◙Supporting Information

A Direct Route to Six and Seven Membered Lactones *via*γ-C(sp^3)–H Activation: A Simple Protocol to Build Molecular Complexity

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General Consideration:

Reagent Information. Unless otherwise stated, all reactions were carried out in screw cap reaction tubes. All the solvents were bought from commercial sources and were used without further purification Palladium salts and olefins were purchased from Aldrich and TCI-India. Silica gel (100–200 mesh) obtained from SRL Co. was used for column chromatography. Products and starting materials were visualized on TLC plate (Merck, TLC silica gel 60 F254) using UV-light or by staining with $KMnO_4$ solution, followed by heating .A gradient elution using petroleum ether and ethyl acetate was performed, based on Merck aluminum TLC sheets (silica gel $60F_{254}$).

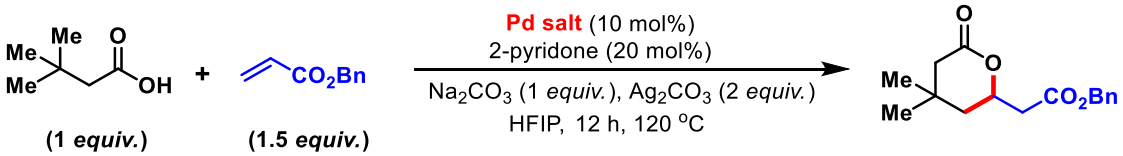
Analytical Information. All compounds are characterized by ^{1}H NMR, ^{13}C NMR spectroscopy, HR-MS and IR. Copies of the ^{1}H NMR, ^{13}C NMR and ^{19}F can be found in the Supporting Information. Unless otherwise stated, all Nuclear Magnetic Resonance spectra were recorded on a Bruker 500 MHz / 400 MHz instrument. All ^{1}H NMR experiments are reported in units, parts per million (ppm), and were measured relative to the signals for residual chloroform (7.26 ppm) in the deuterated solvent, unless otherwise stated. All ^{13}C NMR spectra were reported in ppm relative to deuterochloroform (77.230 ppm), unless otherwise stated, and all were obtained with ^{1}H decoupling. High-resolution mass spectra (HRMS) were recorded on a micro-mass ESI TOF (time of flight) mass spectrometer.In some cases, we observed inseparable non-cyclized form of the lactone as the side product along with the desired cyclized six membered lactone.The diastereomeric ratios are calculated from NMR integration ratios of diastereomericproton peaks.

Optimization details for the γ-C(sp^3)–H olefination of free carboxylic acid:

General procedure for optimization studies:

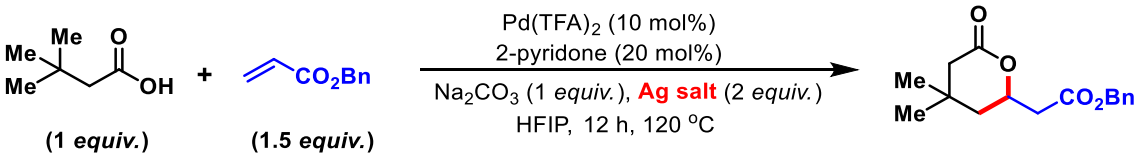
A clean, oven-dried screw cap reaction tube with previously placed magnetic stir–bar was charged with aliphatic carboxylic acid (0.1mmol, 1 *equiv*.), benzyl acrylate (0.15mmol, 1.5 *equiv*.), catalyst (0.01 mmol, 10 mol%), ligand (0.02mmol, 20 mol%), oxidant (0.2mmol, 2 *equiv*.) and an alkali metal base (0.1mmol, 1 *equiv*.) followed by addition of HFIP (1 mL). The reaction mixture was vigorously stirred for 12 h in a preheated oil bath at 120 °C. After stipulated time, the reaction mixture was quenched and cooledto room temperature. 1,3,5-trimethoxybenzene was then added to the reaction mixture as the internal standard. Finally, NMR was recorded.

Table S1: Palladium salt optimization



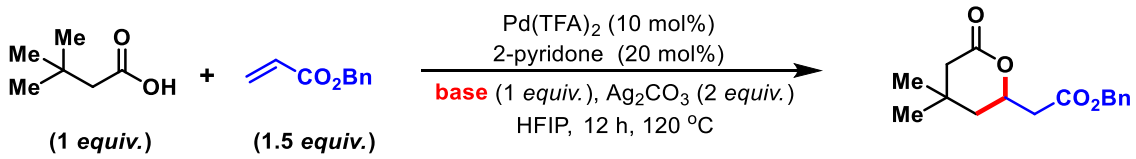
Entry	Catalyst	NMR Yield (%)	Recovered SM (%)
1	$Pd(OAc)_2$	30	59
2	$[Pd(CH_3CN)_2]Cl_2$	22	71
3	$[Pd(PhCN)_2]Cl_2$	trace	91
4	$Pd(OPiv)_2$	35	56
5	**$Pd(TFA)_2$**	**51**	**39**
6	$[Pd(PPh_3)_2]Cl_2$	27	62
7	$[Pd(ferocene)Cl]_2$	trace	89

Table S2: Oxidant optimization



Entry	Oxidant	NMR Yield (%)	Recovered SM (%)
1	AgOAc	20	72
2	**Ag_2CO_3**	**51**	**42**
3	Ag_2O	42	47
4	Ag_2SO_4	11	76
5	AgTFA	34	58
6	Ag_3PO_4	trace	88

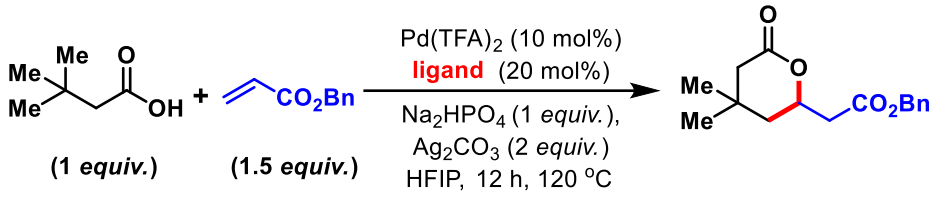
Table S3: Base optimization



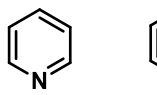
Entry	Base	NMR Yield (%)	Recovered SM (%)
1	**Na_2HPO_4**	**56**	**38**
2	$NaHCO_3$	37	53
3	NaOAc	46	43
4	Na_2CO_3	51	41
5	Na_3PO_4	12	76
6	CF_3CO_2Na	trace	90
7	$NaHSO_4.H_2O$	trace	86
8	K_2CO_3	8	78
9	K_2HPO_4	24	63

10	K_2SO_4	18	70
11	$KHCO_3$	trace	86
12	KOAc	34	54
13	LiCl	18	70
14	$LiOH.H_2O$	16	75
15	LiOAc	12	71
16	$Li_2SO_{4.}H_2O$	19	69
17	Cs_2CO_3	0	81

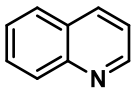
Table S4: Ligand optimization



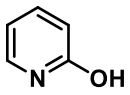
(1 *equiv.*) (1.5 *equiv.*)



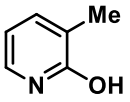
L1, 0%, (91)*



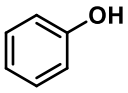
L2, 5%, (80)*



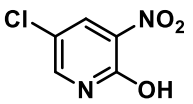
L3, 56%, (34)*



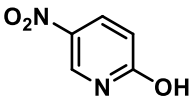
L4, 40%, (49)*



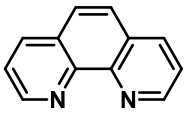
L5, 42%, (42)*



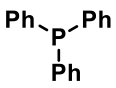
L6, 32%, (54)*



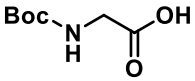
L7, 37%, (51)*



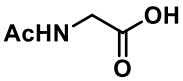
L8, 0%, (86)*



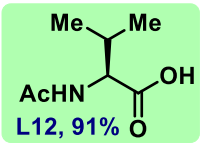
L9, 0%, (93)*



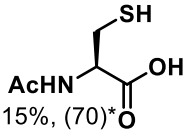
L10, 22%, (68)*



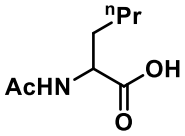
L11, 54%, (31)*



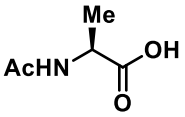
L12, 91%



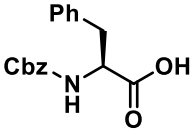
L13, 15%, (70)*



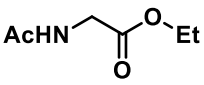
L14, 52%, (36)*



L15, 33%, (52)*



L16, 45%, (44)*



L17, 15%, (74)*

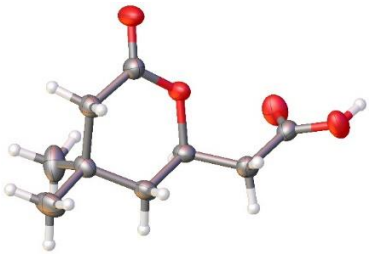
* Recovered/unreacted starting material. Yields measured by NMR

General procedure for six membered lactone formation(GP1) (Figure 4 &5):

A clean, oven-dried screw cap reaction tube with previously placed magnetic stir–bar was charged with aliphatic carboxylic acid(0.2 mmol, 1 *equiv*.), olefin (0.3mmol, 1.5*equiv*.), palladium (II) trifluoroacetate (6.6 mg, 0.02 mmol, 10 mol%), ligand **L12** (6.3 mg, 0.04 mmol, 20 mol%), Ag_2CO_3 (110 mg, 0.4 mmol, 2 *equiv*.) and disodium hydrogen phosphate (28 mg, 0.2 mmol, 1*equiv*.) followed by addition of HFIP (1 mL). The reaction mixture was vigorously stirred for 12 h in a preheated oil bath at 120 °C. After stipulated time, the reaction mixture was cooled to room temperature and filtered through a celite bed using ethyl acetate as the eluent (30 mL). The diluted ethyl acetate solution of the reaction mixture was subsequently washed with saturated brine solution (2 x 10 mL) followed by water (2 x 10 mL). The ethyl acetate layer was dried over anhydrous Na_2SO_4 and the volatiles were removed under vacuum. The crude reaction mixture was purified by column chromatography using silica gel and petroleum-ether / ethyl acetate as the eluent to give the desired six membered lactone as the product.

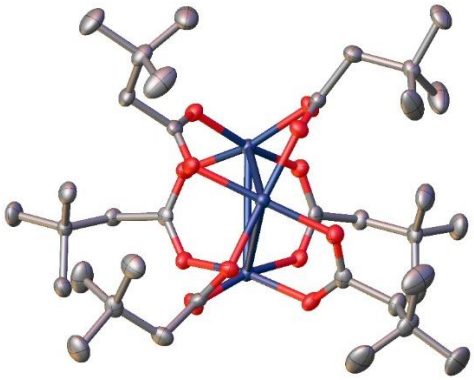
General procedure for seven membered lactone formation(GP2) (Figure 6):

A clean, oven-dried screw cap reaction tube with previously placed magnetic stir–bar was charged with aliphatic carboxylic acid (0.2 mmol, 1 *equiv*.), maleimide (0.3 mmol, 1.5 *equiv*.), palladium(II) trifluoroacetate (6.6 mg, 0.02 mmol, 10 mol%), ligand **L12** (6.3 mg, 0.04 mmol, 20 mol%), Ag_2CO_3 (110 mg, 0.4 mmol, 2 *equiv*.) and disodium hydrogen phosphate (0.2 mmol, 1 *equiv*.) followed by addition of HFIP (1 mL). The reaction mixture was vigorously stirred for 16 h in a preheated oil bath at 100 °C. After stipulated time, the reaction mixture was cooled to room temperature and filtered through a celite bed using ethyl acetate as the eluent (30 mL). The diluted ethyl acetate solution of the reaction mixture was subsequently washed with saturated brine solution (2 x 10 mL) followed by water (2 x 10 mL). The ethyl acetate layer was dried over anhydrous Na_2SO_4 and the volatiles were removed under vacuum. The crude reaction mixture was purified by column chromatography using silica gel and petroleum-ether / ethyl acetate as the eluent to give the desired seven membered lactone as the product.



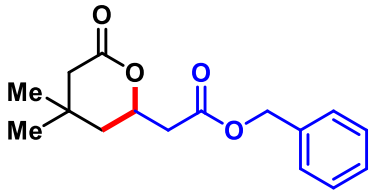
Crystal Data of 5a CCDC 1984975:

Crystal data and structure refinement for $C_9H_{14}O_4$	
Identification code	**5a**
Formula	$C_9H_{14}O_4$
Formula weight(g/mol)	186.20
Temperature/K	150 K
Crystal system	Monoclinic
Space group	P 1 2_1/c 1
a/Å	11.3771(10)
b/Å	8.7126(6)
c/Å	10.1258(8)
α/°	90
β/°	107.359(9)
γ/°	90
Volume/Å^3	958.00(14)
Z	4
P_{calc}g/cm^3	1.291
μ/mm^{-1}	0.101
F(000)	400.0
Crystal size/mm^3	0.0102 x 0.096 x 0.111
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.1360 to 29.9700
Goodness-of-fit on F^2	1.053
R indices (all data)	R1 = 0.0557, wR2 = 0.1444
Largest diff. peak and hole/ e Å^{-3}	0.256 and -0.311



Crystal Data of Intermediate A, CCDC 1984976:

Crystal data and structure refinement for $C_{36}H_{66}O_{12}Pd_3$	
Identification code	**A**
Formula	$C_{36}H_{66}O_{12}Pd_3$
Formula weight (g/mol)	224.46
Temperature/K	150 K
Crystal system	Triclinic
Space group	P -1
a/Å	11.4234(4)
b/Å	12.9659(5)
c/Å	15.7183(6)
α/°	90.714(3)
β/°	97.035(3)
γ/°	107.564(4)
Volume/Å^3	2199.87(15)
Z	9
P_{calc}g/cm^3	1.525
μ/mm^{-1}	1.266
F(000)	1032.0
Crystal size/mm^3	0.082 x 0.09 x 0.091
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	2.051 to 25.000
Goodness-of-fit on F^2	1.036
R indices (all data)	R1 = 0.0321, wR2 = 0.0736
Largest diff. peak and hole/ e Å^{-3}	0.511 and -0.823



Benzyl (R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 4, 1a)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 82% (45 mg, 0.2 mmol)

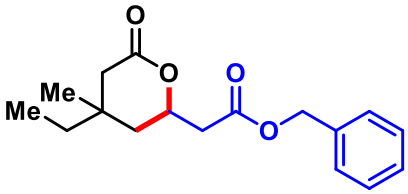
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 – 7.29 (m, 5H), 5.14 (s, 2H), 4.80 (dtd, *J* = 9.6, 6.4, 3.5 Hz, 1H), 2.79 (dd, *J* = 16.1, 6.9 Hz, 1H), 2.60 (dd, *J* = 16.1, 5.8 Hz, 1H), 2.36 (dt, *J* = 16.2, 4.0 Hz, 1H), 2.23 – 2.16 (m, 1H), 1.77 – 1.68 (m, 1H), 1.51 – 1.43 (m, 1H), 1.07 (s, 3H), 1.03 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.28, 169.69, 135.56, 128.71, 128.51, 128.45, 73.72, 66.82, 43.76, 41.67, 40.60, 31.05, 29.93, 27.52.

DEPT-135 (126 MHz, $CDCl_3$) δ 128.64, 128.44, 128.38, 73.65, 66.75, 48.68, 41.59, 40.53, 50.98, 27.44.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{16}H_{20}NaO_4$ *m/z* 299.1254 and found *m/z* 299.1252.

IR (thin film, cm^{-1}): 3035, 2959, 2873, 1780, 1735, 1498, 1456, 1373, 1316, 1233, 1172, 1061.



Benzyl 2-(4-ethyl-4-methyl-6-oxotetrahydro-2H-pyran-2-yl)acetate(Fig 4, 1b)

Lactonizationwas carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 67% (39 mg, 0.2 mmol)

dr: 1.1:1

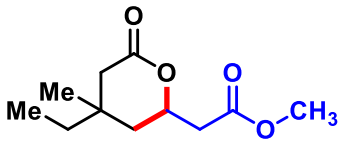
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.32 (m, 10H), 5.18 (d, *J* = 26.2 Hz, 4H), 4.81 (dtd, *J* = 9.7, 6.4, 3.1 Hz, 1.14H), 4.75 – 4.67 (m, 1.05H), 2.87 – 2.79 (m, 2H), 2.60 (ddd, *J* = 16.3, 10.2,

6.1 Hz, 2H), 2.45 – 2.16 (m, 4H), 1.87 (dd, *J* = 14.1, 2.7 Hz, 1H), 1.69 (dd, *J* = 13.9, 1.8 Hz, 1H), 1.53 – 1.29 (m, 6H), 1.06 – 0.98 (m, 6H), 0.90 – 0.83 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.97, 171.75, 169.84, 140.86, 135.64, 128.83, 128.64, 128.60, 128.59, 128.46, 123.25, 73.62, 73.53, 66.98, 66.82, 42.50, 42.12, 40.74, 40.58, 39.90, 39.71, 36.23, 33.18, 32.94, 32.91, 27.76, 27.65, 25.50, 24.89, 8.26, 7.92.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{17}H_{22}NaO_4$ *m/z* 313.1410 and found *m/z* 313.1409.

IR (thin film, cm^{-1}):1056, 1163, 1230, 1310, 1380, 1457, 1499, 1735, 1780, 2968, 2936, 2968.



Methyl 2-(4-ethyl-4-methyl-6-oxotetrahydro-2H-pyran-2-yl)acetate(Fig 4, 1c)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (25:75 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 63% (27 mg, 0.2 mmol)

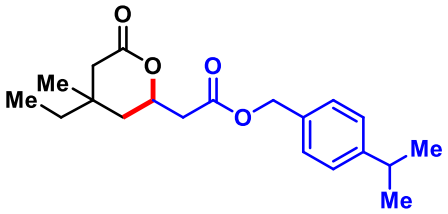
dr: 1.2:1

^{1}H NMR (500 MHz, $CDCl_3$) 4.80 (dd, *J* = 5.3, 3.4 Hz, 0.87H), 4.71 (ddd, *J* = 12.1, 9.9, 6.1 Hz, 1.05H),3.73 (t, *J* = 14.0 Hz, 6H), 2.76 (dd, *J* = 16.2, 6.9 Hz, 2H), 2.61 – 2.51 (m, 2H), 2.47 – 2.17 (m, 4H), 1.90 (dd, *J* = 14.2, 2.1 Hz, 1H), 1.72 (d, *J* = 12.1 Hz, 1H), 1.51 – 1.31 (m, 6H), 1.10 – 0.98 (m, 6H), 0.95 – 0.82 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.02, 171.80, 170.50, 73.68, 73.58, 52.21, 52.11, 42.49, 42.10, 40.56, 40.38, 39.97, 39.76, 36.24, 33.18, 32.95, 32.91, 27.77, 24.91, 8.28, 7.93.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{11}H_{18}NaO_4$ m/z 237.1097 and found m/z 237.1098.

IR (thin film, cm^{-1}): 1056, 1196, 1230, 1313, 1384, 1438, 1459, 1737, 1784, 2883, 2964, 3023.



4-isopropylbenzyl 2-(4-ethyl-4-methyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 4, 1d)

Lactonizationwas carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (30:70 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 55% (36 mg, 0.2 mmol)

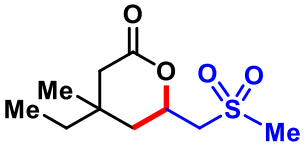
dr: 1.3:1

^{1}H NMR (400 MHz, CDCl3) δ 7.29 (d, J = 8.2 Hz, 4H), 7.23 (d, J = 8.2 Hz, 4H), 5.11 (s, 4H), 4.85 – 4.76 (m, 1.03H), 4.74 – 4.67 (m, 1.29H), 2.92 (dd, J = 13.8, 6.9 Hz, 2H), 2.81 (dd, J = 16.2, 6.6 Hz, 2H), 2.64 – 2.55 (m, 2H), 2.42 (dd, J = 16.1, 1.0 Hz, 1H), 2.32 – 2.15 (m, 3H), 1.90 – 1.85 (m, 1H), 1.69 (dd, J = 14.6, 4.1 Hz, 1H), 1.47 – 1.32 (m, 6H), 1.24 (d, J = 6.9 Hz, 12H), 1.06 – 0.96 (m, 6H), 0.90 – 0.83 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.03, 171.81, 169.90, 149.55, 132.98, 132.95, 128.87, 128.85, 128.72, 126.93, 73.65, 73.56, 66.96, 66.81, 42.53, 42.14, 40.77, 40.61, 39.90, 39.70, 36.25, 34.11, 33.18, 32.94, 32.91, 27.76, 24.89, 24.15, 8.28, 7.94.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{20}H_{28}NaO_4$ m/z 355.1880 and found m/z 355.1879.

IR (thin film, cm^{-1}): 1056, 1127, 1163, 1229, 1309, 1379, 1465, 1737, 1780, 2882, 2932, 2968.



4-ethyl-4-methyl-6-((methylsulfonyl)methyl)tetrahydro-2H-pyran-2-one (Fig 4, 1e)

Lactonizationwas carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (50:50 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 68% (39 mg, 0.2 mmol)

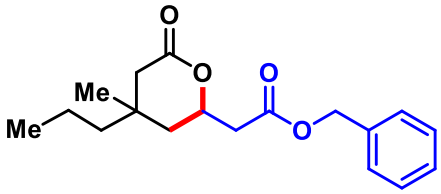
dr: 1.6:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.92 (dd, *J* = 11.8, 9.3 Hz, 1.23H), 4.86 – 4.75 (m, 0.75H),3.44 – 3.34 (m, 2H), 3.12 – 2.95 (m, 8H), 2.48 – 2.19 (m, 4H), 1.91 – 1.70 (m, 2H), 1.61 – 1.23 (m, 6H), 1.14 – 0.84 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.67, 170.42, 170.05, 72.51, 72.35, 72.20, 59.95, 59.92, 59.73, 43.64, 43.47, 42.19, 41.85, 41.39, 39.52, 39.41, 36.14, 33.20, 33.03, 31.09, 30.14, 27.70, 27.61, 25.36, 24.89, 8.23, 7.87.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{10}H_{18}NaO_4S$ m/z 257.0818 and found m/z 257.0820.

IR (thin film, cm^{-1}): 1129, 1246.824, 1306.043, 1378.916, 1466.183, 1742.364, 2933.569, 2970.246, 3022.293.



Benzyl 2-(4-methyl-6-oxo-4-propyltetrahydro-2H-pyran-2-yl)acetate(Fig 4, 1f)

Lactonizationwas carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (25:75 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 67% (41 mg, 0.2 mmol)

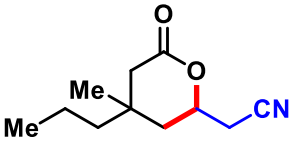
dr: 1:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.31 (m, 10H), 5.22 – 5.14 (m, 4H), 4.80 (tdd, *J* = 9.6, 6.4, 3.3 Hz, 1H), 4.72 (dtd, *J* = 9.8, 6.5, 3.2 Hz, 1H), 2.82 (dd, *J* = 16.1, 6.8 Hz, 2H), 2.60 (dt, *J* = 15.8, 6.4 Hz, 2H), 2.46 – 2.16 (m, 4H), 1.87 (dd, *J* = 14.1, 2.8 Hz, 1H), 1.70 (dd, *J* = 13.9, 2.1 Hz, 1H), 1.51 – 1.25 (m, 10H), 1.00 (dd, *J* = 19.5, 15.0 Hz, 6H), 0.94 – 0.86 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.91, 171.74, 169.83, 135.64, 135.61, 128.84, 128.65, 128.60, 73.60, 73.56, 66.98, 46.33, 43.19, 42.83, 42.54, 40.74, 40.61, 40.28, 40.23, 32.87, 32.83, 28.34, 25.45, 17.17, 16.78, 14.80, 14.76.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{18}H_{24}NaO_4$ m/z 327.1567 and found m/z 327.1568.

IR (thin film, cm^{-1}): 1052, 1246, 1315, 1378, 1488, 1734, 1782, 2957, 2968.



2-(-4-methyl-6-oxo-4-propyltetrahydro-2H-pyran-2-yl)acetonitrile(Fig 4, 1g)

Lactonizationwas carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (40:60 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 66% (26 mg, 0.2 mmol)

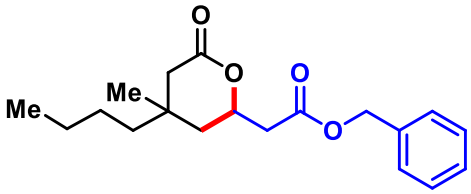
dr: 1.7:1

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.67 – 4.59 (m, 1.22H), 4.55 (dd, *J* = 12.1, 3.6 Hz, 0.73H), 2.82 – 2.71 (m, 4H), 2.48 – 2.23 (m, 4H), 1.83 (dd, *J* = 13.9, 1.8 Hz, 1H), 1.65 (d, *J* = 12.3 Hz, 1H), 1.46 – 1.24 (m, 10H), 1.12 – 1.03 (m, 6H), 0.97 – 0.88 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.43, 170.30, 115.79, 115.76, 72.07, 71.97, 46.14, 42.53, 42.42, 39.56, 39.50, 32.97, 28.00, 24.98, 24.86, 17.21, 16.72, 14.71.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{11}H_{17}NNaO_2$ m/z 218.1151 and found m/z 218.1151.

IR (thin film, cm^{-1}): 1132, 1248, 1380, 1467, 1740, 2258, 2933, 2970.



Benzyl 2-(4-butyl-4-methyl-6-oxotetrahydro-2H-pyran-2-yl)acetate(Fig 4, 1h)

Lactonizationwas carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (30:70 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 78% (49 mg, 0.2 mmol)

dr: 1:1

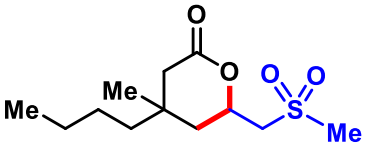
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 10H), 5.15 (d, *J* = 28.6 Hz, 4H), 4.77 (tdd, *J* = 9.5, 6.3, 3.2 Hz, 1.06H), 4.70 (ddd, *J* = 12.1, 9.7, 6.3 Hz, 1.04H), 2.83 – 2.76 (m, 2H), 2.61 – 2.54 (m, 2H), 2.40 (d, *J* = 16.1 Hz, 1H), 2.29 (d, *J* = 16.6 Hz, 1H), 2.17 (dd, *J* = 24.0, 11.1 Hz,

2H), 1.84 (dd, *J* = 14.1, 2.5 Hz, 1H), 1.67 (dd, *J* = 13.8, 1.7 Hz, 1H), 1.47 – 1.21 (m, 14H), 1.04 – 0.96 (m, 6H), 0.87 (dd, *J* = 12.0, 7.0 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.93, 171.76, 169.84, 135.64, 135.61, 128.83, 128.65, 128.60, 73.61, 73.57, 66.99, 66.98, 43.69, 42.86, 42.56, 40.74, 40.62, 40.49, 40.27, 40.18, 32.77, 32.74, 28.32, 26.06, 25.67, 25.45, 23.37, 14.20.

HRMS (ESI-QTOF): [M+H]+ calculated for $C_{19}H_{27}O_4$ m/z 319.1904 and found m/z 319.1900.

IR (thin film, cm^{-1}): 1032, 1122, 1246, 1312, 1378, 1475, 1735, 1782, 2942, 2976.



4-butyl-4-methyl-6-((methylsulfonyl)methyl)tetrahydro-2H-pyran-2-one (Fig 4, 1i)

Lactonizationwas carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (35:65 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 60% (31 mg, 0.2 mmol)

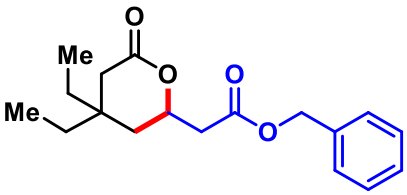
dr: 1.9:1

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.92 (t, *J* = 10.4 Hz, 1.31H), 4.84 (t, *J* = 10.5 Hz, 0.68H),3.39 (dt, *J* = 14.2, 7.2 Hz, 2H), 3.11 – 2.94 (m, 8H), 2.51 – 2.22 (m, 4H), 1.75 – 1.71 (m, 1H), 1.60 (d, *J* = 12.9 Hz, 1H), 1.53 – 1.22 (m, 14H), 1.07 (d, *J* = 36.9 Hz, 6H), 0.91 (dd, *J* = 14.7, 7.5 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 170.60, 170.38, 72.35, 72.26, 60.06, 59.87, 43.62, 43.54, 42.33, 40.62, 40.03, 32.92, 28.36, 25.66, 25.54, 23.30, 14.16.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{12}H_{22}NaO_4S$ m/z 285.1131 and found m/z 285.1132.

IR (thin film, cm^{-1}): 1036, 1242, 1358, 1470, 1734, 2926, 2978



Benzyl 2-(4,4-diethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 4, 1j)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (30:70 v/v).

Appearance: Sticky yellow liquid.

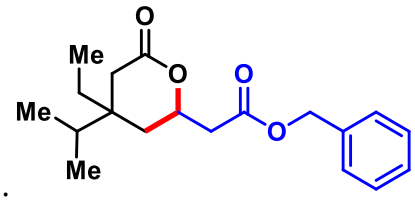
Isolated yield: 63% (38 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 9.4, 6.3 Hz, 5H), 5.18 (d, *J* = 20.8 Hz, 2H), 4.84 – 4.69 (m, 1H), 2.83 (ddd, *J* = 16.3, 6.6, 4.0 Hz, 1H), 2.60 (ddd, *J* = 16.1, 8.9, 4.2 Hz, 1H), 2.47 – 2.20 (m, 2H), 1.91 – 1.67 (m, 1H), 1.52 – 1.24 (m, 5H), 1.08 – 0.82 (m, 6H).

^{13}C NMR (101 MHz, CDCl3) δ 171.74, 169.85, 141.37, 135.62, 128.85, 128.62, 73.61, 67.01, 46.35, 42.55, 40.75, 32.89, 25.47, 16.80, 14.77.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{18}H_{24}NaO_4$ m/z 327.1567 and found m/z 327.1566.

IR (thin film, cm^{-1}): 1125, 1252, 1312, 1382, 1476, 1737, 2926, 2968.



Benzyl 2-(4-ethyl-4-isopropyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 4,1k)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (30:70 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 57% (36 mg, 0.2 mmol)

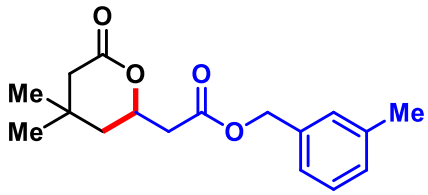
dr: 1.2:1

^{1}H NMR (400 MHz, $CDCl_3$)δ 7.36 (t, *J* = 4.1 Hz, 10H), 5.18 (d, *J* = 21.1 Hz, 4H), 4.81 (tdd, *J* = 9.6, 6.4, 3.2 Hz, 1.33H), 4.76 – 4.67 (m, 1.11H), 2.83 (dd, *J* = 16.1, 6.8 Hz, 2H), 2.66 – 2.57 (m, 2H), 2.42 – 2.20 (m, 4H), 1.88 (dd, *J* = 14.1, 2.7 Hz, 1H), 1.70 (dd, *J* = 13.9, 1.9 Hz, 1H), 1.53 – 1.20 (m, 10H), 1.11 – 0.95 (m, 10H), 0.86 (q, *J* = 7.6 Hz, 6H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 171.94, 171.72, 169.84, 135.66, 135.63, 128.84, 128.65, 128.60, 73.62, 73.53, 66.98, 42.52, 42.13, 40.76, 40.60, 39.93, 39.75, 36.25, 33.20, 32.96, 32.92, 27.77, 24.91, 8.27, 7.93.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{19}H_{26}NaO_4$ m/z 341.1723 and found m/z 341.1722.

IR (thin film, cm^{-1}): 1030, 1122, 1258, 1307, 1380, 1512, 1735, 2926, 2968.



3-methylbenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2a)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

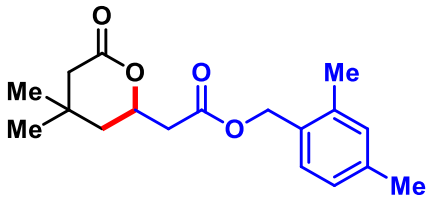
Isolated yield: 72% (42 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.23 (m, *J* = 7.2 Hz, 1H), 7.18 – 7.12 (m, 3H), 5.12 (s, 2H), 4.82 (dtd, *J* = 9.9, 6.4, 3.5 Hz, 1H), 2.81 (dd, *J* = 16.1, 6.8 Hz, 1H), 2.61 (dd, *J* = 16.1, 6.0 Hz, 1H), 2.41 – 2.33 (m, 4H), 2.22 (d, *J* = 16.6 Hz, 1H), 1.75 (ddd, *J* = 13.9, 3.3, 1.6 Hz, 1H), 1.54 – 1.44 (m, 1H), 1.10 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.37, 169.81, 138.55, 135.52, 129.37, 129.28, 128.72, 125.61, 73.82, 67.01, 43.87, 41.82, 40.73, 31.16, 30.04, 27.63, 21.52.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{17}H_{22}NaO_4$ m/z 313.1410 and found m/z 313.1410.

IR (thin film, cm^{-1}): 1035, 1128, 1160, 1233, 1315, 1376, 1466, 1611, 1735, 1774, 2885, 2969, 3022.



2,4-dimethylbenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2b)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

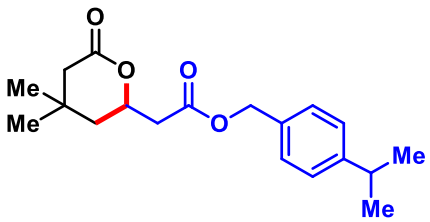
Isolated yield: 57% (35 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (d, *J* = 7.6 Hz, 1H), 7.04 – 6.98 (m, 2H), 5.14 (s, 2H), 4.80 (dtd, *J* = 9.9, 6.4, 3.5 Hz, 1H), 2.79 (dd, *J* = 16.1, 6.7 Hz, 1H), 2.58 (dd, *J* = 16.1, 6.0 Hz, 1H), 2.40 – 2.35 (m, 1H), 2.32 (s, 6H), 2.21 (d, *J* = 16.6 Hz, 1H), 1.75 (dd, *J* = 13.9, 1.7 Hz, 1H), 1.52 – 1.45 (m, 1H), 1.10 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.33, 169.88, 138.89, 137.29, 131.51, 130.63, 129.98, 126.90, 73.84, 65.35, 43.92, 41.90, 40.77, 31.19, 30.08, 27.68, 21.30, 19.03.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{18}H_{24}NaO_4$ m/z 327.1567 and found m/z 327.1565.

IR (thin film, cm^{-1}): 1035, 1128, 1160, 1240, 1312, 1379, 1467, 1735, 1788, 2885, 2933, 2970.



4-isopropylbenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2c)

Lactonizationwas carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

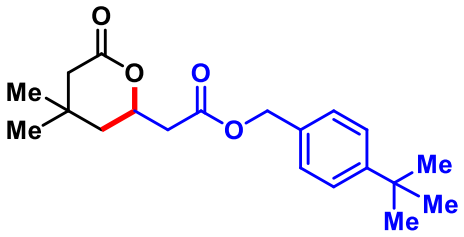
Isolated yield: 78% (50 mg, 0.2 mmol)

^{1}H NMR (400 MHz, CDCl3) δ 7.29 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 5.12 (s, 2H), 4.81 (dtd, J = 9.8, 6.4, 3.5 Hz, 1H), 2.91 (dt, J = 13.8, 6.9 Hz, 1H), 2.81 (dd, J = 16.1, 6.7 Hz, 1H), 2.60 (dd, J = 16.1, 6.0 Hz, 1H), 2.38 (dd, J = 16.6, 1.6 Hz, 1H), 2.21 (d, J = 16.6 Hz, 1H), 1.74 (ddd, J = 13.9, 3.4, 1.6 Hz, 1H), 1.48 (dd, J = 13.7, 12.2 Hz, 1H), 1.24 (d, J = 6.9 Hz, 6H), 1.09 (s, 3H), 1.05 (s, 3H).

^{13}C NMR(126 MHz, $CDCl_3$) δ 171.40, 169.84, 149.50, 132.97, 128.81, 126.90, 73.82, 66.92, 43.87, 41.81, 40.74, 34.08, 31.16, 30.04, 27.63, 24.12.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{19}H_{26}NaO_4$ m/z 341.1723 and found m/z 341.1723.

IR (thin film, cm^{-1}): 1035, 1057, 1172, 1231, 1316, 1373, 1465, 1516, 1735, 1784, 2873, 2961.



4-(tert-butyl)benzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2d)

Lactonizationwas carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

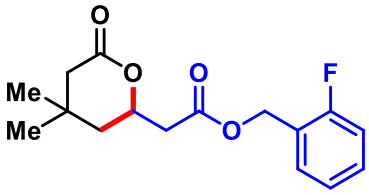
Isolated yield: 77% (51 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 8.4, 2.1 Hz, 2H), 7.29 (d, *J* = 8.3 Hz, 2H), 5.12 (s, 2H), 4.81 (dtd, *J* = 9.9, 6.4, 3.5 Hz, 1H), 2.81 (dd, *J* = 16.1, 6.7 Hz, 1H), 2.60 (dd, *J* = 16.1, 6.0 Hz, 1H), 2.38 (dt, *J* = 16.8, 2.8 Hz, 1H), 2.21 (d, *J* = 16.6 Hz, 1H), 1.74 (ddd, *J* = 13.9, 3.4, 1.6 Hz, 1H), 1.52 – 1.44 (m, 1H), 1.31 (s, 9H), 1.09 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.41, 169.87, 151.78, 132.63, 128.54, 125.78, 73.84, 66.86, 43.90, 41.85, 40.77, 34.82, 32.00, 31.49, 31.19, 30.06, 27.66.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{20}H_{28}NaO_4$ m/z 355.1880 and found m/z 355.1878.

IR (thin film, cm^{-1}): 1035, 1172, 1234, 1316, 1372, 1466, 1518, 1738, 1786, 2870, 2960.



2-fluorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2e)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 65% (38 mg, 0.2 mmol)

^{1}H NMR(400 MHz, $CDCl_3$) δ 7.42 – 7.31 (m, 2H), 7.15 (t, *J* = 7.5 Hz, 1H), 7.08 (t, *J* = 9.1 Hz, 1H), 5.22 (s, 2H), 4.81 (dtd, *J* = 9.8, 6.4, 3.5 Hz, 1H), 2.82 (dd, *J* = 16.1, 6.7 Hz, 1H), 2.61 (dd, *J*

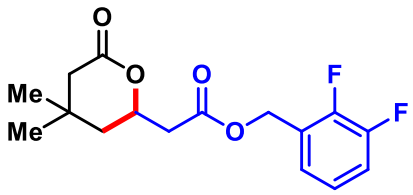
= 16.1, 6.1 Hz, 1H), 2.43 – 2.36 (m, 1H), 2.22 (d, *J* = 16.6 Hz, 1H), 1.76 (ddd, *J* = 13.9, 3.3, 1.6 Hz, 1H), 1.53 – 1.46 (m, 1H), 1.10 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.33, 169.66, 162.45 (d, *J* = 249.44 Hz), 159.98, 141.07, 131.03, 130.99, 130.71, 130.63 (d, *J* = 8.2 Hz), 124.45, 124.41, 123.02, 122.88, 122.74, 115.82, 115.61, 77.55, 77.23, 76.91, 73.75, 60.92, 60.87, 43.87, 41.79, 40.62, 31.17, 30.05, 27.63.

^{19}F NMR (471 MHz, $CDCl_3$) δ -117.86.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{16}H_{19}FNaO4$ m/z 317.1160 and found m/z 317.1156.

IR (thin film, cm^{-1}): 1034, 1060, 1151, 1169, 1231, 1316, 1373, 1457, 1494, 1589.191 1620, 1735, 1784, 2959, 2975.



2,3-difluorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2f)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 69% (43 mg, 0.2 mmol)

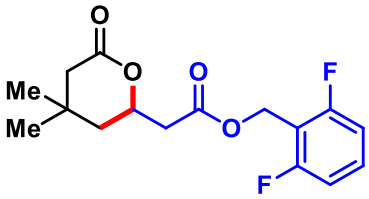
^{1}H NMR(500 MHz, CDCl3) δ 7.18 – 7.11 (m, 2H), 7.10 – 7.06 (m, 1H), 5.22 (s, 2H), 4.83 – 4.77 (m, 1H), 2.80 (dd, J = 16.1, 6.9 Hz, 1H), 2.61 (dd, J = 16.1, 5.8 Hz, 1H), 2.40 – 2.36 (m, 1H), 2.22 (d, J = 16.6 Hz, 1H), 1.78 – 1.72 (m, 1H), 1.53 – 1.47 (m, 1H), 1.10 (s, 3H), 1.05 (s, 3H).

^{13}C NMR(101 MHz, CDCl3) δ 171.29, 169.56, 151.92 (d, *J* = 249.42 Hz), 151.80 (d, *J* = 251.47 Hz), 150.48 (d, *J* = 13.1 Hz), 150.35, 149.45, 149.32, 147.99, 147.86, 125.51, 125.48, 125.46, 125.29, 125.18, 124.51, 124.46, 124.44, 124.40 (dd, J = 6.7, 4.8 Hz), 117.89, 117.72 117.81 (d, J = 17.1 Hz), 73.71, 60.32, 60.29, 60.25 (m), 43.85, 41.77, 40.57, 31.15, 30.05, 27.61.

^{19}F NMR (471 MHz, $CDCl_3$) δ -137.94, -137.99, -142.63, -142.68.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{16}H_{18}F_2NaO_4$ m/z 335.1065 and found m/z 335.1064.

IR (thin film, cm^{-1}): 1034, 1074, 1161, 1234, 1288, 1315, 1374, 1492, 1599, 1631, 1738, 1784, 2877, 2965.



2,6-difluorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2g)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 71% (44 mg, 0.2 mmol)

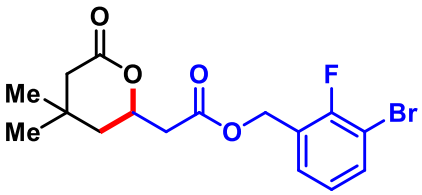
^{1}H NMR(500 MHz, $CDCl_3$) δ 7.32 (dq, *J* = 8.3, 6.5 Hz, 1H), 6.94 – 6.88 (m, 2H), 5.23 (s, 2H), 4.78 (dtd, *J* = 9.8, 6.4, 3.4 Hz, 1H), 2.80 (dd, *J* = 16.2, 6.4 Hz, 1H), 2.58 (dd, *J* = 16.2, 6.4 Hz, 1H), 2.37 (dt, *J* = 16.9, 4.9 Hz, 1H), 2.21 (d, *J* = 16.6 Hz, 1H), 1.77 (ddd, *J* = 13.9, 3.3, 1.5 Hz, 1H), 1.52 – 1.45 (m, 1H), 1.09 (s, 3H), 1.04 (s, 3H).

^{13}C NMR(101 MHz, CDCl3) δ 171.36, 169.45, 163.22, 163.16, 160.73, 160.65(d, *J* = 251.1 Hz), 131.31, 131.21, 131.10 (t, *J* = 10.5 Hz),, 111.72, 111.66, 111.60, 111.53, 111.47, 73.66, 54.60, 43.83, 41.72, 40.42, 31.13, 30.00, 27.60.

^{19}F NMR (471 MHz, $CDCl_3$) δ -114.25, -114.27.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{16}H_{18}F_2NaO_4$ m/z 335.1065 and found m/z 335.1067.

IR (thin film, cm^{-1}): 1035, 1058, 1171, 1236, 1273, 1316, 1373, 1473, 1595, 1629, 1741, 1786, 2932, 2960.



3-bromo-2-fluorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2h)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 67% (50 mg, 0.2 mmol)

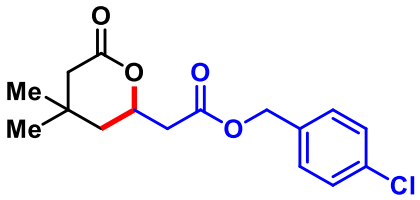
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.51 (m, 1H), 7.35 (dd, *J* = 10.2, 3.9 Hz, 1H), 7.04 (t, *J* = 7.8 Hz, 1H), 5.22 (s, 2H), 4.84 – 4.76 (m, 1H), 2.81 (dd, *J* = 16.1, 6.9 Hz, 1H), 2.62 (dd, *J* = 16.1, 5.8 Hz, 1H), 2.39 (dt, *J* = 16.9, 3.4 Hz, 1H), 2.23 (d, *J* = 16.6 Hz, 1H), 1.76 (ddd, *J* = 13.9, 3.3, 1.6 Hz, 1H), 1.55 – 1.46 (m, 1H), 1.11 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.28, 169.58, 158.77 (d, *J* = 249.39 Hz), 156.29, 134.11, 129.95 (d, *J* = 3.3 Hz), 129.92, 125.45, 125.40 (d, *J* = 4.6 Hz), 124.61, 124.45, 109.62, 109.41, 73.73, 60.81, 60.77, 43.88, 41.81, 40.62, 31.19, 30.09, 27.65.

^{19}F NMR (471 MHz, $CDCl_3$) δ -111.15.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{16}H_{18}BrFNaO_4$ m/z 395.0265 and found m/z 395.0266.

IR (thin film, cm^{-1}): 1035, 1073, 1172, 1231, 1316, 1374, 1456, 1493, 1740, 1781, 2962.



4-chlorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2i)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

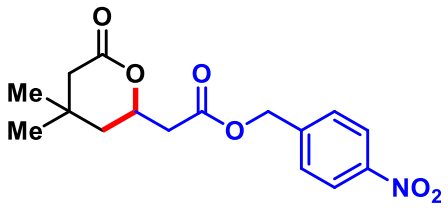
Isolated yield: 70% (43 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 5.11 (s, 2H), 4.81 (dtd, *J* = 10.5, 6.8, 3.5 Hz, 1H), 2.79 (dd, *J* = 16.1, 7.0 Hz, 1H), 2.60 (dd, *J* = 16.1, 5.7 Hz, 1H), 2.42 – 2.36 (m, 1H), 2.22 (d, *J* = 16.6 Hz, 1H), 1.74 (ddd, *J* = 13.9, 3.2, 1.4 Hz, 1H), 1.55 – 1.45 (m, 1H), 1.10 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.31, 169.76, 134.57, 134.16, 129.95, 129.04, 73.78, 66.14, 43.89, 41.85, 40.72, 31.19, 30.09, 27.66.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{16}H_{19}ClNaO_4$ m/z 333.0864 and found m/z 333.0863.

IR (thin film, cm^{-1}): 1035, 1091, 1171, 1241, 1316, 1373, 1466, 1494, 1738, 1772, 2875, 2959.



4-nitrobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2j)

Lactonizationwas carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

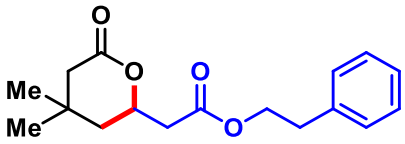
Isolated yield: 71% (45 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (d, *J* = 8.7 Hz, 2H), 7.52 (d, *J* = 8.6 Hz, 2H), 5.25 (s, 2H), 4.83 (tdd, *J* = 8.3, 5.1, 3.6 Hz, 1H), 2.82 (dd, *J* = 16.1, 7.5 Hz, 1H), 2.66 (dd, *J* = 16.1, 5.1 Hz, 1H), 2.40 (dd, *J* = 16.6, 1.5 Hz, 1H), 2.24 (d, *J* = 16.6 Hz, 1H), 1.76 (ddd, *J* = 13.9, 3.4, 1.6 Hz, 1H), 1.58 – 1.48 (m, 1H), 1.11 (s, 3H), 1.07 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.12, 169.63, 148.00, 142.89, 128.64, 124.06, 73.74, 65.41, 43.86, 41.85, 40.67, 31.18, 30.12, 27.64.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{16}H_{19}NNaO_6$ m/z 344.1105 and found m/z 344.1105.

IR (thin film, cm^{-1}): 1010, 1234, 1346, 1467, 1522, 1607, 1738, 1774, 2872, 2959.



Phenethyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2k)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

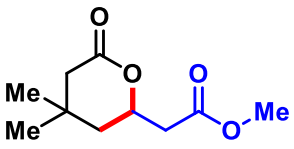
Isolated yield: 62% (36 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.4 Hz, 2H), 7.23 (dd, *J* = 12.0, 7.1 Hz, 3H), 4.75 (dtd, *J* = 9.9, 6.4, 3.5 Hz, 1H), 4.34 (t, 2H), 2.95 (t, *J* = 7.0 Hz, 2H), 2.75 (dd, *J* = 16.0, 6.8 Hz, 1H), 2.75 (dd, *J* = 16.0, 6.8 Hz, 1H), 2.53 (dd, *J* = 16.0, 6.1 Hz, 1H), 2.37 (dd, *J* = 16.6, 1.6 Hz, 1H), 2.21 (d, *J* = 16.6 Hz, 1H), 1.71 (ddd, *J* = 13.9, 3.3, 1.6 Hz, 1H), 1.45 (dd, *J* = 13.7, 12.3 Hz, 1H), 1.08 (s, 3H), 1.05 (s, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.37, 169.88, 137.76, 129.08, 128.76, 126.86, s73.84, 65.51, 43.92, 41.87, 40.81, 35.18, 31.19, 30.05, 27.64.

HRMS (ESI-QTOF): [M+Na]+ calculated for $C_{17}H_{22}NaO_4$ m/z 313.1410 and found m/z 313.1414.

IR (thin film, cm^{-1}): 1034, 1127, 1216, 1378, 1467.640, 1669, 1735, 1776, 2933, 2969.



Methyl (R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2l)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

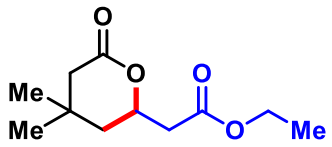
Isolated yield: 80% (32 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.84 – 4.76 (m, 1H), 3.70 (s, 3H), 2.79 – 2.71 (m, 1H), 2.55 (dd, *J* = 16.1, 5.8 Hz, 1H), 2.41 – 2.35 (m, 1H), 2.22 (d, *J* = 16.6 Hz, 1H), 1.79 – 1.75 (m, 1H), 1.53 – 1.45 (m, 1H), 1.10 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.39, 170.43, 73.85, 52.17, 43.86, 41.85, 40.54, 31.16, 30.04, 27.62.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{10}H_{16}NaO_4$ *m/z* 223.0941 and found *m/z* 223.0937.

IR (thin film, cm^{-1}):2970, 2877, 1782, 1734, 1467, 1437, 1378, 1316, 1242, 1160, 1035.



Ethyl (R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2m)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

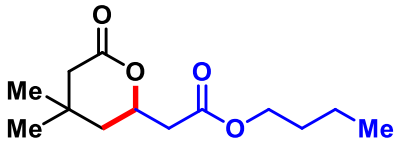
Isolated yield: 81% (35 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.83 – 4.75 (m, 1H), 4.18 – 4.12 (m, 2H), 2.74 (dd, *J* = 16.1, 6.8 Hz, 1H), 2.54 (dd, *J* = 16.1, 5.9 Hz, 1H), 2.41 – 2.35 (m, 1H), 2.23 (t, *J* = 11.8 Hz, 1H), 1.79 – 1.75 (m, 1H), 1.49 (dd, *J* = 13.7, 12.3 Hz, 1H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.10 (s, 3H), 1.05 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.46, 169.99, 73.89, 61.13, 43.88, 41.88, 40.73, 31.17, 30.04, 27.66.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{11}H_{18}NaO_4$ *m/z* 237.1097 and found *m/z* 237.1097.

IR (thin film, cm^{-1}): 2986, 2961, 1782, 1734, 1467, 1372, 1316, 1235, 1192, 1035.



Butyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2n)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

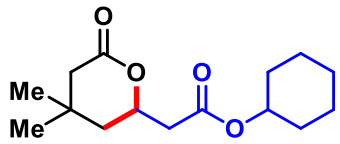
Isolated yield: 78% (38 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.79 (dtd, *J* = 9.5, 6.2, 3.2 Hz, 1H), 4.10 (td, *J* = 6.7, 1.1 Hz, 2H), 2.75 (dd, *J* = 16.1, 6.8 Hz, 1H), 2.55 (dd, *J* = 16.1, 6.1 Hz, 1H), 2.38 (dt, *J* = 16.5, 4.4 Hz, 1H), 2.23 (d, *J* = 16.6 Hz, 1H), 1.78 (ddd, *J* = 13.9, 3.4, 1.6 Hz, 1H), 1.61 (dt, *J* = 14.6, 6.8 Hz, 2H),

1.50 (dd, *J* = 13.7, 12.2 Hz, 1H), 1.38 (dt, *J* = 15.0, 7.4 Hz, 2H), 1.11 (s, 3H), 1.06 (s, 3H), 0.92 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.45, 170.08, 73.90, 65.06, 43.91, 41.93, 40.75, 31.20, 30.72, 30.06, 27.70, 19.27, 13.86.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{13}H_{22}NaO_4$ *m/z* 265.1410 and found *m/z* 265.1412. **IR** (thin film, cm^{-1}): 1035, 1060, 1151, 1176, 1237, 1316, 1467, 1737, 1782, 2874, 2960.



Cyclohexyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2o)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

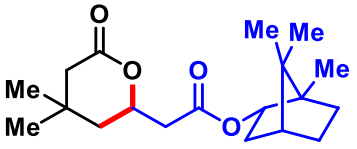
Isolated yield: 67% (36 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.82 – 4.76 (m, 2H), 2.75 (dd, *J* = 15.9, 6.5 Hz, 1H), 2.54 (dd, *J* = 15.9, 6.3 Hz, 1H), 2.42 – 2.37 (m, 1H), 2.23 (d, *J* = 16.6 Hz, 1H), 1.85 (d, *J* = 4.7 Hz, 2H), 1.78 (ddd, *J* = 13.3, 3.0, 1.3 Hz, 1H), 1.74 – 1.68 (m, 2H), 1.57 – 1.33 (m, 7H), 1.11 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.52, 169.43, 73.99, 73.65, 43.95, 41.96, 41.08, 31.76, 31.24, 30.08, 27.76, 25.49, 23.91.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{15}H_{24}NaO_4$ *m/z* 291.1567 and found *m/z* 291.1567.

IR (thin film, cm^{-1}):1014, 1034, 1123, 1152, 1176, 1231, 1316, 1451, 1729, 1786, 2860, 2936.



(1R,2S,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2p)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

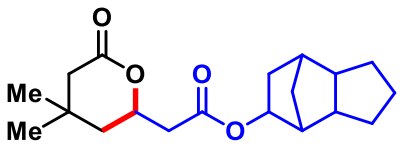
Isolated yield: 66% (42 mg, 0.2 mmol)

^{1}H NMR 1H NMR (400 MHz, CDCl3) δ 4.78 (dddt, J = 12.8, 9.6, 6.4, 3.3 Hz, 1H), 4.72 – 4.65 (m, 1H), 2.75 (ddd, J = 16.0, 6.7, 3.8 Hz, 1H), 2.56 – 2.49 (m, 1H), 2.38 (dd, J = 16.6, 1.5 Hz, 1H), 2.23 (d, J = 16.6 Hz, 1H), 1.85 – 1.68 (m, 5H), 1.59 – 1.45 (m, 2H), 1.16 (dd, J = 9.2, 3.6 Hz, 1H), 1.11 (s, 3H), 1.06 (s, 3H), 1.02 (dd, J = 12.5, 7.0 Hz, 1H), 0.95 (d, J = 7.3 Hz, 3H), 0.87 – 0.80 (m, 6H).

^{13}C NMR (126 MHz, CDCl3) δ 171.42, 169.46, 169.41, 82.03, 81.94, 73.93, 73.91, 48.96, 48.89, 47.14, 45.18, 43.94, 41.97, 41.25, 41.15, 39.00, 38.92, 33.91, 33.87, 31.24, 27.76, 27.71, 27.18, 20.26, 20.09, 20.04, 11.75, 11.66.

HRMS (ESI-QTOF): $[M+Na]^{+}$ calculated for $C_{19}H_{30}NaO_4$ *m/z* 345.2036 and found *m/z* 345.2032.

IR (thin film, cm^{-1}): 1052, 1176, 1233, 1314, 1372, 1456, 1734, 1792, 2876, 2956.



Octahydro-1H-4,7-methanoinden-5-yl-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2q)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 78% (50 mg, 0.2 mmol)

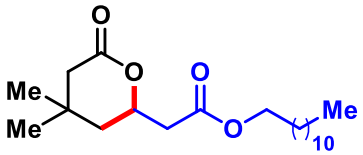
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.77 (dtd, *J* = 9.8, 6.4, 3.4 Hz, 1H), 4.59 (d, *J* = 6.6 Hz, 1H), 2.72 (ddd, *J* = 16.0, 6.5, 3.1 Hz, 1H), 2.51 (ddd, *J* = 16.0, 6.2, 1.9 Hz, 1H), 2.38 (dt, *J* = 16.7, 4.2 Hz, 1H), 2.23 (d, *J* = 16.6 Hz, 1H), 2.04 (dd, *J* = 16.3, 6.9 Hz, 2H), 1.92 – 1.71 (m, 6H), 1.53 – 1.45

(m, 1H), 1.43 – 1.32 (m, 2H), 1.28 – 1.19 (m, 3H), 1.11 (s, 3H), 1.06 (s, 3H), 0.98 – 0.87 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.54, 169.83, 78.05, 73.99, 47.39, 46.25, 43.93, 43.10, 41.93, 40.98, 40.96, 39.72, 39.21, 39.18, 32.16, 31.82, 31.23, 30.07, 29.58, 27.89, 27.75.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{19}H_{28}NaO_4$ *m/z* 343.1880 and found *m/z* 343.1875.

IR (thin film, cm^{-1}**):** 1041, 1192, 1238, 1315, 1373, 1735, 1790, 2866, 2952.



Dodecyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2r)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

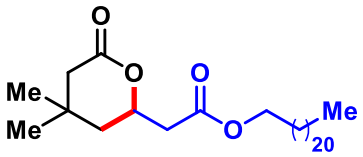
Isolated yield: 76% (57 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.78 (dtd, *J* = 9.9, 6.4, 3.4 Hz, 1H), 4.08 (t, *J* = 6.8 Hz, 2H), 2.74 (dd, *J* = 16.1, 6.7 Hz, 1H), 2.53 (dd, *J* = 16.1, 6.1 Hz, 1H), 2.41 – 2.34 (m, 1H), 2.25 – 2.18 (m, 1H), 1.77 (ddd, *J* = 13.9, 3.4, 1.6 Hz, 1H), 1.60 (dt, *J* = 13.9, 6.8 Hz, 2H), 1.48 (dd, *J* = 13.8, 12.2 Hz, 1H), 1.30 – 1.22 (m, 18H), 1.10 (s, 3H), 1.05 (s, 3H), 0.85 (t, *J* = 6.8 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 171.39, 170.02, 73.86, 65.31, 43.87, 41.89, 40.72, 32.05, 31.16, 30.02, 29.78, 29.76, 29.71, 29.65, 29.48, 29.37, 28.66, 27.66, 26.03, 22.82, 14.26.

HRMS (ESI-QTOF): $[M+H]^+$ calculated for $C_{21}H_{38}NaO_4$ *m/z* 377.2662 and found *m/z* 377.2663.

IR (thin film, cm^{-1}): 1034, 1060, 1172, 1232, 1314, 1372, 1466, 1736, 1792, 2855, 2925, 2962.



Docosyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2s)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

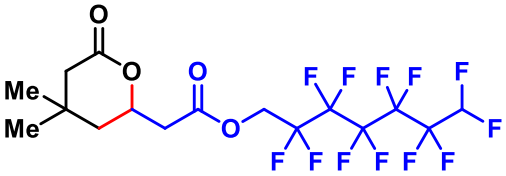
Isolated yield: 73% (72 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.82 – 4.75 (m, 1H), 4.09 (t, *J* = 6.8 Hz, 2H), 2.75 (dd, *J* = 16.1, 6.7 Hz, 1H), 2.54 (dd, *J* = 16.1, 6.1 Hz, 1H), 2.41 – 2.36 (m, 1H), 2.25 – 2.19 (m, 1H), 1.78 (dd, *J* = 13.9, 1.7 Hz, 1H), 1.65 – 1.59 (m, 2H), 1.53 – 1.46 (m, 1H), 1.31 – 1.23 (m, *J* = 22.5 Hz, 38H), 1.11 (s, 3H), 1.06 (s, 3H), 0.86 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.36, 170.03, 77.48, 77.23, 76.98, 73.87, 65.34, 43.90, 41.94, 40.75, 32.10, 31.19, 30.05, 29.88, 29.83, 29.75, 29.69, 29.54, 29.41, 28.70, 27.69, 26.07, 22.86, 14.28.

HRMS (ESI-QTOF): $[M+H]^+$ calculated for $C_{31}H_{59}O_4$ *m/z* 495.4408 and found *m/z* 495.4405.

IR (thin film, cm^{-1}): 1035, 1060, 1153, 1175, 1233, 1315, 1372, 1467, 1737, 1784, 2853, 2923.



2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate (Fig 5, 2t)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 68% (68 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.06 (tt, *J* = 51.8, 5.0 Hz, 1H), 4.82 (dt, *J* = 12.0, 6.3 Hz, 1H), 4.64 (dq, *J* = 39.9, 13.3 Hz, 2H), 2.87 (dd, *J* = 16.3, 7.0 Hz, 1H), 2.70 (dd, *J* = 16.4, 5.6 Hz, 1H),

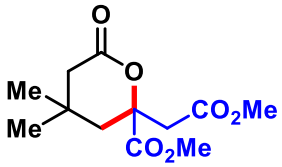
2.44 – 2.37 (m, 1H), 2.25 (d, *J* = 16.7 Hz, 1H), 1.77 (dd, *J* = 13.9, 1.6 Hz, 1H), 1.57 – 1.49 (m, 1H), 1.12 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.04, 168.41, 121.30, 111.32, 110.99, 110.76, 110.02 (t, *J* = 251.77 Hz), 109.77, 109.53, 109.14, 108.89 (t, *J* = 256.34 Hz), 108.65, 108.00, 107.75, 107.50 (t, *J* = 31.5 Hz), 106.01, 105.72, 105.48, 97.11, 73.32, 60.15, 59.93, 59.72 (t, *J* = 26.9 Hz), 43.83, 41.68, 40.19, 31.16, 30.11, 27.53.

^{19}F NMR (471 MHz, $CDCl_3$) δ -119.45, -122.15, -123.41, -129.39, -137.00.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{16}H_{16}F_{12}NaO_4$ *m/z* 523.0749 and found *m/z* 523.0746.

IR (thin film, cm^{-1}):950, 1129, 1160, 1308, 1379, 1407, 1467, 1761, 1738, 2729, 2884, 2970.



Methyl 2-(2-methoxy-2-oxoethyl)-4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-carboxylate (Fig 5, 2u)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

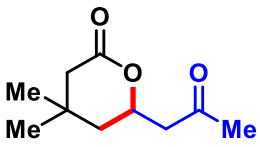
Isolated yield: 51% (26 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 3H), 3.69 (s, 3H), 3.03 (d, *J* = 15.9 Hz, 1H), 2.82 (d, *J* = 15.9 Hz, 1H), 2.42 (d, *J* = 16.4 Hz, 1H), 2.29 (dd, *J* = 21.9, 15.5 Hz, 2H), 1.92 (d, *J* = 14.4 Hz, 1H), 1.07 (s, 3H), 1.02 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 172.40, 170.09, 168.89, 81.50, 53.45, 52.36, 44.90, 43.39, 43.05, 31.40, 30.28, 28.58.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{12}H_{18}NaO_6$ *m/z* 281.0996 and found *m/z* 281.0997.

IR (thin film, cm^{-1}):1056, 1120, 1172, 1214, 1275, 1373, 1438, 1743, 1766, 1776, 2876, 2959.



4,4-dimethyl-6-(2-oxopropyl)tetrahydro-2H-pyran-2-one (Fig 5, 2v)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

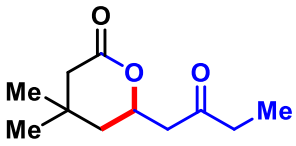
Isolated yield: 56% (21 mg, 0.2 mmol)

^{1}H NMR (400 MHz, CDCl3) δ 4.83 (dtd, J = 9.3, 6.2, 3.2 Hz, 1H), 2.94 (dd, J = 17.0, 6.5 Hz, 1H), 2.61 (dd, J = 17.0, 5.8 Hz, 1H), 2.42 – 2.35 (m, 1H), 2.26 – 2.17 (m, 4H), 1.78 (ddd, J = 13.9, 3.3, 1.6 Hz, 1H), 1.47 – 1.39 (m, 1H), 1.12 (s, 3H), 1.06 (s, 3H).

^{13}C NMR 13C NMR (101 MHz, CDCl3) δ 205.31, 171.72, 73.56, 49.06, 43.96, 42.20, 31.27, 30.10, 27.87.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{10}H_{16}NaO_3$ *m/z* 207.0992 and found *m/z* 207.0992.

IR (thin film, cm^{-1}): 1031, 1112, 1197, 1240, 1288, 1373, 1464, 1719, 1737, 2932, 2960.



4,4-dimethyl-6-(2-oxobutyl)tetrahydro-2H-pyran-2-one (Fig 5, 2w)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

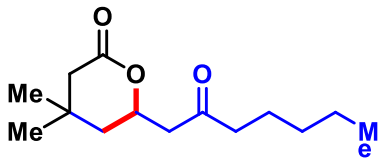
Isolated yield: 72% (28 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.85 (dtd, *J* = 9.5, 6.1, 3.4 Hz, 1H), 2.91 (dd, *J* = 16.7, 6.6 Hz, 1H), 2.61 – 2.55 (m, 1H), 2.52 – 2.47 (m, 2H), 2.36 (t, *J* = 6.8 Hz, 1H), 2.22 (d, *J* = 16.6 Hz, 1H), 1.78 (dd, *J* = 13.9, 1.8 Hz, 1H), 1.47 – 1.39 (m, 1H), 1.12 (s, 3H), 1.05 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 208.11, 171.81, 73.77, 47.87, 43.96, 42.28, 37.38, 31.28, 27.89, 7.65.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{11}H_{18}NaO_3$ *m/z* 221.1148 and found *m/z* 221.1147.

IR (thin film, cm^{-1}):1031, 1112, 1197, 1240, 1288, 1373, 1464, 1719, 1741, 2932, 2960.



4,4-dimethyl-6-(2-oxopropyl)tetrahydro-2H-pyran-2-one (Fig 5, 2x)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (20:80 v/v).

Appearance: Sticky yellow liquid.

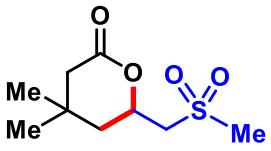
Isolated yield: 70% (34 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.84 (dtd, *J* = 9.4, 6.1, 3.3 Hz, 1H), 2.91 (dd, *J* = 16.9, 6.3 Hz, 1H), 2.61 – 2.53 (m, 1H), 2.43 (ddd, *J* = 27.6, 13.8, 10.7 Hz, 3H), 2.25 – 2.19 (m, 1H), 1.81 – 1.75 (m, 1H), 1.57 (dt, *J* = 14.8, 7.4 Hz, 2H), 1.47 – 1.38 (m, 1H), 1.30 (dd, *J* = 11.6, 5.4 Hz, 4H), 1.12 (s, 3H), 1.05 (s, 3H), 0.88 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 207.80, 171.81, 73.70, 48.17, 44.14, 43.99, 42.29, 31.46, 31.29, 30.11, 27.91, 23.34, 22.63, 14.11.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{14}H_{24}NaO_3$ *m/z* 263.1618 and found *m/z* 263.1613.

IR (thin film, cm^{-1}): 1039, 1129, 1161, 1231, 1305, 1377, 1410, 1466, 1636, 2886, 2936, 2971.



(R)-4,4-dimethyl-6-((methylsulfonyl)methyl)tetrahydro-2H-pyran-2-one (Fig 5, 2y)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (30:70 v/v).

Appearance: Sticky yellow liquid.

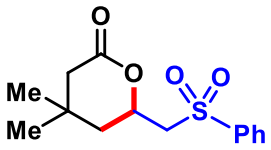
Isolated yield: 61% (27 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.94 (ddd, J = 11.6, 7.5, 4.3 Hz, 1H), 3.39 (dd, J = 15.0, 9.2 Hz, 1H), 3.11 – 3.06 (m, 4H), 2.43 (dd, J = 16.7, 1.3 Hz, 1H), 2.27 (d, J = 16.7 Hz, 1H), 1.79 (ddd, J = 13.9, 3.4, 1.4 Hz, 1H), 1.64 – 1.57 (m, 1H), 1.14 (s, 3H), 1.09 (s, 3H).

^{13}C NMR (101 MHz, CDCl3) δ 170.04, 72.53, 60.00, 43.69, 43.52, 41.48, 31.14, 30.19, 27.67.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_9H_{16}NaO_2S$ *m/z* 243.0662 and found *m/z* 243.0663.

IR (thin film, cm^{-1}): 2970, 2882, 1784, 1735, 1655, 1467, 1408, 1379, 1301, 1254, 1128, 1032.



4,4-dimethyl-6-((phenylsulfonyl)methyl)tetrahydro-2H-pyran-2-one(Fig 5, 2z)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (35:65 v/v).

Appearance: Sticky yellow liquid.

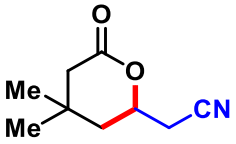
Isolated yield: 68% (38 mg, 0.2 mmol)

1H NMR (400 MHz, CDCl3) δ 7.95 – 7.92 (m, 2H), 7.72 – 7.67 (m, 1H), 7.62 – 7.57 (m, 2H), 4.87 (dtd, *J* = 9.4, 5.9, 3.5 Hz, 1H), 3.56 (dd, *J* = 14.5, 5.7 Hz, 1H), 3.31 (dd, *J* = 14.5, 6.2 Hz, 1H), 2.37 (dd, *J* = 16.6, 1.6 Hz, 1H), 2.21 (d, *J* = 16.7 Hz, 1H), 2.00 (ddd, *J* = 14.1, 3.5, 1.6 Hz, 1H), 1.57 (dd, *J* = 14.0, 12.2 Hz, 1H), 1.11 (s, 3H), 1.06 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.21, 139.68, 134.46, 129.64, 128.32, 71.89, 61.26, 43.86, 42.13, 31.12, 30.21, 27.61.

HRMS (ESI-QTOF): $[M+H]^+$ calculated for $C_{14}H_{19}O_4S$ *m/z* 283.0926 and found *m/z* 283.0928.

IR (thin film, cm^{-1}): 1035, 1125, 1381, 1470, 1650, 1736, 1784, 2926, 2970.



(R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetonitrile (Fig 5, 2ab)

Lactonization was carried out following the general procedure (GP1).

Eluent: ethyl acetate/ petroleum ether (35:65 v/v).

Appearance: Sticky yellow liquid.

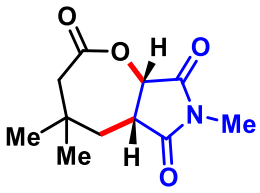
Isolated yield: 70% (23 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.68 – 4.58 (m, 1H), 2.80 – 2.74 (m, 2H), 2.42 (dd, *J* = 16.9, 1.7 Hz, 1H), 2.28 (d, *J* = 16.8 Hz, 1H), 1.84 (ddd, *J* = 13.8, 3.3, 1.8 Hz, 1H), 1.69 – 1.61 (m, 1H), 1.11 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 170.05, 115.79, 72.25, 43.69, 41.05, 30.93, 30.15, 27.05, 24.92.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_9H_{13}NNaO_2$ *m/z* 190.0838 and found *m/z* 190.0838.

IR (thin film, cm^{-1}): 2962, 2875, 2255, 1735, 1471, 1374, 1244, 1223, 1094.



4,4,7-trimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione (Fig 6, 3a)

Lactonization was carried out following the general procedure (GP2).

Eluent: ethyl acetate/ petroleum ether (30:70 v/v).

Appearance: Sticky yellow liquid.

Isolated yield: 58% (26 mg, 0.2 mmol)

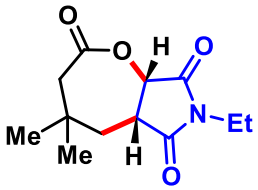
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.75 (d, *J* = 2.1 Hz, 1H), 3.02 (s, 3H), 2.97 (t, *J* = 3.0 Hz, 1H), 2.77 (dd, *J* = 12.4, 7.5 Hz, 2H), 2.51 (d, *J* = 17.2 Hz, 1H), 2.36 (d, *J* = 17.1 Hz, 1H), 1.29 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 177.38, 175.60, 174.71, 84.85, 44.37, 40.16, 39.95, 29.86, 25.78, 25.48, 23.09.

DEPT-135 (126 MHz, $CDCl_3$) δ 84.65, 44.17, 39.95, 29.65, 25.57, 25.29, 22.90.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{11}H_{15}NNaO_4$ *m/z* 248.0893 and found *m/z* 248.0897.

IR (thin film, cm^{-1}): 1128, 1161, 1237, 1289, 1379, 1700, 1779, 2934, 2970.



4,4,7-trimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione (Fig 6, 3b)

Lactonization was carried out following the general procedure (GP2).

Eluent: ethyl acetate/ petroleum ether (30:70 v/v).

Appearance: Sticky yellow liquid.

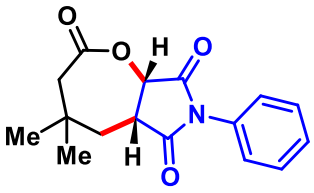
Isolated yield: 52% (25 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.75 (d, *J* = 1.9 Hz, 1H), 3.58 (q, *J* = 7.2 Hz, 2H), 2.99 – 2.94 (m, 1H), 2.79 – 2.72 (m, 2H), 2.51 (d, *J* = 17.1 Hz, 1H), 2.36 (d, *J* = 17.1 Hz, 1H), 1.28 (s, 3H), 1.17 (t, *J* = 7.2 Hz, 3H), 1.08 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 177.20, 175.42, 174.79, 84.86, 44.39, 40.07, 39.96, 34.49, 29.86, 25.74, 23.10, 13.17.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{12}H_{17}NNaO_4$ *m/z* 262.1050 and found *m/z* 262.1047.

IR (thin film, cm^{-1}):1129, 1160, 1227, 1305, 1379, 1407, 1466, 1701, 1774, 2886, 2933, 2971.



4,4-dimethyl-7-phenyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione (Fig 6, 3c)

Lactonization was carried out following the general procedure (GP2).

Eluent: ethyl acetate/ petroleum ether (30:70 v/v).

Appearance: Sticky yellow liquid.

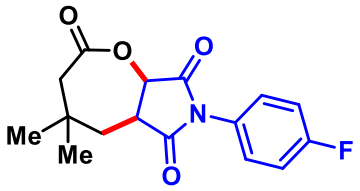
Isolated yield: 51% (29 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$**)** δ 7.48 (t, *J* = 7.4 Hz, 2H), 7.41 (d, *J* = 6.8 Hz, 1H), 7.29 (d, *J* = 7.7 Hz, 2H), 4.85 (s, 1H), 3.20 – 3.15 (m, 1H), 3.02 – 2.89 (m, 2H), 2.58 – 2.52 (m, 1H), 2.40 (d, *J* = 17.1 Hz, 1H), 1.32 (s, 3H), 1.13 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.42, 174.75, 174.53, 131.77, 129.49, 129.12, 126.64, 84.89, 44.40, 40.28, 40.08, 30.04, 25.76, 23.19.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{16}H_{17}NNaO_4$ *m/z* 310.1050and found *m/z* 310.1047.

IR (thin film, cm^{-1}): 1135, 1251, 1302, 1420, 1476, 1709, 1763, 2941, 2981.



7-(4-fluorophenyl)-4,4-dimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione (Fig 6, 3d)

Lactonization was carried out following the general procedure (GP2).

Eluent: ethyl acetate/ petroleum ether (30:70 v/v).

Appearance: Sticky brown gummy

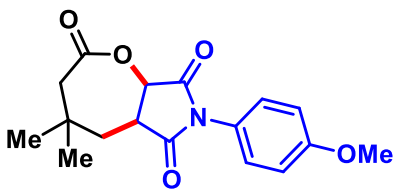
Isolated yield: 39% (24 mg, 0.2 mmol)

1H NMR (400 MHz, $CDCl_3$**)** δ 7.31 – 7.27 (m, 2H), 7.20 – 7.15 (m, 2H), 4.85 (d, *J* = 1.8 Hz, 1H), 3.20 – 3.14 (m, 1H), 2.99 – 2.89 (m, 2H), 2.58 – 2.53 (m, 1H), 2.40 (d, *J* = 17.1 Hz, 1H), 1.32 (s, 3H), 1.13 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$**)** δ 176.20, 174.51, 174.24, 128.34, 128.27, 116.43, 116.25, 84.63, 44.14, 40.03, 39.87, 29.73, 25.56, 23.00.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{16}H_{16}FNNaO_4$ *m/z* 328.0956 and found *m/z* 328.0952.

IR (thin film, cm^{-1}): 1132, 1261, 1307, 1440, 1456, 1729, 1783, 2921, 2991.



7-(4-methoxyphenyl)-4,4-dimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione (Fig 6, 3e)

Lactonization was carried out following the general procedure (GP2).

Eluent: ethyl acetate/ petroleum ether (35:65 v/v).

Appearance: Sticky brown gummy

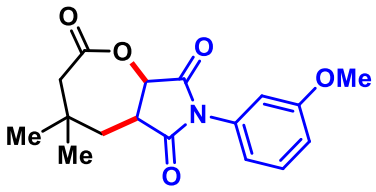
Isolated yield: 40% (25 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$**)** δ 7.21 – 7.18 (m, 2H), 7.00 – 6.98 (m, 2H), 4.85 (s, 1H), 3.83 (s, 3H), 3.18 – 3.13 (m, 1H), 2.98 – 2.87 (m, 2H), 2.55 (d, *J* = 17.1 Hz, 1H), 2.40 (d, *J* = 17.1 Hz, 1H), 1.32 (s, 3H), 1.13 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$**)** δ 176.66, 174.82, 174.77, 159.91, 127.87, 127.67, 114.80, 84.91, 67.23, 55.73, 44.41, 40.22, 40.06, 37.39, 29.98, 25.77, 23.18.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{17}H_{19}NNaO_5$ *m/z* 340.1155 and found *m/z* 340.1156.

IR (thin film, cm^{-1}):1112, 1241, 1315, 1432, 1486, 1708, 1753, 2901, 2961.



7-(3-methoxyphenyl)-4,4-dimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione (Fig 6, 3f)

Lactonization was carried out following the general procedure (GP2).

Eluent: ethyl acetate/ petroleum ether (35:65 v/v).

Appearance: Sticky brown gummy

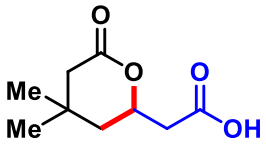
Isolated yield: 45% (28 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38 (t, *J* = 8.1 Hz, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 1H), 6.81 (d, *J* = 1.8 Hz, 1H), 4.85 (d, *J* = 1.5 Hz, 1H), 3.81 (s, 3H), 3.19 – 3.15 (m, 1H), 3.00 – 2.89 (m, 2H), 2.55 (d, *J* = 17.1 Hz, 1H), 2.40 (d, *J* = 17.1 Hz, 1H), 1.32 (s, 3H), 1.13 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.36, 174.78, 174.47, 160.36, 130.20, 118.87, 115.23, 112.32, 84.87, 55.69, 44.38, 40.27, 40.06, 30.02, 25.75, 23.18.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{17}H_{19}NNaO_5$ *m/z* 340.1155 and found *m/z* 340.1157.

IR (thin film, cm^{-1}): 1106, 1232, 1312, 1445, 1497, 1710, 1770, 2921, 2971.



2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetic acid (Fig 9, 4a)

Procedure for the selective hydrolysis of ester:

To a 6NHCl (2 mL) was added **1a** (0.2 mmol) then the mixture was heated to 80°C on a preheated oil bath until TLC showed that the **1a** was fully consumed. The reaction mixture was then cooled to room temperature and extracted with DCM. The organic phase was dried over anhydrous Na_2SO_4, and the solvent was removed under vacuum. The residue was purified by column chromatography using silica gel and petroleum-ether /ethyl acetate as the eluent to afford **4a** in 84% yield.

Eluent: ethyl acetate/ petroleum ether (60:40 v/v).

Appearance: Colorless solid.

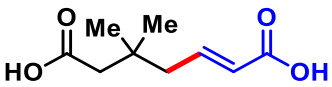
Isolated yield: 84% (31 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.82 (tdd, *J* = 7.4, 5.6, 3.6 Hz, 1H), 2.79 (dd, *J* = 16.4, 7.3 Hz, 1H), 2.62 (dd, *J* = 16.3, 5.5 Hz, 1H), 2.41 (dd, *J* = 16.7, 1.3 Hz, 1H), 2.25 (d, *J* = 16.7 Hz, 1H), 1.83 – 1.76 (m, 1H), 1.57 – 1.48 (m, 1H), 1.12 (s, 3H), 1.08 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 174.86, 171.83, 73.84, 43.83, 41.70, 40.55, 31.14, 30.07, 27.52.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_9H_{14}NaO_4$ *m/z* 209.0784 and found *m/z* 209.0785.

IR (thin film, cm^{-1}): 1130, 1160, 1214, 1315, 1378, 1467, 1719, 1734, 2932, 2970.



(E)-5,5-dimethylhept-2-enedioic acid (Fig 9, 4b)

General procedure for the synthesis of unsaturated dicarboxylic acid (GP3):

To a solution of **1a** (0.2mmol) in EtOH/H_2O (4.0/4.0 mL) was added NaOH (4.0 equiv.), then the mixture was heated to reflux until TLC showed that the **1a** was fully consumed. The reaction mixture was then cooled to room temperature, and 4M HCl was added until the pH of the mixture reached to 3, followed by extraction with EtOAc (30 mL). Then the organic layer was dried on anhydrous Na_2SO_4 and solvent was removed under vacuum. The residue was purified

by column chromatography using silica gel and petroleum-ether /ethyl acetate as the eluent to afford **4b** in 75% yield.

Eluent: ethyl acetate/ petroleum ether (70:30 v/v).

Appearance: Colorless solid.

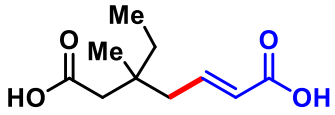
Isolated yield: 75% (28 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (dt, *J* = 15.6, 7.9 Hz, 1H), 5.88 (d, *J* = 15.5 Hz, 1H), 2.32 (d, *J* = 7.8 Hz, 2H), 2.27 (s, 2H), 1.09 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.48, 171.85, 148.50, 123.86, 77.55, 77.23, 76.91, 45.71, 44.47, 34.07, 27.66.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_9H_{14}NaO_4$ *m/z* 209.0784 and found *m/z* 209.0782.

IR (thin film, cm^{-1}): 1034, 1124, 1217, 1283, 1373, 1409, 1467, 1508, 1650, 1700, 1735, 2964, 3022.



(E)-5-ethyl-5-methylhept-2-enedioic acid(Fig 9, 4c)

Unsaturated dicarboxylic acid was synthesized following the general procedure (GP3).

Eluent: ethyl acetate/ petroleum ether (60:40 v/v).

Appearance: Colorless solid.

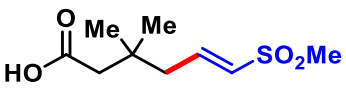
Isolated yield: 81% (32 mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.94 (d, *J* = 15.7 Hz, 1H), 5.60 – 5.53 (m, 1H), 3.68 (d, *J* = 7.4 Hz, 2H), 2.84 (s, 3H), 2.37 (s, 2H), 1.19 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.57, 148.74, 114.59, 58.94, 46.61, 38.92, 36.17, 27.42.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_9H_{16}NaO_4S$ *m/z* 243.0662 and found *m/z* 243.0661.

IR (thin film, cm^{-1}): 1118, 1242, 1290, 1368, 1409, 1472, 1725, 2932, 2967.



(E)-3,3-dimethyl-6-(methylsulfonyl)hex-5-enoic acid (Fig 9, 4d)

Unsaturated sulphone acid was synthesized following the general procedure (GP3).

Eluent: ethyl acetate/ petroleum ether (60:40 v/v).

Appearance: Colorless solid.

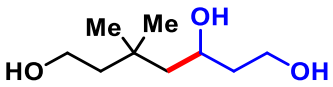
Isolated yield: 82% (36 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (dt, *J* = 15.6, 7.8 Hz, 1H), 5.88 (d, *J* = 15.5 Hz, 1H), 2.33 (td, *J* = 13.8, 7.6 Hz, 2H), 2.24 (t, *J* = 8.7 Hz, 2H), 1.51 – 1.39 (m, 2H), 1.06 (s, 3H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 178.38, 171.54, 148.47, 123.70, 43.21, 42.20, 36.94, 32.89, 24.73, 8.23.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_{10}H_{16}NaO_4$ *m/z* 223.0941 and found *m/z* 223.0942.

IR (thin film, cm^{-1}): 1034, 1124, 1217, 1283, 1373, 1409, 1467, 1508, 1650, 1700, 1735, 2964, 3022.



5,5-dimethylheptane-1,3,7-triol (Fig 9, 4e)

Procedure for the triol synthesis:

To a solution of **1a** (0.2 mmol) in THF (2.0 mL) was added 0.8 mL of LAH solution (1.0 M in THF), then the mixture was stirred at room temperature until TLC showed that the **1a** was fully consumed. Then the reaction was cooled to 0 ºC and quenched by saturated Na_2SO_4 solution. The reaction mixture was extracted with DCM and organic phase was dried over anhydrous Na_2SO_4.Solvent was removed under vacuum and the residue was purified by column chromatography using silica gel and petroleum-ether /ethyl acetate as the eluent to afford **4d** in 80% yield.

Eluent: ethyl acetate/ petroleum ether (50:50 v/v).

Appearance: Colorless gummy.

Isolated yield: 80% (8 mg, 0.2 mmol)

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.01 (d, *J* = 7.8 Hz, 1H), 3.86 – 3.61 (m, 6H), 1.84 (dt, *J* = 14.1, 7.0 Hz, 1H), 1.75 – 1.56 (m, 3H), 1.42 (dt, *J* = 14.3, 5.1 Hz, 1H), 1.26 (d, *J* = 13.8 Hz, 1H), 0.95 (s, 3H), 0.93 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 77.55, 77.23, 76.91, 68.87, 61.35, 59.48, 48.69, 42.89, 40.72, 32.28, 29.38, 29.06.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_9H_{20}NaO_3$ *m/z* 199.1305 and found *m/z* 199.1306.

IR (thin film, cm^{-1}): 1128, 1160, 1304, 1379, 1408, 1467, 2929, 2969, 3325, 3335, 3352.

3,3-dimethylheptanedioic acid (Fig 9, 4f)

Hydrogenation of unsaturated dicarboxylic acid:

A solution of **4b** (0.1mmol) and Pd/C (0.01 mmol, 10 mol%) in MeOH (2.0 mL) fitted with H_2 balloon was stirred at room temperature for 12 h. After completion of the reaction solvent was removed under vacuum and residue was filtered through celite using EtOAc.Then the organic layer was dried on anhydrous Na_2SO_4 and solvent was removed under vacuum. The residue was purified by column chromatography using silica gel and petroleum-ether /ethyl acetate as the eluent to afford **4c** in 70% yield.

Eluent: ethyl acetate/ petroleum ether (60:40 v/v).

Appearance: Colorless solid.

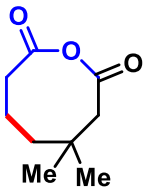
Isolated yield: 70% (26 mg, 0.2 mmol)

^{1}H NMR (400 MHz, CD_3CN) δ 2.24 (t, *J* = 7.4 Hz, 2H), 2.17 (s, 2H), 1.59 – 1.50 (m, 2H), 1.35 – 1.29 (m, 2H), 0.98 (s, 6H).

^{13}C NMR (101 MHz, CD_3CN) δ 175.82, 174.51, 45.90, 42.11, 34.88, 33.49, 27.41, 20.43.

HRMS (ESI-QTOF): $[M+Na]^+$ calculated for $C_9H_{16}NaO_4$ *m/z* 211.0941and found *m/z* 211.0943.

IR (thin film, cm^{-1}): 1051, 1215, 1467, 1706, 1715, 2927, 2961.



4,4-dimethyloxocane-2,8-dione (Fig 9, 4g)

Procedure for the eight membered anhydride synthesis:

Amixture of **4c** (0.1mmol) and $SOCl_2$ (0.4 mmol, 4 equiv.) was stirred at room temperature for 12 h. After completion of reaction volatiles are removed under vacuum and extracted with

EtOAc, then the organic fraction was washed with saturated $NaHCO_3$. Organic phase was dried overanhydrous Na_2SO_4 and solvent was removed under vacuum to afford desired product 4e in 90 yield.

Appearance: White solid.

Isolated yield: 90% (31mg, 0.2 mmol)

^{1}H NMR (500 MHz, $CDCl_3$) δ 2.35 (t, *J* = 6.7 Hz, 2H), 2.26 (s, 2H), 1.66 (ddd, *J* = 13.7, 10.9, 6.9 Hz, 2H), 1.44 – 1.38 (m, 2H), 1.04 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 180.39, 178.93, 45.48, 40.23, 34.63, 33.34, 28.03, 19.79.

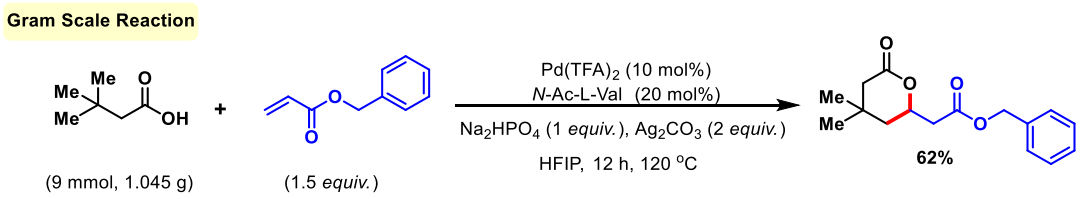
HRMS (ESI-QTOF): $[M+H]^+$ calculated for $C_9H_{15}O_3$ *m/z* 171.1016 and found *m/z* 171.1018.

IR (thin film, cm^{-1}): 755, 933, 1051, 1216, 1285, 1411, 1703, 2963, 3024.

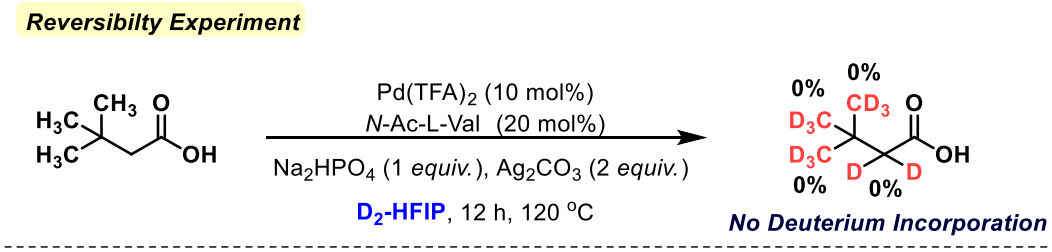
Gram scale synthesis:

A clean, oven-dried screw cap reaction tube with previously placed magnetic stir–bar was charged with aliphatic carboxylic acid (9 mmol), olefin (13.5 mmol), palladium(II) trifluoroacetate (0.9 mmol), ligand (1.8 mmol), Ag_2CO_3 (18 mmol) and disodium hydrogen phosphate (9 mmol) followed by addition of HFIP (10 mL). The reaction mixture was vigorously stirred for 12 h in a preheated oil bath at 120 °C. After stipulated time, the reaction mixture was cooled to room temperature and filtered through a celite bed using ethyl acetate as the eluent (30 mL). The diluted ethyl acetate solution of the reaction mixture was subsequently washed with saturated brine solution (2 x 30 mL) followed by water (2 x 30 mL). The ethyl acetate layer was dried over anhydrous Na_2SO_4 and the volatiles were removed under vacuum. The crude reaction mixture was purified by column chromatography.

Isolated yield: 62% (1.54 g, 9 mmol)



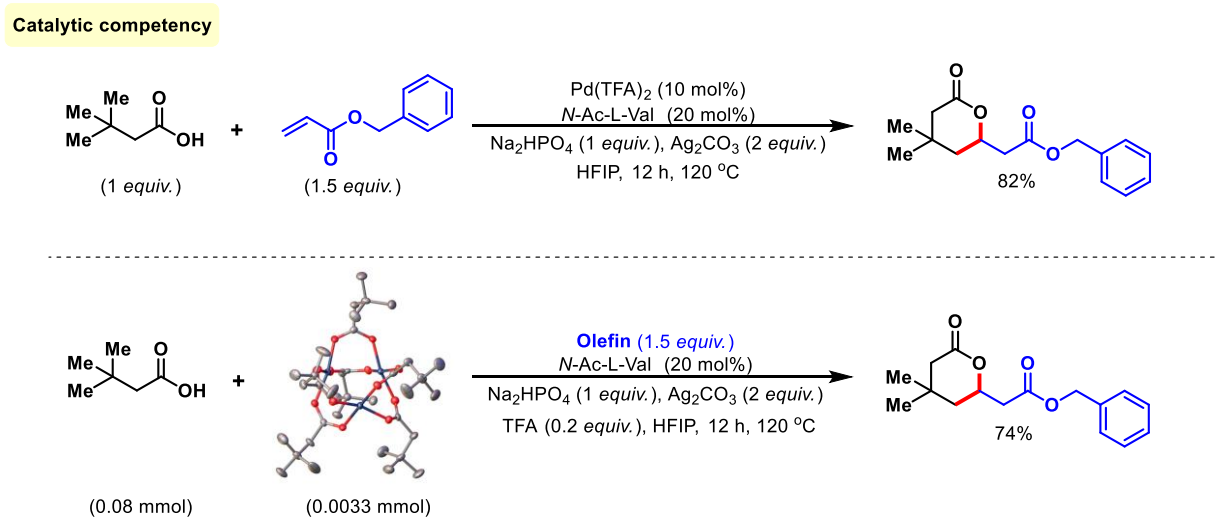
Reversibility Experiment



Reversibility of the γ-C−H activation step was performed by using D_2-HFIP at high temperature 120 ˚C. No deuterium scrambling was observed in the recovered starting material. Similarly, almost no deuterium depletion was observed when the deuterated substrate was subjected to reversibility experiment under the same reaction condition. These experiments suggest the irreversible nature of the C–H activation step and it is likely to be the rate determining step of the reaction. Interestingly, kinetic isotope effect study of 3,3-dimethylbutanoic acid gave a value of 2.3, which is in agreement with our hypothesis that C–H activation is the r.d.s. of the reaction.

Also order determination study showed that reaction follows first order kinetics w.r.t. acid and fraction order w.r.t. olefin which further supports acid is present in the r.d.s.

Catalytic Competency:

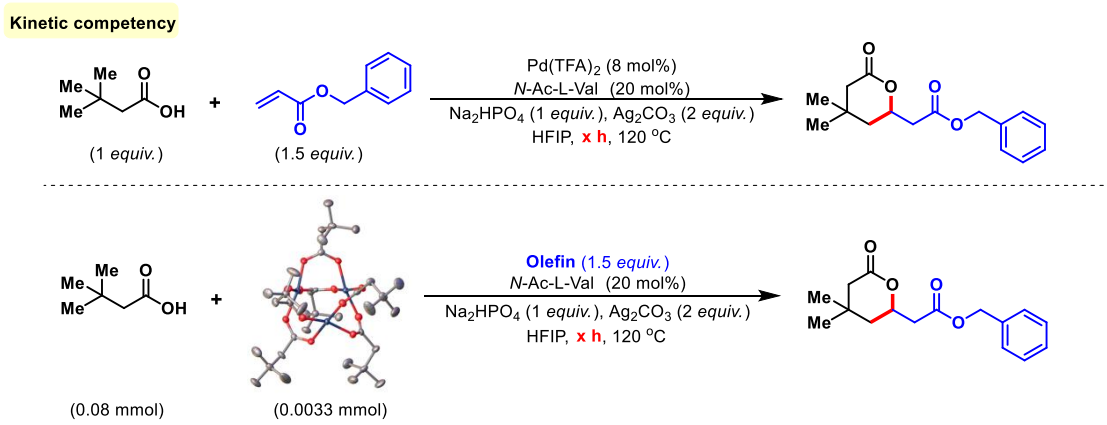


A Clean, oven-dried screw cap reaction tube with previously placed magnetic stir–bar was charged with aliphatic carboxylic acid (0.08 mmol), complex (0.0033 mmol), olefin (1.5 equiv.), ligand (20 mol%), Ag_2CO_3 (2 equiv.) and disodium hydrogen phosphate (1 equiv.) followed by addition of TFA (0.2 equiv.), and HFIP (1 mL). The reaction mixture was vigorously stirred for 12 h in a preheated oil bath at 120 °C. After stipulated time, the reaction mixture was cooled to room temperature and filtered through a celite bed using ethyl acetate as the eluent (30 mL). The diluted ethyl acetate solution of the reaction mixture was subsequently washed with saturated brine solution (2 x 10 mL) followed by water (2 x 10 mL). The ethyl acetate layer was dried over anhydrous Na_2SO_4 and the volatiles were removed under vacuum. The crude reaction mixture was purified by column chromatography using silica gel and petroleum-ether / ethyl acetate as the eluent.

Isolated yield: 74%

Kinetic competency:

Kinetic competency studies were carried out using 3,3-dimethylbutanoic acid as the model substrate and benzyl acrylate as the olefin coupling partner. Two different set of reaction were performed using palladium trifluoroacetate and the complex. Product concentration was plotted against time at different time interval.



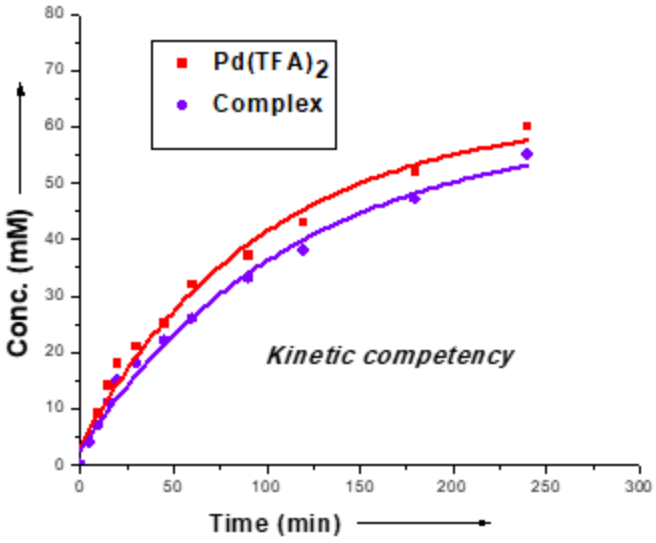


Figure S1: Kinetic competency study

Kinetic experiments:

Kinetic studies were performed under standard reaction conditions with 3,3-dimethylbutanoic acid as the model substrate and benzyl acrylate as the olefin coupling partner. Here, each set of reactions were carried out in different screw cap reaction tubes changing the concentration of the reactant one at a time from the standard condition. Rate of the reaction was determined with respect to both 3,3-dimethylbutanoic acid and benzyl acrylate. Product concentration of the reaction was plotted against time (min).

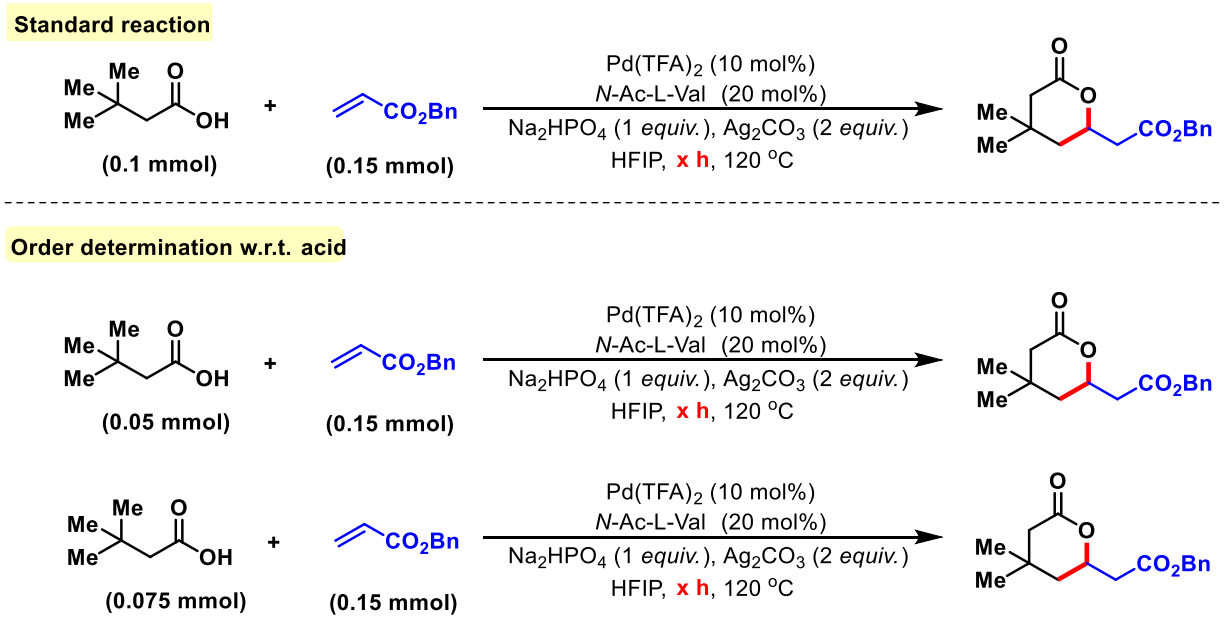
Kinetic dependence of reaction components:

As both acid and olefin were involved in this reaction, we can assume the rate of the reaction is dependent on the concentration of acid and olefin.

So, Rate = k. $[acid]^x[olefin]^y$ (1)

Determination of order with respect to acid:

Run	Acid	olefin	$Pd(TFA)_2$ (mmol)	Ag_2CO_3 (mmol)	*N*-Ac-L-Val (mmol)	Na_2HPO_4 (mmol)	HFIP (mL)
1	0.1	0.15	0.01	0.2	0.02	0.1	1
2	0.05	0.15	0.01	0.2	0.02	0.1	1
3	0.075	0.15	0.01	0.2	0.02	0.1	1



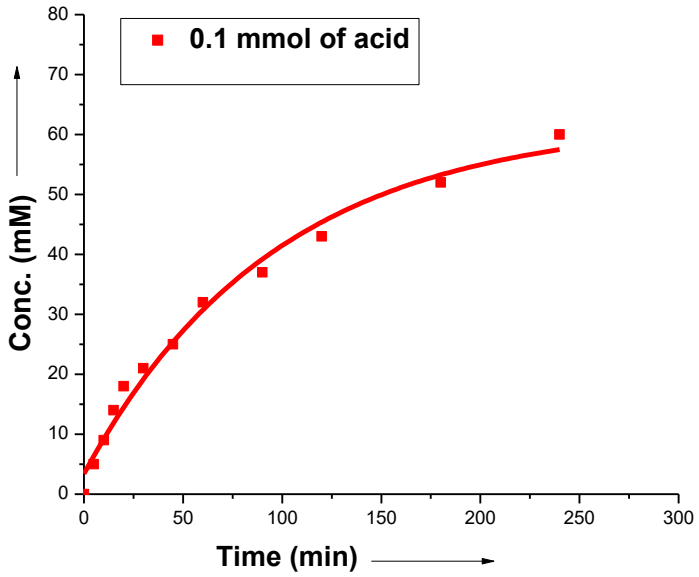


Figure S2: Product formation plot under standard condition (run 1)

From the different set of experiment the following product formation plot was observed:

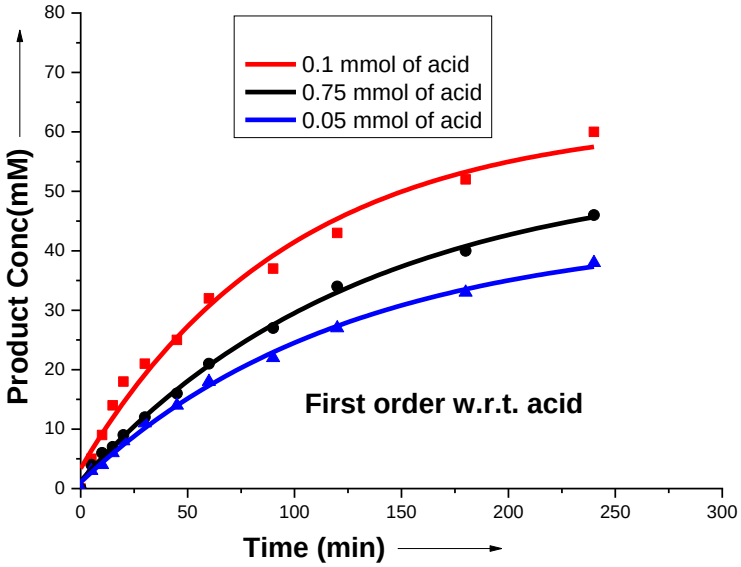


Figure S3: Product formation plot in run 1, 2& 3.

From the equation (1) we got, Rate = k. $[Acid]^x[Olefin]^y$

For run 1, initial rate = Rate 1

So, Rate 1 = k. $[Acid]^x[Olefin]^y$

or, 0.450 $(mmol^{-1}.min^{-1})$ = k. $[0.1]^x [0.15]^y$ (2)

For run 2, initial rate = Rate 2

So, Rate 2 = k. $[Acid]^x[Olefin]^y$

or, 0.223 $(mmol^{-1}.min^{-1})$ = k . $[0.05]^x[0.15]^y$ (3)

Hence from equation (2) and (3)

We get, $[Rate\ 1/ Rate\ 2] = [0.1/ 0.05]^x$

or, x = [log (Rate 1) – log (Rate 2)] / [log (0.1) – log (0.05)]

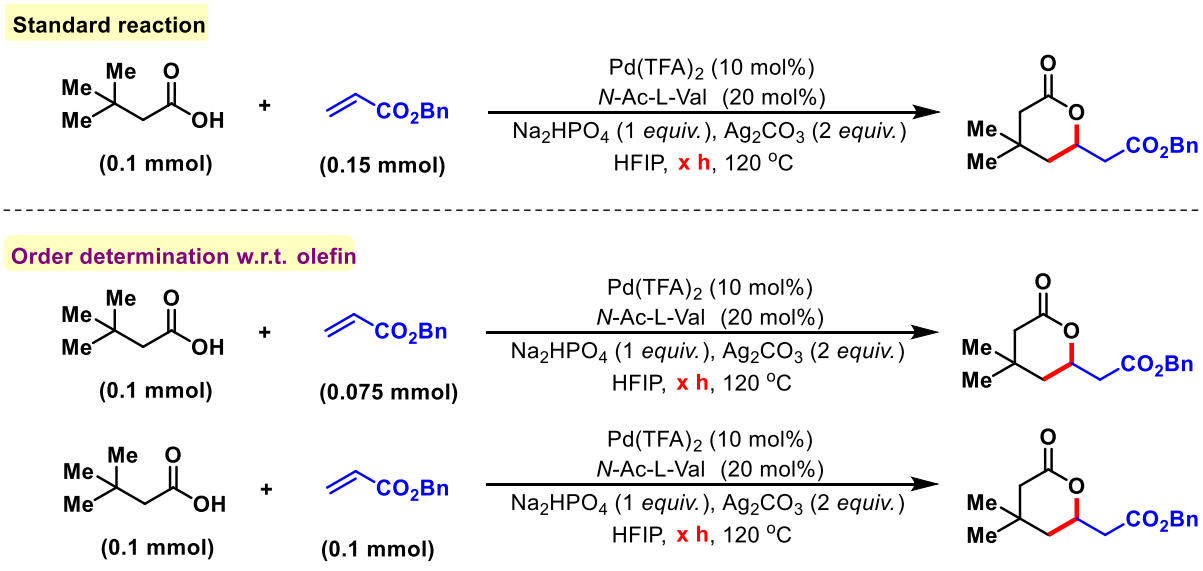
or, x = [log (0.450) – log (Rate 0.223)] / [log (0.1) – log (0.05)]

or, x = 1.01

So, order with respect to aliphatic acid is ~ 1

Determination of order with respect to Olefin:

Run	Acid	Olefin	$Pd(TFA)_2$ (mmol)	Ag_2CO3 (mmol)	*N*-Ac-L-Val (mmol)	Na_2HPO_4 (mmol)	HFIP (mL)
1	0.1	0.15	0.01	0.2	0.02	0.1	1
4	0.1	0.075	0.01	0.2	0.02	0.1	1
5	0.1	0.1	0.01	0.2	0.02	0.1	1



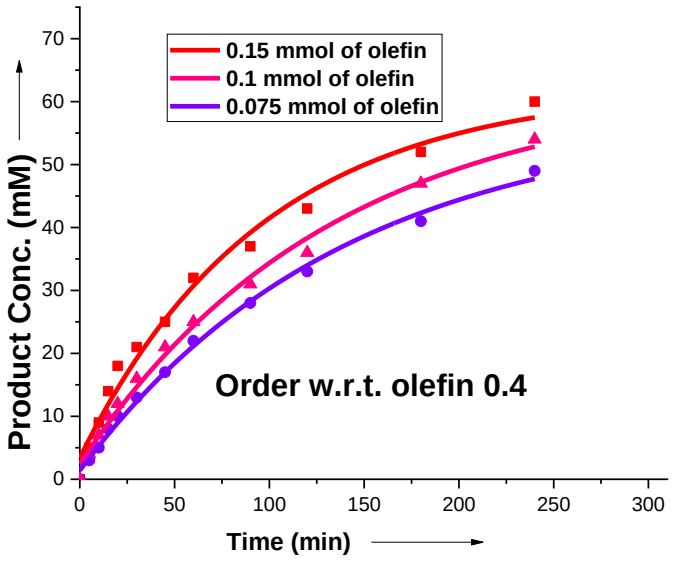


Figure S4: Product formation plot in run 1, 4 & 5.

From the equation (1) we got, Rate = k. $[Acid]^x[Olefin]^y$

For run 1, initial rate = Rate 1

So, Rate 1 = k. $[Acid]^x[Olefin]^y$

or, 0.450 $(mmol^{-1}.min^{-1})$ = k . $[0.1]^x[0.15]^y$ (2)

For run 4, initial rate = Rate 4

So, Rate 4 = k. $[Acid]^x[Olefin]^y$

or, 0.342 $(mmol^{-1}.min^{-1})$ = k . $[0.1]^x[0.075]^y$ (4)

Hence from equation (2) and (4)

We get, $[Rate\ 1/ Rate\ 4] = [0.2/ 0.1]^y$

or, y = [log (Rate 1) – log (Rate 4)] / [log (0.2) – log (0.1)]

or, y = [log (0.450) – log (Rate 0.342)] / [log (0.2) – log (0.1)]

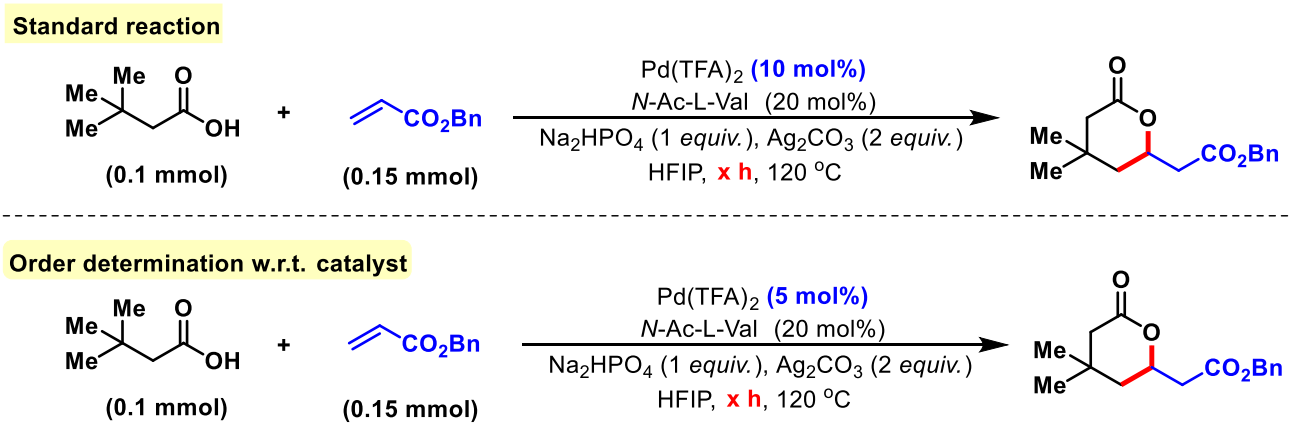
or, y = 0.4

So, order with respect to olefin is ~ 0.4

Determination of order with respect to Catalyst:

Order of the catalyst is determined by using normalized time scale method.[2]Two sets of reactions were carried out with different concentration of the catalyst used.

Run	Acid	Olefin	$Pd(TFA)_2$ (mmol)	Ag_2CO3 (mmol)	*N*-Ac-L-Val (mmol)	Na_2HPO_4 (mmol)	HFIP (mL)
1	0.1	0.15	0.01	0.2	0.02	0.1	1
6	0.1	0.15	0.005	0.2	0.02	0.1	1



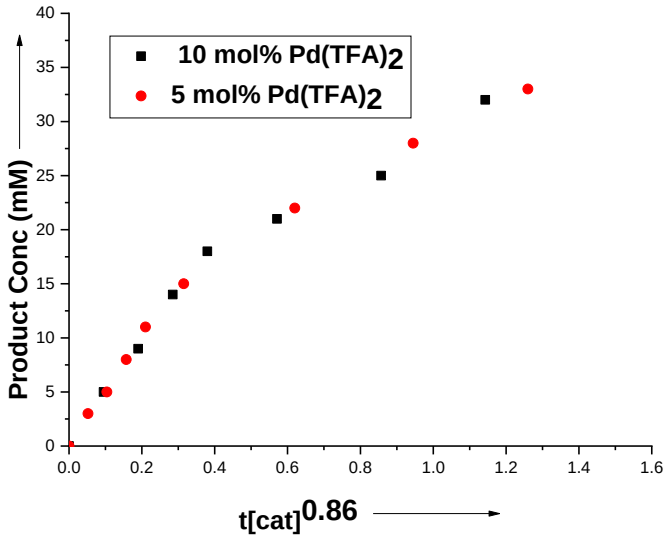


Figure S5: Product formation plot in run 1 & 6.

Order of the catalyst is 0.86.

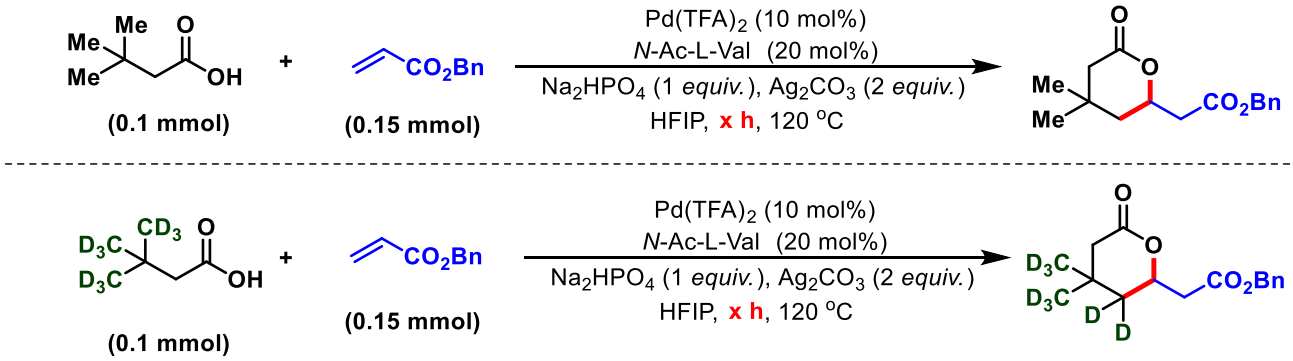
Kinetic isotope effect experiment:

Kinetic isotopic study was performed under the standard condition by using the deuterium containing substrate.

Run	Acid	Olefin	$Pd(TFA)_2$ (mmol)	Ag_2CO3 (mmol)	*N*-Ac-L-Val (mmol)	Na_2HPO_4 (mmol)	HFIP (mL)
1	0.1	0.15	0.01	0.2	0.02	0.1	1

Run	Deuterated Acid	Olefin	$Pd(TFA)_2$ (mmol)	Ag_2CO3 (mmol)	*N*-Ac-L-Val (mmol)	Na_2HPO_4 (mmol)	HFIP (mL)
7	0.1	0.15	0.01	0.2	0.02	0.1	1

Kinetic isotopic effect



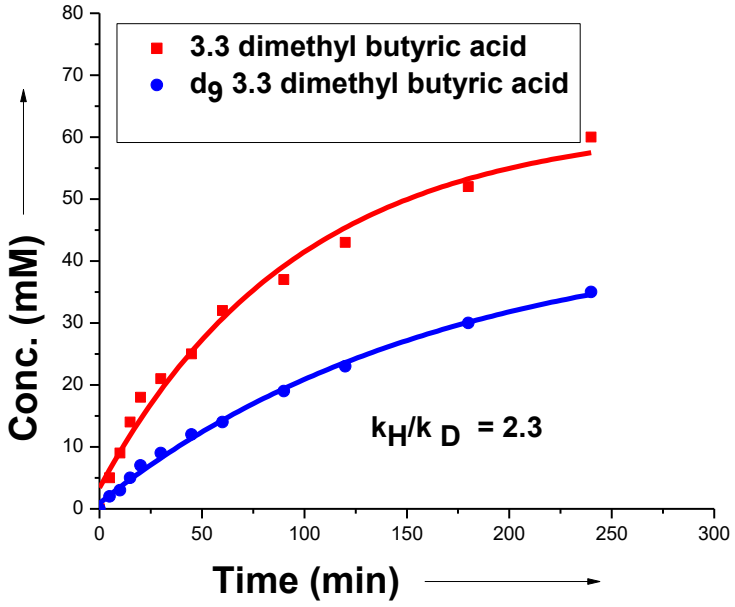


Figure S6: Product formation plot in run 1 &7

Now, Rate = k. $[Acid]^x[Olefin]^y$

For run 1, initial rate = Rate 1

So, Rate 1 = k_H. $[Acid]^x[Olefin]^y$

or, 0.450 ($mmol^{-1}.min^{-1}$) = k_H . $[0.1]^x[0.15]^y$ (1)

For run 7, initial rate = Rate 7

So, Rate 7 = k_D. $[Acid]^x[Olefin]^y$

or, 0.195 ($mmol^{-1}.min^{-1}$) = k_D. $[0.1]^x[0.15]^y$ (5)

So, from equation (1) and (5) we get

k_H / k_D = Rate 1 / Rate 7

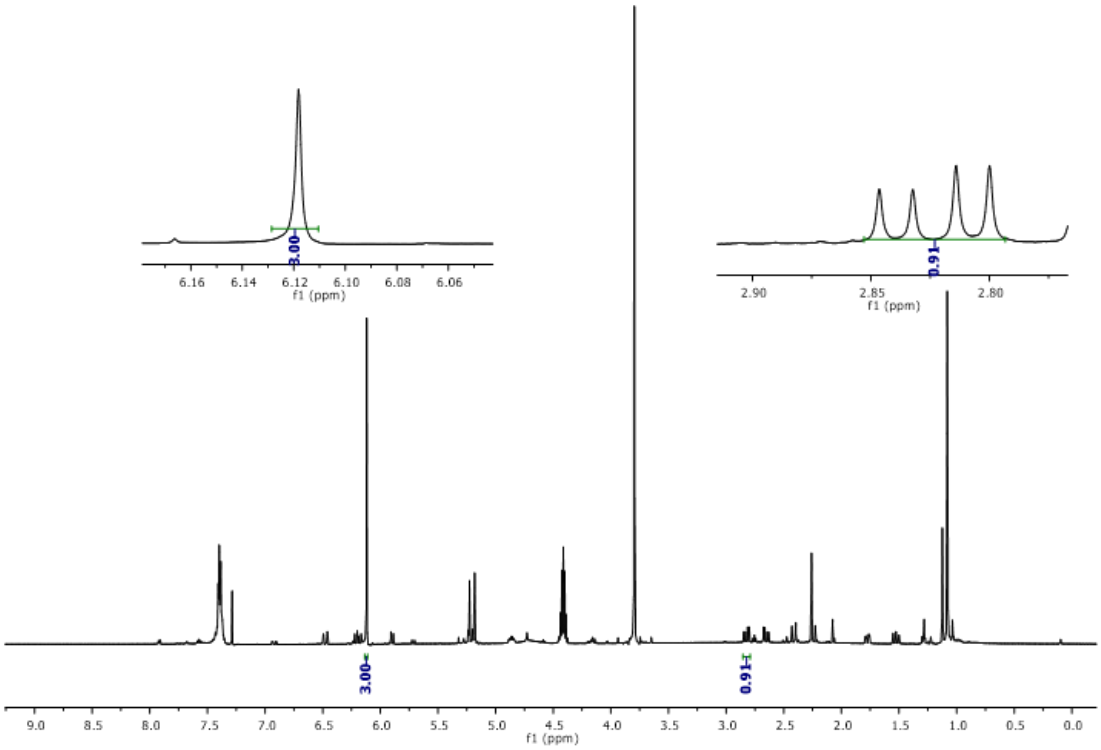
or, k_H / k_D = 0.450 ($mmol^{-1}.min^{-1}$) / 0.195 ($mmol^{-1}.min^{-1}$)

or, k_H / k_D = 2.3

Therefore, primary kinetic isotope effect was observed in the present reaction. This clearly suggest C–H activation is the rate determining step of the reaction.

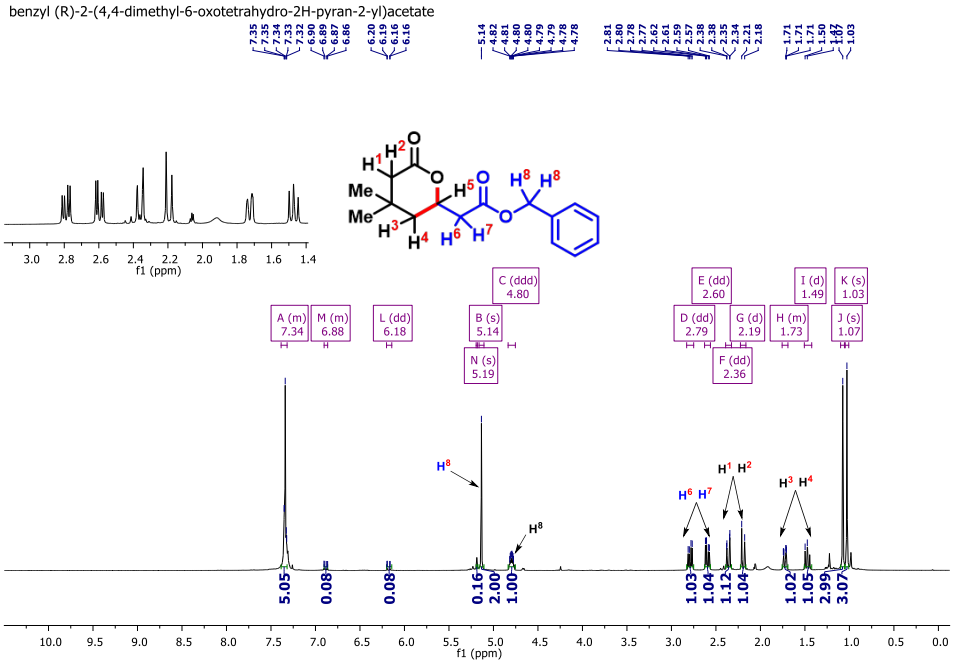
Reference:

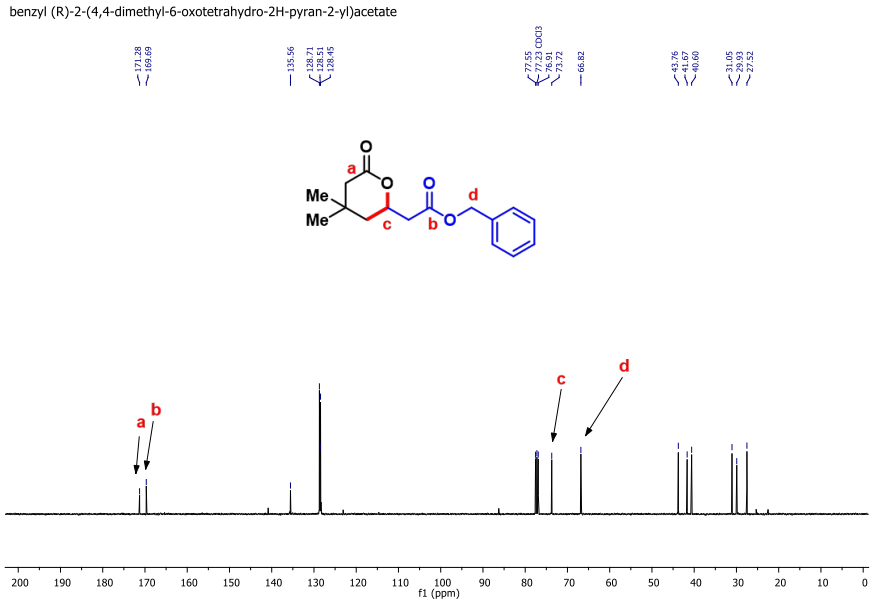
1. K. K. Ghosh, A. Uttry, A. Mondal, F.Ghiringhelli, P. Wedi. M. Van Gemmeren, *Angew. Chem. Int. Ed.***2020**, DOI:https://doi.org/10.1002/anie.202002362
2. J. Burés, *Angew. Chem. Int. Ed.*, 2016,**55**, 2028.



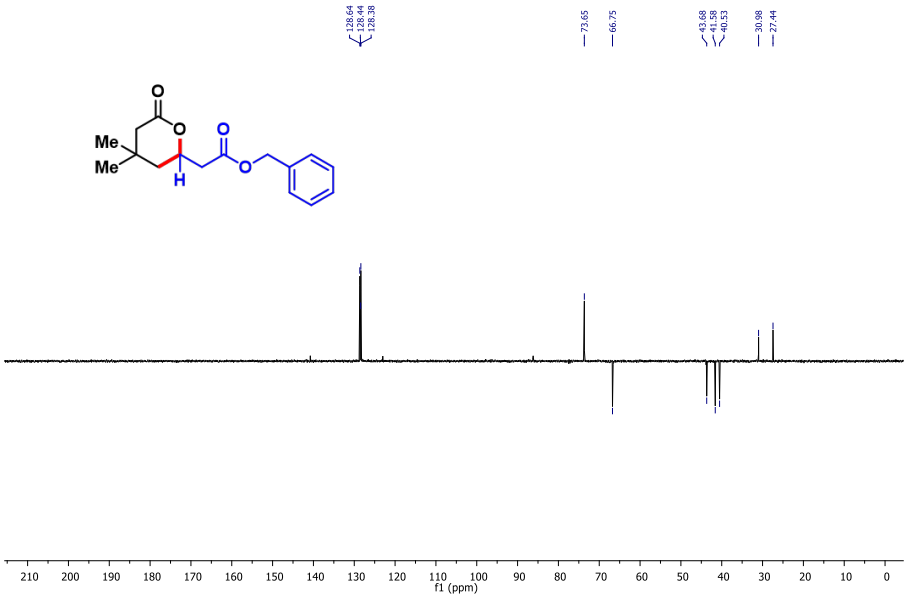
Internal standard: 1,3,5-Trimethoxy benzene

NMR Spectra

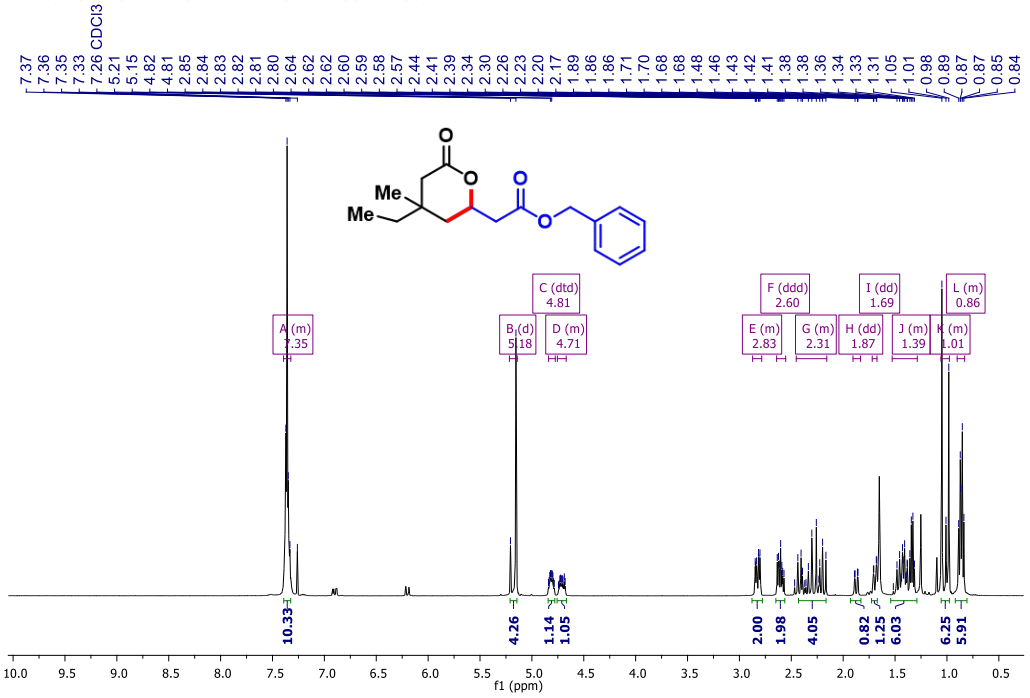

benzyl (R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate
A (m) 7.34
M (m) 6.88
L (dd) 6.18
B (s) 5.14
C (ddd) 4.80
N (s) 5.19
D (dd) 2.79
E (dd) 2.60
F (dd) 2.36
G (d) 2.19
H (m) 1.73
I (d) 1.49
J (s) 1.07
K (s) 1.03
f1 (ppm)


benzyl (R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate
f1 (ppm)

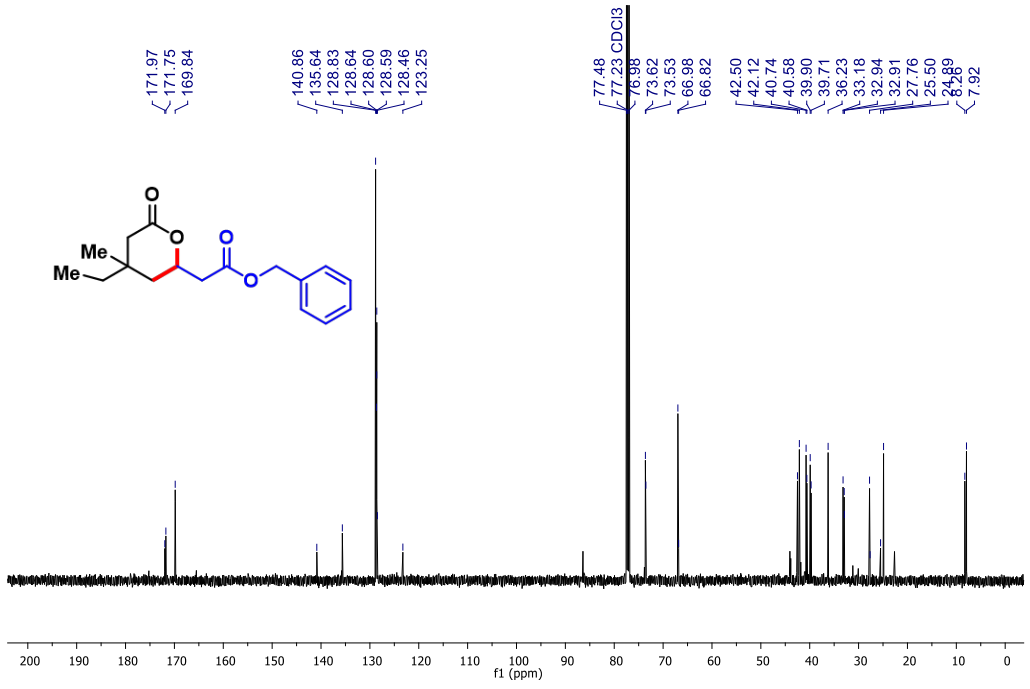
benzyl (R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



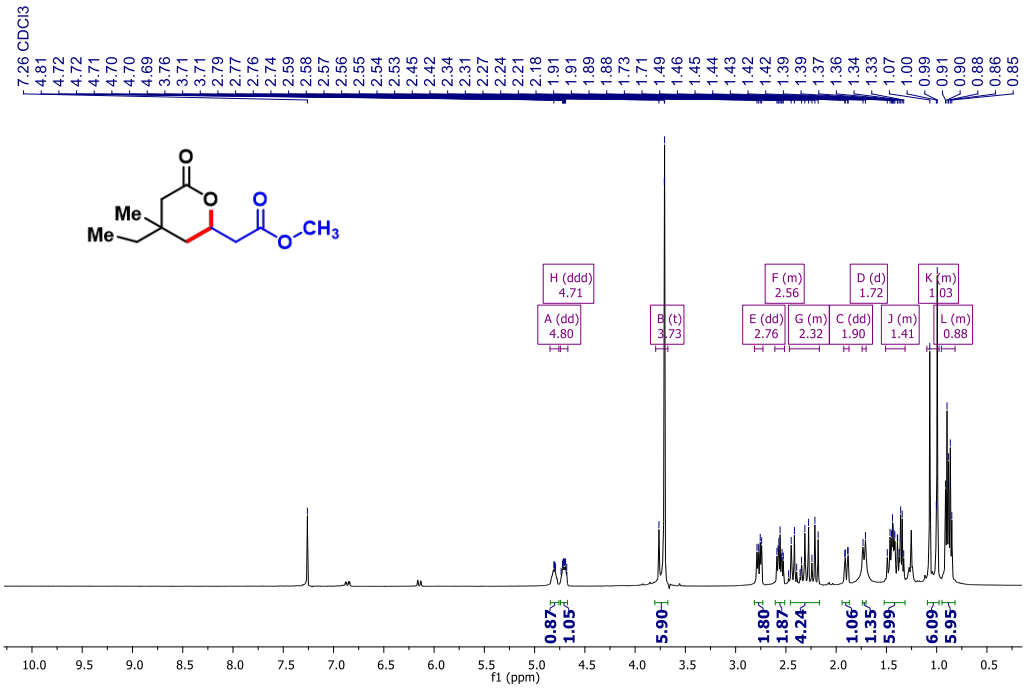
benzyl 2-(4-ethyl-4-methyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



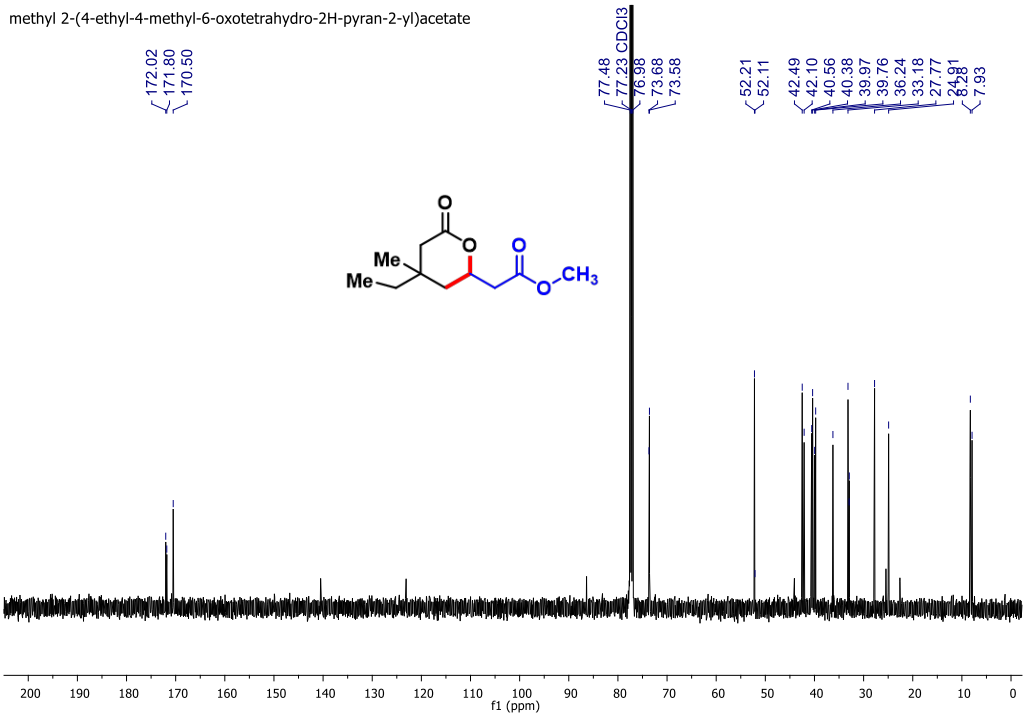
benzyl 2-(4-ethyl-4-methyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



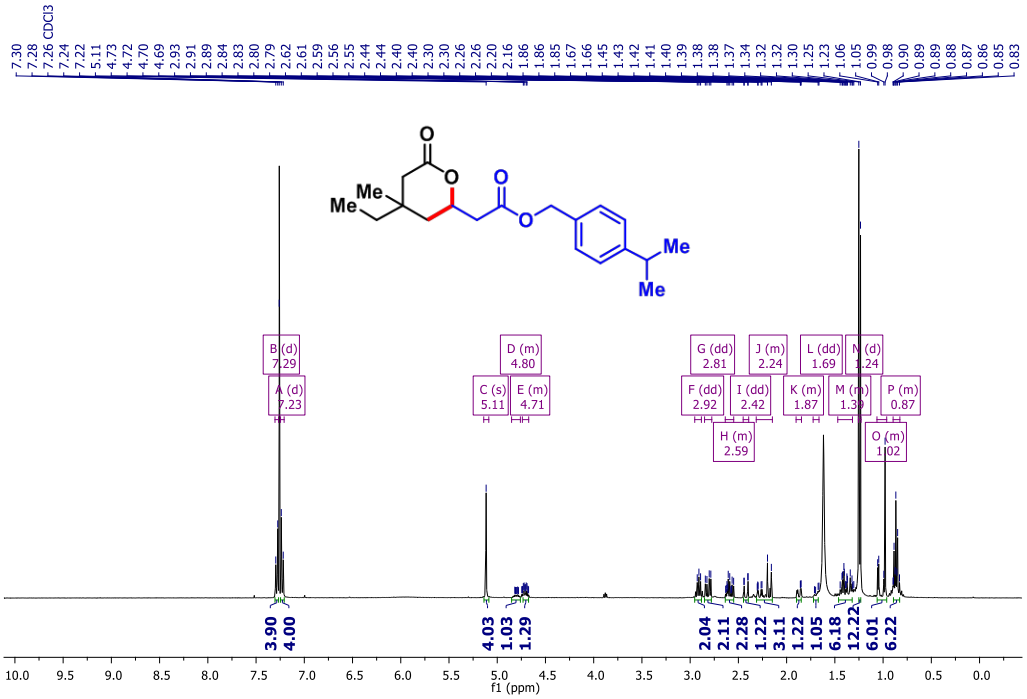
methyl 2-(4-ethyl-4-methyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



methyl 2-(4-ethyl-4-methyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



4-isopropylbenzyl 2-(4-ethyl-4-methyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



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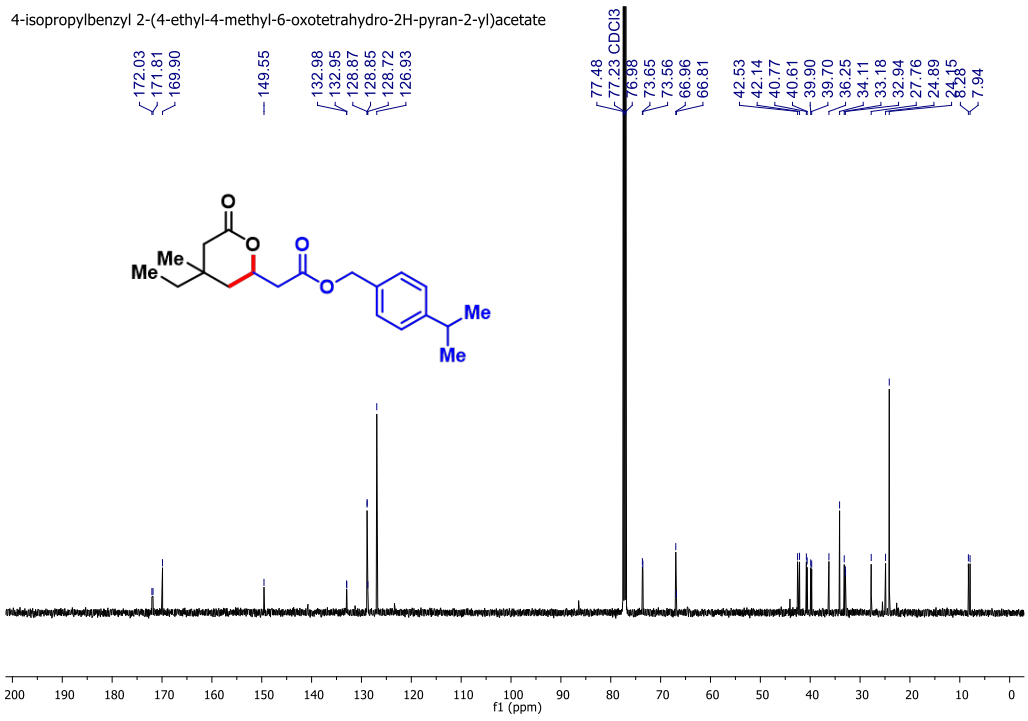
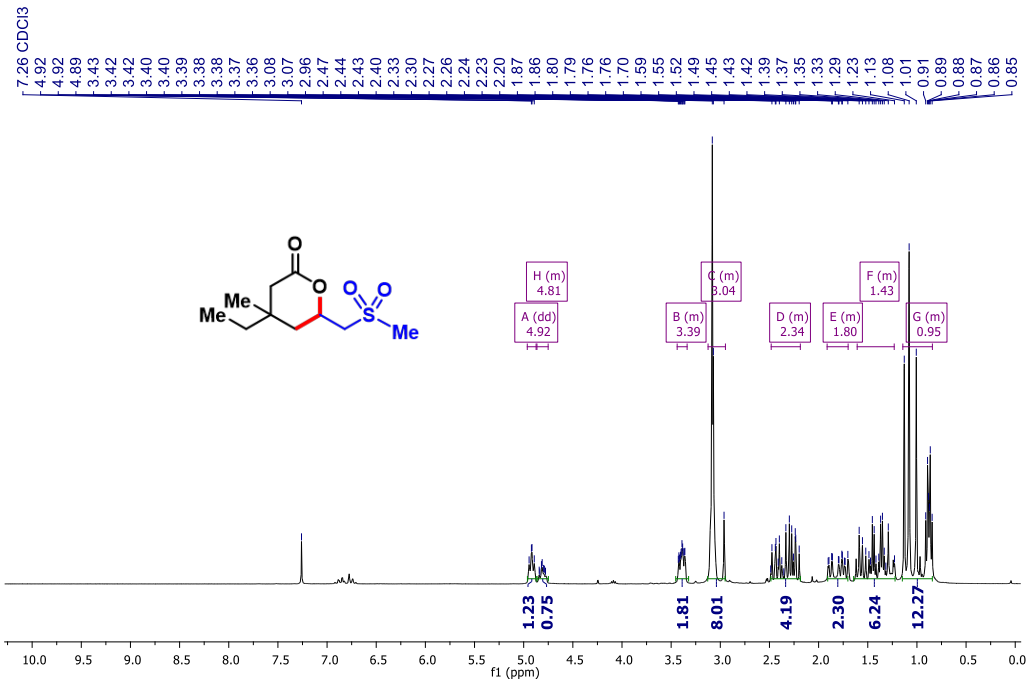


4-ethyl-4-methyl-6-((methylsulfonyl)methyl)tetrahydro-2H-pyran-2-one



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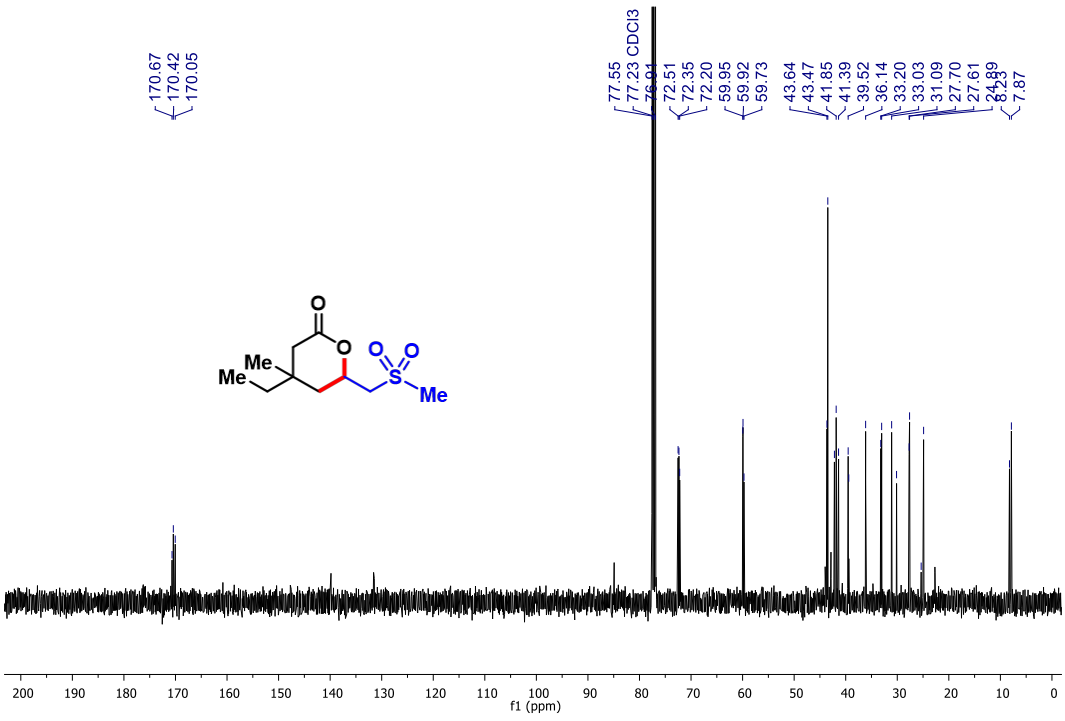
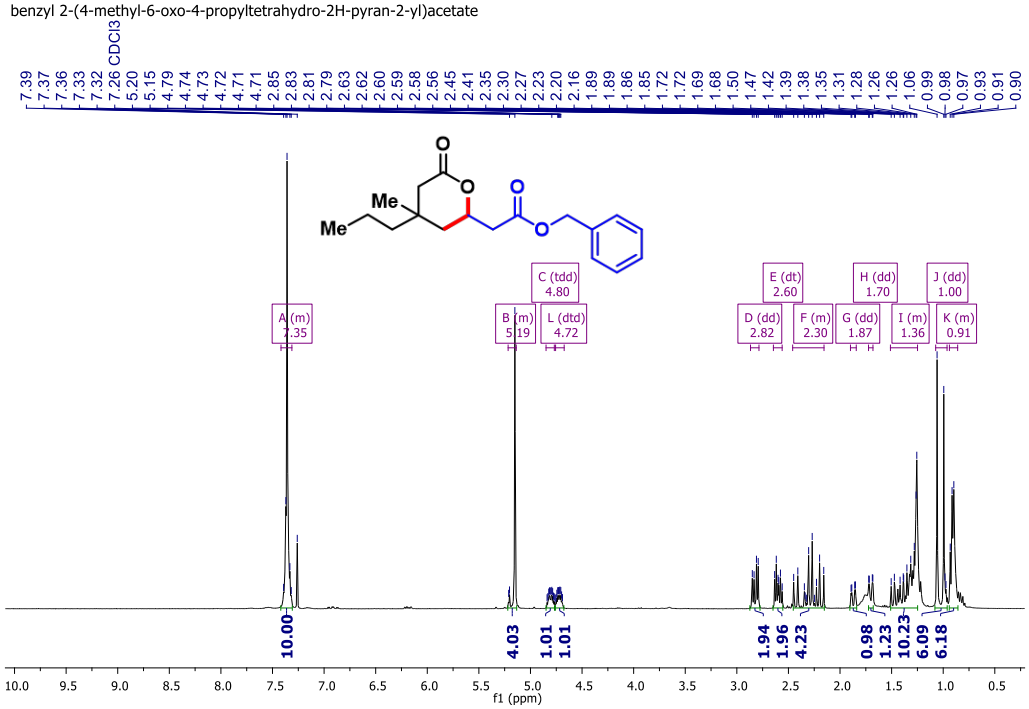


benzyl 2-(4-methyl-6-oxo-4-propyltetrahydro-2H-pyran-2-yl)acetate



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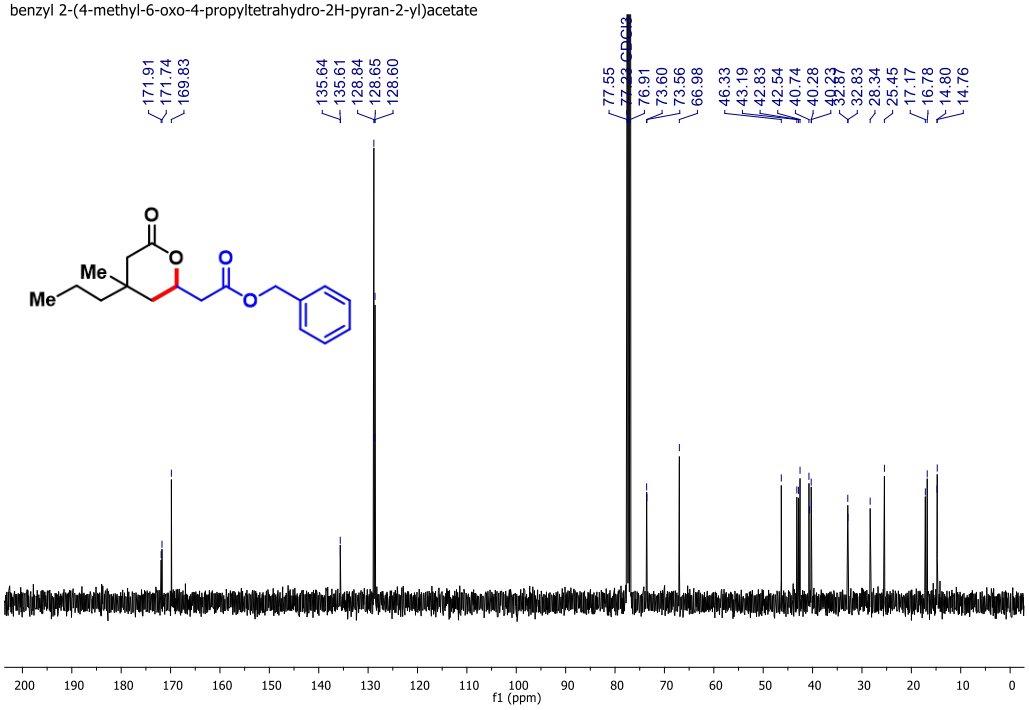
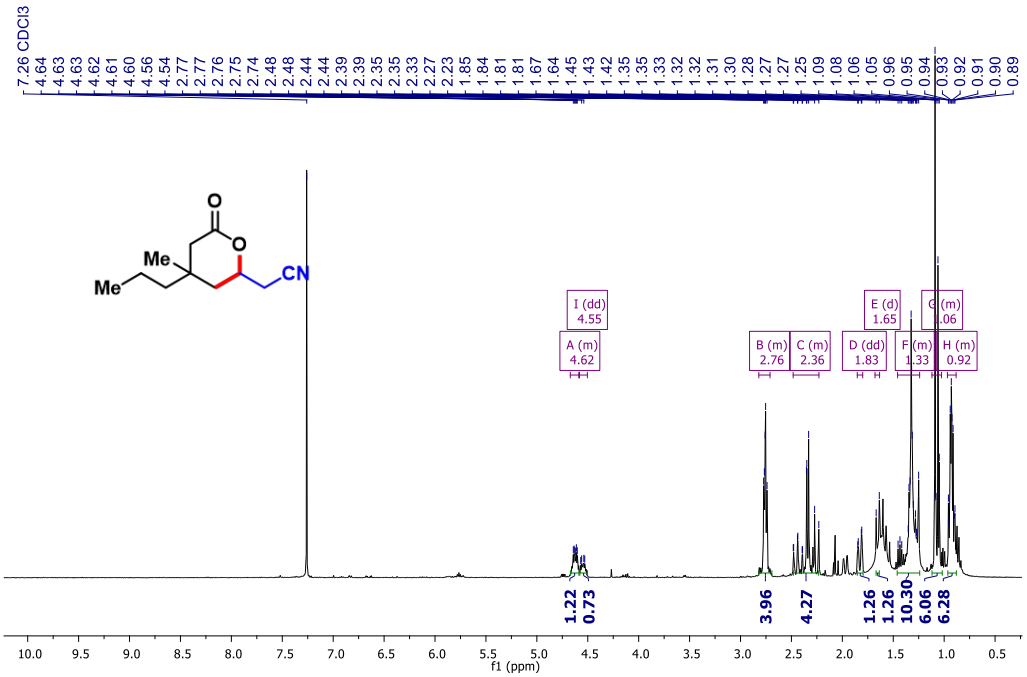


2-(4-methyl-6-oxo-4-propyltetrahydro-2H-pyran-2-yl)acetonitrile



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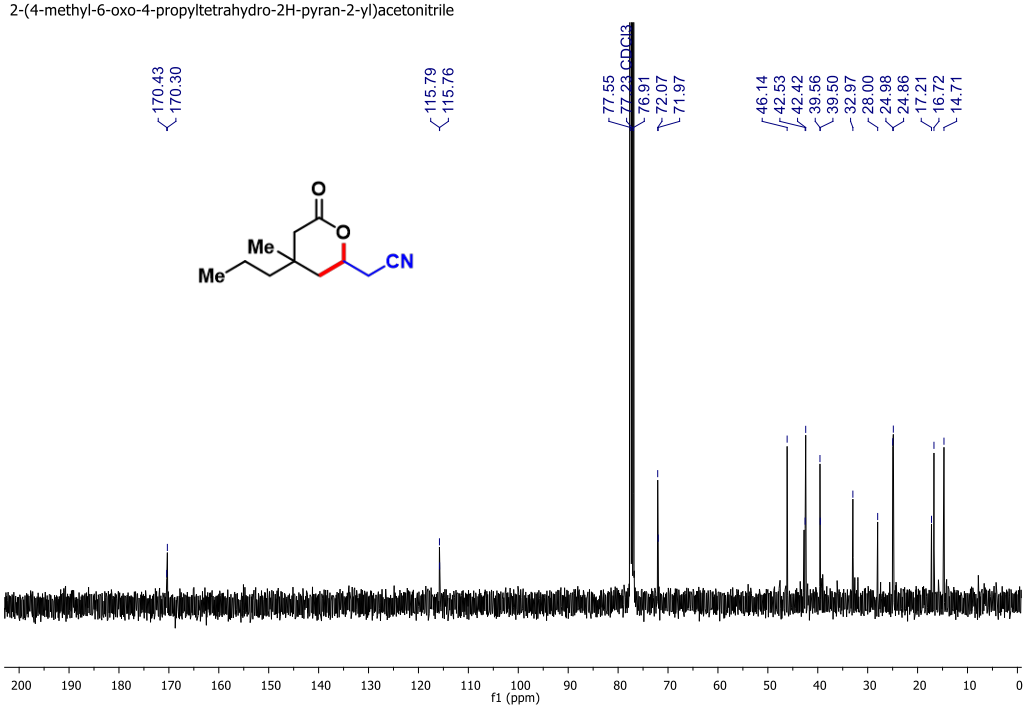

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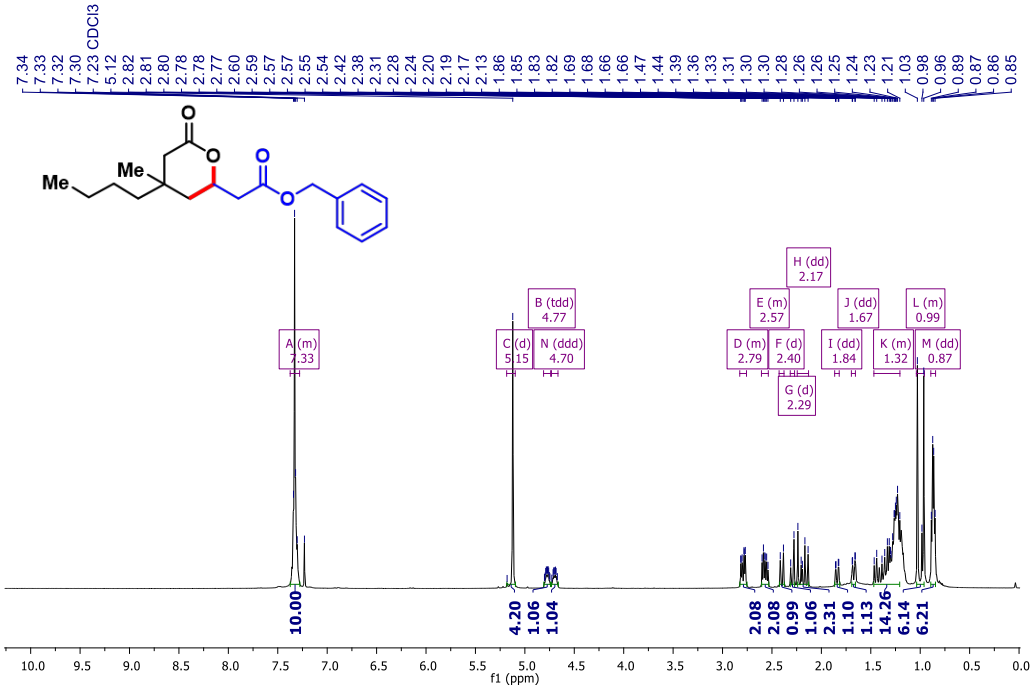

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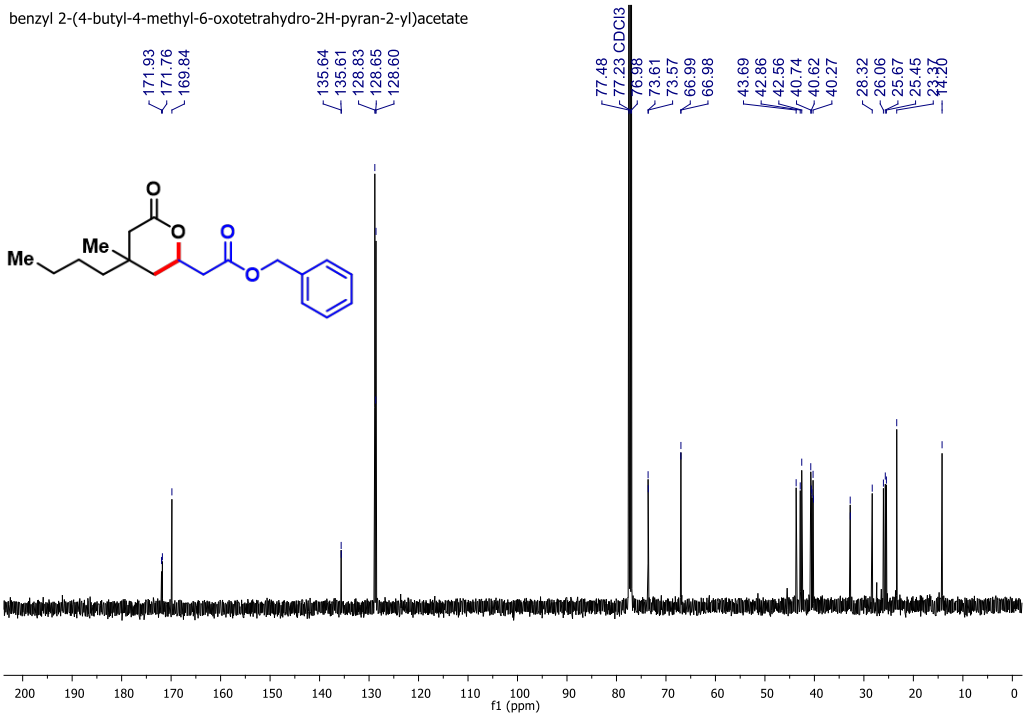
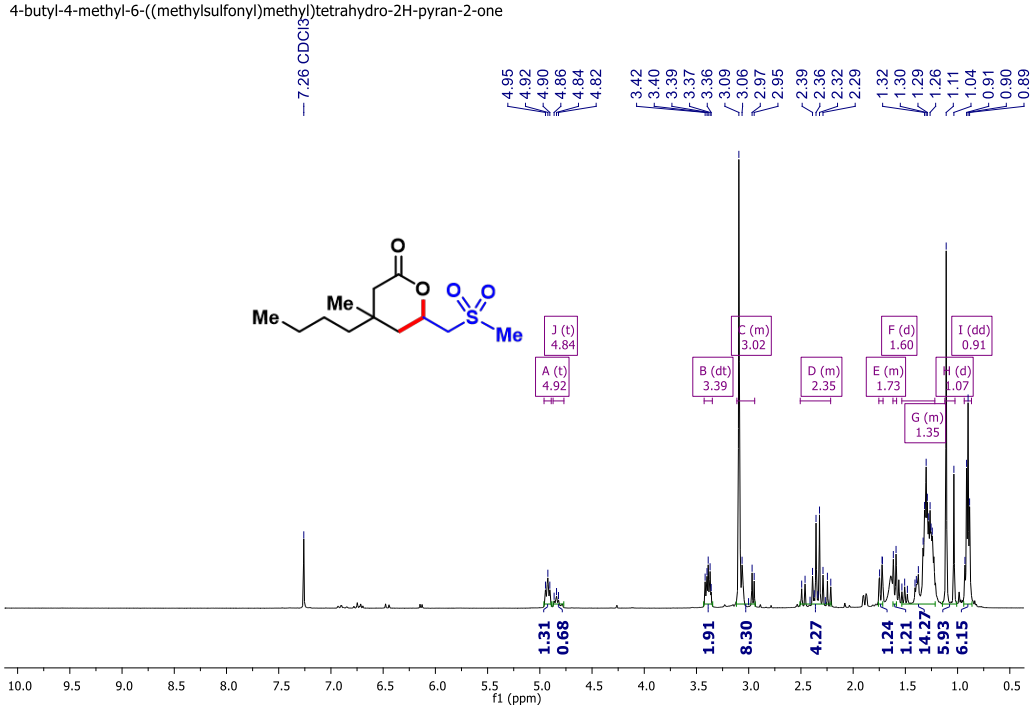


4-butyl-4-methyl-6-((methylsulfonyl)methyl)tetrahydro-2H-pyran-2-one



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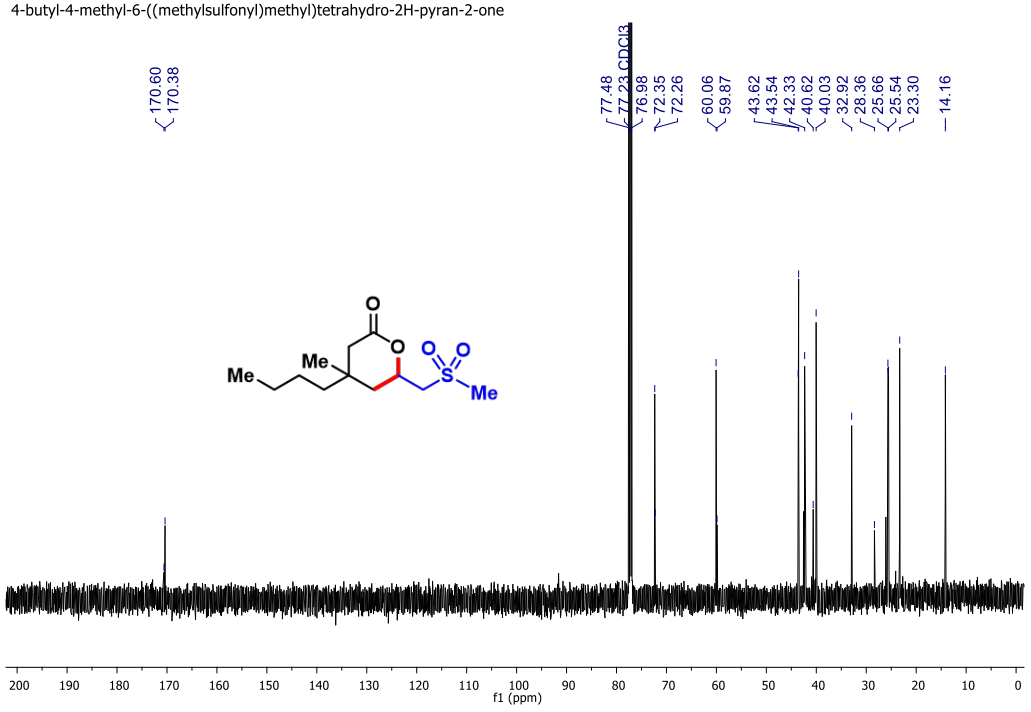
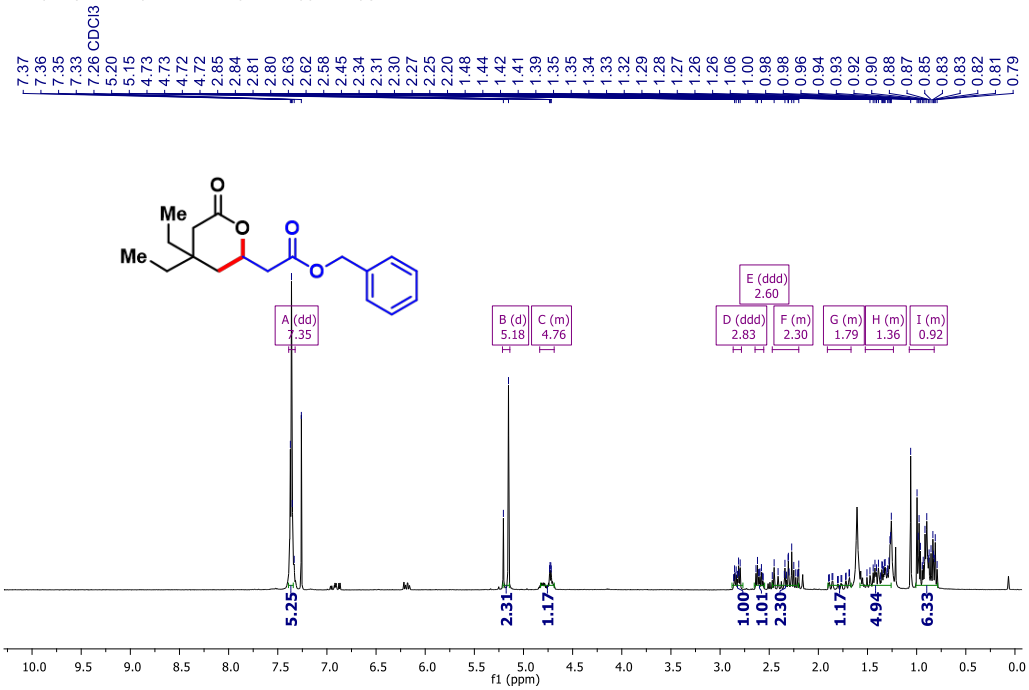


benzyl 2-(4,4-diethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



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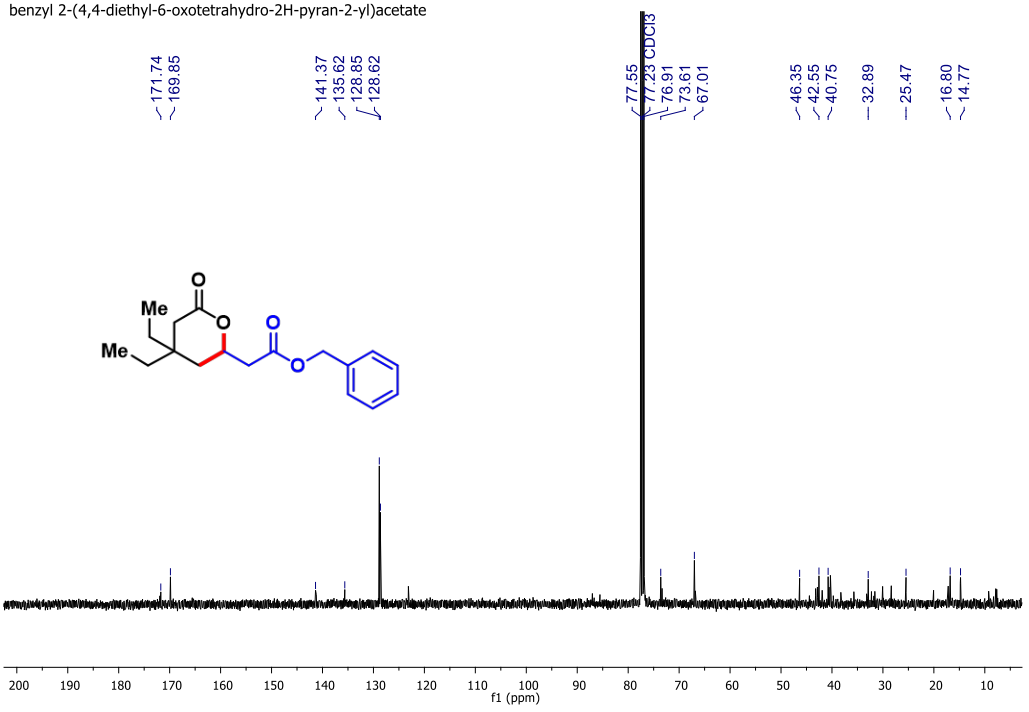
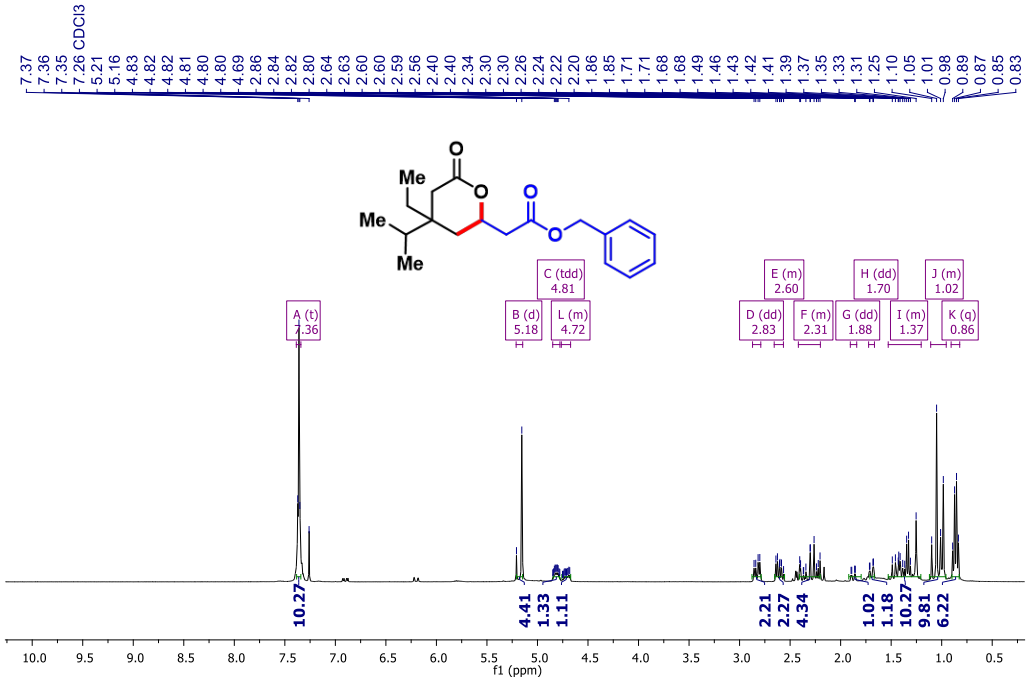


benzyl 2-(4-ethyl-4-isopropyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



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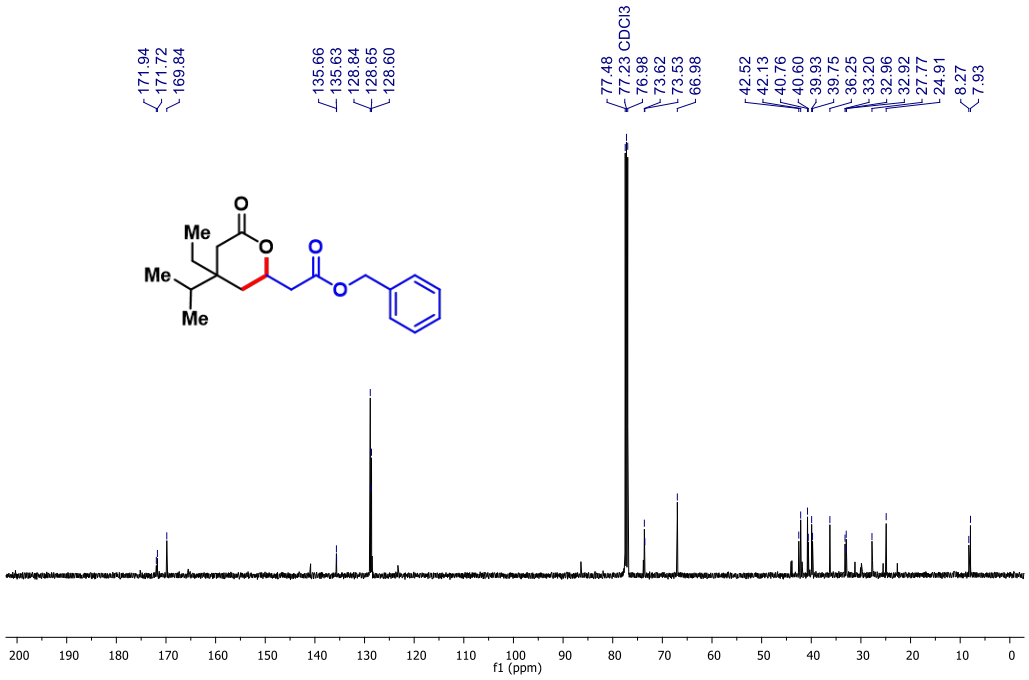

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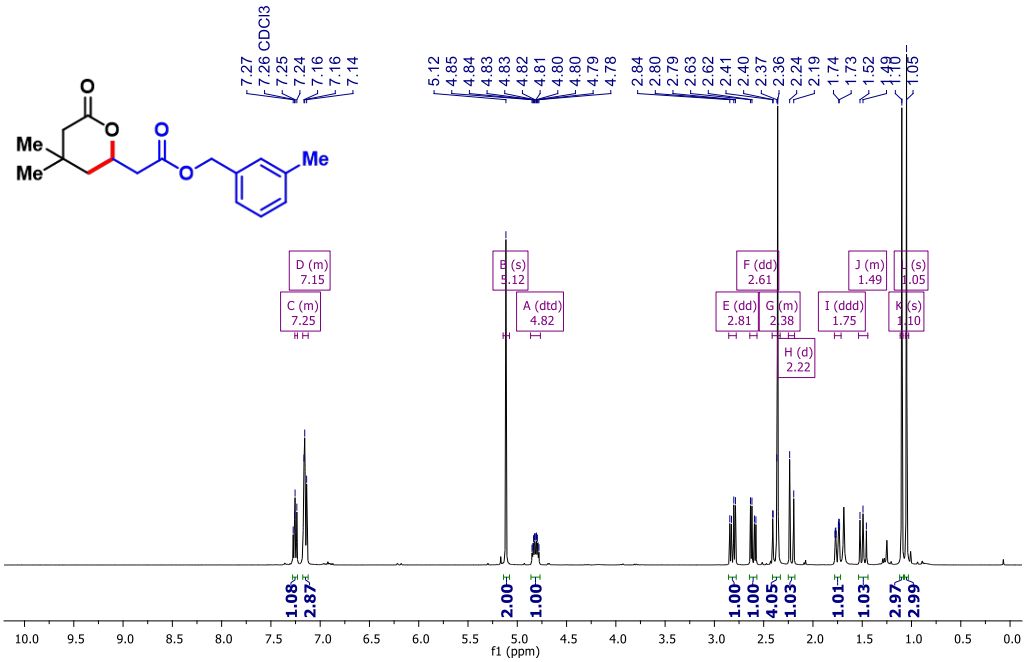

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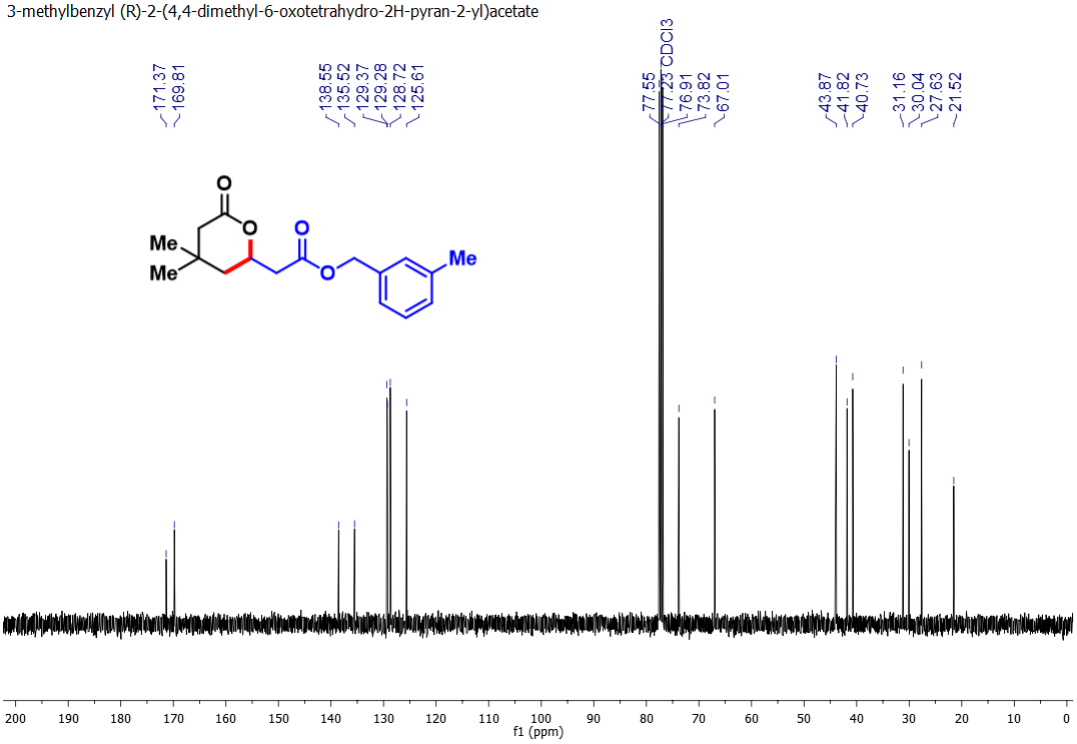

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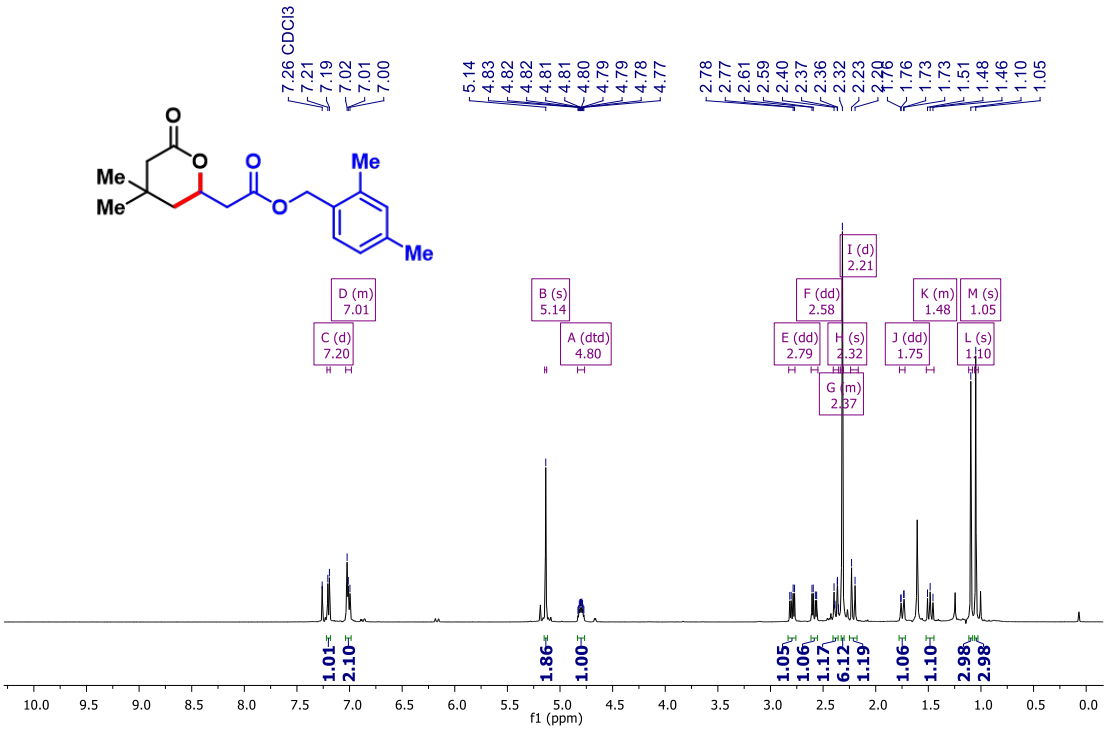

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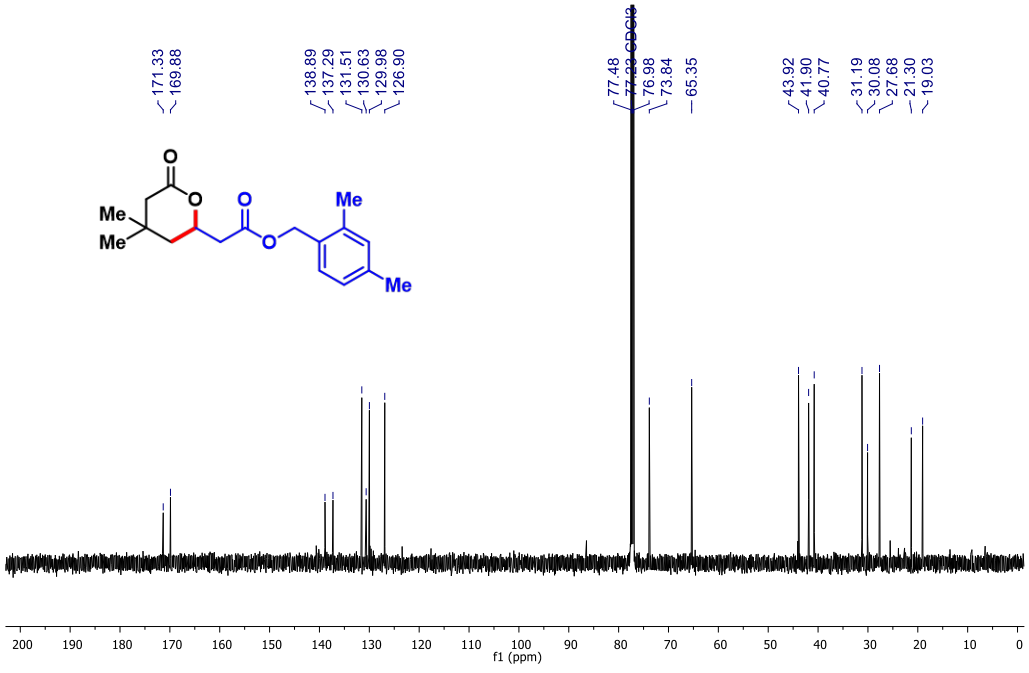
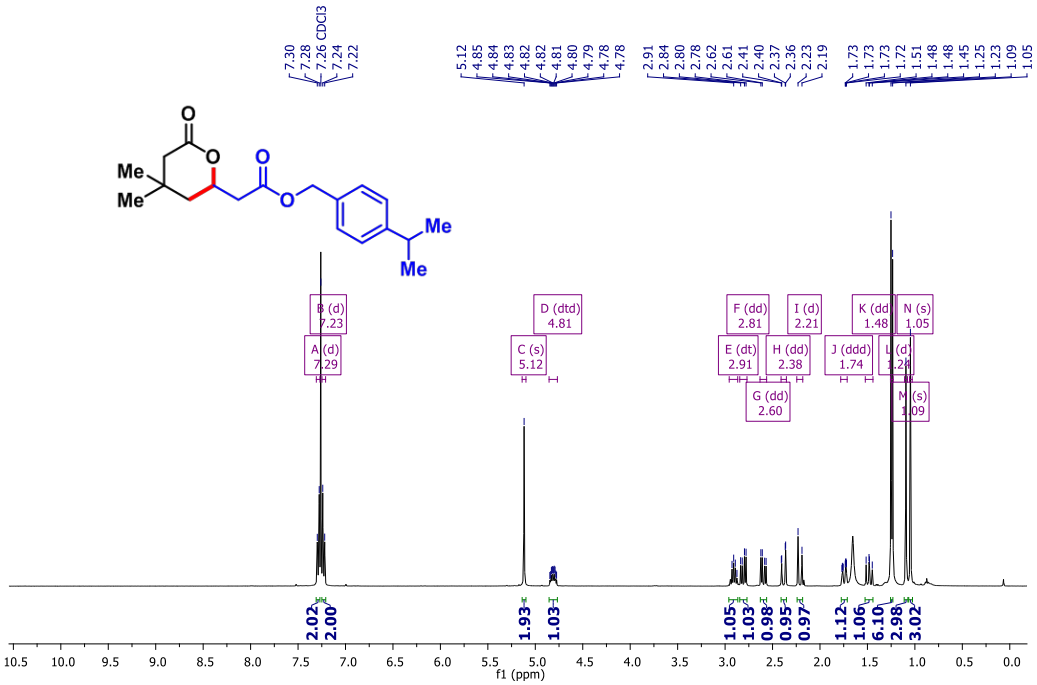


4-isopropylbenzyl-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



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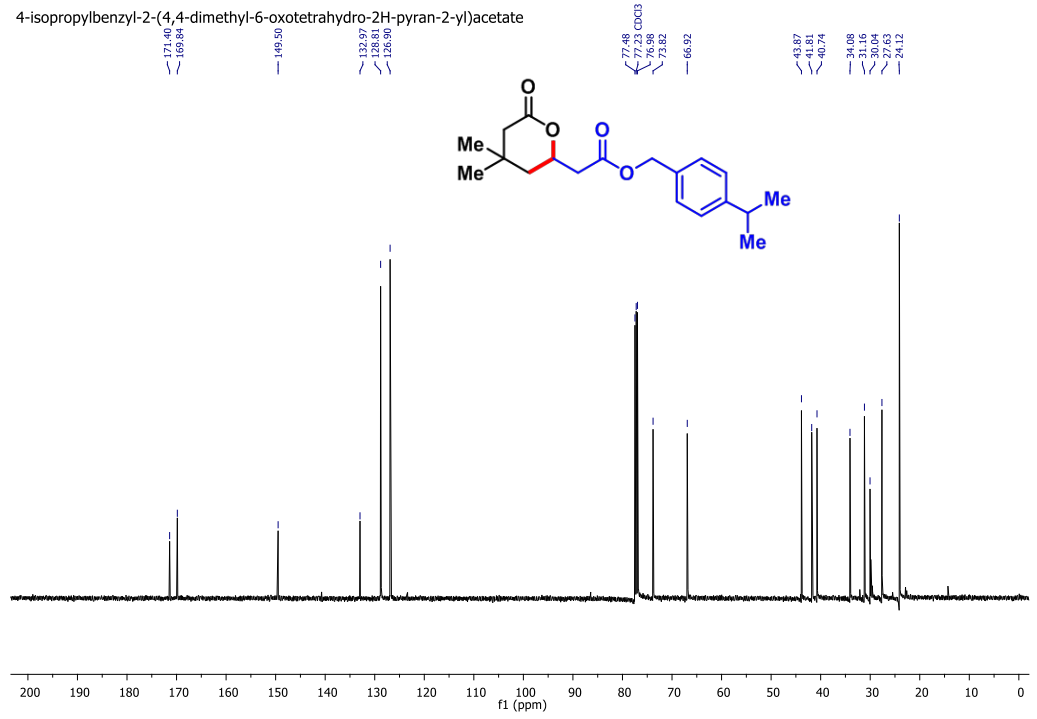

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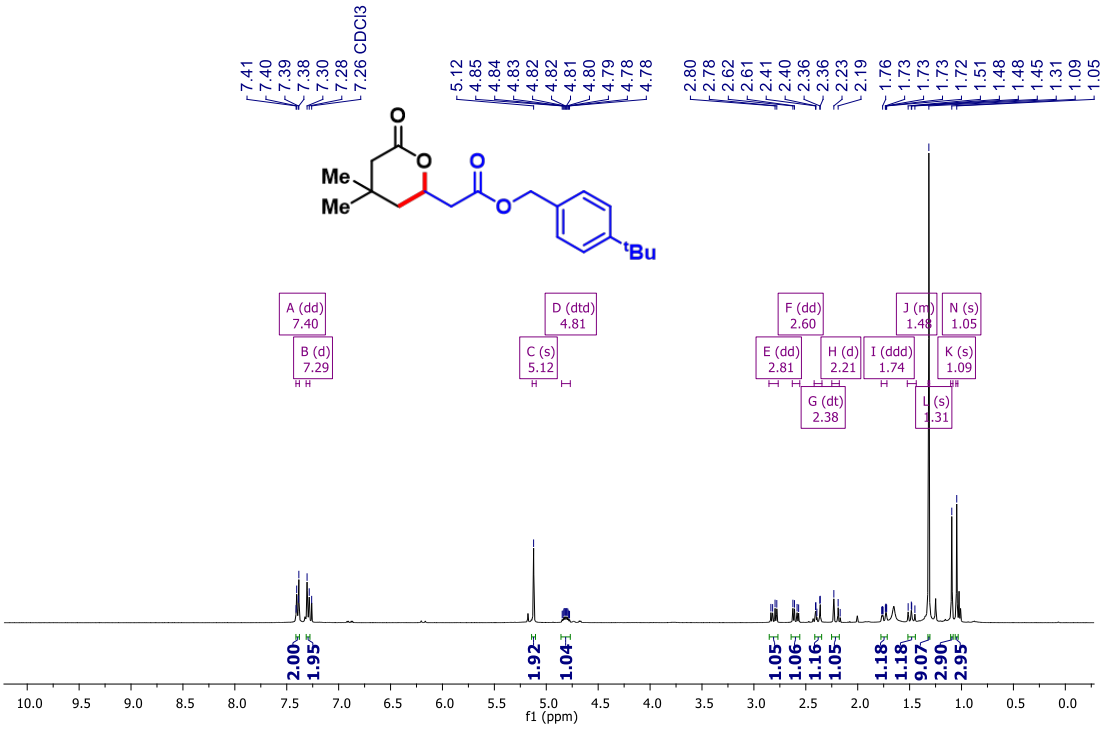

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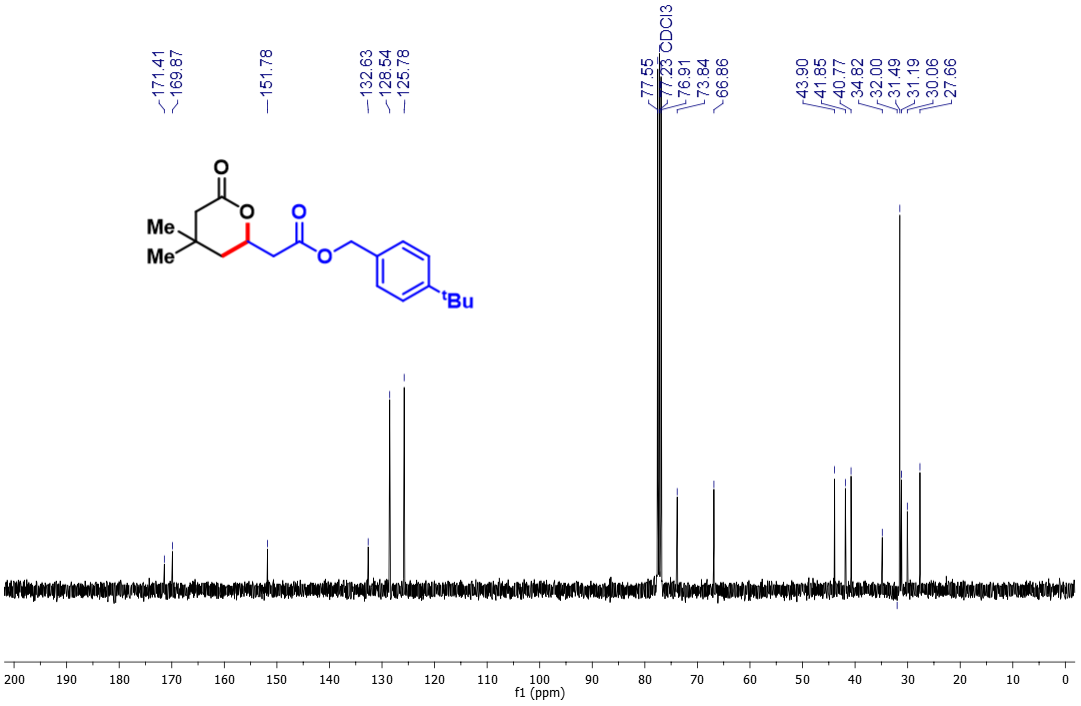

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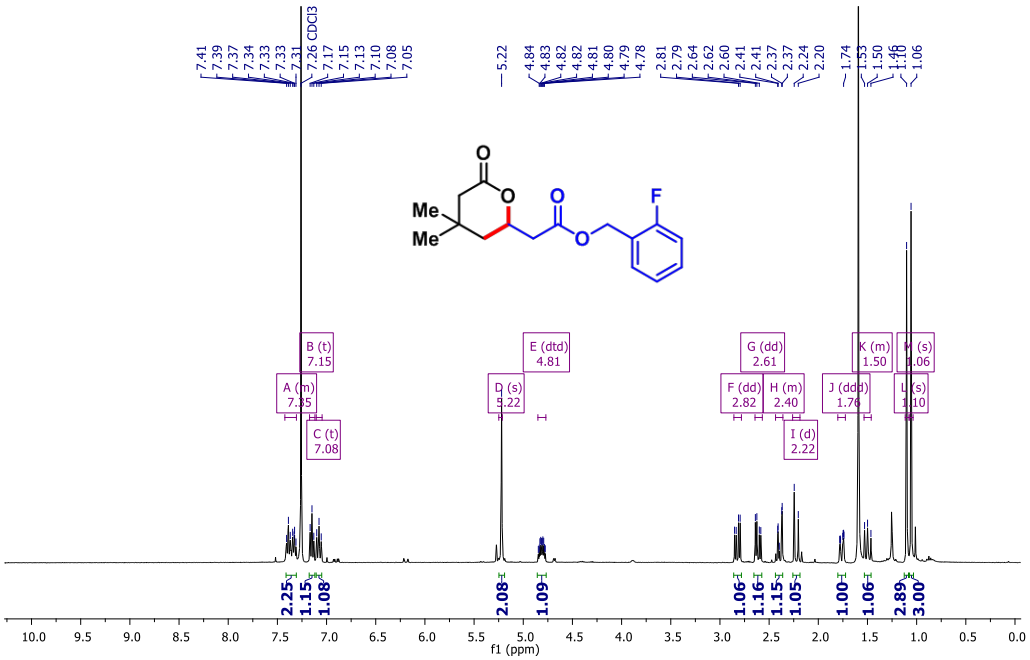
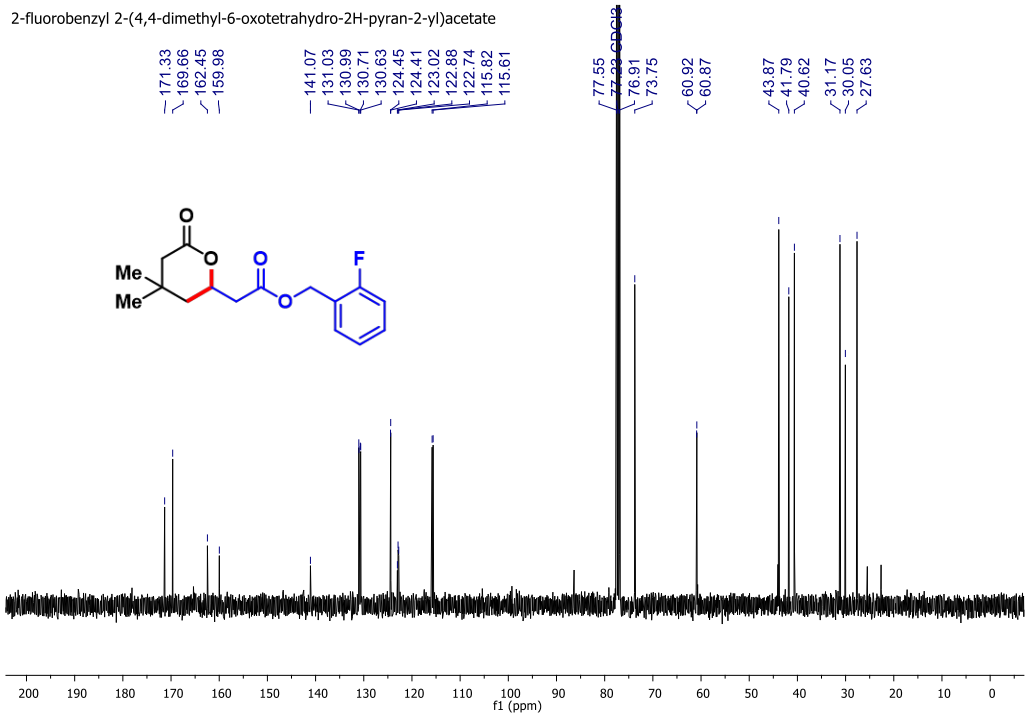
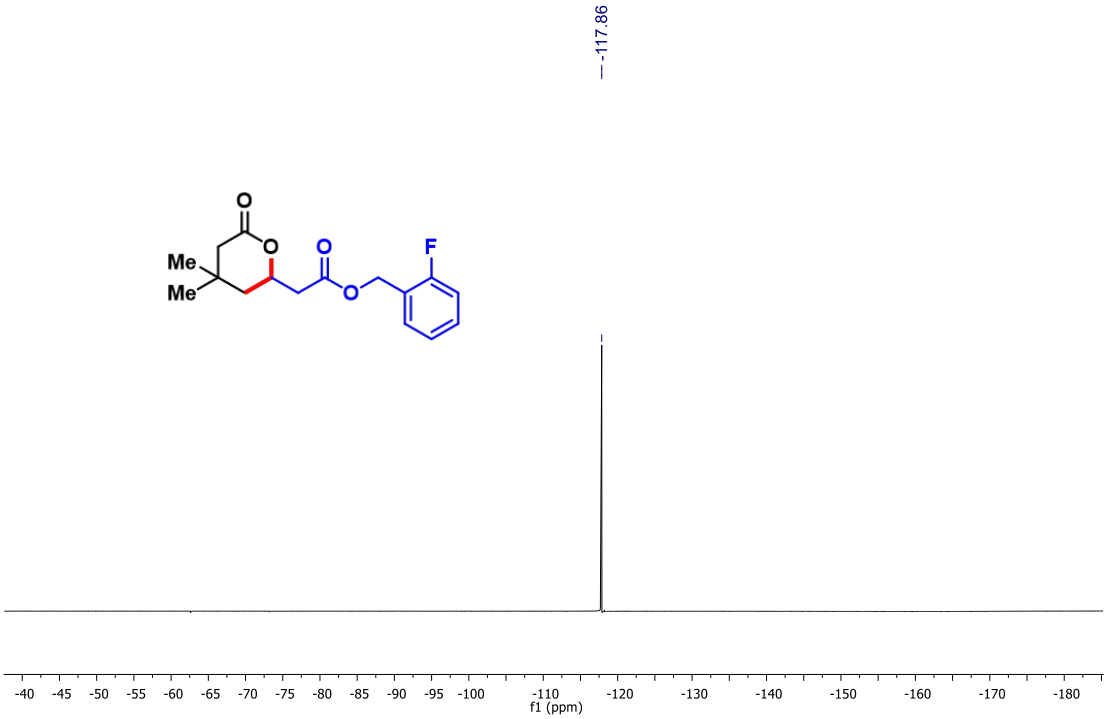


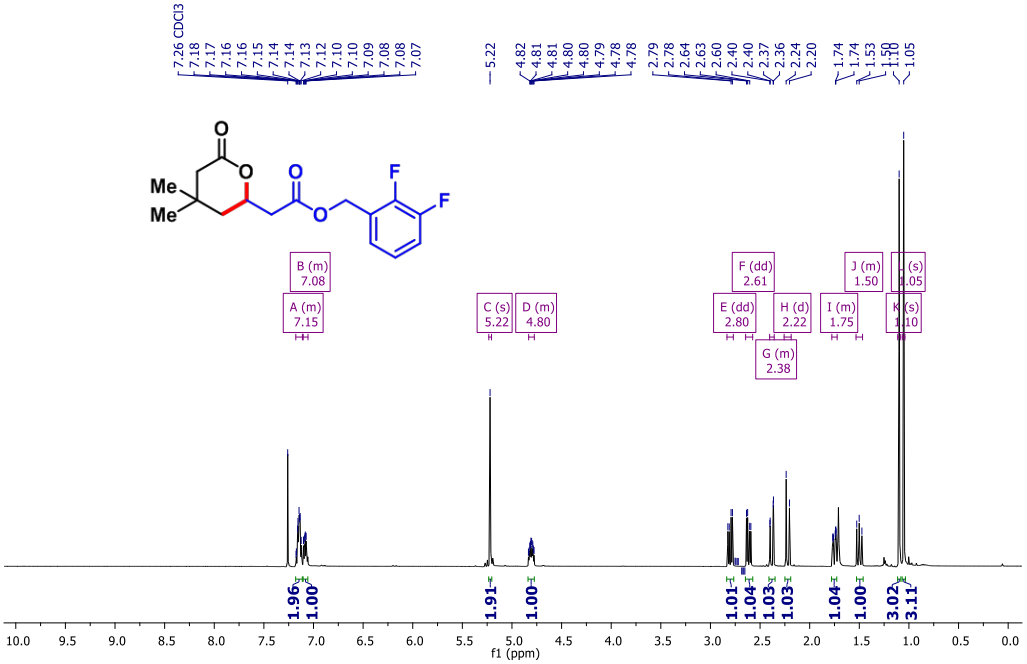
2-fluorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



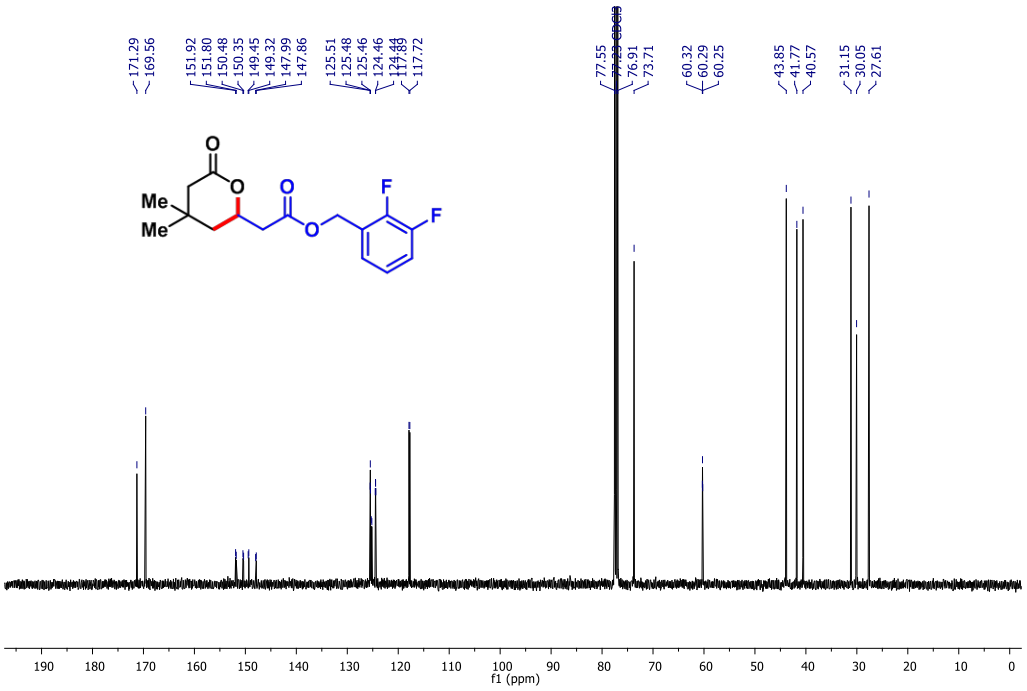
2-fluorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



2,3-difluorobenzyl-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate

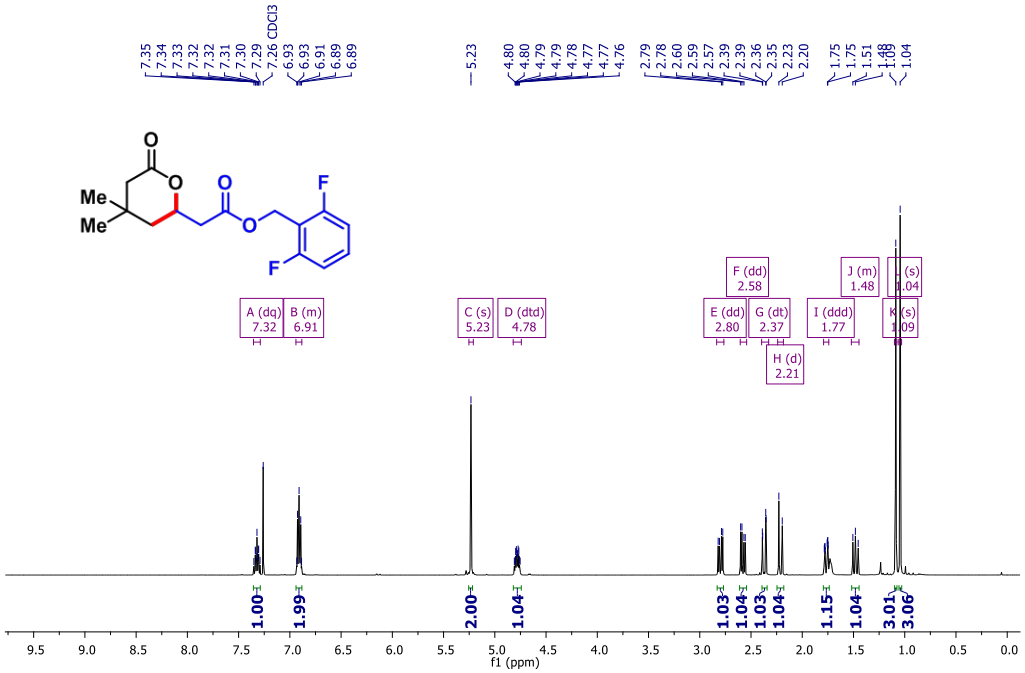


2,3-difluorobenzyl-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate

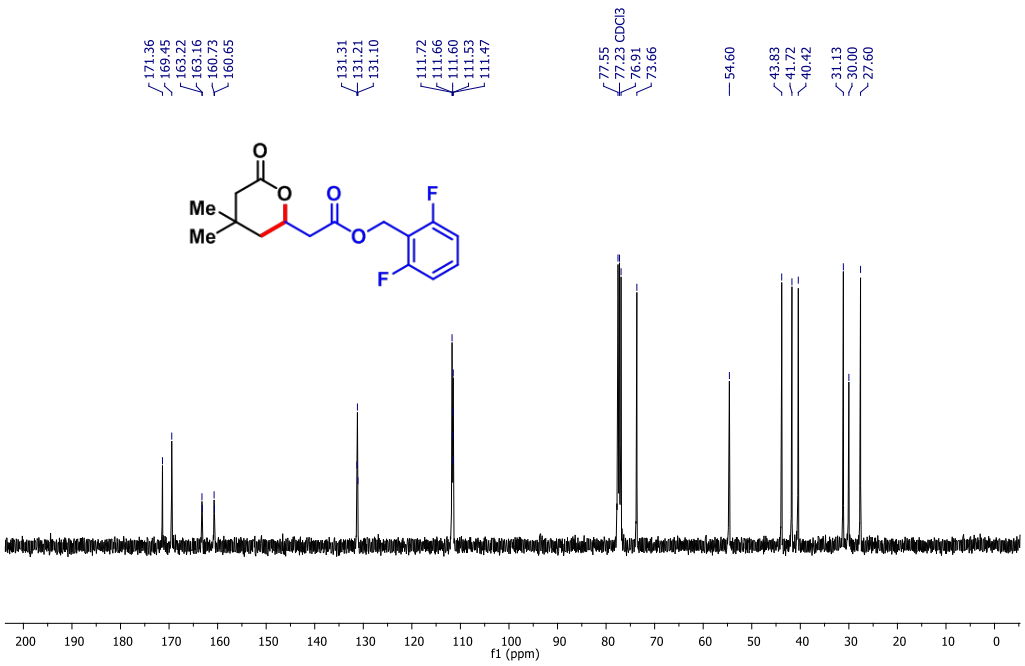


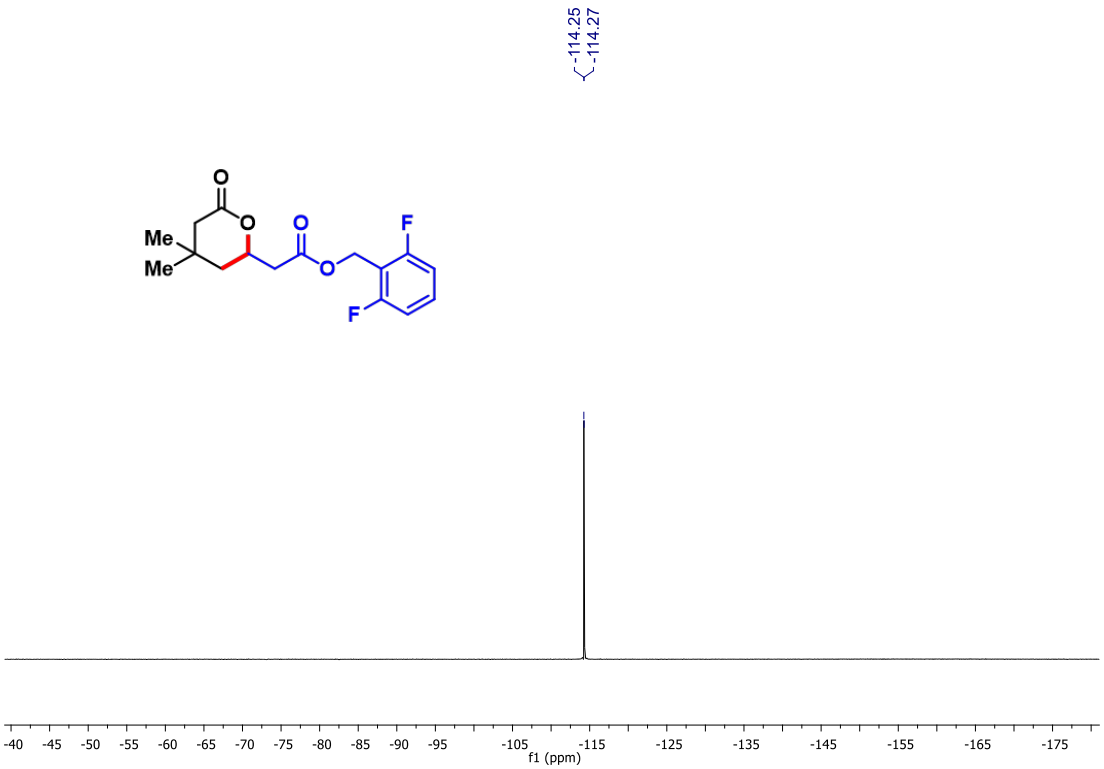
2,3-difluorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate

2,6-difluorobenzyl-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



2,6-difluorobenzyl-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate

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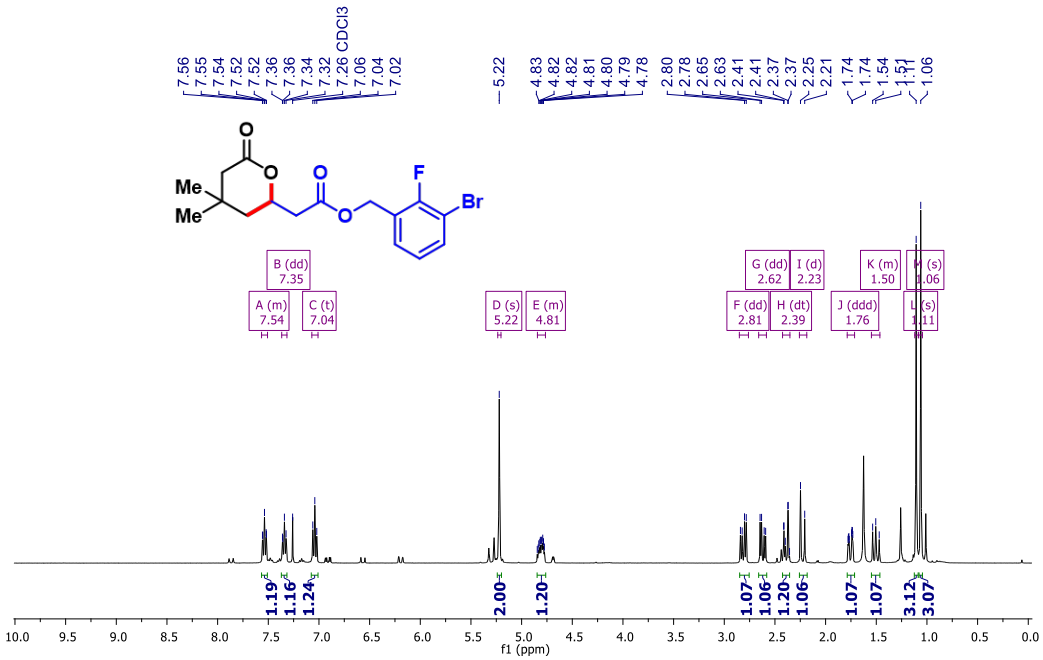
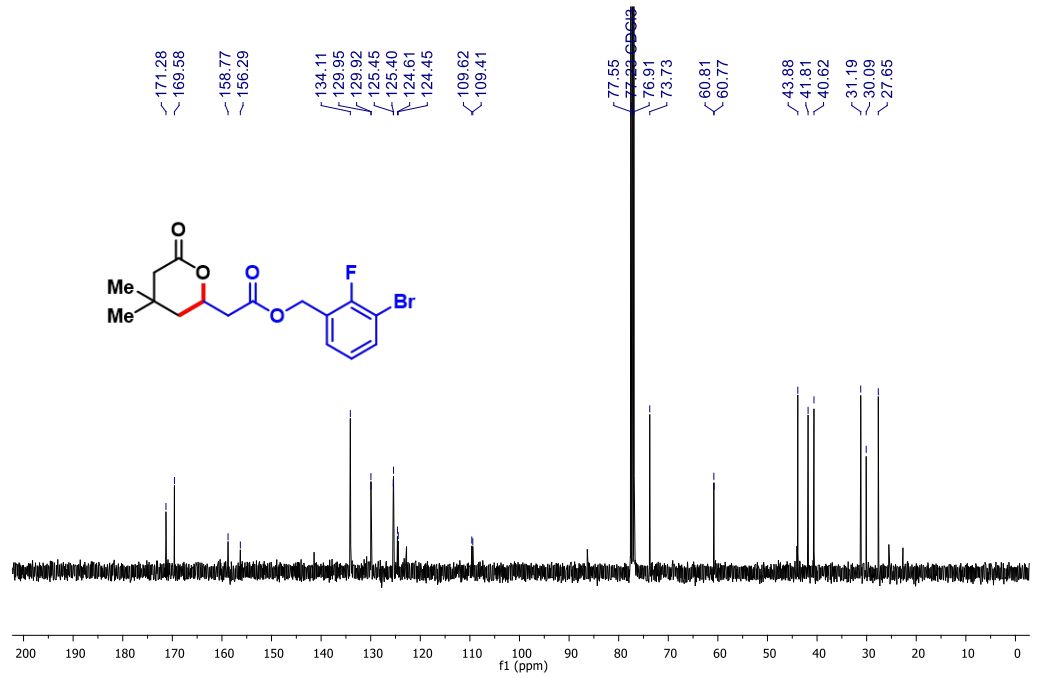
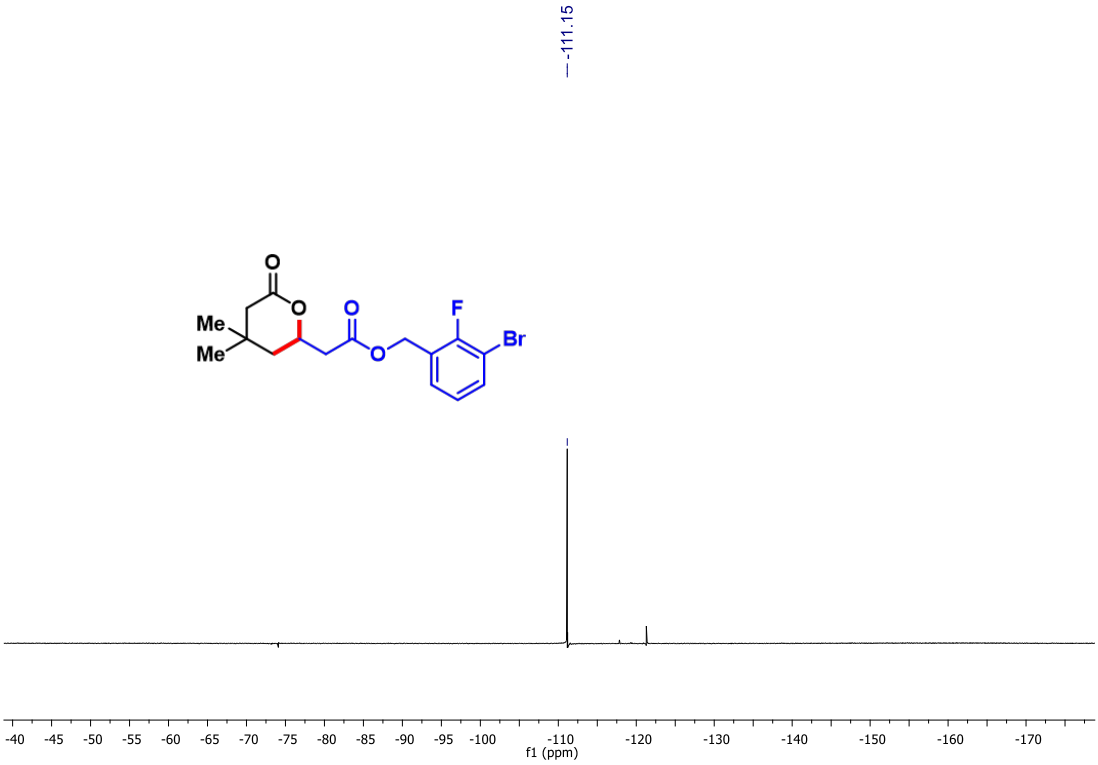
-114.27
O
O
O
O
Me
Me
F
F
-40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -105 -115 -125 -135 -145 -155 -165 -175
f1 (ppm)

3-bromo-2-fluorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate

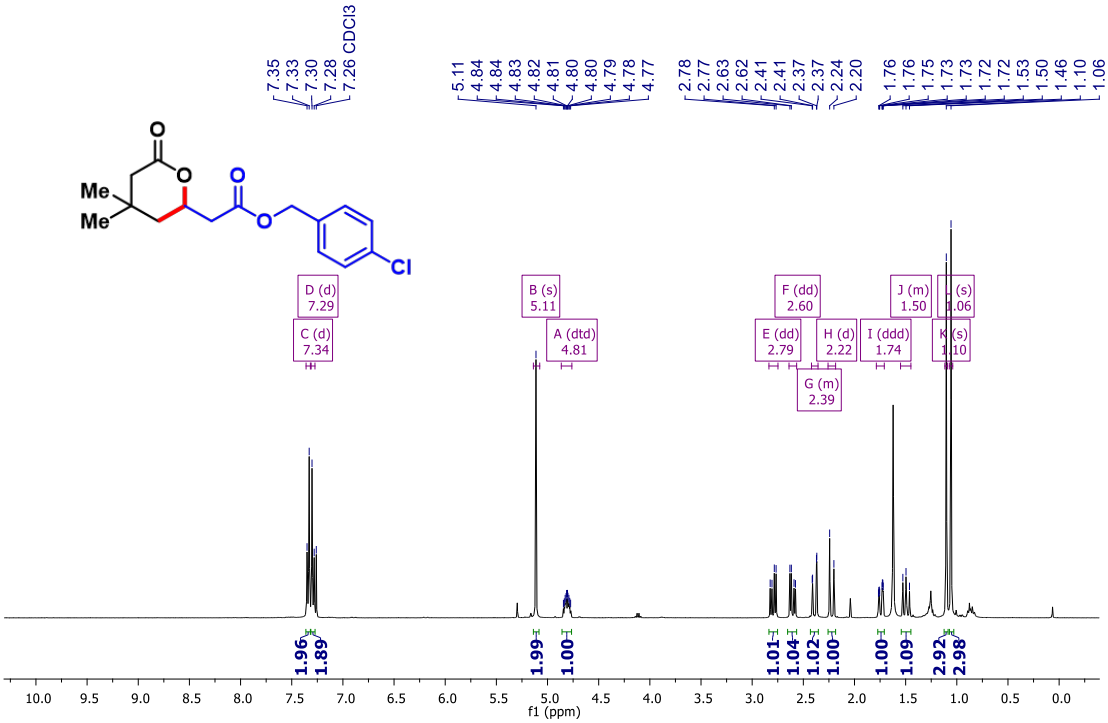


3-bromo-2-fluorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate

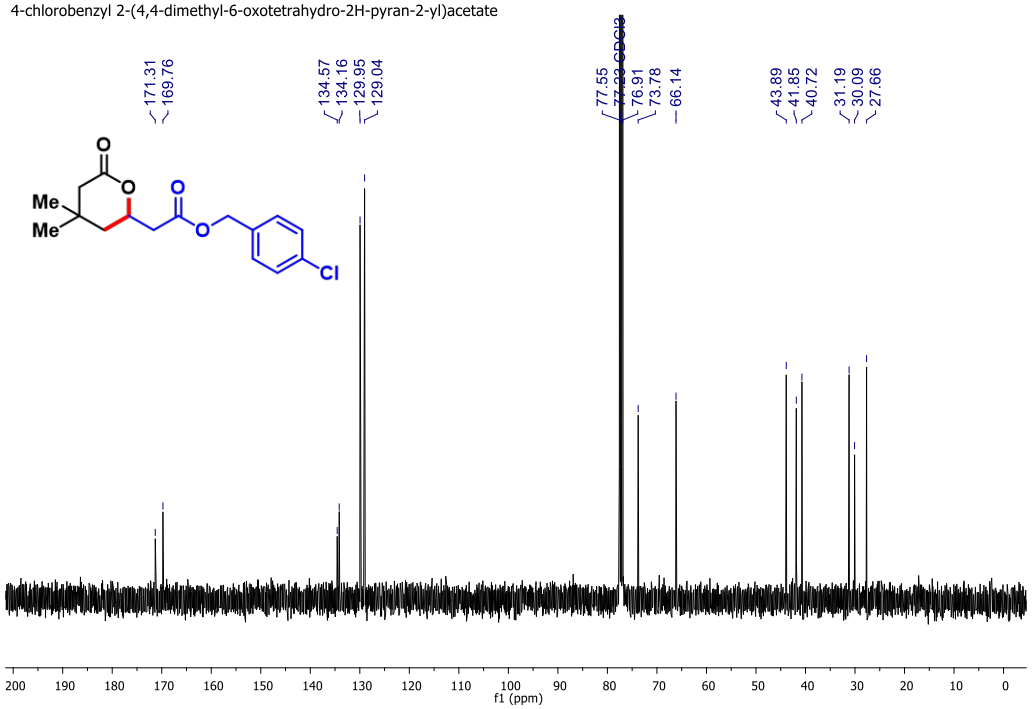



-111.15
O
O
Me
Me
O
O
F
Br
-40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -110 -120 -130 -140 -150 -160 -170
f1 (ppm)

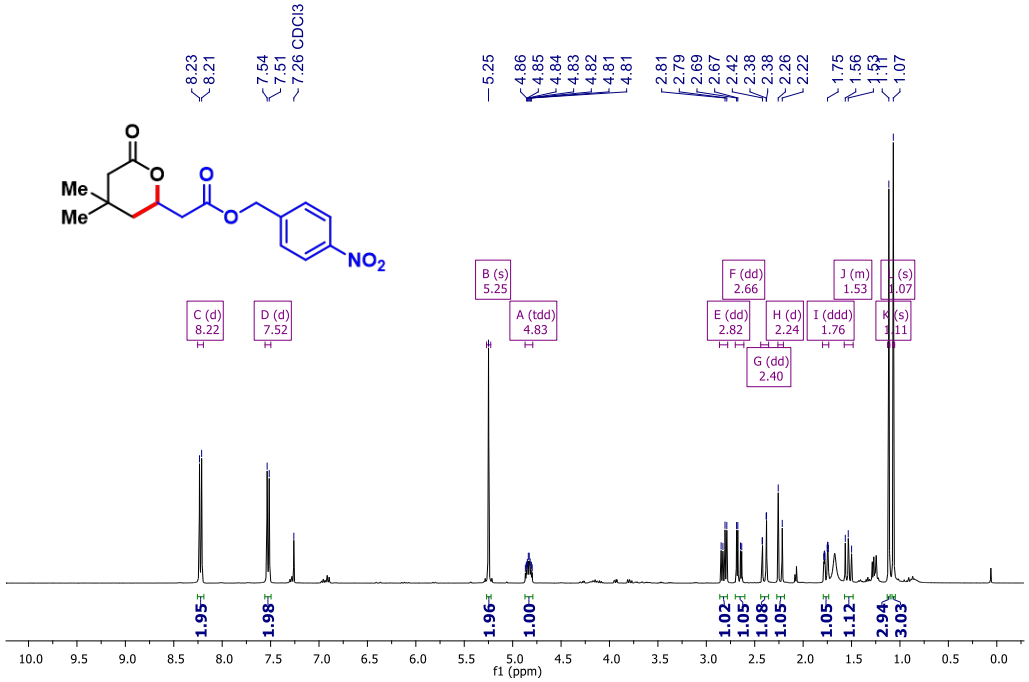
4-chlorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



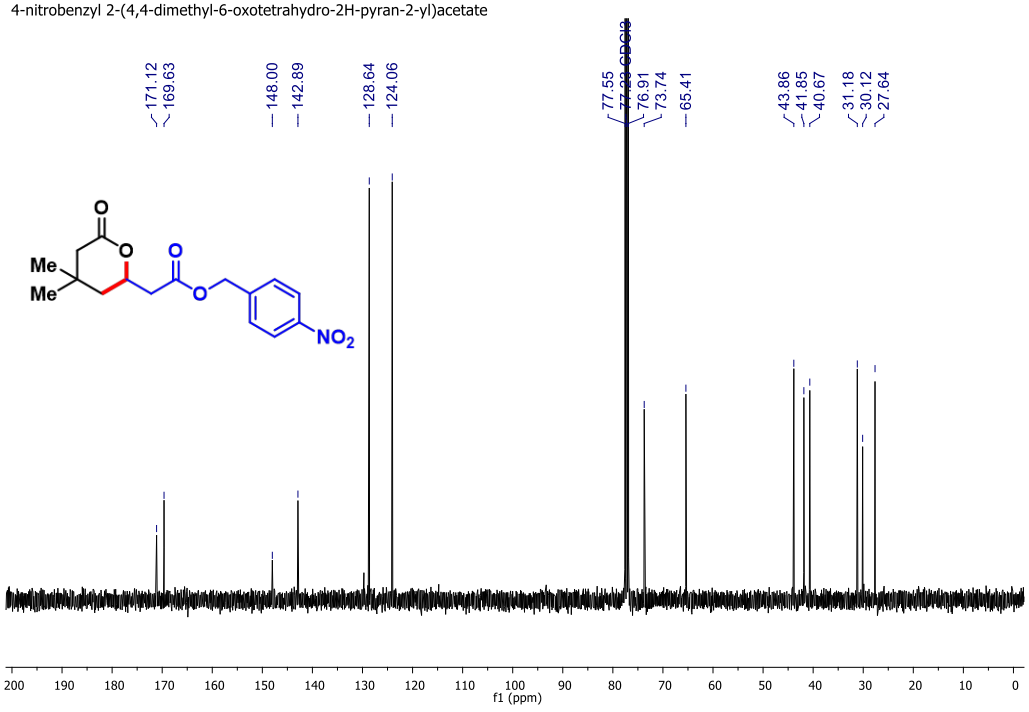
4-chlorobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



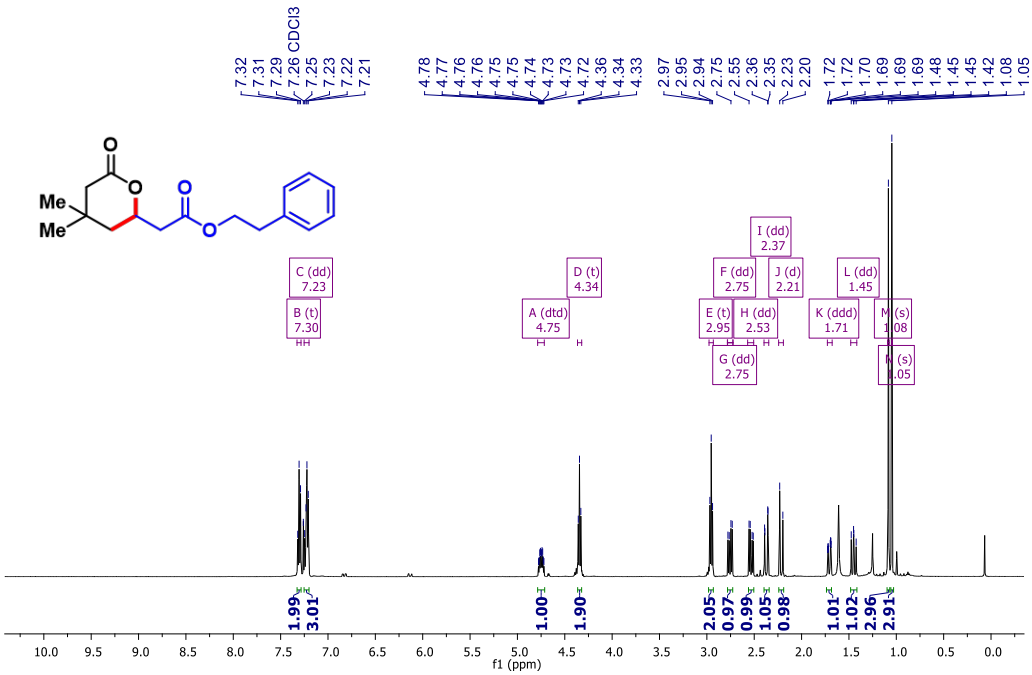
4-nitrobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



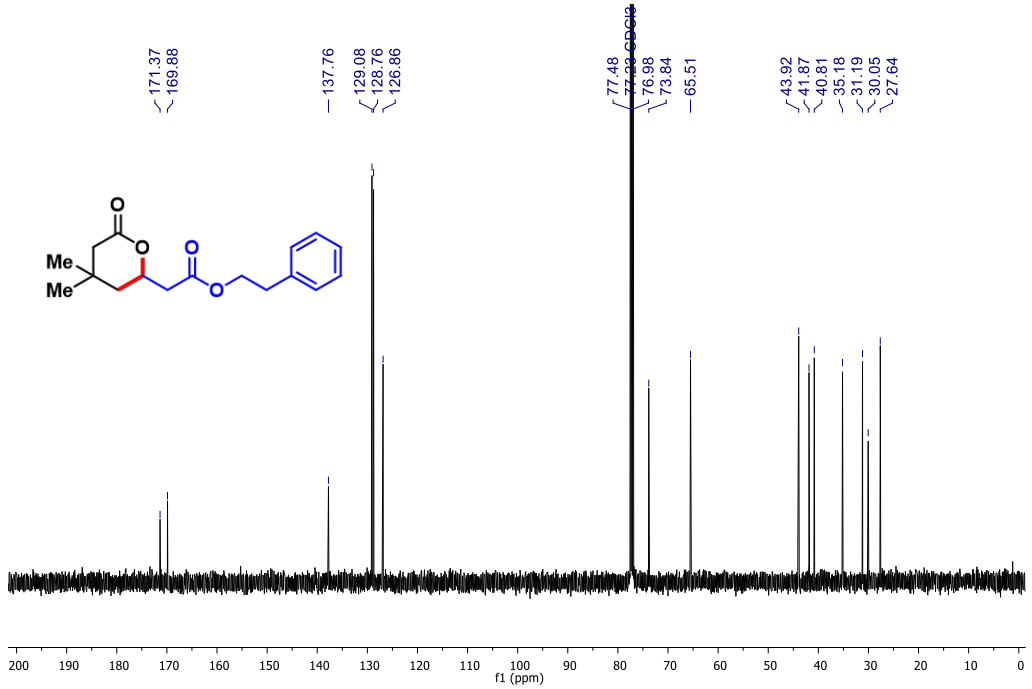
4-nitrobenzyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



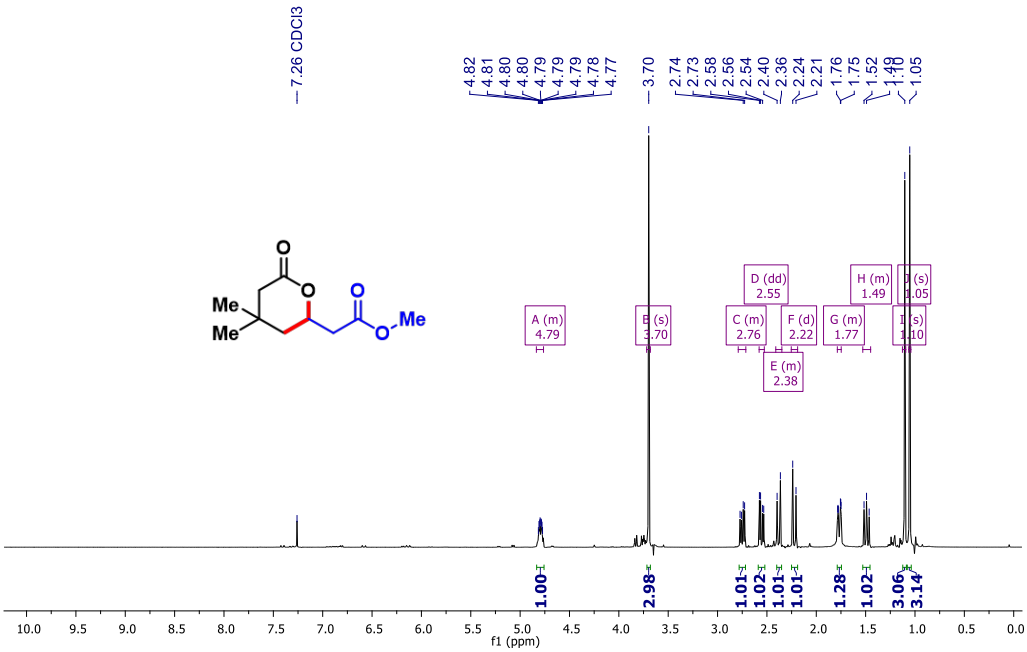
phenethyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



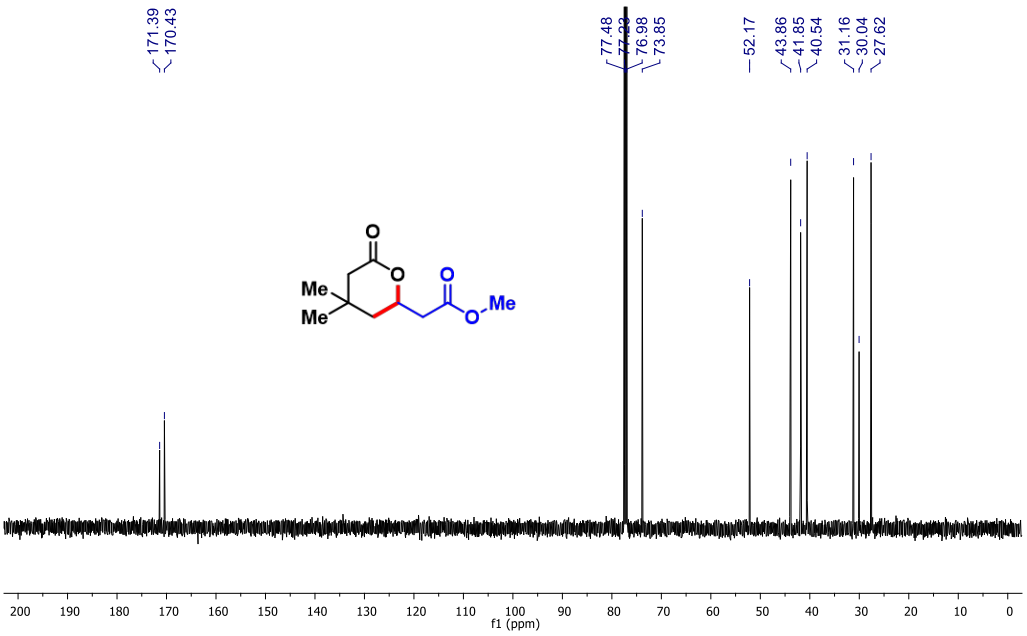
phenethyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



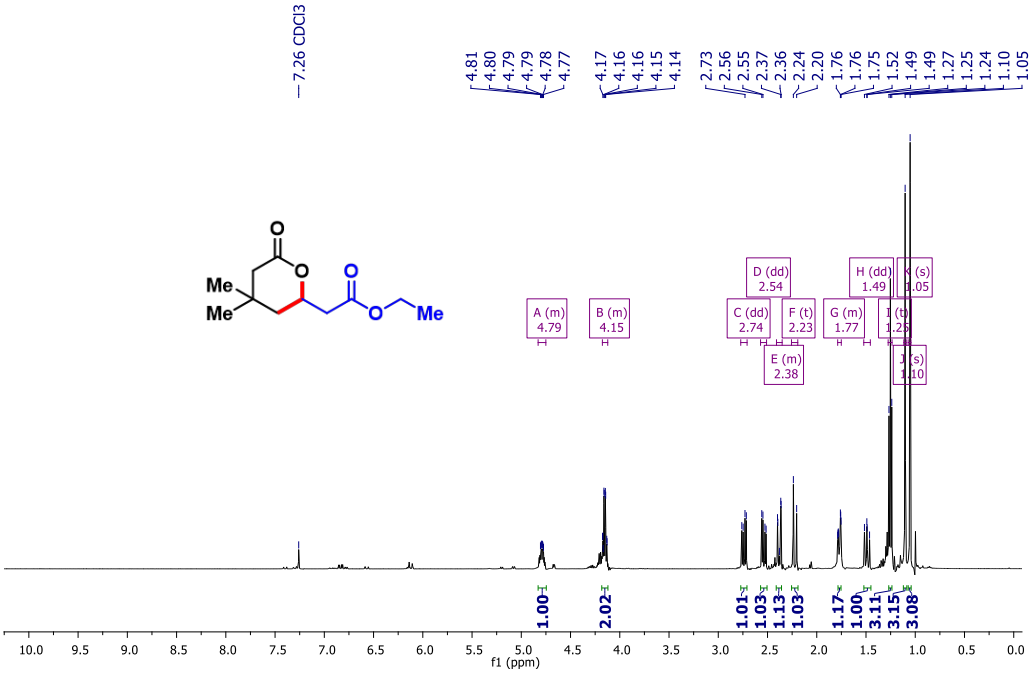
methyl (R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



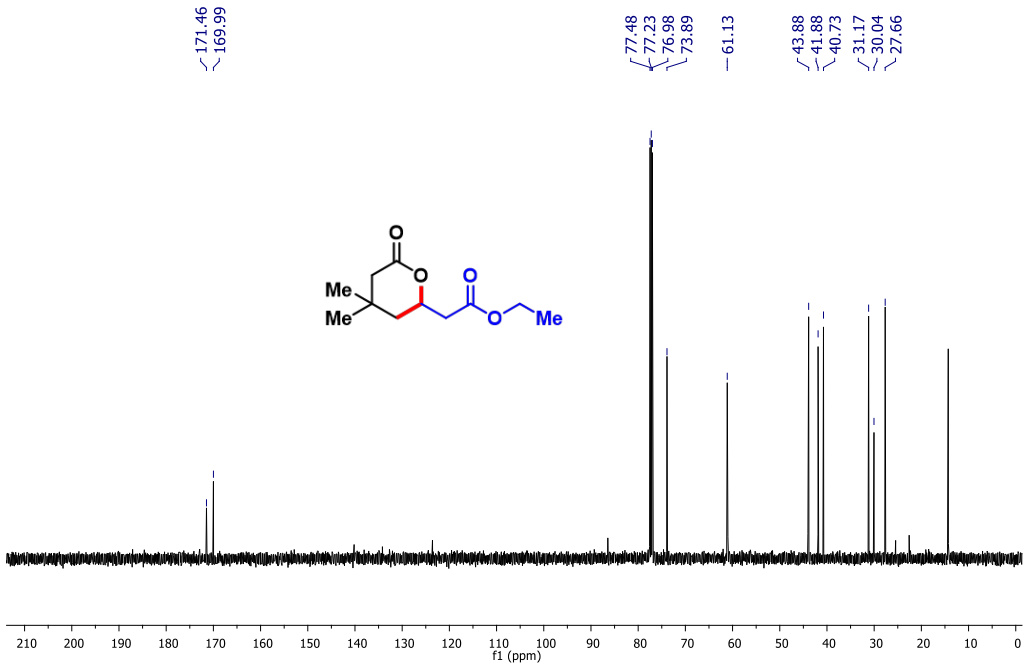
methyl (R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



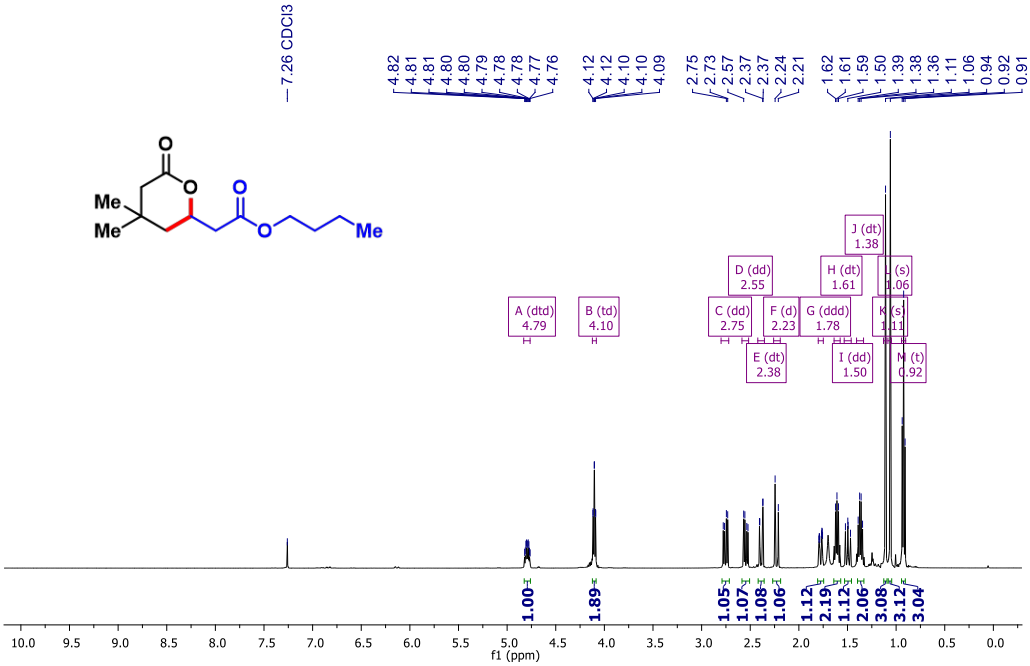
ethyl (R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



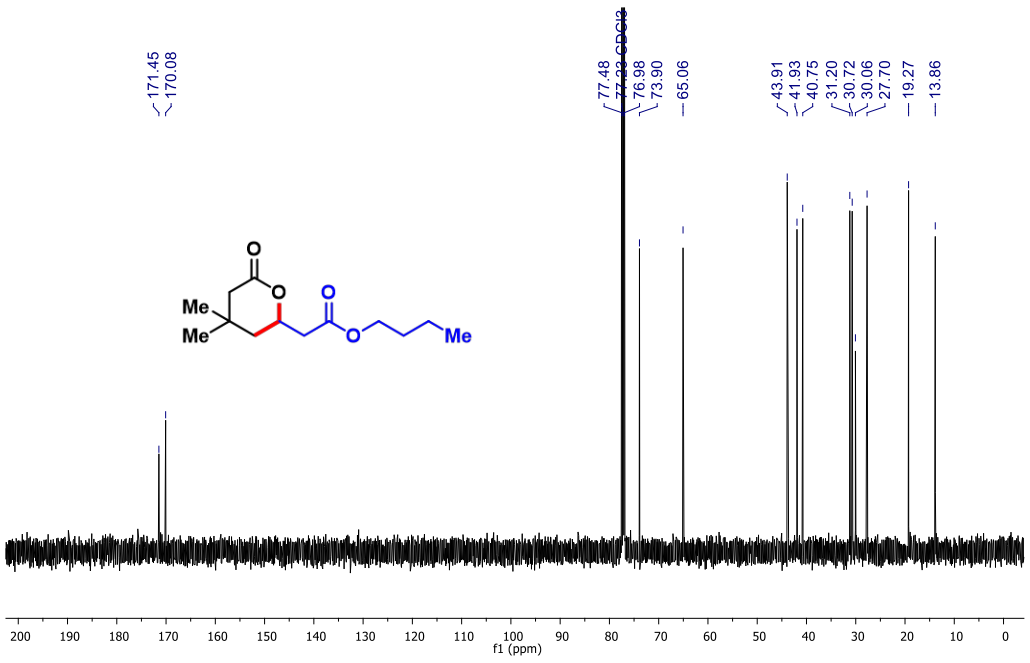
ethyl (R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



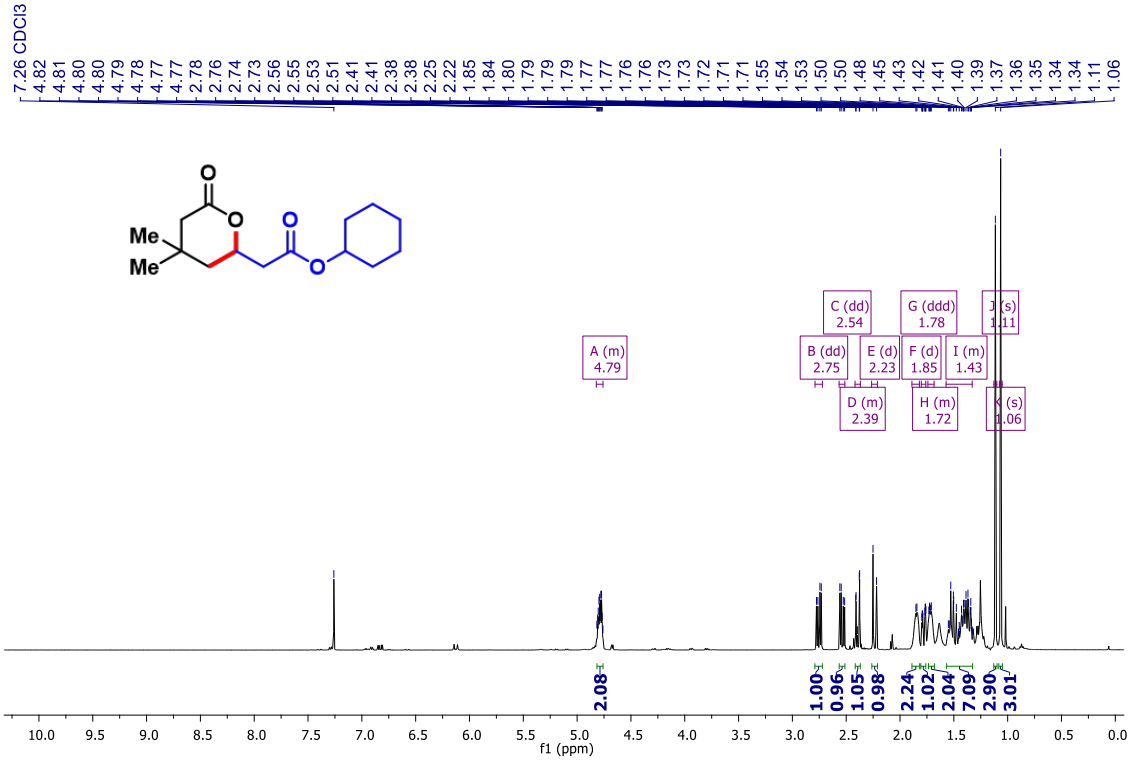
butyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



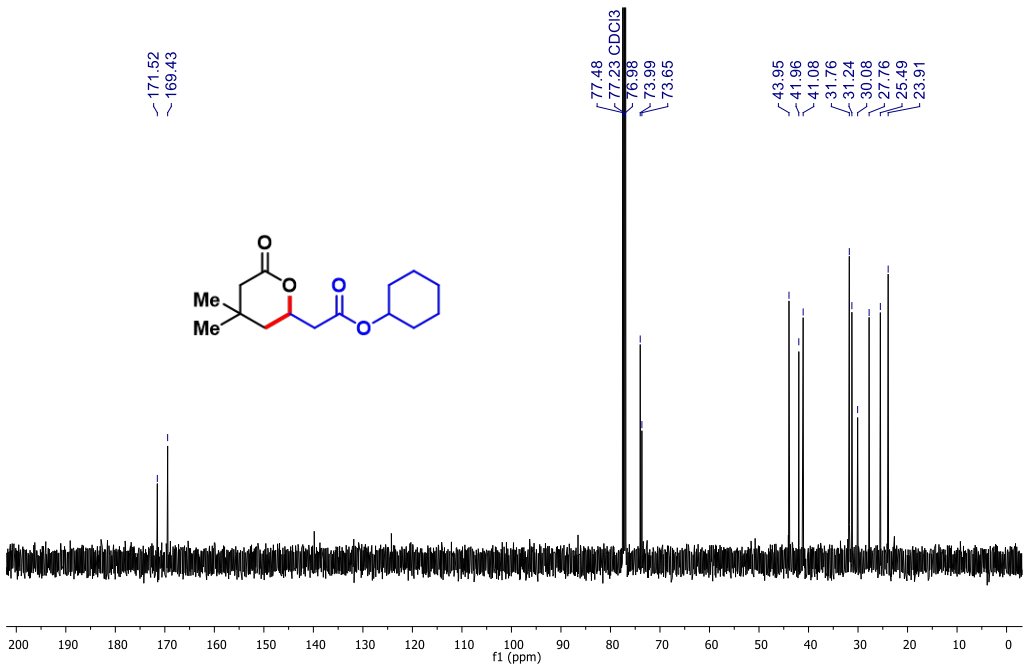
butyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



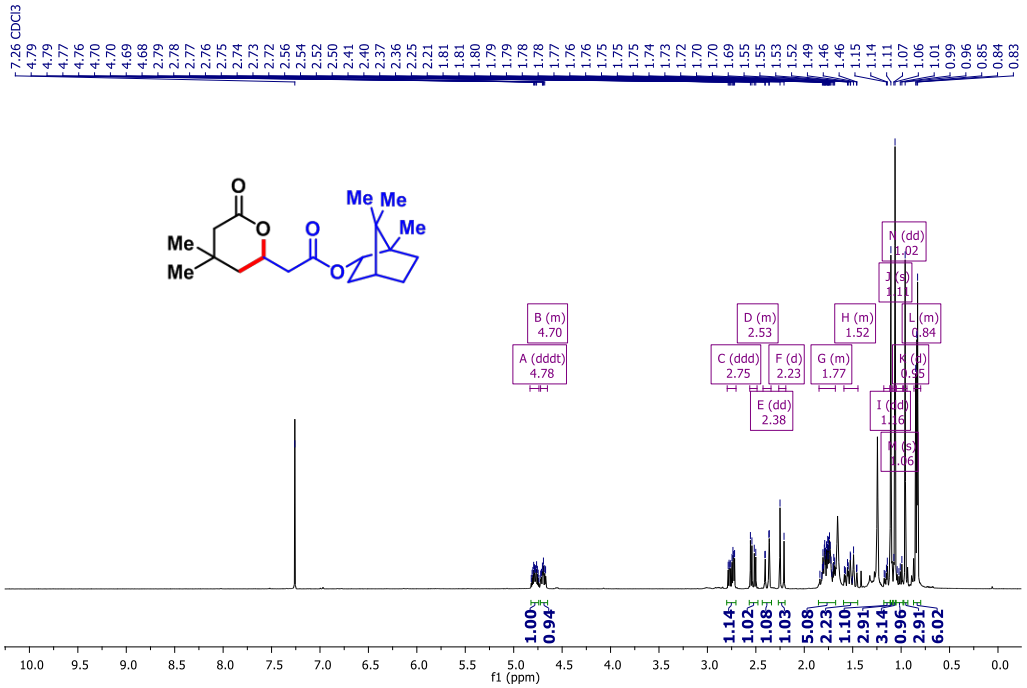
cyclohexyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



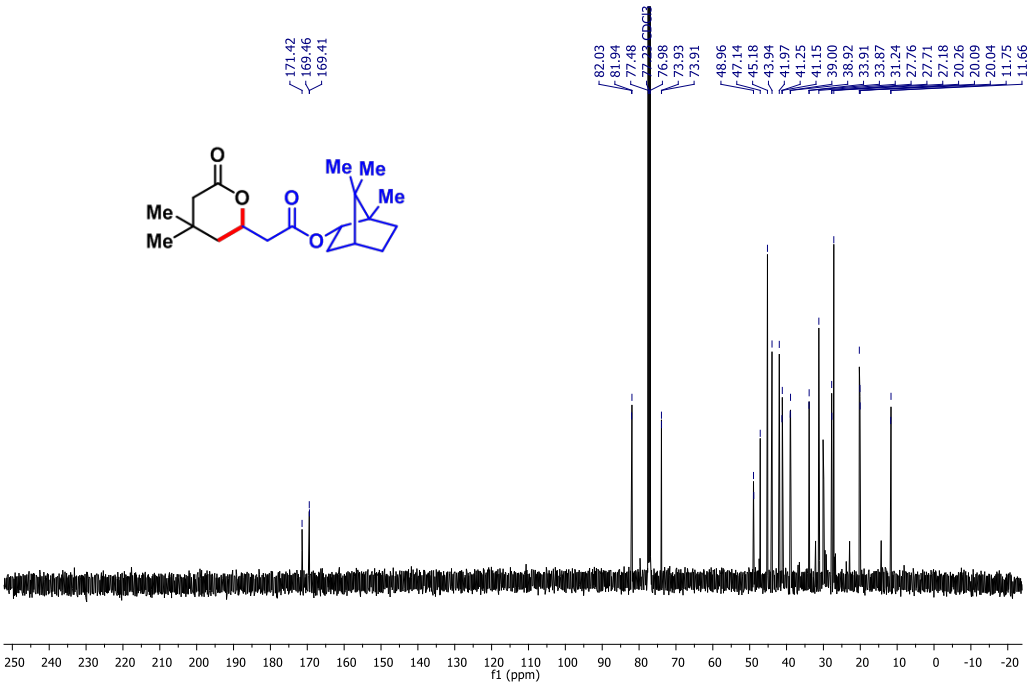
cyclohexyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



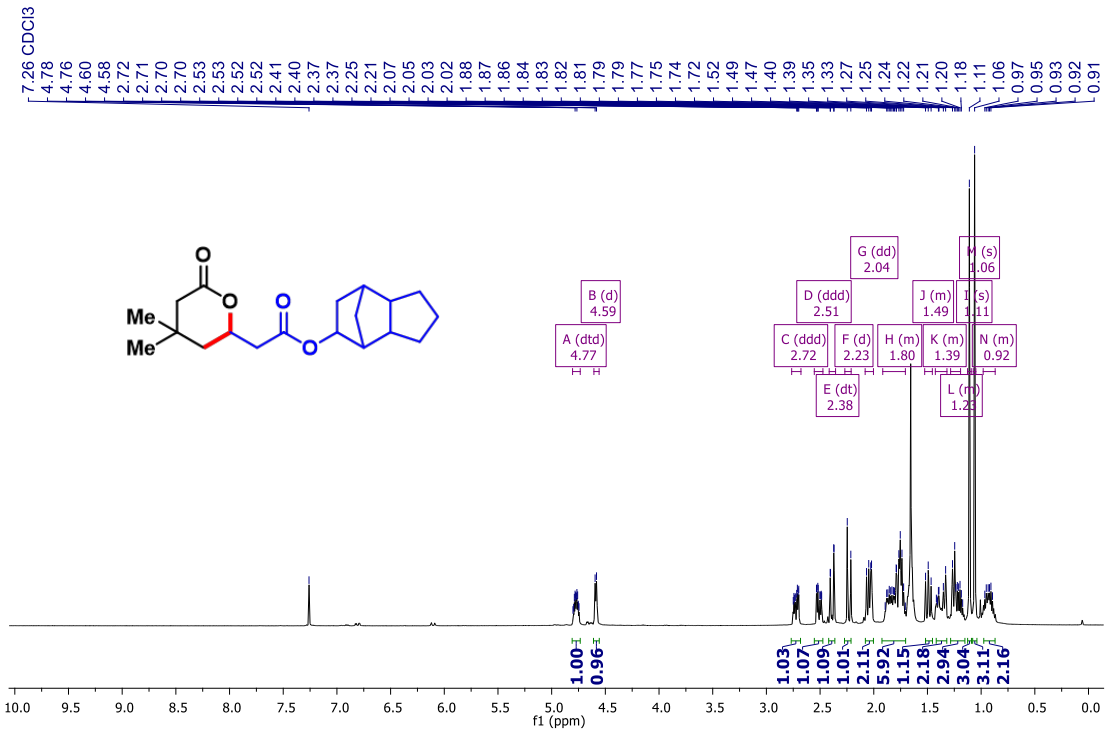
1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



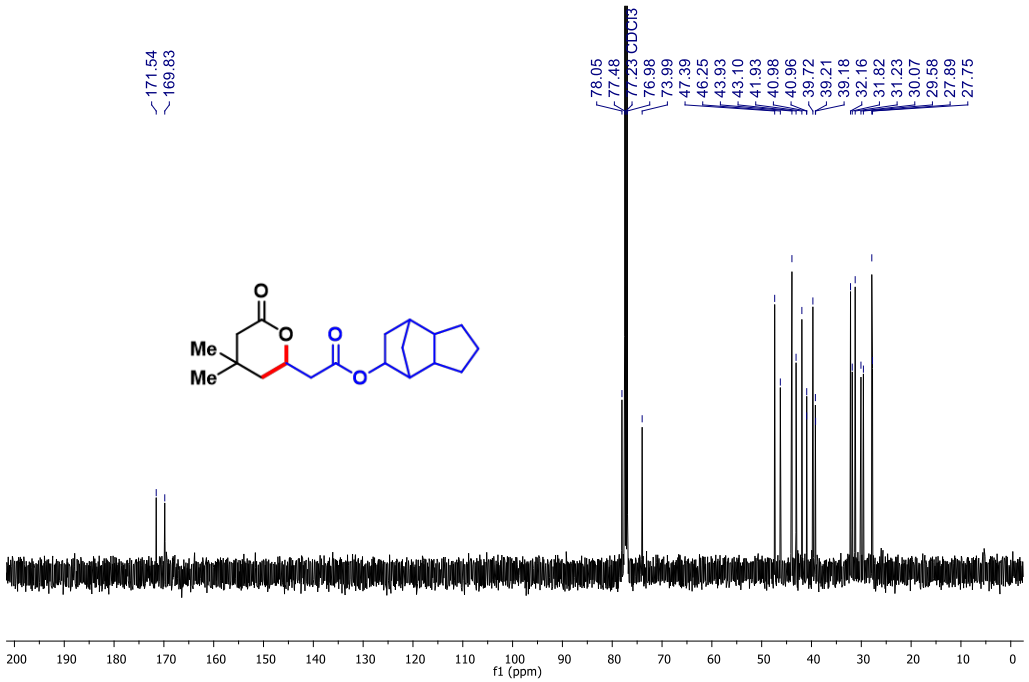
1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



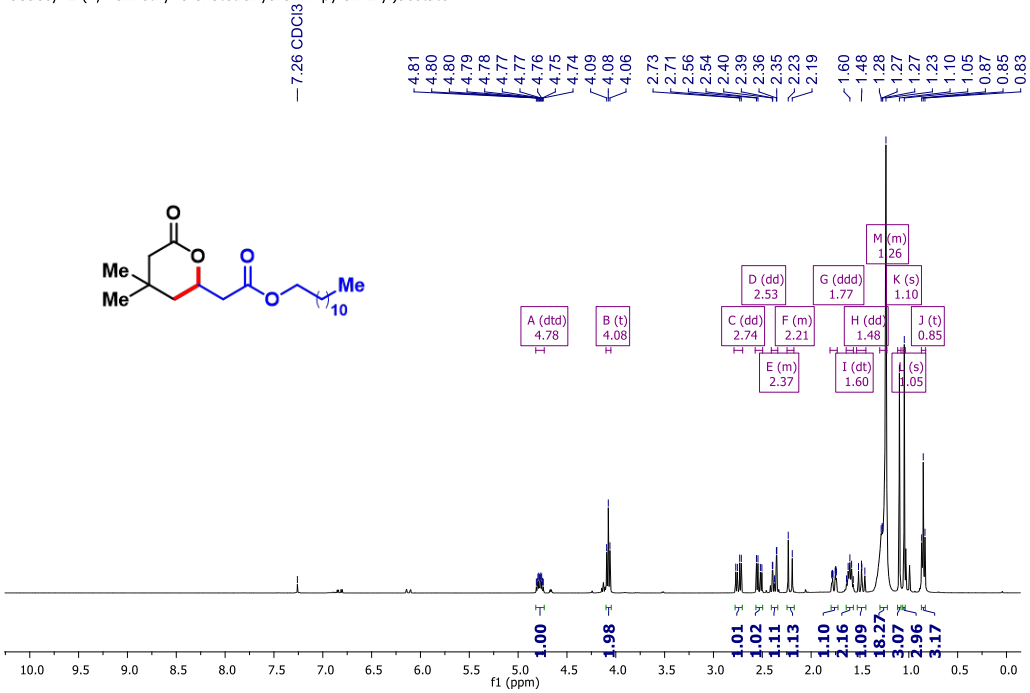
octahydro-1H-4,7-methanoinden-5-yl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



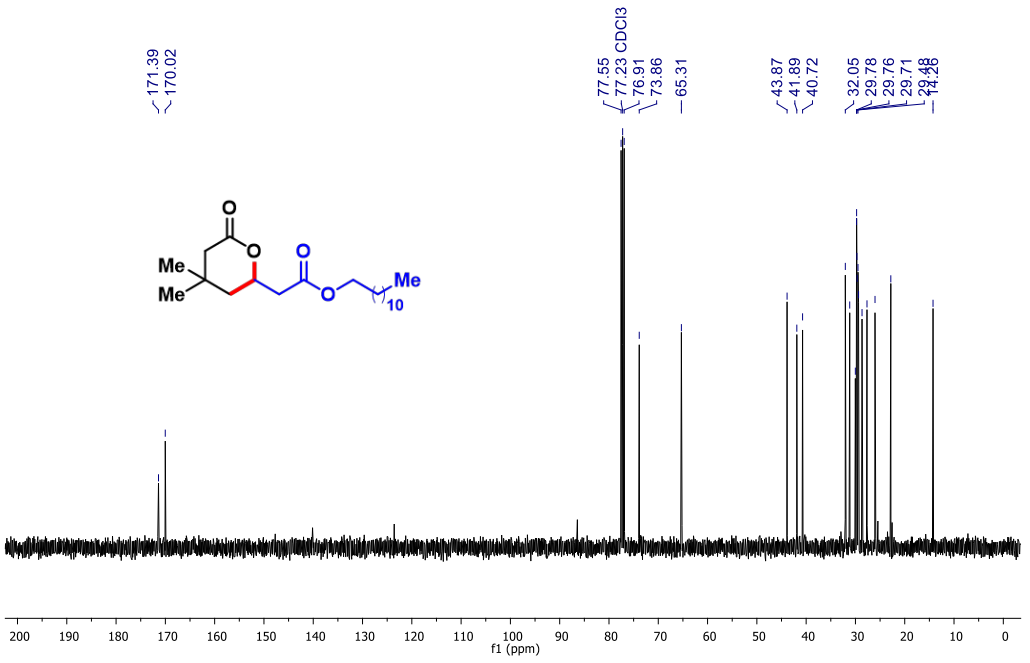
octahydro-1H-4,7-methanoinden-5-yl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



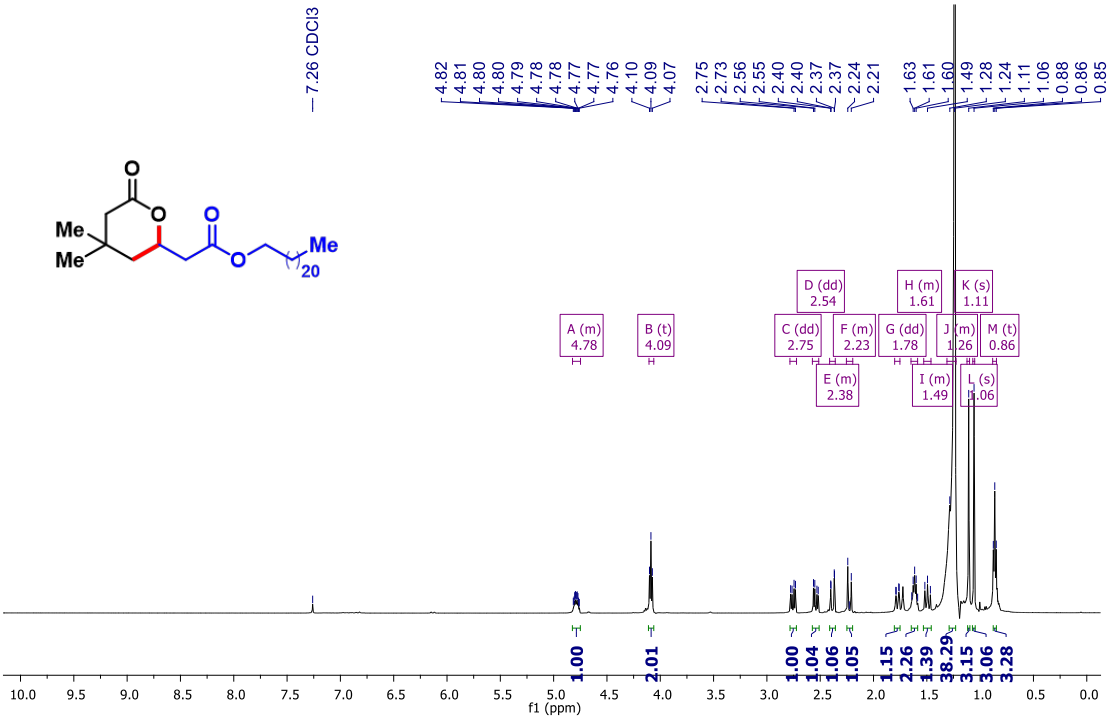
dodecyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



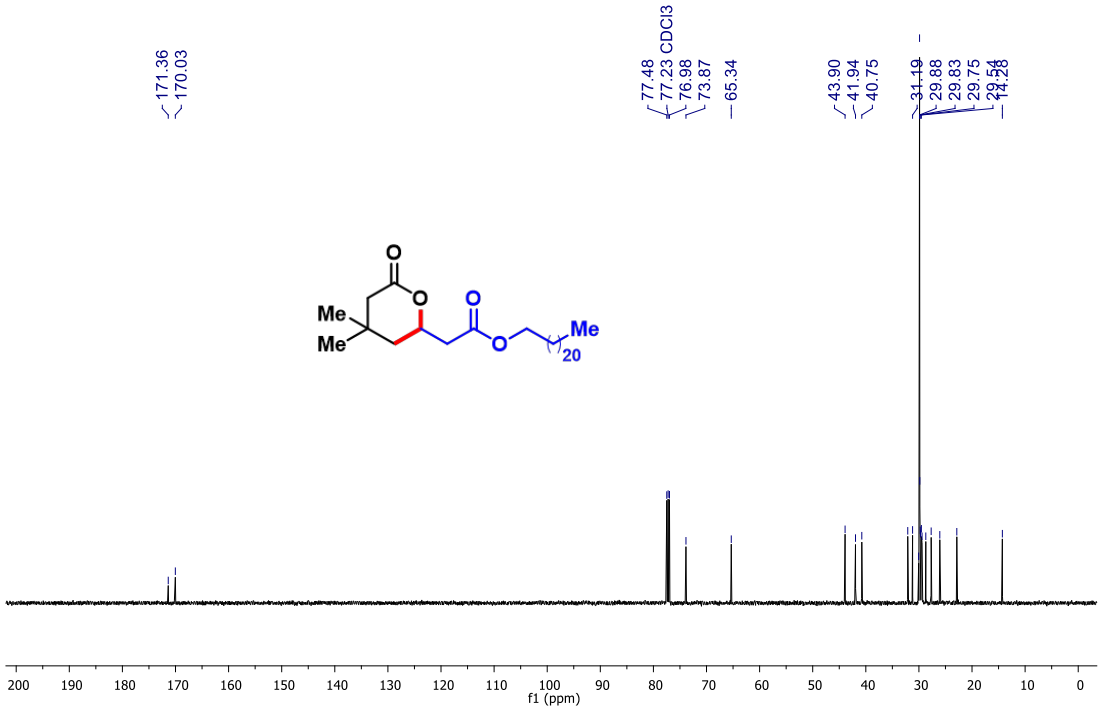
dodecyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



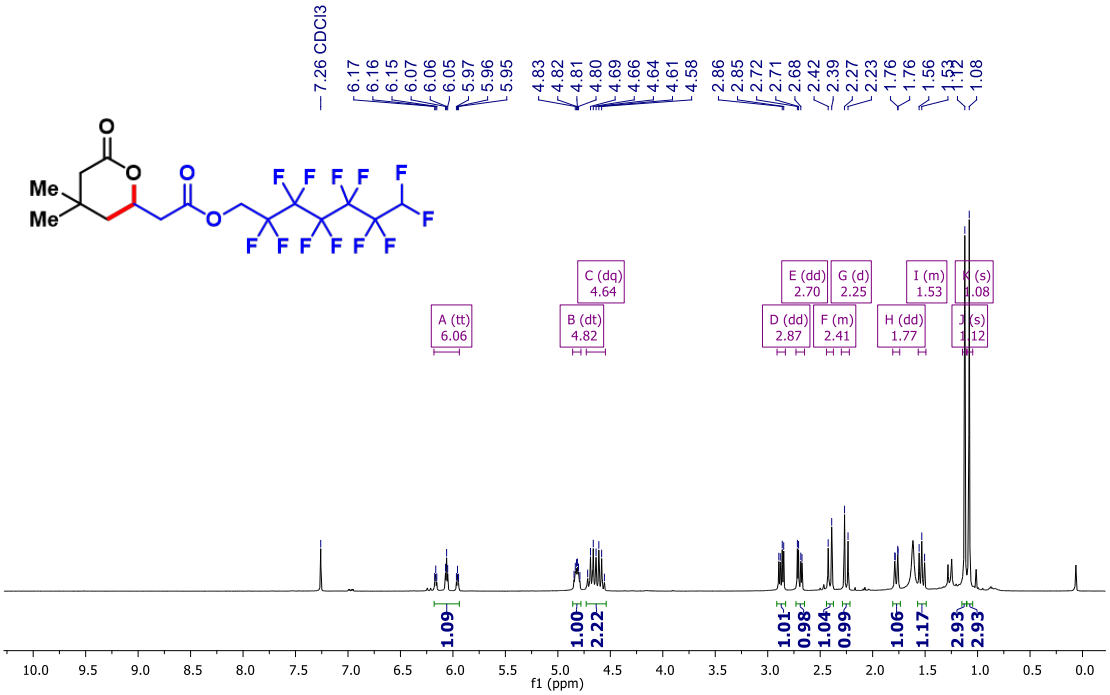
docosyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



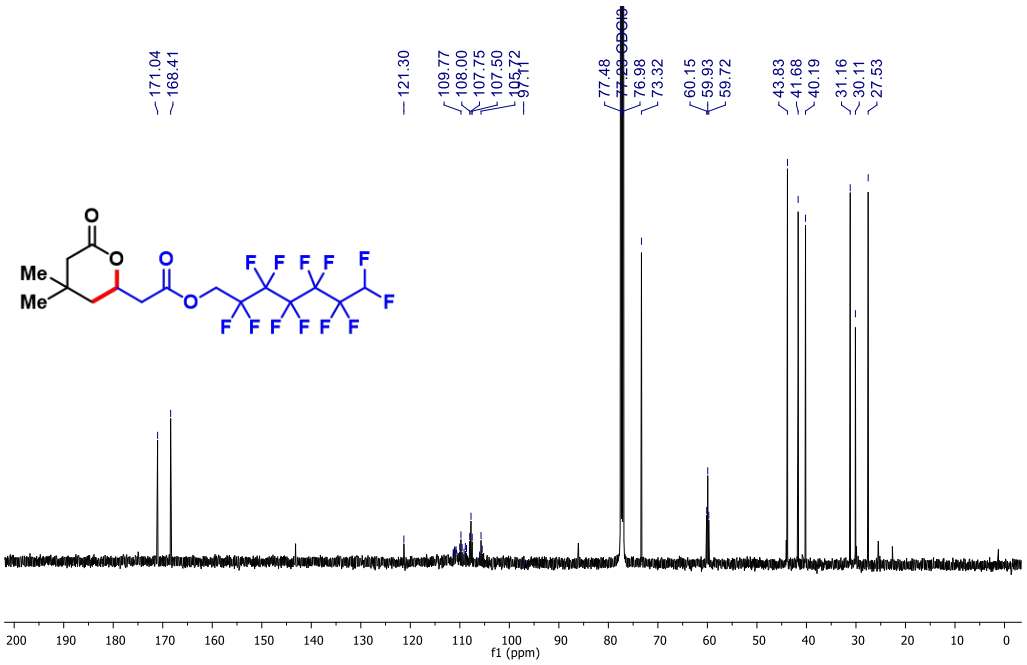
docosyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



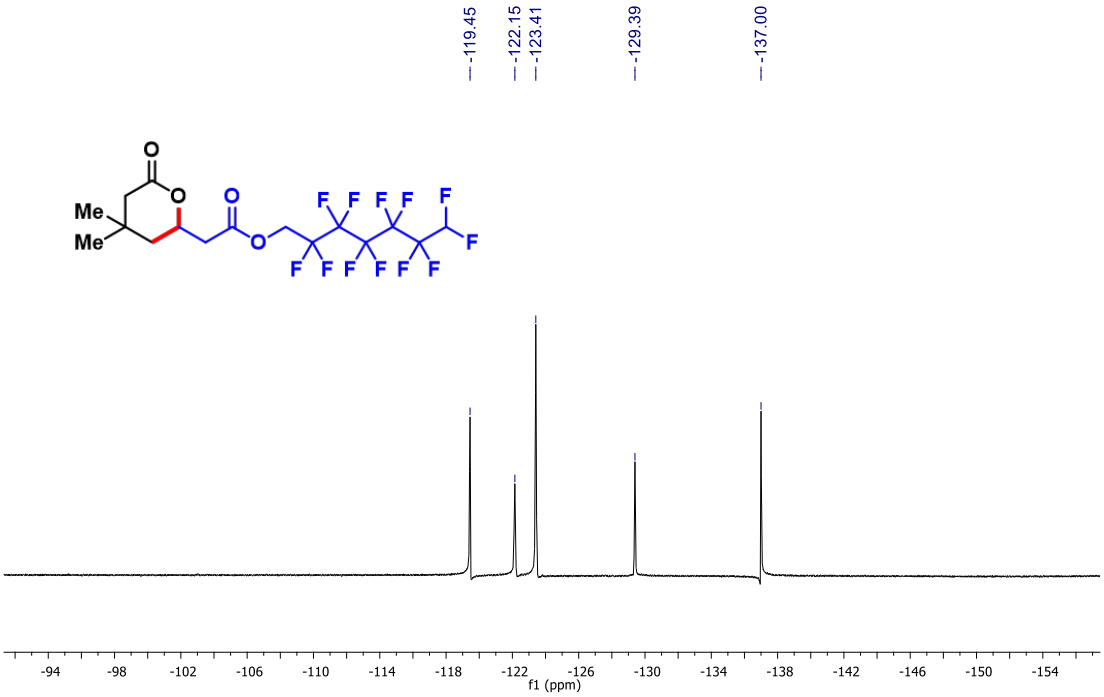
2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



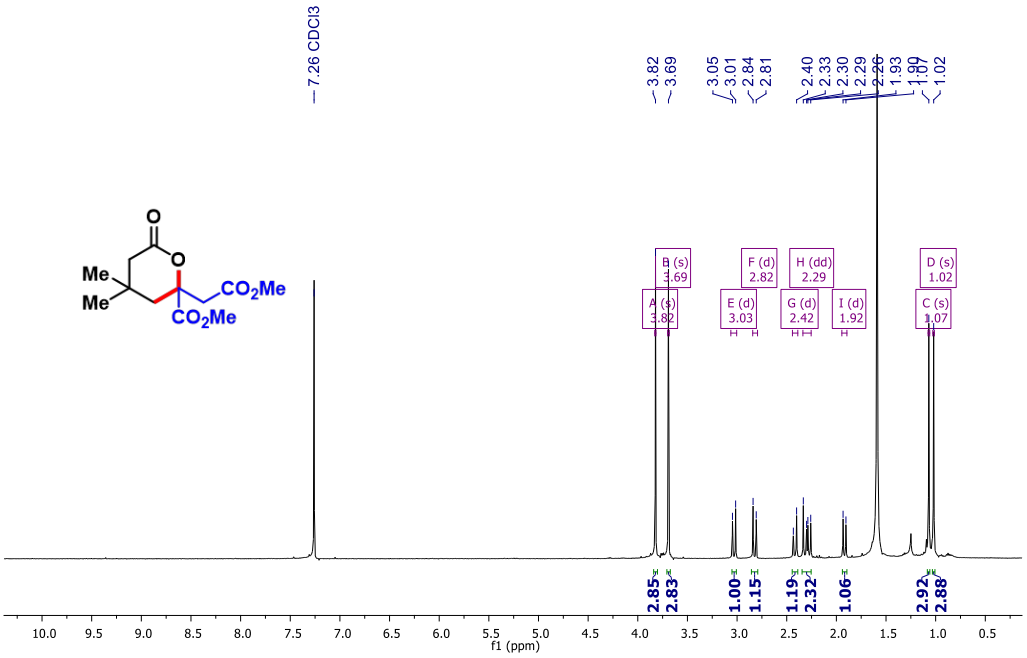
2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



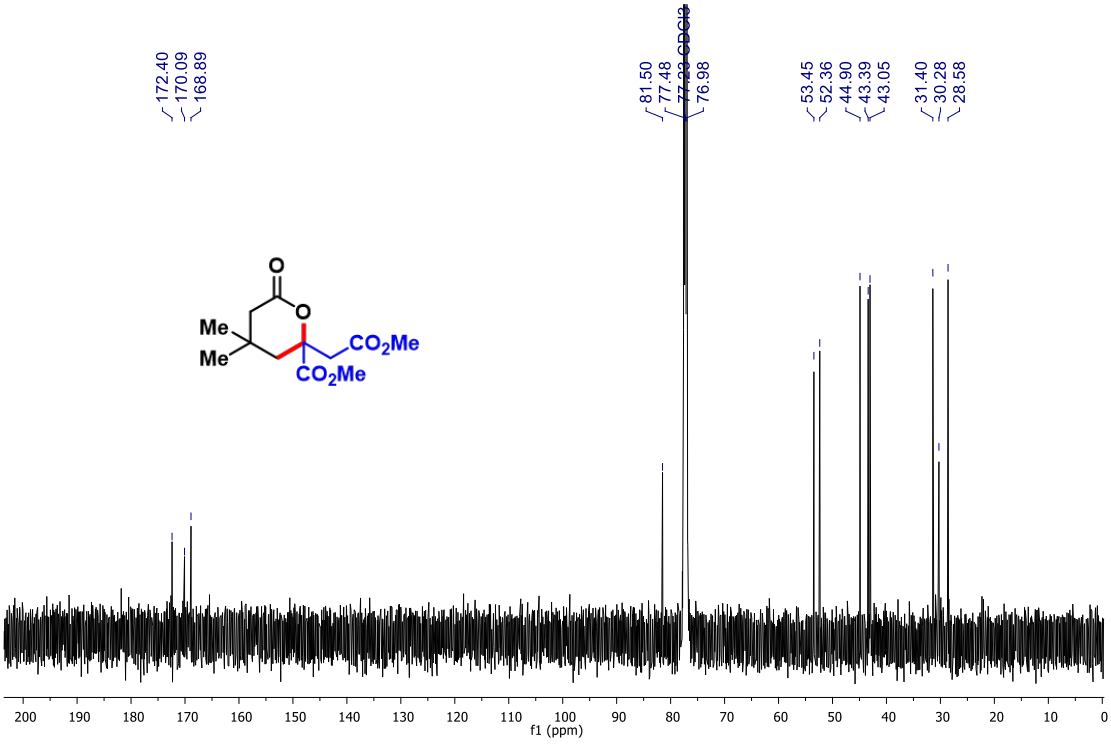
2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoroheptyl 2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetate



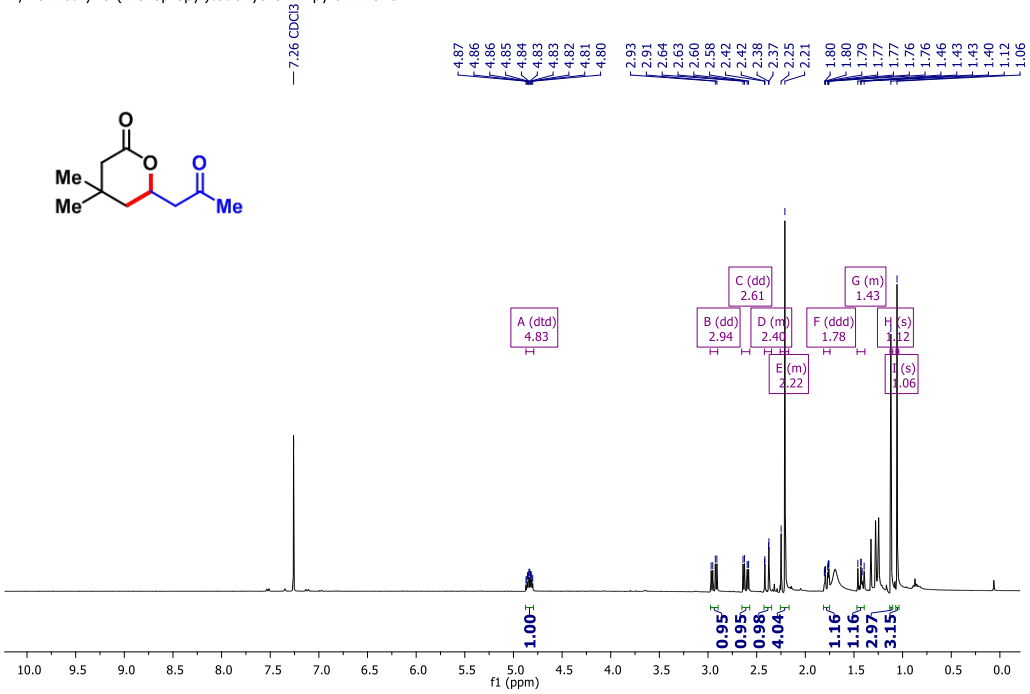
methyl 2-(2-methoxy-2-oxoethyl)-4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-carboxylate



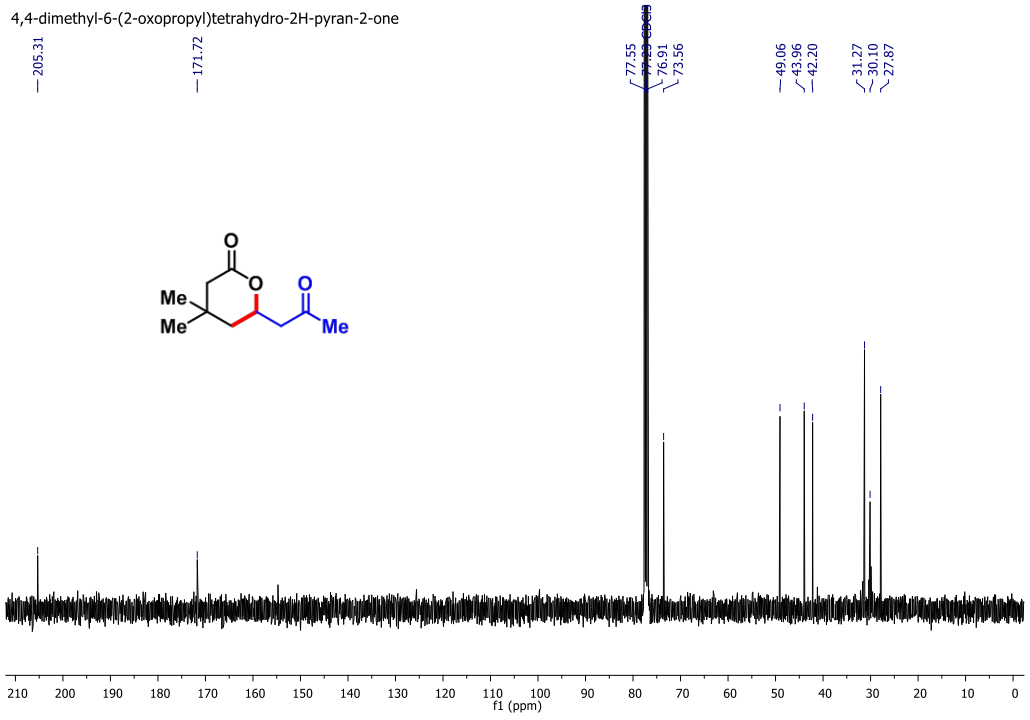
methyl 2-(2-methoxy-2-oxoethyl)-4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-carboxylate



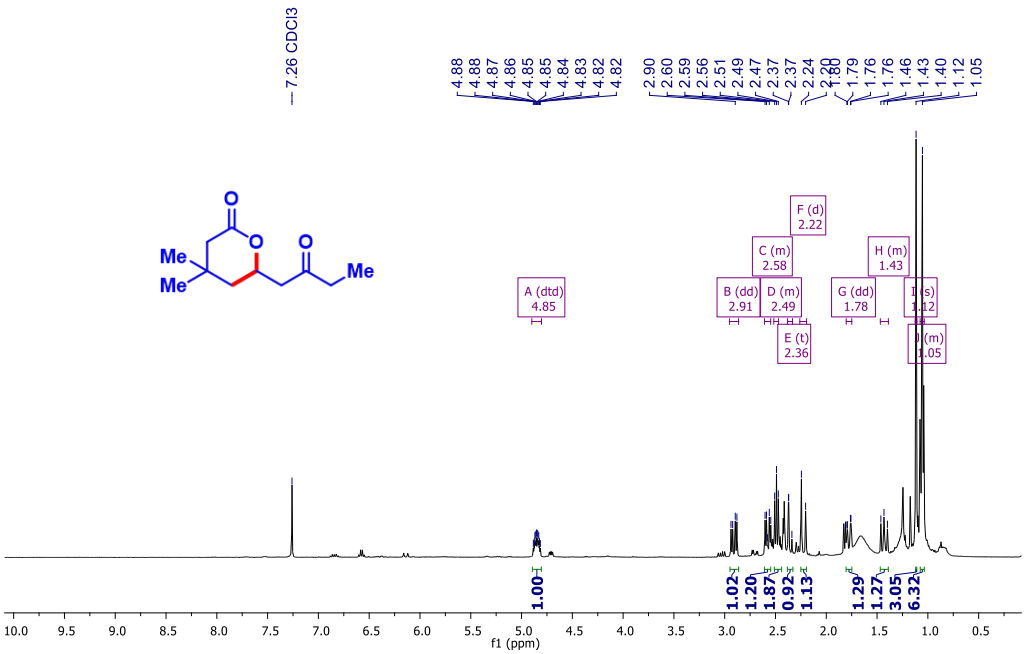
4,4-dimethyl-6-(2-oxopropyl)tetrahydro-2H-pyran-2-one



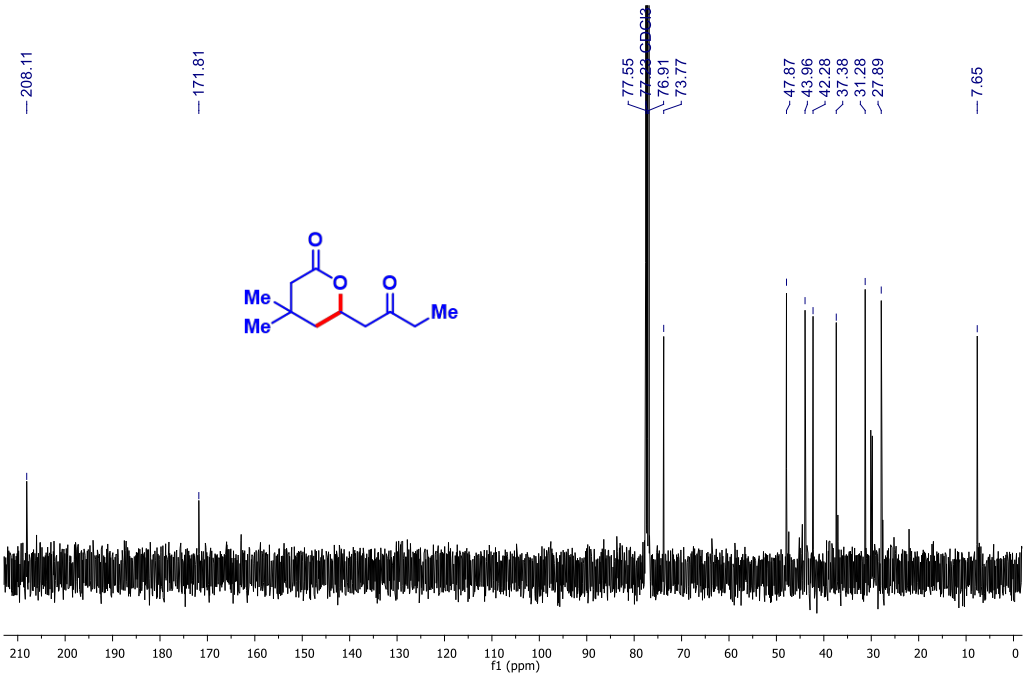
4,4-dimethyl-6-(2-oxopropyl)tetrahydro-2H-pyran-2-one



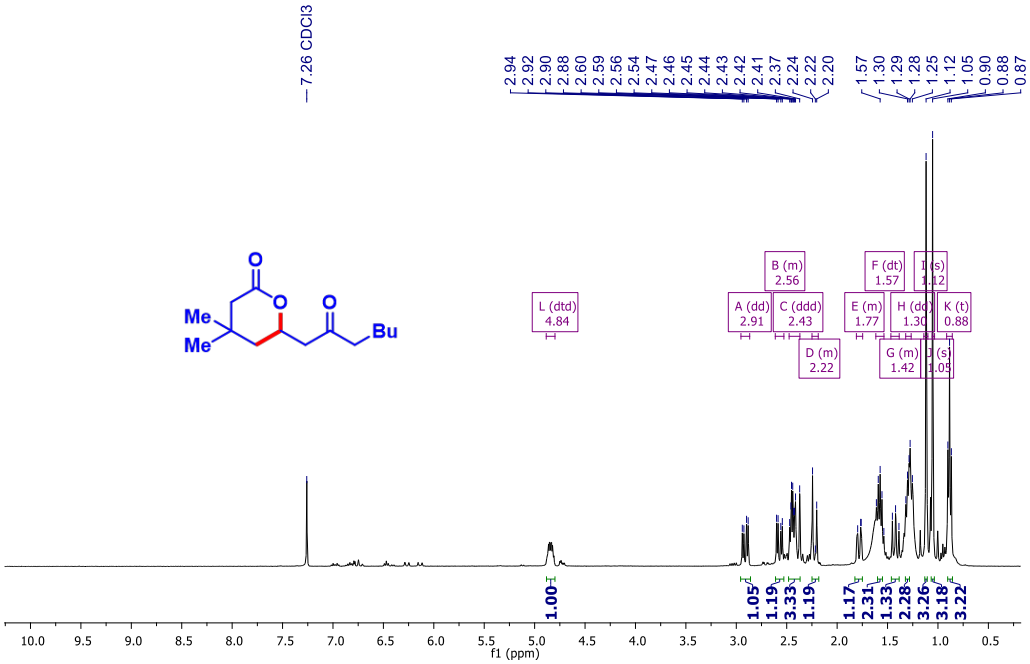
4,4-dimethyl-6-(2-oxobutyl)tetrahydro-2H-pyran-2-one



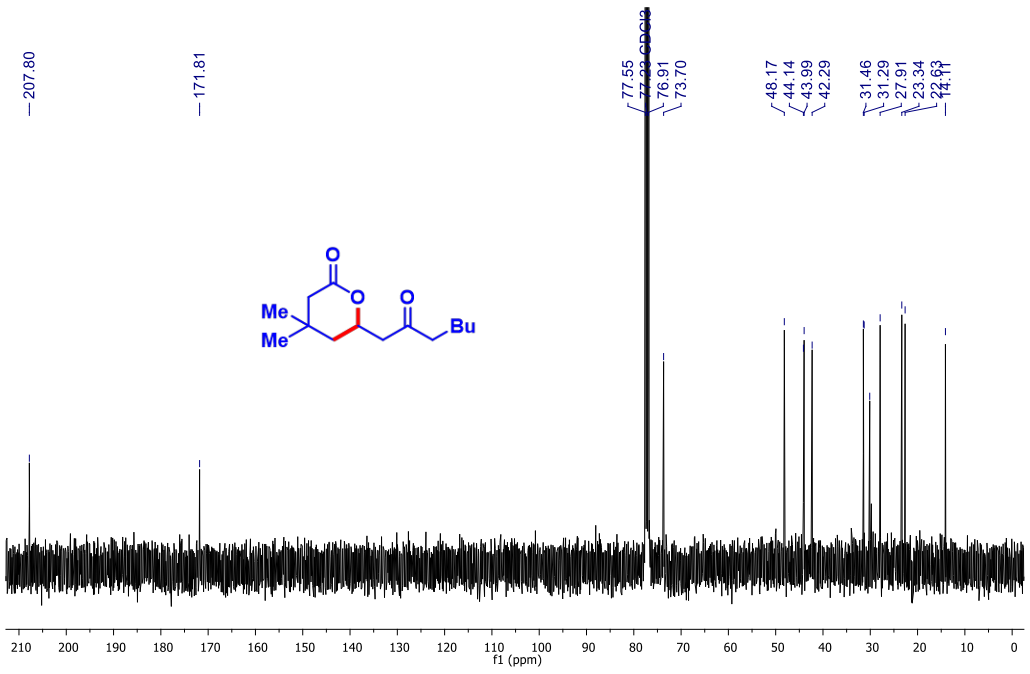
4,4-dimethyl-6-(2-oxobutyl)tetrahydro-2H-pyran-2-one



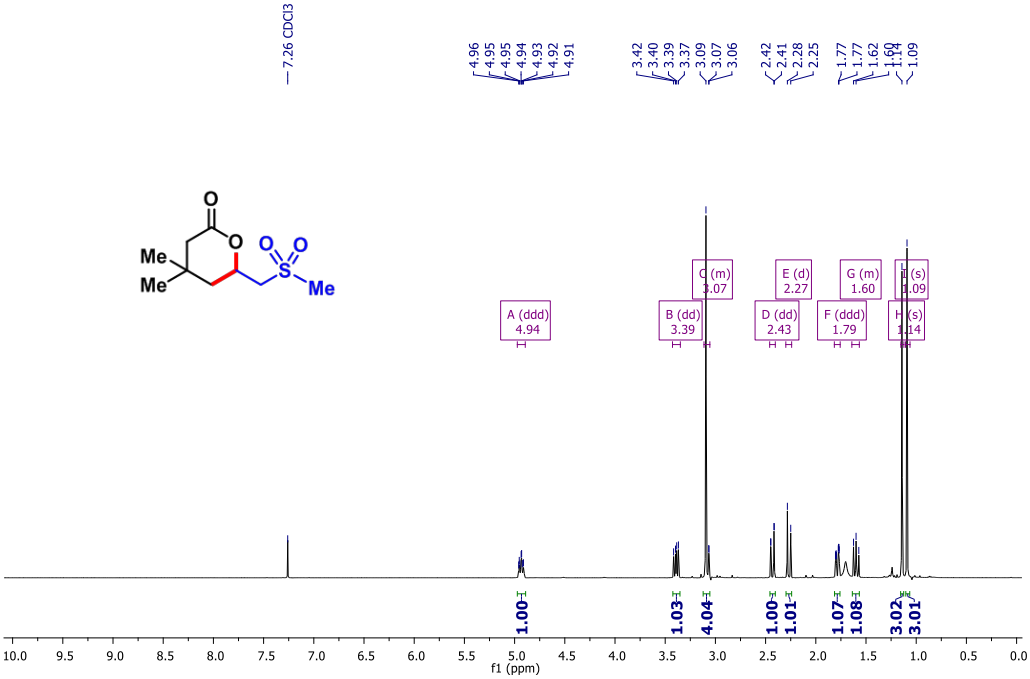
4,4-dimethyl-6-(2-oxoheptyl)tetrahydro-2H-pyran-2-one



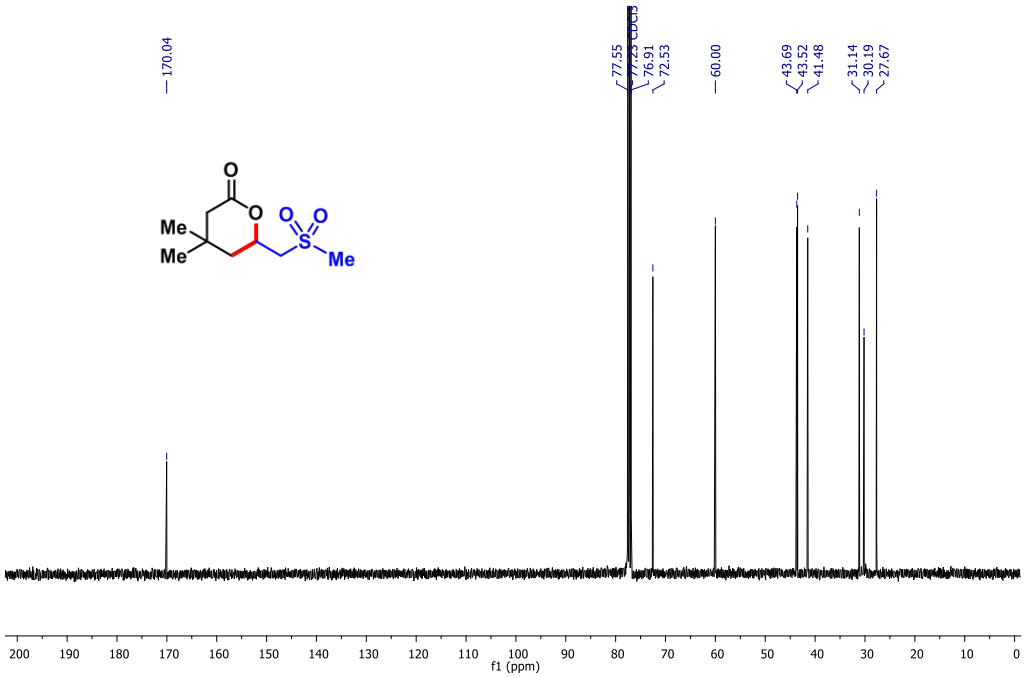
4,4-dimethyl-6-(2-oxoheptyl)tetrahydro-2H-pyran-2-one



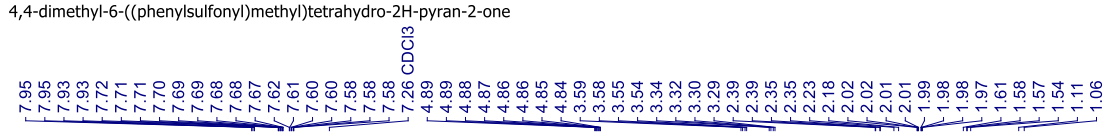
4,4-dimethyl-6-((methylsulfonyl)methyl)tetrahydro-2H-pyran-2-one

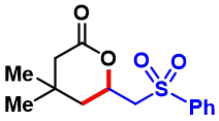


4,4-dimethyl-6-((methylsulfonyl)methyl)tetrahydro-2H-pyran-2-one

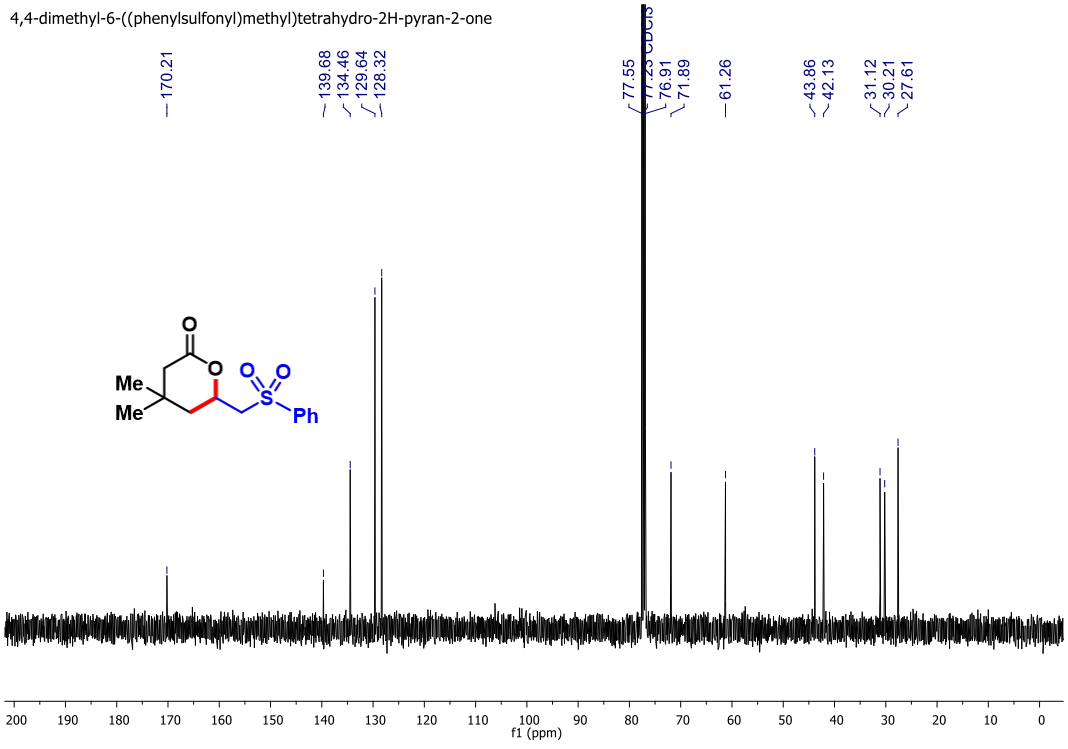


4,4-dimethyl-6-((phenylsulfonyl)methyl)tetrahydro-2H-pyran-2-one

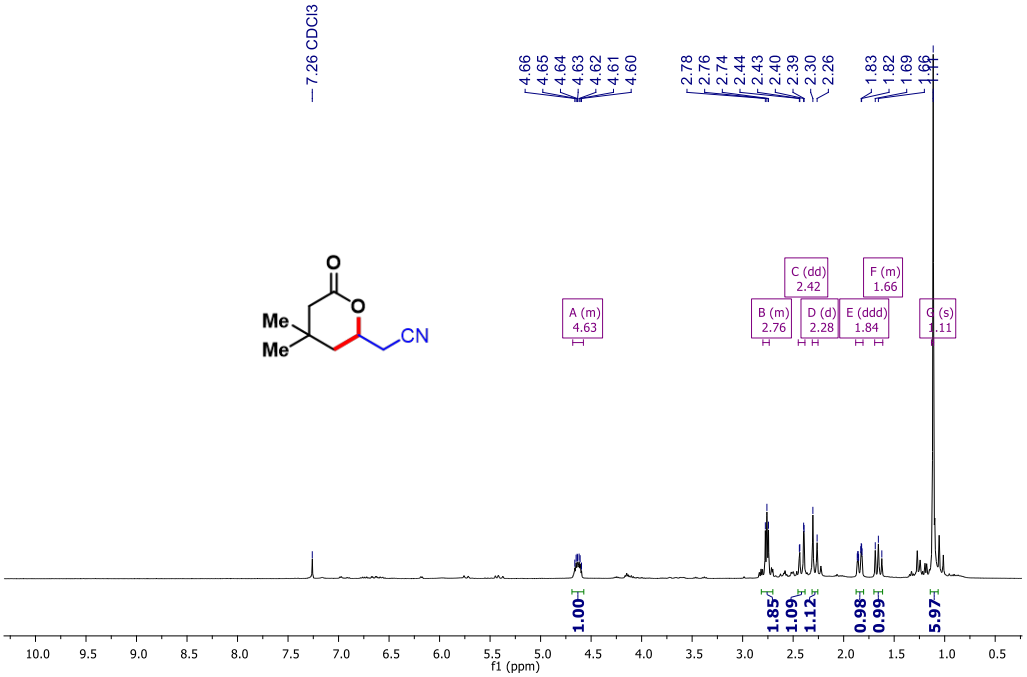




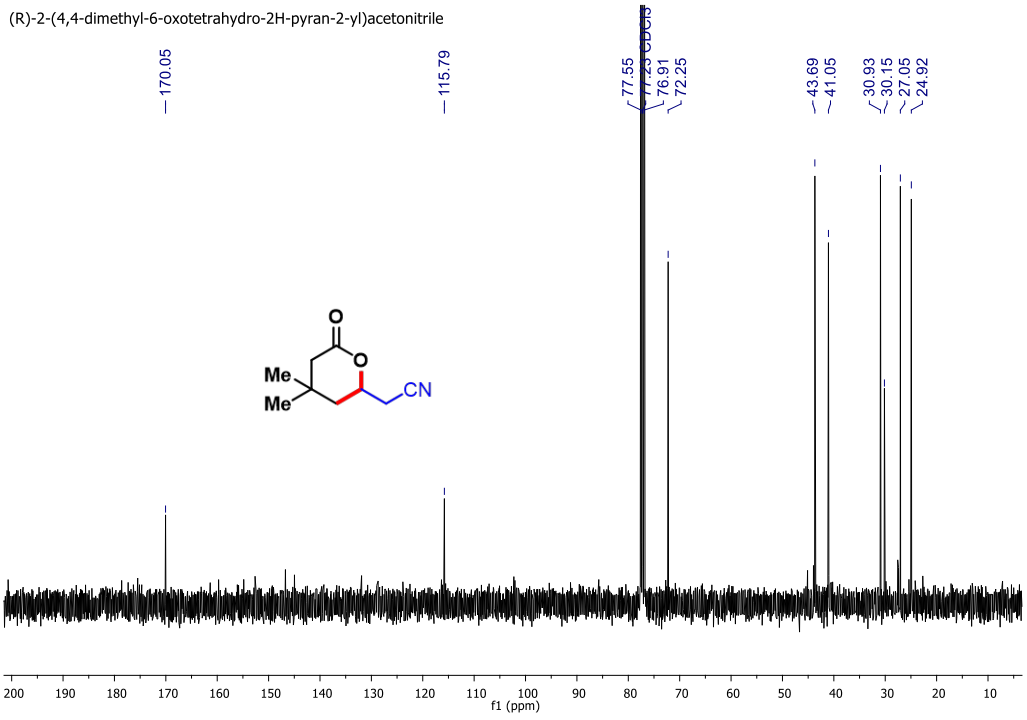
4,4-dimethyl-6-((phenylsulfonyl)methyl)tetrahydro-2H-pyran-2-one



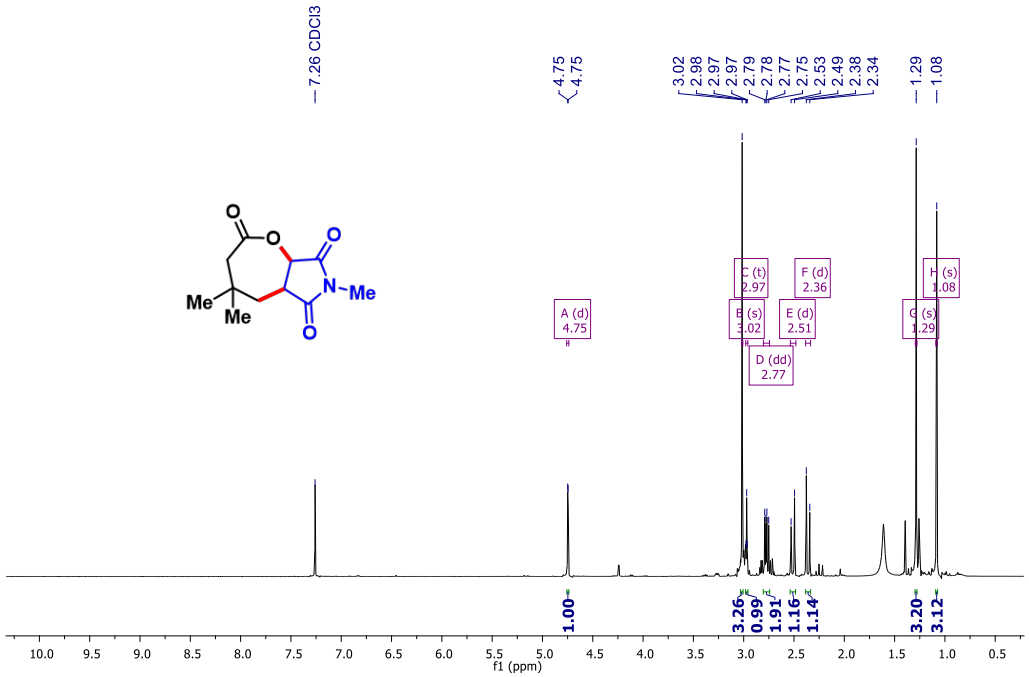
(R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetonitrile



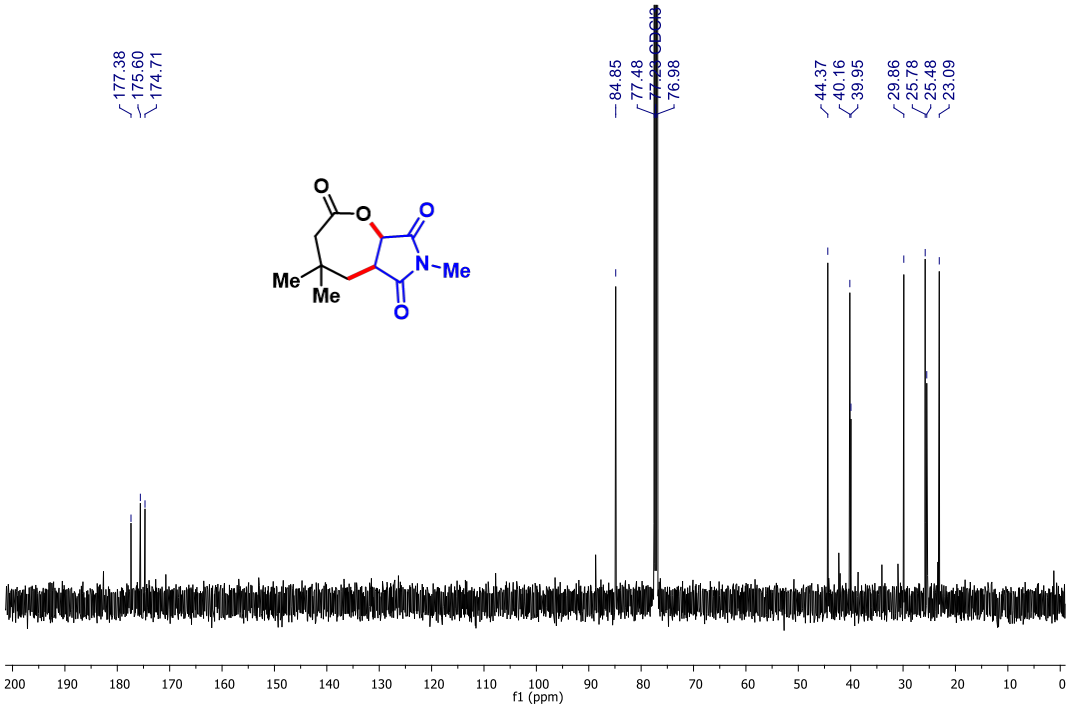
(R)-2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetonitrile



4,4,7-trimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione



4,4,7-trimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione



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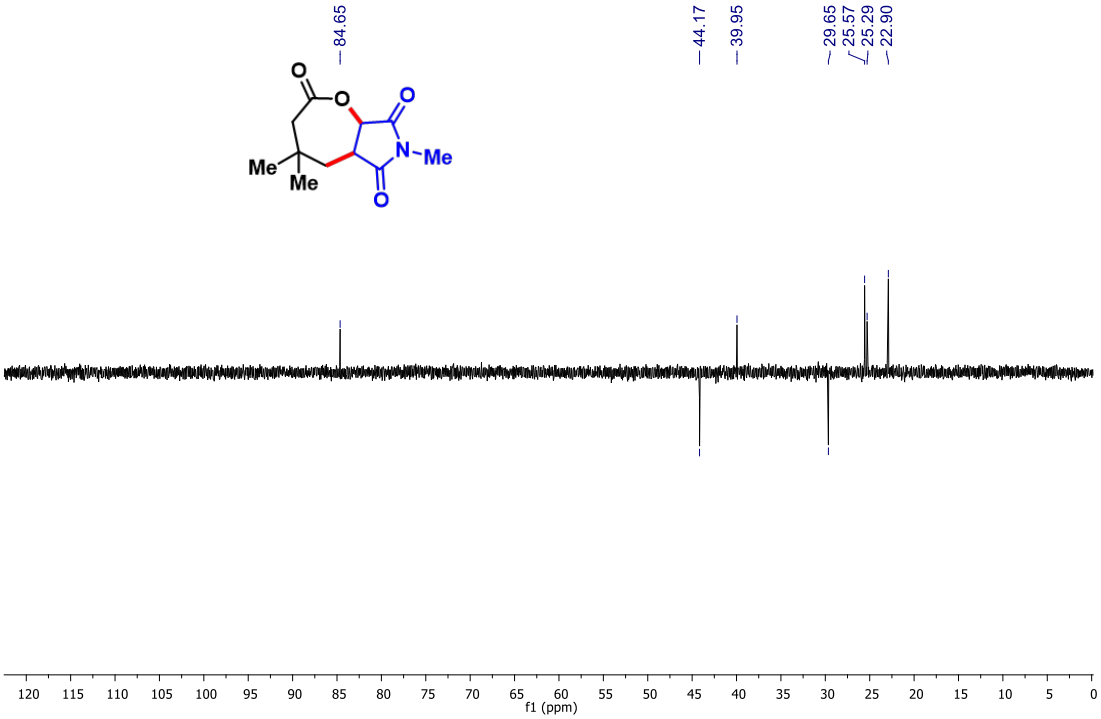
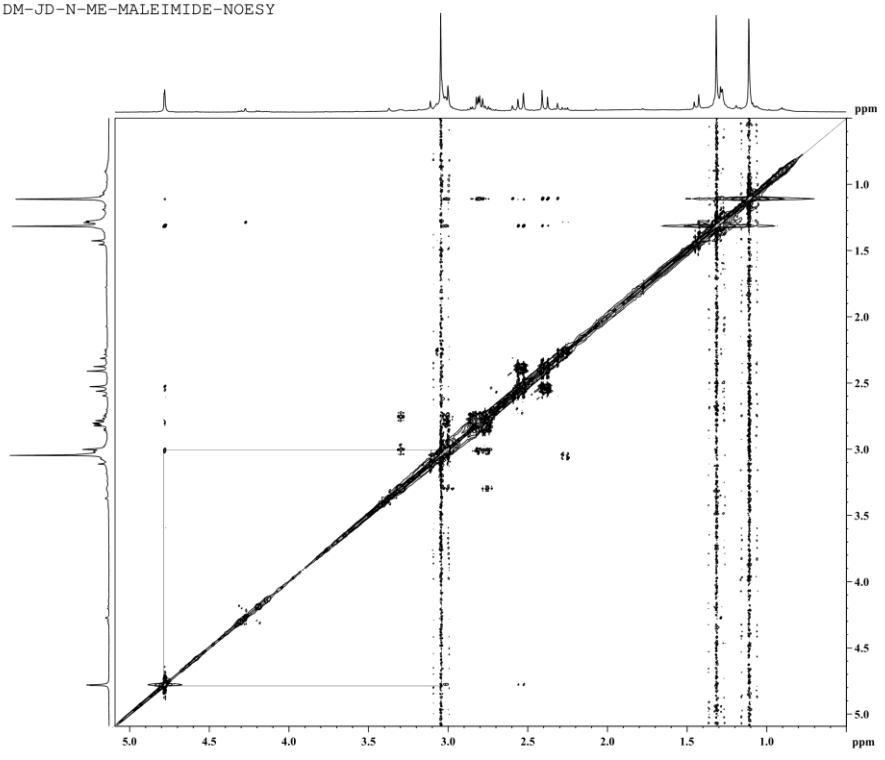


DM-JD-N-ME-MALEIMIDE-NOESY




```
Current Data Parameters
NAME      DM-JD-N-ME-MALEIMIDE-NOESY
EXPNO                 2
PROCNO                1

F2 - Acquisition Parameters
Date_          20191130
Time               0.28
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG        noesygpph
TD                 2048
SOLVENT           CDCl3
NS                   16
DS                    0
SWH           2520.161 Hz
FIDRES        1.230548 Hz
AQ            0.4063232 sec
RG                15.73
DW              198.400 usec
DE                6.50 usec
TE                294.6 K
D0           0.00018140 sec
D1           1.00000000 sec
D8           0.60000002 sec
D16          0.00020000 sec
IN0          0.00039680 sec

======== CHANNEL f1 ========
SFO1        500.1312866 MHz
NUC1               1H
P1                13.35 usec
P2                26.70 usec
PLW1       16.00000000 W

====== GRADIENT CHANNEL =====
GPNAM[1]     SMSQ10.100
GPZ1              40.00 %
P16             1000.00 usec

F1 - Acquisition parameters
TD                 808
SFO1          500.1313 MHz
FIDRES        6.238023 Hz
SW              5.039 ppm
FnMODE            TPPI

F2 - Processing parameters
SI                1024
SF          500.1300000 MHz
WDW               QSINE
SSB                   2
LB                    0 Hz
GB                    0
PC                 1.00

F1 - Processing parameters
SI                1024
MC2               TPPI
SF          500.1300000 MHz
WDW               QSINE
SSB                   2
LB                    0 Hz
GB                    0
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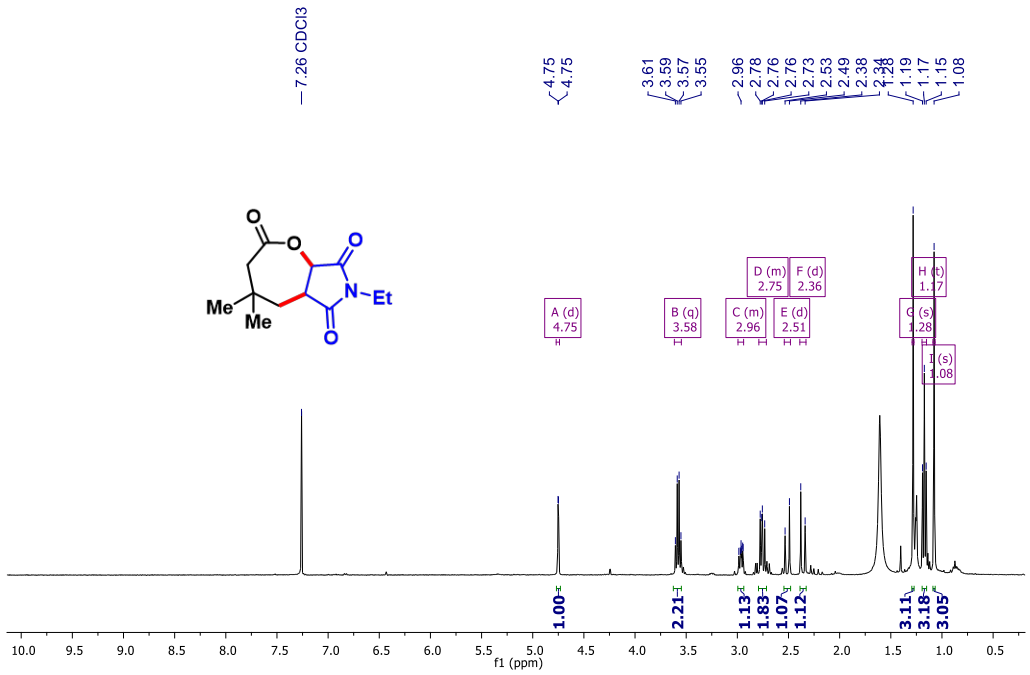
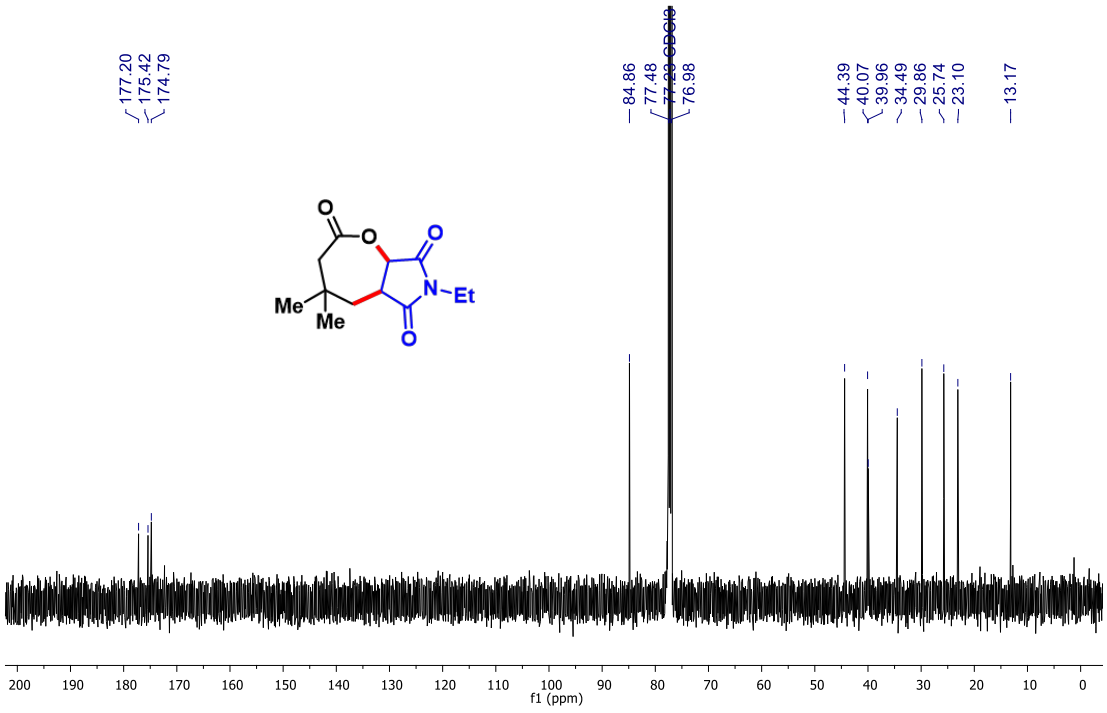
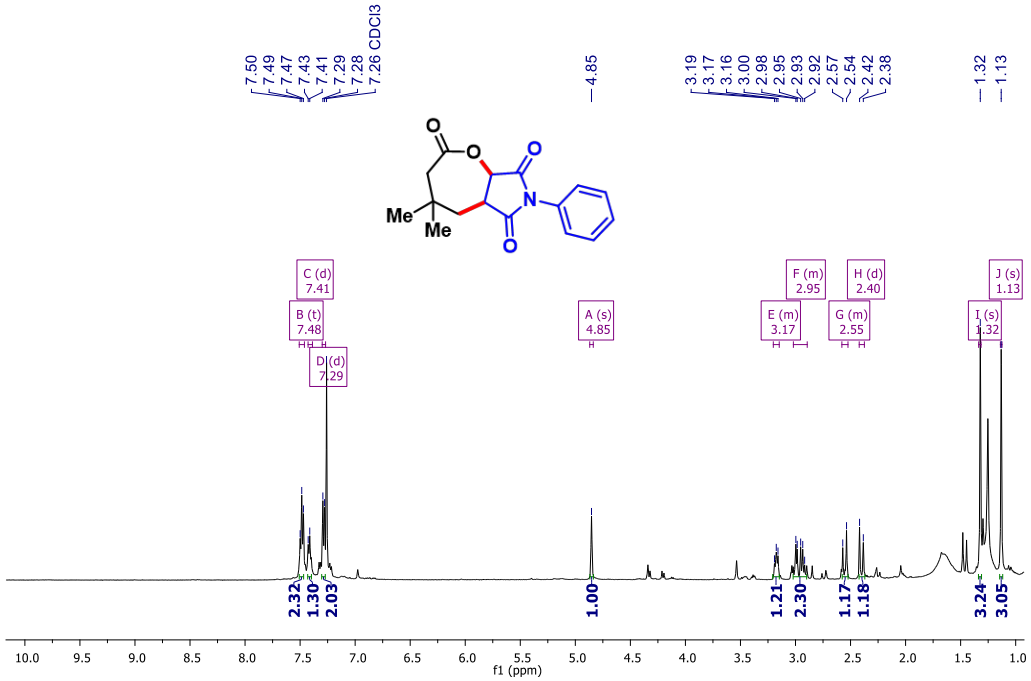
7-ethyl-4,4-dimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione



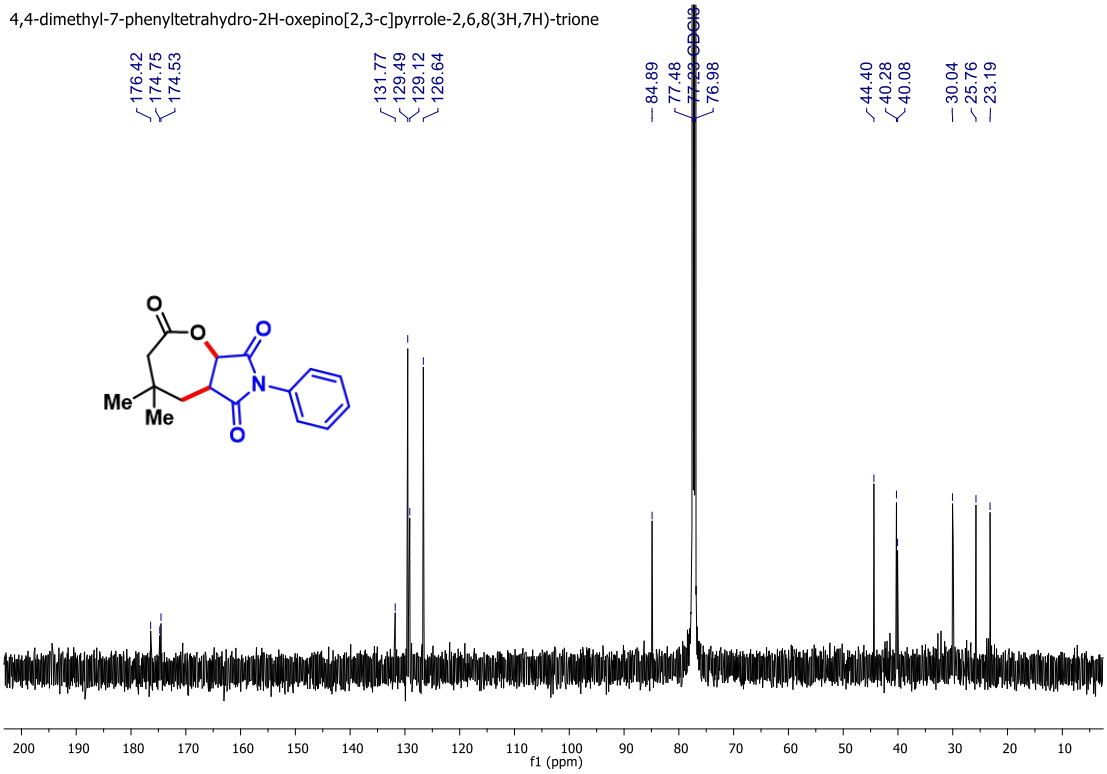
7-ethyl-4,4-dimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione

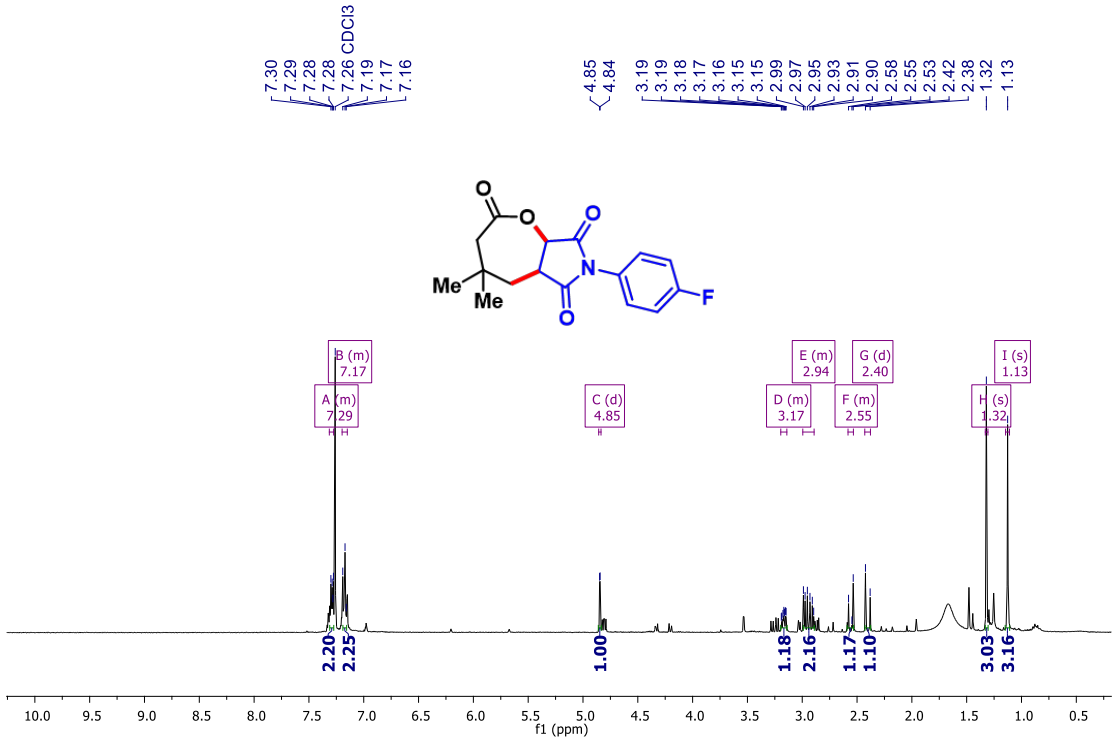


4,4-dimethyl-7-phenyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione

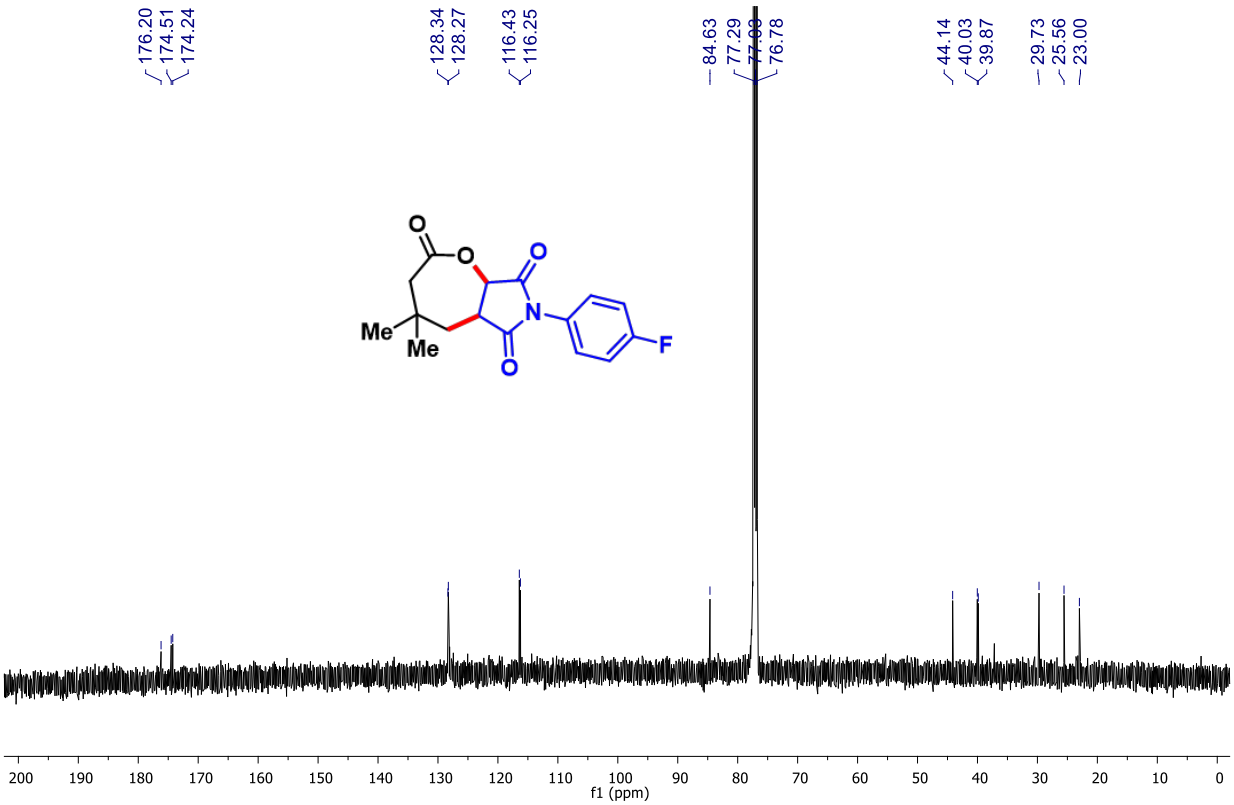


4,4-dimethyl-7-phenyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione

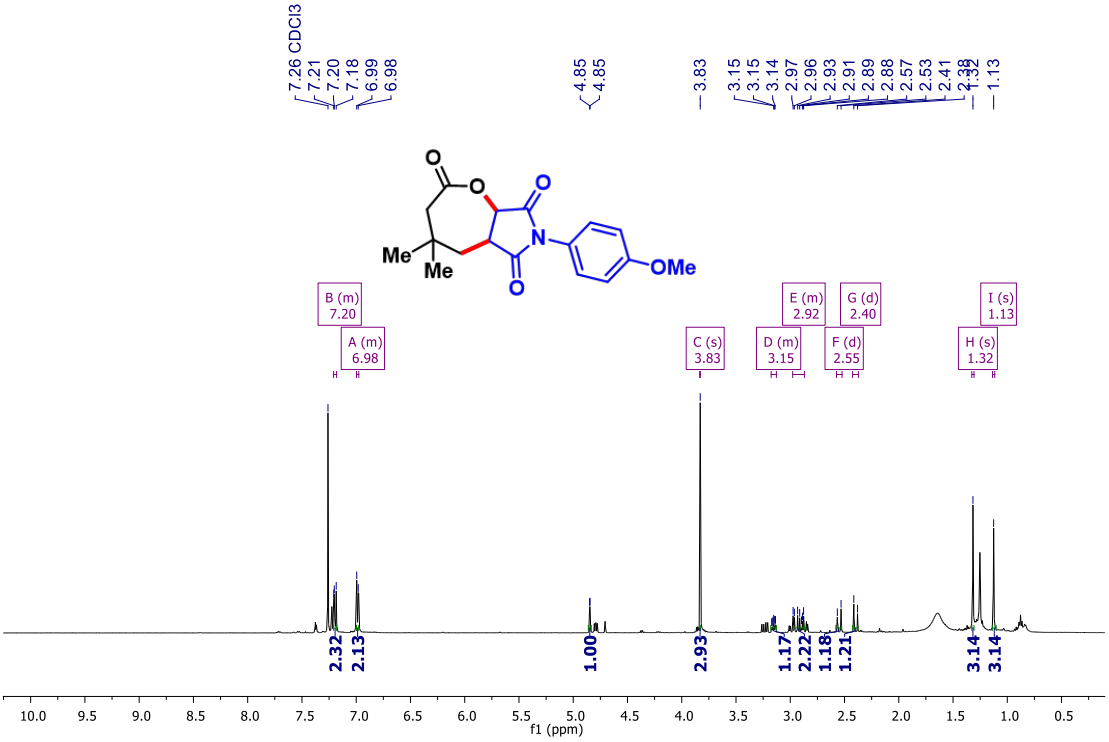




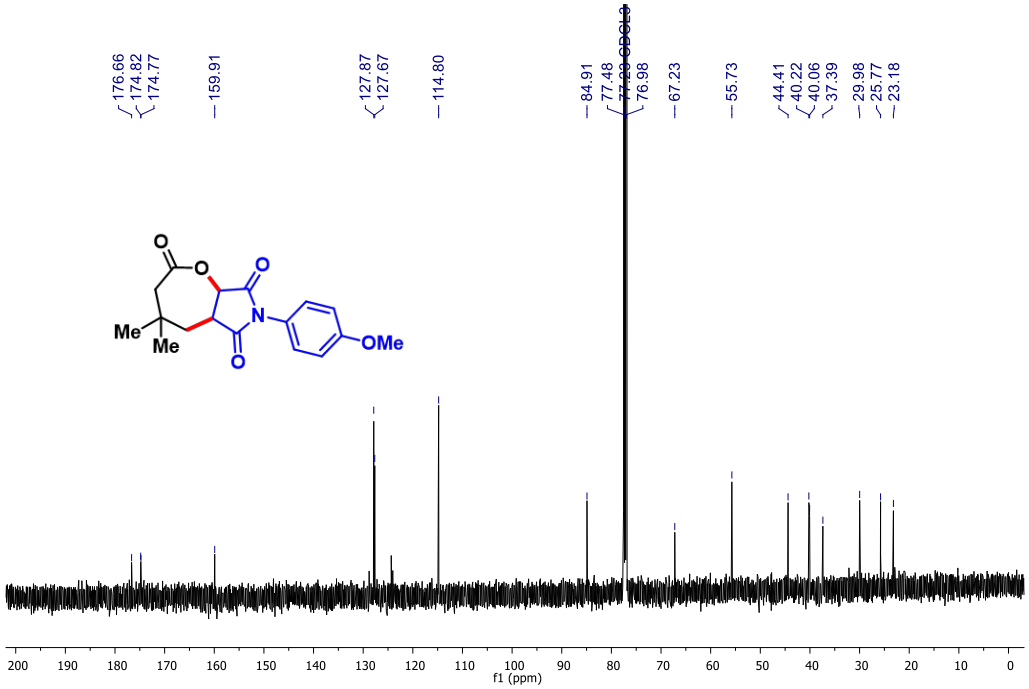
7-(4-fluorophenyl)-4,4-dimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione



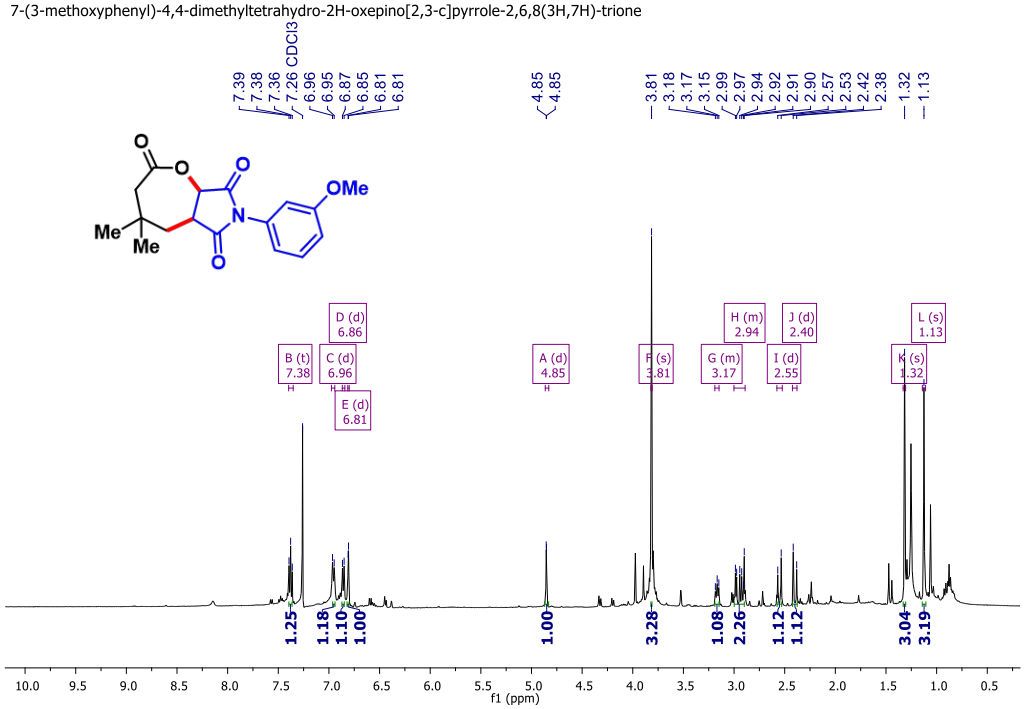
7-(4-methoxyphenyl)-4,4-dimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione



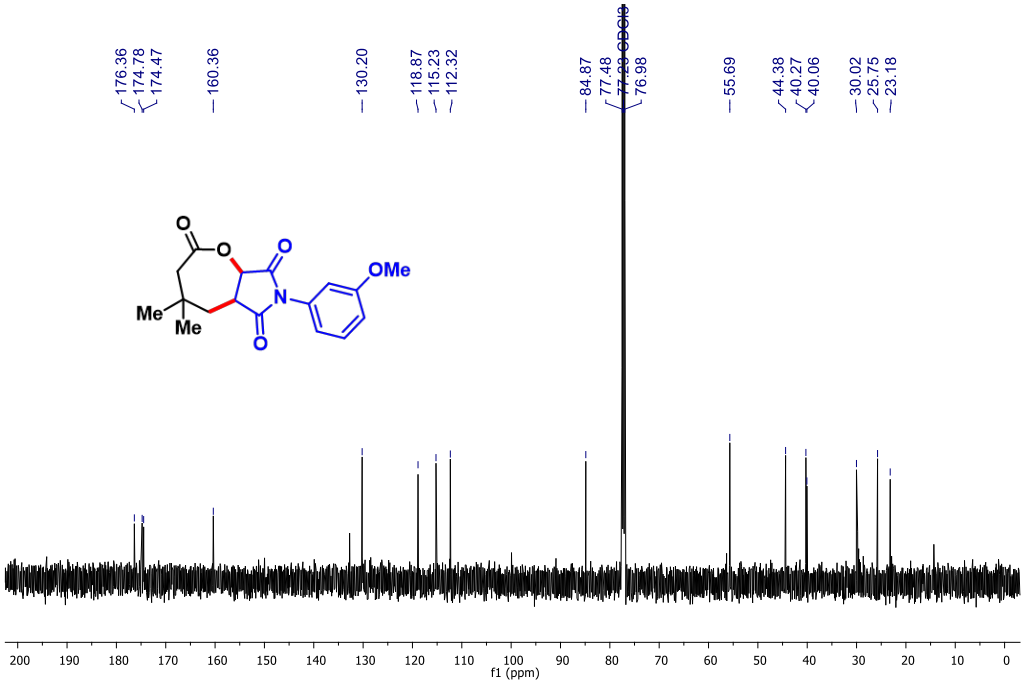
7-(4-methoxyphenyl)-4,4-dimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione



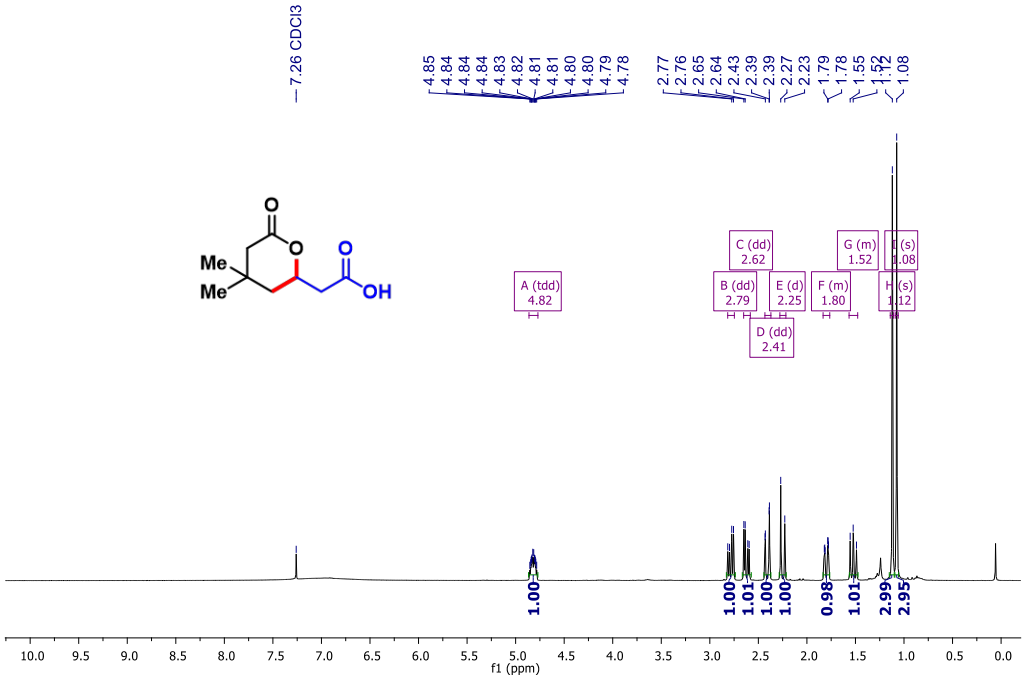
7-(3-methoxyphenyl)-4,4-dimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione



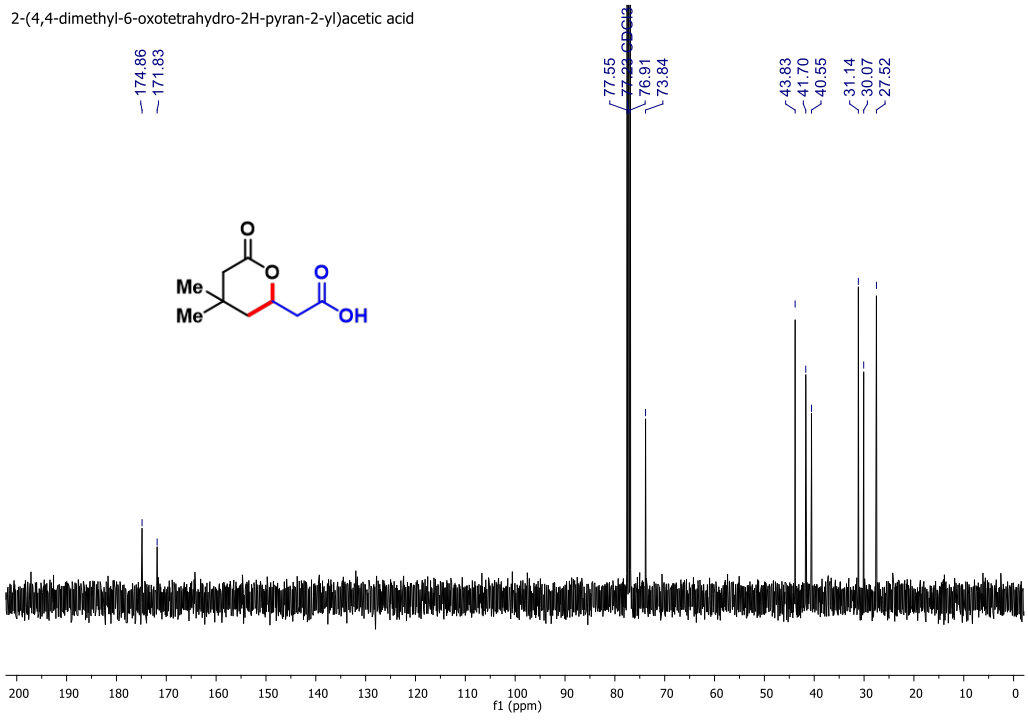
7-(3-methoxyphenyl)-4,4-dimethyltetrahydro-2H-oxepino[2,3-c]pyrrole-2,6,8(3H,7H)-trione



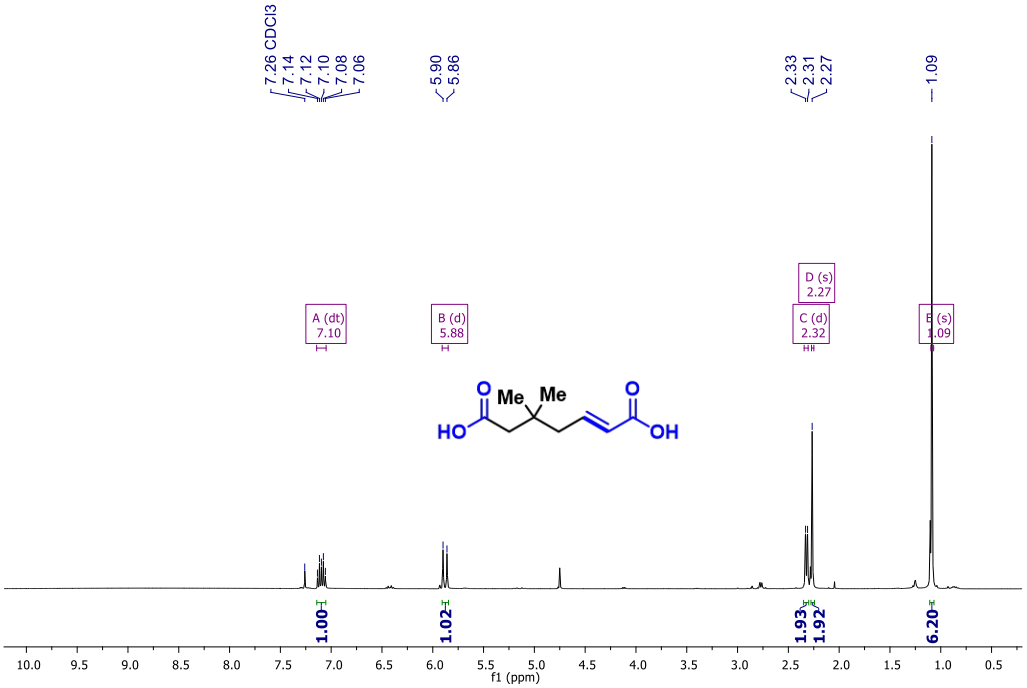
2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetic acid



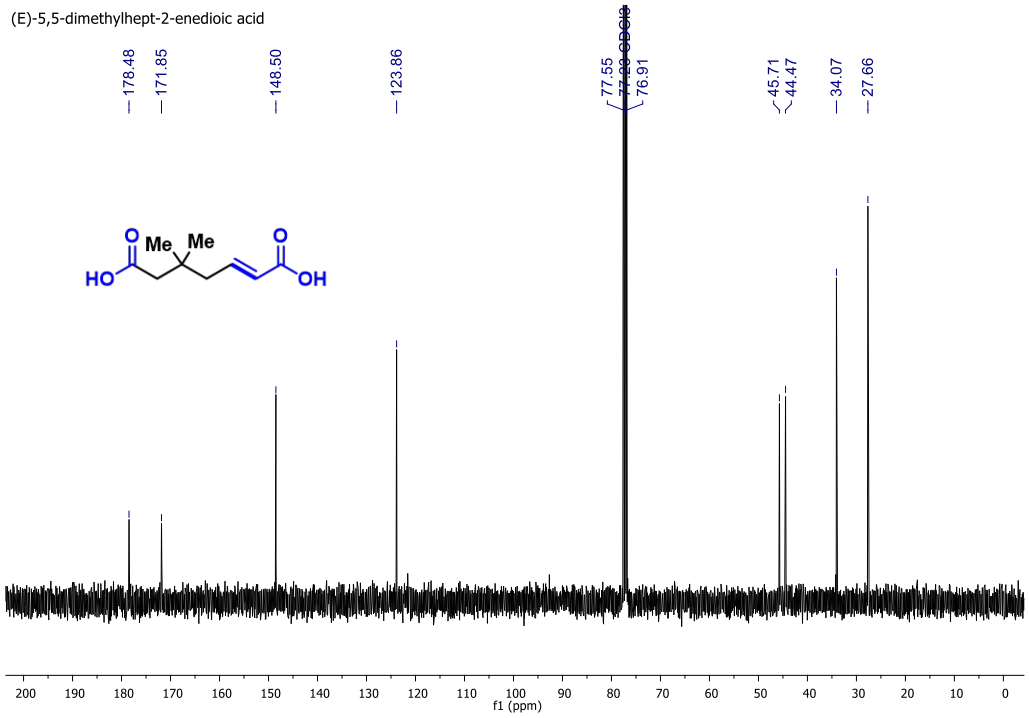
2-(4,4-dimethyl-6-oxotetrahydro-2H-pyran-2-yl)acetic acid



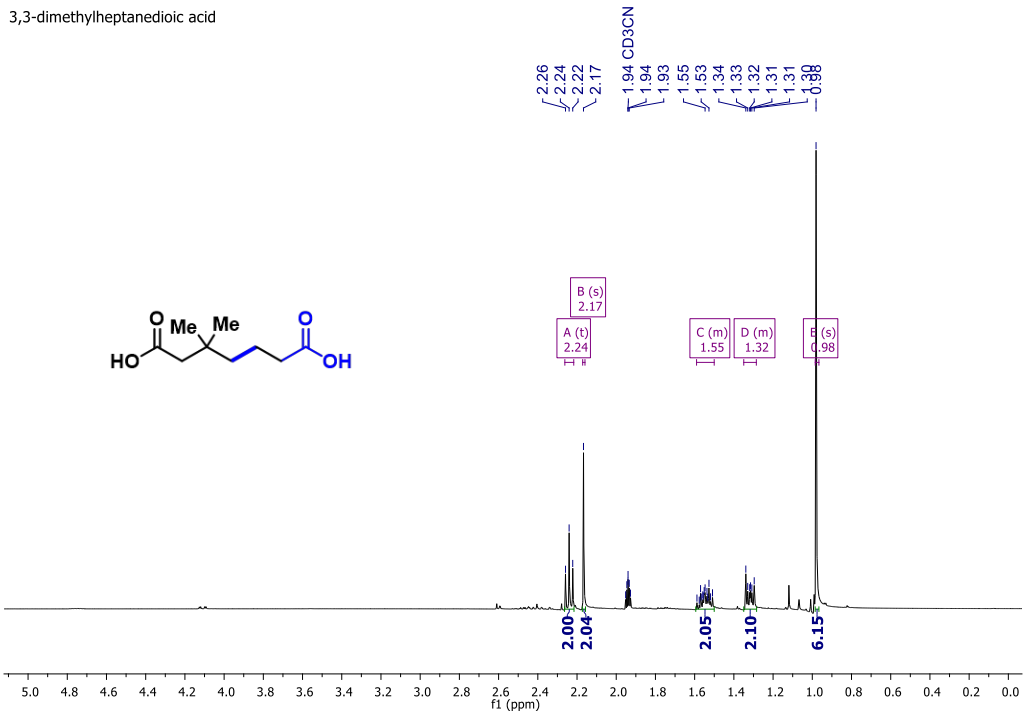
(E)-5,5-dimethylhept-2-enedioic acid



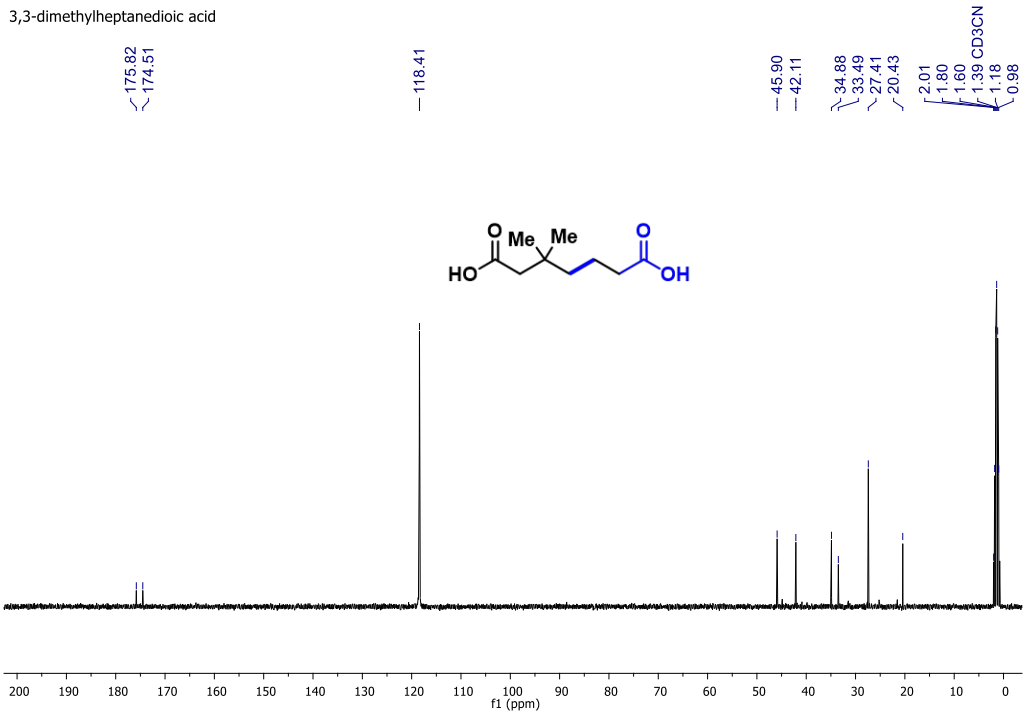
(E)-5,5-dimethylhept-2-enedioic acid



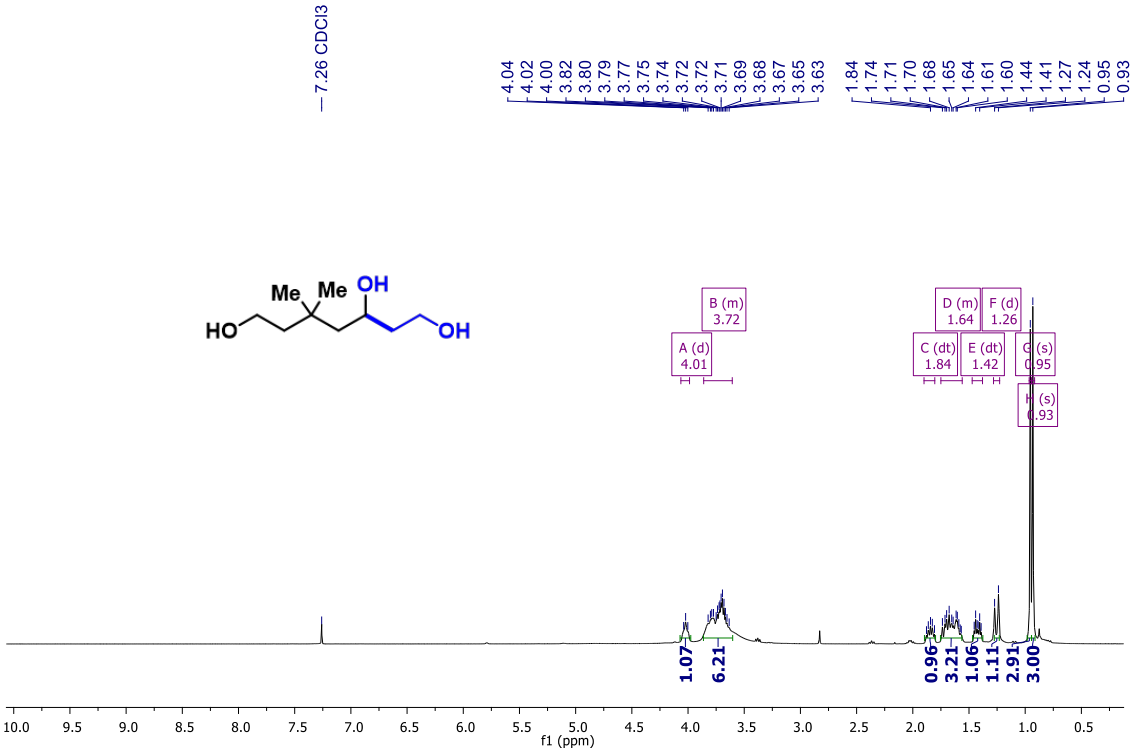
3,3-dimethylheptanedioic acid



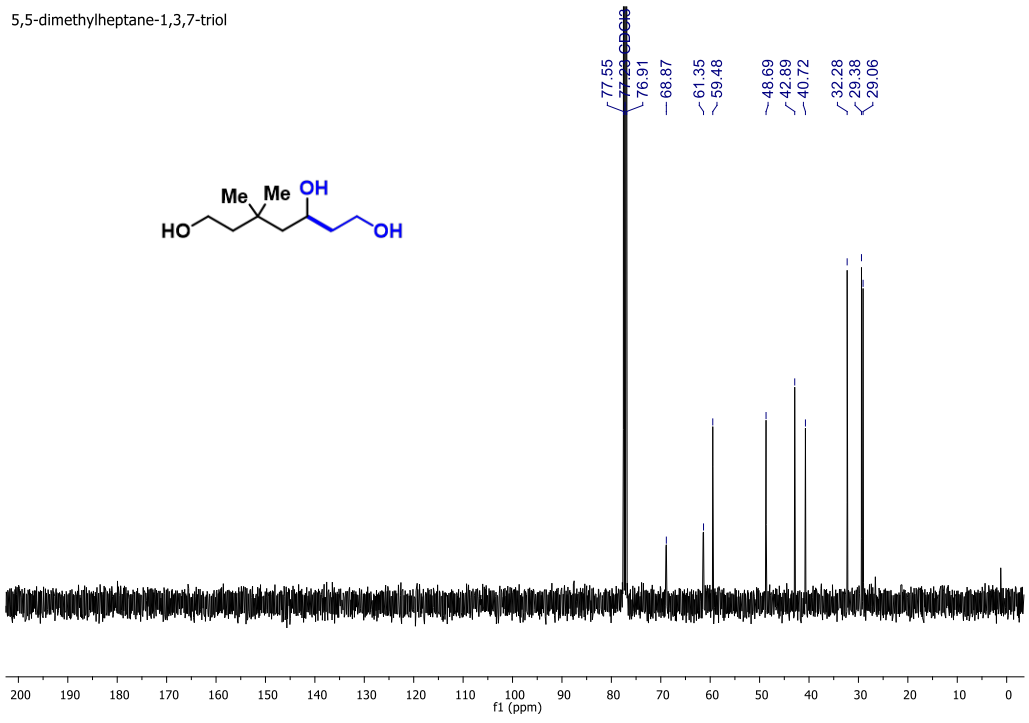
3,3-dimethylheptanedioic acid



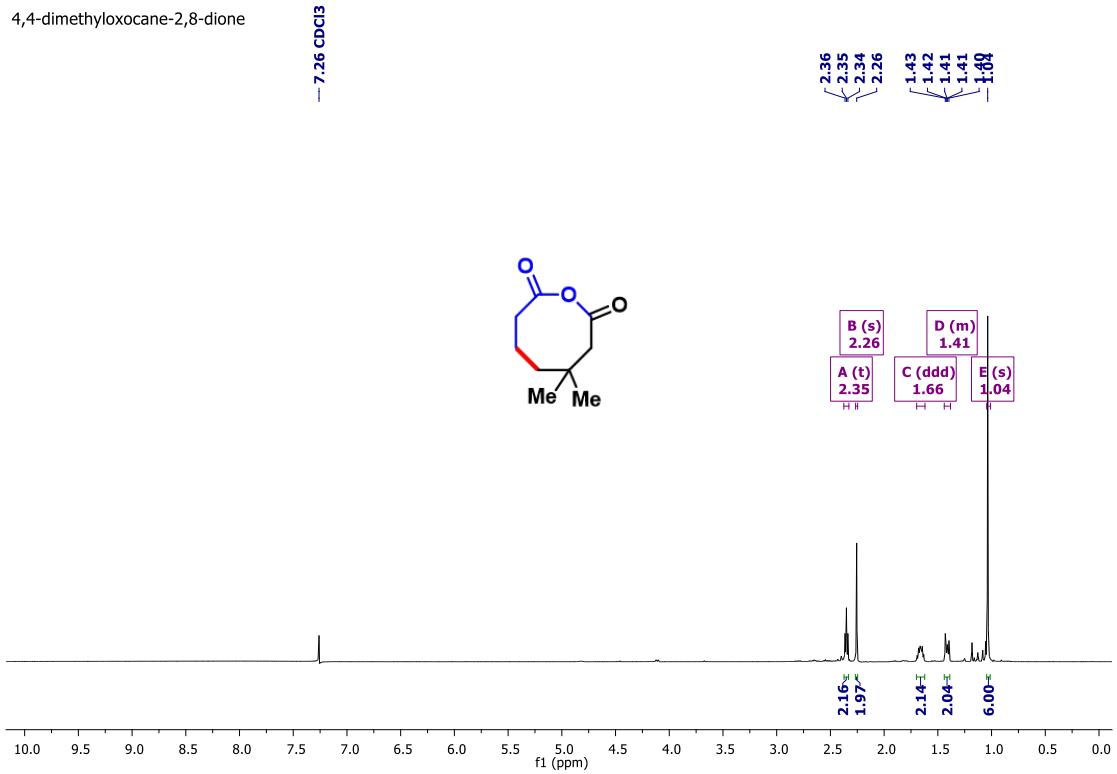
5,5-dimethylheptane-1,3,7-triol



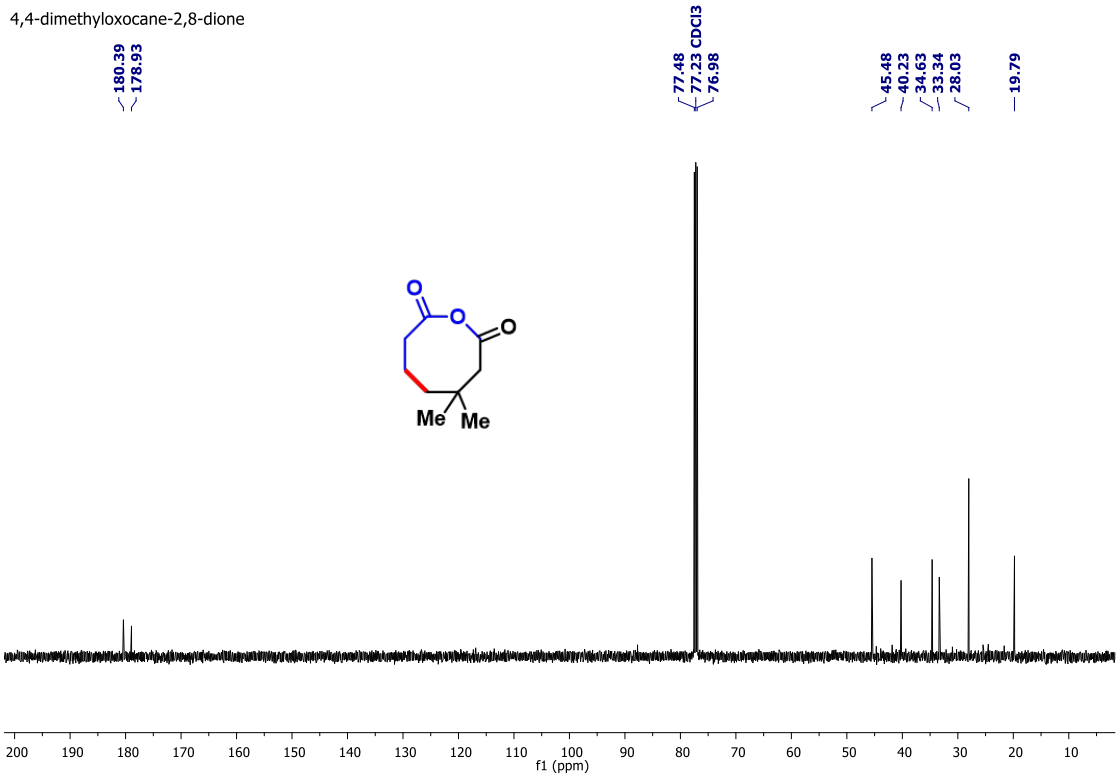
5,5-dimethylheptane-1,3,7-triol



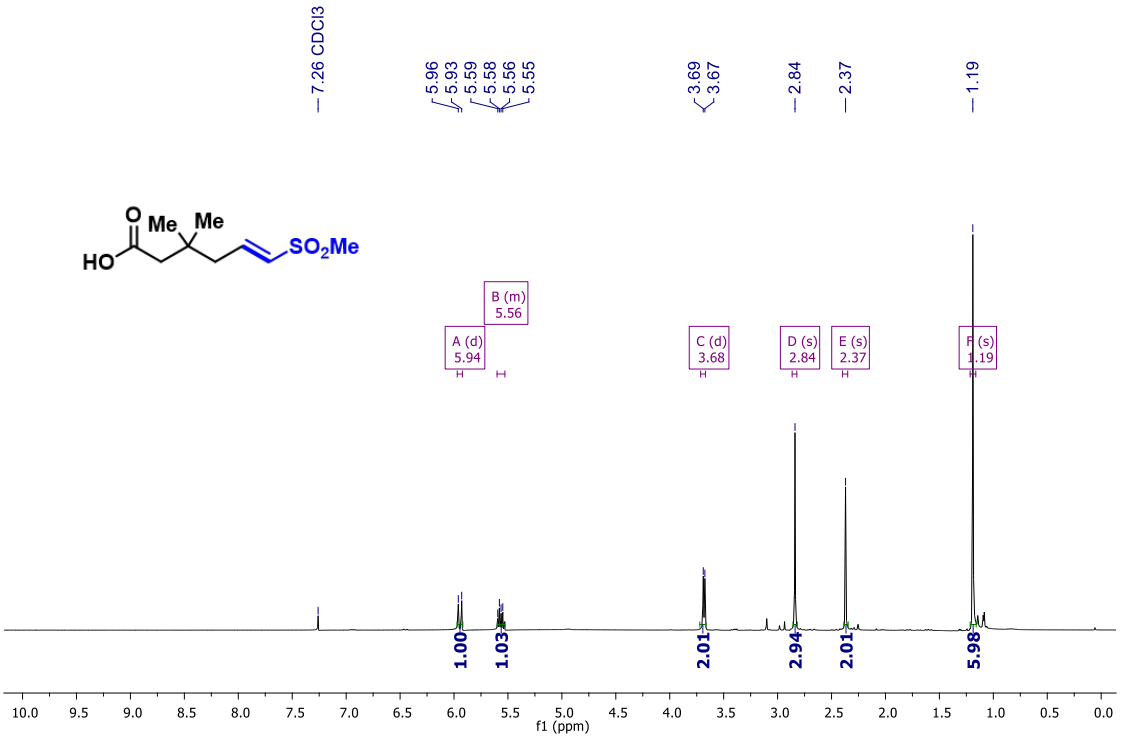
4,4-dimethyloxocane-2,8-dione



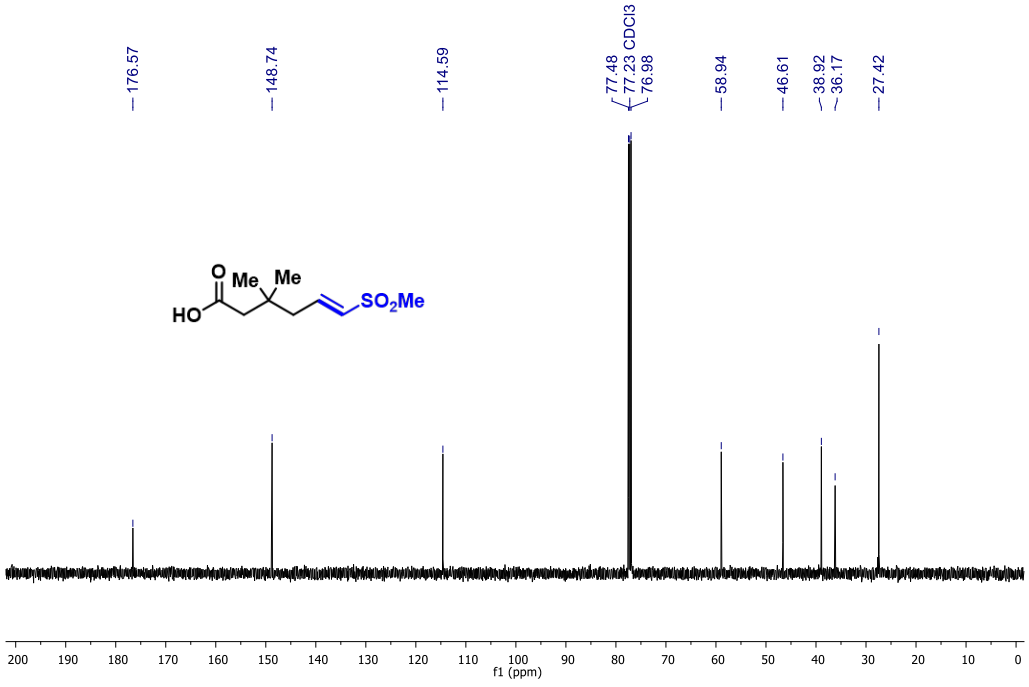
4,4-dimethyloxocane-2,8-dione



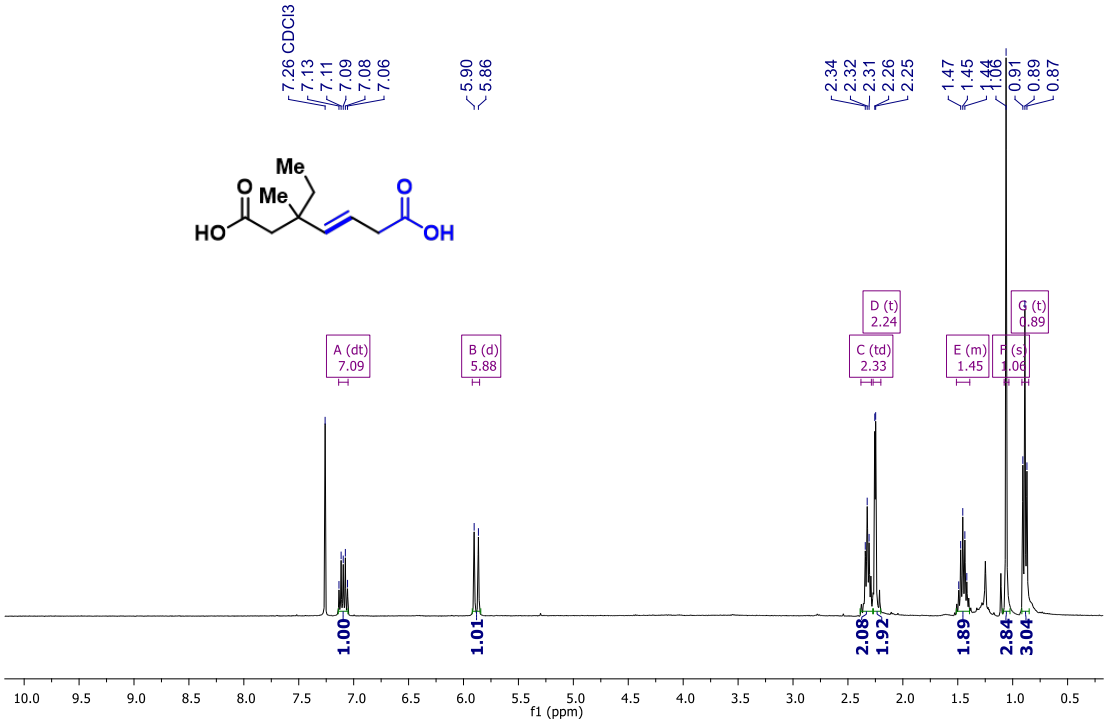
(E)-3,3-dimethyl-6-(methylsulfonyl)hex-5-enoic acid



(E)-5-ethyl-5-methylhept-3-enedioic acid



(E)-5-ethyl-5-methylhept-3-enedioic acid



(E)-5-ethyl-5-methylhept-3-enedioic acid