Supporting Information for:
Carbonylation of Epoxides to Substituted 3-Hydroxy-δ-Lactones

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General Considerations:
All manipulations of air- and/or water-sensitive compounds were carried out using standard Schlenk line techniques or in an MBraun Unilab drybox under an atmosphere of dry nitrogen. NMR spectra were recorded using Varian Mercury or Inova spectrometers (^{1}H NMR, 300 MHz; ^{13}C NMR, 75 MHz and 125 MHz; ^{19}F NMR, 470 MHz) and referenced against residual solvent shifts for ^{1}H and ^{13}C NMR and hexafluorobenzene for ^{19}F NMR spectra. ^{1}H NMR and ^{13}C NMR spectra of the product 3HLs were identified by comparison to published spectra for 4-hydroxy-6-pentyl-δ-lactone (**7**),[1] 4-hydroxy-6-methyl-δ-lactone (**7a**),[2] 4-hydroxy-6-phenyl-δ-lactone (**7c**),[3] 6-ethyl-4-hydroxy-6-methyl-δ-lactone (**7d**),[4] 6-(*tert*-butyldimethylsiloxymethyl)-4-hydroxy-δ-lactone (**7i**),[5] and 6-chloromethyl-4-hydroxy-δ-lactone (**7j**).[6] All epoxides and lactones were prepared as racemic mixtures of diastereomers, except where noted. Mass spectra were acquired using a JEOL GCMate II mass spectrometer operating at 3000 resolving power for high resolution measurements in positive ion mode and an electron ionization potential of 70 eV. Samples were introduced via a GC inlet using an Agilent HP 6890N GC equipped with a 30 m (0.25 μm i.d.) HP-5ms capillary GC column. The carrier gas was helium with a flow rate of 1 mL/min. Samples were introduced into the GC using a split/splitless injector at 230 ˚C with a split ratio of 10:1. Lactones **7b**, **(*R*,*R*)-7b**, **7g**, and **7h** were analyzed using direct injection into the mass spectrometer to avoid dehydration in the GC. Optical rotations were measured on a Perkin-Elmer 241 digital polarimeter and are reported in the following format: $[\alpha]^T_D$ *r* (*c*, solvent), where *T* = temperature in °C, *D* refers to the sodium D line (589 nm), *r* is the measured rotation, and *c* is the concentration in g/dL. IR spectra were measured on a Mattson RS-10500 Research Series FTIR. In situ IR data were collected using a 100-mL Parr reactor modified for use with a Mettler-Toledo ReactIR 4000 Reaction Analysis System fitted with a Sentinel DiComp high-pressure probe, and analyzed with ReactIR software version 2.21. All other carbonylation reactions were performed in a custom-built six-well reactor[7] heated on a hot plate and equipped with magnetic stir bars. *All carbonylation reactions were performed in a well-ventilated fume hood equipped with a CO sensor, as carbon monoxide is a highly toxic gas.*

Materials:
Tetrahydrofuran (THF) was dried over a column of alumina and degassed by sparging with dry nitrogen. Diethyl ether was dried and deoxygenated on columns of alumina and Q5 copper, respectively. 1,2-Dimethoxyethane (DME) was transferred under reduced pressure from sodium/benzophenone. 1,2-Epoxyhexane, 1,1,2,2-tetrafluoroethylglycidyl ether, epichlorohydrin, *tert*-butyldimethylsilylglycidyl ether, hexanal, cyclopentanone, cyclododecanone, 4-pentene-2-ol, 4-phenyl-1-buten-4-ol, allyl magnesium bromide, vinyl

magnesium bromide, copper iodide, *meta*-chloroperbenzoic acid (*m*CPBA), and peracetic acid were purchased from Aldrich and used as received. Sodium acetate (anhydrous), 2-butanone, and acetic acid were purchased from Mallinckrodt. 1,6-Heptadien-4-ol was purchased from Acros. *para*-Toluene sulfonic acid was purchased from Fischer. Dicobalt octacarbonyl and (1*R*, 2*R*)-(-)-1,2-cyclohexanediamino-*N*,*N*′-bis(3,5-di-*t*-butylsalicylidene)cobalt were purchased from Strem. Research-grade carbon monoxide (99.99% min.) was purchased from Matheson and used without purification. Catalysts **1**,[8] **2**,[9] **3**,[10] **4**,[11] and **5**[12] and $Ph_3SiCo(CO)_4$[13] were prepared according to literature procedures. 4-Hydroxy-1,2-epoxynonane (**6**),[14] 4-hydroxy-1,2-epoxypentane (**6a**),[15] 4-hydroxy-4-phenyl epoxybutane (**6c**),[16] 4-hydroxy-4-methyl-1,2-epoxyhexane (**6d**),[17] 1-(2,3-epoxypropyl)-cyclopentan-1-ol (**6e**),[18] and 4-hydroxy-1,6-heptadiene monoepoxide (**6g**)[19] were synthesized in an analogous manner to those in the Experimental Section and characterized by comparison to literature reports. Solid epoxides were dried under vacuum and liquid epoxides were dried over activated 4Å molecular sieves and degassed three times by freeze-pump-thaw cycles.

Experimental Section:

4-Hydroxy-1,2-epoxyoctane (6b): Copper iodide (0.79 g, 4.1 mmol) was added to a 250-mL oven-dried three-neck round-bottom flask and diluted with 40 mL dry THF. Vinyl magnesium bromide (1.0 M solution in diethyl ether, 50 mL, 50 mmol) was slowly added to the flask and stirred for 20 minutes. The flask was then cooled to -78 ˚C and a solution of 1,2-epoxyhexane (4.15 g, 41 mmol) in 30 mL THF was slowly added via an addition funnel under nitrogen. The reaction was slowly warmed to room temperature over the course of 16 hours, then cooled to 0 ˚C and quenched with saturated ammonium chloride. The aqueous layer was extracted with diethyl ether and the combined organic layers were evaporated in vacuo.

The crude homoallylic alcohol was epoxidized by diluting in CH_2Cl_2 (~1 M solution) and slowly adding *m*CPBA (11 g, 66 mmol) to the solution at 0 ˚C. The reaction was warmed to room temperature and stirred for 18 hours, at which time it was cooled back to 0 ˚C and quenched with 10% sodium bisulfite (aq). The organic layer was extracted twice with sat. $NaHCO_3$ (aq) and sat. NaCl (aq) and dried over $MgSO_4$. Solvent was removed in vacuo and the crude epoxide was distilled at 65 ˚C under vacuum to afford pure **6b** (1.8 g, 34%, *syn*:*anti* ca. 50:50) as a racemic mixture of diastereomers. ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 0.85 (t, ^3J = 6.5 Hz, 6H), 1.18-1.59 (m, 12H), 1.70-1.82 (m, 2H), 2.38-2.58 (m, 4H), 2.70-2.80 (m, 2H), 3.00-3.15 (m, 2H), 3.69-3.87 (m, 2H); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) 14.15, 22.78, 27.79, 27.85, 37.25, 37.43, 39.35, 39.87, 46.75, 47.12, 50.38, 50.72, 69.30, 70.44.

1-(2,3-Epoxypropyl)-cyclododecan-1-ol (6f): An oven-dried 500-mL three-neck round-bottom flask was charged with cyclododecanone (6.00 g, 32.9 mmol) and 50 mL dry THF. A 100-mL addition funnel with allyl magnesium bromide (1.0 M solution in THF, 36.2 mL, 36.2 mmol) was attached and the flask was cooled in an ice bath for 10 minutes. The Grignard was slowly dripped in over the course of 30 minutes while stirring at 0 ˚C under nitrogen. After addition, the ice bath was removed and the reaction mixture was stirred for 4 hours at room temperature under nitrogen. Excess Grignard was quenched by slowly

adding water to the reaction mixture cooled to 0 ˚C, and the product was extracted three times with diethyl ether. The organic layer was dried over Na_2SO_4 and solvent was removed under vacuum to obtain the homoallylic alcohol that was used without further purification.

The epoxide was synthesized by addition of peracetic acid (32% solution in dilute acetic acid, 16.6 mL, 79.0 mmol) to a CH_2Cl_2 solution of crude homoallylic alcohol and sodium acetate (4.05 g, 49.4 mmol) at 0 ˚C; the reaction was stirred at room temperature for 18 h. Excess peroxide was quenched with a 10% aqueous solution of sodium bisulfite and the organic layer was washed 3 times with water and brine. Evaporation of solvent yielded crude epoxide which was recrystallized from hot hexanes (5 mL) to afford colorless crystals of **6f** (5.03 g, 64%) as a racemic mixture. ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 1.22-1.86 (m, 25H), 2.48 (dd, ^3J = 2.8 Hz, ^2J = 5.1Hz, 1H), 2.80 (dd, ^3J = 3.9 Hz, ^2J = 5.1 Hz, 1H), 3.19 (dddd, ^3J = 2.7 Hz, ^3J = 3.0 Hz, ^3J = 4.2 Hz, ^3J = 5.1 Hz, 1H); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) 19.59, 19.80, 22.24, 22.71, 26.18, 26.56, 26.60, 34.91, 35.05, 43.25, 46.99, 49.24, 75.47. Note: Two peaks were not visible due to degeneracy.

5-(1,1,2,2-Tetrafluoroethoxy)-4-hydroxy-1,2-epoxypentane (6h): Copper iodide (0.52 g, 2.7 mmol) was added to a 250-mL oven-dried three-neck round-bottom flask and diluted with 25 mL dry THF. Vinyl magnesium bromide (1.0 M solution in diethyl ether, 27 mL, 27 mmol) was slowly added to the flask and stirred for 20 minutes. The flask was then cooled to -78 ˚C and a solution of 1,1,2,2-tetrafluoroethyl glycidyl ether (5.2 g, 30 mmol) in 20 mL THF was slowly added via an addition funnel under nitrogen. The reaction was slowly warmed to room temperature over the course of 16 hours, then cooled to 0 ˚C and quenched with saturated ammonium chloride. The aqueous layer was extracted with diethyl ether and the combined organic layers were evaporated in vacuo.

The crude homoallylic alcohol was epoxidized by diluting in CH_2Cl_2 (~1 M solution) and slowly adding *m*CPBA (8.5 g, 49 mmol) to the solution at 0 ˚C. The reaction was warmed to room temperature and stirred for 18 hours, at which time it was cooled back to 0 ˚C and quenched with 10% sodium bisulfite (aq). The organic layer was extracted twice with sat. $NaHCO_3$ (aq) and sat. NaCl (aq) and dried over $MgSO_4$. Solvent was removed in vacuo and the crude epoxide was distilled at 60 ˚C under vacuum to afford pure **6h** (2.2 g, 33%, *syn*:*anti* ca. 50:50) as a racemic mixture of diastereomers. ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 1.49-1.65 (m, 2H), 1.94-2.05 (m, 1H), 2.40 (d, ^3J = 3.8 Hz, 1H), 2.55 (dd, ^3J = 2.7 Hz, ^3J = 4.8 Hz, 1H), 2.61 (dd, ^3J = 2.7 Hz, ^3J = 4.8 Hz, 1H), 2.82 (dd, ^3J = 4.1 Hz, ^3J = 4.7 Hz, 1H), 2.86 (dd, ^3J = 4.1 Hz, ^3J = 4.7 Hz, 1H), 3.10-3.20 (m, 2H), 3.91 (dd, ^3J = 7.0 Hz, ^2J = 10.0 Hz, 1H), 4.00 (pseudo-d, 2H), 4.04 (dd, ^3J = 3.9 Hz, ^2J = 10.0 Hz, 1H), 4.07-4.20 (m, 2H), 5.74 (tt, ^3J = 2.5 Hz, ^2J = 53.3 Hz, 2H); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) 35.55, 35.82, 46.77, 47.25, 49.60, 49.72, 67.54, 67.91 (t, ^3J = 4.6 Hz), 68.14, 68.15 (t, ^3J = 4.6 Hz), 107.87 (tt, ^2J = 42 Hz, J = 249 Hz) Note: The CF_2 carbon was not definitively identified.

5-(*tert*-Butyldimethylsilyloxy)-4-hydroxy-1,2-epoxypentane (6i): Copper iodide (0.36 g, 1.9 mmol) was added to a 250-mL oven-dried three-neck round-bottom flask and diluted with 20 mL dry THF. Vinyl magnesium bromide (1.0 M solution in diethyl ether, 23 mL, 23 mmol) was slowly added to the flask and stirred for 20 minutes. The flask was then cooled to -78 ˚C and a solution of *tert*-butyldimethylsilyl glycidyl ether (3.6 g, 19

mmol) in 10 mL THF was slowly added via an addition funnel under nitrogen. The reaction was slowly warmed to room temperature over the course of 16 hours, then cooled to 0 ˚C and quenched with sat. NH_4Cl (aq). The aqueous layer was extracted with diethyl ether and the combined organic layers were evaporated in vacuo.

The epoxide was synthesized by addition of peracetic acid (32% solution in dilute acetic acid, 9.6 mL, 46 mmol) to a CH_2Cl_2 solution of crude homoallylic alcohol and sodium acetate (2.3 g, 28 mmol) at 0 ˚C; the reaction was stirred at room temperature for 18 h. Excess peroxide was quenched with 10% sodium bisulfite (aq) and the organic layer was washed 3 times with water and brine. Evaporation of solvent yielded crude epoxide which was purified by column chromatography with 30% ethyl acetate in hexanes to afford **6i** (2.5 g, 58%, *syn*:*anti* ca. 50:50) as a racemic mixture of diastereomers. ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 0.035 (s, 12H), 0.86 (s, 18H), 1.37-1.83 (m, 4H), 2.46-2.51 (m, 2H), 2.63 (d, ^3J = 3.6 Hz, 1H), 2.67 (d, ^3J = 3.6 Hz, 1H), 2.73 (t, ^3J = 4.8, 1H), 2.77 (t, ^3J = 4.8 Hz, 1H), 3.02-3.12 (m, 2H), 3.37-3.66 (m, 4H), 3.75-3.90 (m, 2H); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) -5.28, -5.24, 18.40, 25.99, 35.83, 36.16, 46.83, 47.32, 49.84, 49.94, 66.91, 67.23, 69.88, 69.98.

5-Chloro-4-hydroxy-1,2-epoxypentane (6j): Copper iodide (2.3 g, 12 mmol) was added to a 500-mL oven-dried three-neck round-bottom flask and diluted with 100 mL dry THF. Epicholorohydrin (12 g, 130 mmol) was added to the flask which was equipped with an addition funnel and cooled to -78 ˚C. Vinyl magnesium bromide (1.0 M solution in diethyl ether, 120 mL, 120 mmol) was slowly added to the flask and stirred for 30 minutes, then warmed to room temperature and stirred for 16 hours. The reaction was cooled to 0 ˚C and quenched with sat. NH_4Cl (aq). The organic layer was pushed through a plug of silica to remove magnesium salts and excess epichlorohydrin was removed in vacuo.

The homoallylic alcohol was epoxidized with peracetic acid as in **6i**. The crude epoxide was purified by column chromatography using 30% ethyl acetate in hexanes to afford **6j** (2.5 g, 15%, *syn*:*anti* ca. 50:50) as a racemic mixture of diastereomers. ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 1.43-1.69 (m, 2H), 1.87-2.00 (m, 2H), 2.49 (dd, ^3J = 2.7 Hz, ^2J = 4.8 Hz, 1H), 2.53 (dd, ^3J = 3.0 Hz, ^2J = 4.8 Hz, 1H), 2.75 (t, ^3J = 4.5 Hz, 1H), 2.79 (t, ^3J = 4.5 Hz, 1H), 3.02-3.13 (m, 2H), 3.09 (d, ^3J = 4.8, 1H), 3.16 (d, ^3J = 4.8 Hz, 1H), 3.41-3.63 (m, 4H), 3.93-4.07 (m, 2H); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) 36.83, 36.95, 46.67, 47.28, 49.56, 49.66, 49.69, 49.83, 69.35, 69.71.

(*2R,4R*)-4-Hydroxy-1,2-epoxyoctane ((*R,R*)-6b): (*R*)-1,2-Epoxyhexane was prepared as reported by Jacobsen and coworkers.[20] Ring opening of the optically pure epoxide by vinyl magnesium bromide followed by epoxidation with *m*CPBA were performed in an analogous manner as **6h** to give a 1:1 mixture of diastereomers. The diastereomers were resolved using Jacobsen HKR conditions. The epoxide (2.67 g, 18.5 mmol) was diluted in 2.5 mL THF. To this solution was added (1*R*, 2*R*)-(-)-1,2-cyclohexanediamino-*N*,*N*′-bis(3,5-di-*t*-butylsalicylidene)cobalt (56.2 mg, 0.93 mmol) and glacial acetic acid (21.2 μL, 0.37 mmol). The solution was cooled to 0 ˚C and water (183 μL, 10.2 mmol) was added dropwise. After stirring at room temperature for 24 hours, THF was removed in vacuo and the residue was distilled under vacuum at 65 ˚C to afford **(*R,R*)-6b** (1.18 g, 13% from racemic 1,2-epoxyhexane, >99:1 *syn*:*anti*) as a colorless oil. ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 0.85 (t, ^3J = 6.9 Hz, 3H), 1.17-1.81 (m, 8H), 2.42-2.49 (m, 1H), 2.47 (d,

^3J = 4.2 Hz, 1H), 2.72 (t, ^3J = 4.2 Hz, 1H), 2.99-3.07 (m, 1H), 3.74-3.86 (m, 1H); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) 14.13, 22.75, 27.77, 37.22, 39.84, 46.73, 50.69, 70.38.

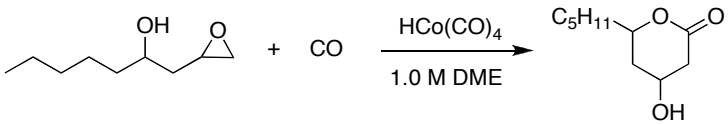
Preparation of $HCo(CO)_4$: This procedure was adapted from a similar synthesis of $HCo(CO)_4$.[21] In the glove box, $Ph_3SiCo(CO)_4$ (0.12 mmol) and *p*-toluenesulfonic acid (0.12 mmol) were weighed into separate flame-dried vials. DME (6.0 mL) was divided evenly into each vial to completely dissolve the catalyst components. The two solutions were combined to form a colorless solution of $HCo(CO)_4$ (0.05 M in DME) which was used immediately. Note: $HCo(CO)_4$ must be used immediately after preparation to ensure reproducible catalytic activity.

Carbonylation of Homoglycidols: In a custom-built, six-well, high pressure stainless steel reactor, six oven-dried vials (8 mL) were charged with epoxide (1.0 mmol) and magnetic stir bars. Freshly prepared $HCo(CO)_4$ solution (1.0 mL, 0.05 M in DME) was transferred to each vial via syringe. The reactor was then sealed, pressured to 800 psi CO, and heated at 60 ˚C for 24 hours while stirring. After the reaction time, the reactor was cooled in dry ice for 10 minutes and the wells were vented in a well-ventilated fume hood.

Crude ^{1}H NMR spectra were obtained by removing an aliquot of reaction mixture and passing it through a plug of silica with $CDCl_3$. Reactions that cleanly produced δ-lactone were purified by chromatography. The crude reaction mixture was concentrated to an oil under vacuum. This crude product was passed through silica gel, first using 30% ethyl acetate in hexanes to remove catalyst residue, then with 70% ethyl acetate in hexanes to elute the δ-lactone product. On a small scale, the isolated 3HLs were sometimes contaminated with small amounts (<5%) of catalyst residue. The contamination was most dramatic with the alkyl-substituted homoglycidols (**7**-**7b**), leading to lower isolated yields. The product 3HL was obtained by removing solvent in vacuo and analyzed by comparison to literature reports, or fully characterized in the case of unreported compounds.

Optimization of Carbonylation Conditions: Using the above general procedure for homoglycidol carbonylation by $HCo(CO)_4$, CO pressure, temperature, catalyst loading, and reaction time were varied to determine the optimal conditions (Table S1).

Table S1: Reaction conditions for homoglycidol carbonylation.



Entry	Epoxide: Catalyst	CO Pressure (psi)	Time (h)	Temperature (˚C)	Conversion[a] (%)
1	20:1	100	48	23	47
2	20:1	800	6	60	99
3	20:1	800	6	80	99[b]
4	50:1	800	24	60	99
5	100:1	800	24	60	30
6	200:1	800	24	60	NR[c]

[a] Conversions determined by ^{1}H NMR spectroscopy. [b] Product contaminated with unknown impurities. [c] NR = No Reaction; only starting material detected.

Carbonylation of 4-hydroxy-1,2-epoxynonane (6) monitored by in situ IR spectroscopy: The adapted Parr reactor was dried under vacuum overnight and brought into the glove box. A solution of **6** (0.79 g, 5.0 mmol) in 5.0 mL DME was drawn into a 10 mL glass syringe. Another solution containing $HCo(CO)_4$ (0.1 mmol in 5.0 mL DME) was drawn into a separate glass syringe. The needles from each syringe were inserted through a septum covering the injection port of the reactor. The reactor was removed from the glove box, connected to the ReactIR, and a background spectrum was recorded. Following the background, both the epoxide and catalyst solutions were injected into the reactor, which was then pressured to 800 psi with CO. While IR spectra were recorded every two minutes, the reactor was heated to 60 ˚C using a heating jacket. The formation of δ-lactone (**7**) and β-lactone (**8**) was monitored by the emergence of their carbonyl stretches at 1744 cm^{-1} and 1827 cm^{-1}, repectively (Figure S1). The reaction was allowed to proceed until the lactone absorbance was constant, at which time the reactor was cooled and vented. The crude reaction mixture was analyzed by ^{1}H NMR spectroscopy.

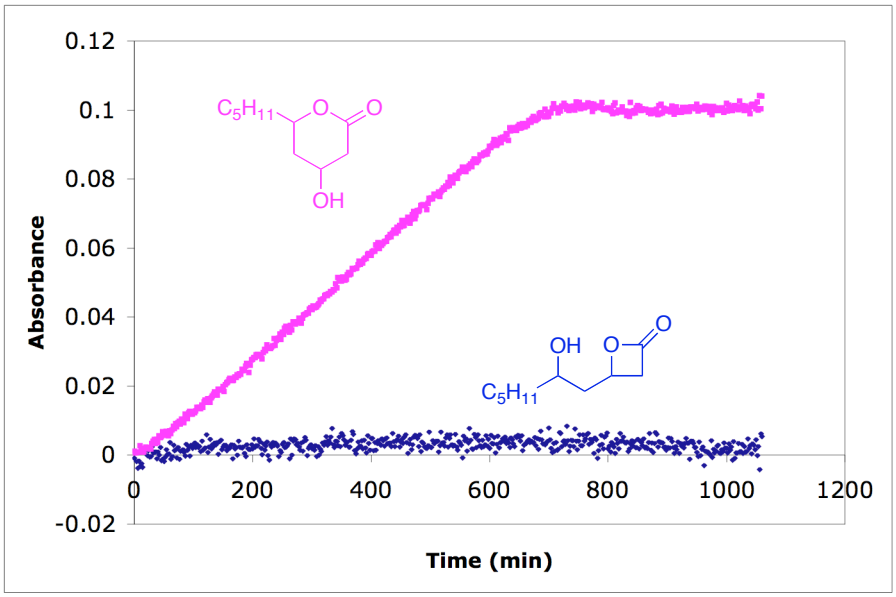


Figure S1: Carbonylation of 4-hydroxy-1,2-epoxynonane (**6**) monitored by in situ IR spectroscopy.

Isomerization of β-lactone (8) monitored by in situ IR spectroscopy: A mixture of **7** and **8** was prepared under standard carbonylation conditions using catalyst **1** (see Table 1, entry 1). Catalyst residue was removed by passing the crude reaction mixture though a plug of silica with CH_2Cl_2 and removing solvent in vacuo. The lactone mixture was then dried over activated 4 Å molecular sieves and degassed three times by freeze-pump-thaw cycles.

The dried Parr reactor was connected to the React-IR and a background spectrum was acquired. Next, 930 mg (5.0 mmol) of **7**/**8** in 5 mL DME was added to the reactor which was pressured to 800 psi with CO. The reactor was heated to 60 ˚C while acquiring

a spectrum every minute until the absorbances (CO stretches measured at 1744 cm^{-1} and 1827 cm^{-1} for δ-lactone and β-lactone, respectively) of the two lactones remained constant. The reactor was then carefully vented to 50 psi CO and a solution of 0.1 mmol $HCo(CO)_4$ in 5 mL DME was added via syringe through the injector port. The reactor was then repressured to 800 psi CO and the absorbances of **7** and **8** were monitored by continuing to acquire IR spectra every minute. The profile of the IR spectra is shown in Figure S2. Since no isomerization of **8** to **7** is observed under the reaction conditions, **8** is eliminated as a possible intermediate in the carbonylation of **6** to **7**.

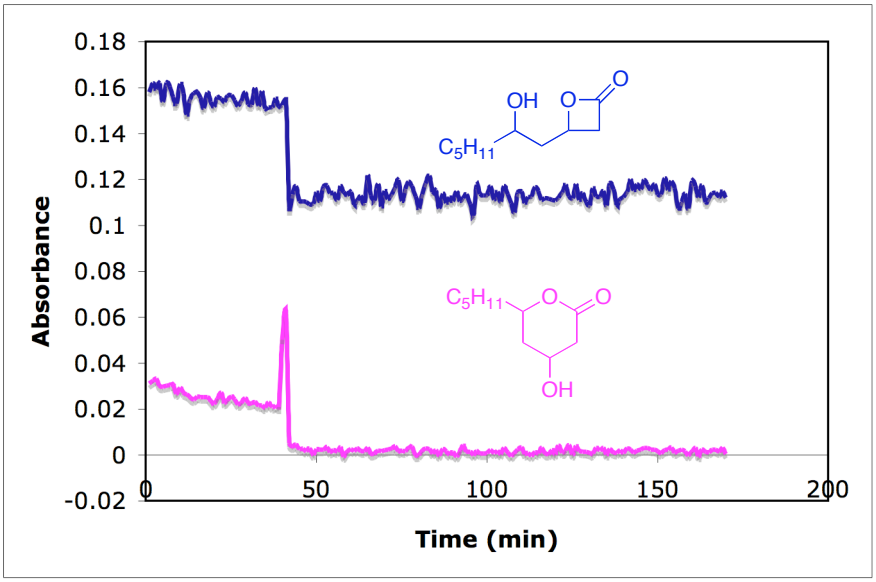
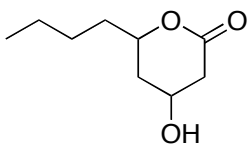


Figure S2: β-Lactone **8** and δ-lactone **7** under standard reaction conditions monitored by in situ IR spectroscopy. The spike and subsequent drop in absorbances at 40 minutes is due to venting the CO pressure in the reactor and dilution of the reaction mixture by addition of catalyst solution. The unchanging absorbances of both lactones after catalyst addition indicates that **7** is not formed from **8**, and therefore **8** is not an intermediate in the carbonylation reaction.

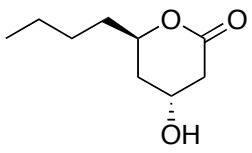
Characterization of New δ-Lactones:



7b

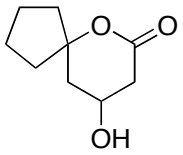
6-Butyl-4-hydroxy-δ-lactone (**7b**): ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 0.89 (t, ^3J = 6.9 Hz, 6H), 1.21-1.79 (m, 14H), 1.96 (dddd, ^4J = 1.6 Hz, ^3J = 3.6 Hz, ^3J = 5.4 Hz, ^2J = 14.4 Hz, 1H), 2.24 (dddd, ^4J = 1.1 Hz, ^3J = 2.8 Hz, ^3J = 5.1 Hz, ^2J = 13.8 Hz, 1H), 2.43 (dd, ^3J = 7.8 Hz, ^2J = 17.1 Hz, 1H), 2.59 (ddd, ^4J = 1.6 Hz, ^3J = 3.6 Hz, ^2J = 17.7, 1H), 2.69 (dd, ^3J = 4.8 Hz, ^2J = 17.7 Hz, 1H), 2.79-2.97 (m, 3H), 4.12-4.29 (m, 2H), 4.30-4.39 (m, 1H), 4.68 (dddd, ^3J = 3.1 Hz, ^3J = 5.1 Hz, ^3J = 7.5 Hz, ^3J = 11.1 Hz, 1H); ^{13}C NMR (δ, $CDCl_3$,

75 MHz) 14.08, 14.10, 22.58, 22.62, 27.12, 35.35, 35.94, 37.91, 38.77, 39.66, 62.70, 63.88, 76.34, 77.72, 171.41, 171.59. IR (neat, NaCl): ν_{CO} = 1719 cm^{-1}, ν_{OH} = 3420 cm^{-1}. HRMS (EI) calculated ($C_9H_{16}O_3$) 172.1100; measured 172.1102, fit 1.4 ppm.



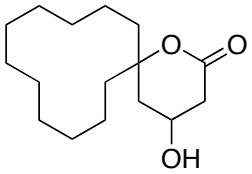
(*R,R*)-7b

(*4R, 6R*)-6-Butyl-4-hydroxy-δ-lactone (***R,R*-7b**): ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 0.89 (t, ^3J = 6.9 Hz, 3H), 1.24-1.76 (m, 7H), 1.95 (dddd, ^4J = 1.6 Hz, ^3J = 4.8 Hz, ^3J = 3.3 Hz, ^2J = 14.4 Hz, 1H), 2.58 (ddd, ^4J = 1.6 Hz, ^3J = 3.6 Hz, ^2J = 17.7 Hz, 1H), 2.68 (dd, ^3J = 4.8 Hz, ^2J = 17.7 Hz, 1H), 2.97 (d, ^3J = 3.3 Hz, 1H), 4.30-4.37 (m, 1H), 4.67 (dddd, ^3J = 3.1 Hz, ^3J = 5.1 Hz, ^3J = 7.5 Hz, ^3J = 11.1 Hz, 1H); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) 14.09, 22.61, 27.11, 35.33, 35.94, 38.74, 62.65, 76.34, 171.45. IR (neat, NaCl): ν_{CO} = 1719 cm^{-1}, ν_{OH} = 3423 cm^{-1}. HRMS (EI) calculated ($C_9H_{16}O_3$) 172.1100; measured 172.1102, fit 1.4 ppm. $[\alpha]^{23}_D$ +32.6 (*c* = 1.0, $CHCl_3$).[22]



7e

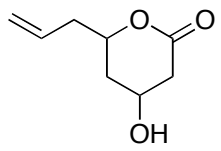
9-Hydroxy-6-oxaspiro(4.5)-decan-7-one (**7e**): ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 1.56-2.17 (m, 11H), 2.42 (dd, ^3J = 8.4 Hz, ^2J = 17.7 Hz, 1H), 2.93 (ddd, ^4J = 1.6 Hz, ^3J = 6.0 Hz, ^2J = 17.7 Hz, 1H), 4.26 (dddd, ^3J = 3.9 Hz, ^3J = 4.5 Hz, ^3J = 6.9 Hz, ^3J = 7.5 Hz, 1H); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) 23.58, 24.01, 39.57, 39.85, 40.67, 41.48, 63.30, 91.40, 170.50. IR (neat, NaCl): ν_{CO} = 1724 cm^{-1}, ν_{OH} = 3420 cm^{-1}. HRMS (EI) calculated ($C_9H_{14}O_3$) 170.0943; measured 170.0939, fit -2.4 ppm.



7f

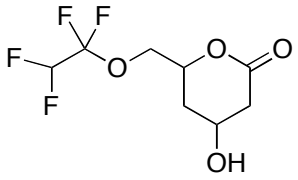
4-Hydroxy-1-oxaspiro(5.11)heptadecan-2-one (**7f**): ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 1.21-1.64 (m, 21H), 1.17-2.01 (m, 3H), 2.17 (ddd, ^4J = 1.7 Hz, ^3J = 4.5 Hz, ^2J = 13.5 Hz, 1H),

2.38 (dd, ^3J = 9.0 Hz, ^2J = 17.7 Hz, 1H), 2.96 (ddd, ^4J = 1.8 Hz, ^3J = 6.0 Hz, ^2J = 17.7 Hz, 1H), 4.27 (dddd, ^3J = 3.3 Hz, ^3J = 4.5 Hz, ^3J = 5.7 Hz, ^3J = 8.1 Hz, 1H); ^{13}C NMR (δ, $CDCl_3$, 75 MHz) 19.06, 19.75, 22.13, 22.57, 22.64, 26.11, 26.25, 33.69, 36.22, 39.88, 41.02, 62.59, 86.07, 170.02. IR (neat, NaCl): ν_{CO} = 1707 cm^{-1}, ν_{OH} = 3423 cm^{-1}. HRMS (EI) calculated ($C_{16}H_{28}O_3$) 268.2039; measured 268.2025, fit -1.4 ppm.



7g

6-Allyl-4-hydroxy-δ-lactone (**7g**): ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 1.53-1.80 (m, 2H), 1.97 (dddd, ^4J = 1.8 Hz, ^3J = 3.4 Hz, ^3J = 5.0 Hz, ^2J = 14.5 Hz, 1H), 2.26 (dddd, ^4J = 1.2 Hz, ^3J = 2.9 Hz, ^3J = 4.8 Hz, ^2J = 13.6 Hz, 1H), 2.35-2.57 (m, 5H), 2.61 (ddd, ^4J = 1.7 Hz, ^3J = 3.5 Hz, ^2J = 17.7 Hz, 1H), 2.71 (dd, ^3J = 4.7 Hz, ^2J = 17.7 Hz, 1H), 2.90 (ddd, ^4J = 1.1 Hz, ^3J = 5.9 Hz, ^2J = 17.1 Hz, 1H), 4.18-4.31 (m, 2H), 4.39 (dddd, ^3J = 3.7 Hz, ^3J = 3.7 Hz, ^3J = 3.7 Hz, ^3J = 10.8 Hz, 1H), 4.77 (dddd, ^3J = 3.1 Hz, ^3J = 6.1 Hz, ^3J = 9.1 Hz, ^3J = 11.7 Hz, 1H), 5.07-5.21 (m, 4H), 5.72-5.90 (m, 2H); ^{13}C NMR (δ, $CDCl_3$, 125 MHz) 35.28, 37.36, 38.75, 39.69, 39.78, 39.83, 62.86, 64.03, 75.29, 76.73, 119.03, 119.27, 132.29, 132.56, 170.63, 170.79. IR (neat, NaCl): ν_{CO} = 1733 cm^{-1}, ν_{OH} = 3427 cm^{-1}. HRMS (EI) calculated ($C_5H_7O_3$) 115.0395; measured 115.0393, fit -2.0 ppm.



7h

6-(1,1,2,2-Tetrafluoroethoxymethyl)-4-hydroxy-δ-lactone (**7h**): ^{1}H NMR (δ, $CDCl_3$, 300 MHz) 1.67-2.02 (m, 4H), 2.30 (dddd, ^4J = 1.5 Hz, ^3J = 3.6 Hz, ^3J = 5.1 Hz, ^2J = 13.8 Hz, 1H), 2.52 (dd, ^3J = 8.1, ^2J = 17.4 Hz, 1H), 2.60-2.69 (m, 1H), 2.75 (dd, ^3J = 4.2 Hz, ^2J = 18.0 Hz, 1H), 2.94 (ddd, ^4J = 1.3 Hz, ^3J = 5.7 Hz, ^2J = 17.4 Hz, 1H), 4.10 (dd, ^3J = 4.5 Hz, ^2J = 10.8 Hz, 1H), 4.15 (d, ^3J = 4.8 Hz, 1H), 4.22 (dd, ^3J = 3.6 Hz, ^2J = 10.8 Hz, 1H), 4.23-4.38 (m, 1H), 4.44-4.54 (m, 2H), 4.97 (dddd, ^3J = 4.0 Hz, ^3J = 4.0 Hz, ^3J = 4.0 Hz, ^3J = 10.7 Hz, 1H), 5.75 (tt, ^3J = 2.7 Hz, ^2J = 54.0 Hz, 2H); ^{13}C NMR (δ, $CDCl_3$, 125 MHz) 31.51, 33.60, 38.60, 39.50, 62.49, 63.51, 65.32 (t, ^3J = 5.0 Hz), 65.49 (t, ^3J = 5.0 Hz), 73.22, 74.44, 107.71 (tt, ^2J = 41.3 Hz, J = 248.8 Hz), 107.75 (tt, ^2J = 41.3 Hz, J = 248.8 Hz), 169.65, 169.72; Note: The CF_2 carbon was not definitively identified. ^{19}F NMR (δ, $CDCl_3$, 470 MHz) -94.81, -139.88. IR (neat, NaCl): ν_{CO} = 1732 cm^{-1}, ν_{OH} = 3428 cm^{-1}. HRMS (EI) calculated ($C_8H_{10}O_4F_4$) 246.0515; measured 246.0518, fit 1.1 ppm.

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(21) Byrne, C. M.; Church, T. L.; Kramer, J. W.; Lobkovsky, E. B.; Coates, G. W. *Manuscript in Preparation*.
(23) The *R,R* diastereomer of 6-pentyl-4-hydroxy-δ-lactone has been reported: $[\alpha]^{23}_{D}$ +32.1 (*c* = 0.92, $CHCl_3$). Romeyke, Y.; Keller, M.; Kluge, H.; Grabley, S.; Hammann, P. *Tetrahedron* **1991**, *47*, 3335-3339. The optical rotation of **(*R,R*)-7b** is in line with the literature report for the analogous compound in both magnitude and direction of rotation.

Figure S3: ^{1}H NMR spectrum of 6-methyl-4-hydroxy-δ-lactone (**7a**)
$CDCl_3$, 300 MHz

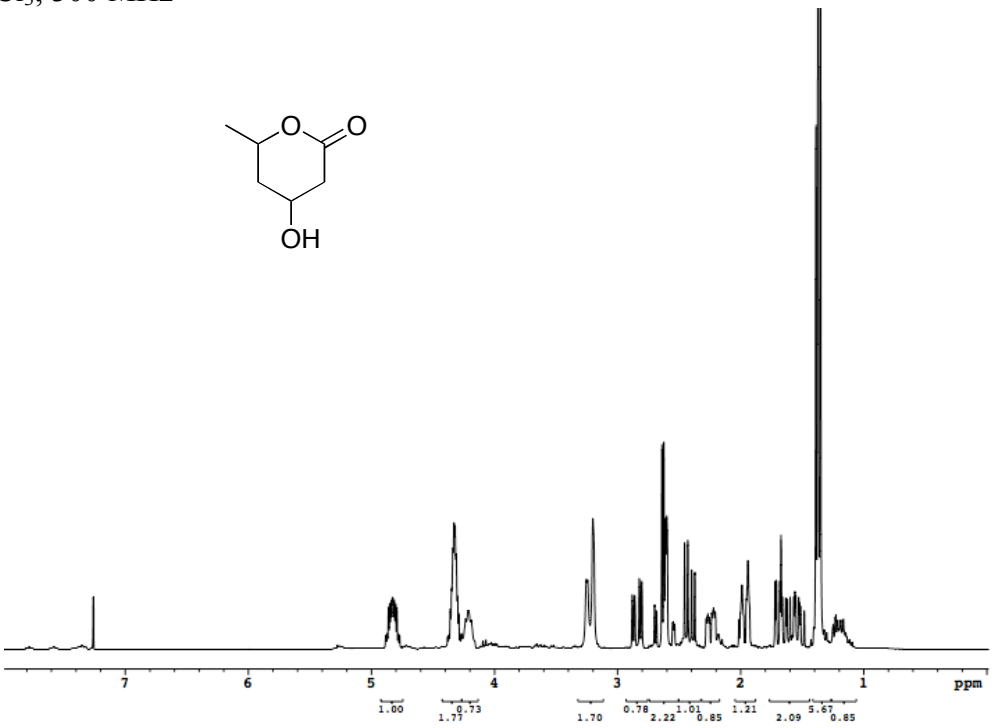

Figure S4: ^{13}C NMR spectrum of 6-methyl-4-hydroxy-δ-lactone (**7a**)
$CDCl_3$, 75 MHz

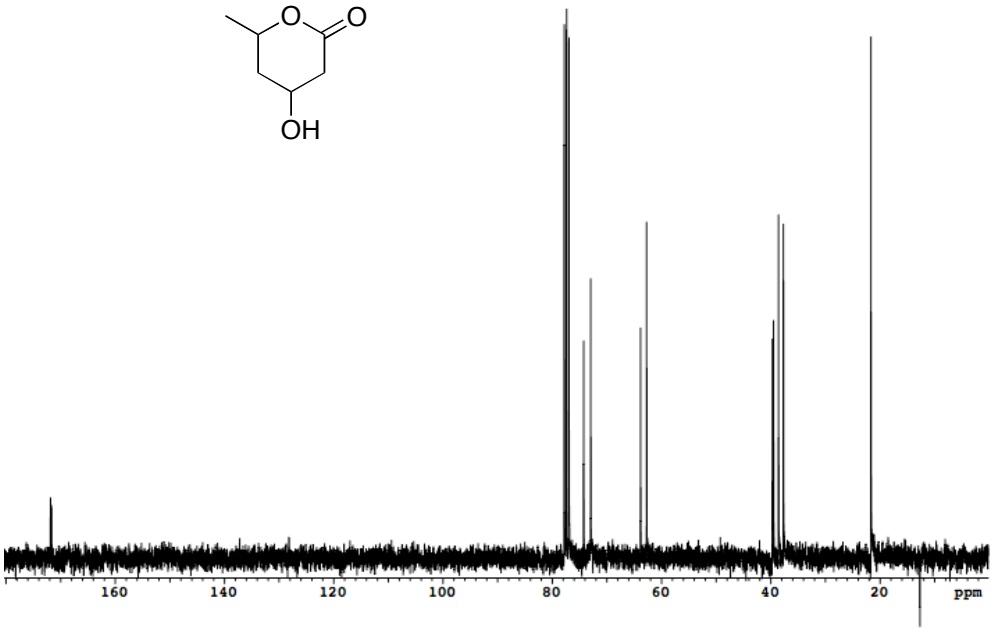

Figure S5: ^{1}H NMR spectrum of 6-butyl-4-hydroxy-δ-lactone (**7b**)
$CDCl_3$, 300 MHz

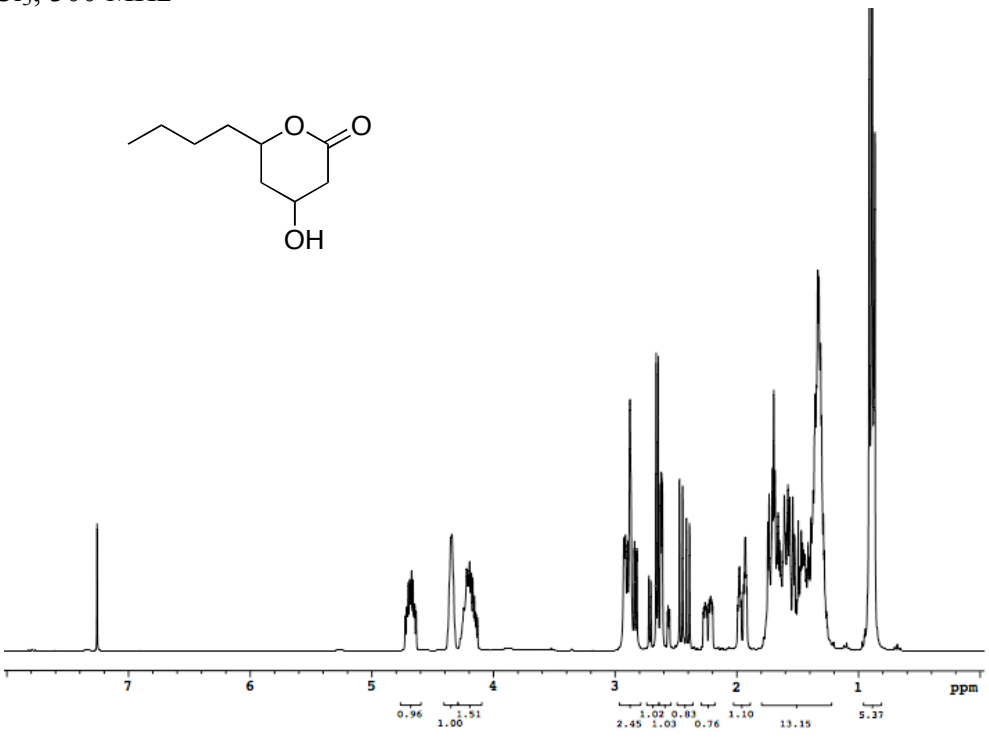

Figure S6: ^{13}C NMR spectrum of 6-butyl-4-hydroxy-δ-lactone (**7b**)
$CDCl_3$, 75 MHz

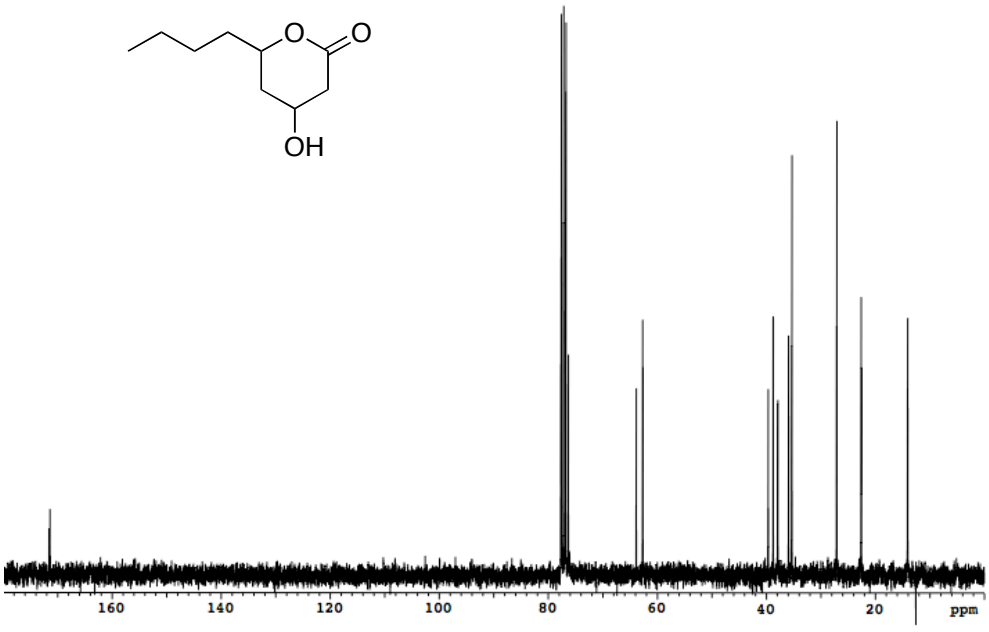

Figure S7: ^{1}H NMR spectrum of (*4R, 6R*)-6-butyl-4-hydroxy-δ-lactone (***R,R*-7b**) $CDCl_3$, 300 MHz

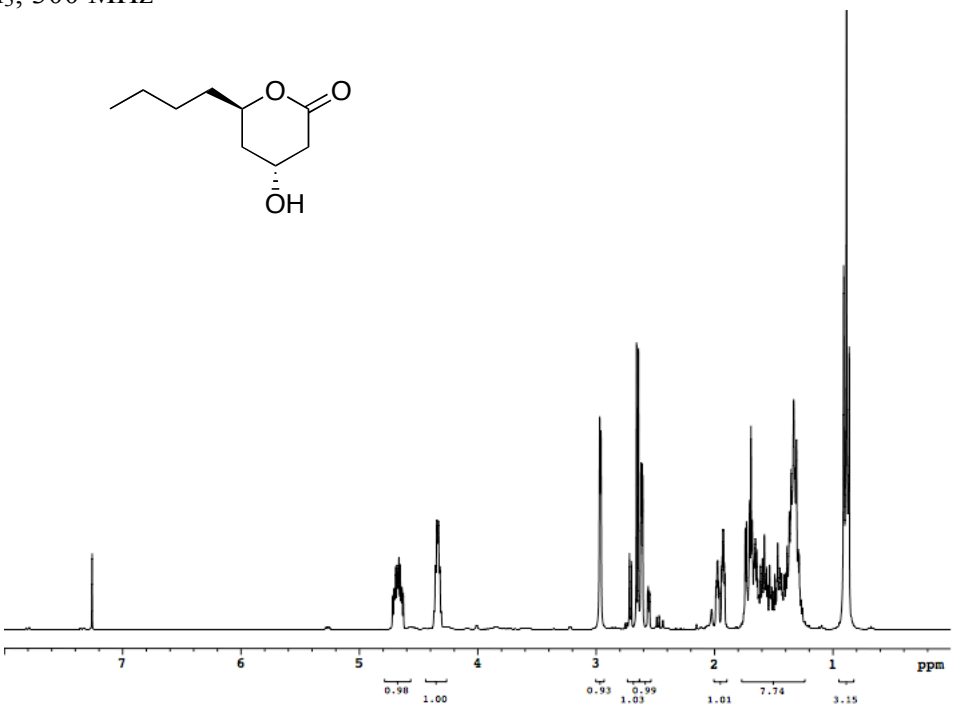

Figure S8: ^{1}H NMR spectrum of (*4R, 6R*)-6-butyl-4-hydroxy-δ-lactone (***R,R*-7b**) $CDCl_3$, 75 MHz

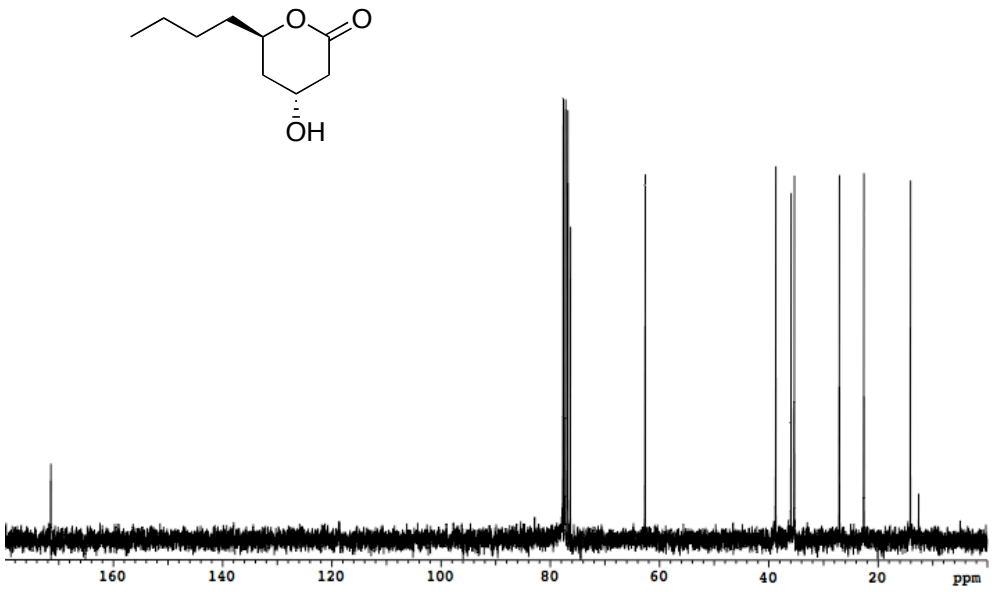

Figure S9: ^{1}H NMR spectrum of 6-phenyl-4-hydroxy-δ-lactone (**7c**)
$CDCl_3$, 300 MHz

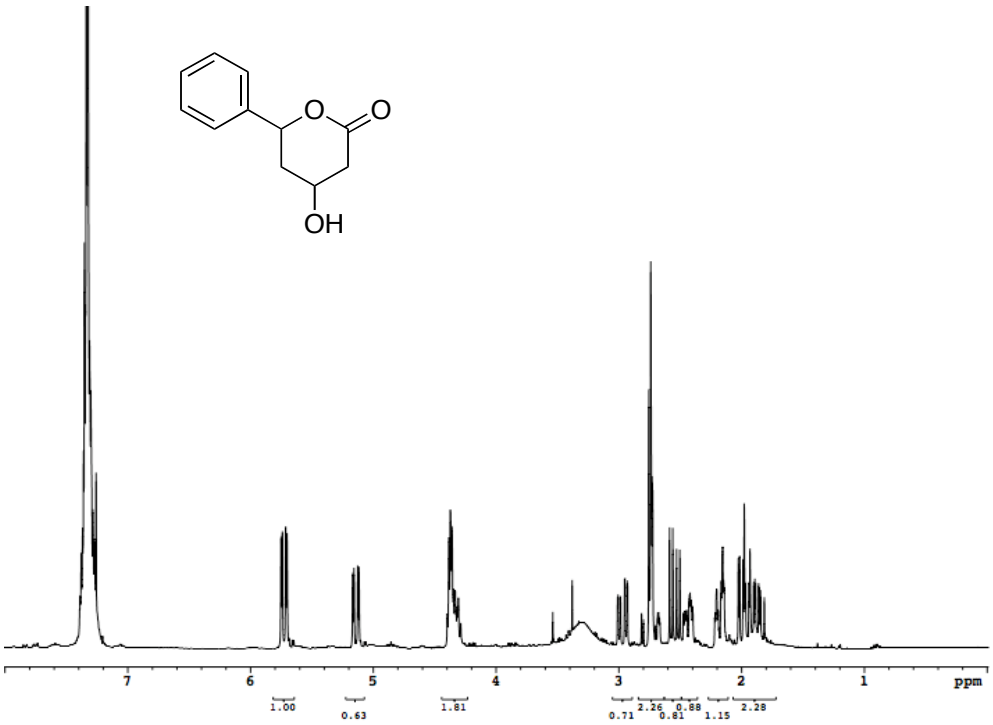

Figure S10: ^{13}C NMR spectrum of 6-phenyl-4-hydroxy-δ-lactone (**7c**)
$CDCl_3$, 125 MHz

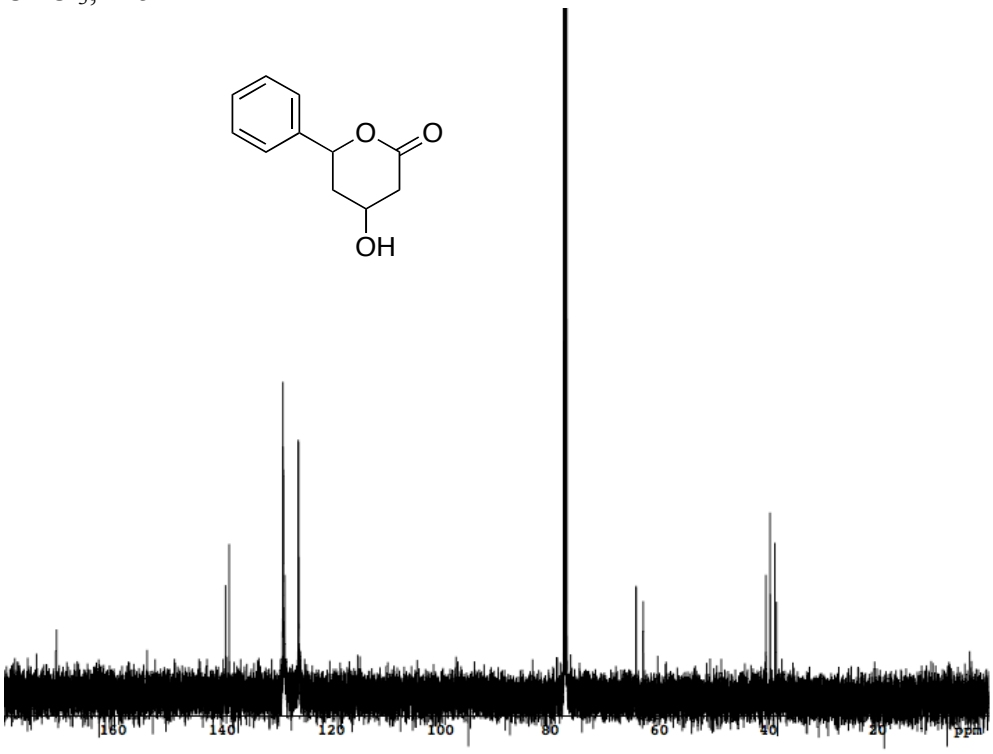

Figure S11: ^{1}H NMR spectrum of 6-ethyl-6-methyl-4-hydroxy-δ-lactone (**7d**) $CDCl_3$, 300 MHz

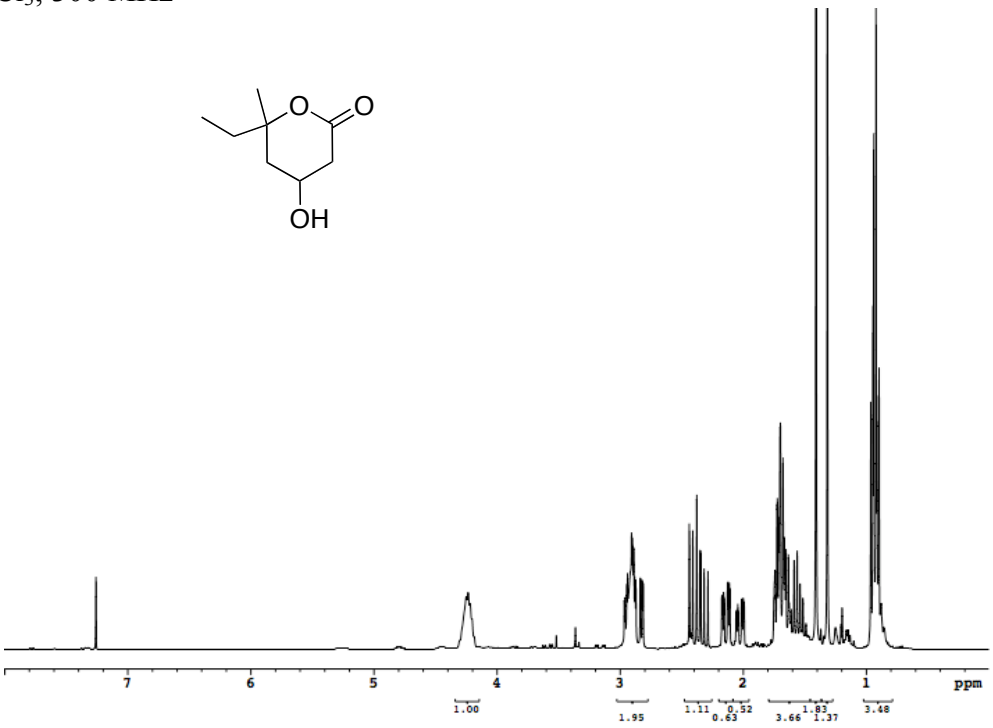

Figure S12: ^{13}C NMR spectrum of 6-ethyl-6-methyl-4-hydroxy-δ-lactone (**7d**) $CDCl_3$, 75 MHz

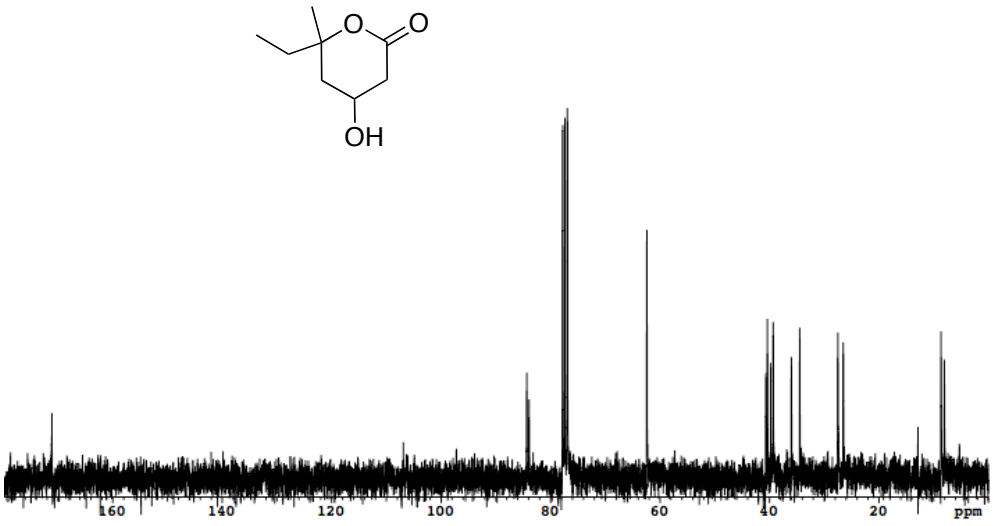

Figure S13: ^{1}H NMR spectrum of 9-hydroxy-6-oxaspiro(4.5)-decan-7-one (**7e**) $CDCl_3$, 300 MHz

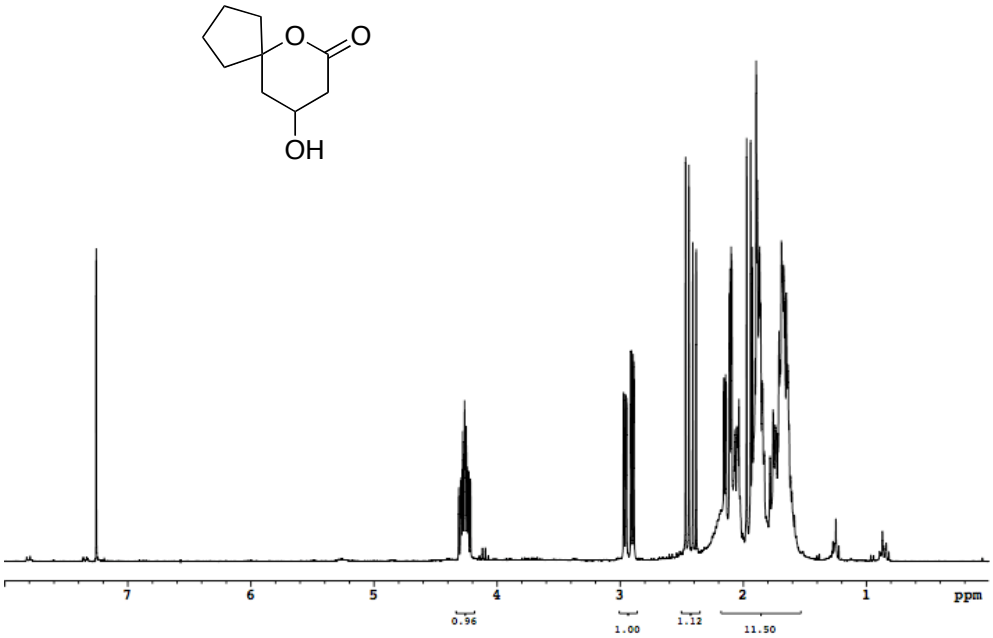

Figure S14: ^{13}C NMR spectrum of 9-hydroxy-6-oxaspiro(4.5)-decan-7-one (**7e**) $CDCl_3$, 75 MHz

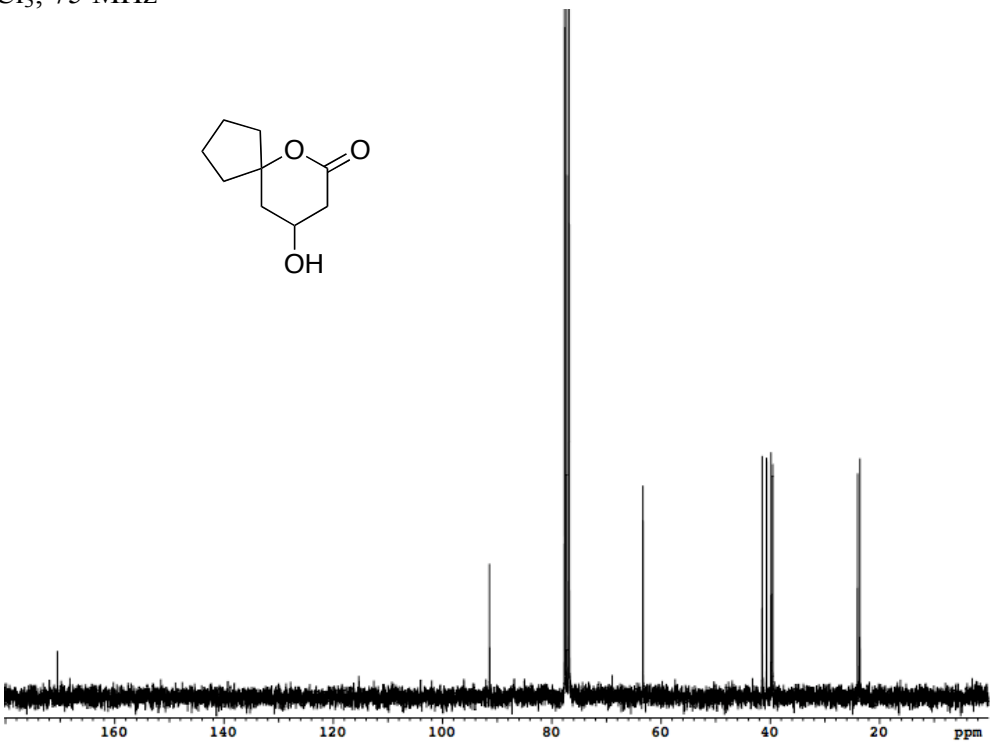

Figure S15: ^{1}H NMR spectrum of 4-hydroxy-1-oxaspiro(5.11)heptadecan-2-one (**7f**) $CDCl_3$, 300 MHz

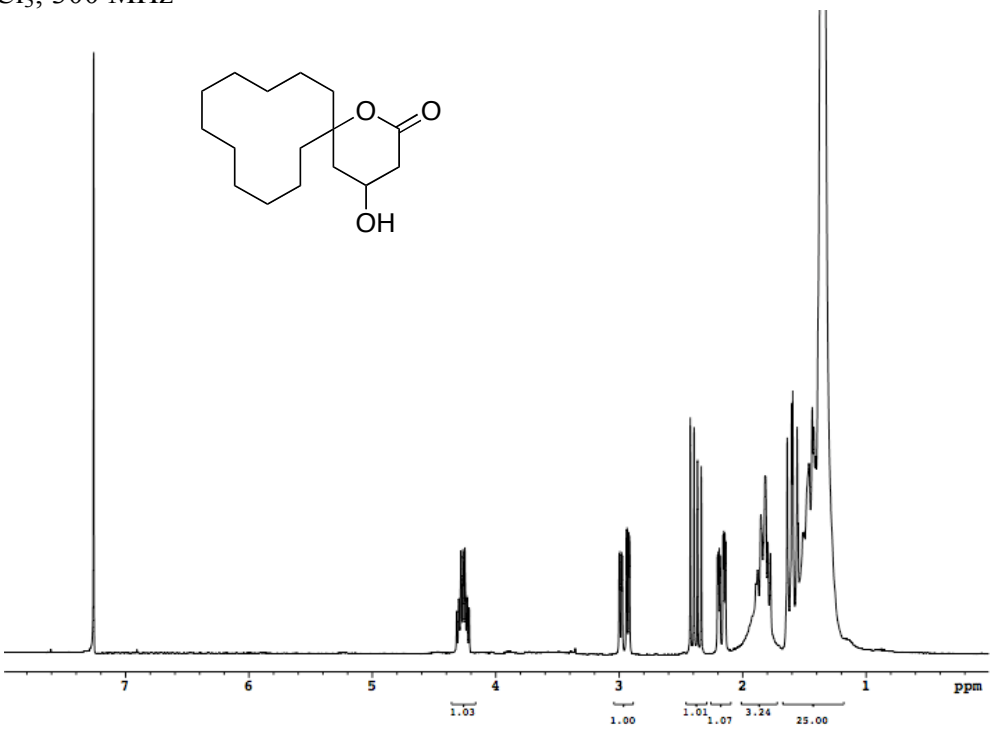

Figure S16: ^{13}C NMR specrum of 4-hydroxy-1-oxaspiro(5.11)heptadecan-2-one (**7f**) $CDCl_3$, 75 MHz

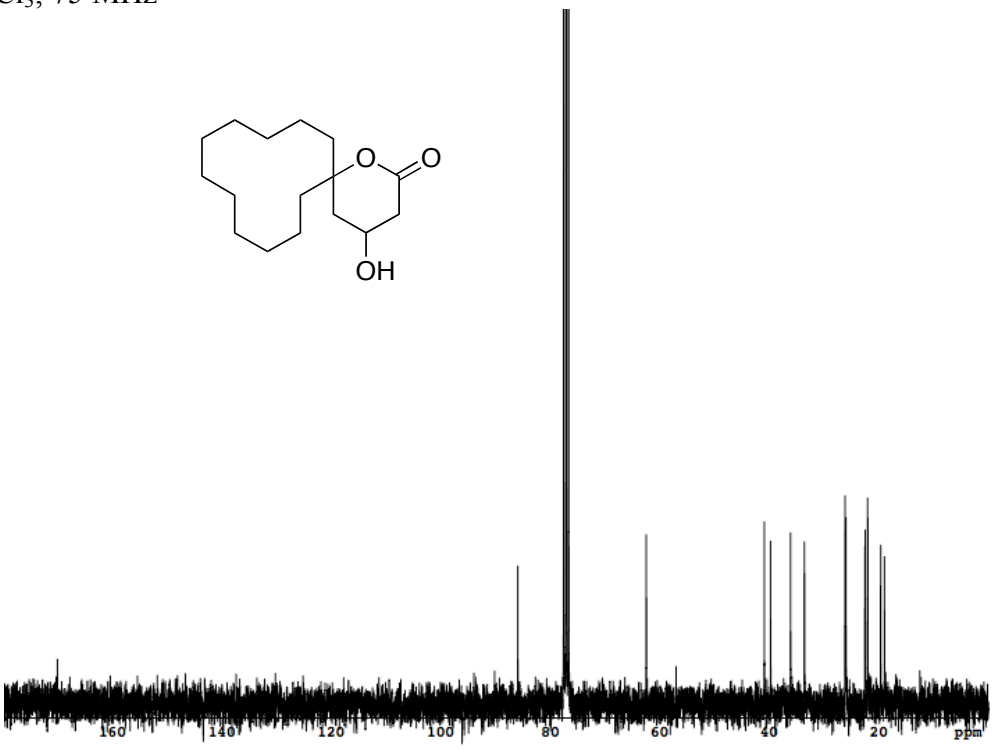

Figure S17: ^{1}H NMR spectrum of 6-allyl-4-hydroxy-δ-lactone (**7g**)
$CDCl_3$, 300 MHz

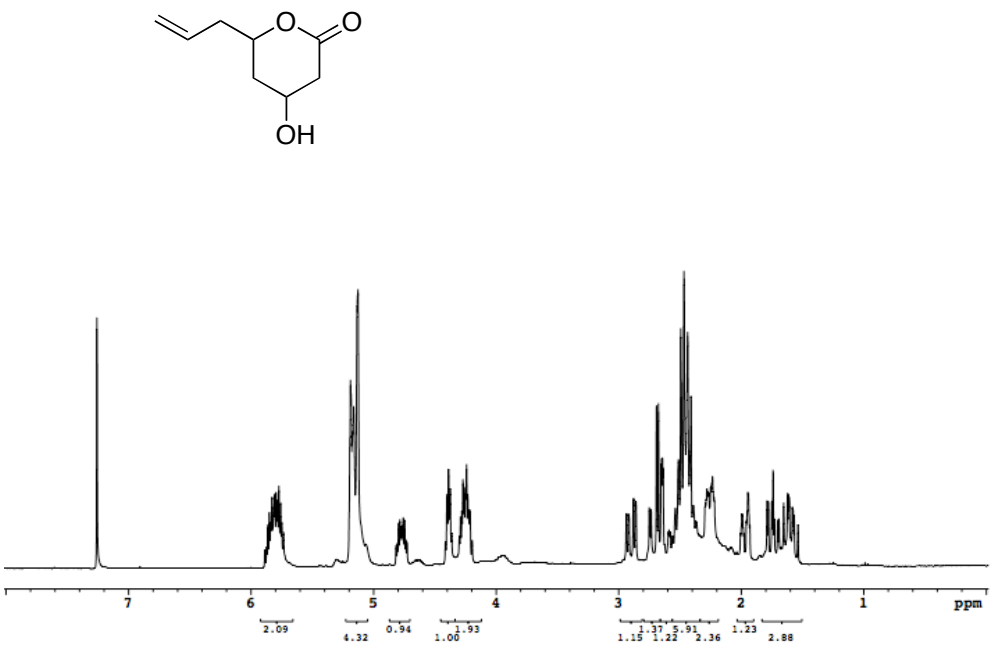

Figure S18: ^{13}C NMR spectrum of 6-allyl-4-hydroxy-δ-lactone (**7g**)
$CDCl_3$, 125 MHz

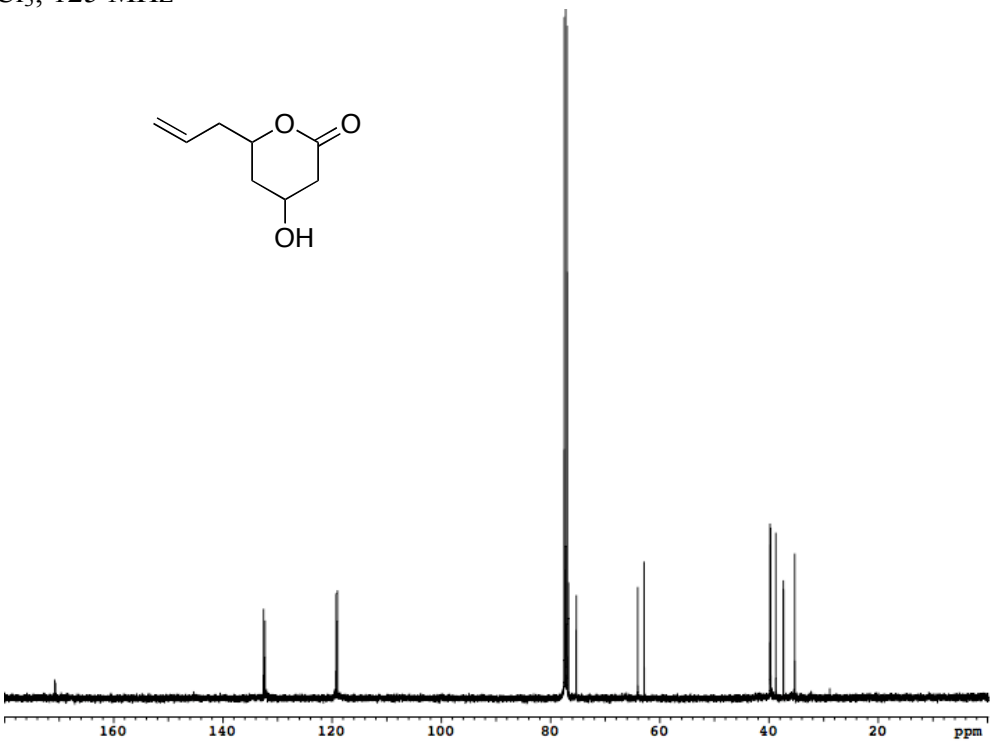

Figure S19: ^{1}H NMR spectrum of 6-(1,1,2,2-tetrafluoroethoxymethyl)-4-hydroxy-δ-lactone (**7h**)
$CDCl_3$, 300 MHz

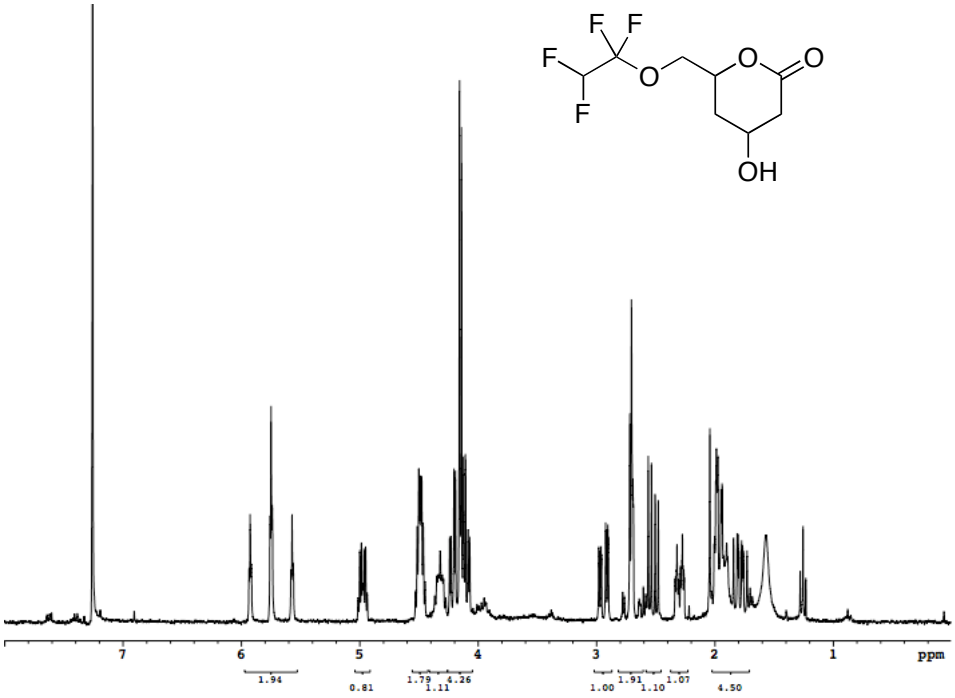

Figure S20: ^{13}C NMR spectrum of 6-(1,1,2,2-tetrafluoroethoxymethyl)-4-hydroxy-δ-lactone (**7h**)
$CDCl_3$, 125 MHz

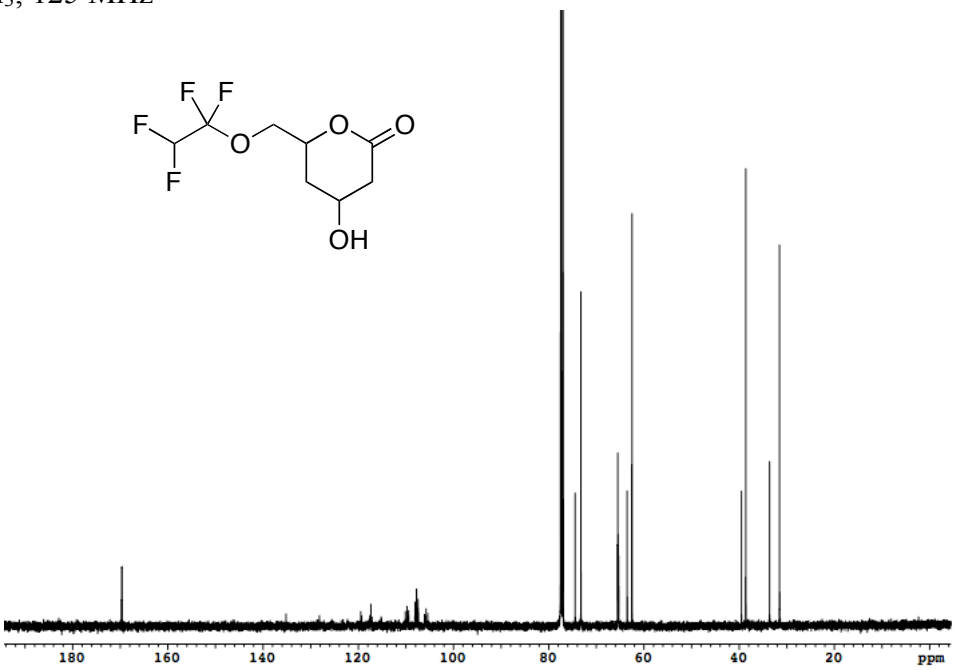

Figure S21: ^{19}F NMR spectrum of 6-(1,1,2,2-tetrafluoroethoxymethyl)-4-hydroxy-δ-lactone (**7h**)
$CDCl_3$, 470 MHz

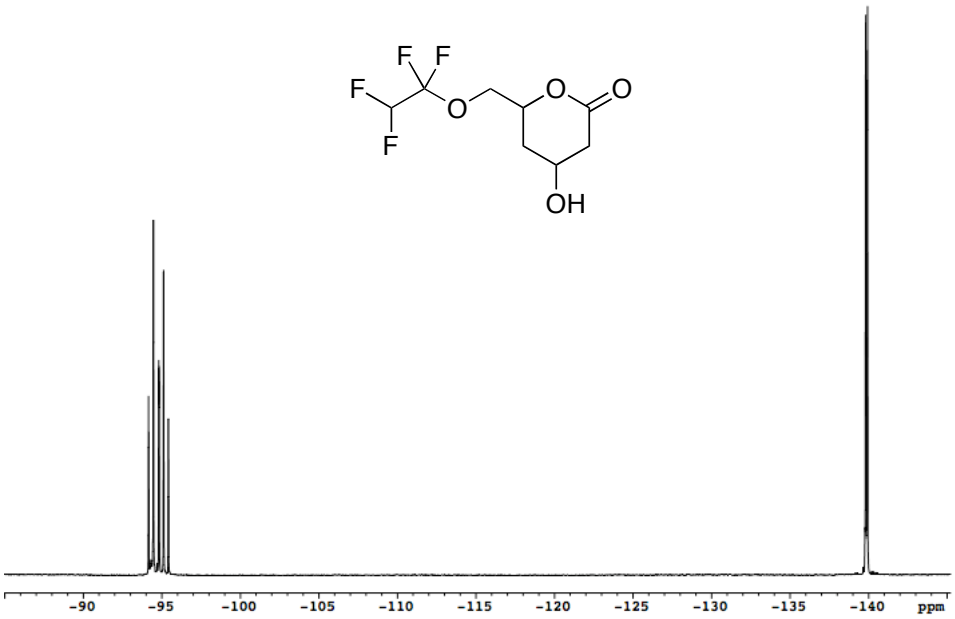

Figure S22: ^{1}H NMR spectrum of 6-(tertbutyldimethylsiloxymethyl)-4-hydroxy-δ-lactone (**7i**)
$CDCl_3$, 300 MHz

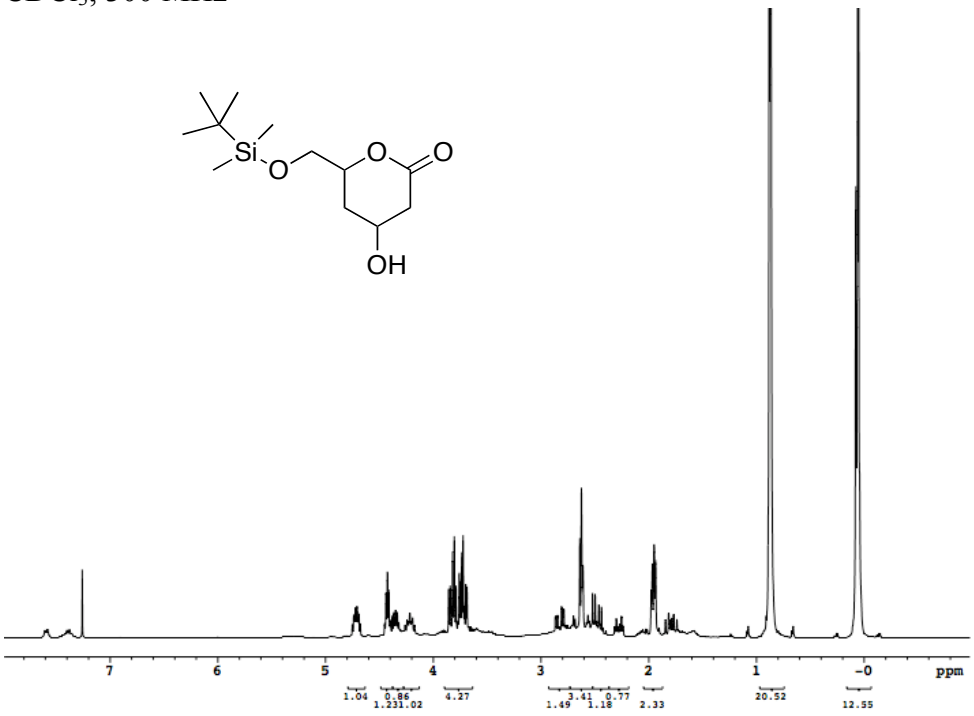

Figure S23: ^{13}C NMR spectrum of 6-(tertbutyldimethylsiloxymethyl)-4-hydroxy-δ-lactone (**7i**)
$CDCl_3$, 75 MHz

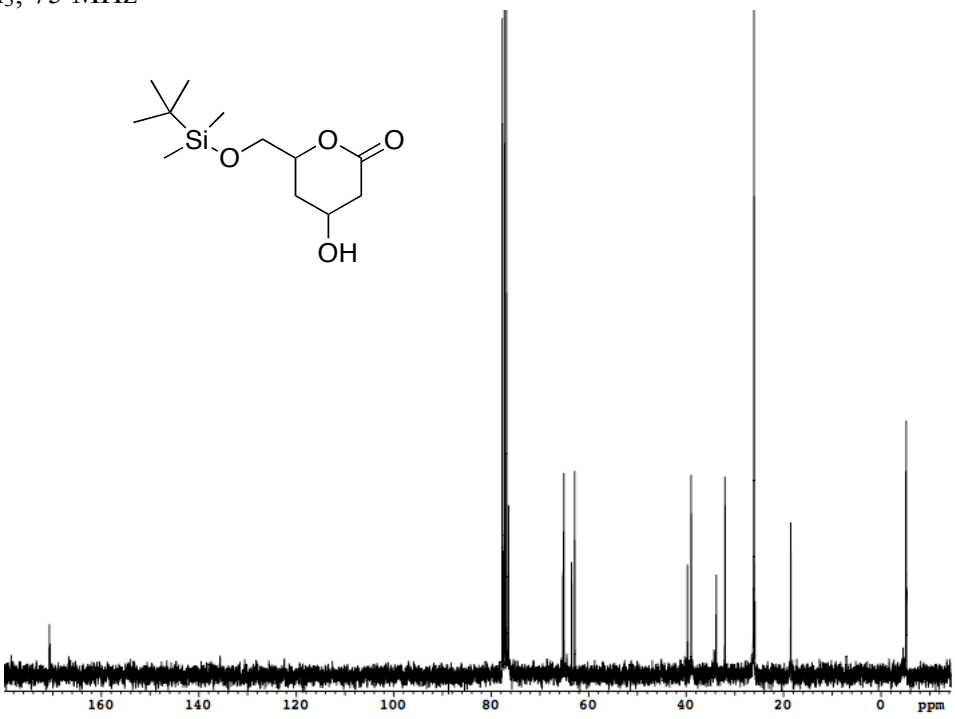

Figure S24: ^{1}H NMR spectrum of 6-(chloromethyl)-4-hydroxy-δ-lactone (**7j**)
$CDCl_3$, 300 MHz

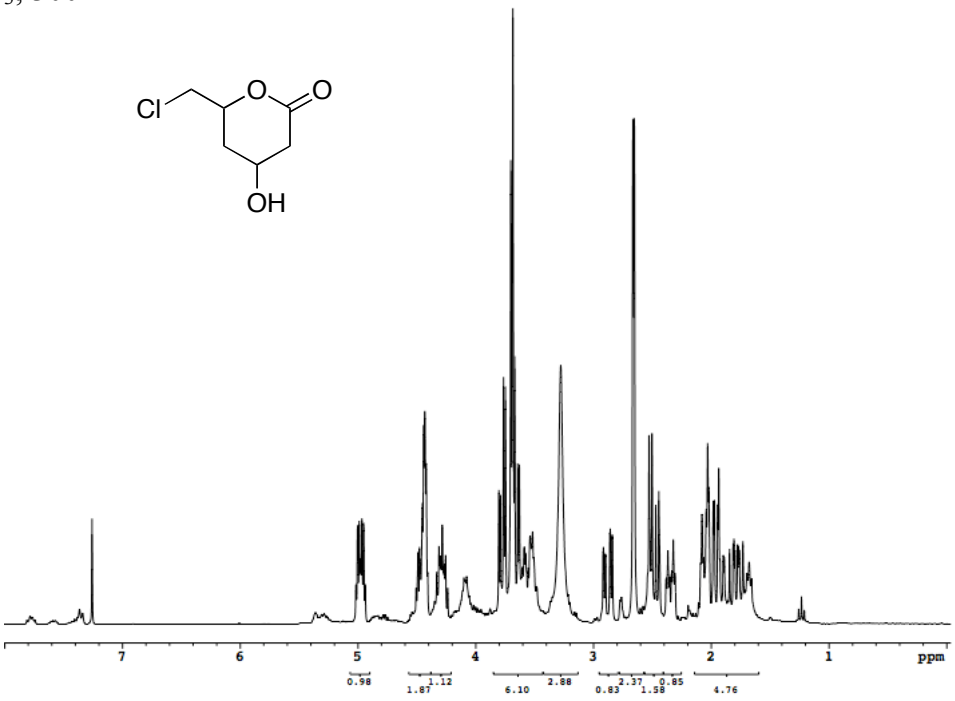

Figure S25: ^{13}C NMR spectrum of 6-(chloromethyl)-4-hydroxy-δ-lactone (**7j**)
$CDCl_3$, 75 MHz