Synthesis of β,γ-Unsaturated Aliphatic Acids via Ligand-Enabled Dehydrogenation

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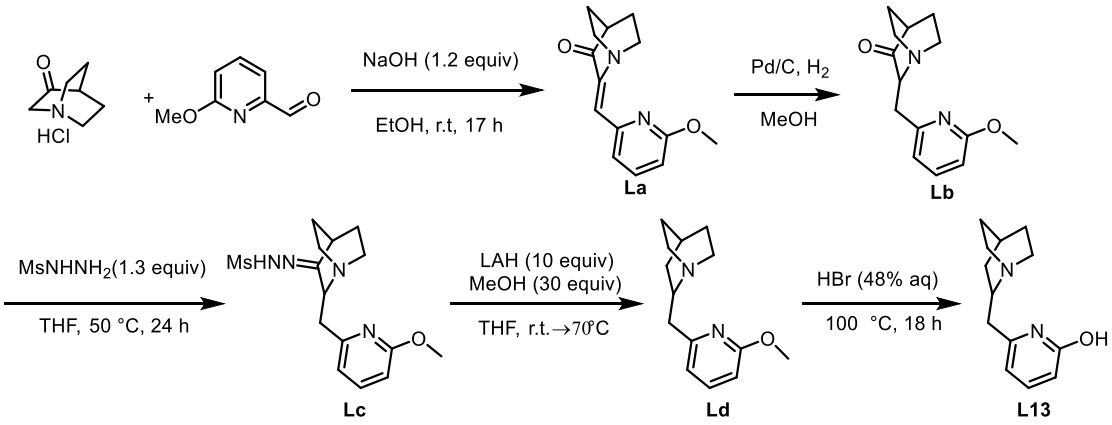
1. General Information:

$Pd(OAc)_2$ was purchased from Strem. Solvents were obtained from Sigma-Aldrich, Alfa-Aesar, and Acros, and used directly without further purification. Other reagents were purchased at the highest commercial quality and used without further purification unless otherwise stated. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254 or Merck pre-coated aluminium-backed silica gel F254 plates. ^{1}H NMR spectra were recorded on Bruker AMX-400 or Bruker DRX-600 instruments. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants, *J*, were reported in the Hertz unit (Hz). ^{13}C NMR spectra were recorded on Bruker DRX-600 and were fully decoupled by broad band proton decoupling. ^{19}F NMR Spectra were recorded on Bruker AMX-400 spectrometer (376 MHz) and were fully decoupled by broadband proton decoupling. Chemical shifts were referenced to the appropriate residual solvent peaks (*35*). Column chromatography was performed using E. Merck silica (60, particle size 0.043–0.063 mm), and pTLC was performed on Merck silica plates (60F-254). High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight).

2. Experimental Section for β, γ-Dehydrogenation Formation

2.1. Optimized Procedure for the Preparation of Ligands L13-L16

Procedure A: Synthesis of 6-(quinuclidin-2-ylmethyl)pyridin-2-ol (L13)



Synthesis of La

To a solution of quinuclidine-3-one hydrochloride (50 mmol, 1.0 equiv., 8.08g) in EtOH (50 mL) at 23 °C was added NaOH (50% in H_2O, 60 mmol, 1.2 equiv., 4.8 g). The resulting solution was stirred for 5 min before 6-methoxypicolinaldehyde (50 mmol, 1.0 equiv., 6.86 g) in 15 mL EtOH was added. The reaction mixture was continued to stir overnight. Upon completion, the yellow solid was filtered and washed with 30 ml H_2O. The solid was dried in high vacuum and used directly in the next step. (70%~90% yield).

Synthesis of Lb

To a solution of **La** (37.8 mmol, 1.0 equiv, 9.22 g) in anhydrous MeOH (100 mL) at 23 °C was added Pd/C (10 wt. %, 922 mg.). Then, H2 in a balloon was applied. The resulting suspension was continued to stir for 5 h. Upon completion (monitored by TLC), the reaction mixture was filtered through celite to remove the Pd/C. The filtrate was concentrated under vacuum and purified through flash column chromatography (eluent: ethyl acetate) to afford **Lb** with 63% yield (5.89g).

Note: long reaction time will result in by-product formation.

Synthesis of Lc

A solution of **Lb** (17.3 mmol, 1.0 equiv, 4.25 g) and $MsNHNH_2$ (25.9 mmol, 1.5 equiv, 2.86 g) in THF (30 mL) was heated to 50 °C and stirred for 24 hours. Upon completion (determined by TLC monitoring), the reaction mixture was cooled to room temperature and passed through filtration paper. The solid was washed with EA (20 mL). Then the solid was dried in high vacuum to get 5.5 g of 3 (94 % yield)

Synthesis of Ld

To a solution of LAH (1 M in THF) (30 mmol, 6.0 equiv., 30 mL) at 0 °C under N_2 was added MeOH (90 mmol, 18 equiv., 3.64 mL) dropwise over 20 min and stirred for additional 10 min. Then, the resulting solution was added dropwise over 30 min to a solution of **Lc** (5 mmol, 1.0 equiv.,1.69 g) in THF (160 mL) at 0 °C under N_2. After the addition, the reaction mixture was heated to 70 °C and stirred overnight (~18 h). Upon completion (monitored by TLC), the mixture was cooled to room temperature and treated with saturated $NaHCO_3$ aqueous solution (20 mL) dropwise. The generated white solid was filtered and washed with ethyl acetate (50 mL). The filtrate was concentrated under vacuum and purified with flash column chromatography (eluent: MeOH/ethyl acetate/Et_3N = 50:50:1) to afford 4 with 55% yield (646 mg).

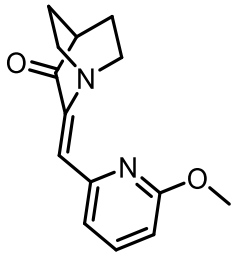
Note: There is some solubility of **Ld** in H_2O. Too much of the saturated $NaHCO_3$ solution will reduce the yield.

Synthesis of L13

A solution of **Ld** (1.48 mmol, 343 mg) in 2 mL HBr (48% aq) in a sealed vial was heated to 100 °C and stirred overnight. Upon completion (monitored by TLC), the reaction mixture was cooled to room temperature and basified with saturated $NaHCO_3$. The resulting mixture was concentrated under vacuum to remove all solvent and extracted with $CHCl_3$ (50 mL*3). The extracts were combined, dried over anhydrous

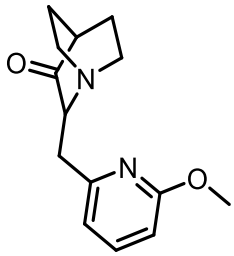
Na_2SO_4, and purified with flash column chromatography (eluent: MeOH/ethyl acetate/Et_3N = 50:50:1) to afford **L13** with 53% yield (171 mg).

Note: After the reaction mixture was basified, all aqueous solution should be removed due to the solubility of the product in it. Other demethylation conditions might give a higher yield.



(*Z*)-2-((6-methoxypyridin-2-yl)methylene)quinuclidin-3-one (La)

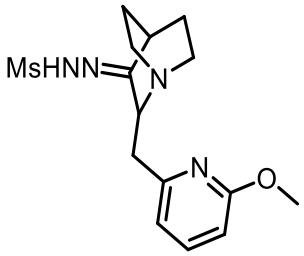
Yellow solid, ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.17 (dd, J = 7.4, 0.8 Hz, 1H), 7.57 (ddd, J = 8.0, 7.4, 0.5 Hz, 1H), 7.08 (s, 1H), 6.67 (dd, J = 8.2, 0.8 Hz, 1H), 3.92 (s, 3H), 3.21 – 3.12 (m, 2H), 3.06 – 2.96 (m, 2H), 2.65 (p, J = 3.0 Hz, 1H), 2.04 (td, J = 7.9, 3.1 Hz, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.0, 163.6, 150.6, 146.7, 138.6, 126.0, 120.5, 111.2, 53.4, 47.5, 40.4, 25.9. HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{17}N_2O_2^+$ $[M+H]^+$ 245.1290, found 245.1289.



2-((6-methoxypyridin-2-yl)methyl)quinuclidin-3-one (Lb)

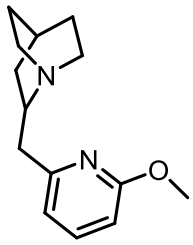
White solid, ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48-7.45 (m, 1H), 6.74 (d, J = 7.2 Hz, 1H), 6.55 (d, J = 8.4Hz, 1H), 3.92 (dd, J = 10.7, 4.1 Hz, 1H), 3.90-3.89 (m, 3H), 3.27 (dd, J = 15.0, 3.6 Hz, 1H), 3.26 – 3.17 (m, 1H), 3.14-3.06 (m, 1H), 2.98 – 2.89 (m, 1H), 2.89 – 2.80 (m, 2H), 2.50 – 2.44 (m, 1H), 2.07 – 1.94 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$)

δ 221.7, 163.8, 156.4, 139.0, 115.9, 108.4, 69.8, 53.3, 49.0, 41.3, 40.3, 36.0, 27.0, 25.2. HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{19}N_2O_2^+$ $[M+H]^+$ 247.1447, found 247.1445.



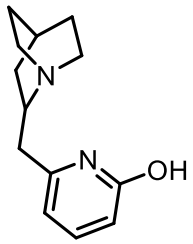
(*Z*)-*N*'-(2-((6-methoxypyridin-2-yl)methyl)quinuclidin-3-ylidene)methanesulfonohydrazide (Lc)

White solid, NMR data was reported for the major diastereomer of the mixture. (Note: the NMR spectra of **Lc** is the Z/E isomer of hydrazone. This intermediate was reduced in the following step without purification.) ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.84 (s, 1H), 7.53 (dd, J = 8.3, 7.1 Hz, 1H), 6.79 (d, J = 7.2 Hz, 1H), 6.67 (d, J = 8.3 Hz, 1H), 4.05 (dd, J = 6.0, 3.3 Hz, 1H), 4.03 (s, 3H), 3.37 – 3.27 (m, 1H), 3.23 – 3.17 (m, 1H), 3.09 (s, 3H), 3.06 – 3.02 (m, 1H), 2.99 – 2.91 (m, 1H), 2.92 – 2.83 (m, 1H), 2.78 – 2.74 (m, 1H), 2.73 – 2.71 (m, 1H), 1.94 – 1.84 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 221.7, 163.8, 156.4, 139.0, 115.9, 108.4, 69.8, 53.3, 49.0, 41.3, 40.3, 36.0, 27.0, 25.2. HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{23}N_4O_3S^+$ $[M+H]^+$ 339.1491, found 339.1487.



2-((6-methoxypyridin-2-yl)methyl)quinuclidine (Ld)

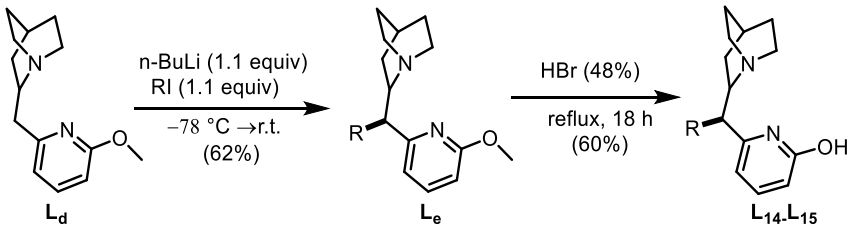
Sticky liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 (dd, J = 8.2, 7.2 Hz, 1H), 6.73 (dd, J = 7.2, 0.7 Hz, 1H), 6.53 (dd, J = 8.2, 0.8 Hz, 1H), 3.91 (s, 3H), 3.38 – 3.28 (m, 1H), 3.16 – 3.06 (m, 1H), 2.99 – 2.89 (m, 3H), 2.82 – 2.71 (m, 2H), 1.79 – 1.72 (m, 1H), 1.69 – 1.61 (m, 1H), 1.56 – 1.43 (m, 4H), 1.29 – 1.18 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.7, 157.9, 138.8, 116.1, 107.6, 55.9, 53.3, 50.1, 43.8, 41.9, 33.7, 27.1, 25.8, 22.1. HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{21}N_2O^+$ $[M+H]^+$ 233.1654, found 233.1662.



6-(quinuclidin-2-ylmethyl)pyridin-2-ol (L13)

White solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.27 – 7.23 (m, 1H), 6.38 (dt, J = 9.1, 1.0 Hz, 1H), 5.94 (d, J = 6.8 Hz, 1H), 3.21 (q, J = 8.9 Hz, 1H), 3.15 – 2.99 (m, 3H), 2.95 – 2.85 (m, 2H), 2.39 (dd, J = 16.1, 3.3 Hz, 1H), 1.94 – 1.82 (m, 2H), 1.65 – 1.52 (m, 4H), 1.20 – 1.12 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 148.4, 140.8, 117.9, 104.9, 55.7, 49.1, 40.3, 33.9, 33.6, 26.4, 25.1, 21.6. HRMS (ESI-TOF) *m/z* Calcd for $C_{13}H_{18}N_2O^+$, $[M+H]^+$ 219.1497, found 219.1497.

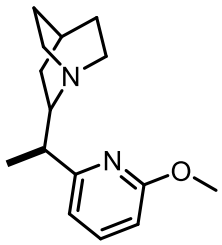
Procedure B: Synthesis of 6-(1-(quinuclidin-2-yl)ethyl)pyridin-2-ol (L14,L15)



To a solution of **L_d** (2.72 mmol, 632 mg) in 8 mL THF at -78 °C under nitrogen atmosphere was added n-BuLi (2.5 M in hexanes) (3.00 mmol, 1.1 equiv, 1.20 mL) dropwise over 20 min. The reaction mixture was allowed to stir for 1 h before the addition of MeI (3.00 mmol, 1.1 equiv., 425.8 mg). The resulting mixture was warmed to room temperature gradually and stirred overnight. After completion, the mixture was concentrated and purified with flash column chromatography (eluent: MeOH/ethyl acetate = 0→50%) to afford **Le** with 62% yield (421 mg).

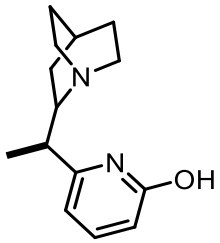
A solution of **Le** (1.36 mmol, 334 mg) in 2 mL HBr (48% aq) in a sealed vial was heated to 100 °C and stirred overnight. Upon completion (monitored by TLC), the reaction mixture was cooled to room temperature and basified with saturated $NaHCO_3$.

The resulting mixture was concentrated under vacuum to remove all solvent and extracted with $CHCl_3$ (50 mL*3). The extracts were combined, dried over anhydrous Na_2SO_4, and purified with flash column chromatography (eluent: MeOH/ethyl acetate/Et_3N = 50:50:1) to afford **L14** with 60% yield (189 mg).



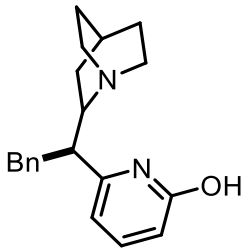
2-(1-(6-methoxypyridin-2-yl)ethyl)quinuclidine (Le)

Colorless liquid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.59 (dd, J = 8.3, 7.2 Hz, 1H), 6.85 (d, J = 7.4 Hz, 1H), 6.72 (dd, J = 8.4, 0.8 Hz, 1H), 3.96 (s, 3H), 3.97 - 3.90 (m, 1H), 3.80 - 3.72 (m, 1H), 3.72 - 3.65 (m, 1H), 3.39 - 3.26 (m, 2H), 3.22 - 3.17 (m, 1H), 2.32 (s, 1H), 2.30 - 2.22 (m, 1H), 2.00 - 1.86 (m, 4H), 1.98 - 1.87 (m, 1H), 1.32 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.9, 156.7, 140.6, 115.9, 111.0, 61.6, 54.1, 49.9, 42.6, 42.4, 30.3, 23.3, 22.5, 21.3, 18.2. HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{23}N_2O^+$, $[M+H]^+$ 247.1810, found 247.1806.



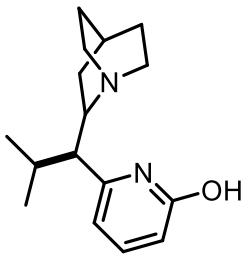
6-(1-(quinuclidin-2-yl)ethyl)pyridin-2-ol (L14)

White solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.34 (s, 1H), 7.29 (dd, J = 9.1, 7.0 Hz, 1H), 6.37 (d, J = 9.1 Hz, 1H), 6.02 (d, J = 7.0 Hz, 1H), 3.06 - 2.91 (m, 3H), 2.90 - 2.77 (m, 2H), 2.72 - 2.62 (m, 1H), 1.88 - 1.82 (m, 2H), 1.60 - 1.47 (m, 4H), 1.33 - 1.25 (m, 1H), 1.21 (d, J = 6.8 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.4, 153.5, 140.7, 118.1, 102.5, 60.5, 48.7, 40.6, 34.6, 32.8, 26.6, 25.2, 21.9, 13.4. HRMS (ESI-TOF) *m/z* Calcd for $C_{14}H_{21}N_2O^+$, $[M+H]^+$ 233.1654, found 233.1664.



6-(2-phenyl-1-(quinuclidin-2-yl)ethyl)pyridin-2-ol (L15)

White solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.05 (s, 1H), 7.21 - 7.11 (m, 4H), 7.01 (d, J = 7.4 Hz, 2H), 6.32 (d, J = 9.1 Hz, 1H), 5.77 (d, J = 6.9 Hz, 1H), 3.16 (q, J = 9.2 Hz, 1H), 3.10 (dd, J = 14.0, 3.0 Hz, 1H), 2.95 - 2.76 (m, 5H), 2.69 – 2.60 (m, 1H), 2.04 – 1.96 (m, 1H), 1.86 (s, 1H), 1.55 – 1.42 (m, 4H), 1.38 – 1.30 (m, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.1, 151.3, 141.1, 139.0, 128.9, 128.5, 126.4, 117.4, 105.9, 58.2, 49.5, 49.2, 41.4, 36.8, 33.7, 26.9, 25.6, 22.3. HRMS (ESI-TOF) *m/z* Calcd for $C_{20}H_{25}N_2O^+$, $[M+H]^+$ 309.1967, found 309.1978.

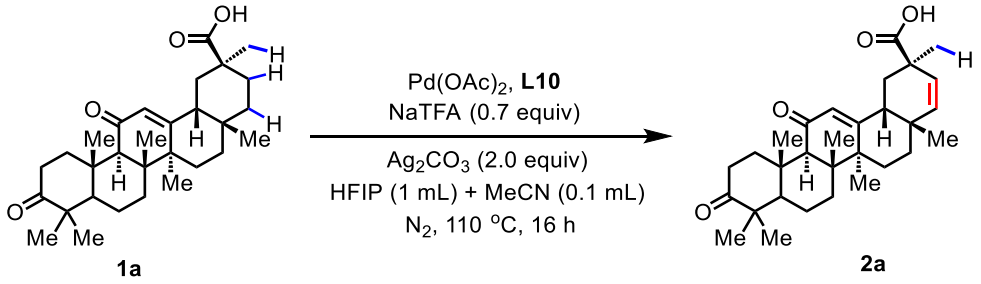


6-(2-methyl-1-(quinuclidin-2-yl)propyl)pyridin-2-ol (L16)

White solid. ^{1}H NMR (600 MHz, $CDCl_3$) δ 11.60 (s, 1H), 7.34 (dd, J = 9.1, 6.9 Hz, 1H), 6.37 (dd, J = 9.1, 1.0 Hz, 1H), 5.95 (dd, J = 7.0, 1.0 Hz, 1H), 3.12 – 3.02 (m, 1H), 2.88 – 2.74 (m, 3H), 2.67 (dd, J = 11.4, 3.8 Hz, 1H), 2.57 – 2.48 (m, 1H), 2.14 – 2.01 (m, 1H), 1.86 – 1.77 (m, 2H), 1.55 – 1.35 (m, 4H), 1.29 – 1.21 (m, 1H), 0.88 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.9 Hz, 3H). ^{13}C NMR (151 MHz, CDCl3) δ 165.1, 150.1, 141.1, 116.9, 106.0, 56.3, 53.3, 49.8, 41.6, 33.2, 27.8, 26.9, 25.8, 22.3, 22.3, 17.0. HRMS (ESI-TOF) *m/z* Calcd for $C_{16}H_{25}N_2O^+$, $[M+H]^+$ 261.1967, found 261.1972.

2.2. Condition Screenings for Dehydrogenation Reaction

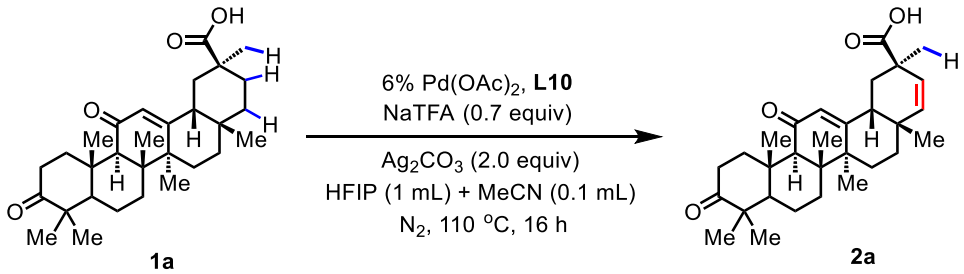
Table S1. Pd Loading Effects[a,b]



entry	Pd amount	yield (%)
1	0.1 mol%	trace
2	0.5 mol%	32 (54)[c]
3	1 mol%	68 (82)[d]
4	2 mol%	78
5	4 mol%	95
6	6 mol%	99
7	8 mol%	99

[a]Conditions: **1a** (0.1 mmol), $Pd(OAc)_2$, **L10** (1.6 equiv. relative to Pd), Ag_2CO_3 (2.0 equiv), NaTFA (0.7 equiv), HFIP (1.0 mL), MeCN (0.1 mL), 110 °C, 16 h. [b]The yields were determined by ^1H NMR using CH_2Br_2 as the internal standard. [c]120 °C. [d]Ag_2CO_3 (1.5 equiv), HFIP (0.5 mL), MeCN (0.05 mL), 120 °C, 24 h.

Table S2. Pd Loading Effects[a,b]

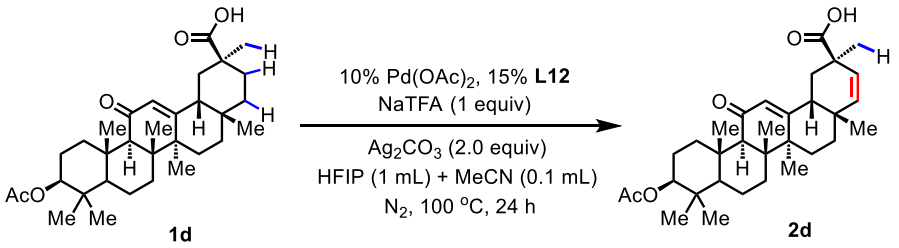


1a 2a

entry	Ligand amount	yield (%)
1	6 mol%	90
2	8 mol%	98
3	10 mol%	99
4	12 mol%	99
5	15 mol%	99

[a]Conditions: **1a** (0.1 mmol), $Pd(OAc)_2$ (6 mol%), **L10**, Ag_2CO_3 (2.0 equiv), NaTFA (0.7 equiv), HFIP (1.0 mL), MeCN (0.1 mL), 110 °C, 16 h. [b]The yields were determined by ^1H NMR using CH_2Br_2 as the internal standard.

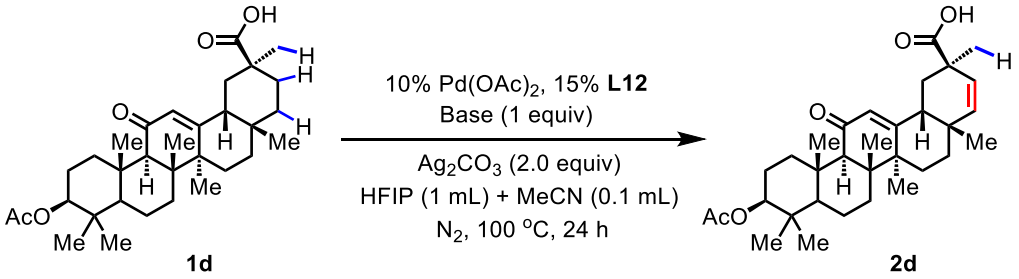
Table S3. Solvent Effects[a,b]



Solvent	yield (%)
HFIP (1 mL)	trace
MeCN (1 mL)	20
HFIP (1 mL) + MeCN (0.1 mL)	88
HFIP (1 mL) + MeCN (0.2 mL)	56
HFIP (1 mL) +DMF (0.1 mL)	12
HFIP (1 mL) + Dioxane (0.1 mL)	22
HFIP (1 mL) + THF (0.1 mL)	12
HFIP (1 mL) + DCE (0.1 mL)	8
HFIP (1 mL) + Tolene (0.1 mL)	21
HFIP (1 mL) + DMSO (0.1 mL)	28
HFIP (1 mL) + ^{t}BuOH (0.1 mL)	8
HFIP (1 mL), no MeCN, 6 mol% $PdCl_2(MeCN)_2$	32
HFIP (1 mL), no MeCN, 6 mol% $PdCl_2(PhCN)_2$	32

[a]Conditions: **1d** (0.1 mmol), $Pd(OAc)_2$ (10 mol%), **L12** (15 mol%), Ag_2CO_3 (2.0 equiv), NaTFA (1.0 equiv), solvent, 100 °C, 24 h. [b]The yields were determined by ^{1}H NMR using CH_2Br_2 as the internal standard.

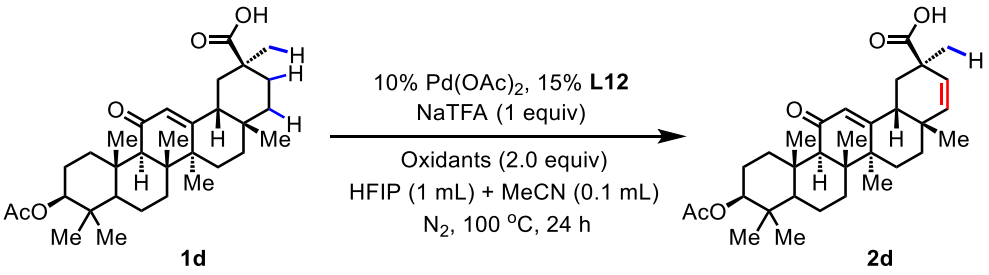
Table S4. Base Effects[a,b]



Base	yield (%)	Base	yield (%)
^{t}BuOK	80	NaOAc	42
K_2HPO_4	80	K_2CO_3	80
NaTFA	88	CsF	76
NaTFA (2.0 equiv)	70	KF	70
LiTFA	69	K_3PO_4	10
$LiOH·H_2O$	64	w/o	84
LiF	70		

[a]Conditions: **1d** (0.1 mmol), $Pd(OAc)_2$ (10 mol%), **L12** (15 mol%), Ag_2CO_3 (2.0 equiv), base, HFIP (1.0 mL), MeCN (0.1 mL), 100 °C, 24 h. [b]The yields were determined by ^{1}H NMR using CH_2Br_2 as the internal standard.

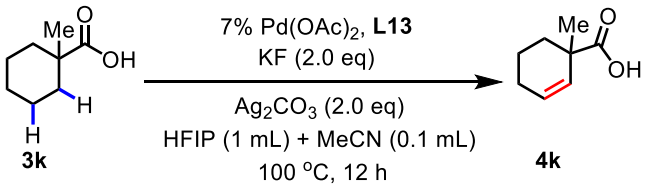
Table S5. Screenings of Oxidants[a,b]



Oxidants	yield (%)	Oxidants	yield (%)
Ag_2CO_3	86	$^tBuOO^tBu$	28
AgOAc	60	w/o	trace
$AgNO_3$	n. d.	No base, Ag_2CO_3	84
Ag_2O	94	No base, Ag_2O	88
$Na_2S_2O_8$	8	No base, AgOAc	54
$NaCO_3$/ 1.5 H_2O_2	8	No base, TBHP in H_2O	18
TBHP in H_2O	35	No base, $^tBuOO^tBu$	8
TBHP in Hexane	36		

[a]Conditions: **1d** (0.1 mmol), $Pd(OAc)_2$ (10 mol%), **L12** (15 mol%), oxidants, NaTFA (1.0 equiv), HFIP (1.0 mL), MeCN (0.1 mL), 100 °C, 24 h. [b]The yields were determined by ^1H NMR using CH_2Br_2 as the internal standard.

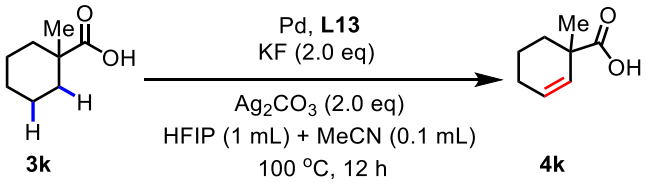
Table S6. Ligand Loading Effects[a,b]



entry	Ligand amount	yield (%)
1	7 mol%	44
2	9 mol%	52
3	11 mol%	58
4	13 mol%	58
5	16 mol%	64
6	20 mol%	62

[a]Conditions: **3k** (0.1 mmol), $Pd(OAc)_2$ (7 mol%), **L13**, Ag_2CO_3 (2.0 equiv), KF (2.0 equiv), HFIP (1.0 mL), MeCN (0.1 mL), 100 °C, 16 h. [b]The yields were determined by ^1H NMR using CH_2Br_2 as the internal standard.

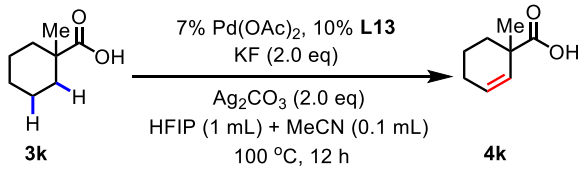
Table S7. Pd Loading Effects[a,b]



entry	Pd	yield (%)
1	2 mol% $Pd(OAc)_2$	32
2	3 mol% $Pd(OAc)_2$	44
3	5 mol% $Pd(OAc)_2$	56
4	6 mol% $Pd(OAc)_2$	58
5	8 mol% $Pd(OAc)_2$	46
6	10 mol% $Pd(OAc)_2$	32
7	6 mol% $Pd(TFA)_2$	54
8	6 mol% $Pd(dba)_2$	54
9	6 mol% $Pd(PhCN)_2Cl_2$	50
10	6 mol% $PdCl_2(MeCN)_2$	50

[a]Conditions: **3k** (0.1 mmol), Pd, **L13** (1.4 equiv. relative to Pd), Ag_2CO_3 (2.0 equiv), KF (2.0 equiv), HFIP (1.0 mL), MeCN (0.1 mL), 100 °C, 12 h. [b]The yields were determined by ^1H NMR using CH_2Br_2 as the internal standard.

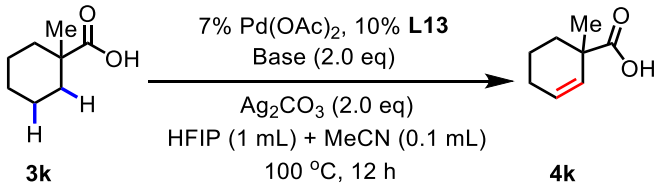
Table S8. Solvent Effects[a,b]



Solvent	yield (%)	Solvent	yield (%)
HFIP (1 mL)	0	HFIP (1 mL) +DMF (0.1 mL)	4
HFIP (1 mL) + MeCN (0.1 mL)	44	HFIP (1 mL) + Dioxane (0.1 mL)	0
THF (1 mL) + MeCN (0.1 mL)	36	HFIP (1 mL) + DMA (0.1 mL)	4
Toluene (1 mL) + MeCN (0.1 mL)	6	HFIP (1 mL) + DCE (0.1 mL)	0
Dioxane (1 mL) + MeCN (0.1 mL)	26	HFIP (1 mL) + Tolene (0.1 mL)	0
DCE (1 mL) + MeCN (0.1 mL)	12	HFIP (1 mL) + DMSO (0.1 mL)	8
DMA (1 mL) +MeCN (0.1 mL)	8	HFIP (1 mL) + EA (0.1 mL)	0
DMF (1 mL) + MeCN (0.1 mL)	0	HFIP (1 mL) + THF	0

[a]Conditions: **3k** (0.1 mmol), $Pd(OAc)_2$ (7 mol%), **L13** (10 mol%), Ag_2CO_3 (2.0 equiv), KF (2.0 equiv), solvent, 100 °C, 12 h. [b]The yields were determined by ^1H NMR using CH_2Br_2 as the internal standard.

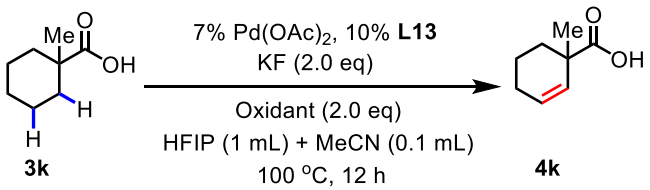
Table S9. Base Effects[a,b]



Base	yield (%)	Base	yield (%)
KTFA	46	LiF (1.0 eq)	50
KTFA (1.0 eq)	56	NaOAc	42
NaTFA	44	NaOAc (1.0 eq)	56
NaTFA (1.0 eq)	56	K_2CO_3	22
LiTFA (1.0 eq)	50	CsF	36
$LiOH·H_2O$	50	$CsHCO_3$	36
$LiOH·H_2O$ (1.0 eq)	56	K_3PO_4	10
LiF	42	w/o	42

[a]Conditions: **3k** (0.1 mmol), $Pd(OAc)_2$ (7 mol%), **L13** (10 mol%), Ag_2CO_3 (2.0 equiv), base (2.0 equiv), HFIP (1.0 mL), MeCN (0.1 mL), 100 °C, 12 h. [b]The yields were determined by ^1H NMR using CH_2Br_2 as the internal standard.

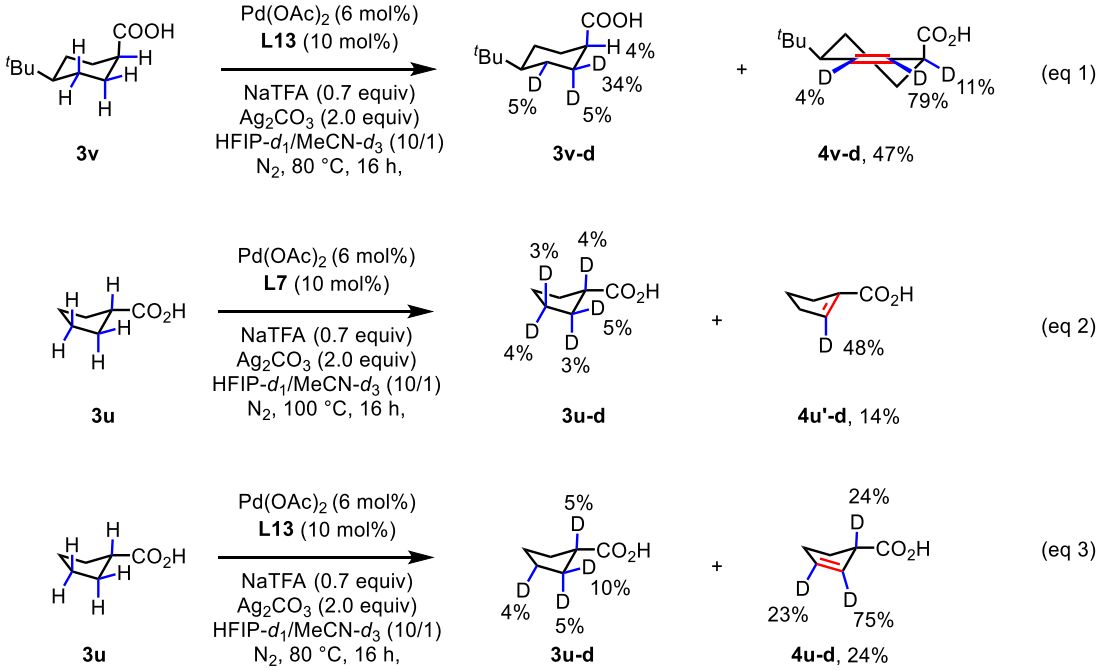
Table S10. Screenings of Oxidants[a,b]



Oxidants	yield (%)	Oxidants	yield (%)
Ag_2CO_3	54	BQ	4
AgOAc	10	H_2O_2	2
AgF	4	TBHP in H_2O	4[c]
AgTFA	0	TBHP in Hexane	2[c]
Ag_2O	32	$^tBuOO^tBu$	2
O_2	2	BQ+O_2	8
$NaCO_3$/ 1.5 H_2O_2	n. d.	w/o	trace

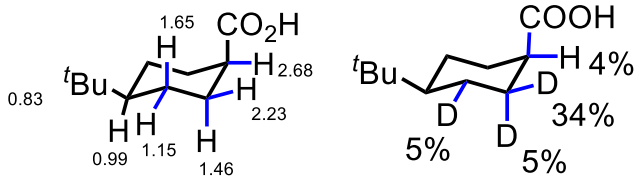
[a]Conditions: **3k** (0.1 mmol), $Pd(OAc)_2$ (7 mol%), **L13** (10 mol%), oxidants, KF (2.0 equiv), HFIP (1.0 mL), MeCN (0.1 mL), 100 °C, 12 h. [b]The yields were determined by ^1H NMR using CH_2Br_2 as the internal standard. [c]At 80 °C.

2.3. H/D Exchange Experiments

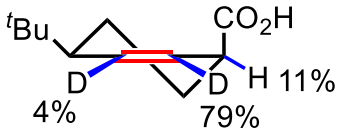


Scheme S1. H/D Exchange Experiments. Conditions: **1** (0.1 mmol), $Pd(OAc)_2$ (6 mol%), **Ligands** (10 mol%), NaTFA (0.7 equiv), Ag_2CO_3 (2.0 equiv), HFIP-d_1/MeCN-d_3 (1.0 mL/ 0.1 mL), N_2, 80-100 °C, 16 h. Isolated yields.

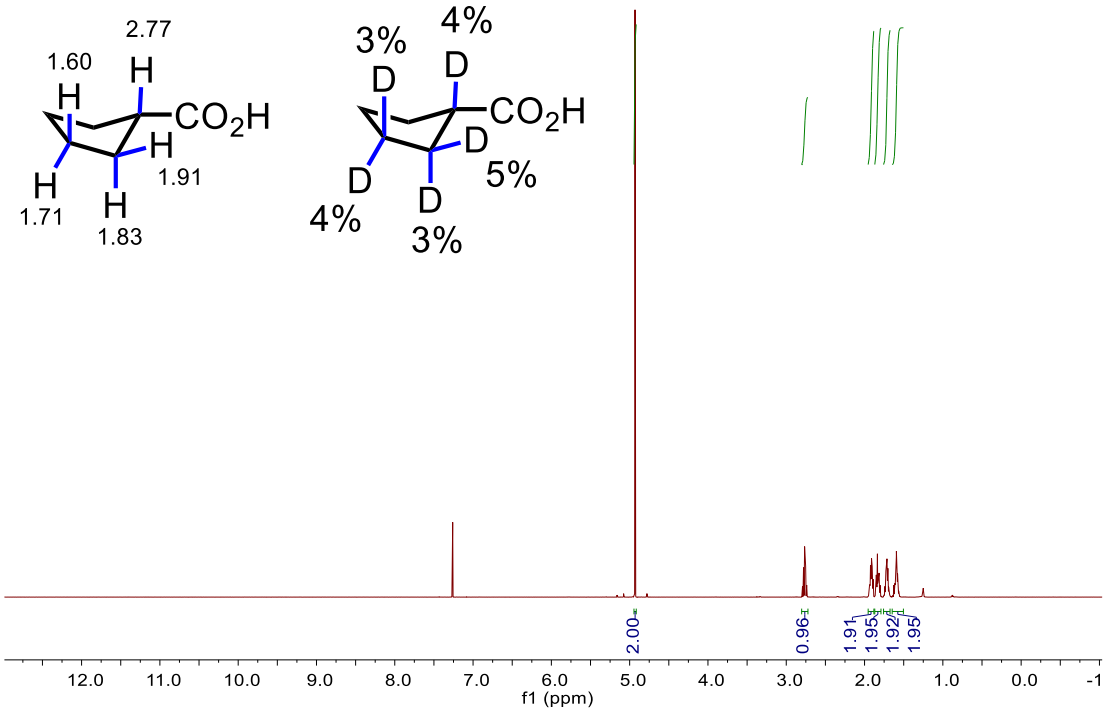
NMR spectrum of 3v-d:



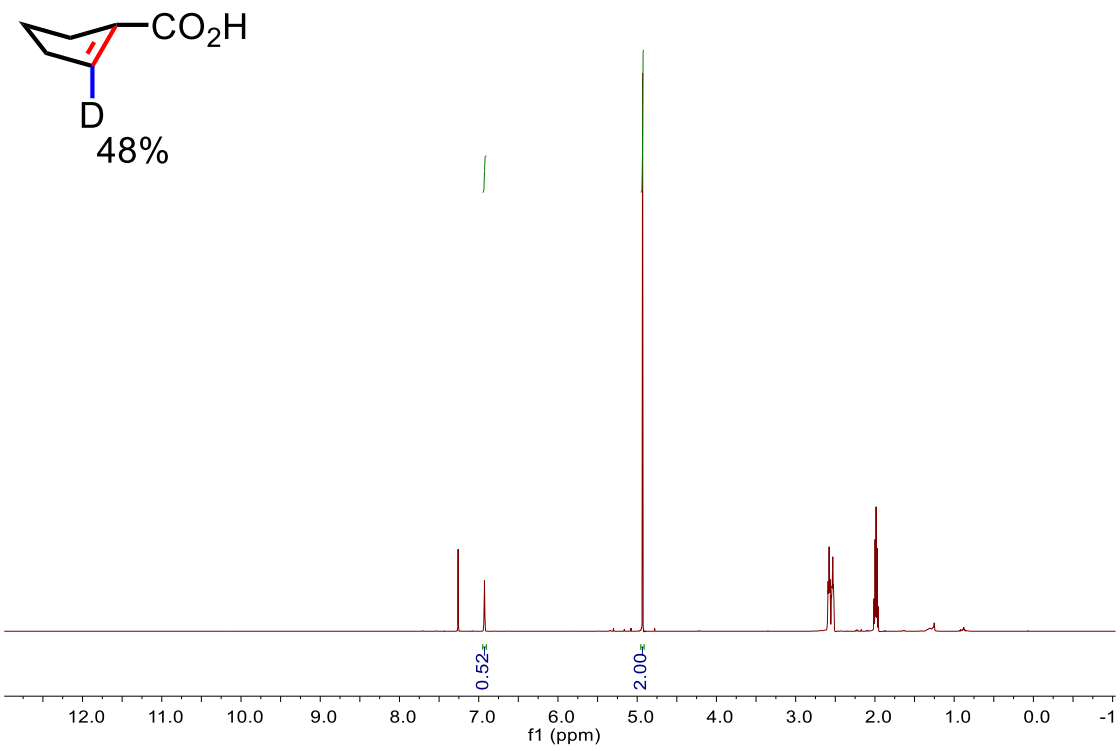
NMR spectrum of 4v-d:



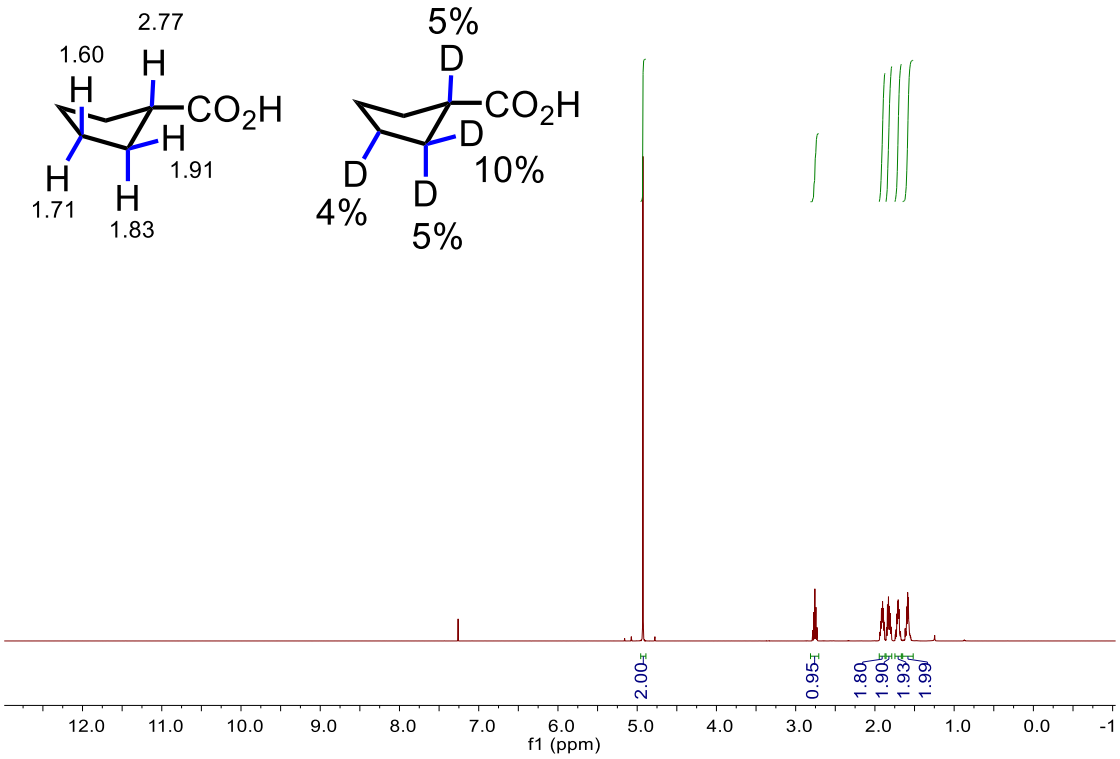
NMR spectrum of 3u-d (L7):



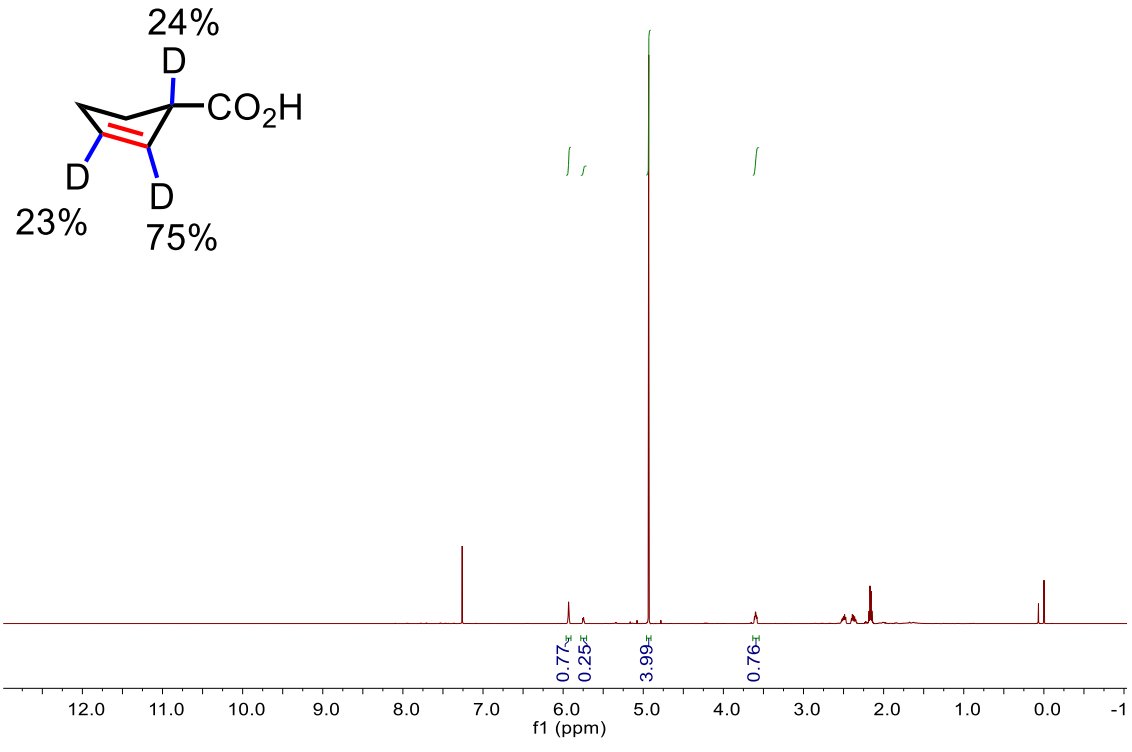
NMR spectrum of 4u'-d (L7):



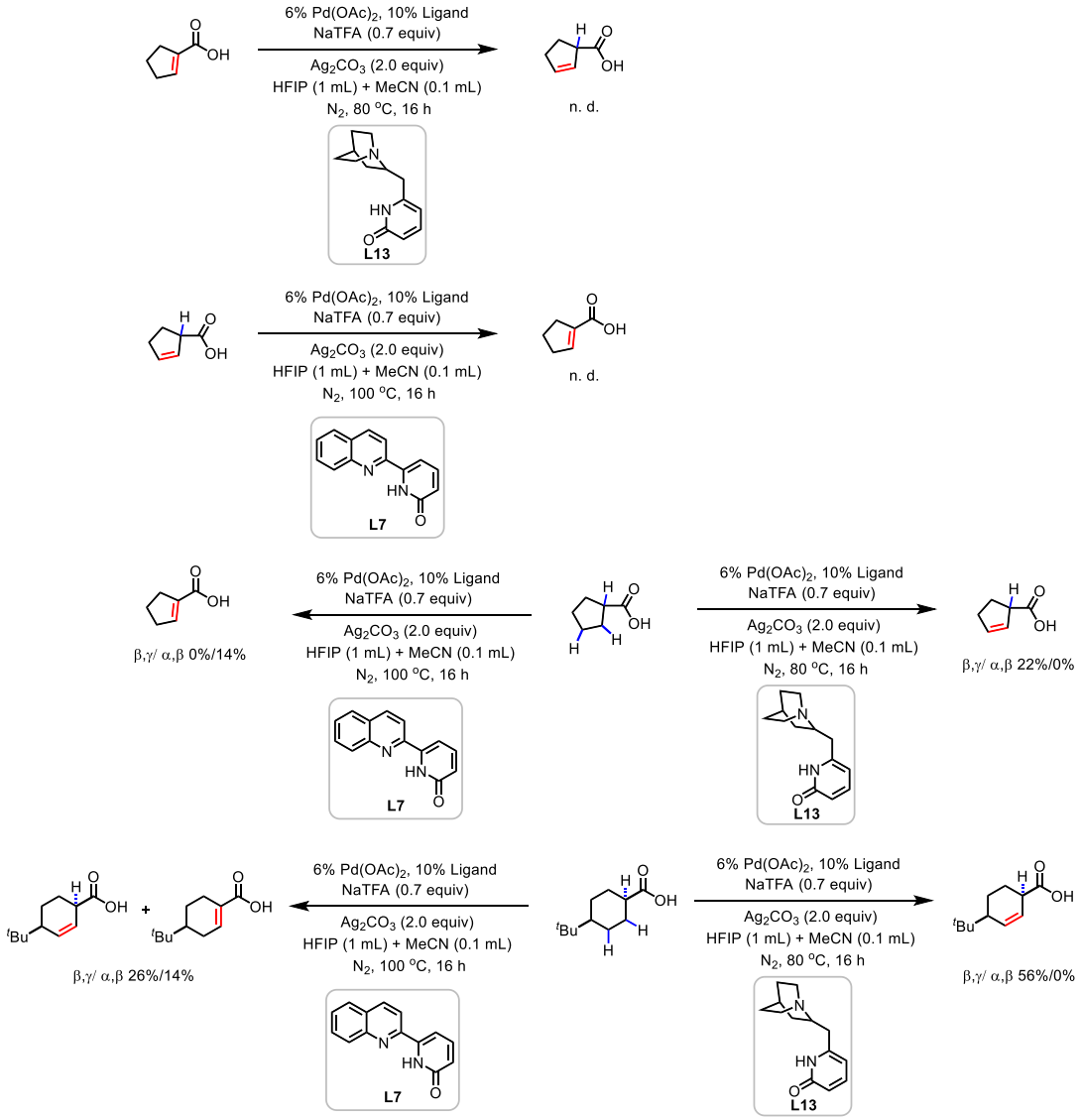
NMR spectrum of 3v-d (L13):



NMR spectrum of 4v-d (L13):

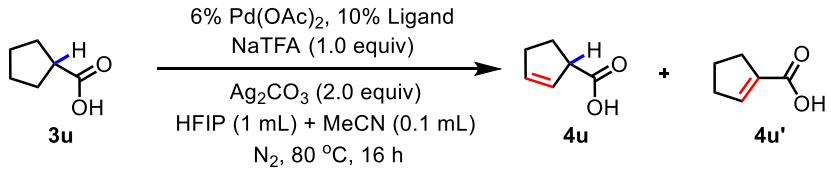


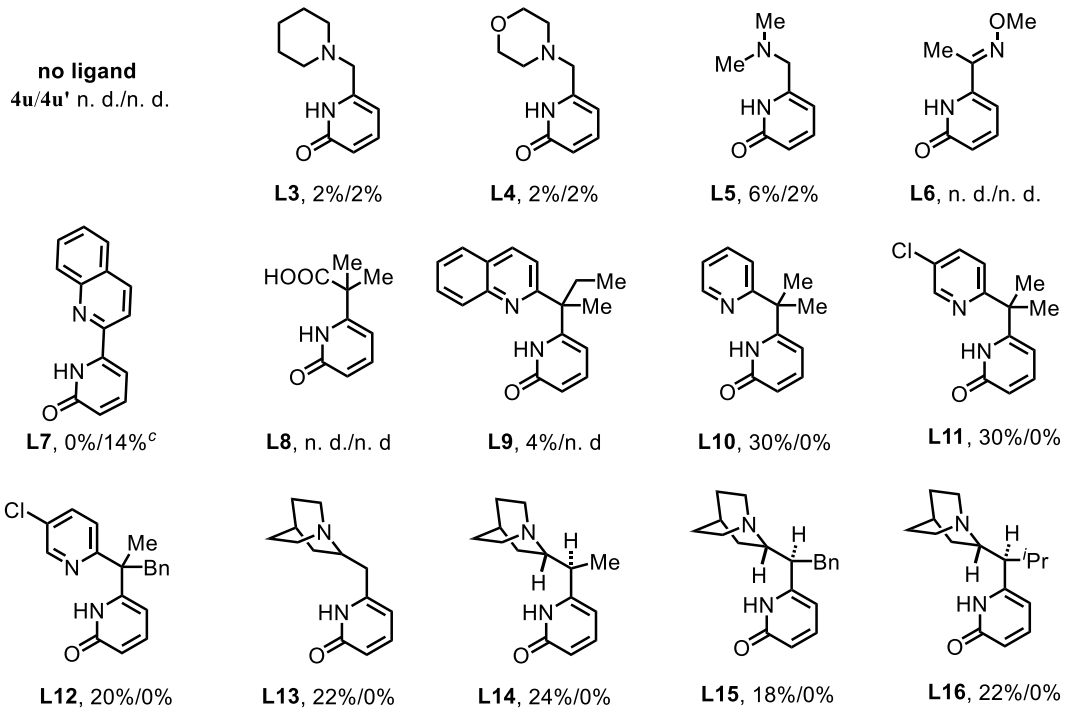
2.4. Switch of Regioselectivity Experiments



Scheme S2. Switch of Regioselectivity Experiments. Conditions: 1 (0.1 mmol), $Pd(OAc)_2$ (6 mol%), Ligand (10 mol%), NaTFA (0.7 equiv), Ag_2CO_3 (2.0 equiv), HFIP /MeCN (1.0 mL/ 0.1 mL), N_2, 80-100 °C, 16 h. The yields were determined by ^1H NMR using CH_2Br_2 as the internal standard.

2.5 Investigation of Ligands for the β,γ-Dehydrogenation of Cyclopentanecarboxylic Acid[a,b]

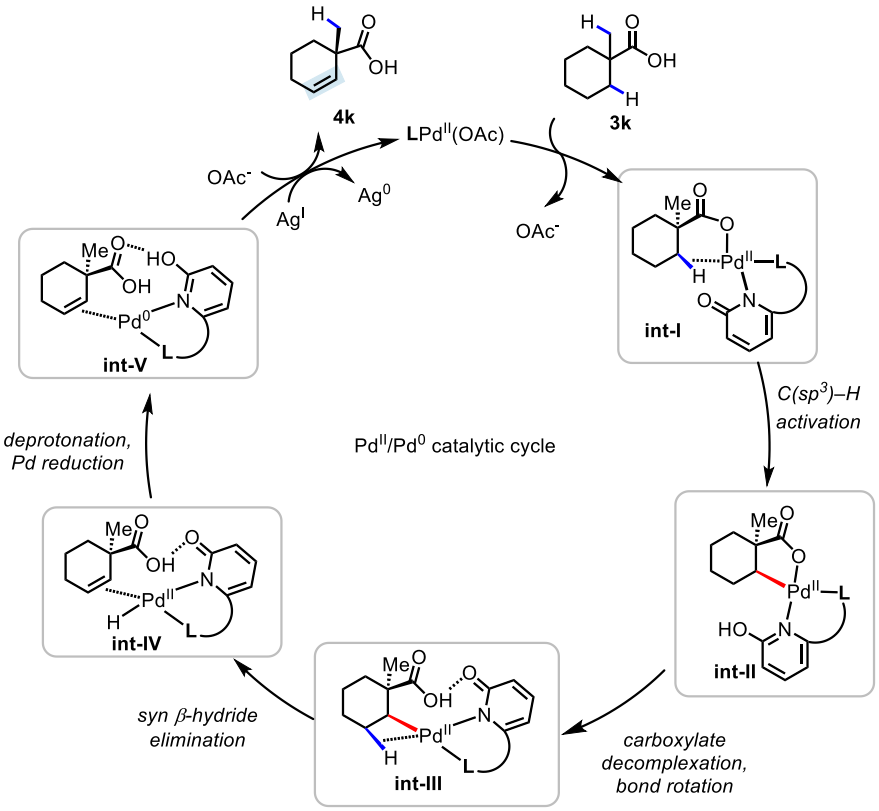




Scheme S3. Investigation of Ligands for the β,γ-Dehydrogenation of Cyclopentanecarboxylic Acid. [a]Conditions: **1a** (0.1 mmol), $Pd(OAc)_2$ (6 mol%), ligand (**L**) (10 mol%), NaTFA (0.7 equiv), Ag_2CO_3 (2.0 equiv), HFIP/MeCN (1.0 mL/0.1 mL), 80 °C, 16 h. [b]The yields were determined by ^1H NMR analysis of the crude product using CH_2Br_2 as the internal standard. [c]100 °C.

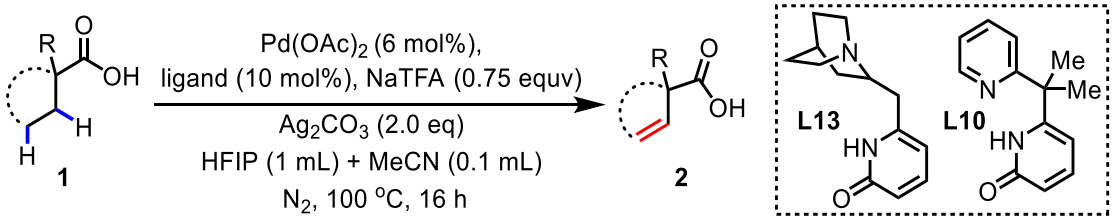
2.6. Proposed Mechanism of β, γ-Dehydrogenation

A general mechanism has been proposed in Scheme S4. Upon generation of the active **L**Pd^{II}(OAc) species, coordination of model substrate **3k** to Pd forms **int-I**, followed by pyridone-assisted CMD-type regioselective cyclopalladation of the β-methylene C−H bond to form **int-II**. Next, dissociation of the substrate carboxylate creates a vacant site for coordination of the adjacent C−H bond in **int-III**. Subsequent syn β-hydride elimination and Pd reduction delivers β,γ-dehydrogenation product **4k**, while Pd^{II} species is regenerated by a Ag^{I} oxidant, closing the catalytic cycle.

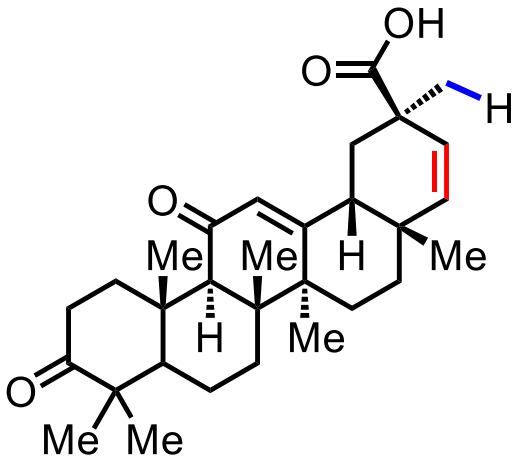


Scheme S4. Proposed Mechanism of β, γ-Dehydrogenation.

2.7. Substrate Scope for the β, γ-Dehydrogenation Reaction

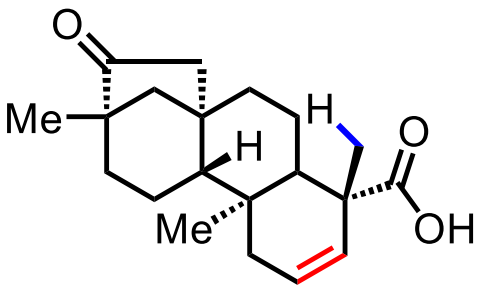


General Procedure for the β, γ-Dehydrogenation Reaction: In a sealed tube equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (1.3 mg, 6 mol%), **Ligand** (10 mol%), the corresponding carboxylic acid substrate (0.10 mmol), Ag_2CO_3 (55.0 mg, 0.2 mmol), NaTFA (10 mg, 0.075 mmol). HFIP (1 ml) and MeCN (0.1 ml) were then added before the tube was briefly flushed with nitrogen. Subsequently, the vial was capped and closed tightly. The reaction mixture was then stirred at the rate of 300 rpm at 100 °C for 16 h. After being allowed to cool to room temperature, the mixture was diluted with ethyl acetate and acidified with 200 µL of formic acid. The mixture was passed through a pad of Celite with acetone as the eluent to remove any insoluble precipitate. The resulting mixture was concentrated, and the residue was isolated using PTLC (Hexane: Ethyl acetate =8:1 to 5:1).



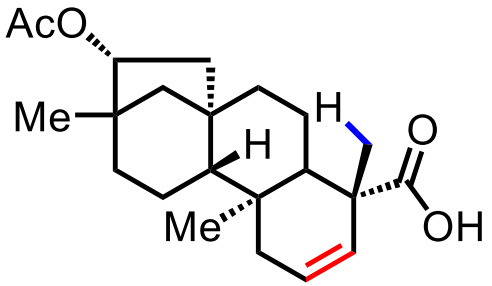
(2*R*,4a*S*,6a*S*,6b*R*,12a*S*,12b*R*,14b*R*)-2,4a,6a,6b,9,9,12a-heptamethyl-10,13-dioxo-1,2,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carboxylic acid (2a)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (46.2 mg, 99% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.96 (s, 1H), 5.59 (dd, *J* = 9.9, 1.6 Hz, 1H), 5.50 (d, *J* = 9.9 Hz, 1H), 2.94 (ddd, *J* = 13.6, 7.2, 4.1 Hz, 1H), 2.62 (ddd, *J* = 15.8, 11.0, 7.2 Hz, 1H), 2.49 (s, 1H), 2.37 (ddd, *J* = 13.5, 6.5, 3.8 Hz, 2H), 2.17 (s, 2H), 2.10 (dt, *J* = 12.9, 2.3 Hz, 1H), 1.84 (td, *J* = 13.8, 4.2 Hz, 1H), 1.76 – 1.64 (m, 3H), 1.61 – 1.36 (m, 4H), 1.34 (s, 3H), 1.31 (s, 3H), 1.27 (s, 3H), 1.24 – 1.20 (m, 1H), 1.17 (s, 3H), 1.10 (s, 3H), 1.06 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 217.4, 200.3, 180.2, 169.6, 138.7, 128.9, 127.8, 61.1, 55.5, 47.9, 47.0, 45.1, 44.5, 44.1, 40.6, 39.8, 36.9, 34.9, 34.4, 32.6, 29.2, 27.3, 26.6, 26.1, 25.9, 21.8, 21.6, 18.9, 18.8, 15.9. HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{41}O_4^-$ $[M-H]^-$ 465.3005, found 465.3008.



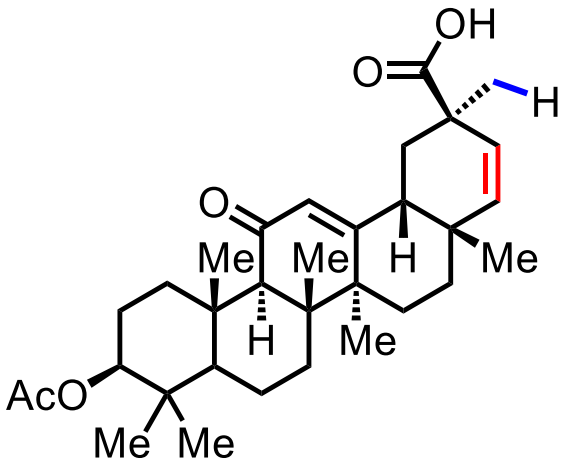
(4*R*,6a*R*,9*S*,11a*R*,11b*S*)-4,9,11b-trimethyl-8-oxo-1,4,4a,5,6,7,8,9,10,11,11a,11b-dodecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylic acid (2b)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (26.9 mg, 85% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.69 – 5.57 (m, 2H), 2.60 (dd, *J* = 18.6, 3.8 Hz, 1H), 2.05 (dd, *J* = 17.6, 4.3 Hz, 1H), 1.99 – 1.92 (m, 1H), 1.84 (d, *J* = 18.6 Hz, 1H), 1.72 – 1.48 (m, 7H), 1.45 – 1.37 (m, 3H), 1.35 (s, 3H), 1.34 – 1.28 (m, 2H), 0.99 (s, 3H), 0.86 (d, *J* = 0.9 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 223.0, 179.9, 130.7, 124.5, 54.1, 54.0, 53.4, 48.9, 47.9, 44.8, 40.7, 40.6, 39.7, 37.5, 36.4, 28.0, 22.0, 20.7, 20.0, 14.4. HRMS (ESI-TOF) *m/z* Calcd for $C_{20}H_{29}O_3^+$ $[M+H]^+$ 317.2117, found 317.2129.



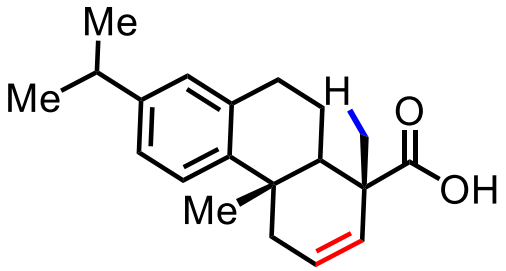
(4*R*,6a*R*,8*R*,11a*R*,11b*S*)-8-acetoxy-4,9,11b-trimethyl-1,4,4a,5,6,7,8,9,10,11,11a,11b-dodecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylic acid (2c)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (25.1 mg, 70% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.64 (ddd, *J* = 10.2, 5.4, 1.9 Hz, 1H), 5.59 (dd, *J* = 10.2, 2.5 Hz, 1H), 4.74 (dd, *J* = 10.8, 4.3 Hz, 1H), 2.05 (s, 4H), 1.89 – 1.74 (m, 4H), 1.69 – 1.58 (m, 2H), 1.57 – 1.46 (m, 3H), 1.40 – 1.21 (m, 7H), 1.07 (ddd, *J* = 11.6, 9.8, 3.7 Hz, 2H), 0.91 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (151 MHz, CDCl3) δ 182.0, 171.6, 130.6, 124.7, 81.7, 54.9, 54.6, 53.4, 45.0, 42.5, 41.6, 40.8, 40.6, 40.2, 36.4, 34.7, 28.1, 25.1, 22.0, 21.3, 20.6, 14.4. HRMS (ESI-TOF) *m/z* Calcd for $C_{22}H_{31}O_4^-$ $[M-H]^-$ 359.2222, found 359.2211.



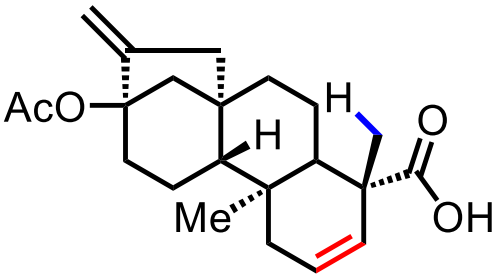
(2*R*,4a*S*,6a*S*,6b*R*,10*S*,12a*S*,12b*R*,14b*R*)-10-acetoxy-2,4a,6a,6b,9,9,12a-heptamethyl-13-oxo-1,2,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carboxylic acid (2d)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (48.0 mg, 94% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.94 (s, 1H), 5.58 (dd, *J* = 9.9, 1.5 Hz, 1H), 5.49 (d, *J* = 9.9 Hz, 1H), 4.51 (dd, *J* = 11.8, 4.7 Hz, 1H), 2.78 (dt, *J* = 13.7, 3.7 Hz, 1H), 2.41 (s, 1H), 2.36 (d, *J* = 13.5 Hz, 1H), 2.10 (dt, *J* = 13.0, 2.2 Hz, 1H), 2.04 (d, *J* = 4.2 Hz, 3H), 1.81 (td, *J* = 13.8, 4.1 Hz, 1H), 1.75 – 1.56 (m, 6H), 1.49 – 1.40 (m, 2H), 1.32 (d, *J* = 9.2 Hz, 6H), 1.22 – 1.14 (m, 5H), 1.12 (s, 3H), 1.05 (td, *J* = 13.6, 3.8 Hz, 1H), 0.92 (s, 3H), 0.87 (s, 6H), 0.80 (dd, *J* = 12.0, 2.1 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 201.0, 180.2, 171.2, 169.2, 138.8, 129.0, 127.8, 80.7, 61.7, 55.2, 46.9, 45.3, 44.5, 43.9, 40.5, 38.9, 38.2, 37.2, 34.9, 33.2, 29.2, 28.2, 27.3, 26.1, 25.8, 23.7, 21.8, 21.5, 19.0, 17.5, 16.9, 16.6. HRMS (ESI-TOF) *m/z* Calcd for $C_{32}H_{47}O_5^+$ $[M+H]^+$ 511.3423, found 511.3438.



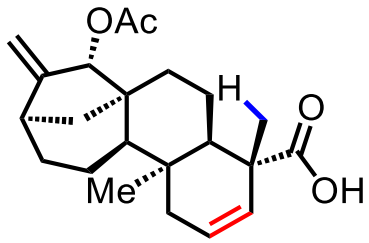
(1*R*,4a*S*)-7-isopropyl-1,4a-dimethyl-1,4,4a,9,10,10a-hexahydrophenanthrene-1-carboxylic acid (2e)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (8.9 mg, 30% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.18 (d, *J* = 8.1 Hz, 1H), 7.03 (d, *J* = 8.1 Hz, 1H), 6.90 (s, 1H), 5.92 – 5.85 (m, 1H), 5.69 (dd, *J* = 10.0, 2.8 Hz, 1H), 2.97 – 2.77 (m, 3H), 2.59 (dd, *J* = 17.1, 6.4 Hz, 1H), 2.54 (dd, *J* = 10.9, 3.8 Hz, 1H), 2.22 (d, *J* = 17.0 Hz, 1H), 1.80 (td, *J* = 12.2, 11.3, 5.1 Hz, 2H), 1.35 (s, 3H), 1.26 (s, 3H), 1.23 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.9, 146.1, 144.5, 135.1, 130.4, 127.0, 126.9, 125.8, 124.4, 48.3, 43.0, 39.5, 36.5, 33.6, 30.8, 29.9, 25.6, 24.1, 21.6, 18.2. HRMS (ESI-TOF) *m/z* Calcd for $C_{20}H_{25}O_2^-$ $[M-H]^-$ 297.1855, found 297.1853.



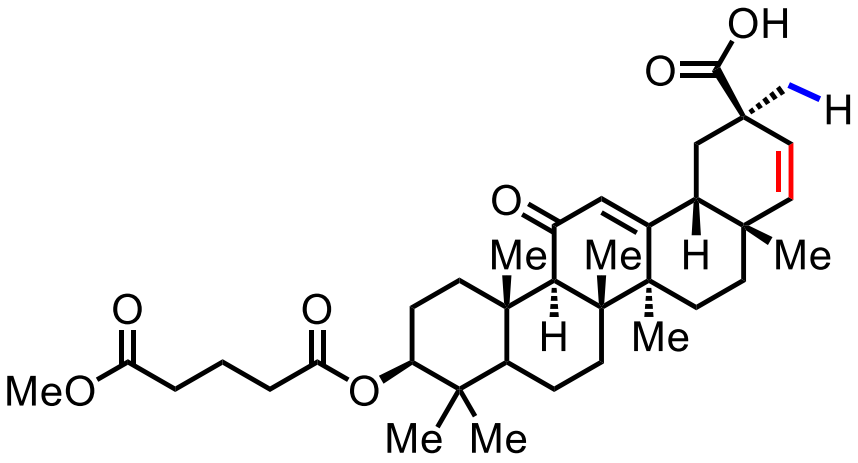
(4*R*,6a*S*,9*R*,11a*R*,11b*S*)-9-acetoxy-4,11b-dimethyl-8-methylene-1,4,4a,5,6,7,8,9,10,11,11a,11b-dodecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylic acid (2f)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (20.1 mg, 56% yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 5.68 – 5.60 (m, 2H), 4.91 (t, *J* = 2.6 Hz, 1H), 4.87 (t, *J* = 2.0 Hz, 1H), 2.55 (dd, *J* = 10.9, 2.6 Hz, 1H), 2.39 – 2.16 (m, 3H), 2.02 (d, *J* = 7.5 Hz, 4H), 1.90 (dq, *J* = 14.0, 3.3 Hz, 1H), 1.82 – 1.67 (m, 4H), 1.66 – 1.56 (m, 3H), 1.54 – 1.40 (m, 2H), 1.37 – 1.29 (m, 4H), 1.06 (d, *J* = 5.5 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.2, 170.0, 152.0, 130.8, 124.7, 103.6, 87.7, 53.3, 52.9, 46.7, 45.1, 42.6, 41.9, 41.5, 40.2, 37.7, 36.8, 28.0, 22.4, 22.0, 20.5, 16.8. HRMS (ESI-TOF) *m/z* Calcd for $C_{22}H_{29}O_4^-$ $[M-H]^-$ 357.2066, found 357.2059.



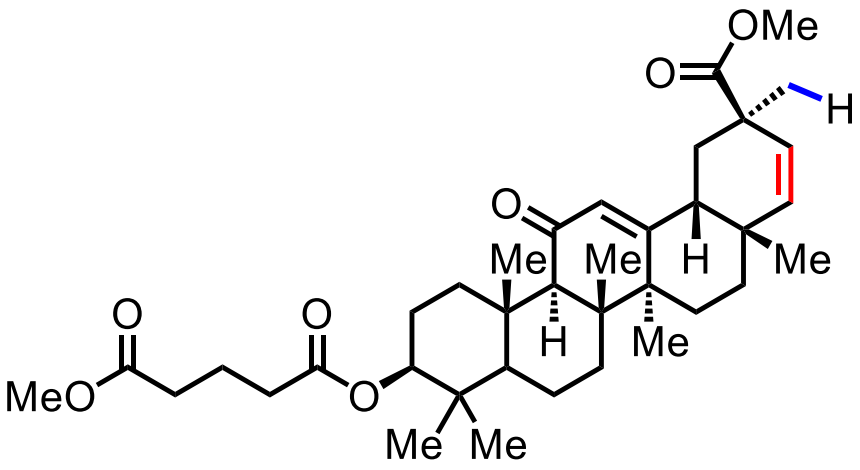
(4*R*,4a*R*,6a*R*,7*S*,9*R*,11a*R*,11b*S*)-7-acetoxy-4,11b-dimethyl-8-methylene-1,4,4a,5,6,7,8,9,10,11,11a,11b-dodecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylic acid (2g)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (19.7 mg, 55% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.68 (ddd, *J* = 10.2, 5.4, 1.9 Hz, 1H), 5.65 – 5.61 (m, 1H), 5.17 (t, *J* = 2.6 Hz, 1H), 4.95 (d, *J* = 2.7 Hz, 1H), 4.90 – 4.86 (m, 1H), 2.69 (s, 1H), 2.27 (dd, *J* = 17.7, 5.6 Hz, 1H), 2.15 (s, 3H), 2.01 (d, *J* = 12.0 Hz, 1H), 1.90 (dq, *J* = 14.0, 3.4 Hz, 1H), 1.80 – 1.66 (m, 3H), 1.55 – 1.46 (m, 4H), 1.45 – 1.40 (m, 2H), 1.34 (s, 3H), 1.29 (dd, *J* = 12.6, 2.7 Hz, 1H), 1.19 (dq, *J* = 12.1, 1.7 Hz, 1H), 1.04 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.0, 171.5, 153.7, 130.6, 125.1, 106.4, 81.7, 52.9, 46.3, 46.1, 45.0, 42.2, 40.7, 38.0, 37.7, 35.8, 33.4, 27.9, 21.7, 21.4, 18.5, 17.2. HRMS (ESI-TOF) *m/z* Calcd for $C_{22}H_{29}O_4^-$ $[M-H]^-$ 357.2066, found 357.2054.



(2*R*,4a*S*,6a*S*,6b*R*,10*S*,12a*S*,12b*R*,14b*R*)-10-((5-methoxy-5-oxopentanoyl)oxy)-2,4a,6a,6b,9,9,12a-heptamethyl-13-oxo-1,2,4a,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-octadecahydropicene-2-carboxylic acid (2h)

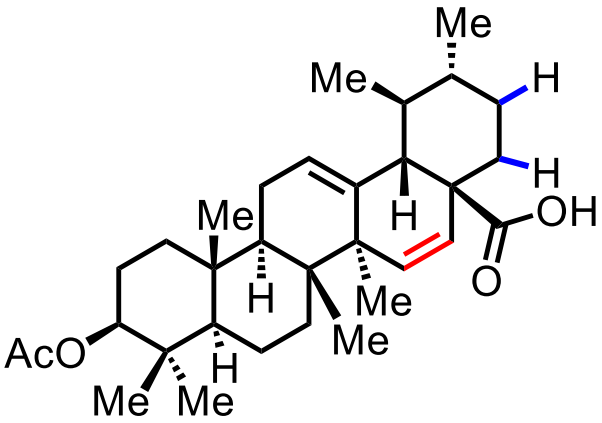
Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (35.8 mg, 60% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.92 (s, 1H), 5.58 (dd, *J* = 9.9, 1.5 Hz, 1H), 5.50 (d, *J* = 9.9 Hz, 1H), 4.53 (dd, *J* = 11.8, 4.7 Hz, 1H), 3.68 (s, 3H), 2.78 (dt, *J* = 13.5, 3.6 Hz, 1H), 2.48 – 2.32 (m, 7H), 2.10 (ddd, *J* = 13.1, 3.0, 1.7 Hz, 1H), 1.99 – 1.92 (m, 2H), 1.82 (td, *J* = 13.7, 4.3 Hz, 1H), 1.75 – 1.53 (m, 5H), 1.49 – 1.34 (m, 3H), 1.32 (d, *J* = 9.8 Hz, 6H), 1.23 – 1.14 (m, 5H), 1.13 (s, 3H), 1.05 (td, *J* = 13.3, 11.6, 4.0 Hz, 1H), 0.92 (s, 3H), 0.87 (d, *J* = 3.5 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 200.8, 180.2, 173.6, 172.8, 169.0, 138.9, 129.0, 127.7, 80.8, 61.7, 55.2, 51.8, 46.9, 45.2, 44.5, 43.9, 40.5, 38.8, 38.2, 37.2, 34.9, 33.9, 33.3, 33.2, 29.2, 28.3, 27.3, 26.1, 25.8, 23.7, 21.8, 20.4, 19.0, 17.5, 16.9, 16.6. HRMS (ESI-TOF) *m/z* Calcd for $C_{36}H_{51}O_7^-$ $[M-H]^-$ 595.3635, found 595.3644.



(3*S*,6a*R*,6b*S*,8a*S*,11*R*,12a*R*,14a*R*,14b*S*)-11-(methoxycarbonyl)-4,4,6a,6b,8a,11,14b-heptamethyl-14-oxo-1,2,3,4,4a,5,6,6a,6b,7,8,8a,11,12,12a,14,14a,14b-octadecahydropicen-3-yl methyl glutarate (2i)

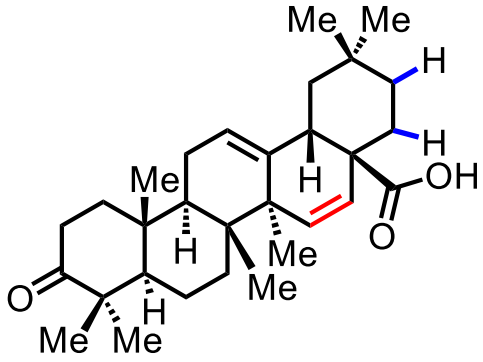
Following General Procedure on a 0.1 mmol scale. After being allowed to cool to room temperature, the mixture was diluted with ethyl acetate and acidified with 200 µL of formic acid. The mixture was passed through a pad of Celite with acetone as the eluent to remove any insoluble precipitate. The resulting reaction mixture was concentrated, followed by the addition of DMF (0.5 mL) Cs_2CO_3 (99.7 mg, 0.03 mmol), and iodomethane (142 mg, 1 mmol). The mixture was stirred at room temperature for 3 h and then diluted with water followed by extraction with ethyl acetate. The organic layer was combined and dried over Na_2SO_4, filtered, and concentrated in vacuo. The residual mixture was isolated using PTLC. The product was obtained as a white solid (41.5 mg, 68% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.73 (s, 1H), 5.54 (dd, *J* = 9.9, 1.6 Hz, 1H), 5.47 (d, *J* = 9.9 Hz, 1H), 4.53 (dd, *J* = 11.8, 4.7 Hz, 1H), 3.68 (d, *J* = 2.3 Hz, 6H), 2.79 (dt, *J* = 13.6, 3.7 Hz, 1H), 2.42 – 2.33 (m, 5H), 2.22 (dt, *J* = 13.6, 2.2 Hz, 1H), 2.07 (ddd, *J* = 13.1, 2.9, 1.7 Hz, 1H), 1.96 (pd, *J* = 7.5, 1.5 Hz, 2H), 1.81 (td, *J* = 13.8, 4.2 Hz, 1H), 1.76 – 1.54 (m, 5H), 1.49 – 1.40 (m, 2H), 1.38 – 1.30 (m, 4H), 1.25 (s, 3H), 1.17 (s, 4H), 1.12 (s, 3H), 1.06 (td, *J* = 13.5, 3.7 Hz, 1H), 0.93 – 0.85 (m, 9H), 0.80 (dd, *J* = 12.0, 2.1 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 200.0, 176.3, 173.6,

172.8, 168.3, 138.5, 129.2, 128.0, 80.8, 61.7, 55.2, 52.3, 51.8, 47.1, 45.1, 44.8, 43.9, 40.9, 38.9, 38.2, 37.1, 34.9, 33.9, 33.3, 33.2, 29.2, 28.3, 27.3, 26.1, 25.8, 23.7, 21.8, 20.4, 19.0, 17.5, 16.9, 16.6. HRMS (ESI-TOF) *m/z* Calcd for $C_{37}H_{55}O_7^+$ $[M+H]^+$ 611.3948, found 611.3932.



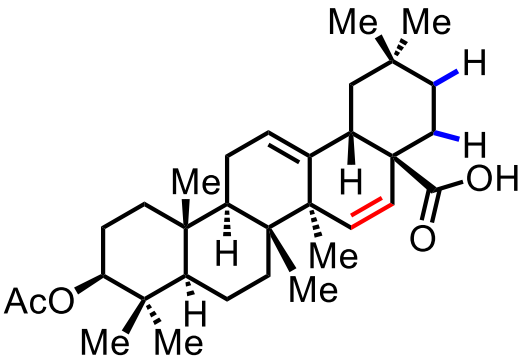
(1*S*,2*R*,4a*S*,6a*S*,6b*R*,8a*R*,10*S*,12a*R*,12b*R*,14b*S*)-10-acetoxy-1,2,6a,6b,9,9,12a-heptamethyl-1,3,4,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-hexadecahydropicene-4a(2*H*)-carboxylic acid (2j)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (28.8 mg, 58% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.64 – 5.54 (m, 2H), 5.35 (d, *J* = 3.5 Hz, 1H), 4.50 (dd, *J* = 10.9, 4.9 Hz, 1H), 2.28 (d, *J* = 11.3 Hz, 1H), 2.05 (s, 3H), 2.01 – 1.91 (m, 2H), 1.83 (ddd, *J* = 18.7, 11.2, 3.6 Hz, 1H), 1.71 – 1.48 (m, 8H), 1.44 – 1.32 (m, 2H), 1.24 – 1.13 (m, 2H), 1.13 – 0.95 (m, 5H), 0.94 – 0.82 (m, 16H), 0.62 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.9, 171.2, 137.2, 136.1, 128.8, 125.7, 81.0, 55.5, 52.6, 48.5, 47.3, 45.0, 39.8, 38.4, 38.2, 38.0, 37.8, 37.3, 37.0, 32.7, 30.9, 28.1, 23.7, 23.4, 23.1, 21.5, 20.9, 18.3, 17.1, 16.9, 16.6, 15.5. HRMS (ESI-TOF) *m/z* Calcd for $C_{32}H_{47}O_4^-$ $[M-H]^-$ 495.3474, found 495.3461.



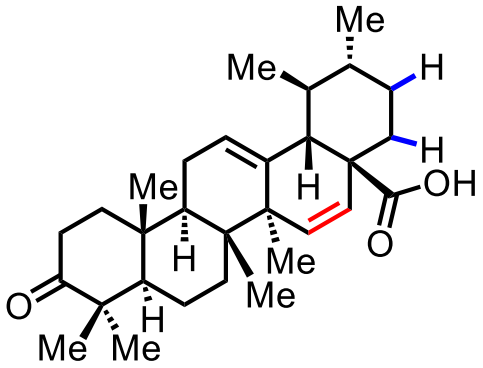
(4a*R*,6a*S*,6b*R*,8a*R*,12a*R*,12b*R*,14b*S*)-2,2,6a,6b,9,9,12a-heptamethyl-10-oxo-1,5,6,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-hexadecahydropicene-4a(2*H*)-carboxylic acid (2k)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (23.5 mg, 52% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.63 (d, *J* = 10.0 Hz, 1H), 5.54 (dd, *J* = 10.1, 1.4 Hz, 1H), 5.46 – 5.42 (m, 1H), 2.90 (dd, *J* = 13.6, 4.0 Hz, 1H), 2.57 (ddd, *J* = 15.6, 11.8, 7.0 Hz, 1H), 2.34 (ddd, *J* = 15.8, 6.3, 3.3 Hz, 1H), 1.98 (ddd, *J* = 18.6, 6.9, 3.4 Hz, 1H), 1.94 – 1.83 (m, 2H), 1.78 (dt, *J* = 13.5, 3.7 Hz, 1H), 1.70 (dd, *J* = 11.1, 6.9 Hz, 1H), 1.62 (td, *J* = 11.8, 5.4 Hz, 1H), 1.50 – 1.39 (m, 3H), 1.32 (dd, *J* = 9.9, 4.6 Hz, 2H), 1.25 (s, 3H), 1.17 (s, 3H), 1.15 – 1.10 (m, 2H), 1.08 (s, 3H), 1.03 (d, *J* = 6.2 Hz, 6H), 0.93 (s, 3H), 0.88 (s, 3H), 0.68 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 217.5, 180.6, 140.6, 136.0, 127.9, 122.9, 55.7, 47.7, 47.7, 46.8, 44.5, 43.2, 42.1, 39.8, 39.3, 37.2, 34.6, 34.3, 33.2, 32.9, 32.3, 30.5, 26.2, 24.6, 23.4, 23.2, 21.7, 19.6, 17.1, 14.9. HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{43}O_3^-$ $[M-H]^-$ 451.3212, found 451.3209.



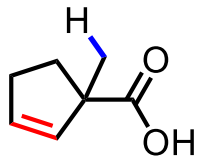
(4a*S*,6a*S*,6b*R*,8a*R*,10*S*,12a*R*,12b*R*,14b*S*)-10-acetoxy-2,2,6a,6b,9,9,12a-heptamethyl-1,3,4,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-hexadecahydropicene-4a(2*H*)-carboxylic acid (2l)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a white solid (28.8 mg, 58% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.60 (d, *J* = 10.0 Hz, 1H), 5.51 (dd, *J* = 10.1, 1.5 Hz, 1H), 5.39 (t, *J* = 3.6 Hz, 1H), 4.49 (dd, *J* = 10.8, 5.2 Hz, 1H), 2.86 (ddd, *J* = 13.5, 4.1, 1.5 Hz, 1H), 2.04 (s, 3H), 1.93 (ddd, *J* = 18.7, 6.9, 3.5 Hz, 1H), 1.85 – 1.69 (m, 3H), 1.65 – 1.53 (m, 6H), 1.42 – 1.34 (m, 1H), 1.24 (dq, *J* = 11.0, 4.5, 3.8 Hz, 3H), 1.15 (s, 3H), 1.13 – 1.01 (m, 3H), 0.91 (d, *J* = 8.1 Hz, 6H), 0.88 – 0.86 (m, 7H), 0.83 (s, 3H), 0.59 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.6, 171.1, 140.4, 136.2, 127.8, 123.1, 81.0, 55.5, 47.6, 47.3, 44.5, 43.1, 41.9, 39.8, 38.2, 37.8, 37.3, 34.6, 33.2, 32.9, 32.7, 30.5, 28.1, 24.6, 23.7, 23.3, 23.2, 21.4, 18.3, 17.3, 16.9, 15.4. HRMS (ESI-TOF) *m/z* Calcd for $C_{32}H_{47}O_4^-$ $[M-H]^-$ 495.3474, found 495.3478.



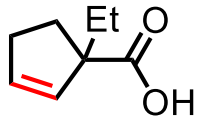
(1*S*,2*R*,4a*S*,6a*S*,6b*R*,8a*R*,12a*R*,12b*R*,14b*S*)-1,2,6a,6b,9,9,12a-heptamethyl-10-oxo-1,3,4,6a,6b,7,8,8a,9,10,11,12,12a,12b,13,14b-hexadecahydropicene-4a(2*H*)-carboxylic acid (2m)

Following General Procedure on 0.1 mmol scale. The product was obtained as a white solid (28.5 mg, 63% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.63 – 5.56 (m, 2H), 5.39 (t, *J* = 3.6 Hz, 1H), 2.57 (ddd, *J* = 15.7, 11.8, 7.0 Hz, 1H), 2.40 – 2.29 (m, 2H), 2.02 (ddd, *J* = 18.5, 6.6, 3.6 Hz, 1H), 1.98 – 1.87 (m, 3H), 1.75 – 1.40 (m, 9H), 1.32 (dd, *J* = 10.2, 4.2 Hz, 1H), 1.24 – 1.14 (m, 2H), 1.10 (d, *J* = 17.2 Hz, 6H), 1.03 (d, *J* = 11.9 Hz, 6H), 0.90 (d, *J* = 6.4 Hz, 3H), 0.86 (d, *J* = 6.4 Hz, 3H), 0.69 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 217.5, 181.1, 137.4, 135.9, 129.0, 125.5, 55.7, 52.7, 48.6, 47.7, 46.7, 45.0, 39.7, 39.3, 38.4, 38.0, 37.2, 36.9, 34.3, 32.2, 30.9, 26.2, 23.5, 23.1, 21.7, 20.9, 19.6, 16.9, 16.6, 15.0. HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{43}O_3^-$ $[M-H]^-$ 451.3212, found 451.3202.



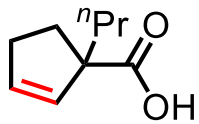
1-methylcyclopent-2-ene-1-carboxylic acid (4a)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a colorless oil (6.8 mg, 54% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.82 (dt, *J* = 5.5, 2.2 Hz, 1H), 5.69 (dt, *J* = 5.6, 2.0 Hz, 1H), 2.53 – 2.38 (m, 3H), 1.80 – 1.71 (m, 1H), 1.34 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.4, 133.7, 131.5, 54.4, 34.2, 30.9, 23.5; HRMS (ESI-TOF) *m/z* Calcd for $C_7H_{11}O_2^+$ $[M+H]^+$ 127.0754, found 127.0747.



1-ethylcyclopent-2-ene-1-carboxylic acid (4b)

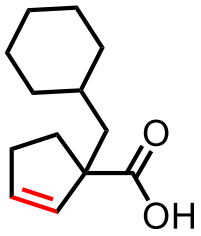
Following General Procedure on a 0.1 mmol scale. The product was obtained as a colorless oil (9.3 mg, 66% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.85 (dt, *J* = 5.6, 2.2 Hz, 1H), 5.70 (dt, *J* = 5.7, 2.1 Hz, 1H), 2.49 – 2.32 (m, 3H), 1.84 – 1.74 (m, 2H), 1.72 – 1.62 (m, 1H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.0, 133.1, 132.9, 60.6, 32.2, 32.0, 31.3, 9.6; HRMS (ESI-TOF) *m/z* Calcd for $C_8H_{13}O_2^+$ $[M+H]^+$ 141.0910, found 141.0915.



1-propylcyclopent-2-ene-1-carboxylic acid (4c)

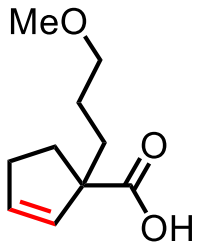
Following General Procedure on a 0.1 mmol scale. The product was obtained as a colorless oil (9.6 mg, 62% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.83 (dt, *J* = 5.6, 2.2 Hz, 1H), 5.71 (dt, *J* = 5.6, 2.1 Hz, 1H), 2.48 – 2.29 (m, 3H), 1.84 – 1.70 (m, 2H), 1.60 (ddd, *J* = 13.3, 11.7, 5.1 Hz, 1H), 1.40 – 1.22 (m, 3H), 0.91 (t, *J* = 7.3 Hz,

3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.5, 133.4, 132.7, 60.1, 40.9, 32.8, 31.9, 18.7, 14.6; HRMS (ESI-TOF) *m/z* Calcd for $C_9H_{15}O_2^+$ $[M+H]^+$ 155.1072, found 155.1066.



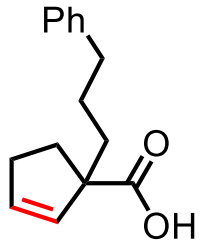
1-(cyclohexylmethyl)cyclopent-2-ene-1-carboxylic acid (4d)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a colorless oil (12.5 mg, 60% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.84 (dt, *J* = 5.6, 2.2 Hz, 1H), 5.75 (dt, *J* = 5.6, 2.0 Hz, 1H), 2.51 – 2.34 (m, 3H), 1.86 – 1.79 (m, 1H), 1.77 – 1.56 (m, 6H), 1.37 (ddtd, *J* = 12.5, 10.1, 6.8, 3.3 Hz, 1H), 1.27 – 1.08 (m, 3H), 1.02 – 0.92 (m, 2H)； ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.9, 134.0, 132.3, 59.2, 45.7, 35.2, 34.3, 34.1, 33.8, 31.7, 26.4, 26.3, 26.3. HRMS (ESI-TOF) *m/z* Calcd for $C_{13}H_{20}O_2^+$ $[M+H]^+$ 209.1542, found 209.1543.



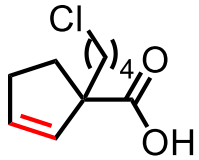
1-(3-methoxypropyl)cyclopent-2-ene-1-carboxylic acid (4e)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a colorless oil (10.7 mg, 58% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.85 (dt, *J* = 5.6, 2.2 Hz, 1H), 5.70 (dt, *J* = 5.6, 2.1 Hz, 1H), 3.37 (t, *J* = 6.4 Hz, 2H), 3.32 (s, 3H), 2.51 – 2.31 (m, 3H), 1.85 – 1.75 (m, 2H), 1.69 (ddd, *J* = 13.2, 11.8, 4.8 Hz, 1H), 1.63 – 1.50 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.0, 133.1, 72.9, 59.7, 58.6, 35.0, 32.7, 32.0, 29.9, 25.6. HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{15}O_3^-$ $[M-H]^-$ 183.1021, found 183.1027.



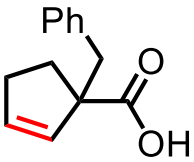
1-(3-phenylpropyl)cyclopent-2-ene-1-carboxylic acid (4f)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a colorless oil (14.3 mg, 62% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 7.8 Hz, 2H), 7.20 – 7.14 (m, 3H), 5.83 (dt, *J* = 5.6, 2.2 Hz, 1H), 5.69 (dt, *J* = 5.6, 2.0 Hz, 1H), 2.64 – 2.57 (m, 2H), 2.48 – 2.32 (m, 3H), 1.86 – 1.74 (m, 2H), 1.72 – 1.56 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.3, 142.2, 133.2, 133.0, 128.5, 128.4, 125.9, 60.0, 38.1, 36.3, 32.7, 32.0, 27.2. HRMS (ESI-TOF) *m/z* Calcd for $C_{15}H_{17}O_2^-$ $[M-H]^-$ 229.1229, found 229.1234.



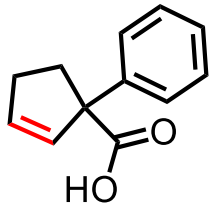
1-(4-chlorobutyl)cyclopent-2-ene-1-carboxylic acid (4g)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a colorless oil (8.9 mg, 44% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.86 (dt, *J* = 5.7, 2.3 Hz, 1H), 5.70 (dt, *J* = 5.6, 2.1 Hz, 1H), 3.53 (t, *J* = 6.7 Hz, 2H), 2.50 – 2.35 (m, 3H), 1.84 – 1.74 (m, 4H), 1.70 – 1.60 (m, 1H), 1.52 – 1.37 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.3, 133.3, 133.0, 59.9, 44.9, 37.6, 33.0, 32.8, 32.0, 22.8. HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{16}ClO_2^+$ $[M+H]^+$ 203.0839, found 203.0835.



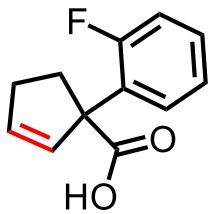
1-benzylcyclopent-2-ene-1-carboxylic acid (4h)

Following General Procedure on a 0.1 mmol scale. The product was obtained as a colorless oil (10.5 mg, 52% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.30 – 7.17 (m, 5H), 5.88 (dt, *J* = 5.7, 2.3 Hz, 1H), 5.75 (dt, *J* = 5.6, 2.1 Hz, 1H), 3.06 (s, 2H), 2.40 (dddt, *J* = 15.5, 8.7, 4.2, 2.2 Hz, 1H), 2.33 (ddd, *J* = 13.1, 9.0, 5.4 Hz, 1H), 2.23 – 2.15 (m, 1H), 1.99 (ddd, *J* = 13.1, 8.7, 4.4 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.6, 137.7, 133.6, 133.0, 130.1, 128.2, 126.6, 61.1, 43.8, 32.7, 31.8. HRMS (ESI-TOF) *m/z* Calcd for $C_{13}H_{13}O_2^-$ $[M-H]^-$ 201.0916, found 201.0923.



1-phenylcyclopent-2-ene-1-carboxylic acid (4i)

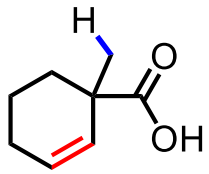
Following General Procedure on a 0.1 mmol scale. The product was obtained as a colorless oil (9.4 mg, 50% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.33 (d, *J* = 4.3 Hz, 4H), 7.26 – 7.22 (m, 1H), 6.12 (dt, *J* = 5.6, 2.2 Hz, 1H), 6.07 (dt, *J* = 5.6, 2.3 Hz, 1H), 2.91 (ddd, *J* = 13.1, 8.4, 4.6 Hz, 1H), 2.51 (dddt, *J* = 16.7, 8.3, 6.0, 2.2 Hz, 1H), 2.41 (dddd, *J* = 14.4, 8.7, 4.6, 2.3 Hz, 1H), 2.06 (ddd, *J* = 13.2, 8.7, 6.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.8, 143.5, 134.7, 132.0, 128.7, 127.1, 126.3, 64.5, 36.3, 32.0; HRMS (ESI-TOF) *m/z* Calcd for $C_{12}H_{13}O_2^+$ $[M+H]^+$ 189.0910, found 189.0911.



1-(2-fluorophenyl)cyclopent-2-ene-1-carboxylic acid (4j)

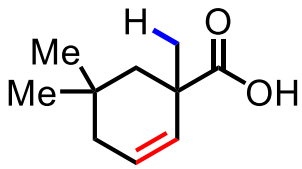
Following General Procedure on a 0.1 mmol scale. The product was obtained as a colorless oil (8.7 mg, 42% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.28 – 7.21 (m,

2H), 7.10 (td, *J* = 7.6, 1.2 Hz, 1H), 7.04 (ddd, *J* = 10.1, 8.6, 1.3 Hz, 1H), 6.16 (dt, *J* = 5.2, 2.3 Hz, 1H), 5.97 (dt, *J* = 5.5, 2.2 Hz, 1H), 3.04 (dddd, *J* = 13.2, 8.6, 4.5, 1.5 Hz, 1H), 2.62 (dddt, *J* = 16.9, 8.5, 6.0, 2.3 Hz, 1H), 2.49 – 2.41 (m, 1H), 1.95 (ddd, *J* = 13.3, 9.0, 6.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.7, 160.44 (d, J = 246.5 Hz), 136.7, 131.51 (d, J = 15.1 Hz), 130.7, 128.90 (d, J = 8.1 Hz), 127.49 (d, J = 4.5 Hz), 124.11 (d, J = 3.4 Hz), 115.75 (d, J = 21.9 Hz), 61.3, 35.0, 32.5; HRMS (ESI-TOF) *m/z* Calcd for $C_{12}H_{12}FO_2^+$ $[M+H]^+$ 207.0821, found 207.0817.



1-methylcyclohex-2-ene-1-carboxylic acid (4k)

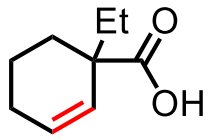
Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (13.2 mg, 64% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.80 (dt, *J* = 10.0, 3.7 Hz, 1H), 5.68 (dtd, *J* = 10.1, 2.2, 0.8 Hz, 1H), 2.20 – 2.10 (m, 1H), 2.06 – 1.92 (m, 2H), 1.71 – 1.60 (m, 2H), 1.47 (ddd, *J* = 13.3, 8.9, 4.4 Hz, 1H), 1.30 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.4, 130.2, 128.7, 43.0, 32.9, 26.4, 24.8, 19.7. HRMS (ESI-TOF) *m/z* Calcd for $C_8H_{13}O_2^+$ $[M+H]^+$ 207.0821, found 207.0830.



1,5,5-trimethylcyclohex-2-ene-1-carboxylic acid (4l)

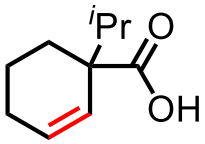
Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (13.0 mg, 77% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.72 (dd, *J* = 2.2, 1.1 Hz, 2H), 2.22 (dt, *J* = 13.6, 1.2 Hz, 1H), 1.85 – 1.72 (m, 2H), 1.30 (s, 3H), 1.28 – 1.24 (m, 1H), 0.96 (s, 3H), 0.86 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 183.5, 129.0,

126.7, 45.8, 42.8, 39.0, 31.6, 28.9, 25.8. HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{17}O_2^+$ $[M+H]^+$ 169.1229, found 169.1228.



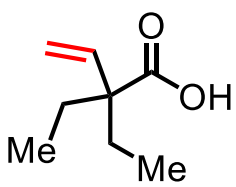
1-ethylcyclohex-2-ene-1-carboxylic acid (4m)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (8.0 mg, 52% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.84 (dt, *J* = 10.1, 3.7 Hz, 1H), 5.72 (dd, *J* = 10.1, 2.6 Hz, 1H), 2.15 (ddd, *J* = 13.2, 6.7, 3.0 Hz, 1H), 2.06 – 1.91 (m, 2H), 1.76 – 1.67 (m, 2H), 1.65 – 1.58 (m, 2H), 1.79 – 1.54 (m, 5H), 1.44 (ddd, *J* = 13.9, 11.1, 3.2 Hz, 1H), 0.90 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.0, 129.4, 129.2, 47.2, 32.9, 30.3, 25.1, 19.8, 8.9. HRMS (ESI-TOF) *m/z* Calcd for $C_9H_{15}O_2^+$ $[M+H]^+$ 155.1072, found 155.1069.



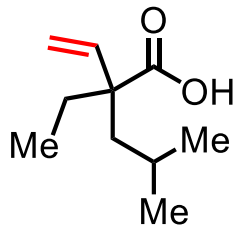
1-isobutylcyclohex-2-ene-1-carboxylic acid (4n)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (8.4 mg, 50% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.82 – 5.72 (m, 2H), 2.13 (ddd, *J* = 13.2, 7.1, 2.8 Hz, 1H), 2.05 – 1.91 (m, 2H), 1.75 (dp, *J* = 13.1, 6.6 Hz, 1H), 1.70 – 1.63 (m, 2H), 1.54 (dd, *J* = 13.8, 6.3 Hz, 1H), 1.48 (ddd, *J* = 13.3, 10.2, 3.3 Hz, 1H), 1.30 (d, *J* = 6.5 Hz, 1H), 0.90 (dd, *J* = 6.6, 4.6 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 182.6, 130.4, 128.4, 48.9, 31.5, 25.1, 24.9, 24.2, 24.1, 19.7. HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{19}O_2^+$ $[M+H]^+$ 169.1223, found 169.1228.



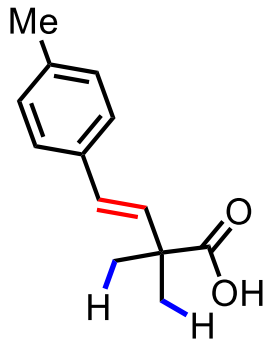
2,2-diethylbut-3-enoic acid (4o)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (6.3 mg, 44% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.97 (dd, *J* = 17.8, 11.0 Hz, 1H), 5.24 (dd, *J* = 11.0, 0.9 Hz, 1H), 5.14 (dd, *J* = 17.7, 0.9 Hz, 1H), 1.76 (q, *J* = 7.4 Hz, 4H), 0.86 (t, *J* = 7.4 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.1, 139.1, 115.3, 53.0, 28.2, 8.8; HRMS (ESI-TOF) *m/z* Calcd for $C_8H_{15}O_2^+$ $[M+H]^+$ 143.1067, found 143.1058.



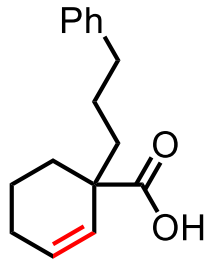
2-ethyl-4-methyl-2-vinylpentanoic acid (4p)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (8.2 mg, 48% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.99 (ddd, *J* = 18.0, 11.3, 0.8 Hz, 1H), 5.32 (dd, *J* = 11.2, 1.2 Hz, 1H), 5.07 (dd, *J* = 18.0, 1.2 Hz, 1H), 2.10 (hept, *J* = 6.8 Hz, 1H), 1.88 – 1.79 (m, 1H), 1.77 – 1.69 (m, 1H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H), 0.84 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.1, 135.0, 116.2, 56.9, 35.2, 26.5, 19.0, 16.9, 9.6. HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{19}O_2^+$ $[M+H]^+$ 171.1385, found 171.1384.



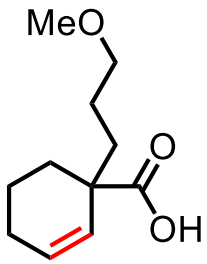
(*E*)-2,2-dimethyl-4-(*p*-tolyl)but-3-enoic acid (4q)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (6.5 mg, 32% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.27 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 6.45 (d, *J* = 16.2 Hz, 1H), 6.35 (d, *J* = 16.2 Hz, 1H), 2.33 (s, 3H), 1.43 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.3, 137.5, 134.2, 132.7, 129.4, 128.6, 126.4, 44.3, 25.1, 21.3. HRMS (ESI-TOF) *m/z* Calcd for $C_{13}H_{17}O_2^+$ $[M+H]^+$ 205.1229, found 205.1231.



1-(3-phenylpropyl)cyclohex-2-ene-1-carboxylic acid (4r)

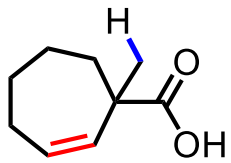
Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (15.6 mg, 64% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.29 – 7.24 (m, 2H), 7.20 – 7.13 (m, 3H), 5.82 (ddd, *J* = 10.1, 4.3, 3.1 Hz, 1H), 5.73 – 5.66 (m, 1H), 2.66 – 2.53 (m, 2H), 2.14 (ddd, *J* = 13.3, 6.7, 3.0 Hz, 1H), 2.05 – 1.89 (m, 2H), 1.79 – 1.55 (m, 6H), 1.44 (ddd, *J* = 13.9, 10.9, 3.3 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.9, 142.2, 129.4, 129.3, 128.5, 128.5, 125.9, 46.8, 39.8, 36.4, 30.7, 26.3, 25.0, 19.8. HRMS (ESI-TOF) *m/z* Calcd for $C_{16}H_{21}O_2^+$ $[M+H]^+$ 245.1542, found 245.1547.



1-(3-methoxypropyl)cyclohex-2-ene-1-carboxylic acid (4s)

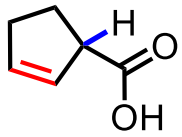
Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (11.5 mg, 58% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.83 (dt, *J* =

10.1, 3.7 Hz, 1H), 5.70 (dt, *J* = 10.1, 2.1 Hz, 1H), 3.36 (t, *J* = 6.2 Hz, 2H), 3.32 (s, 3H), 2.15 (ddd, *J* = 13.3, 6.9, 3.0 Hz, 1H), 1.98 (dttd, *J* = 20.7, 17.9, 5.8, 2.2 Hz, 2H), 1.77 – 1.52 (m, 5H), 1.45 (ddd, *J* = 13.7, 10.8, 3.2 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.7, 129.4, 129.2, 73.0, 58.6, 46.5, 36.6, 30.7, 25.1, 24.7, 19.8. HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{18}O_3^+$ $[M+H]^+$ 199.1334, found 199.1332.



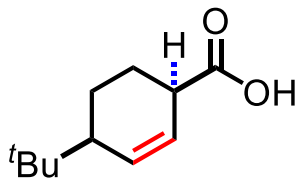
1-methylcyclohept-2-ene-1-carboxylic acid (4t)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (6.8 mg, 44% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.84 (dt, *J* = 11.8, 5.8 Hz, 1H), 5.59 (d, *J* = 11.6 Hz, 1H), 2.16 (q, *J* = 6.0 Hz, 2H), 2.05 (dt, *J* = 13.6, 5.2 Hz, 1H), 1.78 (p, *J* = 6.3 Hz, 2H), 1.66 (dq, *J* = 18.7, 6.5, 6.1 Hz, 2H), 1.53 (dq, *J* = 13.3, 6.3 Hz, 1H), 1.37 (d, *J* = 1.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.2, 134.6, 132.7, 48.4, 37.3, 28.3, 27.7, 27.2, 26.0. HRMS (ESI-TOF) *m/z* Calcd for $C_9H_{15}O_2^+$ $[M+H]^+$ 155.1072, found 155.1071.



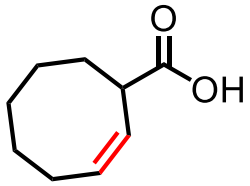
cyclopent-2-ene-1-carboxylic acid (4u)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (2.9 mg, 26% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.94 (dq, *J* = 5.7, 2.4 Hz, 1H), 5.75 (dq, *J* = 5.7, 2.3 Hz, 1H), 3.60 (dddd, *J* = 9.2, 7.3, 4.9, 2.4 Hz, 1H), 2.54 – 2.46 (m, 1H), 2.42 – 2.32 (m, 1H), 2.17 (tdd, *J* = 7.8, 6.3, 1.4 Hz, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.2, 134.6, 128.2, 50.4, 32.4, 26.6. HRMS (ESI-TOF) *m/z* Calcd for $C_6H_9O_2^+$ $[M+H]^+$ 113.0597, found 113.0601.



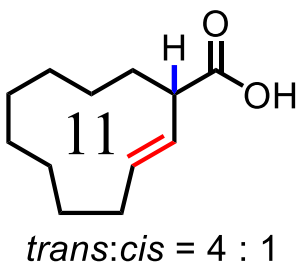
4-(*tert*-butyl)cyclohex-2-ene-1-carboxylic acid (4v)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (10.2 mg, 56% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.92 (dq, *J* = 10.3, 1.8 Hz, 1H), 5.83 (dddd, *J* = 10.3, 4.8, 2.7, 1.3 Hz, 1H), 3.06 (ddt, *J* = 7.0, 4.7, 2.4 Hz, 1H), 2.17 (ddd, *J* = 14.4, 3.7, 2.0 Hz, 1H), 1.85 (ddq, *J* = 10.6, 5.2, 2.6 Hz, 1H), 1.75 – 1.62 (m, 2H), 1.46 (tdd, *J* = 12.4, 10.2, 2.9 Hz, 1H), 0.88 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.9, 133.0, 124.1, 45.7, 39.8, 32.9, 27.4, 24.6, 21.3. HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{19}O_2^+$ $[M+H]^+$ 183.1385, found 183.1385.



(*Z*)-cyclooct-2-ene-1-carboxylic acid (4w)

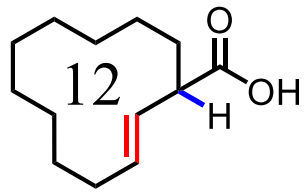
Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (5.2 mg, 34% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.81 (dddd, *J* = 10.1, 8.6, 7.3, 1.2 Hz, 1H), 5.69 (ddd, *J* = 10.4, 8.8, 1.4 Hz, 1H), 3.55 – 3.46 (m, 1H), 2.24 – 2.07 (m, 2H), 2.03 – 1.94 (m, 1H), 1.76 – 1.54 (m, 5H), 1.45 – 1.28 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.2, 131.8, 127.1, 42.2, 33.4, 29.9, 29.3, 26.7, 25.3. HRMS (ESI-TOF) *m/z* Calcd for $C_9H_{15}O_2^+$ $[M+H]^+$ 155.1067, found 155.1069.



trans:*cis* = 4 : 1

(*E*)-cycloundec-2-ene-1-carboxylic acid (4x) and (*Z*)-cycloundec-2-ene-1-carboxylic acid (4x')

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (8.2 mg, 42% yield). NMR was reported as a mixture of mono and didehydrogenation; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.66 – 5.57 (m, 1H), 5.55 – 5.49 (m, 0.7H), 5.32 (td, *J* = 11.0, 2.4 Hz, 0.3H), 3.54 (td, *J* = 11.1, 3.2 Hz, 0.3H), 2.96 (ddd, *J* = 11.4, 9.5, 3.8 Hz, 0.7H), 2.37 (dtd, *J* = 14.8, 12.1, 2.8 Hz, 0.3H), 2.21 (ddddd, *J* = 13.8, 6.1, 4.9, 3.2, 1.5 Hz, 0.7H), 2.11 (dddt, *J* = 14.7, 5.5, 4.1, 2.7 Hz, 0.3H), 2.07 – 1.98 (m, 0.7H), 1.95 (dddd, *J* = 14.0, 9.0, 3.8, 2.2 Hz, 0.7H), 1.79 (ddt, *J* = 14.0, 11.2, 3.0 Hz, 0.3H), 1.69 – 1.56 (m, 2H), 1.54 – 1.40 (m, 3H), 1.40 – 1.20 (m, 6H), 1.20 – 1.09 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.6, 180.4, 135.0, 134.5, 127.5, 127.0, 50.8, 42.8, 34.1, 31.4, 30.5, 27.7, 27.4, 27.3, 26.7, 26.6, 26.2, 26.0, 25.8, 25.6, 24.4, 24.2, 24.1, 23.7. HRMS (ESI-TOF) *m/z* Calcd for $C_{12}H_{19}O_2^-$ $[M-H]^-$ 195.1385, found 195.1392.



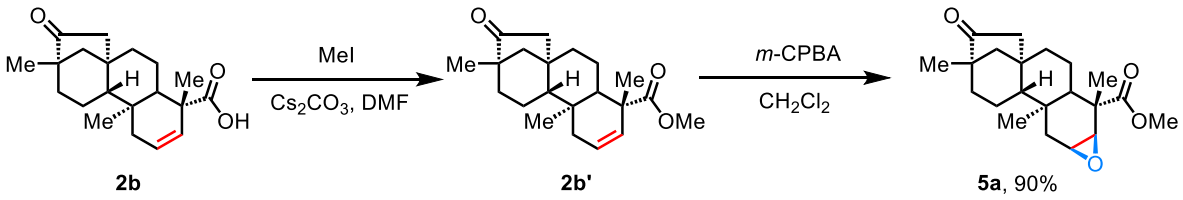
trans:*cis* = 2 : 1

(*E*)-cyclododec-2-ene-1-carboxylic acid (4y) and (*Z*)-cyclododec-2-ene-1-carboxylic acid (4y')

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (10.1 mg, 48% yield). NMR was reported as a mixture of mono and didehydrogenation; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.57 (ddd, *J* = 15.0, 10.3, 4.4 Hz, 0.7H), 5.51 (td, *J* = 11.3, 3.9 Hz, 0.3H), 5.43 (ddd, *J* = 15.3, 9.6, 1.6 Hz, 0.7H), 5.37 (td, *J* = 10.7, 2.1 Hz, 0.3H), 3.53 (ddd, *J* = 10.5, 8.5, 5.6 Hz, 0.3H), 3.01 (ddd, *J* = 11.0, 9.6, 3.6 Hz, 0.7H), 2.48 – 2.38 (m, 0.3H), 2.22 (ddtd, *J* = 11.2, 6.3, 3.3, 1.7 Hz, 0.7H), 2.00 (dtd, *J* = 13.8, 10.6, 3.3 Hz, 0.7H), 1.92 (ddt, *J* = 14.4, 5.2, 3.1 Hz, 0.3H),

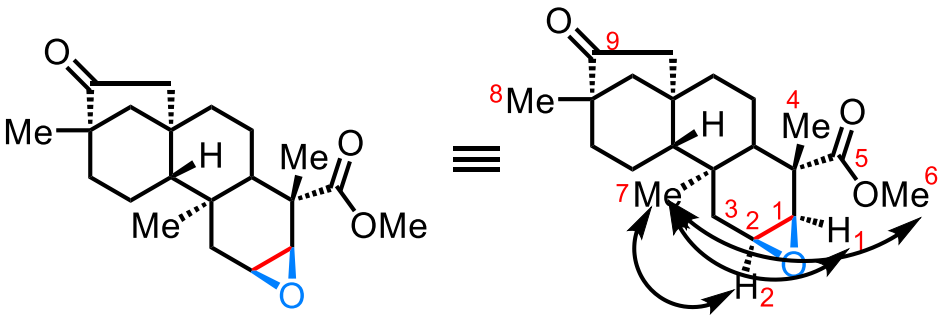
1.88 – 1.75 (m, 1.3H), 1.70 – 1.18 (m, 17H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 180.8, 180.7, 135.3, 133.7, 127.5, 127.4, 49.1, 41.0, 32.3, 30.8, 30.2, 26.8, 26.2, 26.0, 25.0, 24.9, 24.8, 24.6, 24.6, 24.5, 24.3, 24.2, 24.0, 23.7, 22.3, 22.2. HRMS (ESI-TOF) *m/z* Calcd for $C_{13}H_{23}O_2^+$ $[M+H]^+$ 211.1698, found 211.1699.

2.5. Diverse Functionalization of the β,γ-Dehydrogenated Products



To a solution of **2b** (316 mg, 1.0 mmol) in DMF (5 mL) was added Cs_2CO_3 (997 mg, 0.3 mmol) and iodomethane (710 mg, 5.0 mmol). The mixture was stirred at room temperature for 3 h and then diluted with water followed by extraction with ethyl acetate. The organic extracts were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. **2b'** was purified by flash chromatography (95%).[1]

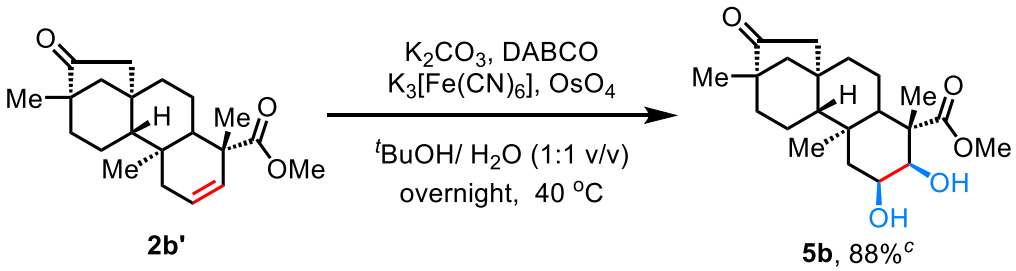
To a solution of compound **2b'** (33 mg, 0.1 mmol) in 1 mL of $CHCl_3$, was added metachloroperbenzoic acid (42 mg, 0.244 mmol) at 0 °C and the reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 24h. Upon completion, the reaction was quenched with 5 mL of saturated $NaHCO_3$ solution. The organic layer was washed with water and then brine. Then, it was dried, filtered, concentrated and purified using preparative TLC with ethyl acetate and hexanes (1/1) as the eluent to get product **5a** as a white solid (31.2 mg, 90% yield).[2] Relative stereochemistry was determined via 2D NMR (See NMR spectra section for details)



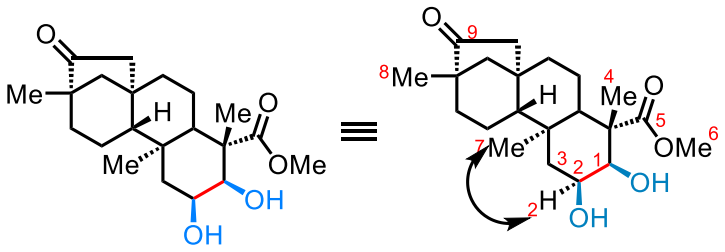
methyl (3*S*,5a*R*,8*S*,10a*S*,10b*R*)-3,8,10a-trimethyl-4-oxotetradecahydro-3,5a-methanocyclohepta[5,6]naphtho[2,3-*b*]oxirene-8-carboxylate (5a)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 3.69 (s, 3H), 3.42 (d, *J* = 3.8 Hz, 1H), 3.29 (dd, *J* = 5.6, 3.9 Hz, 1H), 2.46 (dd, *J* = 18.5, 3.8 Hz, 1H), 1.93 (dd, *J* = 15.4, 5.7 Hz, 1H),

1.89 – 1.84 (m, 1H), 1.76 (d, *J* = 18.6 Hz, 1H), 1.64 – 1.58 (m, 2H), 1.57 (s, 3H), 1.55 – 1.50 (m, 2H), 1.46 – 1.43 (m, 1H), 1.42 (s, 3H), 1.39 – 1.37 (m, 2H), 1.30 – 1.21 (m, 1H), 1.15 (dd, *J* = 12.6, 4.3 Hz, 1H), 0.97 (s, 3H), 0.75 (d, *J* = 1.0 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 222.2, 176.0, 58.2, 54.1, 53.9, 52.6, 51.9, 48.8, 47.7, 47.5, 44.2, 40.5, 39.4, 39.4, 37.4, 35.6, 24.2, 21.0, 20.6, 20.0, 15.7. HRMS (ESI-TOF) *m/z* Calcd for $C_{21}H_{31}O_4^+$ $[M+H]^+$ 347.2222, found 347.2227.

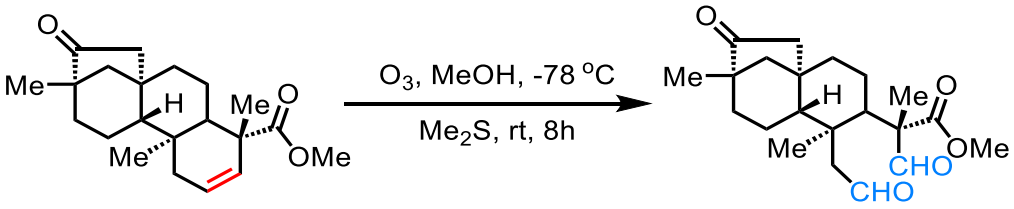


Compound **2b'** (33 mg, 0.1 mmol) and K_2CO_3 (1 mmol) were dissolved in a mixture of ^{t}BuOH and water (1:1 v/v) (3 mL). DABCO (0.1 mmol) and $K_3[Fe(CN)_6]$ (1 mmol) were added and the resulting yellow solution was mixed with 35 µL 4% OsO_4 in water solution (17 µmol). the mixture was heated overnight at 40°C. After cooling, solid Na_2SO_3 (2.8 mmol) was added and stirred for 90 min at rt. The mixture was treated with 1N HCl to pH 5 and extracted three times with 10 mL of diethyl ether. The combined organic extracts were dried with $MgSO_4$ and the solvent was removed under vacuum. The residue was purified by flash chromatography (hexane/ EtOAc = 1/ 2) to afford the **5b** as a white solid (32.0 mg, 88%).[3] The relative stereochemistry was determined via 2D NMR (See NMR spectra section for details)



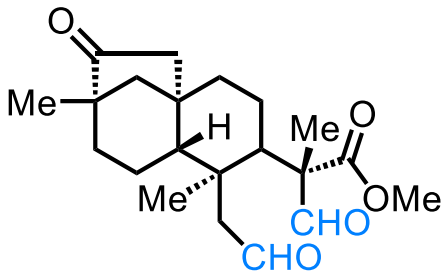
methyl (4*S*,6a*R*,9*S*,11a*R*,11b*S*)-2,3-dihydroxy-4,9,11b-trimethyl-8-oxotetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate (5b)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.21 (ddd, *J* = 12.1, 5.1, 2.9 Hz, 1H), 4.07 (d, *J* = 2.8 Hz, 1H), 3.64 (s, 3H), 2.58 (dd, *J* = 18.6, 3.8 Hz, 1H), 1.84 – 1.59 (m, 9H), 1.59 – 1.48 (m, 2H), 1.44 – 1.37 (m, 2H), 1.35 (s, 3H), 1.31 – 1.21 (m, 4H), 0.97 (s, 3H), 0.70 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 222.4, 177.1, 74.1, 66.1, 54.4, 54.3, 51.6, 48.8, 48.6, 48.4, 48.1, 41.4, 41.3, 39.5, 38.7, 37.3, 24.0, 21.2, 20.5, 19.9, 14.1. HRMS (ESI-TOF) *m/z* Calcd for $C_{21}H_{31}O_5^-$ $[M-H]^-$ 363.2171, found 363.2167.



2b' **5c**, 57%

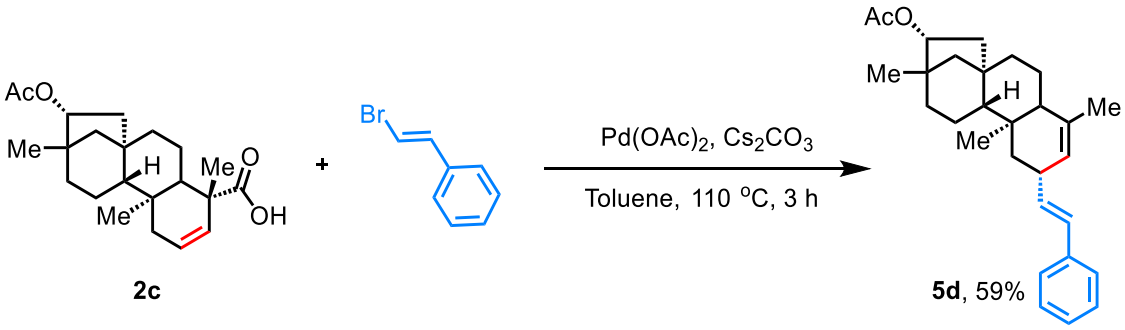
To a solution of compound **2b'** (34 mg, 0.1 mmol) in MeOH (2 mL) at -78 °C, ozone was bubbled through the solution until a blue color appeared. The flow of ozone was then replaced with argon until the blue color disappeared, indicating the removal of excess ozone. The bubbling was then stopped, and the flask was capped with a septum equipped with an argon inlet. Me_2S (12.4 mg, 0.2 mmol) was added slowly to the mixture while still at -78 °C. It was then allowed to warm up to room temperature and stirred for 8 h. The reaction mixture was concentrated under vacuum and the residue was purified by PTLC (hexane/EtOAc = 8/1) to afford the **5c** as a colorless oil (20.6 mg, 57%). The relative stereochemistry was determined via 2D NMR (See NMR spectra section for details)



methyl (2*S*)-2-((1*S*,4a*R*,7*S*,9a*R*)-1,7-dimethyl-6-oxo-1-(2-oxoethyl)decahydro-4a,7-methanobenzo[7]annulen-2-yl)-2-methyl-3-oxopropanoate (5c)

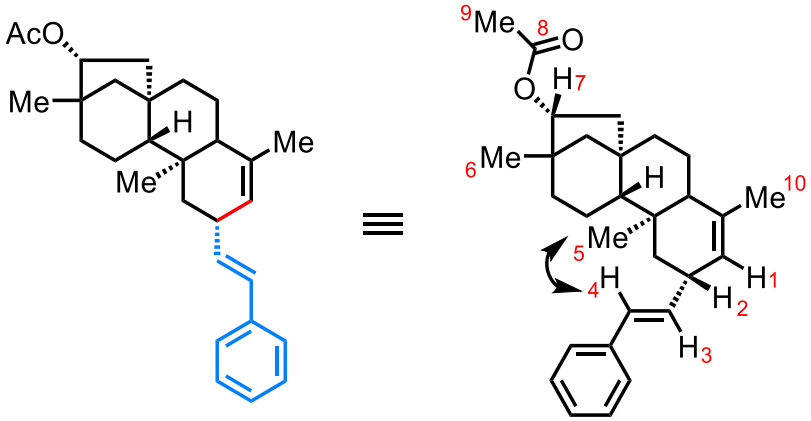
Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (78% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.81 (dd, *J* = 3.1, 1.0 Hz, 1H), 9.69 (s, 1H), 3.68 (s, 3H), 2.98 (dd, *J* = 12.0, 2.4 Hz, 1H), 2.54 (dd, *J* = 18.5, 3.8 Hz, 1H), 2.38 (dd, *J* = 18.7, 3.1 Hz, 1H), 2.21 (dd, *J* = 18.8, 1.0 Hz, 1H), 1.94 (dd, *J* = 12.5, 4.4 Hz, 1H), 1.83 (d, *J* = 18.5 Hz, 1H), 1.73 – 1.58 (m, 6H), 1.48 (dd, *J* = 11.6, 3.8 Hz, 1H), 1.43 – 1.36 (m, 1H), 1.35 (s, 3H), 1.29 (ddt, *J* = 12.9, 7.6, 5.1 Hz, 2H), 0.98 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 221.2, 201.2, 199.6, 173.1, 61.0, 53.8, 52.7,

49.9, 48.8, 48.7, 48.1, 47.2, 41.8, 40.0, 39.6, 36.9, 23.1, 20.4, 19.7, 19.0, 14.7. HRMS (ESI-TOF) *m/z* Calcd for $C_{21}H_{29}O_5^-$ $[M-H]^-$ 361.2015, found 361.2018.



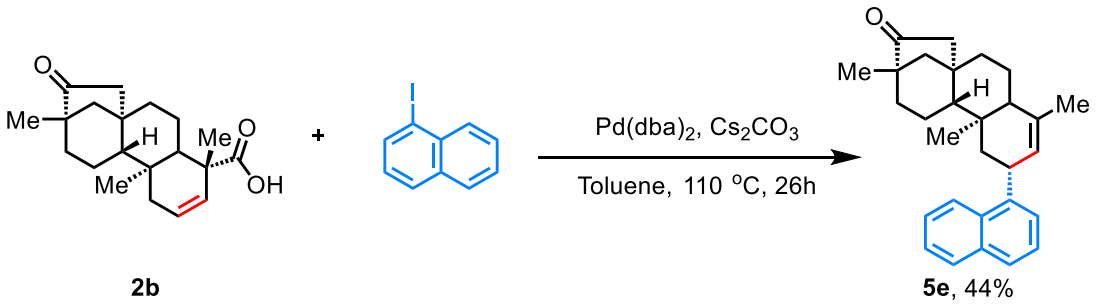
2c **5d**, 59%

The mixture of compound **2c** (0.125 mmol), vinyl bromide (0.1 mmol), Cs_2CO_3 (0.13 mmol), and $Pd(OAc)_2$ (0.005 mmol) in dry toluene (2 mL) was stirred at 110 °C under argon for 3 h. The reaction mixture was purified by PTLC (hexane/EtOAc = 4/1) to afford the **5d** as colorless oil (24.7 mg, 59%).[4] The relative stereochemistry was determined via 2D NMR (See NMR spectra section for details)

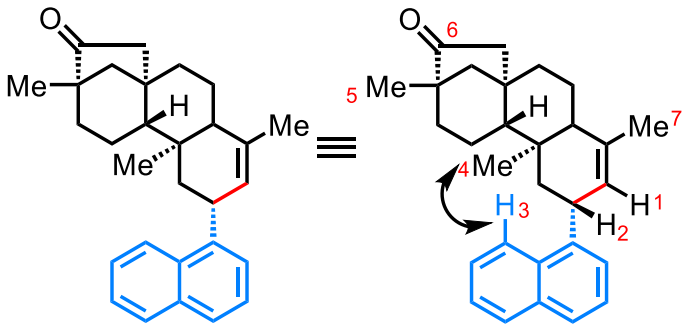


(6a*R*,8*R*,11a*R*,11b*S*)-4,9,11b-trimethyl-2-((*E*)-styryl) 1,2,4a,5,6,7,8,9,10,11,11a, 11b-dodecahydro-6a,9-methanocyclohepta[*a*]naphthalen-8-yl acetate (5d)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.34 – 7.32 (m, 2H), 7.28 (t, *J* = 7.7 Hz, 2H), 7.20 – 7.16 (m, 1H), 6.35 – 6.24 (m, 2H), 5.43 (qd, *J* = 2.8, 1.7 Hz, 1H), 4.72 (dd, *J* = 9.4, 5.9 Hz, 1H), 2.99 (s, 1H), 2.04 (s, 3H), 1.88 (dt, *J* = 10.9, 3.7 Hz, 2H), 1.84 – 1.78 (m, 2H), 1.74 – 1.69 (m, 5H), 1.63 – 1.35 (m, 6H), 1.30 – 1.20 (m, 2H), 1.14 – 1.05 (m, 2H), 0.92 (s, 3H), 0.79 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 171.6, 138.1, 136.8, 136.0, 128.6, 128.1, 126.9, 126.1, 122.6, 81.8, 55.1, 53.8, 48.6, 42.2, 41.9, 41.7, 41.5, 40.6, 36.8, 36.4, 34.7, 25.0, 22.1, 21.8, 21.3, 20.9, 14.6. HRMS (ESI-TOF) *m/z* Calcd for $C_{27}H_{35}^+$ $[M\text{-}OAc]^+$ 359.2739, found 359.2728.



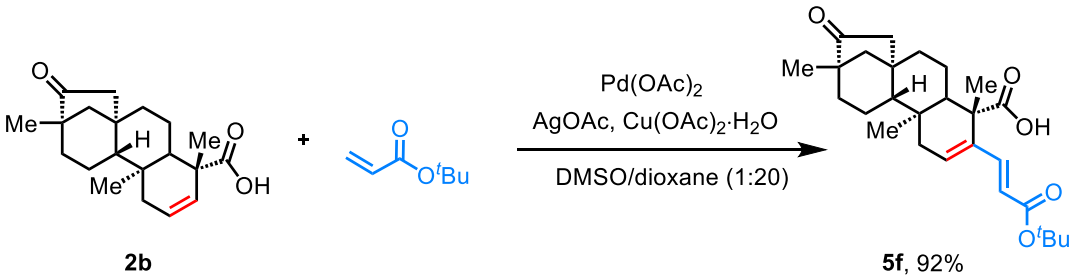
The mixture of compound **2b** (32 mg, 0.1 mmol), 1-Iodonaphthalene (28 mg, 0.11 mmol), Cs_2CO_3 (0.11 mmol), and $Pd_2(dba)_3$ (0.01 mmol) in dry toluene (0.5 mL) was stirred at 110 °C under argon for 26 h. Upon completion, the reaction mixture was extracted with CH_2Cl_2, and washed with 1 M HCl and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by PTLC (hexane/EtOAc = 4/1) to afford the **5e** as a white solid (17.5 mg, 44%).[5] The relative stereochemistry was determined via 2D NMR (See NMR spectra section for details)



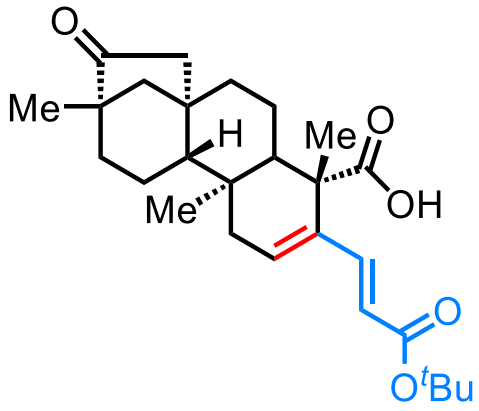
(6a*R*,9*S*,11a*R*,11b*S*)-4,9,11b-trimethyl-2-(naphthalen-1-yl)-1,2,4a,5,6,9,10,11,11a,11b-decahydro-6a,9-methanocyclohepta[*a*]naphthalen-8(7*H*)-one (5e)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.4 Hz, 1H), 7.89 – 7.84 (m, 1H), 7.69 (dd, *J* = 6.6, 2.8 Hz, 1H), 7.49 (dddd, *J* = 23.4, 8.0, 6.8, 1.4 Hz, 2H), 7.41 – 7.36 (m, 2H), 5.75 (dq, *J* = 3.3, 1.6 Hz, 1H), 4.18 (ddt, *J* = 8.5, 6.0, 2.9 Hz, 1H), 2.66 (dd, *J* = 18.7, 3.8 Hz, 1H), 2.07 – 2.01 (m, 1H), 1.99 – 1.89 (m, 3H), 1.86 (dt, *J* = 2.6, 1.4 Hz, 3H), 1.81 (d, *J* = 18.7 Hz, 1H), 1.71 – 1.55 (m, 4H), 1.53 – 1.27 (m, 5H), 1.15 – 0.98

(m, 1H), 0.96 (s, 3H), 0.68 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 222.4, 143.4, 137.1, 134.3, 131.5, 129.2, 126.6, 125.9, 125.4, 125.4, 125.3, 124.0, 123.8, 54.6, 53.5, 49.0, 49.0, 48.2, 43.7, 40.6, 39.4, 37.3, 34.6, 31.1, 22.3, 21.8, 21.1, 20.0, 15.1. HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{35}O^+$ $[M+H]^+$ 399.2688, found 399.2693.



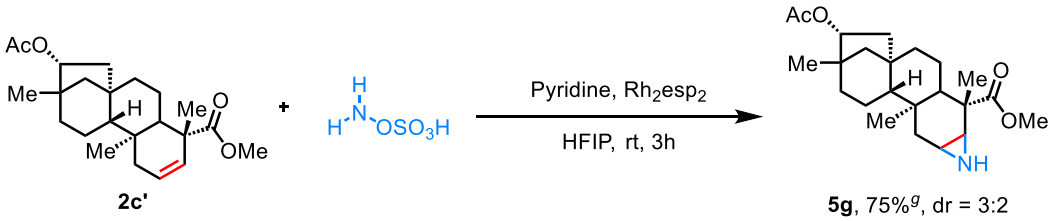
To a solution of compound **2b** (32 mg, 0.1 mmol) in DMSO/dioxane =1/20 (2 mL), AgOAc (0.15 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.1 mmol), $Pd(OAc)_2$ (0.01 mmol) and dry DMSO/dioxane (1:20) were added, followed by the addition of olefin (0.1 mmol). The resulting mixture was kept stirring in a preheated oil bath at 80 °C for 24 h. The reaction mixture was then extracted with ethyl acetate, washed with 10% HCl solution and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by PTLC (hexane/EtOAc = 4/1) to afford the **5f** as a white solid (40.7 mg, 92%).[6]



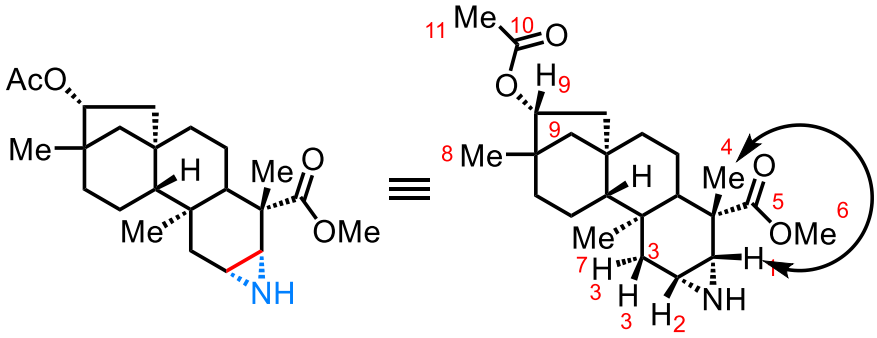
(4*S*,6a*R*,9*S*,11a*R*,11b*S*)-3-((*E*)-3-(*tert*-butoxy)-3-oxoprop-1-en-1-yl)-4,9,11b-trimethyl-8-oxo-1,4,4a,5,6,7,8,9,10,11,11a,11b-dodecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylic acid (5f)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 7.12 (d, *J* = 16.1 Hz, 1H), 6.17 (dd, *J* = 6.7, 2.3 Hz, 1H), 5.76 (d, *J* = 16.1 Hz, 1H), 2.64 (dd, *J* = 18.6, 3.7 Hz, 1H), 2.27 (dd, *J* = 18.3, 6.7 Hz, 1H), 2.01 – 1.92 (m, 1H), 1.88 – 1.53 (m, 7H), 1.47 (s, 9H), 1.45 – 1.37 (m, 6H), 1.37 – 1.20 (m, 3H), 0.99 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 223.7, 177.6, 166.8, 144.7, 137.1, 133.7, 119.3, 80.5, 54.4, 54.0, 54.0, 49.0, 47.9, 46.9,

41.1, 40.5, 39.5, 37.3, 36.0, 28.3, 26.6, 21.8, 20.5, 19.9, 14.8. HRMS (ESI-TOF) *m/z* Calcd for $C_{27}H_{37}O_5^-$ $[M-H]^-$ 441.2641, found 441.2629.

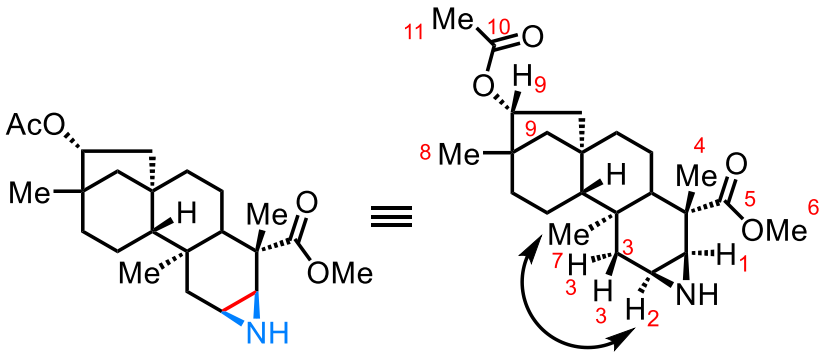


To a solution of compound **2c'** (0.1 mmol) in HFIP (0.25 mL), pyridine (0.12 mmol), the corresponding aminating agent N-H hydroxylamine O-sulfonic acid (0.12 mmol), and $Rh_2(esp)_2$ (0.1 μmol, 1 mol%) were added sequentially. The mixture was stirred at room temperature for 3 h. The reaction mixture was quenched with the addition of saturated aqueous Na_2CO_3 and extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, concentrated under reduced pressure, and purified by PTLC (hexane/EtOAc = 4/1) to afford the **5g** and **5g'** as a white solid (29.2 mg, 75%).[7] The relative stereochemistry was determined via 2D NMR (See NMR spectra section for details)



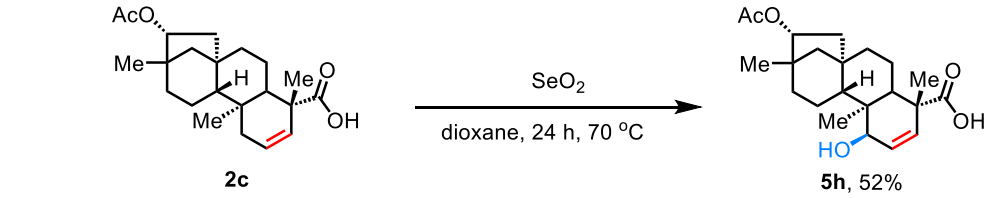
ethyl (4*R*,5a*R*,8*S*,8a*S*,9a*R*,10a*S*,10b*R*)-4-acetoxy-3,8,10a-trimethyltetradecahydro-1*H*-3,5a-methanocyclohepta[5,6]naphtho[2,3-*b*]azirine-8-carboxylate (5g)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.73 (dd, *J* = 10.3, 4.9 Hz, 1H), 3.64 (s, 3H), 2.36 (ddd, *J* = 5.7, 3.9, 1.3 Hz, 1H), 2.24 (d, *J* = 6.1 Hz, 1H), 2.05 (s, 4H), 1.94 (qd, *J* = 13.8, 2.9 Hz, 1H), 1.88 – 1.74 (m, 3H), 1.66 – 1.54 (m, 3H), 1.53 – 1.47 (m, 1H), 1.45 (s, 3H), 1.36 – 1.15 (m, 5H), 1.03 – 0.98 (m, 4H), 0.94 – 0.84 (m, 5H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 176.3, 171.5, 81.6, 57.4, 55.0, 54.0, 51.3, 44.7, 42.7, 41.7, 41.5, 40.5, 38.4, 38.0, 37.2, 34.7, 32.0, 28.8, 25.1, 22.5, 21.4, 20.7, 17.7. HRMS (ESI-TOF) *m/z* Calcd for $C_{23}H_{36}NO_4^+$ $[M+H]^+$ 390.2644, found 390.2659.

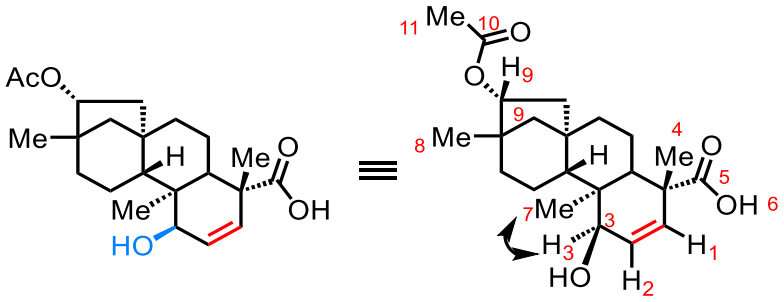


methyl (4*R*,5a*R*,8*S*,8a*R*,9a*S*,10a*S*,10b*R*)-4-acetoxy-3,8,10a-trimethyltetradecahydro-1*H*-3,5a-methanocyclohepta[5,6]naphtho[2,3-*b*]azirine-8-carboxylate (5g')

^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.69 (dd, *J* = 10.8, 4.3 Hz, 1H), 3.66 (s, 3H), 2.67 (d, *J* = 6.3 Hz, 1H), 2.37 (t, *J* = 6.8 Hz, 1H), 2.04 (s, 3H), 1.91 (dd, *J* = 14.6, 7.4 Hz, 1H), 1.80 – 1.73 (m, 3H), 1.65 – 1.52 (m, 3H), 1.46 (ddt, *J* = 25.2, 12.7, 2.7 Hz, 1H), 1.36 (s, 3H), 1.34 – 1.19 (m, 7H), 0.99 (dt, *J* = 12.4, 4.1 Hz, 2H), 0.89 (s, 3H), 0.76 – 0.70 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 177.7, 171.6, 81.8, 55.2, 54.4, 51.7, 47.4, 43.6, 42.3, 41.6, 40.5, 40.1, 39.9, 37.6, 36.0, 34.7, 29.0, 25.2, 25.1, 21.3, 21.1, 20.5, 15.6. HRMS (ESI-TOF) *m/z* Calcd for $C_{23}H_{36}NO_4^+$ $[M+H]^+$ 390.2644, found 390.2653.



To a solution of compound **2c** (0.1 mmol) in dry dioxane (1 mL), SeO_2 (0.23 mmol) was added, and the mixture was kept at 70 °C for 24 h, the mixture was filtered and evaporated under reduced pressure. The residue was purified by PTLC (hexane/EtOAc = 4/1) to afford the **5h** as a colorless oil (19.6 mg, 52%).[8] The relative stereochemistry was determined via 2D NMR (See NMR spectra section for details)

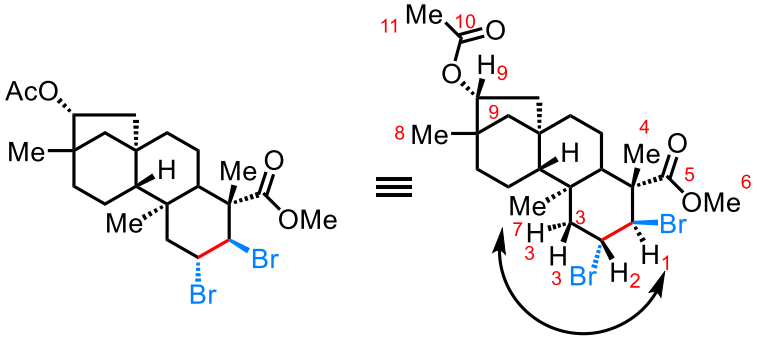


(1*R*,4*R*,6a*R*,8*R*,11a*R*,11b*S*)-8-acetoxy-1-hydroxy-4,9,11b-trimethyl-1,4,4a,5,6,7,8,9,10,11,11a,11b-dodecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylic acid (5h)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.89 (ddd, *J* = 10.1, 5.5, 1.4 Hz, 1H), 5.77 (dd, *J* = 10.0, 1.4 Hz, 1H), 4.73 (dd, *J* = 10.8, 4.2 Hz, 1H), 3.69 (d, *J* = 5.5 Hz, 1H), 2.06 (d, *J* = 1.5 Hz, 3H), 1.92 – 1.76 (m, 5H), 1.65 (qd, *J* = 12.7, 5.6 Hz, 1H), 1.56 (dd, *J* = 10.0, 3.5 Hz, 2H), 1.52 – 1.42 (m, 2H), 1.40 – 1.30 (m, 6H), 1.17 (dd, *J* = 11.6, 2.8 Hz, 1H), 0.92 (d, *J* = 1.5 Hz, 3H), 0.85 (d, *J* = 1.6 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 181.1, 171.7, 134.4, 126.4, 81.8, 68.8, 54.8, 46.8, 45.5, 44.8, 42.1, 41.7, 40.7, 40.5, 40.1, 34.4, 27.8, 25.2, 21.9, 21.4, 20.5, 14.0. HRMS (ESI-TOF) *m/z* Calcd for $C_{22}H_{31}O_5^-$ $[M-H]^-$ 375.2171, found 375.2162.

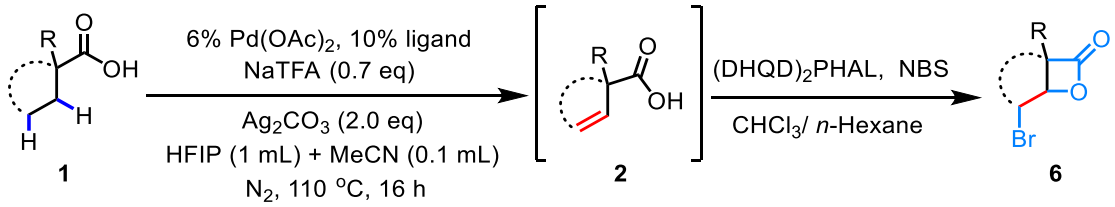
2c' **5i**, 40%

The mixture of NBS (0.3 mmol) and DMSO (0.3 mmol) in DCM (1 mL) was allowed to stir at room temperature until NBS was completely dissolved. Then, compound **2c'** (0.1 mmol) was added. The resulting mixture was stirred at room temperature for 10 min. Upon completion, the mixture was concentrated under reduced pressure and purified by PTLC (hexane/EtOAc = 5/1) to afford the **5i** as a white solid (21.3 mg, 40%).[9] The relative stereochemistry was determined via 2D NMR (See NMR spectra section for details)

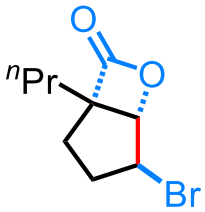


methyl (4*R*,6a*R*,8*R*,11a*R*,11b*S*)-8-acetoxy-2,3-dibromo-4,9,11b-trimethyltetradecahydro-6a,9-methanocyclohepta[*a*]naphthalene-4-carboxylate (5i)

^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.42 (d, *J* = 7.2 Hz, 1H), 4.77 – 4.70 (m, 1H), 4.62 (q, *J* = 6.2 Hz, 1H), 3.68 (s, 3H), 2.24 (d, *J* = 5.9 Hz, 2H), 2.06 (s, 3H), 1.87 – 1.82 (m, 2H), 1.80 (ddt, *J* = 13.2, 5.5, 2.0 Hz, 1H), 1.69 – 1.59 (m, 2H), 1.56 – 1.50 (m, 3H), 1.47 (dd, *J* = 11.5, 2.7 Hz, 1H), 1.40 (s, 3H), 1.38 – 1.33 (m, 2H), 1.28 – 1.20 (m, 1H), 1.19 (s, 3H), 1.05 (td, *J* = 12.4, 3.1 Hz, 2H), 0.91 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.5, 171.5, 81.5, 62.3, 56.8, 54.9, 52.0, 51.7, 49.8, 49.5, 42.2, 41.7, 41.0, 41.0, 38.7, 34.4, 29.8, 28.6, 24.9, 21.8, 21.3, 20.5, 18.3. HRMS (ESI-TOF) *m/z* Calcd for $C_{21}H_{31}Br_2O_2^+$ $[M\text{-}OAc]^+$ 473.0691, found 473.0694.

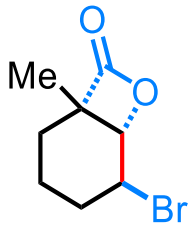


Upon completion of the dehydrogenation, the mixture was acidified with 200 µL of formic acid and filtered by a pad of silica with ethyl acetate. The resulting solution was concentrated. The residue was dissolved in $CHCl_3$/ hexane =1/1 (2 mL) and cooled to 0 °C. To the stirred mixture was added $(DHQD)_2PHAL$ (7.8 mg, 0.01 mmol) and NBS (21.4 mg, 0.12 mmol). The mixture was stirred at room temperature for 3 h and quenched by the addition of saturated aqueous $Na_2S_2O_3$, followed by extraction with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by PTLC (hexane/EtOAc = 8/1- 3/1) to afford the **6a-6i**.



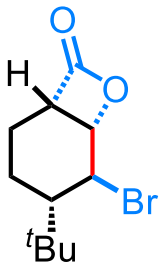
(1*S*,4*S*,5*S*)-4-bromo-1-propyl-6-oxabicyclo[3.2.0]heptan-7-one (6a)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (11.6 mg, 50% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.81 (d, *J* = 1.0 Hz, 1H), 4.46 (d, *J* = 4.5 Hz, 1H), 2.46 – 2.37 (m, 1H), 2.28 (dddt, *J* = 15.4, 6.6, 1.2, 0.6 Hz, 1H), 2.14 (dd, *J* = 13.5, 6.7 Hz, 1H), 2.01 (td, *J* = 13.1, 6.6 Hz, 1H), 1.82 (tdt, *J* = 14.1, 9.1, 7.0 Hz, 2H), 1.65 – 1.53 (m, 1H), 1.47 (ddqd, *J* = 14.6, 11.3, 7.3, 5.7 Hz, 1H), 1.00 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.8, 82.8, 68.7, 50.0, 33.2, 32.7, 29.7, 19.3, 14.4. HRMS (ESI-TOF) *m/z* Calcd for $C_9H_{14}BrO_2^+$ $[M+H]^+$ 233.0177, found 233.0179.



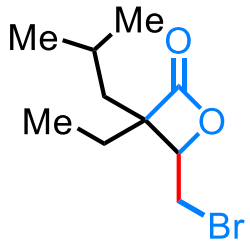
(1*S*,5*S*,6*S*)-5-bromo-1-methyl-7-oxabicyclo[4.2.0]octan-8-one (6b)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (9.8 mg, 45% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.62 (dd, *J* = 3.2, 0.9 Hz, 1H), 4.53 (dt, *J* = 5.0, 3.4 Hz, 1H), 2.42 – 2.33 (m, 1H), 2.14 – 2.06 (m, 1H), 2.00 – 1.86 (m, 3H), 1.78 – 1.67 (m, 1H), 1.46 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 174.3, 78.5, 54.9, 45.6, 25.6, 24.4, 21.3, 16.3. HRMS (ESI-TOF) *m/z* Calcd for $C_8H_{12}BrO_2^+$ $[M+H]^+$ 219.0021, found 219.0020.



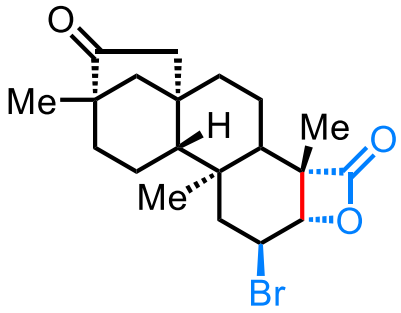
(1*S*,5*S*,6*S*)-5-bromo-4-(*tert*-butyl)-7-oxabicyclo[4.2.0]octan-8-one (6c)

Following General Procedure on 0.1 mmol scale. The product was obtained as a colorless oil (10.7 mg, 41% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.95 (ddd, *J* = 5.5, 2.4, 0.7 Hz, 1H), 4.44 (t, *J* = 2.5 Hz, 1H), 3.87 (tdd, *J* = 5.5, 2.8, 1.2 Hz, 1H), 2.35 (ddd, *J* = 12.7, 7.6, 2.5 Hz, 1H), 2.11 – 2.01 (m, 2H), 1.86 (ddtd, *J* = 14.4, 8.5, 3.2, 1.2 Hz, 1H), 1.45 – 1.33 (m, 1H), 0.95 (s, 9H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 170.3, 72.6, 53.2, 49.4, 44.1, 34.4, 27.2, 20.0, 19.4. HRMS (ESI-TOF) *m/z* Calcd for $C_{11}H_{18}BrO_2^+$ $[M+H]^+$ 261.0490, found 261.0485.



4-(bromomethyl)-3-ethyl-3-isobutyloxetan-2-one (6d)

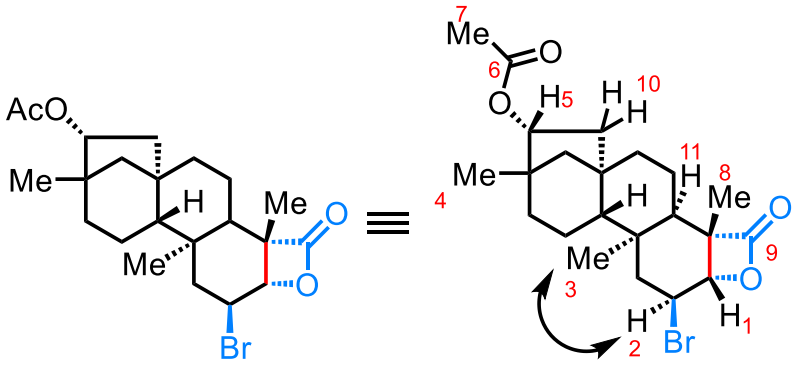
Following General Procedure on 0.1 mmol scale. The product was obtained as a white solid (9.4 mg, 38% yield). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.57 (t, *J* = 7.3 Hz, 1H), 3.69 – 3.62 (m, 1H), 3.53 – 3.42 (m, 1H), 2.22 – 2.15 (m, 1H), 1.90 (dt, *J* = 14.7, 7.3 Hz, 1H), 1.85 – 1.74 (m, 1H), 1.56 (s, 2H), 1.12 – 1.05 (m, 6H), 0.98 (dd, *J* = 6.8, 2.8 Hz, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.5, 75.1, 66.7, 27.8, 27.2, 19.8, 18.1, 17.1, 8.9; HRMS (ESI-TOF) *m/z* Calcd for $C_{10}H_{18}BrO_2^+$ $[M+H]^+$ 249.0490, found 249.0480.



2a*S*,4a*R*,7*S*,9a*R*,9b*S*,11*S*,11a*S*)-11-bromo-2a,7,9b-trimethyldodecahydro-2*H*-4a,7-methanocyclohepta[5,6]naphtho[2,1-*b*]oxete-2,6(5*H*)-dione (6e)

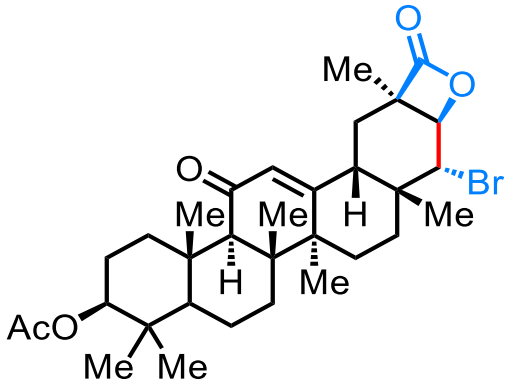
Following General Procedure on 0.1 mmol scale. The product was obtained as a white solid (29.6 mg, 75% yield). The relative stereochemistry was assigned via comparison with that of **6f**. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.72 (d, *J* = 2.5 Hz, 1H), 4.55 (ddd, *J* = 12.6, 6.8, 2.5 Hz, 1H), 2.66 (dd, *J* = 18.7, 3.9 Hz, 1H), 2.49 (dd, *J* = 13.5, 6.9 Hz, 1H), 1.86 (d, *J* = 18.7 Hz, 1H), 1.75 (dtdd, *J* = 16.5, 14.0, 8.8, 6.5 Hz, 3H), 1.65 – 1.53 (m, 8H), 1.47 – 1.36 (m, 2H), 1.35 – 1.22 (m, 3H), 0.98 (d, *J* = 9.7 Hz, 6H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 221.1, 173.4, 84.0, 58.5, 54.3, 52.6, 52.3, 49.1, 48.7, 47.3,

45.6, 40.5, 39.8, 39.3, 36.8, 23.5, 20.7, 20.3, 19.8, 13.0. HRMS (ESI-TOF) *m/z* Calcd for $C_{20}H_{28}BrO_3^+$ $[M+H]^+$ 395.1222, found 395.1220.



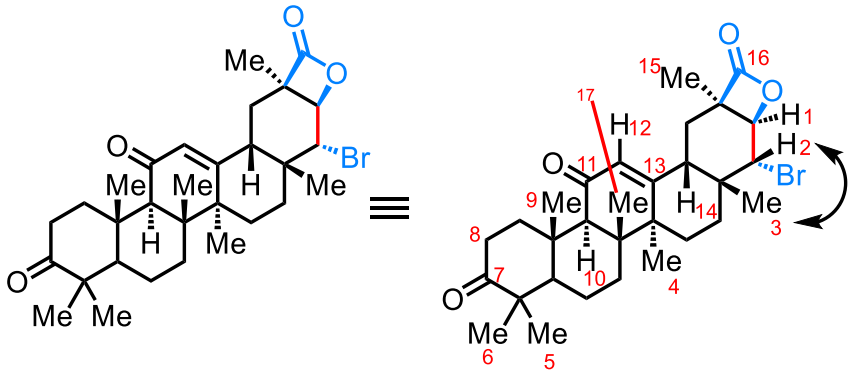
(2a*S*,4a*R*,6*R*,9a*R*,9b*S*,11*S*,11a*S*)-11-bromo-2a,7,9b-trimethyl-2-oxotetradecahydro-2*H*-4a,7-methanocyclohepta[5,6]naphtho[2,1-*b*]oxet-6-yl acetate (6f)

Following General Procedure on 0.1 mmol scale. The product was obtained as a white solid (27.2 mg, 62% yield). The relative stereochemistry was determined via 2D NMR (See NMR spectra section for details). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 4.75 (dd, *J* = 10.8, 4.5 Hz, 1H), 4.70 (d, *J* = 2.5 Hz, 1H), 4.56 (ddd, *J* = 12.8, 6.8, 2.5 Hz, 1H), 2.49 (dd, *J* = 13.5, 6.8 Hz, 1H), 2.06 (s, 3H), 1.90 (dd, *J* = 14.7, 10.7 Hz, 1H), 1.85 – 1.77 (m, 2H), 1.69 – 1.58 (m, 4 H), 1.56 – 1.45 (m, 5H), 1.43 – 1.36 (m, 2H), 1.29 – 1.19 (m, 2H), 1.12 – 1.04 (m, 2H), 0.97 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 173.5, 171.3, 84.2, 81.2, 58.7, 54.9, 53.5, 52.4, 47.5, 46.2, 42.1, 41.7, 41.4, 40.4, 40.0, 34.3, 24.7, 23.6, 21.3, 20.7, 20.3, 13.0. HRMS (ESI-TOF) *m/z* Calcd for $C_{22}H_{32}BrO_4^+$ $[M+H]^+$ 439.1484, found 439.1479.



(3*S*,6a*R*,6b*S*,8a*R*,9*R*,9a*R*,11a*R*,12a*S*,14a*R*,14b*S*)-9-bromo-4,4,6a,6b,8a,11a,14b-heptamethyl-11,14-dioxo-1,3,4,4a,5,6,6a,6b,7,8,8a,9,9a,11,11a,12,12a,14,14a,14b-icosahydro-2*H*-piceno[3,2-*b*]oxet-3-yl acetate (6g)

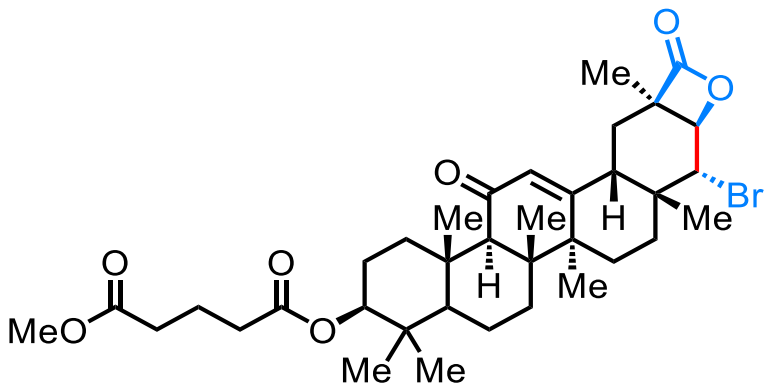
Following General Procedure on 0.1 mmol scale. The product was obtained as a white solid (51.8 mg, 88% yield). The relative stereochemistry was assigned via comparison with that of **6h**. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.67 (s, 1H), 4.91 (d, *J* = 3.4 Hz, 1H), 4.55 – 4.47 (m, 2H), 2.75 (dt, *J* = 13.6, 3.6 Hz, 1H), 2.40 – 2.28 (m, 4H), 2.05 (d, *J* = 0.8 Hz, 3H), 1.81 (td, *J* = 13.9, 3.6 Hz, 1H), 1.76 – 1.67 (m, 2H), 1.67 – 1.59 (m, 2H), 1.52 – 1.40 (m, 5H), 1.33 (s, 3H), 1.25 (s, 3H), 1.19 (d, *J* = 8.5 Hz, 6H), 1.10 (s, 3H), 1.05 (td, *J* = 13.5, 3.7 Hz, 1H), 0.89 – 0.87 (m, 6H), 0.83 – 0.79 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.3, 173.0, 171.2, 164.8, 130.1, 80.7, 79.2, 61.5, 60.8, 58.4, 55.3, 45.9, 44.7, 43.7, 38.9, 38.2, 37.2, 36.5, 35.1, 33.4, 30.1, 29.9, 28.2, 25.6, 23.7, 21.5, 20.8, 19.5, 18.8, 17.5, 16.9, 16.8. HRMS (ESI-TOF) *m/z* Calcd for $C_{32}H_{46}BrO_5^+$ $[M+H]^+$ 589.2529, found 589.2540.



(6a*R*,6b*S*,8a*R*,9*R*,9a*R*,11a*R*,12a*S*,14a*R*,14b*S*)-9-bromo-4,4,6a,6b,8a,11a,14b-heptamethyl-4,4a,5,6,6a,6b,7,8,8a,9,9a,11a,12,12a,14a,14b-hexadecahydro-2*H*-piceno[3,2-*b*]oxete-3,11,14(1*H*)-trione (6h)

Following General Procedure on 0.1 mmol scale. The product was obtained as a white solid (50.1 mg, 92% yield). The relative stereochemistry was determined via 2D NMR (See NMR spectra section for details). ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.71 (d, *J* = 0.9 Hz, 1H), 4.92 (d, *J* = 3.4 Hz, 1H), 4.50 (d, *J* = 3.5 Hz, 1H), 2.91 (ddd, *J* = 13.6,

7.2, 4.0 Hz, 1H), 2.63 (ddd, *J* = 15.9, 11.0, 7.2 Hz, 1H), 2.44 (s, 1H), 2.41 – 2.28 (m, 4H), 1.83 (td, *J* = 13.9, 3.6 Hz, 1H), 1.72 (dd, *J* = 13.3, 2.4 Hz, 1H), 1.70 – 1.63 (m, 1H), 1.57 – 1.51 (m, 3H), 1.47 (s, 3H), 1.46 – 1.37 (m, 2H), 1.37 – 1.29 (m, 5H), 1.28 (s, 3H), 1.21 (s, 3H), 1.14 (s, 3H), 1.10 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 217.1, 198.7, 173.0, 165.3, 130.1, 79.1, 60.8, 60.7, 58.4, 55.6, 47.9, 45.9, 44.5, 43.8, 39.9, 36.9, 36.6, 35.1, 34.3, 33.4, 32.8, 30.2, 26.7, 25.6, 21.6, 20.8, 19.4, 19.0, 18.7, 16.0. HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{40}BrO_4^-$ $[M-H]^-$ 543.2110, found 543.2103.



(3*S*,6a*R*,6b*S*,8a*R*,9*R*,9a*R*,11a*R*,12a*S*,14a*R*,14b*S*)-9-bromo-4,4,6a,6b,8a,11a,14b-heptamethyl-11,14-dioxo-1,3,4,4a,5,6,6a,6b,7,8,8a,9,9a,11,11a,12,12a,14,14a,14b-icosahydro-2*H*-piceno[3,2-*b*]oxet-3-yl methyl glutarate (6i)

Following General Procedure on 0.1 mmol scale. The product was obtained as a white solid (39.1 mg, 58% yield). The relative stereochemistry was assigned via comparison with that of **6h**. ^{1}H NMR (600 MHz, Chloroform-*d*) δ 5.66 (d, *J* = 2.6 Hz, 1H), 4.90 (d, *J* = 3.7 Hz, 1H), 4.56 – 4.45 (m, 2H), 3.67 (d, *J* = 2.7 Hz, 3H), 2.74 (dt, *J* = 13.7, 3.5 Hz, 1H), 2.42 – 2.26 (m, 8H), 1.95 (p, *J* = 7.6 Hz, 2H), 1.80 (td, *J* = 14.0, 3.3 Hz, 1H), 1.75 – 1.55 (m, 7H), 1.52 – 1.40 (m, 6H), 1.35 – 1.24 (m, 5H), 1.22 – 1.14 (m, 6H), 1.09 (s, 3H), 1.08 – 1.01 (m, 1H), 0.87 (d, *J* = 3.4 Hz, 6H), 0.80 (d, *J* = 11.8 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 199.3, 173.5, 173.0, 172.8, 164.8, 130.1, 80.7, 79.2, 61.4, 60.8, 58.4, 55.3, 51.8, 45.9, 44.6, 43.7, 38.9, 38.2, 37.1, 36.5, 35.1, 33.9, 33.4,

33.3, 30.1, 28.2, 25.6, 23.7, 20.8, 20.4, 19.4, 18.8, 17.5, 16.9, 16.8. HRMS (ESI-TOF) *m/z* Calcd for $C_{30}H_{42}BrO_3^+$ $[M\text{-ester}]^+$ 529.2317, found 529.2325.

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Single X-ray Crystal Structures for 2b and 2l

Figure S1. Single crystal X-ray structure (ORTEP) of 2l. The crystals were grown from a concentrated solution of **2l** in Hexanes/$CHCl_3$, using a slow evaporation. X-ray crystallographic data have been deposited in the Cambridge Crystallographic Data Centre database (http://www.ccdc.cam.ac.uk/) under accession code CCDC 2182933.

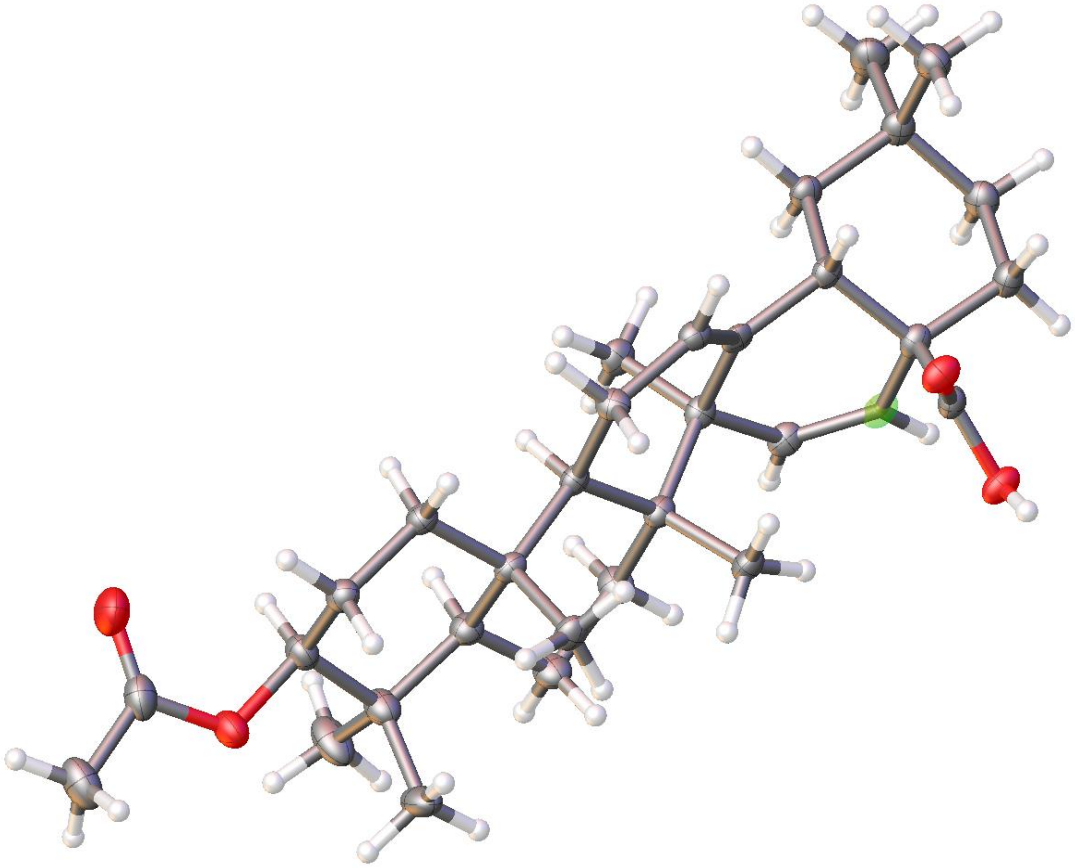
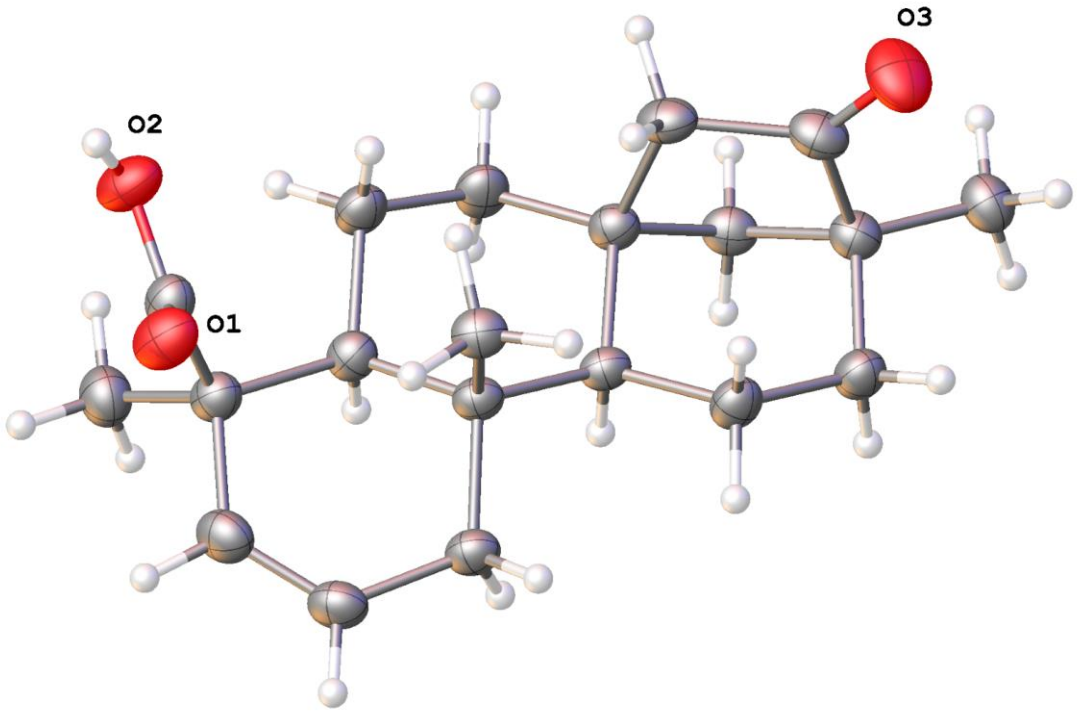


Table 1. Crystal data and structure refinement for Yu161.

Identification code	yu161b_0m
Empirical formula	C32 H48 O4
Formula weight	496.70
Temperature	100.00 K
Wavelength	1.54178 Å
Crystal system	Orthorhombic

Space group	$P2_12_12_1$
Unit cell dimensions	a = 12.7562(3) Å = 90°.
	b = 21.3035(5) Å = 90°.
	c = 33.3169(8) Å = 90°.
Volume	9053.9(4) $Å^3$
Z	12
Density (calculated)	1.093 Mg/m^3
Absorption coefficient	0.547 mm^{-1}
F(000)	3264
Crystal size	0.31 x 0.18 x 0.03 mm^3
Theta range for data collection	2.462 to 69.412°.
Index ranges	-13<=h<=14, -25<=k<=25, -39<=l<=40
Reflections collected	180864
Independent reflections	16551 [R(int) = 0.0507]
Completeness to theta = 67.679°	98.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7532 and 0.6259
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	16551 / 0 / 1001
Goodness-of-fit on F^2	1.017
Final R indices [I>2sigma(I)]	R1 = 0.0311, wR2 = 0.0780
R indices (all data)	R1 = 0.0338, wR2 = 0.0796
Absolute structure parameter	-0.03(3)
Extinction coefficient	0.00017(2)
Largest diff. peak and hole	0.241 and -0.164 $e.Å^{-3}$

Figure S2. Single crystal X-ray structure (ORTEP) of 2b. The crystals were grown from a concentrated solution of **2b** in Hexanes/$CHCl_3$, using a slow evaporation. X-ray crystallographic data have been deposited in the Cambridge Crystallographic Data Centre database (http://www.ccdc.cam.ac.uk/) under accession code CCDC 2168286.

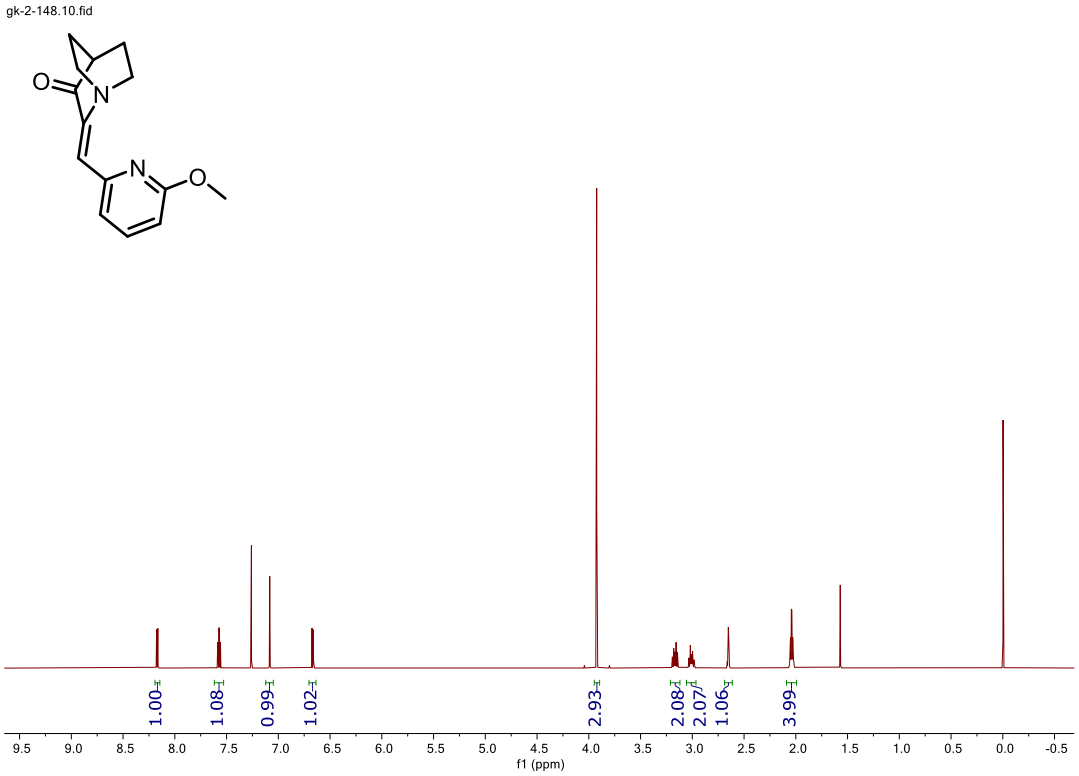


Compound	**yu156_a**
Formula	$C_{20}H_{28}O_3$
$D_{calc.}$/ g cm^{-3}	1.216
m/mm^{-1}	0.631
Formula Weight	316.42
Color	colorless
Shape	needle-shaped
Size/mm^3	0.25×0.12×0.10
T/K	100.15
Crystal System	monoclinic
Flack Parameter	0.06(7)
Space Group	*C*2
a/Å	34.927(2)
b/Å	6.7611(4)
c/Å	15.5355(10)
a/°	90
b/°	109.584(4)
g/°	90
V/Å^3	3456.4(4)
Z	8
Z'	2
Wavelength/Å	1.54178
Radiation type	CuK$_a$
Q_{min}/	2.685
Q_{max}/°	73.232
Measured Refl's.	29320
Indep't Refl's	6648
Refl's I≥2 s(I)	6270
R_{int}	0.0435
Parameters	423
Restraints	1

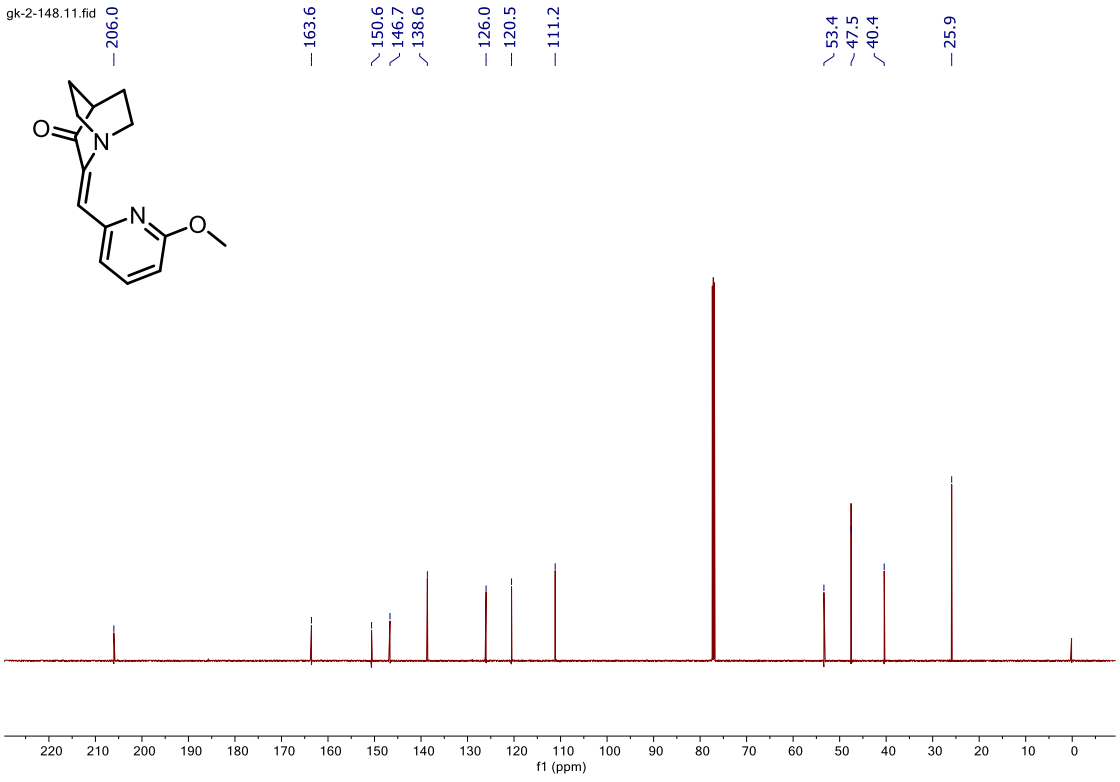
Largest Peak	0.171
Deepest Hole	-0.217
GooF	1.087
wR_2 (all data)	0.0993
wR_2	0.0971
R_1 (all data)	0.0404
R_1	0.0378

NMR Spectrum

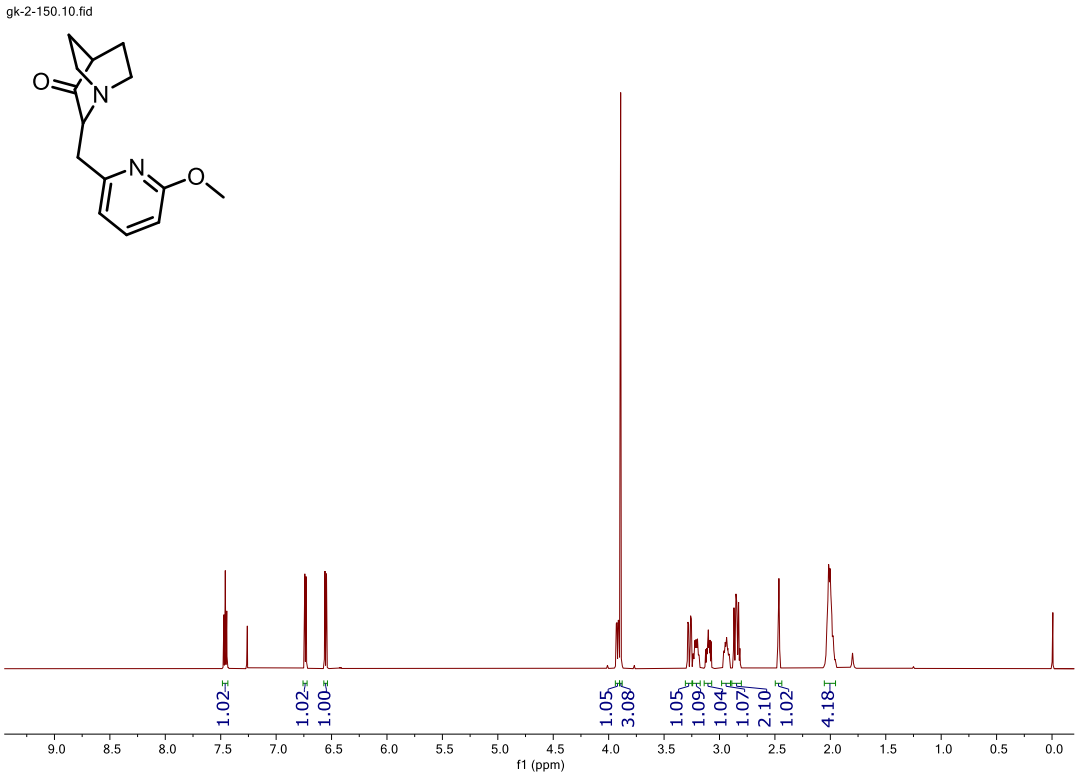
^{1}H NMR of Compound La:



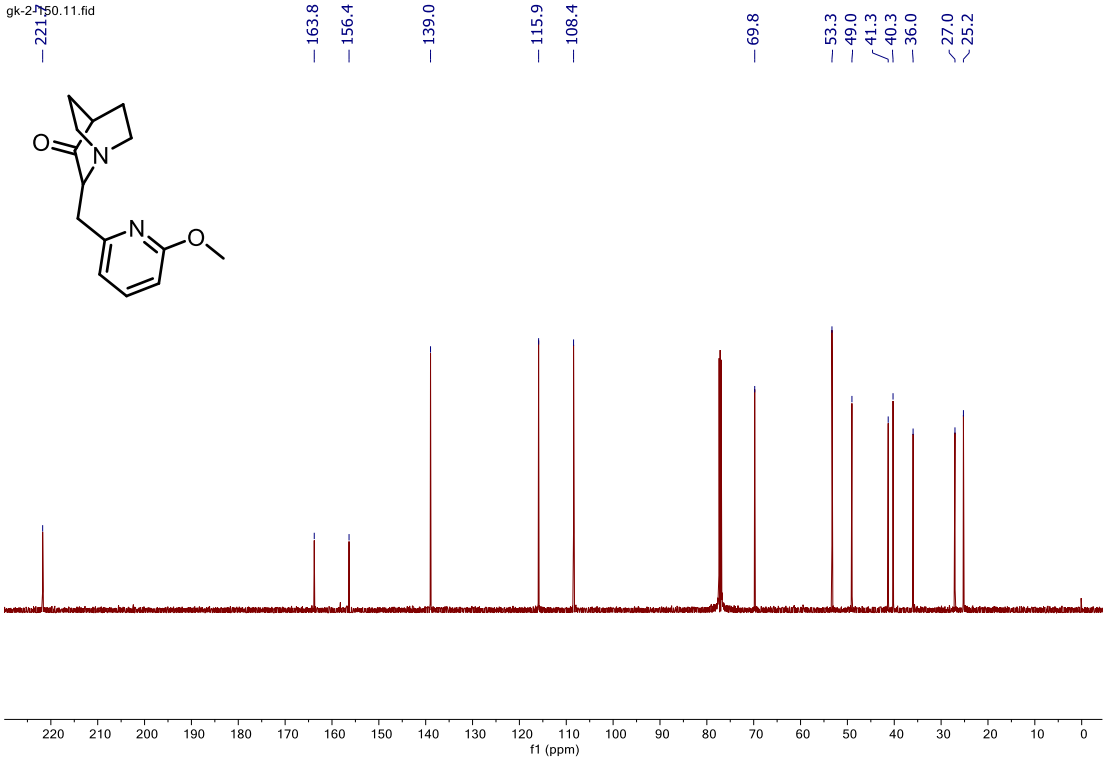
^{13}C NMR of Compound La:



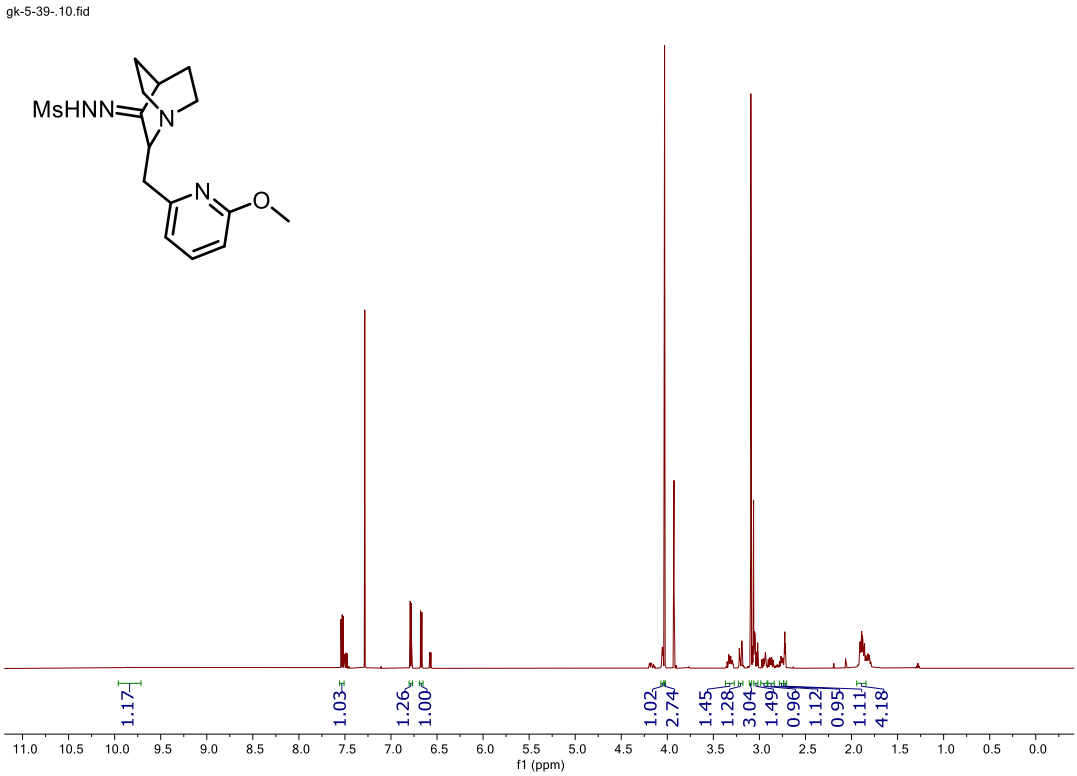
^{1}H NMR of Compound L_b:



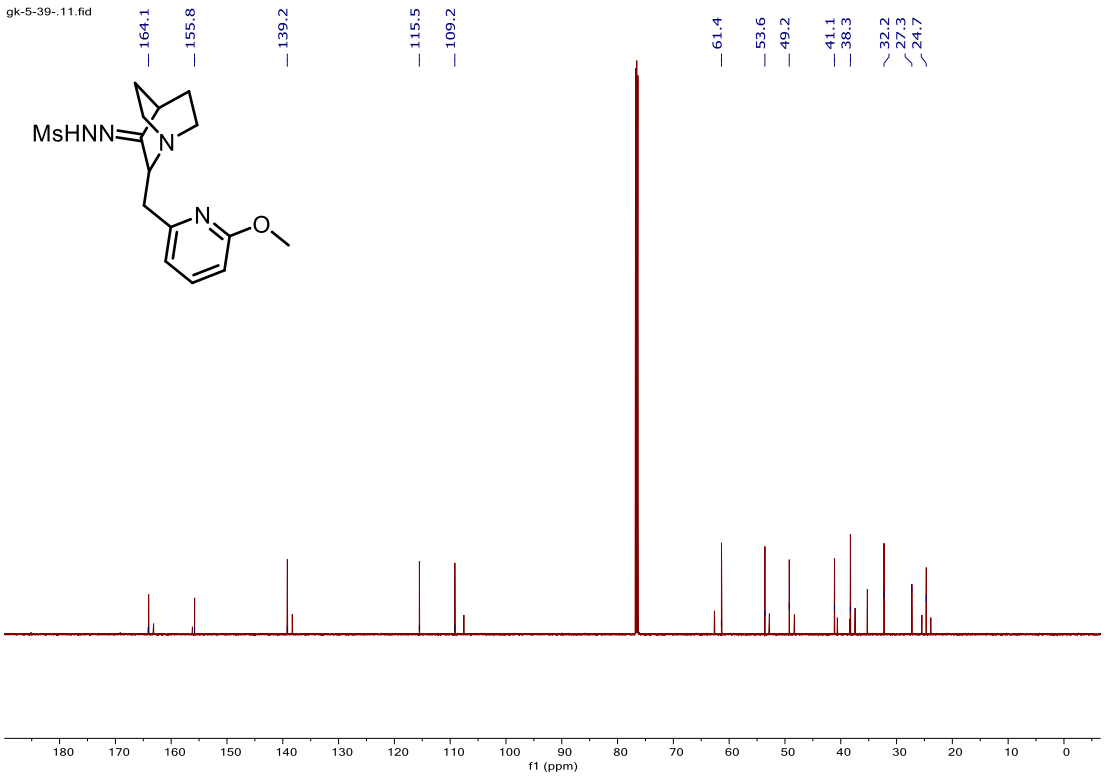
^{13}C NMR of Compound L_b:



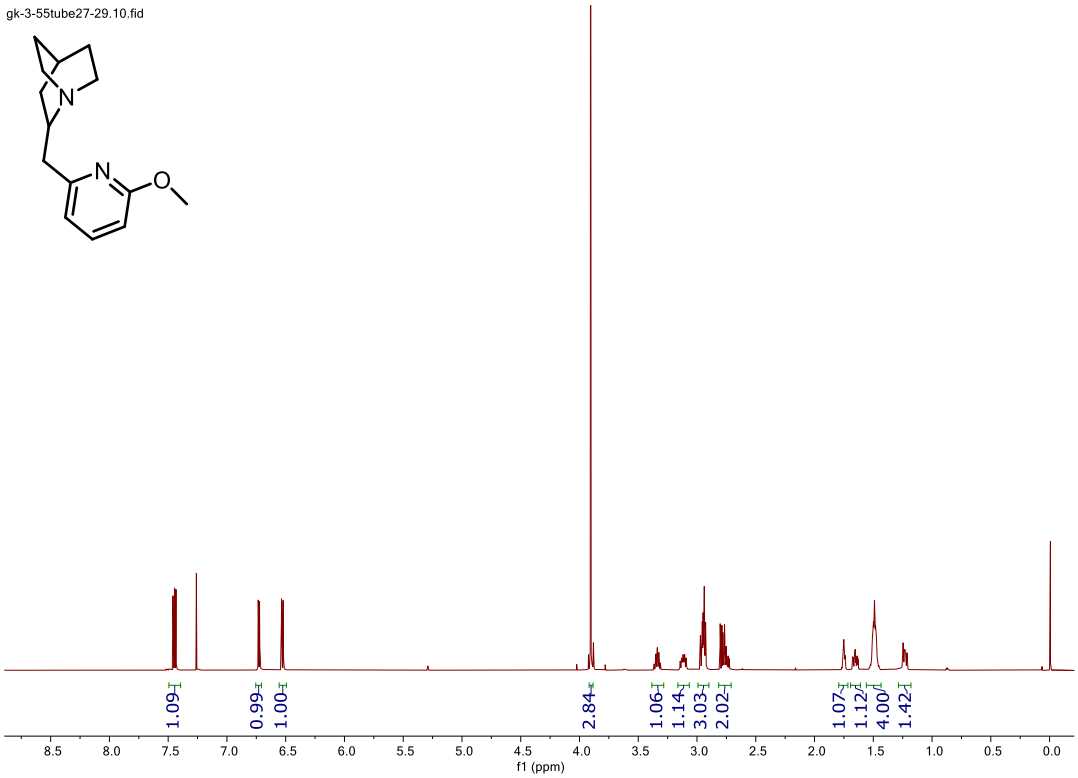
^{1}H NMR of Compound L_C:



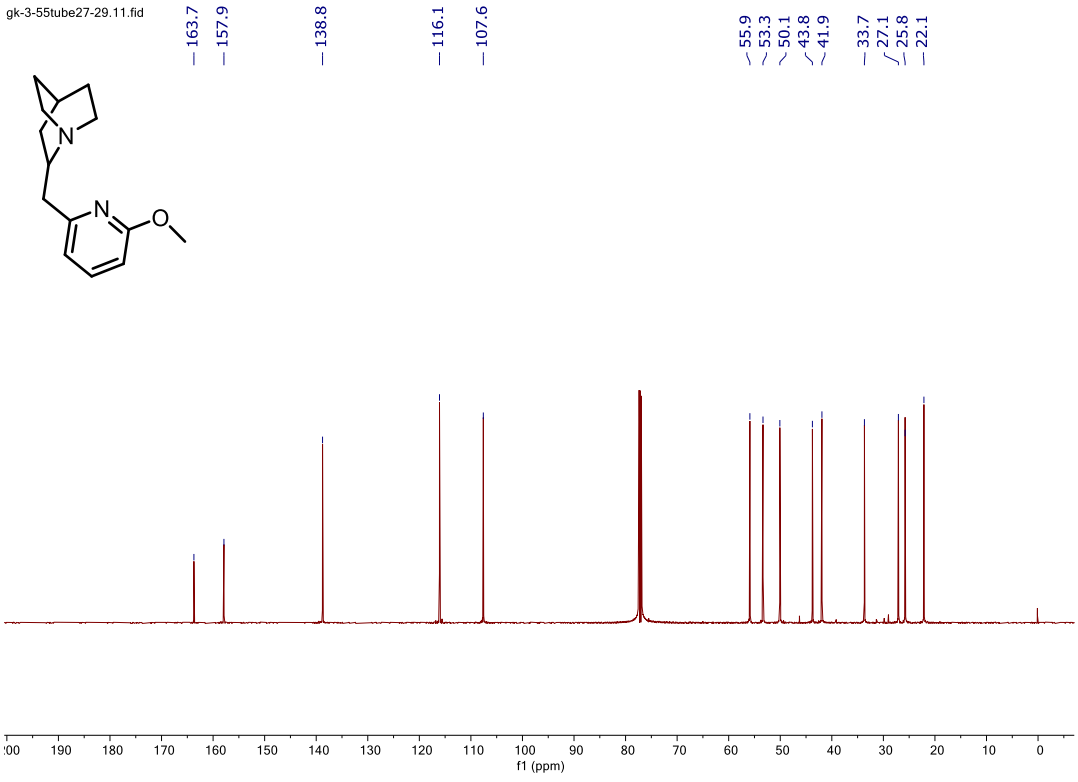
^{13}C NMR of Compound L_C:



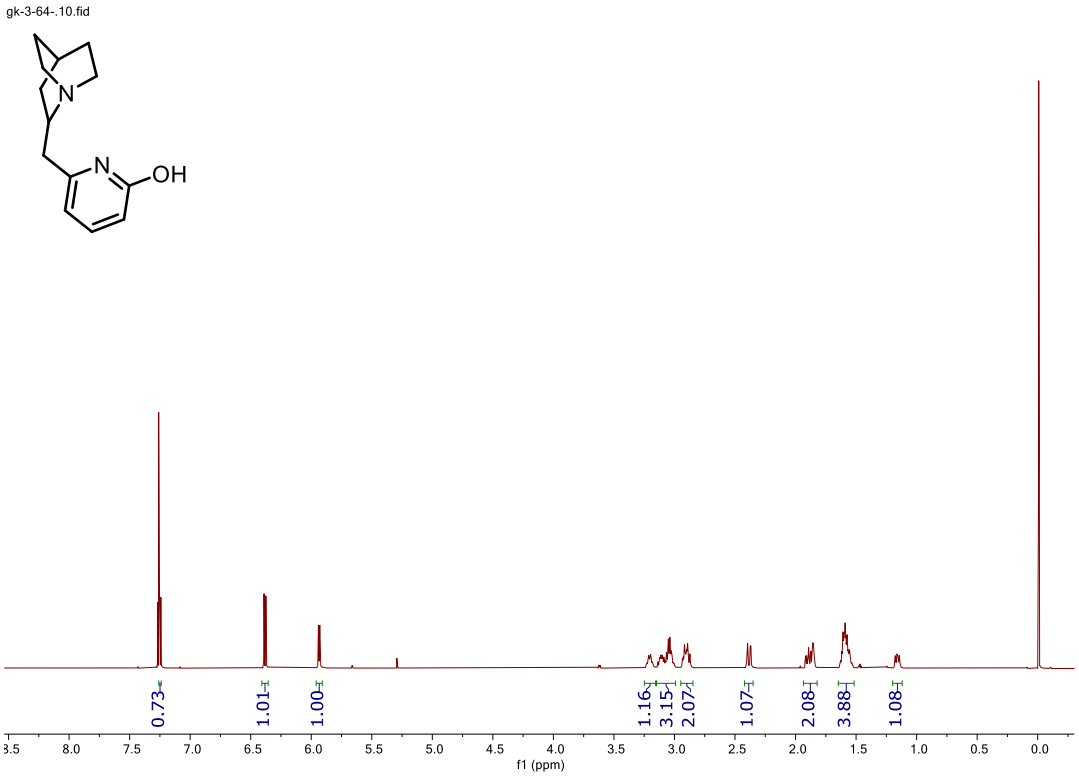
^{1}H NMR of Compound L_d:



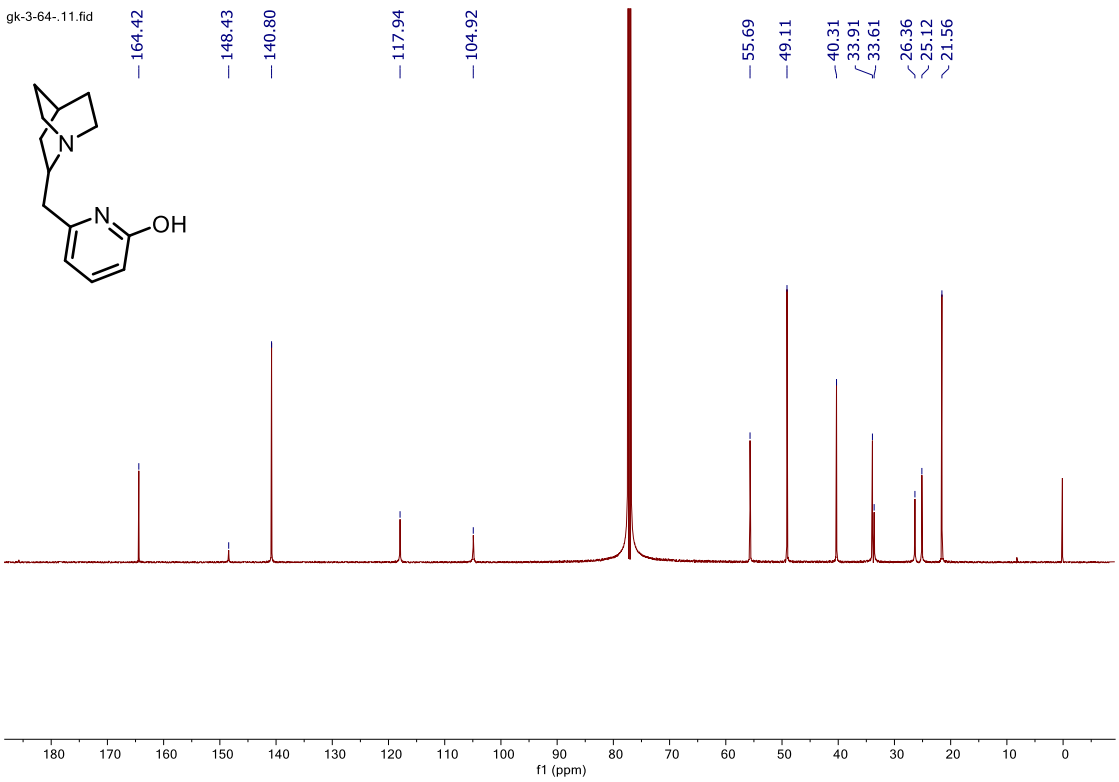
^{13}C NMR of Compound L_d:



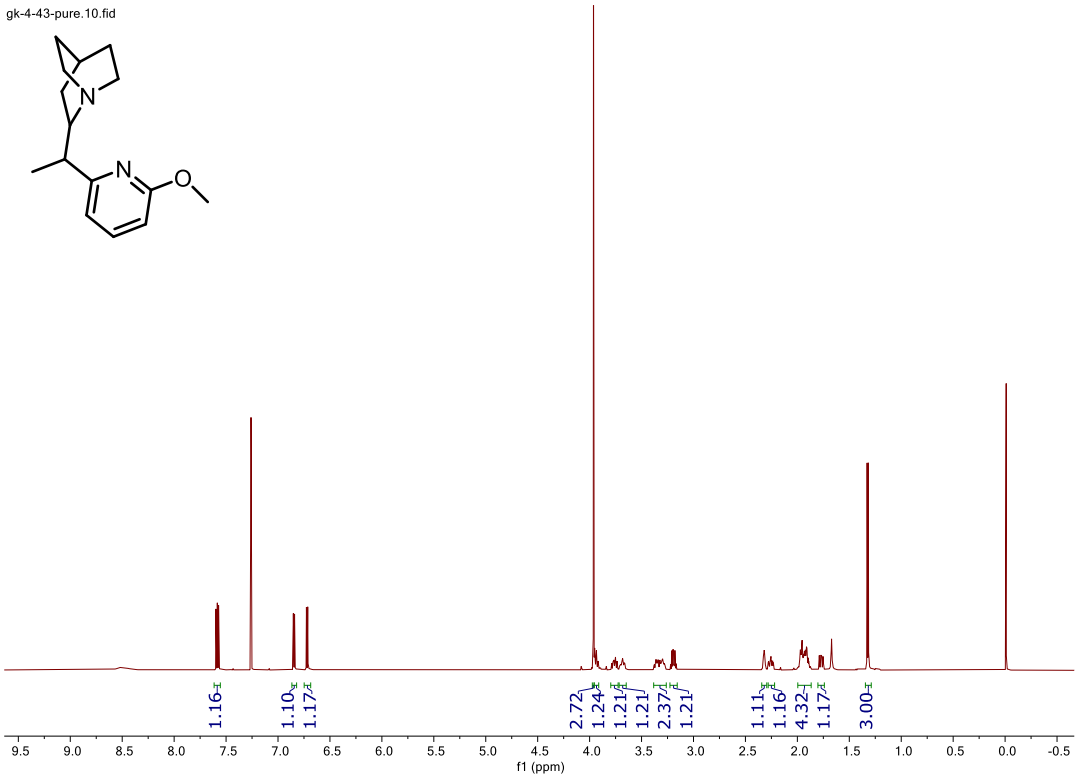
^{1}H NMR of Compound L13:



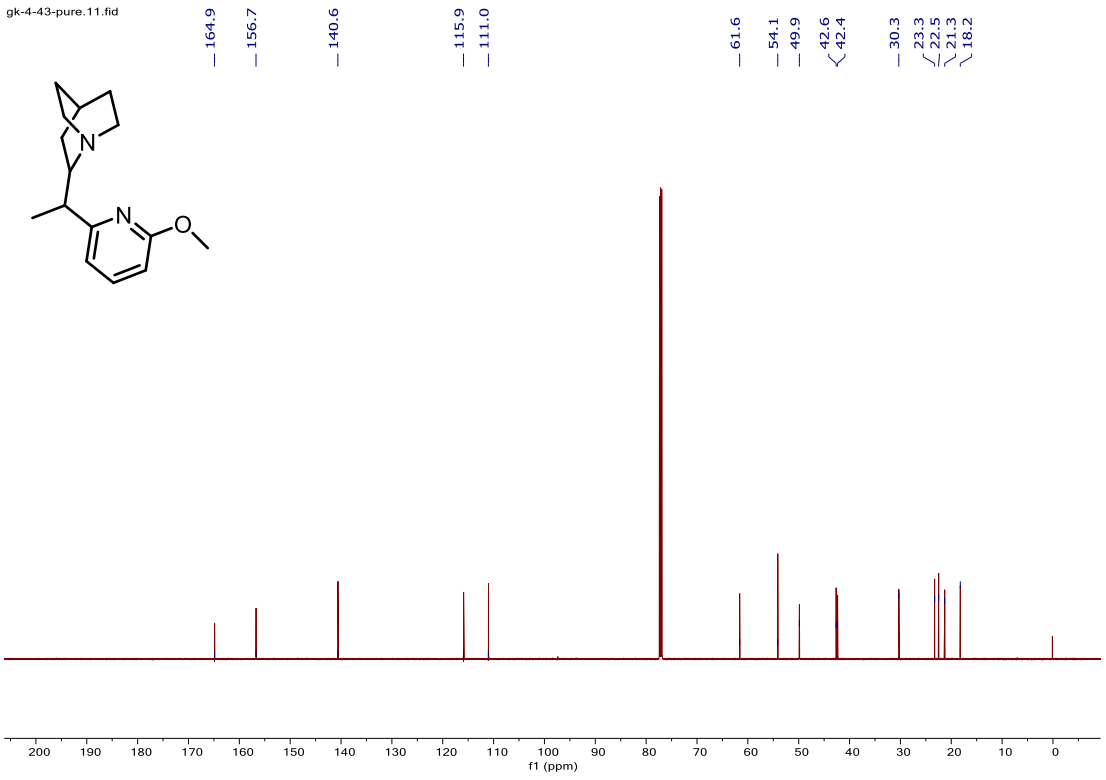
^{13}C NMR of Compound L13:



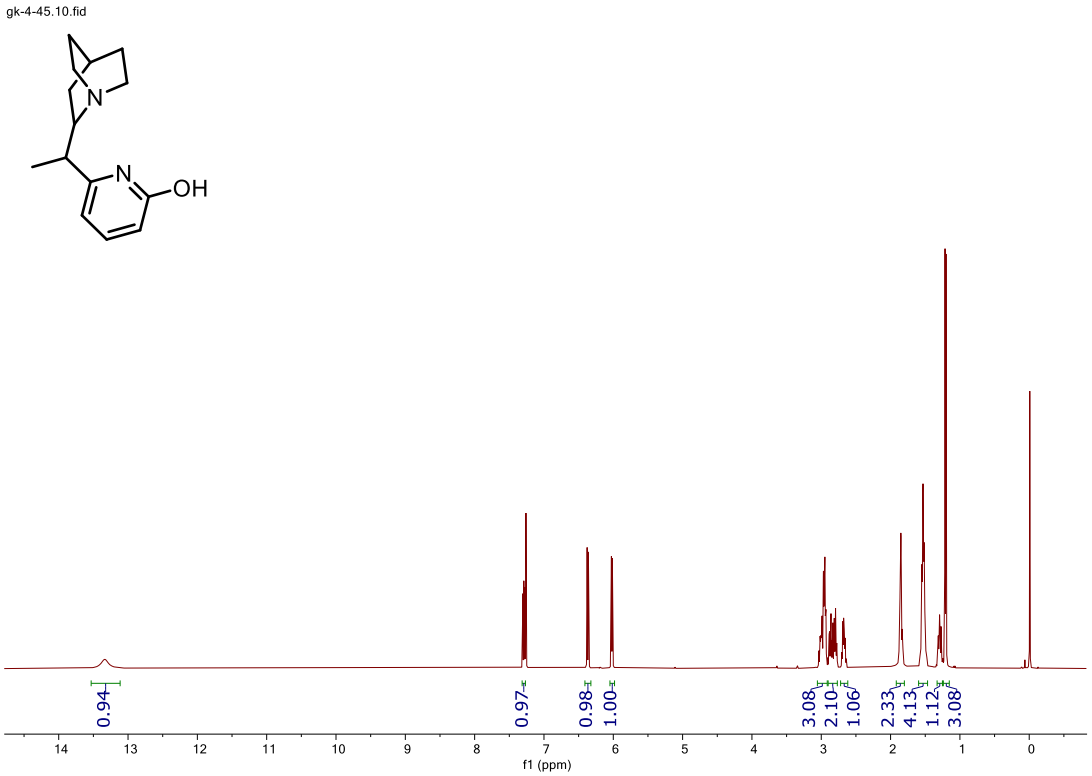
^{1}H NMR of Compound L_e:



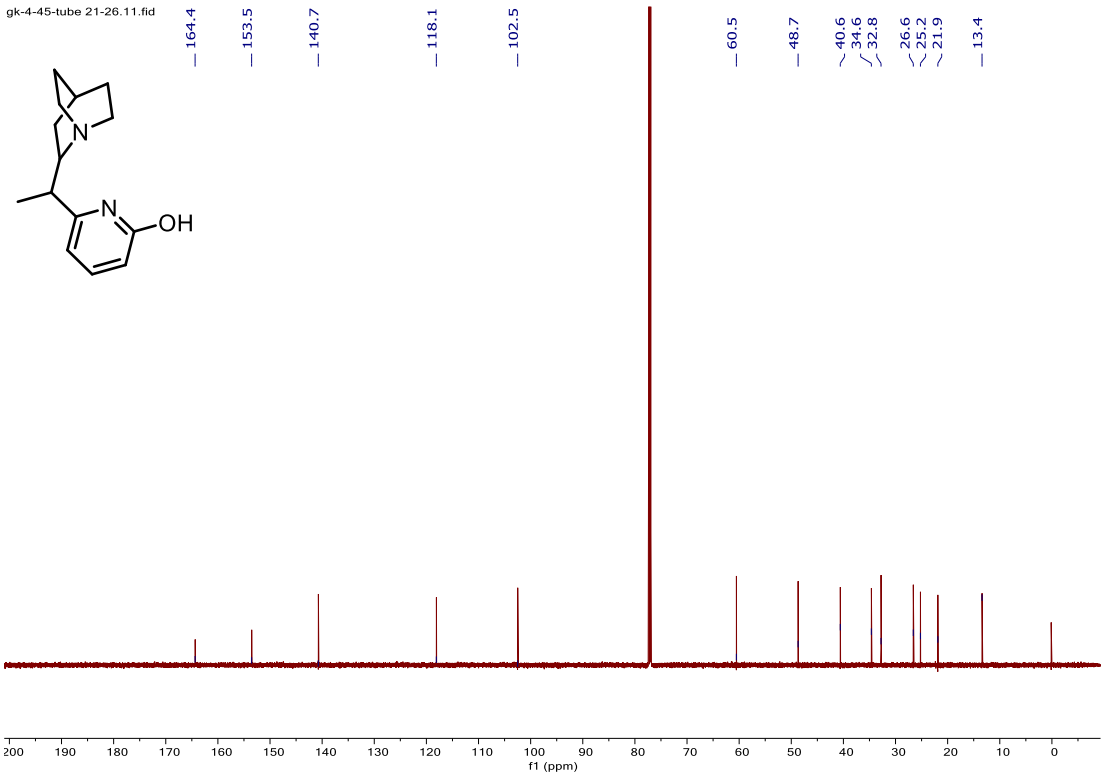
^{13}C NMR of Compound L_e:



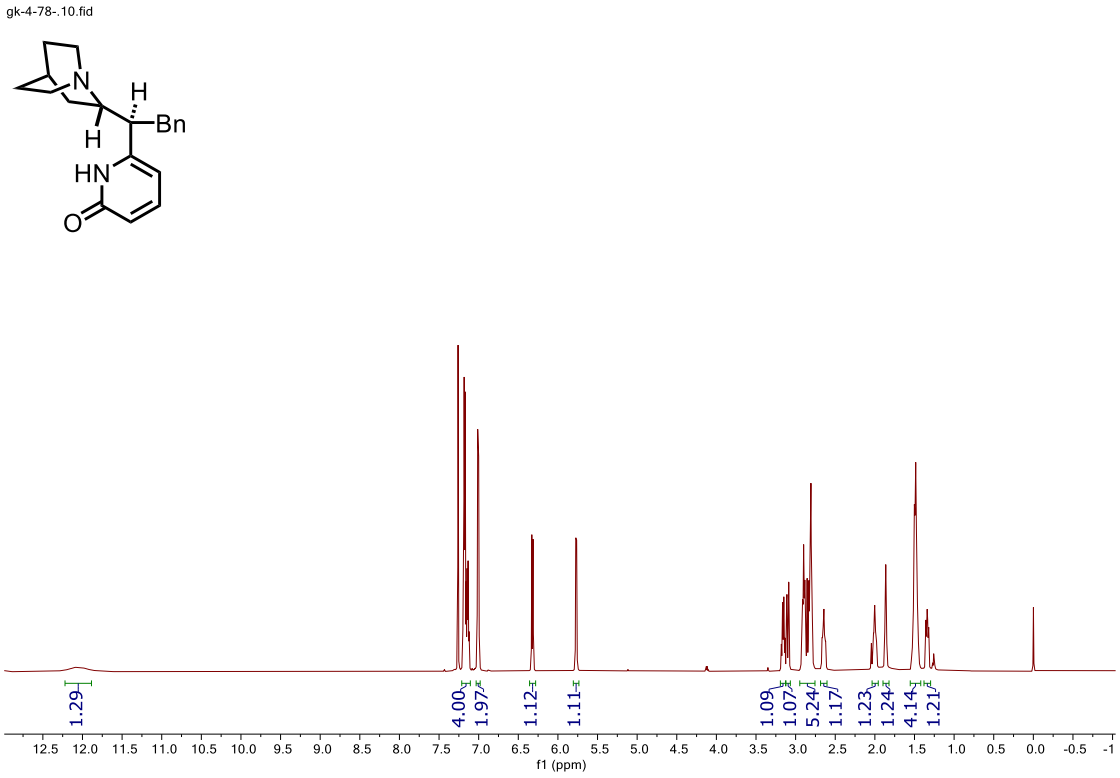
^{1}H NMR of Compound L14:



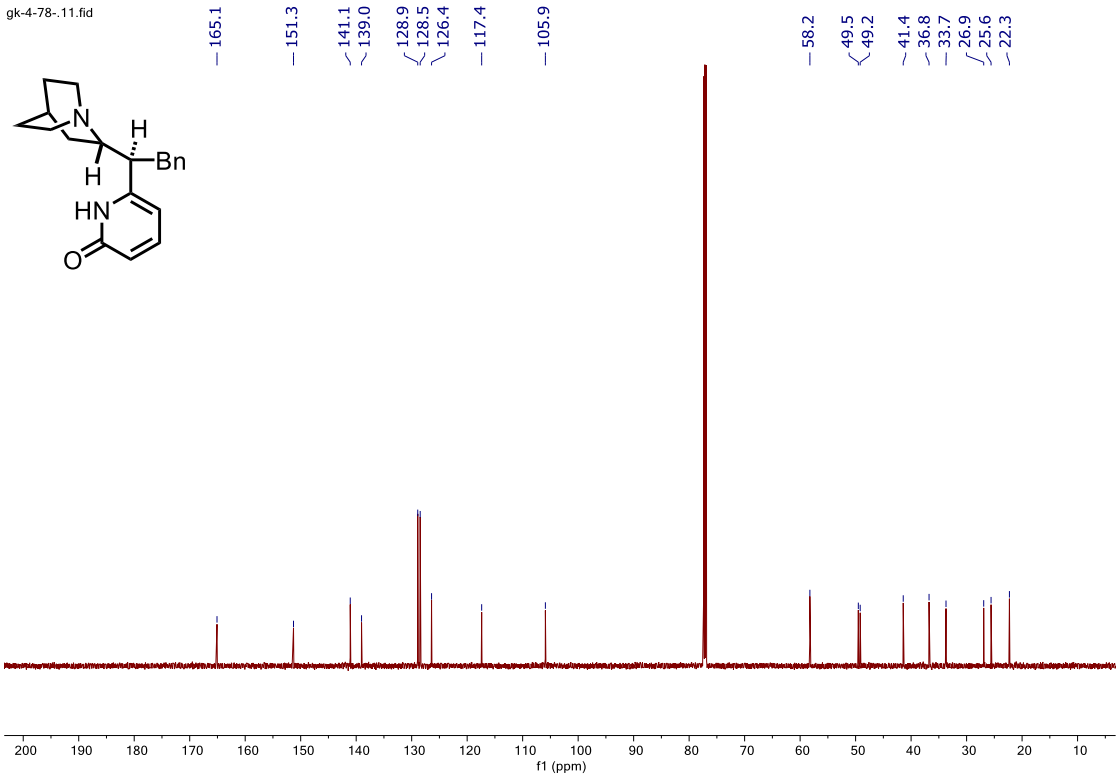
^{13}C NMR of Compound L14:



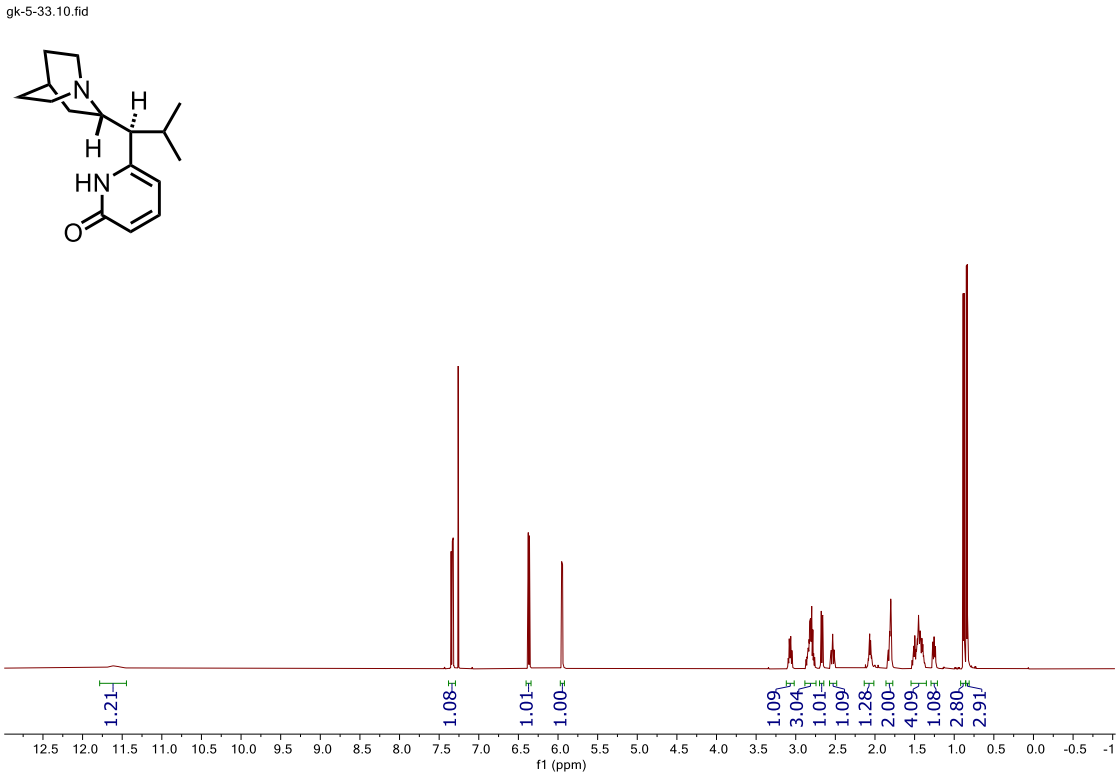
^{1}H NMR of Compound L15:



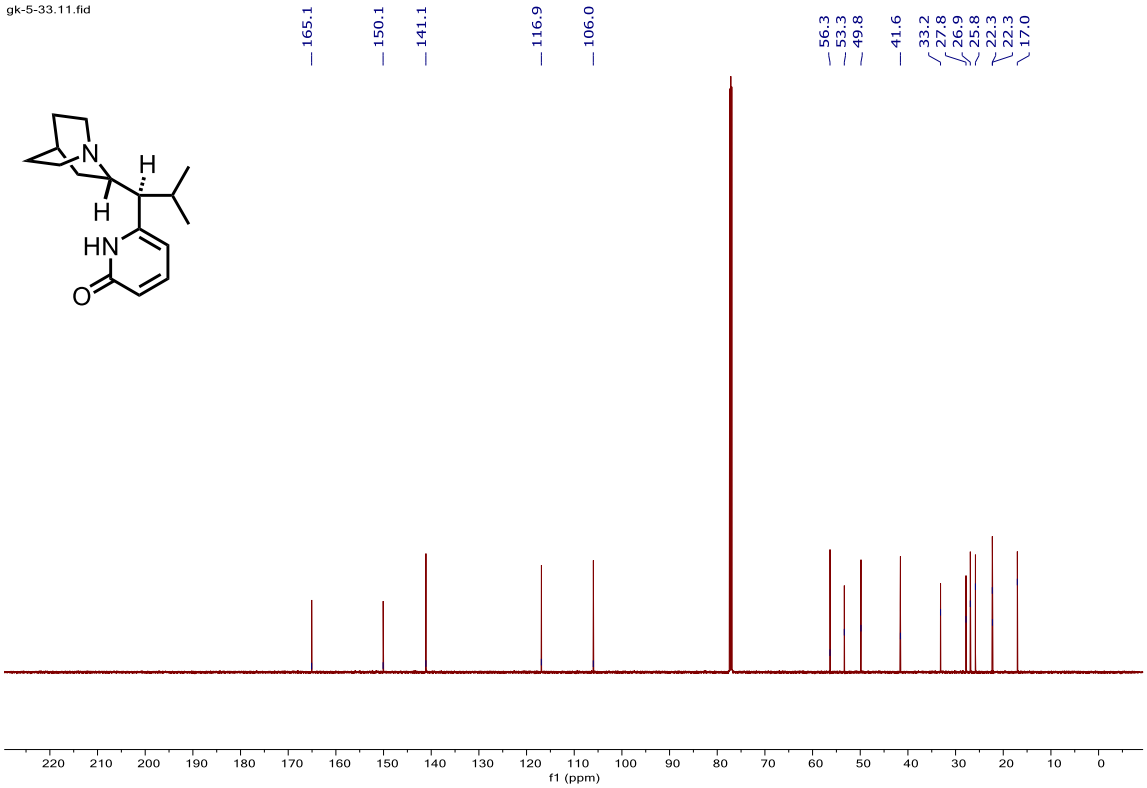
^{13}C NMR of Compound L15:



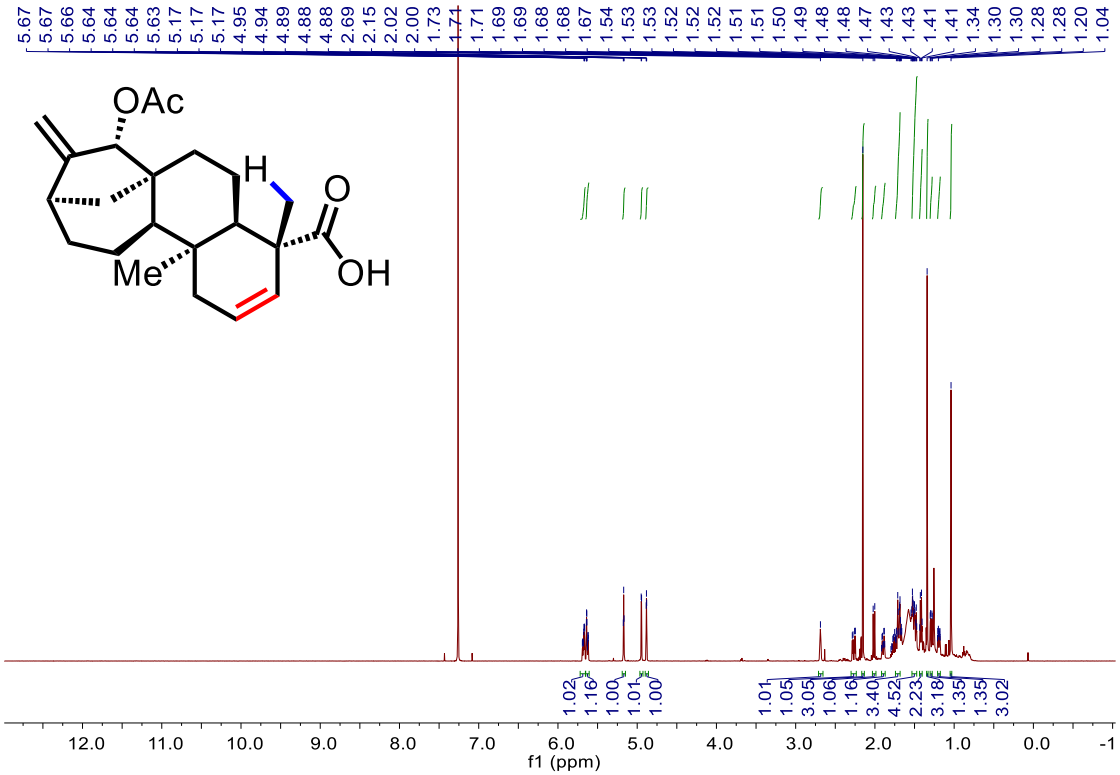
^{1}H NMR of Compound L16:



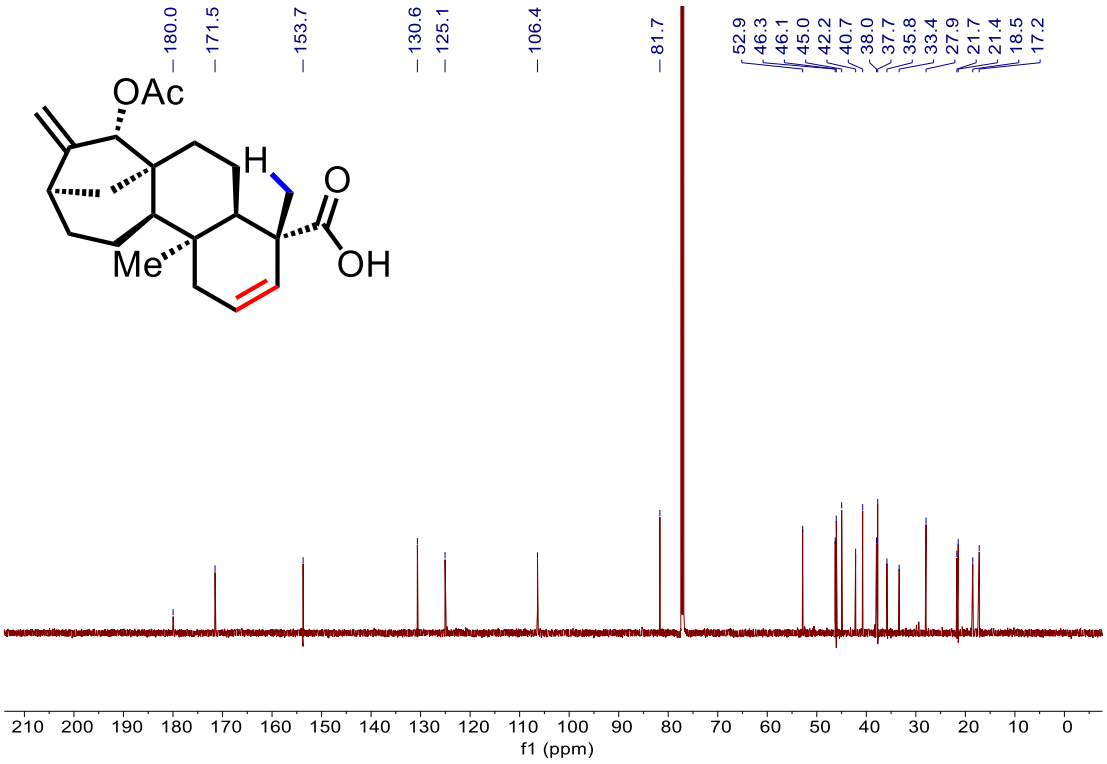
^{13}C NMR of Compound L16:



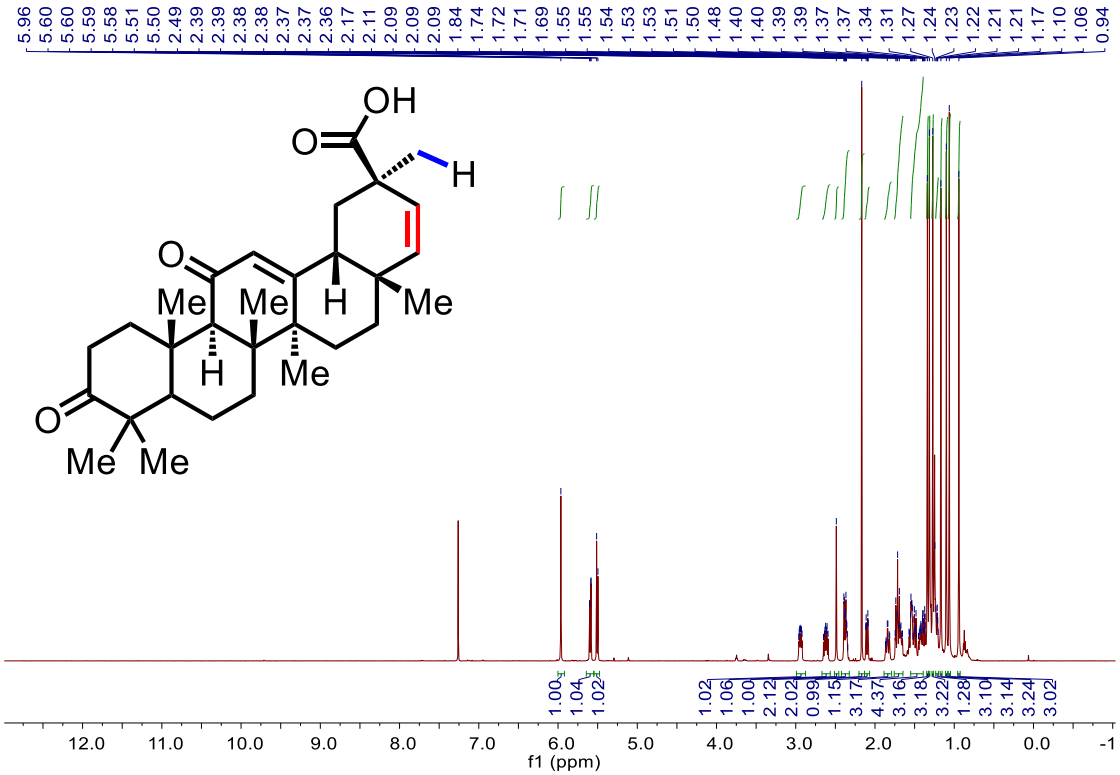
^{1}H NMR of Compound 2g:



^{13}C NMR of Compound 2g:



^{1}H NMR of Compound 2a:



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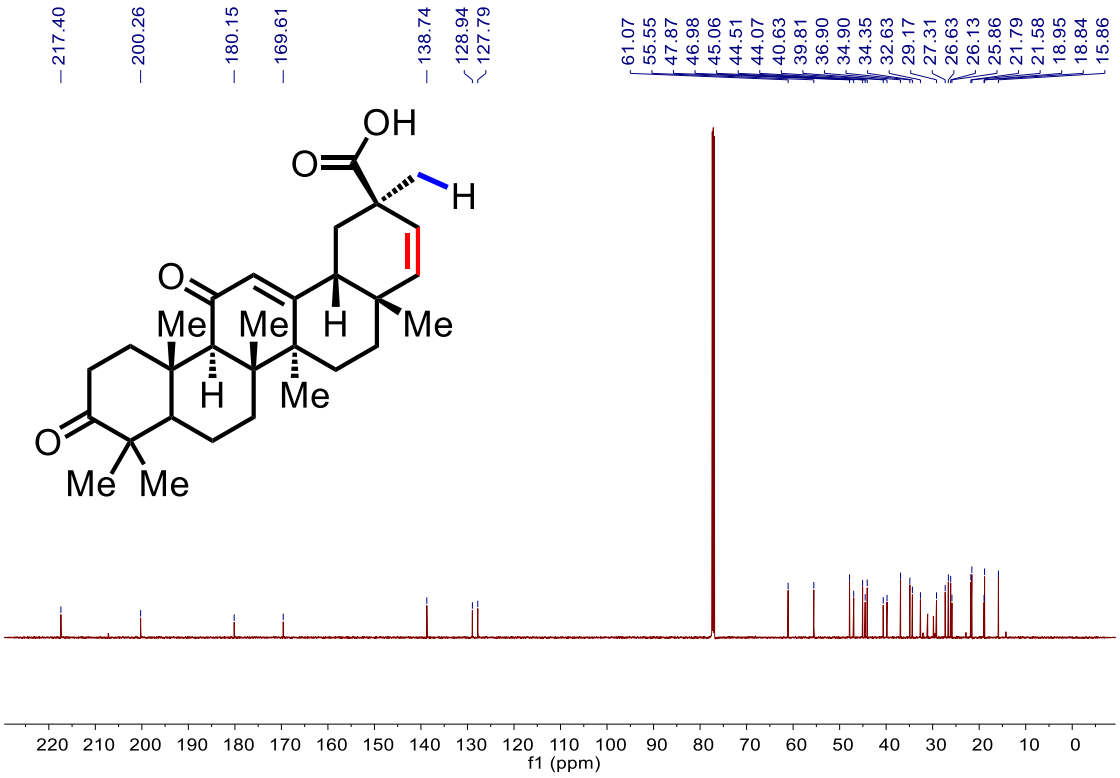
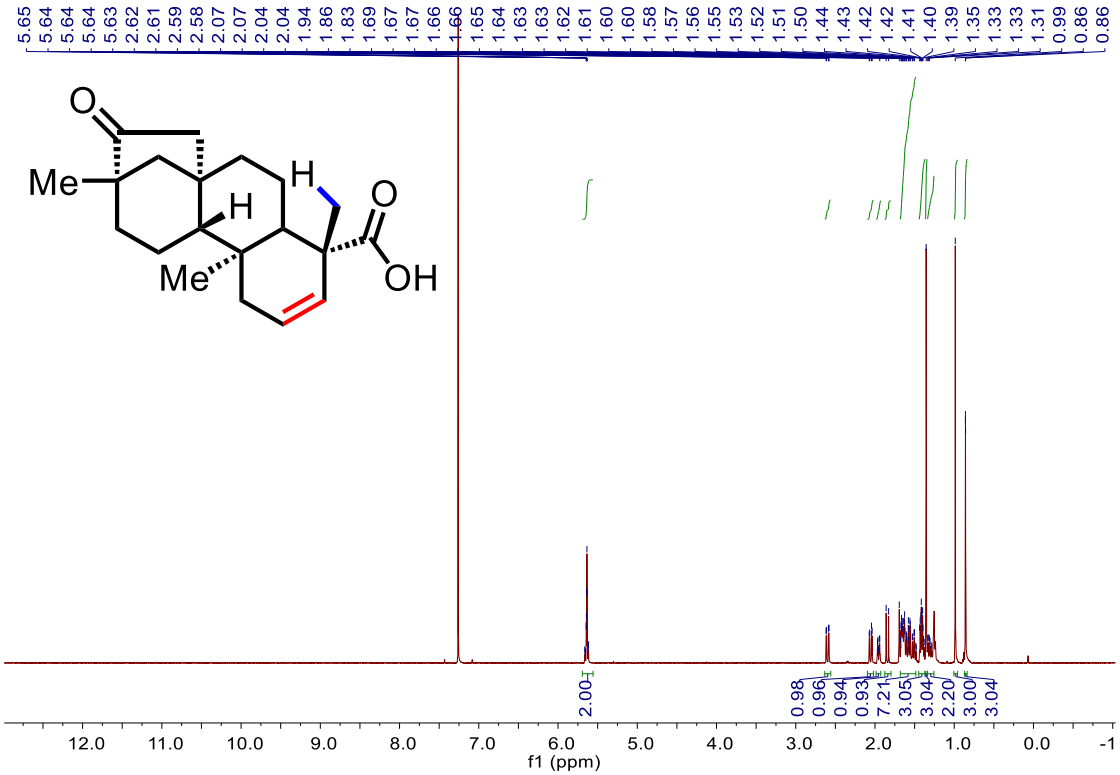
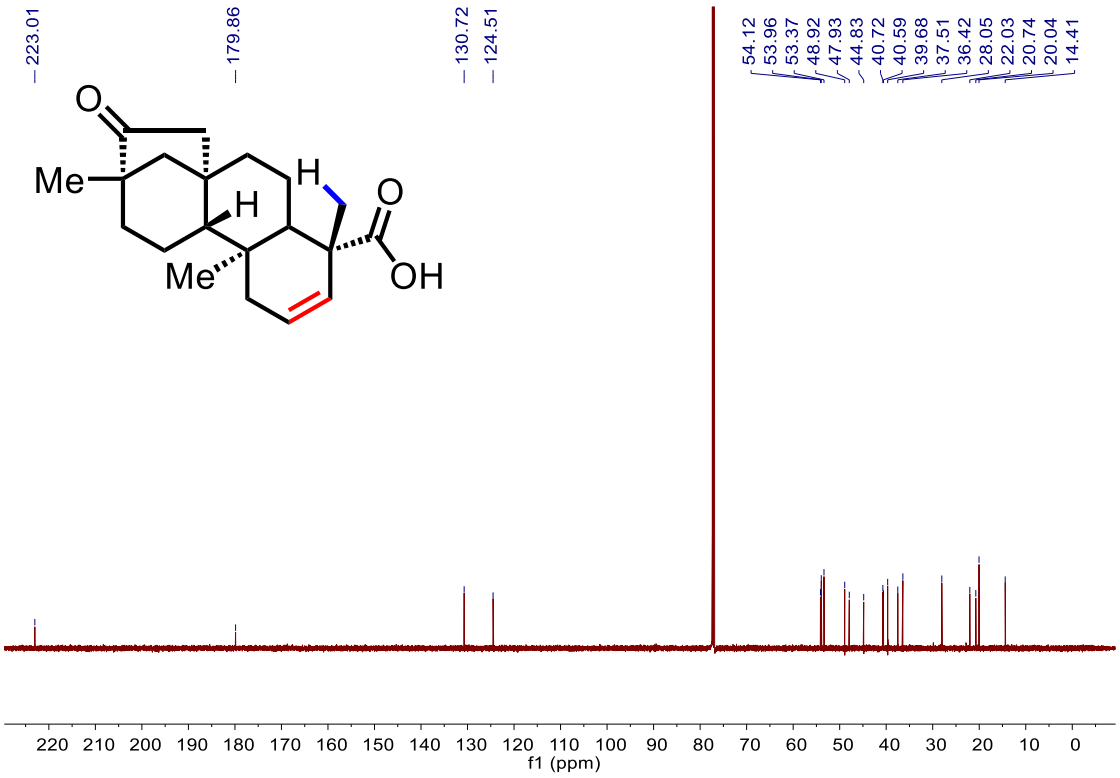


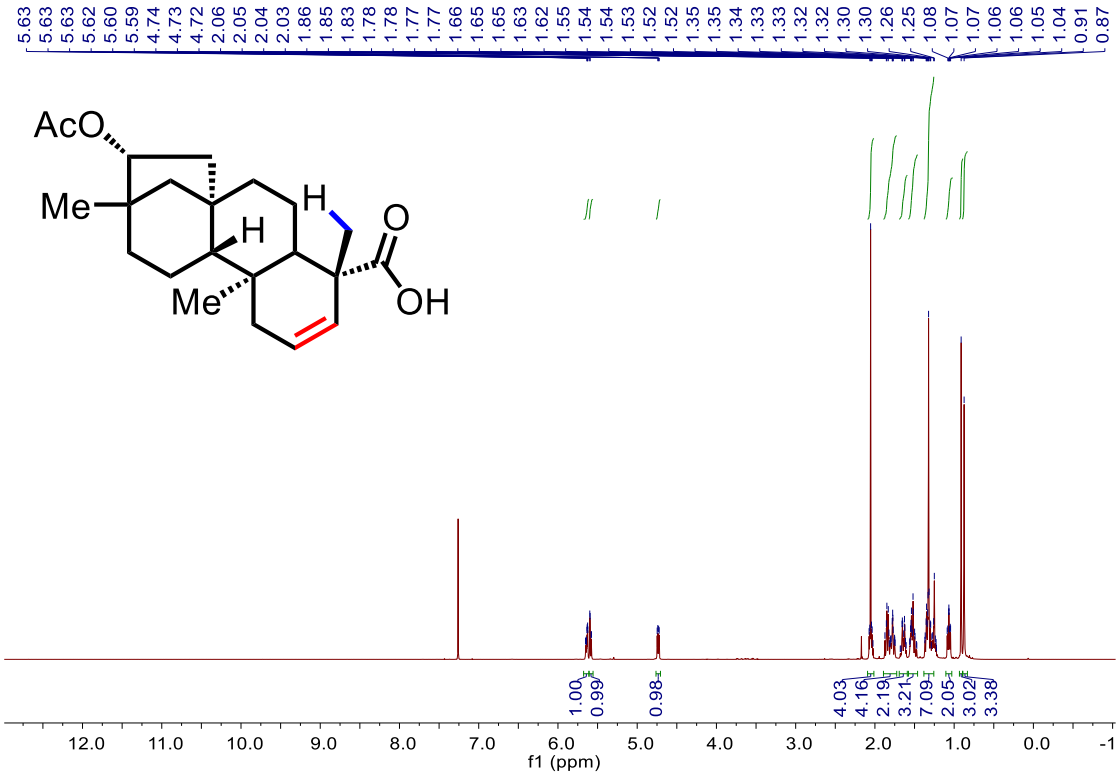
^{1}H NMR of Compound 2b:



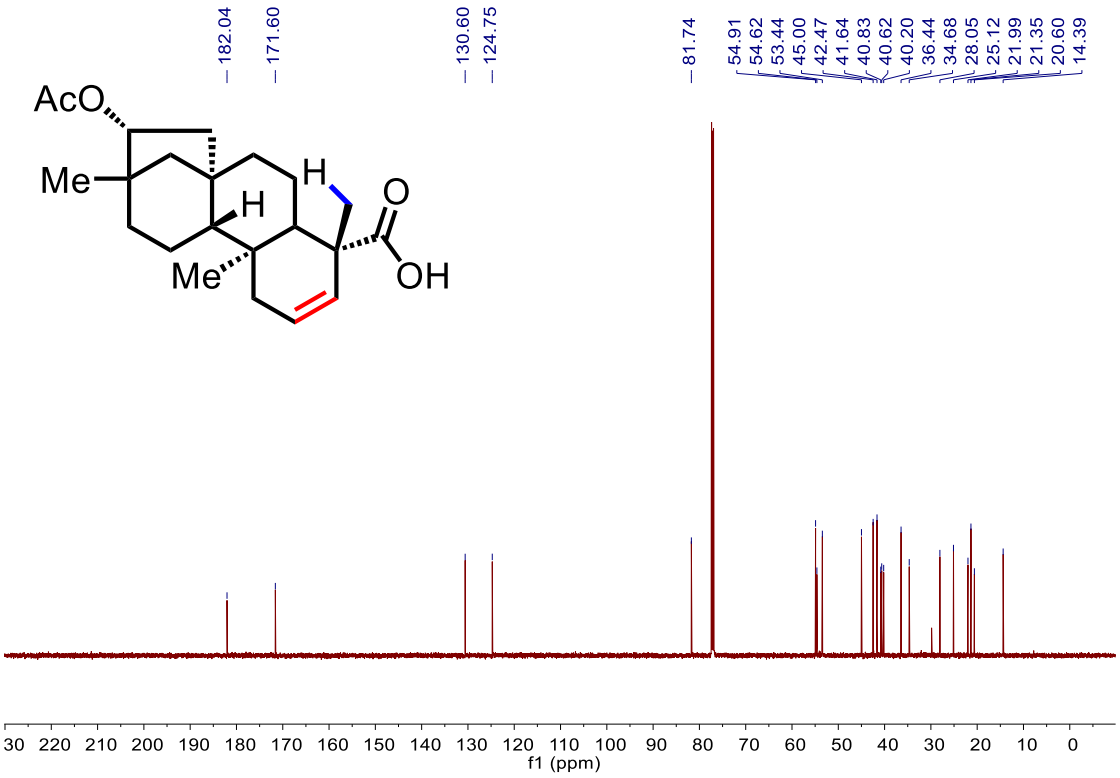
^{13}C NMR of Compound 2b:



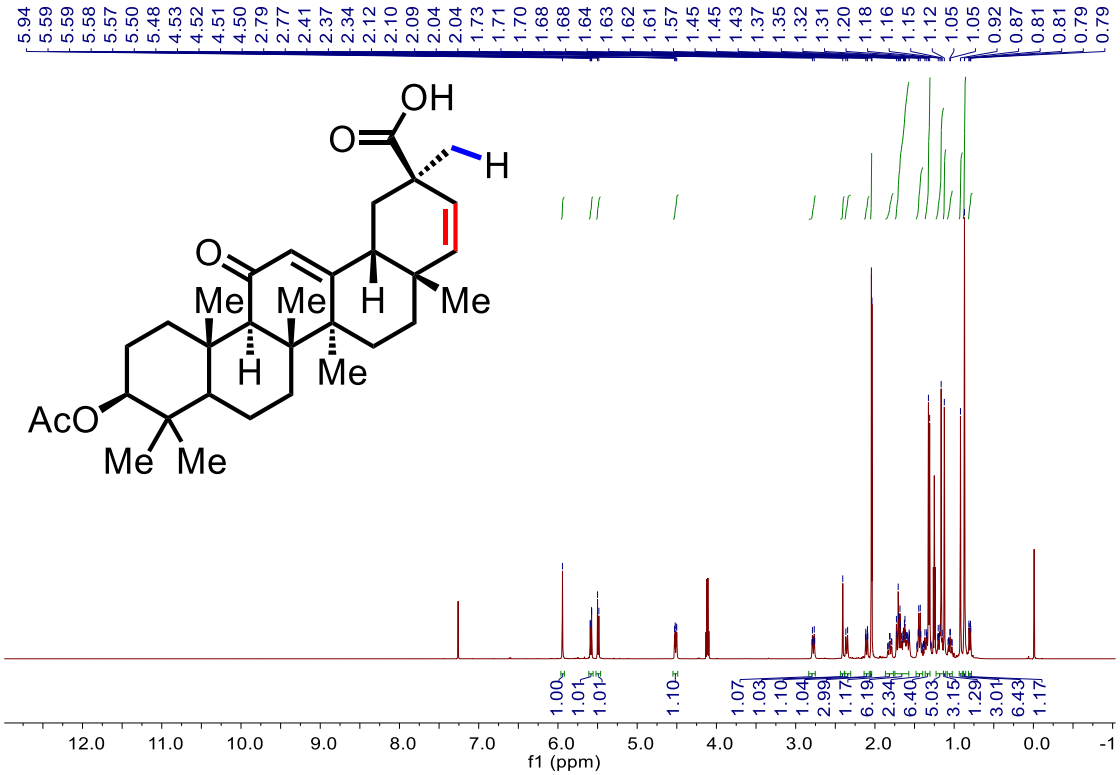
^{1}H NMR of Compound 2c:



^{13}C NMR of Compound 2c:



^{1}H NMR of Compound 2d:



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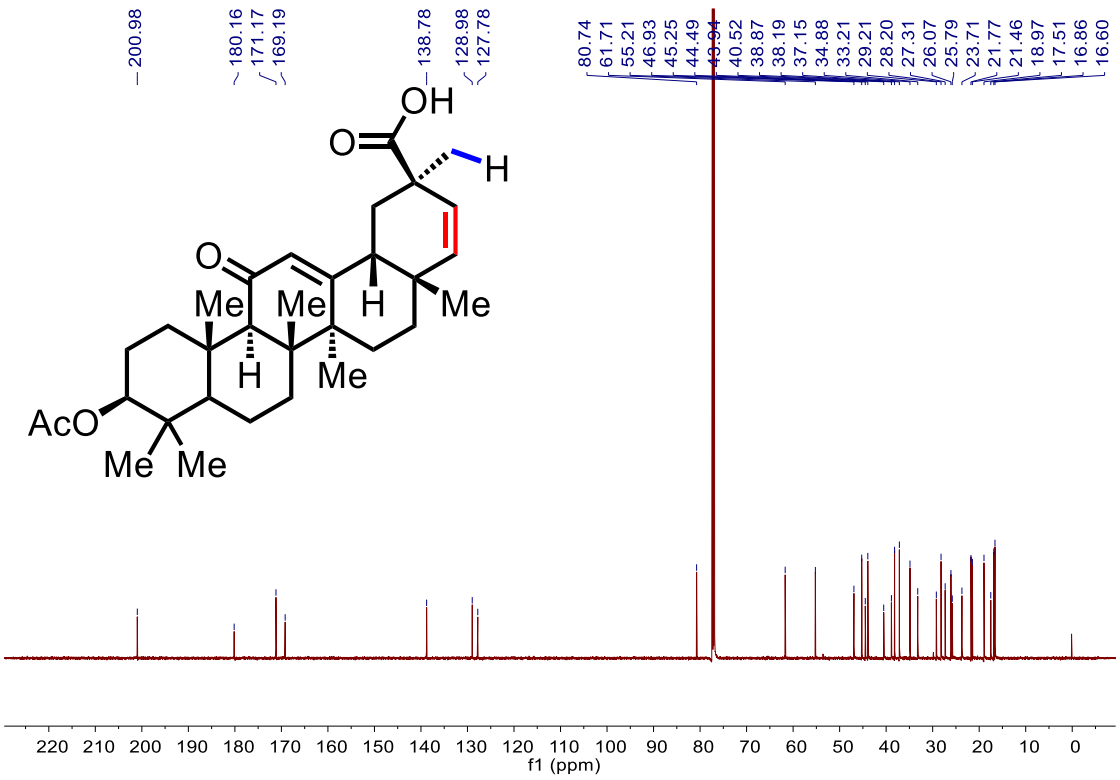

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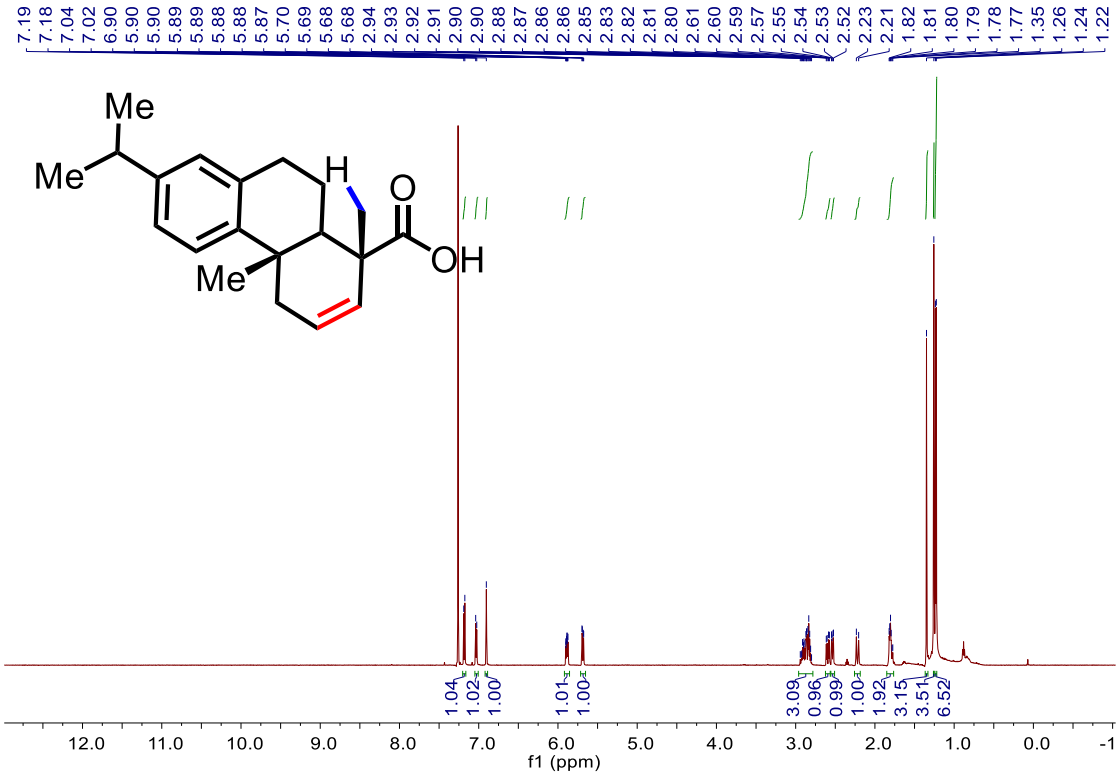

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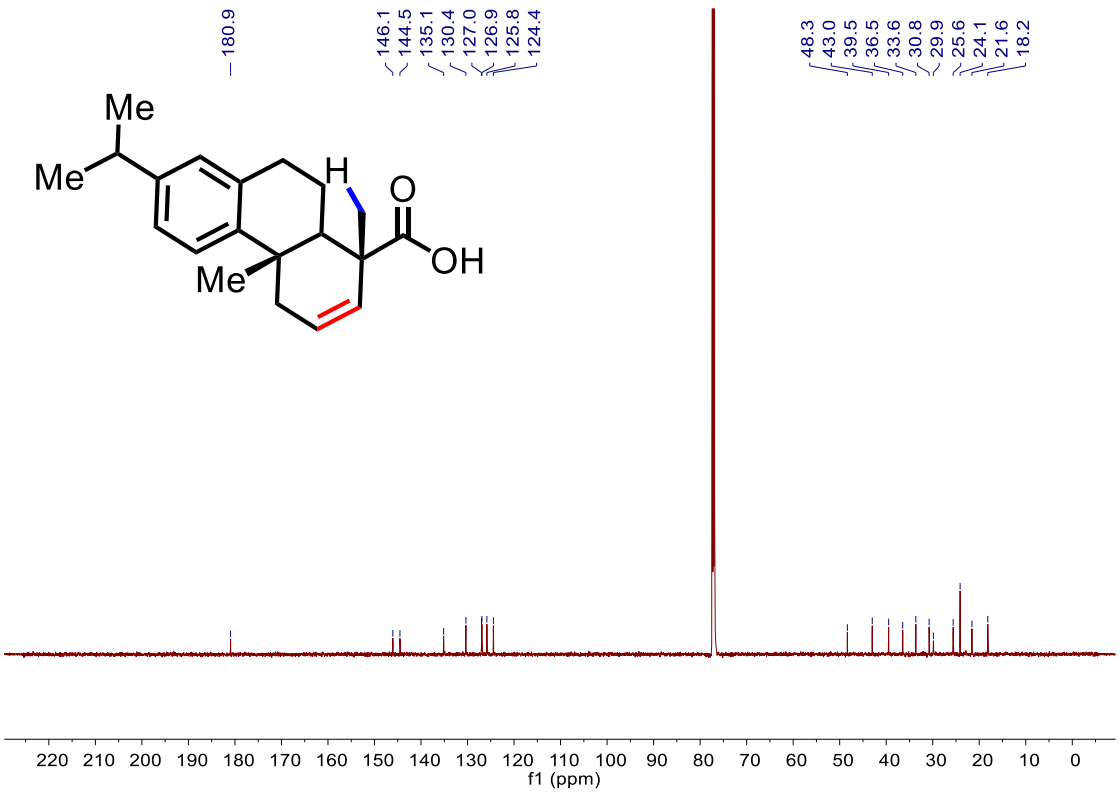
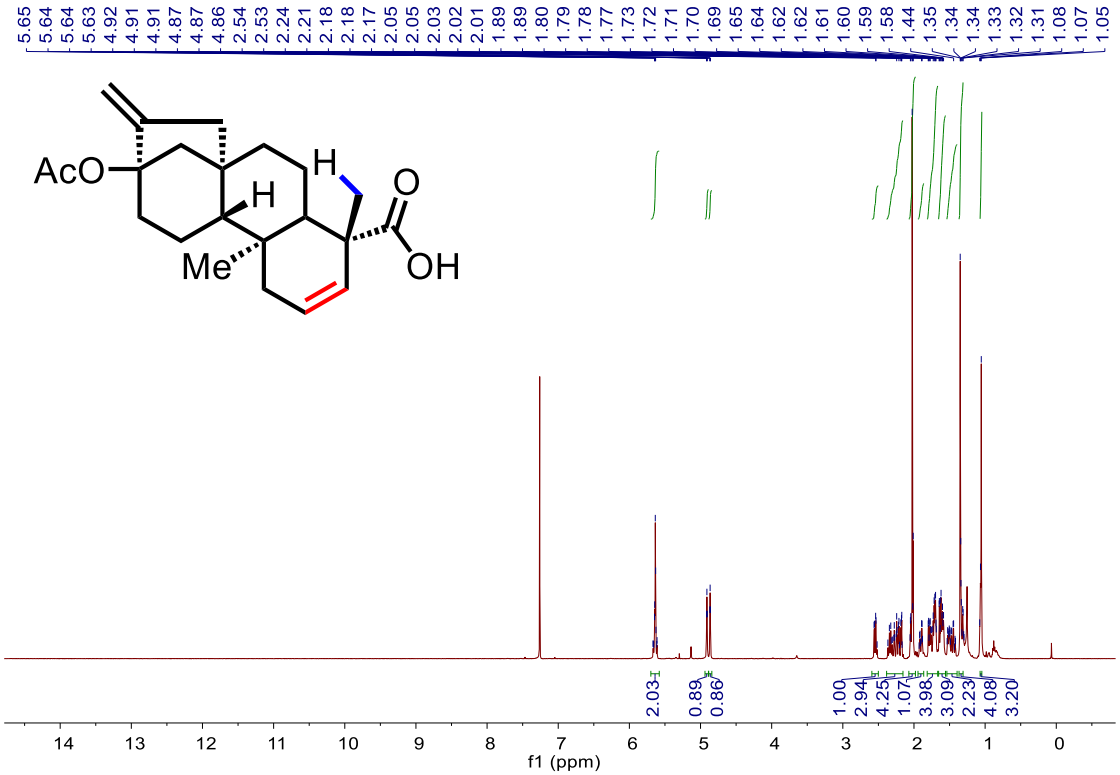


^{1}H NMR of Compound 2f:



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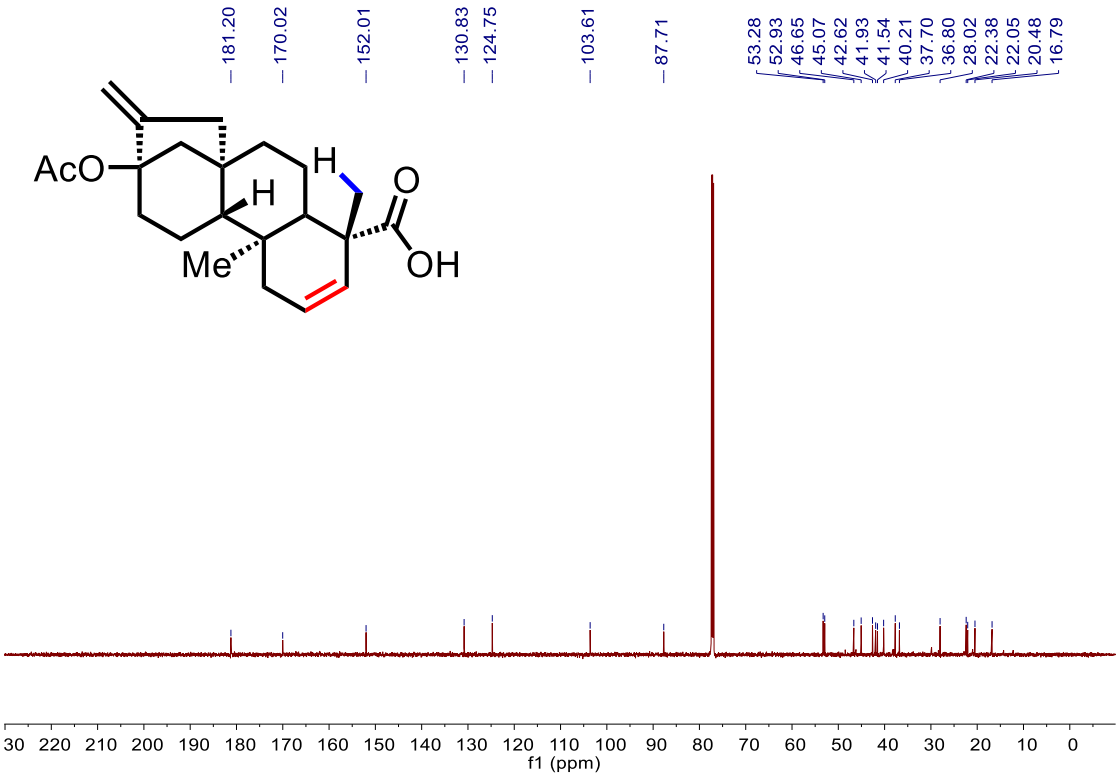
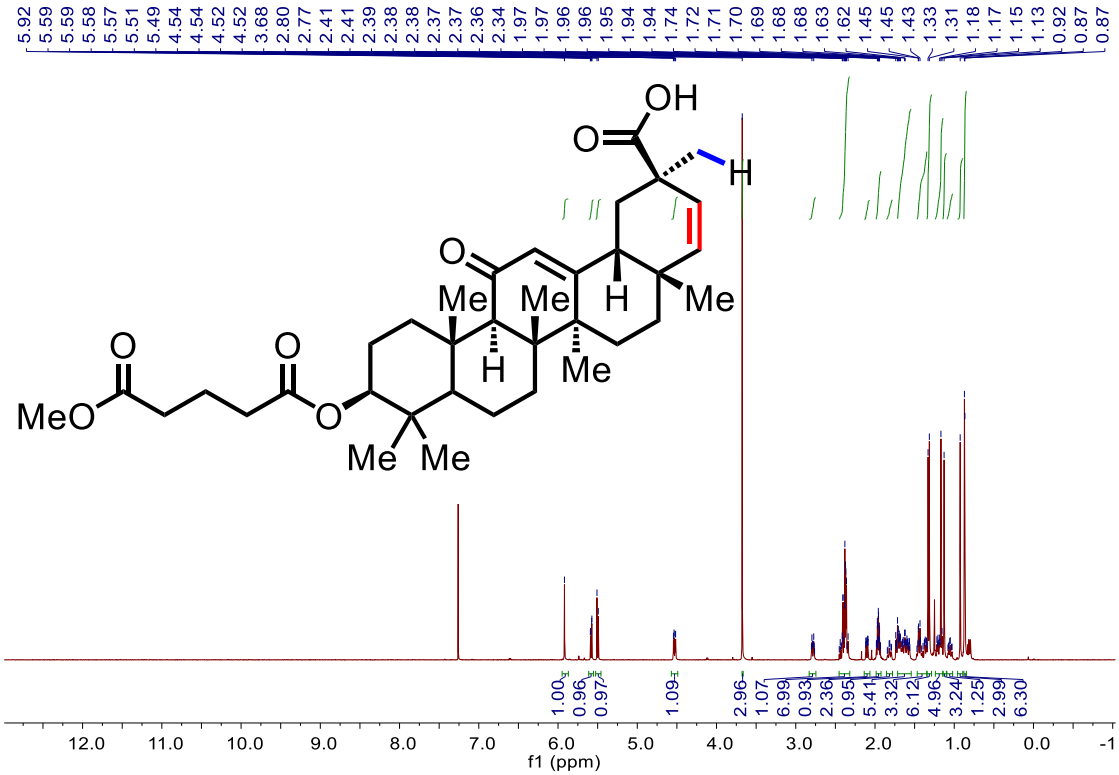
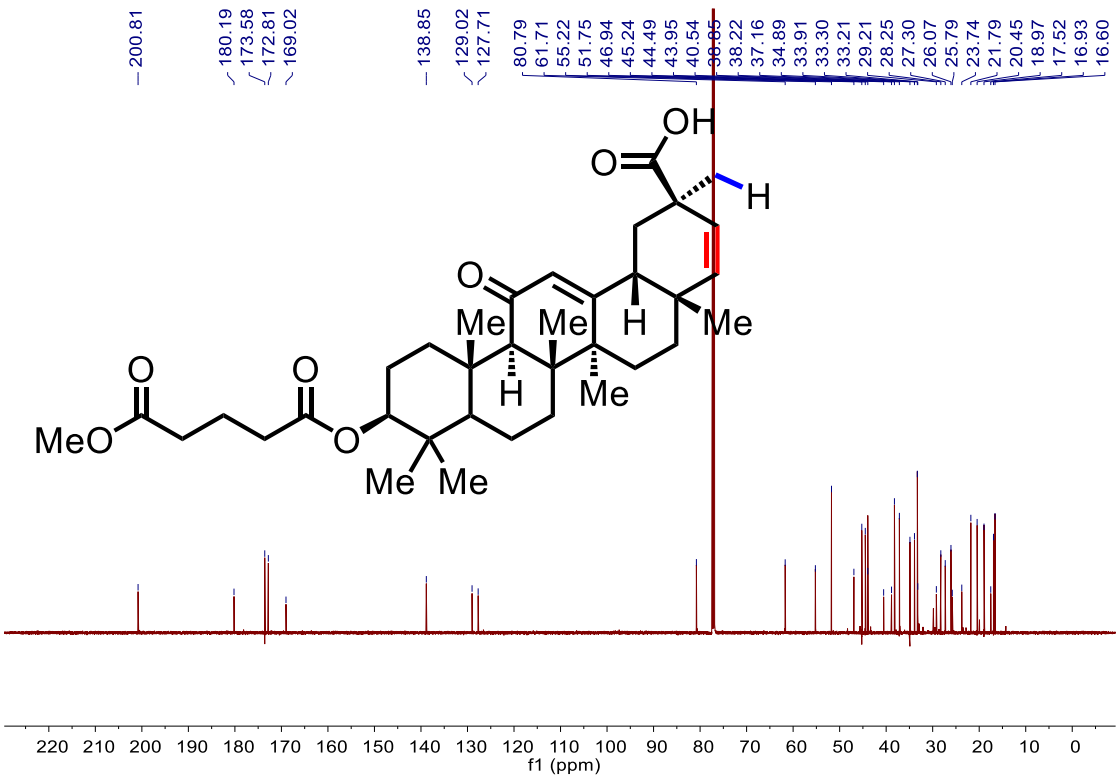


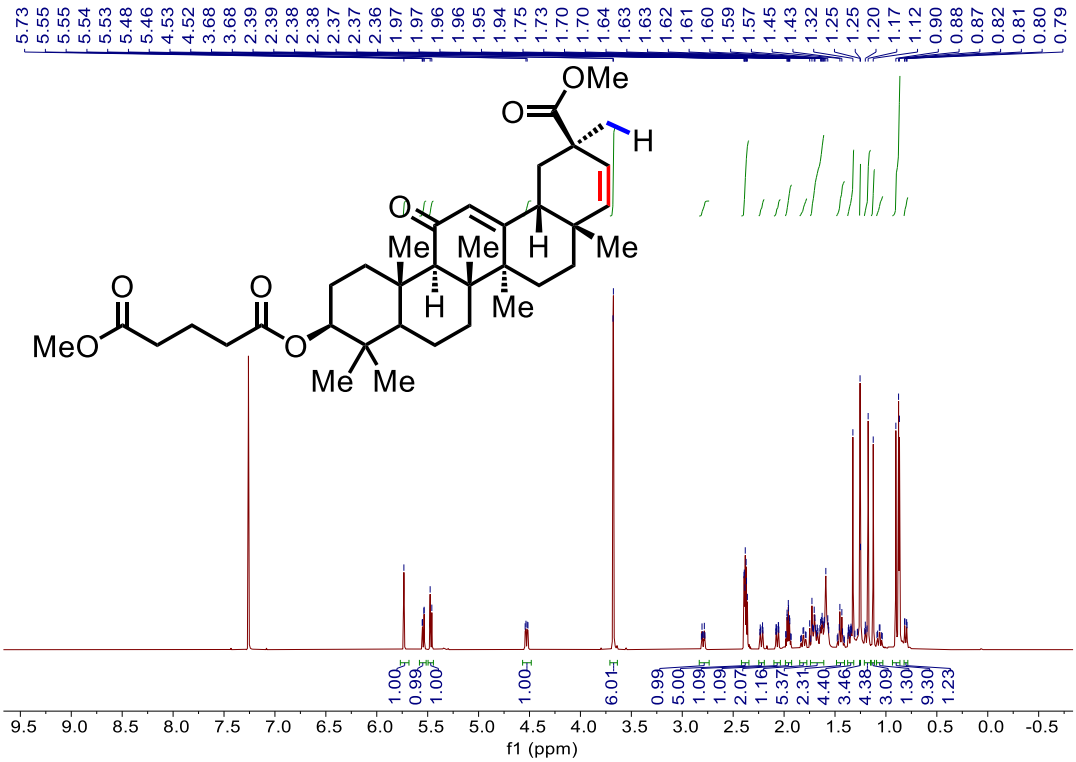
^{1}H NMR of Compound 2h:



^{13}C NMR of Compound 2h:



^{1}H NMR of Compound 2i:



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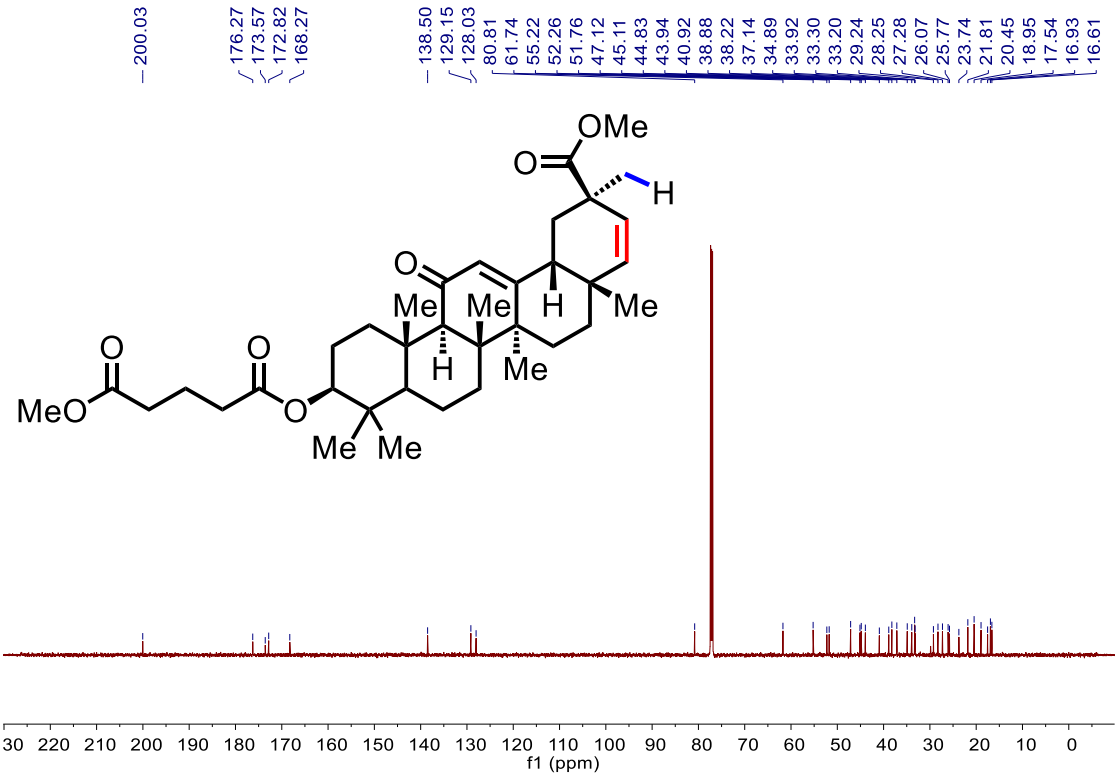

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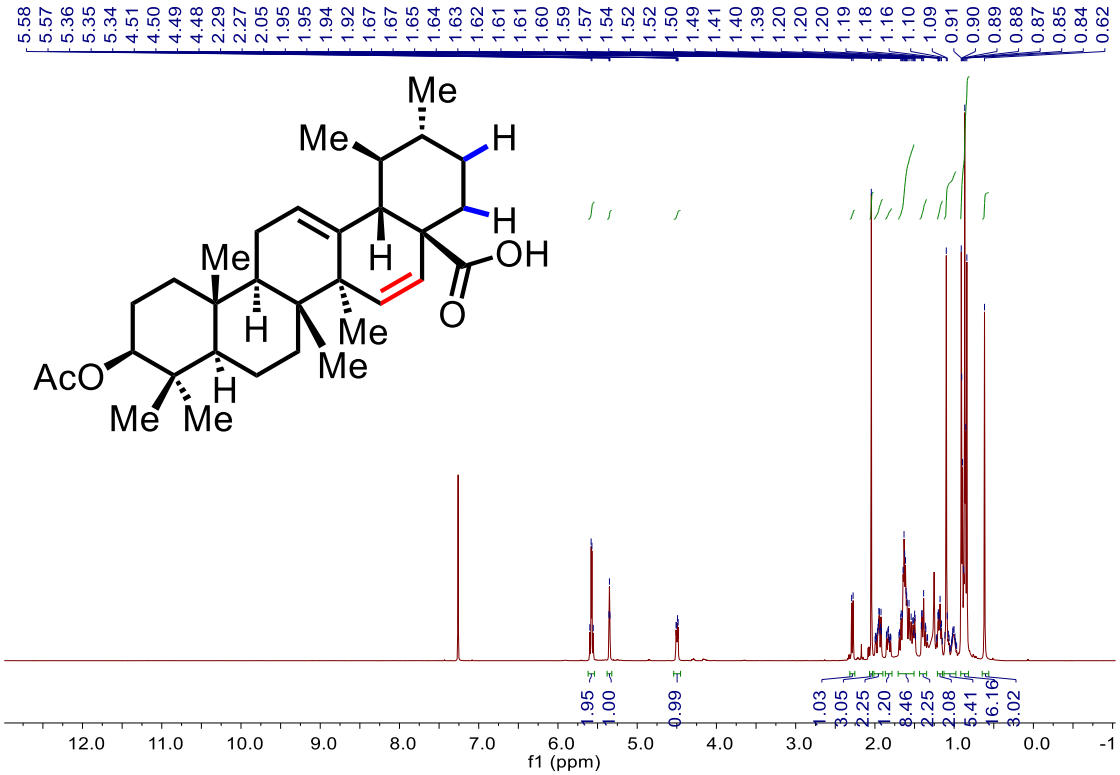

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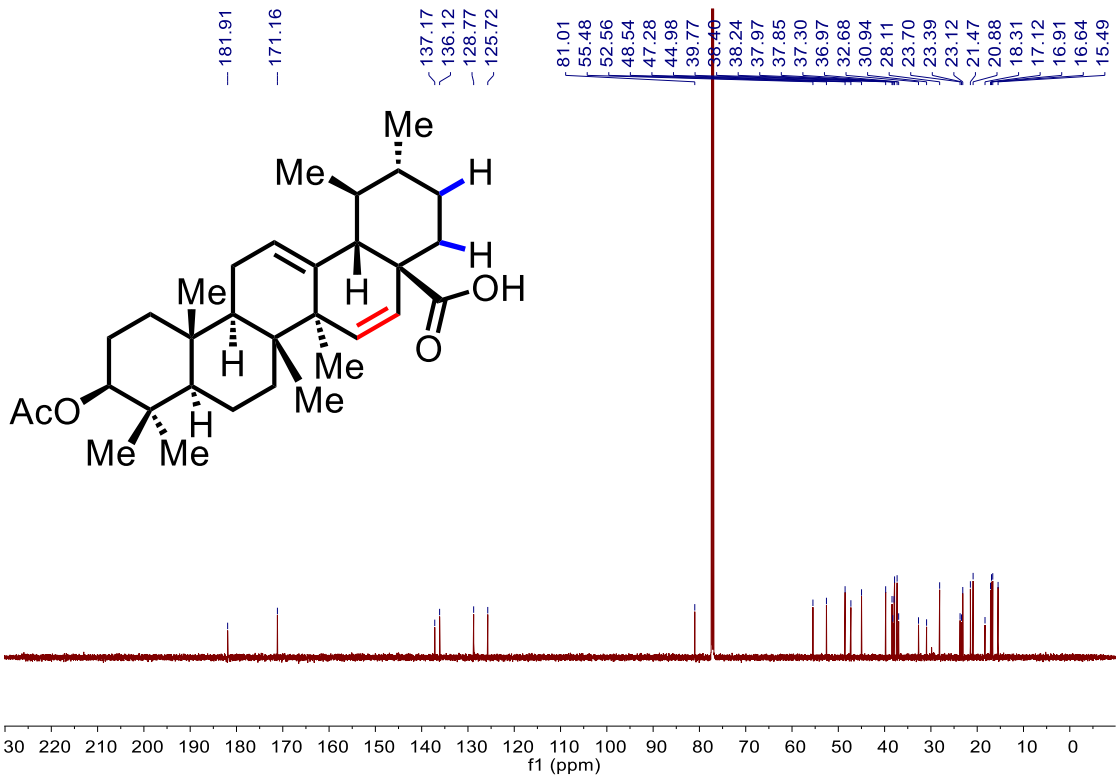

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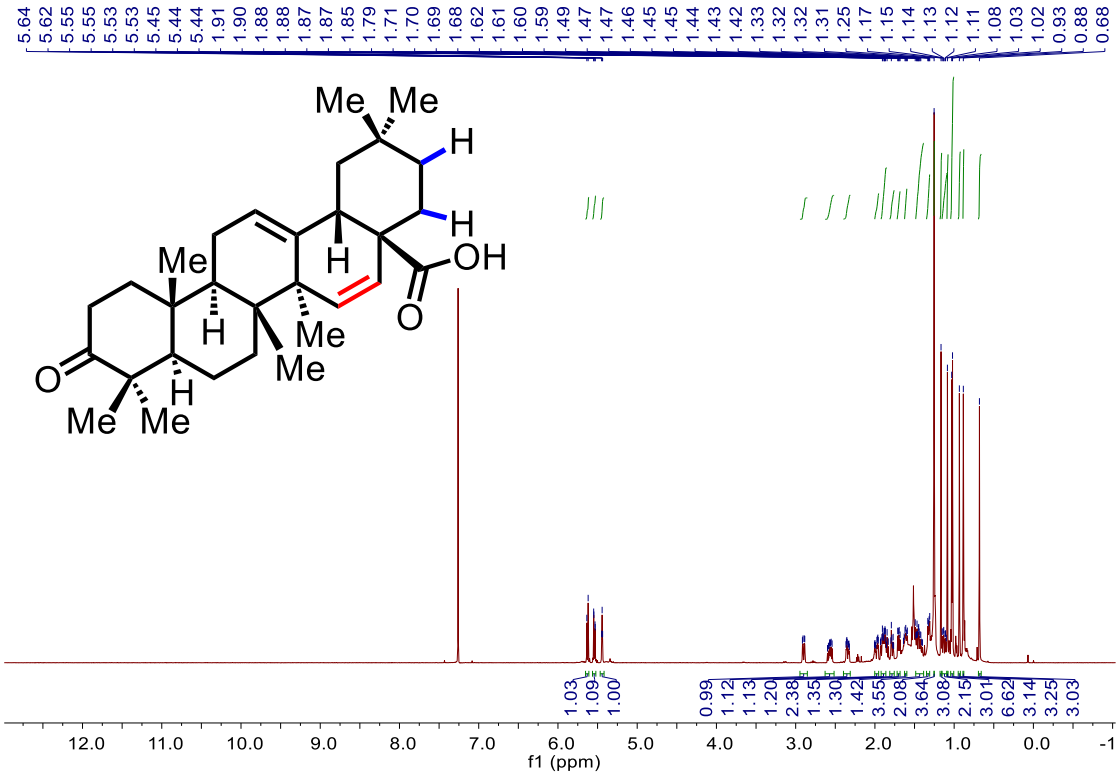

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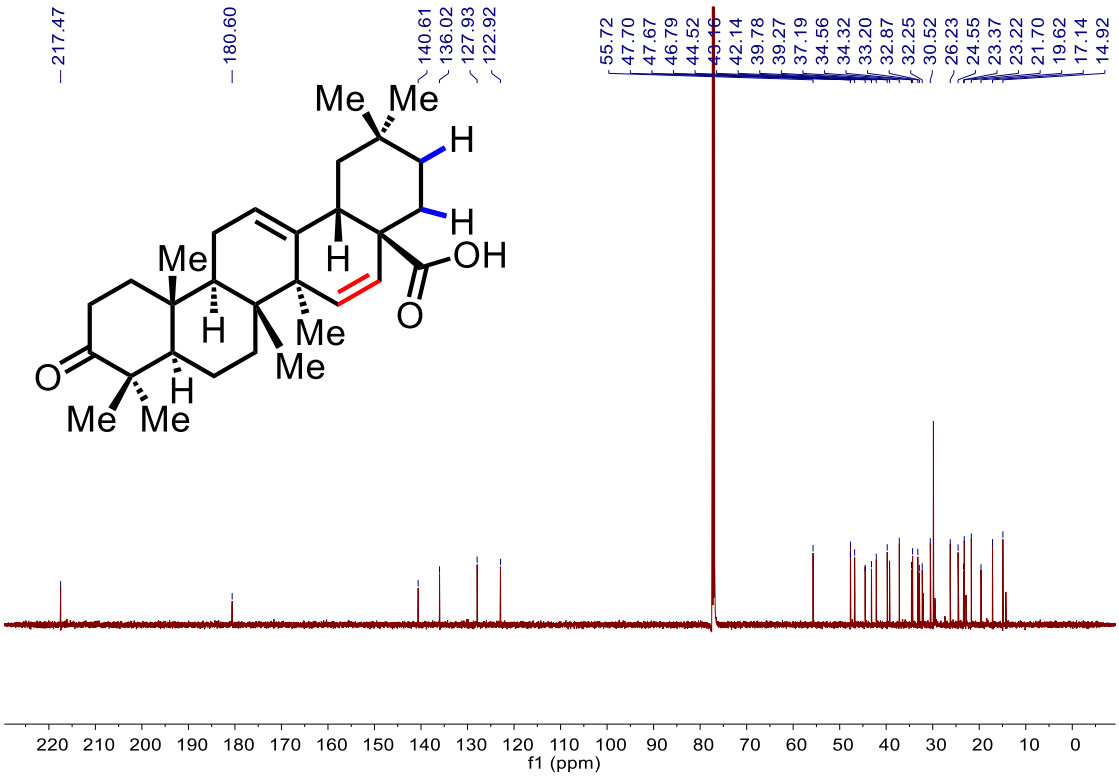

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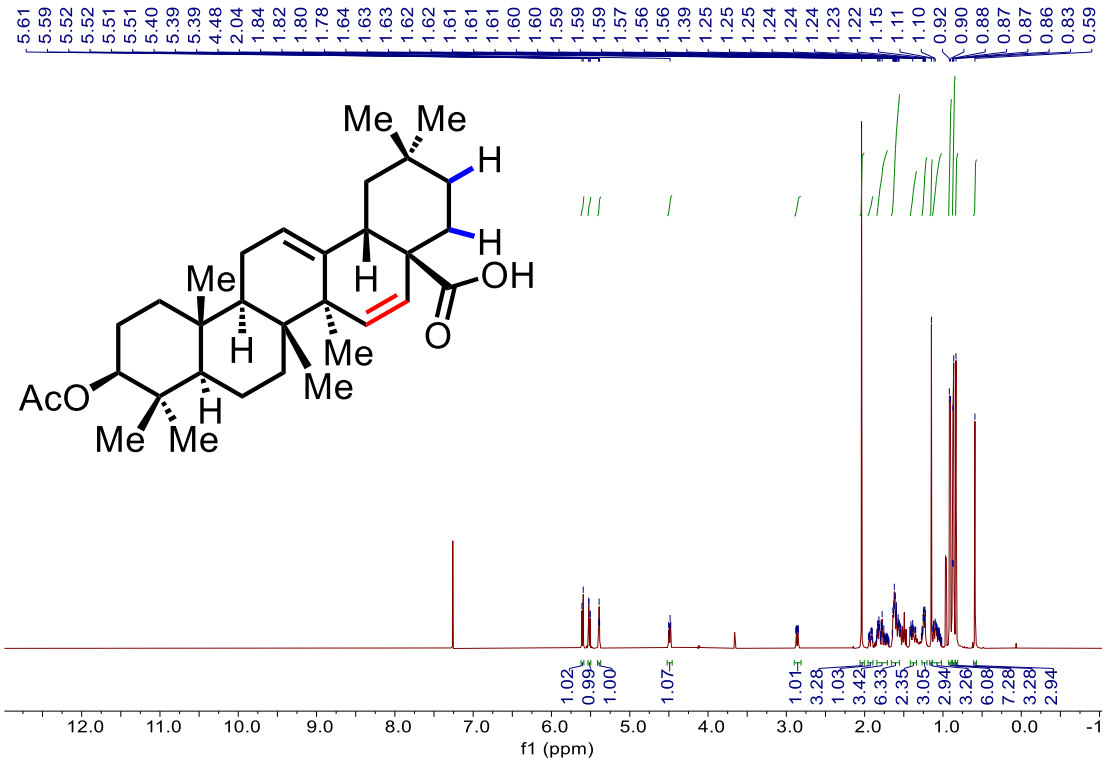
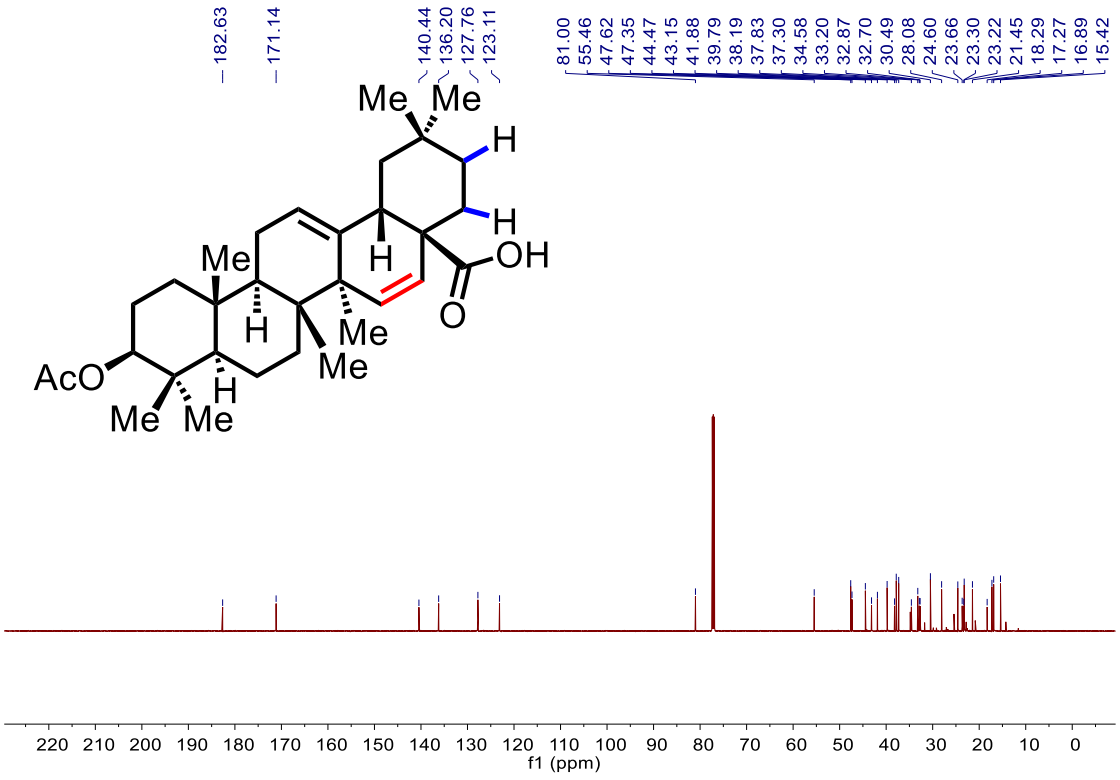
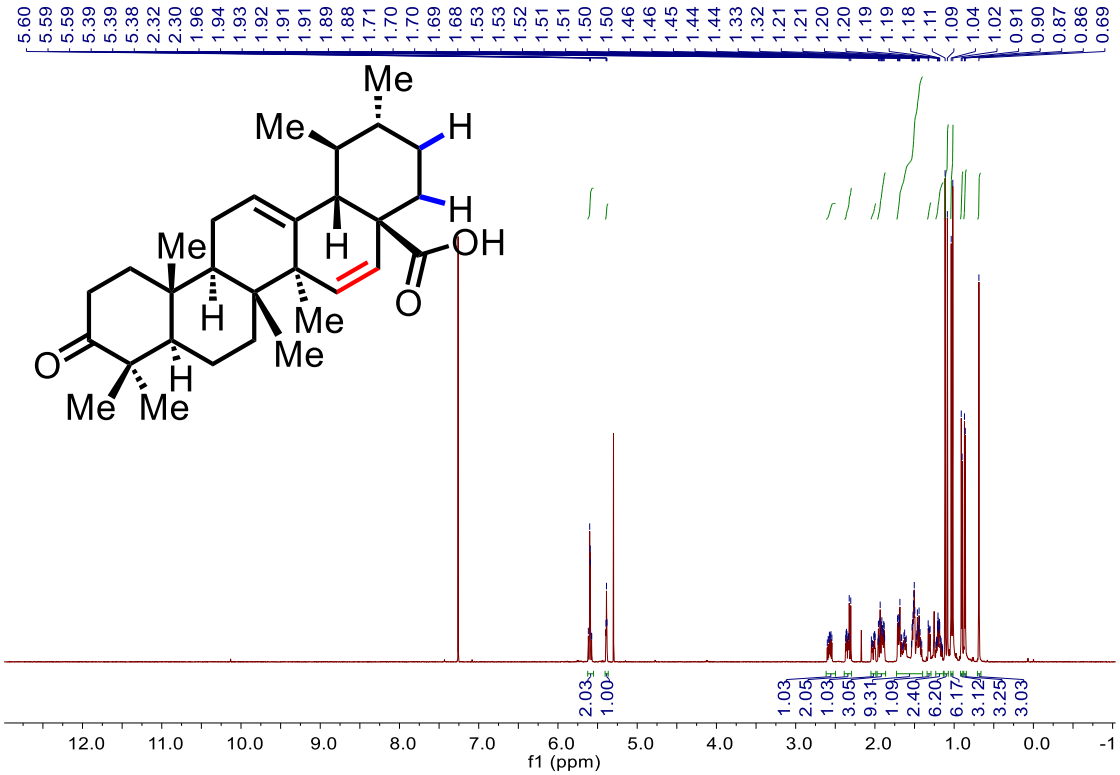


^{13}C NMR of Compound 2l:



^{1}H NMR of Compound 2m:



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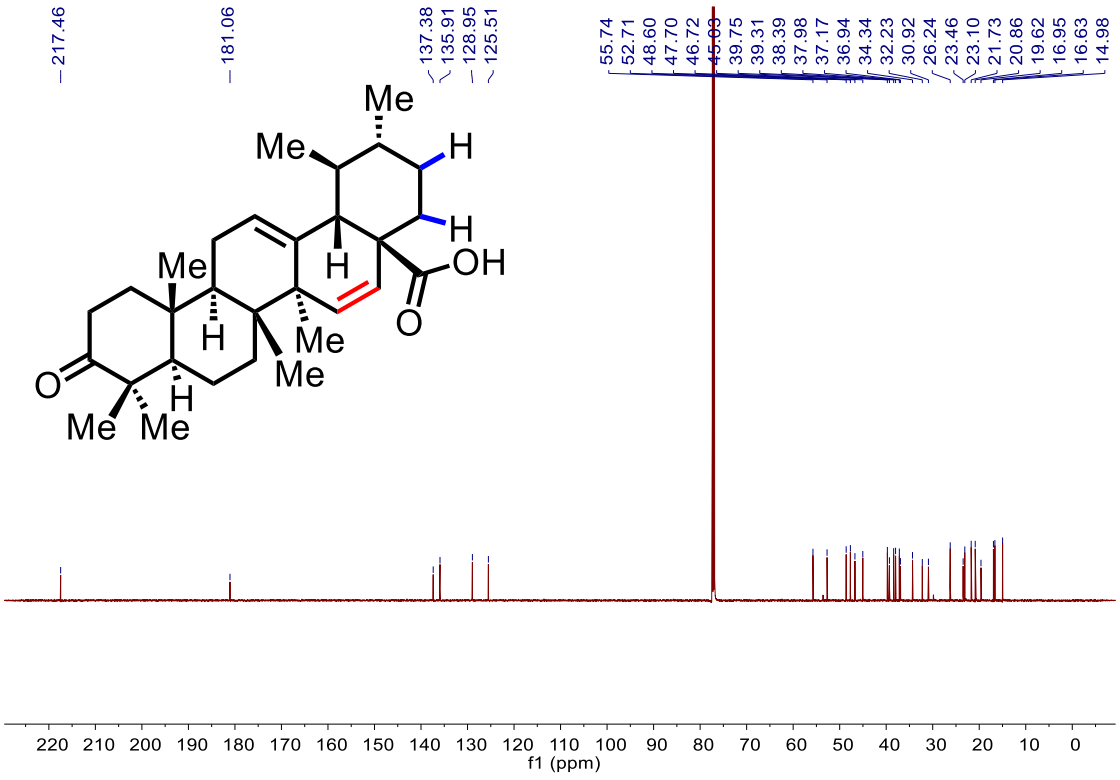
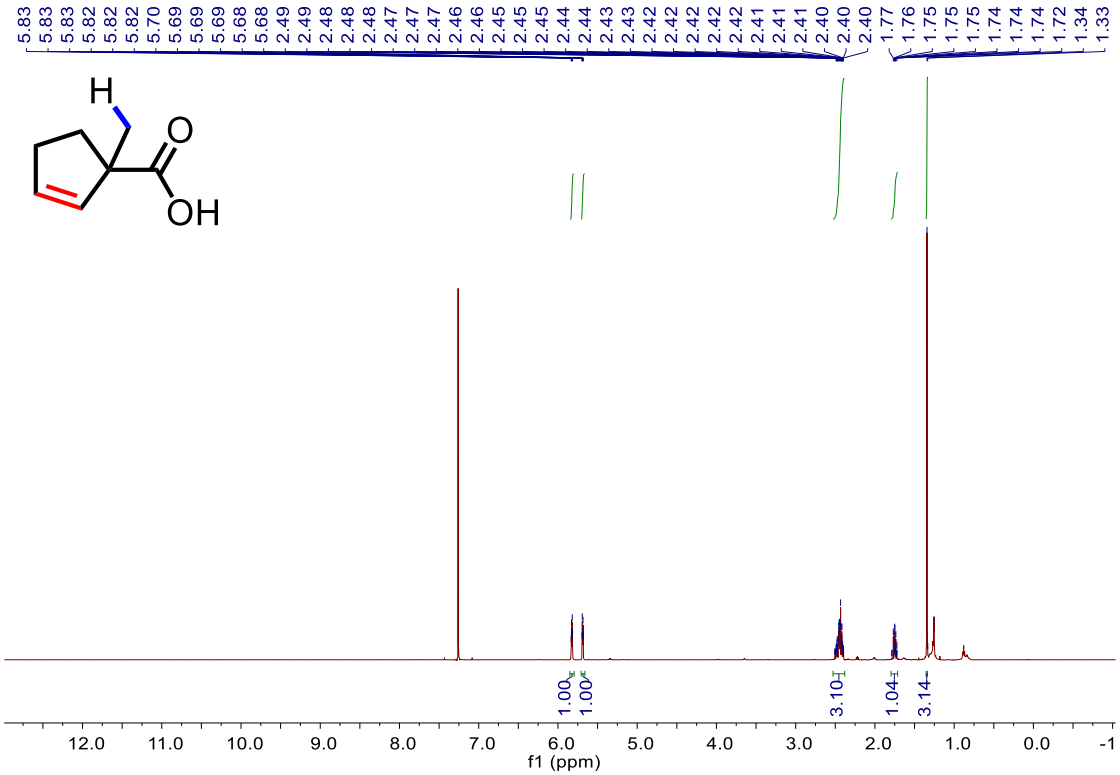
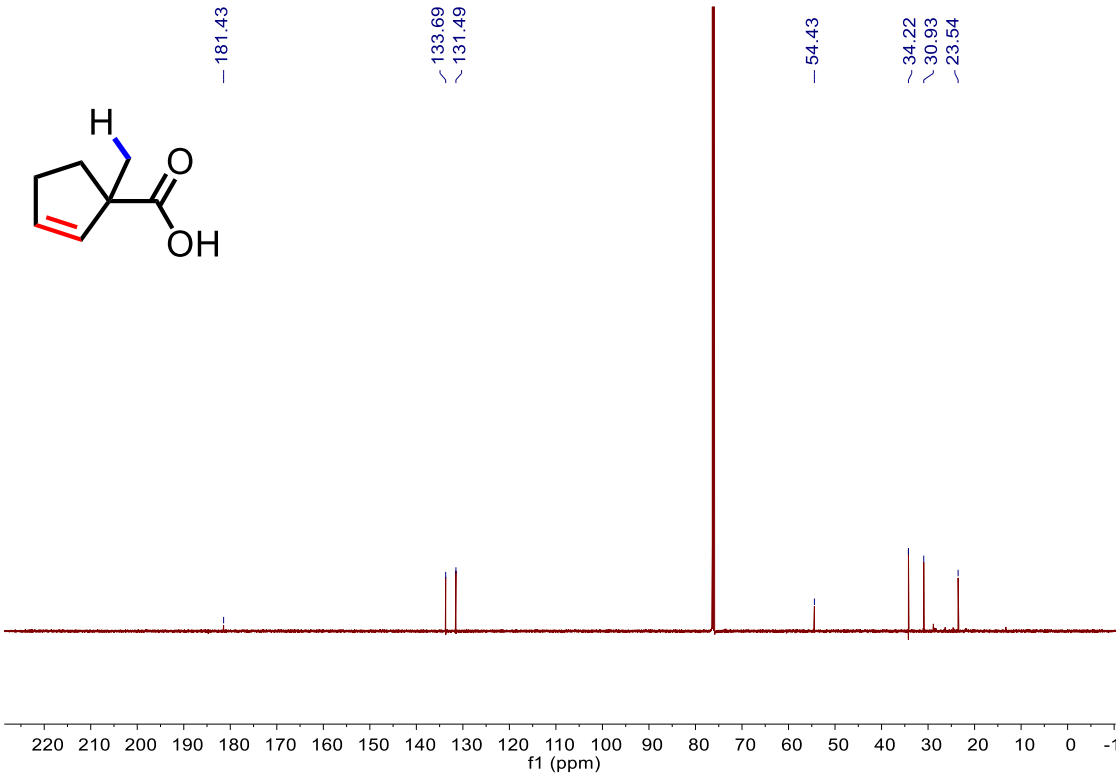


^{1}H NMR of Compound 4a:



^{13}C NMR of Compound 4a:



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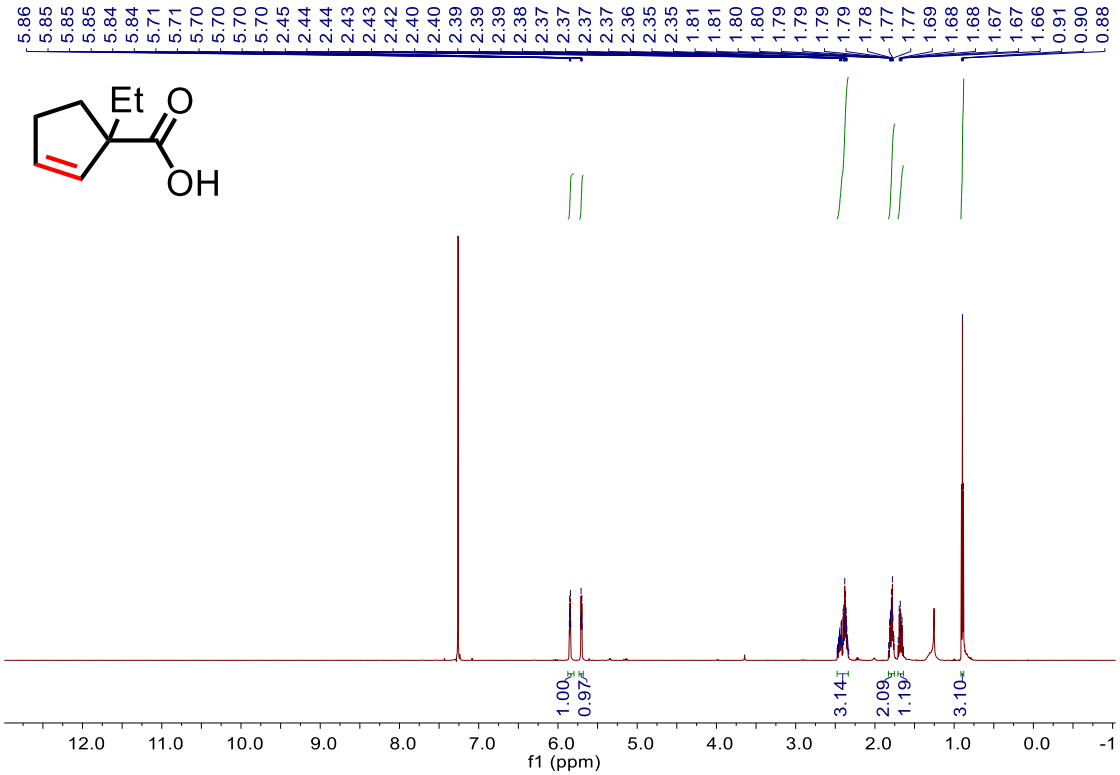
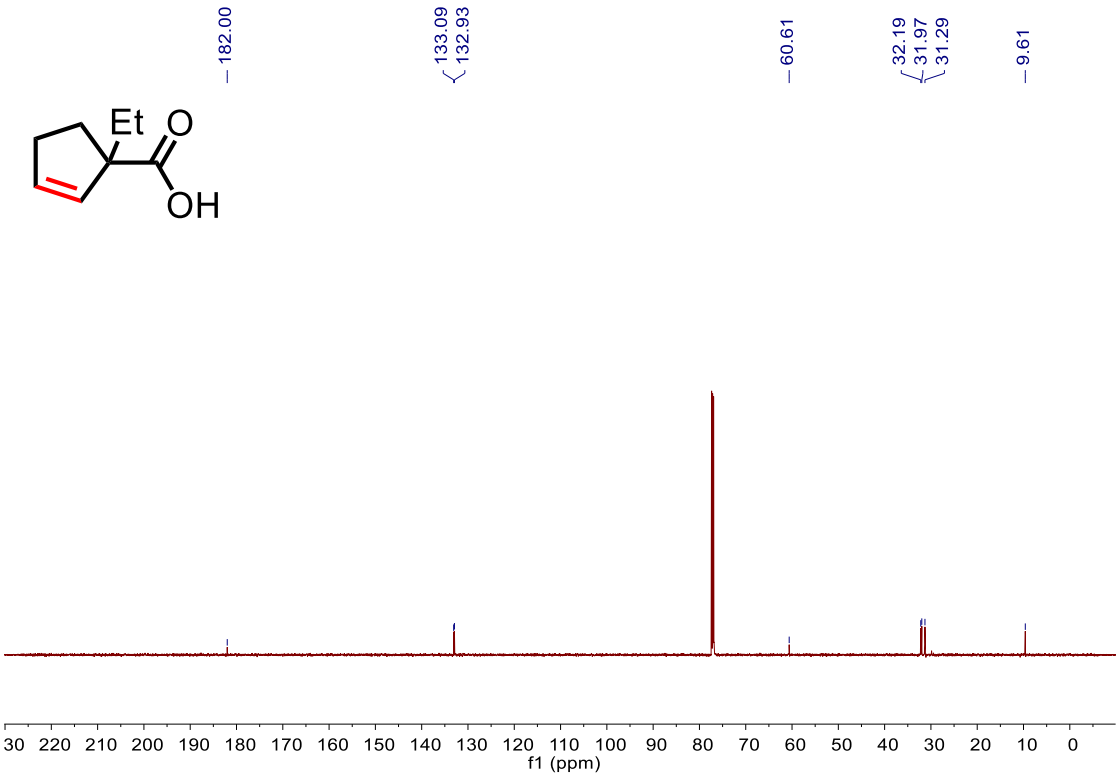
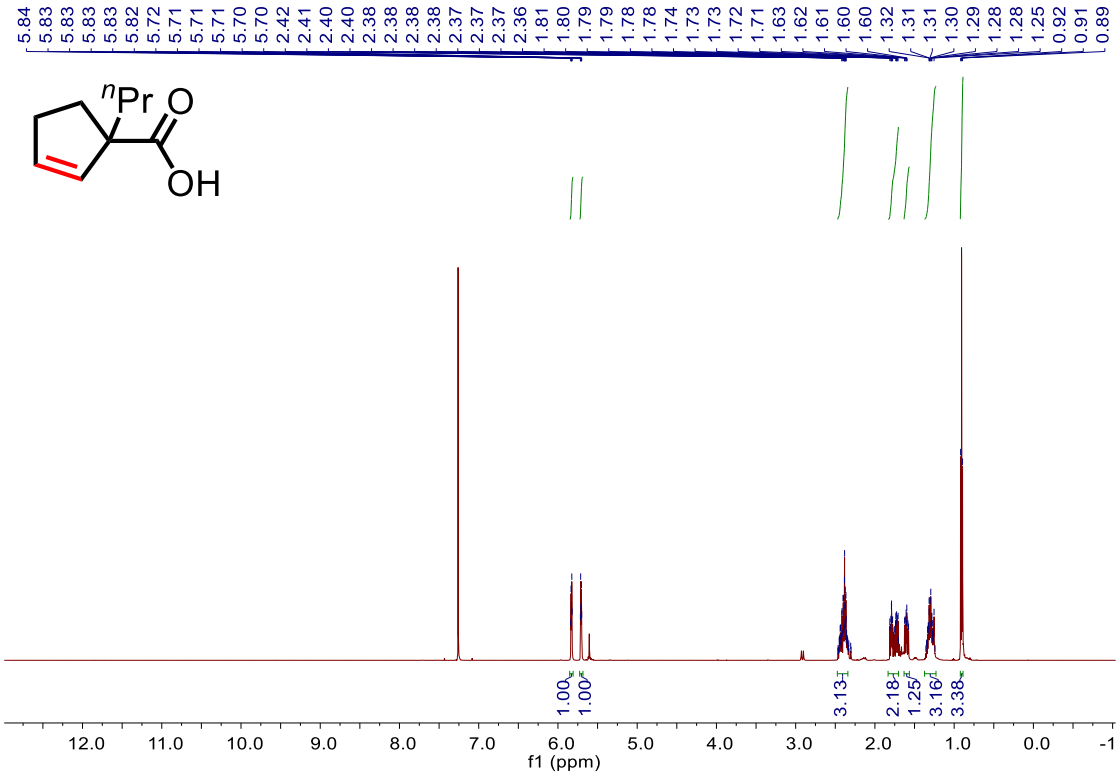


^{13}C NMR of Compound 4b:



^{1}H NMR of Compound 4c:



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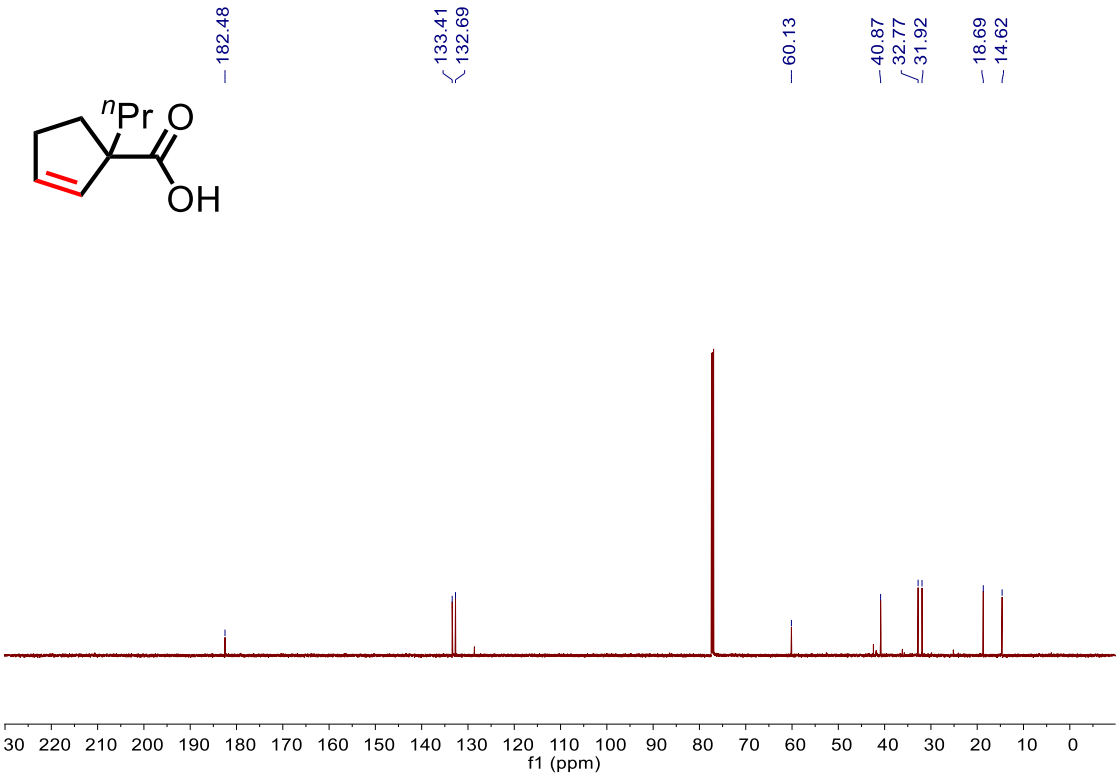
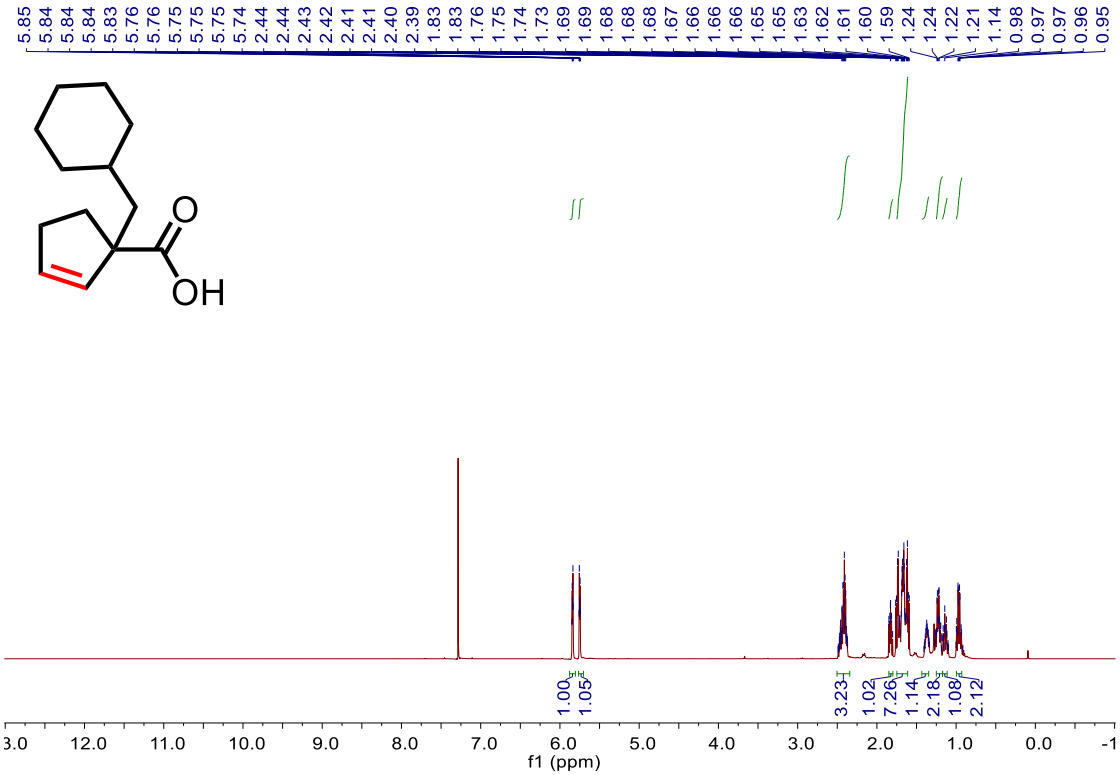


^{1}H NMR of Compound 4d:



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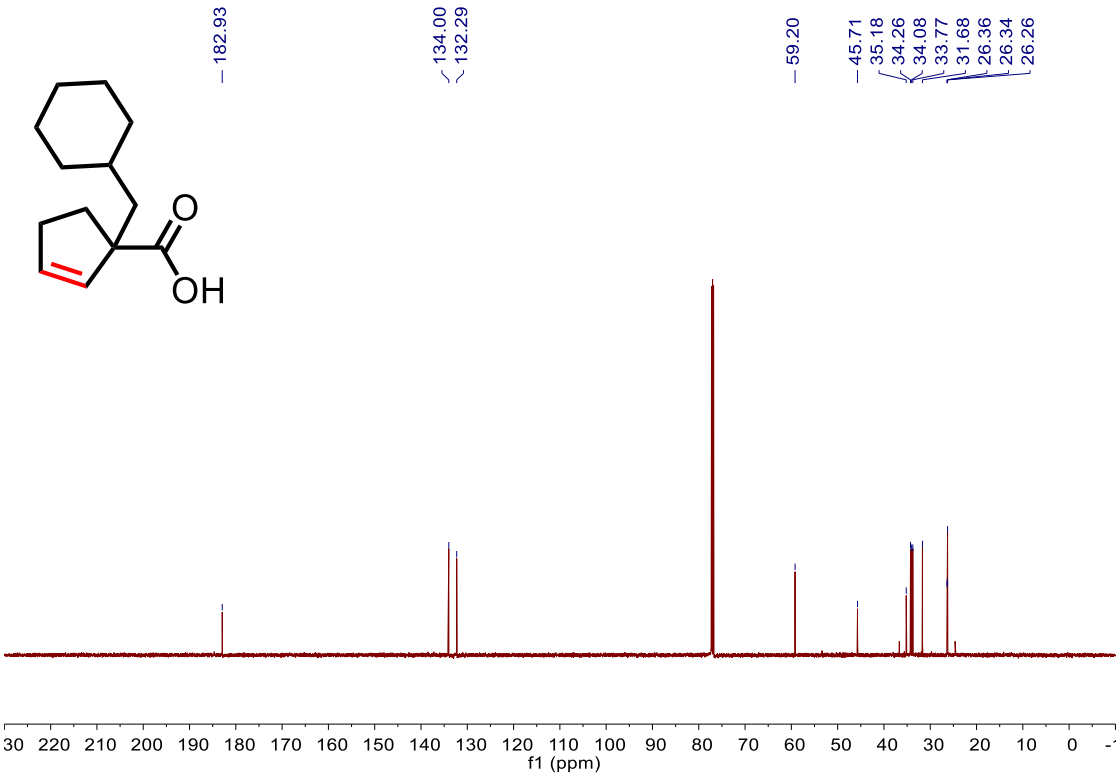

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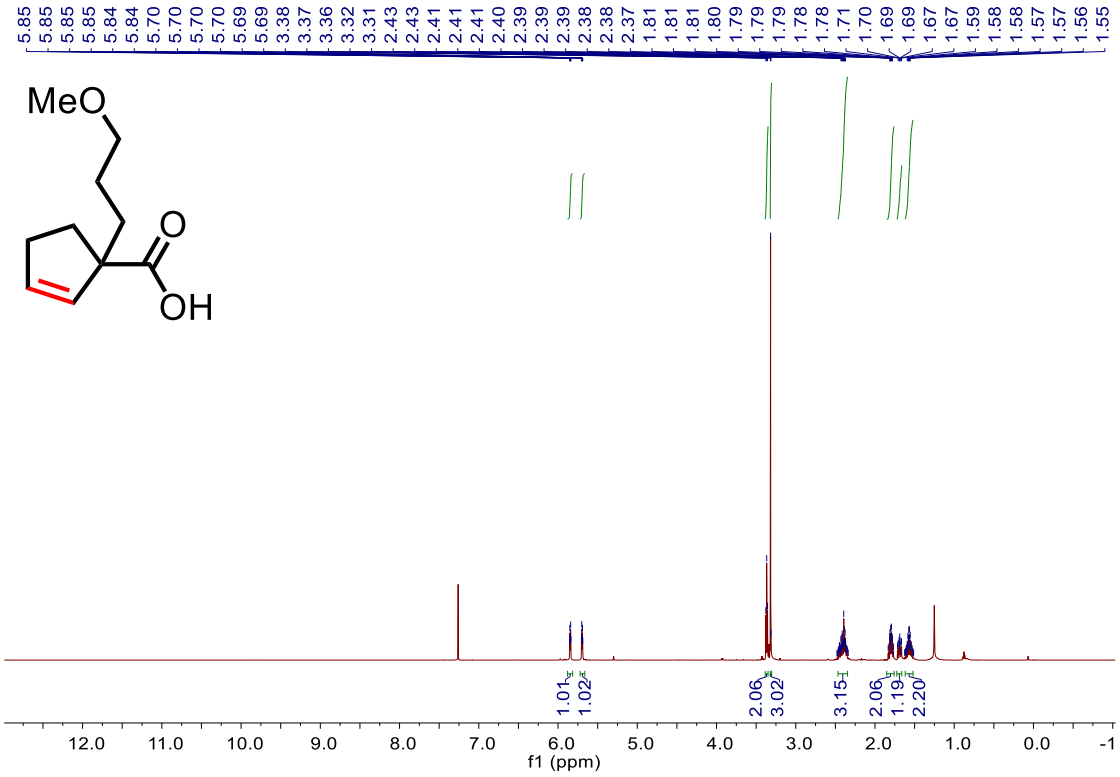

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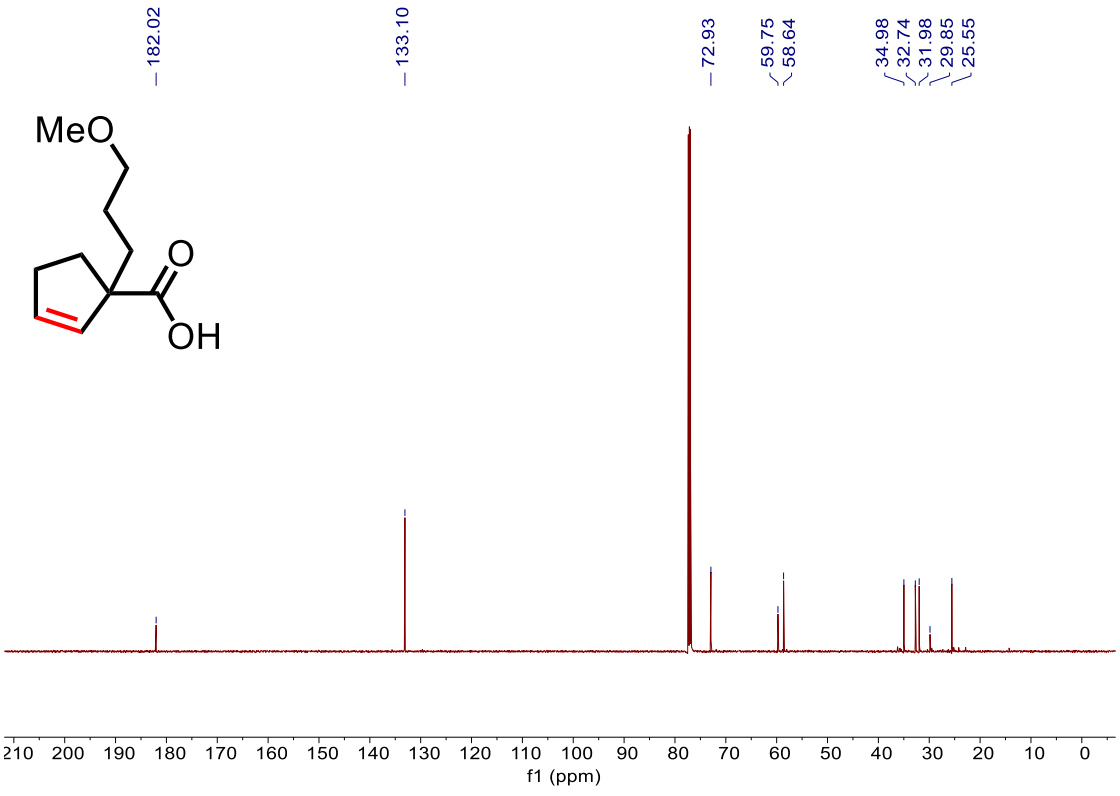
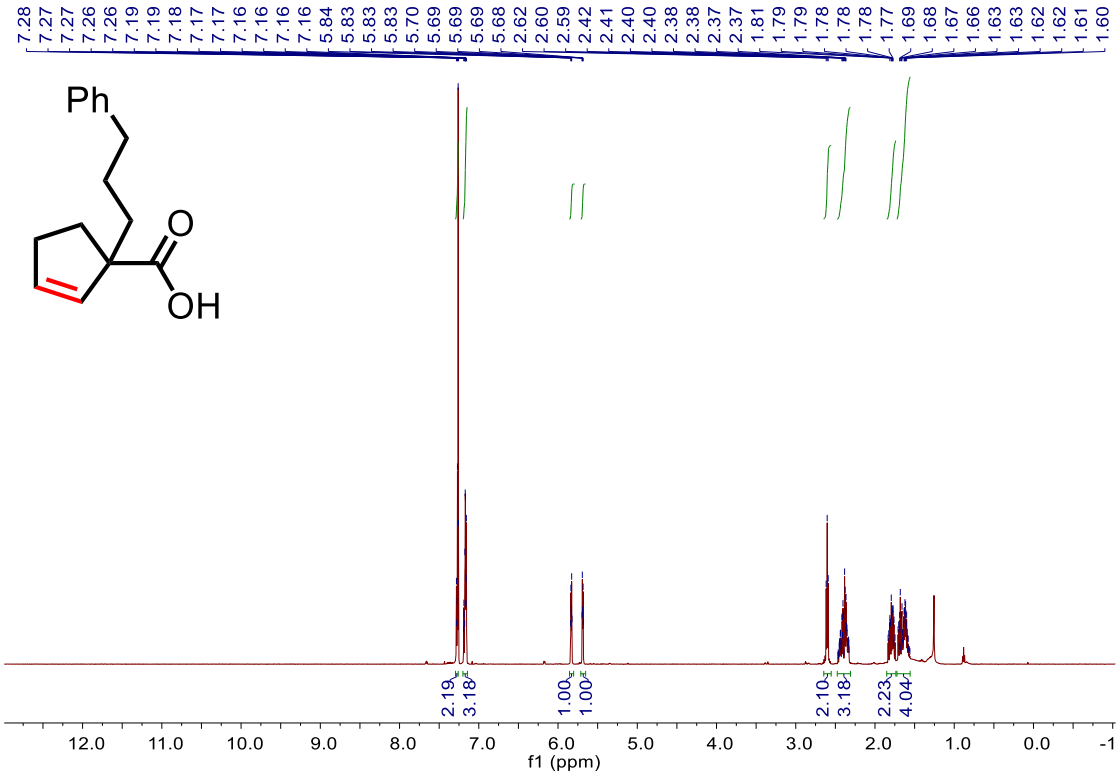


^{1}H NMR of Compound 4f:



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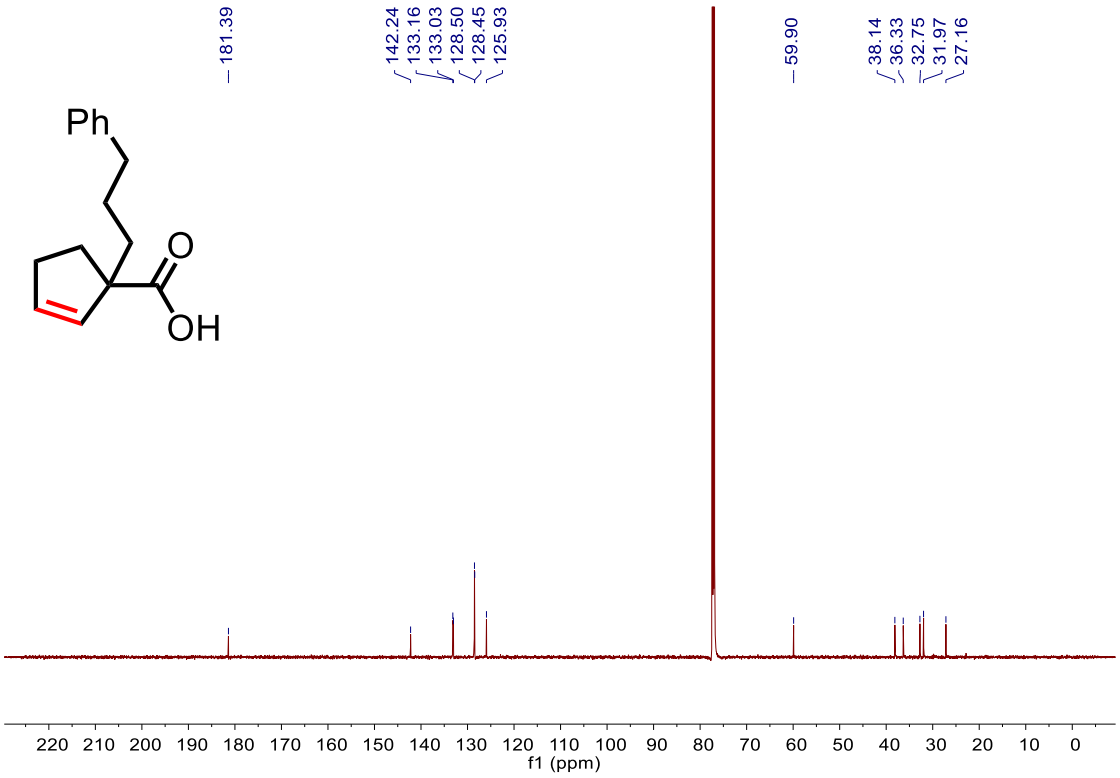
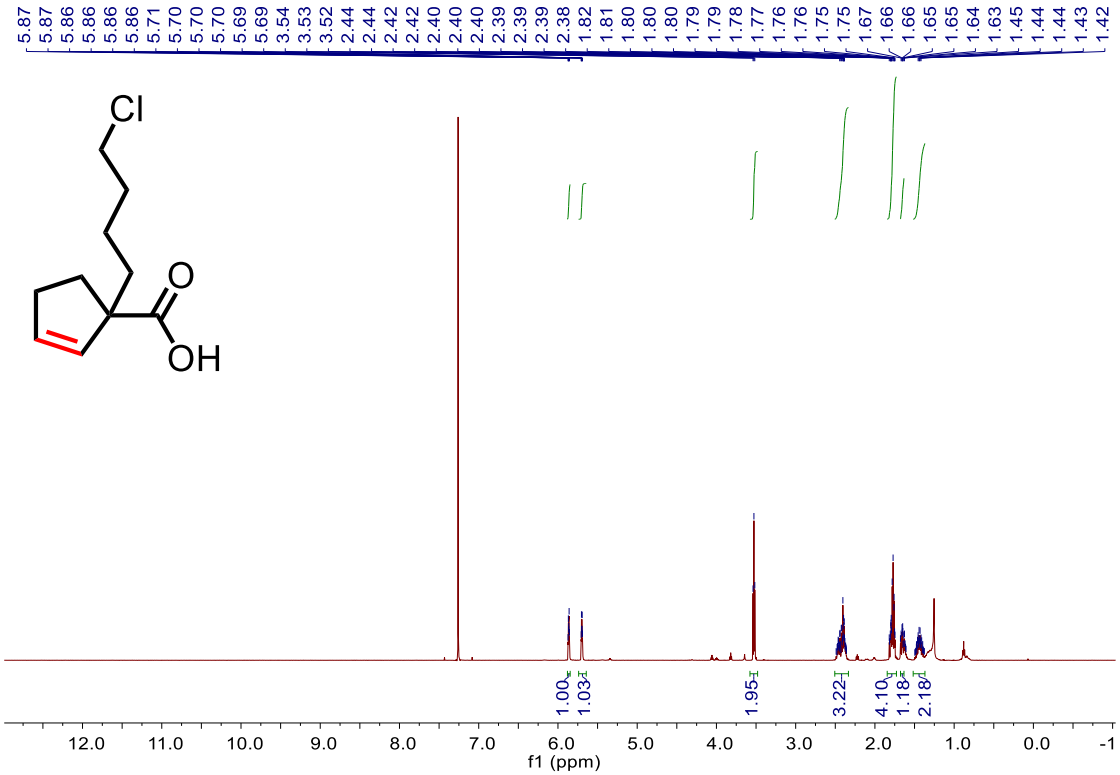
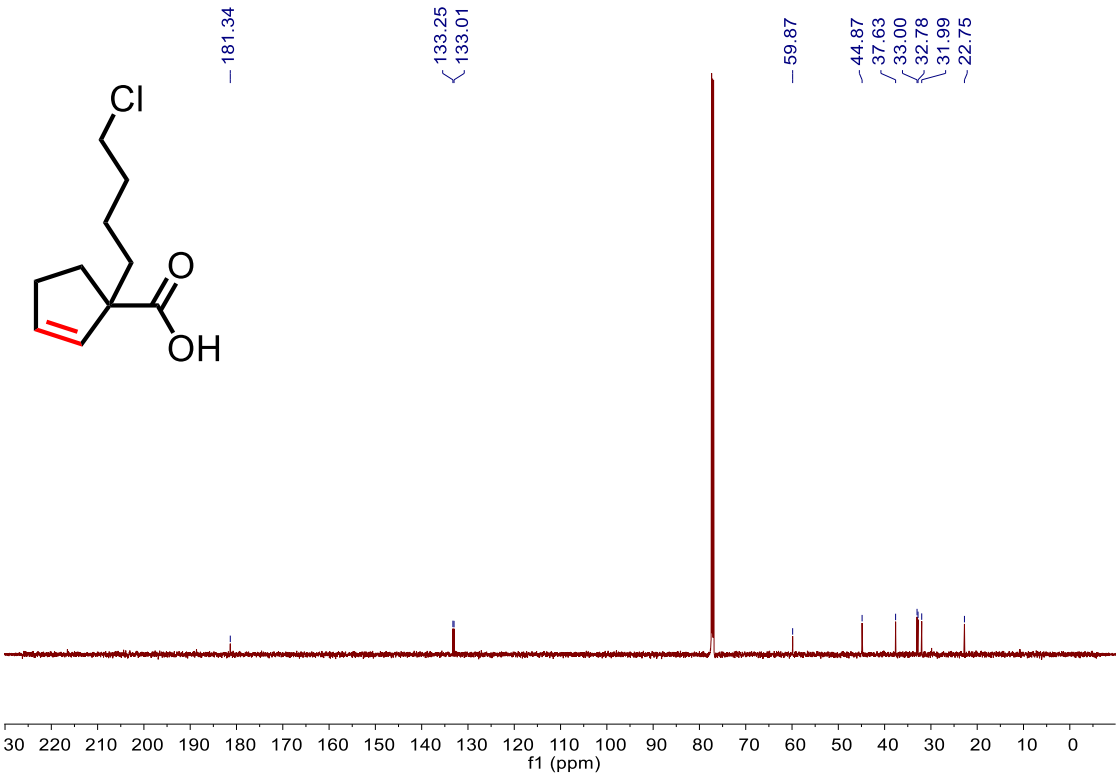


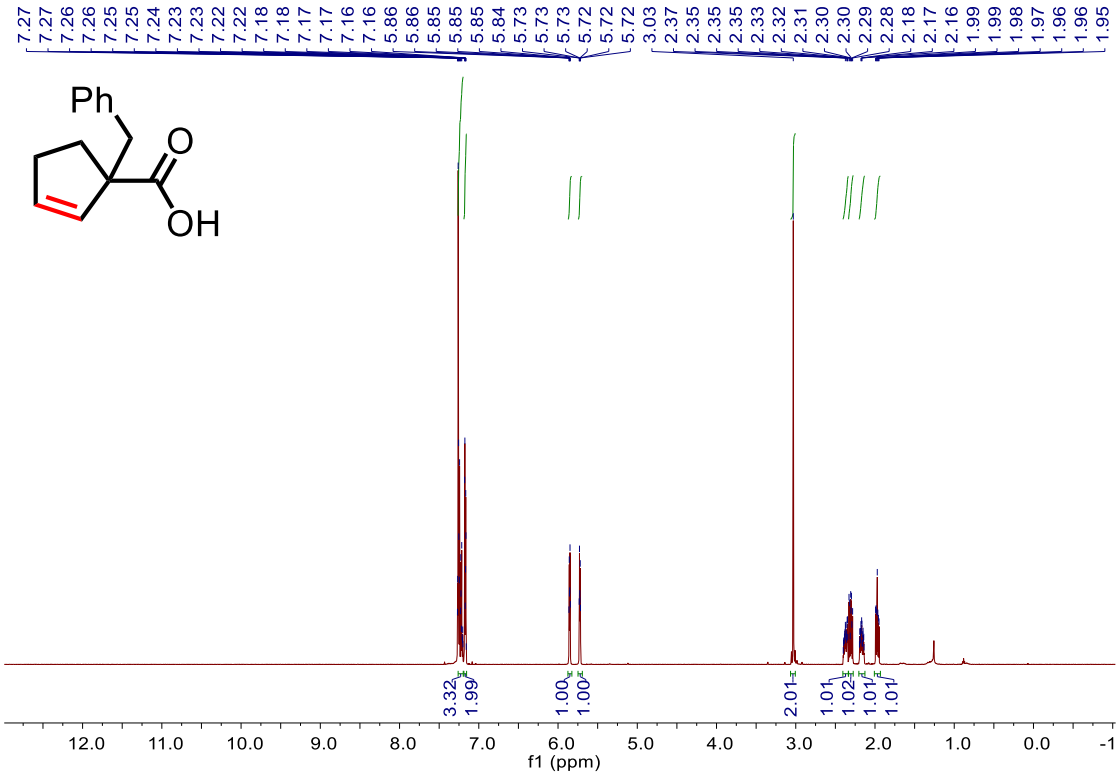
^{1}H NMR of Compound 4g:



^{13}C NMR of Compound 4g:



^{1}H NMR of Compound 4h:



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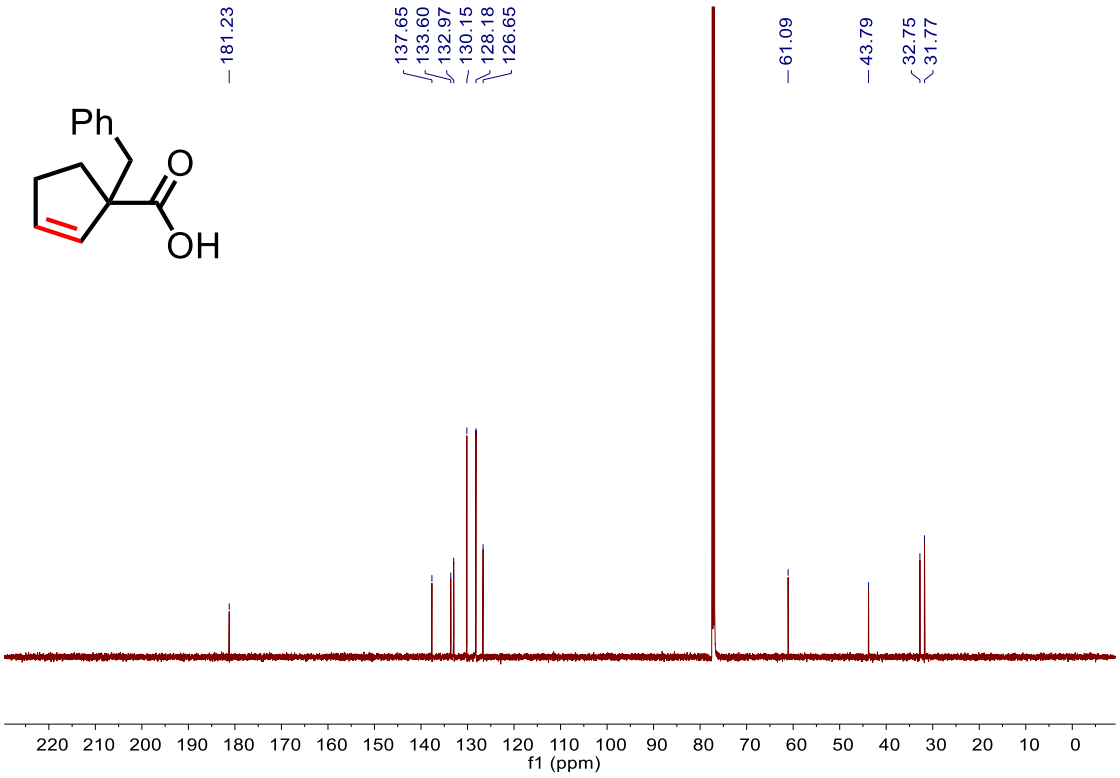
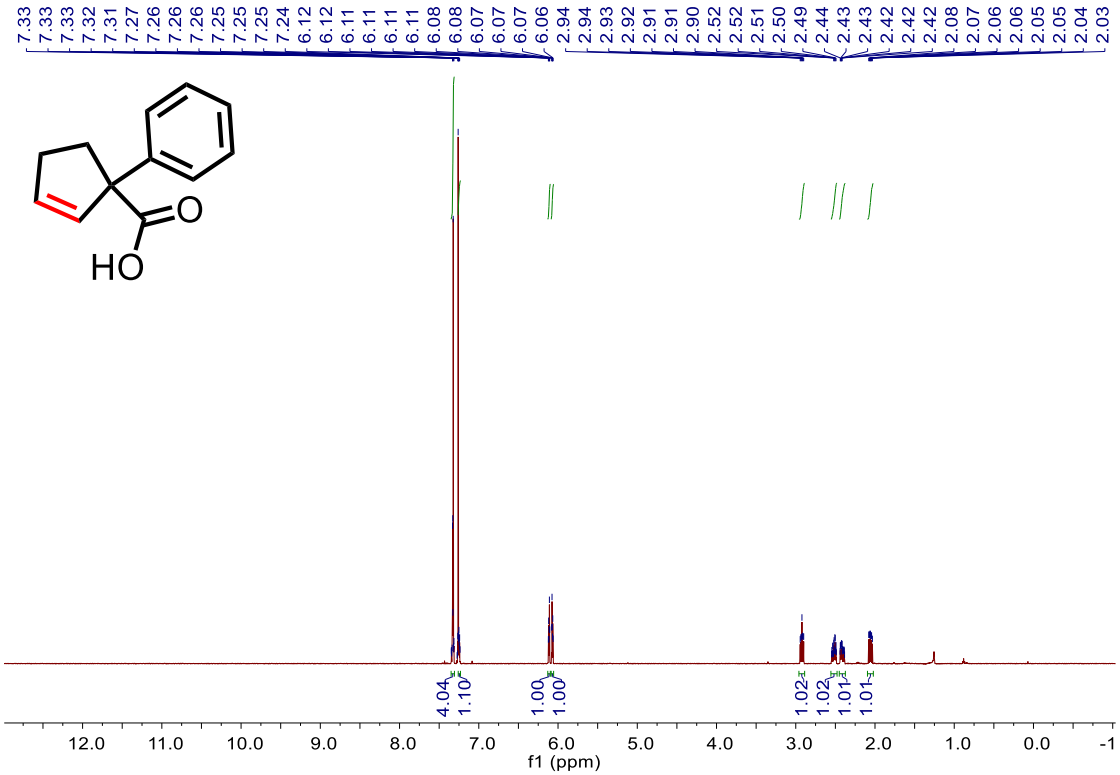
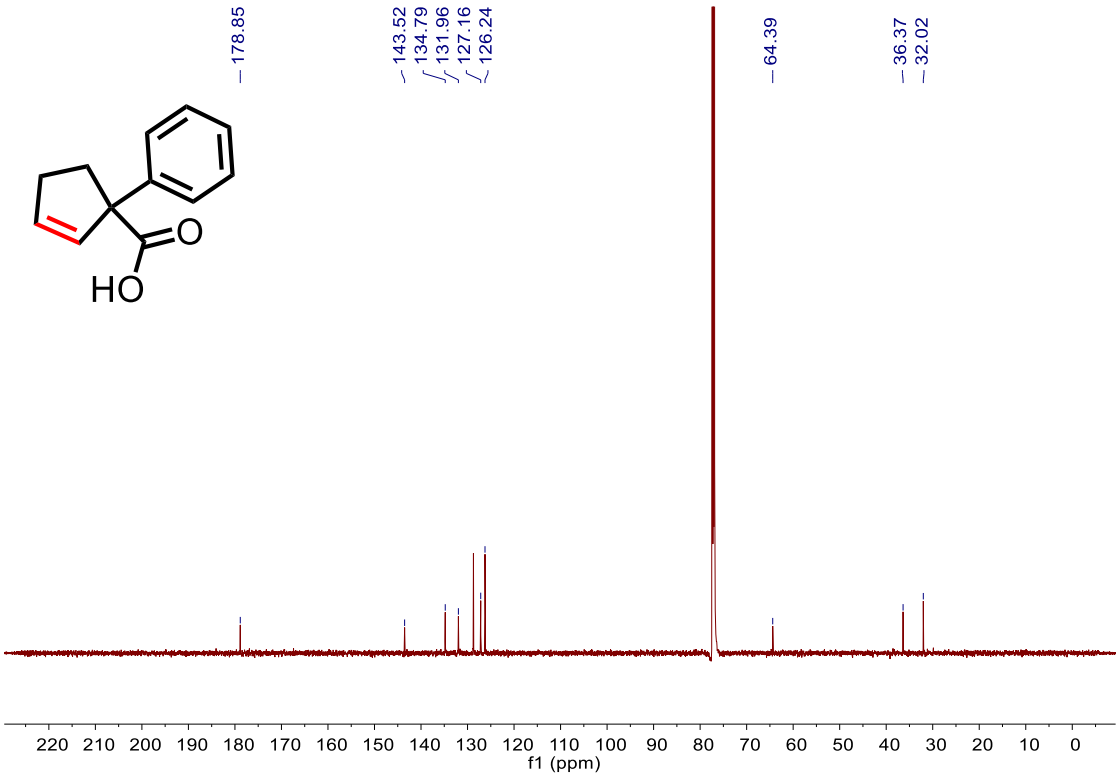


^{1}H NMR of Compound 4i:



^{13}C NMR of Compound 4i:



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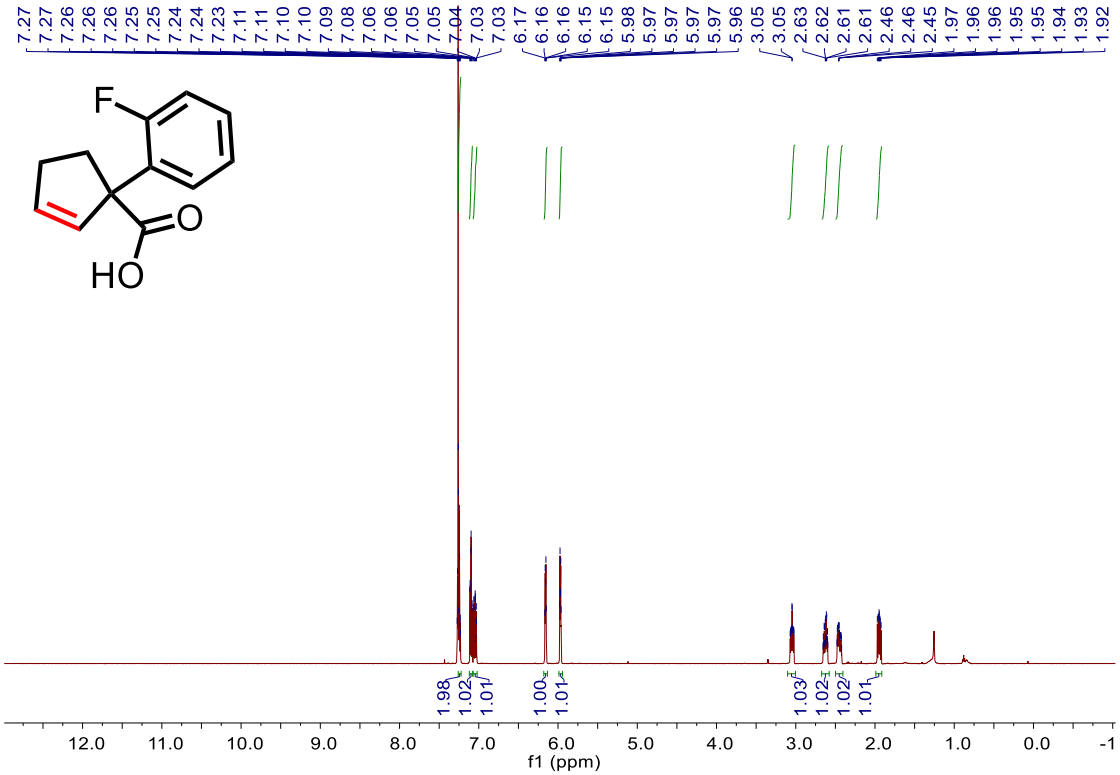

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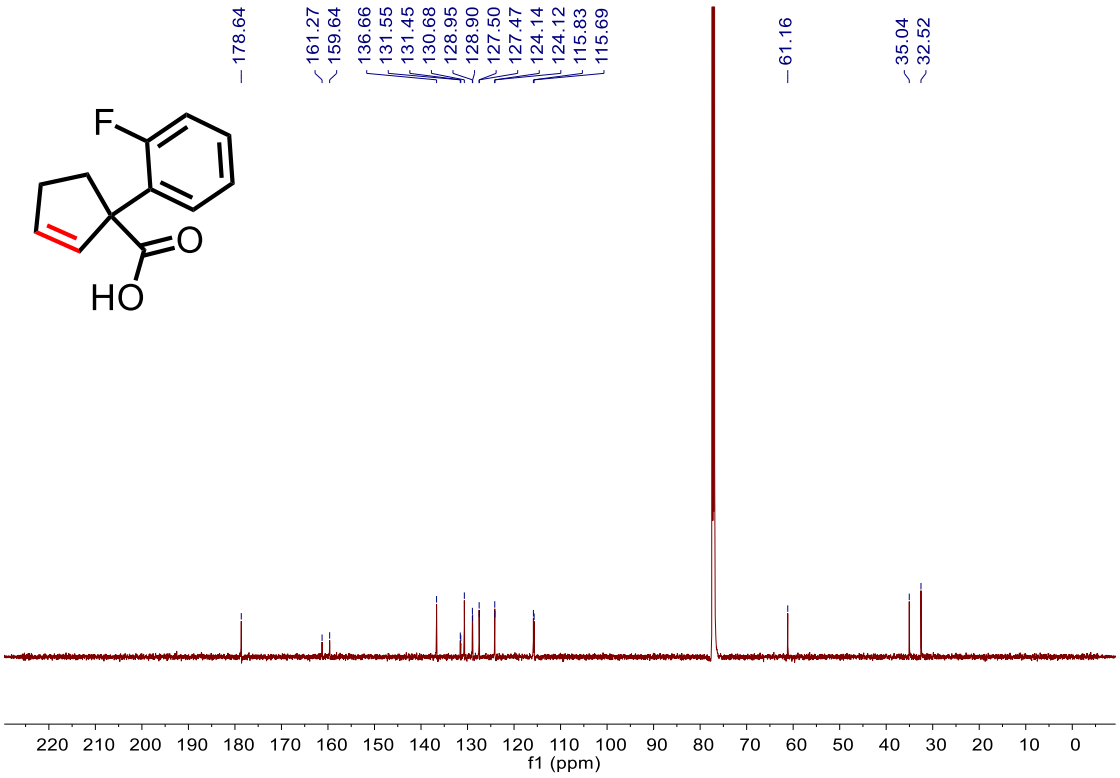
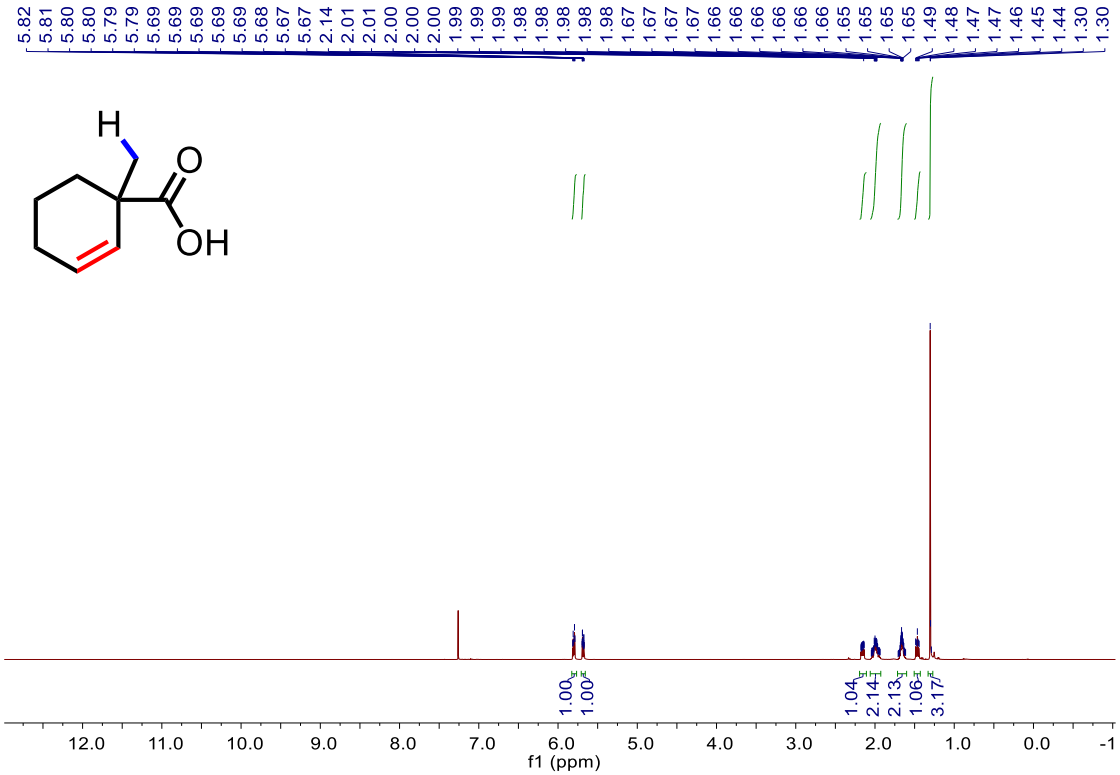
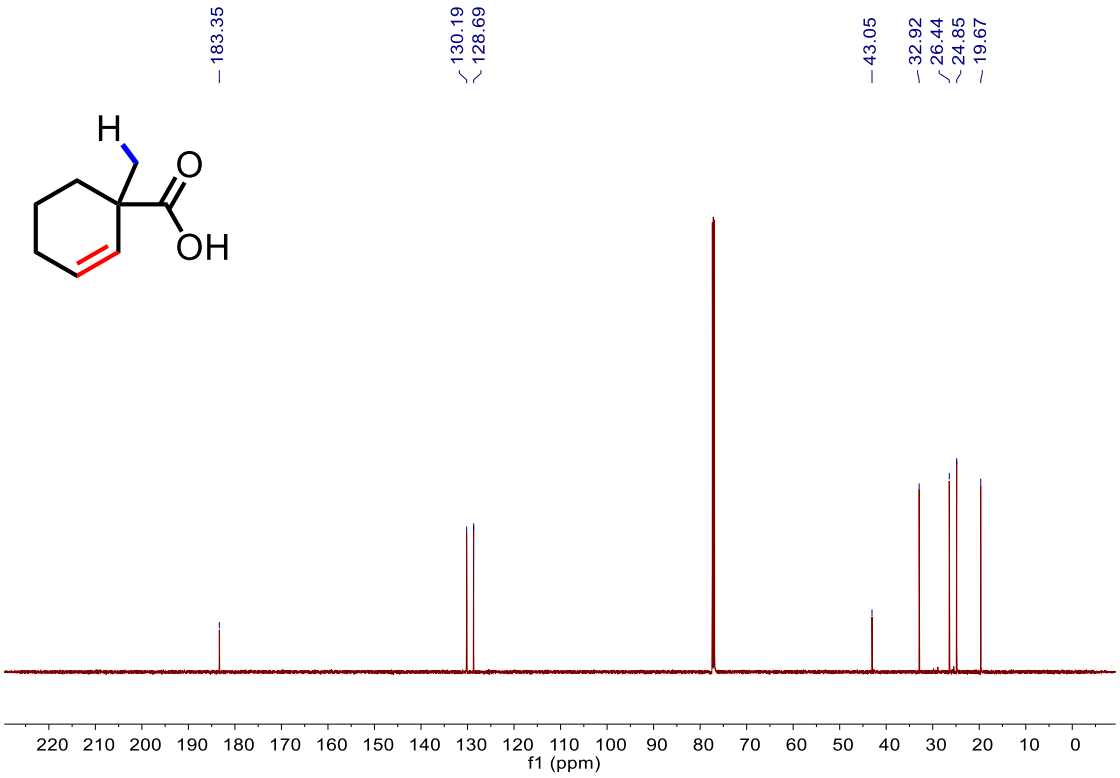


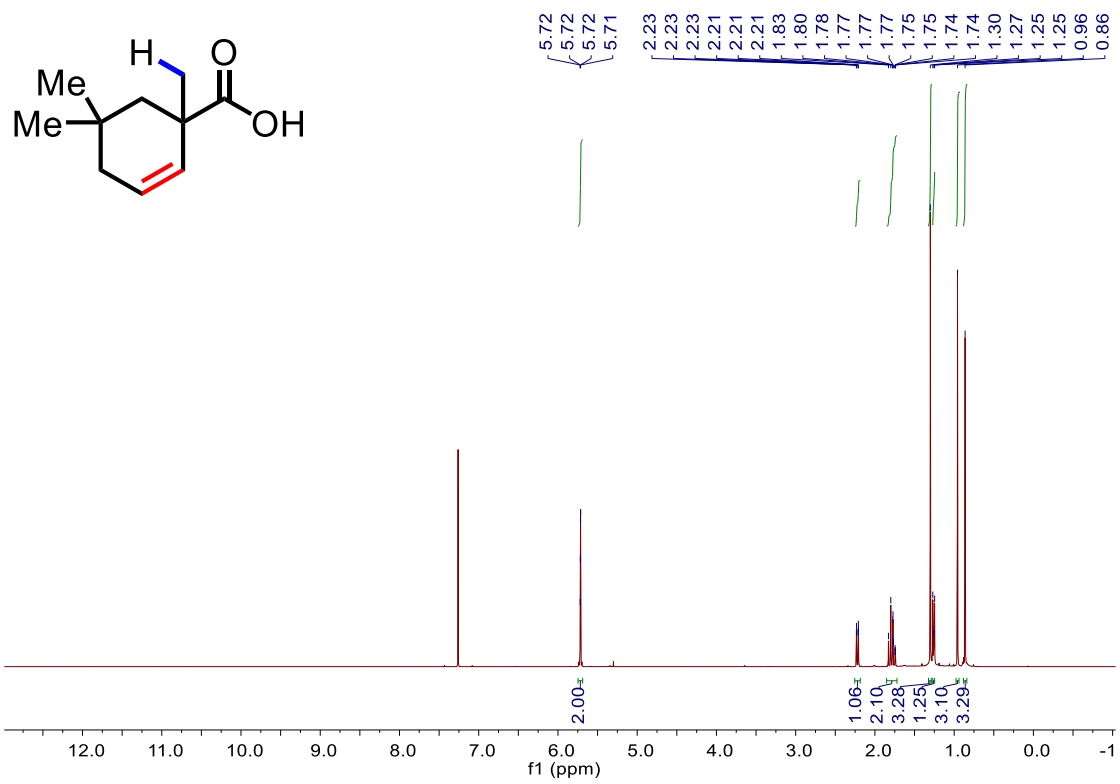
^{1}H NMR of Compound 4k:



^{13}C NMR of Compound 4k:



^{1}H NMR of Compound 4l:



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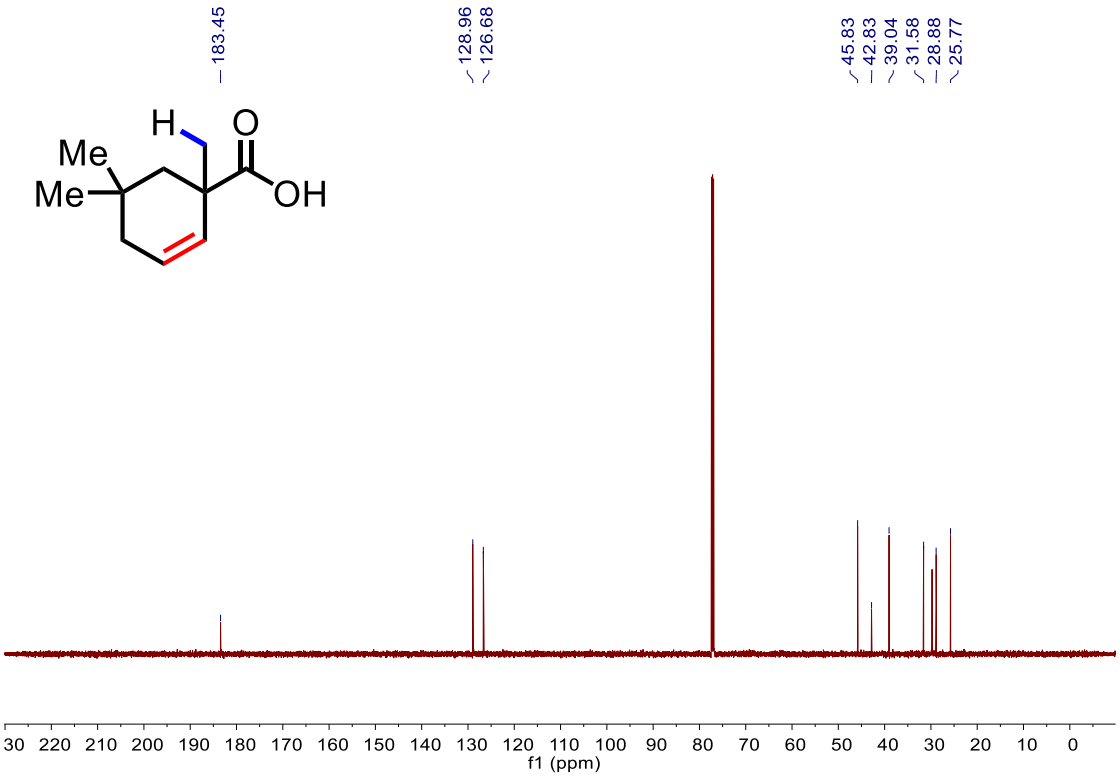
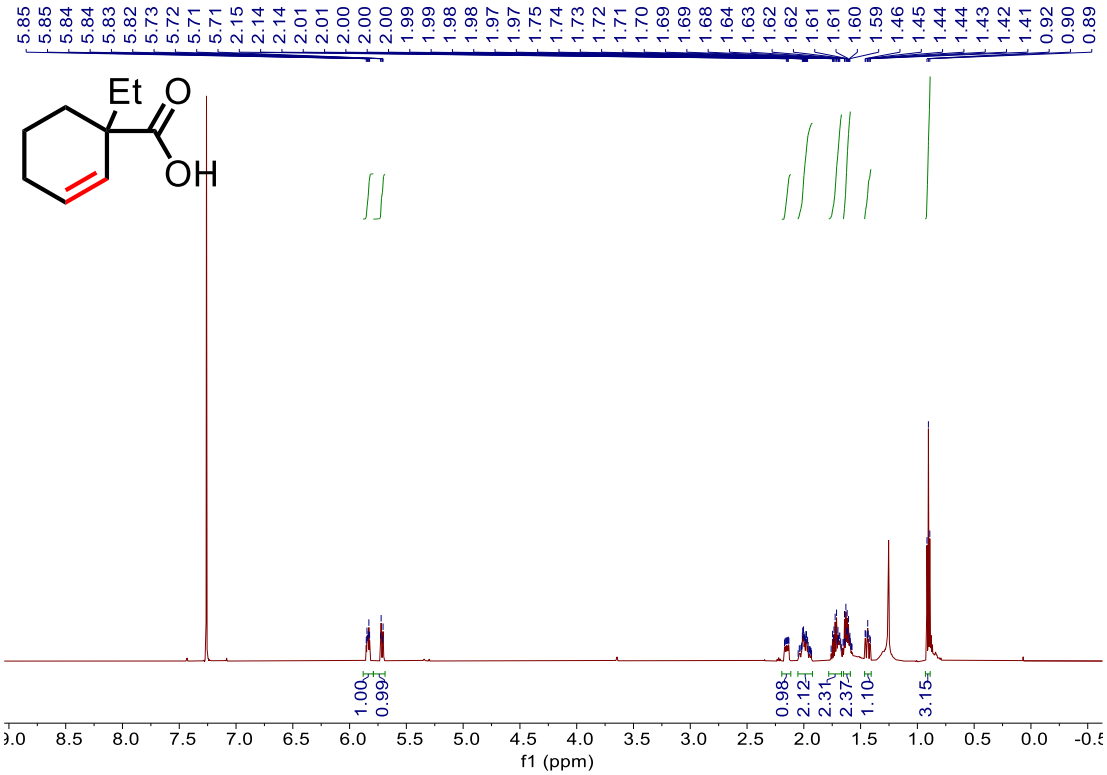


^{1}H NMR of Compound 4m:



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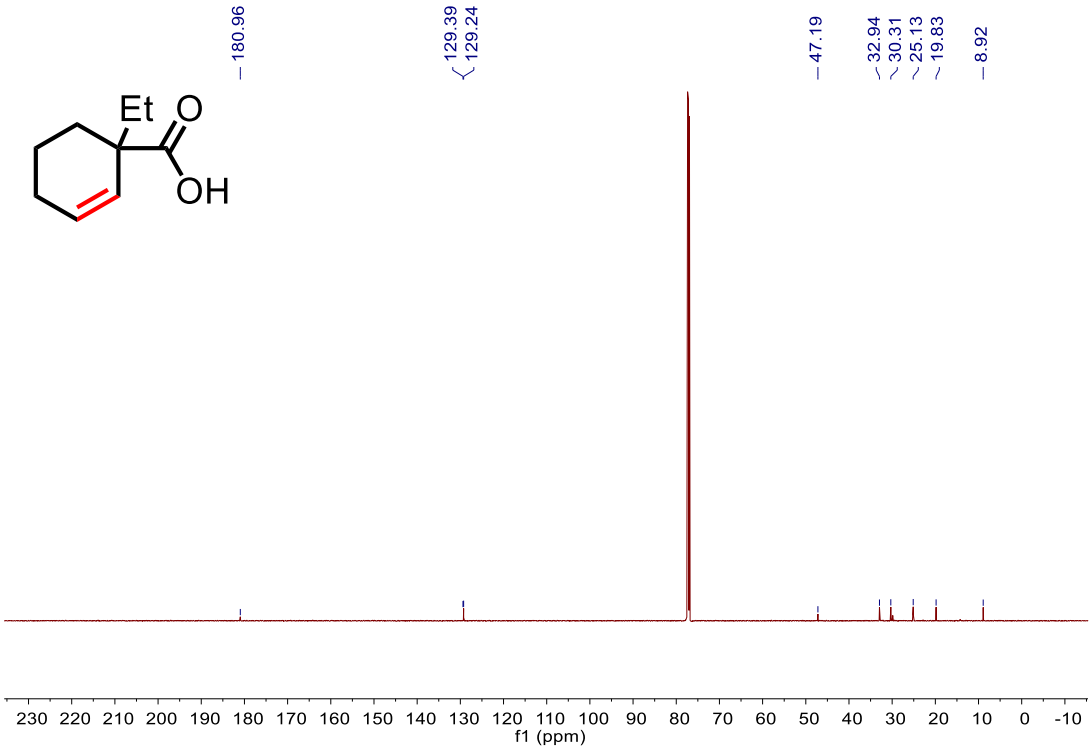

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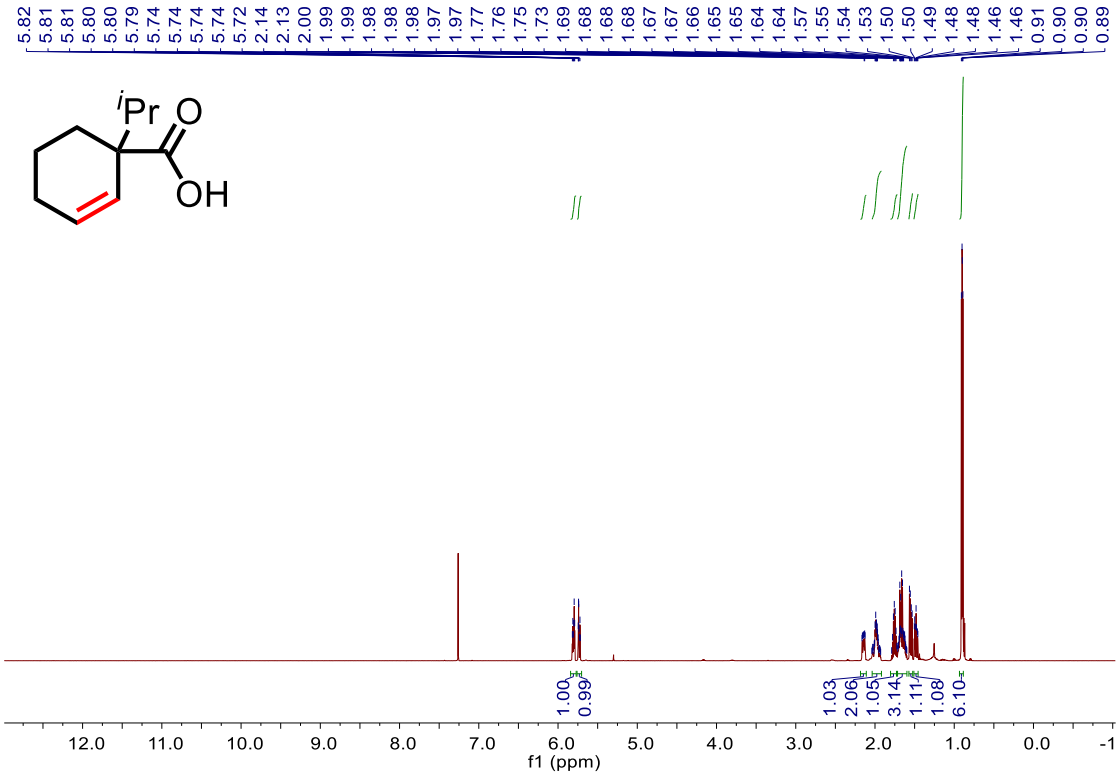

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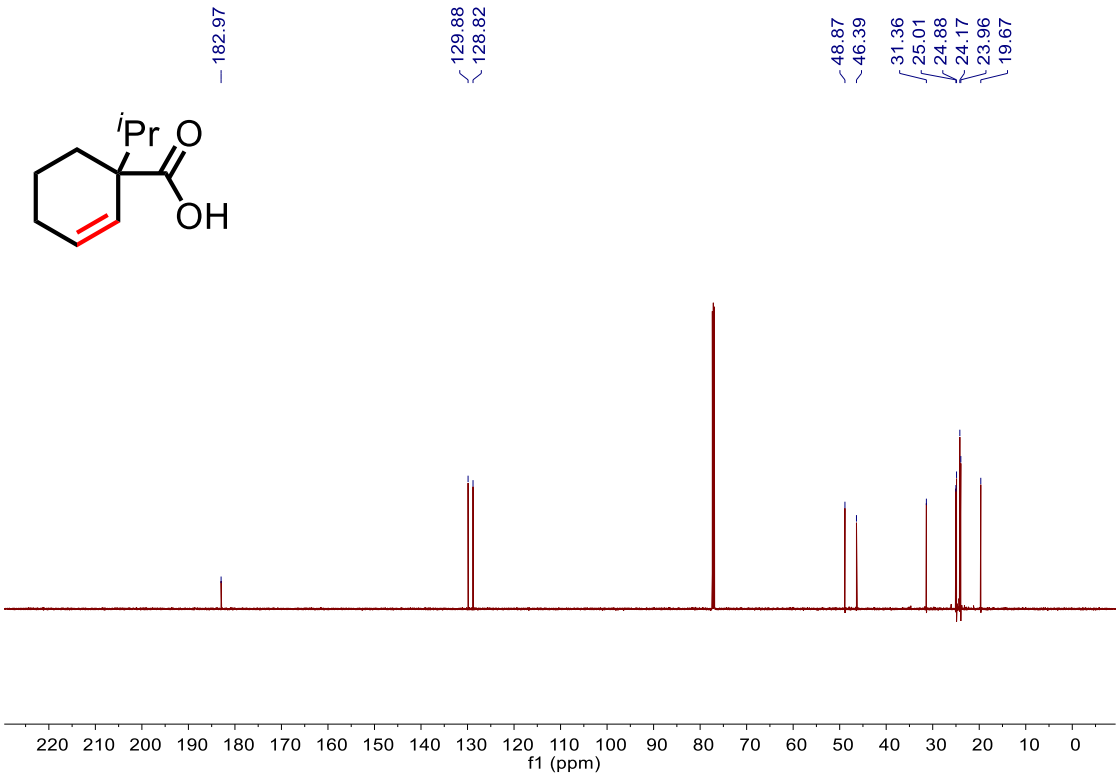
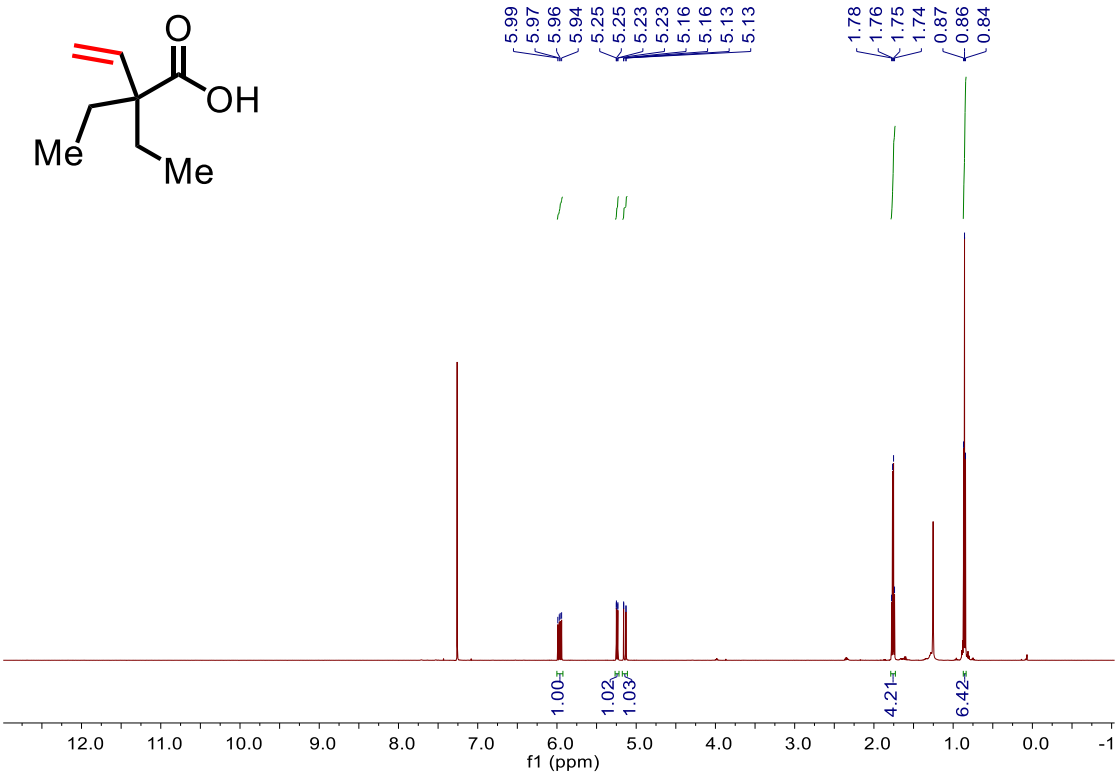
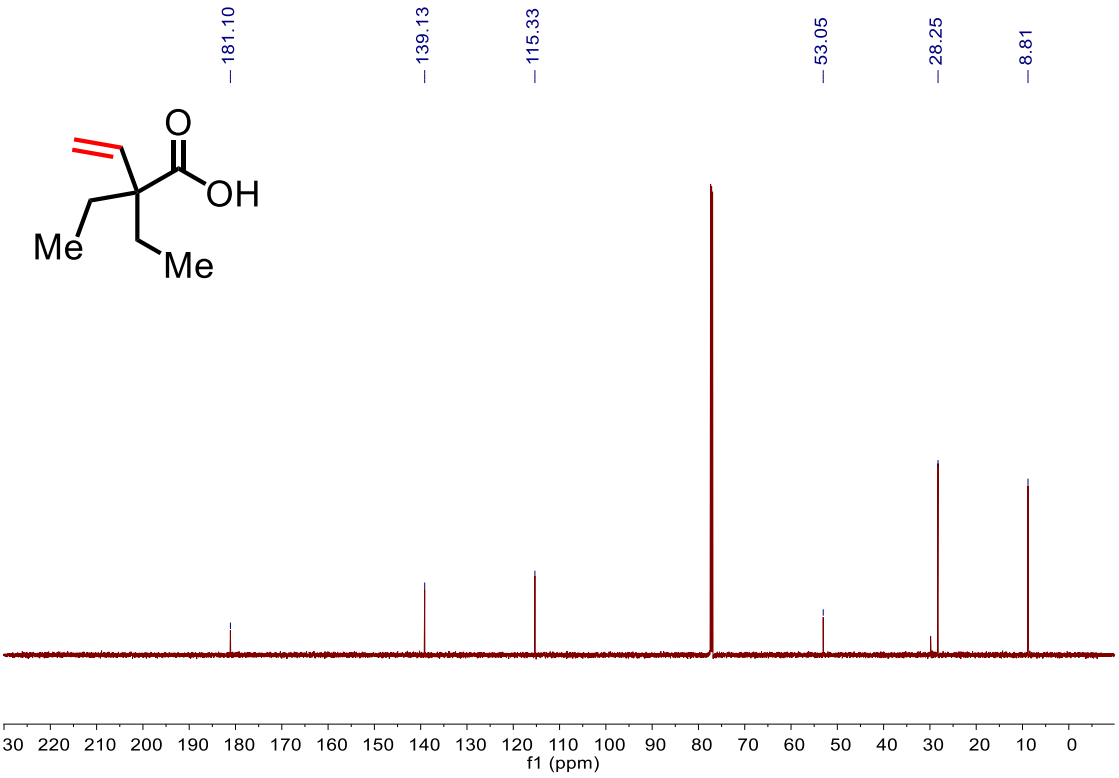


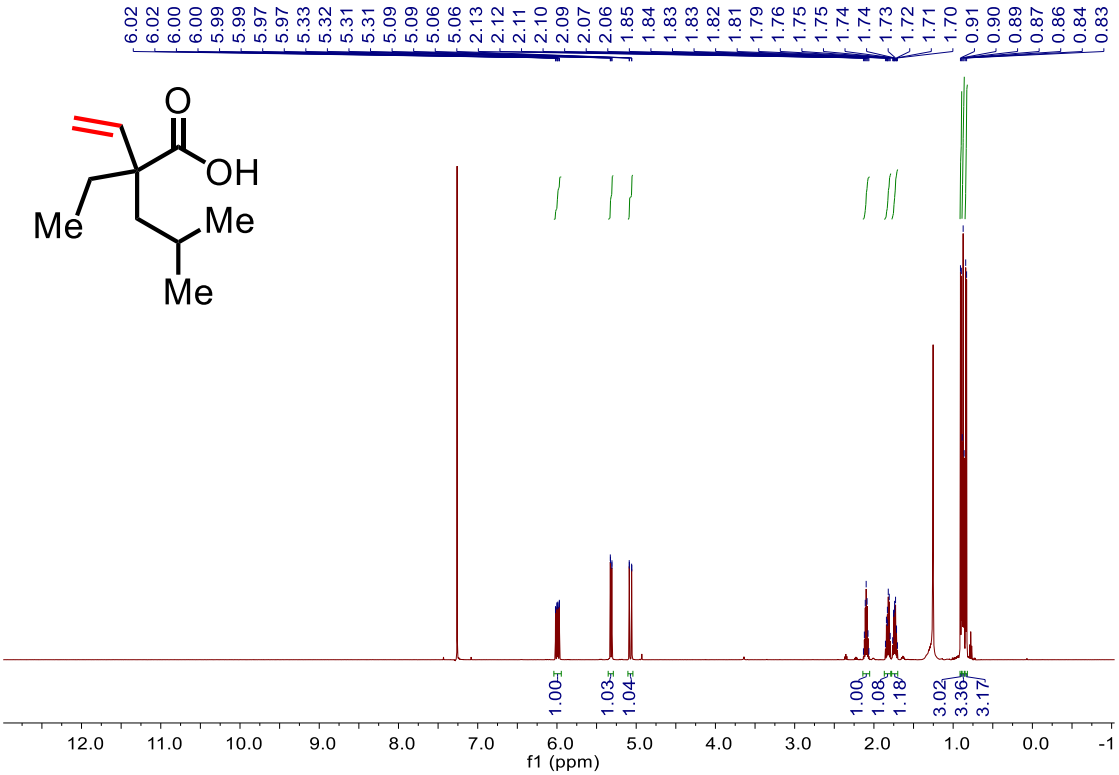
^{1}H NMR of Compound 4o:



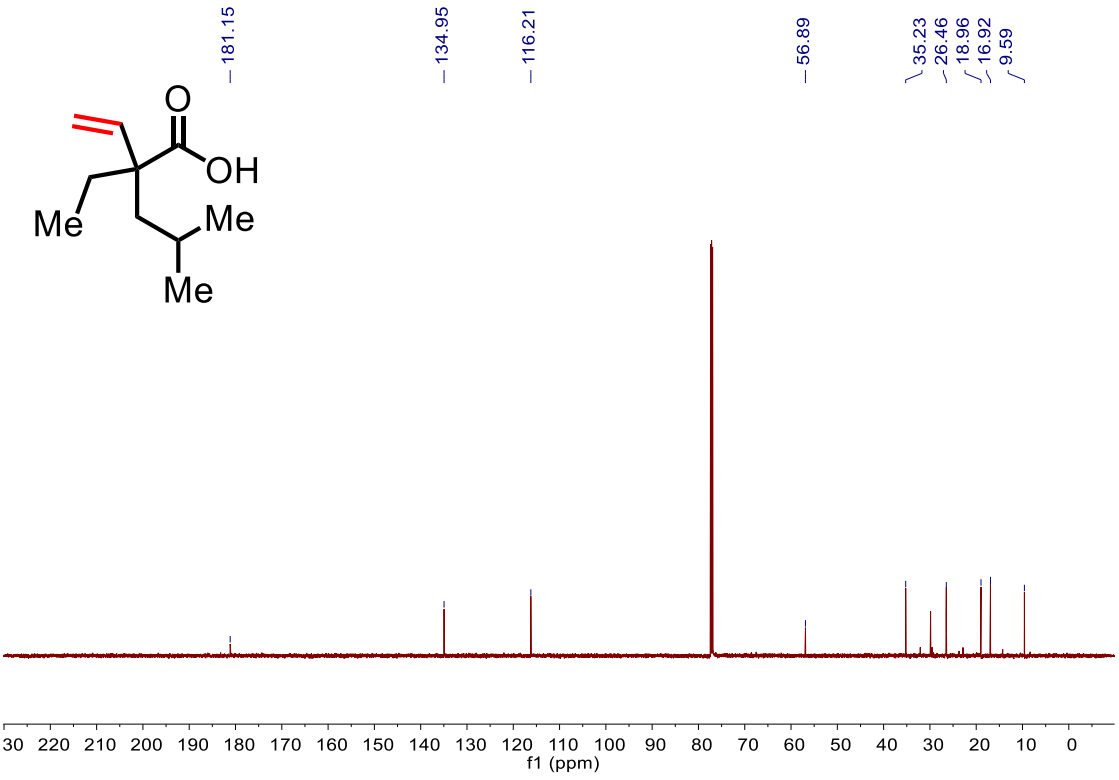
^{13}C NMR of Compound 4o:



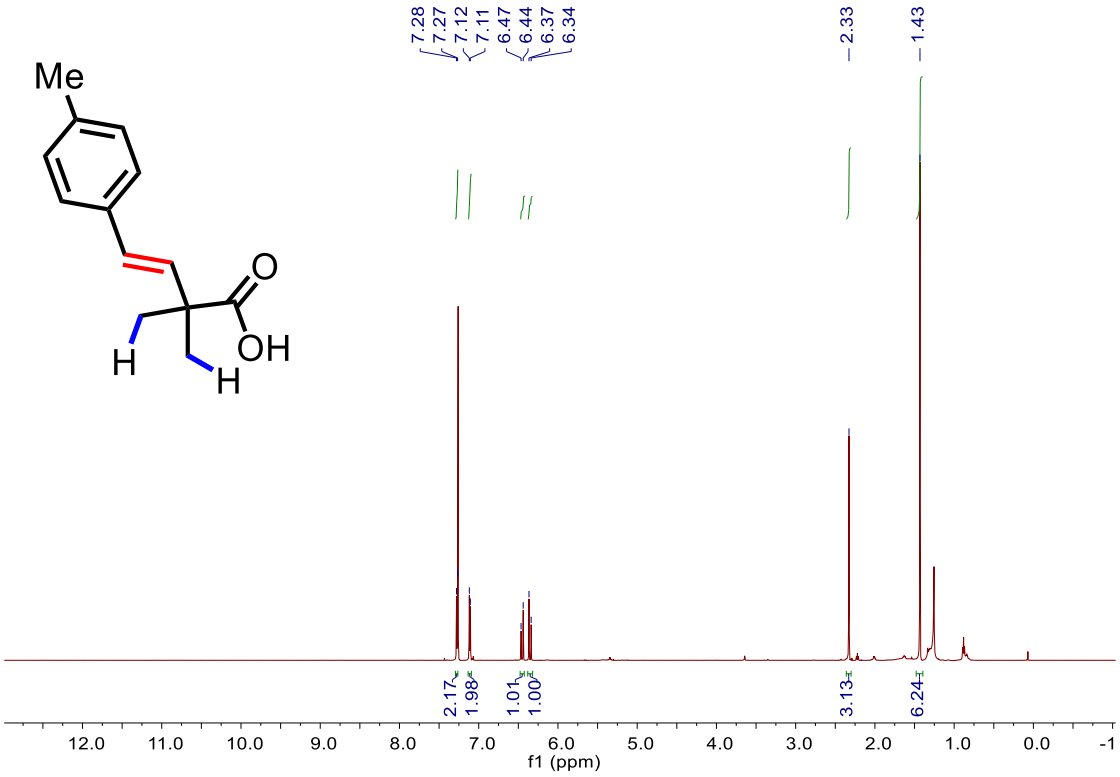
^{1}H NMR of Compound 4p:



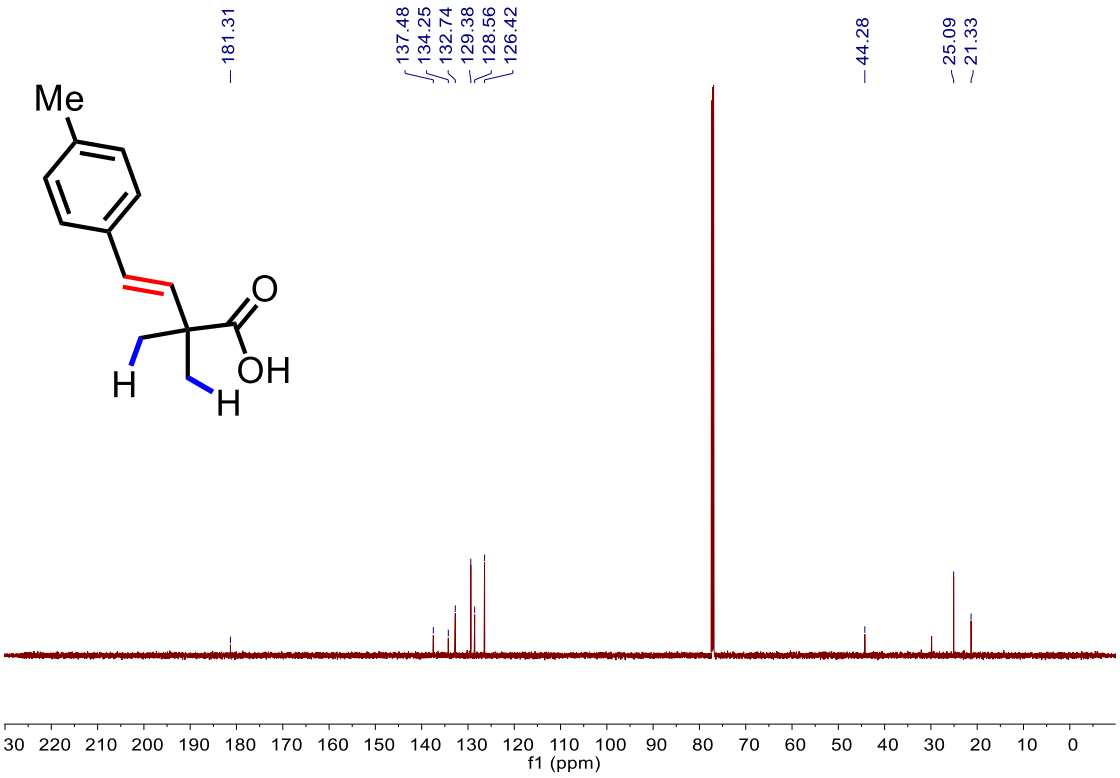
^{13}C NMR of Compound 4p:



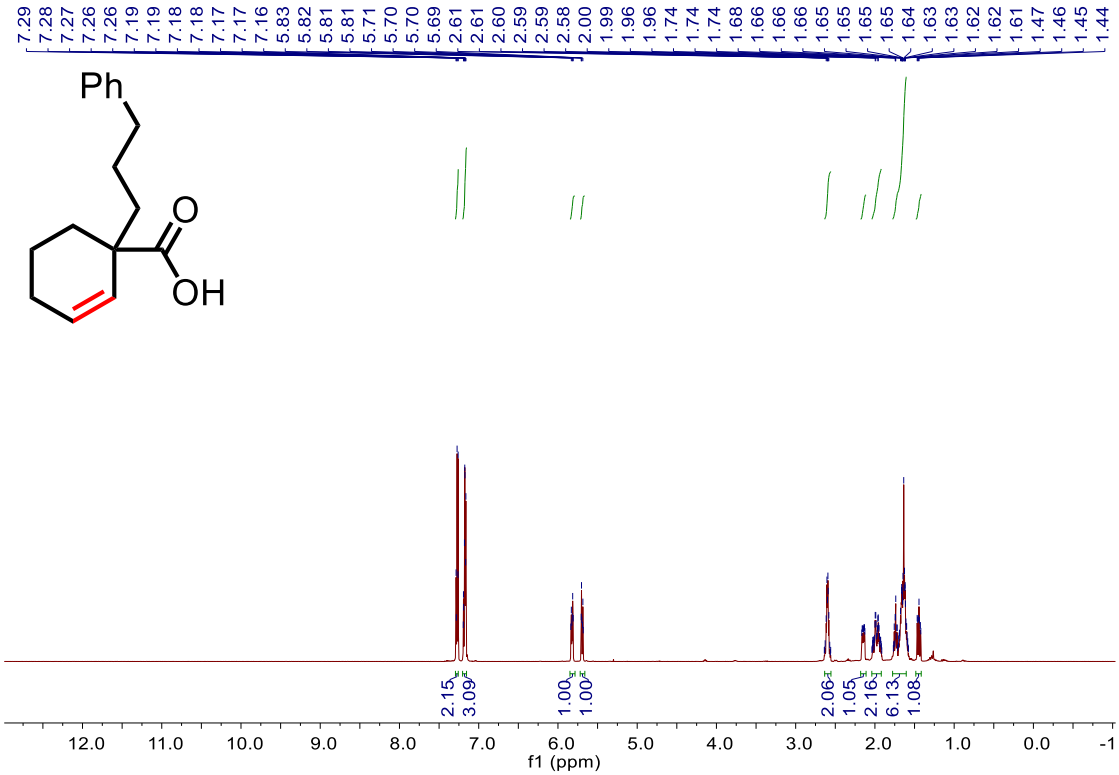
^{1}H NMR of Compound 4q:



^{13}C NMR of Compound 4q:



^{1}H NMR of Compound 4r:



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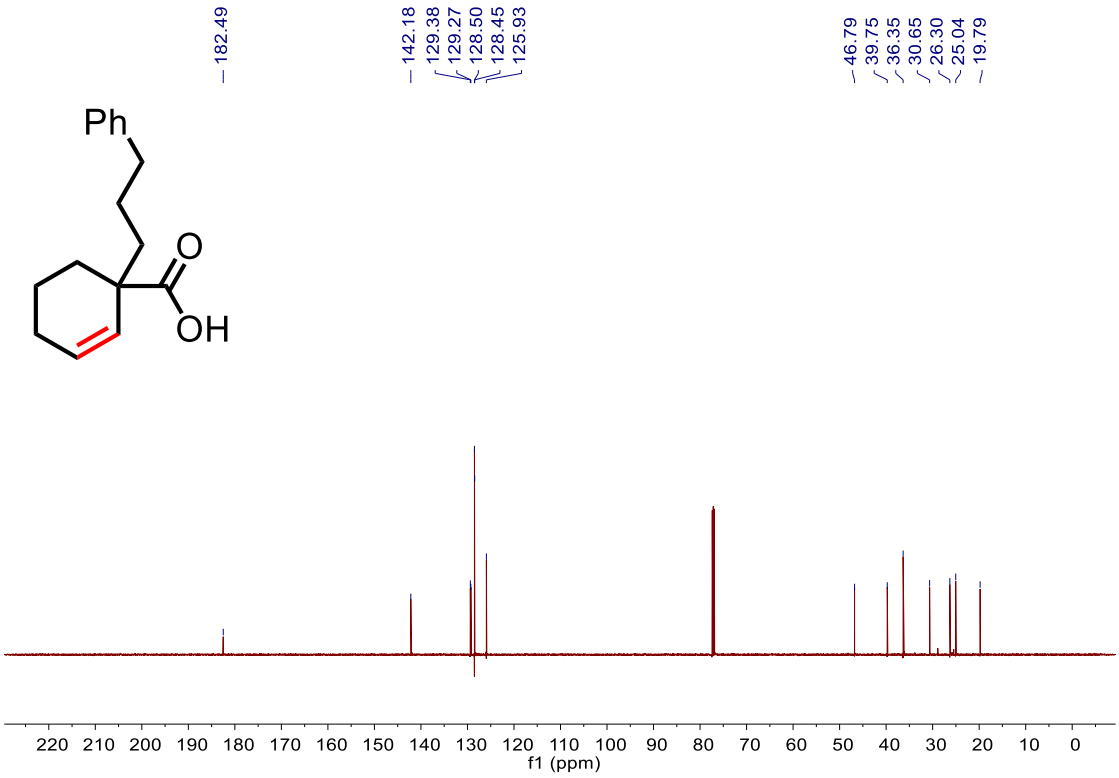
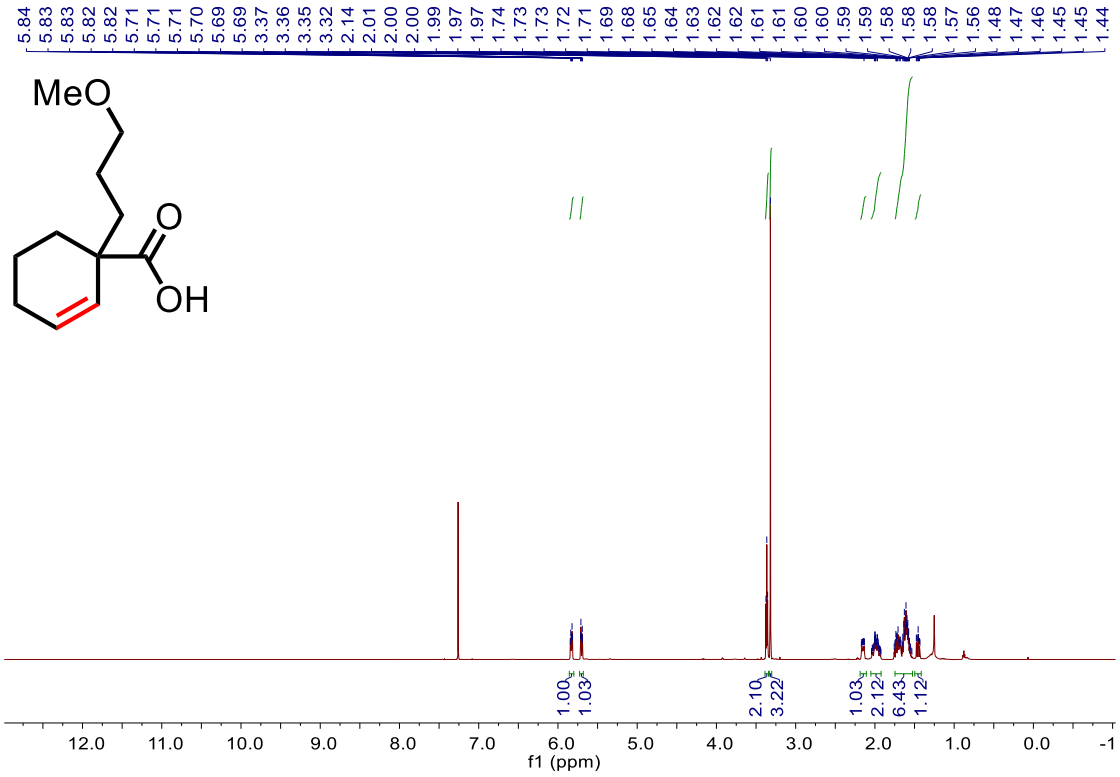
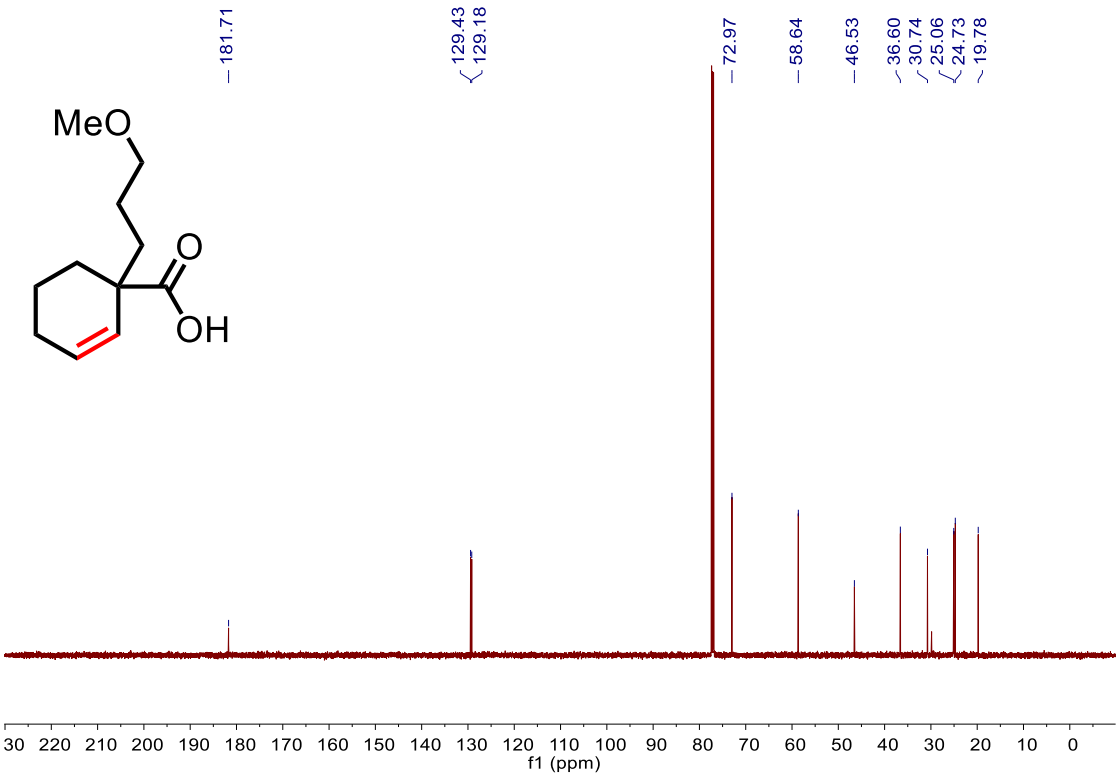


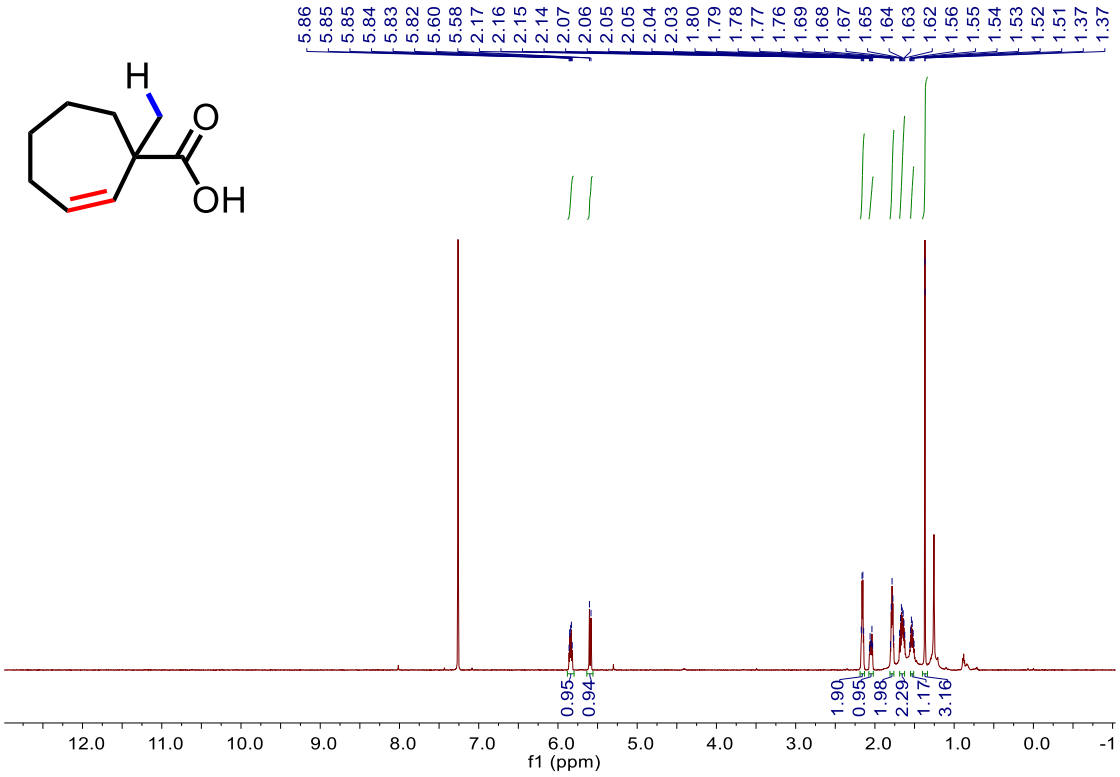
^{1}H NMR of Compound 4s:



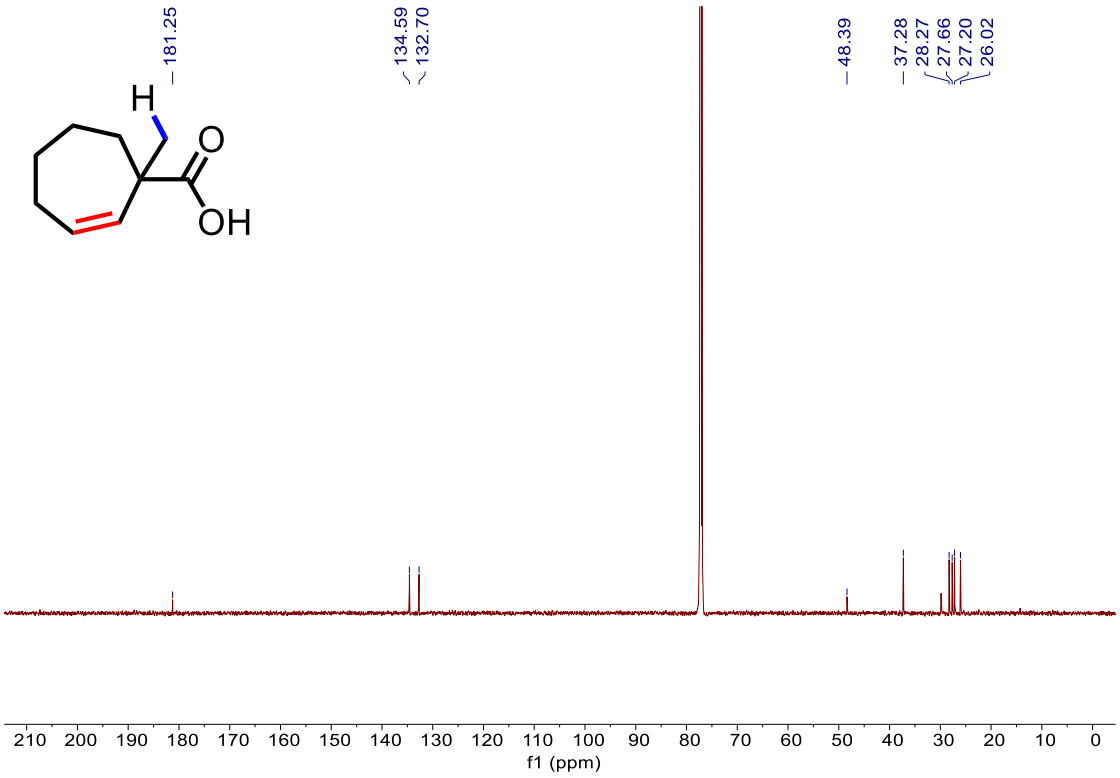
^{13}C NMR of Compound 4s:



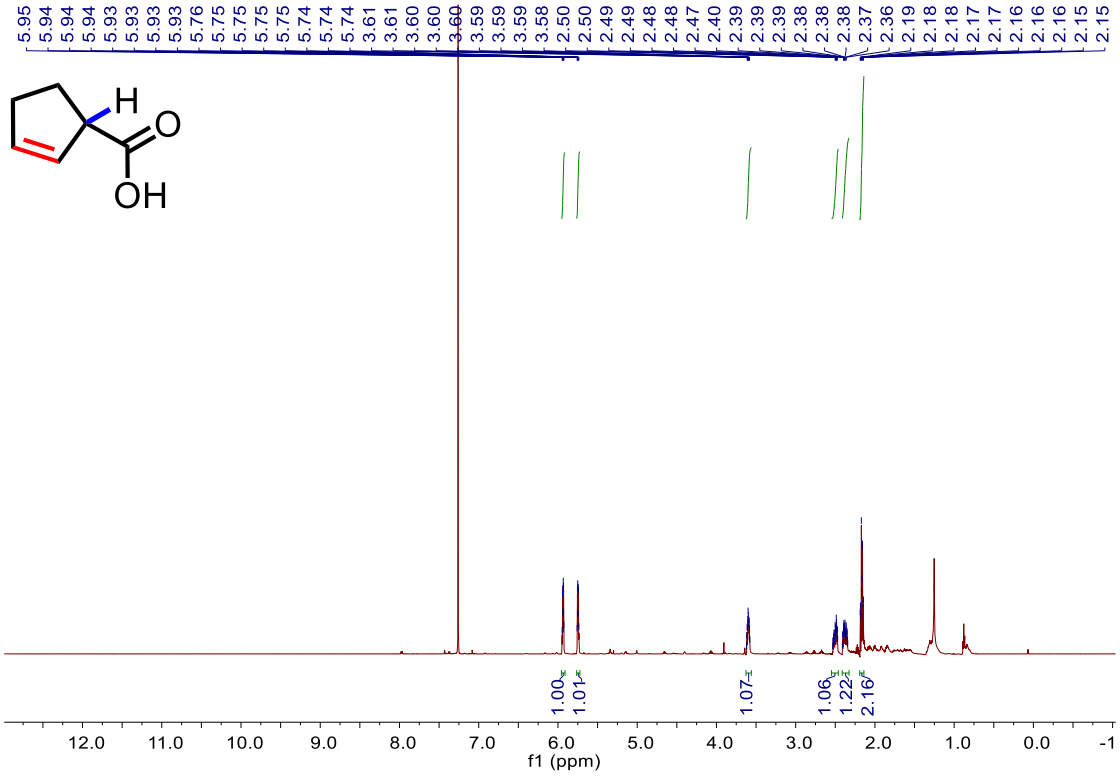
^{1}H NMR of Compound 4t:



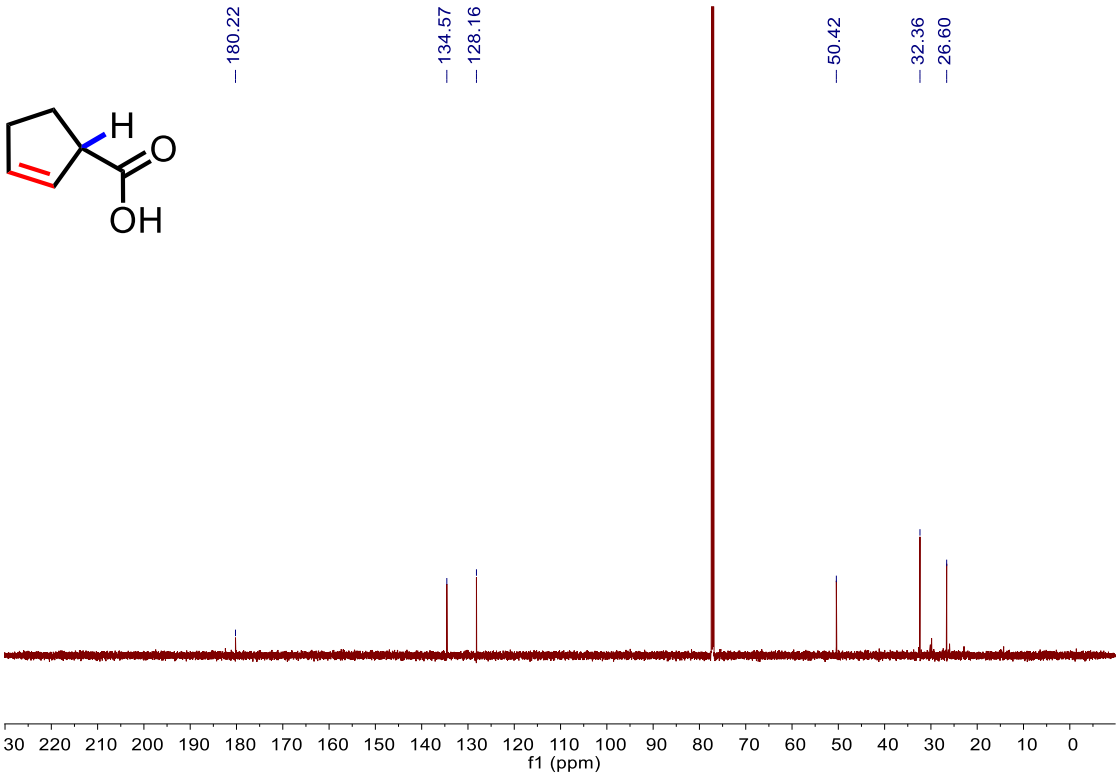
^{13}C NMR of Compound 4t:



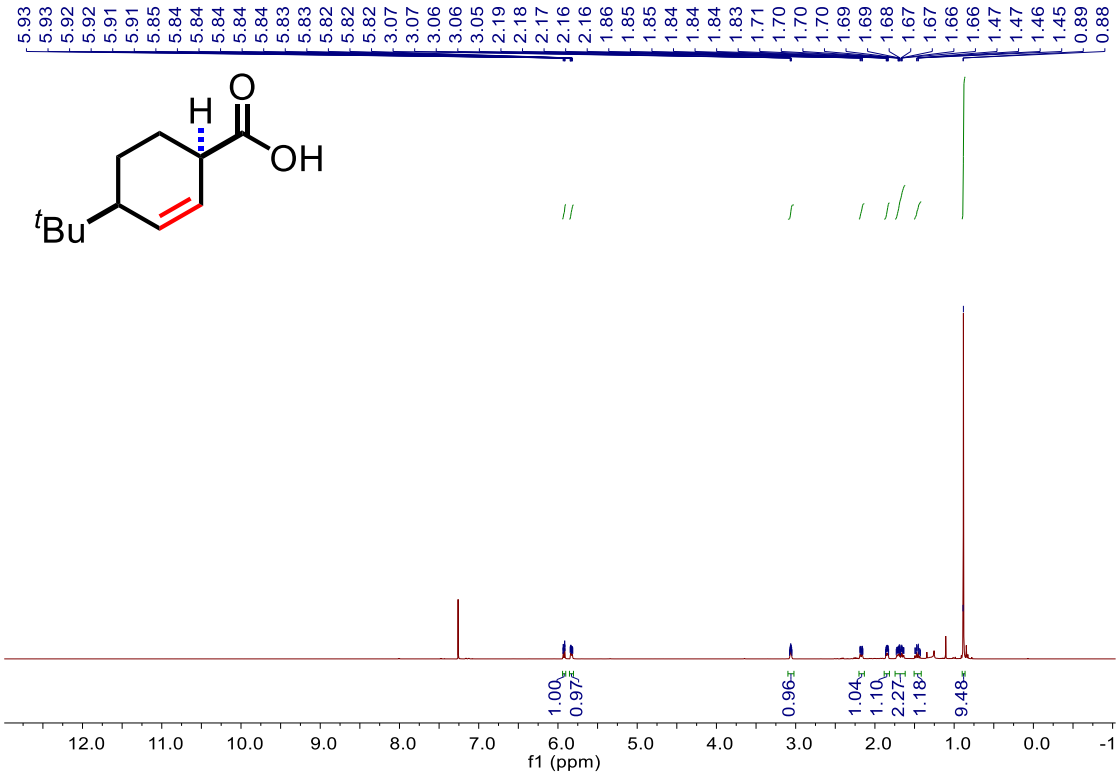
[1]H NMR of Compound 4u:



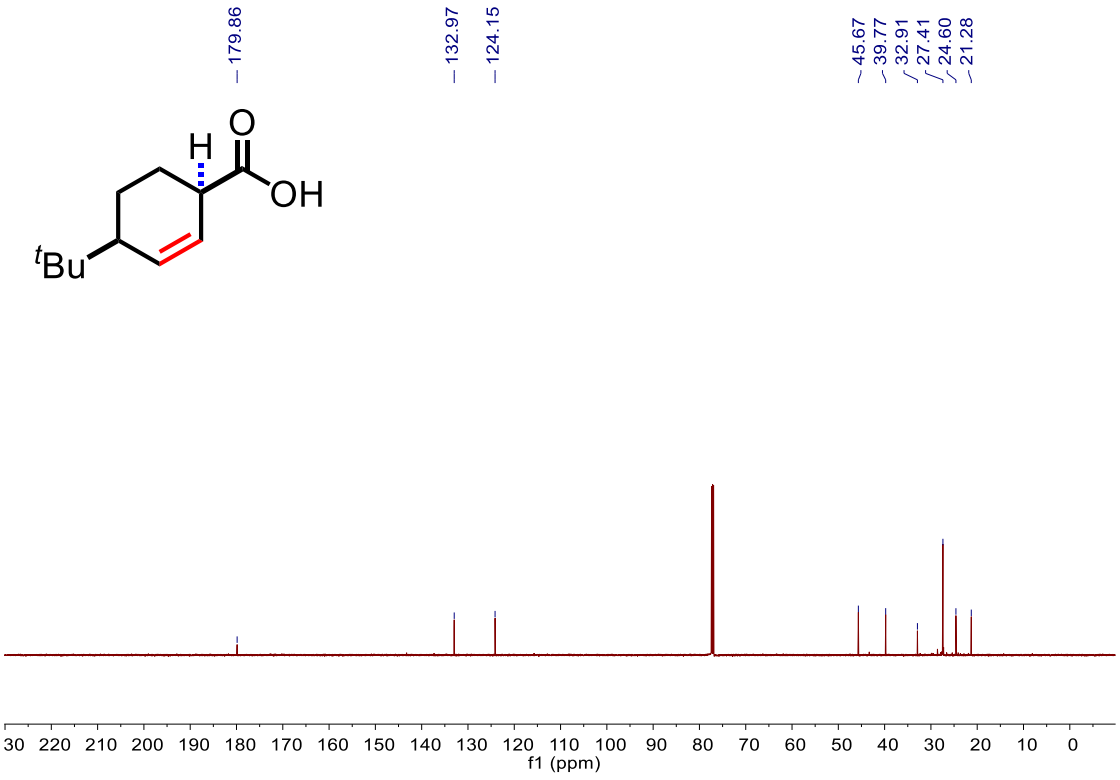
[13]C NMR of Compound 4u:



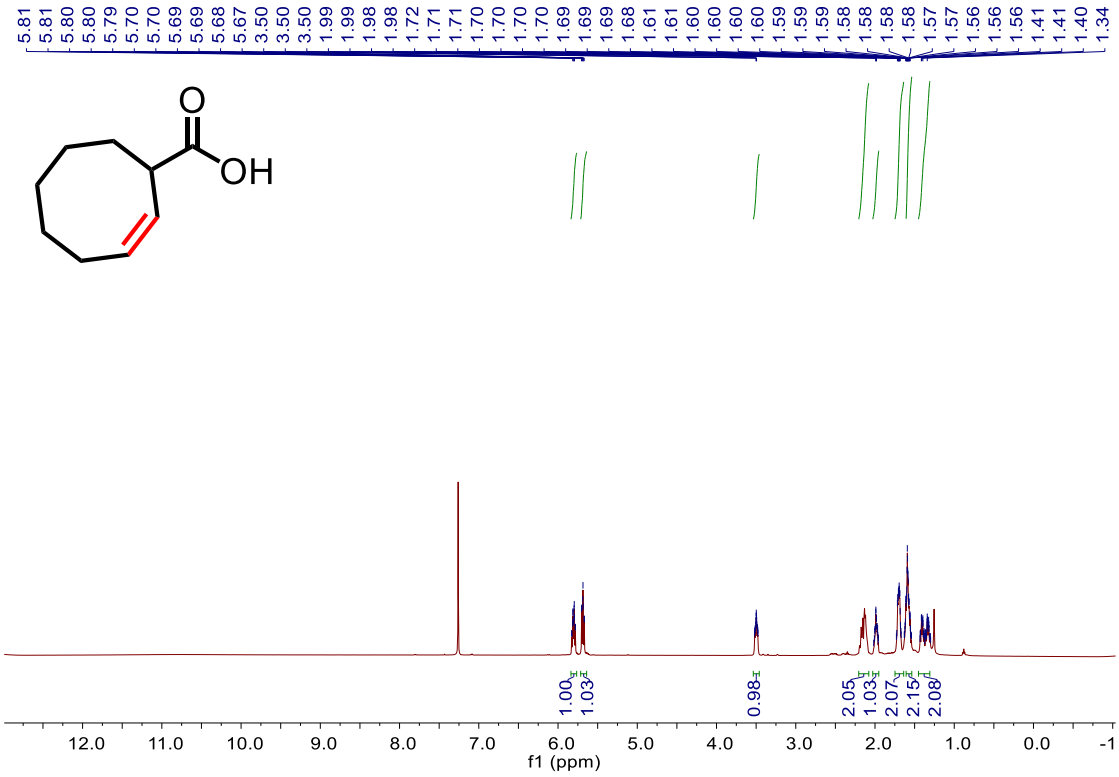
^{1}H NMR of Compound 4v:



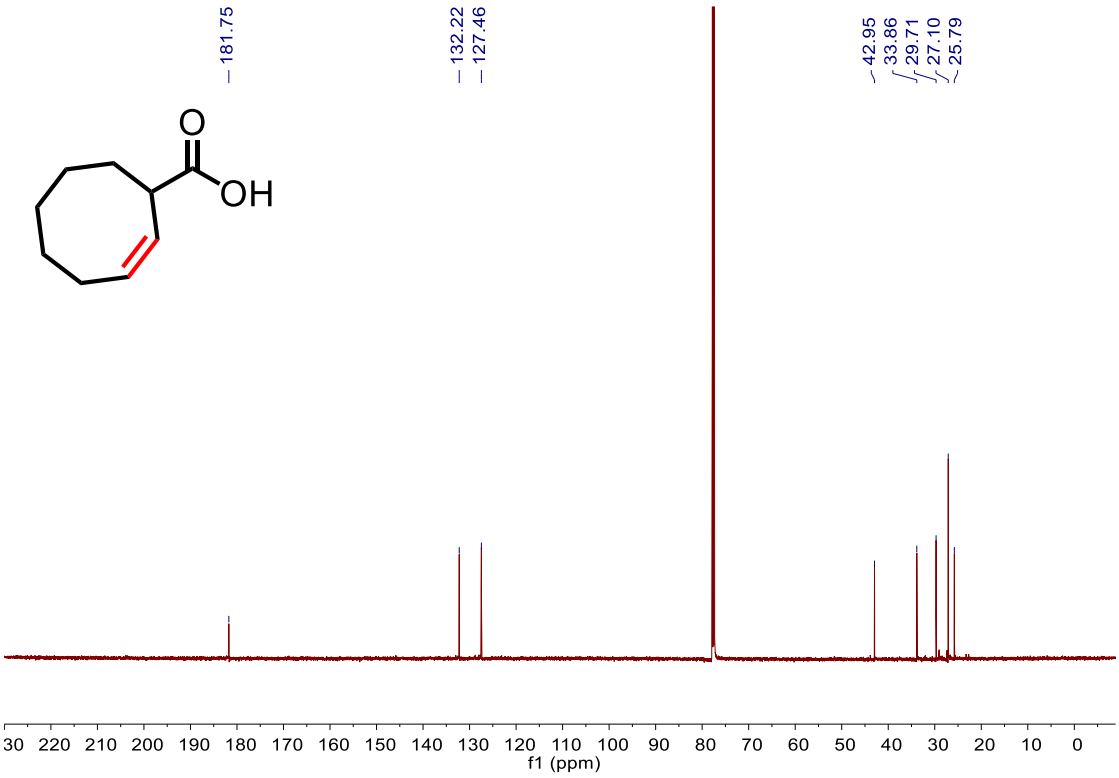
^{13}C NMR of Compound 4v:



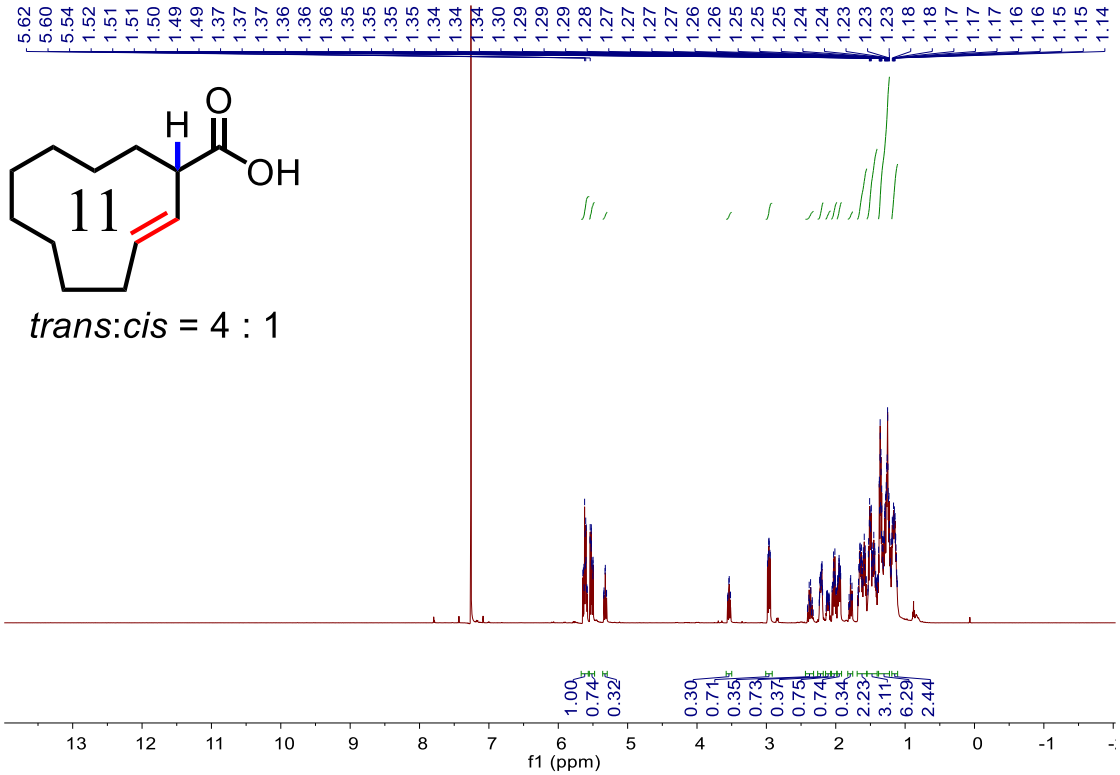
^{1}H NMR of Compound 4w:



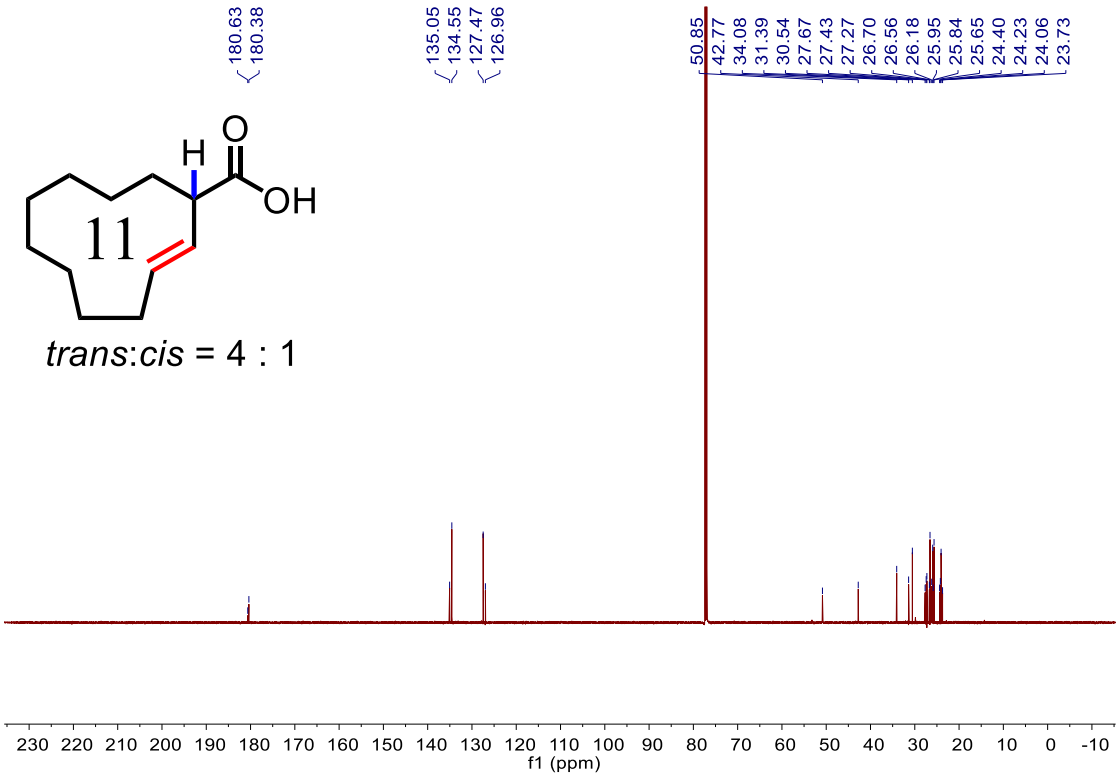
^{13}C NMR of Compound 4w:



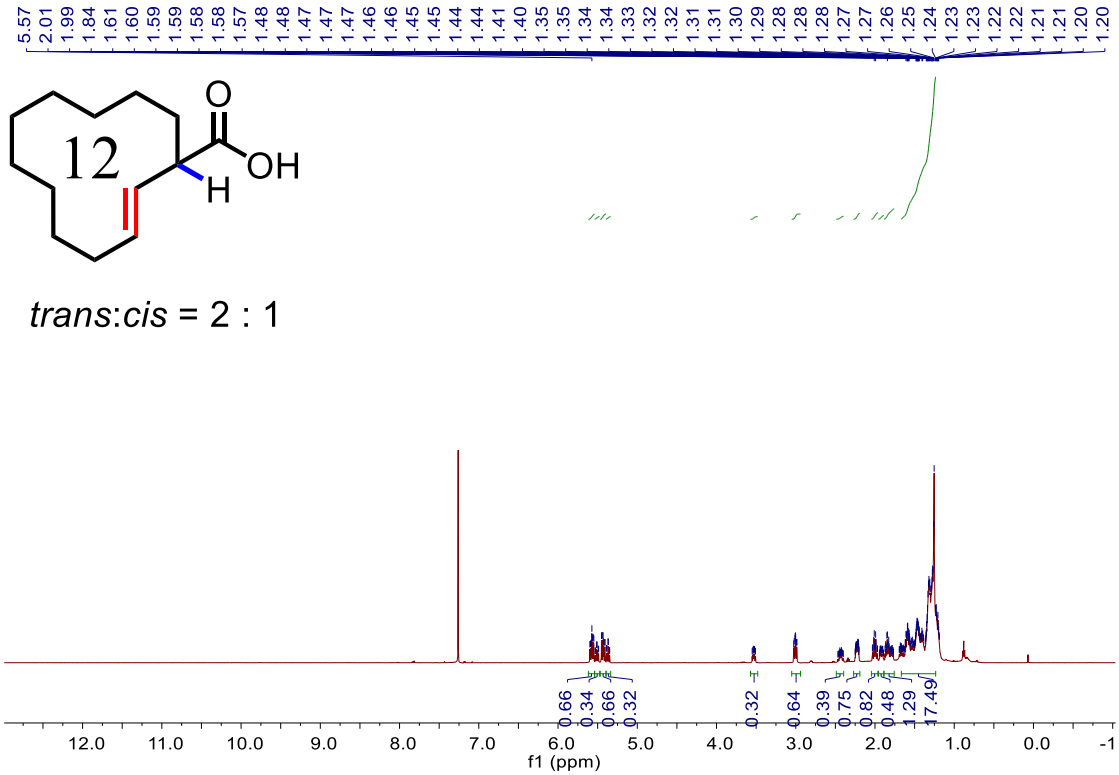
^{1}H NMR of Compound 4x and 4x':



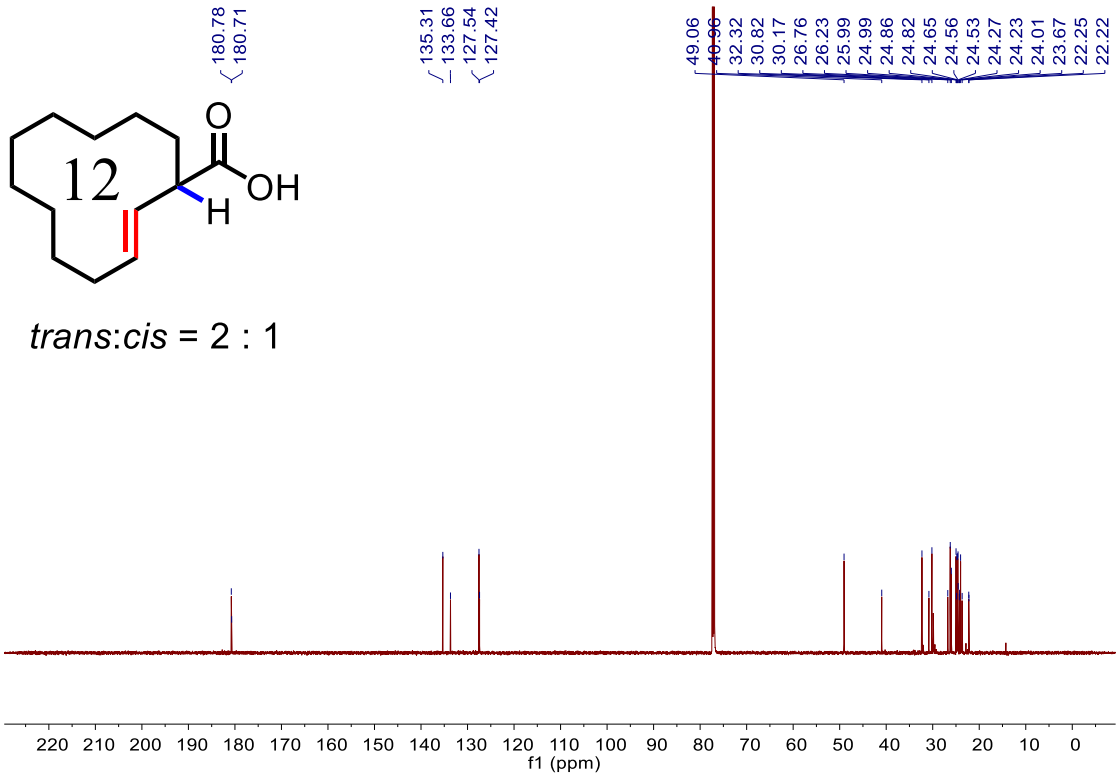
^{13}C NMR of Compound 4x and 4x':



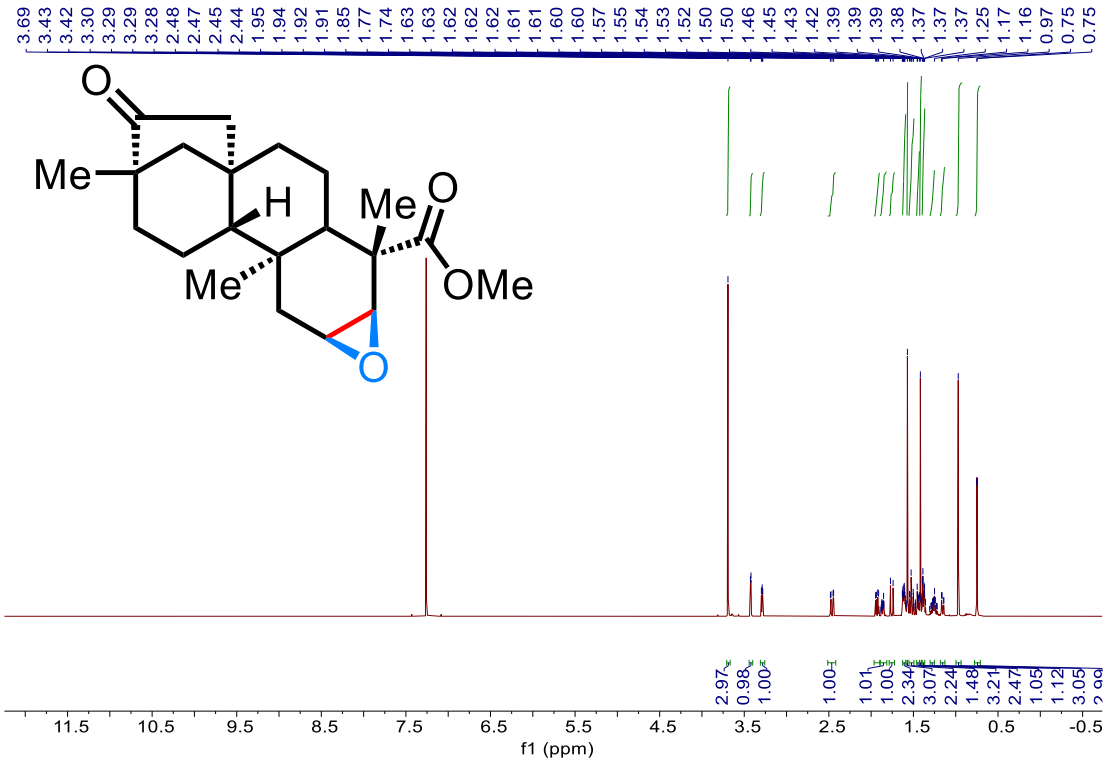
^{1}H NMR of Compound 4y and 4y':



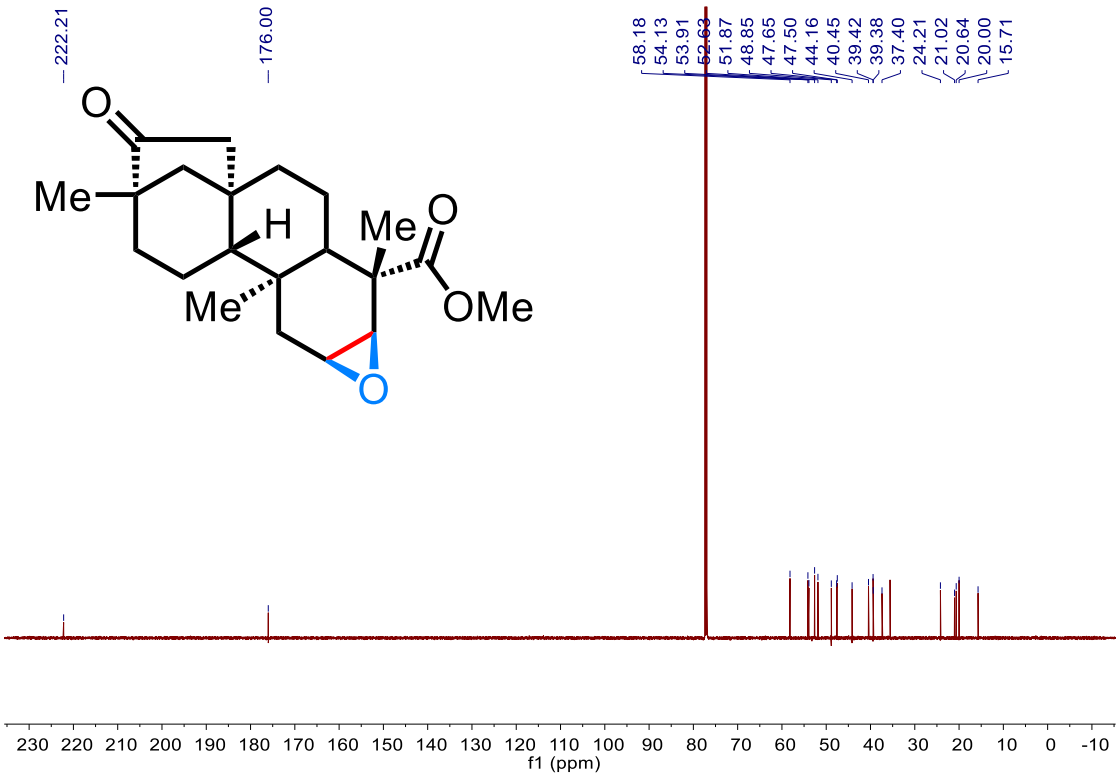
^{13}C NMR of Compound 4y and 4y':



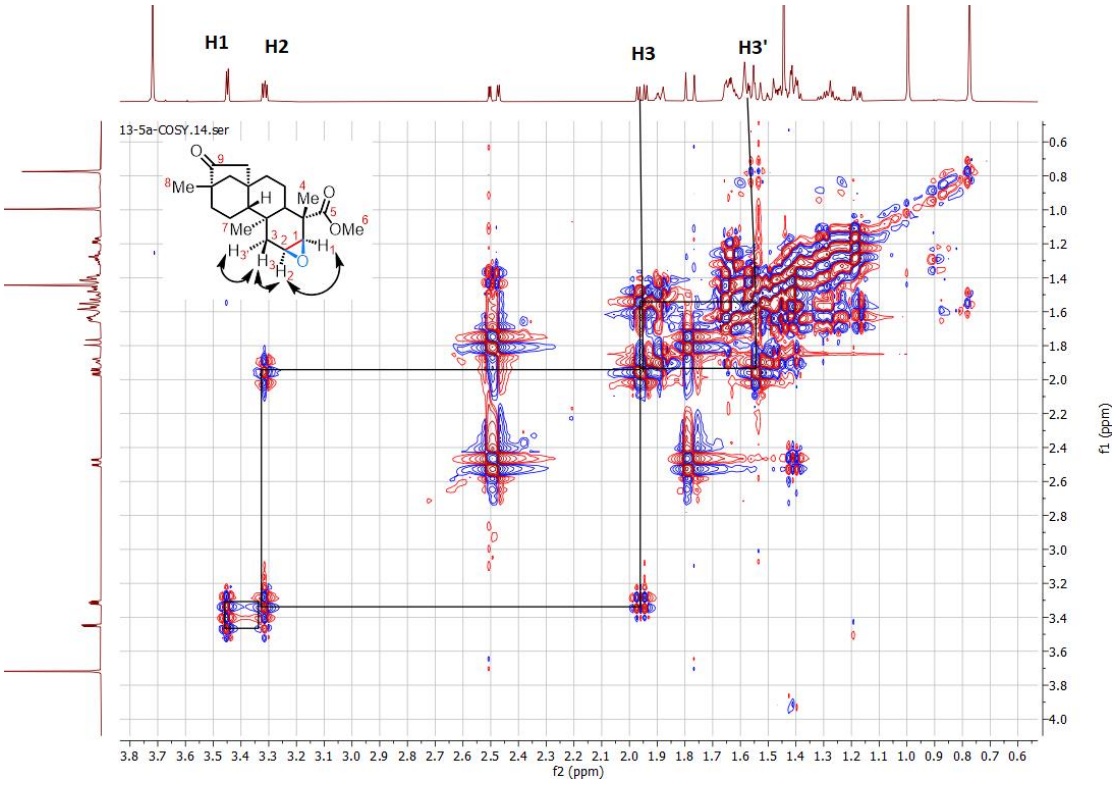
^{1}H NMR of Compound 5a:



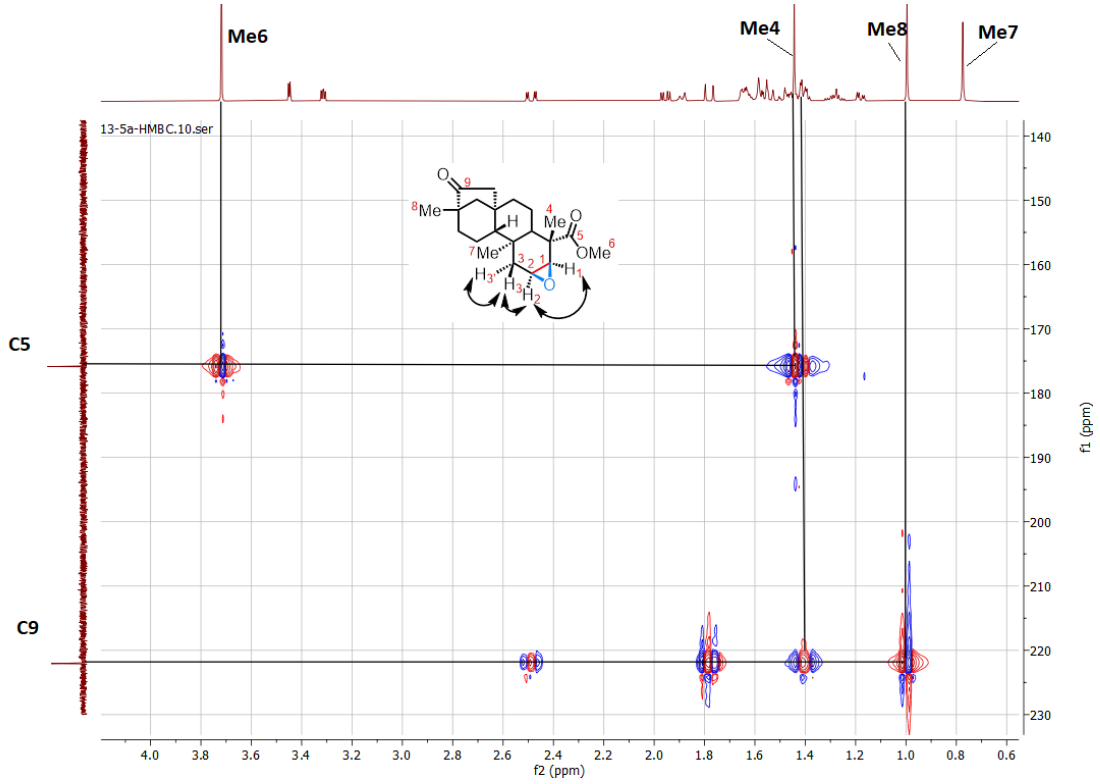
^{13}C NMR of Compound 5a:



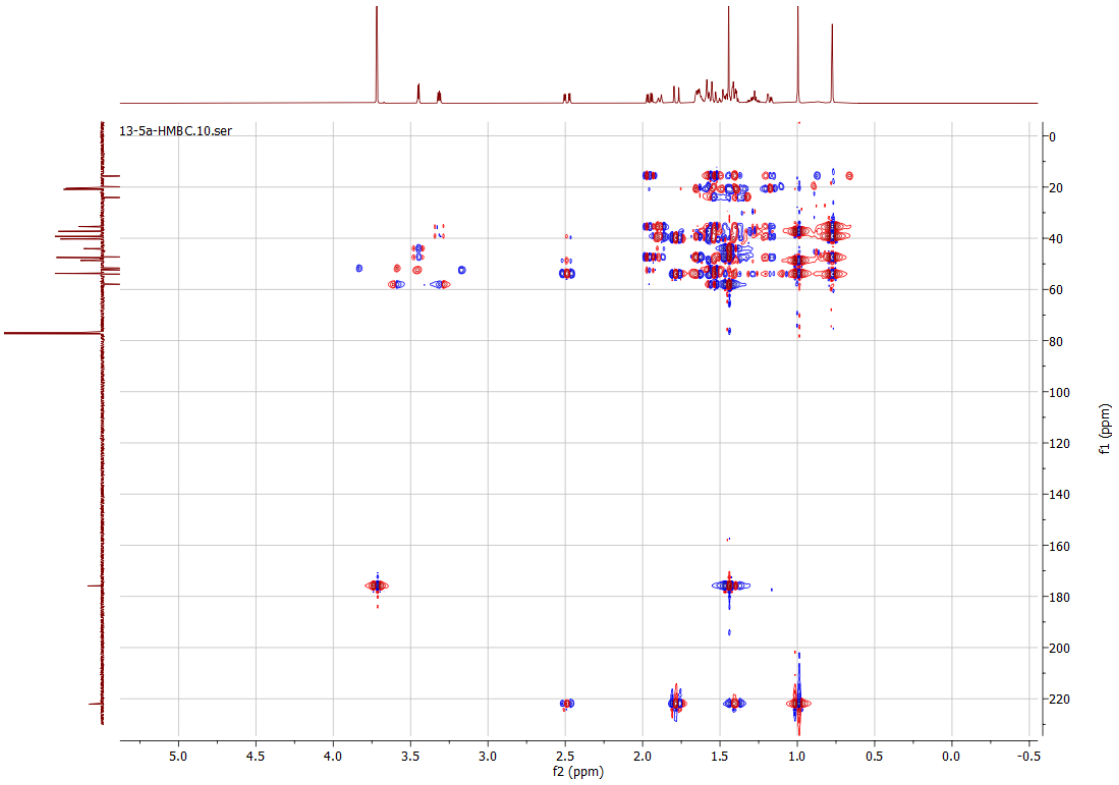
COSY of Compound 5a:



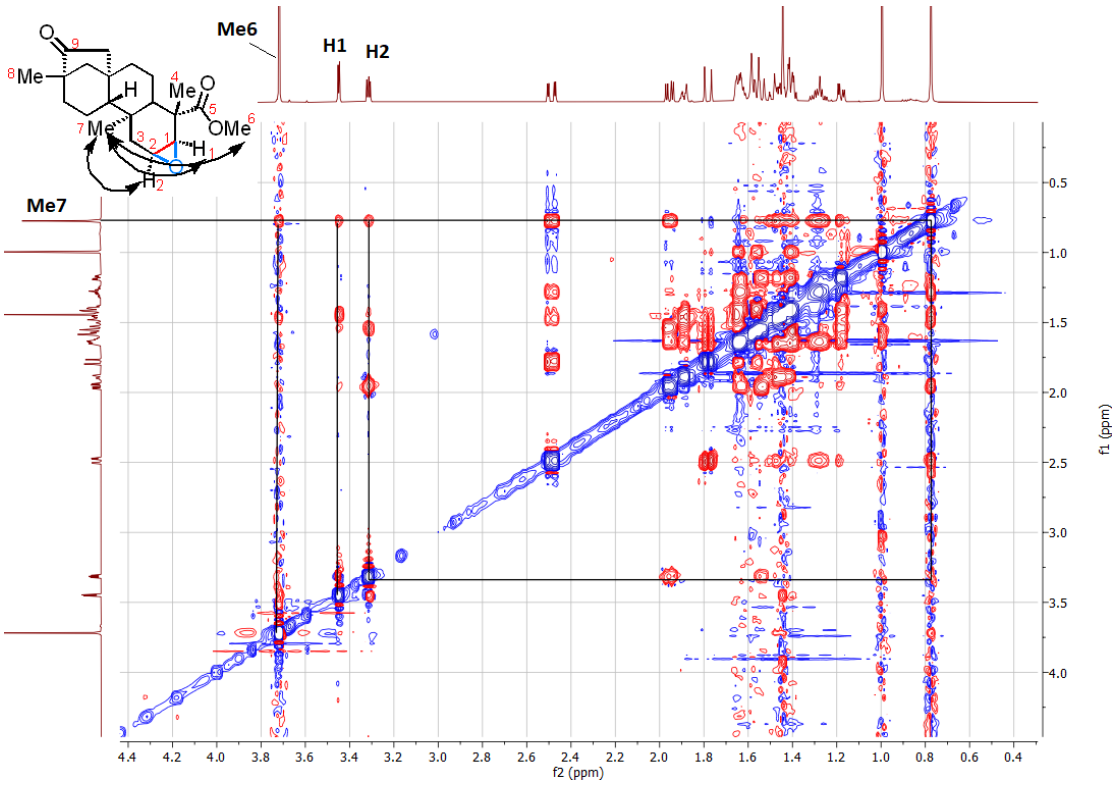
HMBC of Compound 5a:



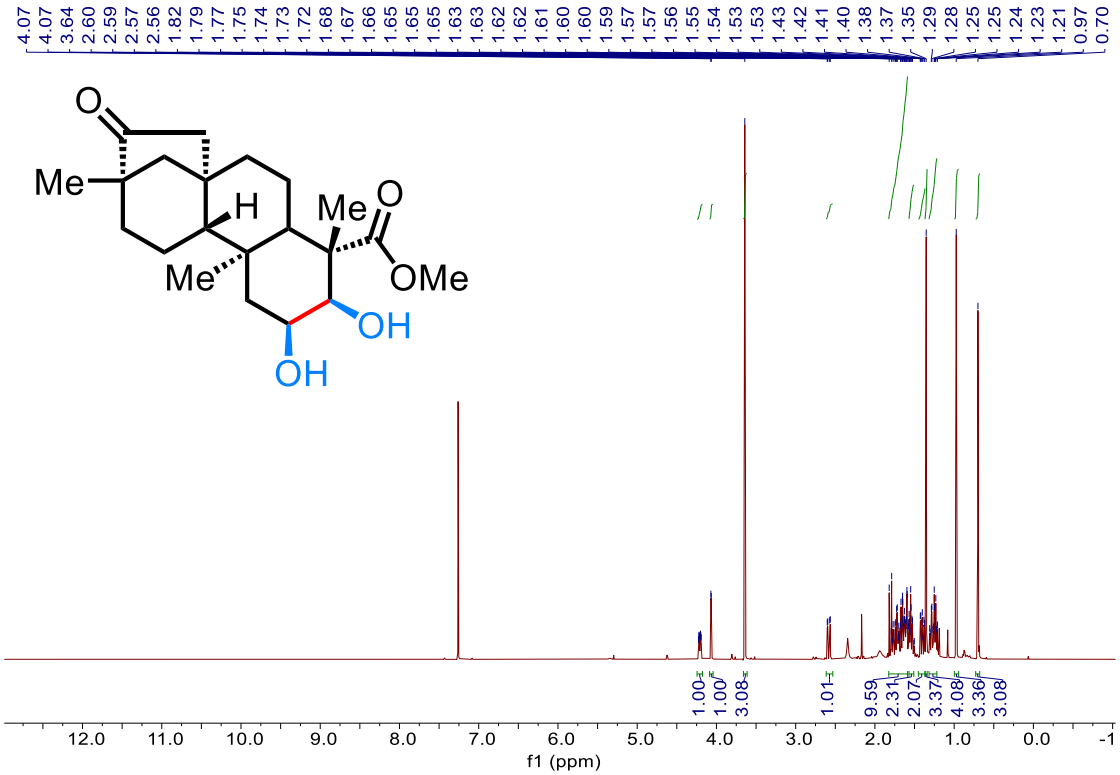
HMBC of Compound 5a (full spectrum):



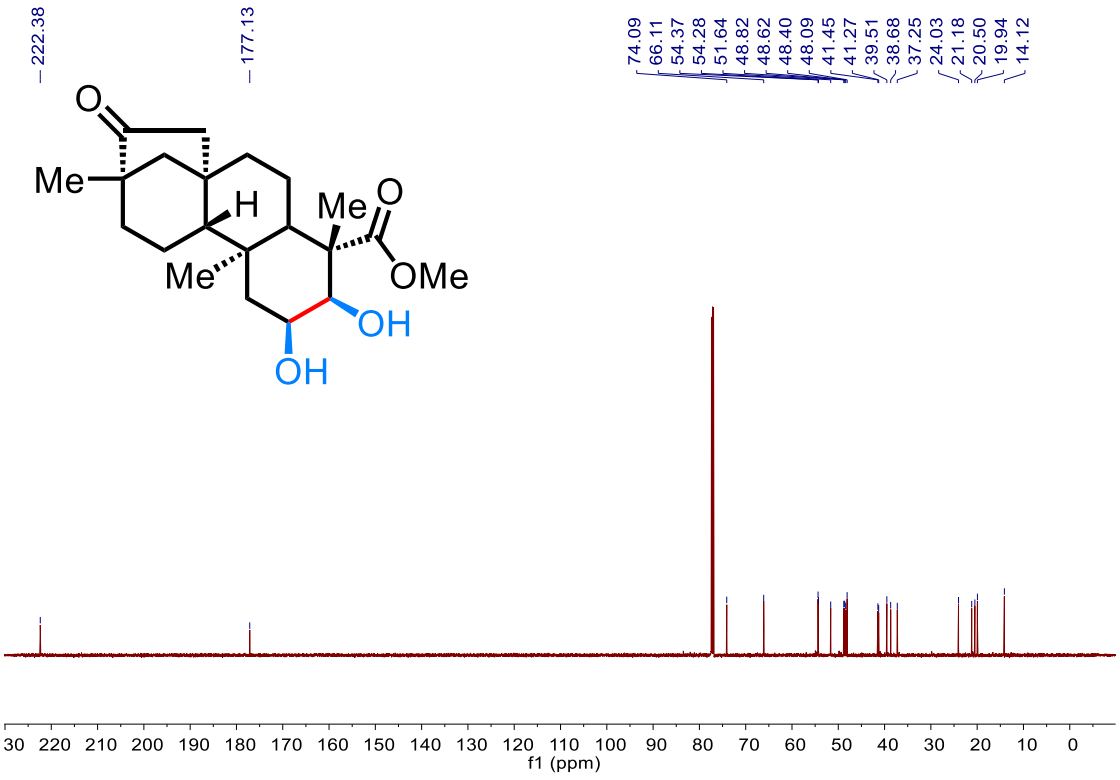
NOE of Compound 5a:



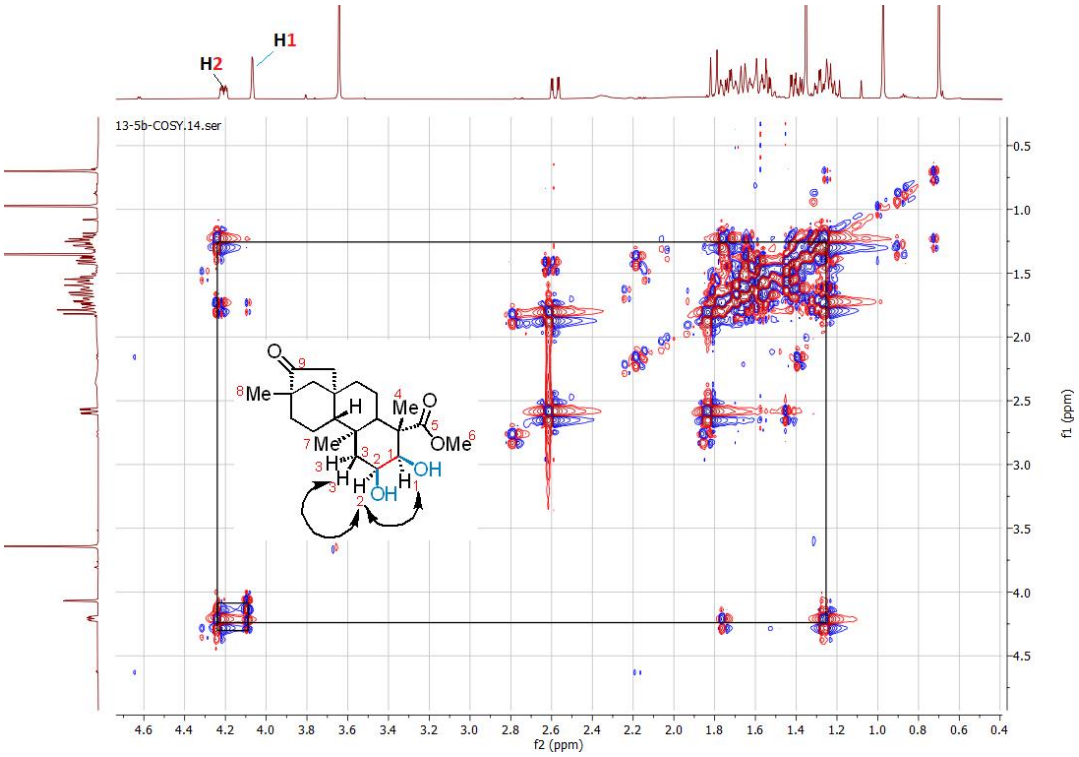
^{1}H NMR of Compound 5b:



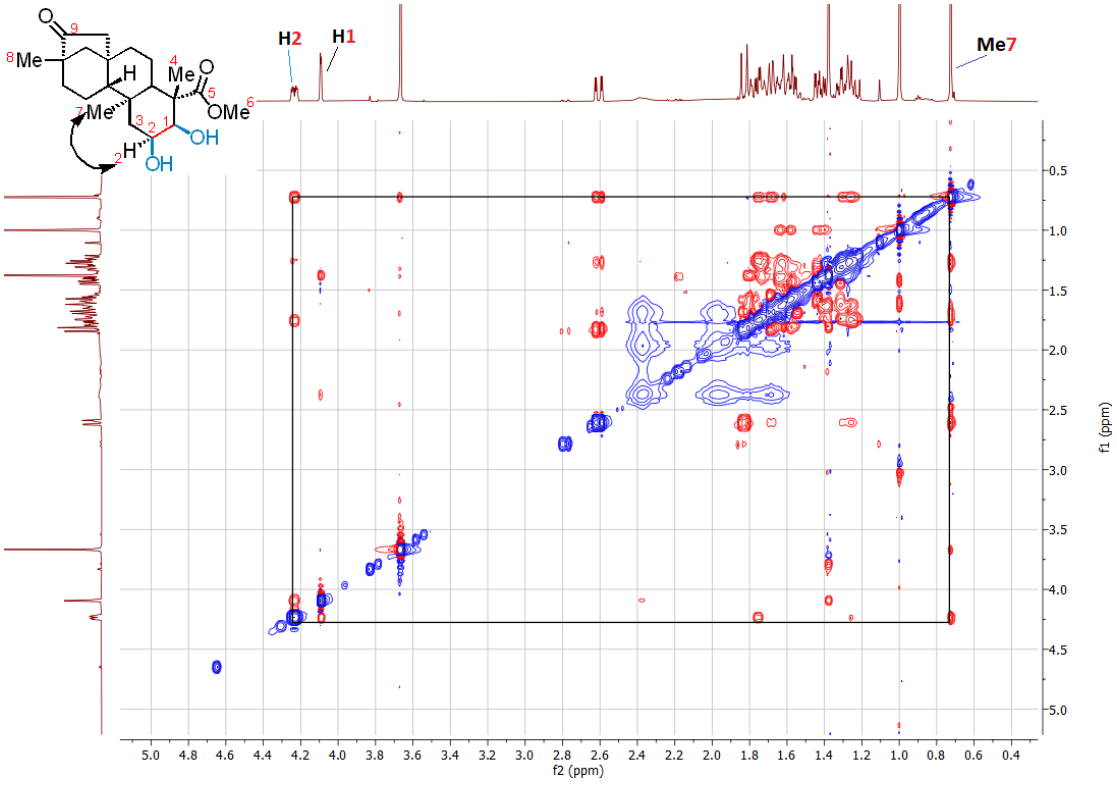
^{13}C NMR of Compound 5b:



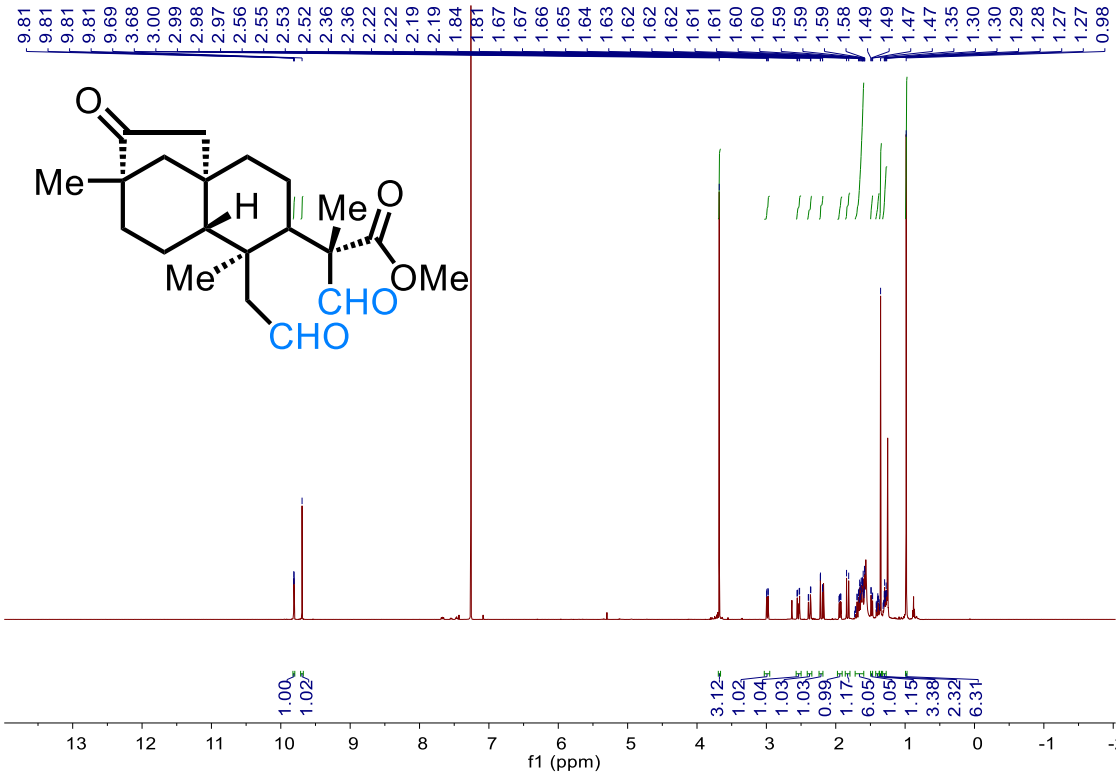
COSY of Compound 5b:



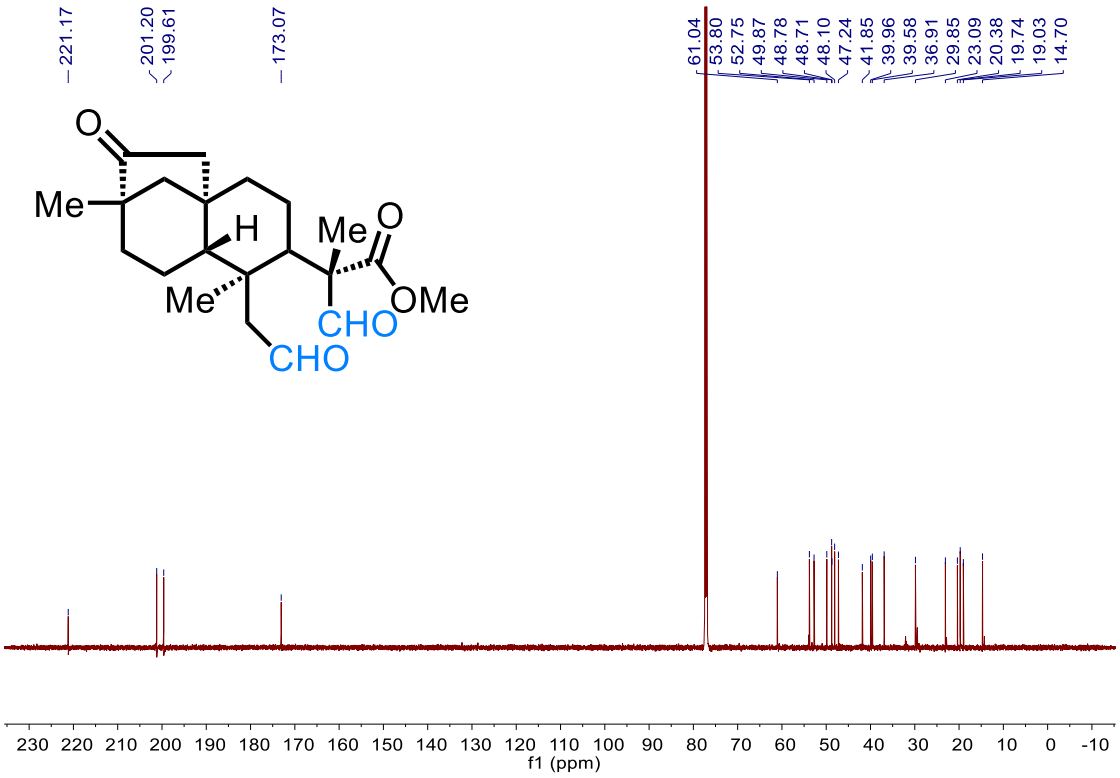
NOE of Compound 5b:



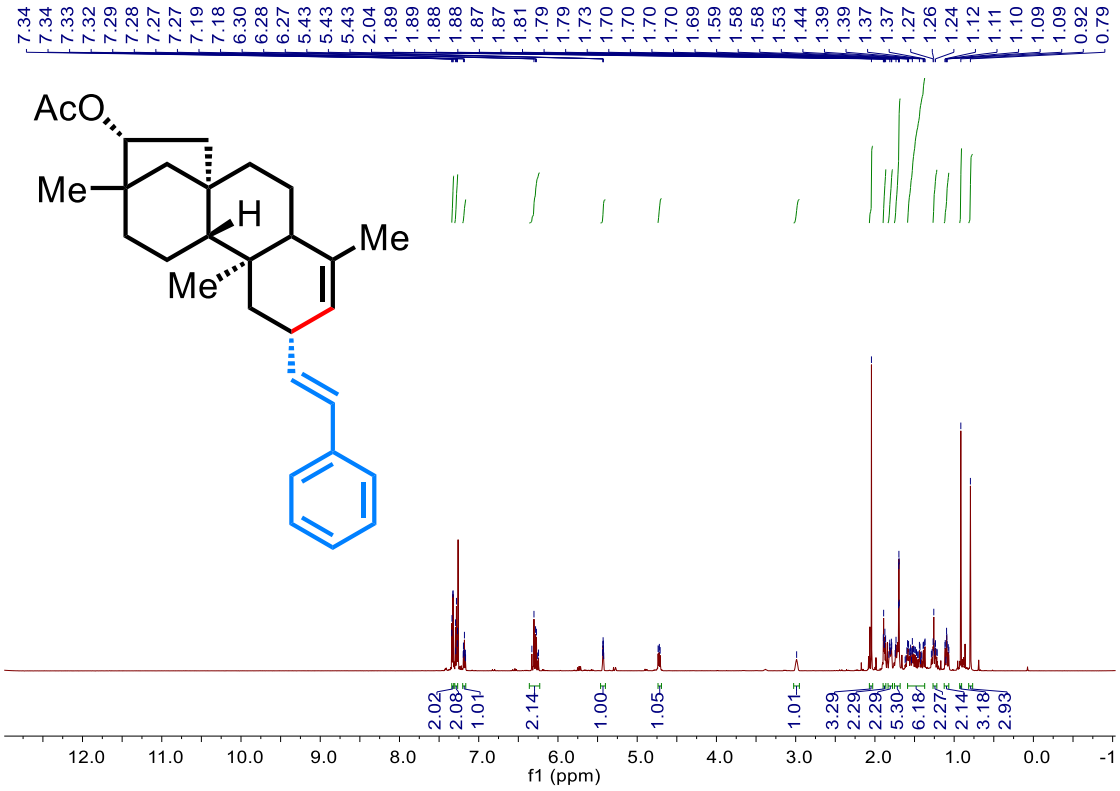
^{1}H NMR of Compound 5c:



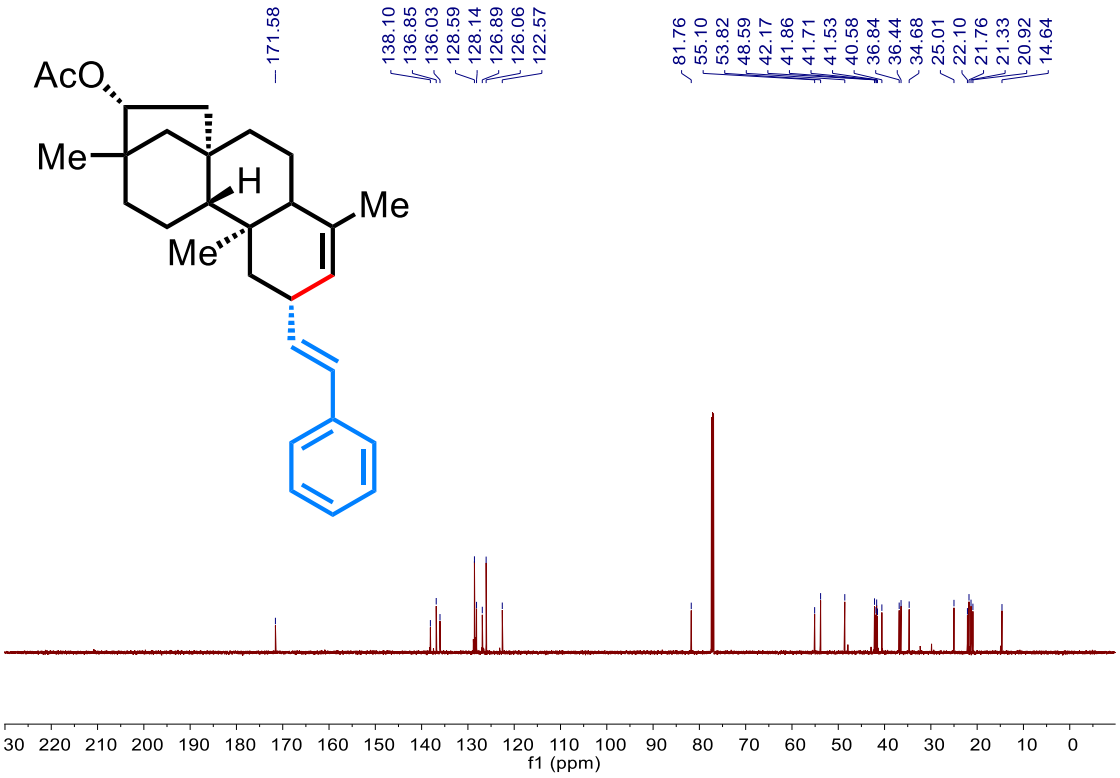
^{13}C NMR of Compound 5c:



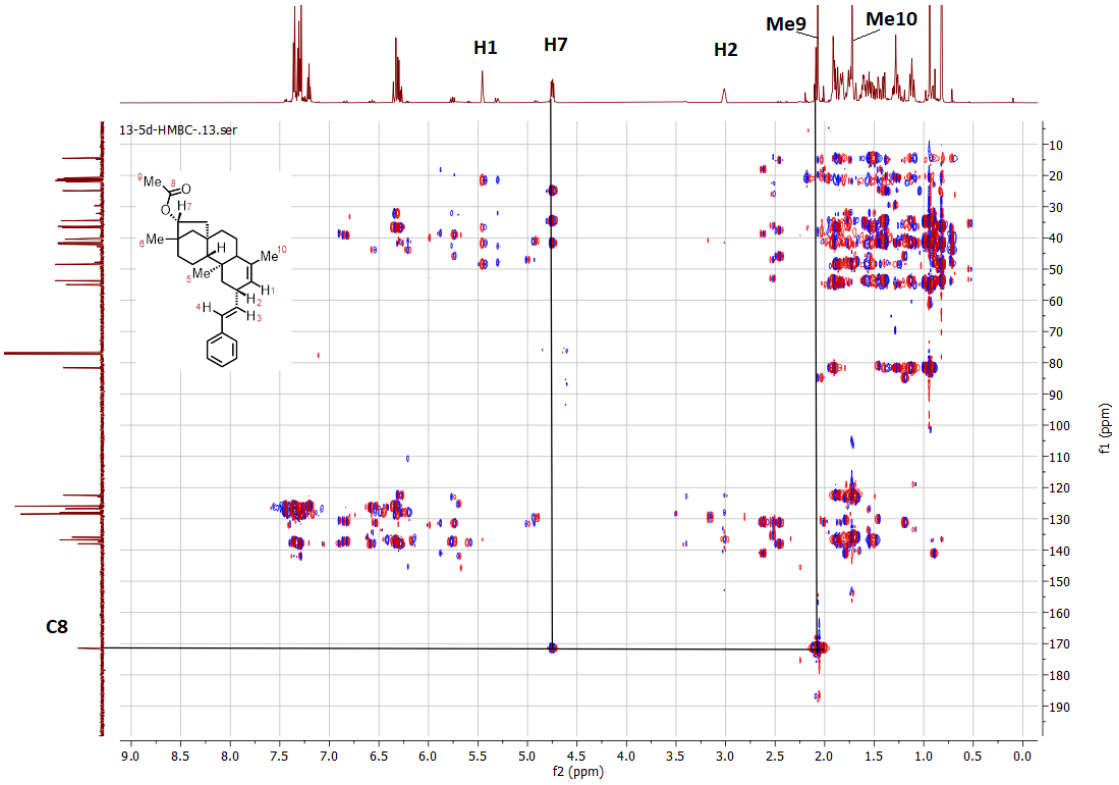
^{1}H NMR of Compound 5d:



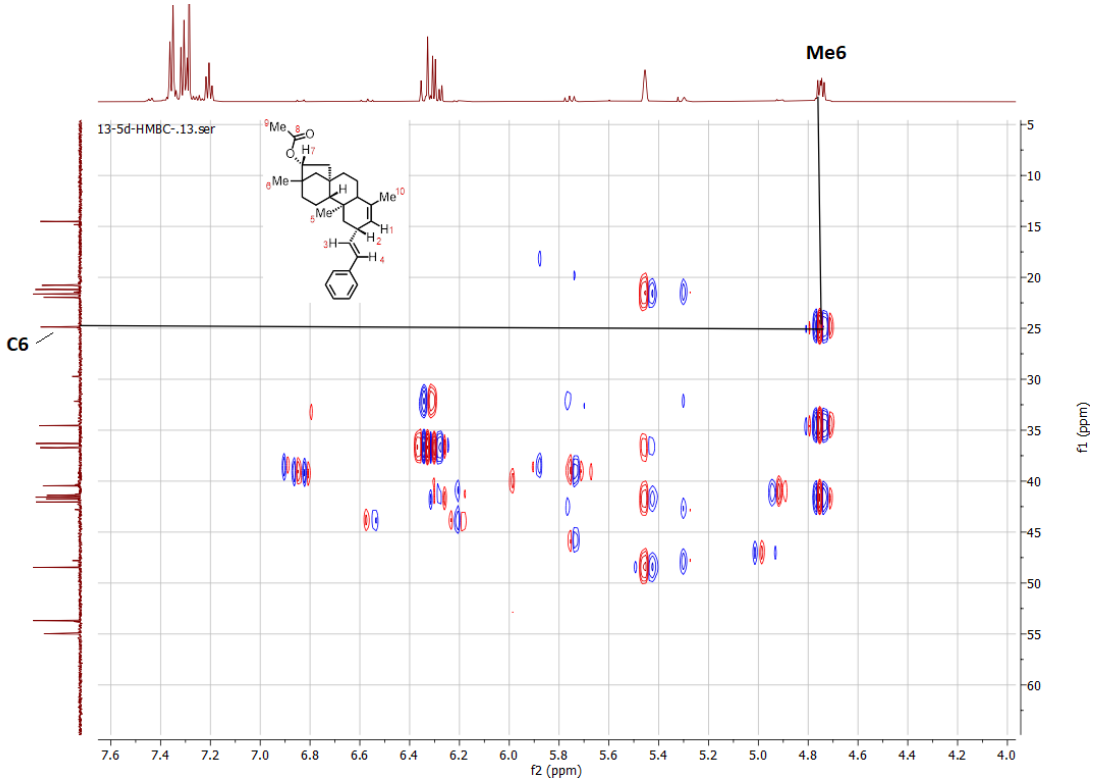
^{13}C NMR of Compound 5d:



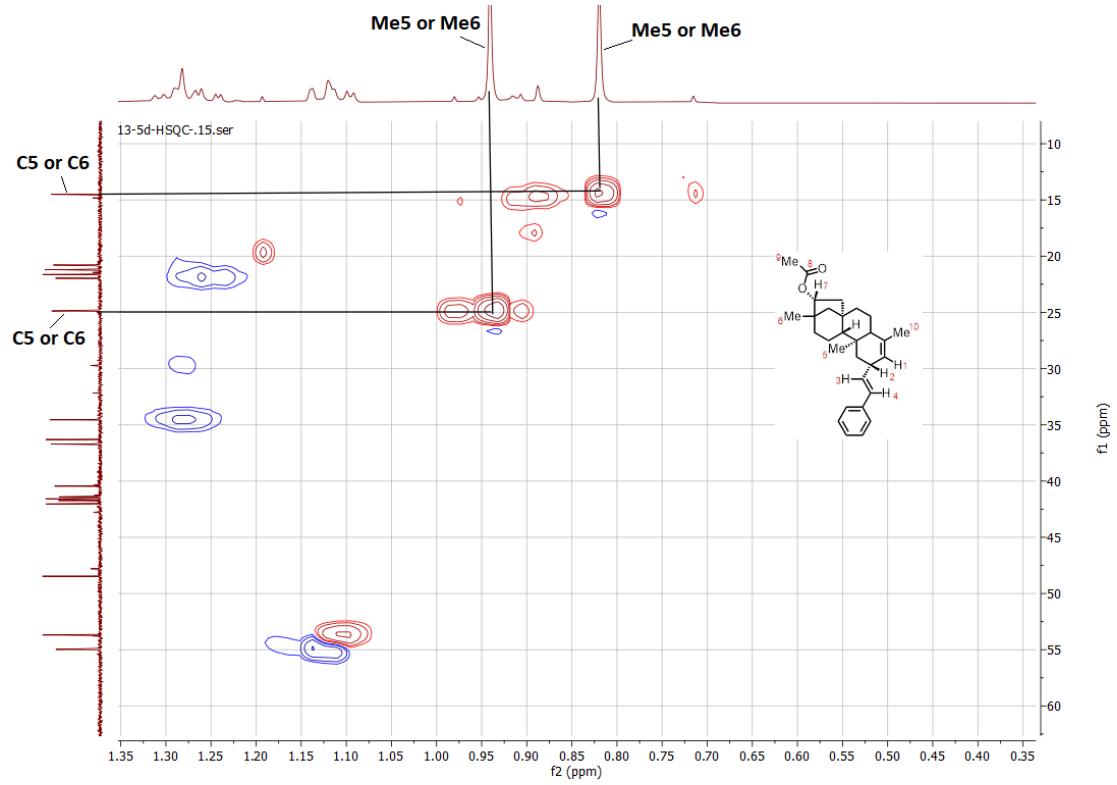
HMBC-1 of Compound 5d:



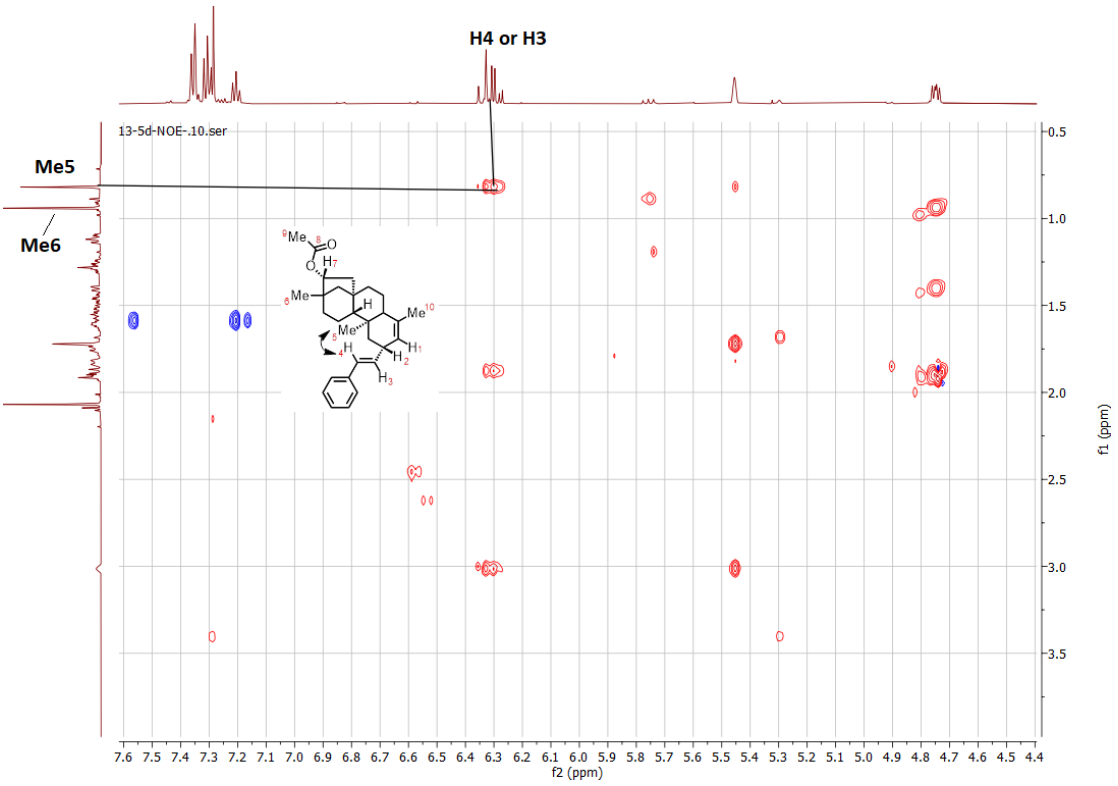
HMBC-2 of Compound 5d:



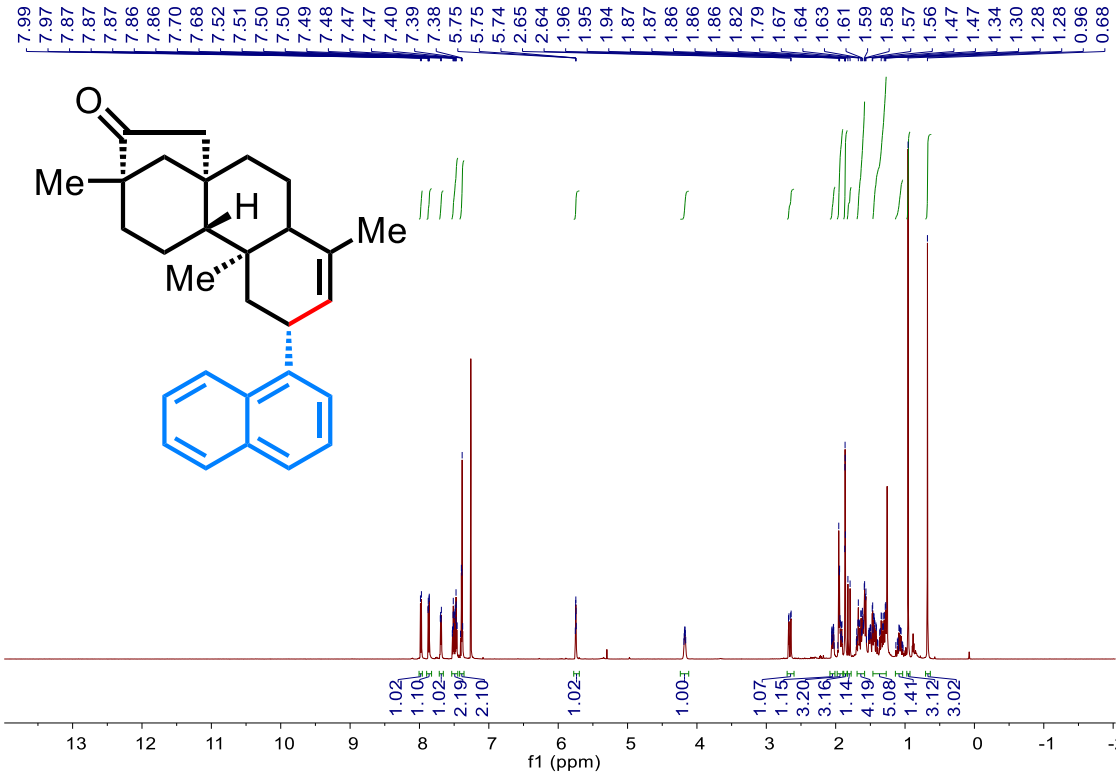
HSQC of Compound 5d:



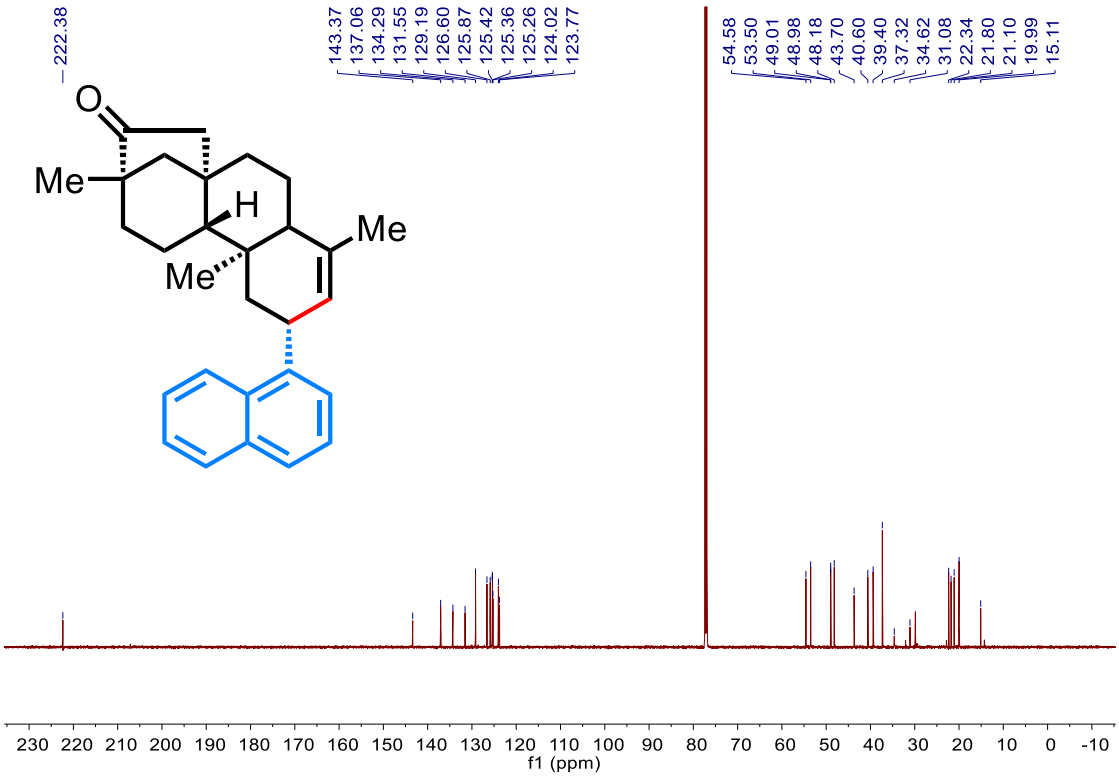
NOE of Compound 5d:



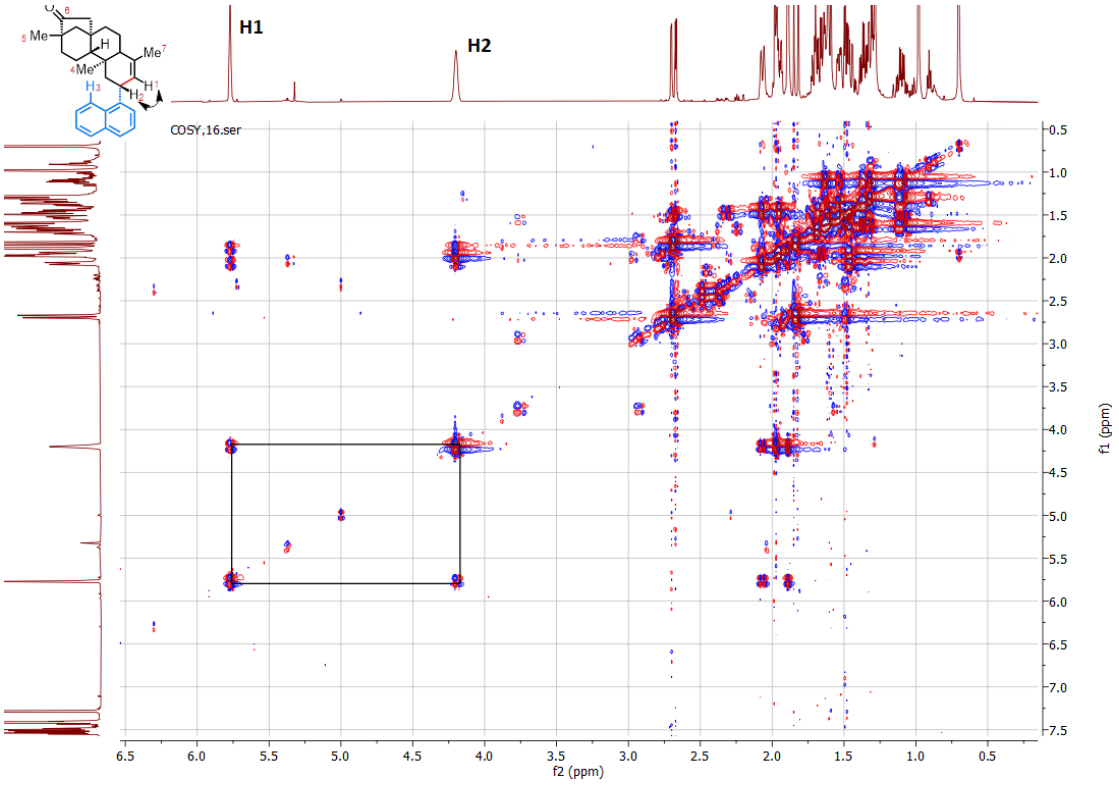
^{1}H NMR of Compound 5e:



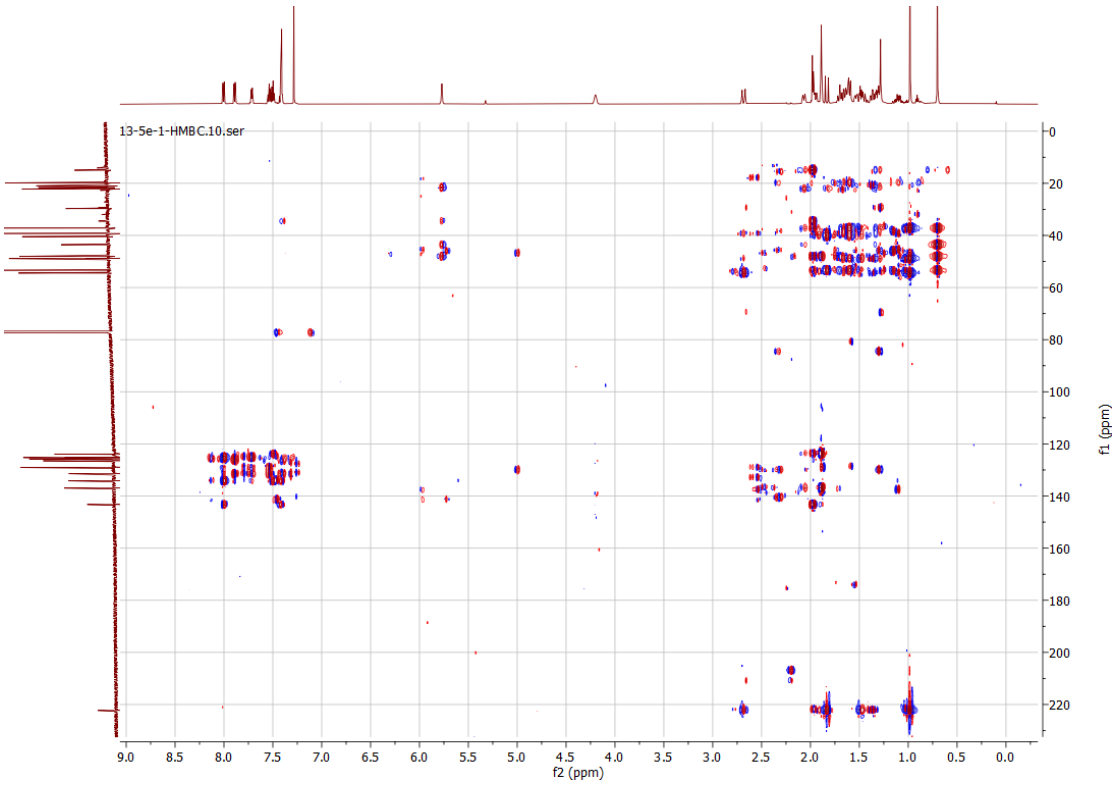
^{13}C NMR of Compound 5e:



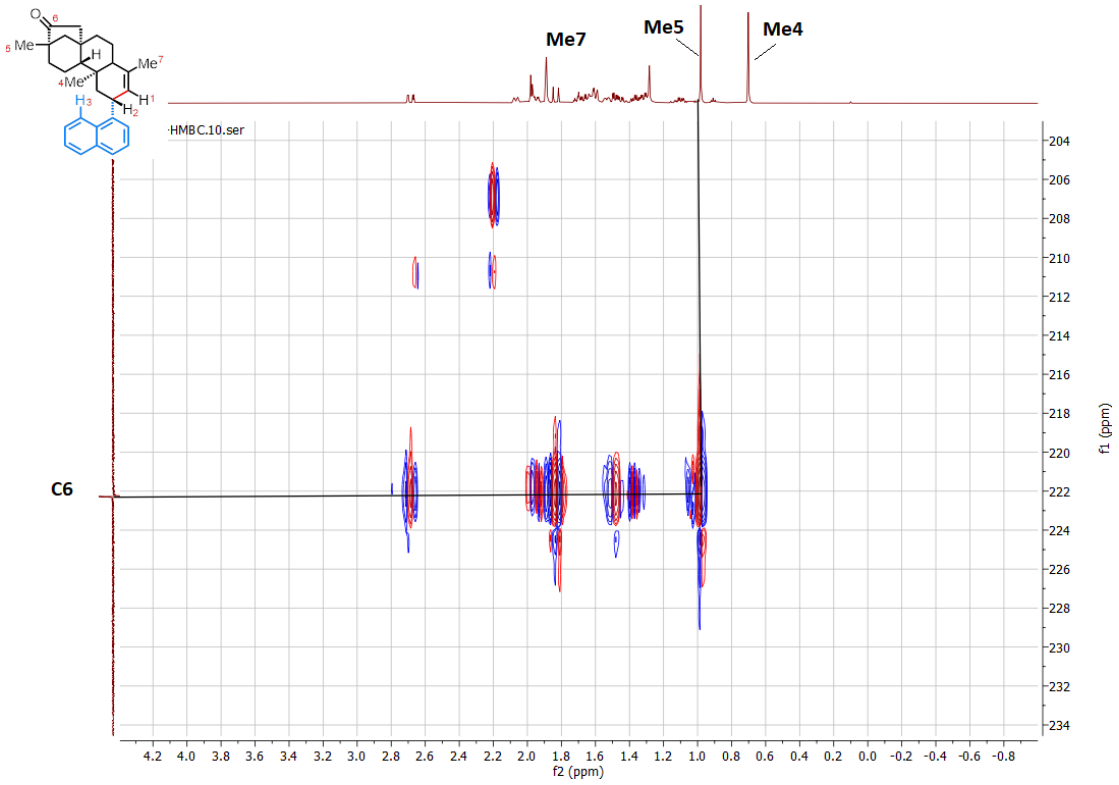
COSY of Compound 5e:



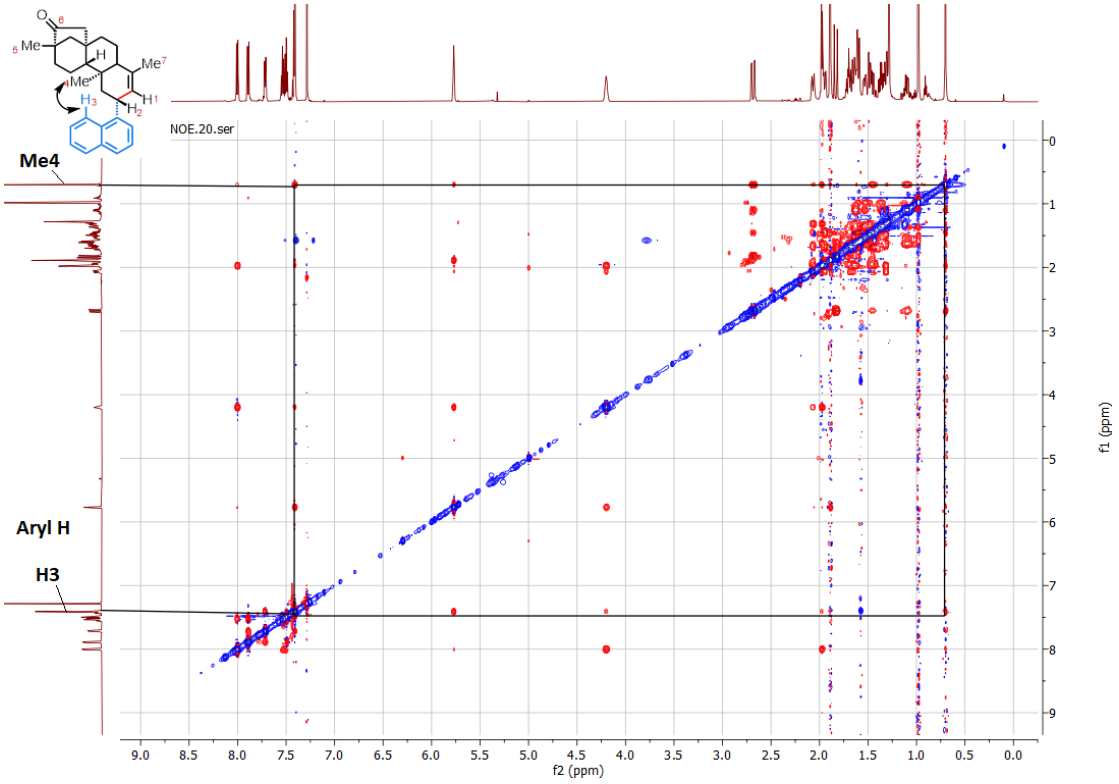
HMBC of Compound 5e (full view):



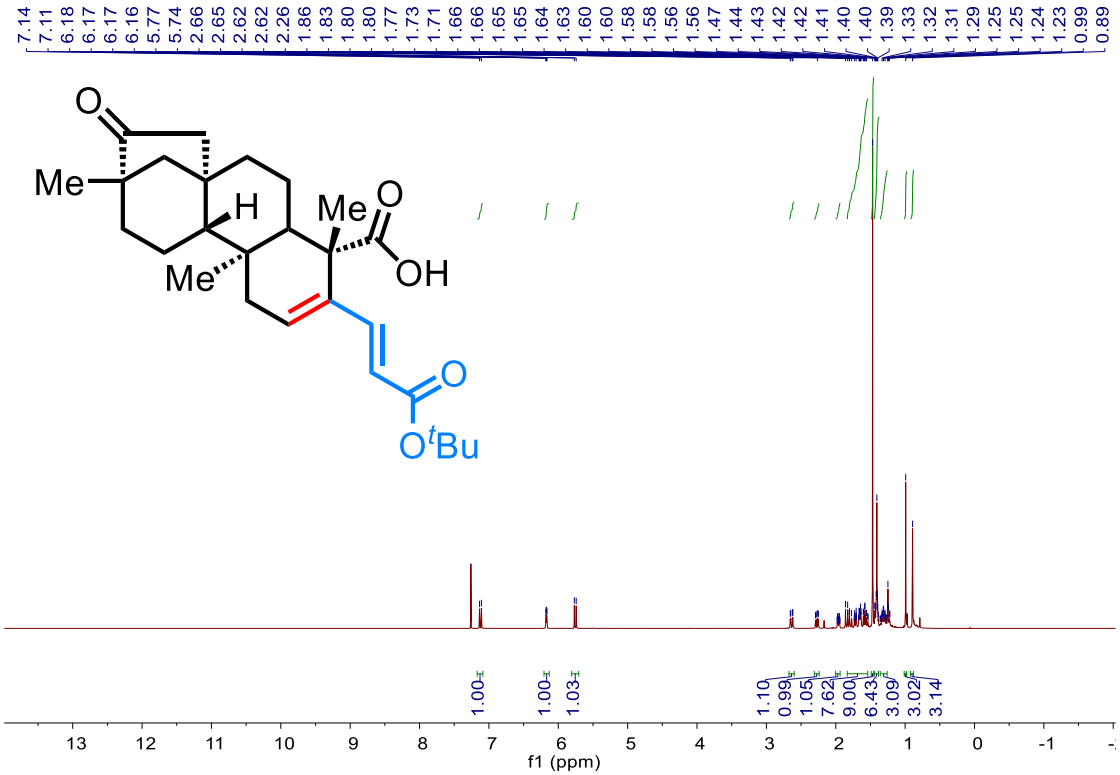
HMBC of Compound 5e:



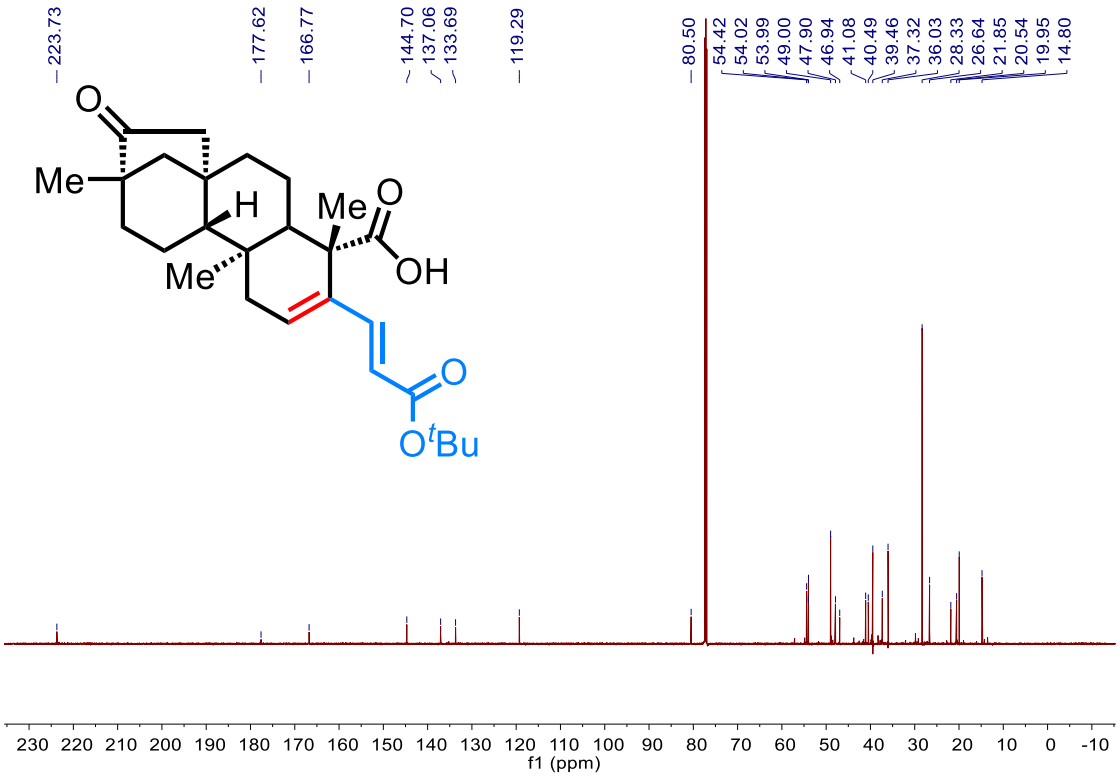
NOE of Compound 5e:



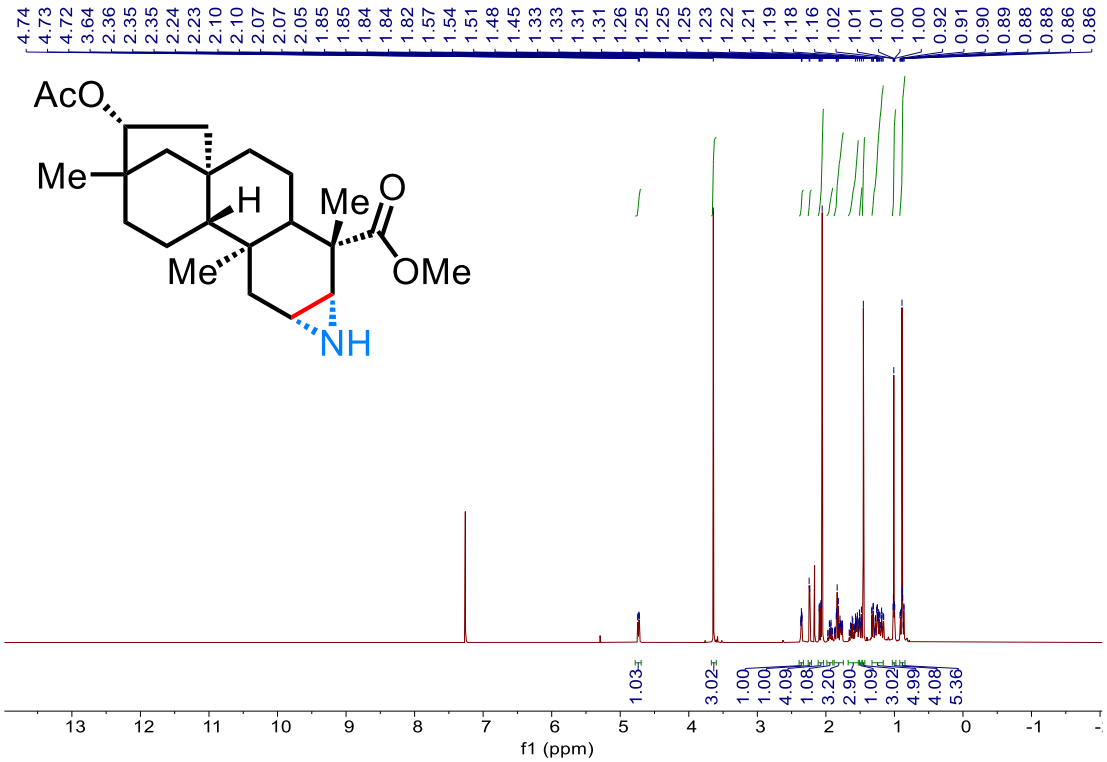
^{1}H NMR of Compound 5f:



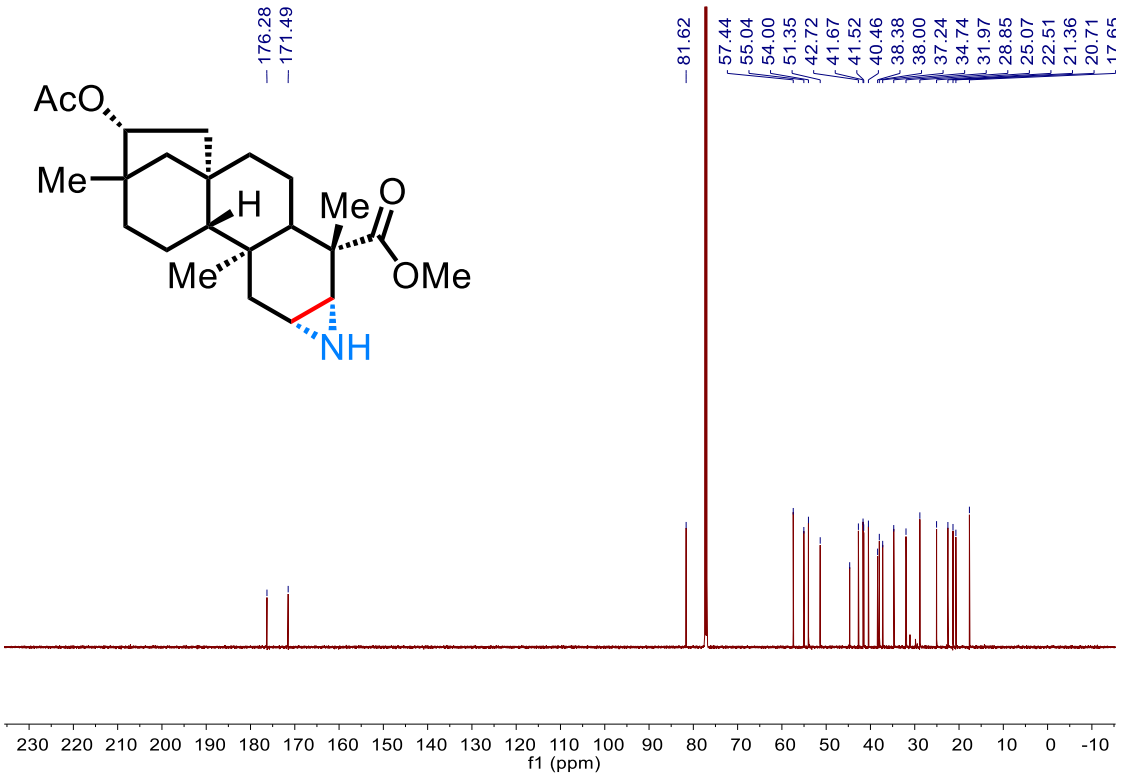
^{13}C NMR of Compound 5f:



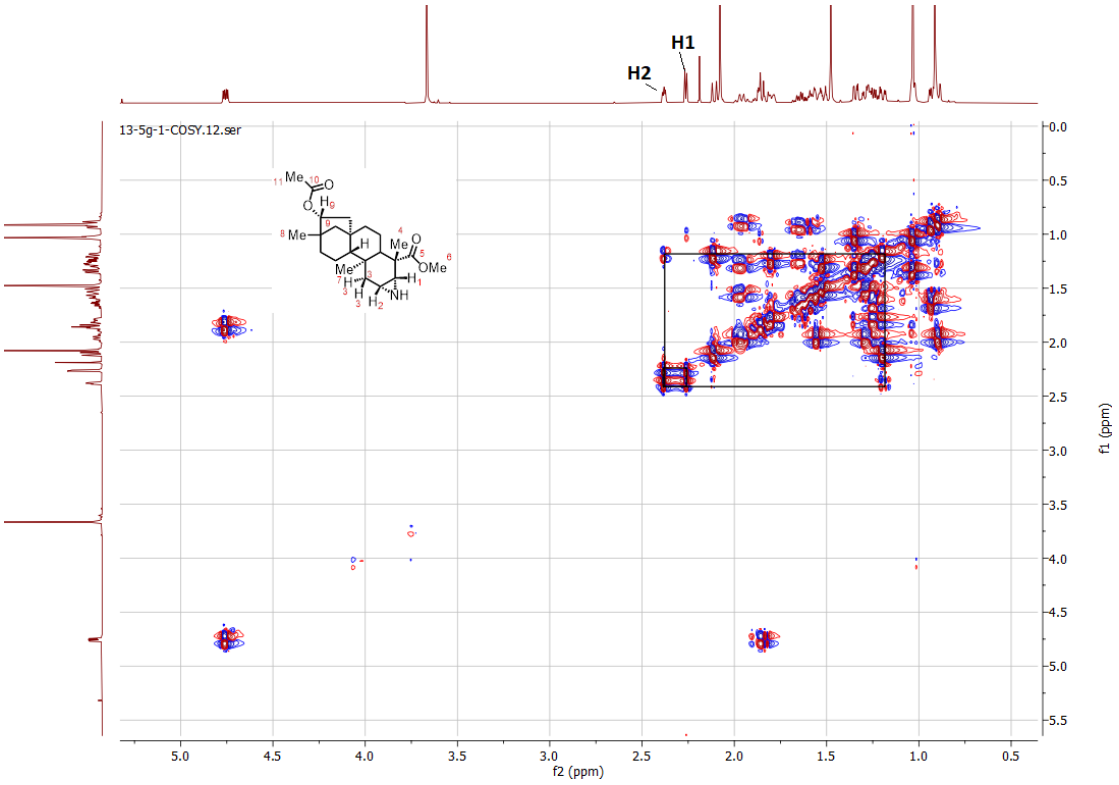
^{1}H NMR of Compound 5g:



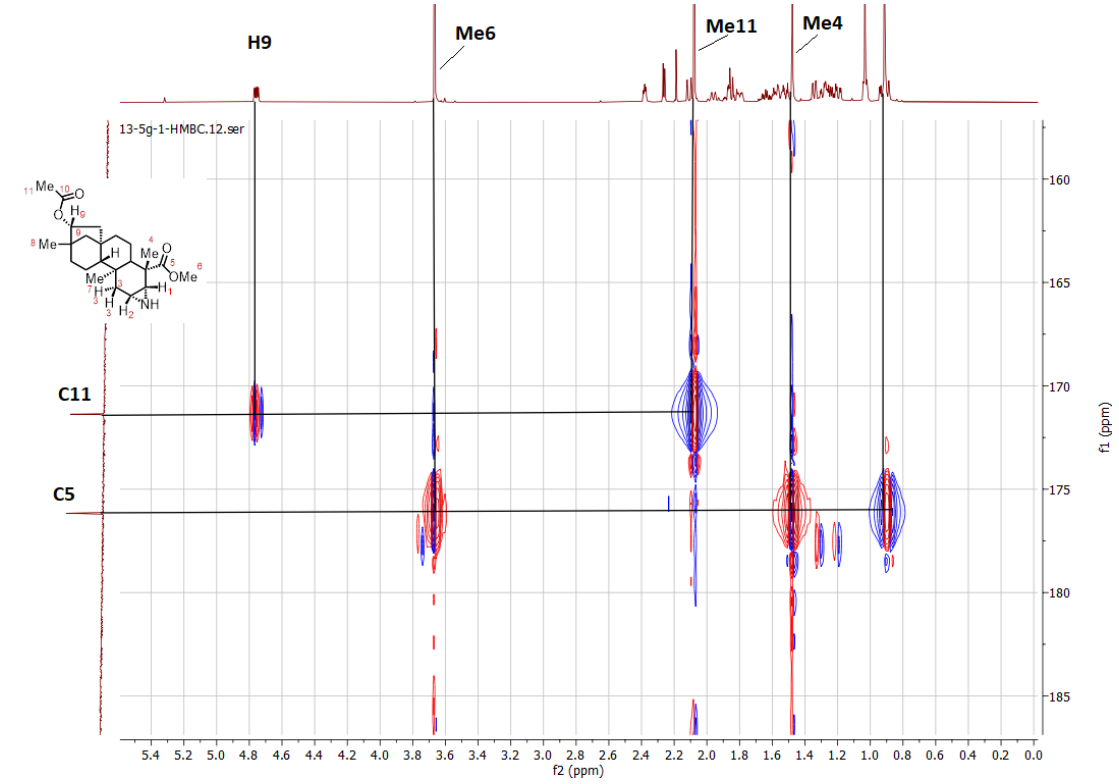
^{13}C NMR of Compound 5g:



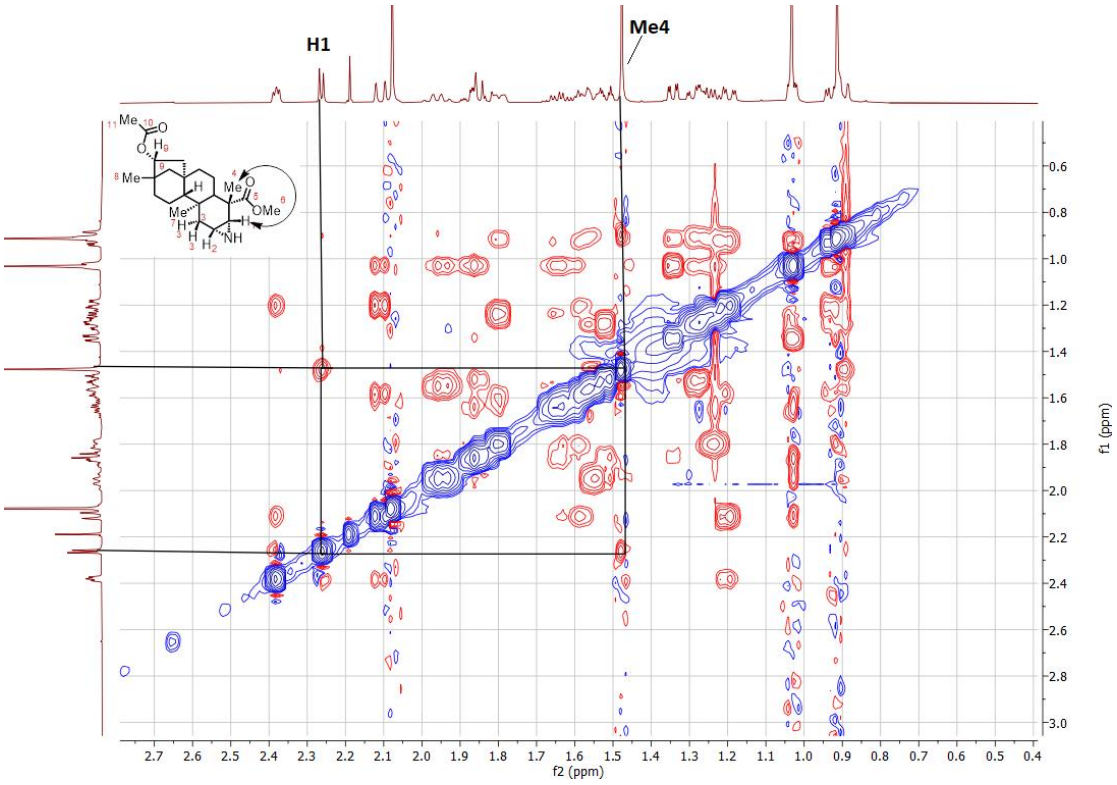
COSY of Compound 5g:



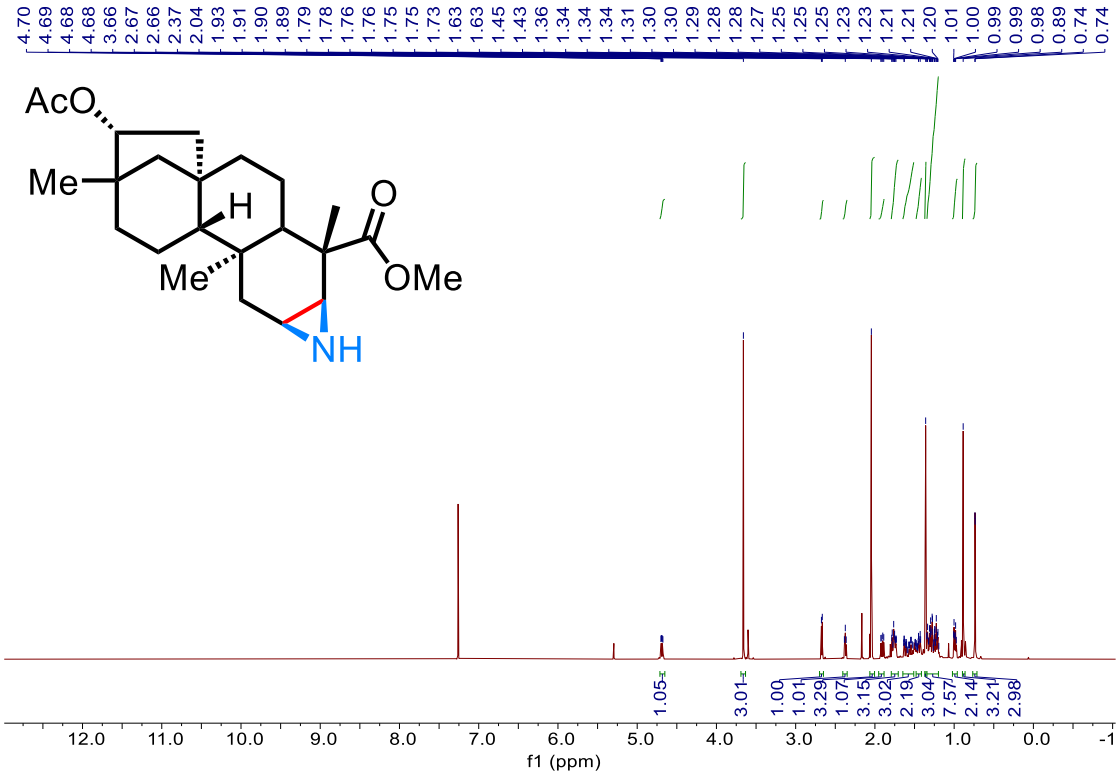
HMBC of Compound 5g:



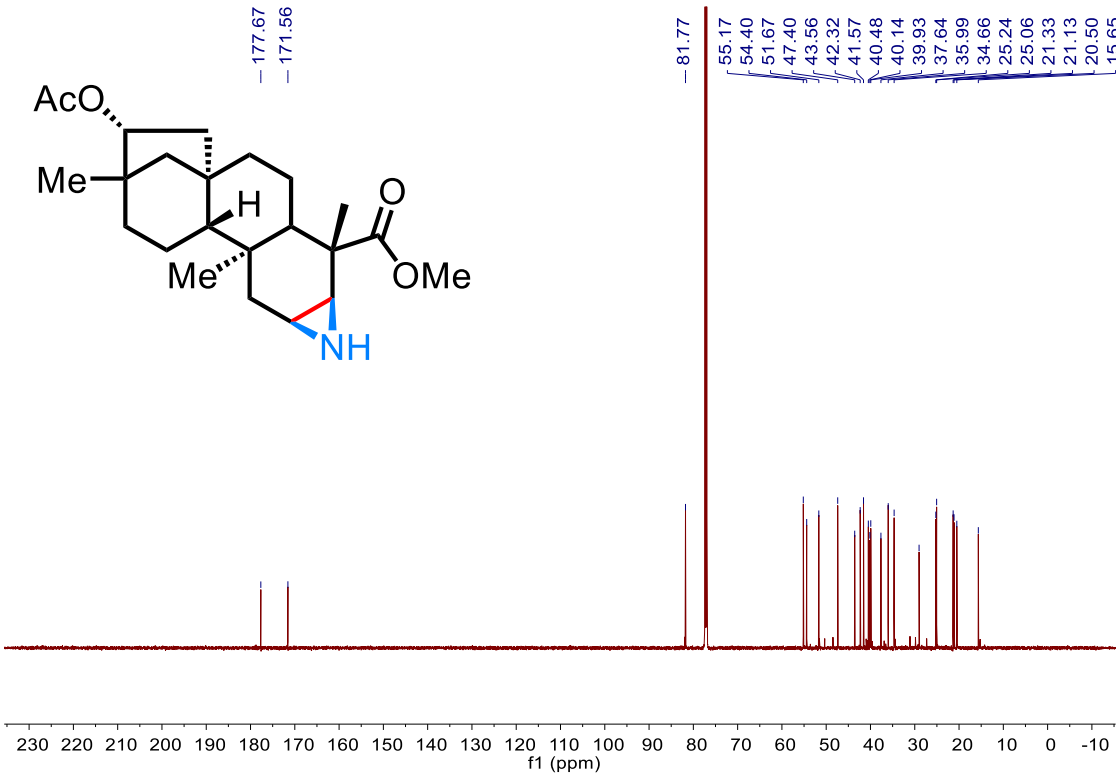
NOE of Compound 5g:



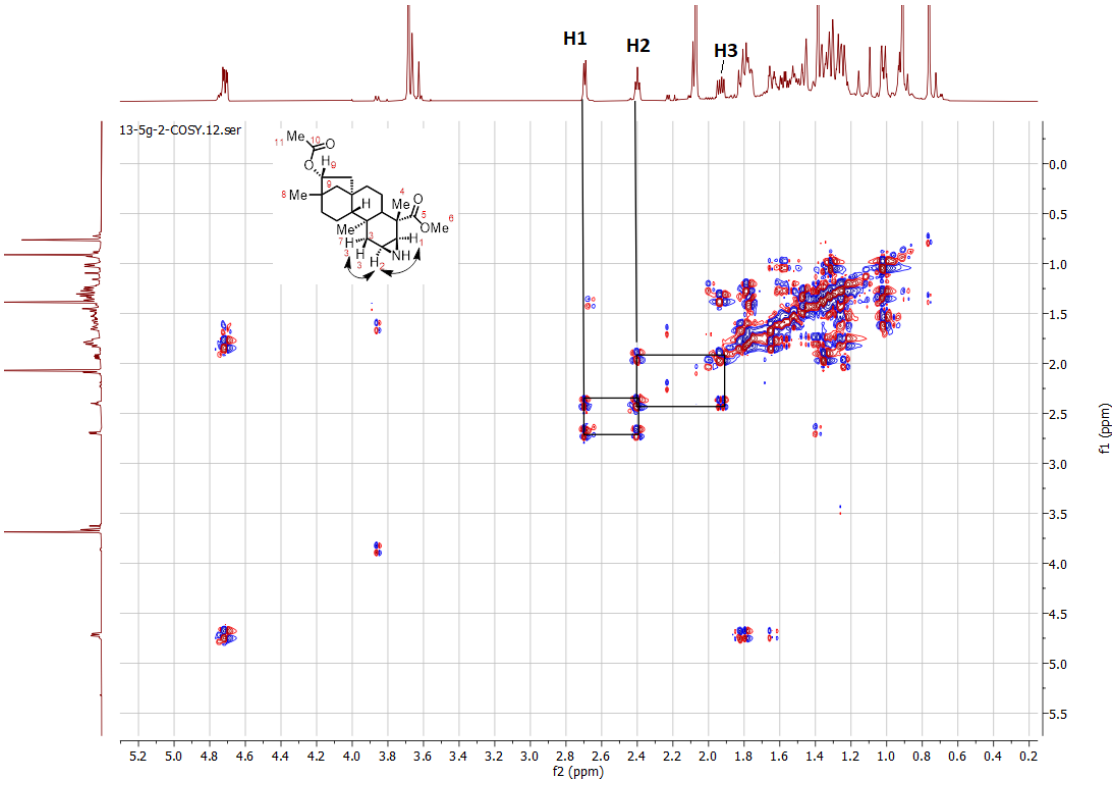
^{1}H NMR of Compound 5g':



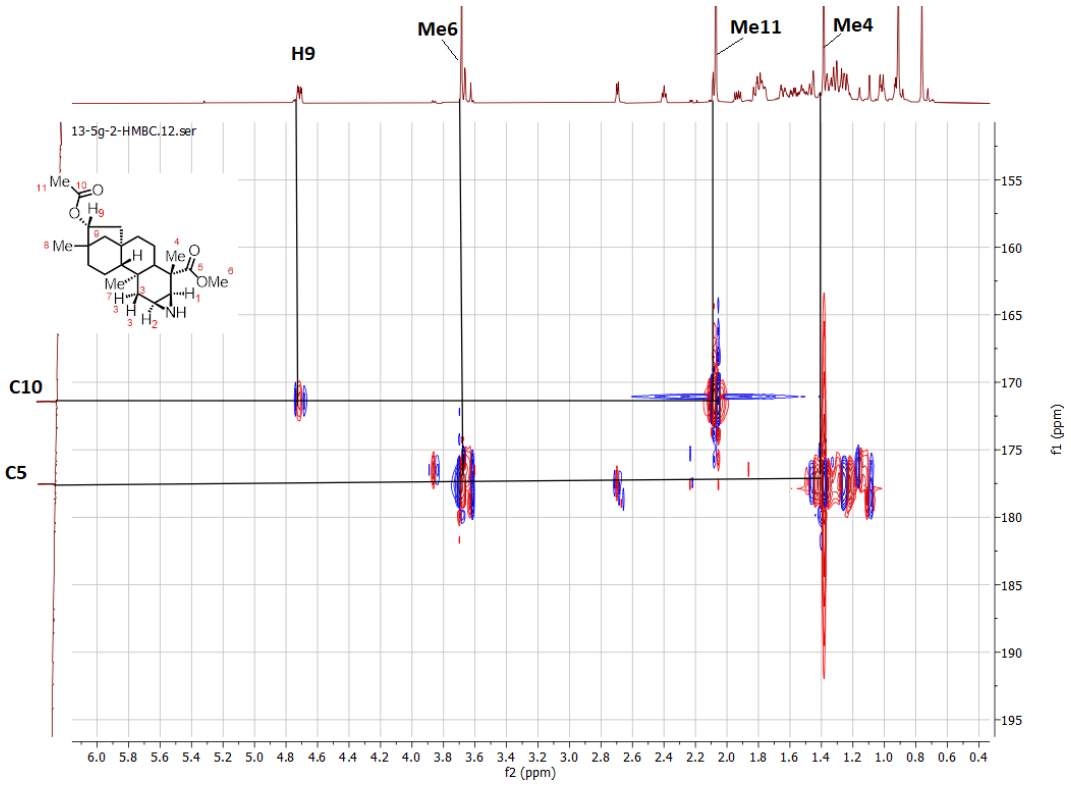
^{13}C NMR of Compound 5g':



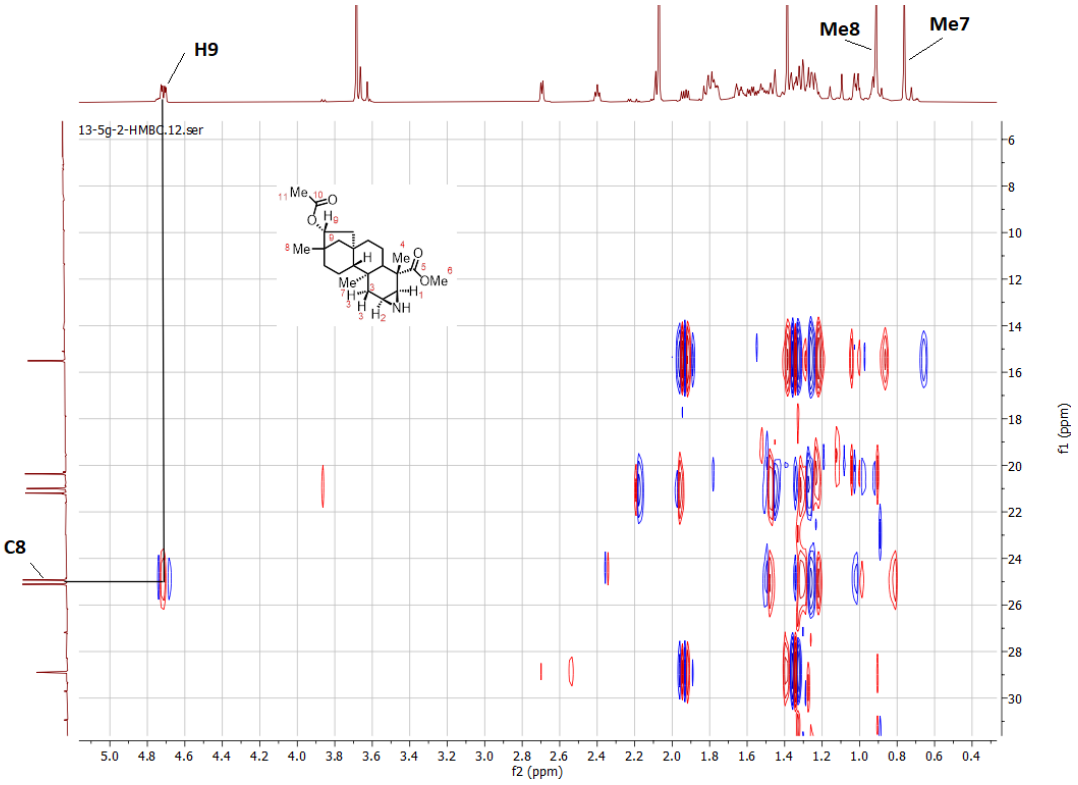
COSY of Compound 5g':



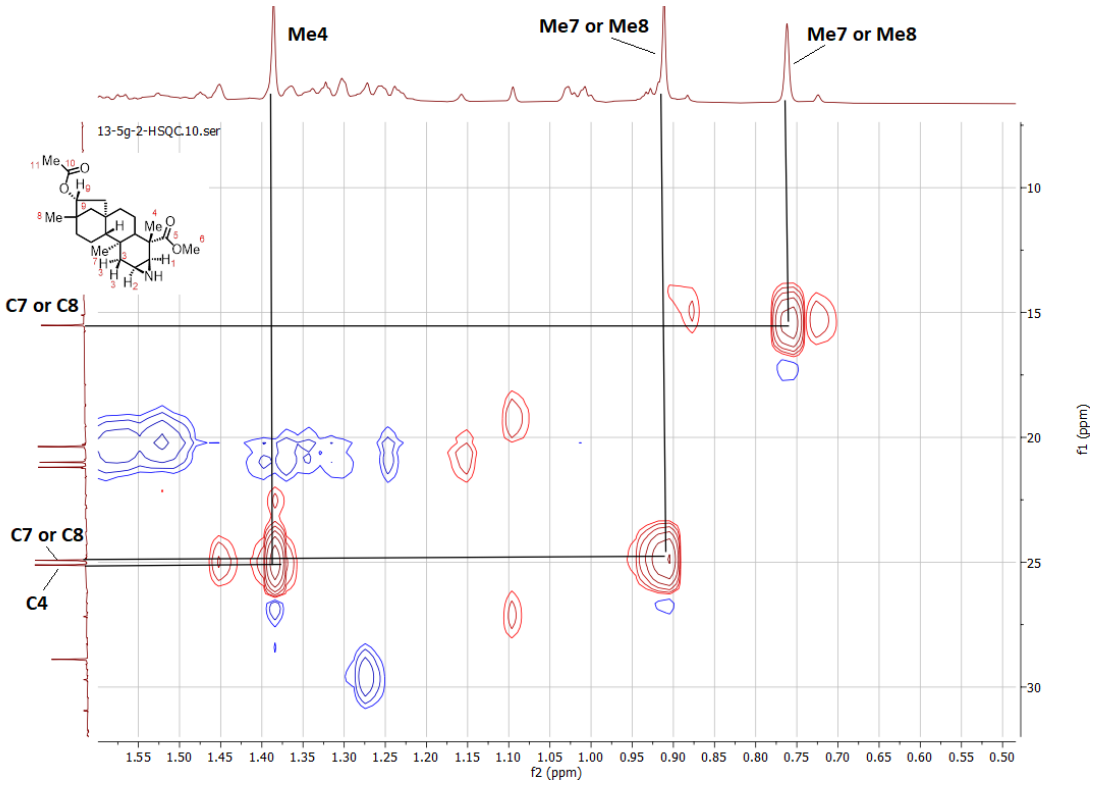
HMBC-1 of Compound 5g':



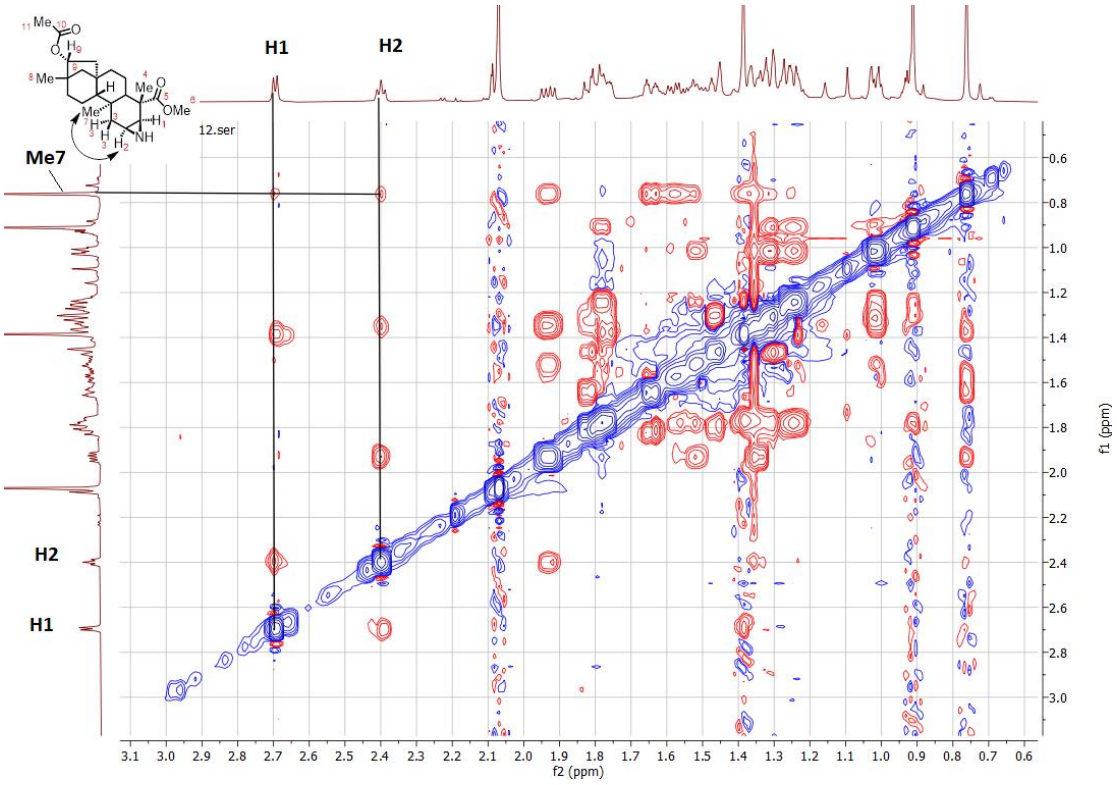
HMBC-2 of Compound 5g':



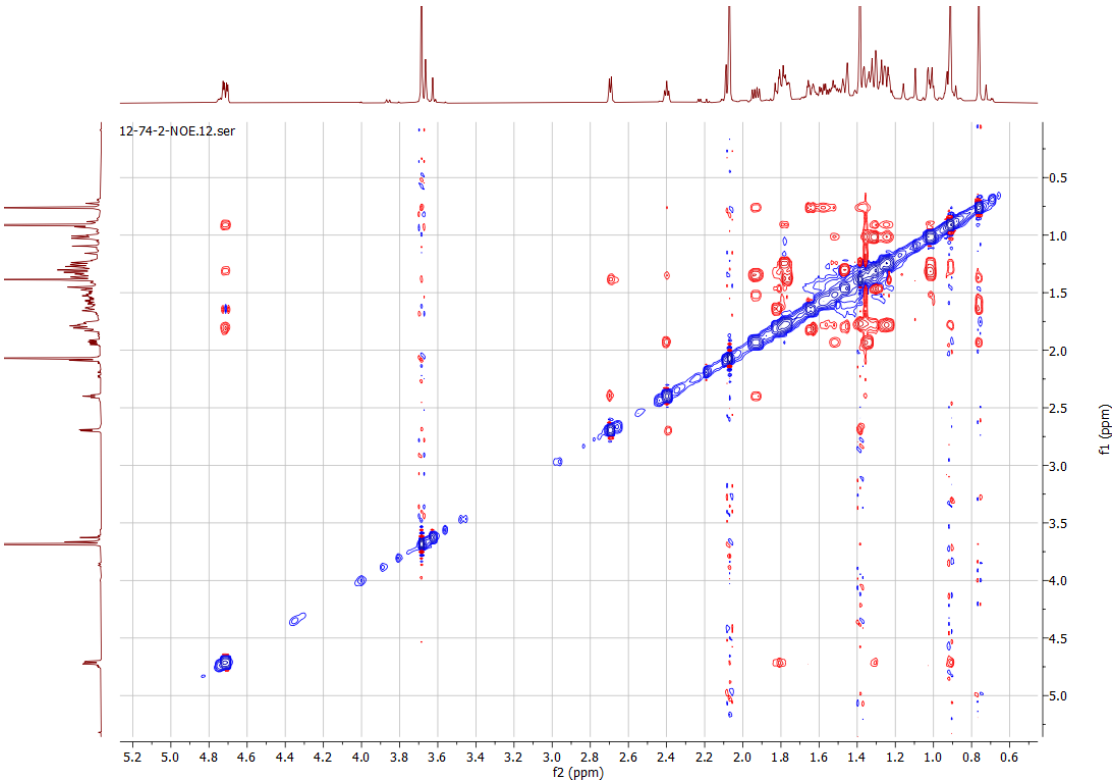
HSQC of Compound 5g':



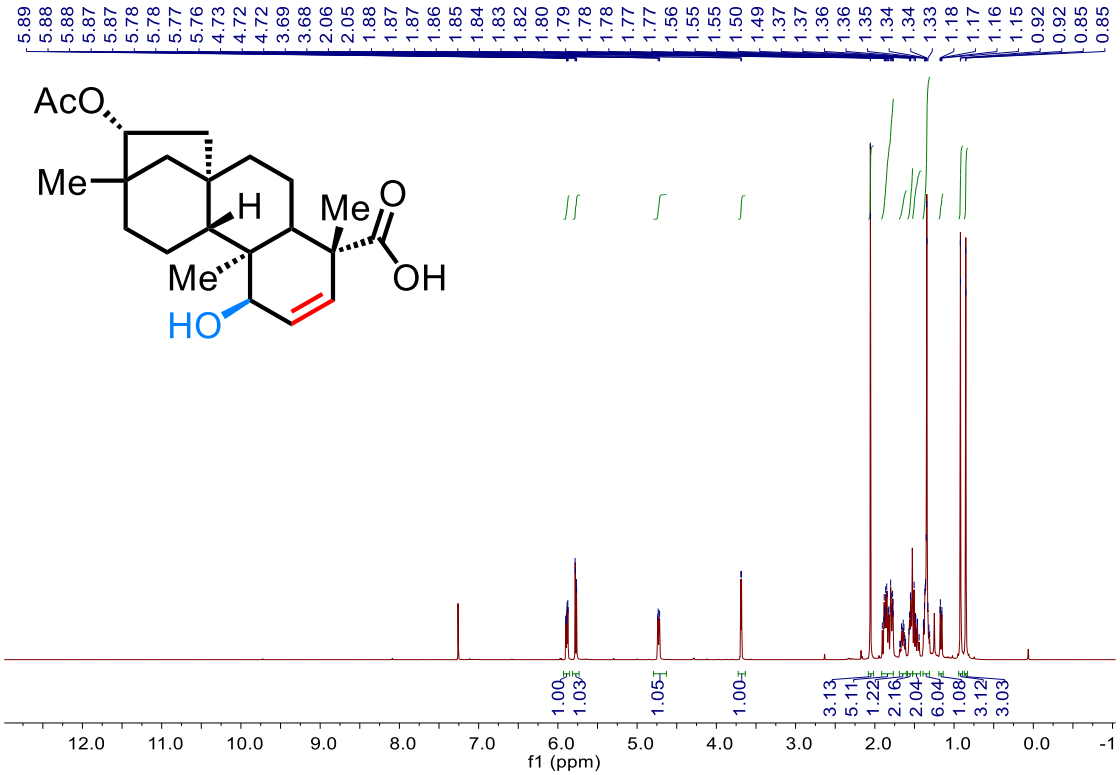
NOE of Compound 5g':



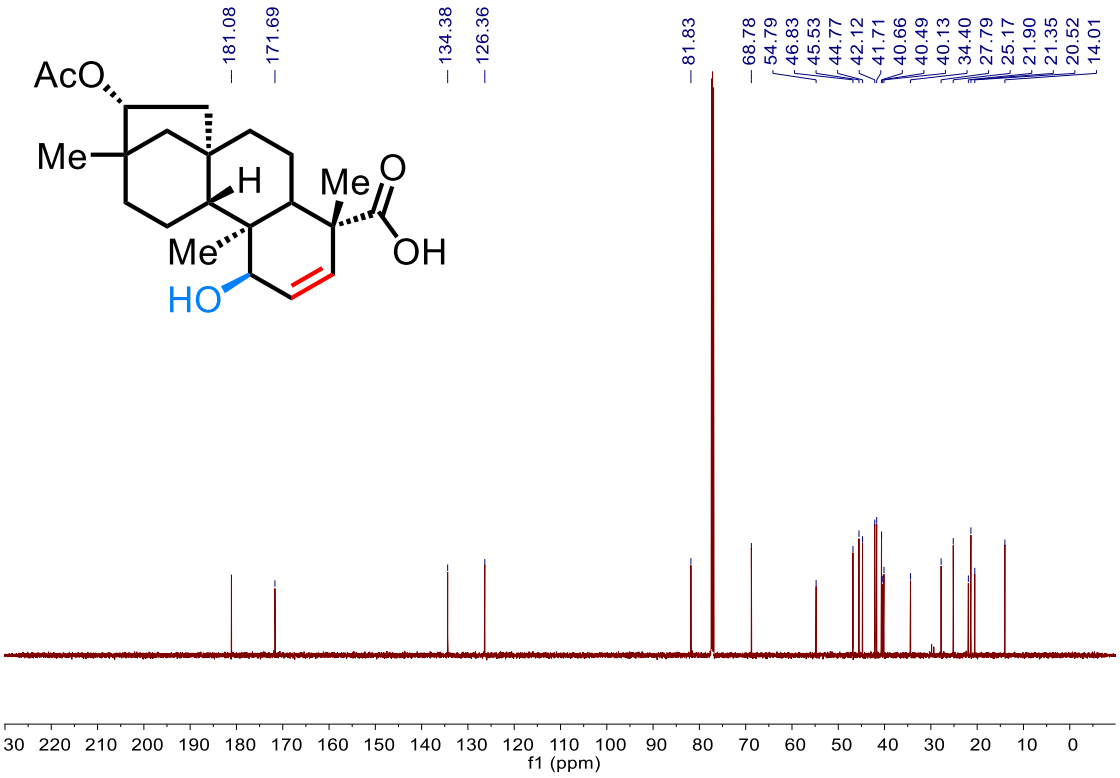
NOE of Compound 5g' (full view):



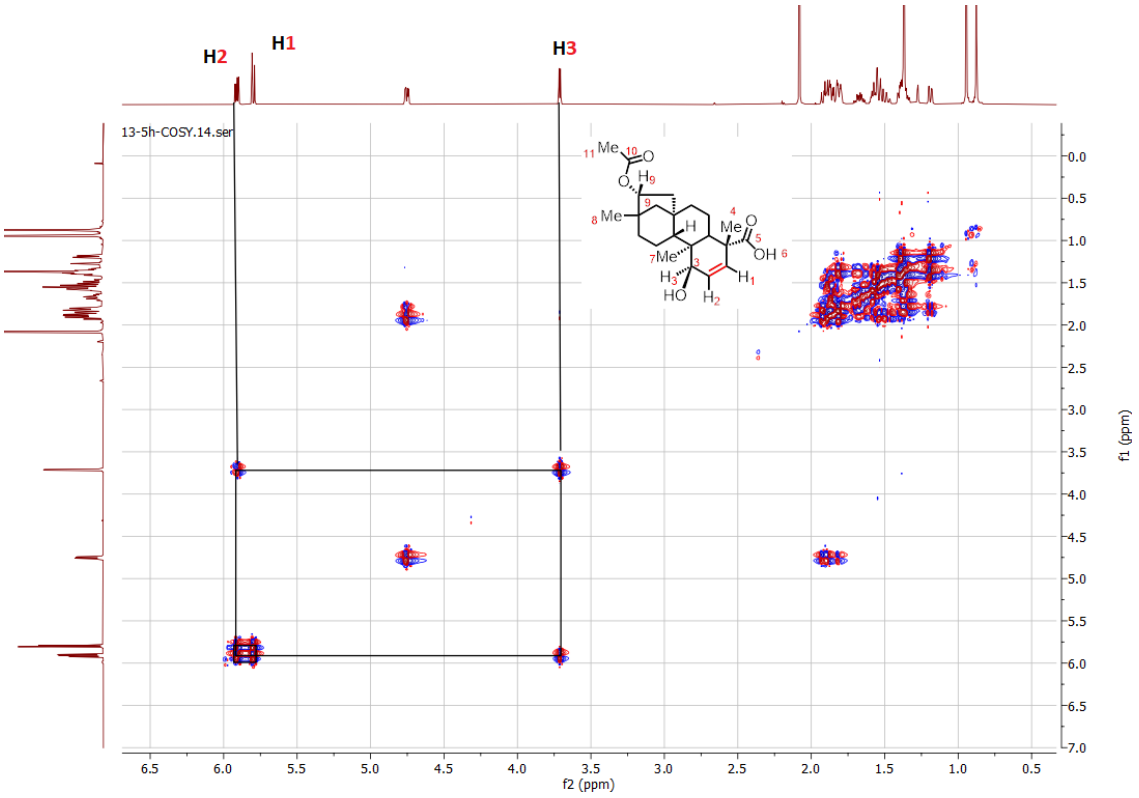
^{1}H NMR of Compound 5h:



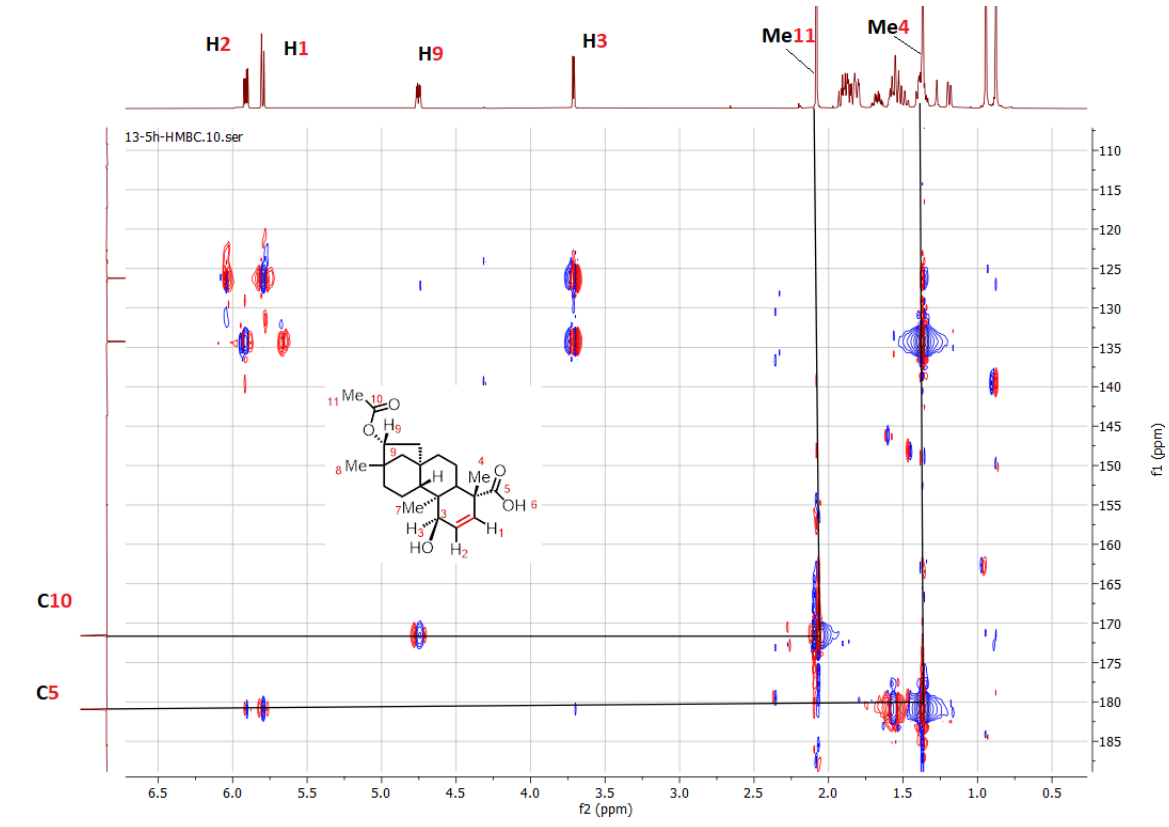
^{13}C NMR of Compound 5h:



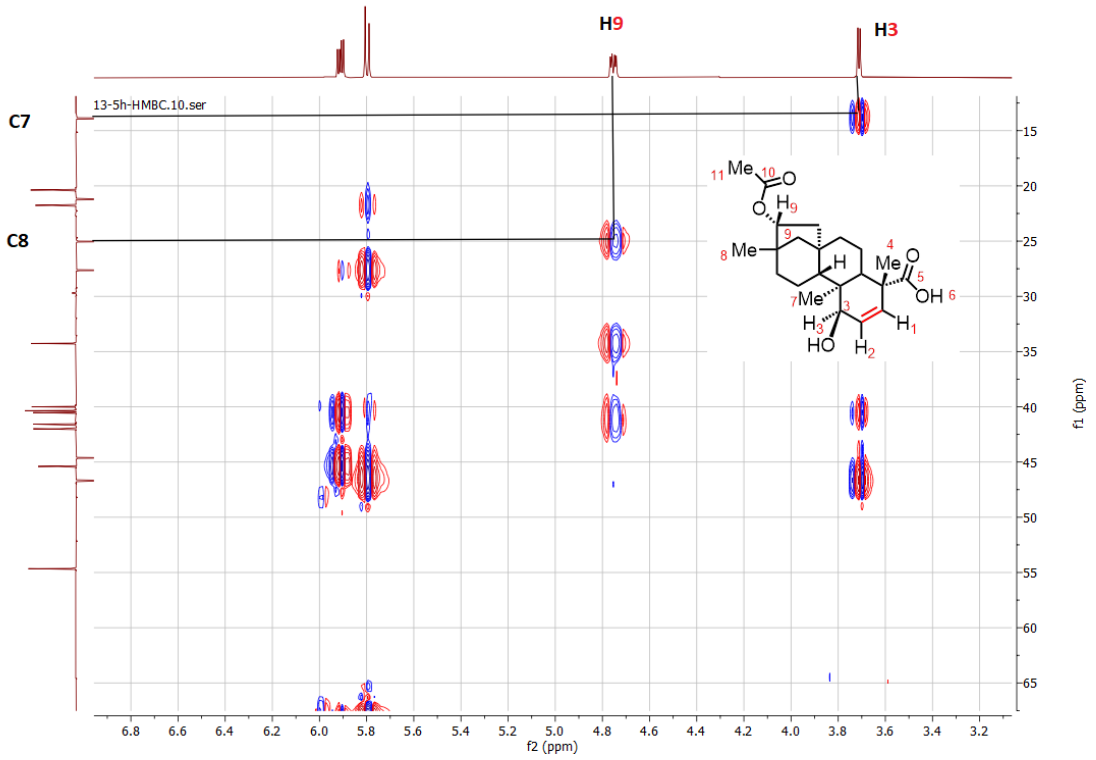
COSY of Compound 5h:



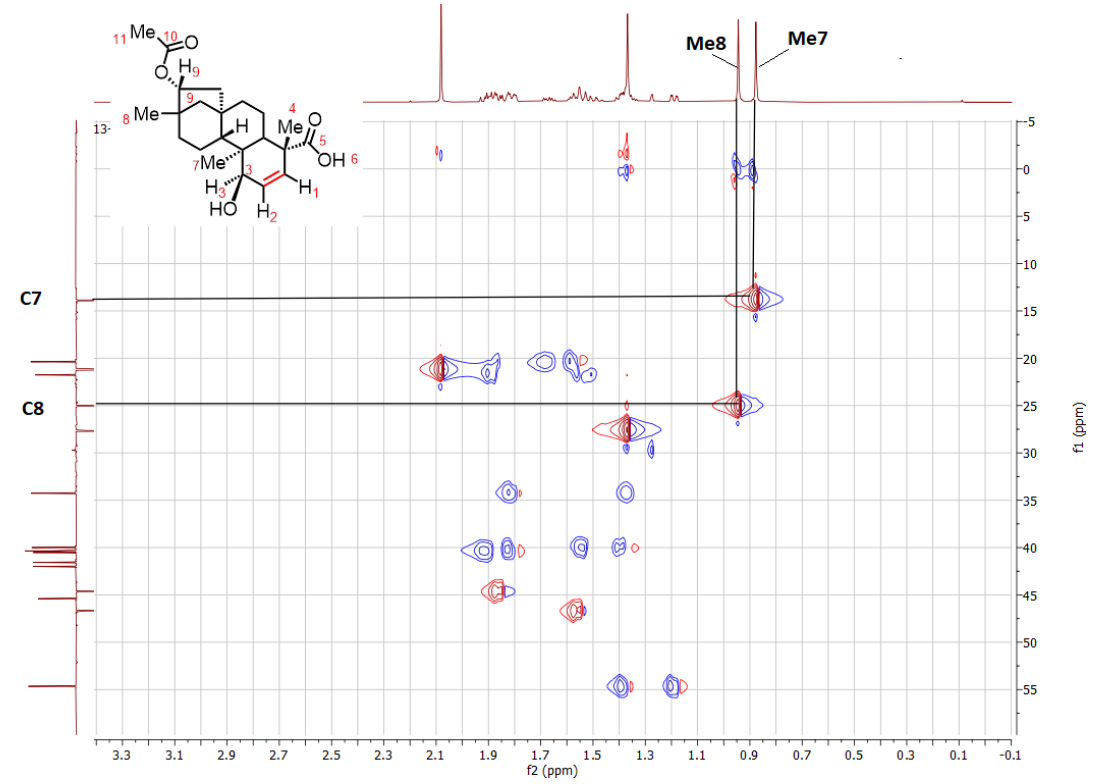
HMBC-1 of Compound 5h:



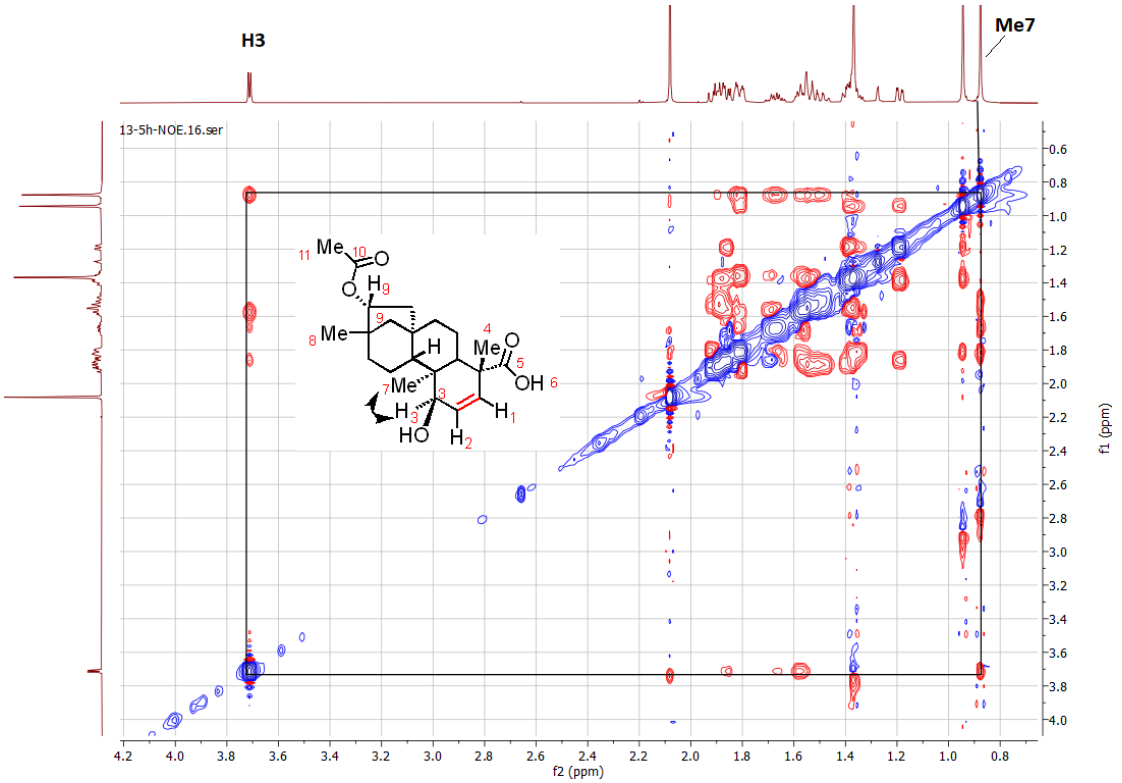
HMBC-2 of Compound 5h:



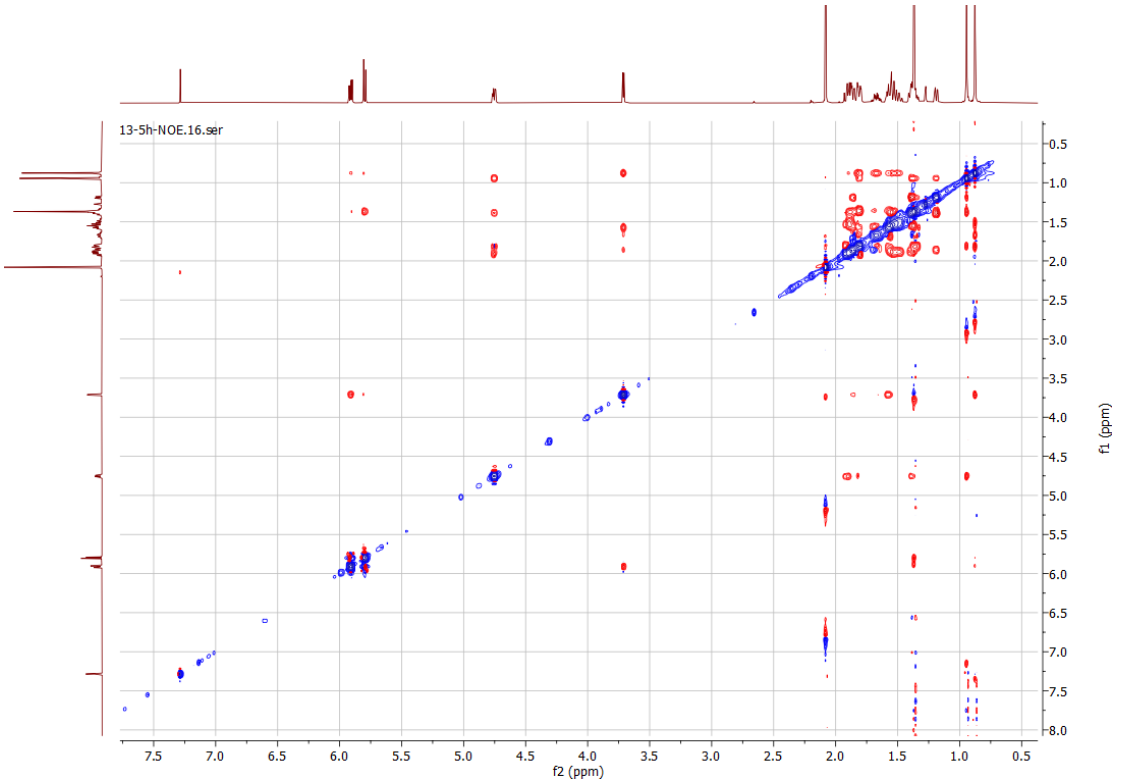
HSQC of Compound 5h:



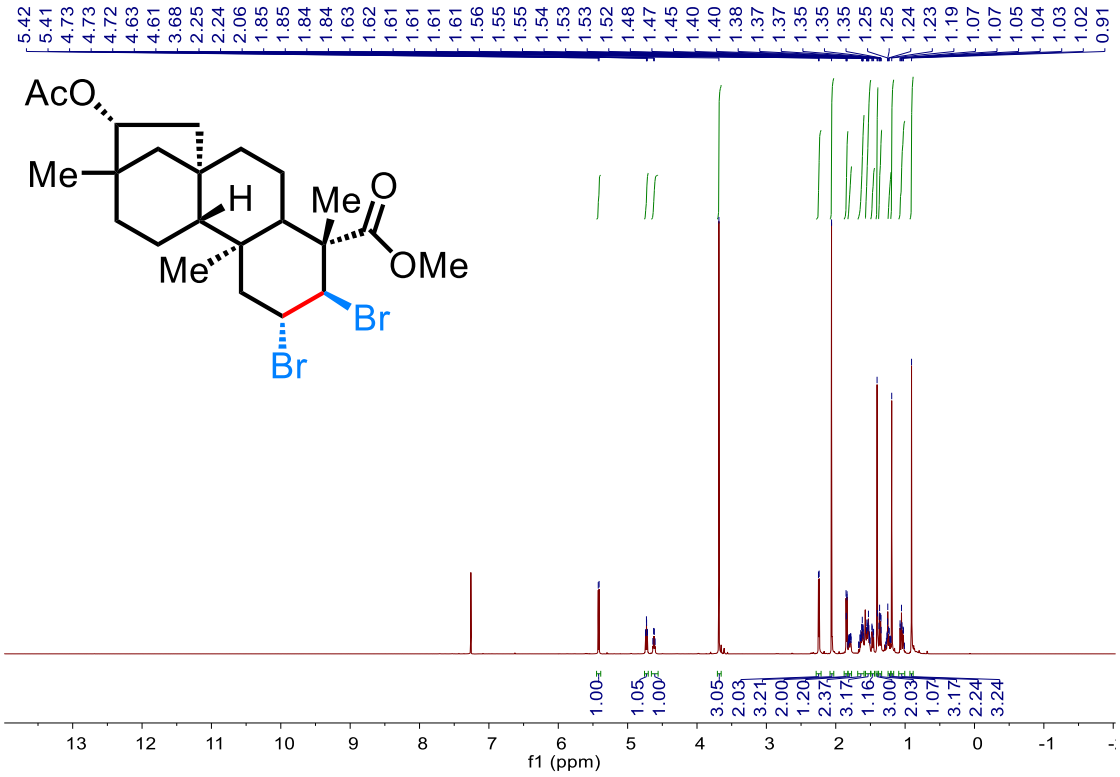
NOE of Compound 5h:



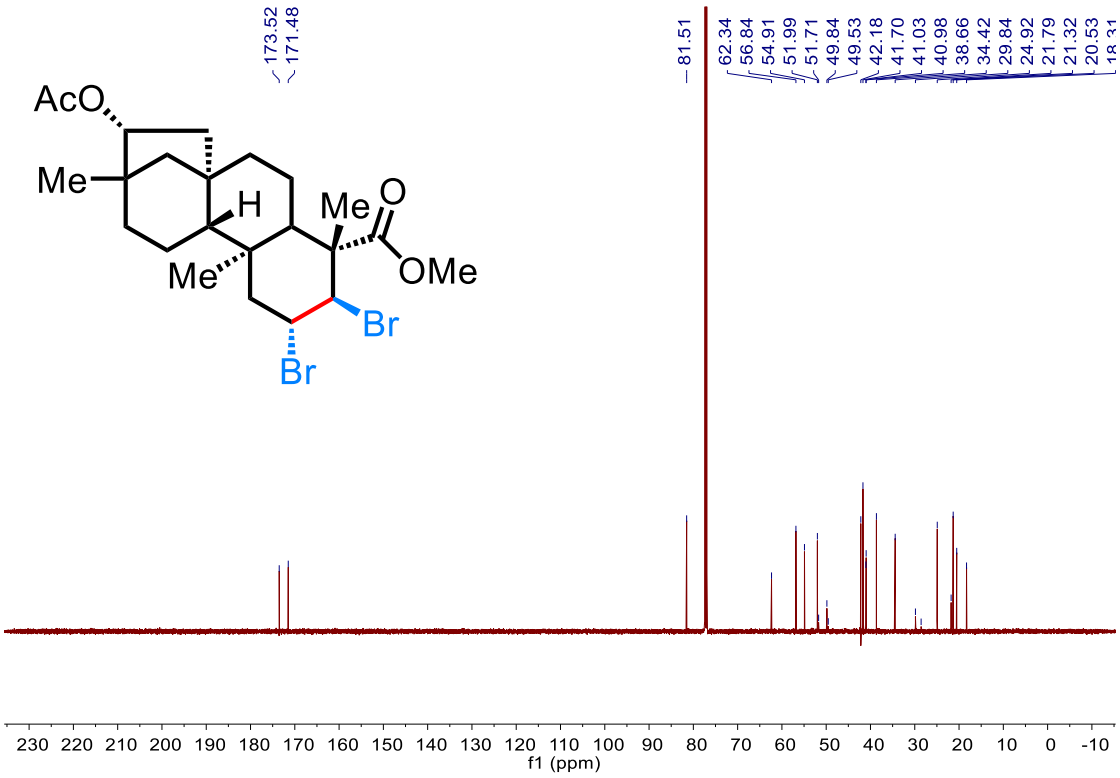
NOE of Compound 5h (full spectrum):



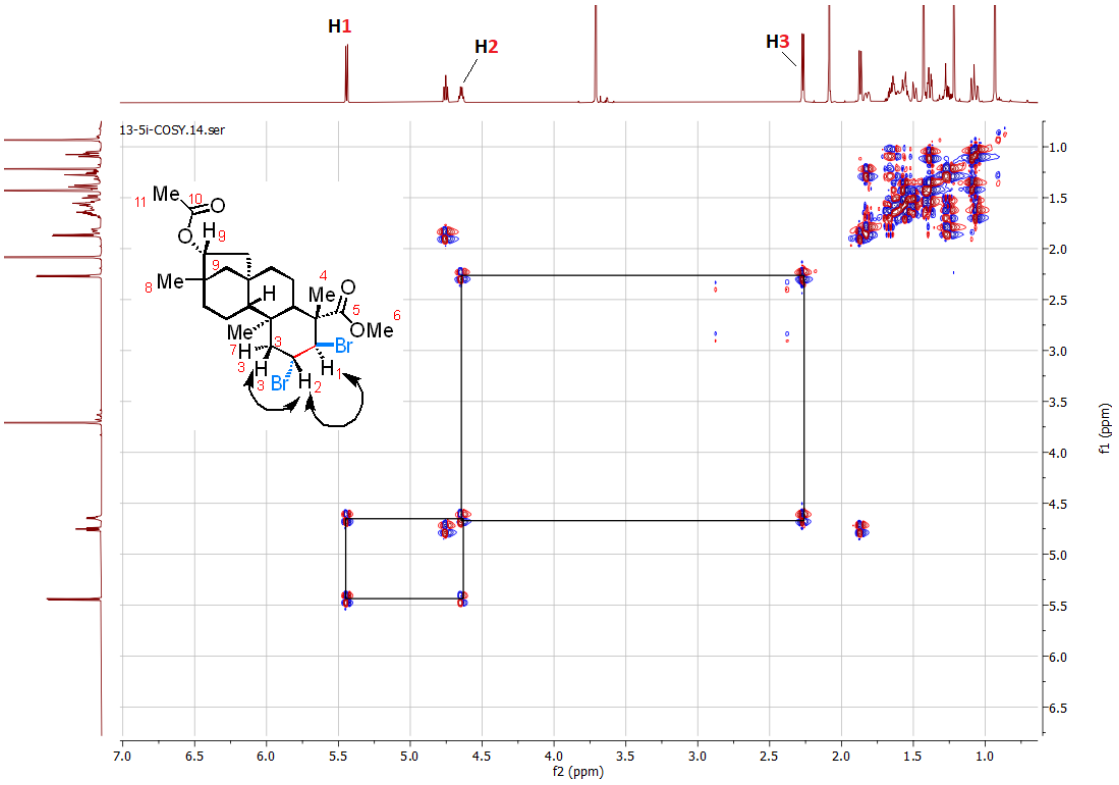
^{1}H NMR of Compound 5i:



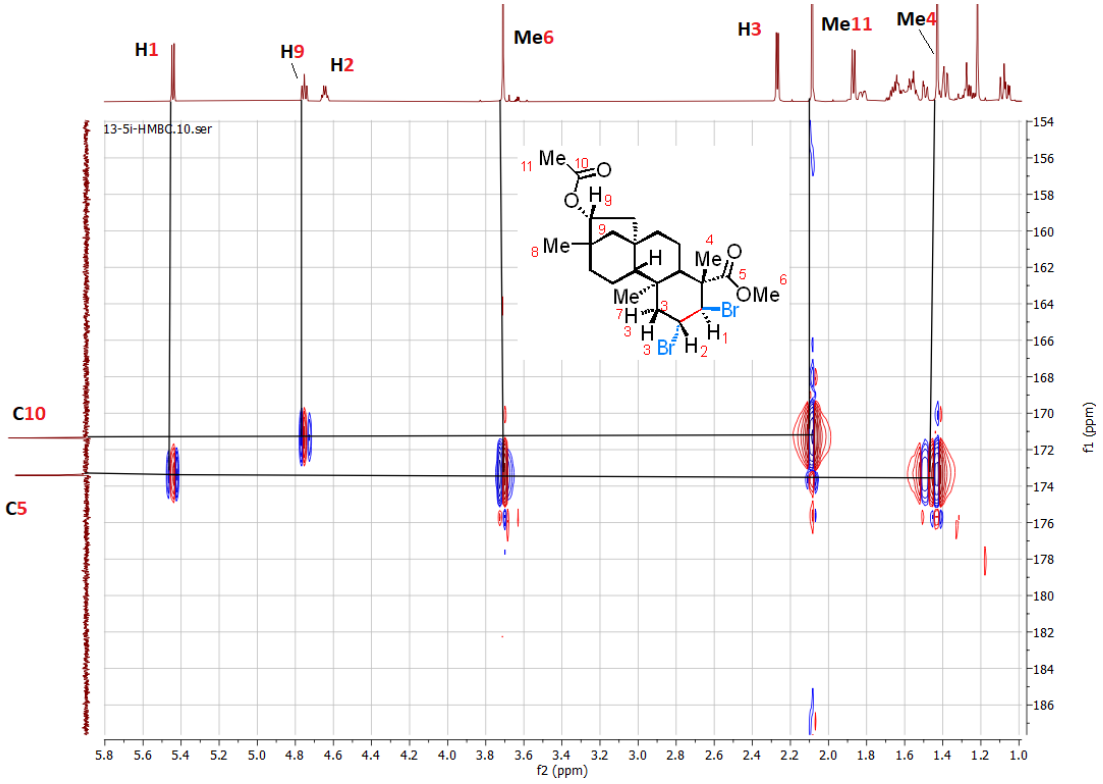
^{13}C NMR of Compound 5i:



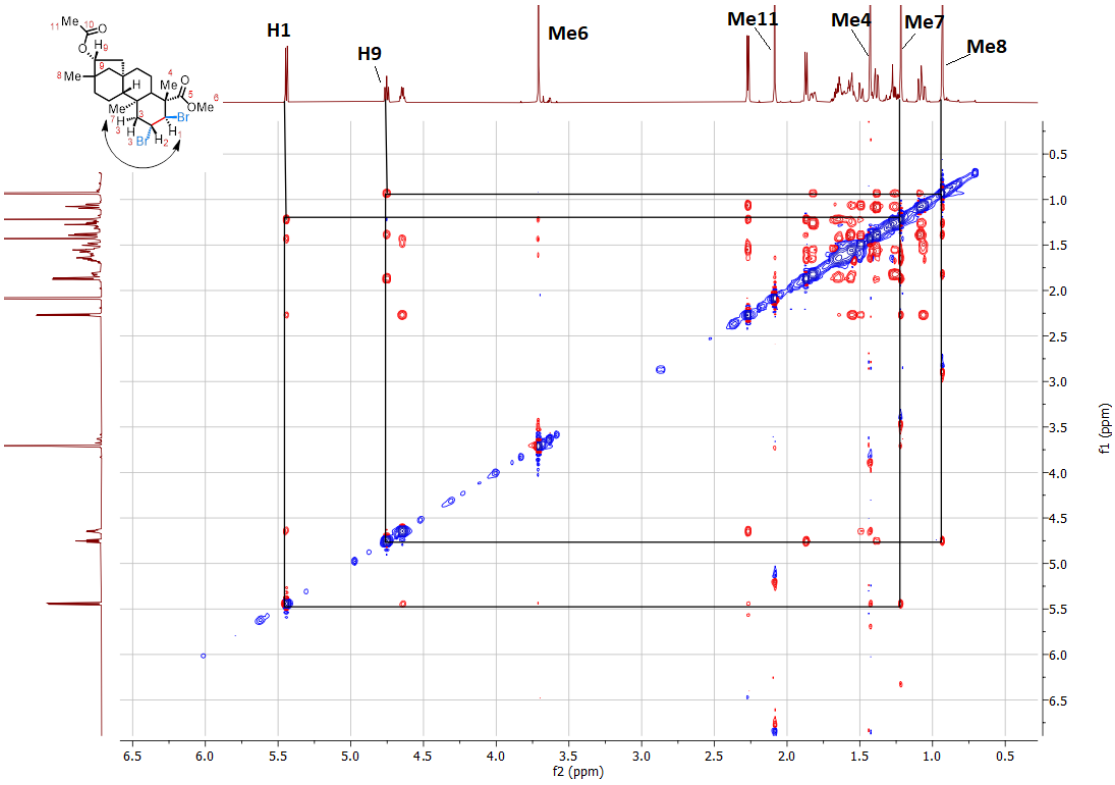
COSY of Compound 5i:



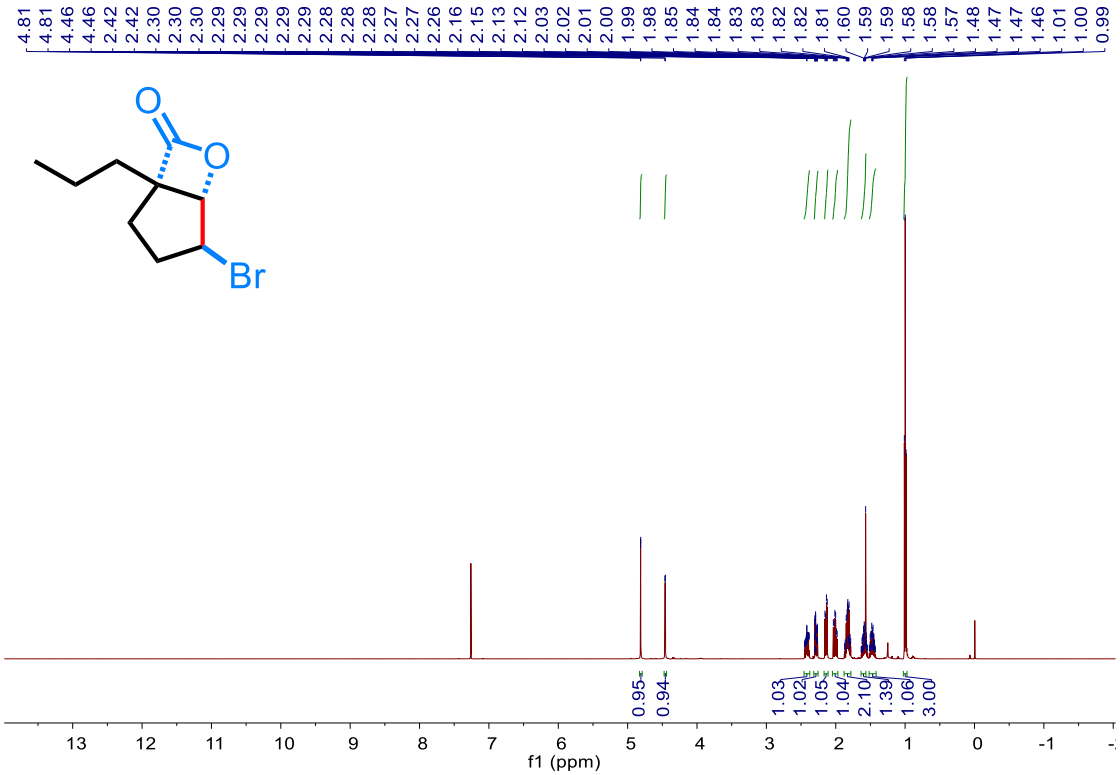
HMBC of Compound 5i:



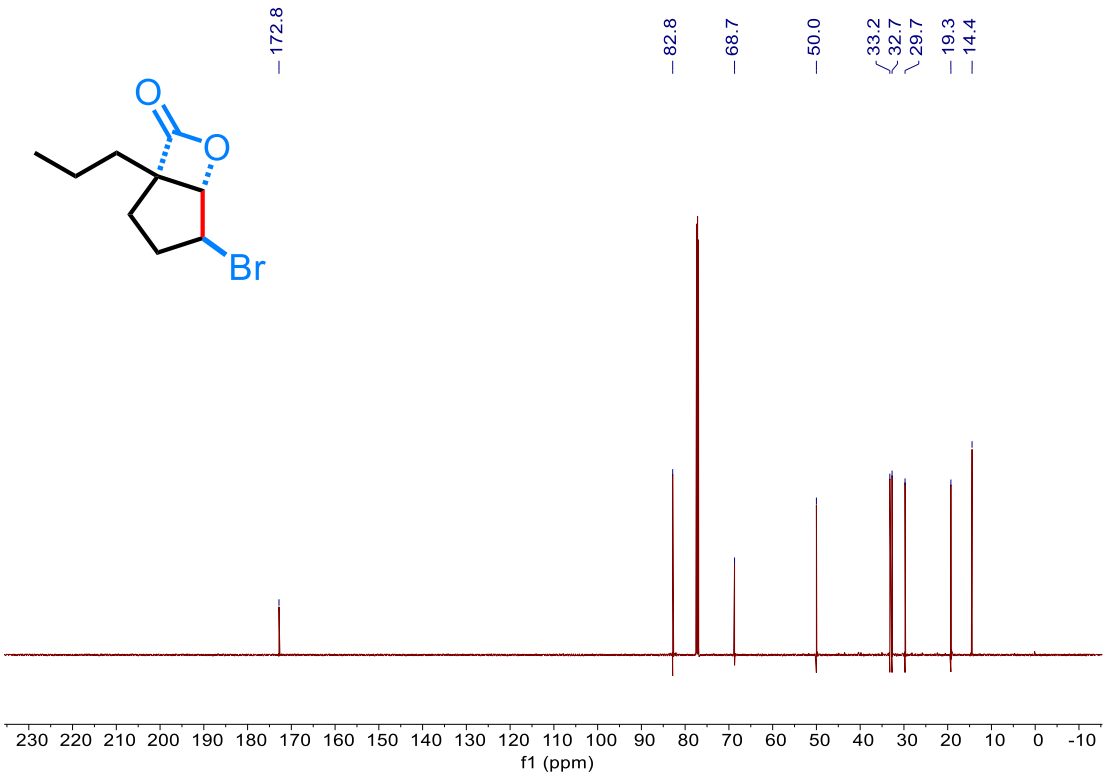
NOE of Compound 5i:



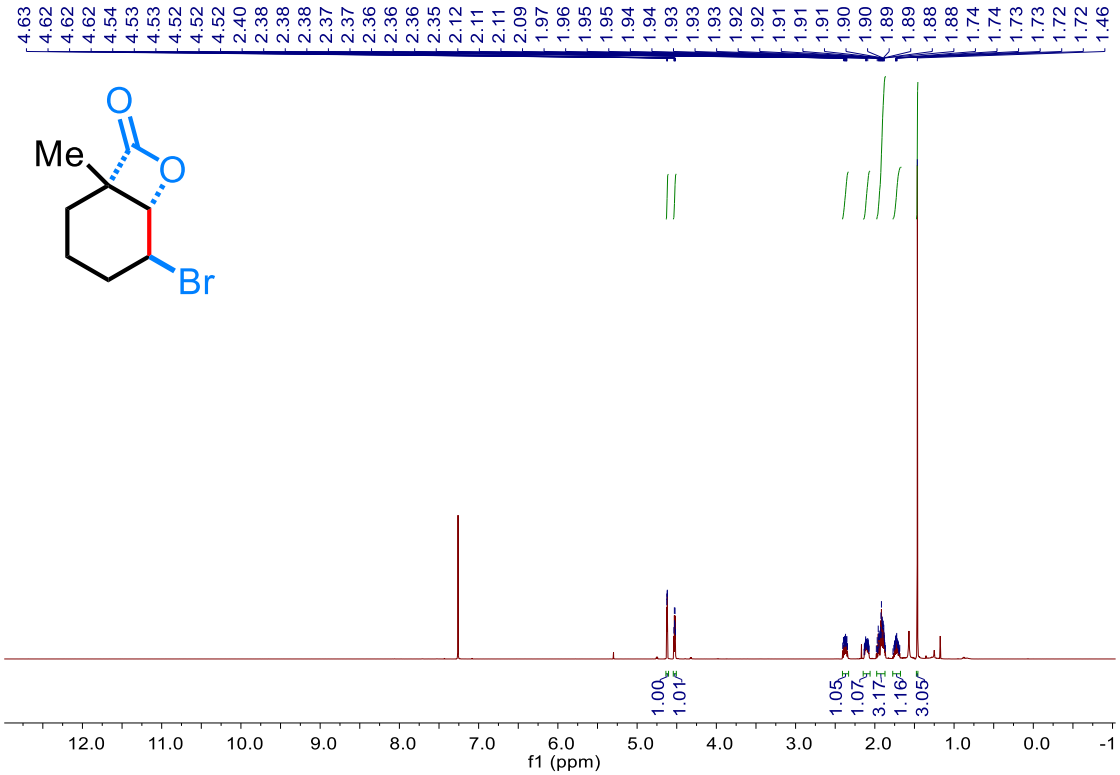
^{1}H NMR of Compound 6a:



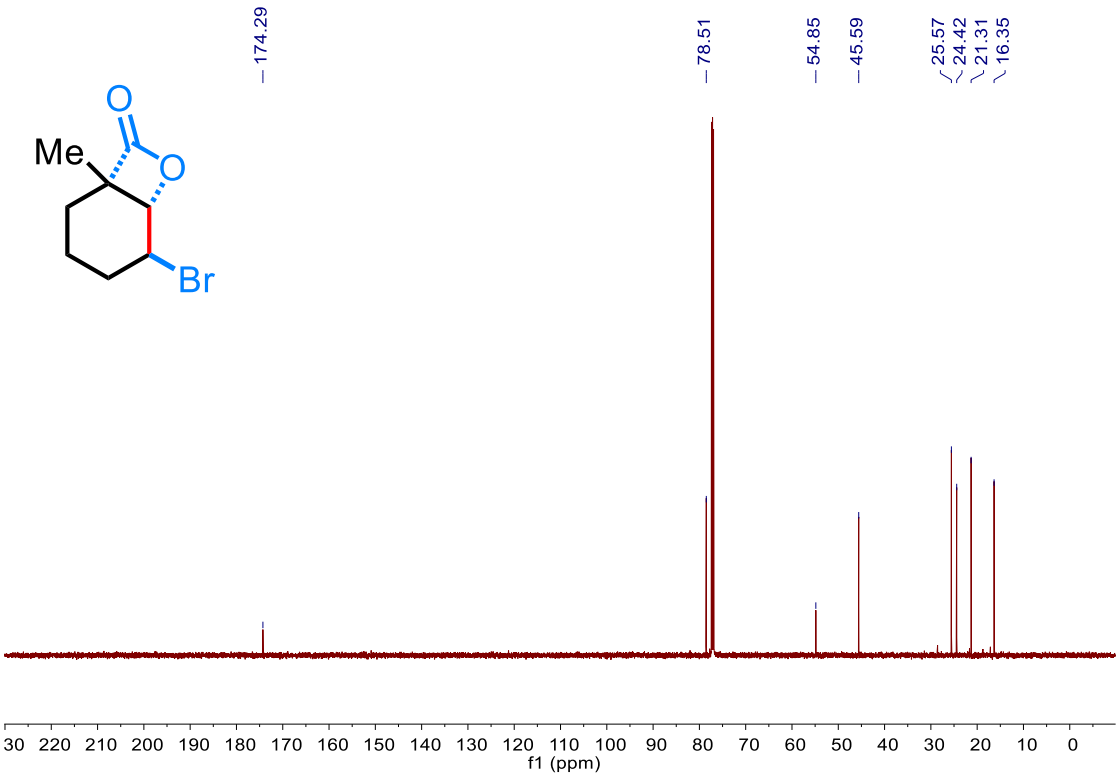
^{13}C NMR of Compound 6a:



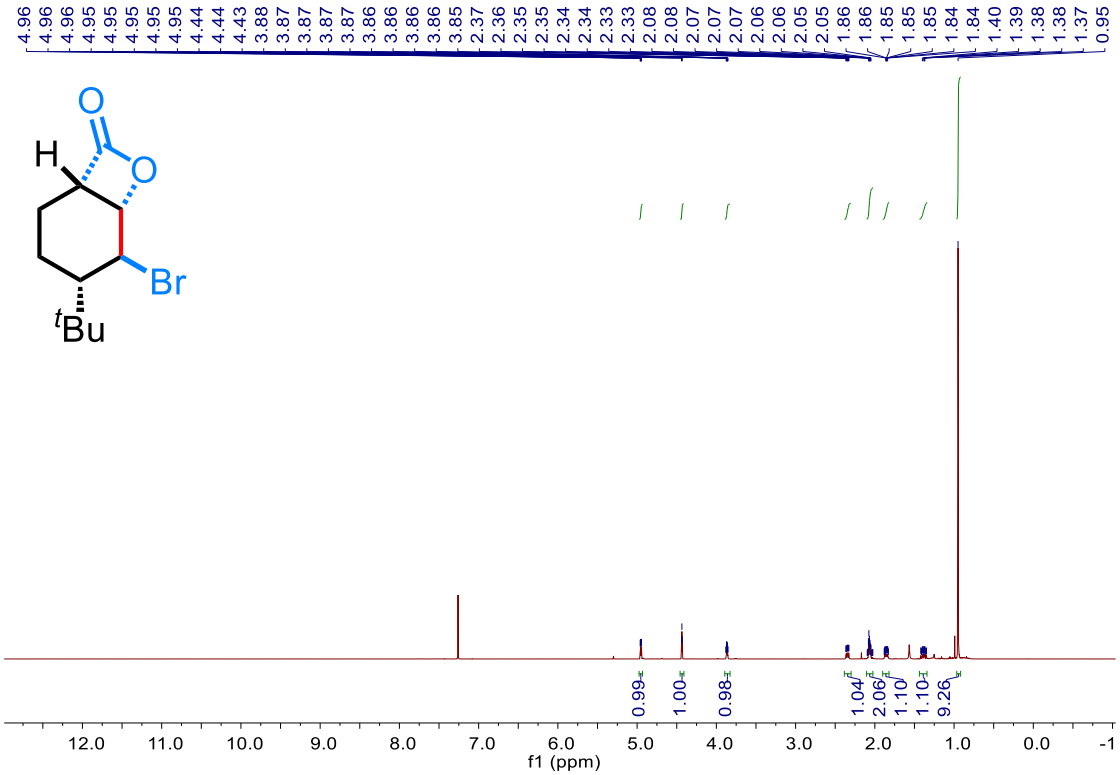
^{1}H NMR of Compound 6b:



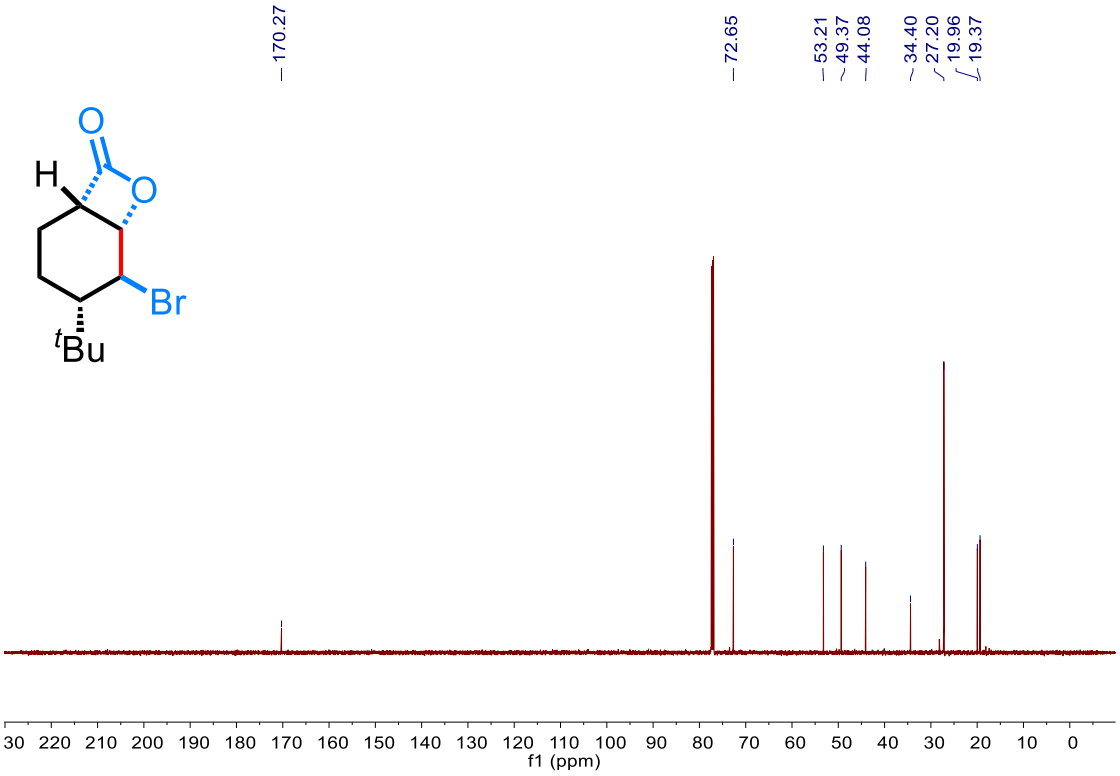
^{13}C NMR of Compound 6b:



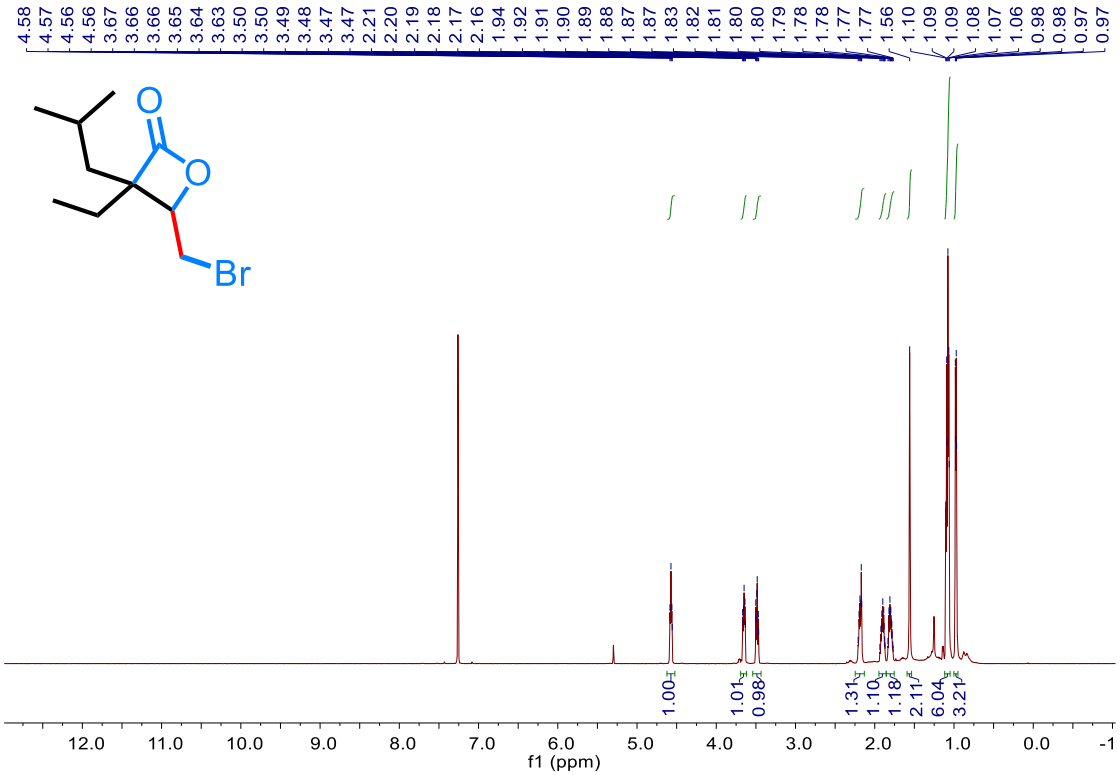
^{1}H NMR of Compound 6c:



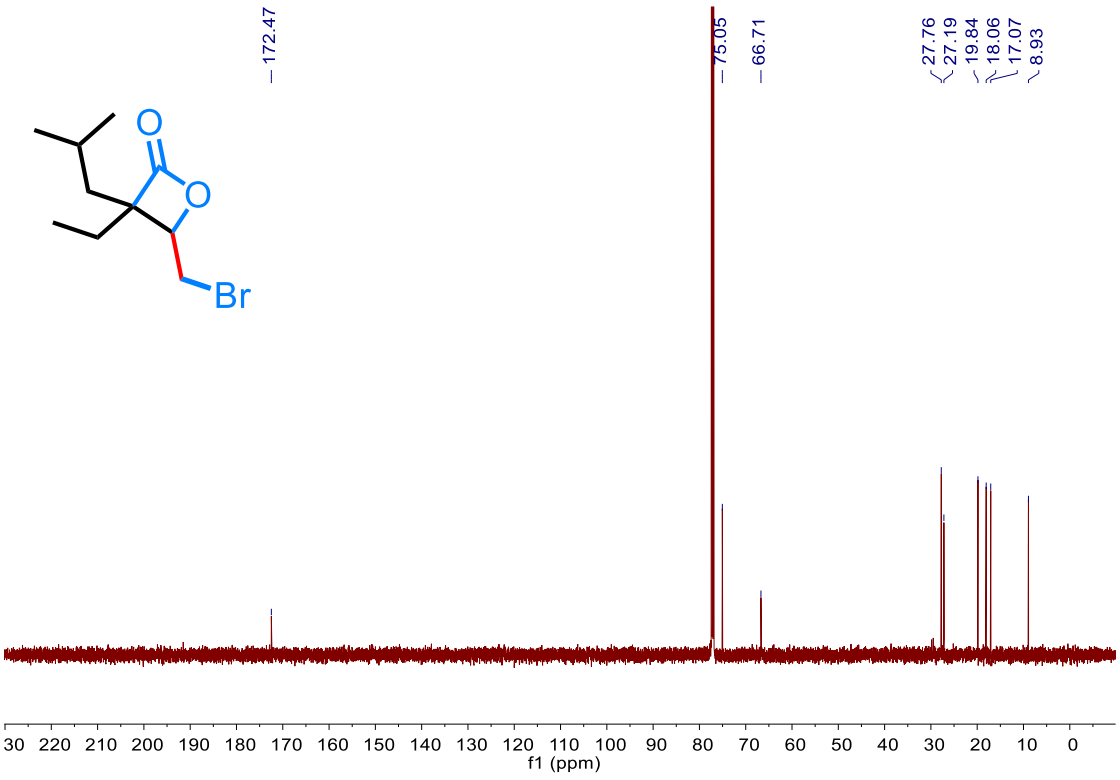
^{13}C NMR of Compound 6c:



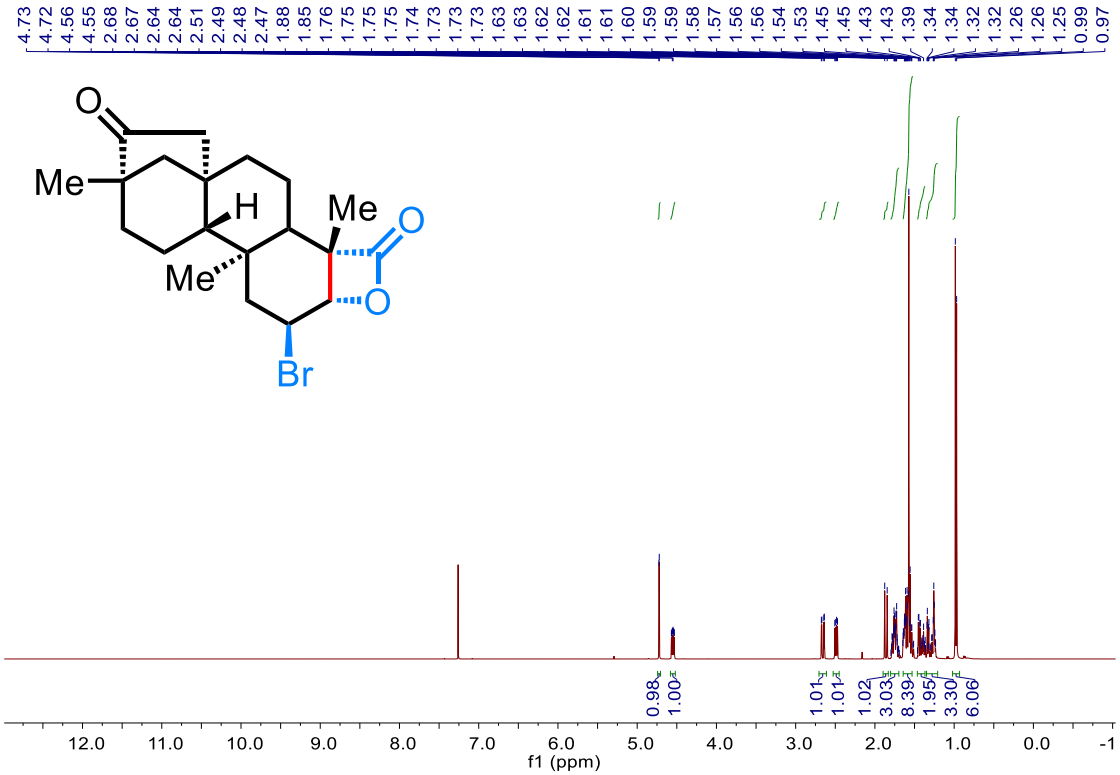
^{1}H NMR of Compound 6d:



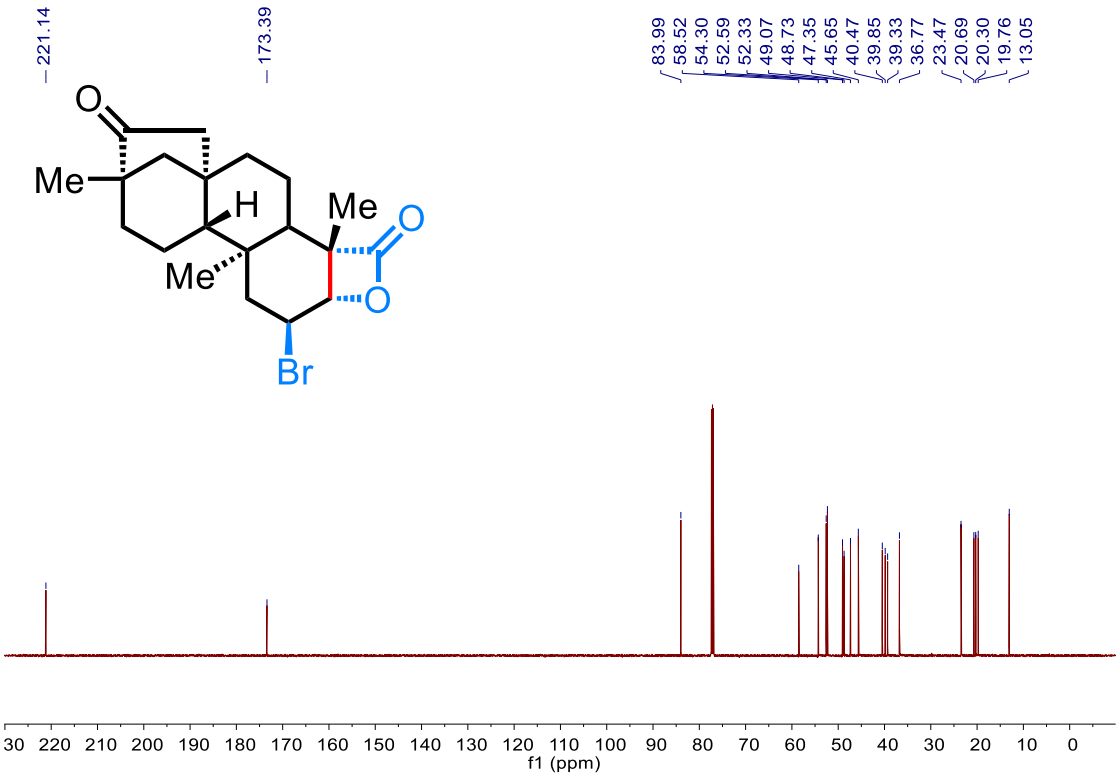
^{13}C NMR of Compound 6d:



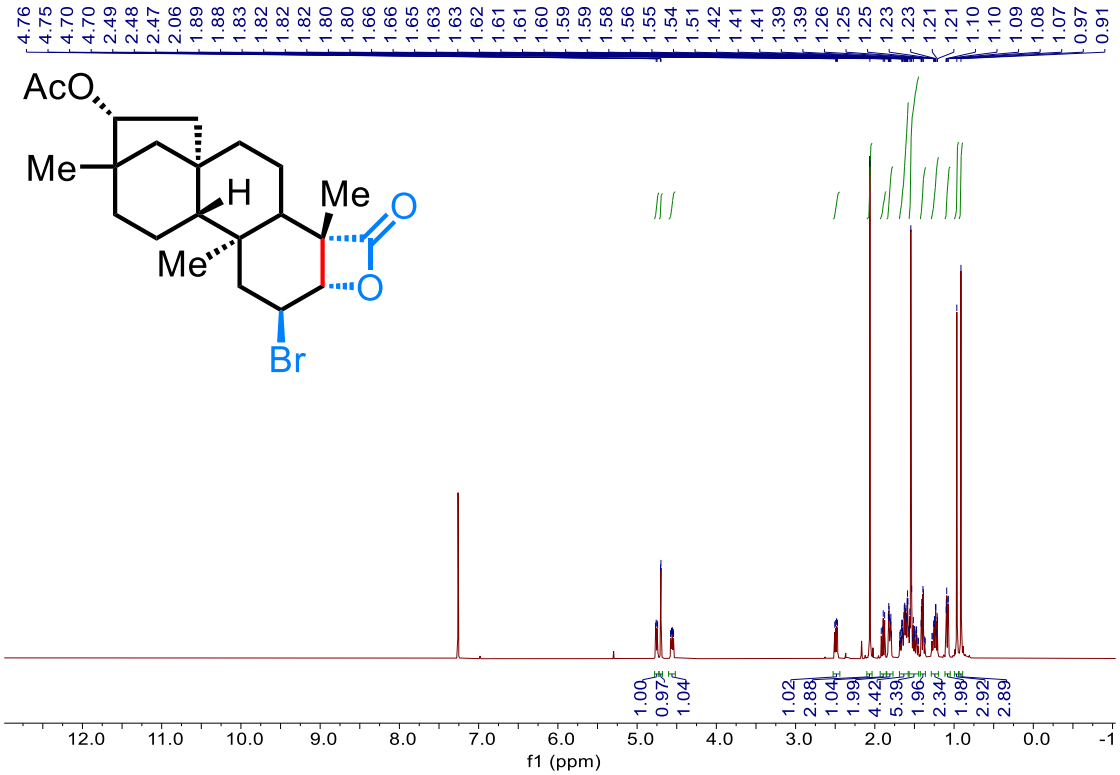
^{1}H NMR of Compound 6e:



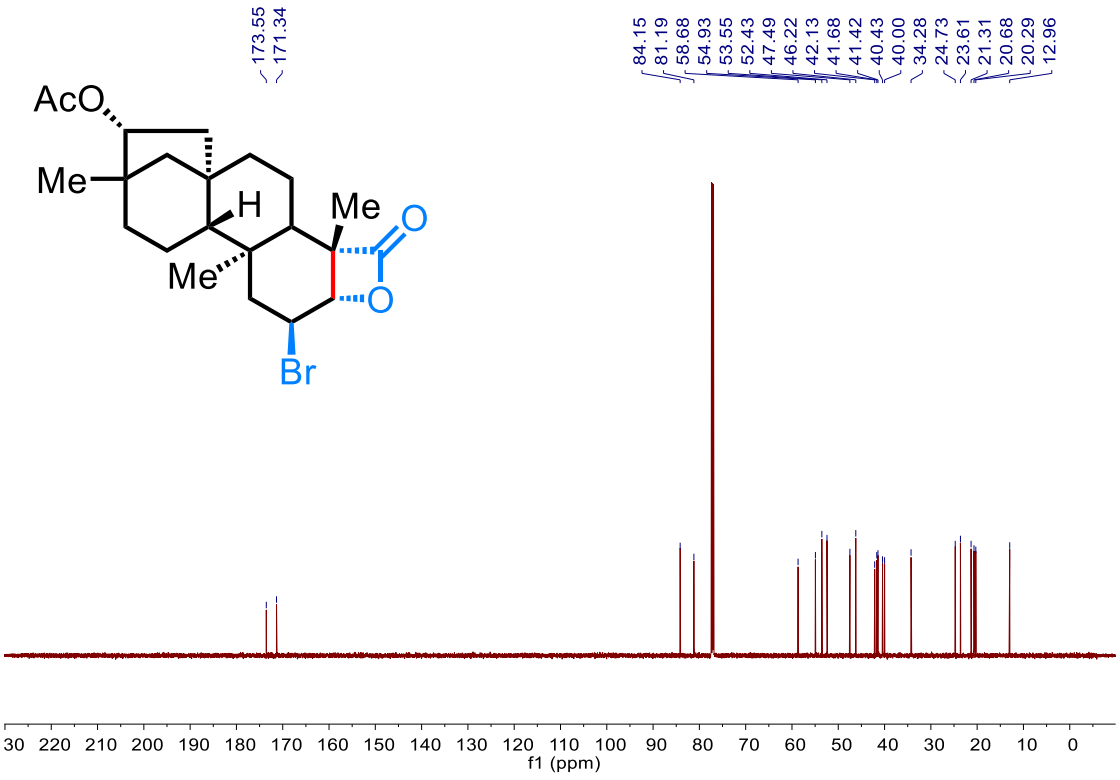
^{13}C NMR of Compound 6e:



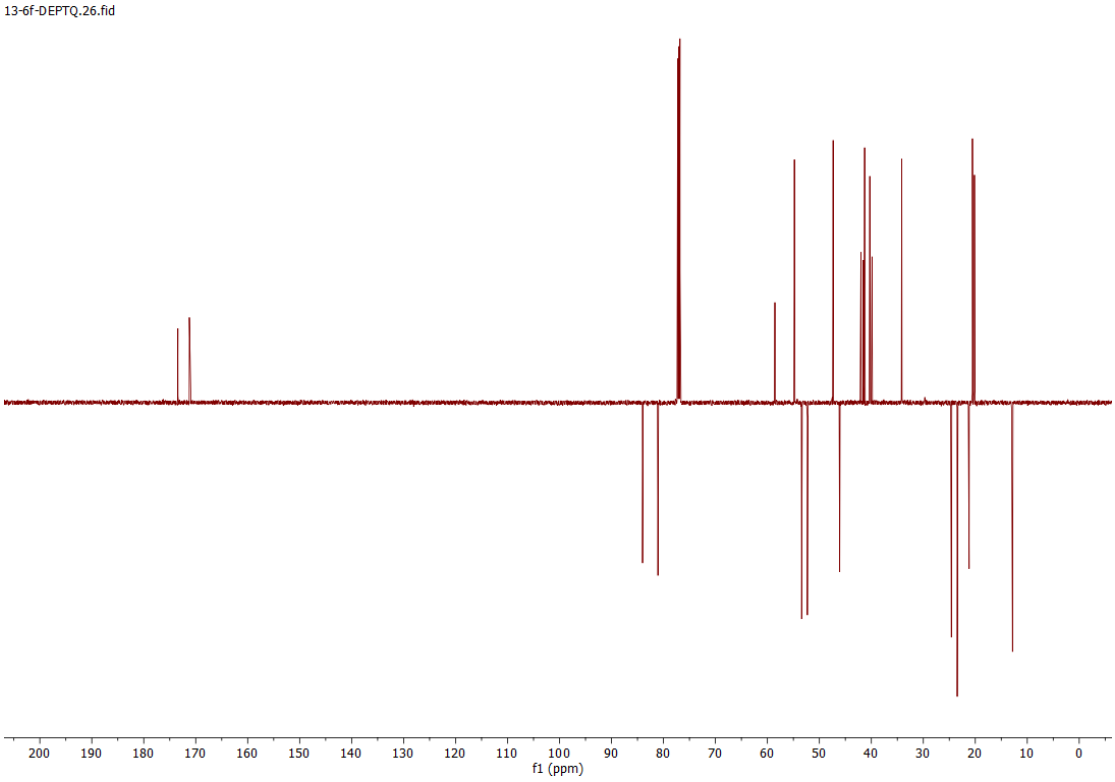
^{1}H NMR of Compound 6f:



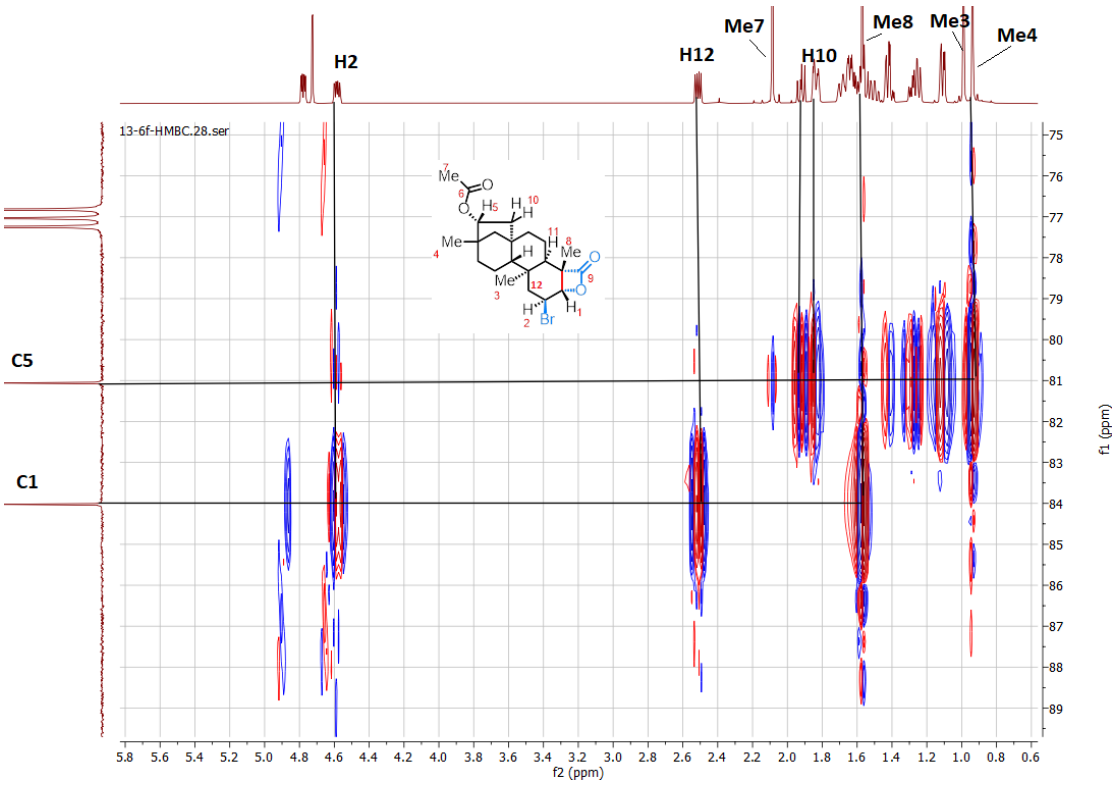
^{13}C NMR of Compound 6f:



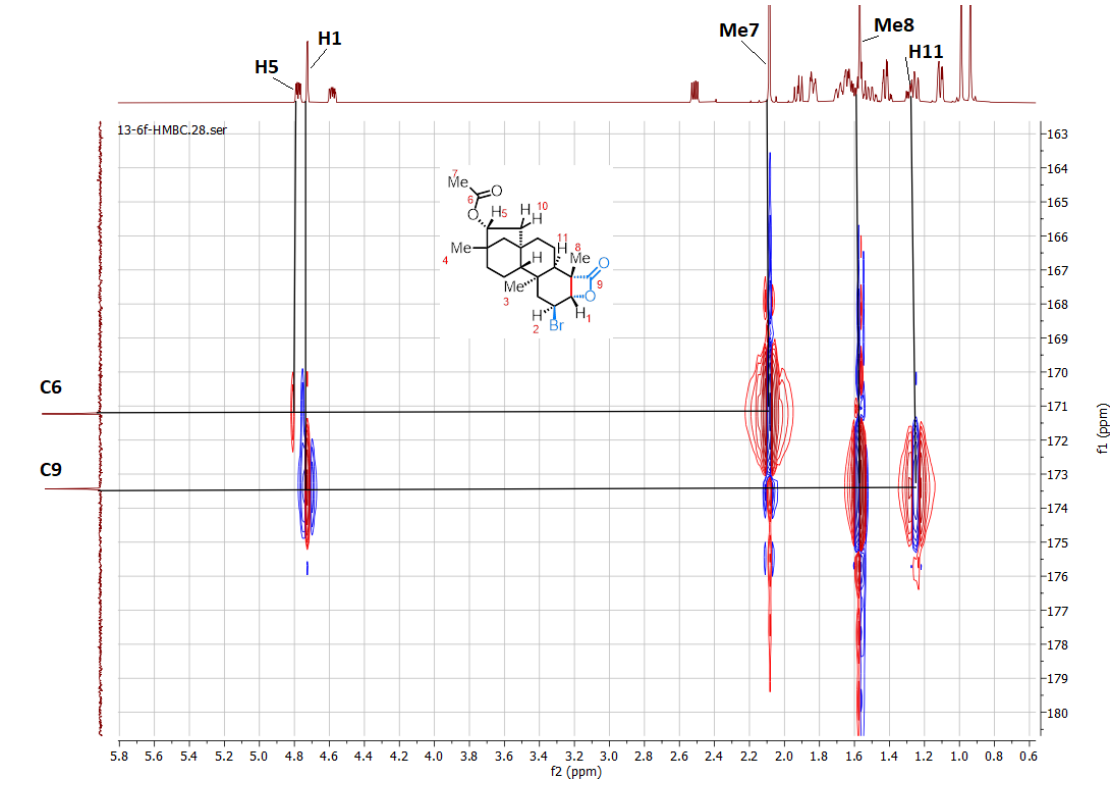
DEPTQ of Compound 6f:



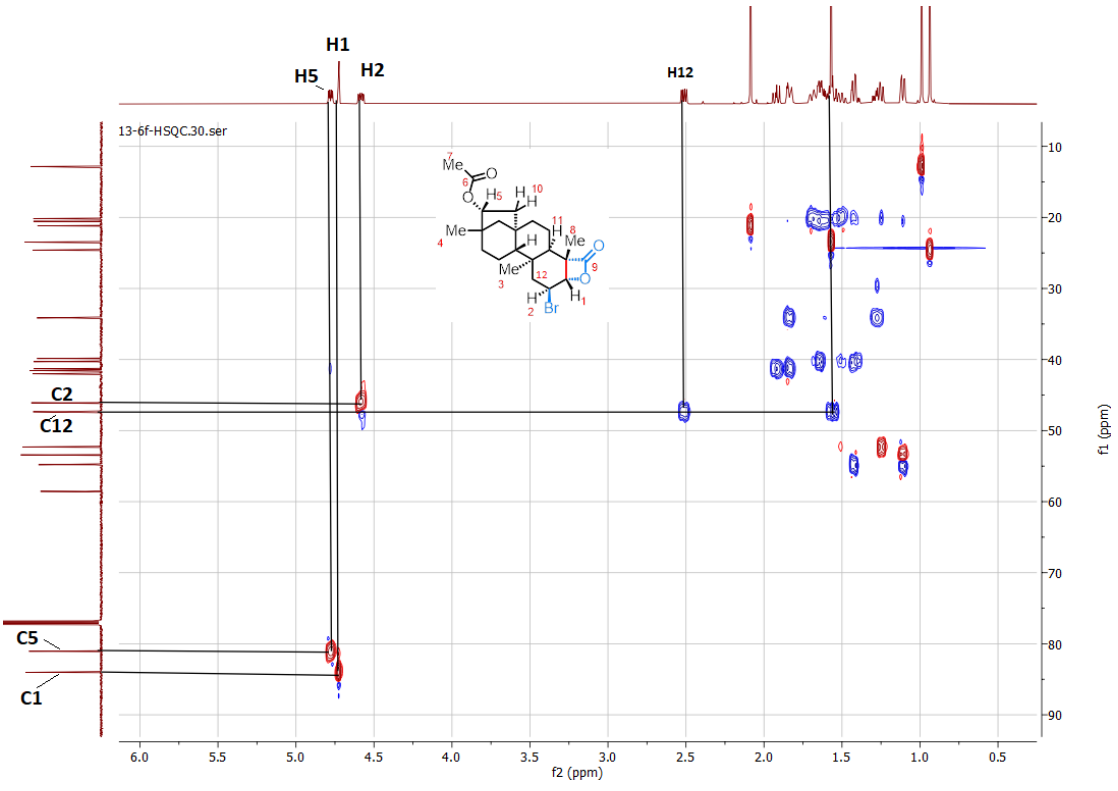
HMBC-1 of Compound 6f:



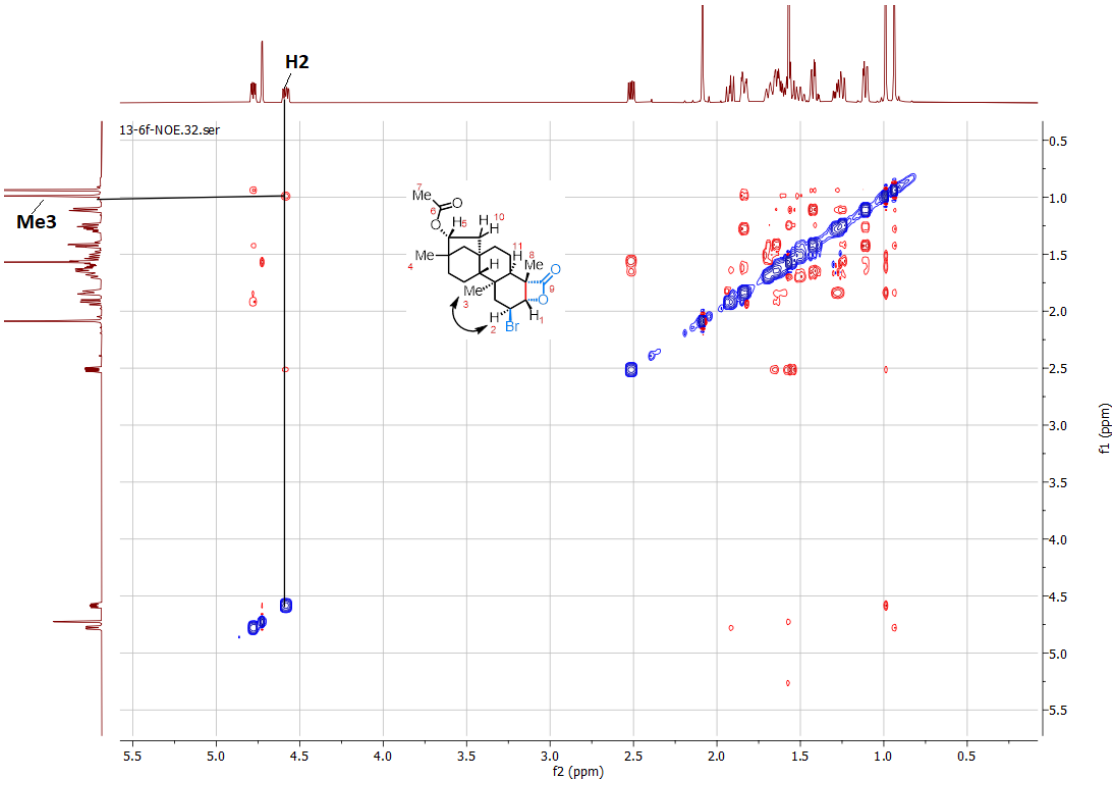
HMBC-2 of Compound 6f:



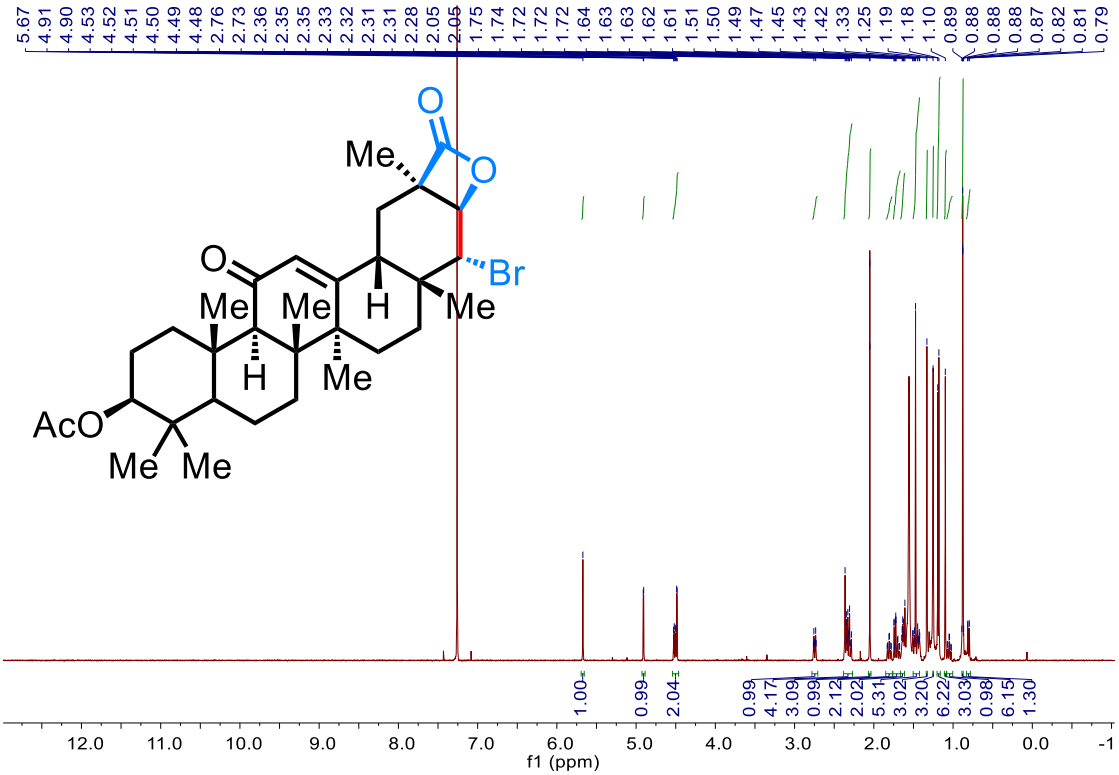
HSQC of Compound 6f:



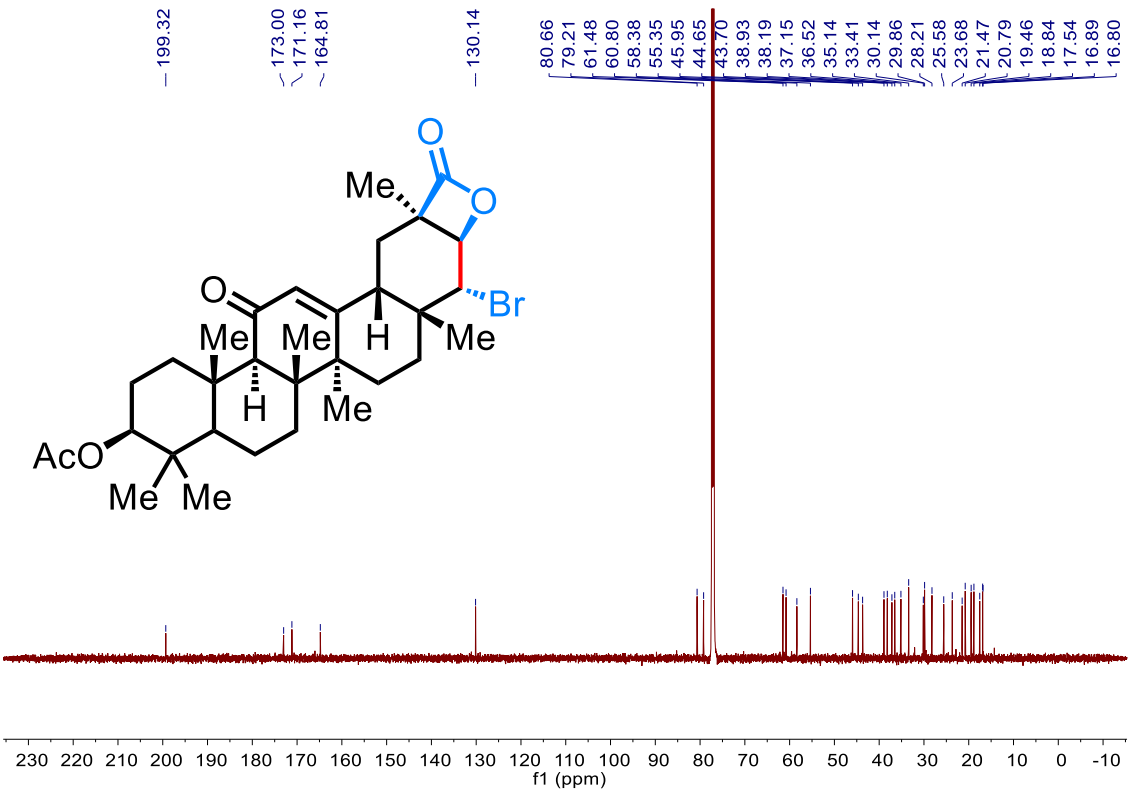
NOE of Compound 6f:



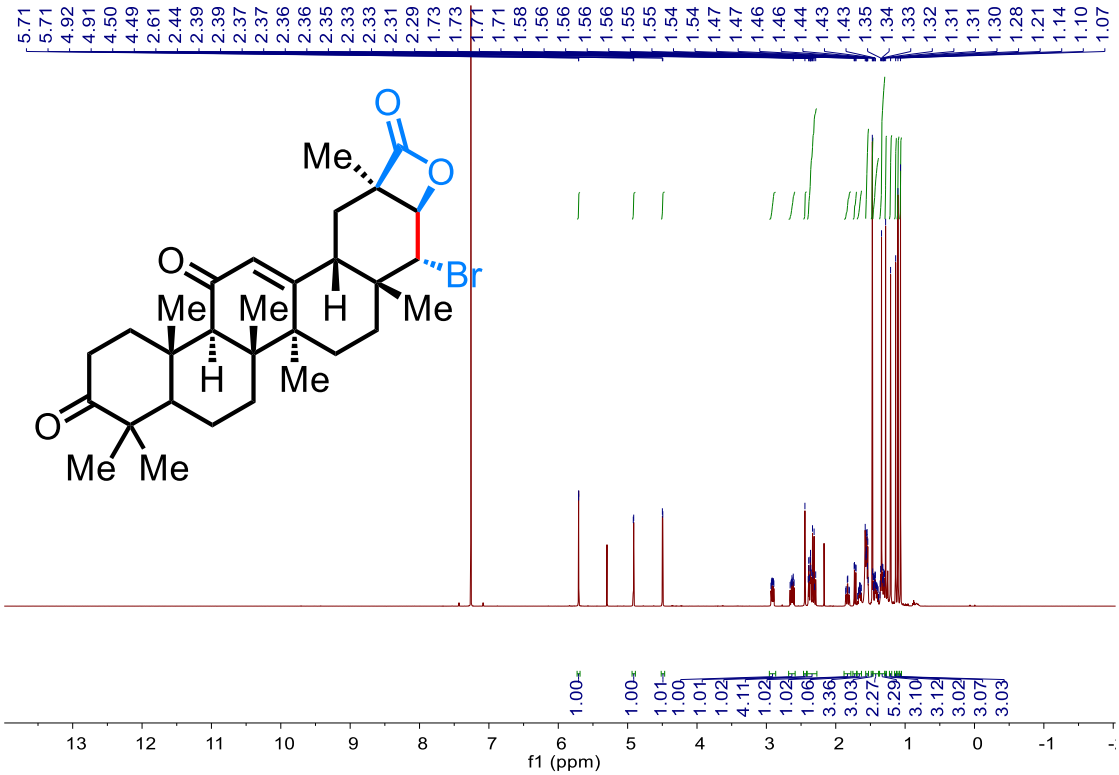
^{1}H NMR of Compound 6g:



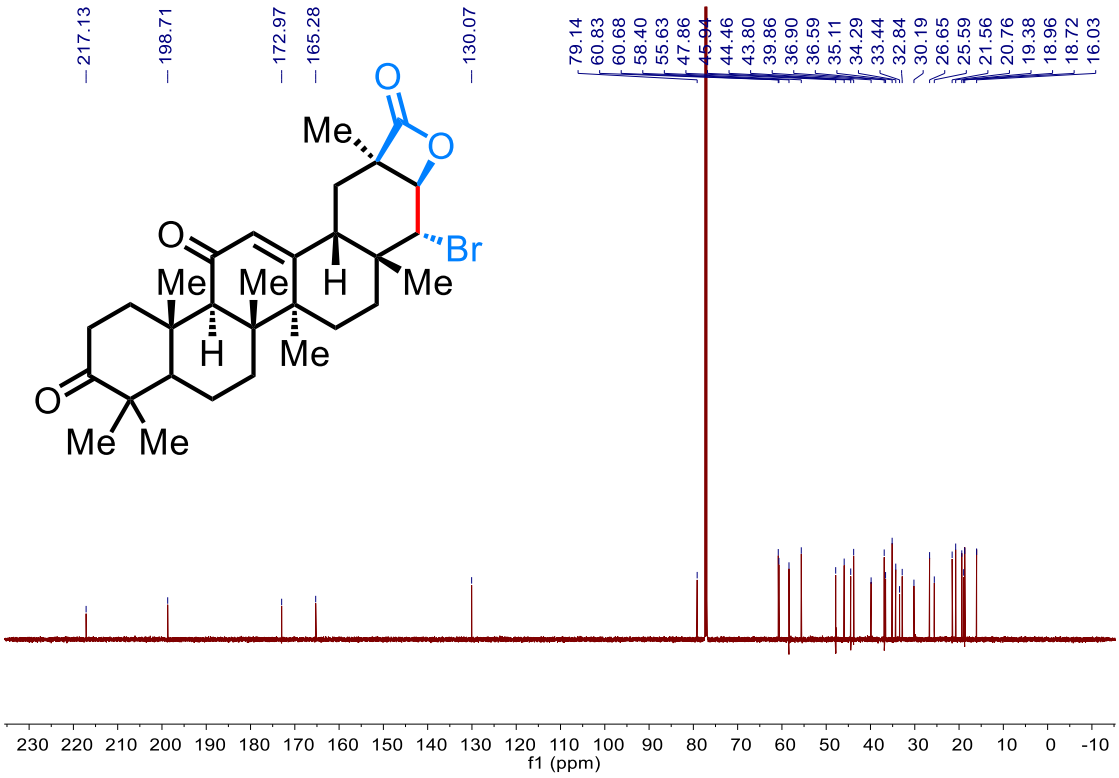
^{13}C NMR of Compound 6g:



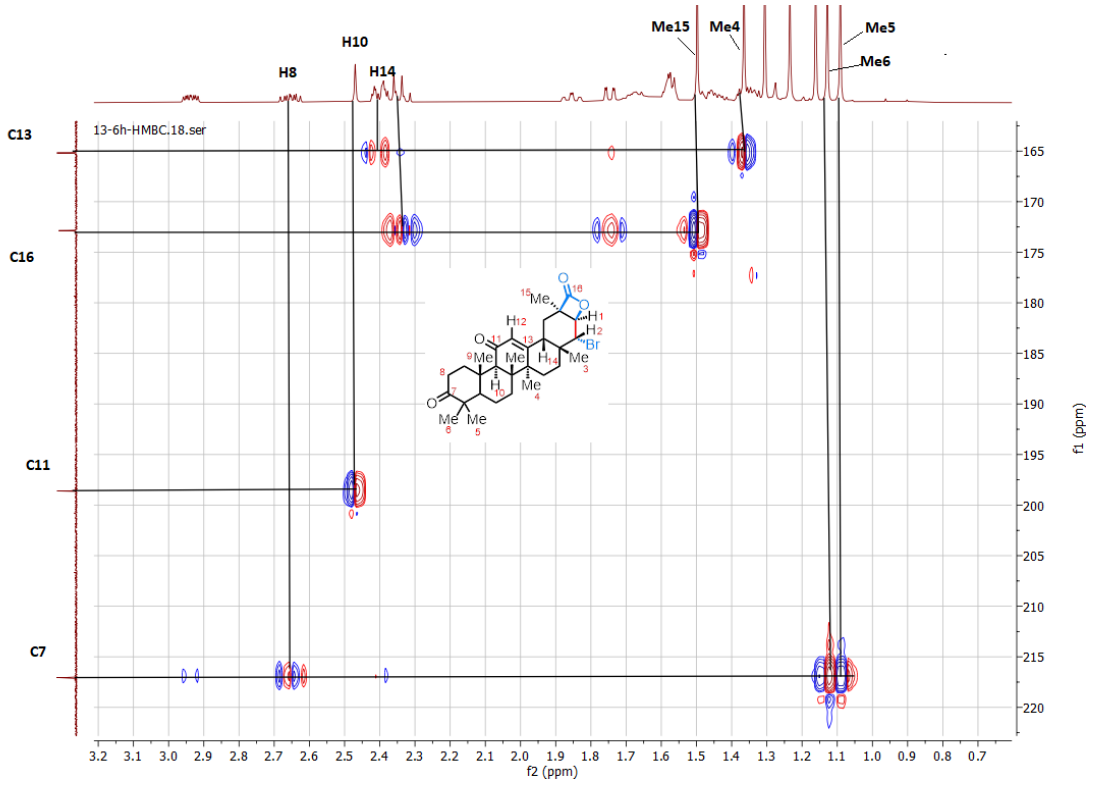
^{1}H NMR of Compound 6h:



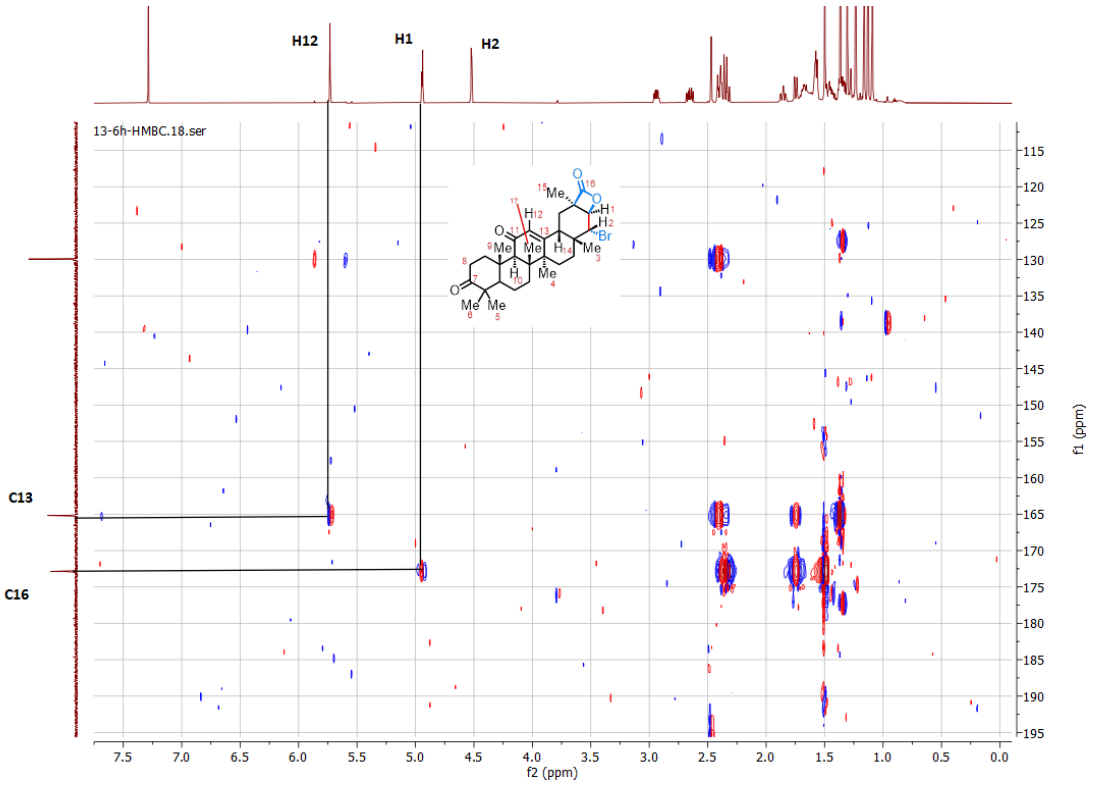
^{13}C NMR of Compound 6h:



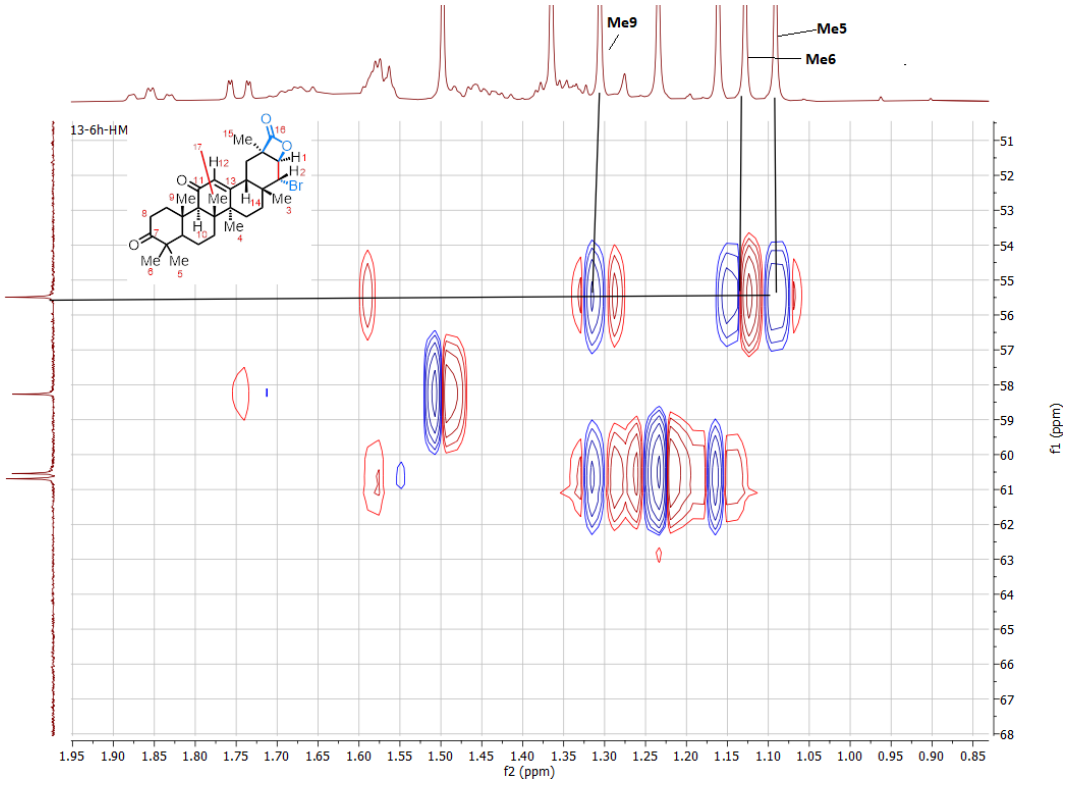
HMBC-1 of Compound 6h:



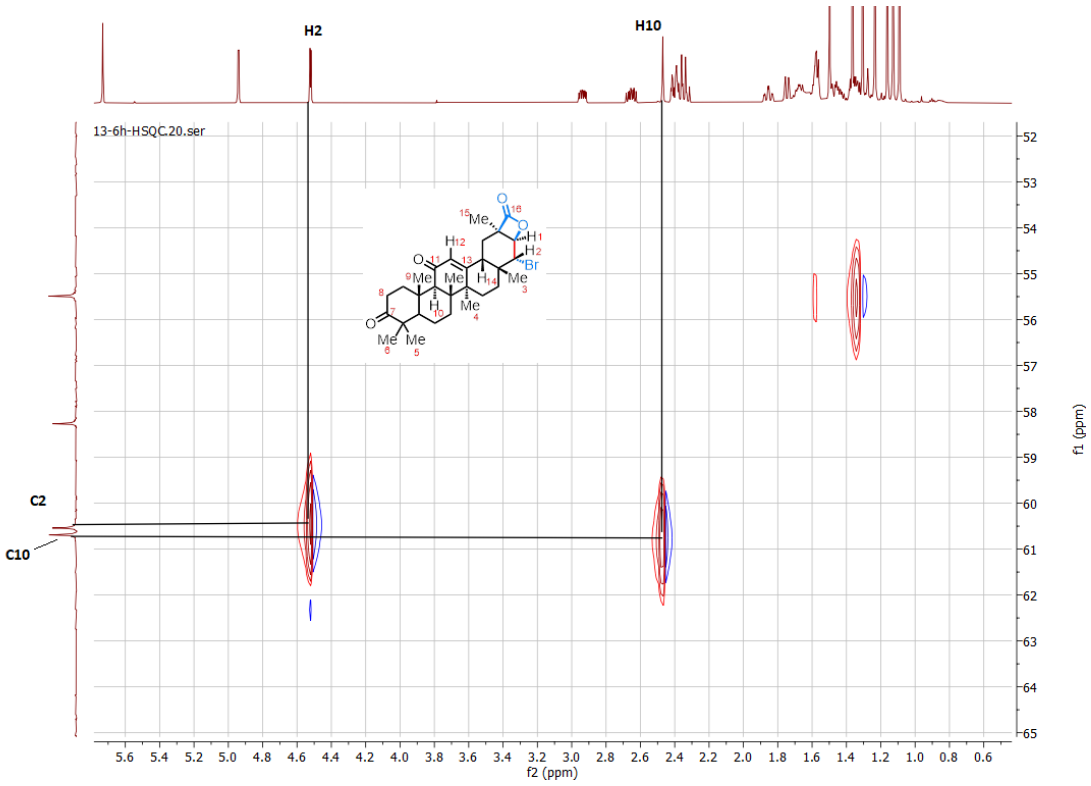
HMBC-2 of Compound 6h:



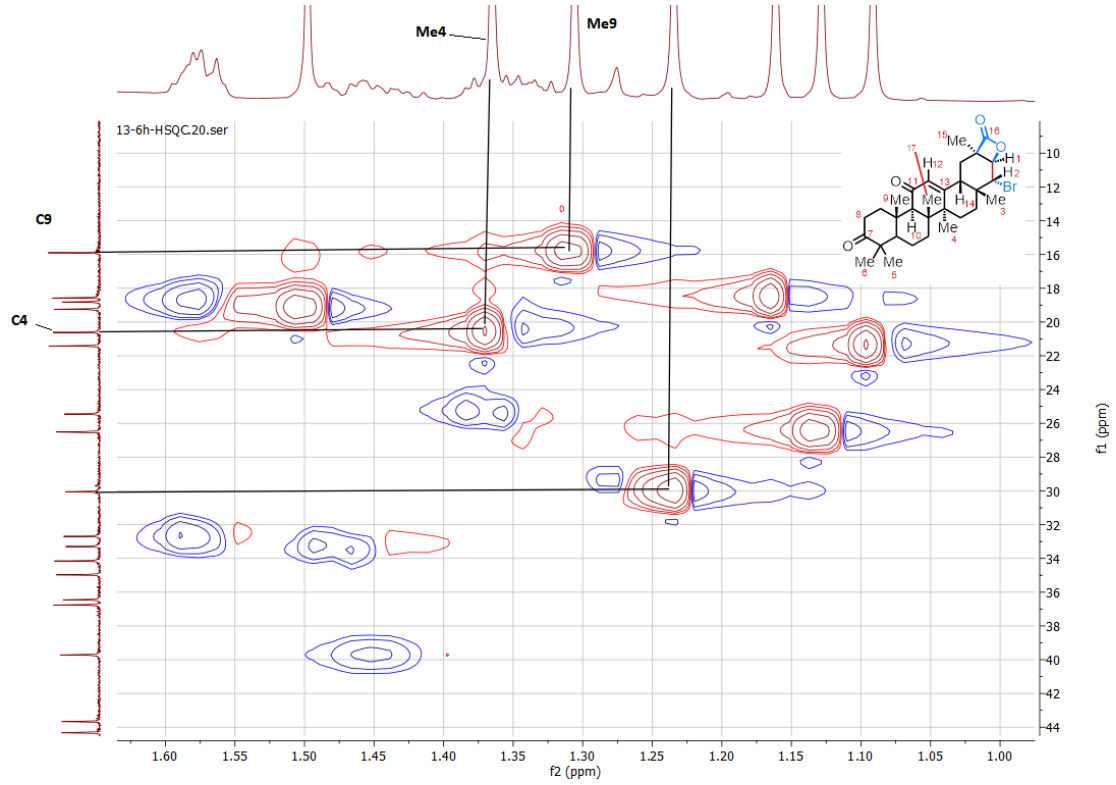
HMBC-3 of Compound 6h:



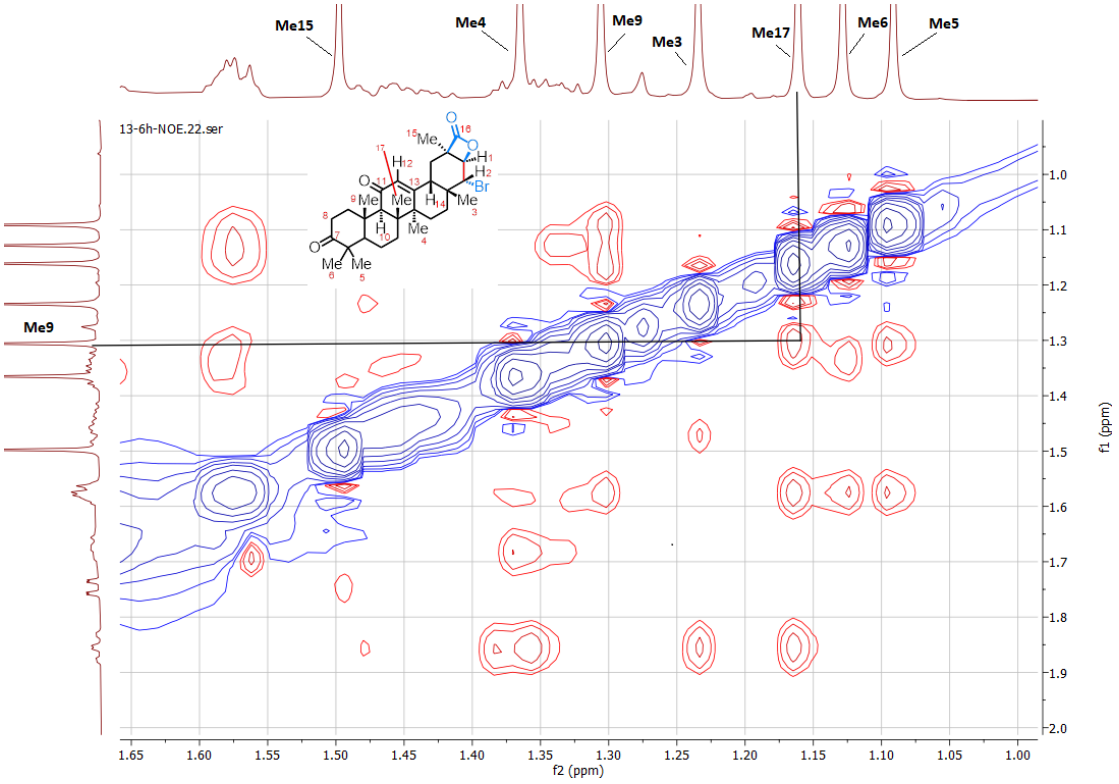
HSQC of Compound 6h:



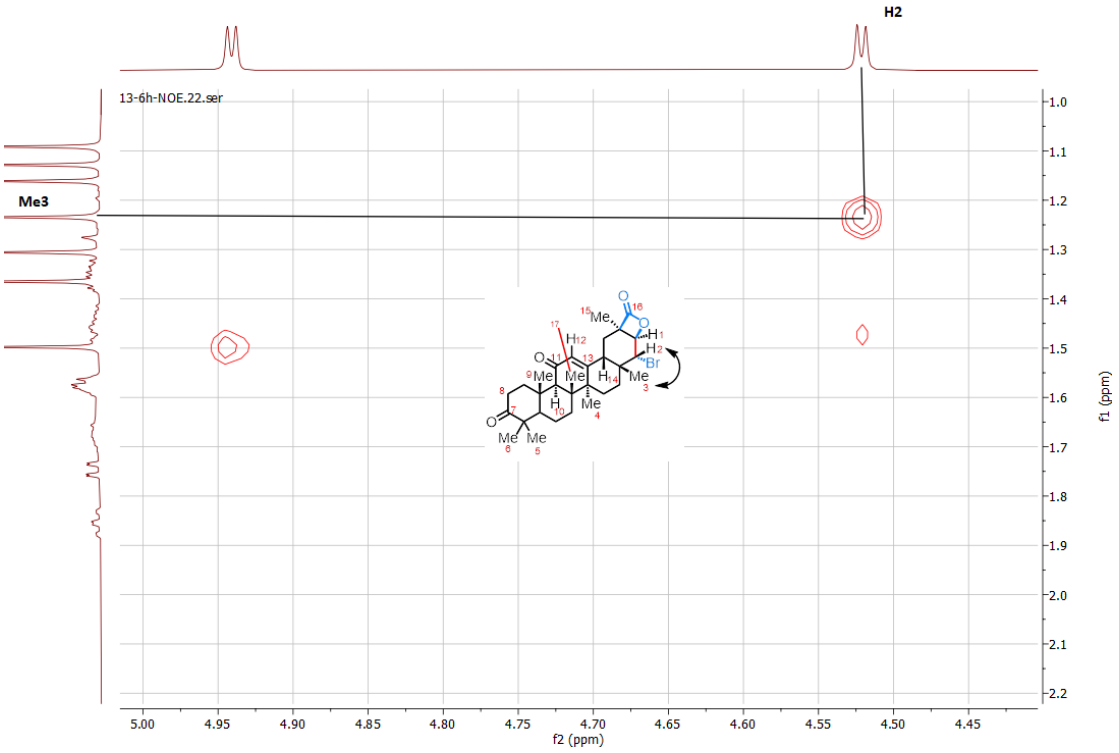
HSQC-2 of Compound 6h:



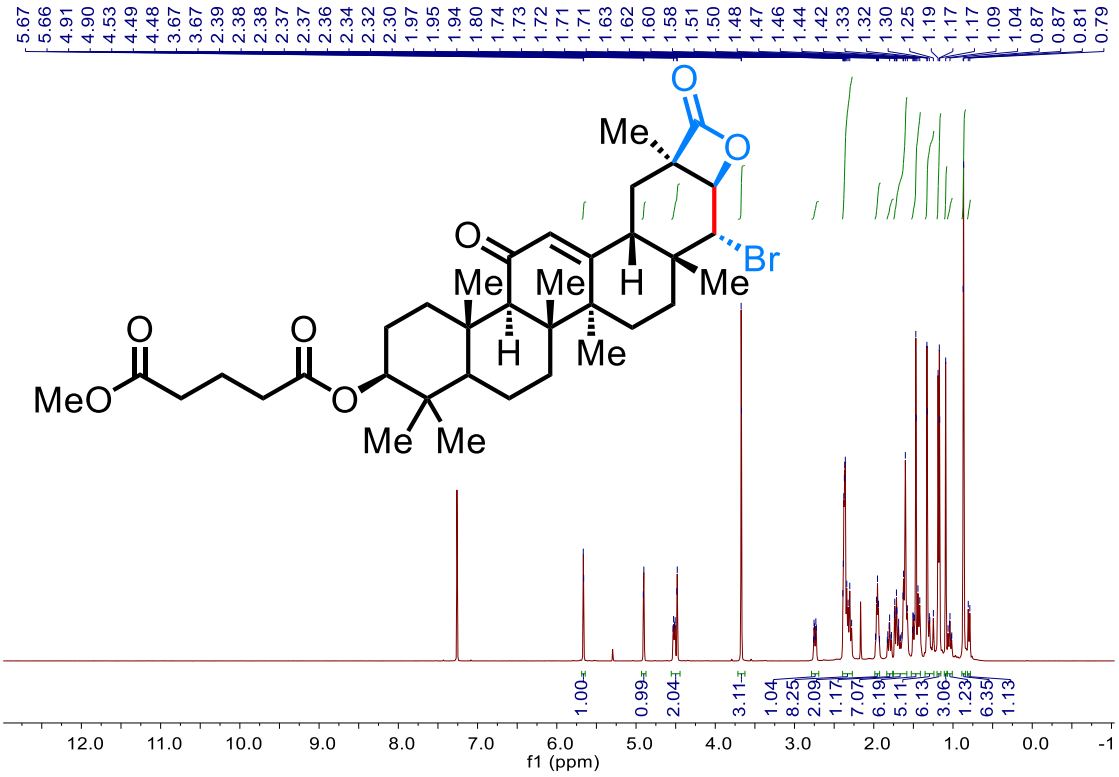
NOE-1 of Compound 6h:



NOE-2 of Compound 6h:



^{1}H NMR of Compound 6i:



^{13}C NMR of Compound 6i: