Electronic Supplementary Information

Allylations of Aryl/Heteroaryl Ketones: Neat, Clean, and Sustainable. Applications to Targets in the Pharma- and Nutraceutical Industries

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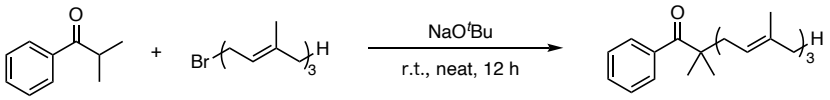
1 General information

Reagents and chemicals were purchased from Sigma-Aldrich, Combi-Blocks, Alfa Aesar, or Acros Organics and used without further purification. NaO^{t}Bu was purchased from Sigma-Aldrich. Heptaprenyl alcohol and 4a-methyl-1,4,4a,9a-tetrahydro-1,4-methanoanthracene-9,10-dione (**32**) was obtained from Anthem Biosciences and used as received. Solanesol and 2,3-dimethoxy-5-methyl-1,4-benzoquinone was purchased from Combi-Blocks (catalog No. QA-3041, QB-8707). Deuterated solvents were purchased from Cambridge Isotope Laboratories. Thin-layer chromatography (TLC) was performed using Silica Gel 60 F254 plates (Merck, 0.25 mm thick). Flash chromatography was performed in an automated Biotage system using Silica Gel 60 (Silicycle, 40-63 nm). ^{1}H and ^{13}C NMR spectra were recorded on either a Bruker Avance III HD 400 MHz (400 MHz for ^{1}H, 100 MHz for ^{13}C), a Bruker Avance NEO 500 MHz (500 MHz for ^{1}H, 125 MHz for ^{13}C) or on a Varian Unity Inova 500 MHz (500 MHz for ^{1}H, 125 MHz for ^{13}C); $CDCl_3$ were used as solvents. Residual peaks for $CHCl_3$ in $CDCl_3$ (^{1}H = 7.26 ppm, ^{13}C = 77.20 ppm) have been assigned. The chemical shifts are reported in part per million (ppm), the coupling constants *J* values are given in Hertz (Hz). The peak patterns are indicated as follows: bs, broad singlet; s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet. HRMS were recorded on a Waters Micromass LCT TOF ES+ Premier mass spectrometer using ESI ionization.

2 Experimental procedures

2.1 Optimization details

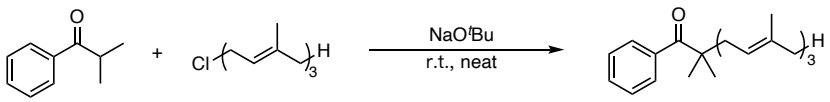
Screening conditions for neat reactions:



Bromide	NaO^{t}Bu	Other	NMR yield[a]
3 equiv	2.4 equiv	2 wt % TPGS-750-M [1 M]	N.R.
3 equiv	2.4 equiv	1 mol % [Pd(μ-Br)^{t}Bu$_3$P]$_2$[b]	N.R.
1.2 equiv	1.5 equiv	-	68% (30% SM)
1.5 equiv	1 equiv	-	70% (27% SM)
1.5 equiv	1.2 equiv	-	80% (15% SM)
1.5 equiv	1.5 equiv	-	99% (no SM)
1.2 equiv	1.5 equiv	10 mol % TBAI	65% (32% SM)
1.2 equiv	1.5 equiv	45 ºC	68% (22% SM)
1.2 equiv	2.4 equiv	45 ºC	83% (3% SM)
1.5 equiv	1.5 equiv	H_2O [0.2 M]	N.R.
1.5 equiv	1.5 equiv	20 min	98% (no SM)

[a]With $C_2H_2Cl_4$ as internal standard. [b]In 2 wt % TPGS-750-M [1 M]

Screening of conditions using an allylic chloride:

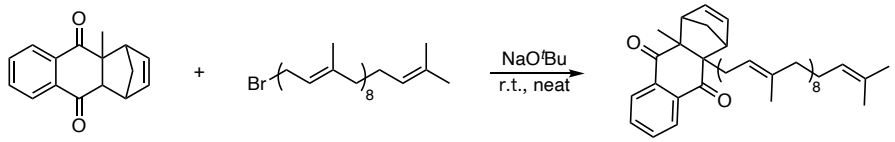


1 equiv 1.5 equiv

Additive	conversion[a]
None	93% (overnight)
10 mol % TBAI	93% (1 h), Full conv. (3 h)
10 mol % KI	84% (1 h), Full conv. (3 h)
5 mol % TBAI	Full conv. (2h)
5 mol % KI	85% (2 h), Full conv. (4 h)
5 mol % NaI	90% (2 h), Full conv. (4 h)
2 mol % KI	Full conv. (3 h)
2 mol % NaI	Full conv. (3 h)
0.5 mol % NaI	89% (3 h), Full conv. (5 h)

[a] By crude NMR

Screening of conditions using solanesyl bromide:

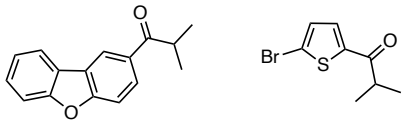


Bromide	NaO^{t}Bu	conversion[a]
1.5 eq	1.5 eq	70%
2 eq	2 eq	79%
1.5 eq	3 eq	34%
3 eq	1.5 eq	85%
3 eq	3 eq	100%

[a] By crude NMR

2.2 Substrate synthesis

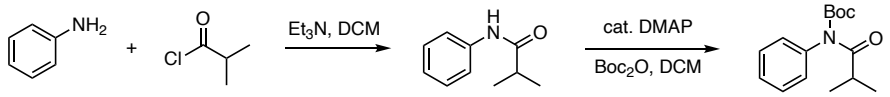
Ketone substrates S1 and S2 were synthesized by Friedel-Crafts acylation using literature procedures 1:



S1 **S2**

To a solution of anhydrous $AlCl_3$ (5.5 mmol, 1.1 equiv) in DCM (5 mL, 1 M), the acid chloride (5.5 mmol, 1.1 equiv) was added dropwise. The reaction mixture was stirred at rt for 10 min, followed by dropwise addition of a solution of arene (5 mmol, 1 equiv). The reaction was slowly heated to 50 ºC and stirred until completion (monitored by TLC, ~3 h). The reaction mixture was cooled to rt and quenched with water, extracted with DCM (3 x 10 mL). The combined organic layer was then washed with sat. $NaHCO_3$ aq (10 mL) and water (10 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel using a mixture of EtOAc and hexanes as elute giving ketones **S1** or **S2** in moderate yields (~70%).

*Amide substrate **S3** was prepared via a literature procedure[2,3]:*



S3

Isobutyryl chloride (5 mmol, 0.53 mL, 1 equiv) was slowly added to a stirred solution of aniline (6 mmol, 0.55 mL, 1.2 equiv) and triethylamine (6 mmol, 0.8 mL, 1.2 equiv) in DCM (0.5 M, 20 mL) at rt. The reaction was stirred at rt for 24 h and then quenched with 1 M HCl (10 mL), then washed with 1 M HCl (2 x10 mL), followed by sat. $NaHCO_3$ aq (2 x10 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure to afford *N*-phenylisobutyramide as an off-white solid in 90% yield.

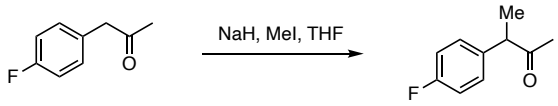
To an oven-dried 50 mL flask, *N*-phenylisobutyramide (3 mmol, 489.7 mg, 1 equiv), DMAP (0.3 mmol, 36.7 mg, 10 mol %) and DCM (15 mL, 0.2 M) was added. Boc_2O (3.9 mmol, 0.9 mL, 1.3 equiv) was added in one portion and the reaction mixture was allowed to stir at rt overnight. The reaction was quenched by adding sat. $NaHCO_3$ aq (10 mL), extracted with EtOAc (3 x 10 mL), and washed with brine (10 mL). The combined organic layer was dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography using a mixture of EtOAc and hexanes as elute give *N*-Boc-protected amide **S3** in 75% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 – 7.32 (m, 3H), 7.11 – 7.05 (m, 2H), 3.64 (heptd, J = 6.7, 1.9 Hz, 1H), 1.41 (d, J = 1.9 Hz, 9H), 1.25 (dd, J = 6.8, 1.9 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 180.48, 152.76, 139.43, 128.92, 128.12, 127.62, 83.00, 34.73, 27.83, 19.59.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{15}H_{21}NO_3$: 263.1521; found 263.1519.

*Preparation of ketone substrate **S4**.*[4]



S4

An oven-dried 100 mL round bottom flask was charged with 60% dispersion of NaH in mineral oil (5.5 mmol, 220 mg, 1.1 equiv), THF (10 mL, 0.5 M), 1-(4-fluorophenyl)propan-2-one (5 mmol, 0.69 mL, 1 equiv), and the resulting mixture was warmed to rt and stirred for 30 min. After 30 min, the mixture was cooled to 0 ºC and methyl iodide (0.5 mL, 8 mmol) was added dropwise. The reaction was stirred at 0 ºC for 1 h, then warmed to rt and stirred for

another 4 h. The reaction was quenched by adding sat. NH_4Cl aq (10 mL), and extracted with Et_2O (3 × 10 mL). The combined organic layer was then washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered, and concentrated. Purification by column chromatography using a mixture of EtOAc and hexanes as elute provide **S5** as a yellow oil in 88% yield.

2.3 General procedure for solvent-free α-allylation reactions

For liquid ketone substrates:

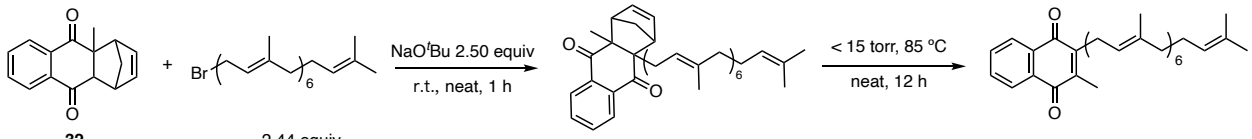
NaO^{t}Bu (0.6 mmol, 57.7 mg, 1.5 equiv) was added to a 1-dram vial in a glovebox. The vial was then capped and removed from the glovebox. Allyl bromide (0.6 mmol, 1.5 equiv) and the ketone (0.4 mmol, 1 equiv) were then added sequentially to the vial. The vial was then capped and stirred vigorously (~1000 RPM). The reaction was monitored by thin-layer chromatography until deemed complete. The reaction mixture was then applied directly to a silica gel column and purified via column chromatography.

For solid ketone substrates:

The ketone (0.4 mmol, 1 equiv) was added to a 1-dram vial, then the vial was placed in a glovebox and NaO^{t}Bu (0.6 mmol, 57.7 mg, 1.5 equiv) was added. The vial was then capped and removed from the glovebox. Allyl bromide (0.6 mmol, 1.5 equiv) was then added and the vial was capped and stirred vigorously (~1000 RPM). The reaction was monitored by thin-layer chromatography until deemed complete. The reaction mixture was then applied directly to a silica gel column and purified via column chromatography.

2.4 Procedures for gram scale syntheses of MK-7, MK-9, and CoQ_9

Gram synthesis of MK-7:

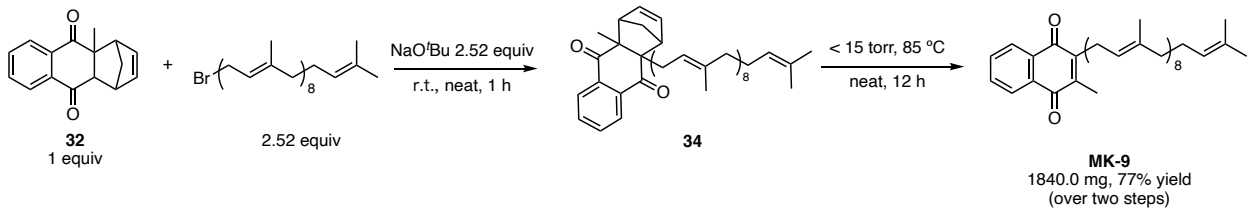


α-Allylation. To a 20 mL oven-dried scintillation vial was added freshly prepared heptaprenyl bromide (1.7 g, 3.05 mmol, 2.44 equiv) and a stir bar. 4a-Methyl-1,4,4a,9a-tetrahydro-1,4-methanoanthracene-9,10-dione (**32**, 297.5 mg, 1.25 mmol, 1.00 equiv) was then added and

allowed to disperse with gentle stirring. NaO^{t}Bu (300 mg, 3.125 mmol, 2.50 equiv) was removed from a glove box in a 1-dram vial and added in one addition to the stirring reaction mixture at rt resulting in a red reaction mixture. The vial was then sealed and stirred rapidly (900 RPM) at rt. After 1 h, the reaction was complete by TLC.

Retro Diels-Alder reaction. The entire reaction mixture was then placed under high vacuum (<15 torr pressure) and heated in a 20 mL scintillation aluminum heating block to 85 °C internal temperature neat with no stirring. The reaction was allowed to heat until constant mass was observed from loss of cyclopentadiene, as well as completion by TLC. The resulting golden oil was then purified by flash chromatography (4% Et_2O/hexanes) and dried under high vacuum resulting in a yellow solid (648.1 mg, 80% yield over two steps). R_f = 0.60 (1:9 Et_2O/hexanes).

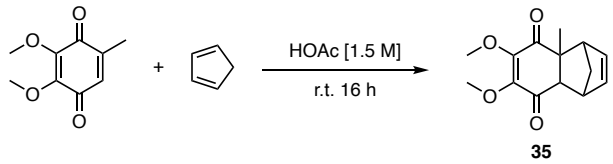
Gram synthesis of MK-9:



α-Allylation. To a 20 mL oven-dried scintillation vial was added freshly prepared solanesyl bromide (5.3 g, 7.65 mmol, 2.52 equiv) and a stir bar. 4a-Methyl-1,4,4a,9a-tetrahydro-1,4-methanoanthracene-9,10-dione (**32**, 722 mg, 3.03 mmol, 1.00 equiv) was then added and allowed to disperse with gentle stirring. NaO^{t}Bu (735 mg, 7.65 mmol, 2.52 equiv) was removed from a glove box in a 1-dram vial and added in one addition to the stirring reaction mixture at rt resulting in a red reaction mixture which warms slightly. The vial was then sealed and stirred rapidly (900 RPM) at rt. After 1 h, the reaction was deemed complete by TLC.

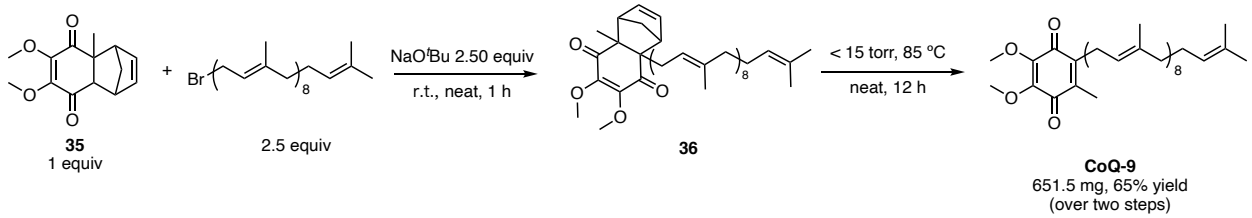
Retro Diels-Alder reaction. The entire reaction mixture was then placed under high vacuum (<15 torr pressure) and heated in a 20 mL scintillation vial aluminum heating block to 85 °C internal temperature neat with no stirring. The reaction was allowed to heat until constant mass was observed from loss of cyclopentadiene as well as completion by TLC. The resulting golden oil was then purified by flash chromatography (eluent: 4% Et_2O/96% hexanes) and dried under hi-vacuum resulting in a yellow solid (1840.0 mg, 77 % yield). R_f = 0.50 (1:9 Et_2O/hexanes).

Gram scale synthesis of CoQ_9:



Cyclopentadiene was freshly distilled from dicyclopentadiene.[5] The dimer was heated in an oven dried round bottom flask with a stir bar in a 180 °C oil bath. The resulting vapors were collected in a water cooled short-path distillation head at 38-40 °C, and the condensed liquid was maintained at below freezing temperature (sodium chloride / ice bath).

To a 50 mL round bottomed flask was added the quinone (CoQ_0; 5 g, 27.45 mmol, 1 equiv) and acetic acid (18 mL, 1.5 M). Freshly distilled cyclopentadiene (2.95 g, 3.8 mL, 1.62 equiv) was then added to the reaction mixture through a septum at rt. The reaction was then allowed to stir overnight at rt and was deemed complete by thin-layer chromatography. The pH of the reaction mixture was then adjusted to 9 (satd. bicarbonate solution, 150 mL) and extracted with diethyl ether (3 x 100 mL). The combined organics were treated with brine, dried over sodium sulfate, filtered, and dried under reduced pressure followed by high vacuum resulting in an opaque oil **35** that yellowed over time (5.39 g, 80% yield).

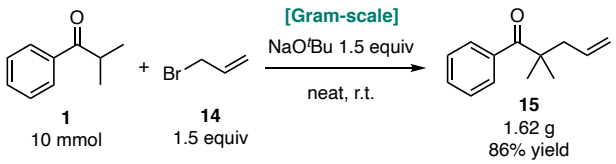


α-Allylation. To a 20 mL scintillation vial was added the Diels-Alder adduct **35** (310 mg, 1.25 mmol, 1 equiv) and freshly prepared solanesyl bromide (2.17 g, 3.125 mmol, 2.5 equiv) along with a stir bar and the slurry was combined at rt with gentle stirring. NaO^{t}Bu (300 mg, 3.125 mmol, 2.5 equiv) was then added in one portion and the stirring speed was increased to 900 RPM, resulting in a bright red slurry. The reaction was allowed to stir at rt for 1 h. The product mixture was then taken up into DCM, dried onto Celite, and purified via a 6-inch silica gel chromatographic column using two column volumes of hexanes, one of 10% Et_2O/hexanes, and four 20% Et_2O/hexanes, giving the product **36** as a yellowish oil (757.4 mg, 70%).

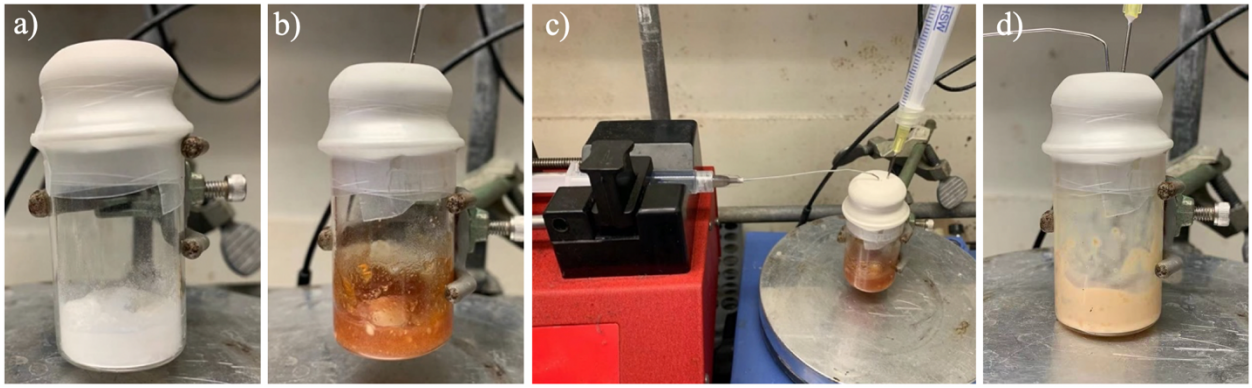
Retro Diels-Alder reaction. The oil **36** from the allylation reaction was dried into a 20 mL scintillation vial, which was then evacuated to <15 torr and heated in an 85 °C aluminum

block. After 16 h, the reaction had turned into a dark red oil and the reaction was complete by thin-layer chromatography. The oil was dried onto Celite and purified using 20% Et_2O/hexanes on a silica gel column. The combined organics were then dried to a red oil which solidified under high vacuum to give CoQ_9 (651.5 mg, 93% yield).

2.5 Larger scale reaction

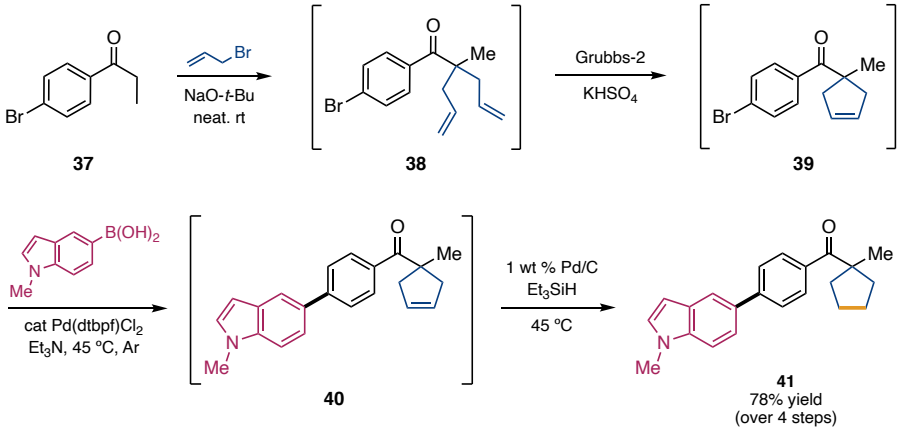


NaO^{t}Bu (1.5 equiv, 15 mmol, 1.442 g) was added to a 20 mL vial in a glovebox. The vial was then capped and removed from the glovebox. Allyl bromide **14** (1.5 equiv, 15 mmol, 1.3 mL) was then added to this vial in one potion. Isobutyrophenone **1** (1 equiv, 10 mmol, 1.5 mL) was then added dropwise to the vial over 15 min via a syringe pump (adding rate 0.1 mL/min). The vial was stirred vigorously (~1000 RPM) during the whole process. After addition, the reaction mixture was allowed to stir for another 30 min. The reaction mixture was then passed through a silica gel pad (eluted with EtOAc) and concentrated under reduced pressure to afford 2,2-dimethyl-1-phenylpent-4-en-1-one (**15**) as a light-yellow oil. (1.62 g, 86% yield).



a) Adding NaO^{t}Bu. b) Adding the allylic bromide in one portion. c) Adding isobutyrophenone dropwise via syringe pump. d) After adding isobutyrophenone and stirring for 30 min.

2.6 1-Pot sequence



Step 1: α-allylation.

1-(4-Bromophenyl)propan-1-one **37** (1 equiv, 0.4 mmol, 85.2 mg) was added to a 1-dram vial, after which the vial was moved to a glovebox and NaO^{t}Bu (1.5 equiv, 1.0 mmol, 96.2 mg) was added. The vial was then capped and removed from the glovebox. Allyl bromide (2.0 equiv, 0.8 mmol, 69.1 µL) was then added and the vial was capped and stirred vigorously (~1000 RPM). The reaction was monitored by thin-layer chromatography until complete.

Step 2: ring-closing metathesis.

To the reaction mixture was added Grubbs 2nd catalyst generation (2 mol %, 0.008 mmol, 6.8 mg) and $KHSO_4$ (0.6 equiv, 0.24 mmol, 32.7 mg). The vial was capped with a rubber septum and then evacuated and backfilled with argon three times. Next, 2 wt % TPGS-750-M solution in water (0.5 M, 0.8 mL) was added via syringe though the septum, then stirred vigorously at rt in an aluminum block placed over an IKA hot plate overnight.

Step 3: Suzuki-Miyaura coupling.

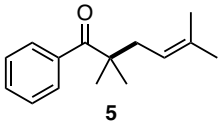
$Pd(dtbpf)Cl_2$ (1 mol %, 0.004 mmol, 2.7 mg) and (1-methyl-1*H*-indol-5-yl)boronic acid (1.5 equiv, 0.60 mmol, 105 mg) were added sequentially to the vial. The vial was then sealed with a fresh rubber septum, and the headspace was purged using argon and a vent needle for 5 min. Next, Et_3N (3 equiv, 1.2 mmol, 0.17 mL) was added via syringe though the septum. The vial was then stirred vigorously at 45 ºC in an aluminum block placed over IKA hot plate for 4 h.

Step 4: olefin hydrogenation.

Pd/C (1 wt % from the supplier; 2000 ppm, 8.5 mg) was added to the reaction mixture. The vial was capped with a rubber septum and Et_3SiH (1.5 equiv, 0.6 mmol, 96 µL) was then added via microsyringe. The vial was stirred vigorously at 45 ºC in an aluminum block placed

over IKA hot plate overnight. Upon completion, the mixture was diluted with EtOAc and then combined directly with silica gel. The volatiles were evaporated under reduced pressure and semi-pure product was purified by flash chromatography over silica gel using 5% EtOAc in hexanes to afford **25** as a light-yellow solid (97.8 mg, 78% overall yield).

2.7 E Factor calculation



5

Mass of product: 86.2 mg (0.4 mmol scale)

Mass of waste: (consider excess reagents)

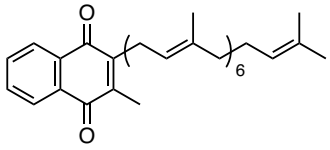
0.5 equiv 3,3-dimethylallylbromide + 0.5 equiv NaOtBu

= 0.4 mmol * 0.5* 149.0 g/mol + 0.4 mmol * 0.5 * 96.1 g/mol

= 29.8 mg + 19.22 mg

= 49.02 mg

E Factor = mass of waste / mass of product = 49.02 mg / 86.2 mg = **0.57**



MK-7

Mass of product: 648.1 mg (1.25 mmol scale)

Mass of waste: (consider excess reagents)

1.44 equiv heptaprenyl bromide + 1.5 equiv NaOtBu + 1 equiv cyclopentadiene

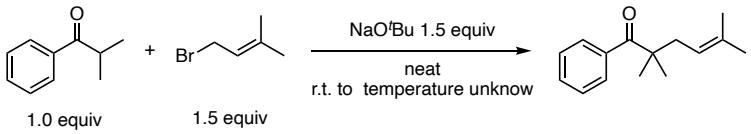
= 1.44 * 1.25 mmol * 696.7 g/mol + 1.25 mmol * 1.5 * 96.1 g/mol + 1.25 mmol * 66.1 g/mol

= 1003 mg + 180 mg + 80.6 mg

= 1265.6 mg

E Factor = mass of waste / mass of ptoduct = 1265.6 mg / 648.1 mg =**1.95**

2.8 Calorimetry data



Procedure: Mixing cell was prepared as follows: 51.5 mg sodium *t*-butoxide (Aldrich, 359270, white solid) in the main tube and 133 mg brownish solution (53 mg isobutyrophenone in 80 mg 3,3-dimethylallylbromide mixed at rt) in the breakable tube, prepared under argon, after equilibration at 30 °C (in the urnace) with mixing.

Prefix of Enthalpy: **-: Exothermic** **+: Endothermic**

SETARAM isotherm setup:

	Atm	Temperature	Duration	Vessel
1.	Argon	30 °C	5 hr	Steel tube glass mixing cell

SETARAM isotherm results:

	Exo. Reaction	Enthalpy	Remarks
1.	Yes	-525 kJ/kg	-

Comment:
A significant exothermal signal (about -525 kJ/kg) is observed after the addition of alpha-Methylpropiophenon / Isobutyrophenon in 3,3 Dimethylallylbromid to NaOtBu.
The measured energy corresponds to an adiabatic temperature increase of about 329°C [estimated heat capacity of the investigated samples: Cp = 1.6 kJ/(kg.K)].

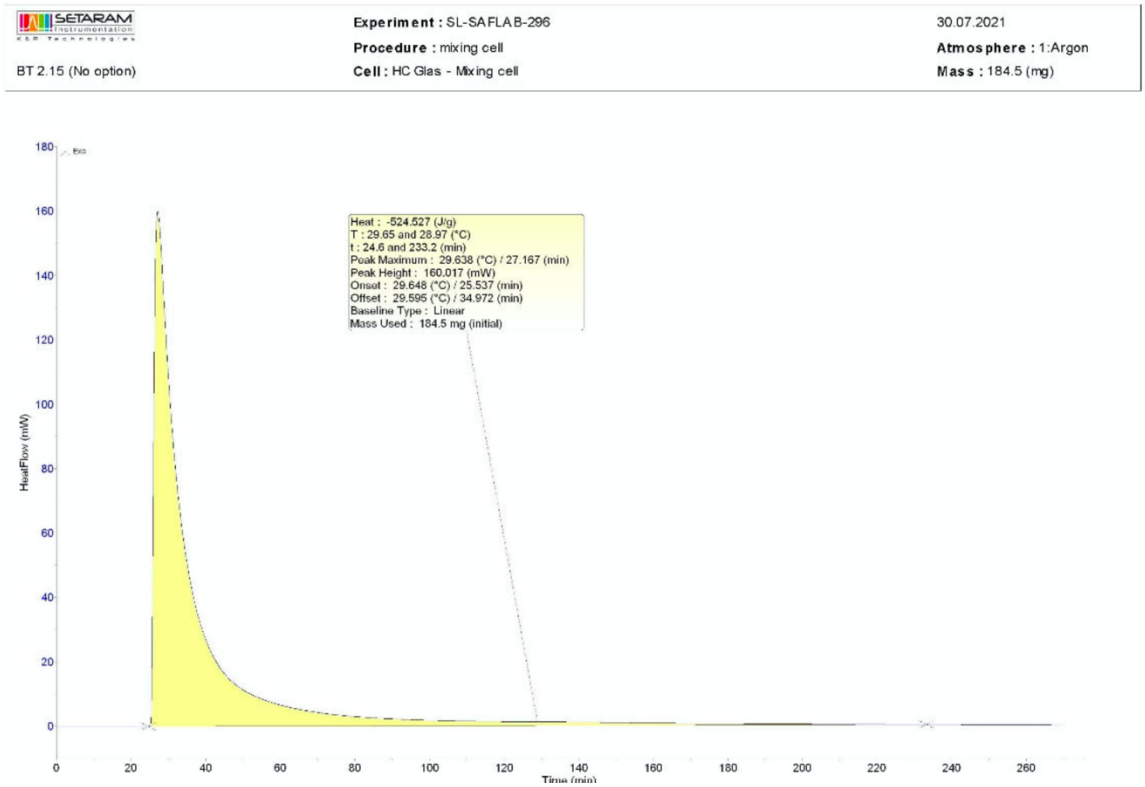


Figure S1 Heatflow *vs.* reaction progress

Prefix of Enthalpy: **-: Exothermic** **+: Endothermic**

SETARAM dynamic setup:

	Atm	Range	Heating Rate	Vessel
2.	Argon	30 °C to 150 °C	6 K/h (0.1 K/min)	Steel tube glass mixing cell
3.	Argon	30 °C to 150 °C	6 K/h (0.1 K/min)	Steel tube glass mixing cell

SETARAM dynamic results:

	Exo. Reaction	Spont. Reac.	Enthalpy	Remarks
1.	Above ca. 40°C	No	-3 kJ/kg	-
2.	Above ca. 70°C	No	-2 kJ/kg	-

Comment:
The dynamic SETARAM thermostability test of the reaction mixture after the isothermal addition shows the onset of a first very weak exothermal reaction starting above ca. 40 °C (approx. -3 kJ/kg) and of a second one starting above ca. 70°C (approx. -2 kJ/kg).

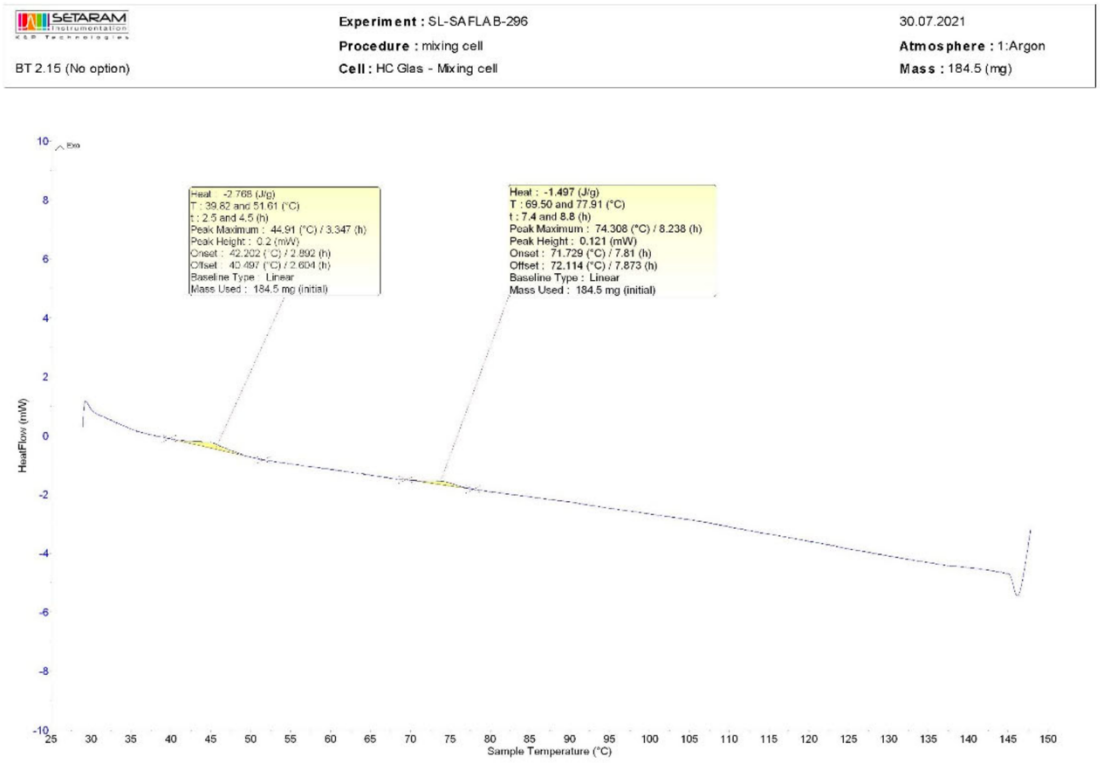
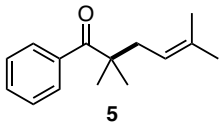


Figure S2 Differential scanning calorimetry (DSC) of reaction mixture

3 Analytical data

HRMS for compound **MK-7**[6], **MK-9**[6] are reported. All other compounds were characterized by ^{1}H and ^{13}C NMR, and HRMS.



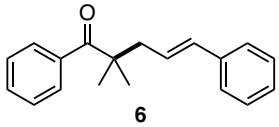
5

Colorless oil, flash chromatography using 2% EtOAc/hexanes; 86.2 mg; 99% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (dq, *J* = 6.9, 1.5 Hz, 2H), 7.48 – 7.44 (m, 1H), 7.41 (ddd, *J* = 8.5, 6.6, 1.5 Hz, 2H), 5.08 (ddq, *J* = 8.9, 6.0, 1.4 Hz, 1H), 2.45 (d, *J* = 7.4 Hz, 2H), 1.70 (t, *J* = 1.5 Hz, 3H), 1.57 (s, 3H), 1.32 (d, *J* = 1.5 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 209.42, 139.36, 134.32, 130.62, 128.03, 127.55, 119.77, 48.38, 38.99, 25.97, 25.77, 17.94.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{15}H_{20}O$: 216.1514; found 216.1513.



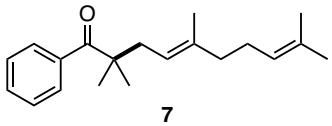
6

Colorless oil, flash chromatography using 2% EtOAc/hexanes; 100.2 mg; 95% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 – 7.66 (m, 2H), 7.53 – 7.47 (m, 1H), 7.46 – 7.42 (m, 2H), 7.32 (dd, *J* = 7.2, 1.4 Hz, 4H), 7.23 (ddt, *J* = 6.6, 5.2, 1.9 Hz, 1H), 6.38 (dt, *J* = 15.9, 1.4 Hz, 1H), 6.17 (dt, *J* = 15.7, 7.5 Hz, 1H), 2.67 (dd, *J* = 7.5, 1.4 Hz, 2H), 1.42 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 208.88, 139.17, 137.39, 133.29, 130.85, 128.51, 128.15, 127.65, 127.20, 126.15, 125.90, 48.17, 44.18, 25.94.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{19}H_{20}O$: 264.1514; found 264.1508.



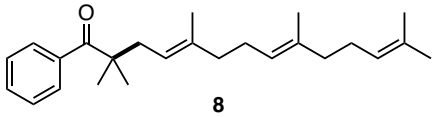
7

Colorless oil, flash chromatography using 3% EtOAc/hexanes; 105.7 mg; 93% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 – 7.61 (m, 2H), 7.49 – 7.44 (m, 1H), 7.44 – 7.38 (m, 2H), 5.14 – 5.03 (m, 2H), 2.46 (d, *J* = 7.4 Hz, 2H), 2.07 – 1.98 (m, 4H), 1.68 (d, *J* = 1.4 Hz, 3H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.56 (d, *J* = 1.3 Hz, 3H), 1.33 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 209.52, 139.42, 137.88, 131.41, 130.58, 128.04, 128.02, 127.53, 124.22, 119.80, 48.40, 39.95, 38.79, 26.56, 25.71, 17.70, 16.22.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{20}H_{28}O$: 284.2140; found 284.2151.



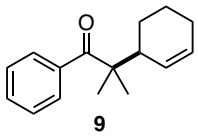
8

Colorless oil, flash chromatography using 3% EtOAc/hexanes; 138.2 mg; 98% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.5 Hz, 2H), 7.49 – 7.35 (m, 3H), 5.08 (t, *J* = 7.7 Hz, 3H), 2.43 (d, *J* = 7.4 Hz, 2H), 2.00 (dq, *J* = 21.5, 8.0 Hz, 8H), 1.68 – 1.52 (m, 12H), 1.30 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.52, 139.41, 137.99, 137.89, 135.21, 135.08, 131.53, 131.28, 130.58, 128.02, 127.56, 127.53, 124.88, 124.40, 124.36, 124.04, 119.81, 119.72, 48.39, 40.25, 39.96, 39.73, 38.77, 32.00, 26.76, 26.61, 26.55, 26.35, 25.74, 25.71, 23.39, 17.69, 17.64, 16.27, 16.21, 16.03.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{25}H_{36}O$: 352.2766; found 352.2749.



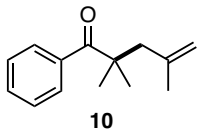
9

Colorless oil, flash chromatography using 3% EtOAc/hexanes; 85.8 mg; 94% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 – 7.59 (m, 2H), 7.49 – 7.32 (m, 3H), 5.80 – 5.72 (m, 1H), 5.50 (dt, *J* = 10.3, 1.9 Hz, 1H), 2.87 (ddt, *J* = 11.3, 6.0, 2.8 Hz, 1H), 1.95 (ddt, *J* = 9.8, 5.3, 1.4 Hz, 2H), 1.77 (dt, *J* = 12.1, 3.6 Hz, 1H), 1.67 (ddt, *J* = 9.6, 5.2, 2.3 Hz, 1H), 1.53 – 1.43 (m, 1H), 1.36 – 1.25 (m, 4H), 1.22 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 209.58, 139.49, 130.66, 129.30, 128.09, 127.60, 127.59, 50.78, 42.39, 25.13, 24.30, 22.66, 22.48, 22.45.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{16}H_{20}$: 228.1514; found 228.1517.



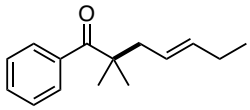
10

Colorless oil, flash chromatography using 2% EtOAc/hexanes; 80.9 mg; quantitative yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.63 (m, 2H), 7.49 – 7.33 (m, 3H), 4.83 – 4.79 (m, 1H), 4.65 (dd, *J* = 2.2, 1.1 Hz, 1H), 2.56 (d, *J* = 1.1 Hz, 2H), 1.64 (t, *J* = 1.1 Hz, 3H), 1.33 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 209.00, 142.44, 139.04, 130.85, 128.07, 127.90, 114.56, 48.39, 47.56, 26.79, 24.39.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{14}H_{18}O$: 202.1358; found 202.1353.



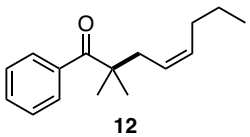
11

Colorless oil, flash chromatography using 3% EtOAc/hexanes; 86.5 mg; quantitative yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 – 7.58 (m, 2H), 7.49 – 7.33 (m, 3H), 5.42 (dtt, *J* = 14.8, 6.1, 1.1 Hz, 1H), 5.30 (dtt, *J* = 15.3, 7.2, 1.3 Hz, 1H), 2.41 (dd, *J* = 7.2, 1.1 Hz, 2H), 2.02 – 1.89 (m, 2H), 1.30 (s, 6H), 0.92 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 209.14, 139.32, 136.04, 130.68, 128.03, 127.61, 124.09, 47.95, 43.72, 25.77, 25.67, 13.85.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{15}H_{20}O$: 216.1514; found 216.1509.



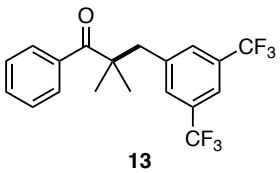
12

Colorless oil, flash chromatography using 3% EtOAc/hexanes; 92.1 mg; quantitative yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.57 (m, 2H), 7.48 – 7.33 (m, 3H), 5.52 – 5.41 (m, 1H), 5.30 (dddt, *J* = 10.9, 9.2, 7.5, 1.7 Hz, 1H), 2.52 – 2.45 (m, 2H), 1.95 (qd, *J* = 7.3, 1.6 Hz, 2H), 1.32 (s, 8H), 0.87 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 209.11, 139.14, 132.74, 130.72, 128.06, 127.61, 124.69, 48.00, 38.03, 29.45, 25.78, 22.69, 13.83.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{16}H_{22}O$: 230.1671; found 230.1681.



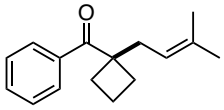
13

Colorless oil, flash chromatography using 3% EtOAc/hexanes; 149.6 mg; quantitative yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.59 – 7.52 (m, 4H), 7.51 – 7.45 (m, 1H), 7.41 (dd, *J* = 8.2, 6.7 Hz, 2H), 3.19 (s, 2H), 1.36 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 208.12, 140.59, 138.82, 131.61, 131.35, 131.20, 131.09, 130.82, 130.58, 130.55, 128.32, 127.47, 126.58, 124.41, 122.24, 120.56, 120.53, 120.50, 120.47, 120.44, 120.07, 48.71, 45.64, 26.09.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{19}H_{16}F_6O$: 374.1105; found 274.1194.



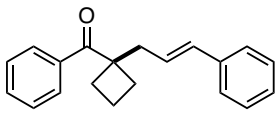
16

Colorless oil, flash chromatography using 3% EtOAc/hexanes; 86.7 mg; 95% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 2H), 7.55 – 7.49 (m, 1H), 7.46 – 7.40 (m, 2H), 5.01 (ddq, *J* = 8.8, 5.8, 1.4 Hz, 1H), 2.75 – 2.65 (m, 4H), 2.18 – 2.05 (m, 3H), 1.89 – 1.80 (m, 1H), 1.64 (d, *J* = 1.4 Hz, 3H), 1.41 (d, *J* = 1.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 204.50, 134.98, 134.40, 132.27, 129.03, 128.25, 118.97, 77.30, 77.05, 76.79, 53.20, 36.94, 30.37, 25.84, 17.73, 15.67.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{16}H_{20}O$: 228.1514; found 228.1525.



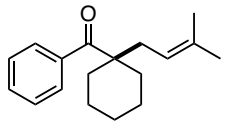
17

Light yellow oil, flash chromatography using 3% EtOAc/hexanes; 110.5 mg; quantitative yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 2H), 7.53 (td, *J* = 7.3, 1.5 Hz, 1H), 7.47 – 7.40 (m, 2H), 7.26 (dd, *J* = 4.2, 1.4 Hz, 4H), 7.19 (q, *J* = 4.0 Hz, 1H), 6.31 (dd, *J* = 15.7, 1.6 Hz, 1H), 6.04 (ddd, *J* = 15.8, 8.0, 6.6 Hz, 1H), 2.89 (d, *J* = 7.3 Hz, 2H), 2.77 – 2.66 (m, 2H), 2.22 (ddd, *J* = 12.6, 8.2, 3.4 Hz, 2H), 2.16 – 1.99 (m, 1H), 1.92 – 1.78 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 204.23, 137.21, 134.90, 133.02, 132.48, 129.11, 128.45, 128.39, 127.23, 126.20, 124.98, 52.92, 41.98, 30.35, 15.55.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{20}H_{20}O$: 276.1514; found 276.1523.



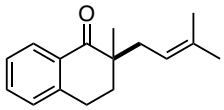
18

Colorless oil, flash chromatography using 3% EtOAc/hexanes; 102.5 mg; quantitative yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 – 7.59 (m, 2H), 7.49 – 7.36 (m, 3H), 5.10 (ddt, *J* = 8.8, 7.3, 1.5 Hz, 1H), 2.49 (d, *J* = 7.4 Hz, 2H), 2.24 – 2.17 (m, 2H), 1.70 (d, *J* = 1.4 Hz, 3H), 1.59 (s, 4H), 1.55 (tt, *J* = 11.2, 3.8 Hz, 3H), 1.44 (ddd, *J* = 13.5, 10.2, 3.5 Hz, 2H), 1.32 (tt, *J* = 7.7, 2.8 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 209.59, 140.32, 134.28, 130.37, 127.98, 127.23, 119.15, 52.96, 37.64, 34.38, 25.97, 23.04, 18.05.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{18}H_{24}O$: 256.1827; found 256.1828.



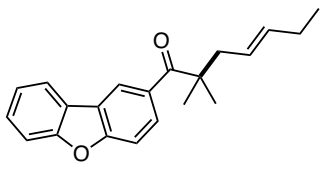
19

Light yellow oil, flash chromatography using 2% EtOAc/hexanes; 88.6 mg; 97% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.47 (td, *J* = 7.4, 1.5 Hz, 1H), 7.35 – 7.30 (m, 1H), 7.24 (d, *J* = 7.7 Hz, 1H), 5.15 (ddt, *J* = 8.4, 7.1, 1.4 Hz, 1H), 2.99 (td, *J* = 6.4, 5.9, 2.1 Hz, 2H), 2.37 (d, *J* = 7.3 Hz, 1H), 2.28 (dd, *J* = 14.4, 7.9 Hz, 1H), 2.10 (ddd, *J* = 13.2, 7.1, 5.8 Hz, 1H), 1.91 (ddd, *J* = 13.6, 6.9, 5.6 Hz, 1H), 1.73 (d, *J* = 1.6 Hz, 3H), 1.62 (d, *J* = 1.4 Hz, 3H), 1.19 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 202.58, 143.40, 134.44, 132.97, 131.74, 128.65, 127.99, 126.58, 119.42, 45.46, 34.97, 33.32, 26.07, 25.50, 21.93, 17.99.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{16}H_{20}O$: 228.1514; found 228.1522.



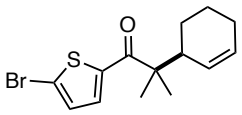
20

Light yellow oil, flash chromatography using 2% EtOAc/hexanes; 112.8 mg; 92% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 1.8 Hz, 1H), 7.98 (dt, *J* = 7.7, 1.1 Hz, 1H), 7.88 (dd, *J* = 8.6, 1.9 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.50 (ddd, *J* = 8.3, 7.2, 1.4 Hz, 1H), 7.38 (td, *J* = 7.5, 1.0 Hz, 1H), 5.47 – 5.40 (m, 1H), 5.39 – 5.31 (m, 1H), 2.51 (dd, *J* = 7.1, 1.2 Hz, 2H), 2.00 – 1.93 (m, 2H), 1.39 (s, 6H), 0.92 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.77, 157.45, 156.75, 136.11, 133.89, 127.78, 127.57, 124.15, 124.08, 123.91, 123.20, 121.23, 120.87, 111.90, 111.07, 48.03, 44.17, 26.21, 25.68, 13.87.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{21}H_{22}O_2$: 306.1620; found 306.1635.



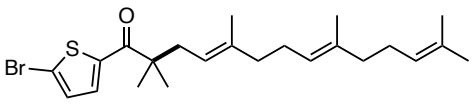
21

Light yellow oil, flash chromatography using 3% EtOAc/hexanes; 125.3 mg; quantitative yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 4.1 Hz, 1H), 7.06 (d, *J* = 4.0 Hz, 1H), 5.77 (ddd, *J* = 7.2, 5.3, 2.1 Hz, 1H), 5.49 (dt, *J* = 10.4, 1.9 Hz, 1H), 2.87 (ddt, *J* = 10.8, 5.4, 2.6 Hz, 1H), 1.99 – 1.92 (m, 2H), 1.76 (dt, *J* = 12.6, 3.8 Hz, 1H), 1.63 (ddt, *J* = 8.0, 4.7, 2.5 Hz, 1H), 1.47 (tdd, *J* = 13.3, 6.5, 4.3 Hz, 1H), 1.31 (s, 4H), 1.21 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 197.73, 144.48, 131.95, 130.81, 129.61, 126.87, 121.35, 50.38, 43.44, 25.04, 24.28, 22.96, 22.40, 21.62.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{14}H_{17}BrOS$: 312.0183; found 312.0172.



22

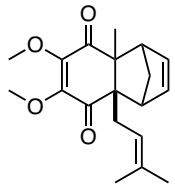
Light yellow oil, flash chromatography using 5% EtOAc/hexanes; 157.3 mg; 90% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 4.1 Hz, 1H), 7.08 (dd, *J* = 4.1, 0.9 Hz, 1H), 5.17 – 5.01 (m, 3H), 2.49 (d, *J* = 7.5 Hz, 2H), 2.03 (dddd, *J* = 29.7, 14.2, 8.0, 3.8 Hz, 8H), 1.71 – 1.57 (m, 12H), 1.34 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 197.55, 144.45, 138.35, 138.25, 135.24, 135.12, 131.96, 131.55, 131.28, 130.74, 124.79, 124.40, 124.36, 123.97, 121.20, 119.35, 119.27, 48.03, 40.20,

39.91, 39.72, 39.20, 32.00, 26.76, 26.61, 26.53, 26.32, 25.74, 25.72, 25.69, 25.61, 23.38, 17.70, 17.64, 16.30, 16.24, 16.03.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{23}H_{33}BrOS$: 436.1436; found 436.1422.



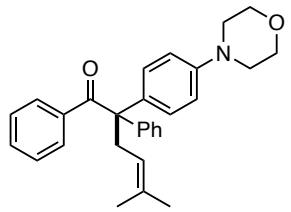
23

Bright yellow oil, flash chromatography using 8% EtOAc/hexanes; 116.3 mg; 92% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.08 – 5.95 (m, 2H), 5.06 (ddp, *J* = 7.7, 5.9, 1.3 Hz, 1H), 3.86 (d, *J* = 15.3 Hz, 6H), 3.10 – 2.94 (m, 2H), 2.76 – 2.66 (m, 1H), 2.43 – 2.32 (m, 1H), 1.79 – 1.73 (m, 1H), 1.64 (t, *J* = 1.4 Hz, 3H), 1.56 (d, *J* = 1.4 Hz, 3H), 1.47 (s, 3H), 1.45 – 1.39 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 198.85, 198.24, 150.79, 149.12, 137.96, 137.19, 134.45, 119.83, 60.30, 59.95, 59.28, 56.07, 54.41, 53.10, 43.44, 36.09, 26.03, 23.38, 17.91.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{19}H_{24}O_4$: 316.1674; found 316.1658.

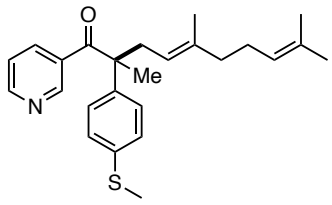


24

Dark yellow oil, flash chromatography using 10% EtOAc/hexanes; 125.8 mg; 74% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.45 (m, 2H), 7.35 – 7.16 (m, 10H), 7.01 – 6.80 (m, 2H), 4.89 (tt, *J* = 7.2, 1.6 Hz, 1H), 3.98 – 3.79 (m, 4H), 3.19 (t, *J* = 4.8 Hz, 4H), 3.10 (d, *J* = 7.1 Hz, 2H), 1.51 (d, *J* = 1.6 Hz, 3H), 1.12 (d, *J* = 1.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 202.21, 142.35, 138.27, 134.68, 131.20, 130.30, 129.54, 129.33, 127.96, 127.75, 126.64, 119.56, 115.25, 66.70, 64.10, 49.32, 38.76, 25.86, 17.53.



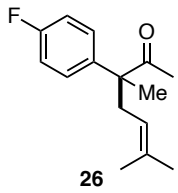
25

Light yellow oil, flash chromatography using 10% EtOAc/hexanes; 122.8 mg; 78% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.59 (m, 1H), 8.57 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.72 (dt, *J* = 8.1, 2.0 Hz, 1H), 7.26 – 7.15 (m, 5H), 5.01 (tq, *J* = 5.4, 1.5 Hz, 1H), 4.88 (ddq, *J* = 8.2, 6.8, 1.5 Hz, 1H), 2.79 (dd, *J* = 14.4, 8.2 Hz, 1H), 2.66 (dd, *J* = 14.6, 6.5 Hz, 1H), 2.48 (s, 3H), 2.02 – 1.88 (m, 4H), 1.67 (d, *J* = 1.4 Hz, 3H), 1.57 (d, *J* = 1.3 Hz, 3H), 1.53 (s, 3H), 1.37 (d, *J* = 1.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 202.13, 151.81, 150.60, 139.52, 138.86, 137.61, 136.79, 132.45, 131.44, 127.01, 126.87, 124.17, 123.01, 118.70, 54.91, 39.96, 37.53, 26.52, 25.73, 23.67, 17.70, 16.07, 15.62.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{25}H_{31}NOS$: 393.2126; found 393.2135.



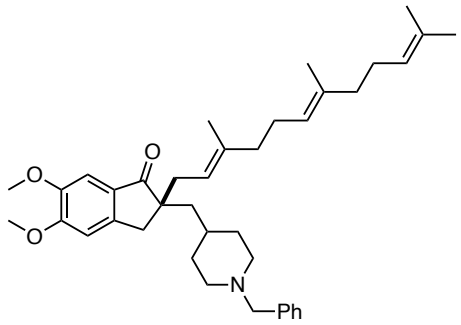
26

Colorless oil, flash chromatography using 3% EtOAc/hexanes; 92.8 mg; 99% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.16 (m, 2H), 7.03 (t, *J* = 8.7 Hz, 2H), 4.86 – 4.79 (m, 1H), 2.65 (dd, *J* = 14.7, 7.6 Hz, 1H), 2.54 (dd, *J* = 14.8, 7.0 Hz, 1H), 1.90 (s, 3H), 1.64 (d, *J* = 1.5 Hz, 3H), 1.54 (s, 3H), 1.42 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 210.61, 162.96, 134.75, 128.12, 128.04, 119.22, 115.58, 115.37, 55.64, 36.10, 25.95, 25.84, 21.56, 17.97.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{15}H_{19}FO$: 234.1420; found 234.2412.

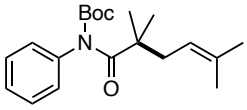


27

Yellow oil, flash chromatography using 5% MeOH/DCM; 205.5 mg; 88% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.07 (m, 6H), 6.86 – 6.75 (m, 1H), 5.11 – 4.62 (m, 3H), 3.94 (d, *J* = 2.9 Hz, 3H), 3.89 (d, *J* = 2.5 Hz, 3H), 3.40 (s, 2H), 2.89 (s, 2H), 2.79 – 2.66 (m, 2H), 2.26 (d, *J* = 7.3 Hz, 2H), 2.07 – 1.71 (m, 10H), 1.71 – 1.52 (m, 12H), 1.52 – 1.36 (m, 4H), 1.32 – 1.19 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 209.73, 155.45, 149.34, 148.36, 138.36, 138.16, 138.04, 135.04, 134.95, 131.47, 131.26, 129.74, 129.72, 129.21, 128.08, 126.87, 124.81, 124.35, 124.01, 119.37, 119.28, 109.73, 107.22, 104.32, 63.36, 56.13, 56.02, 53.74, 53.68, 53.21, 53.19, 43.79, 40.15, 39.88, 39.70, 36.96, 34.06, 33.53, 32.69, 31.89, 26.75, 26.64, 26.54, 26.36, 25.92, 25.74, 25.71, 23.37, 22.46, 17.70, 17.64, 16.36, 16.31, 15.89.



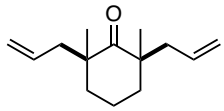
28

Colorless oil, flash chromatography using 5% EtOAc/hexanes; 120.6 mg; 91% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 8.4, 6.9 Hz, 2H), 7.29 – 7.23 (m, 1H), 7.19 – 7.08 (m, 2H), 5.10 (ddt, *J* = 9.0, 7.5, 1.6 Hz, 1H), 2.30 (d, *J* = 7.5 Hz, 2H), 1.68 (d, *J* = 1.6 Hz, 3H), 1.55 (d, *J* = 1.4 Hz, 3H), 1.45 (s, 9H), 1.22 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 184.53, 153.45, 138.89, 134.35, 128.90, 127.43, 127.19, 119.95, 82.37, 48.05, 40.04, 28.00, 26.01, 25.59, 17.96.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{20}H_{29}NO_3$: 331.2148; found 331.2148.



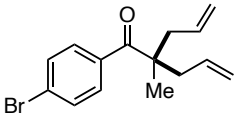
29

Mixture of *cis* and *trans* isomer. Colorless oil, flash chromatography using 5% EtOAc/hexanes. 79.1 mg, 96% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.74 – 5.53 (m, 2H), 5.10 – 4.95 (m, 4H), 2.46 – 2.28 (m, 2H), 2.22 – 2.05 (m, 2H), 1.85 – 1.62 (m, 4H), 1.59 – 1.52 (m, 2H), 1.08 (d, *J* = 16.2 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 219.44, 218.67, 134.60, 134.42, 117.99, 47.60, 47.56, 43.96, 43.93, 36.40, 35.92, 26.11, 25.06, 17.41, 17.37.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{14}H_{22}O$:206.1671; found 206.1681.



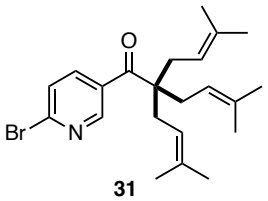
30

Colorless oil, flash chromatography using 2% EtOAc/hexanes; 111.4 mg; 95% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 1.3 Hz, 4H), 5.68 (ddt, *J* = 17.4, 10.2, 7.3 Hz, 2H), 5.08 – 4.96 (m, 4H), 2.64 – 2.54 (m, 2H), 2.41 – 2.32 (m, 2H), 1.27 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 206.83, 138.05, 133.42, 131.39, 129.24, 125.63, 118.67, 51.29, 43.17, 22.73.

HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{15}H_{17}BrO$: 292.0463; found 292.0468.



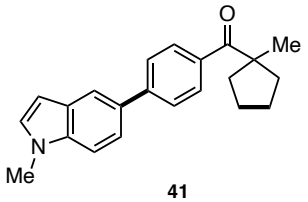
31

White solid, flash chromatography using 4% EtOAc/hexanes; 103.4 mg; 64% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (d, *J* = 2.5 Hz, 1H), 7.68 (dd, *J* = 8.2, 2.5 Hz, 1H), 7.52 (d, *J* = 8.2 Hz, 1H), 5.03 – 4.94 (m, 3H), 2.41 (d, *J* = 7.0 Hz, 6H), 1.67 (d, *J* = 1.8 Hz, 9H), 1.53 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 207.08, 148.60, 143.87, 137.33, 134.95, 134.92, 127.63, 118.68, 55.99, 33.05, 26.04, 17.99.

HRMS (ESI-TOF) *m/z*: $[M+H]^+$ calcd for $C_{22}H_{31}BrNO$: 404.1589; found 404.1590.



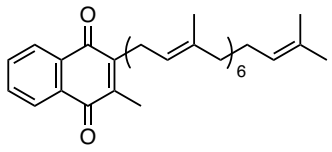
41

Light yellow solid, flash chromatography using 5% EtOAc/hexanes; 99 mg; 78% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.5 Hz, 2H), 7.89 (d, *J* = 1.7 Hz, 1H), 7.71 (d, *J* = 8.5 Hz, 2H), 7.51 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.10 (d, *J* = 3.1 Hz, 1H), 6.56 (dd, *J* = 3.1, 0.9 Hz, 1H), 3.84 (s, 3H), 2.51 – 2.25 (m, 2H), 1.72 (tdt, *J* = 10.4, 7.4, 5.0 Hz, 6H), 1.48 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 205.95, 145.92, 136.65, 134.08, 131.54, 129.79, 129.76, 129.01, 126.78, 121.24, 119.70, 109.64, 101.56, 54.77, 38.09, 32.99, 27.46, 25.40.

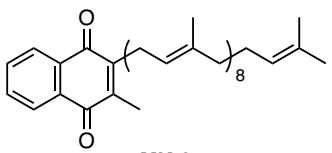
HRMS (ESI-TOF) *m/z*: $[M]^+$ calcd for $C_{22}H_{23}NO$: 317.1780; found 317.1783.



MK-7

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (ddt, *J* = 4.7, 3.1, 2.0 Hz, 2H), 7.68 (dd, *J* = 5.8, 3.3 Hz, 2H), 5.15 – 4.98 (m, 7H), 3.37 (d, *J* = 7.0 Hz, 2H), 2.19 (s, 3H), 2.11 – 1.89 (m, 24H), 1.79 (s, 3H), 1.68 (s, 3H), 1.59 (s, 12H), 1.56 (s, 6H).

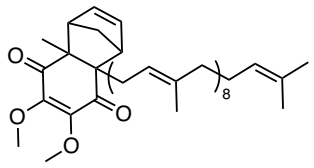
^{13}C NMR (101 MHz, $CDCl_3$): δ 185.4, 184.5, 146.1, 143.3, 137.5, 135.2, 134.9, 134.9, 134.9, 133.3, 133.3, 132.2, 132.1, 131.2, 126.3, 126.2, 124.4, 124.2, 124.1, 123.8, 119.0, 39.7, 39.7, 26.7, 26.7, 26.6, 26.5, 26.0, 25.7, 17.7, 16.4, 16.0, 16.0, 16.0, 12.7.



MK-9

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (ddt, *J* = 4.8, 3.2, 2.0 Hz, 2H), 7.73 – 7.63 (m, 2H), 5.17 – 4.98 (m, 9H), 3.37 (d, *J* = 6.9 Hz, 2H), 2.19 (s, 3H), 2.12 – 1.91 (m, 32H), 1.80 (d, *J* = 1.3 Hz, 3H), 1.68 (d, *J* = 1.4 Hz, 3H), 1.63 – 1.54 (m, 24H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 185.4, 184.5, 146.1, 143.3, 137.5, 135.2, 134.9, 134.9, 134.9, 133.3, 133.2, 132.2, 132.1, 131.2, 126.3, 126.2, 124.4, 124.3, 124.2, 124.2, 124.1, 123.8, 119.1, 39.7, 39.7, 39.7, 29.7, 26.7, 26.7, 26.7, 26.6, 26.5, 26.0, 25.7, 17.7, 16.4, 16.0, 16.0, 16.0, 12.7.

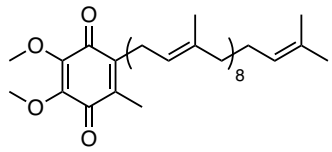


36

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.09 – 6.02 (m, 2H), 5.16 – 5.00 (m, 9H), 3.90 (s, 2H), 3.88 (s, 2H), 3.09 (q, *J* = 1.8, 1.3 Hz, 1H), 3.01 (q, *J* = 2.3, 1.8 Hz, 1H), 2.75 (dd, *J* = 15.2, 7.7 Hz, 1H), 2.47 – 2.37 (m, 1H), 2.05 (q, *J* = 6.7, 5.7 Hz, 16H), 2.01 – 1.91 (m, 18H), 1.81 – 1.71 (m, 2H), 1.68 (q, *J* = 1.4 Hz, 3H), 1.59 (dd, *J* = 9.3, 1.2 Hz, 26H), 1.51 – 1.44 (m, 4H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 198.84, 198.22, 150.82, 149.14, 138.05, 137.98, 137.19, 135.39, 135.03, 134.96, 134.94, 134.92, 134.90, 134.87, 131.22, 124.42, 124.28, 124.27, 124.26, 124.25, 124.23, 124.13, 123.76, 119.63, 60.27, 60.03, 59.33, 56.07, 54.46, 53.15, 43.47, 39.95, 39.75, 39.72, 36.06, 26.77, 26.73, 26.72, 26.69, 26.68, 26.53, 25.69, 23.38, 17.68, 16.39, 16.03, 16.00.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{59}H_{88}O_4Na$: 883.6590; found 883.6572.



CoQ-9

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.15 – 5.03 (m, 9H), 4.93 (tq, *J* = 7.1, 1.4 Hz, 1H), 3.99 (s, 3H), 3.97 (s, 3H), 3.18 (d, *J* = 7.1 Hz, 2H), 2.05 (q, *J* = 6.2, 4.8 Hz, 16H), 2.01 (s, 3H), 2.00 – 1.91 (m, 16H), 1.73 (d, *J* = 1.3 Hz, 3H), 1.67 (d, *J* = 1.4 Hz, 3H), 1.62 – 1.55 (m, 24H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 184.75, 183.90, 144.39, 144.25, 141.68, 138.85, 137.62, 135.24, 134.99, 134.94, 134.92, 134.91, 134.89, 134.87, 131.22, 124.42, 124.29, 124.28,

124.26, 124.25, 124.16, 123.86, 118.87, 61.12, 61.11, 39.75, 39.73, 39.71, 26.78, 26.72, 26.71, 26.70, 26.68, 26.63, 26.52, 25.69, 25.31, 17.67, 16.34, 16.04, 16.02, 16.00, 11.93.

HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd for $C_{54}H_{82}O_4Na$: 817.6111; found 817.6114.

4 References

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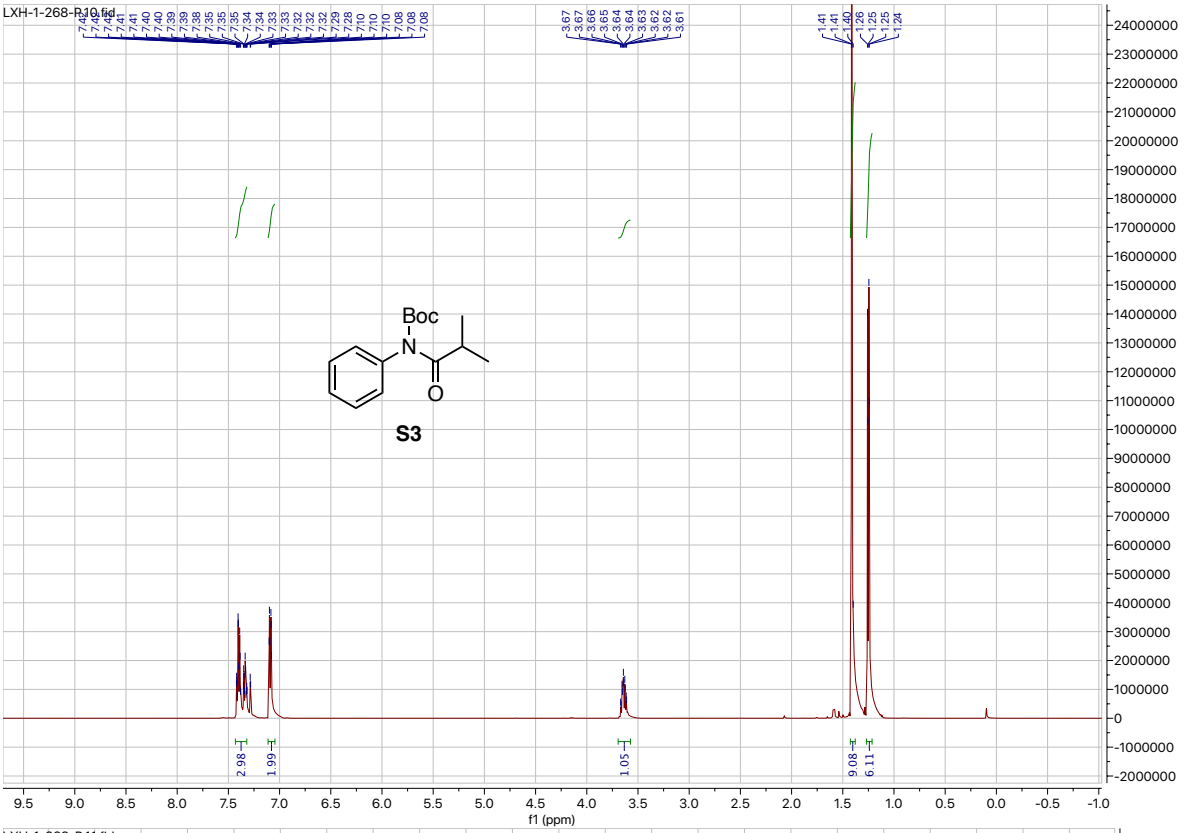
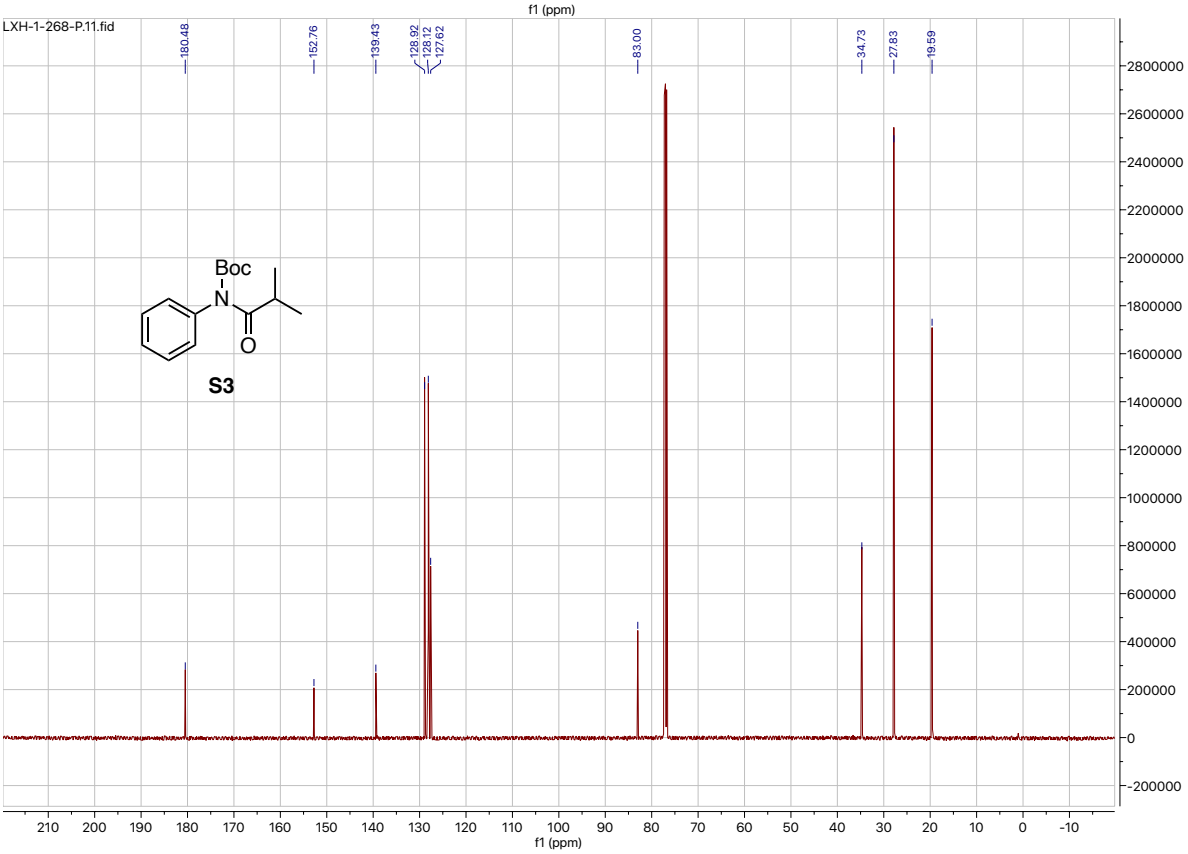
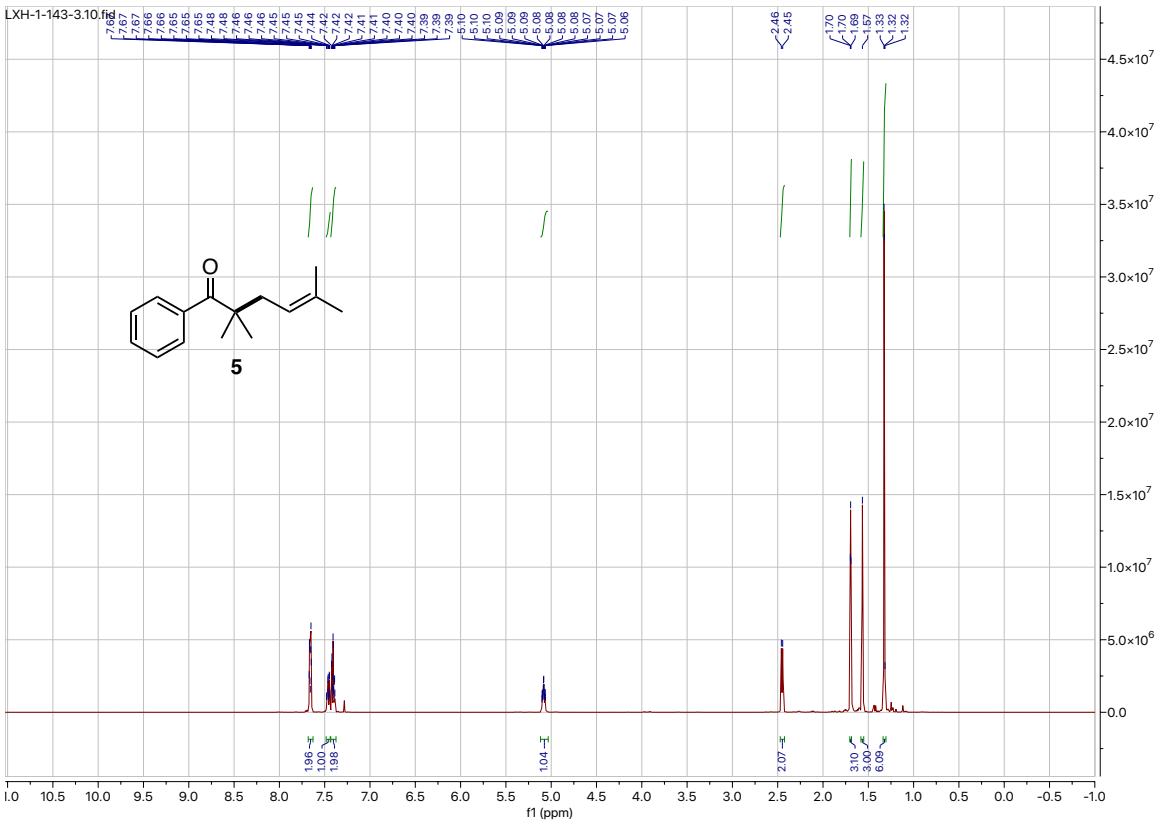
5 NMR Spectra



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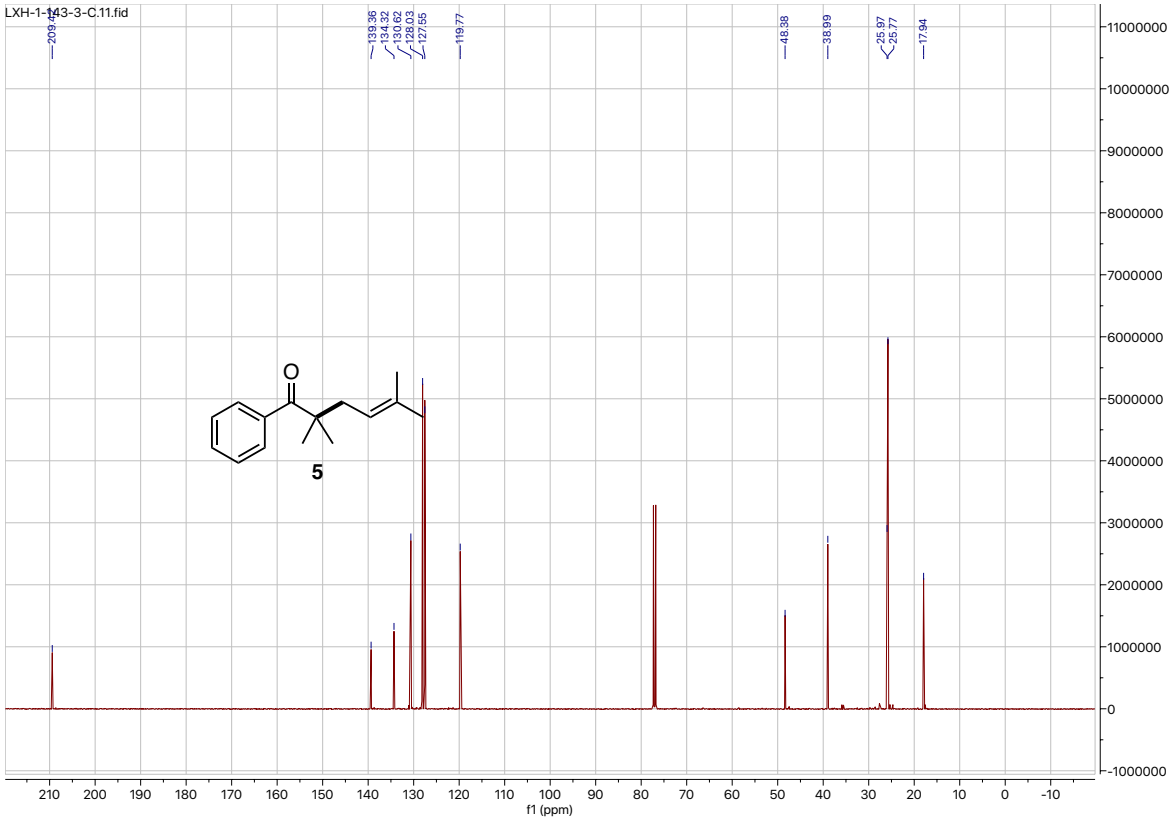
O
5
f1 (ppm)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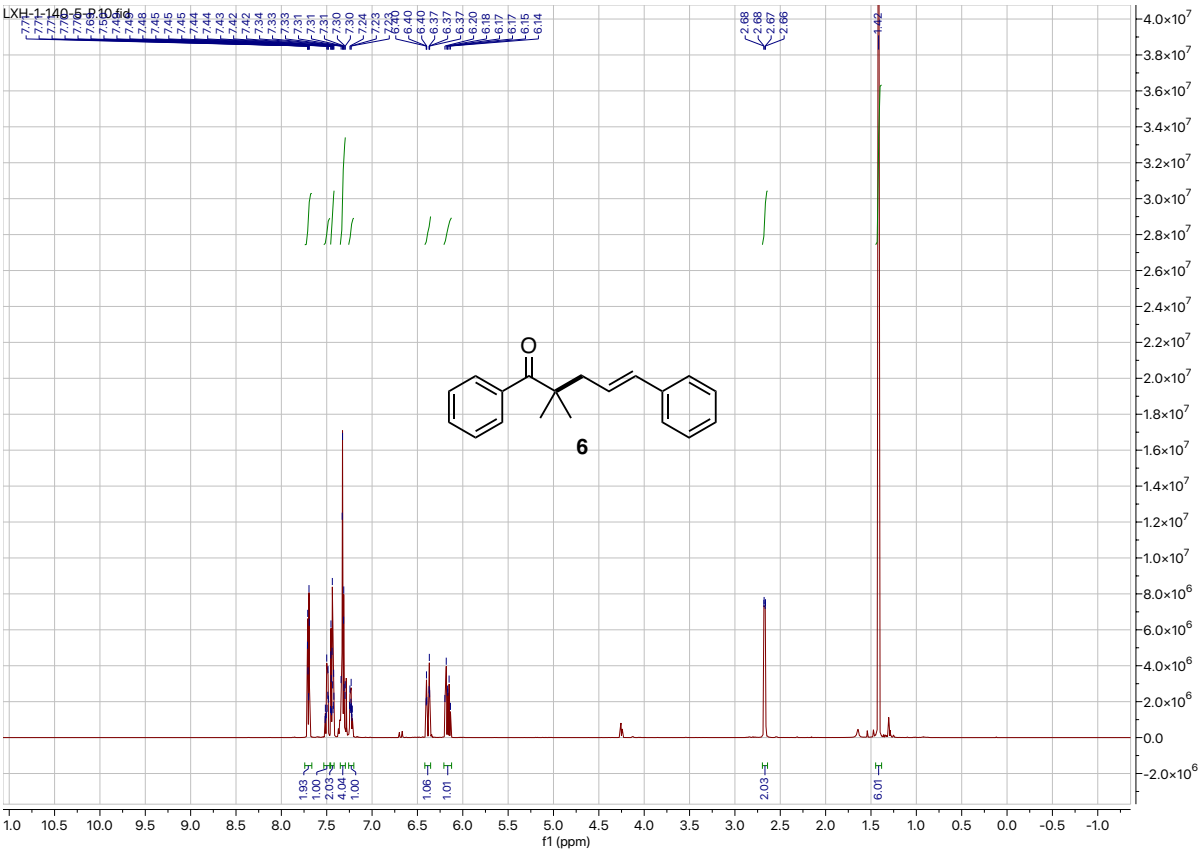
O
5
f1 (ppm)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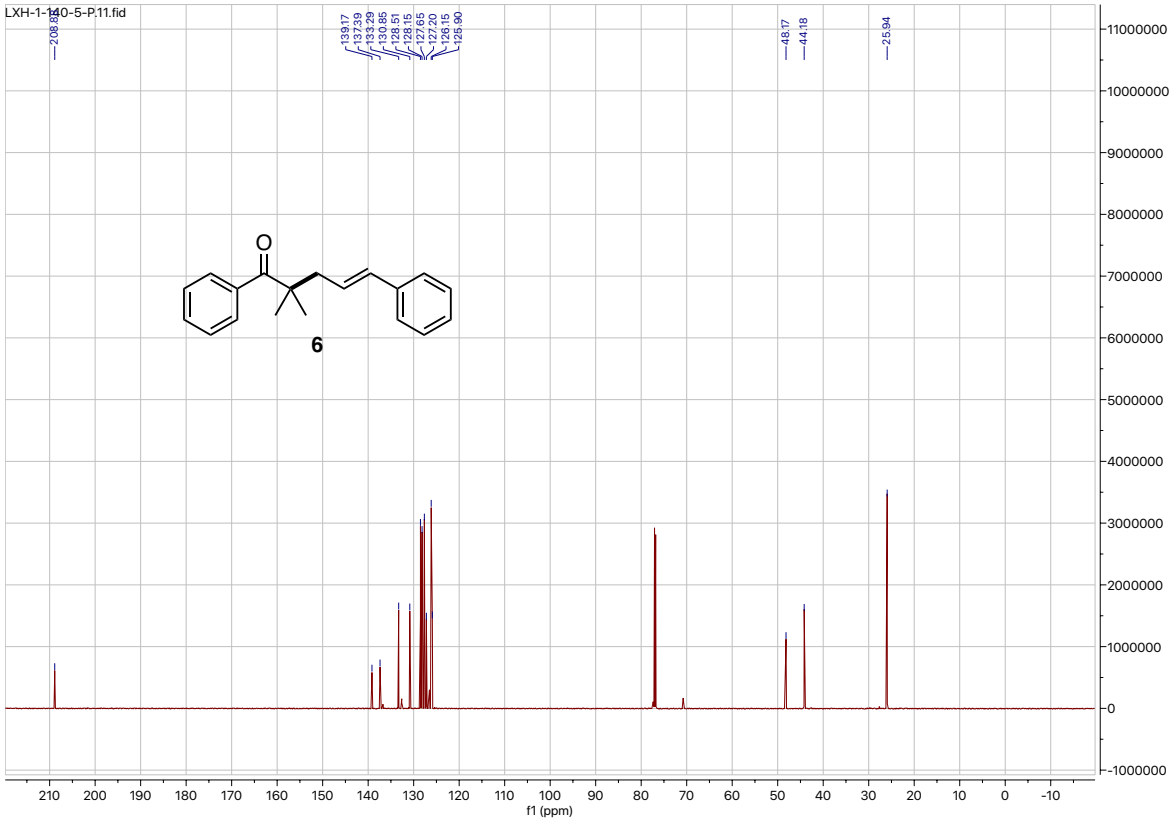
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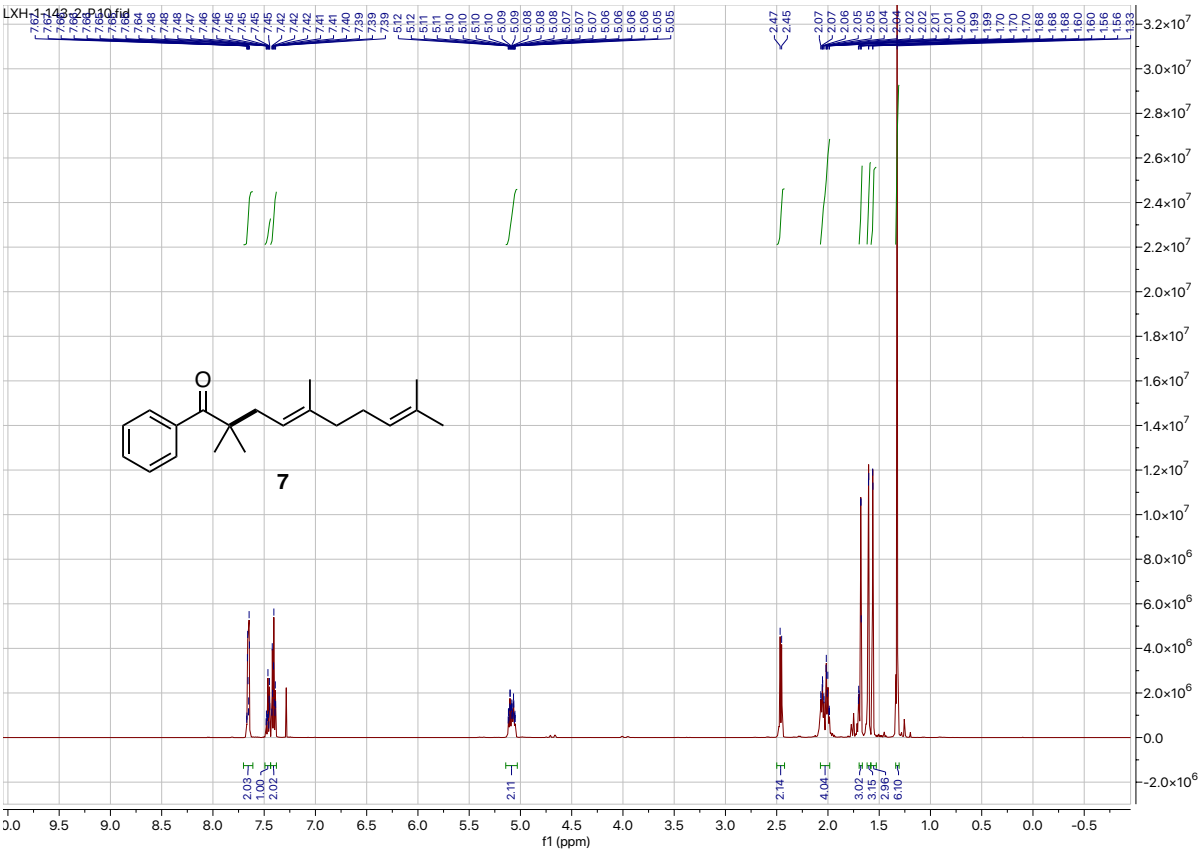
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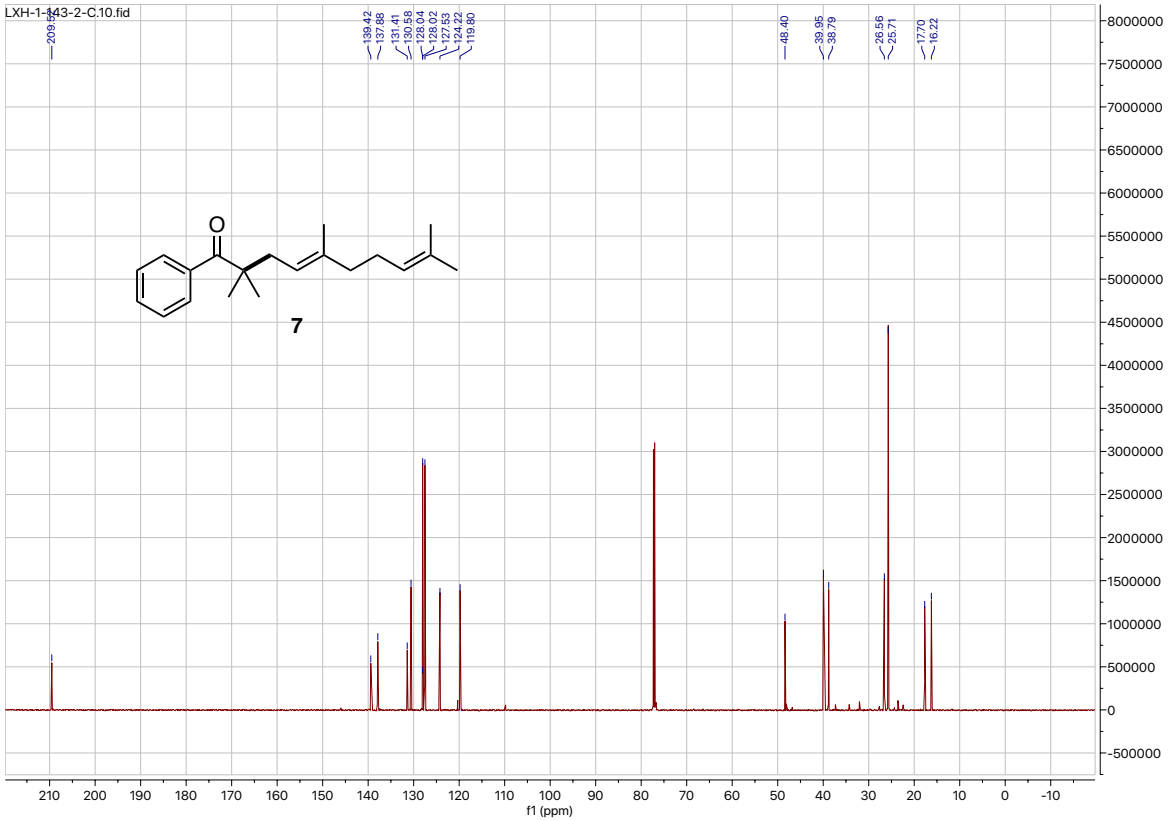
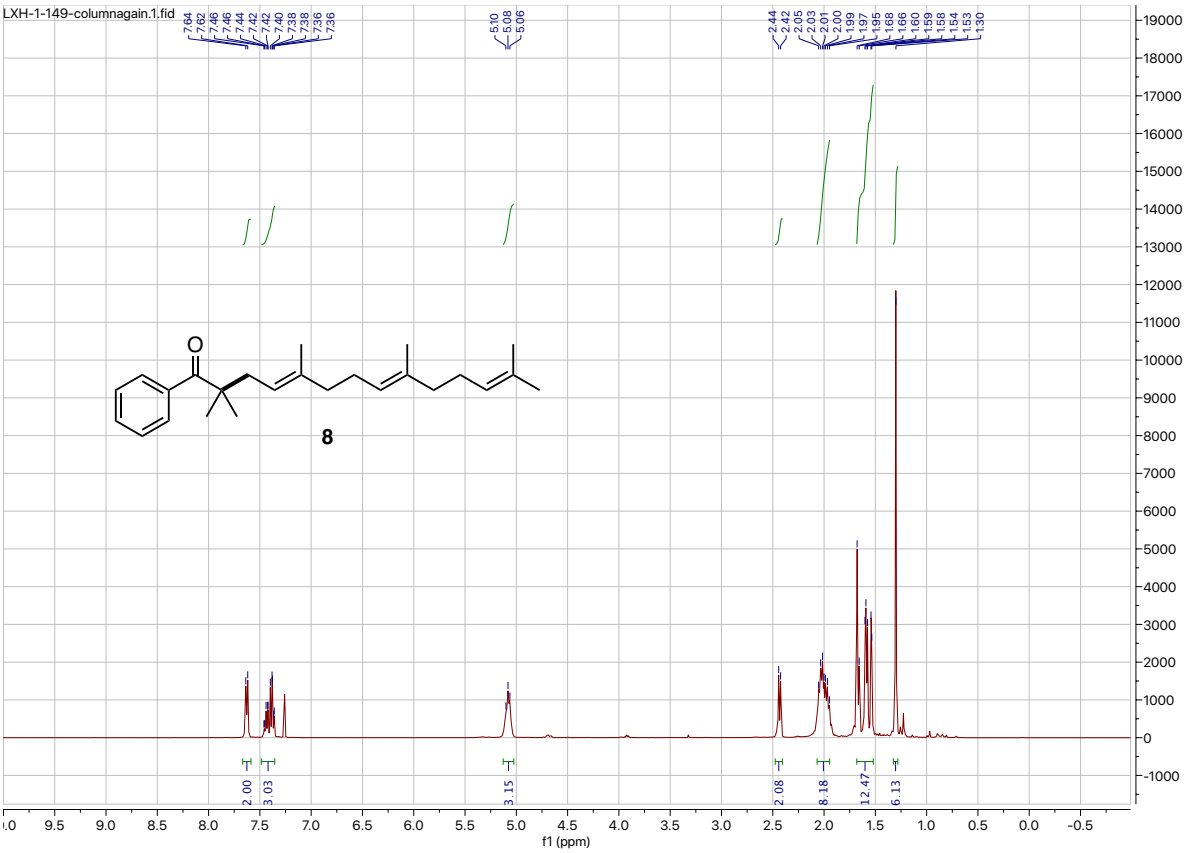
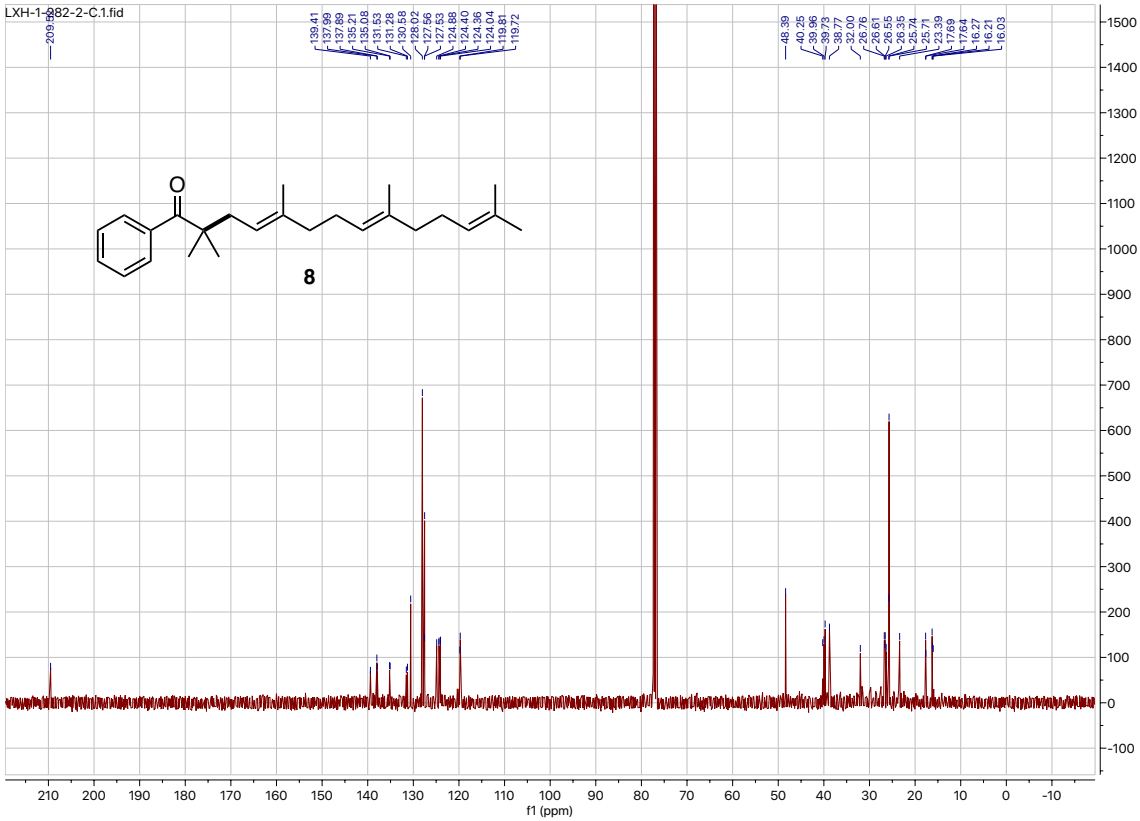
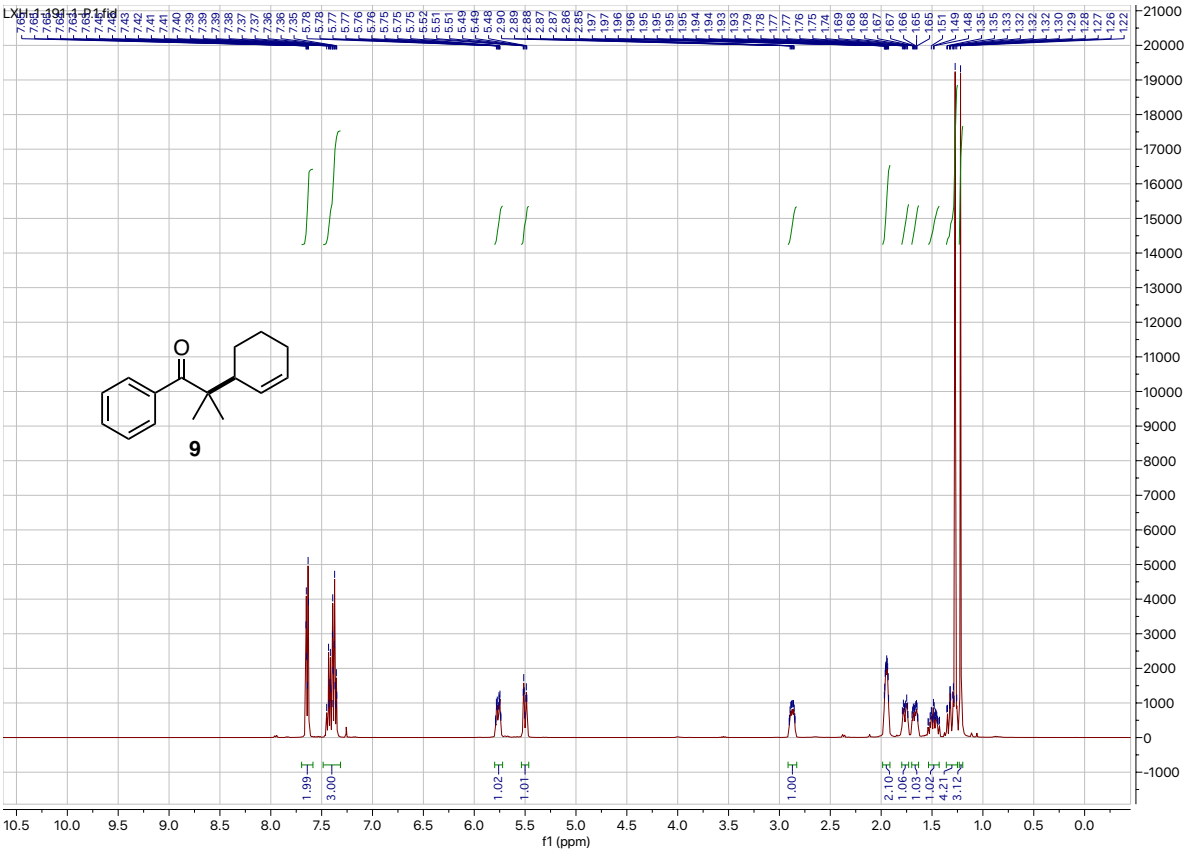
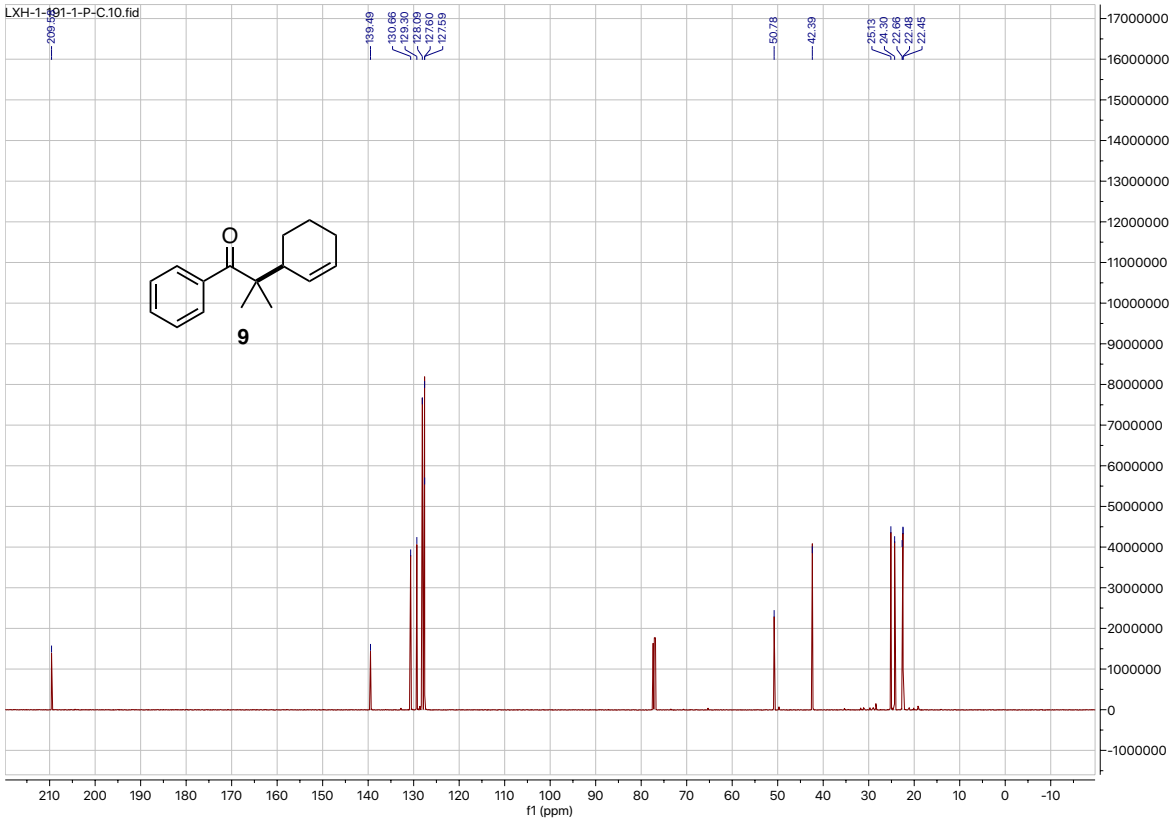
7
f1 (ppm)

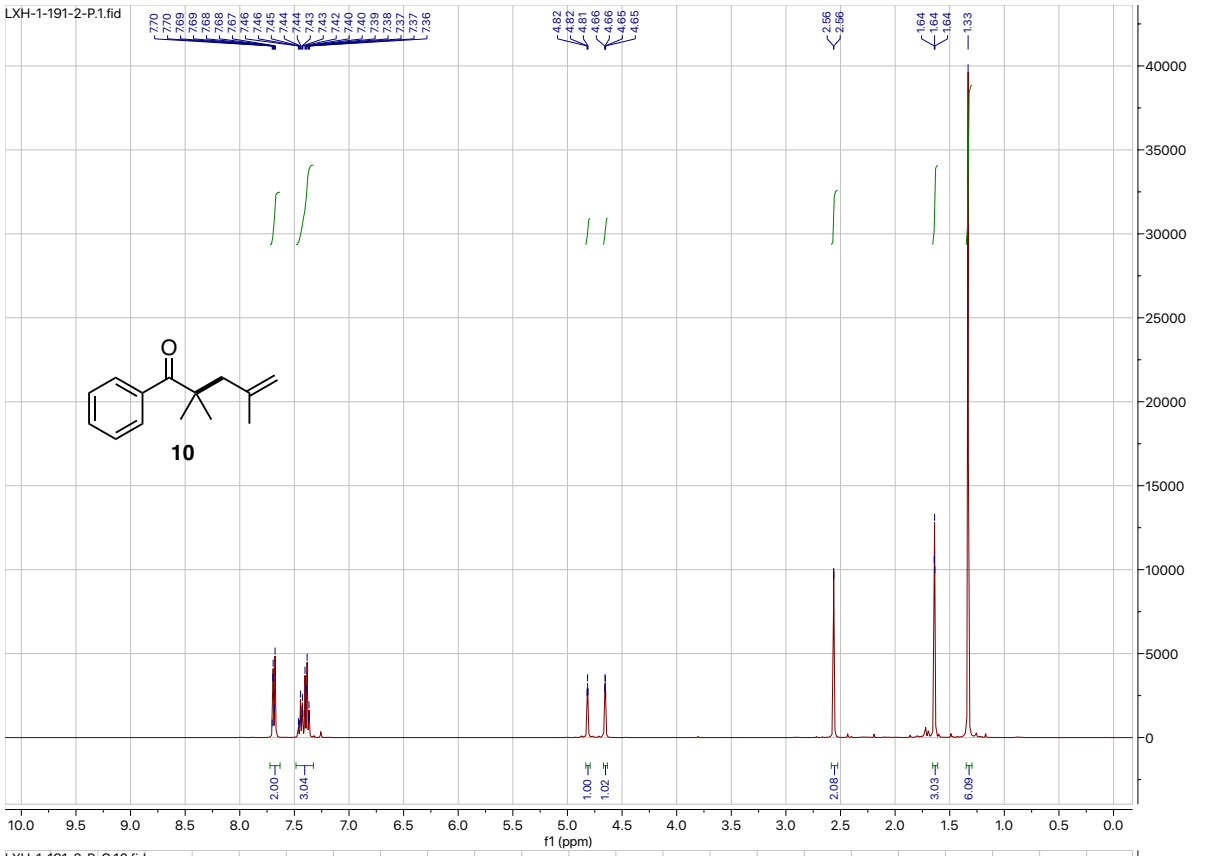

LXH-1-143-2-C.10.fid
7
f1 (ppm)

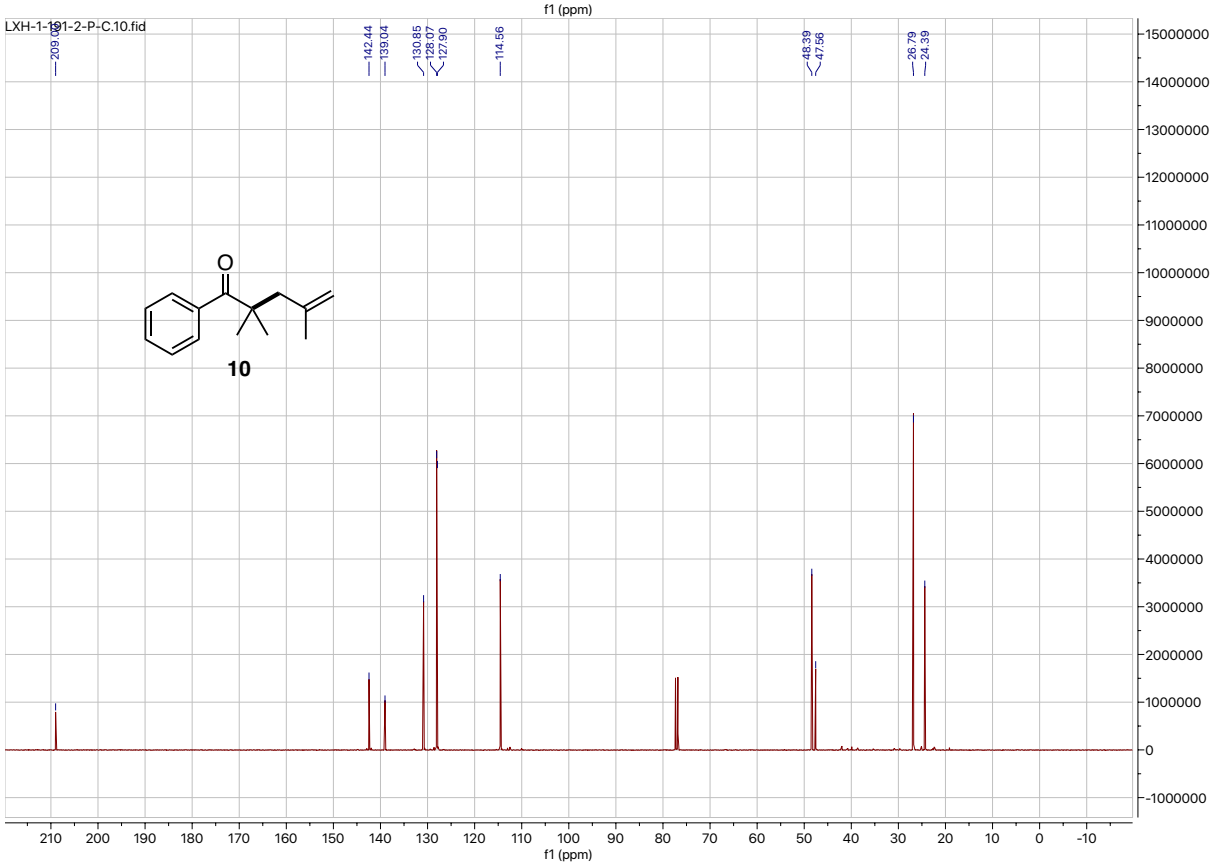

LXH-1-149-columnagain.1.fid
8
f1 (ppm)

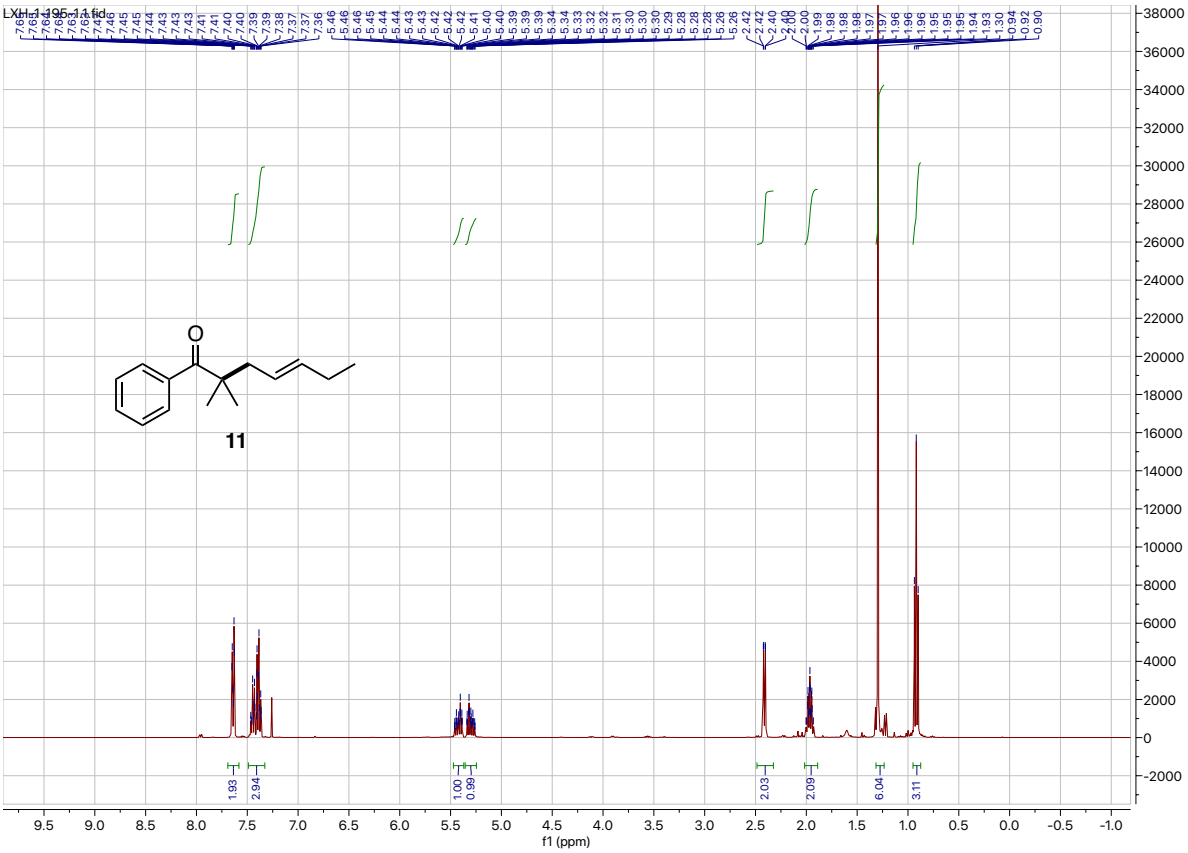

LXH-1-282-2-C.1.fid
8
f1 (ppm)

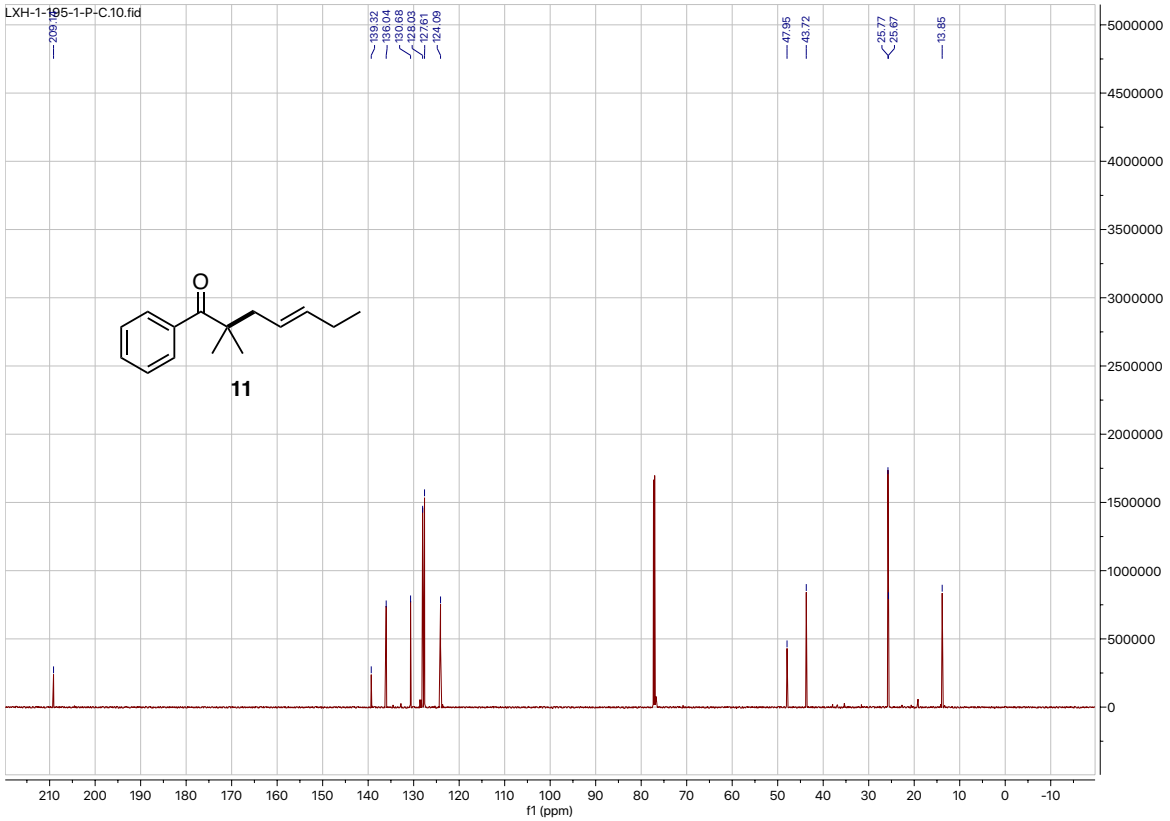

LXH-1-191-1-P1.fid
O
9
1.99
3.00
1.02
1.01
1.00
2.10
1.06
1.03
1.02
4.21
3.12
f1 (ppm)

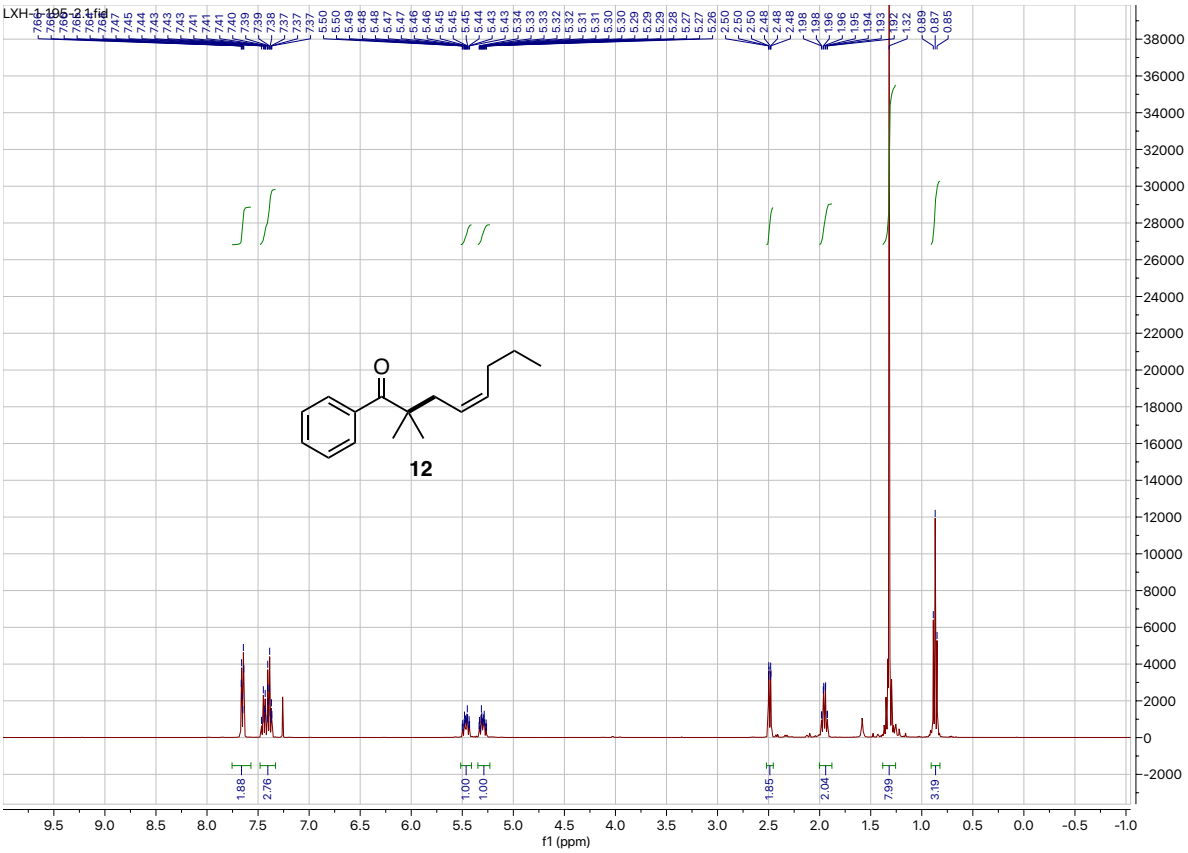

LXH-1-191-1-P-C.10.fid
209.58
139.49
130.66
129.30
128.09
127.60
127.59
50.78
42.39
25.13
24.30
22.66
22.48
22.45
O
9
f1 (ppm)

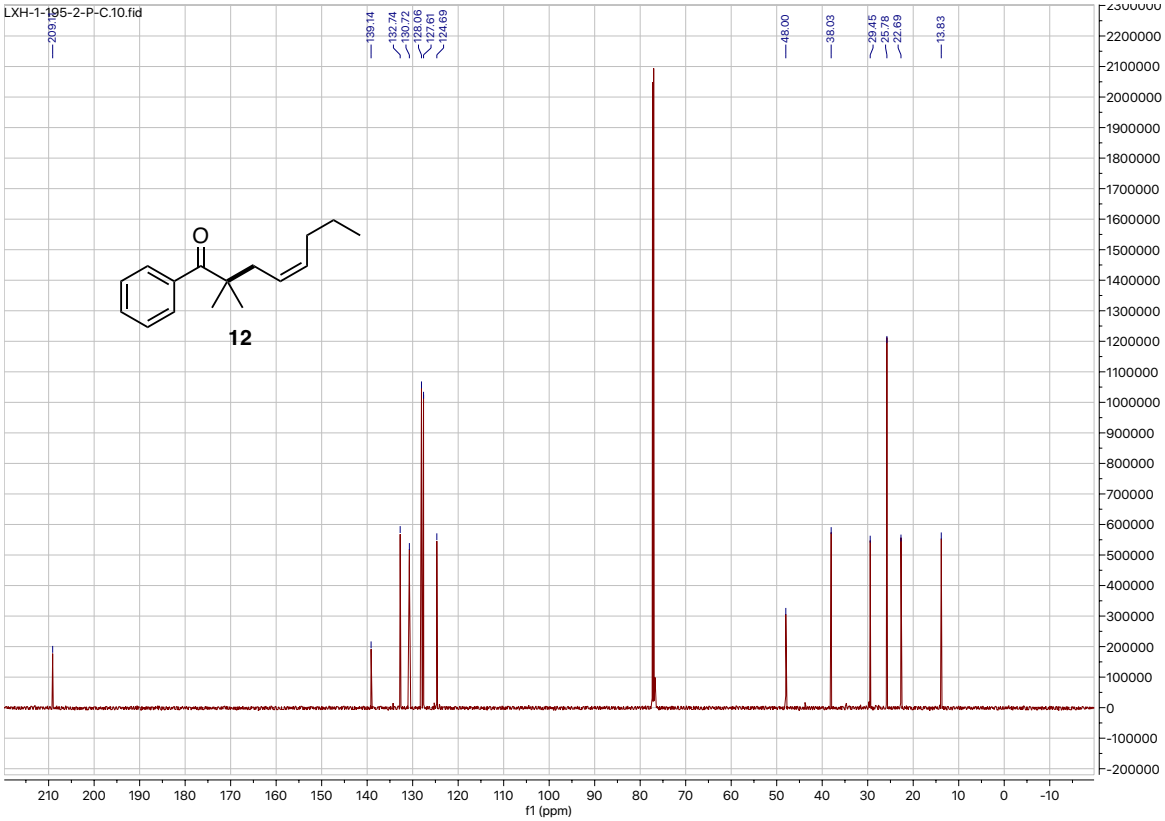

LXH-1-191-2-P.1.fid
7.70
7.70
7.69
7.69
7.68
7.68
7.67
7.67
7.46
7.46
7.45
7.44
7.44
7.43
7.43
7.42
7.40
7.40
7.39
7.38
7.37
7.37
7.36
4.82
4.82
4.81
4.81
4.66
4.66
4.65
4.65
4.65
2.56
2.56
1.64
1.64
1.64
1.33
O
10
2.00
3.04
1.00
1.02
2.08
3.03
6.09
f1 (ppm)

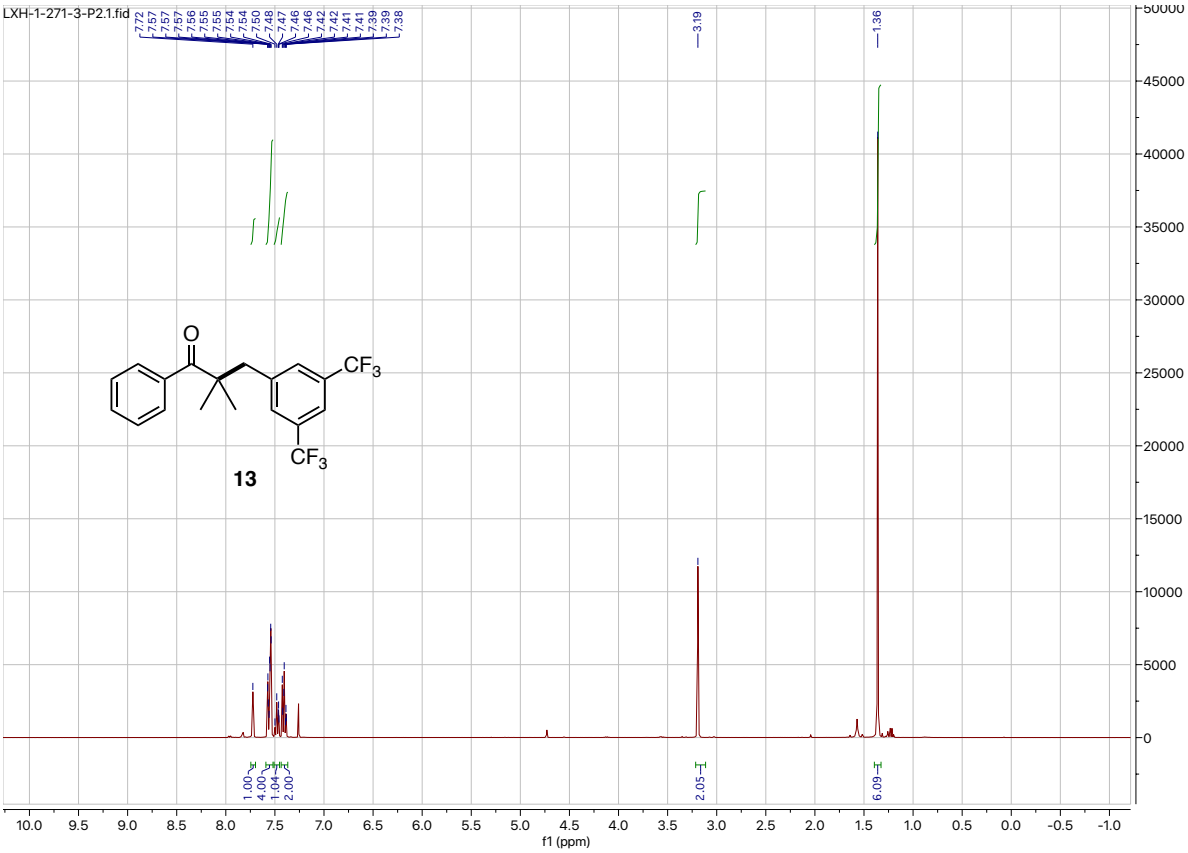

LXH-1-191-2-P-C.10.fid
209.08
142.44
139.04
130.85
128.07
127.90
114.56
48.39
47.56
26.79
24.39
O
10
f1 (ppm)

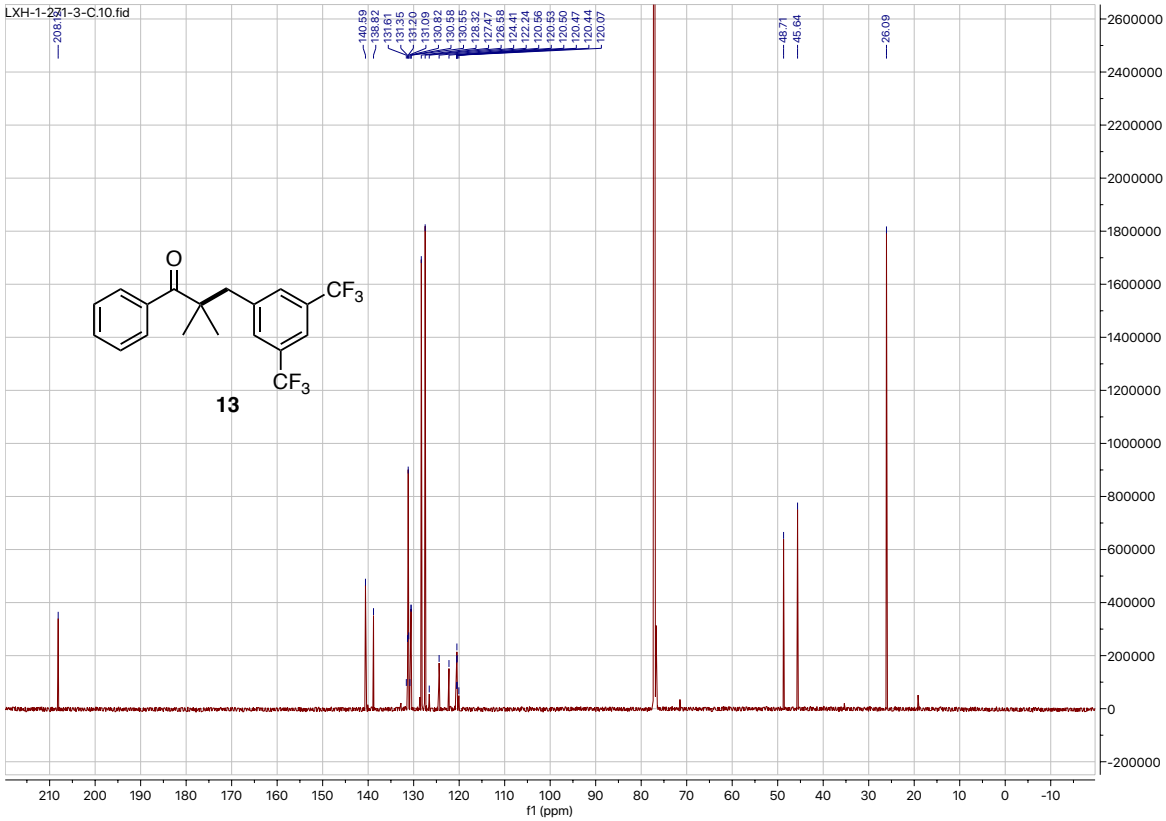

LXH-1-195-1-H.fid
O
11
1.93
2.94
1.00
0.99
2.03
2.09
6.04
3.11
f1 (ppm)

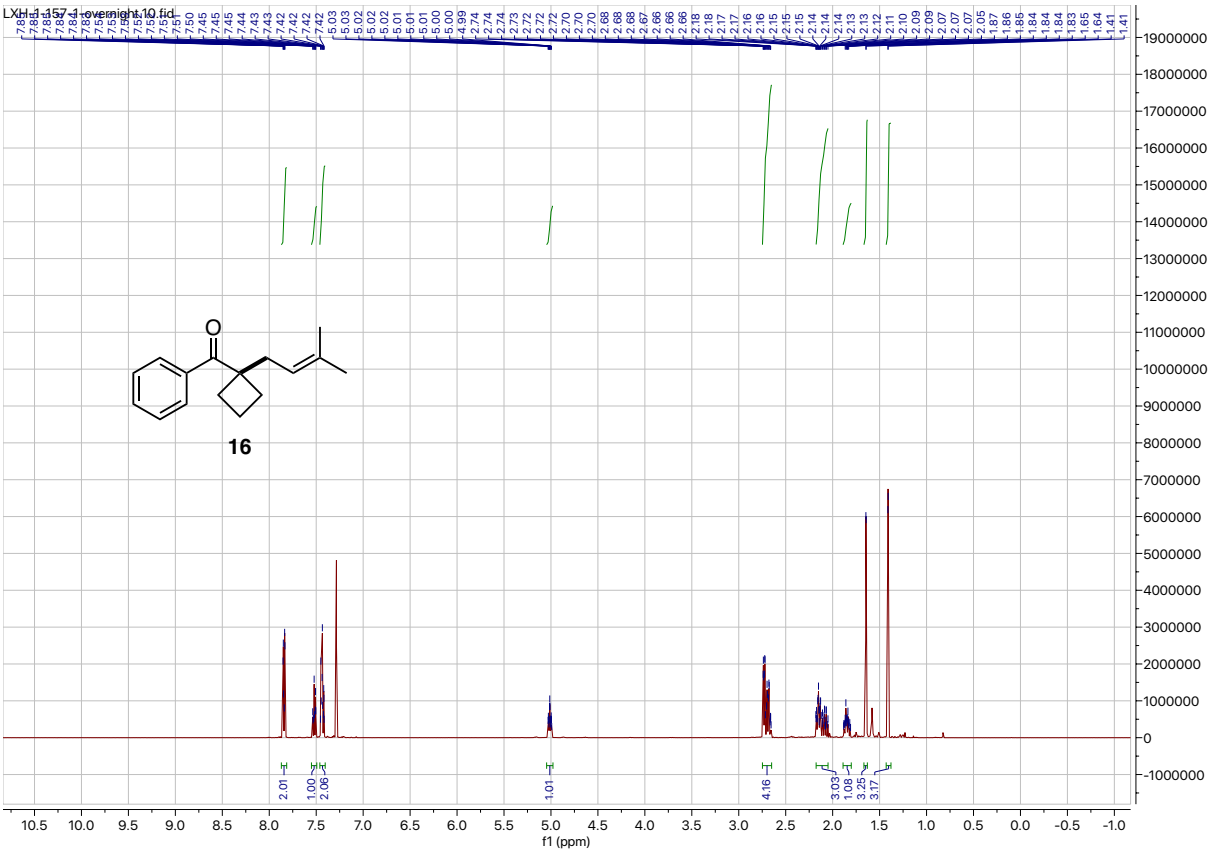

LXH-1-195-1-P-C.10.fid
209.19
139.32
136.04
130.68
128.03
127.61
124.09
47.95
43.72
25.77
25.67
13.85
O
11
f1 (ppm)

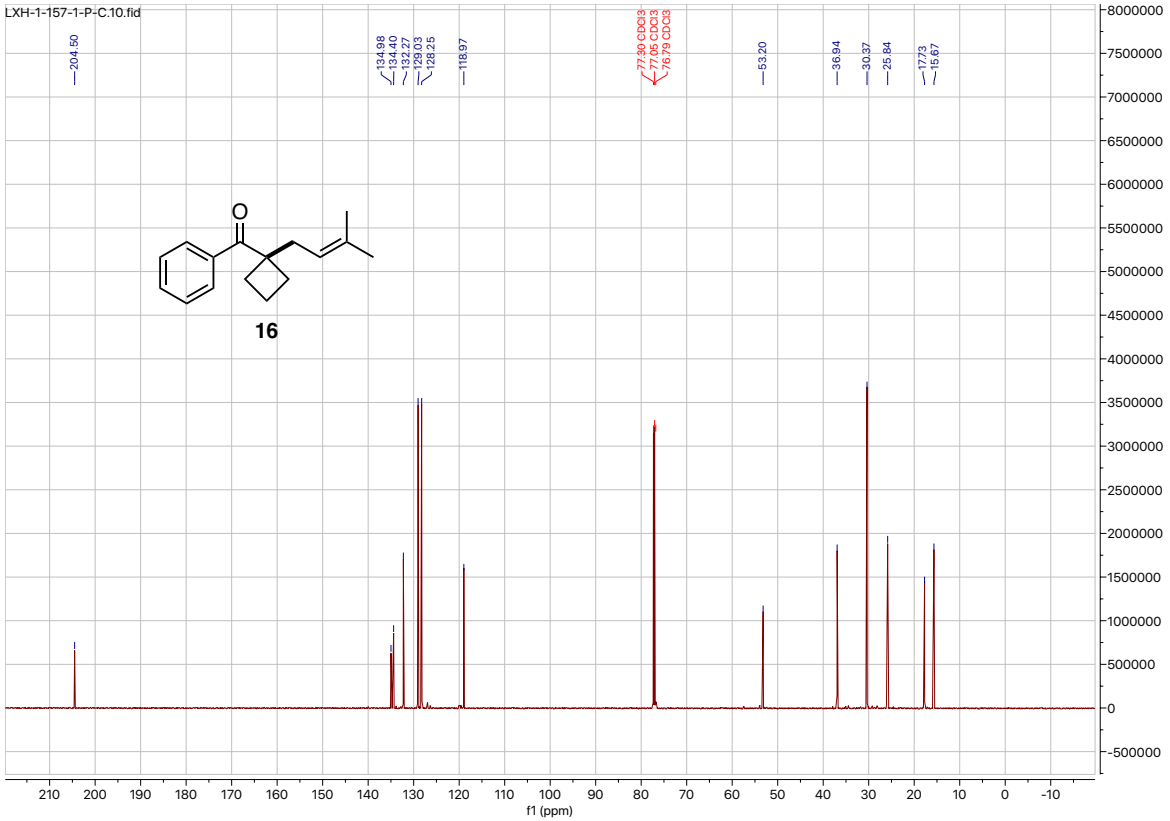

LXH-1-195-2.1.fid
12
1.88
2.76
1.00
1.00
1.85
2.04
7.99
3.19
f1 (ppm)

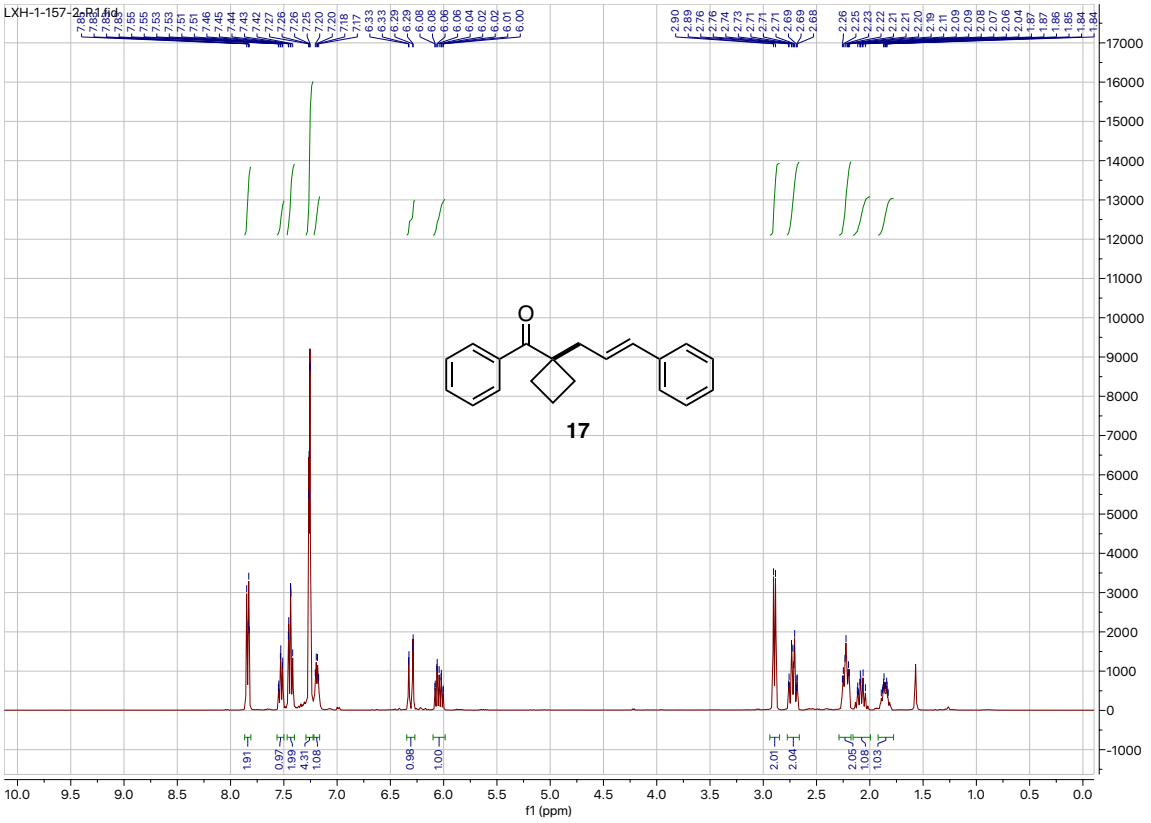

LXH-1-195-2-P-C.10.fid
209.14
139.14
132.74
130.72
128.06
127.61
124.69
48.00
38.03
29.45
25.78
22.69
13.83
12
f1 (ppm)

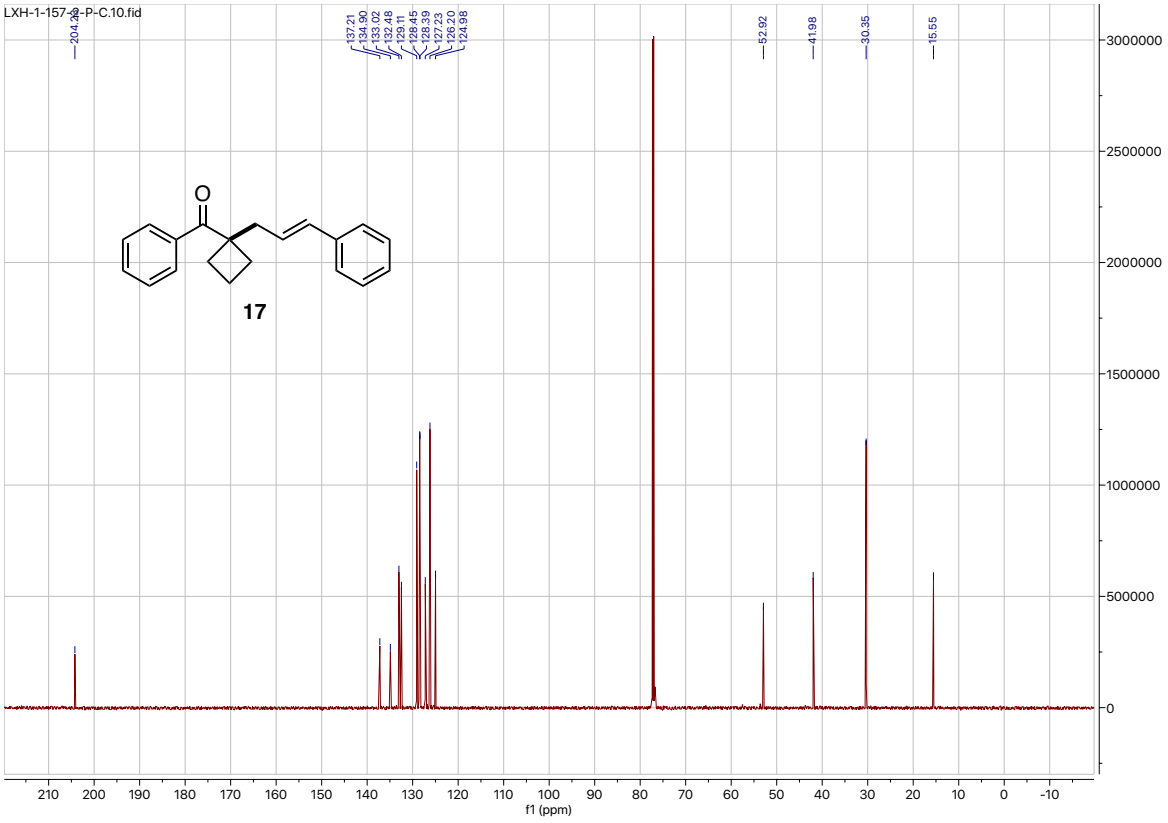

LXH-1-271-3-P2.1.fid
O
CF3
CF3
13
f1 (ppm)

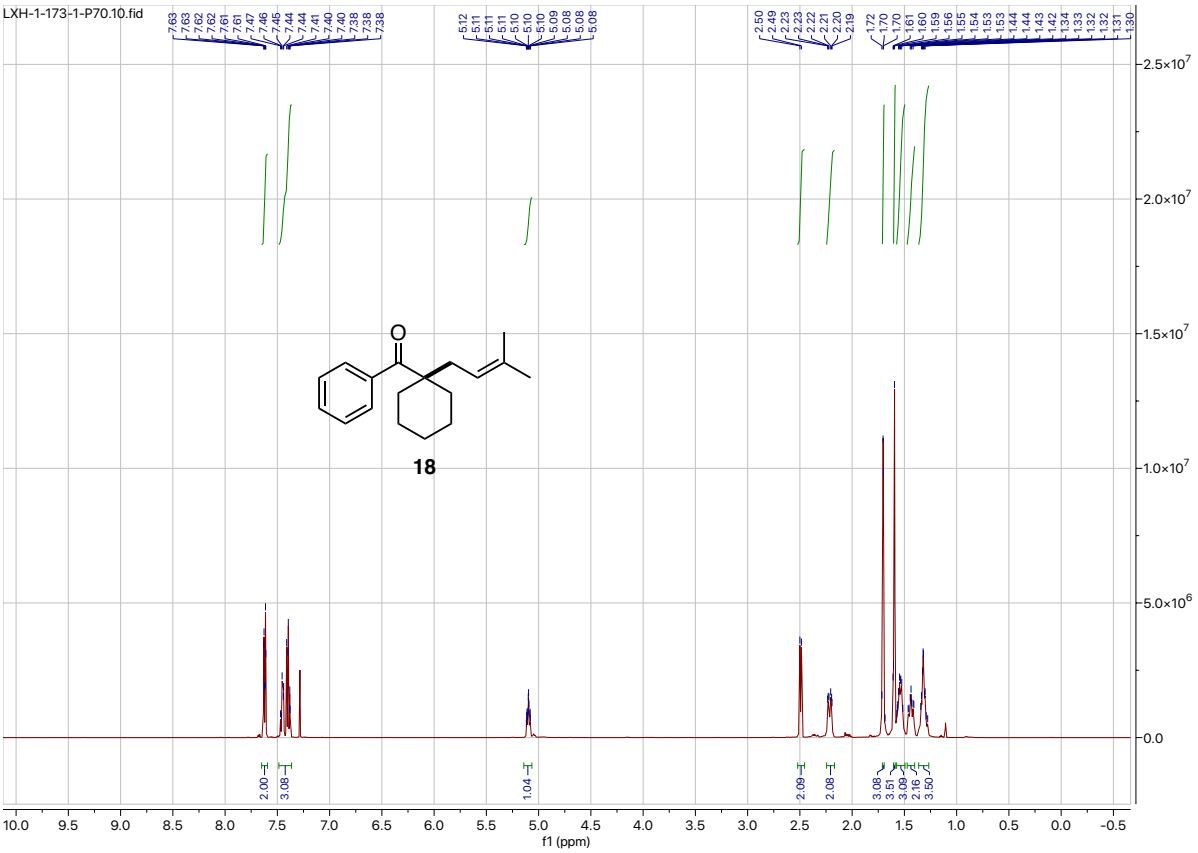

LXH-1-271-3-C.10.fid
O
CF3
CF3
13
f1 (ppm)

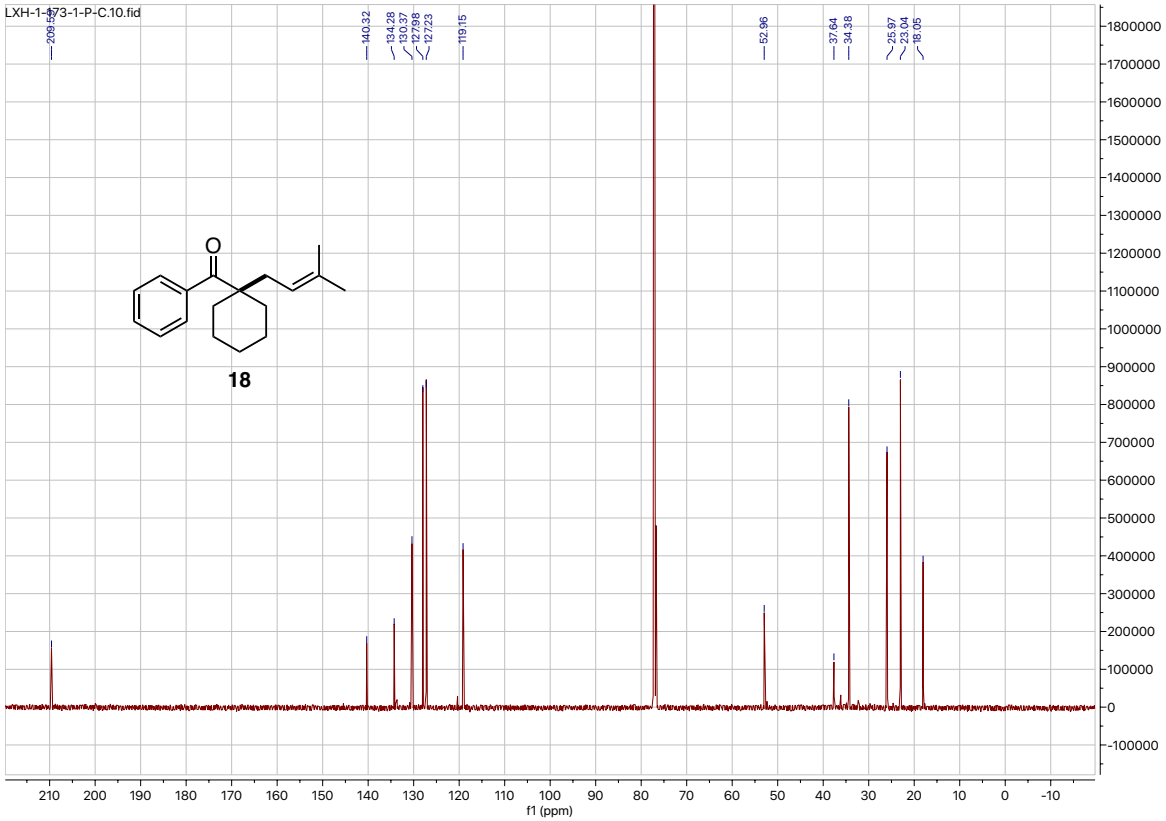

LXH-1-157-1-overnight.10.fid
O
16
2.01
1.00
2.06
1.01
4.16
3.09
1.08
3.25
3.17
f1 (ppm)

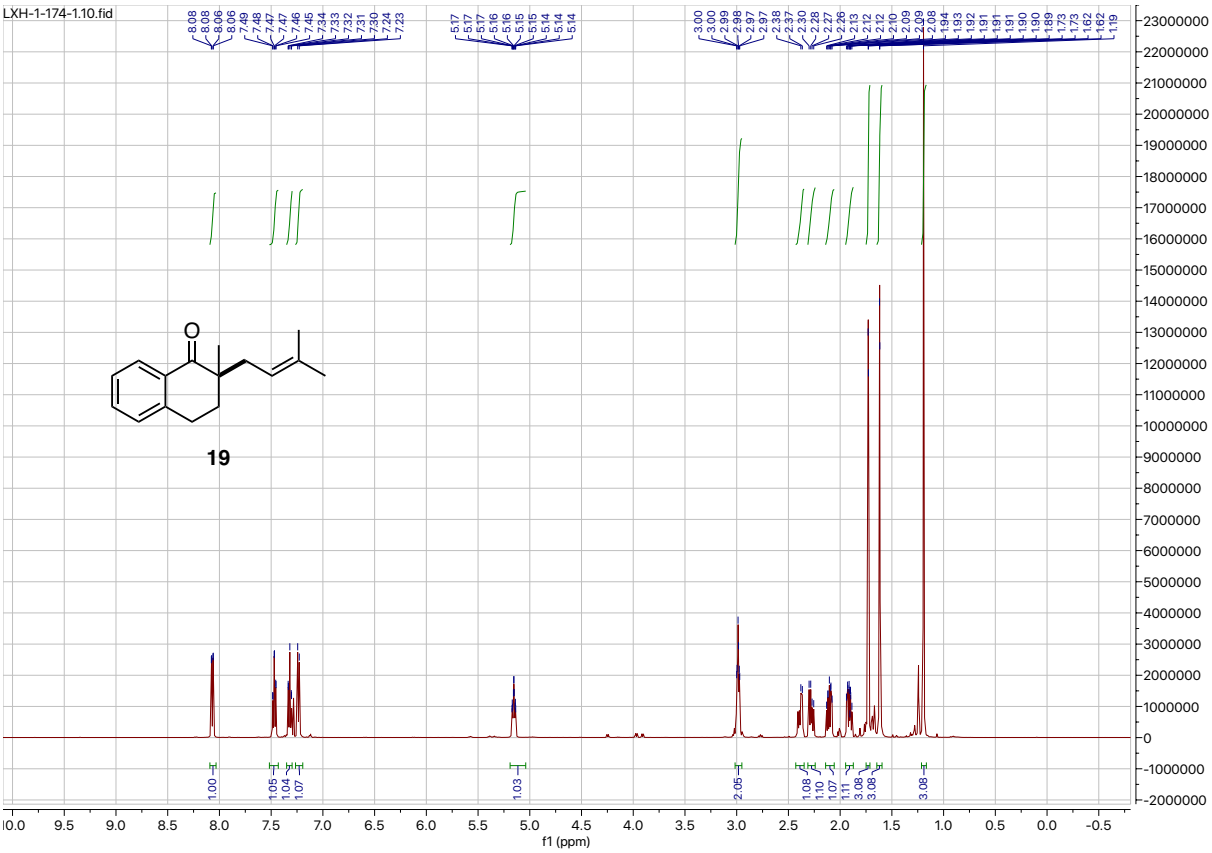

LXH-1-157-1-P-C.10.fid
204.50
134.98
134.40
132.27
129.03
128.25
118.97
77.30 CDCl3
77.05 CDCl3
76.79 CDCl3
53.20
36.94
30.37
25.84
17.73
15.67
O
16
f1 (ppm)

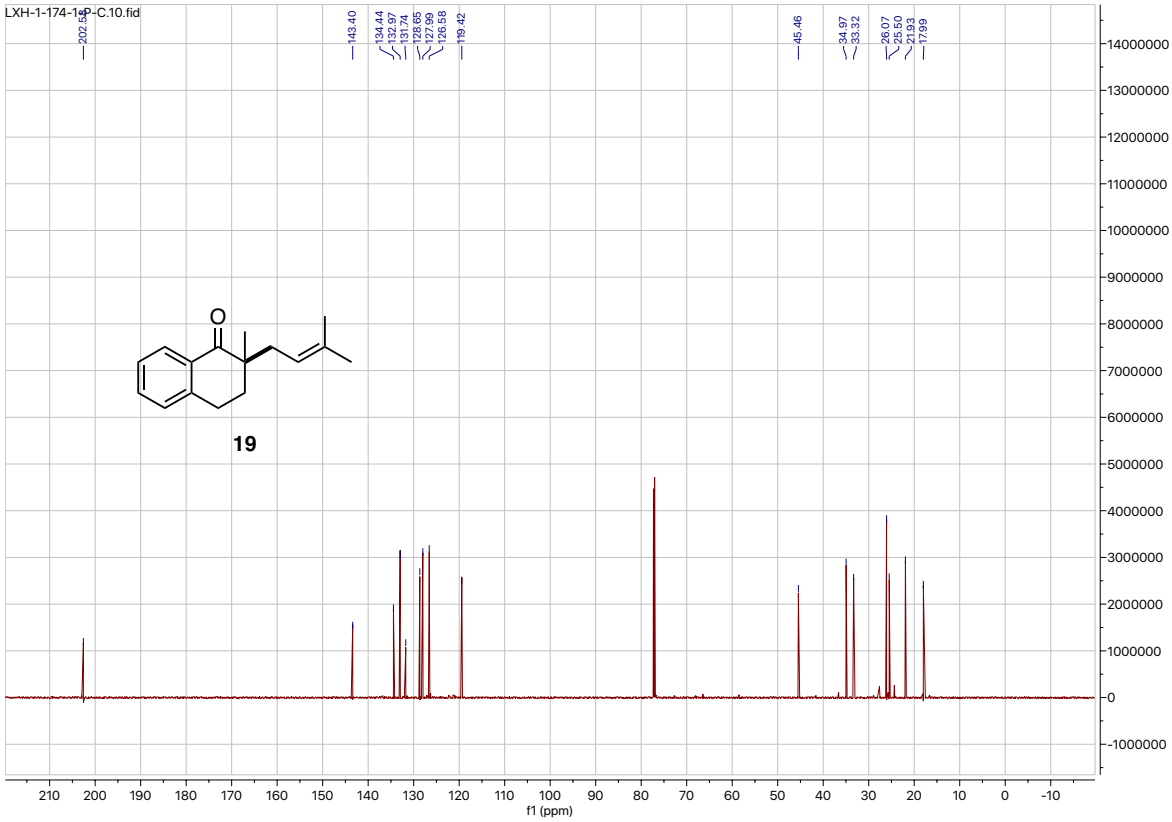

LXH-1-157-2-P1.fid
17

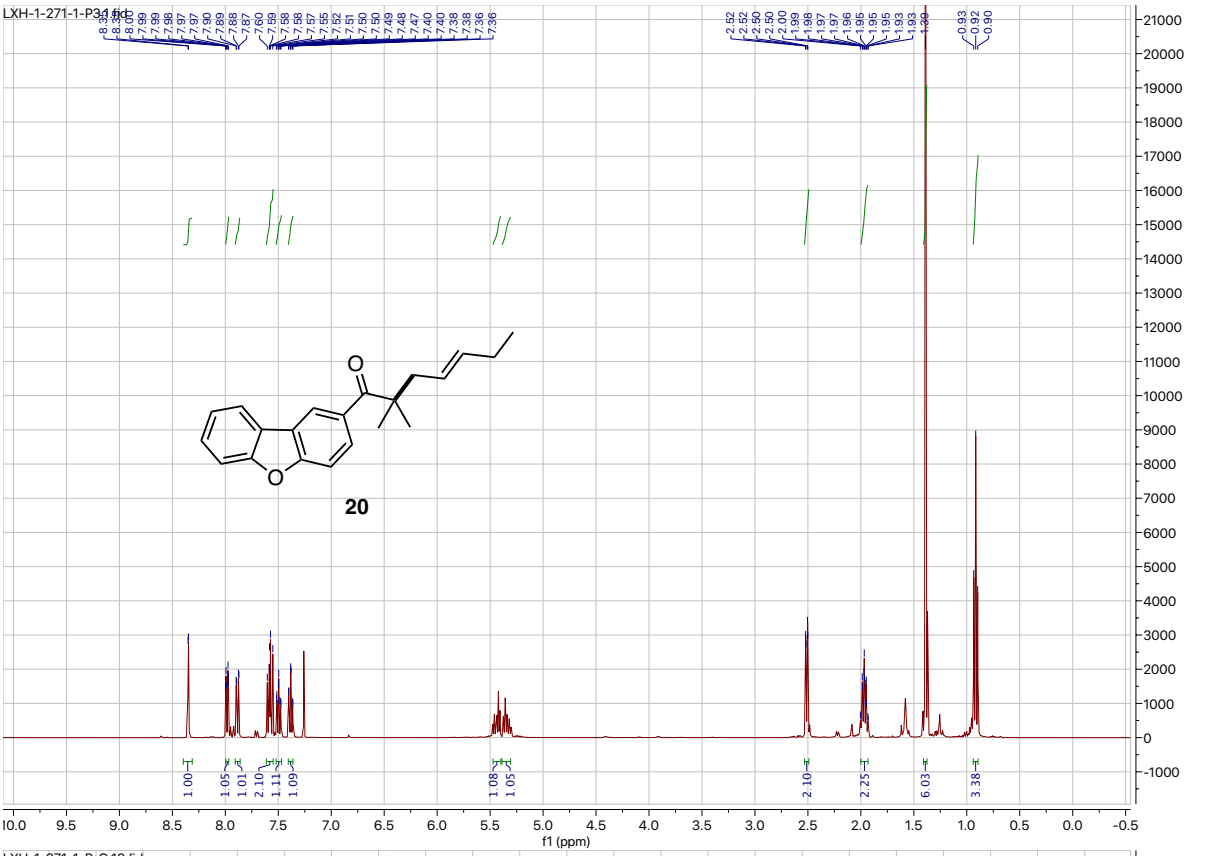

LXH-1-157-2-P-C.10.fid
17

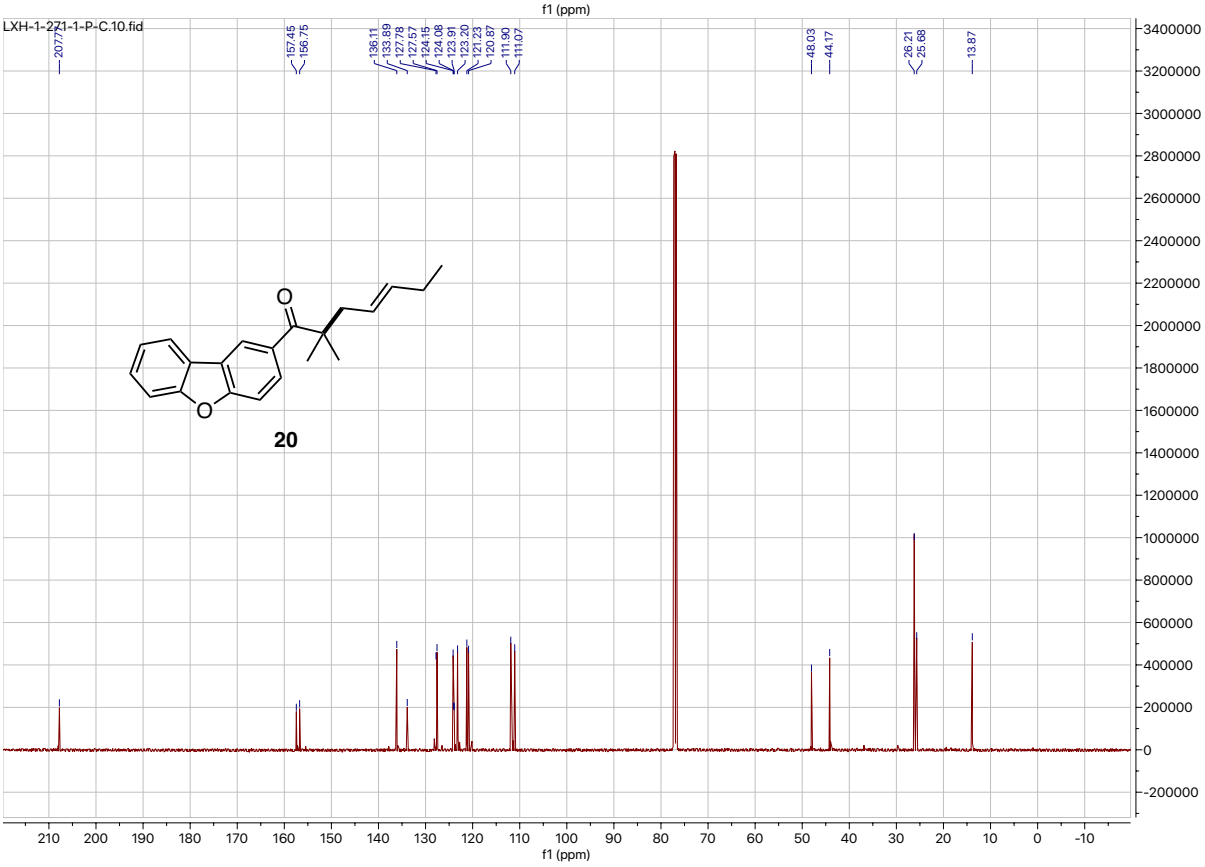

LXH-1-173-1-P70.10.fid
18
f1 (ppm)

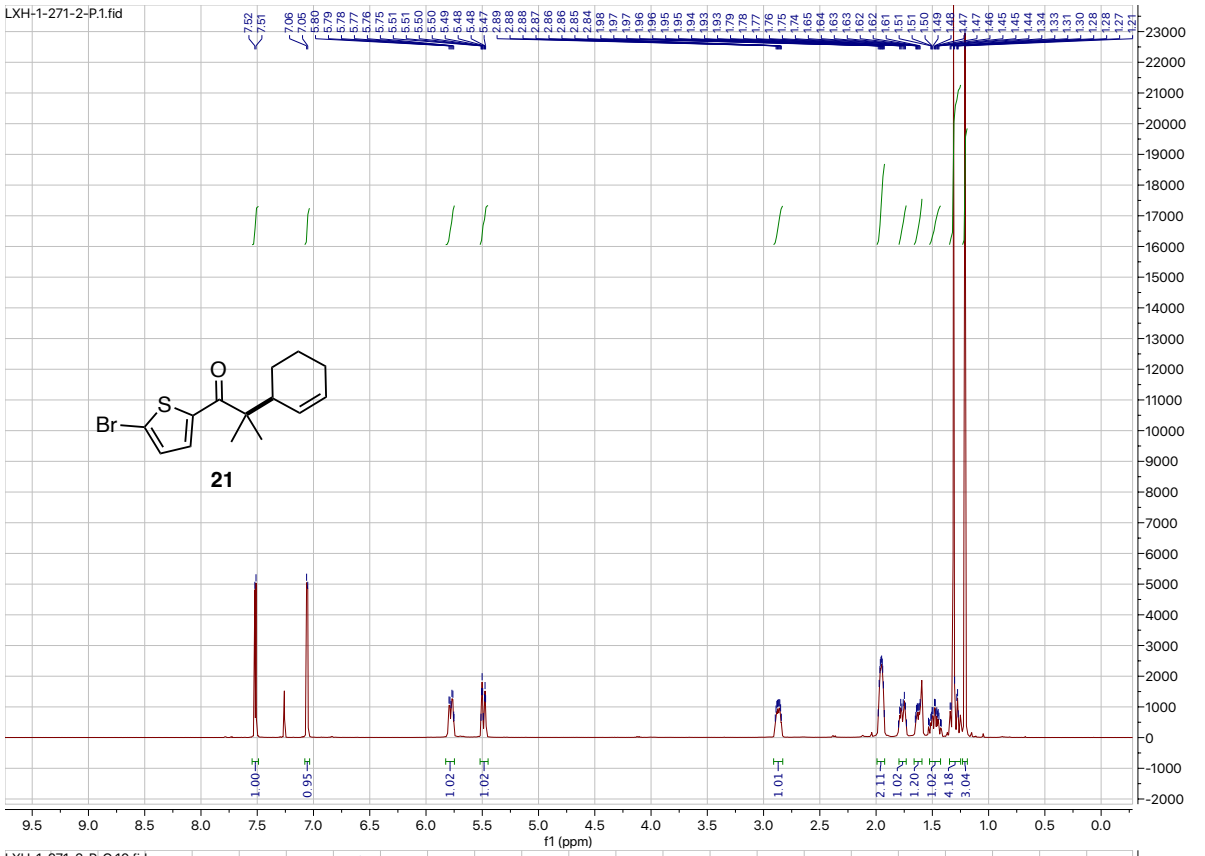

LXH-1-173-1-P-C.10.fid
18
f1 (ppm)

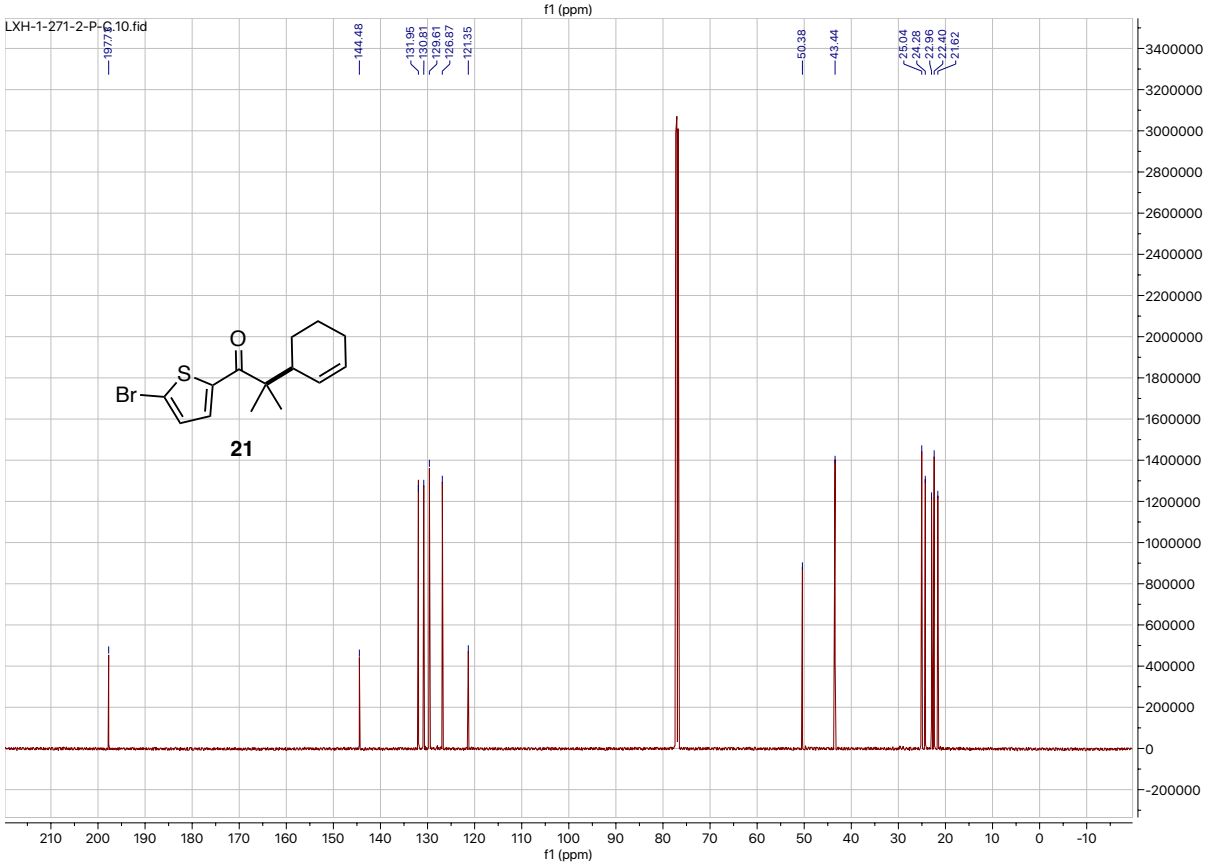

LXH-1-174-1.10.fid
19
f1 (ppm)

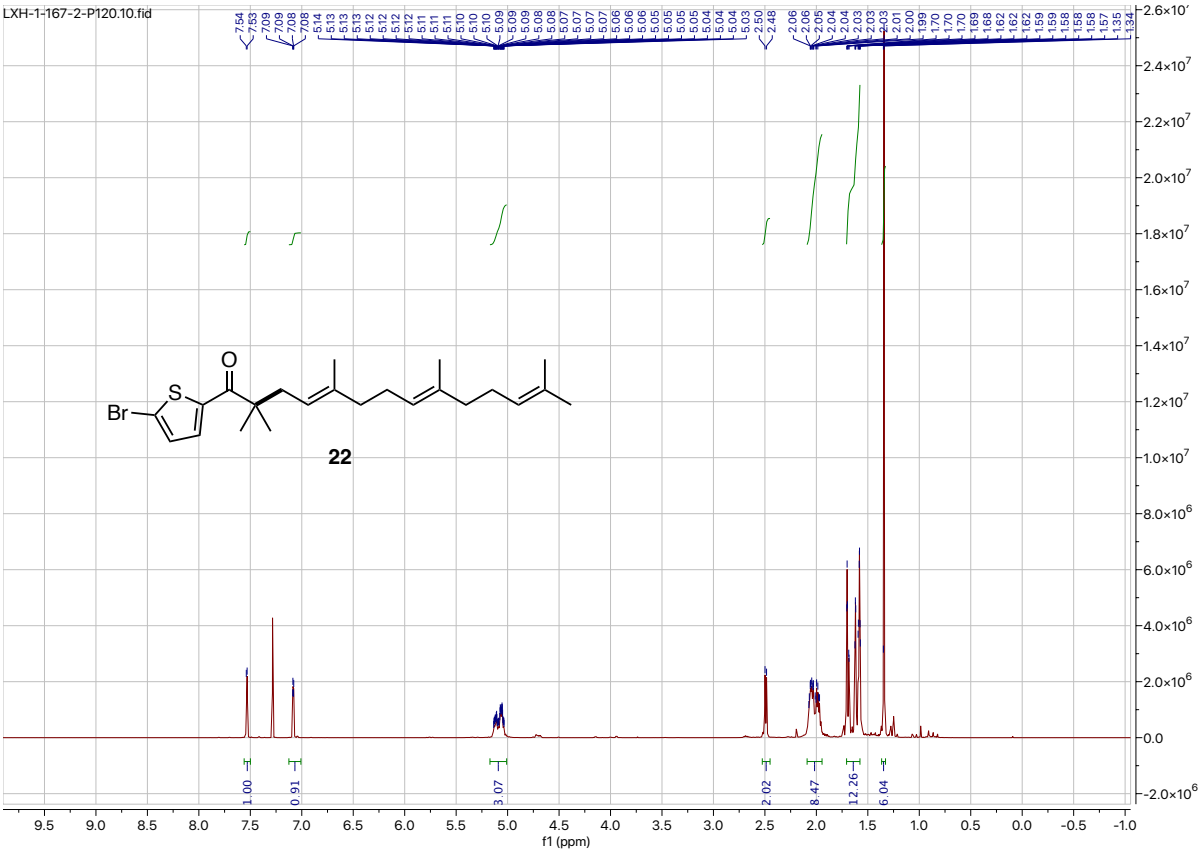

LXH-1-174-1-P-C.10.fid
19
f1 (ppm)

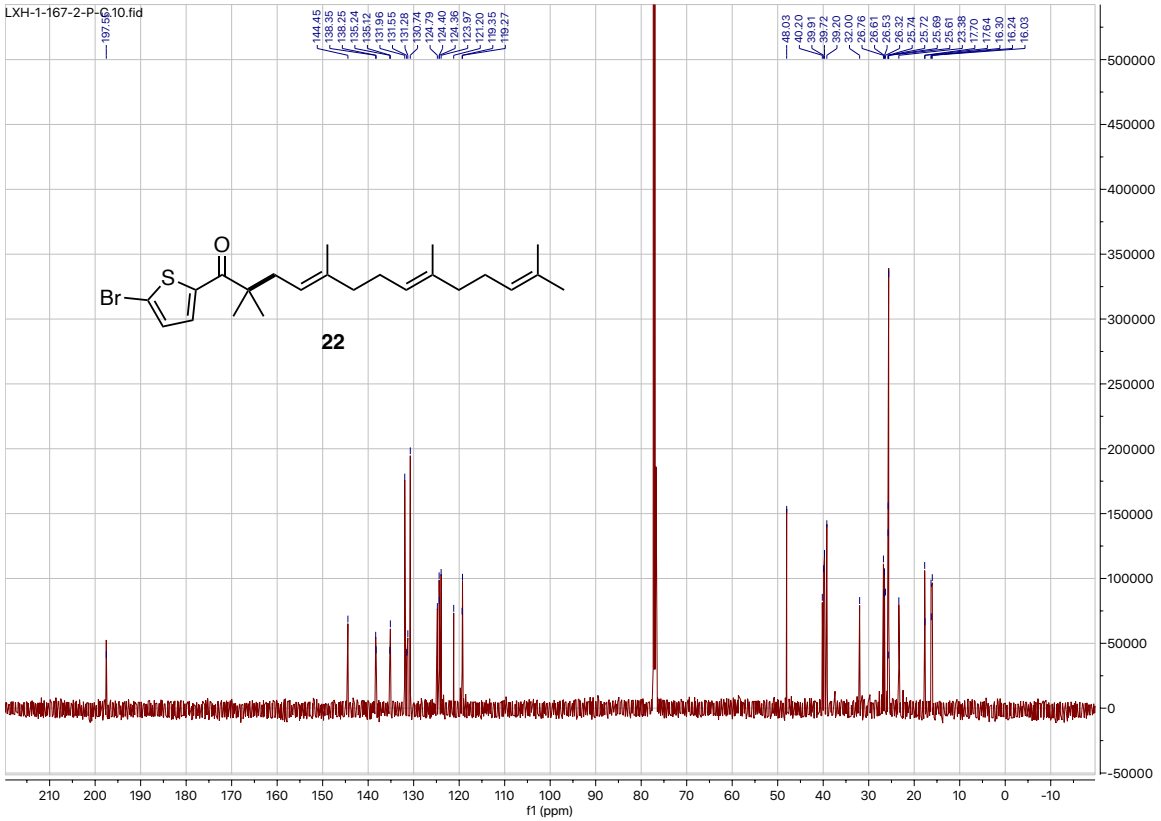

LXH-1-271-1-P3.1.fid
20
f1 (ppm)

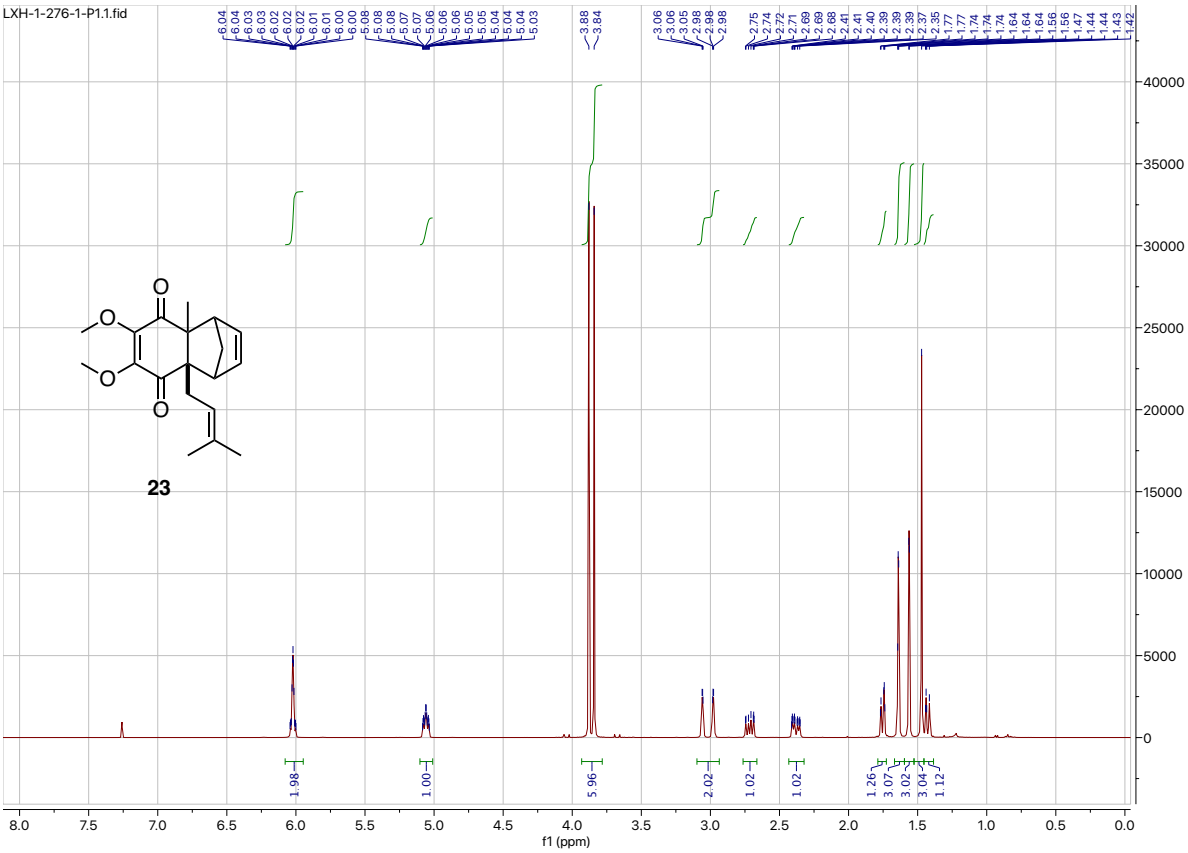

LXH-1-271-1-P-C.10.fid
20
f1 (ppm)

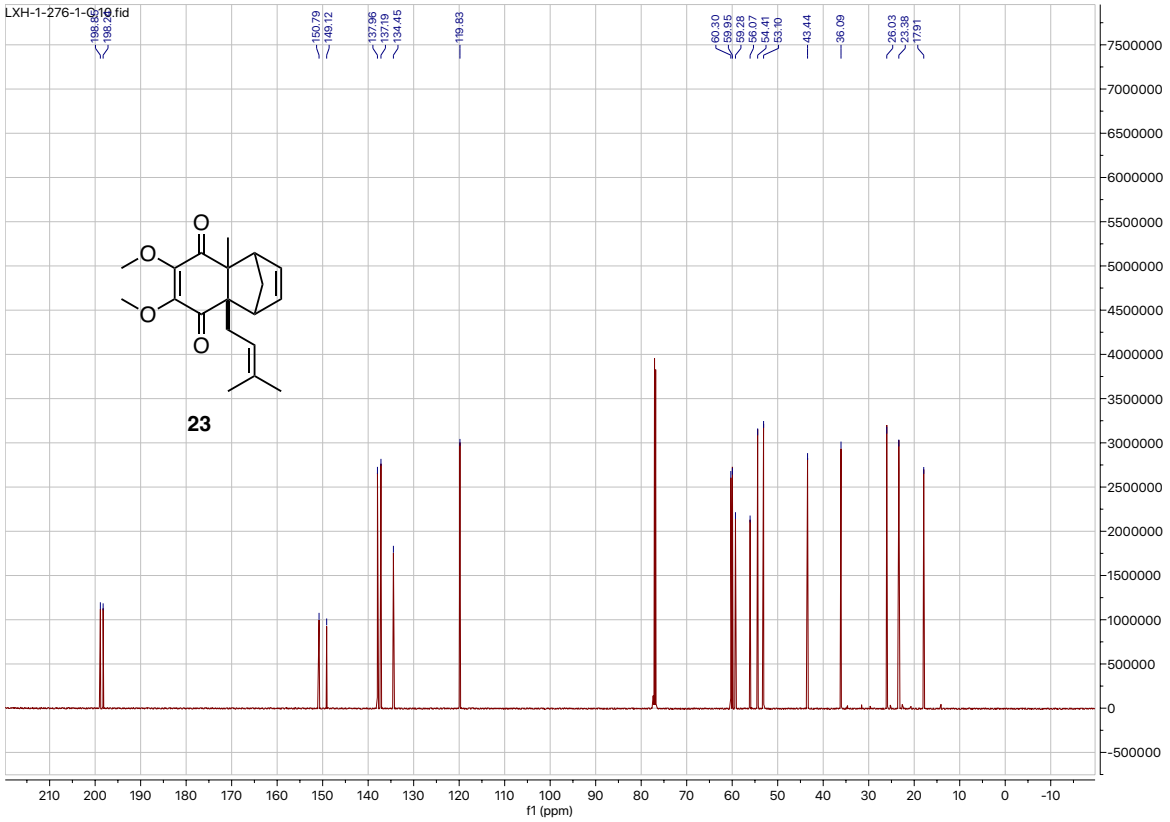

LXH-1-271-2-P.1.fid
f1 (ppm)

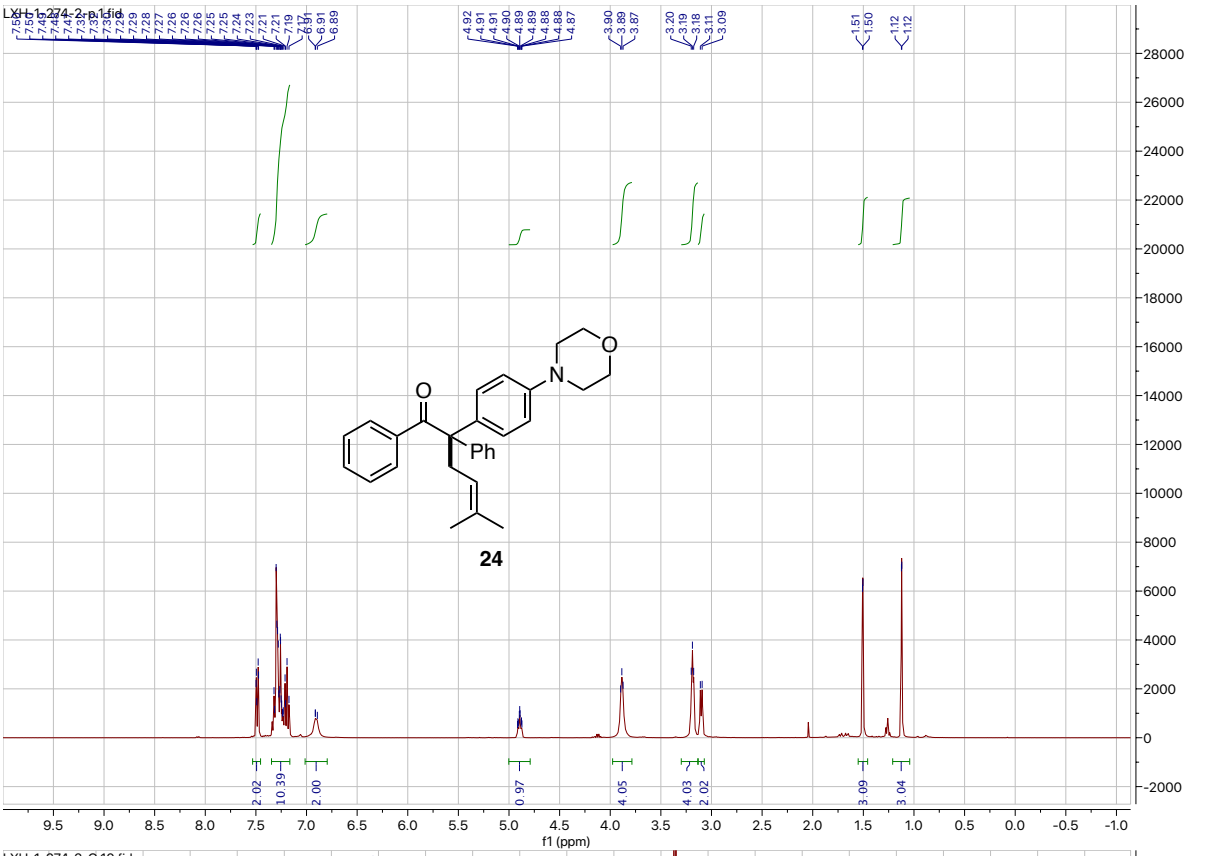

LXH-1-271-2-P-C.10.fid
f1 (ppm)

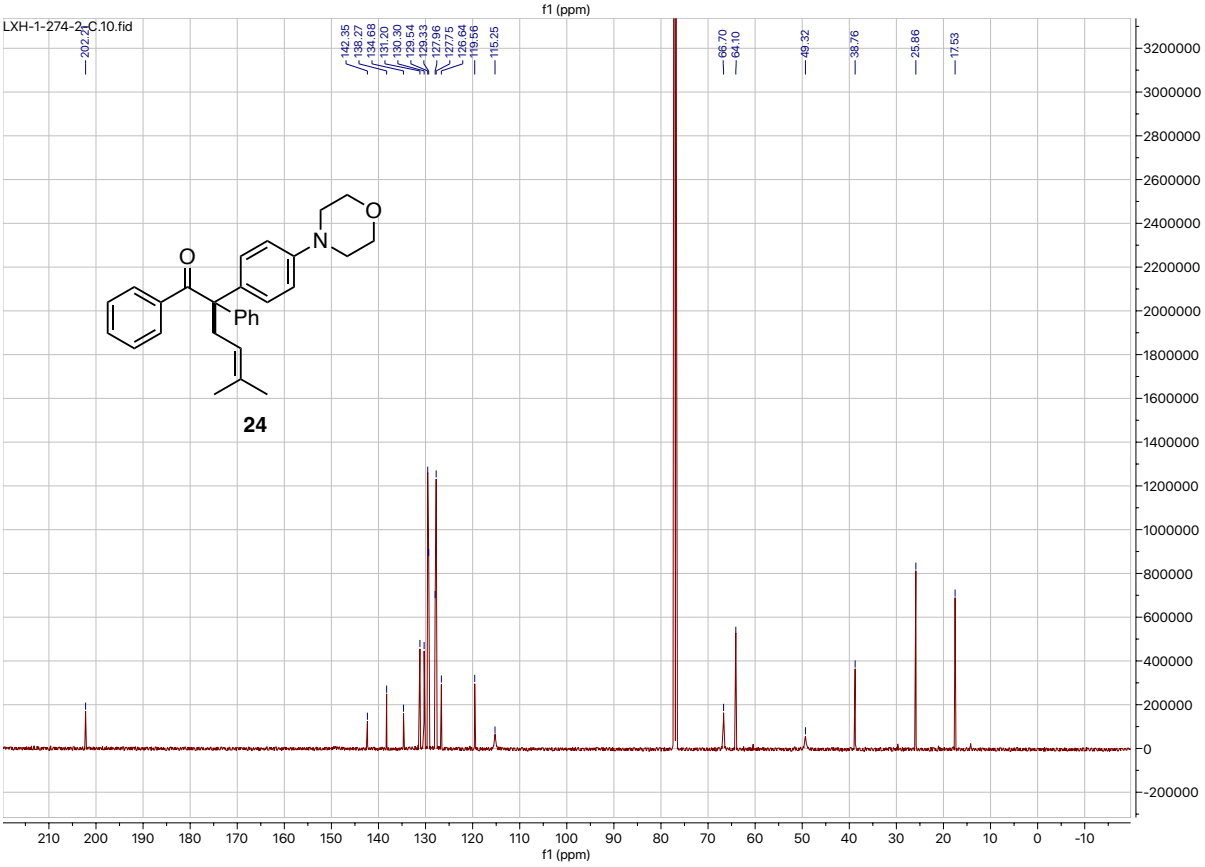

LXH-1-167-2-P120.10.fid
Br
S
O
22
f1 (ppm)

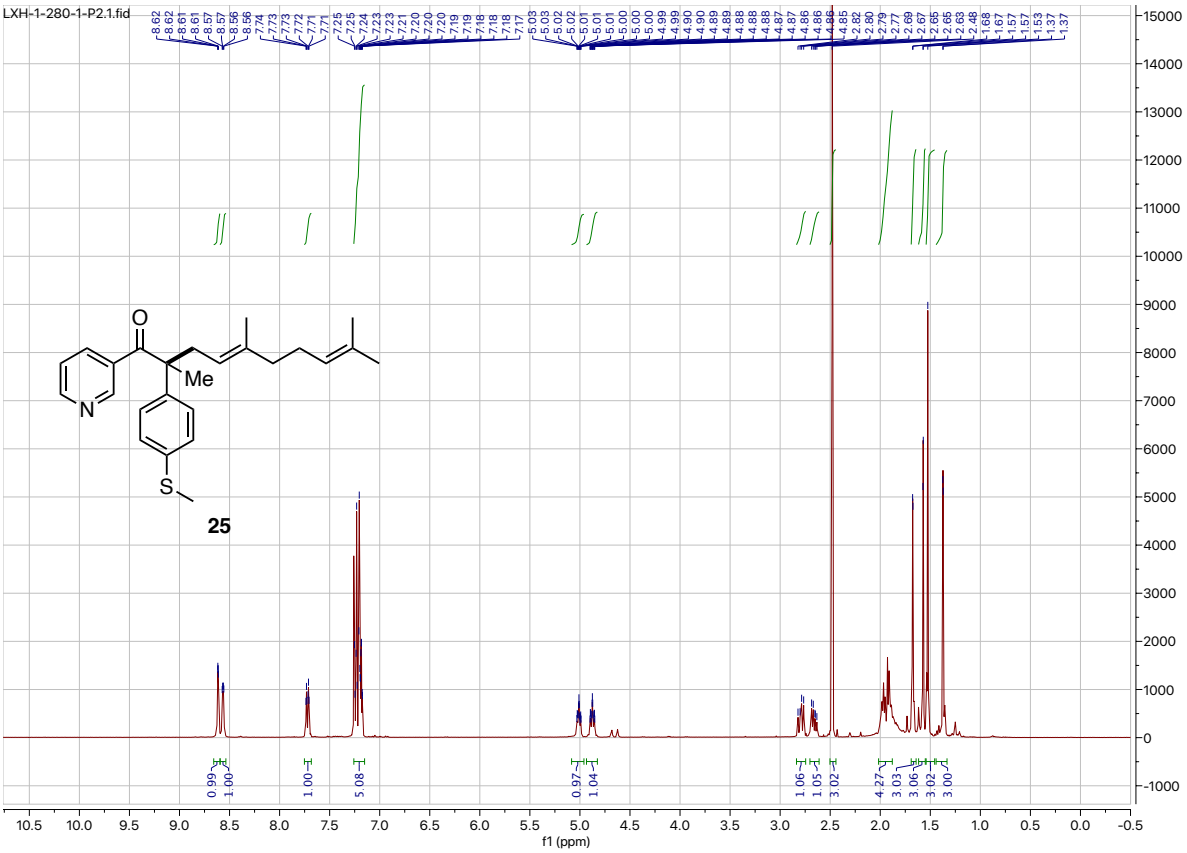

LXH-1-167-2-P-C10.fid
Br
S
O
22
f1 (ppm)

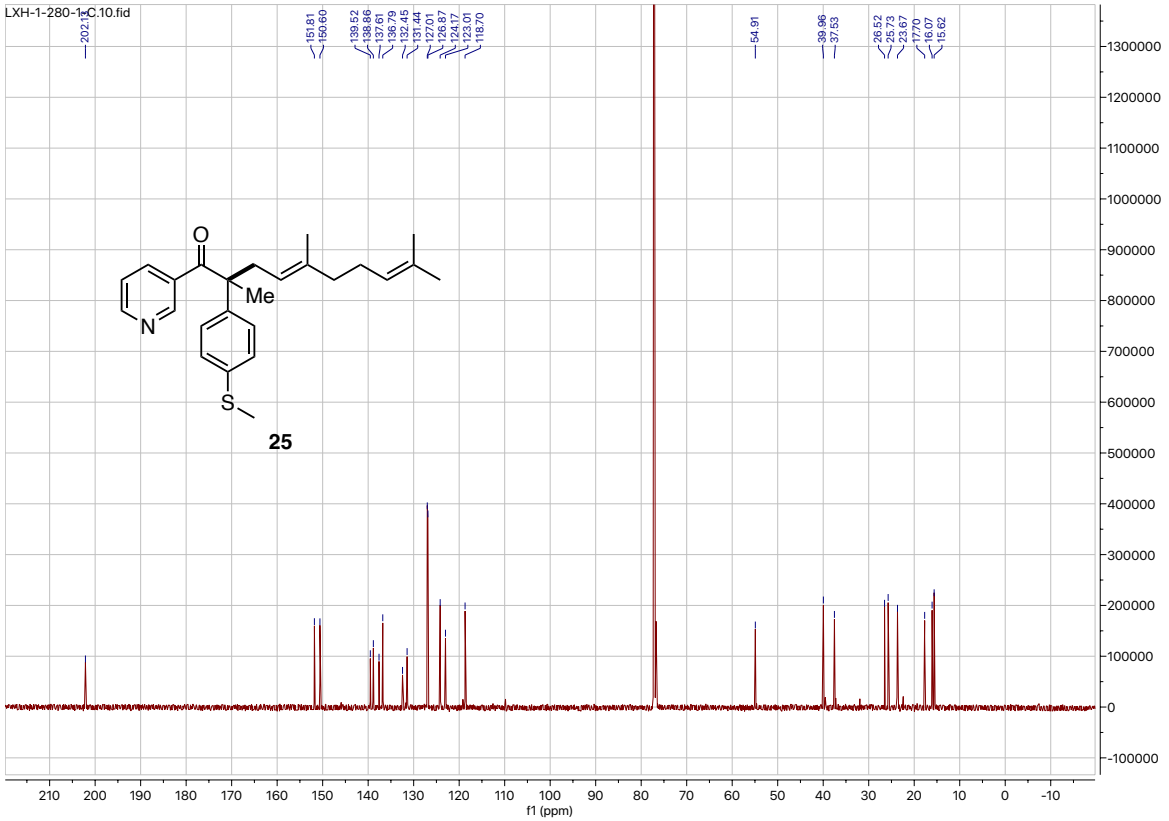

LXH-1-276-1-P1.1.fid
23
f1 (ppm)

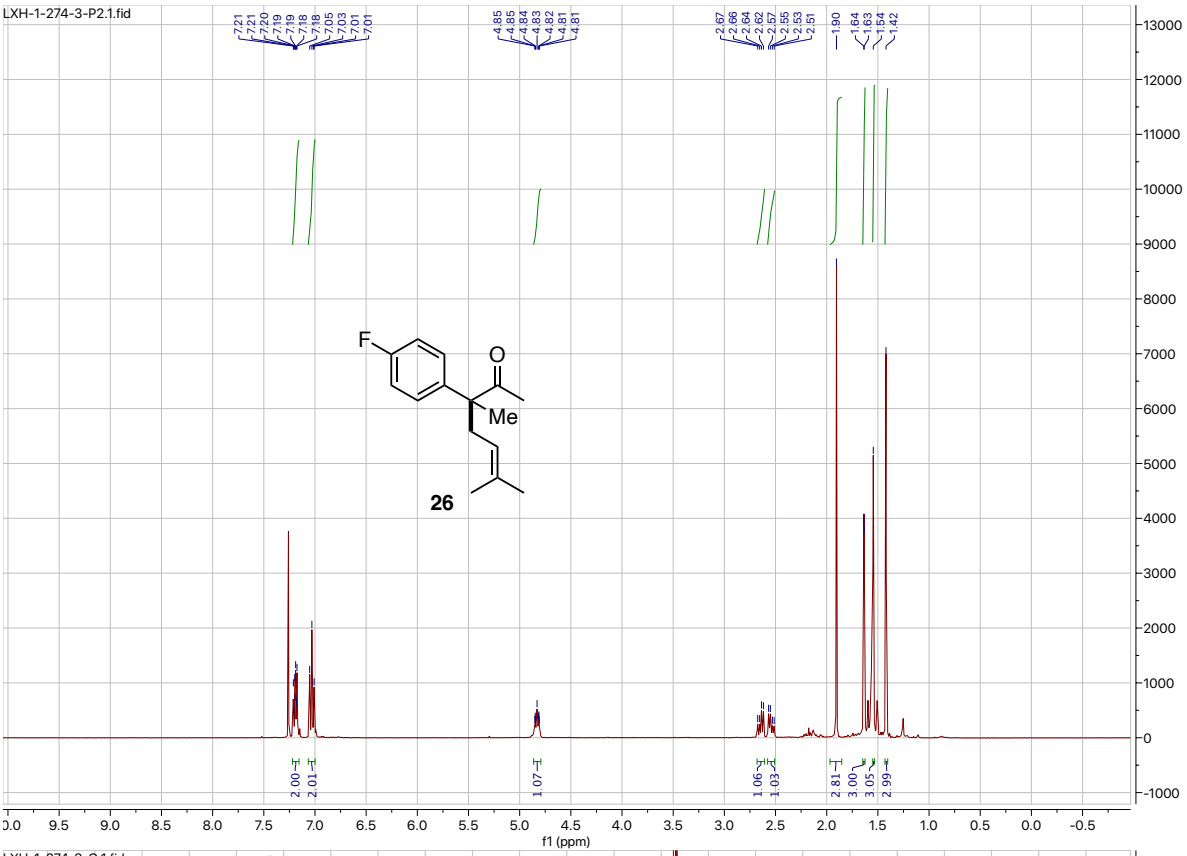

LXH-1-276-1-C13.fid
23
f1 (ppm)

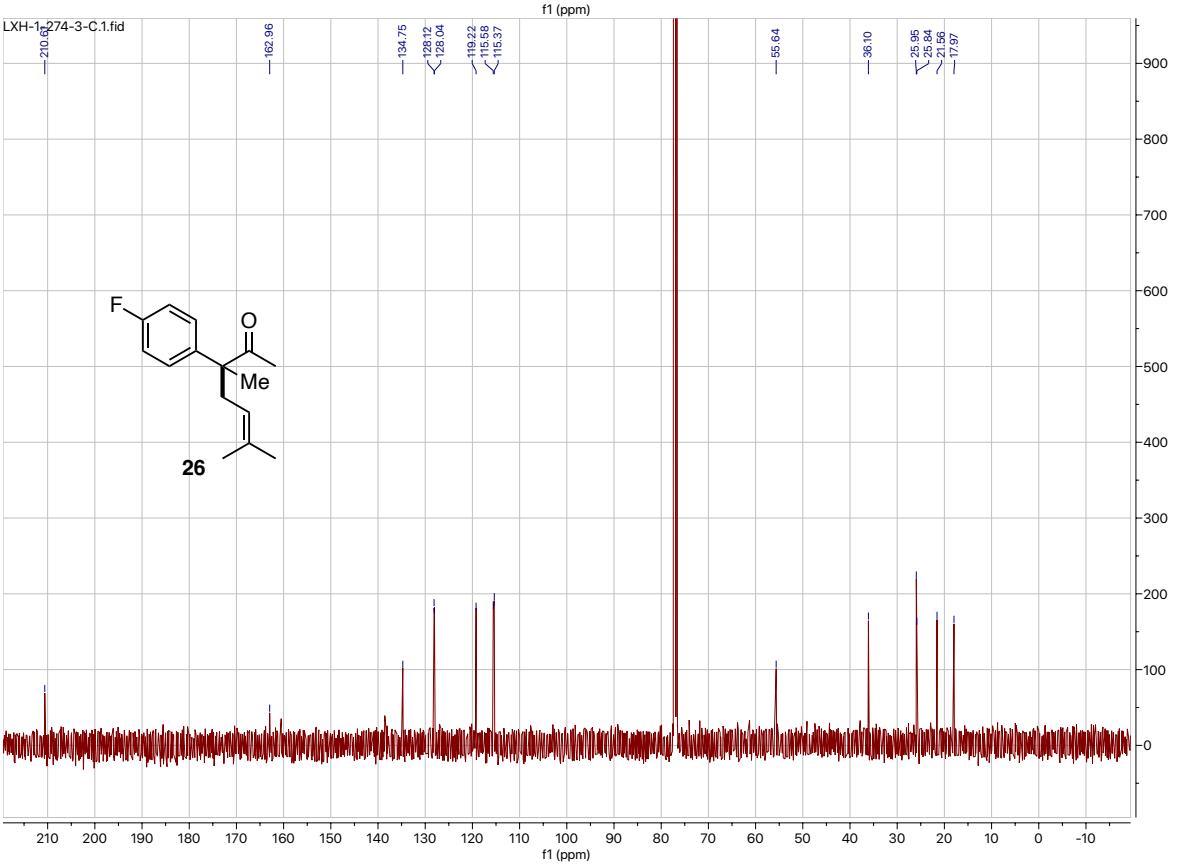

LXH-1-274-2-H.1.fid
24
f1 (ppm)

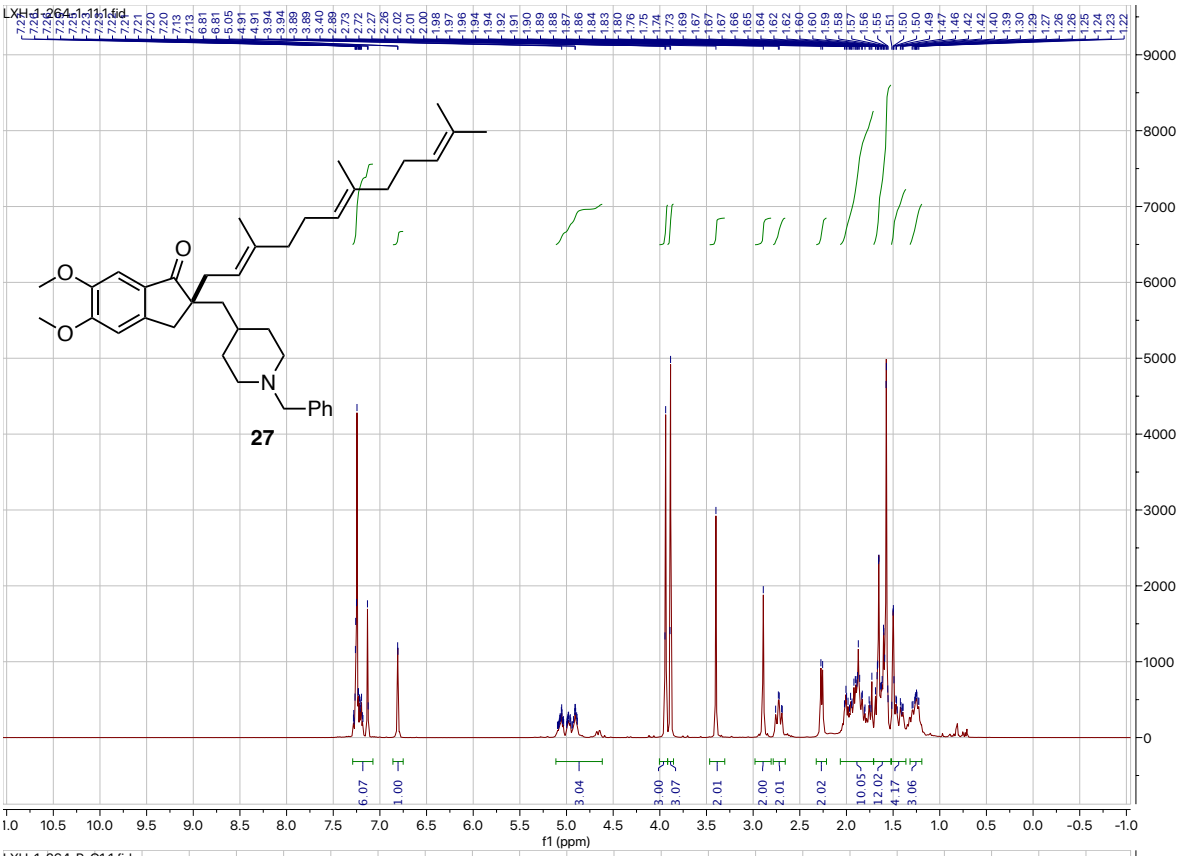

LXH-1-274-2-C.10.fid
24
f1 (ppm)

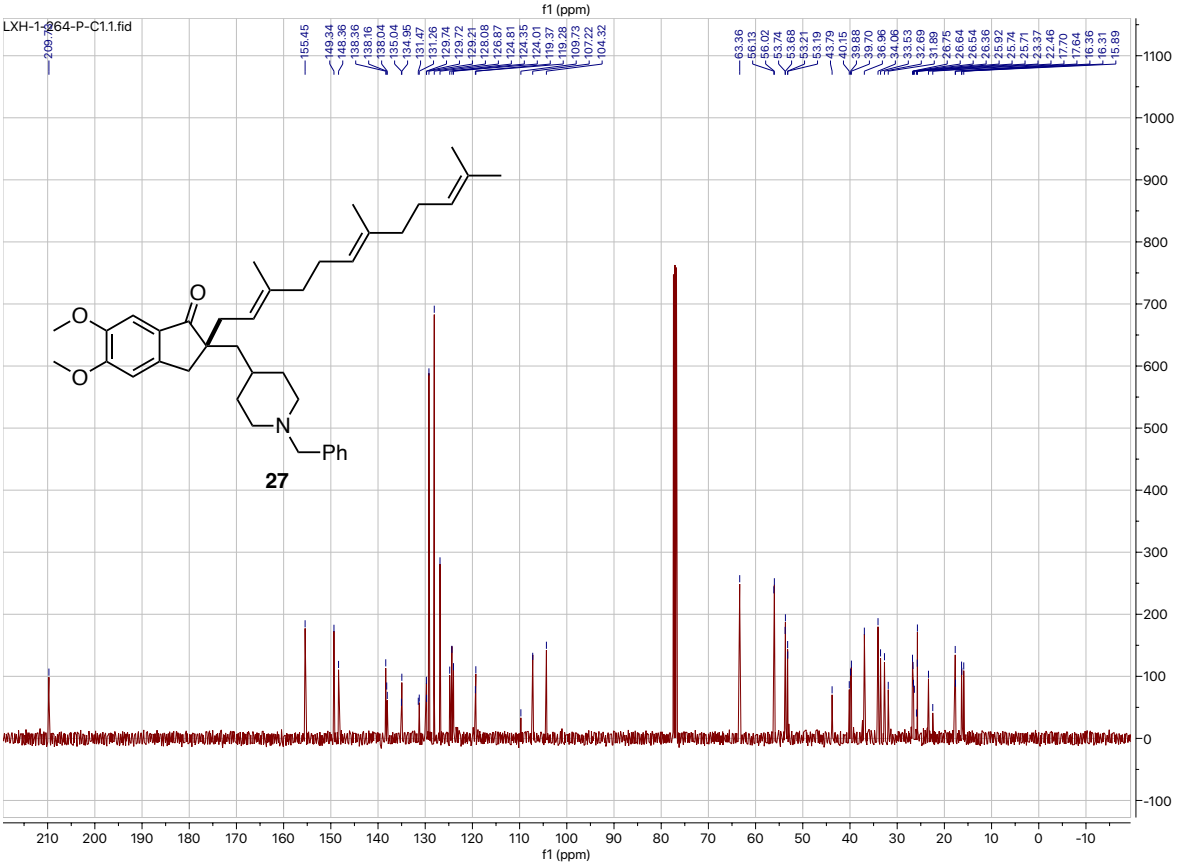

LXH-1-280-1-P2.1.fid
O
Me
N
S
25
f1 (ppm)

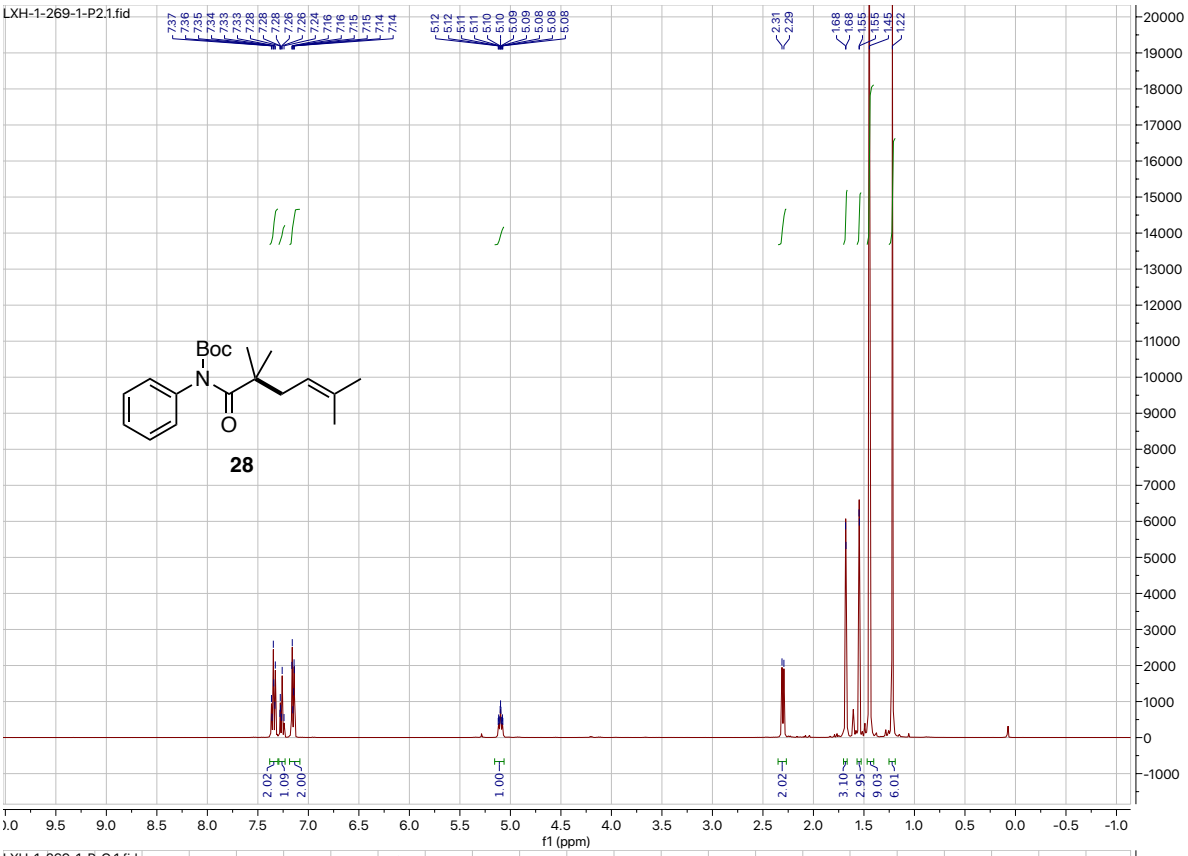

LXH-1-280-1-C.10.fid
O
Me
N
S
25
f1 (ppm)

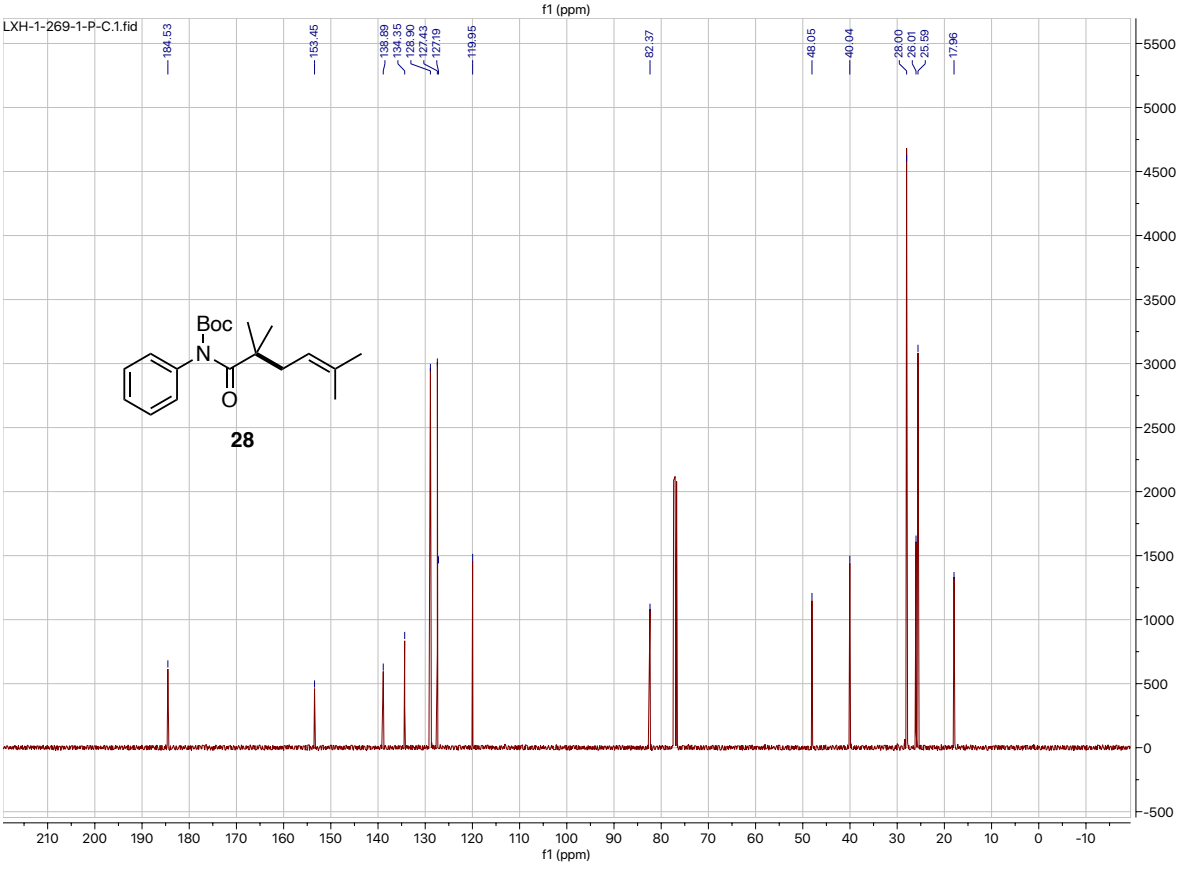

LXH-1-274-3-P2.1.fid
F
O
Me
26
f1 (ppm)

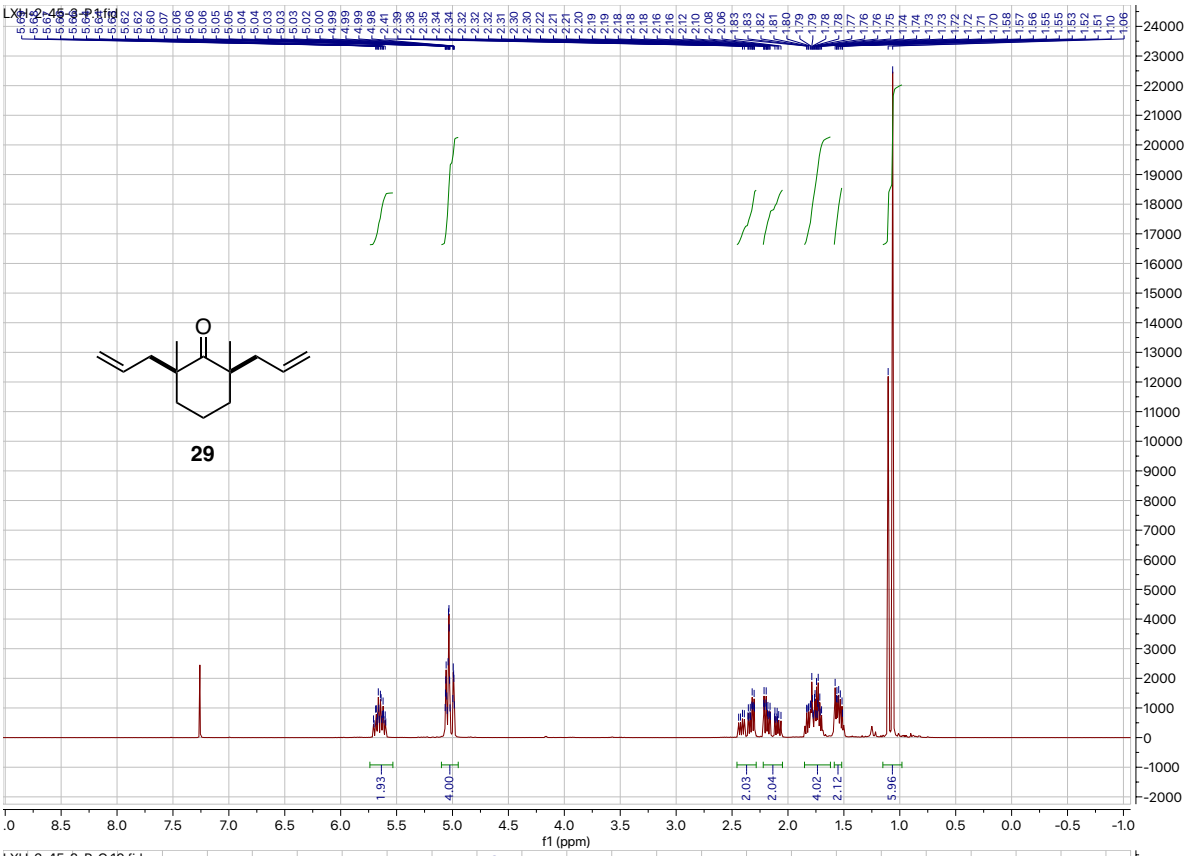

LXH-1-274-3-C.1.fid
F
O
Me
26
f1 (ppm)

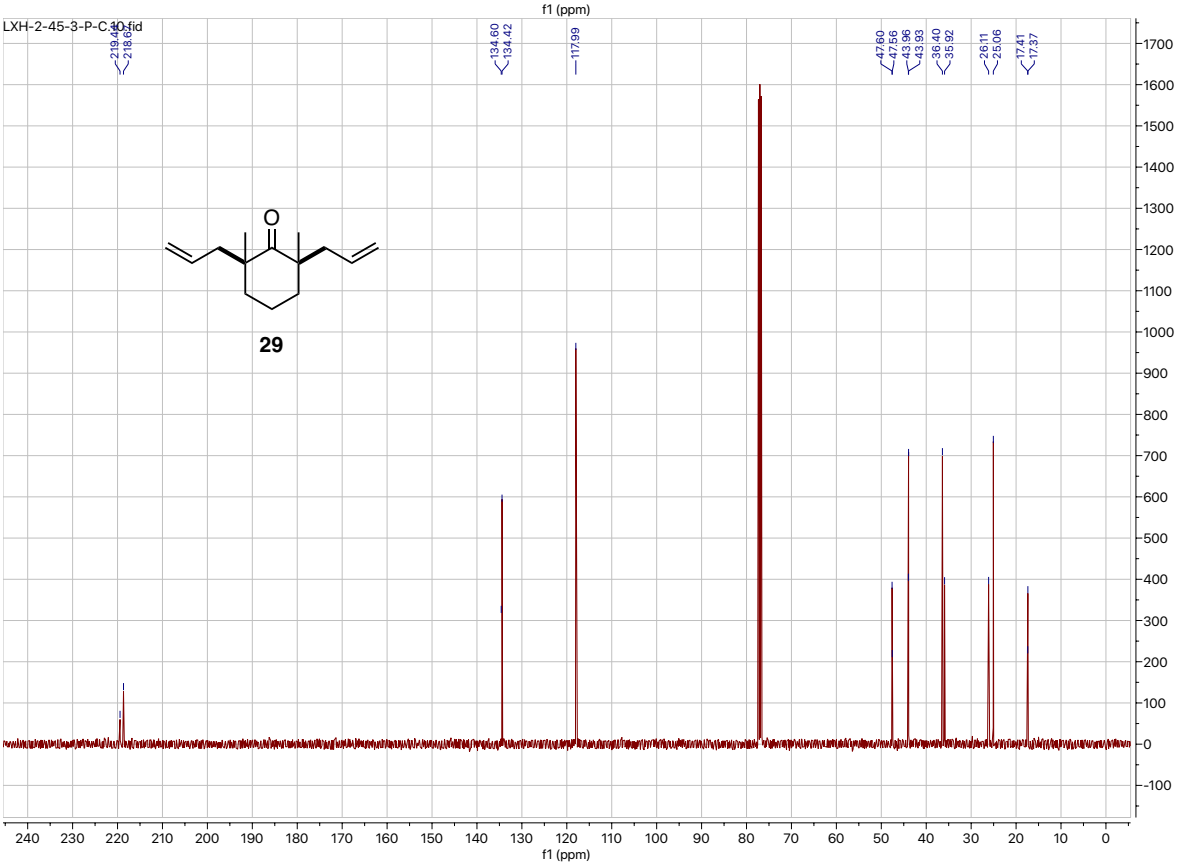

LXH-1-264-1-1.1.fid
O
O
O
N
Ph
27
f1 (ppm)

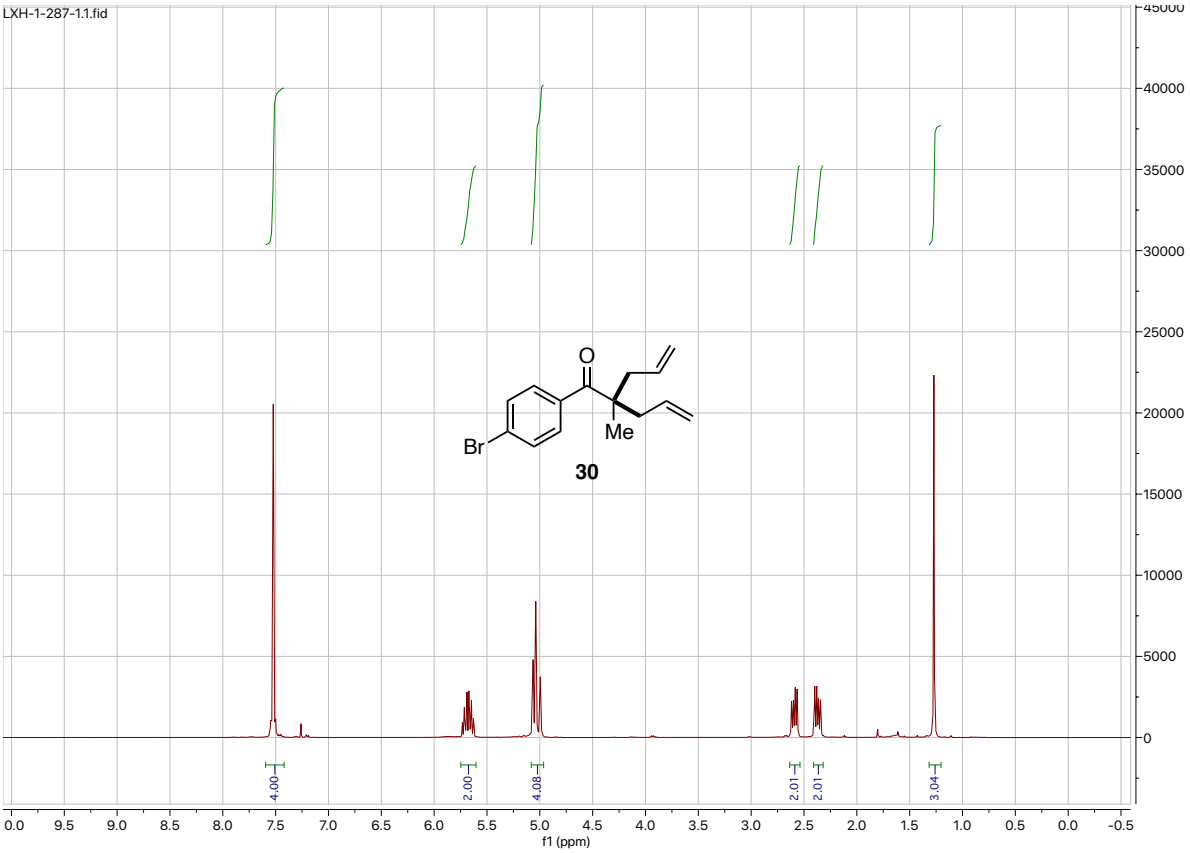

LXH-1-264-P-C1.1.fid
O
O
O
N
Ph
27
f1 (ppm)

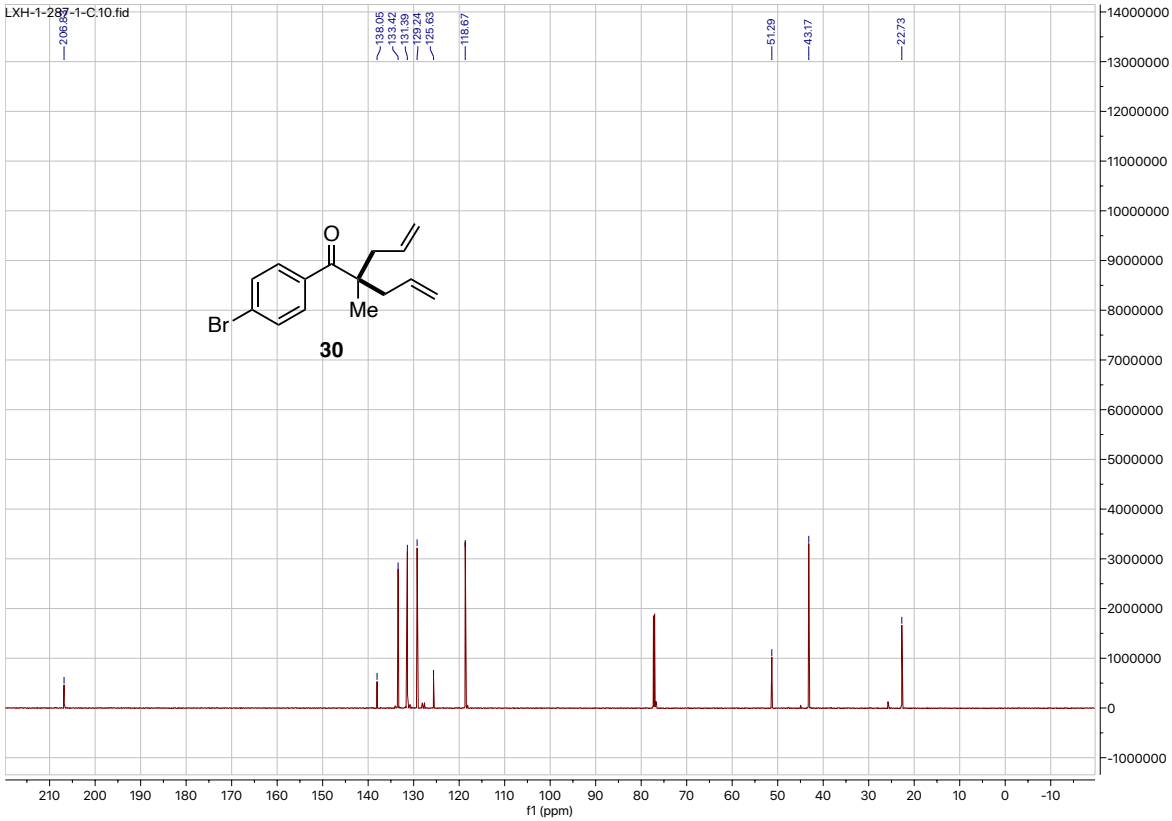

LXH-1-269-1-P2.1.fid
Boc
N
O
28
f1 (ppm)

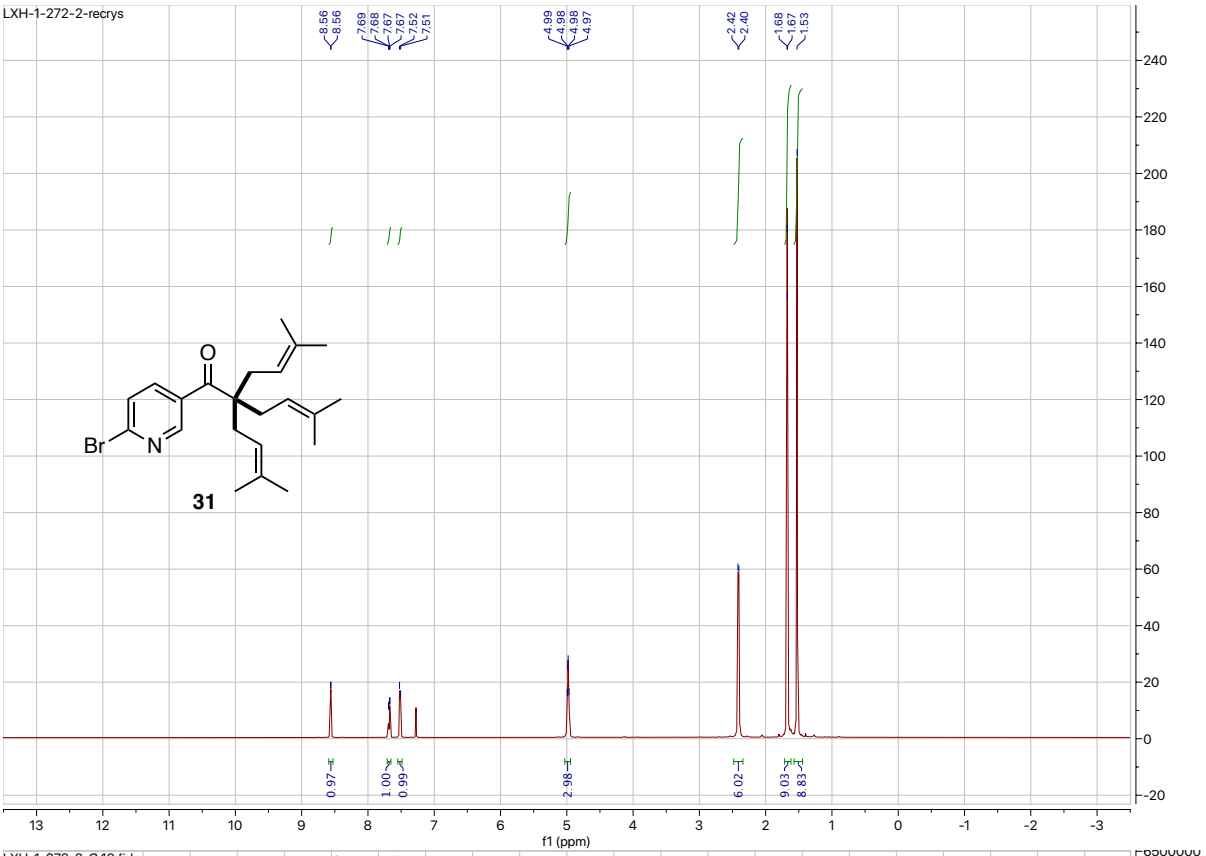

LXH-1-269-1-P-C.1.fid
Boc
N
O
28
f1 (ppm)

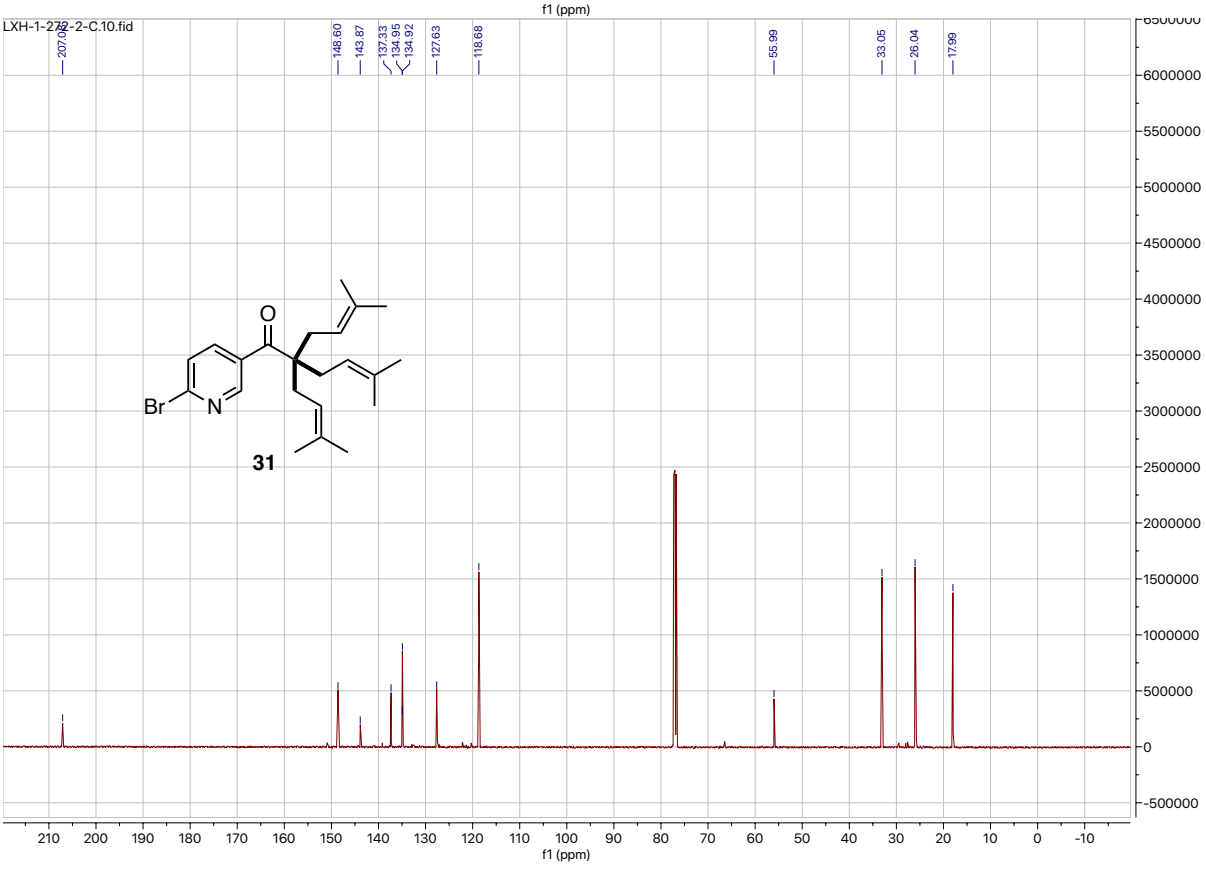

LXH-2-45-3-P1.fid
O
29
1.93
4.00
2.03
2.04
4.02
2.12
5.96
f1 (ppm)

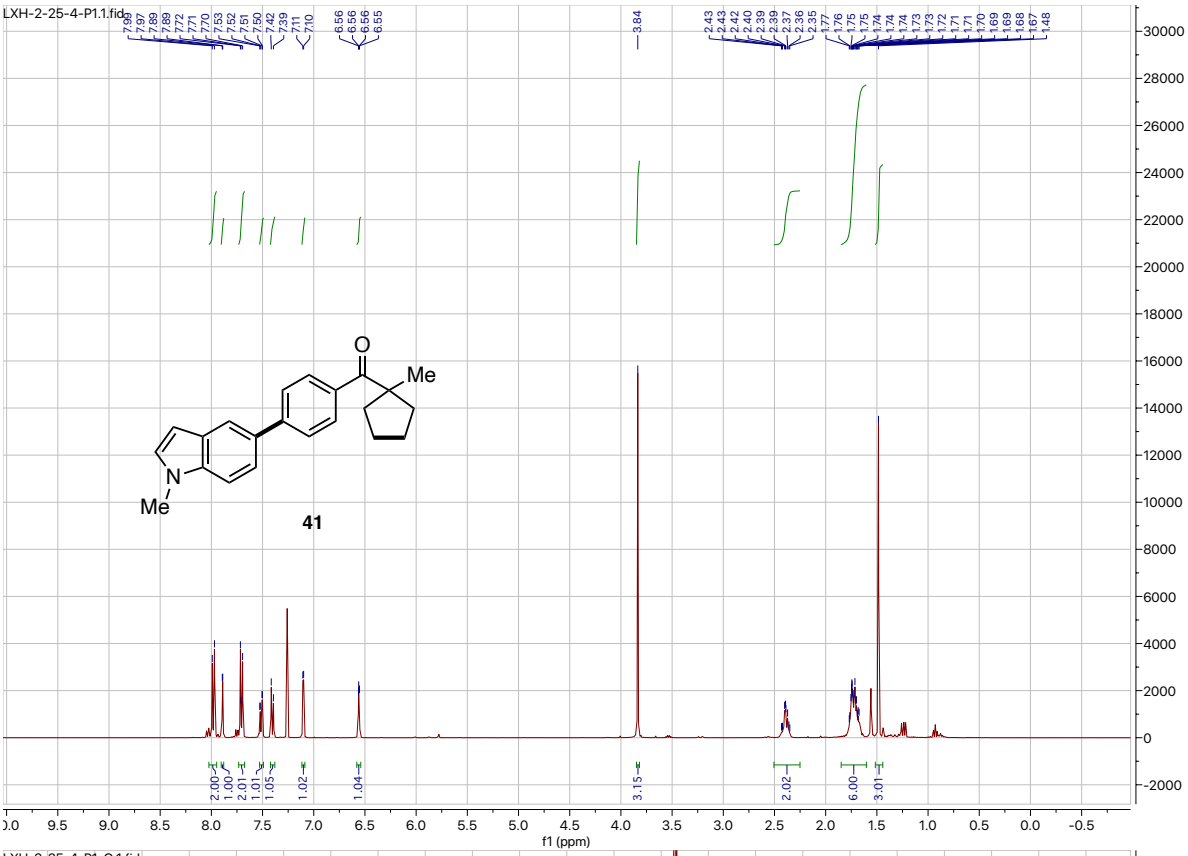

LXH-2-45-3-P-C.10.fid
219.44
218.65
134.60
134.42
117.99
47.60
47.56
43.96
43.93
36.40
35.92
26.11
25.06
17.41
17.37
O
29
f1 (ppm)


LXH-1-287-1.1.fid
O
Br
Me
30
4.00
2.00
4.08
2.01
2.01
3.04
f1 (ppm)


LXH-1-287-1-C.10.fid
206.83
138.05
133.42
131.39
129.24
125.63
118.67
51.29
43.17
22.73
O
Br
Me
30
f1 (ppm)


LXH-1-272-2-recrys
8.56
8.56
7.69
7.68
7.67
7.67
7.52
7.51
4.99
4.98
4.98
4.97
2.42
2.40
1.68
1.67
1.53
0.97
1.00
0.99
2.98
6.02
9.03
8.83
f1 (ppm)
O
Br
N
31


LXH-1-272-2-C.10.fid
207.02
148.60
143.87
137.33
134.95
134.92
127.63
118.68
55.99
33.05
26.04
17.99
f1 (ppm)
O
Br
N
31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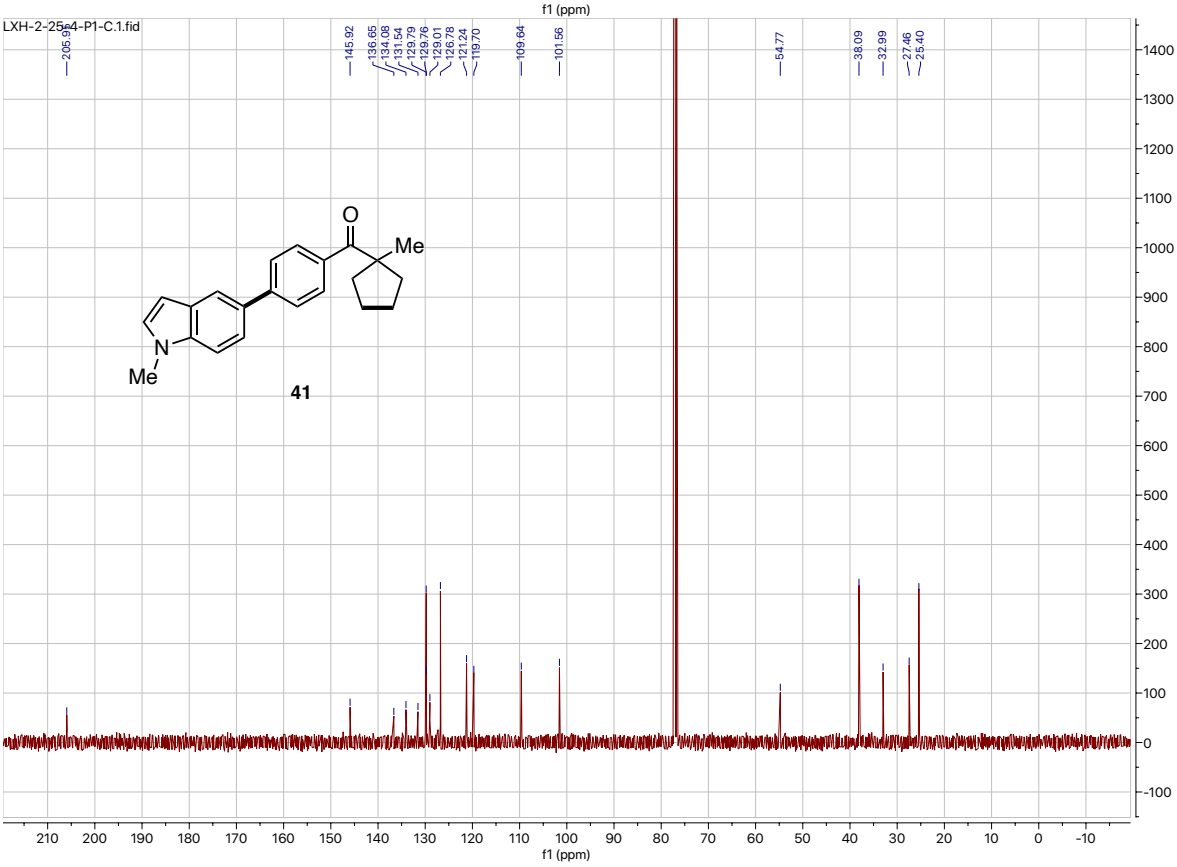
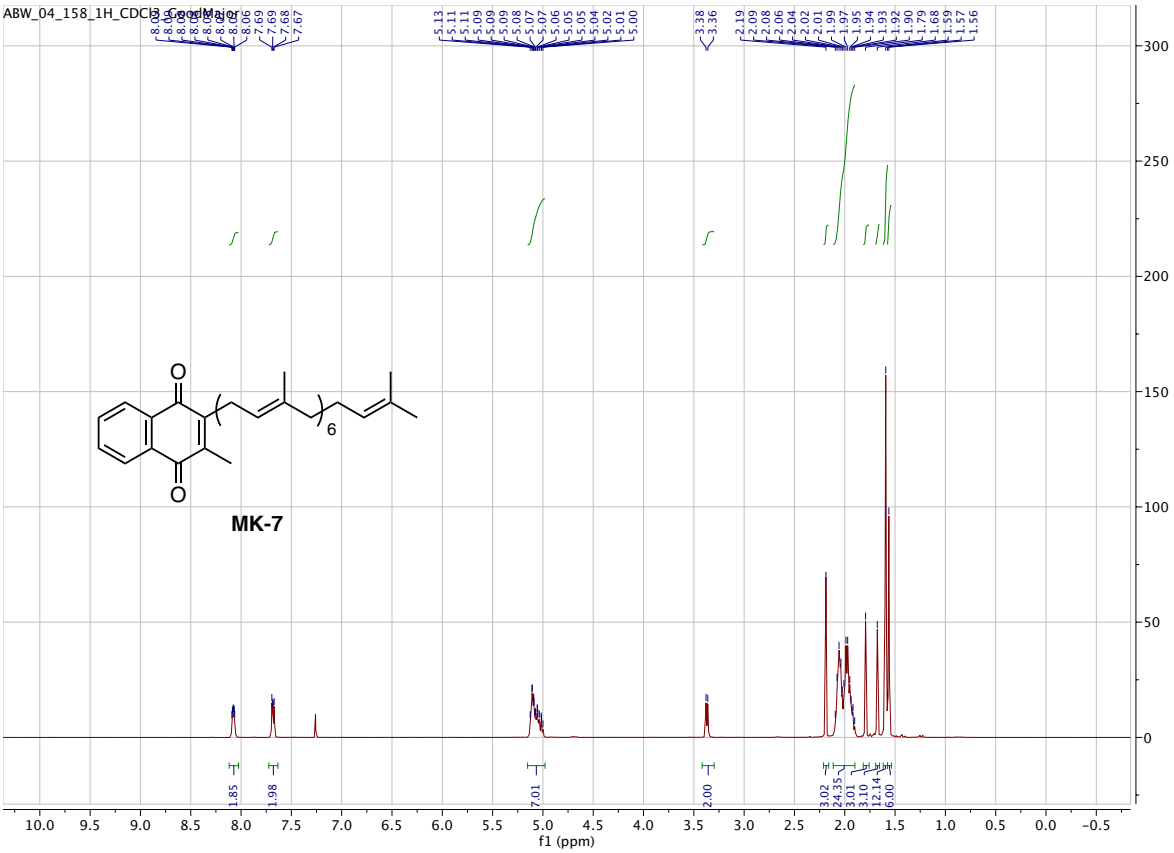
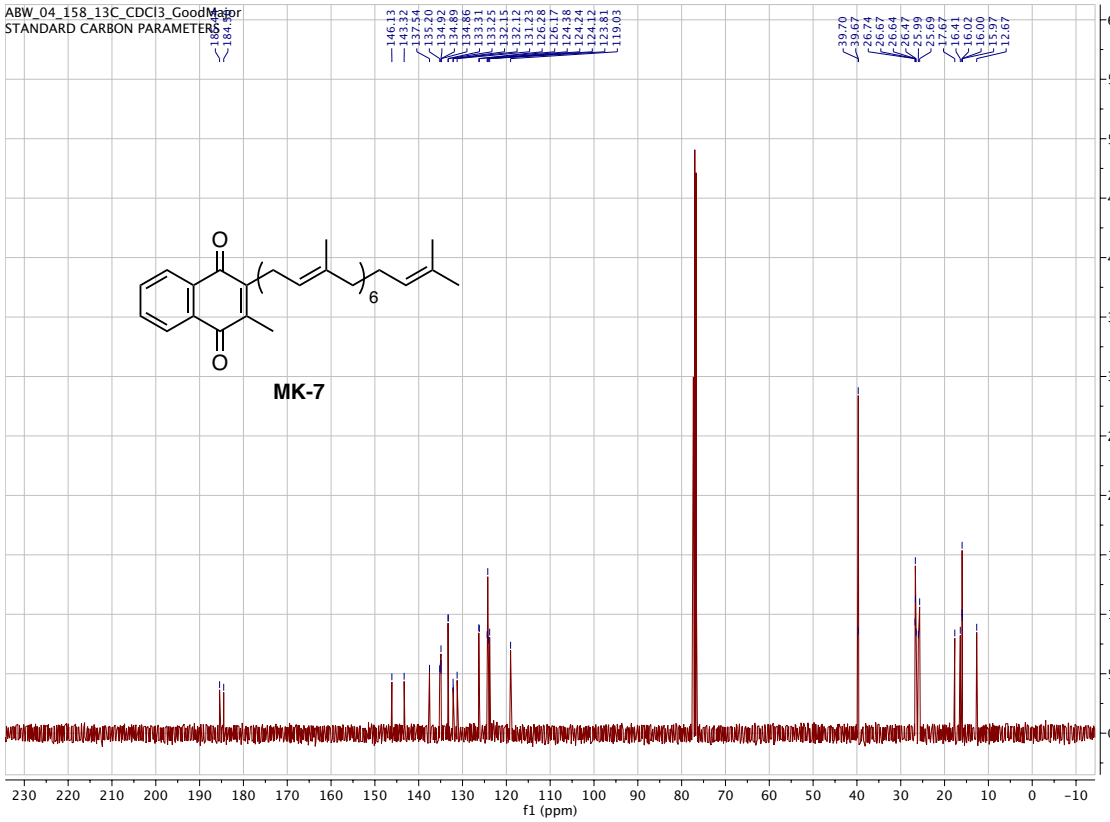
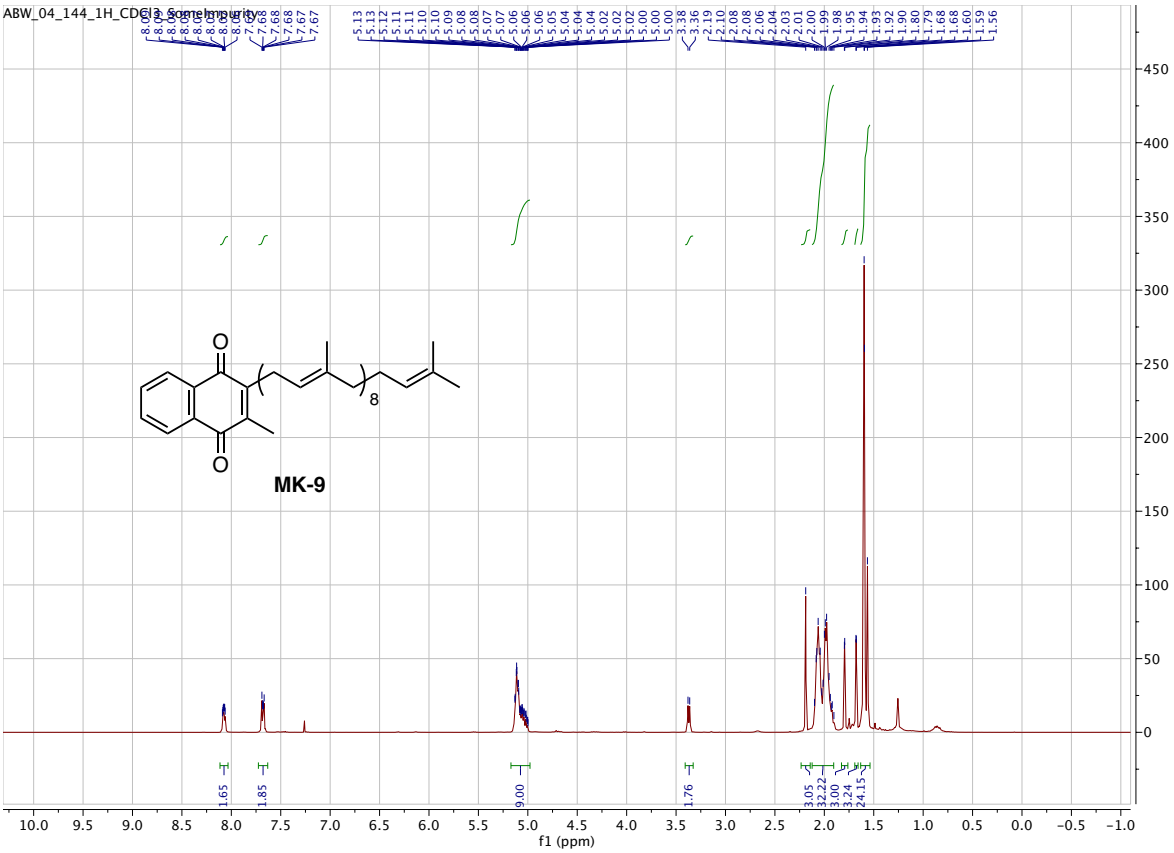
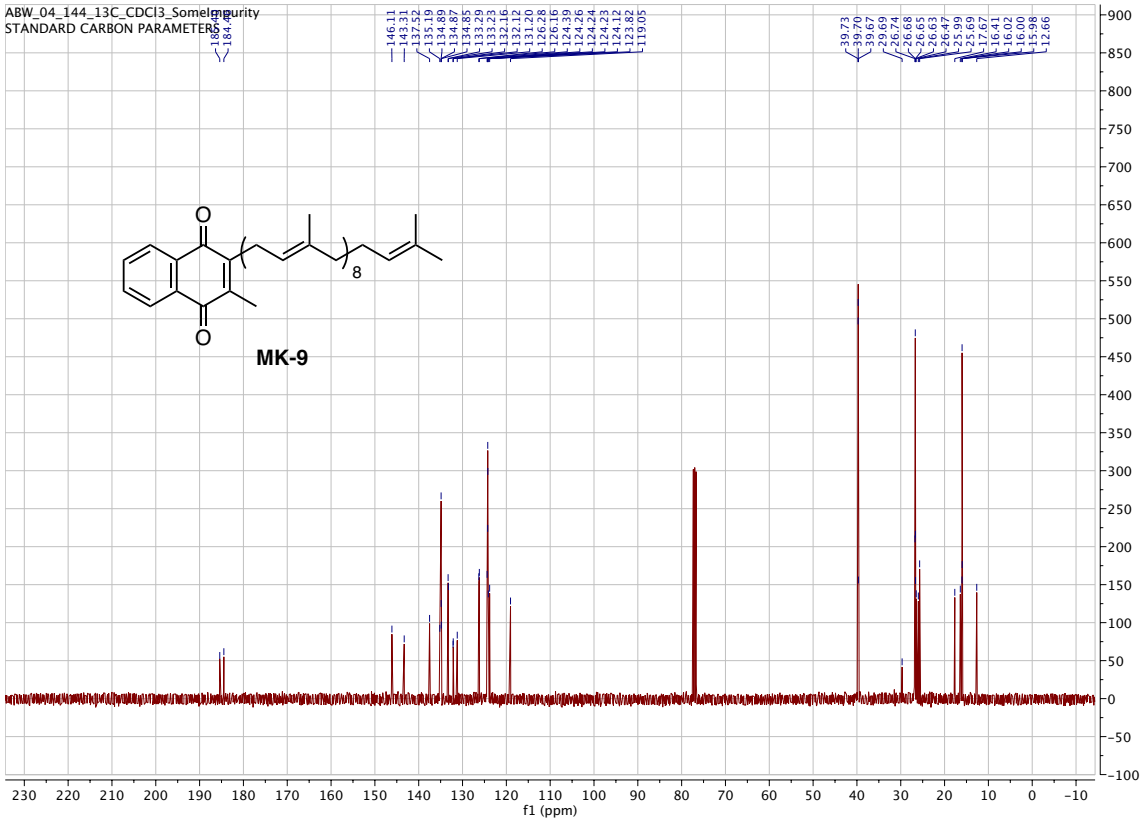
O
Me
N
Me
41
f1 (ppm)

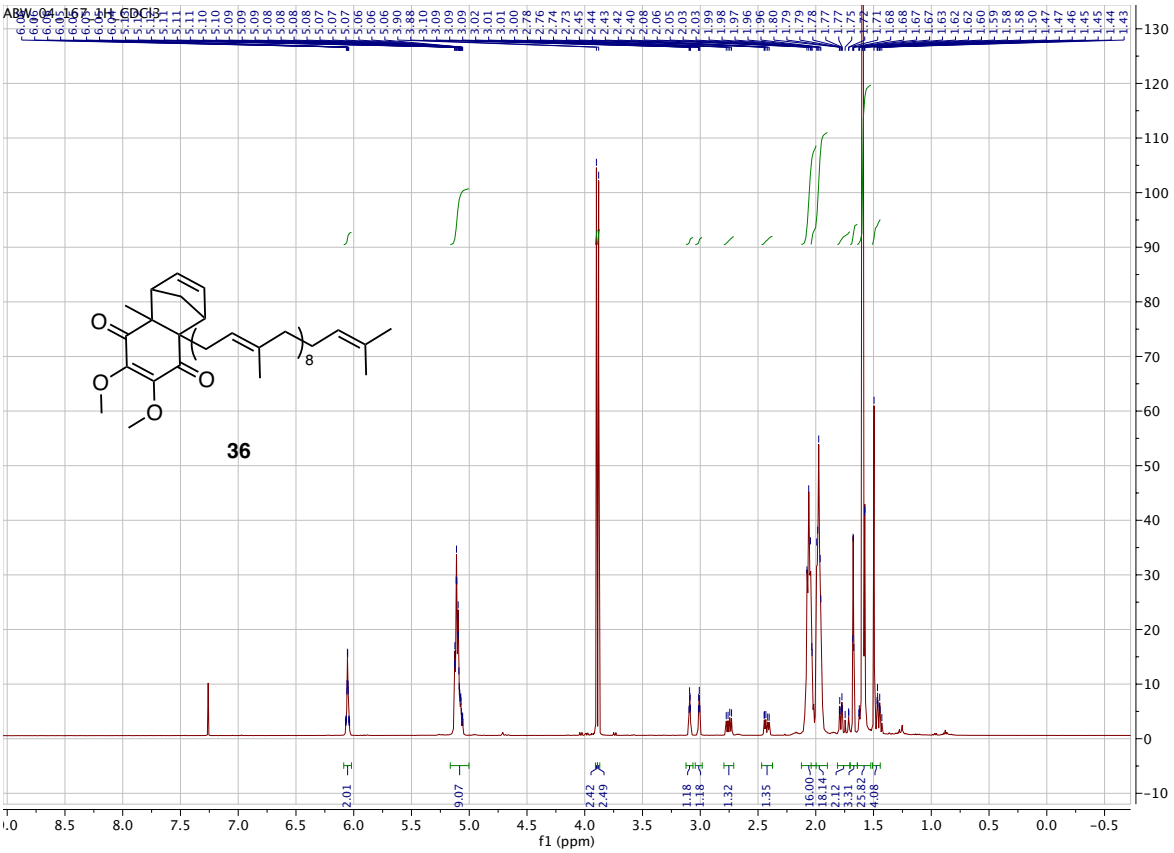

LXH-2-25-4-P1-C.1.fid
O
Me
N
Me
41
f1 (ppm)

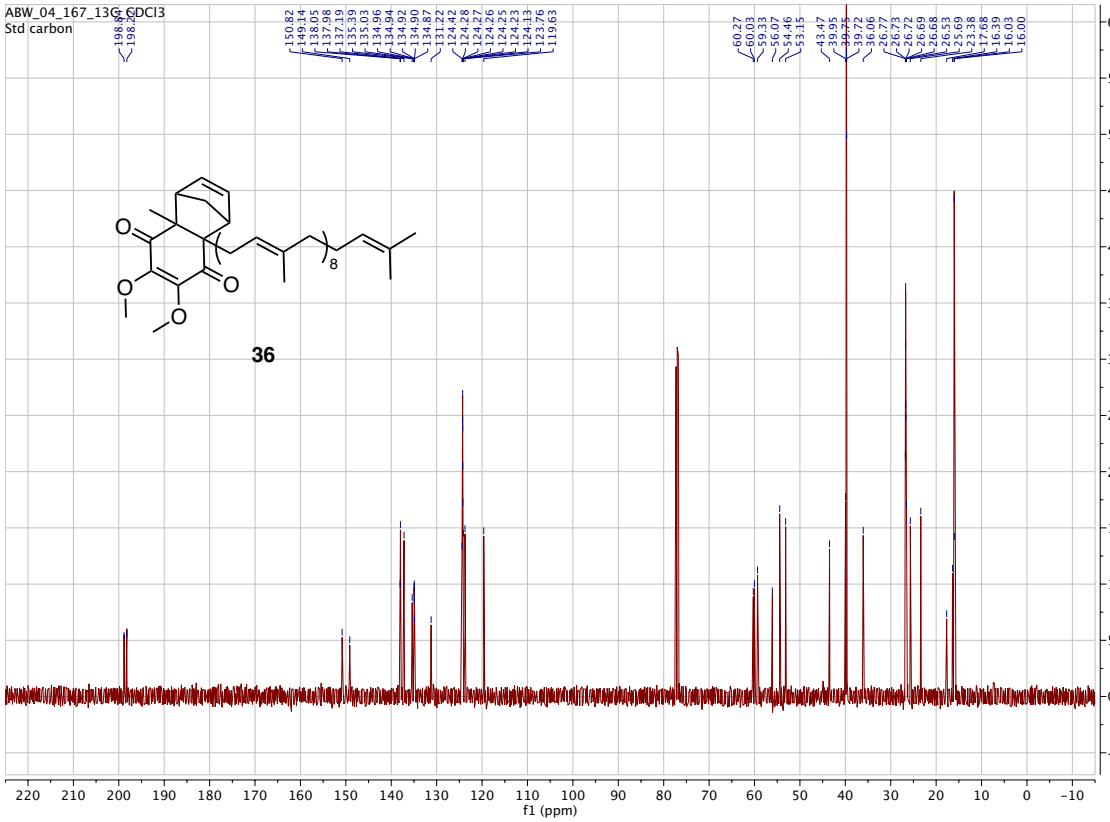

ABW_04_158_1H_CDCl3_GoodMajor
MK-7
f1 (ppm)

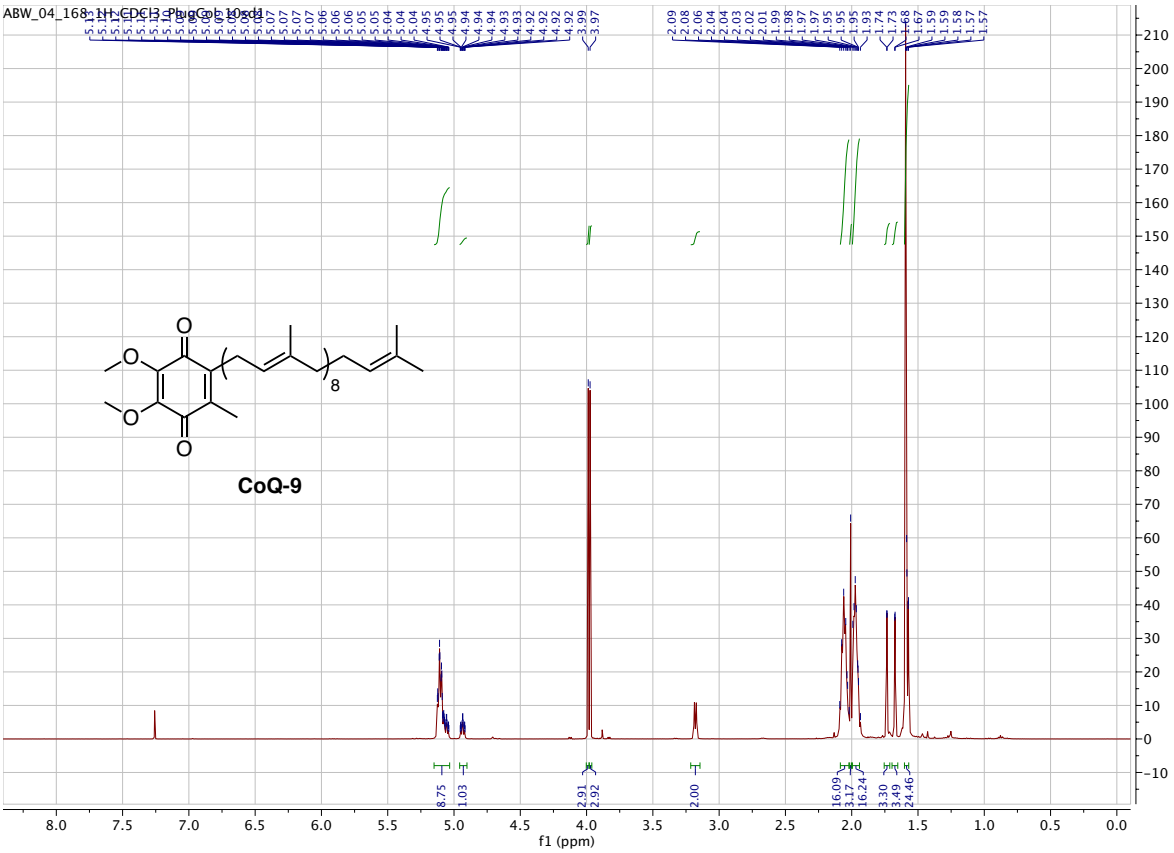

ABW_04_158_13C_CDCl3_GoodMajor
STANDARD CARBON PARAMETERS
MK-7
f1 (ppm)

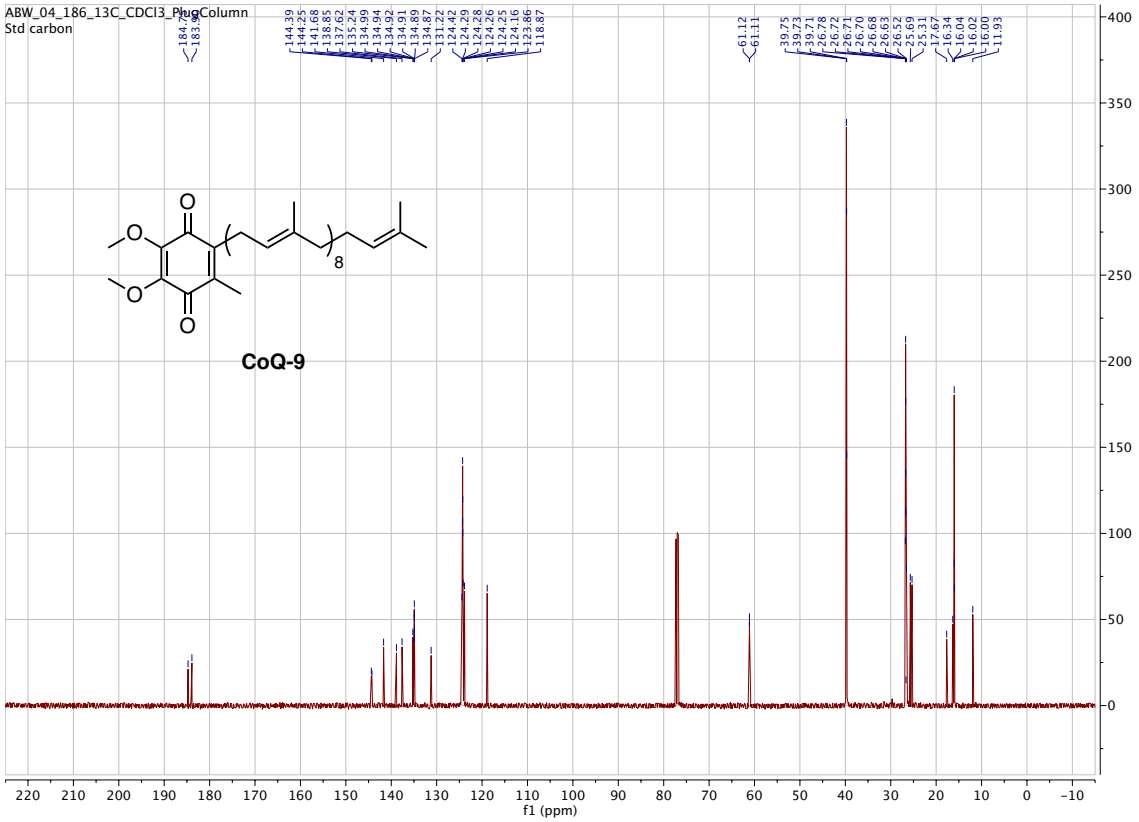

ABW_04_144_1H_CDCl3_Somelmpurity
MK-9
f1 (ppm)


ABW_04_144_13C_CDCl3_Somelmpurity
STANDARD CARBON PARAMETERS
MK-9
f1 (ppm)


ABW_04_167_1H_CDCl3
36
f1 (ppm)


ABW_04_167_13C_CDCl3
Std carbon
36
f1 (ppm)


ABW_04_168_1H_CDCl3_PlugCol_10sd1
CoQ-9
f1 (ppm)


ABW_04_186_13C_CDCl3_PlugColumn
Std carbon
CoQ-9
f1 (ppm)