Nucleophilic Substitution at Quaternary Carbon Stereocenters

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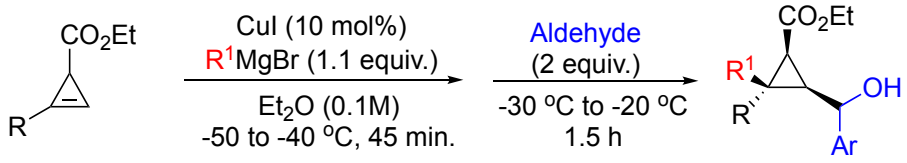
General information

All glassware was flame-dried under vacuum, and cooled under argon prior to use. Unless otherwise stated, all reactions were carried out under positive pressure of argon. Ether and THF were dried from Pure-Solv® Purification System (Innovative Technology©). The newly opened commercial grade dichloromethane was used directly. Copper iodide, copper cyanide, copper bromide dimethyl sulfide, rhodium acetate dimer, methyllithium (1.6 M in diethyl ether), butyllithium (1.6 M in hexane), *tert*-butyllithium (1.7 M in pentane) were purchased from Aldrich. Methylmagnesium bromide (3.0 M in diethyl ether) was purchased from Acros. Ethylmagnesium bromide (2.0 M in diethyl ether), was prepared according to literature and freshly titrated before using with butanol/1,10-phenanthroline. Anhydrous $CuBr_2$, purchased from Sigma Aldrich and used directly. Thin Layer Chromatography (TLC) was performed using Merck© silica gel 60 F254 plates. Column chromatography was performed using Bio-Labsilica gel 60A (0.040-0.063mm). ^{1}H-NMR and ^{13}C-NMR spectra were recorded on a Bruker©spectrometers AVIII400 or Bruker Avance 300 NMR using $CDCl_3$ (unless otherwise specified) as solvent. The GC chromatograms were recorded using Varian© 3800 apparatus with Varian© CP-Sil 8CB® column. HPLC chromatograms were recorded using Agilent© 1100 Series line with CHIRALPAK® OX-H or CHIRALCEL® AY-H.

General Procedure for Starting Materials[1]



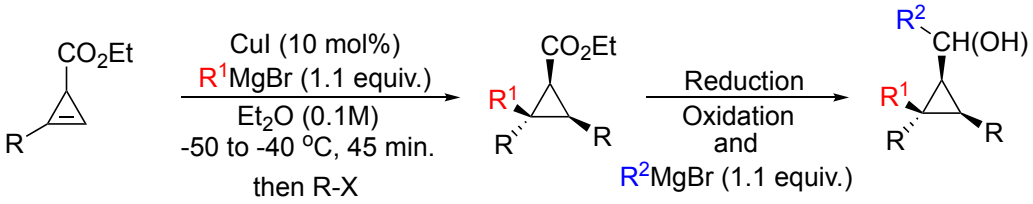
All the starting materials (**1a** to **1p**) were prepared according to the previously developed protocols in our group[1] by modifying the nature of the electrophiles (to aldehydes).

Cyclopropene (1 equiv.) was added to a suspension of CuI (10 mol%) in Et_2O (0.1 M) and alkyl magnesium bromide (1.1 equiv.) was added dropwise at -50 °C. The resulting mixture (yellowish) was then stirred at -50 to -35 °C for 45 minutes. Then, aldehyde (1.5 equiv.) was added and the reaction mixture was warmed to -35 to -20 °C during a period of 1.5 h. An aqueous saturated solution of NH_4Cl was then added. The aqueous layer was extracted twice with Et_2O. The combined organic phases were washed with brine, dried over $NaSO_4$, filtered, and concentrated under reduced pressure. The crude mixture was purified by flash chromatography on silica gel by using a hexanes/Et_2O mixture to get pure products (the diastereomeric ratio on the three stereocenters on the cyclopropyl ring is >95:5:0:0 but the carbinol center is formed as two diastereomers in a 1:1 ratio).

Note: In most of the cases, the diastereomers were separated. In few cases, one of the diastereomer comes along with benzyl alcohol (addition of unreacted Grignard reagent with the aldehyde).

Scale of the reaction: It can be performed from 1 mmol to 50 mmol.

General procedure for the Synthesis of *1q* to *1t*[1,2]



The starting materials (**1q** to **1t**) were prepared according to the previously developed protocols in our group[2] by modifying the nature of the electrophile.

Reduction of the Ester

In a dry round-bottom flask containing the cyclopropyl ester (10 mmol) in 20 mL of THF was added dropwise a solution of DIBAL-H (12 mmol) in hexane (1 M soln.), over a 15 minutes period at 0 °C. When the addition was over, the reaction mixture was stirred for another 30 minutes at room temperature. After completion of the reaction (as monitored by TLC analysis), the reaction mixture was quenched with a saturated aqueous solution of NH_4Cl. The precipitate formed in the flask was dissolved by addition of a solution of 10 mol% HCl or Rochelle salt and the reaction mixture was extracted with Et_2O (3 x 25 mL), dried over $MgSO_4$, filtered and concentrated under vacuum to give the crude alcohol product which was further purified by column chromatography on silica gel using 20-30% diethyl ether in hexane as eluent.

Oxidation of Alcohol

In a round-bottom flask, a solution of cyclopropyl alcohol (5 mmol) and bis(acetoxy)iodobenzene (BAIB) (1.5 equiv) in DCM (20 mL), was added at rt (2,2,6,6-tetramethyl-1-piperidin-1-yl)oxy (TEMPO) (10 mol%). The resulting reaction mixture was stirred for 2 to 4 h. After completion (as monitored by TLC analysis), the reaction mixture was diluted with DCM (20 mL) and washed with a saturated aqueous solution of $Na_2S_2O_3$ (20 mL). The aqueous layer was extracted with DCM (2 x 20 mL) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated under vacuum to give the crude aldehyde product which was further purified by column chromatography on silica gel using 5-10% Et_2O in hexane as eluent.

Characterization data for 1a to 1t.

Ethyl (1S, 2S, 3R)-2-butyl-3-((S)-hydroxy(phenyl)methyl)-2-methylcyclopropane-1-carboxylate (**1a**): **R_f** = 0.5 (ether/hexane = 20:80), colourless syrupy oil, 78% yield, 1:1 dr determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 4H), 7.28 – 7.25 (m, 4H), 7.23 – 7.19 (m, 1H), 7.18 – 7.17 (m, 1H), 5.15 (d, *J* = 9.1 Hz, 1H), 5.02 (d, *J* = 10.1 Hz, 1H), , 4.09 (q, *J* = 7.1 Hz, 2H), 3.96 (ddd, *J* = 9.8, 6.8, 3.2 Hz, 2H), 1.57 (d, *J* = 8.4 Hz, 1H), 1.45 – 1.38 (m, 4H), 1.36 (s, 3H), 1.20 (dd, *J* = 11.9, 4.8 Hz, 14H), 1.09 (t, *J* = 7.1 Hz, 6H), 0.82 (t, *J* = 7.2 Hz, 3H), 0.71 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 171.7, 144.4, 144.0, 128.4, 128.4, 127.4, 127.3, 126.2, 125.9, 125.4, 69.3, 69.0, 60.6, 60.1, 42.6, 42.1, 39.8, 39.7, 30.6, 30.2, 29.4, 29.3, 28.6, 28.2, 22.8, 22.5, 14.4, 14.3, 14.1, 14.0, 12.8, 11.9. HRMS (APCI) calcd. for $C_{18}H_{25}O_2$ [(M+H)-H_2O] 273.1849 found: 273.1853.

Ethyl (1S, 2R, 3R)-2-butyl-3-((S)-hydroxy(phenyl)methyl)-2-methylcyclopropane-1-carboxylate (**1b**): R_f = 0.5 (ether/hexane = 20:80), colourless syrupy oil, 72% yield, 1:1 dr determined by ^{1}H NMR (crude). Isolated both the diastereomers separately.^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.5 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 5.12 (dd, *J* = 10.1, 2.0 Hz, 1H), 4.09 (dddd, *J* = 17.9, 10.8, 7.1, 3.7 Hz, 2H), 2.78 (d, *J* = 3.1 Hz, 1H), 1.72 (ddd, *J* = 13.8, 11.3, 4.9 Hz, 1H), 1.60 (d, *J* = 8.3 Hz, 1H), 1.52 – 1.42 (m, 2H), 1.30 – 1.14 (m, 7H), 1.05 (s, 3H), 0.79 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 144.2, 128.4, 127.3, 126.1, 77.4, 77.1, 76.8, 68.9, 60.6, 41.1, 30.8, 29.5, 28.9, 28.6, 25.8, 23.0, 14.3, 14.1. HRMS (APCI) calcd. for $C_{18}H_{25}O_2$ [(M+H)-H_2O] 273.1849 found: 273.1853.

Ethyl (1S, 2S, 3R)-3-((S)-(4-bromophenyl)(hydroxy)methyl)-2-butyl-2-methylcyclopropane-1-carboxylate (**1c**): R_f = 0.5 (ether/hexane = 20:80), colourless syrupy oil, 74% yield, 1:1 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (dd, *J* = 8.4, 2.1 Hz, 2H), 7.34 (dd, *J* = 8.3, 2.5 Hz, 2H), 7.22 – 7.16 (m, 4H), 5.13 (dd, *J* = 9.7, 2.8 Hz, 1H), 4.97 (d, *J* = 10.0 Hz, 1H), 4.13 – 4.04 (m, 2H), 4.01 – 3.93 (m, 2H), 1.58 (dd, *J* = 8.3, 2.3 Hz, 1H), 1.45 (dd, *J* = 8.9, 2.2 Hz, 1H), 1.37 – 1.31 (m, 6H), 1.20 (ddd, *J* = 11.2, 8.0, 2.2 Hz, 13H), 1.14 – 1.08 (m, 5H), 0.86 – 0.77 (m, 5H), 0.76 – 0.70 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7, 171.6, 143.4, 143.1, 131.5, 131.4, 128.0, 127.7, 121.2, 121.1, 68.8, 68.4, 60.7, 60.2, 42.5, 42.0, 39.5, 30.6, 30.1, 29.4, 29.4, 28.6, 28.2, 22.7, 22.5, 14.3, 14.3, 14.1, 14.0, 12.9, 11.8. HRMS (APCI) calcd. for $C_{18}H_{24}BrO_2$ [(M+H)-H_2O] 351.0954 found: 351.0964.

Ethyl (1S, 2S, 3R)-3-((S)-benzo[d][1,3]dioxol-5-yl(hydroxy)methyl)-2-butyl-2-methylcyclopropane-1-carboxylate (**1d**): R_f = 0.5 (ether/hexane = 20:80), colourless syrupy oil, 70% yield, 1: 0.8 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.84 (dd, *J* = 4.4, 1.6 Hz, 2H), 6.76 (d, *J* = 1.6 Hz, 1H), 6.74 (d, *J* = 1.6 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.63 (d, *J* = 8.0 Hz, 1H), 5.85 (s, 2H), 5.82 (s, 2H), 5.05 (d, *J* = 9.7 Hz, 1H), 4.93 (d, *J* = 10.1 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 4.02 – 3.91 (m, 2H), 1.56 (d, *J* = 8.4 Hz, 1H), 1.43 (d, *J* = 9.0 Hz, 1H), 1.39 – 1.32 (m, 6H), 1.25 – 1.15 (m, 12H), 1.10 (td, *J* = 7.0, 2.9 Hz, 6H), 0.82 (t, *J* = 7.2 Hz, 4H), 0.73 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.6, 171.6, 147.7, 147.6, 146.7, 146.7, 138.5, 138.2, 119.5, 119.2, 108.0, 107.9, 106.8, 106.6, 100.9, 100.87,

69.1, 68.7, 60.5, 60.1, 42.5, 42.1, 39.7, 30.6, 30.0, 29.3, 29.1, 28.6, 28.2, 22.7, 22.5, 14.3, 14.3, 14.1, 134.0, 12.7, 11.8. HRMS (APCI) calcd. for $C_{19}H_{25}O_4$ [(M+H)-H_2O] 317.1747 found: 317.1764.

Ethyl (1S, 2S, 3R)-2-butyl-3-((S)-hydroxy(naphthalen-1-yl)methyl)-2-methylcyclopropane-1-carboxylate (**1e**): R_f = 0.5 (ether/hexane = 20:80), colourless syrupy oil, 76% yield, 1:1 dr by crude NMR, but isolated as one of the major isomers (44% Yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 8.4 Hz, 1H), 7.91 – 7.84 (m, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.58 (d, *J* = 6.4 Hz, 1H), 7.55 – 7.43 (m, 3H), 5.82 (dd, *J* = 10.0, 3.1 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.87 (d, *J* = 3.7 Hz, 1H), 1.97 (dd, *J* = 10.0, 8.4 Hz, 1H), 1.77 (d, *J* = 8.4 Hz, 1H), 1.71 – 1.61 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.30 – 1.23 (m, 2H), 1.18 (s, 3H), 1.13 – 1.05 (m, 2H), 0.74 (t, *J* = 7.1 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ 172.9, 138.9, 134.3, 131.2, 128.8, 128.5, 128.3, 126.0, 125.6, 125.3, 124.7, 124.2, 67.7, 60.7, 42.1, 38.3, 30.4, 29.2, 28.2, 22.4, 14.4, 13.9, 12.4. HRMS (APCI) calcd. for $C_{22}H_{27}O_2$ [(M+H)-H_2O] 323.2006 found: 323.2002.

Ethyl (1S, 2S, 3R)-2-butyl-3-((S)-(2,4-difluorophenyl)(hydroxy)methyl)-2-methylcyclopropane-1-carboxylate (**1f**): R_f = 0.5 (ether/hexane = 20:80), colourless syrupy oil, [Crude-65% yield, 1:1 dr]. Isolated as a one of the single isomers, 42% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dt, *J* = 17.4, 9.6 Hz, 1H), 6.82 (t, *J* = 8.4 Hz, 1H), 6.75 – 6.67 (m, 1H), 5.26 (dd, *J* = 10.0, 3.5 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.02 (d, *J* = 3.3 Hz, 1H), 1.59 (d, *J* = 8.3 Hz, 1H), 1.46 – 1.39 (m, 2H), 1.22 (t, *J* = 7.1 Hz, 5H), 1.14 (d, *J* = 1.1 Hz, 3H), 1.09 – 1.04 (m, 3H), 0.83 (t, *J* = 7.2 Hz, 1H), 0.72 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ δ 172.0 (d, *J* = 162.7 Hz), 161.0 (d, *J* = 12.0 Hz), 128.9 (dd, *J* = 9.7, 6.4 Hz), 111.5 (dd, *J* = 21.0, 3.6 Hz), 103.7 (t, *J* = 25.7 Hz), 63.9 (d, *J* = 2.7 Hz), 60.5 (d, *J* = 58.6 Hz), 42.1, 38.8, 30.4, 29.6, 28.2, 22.4, 14.4, 13.9, 12.3 (d, *J* = 3.5 Hz). HRMS (APCI) calcd. for $C_{18}H_{23}F_2O_2$ [(M+H)-H_2O] 309.1661 found: 309.1677.

Ethyl (1S, 2S, 3R)-2-butyl-3-((S)-furan-2-yl(hydroxy)methyl)-2-methylcyclopropane-1-carboxylate (**1g**): R_f = 0.4 (ether/hexane = 20:80), colourless syrupy oil, 46% yield, 1:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 14.1 Hz, 2H), 6.25 (d, *J* = 17.8 Hz, 2H), 6.16 (dd, *J* = 19.4, 2.9 Hz, 2H), 5.18 (dd, *J* = 9.5, 4.6 Hz, 1H), 5.10 (dd, *J* = 9.8, 4.2 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.96 (p, *J* = 6.9 Hz, 2H), 2.57 (d, *J* = 4.0 Hz, 1H), 2.16 (dt, *J* = 21.5, 9.1 Hz, 2H), 1.91 (d, *J* = 4.9 Hz, 1H), 1.59 (dd, *J* = 6.6, 3.7 Hz, 1H), 1.54 (s, 3H), 1.33 (s, 3H), 1.23 (dd, *J* = 13.3, 6.3 Hz, 10H), 1.10 (t, *J* = 7.1 Hz, 6H), 0.81 (dt, *J* = 20.8, 7.0 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.4, 171.1, 156.0, 142.1, 142.1, 110.1, 105.9, 63.7, 63.4, 60.6, 60.1, 42.4, 42.1, 36.2, 35.7, 29.91, 29.86, 29.3, 28.8, 28.7, 28.2, 22.8, 22.558, 14.4, 14.3, 14.12, 14.07 12.2, 11.6. HRMS (APCI) calcd. for $C_{16}H_{23}O_3$ [(M+H)-H_2O] 263.1642 found: 263.1651.

Ethyl (1S, 2S, 3R)-2-butyl-3-((S)-1-hydroxy-3-phenylprop-2-yn-1-yl)-2-methylcyclopropane-1-carboxylate (**1h**): R_f = 0.6 (ether/hexane = 20:80), colourless syrupy oil, 62% yield, 1:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 6.6, 3.0 Hz, 2H), 7.19 (dd, *J* = 5.0, 1.6 Hz, 3H), 5.02 (d, *J* = 9.6 Hz, 1H), 4.04 (dddd, *J* = 17.8, 10.8, 7.1, 3.7 Hz, 2H), 1.59 (d, *J* = 9.0 Hz, 1H), 1.52 (t, *J* = 9.3 Hz, 1H), 1.32 (dd, *J* = 12.4, 6.0 Hz, 2H), 1.26 (s, 3H), 1.24 – 1.18 (m, 3H), 1.14 (d, *J* = 7.1 Hz, 4H), 0.82 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.2, 171.1, 131.8, 131.7, 128.3, 128.2, 60.6, 60.3, 59.0, 42.2, 42.2, 38.3, 38.1, 30.5, 29.3, 28.6, 22.7, 14.4, 14.2, 14.1, 12.1, 11.5. HRMS (APCI) calcd. for $C_{20}H_{25}O_2$ [(M+H)-H_2O] 297.1849 found: 297.1830.

Ethyl (1S, 2S, 3R)-2-butyl-3-((S)-1-hydroxy-3-(triisopropylsilyl)prop-2-yn-1-yl)-2 methylcyclopropane-1-carboxylate (**1i**): R_f = 0.5 (ether/hexane = 20:80), colourless syrupy oil, 48% yield, single diastereomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.81 (dd, *J* = 9.8, 4.6 Hz, 1H), 4.06 (q, *J* = 7.1 Hz, 2H), 2.21 (d, *J* = 4.6 Hz, 1H), 1.55 – 1.48 (m, 2H), 1.37 – 1.29 (m, 3H), 1.20 (t, *J* = 7.1 Hz, 5H), 1.16 (s, 3H), 1.03 – 0.94 (m, 21H), 0.81 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.0, 107.8, 84.6, 60.5, 58.9, 42.3, 38.2, 29.7, 29.0, 28.6, 22.8, 18.6, 14.3, 14.1, 12.0, 11.2. HRMS (APCI) calcd. for $C_{23}H_{41}O_2Si$ [(M+H)-H_2O] 377.2870 found: 377.2896.

Ethyl (1S, 2S, 3R)-2-hexyl-3-((S)-hydroxy(phenyl)methyl)-2-methylcyclopropane-1-carboxylate (**1j**): R_f = 0.6 (ether/hexane = 20:80), colourless syrupy oil, 72% yield, 1:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.31 (m, 2H), 7.29 – 7.23 (m, 2H), 7.21 – 7.18 (m, 1H), 5.20 (dd, *J* = 9.3, 3.4 Hz, 1H), 4.04 – 3.95 (m, 2H), 1.79 (d, *J* = 3.5 Hz, 1H), 1.47 (d, *J* = 9.0 Hz, 1H), 1.38 (s, 3H), 1.24 – 1.18 (m, 7H), 1.11

(t, *J* = 7.1 Hz, 3H), 0.85 – 0.78 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 144.3, 128.4, 127.5, 126.2, 69.1, 60.1, 42.8, 39.7, 31.9, 30.6, 29.5, 29.3, 26.5, 22.7, 14.3, 14.12 11.9. HRMS (APCI) calcd. for $C_{20}H_{27}O_3$ [(M+H)-H_2O] 315.1955 found: 315.1969.

Ethyl (1S, 2S, 3R)-2-(2-(benzyloxy)ethyl)-3-((S)-hydroxy(phenyl)methyl)-2-methylcyclopropane-1-carboxylate (**1k**): R_f = 0.4 (ether/hexane = 35:65), colourless syrupy oil, 64% yield, 1:0.9 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (s, 2H), 7.31 – 7.15 (m, 18H), 5.14 (d, *J* = 9.0 Hz, 1H), 5.04 (d, *J* = 10.1 Hz, 1H), 4.47 (s, 2H), 4.25 (s, 2H), 4.12 (tt, *J* = 7.1, 3.5 Hz, 2H), 4.04 – 3.96 (m, 2H), 3.68 (td, *J* = 9.2, 5.3 Hz, 1H), 3.57 – 3.50 (m, 1H), 3.40 (q, *J* = 7.0 Hz, 4H), 3.35 – 3.22 (m, 2H), 1.87 – 1.77 (m, 1H), 1.72 (d, *J* = 8.5 Hz, 1H), 1.63 (dd, *J* = 14.0, 7.1 Hz, 1H), 1.54 – 1.46 (m, 1H), 1.40 (s, 3H), 1.24 (s, 3H), 1.13 (td, *J* = 7.1, 4.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.5, 171.4, 144.4, 143.9, 138.3, 137.9, 128.53, 128.50, 128.436, 128.3, 128.0, 127.9, 127.6, 127.5, 127.4, 127.3, 126.1, 125.9, 73.4, 73.0, 69.4, 70.0, 68.0, 67.7, 65.9, 60.7, 60.2, 41.8, 41.7, 40.0, 39.0, 29.4, 29.1, 28.1, 27.4, 15.3, 14.4, 14.3, 13.5, 11.5. HRMS (APCI) calcd. for $C_{23}H_{27}O_3$ [(M+H)-H_2O] 351.1955 found: 351.1980.

Ethyl (1S, 2S, 3R)-2-butyl-3-((R)-1-hydroxyallyl)-2-methylcyclopropane-1-carboxylate (**1l**): R_f = 0.5 (ether/hexane = 15:85), colourless syrupy oil, 65% yield, 1:0.75 dr. ^{1}H NMR (400 MHz, CDCl3) δ 5.85 (dddd, J = 16.2, 12.8, 10.5, 5.5 Hz, 2H), 5.28 – 5.13 (m, 2H), 5.05 (d, J = 10.5 Hz, 1H), 4.99 (d, J = 10.5 Hz, 1H), 4.57 (dd, J = 9.6, 5.5 Hz, 1H), 4.48 (dd, J = 9.7, 5.6 Hz, 1H), 4.15 – 3.92 (m, 4H), 2.47 (s, 1H), 1.84 (s, 1H), 1.50 (t, J = 8.5 Hz, 2H), 1.36 – 1.09 (m, 22H), 0.88 – 0.77 (m, 6H). ^{13}C NMR (101 MHz, CDCl3) δ 172.4, 171.4, 140.3, 140.1, 114.3, 114.0, 68.3, 67.9, 60.4, 60.1, 42.4, 42.2, 37.5, 37.4, 29.7, 29.6, 29.0, 28.7, 28.6, 28.4, 22.7, 22.7, 14.4, 14.3, 14.1, 14.0, 12.3, 11.7. HRMS (APCI) calcd. for $C_{14}H_{23}O_2$ [(M+H)-H_2O] 223.1693 found: 223.1690.

Ethyl (1S, 2S, 3R)-2-butyl-3-((R)-(4-((S)-((1S,2S,3S)-2-butyl-3-(ethoxycarbonyl)-2-methylcyclopropyl)(hydroxy)methyl)phenyl)(hydroxy)methyl)-2-methylcyclopropane-1-carboxylate (**1m**): R_f = 0.5 (ether/hexane = 60:40), colourless syrupy oil, 30% yield, 1:2.5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.26 (m, 7H(2+5)), 5.18 (d, *J* = 8.6 Hz, 1H), 5.03 (t, *J* = 9.9 Hz, 2.5H), 4.12 (q, *J* = 7.1 Hz, 5H), 4.04 – 3.90 (m, 2H), 2.72 (s, 2H), 1.60 (d, *J* = 8.3 Hz, 2H), 1.46 – 1.34 (m, 10H), 1.25 – 1.16 (m, 23H), 1.13 – 1.06 (m, 10H), 0.86 – 0.78 (m, 6H), 0.73 (t, *J* = 6.7 Hz, 8H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.8, 171.6, 143.1, 143.0, 126.3, 126.0, 125.9, 69.3, 68.9, 60.6, 60.1, 42.6, 42.1, 39.7, 39.7, 30.6, 30.2, 29.5, 29.3, 28.7, 28.2, 22.8, 22.6, 14.39, 14.35, 14.1, 14.0, 12.9, 11.9. HRMS (APCI) calcd. for $C_{30}H_{45}O_5$ [(M+H)-H_2O] 485.3262 found: 485.3246.

Benzyl (1S, 2S, 3R)-2-butyl-3-((R)-hydroxy(phenyl)methyl)-2-methylcyclopropane-1-carboxylate (**1n**): R_f = 0.2 (ether/hexane = 20:80), colourless syrupy oil, 65 % yield, 0.66:0.33 dr, isolated as a major single diastereomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.22 (m, 5H), 7.22 – 7.15 (m, 5H), 5.17 (dd, *J* = 9.8, 2.7 Hz, 1H), 5.04 (d, *J* = 12.4 Hz, 1H), 4.91 (d, *J* = 12.4 Hz, 1H), 1.81 (s, 1H), 1.53 (d, *J* = 9.0 Hz, 1H), 1.44 (t, *J* = 9.4 Hz, 1H), 1.38 (s, 3H), 1.37 – 1.31 (m, 2H), 1.31 – 1.20 (m, 4H), 0.82 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.5, 144.2, 136.3, 128.5, 128.5, 128.2, 128.1, 127.5, 126.2, 69.0, 70.0, 42.5, 40.0, 31.1, 29.4, 28.7, 22.8, 14.1, 12.0. HRMS (APCI) calcd. for $C_{23}H_{27}O_2$ [(M+H)-H_2O] 335.2006 found: 335.2010.

(S)-((1R, 2R, 3S)-2-butyl-3-(hydroxymethyl)-2-methylcyclopropyl)(phenyl)methanol (**1o**): R_f = 0.4 (ether/hexane = 50:50), colourless syrupy oil, 85% yield, single diastereomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 2H), 7.22 (dd, *J* = 8.3, 6.0 Hz, 1H), 4.41 (d, *J* = 10.3 Hz, 1H), 3.58 (d, *J* = 6.2 Hz, 2H), 1.81 (s, 1H), 1.63 (s, 1H), 1.37 – 1.30 (m, 2H), 1.27 – 1.18 (m, 7H), 1.13 – 1.06 (m, 1H), 0.90 (t, *J* = 7.4 Hz, 1H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.3, 128.8, 127.9, 126.2, 77.4, 77.1, 76.8, 71.7, 60.1, 42.6, 34.9, 29.5, 29.0, 23.6, 22.9, 14.2, 12.5. HRMS (APCI) calcd. for $C_{16}H_{23}O_2$ [(M+H)-H_2O] 247.1693 found: 247.1704.

Ethyl (1S,2R,3R)-2-butyl-3-((R)-hydroxy(phenyl)methyl)-2-phenylcyclopropane-1-carboxylate (**1p**): Rf = 0.5 (ether/hexane = 20:80), colourless syrupy oil, 59% yield, 80:20 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.04 (m, 10H), 4.92 (d, *J* = 7.7 Hz, 1H), 3.94 – 3.69 (m, 2H), 2.00 (s, 1H), 1.83 (d, *J* = 7.5 Hz, 2H), 1.66 (t, *J* = 11.8 Hz, 1H), 1.36 (d, *J* = 13.0 Hz, 1H), 1.31 – 1.08 (m, 4H), 0.91 (t, *J* = 6.7 Hz, 3H), 0.75 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 144.2, 137.5, 130.8, 128.4, 128.1, 127.7, 126.9,

126.6, 70.0, 60.1, 44.7, 41.2, 38.9, 30.1, 28.8, 22.6, 14.1, 14.1. HRMS (APCI) calcd. for $C_{23}H_{27}O_2$ [(M+H)-H_2O] 335.2010 found: 335.2014.

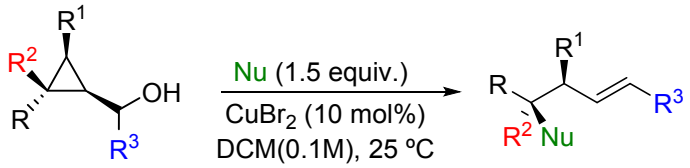
(S)-((1R, 2R, 3S)-3-allyl-2-butyl-2-methylcyclopropyl)(4-methoxyphenyl)methanol (**1q**): R_f = 0.4 (ether/hexane = 20:80), colourless syrupy oil, 70% yield (over two steps-Oxidation and reduction), 1:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.22 (m, 4H), 6.81 (dd, *J* = 8.7, 1.5 Hz, 4H), 6.03 – 5.91 (m, 1H), 5.71 – 5.57 (m, 1H), 5.18 – 5.09 (m, 1H), 5.04 – 4.97 (m, 1H), 4.90 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.83 (dd, *J* = 10.2, 1.8 Hz, 1H), 4.35 (d, *J* = 5.1 Hz, 1H), 4.33 (d, *J* = 5.1 Hz, 1H), 3.73 (s, 6H), 2.27 – 2.20 (m, 2H), 2.04 (ddd, *J* = 7.0, 6.3, 1.2 Hz, 1H), 1.98 – 1.87 (m, 1H), 1.81 (s, 1H), 1.63 (s, 1H), 1.31 (dd, *J* = 10.2, 4.7 Hz, 2H), 1.22 (ddd, *J* = 11.7, 8.6, 5.1 Hz, 4H), 1.12 (s, 3H), 1.07 (dd, *J* = 8.5, 4.2 Hz, 6H), 0.97 (dd, *J* = 6.3, 4.0 Hz, 2H), 0.89 (s, 3H), 0.83 (t, *J* = 7.2 Hz, 3H), 0.78 (dd, *J* = 8.4, 2.0 Hz, 2H), 0.74 – 0.70 (m, 3H), 0.62 (td, *J* = 9.5, 5.3 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 158.9, 139.2, 138.2, 136.8, 136.5, 127.6, 127.4, 116.1, 114.8, 114.7, 114.5, 113.8, 113.7, 71.6, 71.1, 55.3, 55.3, 42.9, 42.8, 33.9, 33.8, 29.2, 29.0, 28.9, 28.4, 26.6, 25.4, 23.0, 22.9, 22.8, 22.6, 14.2, 14.1, 13.1, 12.5. HRMS (APCI) calcd. for $C_{19}H_{27}O$ [(M+H)-H_2O] 271.2056 found: 271.2077.

(S)-((1R, 2R, 3S)-2-butyl-2,3-dimethylcyclopropyl)(4-methoxyphenyl)methanol (**1r**): R_f = 0.4 (ether/hexane = 20:80), colourless syrupy oil, 68% yield (over two steps-Oxidation and reduction), 1:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.22 (m, 4H), 6.83 – 6.76 (m, 4H), 4.20 (s, 1H), 4.18 (s, 1H), 3.72 (s, 3H), 1.74 (s, 2H, -OH), 1.58 (dd, *J* = 12.9, 10.2 Hz, 1H), 1.45 (ddd, *J* = 9.8, 4.8, 2.7 Hz, 1H), 1.32 – 1.17 (m, 8H), 1.06 (d, *J* = 6.2 Hz, 3H), 0.99 (s, 3H), 0.93 – 0.83 (m, 10H), 0.79 (dd, *J* = 7.9, 6.0 Hz, 4H), 0.55 (ddd, *J* = 19.6, 9.6, 5.4 Hz, 1H), 0.47 – 0.39 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 137.2, 137.1, 127.4, 127.0, 113.7, 74.9, 74.5, 55.3, 40.6, 40.2, 36.2, 35.8, 29.3, 29.2, 24.6, 24.5, 23.2, 23.1, 23.99, 22.88, 19.0, 18.7, 14.3, 14.2, 13.9, 13.2. HRMS (APCI) calcd. for $C_{17}H_{25}O$ [(M+H)-H_2O]: 245.1900 found: 245.1889.

(S)-((1R, 2R)-2-butyl-2-methylcyclopropyl)(4-methoxyphenyl)methanol (**1s**): Rf = 0.3 (ether/hexane = 15:85), colourless syrupy oil, 78% yield (over two steps- Oxidation and reduction), 1:1 dr-crude NMR, (isolated as a 1:0.7 dr., may be manual error in isolating separately and combined them). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (dd, *J* = 10.3, 8.1 Hz, 4H), 6.80 (dd, *J* = 8.7, 2.0 Hz, 4H), 4.12 (t, *J* = 9.1 Hz, 2H), 3.72 (d, *J* = 3.2 Hz, 6H), 1.25 (ddd, *J* = 21.5, 12.4, 6.1 Hz, 4H), 1.17 (s, 3H), 1.15 – 1.02 (m, 8H), 0.99 – 0.95 (m, 4H), 0.95 – 0.86 (m, 2H), 0.82 (dd, *J* = 9.1, 5.2 Hz, 3H), 0.73 (t, *J* = 6.8 Hz, 4H), 0.54 (dd, *J* = 8.3, 4.4 Hz, 1H), 0.42 (dd, *J* = 8.8, 4.7 Hz, 1H), 0.32 (t, *J* = 4.9 Hz, 1H), 0.14 (t, *J* = 5.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 136.9, 127.3, 127.1, 113.8, 75.5, 74.9, 55.3, 40.9, 32.3, 31.9, 29.1, 28.6, 23.0, 22.8, 21.2, 20.8, 18.5, 18.3, 18.2, 17.6, 14.2, 14.1. HRMS (APCI) calcd. for $C_{16}H_{23}O$ [(M+H)-H_2O] 231.1743 found: 231.1765.

2-((1R, 2R, 3S)-2-butyl-2-methyl-3-(2-phenylallyl)cyclopropyl)propan-2-ol (**1t**): Prepared according to the general procedure with (3-bromoprop-1-en-2-yl)benzene as electrophile, and the second step is direct addition of 2.5 equiv. of MeMgBr. R_f = 0.5 (ether/hexane = 15:85), colourless syrupy oil, 85% yield, single diastereomer. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 7.7 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 2H), 7.21 – 7.16 (m, 1H), 5.25 (s, 1H), 5.11 (s, 1H), 2.83 (dd, *J* = 17.0, 8.3 Hz, 1H), 2.73 (dd, *J* = 16.9, 6.2 Hz, 1H), 1.28 (s, 4H), 1.26 (s, 4H), 1.23 – 1.14 (m, 3H), 1.13 (s, 3H), 0.99 (d, *J* = 1.4 Hz, 1H), 0.90 (d, *J* = 9.6 Hz, 1H), 0.80 (t, *J* = 7.0 Hz, 3H), 0.72 (dd, *J* = 15.3, 8.8 Hz, 1H), 0.40 (d, *J* = 9.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.9, 142.3, 128.2, 127.3, 126.2, 111.9, 71.9, 44.9, 35.7, 32.9, 31.8, 30.0, 28.9, 26.3, 23.1, 22.4, 14.2, 12.5. HRMS (APCI) calcd. for $C_{20}H_{29}$ [(M+H)-H_2O] 269.2264 found: 269.2276.

General Procedure for Nucleophilic Substitution at the Quaternary Carbon Stereocenters

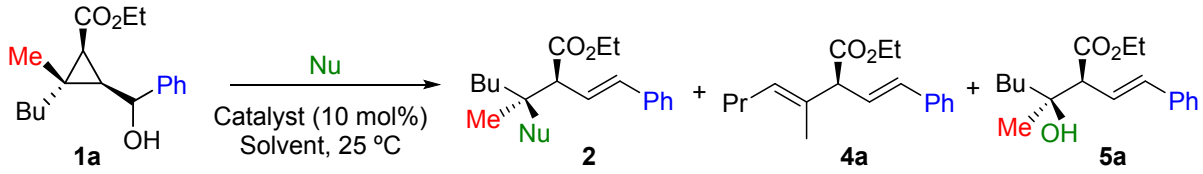


Procedure for Halogenation To a 15 mL oven dried (or flame dried) Schlenk tube, purged with argon, was added $CuBr_2$ (10 mol%) in 2 mL of dichloromethane and sealed with a septum. Then, a solution of cyclopropane carbinol in 1 mL of DCM (0.3 mmol, 1 equiv.) was added with a syringe followed by a dropwise addition of the nucleophile (TMSBr /TMSCl /48% aq. HBF_4) (0.45 mmol, 1.5 equiv.) in one minute at room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with a saturated solution of NH_4Cl (saturated Na_2CO_3 soln. in the case of fluorination) and diluted with DCM. The organic layers were extracted with DCM (3 X 20 mL) dried over $MgSO_4$, filtered and concentrated under vacuum to give the halogenated product, further purified by column chromatography when needed.

Procedure for carboxylation/hydroxylation In a 15 mL dry Schlenk tube containing trichloroacetic acid (1.5 equiv.) in 2 mL of DCM, was added the cyclopropane carbinol derivative (0.3 mmol, 1.0 equiv.) in 1 mL DCM. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with an aqueous saturated solution of NH_4Cl (5mL) and diluted with DCM. The organic layers were washed with saturated solution of Na_2CO_3 (10 mL) and extracted with DCM (3 X 20 mL) dried over $MgSO_4$, filtered and concentrated under vacuum to give the carboxylated product, further purified by column chromatography when needed.

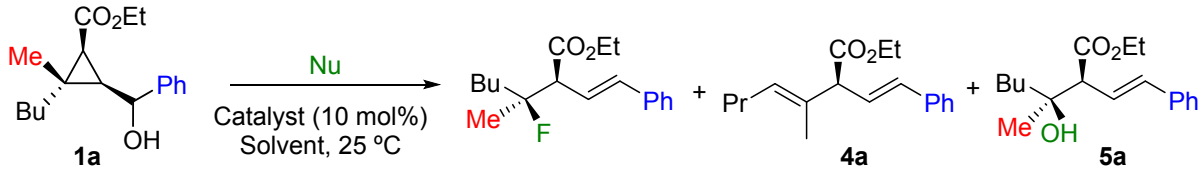
Scale of the reaction: tested up to 5 mmol.

Optimization Table



S. No	Halogen source (equiv.)	Catalyst (mol%)	Solvent (M)	Temp/h ° C	Product (%) 2 + 4a + 5a
1	48% HBr (1.5)	48% HBr	DCM (0.1M)	rt/12h	15 (dr.98:2) + 10 + 08
2	48% HBr (1.5)	PTSA.H_2O	DCM (0.1M)	rt/12h	30 (dr.95:5) + 15 + 10
3	TMSBr (1.5)	PTSA.H_2O	DCM (0.1M)	rt/12h	45 (dr.95:5) + 10 + 04
4	TBAB (1.5)	PTSA.H_2O	DCM (0.1M)	rt/12h	00 + 45 + 15
5	***TMSBr (1.5)***	***$InBr_3$ (10)***	***DCM (0.1M)***	***rt/20 min***	***84 (dr.98:2) + 00 + 02***
6	TMSBr (1.5)	$InBr_3$ (10)	DCM (0.1M)	0/35 min	85 (dr.98:2) + 00 +02
7	TMSBr (1.5)	-	DCM (0.1M)	rt/24h	45 (dr.98:2) + 35 +00
8	TMSBr (1.5)	$InCl_3$(10)	DCM (0.1M)	rt/25 min	84(dr.98:2) + 00 + 00
9	TMSBr (1.5)	$FeCl_3$ (10)	DCM (0.1M)	rt/25 min	80 (dr.75:25) + 10 +02
10	***TMSBr (1.5)***	***$CuBr_2$ (10)***	***DCM (0.1M)***	***rt/ 2h***	***83 (dr.98:2) + 00 + 02***
11	TMSBr (1.5)	$Bi(OTf)_3$(10)	DCM (0.1M)	rt/25 min	70 (dr.65:35) + 15 + 00
12	TMSBr (1.5)	$FeCl_2$ (10)	DCM (0.1M)	rt/25 min	75 (dr.85:15) +10 + 00
13	TMSBr (1.5)	$Cu(OTf)_3$(10)	DCM (0.1M)	**rt/ 2h**	54 (dr.95: 5) + 00 +02
14	TMSCl (1.5)	$CuBr_2$ (10)	DCM (0.1M)	rt/ *2h*	76(dr.98:2) + 05 + 00
15	TFA (1.5)	-	DCM (0.1M)	rt/ *2h*	65(dr.98:2) + 11 + 10
16	TCA (1.5)	-	DCM (0.1M)	rt/ *2h*	67(dr.98:2) + 10 + 10
17	***48% aq.HBF4 (2)***	***$CuBr_2$ (10)***	***DCM (0.1M)***	***rt/ 2h***	***52(dr.98:2) + 05 + 20***
18	48% aq.HBF4 (2)	-	DCM (0.1M)	rt/ *12h*	40(dr.98:2) + 10 + 25

Optimization for the fluorination reaction



S.No	Reaction Conditions	F/OH/EP
1	48% aq. HBF_4 (2equiv), DCM (0.1M), rt, 6h	45/15/5
2	48% aq. HBF_4 (2equiv), CuBr(II) (10 mol%), DCM (0.1M), rt, 1h	55/14/5
3	48% aq. HBF_4 (1equiv), CuBr(II) (10 mol%), DCM (0.1M), rt, 2h	48/12/5
4	48% aq. HBF_4 (1equiv), DCM (0.1M), rt, 6h	46/14/5
6	48% aq. HBF_4 (2equiv), DCM (0.1M), rt, 6h, Argon atm.	52/16/5
7	48% aq. HBF_4 (2equiv), DCM (0.1M), -15 °C, 7h	25/20/41
8	NH_4BF_4 (1equiv), DCM (0.1M), RT, 6h	nr
9	$HBF_4.Et_2O$ (2equiv), DCM (0.1M), RT, 2h	00/00/(47+45)
10	$HBF_4.Et_2O$ (1equiv), DCM (0.1M), -30 °C, 4h	26/4/35
11	KF (2 equiv.), CuBr(II) (10 mol%), DCM (0.1M), rt, 12h	No reaction
12	TBAF(1.2equiv), CuBr(II) (10 mol%), DCM (0.1M), rt, 1h	Complex mixture
13	TBAF(1.2equiv), CuBr(II) (10 mol%), DCM (0.1M), at 0 °C, 3h	Complex mixture

NMR Yield – After work-up, 1 equiv. of *p*-methoxy acetophenone was added into the round bottom flask containing the combined organic layers from the work-up. Either an aliquot from the round bottom flask was taken, evaporated and then submitted to NMR or the organic layer was completely evaporated and the residue was dissolved in an appropriate amount of solvent ($CDCl_3$) to record the NMR. The aromatic protons of p-methoxy acetophenone and the olefinic protons of our product were well distinguished and the integrations could serve as inrenal standard (sample spectrum see at SI-19).

Determination of Diastereomeric ratio

The diastereomeric ratios were determined by ^{1}H NMR spectrum. As can be seen in scheme 2, the two diastereomers **2m** and **2n** were independently prepared and analysis of their NMR (^{1}H,^{13}C and ^{19}F) shows major differences. For all other addition of nucleophiles, allylic hydrogens of the two diastereomers are well distinguished by ^{1}H NMR (see sample spectrum at SI-20).

Characterization data of new compounds

Ethyl (2R, 3S)-3-bromo-3-methyl-2-((E)-styryl)heptanoate (**2a**): R_f = 0.6 (ether/hexane = 05:95), colourless thick oil, 78% yield, 95:5 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 2H), 7.26 (t, *J* = 7.3 Hz, 2H), 7.22 – 7.18 (m, 1H), 6.49 (d, *J* = 15.8 Hz, 1H), 6.25 (dd, *J* = 15.8, 9.6 Hz, 1H), 4.14 (dddd, *J* = 18.0, 10.8, 7.1, 3.7 Hz, 2H), 3.58 (d, *J* = 9.6 Hz, 1H), 1.85 – 1.79 (m, 5H), 1.48 (ddd, *J* = 16.8, 9.1, 6.0 Hz, 2H), 1.30 – 1.19 (m, 5H), 0.87 (t, *J* = 5.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 136.3, 135.1, 128.7, 128.1, 126.6, 124.0, 70.6, 61.5, 61.0, 43.4, 28.5, 27.8, 22.7, 14.2,14.1. HRMS (APCI) calcd. for $C_{18}H_{26}BrO_2$ [M+H]: 353.1116found: 353.1131.

Ethyl (2R, 3S)-3-bromo-2-((E)-4-bromostyryl)-3-methylheptanoate (**2b**): R_f = 0.5 (ether/hexane = 05:95), colourless thick oil, 80% yield, 95:5 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.2 Hz, 2H), 6.41 (d, *J* = 15.9 Hz, 1H), 6.24 (dd, *J* = 15.8, 9.5 Hz, 1H), 4.19 – 4.05 (m, 2H), 3.54 (d, *J* = 9.5 Hz, 1H), 2.21 – 2.09 (m, 4H), 1.79 (s, 3H), 1.29 – 1.15 (m, 5H), 0.85 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 135.3, 133.9, 131.8, 128.1, 124.9, 121.9, 70.6, 61.4, 61.1, 43.3, 28.6, 27.8, 22.7, 14.2, 14.1. HRMS (APCI) calcd. for $C_{18}H_{25}Br_2O_2$ [M+H]: 431.0216 found: 431.0239.

Ethyl (2R, 3S)-2-((E)-2-(benzo[d][1,3] dioxol-5-yl)vinyl)-3-bromo-3-methylheptanoate (**2c**): R_f = 0.4 (ether/hexane = 05:95), colourless thick oil, 75% yield, 95:5 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (d, *J* = 1.0 Hz, 1H), 6.75 (d, *J* = 8.1 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.39 (d, *J* = 15.8 Hz, 1H), 6.06 (dd, *J* = 15.8, 9.6 Hz, 1H), 5.89 (s, 2H), 4.21 – 4.03 (m, 2H), 3.53 (d, *J* = 9.6 Hz, 1H), 1.87 – 1.74 (m, 5H(3+2)), 1.47 (d, *J* = 7.4 Hz, 2H), 1.24 (ddt, *J* = 17.2, 12.0, 8.8 Hz, 5H), 0.85 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 148.1, 147.6, 134.7, 130.8, 122.1, 121.5, 108.3, 105.8, 101.2, 70.8, 61.4, 61.0, 43.3, 28.4, 27.8, 22.7, 14.2, 14.1 HRMS (APCI) calcd. for $C_{19}H_{26}BrO_4$ [M+H]: 397.1014 found: 397.1000.

Ethyl (2R, 3R)-3-bromo-3-methyl-4-oxo-2-((E)-styryl)nonanoate (**2d**): R_f = 0.6 (ether/hexane = 05:95), colourless thick oil, 68% yield, 95:5 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.4 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 2H), 7.22 – 7.15 (m, 1H), 6.48 (d, *J* = 15.8 Hz, 1H), 6.23 (dd, *J* = 15.8, 9.6 Hz, 1H), 4.19 – 4.05 (m, 2H), 3.57 (d, *J* = 9.6 Hz, 1H), 1.86 – 1.77 (m, 5H), 1.49 (dd, *J* = 15.9, 9.2 Hz, 2H), 1.28 – 1.19 (m, 9H), 0.80 (t, *J* = 5.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 136.3, 135.1, 128.7, 128.1, 126.6, 124.0,70.7, 61.5, 61.0, 43.7, 31.6, 29.2, 28.5, 25.5, 22.6, 14.2, 14.1. HRMS (APCI) calcd. for $C_{20}H_{28}BrO_3$ [M+H]: 395.1222found: 395.1212.

Diethyl-2,2'-((1E,1'E)-1,4-phenylenebis(ethene-2,1-diyl))(2R, 2'R, 3S, 3'S)-bis(3-bromo-3 methylheptanoate) (**2e**): R_f = 0.4 (ether/hexane = 15:85), colourless thick oil, 68% yield, 95:5 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (s, 4H), 6.46 (d, *J* = 15.8 Hz, 2H), 6.24 (dd, *J* = 15.8, 9.5 Hz, 2H), 4.23 – 4.05 (m, 4H), 3.56 (d, *J* = 9.5 Hz, 2H), 1.85 – 1.77 (m, 10H), 1.48 (dd, *J* = 15.3, 7.9 Hz, 4H), 1.30 – 1.19 (m, 10H), 0.85 (t, *J* = 7.3 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 136.1, 134.6, 126.9, 124.2, 70.6, 61.5, 61.0, 43.3, 28.5, 27.7, 22.7, 14.2, 14.1. HRMS (APCI) calcd. for $C_{30}H_{45}Br_2O_4$ [M+H]: 627.1685 found: 627.1685.

Ethyl (2R, 3S)-3-chloro-3-methyl-2-((E)-styryl)heptanoate (**2f**): R_f = 0.5 (ether/hexane = 05:95), colourless thick oil, 70% yield, 95:5 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 2H), 7.25 (t, *J* = 7.4 Hz, 2H), 7.21 – 7.17 (m, 1H), 6.47 (d, *J* = 15.9 Hz, 1H), 6.23 (dd, *J* = 15.9, 9.7 Hz, 1H), 4.12 (dddd, *J* = 14.1, 8.6, 7.2, 3.7 Hz, 2H), 3.49 (d, *J* = 9.6 Hz, 1H), 1.84 – 1.69 (m, 2H), 1.62 (s, 3H), 1.50 – 1.41 (2, 4H), 1.27 – 1.18 (m, 5H), 0.85 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1, 136.4, 135.1, 128.7, 128.1, 126.6, 123.7, 73.4, 60.9, 60.7, 42.3, 26.9, 26.4, 22.8, 14.2, 14.1. HRMS (APCI) calcd. for $C_{18}H_{26}ClO_2$ [M+H]: 309.1621found: 309.1608.

Ethyl (2R, 3S)-3-chloro-3-methyl-2-((E)-2-(naphthalen-1-yl)vinyl)heptanoate (**2g**): R_f = 0.5 (ether/hexane = 05:95), colourless thick oil, 60% yield, 95:5 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.2 Hz, 1H), 7.82 – 7.75 (m, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.47 – 7.32 (m, 3H), 7.23 (d, *J* = 15.6 Hz, 1H), 6.26 (dd, *J* = 15.6, 9.7 Hz, 1H), 4.25 – 4.08 (m, 2H), 3.65 (d, *J* = 9.7 Hz, 1H), 1.90 – 1.78 (m, 2H), 1.66 (s, 3H), 1.58 – 1.46 (m, 2H), 1.30 – 1.20 (m, 5H), 0.86 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 134.2, 133.6, 132.6, 131.1, 128.7, 128.4, 127.0, 126.3, 125.9, 125.7, 124.3, 123.7, 73.4, 61.0, 42.3, 27.2, 26.5, 22.9, 14.3, 14.1. HRMS (APCI) calcd. for $C_{22}H_{28}ClO_2$ [M+H]: 359.1778 found: 359.1772.

Ethyl (2R, 3S)-5-(benzyloxy)-3-chloro-3-methyl-2-((E)-styryl)pentanoate (**2h**): R_f = 0.5 (ether/hexane = 10:90), colourless thick oil, 65% yield, 95:5 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.15 (m, 10H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.20 (dd, *J* = 15.8, 9.6 Hz, 1H), 4.44 (s, 2H), 4.16 – 4.04 (m, 2H), 3.77 – 3.63 (m, 2H), 3.55 (d, *J* = 9.6 Hz, 1H), 2.13 (dt, *J* = 10.3, 6.7 Hz, 2H), 1.66 (s, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9, 138.3, 136.3, 135.8, 128.7, 128.5, 128.1, 127.8,127.7, 126.7, 123.2, 73.3, 72.0, 66.9, 61.0 (d, *J* = 2.9 Hz), 41.7, 27.3, 14.3. HRMS (APCI) calcd. for $C_{23}H_{28}ClO_3$ [M+H]: 387.1727 found: 387.1731.

(2R, 3S)-3-chloro-3-methyl-2-((E)-styryl)heptan-1-ol (**2i**): R_f = 0.4 (ether/hexane = 20:80), colourless thick oil, 90% yield, 98:2 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, CDCl3) δ 7.33 (d, J = 7.2 Hz, 2H), 7.26 (t, J = 7.5 Hz, 2H), 7.18 (dd, J = 8.0, 6.5 Hz, 1H), 6.49 (d, J = 15.9 Hz, 1H), 6.10 (dd, J = 15.8, 9.6 Hz, 1H), 3.98 (dd, J = 10.8, 4.0 Hz, 1H), 3.64 (dd, J = 10.8, 9.0 Hz, 1H), 2.57 (td, J = 9.2, 3.9 Hz, 1H), 1.76 (ddd, J = 15.9, 7.8, 3.9 Hz, 2H), 1.48 – 1.35 (m, 5H), 1.25 (dd, J = 14.6, 7.3 Hz, 2H), 0.84 (t, J = 7.3 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ 136.6, 135.4, 128.7, 127.9, 127.0, 126.5, 75.2, 62.4, 56.3, 43.4, 28.2, 26.5, 22.9, 14.1. HRMS (APCI) calcd. for $C_{16}H_{25}ClO$ [M+H]: 267.1516found: 267.1529.

1-((3S, 4S, E)-3-allyl-4-chloro-4-methyloct-1-en-1-yl)-4-methoxybenzene (**2j**): R_f = 0.7 (ether/hexane = 05:95), colourless thick oil, 90% yield, 98:2 dr determined by ^{1}H-NMR, crude product itself clean, no further purification required. ^{1}H NMR (400 MHz, CDCl3) δ 7.22 (d, J = 8.7 Hz, 2H), 6.77 (d, J = 8.8 Hz, 2H), 6.23 (d, J = 15.8 Hz, 1H), 5.80 (dd, J = 15.8, 9.5 Hz, 1H), 5.66 (ddt, J = 17.1, 10.1, 7.0 Hz, 1H), 4.99 – 4.91 (m, 1H), 4.91 – 4.84 (m, 1H), 3.72 (s, 3H), 2.67 – 2.54 (m, 1H), 2.41 – 2.30 (m, 1H), 2.18 – 2.08 (m, 1H), 1.75 (ddd, J = 10.7, 8.3, 5.1 Hz, 2H), 1.49 – 1.33 (m, 5H), 1.24 (dd, J = 14.6, 7.3 Hz, 2H), 0.84 (t, J = 7.3 Hz, 3H). 13C NMR (101 MHz, CDCl3) δ 158.0, 136.1, 131.4, 129.0, 126.3, 126.2, 114.9, 112.9, 76.4, 76.3, 76.0, 75.7, 54.3, 52.9, 42.1, 33.6, 26.3, 25.5, 21.9, 13.0. HRMS (APCI) calcd. for $C_{19}H_{28}ClO$ [M+H]: 307.1823 found: 307.1801.

1-((3S, 4S, E)-4-chloro-3,4-dimethyloct-1-en-1-yl)-4-methoxybenzene (**2k**): R_f = 0.5 (ether/hexane = 05:95), colourless thick oil, 90% yield, single isomer determined by 1H-NMR. ^{1}H NMR (400 MHz, CDCl3) δ 7.27 – 7.19 (m, 2H), 6.81 – 6.74 (m, 2H), 6.27 (d, J = 15.8 Hz, 1H), 5.99 (dd, J = 15.8, 8.8 Hz, 1H), 3.72 (s, 3H), 2.49 (dt, J = 13.6, 6.8 Hz, 1H), 1.79 – 1.63 (m, 2H), 1.48 – 1.32 (m, 5H), 1.24 (dd, J = 14.5, 7.2 Hz, 2H), 1.15 (d, J = 6.7 Hz, 3H), 0.85 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 159.0, 130.5, 130.3, 129.6, 127.3, 114.0, 78.0, 55.4, 48.0, 42.8, 27.3, 26.7, 23.0, 16.5, 14.1. HRMS (APCI) calcd. for $C_{17}H_{26}ClO$ [M+H]: 281.1672found: 281.1684.

(S, E)-1-(4-chloro-4-methyloct-1-en-1-yl)-4-methoxybenzene (**2l**): R_f = 0.5 (ether/hexane = 05:95), colourless thick oil, 79% yield, single isomer determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, CDCl3) δ 7.24 (d, J = 8.7 Hz, 2H), 6.77 (d, J = 8.7 Hz, 2H), 6.32 (d, J = 15.8 Hz, 1H), 6.08 (dt, J = 15.7, 7.2 Hz, 1H), 3.72 (s, 3H), 2.63 – 2.48 (m, 2H), 1.69 (td, J = 10.7, 5.4 Hz, 2H), 1.47 (s, 3H), 1.44 – 1.34 (m, 2H), 1.25 (dd, J = 14.7, 7.3 Hz, 2H), 0.85 (t, J = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 158.0, 131.8, 129.1, 126.3, 122.2, 112.9, 73.1, 54.3, 46.6, 42.6, 28.7, 25.8, 21.8, 13.0. HRMS (APCI) calcd. for $C_{16}H_{24}ClO$ [M+H]: 267.1516found: 267.1522.

Ethyl (2R, 3S)-3-fluoro-3-methyl-2-((E)-styryl)heptanoate (**2m**): R_f = 0.4 (ether/hexane = 05:95), colourless thick oil, (solid after crystallization), 50% yield, 98:2 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.2 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 2H), 7.18 (d, *J* = 7.1 Hz, 1H), 6.44 (d, *J* = 15.9 Hz, 1H), 6.21 (dd, *J* = 15.9, 9.8 Hz, 1H), 4.12 (qd, *J* = 7.1, 2.7 Hz, 2H), 3.40 (dd, *J* = 11.9, 9.8 Hz, 1H), 1.68 – 1.57 (m, 2H), 1.41 – 1.30 (m, 5H), 1.28 – 1.18 (m, 5H), 0.83 (dd, *J* = 9.8, 4.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1 (d, *J* = 3.7 Hz), 136.5, 134.6 , 128.7, 128.0, 126.5, 123.5 (d, *J* = 7.3 Hz), 97.4 (d, *J* = 177.4 Hz), 60.9, 58.3 (d, *J* = 23.8 Hz), 38.3 (d, *J* = 22.4 Hz), 25.3 (d, *J* = 4.2 Hz), 23.0, 21.7 (d, *J* = 24.6 Hz), 14.2, 14.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -147.67. HRMS (ESI-MS) calcd. for $C_{18}H_{25}FNaO_2$ [(M+Na)]: 315.1731 found: 315.1748.

Ethyl (2R, 3R)-3-fluoro-3-methyl-2-((E)-styryl)heptanoate (**2n**): R_f = 0.4 (ether/hexane = 05:95), colourless thick oil, 46% yield, 98:2 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.3 Hz, 2H), 7.24 (t, *J* = 7.5 Hz, 2H), 7.20 – 7.15 (m, 1H), 6.43 (d, *J* = 16.0 Hz, 1H), 6.27 (dd, *J* = 15.9, 9.3 Hz, 1H), 4.11 (qd, *J* = 7.1, 2.4 Hz, 2H), 3.38 (dd, *J* = 15.4, 9.3 Hz, 1H), 1.82 – 1.68 (m, 1H), 1.54 (dt, *J* = 16.7, 5.7 Hz, 1H), 1.36 (d, *J* = 22.1 Hz, 4H), 1.21 (t, *J* = 7.1 Hz, 6H), 0.83 (t, *J* = 8.7, 5.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1 (d, *J* = 7.3 Hz), 136.7, 134.6, 128.6, 127.9, 126.6, 123.4 (d, *J* = 4.8 Hz), 97.0 (d, *J* = 177.7 Hz), 60.9, 58.3 (d, *J* = 23.9 Hz), 37.7 (d, *J* = 22.4 Hz), 25.3 (d, *J* = 4.9 Hz), 23.0, 22.5, 22.2, 14.2, 14.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -147.83. HRMS (ESI-MS) calcd. for $C_{18}H_{25}FNaO_2$ [(M+Na)]: 315.1731 found: 315.1747.

Ethyl (2R,3S)-3-fluoro-3-methyl-2-((E)-2-(naphthalen-1-yl)vinyl)heptanoate (**2o**): R_f = 0.3 (ether/hexane = 05:95), colourless thick oil, 40% yield, 98:2 dr determined by 1H-NMR. ^{1}H NMR (400

MHz, $CDCl_3$) δ 8.00 – 7.94 (m, 1H), 7.76 (dd, *J* = 7.3, 2.1 Hz, 1H), 7.70 (d, *J* = 8.3 Hz, 1H), 7.51 (d, *J* = 7.0 Hz, 1H), 7.45 – 7.34 (m, 3H), 7.19 (d, *J* = 15.6 Hz, 1H), 6.24 (dd, *J* = 15.6, 9.8 Hz, 1H), 4.15 (qd, *J* = 7.1, 3.4 Hz, 2H), 3.56 (dd, *J* = 11.8, 9.9 Hz, 1H), 1.73 – 1.62 (m, 2H), 1.46 – 1.36 (m, 5H), 1.24 (dt, *J* = 11.5, 7.4 Hz, 5H), 0.85 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1 (d, *J* = 3.8 Hz), 134.3, 133.6, 132.0, 131.1, 128.7, 128.3, 126.8 (d, *J* = 7.2 Hz), 126.2, 125.9, 125.7, 124.2, 123.7, 97.4 (d, *J* = 177.7 Hz), 61.0, 58.5 (d, *J* = 23.9 Hz), 38.4 (d, *J* = 22.3 Hz), 25.3 (d, *J* = 4.1 Hz), 23.0, 22.0, 21.8, 14.3, 14.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -147.38. HRMS (ESI-MS) calcd. for $C_{22}H_{27}FNaO_2$ [(M+Na)]: 365.1887 found: 365.1912.

Ethyl (2R, 3S)-2-((E)-2,4-difluorostyryl)-3-fluoro-3-methylheptanoate (**2p**): R_f = 0.3 (ether/hexane = 05:95), colourless thick oil, 55% yield, 98:2 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (td, *J* = 8.6, 6.5 Hz, 1H), 6.81 – 6.67 (m, 2H), 6.52 (d, *J* = 16.1 Hz, 1H), 6.22 (dd, *J* = 16.0, 9.8 Hz, 1H), 4.17 – 4.06 (m, 2H), 3.40 (dd, *J* = 12.6, 9.9 Hz, 1H), 1.69 – 1.54 (m, 2H), 1.42 – 1.33 (m, 5H), 1.31 – 1.17 (m, 5H), 0.84 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9 (d, *J* = 3.8 Hz), 163.7 (d, *J* = 12.2 Hz), 161.3 (dd, *J* = 24.2, 11.9 Hz), 158.9 (d, *J* = 11.7 Hz), 128.3 (dd, *J* = 9.6, 5.1 Hz), 125.9 (d, *J* = 26.6 Hz), 120.7 (dd, *J* = 12.3, 4.0 Hz), 111.6 (dd, *J* = 21.5, 3.7 Hz), 104.1 (t, *J* = 25.7 Hz), 97.2 (d, *J* = 177.9 Hz), 61.0, 58.5 (d, *J* = 23.8 Hz), 38.2 (d, *J* = 22.4 Hz), 25.3 (d, *J* = 4.3 Hz), 22.9, 21.8 (d, *J* = 24.6 Hz), 14.2, 14.0. ^{19}F NMR (377 MHz, $CDCl_3$) δ -106.78 – -111.17 (m), -112.66 – -116.21 (m), -147.81. HRMS (ESI-MS) calcd. for $C_{18}H_{23}F_3NaO_2$ [(M+Na)]: 351.1542 found: 351.1568.

Ethyl (2R, 3R)-3-fluoro-3-methyl-4-oxo-2-((E)-styryl)nonanoate (**2q**): R_f = 0.4 (ether/hexane = 05:95), colourless thick oil, 48% yield, 98:2 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, CDCl3) δ 7.32 (d, *J* = 7.4 Hz, 2H), 7.25 (t, *J* = 7.5 Hz, 2H), 7.18 (dd, *J* = 7.6, 6.7 Hz, 1H), 6.44 (d, *J* = 15.9 Hz, 1H), 6.21 (dd, *J* = 15.9, 9.8 Hz, 1H), 4.12 (qd, *J* = 7.1, 2.6 Hz, 2H), 3.40 (dd, *J* = 11.8, 9.9 Hz, 1H), 1.69 – 1.55 (m, 2H), 1.43 – 1.30 (m, 5H), 1.21 (t, *J* = 7.1 Hz, 10H), 0.80 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1 (d, *J* = 3.7 Hz), 136.5, 134.6, 128.6, 128.0, 126.6, 123.5 (d, *J* = 7.3 Hz), 97.4 (d, *J* = 177.4 Hz), 60.9, 58.3 (d, *J* = 23.8 Hz), 38.6 (d, *J* = 22.3 Hz), 31.8, 29.6, 23.0 (d, *J* = 4.2 Hz), 22.6, 21.7 (d, *J* = 24.6 Hz), 14.2, 14.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -147.56. HRMS (ESI-MS) calcd. for $C_{20}H_{27}FNaO_3$ [(M+Na)]: 357.1842 found: 357.1859.

Ethyl (2R, 3S)-5-(benzyloxy)-3-fluoro-3-methyl-2-((E)-styryl)pentanoate (**2r**): R_f = 0.5 (ether/hexane = 10:90), colourless thick oil, 49% yield, 98:2 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.14 (m, 10H), 6.43 (d, *J* = 15.9 Hz, 1H), 6.18 (dd, *J* = 15.9, 9.7 Hz, 1H), 4.43 (s, 2H), 4.11 (tt, *J* = 7.2, 3.7 Hz, 2H), 3.66 – 3.55 (m, 2H), 3.49 (t, *J* = 10.2 Hz, 1H), 2.10 – 1.90 (m, 2H), 1.43 (d, *J* = 22.2 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.9 (d, *J* = 4.3 Hz), 138.3, 136.4, 135.2, 128.6, 128.5, 128.0, 127.8, 127.7, 126.6, 123.0 (d, *J* = 7.3 Hz), 96.6 (d, *J* = 177.5 Hz), 73.2, 65.5 (d, *J* = 5.1 Hz), 61.0, 58.4 (d, *J* = 24.0 Hz), 38.1 (d, *J* = 21.9 Hz), 22.1 (d, *J* = 24.6 Hz), 14.2. ^{19}F NMR (377 MHz, $CDCl_3$) δ -146.73. HRMS (ESI-MS) calcd. for $C_{23}H_{27}FNaO_3$ [(M+Na)]: 393.1836 found: 393.1859.

Diethyl 2,2'-((1E, 1'E)-1,4-phenylenebis(ethene-2,1-diyl))(2R,2'R,3S,3'S)-bis(3-fluoro-3-methylheptanoate) (**2s**): R_f = 0.4 (ether/hexane = 05:95), white solid, 30% yield, 98:2 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (s, 4H), 6.41 (d, *J* = 15.9 Hz, 2H), 6.20 (dd, *J* = 15.9, 9.7 Hz, 2H), 4.12 (ddt, *J* = 10.8, 7.1, 3.6 Hz, 4H), 3.39 (dd, *J* = 12.2, 9.8 Hz, 2H), 1.68 – 1.56 (m, 4H), 1.42 – 1.33 (m, 10H), 1.28 – 1.18 (m, 10H), 0.84 (t, *J* = 7.2 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.1 (d, *J* = 3.7 Hz), 136.1, 134.1, 126.8, 123.6 (d, *J* = 7.2 Hz), 97.4 (d, *J* = 177.6 Hz), 61.0, 58.3 (d, *J* = 23.8 Hz), 38.3 (d, *J* = 22.3 Hz), 25.3 (d, *J* = 4.1 Hz), 23.0, 21.7 (d, *J* = 24.6 Hz), 14.2, 14.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -147.65. HRMS (APCI) calcd. for $C_{30}H_{45}F_2O_4$ [M+H]: 507.3286found: 506.3236.

Benzyl (2R, 3S)-3-fluoro-3-methyl-2-((E)-styryl)heptanoate (**2t**): R_f = 0.4 (ether/hexane = 10:90), thick oil, 39% yield, 98:2 dr determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.20 (m, 10H), 7.19 – 7.13 (m, 1H), 6.43 (d, *J* = 15.9 Hz, 1H), 6.22 (dd, *J* = 15.9, 9.7 Hz, 1H), 5.16 – 4.99 (m, 2H), 3.46 (dd, *J* = 12.4, 9.7 Hz, 1H), 1.58 (ddd, *J* = 12.4, 11.7, 5.2 Hz, 2H), 1.41 – 1.28 (m, 5H), 1.19 (dd, *J* = 14.9, 5.9 Hz, 3H), 0.80 (t, *J* = 7.3 Hz, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0 (d, *J* = 3.5 Hz), 136.5, 135.8, 134.9, 128.7, 128.6, 128.29, 128.26, 128.0, 126.6, 123.3 (d, *J* = 7.3 Hz), 97.4 (d, *J* = 177.8 Hz), 66.7, 58.2 (d, *J* = 23.7 Hz), 38.3 (d, *J* = 22.3 Hz), 25.3 (d, *J* = 4.2 Hz), 23.0, 21.9, 21.7, 14.1. ^{19}F

NMR (377 MHz, $CDCl_3$) δ -147.53. HRMS (ESI-MS) calcd. for $C_{23}H_{27}FNaO_2$ [(M+Na)]: 377.1887 found: 377.1912.

1-((3S, 4S, E)-3-allyl-4-fluoro-4-methyloct-1-en-1-yl)-4-methoxybenzene (**2u**): R_f = 0.7 (ether/hexane = 05:95), colourless thick oil, 65% yield, 98:2 dr determined by 1H-NMR, crude product itself clean, along with 8% of hydroxylated product. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 2H), 6.80 – 6.75 (m, 2H), 6.26 (d, *J* = 15.8 Hz, 1H), 5.79 (dd, *J* = 15.8, 9.5 Hz, 1H), 5.75 – 5.63 (m, 1H), 4.94 (dd, *J* = 17.1, 1.9 Hz, 1H), 4.91 – 4.84 (m, 1H), 3.71 (s, 3H), 2.46 – 2.37 (m, 1H), 2.17 (td, *J* = 10.1, 3.0 Hz, 1H), 2.10 – 2.00 (m, 1H), 1.39 – 1.16 (m, 6H), 1.10 (s, 3H), 0.85 – 0.80 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 136.9, 131.3, 129.1, 127.0, 126.3, 126.1, 114.5, 112.9, 112.9, 73.4, 54.3, 52.8, 39.0, 33.0, 24.4, 23.1, 22.3, 13.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -149.62. HRMS (APCI) calcd. for $C_{19}H_{27}O$ [(M+H)-HF]: 271.2056 found: 271.2077.

Ethyl (2R, 3S)-3-fluoro-3-methyl-2-((E)-4-phenylbut-1-en-3-yn-1-yl)heptanoate (**2v**): R_f = 0.5 (ether/hexane = 05:95), colourless thick oil, 50% yield, 98:2 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.29 (m, 2H), 7.23 (dd, *J* = 6.8, 3.9 Hz, 3H), 6.19 (dd, *J* = 15.9, 9.9 Hz, 1H), 5.77 (d, *J* = 15.9 Hz, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.40 – 3.28 (m, 1H), 1.67 – 1.51 (m, 2H), 1.44 – 1.29 (m, 5H), 1.22 (dd, *J* = 14.4, 7.2 Hz, 5H), 0.85 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.2 (d, *J* = 4.0 Hz), 136.7 (d, *J* = 7.0 Hz), 131.6 , 128.4, 128.4, 123.0, 114.7, 97.0 (d, *J* = 178.3 Hz), 90.3, 87.1, 61.1, 58.3 (d, *J* = 24.4 Hz), 38.2 (d, *J* = 22.3 Hz), 25.2 (d, *J* = 4.0 Hz), 22.9, 21.7 (d, *J* = 24.6 Hz), 14.2, 14.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -147.39. HRMS (ESI-MS) calcd. for $C_{20}H_{25}FNaO_2$ [(M+Na)]: 339.1731 found: 339.1759.

Ethyl (2R, 3S)-3-fluoro-3-methyl-2-((E)-4-(triisopropylsilyl)but-1-en-3-yn-1-yl)heptanoate (**2w**): R_f = 0.5 (ether/hexane = 05:95), colourless thick oil, 42% yield, 98:2 dr determined by 1H-NMR. (Isolated 42% of yield along with 10% of eliminated product) ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.13 (dd, *J* = 15.9, 9.8 Hz, 1H), 5.60 (d, *J* = 15.9 Hz, 1H), 4.11 (ddd, *J* = 14.3, 7.2, 2.5 Hz, 2H), 3.28 (dd, *J* = 11.6, 10.2 Hz, 1H), 1.65 – 1.54 (m, 2H), 1.37 – 1.27 (m, 5H), 1.25 – 1.16 (m, 5H), 1.01 (s, 21H), 0.88 – 0.81 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3 (d, *J* = 4.1 Hz), 137.2 (d, *J* = 7.0 Hz), 115.1, 104.3, 97.1 (d, *J* = 178.2 Hz), 92.0, 61.1 , 58.2 (d, *J* = 24.3 Hz), 38.2 (d, *J* = 22.3 Hz), 25.2 (d, *J* = 4.0 Hz), 22.9, 21.7 (d, *J* = 24.5 Hz), 18.6, 14.2, 14.0, 11.3. ^{19}F NMR (377 MHz, $CDCl_3$) δ -147.45. HRMS (APCI) calcd. for $C_{23}H_{42}FO_2Si$ [M+H]: 397.2933 found: 397.2962.

Ethyl (2S, 3S)-3-methyl-2-((E)-styryl)-3-(trichloro(oxo)-l6-methoxy)heptanoate (**2x**): R_f = 0.6 (ether/hexane = 05:95), colourless thick oil, 67% yield, 95:5 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.30 (m, 2H), 7.29 – 7.24 (m, 2H), 7.20 (dt, *J* = 7.0, 1.7 Hz, 1H), 6.48 (d, *J* = 15.8 Hz, 1H), 6.17 (dd, *J* = 15.8, 10.0 Hz, 1H), 4.09 (dtd, *J* = 14.4, 7.2, 3.5 Hz, 2H), 3.98 (d, *J* = 10.0 Hz, 1H), 2.19 – 2.04 (m, 1H), 1.84 – 1.72 (m, 1H), 1.57 (s, 3H), 1.26 – 1.15 (m, 7H), 0.86 – 0.77 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 155.9 (d, *J* = 41.5 Hz), 136.2, 135.7, 128.7, 128.2, 126.6, 122.4, 90.9, 61.3, 55.9, 35.8, 25.0, 22.7, 20.9, 14.0. HRMS (APCI) calcd. for $C_{18}H_{25}O_2$ [(M+H)-Cl_3CCO_2H]: 273.1849 found: 273.1861.

Ethyl (2S, 3S)-2-((E)-4-bromostyryl)-3-methyl-3-(trichloro(oxo)-l6-methoxy)heptanoate (**2y**): R_f = 0.4 (ether/hexane = 05:95), colourless thick oil, 70% yield, 95:5 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (t, *J* = 9.1 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 6.41 (d, *J* = 15.9 Hz, 1H), 6.20 (dd, *J* = 15.8, 9.9 Hz, 1H), 4.17 – 4.03 (m, 2H), 3.99 (d, *J* = 9.9 Hz, 1H), 2.09 – 2.00 (m, 1H), 1.87 – 1.77 (m, 1H), 1.62 (s, 3H), 1.36 – 1.16 (m, 7H), 0.83 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 159.9, 135.2, 134.4, 131.8, 128.1, 123.5, 122.0, 90.8, 61.4, 56.0, 35.8, 25.1, 22.8, 20.8, 14.1, 14.0. HRMS (APCI) calcd. for $C_{18}H_{24}BrO_2$ [(M+H)-Cl_3CCO_2H]: 351.0960 found: 351.0960.

Ethyl (2S, 3S)-2-((E)-2-(benzo[d][1,3]dioxol-5-yl)vinyl)-3-methyl-3-(trichloro(oxo)-l6-methoxy)heptanoate (**2z**): R_f = 0.4 (ether/hexane = 05:95), colourless thick oil, 67% yield, 95:5 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.85 (s, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.38 (d, *J* = 15.8 Hz, 1H), 6.02 (dd, *J* = 15.7, 9.9 Hz, 1H), 5.88 (s, 2H), 4.16 – 4.01 (m, 2H), 3.95 (d, *J* = 9.9 Hz, 1H), 2.08 – 1.98 (m, 1H), 1.83 (dt, *J* = 15.1, 7.1 Hz, 1H), 1.61 (s, 3H), 1.35 – 1.14 (m, 7H), 0.83 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 159.9, 148.1, 147.7, 135.1,

130.7, 121.5, 120.7, 108.3, 105.8, 101.2, 91.1, 61.3, 55.9, 35.8, 25.1, 22.8, 20.7, 14.1, 14.0. HRMS (APCI) calcd. for $C_{19}H_{25}O_4$ [(M+H)-Cl_3CCO_2H]: 317.17471 found: 317.1731

Ethyl (2S, 3S)-2-((E)-2,4-difluorostyryl)-3-methyl-3-(trichloro(oxo)-l6-methoxy)heptanoate (**2aa**): R_f = 0.4 (ether/hexane = 05:95), colourless thick oil, 70% yield, 95:5 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (td, *J* = 8.6, 6.4 Hz, 1H), 6.82 – 6.69 (m, 2H), 6.56 (d, *J* = 16.0 Hz, 1H), 6.23 (dd, *J* = 16.0, 10.0 Hz, 1H), 4.17 – 4.09 (m, 1H), 4.09 – 4.02 (m, 1H), 3.98 (d, *J* = 10.0 Hz, 1H), 2.10 – 2.01 (m, 1H), 1.84 (dt, *J* = 21.6, 7.2 Hz, 1H), 1.62 (s, 3H), 1.36 – 1.26 (m, 3H), 1.22 (t, *J* = 7.1 Hz, 4H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 159.9, 128.5, 127.1, 125.0, 120.5, 111.5, 104.2, 90.8, 61.4, 56.4, 35.8, 30.4, 25.1, 22.7, 20.8, 14.1, 13.9. ^{19}F NMR (377 MHz, $CDCl_3$) δ -109.95, -109.97, -113.41, -113.43. HRMS (APCI) calcd. for $C_{18}H_{23}F_2O_2$ [(M+H)-Cl_3CCO_2H]: 309.1661 found: 309.1679.

Ethyl (2S, 3S)-2-((E)-2-(furan-3-yl)vinyl)-3-methyl-3-(trichloro(oxo)-l6-methoxy)heptanoate (**2ab**): The reaction was performed at 0 ^{o}C, in order to reduce the decomposition and byproducts. R_f = 0.6 (ether/hexane = 05:95), colourless thick oil, 40 % yield, 95:5 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 1.7 Hz, 1H), 6.40 – 6.34 (m, 1H), 6.27 (d, *J* = 3.3 Hz, 1H), 6.18 (dd, *J* = 15.7, 10.0 Hz, 1H), 4.22 – 4.17 (m, 1H), 4.14 – 4.08 (m, 1H), 4.01 (d, *J* = 10.0 Hz, 1H), 2.11 (dd, *J* = 15.4, 6.8 Hz, 1H), 1.91 (dt, *J* = 15.1, 7.4 Hz, 1H), 1.69 (s, 3H), 1.35 – 1.23 (m, 7H), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 159.9, 151.8, 142.4, 123.6, 120.9, 111.4, 108.9, 91.1, 61.3, 55.7, 35.8, 31.5, 30.2, 29.7, 25.02, 22.7, 20.6, 14.1, 14.0. HRMS (APCI) calcd. for $C_{18}H_{24}BrO_2$ [(M+H)-Cl_3CCO_2H]: 263.1642found: 263.1661.

Ethyl (2S, 3S)-3-methyl-2-((E)-prop-1-en-1-yl)-3-(2,2,2-trichloroacetoxy)heptanoate (**2ac**): R_f = 0.6 (ether/hexane = 05:95), colourless thick oil, 33% yield along with 20% of eliminated product, 95:5 dr determined by 1H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.26 (dt, *J* = 16.8, 10.3 Hz, 1H), 6.12 (dd, *J* = 15.1, 10.5 Hz, 1H), 5.68 (dd, *J* = 15.1, 10.0 Hz, 1H), 5.17 (d, *J* = 16.5 Hz, 1H), 5.07 (d, *J* = 10.5 Hz, 1H), 4.17 – 3.99 (m, 2H), 3.86 (d, *J* = 10.0 Hz, 1H), 2.04 – 1.90 (m, 1H), 1.86 – 1.73 (m, 1H), 1.57 (s, 3H), 1.32 – 1.25 (m, 4H), 1.22 – 1.15 (m, 4H), 0.87 – 0.76 (m, 3H). ^{13}C NMR (101 MHz, CDCl3) δ 170.6, 159.8, 136.3, 126.4, 118.6, 91.0, 61.2, 55.6, 35.7, 25.0, 22.7, 22.6, 20.6, 14.1, 14.0. HRMS (APCI) calcd. for $C_{14}H_{23}O_2$ [(M+H)-Cl_3CCO_2H]: 223.1693 found: 223.1701.

(4S,5S)-4-((E)-4-methoxystyryl)-5-methylnon-1-en-5-yl 2,2,2-trichloroacetate (**2ad**): R_f = 0.7 (ether/hexane = 05:95), colourless thick oil, 85% yield, 98:2 dr determined by 1H-NMR, crude product itself clean, no further purification required. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.7 Hz, 2H), 6.77 (d, *J* = 8.7 Hz, 2H), 6.29 (d, *J* = 15.8 Hz, 1H), 5.78 – 5.69 (m, 1H), 5.69 – 5.59 (m, 1H), 4.97 – 4.87 (m, 2H), 3.71 (s, 3H), 2.83 (td, *J* = 10.7, 2.7 Hz, 1H), 2.45 – 2.35 (m, 1H), 2.15 – 2.06 (m, 1H), 2.04 – 1.94 (m, 1H), 1.83 (ddd, *J* = 14.4, 11.4, 4.7 Hz, 1H), 1.48 (s, 3H), 1.31 – 1.19 (m, 4H), 0.82 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.9, 159.2, 136.7, 133.2, 129.9, 127.4, 125.7, 116.3, 114.0, 113.9, 93.3, 55.4, 50.3, 35.8, 33.8, 25.2, 22.9, 20.7, 14.1. HRMS (APCI) calcd. for $C_{19}H_{27}O$ [(M+H)-Cl_3CCO_2H]: 271.2056 found: 271.2081.

(S, E)-1-(4-methoxyphenyl)-4-methyloct-1-en-4-yl 2,2,2-trichloroacetate (**2ae**): R_f = 0.7 (ether/hexane = 05:95), colourless thick oil, 90% yield, 98:2 dr determined by 1H-NMR, crude product itself clean, no further purification required. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.7 Hz, 2H), 6.76 (d, *J* = 8.7 Hz, 2H), 6.34 (d, *J* = 15.8 Hz, 1H), 5.99 – 5.89 (m, 1H), 3.72 (s, 3H), 2.75 (ddd, *J* = 14.1, 7.3, 0.7 Hz, 1H), 2.63 (ddd, *J* = 14.3, 7.6, 0.8 Hz, 1H), 1.97 – 1.86 (m, 1H), 1.76 (dt, *J* = 14.3, 7.2 Hz, 1H), 1.49 (s, 3H), 1.33 – 1.23 (m, 4H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 159.1, 133.7, 130.1, 127.3, 127.3, 121.3, 114.0, 91.2, 55.3, 41.6, 37.8, 25.6, 23.2, 22.9, 14.1. HRMS (APCI) calcd. for $C_{16}H_{23}O$ [(M+H)-Cl_3CCO_2H]: 231.1743 found: 231.1764.

(4S, 5S)-5-methyl-4-(2-methylprop-1-en-1-yl)-2-phenylnon-1-en-5-yl 2,2,2-trichloroacetate (**2af**): R_f = 0.5 (ether/hexane = 05:95), colourless thick oil, 75% yield along with a 13% of eliminated product, 95:5 dr determined by 1H NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 7.2 Hz, 2H), 7.23 (d, *J* = 7.0 Hz, 2H), 7.19 – 7.15 (m, 1H), 5.16 (d, *J* = 1.2 Hz, 1H), 4.89 (s, 1H), 4.73 (d, *J* = 10.5 Hz, 1H), 2.97 (dd, *J* = 17.9, 8.0 Hz, 2H), 2.22 (dd, *J* = 13.0, 11.0 Hz, 1H), 1.89 – 1.81 (m, 2H), 1.54 (s, 3H), 1.45 (s, 3H), 1.20 – 1.12 (m, 4H), 1.10 (s, 3H), 0.76 (t, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 145.5,

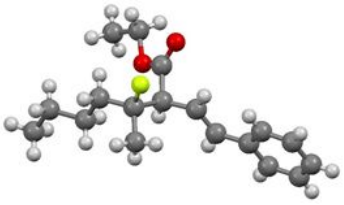
139.6, 134.5, 127.1, 127.1, 126.3, 125.4, 121.6, 113.4, 93.4, 42.3, 34.8, 34.7, 24.9, 24.0, 21.8, 18.9, 17.4, 12.9. HRMS (APCI) calcd. for $C_{20}H_{29}$ [(M+H)-Cl_3CCO_2H]: 269.2264 found: 269.2280.

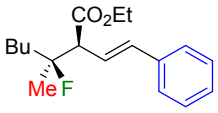
(3S, 4S, E)-1-(4-methoxyphenyl)-3,4-dimethyloct-1-en-4-yl 2,2,2-trichloroacetate (**2ag**): Rf = 0.5 (ether/hexane = 03:97), colourless thick oil, 84% yield, single isomer determined by ^{1}H-NMR. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.19 (m, 2H), 6.80 – 6.74 (m, 2H), 6.33 (d, *J* = 15.8 Hz, 1H), 5.89 (dd, *J* = 15.8, 8.9 Hz, 1H), 3.73 (s, 3H), 3.01 (dq, *J* = 13.9, 7.0 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.81 (ddd, *J* = 14.3, 11.4, 5.0 Hz, 1H), 1.46 (s, 3H), 1.26 (ddt, *J* = 13.1, 9.3, 6.5 Hz, 4H), 1.10 (d, *J* = 6.9 Hz, 3H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 159.1, 131.2, 130.1, 127.9, 127.2, 114.0, 93.6, 91.2, 55.4, 44.0, 35.5, 25.4, 22.9, 20.4, 15.3, 14.1. HRMS (APCI) calcd. for $C_{18}H_{24}BrO_2$ [M-$OCOCCl_3$]: 351.0960 found: 351.0960.

((3S, 4R, E)-4-bromo-3-ethylpent-1-ene-1,4-diyl)dibenzene (**2ah**): R_f = 0.6 (ether/hexane = 05:95), colourless thick oil, 60% yield, 1:1 dr crude NMR, 1:0.63 dr after column purification. ^{1}H NMR (400 MHz, CDCl3) δ 7.43 – 7.12 (m, 19H), 6.42 (d, J = 15.9 Hz, 0.64H), 6.36 (d, J = 15.9 Hz, 1H), 5.96 (dd, J = 15.9, 9.6 Hz, 1H), 5.86 (dd, J = 15.9, 9.7 Hz, 0.62H), 2.30 – 2.22 (m, 1.7H), 1.53 (s, 2H), 1.47 (s, 3H), 1.39 – 1.31 (m, 1.72H), 1.16 (ddd, J = 13.4, 11.2, 7.3 Hz, 1.8H), 0.72 – 0.68 (m, 5.2H). ^{13}C NMR (101 MHz, CDCl3) δ 147.4, 146.4, 137.4, 137.3, 134.0, 133.4, 130.4, 130.2, 128.6, 128.6, 128.0, 127.9 ,127.8, 127.4, 126.8, 126.5, 126.3, 126.2, 126.0, 125.2, 58.1, 57.0, 31.2, 30.7, 29.3, 26.0, 22.3, 22.1, 12.7, 12.7. HRMS (APCI) calcd. for $C_{19}H_{22}Br$ [M+H]: 329.0905 found: 329.0913.

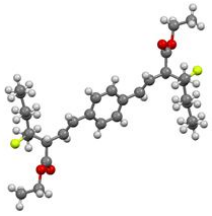
Ethyl (2S, 3R)-3-hydroxy-3-methyl-4-oxo-2-((E)-styryl)nonanoate (**5b**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 2H), 7.25 (dd, *J* = 8.2, 6.7 Hz, 2H), 7.17 (s, 1H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.29 (dd, *J* = 15.9, 9.6 Hz, 1H), 4.13 (tdd, *J* = 10.8, 7.1, 3.7 Hz, 2H), 3.14 (d, *J* = 9.6 Hz, 1H), 1.46 – 1.39 (m, 2H), 1.32 (dd, *J* = 6.1, 3.0 Hz, 2H), 1.21 (dd, *J* = 9.6, 4.6 Hz, 10H), 1.09 (s, 3H), 0.81 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.1, 136.7, 134.6, 128.6, 127.8, 126.5, 124.2, 73.9, 61.1, 58.2, 41.8, 31.8, 29.8, 23.8, 23.7, 22.6, 14.2, 14.1. HRMS (APCI) calcd. for $C_{20}H_{27}O_3$ [(M+H)- Cl_3CCO_2H]: 315.1955 found: 315.1941.

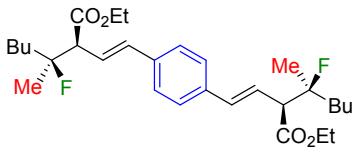
Crystal structure for **2m**. (**CCDC no: 1888232**)

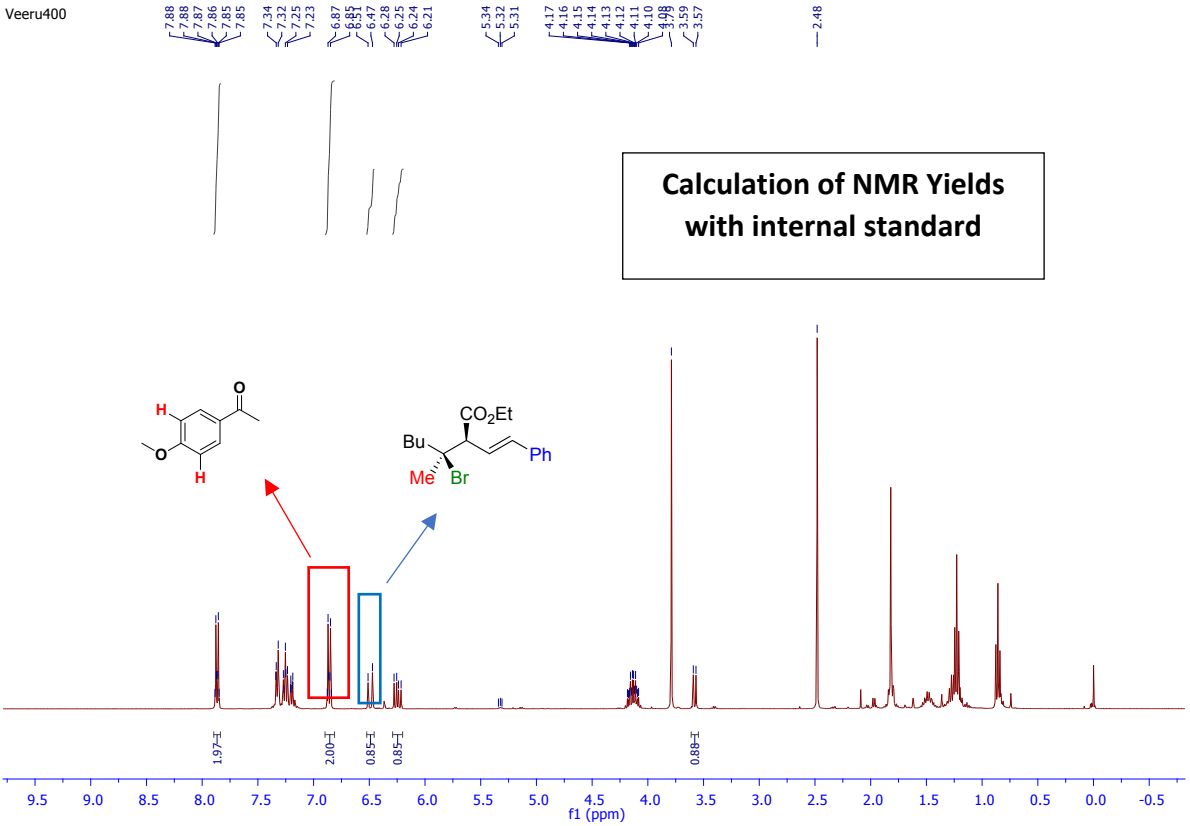


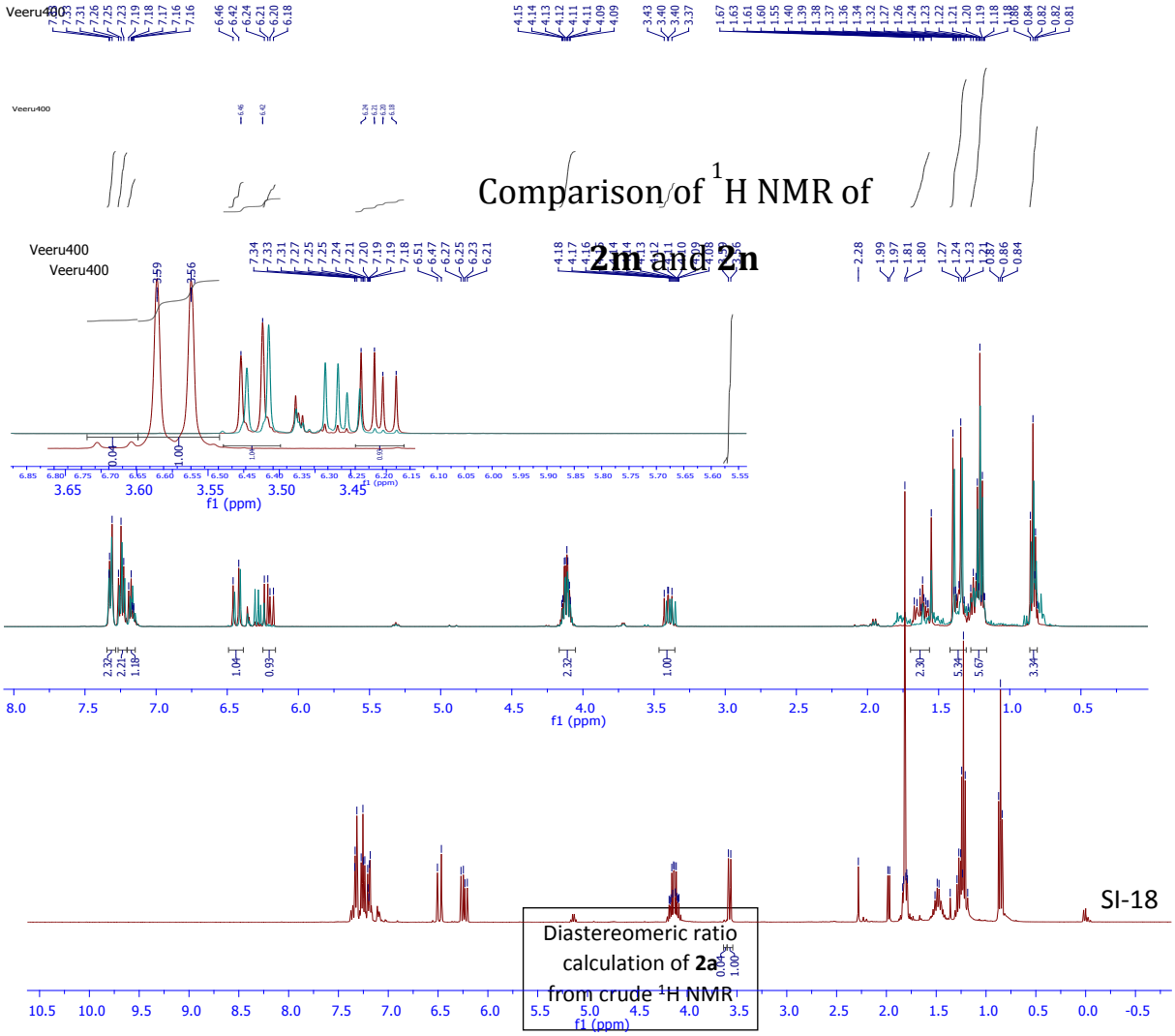


1. Crystal structure for **2s. (CCDC no: 1977388)**



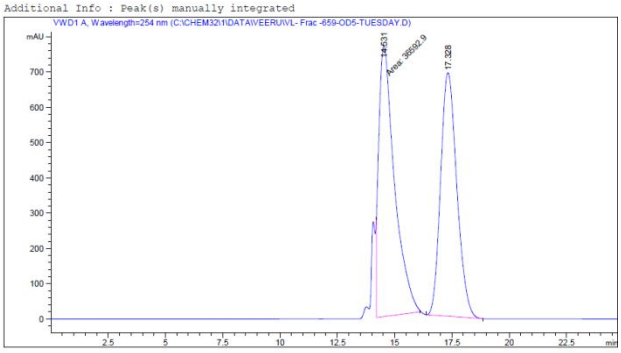



Veeru400
Calculation of NMR Yields
with internal standard
H
O
O
H
CO2Et
Bu
Ph
Me
Br
f1 (ppm)


Veeru400
Comparison of 1H NMR of
2m and 2n
Veeru400
Veeru400
f1 (ppm)
Diastereomeric ratio
calculation of 2a
from crude 1H NMR
f1 (ppm)

2. HPLC data for compound **2q**

Additional Info : Peak(s) manually integrated



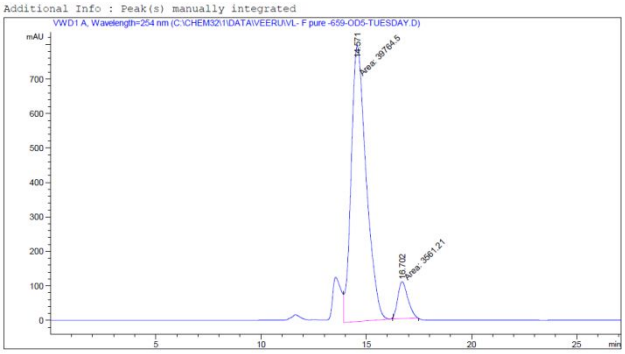
Area Percent Report

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.531	FM	0.7945	3.65929e4	767.58521	51.9048
2	17.328	BB	0.7614	3.39072e4	689.92285	48.0952

Totals : 7.05001e4 1457.50806

*** End of Report ***

Additional Info : Peak(s) manually integrated



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.571	FM T	0.8292	3.97645e4	799.27197	91.7804
2	16.702	MM T	0.5540	3561.21265	107.13142	8.2196

Totals : 4.33257e4 906.40340

*** End of Report ***

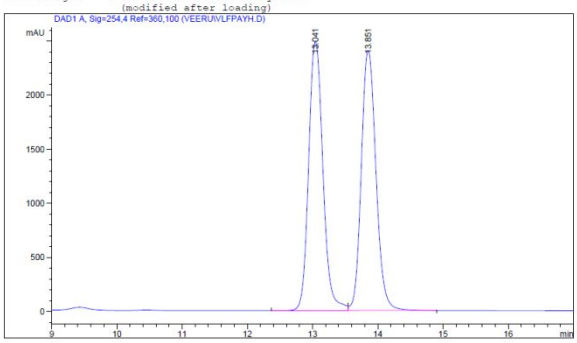
38. HPLC data for compound **5b**

Data File C:\HPCHEM\1\DATA\VEERU\VLFPAYH.D Sample Name: VL-F-P-AY-H

OX-H,97:03(Hexane:IPA), 0.4ML/min, 2microL
VL-OH-RAC-HEX
Trail 1

Injection Date : 10/16/2019 4:53:34 PM
Sample Name : VL-F-P-AY-H Location : Vial 21
Acq. Operator : VEERU
Inj Volume : 2 µl

Acq. Method : C:\HPCHEM\1\METHODS\ZACK.M
Last changed : 10/16/2019 4:51:34 PM by VEERU
(modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\ZACK.M
Last changed : 11/25/2019 5:38:10 PM by YAIR
(modified after loading)



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 5.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.041	BV	0.2354	3.78379e4	2489.06763	50.1792
2	13.851	VB	0.2422	3.75677e4	2406.09888	49.8208

Totals : 7.54056e4 4895.16650

Results obtained with enhanced integrator!

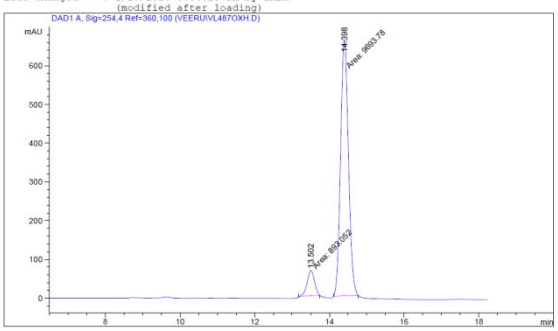
*** End of Report ***

Data File C:\HPCHEM\1\DATA\VEERU\VL487OXH.D Sample Name: VL-486-OHp-OX-H

OX-H,97:3(Hexane:IPA), 0.4ML/min, 2microL
VL-486-OH-pure
Trail 1

Injection Date : 10/7/2019 9:49:43 AM
Sample Name : VL-486-OHp-OX-H Location : Vial 21
Acq. Operator : VEERU
Inj Volume : 2 µl

Acq. Method : C:\HPCHEM\1\METHODS\ZACK.M
Last changed : 10/7/2019 9:49:46 AM by VEERU
(modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\ZACK.M
Last changed : 1/27/2020 5:56:25 PM by YAIR
(modified after loading)



Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Sample Amount : 2.00000 [ng/ul] (not used in calc.)
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=254,4 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.502	MM T	0.2280	893.05188	65.28743	8.4355
2	14.398	MM T	0.2446	9693.78418	660.62085	91.5645

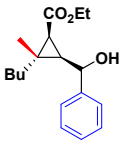
Totals : 1.05868e4 725.90828

Results obtained with enhanced integrator!

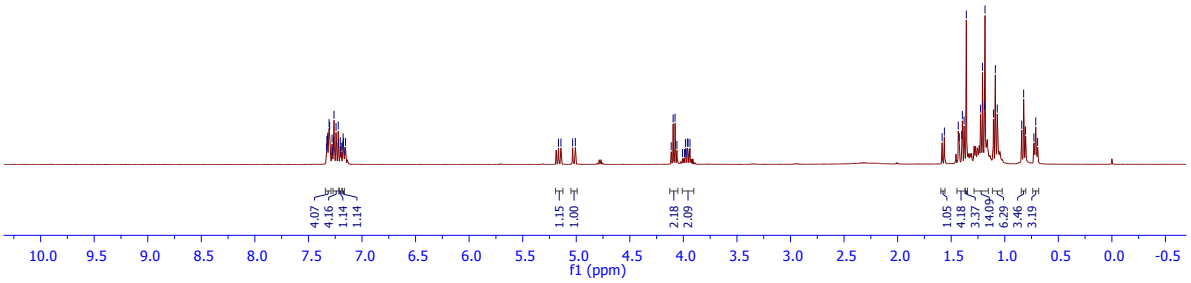
*** End of Report ***

Spectral Data

Veeru4002019



78%, 1:1 dr



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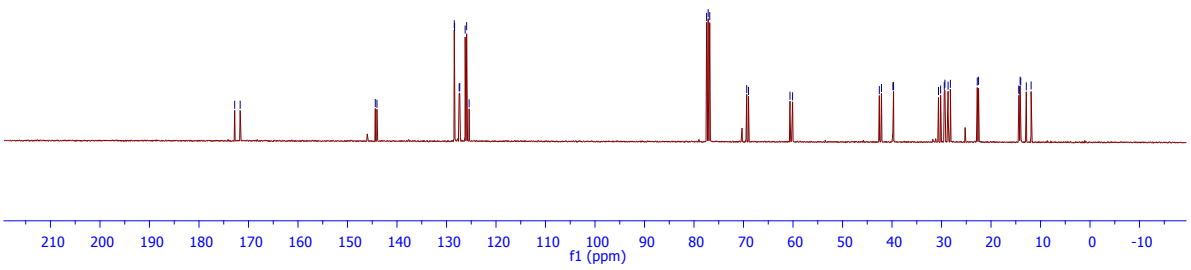

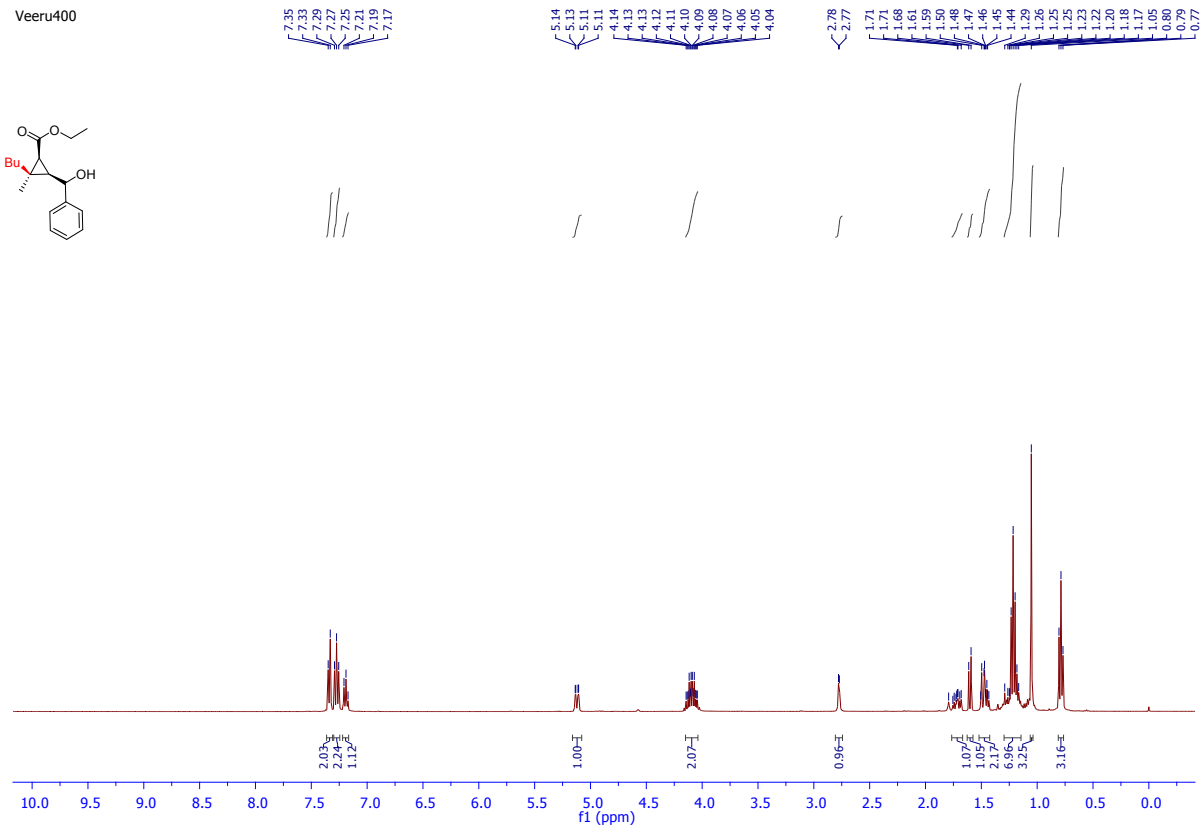
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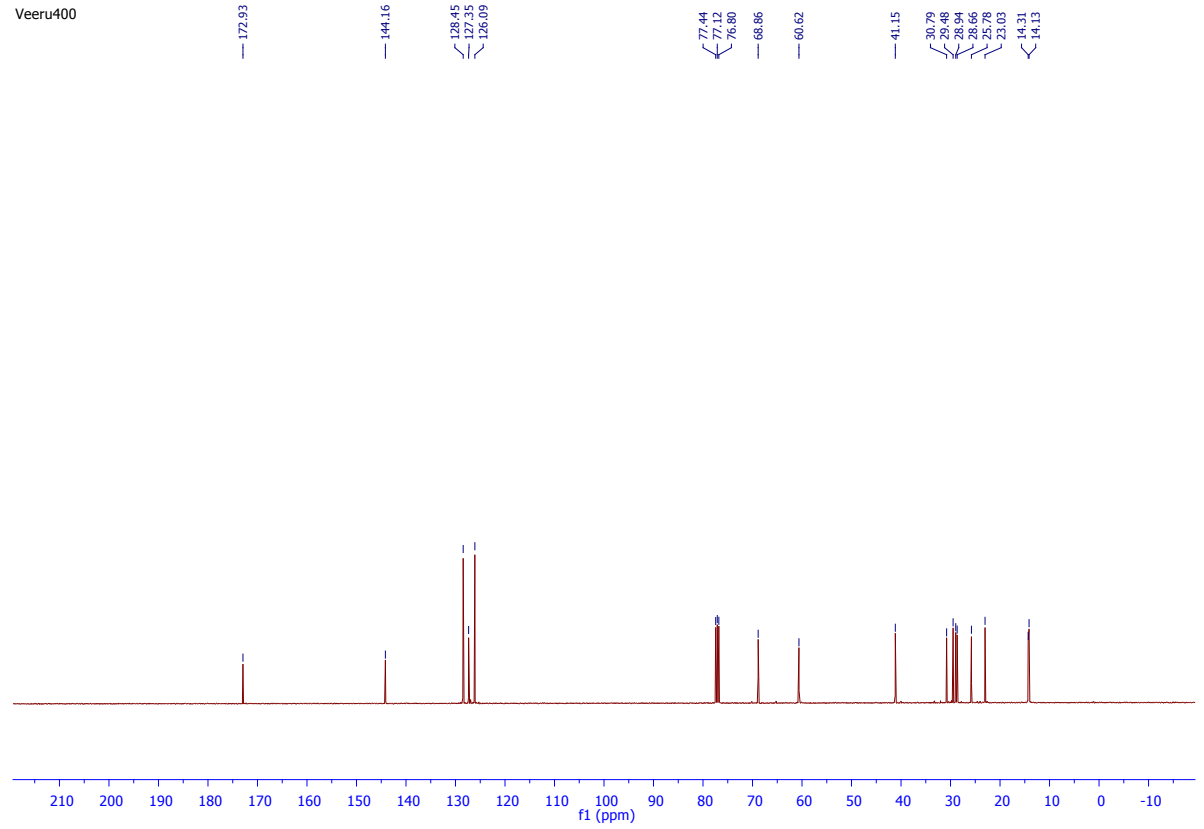
7.29
7.27
7.25
7.21
7.19
7.17
5.14
5.13
5.11
5.11
4.14
4.13
4.13
4.12
4.11
4.10
4.09
4.08
4.07
4.06
4.05
4.04
2.78
2.77
1.71
1.71
1.68
1.61
1.59
1.50
1.48
1.47
1.46
1.45
1.44
1.29
1.26
1.25
1.25
1.23
1.22
1.20
1.18
1.17
1.05
0.80
0.79
0.77
O
O
Bu
OH
2.03
2.24
1.12
1.00
2.07
0.96
1.07
1.05
2.17
6.96
3.25
3.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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144.16
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126.09
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77.12
76.80
68.86
60.62
41.15
30.79
29.48
28.94
28.66
25.78
23.03
14.31
14.13
210
200
190
180
170
160
150
140
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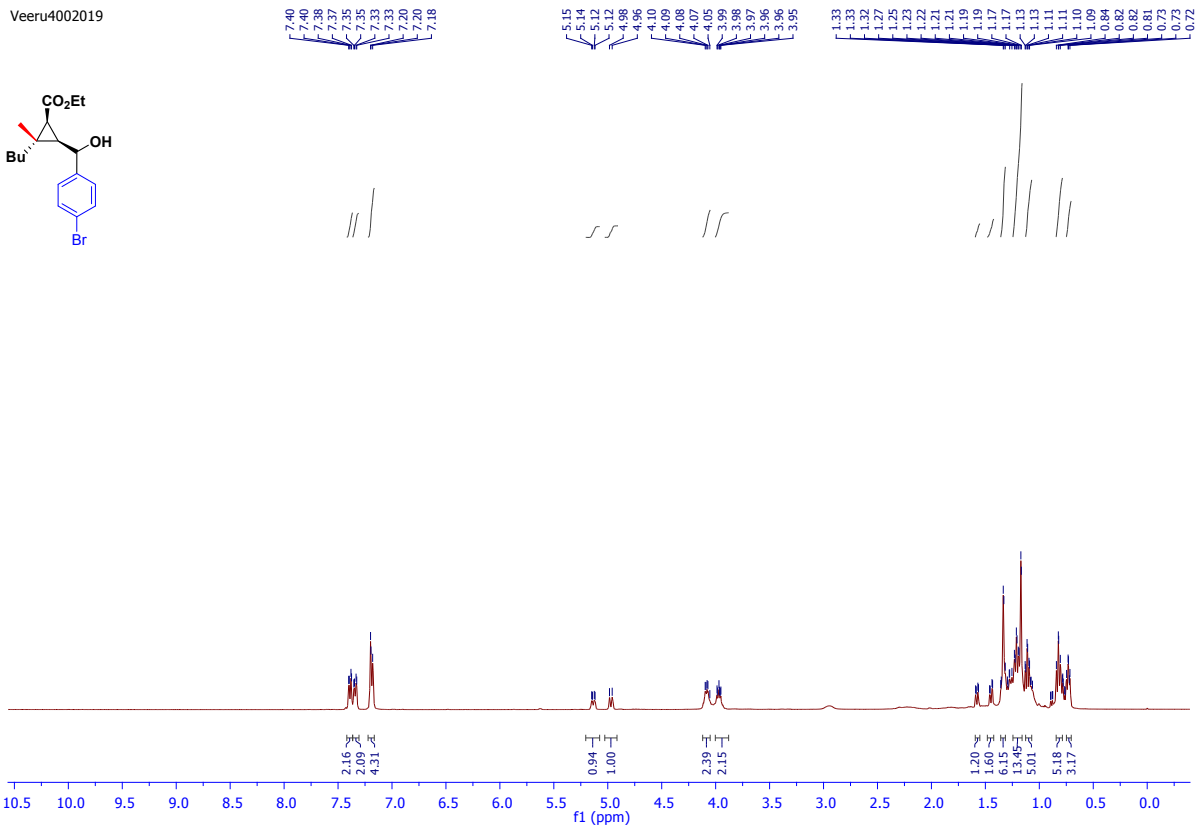
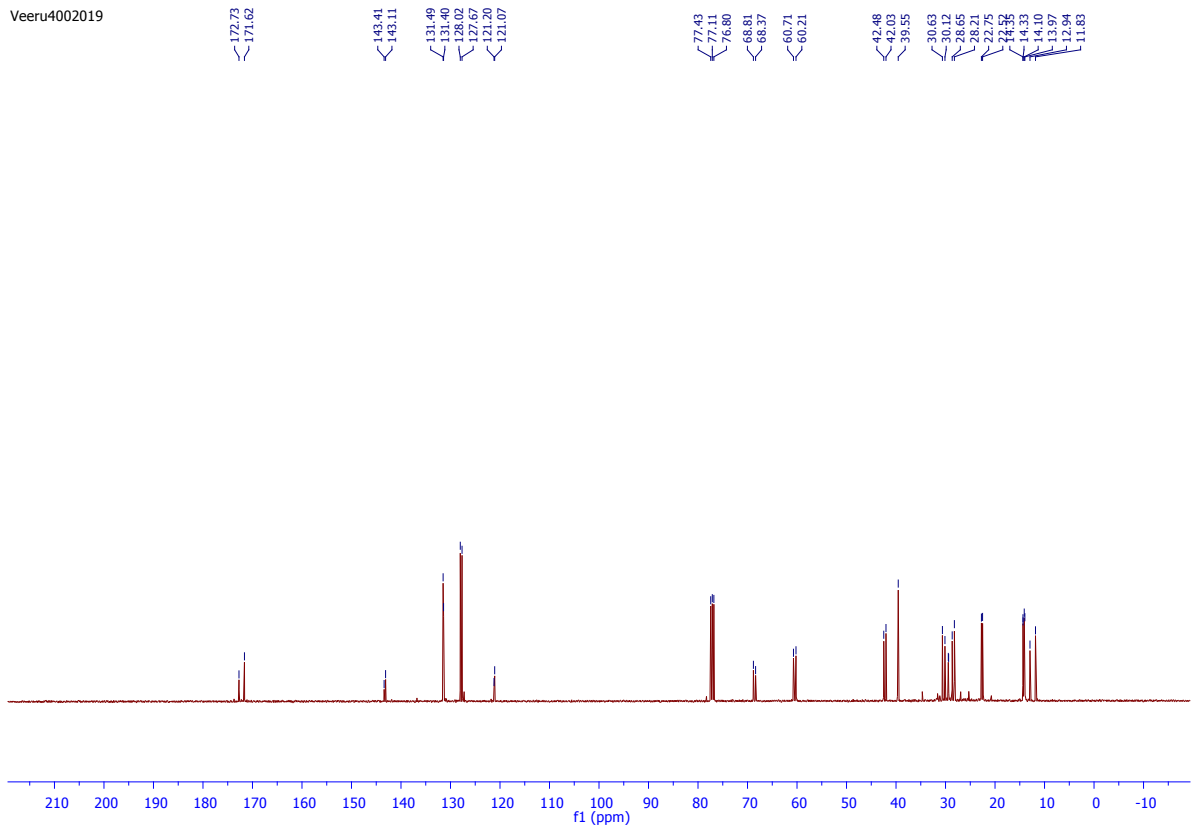
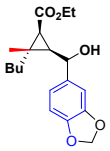
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

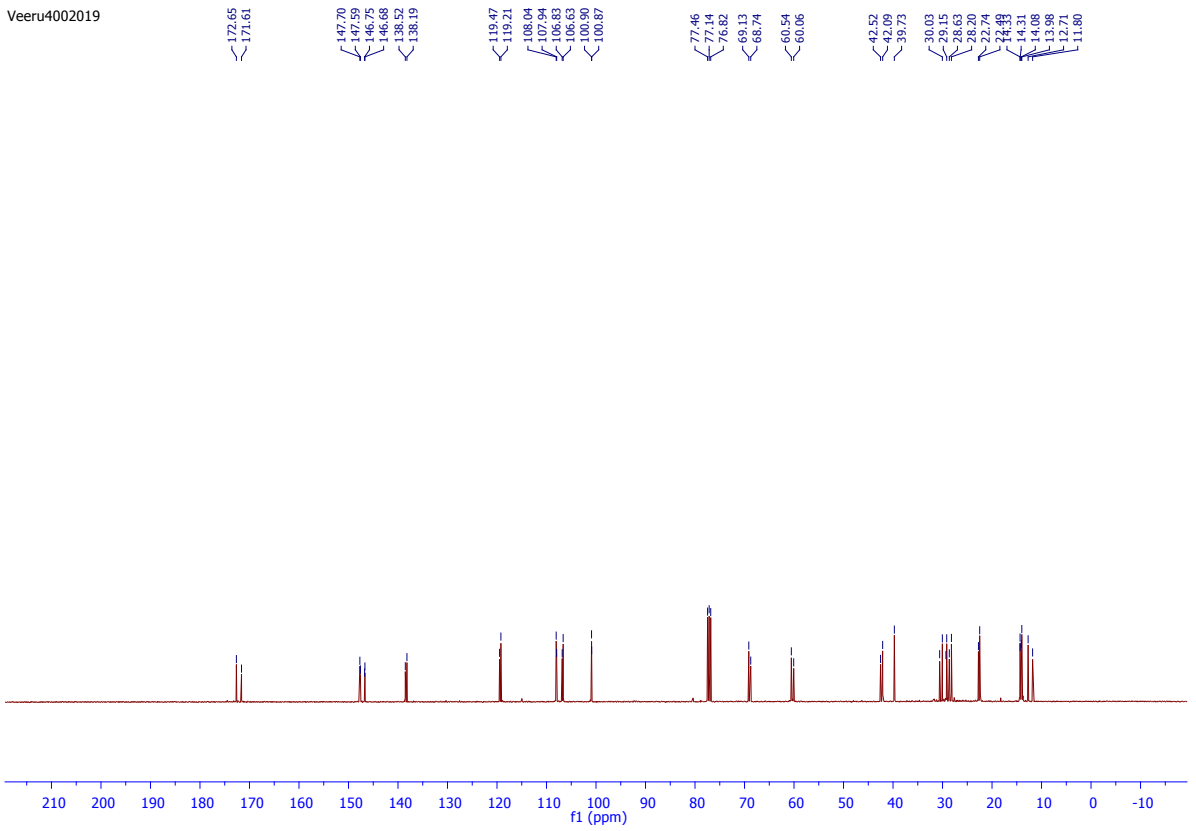

Veeru4002019
CO2Et
OH
Bu
Br
f1 (ppm)


Veeru4002019
f1 (ppm)

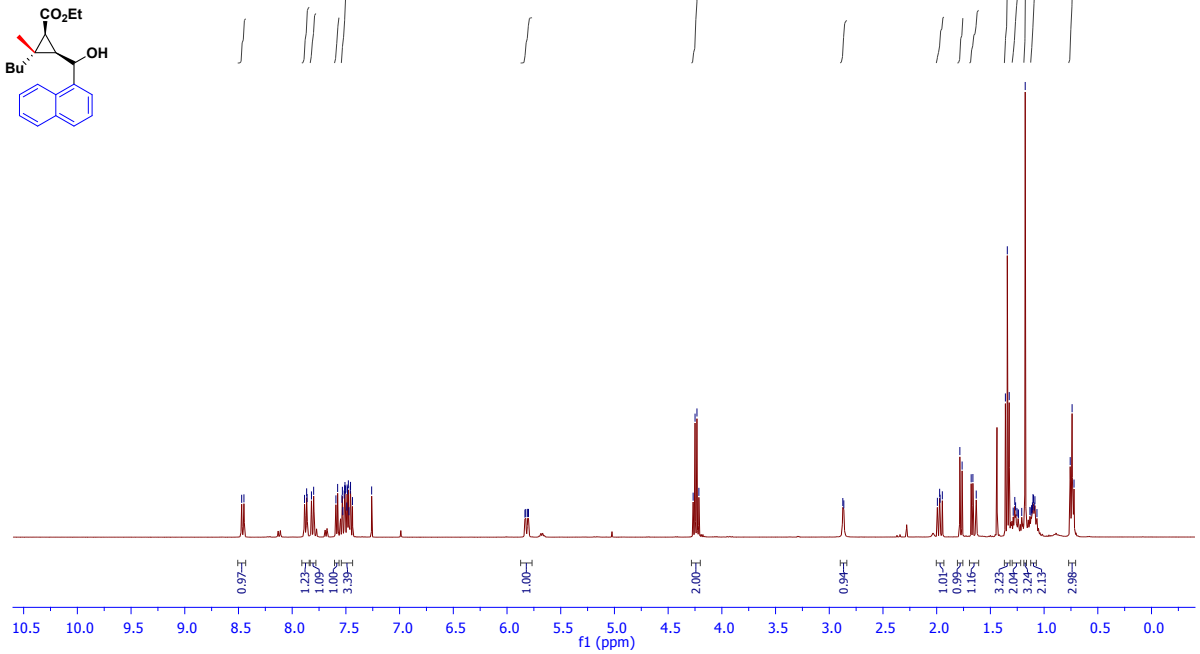
Veeru4002019



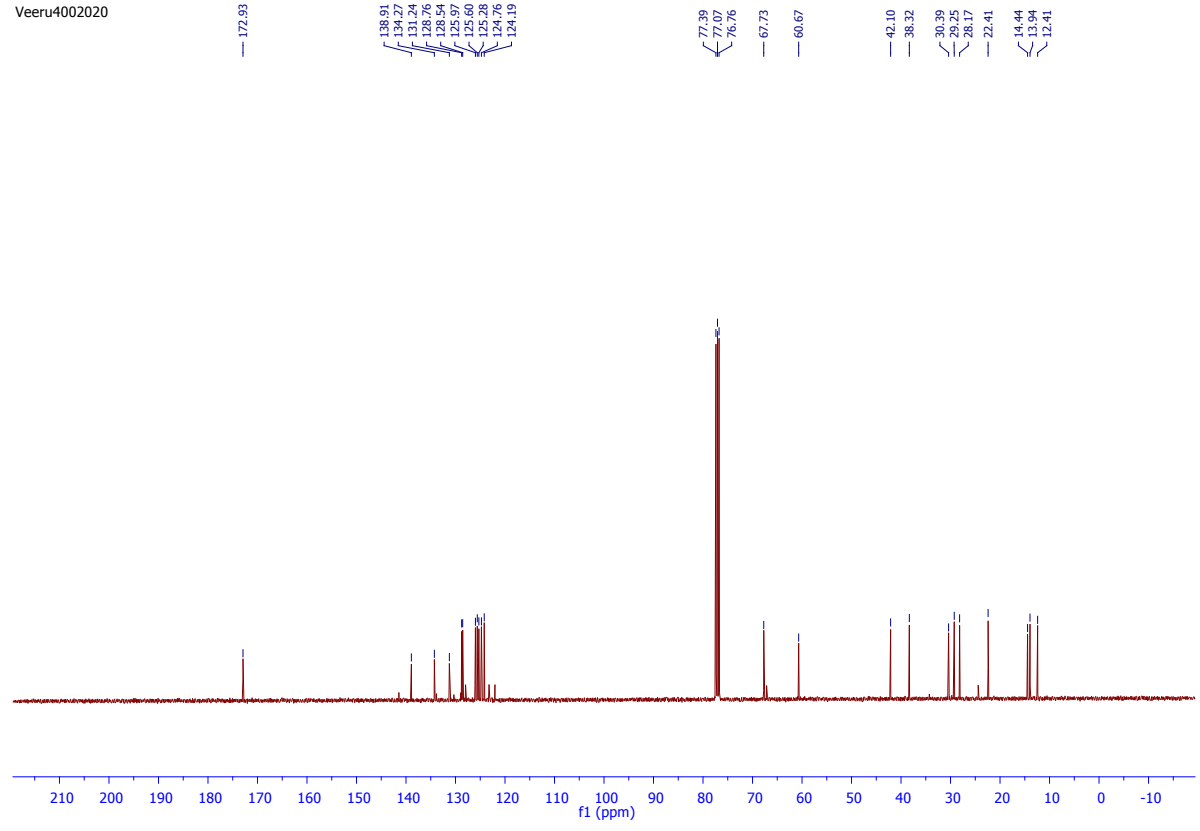
Veeru4002019

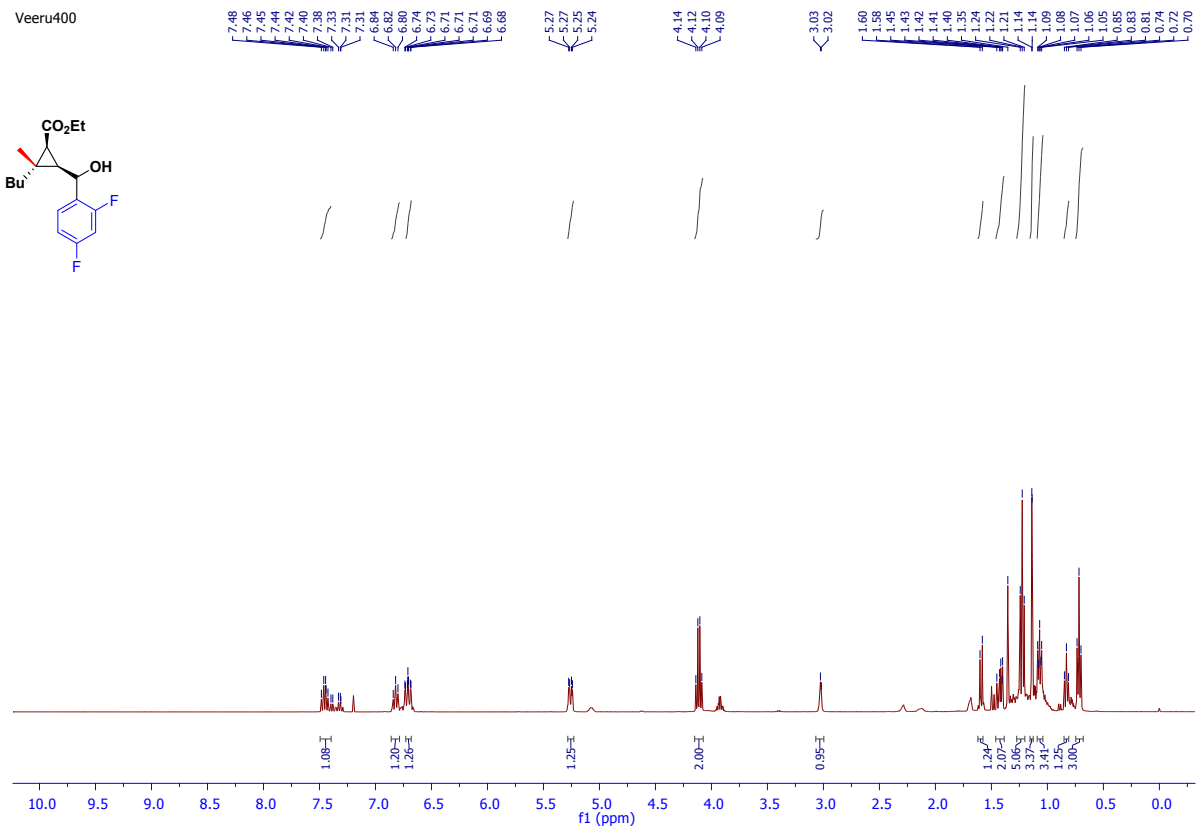


Veeru4002020



Veeru4002020




Veeru400
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7.46
7.45
7.44
7.42
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7.38
7.33
7.31
7.31
6.84
6.82
6.80
6.74
6.73
6.71
6.71
6.71
6.69
6.68
5.27
5.27
5.25
5.24
4.14
4.12
4.10
4.09
3.03
3.02
1.60
1.58
1.45
1.43
1.42
1.41
1.40
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1.24
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1.21
1.14
1.14
1.09
1.08
1.07
1.06
1.05
0.85
0.83
0.81
0.74
0.72
0.70
CO2Et
OH
Bu
F
F
1.08
1.20
1.26
1.25
2.00
0.95
1.24
2.07
5.06
3.37
3.41
1.25
3.00
10.0
9.5
9.0
8.5
8.0
7.5
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6.5
6.0
5.5
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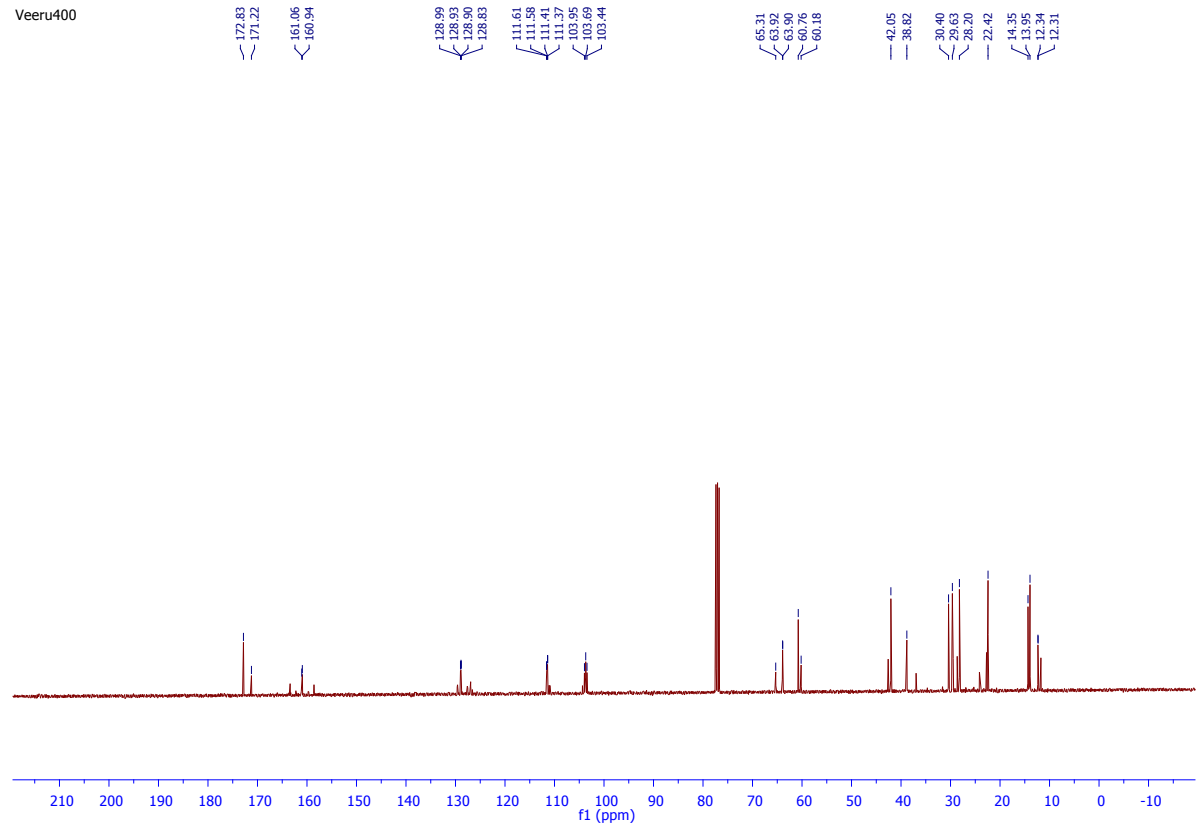
0.0
f1 (ppm)


Veeru400
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171.22
161.06
160.94
128.99
128.93
128.90
128.83
111.61
111.58
111.41
111.37
103.95
103.69
103.44
65.31
63.92
63.90
60.76
60.18
42.05
38.82
30.40
29.63
28.20
22.42
14.35
13.95
12.34
12.31
210
200
190
180
170
160
150
140
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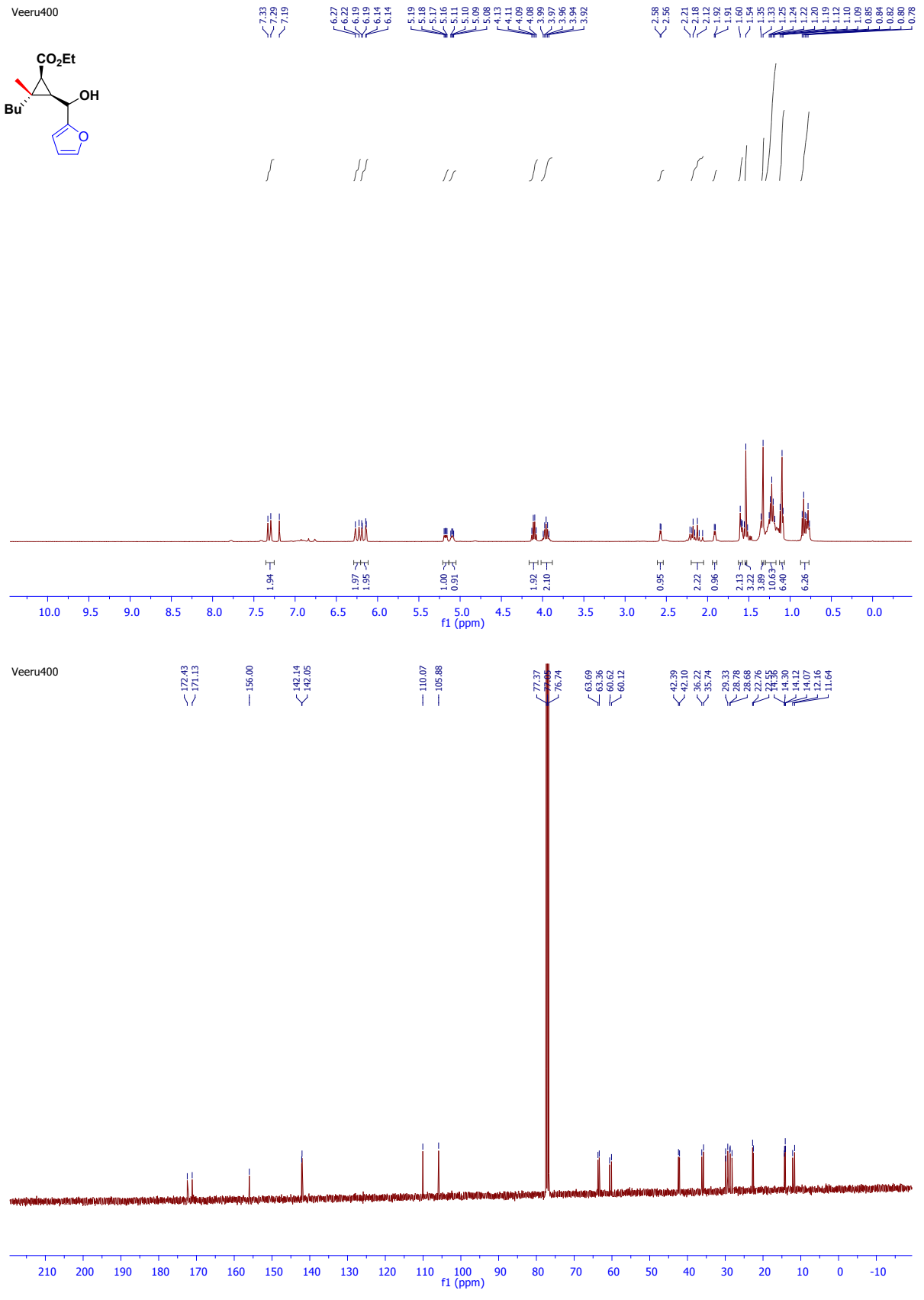
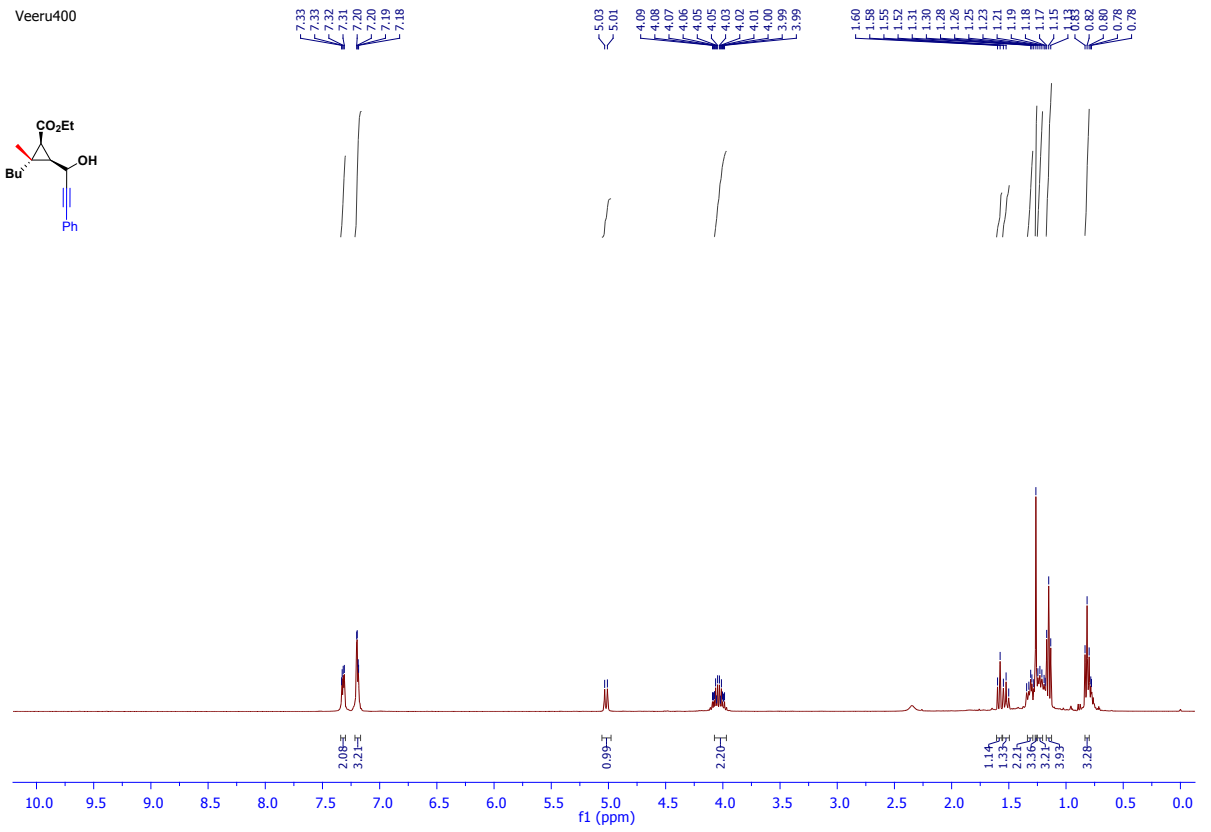
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Veeru400
CO2Et
OH
Bu
O
f1 (ppm)
Veeru400
f1 (ppm)


Veeru400
7.33
7.33
7.32
7.31
7.20
7.20
7.19
7.18
5.03
5.01
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4.08
4.07
4.06
4.05
4.05
4.03
4.02
4.01
4.00
3.99
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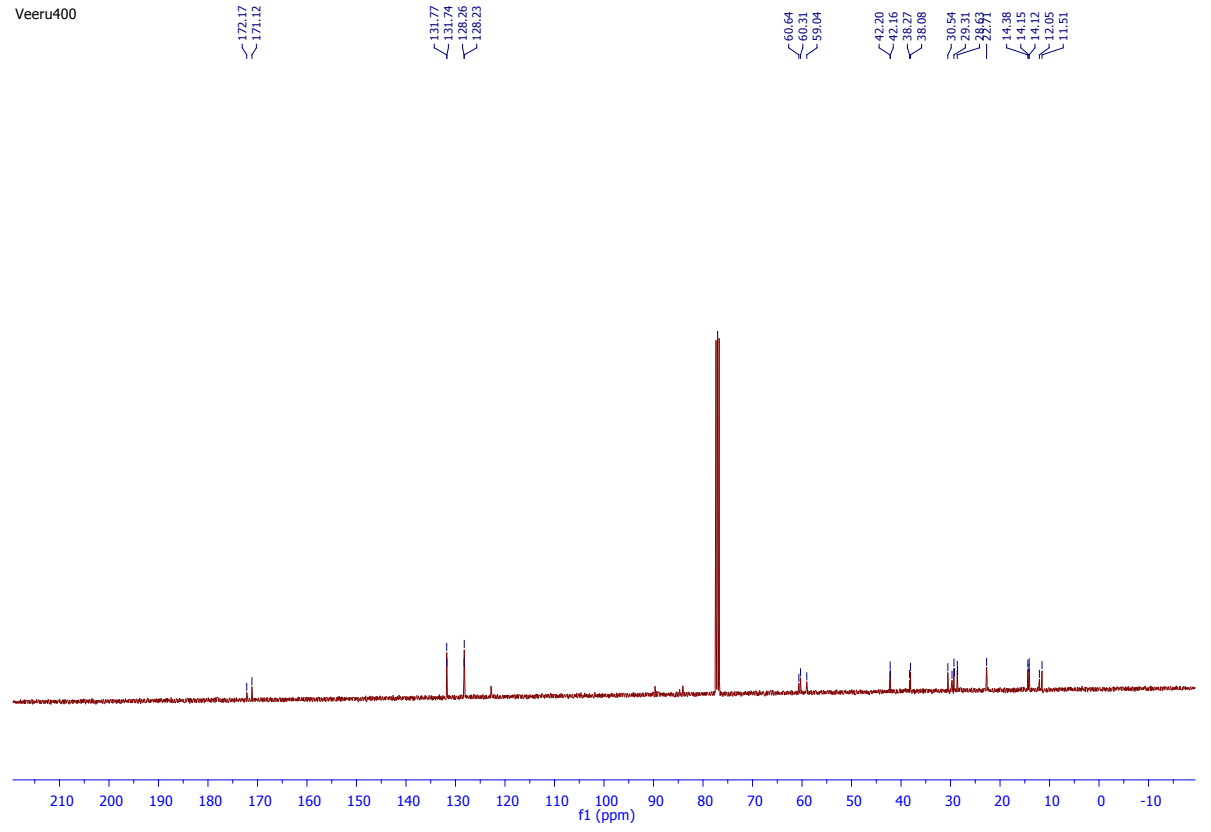
1.28
1.26
1.25
1.23
1.21
1.19
1.18
1.17
1.15
1.13
0.83
0.82
0.80
0.78
0.78
CO2Et
OH
Bu
Ph
2.08
3.21
0.99
2.20
1.14
1.33
2.21
3.36
3.21
3.93
3.28
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


Veeru400
172.17
171.12
131.77
131.74
128.26
128.23
60.64
60.31
59.04
42.20
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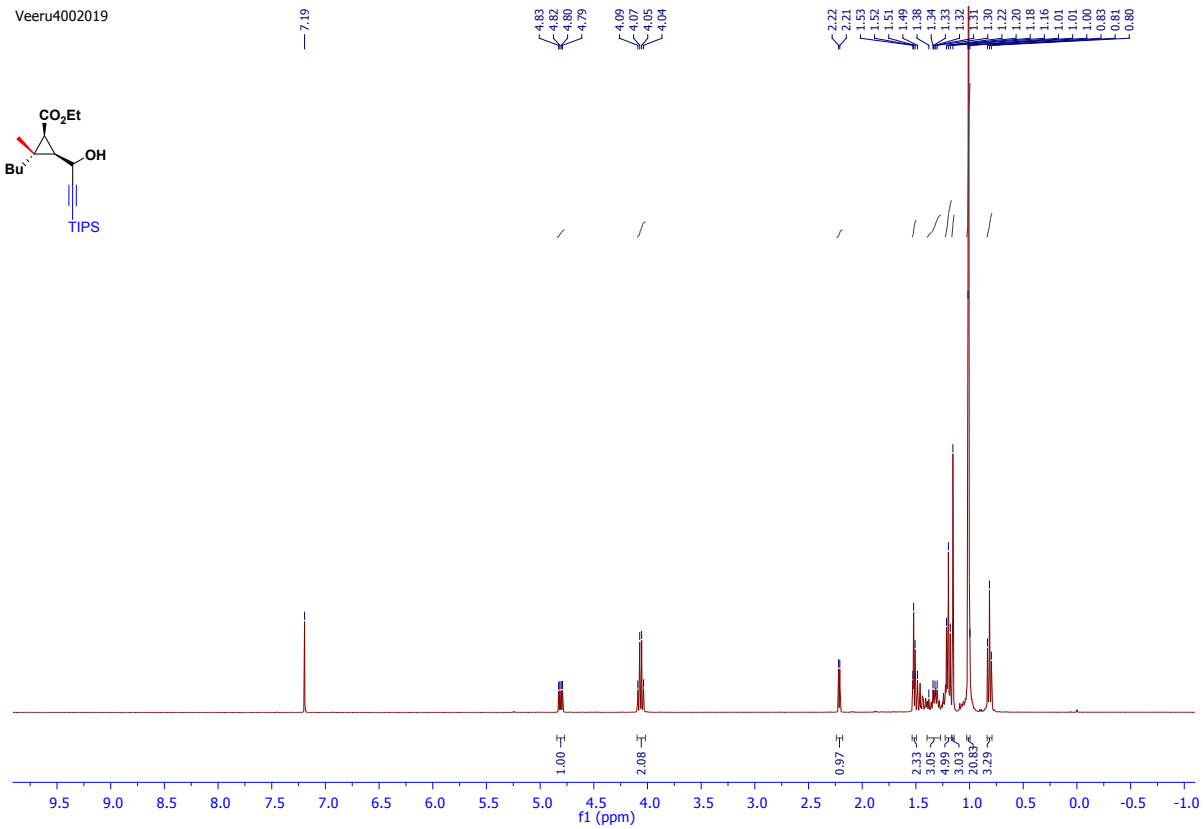
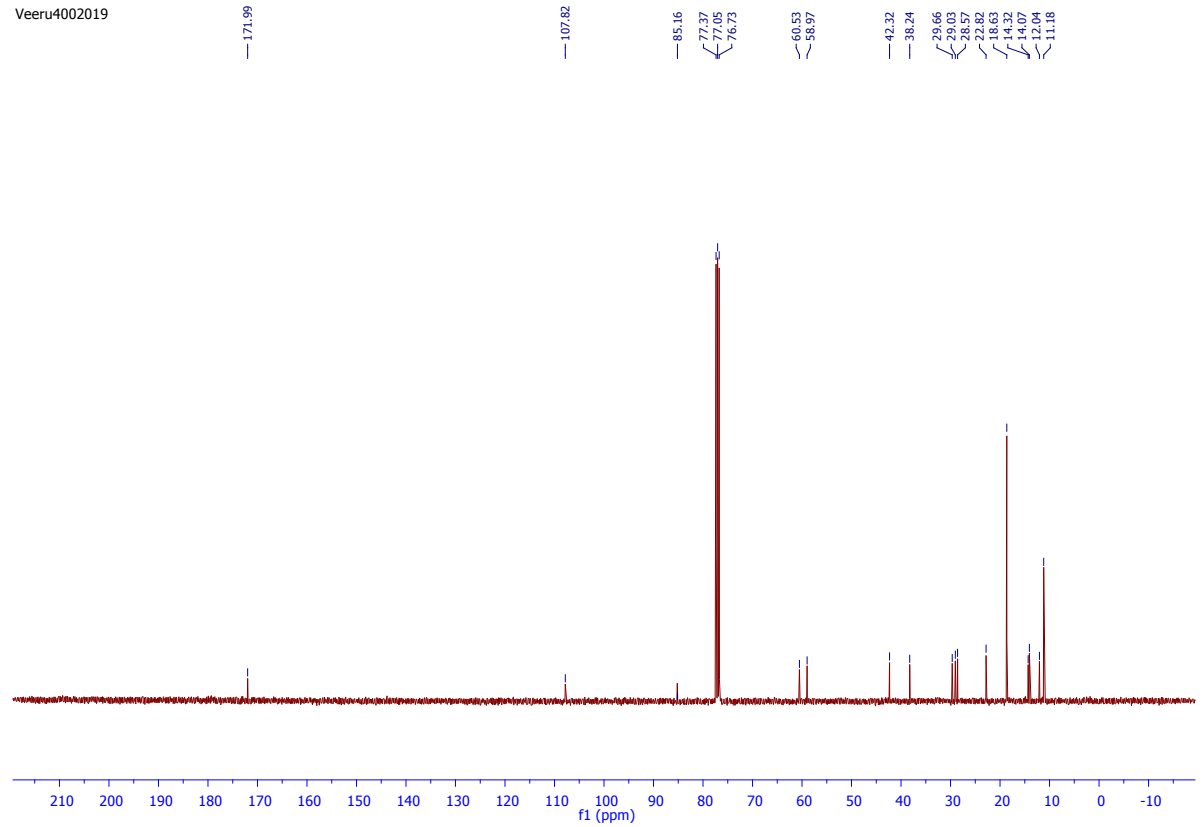
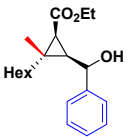
38.27
38.08
30.54
29.31
28.63
22.71
14.38
14.15
14.12
12.05
11.51
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

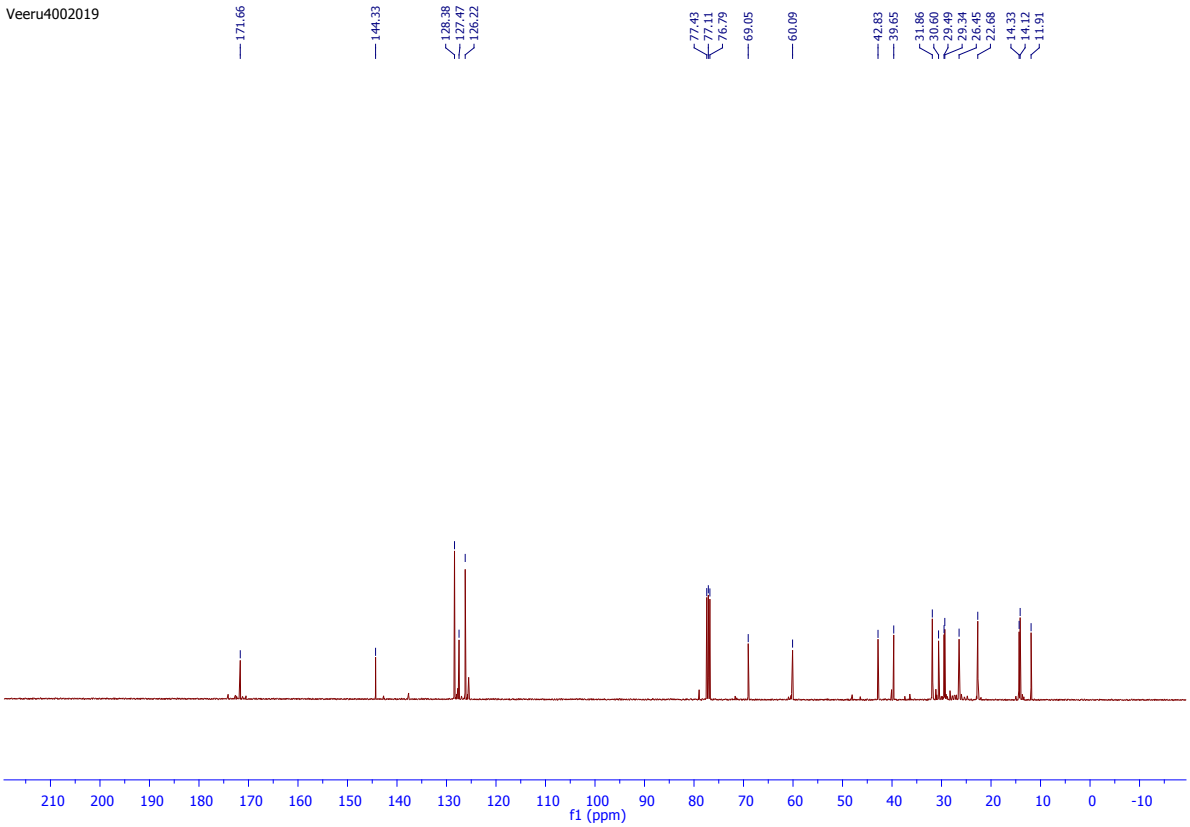

Veeru4002019
7.19
4.83
4.82
4.80
4.79
4.09
4.07
4.05
4.04
2.22
2.21
1.53
1.52
1.51
1.49
1.38
1.34
1.33
1.32
1.31
1.30
1.22
1.20
1.18
1.16
1.01
1.01
1.00
0.83
0.81
0.80
CO2Et
OH
Bu
TIPS
1.00
2.08
0.97
2.33
3.05
4.99
3.03
20.83
3.29
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

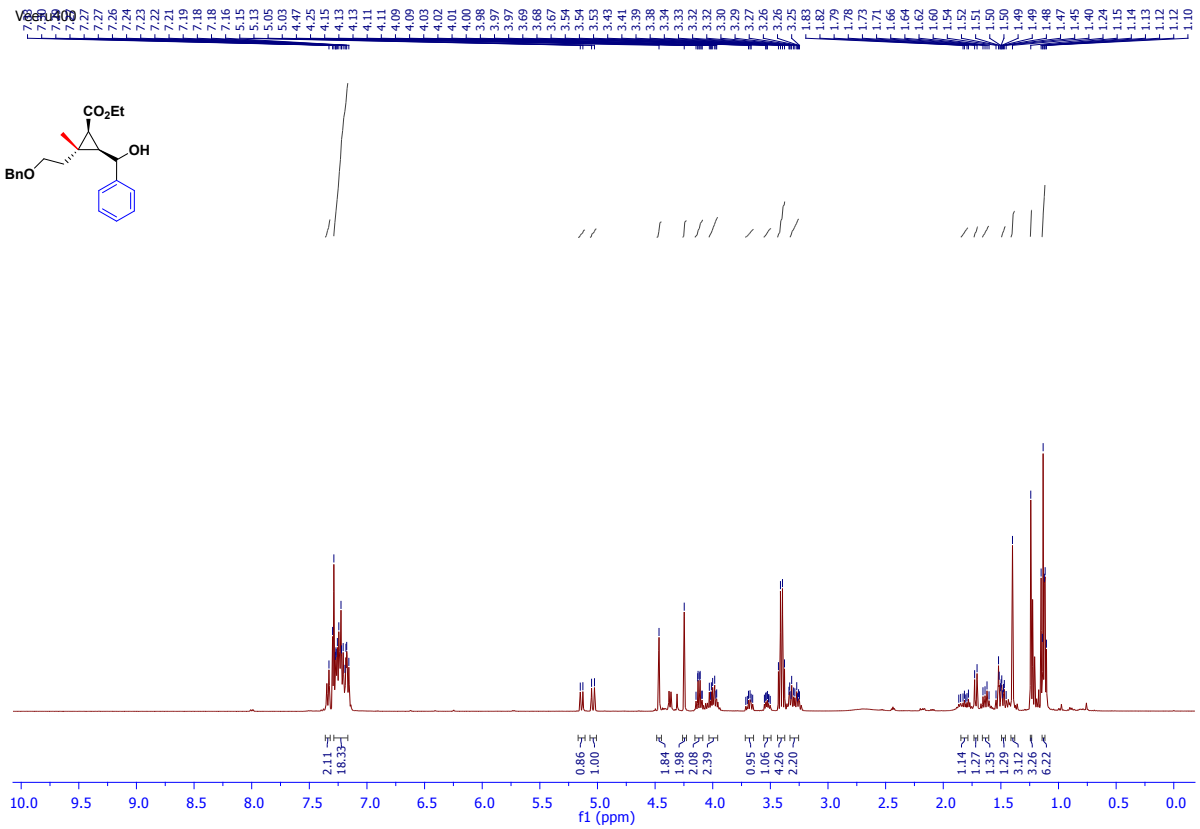

Veeru4002019
171.99
107.82
85.16
77.37
77.05
76.73
60.53
58.97
42.32
38.24
29.66
29.03
28.57
22.82
18.63
14.32
14.07
12.04
11.18
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

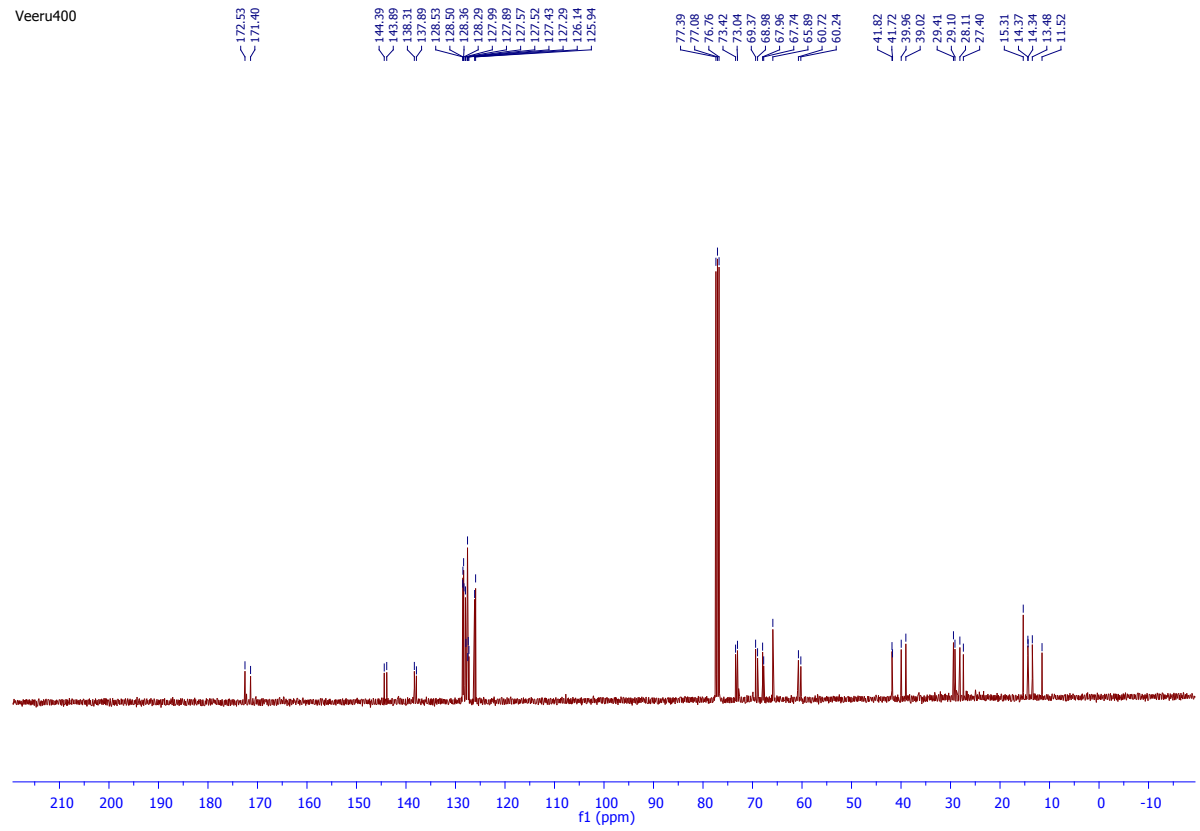
Veeru400



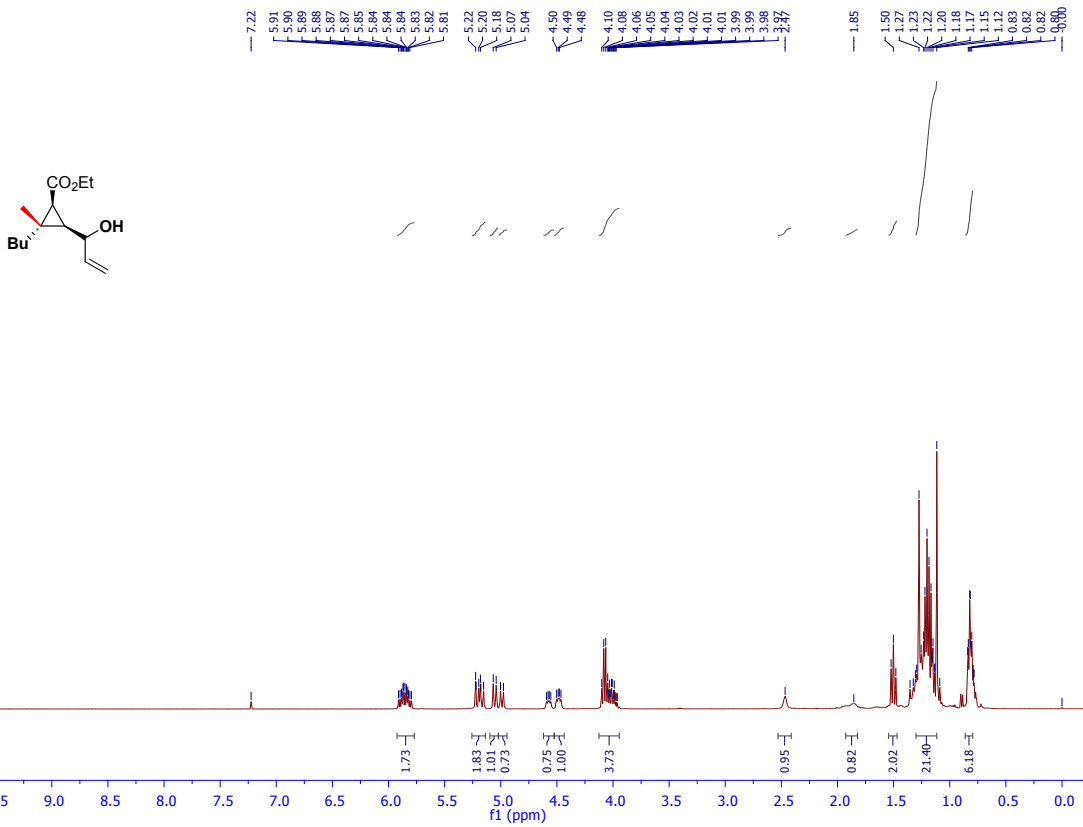
Veeru4002019



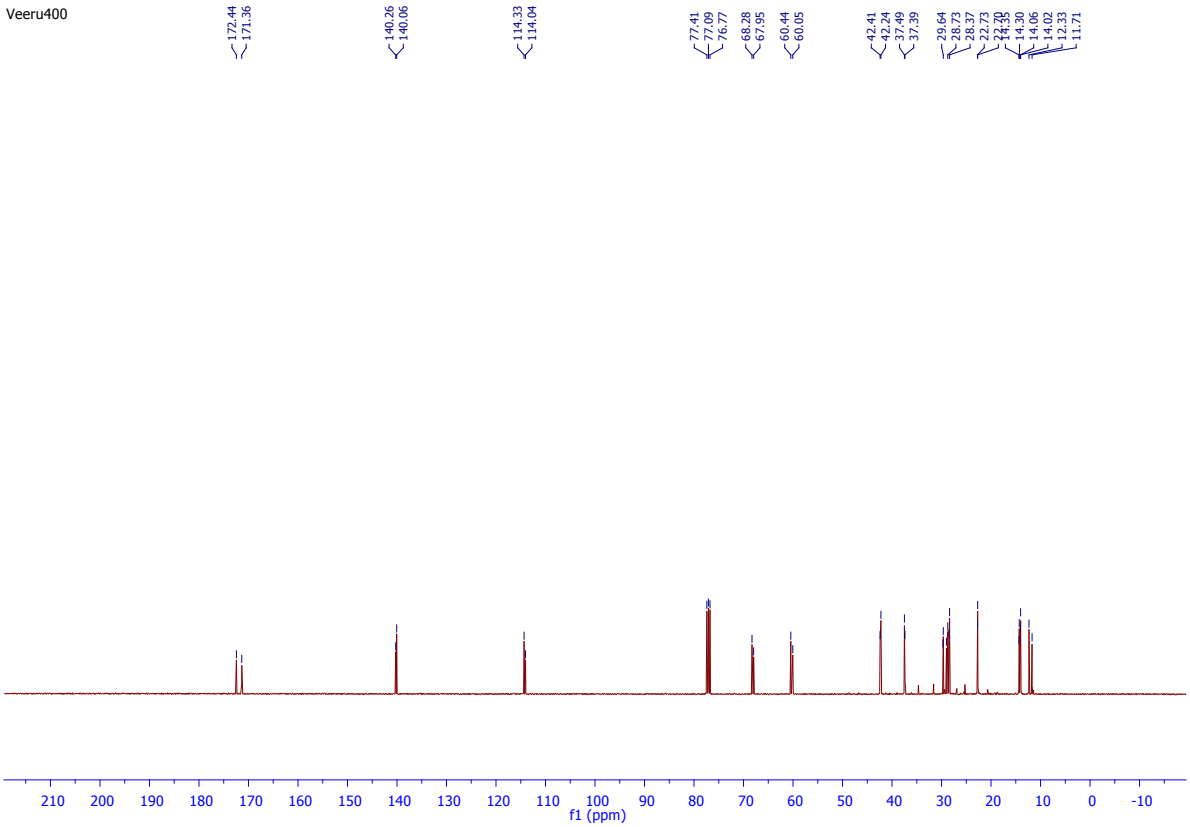

Veeru400
CO2Et
OH
BnO
2.11
18.33
0.86
1.00
1.84
1.98
2.08
2.39
0.95
1.06
4.26
2.20
1.14
1.27
1.35
1.29
3.12
3.26
6.22
f1 (ppm)


Veeru400
f1 (ppm)

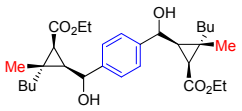
Veeru400



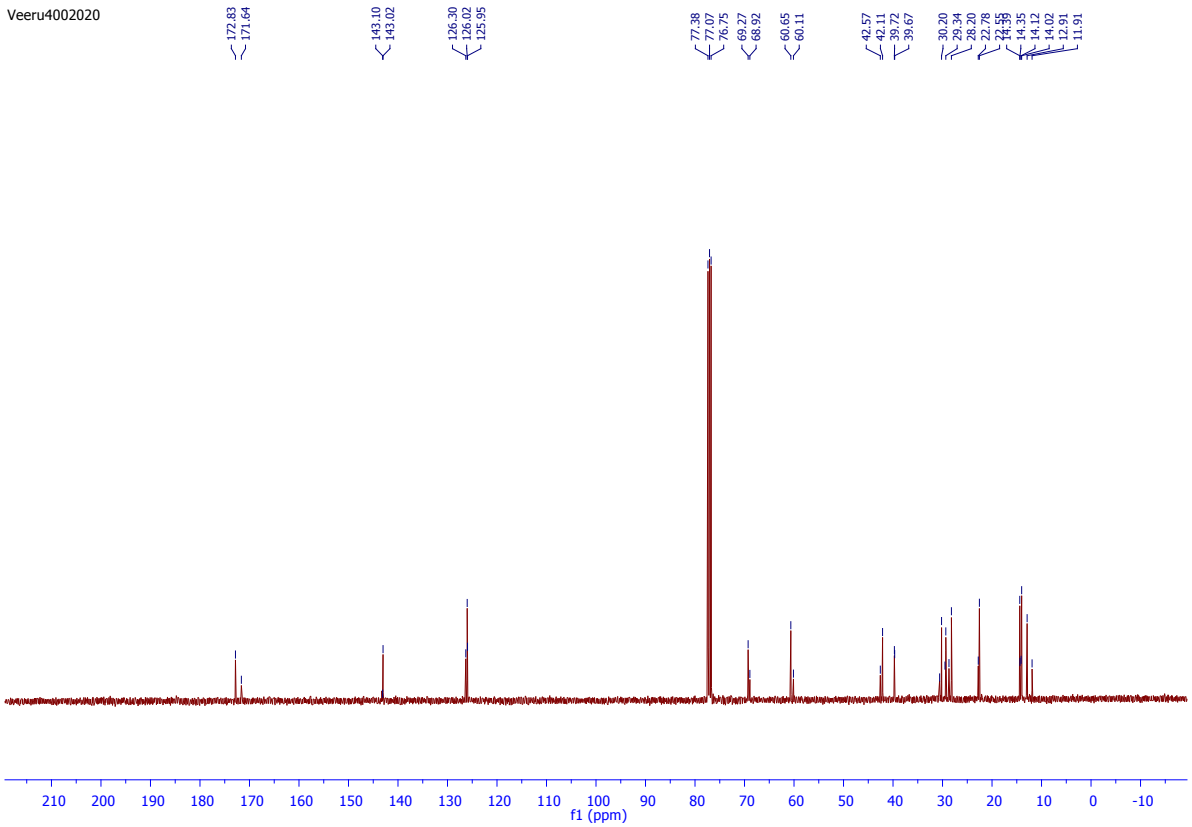
Veeru400



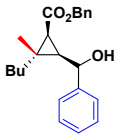
Veeru4002020



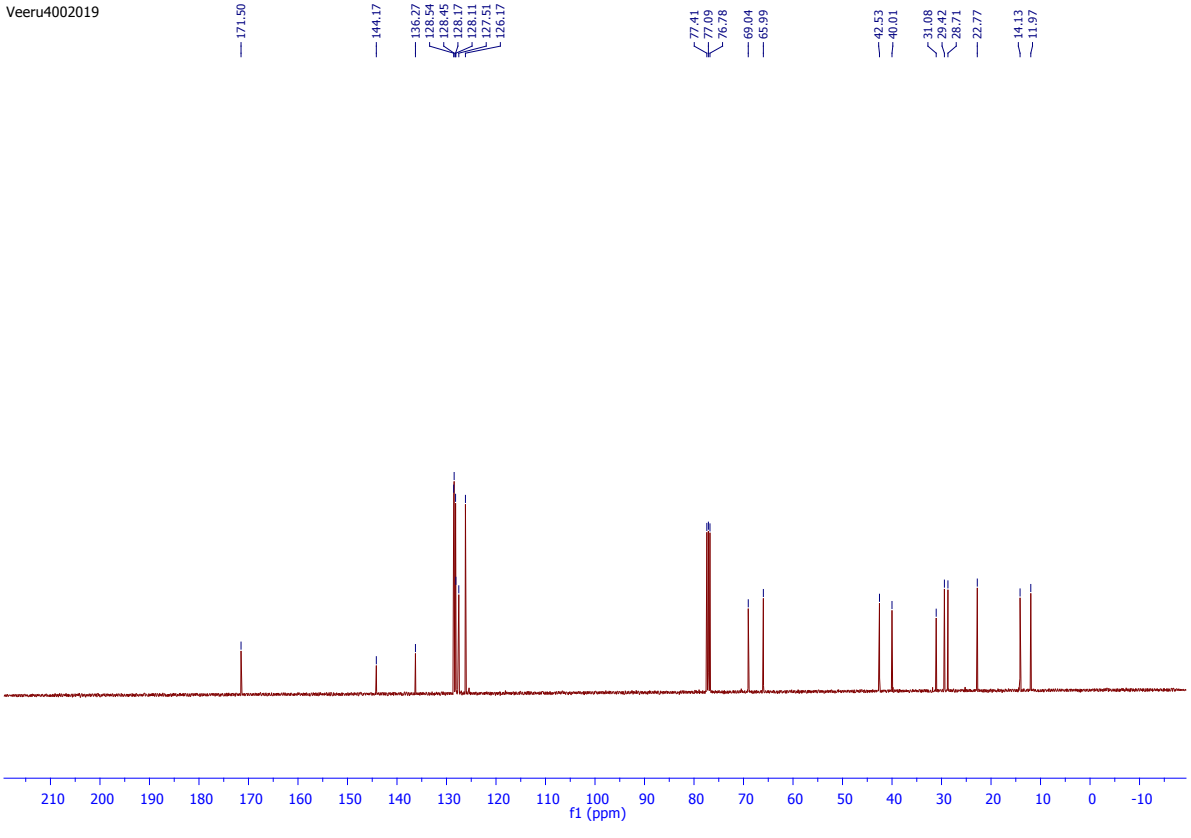
Veeru4002020

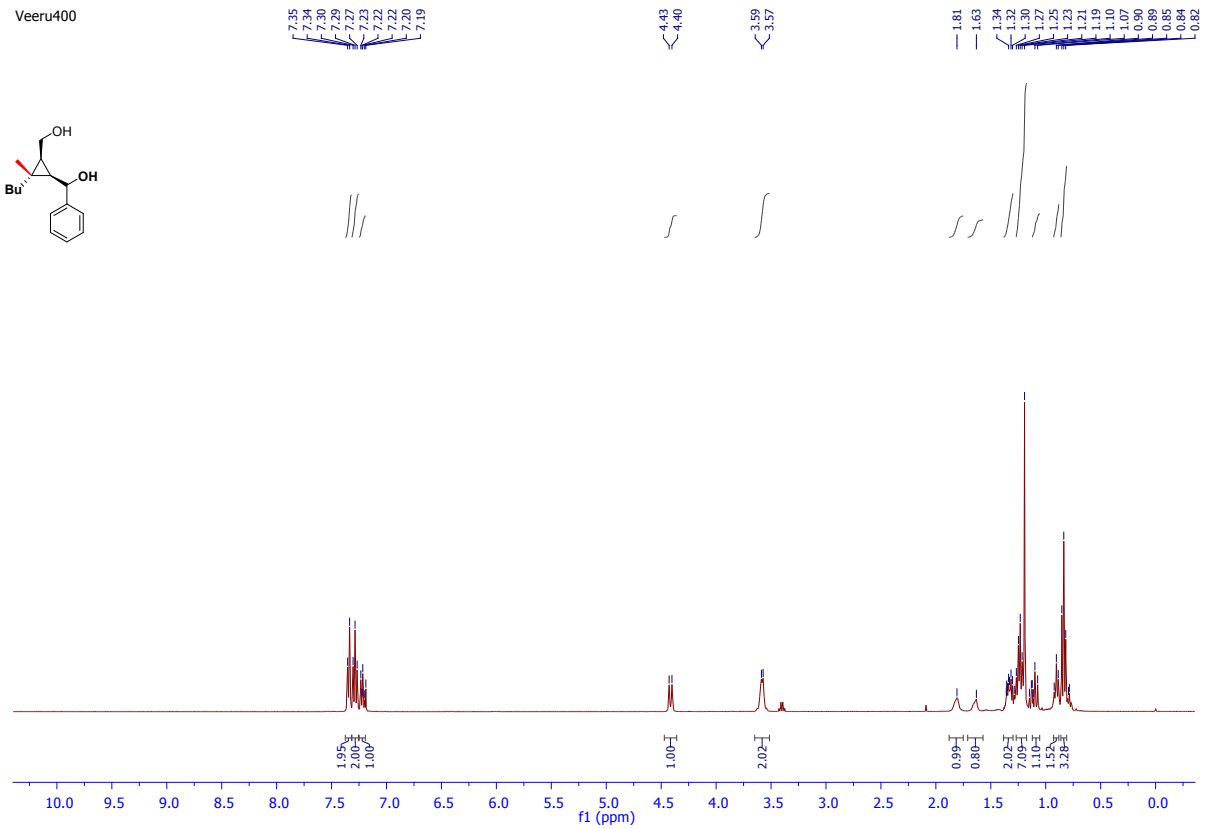


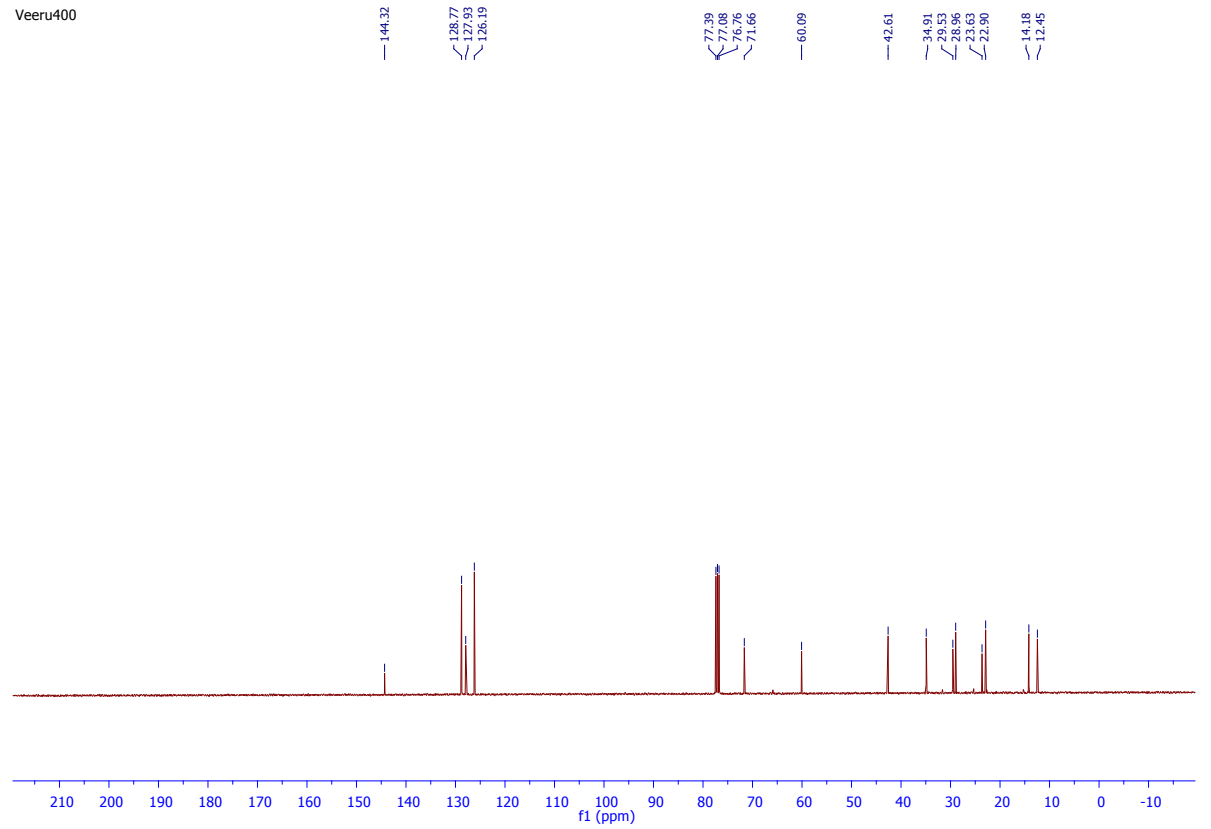
Veeru4002019

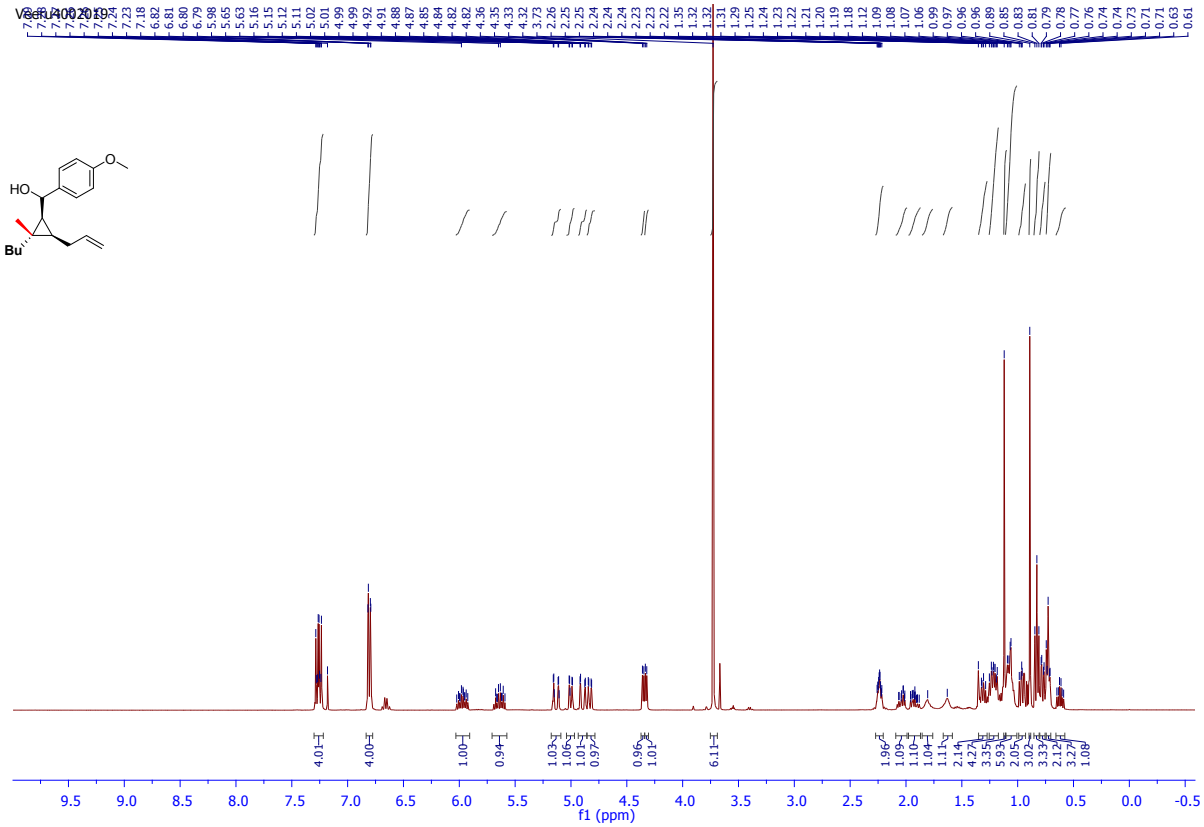


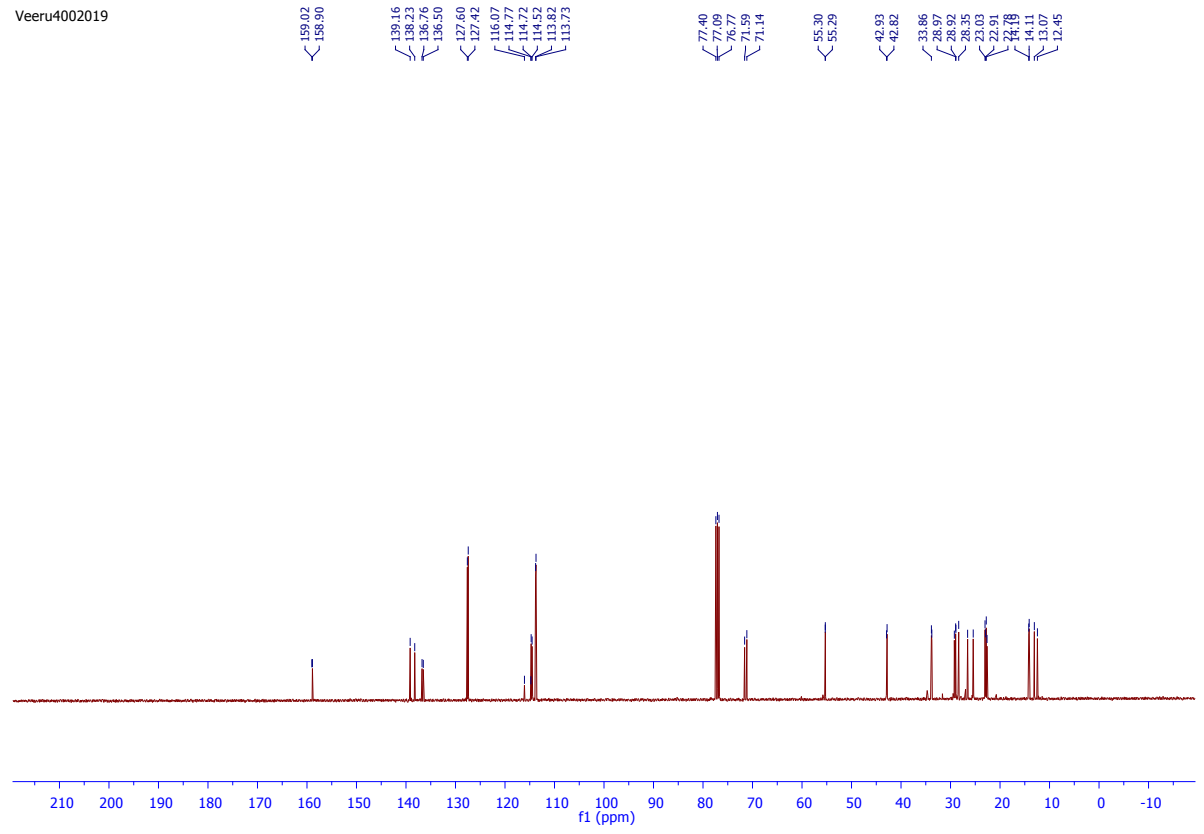
Veeru4002019

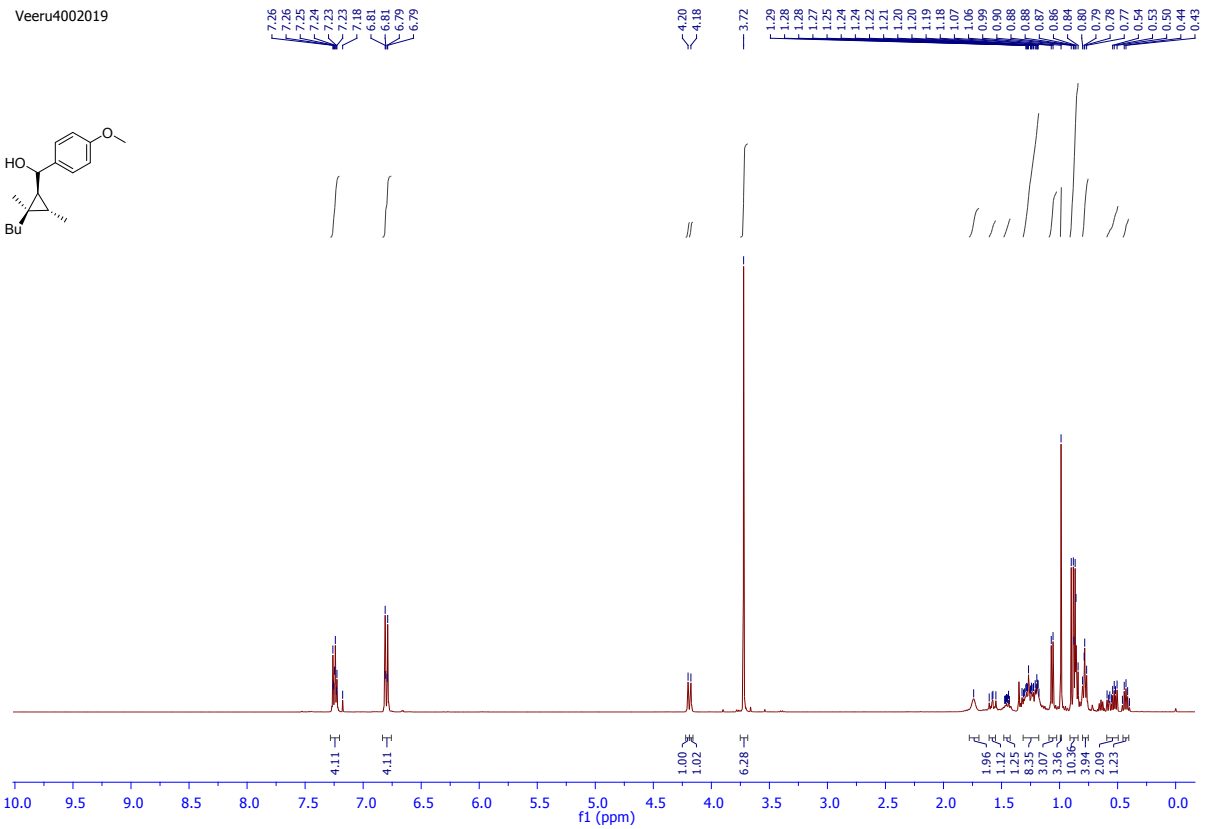


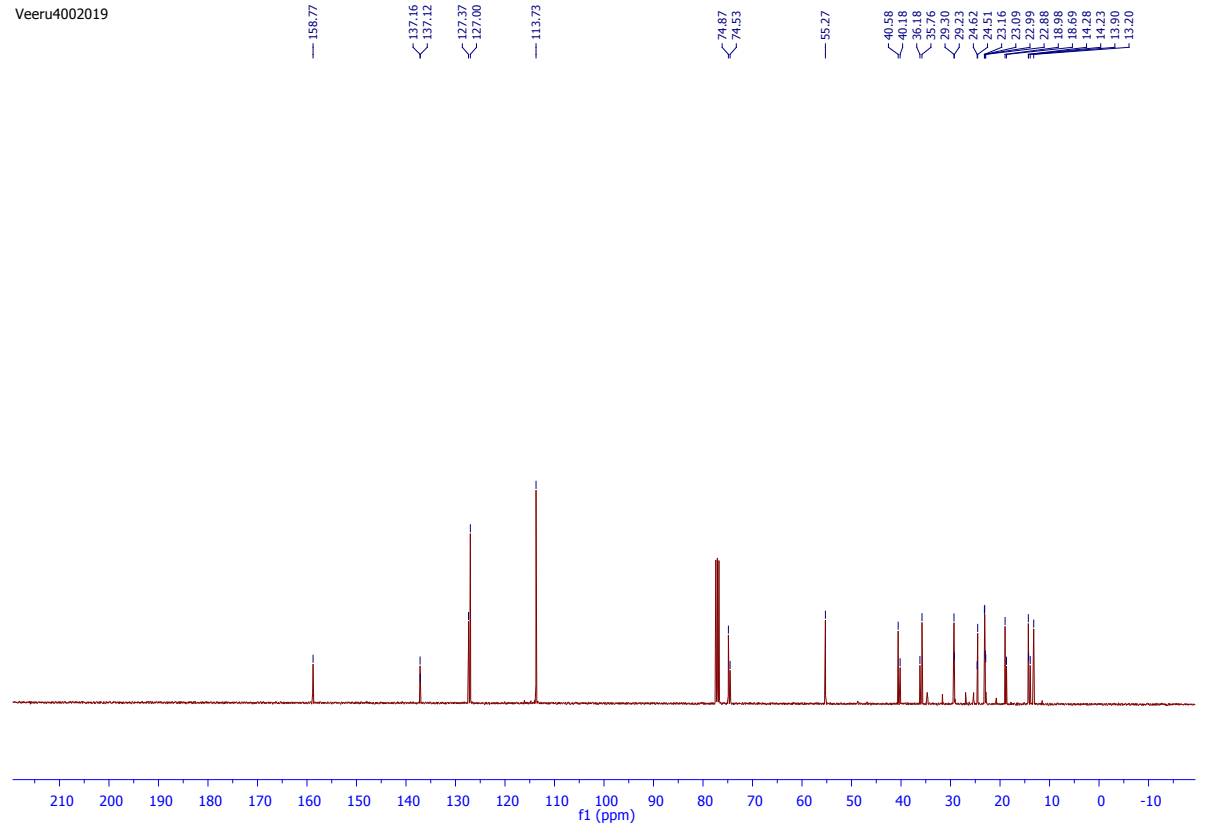

Veeru400
7.35
7.34
7.30
7.29
7.27
7.23
7.22
7.22
7.20
7.19
4.43
4.40
3.59
3.57
1.81
1.63
1.34
1.32
1.30
1.27
1.25
1.23
1.21
1.19
1.10
1.07
0.90
0.89
0.85
0.84
0.82
OH
OH
Bu
1.95
2.00
1.00
1.00
2.02
0.99
0.80
2.02
7.09
1.10
1.52
3.28
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

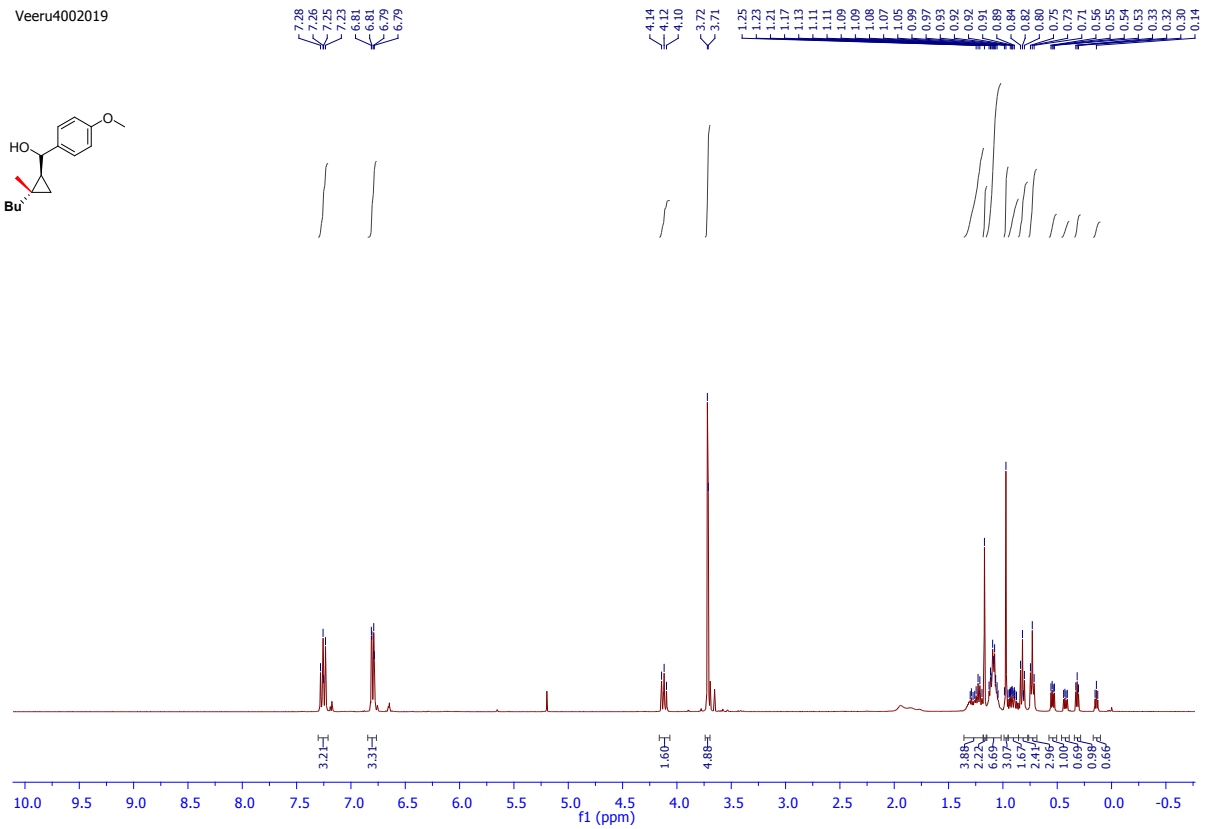

Veeru400
144.32
128.77
127.93
126.19
77.39
77.08
76.76
71.66
60.09
42.61
34.91
29.53
28.96
23.63
22.90
14.18
12.45
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

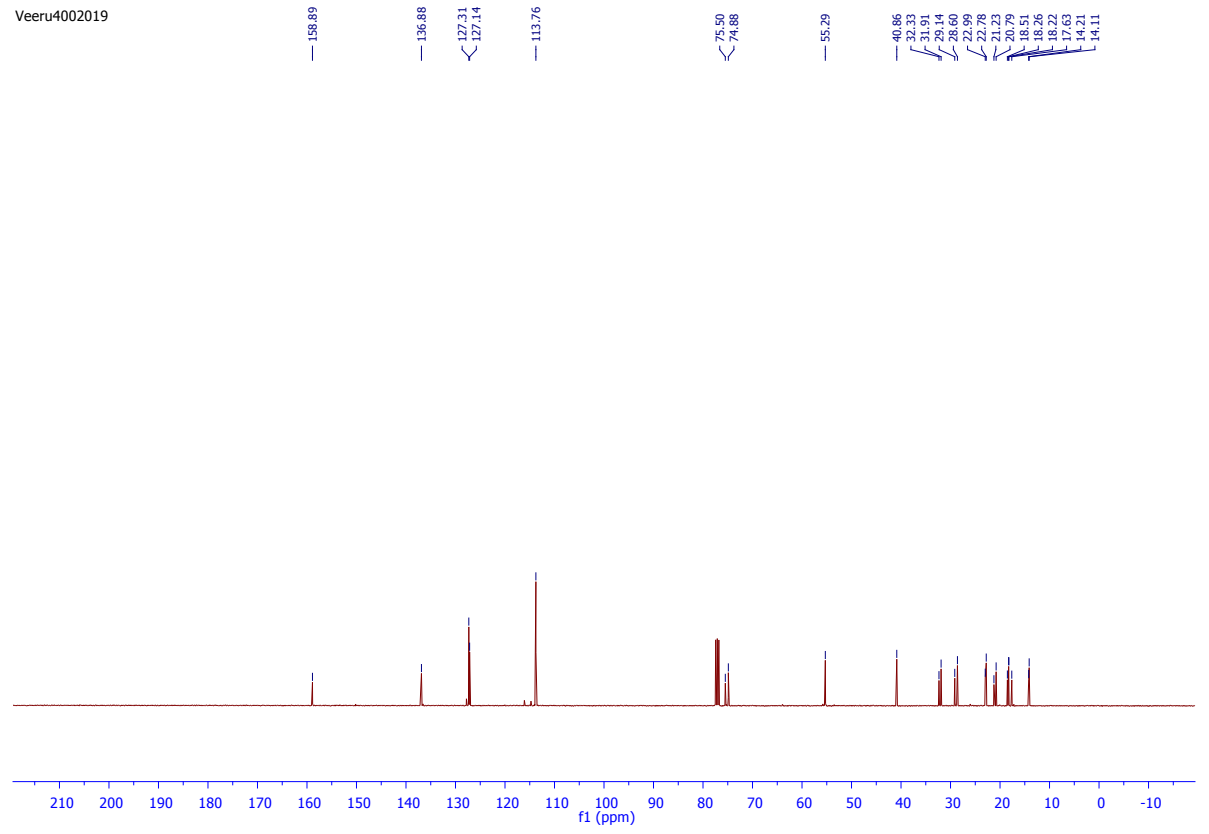

Veeru4002019
HO
O
Bu
4.01
4.00
1.00
0.94
1.03
1.06
1.01
0.97
0.96
1.01
6.11
1.96
1.09
1.10
1.04
1.11
2.14
4.27
3.35
5.93
2.05
3.02
3.39
2.12
3.27
1.08
f1 (ppm)


Veeru4002019
159.02
158.90
139.16
138.23
136.76
136.50
127.60
127.42
116.07
114.77
114.72
114.52
113.82
113.73
77.40
77.09
76.77
71.59
71.14
55.30
55.29
42.93
42.82
33.86
28.97
28.92
28.35
23.03
22.91
14.19
14.11
13.07
12.45
f1 (ppm)

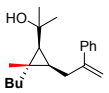

Veeru4002019
HO
O
Bu
f1 (ppm)


Veeru4002019
f1 (ppm)

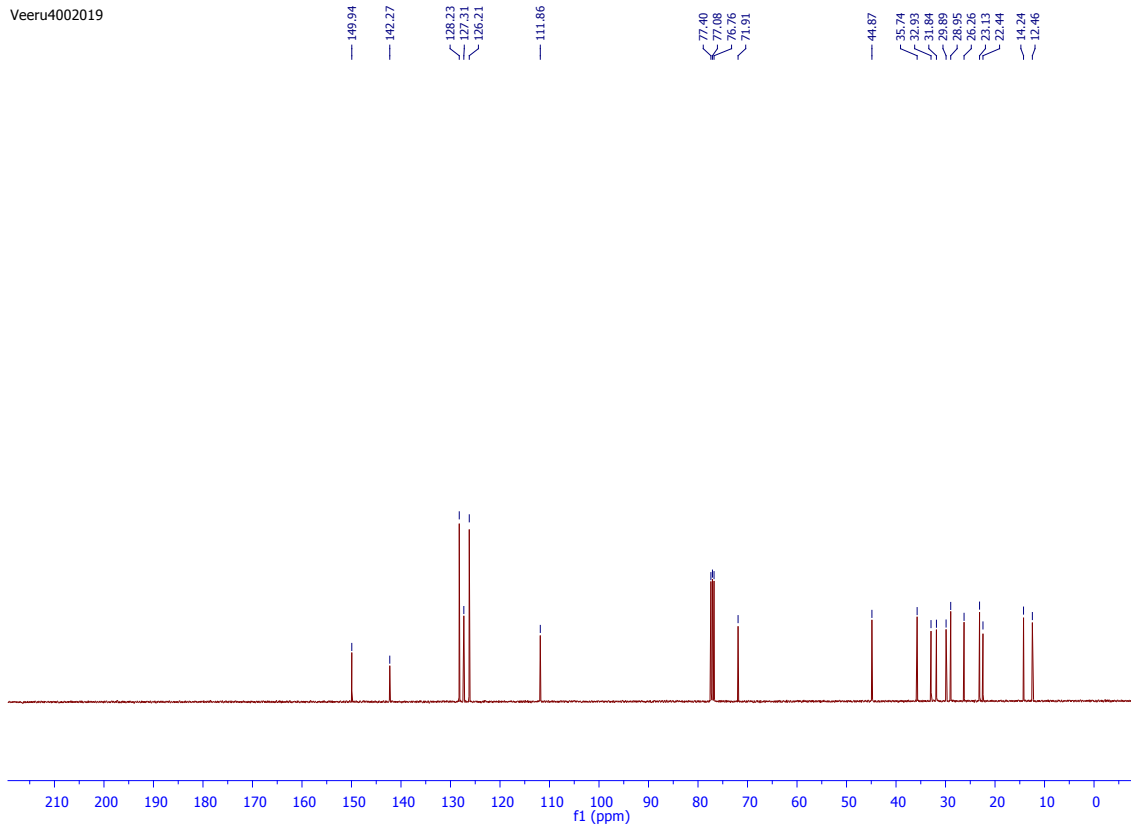

Veeru4002019
HO
O
Bu
f1 (ppm)


Veeru4002019
f1 (ppm)

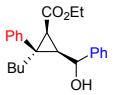
Veeru4002019

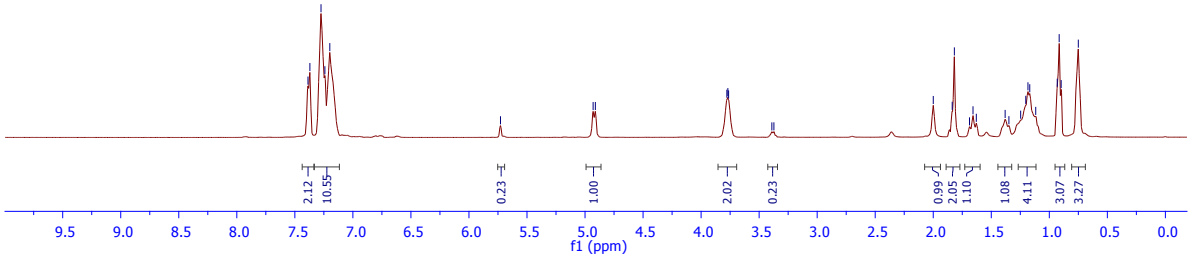


Veeru4002019

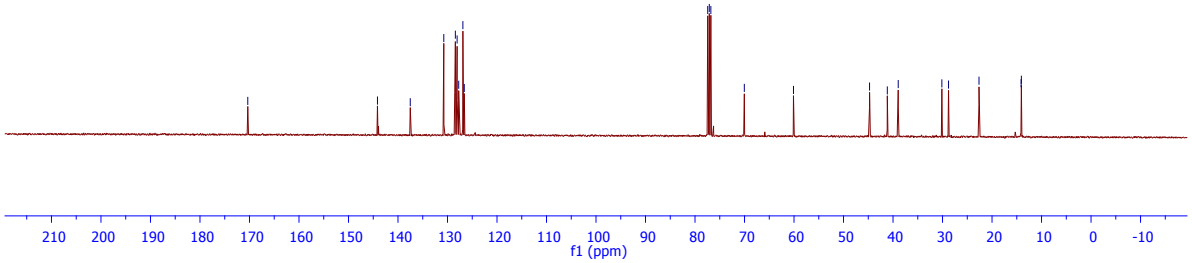


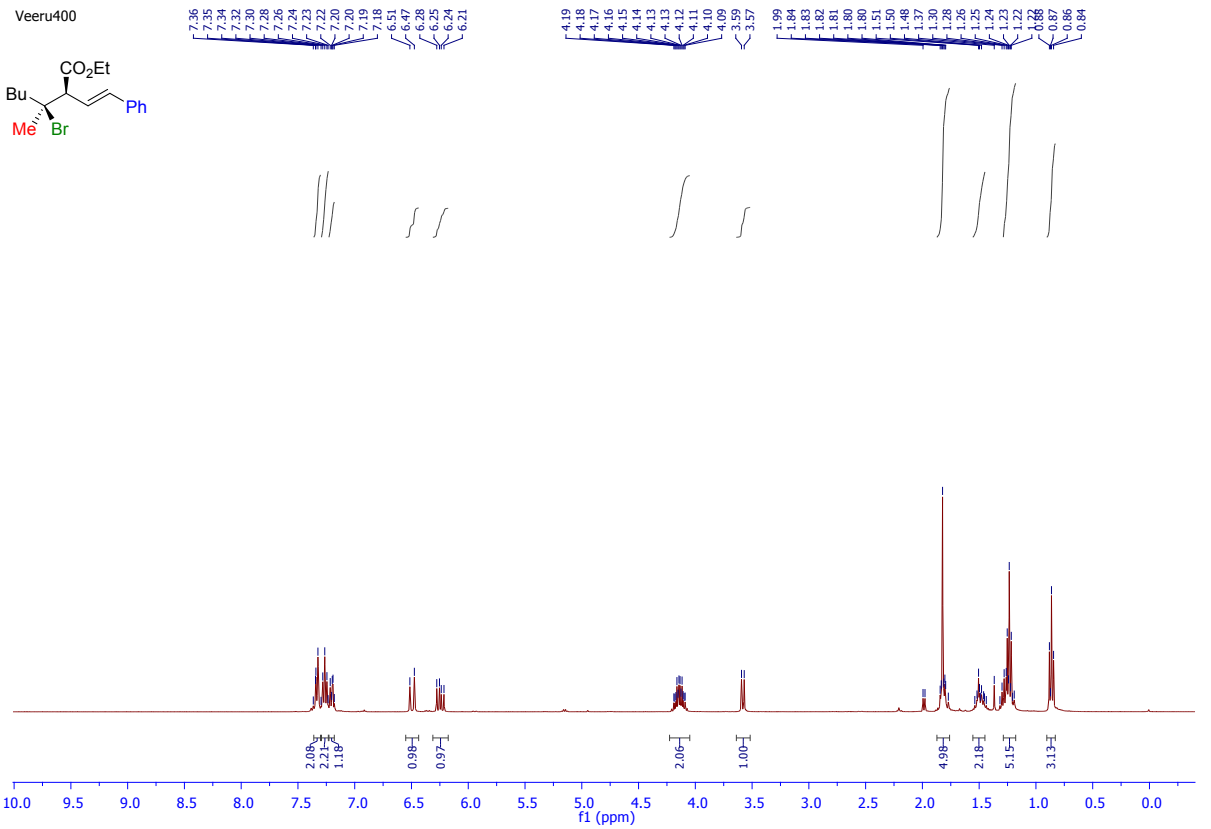
Veeru4002019

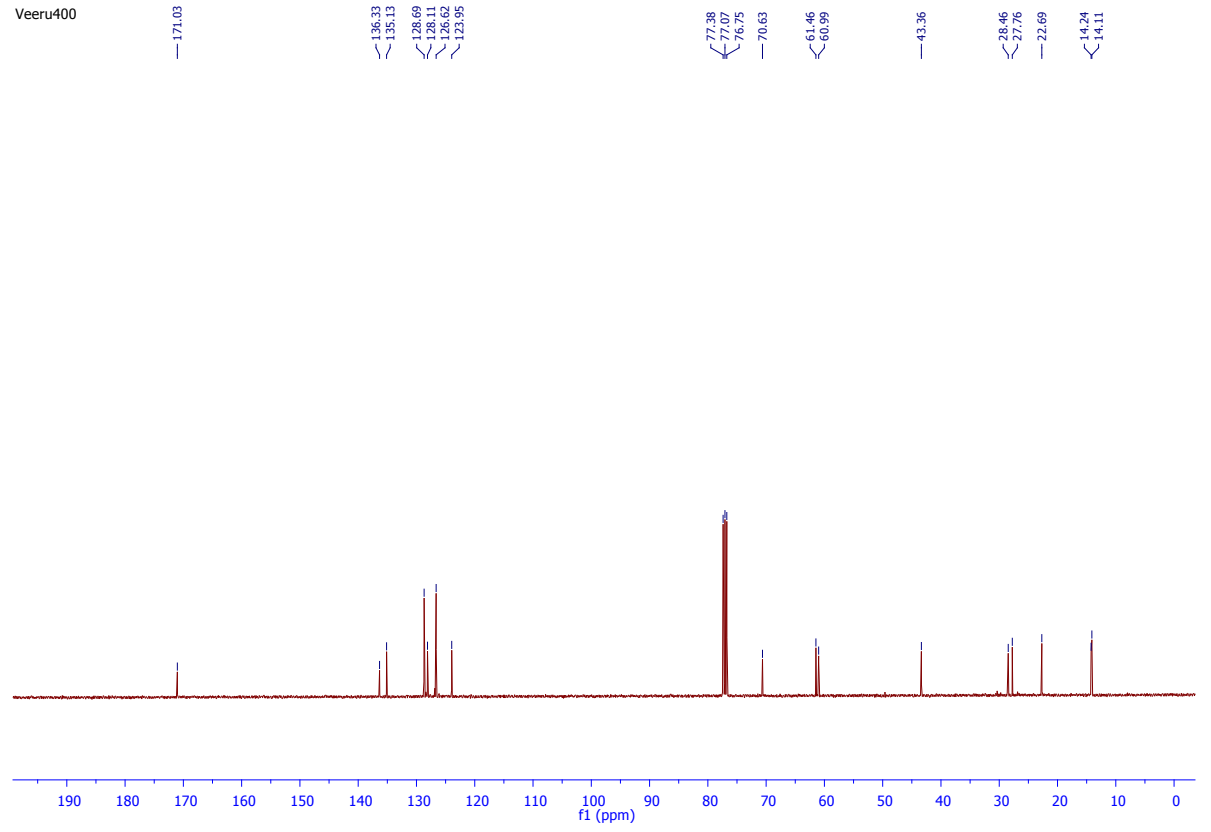


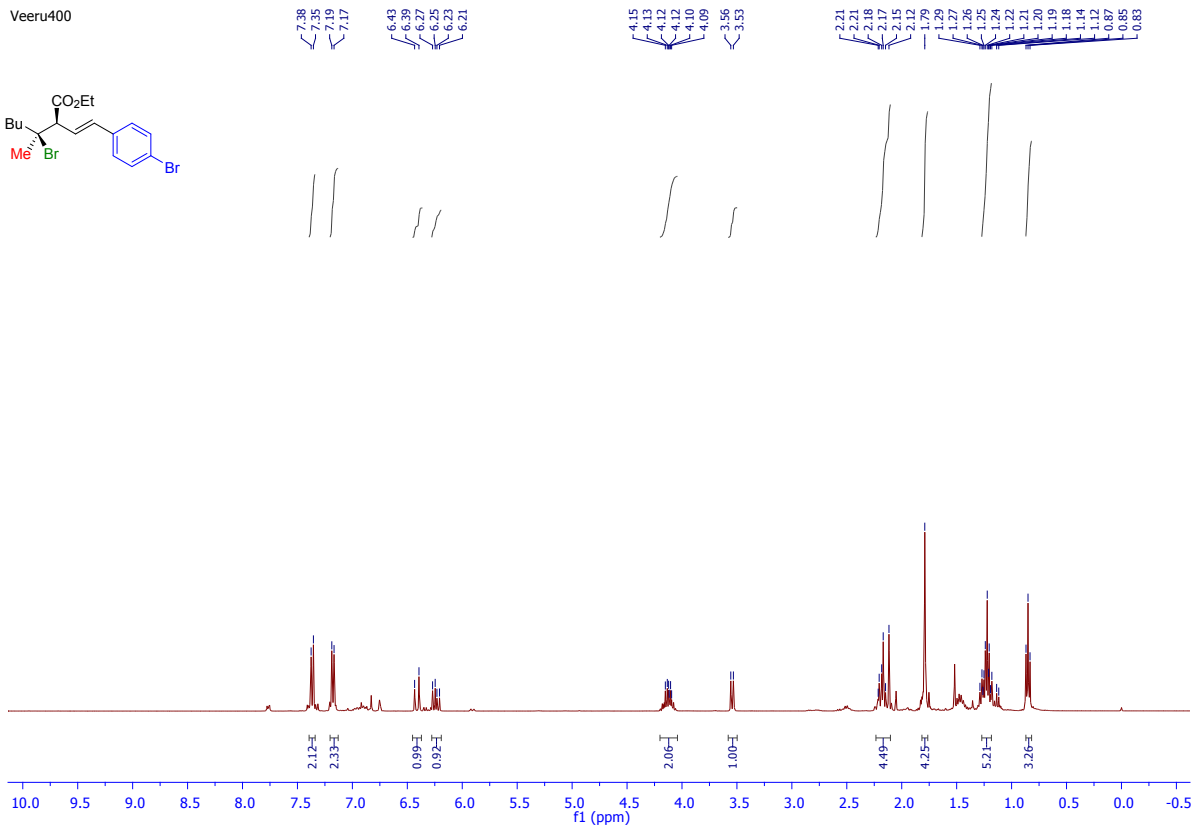


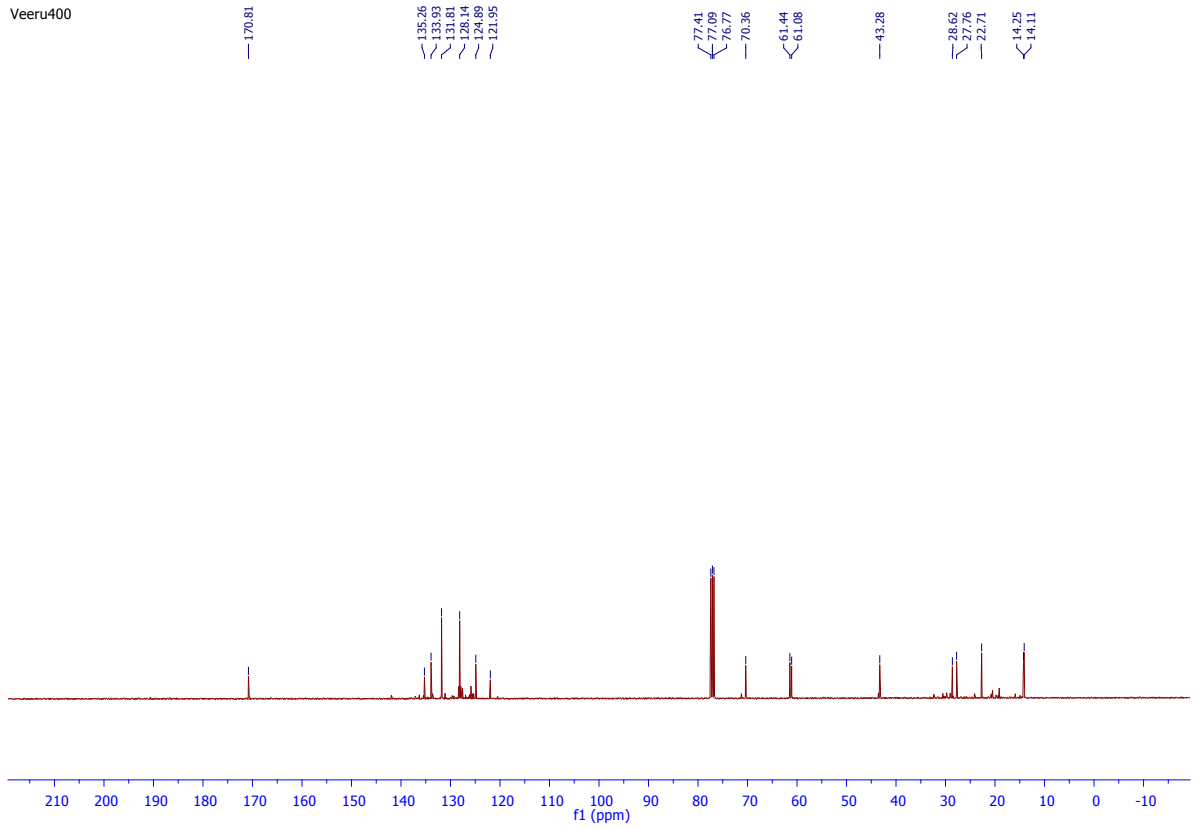
Veeru4002019

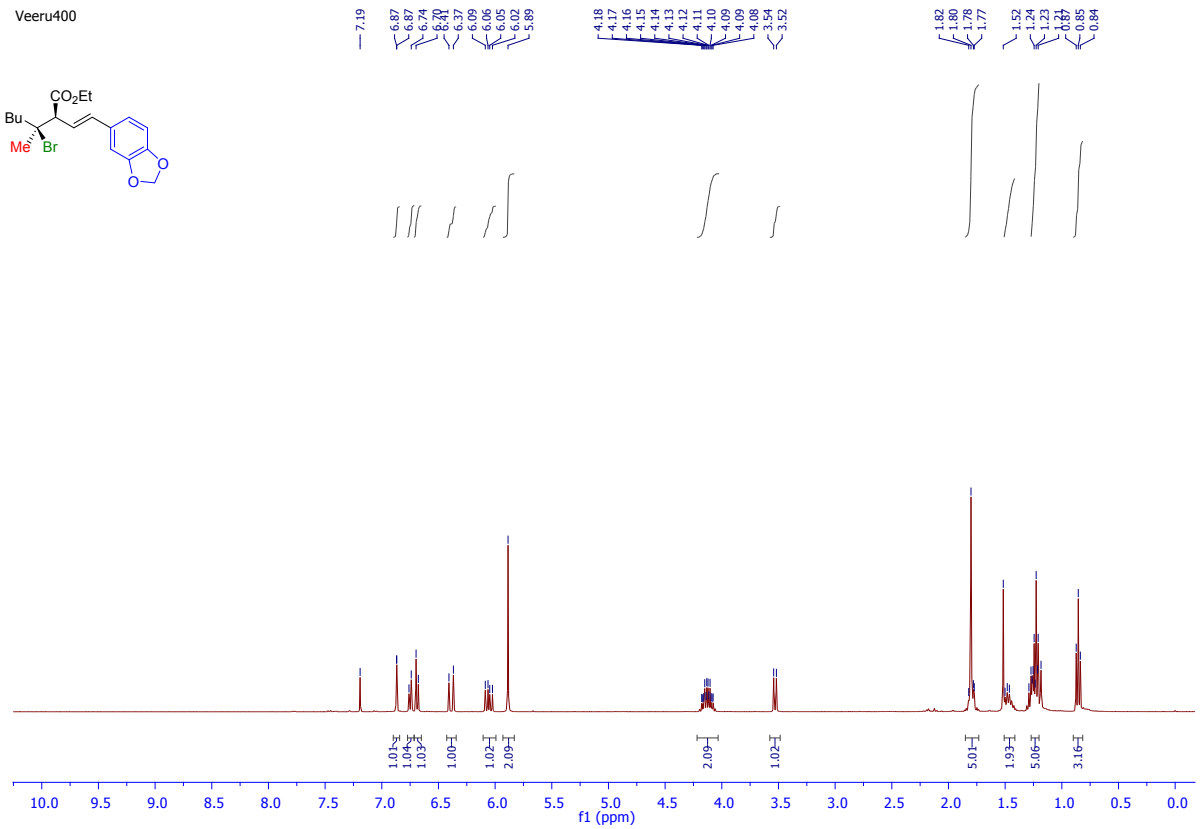


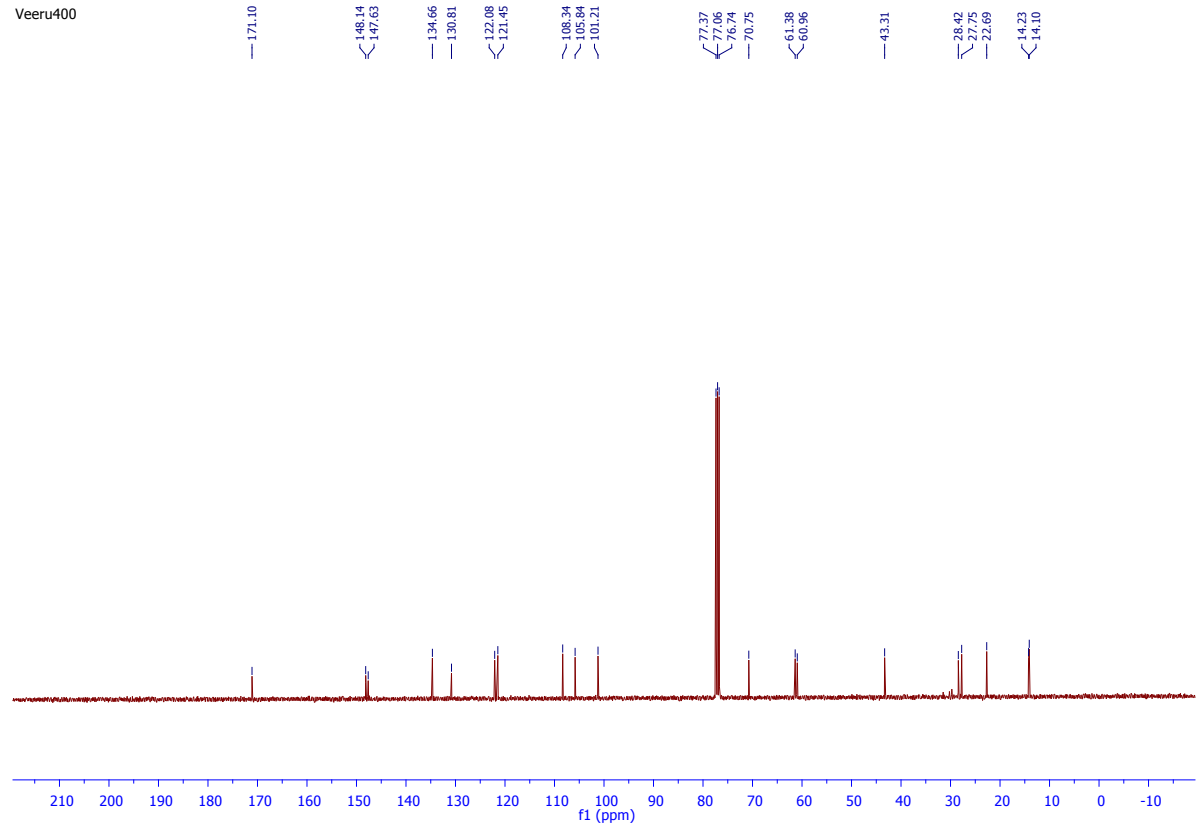

Veeru400
CO2Et
Bu
Ph
Me
Br
7.36 7.35 7.34 7.32 7.30 7.28 7.26 7.24 7.23 7.22 7.20 7.19 7.18 6.51 6.47 6.28 6.25 6.24 6.21
4.19 4.18 4.17 4.16 4.15 4.14 4.13 4.13 4.12 4.11 4.10 4.09 3.59 3.57
1.99 1.84 1.83 1.82 1.81 1.80 1.80 1.51 1.50 1.48 1.37 1.30 1.28 1.26 1.25 1.24 1.23 1.22 0.88 0.87 0.86 0.84
2.08 2.21 1.18 0.98 0.97 2.06 1.00 4.98 2.18 5.15 3.13
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

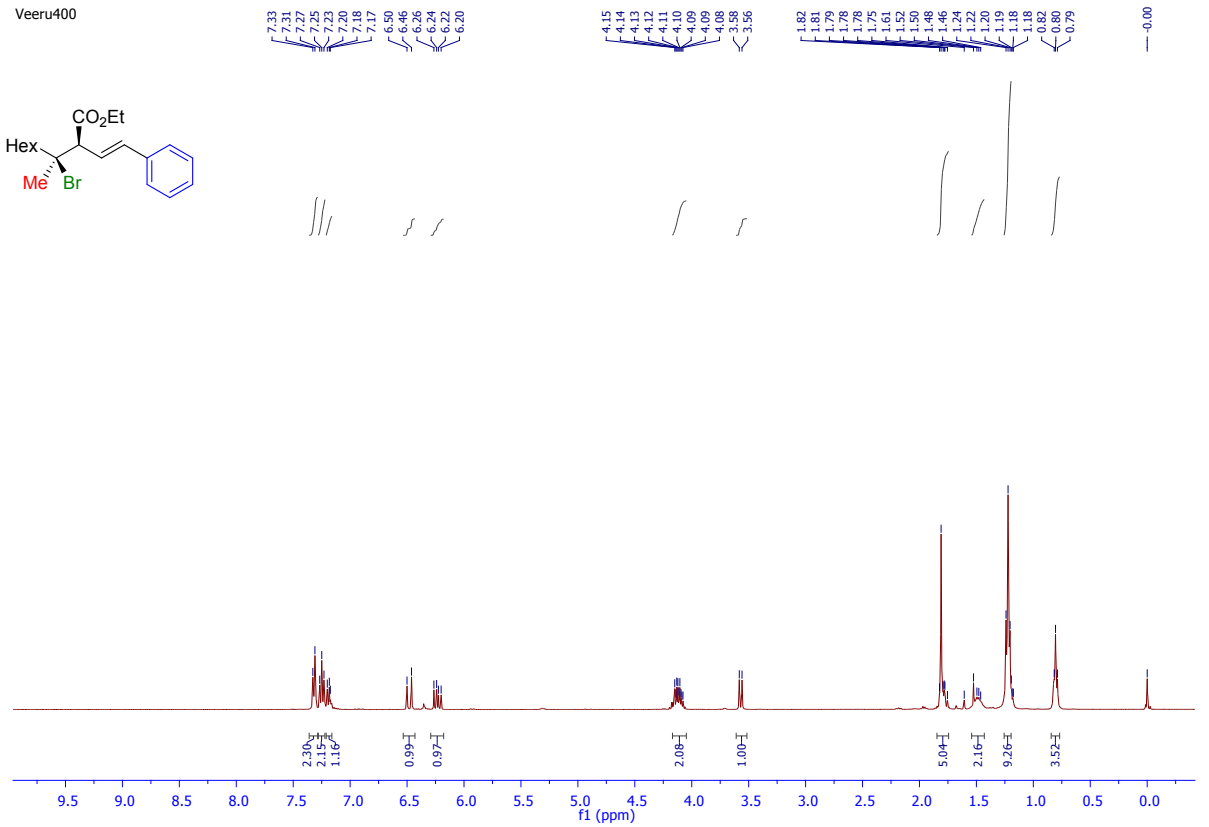

Veeru400
171.03
136.33 135.13 128.69 128.11 126.62 123.95
77.38 77.07 76.75 70.63 61.46 60.99 43.36 28.46 27.76 22.69 14.24 14.11
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

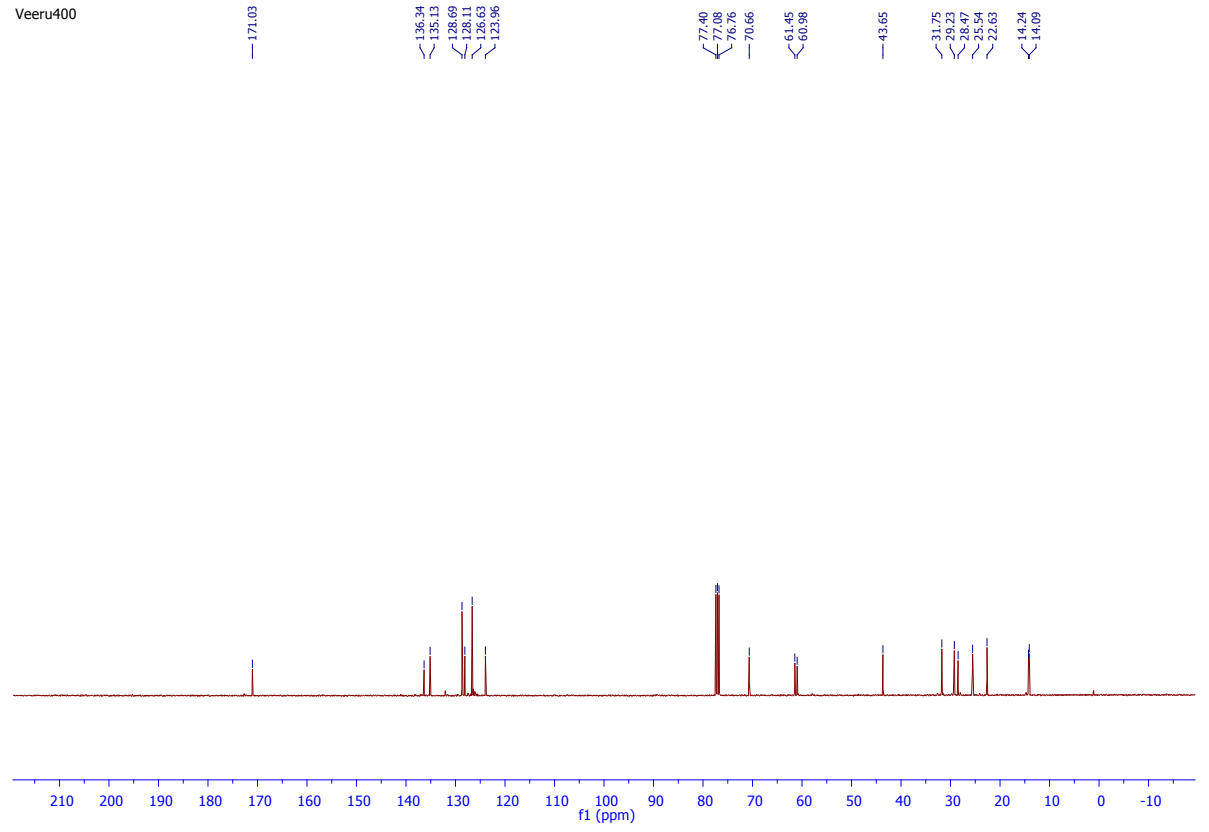

Veeru400
7.38
7.35
7.19
7.17
6.43
6.39
6.27
6.25
6.23
6.21
4.15
4.13
4.12
4.12
4.10
4.09
3.56
3.53
2.21
2.21
2.18
2.17
2.15
2.12
1.29
1.29
1.27
1.26
1.25
1.24
1.22
1.21
1.20
1.19
1.18
1.14
1.12
0.87
0.85
0.83
CO2Et
Bu
Me
Br
Br
2.12
2.33
0.99
0.92
2.06
1.00
4.49
4.25
5.21
3.26
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


Veeru400
170.81
135.26
133.93
131.81
128.14
124.89
121.95
77.41
77.09
76.77
70.36
61.44
61.08
43.28
28.62
27.76
22.71
14.25
14.11
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

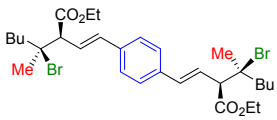

Veeru400
7.19
6.87
6.87
6.74
6.70
6.41
6.37
6.09
6.06
6.05
6.02
5.89
4.18
4.17
4.16
4.15
4.14
4.13
4.12
4.11
4.10
4.09
4.09
4.08
3.54
3.52
1.82
1.80
1.78
1.77
1.52
1.24
1.23
0.87
0.85
0.84
CO2Et
Bu
Me
Br
O
O
1.01
1.04
1.03
1.00
1.02
2.09
2.09
1.02
5.01
1.93
5.06
3.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

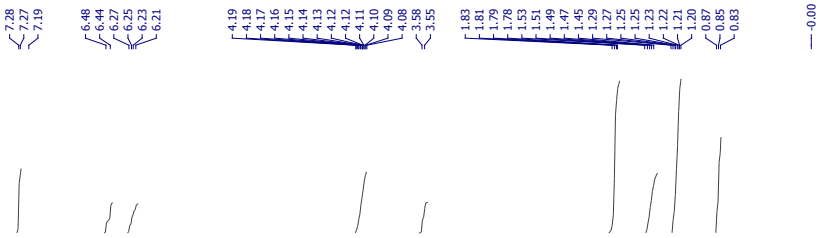

Veeru400
171.10
148.14
147.63
134.66
130.81
122.08
121.45
108.34
105.84
101.21
77.37
77.06
76.74
70.75
61.38
60.96
43.31
28.42
27.75
22.69
14.23
14.10
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

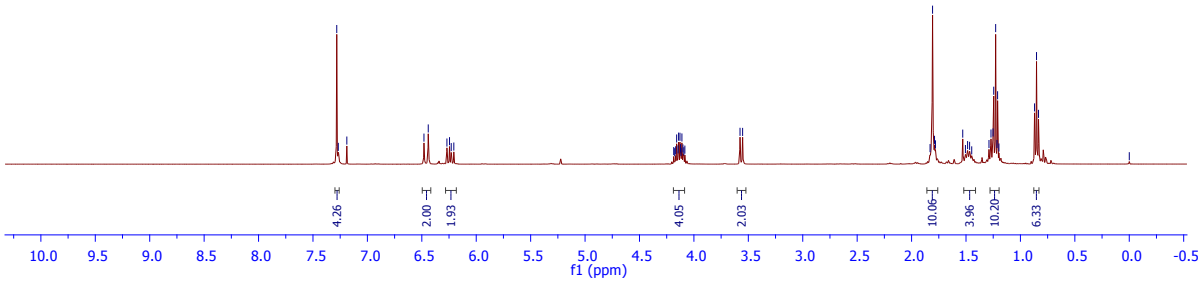

Veeru400
7.33
7.31
7.27
7.25
7.23
7.20
7.18
7.17
6.50
6.46
6.26
6.24
6.22
6.20
4.15
4.14
4.13
4.12
4.11
4.10
4.09
4.09
4.08
3.58
3.56
1.82
1.81
1.79
1.78
1.78
1.75
1.61
1.52
1.50
1.48
1.46
1.24
1.22
1.20
1.19
1.18
0.82
0.80
0.79
-0.00
CO2Et
Hex
Me
Br
2.30
2.15
1.16
0.99
0.97
2.08
1.00
5.04
2.16
9.26
3.52
f1 (ppm)


Veeru400
171.03
136.34
135.13
128.69
128.11
126.63
123.96
77.40
77.08
76.76
70.66
61.45
60.98
43.65
31.75
29.23
28.47
25.54
22.63
14.24
14.09
f1 (ppm)

Veeru4002019







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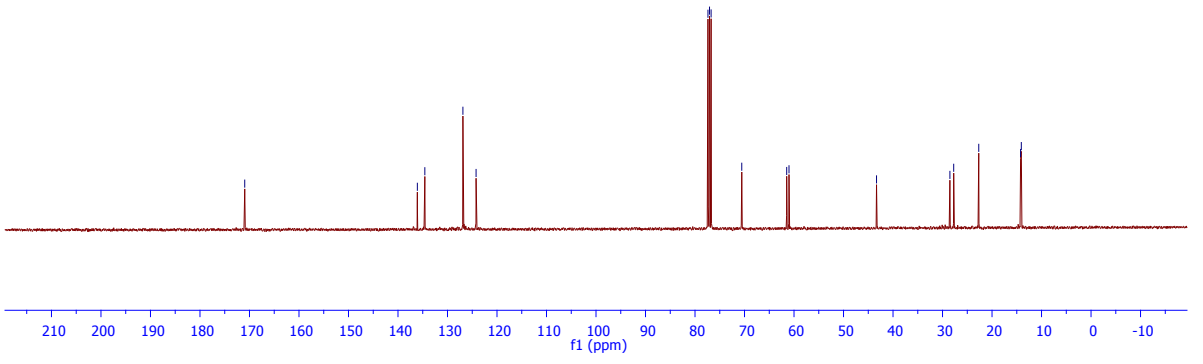
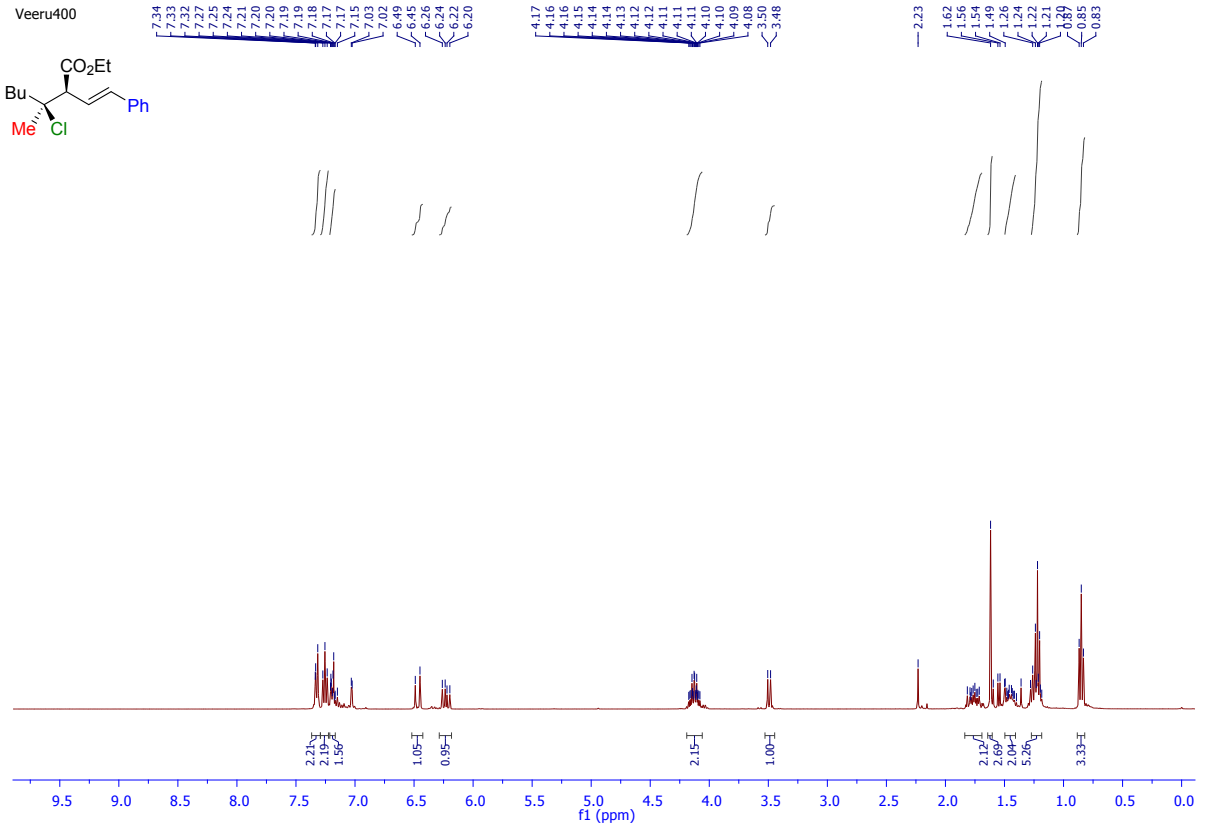
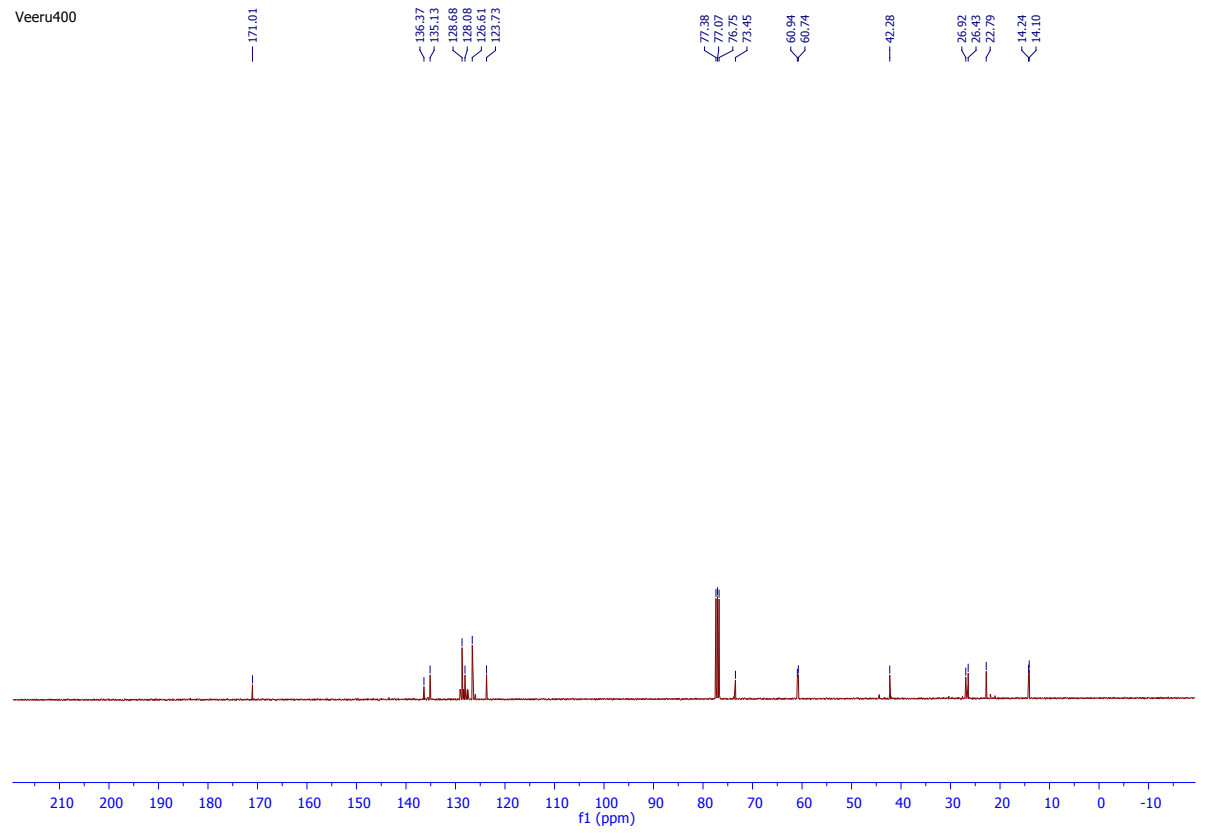



Veeru400
CO2Et
Bu
Ph
Me
Cl
f1 (ppm)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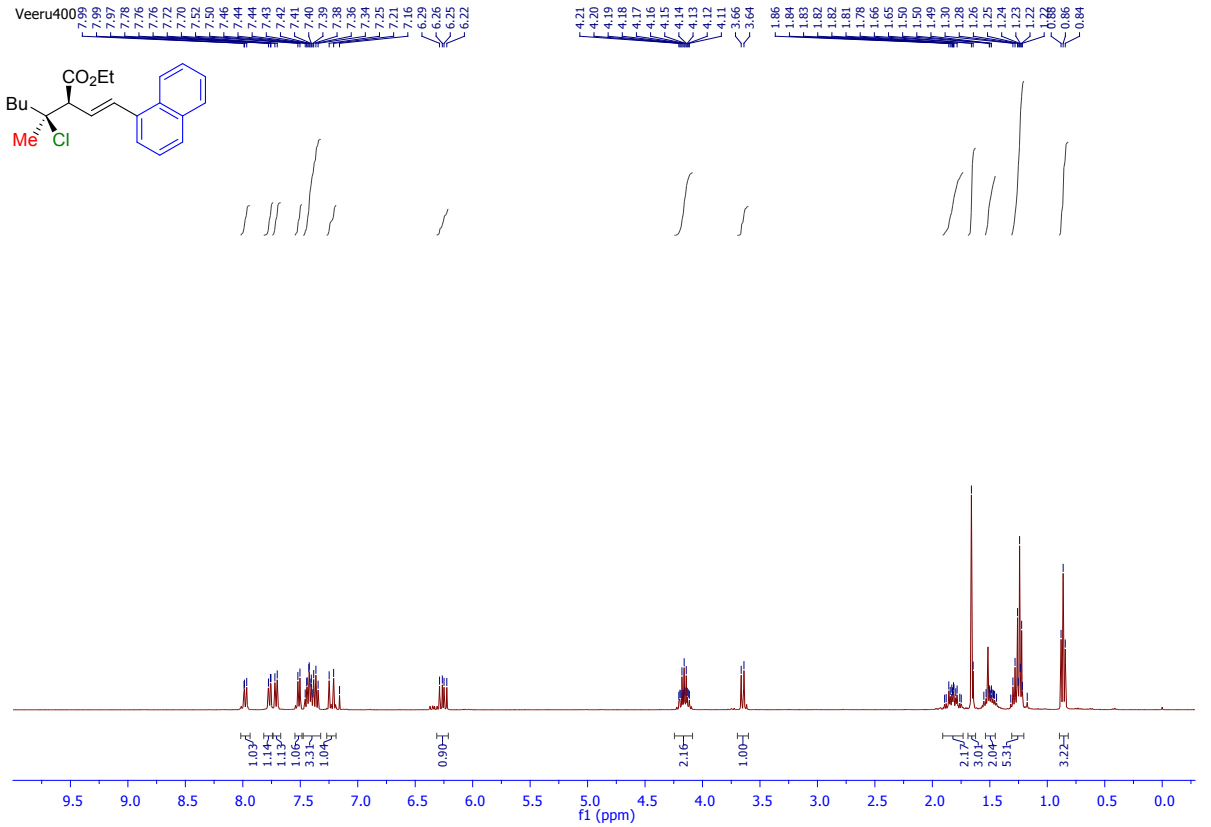
f1 (ppm)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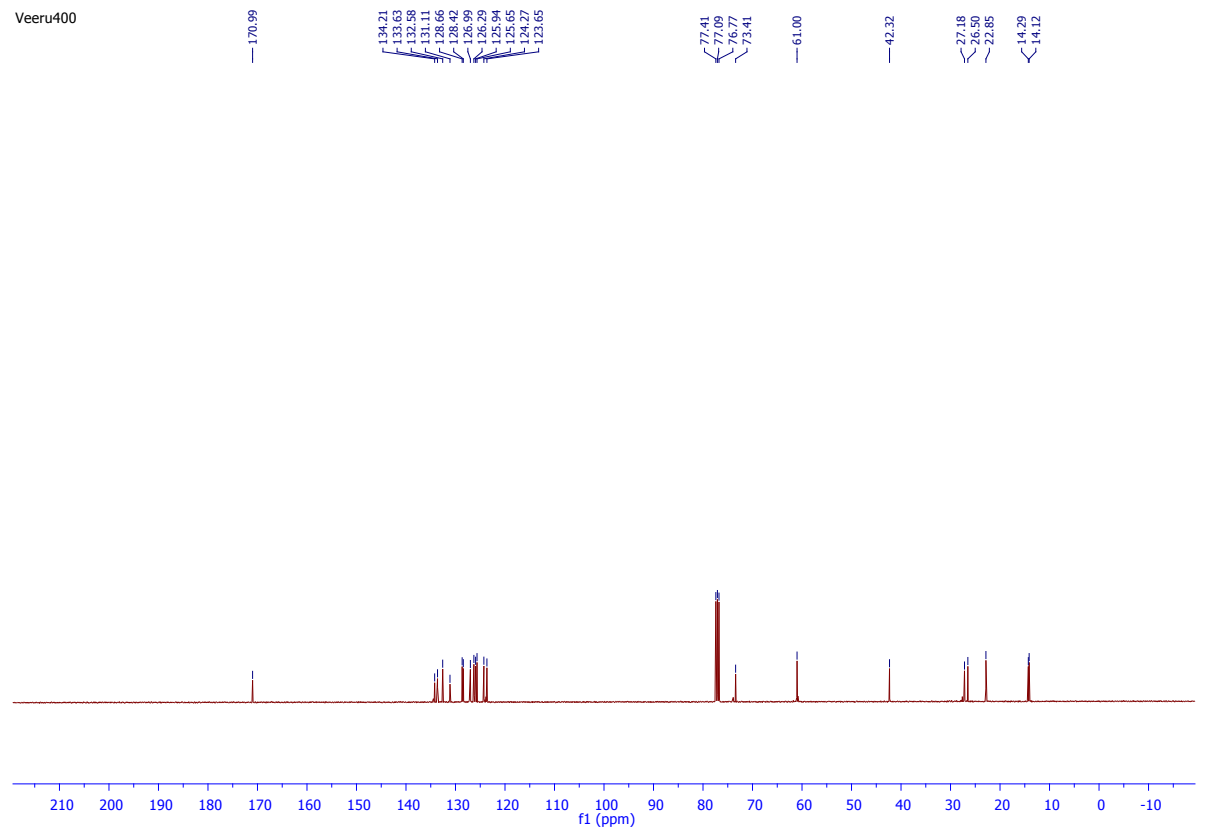
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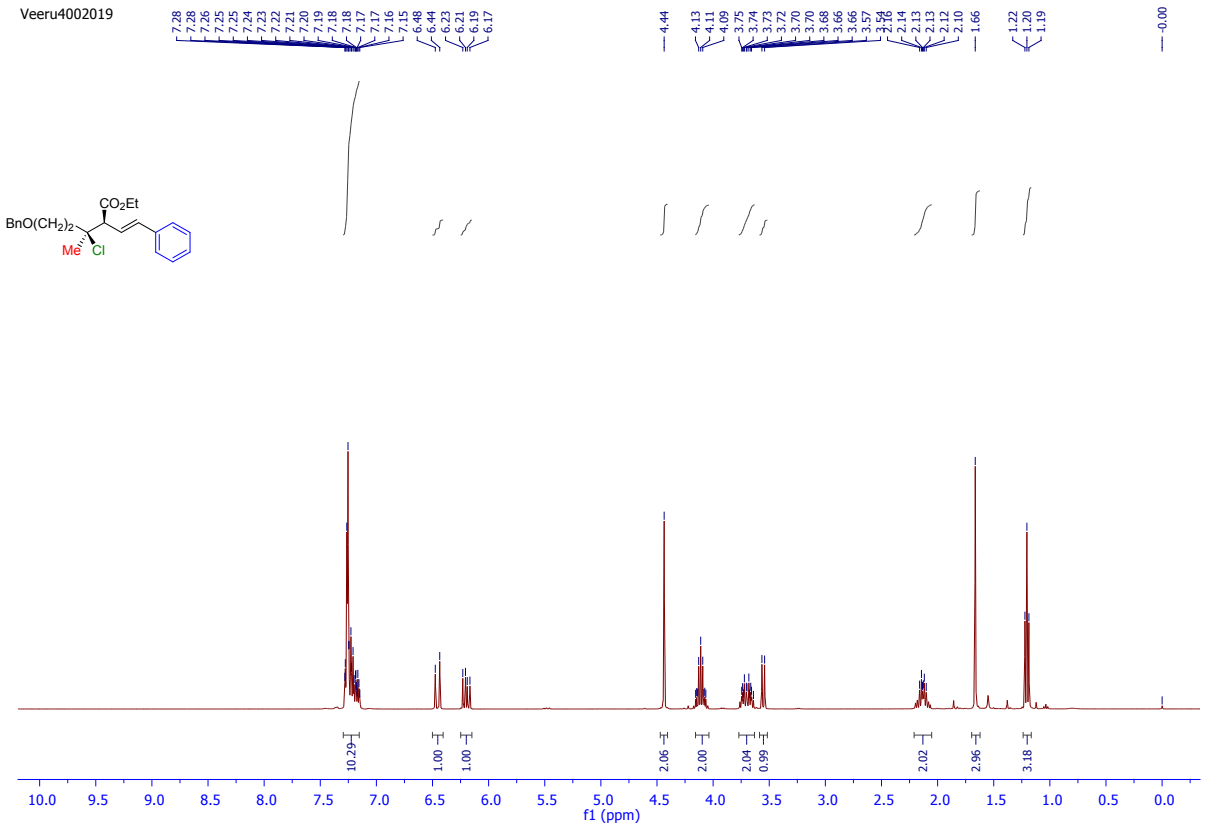
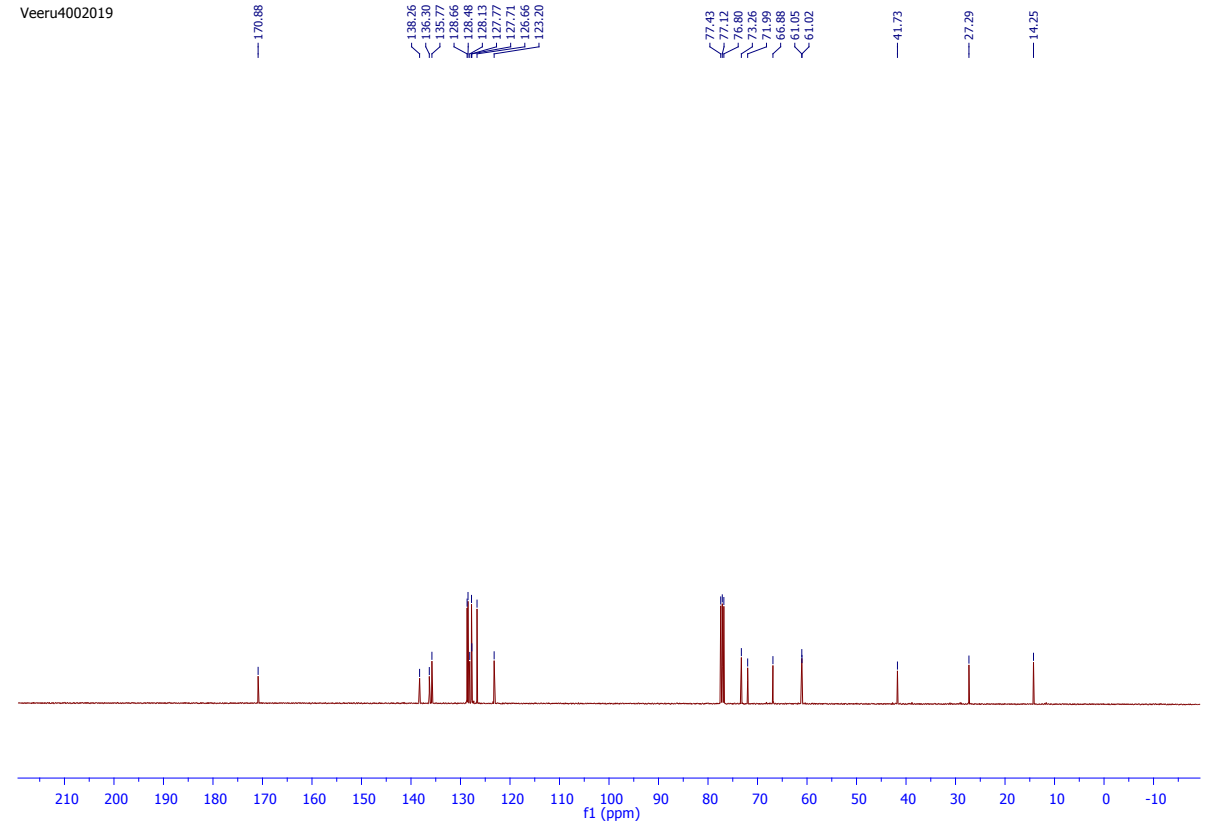
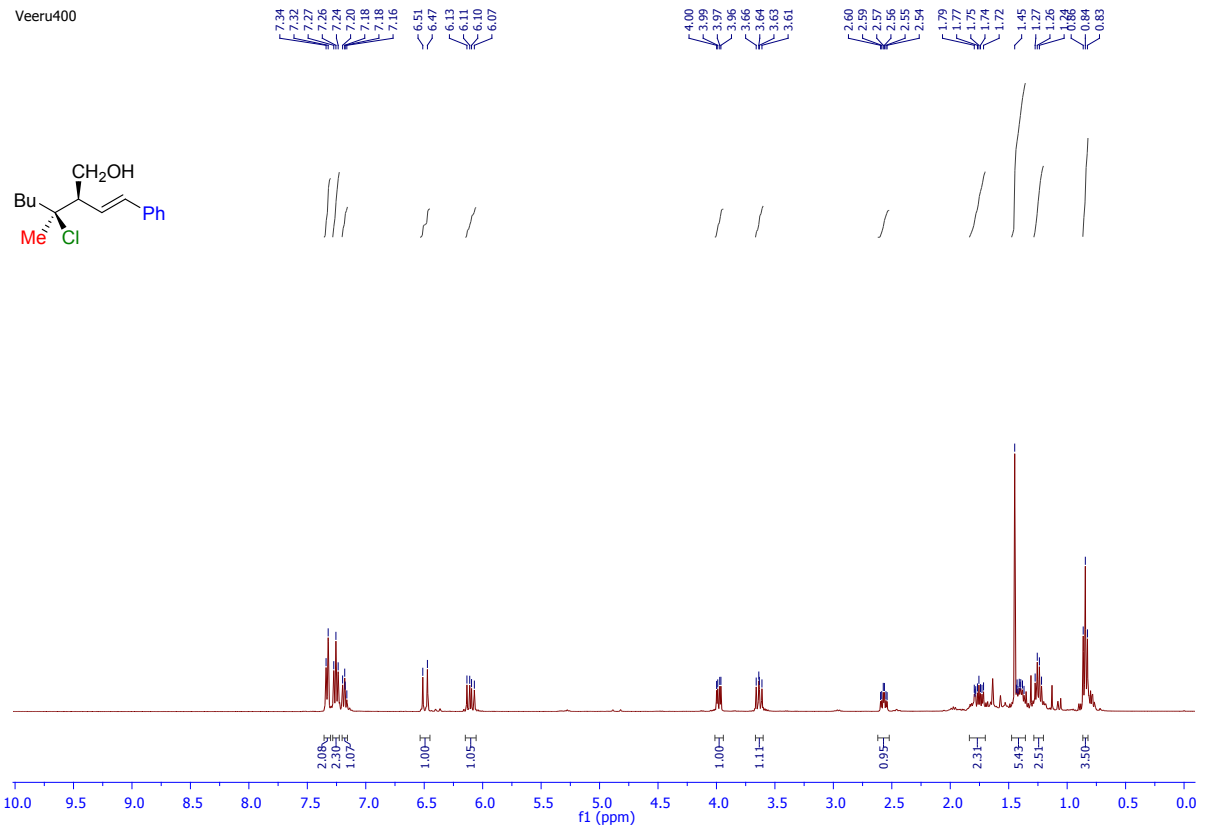

Veeru4002019
7.28 7.28 7.26 7.25 7.25 7.24 7.23 7.22 7.21 7.20 7.19 7.18 7.18 7.17 7.17 7.16 7.15 6.48 6.44 6.23 6.21 6.19 6.17
4.44 4.13 4.11 4.09 3.75 3.74 3.73 3.72 3.70 3.70 3.68 3.66 3.66 3.57 2.14 2.14 2.14 2.13 2.13 2.12 2.10 1.66 1.22 1.20 1.19 0.00
CO2Et
BnO(CH2)2
Me
Cl
10.29 1.00 1.00 2.06 2.00 2.04 0.99 2.02 2.96 3.18
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


Veeru4002019
170.88
138.26 136.30 135.77 128.66 128.48 128.13 127.77 127.71 126.66 123.20
77.43 77.12 76.80 73.26 71.99 66.88 61.05 61.02
41.73
27.29
14.25
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.18
7.18
7.16
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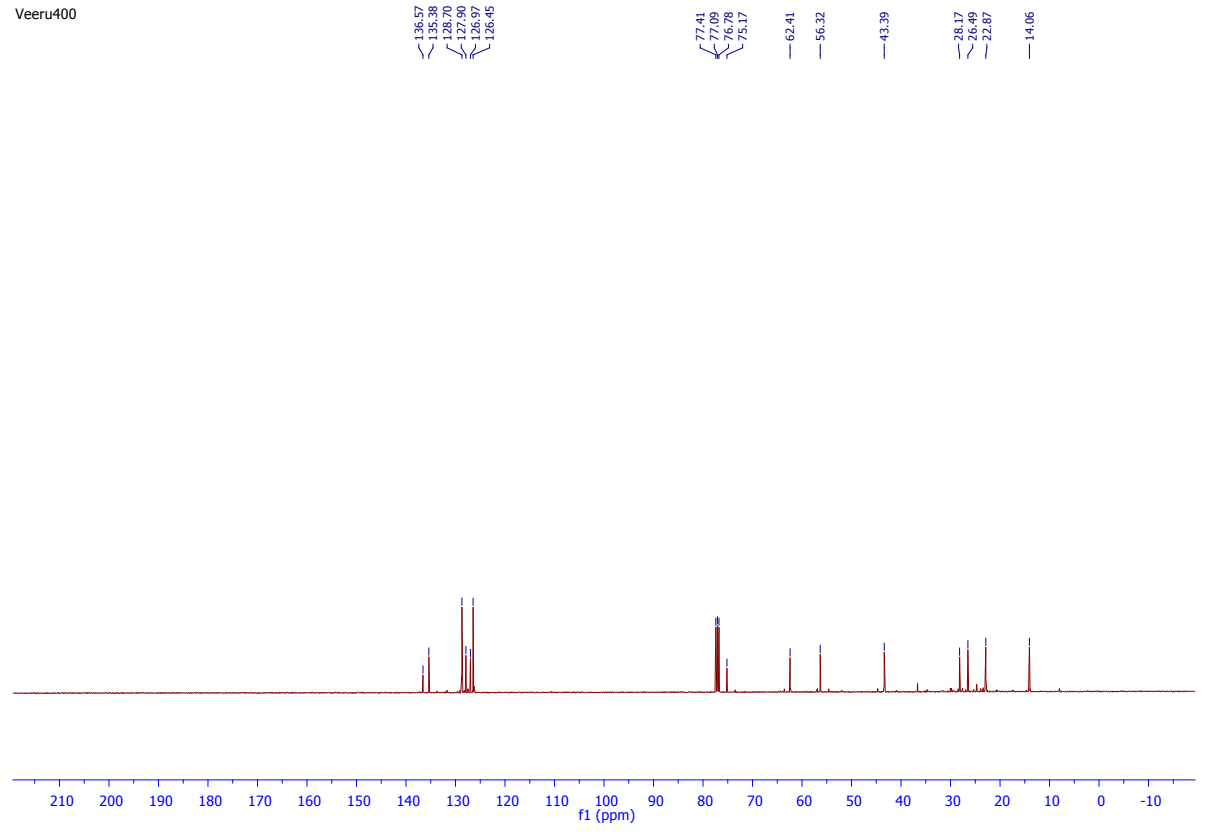
6.13
6.11
6.10
6.07
4.00
3.99
3.97
3.96
3.66
3.64
3.63
3.61
2.60
2.59
2.57
2.56
2.55
2.54
1.79
1.77
1.75
1.74
1.72
1.45
1.27
1.26
0.88
0.84
0.83
CH2OH
Bu
Ph
Me
Cl
2.08
2.30
1.07
1.00
1.05
1.00
1.11
0.95
2.31
5.43
2.51
3.50
f1 (ppm)


Veeru400
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135.38
128.70
127.90
126.97
126.45
77.41
77.09
76.78
75.17
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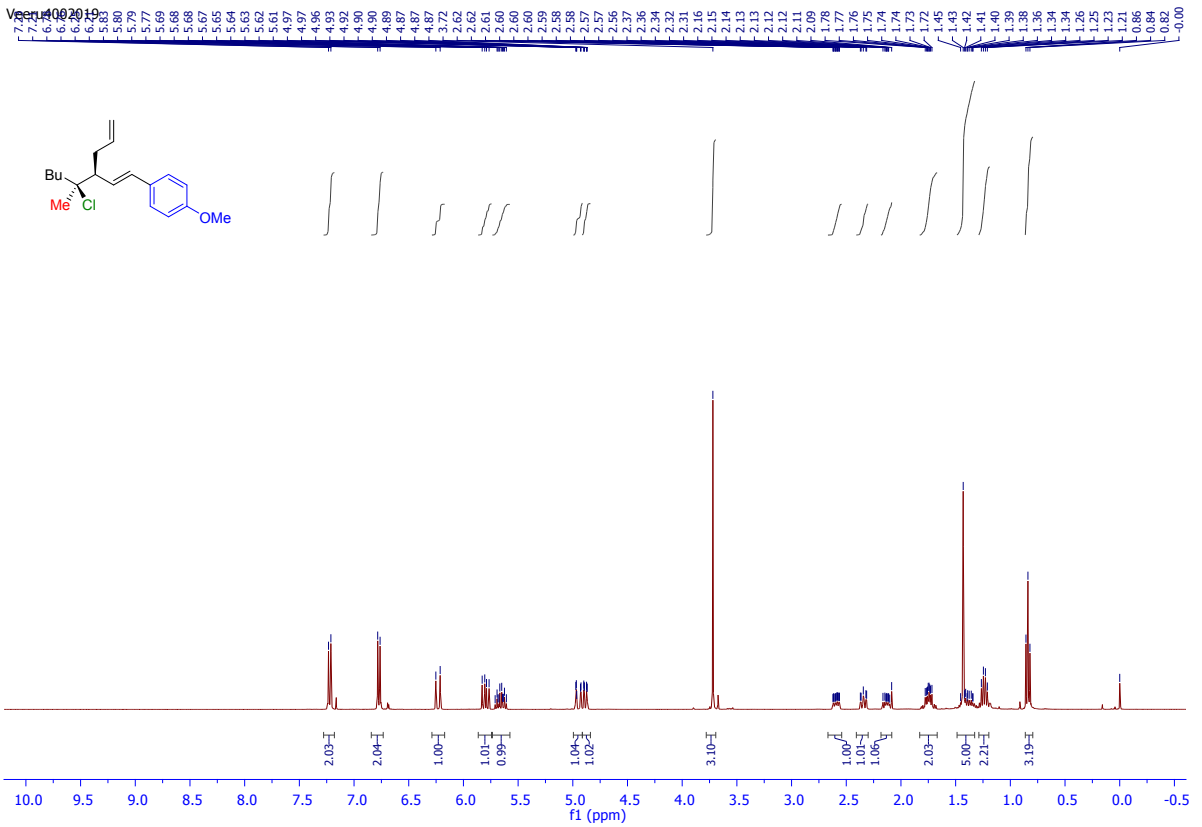
28.17
26.49
22.87
14.06
f1 (ppm)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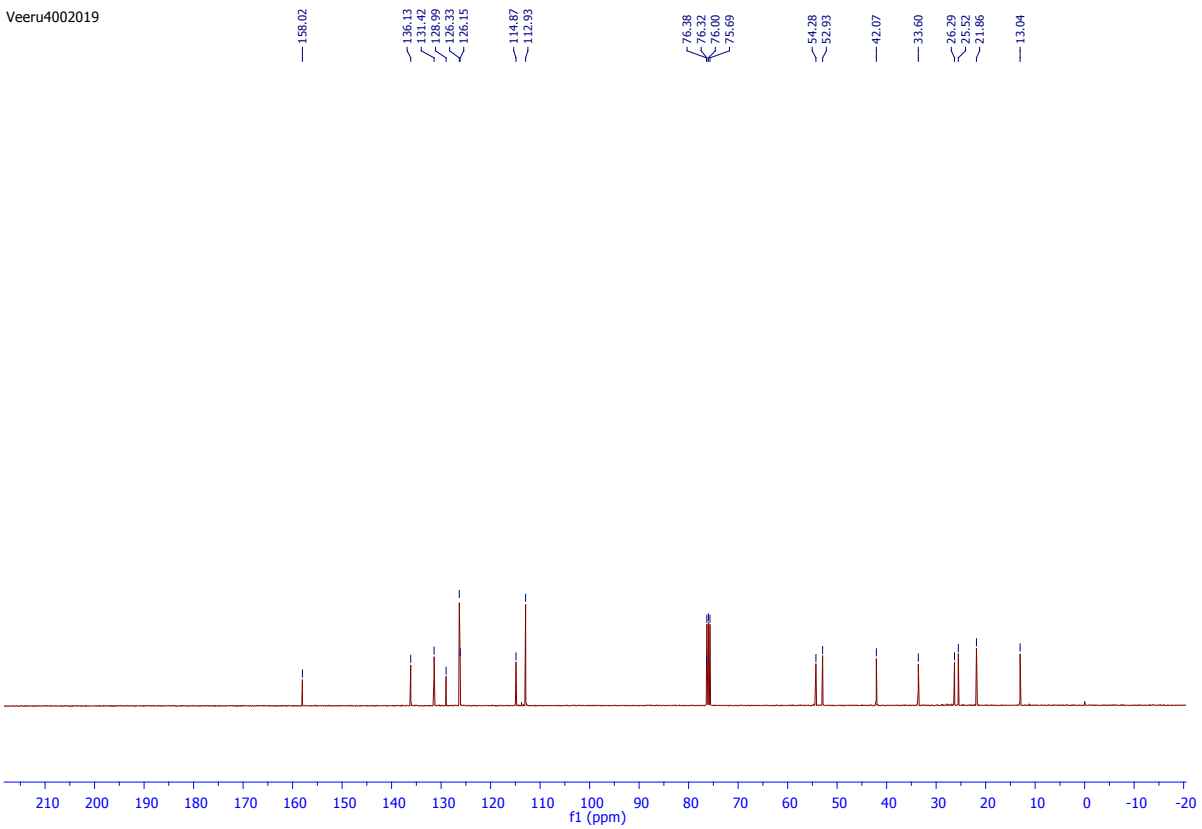
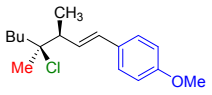
Bu
Me
Cl
OMe
f1 (ppm)


Veeru4002019
f1 (ppm)

Veeru4002019



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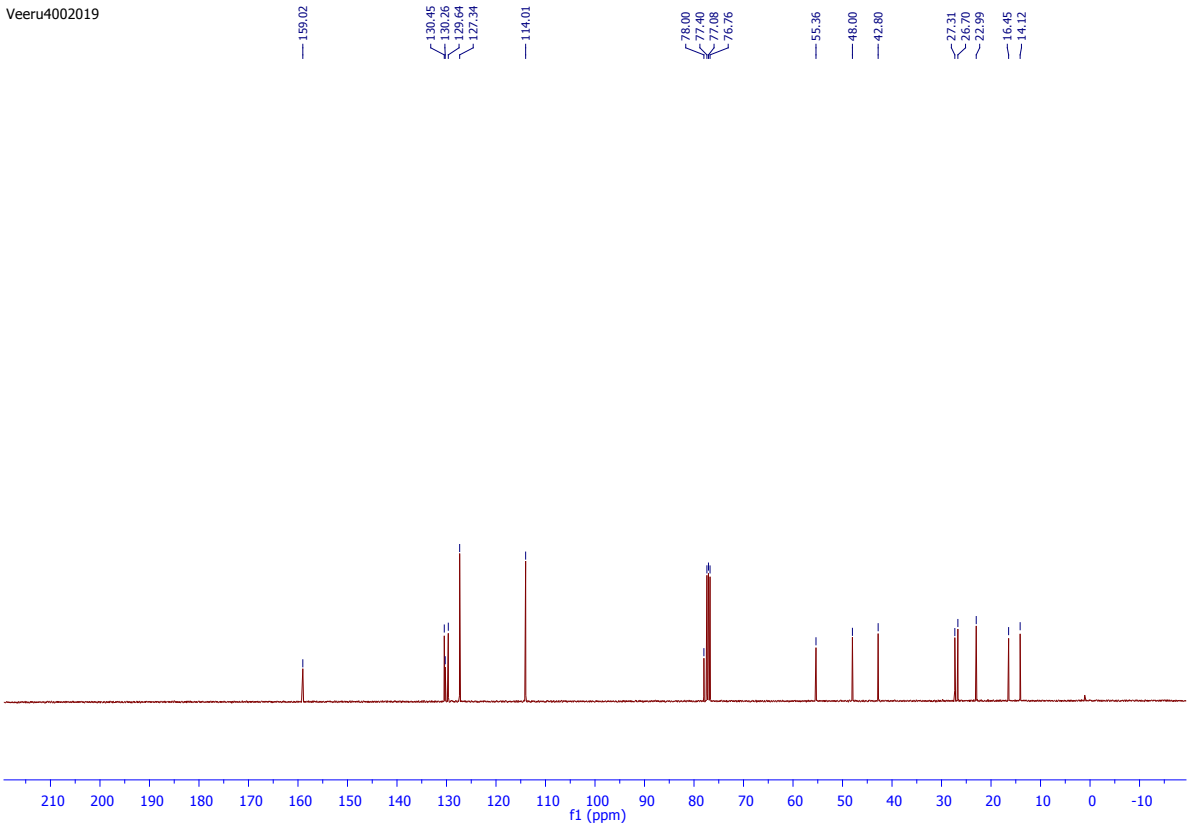

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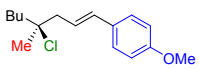

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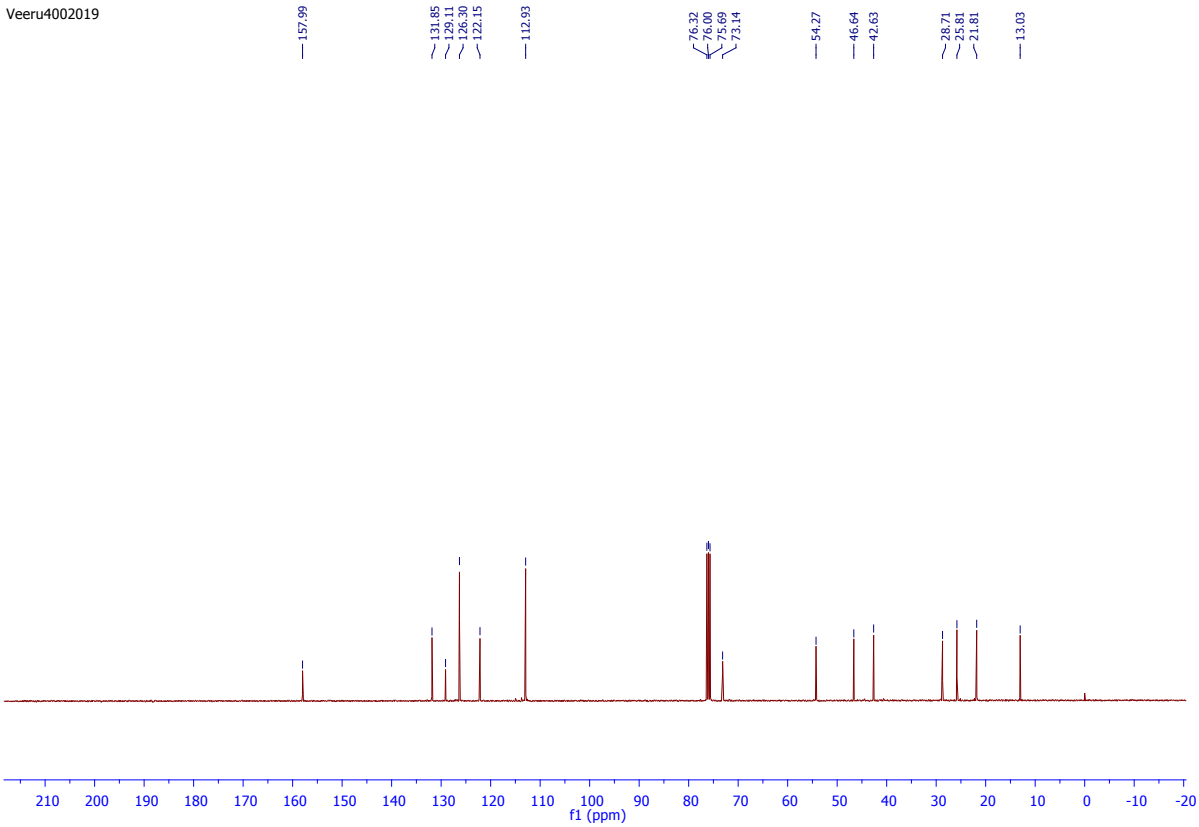

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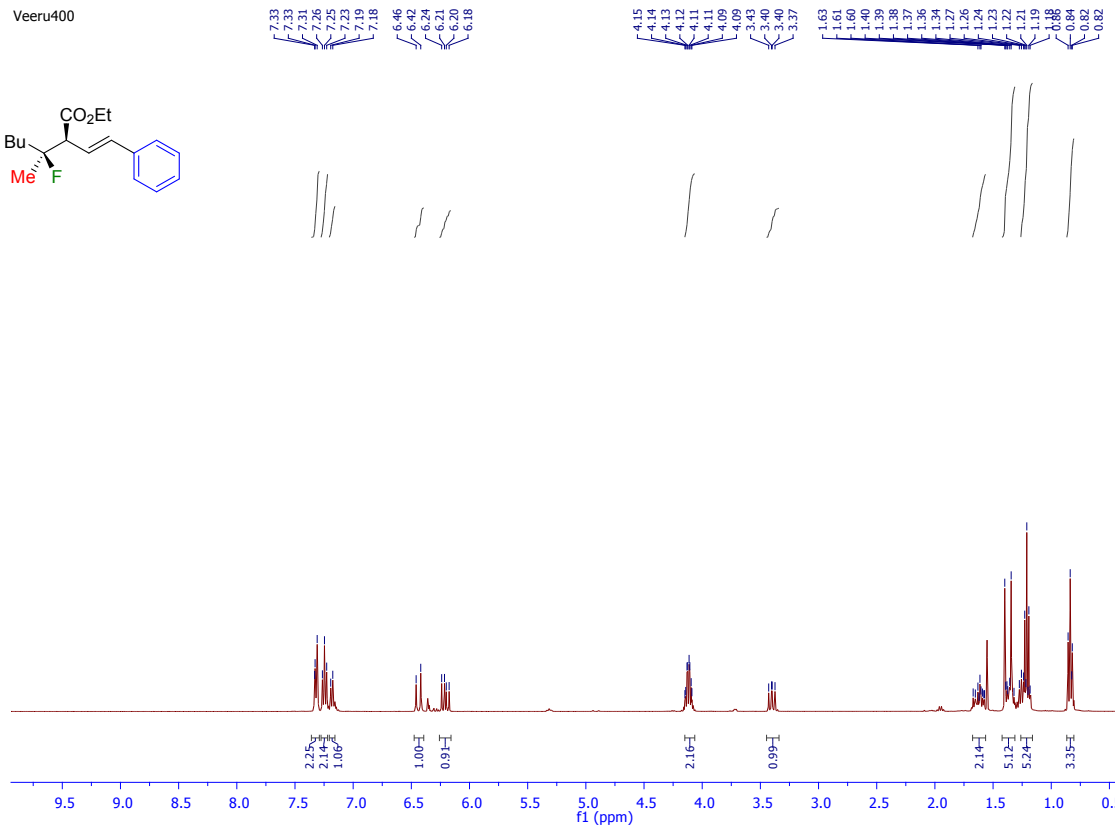

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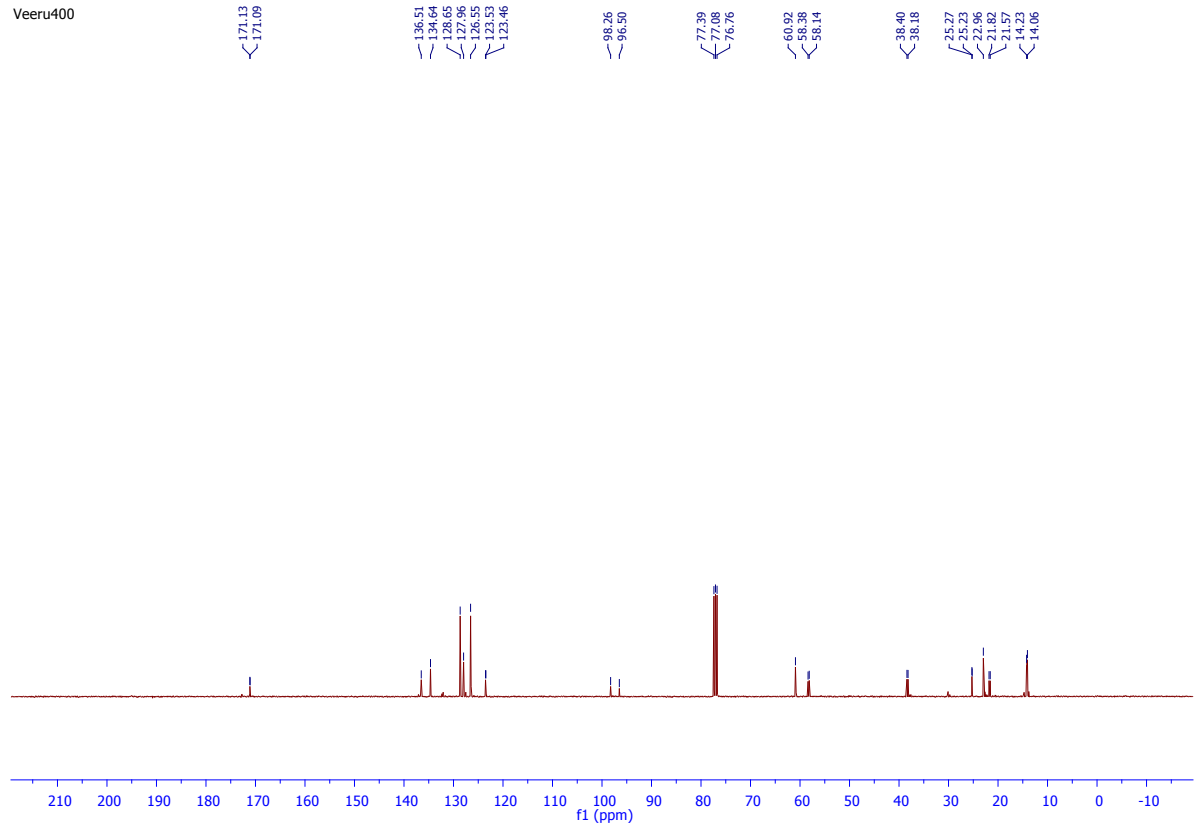

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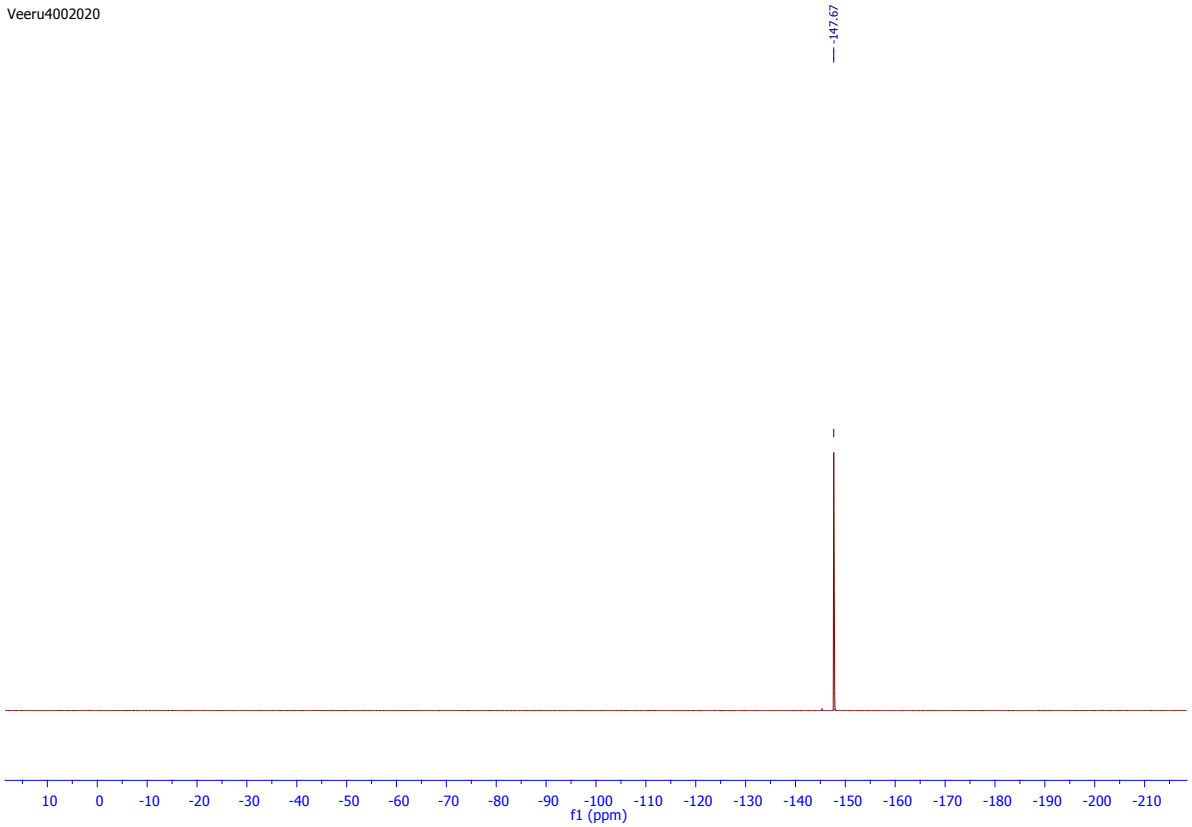

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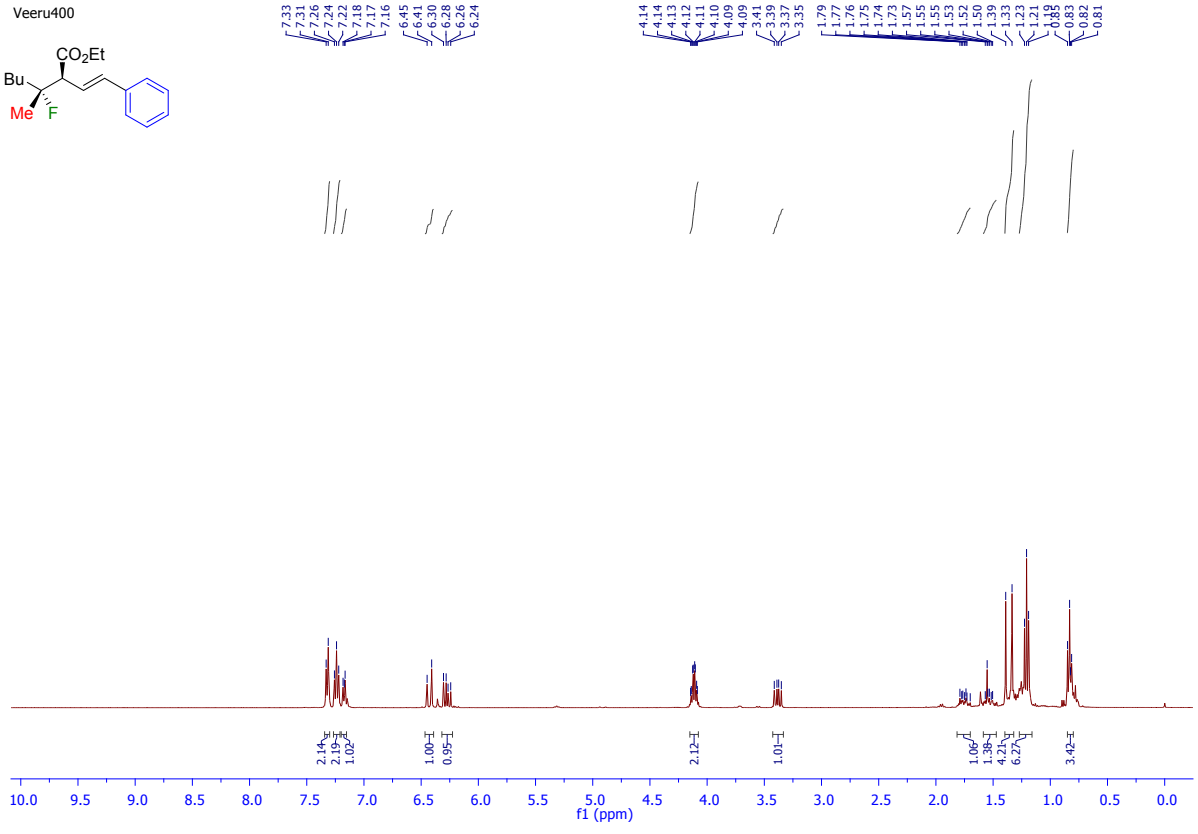

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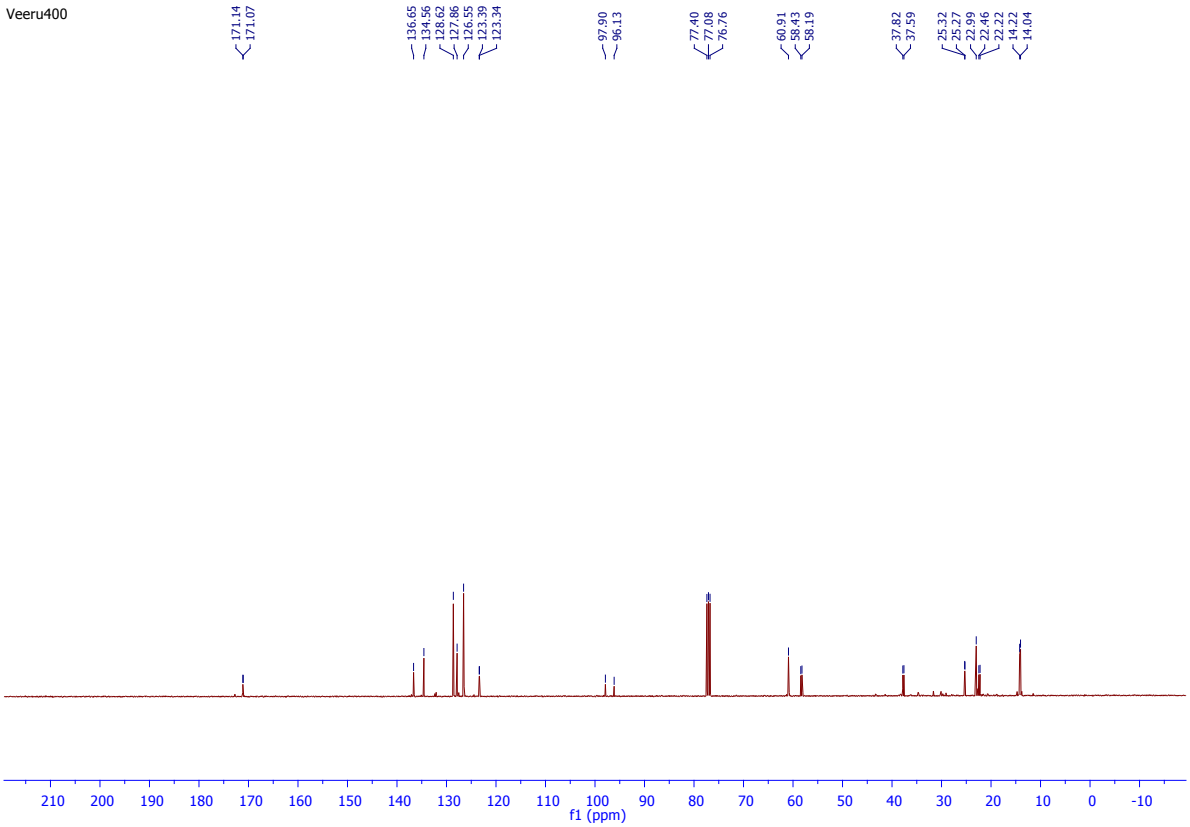

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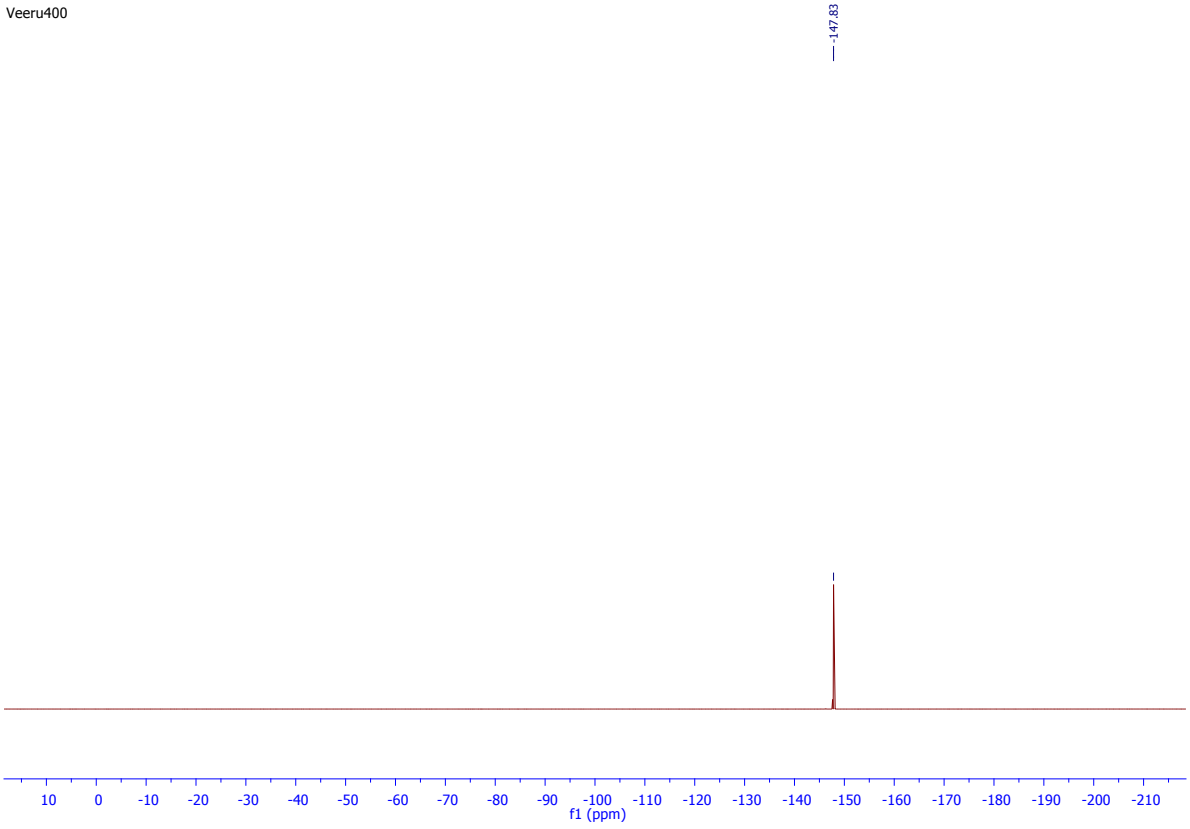
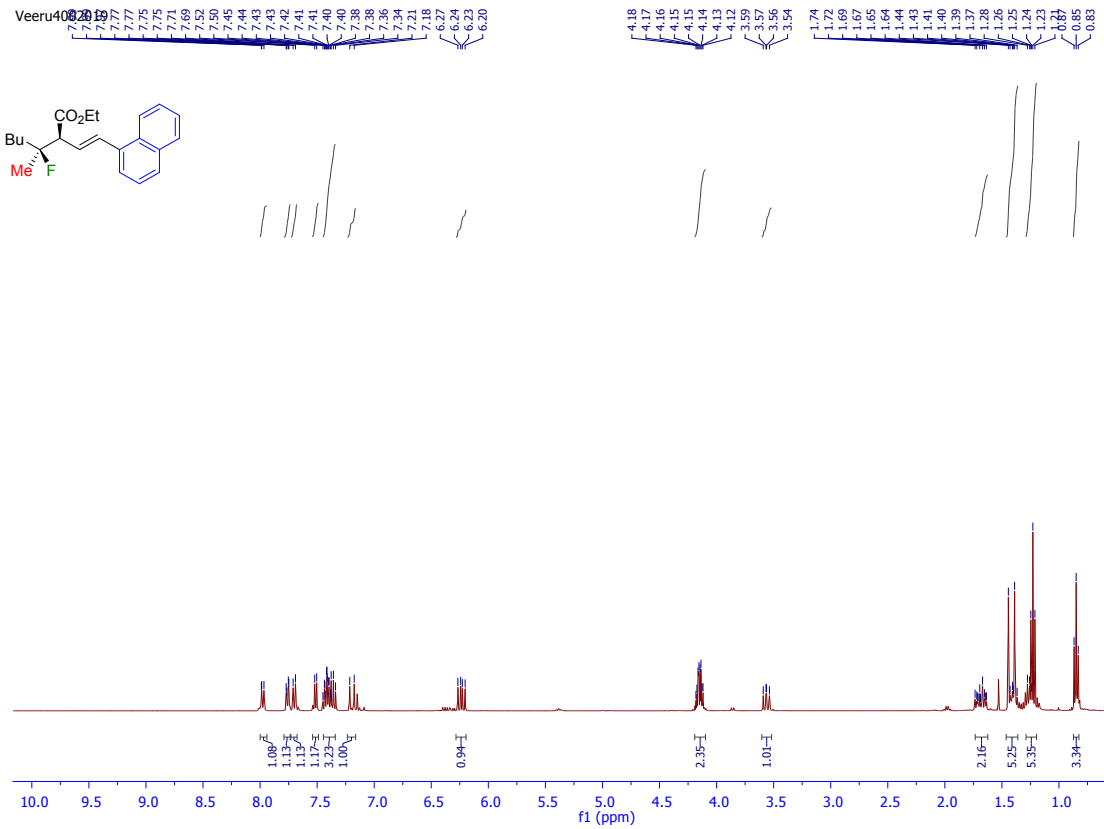
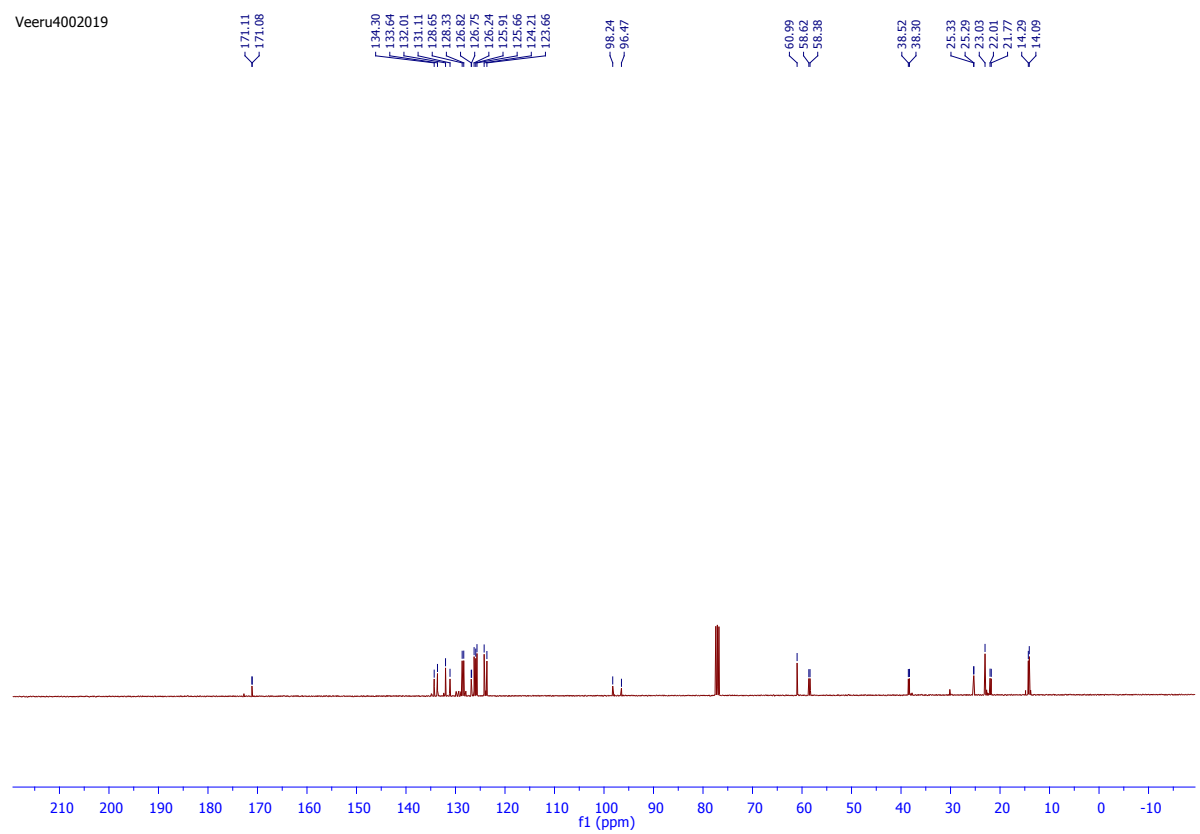
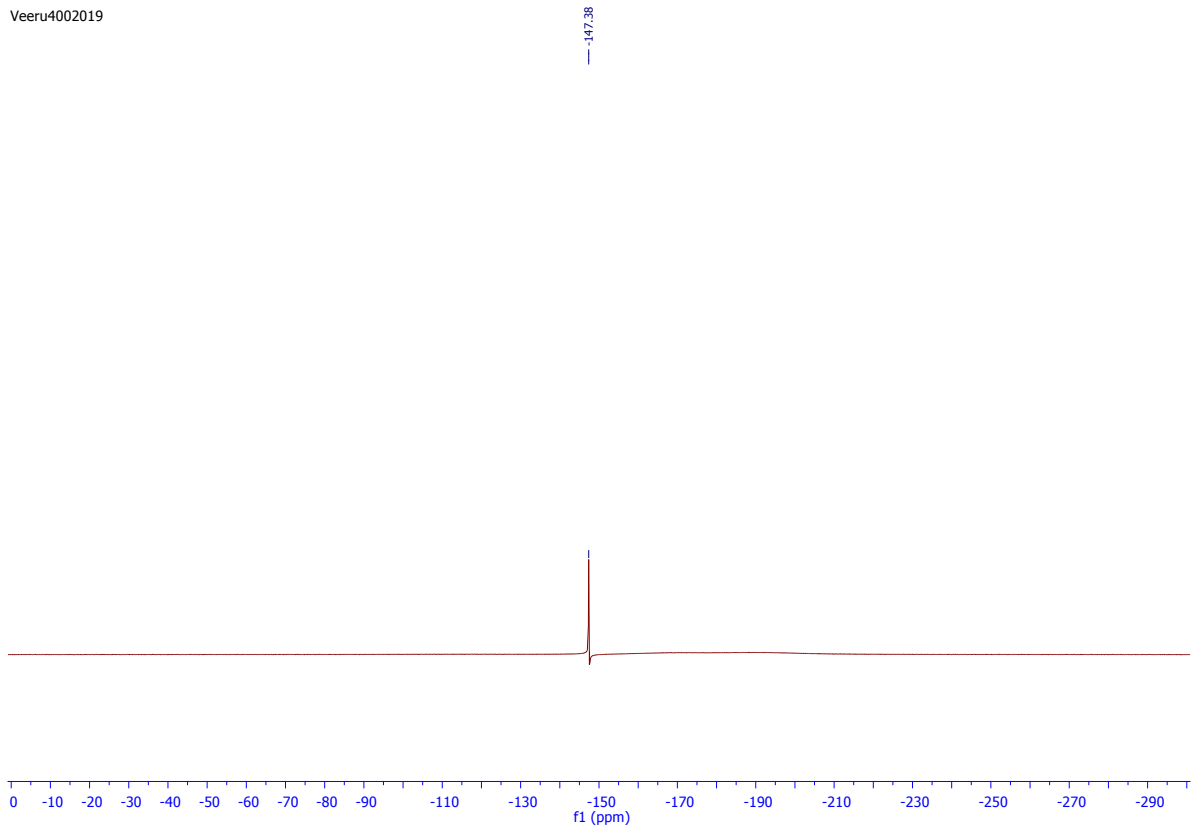



Veeru4002019
CO2Et
Bu
Me
F
f1 (ppm)


Veeru4002019
f1 (ppm)

Veeru4002019



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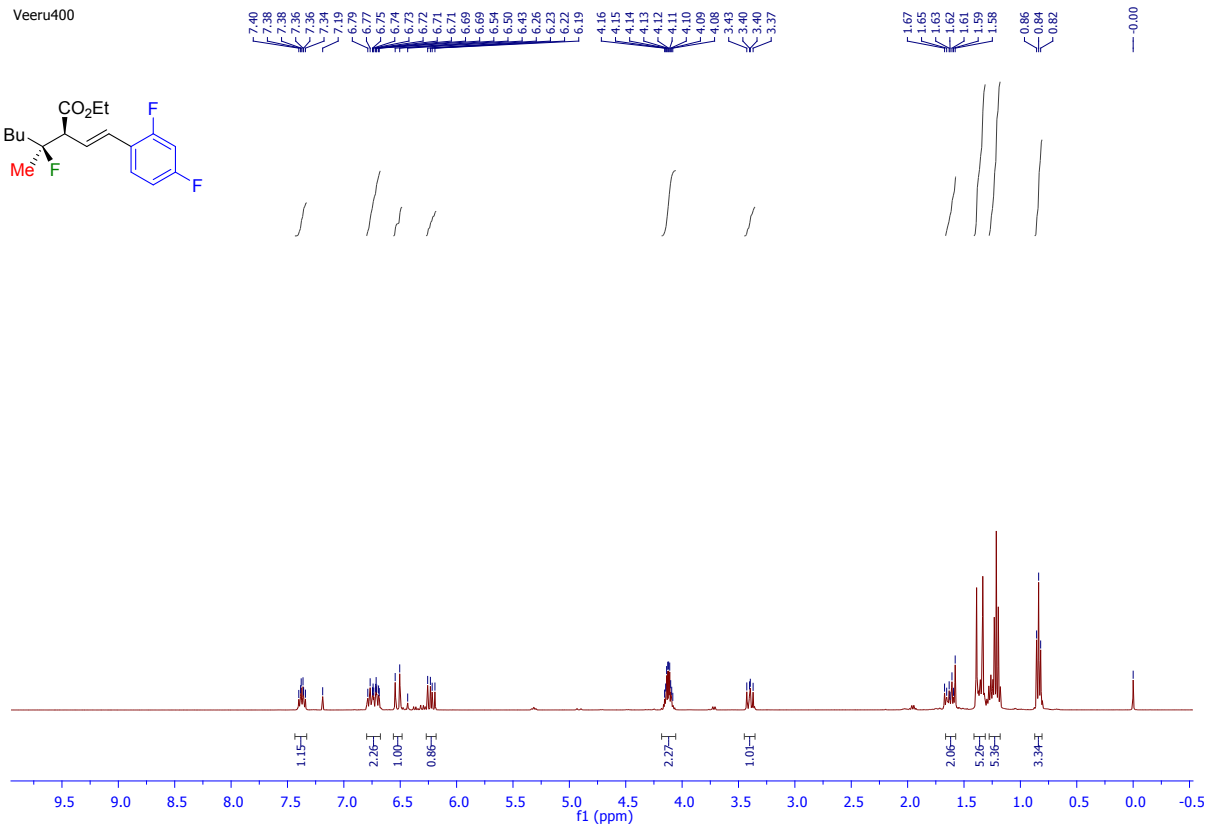

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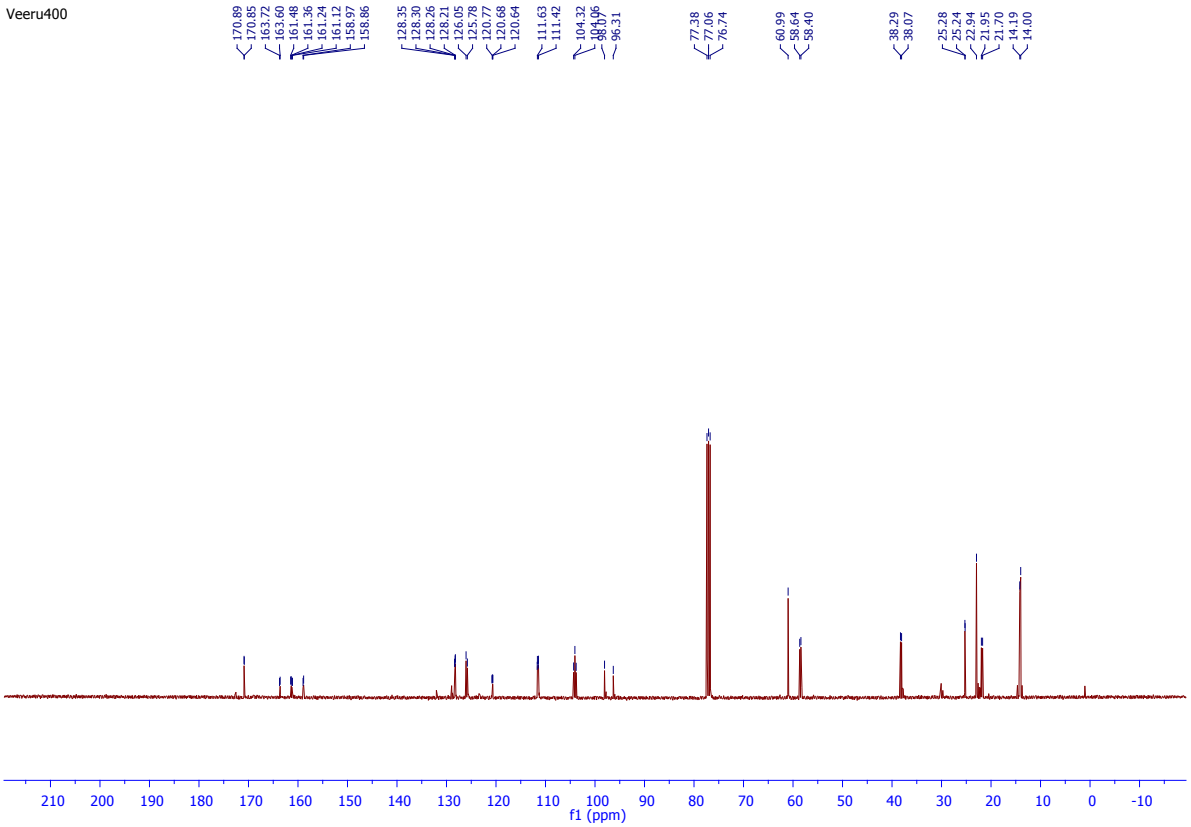

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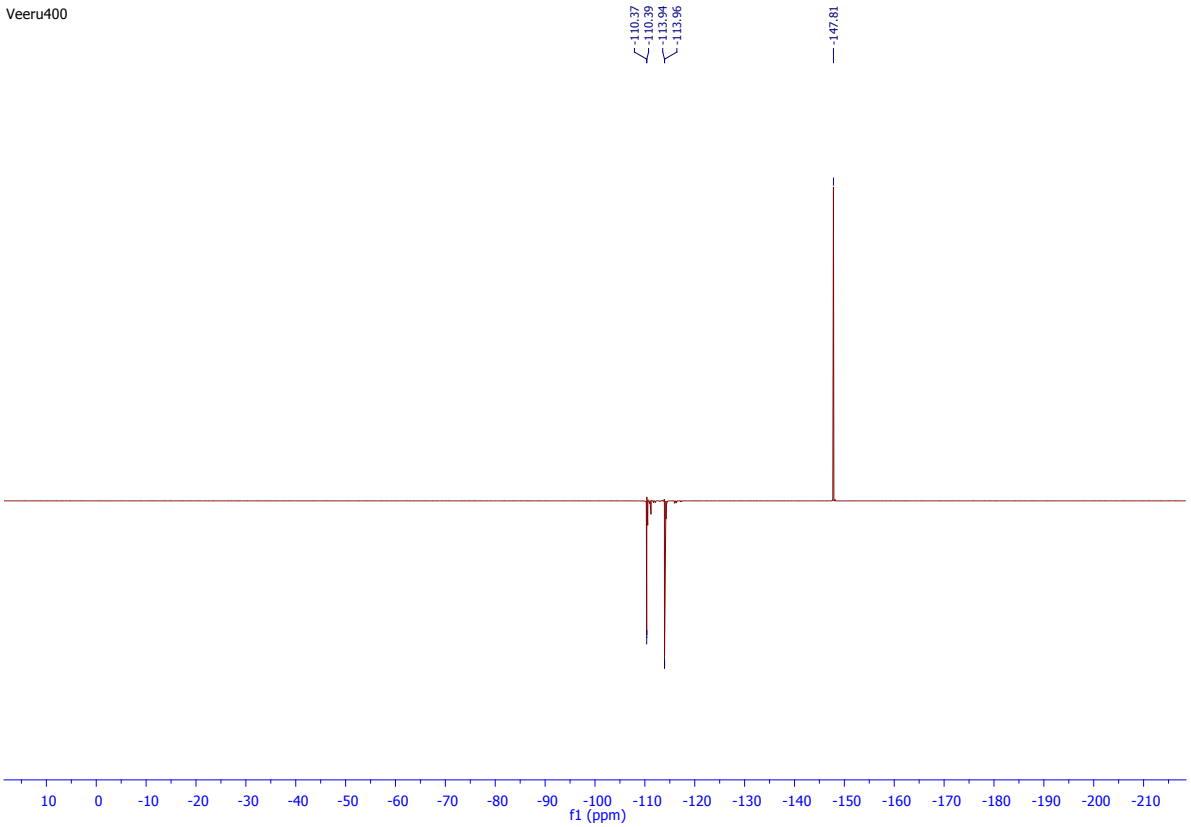
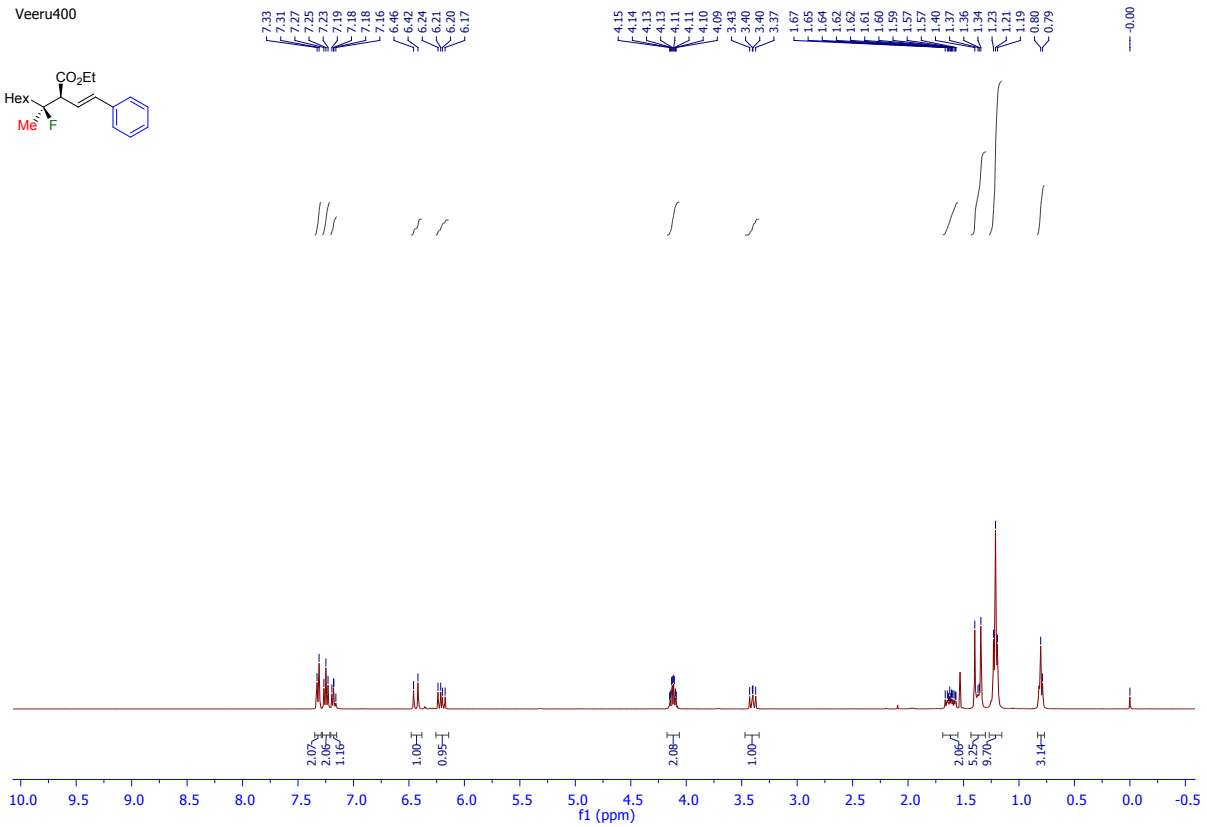
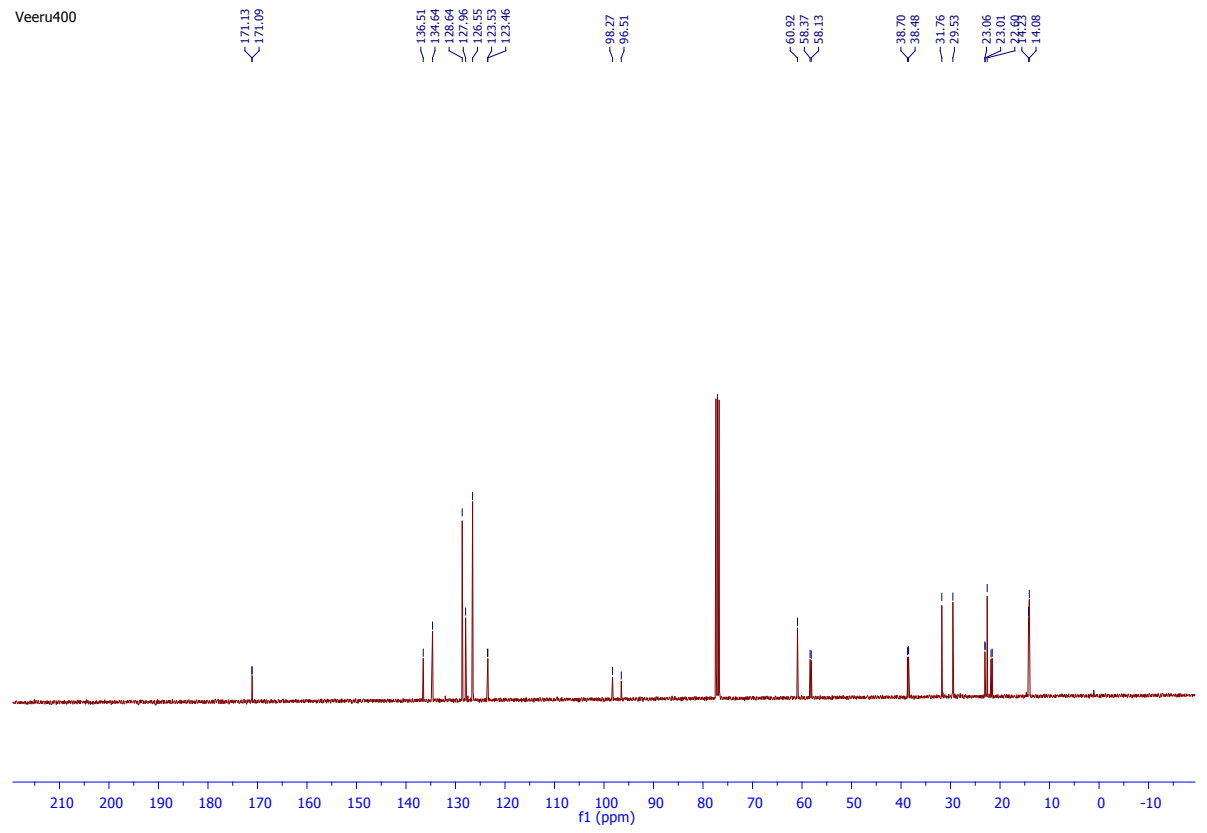
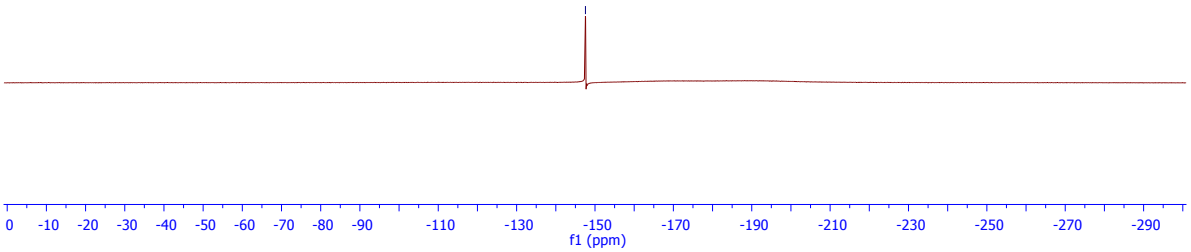



Veeru400
CO2Et
Hex
Me
F
f1 (ppm)


Veeru400
f1 (ppm)

Veeru400 **^{19}F NMR** (377 MHz, $CDCl_3$) δ -147.45.



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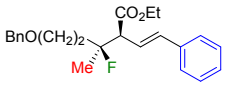

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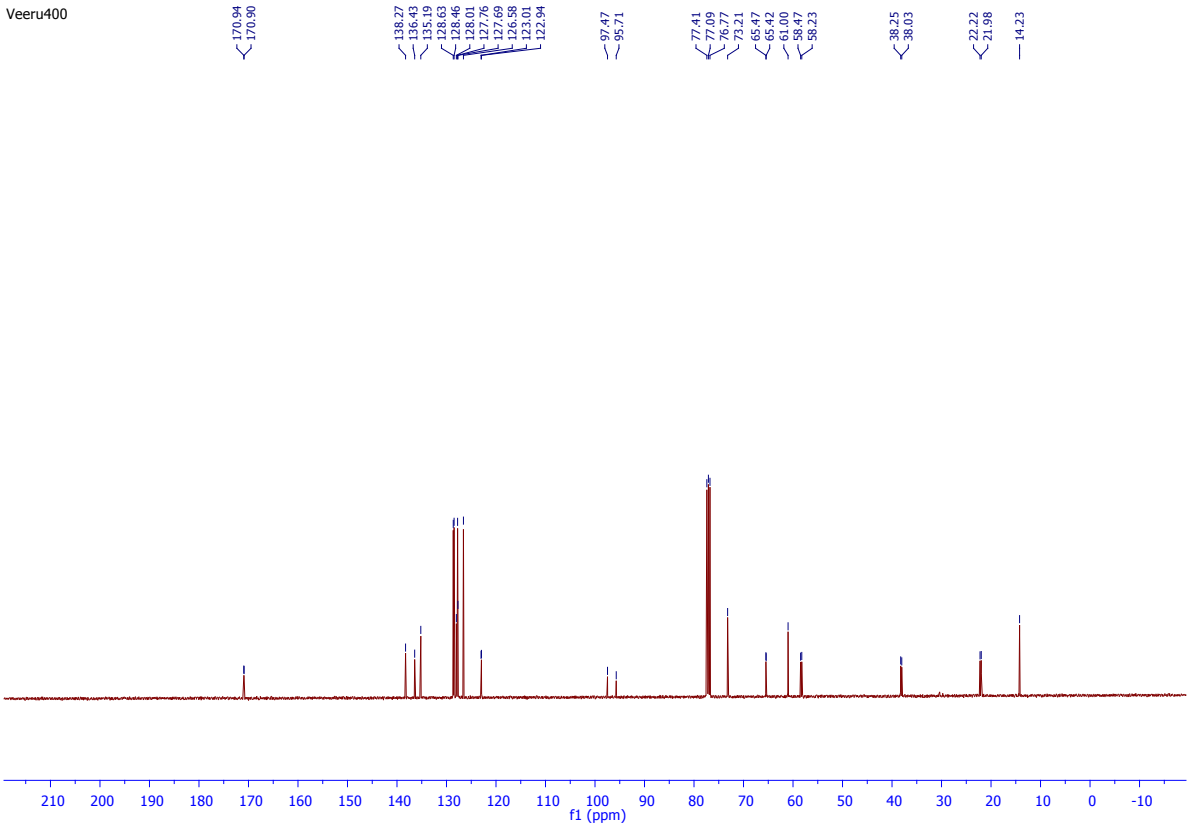

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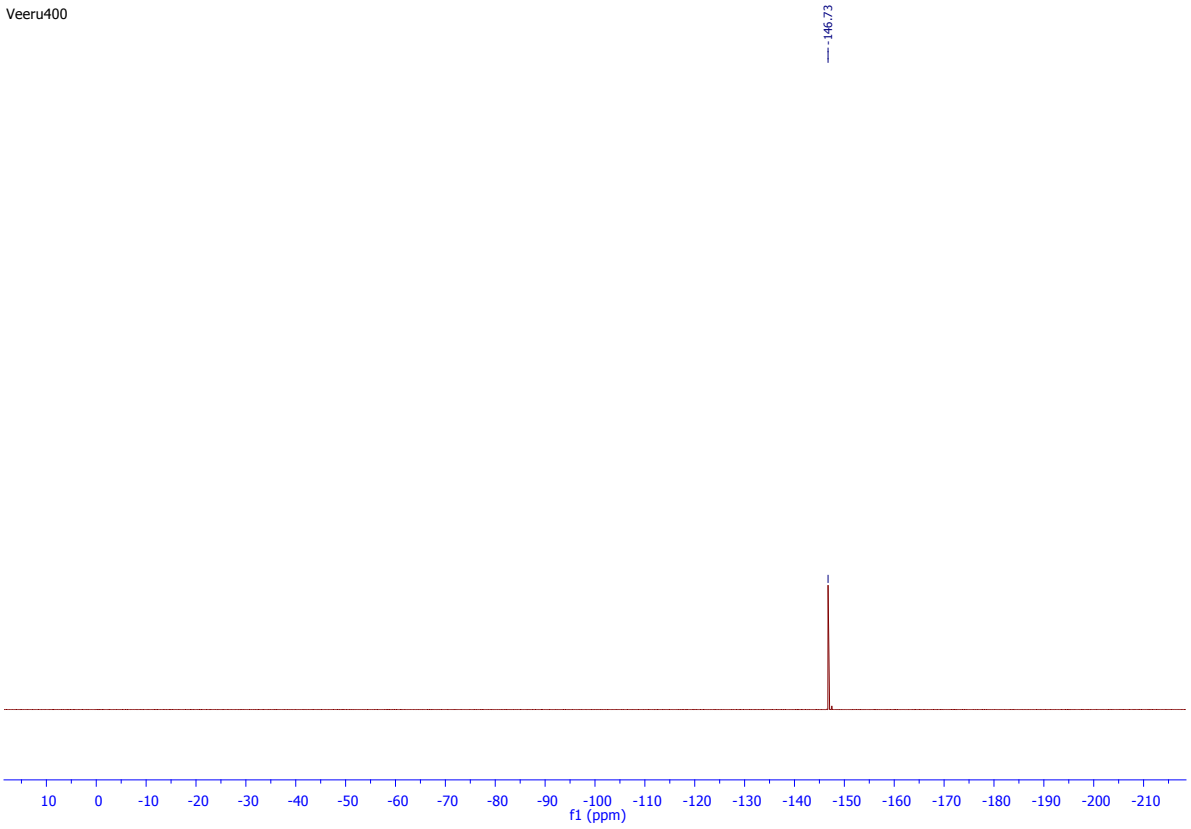
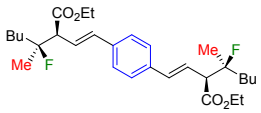
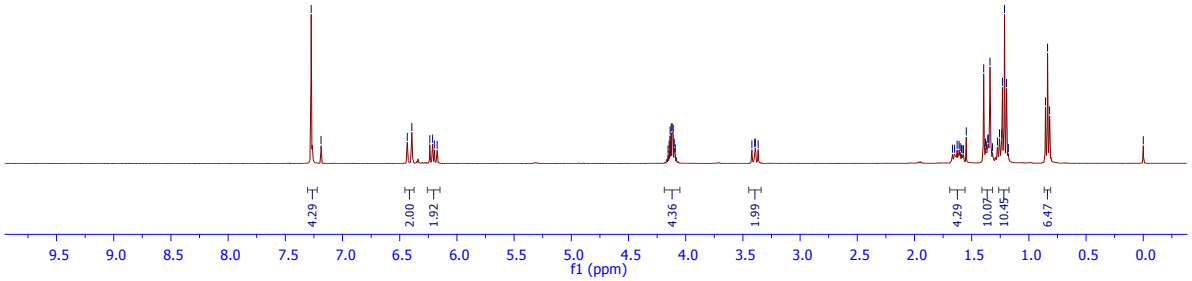


Veeru4002019





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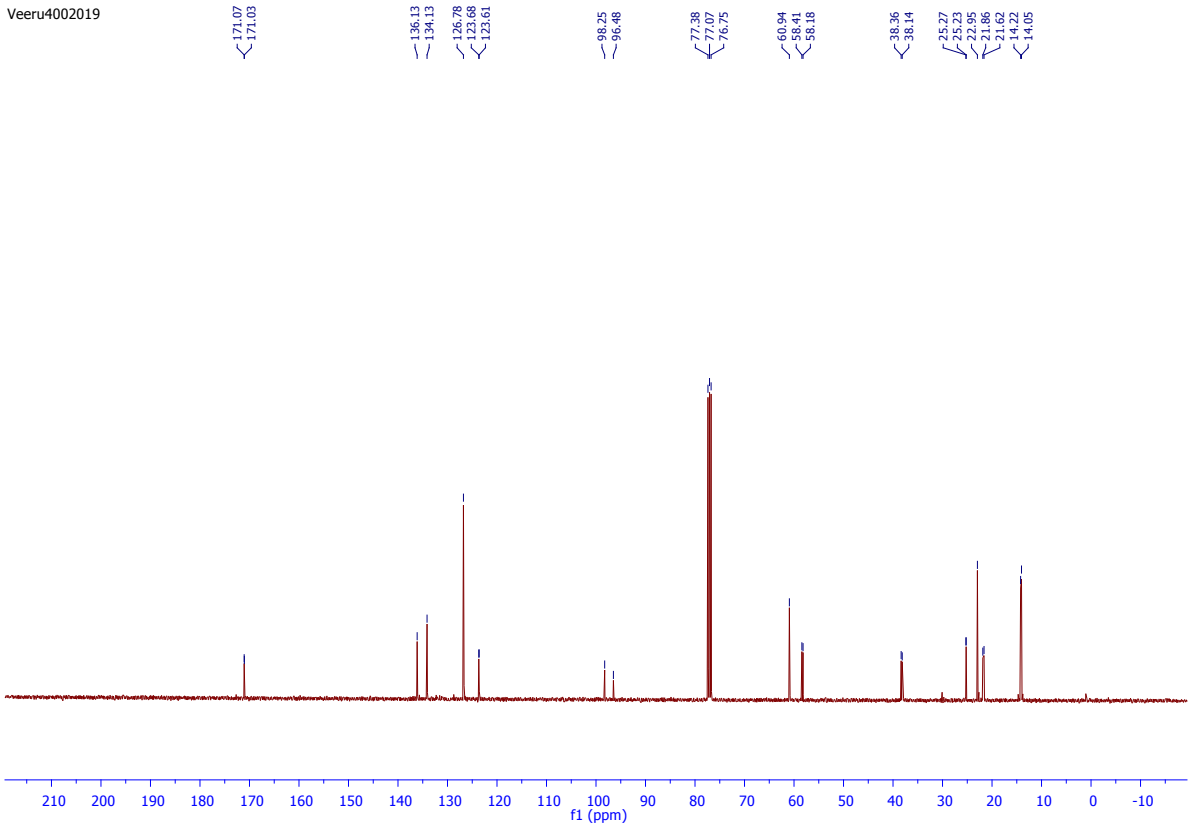

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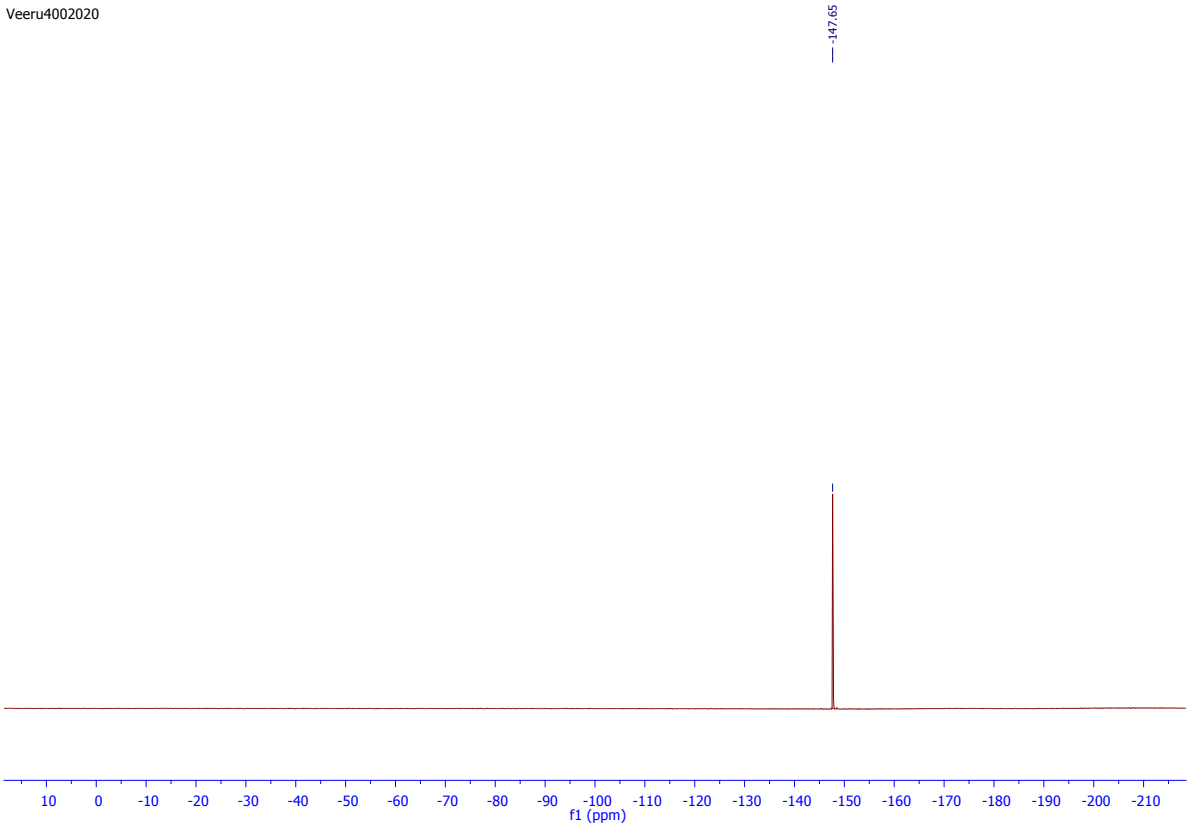

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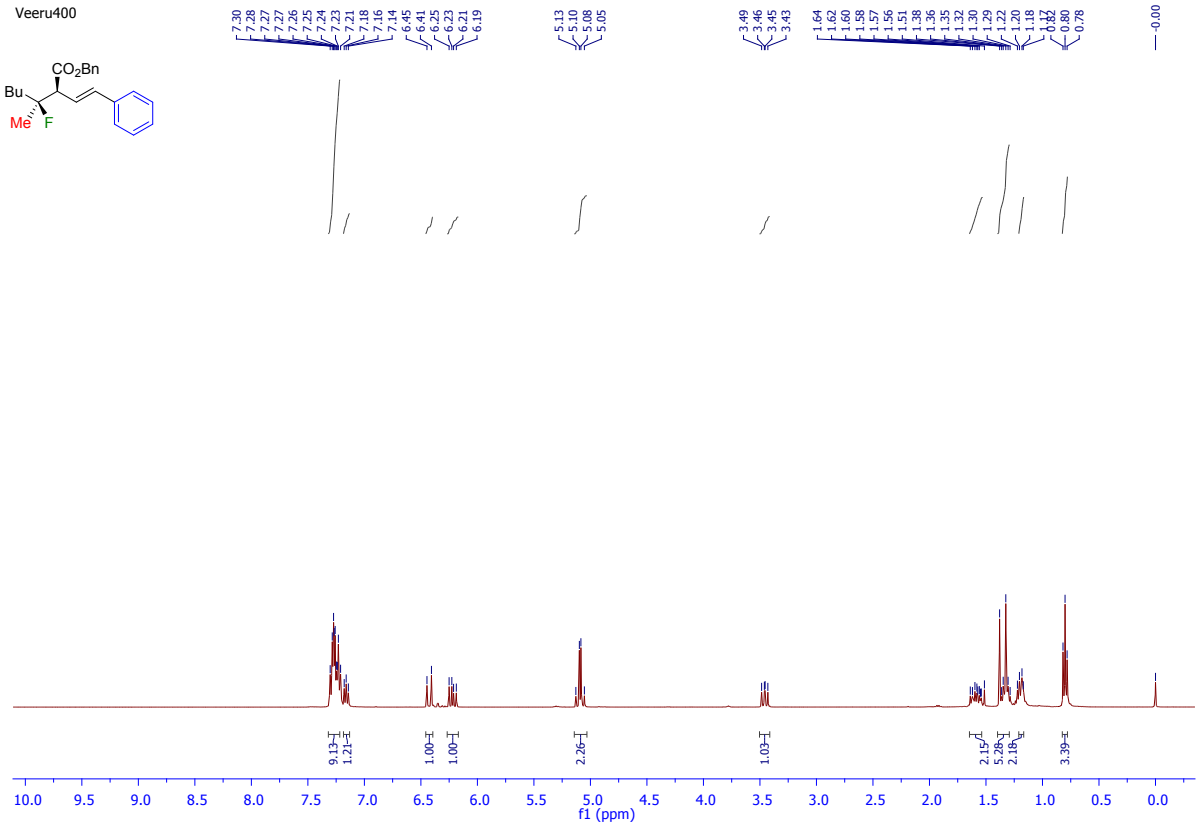

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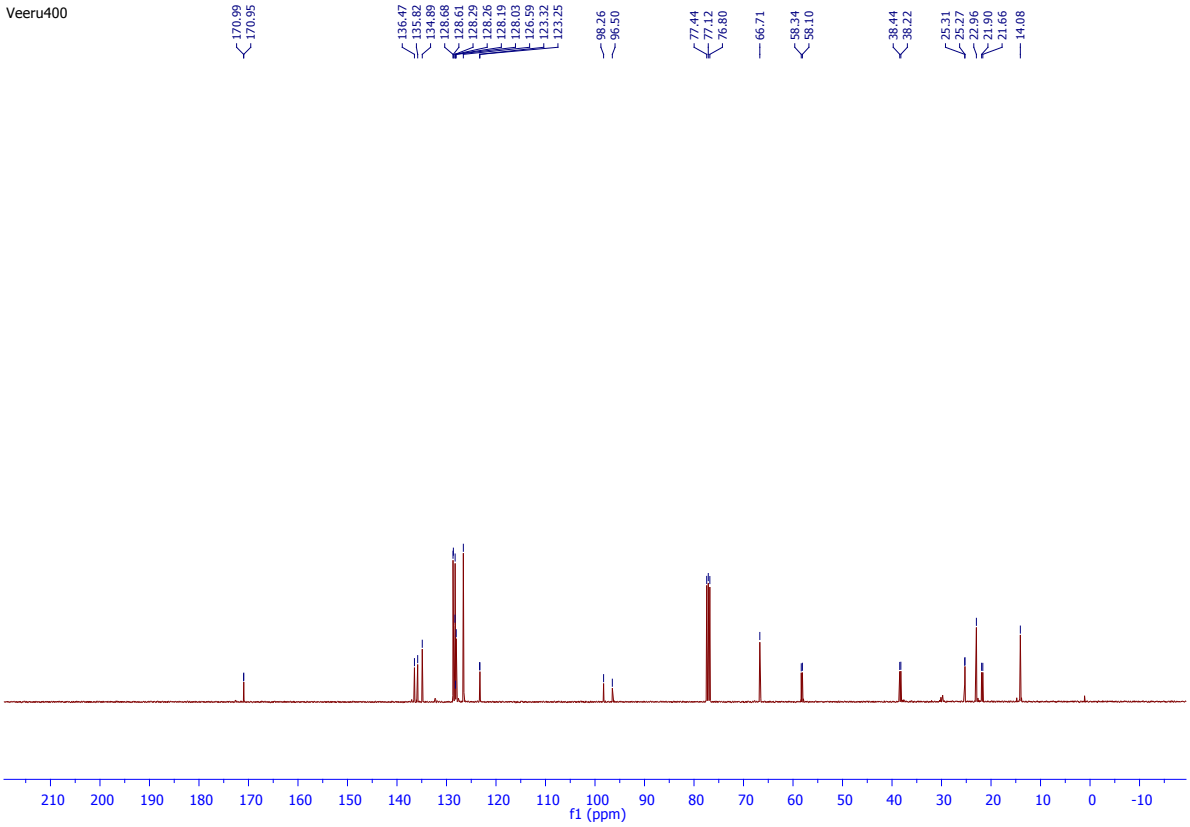

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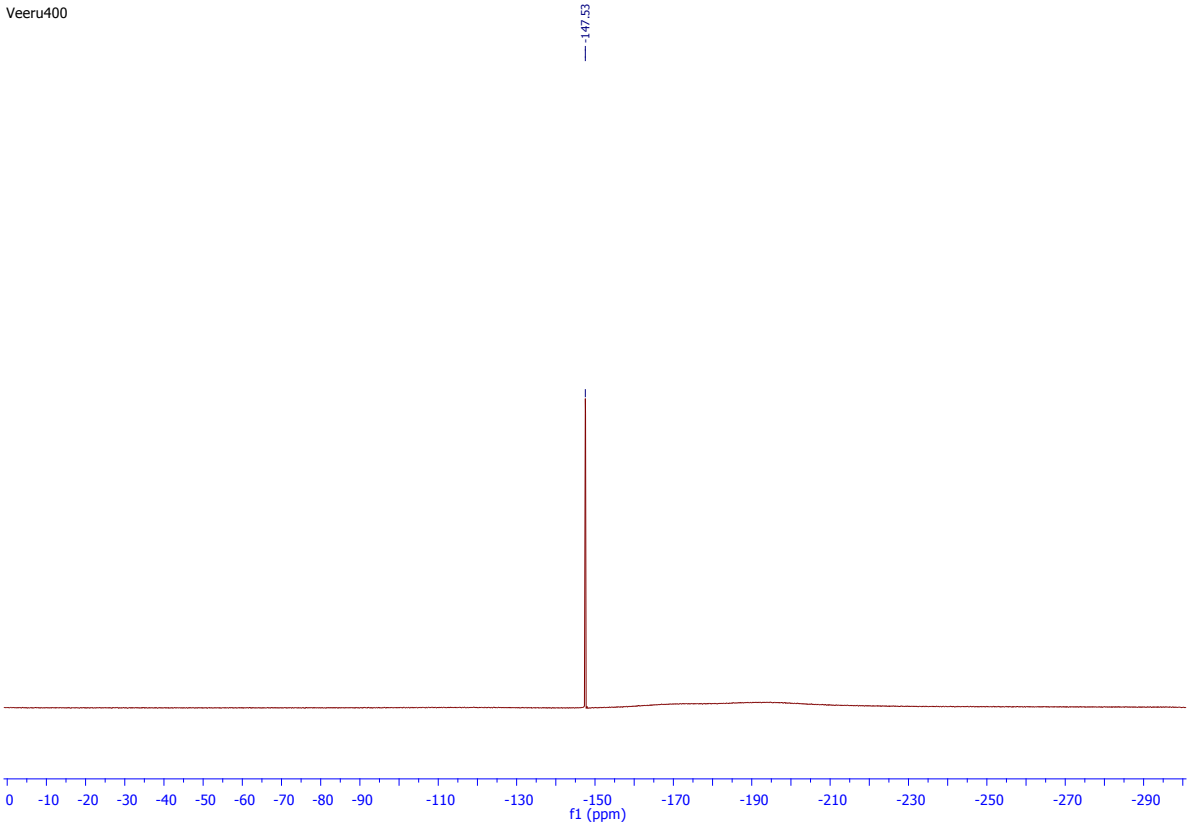

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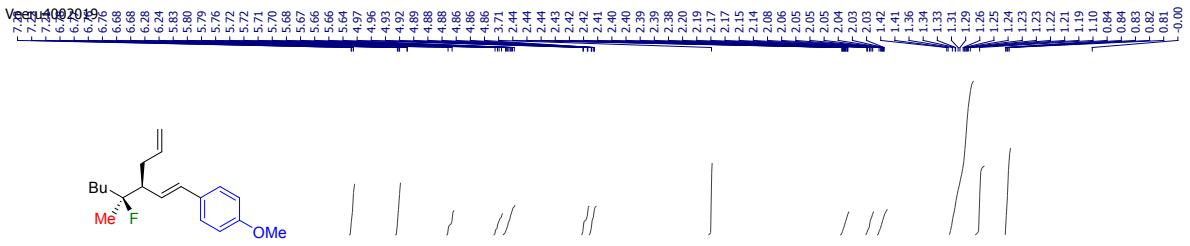
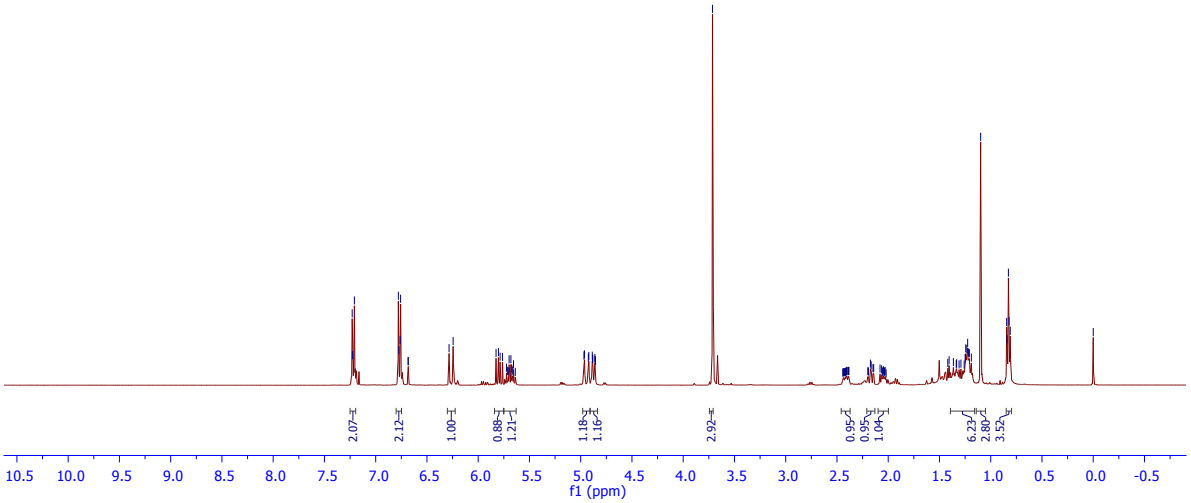


65% along with an inseparable mixture of
18% (out of 65%) eliminated product



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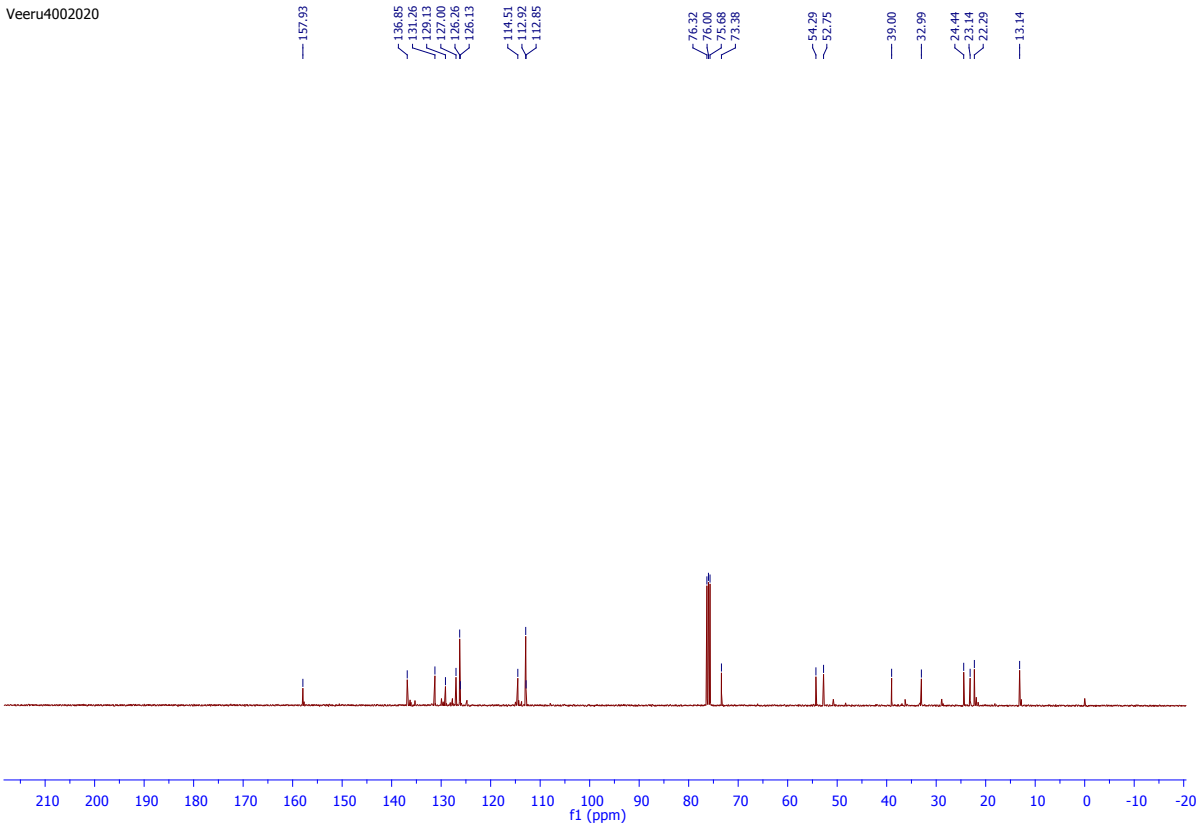

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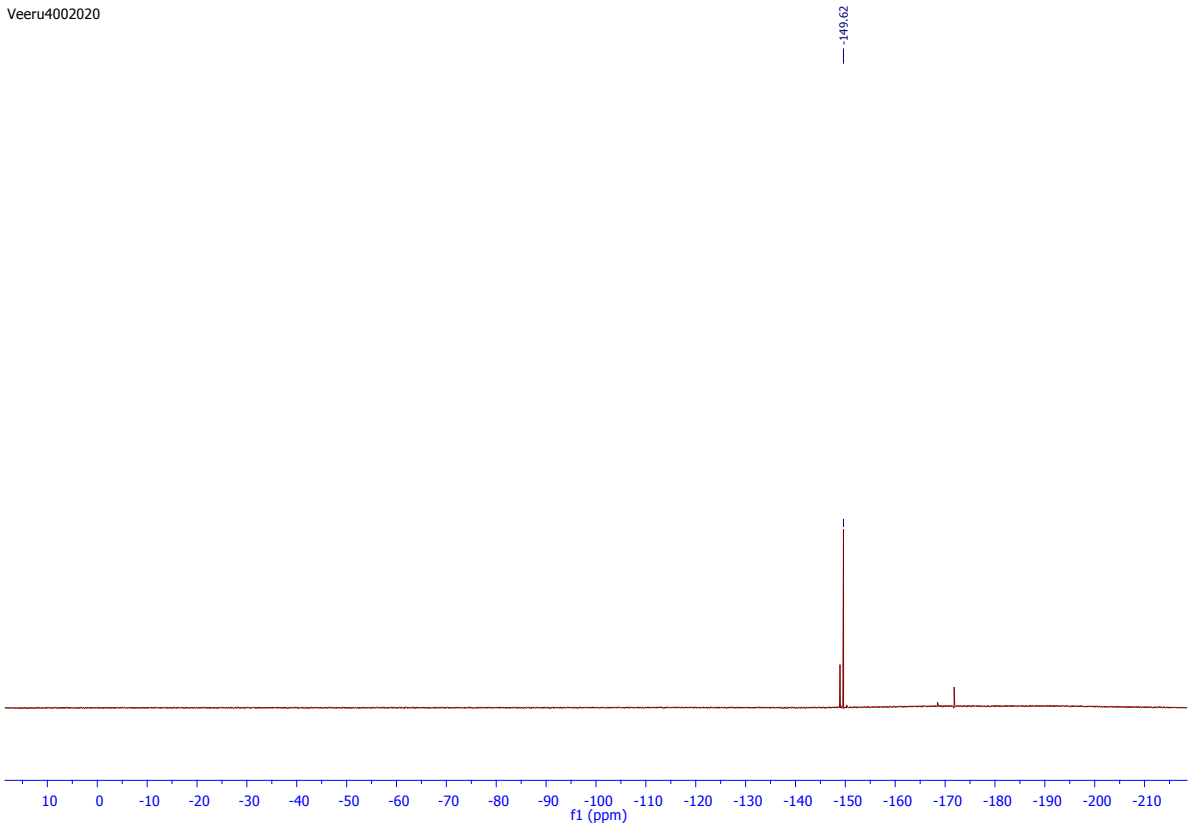

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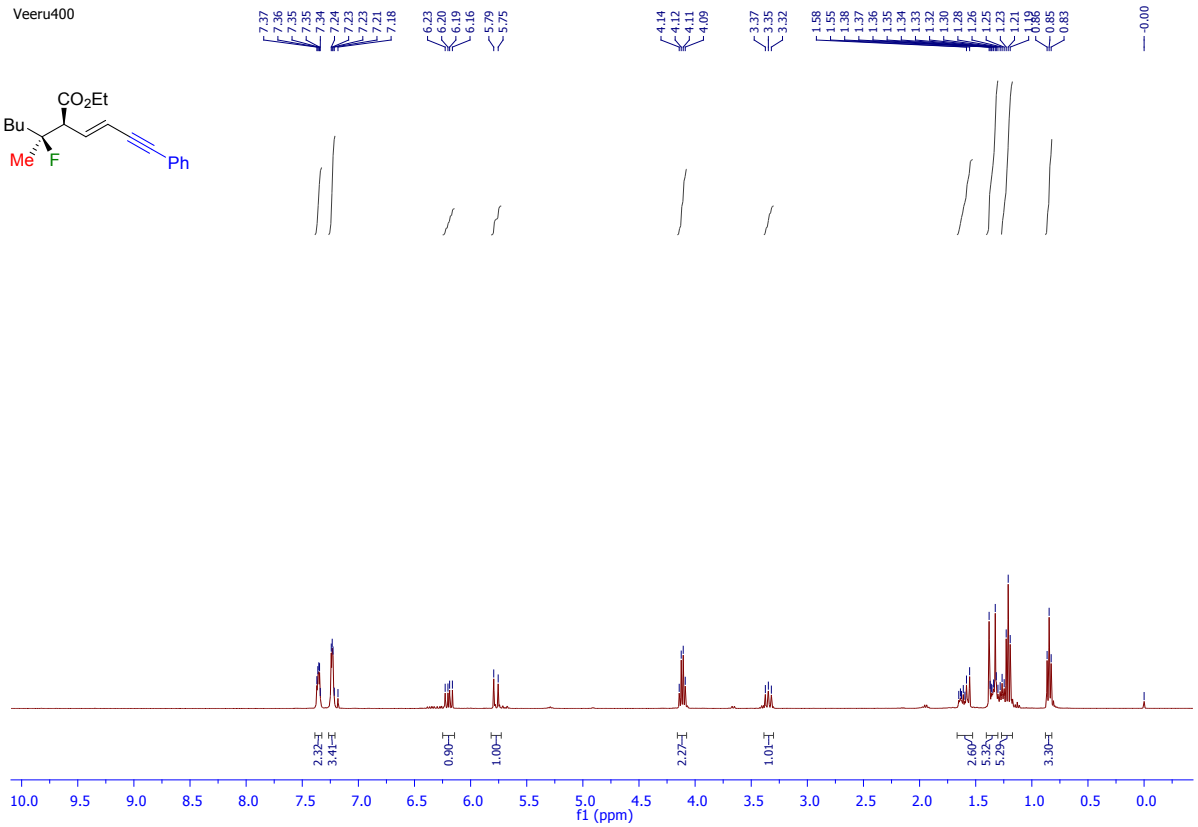

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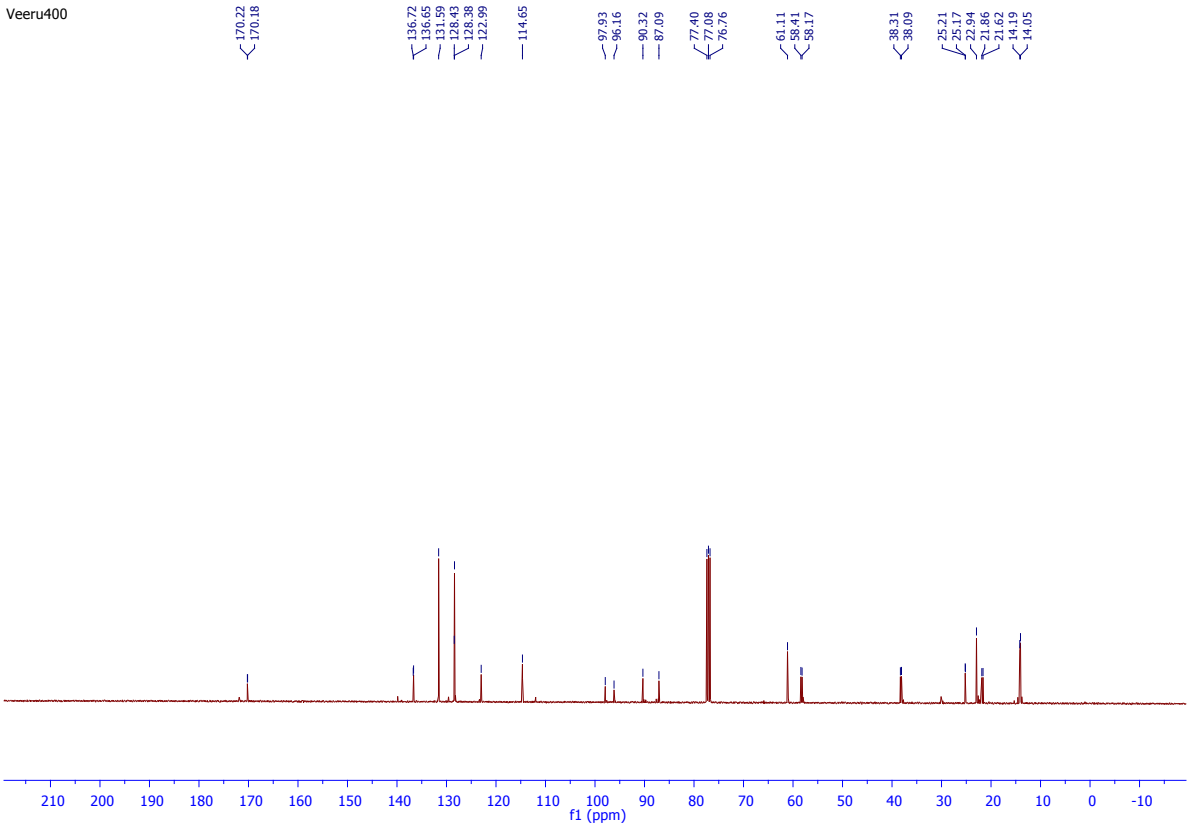

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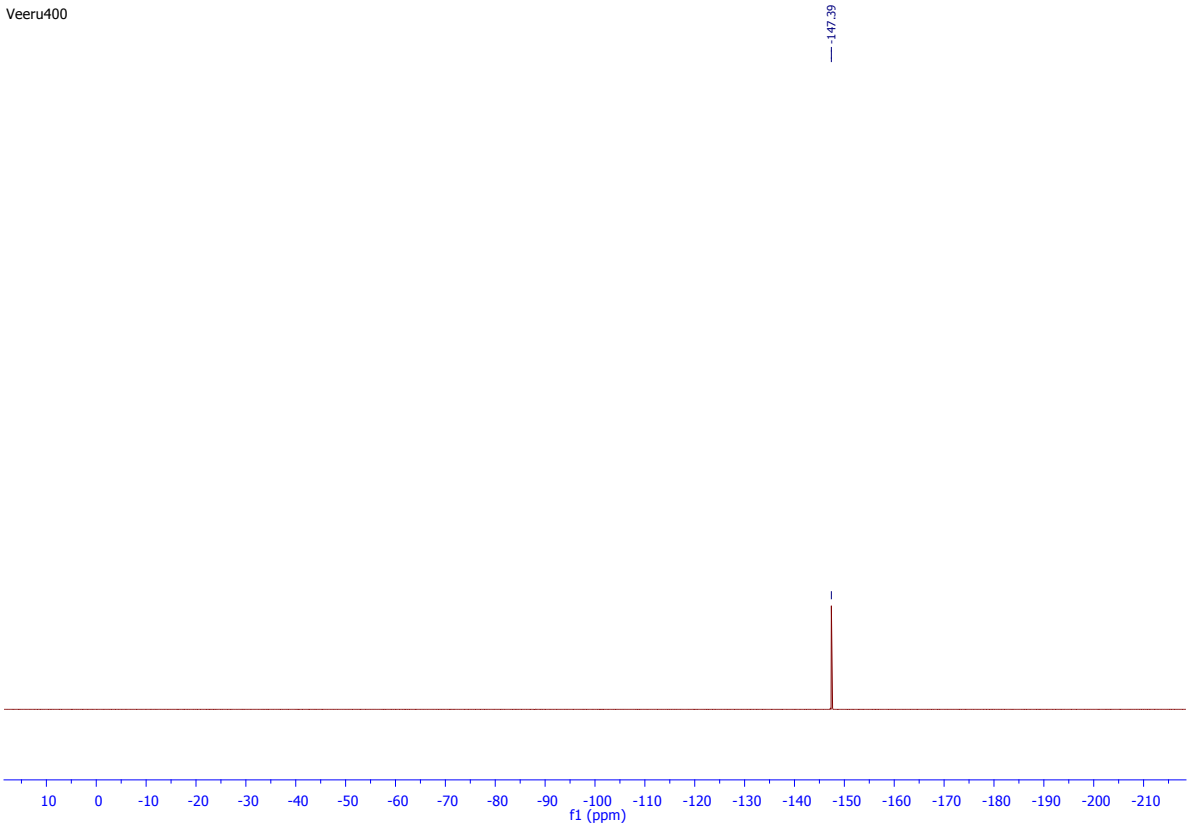

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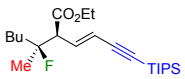

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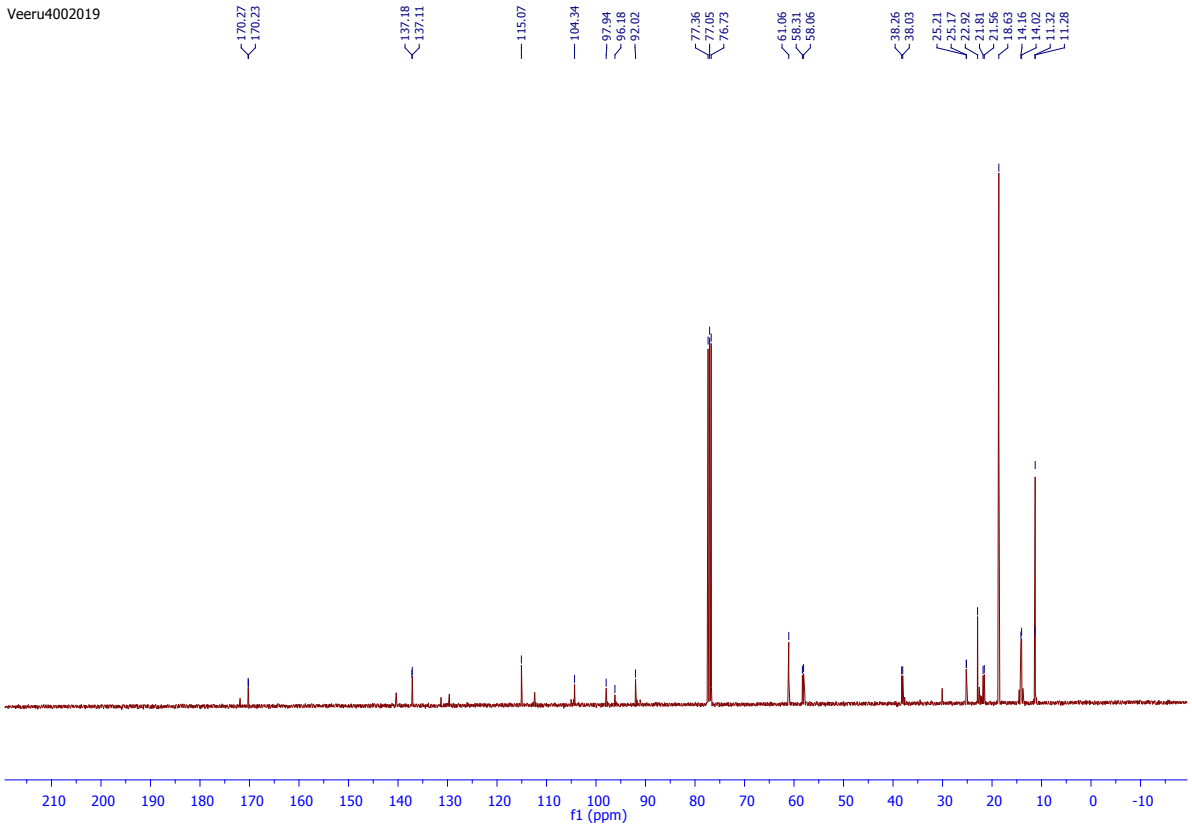
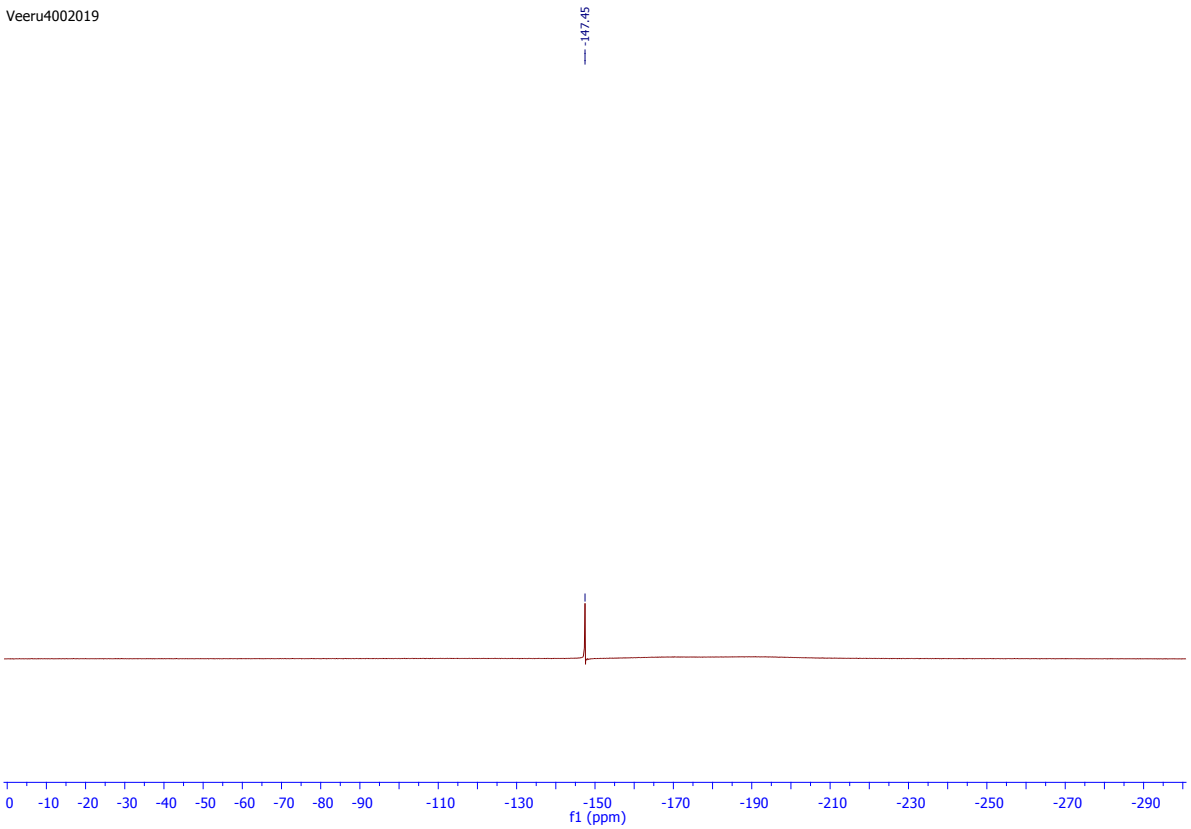


Veeru4002019



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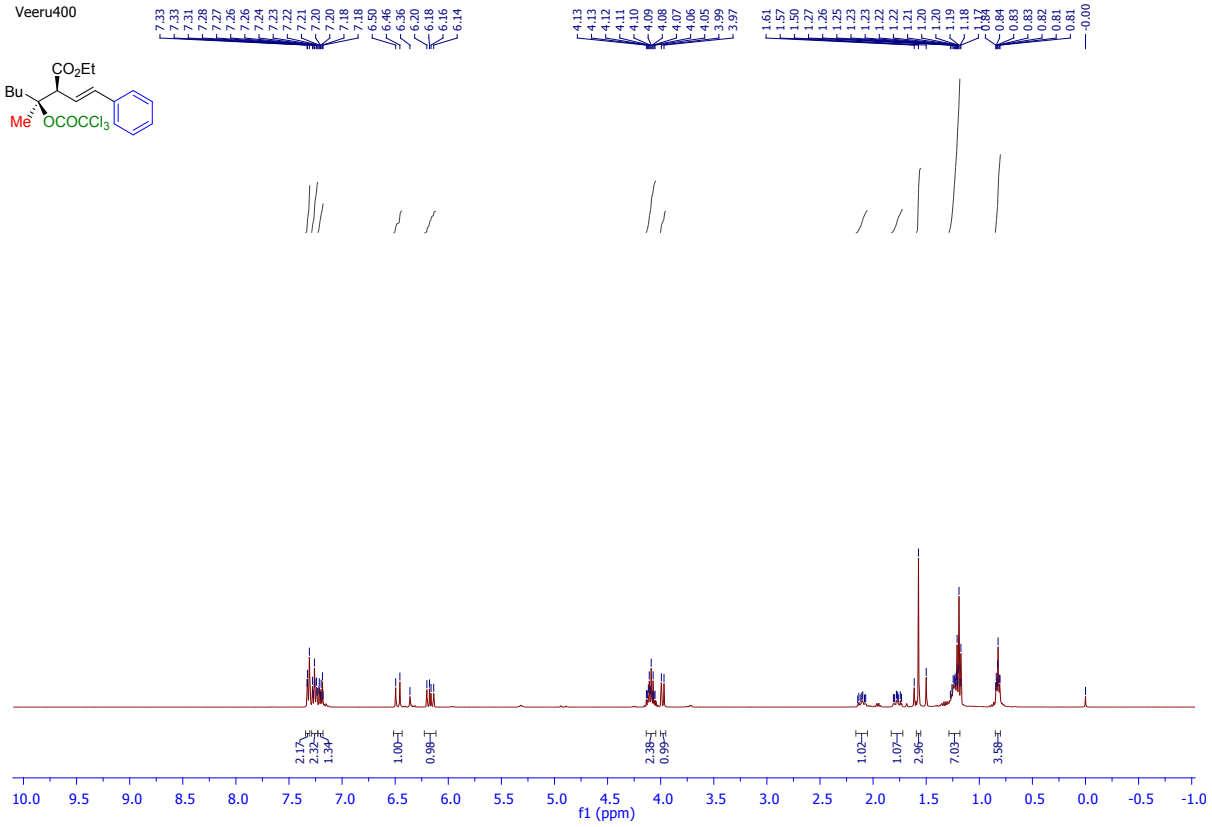

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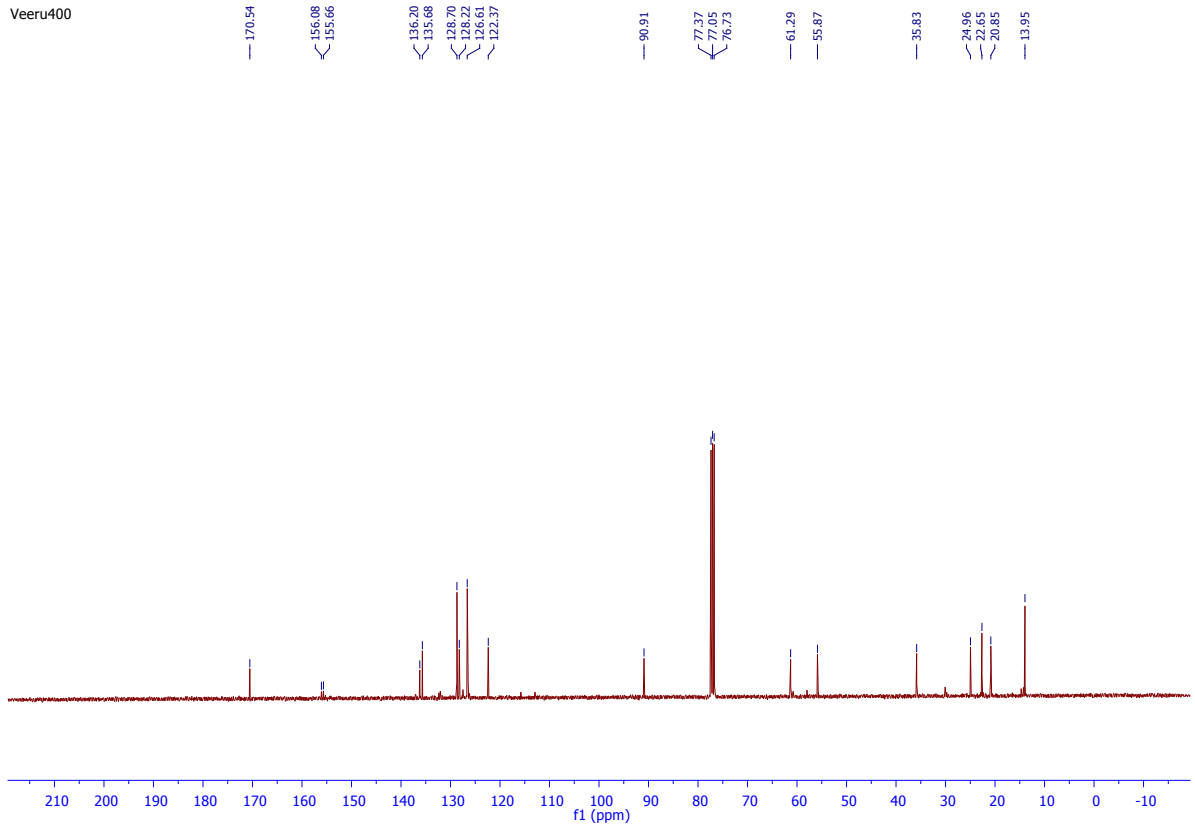

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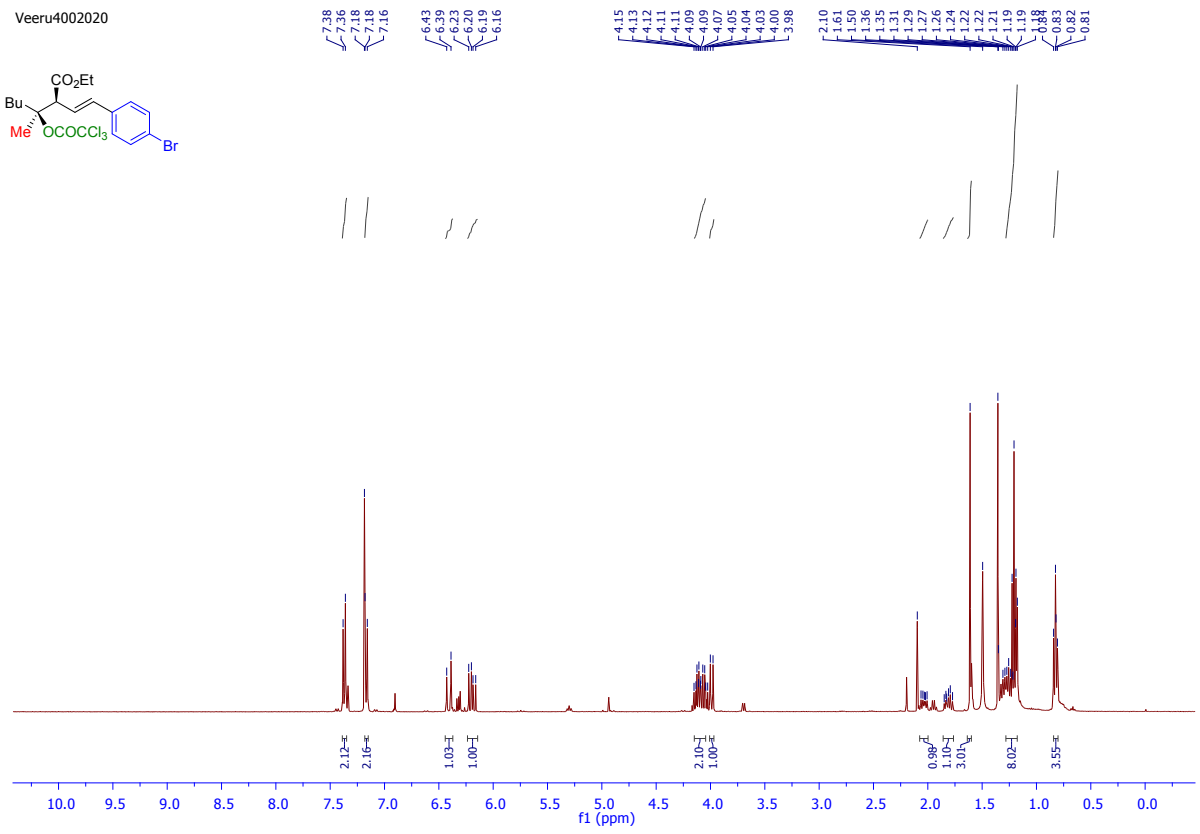

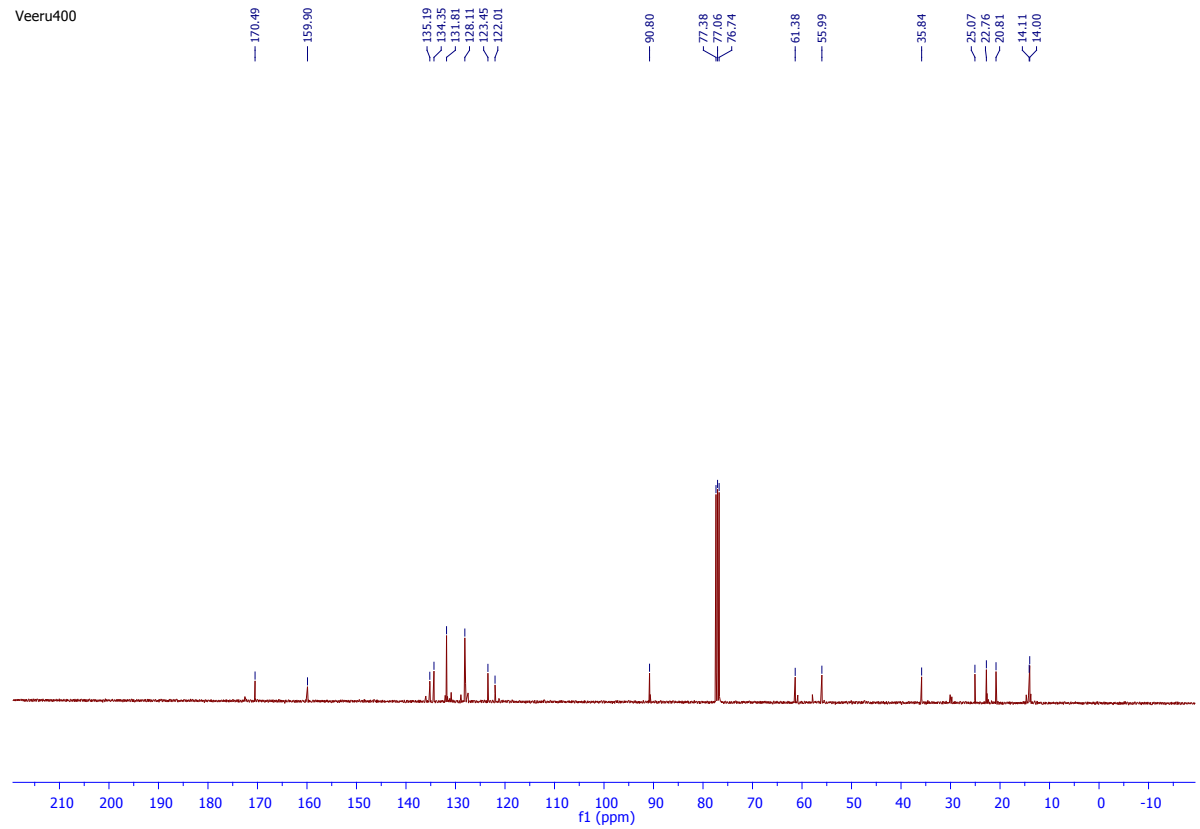
Veeru400
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159.90
135.19
134.35
131.81
128.11
123.45
122.01
90.80
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77.06
76.74
61.38
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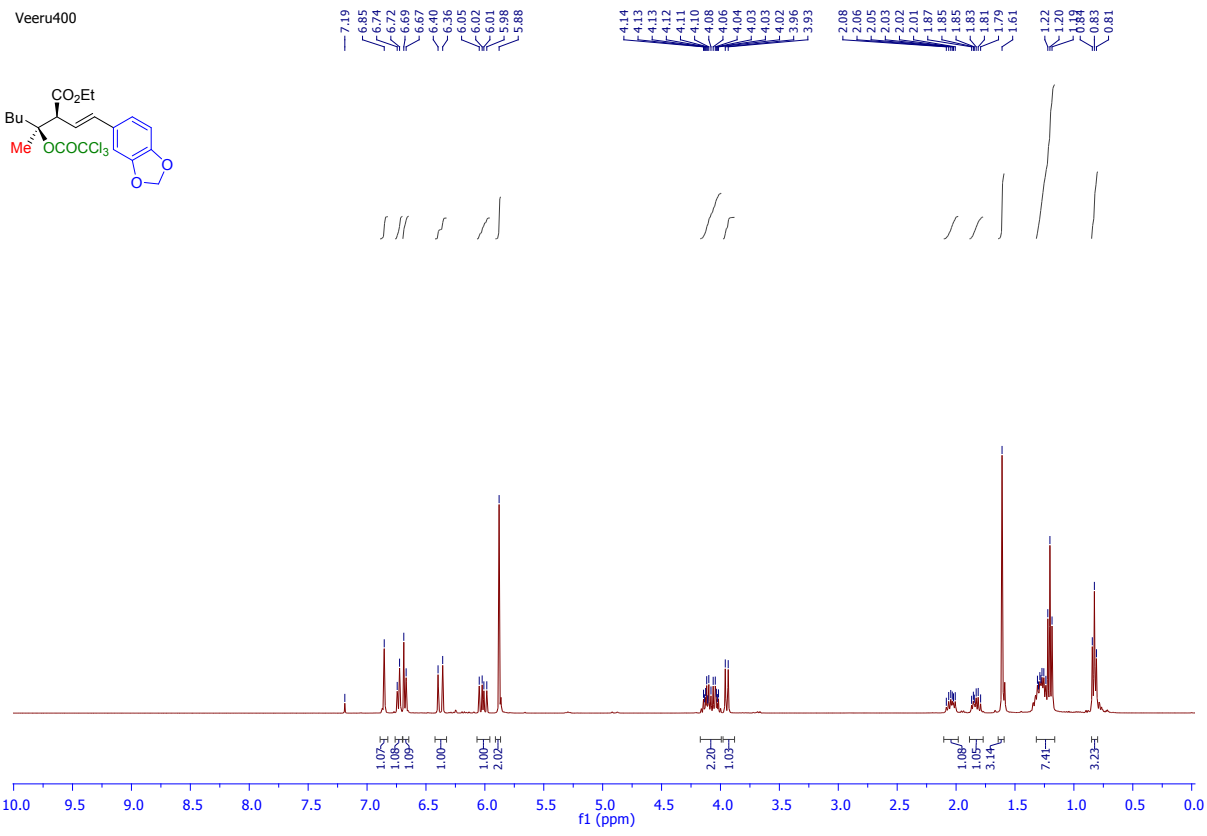
35.84
25.07
22.76
20.81
14.11
14.00
f1 (ppm)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6.67
6.40
6.36
6.05
6.02
6.01
5.98
5.88
4.14
4.13
4.13
4.12
4.11
4.10
4.08
4.06
4.04
4.03
4.03
4.02
3.96
3.93
2.08
2.06
2.05
2.03
2.02
2.01
1.87
1.85
1.85
1.83
1.81
1.79
1.61
1.22
1.20
0.83
0.81
CO2Et
Bu
Me
OCOCCl3
O
O
1.07
1.08
1.09
1.00
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2.20
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1.08
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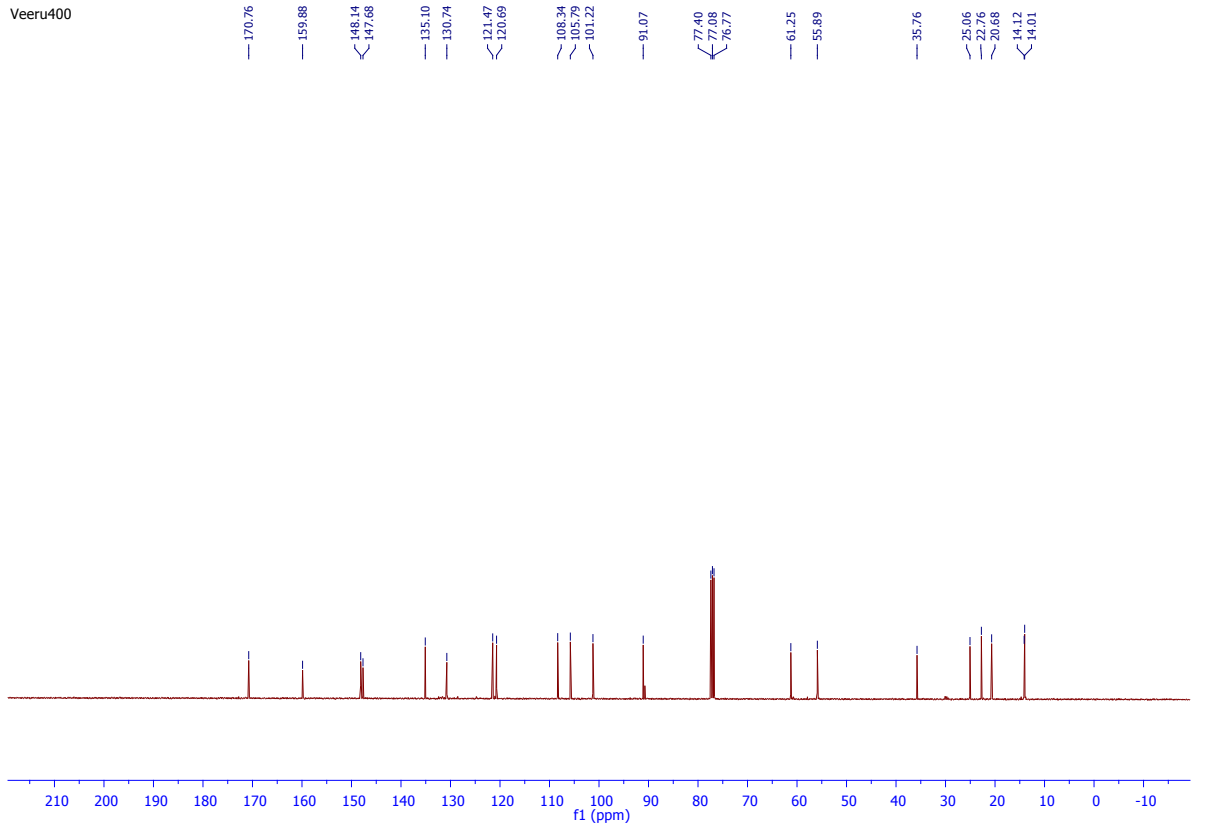
7.41
3.23
f1 (ppm)

Veeru400



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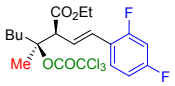

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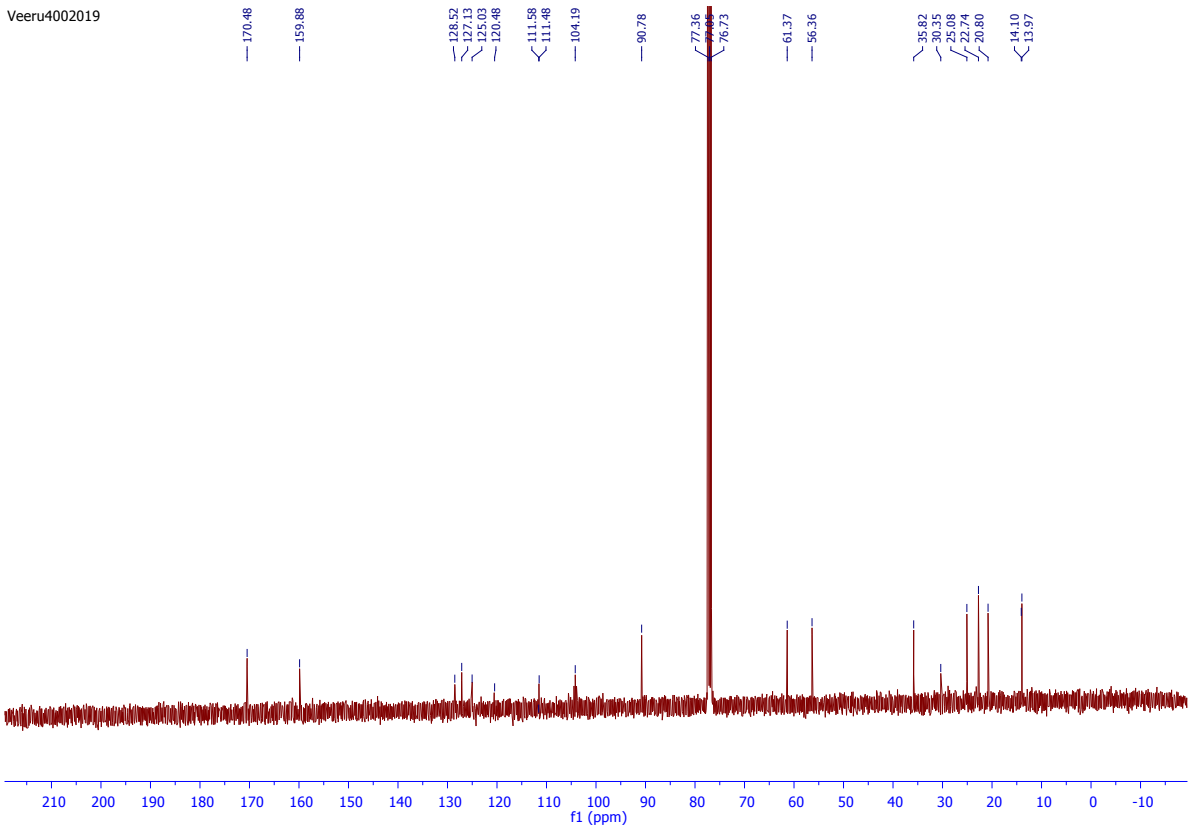

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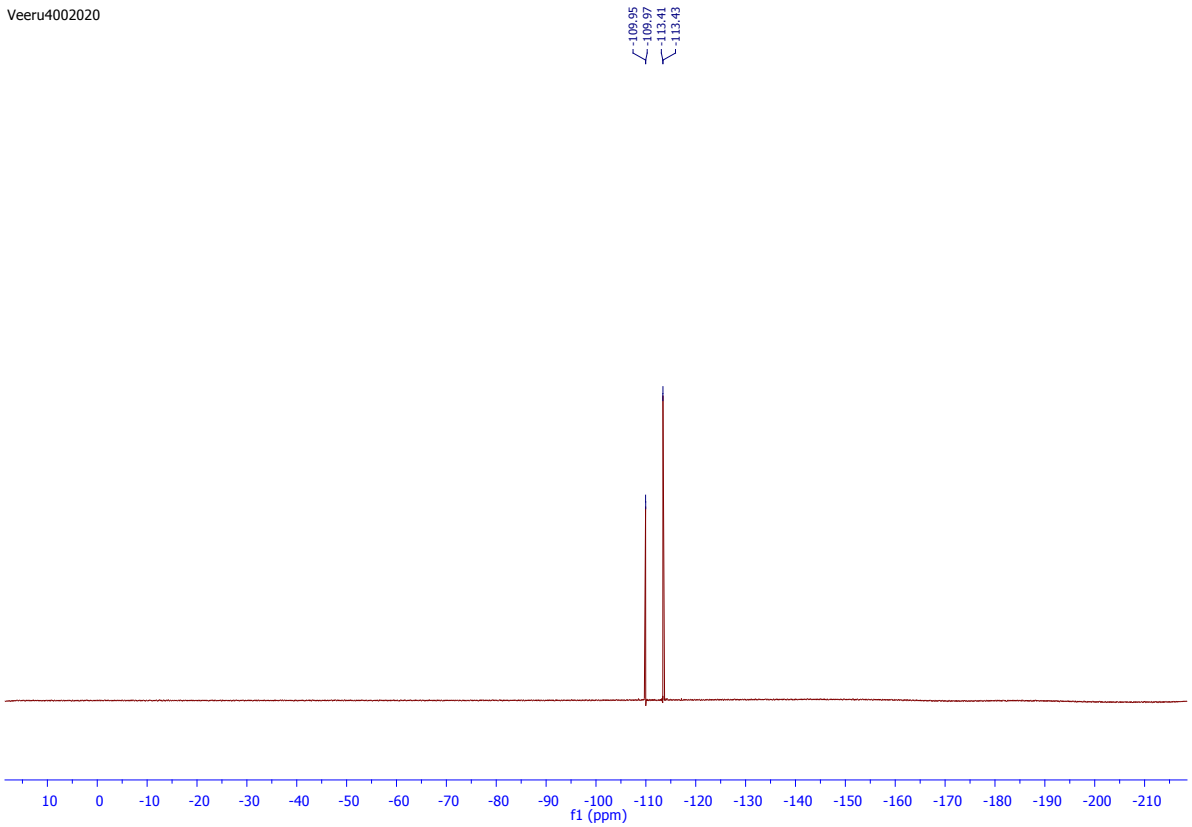

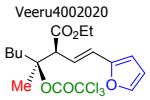
Veeru4002020
CO2Et
Bu
Me
OCOCCl3
O

7.36
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7.26
6.39
6.38
6.38
6.37
6.37
6.35
6.27
6.26
6.21
6.19
6.17
6.15
4.22
4.20
4.19
4.18
4.13
4.11
4.10
4.08
4.02
4.00
2.14
2.12
2.10
2.10
2.08
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1.69
1.57
1.43
1.35
1.34
1.33
1.33
1.29
1.28
1.28
1.26
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0.90
0.88
1.00
2.12
1.04
1.12
1.13
1.15
1.10
1.22
1.04
3.40
7.71
3.35
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
2.5
2.0
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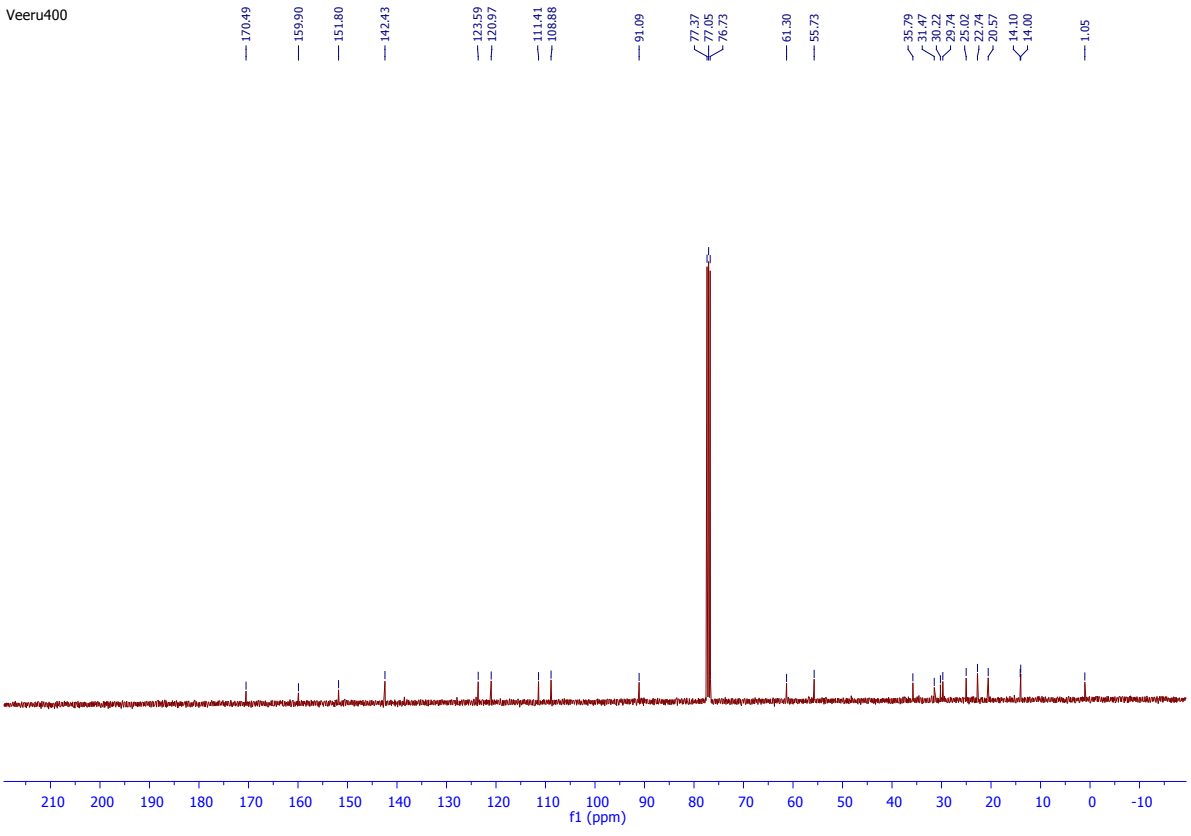
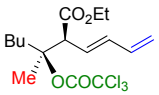
0.5
0.0
f1 (ppm)

Veeru400

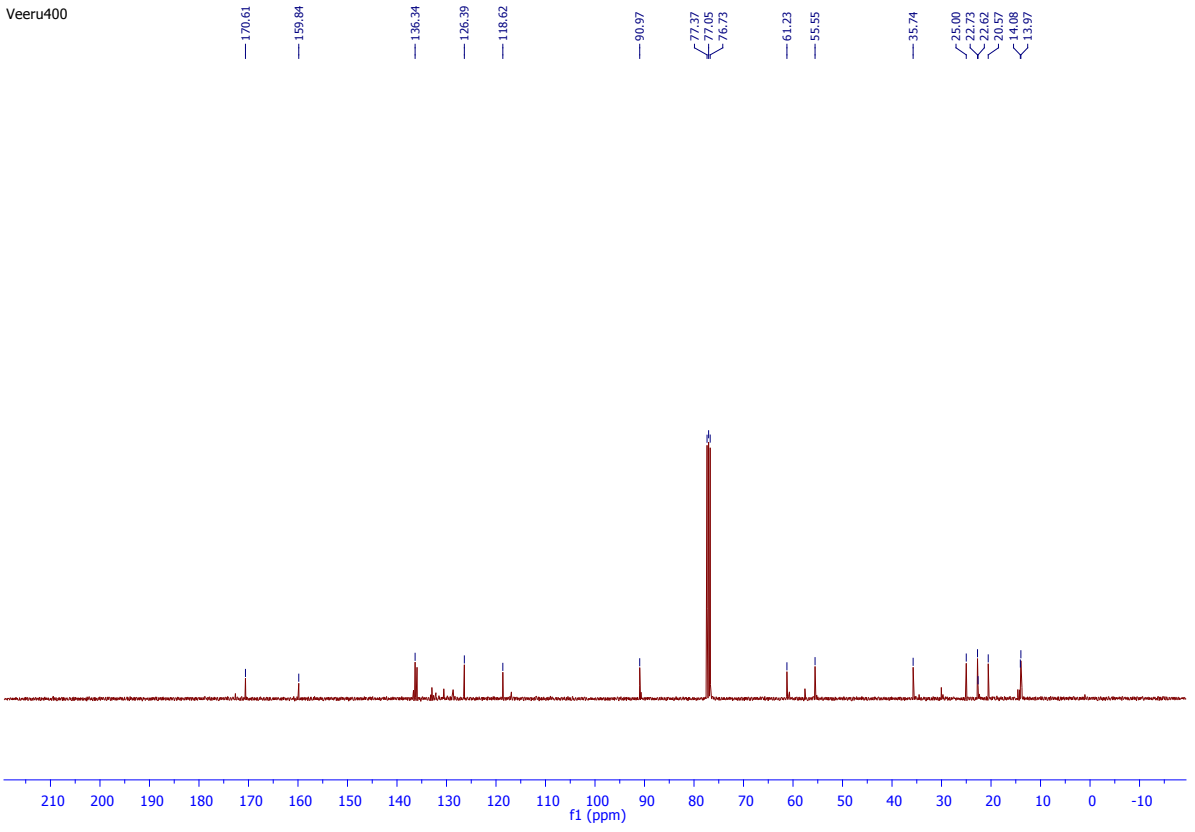

170.49
159.90
151.80
142.43
123.59
120.97
111.41
108.88
91.09
77.37
77.05
76.73
61.30
55.73
35.79
31.47
30.22
29.74
25.02
22.74
20.57
14.10
14.00
1.05
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

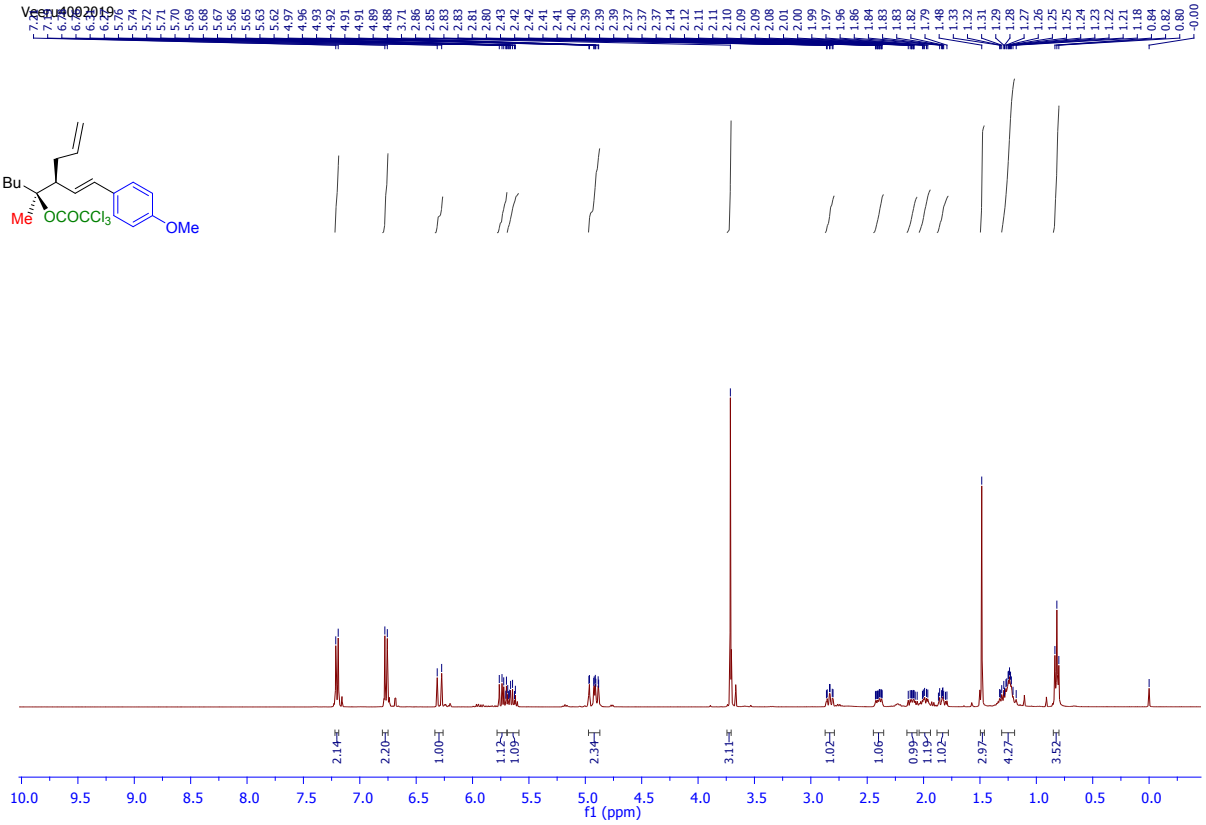
Veeru400

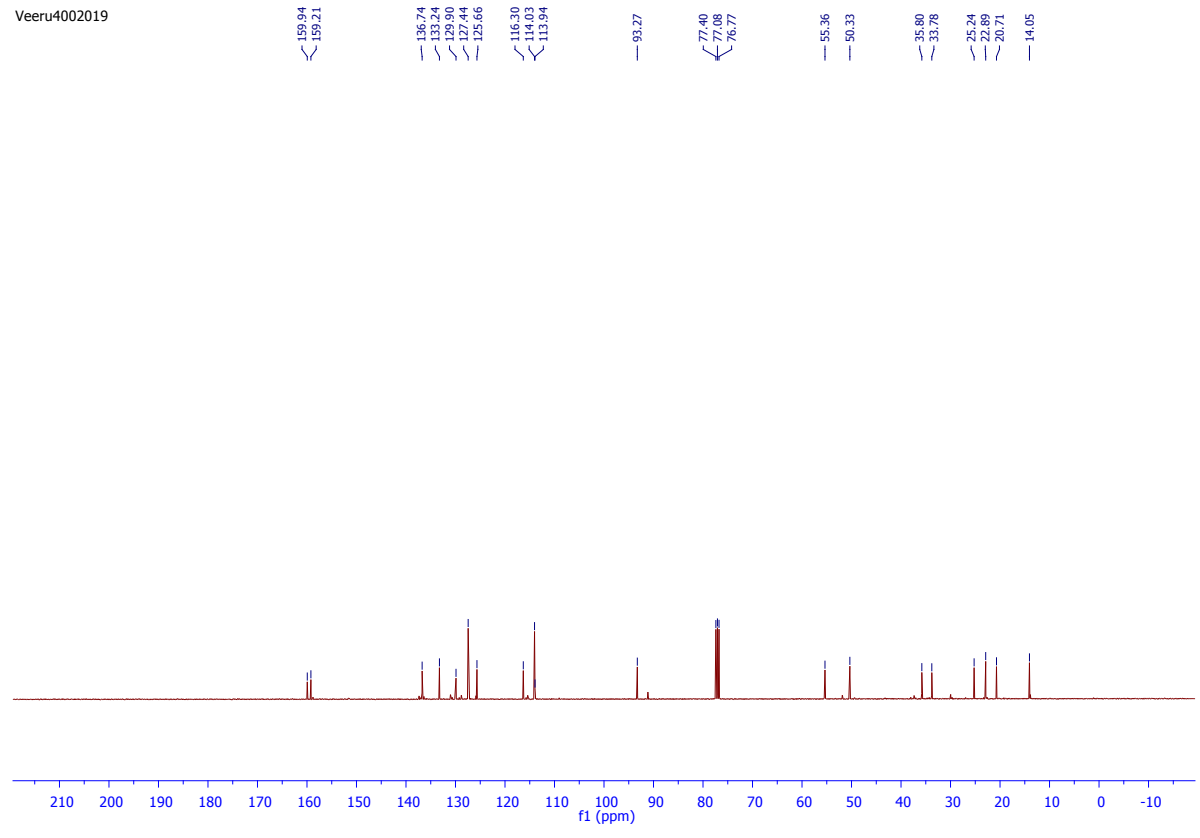


33% product +
20% eliminated product

Veeru400




Veeru4002019
Bu
Me
OCOCCl3
OMe
f1 (ppm)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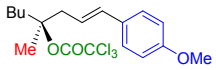
f1 (ppm)

Veeru4002019



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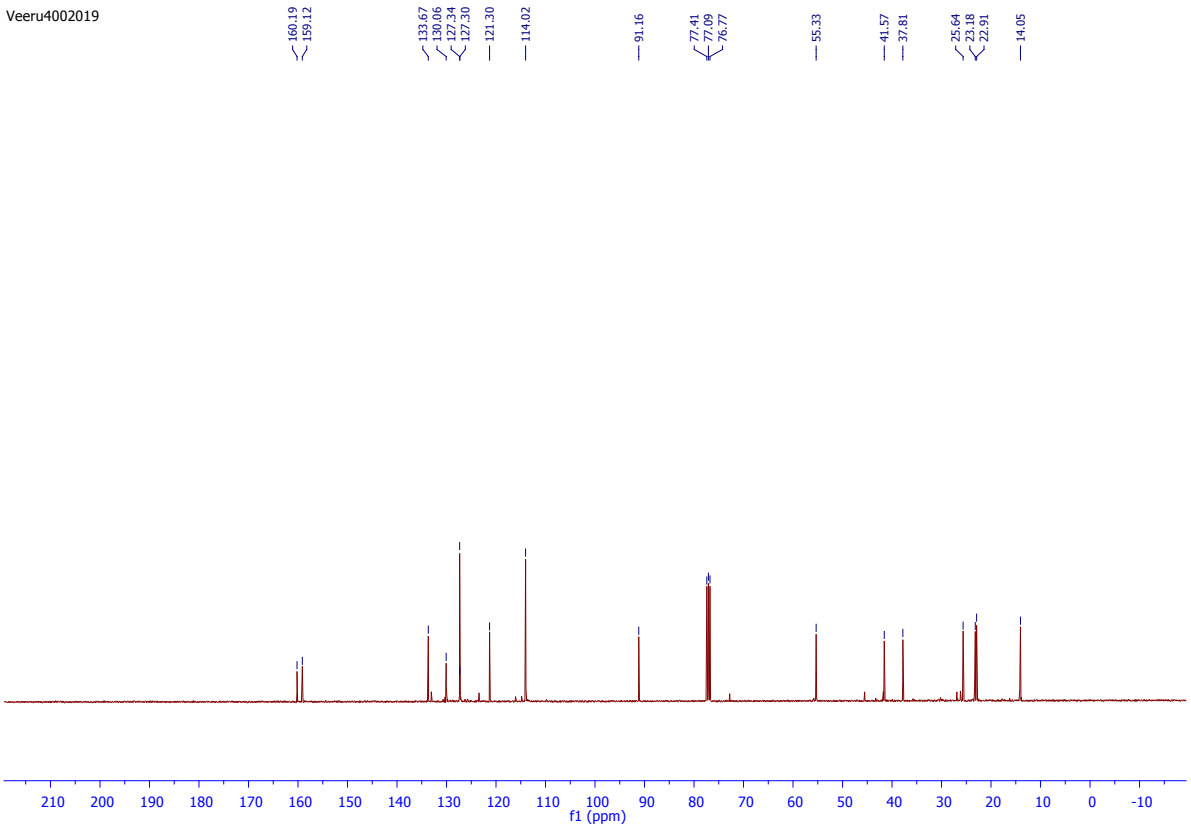

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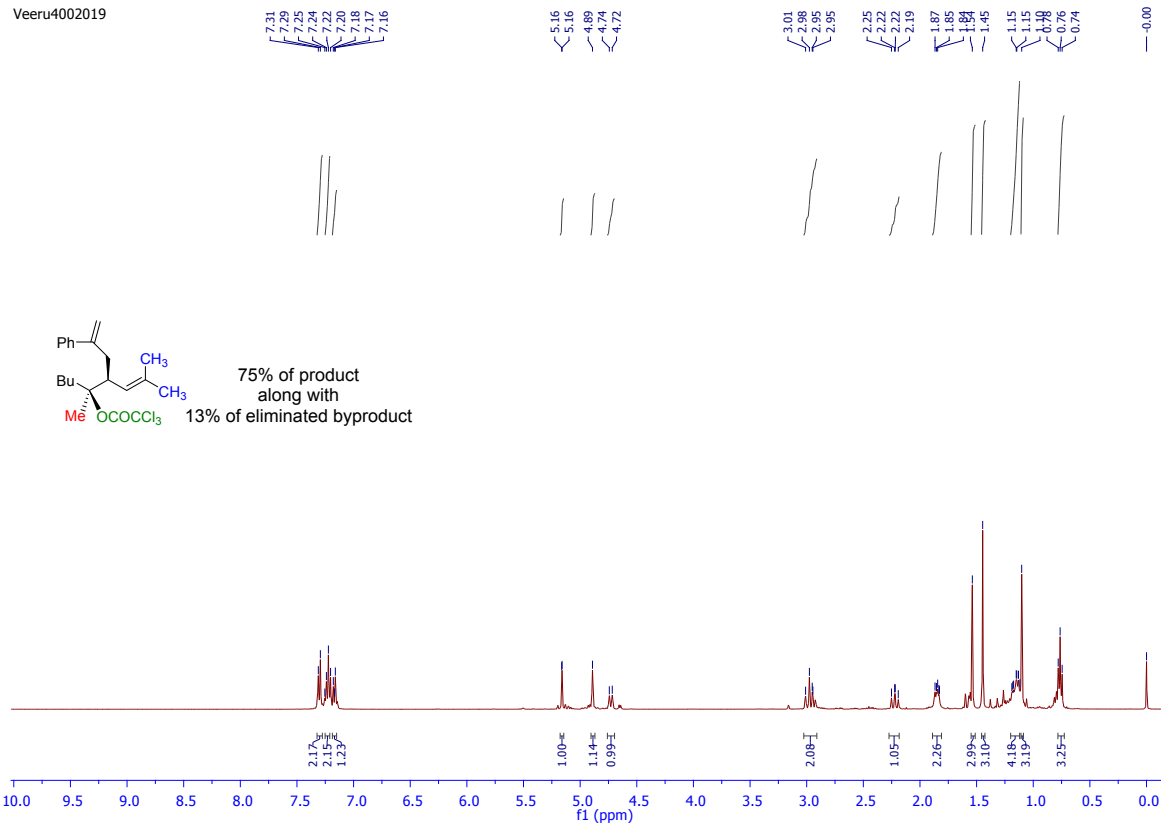

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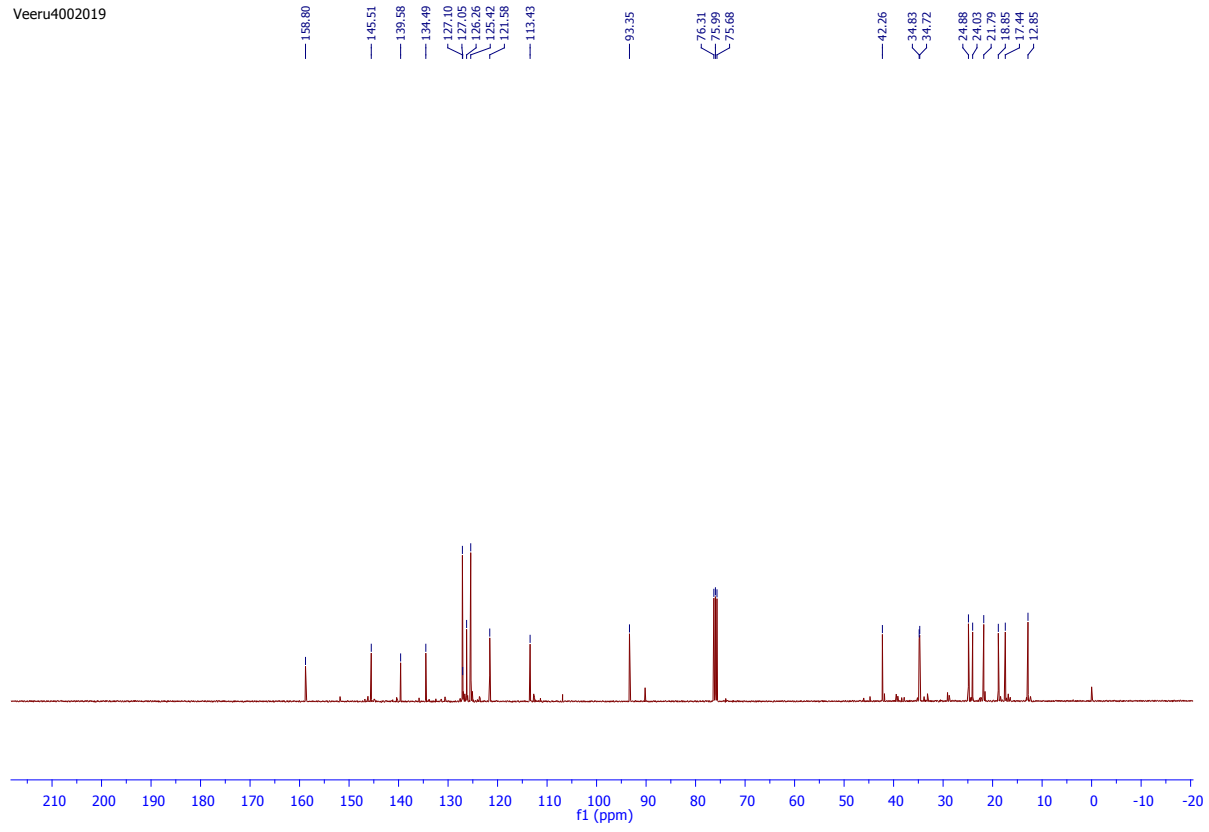

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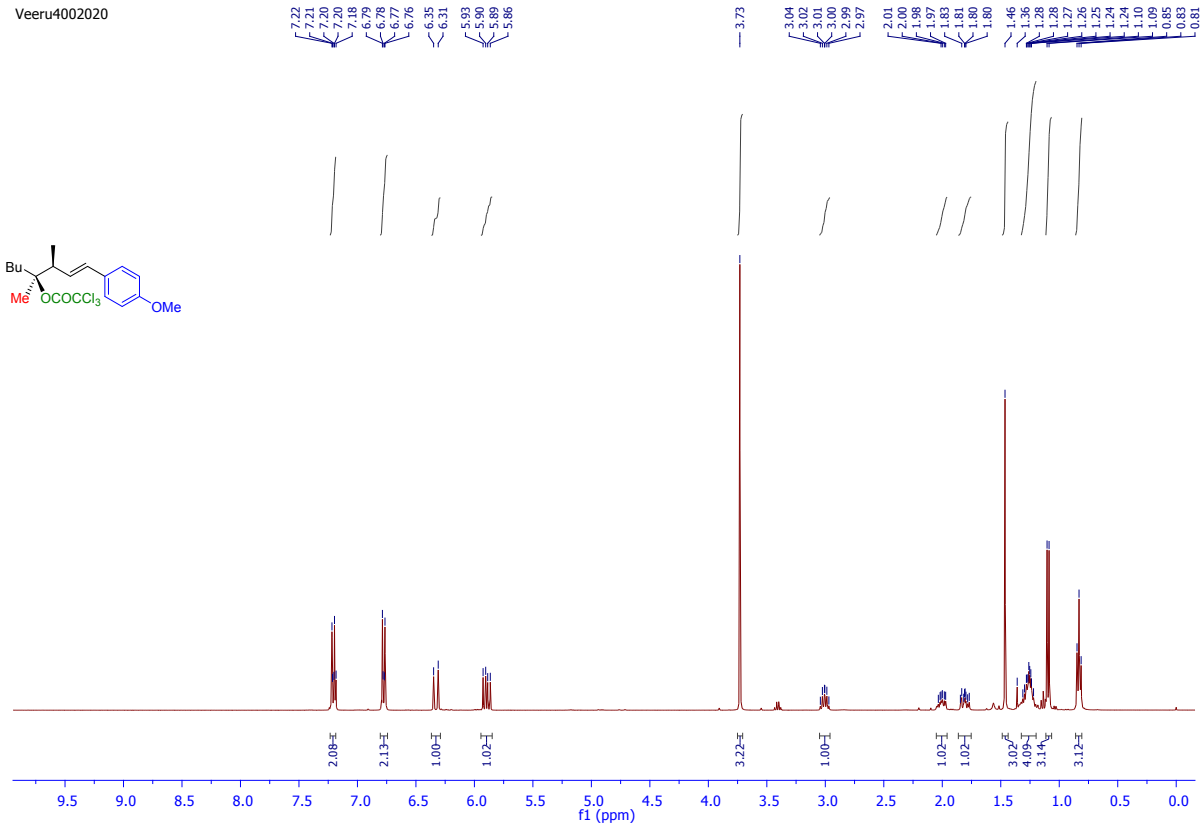

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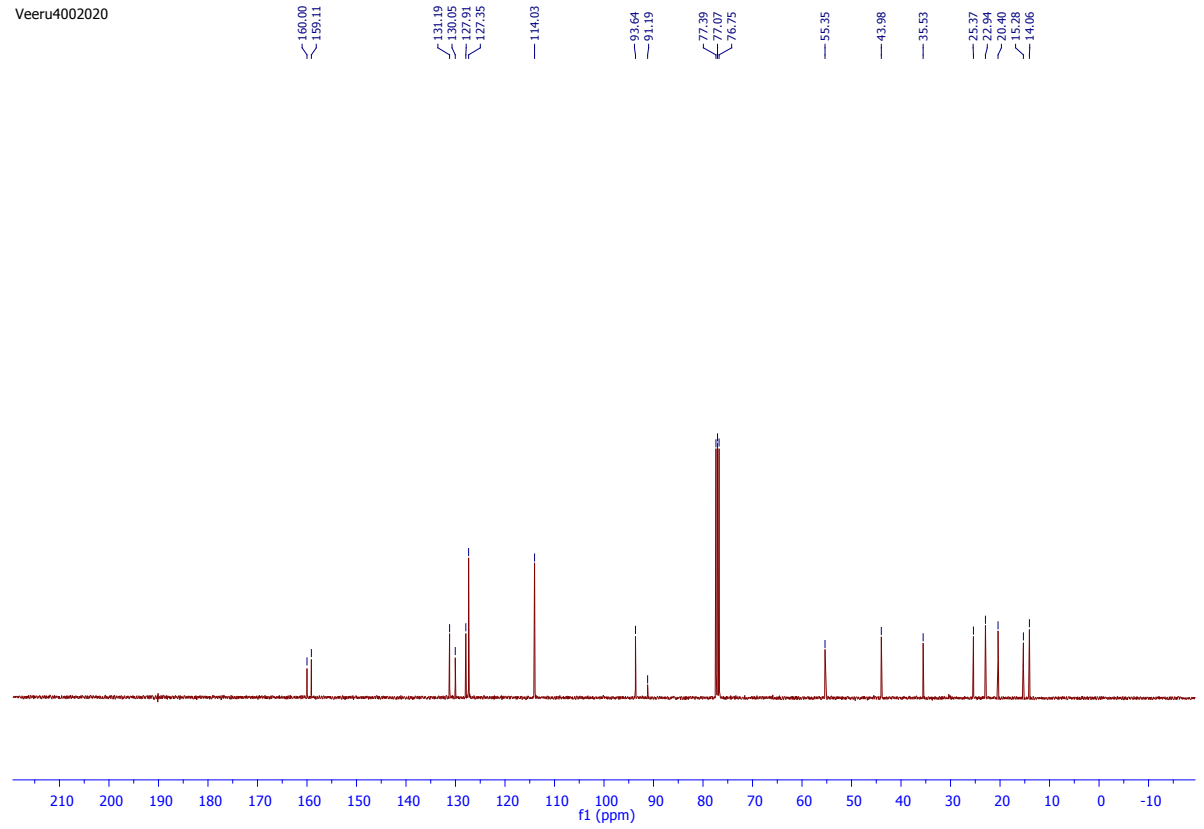

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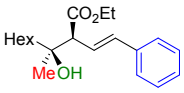

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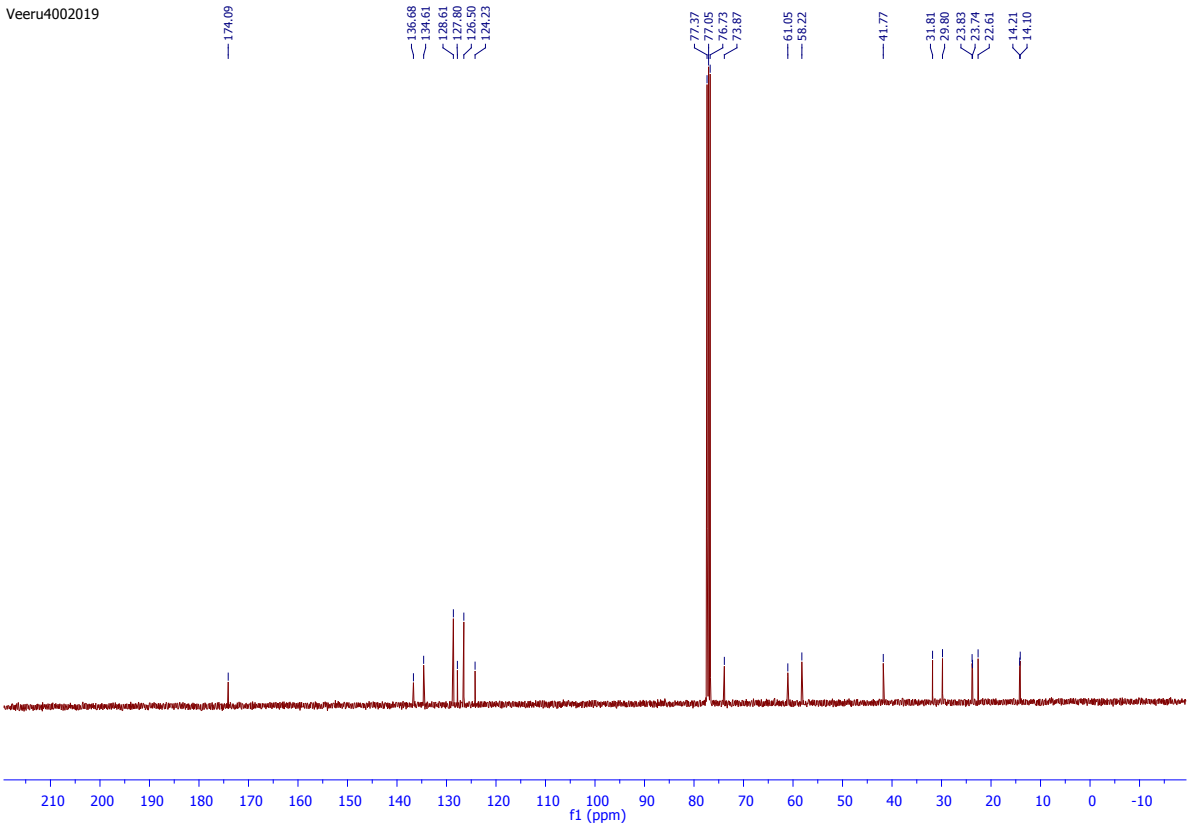
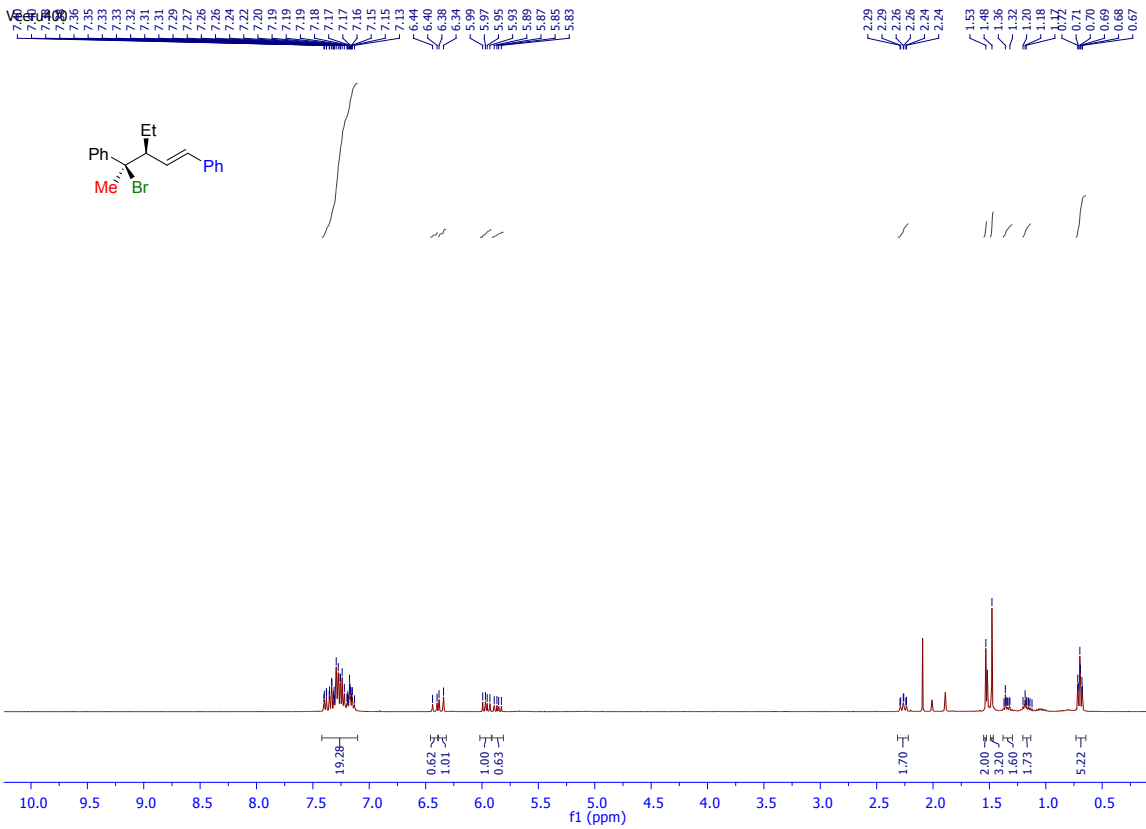
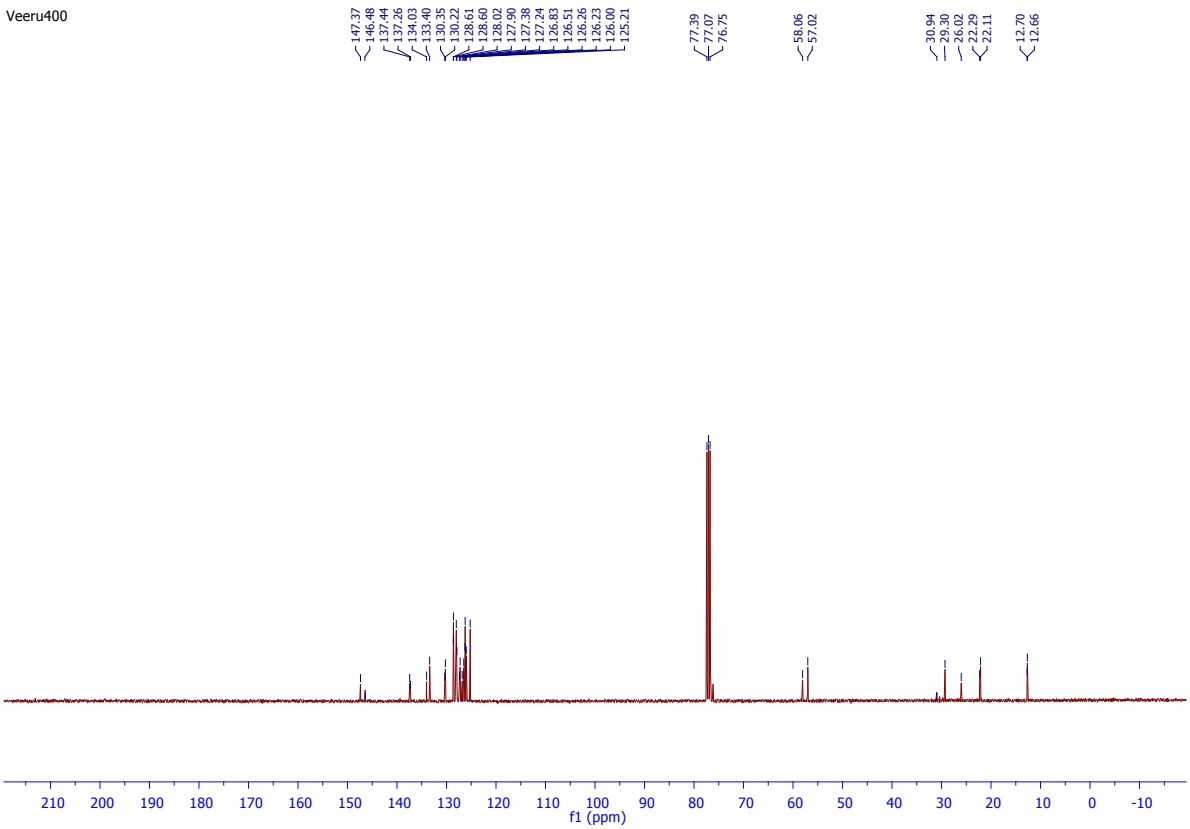



Veeru400
Et
Ph
Ph
Me
Br
f1 (ppm)


Veeru400
f1 (ppm)

References:

Didier, D.; Delaye, P.-O.; Simaan, M.; Island, B.; Eppe, G.; Eijsberg, H.; Kleiner, A.; Knochel, P.; Marek, I. Modulable and Highly Diastereoselective Carbometalation of Cyclopropenes. *Chem. - Eur. J.* **2014**, *20*, 1038− 1048. b) Fa-Guang Zhang, Guillaume Eppe and Ilan Marek., Brook Rearrangement as a Trigger for Ring-Opening strained Carbocycles *Angew. Chem. Int. Ed.* **2016**, *55*, 714-718.

[2]Singh, S., Bruffaerts, J., Vasseur, A. *et al.* A unique Pd-catalysed Heck arylation as a remote trigger for cyclopropane selective ring-opening. *Nat. Commun.* **2017**, *8,* 14200.