

Stereoselective synthesis of 2,3,4-highly substituted oxetanes by intramolecular C–C bond forming Michael addition

Guo-Ming Ho,^{[a],[b]} and Yu-Jang Li*^[a]

^[a] Department of Applied Chemistry, National Chiayi university, 300, Syuefu Road, Chiayi City
600, Taiwan

^[b] Genomics Research Center, Academia Sinica, 128, Section 2, Academia Road, Taipei 115,
Taiwan

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I. General Experimental

NMR Spectroscopy: ^1H and ^{13}C NMR spectra were recorded on Varian Mercury 300 (300 MHz, ^1H ; 75 MHz, ^{13}C), Bruker AVIII 500 (500 MHz, ^1H ; 126 MHz, ^{13}C) or Bruker 600 (600 MHz, ^1H ; 151 MHz, ^{13}C) MHz nuclear magnetic resonance spectrometers. Spectra are referenced relative to residual CDCl_3 ($\delta = 7.26$ ppm, ^1H ; 77.00 ppm, ^{13}C) or C_6D_6 ($\delta = 7.15$ ppm, ^1H ; 128.00 ppm, ^{13}C). Data are reported as follows: chemical shift (multiplicity [s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = mutiple], integration, coupling constant (Hz) and assignment.) (J) refers to the observed coupling constant(s) in Hz. The chemical shift difference in Hz between the signals for protons A and B of an AB quartet is Du . As described in Silverstein, Bassler and Morrill's text, a four line two spin pattern was analyzed as shown in the figure below and by using the equation; $(a-c)=[(Du)^2+JAB^2]^{0.5}$. Letting $(a-c) = x$ and rearranging the equation solves for $Du=[(x)^2-JAB^2]^{0.5}$. For those examples where multiples were recognized as the A and B protons of AB_mx pattern, the chemical shift is reported as the midpoint of the multiplet.

Infrared Spectroscopy: Infrared spectra were recorded using a Bruker ALPHA FT-IR spectrometer equipped with an ATR accessory. Total reflection spectra (specular and diffuse reflection) were collected in-situ in the range of $4000\text{-}500\text{ cm}^{-1}$ at a resolution of 4 cm^{-1} over 24 scans, and were converted into transmission by Bruker OPUS 6.5 software. The time measurement was of 18 s (24 scans) per spectrum. After each measurement the ATR plate was washed with ethanol and dried using tissue paper. Infrared frequencies are reported in reciprocal centimeters (cm^{-1}).

Mass Spectrometry: Mass spectra were recorded on a VG-7035 mass spectrometer at an ionizing voltage of either 70 or 20 eV; alternatively, samples were analyzed by the Instrumental center of National Science Consul at National Chung Hsing University. Mass spectra are reported as m/z values for the parent peak M^+ and /or the major fragments. The values in parentheses refer to the relative peak intensities.

Chromatography: Reaction progress was monitored by analytical thin-layer chromatography on Analtech 250nm hard layer silica gel 60 F-250 plates cut into $1\text{ cm} \times 5\text{ cm}$ sections. Visualization was effected by ultraviolet light (254nm), followed by dipping the plate into the appropriate stain

and then charring on a hot plate. [15% (w/v) solvent of phosphoromolybdic acid and 95% ethanol (PMA)]. Flash chromatography was performed on silica gel 230-400 mesh, eluted with appropriate solvents.

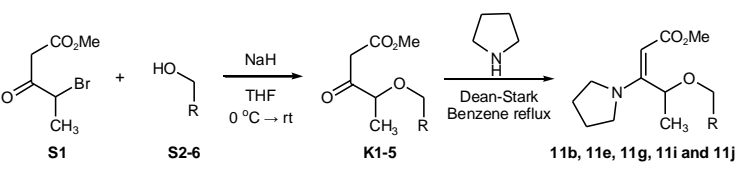
Reaction Setup: Reactions requiring heating were immersed in thermostat-controlled silicon-oil baths. The low temperature baths were dry ice/acetone ($-78\text{ }^{\circ}\text{C}$) and ice water ($4\text{ }^{\circ}\text{C}$). Reactions, which maintained at low temperature for extended periods of time, were kept in Neslab thermostat-controlled Cryobath with stirrer. Reactions other than those in which water was present as a solvent, reagent or by-product were normally performed under a slight positive pressure of nitrogen in vessels, which had been flame-dried under a slow nitrogen flow and sealed with rubber septa. The nitrogen gas was dried by passing it through a drying tube filled with Drierite®. Additions of liquid to the vessels were made via syringe or cannula through septa. Solids were added through open septa. All reactions were stirred with Teflon-coated magnetic stir bars. Removal of solvents was normally accomplished using a Jasco rotary evaporator connected to a vacuum pump.

Solvents and reagents: The following solvents were distilled directly before use, under a slight positive pressure of nitrogen. Diethyl ether, tetrahydrofuran and benzene were distilled from sodium benzophenone ketyl. Dichloromethane and diisopropyl amine were distilled from calcium hydride prior to use. Reagents were purchased from the Aldrich, Fluka, and Acros chemical companies.

II. Experimental Procedures

Secondary γ -allyloxy substituted vinylogous urethanes were prepared from two different sequential approaches. As depicted in **Table S1** and **S2**. Williamson ether synthesis of methyl 4-bromoketoester **S1** with alcohols **S2-6** provided ketoesters **K1-5** in 72%-83% yields, respectively (**Table S1**, entries 1-5). Subsequent condensed with pyrrolidine utilizing Dean-Stark apparatus to provide desired vinylogous urethanes **11b**, **11e**, **11g**, **11i** and **11j** in 98%-99% yields (**Table S1**, entries 1-5). Alternatively, an efficient one-pot reaction can directly convert propargylic alcohols **S7**, **S8**, **S9** and **S10** to corresponding acetylenic esters **E1-9** in 65%-83% yields, respectively (**Table S2**, entries 1-9). Following exposed to pyrrolidine to give desired vinylogous urethanes **11a**, **11c**, **11d**, **11f**, **11h**, **11k**, **11l**, **11m** and **11n** in 98%-99% yields (**Table S2**, entries 1-9).

Table S1 | Preparations of ketoesters and their corresponding vinylogous urethanes.



Entry ^[a]	R	Ester	Yield ^[b]	VU	Yield ^[c]
1	CH=CH ₂	K1	80%	11b	98%
2	C(Me)=CH ₂	K2	77%	11e	99%
3	(<i>E</i>)-CH=CH(CH ₂) ₂ CH ₃	K3	74%	11g	98%
4	(<i>Z</i>)-CH=CH(CH ₂) ₂ CH ₃	K4	72%	11i	98%
5	Ph	K5	83%	11j	98%

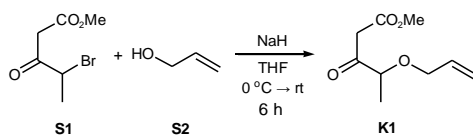
[a] The ketoesters **K1-5** and **S1** were prepared according to literature procedure^[1]. [b] Yields of isolated ketoesters **K1-5** were given after column chromatograph. [c] Pyrrolidine added to a solution of ketoester in benzene followed by heating to reflux for 30 minutes, and yields of VUs were given by directly removed solvent under *vacuo* without further purifications.

Table S2 | Preparations of acetylenic esters and their corresponding vinylogous urethanes.

Entry ^[a]	R ¹	R ²	Ester	Yield ^[b]	VU	Yield ^[c]
1	CHMe ₂	CH=CH ₂	E1	76%	11a	99%
2	cC ₆ H ₁₁	CH=CH ₂	E2	81%	11c	99%
3	CH ₂ CHMe ₂	CH=CH ₂	E3	74%	11d	99%
4	CHMe ₂	C(Me)=CH ₂	E4	76%	11f	99%
5	(CH ₂) ₄ CH ₃	(<i>E</i>)-CH=CH(CH ₂) ₂ CH ₃	E5	70%	11h	99%
6	CHMe ₂	Ph	E6	82%	11k	98%
7	cC ₆ H ₁₁	Ph	E7	83%	11l	99%
8	CH ₂ CHMe ₂	Ph	E8	77%	11m	99%
9	CHMe ₂	naphth	E9	65%	11n	98%

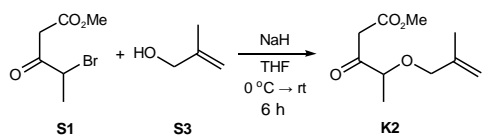
[a] The acetylenic esters **E1-9**^[2] and propargylic alcohols **S7**^[3], **S8**^[4], **S9**^[3] as well as **S10**^[5] were prepared according to literature procedures. [b] Yields of isolated acetylenic esters **E1-9** were given after column chromatograph. [c] Pyrrolidine added to a solution of acetylenic ester in *tert*-butanol followed by heating to reflux for 30 minutes, and yields of VUs were given by directly removed solvent under *vacuo* without further purifications.

General procedure for the synthesis of ketoesters.



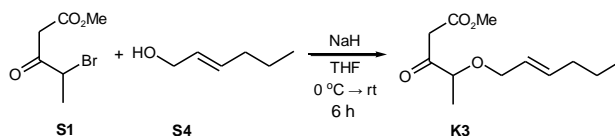
Synthesis of methyl 4-(allyloxy)-3-oxopentanoate (K1). Ketoesters were prepared by literature reported procedure^[1]. To NaH (0.43 g, 60%, 10.6 mmol, pre-washed with *n*-hexane) in a flame-

dried 50 mL round-bottomed three-necked flask with THF (12 mL) at 0 °C was added dropwise a solution of methyl 4-bromo-3-oxopentanoate **S1** (1.0 g, 4.81 mmol, 1.0 equiv.) in THF (4 mL). The reaction mixture was stirred for 30 min at 0 °C, after which a solution of allyl alcohol **S2** (0.36 mL, 5.30 mmol, 1.1 equiv.) in THF (2 mL) was added dropwise into the reaction. The reaction mixture was allowed to warm to room temperature slowly, and stirred for additional 6 hours at ambient temperature. The reaction was quenched by the slow addition of water (20 mL), the reaction mixture was acidified with aqueous HCl (1 M) to pH 4.0, and then extracted with EtOAc (10 mL × 2). The combined organic layer was washed with brine, then dried over anhydrous sodium sulfate, and concentrated to give crude material. Purification by flash column chromatography (*n*-hexane/EtOAc, 10:1) afforded product **K1** as a pale-yellow oil in 80% yield (0.72 g). $R_f = 0.46$ (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3012, 2985, 2954, 2870, 1749, 1722, 1659, 1631, 1438, 1321, 1264, 1228, 1117, 997, 841, 741 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 5.89 (ddt, $J = 17.2, 10.4, 5.6$ Hz, 1H, vinylic H), 5.29 (dd, $J = 17.2, 1.6$ Hz, 1H, geminal-H), 5.21 (dd, $J = 10.4, 1.6$ Hz, 1H, geminal-H), 4.02 (dd, $J = 5.6, 4.2$ Hz, 2H, allylic H), 3.96 (q, $J = 6.8$ Hz, 1H, methine-H), 3.73 (s, 3H, CO₂Me), 3.64 (ABq, $J = 16.2$ Hz, 1H, methylene-H), 3.56 (ABq, $J = 16.2$ Hz, 1H, methylene-H), 1.33 (d, $J = 6.8$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 205.5 (C), 167.8 (C), 133.7 (CH), 117.7 (CH₂), 80.2 (CH), 70.8 (CH₂), 52.3 (CH₃), 44.4 (CH₂), 16.8 (CH₃); **HRMS-EI** calcd for C₉H₁₄O₄, 186.0892 found 186.0899.

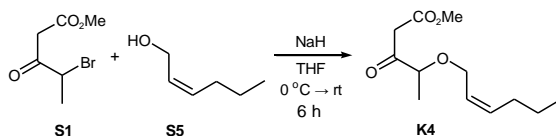


Methyl 4-(2-methylallyloxy)-3-oxopentanoate (K2). Prepared according to the general procedure with NaH (0.43 g, 60%, 10.6 mmol), methyl 4-bromo-3-oxopentanoate **S1** (1.0 g, 4.81 mmol, 1.0 equiv.) and methallyl alcohol **S3** (0.45 mL, 5.30 mmol, 1.1 equiv.) for 6 hours to give product **K2** as a pale-yellow oil in 77% yield (0.74 g). $R_f = 0.47$ (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3010, 2984, 2951, 1752, 1723, 1659, 1461, 1441, 1322, 1259, 1228, 1149, 1003, 902, 813 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 4.97 (s, 1H, geminal-H), 4.91 (s, 1H, geminal-H), 3.97 (q, $J = 7.3$ Hz, 1H, methine-H), 3.90 (s, 2H, allylic H), 3.72 (s, 3H, CO₂Me), 3.65 (ABq, $J = 16.2$ Hz, 1H, methylene-H), 3.58 (ABq, $J = 16.2$ Hz, 1H, methylene-H), 1.74 (s, 3H, vinylic Me),

1.33 (d, $J = 7.3$ Hz, 3H, Me); ^{13}C NMR (75 MHz, CDCl_3) δ 205.5 (C), 167.8 (C), 141.1 (C), 112.7 (CH_2), 80.2 (CH), 73.7 (CH_2), 52.3 (CH_3), 44.4 (CH_2), 19.5 (CH_3), 16.7 (CH_3); HRMS-EI calcd for $\text{C}_{10}\text{H}_{16}\text{O}_4$, 200.1049 found 200.1040.

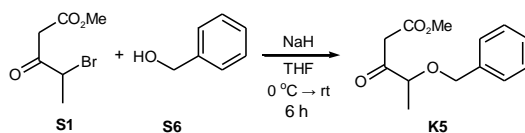


Methyl 4-[(E)-hex-2-enyloxy]-3-oxopentanoate (K3). Prepared according to the general procedure with NaH (0.43 g, 60%, 10.6 mmol), methyl 4-bromo-3-oxopentanoate **S1** (1.0 g, 4.81 mmol, 1.0 equiv.) and *trans*-2-hexen-1-ol **S4** (0.63 mL, 5.30 mmol, 1.1 equiv.) for 6 hours to give product **K3** as a pale-yellow oil in 74% yield (0.82 g). $R_f = 0.51$ (SiO_2 , 4:1 v/v, *n*-hexane/EtOAc); FT-IR (neat) ν 3010, 2958, 2934, 2872, 1749, 1722, 1659, 1632, 1438, 1320, 1263, 1226, 1146, 972, 814 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.71 (dt, $J = 14.4, 6.6$ Hz, 1H, vinylic H), 5.52 (dt, $J = 14.4, 6.2$ Hz, 1H, vinylic H), 4.01–3.96 (m, 3H, allylic and methine-H), 3.73 (s, 3H, CO_2Me), 3.64 (ABq, $J = 16.2$ Hz, 1H, methylene-H), 3.56 (ABq, $J = 16.2$ Hz, 1H, methylene-H), 2.03 (dd, $J = 13.9, 6.2$ Hz, 2H, allylic H), 1.42–1.37 (m, 2H, homoallylic H), 1.33 (d, $J = 6.8$ Hz, 3H, methine-Me), 0.90 (t, $J = 7.3$ Hz, 3H, Me); ^{13}C NMR (75 MHz, CDCl_3) δ 205.5 (C), 167.8 (C), 135.7 (CH), 125.4 (CH), 79.8 (CH), 70.8 (CH_2), 52.2 (CH_3), 44.4 (CH_2), 34.3 (CH_2), 22.1 (CH_2), 16.8 (CH_3), 13.7 (CH_3); HRMS-EI calcd for $\text{C}_{12}\text{H}_{20}\text{O}_4$, 228.1362 found 228.1356.



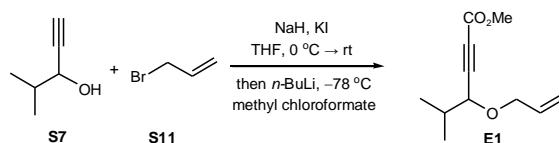
Methyl 4-[(Z)-hex-2-enyloxy]-3-oxopentanoate (K4). Prepared according to the general procedure with NaH (0.43 g, 60%, 10.6 mmol), methyl 4-bromo-3-oxopentanoate **S1** (1.0 g, 4.81 mmol, 1.0 equiv.) and *cis*-2-hexen-1-ol **S5** (0.63 mL, 5.30 mmol, 1.1 equiv.) for 6 hours to give product **K4** as a pale-yellow oil in 72% yield (0.79 g). $R_f = 0.52$ (SiO_2 , 4:1 v/v, *n*-hexane/EtOAc); FT-IR (neat) ν 3013, 2959, 2934, 2873, 1745, 1723, 1659, 1632, 1438, 1369, 1317, 1263, 1225, 1147, 1004, 813 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.66–5.47 (m, 2H, vinylic H), 4.09–4.05 (m, 2H, allylic H), 3.97 (q, $J = 6.8$ Hz, 1H, methine-H), 3.73 (s, 3H, CO_2Me), 3.65 (ABq, $J = 16.2$ Hz, 1H, methylene-H), 3.56 (ABq, $J = 16.2$ Hz, 1H, methylene-H), 2.03 (dd, $J = 14.3, 7.3$

Hz, 2H, allylic H), 1.42–1.38 (m, 2H, homoallylic H), 1.32 (d, $J = 6.8$ Hz, 3H, methine-Me), 0.90 (t, $J = 7.4$ Hz, 3H, Me); ^{13}C NMR (75 MHz, CDCl_3) δ 205.5 (C), 167.8 (C), 134.4 (CH), 125.1 (CH), 80.0 (CH), 65.6 (CH_2), 52.2 (CH_3), 44.3 (CH_2), 29.6 (CH_2), 22.6 (CH_2), 16.8 (CH_3), 13.7 (CH_3); HRMS-EI calcd for $\text{C}_{12}\text{H}_{20}\text{O}_4$, 228.1362 found 228.1357.



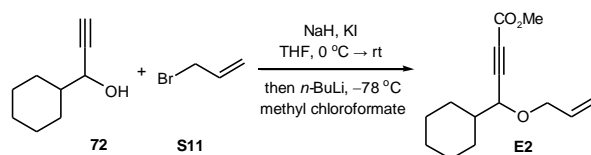
Methyl 4-(benzyloxy)-3-oxopentanoate (K5). Prepared according to the general procedure with NaH (0.43 g, 60%, 10.6 mmol), methyl 4-bromo-3-oxopentanoate **S1** (1.0 g, 4.81 mmol, 1.0 equiv.) and benzyl alcohol **S6** (0.55 mL, 5.30 mmol, 1.1 equiv.) for 6 hours to give product **K5** as a pale-yellow oil in 83% yield (0.94 g). $R_f = 0.55$ (SiO_2 , 4:1 v/v, *n*-hexane/EtOAc); FT-IR (neat) ν 2983, 2953, 1741, 1721, 1655, 1632, 1497, 1319, 1262, 1227, 1148, 1114, 1002, 740, 698 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.38–7.28 (m, 5H, phenyl-H), 4.58 (ABq, $J = 11.6$ Hz, 1H, benzylic H), 4.50 (ABq, $J = 11.6$ Hz, 1H, benzylic H), 4.03 (q, $J = 6.8$ Hz, 1H, methine-H), 3.70 (s, 3H, CO_2Me), 3.66 (ABq, $J = 16.2$ Hz, 1H, methylene-H), 3.58 (ABq, $J = 16.2$ Hz, 1H, methylene-H), 1.37 (d, $J = 6.8$ Hz, 3H, Me); ^{13}C NMR (75 MHz, CDCl_3) δ 205.3 (C), 167.8 (C), 137.2 (C), 128.5 (CH \times 2), 128.0 (CH \times 2), 127.7 (CH), 80.2 (CH), 71.9 (CH_2), 52.2 (CH_3), 44.4 (CH_2), 16.7 (CH_3); HRMS-EI calcd for $\text{C}_{13}\text{H}_{16}\text{O}_4$, 236.1049 found 236.1043.

General procedure for the synthesis of acetylenic esters



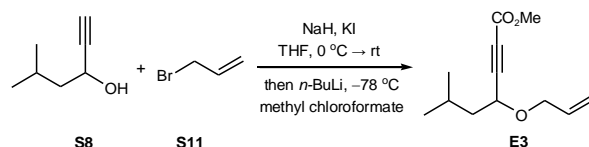
Synthesis of methyl 4-(allyloxy)-5-methylhex-2-ynoate (E1). Acetylenic esters were prepared by modified reported procedure^[2]. To NaH (640 mg, 60%, 16.1 mmol, 1.5 equiv., pre-washed with *n*-hexane) in a 50 mL round-bottomed three-necked flask with THF (5 mL) at 0 °C was added dropwise a solution of 4-methylpent-1-yn-3-ol **S7**^[3] (1.05 g, 10.7 mmol, 1.0 equiv.) in THF (15 mL). The reaction mixture was stirred for 30 minutes at 0 °C. Allyl bromide **S11** (1.02 mL, 11.8 mmol, 1.1 equiv) in THF (6 mL) was added dropwise into the reaction, followed by the addition of KI (1.77 g, 10.7 mmol, 1.0 equiv.). The reaction mixture was allowed to warm to

ambient temperature slowly and stirred for additional 6 hours. Upon TLC showed complete consumption of the starting material, the reaction was cooled to $-78\text{ }^{\circ}\text{C}$ and added *n*-BuLi (1.6 M in *n*-hexane, 8.1 mL, 12.8 mmol, 1.2 equiv.) dropwise over a period of 30 minutes. The reaction mixture was allowed to stir for 1 hour at $-78\text{ }^{\circ}\text{C}$, and then the anion was quenched with methyl chloroformate (1.3 mL, 16.1 mmol, 1.5 equiv.). The reaction mixture was allowed to warm to ambient temperature, and stirred for 1 hour. Water was added and the reaction mixture extracted with diethyl ether (10 mL \times 2). The combined organic layer was washed with brine, dried over anhydrous sodium sulfate, and concentrated to give crude material. Purification by flash column chromatography (*n*-hexane/ethyl acetate, 10:1) afforded product **E1** as a colorless oil in 76% yield (1.60 g). $R_f = 0.46$ (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3010, 2962, 2934, 2875, 2233, 1754, 1720, 1599, 1585, 1468, 1434, 1249, 1129, 1071, 1000, 930, 751 cm^{-1} ; **¹H NMR (300 MHz, CDCl₃)** δ 5.89 (ddt, $J = 17.3, 10.3, 5.1$ Hz, 1H, vinylic H), 5.31 (dd, $J = 17.3, 1.6$ Hz, 1H, geminal-H), 5.20 (dd, $J = 10.3, 1.6$ Hz, 1H, geminal-H), 4.26 (dd, $J = 12.6, 5.1$ Hz, 1H, allylic H), 3.97 (d, $J = 5.8$ Hz, 1H, propargylic H), 3.96–3.90 (m, 1H, allylic H), 3.78 (s, 3H, CO₂Me), 2.04–1.98 (m, 1H, methine-H), 1.03 (d, $J = 6.5$ Hz, 3H, Me), 1.01 (d, $J = 6.5$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 153.7 (C), 133.9 (CH), 117.6 (CH₂), 85.9 (C), 77.8 (C), 73.9 (CH), 70.3 (CH₂), 52.7 (CH₃), 32.9 (CH), 18.4 (CH₃), 17.8 (CH₃); **HRMS-EI** calcd for C₁₁H₁₆O₃, 196.1099 found 196.1106.

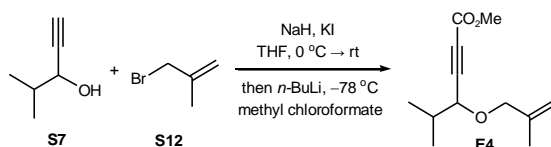


Methyl 4-(allyloxy)-4-cyclohexylbut-2-ynoate (E2). Prepared according to the general procedure with NaH (610 mg, 60%, 15.31 mmol), 1-cyclohexyl-prop-2-yn-1-ol **72**^[4] (1.41 g, 10.2 mmol), KI (1.69 g, 10.20 mmol), allyl bromide **S11** (0.97 mL, 11.2 mmol), *n*-BuLi (7.7 mL, 12.2 mmol) and methyl chloroformate (1.2 mL, 15.3 mmol) to provide product **E2** as a pale-yellow oil in 81% yield (1.95 g). $R_f = 0.47$ (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3012, 2932, 2856, 2234, 1721, 1450, 1351, 1333, 1251, 1174, 1071, 980, 821, 750, 737 cm^{-1} ; **¹H NMR (300 MHz, CDCl₃)** δ 5.88 (ddt, $J = 17.3, 10.3, 5.1$ Hz, 1H, vinylic H), 5.30 (dd, $J = 17.3, 1.6$ Hz, 1H, geminal-H), 5.20 (dd, $J = 10.3, 1.6$ Hz, 1H, geminal-H), 4.25 (dd, $J = 12.6, 5.1$ Hz, 1H, allylic H), 3.96 (d, $J = 6.2$ Hz, 1H, propargylic H), 3.88–3.83 (m, 1H, allylic H), 3.78 (s, 3H,

CO₂Me), 1.82–1.76 (m, 2H, cyclohexyl-H), 1.80–1.60 (m, 5H, cyclohexyl-H), 1.38–1.12 (m, 4H, cyclohexyl-H); ¹³C NMR (75 MHz, CDCl₃) δ 153.8 (C), 133.9 (CH), 117.8 (CH₂), 86.1 (C), 77.8 (C), 73.3 (CH), 70.3 (CH₂), 52.7 (CH₃), 42.3 (CH), 28.7 (CH₂), 28.4 (CH₂), 26.2 (CH₂), 25.8 (CH₂), 25.7 (CH₂); HRMS-EI calcd for C₁₄H₂₀O₃, 236.1412 found 236.1406.

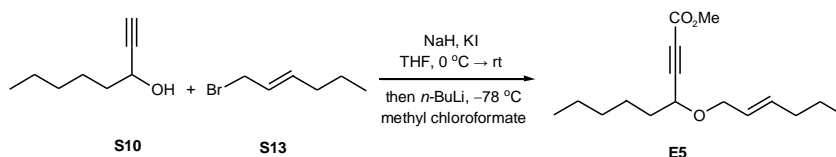


Methyl 4-(allyloxy)-6-methylhept-2-ynoate (E3). Prepared according to the general procedure with NaH (610 mg, 60%, 15.3 mmol), 5-methyl-hex-1-yn-3-ol **S8**^[3] (1.14 g, 10.20 mmol), KI (1.69 g, 10.2 mmol), allyl bromide **S11** (0.97 mL, 11.2 mmol), *n*-BuLi (7.7 mL, 12.2 mmol) and methyl chloroformate (1.2 mL, 15.3 mmol) to provide product **E3** as a colorless oil in 74% yield (1.58 g). *R_f* = 0.50 (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) ν 3011, 2958, 2871, 2234, 1764, 1720, 1599, 1585, 1468, 1434, 1240, 1128, 1083, 1019, 999, 933, 751 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.89 (ddt, *J* = 17.2, 10.3, 6.4 Hz, 1H, vinylic H), 5.31 (dd, *J* = 17.2, 1.5 Hz, 1H, geminal-H), 5.19 (dd, *J* = 10.3, 1.5 Hz, 1H, geminal-H), 4.27–4.20 (m, 2H, allylic and propargylic H), 3.94 (dd, *J* = 12.6, 6.4 Hz, 1H, allylic H), 3.76 (s, 3H, CO₂Me), 1.87–1.83 (m, 1H, methine-H), 1.72 (ddd, *J* = 14.5, 8.0, 6.7 Hz, 1H, methylene-H), 1.57 (ddd, *J* = 14.5, 6.7, 6.1 Hz, 1H, methylene-H), 0.90 (d, *J* = 6.7 Hz, 6H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 153.6 (C), 133.7 (CH), 117.8 (CH₂), 86.8 (C), 77.0 (C), 70.0 (CH), 66.8 (CH₂), 52.7 (CH₃), 43.7 (CH₂), 24.4 (CH), 22.5 (CH₃), 22.2 (CH₃); HRMS-EI calcd for C₁₂H₁₈O₃, 210.1256 found 210.1251.

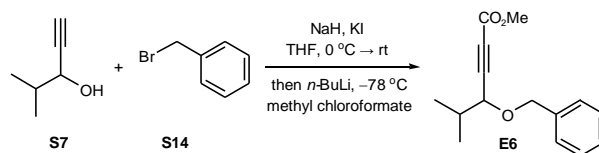


Methyl 4-(2-methylallyloxy)-5-methylhex-2-ynoate (E4). Prepared according to the general procedure with NaH (640 g, 60%, 16.1 mmol), 4-methyl-pent-1-yn-3-ol **S7** (1.05 g, 10.7 mmol), KI (1.77 g, 10.7 mmol), methallyl bromide **S12** (1.19 mL, 11.8 mmol), *n*-BuLi (8.1 mL, 12.8 mmol) and methyl chloroformate (1.3 mL, 16.1 mmol) to provide product **E4** as a colorless oil in 76% yield (1.71 g). *R_f* = 0.46 (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) ν 3012, 2962, 2934, 2875, 2233, 1754, 1720, 1599, 1585, 1468, 1434, 1249, 1129, 1071, 1000, 930, 751 cm⁻¹; ¹H

NMR (300 MHz, CDCl₃) δ 4.99 (s, 1H, geminal-H), 4.91 (s, 1H, geminal-H), 4.13 (ABq, $J = 11.8$ Hz, 1H, allylic H), 3.93 (d, $J = 5.9$ Hz, 1H, propargylic H), 3.89 (ABq, $J = 11.8$ Hz, 1H, allylic H), 3.78 (s, 3H, CO₂Me), 2.05-1.98 (m, 1H, methine-H), 1.74 (s, 3H, vinylic Me), 1.04 (d, $J = 6.5$ Hz, 3H, Me), 1.02 (d, $J = 6.5$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 153.8 (C), 141.4 (C), 113.0 (CH₂), 86.0 (C), 77.7 (C), 73.7 (CH), 73.2 (CH₂), 52.7 (CH₃), 32.9 (CH), 19.6 (CH₃), 18.3 (CH₃), 17.9 (CH₃); **HRMS-EI** calcd for C₁₂H₁₈O₃, 210.1256 found 210.1247.

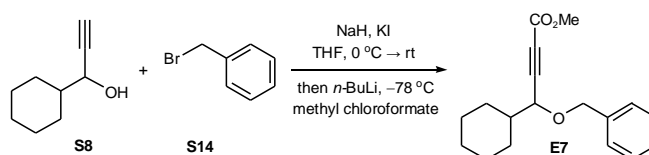


Methyl 4-((E)-hex-2-enyloxy)non-2-ynoate (E5). Prepared according to the general procedure with NaH (610 mg, 60%, 15.4 mmol), oct-1-yn-3-ol **S10**^[51] (1.30 g, 10.3 mmol), KI (1.69 g, 10.3 mmol), allyl bromide **S13** (1.82 g, 11.3 mmol), *n*-BuLi (7.7 mL, 12.3 mmol) and methyl chloroformate (1.2 mL, 15.4 mmol) to provide product **E5** as a colorless oil in 70% yield (1.92 g). $R_f = 0.45$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3010, 2957, 2931, 2863, 2233, 1754, 1721, 1599, 1585, 1462, 1451, 1247, 1097, 1069, 972, 751 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 5.73 (dt, $J = 15.2, 6.7$ Hz, 1H, geminal-H), 5.51 (dt, $J = 15.2, 6.7$ Hz, 1H, geminal-H), 4.23–4.18 (m, 1H, allylic H), 4.16 (t, $J = 6.6$ Hz, 1H, propargylic H), 3.90 (dd, $J = 11.6, 6.7$ Hz, 1H, allylic H), 3.78 (s, 3H, CO₂Me), 2.02 (q, $J = 6.7$ Hz, 2H, allylic H), 1.80–1.74 (m, 2H, homopropargylic H), 1.46–1.22 (m, 8H, pentyl and homoallylic H), 1.91–1.85 (m, 6H, terminal-Me); **¹³C NMR (75 MHz, CDCl₃)** δ 153.7 (C), 135.7 (CH), 125.4 (CH), 87.0 (C), 76.9 (C), 69.9 (CH), 67.8 (CH₂), 52.6 (CH₃), 34.8 (CH₂), 34.3 (CH₂), 31.3 (CH₂), 24.7 (CH₂), 22.4 (CH₂), 22.0 (CH₂), 13.9 (CH₃), 13.6 (CH₃); **HRMS-EI** calcd for C₁₆H₂₆O₃, 266.1882 found 266.1889.

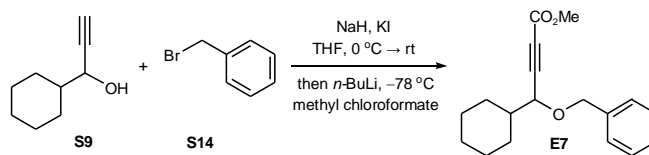


Methyl 4-(benzyloxy)-5-methylhex-2-ynoate (E6). Prepared according to the general procedure with NaH (670 mg, 60%, 16.8 mmol), 4-methyl-pent-1-yn-3-ol **S7** (1.10 g, 11.2 mmol), KI (1.85 g, 11.2 mmol), benzyl bromide **S14** (1.5 mL, 12.3 mmol), *n*-BuLi (8.5 mL, 13.4 mmol) and methyl chloroformate (1.3 mL, 16.8 mmol) to provide product **E6** as a pale-yellow oil in 82%

yield (2.27 g). $R_f = 0.53$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2962, 2874, 2234, 1754, 1720, 1599, 1586, 1465, 1452, 1440, 1383, 1349, 1250, 1088, 1069, 750, 699 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 7.38–7.28 (m, 5H, phenyl-H), 4.83 (ABq, $J = 11.8$ Hz, 1H, benzylic H), 4.50 (ABq, $J = 11.8$ Hz, 1H, benzylic H), 3.97 (d, $J = 5.9$ Hz, 1H, propargylic H), 3.80 (s, 3H, CO₂Me), 2.06–2.02 (m, 1H, methine-H), 1.05 (d, $J = 7.0$ Hz, 3H, Me), 1.03 (d, $J = 7.0$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 153.7 (C), 137.4 (C), 128.3 (CH \times 2), 127.9 (CH \times 2), 127.7 (CH), 85.8 (C), 78.0 (C), 73.8 (CH), 71.1 (CH₂), 52.7 (CH₃), 32.9 (CH), 18.3 (CH₃), 17.9 (CH₃); **HRMS-EI** calcd for C₁₅H₁₈O₃, 246.1256 found 246.1250.

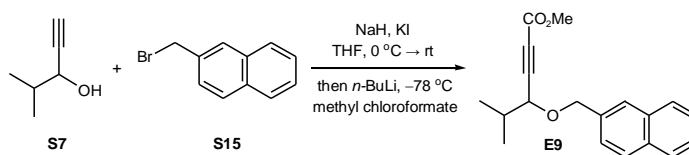


Methyl 4-(benzyloxy)-4-cyclohexylbut-2-ynoate (E7). Prepared according to the general procedure with NaH (610 mg, 60%, 15.3 mmol), 1-cyclohexyl-prop-2-yn-1-ol **S8** (1.41 g, 10.2 mmol), KI (1.70 g, 10.2 mmol), benzyl bromide **S14** (1.34 mL, 11.2 mmol), *n*-BuLi (7.7 mL, 12.2 mmol) and methyl chloroformate (1.18 mL, 15.3 mmol) to provide product **E7** as a pale-yellow oil in 83% yield (2.42 g). $R_f = 0.51$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2929, 2854, 2232, 1718, 1451, 1435, 1249, 1103, 1089, 1071, 750, 698 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 7.37–7.27 (m, 5H, phenyl-H), 4.81 (ABq, $J = 11.8$ Hz, 1H, benzylic H), 4.48 (ABq, $J = 11.8$ Hz, 1H, benzylic H), 3.96 (d, $J = 6.3$ Hz, 1H, propargylic H), 3.80 (s, 3H, CO₂Me), 1.87–1.86 (m, 2H, cyclohexyl-H), 1.73–1.67 (m, 3H, cyclohexyl-H), 1.25–1.10 (m, 6H, cyclohexyl-H); **¹³C NMR (75 MHz, CDCl₃)** δ 153.7 (C), 137.3 (C), 128.3 (CH \times 2), 127.9 (CH \times 2), 127.7 (CH), 86.0 (C), 78.1 (C), 73.1 (CH), 71.1 (CH₂), 52.7 (CH₃), 42.3 (CH), 28.8 (CH₂), 28.5 (CH₂), 26.2 (CH₂), 25.7 (CH₂ \times 2); **HRMS-EI** calcd for C₁₈H₂₂O₃, 286.1569 found 286.1574.



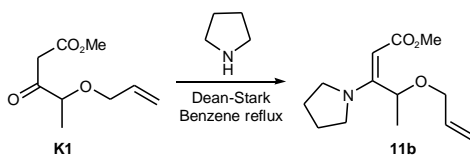
Methyl 4-(benzyloxy)-6-methylhept-2-ynoate (E8). Prepared according to the general procedure with NaH (610 g, 60%, 15.31 mmol), 5-methyl-hex-1-yn-3-ol **S9** (1.14 g, 10.2 mmol),

KI (1.69 g, 10.2 mmol), benzyl bromide **S14** (1.34 mL, 11.2 mmol), *n*-BuLi (7.7 mL, 12.2 mmol) and methyl chloroformate (1.18 mL, 15.3 mmol) to provide product **E8** as a pale-yellow oil in 77% yield (2.04 g). $R_f = 0.51$ (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2958, 2871, 2234, 1754, 1738, 1721, 1599, 1585, 1467, 1441, 1383, 1329, 1250, 1087, 1072, 1025, 749, 698 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 7.39–7.26 (m, 5H, phenyl-H), 4.81 (ABq, $J = 11.6$ Hz, 1H, benzylic H), 4.49 (ABq, $J = 11.6$ Hz, 1H, benzylic H), 4.23 (dd, $J = 8.0, 6.1$ Hz, 1H, propargylic H), 3.80 (s, 3H, CO₂Me), 1.88–1.83 (m, 1H, methine-H), 1.72 (ddd, $J = 14.5, 8.0, 6.7$ Hz, 1H, methylene-H), 1.59–1.55 (m, 1H, methylene-H), 0.91 (d, $J = 6.5$ Hz, 3H, Me), 0.86 (d, $J = 6.5$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 153.8 (C), 137.3 (C), 128.4 (CH \times 2), 128.0 (CH \times 2), 127.9 (CH), 86.9 (C), 77.0 (C), 71.1 (CH), 66.7 (CH₂), 52.8 (CH₃), 43.8 (CH₂), 24.4 (CH), 22.6 (CH₃), 21.9 (CH₃); **HRMS-EI** calcd for C₁₆H₂₀O₃, 260.1412 found 260.1421.

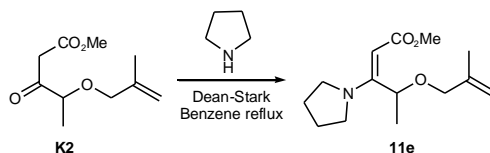


Methyl 4-[(naphthalen-3-yl)methoxy]-5-methylhex-2-ynoate (E9). Prepared according to the general procedure with NaH (670 mg, 60%, 16.8 mmol), 4-methyl-pent-1-yn-3-ol **S7** (1.10 g, 11.2 mmol), KI (1.85 g, 11.2 mmol), 2-bromomethyl-naphthalene **S15** (2.70 g, 12.3 mmol), *n*-BuLi (8.5 mL, 13.4 mmol) and methyl chloroformate (1.3 mL, 16.8 mmol) to provide product **E9** as a pale-yellow oil in 65% yield (2.16 g). $R_f = 0.55$ (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (CHCl₃) ν 2960, 2932, 2873, 2232, 1754, 1720, 1600, 1585, 1468, 1441, 1251, 1071, 949, 856, 817, 750 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 7.85–7.66 (m, 4H, naphthalene-H), 7.49–7.42 (m, 3H, naphthalene-H), 4.97 (ABq, $J = 12.0$ Hz, 1H, benzylic H), 4.67 (ABq, $J = 12.0$ Hz, 1H, O-benzylic H), 3.99 (d, $J = 6.0$ Hz, 1H, propargylic H), 3.80 (s, 3H, CO₂Me), 2.06–2.02 (m, 1H, methine-H), 1.05 (d, $J = 6.6$ Hz, 3H, Me), 1.03 (d, $J = 6.6$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 153.7 (C), 134.7 (C), 133.1 (C), 133.0 (C), 128.2 (CH), 127.8 (CH), 127.6 (CH), 126.9 (CH), 126.1 (CH), 125.9 (CH), 125.8 (CH), 85.8 (C), 78.0 (C), 73.7 (CH), 71.3 (CH₂), 52.7 (CH₃), 32.9 (CH), 18.3 (CH₃), 17.9 (CH₃); **HRMS-EI** calcd for C₁₉H₂₀O₃, 296.1412 found 296.1407.

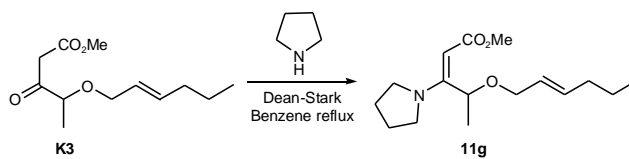
General procedure for the synthesis of vinylogous urethanes from ketoesters



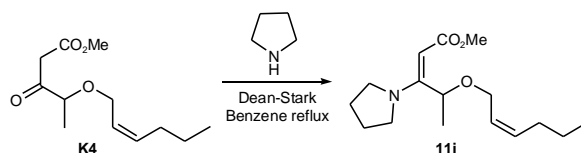
Synthesis of (*E*)-methyl 4-(allyloxy)-3-(pyrrolidin-1-yl)pent-2-enoate (11b**).** To ketoester **K1** (0.30 g, 1.61 mmol, 1.0 equiv.) in 10 mL round-bottom flask was added benzene (4 mL) and pyrrolidine (0.16 mL, 1.94 mmol, 1.2 equiv.), warmed to reflux under Dean-Stark apparatus to remove water. After 30 minutes of stirring, the solvent was removed under *vacuo* to give **11b** as a brown oil in 98% yield (0.38 g) and then used in the next reaction without further purifications. **FT-IR** (neat) ν 2975, 2946, 2870, 1681, 1565, 1445, 1421, 1394, 1343, 1185, 1138, 1099, 1076, 924, 794 cm^{-1} ; **^1H NMR (300 MHz, CDCl_3)** δ 6.06 (q, $J = 6.9$ Hz, 1H, methine-H), 5.89 (ddt, $J = 17.2, 10.5, 5.6$ Hz, 1H, vinylic H), 5.23 (dd, $J = 17.2, 1.7$ Hz, 1H, geminal-H), 5.21 (dd, $J = 10.5, 1.7$ Hz, 1H, geminal-H), 4.45 (s, 1H, α -vinylic H), 3.90 (ddt, $J = 5.6, 3.4, 1.3$ Hz, 2H, allylic H), 3.59 (s, 3H, CO_2Me), 3.42–3.18 (br, 4H, pyrrolidine-H), 1.85–1.78 (m, 4H, pyrrolidine-H), 1.42 (d, $J = 6.9$ Hz, 3H, Me); **^{13}C NMR (75 MHz, CDCl_3)** δ 168.7 (C), 162.3 (C), 134.6 (CH), 116.7 (CH_2), 84.2 (CH), 70.9 (CH), 70.0 (CH_2), 50.0 (CH_3), 49.2 ($\text{CH}_2 \times 2$), 25.1 ($\text{CH}_2 \times 2$), 19.2 (CH_3); **HRMS-EI** calcd for $\text{C}_{13}\text{H}_{21}\text{NO}_3$, 239.1521 found 239.1525.



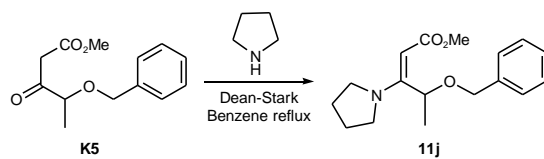
(*E*)-methyl 4-(2-methylallyloxy)-3-(pyrrolidin-1-yl)pent-2-enoate (11e**).** Prepared according to the general procedure with ketoester **K2** (0.32 g, 1.61 mmol) and pyrrolidine (0.16 mL, 1.94 mmol) to give product **11e** as a brown oil in 99% yield (0.40 g). **FT-IR** (neat) ν 2974, 2944, 2871, 1680, 1565, 1444, 1422, 1390, 1343, 1314, 1185, 1136, 1078, 900, 794 cm^{-1} ; **^1H NMR (300 MHz, CDCl_3)** δ 6.05 (q, $J = 6.9$ Hz, 1H, methine-H), 4.94 (s, 1H, geminal-H), 4.84 (s, 1H, geminal-H), 4.45 (s, 1H, α -vinylic H), 3.80 (s, 2H, allylic H), 3.59 (s, 3H, CO_2Me), 3.42–3.18 (br, 4H, pyrrolidine-H), 1.90–1.85 (m, 4H, pyrrolidine-H), 1.71 (s, 3H, vinylic Me), 1.43 (d, $J = 6.9$ Hz, 3H, Me); **^{13}C NMR (75 MHz, CDCl_3)** δ 168.7 (C), 162.3 (C), 142.2 (C), 111.6 (CH_2), 84.2 (CH), 72.9 (CH), 70.9 (CH_2), 50.0 (CH_3), 49.1 ($\text{CH}_2 \times 2$), 25.1 ($\text{CH}_2 \times 2$), 19.7 (CH_3), 19.1 (CH_3); **HRMS-EI** calcd for $\text{C}_{14}\text{H}_{23}\text{NO}_3$, 253.1678 found 253.1681.



(2E)-methyl 4-((E)-hex-2-enyloxy)-3-(pyrrolidin-1-yl)pent-2-enoate (11g). Prepared according to the general procedure with ketoester **K3** (0.37 g, 1.61 mmol) and pyrrolidine (0.16 mL, 1.94 mmol) to give product **11g** as a brown oil in 98% yield (0.45 g). **FT-IR** (neat) ν 2975, 2946, 2871, 1681, 1565, 1445, 1421, 1394, 1343, 1138, 1099, 1076, 924, 794 cm^{-1} ; **^1H NMR (300 MHz, CDCl_3)** δ 6.04 (q, $J = 6.9$ Hz, 1H, methine-H), 5.68 (dt, $J = 14.4, 6.6$ Hz, 1H, vinylic H), 5.52 (dt, $J = 14.4, 6.2$ Hz, 1H, vinylic H), 4.45 (s, 1H, α -vinylic H), 3.84 (t, $J = 5.6$ Hz, 2H, allylic H), 3.60 (s, 3H, CO_2Me), 3.42–3.18 (br, 4H, pyrrolidine-H), 2.03–1.99 (m, 2H, allylic H), 1.91–1.83 (m, 4H, pyrrolidine-H), 1.41 (d, $J = 6.9$ Hz, 3H, Me), 1.32–1.28 (m, 2H, homoallylic H), 0.88 (t, $J = 7.3$ Hz, 3H, terminal-Me); **^{13}C NMR (75 MHz, CDCl_3)** δ 168.6 (C), 162.6 (C), 134.6 (CH), 126.2 (CH), 84.1 (CH), 70.8 (CH), 70.0 (CH_2), 50.0 (CH_3), 49.2 ($\text{CH}_2 \times 2$), 34.4 (CH_2), 26.0 ($\text{CH}_2 \times 2$), 22.1 (CH_2), 19.2 (CH_3), 13.7 (CH_3); **HRMS-EI** calcd for $\text{C}_{16}\text{H}_{27}\text{NO}_3$, 281.1991 found 281.1985.

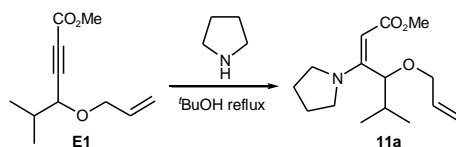


(2E)-methyl 4-((Z)-hex-2-enyloxy)-3-(pyrrolidin-1-yl)pent-2-enoate (11i). Prepared according to the general procedure with ketoester **K4** (0.37 g, 1.61 mmol) and pyrrolidine (0.16 mL, 1.94 mmol) to give product **11i** as a brown oil in 98% yield (0.45 g). **FT-IR** (neat) ν 2960, 2870, 1732, 1682, 1566, 1446, 1421, 1392, 1343, 1315, 1185, 1138, 1099, 1077, 794 cm^{-1} ; **^1H NMR (300 MHz, CDCl_3)** δ 5.97 (q, $J = 6.9$ Hz, 1H, methine-H), 5.46–5.43 (m, 2H, vinylic H), 4.39 (s, 1H, α -vinylic H), 3.92–3.89 (m, 2H, allylic H), 3.52 (s, 3H, CO_2Me), 3.42–3.18 (br, 4H, pyrrolidine-H), 2.01–1.97 (m, 2H, allylic H), 1.82–1.75 (m, 4H, pyrrolidine-H), 1.33 (d, $J = 6.9$ Hz, 3H, Me), 1.31–1.25 (m, 2H, homoallylic H), 0.79 (t, $J = 7.3$ Hz, 3H, terminal-Me); **^{13}C NMR (75 MHz, CDCl_3)** δ 168.4 (C), 162.3 (C), 133.0 (CH), 125.8 (CH), 84.1 (CH), 70.8 (CH), 64.5 (CH_2), 49.8 (CH_3), 48.9 ($\text{CH}_2 \times 2$), 29.3 (CH_2), 24.9 ($\text{CH}_2 \times 2$), 22.4 (CH_2), 19.0 (CH_3), 13.5 (CH_3); **HRMS-EI** calcd for $\text{C}_{16}\text{H}_{27}\text{NO}_3$, 281.1991 found 281.1983.



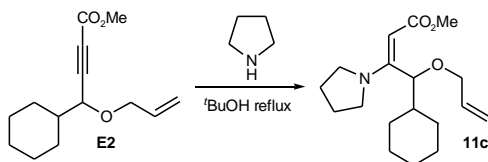
(E)-methyl 4-(benzyloxy)-3-(pyrrolidin-1-yl)pent-2-enoate (11j). Prepared according to the general procedure with ketoester **K5** (0.38 g, 1.61 mmol) and pyrrolidine (0.16 mL, 1.94 mmol) to give product **11j** as a brown oil in 98% yield (0.46 g). **FT-IR** (neat) ν 2977, 2946, 2873, 1717, 1681, 1635, 1565, 1455, 1267, 1139, 1101, 1075, 1043, 795, 735, 699 cm^{-1} ; **^1H NMR (300 MHz, CDCl_3)** δ 7.38–7.28 (m, 5H, phenyl-H), 6.20 (q, $J = 6.9$ Hz, 1H, methine-H), 4.49 (s, 1H, α -vinylic H), 4.47 (ABq, $J = 11.5$ Hz, 1H, benzylic H), 4.41 (ABq, $J = 11.5$ Hz, 1H, benzylic H), 3.62 (s, 3H, CO_2Me), 3.42–3.38 (br, 4H, pyrrolidine-H), 1.86–1.81 (m, 4H, pyrrolidine-H), 1.47 (d, $J = 6.9$ Hz, 3H, Me); **^{13}C NMR (75 MHz, CDCl_3)** δ 168.7 (C), 162.2 (C), 138.3 (C), 128.3 (CH \times 2), 127.7 (CH \times 2), 127.5 (CH), 84.3 (CH), 71.5 (CH and CH_2), 50.1 (CH_3), 49.1 ($\text{CH}_2 \times 2$), 25.1 ($\text{CH}_2 \times 2$), 19.2 (CH_3); **HRMS-EI** calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_3$, 289.1678 found 289.1684.

General procedure for the synthesis of vinylogous urethanes from acetylenic esters

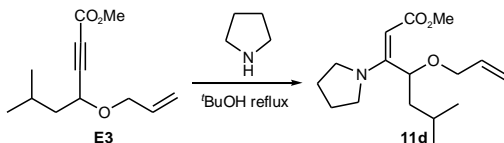


Synthesis of (E)-methyl 4-(allyloxy)-5-methyl-3-(pyrrolidin-1-yl)hex-2-enoate (11a). To a solution of acetylenic ester **E1** (1.05 g, 5.35 mmol) in a 25 mL round-bottom flask with *tert*-butanol (8 mL) as solvent was added pyrrolidine (0.54 mL, 6.42 mmol). The reaction mixture was heated to reflux at 100 $^\circ\text{C}$ for 40 min. After removal of solvent under *vacuo*, product **11a** as a pale-yellow oil was obtained in 99% yield (1.41 g) and then used in the next reaction without further purifications. **FT-IR** (neat) ν 3011, 2964, 2873, 1680, 1569, 1462, 1443, 1423, 1391, 1344, 1257, 1230, 1185, 1138, 1063, 998, 823, 798 cm^{-1} ; **^1H NMR (300 MHz, CDCl_3)** 5.89 (ddt, $J = 17.2, 10.4, 5.6$ Hz, 1H, vinylic H), 5.68 (d, $J = 9.7$ Hz, 1H, methine-H), 5.23 (dd, $J = 17.2, 1.9$ Hz, 1H, geminal-H), 5.10 (dd, $J = 10.4, 1.9$ Hz, 1H, geminal-H), 4.59 (s, 1H, α -vinylic H), 3.92 (d, $J = 5.6$ Hz, 2H, allylic H), 3.60 (s, 3H, CO_2Me), 3.60–3.57 (br, 2H, pyrrolidine-H), 3.28 (br, 2H, pyrrolidine-H), 2.00–1.65 (m, 5H, pyrrolidine- and methine-H), 1.09 (d, $J = 6.4$ Hz, 3H,

Me), 0.84 (d, $J = 6.4$ Hz, 3H, Me); ^{13}C NMR (75 MHz, CDCl_3) δ 168.9 (C), 160.3 (C), 134.9 (CH), 116.3 (CH_2), 86.9 (CH), 79.9 (CH), 70.4 (CH_2), 50.0 (CH_3), 49.0 ($\text{CH}_2 \times 2$), 30.9 (CH), 25.0 ($\text{CH}_2 \times 2$), 20.4 (CH_3), 18.3 (CH_3); HRMS-EI calcd for $\text{C}_{15}\text{H}_{25}\text{NO}_3$, 267.1834 found 267.1823.

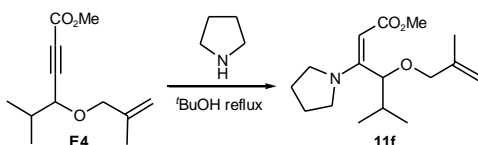


(E)-methyl 4-(allyloxy)-4-cyclohexyl-3-(pyrrolidin-1-yl)but-2-enoate (11c). Prepared according to the general procedure with acetylenic ester **E2** (1.20 g, 5.10 mmol) and pyrrolidine (0.50 mL, 6.12 mmol) to give product **11c** as a brown oil in 99% yield (1.55 g). FT-IR (neat) ν 3009, 2928, 2853, 1738, 1727, 1710, 1680, 1658, 1631, 1606, 1568, 1450, 1423, 1392, 1344, 1181, 1130, 1084, 1060, 994, 922, 796, 766, 734 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 5.89 (ddt, $J = 17.2, 10.4, 5.6$ Hz, 1H, vinylic H), 5.75 (d, $J = 9.6$ Hz, 1H, methine-H), 5.22 (dd, $J = 17.2, 1.9$ Hz, 1H, geminal-H), 5.11 (dd, $J = 10.4, 1.9$ Hz, 1H, geminal-H), 4.58 (s, 1H, α -vinylic H), 3.92 (d, $J = 5.6$ Hz, 2H, allylic H), 3.60 (s, 3H, CO_2Me), 3.58 (br, 2H, pyrrolidine-H), 3.28–3.26 (br, 2H, pyrrolidine-H), 2.22–2.18 (m, 1H, methine-H), 1.85–1.78 (m, 4H, pyrrolidine-H), 1.75–1.62 (m, 4H, cyclohexyl-H), 1.44–1.20 (m, 6H, cyclohexyl-H); ^{13}C NMR (75 MHz, CDCl_3) δ 168.8 (C), 159.9 (C), 134.8 (CH), 116.3 (CH_2), 86.8 (CH), 78.8 (CH), 70.2 (CH_2), 49.9 (CH_3), 48.9 ($\text{CH}_2 \times 2$), 40.4 (CH), 31.1 (CH_2), 30.2 (CH_2), 26.1 (CH_2), 26.0 (CH_2), 25.9 (CH_2), 24.9 ($\text{CH}_2 \times 2$); HRMS-EI calcd for $\text{C}_{18}\text{H}_{29}\text{NO}_3$, 307.2147 found 307.2153.

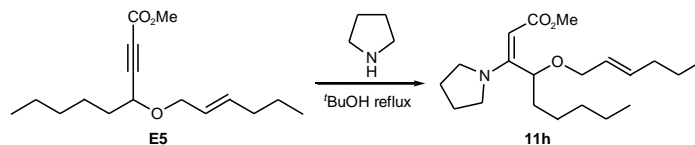


(E)-methyl 4-(allyloxy)-6-methyl-3-(pyrrolidin-1-yl)hept-2-enoate (11d). A Prepared according to the general procedure with acetylenic ester **E3** (1.07 g, 5.10 mmol) and pyrrolidine (0.50 mL, 6.12 mmol) to give product **11d** as a pale-yellow oil in 99% yield (1.42 g). FT-IR (neat) ν 2953, 2870, 1681, 1566, 1483, 1462, 1443, 1422, 1391, 1344, 1267, 1185, 1137, 1085, 1064, 1041, 990, 923, 907, 795 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 6.03 (dd, $J = 9.7, 3.9$ Hz, 1H, methine-H), 5.90 (ddt, $J = 17.2, 10.4, 5.6$ Hz, 1H, vinylic H), 5.23 (dd, $J = 17.2, 1.9$ Hz, 1H,

geminal-H), 5.12 (dd, $J = 10.4, 1.9$ Hz, 1H, geminal-H), 4.47 (s, 1H, α -vinylic H), 3.90 (d, $J = 5.6$ Hz, 2H, allylic H), 3.61 (s, 3H, CO₂Me), 3.60–3.57 (br, 2H, pyrrolidine-H), 3.38–3.36 (br, 2H, pyrrolidine-H), 1.98–1.62 (m, 6H, methine-, methylene- and pyrrolidine-H), 1.41–1.39 (m, 1H, methylene-H), 0.98 (d, $J = 6.7$ Hz, 3H, Me), 0.96 (d, $J = 6.7$ Hz, 3H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 168.6 (C), 162.0 (C), 134.8 (CH), 116.6 (CH₂), 84.7 (CH), 73.3 (CH), 70.2 (CH₂), 50.1 (CH₃), 49.2 (CH₂ \times 2), 42.4 (CH₂), 25.2 (CH and CH₂ \times 2), 23.5 (CH₃), 21.8 (CH₃); HRMS-EI calcd for C₁₆H₂₇NO₃, 281.1991 found 281.1998.

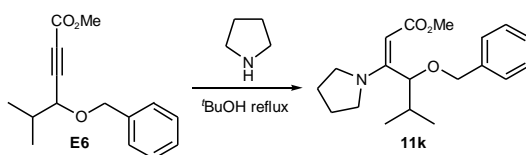


(E)-methyl 4-(2-methylallyloxy)-5-methyl-3-(pyrrolidin-1-yl)hex-2-enoate (11f). Prepared according to the general procedure with acetylenic ester **E4** (1.07 g, 5.10 mmol) and pyrrolidine (0.50 mL, 6.12 mmol) to give product **11f** as a pale-yellow oil in 99% yield (1.42 g). FT-IR (neat) ν 2955, 2871, 1681, 1568, 1483, 1462, 1443, 1422, 1391, 1344, 1267, 1185, 1137, 1064, 998, 923, 798 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) 5.65 (d, $J = 9.7$ Hz, 1H, methine-H), 4.92 (s, 1H, geminal-H), 4.81 (s, 1H, geminal-H), 4.59 (s, 1H, α -vinylic H), 3.80 (s, 2H, allylic H), 3.59 (s, 3H, CO₂Me), 3.60–3.58 (br, 2H, pyrrolidine-H), 3.30–3.28 (br, 2H, pyrrolidine-H), 2.00–1.65 (m, 5H, pyrrolidine- and methine-H), 1.71 (s, 3H, vinylic Me), 1.12 (d, $J = 6.4$ Hz, 3H, Me), 0.84 (d, $J = 6.4$ Hz, 3H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 168.9 (C), 160.3 (C), 142.5 (C), 111.5 (CH₂), 87.0 (CH), 79.9 (CH), 73.4 (CH₂), 50.0 (CH₃), 49.0 (CH₂ \times 2), 31.0 (CH), 25.0 (CH₂ \times 2), 20.4 (CH₃), 19.7 (CH₃), 18.3 (CH₃); HRMS-EI calcd for C₁₆H₂₇NO₃, 281.1991 found 281.1998.

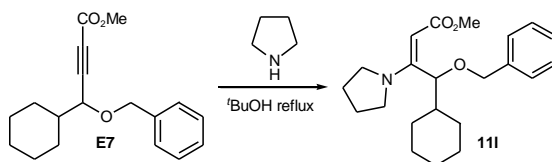


(2E)-methyl 4-((E)-hex-2-enyloxy)-3-(pyrrolidin-1-yl)non-2-enoate (11h). Prepared according to the general procedure with acetylenic ester **E5** (1.35 g, 5.10 mmol) and pyrrolidine (0.50 mL, 6.12 mmol) to give product **11h** as a pale-yellow oil in 99% yield (1.70 g). FT-IR (neat) ν 2956, 2930, 2871, 1687, 1567, 1462, 1443, 1422, 1383, 1344, 1184, 1138, 1090, 1064, 1042, 970, 796 ; ¹H NMR (300 MHz, CDCl₃) δ 5.89 (dd, $J = 9.1, 4.4$ Hz, 1H, methine-H), 5.64 (dt, $J = 15.4, 6.3$

Hz, 1H, vinylic H), 5.52 (dt, $J = 15.4, 6.8$ Hz, 1H, vinylic H), 4.47 (s, 1H, α -vinylic H), 3.85 (d, $J = 6.3$ Hz, 2H, allylic H), 3.60 (s, 3H, CO₂Me), 3.52–3.50 (br, 2H, pyrrolidine-H), 3.38–3.36 (br, 2H, pyrrolidine-H), 1.99 (dd, $J = 14.1, 6.8$ Hz, 2H, allylic H), 1.90–1.85 (m, 4H, pyrrolidine-H), 1.78–1.75 (m, 2H, methylene-H), 1.62–1.22 (m, 8H, homoallylic and pentyl-H), 0.88 (t, $J = 7.3$ Hz, 3H, Me), 0.87 (t, $J = 7.3$ Hz, 3H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 168.5 (C), 161.9 (C), 134.2 (CH), 126.2 (CH), 84.7 (CH), 74.2 (CH), 70.1 (CH₂), 49.8 (CH₃), 49.0 (CH₂ \times 2), 34.2 (CH₂), 33.6 (CH₂), 31.6 (CH₂), 25.8 (CH₂), 24.9 (CH₂ \times 2), 22.4 (CH₂), 22.0 (CH₂), 13.9 (CH₃), 13.5 (CH₃); HRMS-EI calcd for C₂₀H₃₅NO₃, 337.2617 found 337.2626.

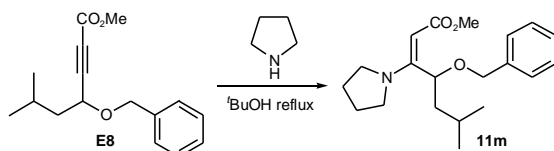


(E)-methyl 4-(benzyloxy)-5-methyl-3-(pyrrolidin-1-yl)hex-2-enoate (11k). Prepared according to the general procedure with acetylenic ester **E6** (1.25 g, 5.10 mmol) and pyrrolidine (0.50 mL, 6.12 mmol) to give product **11k** as a pale-yellow oil in 98% yield (1.59 g). FT-IR (neat) ν 2963, 2870, 1680, 1568, 1462, 1452, 1423, 1383, 1344, 1265, 1185, 1136, 1063, 998, 948, 896, 797, 748, 736, 699 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.18 (m, 5H, phenyl-H), 5.83 (d, $J = 9.7$ Hz, 1H, methine-H), 4.64 (s, 1H, α -vinylic H), 4.53 (ABq, $J = 11.5$ Hz, 1H, benzylic-H), 4.47 (ABq, $J = 11.5$ Hz, 1H, benzylic-H), 3.63 (s, 3H, CO₂Me), 3.62–3.58 (br, 2H, pyrrolidine-H), 3.31–3.28 (br, 2H, pyrrolidine-H), 2.04–1.20 (m, 1H, methine-H), 1.88–1.80 (m, 4H, pyrrolidine-H), 1.17 (d, $J = 6.4$ Hz, 3H, Me), 0.89 (d, $J = 6.4$ Hz, 3H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 168.9 (C), 160.1 (C), 138.7 (C), 128.1 (CH \times 2), 127.7 (CH \times 2), 127.3 (CH), 87.1 (CH), 80.4 (CH), 71.8 (CH₂), 50.0 (CH₃), 49.0 (CH₂ \times 2), 30.9 (CH), 25.0 (CH₂ \times 2), 20.4 (CH₃), 18.3 (CH₃); HRMS-EI calcd for C₁₉H₂₇NO₃, 317.1991 found 317.1992.

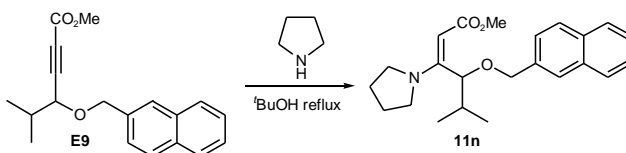


(E)-methyl 4-(benzyloxy)-4-cyclohexyl-3-(pyrrolidin-1-yl)but-2-enoate (11l). Prepared according to the general procedure with acetylenic ester **E7** (1.46 g, 5.10 mmol) and pyrrolidine (0.50 mL, 6.12 mmol) to give product **11l** as a brown oil in 99% yield (1.81 g). FT-IR (neat) ν

2927, 2852, 1743, 1726, 1682, 1568, 1451, 1422, 1389, 1344, 1265, 1182, 1137, 1086, 1060, 906, 889, 797, 736, 699 cm^{-1} ; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.34–7.25 (m, 5H, phenyl-H), 5.88 (d, $J = 9.6$ Hz, 1H, methine-H), 4.61 (s, 1H, γ -vinylicH), 4.49 (ABq, $J = 11.6$ Hz, 1H, benzylic H), 4.44 (ABq, $J = 11.6$ Hz, 1H, benzylic H), 3.62 (s, 3H, CO_2Me), 3.60–3.57 (br, 2H, pyrrolidine-H), 3.31–3.26 (br, 2H, pyrrolidine-H), 2.23–2.18 (m, 1H, cyclohexyl-H), 1.85–1.80 (m, 4H, pyrrolidine-H), 1.80–1.62 (m, 4H, cyclohexyl-H), 1.43–1.41 (m, 2H, cyclohexyl-H), 1.16–1.13 (m, 4H, cyclohexyl-H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 168.9 (C), 159.9 (C), 138.7 (C), 128.2 ($\text{CH} \times 2$), 127.7 ($\text{CH} \times 2$), 127.3 (CH), 87.0 (CH), 79.5 (CH), 71.8 (CH_2), 50.0 (CH_3), 49.0 ($\text{CH}_2 \times 2$), 40.5 (CH), 30.9 (CH_2), 28.2 (CH_2), 26.2 (CH_2), 26.1 (CH_2), 26.0 (CH_2), 24.9 ($\text{CH}_2 \times 2$); HRMS-EI calcd for $\text{C}_{22}\text{H}_{31}\text{NO}_3$, 357.2304 found 357.2307.

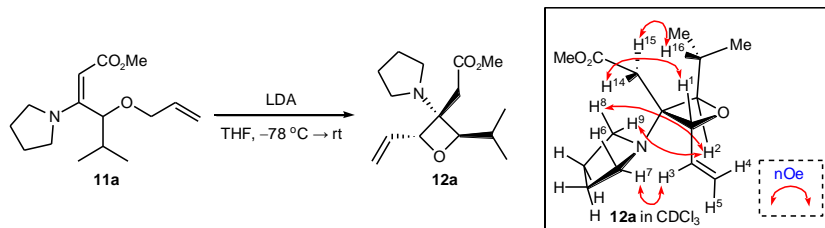


(E)-methyl 4-(benzyloxy)-6-methyl-3-(pyrrolidin-1-yl)hept-2-enoate (11m). Prepared according to the general procedure with acetylenic ester **E8** (1.33 g, 5.10 mmol) and pyrrolidine (0.50 mL, 6.12 mmol) to give product **11m** as a brown oil in 99% yield (1.68 g). **FT-IR** (neat) ν 2954, 2869, 1679, 1566, 1462, 1423, 1384, 1265, 1184, 1138, 1088, 1041, 991, 923, 795, 748, 736, 698 cm^{-1} ; $^1\text{H NMR}$ (300 MHz, CDCl_3) δ 7.42–7.26 (m, 5H, phenyl-H), 6.15 (dd, $J = 9.8$, 3.8 Hz, 1H, methine-H), 4.50 (s, 1H, γ -vinylicH), 4.46 (ABq, $J = 11.6$ Hz, 1H, benzylic H), 4.42 (ABq, $J = 11.6$ Hz, 1H, benzylic H), 3.62 (s, 3H, CO_2Me), 3.60–3.57 (br, 2H, pyrrolidine-H), 3.30–3.26 (br, 2H, pyrrolidine-H), 1.98–1.72 (m, 6H, methylene-, methine- and pyrrolidine-H), 1.43–1.41 (m, 1H, methylene-H), 0.98 (d, $J = 6.7$ Hz, 3H, Me), 0.96 (d, $J = 6.7$ Hz, 3H, Me); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) δ 168.6 (C), 161.9 (C), 138.5 (C), 128.2 ($\text{CH} \times 2$), 127.7 ($\text{CH} \times 2$), 127.4 (CH), 84.8 (CH), 73.8 (CH), 71.5 (CH_2), 50.1 (CH_3), 49.2 ($\text{CH}_2 \times 2$), 42.4 (CH_2), 25.2 (CH), 24.3 ($\text{CH}_2 \times 2$), 23.4 (CH_3), 21.7 (CH_3); HRMS-EI calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_3$, 331.2147 found 331.2142.



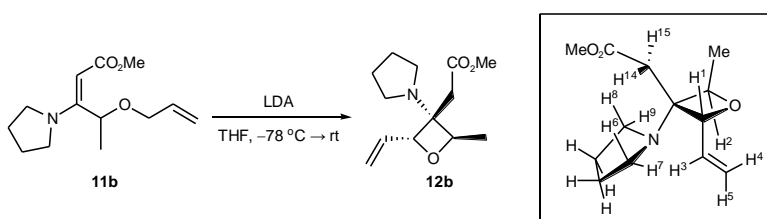
(E)-methyl 4-[(naphthalen-3-yl)methoxy]-5-methyl-3-(pyrrolidin-1-yl)hex-2-enoate (11n). Prepared according to the general procedure with acetylenic ester **E9** (1.52 g, 5.10 mmol) and pyrrolidine (0.50 mL, 6.12 mmol) to give product **11n** as a brown oil in 98% yield (1.85 g). **FT-IR** (neat) ν 2963, 2871, 1754, 1687, 1567, 1442, 1423, 1383, 1345, 1265, 1137, 1063, 947, 895, 856, 817, 796, 752; **^1H NMR (300 MHz, CDCl_3)** δ 7.85–7.66 (m, 4H, naphthalene-H), 7.51–7.42 (m, 3H, naphthalene-H), 5.81 (d, $J = 9.7$ Hz, 1H, methine-H), 4.51 (ABq, $J = 11.5$ Hz, 1H, benzylic H), 4.63 (s, 1H, γ -vinylicH), 4.45 (ABq, $J = 11.5$ Hz, 1H, benzylic H), 3.62 (s, 3H, CO_2Me), 3.60–3.58 (br, 2H, pyrrolidine-H), 3.30–3.27 (br, 2H, pyrrolidine-H), 2.02–2.00 (m, 1H, methine-H), 1.86–1.80 (m, 4H, pyrrolidine-H), 1.14 (d, $J = 6.4$ Hz, 3H, Me), 0.86 (d, $J = 6.4$ Hz, 3H, Me); **^{13}C NMR (75 MHz, CDCl_3)** δ 168.9 (C), 160.1 (C), 136.2 (C), 133.2 (C), 132.8 (C), 127.8 (CH \times 2), 127.6 (CH), 126.4 (CH), 126.0 (CH), 125.9 (CH), 125.7 (CH), 87.2 (CH), 80.5 (CH), 72.0 (CH_2), 50.0 (CH_3), 49.0 ($\text{CH}_2 \times 2$), 31.0 (CH), 25.0 ($\text{CH}_2 \times 2$), 20.5 (CH_3), 18.3 (CH_3); **HRMS-EI** calcd for $\text{C}_{23}\text{H}_{29}\text{NO}_3$, 367.2147 found 367.2142.

General procedure for the synthesis of 2,3,3,4-tetrasubstituted oxetanes

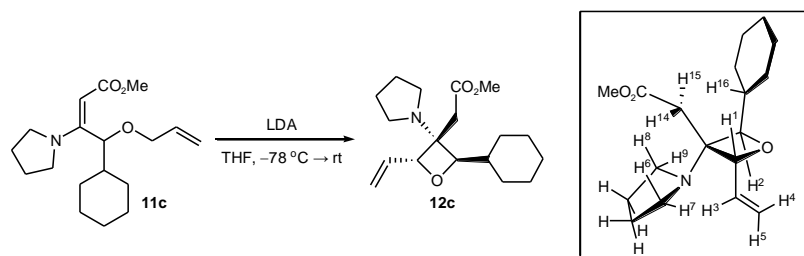


Synthesis of [(2*R*,3*R*,4*R*)-2-isopropyl-3-pyrrolidin-1-yl-4-vinyl-oxetan-3-yl]-acetic acid methyl ester (12a**).** To compound **11a** (200 mg, 0.75 mmol, 1.0 equiv.) with THF (7.5 mL) at -78 °C in a flame-dried 25 mL round-bottomed flask was added a solution of LDA (1.9 mL, 1.87 mmol, 2.5 equiv., 1.0 *N* in THF/*n*-hexane). The reaction mixture was stirred for 1 hour at -78 °C, which was then removed the dry-ice bath and allowed to warm to ambient temperature over a period of 10 minutes. The reaction was quenched by the addition of aqueous ammonium chloride solution (1.0 M, 2.0 mL), the reaction mixture was extracted with EtOAc (6 mL \times 2). The combined organic layer was washed with brine, then dried over anhydrous sodium sulfate, and concentrated to give crude material. Purification by flash column chromatography (*n*-hexane/EtOAc, 10:1) to afford oxetane **12a** (152 mg, 0.57 mmol) as a pale-yellow solid in 76%

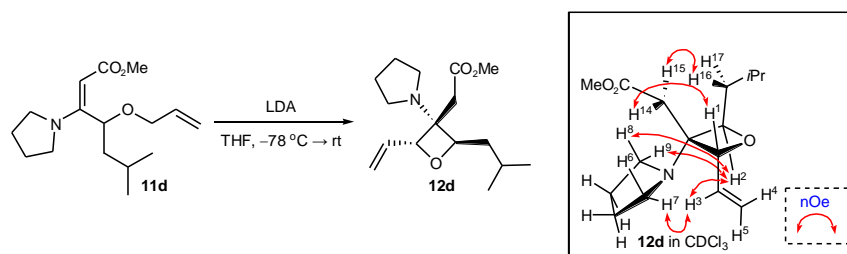
yield. m.p. 44.5–47.5 °C (recrystallized from hexanes: EtOAc (4:1)); $R_f = 0.33$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2960, 2874, 2808, 1735, 1717, 1699, 1558, 1541, 1521, 1508, 1472, 1457, 1435, 1387, 1363, 1338, 1257, 1196, 1177, 1153, 1129, 1057, 995, 935, 923, 884 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 6.39 (ddd, $J = 17.3, 10.3, 7.5$ Hz, 1H, H³), 5.39 (ddd, $J = 17.3, 2.0, 1.1$ Hz, 1H, H⁴), 5.26 (ddd, $J = 10.3, 2.0, 1.0$ Hz, 1H, H⁵), 5.11 (ddd, $J = 7.5, 1.1, 1.0$ Hz, 1H, H¹), 4.16 (d, $J = 11.4$ Hz, 1H, H²), 3.66 (s, 3H, OMe), 2.81 (s, 2H, H¹⁴ and H¹⁵), 2.66–2.63 (m, 2H, H⁷ and H⁹), 2.50–2.47 (m, 2H, H⁶ and H⁸), 1.94–1.92 (m, 1H, H¹⁶), 1.69–1.65 (m, 4H, H¹⁰, H¹¹, H¹² and H¹³), 0.95 (d, $J = 6.4$ Hz, 3H, Me²), 0.83 (d, $J = 6.4$ Hz, 3H, Me¹); **¹³C NMR (75 MHz, CDCl₃)** δ 172.7 (C), 136.3 (CH), 118.0 (CH₂), 91.4 (CH), 85.8 (CH), 65.3 (C), 51.5 (CH₃), 46.8 (CH₂ × 2), 32.2 (CH), 30.6 (CH₂), 23.6 (CH₂ × 2), 18.5 (CH₃), 18.3 (CH₃); **HRMS-EI** calcd for C₁₅H₂₅NO₃, 267.1834 found 267.1845.



Synthesis of [(2*R*,3*R*,4*R*)-2-methyl-3-pyrrolidin-1-yl-4-vinyl-oxetan-3-yl]-acetic acid methyl ester (12b**).** Prepared according to the representative procedure with compound **11b** (180 mg, 0.75 mmol) and LDA to give oxetane **12b** (112 mg, 0.47 mmol) as a pale-yellow oil in 62% yield. $R_f = 0.25$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2966, 2874, 1736, 1461, 1367, 1332, 1261, 1197, 1062, 919, 867 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 6.39 (ddd, $J = 17.4, 10.3, 7.3$ Hz, 1H, H³), 5.39 (ddd, $J = 17.4, 1.9, 1.2$ Hz, 1H, H⁴), 5.26 (ddd, $J = 10.3, 1.9, 1.0$ Hz, 1H, H⁵), 5.08 (d, $J = 7.2$ Hz, 1H, H¹), 4.87 (q, $J = 6.4$ Hz, 1H, H²), 3.66 (s, 3H, OMe), 2.79 (ABq, $J = 15.1$ Hz, 1H, H¹⁴), 2.73 (ABq, $J = 15.1$ Hz, 1H, H¹⁵), 2.63–2.60 (m, 2H, H⁷ and H⁹), 2.51–2.49 (m, 2H, H⁶ and H⁸), 1.77–1.72 (m, 4H, H¹⁰, H¹¹, H¹² and H¹³), 1.31 (d, $J = 6.4$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 172.6 (C), 135.8 (CH), 117.8 (CH₂), 87.0 (CH), 82.5 (CH), 65.2 (C), 51.6 (CH₃), 46.2 (CH₂ × 2), 32.5 (CH₂), 23.8 (CH₂ × 2), 17.7 (CH₃); **HRMS-EI** calcd for C₁₃H₂₁NO₃, 239.1521 found 239.1524.

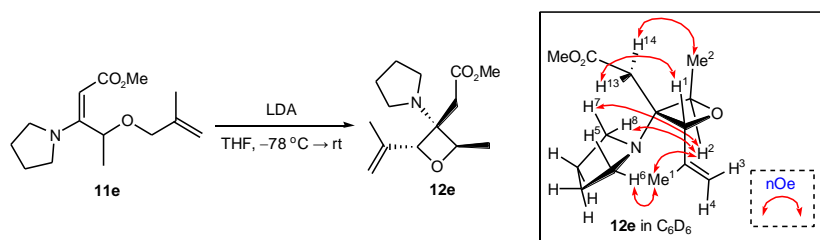


Synthesis of [(2*R*,3*R*,4*R*)-2-cyclohexyl-3-pyrrolidin-1-yl-4-vinyl-oxetan-3-yl]-acetic acid methyl ester (12c**).** Prepared according to the representative procedure with compound **11c** (230 mg, 0.75 mmol) and LDA to give oxetane **12c** (161 mg, 0.52 mmol) as a pale-yellow oil in 70% yield. $R_f = 0.41$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2926, 2852, 2807, 1735, 1717, 1699, 1684, 1652, 1636, 1558, 1541, 1521, 1508, 1449, 1436, 1338, 1258, 1196, 1176, 1153, 1129, 1056, 1046, 1016, 989, 923, 882 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 6.35 (ddd, $J = 17.6, 10.3, 7.5$ Hz, 1H, H³), 5.34 (ddd, $J = 17.3, 1.8, 0.9$ Hz, 1H, H⁴), 5.21 (dd, $J = 10.3, 2.0, 0.8$ Hz, 1H, H⁵), 5.07 (d, $J = 7.5$ Hz, 1H, H¹), 4.22 (d, $J = 10.4$ Hz, 1H, H²), 3.62 (s, 3H, OMe), 2.79 (s, 3H, H¹⁴ and H¹⁵), 2.62–2.58 (m, 2H, H⁷ and H⁹), 2.42–2.38 (m, 2H, H⁶ and H⁸), 1.93–1.89 (m, 1H, H¹⁷), 1.68–1.47 (m, 8H, H¹⁶, H¹⁸–H²⁰ and H²³–H²⁶), 1.12–1.09 (m, 4H, H¹⁰, H¹¹, H¹² and H¹³), 0.85–0.77 (m, 2H, H²¹ and H²²); **¹³C NMR (75 MHz, CDCl₃)** δ 172.6 (C), 136.2 (CH), 117.9 (CH₂), 89.9 (CH), 85.8 (CH), 65.3 (C), 51.5 (CH₃), 46.7 (CH₂ × 2), 40.2 (CH), 31.8 (CH₂), 28.9 (CH₂), 28.0 (CH₂), 26.3 (CH₂), 25.4 (CH₂ × 2), 23.4 (CH₂ × 2); **HRMS-EI** calcd for C₁₈H₂₉NO₃, 307.2147 found 307.2141.

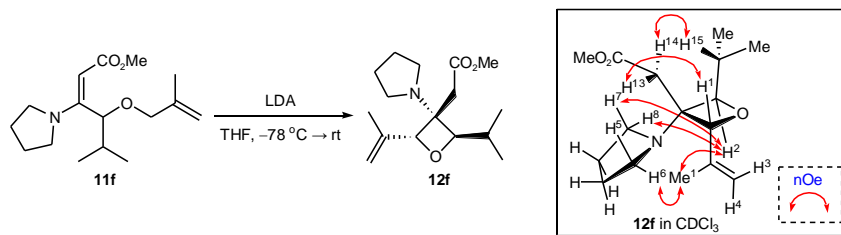


Synthesis of [(2*R*,3*R*,4*R*)-2-isobutyl-3-pyrrolidin-1-yl-4-vinyl-oxetan-3-yl]-acetic acid methyl ester (12d**).** Prepared according to the representative procedure with compound **11d** (210 mg, 0.75 mmol) and LDA to give oxetane **12d** (143 mg, 0.51 mmol) as a pale-yellow oil in 68% yield. $R_f = 0.40$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2954, 2872, 2810, 1736, 1717, 1699, 1653, 1636, 1558, 1541, 1521, 1508, 1457, 1435, 1396, 1386, 1362, 1338, 1245, 1197, 1177, 1147, 1133, 1074, 1009, 987, 921, 879 cm⁻¹; **¹H NMR (500 MHz, CDCl₃)** δ 6.39 (ddd, $J =$

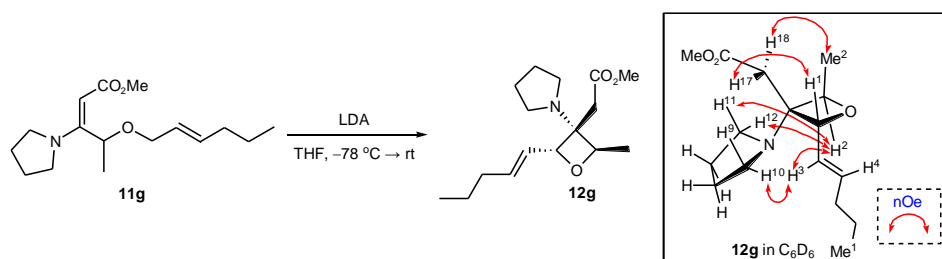
17.2, 10.3, 7.5 Hz, 1H, H³), 5.39 (ddd, $J = 17.2, 2.0, 1.1$ Hz, 1H, H⁴), 5.26 (ddd, $J = 10.3, 2.0, 1.0$ Hz, 1H, H⁵), 5.09 (ddd, $J = 7.5, 1.1, 1.0$ Hz, 1H, H¹), 4.77 (dd, $J = 11.4, 3.0$ Hz, 1H, H²), 3.65 (s, 3H, OMe), 2.79 (ABq, $J = 15.2$ Hz, 1H, H¹⁴), 2.73 (ABq, $J = 15.2$ Hz, 1H, H¹⁵), 2.65–2.61 (m, 2H, H⁷ and H⁹), 2.49–2.45 (m, 2H, H⁶ and H⁸), 1.73–1.60 (m, 6H, H¹⁷, H¹⁸ and H¹⁰–H¹³), 1.31 (ddd, $J = 13.7, 8.0, 3.0$ Hz, 1H, H¹⁶), 0.94 (d, $J = 6.4$ Hz, 3H, Me), 0.82 (d, $J = 6.4$ Hz, 3H, Me); ¹³C NMR (126 MHz, CDCl₃) δ 172.8 (C), 135.9 (CH), 117.9 (CH₂), 86.8 (CH), 84.9 (CH), 65.2 (C), 51.6 (CH₃), 46.3 (CH₂ × 2), 41.2 (CH₂), 32.2 (CH₂), 24.7 (CH), 23.7 (CH₂ × 2), 22.4 (CH₃), 22.1 (CH₃); HRMS-EI calcd for C₁₆H₂₇NO₃, 281.1991 found 281.1998.



Synthesis of [(2*R*,3*R*,4*R*)-2-isopropenyl-4-methyl-3-pyrrolidin-1-yl-oxetan-3-yl]-acetic acid methyl ester (12e). Prepared according to the representative procedure with compound **11e** (190 mg, 0.75 mmol) and LDA to give oxetane **12e** (127 mg, 0.50 mmol) as a colorless oil in 67% yield. $R_f = 0.35$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2967, 1736, 1460, 1437, 1379, 1331, 1263, 1196, 1141, 1062, 1023, 952, 897 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 5.15 (s, 1H, H³), 5.12 (s, 1H, H¹), 4.98 (q, $J = 6.5$ Hz, 1H, H²), 4.96 (s, 1H, H⁴), 3.66 (s, 3H, OMe), 2.86 (ABq, $J = 14.8$ Hz, 1H, H¹³), 2.77 (ABq, $J = 14.8$ Hz, 1H, H¹⁴), 2.71–2.68 (m, 2H, H⁶ and H⁸), 2.51–2.47 (m, 2H, H⁵ and H⁷), 1.94 (s, 3H, Me¹), 1.68–1.62 (m, 4H, H¹⁰–H¹³), 1.31 (d, $J = 6.5$ Hz, 3H, Me²); ¹³C NMR (75 MHz, CDCl₃) δ 172.7 (C), 144.6 (C), 113.3 (CH₂), 89.6 (CH), 81.7 (CH), 65.6 (C), 51.5 (CH₃), 46.2 (CH₂ × 2), 34.7 (CH₂), 23.9 (CH₂ × 2), 19.0 (CH₃), 18.0 (CH₃); ¹H NMR (600 MHz, C₆D₆) δ 5.44 (s, 1H, H³), 5.29 (s, 1H, H¹), 5.02 (s, 1H, H⁴), 4.87 (q, $J = 6.6$ Hz, 1H, H²), 3.28 (s, 3H, OMe), 2.67–2.64 (m, 2H, H⁶ and H⁸), 2.60 (ABq, $J = 14.9$ Hz, 1H, H¹³), 2.54 (ABq, $J = 14.9$ Hz, 1H, H¹⁴), 2.40–2.37 (m, 2H, H⁵ and H⁷), 2.09 (s, 3H, Me¹), 1.44–1.42 (m, 4H, H¹⁰–H¹³), 1.10 (d, $J = 6.6$ Hz, 3H, Me²); ¹³C NMR (151 MHz, C₆D₆) δ 172.0 (C), 145.7 (C), 113.1 (CH₂), 89.5 (CH), 81.2 (CH), 65.9 (C), 50.8 (CH₃), 46.5 (CH₂ × 2), 34.9 (CH₂), 24.1 (CH₂ × 2), 19.4 (CH₃), 18.2 (CH₃); **HRMS-EI** calcd for C₁₄H₂₃NO₃, 253.1678 found 253.1670.

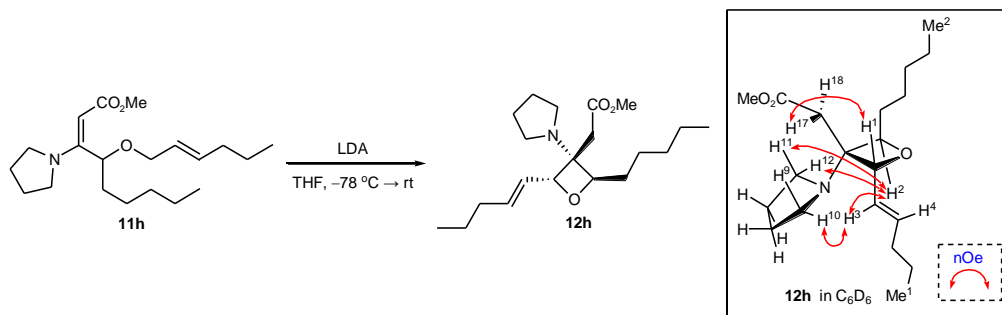


Synthesis of [(2*R*,3*R*,4*R*)-2-isopropenyl-4-isopropyl-3-pyrrolidin-1-yl-oxetan-3-yl]-acetic acid methyl ester (12f**).** Prepared according to the representative procedure with compound **11f** (210 mg, 0.75 mmol) and LDA to give oxetane **12f** (149 mg, 0.53 mmol) as a colorless oil in 71% yield. $R_f = 0.50$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2960, 2873, 2814, 1736, 1717, 1699, 1684, 1652, 1636, 1558, 1541, 1521, 1507, 1457, 1448, 1387, 1364, 1338, 1259, 1195, 1176, 1155, 1131, 1057, 1036, 997, 963, 898, 752 cm⁻¹; **¹H NMR (500 MHz, CDCl₃)** δ 5.17 (s, 1H, H³), 5.13 (s, 1H, H¹), 4.95 (s, 1H, H⁴), 4.28 (d, $J = 10.5$ Hz, 1H, H²), 3.66 (s, 3H, OMe), 2.90 (ABq, $J = 14.8$ Hz, 1H, H¹³), 2.83 (ABq, $J = 14.8$ Hz, 1H, H¹⁴), 2.72–2.68 (m, 2H, H⁶ and H⁸), 2.55–2.51 (m, 2H, H⁵ and H⁷), 1.97 (s, 3H, Me¹), 1.86 (td, $J = 12.8, 10.5$ Hz, 1H, H¹⁵), 1.65–1.59 (m, 4H, H⁹–H¹²), 0.95 (d, $J = 6.4$ Hz, 3H, Me), 0.82 (d, $J = 6.4$ Hz, 3H, Me); **¹³C NMR (126 MHz, CDCl₃)** δ 172.7 (C), 145.2 (C), 113.4 (CH₂), 91.1 (CH), 88.2 (CH), 65.7 (C), 51.5 (CH₃), 46.7 (CH₂ × 2), 34.2 (CH₂), 30.4 (CH), 23.8 (CH₂ × 2), 19.0 (CH₃), 18.7 (CH₃), 18.4 (CH₃); **HRMS-EI** calcd for C₁₆H₂₇NO₃, 281.1991 found 281.1996.



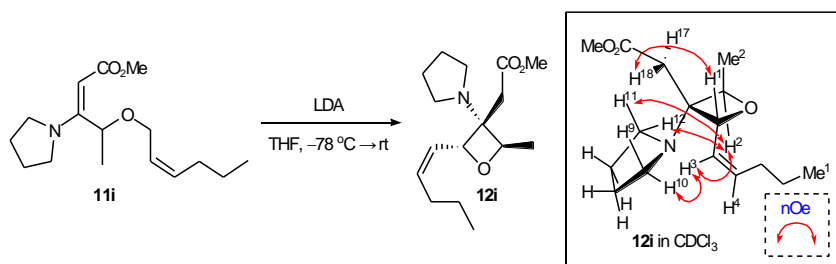
Synthesis of [(2*R*,3*R*,4*R*)-2-methyl-4-(*E*)-pent-1-enyl-3-pyrrolidin-1-yl-oxetan-3-yl]-acetic acid methyl ester (12g**).** Prepared according to the representative procedure with compound **11g** (210 mg, 0.75 mmol) and LDA to give oxetane **12g** (137 mg, 0.49 mmol) as a pale-yellow oil in 65% yield. $R_f = 0.28$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2960, 2931, 2873, 1733, 1456, 1436, 1374, 1196, 1140, 1070, 969, 945 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 6.02 (dd, $J = 15.4, 8.3$ Hz, 1H, H³), 5.73 (dt, $J = 15.4, 6.7$ Hz, 1H, H⁴), 4.97 (d, $J = 8.3$ Hz, 1H, H¹), 4.81 (q, $J = 6.5$ Hz, 1H, H²), 3.61 (s, 3H, OMe), 2.71 (s, 2H, H¹⁷ and H¹⁸), 2.60–2.57 (m, 2H, H¹⁰ and H¹²),

2.46–2.44 (m, 2H, H⁹ and H¹¹), 2.03 (dd, $J = 13.5, 6.7$ Hz, 2H, H⁵ and H⁶), 1.68–1.60 (m, 4H, H¹³–H¹⁶), 1.42–1.37 (m, 2H, H⁷ and H⁸), 1.25 (d, $J = 6.5$ Hz, 3H, Me²), 0.86 (t, $J = 7.3$ Hz, 3H, Me¹); ¹³C NMR (75 MHz, CDCl₃) δ 172.7 (C), 135.2 (CH), 127.7 (CH), 86.8 (CH), 82.3 (CH), 65.0 (C), 51.4 (CH₃), 46.0 (CH₂ × 2), 34.4 (CH₂), 32.3 (CH₂), 23.7 (CH₂ × 2), 22.0 (CH₂), 17.7 (CH₃), 13.6 (CH₃); ¹H NMR (600 MHz, C₆D₆) δ 6.27 (dd, $J = 15.4, 7.8$ Hz, 1H, H³), 5.86 (dt, $J = 15.4, 6.7$ Hz, 1H, H⁴), 5.25 (d, $J = 7.8$ Hz, 1H, H¹), 4.86 (q, $J = 6.5$ Hz, 1H, H²), 3.30 (s, 3H, OMe), 2.61–2.58 (m, 2H, H¹⁰ and H¹²), 2.56 (s, 2H, H¹⁷ and H¹⁸), 2.44–2.41 (m, 2H, H⁹ and H¹¹), 1.99 (dd, $J = 13.5, 6.7$ Hz, 2H, H⁵ and H⁶), 1.52–1.48 (m, 4H, H¹³–H¹⁶), 1.35–1.29 (m, 2H, H⁷ and H⁸), 1.14 (d, $J = 6.5$ Hz, 3H, Me²), 0.82 (t, $J = 7.3$ Hz, 3H, Me¹); ¹³C NMR (151 MHz, C₆D₆) δ 172.3 (C), 134.0 (CH), 129.3 (CH), 86.8 (CH), 81.9 (CH), 65.4 (C), 50.9 (CH₃), 46.3 (CH₂ × 2), 34.8 (CH₂), 32.7 (CH₂), 24.1 (CH₂ × 2), 22.5 (CH₂), 17.9 (CH₃), 13.8 (CH₃); HRMS-EI calcd for C₁₆H₂₇NO₃, 281.1991 found 281.1989.

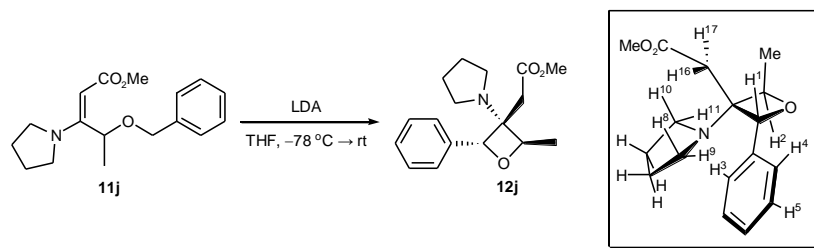


Synthesis of [(2*R*,3*R*,4*R*)-2-(*E*)-pent-1-enyl-4-pentyl-3-pyrrolidin-1-yl-oxetan-3-yl]-acetic acid methyl ester (12h). Prepared according to the representative procedure with compound **11h** (250 mg, 0.74 mmol) and LDA to give oxetane **12h** (167 mg, 0.50 mmol) as a pale-yellow oil in 67% yield. $R_f = 0.52$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); FT-IR (neat) ν 2957, 2931, 2872, 1737, 1665, 1641, 1632, 1461, 1436, 1374, 1334, 1195, 1178, 1151, 1132, 1102, 1005, 968, 945, 910, 893 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.04 (ddt, $J = 15.4, 8.4, 1.4$ Hz, 1H, H³), 5.76 (dt, $J = 15.4, 6.5$ Hz, 1H, H⁴), 5.01 (d, $J = 8.4$ Hz, 1H, H¹), 4.61 (dd, $J = 9.5, 3.6$ Hz, 1H, H²), 3.64 (s, 3H, OMe), 2.74 (s, 2H, H¹⁷ and H¹⁸), 2.50–2.46 (m, 2H, H¹⁰ and H¹²), 2.63–2.59 (m, 2H, H⁹ and H¹¹), 2.05 (q, $J = 7.0$ Hz, 2H, H⁵ and H⁶), 1.70–1.62 (m, 5H, H¹³–H¹⁶ and H¹⁸), 1.54–1.51 (m, 1H, H¹⁹), 1.44–1.40 (m, 3H, H⁷, H⁸ and H²¹), 1.30–1.18 (m, 5H, H²²–H²⁶), 0.89 (t, $J = 7.2$ Hz, 3H, Me²), 0.87 (t, $J = 7.0$ Hz, 3H, Me¹); ¹³C NMR (75 MHz, CDCl₃) δ 172.8 (C), 135.5 (CH), 127.8 (CH), 86.6 (CH), 86.3 (CH), 65.0 (C), 51.5 (CH₃), 46.2 (CH₂ × 2), 34.5 (CH₂), 32.5 (CH₂), 32.4 (CH₂),

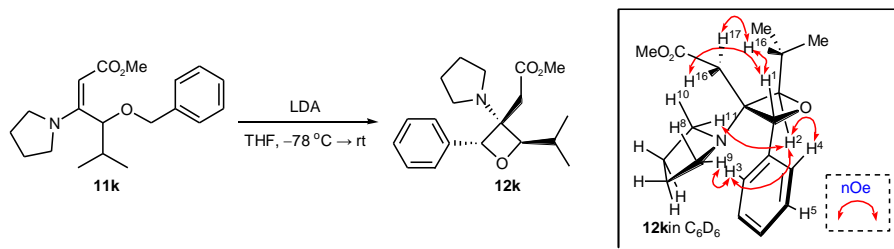
31.8 (CH₂), 24.9 (CH₂), 23.8 (CH₂ × 2), 22.5 (CH₂), 22.1 (CH₂), 13.9 (CH₃), 13.7 (CH₃); ¹H NMR (600 MHz, C₆D₆) δ 6.30 (ddt, *J* = 15.5, 7.7, 1.0 Hz, 1H, H³), 5.89 (dt, *J* = 15.5, 6.8 Hz, 1H, H⁴), 5.28 (d, *J* = 7.7 Hz, 1H, H¹), 4.75 (dd, *J* = 9.8, 3.6 Hz, 1H, H²), 3.32 (s, 3H, OMe), 2.68–2.64 (m, 2H, H¹⁰ and H¹²), 2.61 (s, 2H, H¹⁷ and H¹⁸), 2.51–2.48 (m, 2H, H⁹ and H¹¹), 1.98 (q, *J* = 7.1 Hz, 2H, H⁵ and H⁶), 1.67–1.62 (m, 1H, H²⁰), 1.56–1.50 (m, 5H, H¹³–H¹⁶ and H²¹), 1.45–1.41 (m, 1H, H¹⁹), 1.35–1.30 (m, 2H, H⁷ and H⁸), 1.28–1.27 (m, 5H, H²²–H²⁶), 0.87 (t, *J* = 7.3 Hz, 3H, Me²), 0.83 (t, *J* = 7.4 Hz, 3H, Me¹); ¹³C NMR (151 MHz, C₆D₆) δ 172.3 (C), 133.9 (CH), 128.1 (CH), 86.6 (CH), 85.9 (CH), 65.6 (C), 50.9 (CH₃), 46.6 (CH₂ × 2), 34.8 (CH₂), 32.8 (CH₂), 32.7 (CH₂), 32.2 (CH₂), 25.6 (CH₂), 24.2 (CH₂ × 2), 22.9 (CH₂), 22.3 (CH₂), 14.2 (CH₃), 13.8 (CH₃); HRMS-EI calcd for C₂₀H₃₅NO₃, 337.2617 found 337.2608.



Synthesis of [(2*R*,3*R*,4*R*)-2-methyl-4-(*Z*)-pent-1-enyl-3-pyrrolidin-1-yl-oxetan-3-yl]-acetic acid methyl ester (12i). Prepared according to the representative procedure with compound **11i** (210 mg, 0.75 mmol) and LDA to give oxetane **12i** (130 mg, 0.46 mmol) as a pale-yellow oil in 62% yield. *R_f* = 0.28 (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) ν 2961, 2930, 2873, 1736, 1461, 1440, 1266, 1198, 1141, 1066, 942 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.12 (ddt, *J* = 11.1, 9.7, 1.5 Hz, 1H, H³), 5.66 (dt, *J* = 11.1, 7.5 Hz, 1H, H⁴), 5.43 (d, *J* = 9.7 Hz, 1H, H¹), 4.89 (q, *J* = 6.5 Hz, 1H, H²), 3.66 (s, 3H, OMe), 2.77 (s, 2H, H¹⁷ and H¹⁸), 2.62–2.58 (m, 2H, H¹⁰ and H¹²), 2.46–2.42 (m, 2H, H⁹ and H¹¹), 2.21–2.08 (m, 2H, H⁵ and H⁶), 1.68–1.62 (m, 4H, H¹³–H¹⁶), 1.43–1.36 (m, 2H, H⁷ and H⁸), 1.28 (d, *J* = 6.5 Hz, 3H, Me²), 0.92 (t, *J* = 7.3 Hz, 3H, Me¹); ¹³C NMR (75 MHz, CDCl₃) δ 172.9 (C), 134.6 (CH), 126.9 (CH), 82.9 (CH), 80.6 (CH), 65.1 (C), 51.6 (CH₃), 45.8 (CH₂ × 2), 32.1 (CH₂), 29.4 (CH₂), 23.7 (CH₂ × 2), 22.8 (CH₂), 17.6 (CH₃), 13.8 (CH₃); HRMS-EI calcd for C₁₆H₂₇NO₃, 281.1991 found 281.1984.

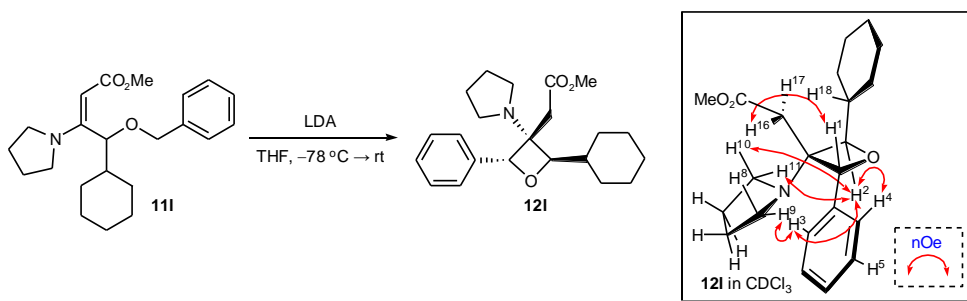


Synthesis of [(2*R*,3*R*,4*R*)-2-methyl-4-phenyl-3-pyrrolidin-1-yl-oxetan-3-yl]-acetic acid methyl ester (12j**).** Prepared according to the representative procedure with compound **11j** (220 mg, 0.76 mmol) and LDA to give oxetane **12j** (176 mg, 0.61 mmol) as a colorless oil in 80% yield. $R_f = 0.47$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2966, 2874, 2809, 1735, 1711, 1602, 1558, 1541, 1588, 1460, 1435, 1379, 1333, 1264, 1196, 1178, 1140, 1069, 983, 890, 747, 697 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 7.58 (d, $J = 7.5$ Hz, 2H, H³ and H⁴), 7.36–7.28 (m, 3H, H⁵, H⁶ and H⁷), 5.82 (s, 1H, H¹), 5.08 (q, $J = 6.4$ Hz, 1H, H²), 3.69 (s, 3H, OMe), 2.93 (ABq, $J = 15.1$ Hz, 1H, H¹⁶), 2.83 (ABq, $J = 15.1$ Hz, 1H, H¹⁷), 2.25 (br, 2H, H⁸ and H¹⁰), 2.17 (br, 2H, H⁹ and H¹¹), 1.41 (d, $J = 6.4$ Hz, 3H, Me), 1.42–1.38 (m, 4H, H¹²–H¹⁵); **¹³C NMR (75 MHz, CDCl₃)** δ 172.6 (C), 139.3 (C), 127.6 (CH \times 3), 127.4 (CH \times 2), 87.5 (CH), 82.7 (CH), 65.6 (C), 51.6 (CH₃), 45.8 (CH₂ \times 2), 33.5 (CH₂), 23.6 (CH₂ \times 2), 18.2 (CH₃); HRMS-EI calcd for C₁₇H₂₃NO₃, 289.1678 found 289.1685.



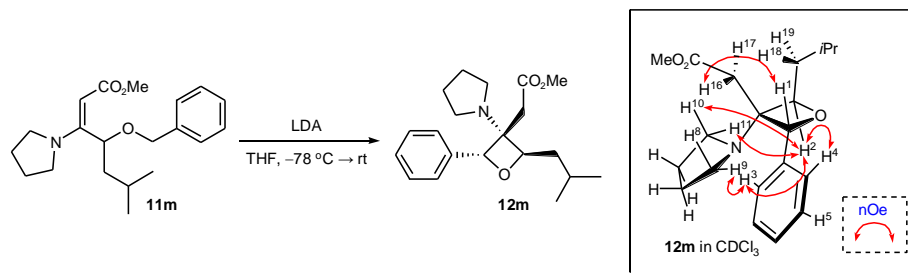
Synthesis of [(2*R*,3*R*,4*R*)-2-isopropyl-4-phenyl-3-pyrrolidin-1-yl-oxetan-3-yl]-acetic acid methyl ester (12k**).** Prepared according to the representative procedure with compound **11k** (240 mg, 0.76 mmol) and LDA to give oxetane **12k** (204 mg, 0.64 mmol) as a colorless oil in 85% yield. $R_f = 0.53$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2959, 2872, 2808, 1735, 1717, 1698, 1684, 1653, 1558, 1541, 1521, 1496, 1472, 1457, 1436, 1387, 1363, 1339, 1314, 1259, 1195, 1176, 1154, 1120, 1095, 1053, 1001, 934, 892, 750, 698 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 7.62 (d, $J = 7.5$ Hz, 2H, H³ and H⁴), 7.34–7.25 (m, 3H, H⁵, H⁶ and H⁷), 5.82 (s, 1H, H¹), 4.37 (d, $J = 10.5$ Hz, 1H, H²), 3.69 (s, 3H, OMe), 2.98 (ABq, $J = 15.3$ Hz, 1H, H¹⁶), 2.88 (ABq, $J = 15.3$

Hz, 1H, H¹⁷), 2.24–2.20 (m, 2H, H⁸ and H¹⁰), 2.11–2.04 (m, 3H, H⁹, H¹¹ and H¹⁸), 1.46–1.31 (m, 4H, H¹²–H¹⁵), 1.13 (d, *J* = 6.4 Hz, 3H, Me), 0.87 (d, *J* = 6.4 Hz, 3H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 172.7 (C), 139.7 (C), 128.1 (CH × 2), 127.4 (CH), 127.3 (CH × 2), 91.9 (CH), 86.0 (CH), 65.4 (C), 51.6 (CH₃), 46.1 (CH₂ × 2), 32.6 (CH₂), 30.7 (CH), 23.4 (CH₂ × 2), 18.5 (CH₃ × 2); ¹H NMR (600 MHz, C₆D₆) δ 7.92 (d, *J* = 7.3 Hz, 2H, H³ and H⁴), 7.25 (dd, *J* = 7.6, 7.3 Hz, 2H, H⁵ and H⁷), 7.15–7.13 (m, 1H, H⁶), 6.03 (s, 1H, H¹), 4.34 (d, *J* = 10.4 Hz, 1H, H²), 3.31 (s, 3H, OMe), 2.72 (s, 2H, H¹⁶ and H¹⁷), 2.20–2.15 (m, 4H, H⁸–H¹¹), 1.84–1.78 (m, 1H, H¹⁸), 1.28–1.19 (m, 4H, H¹²–H¹⁵), 1.10 (d, *J* = 6.6 Hz, 3H, Me), 0.60 (d, *J* = 6.7 Hz, 3H, Me); ¹³C NMR (151 MHz, C₆D₆) δ 172.3 (C), 140.9 (C), 128.5 (CH × 2), 127.6 (CH), 127.5 (CH × 2), 91.4 (CH), 86.2 (CH), 65.9 (C), 51.0 (CH₃), 46.5 (CH₂ × 2), 33.1 (CH₂), 30.9 (CH), 23.7 (CH₂ × 2), 18.7 (CH₃), 18.5 (CH₃); HRMS-EI calcd for C₁₉H₂₇NO₃, 317.1991 found 317.1999.

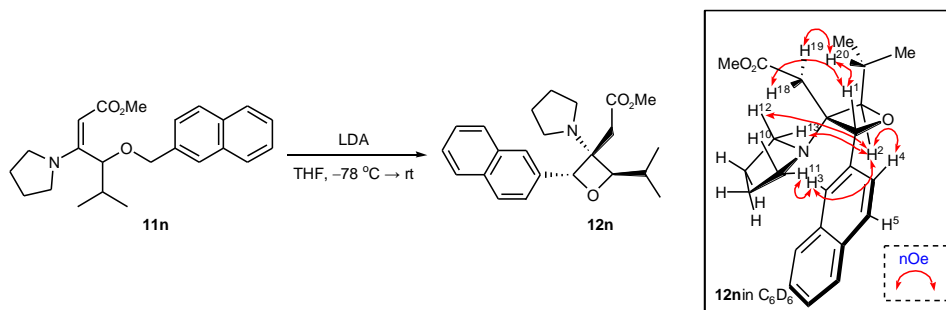


Synthesis of [(2*R*,3*R*,4*R*)-2-cyclohexyl-4-phenyl-3-pyrrolidin-1-yl-oxetan-3-yl]-acetic acid methyl ester (121**).** Prepared according to the representative procedure with compound **111** (260 mg, 0.73 mmol) and LDA to give oxetane **121** (214 mg, 0.60 mmol) as a pale-yellow oil in 82% yield. *R_f* = 0.47 (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) ν 2925, 2851, 2806, 1735, 1699, 1684, 1559, 1450, 1436, 1338, 1263, 1194, 1174, 1154, 1131, 1030, 996, 887, 752, 698 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.62 (dd, *J* = 8.2, 1.5 Hz, 2H, H³ and H⁴), 7.32–7.25 (m, 3H, H⁵, H⁶ and H⁷), 5.81 (s, 1H, H¹), 4.47 (d, *J* = 10.5 Hz, 1H, H²), 3.69 (s, 3H, OMe), 3.00 (ABq, *J* = 15.3 Hz, 1H, H¹⁶), 2.89 (ABq, *J* = 15.3 Hz, 1H, H¹⁷), 2.22–2.18 (m, 2H, H⁸ and H¹⁰), 2.11–2.05 (m, 3H, H⁹, H¹¹ and H¹⁹), 1.78–1.69 (m, 4H, H¹⁸, H²¹, H²² and H²⁶), 1.58–1.56 (m, 1H, H²⁸), 1.45–1.42 (m, 2H, H¹² and H¹³), 1.35–1.21 (m, 5H, H¹⁴, H¹⁵, H²³, H²⁴ and H²⁵), 0.94–0.90 (m, 2H, H¹⁹ and H²⁷); ¹³C NMR (126 MHz, CDCl₃) δ 172.8 (C), 139.7 (C), 128.1 (CH × 2), 127.4 (CH), 127.3 (CH × 2), 90.6 (CH), 86.3 (CH), 65.6 (C), 51.6 (CH₃), 46.2 (CH₂ × 2), 40.5 (CH), 32.7 (CH₂), 29.0 (CH₂), 28.3 (CH₂), 26.4 (CH₂), 25.5 (CH₂ × 2), 23.4 (CH₂ × 2); HRMS-EI calcd for

C₂₂H₃₁NO₃, 357.2304 found 357.2312.



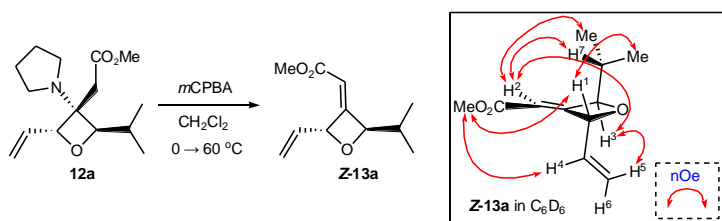
Synthesis of [(2*R*,3*R*,4*R*)-2-isobutyl-4-phenyl-3-pyrrolidin-1-yl-oxetan-3-yl]-acetic acid methyl ester (12m**).** Prepared according to the representative procedure with compound **11m** (250 mg, 0.76 mmol) and LDA to give oxetane **12m** (198 mg, 0.60 mmol) as a pale-yellow oil in 79% yield. $R_f = 0.51$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2954, 2930, 2807, 1734, 1717, 1699, 1653, 1617, 1558, 1541, 1507, 1489, 1457, 1435, 1363, 1339, 1260, 1196, 1176, 1147, 1075, 1030, 985, 892, 884, 750, 698 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 7.52 (d, $J = 7.5$ Hz, 2H, H³ and H⁴), 7.25–7.18 (m, 3H, H⁵, H⁶ and H⁷), 5.74 (s, 1H, H¹), 4.90 (dd, $J = 9.9, 2.9$ Hz, 1H, H²), 3.62 (s, 3H, OMe), 2.86 (ABq, $J = 15.2$ Hz, 1H, H¹⁶), 2.72 (ABq, $J = 15.2$ Hz, 1H, H¹⁷), 2.19–2.14 (m, 2H, H⁸ and H¹⁰), 2.10–2.06 (m, 2H, H⁹ and H¹¹), 1.77–1.69 (m, 1H, H²⁰), 1.68–1.64 (m, 1H, H¹⁸), 1.39–1.24 (m, 5H, H¹⁹ and H¹²–H¹⁵), 0.92 (d, $J = 6.4$ Hz, 3H, Me), 0.91 (d, $J = 6.4$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 172.7 (C), 139.6 (C), 127.8 (CH \times 2), 127.5 (CH), 127.4 (CH \times 2), 87.4 (CH), 85.2 (CH), 65.6 (C), 51.6 (CH₃), 45.8 (CH₂ \times 2), 41.6 (CH₂), 33.2 (CH₂), 24.9 (CH), 23.6 (CH₂ \times 2), 23.4 (CH₃), 22.3 (CH₃); **HRMS-EI** calcd for C₂₀H₂₉NO₃, 331.2147 found 331.2140.



Synthesis of [(2*R*,3*R*,4*R*)-2-isopropyl-4-naphthalen-2-yl-3-pyrrolidin-1-yl-oxetan-3-yl]-acetic acid methyl ester (12n**).** Prepared according to the representative procedure with compound **11n** (270 mg, 0.74 mmol) and LDA to give oxetane **12n** (176 mg, 0.48 mmol) as a

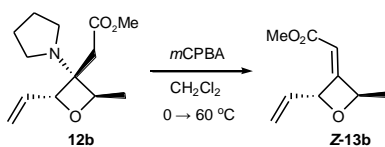
pale-yellow oil in 65% yield. $R_f = 0.55$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2959, 2872, 2808, 1735, 1631, 1601, 1509, 1461, 1435, 1365, 1332, 1262, 1195, 1175, 1154, 1125, 1053, 1001, 966, 952, 890, 857, 813, 745 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 8.05 (s, 1H, H³), 7.89–7.78 (m, 4H, H⁴, H⁵, H⁶ and H⁹), 7.47–7.44 (m, 2H, H⁷ and H⁸), 6.01 (s, 1H, H¹), 4.37 (d, $J = 10.2$ Hz, 1H, H²), 3.72 (s, 3H, OMe), 3.05 (ABq, $J = 15.3$ Hz, 1H, H¹⁸), 2.95 (ABq, $J = 15.3$ Hz, 1H, H¹⁹), 2.26 (br, 2H, H¹⁰ and H¹²), 2.16–2.06 (m, 3H, H¹¹, H¹³ and H²⁰), 1.39–1.28 (m, 4H, H¹⁴–H¹⁷), 1.08 (d, $J = 6.6$ Hz, 3H, Me), 0.91 (d, $J = 6.6$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 172.7 (C), 137.4 (C), 133.0 (C), 132.8 (C), 128.2 (CH), 127.5 (CH), 126.9 (CH), 126.7 (CH), 126.3 (CH), 125.6 (CH), 125.5 (CH), 91.9 (CH), 86.2 (CH), 65.8 (C), 51.6 (CH₃), 46.3 (CH₂ × 2), 32.9 (CH₂), 30.8 (CH), 23.5 (CH₂ × 2), 18.5 (CH₃ × 2); **¹H NMR (600 MHz, C₆D₆)** δ 8.38 (s, 1H, H³), 8.16 (dd, $J = 8.7, 1.6$ Hz, 1H, H⁴), 7.75–7.74 (m, 2H, H⁵ and H⁹), 7.66–7.64 (m, 1H, H⁶), 7.24–7.21 (m, 2H, H⁷ and H⁸), 6.21 (s, 1H, H¹), 4.45 (d, $J = 10.5$ Hz, 1H, H²), 3.35 (s, 3H, OMe), 2.76 (ABq, $J = 14.9$ Hz, 1H, H¹⁸), 2.75 (ABq, $J = 14.9$ Hz, 1H, H¹⁹), 2.78–2.14 (m, 4H, H¹⁰–H¹³), 1.89–1.83 (m, 1H, H²⁰), 1.17–1.14 (m, 2H, H¹⁴–H¹⁵), 1.14 (d, $J = 6.4$ Hz, 3H, Me), 1.12–1.08 (m, 2H, H¹⁶–H¹⁷), 0.62 (d, $J = 6.6$ Hz, 3H, Me); **¹³C NMR (151 MHz, C₆D₆)** δ 172.3 (C), 138.8 (C), 133.6 (C), 133.5 (C), 128.5 (CH), 127.9 (CH), 127.3 (CH), 127.1 (CH), 126.9 (CH), 125.9 (CH), 125.8 (CH), 91.5 (CH), 86.5 (CH), 66.2 (C), 51.1 (CH₃), 46.6 (CH₂ × 2), 33.2 (CH₂), 30.9 (CH), 23.7 (CH₂ × 2), 18.7 (CH₃), 18.5 (CH₃); **HRMS-EI** calcd for C₂₃H₂₉NO₃, 367.2147 found 367.2141.

General procedure for the Cope elimination reaction



Synthesis of (Z)-[(2*R*,4*R*)-2-isopropyl-4-vinyl-oxetan-3-(*Z*)-ylidene]-acetic acid methyl ester (E-13a**). *m*-CPBA (77%; 100 mg, 4.49 mmol, 1.2 equiv.) was added at 0 °C to an oxetane **12a** (100 mg, 3.74 mmol, 1.0 equiv.) in a 10 mL flask with CH₂Cl₂ (4.0 mL). The mixture was stirred for 30 minutes at 0 °C, and then heated to 60 °C for an additional 30 minutes by switching the ice/water bath to an oil bath. The reaction was quenched by the addition of saturated sodium**

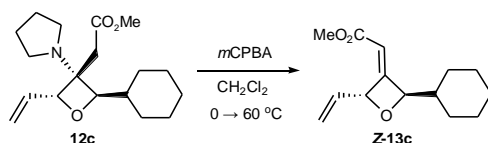
thiosulfate (2.0 mL) and washed with saturated sodium bicarbonate (3 mL \times 2), extracted with CH₂Cl₂ (3 mL \times 2). The combined organic layer was washed with brine, and dried over anhydrous sodium sulfate, followed by concentration to afford the crude material. Purification by flash column chromatography (*n*-hexane/EtOAc, 10:1) to provide a single diastereomer **Z-13a** (66 mg, 3.37 mmol) as colorless oil in 90% yield. $R_f = 0.56$ (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2962, 2931, 2874, 1724, 1699, 1653, 1636, 1558, 1541, 1533, 1457, 1436, 1397, 1386, 1363, 1341, 1269, 1219, 1197, 1102, 1032, 1008, 970, 926, 906, 890 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 6.22 (ddd, $J = 15.8, 10.2, 5.2$ Hz, 1H, H⁴), 5.74 (br, 1H, H¹), 5.66 (dd, $J = 2.5, 2.1$ Hz, 1H, H²), 5.52 (dd, $J = 15.8, 1.3$ Hz, 1H, H⁵), 5.29 (dd, $J = 10.2, 1.3$ Hz, 1H, H⁶), 5.03 (ddd, $J = 6.4, 4.6, 2.1$ Hz, 1H, H³), 3.70 (s, 3H, OMe), 2.05–1.96 (m, 1H, H⁷), 1.02 (d, $J = 6.8$ Hz, 3H, Me), 0.99 (d, $J = 6.8$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 165.0 (C), 163.5 (C), 134.1 (CH), 116.5 (CH₂), 110.7 (CH), 90.5 (CH), 86.7 (CH), 51.2 (CH₃), 32.9 (CH), 16.9 (CH₃), 16.8 (CH₃); **¹H NMR (600 MHz, C₆D₆)** δ 6.47 (ddd, $J = 17.1, 10.5, 4.6$ Hz, 1H, H⁴), 5.86 (br, 1H, H¹), 5.71 (ddd, $J = 17.1, 1.8, 1.5$ Hz, 1H, H⁵), 5.51 (dd, $J = 2.6, 2.1$ Hz, 1H, H²), 5.21 (ddd, $J = 10.5, 1.8, 1.7$ Hz, 1H, H⁶), 4.71 (ddd, $J = 6.5, 4.6, 2.1$ Hz, 1H, H³), 3.30 (s, 3H, OMe), 1.69 (qqd, $J = 6.8, 6.8, 6.5$ Hz, 1H, H⁷), 0.84 (d, $J = 6.8$ Hz, 3H, Me), 0.76 (d, $J = 6.8$ Hz, 3H, Me); **¹³C NMR (151 MHz, C₆D₆)** δ 164.8 (C), 164.4 (C), 134.9 (CH), 115.3 (CH₂), 110.7 (CH), 90.3 (CH), 86.6 (CH), 50.8 (CH₃), 33.2 (CH), 17.0 (CH₃), 16.9 (CH₃); **HRMS-EI** calcd for C₁₁H₁₆O₃, 196.1099 found 196.1105.



(Z)-[(2R,4R)-2-methyl-4-vinyl-oxetan-3-(Z)-ylidene]-acetic acid methyl ester (Z-13b).

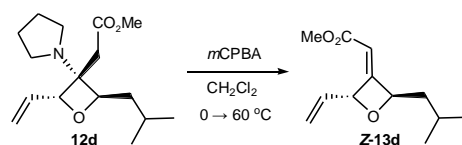
According to the general procedure, oxetane **12b** (90 mg, 3.76 mmol) was reacted to give a single diastereomer **Z-13b** (56 mg, 3.31 mmol) as a pale-yellow oil in 88% yield. $R_f = 0.40$ (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2981, 2937, 1726, 1658, 1641, 1439, 1402, 1371, 1221, 1166, 1097, 1077, 1023, 954, 885 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 6.22 (ddd, $J = 17.1, 10.4, 5.1$ Hz, 1H, H⁴), 5.86 (br, 1H, H¹), 5.59 (dd, $J = 2.5, 2.1$ Hz, 1H, H²), 5.53 (dd, $J = 17.1, 1.6$ Hz, 1H, H⁵), 5.44–5.40 (m, 1H, H³), 5.29 (dd, $J = 10.4, 1.5$ Hz, 1H, H⁶), 3.71 (s, 3H, OMe), 1.50 (d, $J = 6.5$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 165.4 (C), 165.2 (C), 133.9

(CH), 116.2 (CH₂), 110.2 (CH), 86.9 (CH), 82.6 (CH), 51.4 (CH₃), 21.0 (CH₃); **HRMS-EI** calcd for C₉H₁₂O₃, 168.0786 found 168.0791.



(Z)-[(2R,4R)-2-cyclohexyl-4-vinyl-oxetan-3-(Z)-ylidene]-acetic acid methyl ester (Z-13c).

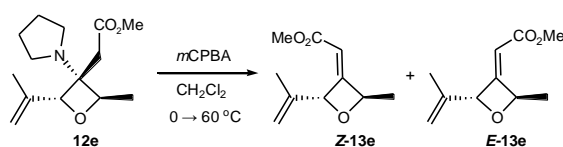
According to the general procedure, oxetane **12c** (110 mg, 3.60 mmol) was reacted to give a single diastereomer **Z-13c** (77 mg, 3.28 mmol) as a pale-yellow oil in 91% yield. **R_f** = 0.58 (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3049, 2926, 2854, 1724, 1699, 1653, 1638, 1558, 1541, 1508, 1449, 1436, 1341, 1268, 1218, 1197, 1144, 1114, 1087, 1024, 1001, 988, 968, 924, 890, 749 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 6.21 (ddd, *J* = 17.1, 10.4, 5.0 Hz, 1H, H⁴), 5.73 (ddd, *J* = 5.0, 4.5, 2.5 Hz, 1H, H¹), 5.65 (dd, *J* = 2.5, 2.1 Hz, 1H, H²), 5.50 (dd, *J* = 17.1, 1.6 Hz, 1H, H⁵), 5.28 (dd, *J* = 10.4, 1.6 Hz, 1H, H⁶), 5.04 (ddd, *J* = 6.5, 4.5, 2.1 Hz, 1H, H³), 3.70 (s, 3H, OMe), 1.80–1.67 (m, 5H, H⁷–H⁹, H¹⁶ and H¹⁷), 1.24–0.90 (m, 6H, H¹⁰–H¹⁵); **¹³C NMR (75 MHz, CDCl₃)** δ 165.1 (C), 163.7 (C), 134.2 (CH), 116.5 (CH₂), 110.7 (CH), 89.9 (CH), 86.9 (CH), 51.2 (CH₃), 42.7 (CH), 29.6 (CH₂), 27.3 (CH₂), 27.1 (CH₂), 25.7 (CH₂), 25.6 (CH₂); **¹H NMR (600 MHz, C₆D₆)** δ 6.50 (ddd, *J* = 17.0, 10.3, 4.4 Hz, 1H, H⁴), 5.88 (br, m, 1H, H¹), 5.73 (ddd, *J* = 17.0, 1.7, 1.4 Hz, 1H, H⁵), 5.54 (dd, *J* = 2.6, 2.1 Hz, 1H, H²), 5.22 (dd, *J* = 10.3, 1.9, 1.4 Hz, 1H, H⁶), 4.76 (ddd, *J* = 6.4, 4.5, 2.1 Hz, 1H, H³), 3.31 (s, 3H, OMe), 1.80–1.78 (m, 1H, H⁸), 1.61–1.51 (m, 4H, H⁹, H¹⁰, H¹⁶ and H¹⁷), 1.48–1.42 (m, 1H, H⁷), 1.09–0.90 (m, 5H, H¹¹–H¹⁵); **¹³C NMR (151 MHz, C₆D₆)** δ 164.9 (C), 164.6 (C), 135.0 (CH), 115.4 (CH₂), 110.6 (CH), 89.6 (CH), 86.8 (CH), 50.8 (CH₃), 42.9 (CH), 27.6 (CH₂), 27.3 (CH₂), 26.5 (CH₂), 26.0 (CH₂), 25.9 (CH₂); **HRMS-EI** calcd for C₁₄H₂₀O₃, 236.1412 found 236.1411.



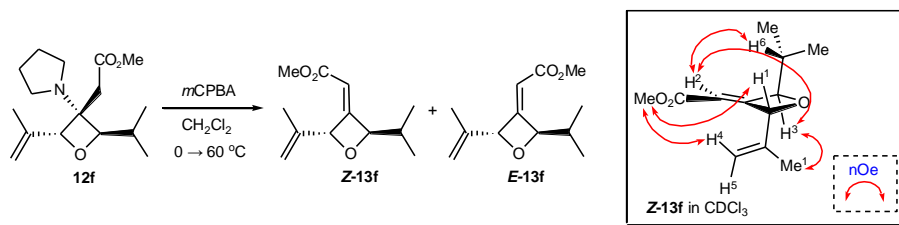
(Z)-[(2R,4R)-2-isobutyl-4-vinyl-oxetan-3-(Z)-ylidene]-acetic acid methyl ester (Z-13d).

According to the general procedure, oxetane **12d** (100 mg, 3.55 mmol) was reacted to give a single diastereomer **Z-13d** (67 mg, 3.20 mmol) as a pale-yellow oil in 90% yield. **R_f** = 0.57

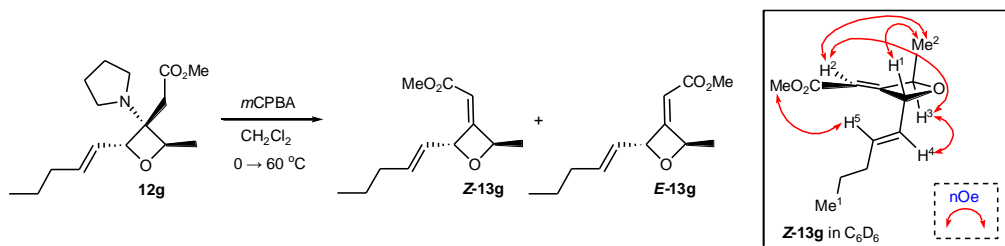
(SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2965, 2876, 1724, 1699, 1653, 1638, 1559, 1542, 1436, 1341, 1269, 1219, 1197, 1032, 1008, 970, 927, 890 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 6.21 (ddd, $J = 17.1, 10.4, 5.3$ Hz, 1H, H⁴), 5.81 (br, 1H, H¹), 5.60 (dd, $J = 2.5, 2.1$ Hz, 1H, H²), 5.52 (ddd, $J = 17.1, 1.8, 1.6$ Hz, 1H, H⁵), 5.49–5.33 (m, 1H, H³), 5.29 (ddd, $J = 10.4, 1.6, 1.3$ Hz, 1H, H⁶), 3.70 (s, 3H, OMe), 1.89–1.78 (m, 2H, H⁷ and H⁸), 1.61–1.51 (m, 1H, H⁹), 0.96 (d, $J = 6.5$ Hz, 3H, Me), 0.95 (d, $J = 6.5$ Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 165.2 (C \times 2), 134.0 (CH), 116.4 (CH₂), 110.1 (CH), 86.9 (CH), 84.9 (CH), 51.3 (CH₃), 44.5 (CH₂), 24.5 (CH), 23.0 (CH₃), 22.3 (CH₃); HRMS-EI calcd for C₁₂H₁₈O₃, 210.1256 found 210.1248.



(Z)- and (E)-[(2*R*,4*R*)-2-isopropenyl-4-methyl-oxetan-3-ylidene]-acetic acid methyl esters (Z-13e**) and (**E-13e**).** According to the general procedure, oxetane **12e** (90 mg, 3.55 mmol) was reacted to give a 75:25 mixture of diastereomers **Z-13e** and **E-13e** (*d.r.* was determined from the crude ¹H NMR spectrum of the reaction) as a pale-yellow oil in 88% yield (57 mg, 3.13 mmol). **Z-13e:** $R_f = 0.52$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2986, 2939, 1736, 1450, 1357, 1227, 1164, 1097, 1055, 954, 885 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 5.59–5.57 (m, 3H, H¹, H² and H³), 5.10 (s, 1H, H⁴), 4.98 (s, 1H, H⁵), 3.71 (s, 3H, OMe), 1.82 (s, 3H, Me¹), 1.64 (d, $J = 6.6$ Hz, 3H, Me²); **¹³C NMR (75 MHz, CDCl₃)** δ 165.5 (C), 165.2 (C), 142.3 (C), 113.8 (CH₂), 110.6 (CH), 88.1 (CH), 84.8 (CH), 51.4 (CH₃), 19.8 (CH₃), 17.0 (CH₃); HRMS-EI calcd for C₁₀H₁₄O₃, 182.0943 found 182.0945; **E-13e:** $R_f = 0.41$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2985, 2936, 1732, 1684, 1647, 1636, 1456, 1362, 1226, 1170, 1096, 1058, 953, 881 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 5.79 (ddd, $J = 4.1, 2.5, 0.6$ Hz, 1H, H¹), 5.68 (dd, $J = 2.5, 2.3$ Hz, 1H, H²), 5.44–5.38 (m, 1H, H³), 5.10 (s, 1H, H⁴), 5.04 (s, 1H, H⁵), 3.67 (s, 3H, OMe), 1.88 (s, 3H, Me¹), 1.50 (d, $J = 6.5$ Hz, 3H, Me²); **¹³C NMR (75 MHz, CDCl₃)** δ 165.2 (C), 164.7 (C), 141.6 (C), 115.5 (CH₂), 111.5 (CH), 90.7 (CH), 82.9 (CH), 51.2 (CH₃), 21.2 (CH₃), 17.6 (CH₃); **HRMS-EI** calcd for C₁₀H₁₄O₃, 182.0943 found 182.0945.

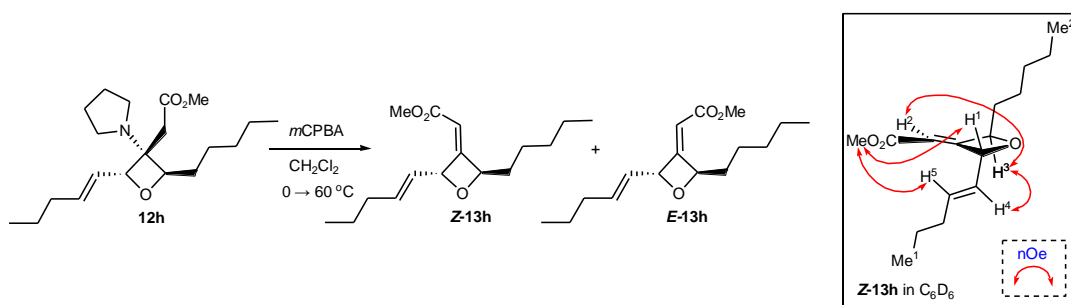


(Z)- and (E)-[(2R,4R)-2-isopropenyl-4-isopropyl-oxetan-3-ylidene]-acetic acid methyl esters (Z-13f) and (E-13f). According to the general procedure, oxetane **12f** (100 mg, 3.55 mmol) was reacted to give a 72:28 mixture of diastereomers **Z-13f** and **E-13f** (*d.r.* was determined from the crude ^1H NMR spectrum of the reaction) as a colorless oil in 85% yield (64 mg, 3.04 mmol). **Z-13f**: $R_f = 0.53$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3080, 2963, 2875, 1725, 1699, 1652, 1558, 1541, 1521, 1508, 1472, 1457, 1436, 1363, 1342, 1274, 1219, 1197, 1102, 1039, 1016, 975, 937, 903, 877 cm^{-1} ; ^1H NMR (300 MHz, CDCl₃) δ 5.73 (dd, $J = 2.5, 2.1$ Hz, 1H, H²), 5.68 (dd, $J = 4.4, 2.5$ Hz, 1H, H¹), 5.07 (s, 1H, H⁴), 5.03 (s, 1H, H⁵), 4.98 (ddd, $J = 6.4, 4.4, 2.1$ Hz, 1H, H³), 3.65 (s, 3H, OMe), 2.05–1.99 (m, 1H, H⁶), 1.85 (s, 3H, Me¹), 1.01 (d, $J = 6.8$ Hz, 3H, Me), 0.99 (d, $J = 6.8$ Hz, 3H, Me); ^{13}C NMR (75 MHz, CDCl₃) δ 165.0 (C), 162.6 (C), 141.6 (C), 115.9 (CH), 112.0 (CH₂), 90.9 (CH), 90.7 (CH), 51.0 (CH₃), 33.1 (CH), 17.2 (CH₃), 17.0 (CH₃), 16.8 (CH₃); **HRMS-EI** calcd for C₁₂H₁₈O₃, 210.1256 found 210.1263; **E-13f**: $R_f = 0.47$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3078, 2966, 2876, 1725, 1699, 1652, 1558, 1542, 1524, 1457, 1436, 1363, 1343, 1272, 1219, 1197, 1102, 1038, 1016, 976, 935, 903, 879 cm^{-1} ; ^1H NMR (300 MHz, CDCl₃) δ 5.60 (dd, $J = 2.4, 2.0$ Hz, 1H, H²), 5.42 (br, 1H, H¹), 5.40–5.37 (m, 1H, H³), 5.02 (s, 1H, H⁴), 4.98 (s, 1H, H⁵), 3.70 (s, 3H, OMe), 2.46–2.41 (m, 1H, H⁶), 1.82 (s, 3H, Me¹), 1.06 (d, $J = 6.8$ Hz, 3H, Me), 1.02 (d, $J = 6.8$ Hz, 3H, Me); ^{13}C NMR (75 MHz, CDCl₃) δ 165.3 (C), 163.8 (C), 142.6 (C), 114.2 (CH), 111.2 (CH₂), 92.8 (CH), 89.3 (CH), 51.3 (CH₃), 30.3 (CH), 18.2 (CH₃), 16.9 (CH₃), 15.5 (CH₃). **HRMS-EI** calcd for C₁₂H₁₈O₃, 210.1256 found 210.1248.



(Z)- and (E)-[(2R,4R)-2-methyl-4-((E)-pent-1-enyl)-oxetan-3-ylidene]-acetic acid methyl

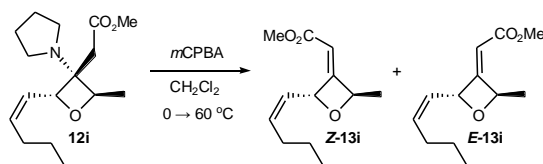
ester (**Z-13g**) and (**E-13g**). According to the general procedure, oxetane **12g** (100 mg, 3.55 mmol) was reacted to give a 90:10 mixture of inseparable diastereomers **Z-13g** and **E-13g** (*d.r.* was determined from the crude ^1H NMR spectrum of the reaction) as a pale-yellow oil in 86% yield (64 mg, 3.04 mmol). **Z-13g**: $R_f = 0.49$ (SiO_2 , 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2960, 2935, 2874, 1725, 1678, 1658, 1642, 1439, 1352, 1257, 1095, 1030, 923, 883 cm^{-1} ; **^1H NMR (600 MHz, C_6D_6)** δ 6.05–6.04 (m, 2H, H^4 and H^5), 5.96 (ddd, $J = 4.3, 3.2, 2.5$ Hz, 1H, H^1), 5.38 (dd, $J = 2.5, 2.0$ Hz, 1H, H^2), 5.07 (ddq, $J = 6.5, 4.3, 2.0$ Hz, 1H, H^3), 3.31 (s, 3H, OMe), 1.99–1.96 (m, 2H, H^6 and H^7), 1.35–1.29 (m, 2H, H^8 and H^9), 1.13 (d, $J = 6.5$ Hz, 3H, Me^2), 0.82 (t, $J = 7.4$ Hz, 3H, Me^1); **^{13}C NMR (151 MHz, C_6D_6)** δ 167.1 (C), 164.9 (C), 132.8 (CH), 127.1 (CH), 109.9 (CH), 86.8 (CH), 81.9 (CH), 50.7 (CH_3), 34.5 (CH_2), 22.6 (CH_2), 21.0 (CH_3), 13.7 (CH_3); **HRMS-EI** calcd for $\text{C}_{12}\text{H}_{18}\text{O}_3$, 210.1256 found 210.1261; **E-13g**: $R_f = 0.49$ (SiO_2 , 4:1 *v/v*, *n*-hexane/EtOAc); **^1H NMR (600 MHz, C_6D_6)** δ 5.67–5.63 (m, 1H, H^3), 5.55–5.54 (m, 1H, H^4 and H^5), 5.50 (dd, $J = 2.5, 2.0$ Hz, 1H, H^2), 5.39–5.38 (m, 1H, H^1), 3.29 (s, 3H, OMe), 1.83–1.79 (m, 2H, H^6 and H^7), 1.68 (d, $J = 6.5$ Hz, 3H, Me^2), 1.23–1.18 (m, 2H, 2H, H^8 and H^9), 0.76 (t, $J = 7.4$ Hz, 3H, Me^1); **^{13}C NMR (151 MHz, C_6D_6)** δ 167.7 (C), 165.0 (C), 135.4 (CH), 128.7 (CH), 110.8 (CH), 85.7 (CH), 84.1 (CH), 50.8 (CH_3), 34.3 (CH_2), 22.2 (CH_2), 20.2 (CH_3), 13.6 (CH_3); **HRMS-EI** calcd for $\text{C}_{12}\text{H}_{18}\text{O}_3$, 210.1256 found 210.1261.



(**Z**)- and (**E**)-[(2*R*,4*R*)-2-pentyl-4-(*E*)-pent-1-enyl]-oxetan-3-ylidene]-acetic acid methyl ester (**Z-13h**) and (**E-13h**). According to the general procedure, oxetane **12h** (120 mg, 3.56 mmol) was reacted to give a 93:7 mixture of inseparable diastereomers **Z-13h** and **E-13h** (*d.r.* was determined from the crude ^1H NMR spectrum of the reaction) as a pale-yellow oil in 82% yield (78 mg, 2.92 mmol). **Z-13h**: $R_f = 0.66$ (SiO_2 , 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2957, 2390, 2872, 2861, 1726, 1701, 1461, 1436, 1343, 1267, 1209, 1195, 1126, 1105, 1032, 1022, 973, 925, 900 cm^{-1} ; **^1H NMR (600 MHz, C_6D_6)** δ 6.12–6.05 (m, 2H, H^4 and H^5), 5.97 (br,

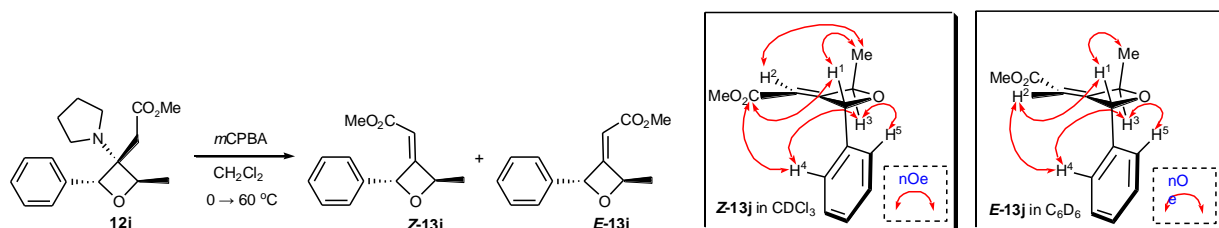
1H, H¹), 5.59 (dd, $J = 2.4, 2.0$ Hz, 1H, H²), 5.07–5.04 (m, 1H, H³), 3.33 (s, 3H, OMe), 2.00–1.98 (m, 2H, H⁶ and H⁷), 1.66–1.60 (m, 1H, H¹⁰), 1.47–1.43 (m, 1H, H¹¹), 1.39–1.27 (m, 5H, H⁸, H⁹ and H¹²–H¹⁴), 1.22–1.14 (m, 3H, H¹⁵–H¹⁷), 0.83 (t, $J = 7.0$ Hz, 3H, Me¹), 0.82 (t, $J = 7.3$ Hz, 3H, Me²); ¹³C NMR (151 MHz, C₆D₆) δ 166.5 (C), 164.9 (C), 132.9 (CH), 127.2 (CH), 110.0 (CH), 86.9 (CH), 85.7 (CH), 50.8 (CH₃), 35.6 (CH₂), 34.6 (CH₂), 31.9 (CH₂), 24.3 (CH₂), 22.8 (CH₂), 22.6 (CH₂), 14.1 (CH₃), 13.7 (CH₃); HRMS-EI calcd for C₁₆H₂₆O₃, 266.1882 found 266.1886.

E-13h: $R_f = 0.66$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); ¹H NMR (600 MHz, C₆D₆) δ 5.67–5.64 (m, 1H, H³), 5.61–5.54 (m, 3H, H⁴–H⁵ and H³), 5.39–5.38 (m, 1H, H¹), 3.31 (s, 3H, OMe), 2.20–2.17 (m, 1H, H¹⁰), 2.10–2.07 (m, 1H, H¹¹), 1.85–1.80 (m, 2H, H⁶ and H⁷), 1.37–1.15 (m, 8H, H⁸, H⁹ and H¹²–H¹⁷), 0.90 (t, $J = 7.3$ Hz, 3H, Me²), 0.77 (t, $J = 7.1$ Hz, 3H, Me¹); ¹³C NMR (151 MHz, C₆D₆) δ 166.9 (C), 165.2 (C), 135.4 (CH), 128.8 (CH), 110.9 (CH), 87.8 (CH), 86.1 (CH), 50.8 (CH₃), 34.4 (CH₂), 33.7 (CH₂), 32.0 (CH₂), 24.7 (CH₂), 23.1 (CH₂), 22.9 (CH₂), 14.2 (CH₃), 13.7 (CH₃); HRMS-EI calcd for C₁₆H₂₆O₃, 266.1882 found 266.1886.



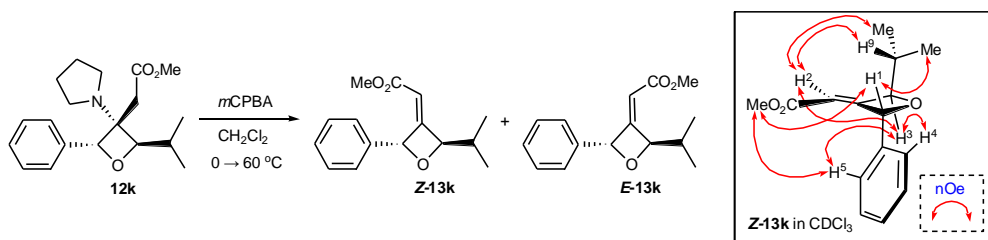
(Z)- and (E)-[(2R,4R)-2-methyl-4-((Z)-pent-1-enyl)-oxetan-3-ylidene]-acetic acid methyl esters (Z-13i) and (E-13i). According to the general procedure, oxetane **12i** (100 mg, 3.55 mmol) was reacted to give a 83:17 mixture of diastereomers **Z-13i** and **E-13i** (*d.r.* was determined from the crude ¹H NMR spectrum of the reaction) as a pale-yellow oil in 80% yield (60 mg, 2.84 mmol). **Z-13i**: $R_f = 0.47$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); FT-IR (neat) ν 2961, 2935, 2875, 1740, 1725, 1692, 1658, 1214, 1163, 1095, 1021 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.16 (ddd, $J = 8.1, 4.3, 2.4$ Hz, 1H, H⁴), 5.73–5.69 (m, 2H, H⁵ and H¹), 5.60 (dd, $J = 2.5, 2.0$ Hz, 1H, H²), 5.44 (ddq, $J = 6.5, 4.3, 2.0$ Hz, 1H, H³), 3.67 (s, 3H, OMe), 2.27–2.10 (m, 2H, H⁶ and H⁷), 1.49 (d, $J = 6.5$ Hz, 3H, Me²), 1.44–1.39 (m, 2H, H⁸ and H⁹), 0.94 (t, $J = 7.3$ Hz, 3H, Me¹); ¹³C NMR (75 MHz, CDCl₃) δ 166.6 (C), 165.1 (C), 135.8 (CH), 125.6 (CH), 110.7 (CH), 82.4 (CH), 82.2 (CH), 51.3 (CH₃), 29.7 (CH₂), 22.7 (CH₂), 21.3 (CH₃), 13.8 (CH₃); HRMS-EI calcd for C₁₂H₁₈O₃, 210.1256 found 210.1253; **E-13i**: $R_f = 0.40$ (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); FT-IR (neat) ν 2960, 2935, 2874, 1724, 1692, 1659, 1216, 1162, 1093, 1025 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 6.04 (ddd, $J = 7.3, 4.3, 2.2$ Hz, 1H, H⁴), 5.73–5.63 (m, 2H, H⁵ and H¹), 5.56 (ddq, $J = 6.5, 4.3,$

2.0 Hz, 1H, H³), 5.52 (dd, $J = 2.4, 2.0$ Hz, 1H, H²), 3.71 (s, 3H, OMe), 2.23–2.02 (m, 2H, H⁶ and H⁷), 1.63 (d, $J = 6.5$ Hz, 3H, Me²), 1.44–1.34 (m, 2H, H⁸ and H⁹), 0.91 (t, $J = 7.3$ Hz, 3H, Me¹); ¹³C NMR (75 MHz, CDCl₃) δ 167.2 (C), 165.3 (C), 135.8 (CH), 127.3 (CH), 110.7 (CH), 84.5 (CH), 80.7 (CH), 51.3 (CH₃), 29.8 (CH₂), 22.7 (CH₂), 19.9 (CH₃), 13.6 (CH₃); HRMS-EI calcd for C₁₂H₁₈O₃, 210.1256 found 210.1261.

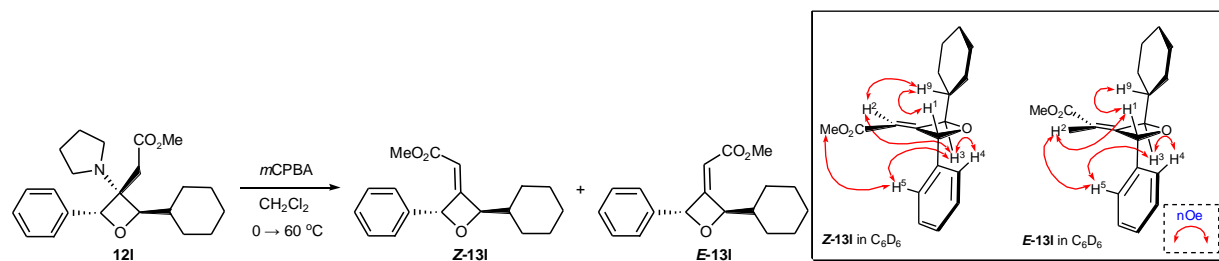


(Z)- and (E)-[(2R,4R)-2-methyl-4-phenyl-oxetan-3-ylidene]-acetic acid methyl esters (Z-13j) and (E-13j). According to the general procedure, oxetane **12j** (100 mg, 3.45 mmol) was reacted to give a 91:9 mixture of diastereomers **Z-13j** and **E-13j** (*d.r.* was determined from the crude ¹H NMR spectrum of the reaction) as a pale-yellow oil in 91% yield (69 mg, 3.15 mmol). **Z-13j**: *R_f* = 0.40 (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) ν 3036, 2981, 2951, 1722, 1665, 1642, 1449, 1438, 1327, 1259, 1201, 1174, 1032, 700 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.52 (dd, $J = 8.2, 1.5$ Hz, 2H, H⁴ and H⁵), 7.41–7.29 (m, 3H, H⁶, H⁷ and H⁸), 6.36 (dd, $J = 4.1, 2.5$ Hz, 1H, H¹), 5.68 (dd, $J = 2.5, 2.1$ Hz, 1H, H²), 5.64 (qdd, $J = 6.4, 4.1, 2.1$ Hz, 1H, H³), 3.56 (s, 3H, OMe), 1.59 (d, $J = 6.5$ Hz, 3H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 165.6 (C), 164.8 (C), 138.8 (C), 128.4 (CH), 128.3 (CH × 2), 127.2 (CH × 2), 111.0 (CH), 88.5 (CH), 83.5 (CH), 51.2 (CH₃), 21.3 (CH₃); HRMS-EI calcd for C₁₃H₁₄O₃, 218.0943 found 218.0935; **E-13j**: *R_f* = 0.44 (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) ν 3032, 2950, 1724, 1669, 1646, 1447, 1438, 1325, 1260, 1201, 1176, 1032, 1023, 698 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.40 (dd, $J = 8.2, 1.5$ Hz, 2H, H⁴ and H⁵), 7.39–7.33 (m, 3H, H⁶, H⁷ and H⁸), 6.20 (dd, $J = 4.5, 2.0$ Hz, 1H, H¹), 5.74 (qdd, $J = 6.4, 4.5, 2.5$ Hz, 1H, H³), 5.52 (dd, $J = 2.5, 2.0$ Hz, 1H, H²), 3.69 (s, 3H, OMe), 1.74 (d, $J = 6.8$ Hz, 3H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 166.5 (C), 165.3 (C), 139.2 (C), 128.7 (CH × 2), 128.6 (CH), 126.0 (CH × 2), 111.3 (CH), 86.3 (CH), 85.2 (CH), 51.4 (CH₃), 19.9 (CH₃); ¹H NMR (600 MHz, C₆D₆) δ 7.25 (dd, $J = 7.7, 1.5$ Hz, 2H, H⁴ and H⁵), 7.13 (dd, $J = 7.7, 7.3$ Hz, 2H, H⁶ and H⁸), 7.06 (dd, $J = 7.3, 1.5$ Hz, 2H, H⁷), 5.87 (dd, $J = 4.4, 2.1$ Hz, 1H, H¹), 5.74 (qdd, $J = 6.5, 4.4, 2.4$ Hz, 1H, H³), 5.39 (dd, $J = 2.4, 2.1$ Hz, 1H, H²), 3.24 (s, 3H, OMe), 1.74 (d, $J =$

6.5 Hz, 3H, Me); ^{13}C NMR (151 MHz, C_6D_6) δ 167.3 (C), 164.9 (C), 140.3 (C), 128.8 (CH \times 2), 128.4 (CH), 126.2 (CH \times 2), 111.2 (CH), 86.0 (CH), 85.1 (CH), 50.8 (CH₃), 20.1 (CH₃); HRMS-EI calcd for $\text{C}_{13}\text{H}_{14}\text{O}_3$, 218.0943 found 218.0936.

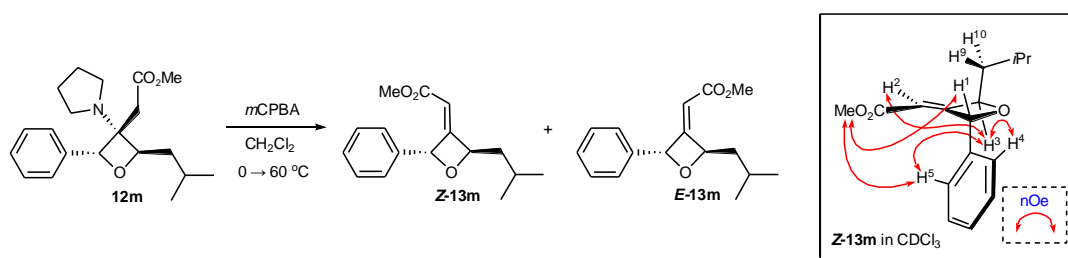


(Z)- and (E)-[(2R,4R)-2-isopropyl-4-phenyl-oxetan-3-ylidene]-acetic acid methyl esters (Z-13k) and (E-13k). According to the general procedure, oxetane **12k** (110 mg, 3.47 mmol) was reacted to give a 90:10 mixture of diastereomers **Z-13k** and **E-13k** (*d.r.* was determined from the crude ^1H NMR spectrum of the reaction) as a colorless oil in 93% yield (80 mg, 3.23 mmol). **Z-13k**: R_f = 0.49 (SiO_2 , 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) ν 3032, 2962, 2930, 2892, 2873, 1722, 1699, 1653, 1558, 1541, 1521, 1507, 1490, 1456, 1436, 1339, 1270, 1220, 1200, 1101, 1032, 1006, 999, 949, 906, 893, 867, 748, 696, 661 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.49 (dd, J = 8.2, 1.5 Hz, 2H, H^4 and H^5), 7.38–7.35 (m, 2H, H^6 and H^8), 7.32–7.29 (m, 1H, H^7), 6.23 (dd, J = 4.4, 2.7 Hz, 1H, H^1), 5.77 (dd, J = 2.7, 2.1 Hz, 1H, H^2), 5.26 (ddd, J = 6.8, 4.4, 2.1 Hz, 1H, H^3), 3.51 (s, 3H, OMe), 2.15–2.08 (m, 1H, H^9), 1.09 (d, J = 6.7 Hz, 3H, Me), 1.06 (d, J = 6.7 Hz, 3H, Me); ^{13}C NMR (126 MHz, CDCl_3) δ 164.6 (C), 163.8 (C), 139.0 (C), 128.3 (CH), 128.2 (CH \times 2), 127.5 (CH \times 2), 111.6 (CH), 91.4 (CH), 88.6 (CH), 51.0 (CH₃), 33.1 (CH), 17.0 (CH₃), 16.9 (CH₃); HRMS-EI calcd for $\text{C}_{15}\text{H}_{18}\text{O}_3$, 246.1256 found 246.1254; **E-13k**: R_f = 0.45 (SiO_2 , 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) ν 3029, 2962, 2932, 2873, 1722, 1699, 1653, 1521, 1507, 1490, 1456, 1438, 1338, 1271, 1222, 1200, 1100, 1031, 1005, 999, 949, 907, 893, 867, 698 cm^{-1} ; ^1H NMR (300 MHz, CDCl_3) δ 7.43–7.31 (m, 5H, H^4 – H^8), 6.02 (dd, J = 4.5, 2.0 Hz, 1H, H^1), 5.59 (ddd, J = 4.5, 2.6, 2.4 Hz, 1H, H^3), 5.55 (dd, J = 2.4, 2.0 Hz, 1H, H^2), 3.68 (s, 3H, OMe), 2.54–2.49 (m, 1H, H^9), 1.16 (d, J = 6.8 Hz, 3H, Me), 1.08 (d, J = 6.8 Hz, 3H, Me); ^{13}C NMR (75 MHz, CDCl_3) δ 165.4 (C), 164.9 (C), 139.3 (C), 128.7 (CH \times 2), 128.6 (CH), 126.2 (CH \times 2), 112.1 (CH), 93.3 (CH), 87.3 (CH), 51.3 (CH₃), 30.6 (CH), 18.3 (CH₃), 15.7 (CH₃); HRMS-EI calcd for $\text{C}_{15}\text{H}_{18}\text{O}_3$, 246.1256 found 246.1251.



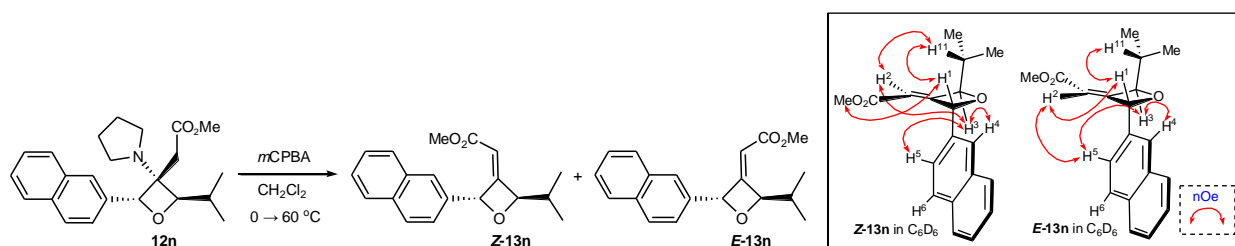
(Z)- and (E)-[(2R,4R)-2-cyclohexyl-4-phenyl-oxetan-3-ylidene]-acetic acid methyl esters (Z-13I**) and (**E-13I**).** According to the general procedure, oxetane **12I** (120 mg, 3.36 mmol) was reacted to give a 92:8 mixture of diastereomers **Z-13I** and **E-13I** (*d.r.* was determined from the crude ^1H NMR spectrum of the reaction) as a colorless oil in 91% yield (88 mg, 3.06 mmol). **Z-13I**: $R_f = 0.53$ (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3032, 2927, 2853, 1723, 1699, 1451, 1435, 1339, 1270, 1219, 1199, 1114, 1031, 953, 886, 864, 748, 696 cm^{-1} ; **^1H NMR (300 MHz, CDCl₃)** δ 7.47 (dd, $J = 8.2, 1.5$ Hz, 2H, H⁴ and H⁵), 7.39–7.27 (m, 3H, H⁶, H⁷ and H⁸), 6.22 (dd, $J = 4.4, 2.6$ Hz, 1H, H¹), 5.76 (dd, $J = 2.6, 2.0$ Hz, 1H, H²), 5.28 (ddd, $J = 6.4, 4.4, 2.0$ Hz, 1H, H³), 3.50 (s, 3H, OMe), 1.95–1.64 (m, 6H, H¹⁸, H¹⁰, H¹³, H¹⁷, H⁹ and H¹⁵), 1.32–1.15 (m, 5H, H¹¹, H¹⁹, H¹², H¹⁴ and H¹⁶); **^{13}C NMR (75 MHz, CDCl₃)** δ 164.7 (C), 163.9 (C), 139.1 (C), 128.4 (CH), 128.3 (CH \times 2), 127.5 (CH \times 2), 111.6 (CH), 90.7 (CH), 88.7 (CH), 51.1 (CH₃), 42.9 (CH), 27.5 (CH₂), 27.3 (CH₂), 26.2 (CH₂), 25.7 (CH₂), 25.6 (CH₂); **^1H NMR (600 MHz, C₆D₆)** δ 7.59 (dd, $J = 7.4, 1.3$ Hz, 2H, H⁴ and H⁵), 7.29 (dd, $J = 7.7, 7.4$ Hz, 2H, H⁶ and H⁸), 7.11–7.09 (dd, $J = 7.7, 1.3$ Hz, 1H, H⁷), 6.33 (dd, $J = 4.4, 2.5$ Hz, 1H, H¹), 5.62 (dd, $J = 2.5, 2.1$ Hz, 1H, H²), 4.97 (ddd, $J = 6.4, 4.4, 2.1$ Hz, 1H, H³), 3.13 (s, 3H, OMe), 1.89 (m, 1H, H¹⁸), 1.66–1.62 (m, 3H, H¹⁰, H¹³ and H¹⁷), 1.58–1.53 (m, 2H, H⁹ and H¹⁵), 1.15–1.08 (m, 5H, H¹¹, H¹⁹, H¹², H¹⁴ and H¹⁶); **^{13}C NMR (151 MHz, C₆D₆)** δ 164.8 (C), 164.4 (C), 140.2 (C), 128.3 (CH \times 2), 128.3 (CH), 128.2 (CH \times 2), 111.6 (CH), 90.5 (CH), 88.7 (CH), 50.6 (CH₃), 43.1 (CH), 27.8 (CH₂), 27.4 (CH₂), 26.6 (CH₂), 26.1 (CH₂), 26.0 (CH₂); **HRMS-EI** calcd for C₁₈H₂₂O₃, 286.1569 found 286.1567; **E-13I**: $R_f = 0.59$ (SiO₂, 4/1, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3030, 2928, 2854, 1722, 1699, 1451, 1436, 1338, 1272, 1219, 1199, 1115, 1032, 953, 887, 864, 748, 698 cm^{-1} ; **^1H NMR (300 MHz, CDCl₃)** δ 7.42–7.31 (m, 5H, H⁴–H⁸), 6.01 (dd, $J = 4.1, 2.0$ Hz, 1H, H¹), 5.56 (ddd, $J = 4.1, 2.4, 2.5$ Hz, 1H, H³), 5.54 (dd, $J = 2.5, 2.0$ Hz, 1H, H²), 3.68 (s, 3H, OMe), 2.18–2.17 (m, 1H, H⁹), 1.90–1.55 (m, 4H, H¹¹, H¹⁰, H¹⁸ and H¹⁹), 1.43–1.22 (m, 6H, H¹²–H¹⁷); **^{13}C NMR (75 MHz, CDCl₃)** δ 165.4 (C), 164.9 (C), 139.3 (C), 128.7 (CH \times 2), 128.6 (CH), 126.3 (CH \times 2),

112.0 (CH), 93.0 (CH), 87.4 (CH), 51.3 (CH₃), 40.3 (CH), 28.5 (CH₂), 26.3 (CH₂), 26.2 (CH₂), 26.1 (CH₂), 26.0 (CH₂); ¹H NMR (600 MHz, C₆D₆) δ 7.28 (dd, *J* = 7.3, 1.3 Hz, 2H, H⁴ and H⁵), 7.13 (dd, *J* = 7.8, 7.3 Hz, 2H, H⁶ and H⁸), 7.11–7.09 (dd, *J* = 7.8, 1.3 Hz, 1H, H⁷), 5.82 (dd, *J* = 4.5, 2.1 Hz, 1H, H¹), 5.69 (ddd, *J* = 4.5, 3.4, 2.5 Hz, 1H, H³), 5.50 (dd, *J* = 2.5, 2.1 Hz, 1H, H²), 3.25 (s, 3H, OMe), 2.45–2.39 (m, 1H, H⁹), 1.96–1.93 (m, 1H, H¹⁹), 1.79–1.73 (m, 2H, H¹⁰ and H¹³), 1.68–1.60 (m, 4H, H¹¹, H¹⁵, H¹⁷ and H¹⁸), 1.31–1.14 (m, 3H, H¹², H¹⁴ and H¹⁶); ¹³C NMR (151 MHz, C₆D₆) δ 165.6 (C), 165.1 (C), 140.5 (C), 128.9 (CH × 2), 128.5 (CH), 126.3 (CH × 2), 112.1 (CH), 92.8 (CH), 87.2 (CH), 50.8 (CH₃), 40.8 (CH), 28.9 (CH₂), 26.8 (CH₂), 26.6 (CH₂), 26.5 (CH₂), 26.4 (CH₂); HRMS-EI calcd for C₁₈H₂₂O₃, 286.1569 found 286.1562.



(Z)- and (E)-[(2*R*,4*R*)-2-isobutyl-4-phenyl-oxetan-3-ylidene]-acetic acid methyl esters (Z-13m**) and (**E-13m**).** According to the general procedure, oxetane **12m** (110 mg, 3.32 mmol) was reacted to give a 72:28 mixture of diastereomers **Z-13m** and **E-13m** (*d.r.* was determined from the crude ¹H NMR spectrum of the reaction) as a colorless oil in 89% yield (77 mg, 2.95 mmol). **Z-13m**: *R_f* = 0.51 (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) ν 3032, 2955, 2927, 2871, 1723, 1699, 1685, 1653, 1617, 1558, 1541, 1521, 1507, 1489, 1456, 1436, 1333, 1218, 1200, 1137, 1107, 1020, 952, 935, 896, 865, 831, 767, 744, 697, 662 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.50 (dd, *J* = 8.2, 1.5 Hz, 2H, H⁴ and H⁵), 7.39–7.36 (m, 2H, H⁶ and H⁸), 7.33–7.30 (m, 1H, H⁷), 6.32 (dd, *J* = 4.3, 2.7 Hz, 1H, H¹), 5.71 (dd, *J* = 2.7, 2.1 Hz, 1H, H²), 5.62–5.58 (m, 1H, H³), 3.54 (s, 3H, OMe), 1.98–1.90 (m, 1H, H¹⁰), 1.88–1.84 (m, 1H, H¹¹), 1.68–1.63 (m, 1H, H⁹), 0.94 (d, *J* = 6.5 Hz, 3H, Me), 0.93 (d, *J* = 6.5 Hz, 3H, Me); ¹³C NMR (126 MHz, CDCl₃) δ 165.4 (C), 164.8 (C), 139.0 (C), 128.4 (CH), 128.3 (CH × 2), 127.4 (CH × 2), 110.9 (CH), 88.6 (CH), 85.8 (CH), 51.1 (CH₃), 44.8 (CH₂), 24.6 (CH), 23.0 (CH₃), 22.3 (CH₃); HRMS-EI calcd for C₁₆H₂₀O₃, 260.1412 found 260.1416; **E-13m**: *R_f* = 0.57 (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) ν 3030, 2953, 2928, 2869, 1722, 1699, 1686, 1653, 1617, 1558, 1541, 1522, 1507, 1489, 1457, 1436, 1336, 1218, 1200, 1137, 1106, 1021, 952, 935, 896, 865, 767, 744, 698 cm⁻¹; ¹H NMR

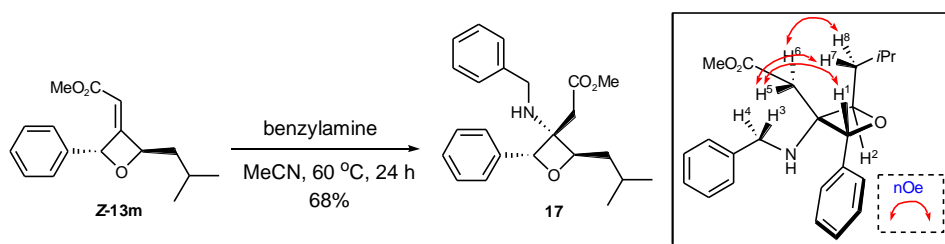
(300 MHz, CDCl₃) δ 7.43–7.33 (m, 5H, H⁴–H⁸), 6.16 (dd, *J* = 4.4, 2.1 Hz, 1H, H¹), 5.72–5.69 (m, 1H, H³), 5.50 (dd, *J* = 2.5, 2.3 Hz, 1H, H²), 3.69 (s, 3H, OMe), 2.00–1.93 (m, 3H, H⁹–H¹¹), 1.02 (d, *J* = 6.5 Hz, 3H, Me), 0.99 (d, *J* = 6.5 Hz, 3H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 166.4 (C), 165.3 (C), 139.2 (C), 128.8 (CH × 2), 128.7 (CH), 126.3 (CH × 2), 111.2 (CH), 87.5 (CH), 86.5 (CH), 51.4 (CH₃), 42.3 (CH₂), 24.5 (CH), 23.6 (CH₃), 21.6 (CH₃); HRMS-EI calcd for C₁₆H₂₀O₃, 260.1412 found 260.1417.



(Z)- and (E)-[(2*R*,4*R*)-2-isopropyl-4-naphthalen-2-yl-oxetan-3-ylidene]-acetic acid methyl esters (Z-13n**) and (**E-13n**).** According to the general procedure, oxetane **12n** (120 mg, 3.27 mmol) was reacted to give a 89:11 mixture of diastereomers **Z-13n** and **E-13n** (*d.r.* was determined from the crude ¹H NMR spectrum of the reaction) as a colorless oil in 88% yield (86 mg, 2.86 mmol). **Z-13n**: *R_f* = 0.49 (SiO₂, 4:1 *v/v*, *n*-hexane/EtOAc); FT-IR (neat) *v* 2962, 2873, 1722, 1698, 1541, 1507, 1456, 1435, 1339, 1270, 1219, 1199, 1100, 1032, 998, 949, 893, 867, 747, 696 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ 7.95 (s, 1H, H⁴), 7.88–7.81 (m, 3H, H⁵, H⁶ and H¹⁰), 7.62 (dd, *J* = 8.6, 1.8 Hz, 1H, H⁷), 7.51–7.45 (m, 2H, H⁸ and H⁹), 6.40 (dd, *J* = 4.4, 2.5 Hz, 1H, H¹), 5.81 (dd, *J* = 2.5, 2.0 Hz, 1H, H²), 5.35 (ddd, *J* = 6.8, 4.4, 2.0 Hz, 1H, H³), 3.48 (s, 3H, OMe), 2.20–2.13 (m, 1H, H¹¹), 1.12 (d, *J* = 6.7 Hz, 3H, Me), 1.10 (d, *J* = 6.7 Hz, 3H, Me); ¹³C NMR (75 MHz, CDCl₃) δ 164.6 (C), 163.8 (C), 136.5 (C), 133.4 (C), 133.1 (C), 128.2 (CH), 128.1 (CH), 127.7 (CH), 126.9 (CH), 126.2 (CH), 126.0 (CH), 125.2 (CH), 111.8 (CH), 91.6 (CH), 88.8 (CH), 51.2 (CH₃), 33.3 (CH), 17.1 (CH₃), 17.0 (CH₃); ¹H NMR (600 MHz, C₆D₆) δ 8.02 (d, *J* = 0.6 Hz, 1H, H⁴), 7.76 (dd, *J* = 8.4, 1.6 Hz, 1H, H⁵), 7.69–7.68 (m, 2H, H⁶ and H¹⁰), 7.62–7.60 (m, 1H, H⁷), 7.26–7.23 (m, 2H, H⁸ and H⁹), 6.49 (dd, *J* = 4.4, 2.6 Hz, 1H, H¹), 5.65 (dd, *J* = 2.6, 2.1 Hz, 1H, H²), 5.00 (ddd, *J* = 6.4, 4.4, 2.1 Hz, 1H, H³), 3.07 (s, 3H, OMe), 1.84 (qqd, *J* = 6.8, 6.8, 6.4 Hz, 1H, H¹¹), 0.97 (d, *J* = 6.8 Hz, 3H, Me), 0.88 (d, *J* = 6.8 Hz, 3H, Me); ¹³C NMR (151 MHz, C₆D₆) δ 164.6 (C), 164.3 (C), 137.5 (C), 133.9 (C), 133.7 (C), 128.5 (CH), 128.3 (CH), 127.9 (CH), 127.6 (CH), 126.3 (CH), 126.2 (CH), 125.8 (CH), 111.8 (CH), 91.3

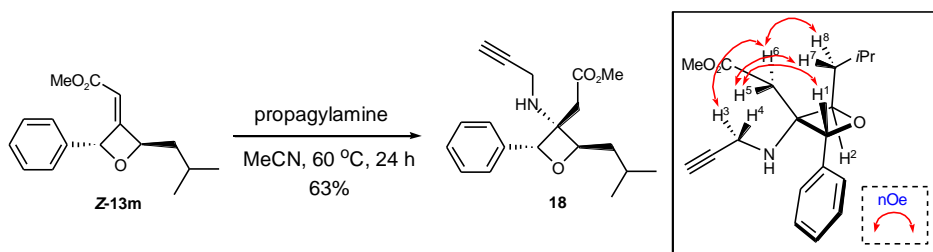
(CH), 88.8 (CH), 50.6 (CH₃), 33.5 (CH), 17.2 (CH₃), 17.0 (CH₃); **HRMS-EI** calcd for C₁₉H₂₀O₃, 296.1412 found 296.1410; **E-13n**: **R_f** = 0.54 (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2963, 2872, 1723, 1697, 1541, 1507, 1456, 1436, 1340, 1269, 1220, 1200, 1100, 1032, 997, 949, 893, 867, 746, 698 cm⁻¹; **¹H NMR (300 MHz, CDCl₃)** δ 7.89–7.82 (m, 4H, H⁴–H⁶ and H¹⁰), 7.54–7.47 (m, 3H, H⁷–H⁹), 6.18 (dd, *J* = 4.5, 1.8 Hz, 1H, H¹), 5.67 (ddd, *J* = 4.5, 2.6, 2.2 Hz, 1H, H³), 5.57 (dd, *J* = 2.2, 1.8 Hz, 1H, H²), 3.68 (s, 3H, OMe), 2.59–2.53 (m, 1H, H¹¹), 1.12 (d, *J* = 6.8 Hz, 3H, Me), 1.08 (d, *J* = 6.8 Hz, 3H, Me); **¹³C NMR (75 MHz, CDCl₃)** δ 165.4 (C), 164.9 (C), 136.7 (C), 133.4 (C), 133.1 (C), 128.8 (CH), 128.1 (CH), 127.7 (CH), 126.4 (CH), 126.3 (CH), 125.5 (CH), 123.7 (CH), 112.2 (CH), 93.5 (CH), 87.5 (CH), 51.4 (CH₃), 30.6 (CH), 18.3 (CH₃), 15.8 (CH₃); **¹H NMR (600 MHz, C₆D₆)** δ 7.69 (s, 1H, H⁴), 7.63–7.59 (m, 3H, H⁶, H¹⁰ and H⁷), 7.40 (dd, *J* = 8.5, 1.6 Hz, 1H, H⁵), 7.27–7.23 (m, 2H, H⁸ and H⁹), 5.94 (dd, *J* = 4.4, 1.7 Hz, 1H, H¹), 5.76 (ddd, *J* = 4.4, 2.8, 2.3 Hz, 1H, H³), 5.52 (dd, *J* = 2.3, 1.7 Hz, 1H, H²), 3.26 (s, 3H, OMe), 2.76 (qqd, *J* = 7.1, 6.8, 2.8 Hz, 1H, H¹¹), 1.25 (d, *J* = 6.8 Hz, 3H, Me), 1.17 (d, *J* = 7.1 Hz, 3H, Me); **¹³C NMR (151 MHz, C₆D₆)** δ 165.5 (C), 165.1 (C), 137.8 (C), 133.9 (C), 133.8 (C), 128.9 (CH), 128.5 (CH), 128.1 (CH), 126.5 (CH), 126.4 (CH), 125.5 (CH), 124.0 (CH), 112.4 (CH), 93.2 (CH), 87.3 (CH), 51.8 (CH₃), 31.0 (CH), 18.6 (CH₃), 16.1 (CH₃); **HRMS-EI** calcd for C₁₉H₂₀O₃, 296.1412 found 296.1420.

General procedure for the conjugate addition of primary amine



Synthesis of β -oxetanyl containing amino ester 17. Benzylamine (0.21 mL, 1.92 mmol, 10.0 equiv) was added to the oxetane **Z-13m** (50 mg, 0.19 mmol, 1.0 equiv) in acetonitrile (1.0 mL). The resulting mixture was stirred at 60 °C for 24 h, and the cooled to ambient temperature. The solvent was removed by rotary evaporation. The crude residue was purified by flash-column chromatography (*n*-hexane/EtOAc, 10:1) to afford oxetane **17** (48 mg, 0.13 mmol) as a pale-yellow oil in 68% yield. **R_f** = 0.50 (SiO₂, 4:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 2953, 2928,

1736, 1454, 1436, 1200, 1176, 988, 745, 700 cm^{-1} ; $^1\text{H NMR}$ (600 MHz, C_6D_6) δ 7.75 (d, $J = 7.6$ Hz, 2H, Ph-H), 7.22 (t, $J = 7.7$ Hz, 2H, Ph-H), 7.08 (t, $J = 7.4$ Hz, 2H, Ph-H), 7.03–7.00 (m, 4H, Ph-H), 6.98–6.95 (m, 1H, Ph-H), 5.90 (s, 1H, H^1), 4.74 (dd, $J = 10.3, 2.7$ Hz, 1H, H^2), 3.47 (ABq , $J = 12.9$ Hz, 1H, H^3), 3.34 (s, 3H, OMe), 3.33 (ABq , $J = 12.9$ Hz, 1H, H^4), 2.83 (ABq , $J = 14.8$ Hz, 1H, H^5), 2.74 (ABq , $J = 14.8$ Hz, 1H, H^6), 1.82–1.75 (m, 1H, H^9), 1.56 (ddd, $J = 13.3, 10.3, 5.6$ Hz, 1H, H^7), 1.08 (ddd, $J = 13.3, 7.6, 2.8$ Hz, 1H, H^8), 0.99 (d, $J = 6.7$ Hz, 1H, CH_3), 0.88 (d, $J = 6.6$ Hz, 1H, CH_3); $^{13}\text{C NMR}$ (151 MHz, C_6D_6) δ 171.5 (C), 140.8 (C), 139.2 (C), 128.5 (CH \times 2), 128.4 (CH \times 2), 128.2 (CH \times 2), 127.8 (CH), 127.1 (CH), 127.0 (CH \times 2), 88.6 (CH), 88.3 (CH), 62.8 (C), 51.0 (CH_3), 46.9 (CH_2), 41.7 (CH_2), 37.3 (CH_2), 25.5 (CH), 23.5 (CH_3), 22.5 (CH_3); HRMS-EI calcd for $\text{C}_{23}\text{H}_{29}\text{NO}_3$, 367.2147 found 367.2141.



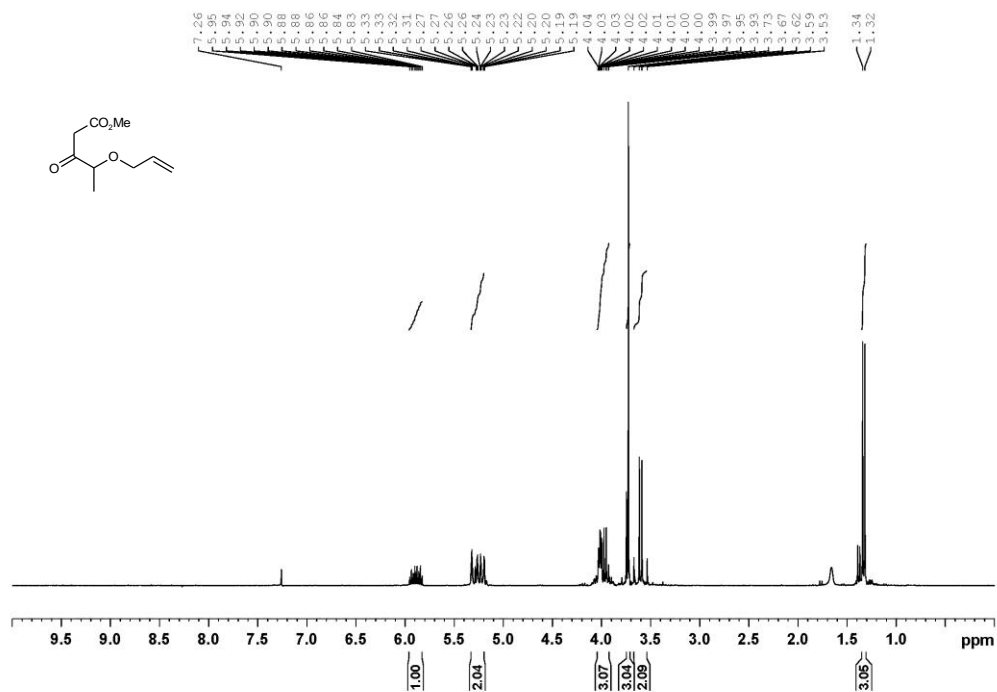
Synthesis of β -oxetanyl containing amino ester 18. Prepared according to the above procedure, compound **Z-13m** (50 mg, 0.19 mmol, 1.0 equiv) was reacted with propargylamine (0.12 mL, 1.92 mmol, 10.0 equiv) to give oxetane **18** (38 mg, 0.12 mmol) as a pale-yellow oil in 63% yield. $R_f = 0.55$ (SiO_2 , 7:1 v/v, *n*-hexane/EtOAc); **FT-IR** (neat) ν 3303, 2955, 2926, 2232, 2111, 1735, 1452, 1206, 1173, 986, 742, 702 cm^{-1} ; $^1\text{H NMR}$ (600 MHz, C_6D_6) δ 7.71 (d, $J = 7.7$ Hz, 2H, Ph-H), 7.24 (t, $J = 7.7$ Hz, 2H, Ph-H), 7.10 (t, $J = 7.4$ Hz, 1H, Ph-H), 5.91 (s, 1H, H^1), 4.96 (dd, $J = 10.5, 2.2$ Hz, 1H, H^2), 3.31 (s, 3H, OMe), 3.06 (ABq , $J = 17.4$ Hz, 1H, H^3), 2.09 (ABq , $J = 17.4$ Hz, 1H, H^4), 2.79 (ABq , $J = 14.7$ Hz, 1H, H^5), 2.68 (ABq , $J = 14.7$ Hz, 1H, H^6), 1.91–1.85 (m, 1H, H^9), 1.64 (t, $J = 2.4$ Hz, 1H, acetylene-H), 1.55 (ddd, $J = 13.6, 10.5, 5.9$ Hz, 1H, H^7), 1.38 (ddd, $J = 13.6, 7.9, 2.3$ Hz, 1H, H^8), 1.03 (d, $J = 6.7$ Hz, 1H, CH_3), 0.94 (d, $J = 6.6$ Hz, 1H, CH_3); $^{13}\text{C NMR}$ (151 MHz, C_6D_6) δ 171.3 (C), 138.8 (C), 128.5 (CH \times 2), 127.8 (CH), 127.0 (CH \times 2), 89.3 (CH), 88.3 (CH), 83.3 (C), 71.4 (CH), 62.5 (C), 51.0 (CH_3), 41.8 (CH_2), 36.8 (CH_2), 31.9 (CH_2), 25.6 (CH), 23.6 (CH_3), 22.5 (CH_3); HRMS-EI calcd for $\text{C}_{19}\text{H}_{25}\text{NO}_3\text{Na}$, 338.1732 found 338.1726.

III. References

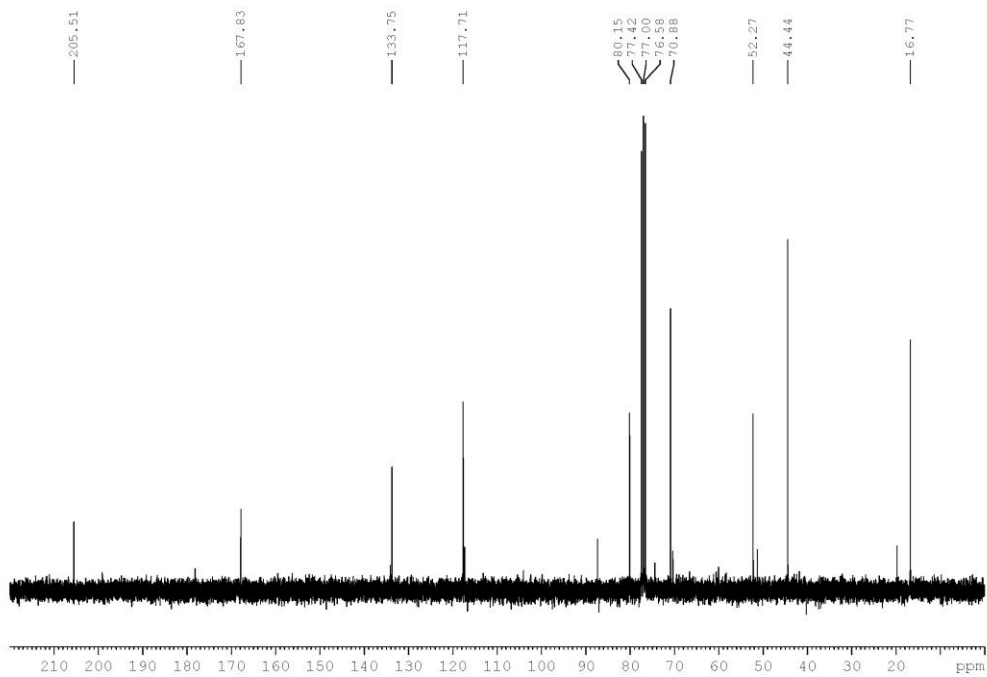
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- [2] I. D. Jurberg, Y. Odabachian, F. Gagosz, *J. Am. Chem. Soc.* **2010**, *132*, 3543-3552.
- [3] S. Braverman, T. Pechenick-Azizi, H. E. Gottlieb, M. Sprecher, *Synthesis* **2011**, *2011*, 1741-1750.
- [4] J. Barluenga, F. J. Fañanás, R. Sanz, C. Marcos, *Chem. Eur. J.* **2005**, *11*, 5397-5407.
- [5] Y. K. Booth, W. Kitching, J. J. De Voss, *ChemBioChem* **2011**, *12*, 155-172.
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IV. NMR spectra

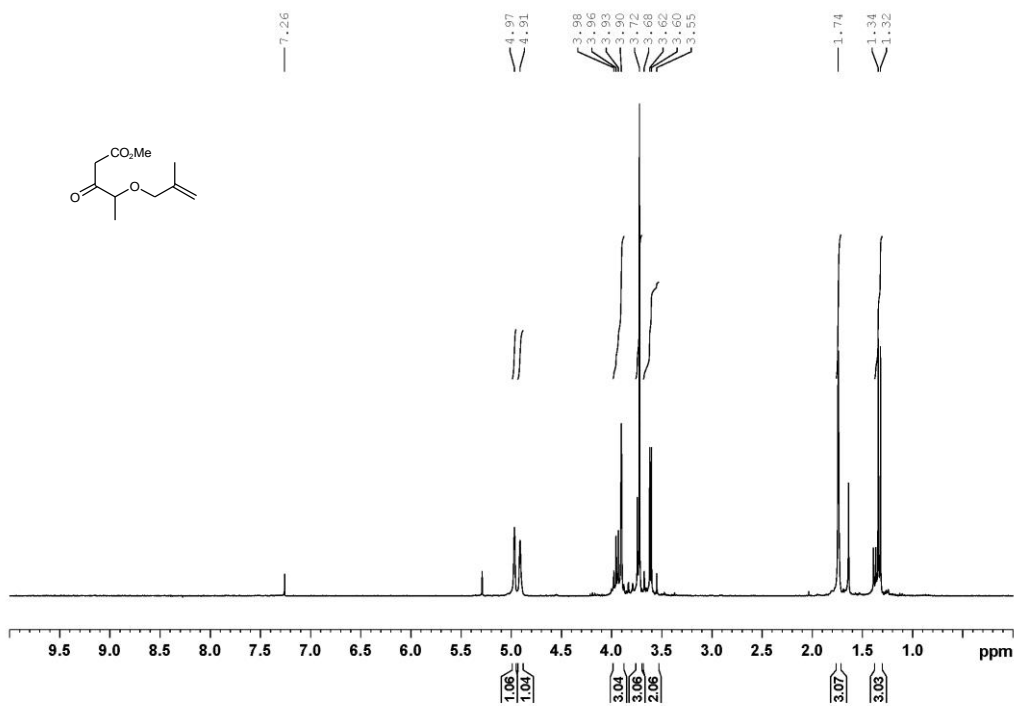
^1H NMR Spectrum of **K1** in CDCl_3



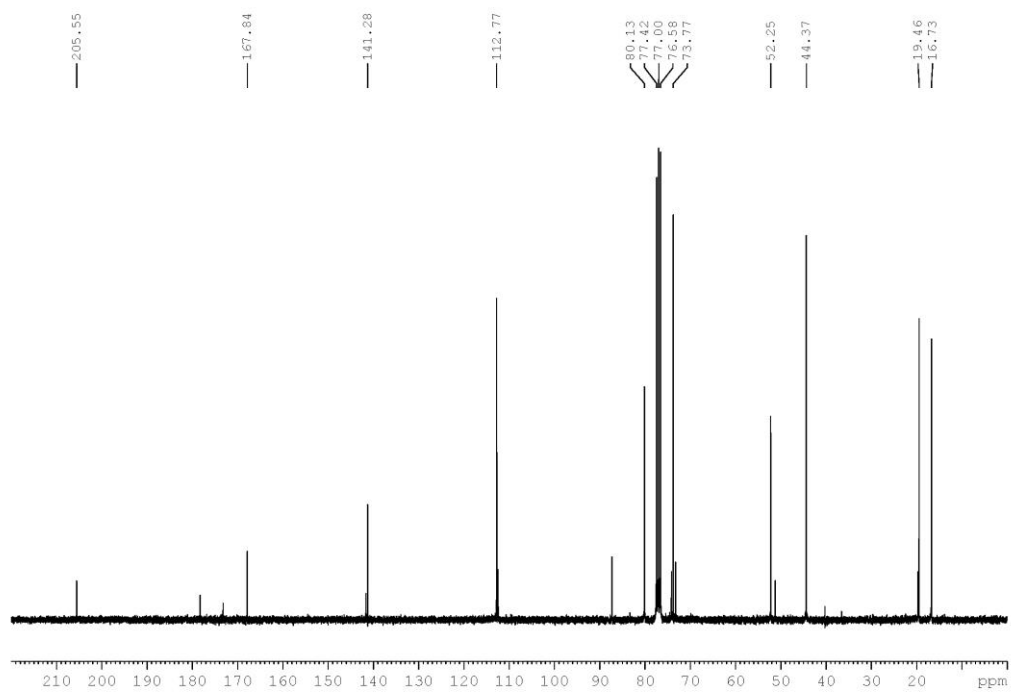
^{13}C NMR Spectrum of **K1** in CDCl_3



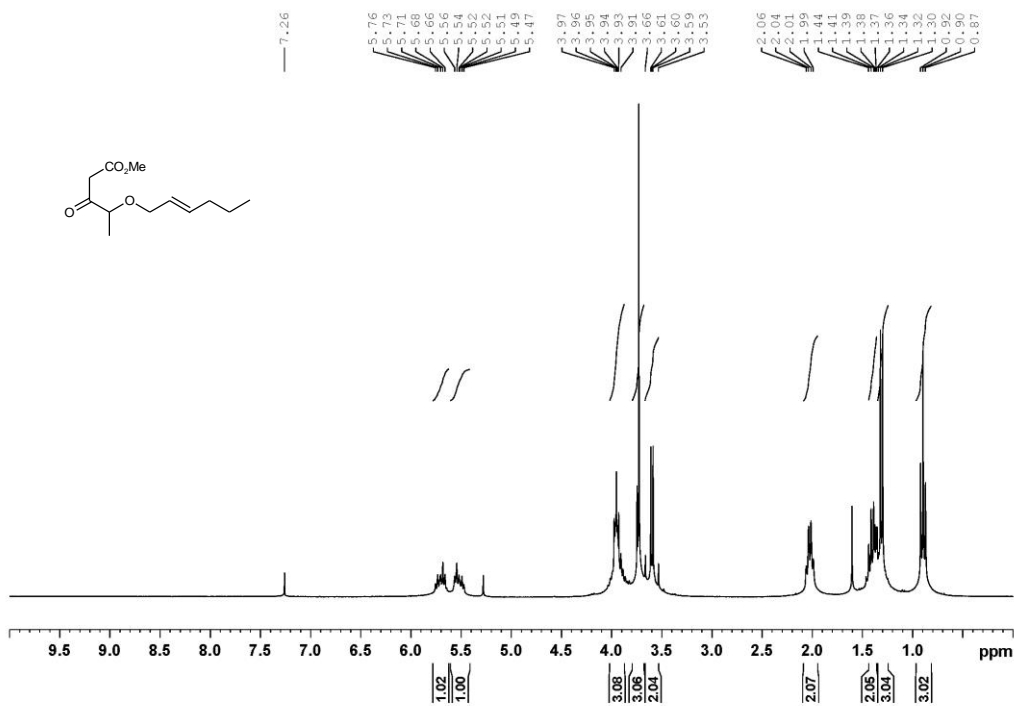
¹H NMR Spectrum of **K2** in CDCl₃



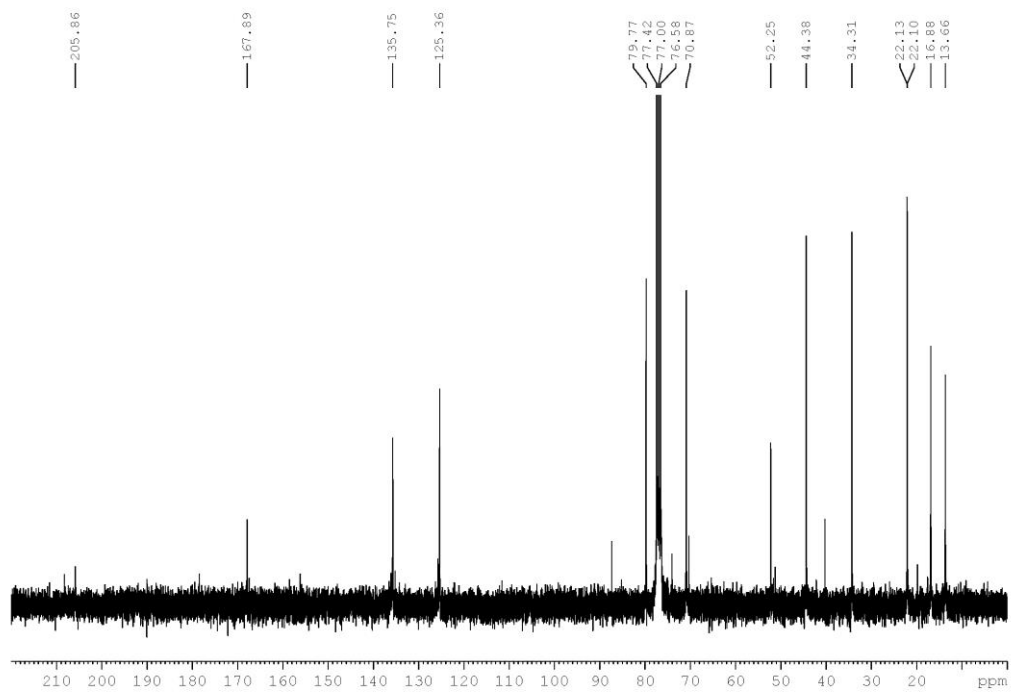
¹³C NMR Spectrum of **K2** in CDCl₃



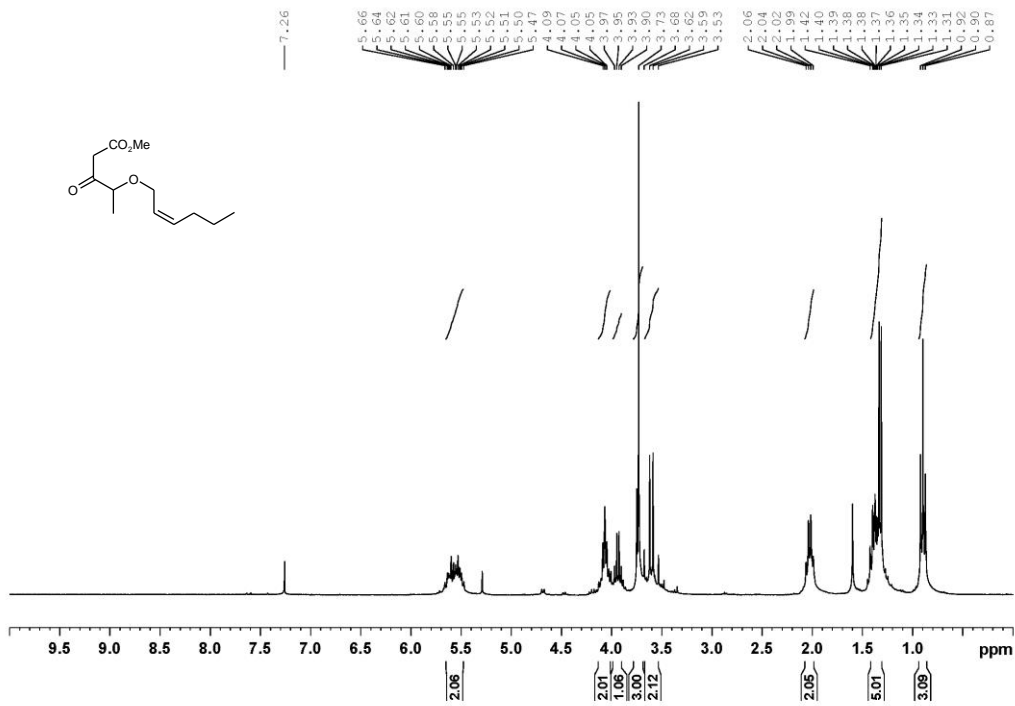
¹H NMR Spectrum of **K3** in CDCl₃



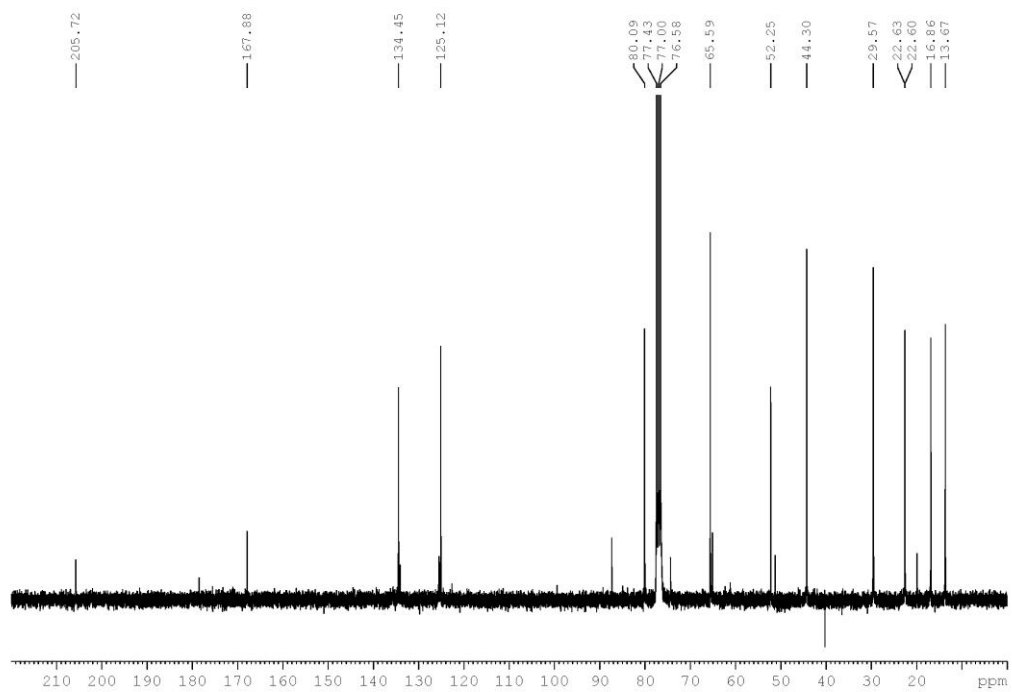
¹³C NMR Spectrum of **K3** in CDCl₃



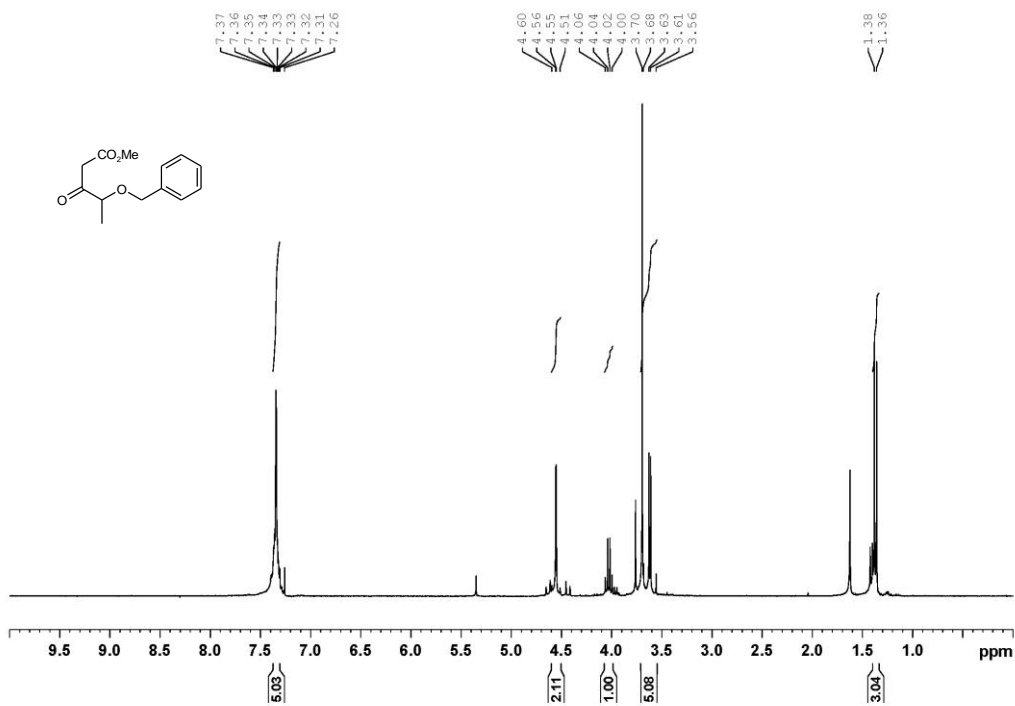
¹H NMR Spectrum of **K4** in CDCl₃



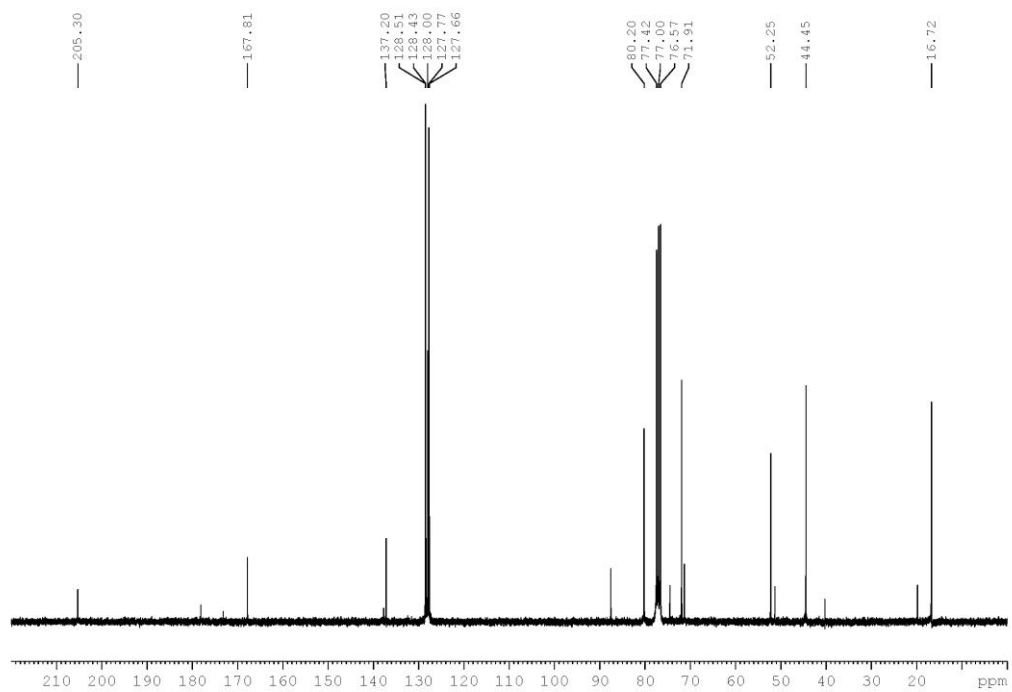
¹³C NMR Spectrum of **K4** in CDCl₃



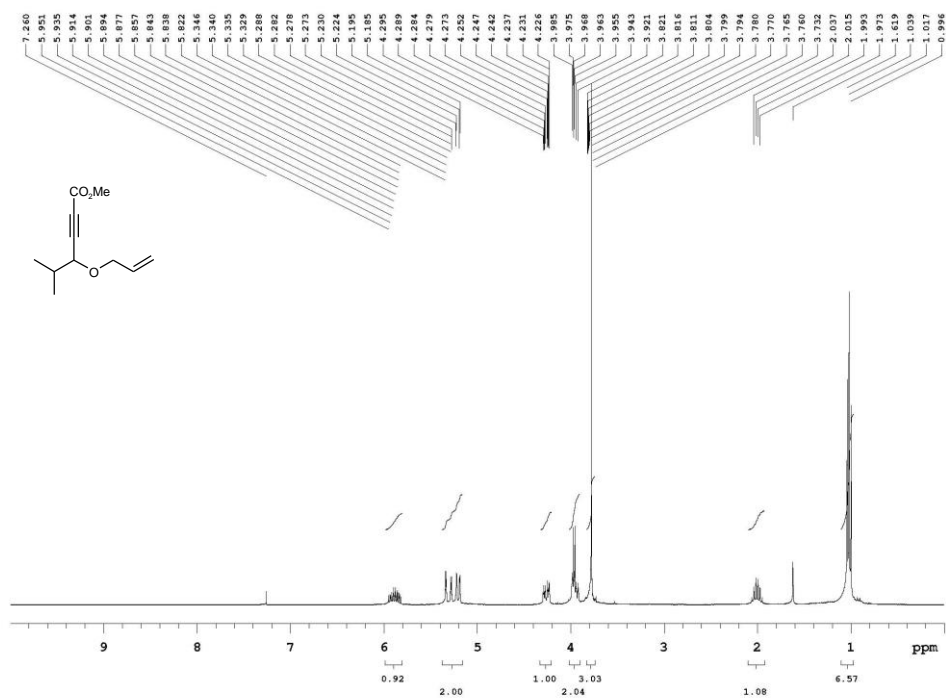
¹H NMR Spectrum of **K5** in CDCl₃



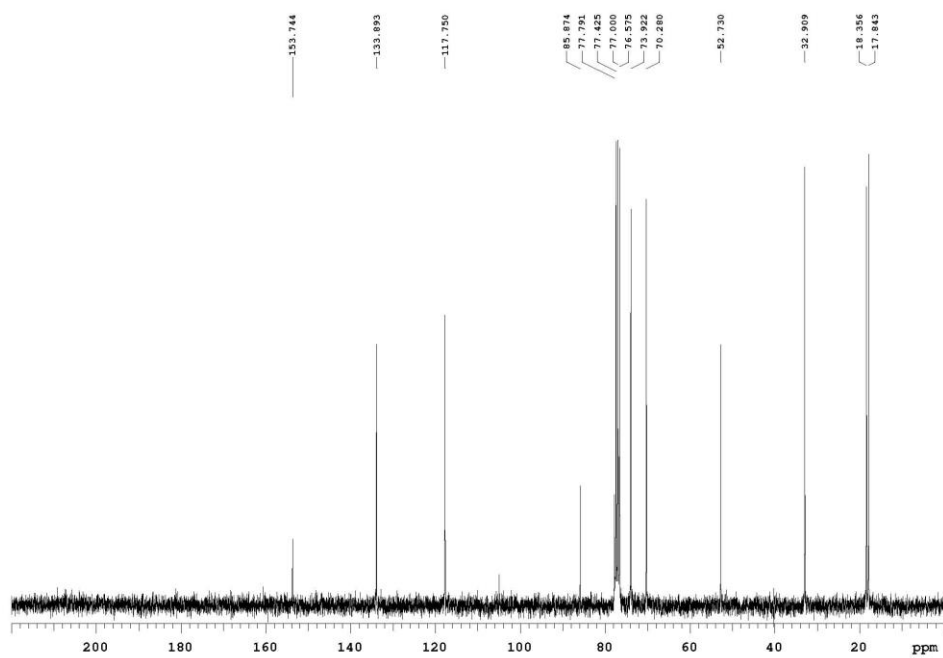
¹³C NMR Spectrum of **K5** in CDCl₃



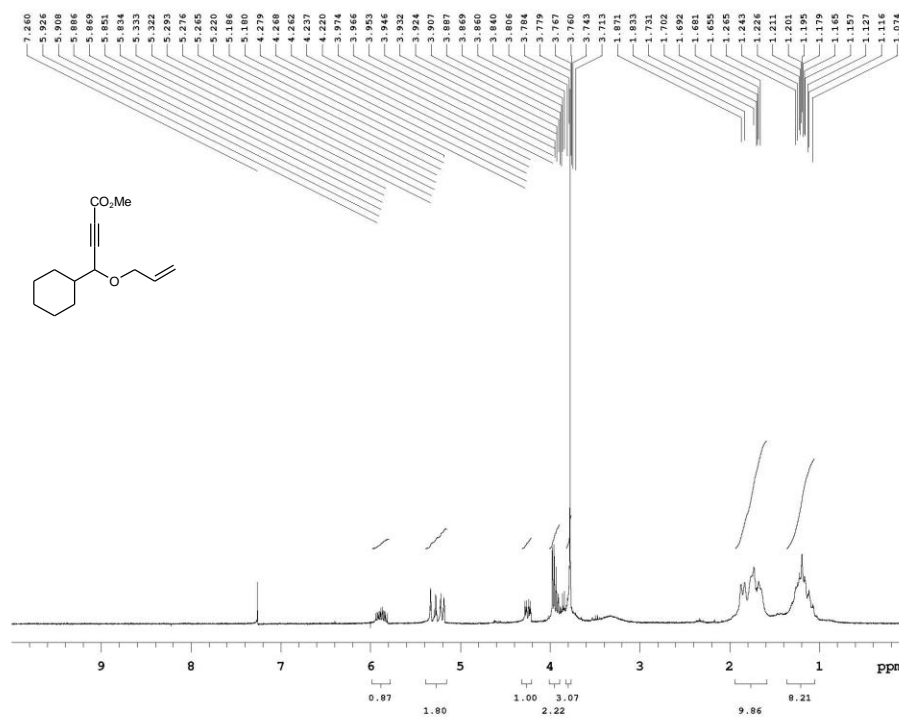
^1H NMR Spectrum of **E1** in CDCl_3



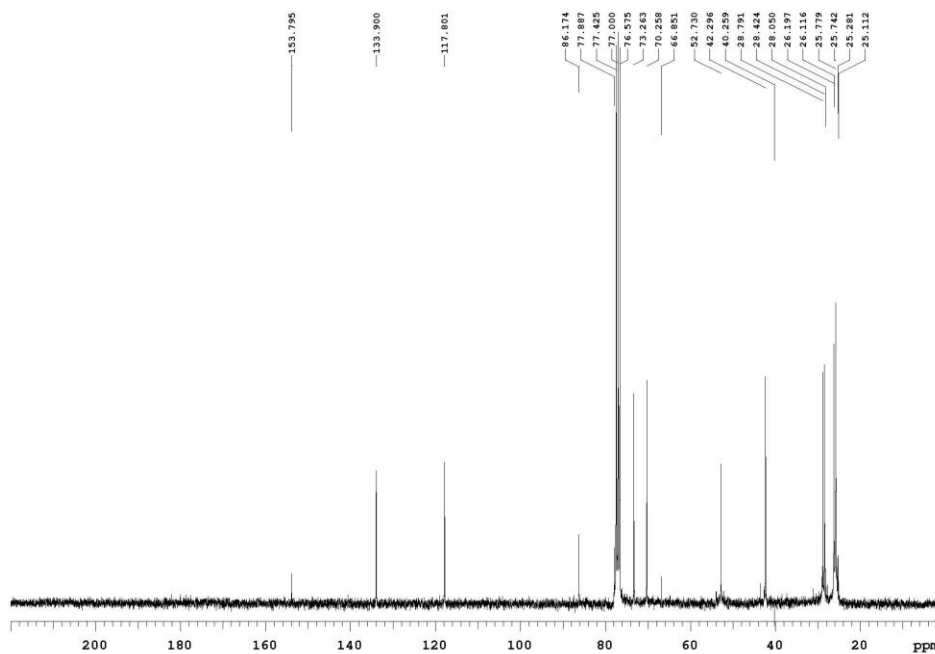
^{13}C NMR Spectrum of **E1** in CDCl_3



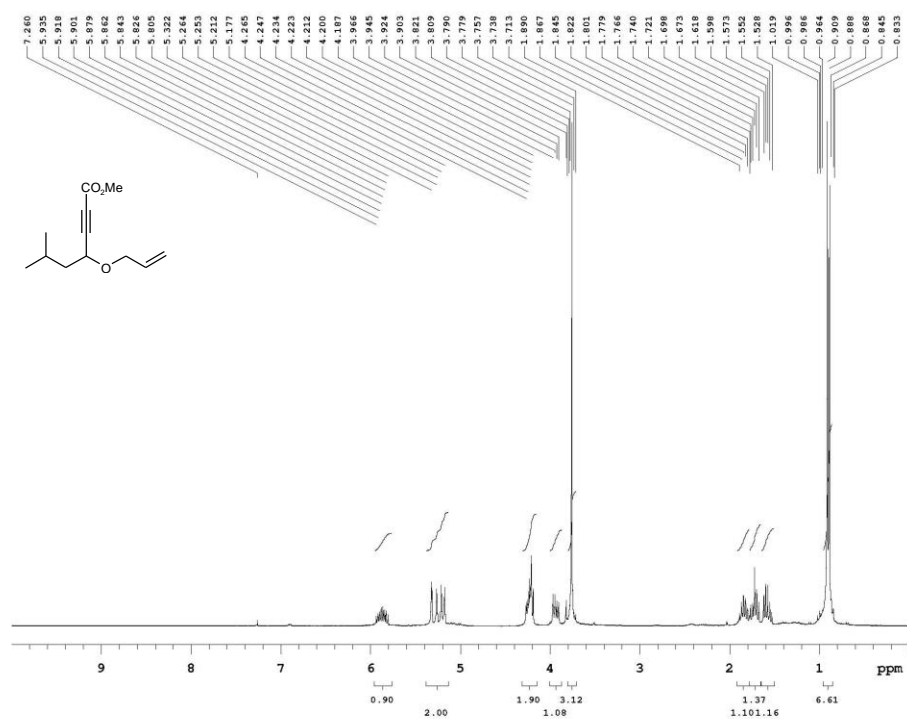
¹H NMR Spectrum of **E2** in CDCl₃



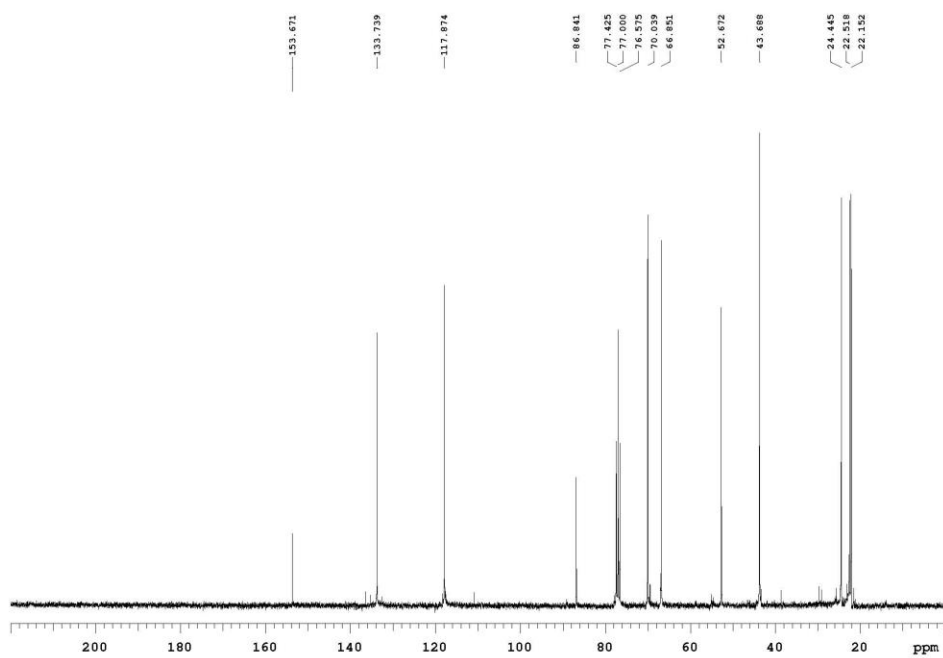
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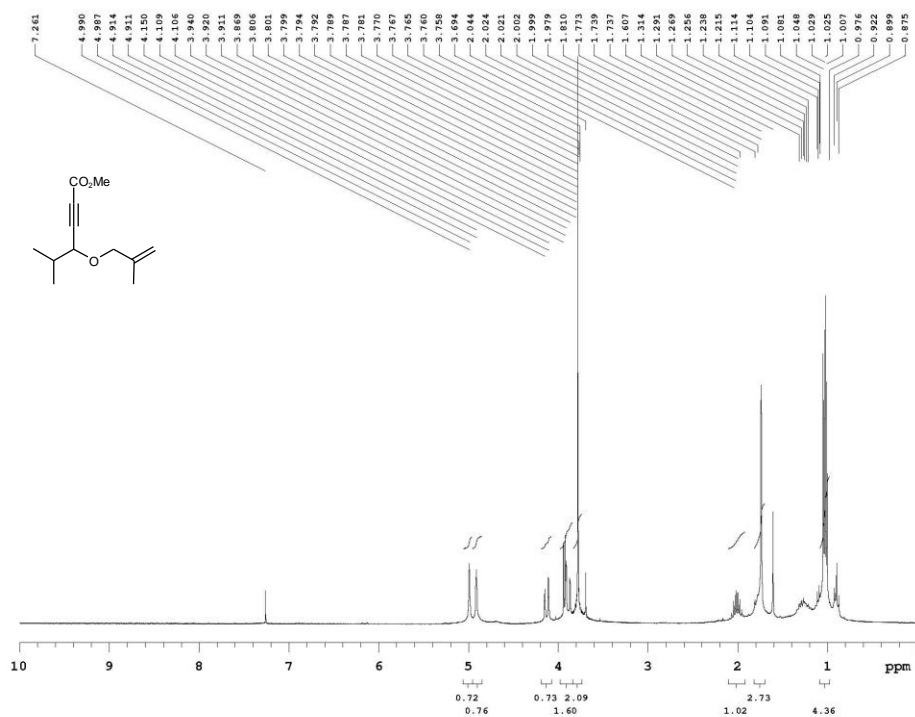
¹H NMR Spectrum of **E3** in CDCl₃



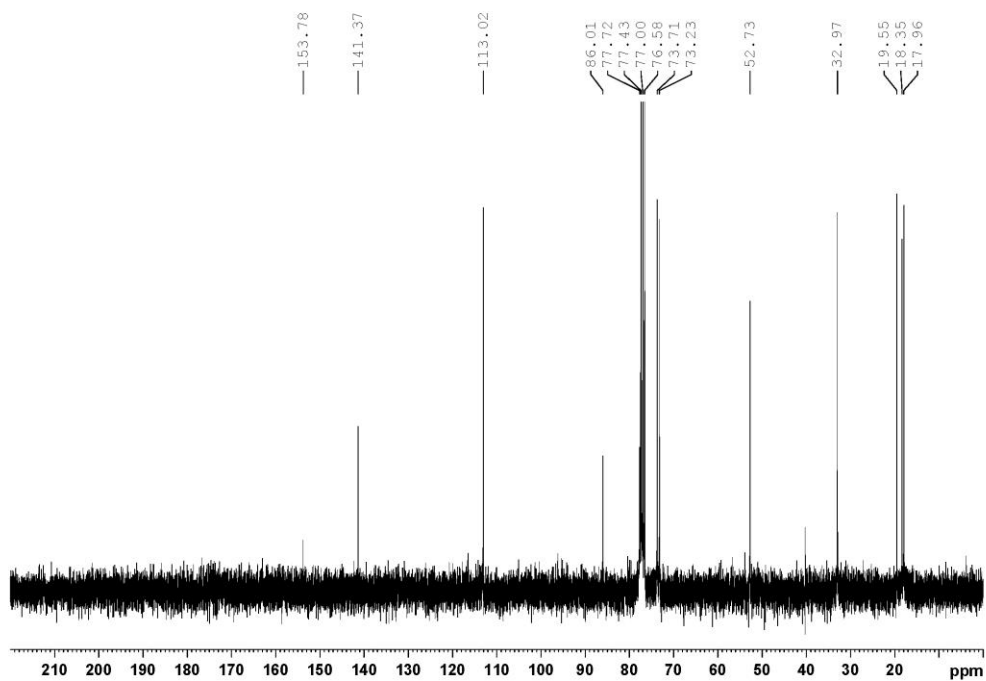
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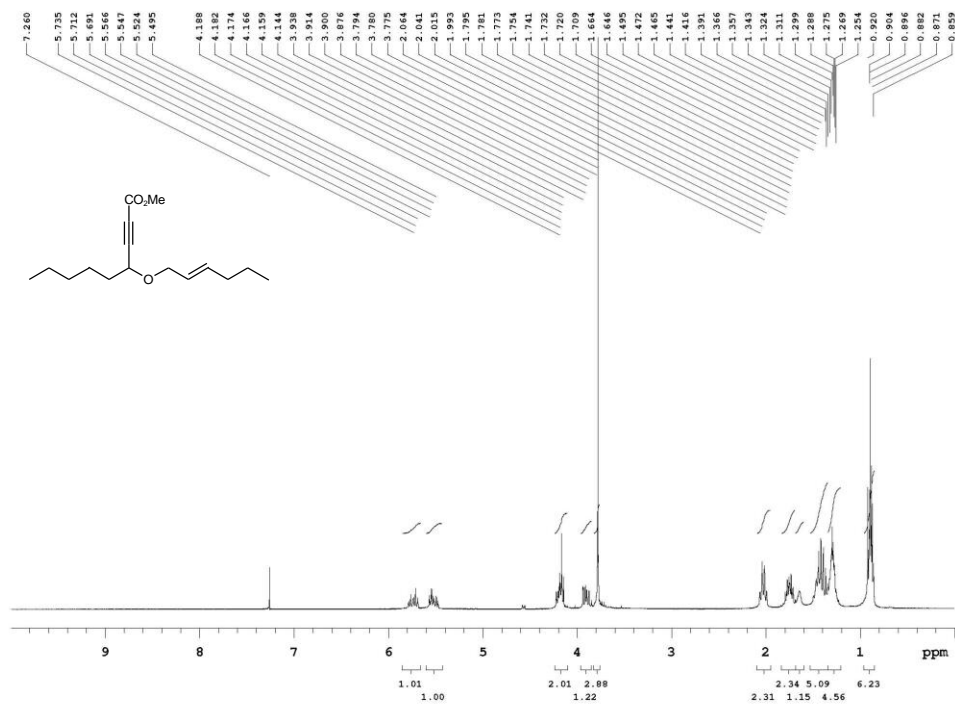
¹H NMR Spectrum of **E4** in CDCl₃



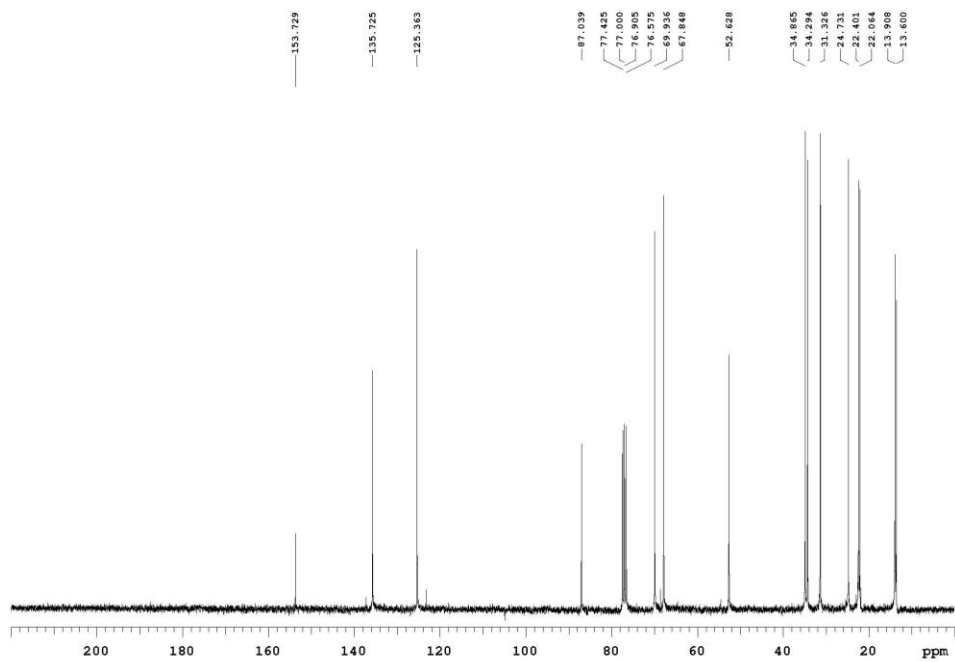
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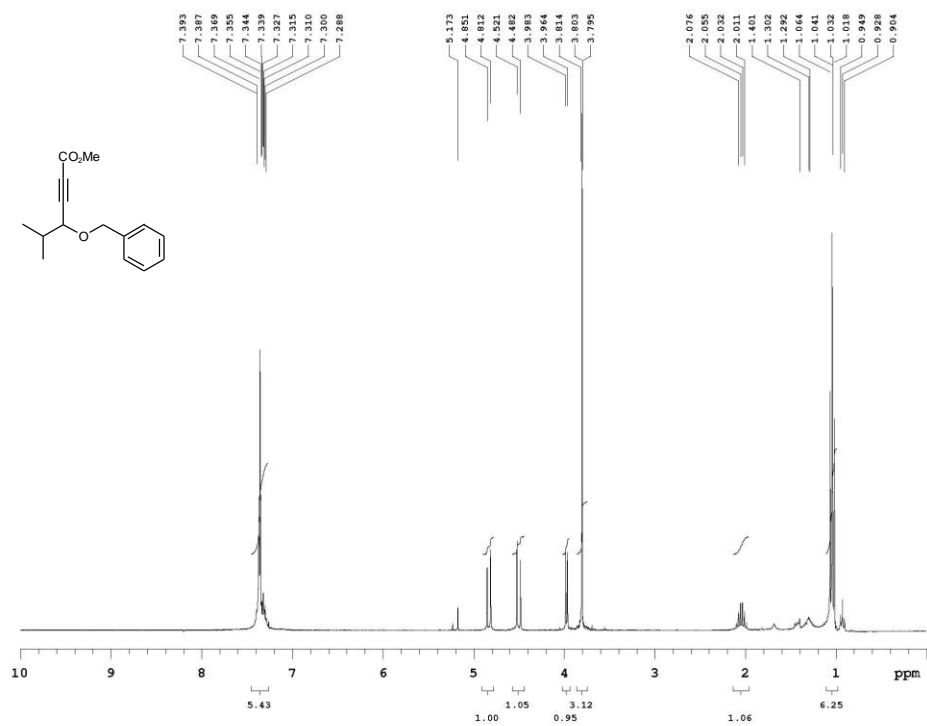
^1H NMR Spectrum of **E5** in CDCl_3



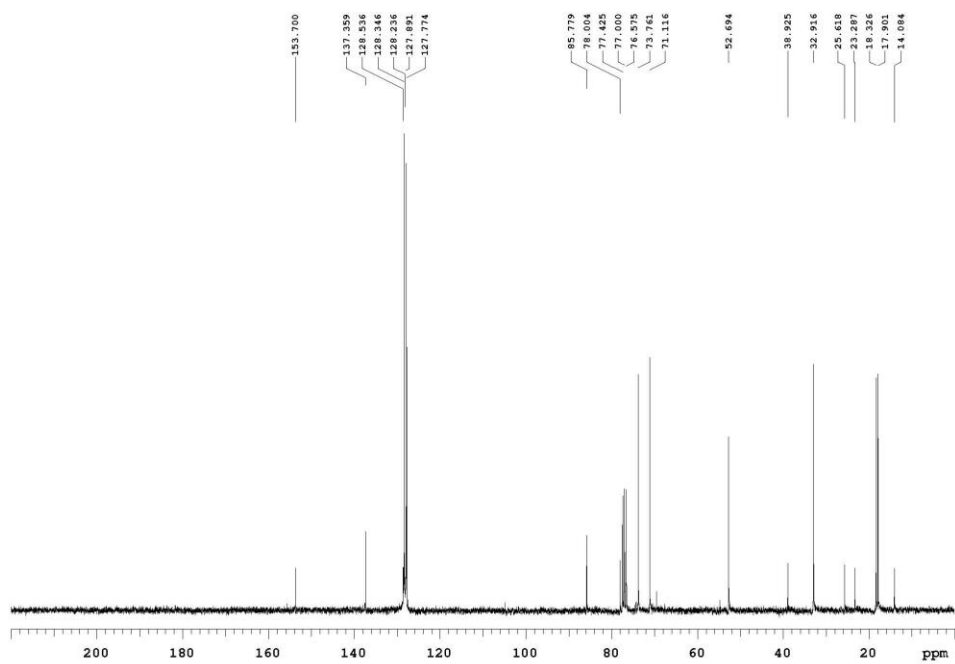
^{13}C NMR Spectrum of **E5** in CDCl_3



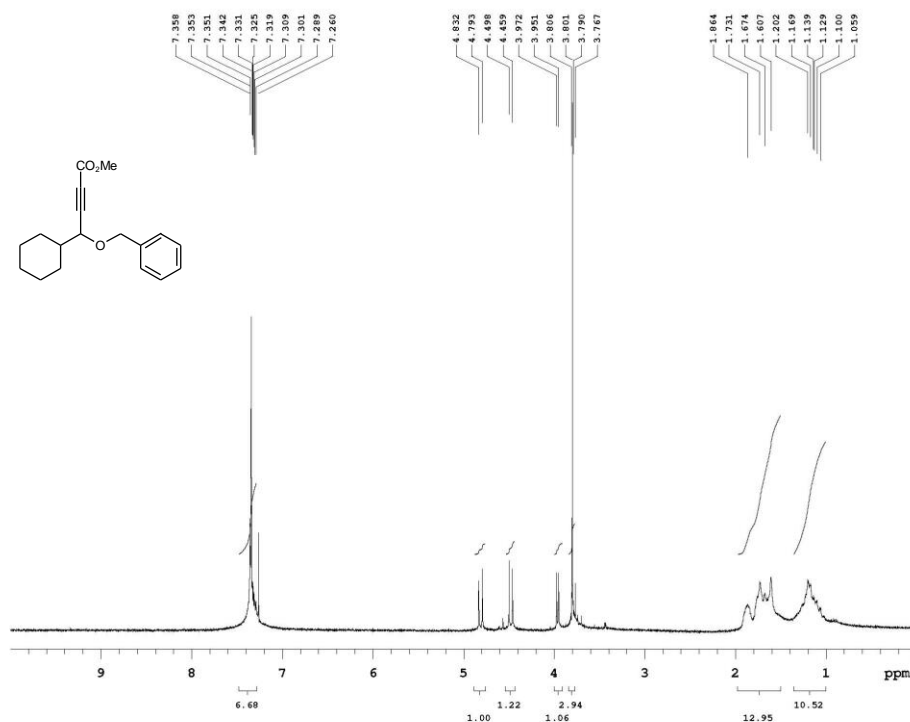
^1H NMR Spectrum of **E6** in CDCl_3



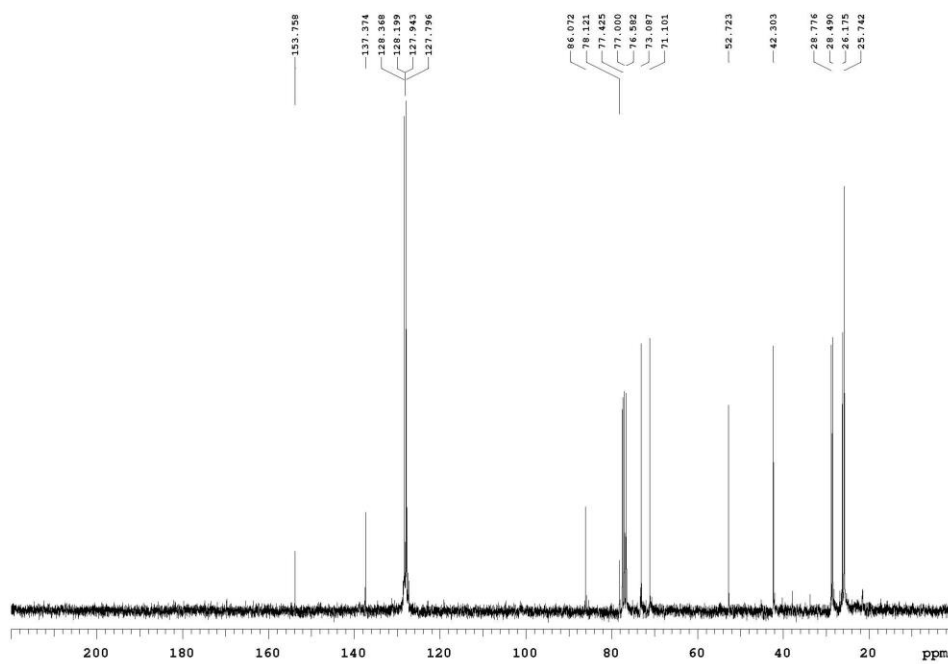
^{13}C NMR Spectrum of **E6** in CDCl_3



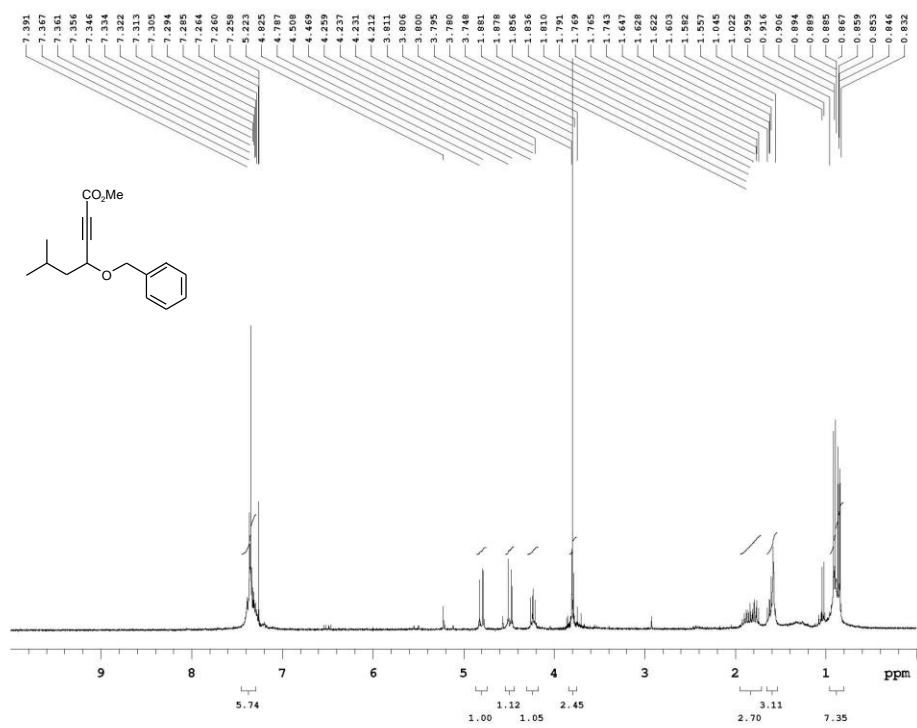
¹H NMR Spectrum of **E7** in CDCl₃



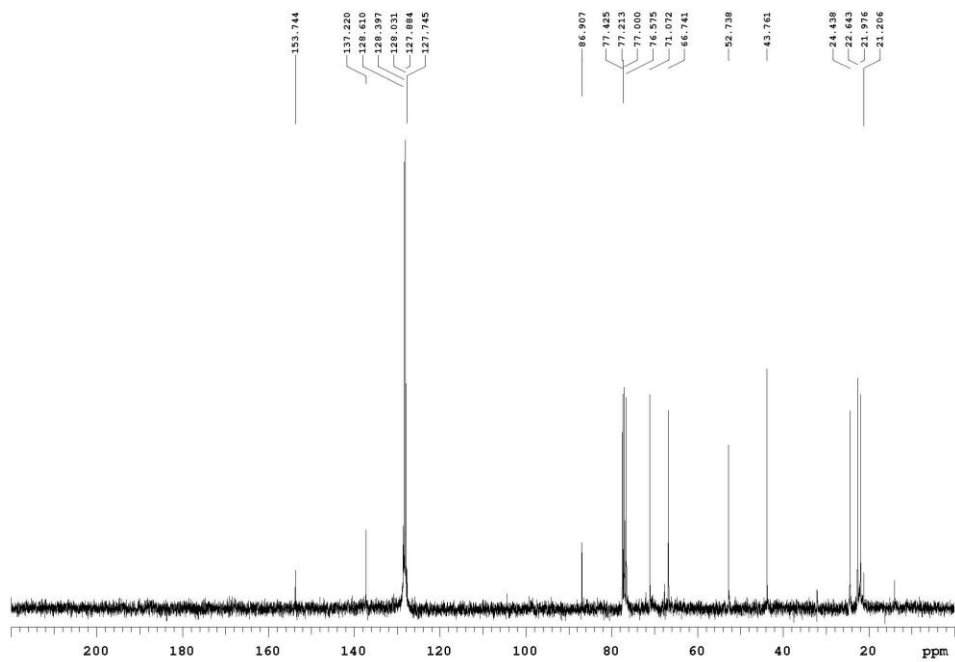
¹³C NMR Spectrum of **E7** in CDCl₃



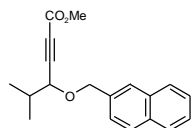
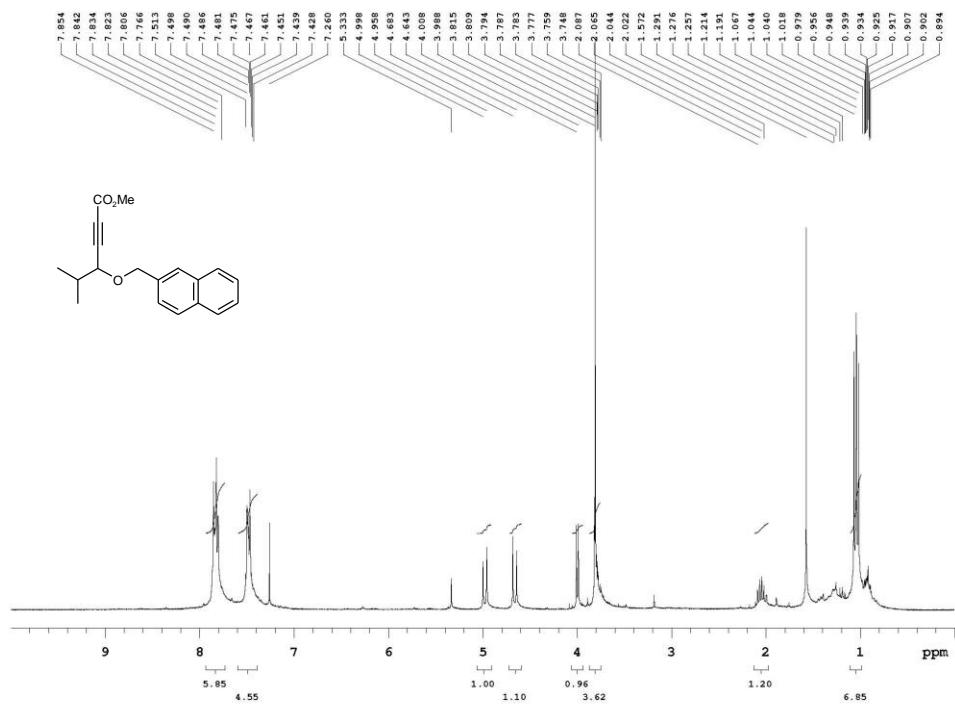
^1H NMR Spectrum of **E8** in CDCl_3



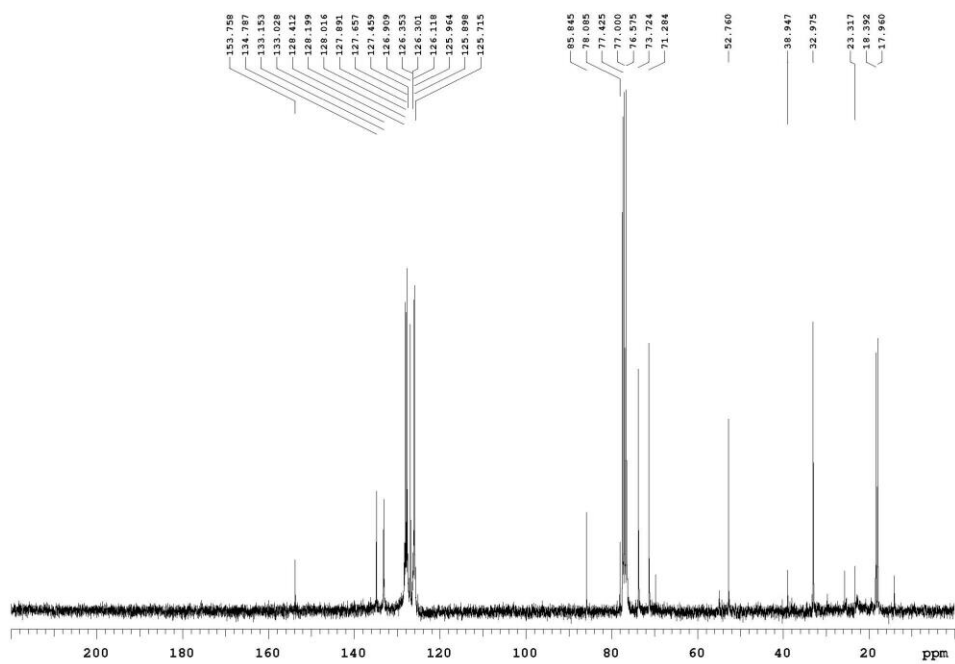
^{13}C NMR Spectrum of **E8** in CDCl_3



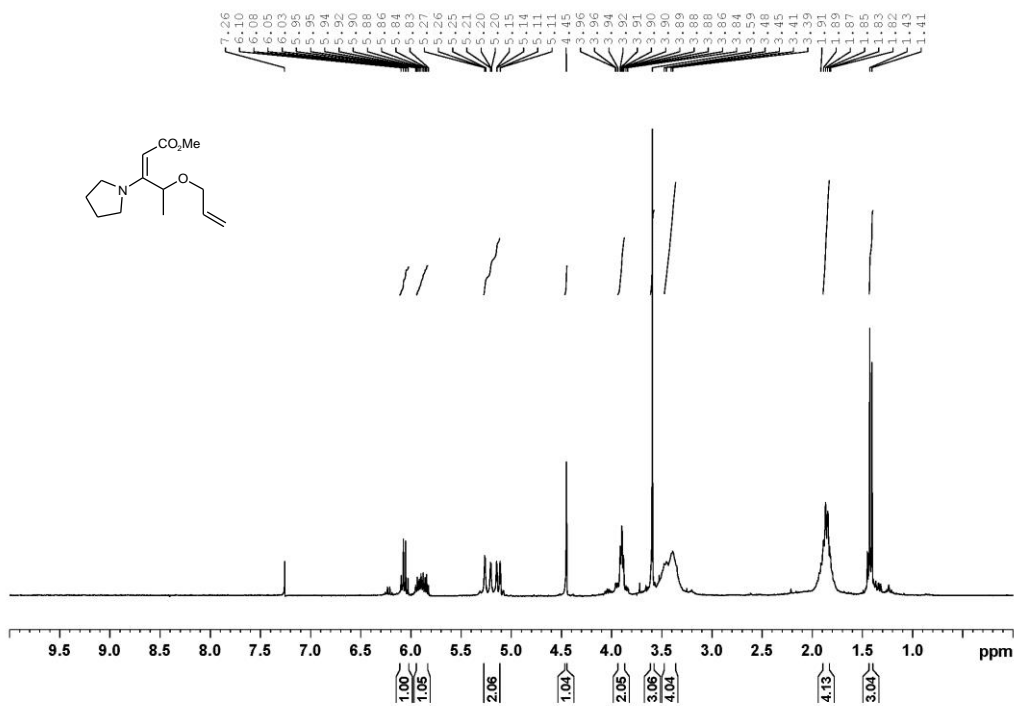
¹H NMR Spectrum of **E9** in CDCl₃



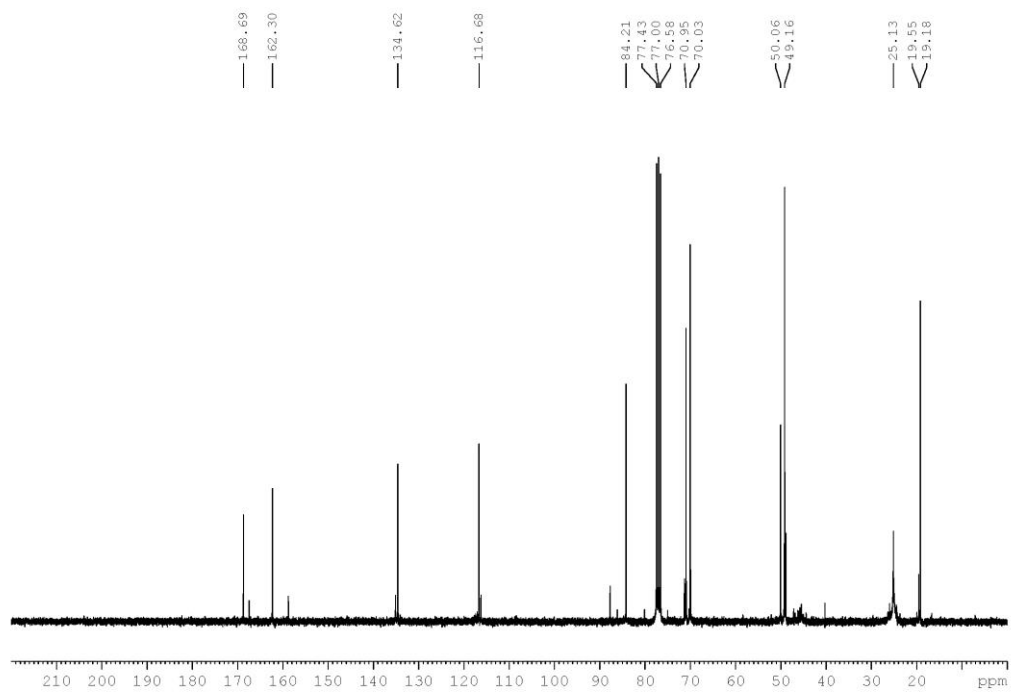
¹³C NMR Spectrum of **E9** in CDCl₃



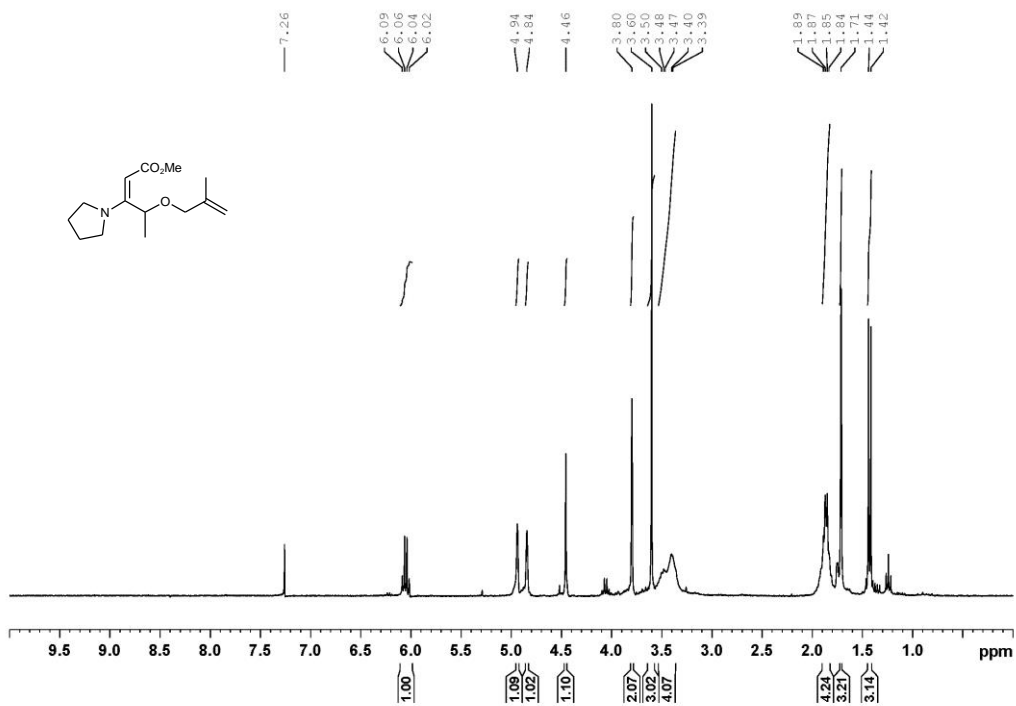
¹H NMR Spectrum of **11b** in CDCl₃



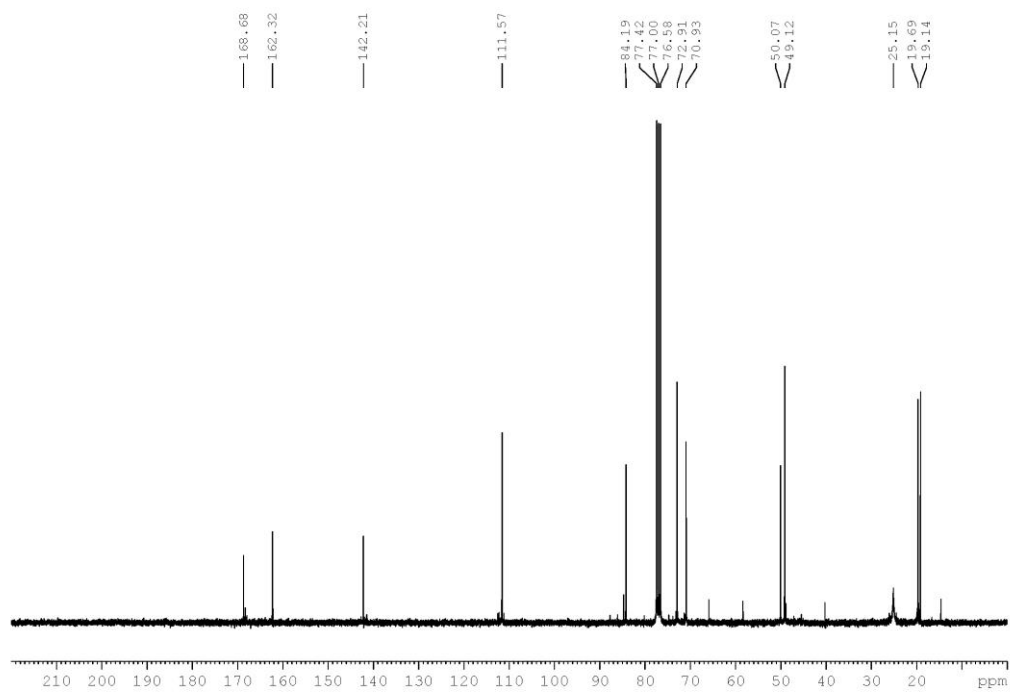
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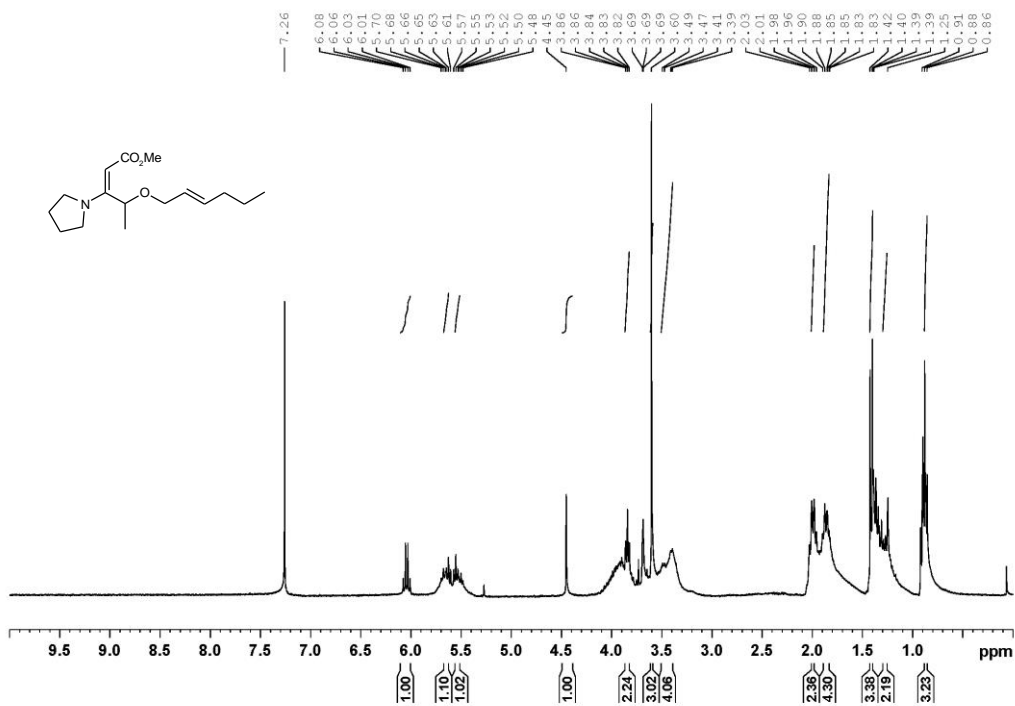
^1H NMR Spectrum of **11e** in CDCl_3



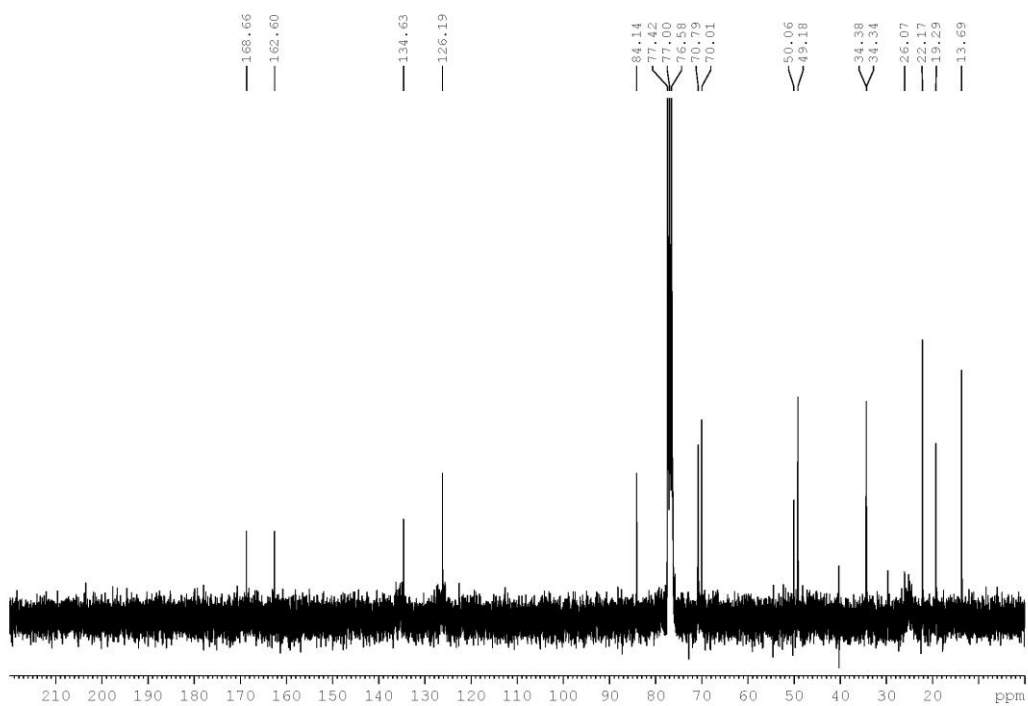
^{13}C NMR Spectrum of **11e** in CDCl_3



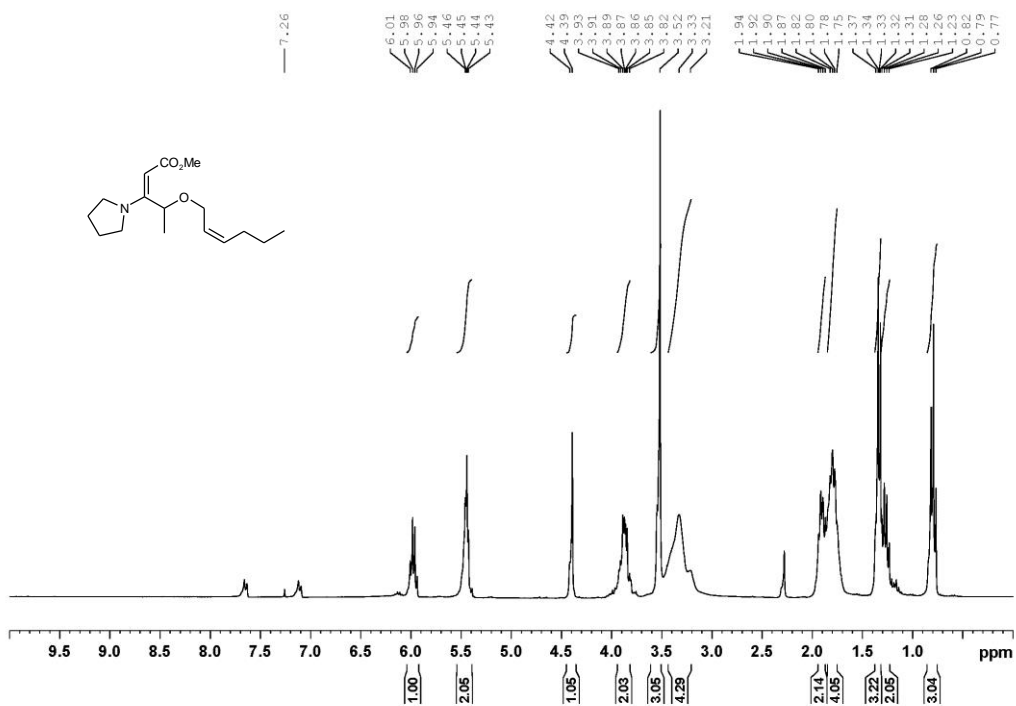
¹H NMR Spectrum of **11g** in CDCl₃



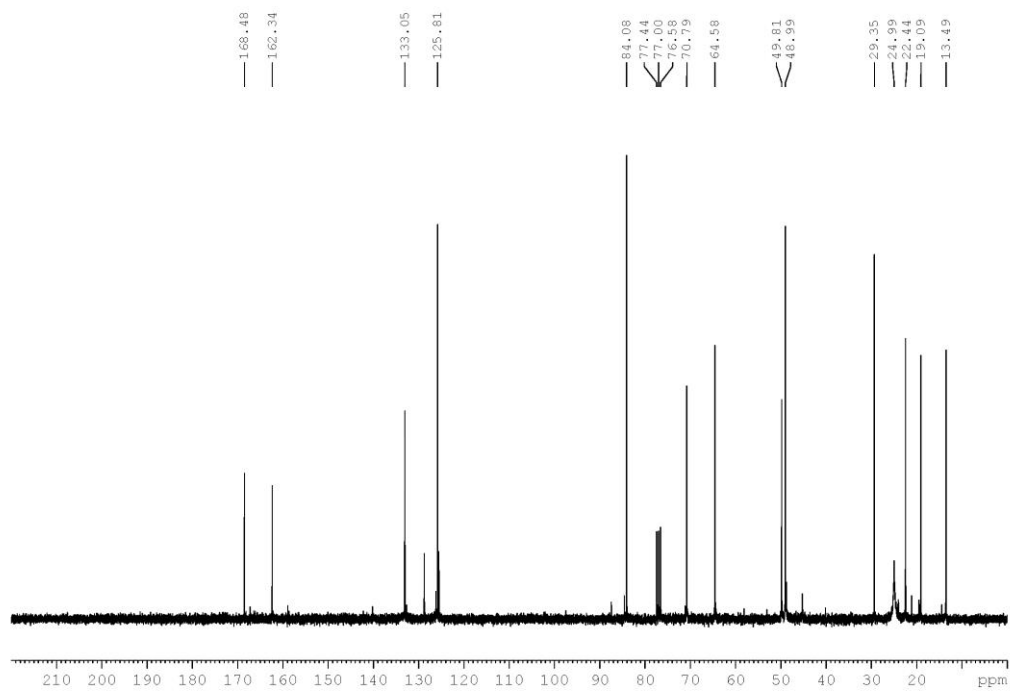
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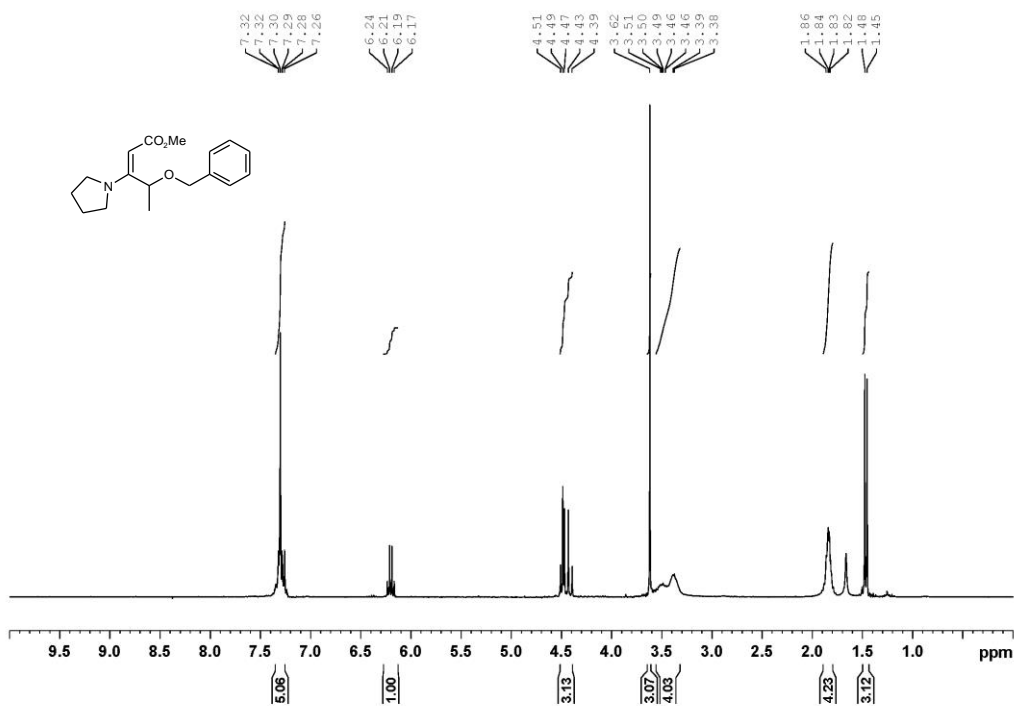
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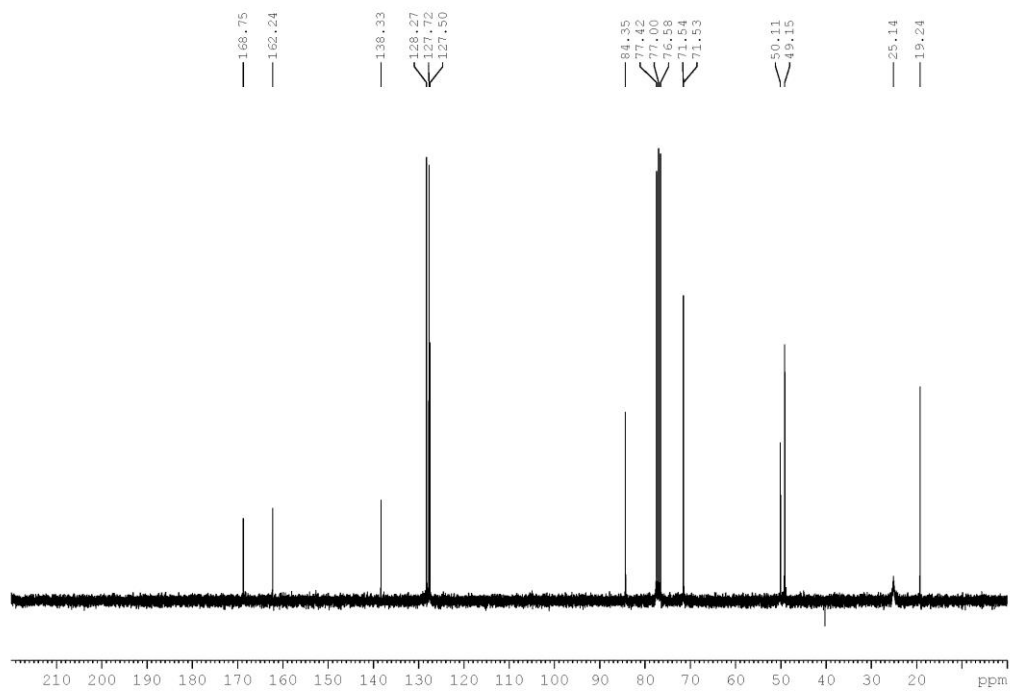
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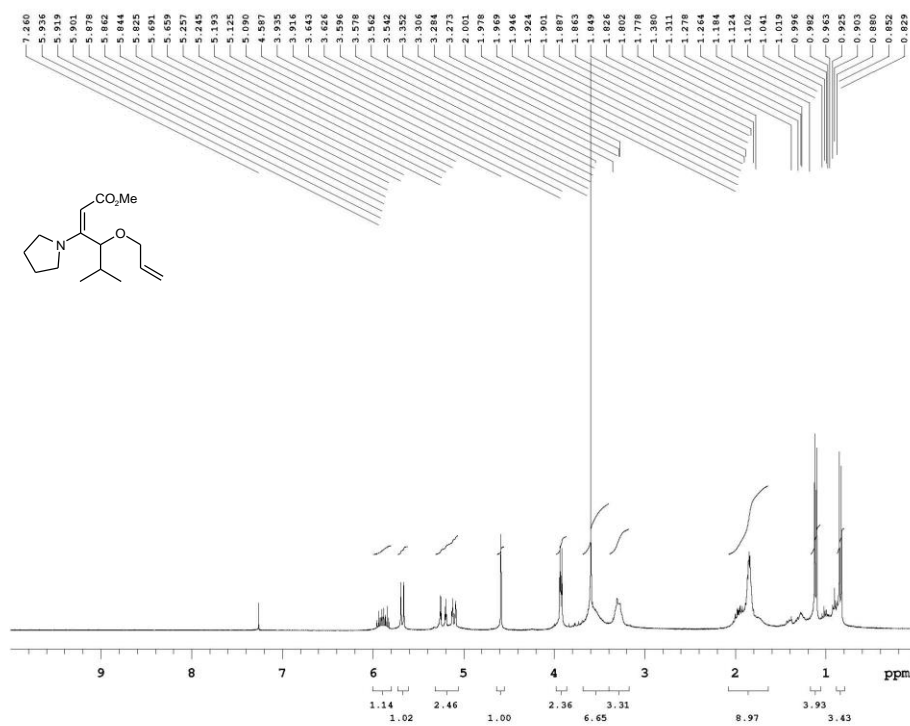
¹H NMR Spectrum of **11j** in CDCl₃



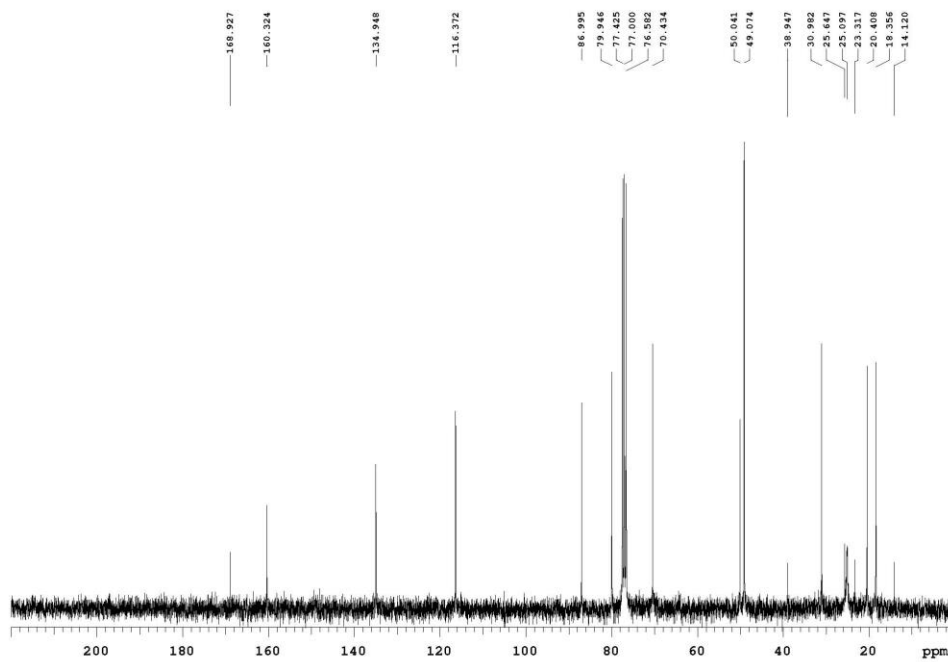
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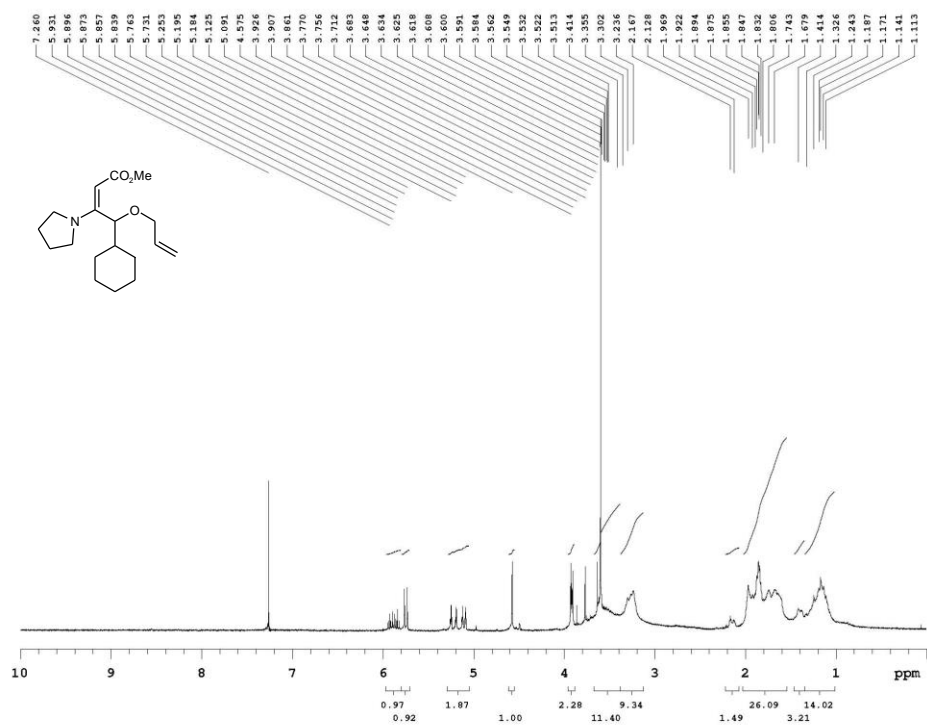
¹H NMR Spectrum of **11a** in CDCl₃



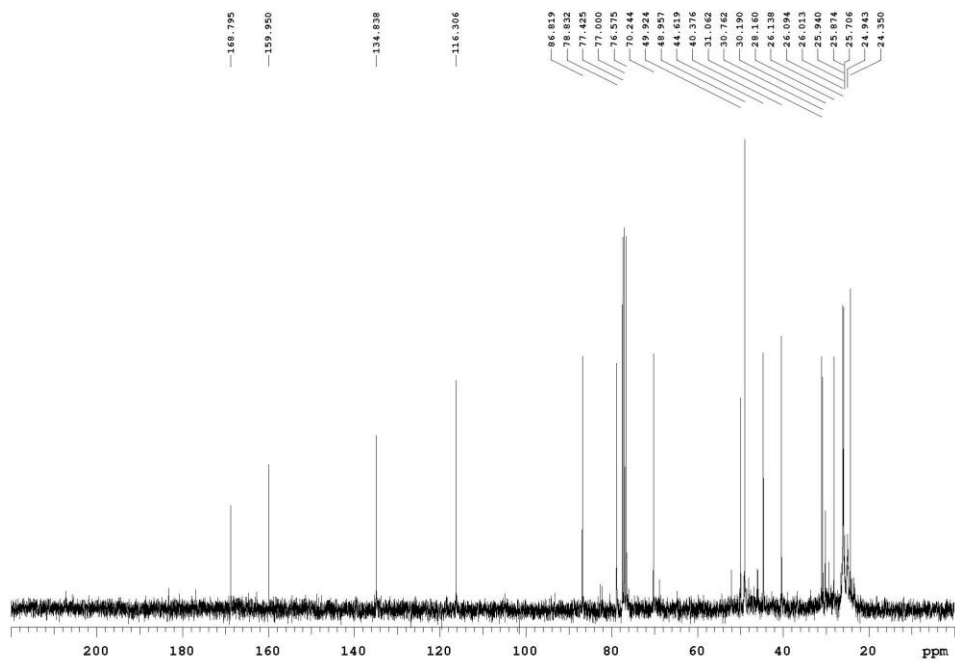
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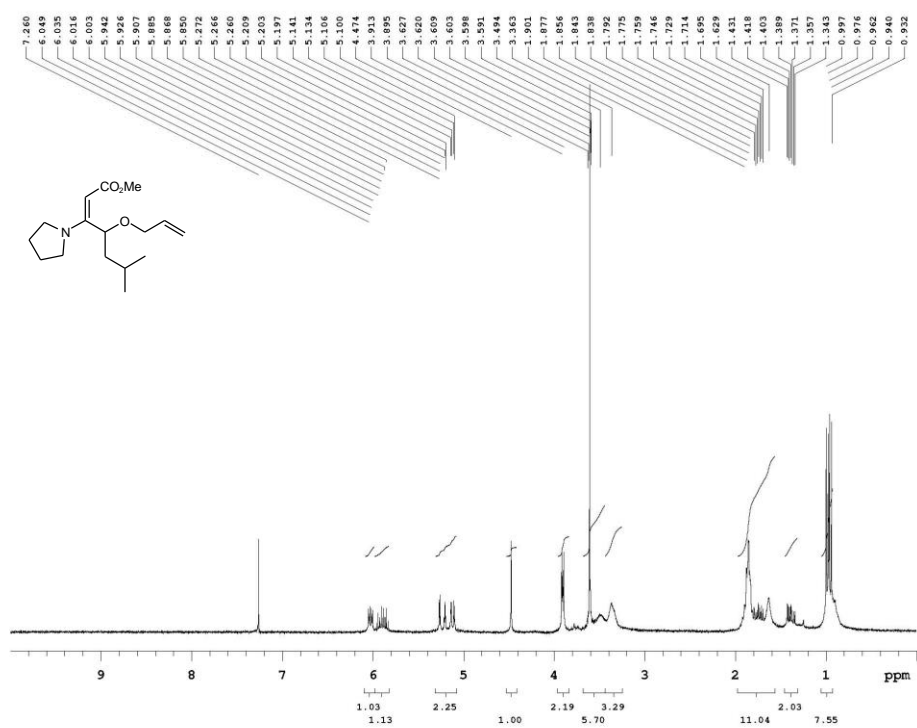
¹H NMR Spectrum of **11c** in CDCl₃



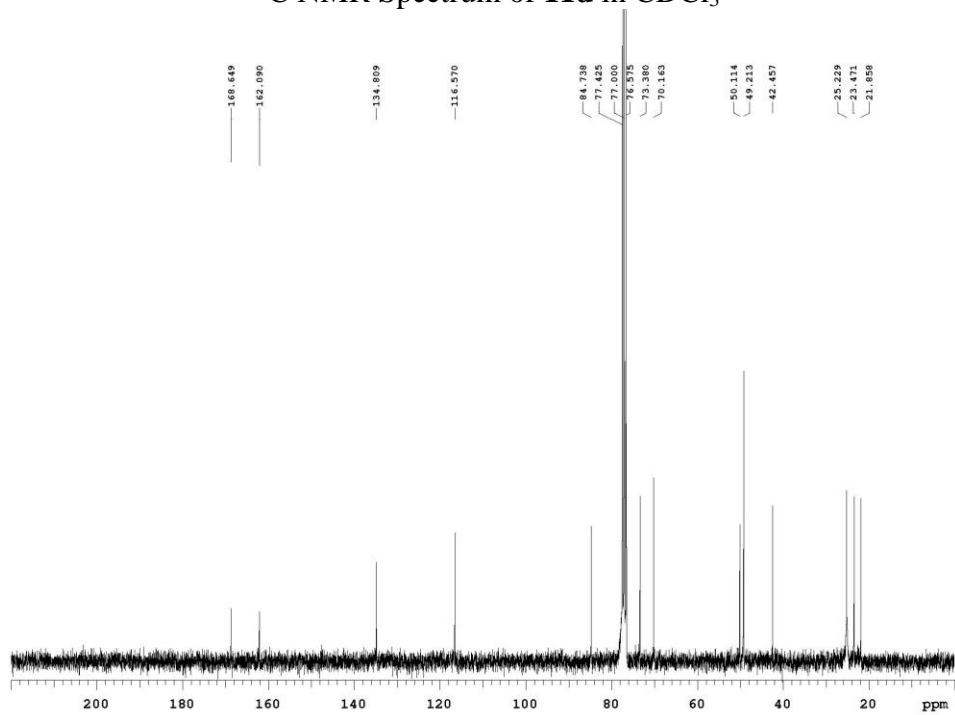
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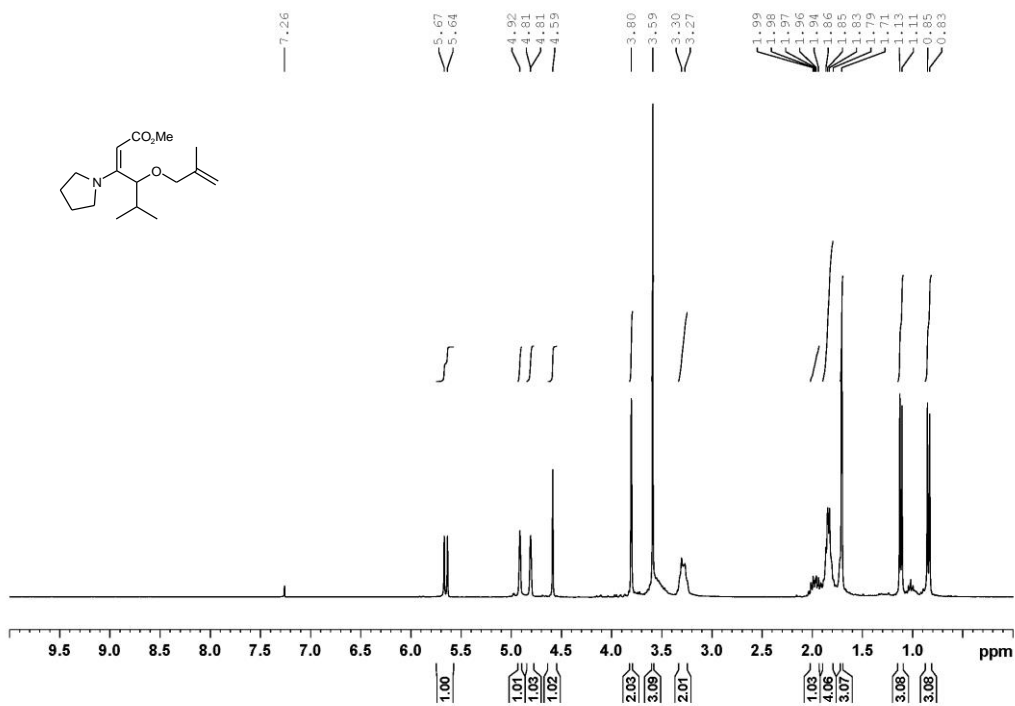
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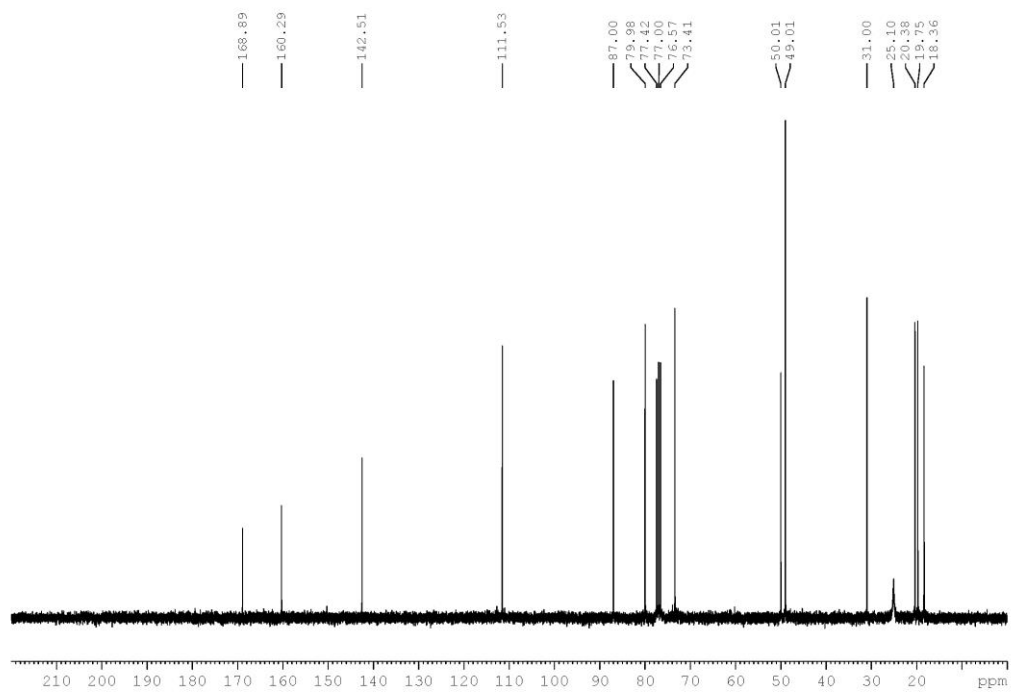
¹³C NMR Spectrum of **11d** in CDCl₃



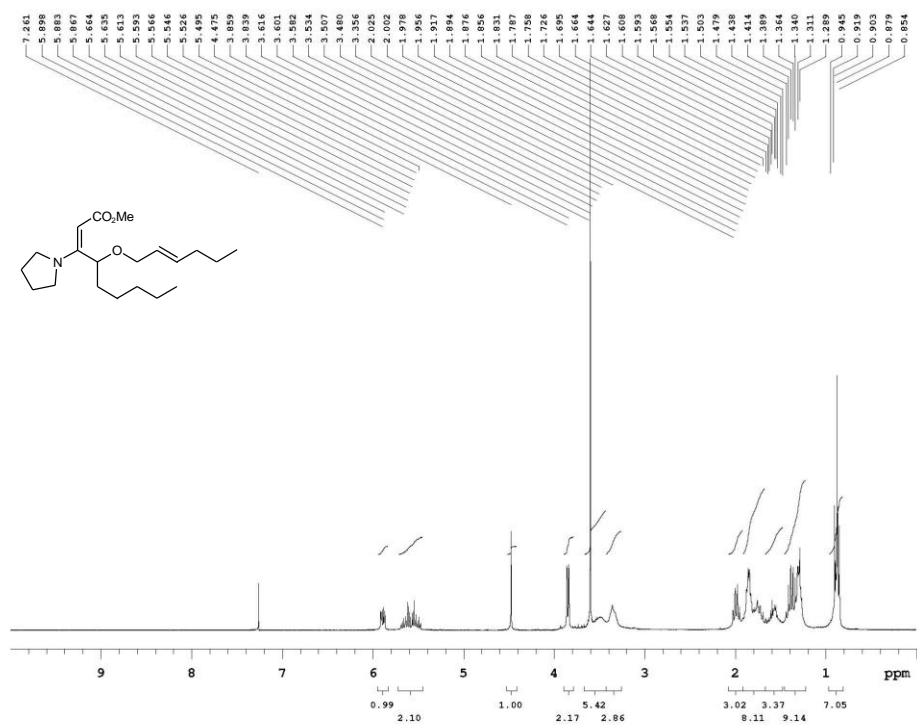
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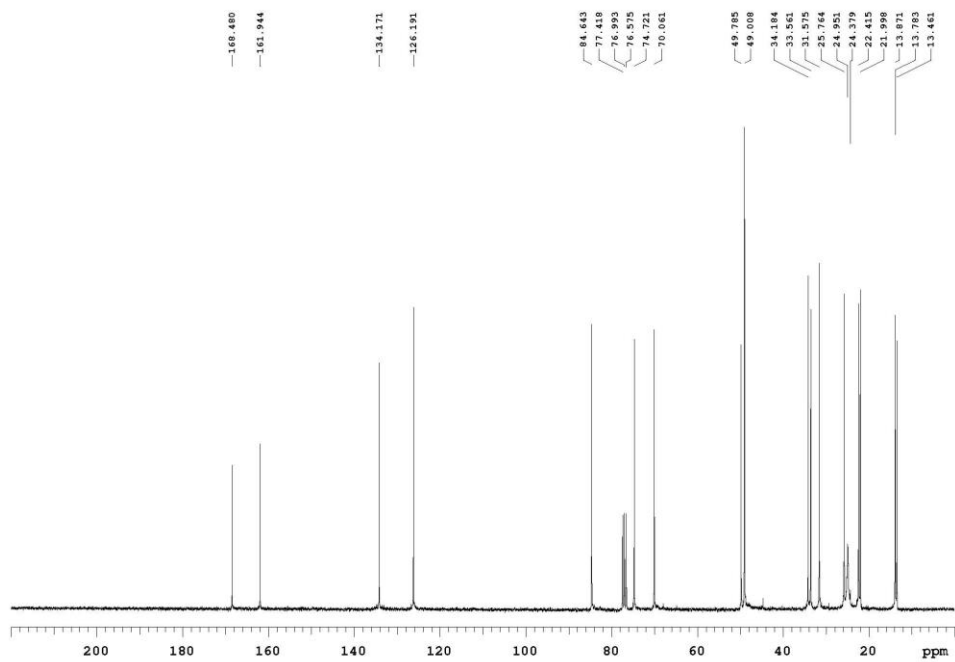
^{13}C NMR Spectrum of **11f** in CDCl_3



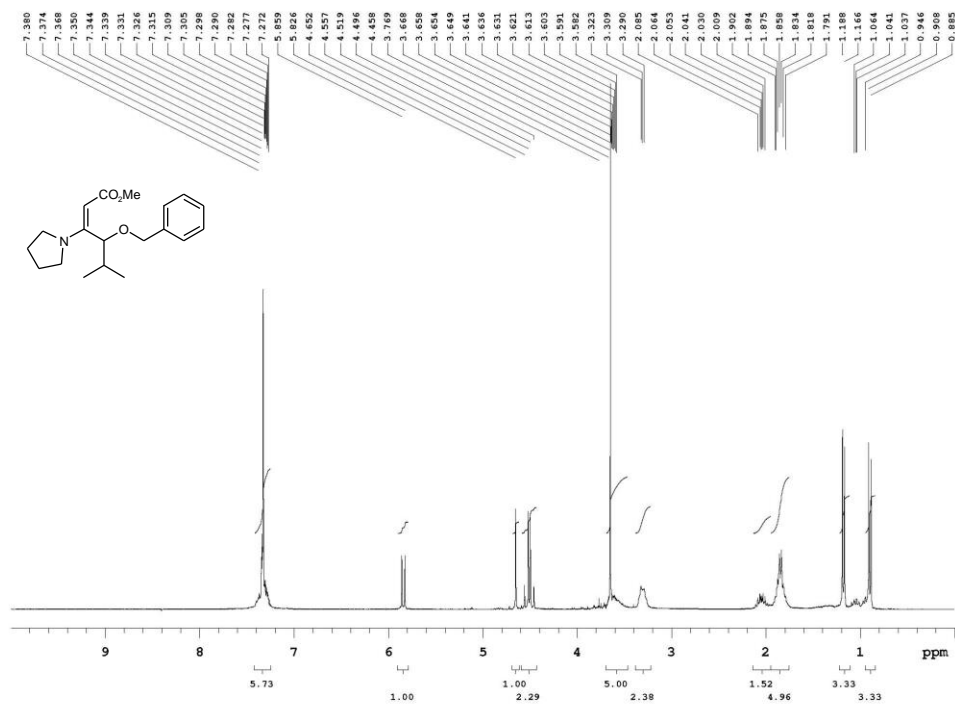
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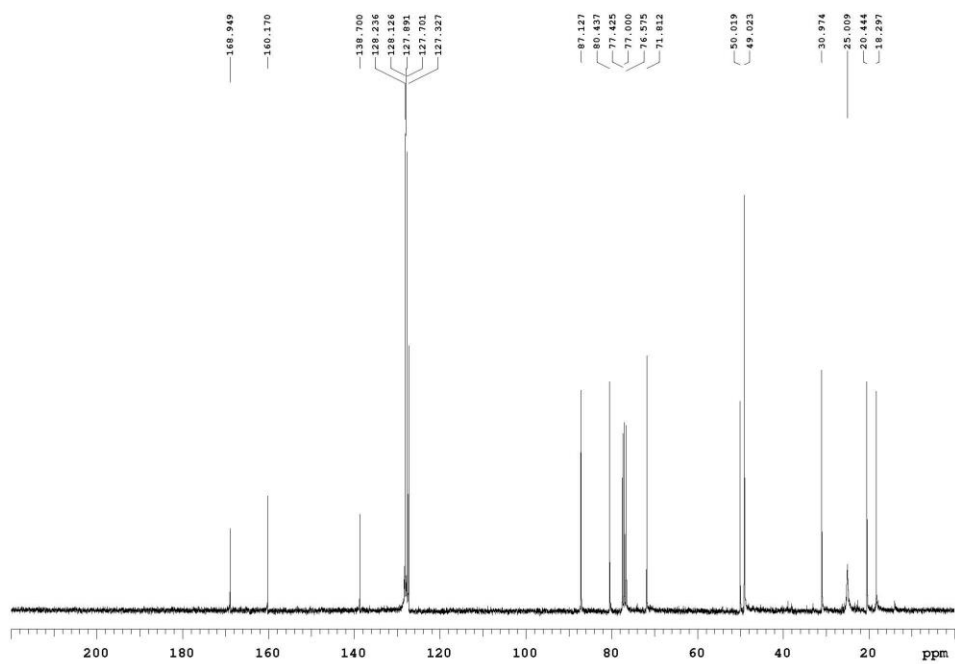
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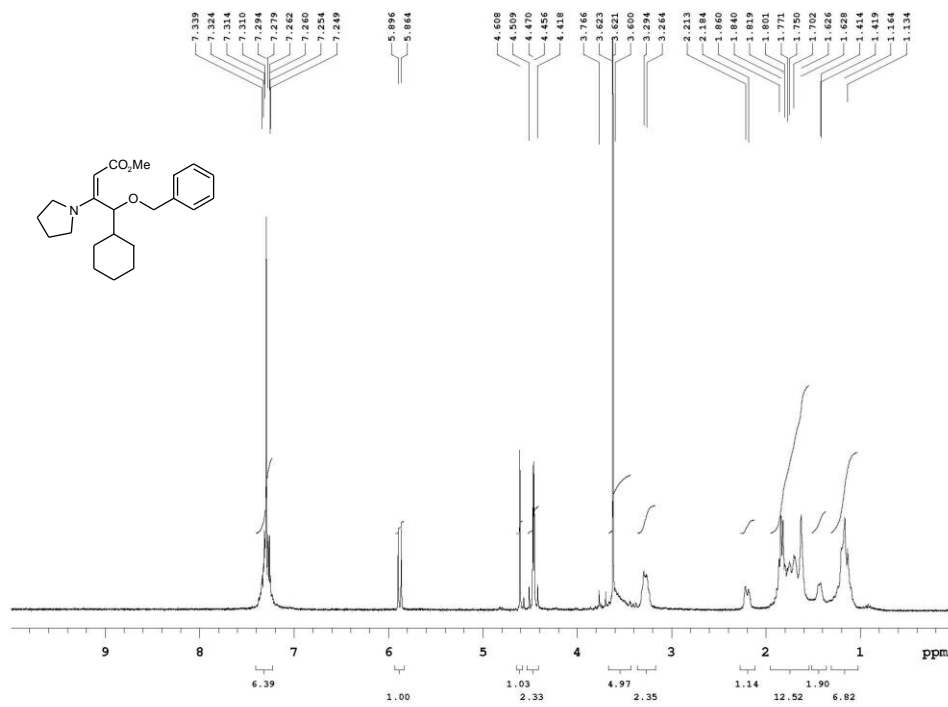
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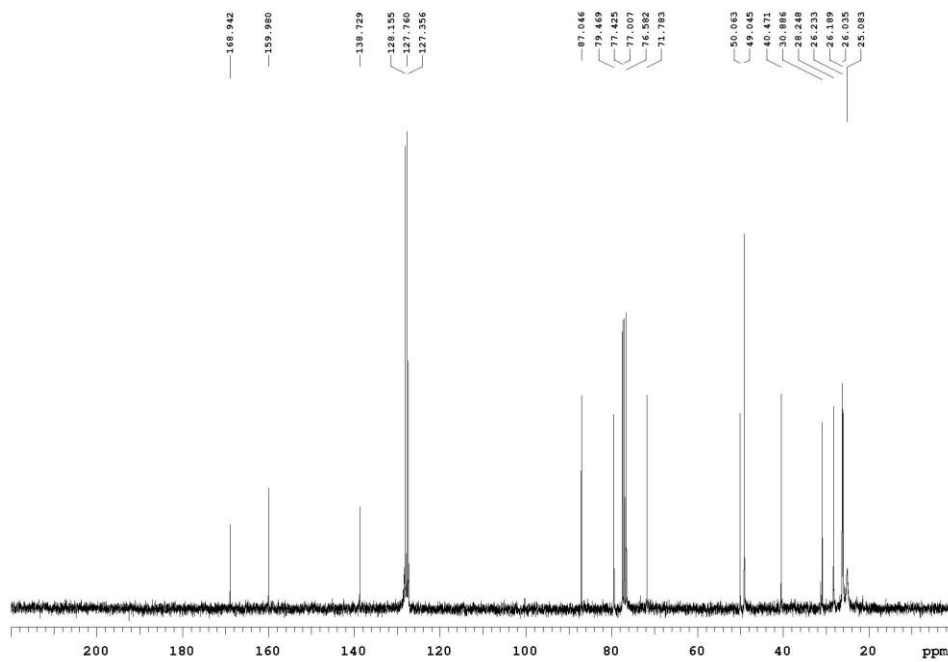
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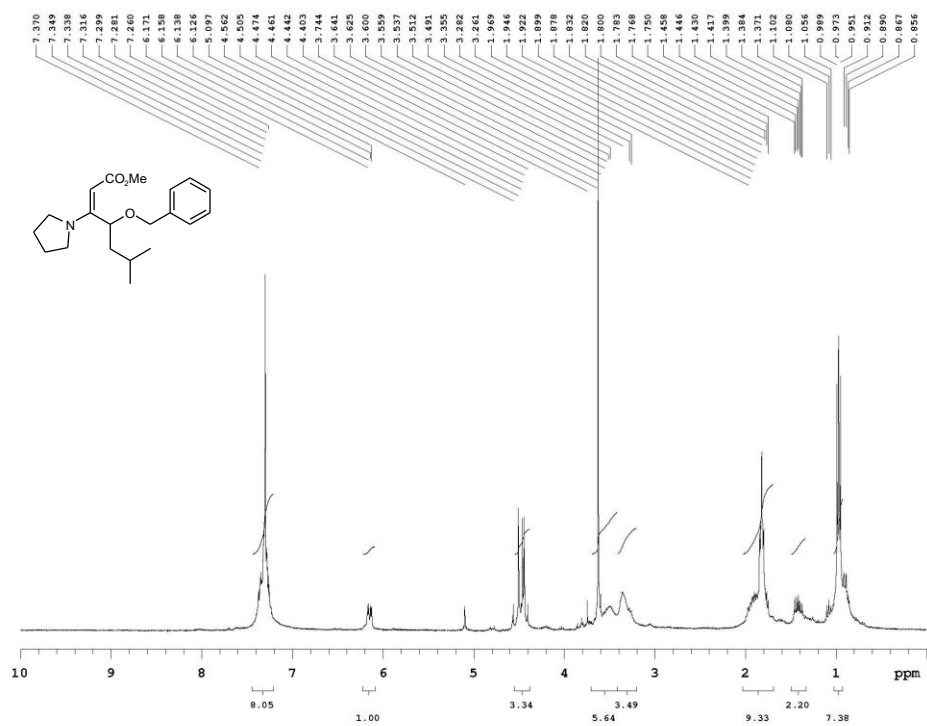
¹H NMR Spectrum of **11l** in CDCl₃



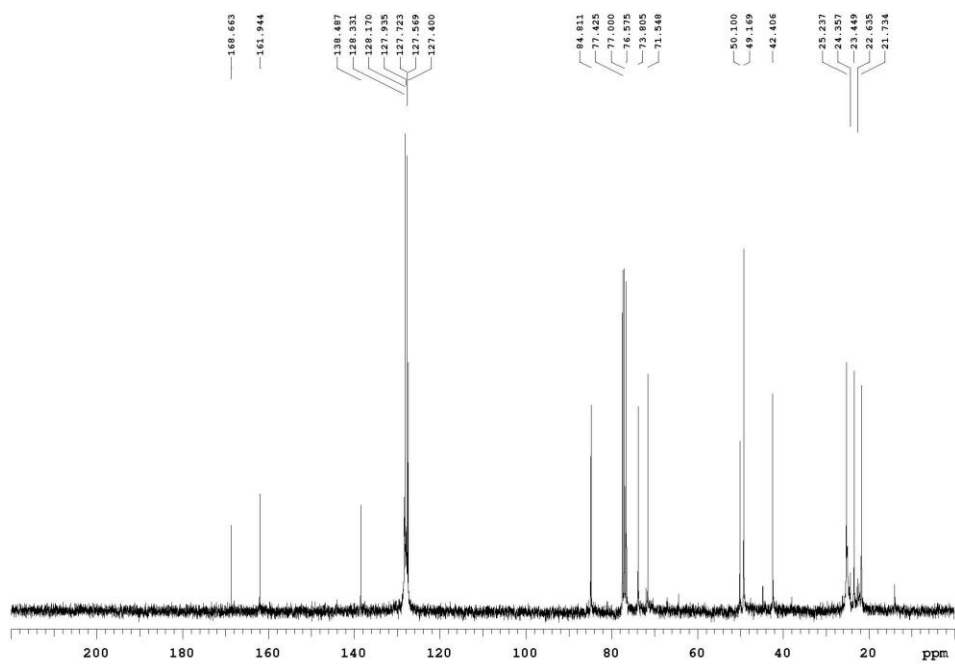
¹³C NMR Spectrum of **11l** in CDCl₃



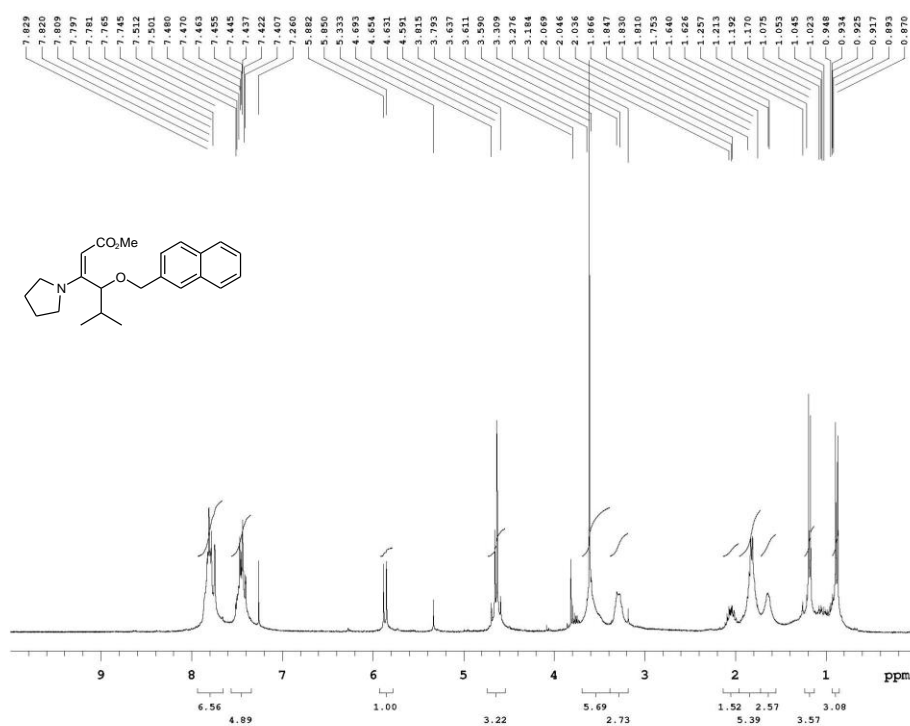
^1H NMR Spectrum of **11m** in CDCl_3



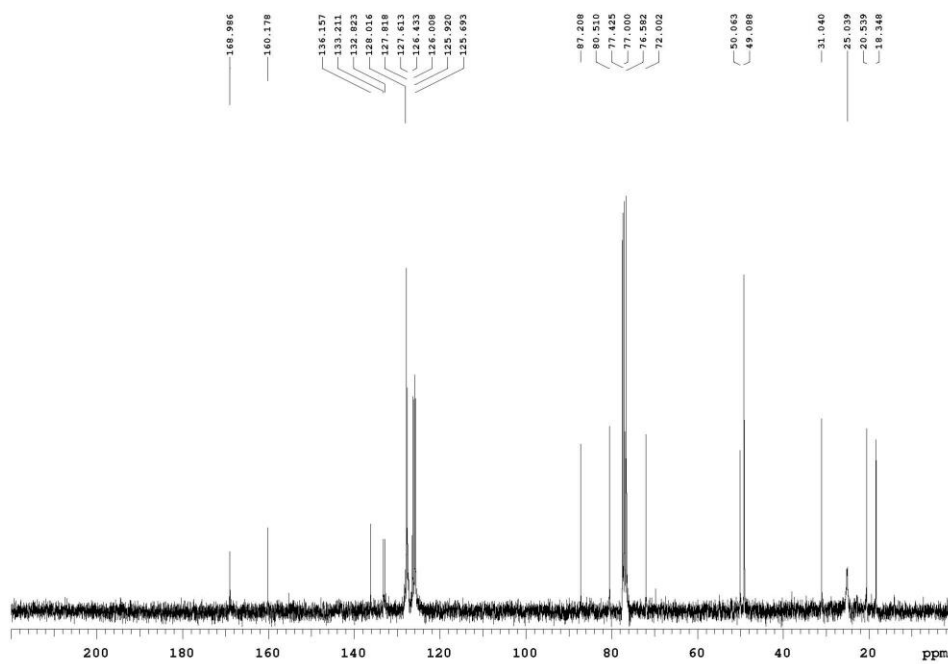
^{13}C NMR Spectrum of **11m** in CDCl_3



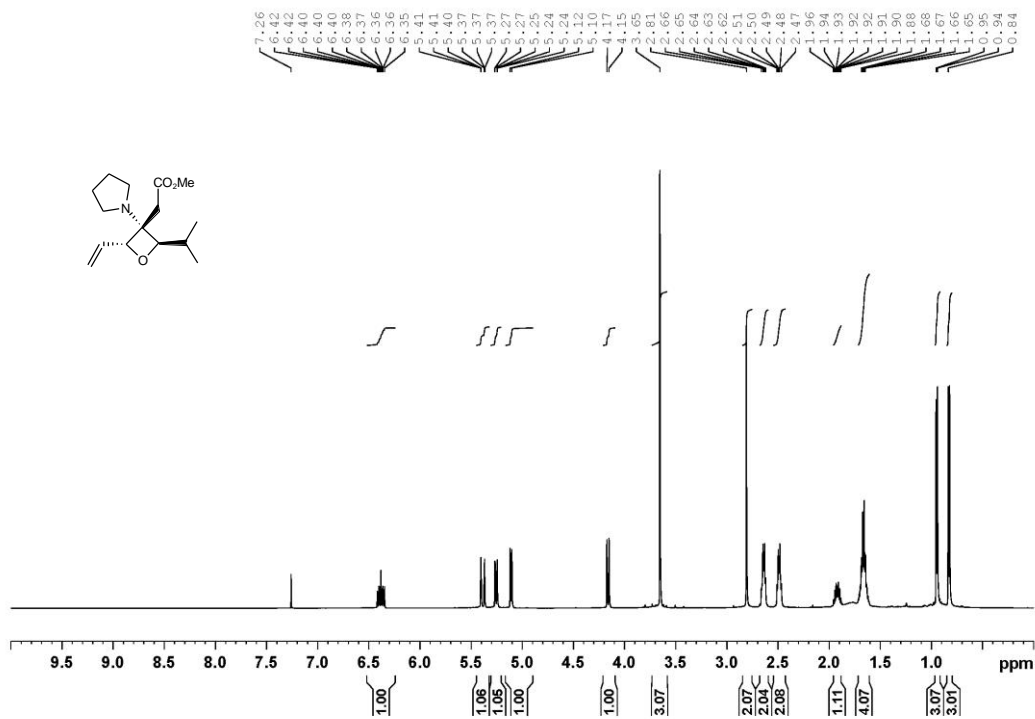
¹H NMR Spectrum of **11n** in CDCl₃



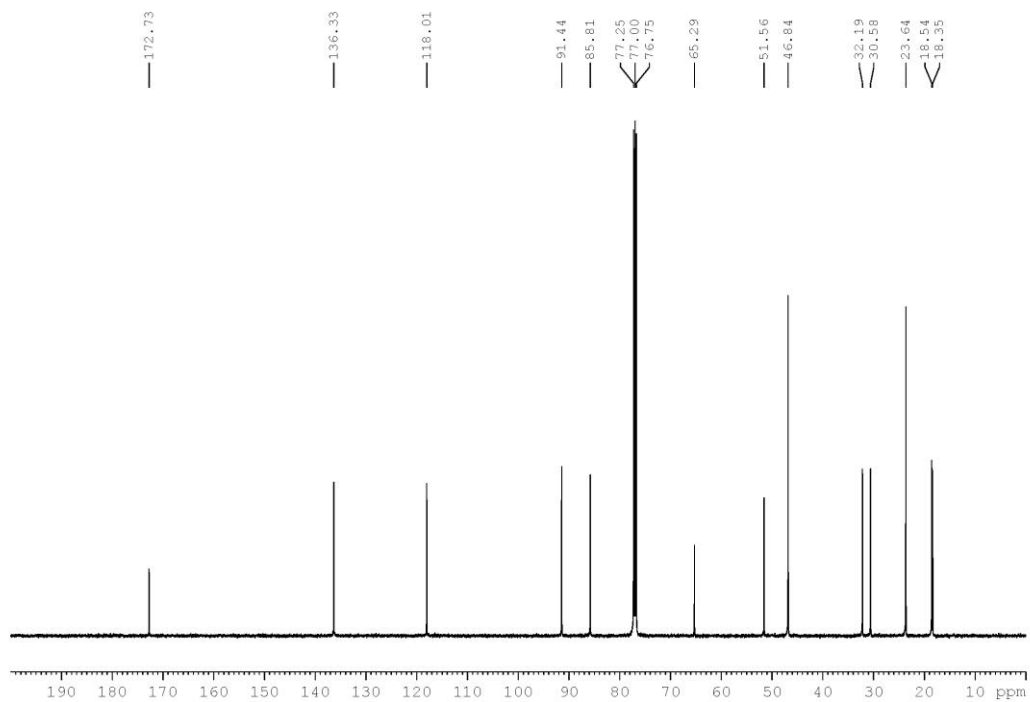
¹³C NMR Spectrum of **11n** in CDCl₃



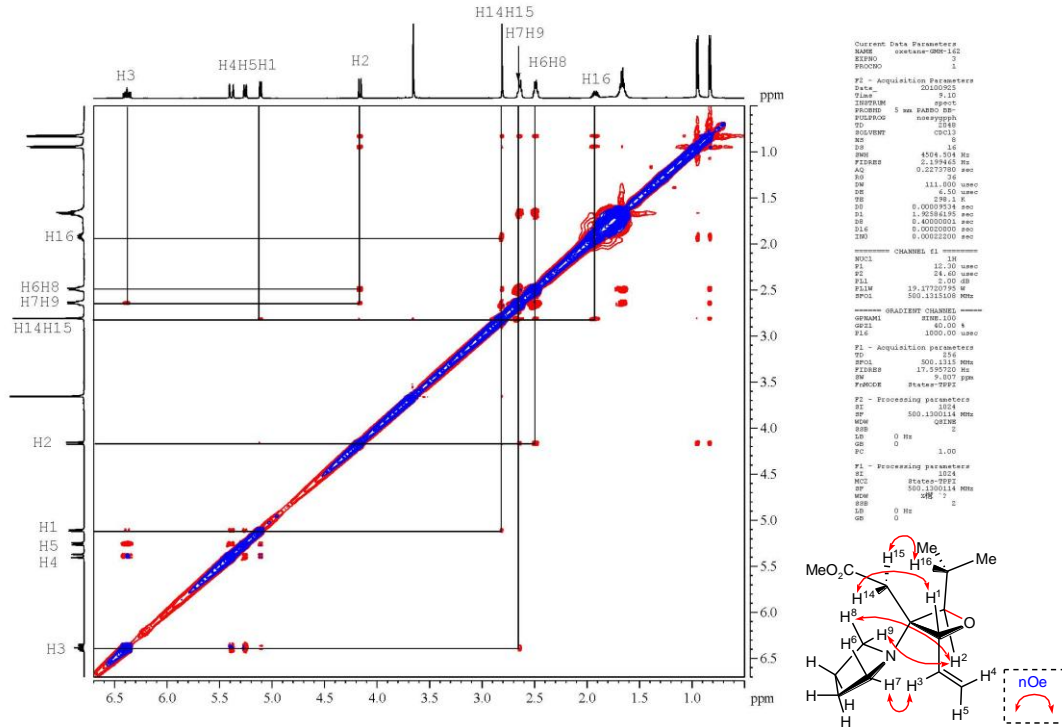
¹H NMR Spectrum of **12a** in CDCl₃



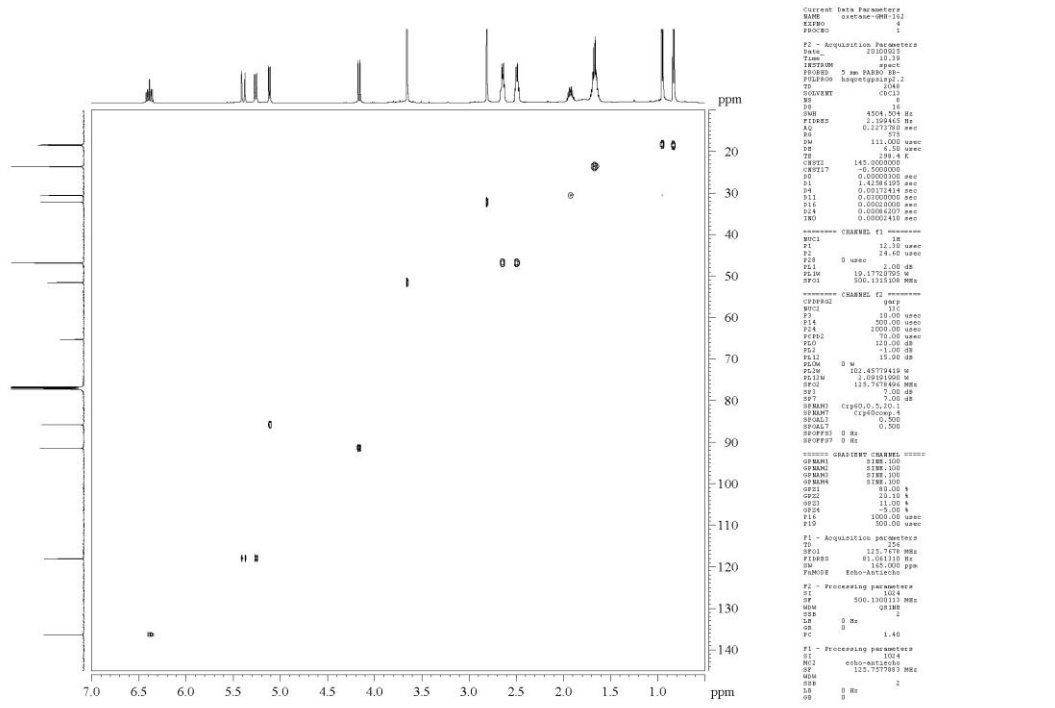
¹³C NMR Spectrum of **12a** in CDCl₃



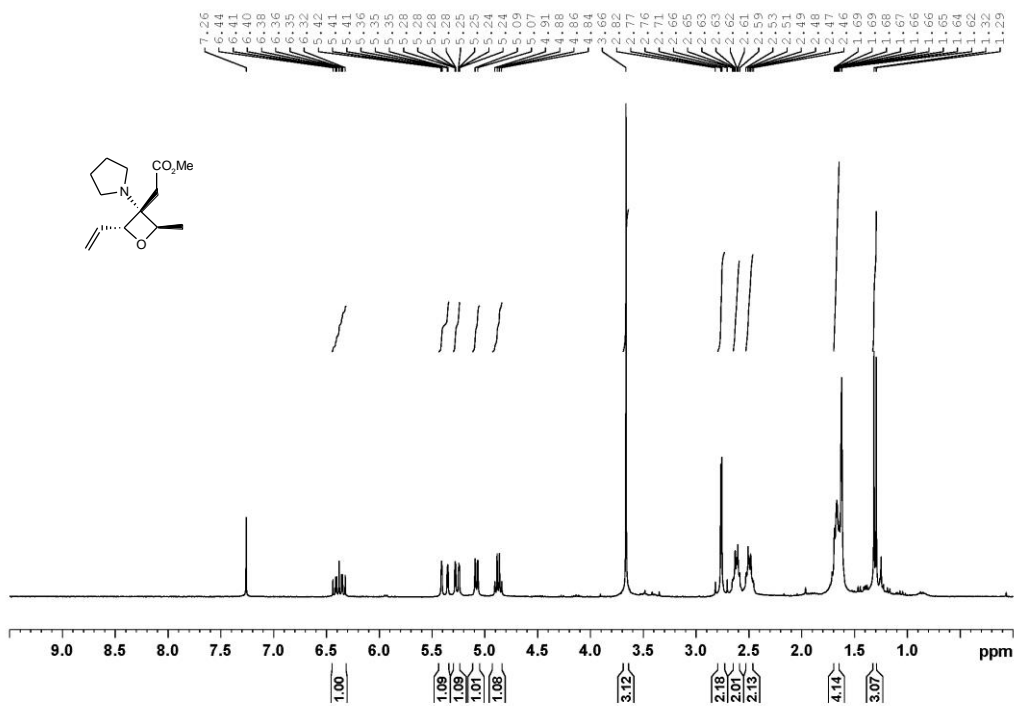
NOESY Spectrum of 12a in CDCl₃



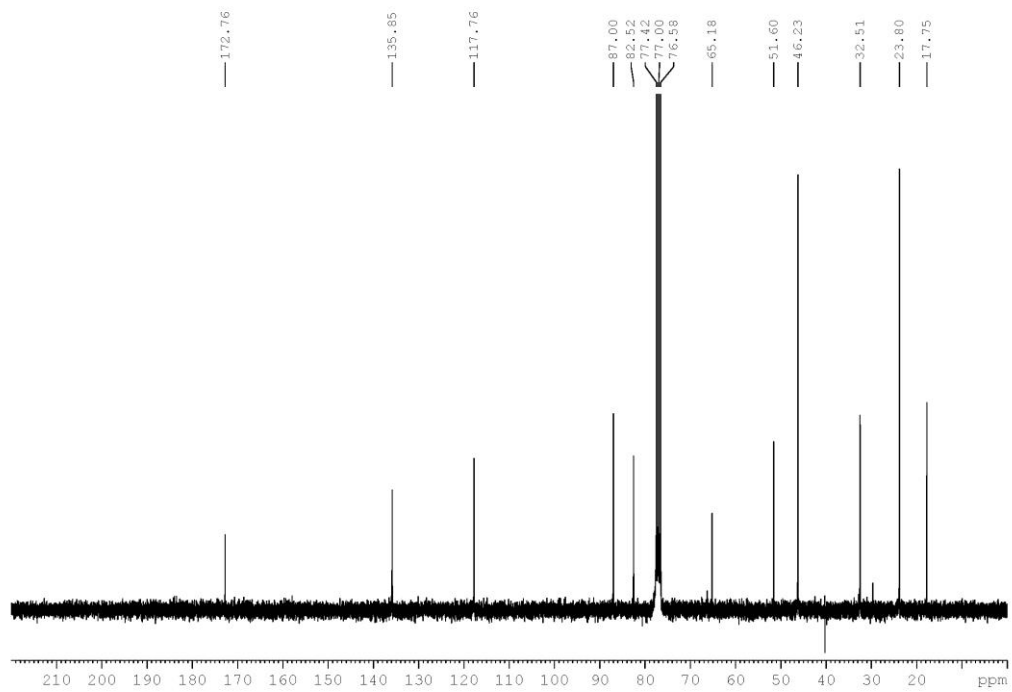
HSQC Spectrum of 12a in CDCl₃



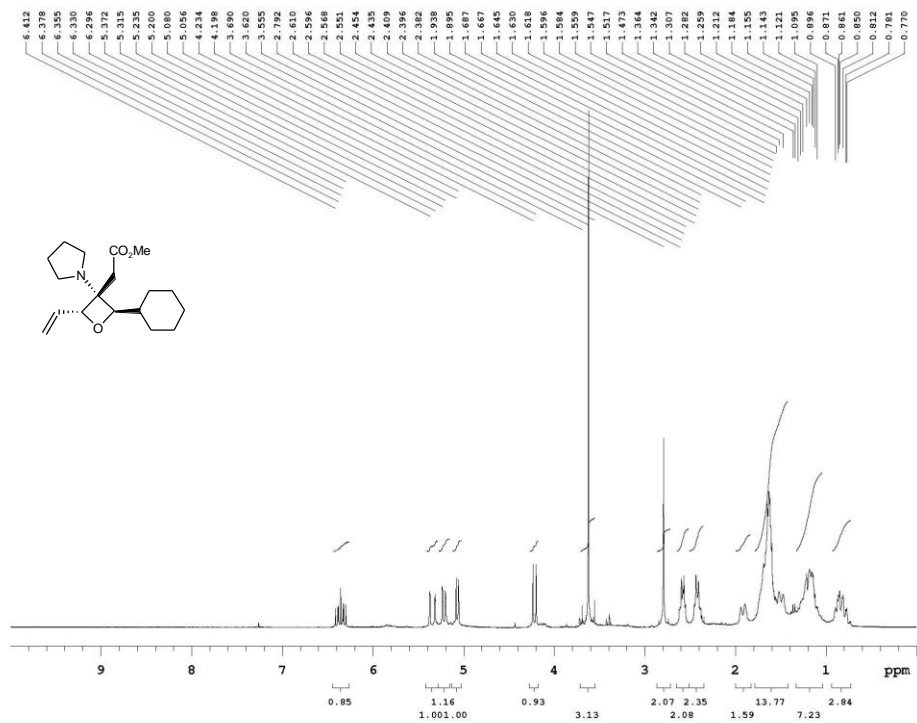
¹H NMR Spectrum of **12b** in CDCl₃



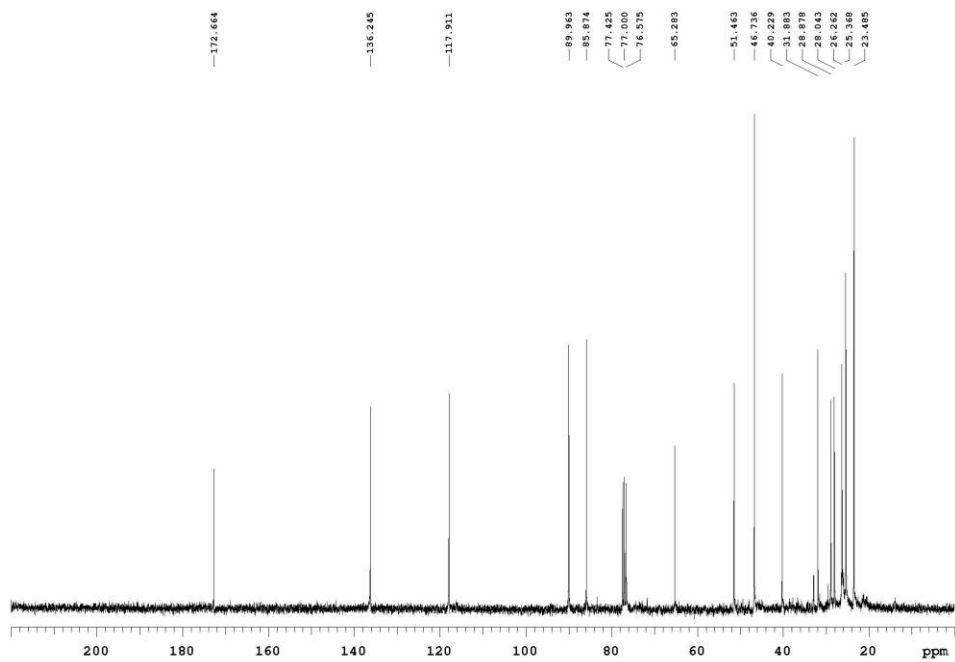
¹³C NMR Spectrum of **12b** in CDCl₃



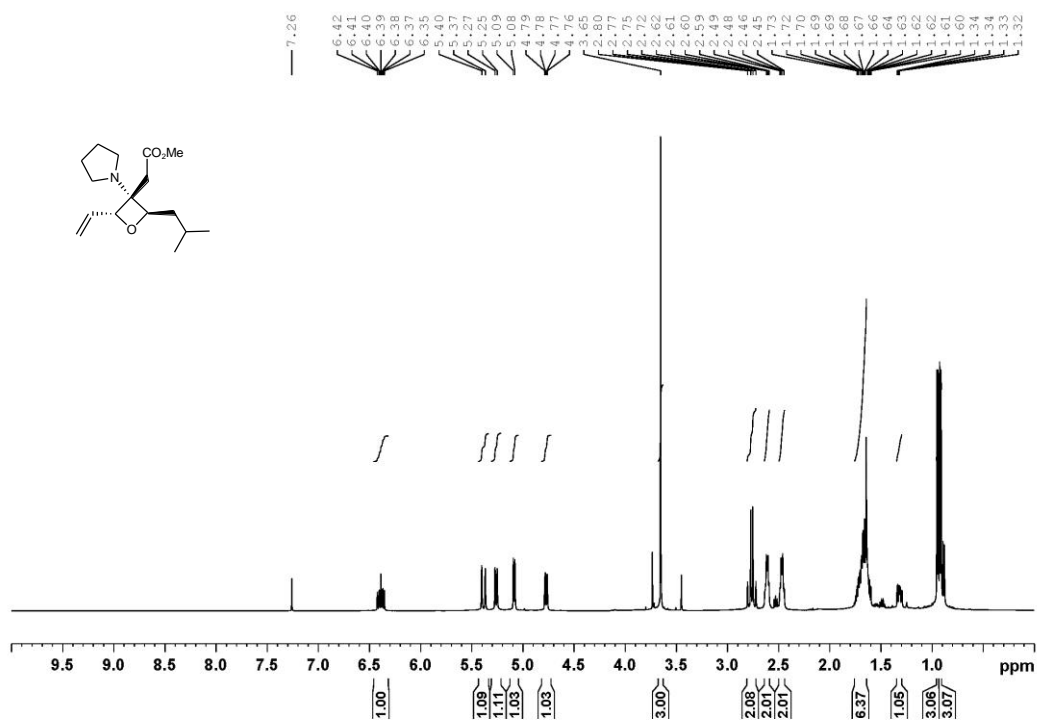
^1H NMR Spectrum of **12c** in CDCl_3



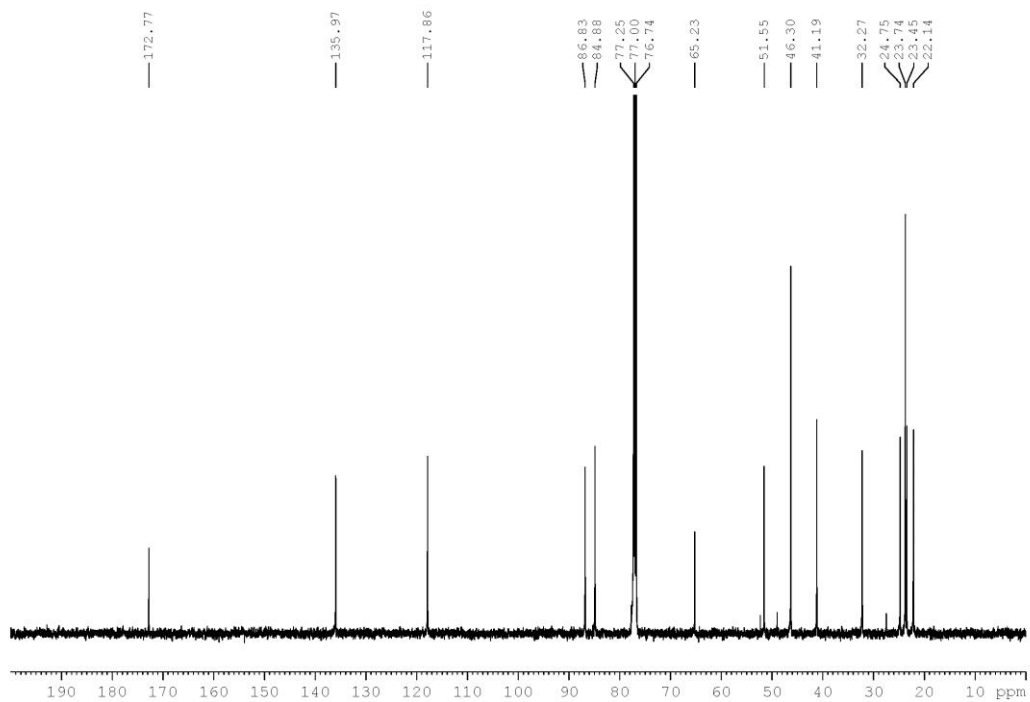
^{13}C NMR Spectrum of **12c** in CDCl_3



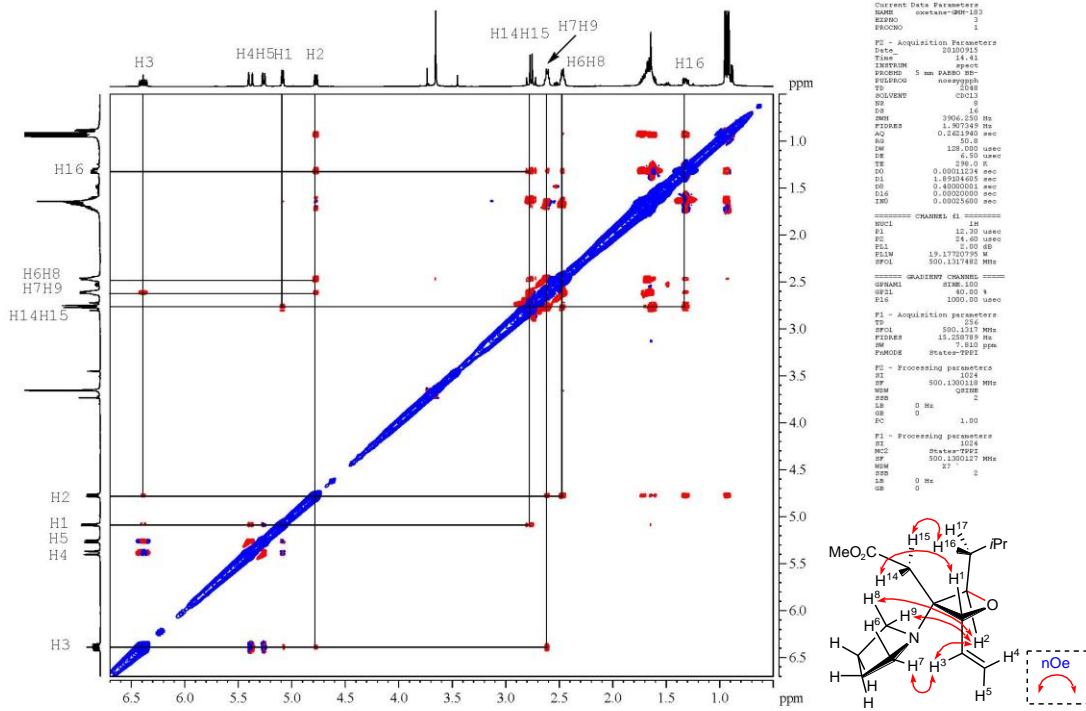
¹H NMR Spectrum of **12d** in CDCl₃



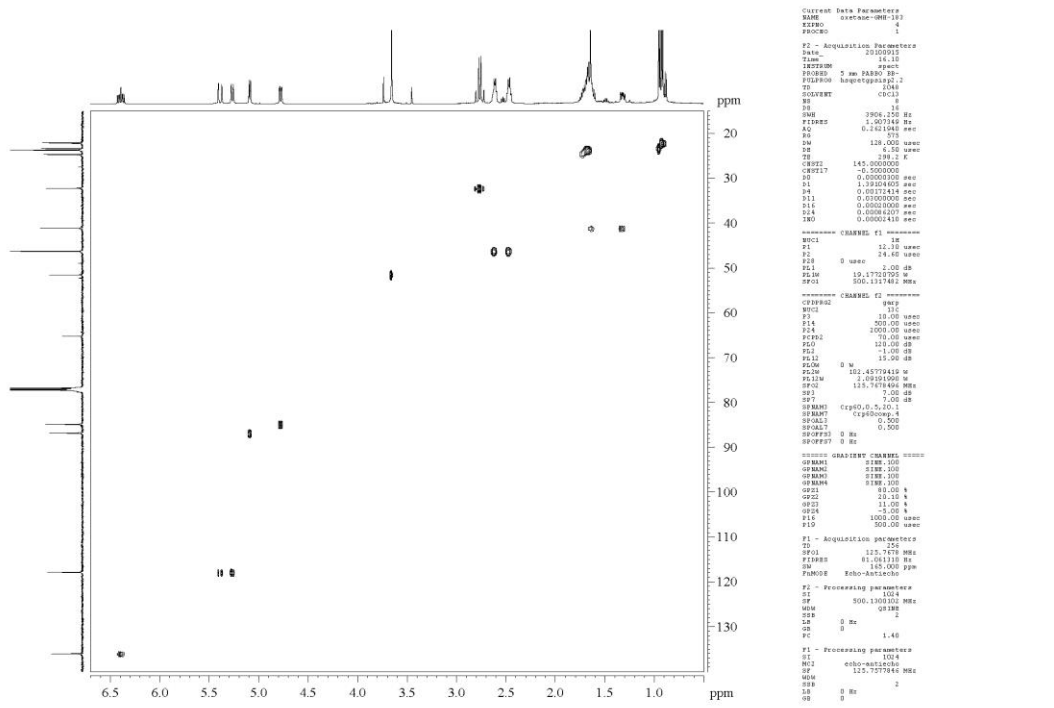
¹³C NMR Spectrum of **12d** in CDCl₃



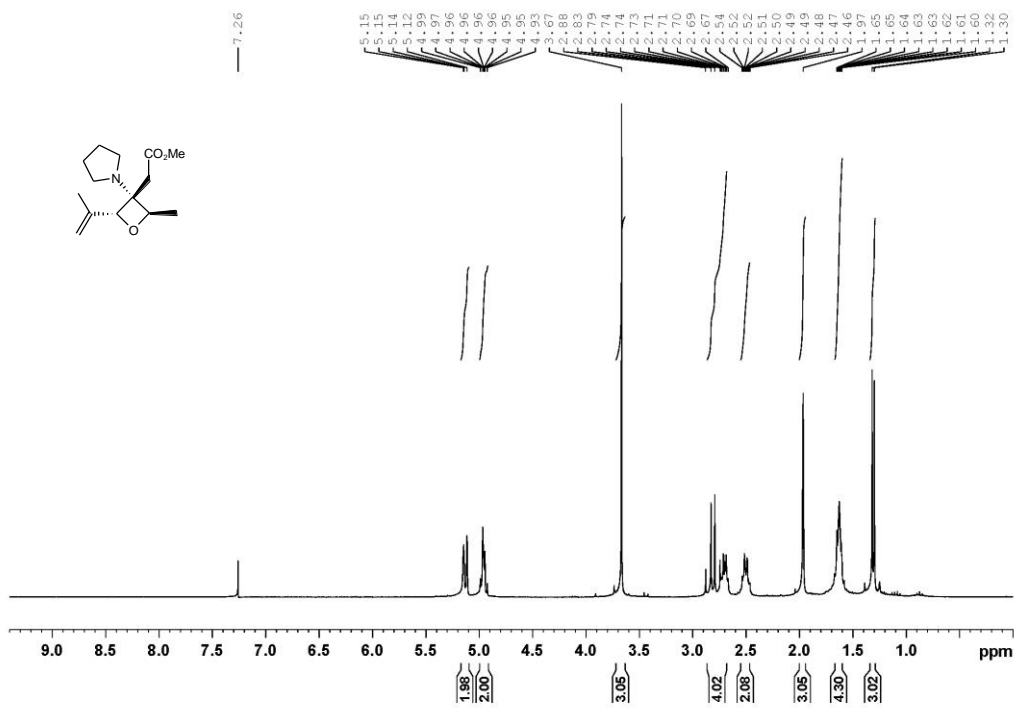
NOESY Spectrum of 12d in CDCl₃



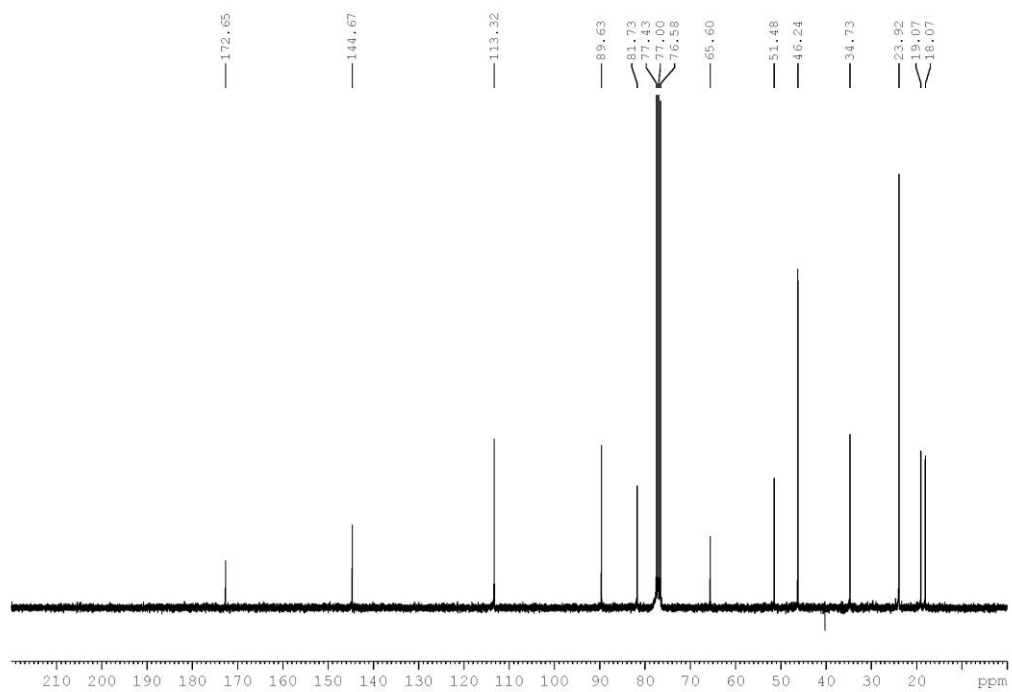
HSCOC Spectrum of 12d in CDCl₃



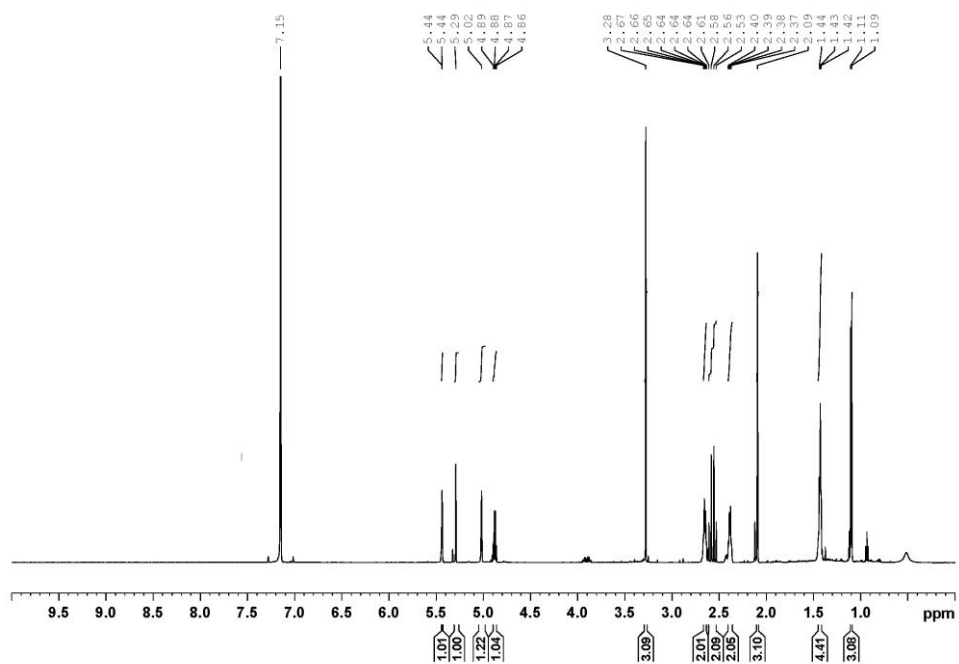
^1H NMR Spectrum of **12e** in CDCl_3



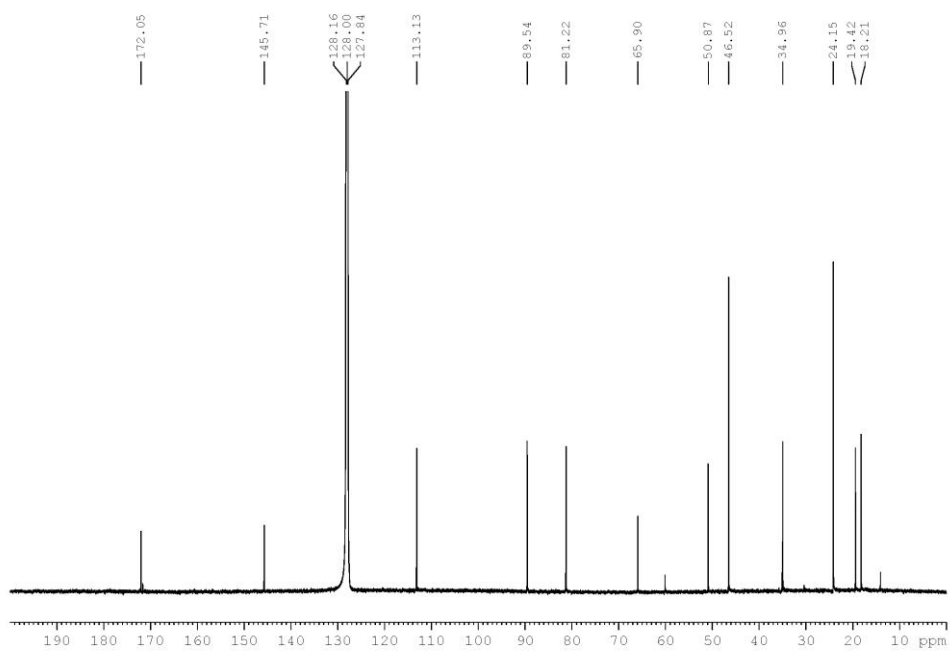
^{13}C NMR Spectrum of **12e** in CDCl_3



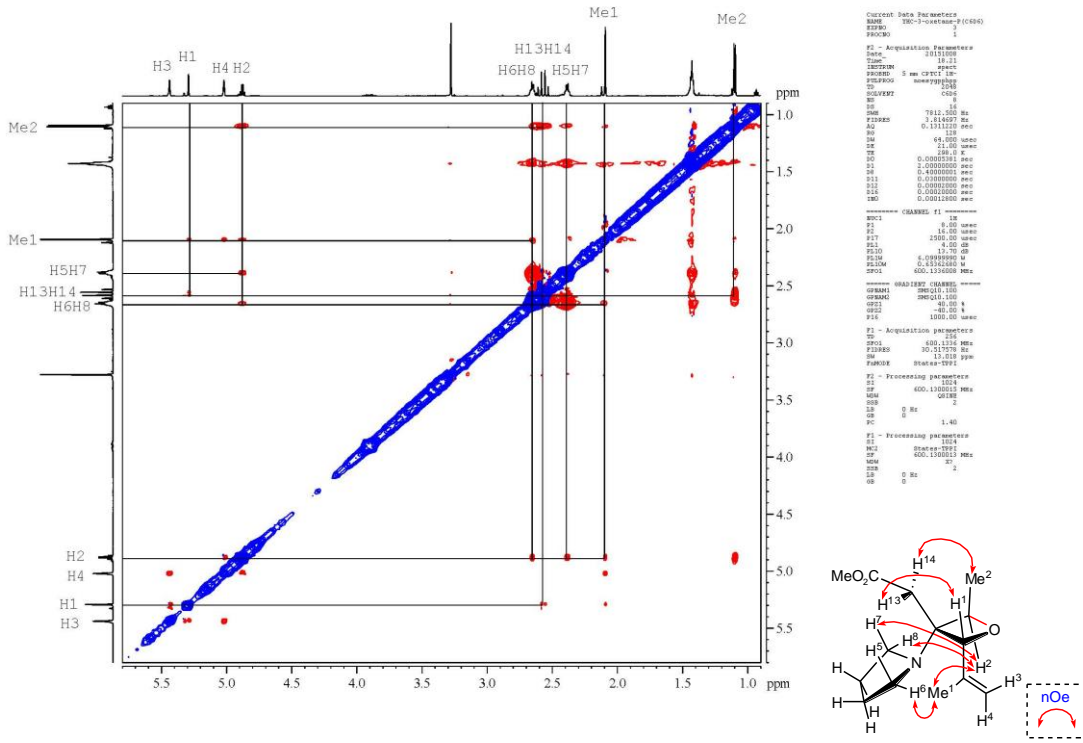
^1H NMR Spectrum of **12e** in C_6D_6



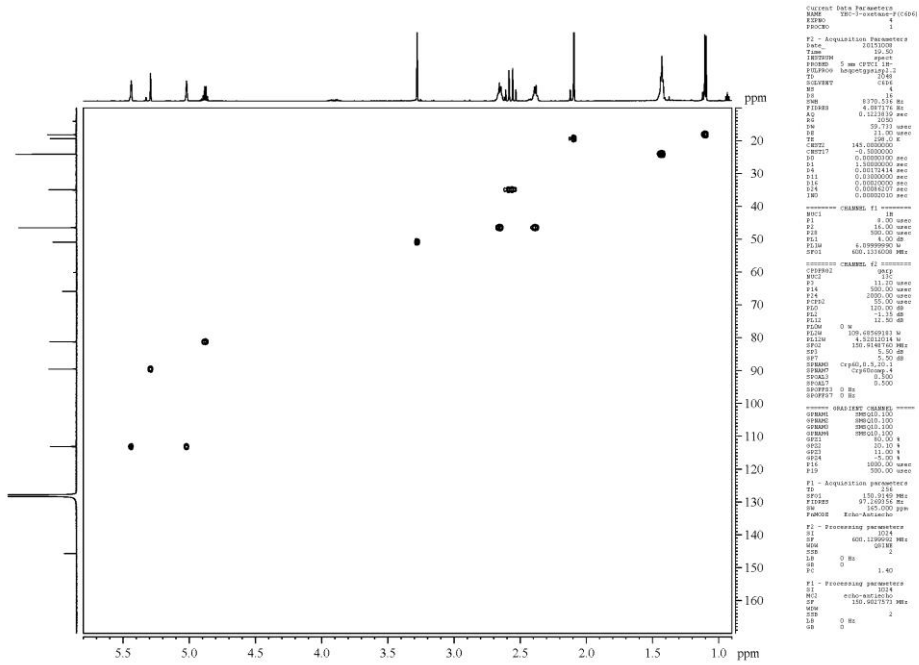
^{13}C NMR Spectrum of **12e** in C_6D_6



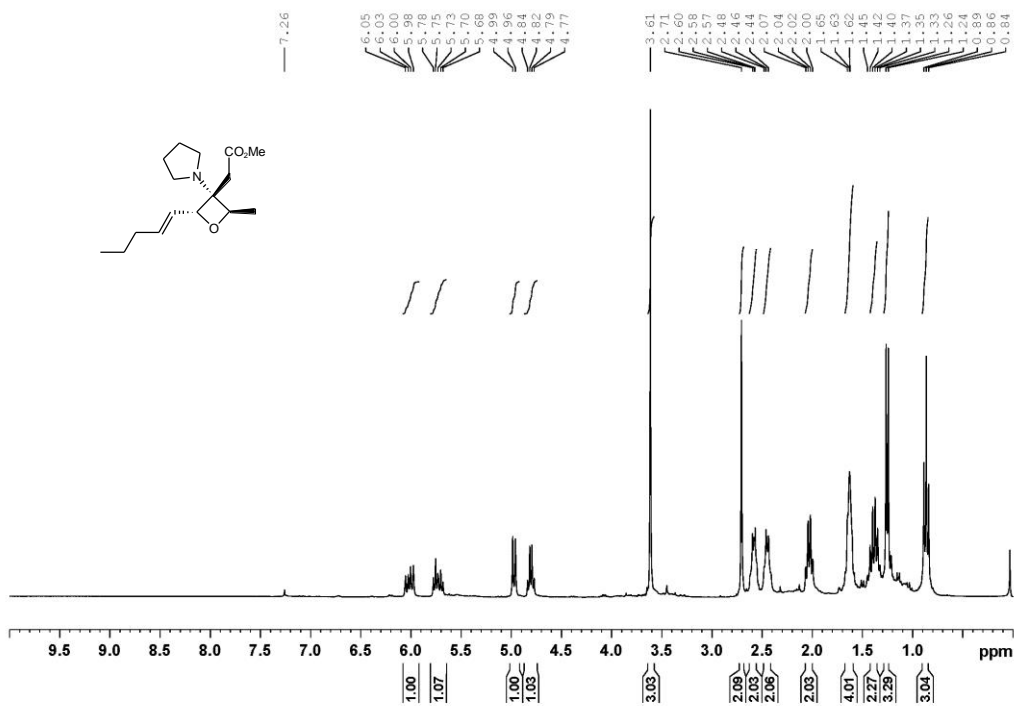
NOESY Spectrum of 12e in C₆D₆



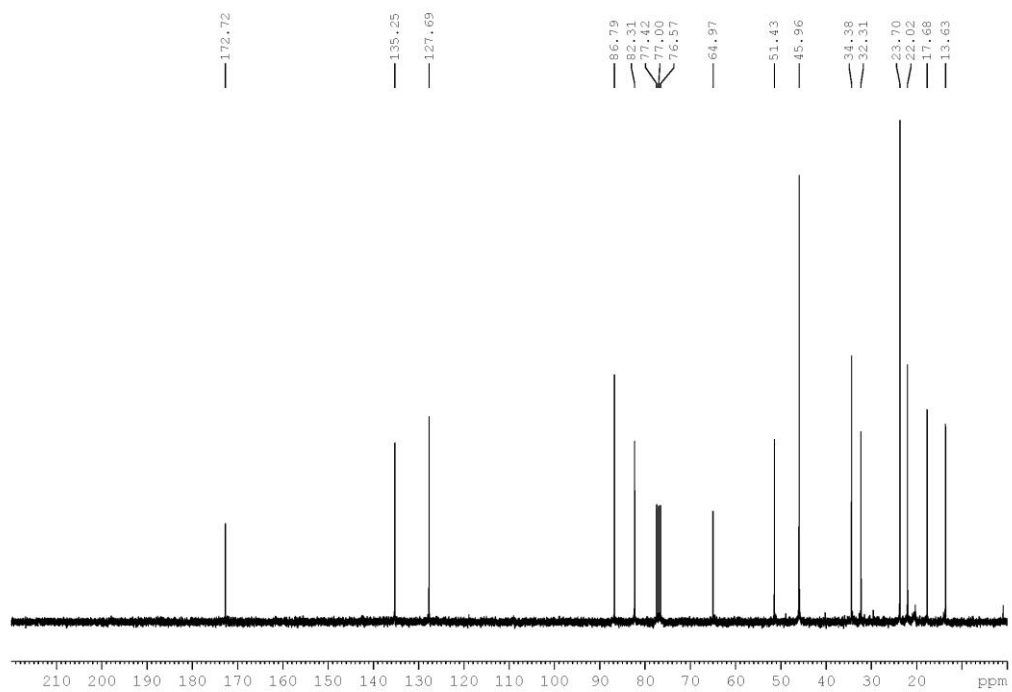
HSQC Spectrum of 12e in C₆D₆



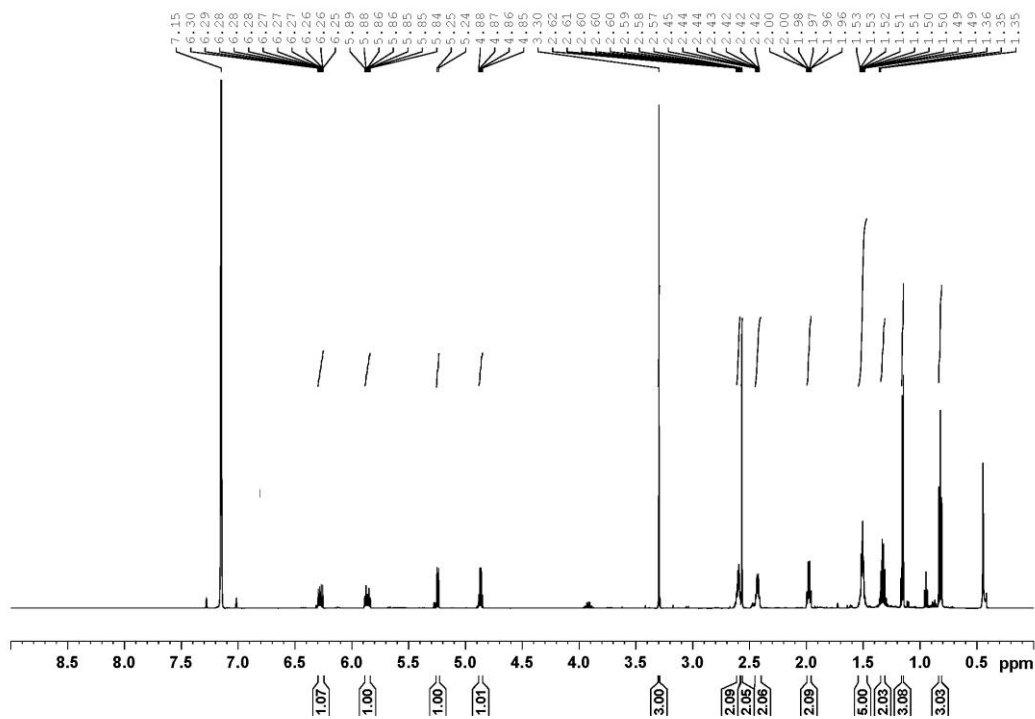
¹H NMR Spectrum of **12g** in CDCl₃



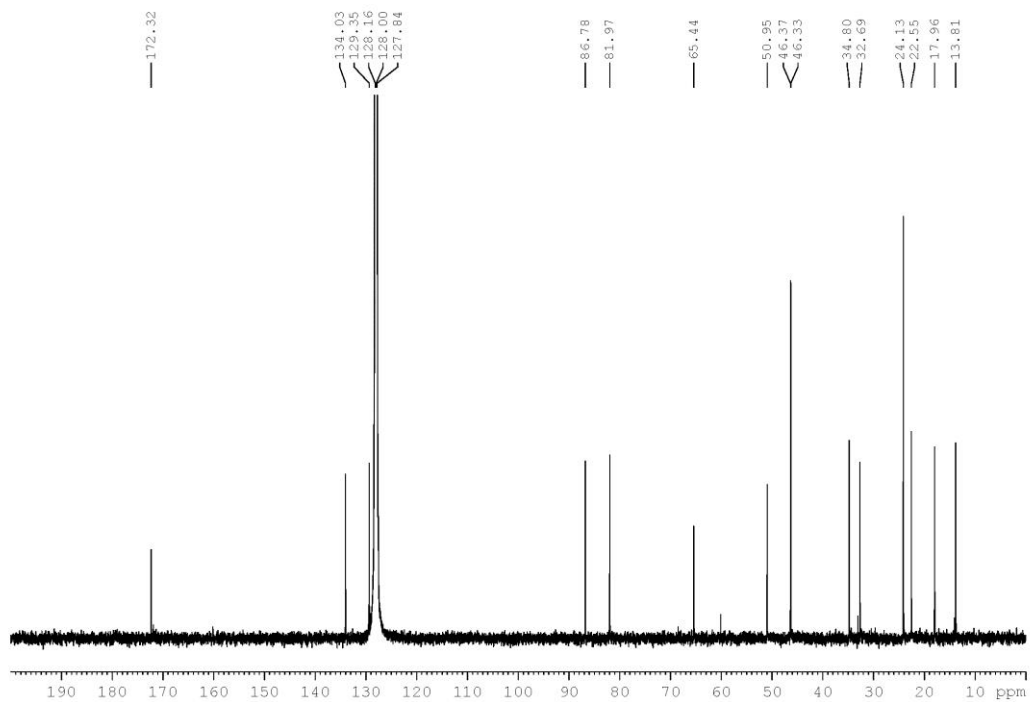
¹³C NMR Spectrum of **12g** in CDCl₃



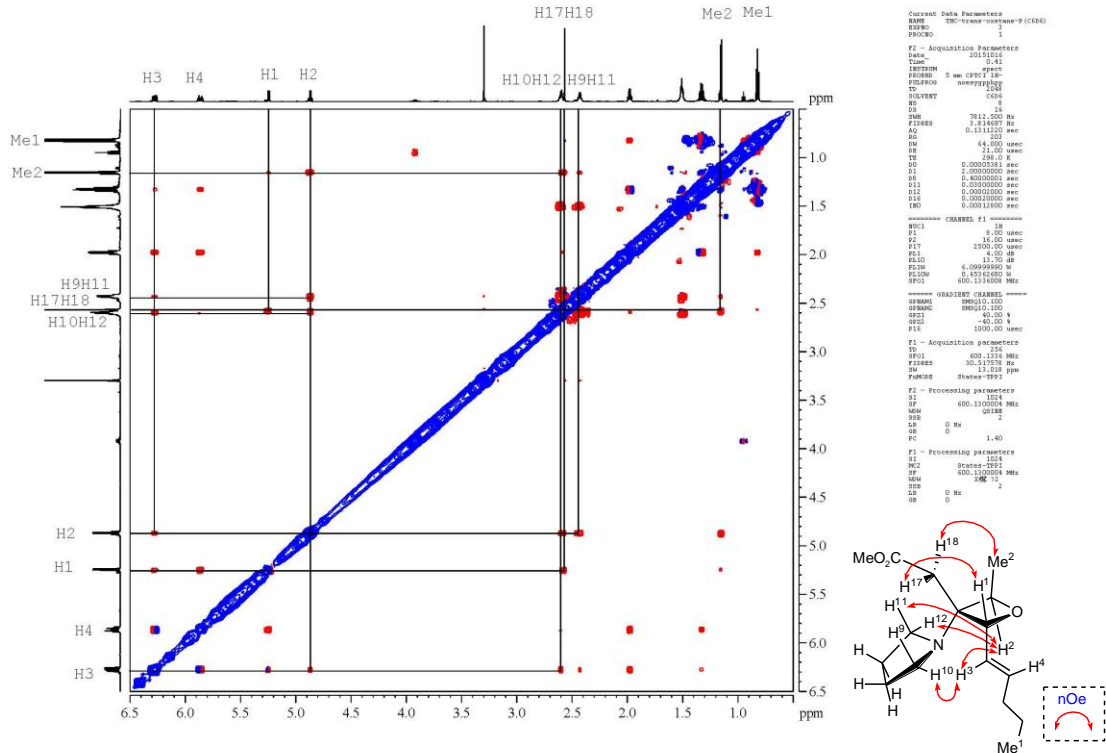
^1H NMR Spectrum of **12g** in C_6D_6



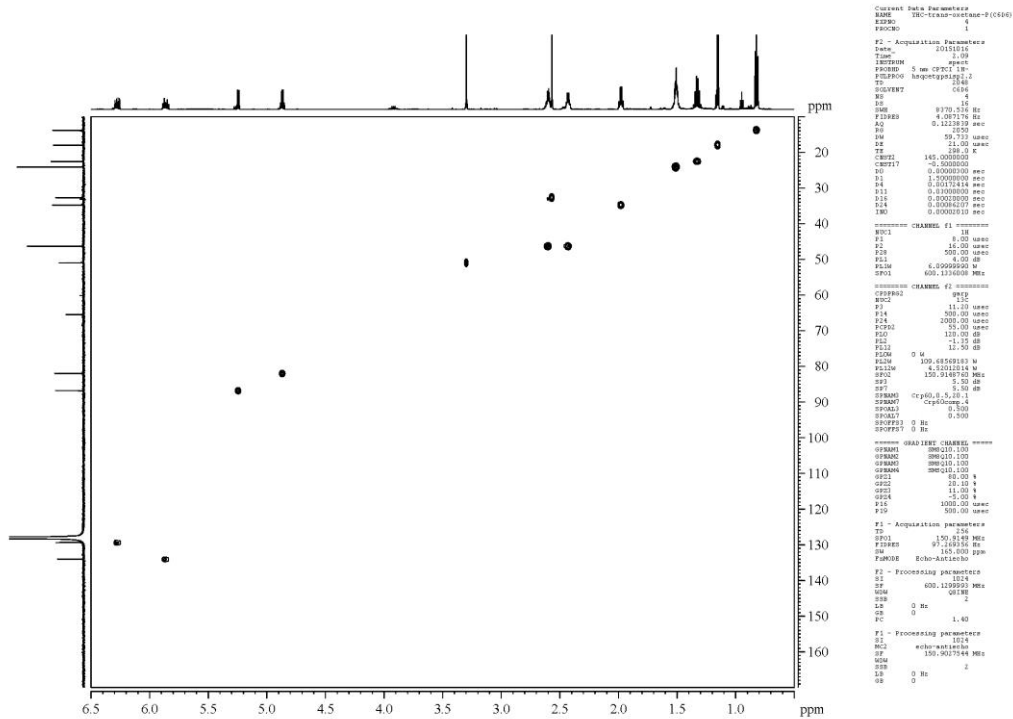
^{13}C NMR Spectrum of **12g** in C_6D_6



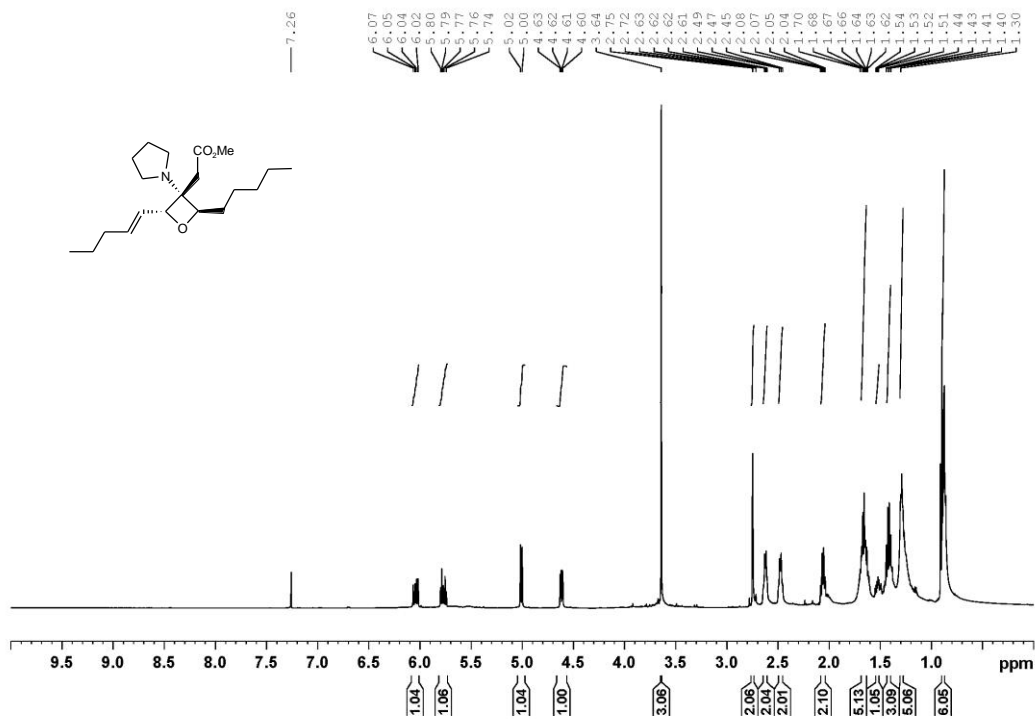
NOESY Spectrum of 12g in C₆D₆



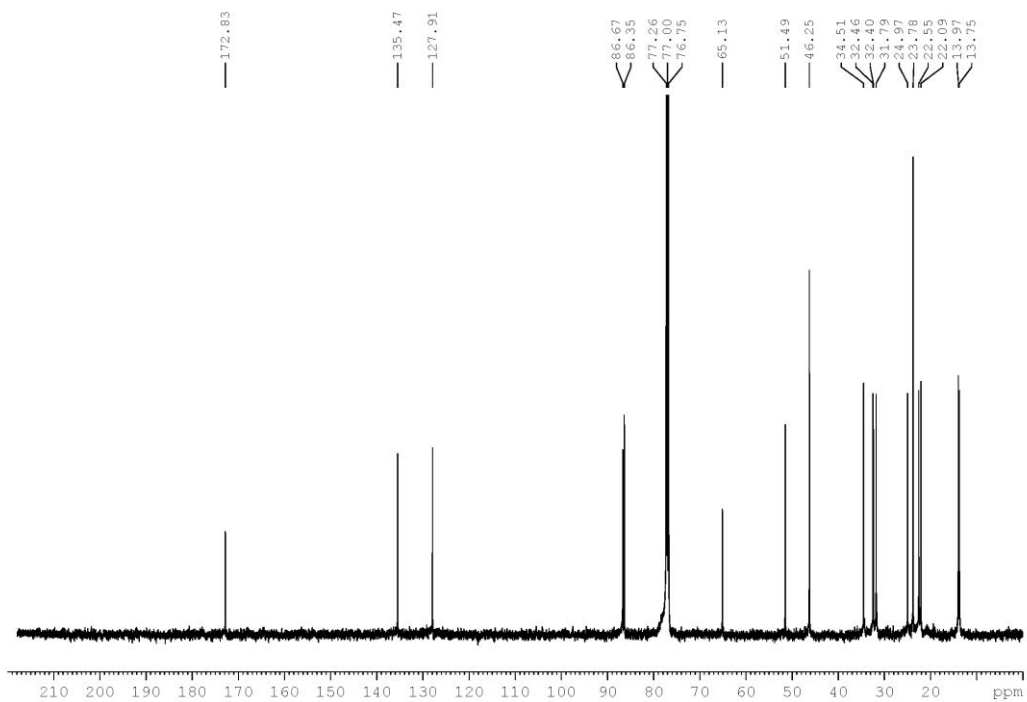
HSQC Spectrum of 12g in C₆D₆



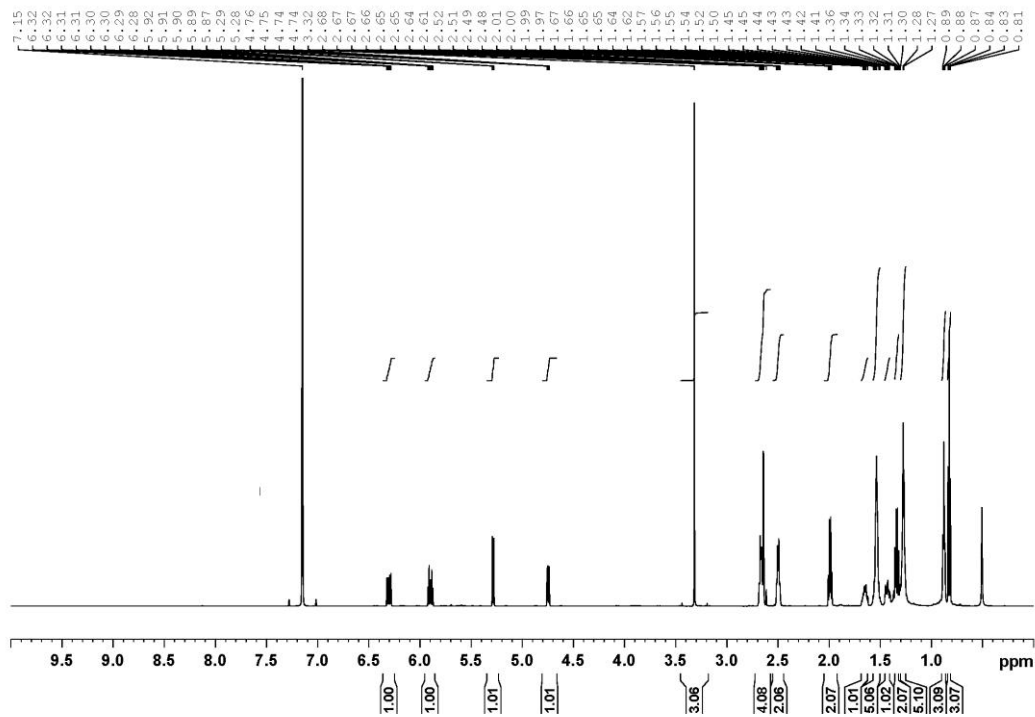
^1H NMR Spectrum of **12h** in CDCl_3



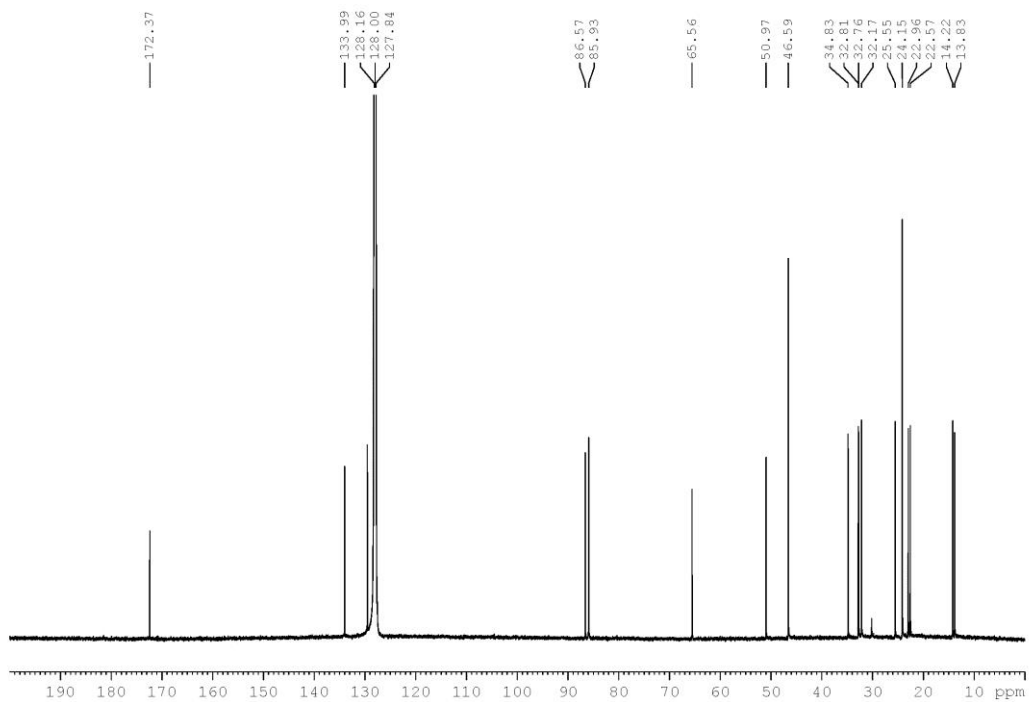
^{13}C NMR Spectrum of **12h** in CDCl_3



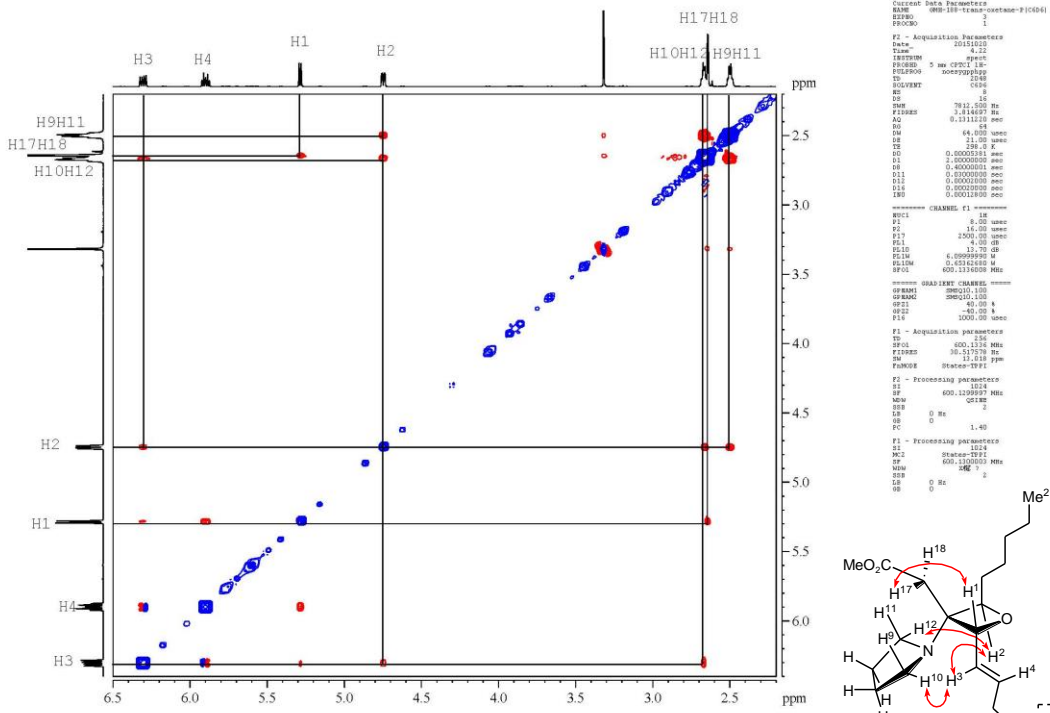
^1H NMR Spectrum of **12h** in C_6D_6



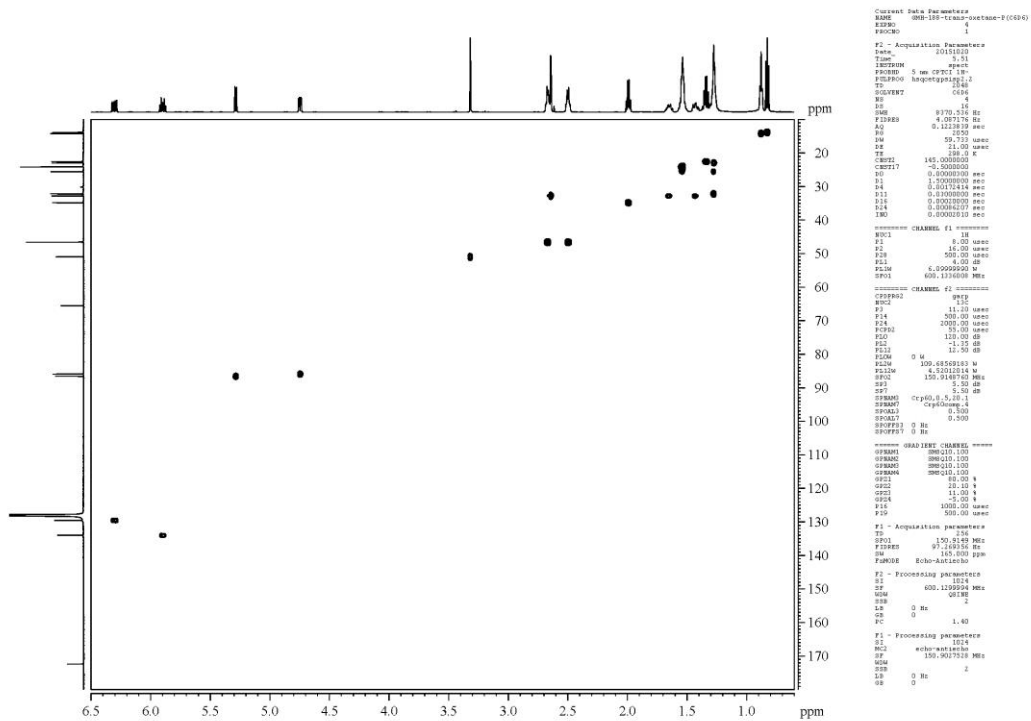
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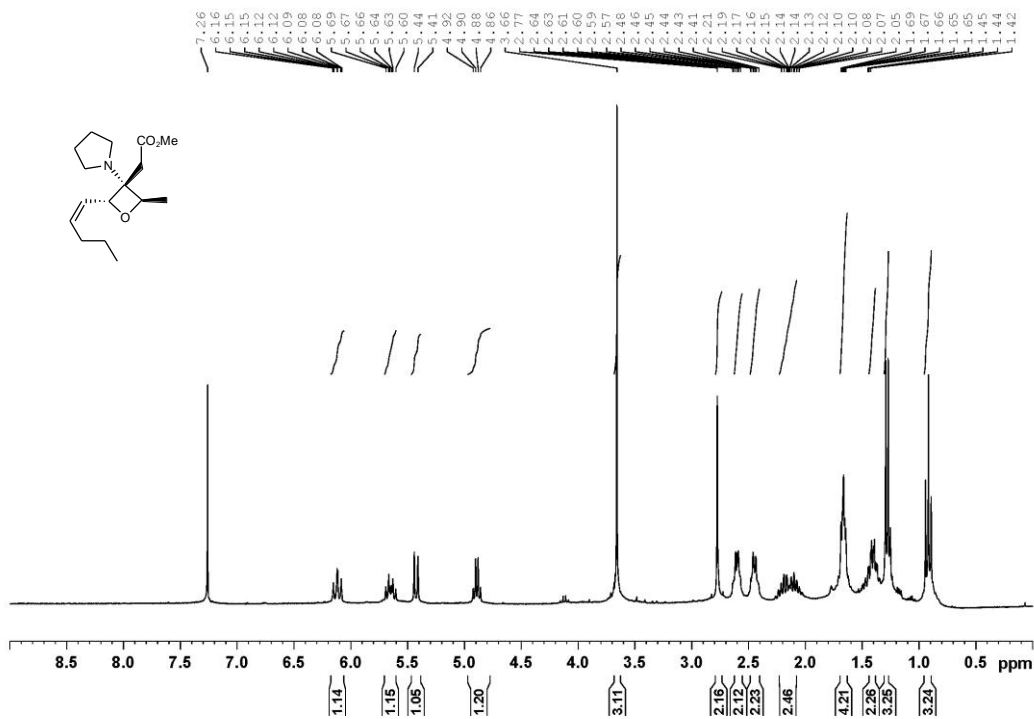
NOESY Spectrum of 12h in C₆D₆



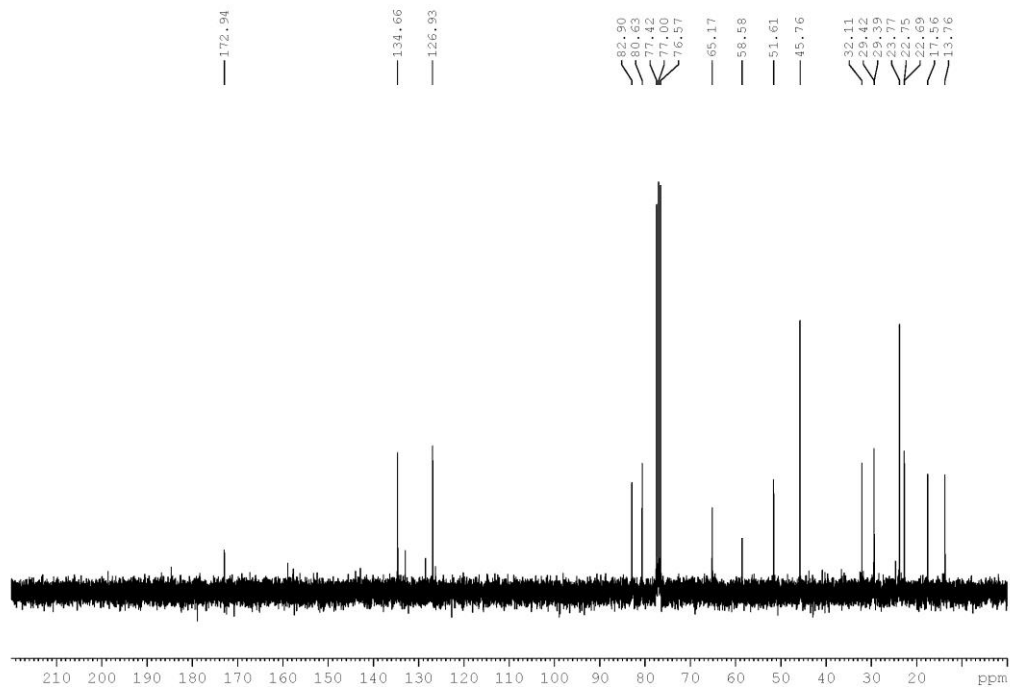
HSQC Spectrum of 12h in C₆D₆



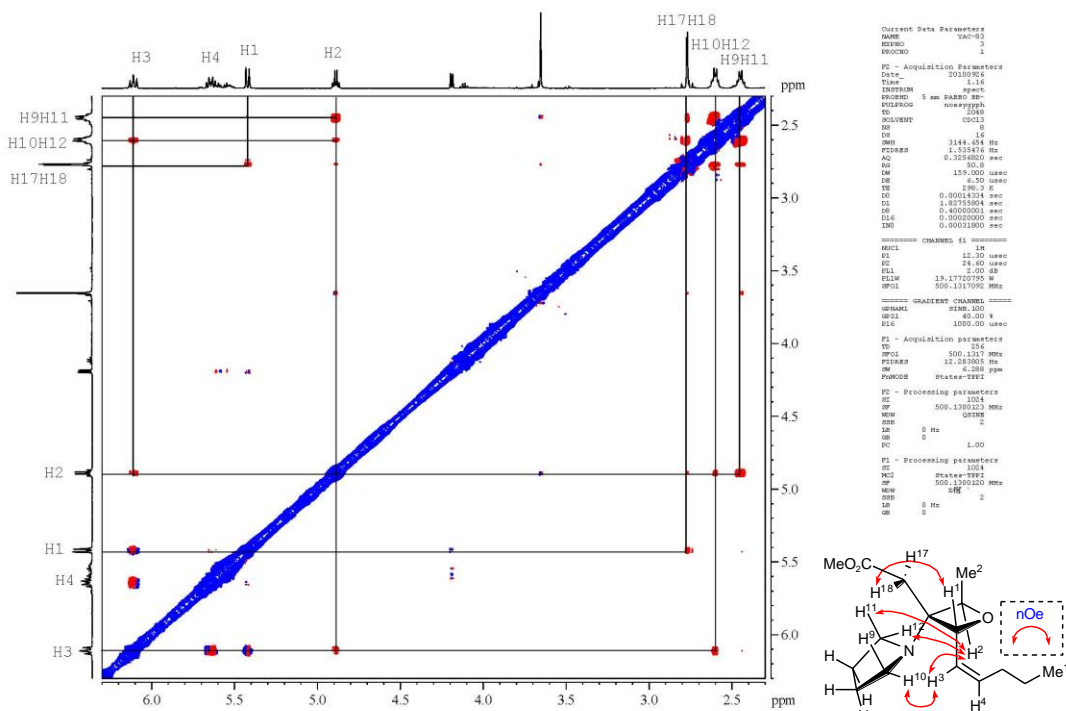
¹H NMR Spectrum of **12i** in CDCl₃



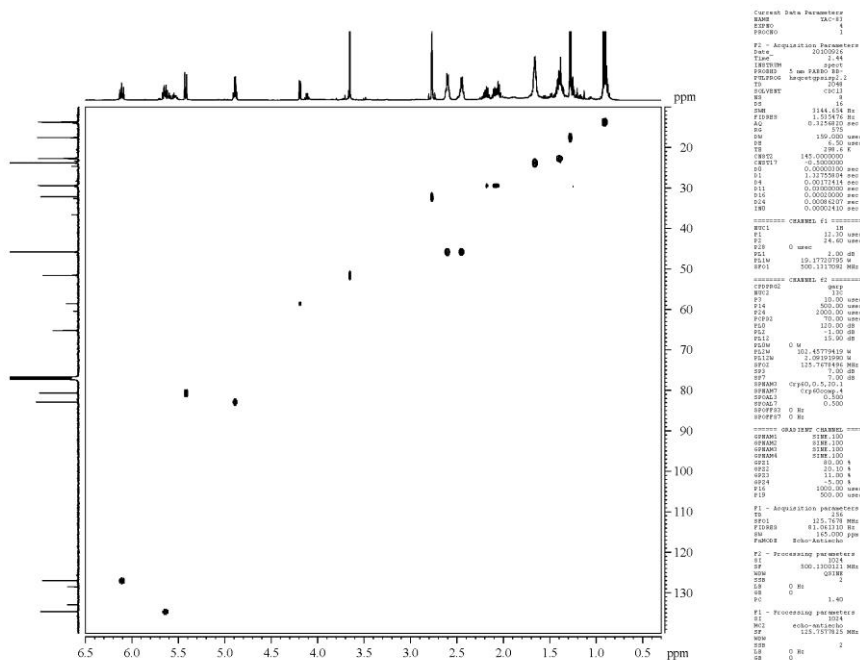
¹³C NMR Spectrum of **12i** in CDCl₃



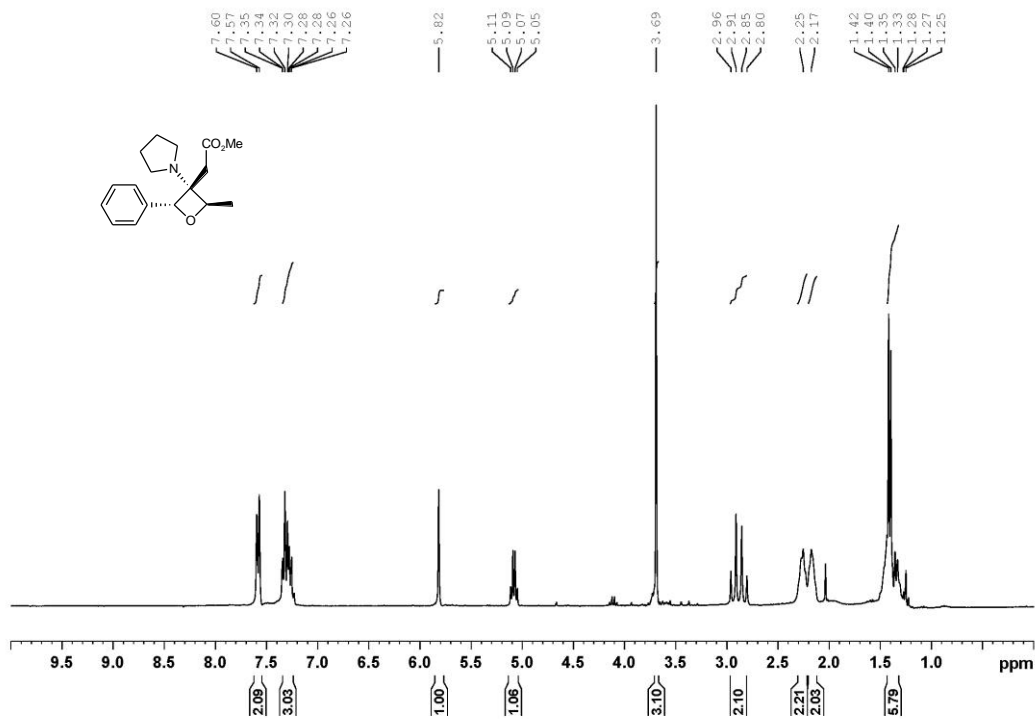
NOESY Spectrum of **12i** in CDCl₃



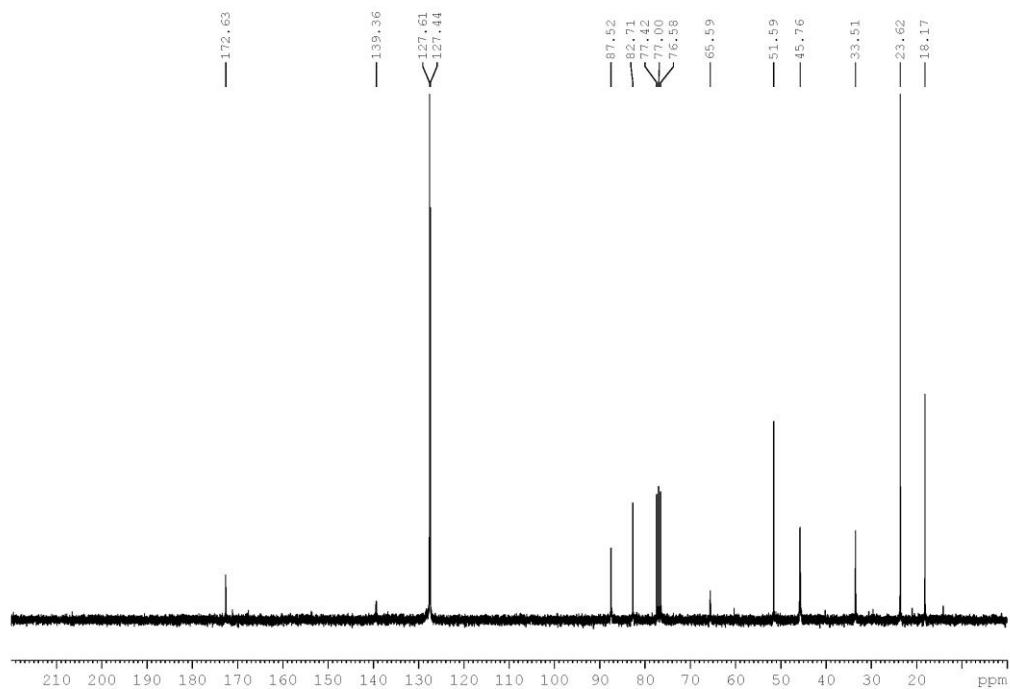
HSQC Spectrum of **12i** in CDCl₃



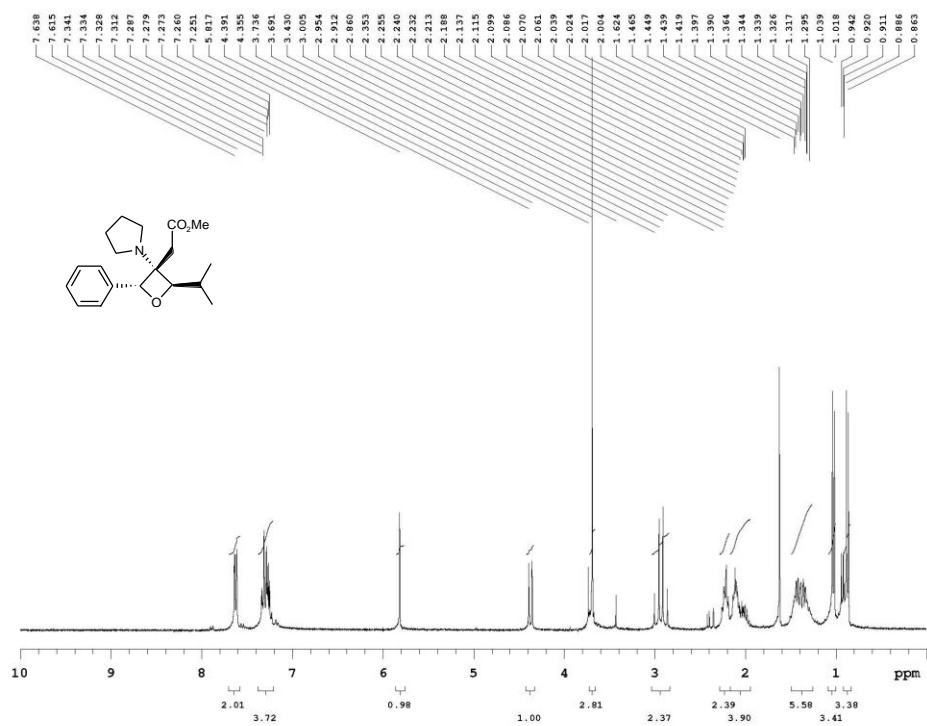
¹H NMR Spectrum of **12j** in CDCl₃



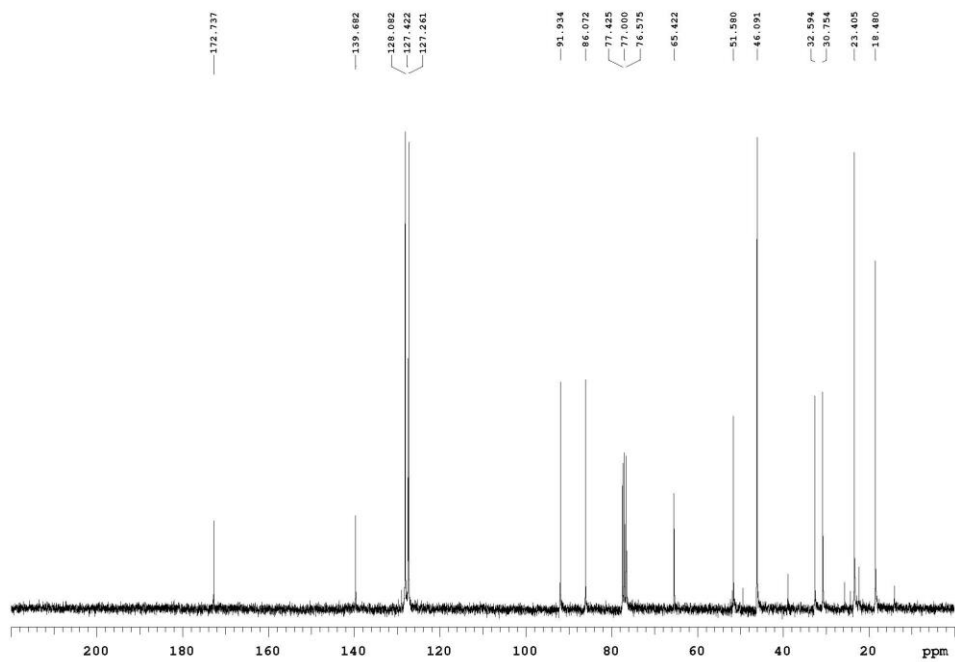
¹³C NMR Spectrum of **12j** in CDCl₃



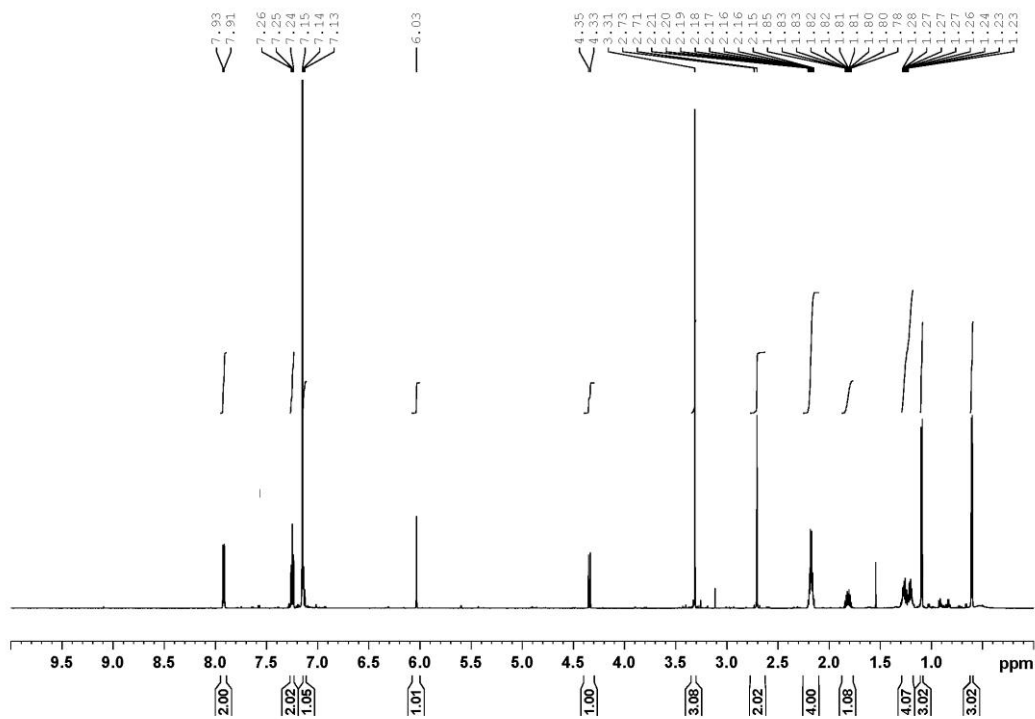
^1H NMR Spectrum of **12k** in CDCl_3



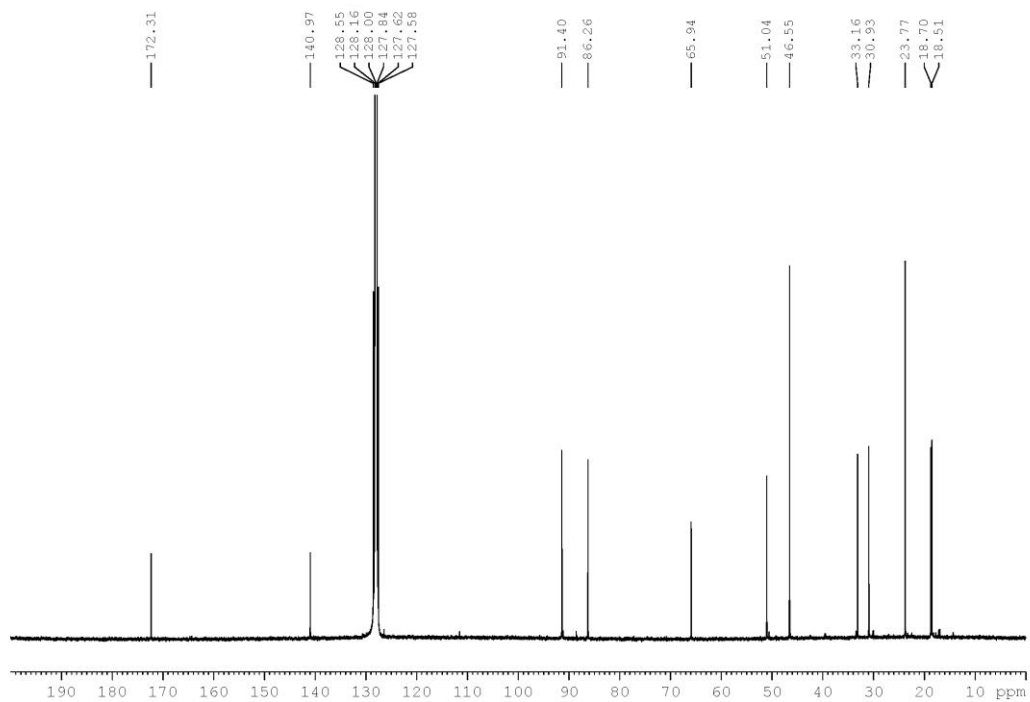
^{13}C NMR Spectrum of **12k** in CDCl_3



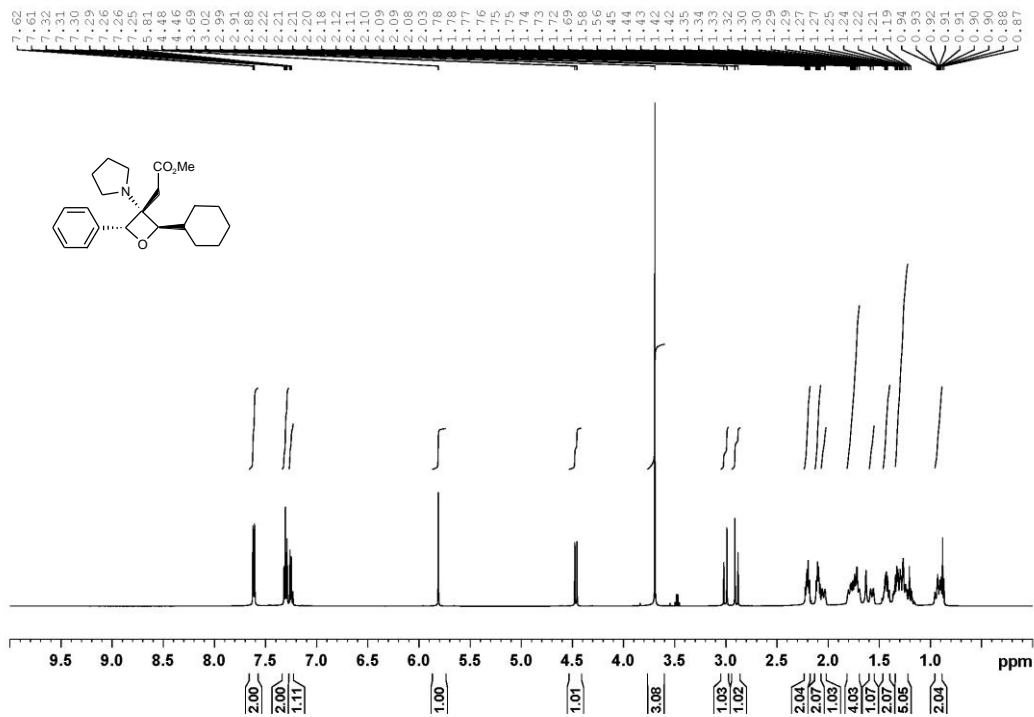
^1H NMR Spectrum of **12k** in C_6D_6



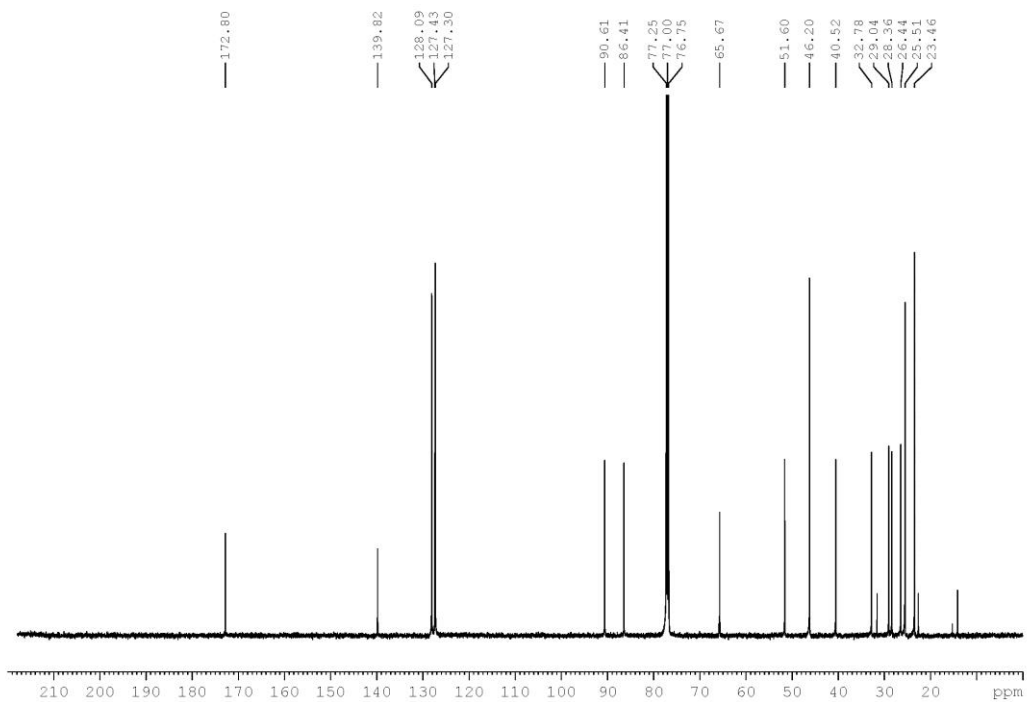
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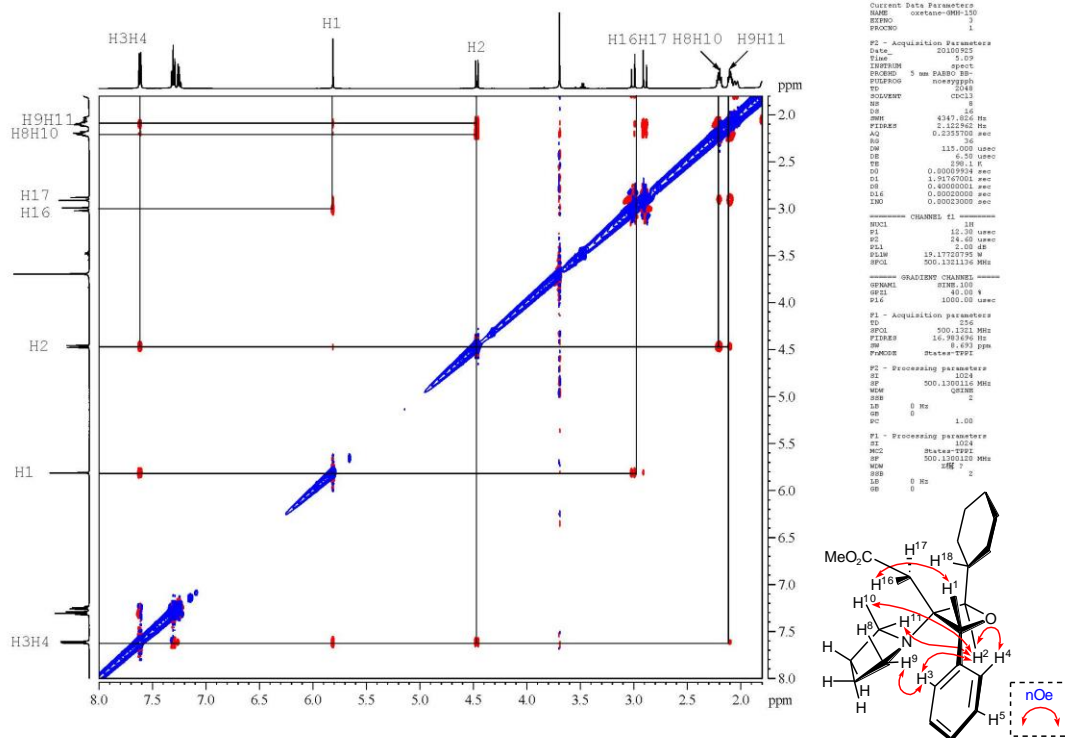
¹H NMR Spectrum of **12l** in CDCl₃



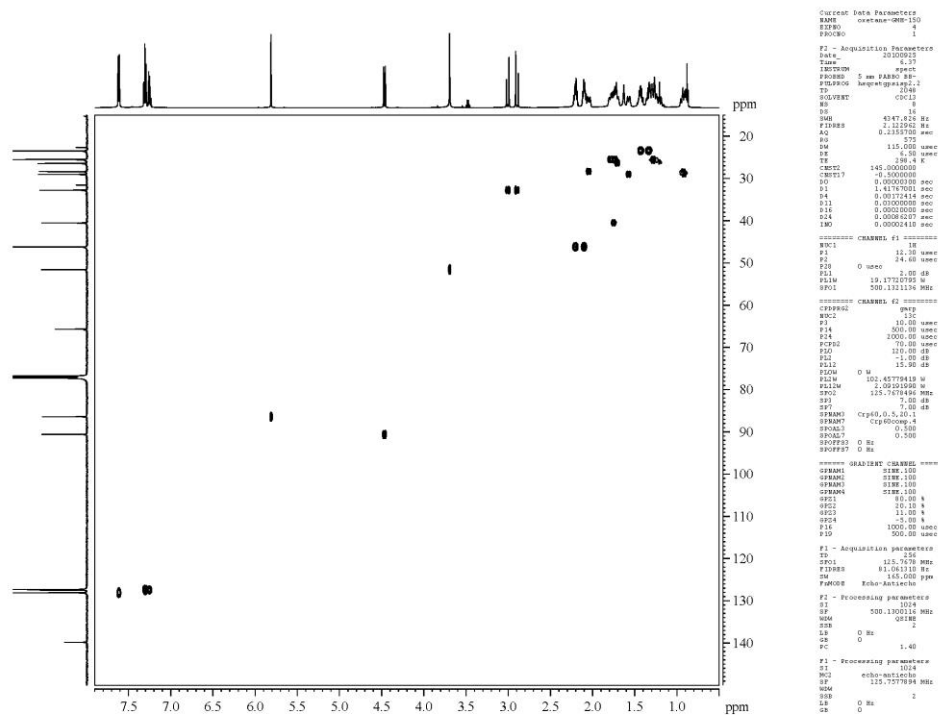
¹³C NMR Spectrum of **12l** in CDCl₃



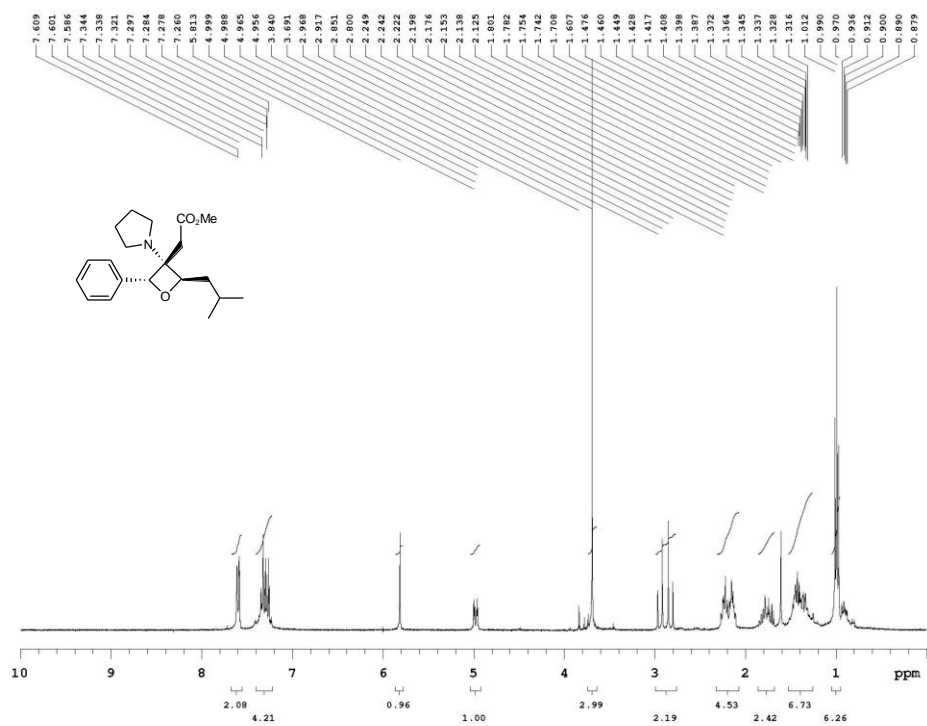
NOESY Spectrum of **12l** in CDCl₃



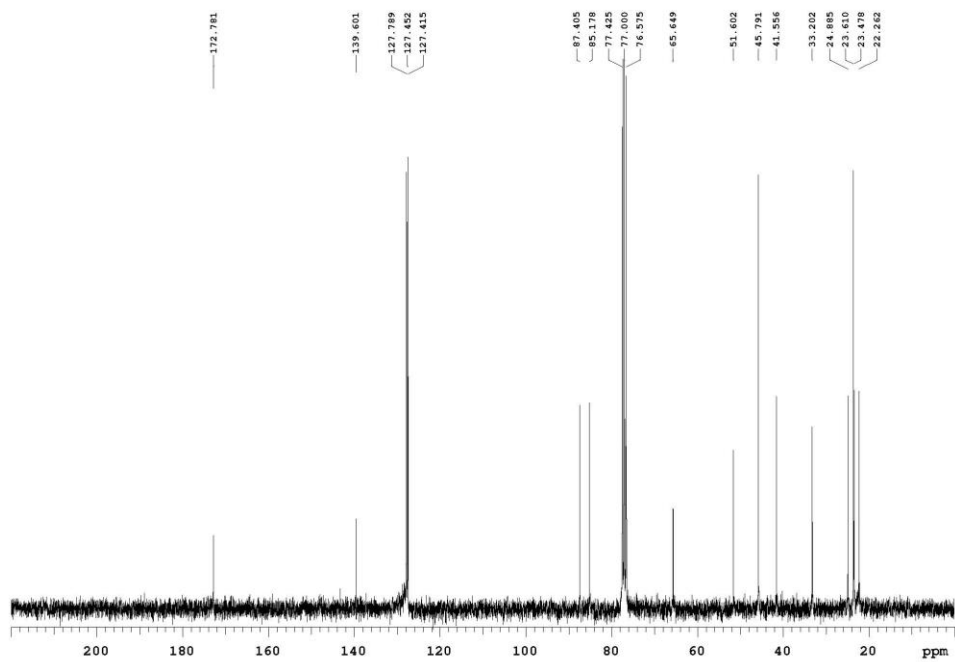
HSQC Spectrum of **12l** in CDCl₃



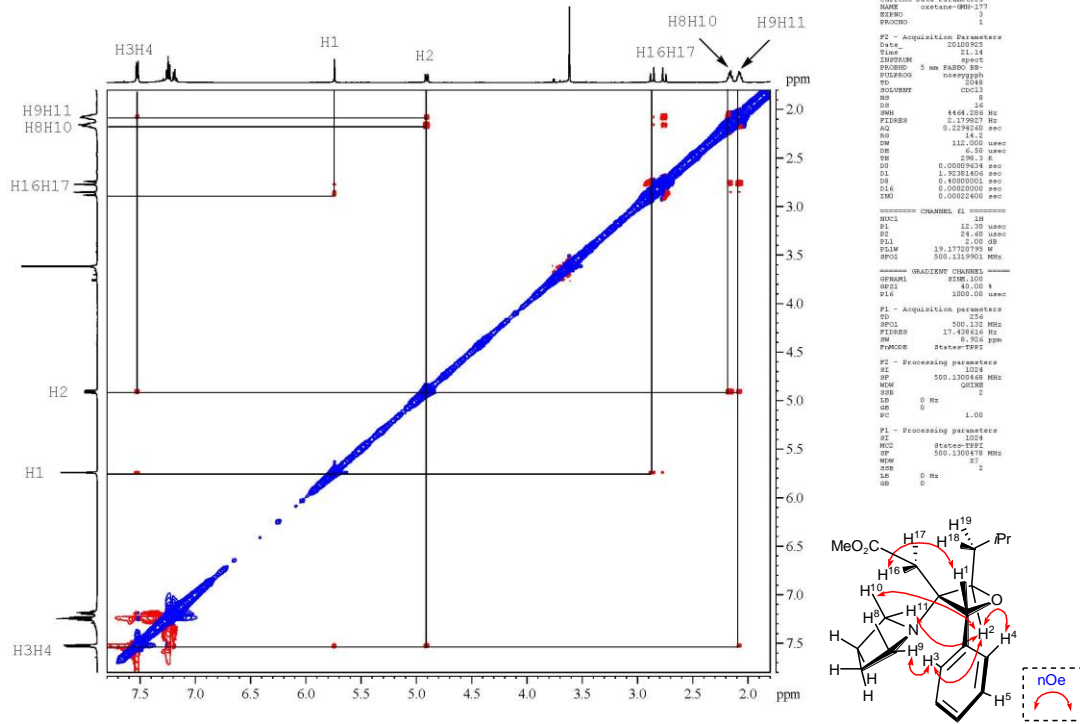
¹H NMR Spectrum of **12m** in CDCl₃



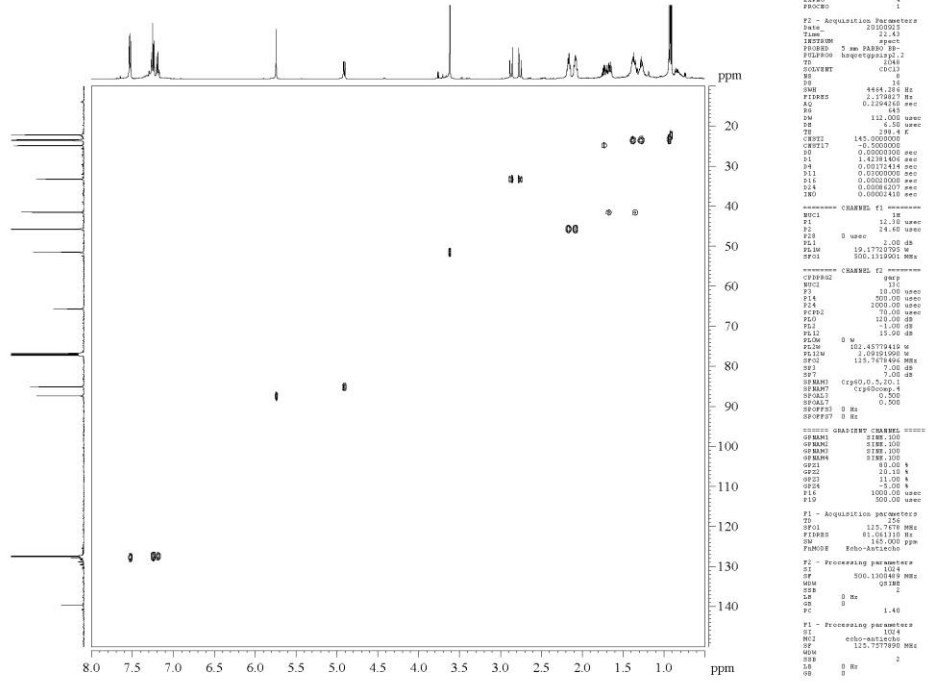
¹³C NMR Spectrum of **12m** in CDCl₃



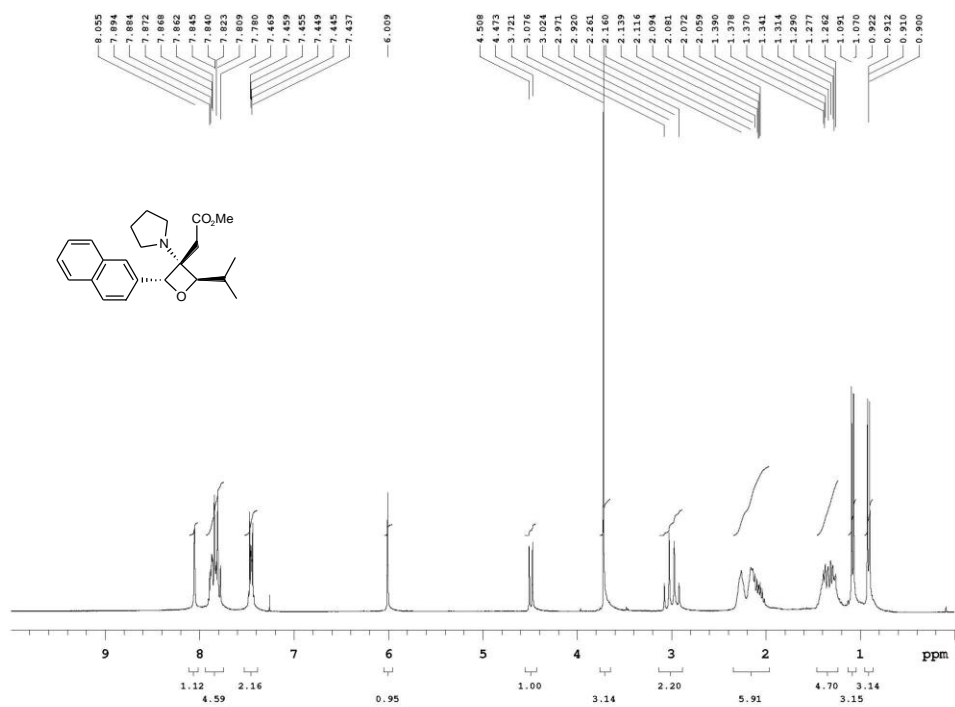
NOESY Spectrum of 12m in CDCl₃



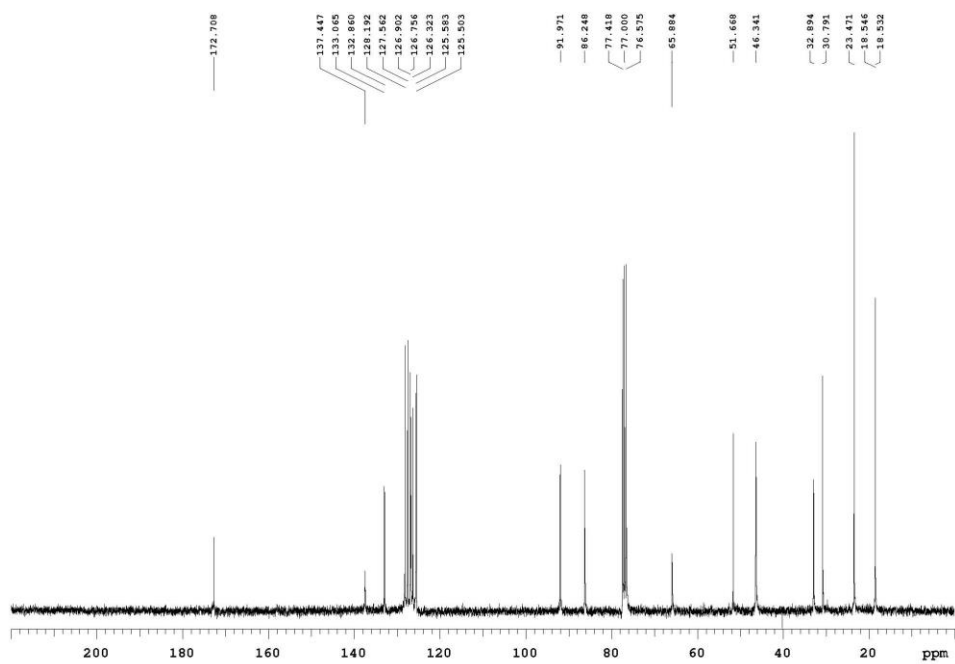
HSQC Spectrum of 12m in CDCl₃



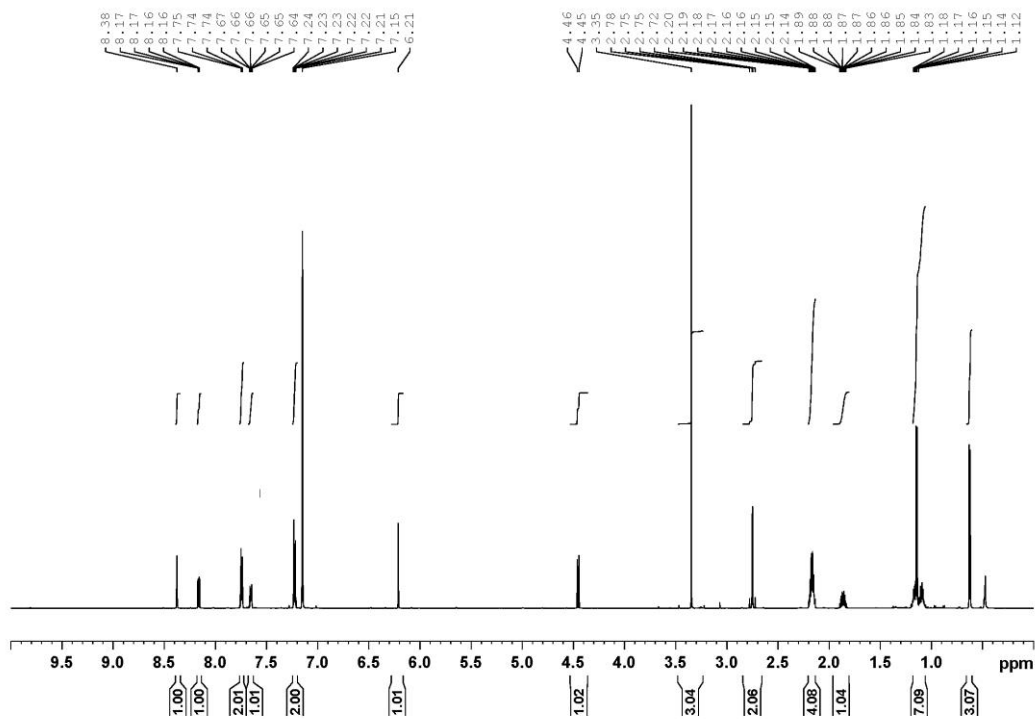
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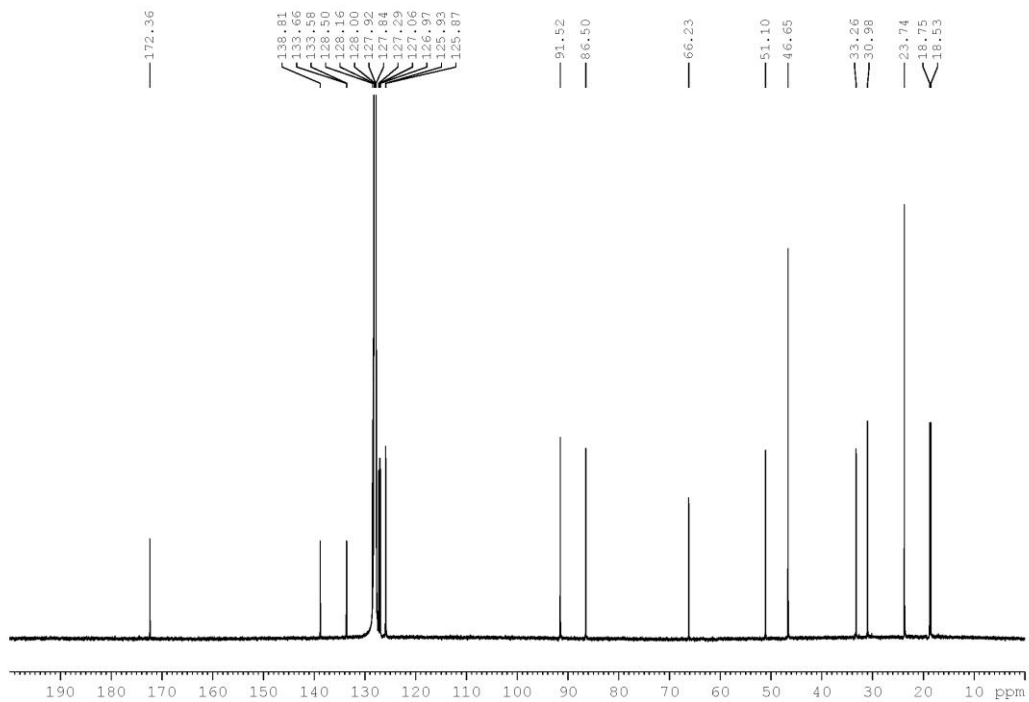
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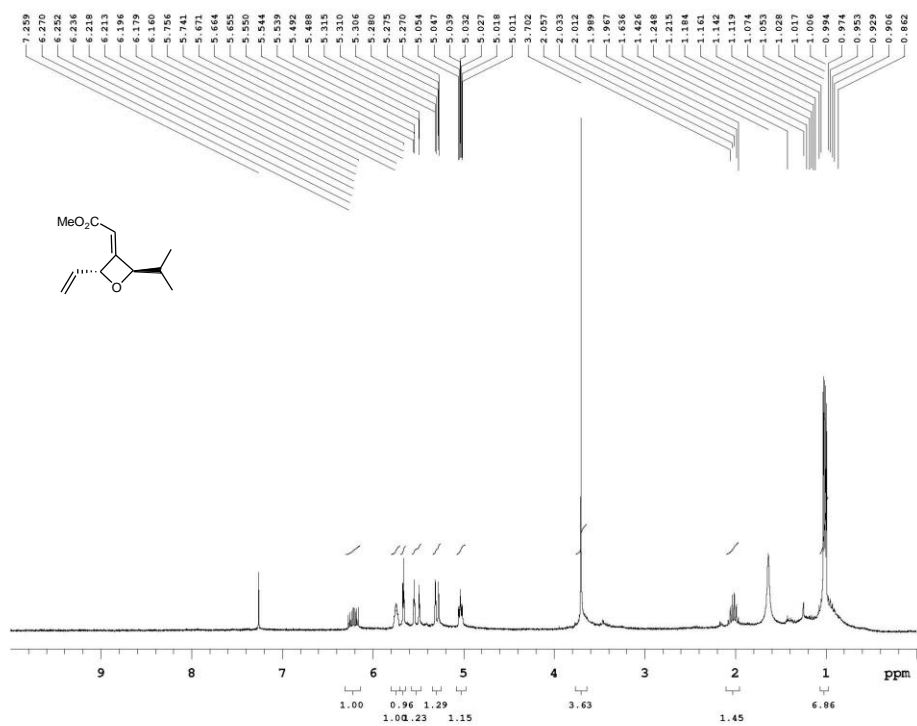
^1H NMR Spectrum of **12n** in C_6D_6



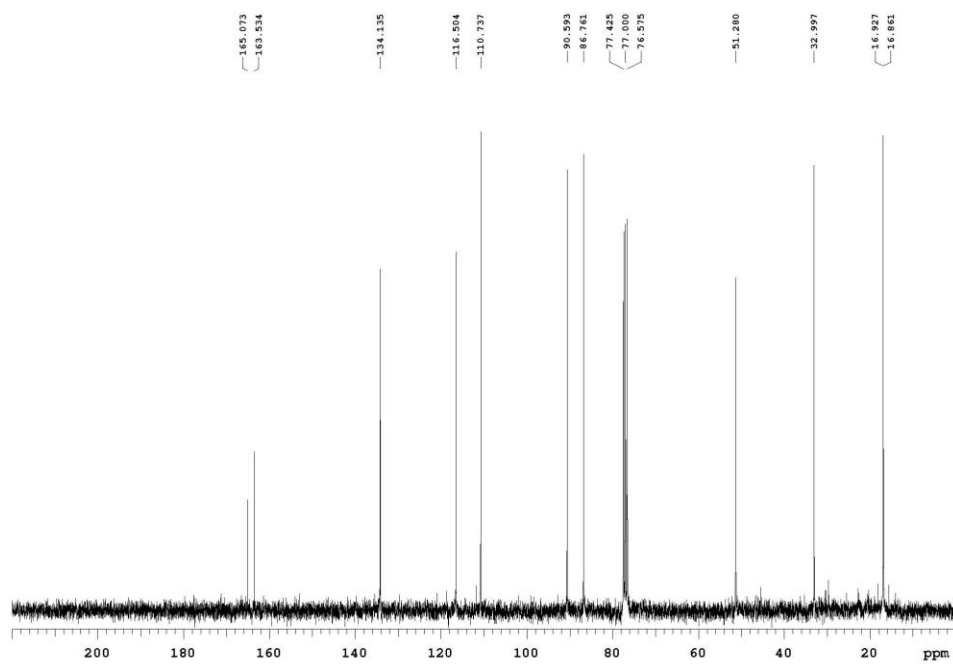
^{13}C NMR Spectrum of **12n** in C_6D_6



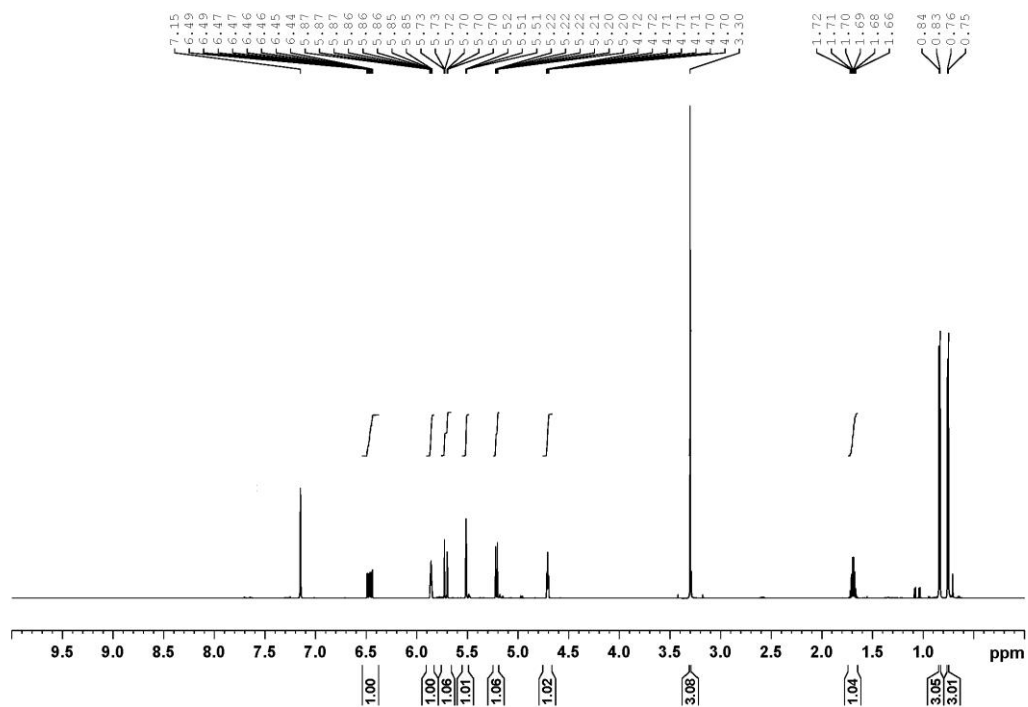
^1H NMR Spectrum of **Z-13a** in CDCl_3



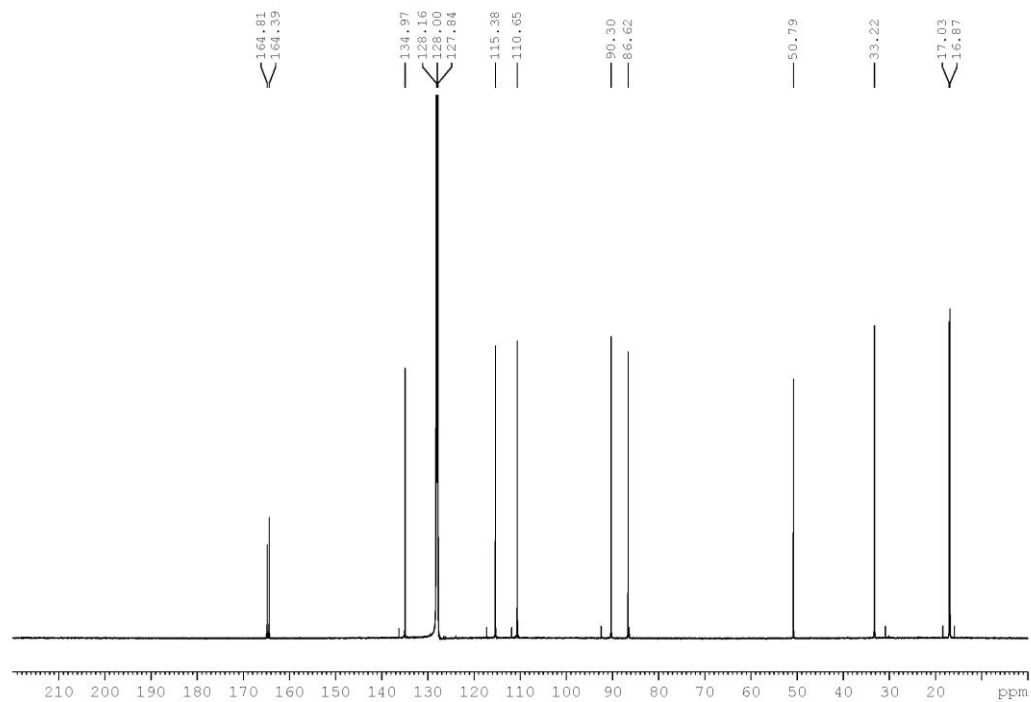
^{13}C NMR Spectrum of **Z-13a** in CDCl_3



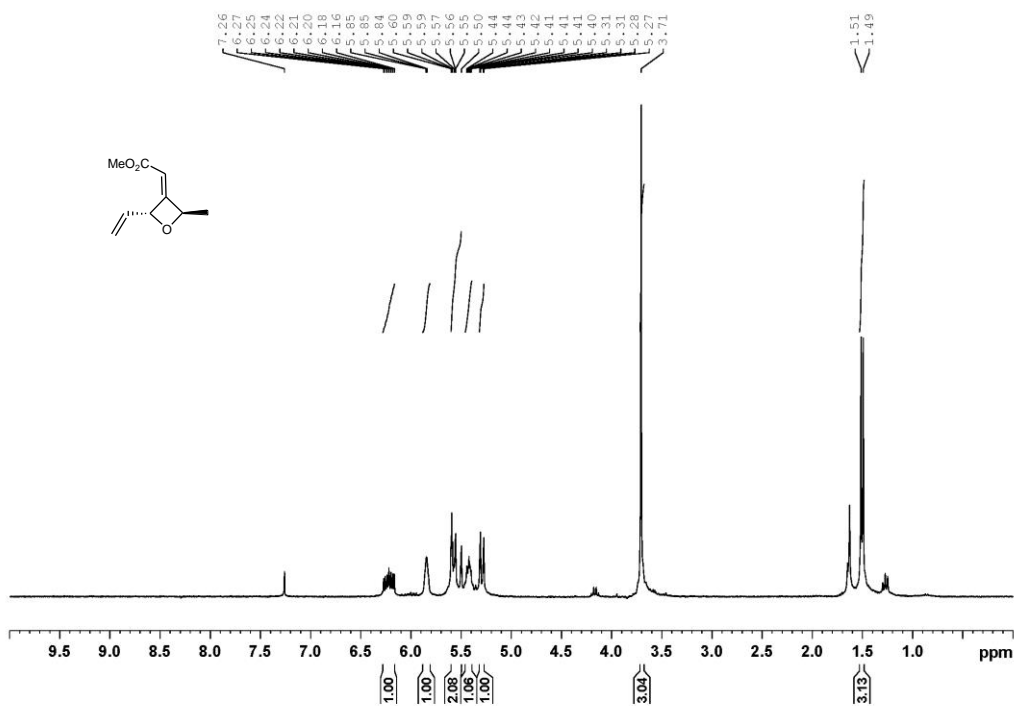
^1H NMR Spectrum of **Z-13a** in C_6D_6



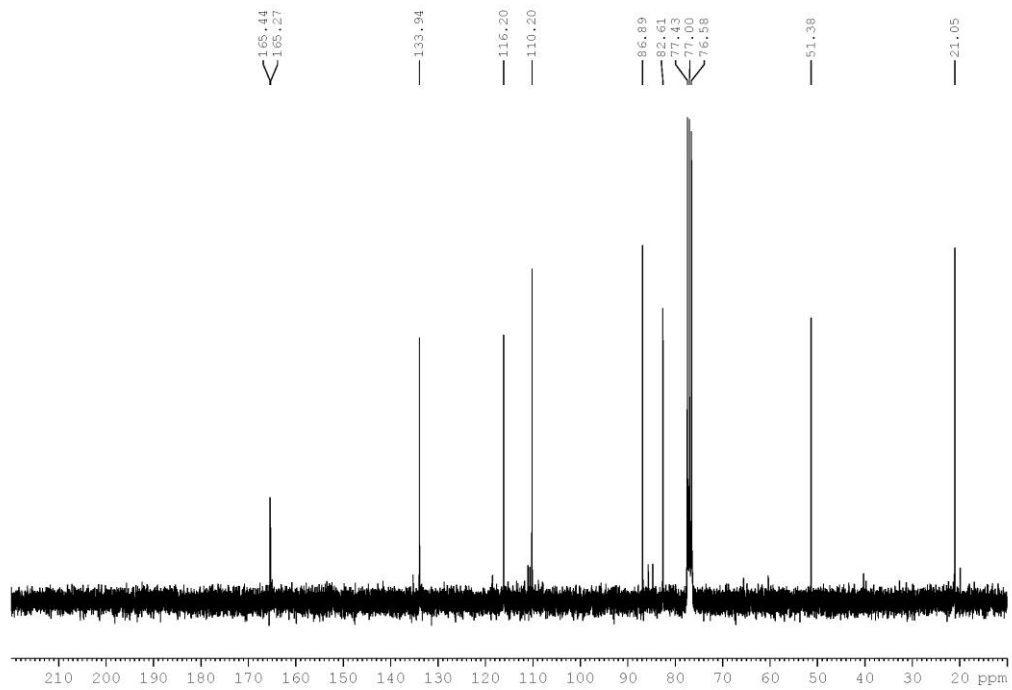
^{13}C NMR Spectrum of **Z-13a** in C_6D_6



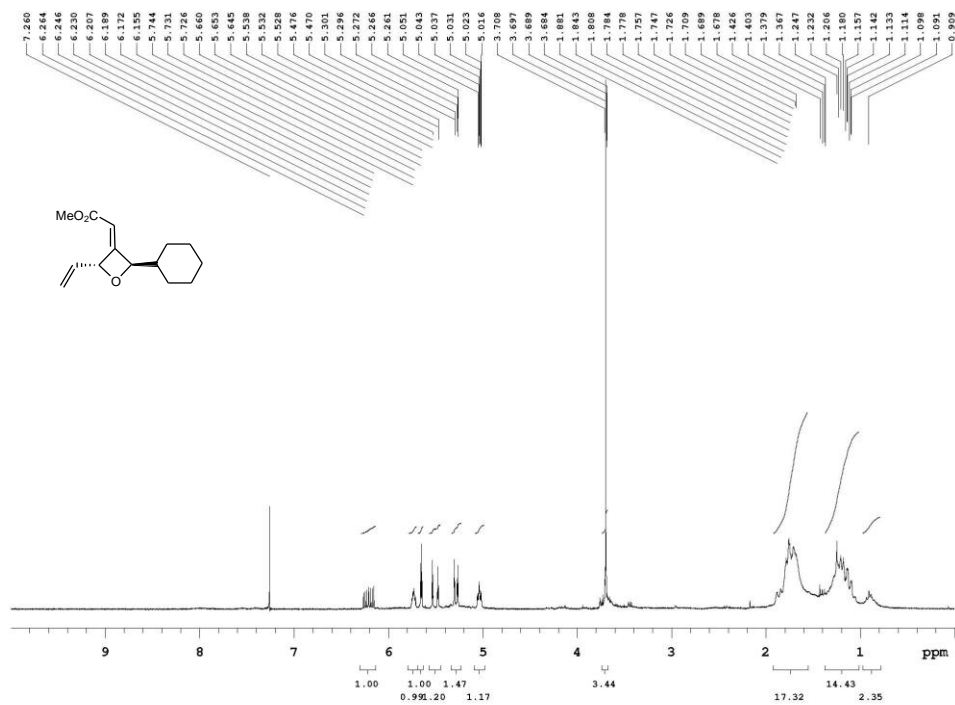
¹H NMR Spectrum of **Z-13b** in CDCl₃



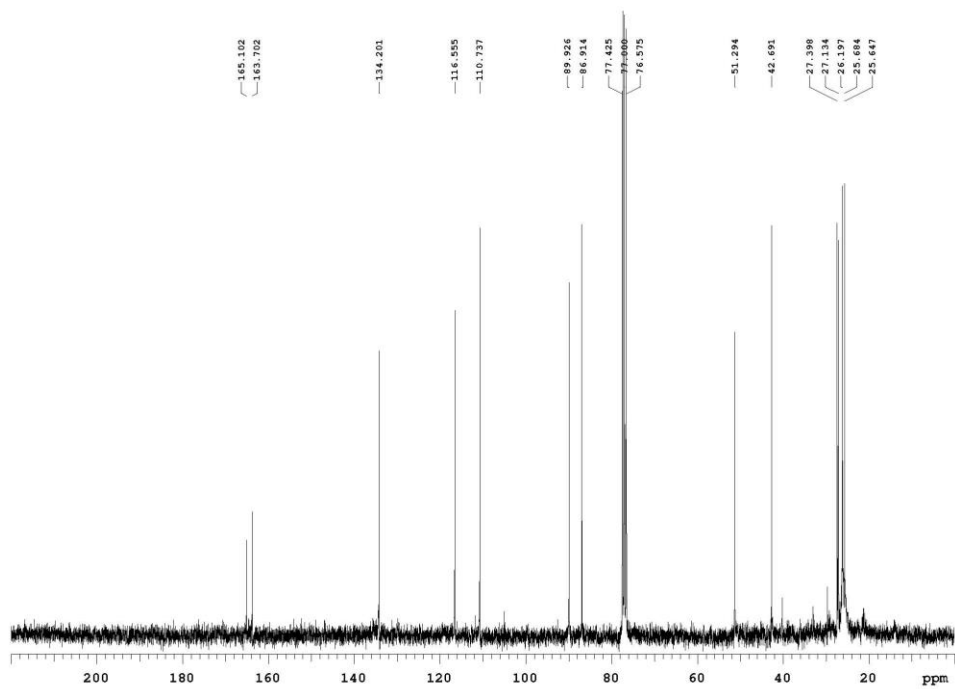
¹³C NMR Spectrum of **Z-13b** in CDCl₃



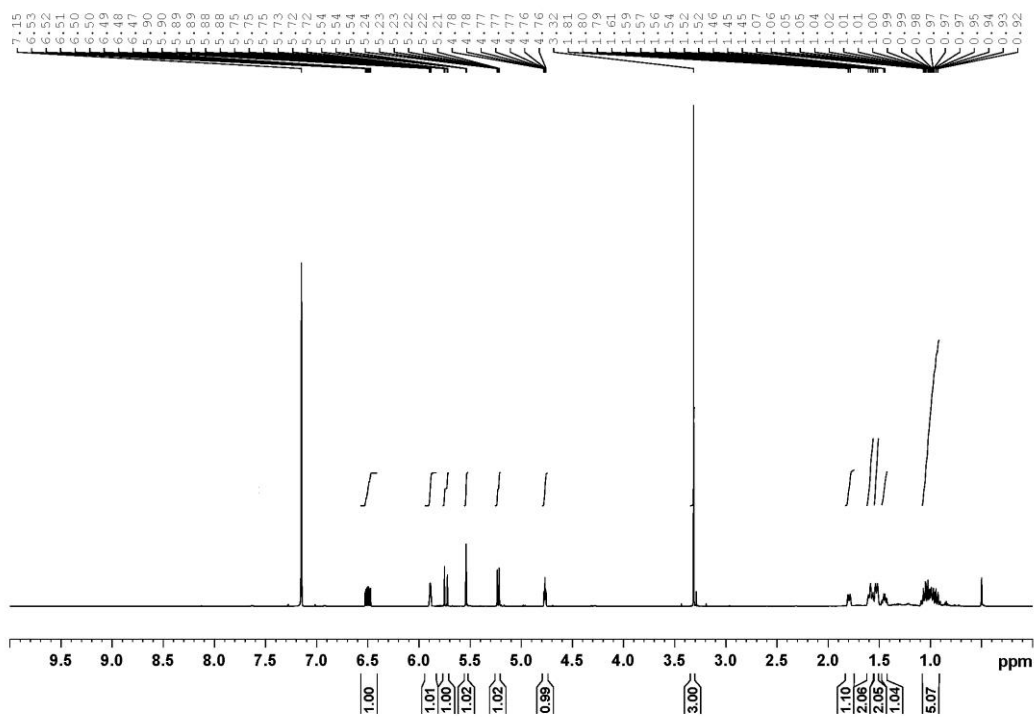
^1H NMR Spectrum of **Z-13c** in CDCl_3



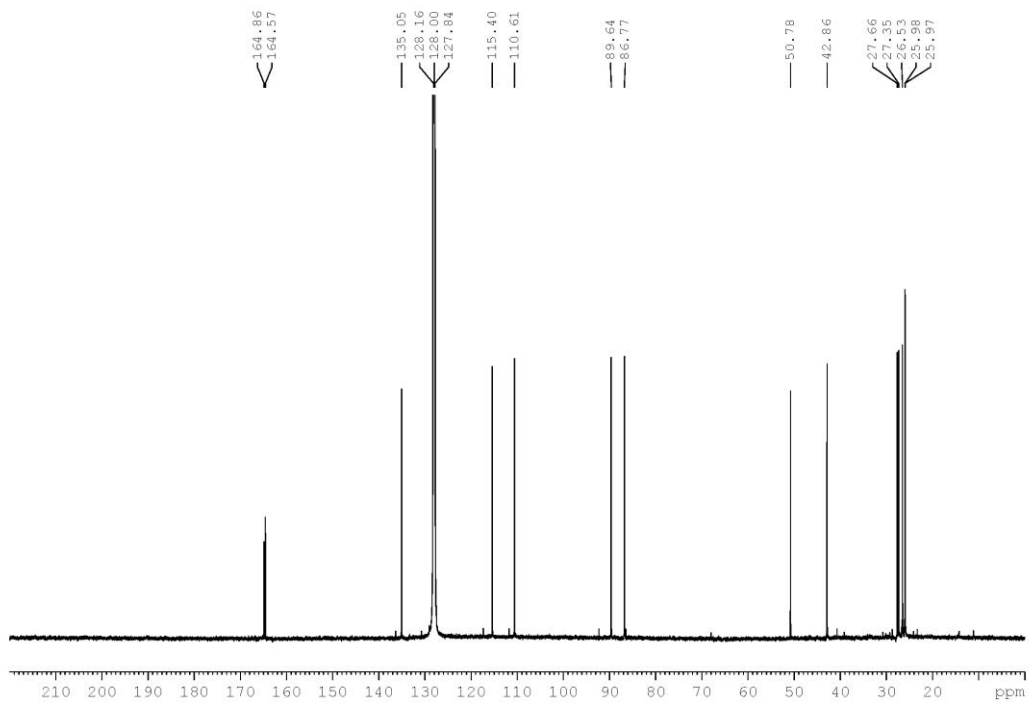
^{13}C NMR Spectrum of **Z-13c** in CDCl_3



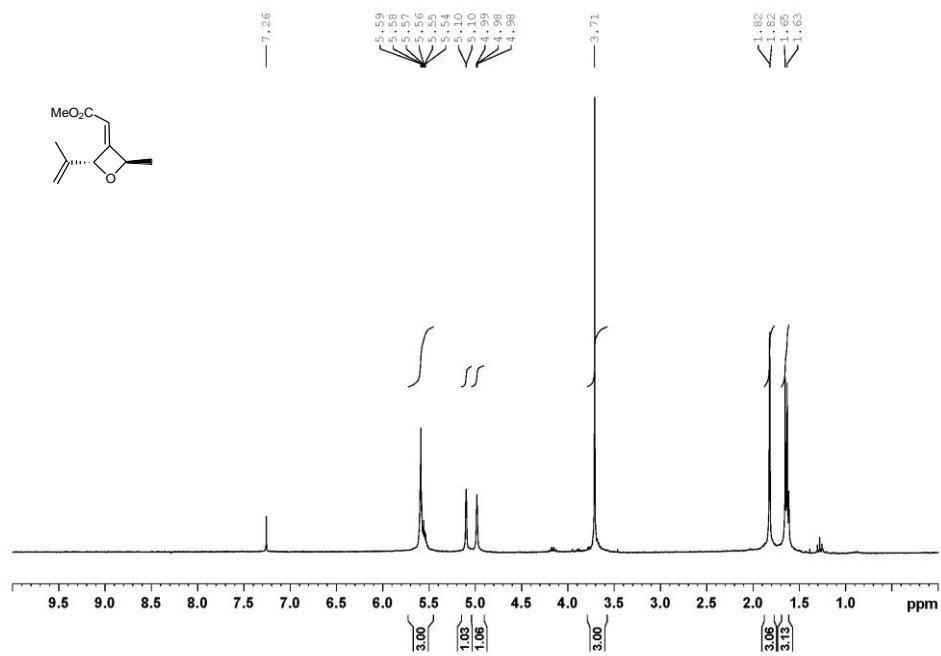
¹H NMR Spectrum of **Z-13c** in C₆D₆



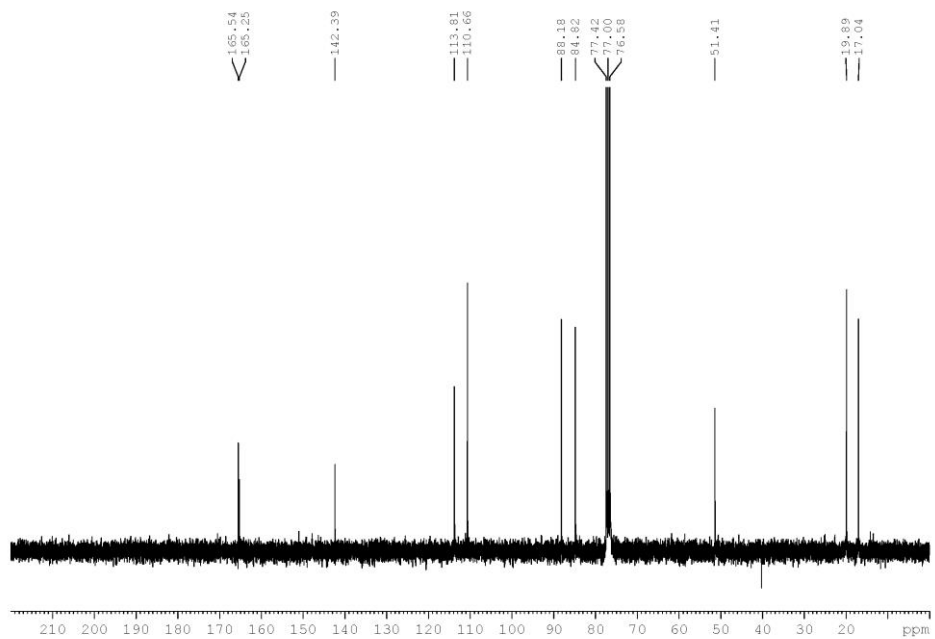
¹³C NMR Spectrum of **Z-13c** in C₆D₆



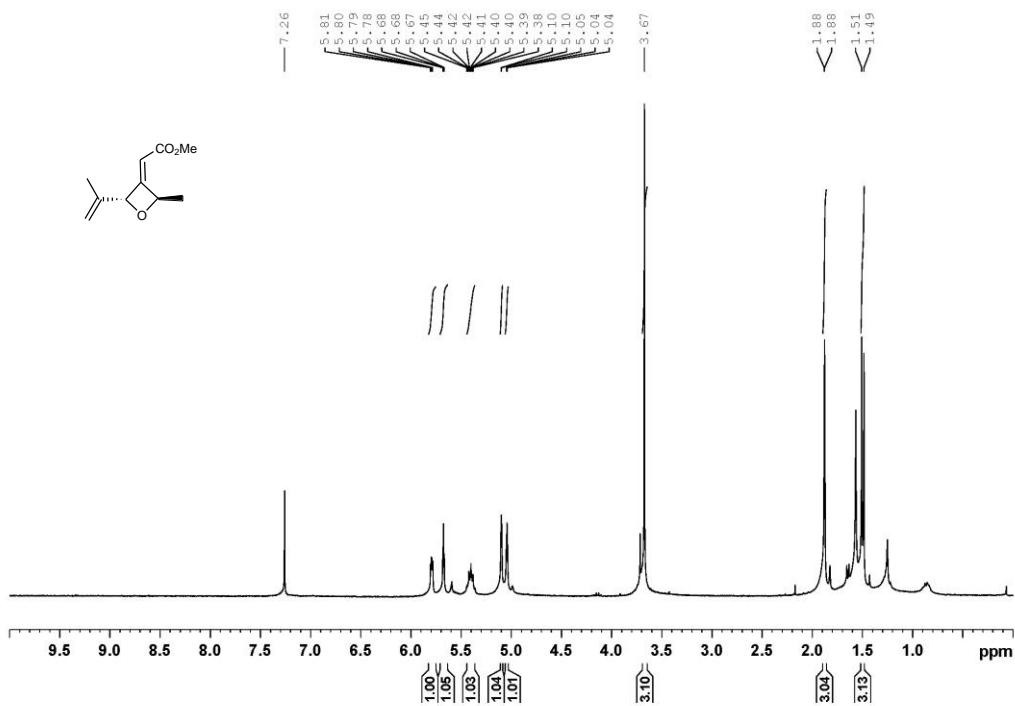
¹H NMR Spectrum of **Z-13e** in CDCl₃



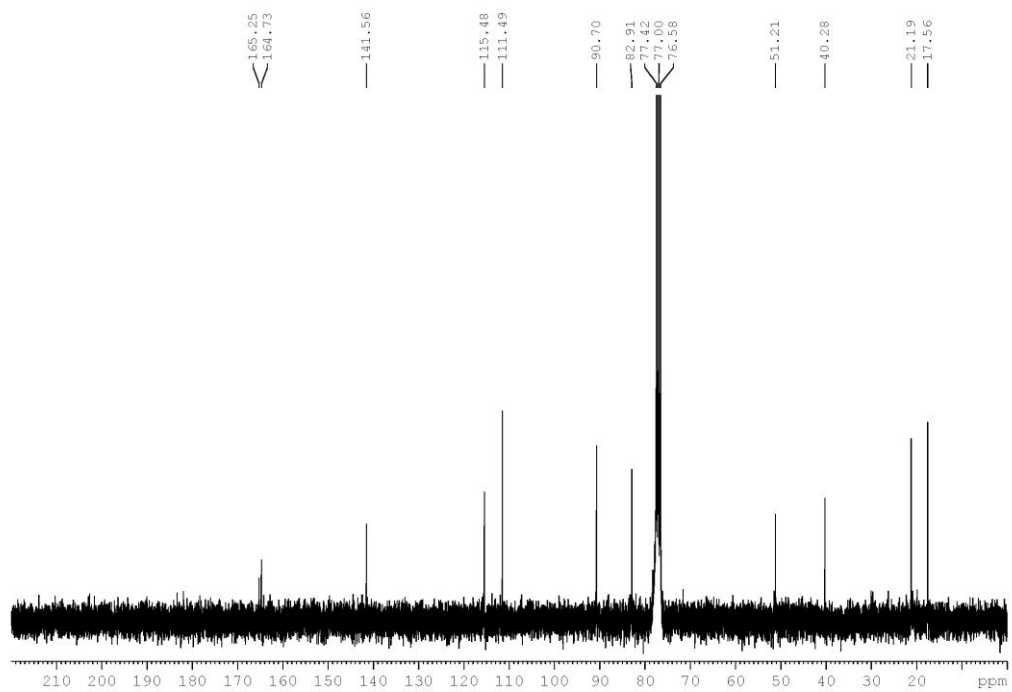
¹³C NMR Spectrum of **Z-13e** in CDCl₃



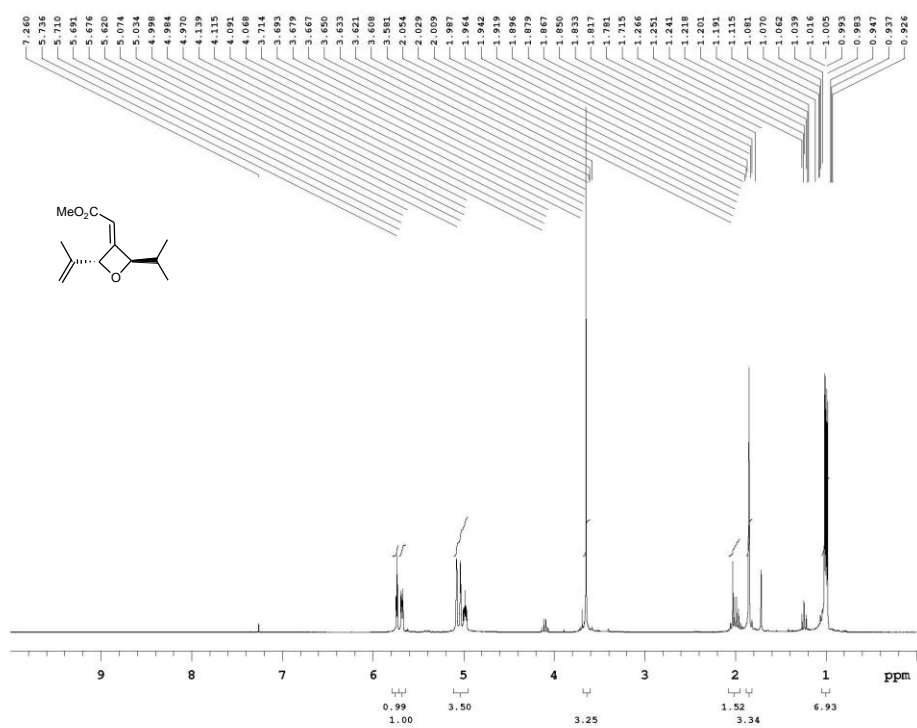
^1H NMR Spectrum of *E*-13e in CDCl_3



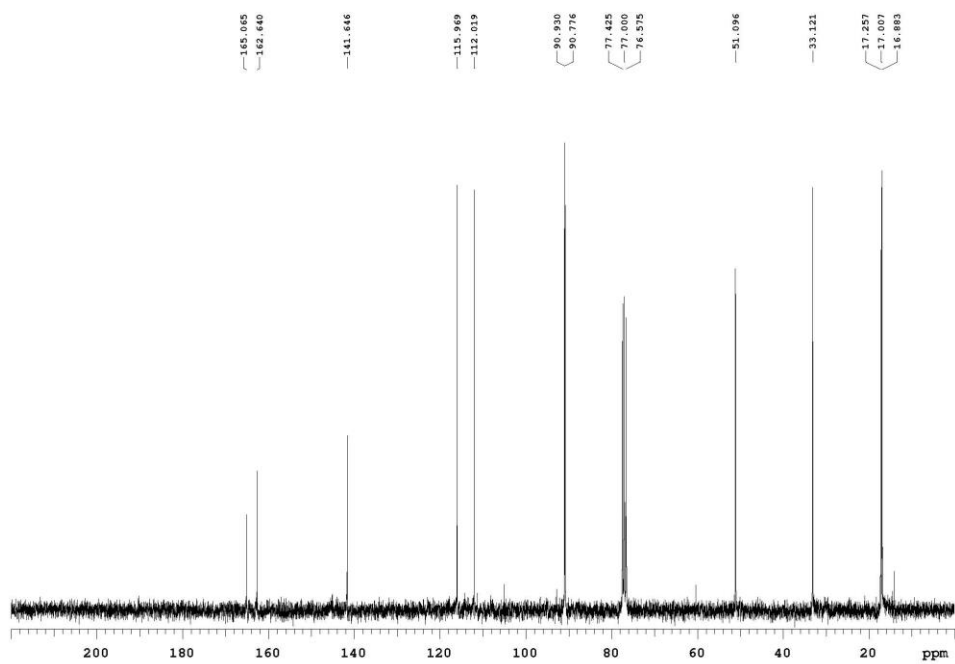
^{13}C NMR Spectrum of *E*-13e in CDCl_3



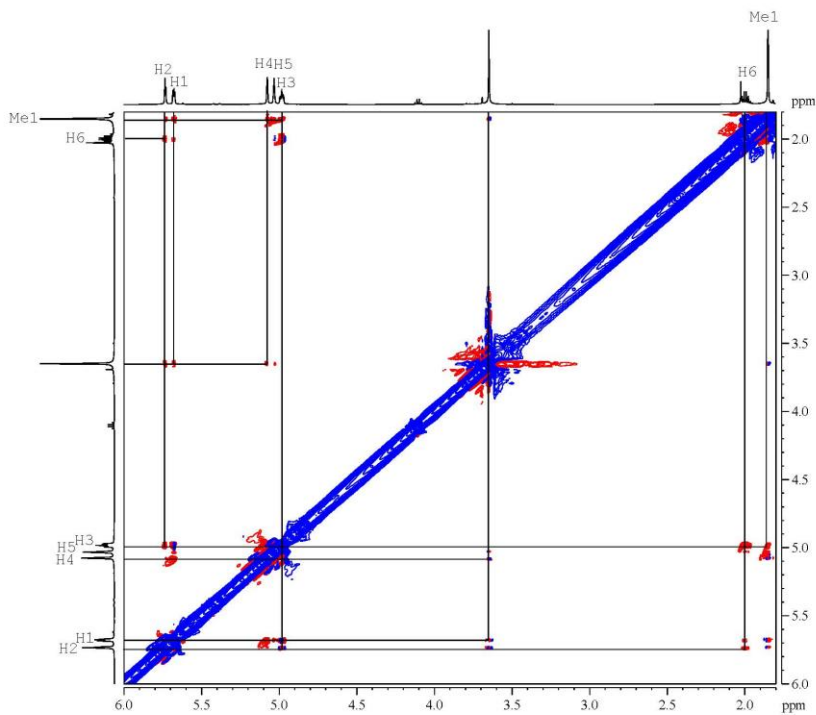
¹H NMR Spectrum of **Z-13f** in CDCl₃



¹³C NMR Spectrum of **Z-13f** in CDCl₃



NOESY Spectrum of Z-13f in CDCl₃



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PROCNO       1

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DS           4
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SQ          135.000 usec
DE          6.50 usec
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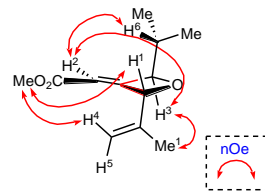
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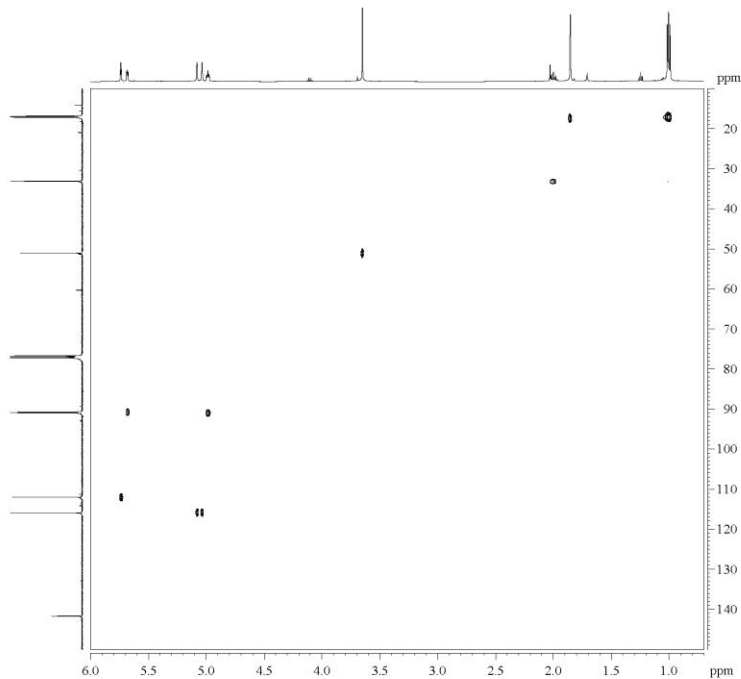
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HSQC Spectrum of Z-13f in CDCl₃



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d11         0.4000000 sec
d12         0.0000000 sec
IMB         0.0007000 sec

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PL           0.00 dB
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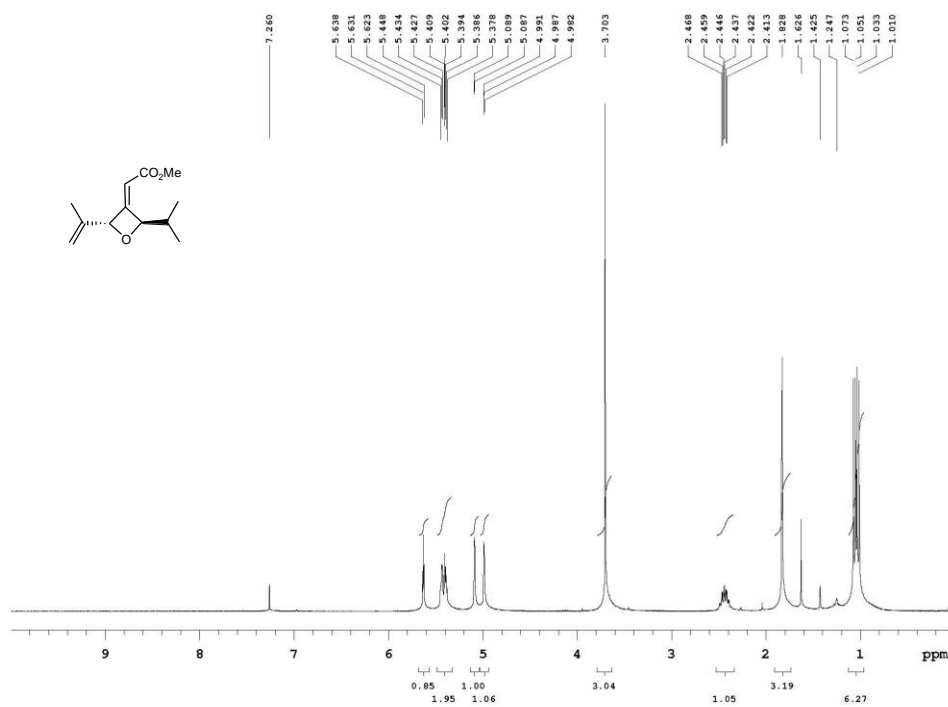
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P1B          1000.00 usec

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RG          655.000
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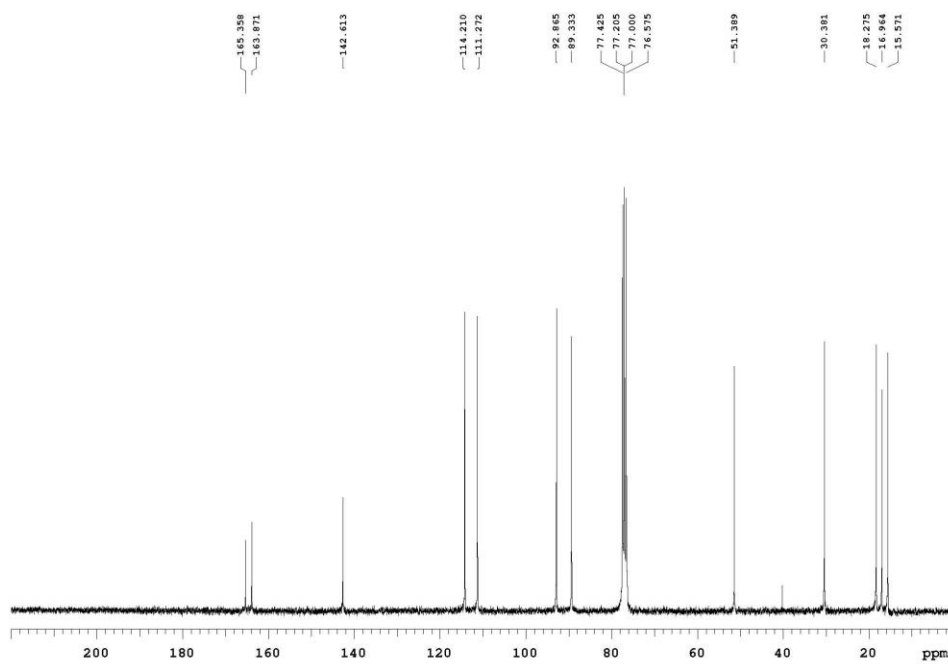
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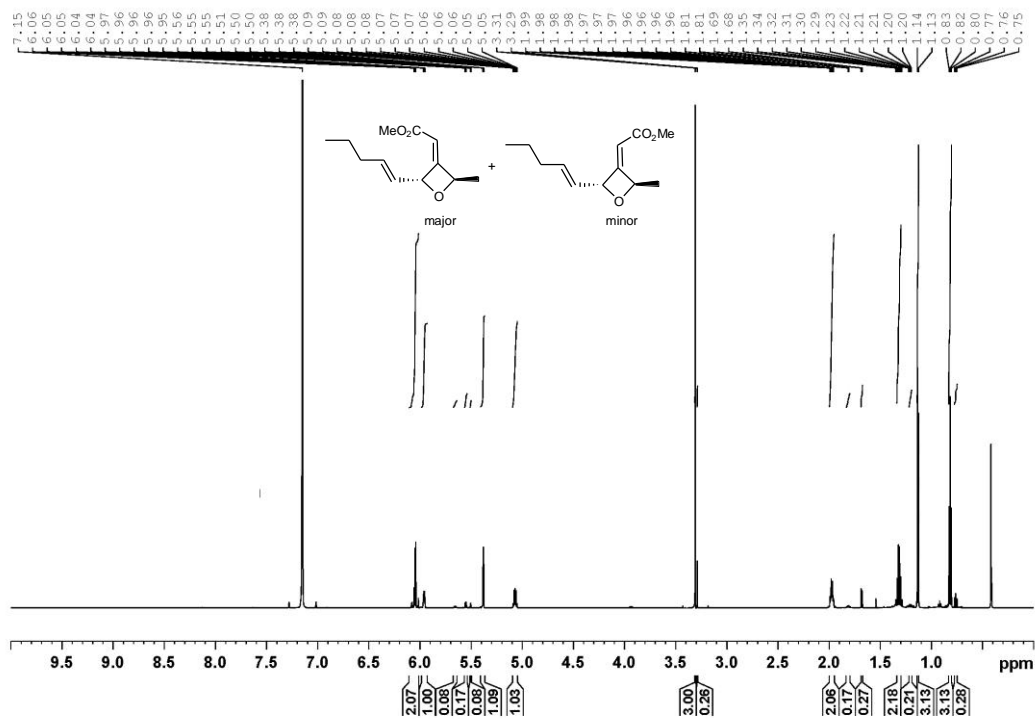
¹H NMR Spectrum of *E*-13f in CDCl₃



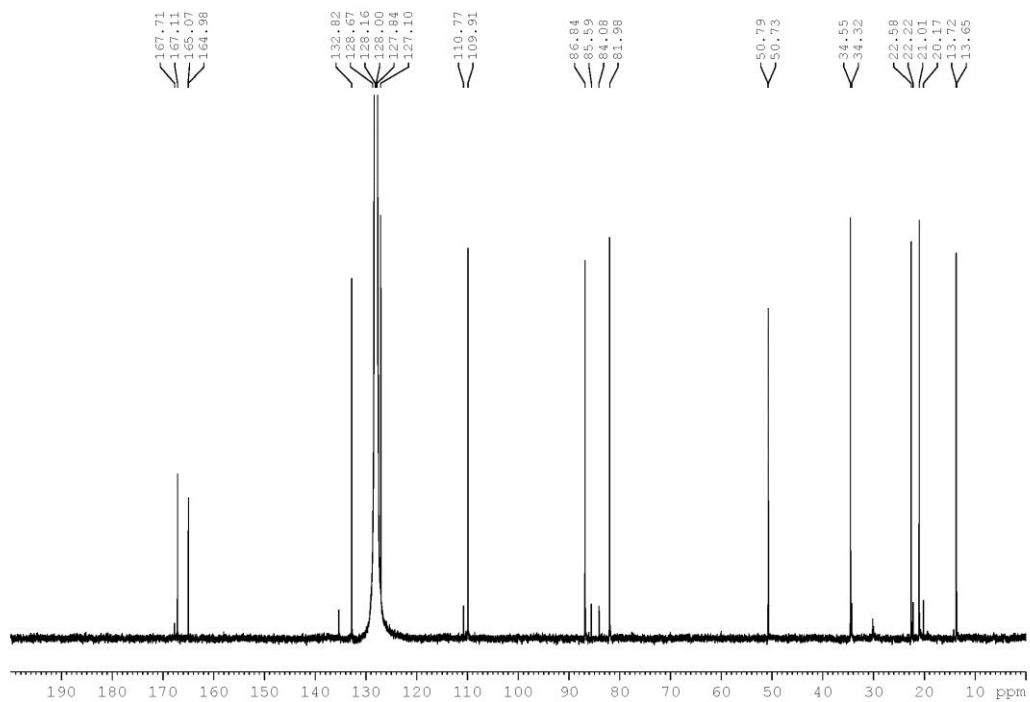
¹³C NMR Spectrum of *E*-13f in CDCl₃



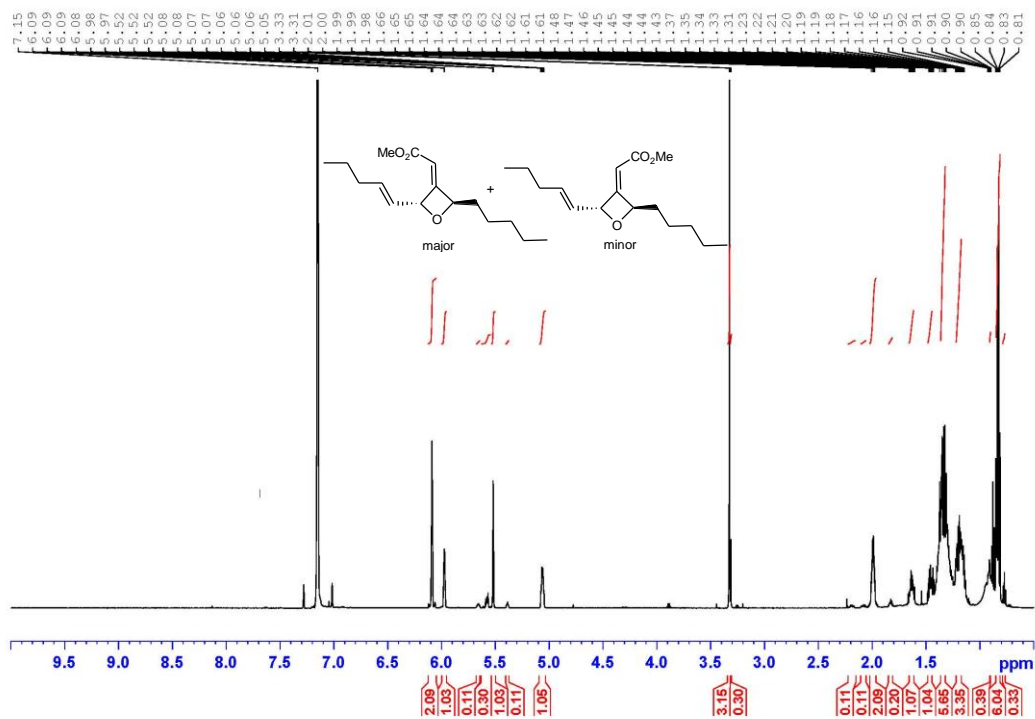
^1H NMR Spectra of *Z*-13g and *E*-13g in C_6D_6



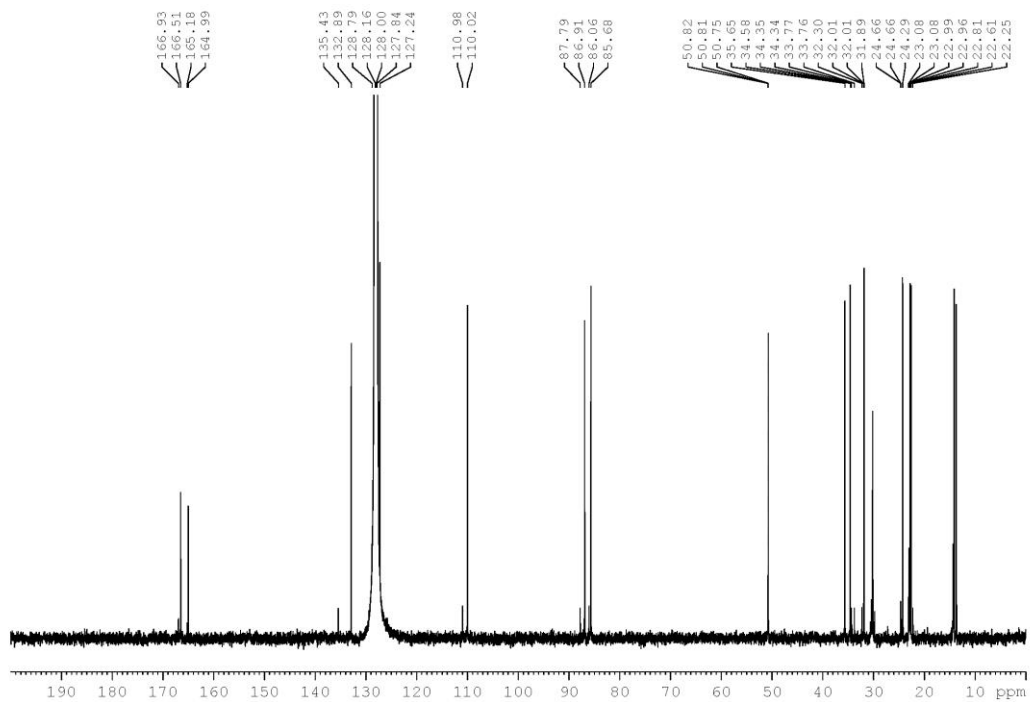
^{13}C NMR Spectra of *Z*-13g and *E*-13g in C_6D_6



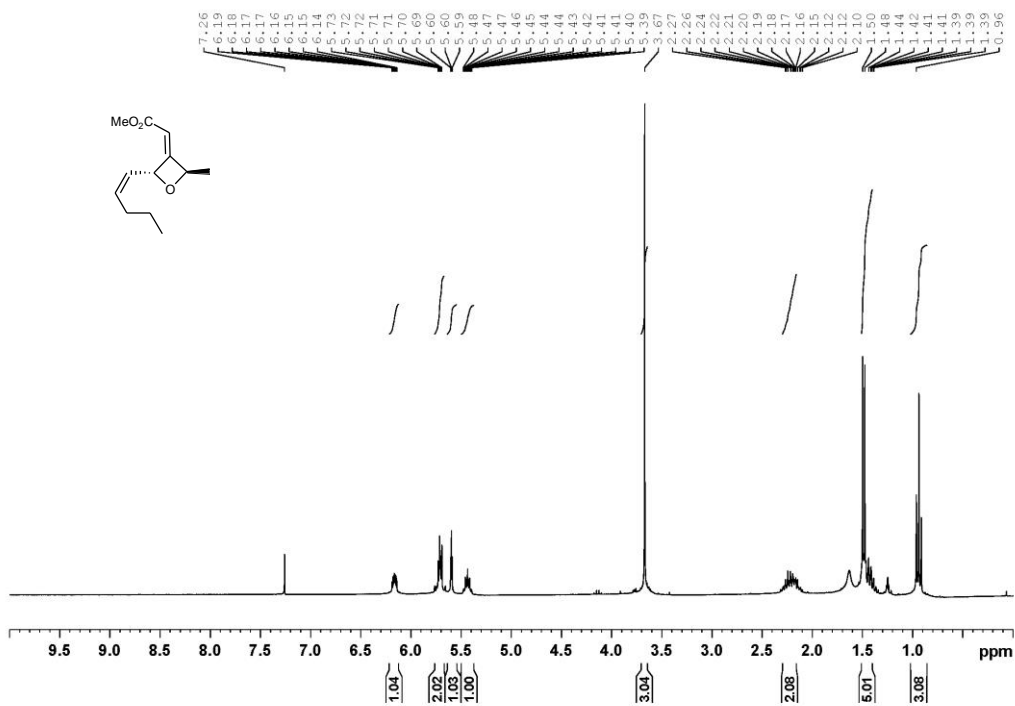
¹H NMR Spectra of *Z*-13h and *E*-13h in C₆D₆



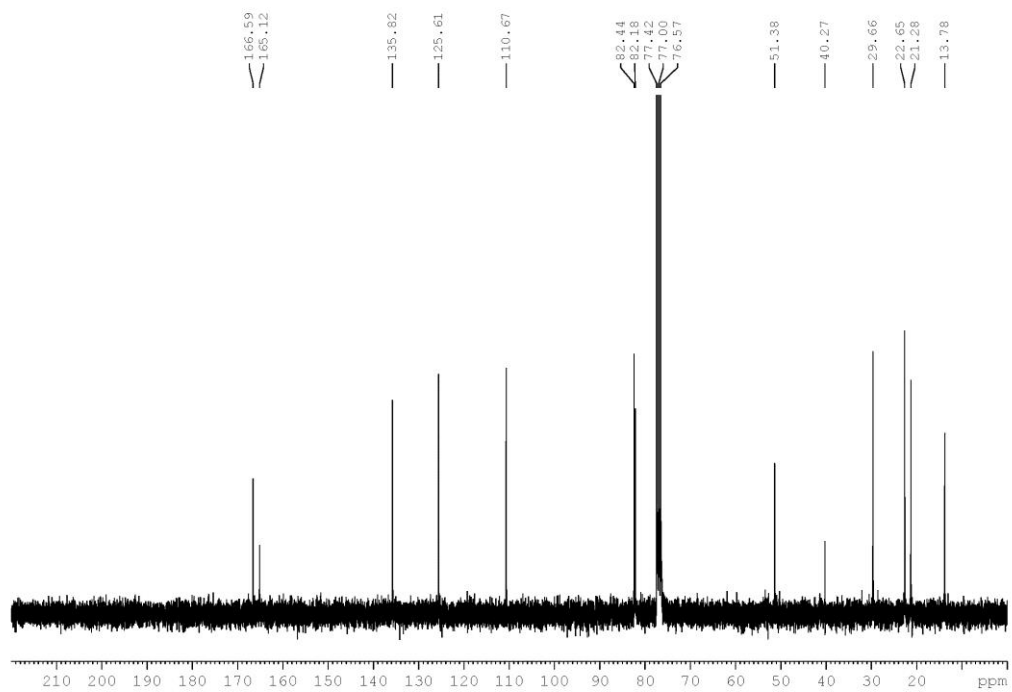
¹³C NMR Spectra of *Z*-13h and *E*-13h in C₆D₆



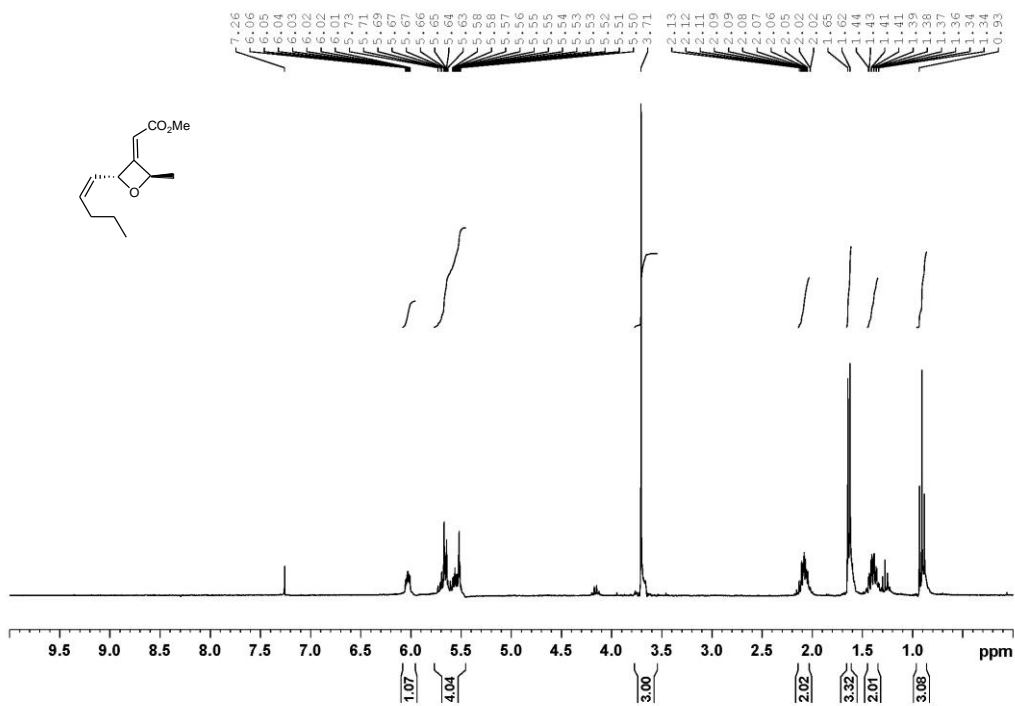
¹H NMR Spectrum of **Z-13i** in CDCl₃



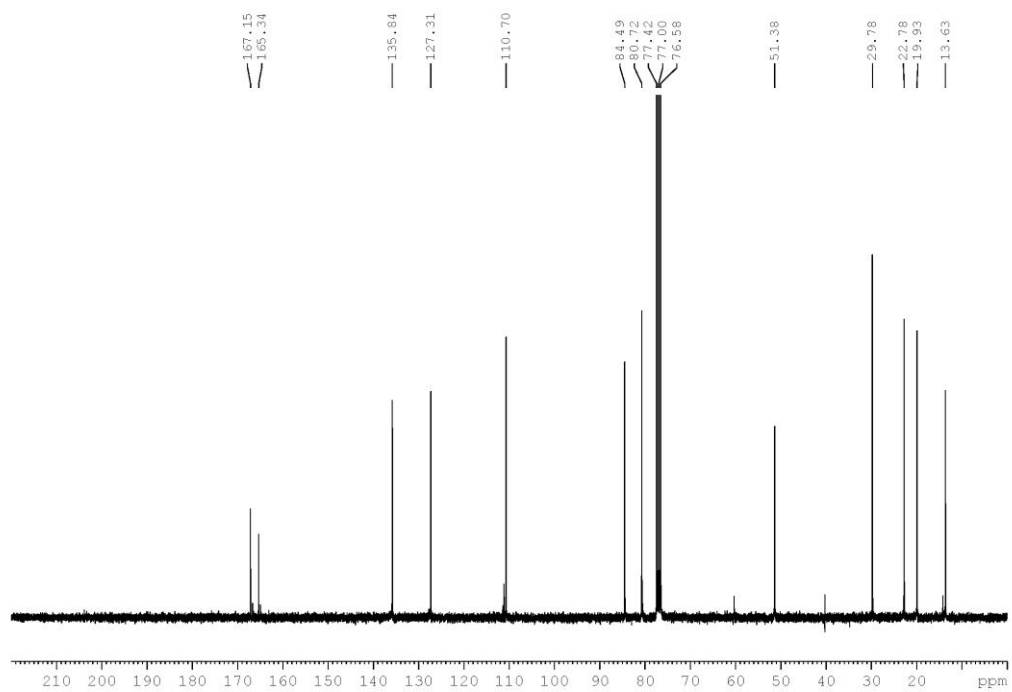
¹³C NMR Spectrum of **Z-13i** in CDCl₃



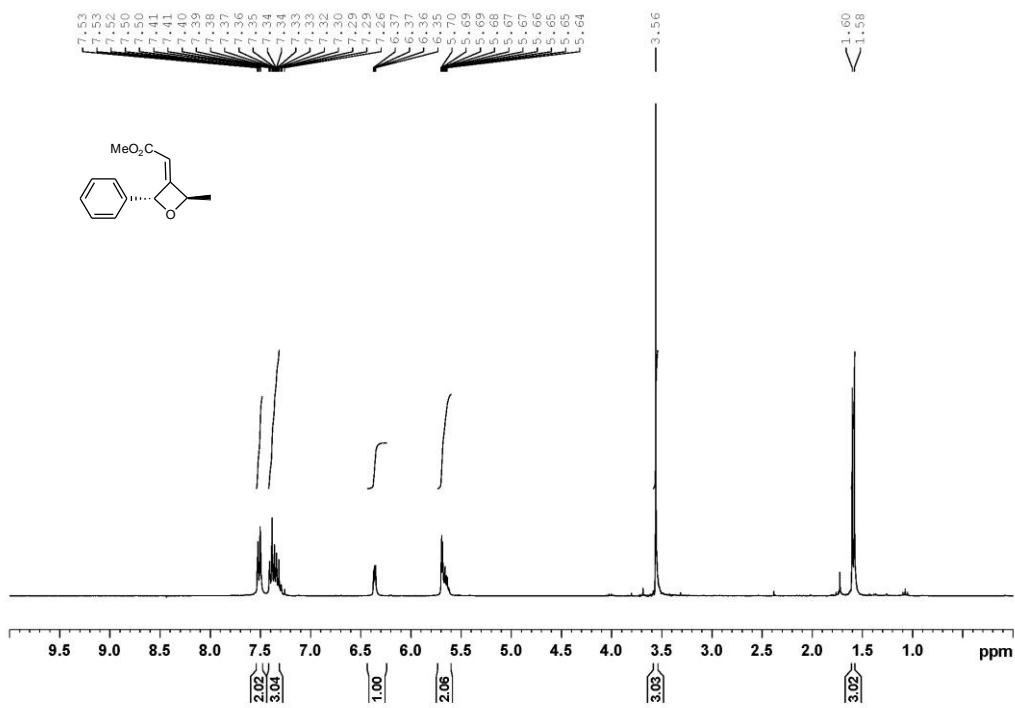
^1H NMR Spectrum of *E*-13i in CDCl_3



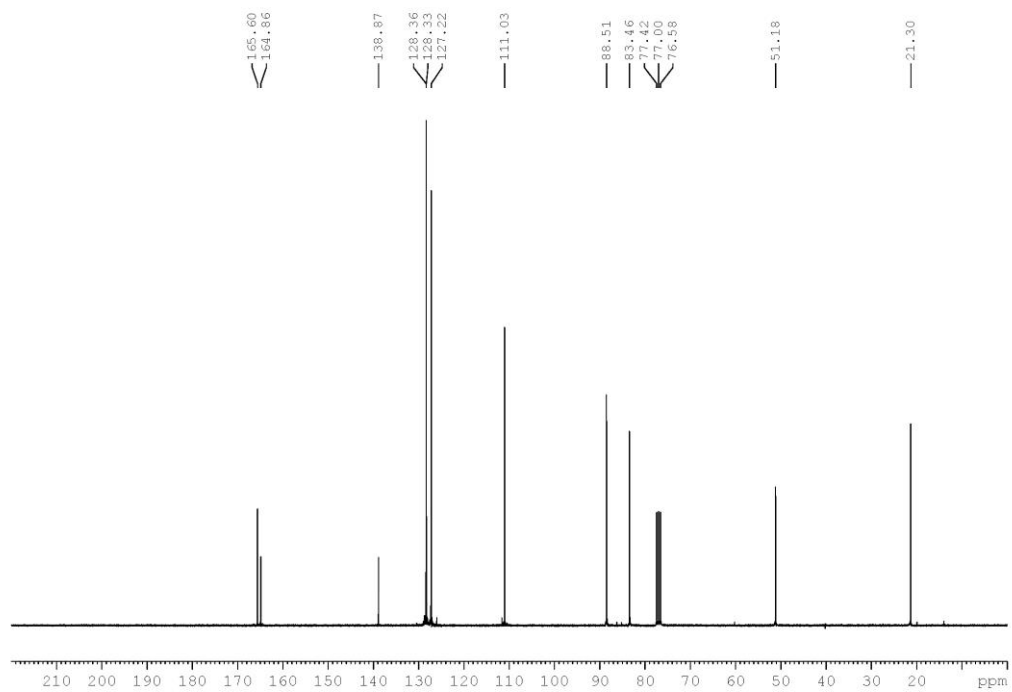
^{13}C NMR Spectrum of *E*-13i in CDCl_3



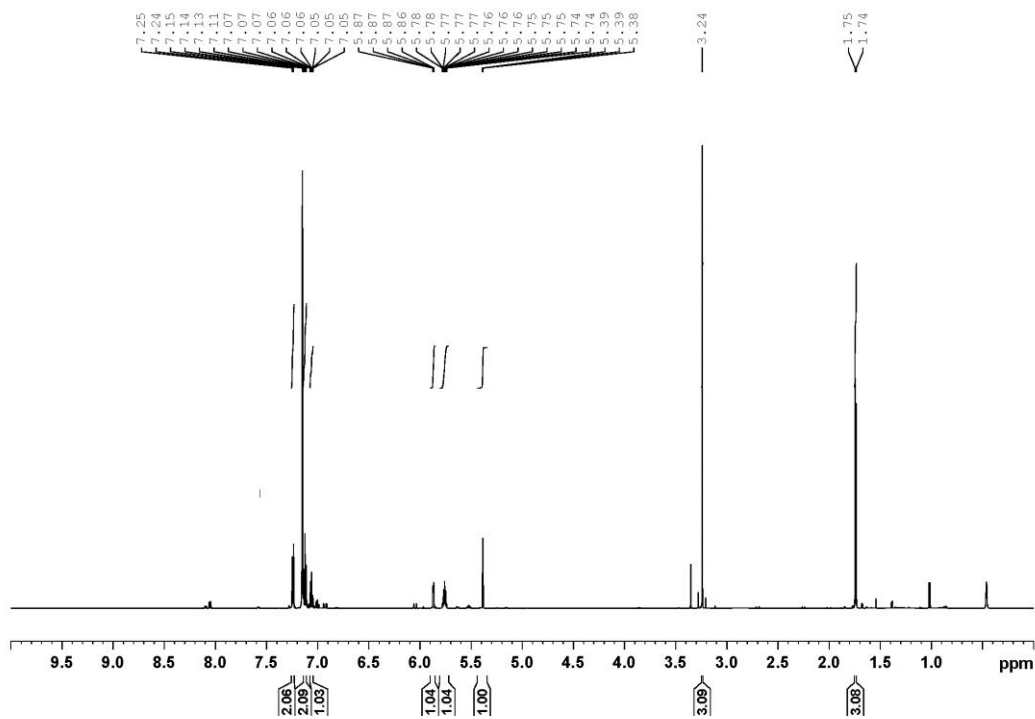
¹H NMR Spectrum of **Z-13j** in CDCl₃



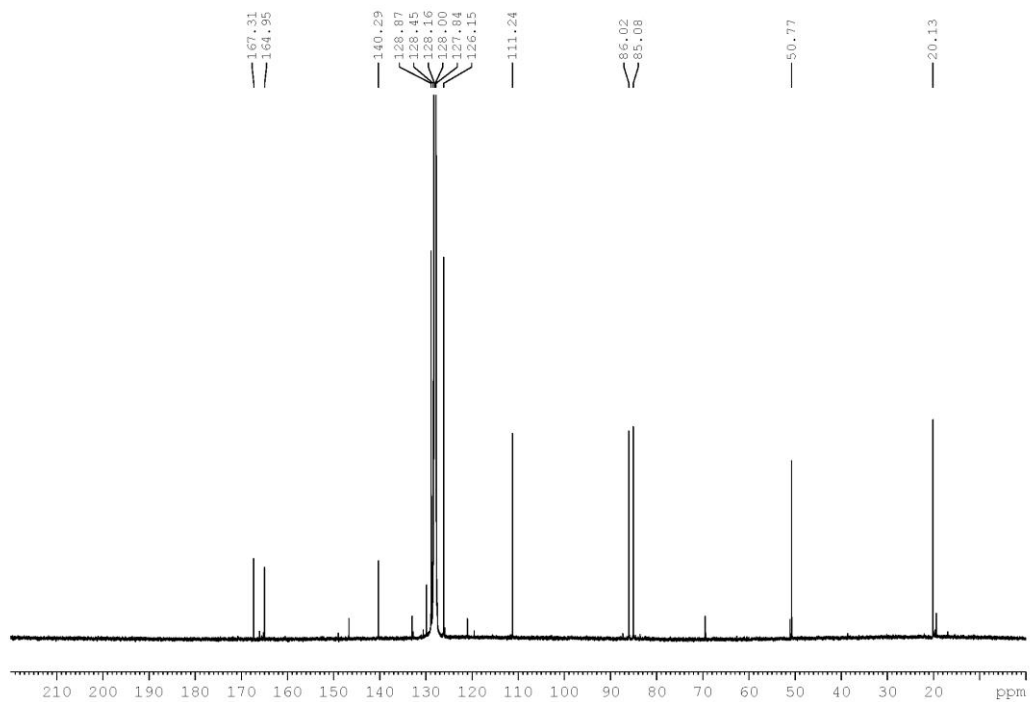
¹³C NMR Spectrum of **Z-13j** in CDCl₃



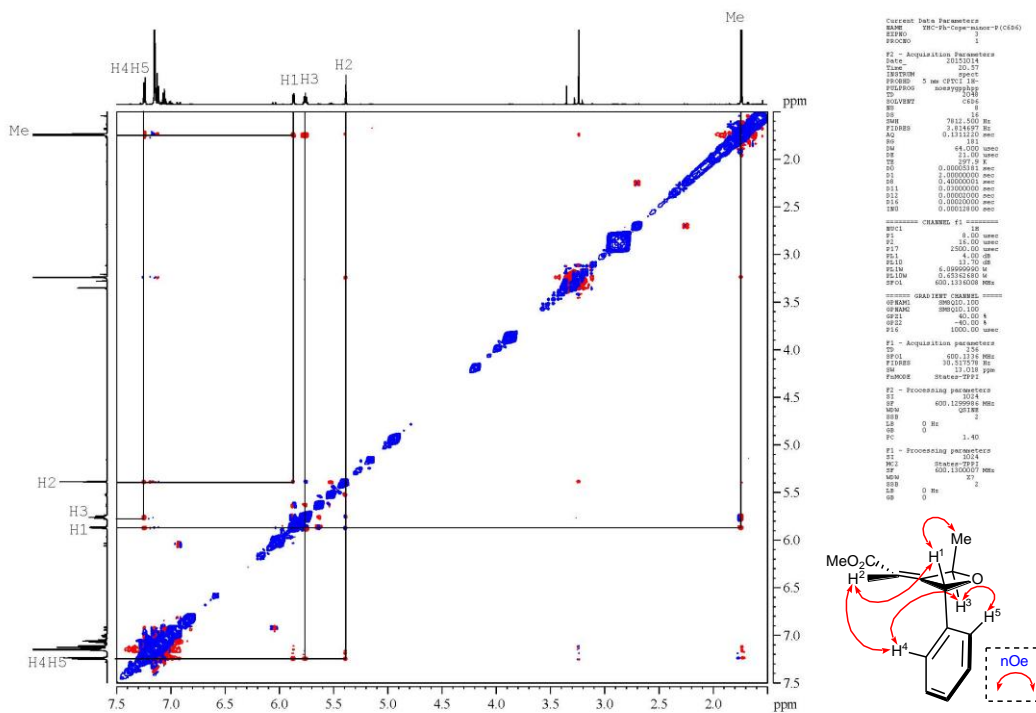
^1H NMR Spectrum of *E*-13j in C_6D_6



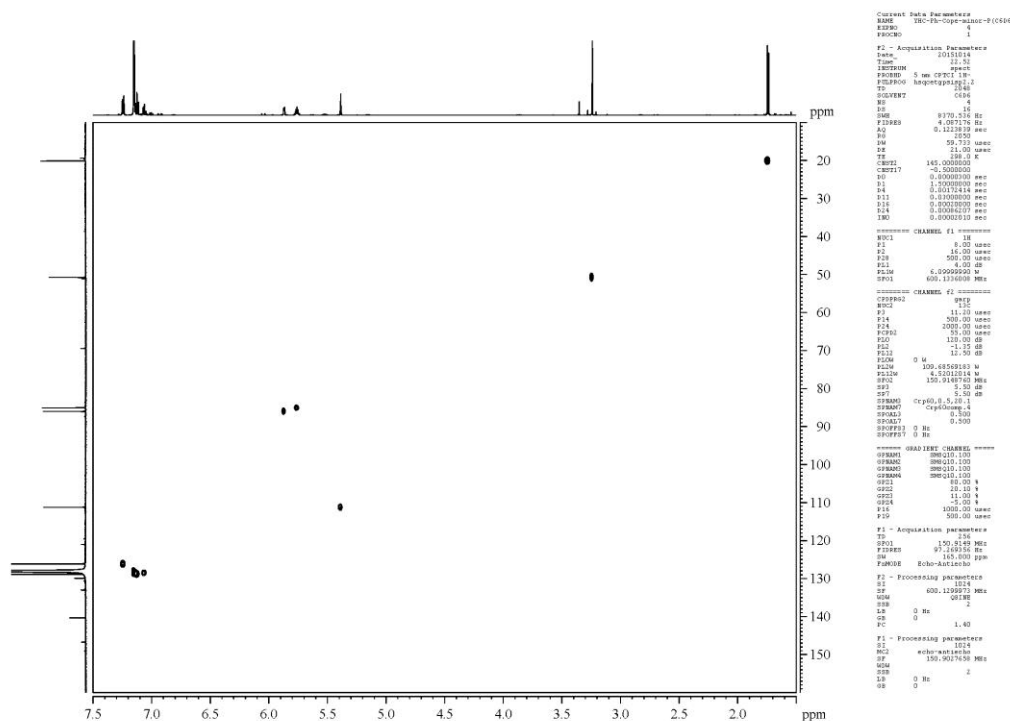
^{13}C NMR Spectrum of *E*-13j in C_6D_6



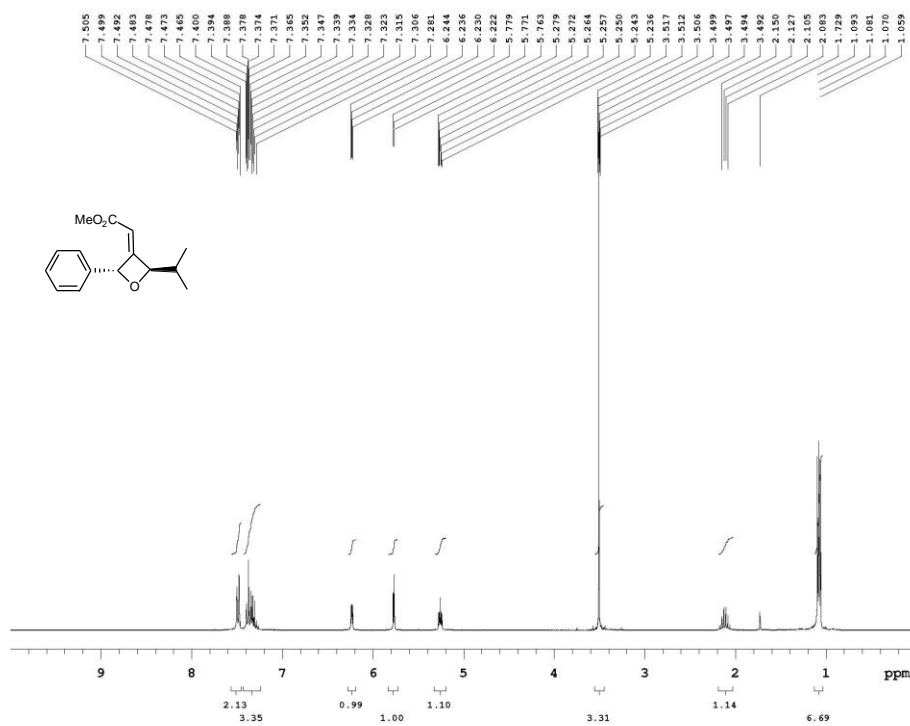
NOESY Spectrum of *E*-13j in C₆D₆



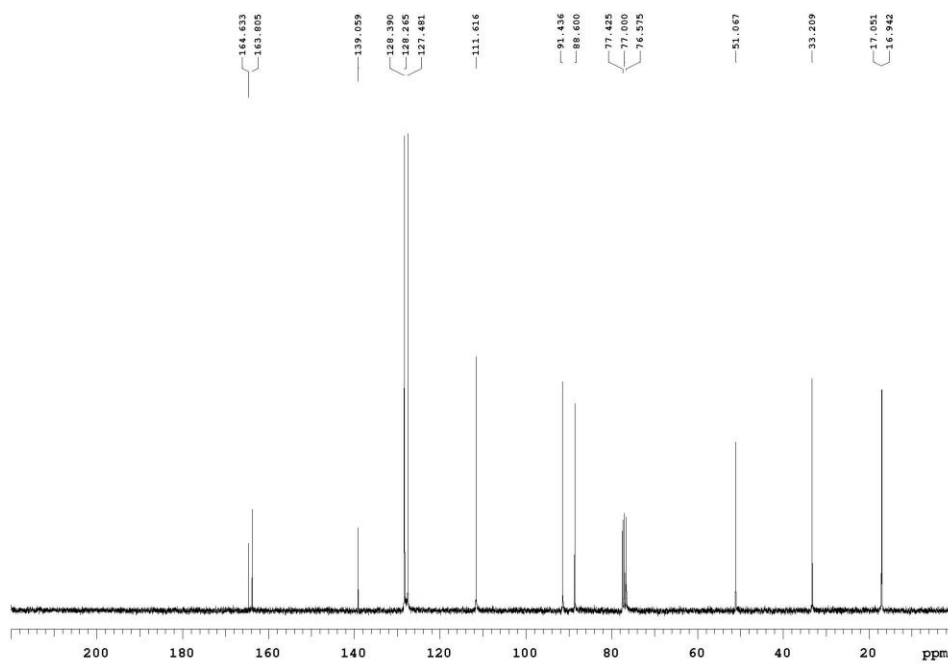
HSQC Spectrum of *E*-13j in C₆D₆



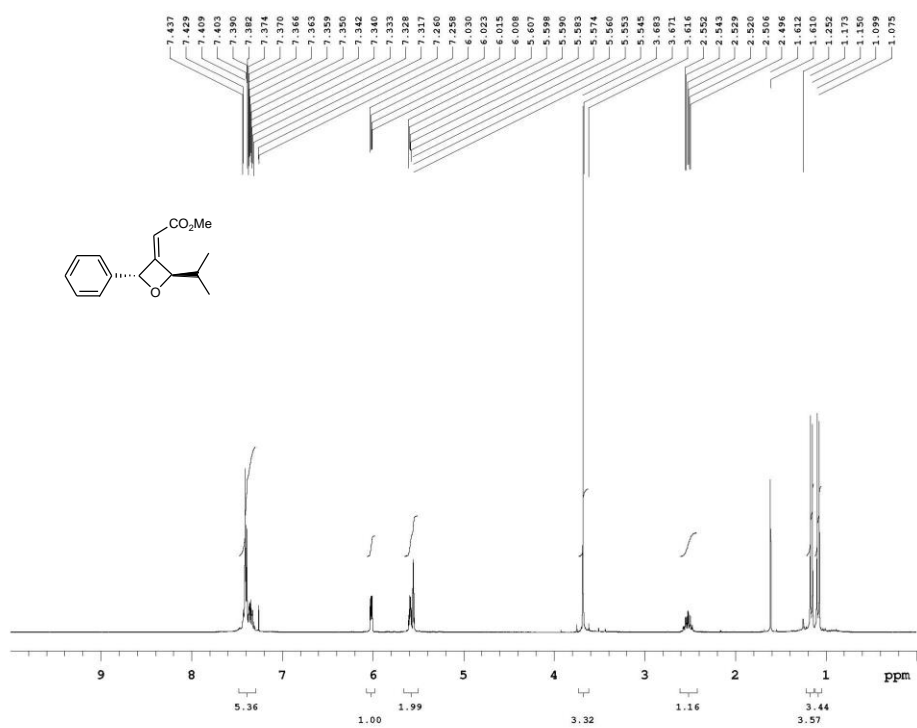
¹H NMR Spectrum of **Z-13k** in CDCl₃



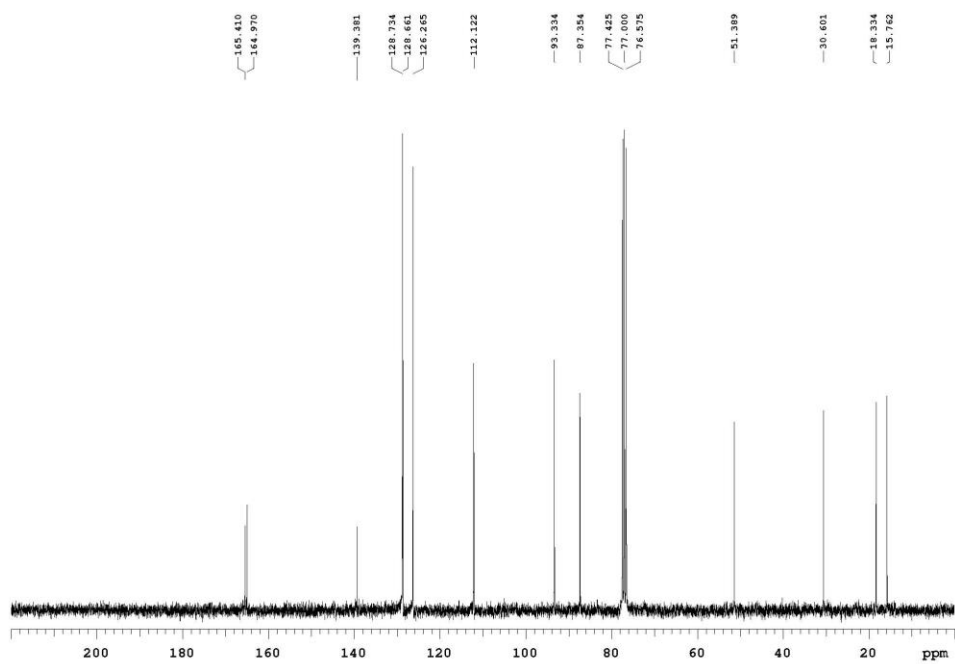
¹³C NMR Spectrum of **Z-13k** in CDCl₃



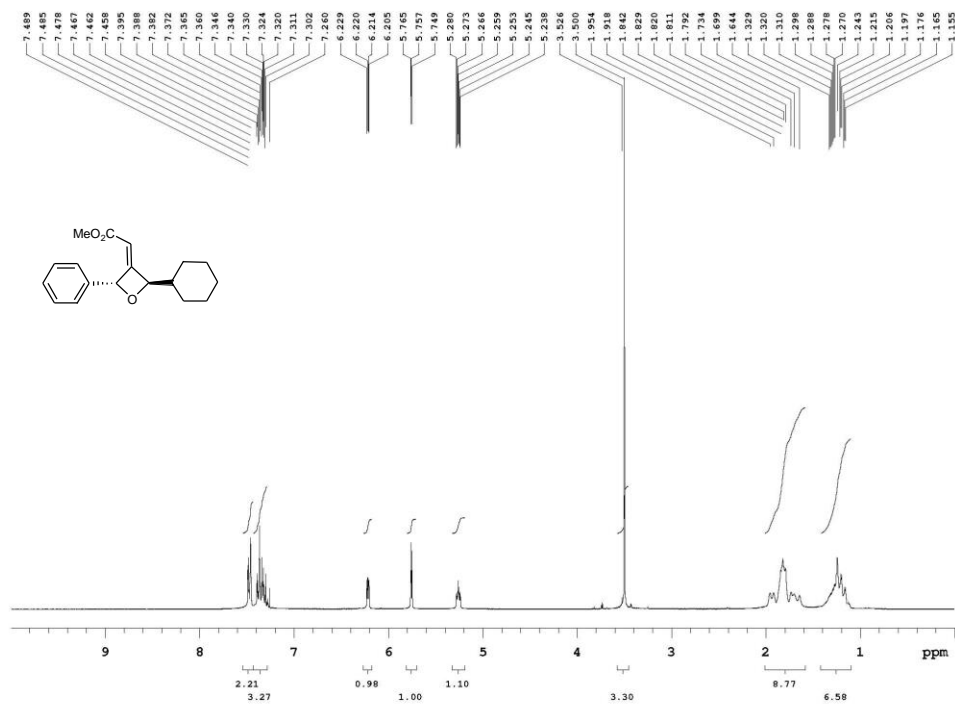
¹H NMR Spectrum of *E*-13k in CDCl₃



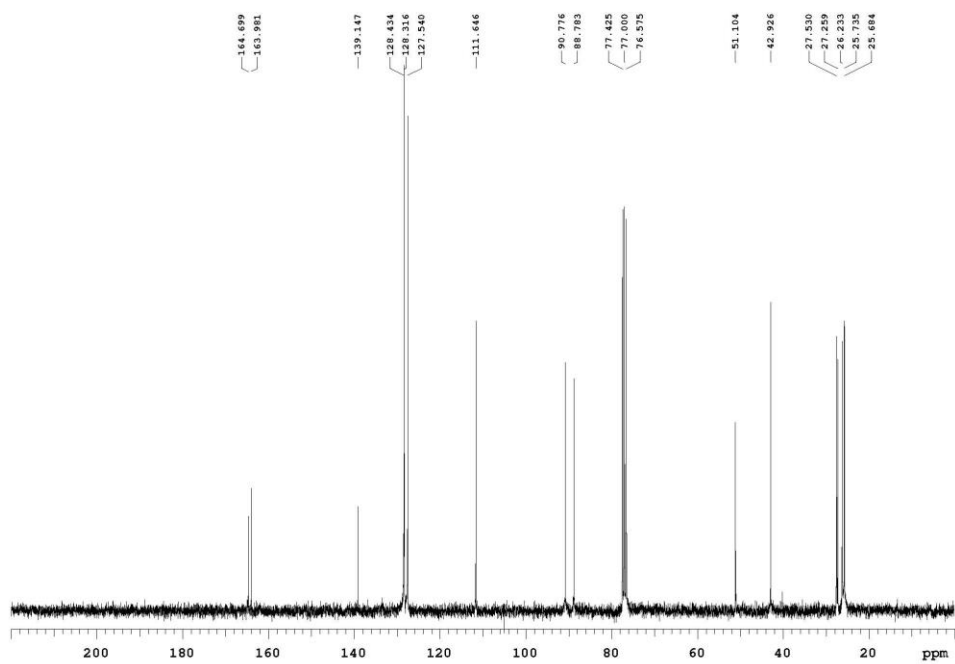
¹³C NMR Spectrum of *E*-13k in CDCl₃



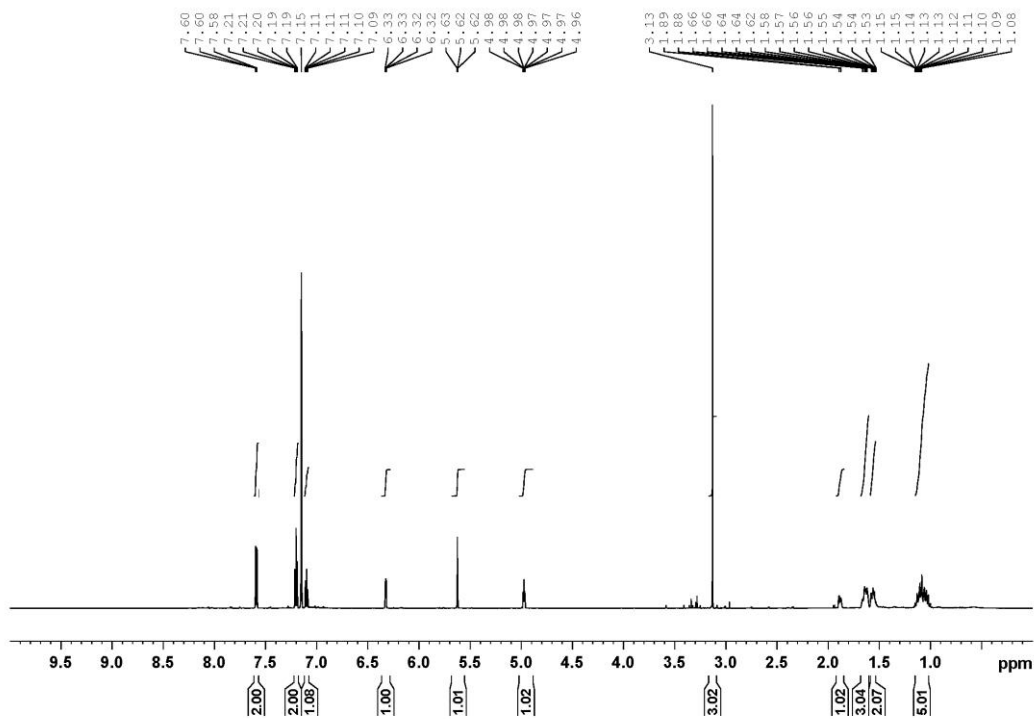
¹H NMR Spectrum of **Z-131** in CDCl₃



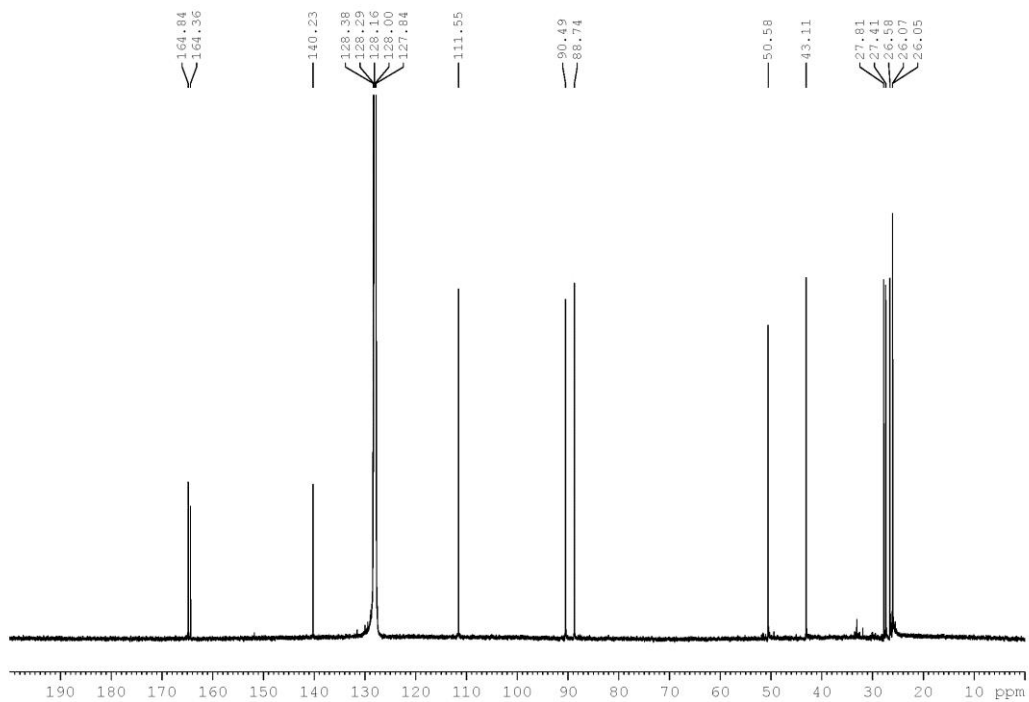
¹³C NMR Spectrum of **Z-131** in CDCl₃



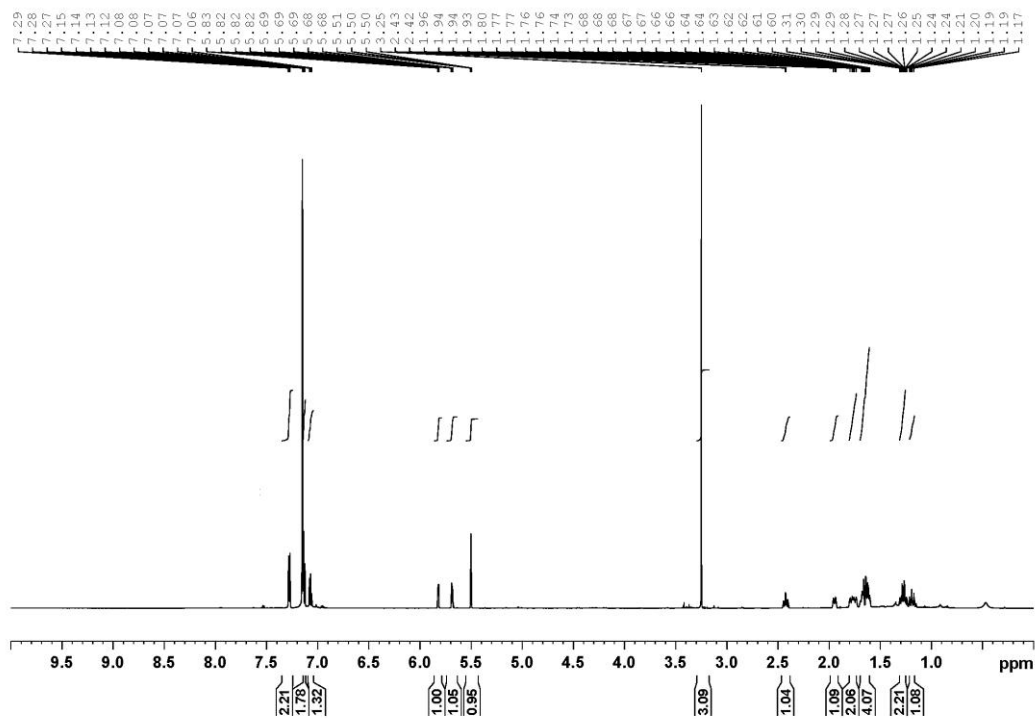
¹H NMR Spectrum of Z-131 in C₆D₆



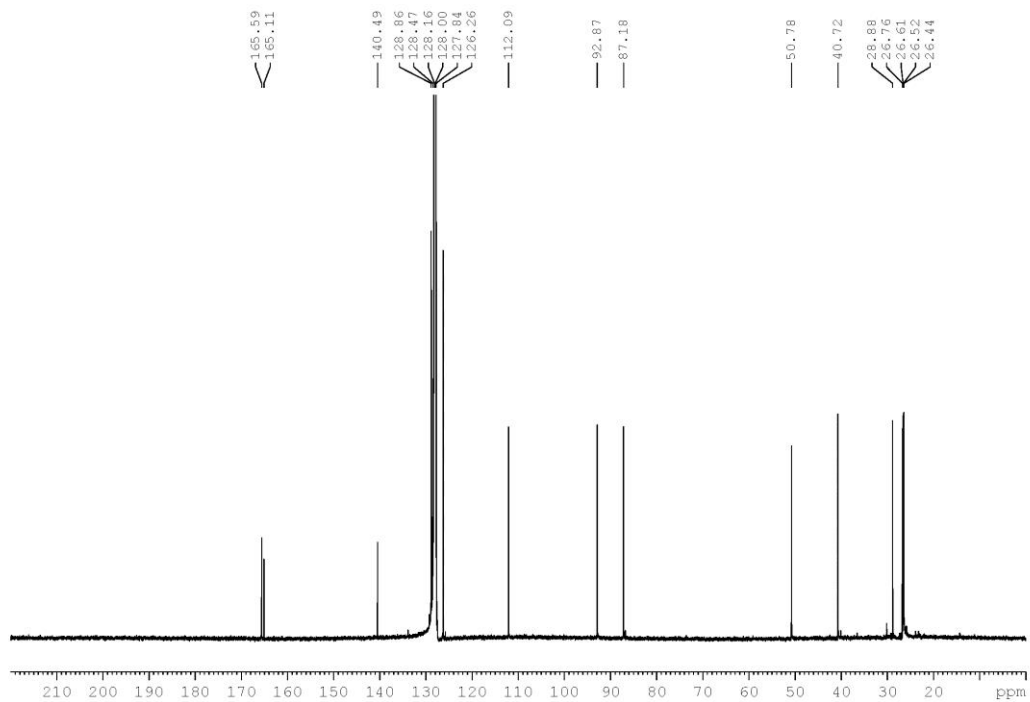
¹³C NMR Spectrum of Z-131 in C₆D₆



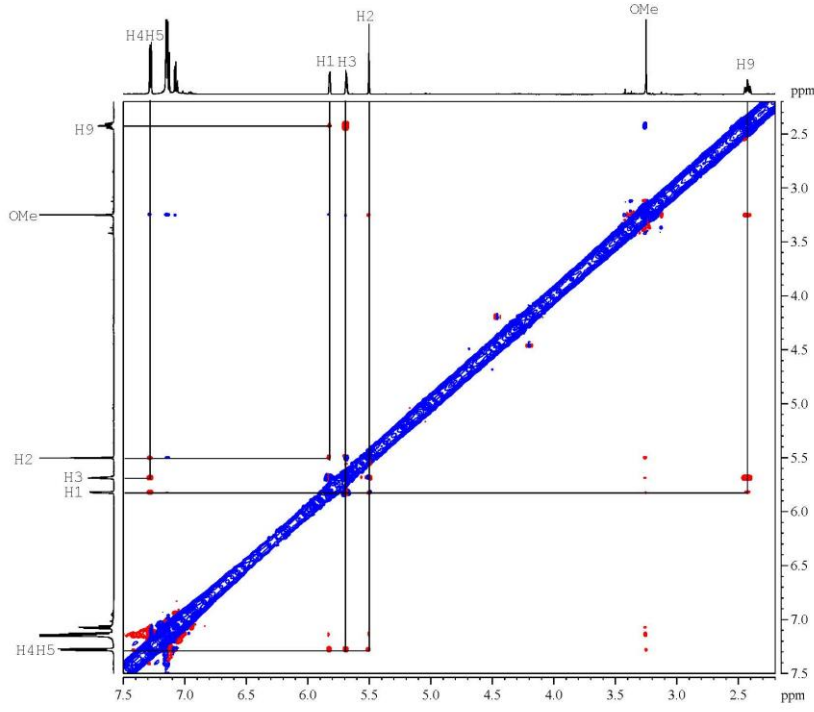
¹H NMR Spectrum of *E*-13l in C₆D₆



¹³C NMR Spectrum of *E*-13l in C₆D₆



NOESY Spectrum of *E*-131 in C₆D₆

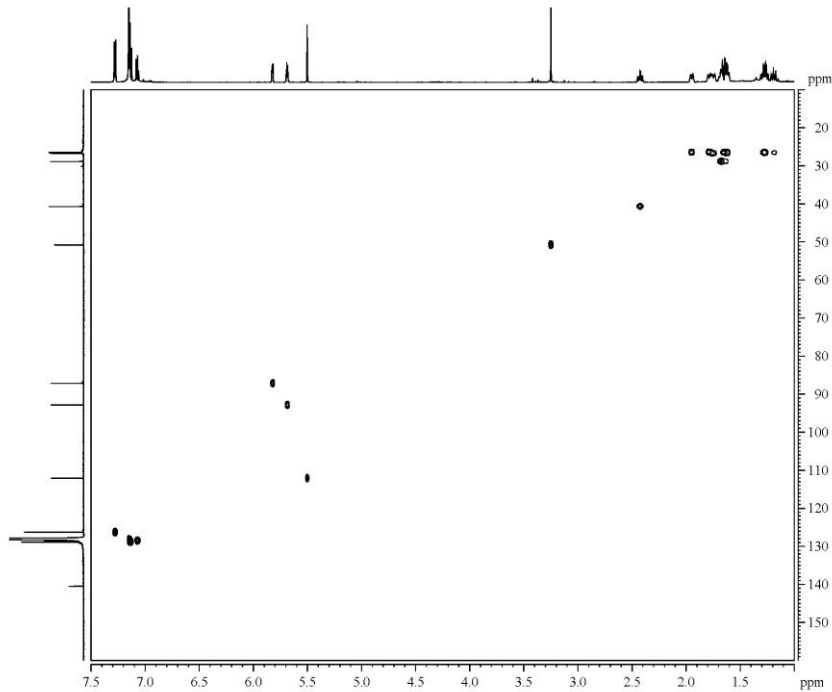


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PROCNO 1
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PULPROG zgpg30
TD 65536
SOLVENT cdm
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DS 2
SWH 7012.200 Hz
F2FREQ 314.457 MHz
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RG 64
AQ 64.000 usec
DE 21.00 usec
TE 300.2
SI 0.0000011 sec
SFO 1.0000000 sec
SF 0.4000001 sec
SF 0.0000000 sec
SF 0.0000000 sec
SF 0.0000000 sec
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SF 0.0001000 sec
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PC 15.00 usec
PT 2000.00 usec
PR 4.00 dB
PL1 12.70 dB
PL2 0.0000000 dB
PL3 0.0000000 dB
PL4 0.0000000 dB
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PT 3000.00 usec
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WDW EM
SSB 0 Hz
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GB 0
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F1 - Processing parameters
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SF 600.135000 MHz
WDW EM
SSB 0 Hz
LB 2
GB 0
PC 1.40
F2 - Acquisition Parameters
SI 134
SF 600.135000 MHz
WDW EM
SSB 0 Hz
LB 2
GB 0
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F2 - Processing parameters
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SSB 0 Hz
LB 2
GB 0
PC 1.40

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HSQC Spectrum of *E*-131 in C₆D₆

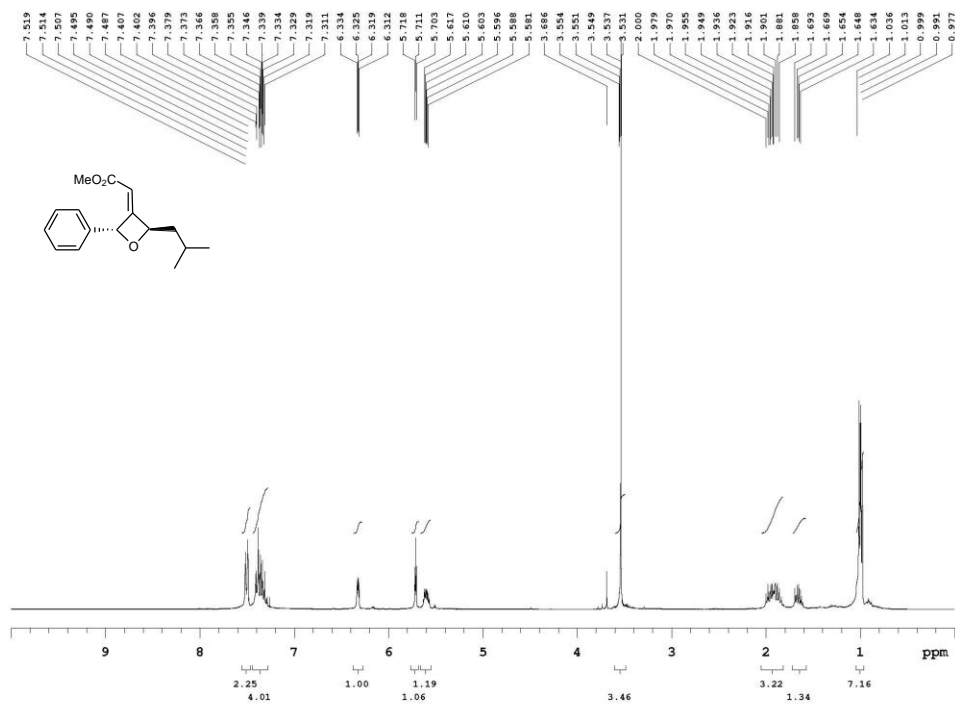


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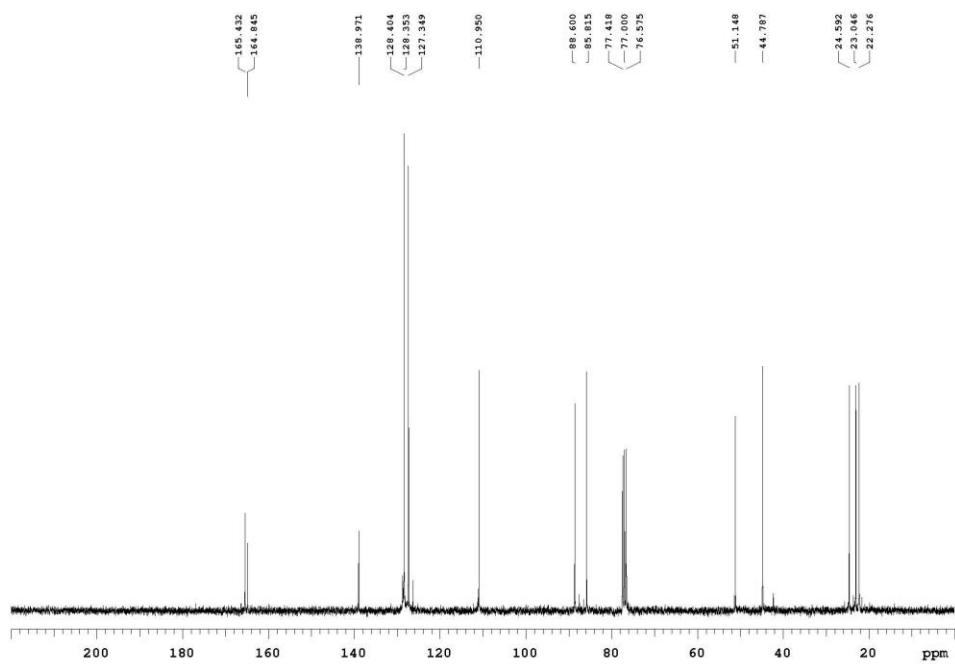
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PROCNO 1
F2 - Acquisition Parameters
Date_ 20151007
Time 17:45
INSTRUM spect
PROBHD 5 mm CPYX 1H
PULPROG zgpg30
TD 65536
SOLVENT cdm
NS 2
DS 2
SWH 7012.200 Hz
F2FREQ 314.457 MHz
AQ 0.111111 sec
RG 64
AQ 64.000 usec
DE 21.00 usec
TE 300.2
SI 0.0000011 sec
SFO 1.0000000 sec
SF 0.4000001 sec
SF 0.0000000 sec
SF 0.0000000 sec
SF 0.0000000 sec
SF 0.0001000 sec
SF 0.0001000 sec
===== CHANNEL f1 =====
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PC 15.00 usec
PT 2000.00 usec
PR 4.00 dB
PL1 12.70 dB
PL2 0.0000000 dB
PL3 0.0000000 dB
PL4 0.0000000 dB
===== GRABBER CHANNEL =====
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OPRG2 SMOULD100
PC 40.00 usec
PT 3000.00 usec
F1 - Acquisition Parameters
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SF 600.135000 MHz
WDW EM
SSB 0 Hz
LB 2
GB 0
PC 1.40
F1 - Processing parameters
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SSB 0 Hz
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GB 0
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WDW EM
SSB 0 Hz
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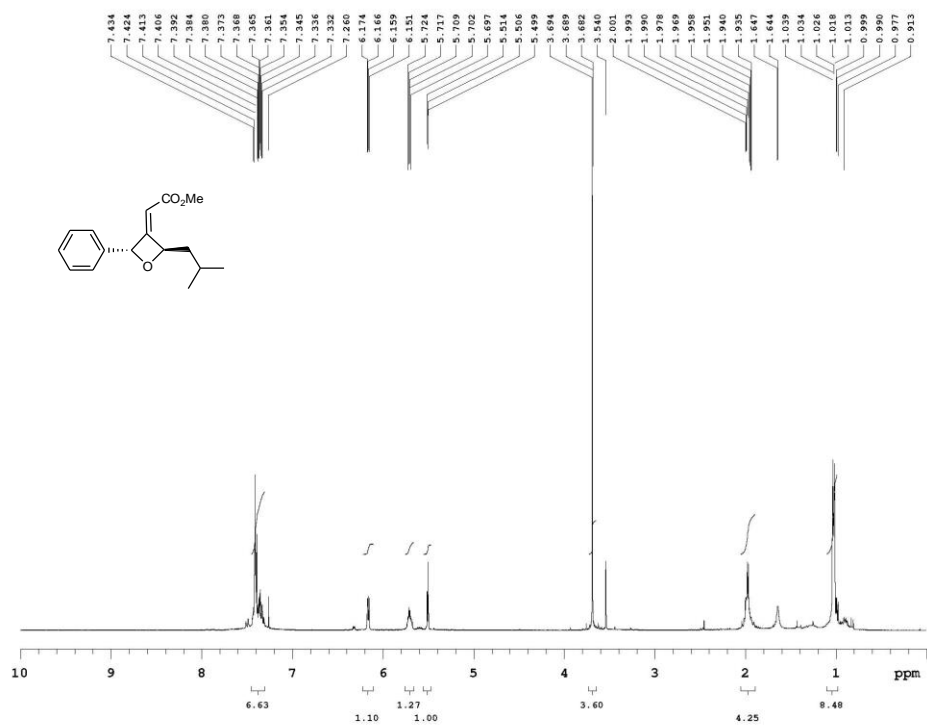
¹H NMR Spectrum of **Z-13m** in CDCl₃



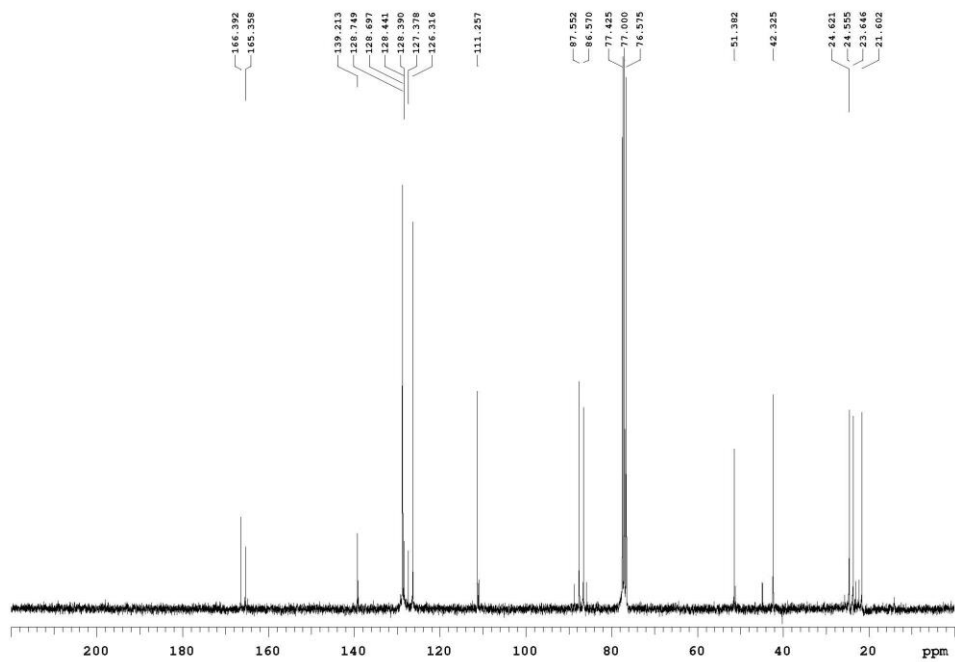
¹³C NMR Spectrum of **Z-13m** in CDCl₃



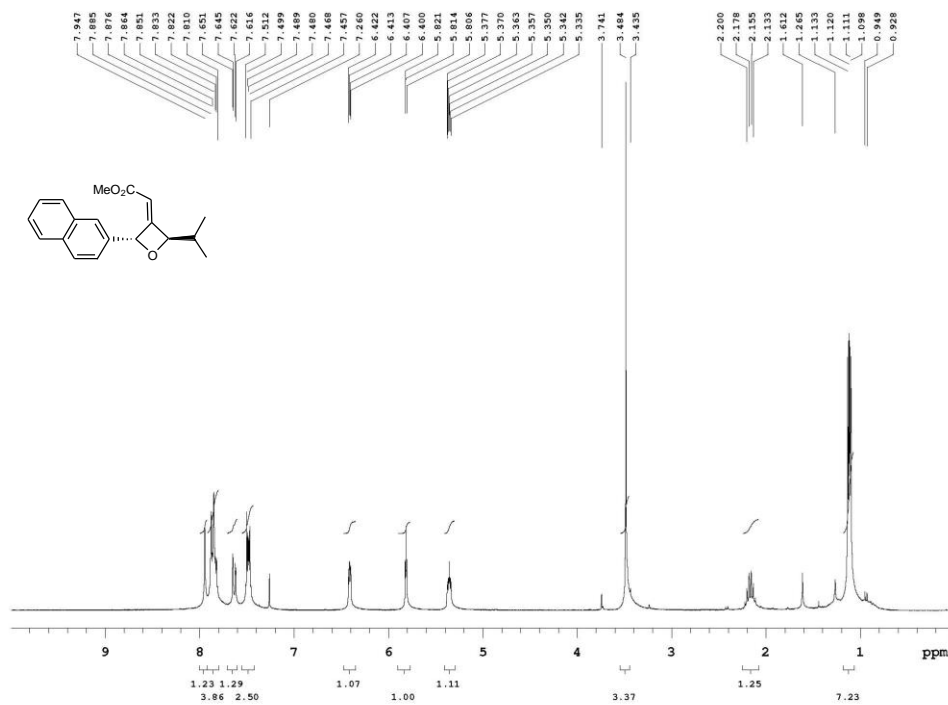
^1H NMR Spectrum of *E*-13m in CDCl_3



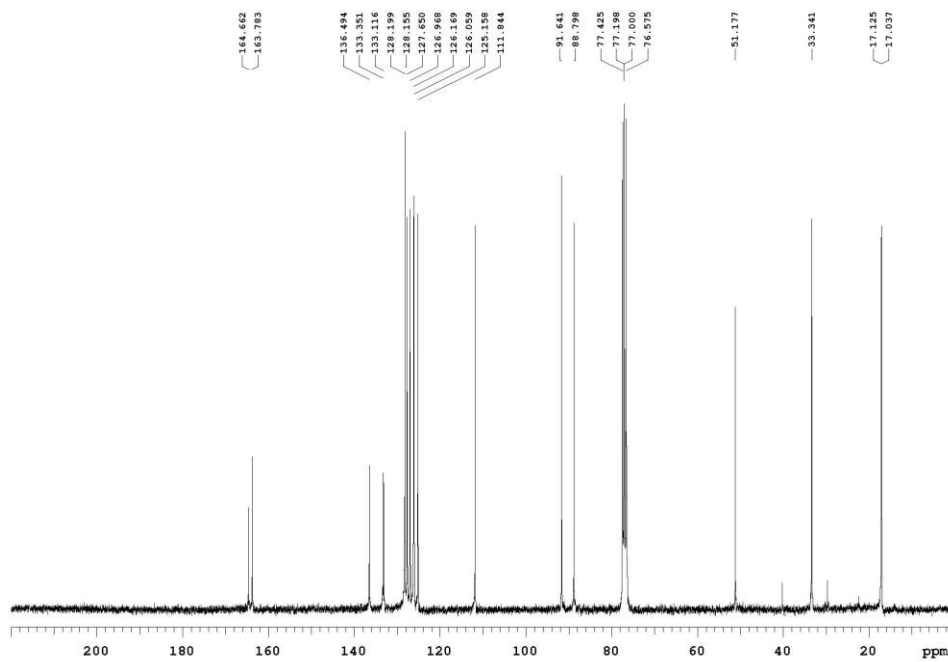
^{13}C NMR Spectrum of *E*-13m in CDCl_3



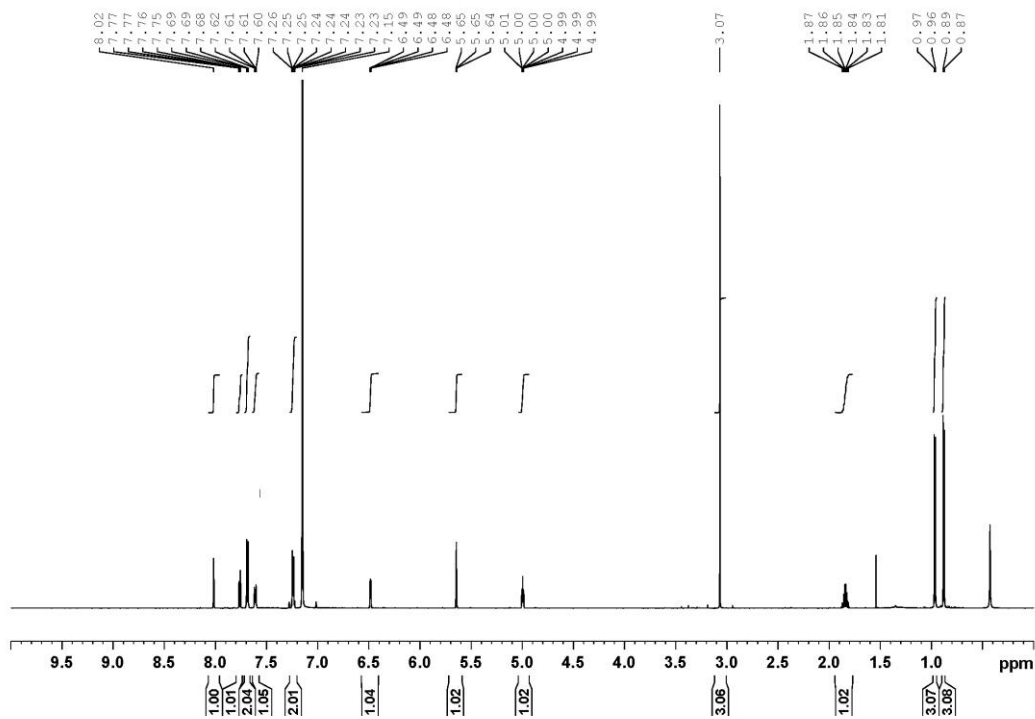
^1H NMR Spectrum of **Z-13n** in CDCl_3



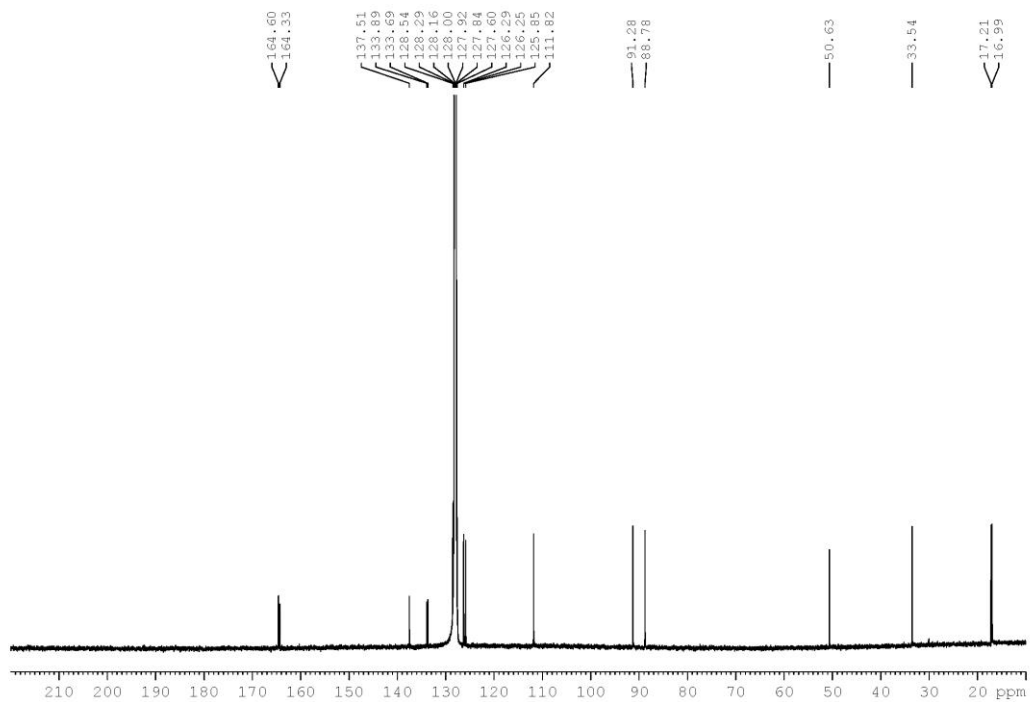
^{13}C NMR Spectrum of **Z-13n** in CDCl_3



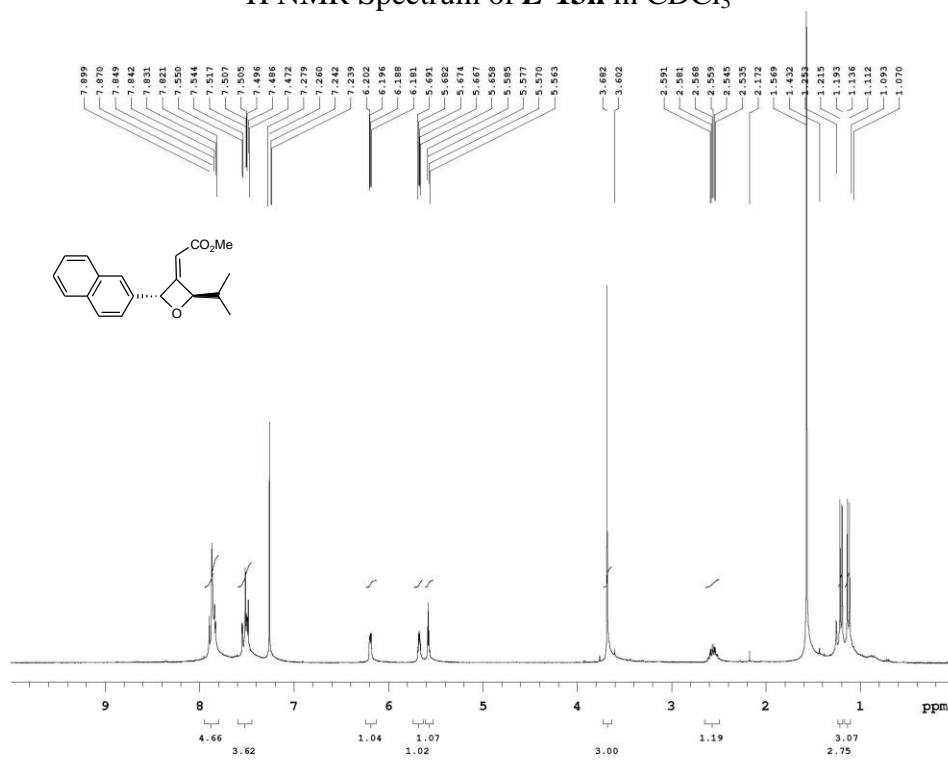
¹H NMR Spectrum of **Z-13n** in C₆D₆



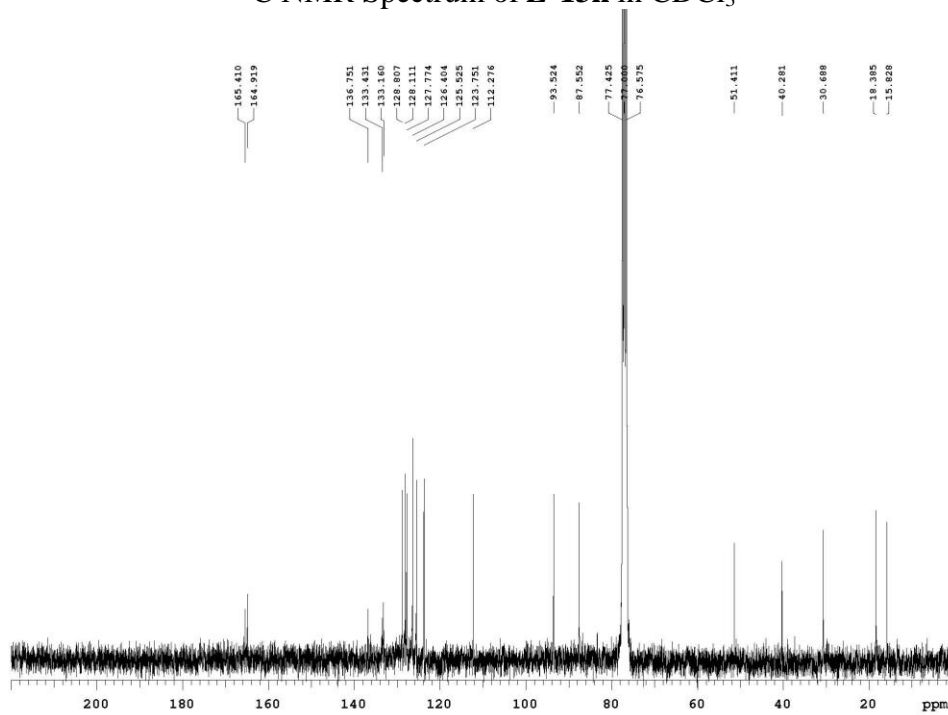
¹³C NMR Spectrum of **Z-13n** in C₆D₆



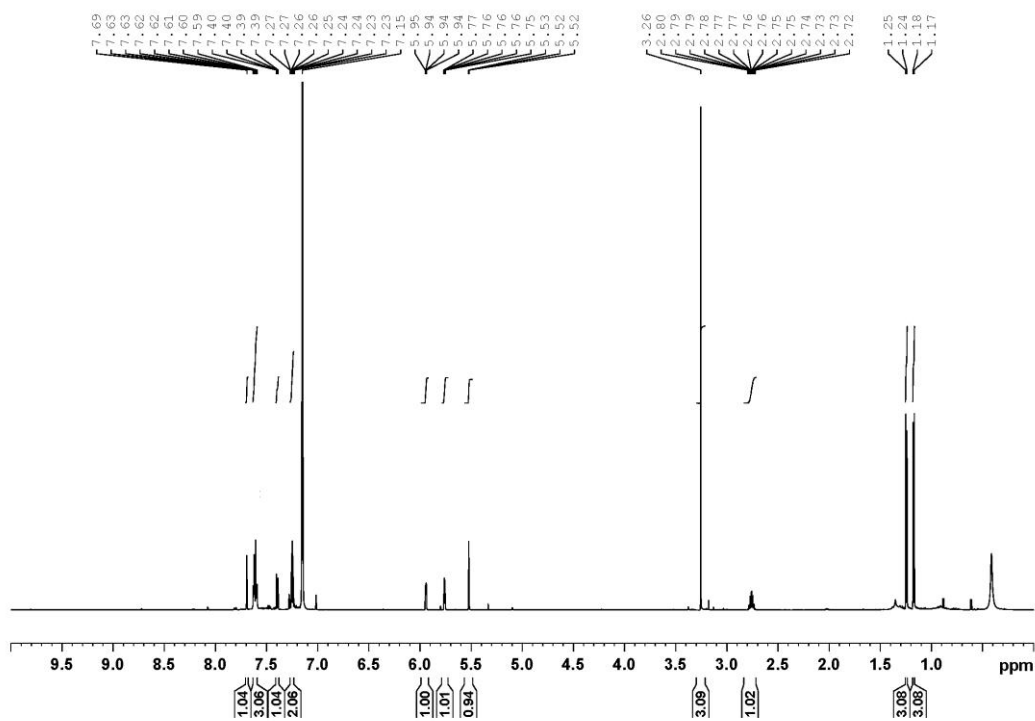
^1H NMR Spectrum of *E*-13n in CDCl_3



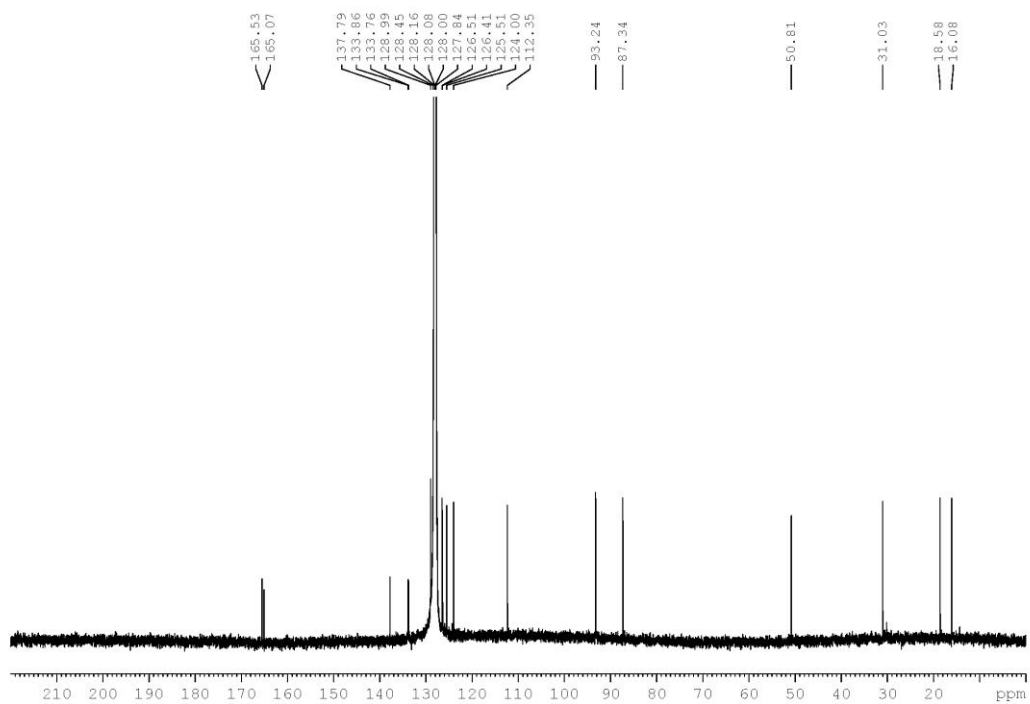
^{13}C NMR Spectrum of *E*-13n in CDCl_3



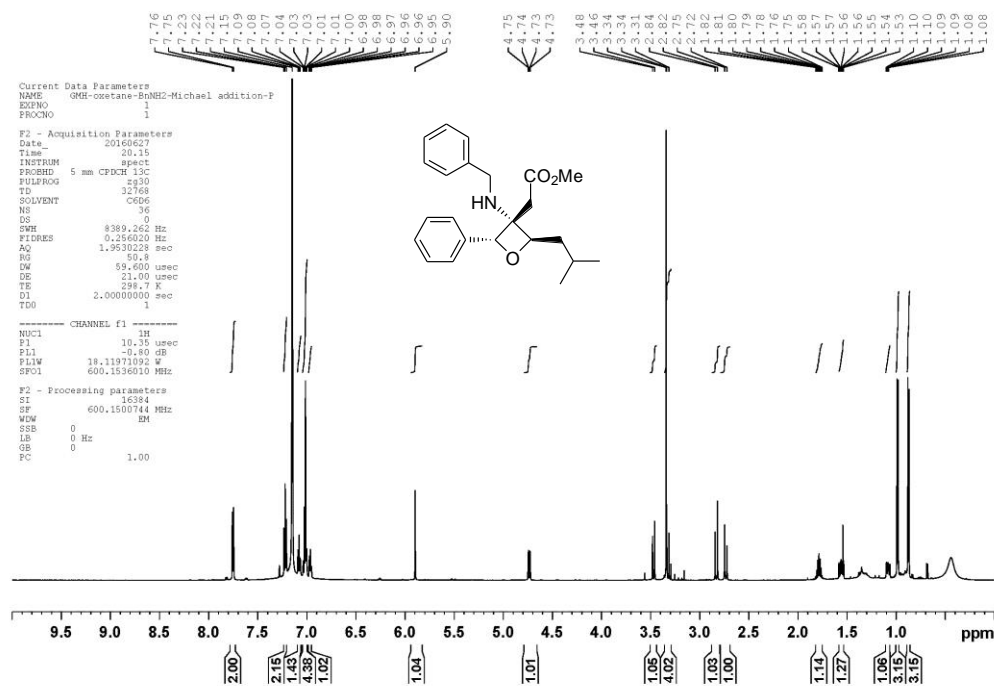
^1H NMR Spectrum of *E*-13n in C_6D_6



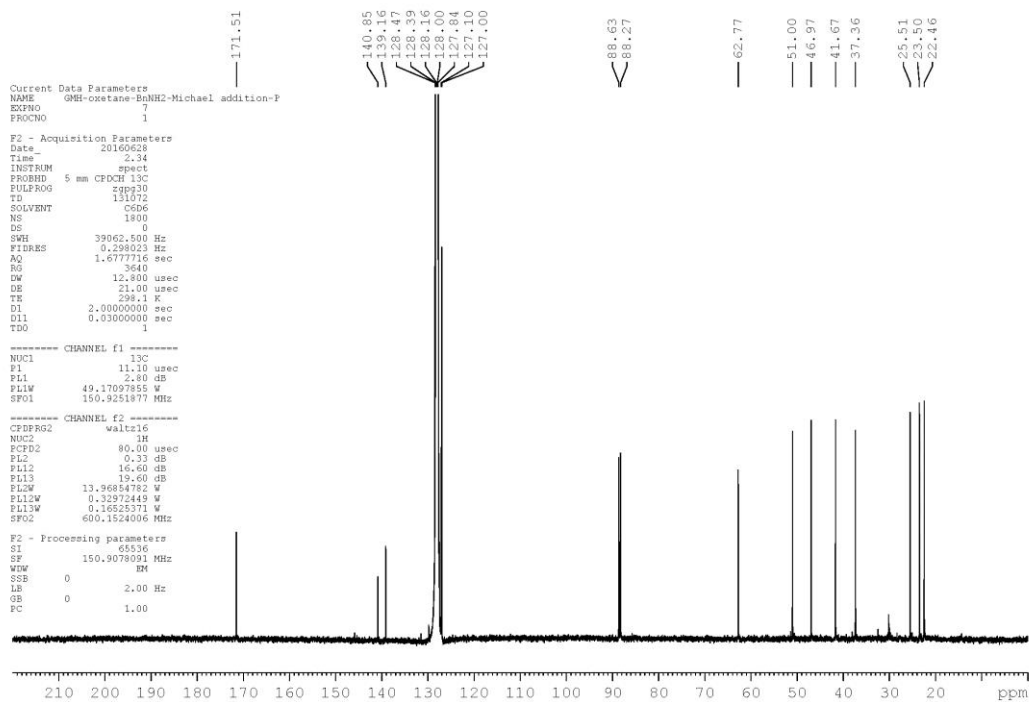
^{13}C NMR Spectrum of *E*-13n in C_6D_6



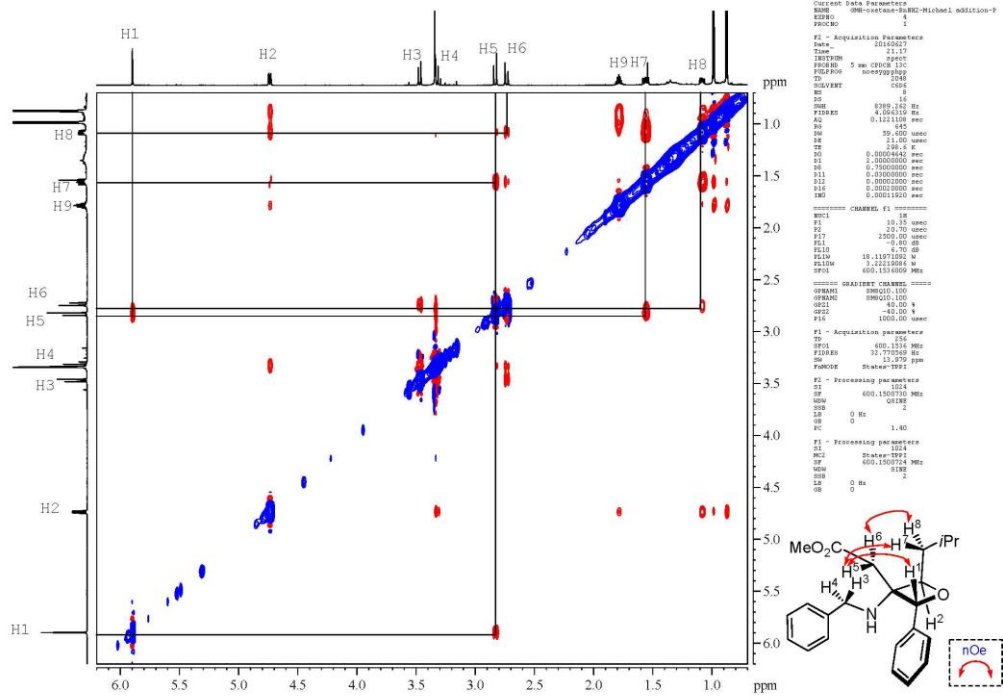
¹H NMR Spectrum of 17 in C₆D₆



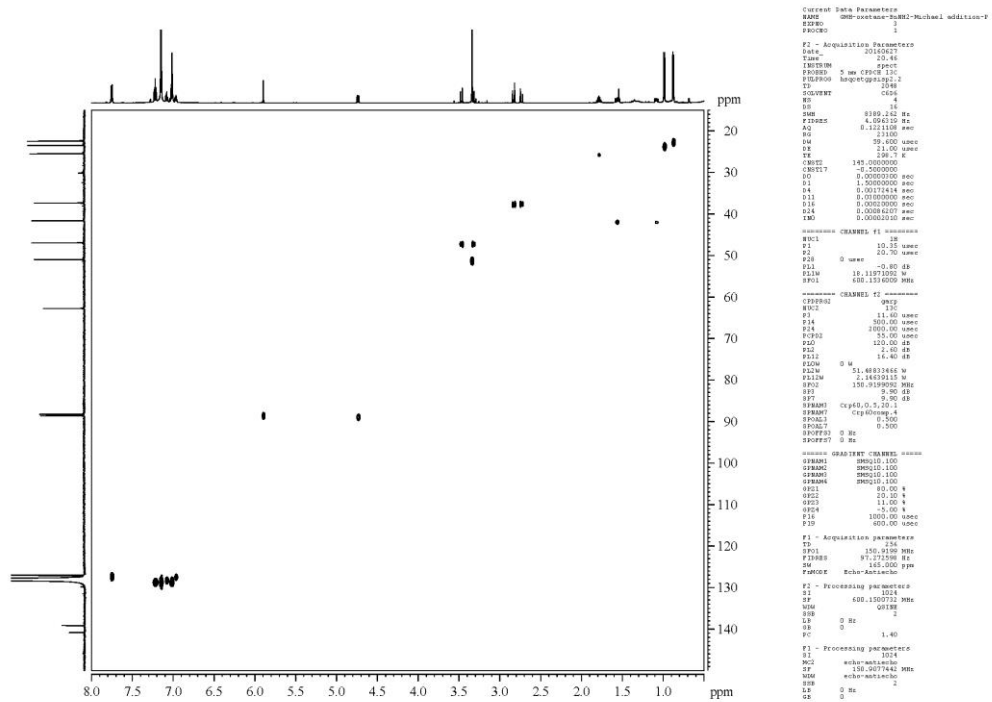
¹³C NMR Spectrum of 17 in C₆D₆



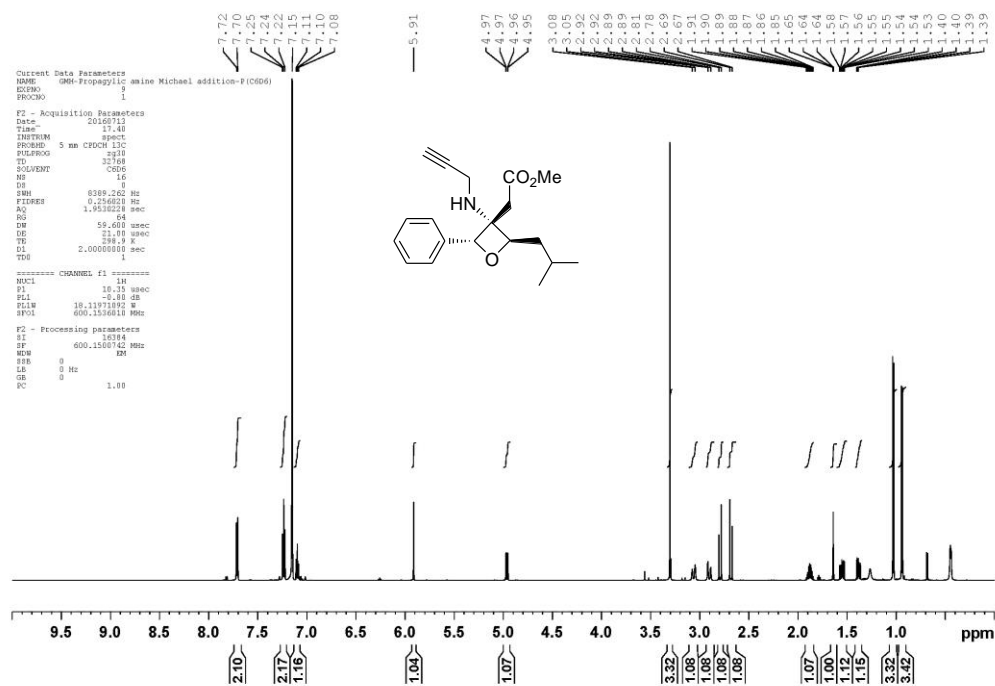
NOESY Spectrum of 17 in C₆D₆



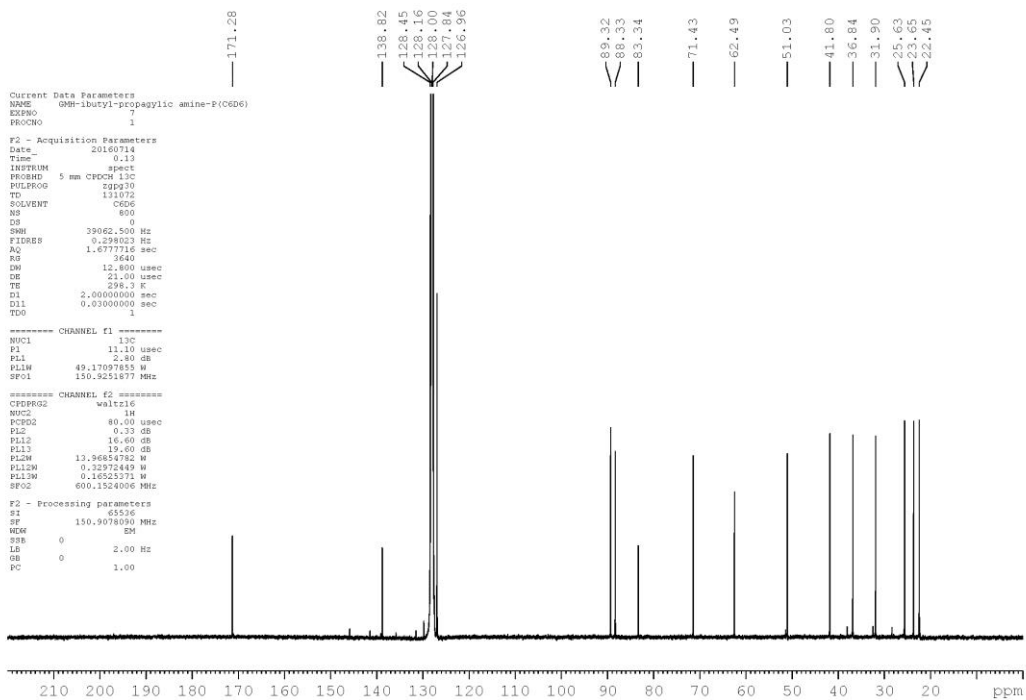
HSQC Spectrum of 17 in C₆D₆



¹H NMR Spectrum of **18** in C₆D₆



¹³C NMR Spectrum of **18** in C₆D₆



V. X-Ray Structure and Crystallographic Data

Single crystal X-ray structure (ORTEP) of oxetane 25a. The crystals were grown from hexanes: EtOAc (4:1), using a slow evaporation method (ellipsoids are set at 50% probability). X-ray crystallographic data have been deposited in the Cambridge Crystallographic Data Centre database (<http://www.ccdc.cam.ac.uk/>) under accession code CCDC 1437743.

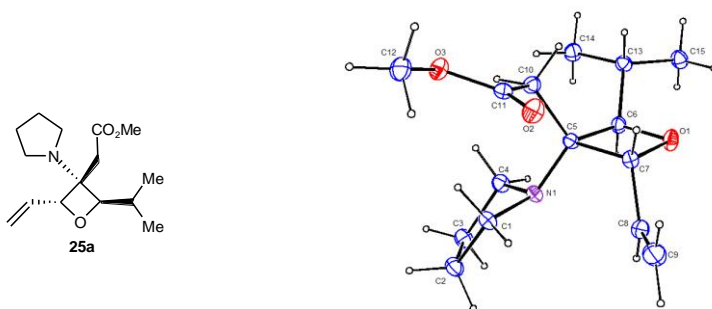


Table 1. Crystal data and structure refinement for i15955.

Identification code	i15955	
Empirical formula	C ₁₅ H ₂₅ N O ₃	
Formula weight	267.36	
Temperature	100.0(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 2 ₁ /n	
Unit cell dimensions	a = 11.3879(3) Å	α = 90°.
	b = 10.6012(3) Å	β = 98.506(2)°.
	c = 12.1055(3) Å	γ = 90°.
Volume	1445.37(7) Å ³	
Z	4	
Density (calculated)	1.229 Mg/m ³	
Absorption coefficient	0.084 mm ⁻¹	
F(000)	584	
Crystal size	0.320 x 0.180 x 0.120 mm ³	
Theta range for data collection	2.292 to 27.101°.	
Index ranges	-14 ≤ h ≤ 14, -13 ≤ k ≤ 13, -15 ≤ l ≤ 15	
Reflections collected	55506	
Independent reflections	3195 [R(int) = 0.0498]	
Completeness to theta = 25.000°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9705 and 0.9044	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3195 / 0 / 176	
Goodness-of-fit on F ²	1.035	

Final R indices [$I > 2\sigma(I)$]	R1 = 0.0347, wR2 = 0.0777
R indices (all data)	R1 = 0.0495, wR2 = 0.0877
Extinction coefficient	0.0029(7)
Largest diff. peak and hole	0.309 and -0.181 e.Å ⁻³

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{Å}^2 \times 10^3$) for i15955. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
O(1)	7935(1)	5323(1)	3980(1)	22(1)
O(2)	5524(1)	6117(1)	6245(1)	23(1)
O(3)	5433(1)	4495(1)	7417(1)	21(1)
N(1)	8684(1)	5050(1)	6606(1)	16(1)
C(1)	8351(1)	5730(1)	7566(1)	19(1)
C(2)	9472(1)	5654(1)	8434(1)	22(1)
C(3)	10085(1)	4429(1)	8136(1)	23(1)
C(4)	9293(1)	3919(1)	7103(1)	20(1)
C(5)	7736(1)	4829(1)	5673(1)	15(1)
C(6)	8241(1)	4213(1)	4673(1)	16(1)
C(7)	7477(1)	5988(1)	4879(1)	16(1)
C(8)	8130(1)	7179(1)	5185(1)	20(1)
C(9)	7616(1)	8284(1)	5218(1)	29(1)
C(10)	6613(1)	4207(1)	6001(1)	18(1)
C(11)	5821(1)	5068(1)	6550(1)	17(1)
C(12)	4619(1)	5226(1)	7971(1)	24(1)
C(13)	7720(1)	3017(1)	4117(1)	18(1)
C(14)	8058(1)	1873(1)	4861(1)	21(1)
C(15)	8156(1)	2841(1)	2994(1)	22(1)