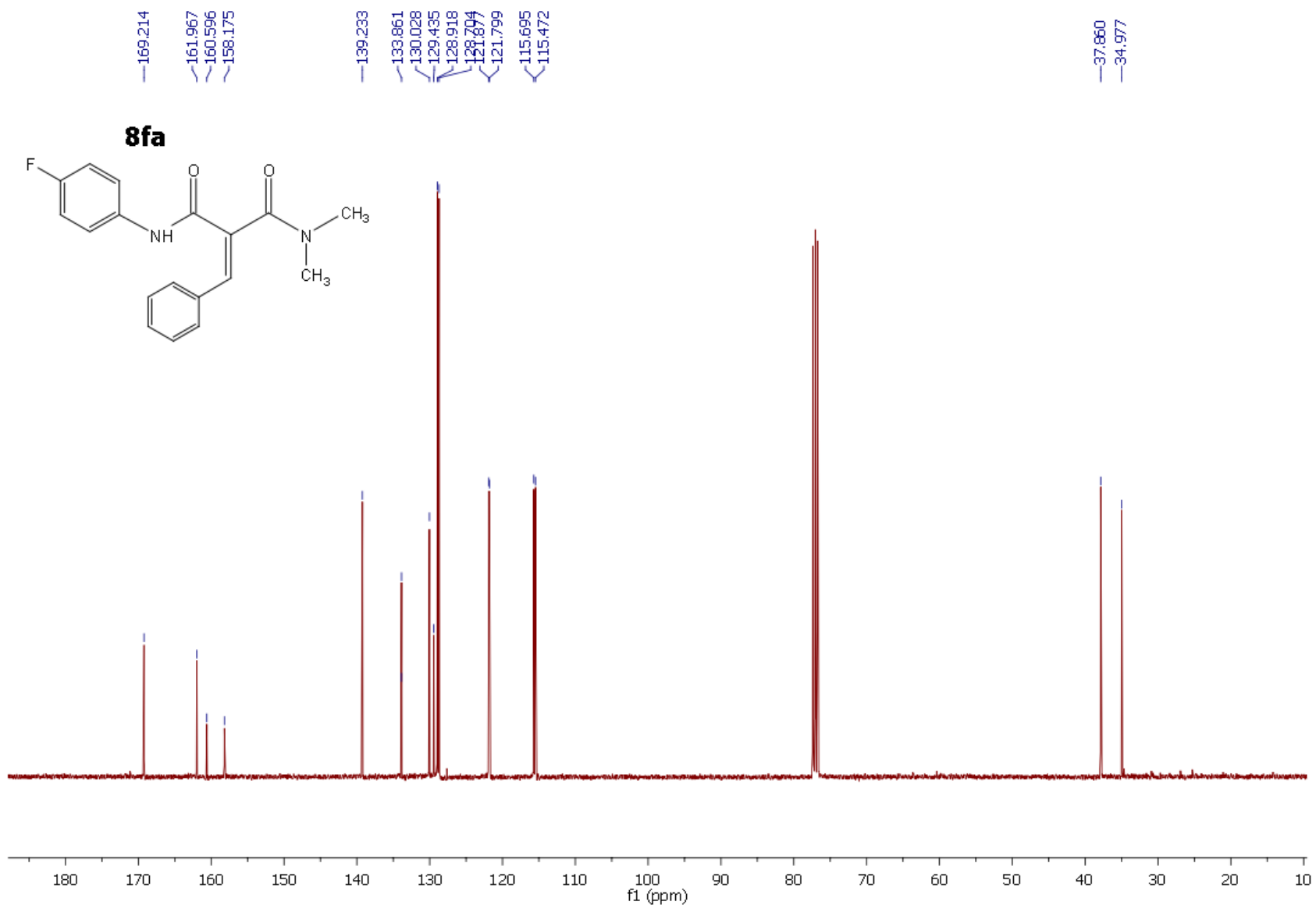


S41

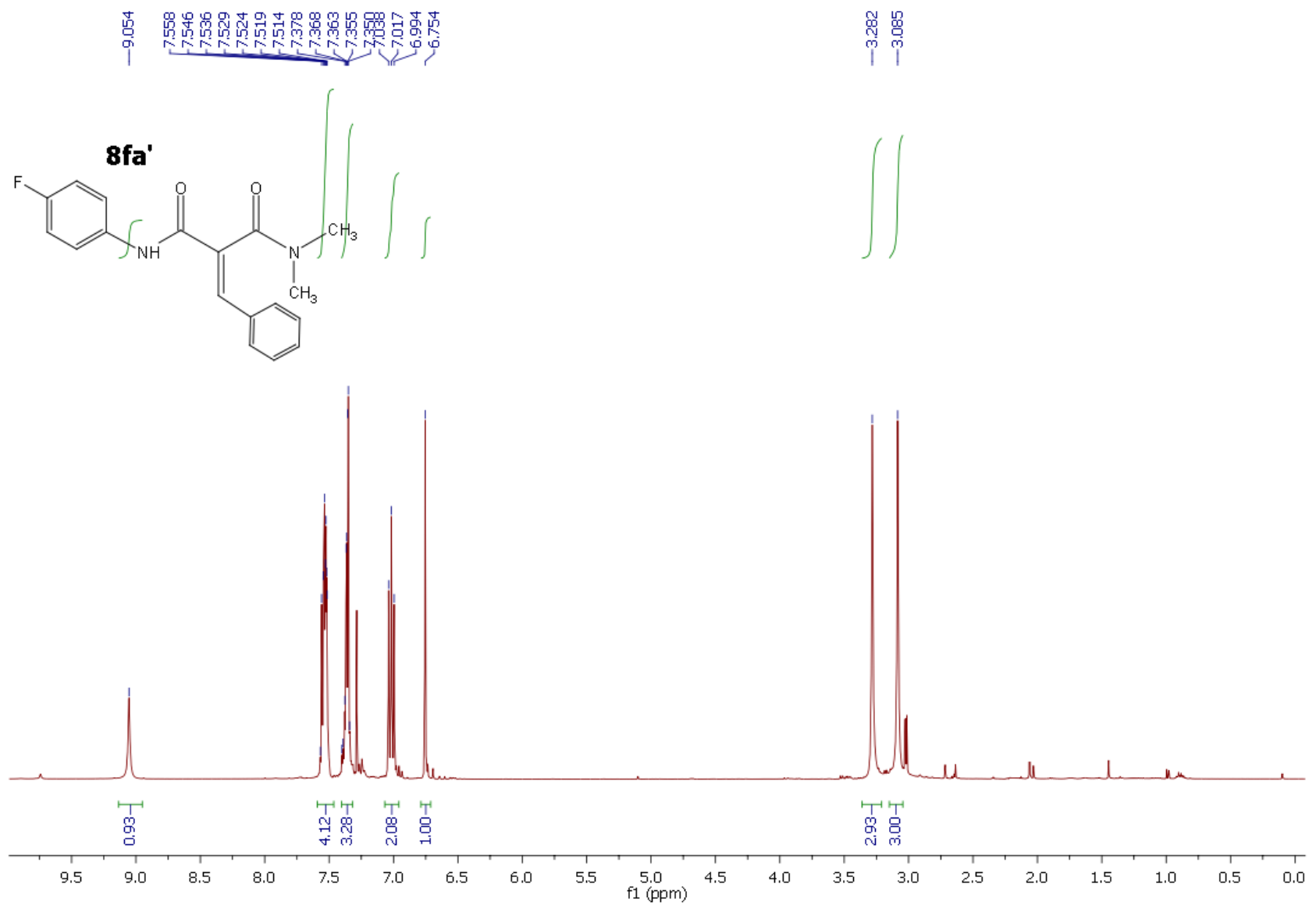




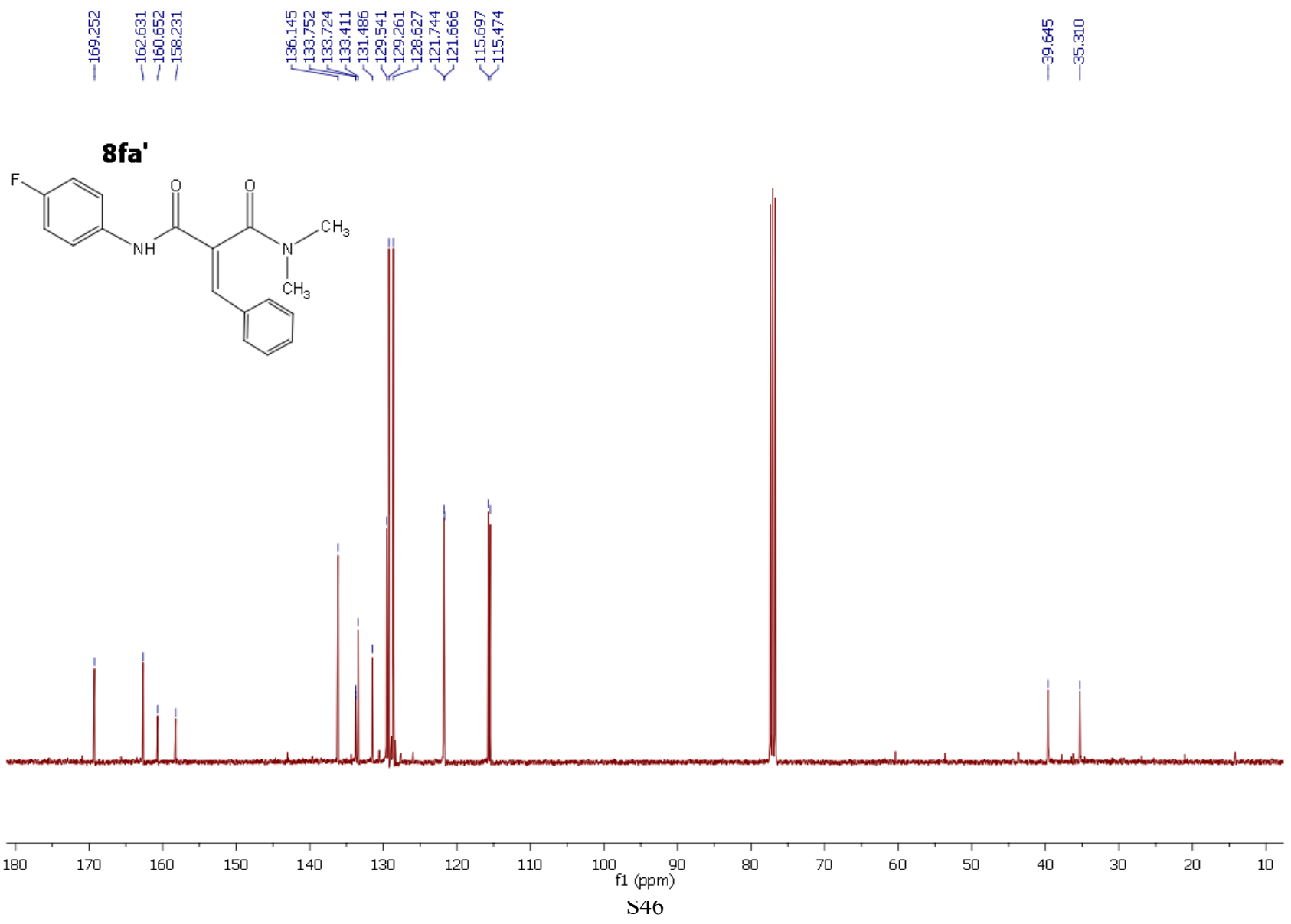
S43

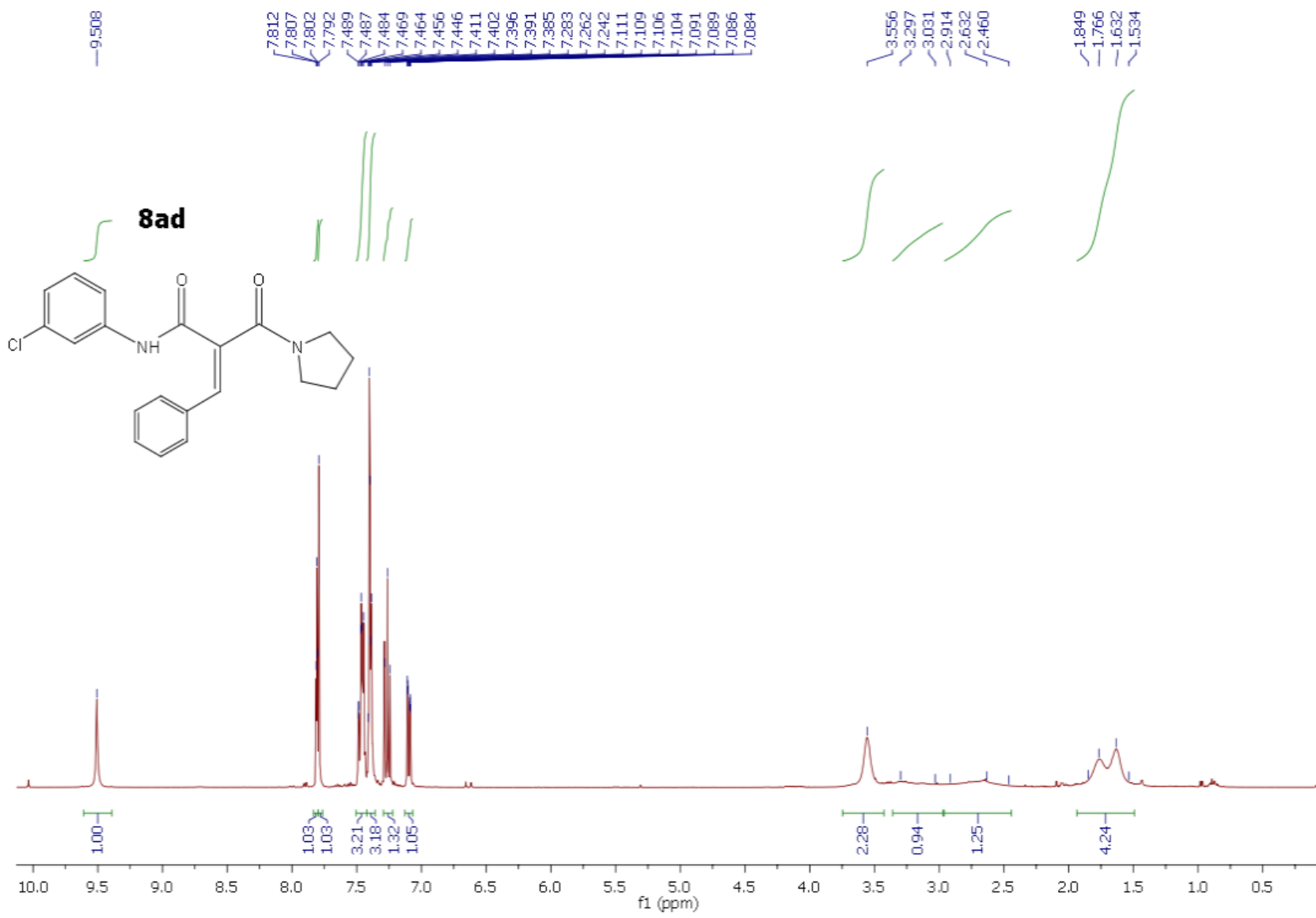


S44

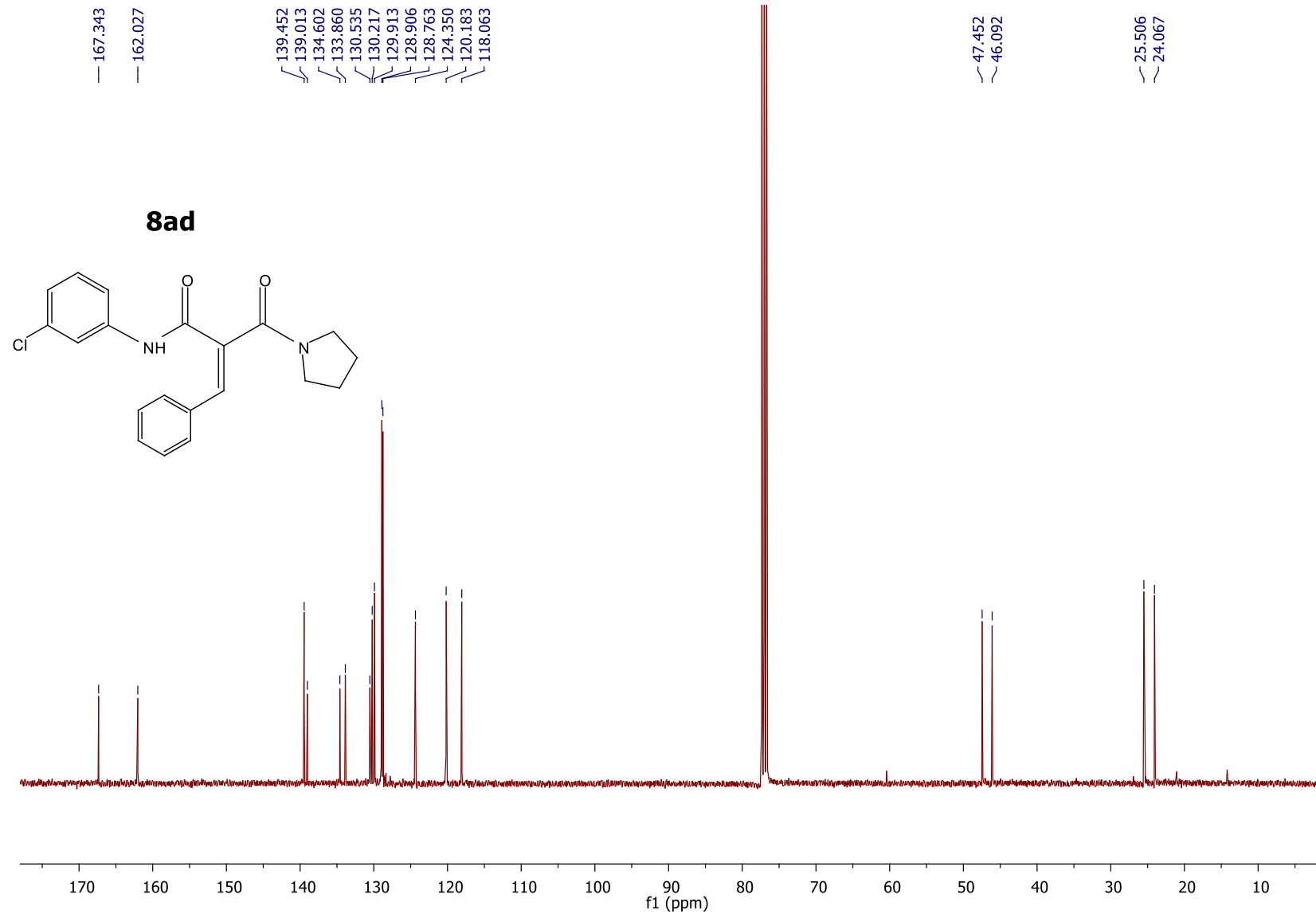


S45

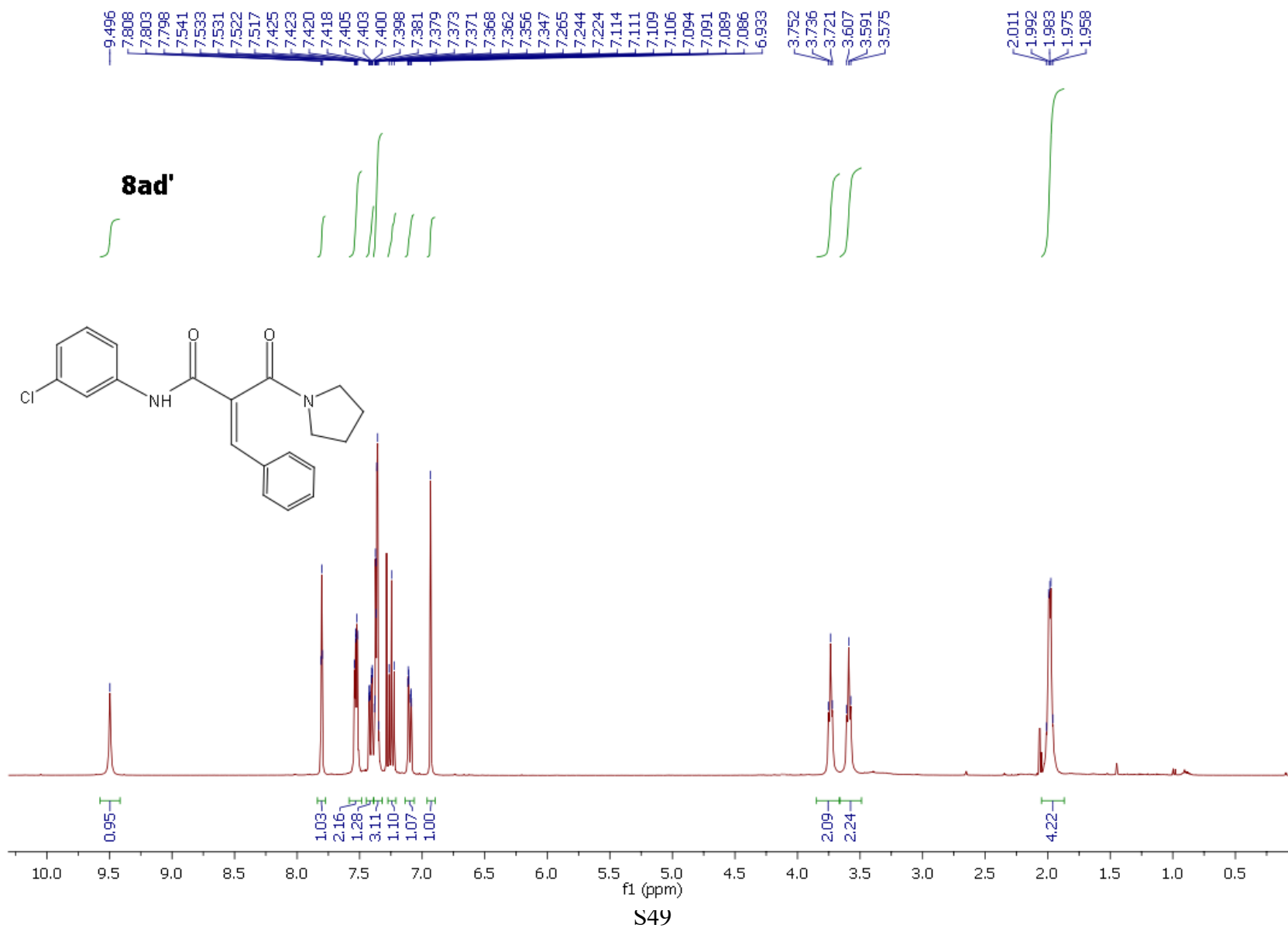


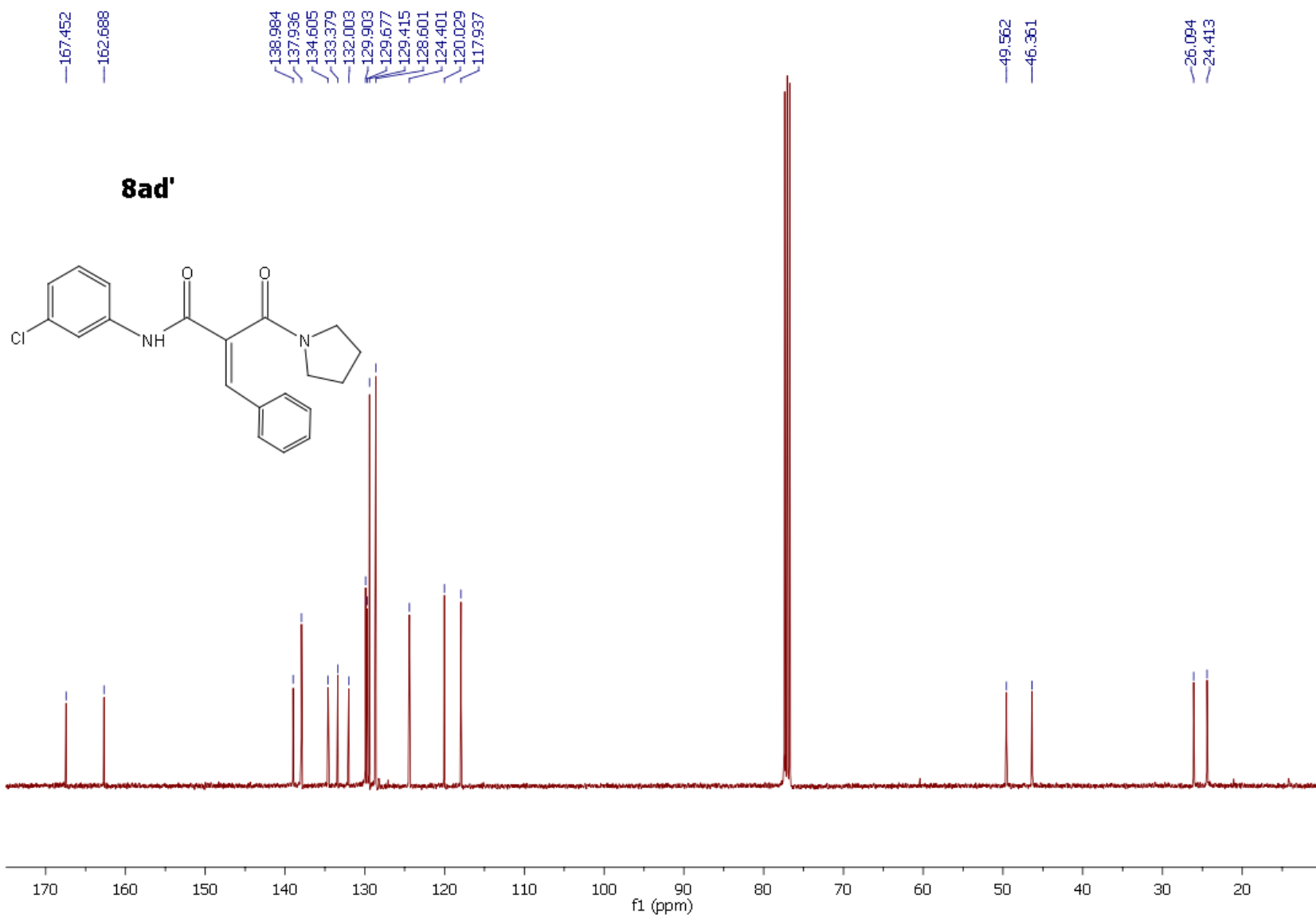


S47

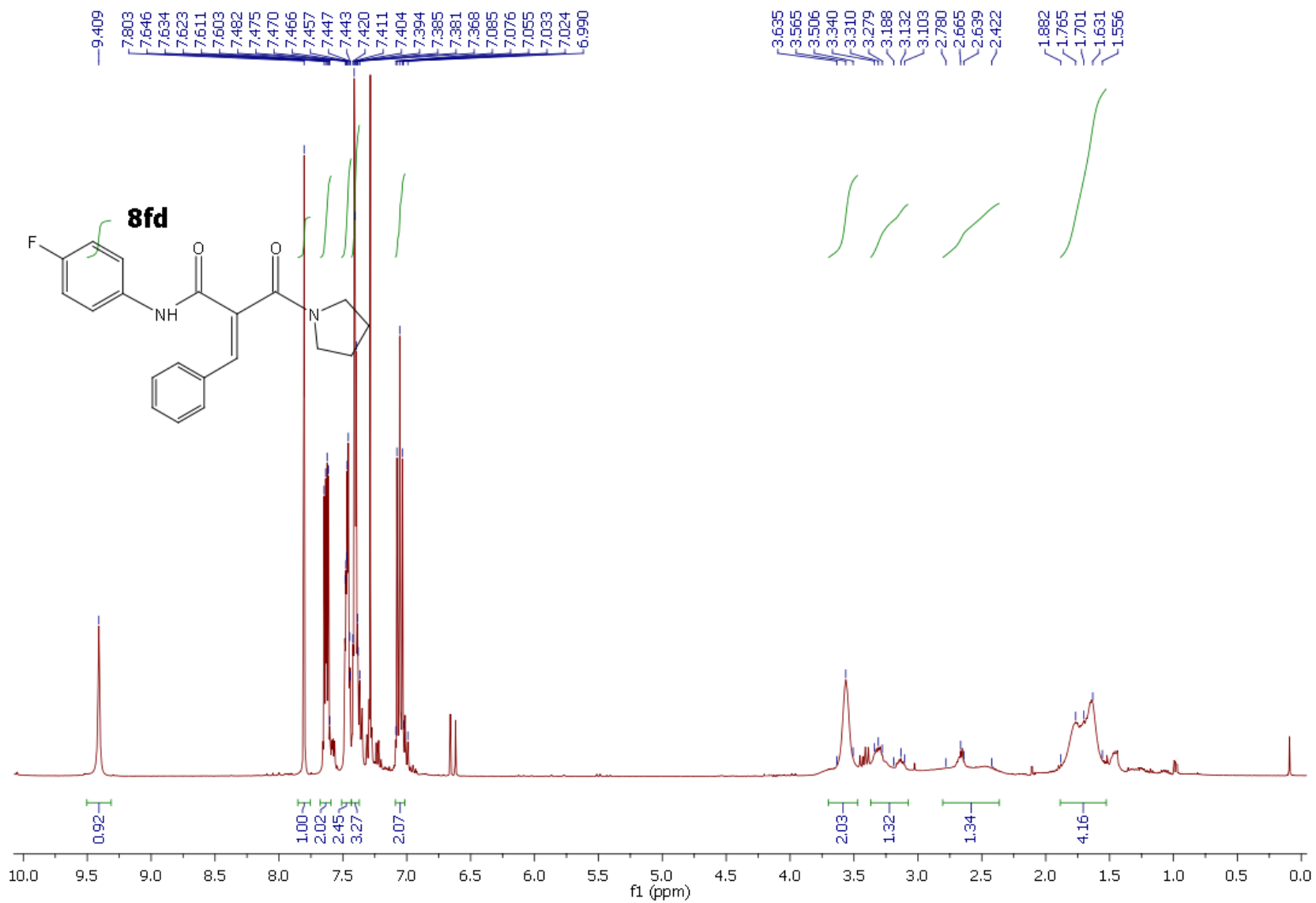


S48

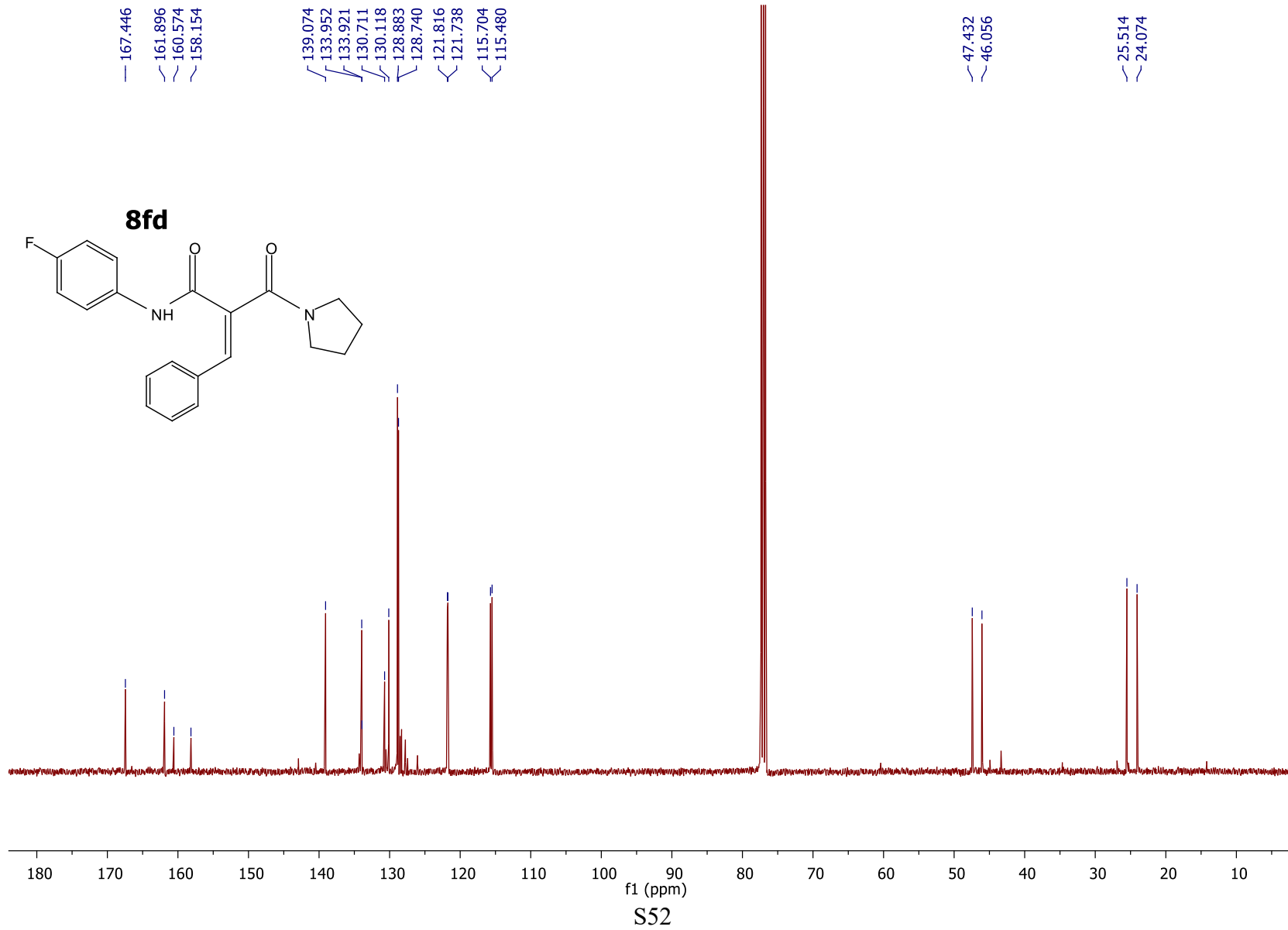
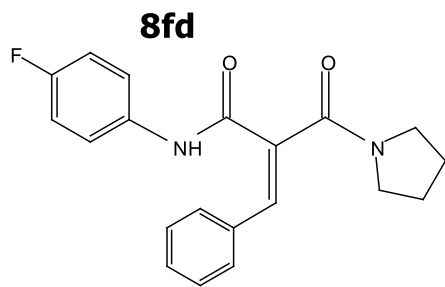


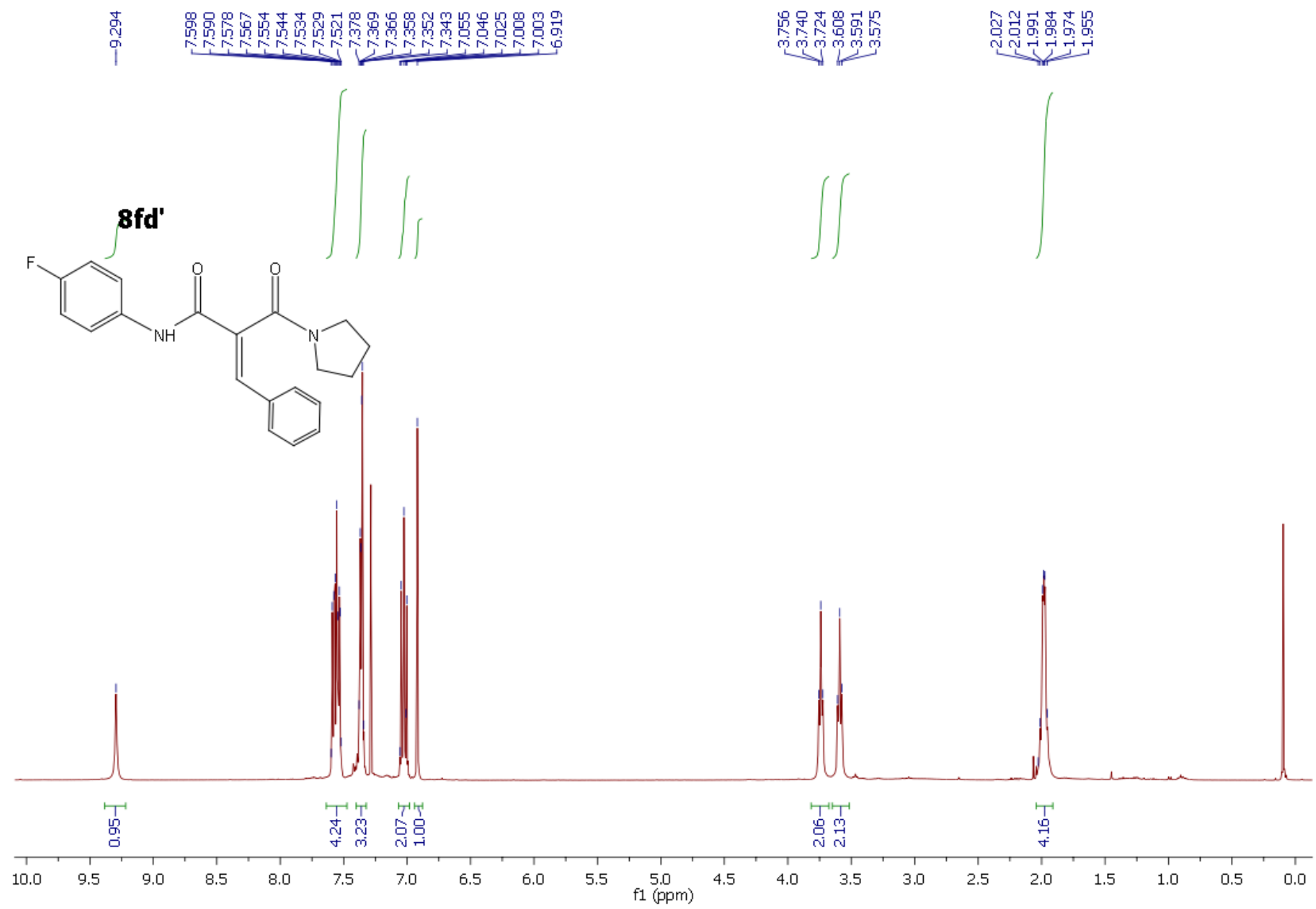


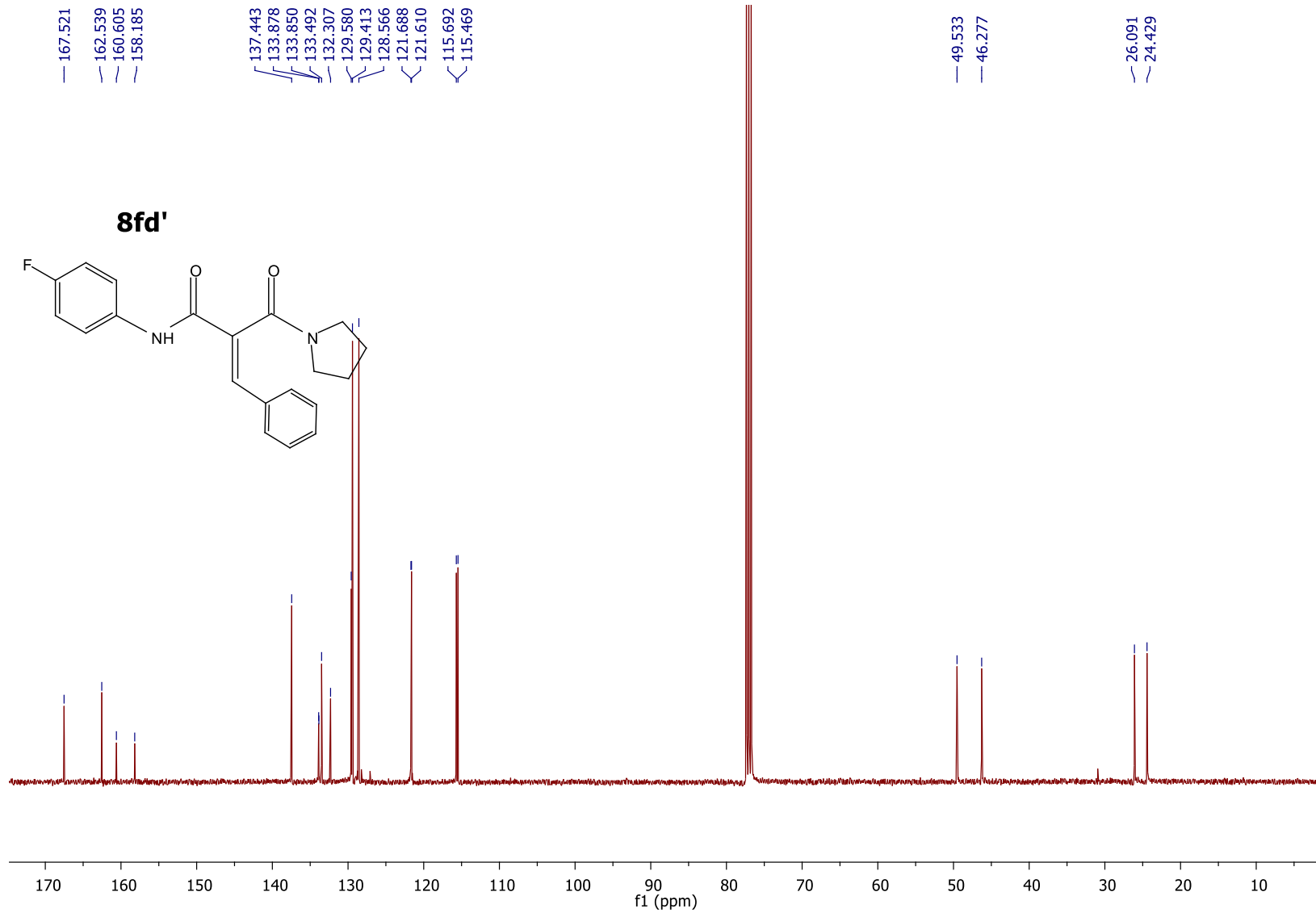
S50



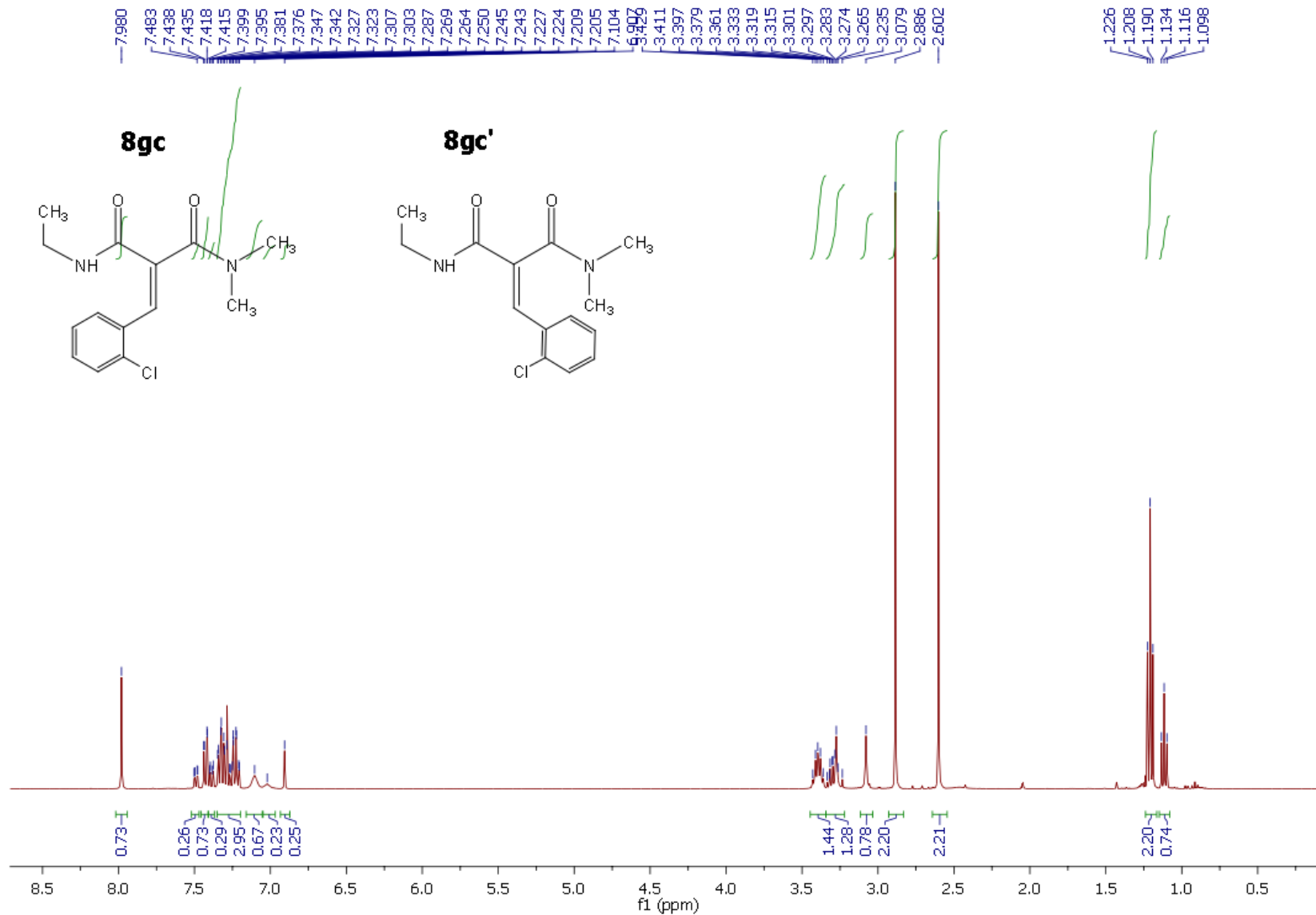
S51



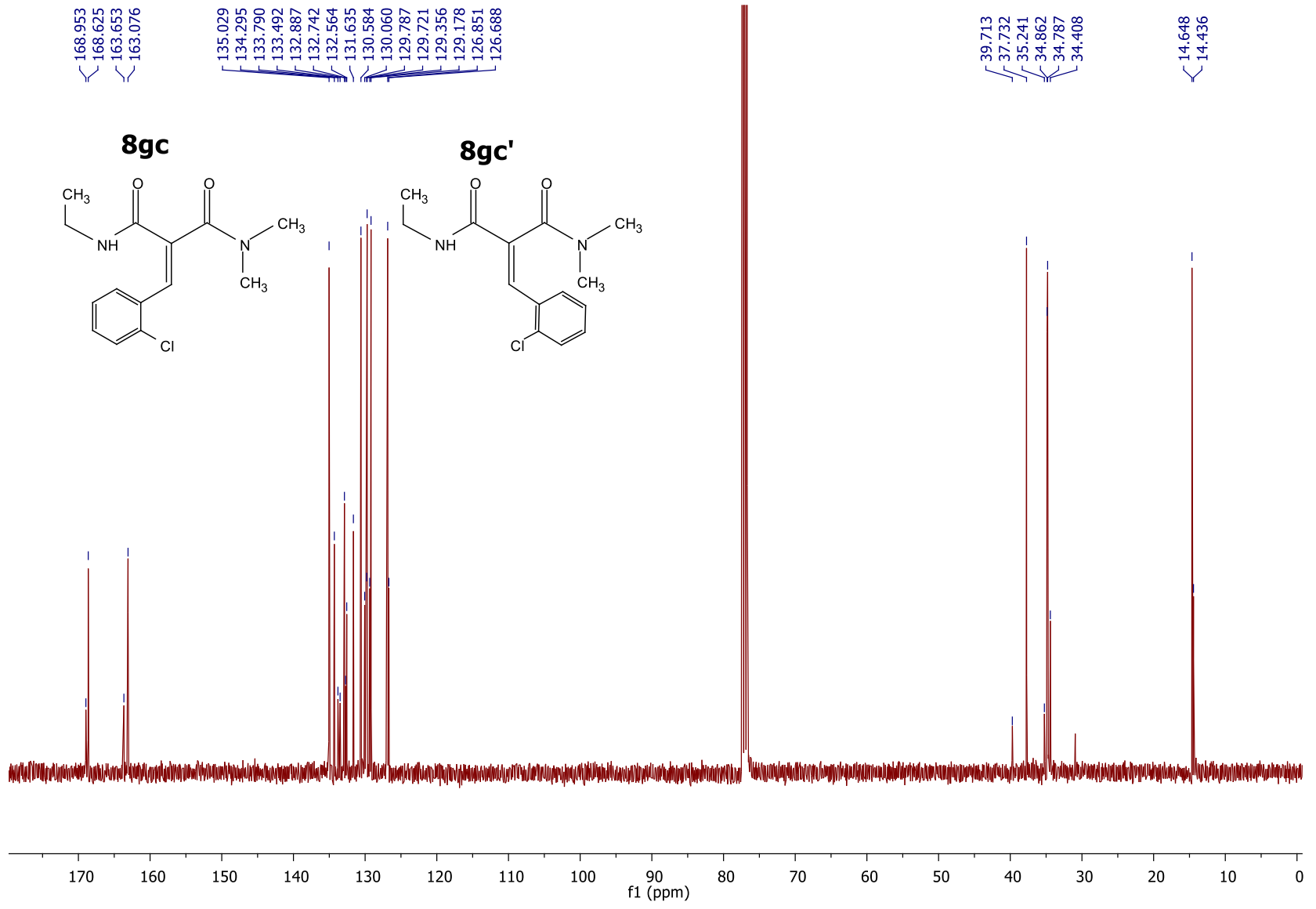




S54



S55



S56

References

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- [2] P. Punda, Ł. Ponikiewski and S. Makowiec, *Helv. Chim. Acta.*, 2013, **96**, 2081-2091.
- [3] N. Pawelska, Ł. Ponikiewski and S. Makowiec, *J. Fluorine Chem.*, 2012, **144**, 65-68.
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