Supplementary Information

Geminal dihalogen isosteric replacement in hydrated AI-2 affords analogs that potently modulate quorum sensing

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Table of contents

1. Supplemental figures, tables and schemes

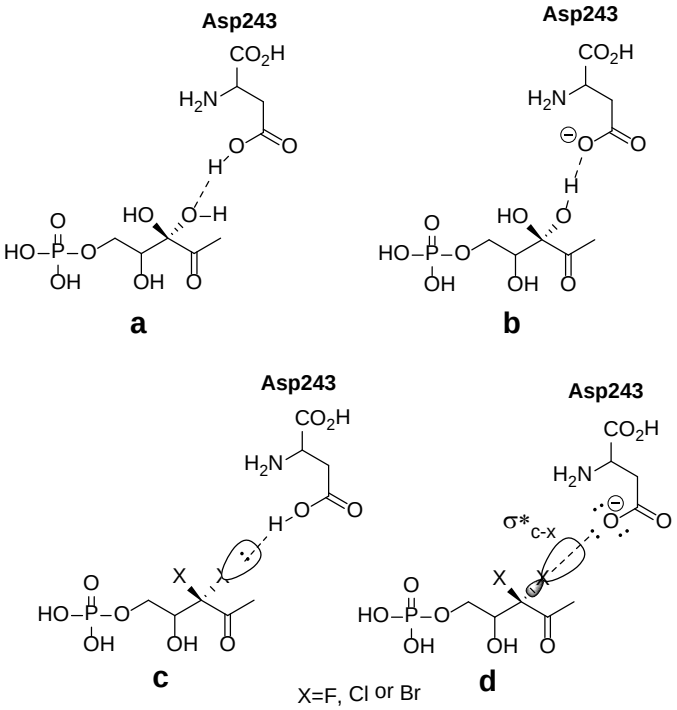


Figure S1. Postulated binding mode of AI-2 and dihalogenated AI-2 with Asp-243. **a)** carboxylic acid as hydrogen donor to form hydrogen bond with one of the hydroxyl groups on P-AI-2. **b)** one of the hydroxyl groups on P-AI-2 as hydrogen donor to form hydrogen bond with carboxylate. **c)** Halogens partaking in hydrogen bonding and **d)** halogen bonding.

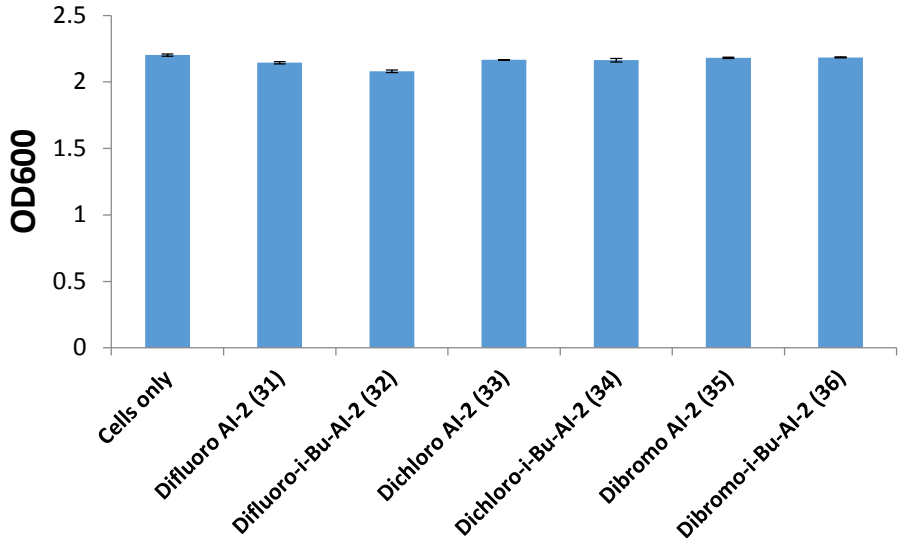


Figure S2. OD_{600} value of *E. coli* LW7 (*luxS*$^-$) after 24 hrs growth in the presence of AI-2 analogs (100 μM).

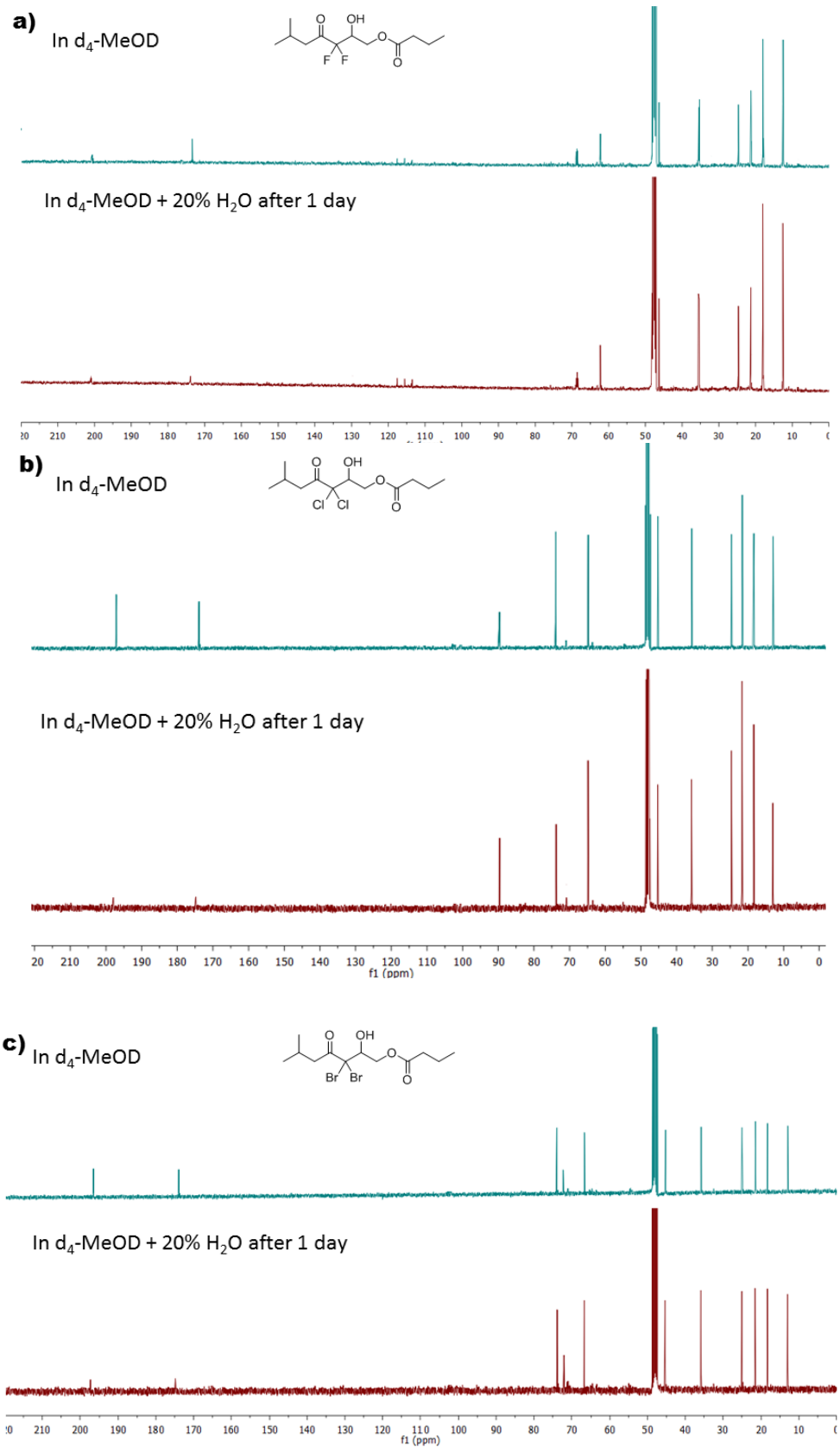

a)
In d4-MeOD
In d4-MeOD + 20% H2O after 1 day
b)
In d4-MeOD
In d4-MeOD + 20% H2O after 1 day
f1 (ppm)
c)
In d4-MeOD
In d4-MeOD + 20% H2O after 1 day
f1 (ppm)

Figure S3. ^{13}C NMR of dihalogen isobutyl AI-2 analogs (**32, 34** and **36**) in d_4-MeOD and d_4-MeOD + 20% H_2O after 1 day. **a)** Difluoro-i-Bu-AI-2, **32**; **b)** Dichloro-i-Bu-AI-2, **32**; **a)** Dibromo-i-Bu-AI-2, **32**. In the presence of water, the keto group in the geminal dihalogen analogs is still present.

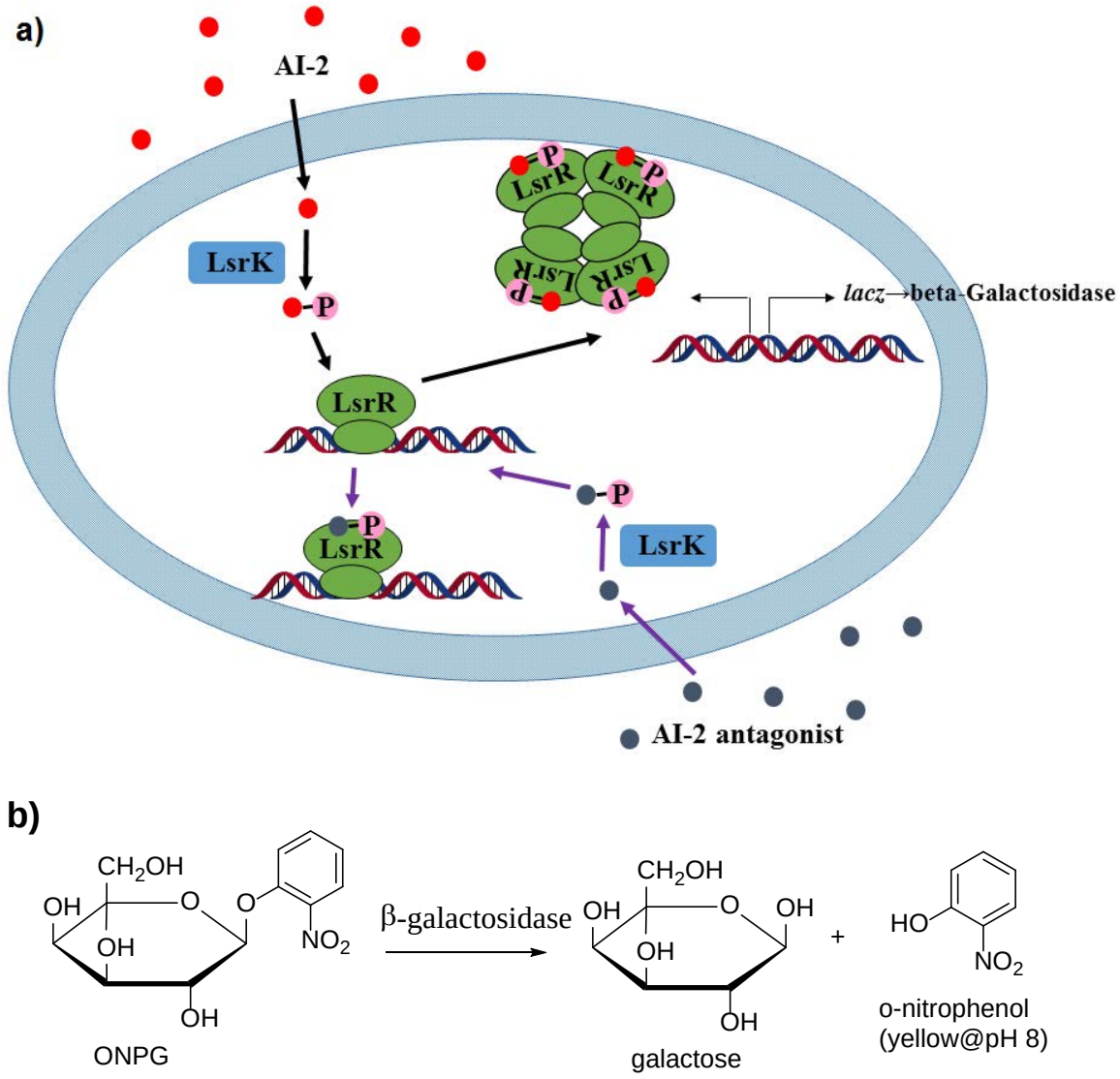


Figure S4. Mechanism of *β*-galactosidase assay. **a**) LsrR is a transcriptional repressor, which binds to DNA and inhibits transcription. Phospho-AI-2 or AI-2-based agonists binds to LsrR to cause de-repression of LsrR (i.e. LsrR/AI-2 complex no longer binds near the promoter region), resulting in the transcription of *lacz*, gene (i.e. concentration of mRNA for *β*-galactosidase increases, leading to an increase in *β*-galactosidase). On the other hand, AI-2-based antagonists bind to LsrR to keep the transcriptional repressor

bound to the DNA to prevent *lacz* expression. **b)** *β*-galactosidase is a hydrolase enzyme. In this assay, ONPG is added to bacterial culture. Once QS is turned on and *β*-galactosidase is produced, ONPG will be hydrolyzed to galactose and o-nitrophenol, which is yellow colored at basic condition. QS can be quantified based on the production of o-nitrophenol monitored by UV-Vis.

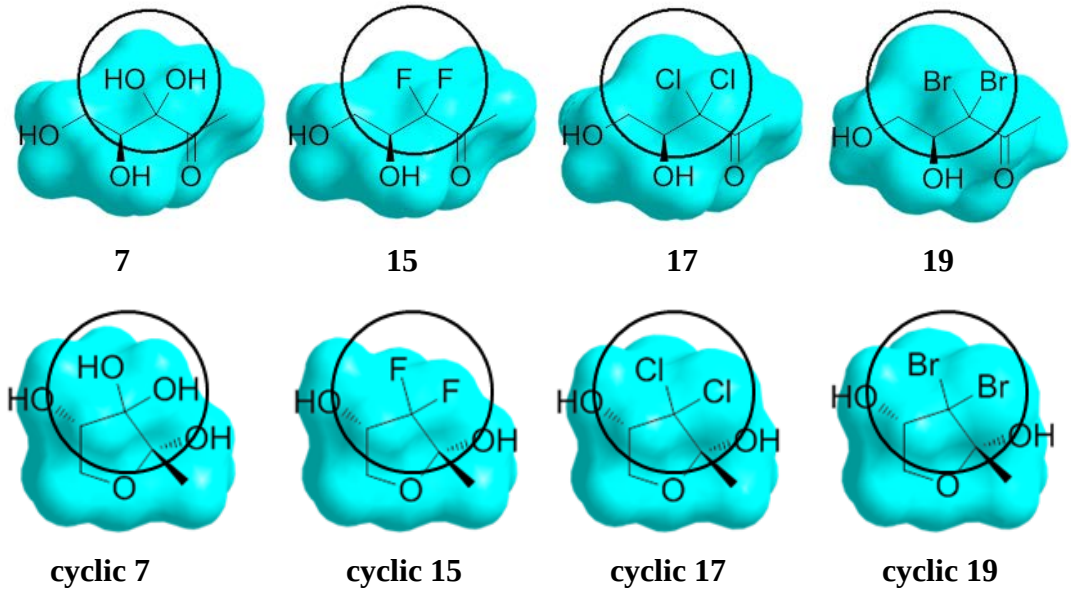


Figure S5. Linear and cyclized forms of geminal dihalogenated analogs of AI-2. The difluoro analog is smaller than the natural analog **7** whereas the dichloro and dibromo analogs are bigger than **7**.

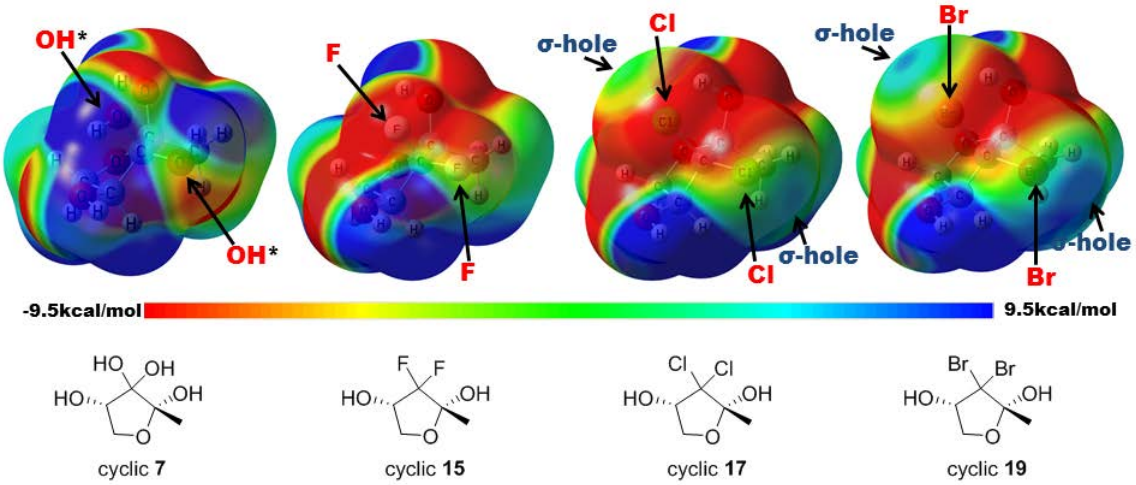


Figure S6. Molecular surface electrostatic potential of AI-2 and analogs in simplified models (cyclic forms). Color ranges from -9.5 kcal/mol (red) to 9.5 kcal/mol (blue). Important atoms and σ-hole were labeled.

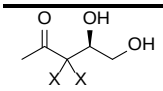
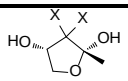
	X	Compd.	Mol. weight	Mol. volume/Å^3	C-X bond lenghth/Å^2	Molecular dipole moment/D
	-OH	**7**	150.13	120.33	1.40	4.24
	-F	**15**	154.11	115.08	1.37	3.20
	-Cl	**17**	187.02	137.98	1.81	3.02
	-Br	**19**	275.92	149.46	2.00	2.97
	-OH	**Cyclic 7**	150.13	118.14	1.41	4.23
	-F	**Cyclic 15**	154.11	110.84	1.38	3.02
	-Cl	**Cyclic 17**	187.02	132.77	1.80	3.30
	-Br	**Cyclic 19**	275.92	144.87	1.96	3.12

Table S1. Comparison of properties of AI-2 and analogs.

2. Bioassay procedures

***β*-galactosidase assay:** *E. coli* ZK126 (Wild-type strain derivative, W3110 *ΔlacU160-tna2*) and LW7 (ZK126 *ΔluxS*) were grown in the presence of ampicillin overnight. The overnight culture was diluted 40 times and grew at 37 °C until OD_{600} reached 0.8. The cells were spun down and the cell pellet was resuspend in PBS. To 500 μL aliquots of the resuspended cells was added the AI-2 analogs and the bacteria were grown at 37 °C for 2 hours. The cells were then spun down and the cell pellet was resuspend in Z-buffer (500 μL). 250 μL of the cell suspension was used for the OD_{600} measurement. The rest of cell suspension (250 μl) was mixed with 25 μL of CH_3Cl and 12.5 μL of 0.1% SDS and incubated at room temperature for 5 min. After adding 50 μL of ONPG (4 mg/ml in Z-buffer), samples were incubated at 28 °C for 40 min and 125 μL of 1 M sodium carbonate solution was added to stop the reaction. The sample was centrifuged at 4 °C for 5 min and OD_{420} and OD_{550} were measured using Molecular Devices SpectraMax M5^e microplate reader.

β-galactosidase units was calculated using the following equation:

β-galactosidase units=1000 x (OD_{420} – (1.75 x OD_{550}) / (0.25 (ml) x 40 (min) x OD_{600}))

Flow cytometry assay: *E.coli* W3110 pCT6[1] + pET200-EGFP-Lys[2] was cultured from colony in Luria-Bertani medium supplemented with ampicillin and kanamycin. At OD_{600} 0.1, cultures were supplemented with 20 μM of the AI-2 analog (or an equivalent volume of DMSO for negative controls) and incubated in triplicate for 6 h at 37 °C with shaking

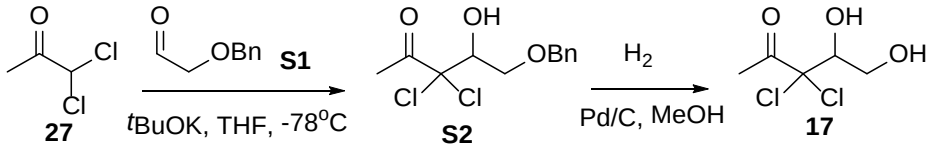
(250 rpm). The *E.coli* green fluorescence response was determined using fluorescence microscopy (Olympus BX60) and flow cytometric analysis. Samples were analyzed by flow cytometery (FACS CantoII, BD 394 Biosciences), using a 488 nm laser and 530/30 filter set with 50000 gated events analyzed per sample.

3. Chemical synthesis procedures and characterization of new compounds

All reagents were obtained commercially unless otherwise noted. Reactions were performed using oven-dried glassware under an atmosphere of argon. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Dry tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled over sodium prior to use and dry dichloromethane (DCM) was distilled over CaH_2 prior to use. Thin-layer chromatography (TLC) was performed on Merck Kieselgel 60 F254 plates. Visualization of the developed chromatogram was accomplished by UV light or by staining with $KMnO_4$ solution. Chromatographic purification of products was accomplished using flash column chromatography on silica gel (230 X 400 mesh) or GRACE Reveleris® X2 flash Chromatography system with Reveleris® flash cartridges (40 µM silica). Compounds purified by chromatography on silica gel were typically applied to the absorbent bed using the indicated solvents conditions with a minimum amount of added dichloromethane as needed for solubility. Solvents were removed from the reaction mixture or combined organic extracts by concentration under reduced pressure using an evaporator with bath at 30–40 ^{o}C. Elevated temperatures were obtained using thermostat-controlled silicone oil baths. Low temperatures were obtained by ice bath or by mixing dry-ice with organic solvents. NMR spectra were measured on Bruker AV-400, Bruker DRX-400 (^{1}H at 400 MHz, ^{13}C at 100MHz), Bruker DRX-500 (^{1}H at 500 MHz, ^{13}C at 125MHz) or Bruker AVIII-600 (^{1}H at 600 MHz, ^{13}C at 150MHz). Data for ^{1}H -NMR spectra are reported as follows: chemical shift (ppm, relative to residual solvent peaks or indicated external standards; s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, td = triplet of doublets, m = multiplet), coupling constant (Hz), and integration. Data for ^{13}C -NMR are reported in terms of chemical shift (ppm) relative to residual solvent peak. Mass spectra (MS) and high resolution mass spectra (HRMS) were

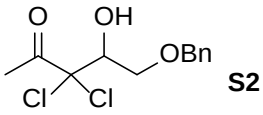
recorded by JEOL AccuTOF-CS (ESI positive, needle voltage 1800~2400 eV). Infrared spectra (IR) were recorded by a ThermoNicolet IR200 Spectrometer.

*Initial attempt to make dichloro AI-2 **17**:*



Scheme S1. Initial attempt to make dichloro AI-2 **17**.

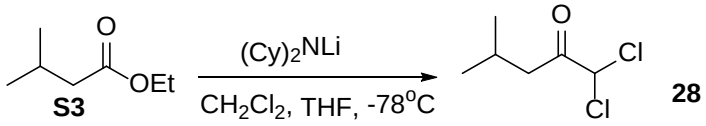
To a stirred suspension of *t*BuOK (6 mg, 0.1 equiv) in anhydrous THF was added 1,1-dichloro-2-propanone **27** (50 µL, 0.5 mmol), followed by benzyloxyacetaldehyde **S1** (70 µL, 1 equiv) at -78°C under argon. The reaction was allowed to warm up to room temperature gradually and stirred overnight. Then the reaction was quenched by saturated NH_4Cl (aq) carefully at 0 °C. The organic layer was separated and the aqueous layer was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$. The product was purified by silica column chromatography (EtOAc: Hexanes = 1: 8, *v/v*) and **S1** was obtained as 93 mg clear oil (67 % yield). To make dichloro AI-2 **17**, **S2** (39 mg, 0.14 mmol) was dissolved in 2 ml methanol, which was suspended with Pd/C (5% on carbon, 29 mg, 10 mol%). The reaction flask was vacuumed and then charged by H_2 balloon. The reaction was stirred at room temperature overnight. Then Pd/C was filtered out and the filtrate was evaporated at reduced pressure. However, the product **17** was volatile and left the flask empty.

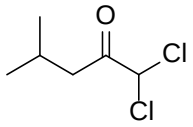


5-(benzyloxy)-3,3-dichloro-4-hydroxypentan-2-one (S2):

S1 was obtained as 93 mg clear oil (67 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 7.42-7.30 (5H, m), 4.65-4.58 (2H, m), 4.58-4.51 (1H, m), 3.98-3.90 (1H, m), 3.81-3.73 (1H, m), 3.23 (1H, d, J = 5.2 Hz), 2.52 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 196.4, 137.8, 128.9, 128.4, 128.2, 89.0, 75.4, 74.0, 70.4, 24.8. HRMS (ESI^+) m/z calcd. for $C_{12}H_{15}Cl_2O_3$ $[M+H]^+$ 277.0398, found 277.0422.

Synthesis of the starting materials for dihalogen AI-2 analogs:

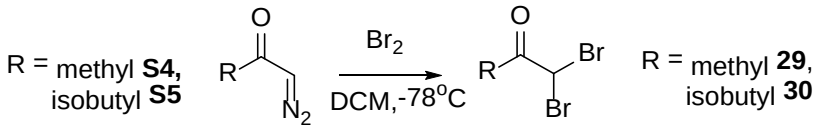




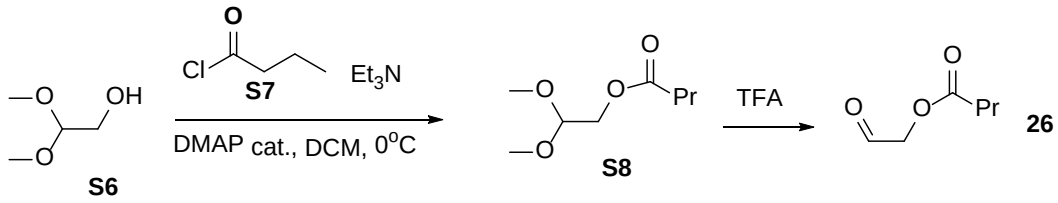
28

1,1-dichloro-4-methylpentan-2-one (28):

The synthesis was similar to the reference.[3] Generally, to a stirred solution of dichloromethane (10 mmol, 0.64 ml) and ethyl isovalerate **S3** (5 mmol, 0.75 ml) in anhydrous THF (10 ml), was added a solution of lithium dicyclohexylamide in 10 ml anhydrous THF over 10 min at -78 °C under argon. The resulting mixture was stirred for another 20 min at -78 °C and then carefully quenched with 6 M HCl (aq). The reaction was allowed to warm up slowly and then the white precipitate was filtered off. The filtrate was extracted with Et_2O (5ml x 3) and organic layer was dried with $MgSO_4$. The solvent was carefully removed *in vacuo* to avoid the loss of volatile product **28**. The product was obtained as 0.75 g slightly yellow liquid (89% yield) and used for the next step without purification.



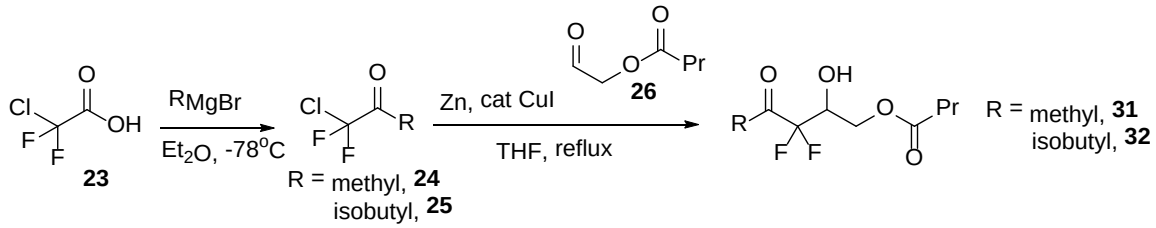
The starting diazocarbonyls **S4** and **S5** were obtained using the same method reported by our group.[4] To a stirred solution of the diazocarbonyl (3 mmol) in anhydrous DCM (10 ml) was added a solution Br_2 (1.2 equiv, 0.18 ml) in in anhydrous DCM (5 ml) dropwise at -78 °C. The resulting solution was allowed to warm up to room temperature in 1 hr and then the reaction was quenched by saturated $NaHSO_3$ (aq). The organic layer was separated and dried with $MgSO_4$. The solvent was carefully removed *in vacuo* to avoid the loss of volatile product **29**/**30**. The yield was quantitatively and if necessary, the product could be purified by a short column with 100% hexanes.



The synthesis was similar to the reference.[5] Generally, To a solution of 2,2-dimethoxyethanol **S6** (5 mmol, 0.51 ml), DMAP (catalytic) and dry Et_3N (1.1 equiv, 0.71 ml) in anhydrous DCM, was added butyryl chloride **S7** (1 equiv, 0.50 ml) dropwise at 0 ^oC under argon. The reaction was allowed to warm up to room temperature and stirred overnight. The resulting solution was washed with saturated $NaHCO_3$ (aq) and brine, then dried with $MgSO_4$. The solvent was removed at reduced pressure and the product **S8** was obtained as clear oil at quantitative yield without further purification.

A well-stirred solution of **S8** (5 mmol) in DCM (25 ml) was treated with TFA (9.75 equiv, 3.8 ml) and water (10 equiv, 0.9 ml) at room temperature. After stirring for 5 hr, the solution was evaporated and the crude product was purified by flash silica chromatography (EtOAc: Hexanes = 1: 2, *v/v*). The product **26** was obtained as clear thick oil (560 mg, 86% yield).

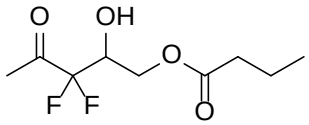
Synthesis of difluoro AI-2 analogs:



The synthesis was similar to the reference.[6] Generally, a solution of corresponding Grignard reagent (2M in Et_2O, 30 mmol) was slowly added a solution of chlorodifluoroacetic acid **23** (10 mmol, 0.84 ml) in anhydrous diethyl ether at -20 ^oC under argon. The resulting mixture was kept stirring for another 12 hr. Then the reaction mixture was hydrolyzed with 6M HCl (aq) below 0 ^oC and stirred for 1 hr at room temperature. The resuting mixture was extracted with diethyl ether (10 ml x 3) and the combined organic layer was washed with saturated $NaHCO_3$ (aq) and brine, then dried

with $MgSO_4$ and finally concentrated in mild vacuum to avoid the loss of volatile product **24/25**. Products were obtained in high yield without further purification.

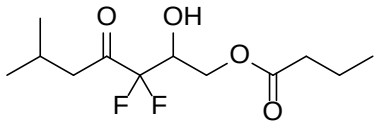
Acid-activated Zn powder (3 equiv, 149 mg) and CuI (0.1 equiv, 8 mg) were suspended in anhydrous THF and stirred for 0.5 hr at room temperature under argon. To the resulting mixture was added a solution of corresponding chlorodifluoromethyl ketone **24/25** (100 mg, 0.76 mmol) and **26** in anhydrous THF. The mixture was refluxed for 4 hr and then cooled down to room temperature. The reaction mixture was then filtered with Celite and the filtrate was concentrated under vacuum. The products of difluoro AI-2 analogs **31/32** were purified by flash silica chromatography (EtOAc: Hexanes = 1: 6, *v/v*).



31

3,3-difluoro-2-hydroxy-4-oxopentyl butyrate (31):

31 was obtained as 60 mg clear oil (35 % yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ ppm = 4.45-4.26 (3H, m), 3.00-2.92 (1H, m), 2.45-2.40 (3H, m), 2.37 (2H, t, *J* = 7.4 Hz), 1.70 (2H, dd, *J* = 14.8, 7.4 Hz), 0.99 (3H, t, *J* = 7.4 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ ppm = 198.8 (t, *J* = 31.2 Hz), 174.0, 114.4 (t, *J* = 253.8 Hz), 69.9 (m), 62.7, 35.8, 25.2, 18.2, 13.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ ppm = -113.54 (1F, dd, *J* = 279.2, 6.4 Hz), -123.21 (1F, dd, *J* = 280.7, 15.6 Hz). HRMS (ESI^+) m/z calcd. for $C_9H_{15}F_2O_4$ $[M+H]^+$ 225.0938, found 225.0923.

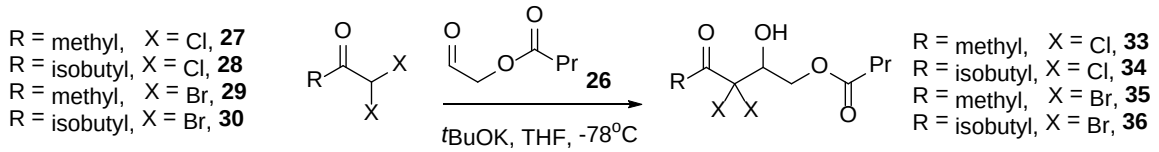


32

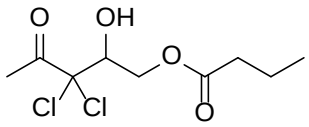
3,3-difluoro-2-hydroxy-6-methyl-4-oxoheptyl butyrate (32):

32 was obtained as 93 mg clear oil (67 % yield). ^{1}H NMR (400 MHz, CD_2Cl_2) δ ppm = 4.41-4.26 (3H, m), 3.14-3.02 (1H, m), 2.64 (2H, d, *J* = 6.7 Hz), 2.36 (2H, t, *J* = 7.4 Hz), 2.27-2.16 (1H, m), 1.74-1.60 (2H, m), 1.02-0.90 (9H, m). ^{13}C NMR (125 MHz, CD_2Cl_2) δ ppm = 200.6 (t, *J* = 27.5 Hz), 173.8, 114.7 (t, *J* = 255.0 Hz), 69.8 (t, *J* = 27.5 Hz), 62.6, 46.2, 35.7, 23.4, 22.0, 18.2, 13.2. ^{19}F NMR (376 MHz, CD_2Cl_2) δ ppm = -114.30 (1F, dd, *J* = 276.3, 6.3 Hz), -124.34 (1F, dd, *J* = 275.5, 17.7 Hz). HRMS (ESI^+) m/z calcd. for $C_{12}H_{24}F_2NO_4$ $[M+NH_4]^+$ 284.1673, found 284.1690.

Synthesis of dichloro and dibromo AI-2 analogs:



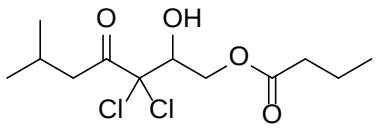
Generally, to a stirred suspension of *t*BuOK (0.1 equiv) in anhydrous THF was added a solution of corresponding dihalogen ketone (1 equiv) and **26** (1 equiv) in anhydrous THF at -78^{o}C under argon. The reaction was allowed to warm up to room temperature gradually and stirred overnight. Then the reaction was quenched by saturated NH_4Cl (aq) carefully at 0 ^{o}C. The organic layer was separated and the aqueous layer was extracted with EtOAc three times. The combined organic phase was dried over $MgSO_4$. The product was purified by silica column chromatography (EtOAc: Hexanes = 1: 6, *v/v*)



33

3,3-dichloro-2-hydroxy-4-oxopentyl butyrate (33):

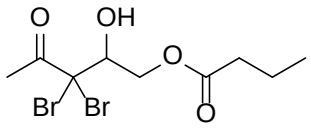
33 was obtained as 51 mg clear oil (64% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 4.63-4.52 (2H, m), 4.47-4.35 (1H, m), 3.23 (1H, s, br), 2.57 (3H, s), 2.37 (2H, t, J = 7.4 Hz), 1.70 (2H, dd, J = 14.8, 7.4 Hz), 0.98 (3H, t, J = 7.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 196.7, 174.2, 87.4, 74.7, 64.7, 36.4, 24.2, 18.7, 14.0. HRMS (ESI^{+}) m/z calcd. for $C_9H_{15}Cl_2O_4$ $[M+H]^{+}$ 257.0347, found 257.0340.



34

3,3-dichloro-2-hydroxy-6-methyl-4-oxoheptyl butyrate (34):

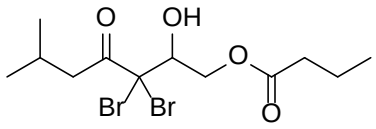
34 was obtained as 74 mg clear oil (61% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 4.62-4.51 (2H, m), 4.44-4.34 (1H, m), 3.22 (1H, s, br), 2.81 (2H, dd, J = 6.9, 1.4 Hz), 2.36 (2H, t, J = 7.4 Hz), 2.29-2.18 (1H, m), 1.69 (2H, dd, J = 14.9, 7.4 Hz), 1.03-0.86 (9H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 198.6, 174.2, 87.6, 74.7, 64.8, 45.0, 36.4, 25.0, 22.7, 22.5, 18.7, 14.0. HRMS (ESI^{+}) m/z calcd. for $C_{12}H_{21}Cl_2O_4$ $[M+H]^{+}$ 299.0817, found 299.0821.



35

3,3-dibromo-2-hydroxy-4-oxopentyl butyrate (35):

35 was obtained as 74 mg clear oil (61% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 4.75-4.65 (1H, m), 4.48-4.36 (2H, m), 3.37 (1H, s, br), 2.72 (3H, s), 2.38 (2H, t, J = 7.4 Hz), 1.70 (2H, dd, J = 14.9, 7.4 Hz), 0.98 (3H, t, J = 7.4 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 196.9, 174.2, 75.0, 69.4, 66.5, 36.4, 24.8, 18.8, 14.1. HRMS (ESI^+) m/z calcd. for $C_9H_{15}Br_2O_4$ $[M+H]^+$ 346.9317, found 346.9340.

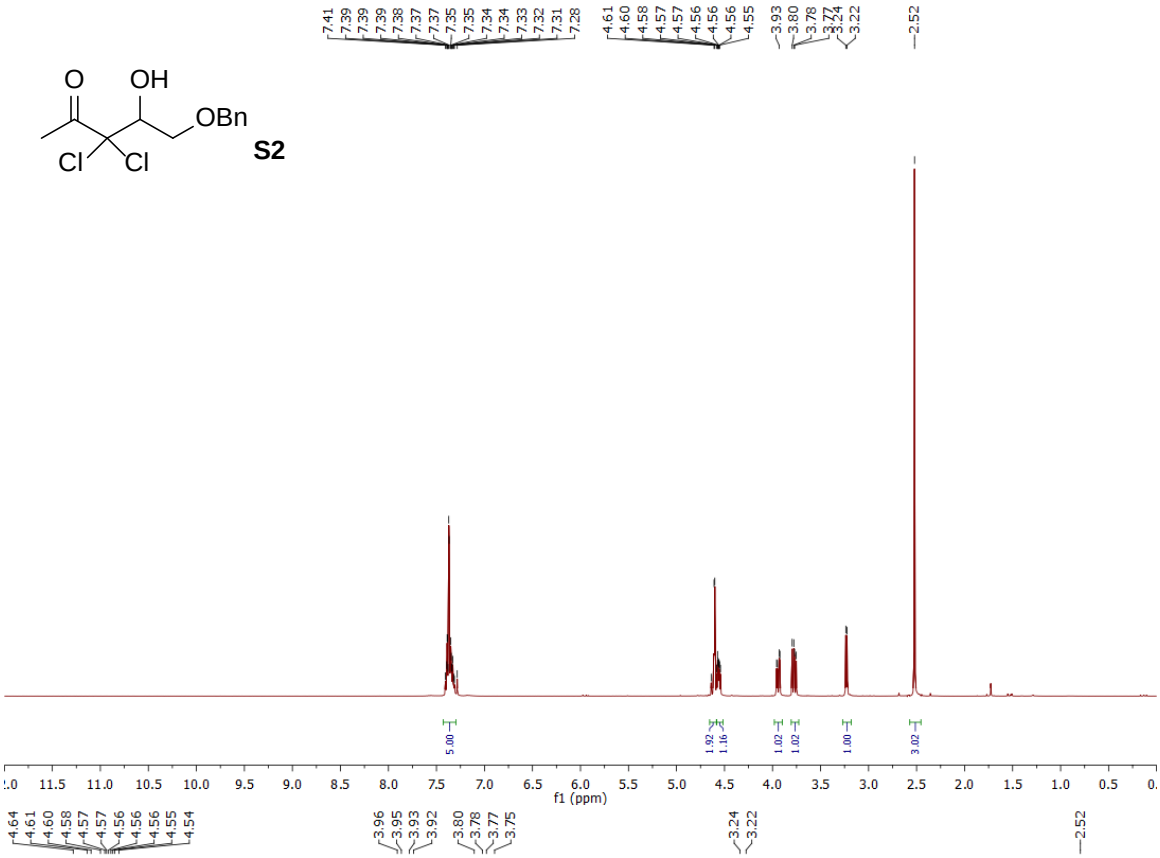


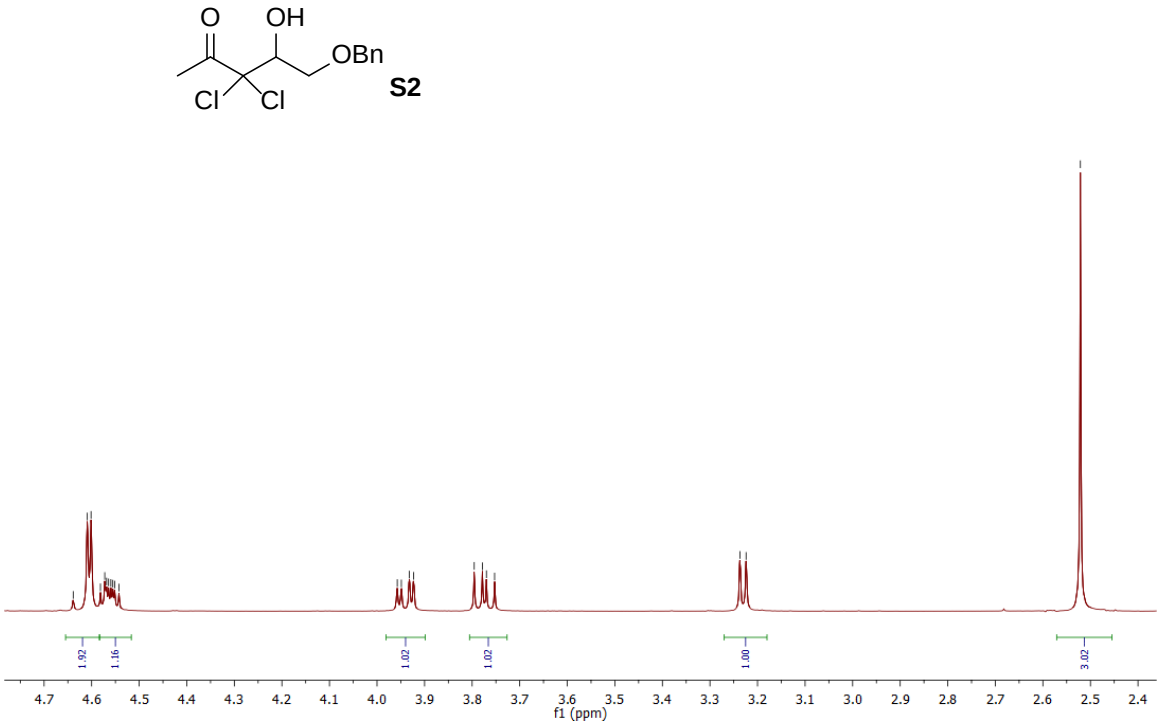
36

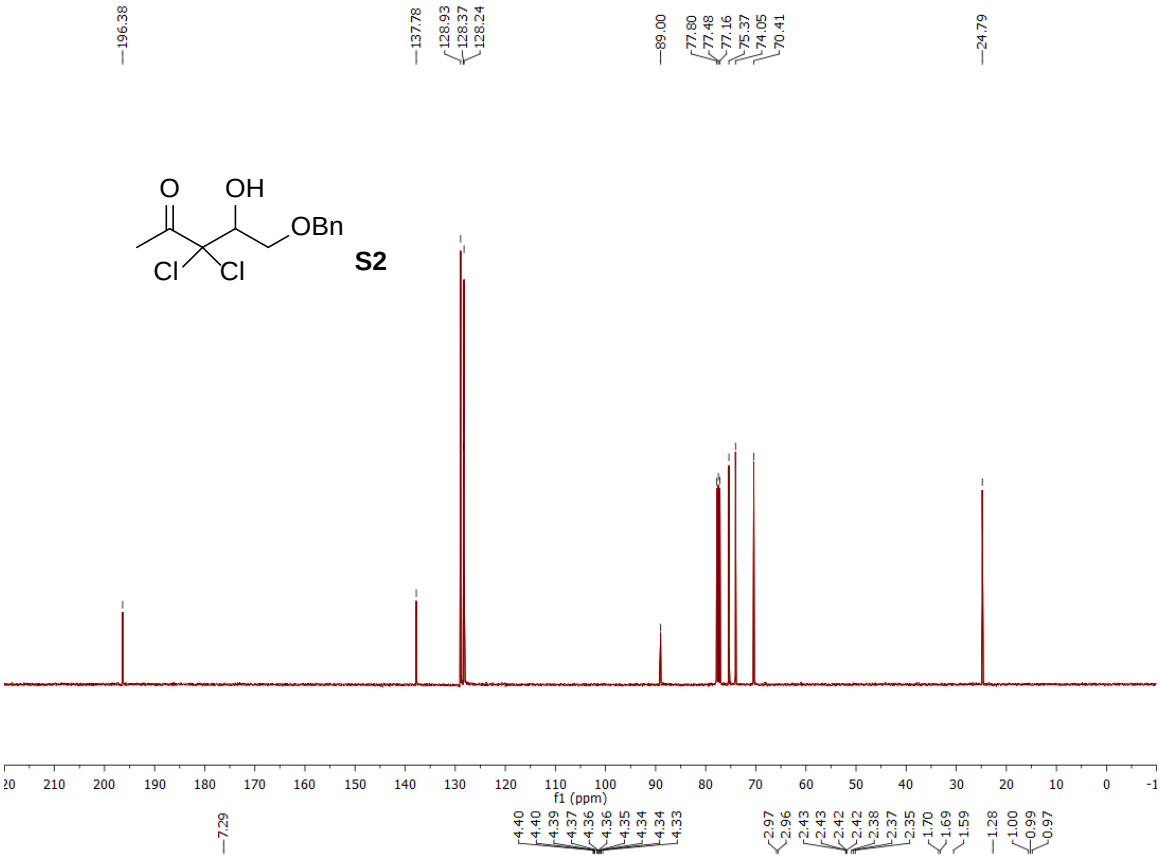
3,3-dibromo-2-hydroxy-6-methyl-4-oxoheptyl butyrate (36):

36 was obtained as 53 mg clear oil (40% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ ppm = 4.73-4.64 (1H, m), 4.50-4.34 (2H, m), 3.38 (1H, s, br), 2.99 (2H, dd, J = 6.9, 2.9 Hz), 2.37 (2H, d, J = 7.4 Hz), 2.32-2.18 (1H, m), 1.70 (2H, dd, J = 14.8, 7.4 Hz), 1.04-0.90 (9H, m). ^{13}C NMR (100 MHz, $CDCl_3$) δ ppm = 198.7, 174.2, 75.0, 70.1, 66.6, 45.5, 36.4, 25.4, 22.7, 22.5, 18.8, 14.1. HRMS (ESI^+) m/z calcd. for $C_{12}H_{21}Br_2O_4$ $[M+H]^+$ 388.9786, found 388.9804.

4. NMR spectra



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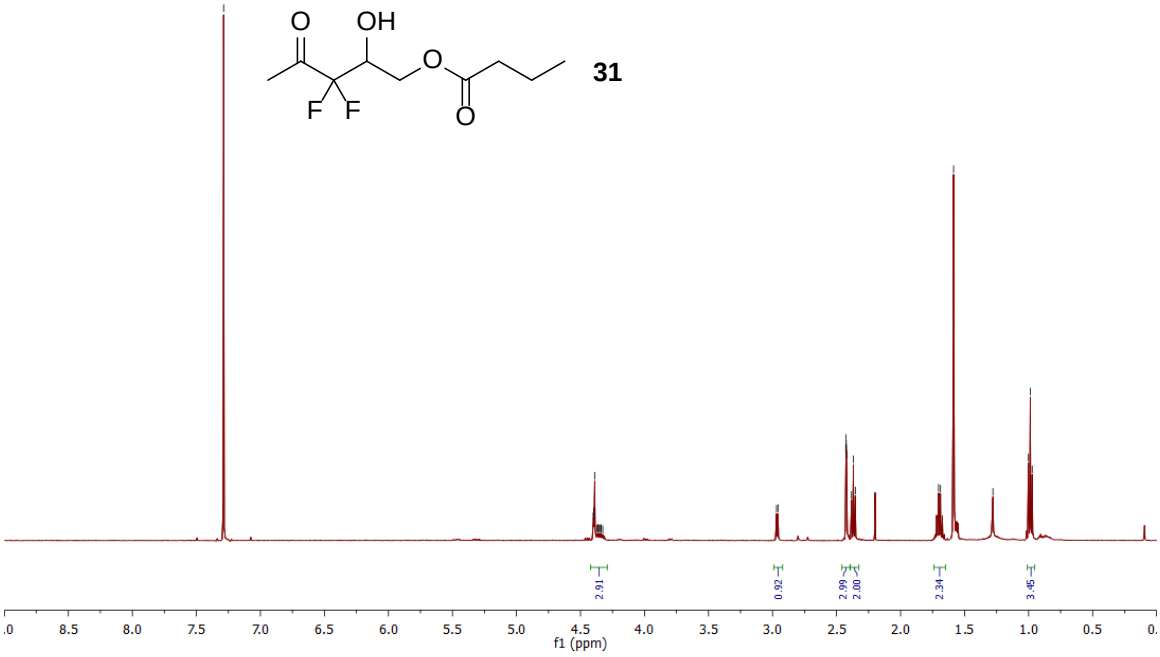
128.93
128.37
128.24
89.00
77.80
77.48
77.16
75.37
74.05
70.41
24.79
O
OH
OBn
Cl
Cl
S2
f1 (ppm)
7.29
4.40
4.40
4.39
4.37
4.36
4.36
4.35
4.34
4.34
4.33
2.97
2.96
2.43
2.43
2.42
2.42
2.38
2.37
2.35
1.70
1.69
1.59
1.28
1.00
0.99
0.97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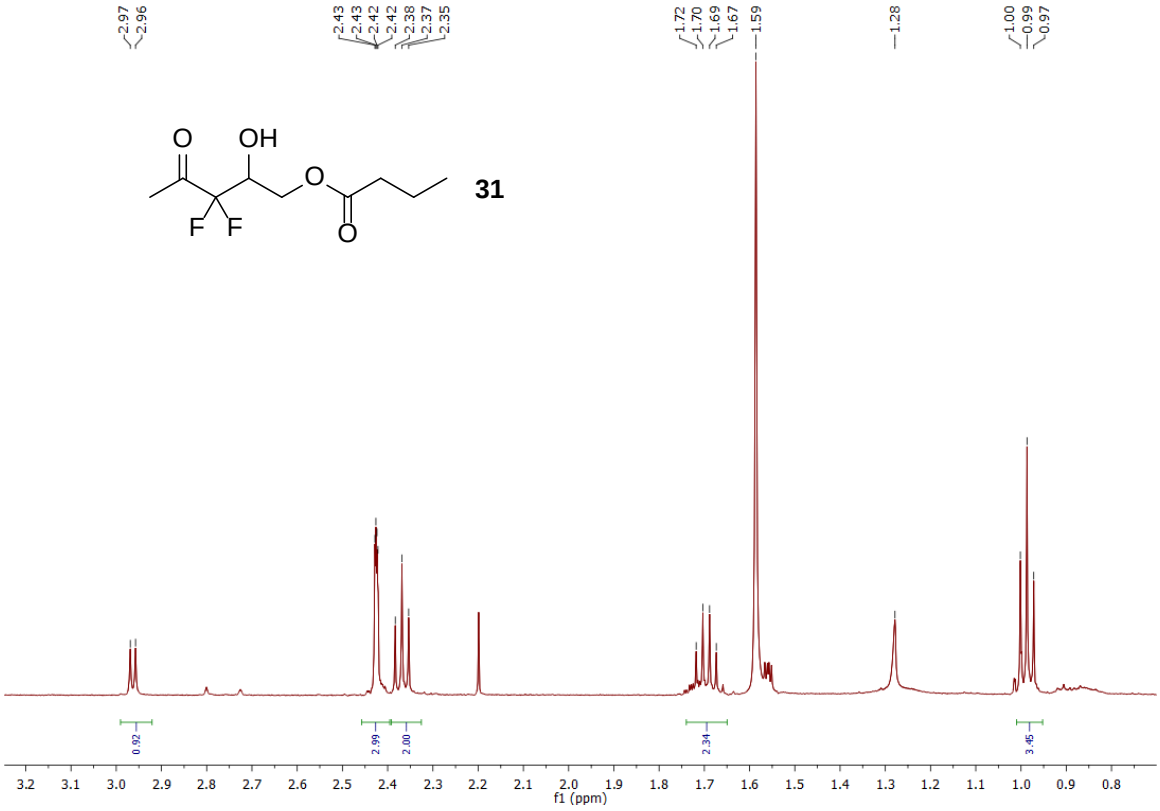
OH
O
F
F
O
31
2.91
0.92
2.99
2.00
2.34
3.45
f1 (ppm)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1.70
1.69
1.67
1.59
1.28
1.00
0.99
0.97
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OH
O
F
F
O
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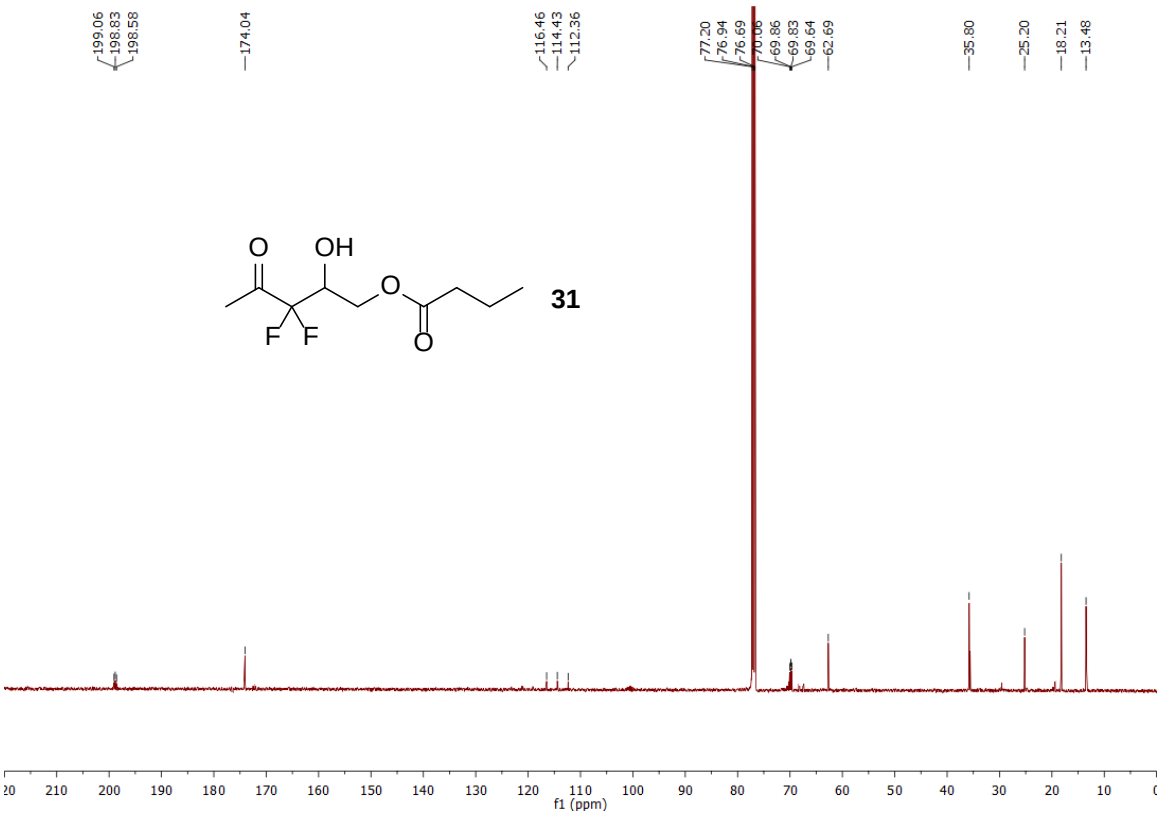
0.92
2.99
2.00
2.34
3.45
f1 (ppm)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76.94
76.69
70.06
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69.83
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35.80
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18.21
13.48
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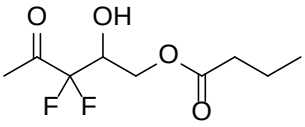
OH
O
F
F
O
31
f1 (ppm)


O
OH
O
F
F
O

31

-113.16
-113.18
-113.90
-113.92
-122.81
-122.85
-123.56
-123.60
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f1 (ppm)
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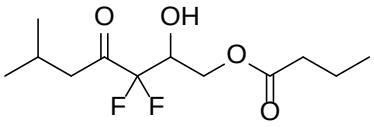
5.36
5.36
4.36
4.35
4.35
4.33
3.09
3.08
2.65
2.64
2.38
2.36
2.34
2.22
2.20
1.72
1.70
1.68
1.67
1.65
0.99
0.98
0.96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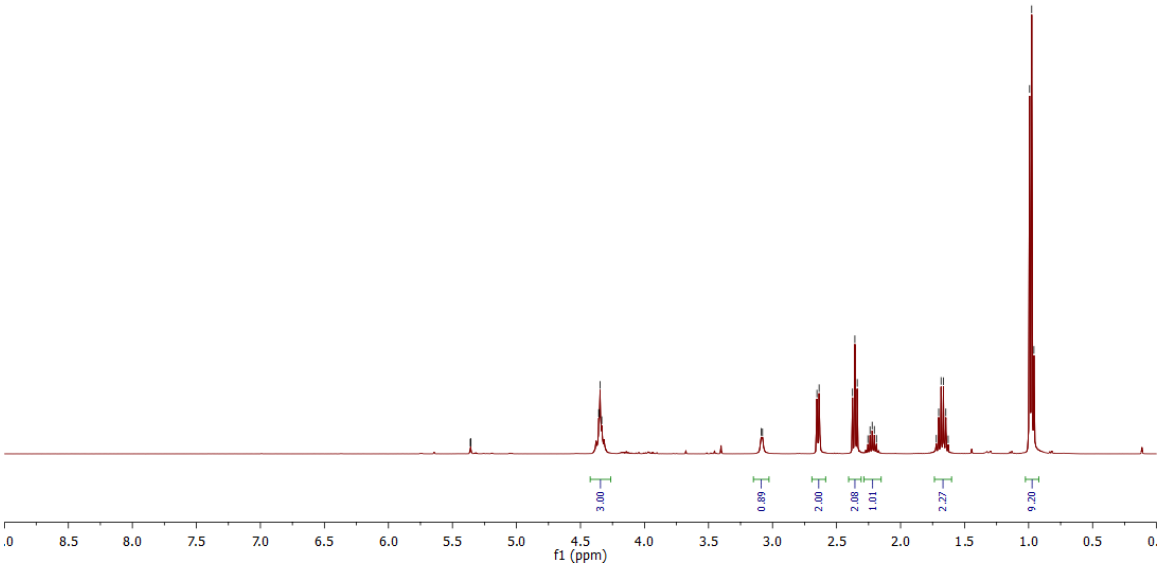
OH
O
F
F
O

32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2.00
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1.01
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9.20
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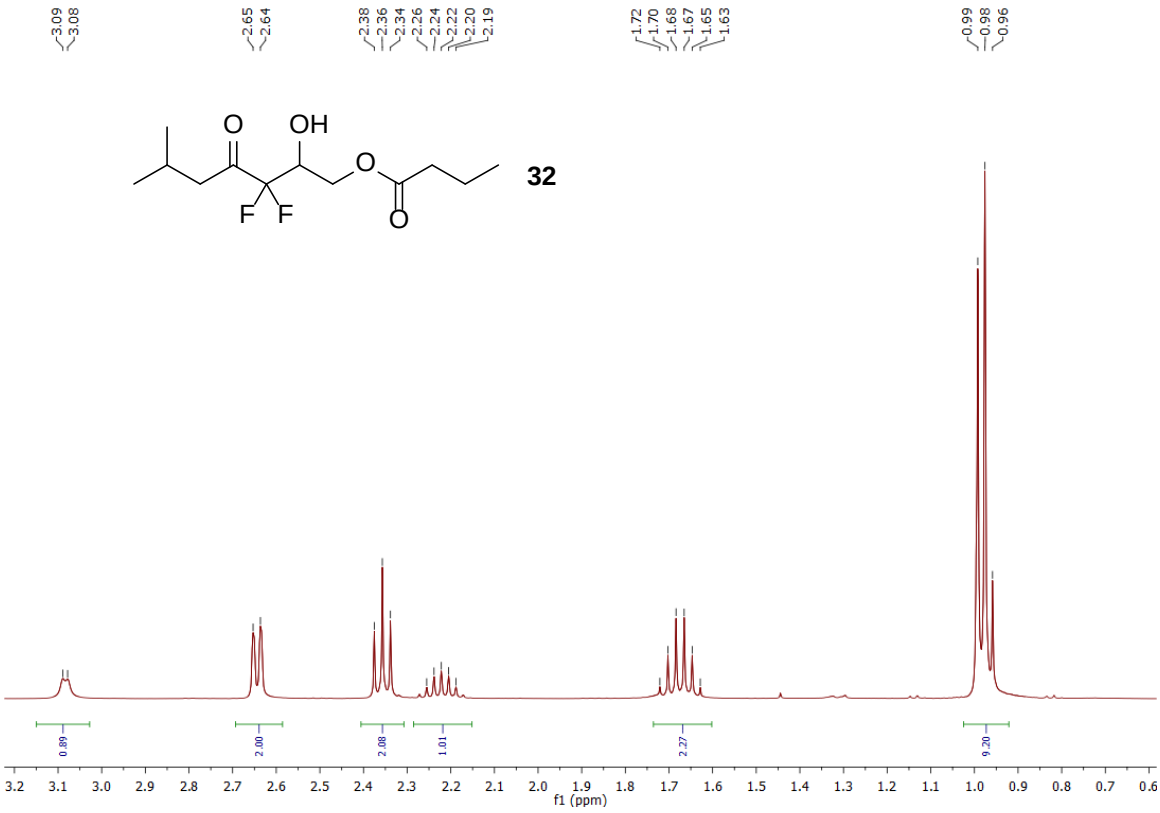
f1 (ppm)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3.08
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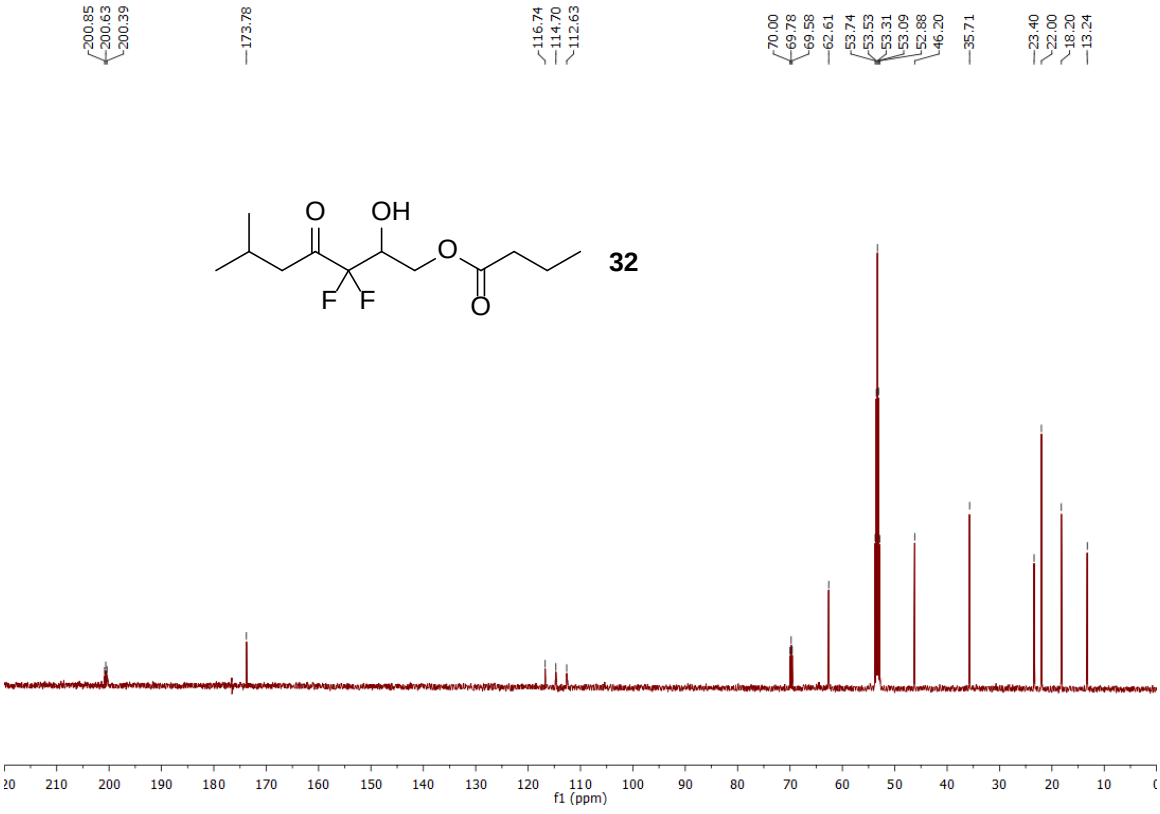
2.36
2.34
2.26
2.24
2.22
2.20
2.19
1.72
1.70
1.68
1.67
1.65
1.63
0.99
0.98
0.96
O
OH
O
F F
O
32
0.89
2.00
2.08
1.01
2.27
9.20
f1 (ppm)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69.58
62.61
53.74
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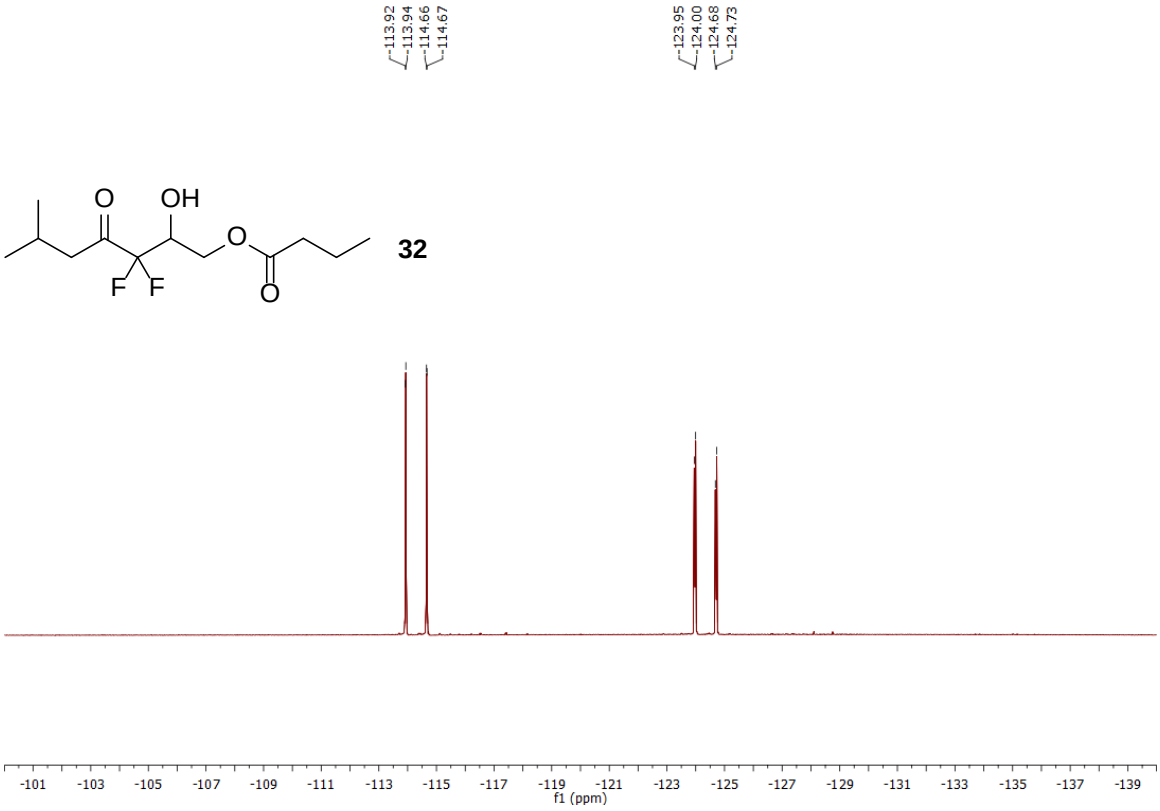
53.31
53.09
52.88
46.20
35.71
23.40
22.00
18.20
13.24
O
OH
O
F F
O
32
f1 (ppm)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-124.68
-124.73
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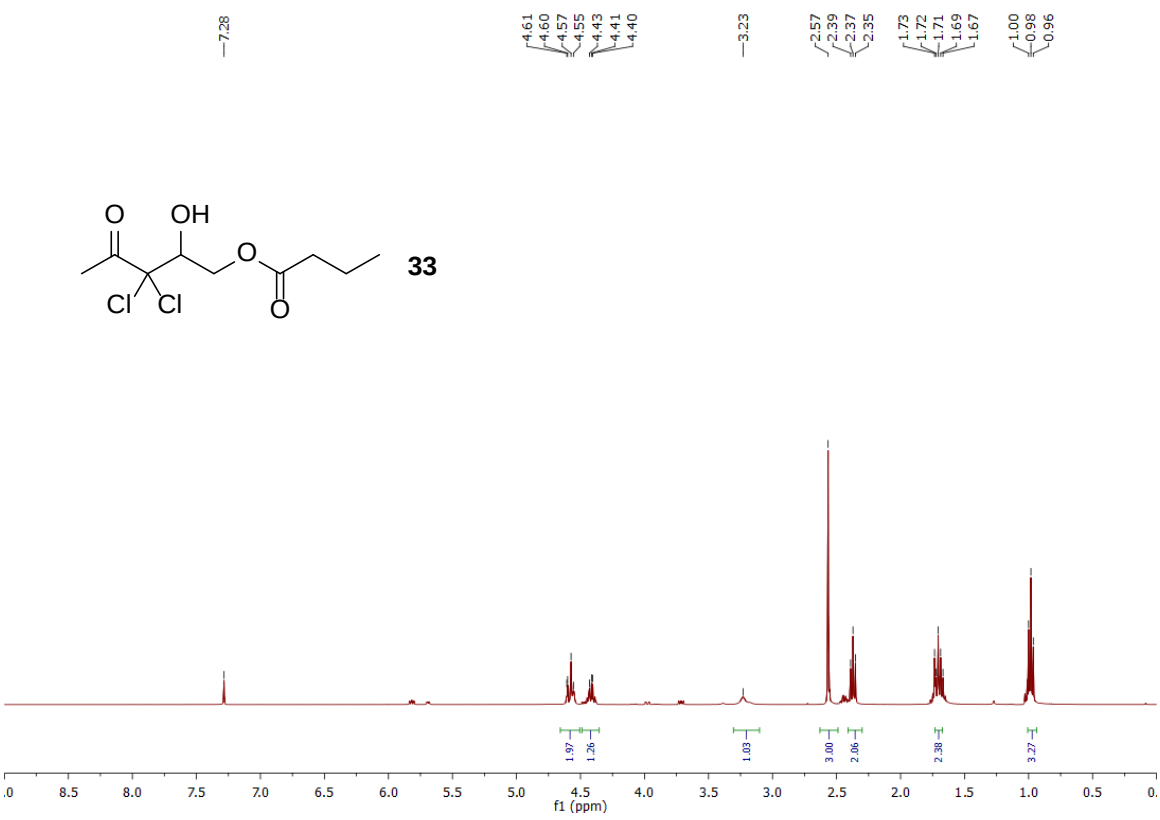
OH
O
F
F
O
32
-101 -103 -105 -107 -109 -111 -113 -115 -117 -119 -121 -123 -125 -127 -129 -131 -133 -135 -137 -139
f1 (ppm)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4.43
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4.40
3.23
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2.39
2.37
2.35
1.73
1.72
1.71
1.69
1.67
1.00
0.98
0.96
O
OH
O
Cl
Cl
O
33
1.97
1.26
1.03
3.00
2.06
2.38
3.27
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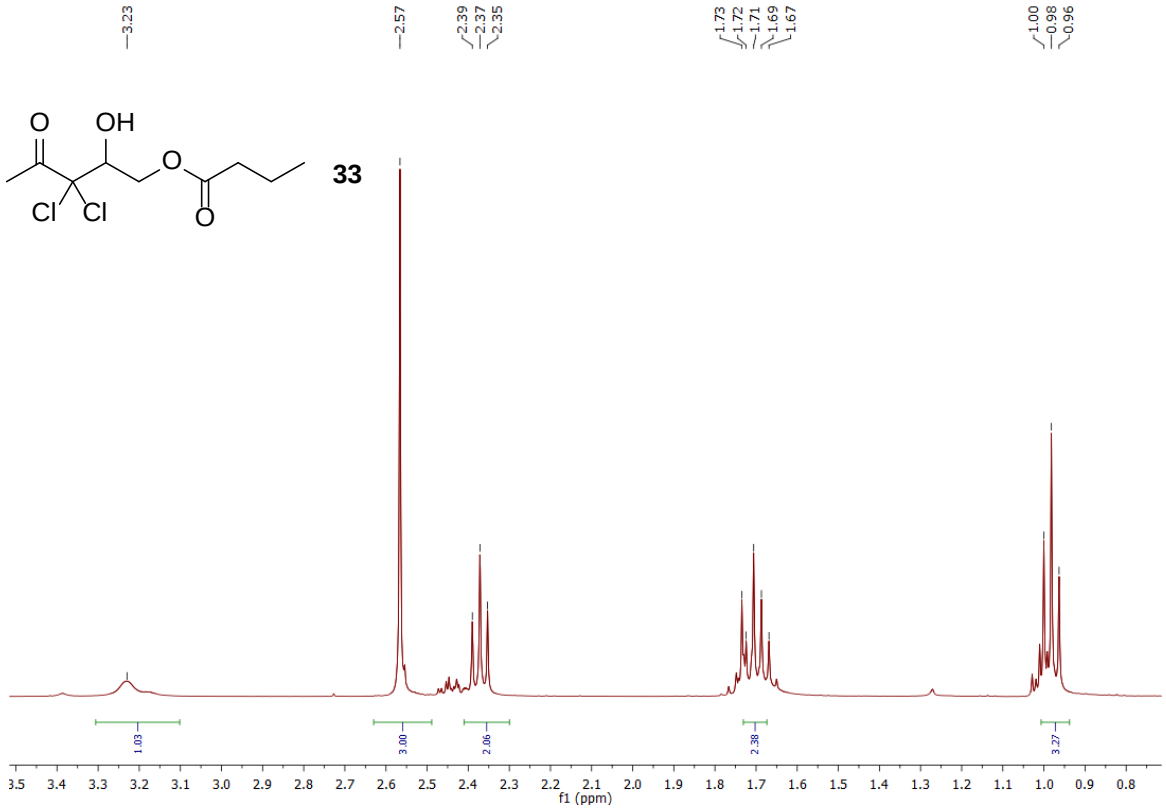
f1 (ppm)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2.06
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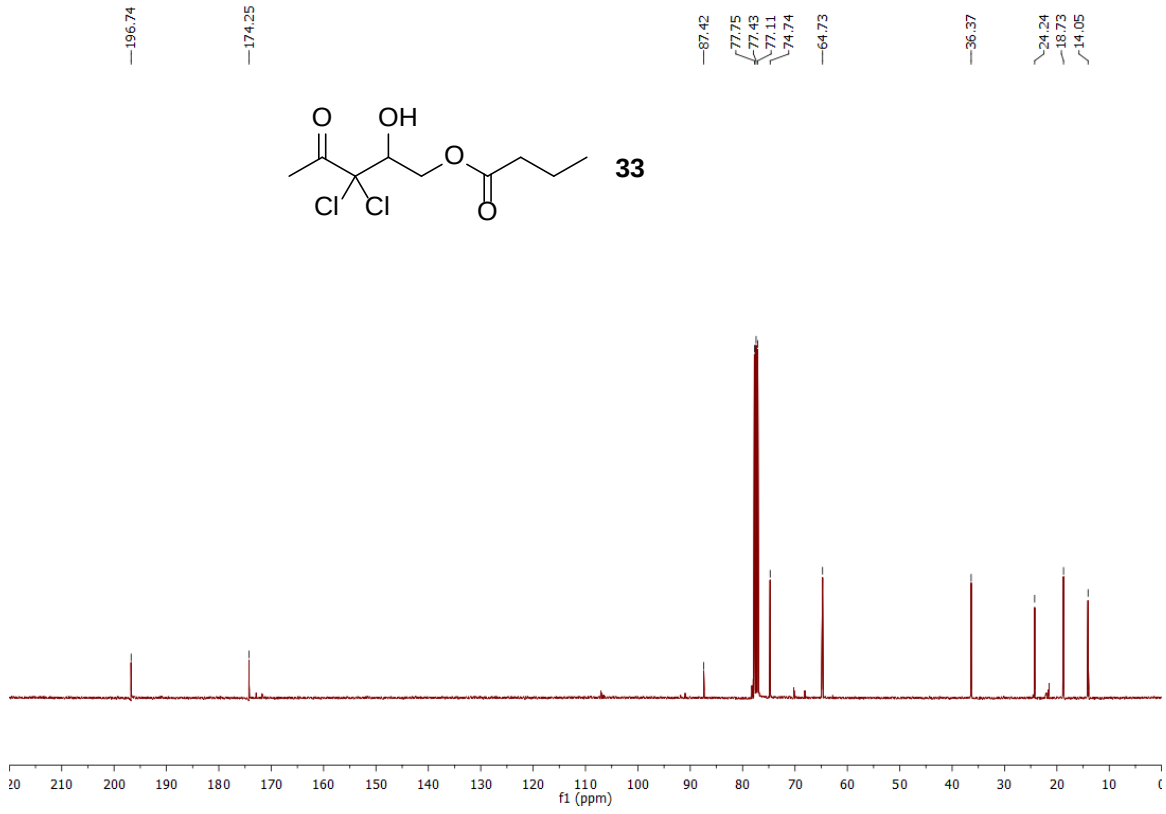
3.27
f1 (ppm)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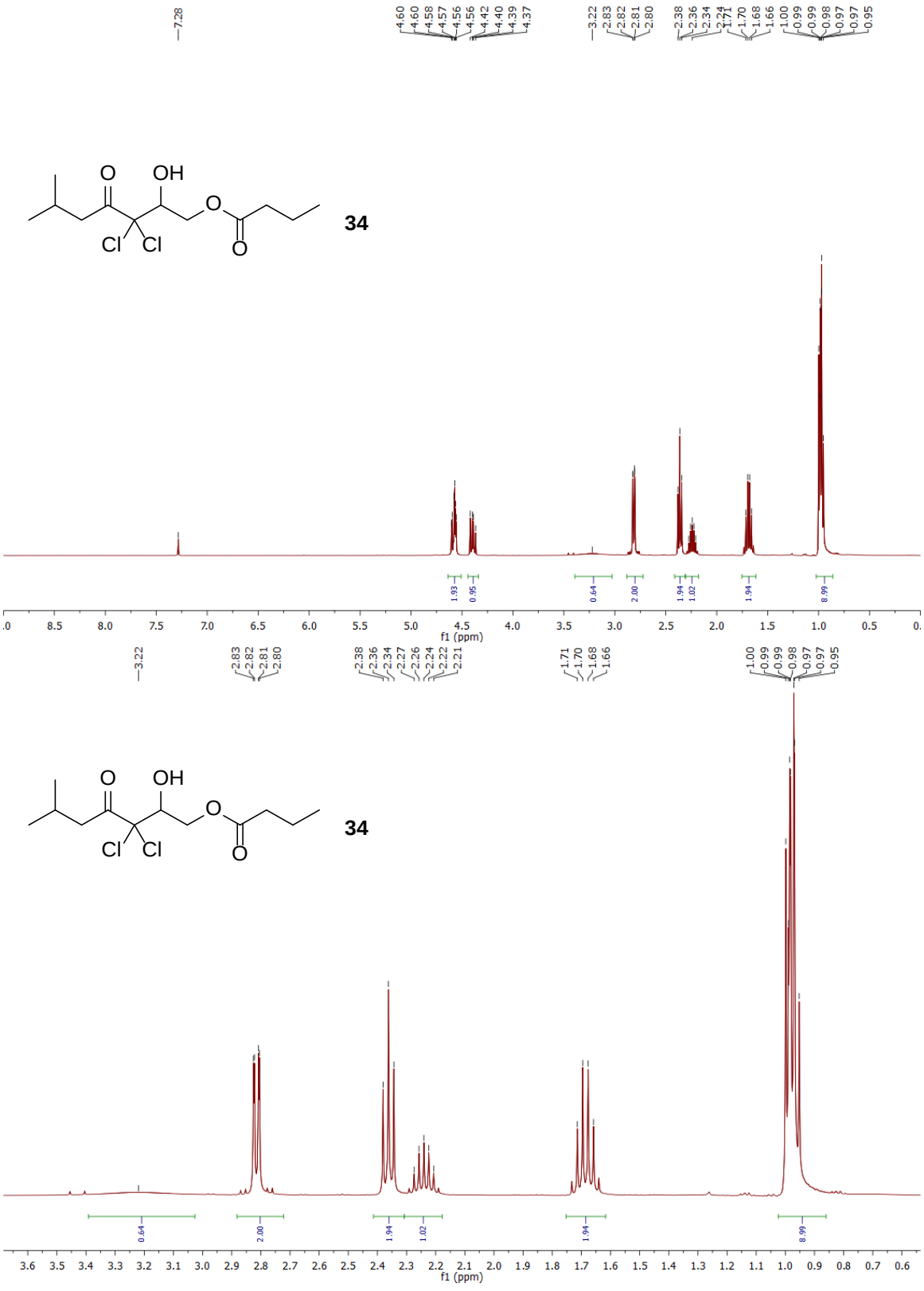
OH
O
Cl
Cl
O
33
f1 (ppm)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4.56
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4.39
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2.38
2.36
2.34
2.27
2.24
2.21
1.71
1.70
1.68
1.66
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0.98
0.97
0.97
0.95
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Cl
Cl
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0.95
0.64
2.00
1.94
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1.94
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f1 (ppm)
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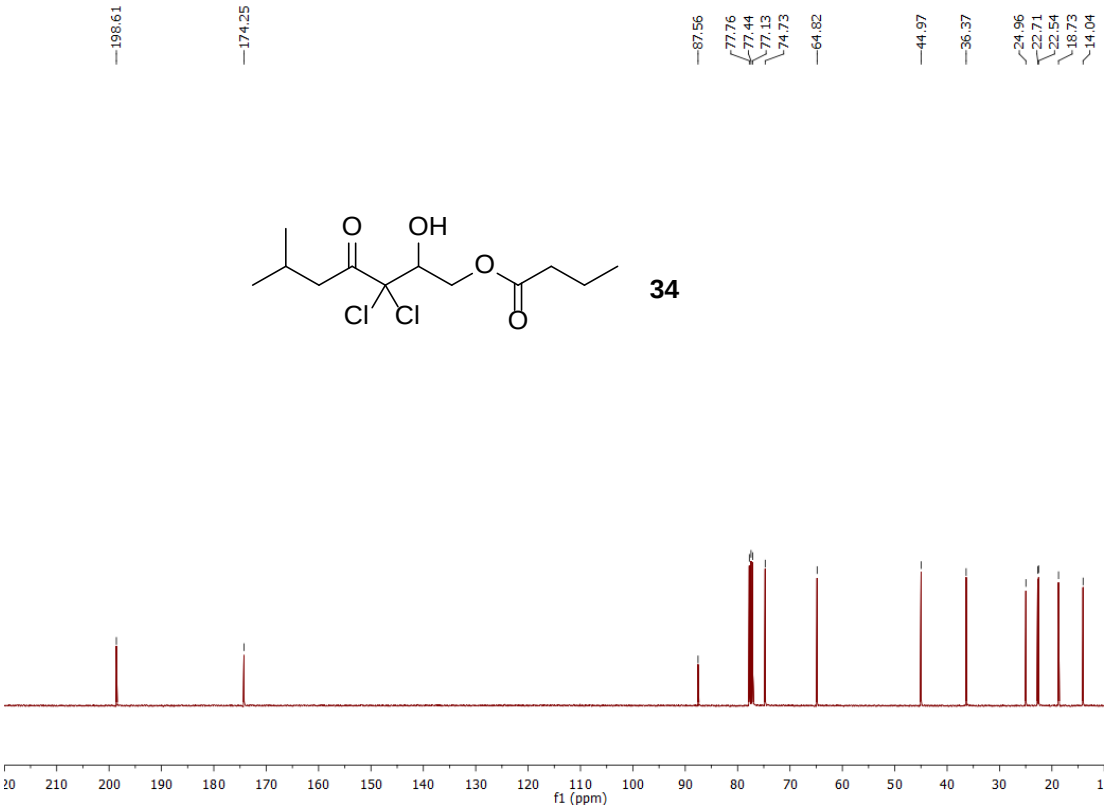
2.00
1.94
1.02
1.94
8.99
f1 (ppm)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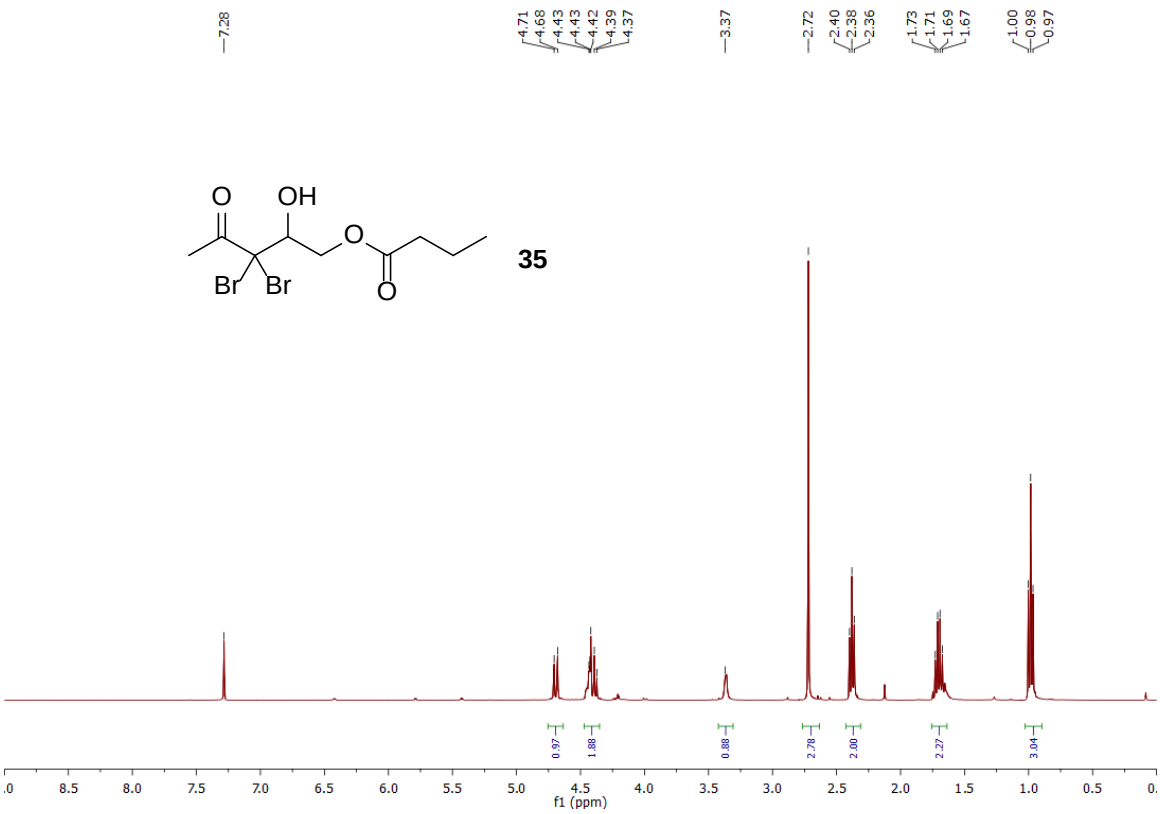
OH
O
Cl
Cl
O
f1 (ppm)

34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2.36
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1.71
1.69
1.67
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0.97
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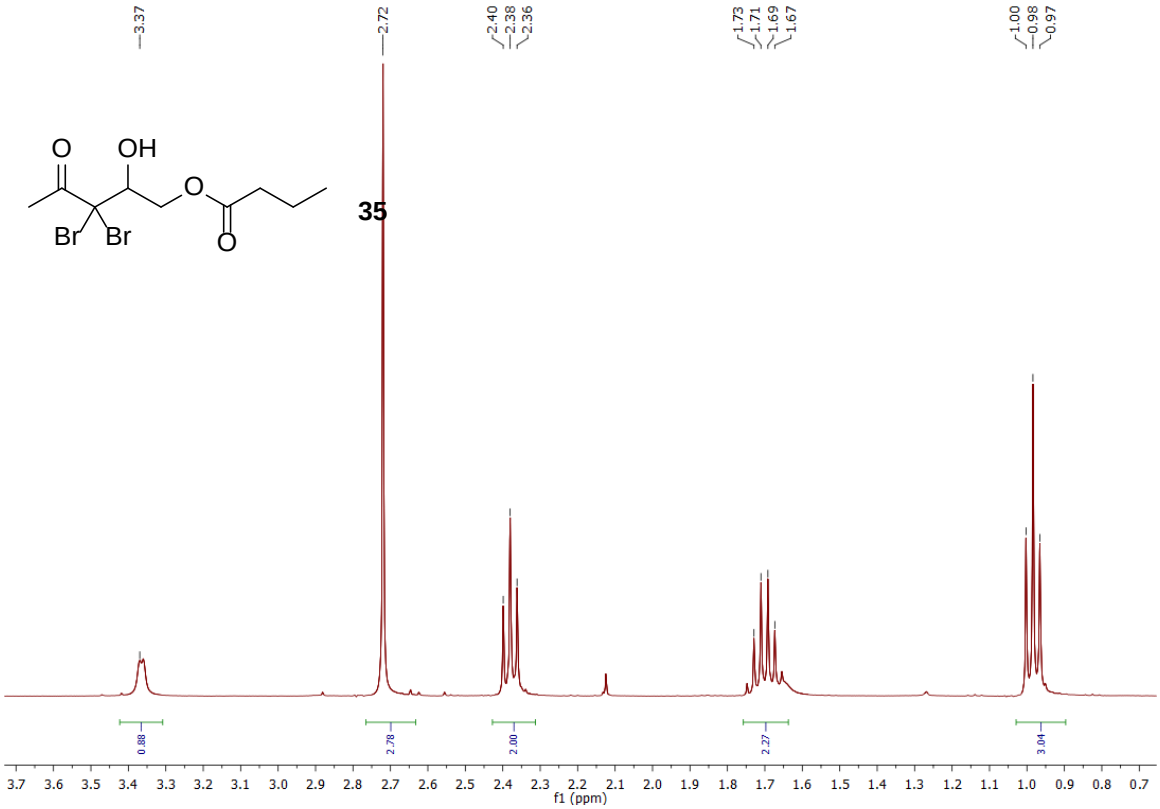
f1 (ppm)

35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Br
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2.00
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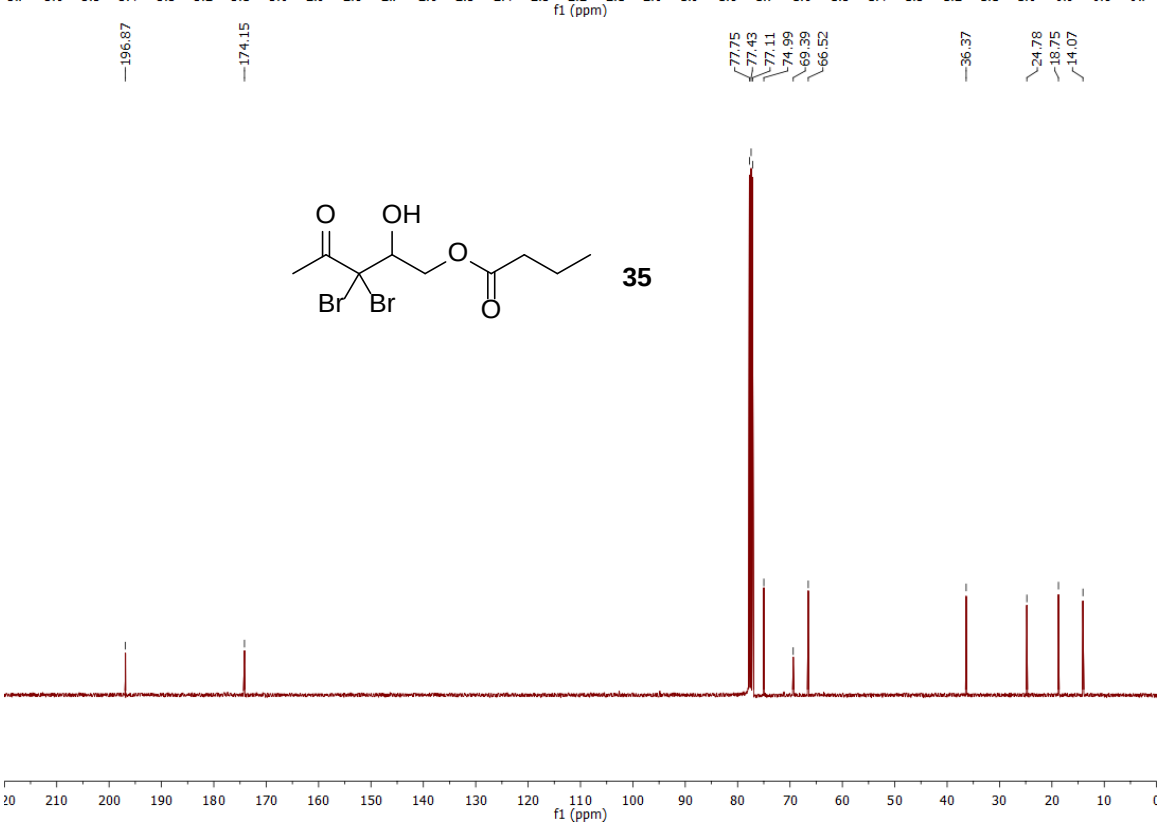
f1 (ppm)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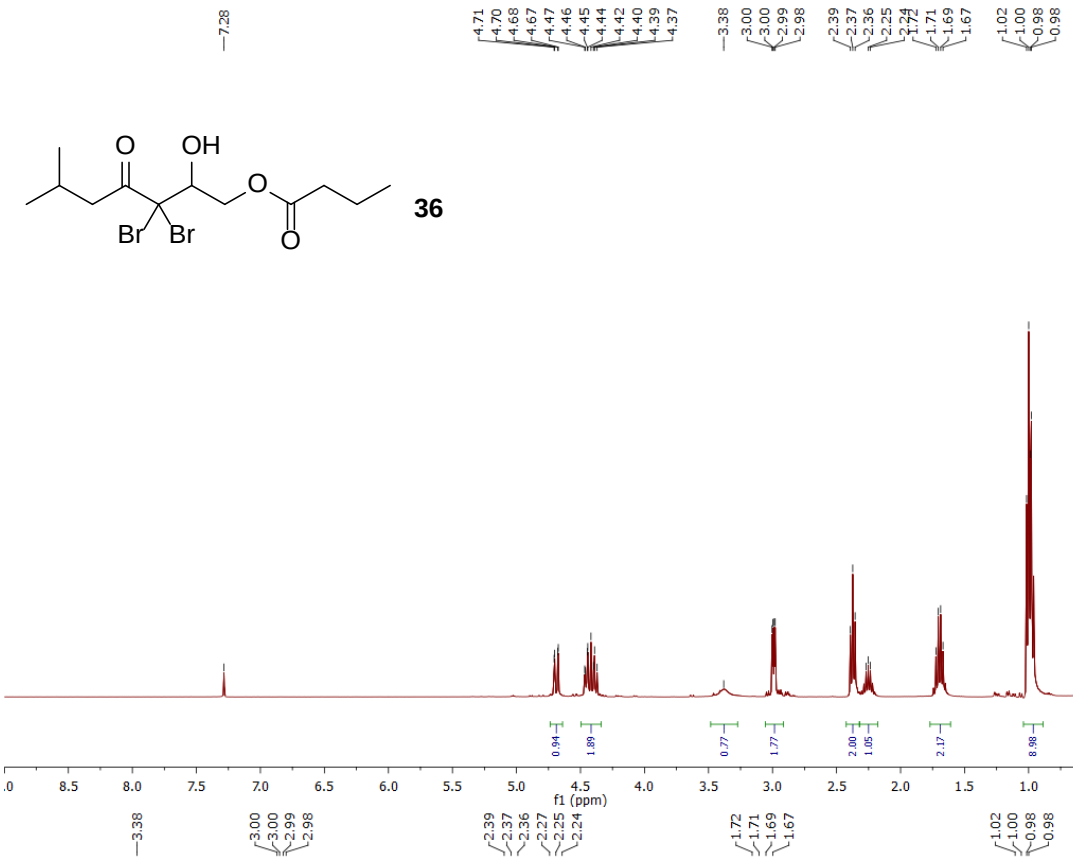
f1 (ppm)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2.98
2.39
2.37
2.36
2.25
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1.72
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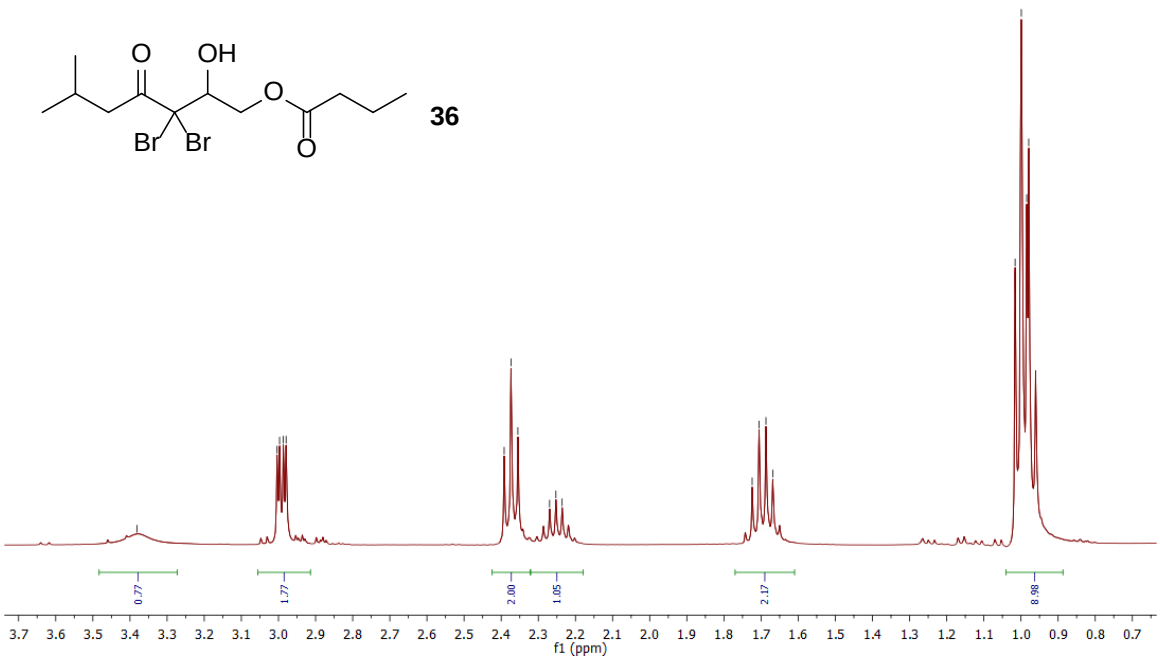
f1 (ppm)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1.05
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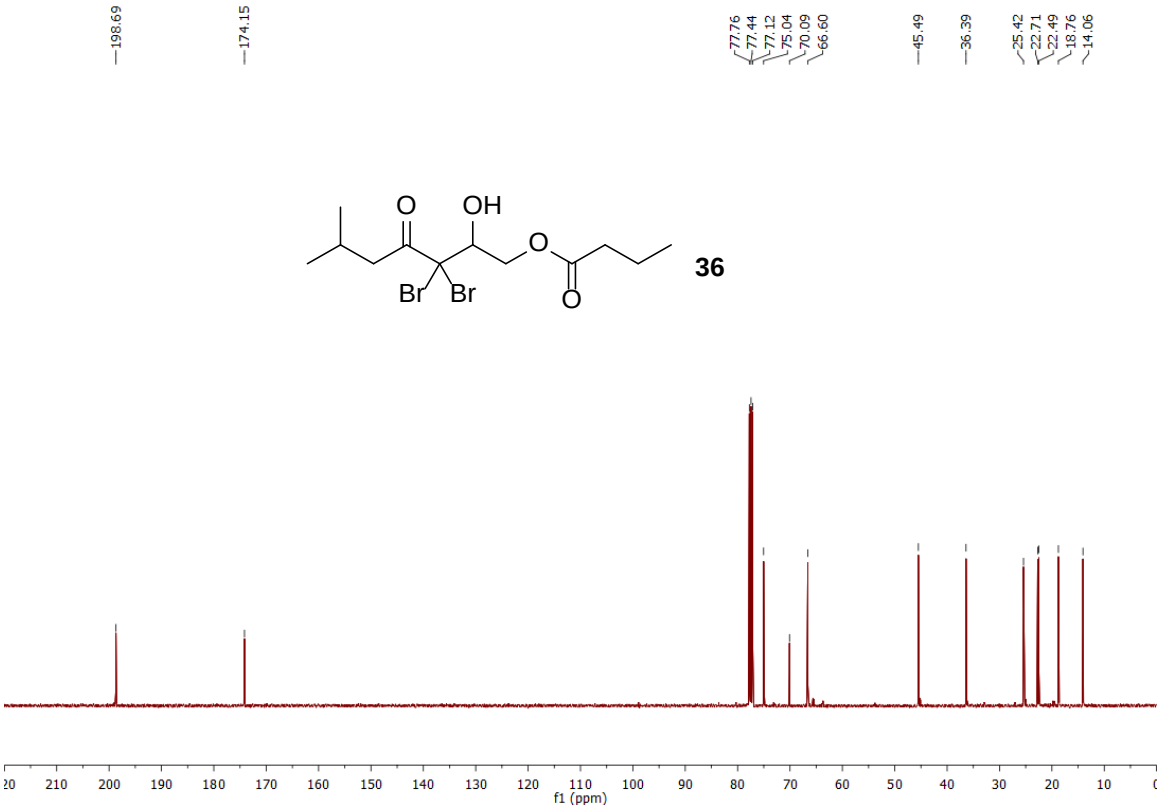
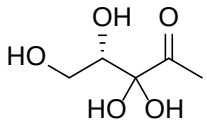
8.98
f1 (ppm)



5. Gaussian calculation results.

All the structures interested were optimized at B3LYP/6-31g(d) level using Gaussian 09.[7] A polarizable continuum model (PCM) was used as the SCRF method when solvation effect (water) is considered.



7

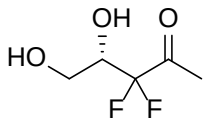
Total energy of the optimized structure: -572.6433216 a.u.

Number of imaginary frequencies: 0

Cartesian Coordinates:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.203529	1.564230	0.149776
2	6	0	-1.161643	0.160716	-0.438110
3	6	0	-0.005068	-0.722572	0.100486

4	6	0	1.400010	-0.177156	-0.262557
5	8	0	-0.096917	-0.865156	1.492751
6	8	0	-0.219802	-1.970875	-0.552828
7	6	0	2.294892	0.311235	0.848482
8	8	0	-0.041320	2.259358	-0.289077
9	8	0	-2.382792	-0.468146	-0.058650
10	8	0	1.740320	-0.195874	-1.431677
11	1	0	-2.123157	2.055491	-0.196962
12	1	0	-1.245344	1.495284	1.244615
13	1	0	-1.060350	0.218349	-1.529707
14	1	0	-1.045966	-1.005460	1.677626
15	1	0	0.303079	-2.638782	-0.077017
16	1	0	2.501349	-0.504452	1.550804
17	1	0	3.230649	0.681825	0.424713
18	1	0	1.796520	1.103835	1.413455
19	1	0	0.028204	3.076979	0.227259
20	1	0	-2.328862	-1.376244	-0.407391



15

Total energy of the optimized structure: -620.6888831 a.u.

Number of imaginary frequencies: 0

Cartesian Coordinates:

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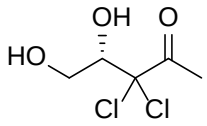
1	6	0	-1.346482	1.469234	0.095975
2	6	0	-1.207153	0.049106	-0.441618
3	6	0	0.023638	-0.658602	0.150399
4	6	0	1.391942	-0.129531	-0.339161
5	9	0	-0.029149	-0.629865	1.522739
6	9	0	-0.037706	-1.989216	-0.213513
7	6	0	2.366908	0.362356	0.695577
8	8	0	-0.146697	2.167660	-0.211813
9	8	0	-2.386246	-0.644003	-0.087201
10	8	0	1.626179	-0.191043	-1.531376
11	1	0	-2.223879	1.935318	-0.374371
12	1	0	-1.524820	1.417874	1.178452
13	1	0	-1.056847	0.076518	-1.531676
14	1	0	1.914263	1.163519	1.286625
15	1	0	2.619911	-0.451594	1.386549

16	1	0	3.271817	0.721816	0.201636
17	1	0	-0.097665	2.971629	0.353566
18	1	0	-2.420082	-1.479647	-0.607731



17

Total energy of the optimized structure: -1341.3842177 a.u.

Number of imaginary frequencies: 0

Cartesian Coordinates:

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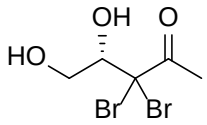
1	6	0	-1.509572	-1.629098	-0.132275
2	6	0	-0.118003	-1.222030	-0.619205
3	6	0	0.373100	0.105392	0.035867
4	6	0	-0.433153	1.338889	-0.497858
5	17	0	0.372099	-0.031032	1.838856
6	17	0	2.102776	0.386759	-0.498432
7	6	0	-1.008332	2.336402	0.469335
8	8	0	-2.378142	-0.509965	-0.252873
9	8	0	0.722786	-2.314220	-0.335751
10	8	0	-0.518052	1.447105	-1.703506
11	1	0	-1.846287	-2.472145	-0.749944
12	1	0	-1.430706	-1.975577	0.904948
13	1	0	-0.153612	-1.000555	-1.692768
14	1	0	-0.218851	2.767995	1.094143
15	1	0	-1.502809	3.125154	-0.100107
16	1	0	-1.725323	1.847404	1.133977
17	1	0	-3.166894	-0.681044	0.284235
18	1	0	1.534642	-2.219282	-0.859828



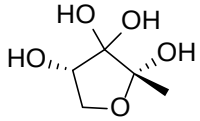
19

Total energy of the optimized structure: -5564.4100094 a.u.

Number of imaginary frequencies: 0

Cartesian Coordinates:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	2.035562	0.054599	1.542411
2	6	0	0.517330	0.237038	1.489021
3	6	0	-0.032182	0.180165	0.036869
4	6	0	0.366362	1.432359	-0.801828
5	35	0	0.431872	-1.537737	-0.806352
6	35	0	-2.029613	0.251211	0.152736
7	6	0	0.966670	1.261472	-2.170320
8	8	0	2.631874	0.978000	0.641148
9	8	0	-0.017420	-0.768165	2.315697
10	8	0	0.134985	2.515756	-0.303900
11	1	0	2.357583	0.230312	2.577443
12	1	0	2.273233	-0.982722	1.279610
13	1	0	0.257100	1.242230	1.845845
14	1	0	0.278583	0.714053	-2.823663
15	1	0	1.168374	2.249333	-2.587656
16	1	0	1.890857	0.680882	-2.109611
17	1	0	3.550870	0.705224	0.496017
18	1	0	-0.973648	-0.609445	2.398097



cyclic **7**

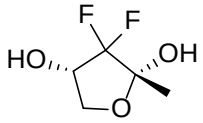
Total energy of the optimized structure: -572.6508389 a.u.

Number of imaginary frequencies: 0

Cartesian Coordinates:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.252736	0.371585	-0.564494
2	6	0	-0.714961	1.682871	-0.003230
3	8	0	0.705692	1.554326	-0.077756
4	6	0	1.117464	0.174041	0.050210
5	6	0	-0.226147	-0.638777	-0.017305
6	8	0	-2.560420	0.112147	-0.068078
7	8	0	1.785650	-0.036243	1.264458
8	6	0	2.101118	-0.113585	-1.072897
9	8	0	-0.203990	-1.773715	-0.844579
10	8	0	-0.577499	-0.975958	1.306682
11	1	0	-1.230942	0.366245	-1.659131

12	1	0	-1.010663	2.560262	-0.583638
13	1	0	-1.059673	1.810764	1.033441
14	1	0	-2.964132	-0.570731	-0.629002
15	1	0	1.088633	-0.182992	1.931715
16	1	0	1.633528	0.040827	-2.048096
17	1	0	2.951701	0.568445	-0.977535
18	1	0	2.467919	-1.141848	-1.014211
19	1	0	0.333833	-2.449665	-0.397246
20	1	0	-1.554114	-0.902570	1.344185



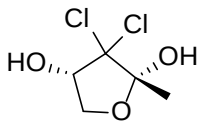
cyclic **15**

Total energy of the optimized structure: -620.6812635 a.u.

Number of imaginary frequencies: 0

Cartesian Coordinates:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-1.285222	0.335658	-0.523979
2	6	0	-0.782180	1.644092	0.083722
3	8	0	0.649086	1.559890	0.017300
4	6	0	1.105689	0.195288	0.022409
5	6	0	-0.216395	-0.626655	-0.000121
6	8	0	-2.597773	0.057114	-0.099300
7	8	0	1.870682	-0.079134	1.160378
8	6	0	1.996579	-0.033362	-1.188501
9	1	0	-1.201798	0.368128	-1.618249
10	1	0	-1.098773	2.529391	-0.471318
11	1	0	-1.132097	1.726127	1.121967
12	1	0	-2.940565	-0.678589	-0.631885
13	1	0	1.266996	-0.132304	1.921281
14	1	0	1.450810	0.159310	-2.115469
15	1	0	2.843559	0.656151	-1.131192
16	1	0	2.371617	-1.059597	-1.199857
17	9	0	-0.532877	-0.992168	1.290122
18	9	0	-0.116738	-1.781355	-0.719396



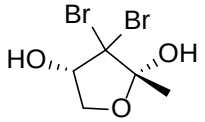
cyclic **17**

Total energy of the optimized structure: -1341.3884811 a.u.

Number of imaginary frequencies: 0

Cartesian Coordinates:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	-0.876672	0.827794	-0.849972
2	6	0	-0.115227	2.048189	-0.315637
3	8	0	1.141722	1.570078	0.190377
4	6	0	1.274091	0.147442	0.055444
5	6	0	-0.233817	-0.308332	-0.021676
6	8	0	-2.256952	1.016500	-0.705973
7	8	0	1.977587	-0.350235	1.140766
8	6	0	2.091922	-0.199740	-1.186894
9	17	0	-0.479660	-1.932688	-0.758034
10	17	0	-0.945463	-0.325625	1.649712
11	1	0	-0.612550	0.638083	-1.897452
12	1	0	0.060976	2.793811	-1.096290
13	1	0	-0.684341	2.508196	0.499462
14	1	0	-2.717074	0.357745	-1.251672
15	1	0	1.516526	-0.067664	1.950986
16	1	0	1.594563	0.123510	-2.104211
17	1	0	3.045741	0.328031	-1.104158
18	1	0	2.282618	-1.273252	-1.244144



cyclic **19**

Total energy of the optimized structure: -5564.4136272 a.u.

Number of imaginary frequencies: 0

Cartesian Coordinates:

Center Number	Atomic Number	Atomic Type	Coordinates (Angstroms) X	Y	Z
1	6	0	0.496505	0.159023	1.583279
2	6	0	1.903534	0.715166	1.330244
3	8	0	1.832091	1.475733	0.113114
4	6	0	0.534509	1.395912	-0.507270
5	6	0	-0.048209	0.092521	0.145407
6	8	0	0.567144	-1.046699	2.292806

7	8	0	0.683035	1.347516	-1.883845
8	6	0	-0.271944	2.658254	-0.205234
9	35	0	-1.998131	-0.066186	0.082109
10	35	0	0.724995	-1.495230	-0.761059
11	1	0	-0.116393	0.894783	2.119889
12	1	0	2.244833	1.358840	2.145731
13	1	0	2.607678	-0.114842	1.205327
14	1	0	-0.333929	-1.295045	2.559715
15	1	0	1.178054	0.535680	-2.102740
16	1	0	-0.435908	2.786110	0.867357
17	1	0	0.307893	3.509424	-0.572105
18	1	0	-1.236974	2.636935	-0.715091

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