

SUPPORTING INFORMATION**Room Temperature, Reductive Alkylation of Activated Methylene Compounds: Carbon-Carbon Bond Formation Driven by the Rhodium-Catalyzed, Water-Gas Shift Reaction**Scott E. Denmark,* Malek Y. S. Ibrahim,[†] Andrea Ambrosi[†]

*Roger Adams Laboratory, Department of Chemistry, University of Illinois,
Urbana, Illinois, 61801
sdenmark@illinois.edu*

Table of Contents

General Experimental	S2
Literature Preparations	S4
General Procedure I: Catalyst Screening and Conditions Optimization: Reaction of Ethyl Cyanoacetate with Benzaldehyde (Tables 1 and 2, Figures 3 and 4)	S5
General Procedure II: Water and Base Optimization: Reduction of 9aa (Tables 3, 4, 10, 11, Figure 5, Scheme 7)	S6
General Procedure III: Rh/TiO ₂ Synthesis and Recycle (Table 1, entry 10)	S6
General Procedure IV: Reaction of Ethyl Cyanoacetate with Aldehydes (Table 5)	S8
General Procedure V: Reaction of Ethyl Cyanoacetate with Cyclic Ketones (Table 6)	S30
General Procedure VI: Reaction of Ethyl Cyanoacetate with Acyclic Ketones (Table 7)	S36
General Procedure VII: Reaction of Other Active Methylene Compounds with Aldehydes in One Step (Table 8)	S38
General Procedure VIII: Reaction of Other Active Methylene Compounds with Benzaldehyde in Two Steps (Table 9)	S43
Deuterium Incorporation Experiment (Scheme 6)	S47
References	S49
NMR Spectra	S50

General Experimental

All reactions were performed in glass vials under an atmosphere of carbon monoxide, unless noted otherwise. Glass vials were put in a stainless steel, bolted-closure autoclave with a removable top section fitted with an inlet and outlet needle valves and a pressure gauge.

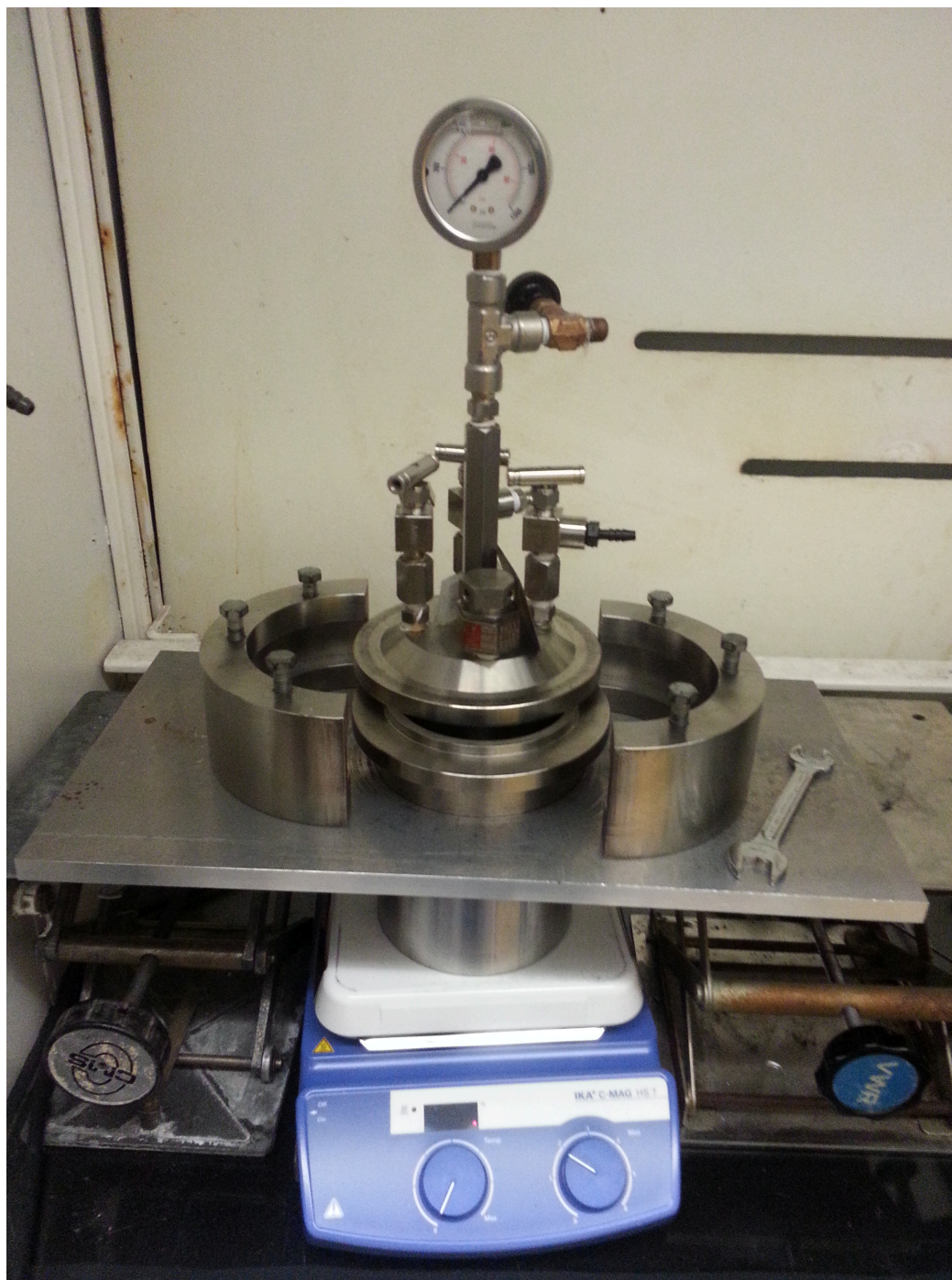


Figure S1. Pressure autoclave setup used for reductive alkylation.

Reaction solvent acetonitrile (Aldrich, HPLC grade) was distilled over CaH_2 and further dried over 4 Å molecular sieves. Reaction solvent tetrahydrofuran (Fisher, HPLC grade) was dried by percolation through two columns packed with neutral alumina under a positive pressure of argon. Reaction solvent toluene (Fisher, ACS grade) was dried by percolation through a column packed with neutral alumina and a column packed with Q5 reactant, a supported copper catalyst for scavenging oxygen, under a positive pressure of argon. Reaction solvent dioxane (Macron, ACS grade) was distilled over sodium and further dried over 4 Å molecular sieves. Reaction solvent methanol (Optima, HPLC grade) was distilled over magnesium and further dried over 3 Å molecular sieves. Reaction solvent ethanol (Decon, 200 proof) was distilled over magnesium and further dried over 4 Å molecular sieves. Reaction solvents *N,N*-dimethylformamide (Fisher, ACS grade), and dimethyl sulfoxide (Fisher, ACS grade) were dried by percolation through two columns packed with Linde type 4 Å molecular sieves under a positive pressure of argon and further dried over 4 Å molecular sieves. Reaction solvents 2-ethoxyethanol (Aldrich, ACS grade), Butyronitrile (Aldrich, >99%), and 2-propanol (Fisher, ACS grade) were dried over 4 Å molecular sieves. Solvents for filtration and chromatography were certified ACS grade.

^1H and ^{13}C NMR spectra were recorded on Varian Unity 500, Varian VXR 500, Varian Unity Inova 500 NB, or Bruker Avance III HD 500 spectrometers (500 MHz, ^1H ; 126 MHz, ^{13}C). Spectra are referenced to residual chloroform (δ 7.26 ppm, ^1H ; δ 77.0 ppm, ^{13}C), CFCl_3 (10% in CDCl_3) as an external reference for ^{19}F NMR (δ 0.00 ppm ^{19}F). Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), sept (septet), m (multiplet) and br (broad). Coupling constants, J , are reported in Hertz. All assignments are corroborated by ^{13}C APT and/or 2D experiments (COSY, HSQC).

Elemental analyses were performed by the University of Illinois Microanalytical Service Laboratory, or by Robertson Microlit Laboratories. Mass Spectrometry was performed by the University of Illinois Mass Spectrometer Center. Electron Impact (EI) spectra were recorded on a Waters 70-VSE spectrometer. Electrospray Ionization (ESI) spectra were recorded on Waters Q-TOF Ultima or Waters Synapt G2-Si spectrometers. Data are reported in the form of m/z . Infrared spectra (IR) were recorded on a Perkin Elmer Spectrum Two ATR spectrometer using neat sample. Peaks are reported in cm^{-1} with indicated relative intensities: s (strong, 67-100%); m

(medium, 34-66%), w (weak, 0-33%). Kugelrohr distillations were performed on a Büchi GKR-50 Kugelrohr and boiling points correspond to uncorrected air bath temperatures (ABT). Melting points were obtained in a vacuum-sealed capillary tube using a Thomas Hoover melting point apparatus and are corrected. Analytical thin-layer chromatography was performed on Merck silica gel plates with QF-254 indicator. Visualization was accomplished with UV (254). Column chromatography was performed using 230-400 mesh silica gel purchased from Silicycle.

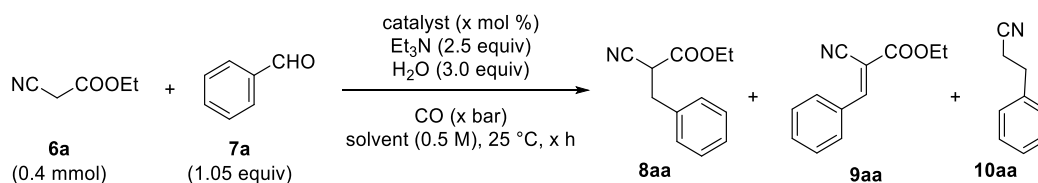
Analytical gas chromatography (GC) was performed using a Hewlett Packard 5890 Series II Gas Chromatograph fitted with a flame ionization detector (H_2 carrier gas, 1 mL/min) Injections were made on a Hewlett-Packard HP-1 (30 meter) capillary column. The injector temperature was 250 °C, the detector temperature was 300 °C, with a split ratio of 100:1. Retention times (t_R) and integrated ratios were obtained using Agilent Chemstation Software.

Hydrocinnamaldehyde (Alfa), pyridine (Fisher), triethylamine (Fisher), benzaldehyde (Aldrich), furfural (Alfa), 4-(trifluoromethyl)benzaldehyde (Oakwood), isobutyraldehyde (Aldrich), isovaleraldehyde (Aldrich) were distilled prior to use. $RhCl_3$ hydrate was purchased from Pressure and used as received. All metal-carbonyl complexes were purchased from Strem, stored and handled in a drybox, and used as received. All other reagents and solvents were purchased from Aldrich, Fisher, Oakwood, or Strem and used as received.

Literature Preparations

The following compounds were prepared according to published procedures: **9aa**,¹ **9af**,² **7h**,³ **7v**,⁴ **7w**.⁵

General Procedure I: Catalyst Screening and Conditions Optimization: Reaction of Ethyl Cyanoacetate with Benzaldehyde (Tables 1 and 2, Figures 3 and 4)



The catalyst was added to a 4-mL glass vial, followed by solvent, ethyl cyanoacetate **6a**, benzaldehyde **7a**, deionized water, triethylamine, and mesitylene as internal standard. A stir bar was added, and the vial was placed in an autoclave. The autoclave was pressurized with CO and vented three times, and then pressurized to the specified pressure. The mixture was stirred at room temperature for the indicated time. After venting and purging the autoclave with nitrogen, the vial was removed. An aliquot was taken and diluted in EtOAc before being passed through a short silica column and injected into a HP-1 GC column (25 m, 0.2 mm ID, 0.33 μm thickness). The column oven temperature program was as follows: 100 °C for 3 minutes, 100 °C to 260 °C at 20 °C /min, then 260 °C for 1 minute.

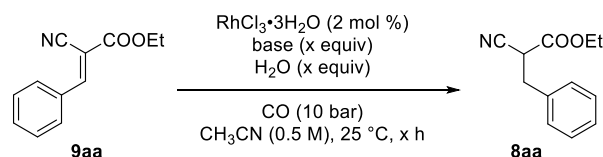
GC response factors were established by the following equation using mesitylene as the internal standard:

$$\text{Response Factor} = \frac{(\text{mmols of compound})}{(\text{area of compound})} \times \frac{(\text{area of mesitylene})}{(\text{mmol of mesitylene})}$$

Three samples containing a known amount of the desired compound and mesitylene were prepared and dissolved in EtOAc. A small portion of each sample was diluted further to 1 mL. An aliquot of each sample was injected into GC in triplicates. The average of 9 response factors was used to monitor reductive alkylation reactions.

Table S1. GC calibration factors.

compound	response factor	<i>t_R</i> (min)
6a	2.82	2.62
7a	1.52	3.00
8aa	0.76	8.88
9aa	0.81	9.79
10aa	0.98	6.02
mesitylene	-	3.27

General Procedure II: Water and Base Optimization: Reduction of 9aa (Tables 3, 4, 10, 11, Figure 5, Scheme 7)

$\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (2.1 mg) was added to a 4-mL glass vial, followed by acetonitrile (0.8 mL), ethyl-2-cyano-3-phenylacrylate **9aa**, deionized water, base, and mesitylene as internal standard. A stir bar was added, and the vial was placed in an autoclave. The autoclave was pressurized with CO and vented three times, and then pressurized to 10 bar. The reaction was stirred at room temperature for the indicated time. After venting and purging the autoclave with nitrogen, the vial was removed. An aliquot was taken and diluted in EtOAc before being passed on a short silica column and injected to a GC. The analysis and calibration factors used are described above.

General Procedure III: Rh/TiO₂ Synthesis and Recycle (Table 1, entry 10)

One gram TiO_2 (P25, Acros) was washed with 300 mL deionized water (18.2 $\text{M}\Omega \cdot \text{cm}$) and dried at 100°C in static air. Rhodium chloride solution was prepared by dissolving 51 mg of $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ in 50 mL deionized water and the pH of the solution was adjusted to 11 by adding sat. aq. NH_4OH solution. The dried TiO_2 was dispersed in the solution and stirred for 24 h at room temperature. The slurry was centrifuged and the recovered solid was washed with deionized water three times and then dried under vacuum at 60°C overnight. The dried catalyst was reduced under flowing hydrogen at 100°C for 30 min and cooled down to room temperature before exposure to air.

The Rh/ TiO_2 catalyst used for reductive alkylation was recovered from the reaction mixture by centrifugation (10000 rpm) and was washed with acetonitrile (1 mL) before being reused for the next reaction cycle. The yield of **8aa** was 98% for the first reaction cycle versus 6% for the second.

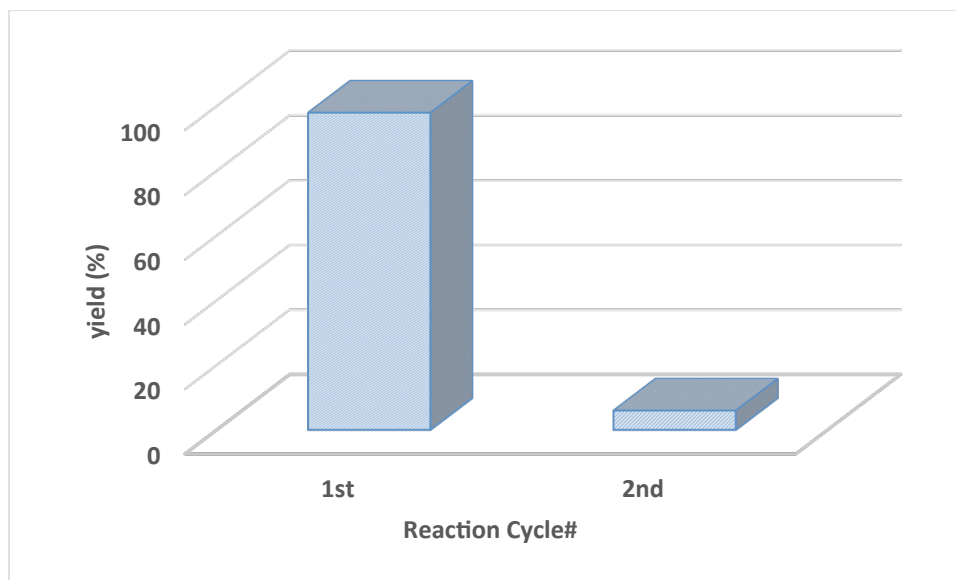
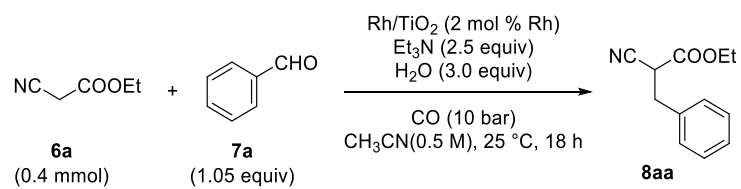
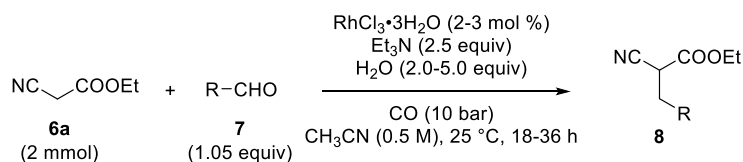
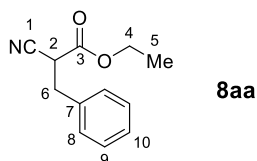


Figure S2. Recycle-ability of Rh supported nanoparticles catalyst.

General Procedure IV: Reaction of Ethyl Cyanoacetate with Aldehydes (Table 5)

RhCl₃·3H₂O was added to a 40-mL glass vial, followed by acetonitrile, ethyl cyanoacetate **6a**, the aldehyde **7**, deionized water, and triethylamine. A stir bar was added, and the vial was placed in an autoclave. The autoclave was pressurized with CO and vented three times, and then pressurized to 10 bar. The reaction was stirred at room temperature for the indicated time. After venting and purging the autoclave with nitrogen, the vial was removed. The volatiles were removed by rotary evaporation (25-30 °C, 15 mmHg), then the residue was dissolved in CH₂Cl₂, and was loaded on silica gel (1 g). The crude mixture was purified by silica gel column chromatography (2.5 x 20-25 cm), followed by distillation or recrystallization.

Ethyl 2-Cyano-3-phenylpropanoate (8aa)

Following General Procedure IV, RhCl₃·3H₂O (10.5 mg, 0.04 mmol, 2 mol %), CH₃CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), benzaldehyde (0.214 mL, 2.1 mmol, 1.05 equiv), H₂O (0.108 mL, 6.0 mmol, 3.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 24 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O 80:20), followed by Kugelrohr distillation, afforded **8aa** (363 mg, 89%) as a colorless oil. The spectral data matched those previously reported in the literature.⁶

Data for 8aa:

bp: 192 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, CDCl₃)

δ 7.38 – 7.26 (m, 5 H, C(aryl)H), 4.24 (q, *J* = 7.1 Hz, 2 H, C(4)H₂), 3.72 (dd, *J* =

8.4, 5.8 Hz, 1 H, C(2)H), 3.28 (dd, $J = 13.8, 5.8$ Hz, 1 H, C(6)H), 3.20 (dd, $J = 13.8, 8.4$ Hz, 1 H, C(6)H'), 1.27 (t, $J = 7.1$ Hz, 3 H, C(5)H₃)

¹³C NMR: (126 MHz, CDCl₃)

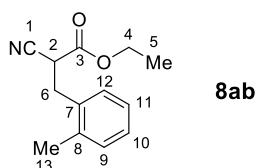
δ 165.5 C(3), 135.4 C(7), 129.0, 128.8, 127.7 C(10), 116.0 C(1), 62.8 C(4), 39.6 C(2), 35.9 C(6), 13.9 C(5)

HRMS: (EI)

m/z : [M]⁺ Calcd for C₁₂H₁₃NO₂: 203.0946; Found: 203.0950

TLC: R_f 0.21 (pentane/Et₂O, 80:20) [silica gel, UV, iodine]

Ethyl 2-Cyano-3-(2-tolyl)propanoate (**8ab**)



8ab

Following General Procedure IV, RhCl₃·3H₂O (10.5 mg, 0.04 mmol, 2 mol %), CH₃CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), *o*-tolualdehyde (0.243 mL, 2.1 mmol, 1.05 equiv), H₂O (0.108 mL, 6.0 mmol, 3.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 24 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 85:15), followed by Kugelrohr distillation, afforded **8ab** (383 mg, 88%) as a colorless oil.

Data for **8ab**:

bp: 209 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, CDCl₃)

δ 7.24 – 7.16 (m, 4 H, C(aryl)H), 4.31 – 4.22 (m, 2 H, C(4)H₂), 3.67 (dd, $J = 9.4, 6.0$ Hz, 1 H, C(2)H), 3.34 (dd, $J = 14.1, 6.0$ Hz, 1 H, C(6)H), 3.19 (dd, $J = 14.1, 9.4$ Hz, 1 H, C(6)H'), 2.37 (s, 3 H, C(13)H₃), 1.29 (t, $J = 7.2$ Hz, 3 H, C(5)H₃)

¹³C NMR: (126 MHz, CDCl₃)

δ 165.7 C(3), 136.2 C(7), 133.6 C(8), 130.8, 129.6, 127.8, 126.4, 116.2 C(1), 62.9 C(4), 38.4 C(2), 33.1 C(6), 19.2 C(13), 13.9 C(5)

IR: (neat)

2983 (w), 2250 (w), 1741 (s), 1455 (w), 1370 (w), 1259 (m), 1200 (m), 1160 (m), 1027 (m), 860 (w), 753 (s)

HRMS: (EI)

m/z : $[M]^+$ Calcd for $C_{13}H_{15}NO_2$: 217.1103; Found: 217.1103

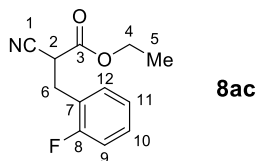
TLC: R_f 0.30 (pentane/Et₂O, 80:20) [silica gel, UV, iodine]

Analysis: $C_{13}H_{15}NO_2$

Calcd: C, 71.87; H, 6.96; N, 6.45

Found: C, 71.95; H, 6.95; N, 6.57

Ethyl 2-Cyano-3-(2-fluorophenyl)propanoate (**8ac**)



Following General Procedure IV, $RhCl_3 \cdot 3H_2O$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 2-fluorobenzaldehyde (0.221 mL, 2.1 mmol, 1.05 equiv), H_2O (0.108 mL, 6.0 mmol, 3.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 24 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 85:15), followed by Kugelrohr distillation, afforded **8ac** (407 mg, 92%) as a colorless oil. The spectral data matched those previously reported in the literature.⁷

Data for 8ac:

bp: 188 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, $CDCl_3$)

δ 7.34 – 7.27 (m, 2 H, C(10)H, C(12)H), 7.13 (td, $J = 7.5, 1.1$ Hz, 1 H, C(11)H), 7.10 – 7.04 (m, 1 H, C(9)H), 4.28 – 4.21 (m, 2 H, C(4)H₂), 3.81 (dd, $J = 8.8, 6.4$ Hz, 1 H, C(2)H), 3.38 (dd, $J = 14.0, 6.4$ Hz, 1 H, C(6)H), 3.19 (dd, $J = 13.9, 8.8$ Hz, 1 H, C(6)H'), 1.28 (t, $J = 7.2$ Hz, 3 H, C(5)H₃)

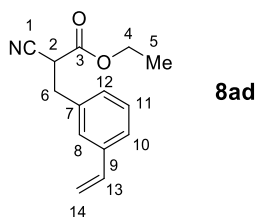
^{13}C NMR: (126 MHz, CDCl_3)
 δ 165.2 C(3), 161.0 (d, $J = 246.4$ Hz, C(8)), 131.4 (d, $J = 3.9$ Hz, C(12)), 129.7 (d, $J = 8.2$ Hz, C(10)), 124.4 (d, $J = 3.6$ Hz, C(11)), 122.3 (d, $J = 15.2$ Hz, C(7)), 115.8 C(1), 115.5 (d, $J = 21.6$ Hz, C(9)), 62.9 C(4), 37.9 (d, $J = 1.6$ Hz, C(2)), 29.5 (d, $J = 2.4$ Hz, C(6)), 13.81 C(5)

^{19}F NMR: (470 MHz, CDCl_3)
 δ -118.2

HRMS: (EI)
 m/z : $[\text{M}]^+$ Calcd for $\text{C}_{12}\text{H}_{12}\text{FNO}_2$: 221.0852; Found: 221.0851

TLC: R_f 0.29 (pentane/ Et_2O , 80:20) [silica gel, UV, iodine]

Ethyl 2-Cyano-3-(3-vinylphenyl)propanoate (**8ad**)



Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 3-vinylbenzaldehyde (0.267 mL, 2.1 mmol, 1.05 equiv), H_2O (0.108 mL, 6.0 mmol, 3.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 24 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 80:20) afforded **8ad** (423 mg, 92%) as a pale yellow oil. **8ad** underwent polymerization over the course of a few hours at room temperature.

Data for **8ad**:

^1H NMR: (500 MHz, CDCl_3)
 δ 7.38 – 7.28 (m, 3 H, C(8)H, C(10)H, C(11)H), 7.17 (d, $J = 7.3$ Hz, 1 H, C(12)H), 6.70 (dd, $J = 17.6, 10.9$ Hz, 1 H, C(13)H), 5.76 (d, $J = 17.6$ Hz, 1 H, C(14) H_{trans}), 5.27 (d, $J = 10.9$ Hz, 1 H, C(14) H_{cis}), 4.24 (q, $J = 7.1$ Hz, 2 H, C(4) H_2), 3.73 (dd, $J = 8.4, 5.9$ Hz, 1 H, C(2)H), 3.27 (dd, $J = 13.8, 5.8$ Hz, 1 H, C(6)H), 3.19 (dd, $J = 13.8, 8.4$ Hz, 1 H, C(6)H'), 1.26 (t, $J = 7.1$ Hz, 3 H,

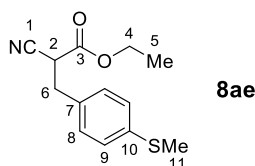
C(5)H₃)

¹³C NMR: (126 MHz, CDCl₃)
 δ 165.5 C(3), 138.1 C(9), 136.3 C(13), 135.5 C(7), 129.0C(11), 128.4 C(12),
 126.8 C(8), 125.6 C(10), 116.1 C(1), 114.5 C(14), 62.9 C(4), 39.6 C(2), 35.6
 C(6), 13.9 C(5)

HRMS: (EI)
 m/z : [M]⁺ Calcd for C₁₄H₁₅NO₂: 229.1103; Found: 229.1113

TLC: R_f 0.31 (pentane/Et₂O, 80:20) [silica gel, UV, iodine]

Ethyl 2-Cyano-3-(4-(methylthio)phenyl)propanoate (**8ae**)



Following General Procedure IV, RhCl₃·3H₂O (10.5 mg, 0.04 mmol, 2 mol %), CH₃CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 4-(methylthio)benzaldehyde (0.279 mL, 2.1 mmol, 1.05 equiv), H₂O (0.108 mL, 6.0 mmol, 3.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial. which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 24 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 80:20), followed by Kugelrohr distillation, afforded **8ae** (365 mg, 73%) as a yellow oil.

Data for **8ae**:

bp: 244 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, CDCl₃)
 δ 7.22 (d, J = 8.6 Hz, 2 H, C(9)H), 7.19 (d, J = 8.5 Hz, 2 H, C(8)H), 4.24 (q, J =
 7.1 Hz, 2 H, C(4)H₂), 3.69 (dd, J = 8.3, 5.8 Hz, 1 H, C(2)H), 3.23 (dd, J = 13.9,
 5.8 Hz, 1 H, C(6)H), 3.15 (dd, J = 13.9, 8.3 Hz, 1 H, C(6)H'), 2.47 (s, 3 H,
 C(11)H₃), 1.28 (t, J = 7.1 Hz, 3 H, C(5)H₃)

¹³C NMR: (126 MHz, CDCl₃)
 δ 165.4 C(3), 138.1 C(10), 131.9 C(7), 129.4 C(8), 126.8 C(9), 116.0 C(1), 62.9
 C(4), 39.6 C(2), 35.1 C(6), 15.6 C(11), 13.9 C(5)

IR: (neat)

2983 (w), 2923 (w), 2250 (w), 1739 (s), 1601 (w), 1495 (m), 1441 (w), 1369 (w), 1257 (m), 1193 (m), 1094 (m), 1025 (m), 856 (w), 830 (w), 804 (m)

HRMS: (EI)

m/z : $[M]^+$ Calcd for $C_{13}H_{15}NO_2S$: 249.0823; Found: 249.0826

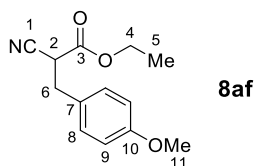
TLC: R_f 0.16 (pentane/Et₂O, 80:20) [silica gel, UV, iodine]

Analysis: $C_{13}H_{15}NO_2S$

Calcd: C, 62.63; H, 6.06; N, 5.62

Found: C, 62.53; H, 5.99; N, 5.58

Ethyl 2-Cyano-3-(4-methoxyphenyl)propanoate (**8af**)



Following General Procedure IV, $RhCl_3 \cdot 3H_2O$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), *p*-anisaldehyde (0.256 mL, 2.1 mmol, 1.05 equiv), H_2O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 70:30), followed by Kugelrohr distillation, afforded **8af** (433 mg, 93%) as a colorless oil. The spectral data matched those previously reported in the literature.⁷

Data for **8af**:

bp: 210 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, $CDCl_3$)

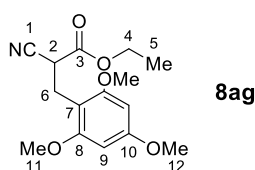
δ 7.19 (d, $J = 8.6$ Hz, 2 H, C(8)H), 6.87 (d, $J = 8.6$ Hz, 2 H, C(9)H), 4.24 (q, $J = 7.1$ Hz, 2 H, C(4)H₂), 3.80 (s, 3 H, C(11)H₃), 3.68 (dd, $J = 8.3, 5.8$ Hz, 1 H, C(2)H), 3.22 (dd, $J = 13.9, 5.8$ Hz, 1 H, C(6)H), 3.15 (dd, $J = 13.9, 8.3$ Hz, 1 H, C(6)H'), 1.28 (t, $J = 7.1$ Hz, 3 H, C(5)H₃)

^{13}C NMR: (126 MHz, CDCl_3)
 δ 165.5 C(3), 159.1 C(10), 130.1 C(8), 127.2 C(7), 116.2 C(1), 114.2 C(9), 62.8 C(4), 55.2 C(11), 39.9 C(2), 35.0 C(6), 13.9 C(5)

HRMS: (EI)
 m/z : $[\text{M}]^+$ Calcd for $\text{C}_{13}\text{H}_{15}\text{NO}_3$: 233.1052; Found: 233.1056

TLC: R_f 0.15 (pentane/ Et_2O , 80:20) [silica gel, UV, iodine]

Ethyl 2-Cyano-3-(2,4,6-trimethoxyphenyl)propanoate (**8ag**)



Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 2,4,6-trimethoxybenzaldehyde (412 mg, 2.1 mmol, 1.05 equiv), H_2O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 1:1), followed by recrystallization (hexane/acetone 90:10), afforded **8ag** (535 mg, 91%) as a white, crystalline solid.

Data for **8ag**:

mp: 81-82 °C (hexane/acetone, 90:10)

^1H NMR: (500 MHz, CDCl_3)
 δ 6.12 (s, 2 H, C(9)H), 4.23 (q, $J = 7.1$ Hz, 2 H, C(4)H₂), 3.89 – 3.75 (m, 10H, C(2)H, C(11)H₃, C(12)H₃), 3.29 (dd, $J = 13.3, 9.2$ Hz, 1 H, C(6)H), 3.19 (dd, $J = 13.4, 6.8$ Hz, 1 H, C(6)H'), 1.30 (t, $J = 7.1$ Hz, 3 H, C(5)H₃)

^{13}C NMR: (126 MHz, CDCl_3)
 δ 166.4 C(3), 160.7 C(10), 159.1 C(8), 116.8 C(1), 104.2 C(7), 90.4 C(9), 62.4 C(4), 55.6 C(11), 55.3 C(12), 37.1 C(2), 23.6 C(6), 13.9 C(5)

IR: (neat)
3004 (w), 2948 (w), 2836 (w), 2252 (w), 1732 (s), 1597 (s), 1501 (m), 1469 (m),

1459 (m), 1420 (m), 1370 (w), 1343 (w), 1272 (m), 1194 (s), 1147 (s), 1120 (s),
1056 (m), 1038 (m), 995 (w), 946 (m), 820 (s), 809 (s)

HRMS: (EI)

m/z : $[M]^+$ Calcd for $C_{15}H_{19}NO_5$: 293.1263; Found: 293.1269

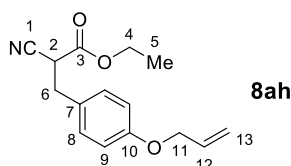
TLC: R_f 0.08 (pentane/Et₂O, 80:20) [silica gel, UV, iodine]

Analysis: $C_{15}H_{19}NO_5$

Calcd: C, 61.42; H, 6.53; N, 4.78

Found: C, 61.30; H, 6.58; N, 4.79

Ethyl 3-(4-(Allyloxy)phenyl)-2-cyanopropanoate (**8ah**)



Following General Procedure IV, $RhCl_3 \cdot 3H_2O$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 4-allyloxybenzaldehyde (0.322 mL, 2.1 mmol, 1.05 equiv), H_2O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 80:20) afforded **8ah** (450 mg, 87%) as a colorless oil.

Data for 8ah:

1H NMR: (500 MHz, $CDCl_3$)

δ 7.18 (d, $J = 8.5$ Hz, 2 H, C(8)H), 6.88 (d, $J = 8.6$ Hz, 2 H, C(9)H), 6.05 (ddt, $J = 16.9, 10.3, 5.2$ Hz, 1 H, C(12)H), 5.41 (ddd, $J = 17.3, 2.9, 1.4$ Hz, 1 H, C(13)_{H_{trans}}), 5.29 (ddd, $J = 10.5, 2.3, 1.2$ Hz, 1 H, C(13)_{H_{cis}}), 4.52 (dt, $J = 5.3, 1.3$ Hz, 2 H, C(11)_{H₂}), 4.23 (q, $J = 7.1$ Hz, 2 H, C(4)_{H₂}), 3.67 (dd, $J = 8.2, 5.8$ Hz, 1 H, C(2)H), 3.21 (dd, $J = 13.9, 5.8$ Hz, 1 H, C(6)H), 3.14 (dd, $J = 13.9, 8.3$ Hz, 1 H, C(6)H'), 1.27 (t, $J = 7.2$ Hz, 3 H, C(5)_{H₃})

^{13}C NMR: (126 MHz, $CDCl_3$)

δ 165.5 C(3), 158.1 C(10), 133.1 C(12), 130.1 C(8), 127.4 C(7), 117.6 C(13),

116.2 C(1), 114.9 C(9), 68.7 C(11), 62.8 C(4), 39.9 C(2), 34.9 C(6), 13.9 C(5)

IR: (neat)

2984 (w), 2924 (w), 2868 (w), 2254 (w), 1888 (w), 1725 (s), 1612 (w), 1511 (s), 1443 (w), 1430 (w), 1371 (m), 1345 (w), 1298 (m), 1247 (s), 1216 (s), 1180 (s), 1111 (m), 1022 (s), 997 (m), 943 (s), 744 (m), 646 (m)

HRMS: (EI)

m/z : $[M]^+$ Calcd for $C_{15}H_{17}NO_3$: 259.1208; Found: 259.1197

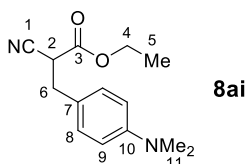
TLC: R_f 0.19 (pentane/Et₂O, 80:20) [silica gel, UV, iodine]

Analysis: $C_{15}H_{17}NO_3$

Calcd: C, 69.48; H, 6.61; N, 5.40

Found: C, 69.36; H, 6.49; N, 5.55

Ethyl 2-Cyano-3-(4-(dimethylamino)phenyl)propanoate (**8ai**)



Following General Procedure IV, $RhCl_3 \cdot 3H_2O$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 4-dimethylaminobenzaldehyde (313 mg, 2.1 mmol, 1.05 equiv), H_2O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 70:30), followed by Kugelrohr distillation, afforded **8ai** (445 mg, 90%) as a yellow oil.

Data for **8ai**:

bp: 220 °C (ABT, 0.5 mmHg)

1H NMR: (500 MHz, $CDCl_3$)

δ 7.13 (d, $J = 8.7$ Hz, 2 H, C(8)H), 6.69 (d, $J = 8.7$ Hz, 2 H, C(9)H), 4.23 (q, $J = 7.1$ Hz, 2 H, C(4)H₂), 3.65 (dd, $J = 8.3, 5.8$ Hz, 1 H, C(2)H), 3.18 (dd, $J = 13.9, 5.8$ Hz, 1 H, C(6)H), 3.11 (dd, $J = 13.9, 8.3$ Hz, 1 H, C(6)H'), 2.94 (s, 6H, C(11)H₃), 1.28 (t, $J = 7.1$ Hz, 3 H, C(5)H₃)

^{13}C NMR: (126 MHz, CDCl_3)
 δ 165.7 C(3), 150.0 C(10), 129.7 C(8), 122.7 C(7), 116.4 C(1), 112.6 C(9), 62.7 C(4), 40.5 C(11), 40.1 C(2), 35.1 C(6), 13.9 C(5)

IR: (neat)
 2983 (w), 2936 (w), 2804 (w), 2249 (w), 1739 (s), 1614 (s), 1522 (s), 1477 (w), 1444 (m), 1342 (m), 1257 (m), 1193 (s), 1162 (s), 1026 (m), 946 (m), 856 (w), 804 (m)

HRMS: (EI)
 m/z : $[\text{M}]^+$ Calcd for $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_2$: 246.1368; Found: 246.1365

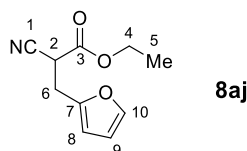
TLC: R_f 0.13 (pentane/ Et_2O , 80:20) [silica gel, UV, iodine]

Analysis: $\text{C}_{14}\text{H}_{18}\text{N}_2\text{O}_2$

Calcd: C, 68.27; H, 7.37; N, 11.37

Found: C, 68.11; H, 7.07; N, 11.47

Ethyl 2-Cyano-3-(furan-2-yl)propanoate (**8aj**)



Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), furfural (0.174 mL, 2.1 mmol, 1.05 equiv), H_2O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 80:20), followed by Kugelrohr distillation, afforded **8aj** (313 mg, 81%) as a pale yellow oil. The spectral data matched those previously reported in the literature.⁸

Data for **8aj**:

bp: 188 °C (ABT, 0.5 mmHg)

^1H NMR: (500 MHz, CDCl_3)

δ 7.37 – 7.35 (m, 1 H, C(10)H), 6.33 (dd, $J = 3.0, 2.0$ Hz, 1 H, C(9)H), 6.25 (d, J

= 3.2 Hz, 1 H, C(8)H), 4.27 (q, $J = 7.1$ Hz, 2 H, C(4)H₂), 3.82 (dd, $J = 7.9, 6.1$ Hz, 1 H, C(2)H), 3.33 (dd, $J = 15.1, 6.1$ Hz, 1 H, C(6)H), 3.27 (dd, $J = 15.1, 8.0$ Hz, 1 H, C(6)H'), 1.31 (t, $J = 7.1$ Hz, 3 H, C(5)H₃)

¹³C NMR: (126 MHz, CDCl₃)

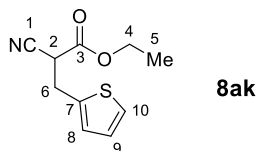
δ 165.1 C(3), 148.8 C(7), 142.5 C(10), 115.8 C(1), 110.5 C(9), 108.3 C(8), 63.0 C(4), 37.0 C(2), 28.5 C(6), 13.9 C(5)

HRMS: (EI)

m/z : [M]⁺ Calcd for C₁₀H₁₁NO₃:193.0739; Found: 193.0731

TLC: R_f 0.28 (pentane/Et₂O 80:20) [silica gel, UV, iodine]

Ethyl 2-Cyano-3-(thiophen-2-yl)propanoate (**8ak**)



Following General Procedure IV, RhCl₃·3H₂O (10.5 mg, 0.04 mmol, 2 mol %), CH₃CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 2-thiophenecarboxaldehyde (0.196 mL, 2.1 mmol, 1.05 equiv), H₂O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 80:20), followed by Kugelrohr distillation, afforded **8ak** (397 mg, 95%) as a pale yellow oil. The spectral data matched those previously reported in the literature.⁷

Data for **8ak**:

bp: 185 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, CDCl₃)

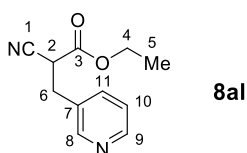
δ 7.23 (dd, $J = 5.1, 1.1$ Hz, 1 H, C(10)H), 7.01 (d, $J = 2.8$ Hz, 1 H, C(8)H), 6.97 (dd, $J = 5.0, 3.5$ Hz, 1 H, C(9)H), 4.27 (q, $J = 7.2$ Hz, 2 H, C(4)H₂), 3.76 (dd, $J = 7.5, 6.0$ Hz, 1 H, C(2)H), 3.54 – 3.42 (m, 2 H, C(6)H₂), 1.30 (t, $J = 7.1$ Hz, 3 H, C(5)H₃)

^{13}C NMR: (126 MHz, CDCl_3)
 δ 165.0 C(3), 136.6 C(7), 127.3 C(8), 127.2 C(9), 125.3 C(10), 115.9 C(1), 63.1 C(4), 39.9 C(2), 29.9 C(6), 13.9 C(5)

HRMS: (EI)
 m/z : $[\text{M}]^+$ Calcd for $\text{C}_{10}\text{H}_{11}\text{NO}_2\text{S}$: 209.0511; Found: 209.0512

TLC: R_f 0.23 (pentane/ Et_2O , 80:20) [silica gel, UV, iodine]

Ethyl 2-Cyano-3-(pyridin-3-yl)propanoate (**8al**)



Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 3-pyridinecarboxaldehyde (0.197 mL, 2.1 mmol, 1.05 equiv), H_2O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography ($\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$, 80:20), followed by Kugelrohr distillation, afforded **8al** (356 mg, 87%) as a pale yellow oil.

Data for **8al**:

bp: 205 °C (ABT, 0.5 mmHg)

^1H NMR: (500 MHz, CDCl_3)
 δ 8.55 (dd, $J = 4.8, 1.6$ Hz, 1 H, C(9)H), 8.52 (d, $J = 2.1$ Hz, 1 H, C(8)H), 7.65 (dt, $J = 7.9, 1.9$ Hz, 1 H, C(11)H), 7.28 (dd, $J = 7.8, 4.8$ Hz, 1 H, C(10)H), 4.24 (q, $J = 7.1$ Hz, 2 H, C(4)H₂), 3.75 (dd, $J = 8.0, 5.9$ Hz, 1 H, C(2)H), 3.27 (dd, $J = 14.1, 5.9$ Hz, 1 H, C(6)H), 3.21 (dd, $J = 14.1, 8.0$ Hz, 1 H, C(6)H'), 1.26 (t, $J = 7.2$ Hz, 3 H, C(5)H₃)

^{13}C NMR: (126 MHz, CDCl_3)
 δ 164.9 C(3), 150.2 C(8), 149.2 C(9), 136.6 C(11), 130.8 C(7), 123.5 C(10), 115.6 C(1), 63.1 C(4), 39.0 C(2), 32.6 C(6), 13.8 C(5)

IR: (neat)

2985 (w), 2940 (w), 2251 (w), 1738 (s), 1576 (w), 1480 (w), 1426 (m), 1370 (w), 1252 (m), 1205 (m), 1106 (w), 1028 (s), 857 (w), 796 (w), 713 (s)

HRMS: (EI)

m/z : $[M]^+$ Calcd for $C_{11}H_{12}N_2O_2$: 204.0899; Found: 204.0907

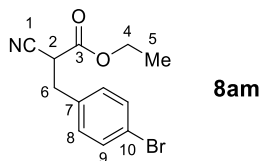
TLC: R_f 0.19 (CH_2Cl_2/Et_2O , 80:20) [silica gel, UV, iodine]

Analysis: $C_{11}H_{12}N_2O_2$

Calcd: C, 64.69; H, 5.92; N, 13.72

Found: C, 64.96; H, 6.13; N, 13.49

Ethyl 3-(4-Bromophenyl)-2-cyanopropanoate (**8am**)



Following General Procedure IV, $RhCl_3 \cdot 3H_2O$ (15.8 mg, 0.06 mmol, 3 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 4-bromobenzaldehyde (389 mg, 2.1 mmol, 1.05 equiv), H_2O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 36 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 75:25), followed by Kugelrohr distillation, afforded **8am** (461 mg, 82%) as a white solid. The spectral data matched those previously reported in the literature.⁷

Data for **8am**:

bp: 234 °C (ABT, 0.5 mmHg)

mp: 39-40 °C

1H NMR: (500 MHz, $CDCl_3$)

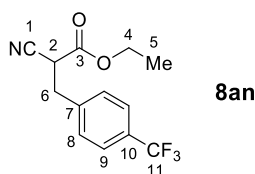
δ 7.47 (d, $J = 8.4$ Hz, 2 H, C(9)H), 7.16 (d, $J = 8.4$ Hz, 2 H, C(8)H), 4.24 (q, $J = 7.1$ Hz, 2 H, C(4)H₂), 3.70 (dd, $J = 8.2, 5.8$ Hz, 1 H, C(2)H), 3.23 (dd, $J = 13.9, 5.8$ Hz, 1 H, C(6)H), 3.16 (dd, $J = 13.9, 8.2$ Hz, 1 H, C(6)H'), 1.28 (t, $J = 7.1$ Hz, 3 H, C(5)H₃)

^{13}C NMR: (126 MHz, CDCl_3)
 δ 165.2 C(3), 134.2 C(7), 132.0 C(9), 130.8 C(8), 121.9 C(10), 115.8 C(1), 63.1 C(4), 39.3 C(2), 35.0 C(6), 13.9 C(5)

HRMS: (EI)
 m/z : $[\text{M}]^+$ Calcd for $\text{C}_{12}\text{H}_{12}\text{BrNO}_2$: 281.0051; Found: 281.0050

TLC: R_f 0.20 (pentane/ Et_2O , 80:20) [silica gel, UV, iodine]

Ethyl 2-Cyano-3-(4-(trifluoromethyl)phenyl)propanoate (**8an**)



Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (15.8 mg, 0.06 mmol, 3 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 4-(trifluoromethyl)benzaldehyde (0.287 mL, 2.1 mmol, 1.05 equiv), H_2O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 36 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 70:30), followed by Kugelrohr distillation and recrystallization (pentane), afforded **8an** (294 mg, 54%) as a white, crystalline solid.

Data for **8an**:

bp: 203 °C (ABT, 0.5 mmHg)

mp: 33-34 °C (pentane)

^1H NMR: (500 MHz, CDCl_3)
 δ 7.61 (d, $J = 8.1$ Hz, 2 H, C(9)H), 7.41 (d, $J = 8.1$ Hz, 2 H, C(8)H), 4.25 (q, $J = 7.1$ Hz, 2 H, C(4)H₂), 3.75 (dd, $J = 8.3, 5.8$ Hz, 1 H, C(2)H), 3.33 (dd, $J = 13.9, 5.8$ Hz, 1 H, C(6)H), 3.26 (dd, $J = 13.9, 8.3$ Hz, 1 H, C(6)H'), 1.28 (t, $J = 7.2$ Hz, 3 H, C(5)H₃)

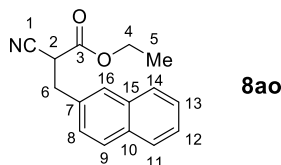
^{13}C NMR: (126 MHz, CDCl_3)
 δ 165.1 C(3), 139.3 C(7), 130.2 (q, $J = 32.6$ Hz, C(10)), 129.5 C(8), 125.8 (q, $J = 3.7$ Hz, C(9)), 123.9 (q, $J = 272.0$ Hz, C(11)), 115.7 C(1), 63.2 C(4), 39.1 C(2),

35.2 C(6), 13.9 C(5)

 ^{19}F NMR: (470 MHz, CDCl_3) δ -63.07IR: (neat)2988 (w), 2251 (w), 1742 (m), 1619 (w), 1447 (w), 1421 (w), 1322 (s) 1263 (m),
1161 (m), 1109 (s), 1066 (s), 1019 (m), 855 (w), 819 (w) 734 (w)HRMS: (EI) m/z : $[\text{M}]^+$ Calcd for $\text{C}_{13}\text{H}_{12}\text{F}_3\text{NO}_2$: 271.0820; Found: 271.0821TLC: R_f 0.17 (pentane/ Et_2O , 80:20) [silica gel, UV, iodine]Analysis: $\text{C}_{13}\text{H}_{12}\text{F}_3\text{NO}_2$

Calcd: C, 57.57; H, 4.46; N, 5.16

Found: C, 57.70; H, 4.44; N, 5.40

Ethyl 2-Cyano-3-(naphthalen-2-yl)propanoate (8ao)

Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (15.8 mg, 0.06 mmol, 3 mol %), CH_3CN (2.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 2-naphthaldehyde (328 mg, 2.1 mmol, 1.05 equiv), H_2O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 36 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 70:30), followed by Kugelrohr distillation, afforded **8ao** (349 mg, 69%) as a white solid.

Data for 8ao:bp: 251 °C (ABT, 0.5 mmHg)mp: 42-43 °C ^1H NMR: (500 MHz, CDCl_3) δ 7.86 – 7.79 (m, 3 H, C(9)H, C(11)H, C(14)H), 7.75 (s, 1 H, C(16)H), 7.53 – 7.46 (m, 2 H, C(12), C(13)), 7.39 (dd, J = 8.4, 1.8 Hz, 1 H, C(8)), 4.24 (qd, J =

7.1, 0.5 Hz, 2 H, C(4)H₂), 3.82 (dd, $J = 8.4, 5.9$ Hz, 1 H, C(2)H), 3.45 (dd, $J = 13.9, 5.8$ Hz, 1 H, C(6)H), 3.37 (dd, $J = 13.9, 8.4$ Hz, 1 H, C(6)H'), 1.25 (t, $J = 7.2$ Hz, 3 H, C(5)H₃)

¹³C NMR: (126 MHz, CDCl₃)

δ 165.4 C(3), 133.3 C(7), 132.7, 132.6, 128.6 C(9), 128.0 C(16), 127.7, 127.6, 126.6 C(8), 126.3, 126.1, 116.1 C(1), 62.9 C(4), 39.5 C(2), 35.8 C(6), 13.8 C(5)

IR: (neat)

3051 (w), 2984 (w), 2938 (w), 2906 (w), 2250 (w), 1731 (s), 1600 (w), 1507 (w), 1463 (w), 1368 (w), 1245 (s), 1095 (w), 1028 (m), 903 (m), 852 (m), 821 (m), 803 (m), 749 (s)

HRMS: (EI)

m/z : [M]⁺ Calcd for C₁₆H₁₅NO₂: 253.1103; Found: 253.1096

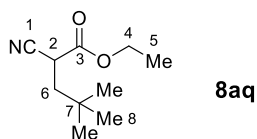
TLC: R_f 0.17 (pentane/Et₂O, 80:20) [silica gel, UV, iodine]

Analysis: C₁₆H₁₅NO₂

Calcd: C, 75.87; H, 5.97; N, 5.53

Found: C, 75.86; H, 5.91; N, 5.54

Ethyl 2-Cyano-4,4-dimethylpentanoate (**8aq**)



Following General Procedure IV, RhCl₃·3H₂O (10.5 mg, 0.04 mmol, 2 mol %), CH₃CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), pivaldehyde (0.228 mL, 2.1 mmol, 1.05 equiv), H₂O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 90:10), followed by Kugelrohr distillation, afforded **8aq** (329 mg, 90%) as a colorless oil.

Data for **8aq**:

bp: 130 °C (ABT, 0.5 mmHg)

^1H NMR: (500 MHz, CDCl_3)

δ 4.26 (q, $J = 7.2$ Hz, 2 H, C(4) H_2), 3.42 (dd, $J = 8.6, 4.6$ Hz, 1 H, C(2)H), 1.95 (dd, $J = 14.2, 4.6$ Hz, 1 H, C(6)H), 1.89 (dd, $J = 14.2, 8.6$ Hz, 1 H, C(6)H'), 1.32 (t, $J = 7.2$ Hz, 3 H, C(5) H_3), 1.00 (s, 9H, C(8) H_3)

^{13}C NMR: (126 MHz, CDCl_3)

δ 166.8 C(3), 117.7 C(1), 62.8 C(4), 43.2 C(6), 33.6 C(2), 30.7 C(7), 28.9 C(8), 13.9 C(5)

IR: (neat)

2960 (w), 2249 (w), 1743 (s), 1477 (w), 1399 (w), 1369 (m), 1244 (m), 1195 (m), 1028 (m), 916 (w), 856 (w)

HRMS: (EI)

m/z : $[\text{MH}]^+$ Calcd for $\text{C}_{10}\text{H}_{18}\text{NO}_2$: 184.1338; Found: 184.1338

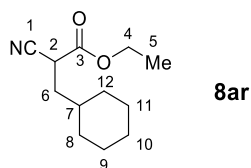
TLC: R_f 0.48 (pentane/ Et_2O , 80:20) [silica gel, iodine]

Analysis: $\text{C}_{10}\text{H}_{17}\text{NO}_2$

Calcd: C, 65.54; H, 9.35; N, 7.64

Found: C, 65.75; H, 9.33; N, 7.79

Ethyl 2-Cyano-3-cyclohexylpropanoate (**8ar**)



Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), cyclohexanecarboxaldehyde (0.254 mL, 2.1 mmol, 1.05 equiv), H_2O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 90:10), followed by Kugelrohr distillation, afforded **8ar** (404 mg, 97%) as a colorless oil.

Data for **8ar**:

bp: 158 °C (ABT, 0.5 mmHg)

^1H NMR: (500 MHz, CDCl_3)

δ 4.25 (q, $J = 7.1$ Hz, 2 H, C(4) H_2), 3.54 (dd, $J = 9.4, 6.2$ Hz, 1 H, C(2)H), 1.89 – 1.77 (m, 2 H, C(6) H_2), 1.77 – 1.63 (m, 5 H, C(8-12) H_{eq}), 1.57 – 1.47 (m, 1 H, C(7)H), 1.31 (t, $J = 7.1$ Hz, 3 H, C(5) H_3), 1.29 – 1.20 (m, 2 H, C(9) H_{ax} , C(11) H_{ax}), 1.19 – 1.09 (m, 1 H, C(10) H_{ax}), 1.02 – 0.84 (m, 2 H, C(8) H_{ax} , C(12) H_{ax})

^{13}C NMR: (126 MHz, CDCl_3)

δ 166.5 C(3), 116.7 C(1), 62.7 C(4), 37.0 C(6), 35.3 C(2), 35.2 C(7), 33.0 C(12), 31.9 C(8), 26.1 C(10), 25.8 C(9), 25.7 C(11), 13.9 C(5)

IR: (neat)

2984 (w), 2924 (m), 2852 (w), 2249 (w), 1742 (s), 1449 (m), 1321 (w), 1247 (m), 1188 (m), 1096 (w), 1023 (m), 855 (w)

HRMS: (EI)

m/z : $[\text{M}-\text{H}]^+$ Calcd for $\text{C}_{12}\text{H}_{18}\text{NO}_2$: 208.1338; Found: 208.1340

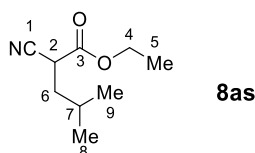
TLC: R_f 0.52 (pentane/ Et_2O , 80:20) [silica gel, iodine]

Analysis: $\text{C}_{12}\text{H}_{19}\text{NO}_2$

Calcd: C, 68.87; H, 9.15; N, 6.69

Found: C, 69.15; H, 9.00; N, 6.88

Ethyl 2-Cyano-4-methylpentanoate (**8as**)



Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), isobutyraldehyde (0.192 mL, 2.1 mmol, 1.05 equiv), H_2O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 90:10), followed by Kugelrohr distillation, afforded **8as** (307 mg, 91%) as a colorless oil.

Data for 8as:

bp: 121 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, CDCl₃)

δ 4.26 (q, *J* = 7.1 Hz, 2 H, C(4)H₂), 3.51 (dd, *J* = 9.3, 5.9 Hz, 1 H, C(2)H), 1.91 – 1.81 (m, 2 H, C(6)H, C(7)H), 1.81 – 1.74 (m, 1 H, C(6)H'), 1.32 (t, *J* = 7.1 Hz, 3 H, C(5)H₃), 0.99 (d, *J* = 6.3 Hz, 3 H, C(8)H₃), 0.96 (d, *J* = 6.4 Hz, 3 H, C(9)H₃)

¹³C NMR: (126 MHz, CDCl₃)

δ 166.4 C(3), 116.6 C(1), 62.7 C(4), 38.3 C(6), 35.9 C(2), 26.0 C(7), 22.4 C(8), 21.2 C(9), 13.9 C(5)

IR: (neat)

2962 (w), 2875 (w), 2249 (w), 1742 (s), 1470 (w), 1390 (w), 1370 (w), 1265 (m), 1244 (m), 1185 (m), 1113 (w), 1023 (m), 927 (w), 857 (w)

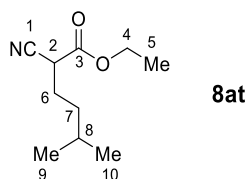
HRMS: (EI)

m/z: [M]⁺ Calcd for C₉H₁₅NO₂: 169.1103; Found: 169.1106

TLC: *R_f* 0.36 (pentane/Et₂O, 80:20) [silica gel, iodine]Analysis: C₉H₁₅NO₂

Calcd: C, 63.88; H, 8.93; N, 8.28

Found: C, 63.89; H, 9.17; N, 8.39

Ethyl 2-Cyano-5-methylhexanoate (8at)

Following General Procedure IV, RhCl₃·3H₂O (10.5 mg, 0.04 mmol, 2 mol %), CH₃CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), isovaleraldehyde (0.230 mL, 2.1 mmol, 1.05 equiv), H₂O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 90:10), followed by Kugelrohr distillation,

afforded **8at** (347 mg, 95%) as a colorless oil. The spectral data matched those previously reported in the literature.⁷

Data for **8at**:

bp: 138 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, CDCl₃)

δ 4.26 (q, *J* = 7.1 Hz, 2 H, C(4)H₂), 3.46 (dd, *J* = 7.6, 6.4 Hz, 1 H, C(2)H), 2.03 – 1.86 (m, 2 H, C(6)H₂), 1.66 – 1.55 (m, 1 H, C(8)H), 1.42 – 1.35 (m, 2 H, C(7)H₂), 1.32 (t, *J* = 7.1 Hz, 3 H, C(5)H₃), 0.92 (d, *J* = 6.6 Hz, 3 H, C(9)H₃), 0.91 (d, *J* = 6.6 Hz, 3 H, C(10)H₃)

¹³C NMR: (126 MHz, CDCl₃)

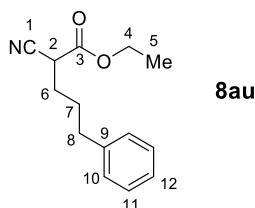
δ 166.2 C(3), 116.6 C(1), 62.7 C(4), 37.7 C(2), 35.6 C(7), 27.8 C(6), 27.5 C(8), 22.3 C(9), 22.1 C(10), 14.0 C(5)

HRMS: (ESI)

m/z: [MH]⁺ Calcd for C₁₀H₁₈NO₂: 184.1338; Found: 184.1339

TLC: *R_f* 0.37 (pentane/Et₂O, 80:20) [silica gel, iodine]

Ethyl 2-Cyano-5-phenylpentanoate (8au)



Following General Procedure IV, RhCl₃·3H₂O (10.5 mg, 0.04 mmol, 2 mol %), CH₃CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), hydrocinnamaldehyde (0.277 mL, 2.1 mmol, 1.05 equiv), H₂O (0.108 mL, 6.0 mmol, 3.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 24 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 80:20), followed by Kugelrohr distillation, afforded **8au** (329 mg, 71%) as a colorless oil. The spectral data matched those previously reported in the literature.⁷

Data for **8au**:

bp: 211 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, CDCl₃)

δ 7.30 (t, *J* = 7.5 Hz, 2 H, C(11)H), 7.21 (t, *J* = 7.4 Hz, 1 H, C(12)H), 7.18 (d, *J* = 7.4 Hz, 2 H, C(10)H), 4.25 (q, *J* = 7.1 Hz, 2 H, C(4)H₂), 3.48 (t, *J* = 6.8 Hz, 1 H, C(2)H), 2.69 (t, *J* = 7.5 Hz, 2 H, C(8)H₂), 2.01 – 1.94 (m, 2 H, C(6)H₂), 1.90 – 1.79 (m, 2 H, C(7)H₂), 1.31 (t, *J* = 7.1 Hz, 3 H, C(5)H₃)

¹³C NMR: (126 MHz, CDCl₃)

δ 166.0 C(3), 140.8 C(9), 128.5 C(11), 128.3 C(10), 126.2 C(12), 116.4 C(1), 62.8 C(4), 37.4 C(2), 34.9 C(8), 29.2 C(6), 28.3 C(7), 14.0 C(5)

HRMS: (EI)

m/z: [M]⁺ Calcd for C₁₄H₁₇NO₂: 231.1259; Found: 231.1267

TLC: *R*_f 0.28 (pentane/Et₂O, 80:20) [silica gel, UV, iodine]

Table 5, entry 16

Following General Procedure IV, RhCl₃·3H₂O (15.8 mg, 0.06 mmol, 3 mol %), CH₃CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 4-nitrobenzaldehyde (317 mg, 2.1 mmol, 1.05 equiv), H₂O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 36 h followed by standard workup. Analysis of the reaction mixture by GC-MS showed only trace amounts of **8ap**, and **9ap'** as the major product.

Table 5, entry 22

Following General Procedure IV, RhCl₃·3H₂O (15.8 mg, 0.06 mmol, 3 mol %), CH₃CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 4-(2-trimethylsilylethynyl)benzaldehyde (425 mg, 2.1 mmol, 1.05 equiv), H₂O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial. which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 24 h followed by standard workup. The conversion to **8av** was determined to be 19% by analysis of the crude reaction mixture by ¹H NMR (based on mesitylene (0.096 mL, 0.5 mmol) as the standard), with **9av** being the major component of the mixture.

Table 5, entry 23

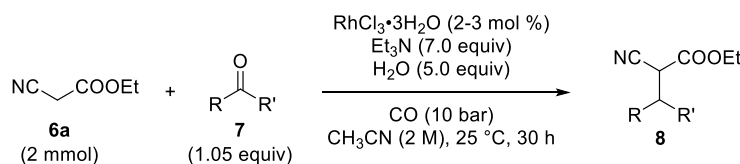
Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 4-prop-2-ynoxybenzaldehyde (336 mg, 2.1 mmol, 1.05 equiv), H_2O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Analysis of the reaction mixture by GC-MS and ^1H NMR showed no **8aw**, and **9aw** as the major product.

Table 5, entry 24

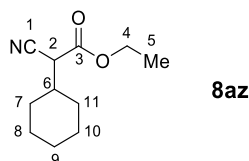
Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (15.8 mg, 0.06 mmol, 3 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 2-hydroxybenzaldehyde (223.6 mL, 2.1 mmol, 1.05 equiv), H_2O (0.108 mL, 6.0 mmol, 3.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Analysis of the reaction mixture by GC-MS and ^1H NMR (based on mesitylene (0.096 mL, 0.5 mmol) as the standard) showed **9ax'** as the major component of the mixture.

Table 5, entry 25

Following General Procedure IV, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (15.8 mg, 0.06 mmol, 3 mol %), CH_3CN (4.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 2-hydroxybenzaldehyde (223.6 mL, 2.1 mmol, 1.05 equiv), H_2O (0.072 mL, 4.0 mmol, 2.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 18 h followed by standard workup. Analysis of the reaction mixture by GC-MS and ^1H NMR (based on mesitylene (0.096 mL, 0.5 mmol) as the standard) showed a mixture of *cis*- and *trans*- isomers of the mono- and dienoates with 15% yield of **8au**.

General Procedure V: Reaction of Ethyl Cyanoacetate with Cyclic Ketones (Table 6)

$\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ was added to a 40-mL glass vial, followed by acetonitrile, ethyl cyanoacetate **6a**, the ketone **7**, deionized water, and triethylamine. A stir bar was added, and the vial was placed in an autoclave. The autoclave was pressurized with CO and vented three times, and then pressurized to 10 bar. The reaction was stirred at room temperature for the indicated time. After venting and purging the autoclave with nitrogen, the vial was removed. The volatiles were removed by rotary evaporation ($25\text{-}30^\circ\text{C}$, 15 mmHg), the residue was dissolved in CH_2Cl_2 , and loaded on silica gel (1 g). The crude mixture was purified by silica gel column chromatography (2.5 x 20-25 cm), followed by distillation.

Ethyl 2-Cyano-2-cyclohexylacetate (8az)

Following General Procedure V, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (1.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), cyclohexanone (0.217 mL, 2.1 mmol, 1.05 equiv), H_2O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et_3N (1.95 mL, 14.0 mmol, 7.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 30 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 95:5), followed by Kugelrohr distillation, afforded **8az** (364 mg, 93%) as a colorless oil. The spectral data matched those previously reported in the literature.⁸

Data for 8az:

bp: 178°C (ABT, 0.5 mmHg)

^1H NMR: (500 MHz, CDCl_3)

δ 4.28 – 4.23 (m, 2 H, C(4) H_2), 3.36 (d, $J = 5.7$ Hz, 1 H, C(2)H), 2.10 – 1.96 (m,

1 H, C(6)H), 1.86 – 1.64 (m, 5 H, C(7-11) H_{eq}), 1.31 (t, $J = 7.1$ Hz, 3 H, C(5) H_3),
1.29 – 1.10 (m, 5 H, C(7-11) H_{ax})

^{13}C NMR: (126 MHz, $CDCl_3$)

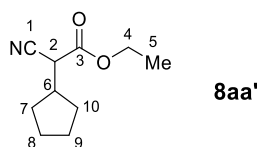
δ 165.8 C(3), 115.7 C(1), 62.5 C(4), 44.5 C(2), 38.8 C(6), 31.0, 29.3, 25.7, 25.5,
25.4, 14.0 C(5)

HRMS: (ESI)

m/z : $[MH]^+$ Calcd for $C_{11}H_{18}NO_2$: 196.1338; Found: 196.1332

TLC: R_f 0.48 (pentane/ Et_2O , 80:20) [silica gel, iodine]

Ethyl 2-Cyano-2-cyclopentylacetate (**8aa'**)



Following General Procedure V, $RhCl_3 \cdot 3H_2O$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (1.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), cyclopentanone (0.186 mL, 2.1 mmol, 1.05 equiv), H_2O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et_3N (1.95 mL, 14.0 mmol, 7.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 30 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 85:15), followed by Kugelrohr distillation, afforded **8aa'** (285 mg, 79%) as a colorless oil.

Data for **8aa'**:

bp: 147 °C (ABT, 0.5 mmHg)

1H NMR: (500 MHz, $CDCl_3$)

δ 4.29 – 4.22 (m, 2 H, C(4) H_2), 3.49 (d, $J = 6.7$ Hz, 1 H, C(2)H), 2.48 (h, $J = 7.0$ Hz, 1 H, C(6)H), 1.95 – 1.81 (m, 2 H, C(7)H, C(10)H), 1.79 – 1.68 (m, 2 H, C(8)H, C(9)H), 1.66 – 1.55 (m, 2 H, C(8)H', C(9)H'), 1.53 – 1.36 (m, 2 H, C(7)H', C(10)H'), 1.31 (t, $J = 7.1$ Hz, 3 H, C(5) H_3)

^{13}C NMR: (126 MHz, $CDCl_3$)

δ 166.1 C(3), 116.0 C(1), 62.5 C(4), 42.5 C(2), 40.1 C(6), 30.7 C(7), 29.7 C(10),
25.0 C(8), 24.9 C(9), 14.0 C(5)

IR: (neat)

3395 (w), 3209 (w), 2958 (w), 2872 (w), 2252 (w), 1740 (s) 1668 (w), 1614 (w),
1514 (w), 1392 (w), 1369 (w), 1246 (s), 1186 (s), 1028 (s), 854 (w), 814 (w)

HRMS: (ESI)

m/z : $[MH]^+$ Calcd for $C_{10}H_{16}NO_2$: 182.1181; Found: 182.1177

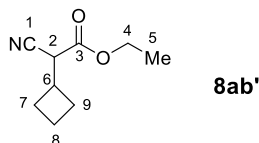
TLC: R_f 0.44 (pentane/Et₂O, 80:20) [silica gel, iodine]

Analysis: $C_{10}H_{15}NO_2$

Calcd: C, 66.27; H, 8.34; N, 7.73

Found: C, 65.94; H, 8.25; N, 7.60

Ethyl 2-Cyano-2-cyclobutylacetate (**8ab'**)



Following General Procedure V, $RhCl_3 \cdot 3H_2O$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (1.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), cyclobutanone (0.149 mL, 2.1 mmol, 1.05 equiv), H_2O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et_3N (1.95 mL, 14.0 mmol, 7.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 30 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 90:10), followed by Kugelrohr distillation, afforded **8ab'** (157 mg, 47%) as a colorless oil. The spectral data matched those previously reported in the literature.⁹

Data for **8ab'**:

bp: 95 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, $CDCl_3$)

δ 4.22 (q, $J = 7.1$ Hz, 2 H, C(4)H₂), 3.49 (d, $J = 7.3$ Hz, 1 H, C(2)H), 2.91 (h, $J = 8.1$ Hz, 1 H, C(6)H), 2.20 – 2.10 (m, 2 H, C(7)H, C(9)H), 2.08 – 1.82 (m, 4 H, C(7)H', C(8)H₂, C(9)H'), 1.29 (t, $J = 7.1$ Hz, 3 H, C(5)H₃)

¹³C NMR: (126 MHz, $CDCl_3$)

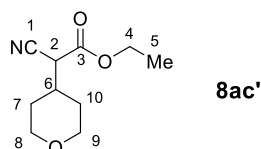
δ 165.4 C(3), 115.6 C(1), 62.5 C(4), 43.1 C(2), 35.1 C(6), 26.5 C(7), 25.8 C(9), 17.7 C(8), 14.0 C(5)

HRMS: (ESI)

m/z : $[MH]^+$ Calcd for $C_9H_{14}NO_2$: 168.1025; Found: 168.1019

TLC: R_f 0.42 (pentane/Et₂O, 80:20) [silica gel, iodine]

Ethyl 2-Cyano-2-(tetrahydro-2 H-pyran-4-yl)acetate (8ac'**)**



Following General Procedure V, $RhCl_3 \cdot 3H_2O$ (10.5 mg, 0.04 mmol, 2 mol %), CH_3CN (1.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), tetrahydro-pyran-4-one (0.194 mL, 2.1 mmol, 1.05 equiv), H_2O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et_3N (1.95 mL, 14.0 mmol, 7.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 30 h followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 70:30), followed by Kugelrohr distillation, afforded **8ac'** (304 mg, 77%) as a colorless oil that slowly solidified at room temperature.

Data for **8ac'**:

bp: 185 °C (ABT, 0.5 mmHg)

mp: 39-40 °C

¹H NMR: (500 MHz, $CDCl_3$)

δ 4.32 – 4.23 (m, 2 H, C(4)H₂), 4.07 – 3.98 (m, 2 H, C(8)H_{eq}, C(9)H_{eq}), 3.45 – 3.37 (m, 3 H, C(2)H, C(8)H_{ax}, C(9)H_{ax}), 2.35 – 2.21 (m, 1 H, C(6)H), 1.75 – 1.67 (m, 1 H, C(7)H₂), 1.67 – 1.57 (m, 2 H, C(10)H₂), 1.36 – 1.28 (t, $J = 7.2$ Hz, 3 H, C(5)H₃)

¹³C NMR: (126 MHz, $CDCl_3$)

δ 165.2 C(3), 115.1 C(1), 67.19 C(8), 67.16 C(9), 62.9 C(4), 43.8 C(2), 36.1 C(6), 30.6 C(7), 29.4 C(10), 14.1 C(5)

IR: (neat)

2934 (w), 2920 (m), 2856 (m), 2246 (w), 1737 (s), 1468 (m), 1446 (m), 1371 (m), 1305 (m), 1246 (s), 1208 (s), 1090 (s), 1022 (s), 1010 (s), 986 (s), 855 (s), 770 (m)

HRMS: (EI)

m/z : $[M]^+$ Calcd for $C_{10}H_{15}NO_3$: 197.1052; Found: 197.1055

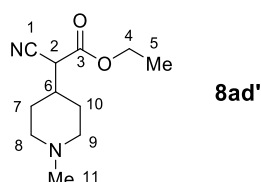
TLC: R_f 0.28 (pentane/Et₂O, 70:30) [silica gel, iodine]

Analysis: $C_{10}H_{15}NO_3$

Calcd: C, 60.90; H, 7.67; N, 7.10

Found: C, 60.86; H, 7.53; N, 7.04

Ethyl 2-Cyano-2-(1-methylpiperidin-4-yl)acetate (**8ad'**)



Following General Procedure V, $RhCl_3 \cdot 3H_2O$ (15.8 mg, 0.06 mmol, 3 mol %), CH_3CN (1.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), *N*-methyl-4-piperidinone (0.246 mL, 2.1 mmol, 1.05 equiv), H_2O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et_3N (1.95 mL, 14.0 mmol, 7.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 30 h followed by standard workup. Purification by silica gel column chromatography (EtOAc/MeOH/ NH_4OH , 90:9:1), followed by Kugelrohr distillation, afforded **8ad'** (352 mg, 89%) as a clear, colorless oil which rapidly discolored in air.

Data for 8ad':

bp: 135 °C (ABT, 0.5 mmHg)

1H NMR: (500 MHz, $CDCl_3$)

δ 4.24 – 4.15 (m, 2 H, C(4)H₂), 3.30 (d, $J = 6.6$ Hz, 1 H, C(2)H), 2.88 – 2.78 (m, 2 H, C(8)H_{eq}, C(9)H_{eq}), 2.19 (s, 3 H, C(11)H₃), 1.98 – 1.83 (m, 3 H, C(6)H, C(8)H_{ax}, C(9)H_{ax}), 1.77 – 1.69 (m, 1 H, C(7)H_{eq}), 1.67 – 1.59 (m, 1 H, C(10)H_{eq}), 1.57 – 1.45 (m, 2 H, C(7)H_{ax}, C(10)H_{ax}), 1.25 (t, $J = 7.1$ Hz, 3 H, C(5)H₃)

^{13}C NMR: (126 MHz, $CDCl_3$)

δ 165.5 C(3), 115.3 C(1), 62.7 C(4), 55.1 C(8), 55.0 C(9), 46.1 C(11), 43.6 C(2), 36.7 C(6), 30.2 C(10), 29.1 C(7), 14.0 C(5)

IR: (neat)

2939 (w), 2849 (w), 2785 (w), 2686 (w), 2249 (w), 1739 (s), 1466 (w), 1448 (m),
1380 (w), 1369 (w), 1280 (m), 1250 (m), 1197 (m), 1179 (m), 1139 (m), 1093
(w), 1066 (w), 1028 (m), 985 (w), 853 (w), 765 (w)

HRMS: (EI)

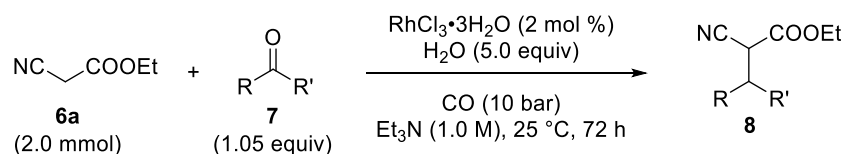
m/z : $[M]^+$ Calcd for $C_{11}H_{18}N_2O_2$: 210.1364; Found: 210.1368

TLC: R_f 0.45 (EtOAc/MeOH/NH₄OH, 90:9:1) [silica gel, iodine]

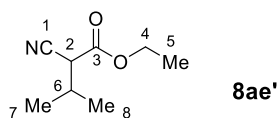
Analysis: $C_{11}H_{18}N_2O_2$

Calcd: C, 62.83; H, 8.63; N, 13.32

Found: C, 62.40; H, 8.40; N, 13.27

General Procedure VI: Reaction of Ethyl Cyanoacetate with Acyclic Ketones (Table 7)

$\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ was added to a 40-mL glass vial, followed by triethylamine, ethyl cyanoacetate **6a**, the ketone **7**, and deionized water. A stir bar was added, and the vial was placed in an autoclave. The autoclave was pressurized with CO and vented three times, and then pressurized to 10 bar. The reaction was stirred at room temperature for the indicated time. After venting and purging the autoclave with nitrogen, the vial was removed. The volatiles were removed by rotary evaporation (25–30 °C, 15 mmHg), the residue was dissolved in CH_2Cl_2 , and loaded on silica gel (1 g). The crude mixture was purified by silica gel column chromatography (2.5 x 20–25 cm), followed by distillation.

Ethyl 2-Cyano-3-methylbutanoate (8ae')

Following General Procedure VI, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), triethylamine (2.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), acetone (0.154 mL, 2.1 mmol, 1.05 equiv), and H_2O (0.180 mL, 10.0 mmol, 5.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 72 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 90:10), followed by Kugelrohr distillation, afforded **8ae'** (146 mg, 47%) as a colorless oil. The spectral data matched those previously reported in the literature.⁶

Data for 8ae':

bp: 93 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, CDCl_3)

δ 4.30 – 4.22 (m, 2 H, C(4) H_2), 3.38 (d, $J = 5.4$ Hz, 1 H, C(2)H), 2.46 – 2.35 (m, 1 H, C(6)H), 1.31 (t, $J = 7.2$ Hz, 3 H, C(5) H_3), 1.12 (d, $J = 6.9$ Hz, 3 H, C(7) H_3), 1.09 (d, $J = 6.8$ Hz, 3 H, C(8) H_3)

^{13}C NMR: (126 MHz, CDCl_3)
 δ 165.9 C(3), 115.5 C(1), 62.6 C(4), 45.3 C(2), 30.0 C(6), 20.7 C(7), 18.8 C(8),
14.0 C(5)

HRMS: (EI)
 m/z : $[\text{M}]^+$ Calcd for $\text{C}_8\text{H}_{13}\text{NO}_2$: 155.0944; Found: 155.0946

TLC: R_f 0.19 (pentane/ Et_2O , 90:10) [silica gel, iodine]

Table 7, entry 2

Following General Procedure VI, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), Et_3N (2.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 3-pentanone (0.222 mL, 2.1 mmol, 1.05 equiv), and H_2O (0.180 mL, 10.0 mmol, 5.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 72 h followed by standard workup. Analysis of the reaction mixture by GC-MS and ^1H NMR (based on mesitylene as the standard) showed no product formation.

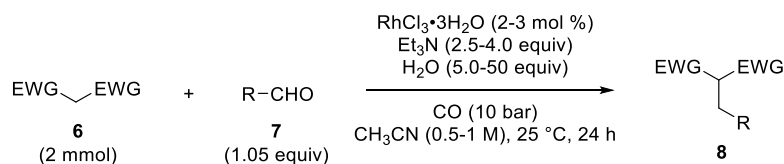
Table 7, entry 3

Following General Procedure VI, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), Et_3N (2.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), 2,4-dimethyl-3-pentanone (0.297 mL, 2.1 mmol, 1.05 equiv), and H_2O (0.180 mL, 10.0 mmol, 5.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 72 h followed by standard workup. Analysis of the reaction mixture by GC-MS and ^1H NMR (based on mesitylene (0.096 mL, 0.5 mmol) as the standard) showed no product formation.

Table 7, entry 4

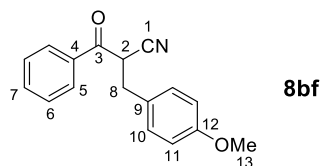
Following General Procedure VI, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (10.5 mg, 0.04 mmol, 2 mol %), Et_3N (2.0 mL), ethyl cyanoacetate (0.213 mL, 2.0 mmol), benzophenone (383 mg, 2.1 mmol, 1.05 equiv), and H_2O (0.180 mL, 10.0 mmol, 5.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 72 h followed by standard workup. Analysis of the reaction mixture by GC-MS and ^1H NMR (based on mesitylene (0.096 mL, 0.5 mmol) as the standard) showed no product formation.

General Procedure VII: Reaction of Other Active Methylene Compounds with Aldehydes in One Step (Table 8)



$\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ was added to a 40-mL glass vial, followed by acetonitrile, the active methylene compound **6**, the aldehyde **7**, deionized water, and triethylamine. A stir bar was added, and the vial was placed in an autoclave. The autoclave was pressurized with CO and vented three times, and then pressurized to 10 bar. The reaction was stirred at room temperature for the indicated time. After venting and purging the autoclave with nitrogen, the vial was removed. The volatiles were removed by rotary evaporation (25-30 °C, 15 mmHg), the residue was dissolved in CH_2Cl_2 , and loaded on silica gel (1 g). The crude mixture was purified by silica gel column chromatography (2.5 x 20-25 cm), followed by distillation or recrystallization.

2-(4-Methoxybenzyl)-3-oxo-3-phenylpropanenitrile (**8bf**)



Following General Procedure VII, $\text{RhCl}_3 \cdot 3\text{H}_2\text{O}$ (15.8 mg, 0.06 mmol, 3 mol %), CH_3CN (3.0 mL), benzoylacetonitrile (290 mg, 2.0 mmol), *p*-anisaldehyde (0.256 mL, 2.1 mmol, 1.05 equiv), H_2O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et_3N (1.12 mL, 8.0 mmol, 4.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 24 h followed by standard workup. Purification by silica gel column chromatography (pentane/ Et_2O , 75:25 to 50:50), followed by Kugelrohr distillation, afforded **8bf** (463 mg, 87%) as a yellow oil.

Data for **8bf**:

bp: 256 °C (ABT, 0.5 mmHg)

$^1\text{H NMR}$: (500 MHz, CDCl_3)

δ 7.95 (dd, $J = 8.4, 1.2$ Hz, 2 H, C(5)H), 7.65 (t, $J = 7.4$ Hz, 1 H, C(7)H), 7.51 (t,

$J = 7.8$ Hz, 2 H, C(6)H), 7.20 (d, $J = 8.7$ Hz, 2 H, C(10)H), 6.86 (d, $J = 8.7$ Hz, 2 H, C(11)H), 4.51 (dd, $J = 8.8, 5.8$ Hz, 1 H, C(2)H), 3.78 (s, 3 H, C(13)H₃), 3.30 (dd, $J = 14.1, 5.8$ Hz, 1 H, C(8)H), 3.19 (dd, $J = 14.1, 8.8$ Hz, 1 H, C(8)H')

¹³C NMR: (126 MHz, CDCl₃)

δ 190.2 C(3), 159.0 C(12), 134.5 C(7), 134.0 C(4), 130.1 C(10), 129.1 C(6), 128.7 C(5), 127.8 C(9), 117.0 C(1), 114.2 C(11), 55.2 C(13), 42.1 C(2), 34.8 C(8)

IR: (neat)

3003 (w), 2935 (w), 2836 (w), 2249 (w), 1688 (m), 1611 (m), 1596 (m), 1582 (m), 1512 (s), 1448 (m), 1301 (m), 1246 (s), 1178 (s), 1110 (w), 1030 (m), 949 (w), 874 (w), 810 (m), 744 (m), 690 (s)

HRMS: (EI)

m/z : [M]⁺ Calcd for C₁₇H₁₅NO₂: 265.1103; Found: 265.1111

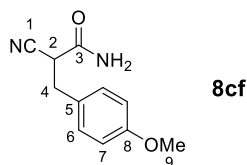
TLC: R_f 0.16 (pentane/Et₂O, 70:30) [silica gel, UV, iodine]

Analysis: C₁₇H₁₅NO₂

Calcd: C, 76.96; H, 5.70; N, 5.28

Found: C, 76.63; H, 5.61; N, 5.23

2-Cyano-3-(4-methoxyphenyl)propanamide (8cf)



Following General Procedure VII, RhCl₃·3H₂O (10.5 mg, 0.04 mmol, 2 mol %), CH₃CN (4.0 mL), 2-cyanoacetamide (168, 2.0 mmol), *p*-anisaldehyde (0.256 mL, 2.1 mmol, 1.05 equiv), H₂O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et₃N (1.12 mL, 8.0 mmol, 4.0 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 24 h followed by standard workup. After evaporation of the volatiles (25-30 °C, 15 mmHg), the residue was suspended in Et₂O and filtered. The solid residue was redissolved in acetone and filtered through a silica plug eluting with acetone. The filtrate

was concentrated to provide an off-white solid. Recrystallization (EtOH, abs.) afforded **8cf** (344 mg, 84%) as a white, crystalline solid.

Data for **8cf**:

mp: 170-171 °C (EtOH)

¹H NMR: (500 MHz, *d*₆-acetone)

δ 7.26 (d, *J* = 8.6 Hz, 2 H, C(6)H), 7.20 (br s, 1 H, NH), 6.88 (d, *J* = 8.7 Hz, 2 H, C(7)H), 6.78 (br s, 1 H, NH), 3.86 (dd, *J* = 8.5, 6.6 Hz, 1 H, C(2)H), 3.78 (s, 3 H, C(9)H₃), 3.20 (dd, *J* = 13.8, 6.6 Hz, 1 H, C(4)H), 3.08 (dd, *J* = 13.8, 8.5 Hz, 1 H, C(4)H')

¹³C NMR: (126 MHz, *d*₆-acetone)

δ 167.2 C(3), 159.9 C(8), 131.1 C(6), 129.7 C(5), 118.8, C(1) 114.7 C(7), 55.5 C(9), 41.0 C(2), 35.9 C(4)

IR: (neat)

3397 (m), 3321 (w), 3274 (w), 3210 (w), 3042 (w), 2942 (w), 2843 (w), 2252 (w), 1669 (s), 1611 (m), 1584 (w), 1514 (s), 1455 (w), 1406 (m), 1325 (w), 1304 (m), 1240 (s), 1173 (m), 1119 (w), 1027 (s), 895 (w), 825 (s), 815 (m), 736 (w)

HRMS: (EI)

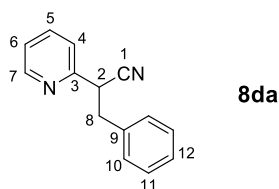
m/z: [M]⁺ Calcd for C₁₁H₁₂N₂O₂: 204.0899; Found: 204.0899

Analysis: C₁₁H₁₂N₂O₂

Calcd: C, 64.69; H, 5.92; N, 13.72

Found: C, 64.39; H, 5.93; N, 13.61

3-Phenyl-2-(pyridin-2-yl)propanenitrile (8da)



Following General Procedure VII, RhCl₃·3H₂O (15.8 mg, 0.06 mmol, 3 mol %), CH₃CN (1.0 mL), 2-pyridylacetonitrile (0.223 mL, 2.0 mmol), benzaldehyde (0.214 mL, 2.1 mmol, 1.05 equiv), H₂O (1.80 mL, 100.0 mmol, 50.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The

reaction was stirred at room temperature for 72 h followed by standard workup. Purification by silica gel column chromatography (CH₂Cl₂/EtOAc, 80:20), followed by recrystallization (hexane/Et₂O 90:10), afforded **8da** (283 mg, 68%) as a white, crystalline solid. The spectral data matched those previously reported in the literature.¹⁰

Data for **8da**:

mp: 62-64 °C (hexane/Et₂O, 90:10)

¹H NMR: (500 MHz, CDCl₃)

δ 8.64 (d, *J* = 4.6 Hz, 1 H, C(7)H), 7.67 (td, *J* = 7.7, 1.5 Hz, 1 H, C(5)H), 7.32 – 7.26 (m, 5 H, C(4)H, C(6)H, C(11)H, C(12)H), 7.17 (d, *J* = 6.7 Hz, 2 H, C(10)H), 4.21 (dd, *J* = 8.6, 5.9 Hz, 1 H, C(2)H), 3.37 (dd, *J* = 13.6, 5.8 Hz, 1 H, C(8)H), 3.26 (dd, *J* = 13.6, 8.7 Hz, 1 H, C(8)H')

¹³C NMR: (126 MHz, CDCl₃)

δ 154.5 C(3), 150.0 C(7), 137.2 C(5), 136.2 C(9), 129.2 C(10), 128.6 C(11), 127.4, 123.1, 122.2, 119.6 C(1), 42.0 C(2), 40.0 C(8)

HRMS: (ESI)

m/z: [MH]⁺ Calcd for C₁₄H₁₃N₂: 209.1079; Found: 209.1086

TLC: *R_f* 0.50 (CH₂Cl₂/Et₂O, 80:20) [silica gel, UV, iodine]

Table 8, entry 4

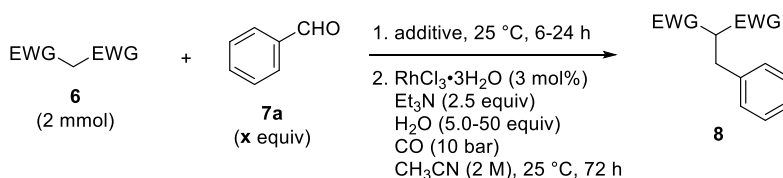
Following General Procedure VII, RhCl₃·3H₂O (15.8 mg, 0.06 mmol, 3 mol %), CH₃CN (4.0 mL), malononitrile (132 mg, 2.0 mmol), benzaldehyde (0.214 mL, 2.1 mmol, 1.05 equiv), H₂O (0.900 mL, 25.0 mmol, 25.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 72 h followed by standard workup. The conversion to **8ea** was determined to be 54% by analysis of the crude reaction mixture by ¹H NMR (based on mesitylene (0.096 mL, 0.5 mmol) as the standard).

Table 8, entry 5

Following General Procedure VII, RhCl₃·3H₂O (15.8 mg, 0.06 mmol, 3 mol %), CH₃CN (4.0 mL), N, N dimethylbarbituric acid (312 mg, 2.0 mmol), benzaldehyde (0.214 mL, 2.1 mmol, 1.05 equiv), H₂O (0.900 mL, 25.0 mmol, 25.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv)

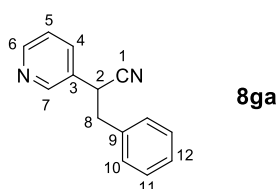
were sequentially added to a 40-mL vial which was then placed in an autoclave and pressurized. The reaction was stirred at room temperature for 24 h followed by standard workup. The conversion to **8fa** was determined to be 23% by analysis of the crude reaction mixture by ¹H NMR (based on mesitylene (0.096 mL, 0.5 mmol) as the standard).

General Procedure VIII: Reaction of Other Active Methylene Compounds with Benzaldehyde in Two Steps (Table 9)



1,5-Diazabicyclo[4.3.0]non-5-ene (DBN) or L-proline was added to a 40-mL glass vial, followed by the active methylene compound **6**, benzaldehyde **7a**, deionized water, and triethylamine, and the reaction mixture was stirred using a stir bar for the specified length of time. $\text{RhCl}_3\cdot 3\text{H}_2\text{O}$ was added to the glass vial, followed by acetonitrile, additional deionized water, and triethylamine. The vial was placed in an autoclave. The autoclave was pressurized with CO and vented three times, and then pressurized to 10 bar. The reaction was stirred at room temperature for the indicated time. After venting and purging the autoclave with nitrogen, the vial was removed. The volatiles were removed by rotary evaporation (25-30 °C, 15 mmHg), the residue was dissolved in CH_2Cl_2 , and loaded on silica gel (1 g). The crude mixture was purified by silica gel column chromatography (2.5 x 20-25 cm), followed by distillation or recrystallization.

3-Phenyl-2-(pyridin-3-yl)propanenitrile (**8ga**)



Following General Procedure VIII, 3-pyridylacetonitrile (0.212 mL, 2.0 mmol), benzaldehyde (0.214 mL, 2.1 mmol, 1.05 equiv), and DBN (0.012 mL, 0.1 mmol, 0.05 equiv) were sequentially added to a 40-mL vial and the reaction was stirred at room temperature for 6 h under air. $\text{RhCl}_3\cdot 3\text{H}_2\text{O}$ (15.8 mg, 0.06 mmol, 3 mol %), CH_3CN (1.0 mL), H_2O (1.80 mL, 100.0 mmol, 50.0 equiv), and Et_3N (0.70 mL, 5.0 mmol, 2.5 equiv) were added to the vial and the vial was transferred to an autoclave where the reaction was stirred at room temperature for 72 h under CO followed by standard workup. Purification by silica gel column chromatography

(CH₂Cl₂/EtOAc, 90:10), followed by recrystallization (hexane/benzene, 90:10), afforded **8ga** (325 mg, 78%) as a white, crystalline solid. The spectral data matched those previously reported in the literature.¹⁰

Data for 8ga:

mp: 60-61 °C (hexane/benzene, 90:10)

¹H NMR: (500 MHz, CDCl₃)

δ 8.58 (dd, *J* = 4.8, 1.4 Hz, 1 H, C(6)H), 8.46 (d, *J* = 2.1 Hz, 1 H, C(7)H), 7.61 – 7.55 (m, 1 H, C(4)H), 7.34 – 7.27 (m, 4 H, C(5)H, C(11)H, C(12)H), 7.10 (dd, *J* = 7.4, 1.6 Hz, 2 H, C(10)H), 4.11 – 4.01 (m, 1 H, C(2)H), 3.23 (dd, *J* = 13.6, 7.9 Hz, 1 H, C(8)H), 3.14 (dd, *J* = 13.6, 6.7 Hz, 1 H, C(8)H')

¹³C NMR: (126 MHz, CDCl₃)

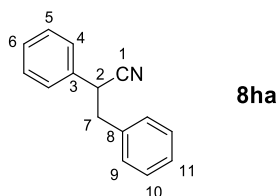
δ 149.6 C(6), 148.8 C(7), 135.2 C(9), 134.9 C(4), 130.9 C(3), 129.1 C(10), 128.7 C(11), 127.6 C(12), 123.6 C(5), 119.3 C(1), 41.7 C(8), 37.1 C(2)

HRMS: ESI

m/z: [MH]⁺ Calcd for C₁₄H₁₃N₂: 209.1079; Found: 209.1081

TLC: *R_f* 0.21 (CH₂Cl₂/EtOAc, 90:10) [silica gel, UV, iodine]

2,3-Diphenylpropanenitrile (8ha)



Following General Procedure VIII, phenylacetonitrile (0.231 mL, 2.0 mmol), benzaldehyde (0.214 mL, 2.1 mmol, 1.05 equiv), and DBN (0.012 mL, 0.1 mmol, 0.05 equiv) were sequentially added to a 40-mL vial and the reaction was stirred at room temperature for 6 h under air. RhCl₃·3H₂O (15.8 mg, 0.06 mmol, 3 mol %), CH₃CN (1.0 mL), H₂O (1.80 mL, 100.0 mmol, 50.0 equiv), and Et₃N (0.70 mL, 5.0 mmol, 2.5 equiv) were added to the vial and the vial was transferred to an autoclave where the reaction was stirred at room temperature for 72 h under CO followed by standard workup. Purification by silica gel column chromatography (pentane/CH₂Cl₂ 70:30), followed by recrystallization (pentane/CH₂Cl₂, 95:5), afforded **8ha** (261

mg, 63%) as a white, crystalline solid. The spectral data matched those previously reported in the literature.¹⁰

Data for **8ha:**

mp: 56-57 °C (pentane/CH₂Cl₂, 95:5)

¹H NMR: (500 MHz, CDCl₃)

δ 7.39 – 7.25 (m, 8H), 7.17 – 7.12 (m, 2 H), 4.00 (dd, *J* = 8.4, 6.4 Hz, 1 H, C(2)H), 3.20 (dd, *J* = 13.6, 8.4 Hz, 1 H, C(7)H), 3.14 (dd, *J* = 13.6, 6.4 Hz, 1 H, C(7)H')

¹³C NMR: (126 MHz, CDCl₃)

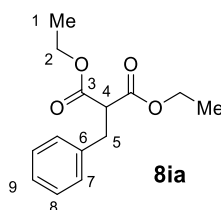
δ 136.3, 135.2, 129.2, 129.0, 128.6, 128.9, 127.5, 127.4, 120.4 C(1), 42.2 C(7), 39.8 C(2)

HRMS: (EI)

m/z: [M]⁺ Calcd for C₁₅H₁₃N: 207.1048; Found: 207.1055

TLC: *R_f* 0.21 (pentane/CH₂Cl₂, 70:30) [silica gel, UV, iodine]

Diethyl 2-Benzylmalonate (8ia**)**



Following General Procedure VIII, diethyl malonate (0.304 mL, 2.0 mmol), benzaldehyde (0.408 mL, 4 mmol, 2 equiv), L-proline (23 mg, 0.2 mmol, 0.1 equiv), H₂O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et₃N (0.28 mL, 2.0 mmol, 1 equiv) were sequentially added to a 40-mL vial and the reaction was stirred at room temperature for 24 h under air. RhCl₃·3H₂O (15.8 mg, 0.06 mmol, 3 mol %), CH₃CN (1.0 mL), and additional Et₃N (0.42 mL, 3.0 mmol, 1.5 equiv) were added to the vial and the vial was transferred to an autoclave where the reaction was stirred at room temperature for 48 h under CO followed by standard workup. Purification by silica gel column chromatography (pentane/Et₂O, 90:10), followed by Kugelrohr distillation, afforded **8ia** (353 mg, 70%) as a colorless oil. The spectral data matched those previously reported in the literature.¹¹

Data for 8ia:

bp: 168 °C (ABT, 0.5 mmHg)

¹H NMR: (500 MHz, CDCl₃)

δ 7.30 – 7.24 (m, 2 H, C(8)H), 7.24 – 7.18 (m, 3 H, C(7)H, C(9)H), 4.23 – 4.09 (m, 4 H, C(2)H₂), 3.65 (t, *J* = 7.9 Hz, 1 H, C(4)H), 3.22 (d, *J* = 7.9 Hz, 2 H, C(5)H₂), 1.20 (t, *J* = 7.2 Hz, 6H, C(1)H₃)

¹³C NMR: (126 MHz, CDCl₃)

δ 168.9 C(3), 137.9 C(6), 128.9 C(8), 128.5 C(7), 126.7 C(9), 61.4 C(2), 53.9 C(4), 34.7 C(5), 14.0 C(1)

HRMS: (EI)

m/z: [M]⁺ Calcd for C₁₄H₁₈O₄: 250.1205; Found: 250.1199

TLC: *R_f* 0.38 (pentane/Et₂O, 80:20) [silica gel, UV, iodine]

Table 9, entry 4

Following General Procedure VIII, ethyl benzoylacetate (0.346 mL, 2.0 mmol), benzaldehyde (0.407 mL, 4.0 mmol, 2.0 equiv), H₂O (0.180 mL, 10.0 mmol, 5.0 equiv), and Et₃N (0.280 mL, 2.0 mmol, 1.0 equiv) were sequentially added to a 40-mL vial and stirred under air for 24 h. RhCl₃·3H₂O (15.8 mg, 0.06 mmol, 3 mol %), CH₃CN (1.0 mL), and additional Et₃N (0.420 mL, 3.0 mmol, 1.5 equiv) were added and the reaction was stirred at room temperature for 48 h under CO followed by standard workup. The conversion to **8ja** was determined to be 33% by analysis of the crude reaction mixture by ¹H NMR (based on mesitylene (0.096 mL, 0.5 mmol) as the standard).

Deuterium Incorporation Experiment (Scheme 6)

In the glove box, $\text{Rh}_4(\text{CO})_{12}$ (3.7 mg, 0.005 mmol, 1.25 mol %) was added to a 10-mL glass vial. The vial was sealed and removed from the glove box. Acetonitrile (0.8 mL), the pre-formed Knoevenagel condensation adduct **9af** (93 mg, 0.4 mmol), D_2O (0.108 mL, 6.0 mmol, 15.0 equiv), and triethylamine (0.139 mL, 1.0 mmol, 2.5 equiv) were sequentially added to the vial. A stir bar was added, and the vial was placed in an autoclave. The autoclave was pressurized with CO and vented three times, and then pressurized to 10 bar. The reaction was stirred at room temperature for 24 h. After venting and purging the autoclave with nitrogen, the vial was removed. The volatiles were removed by rotary evaporation (25-30 °C, 15 mmHg), the residue was dissolved in CH_2Cl_2 , and filtered through a silica plug (eluting with CH_2Cl_2). Deuterium incorporation at C(3) was determined to be 92% by mass spectrometry analysis (ESI) of the filtrate.^{12,13}

Table S2. Calculations of deuterium incorporation in **8af(D)**.

		234 (M)	235	236	237
Non-D	nonD intensity	15203872	2910345	747420	899825
	nonD ratio	1.00	0.19	0.05	0.06
D	enriched intensity	6970923	31087942	5421365	2894631
	contribution of non-D	6970923	1334383	342689	412567
	intensity due to D	0	29753559	5078676	2482064
	% enrichment	0	96	94	86
	% average	92			

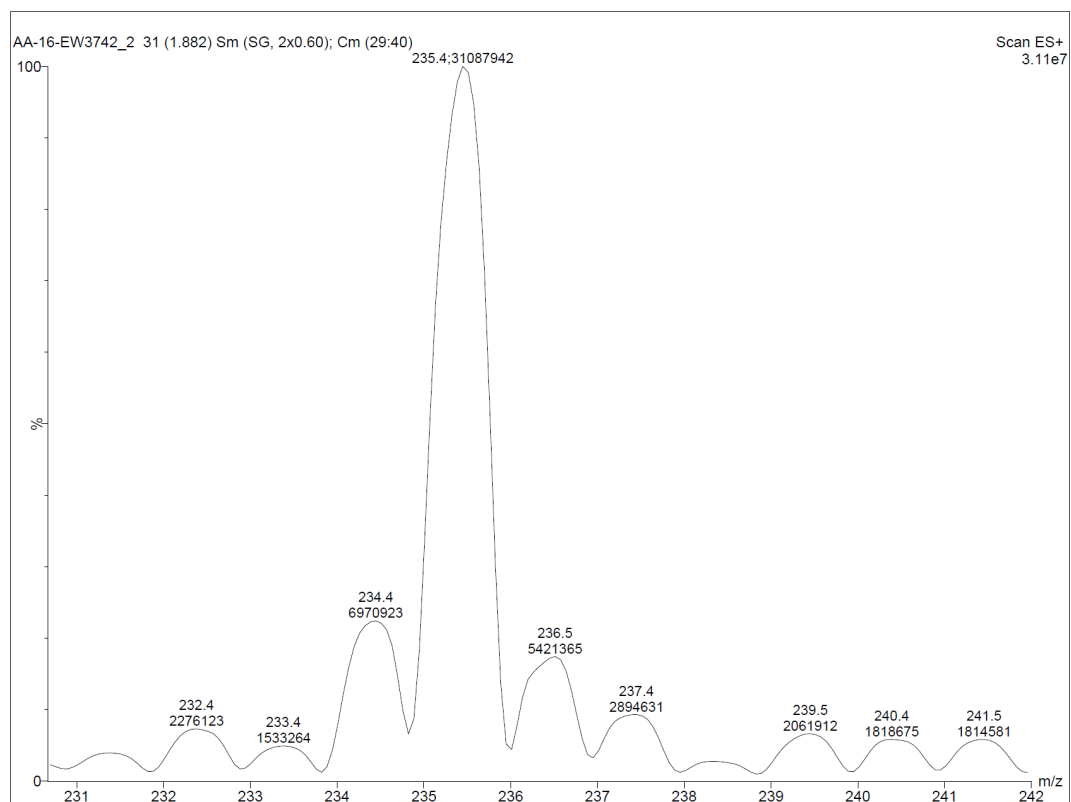
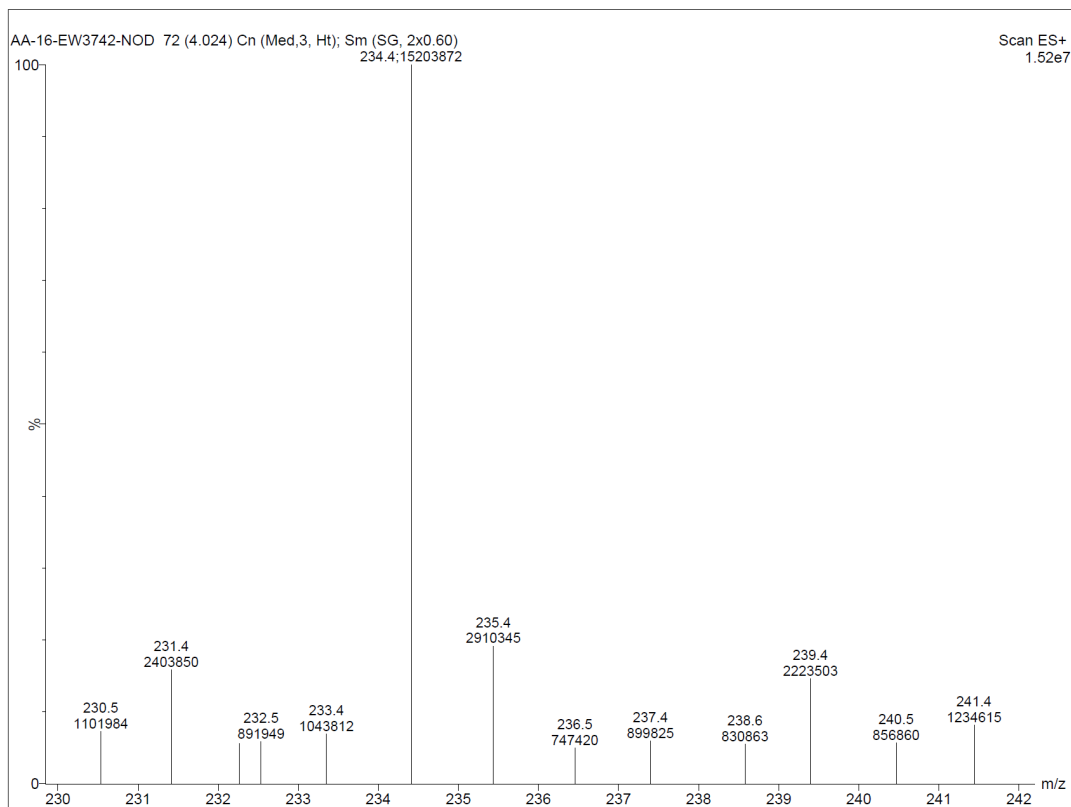
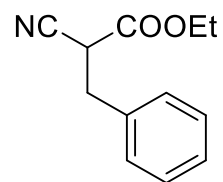
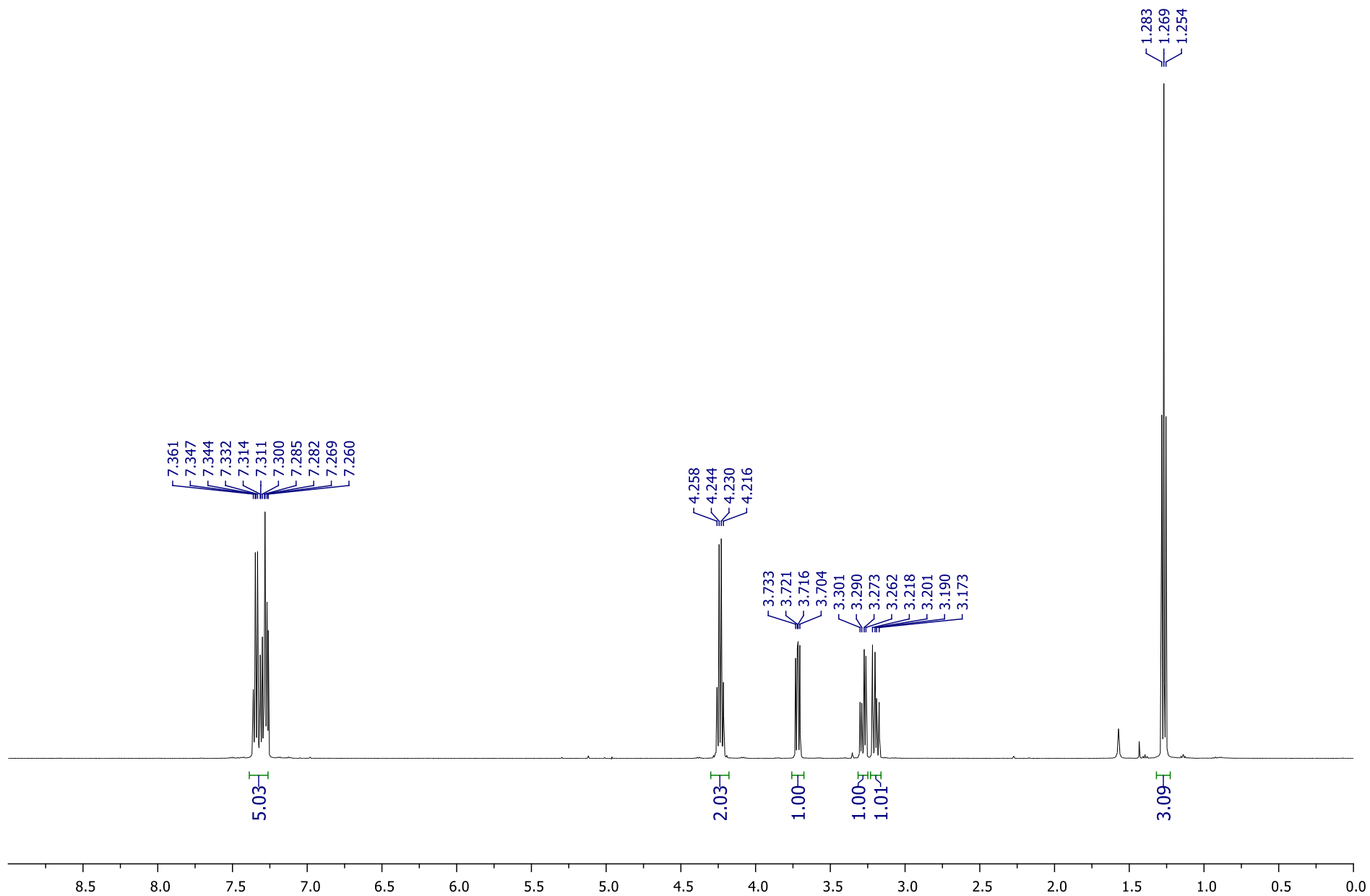
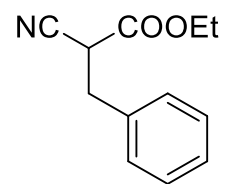
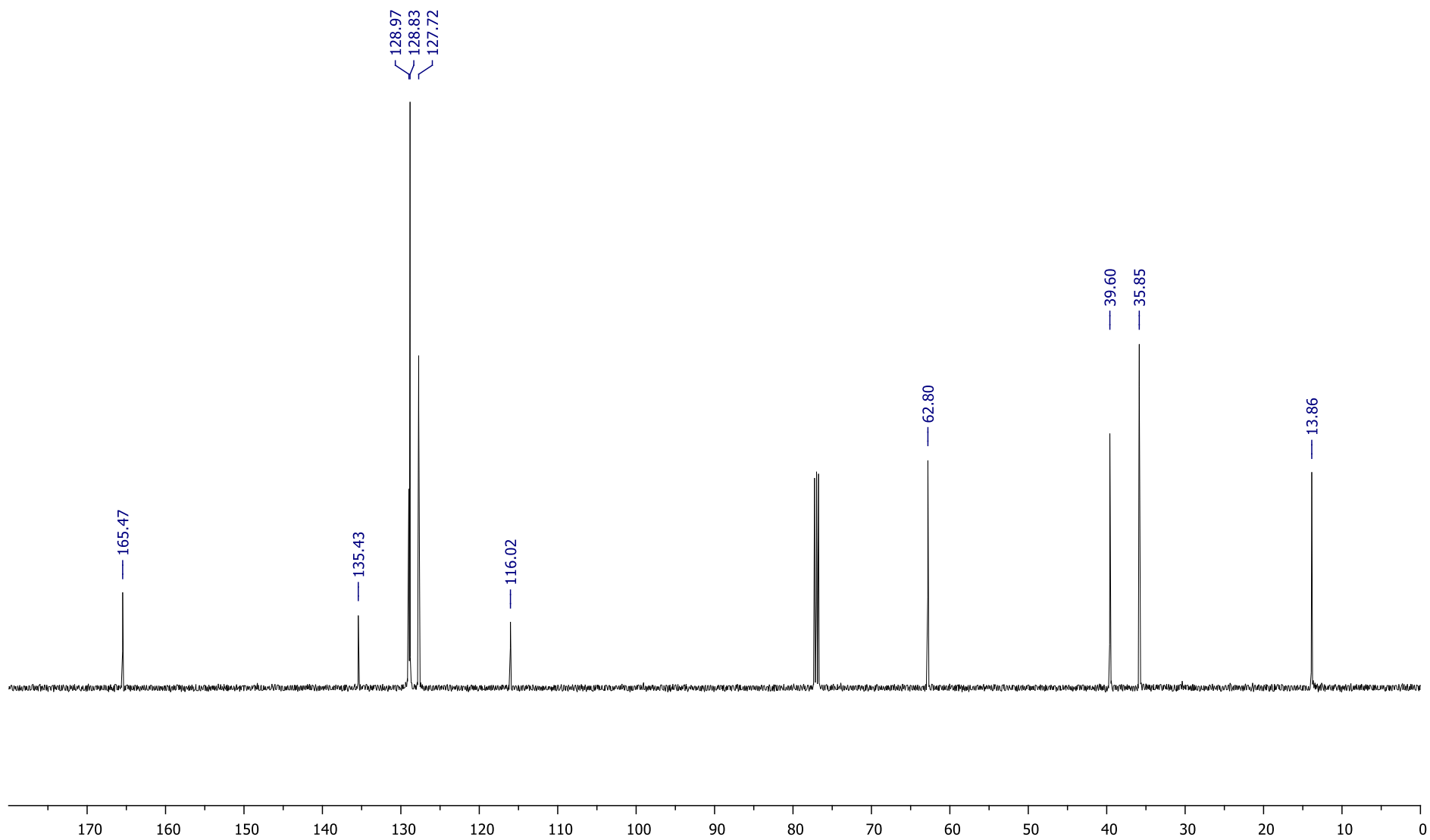


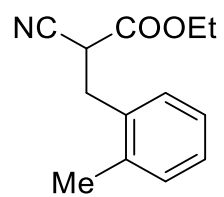
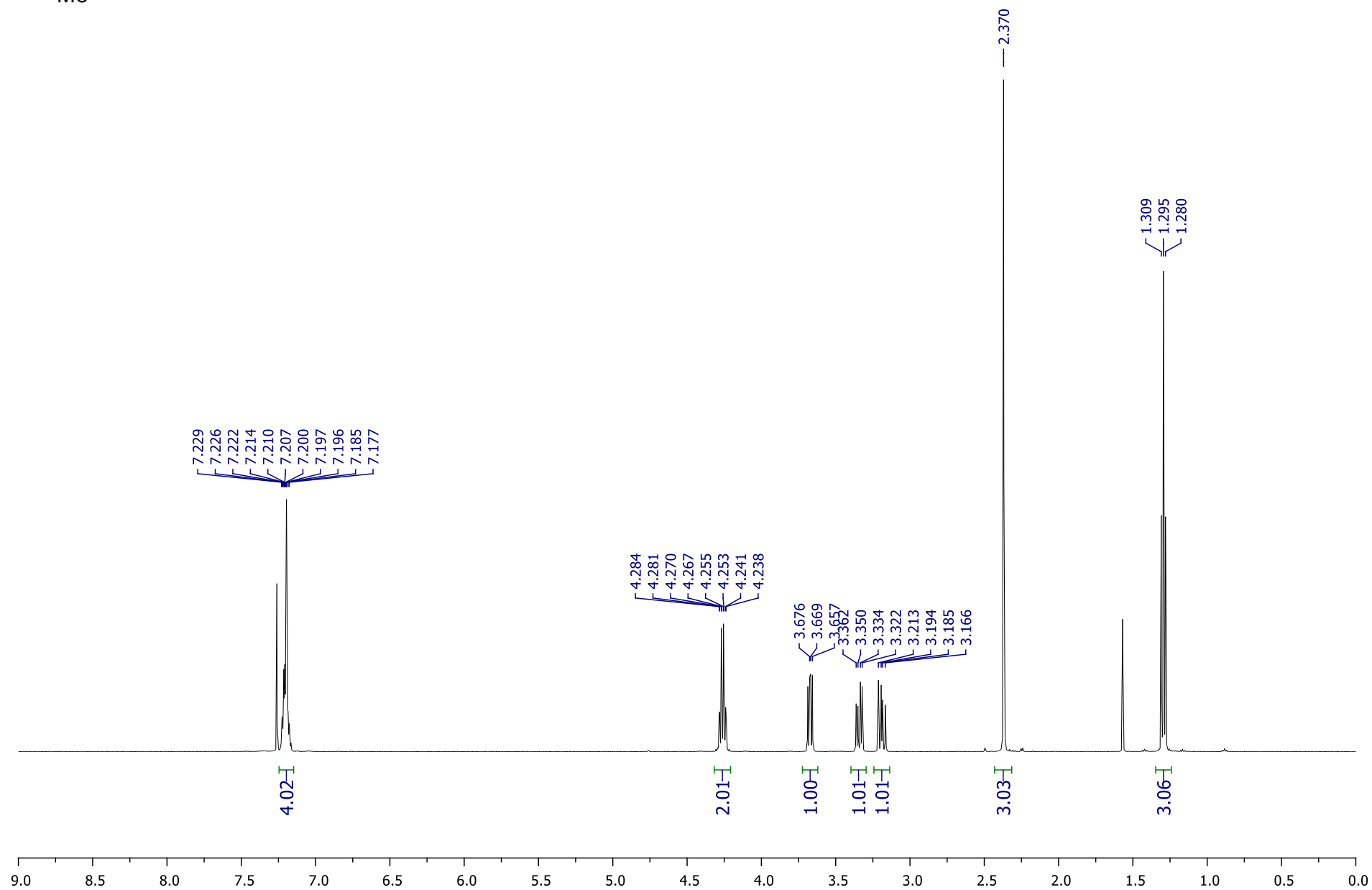
Figure S3. Mass-spec signal of $\delta af(D)$.

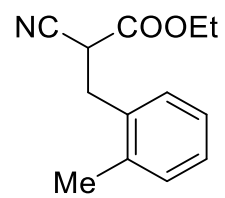
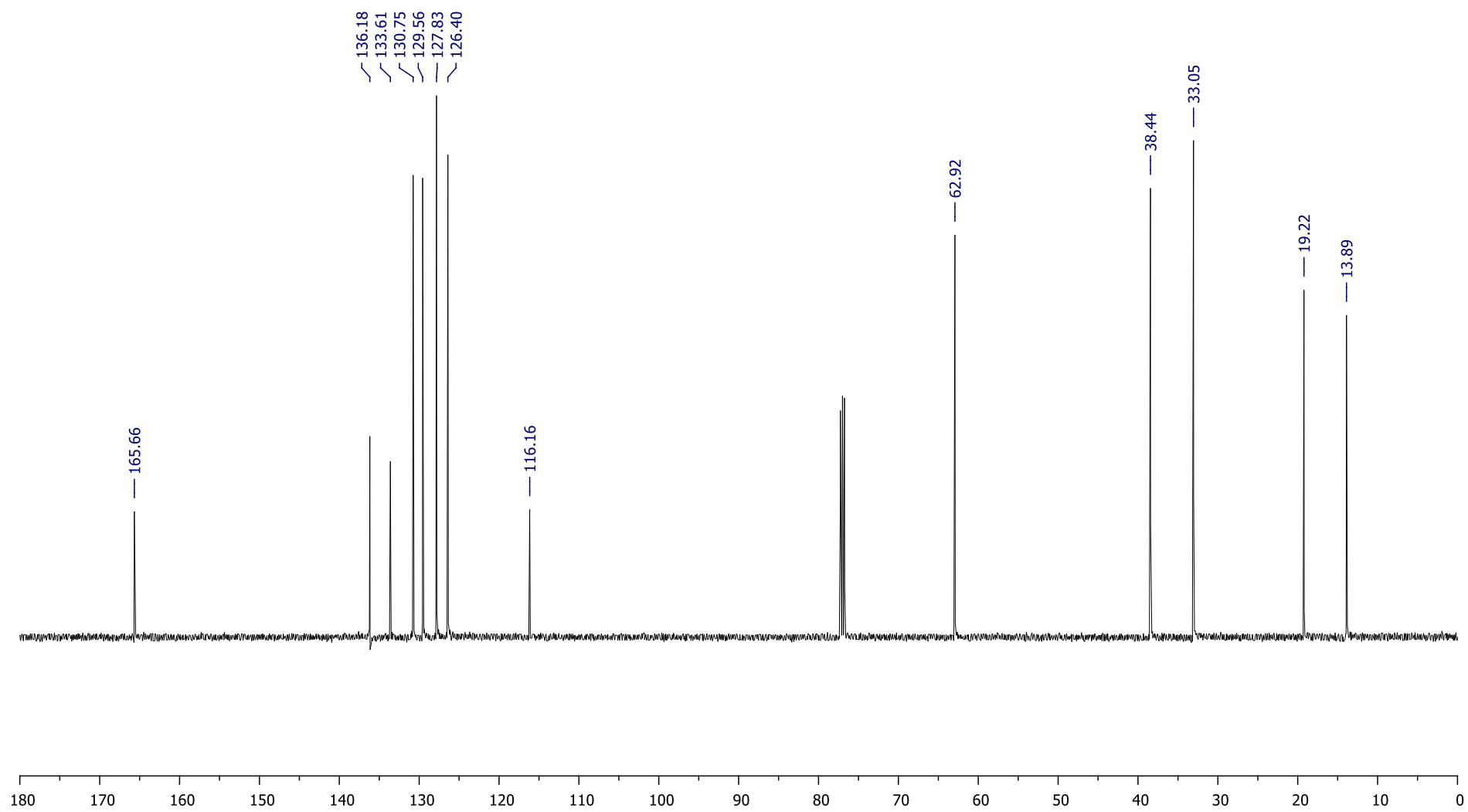
References

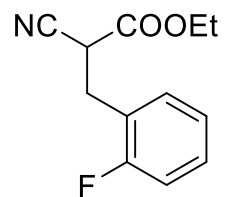
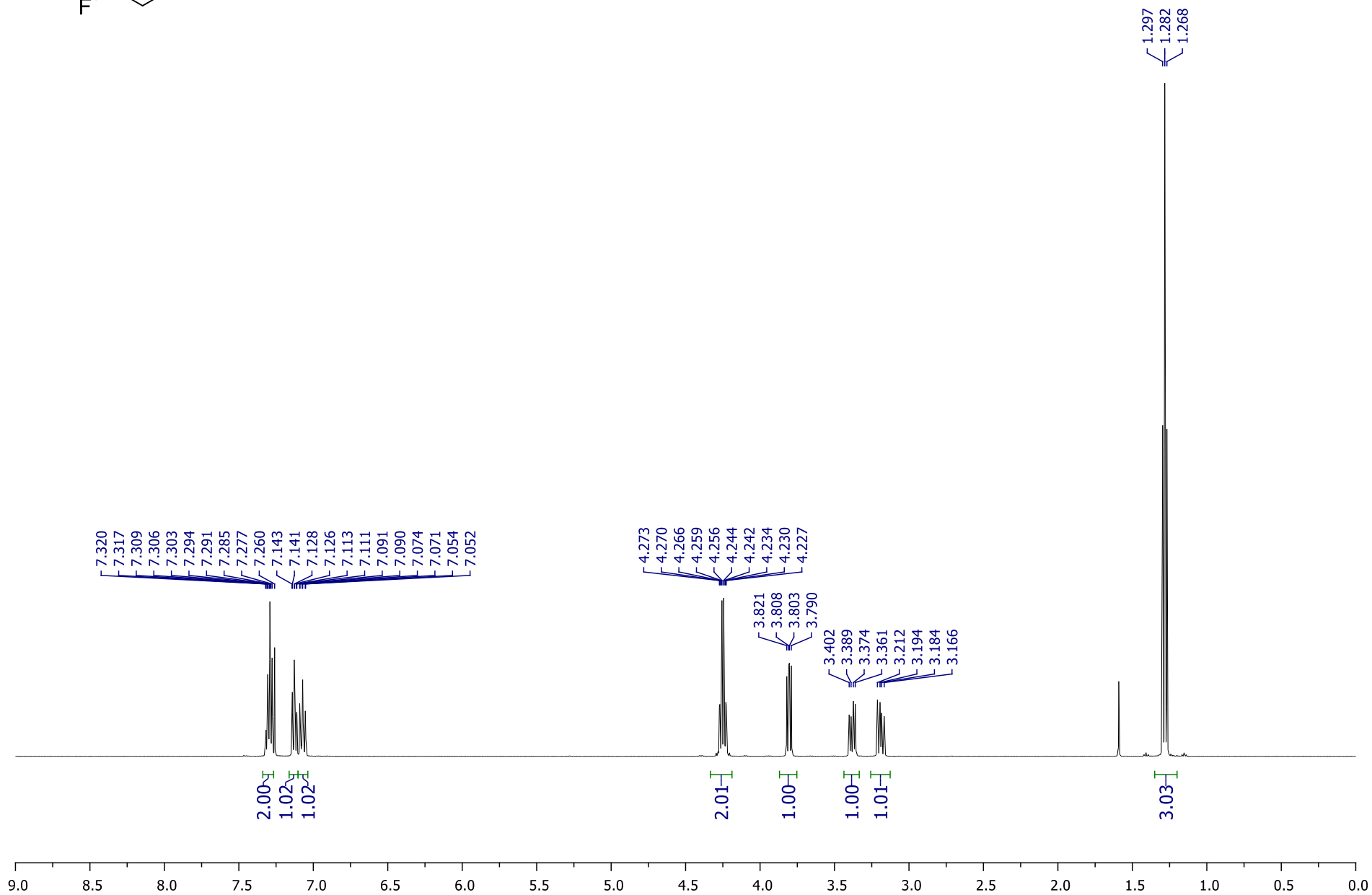
- (1) Yu, Y.-Q.; Wang, Z.-L. *J. Chin. Chem. Soc.* **2013**, *60*, 288-292.
- (2) Ying, A.-G.; Wu, C.-L.; He, G.-H. *Asian J. Chem.* **2012**, *24*, 653-656.
- (3) Gaspar, B.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2007**, *46*, 4519-4522.
- (4) Thorand, S.; Krause, N. *J. Org. Chem.* **1998**, *63*, 8551-8553.
- (5) Yu, B.; Qi, P.-P.; Shi, X.-J.; Huang, R.; Guo, H.; Zheng, Y.-C.; Yu, D.-Q.; Liu, H.-M. *Eur. J. Med. Chem.* **2016**, *117*, 241-255.
- (6) Mallia, C. J.; Englert, L.; Walter, G. C.; Baxendale, I. R. *Beilstein J. Org. Chem.* **2015**, *11*, 875-883.
- (7) Ramachary, D. B.; Reddy, G. B. *Org. Biomol. Chem.* **2006**, *4*, 4463-4468.
- (8) Ranu, B. C.; Samanta, S. *Tetrahedron* **2003**, *59*, 7901-7906.
- (9) Ramachary, D. B.; Kishor, M.; Reddy, Y. V. *Eur. J. Org. Chem.* **2008**, 975-993.
- (10) Löfberg, C.; Grigg, R.; Whittaker, M. A.; Keep, A.; Derrick, A. *J. Org. Chem.* **2006**, *71*, 8023-8027.
- (11) Doni, E.; Mondal, B.; O'Sullivan, S.; Tuttle, T.; Murphy, J. A. *J. Am. Chem. Soc.* **2013**, *135*, 10934-10937.
- (12) Deuterium incorporation was determined as described in Olsen, M. T.; Barton, B. E.; Rauchfuss, T. B. *Inorg. Chem.* **2009**, *48*, 7507-7509.
- (13) Previous control experiments had shown that, under similar reaction conditions, **9af** is completely reduced to **8af(D)**, and no deuterium incorporation is observed at C(2) (as determined by ¹H NMR analysis).

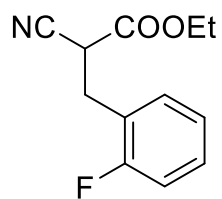
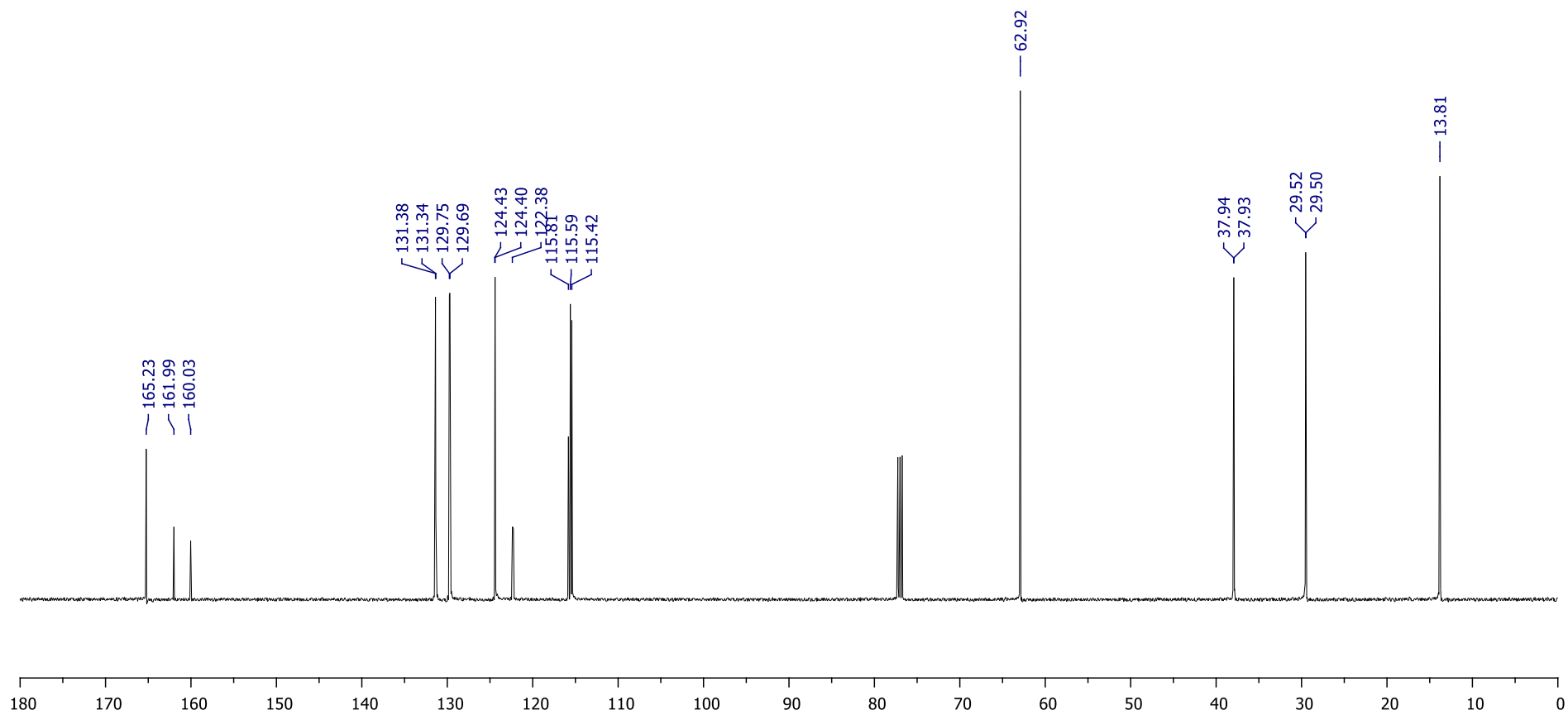
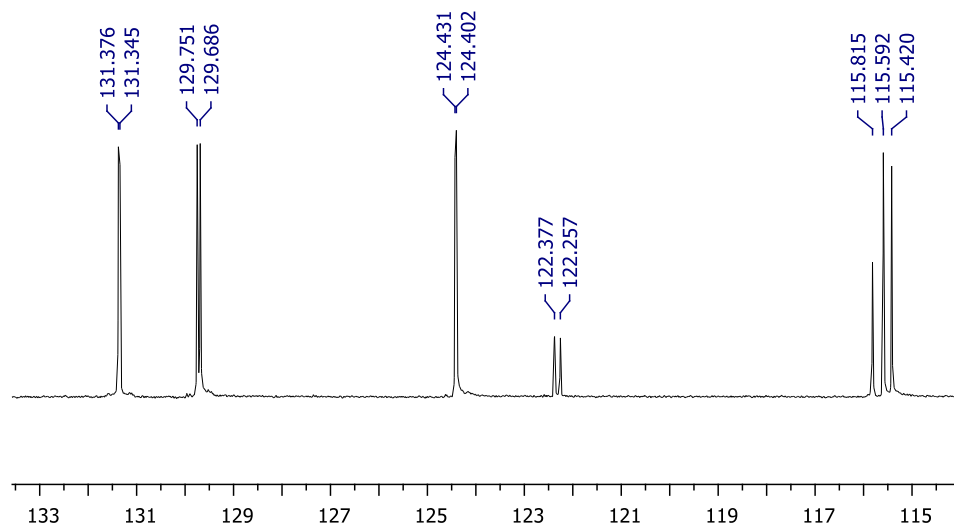
**8aa**

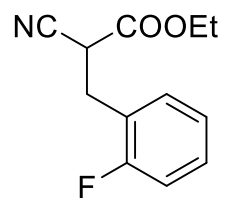
**8aa**

**8ab**

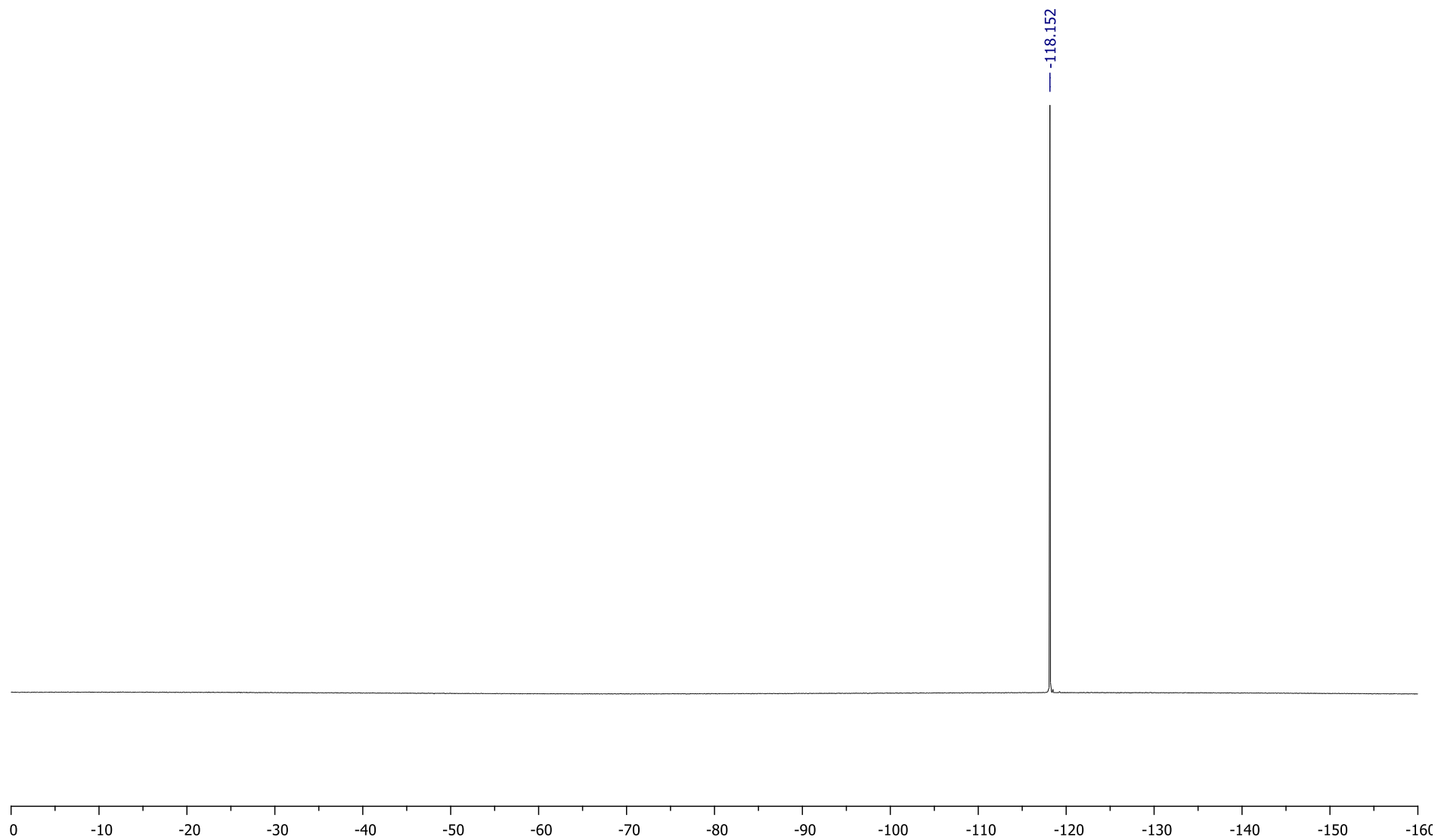
**8ab**

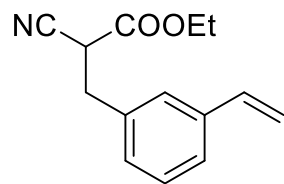
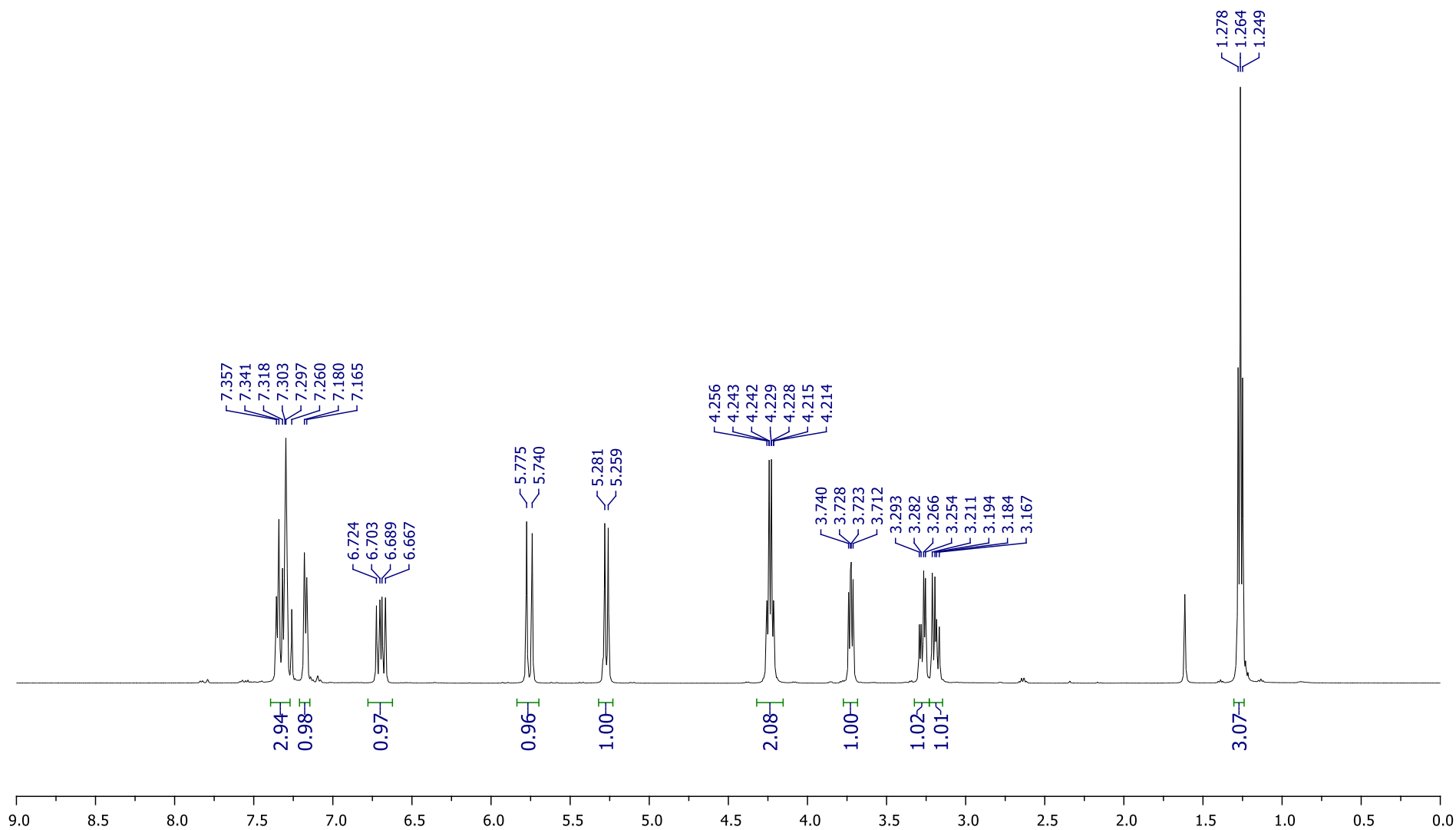
**8ac**

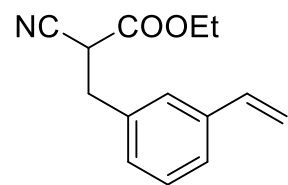
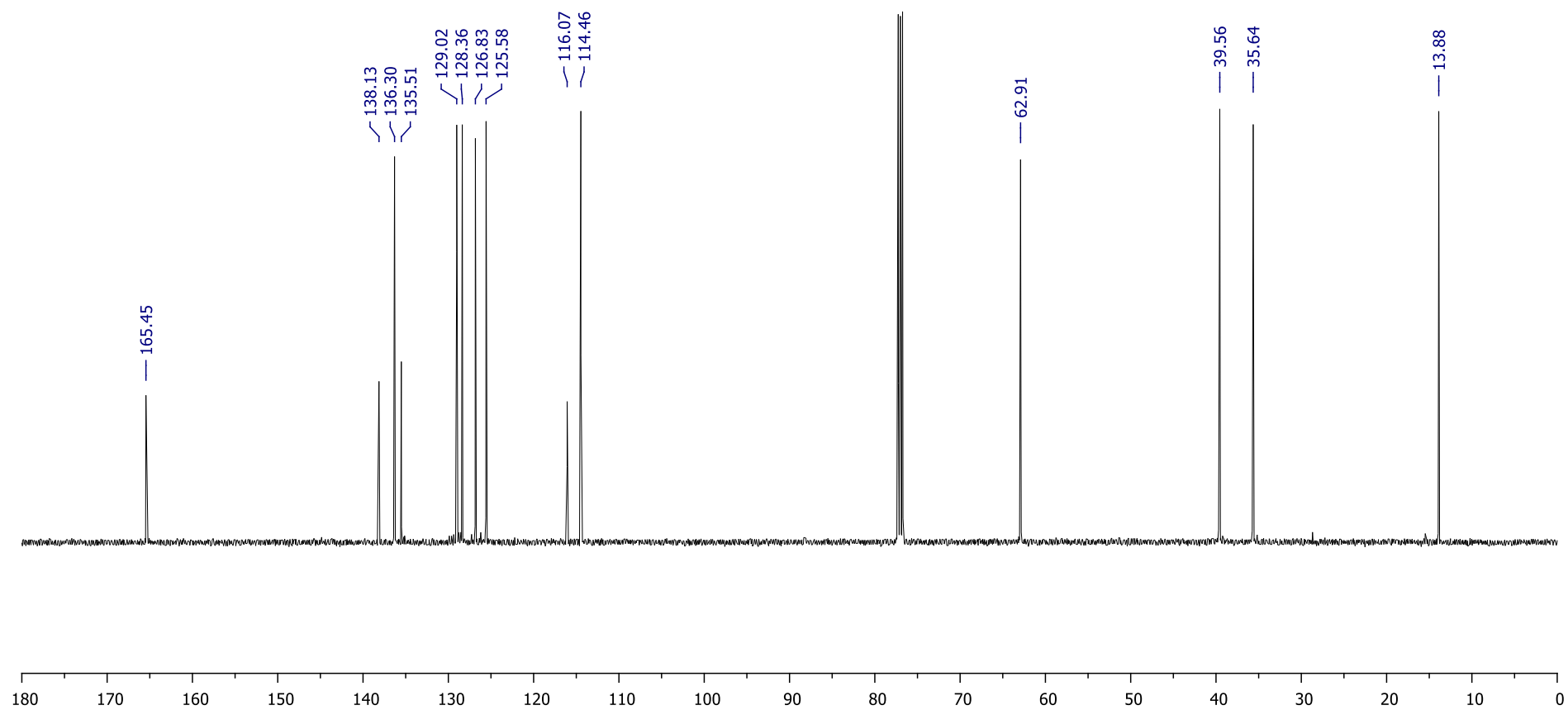
**8ac**

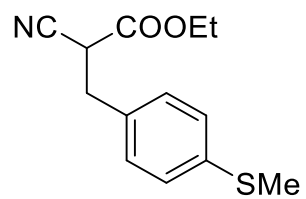
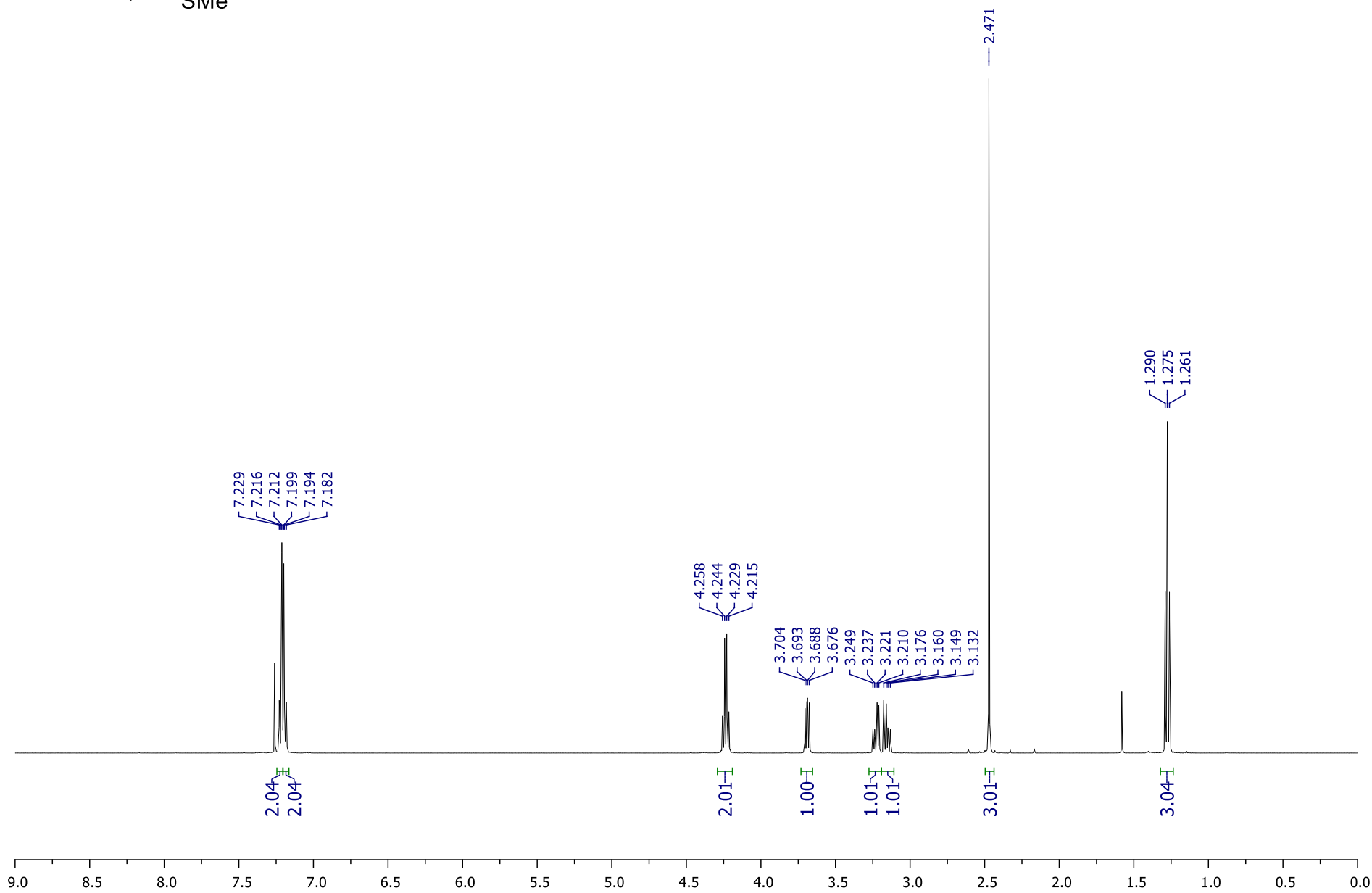


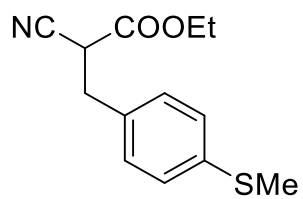
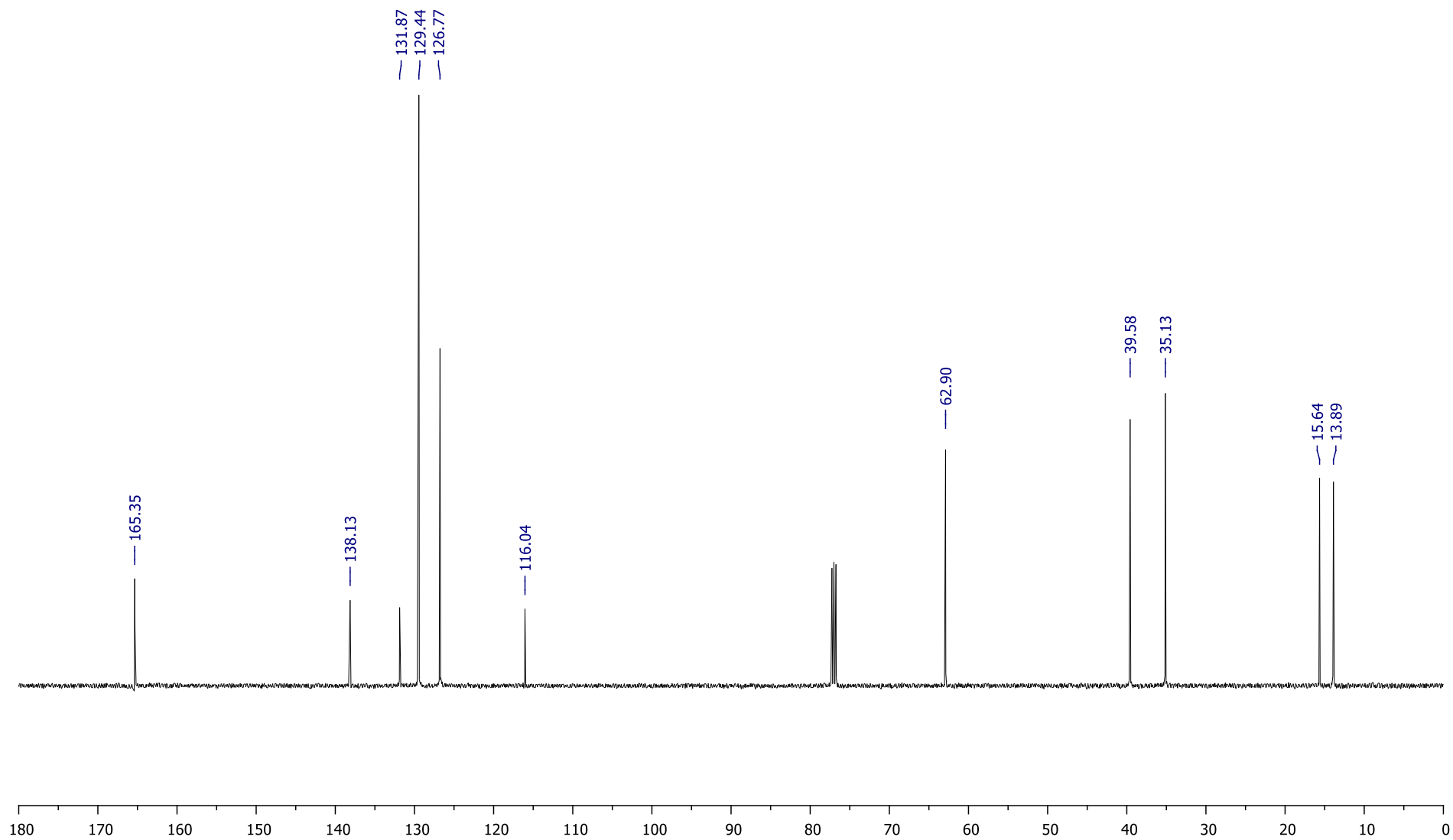
8ac

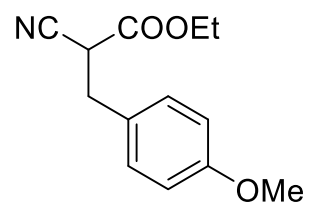
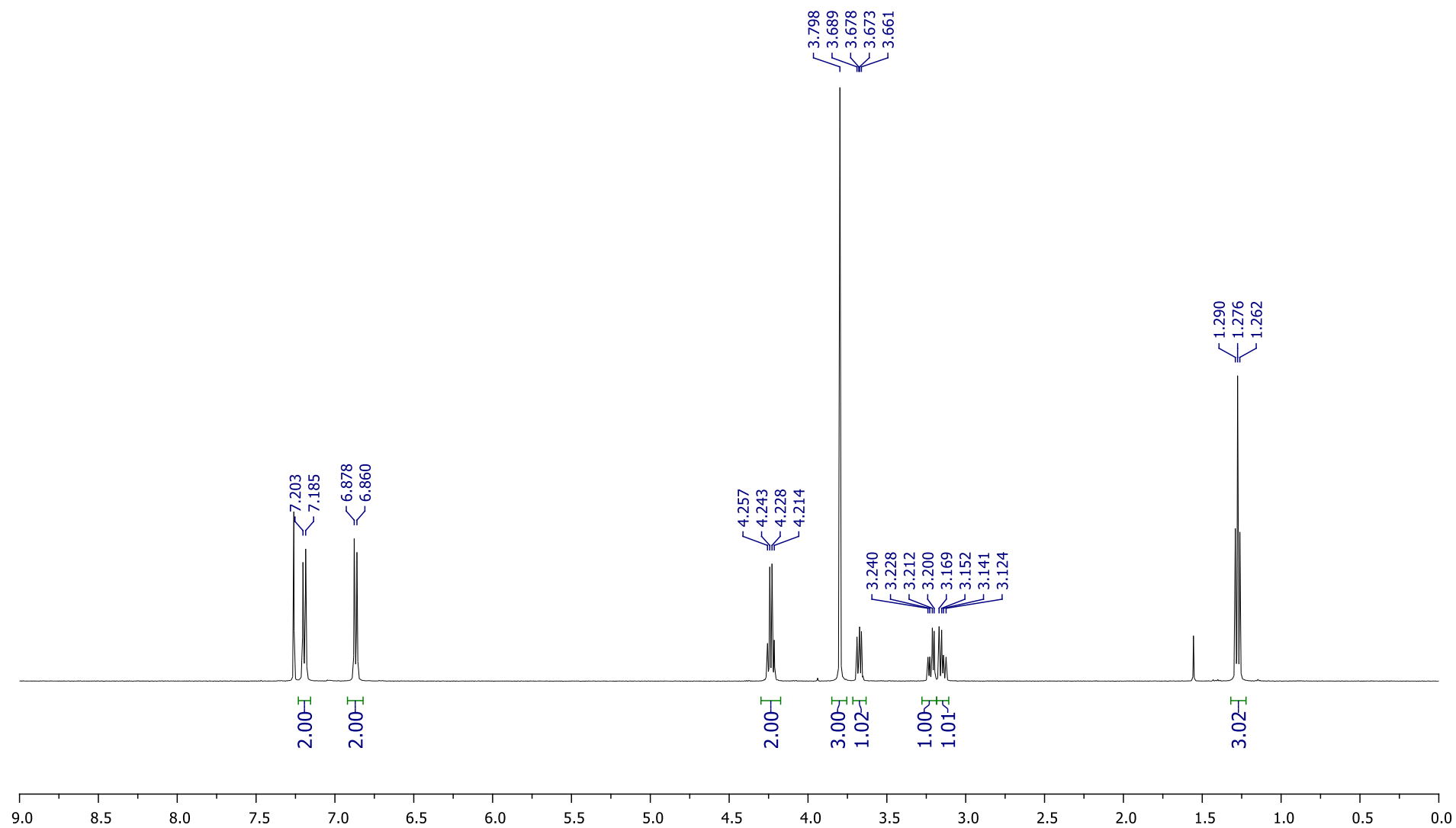


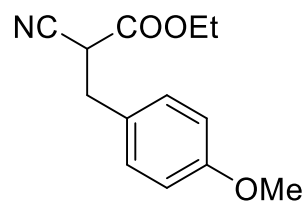
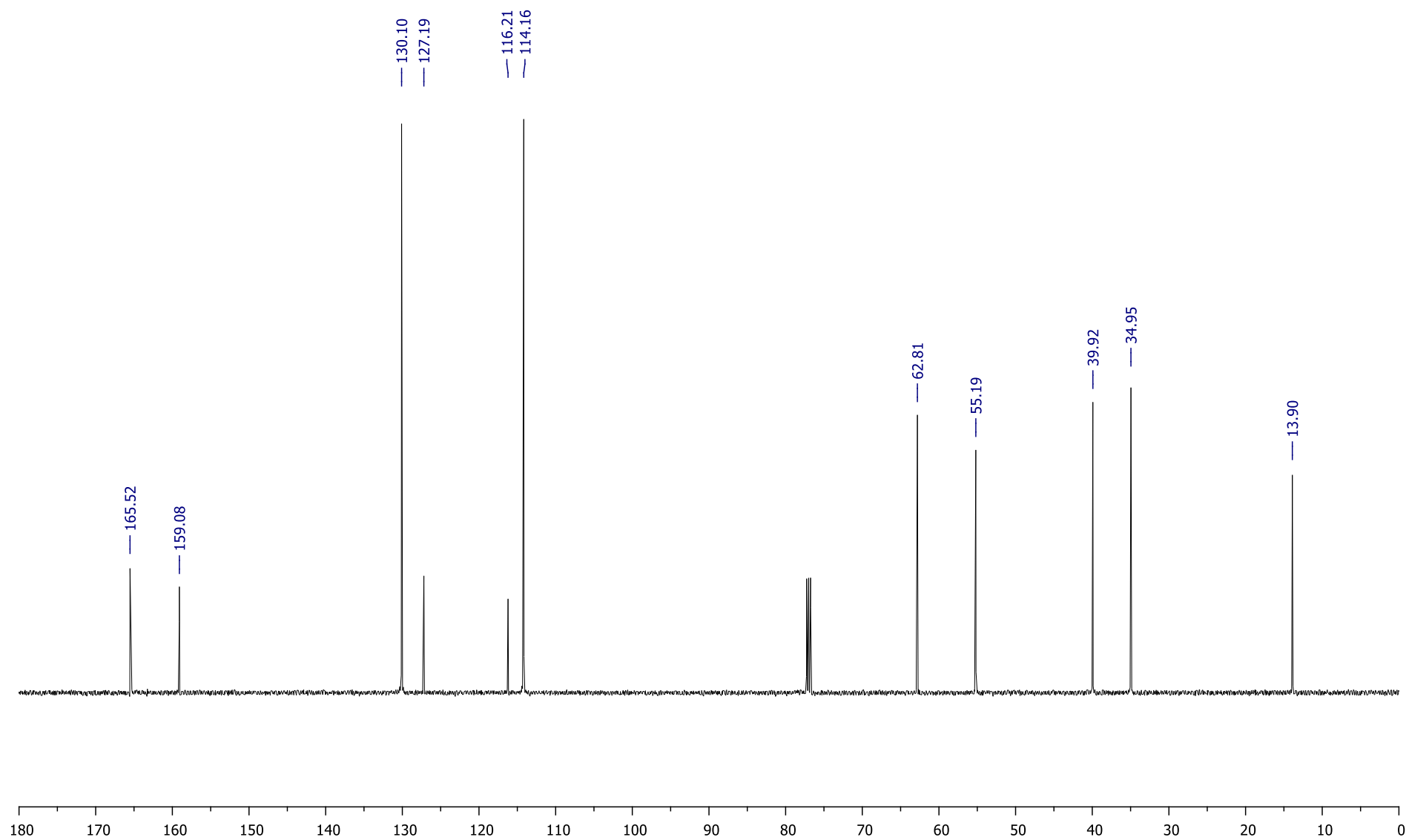
**8ad**

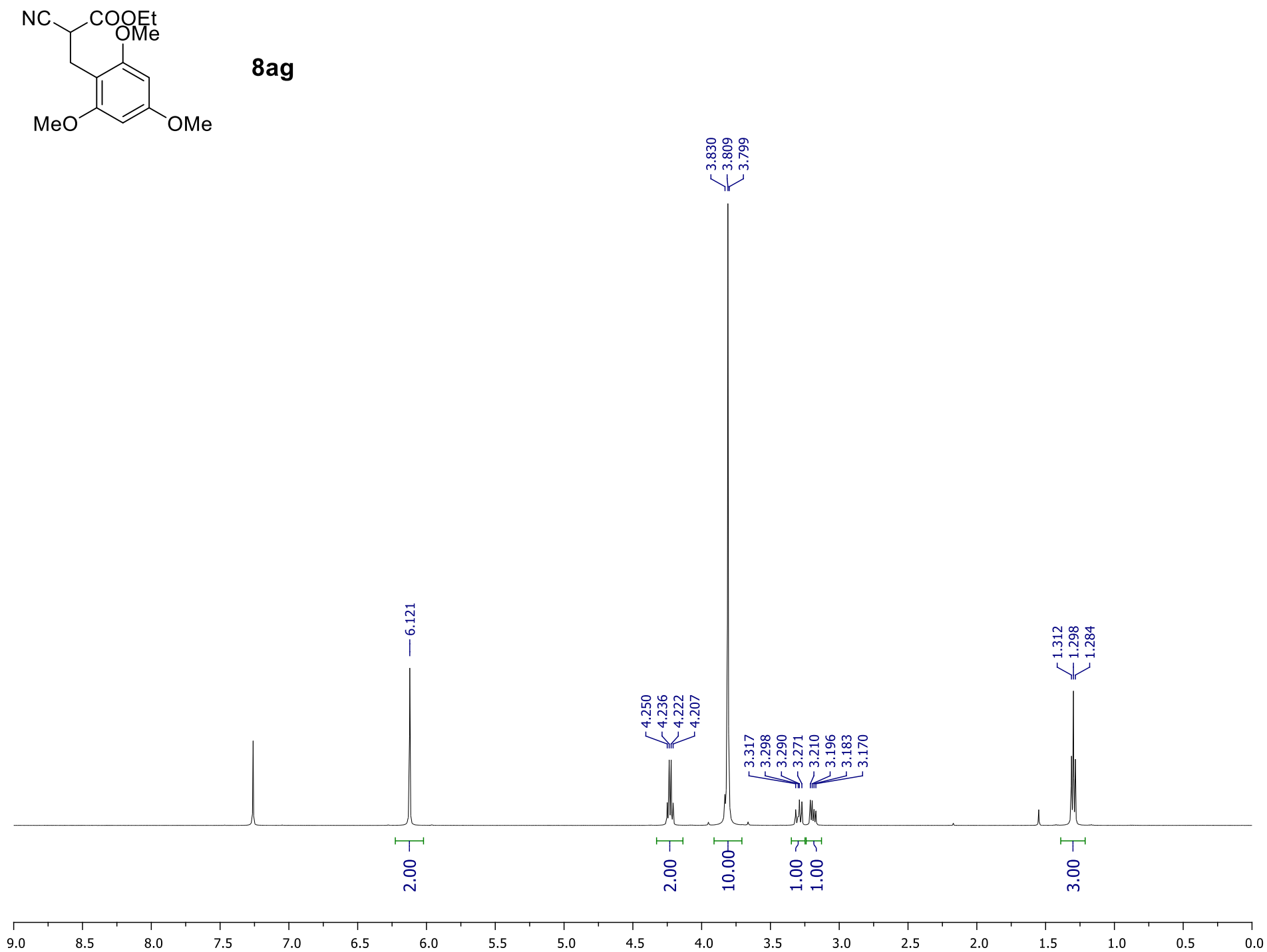
**8ad**

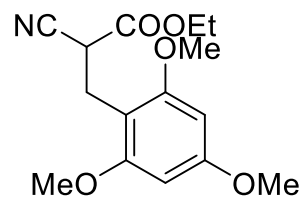
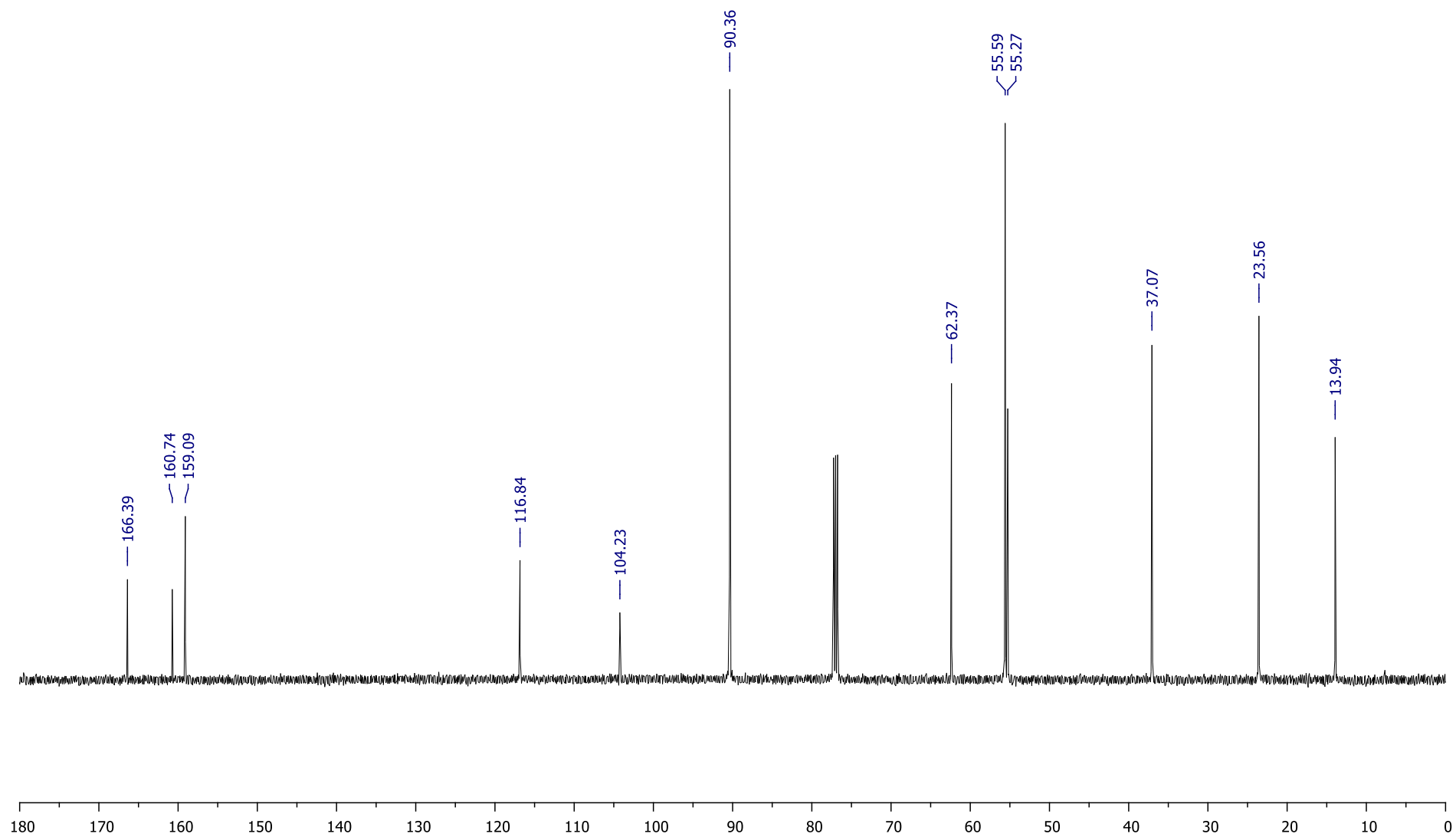
**8ae**

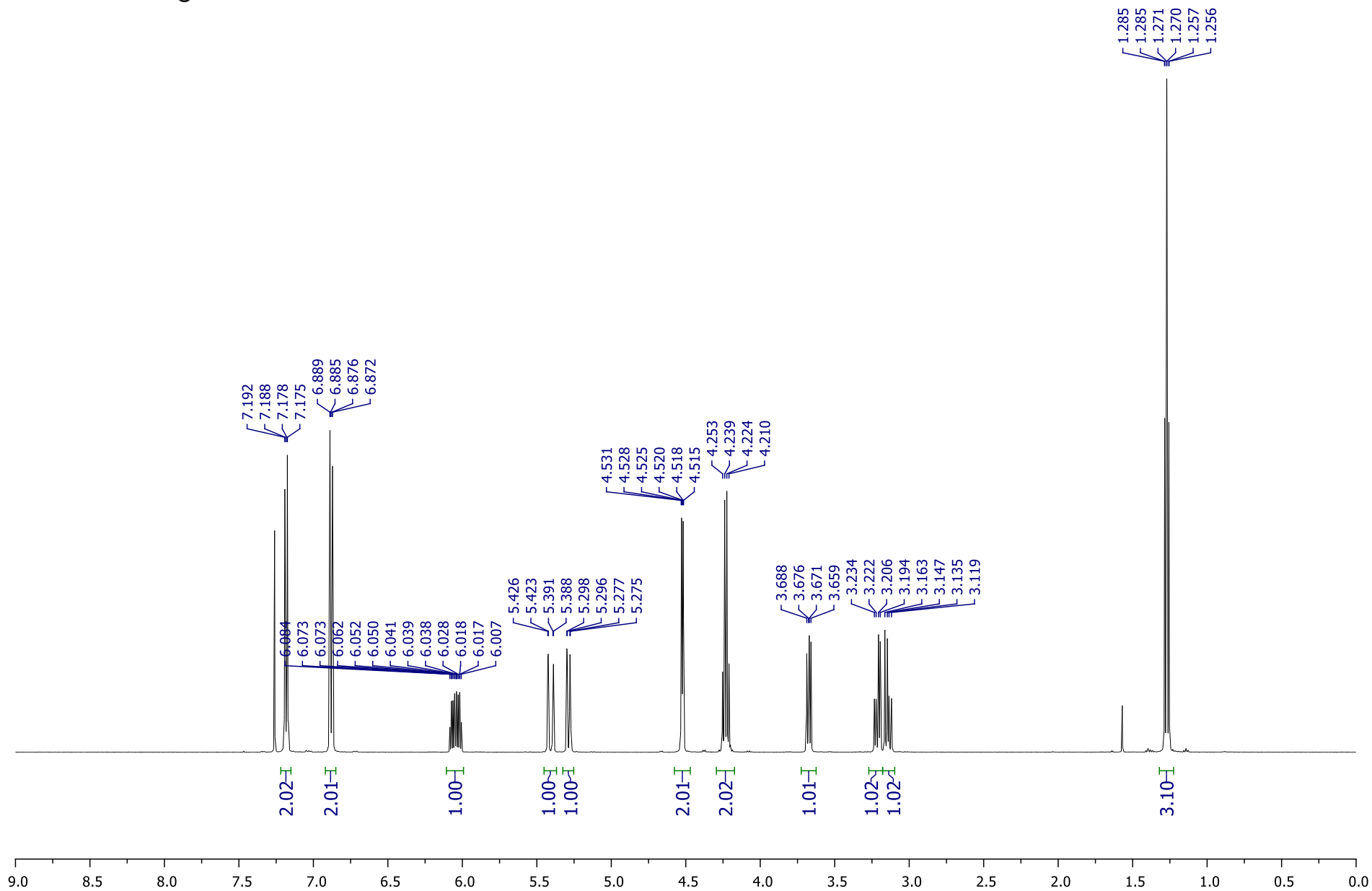
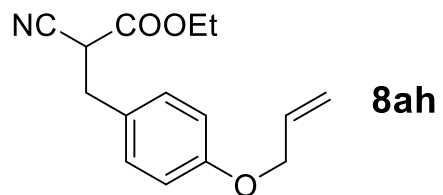
**8ae**

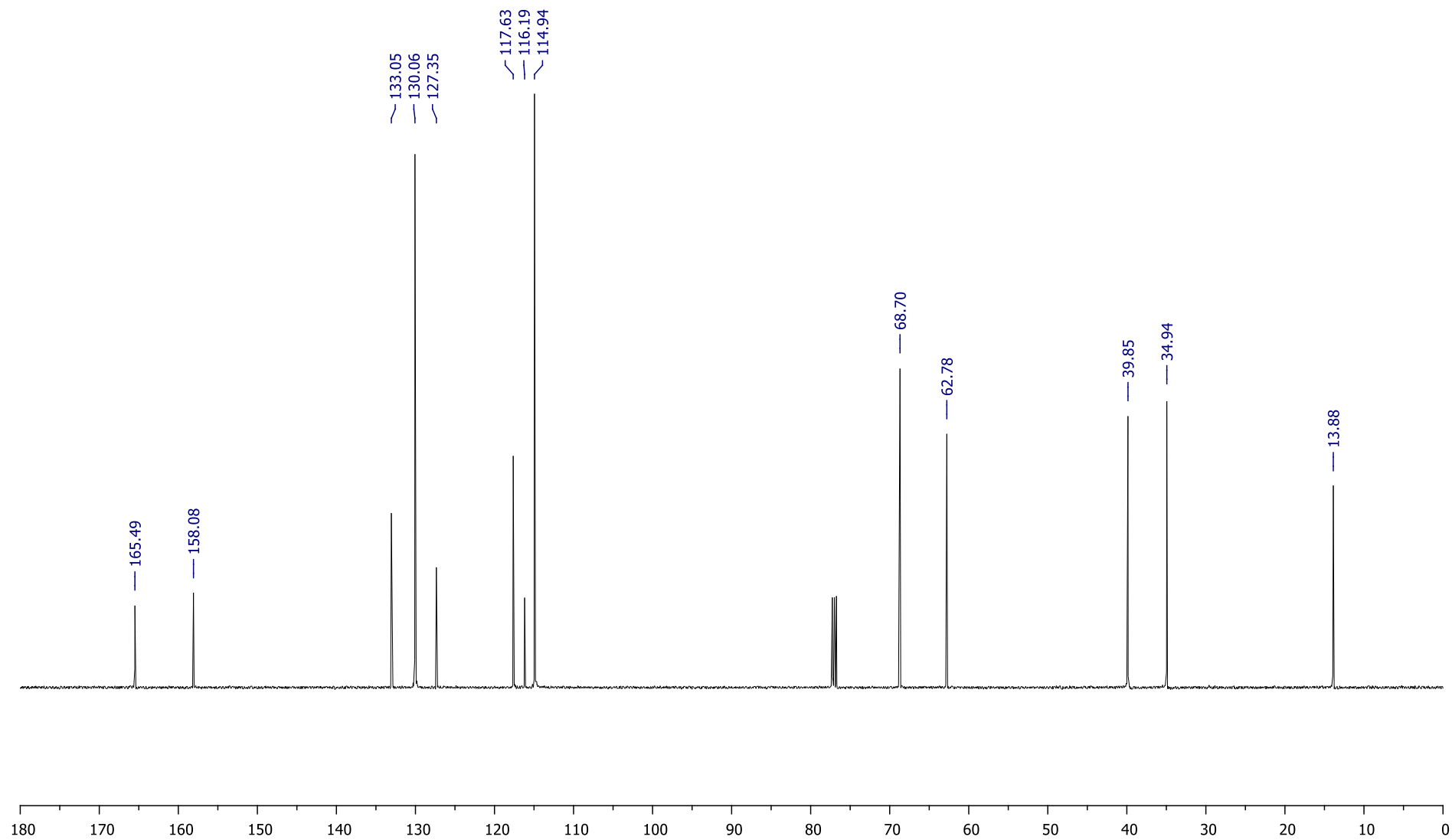
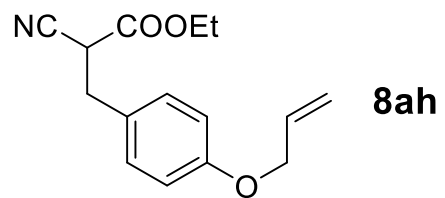
**8af**

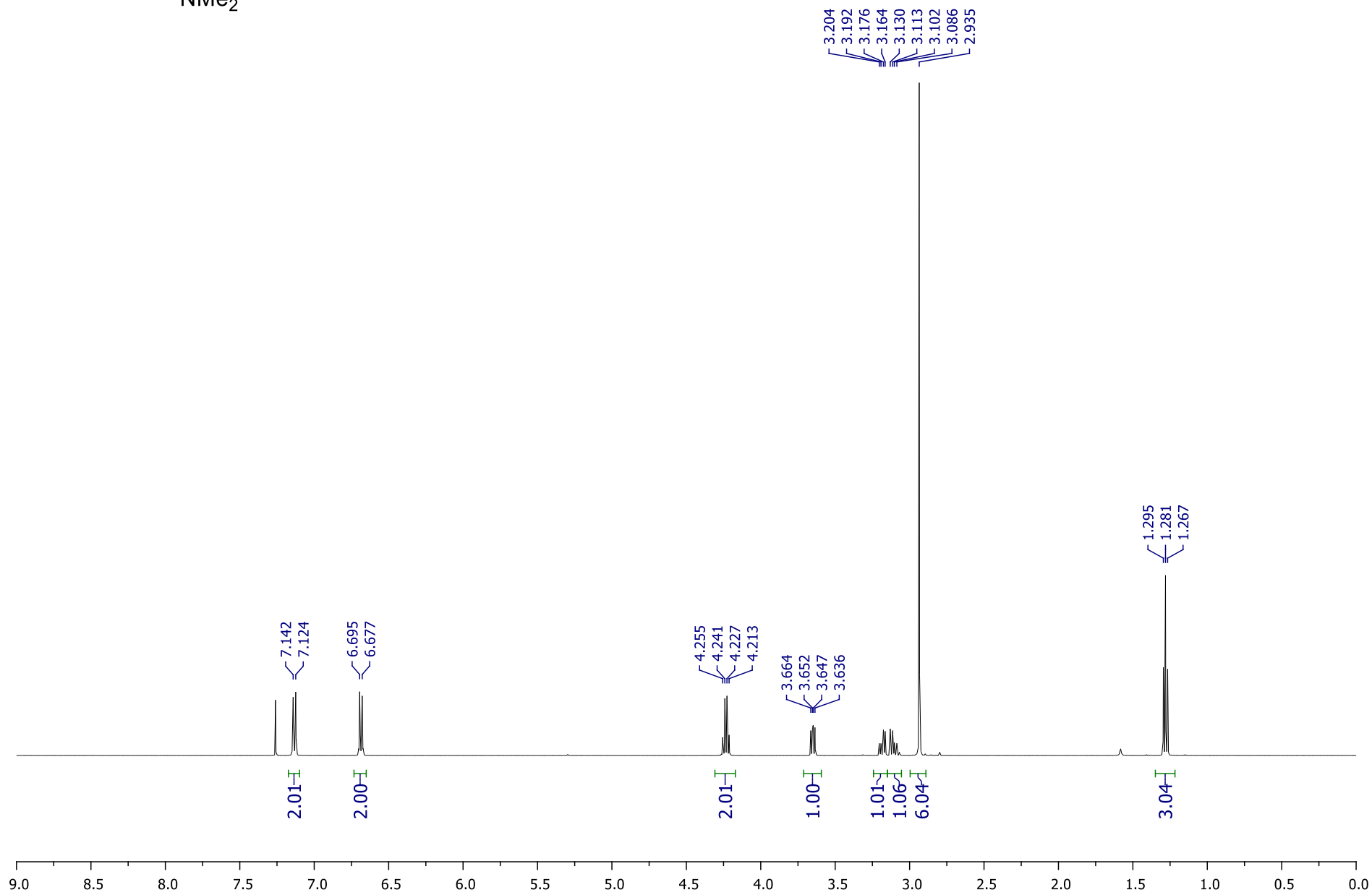
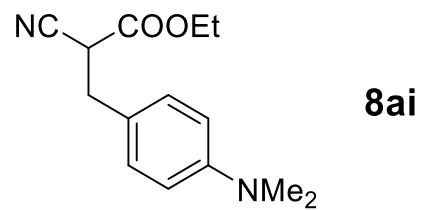
**8af**

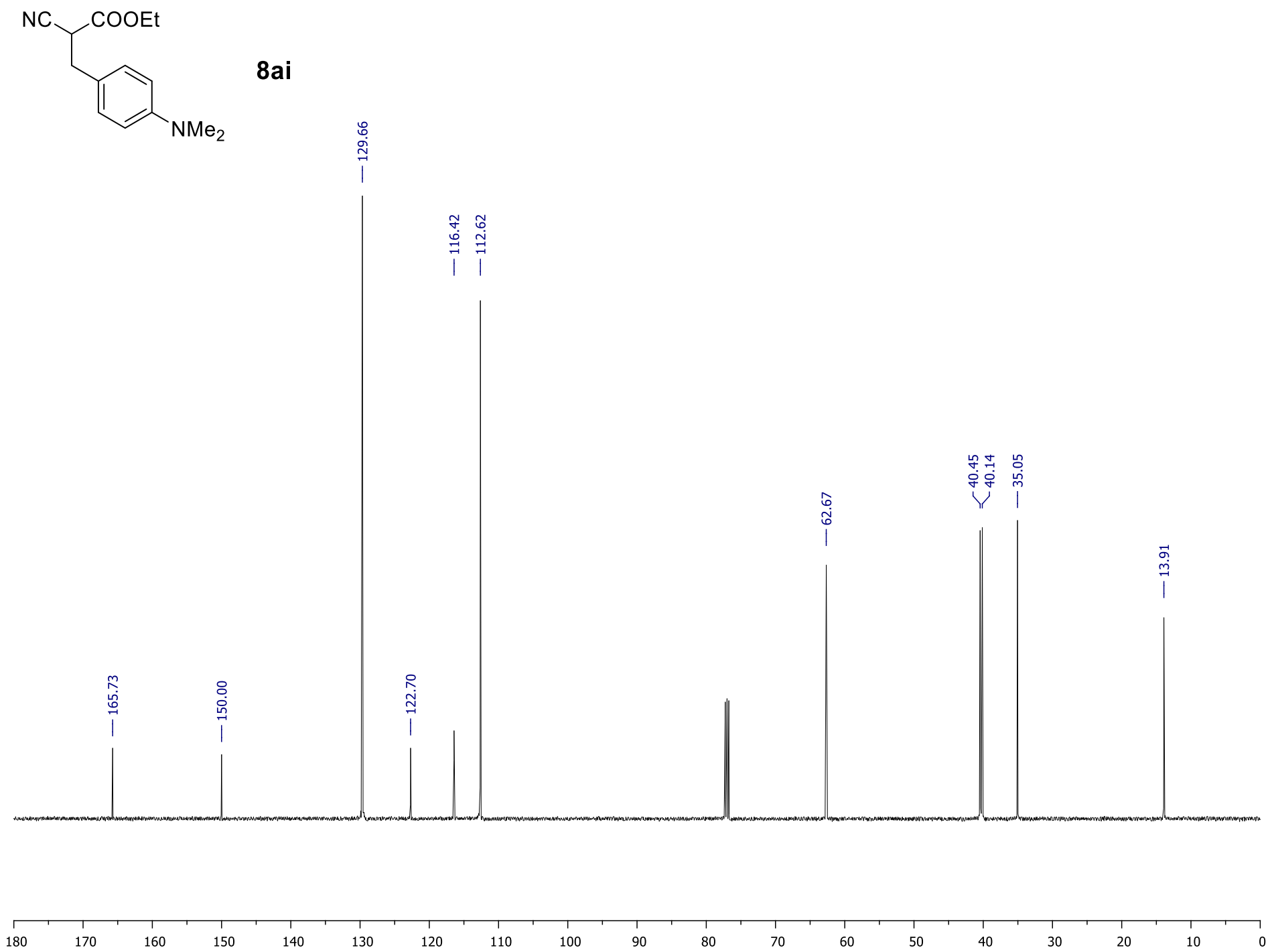


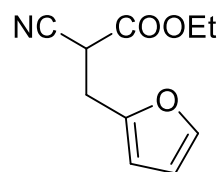
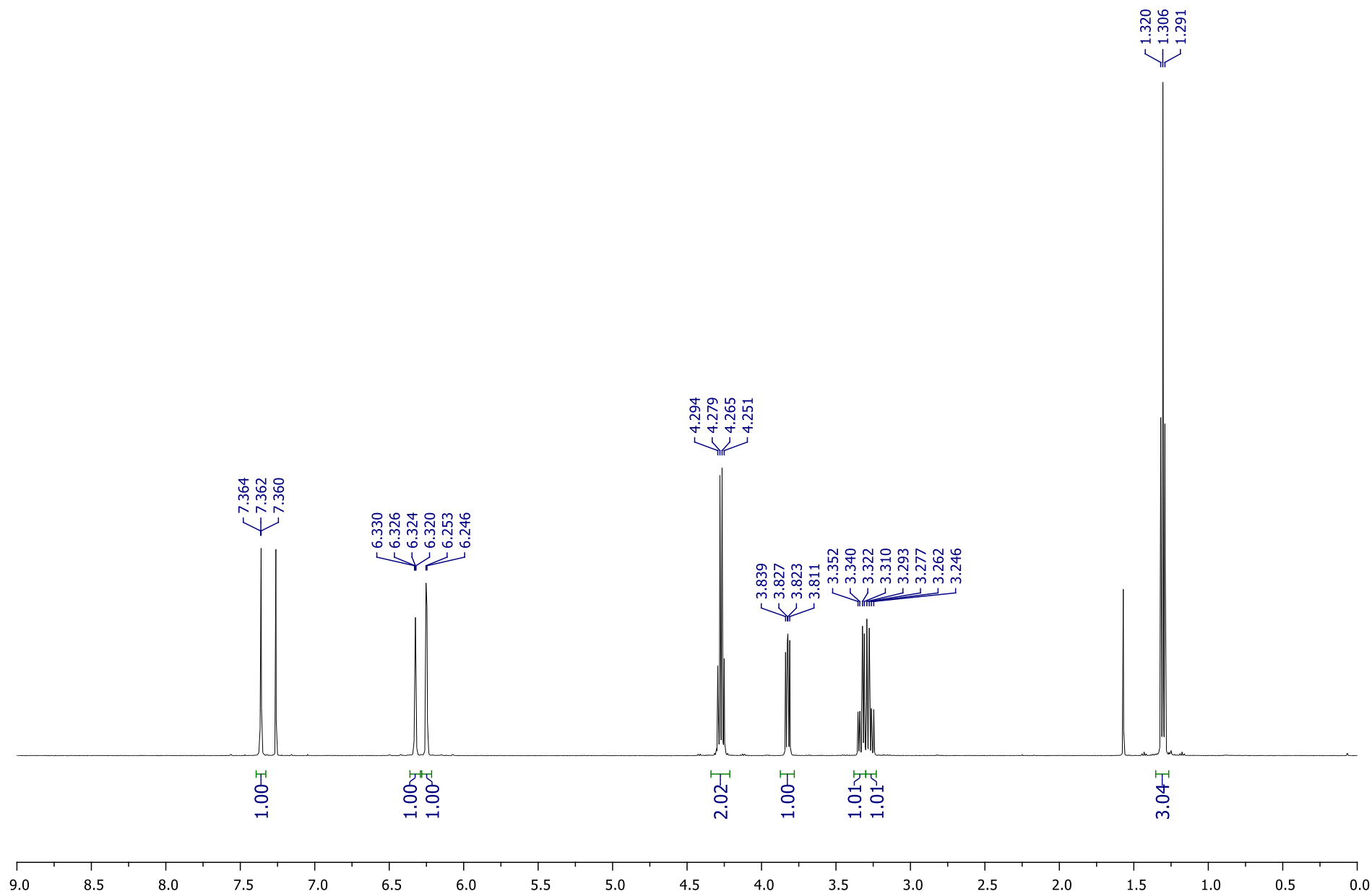
**8ag**

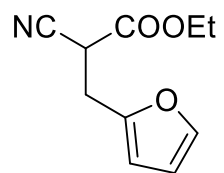
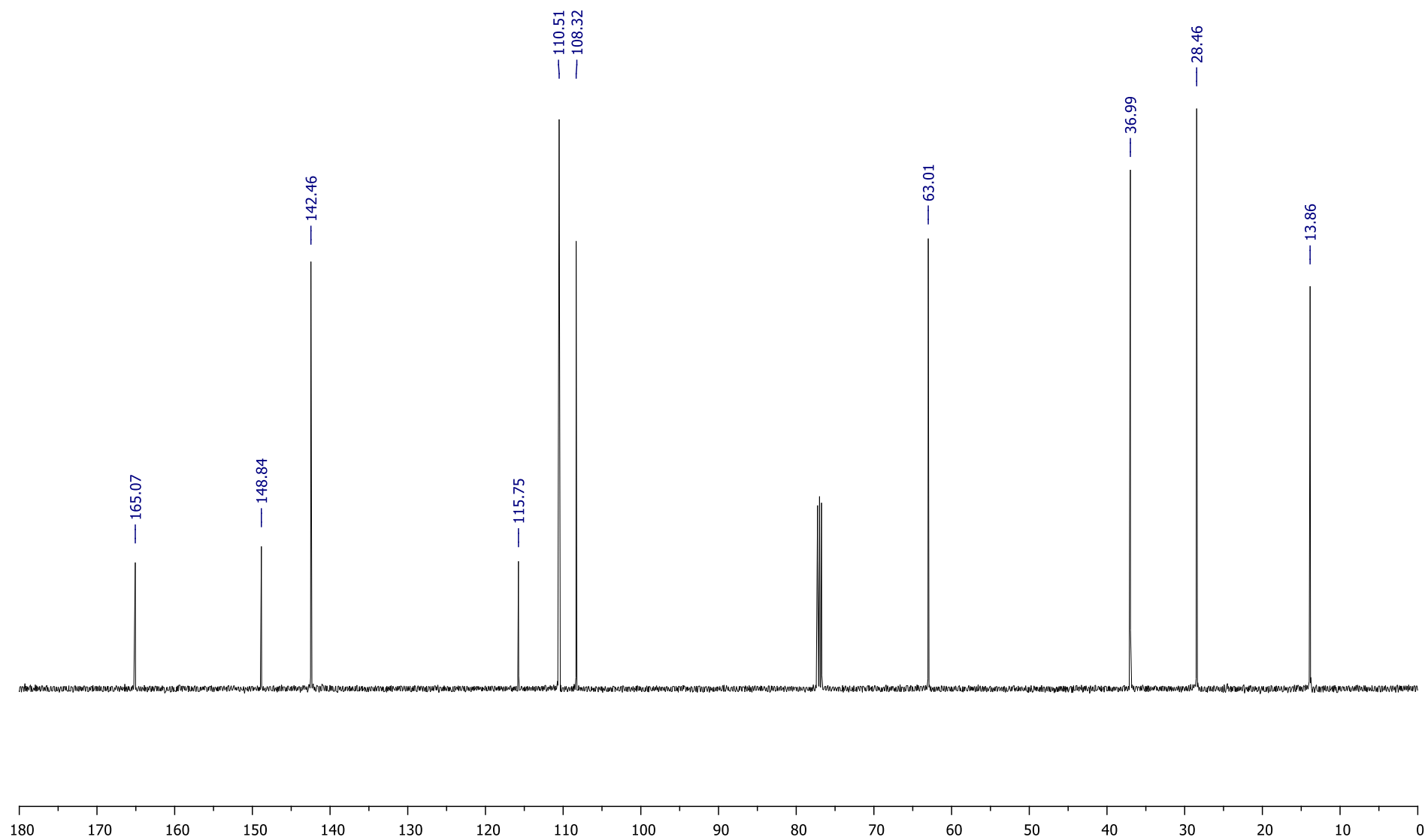


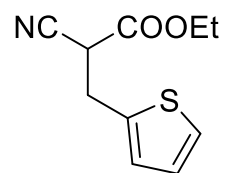
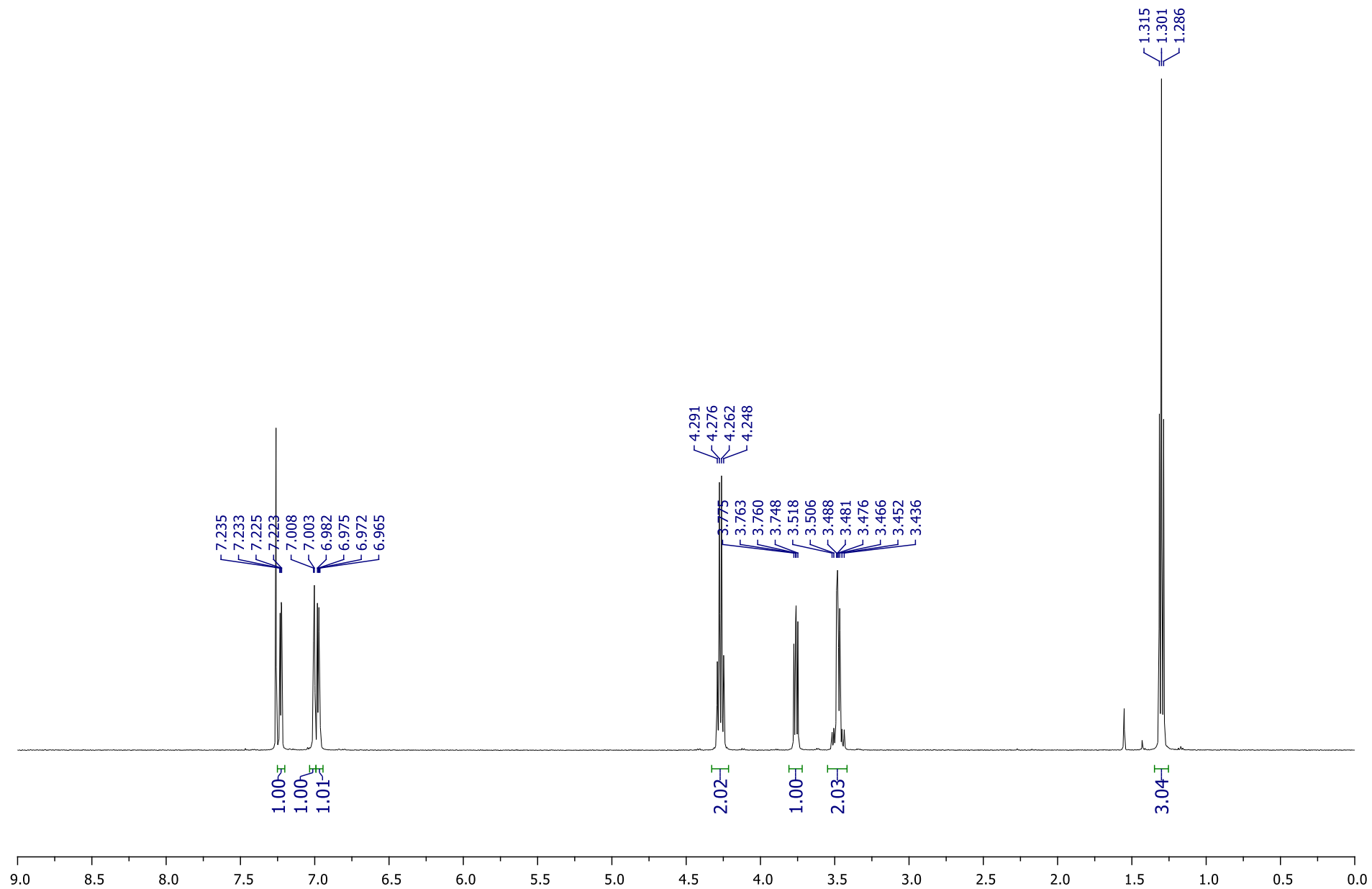


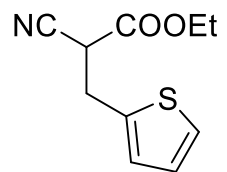
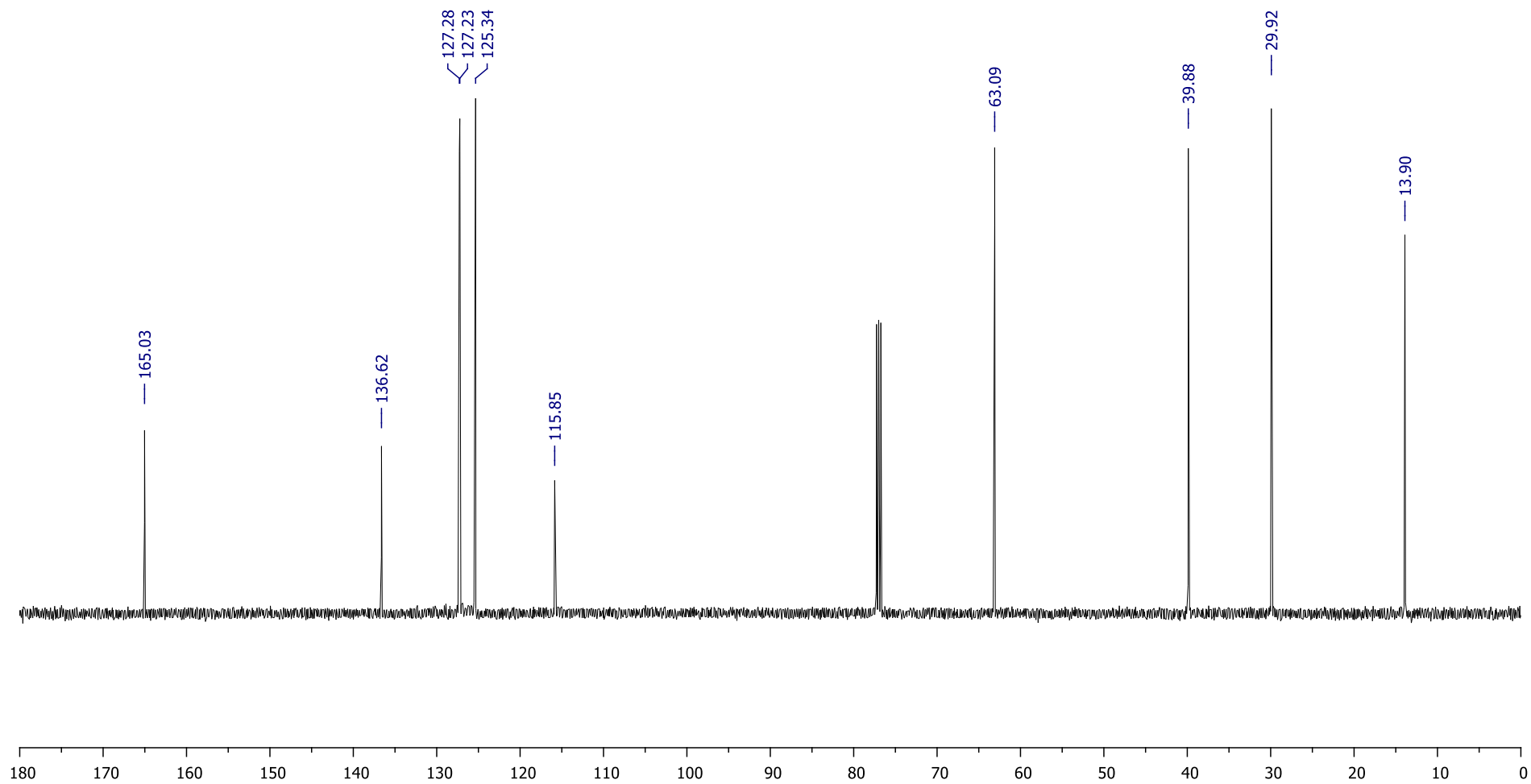


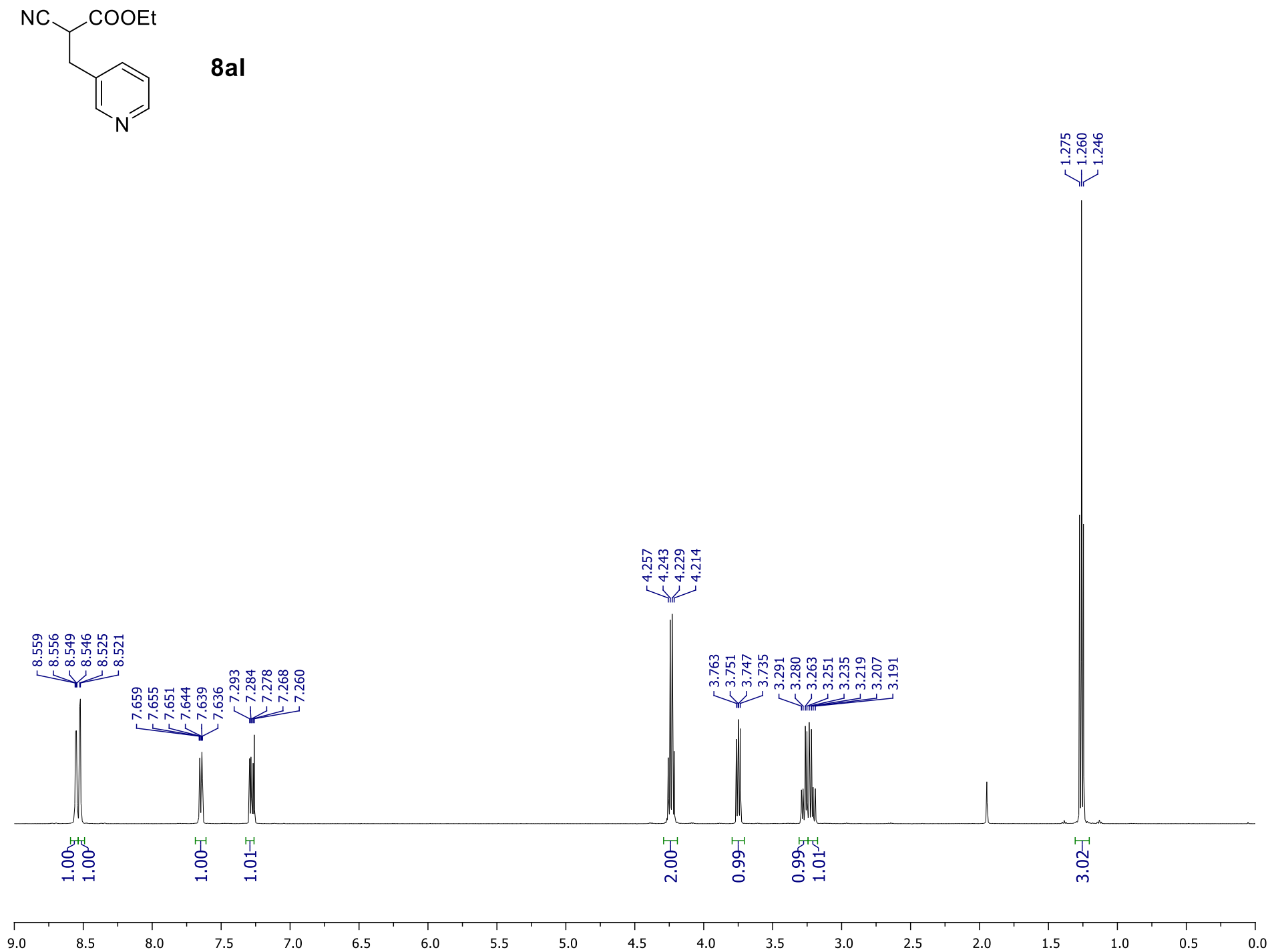


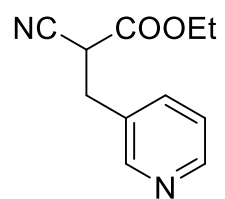
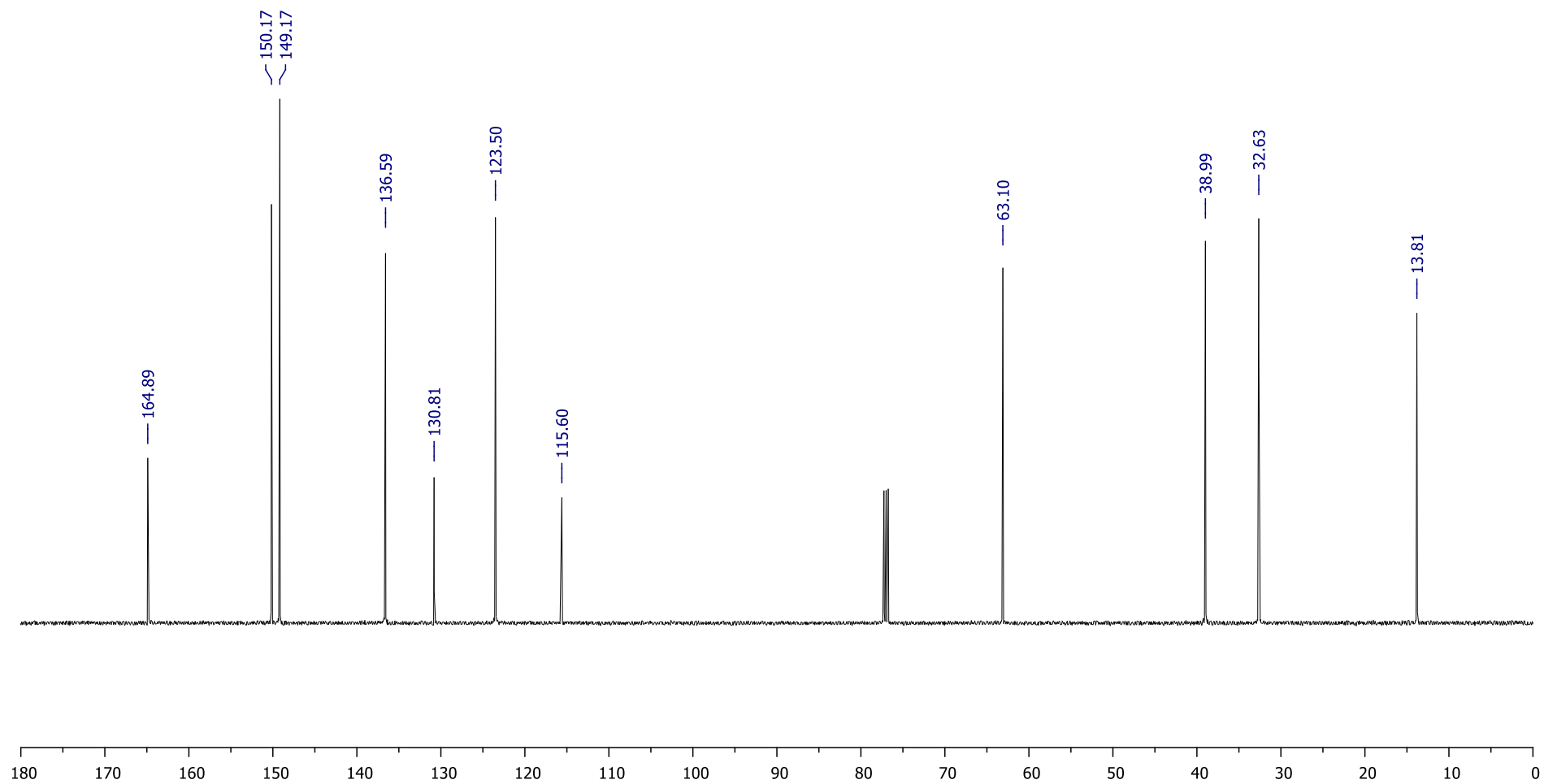
**8aj**

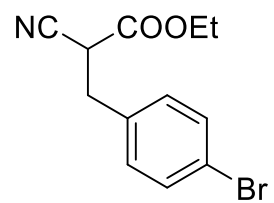
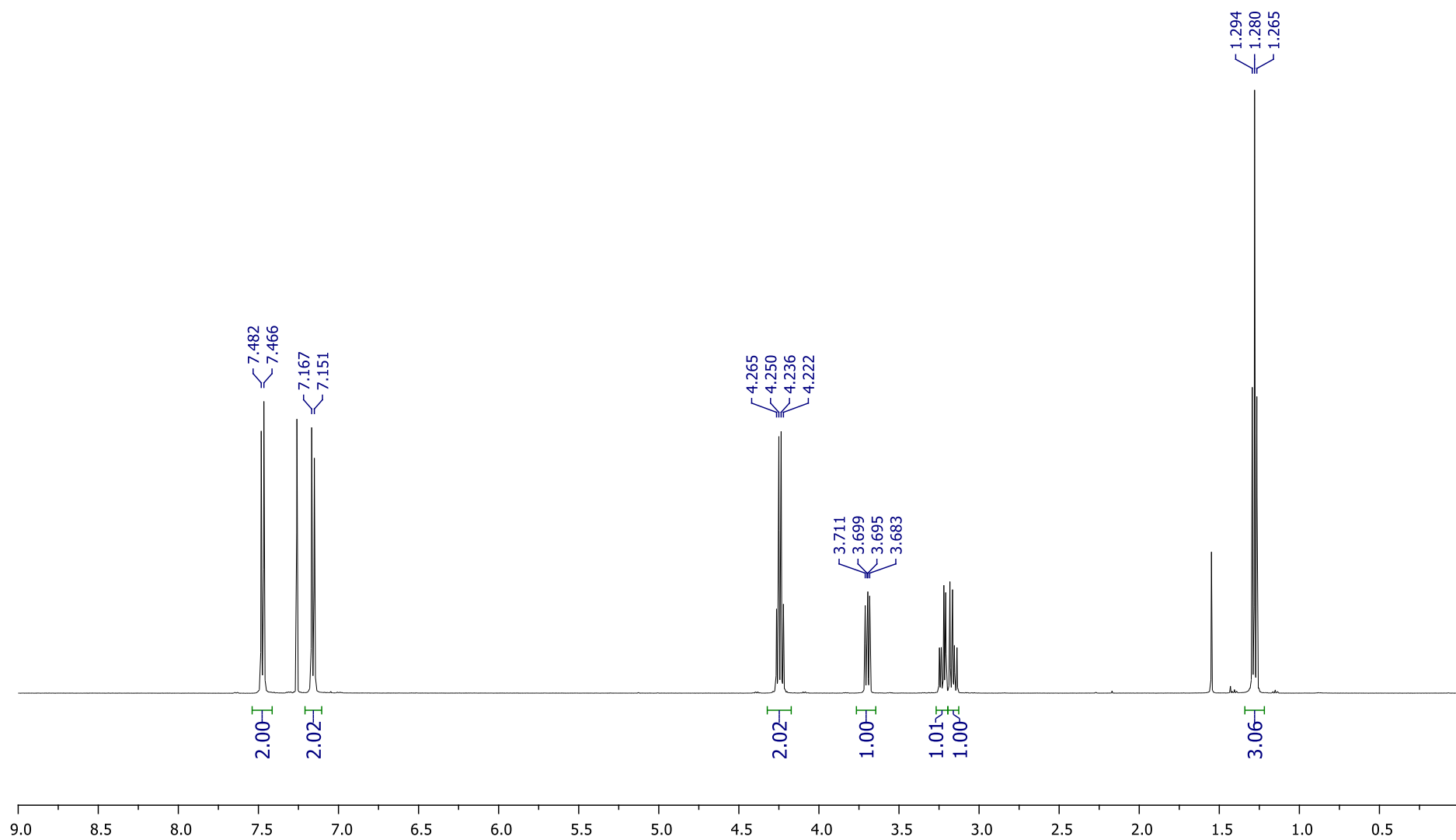
**8aj**

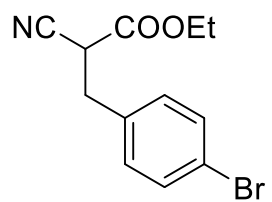
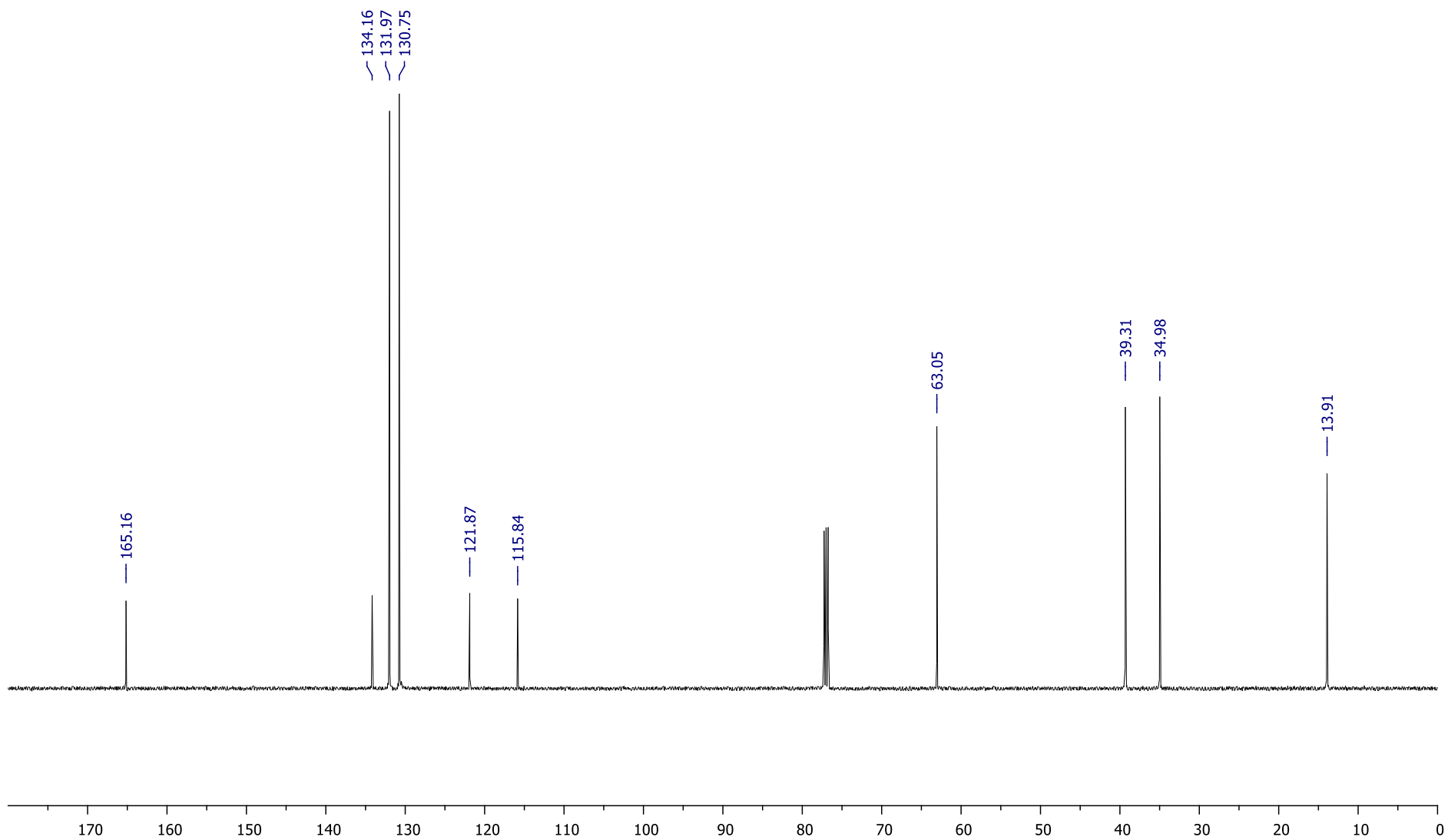
**8ak**

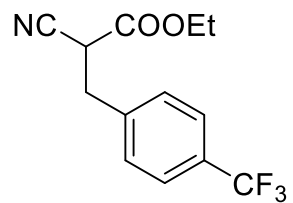
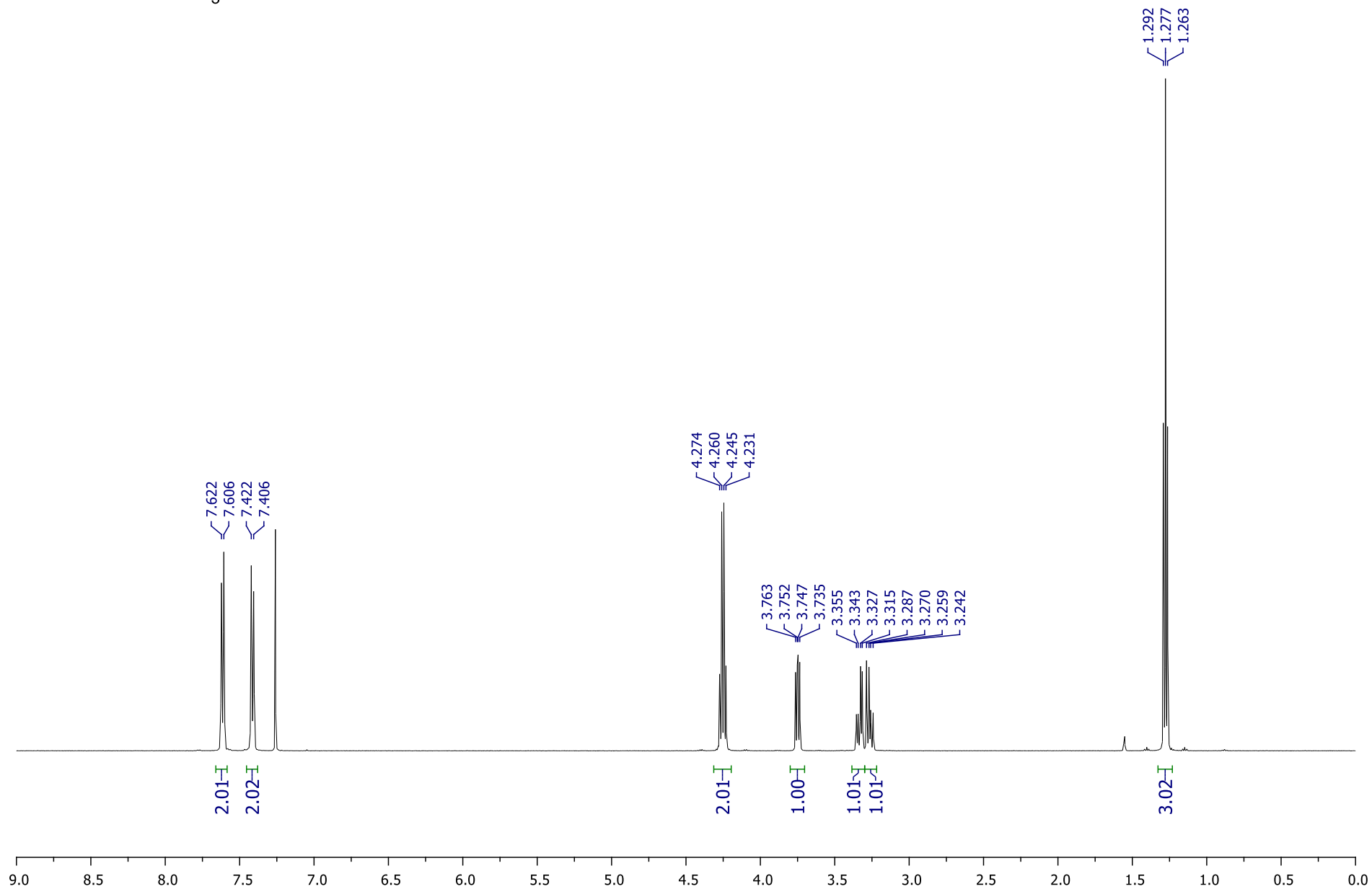
**8ak**

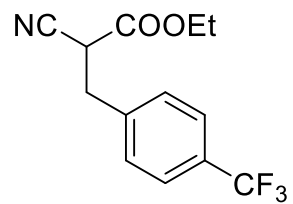
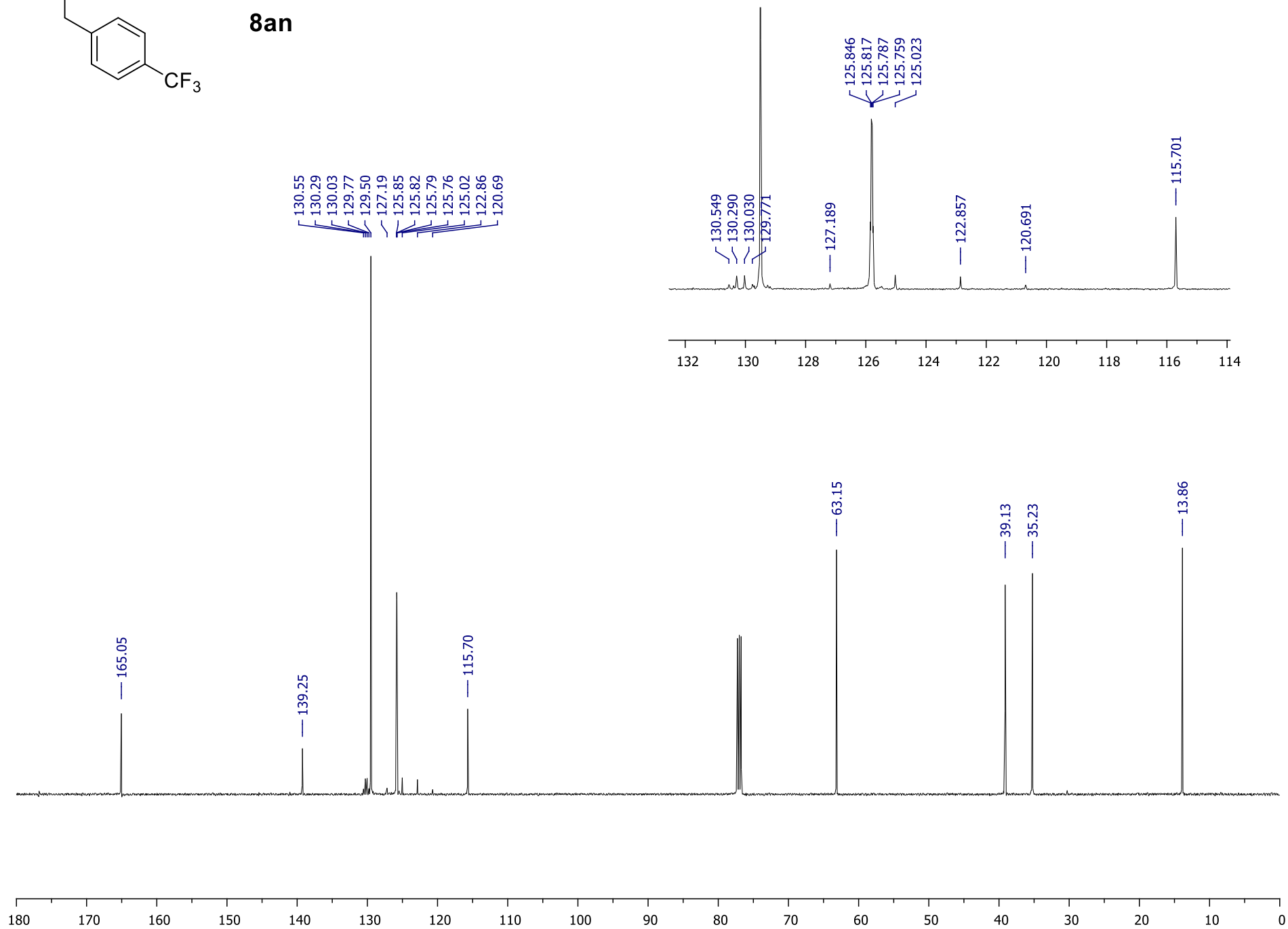


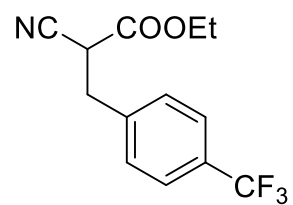
**8aI**

**8am**

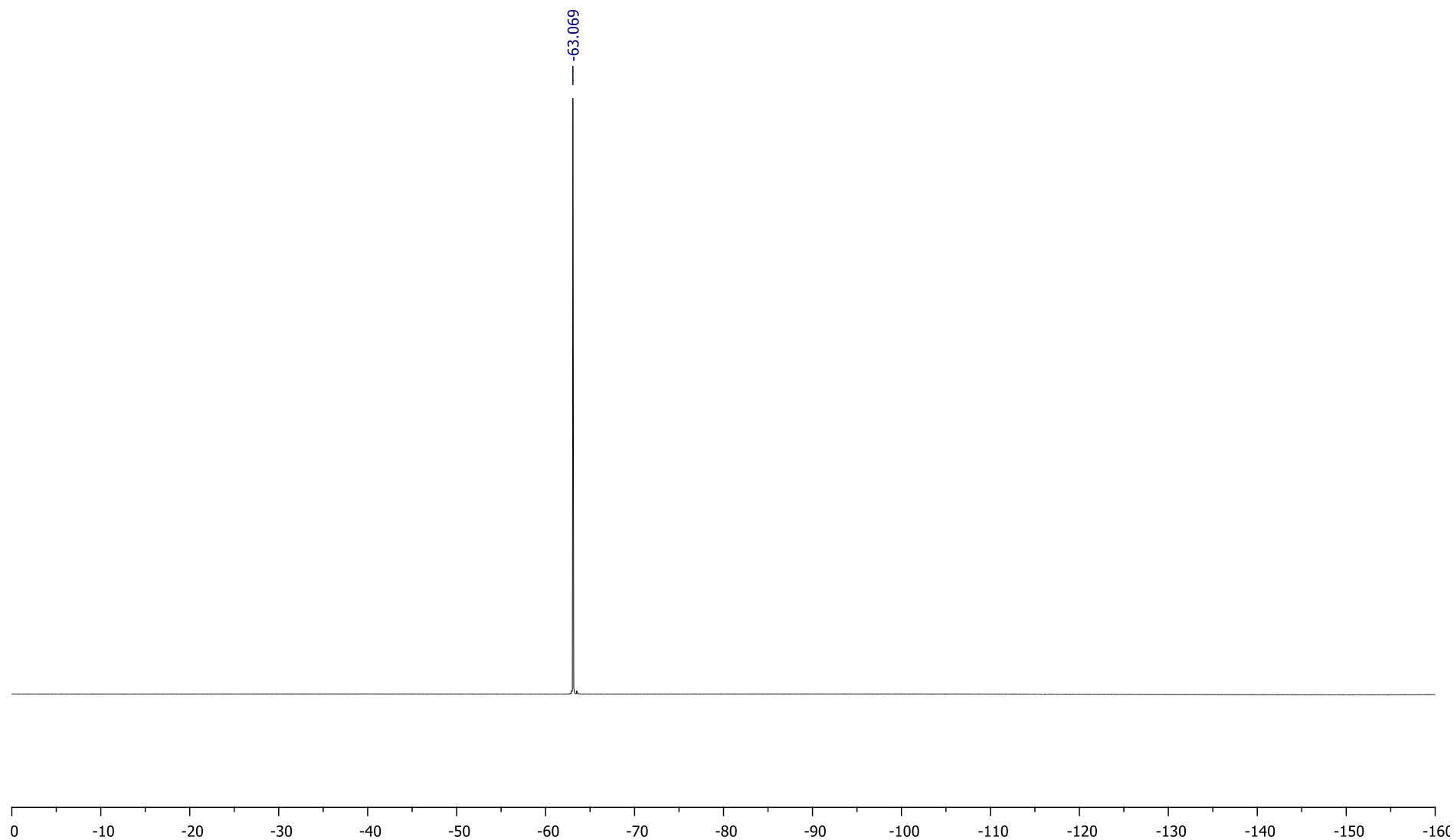
**8am**

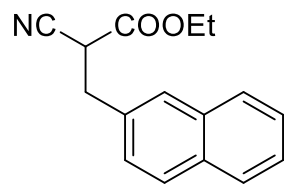
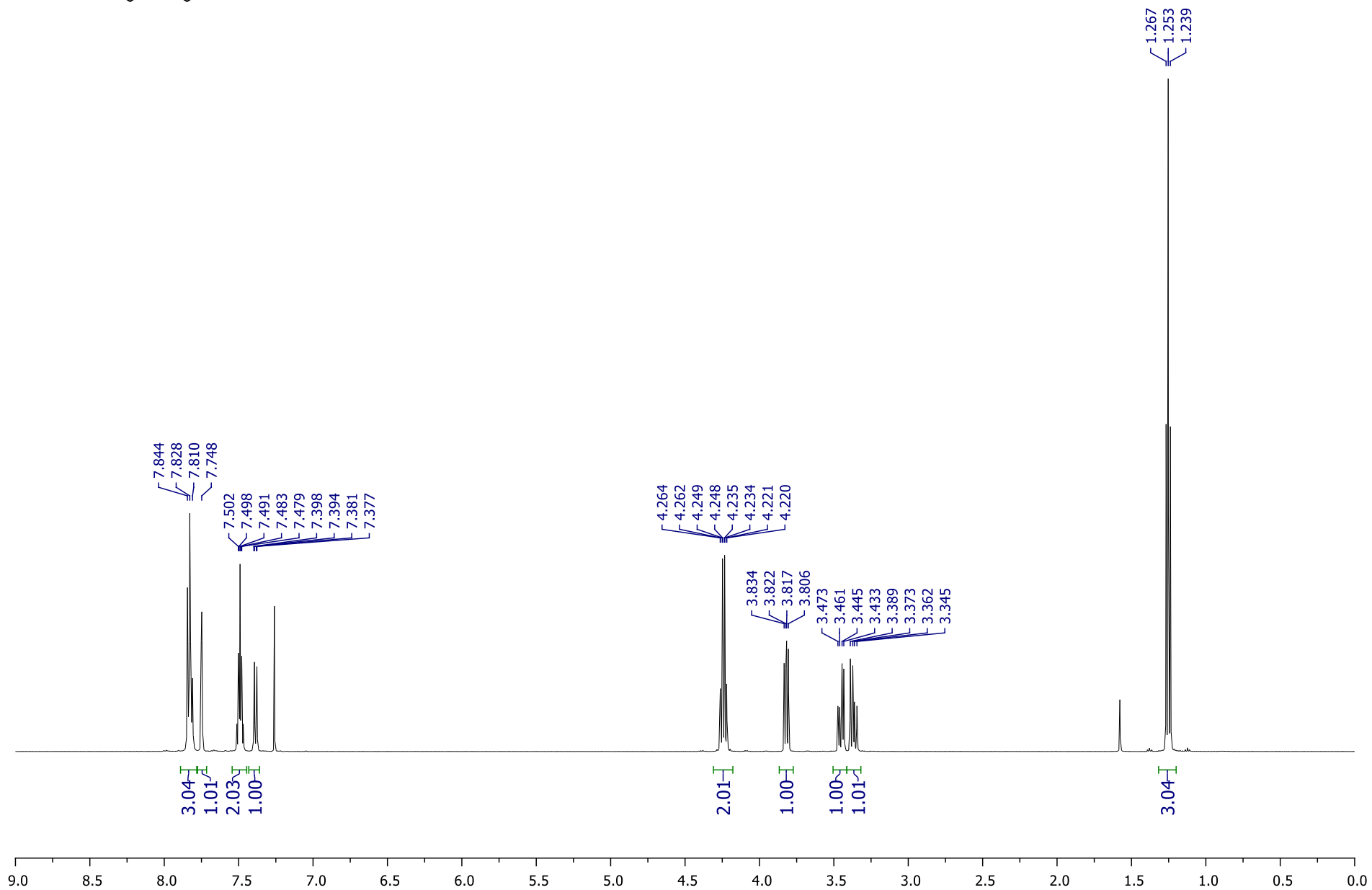
**8an**

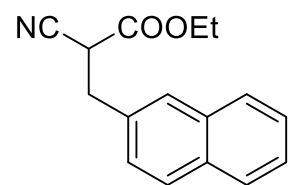
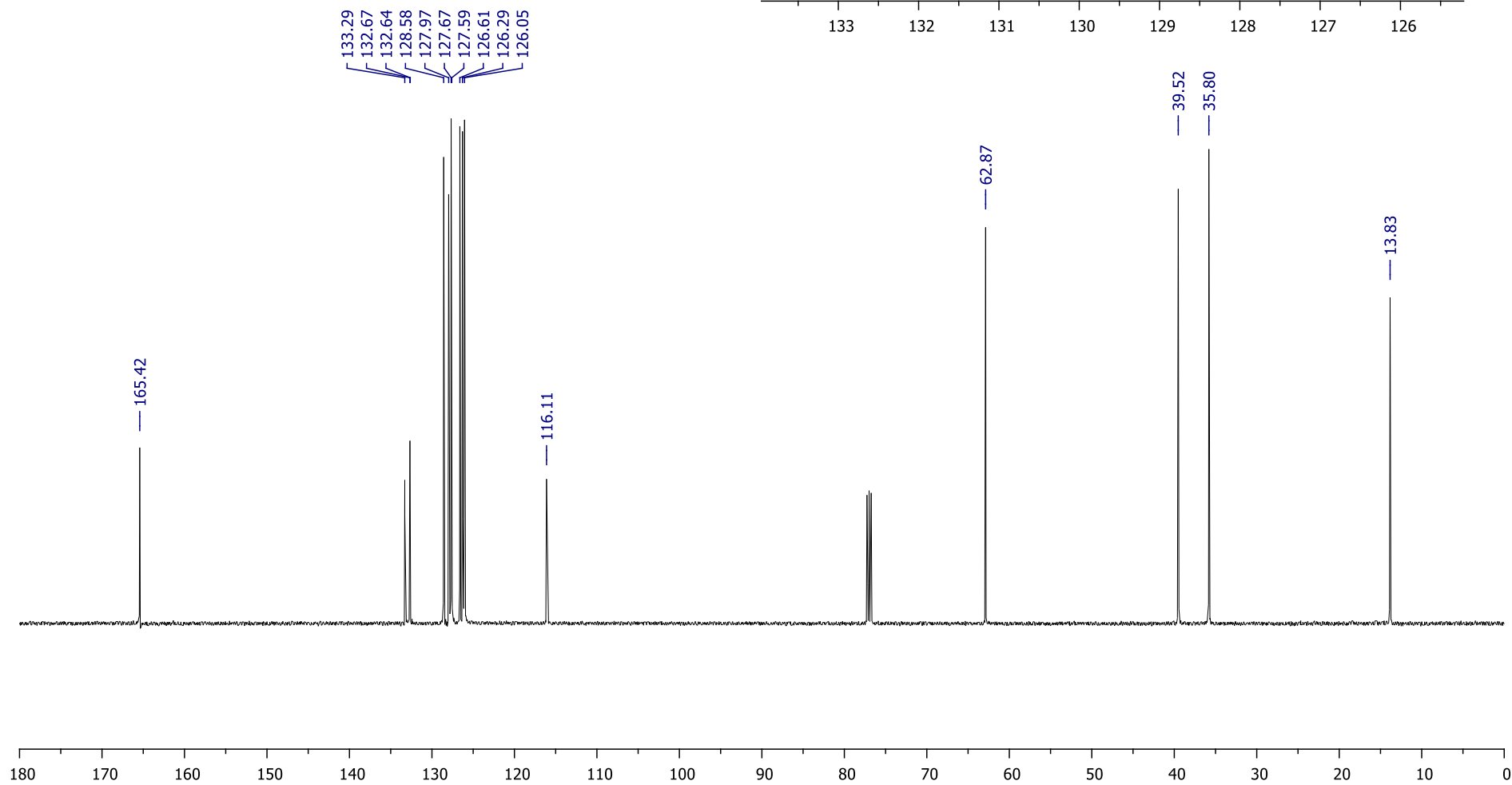
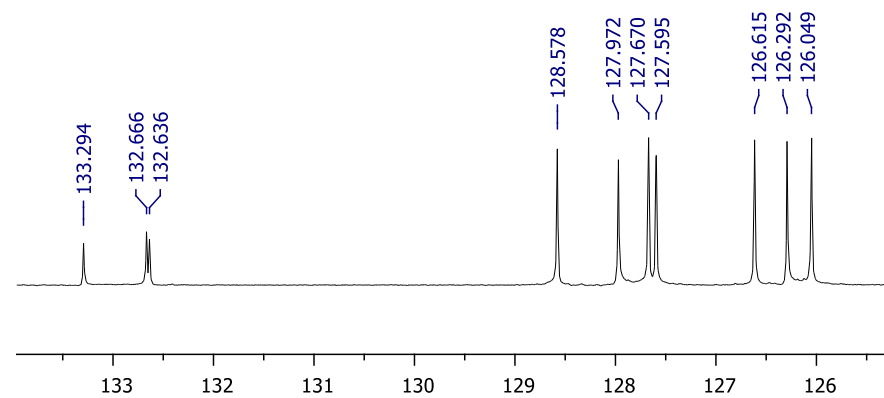
**8an**

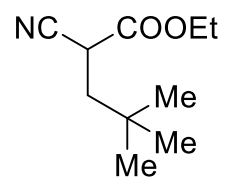
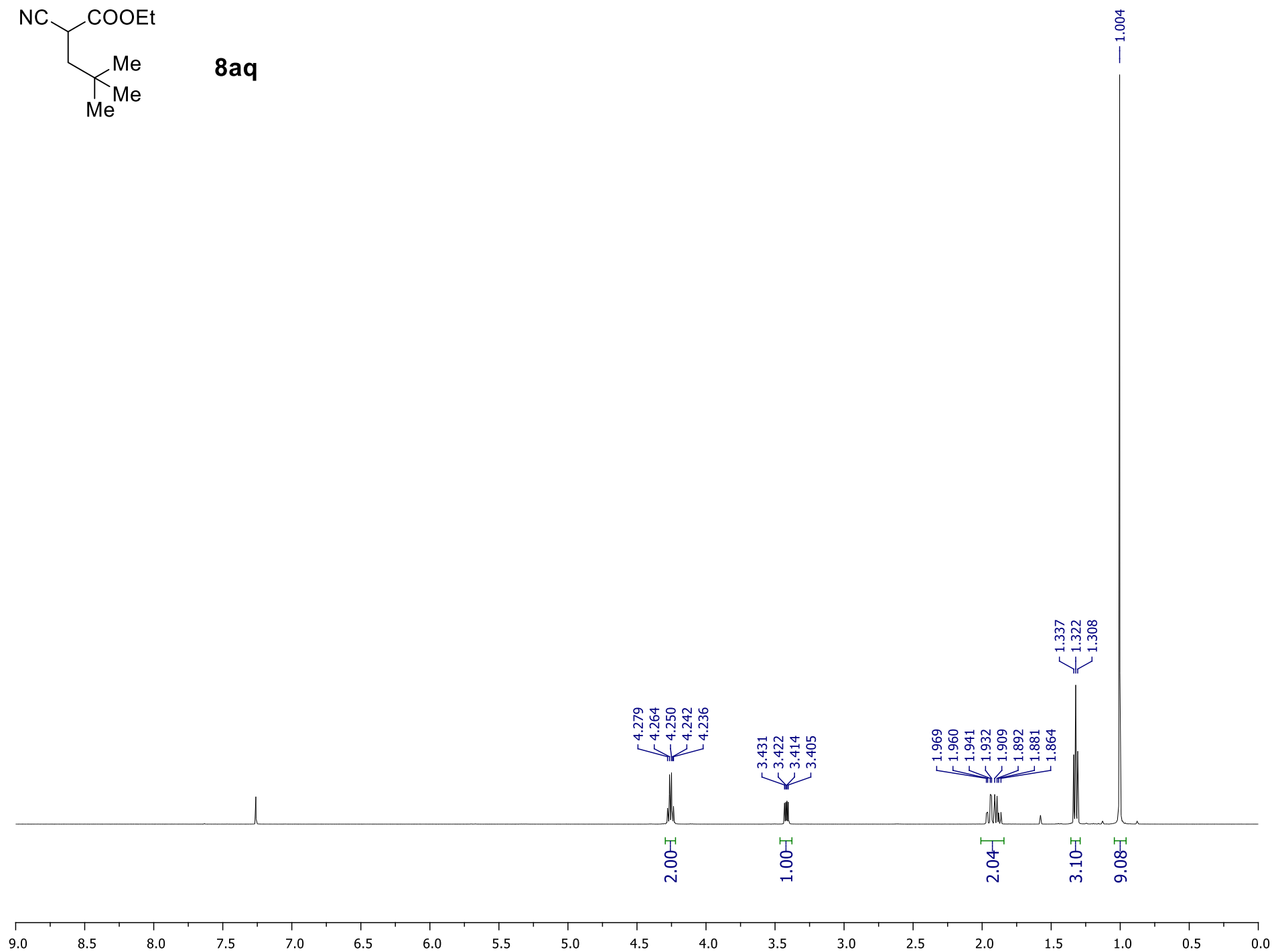


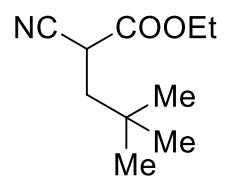
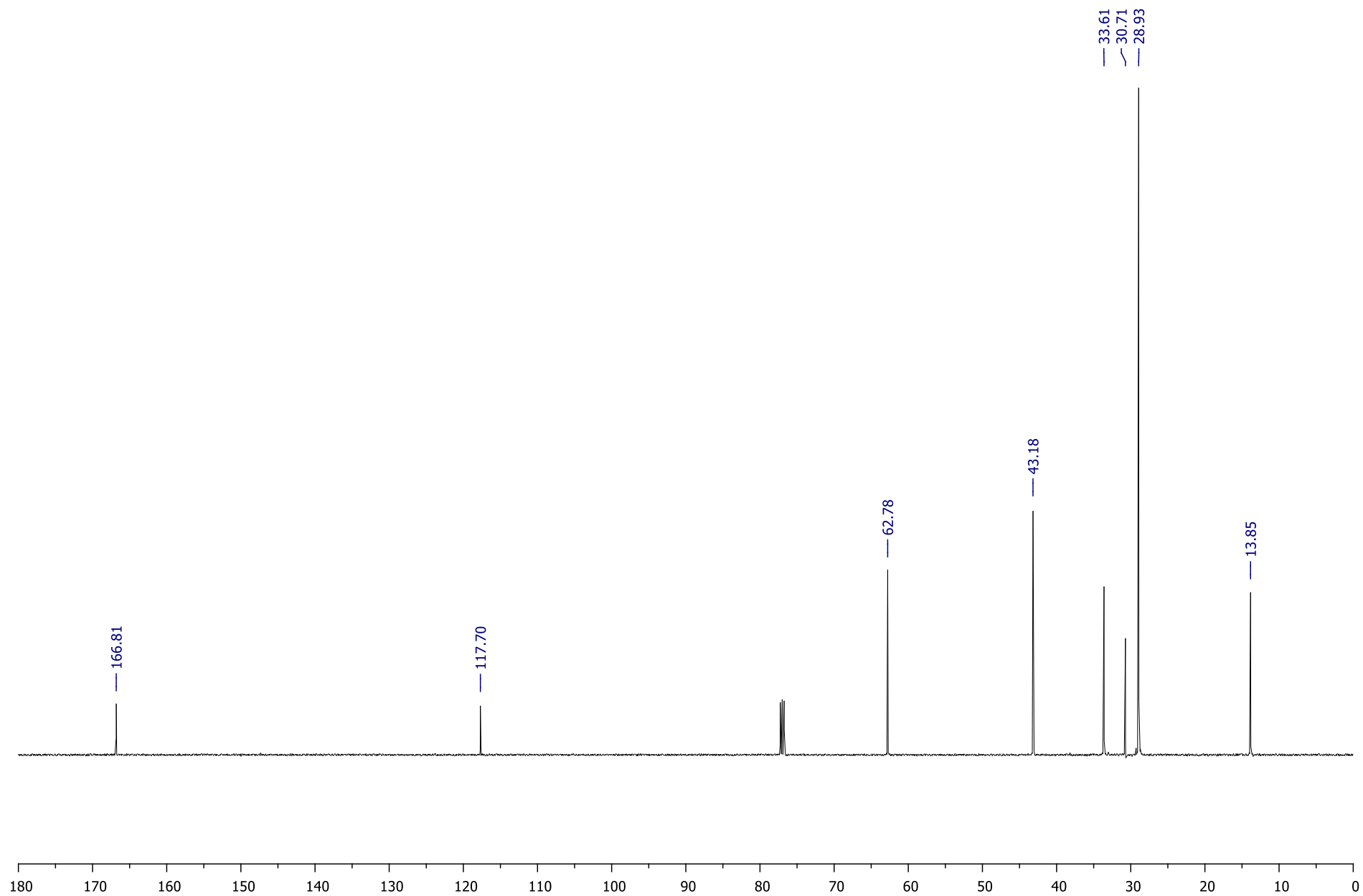
8an

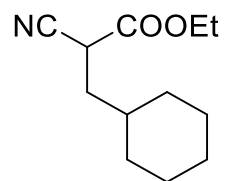
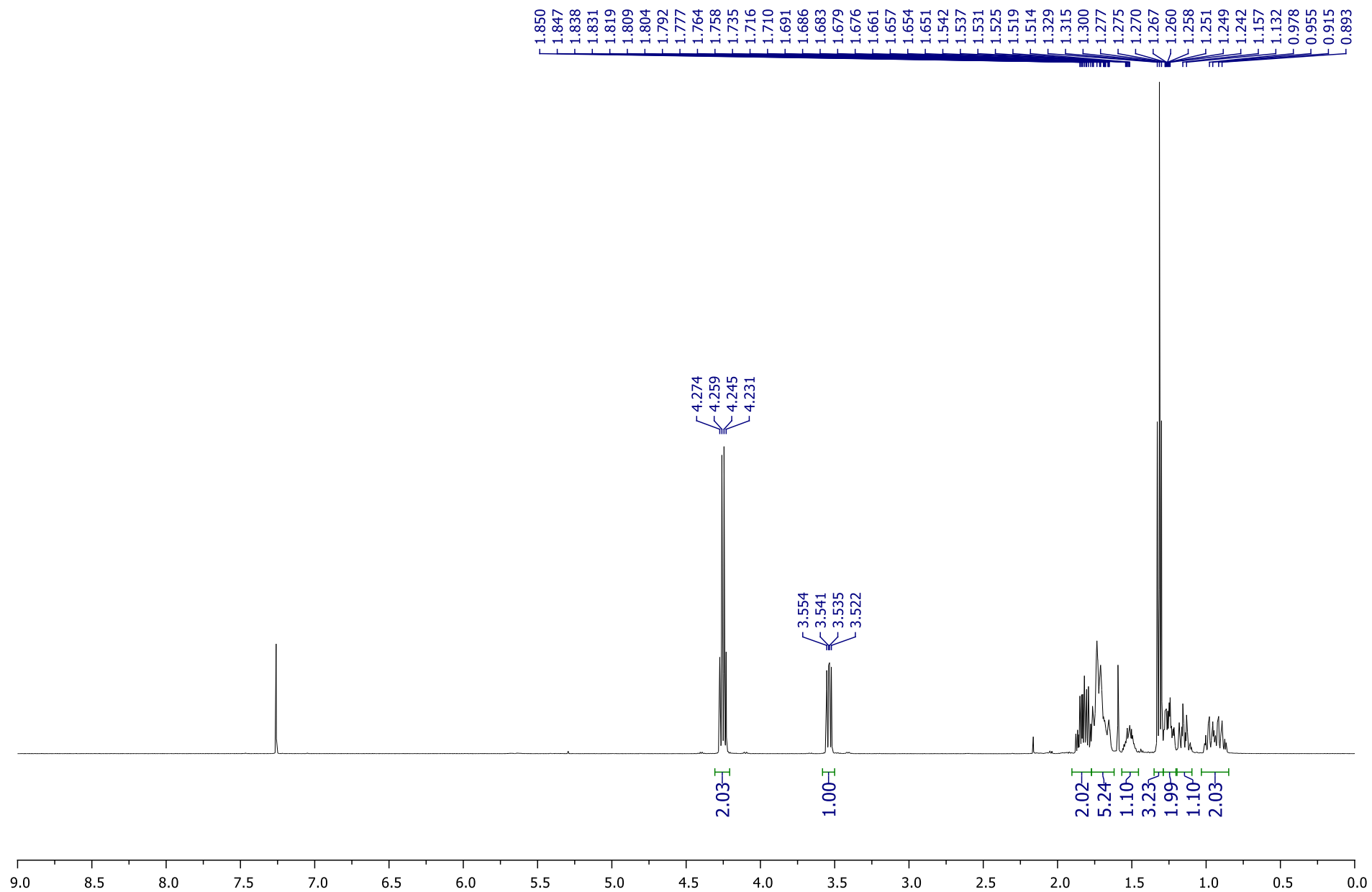


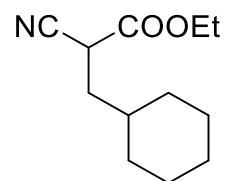
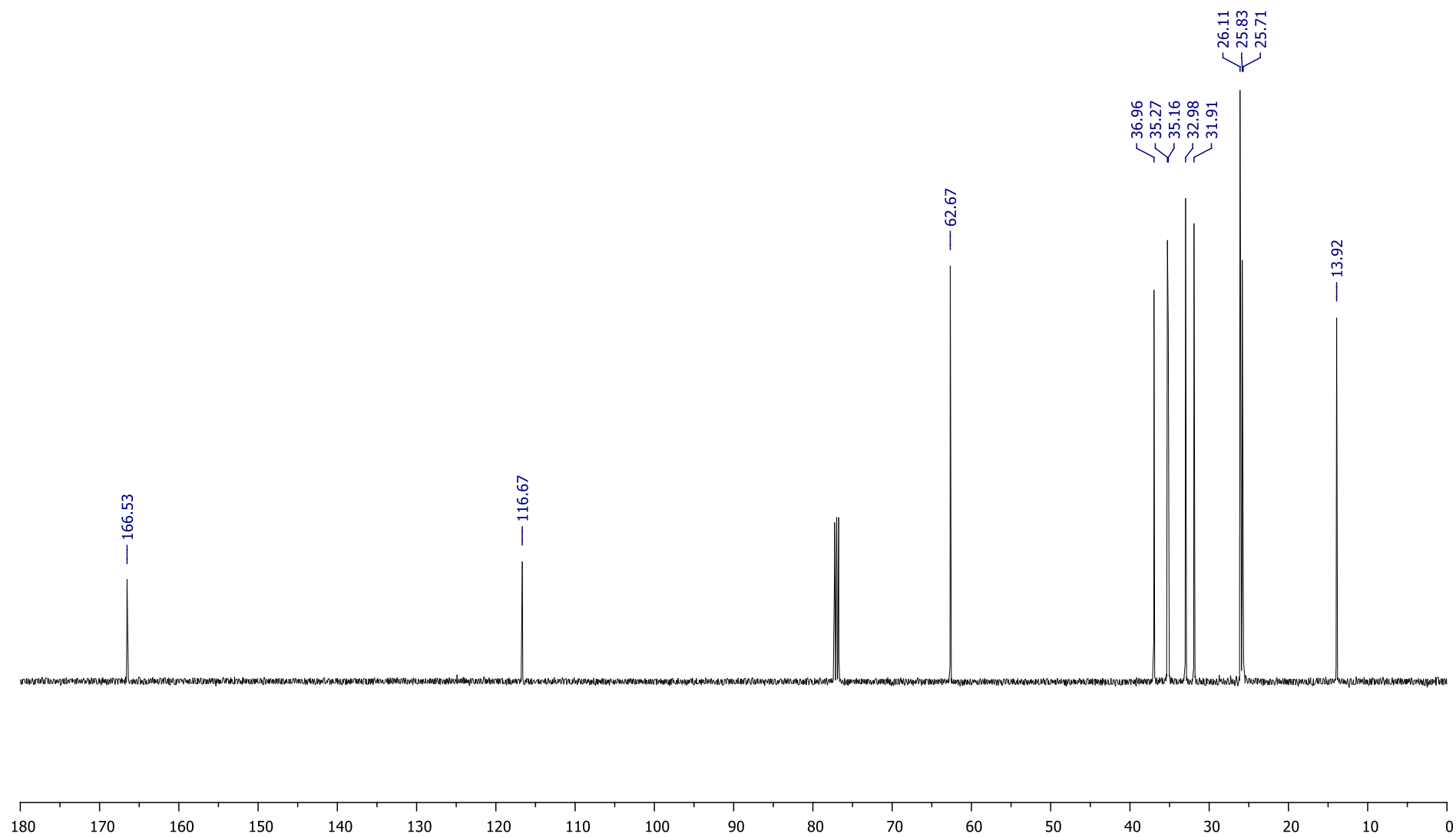
**8ao**

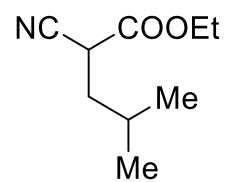
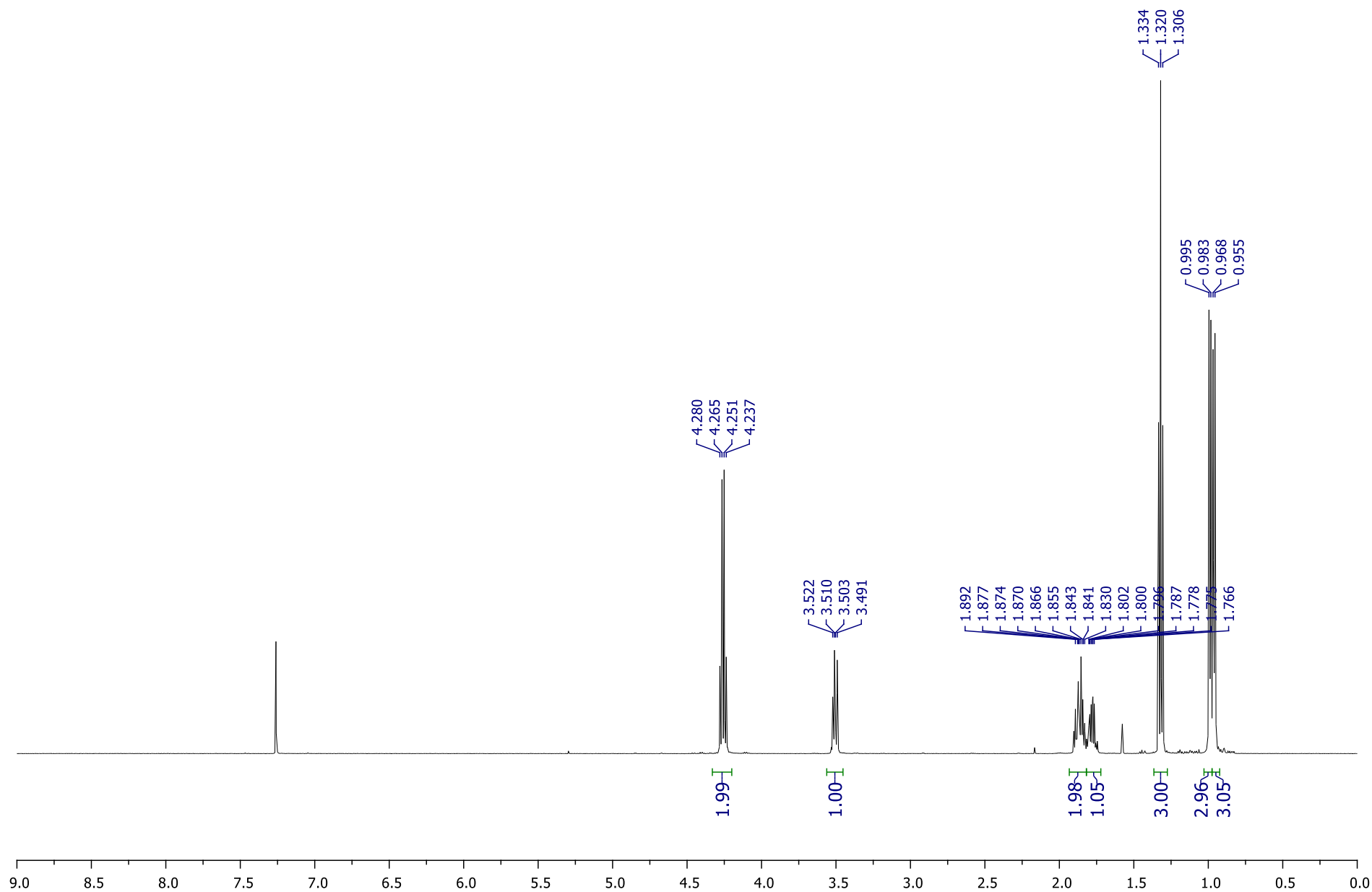
**8ao**

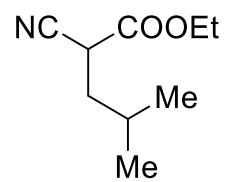
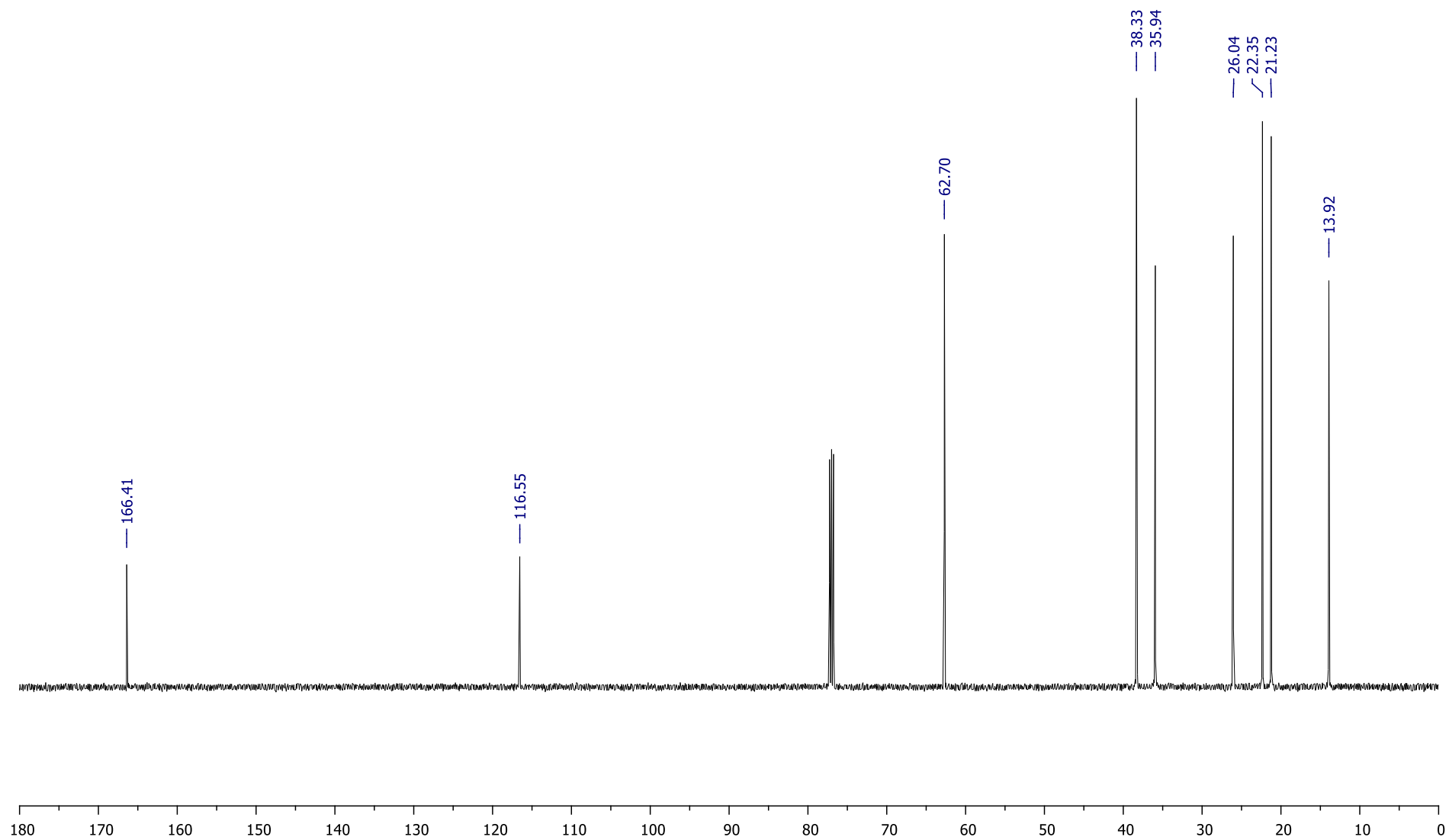
**8aq**

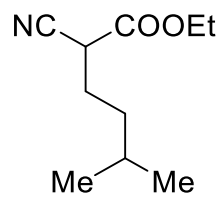
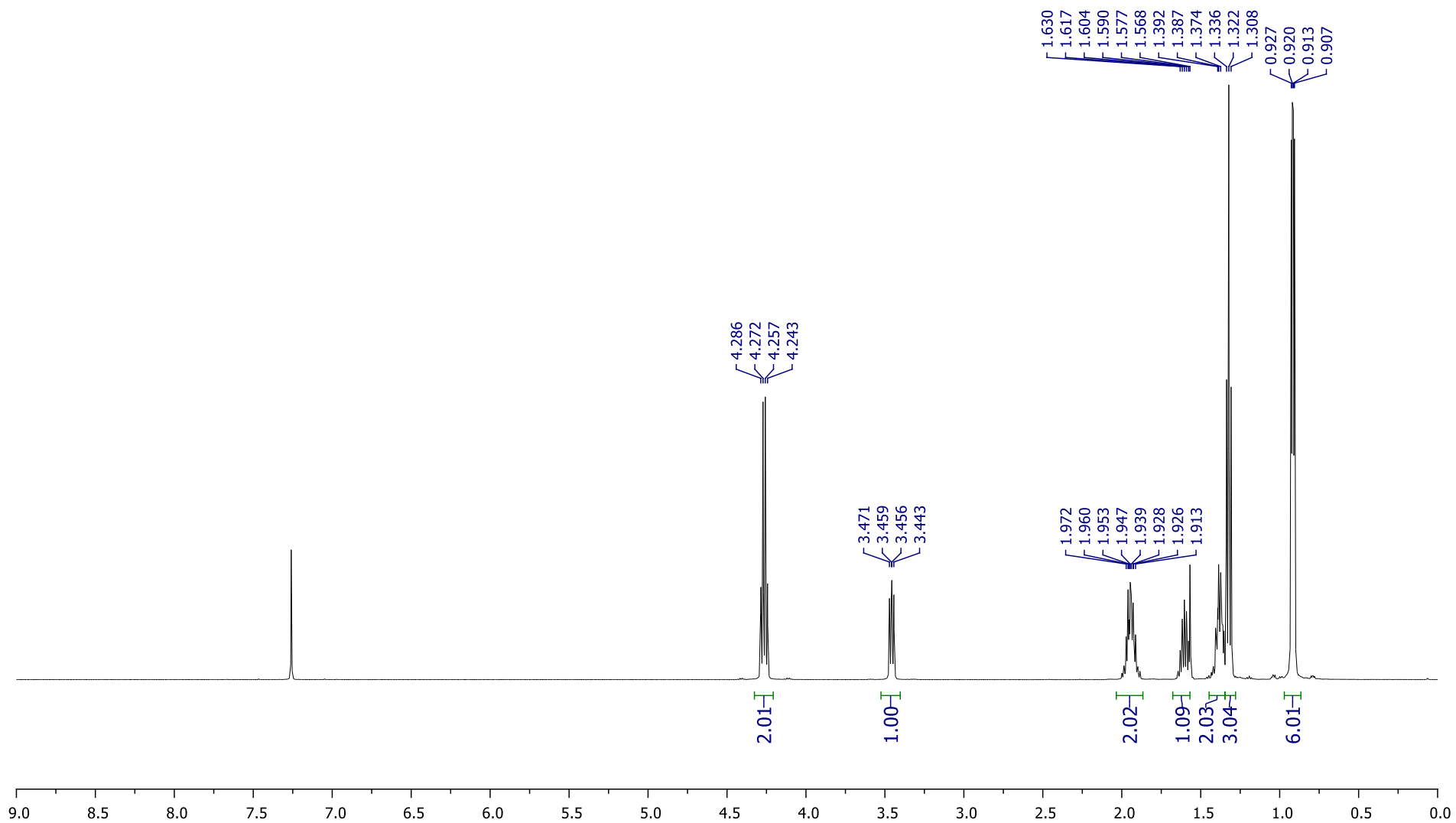
**8aq**

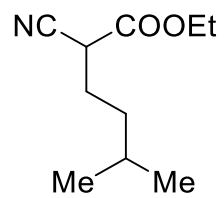
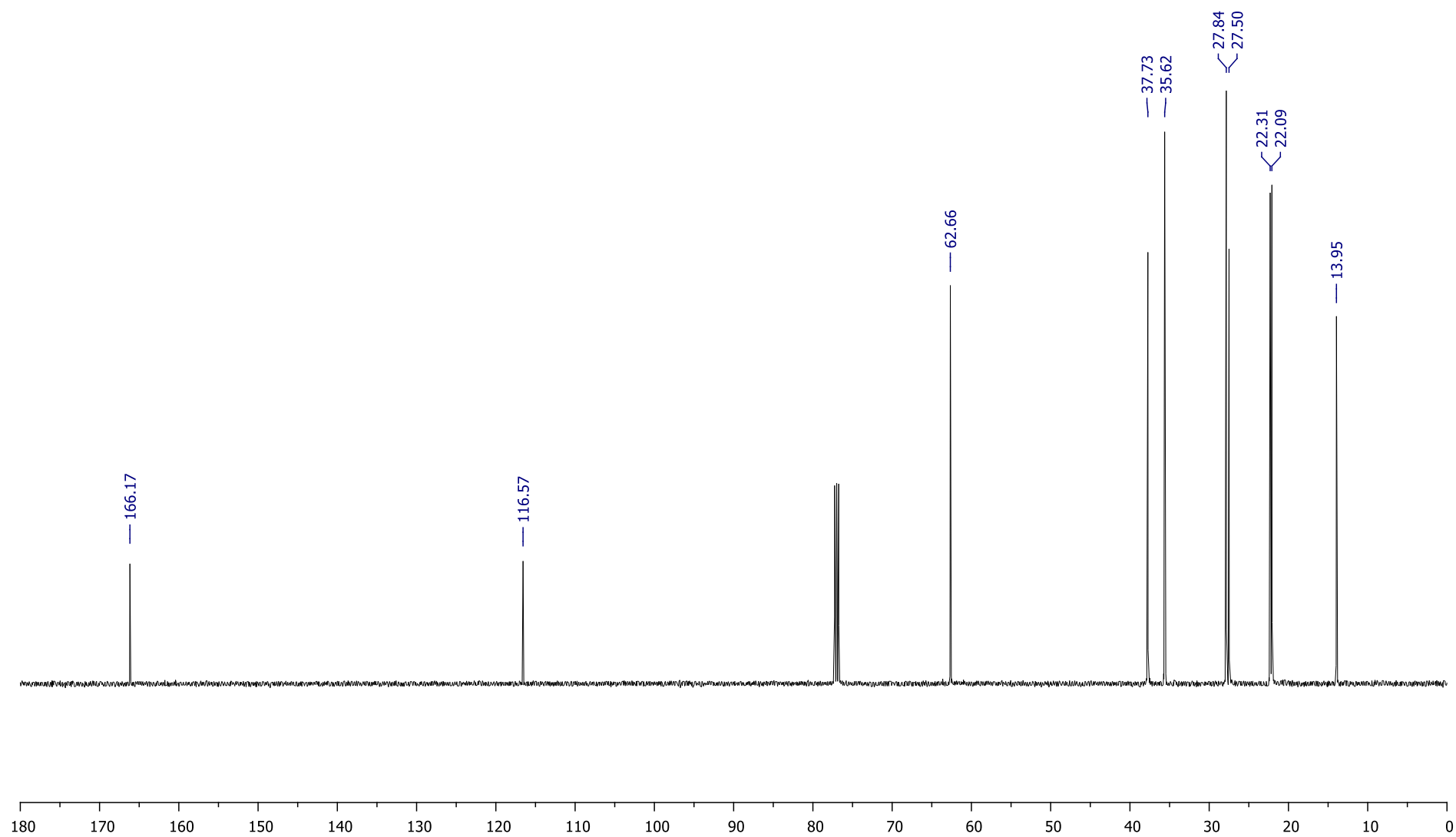
**8ar**

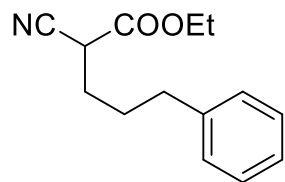
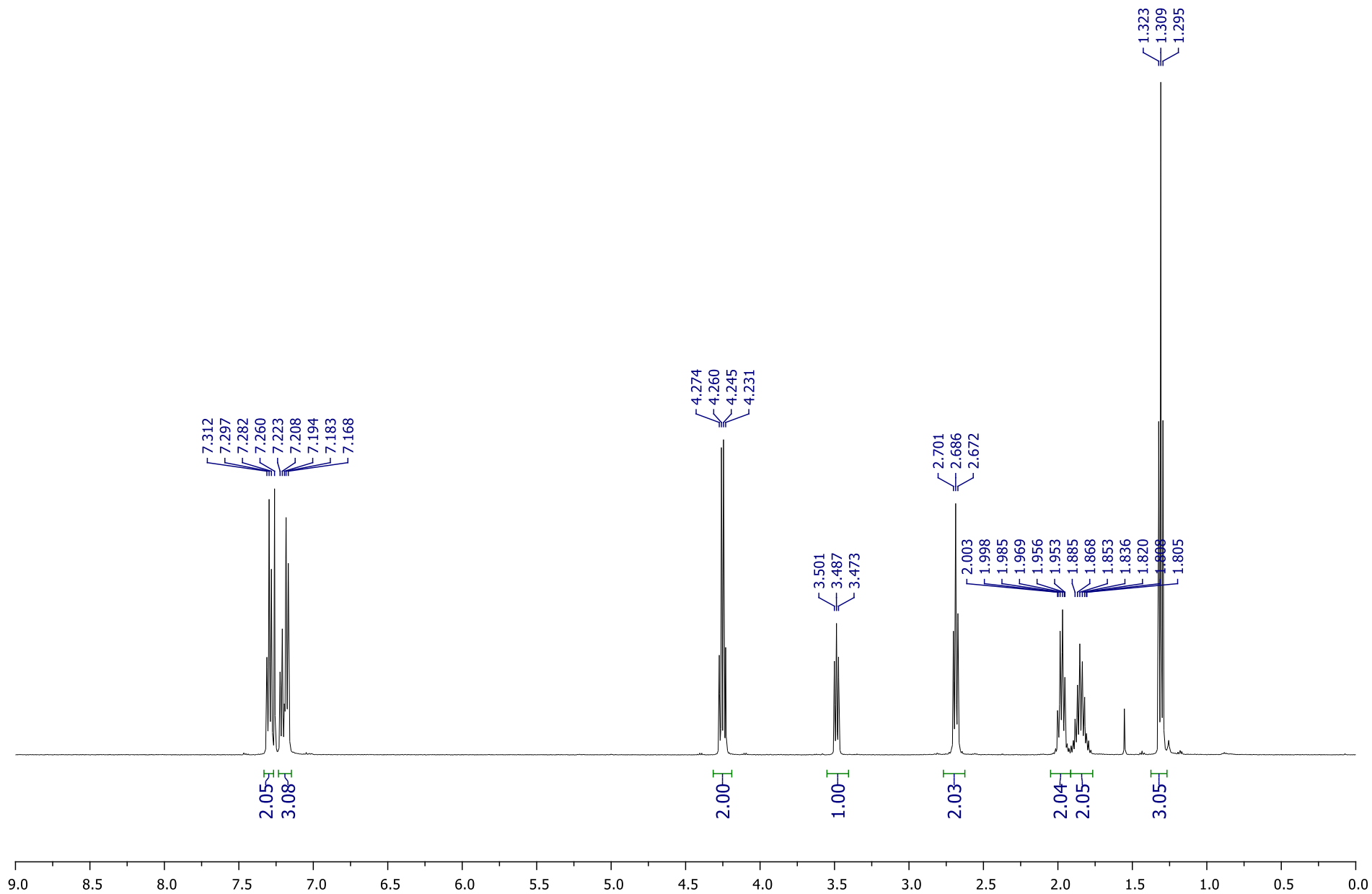
**8ar**

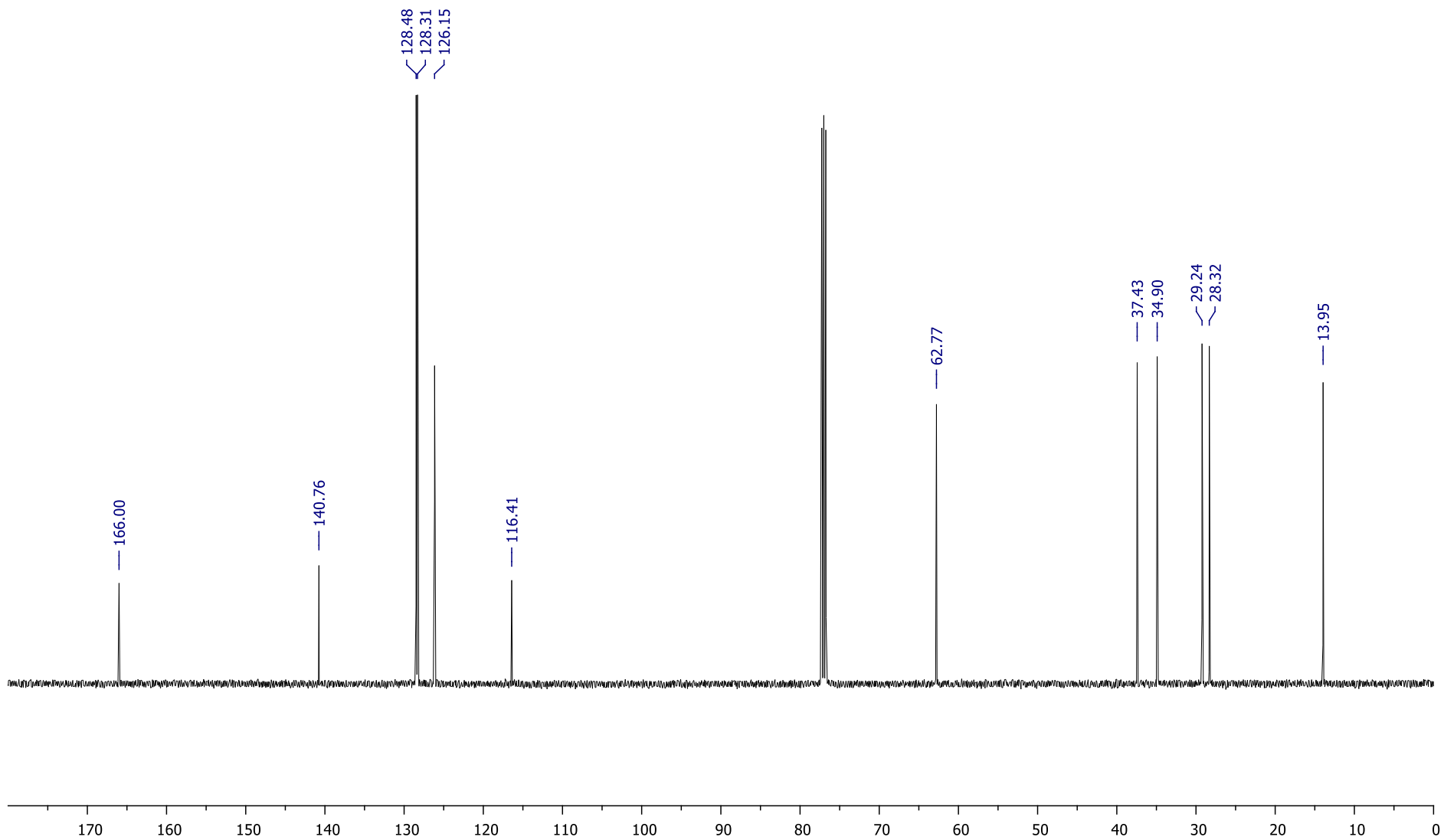
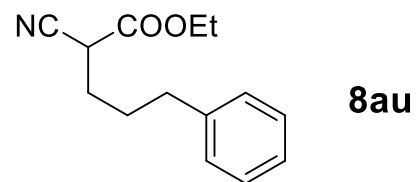
**8as**

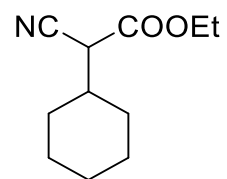
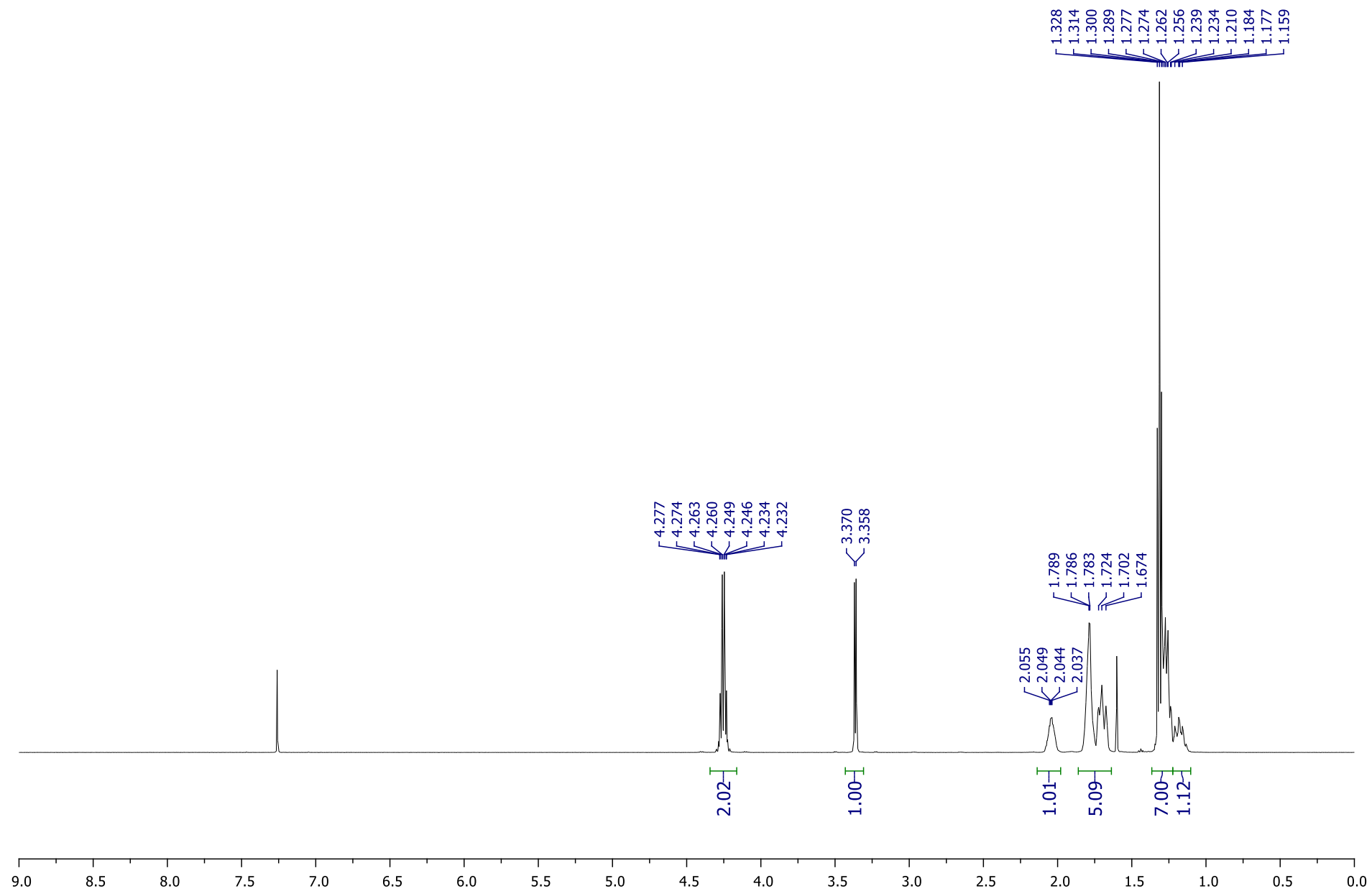
**8as**

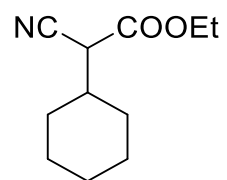
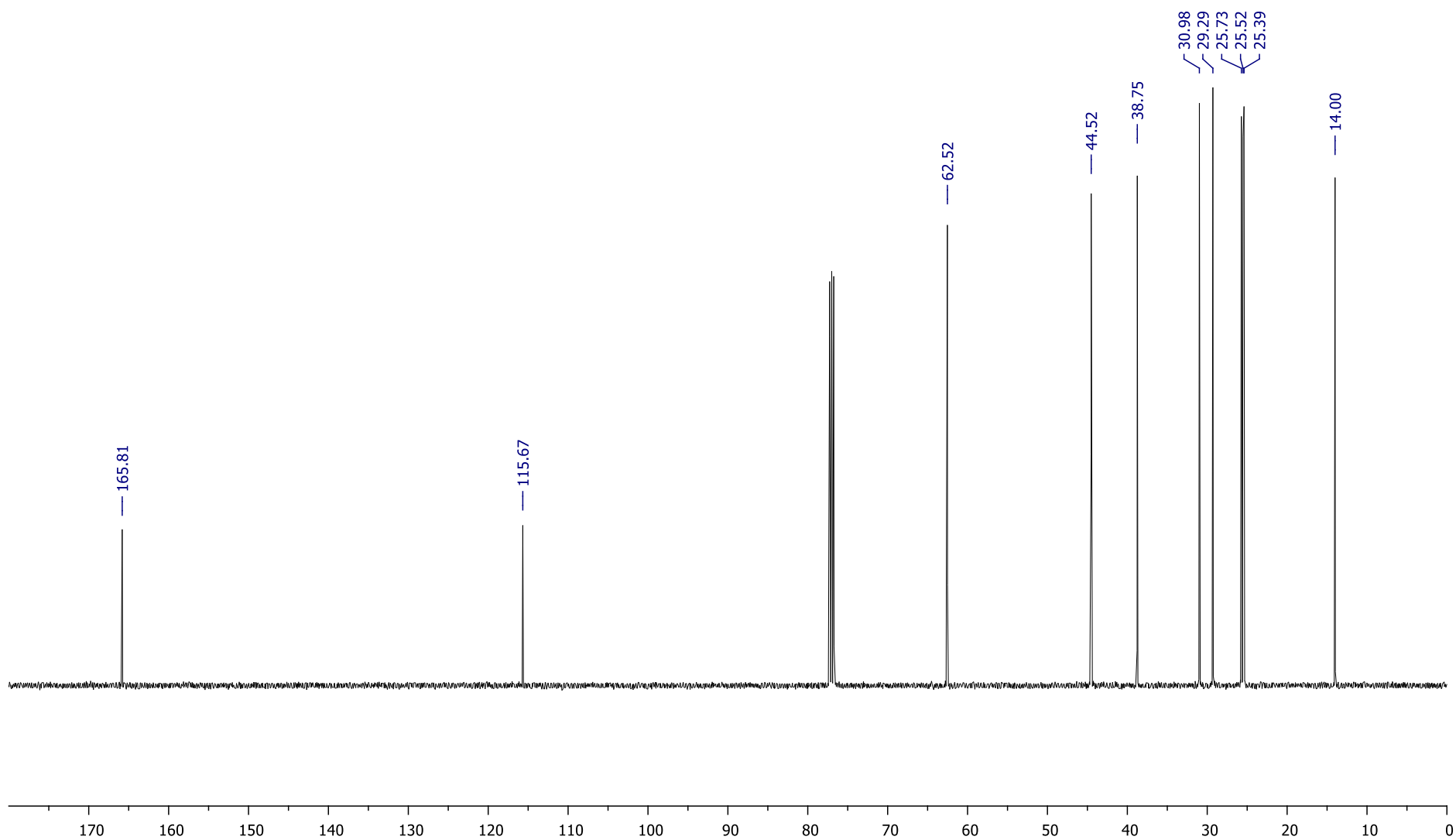
**8at**

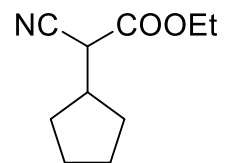
**8at**

**8au**

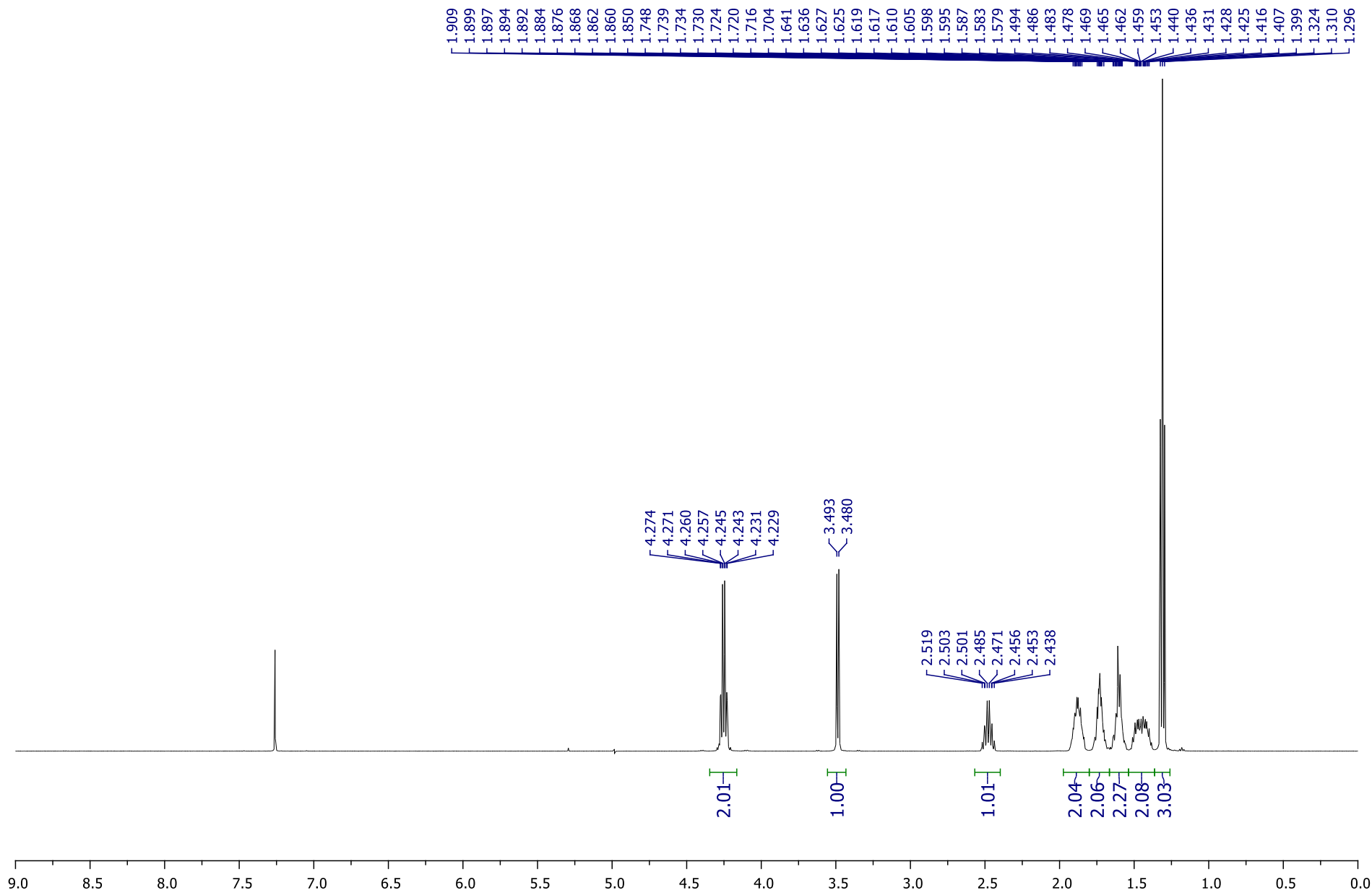


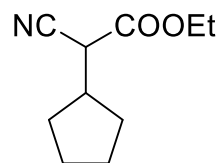
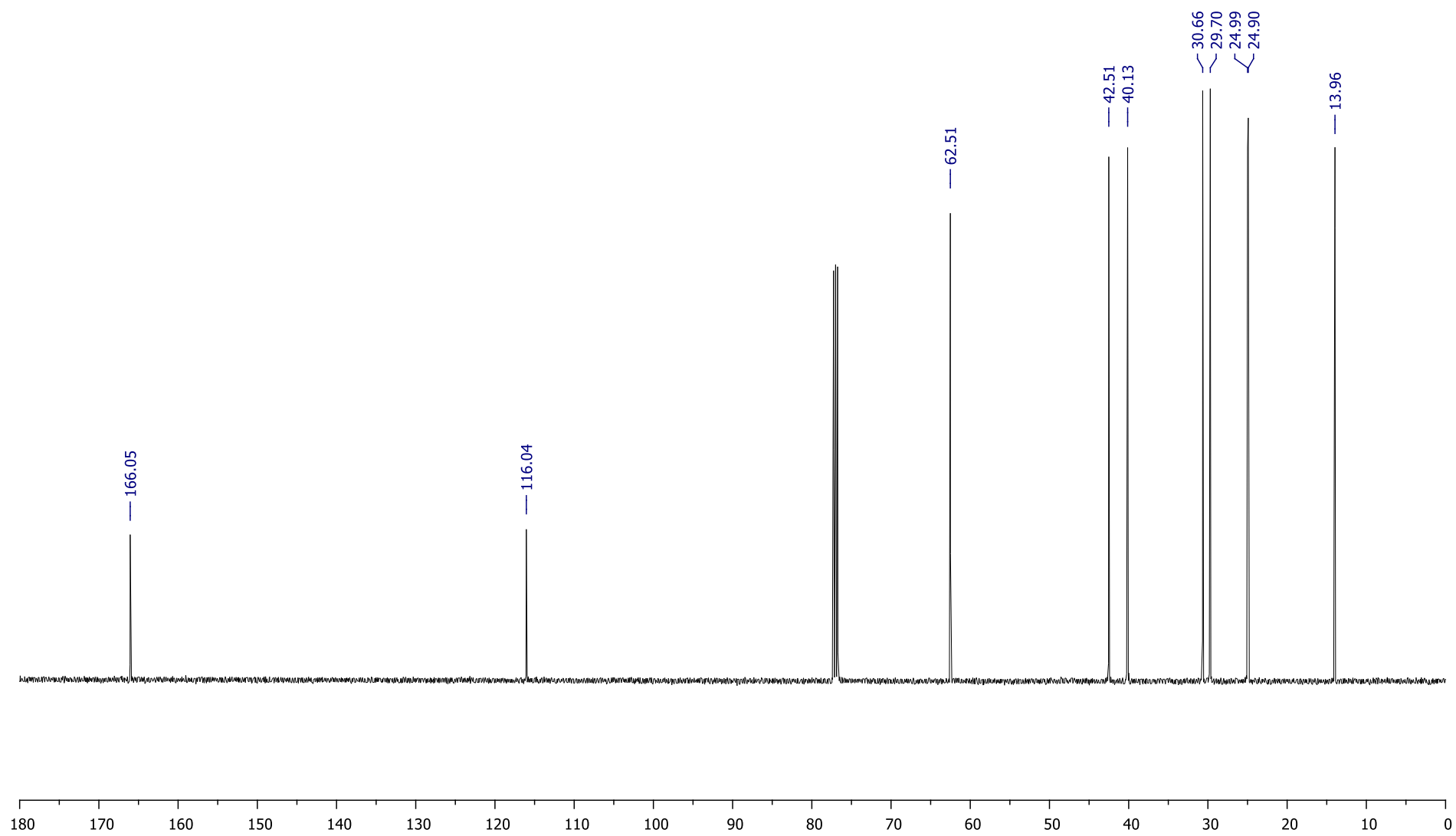
**8az**

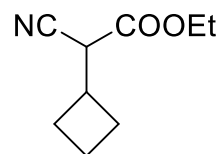
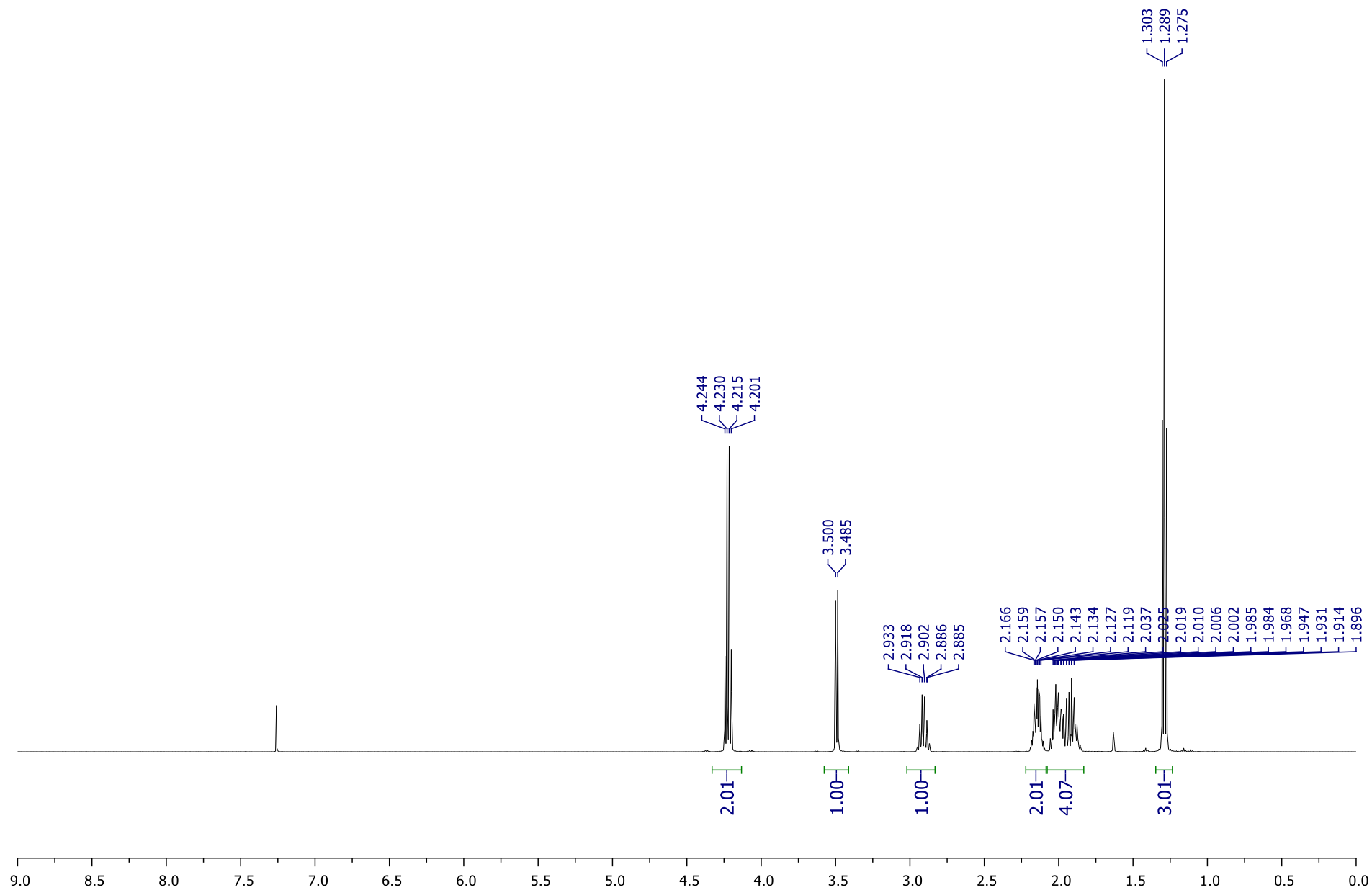
**8az**

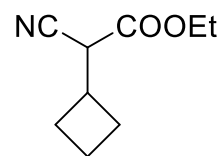
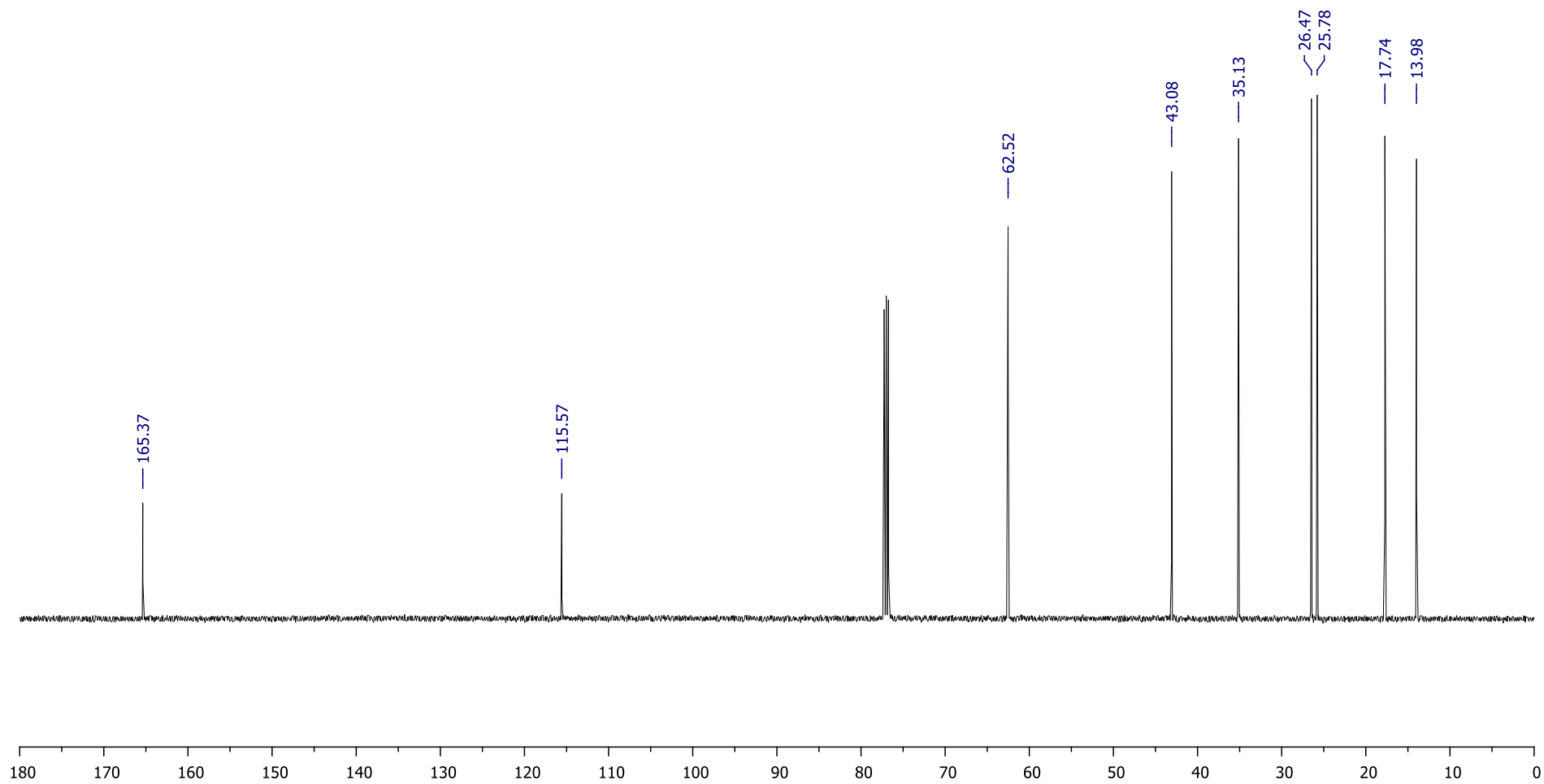


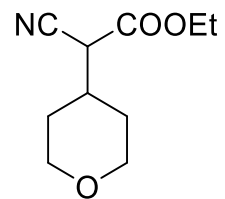
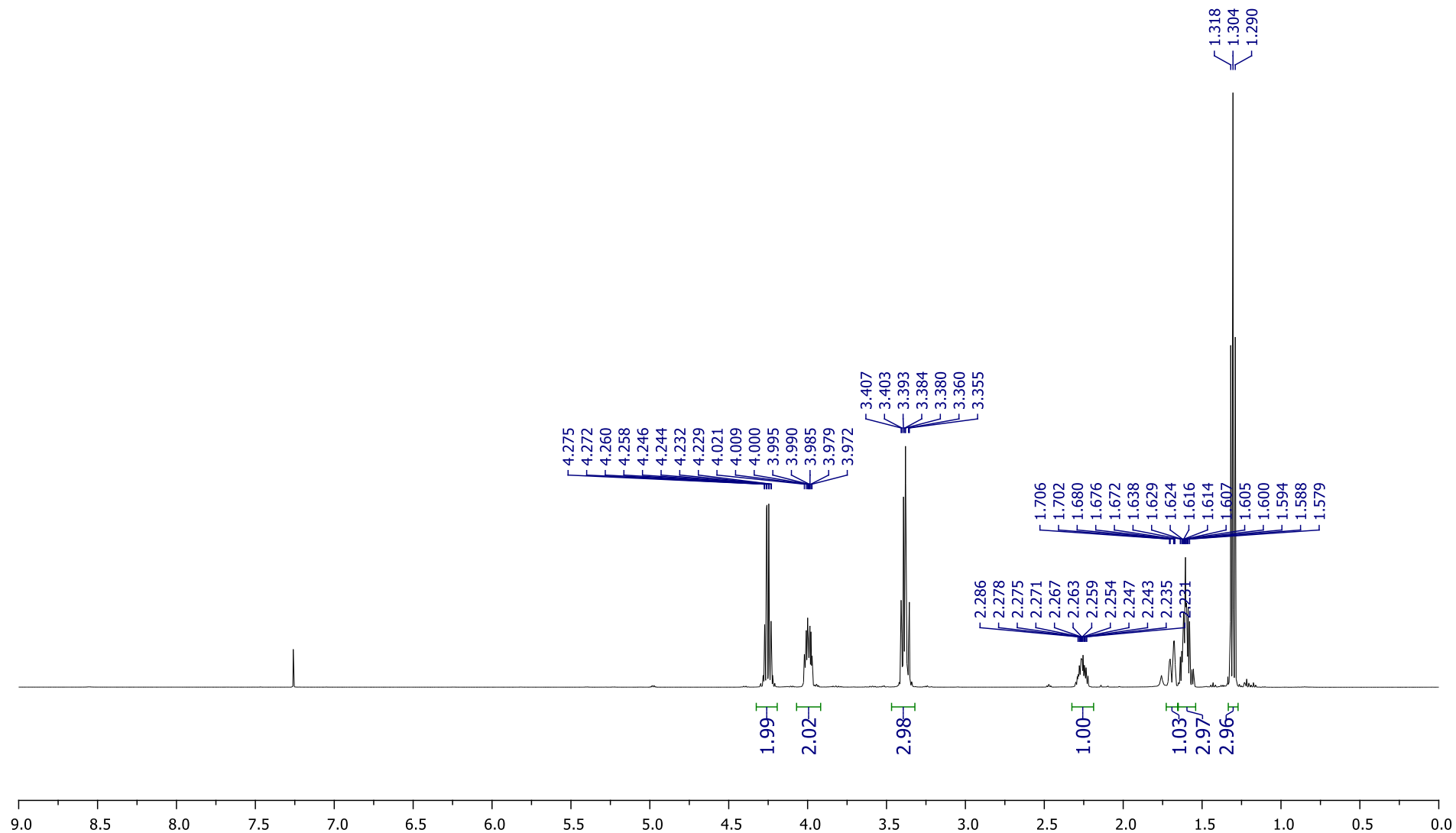
8aa'

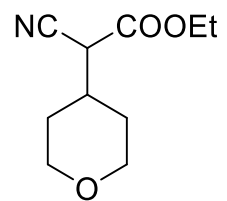
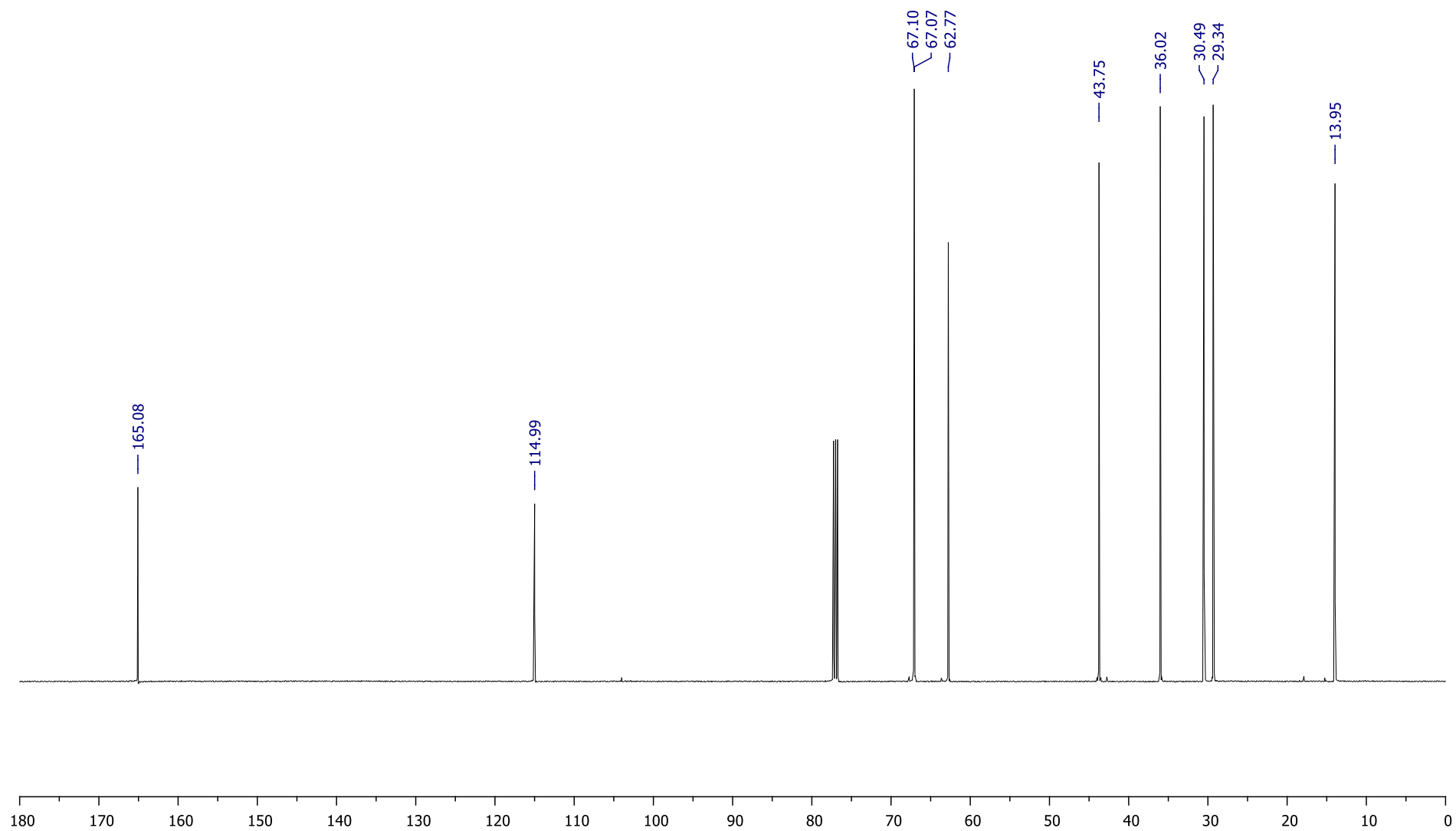


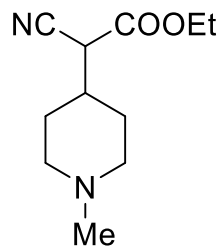
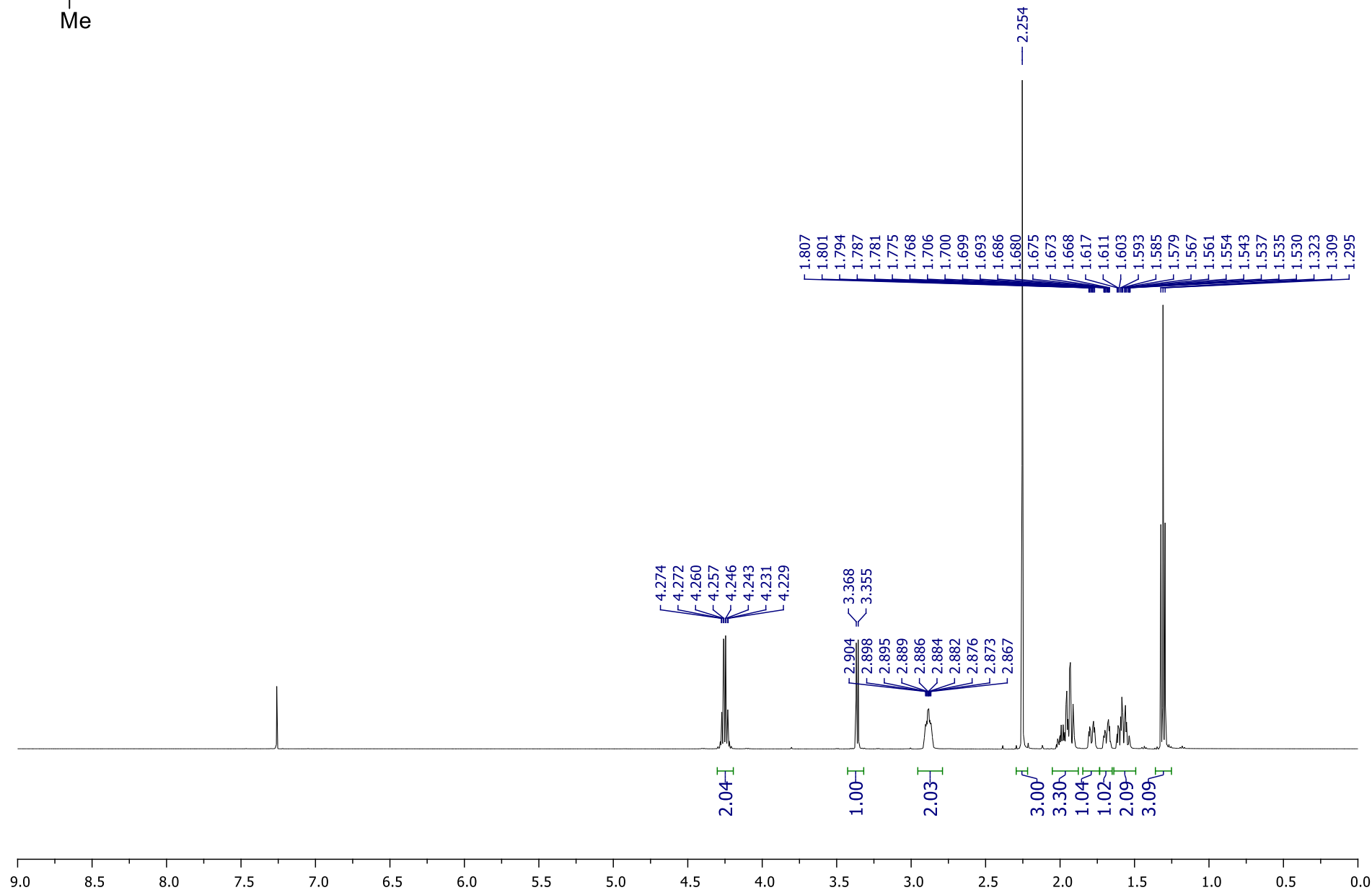
**8aa'**

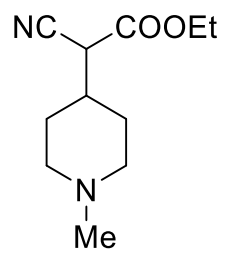
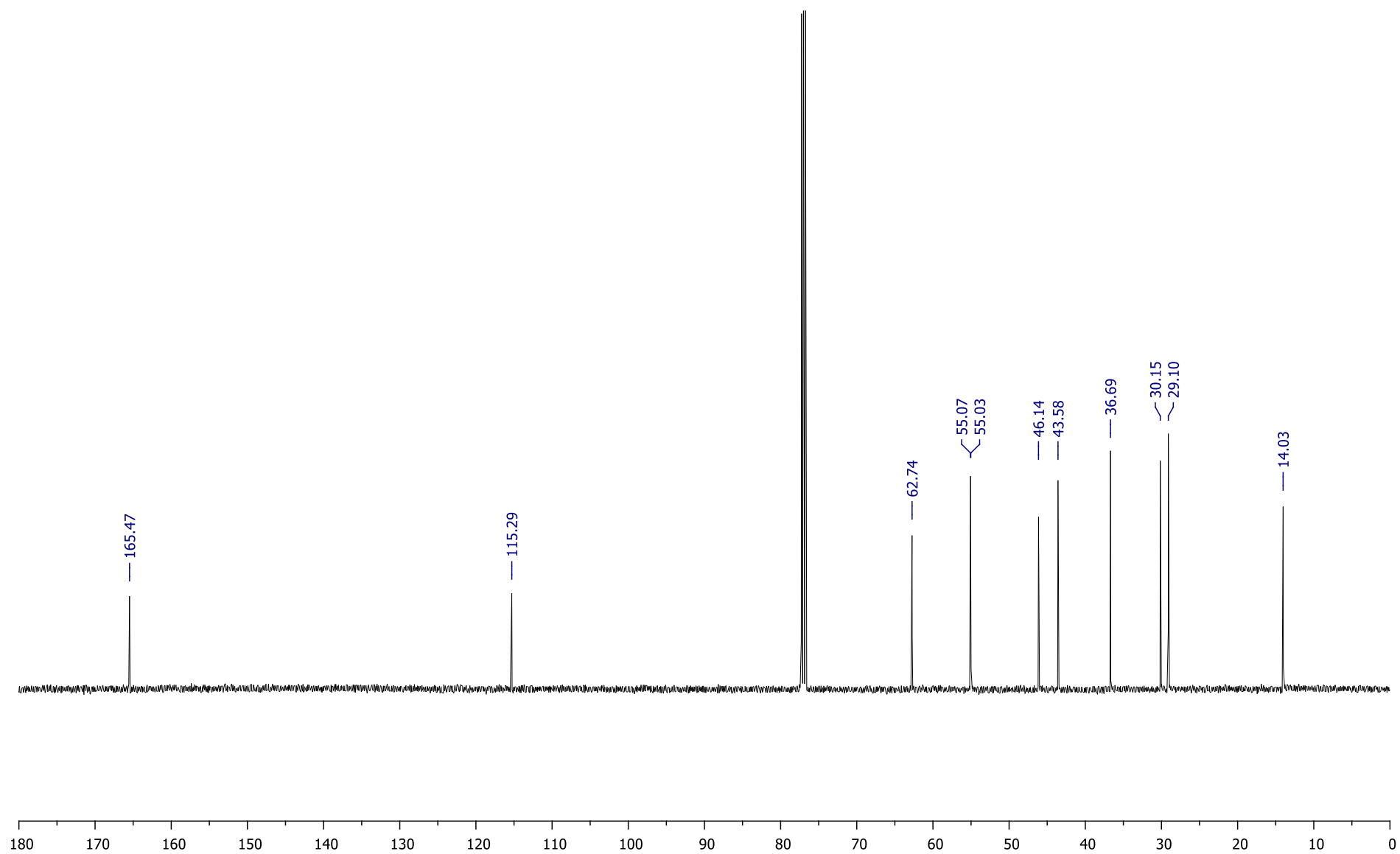
**8ab'**

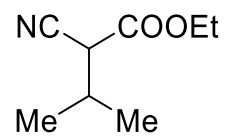
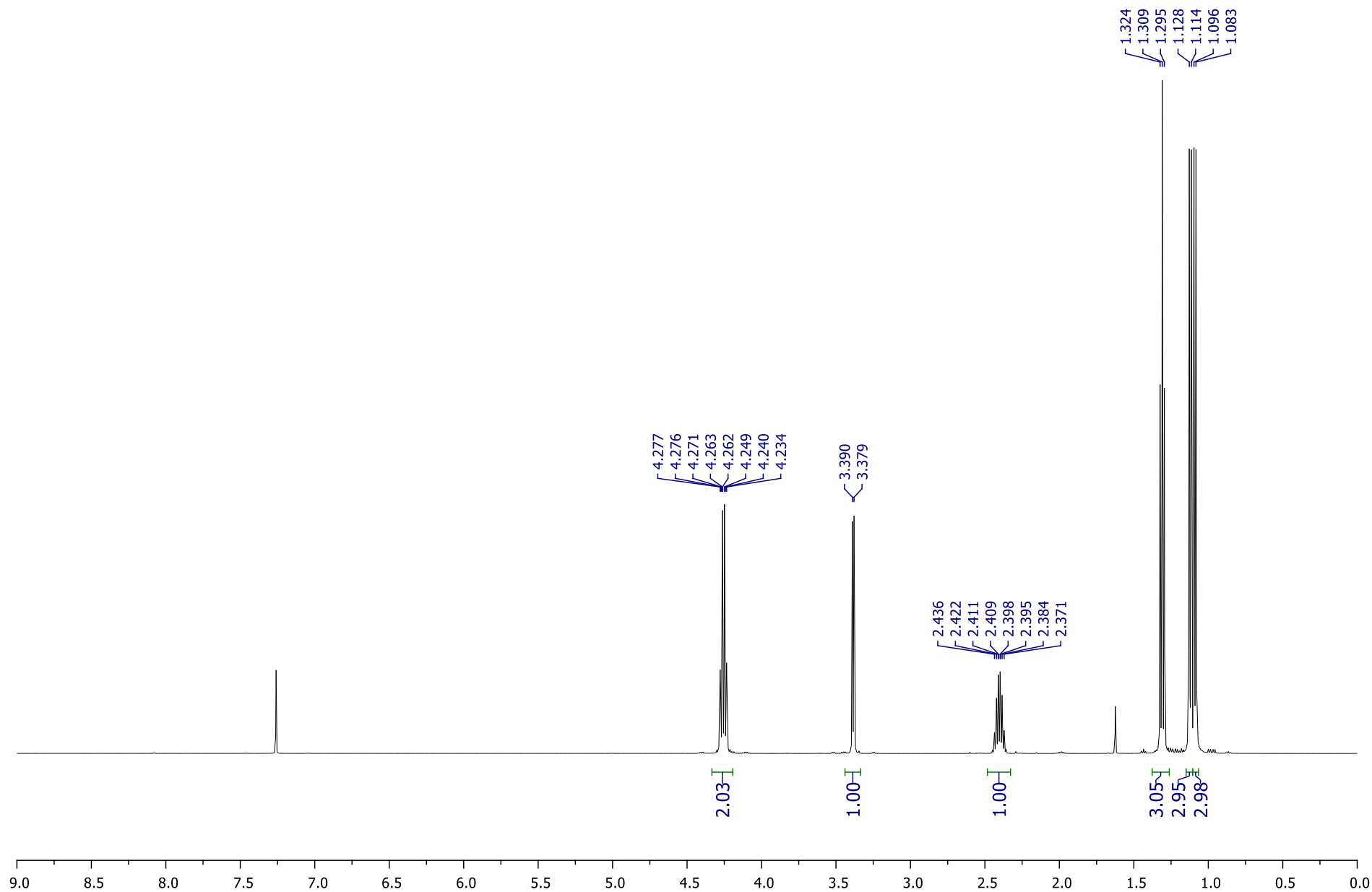
**8ab'**

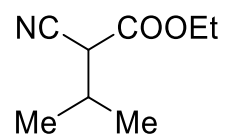
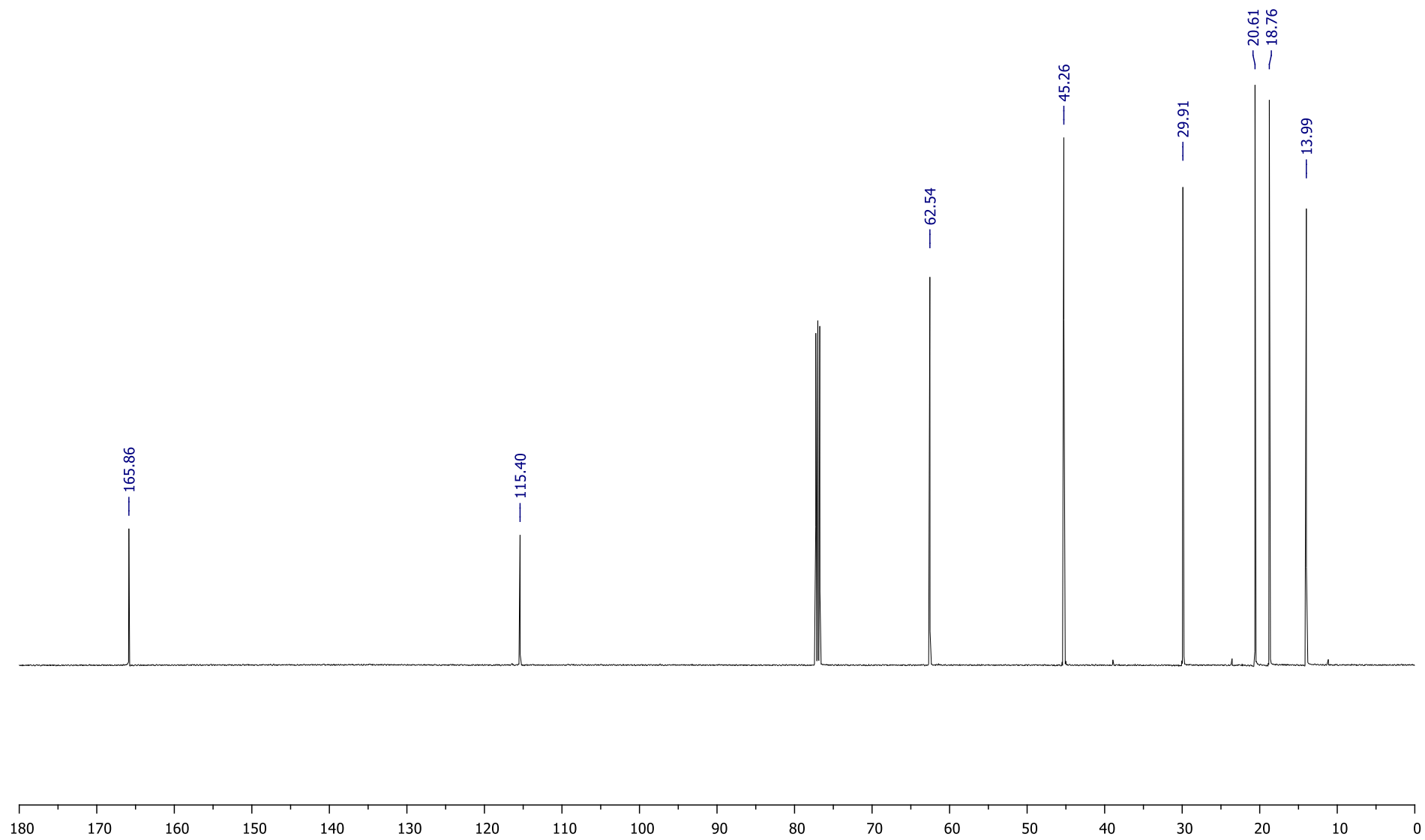
**8ac'**

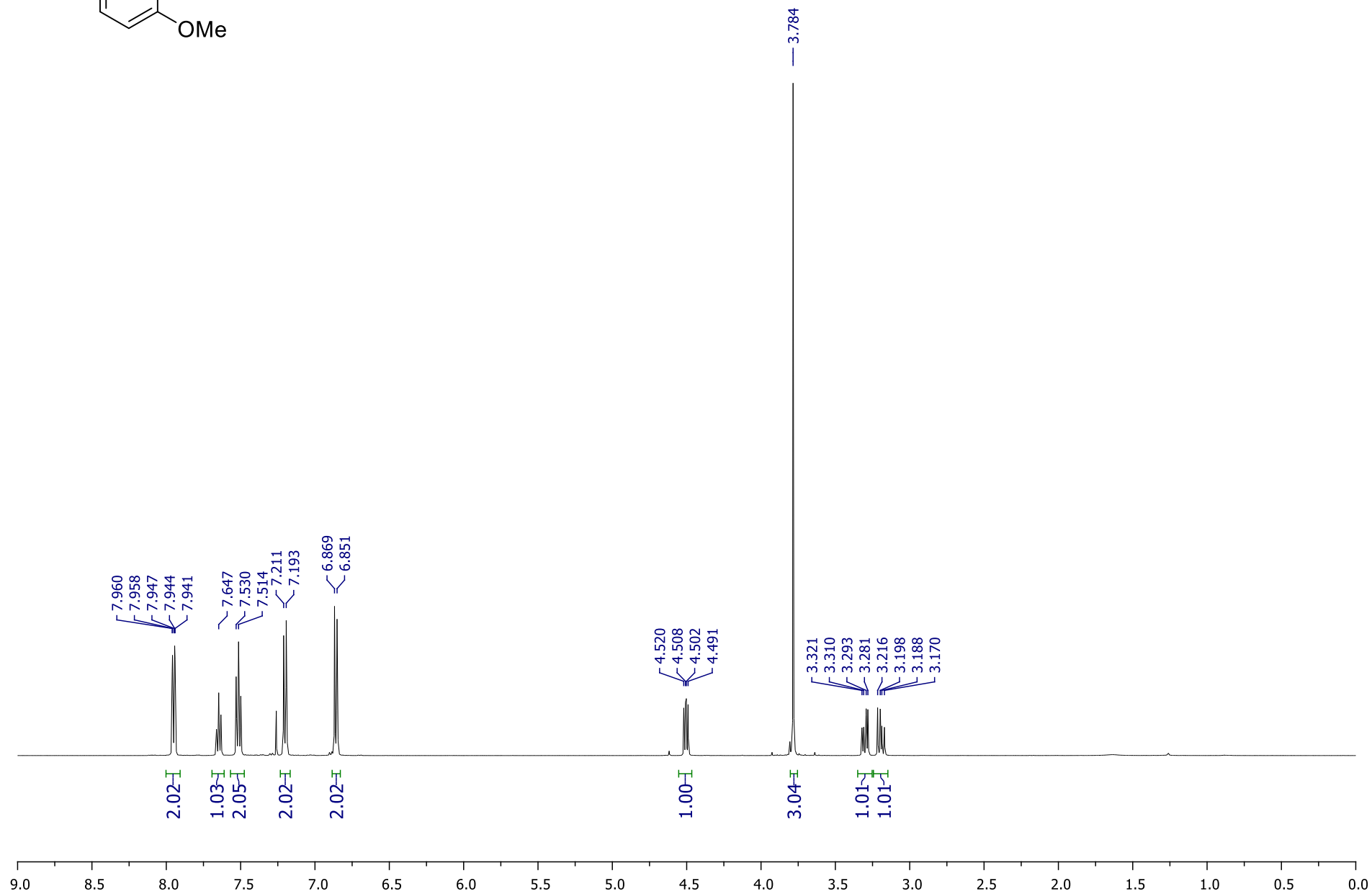
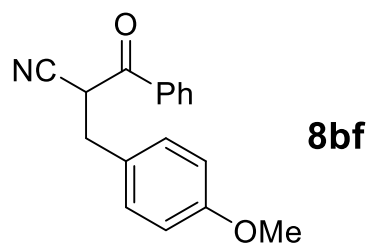
**8ac'**

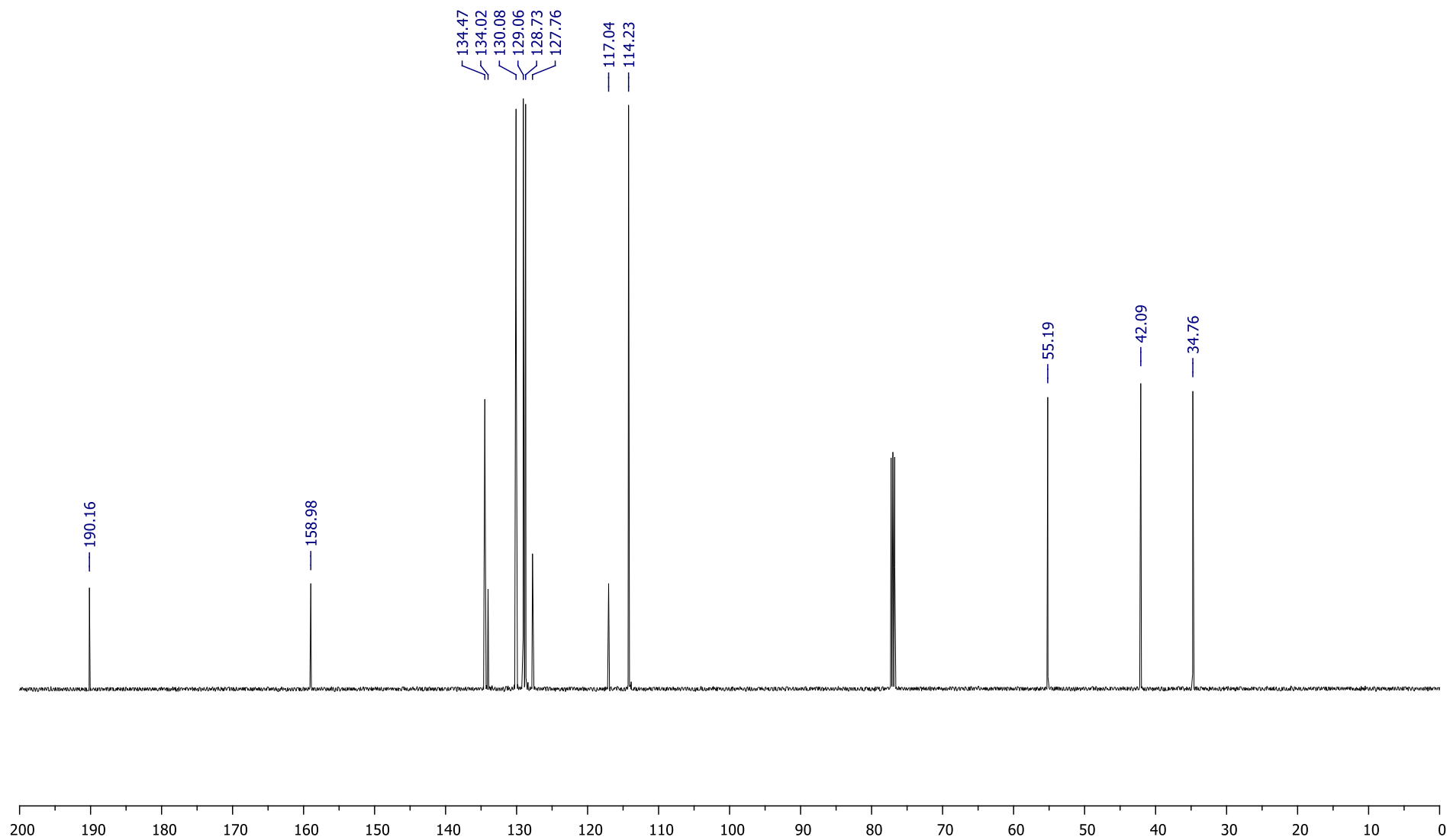
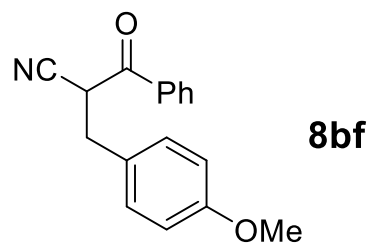
**8ad'**

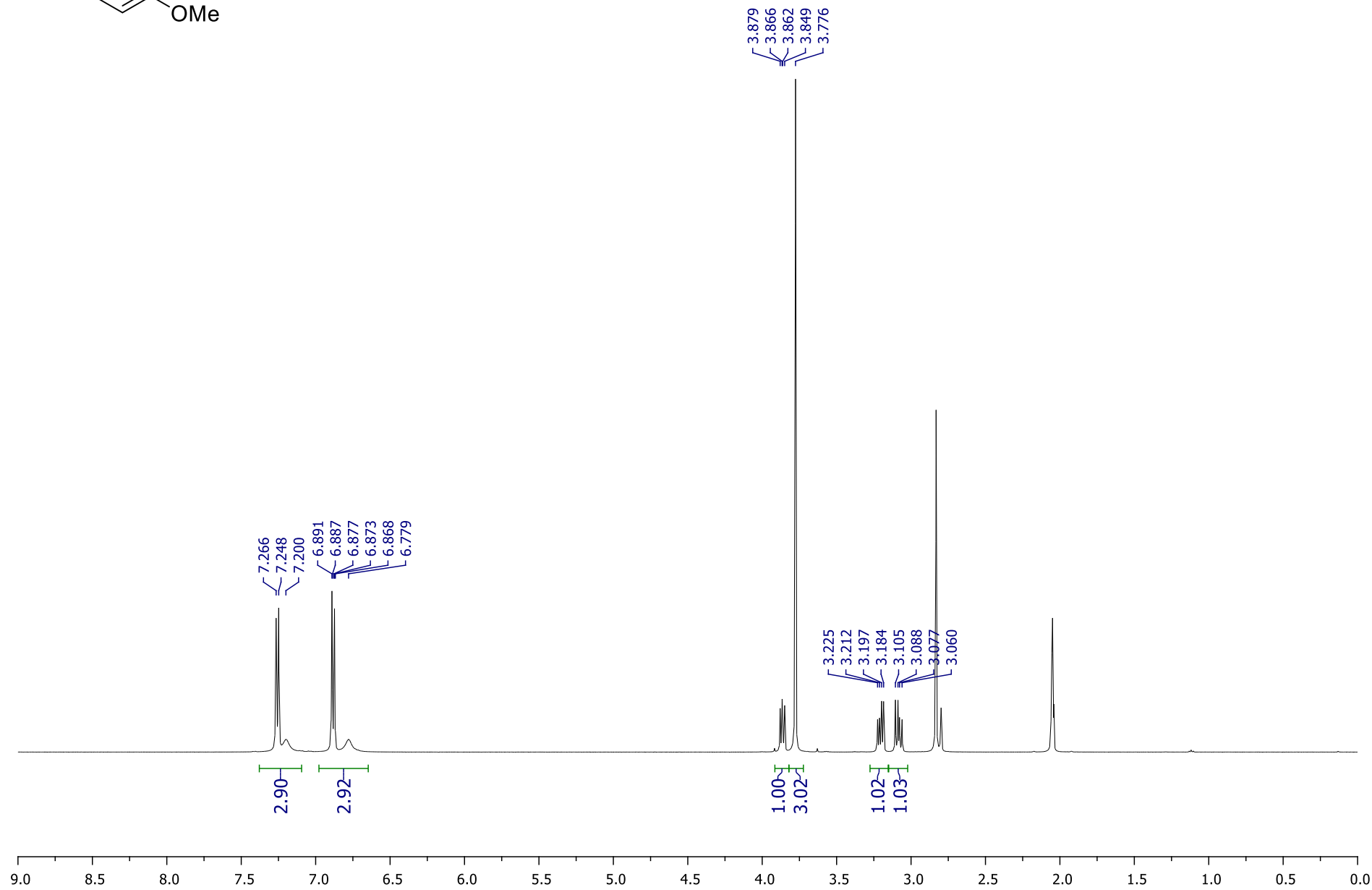
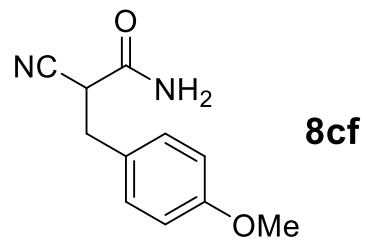
**8ad'**

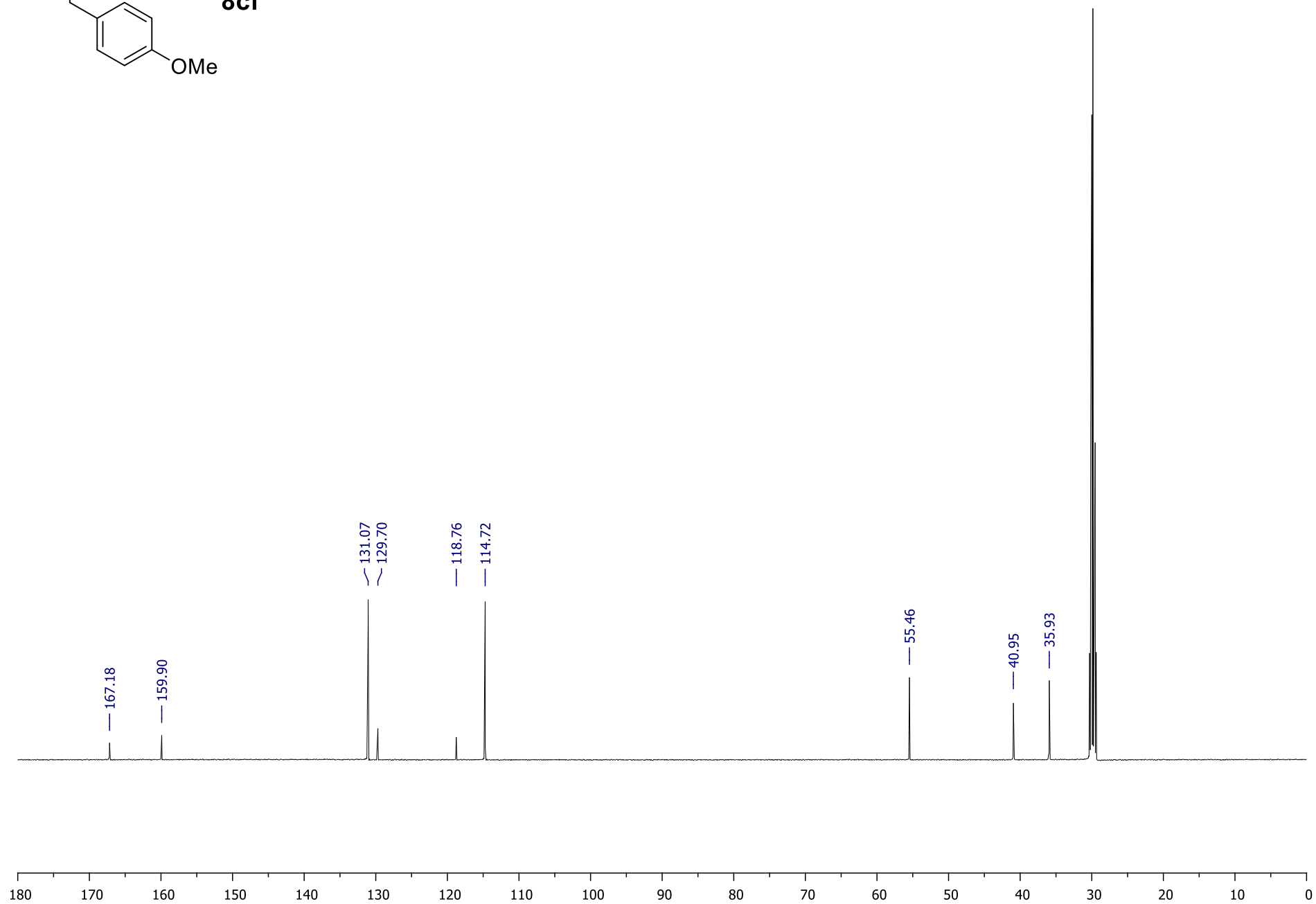
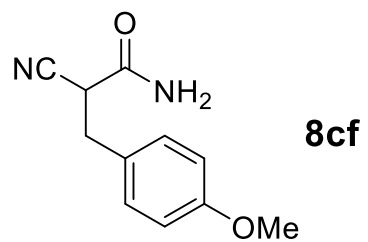
**8ae'**

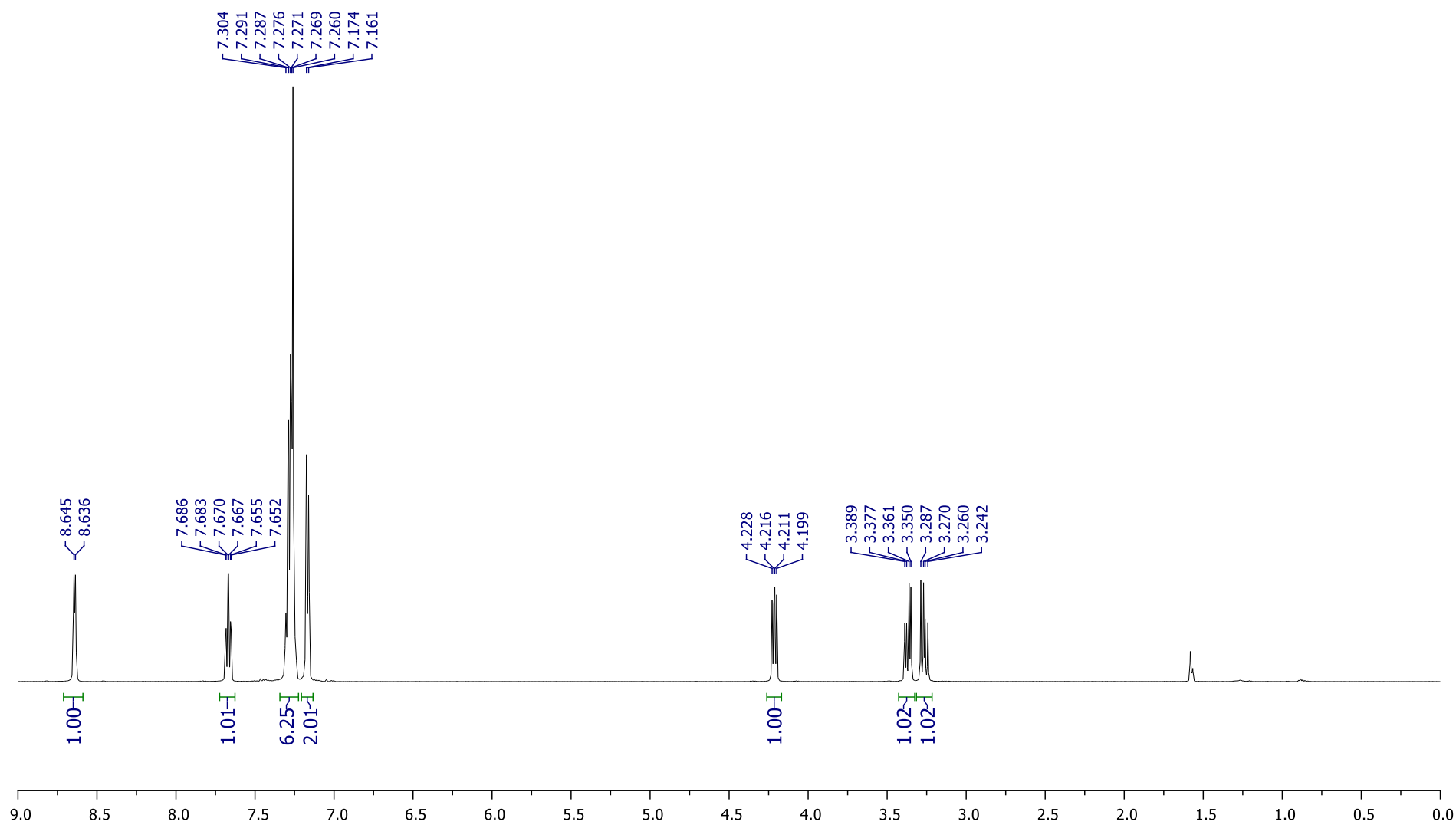
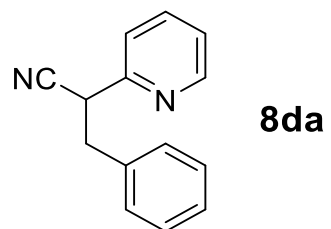
**8ae'**

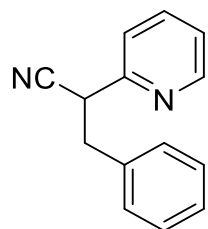
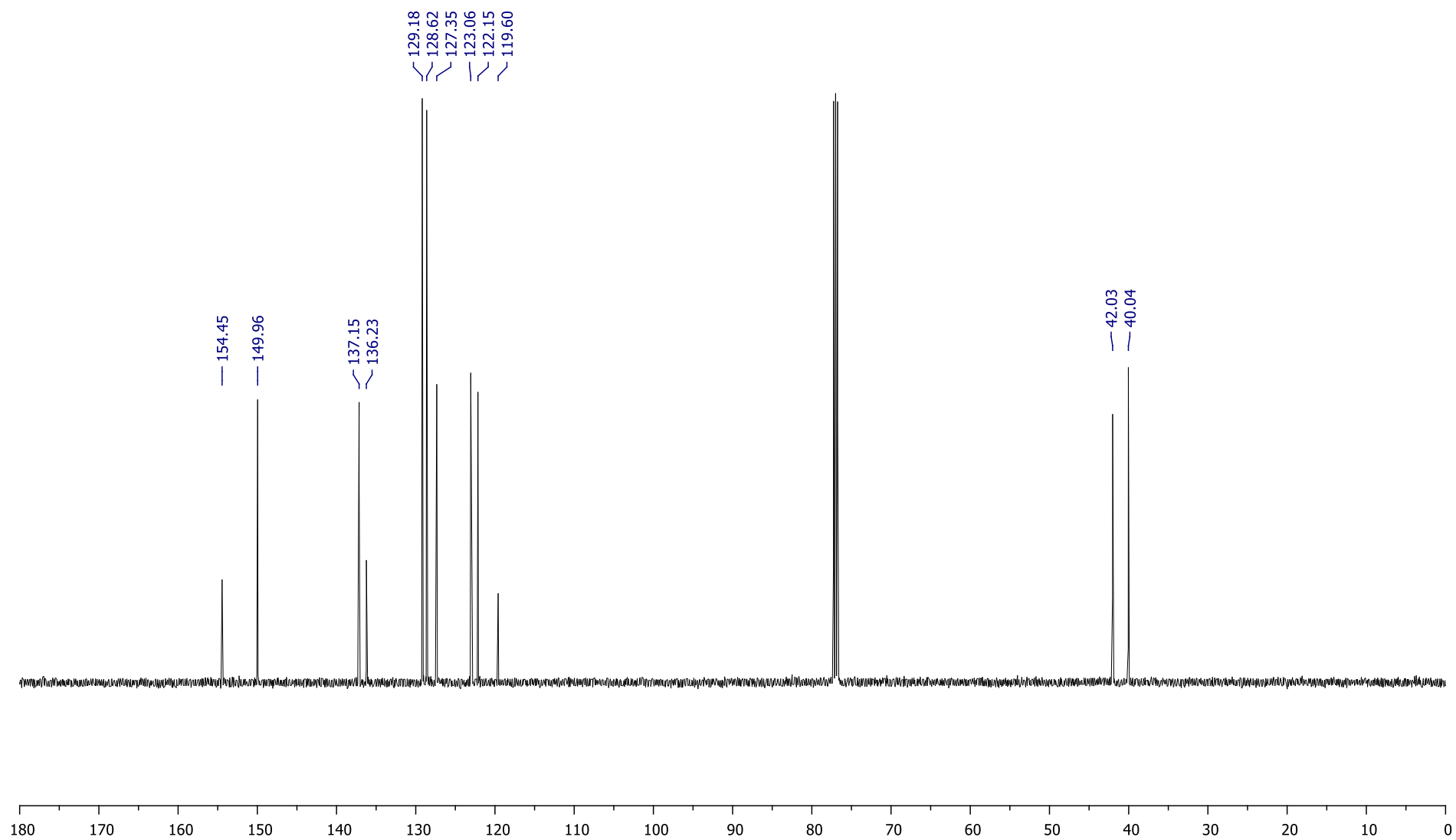


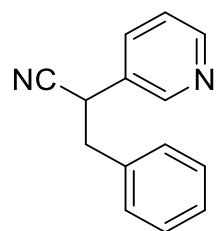




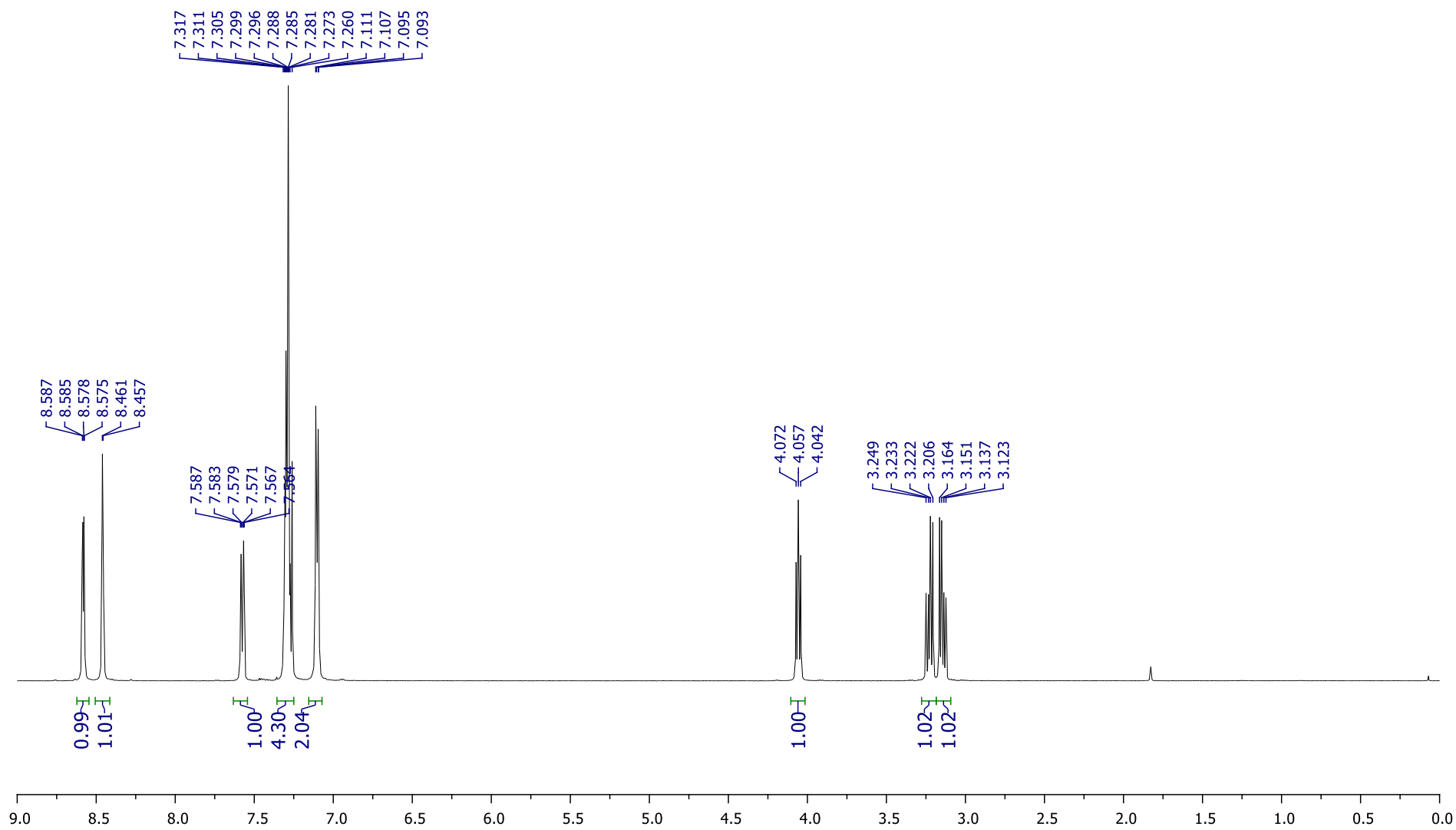


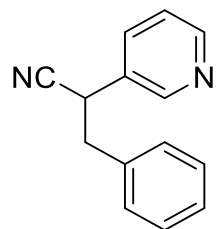
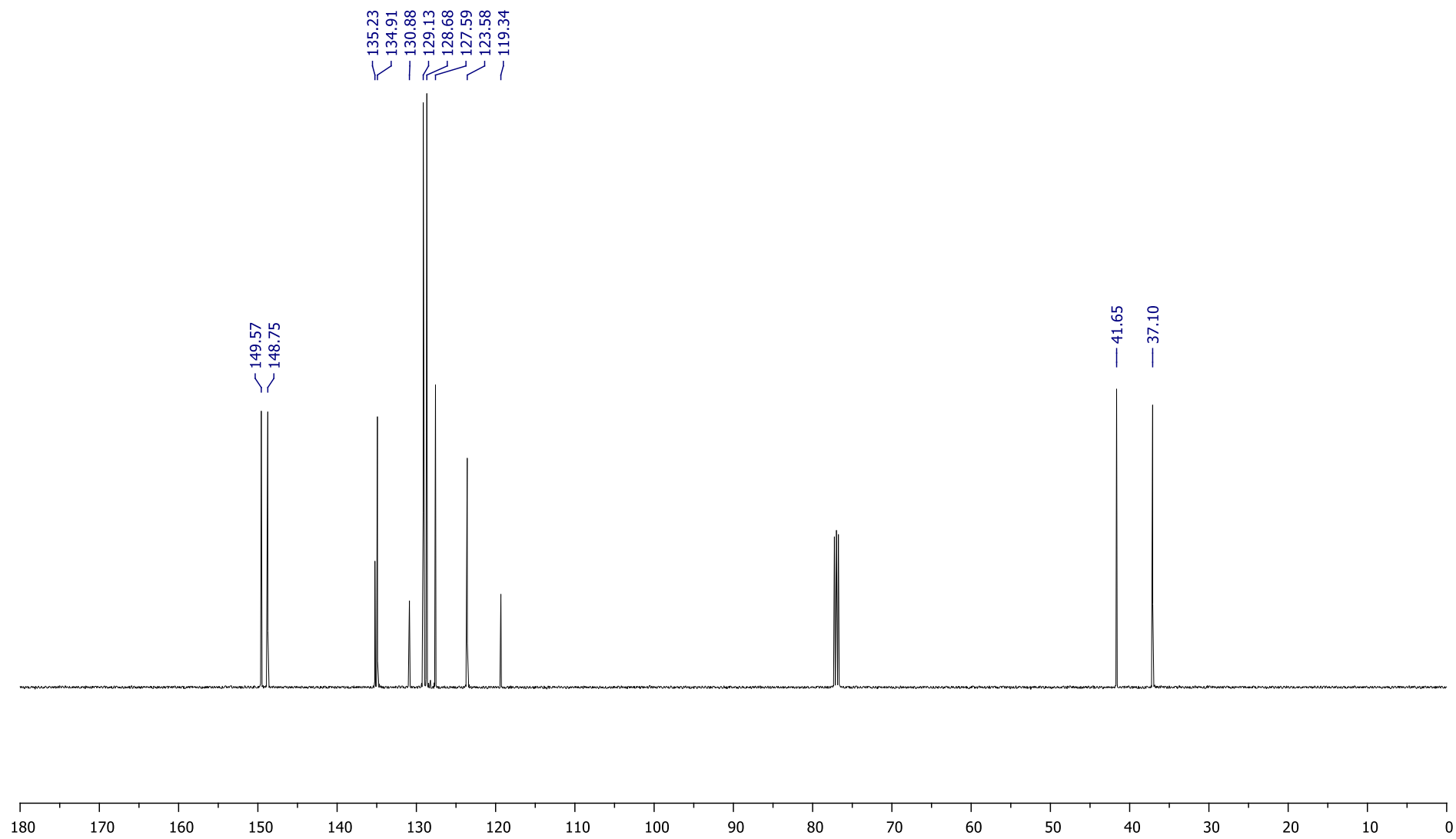


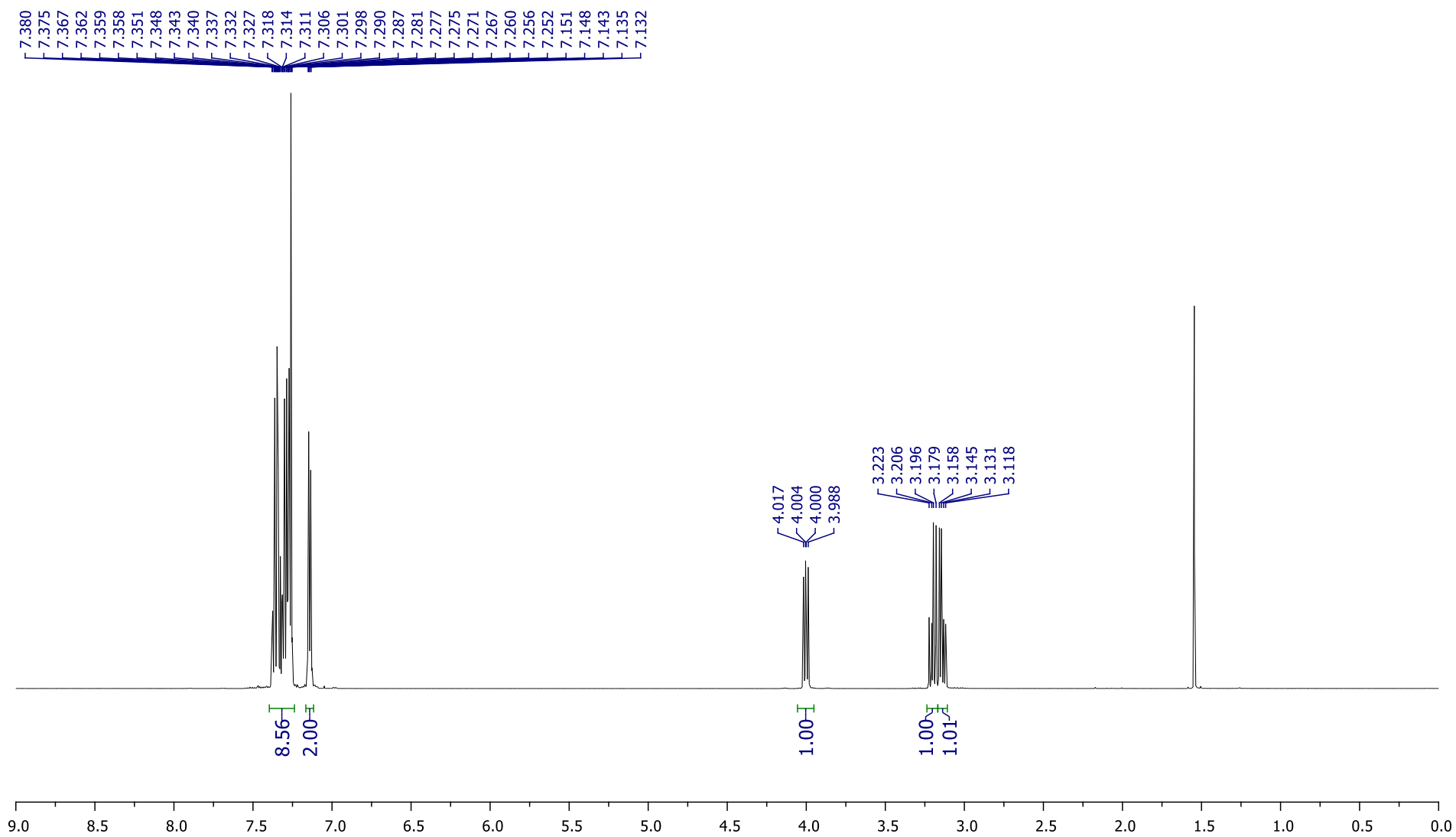
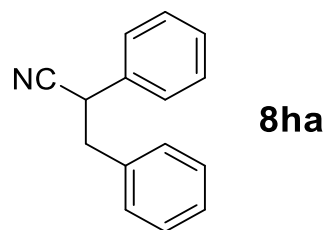
**8da**

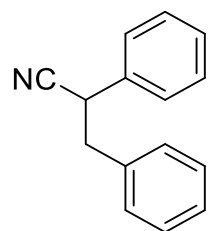
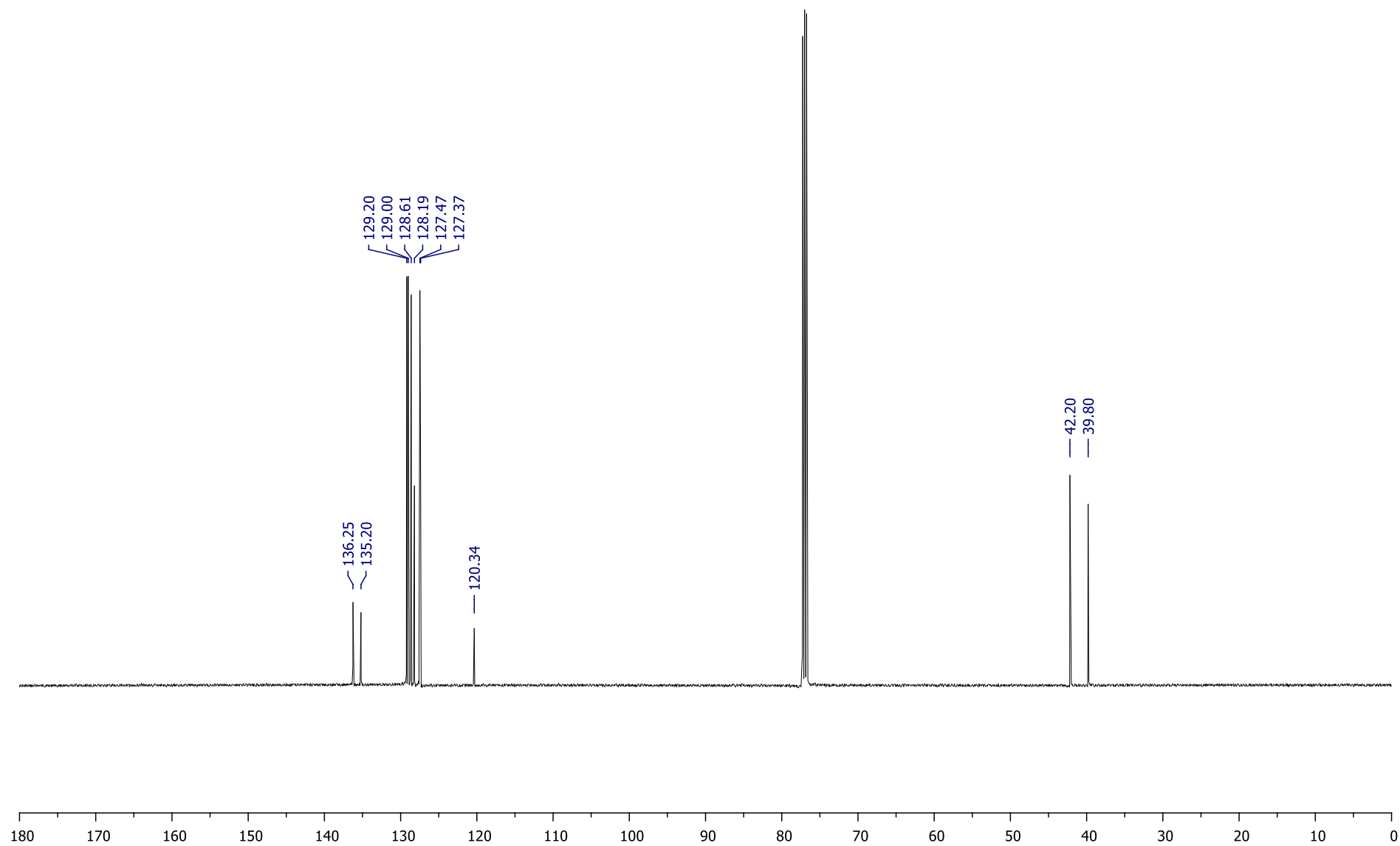


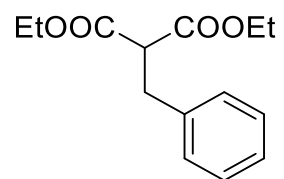
8ga



**8ga**



**8ha**

**8la**