Chapter 3

SYNTHESIS OF β-FLUORINATED CARBONYL COMPOUNDS BY NITRITE-MODIFIED WACKER OXIDATION

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The work described was conducted in collaboration with Dr. Daniel Ziegler, who performed mechanistic experiments, as well as with Brian Carr and Dr. Zachary Wickens, who conceived the project and developed reaction conditions.

Abstract

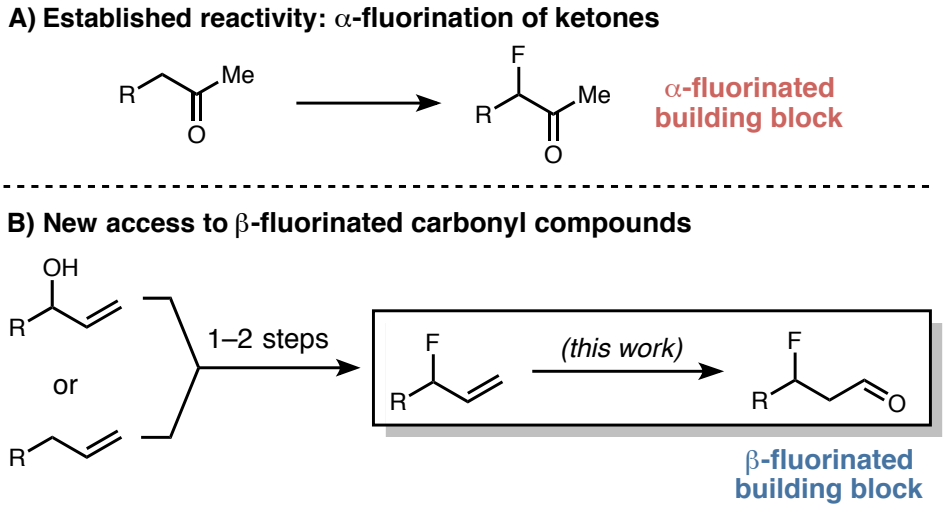
An aldehyde-selective Wacker-type oxidation of allylic fluorides employing a nitrite catalyst is described. The method represents a direct route to prepare β-fluorinated aldehydes. Allylic fluorides bearing a variety of functional groups are transformed in high yield and very high regioselectivity. Additionally, crude aldehyde products serve as versatile intermediates, enabling access to a diverse array of fluorinated building blocks. Preliminary mechanistic investigations suggest that inductive effects have a strong influence on the rate and regioselectivity of oxidation.

Introduction

The demand for organofluorine compounds is rapidly growing as a result of their prevalence in the pharmaceutical,[1] agrochemical,[2] and materials[3] industries. Due to a low abundance of fluorinated chemical feedstocks,[4] the development of efficient routes toward organofluorine building blocks has been recognized as an important challenge in the synthetic community.[5] Traditional fluorination protocols typically employ harsh reagents such as diethylaminosulfur trifluoride (DAST), restricting their tolerance of functional groups. Consequently, careful selection of an appropriate fluorinating agent must often be performed on a case-by-case basis.[6]

Significant progress has been made toward mild, catalytic alkyl fluorination, with much of this work dedicated to installing fluorine atoms adjacent to π systems (Scheme 3.1A).[7] α-Fluorination of carbonyl compounds is achieved efficiently via organo- and transition-metal catalysis.[8] Allylic fluorides can also be readily prepared by regio- and enantioselective methods.[7a-d,f,h] For example, Ir-catalyzed allylic substitution[7d,h] and Pd-catalyzed C–H fluorination[7f] methods can serve as convenient approaches to allylic fluorides.

Despite the depth of research dedicated to α-fluorination of activated π systems, catalytic installation of fluorine β to functional groups remains a major challenge.[9] One promising strategy enables the syntheses of β- and γ- fluorinated ketones via catalytic ring opening of strained cyclopropanols and cyclobutanols, respectively.[10] Alternative methods amenable to producing β-fluorinated carbonyl compounds have been reported,[11] but a general solution employing simple starting materials has yet to be developed. Herein, we report a catalytic approach to directly access β-fluorinated aldehydes from readily accessible allylic fluorides (Scheme 3.1B).



Scheme 3.1. Strategies toward alkylfluorine compounds.

The Wacker reaction is a powerful method[12] for the oxidation of olefins that typically favors Markovnikov selectivity.[13] However, in the presence of proximal functional groups, regioselectivity of oxidation can be difficult to rationally predict.[14] In our recent study of a dicationic Pd-catalyzed Wacker-type oxidation of internal olefins,[15]

inductively withdrawing trifluoromethyl groups were found to substantially enhance selectivity for distal oxidation.[16] In fact, even the oxidation of a terminal olefin, 4,4,4-trifluoro-1-butene, occurred with modest anti-Markovnikov selectivity (3:1 aldehyde/ketone). We therefore reasoned that modified Wacker conditions, combined with the inductive influence of allylic fluorides, could be employed as a general strategy for the synthesis of β-fluorinated aldehydes under mild conditions.

Development of Reaction Conditions

The model allylic fluoride **A** was initially subjected to a range of Wacker-type oxidation conditions toward optimization of aldehyde selectivity.[17] Traditional Tsuji-Wacker conditions proved poorly suited for oxidation of the electron deficient allylic fluoride, resulting in defluorination and no aldehyde selectivity (Figure 3.1a). When subjected to our previously reported dicationic palladium system, this substrate was oxidized in moderate yield with preference for the aldehyde (3:1 aldehyde/ketone; Figure 3.1b), revealing some innate aldehyde selectivity of the substrate.

To emphasize this effect, we next explored nitrite ligands[18] and exogenous nitrite co-catalysts, utilized by Feringa and our own group, respectively, for the catalyst-controlled oxidation of terminal olefins to aldehydes. When **A** was subjected to Feringa's conditions, catalyzed by $[PdNO_2Cl(MeCN)_2]$,[19] high aldehyde selectivity was observed (18:1 aldehyde/ketone), albeit in poor yield (Figure 3.1c). Our group recently developed a Wacker system that employs an exogenous nitrite catalyst in a tBuOH/$MeNO_2$ solvent system, which oxidizes unbiased terminal olefins with anti-Markovnikov selectivity.[20] This nitrite co-catalyzed system oxidized allylic fluoride **A** in moderate yield and high selectivity (26:1 aldehyde/ketone; Figure 3.1d). Further optimization, involving exclusion of water from the reaction system, increased nitromethane concentration, and even a reduction in catalyst loading, resulted in very high selectivity for aldehyde formation (36:1 aldehyde/ketone) in high yield (77%; Figure 3.1e). Since the use of tBuOH has been established as a strategy to enhance aldehyde selectivity in Wacker-type oxidations,[21,22] the importance of the nitrite catalyst and nitromethane as a cosolvent was assessed. Elimination

of these components from the optimized conditions led to diminished aldehyde selectivity (8:1 aldehyde/ketone) and formation of defluorination products (Figure 3.1f).[23]

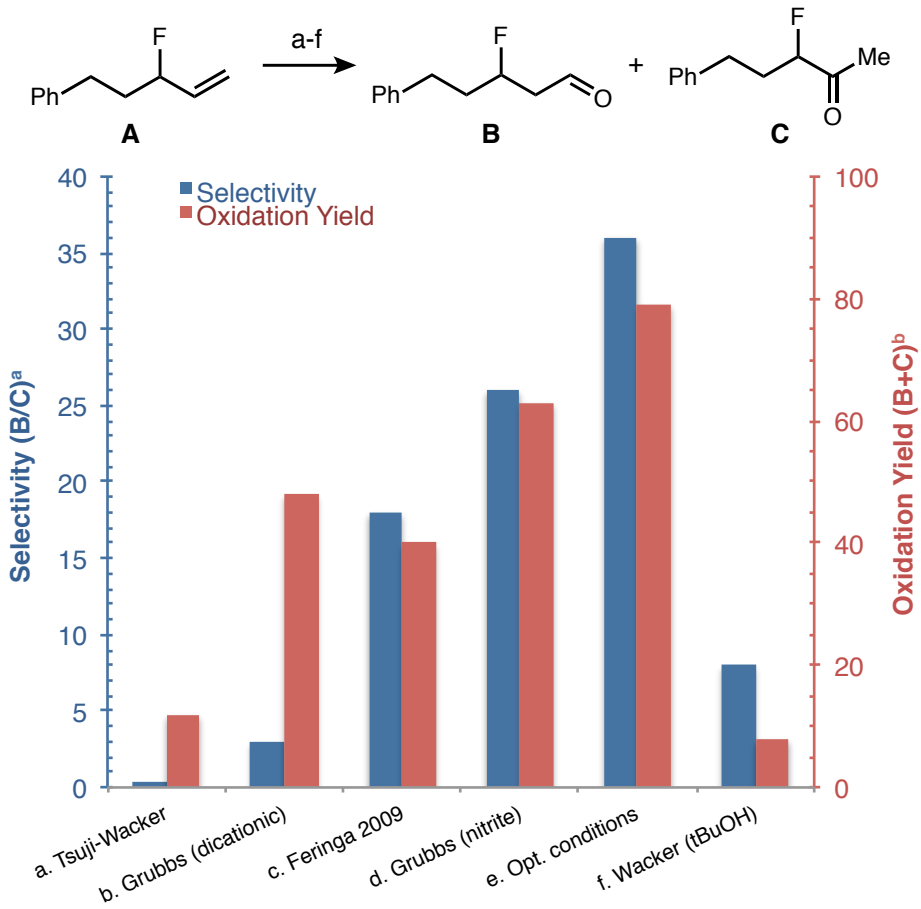
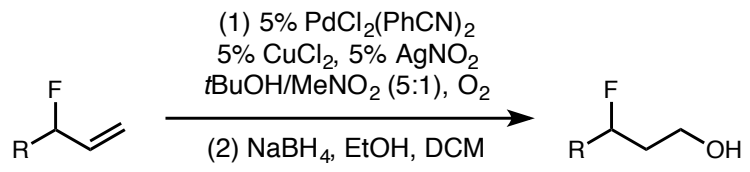


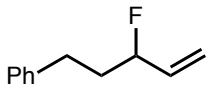
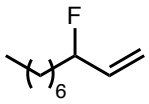
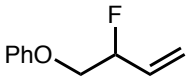
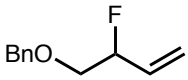
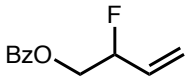
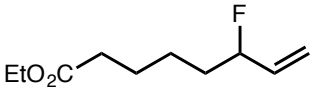
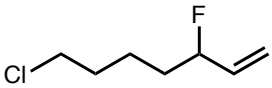
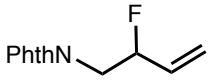
Figure 3.1. Comparison of oxidation conditions with a model substrate. (a) Selectivity (aldehyde/ketone) determined by ^{1}H NMR analysis. (b) Oxidation yield (aldehyde + ketone) determined by ^{1}H NMR analysis versus an internal standard. Only fluorinated products are included. (See Table 3.1 for standard conditions).

Reaction Scope

With optimized conditions in hand, we next explored the reaction scope, and found the method to be well suited for regioselective oxidation of allylic fluorides bearing a variety of functional groups.[24] Branched allylic fluorides without added bias were oxidized to the corresponding β-fluorinated aldehydes in high yield and ≥20:1 selectivity, with an ester and alkyl chloride being well tolerated (Table 3.1, entries 1, 2, 6, and 7). High

Table 3.1. Nitrite-Modified Wacker Oxidations of Allylic Fluorides: Substrate Scope



entry	substrate	yield[a]	selectivity[b]
1		82	≥20:1
2		87	≥20:1
3		94	≥20:1
4		93	≥20:1
5		93	≥20:1
6		72	≥20:1
7		81[c]	≥20:1
8		77	≥20:1

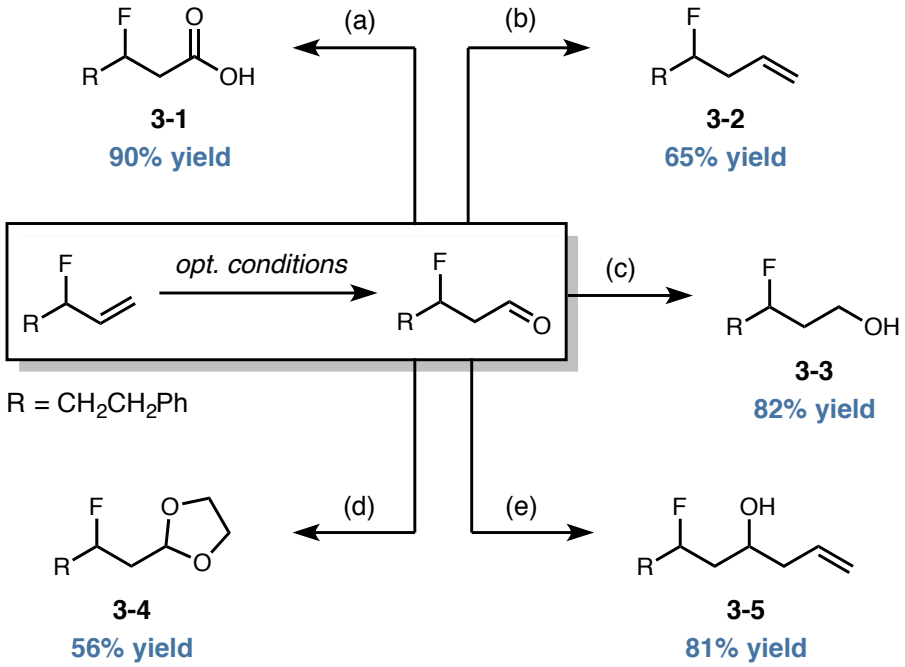
[a]Yield of purified product following $NaBH_4$ reduction. [b]Selectivity (aldehyde:ketone) determined by ^1H NMR analysis of crude reaction mixture prior to reduction. [c]Yield of aldehyde determined by ^1H NMR analysis versus an internal standard.

aldehyde selectivities were maintained for allylic fluorides bearing an additional directing group. Olefins with phenyl and benzyl ethers, benzoate, and phthalimide branches were oxidized to the corresponding aldehydes with only trace levels of ketone detected (entries

3, 4, 5, and 8, respectively). When comparing previous nitrite-modified Wacker oxidations of functionalized olefins, fluoride has shown to be an exceptionally potent directing group.

Derivatization of Products

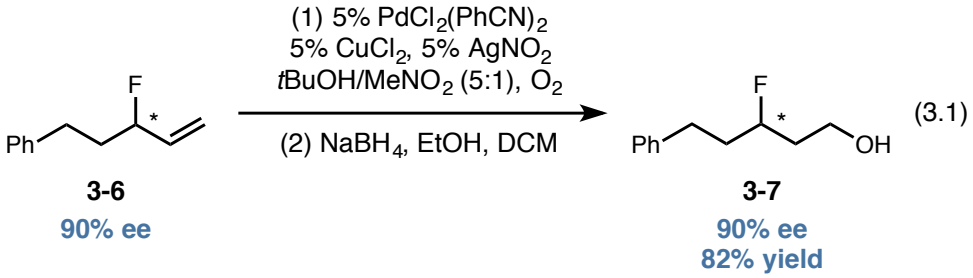
Despite the relative instability of β-fluorinated aldehydes, the high purity of the crude products allows for direct transformation to a variety of organofluorine compounds. Reaction with Oxone furnished the β-fluorinated carboxylic acid **3-1** in excellent yield (Scheme 3.2a). Wittig olefination and protection of the carbonyl were achieved in synthetically useful yields in spite of potential base or acid lability of the fluoride (Scheme 3.2b, d). The aldehyde was reduced nearly quantitatively to γ-fluorinated alcohol **3-3** (Scheme 3.2c). Furthermore, nucleophilic addition to aldehydes provides access to a range of new fluorinated building blocks, demonstrated by the addition of allylB(pin) to produce



Scheme 3.2. Derivatization of a β-fluorinated aldehyde crude product. All derivatizations performed using crude Wacker oxidation product. Yields reported over 2 steps. (a) Oxone, DMF. (b) $MePPh_3Br$, *n*BuLi, THF. (c) $NaBH_4$, DCM/EtOH. (d) *p*TsOH, ethylene glycol, mol. sieves. (e) AllylB(pin), DCM.

homoallylic alcohol **3-5** (Scheme 3.2e). Overall, the efficient preparation of β-fluorinated aldehydes via Wacker-type oxidation serves as a unique synthetic handle to produce diverse fluorinated molecules.

In order to investigate how our method may be used to generate stereodefined organofluorines, we were interested in the aldehyde-selective oxidation of enantioenriched allylic fluoride **3-6**.[7h] Under the optimal reaction conditions, oxidation occurred without erosion of enantiopurity,[25] allowing for the isolation of enantioenriched fluorinated product **3-7** in good yield and ee (Eq. 3.1). This result suggests that Pd-catalyzed olefin isomerization does not occur on the time scale of oxidation to the aldehyde product.



(3.1)

Mechanistic Insights

Having demonstrated the synthetic utility of the transformation, we sought to gain insight into the role of the fluoride in influencing regioselectivity and reactivity. To this end, a study of the distance dependence of regioselectivity on fluoride proximity was conducted. Three alkyl fluoride isomers were synthesized with systematic variation of the distance between fluoride and olefin. The oxidations of these compounds under our standard conditions were then compared along with that of 1-decene (Figure 3.2). The high aldehyde selectivity (96%) in the case of the allylic fluoride (n = 0) depreciates as n increases. A strong preference for oxidation to the aldehyde is maintained in the reaction of a homoallylic fluoride (n = 1), suggesting that this method can provide a convenient route to γ-fluorinated aldehydes. However, aldehyde selectivity diminishes for the analogue fluorinated in a more distal position (n = 2), and poor regioselectivity is observed in the oxidation of the unbiased olefin 1-decene (58%).[26] The gradual loss in selectivity as

fluoride substitution is placed further from the olefin is consistent with a key inductive effect that enhances regioselectivity under these nitrite-modified Wacker conditions.

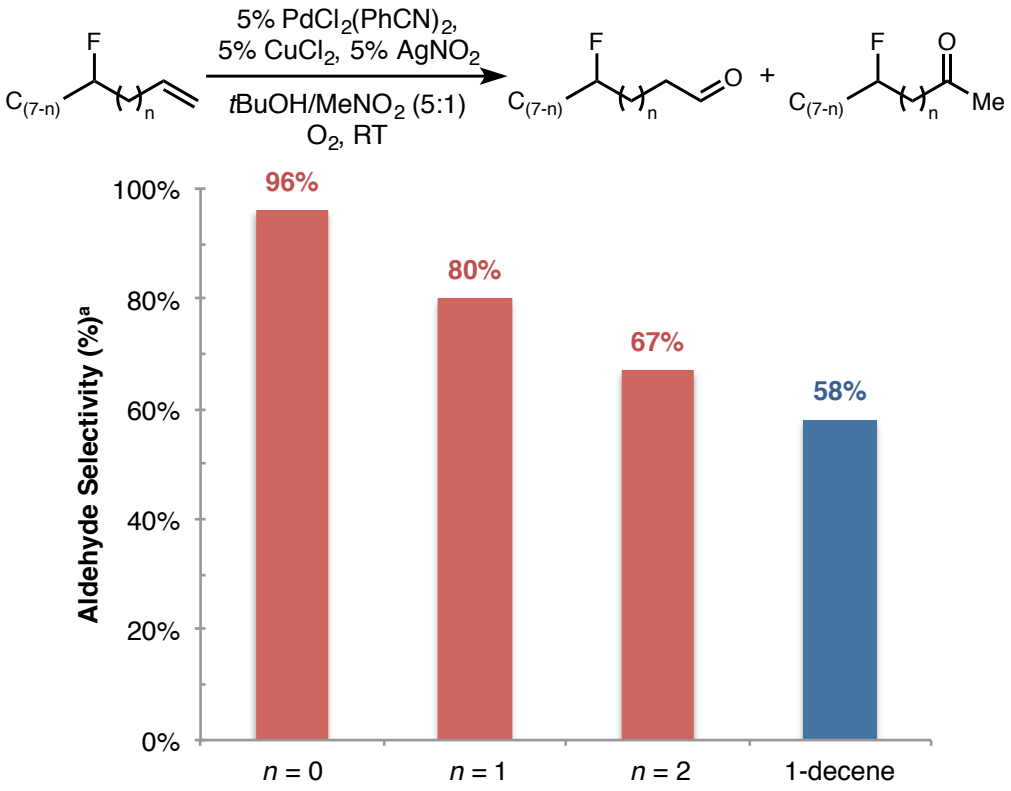


Figure 3.2. Influence of fluoride proximity on regioselectivity of oxidation. [a]Selectivity (aldehyde/total oxidation yield) determined by ^{1}H NMR analysis.

The relative rates of conversion of a fluorinated and non-fluorinated olefin were studied in order to further elucidate the effect of fluoride substitution (Figure 3.3). Individual rate comparisons of the two compounds show that the more electron deficient fluorinated olefin reacts at an accelerated rate relative to the unfunctionalized olefin (Figure 3.3A). However, when the two olefins were oxidized in competition in a 1:1 ratio, the non-fluorinated olefin was consumed 2.3 times faster than the allylic fluoride, potentially due to saturation of the catalyst with non-fluorinated olefin (Figure 3.3B). This inversion of relative reactivity, which results from a decrease in the rate of conversion of the fluorinated olefin rather than an increase in the rate of conversion of the non-fluorinated olefin,

suggests that stronger olefin coordination does not inherently lead to accelerated rate of oxidation.

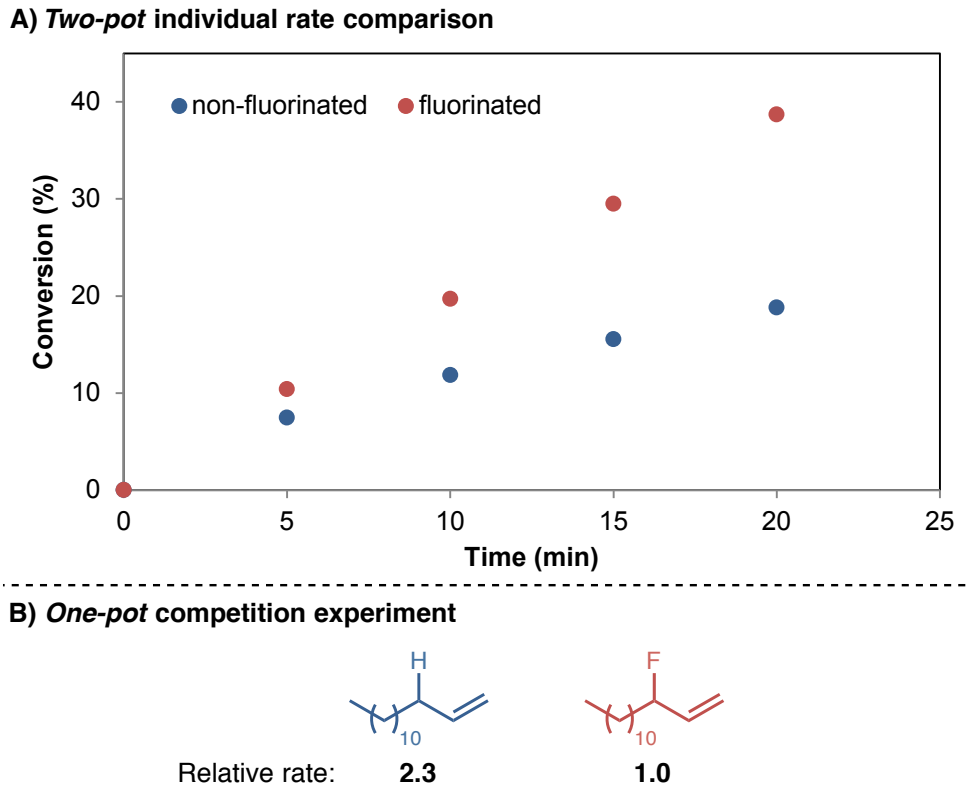


Figure 3.3. Individual rate and competition experiments performed to measure relative rates of conversion.

Conclusion

In summary, we have developed a practical synthesis of β-fluorinated aldehydes from readily accessible allylic fluorides. This method represents a rare example of catalysis to produce β-fluorinated carbonyl compounds under procedurally simple conditions. Direct transformation of crude aldehyde products demonstrates the versatility of β-fluorinated aldehyde building blocks. Preliminary mechanistic studies are consistent with inductive effects having a significant influence on both the regioselectivity and rate of oxidation and will facilitate further study of this new catalytic system.

Experimental Section

General Information

Anhydrous ether and dichloromethane used for substrate syntheses were purified and dried using a solvent-purification system containing activated alumina. All other solvents were purchased anhydrous with Sure/Seal^{TM} septa from Sigma Aldrich and used without further purification. All reagents and standards were purchased from Sigma Aldrich and used without further purification. All metal salts were purchased from Sigma Aldrich or Strem and used without further purification. NMR analysis was performed on the following instruments at ambient temperature: Varian 300 MHz, Varian 400 MHz, Varian 500 MHz, Bruker 400 MHz spectrometers. High-resolution mass spectra were provided by the California Institute of Technology Mass Spectrometry Facility using a JEOL JMS- 600H High Resolution Mass Spectrometer.

Optimization of Reaction Conditions (Figure 3.1)

For all reactions in Figure 1: Following work up procedure, nitrobenzene (0.1 mmol, 10.3 μL) was added as a standard, and ^{1}H NMR analysis of the crude product was performed to determine yield and selectivity.

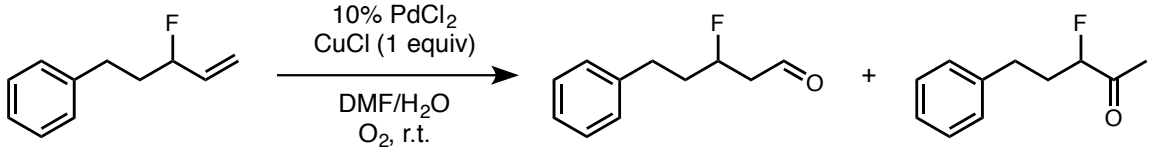


Figure 1a: Tsuji-Wacker conditions. The model substrate (0.1 mmol, 16.4 mg) was reacted using the "Procedure for Tsuji-Wacker oxidations" reported by Grubbs.[20b] Oxidation yield: 12%. Selectivity: 0.3:1 (aldehyde/ketone).

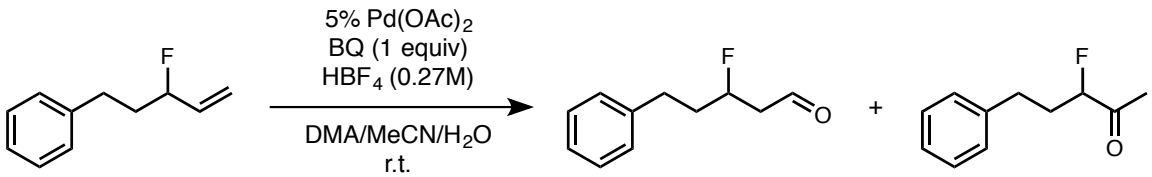


Figure 1b: Grubbs (dicationic) conditions.[15a] The model substrate (0.1 mmol, 16.4 mg) was reacted using "General Procedure 2" reported by Grubbs. Following overnight reaction in a 1-dram vial, the work up procedure was followed. Oxidation yield: 48%. Selectivity: 3:1 (aldehyde/ketone).

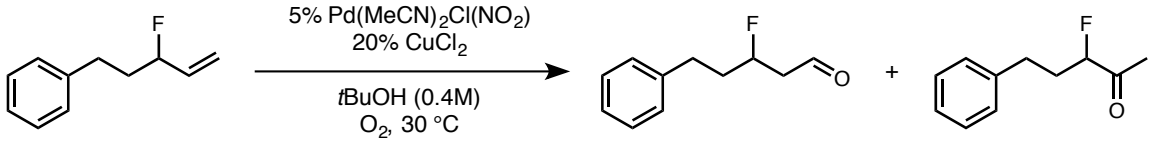


Figure 1c: Feringa conditions.[19] The model substrate (0.1 mmol, 16.4 mg) was reacted using the "General procedure for oxidation reactions with $Pd(MeCN)_2Cl(NO_2)/CuCl_2$" reported by Feringa. Following overnight reaction in a 1-dram vial, the work up procedure was followed. Oxidation yield: 40%. Selectivity: 18:1 (aldehyde/ketone).

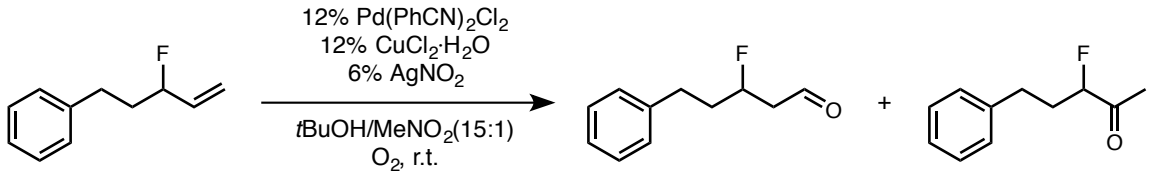


Figure 1d: Grubbs (nitrite) conditions.[20a] The model substrate (0.1 mmol, 16.4 mg) was reacted using the "Procedure (C) for small-scale oxidation of alkenes (NMR analysis)" reported by Grubbs. A 1-dram vial was used for the reaction, and, following sparging, the oxygen balloon was removed for the course of the reaction. Oxidation yield: 63%. Selectivity: 26:1 (aldehyde/ketone).

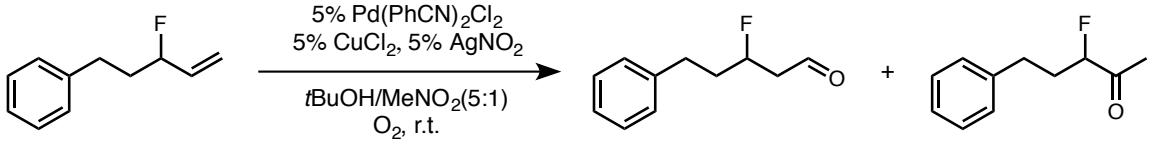


Figure 1e: Optimized conditions. A 1-dram vial equipped with a septum cap and magnetic stir bar was charged with $CuCl_2$ (0.7 mg, 0.005 mmol, 0.05 equiv), $AgNO_2$ (0.8 mg, 0.005 mmol, 0.05 equiv), and $Pd(PhCN)_2Cl_2$ (1.9 mg, 0.005 mmol, 0.05 equiv). The atmosphere was then purged using an oxygen-filled balloon for ~30 seconds. *Tert*-butanol (0.88 mL) was then added via syringe, followed by nitromethane (0.18 mL). This mixture

was sparged using an oxygen-filled balloon for ~60 seconds. (3-fluoropent-4-en-1-yl)benzene (0.1 mmol, 16.4 mg) was injected via glass syringe, the balloon was removed, and the septum cap was greased. The reaction mixture was stirred for 4 hours at room temperature. Upon completion, the solvent was removed via rotary evaporation. The reaction crude was resuspended in dichloromethane and filtered through a glass pipet containing celite, which was washed with dichloromethane. Dichloromethane was removed via rotary evaporation. Oxidation yield: 79%. Selectivity: 36:1 (aldehyde/ketone).

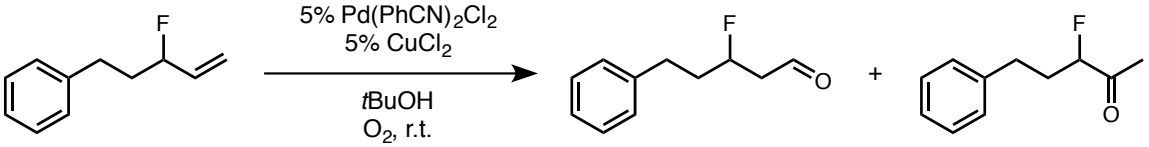


Figure 1f: Wacker conditions in *t*BuOH. A 1-dram vial equipped with a septum cap and magnetic stir bar was charged with $CuCl_2$ (0.7 mg, 0.005 mmol, 0.05 equiv) and $Pd(PhCN)_2Cl_2$ (1.9 mg, 0.005 mmol, 0.05 equiv). The atmosphere was then purged using an oxygen-filled balloon for ~30 seconds. *Tert*-butanol (1.06 mL) was then added via syringe. This mixture was sparged using an oxygen-filled balloon for ~60 seconds. (3-fluoropent-4-en-1-yl)benzene (0.1 mmol, 16.4 mg) was injected via glass syringe, the balloon was removed, and the septum cap was greased. The reaction mixture was stirred overnight at room temperature. Upon completion, the solvent was removed via rotary evaporation. The reaction crude was resuspended in dichloromethane and filtered through a glass pipet containing celite, which was washed with dichloromethane. Dichloromethane was removed via rotary evaporation. Oxidation yield: 8%. Selectivity: 8:1 (aldehyde/ketone).

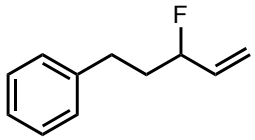
Preparation of Allylic Fluorides

General Procedure A: Synthesis of Allylic Fluorides.[7d] $[IrClCOD]_2$ (0.025 equiv) was weighed into a 50 mL polypropylene centrifuge tube equipped with a large stir bar. A first portion of anhydrous ether (30% of the total solvent volume, 0.83 M relative to trichloroacetimidate) was added to the tube, followed by TEA·3HF (3 equiv). The trichloroacetimidate (1.0 equiv) was then dissolved in a second portion of anhydrous ether and added to the reaction vessel, bringing the final concentration of trichloroacetimidate to

0.25 M. The polypropylene tube was closed tightly, and the reaction was stirred vigorously at room temperature for 2 hours. Upon completion, the crude mixture was allowed to separate into two layers. A glass pipette was used to transfer the organic layer to a separatory funnel containing a saturated solution of $NaHCO_3$. Ether was added to the polypropylene tube followed by 2 minutes of vigorous stirring. The organic layer was again transferred to the separatory funnel, and this step was repeated once more. The combined organic layers were separated, and the remaining bicarb solution extracted once with ether. After drying over Na_2SO_4, the solvent was removed by rotary evaporation. The residue was purified by flash chromatography (ether/pentane).

General Procedure B: Fluorinaton of Alcohols. A three-neck round bottom flask was equipped with an addition funnel and two septa. The system was purged with argon, and DAST (0.85 mL, 6.40 mmol, 1 equiv) and anhydrous DCM (6 mL) were added to the flask via syringe. The round-bottom flask was cooled to -78 °C and stirred. The alcohol (1.0 g, 1 equiv) was dissolved in 6 mL anhydrous DCM, transferred to the addition funnel, and added dropwise over 30 minutes. The reaction was allowed to slowly warm to room temperature and stirred overnight. Following reaction completion, the crude mixture was cooled to 0 °C for quenching. One neck previously closed with a septum was opened and saturated $NaHCO_3$ solution was slowly added via addition funnel to bring the mixture to basic pH. The mixture was then stirred for 1 hour at room temperature. The layers were separated, and the organic layer washed with brine. The solvent was removed by rotary evaporation, and the residue was purified by column chromatography.

The yields have not been optimized.



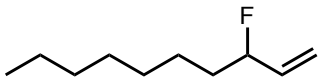
(3-fluoropent-4-en-1-yl)benzene. The fluoride was prepared according to General Procedure A from the corresponding trichloroacetimidate, 5-phenylpent-1-en-3-yl 2,2,2-trichloroacetimidate. The product was purified by flash chromatography (1% ether/pentane). Colorless oil (1.84 g, 68% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35–7.29 (m, 2H), 7.25–7.19 (m, 3H), 6.00–5.86 (m, 1H), 5.40–5.31 (m, 1H), 5.26 (dt, 1H, *J* = 10.7, 1.3 Hz), 4.99–4.82 (m, 1H), 2.86–2.69 (m, 2H), 2.14–1.86 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.5, 136.7 (d, *J* = 20.2 Hz), 128.8, 126.4, 117.4 (d, *J* = 12.6 Hz), 93.0 (d, *J* = 167.6 Hz), 37.2 (d, *J* = 21.4 Hz), 31.3 (d, *J* = 5.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -178.86 (ddddd, *J* = 48.5, 28.0, 17.3, 14.2, 3.5 Hz).

MS (EI) *m/z* (M^+) calcd for $C_{11}H_{13}F$: 164.1001, found: 164.0982.



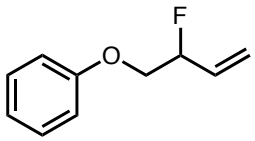
3-fluorodec-1-ene. The fluoride was prepared according to General Procedure A from the corresponding trichloroacetimidate, dec-1-en-3-yl 2,2,2-trichloroacetimidate. The product was purified by flash chromatography (pentane). Colorless oil (250 mg, 32% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 (dddd, 1H, *J* = 16.9, 14.0, 10.6, 6.1 Hz), 5.30 (ddt, 1H, *J* = 17.3, 3.6, 1.4 Hz), 5.21 (dt, 1H, *J* = 10.6, 1.3 Hz), 4.94–4.78 (m, 1H), 1.79–1.52 (m, 2H), 1.49–1.21 (m, 10H), 0.92–0.81 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 137.2 (d, *J* = 20.2 Hz), 117.1 (d, *J* = 11.3 Hz), 94.1 (d, *J* = 167.6 Hz), 35.6 (d, *J* = 21.4 Hz), 32.1, 29.7, 29.5, 25.0 (d, *J* = 5.0 Hz), 23.0, 14.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -176.74 (ddddd, *J* = 48.1, 26.2, 17.7, 13.9, 3.6 Hz).

MS (EI) *m/z* (M^+–HF) calcd for $C_{10}H_{18}$: 138.1408, found: 138.1430.



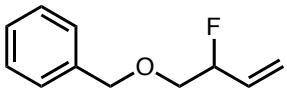
((2-fluorobut-3-en-1-yl)oxy)benzene. The fluoride was prepared according to General Procedure A from the corresponding trichloroacetimidate, 1-phenoxybut-3-en-2-yl 2,2,2-trichloroacetimidate. The product was purified by flash chromatography (5% ether/pentane). Colorless oil (1.20 g, 77% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.02–6.97 (m, 1H), 6.96–6.91 (m, 2H), 6.08–5.96 (m, 1H), 5.53 (ddt, 1H, *J* = 17.3, 3.0, 1.3 Hz), 5.40 (dt, 1H, *J* = 10.8, 1.3 Hz), 5.35–5.18 (m, 1H), 4.20–4.04 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 132.8 (d, *J* = 20.2 Hz), 129.9, 121.6, 119.5 (d, *J* = 11.3 Hz), 115.0, 91.5 (d, *J* = 173.9 Hz), 70.0 (d, *J* = 23.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -185.41 (ddddd, *J* = 48.7, 24.7, 19.8, 14.8, 3.1 Hz).

MS (EI) *m/z* (M^+) calcd for $C_{10}H_{11}FO$: 166.0794, found: 166.0788.



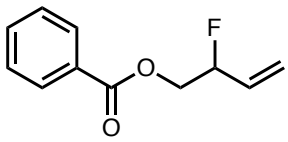
(((2-fluorobut-3-en-1-yl)oxy)methyl)benzene. The fluoride was prepared according to General Procedure A from the corresponding trichloroacetimidate, 1-(benzyloxy)but-3-en-2-yl 2,2,2-trichloroacetimidate. The product was purified by flash chromatography (5% ether/pentane). Colorless oil (144 mg, 52% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41–7.25 (m, 5H), 5.90 (dddd, 1H, *J* = 17.3, 15.1, 10.8, 5.7 Hz), 5.43 (ddt, 1H, *J* = 17.3, 2.9, 1.4 Hz), 5.31 (dt, 1H, *J* = 10.8, 1.3 Hz), 5.18–5.01 (m, 1H), 4.68–4.54 (m, 2H), 3.68–3.54 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.1, 133.3 (d, *J* = 20.2 Hz), 128.8, 128.10, 128.06, 118.8 (d, *J* = 11.3 Hz), 92.6 (d, *J* = 171.4 Hz), 73.8, 72.3 (d, *J* = 22.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -184.63 – -185.09 (m).

MS (EI) *m/z* (M^+) calcd for $C_{11}H_{13}FO$: 180.0950, found: 180.0952.



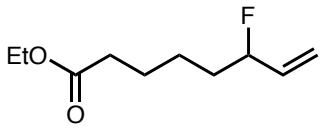
2-fluorobut-3-en-1-yl benzoate. The fluoride was prepared according to General Procedure A from the corresponding trichloroacetimidate, 2-(2,2,2-trichloro-1-iminoethoxy)but-3-en-1-yl benzoate. The product was purified by flash chromatography (10% ether/pentane). Colorless oil (344 mg, 60% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11–8.04 (m, 2H), 7.62–7.54 (m, 1H), 7.49–7.42 (m, 2H), 5.96 (dddd, 1H, *J* = 17.4, 15.1, 10.8, 5.7 Hz), 5.52 (ddt, 1H, *J* = 17.3, 2.8, 1.3 Hz), 5.40 (dt, 1H, *J* = 10.8, 1.2 Hz), 5.32–5.17 (m, 1H), 4.52 (ddd, 1H, *J* = 26.6, 12.4, 3.0 Hz), 4.42 (ddd, 1H, *J* = 20.4, 12.4, 7.0 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.5, 133.6, 132.3 (d, J = 20.2 Hz), 130.1, 130.0, 128.8, 119.8 (d, J = 11.3 Hz), 91.0 (d, J = 173.9 Hz), 66.1 (d, J = 22.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -186.05 (ddddd, J = 48.7, 26.5, 20.4, 15.0, 3.0 Hz).

MS (EI) *m/z* (M^+) calcd for $C_{11}H_{11}FO_2$: 194.0743, found: 194.0721.



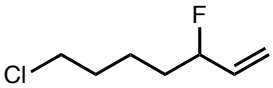
ethyl 6-fluorooct-7-enoate. The fluoride was prepared according to General Procedure A from the corresponding trichloroacetimidate, ethyl 6-(2,2,2-trichloro-1-iminoethoxy)oct-7-enoate. The product was purified by flash chromatography (10% ether/pentane). Colorless oil (124 mg, 55% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (dddd, 1H, J = 17.3, 14.0, 10.6, 6.1 Hz), 5.30 (ddt, 1H, J = 17.3, 3.6, 1.4 Hz), 5.21 (dt, 1H, J = 10.6, 1.3 Hz), 4.98–4.73 (m, 1H), 4.12 (q, 2H, J = 7.1 Hz), 2.31 (t, 2H, J = 7.5 Hz), 1.82–1.33 (m, 6H), 1.25 (t, 3H, J = 7.1 Hz).

^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 136.8 (d, J = 20.2 Hz), 117.3 (d, J = 12.1 Hz), 93.7 (d, J = 167.7 Hz), 60.6, 35.2 (d, J = 22.2 Hz), 34.5, 25.0, 24.6 (d, J = 5.0 Hz), 14.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -177.17 – -177.57 (m).

MS (EI) *m/z* (M^+) calcd for $C_{10}H_{17}FO_2$: 188.1201, found: 188.1185.



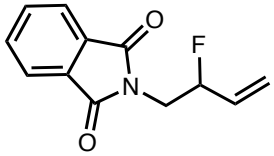
7-chloro-3-fluorohept-1-ene. The fluoride was prepared according to General Procedure A from the corresponding trichloroacetimidate, 7-chlorohept-1-en-3-yl 2,2,2-trichloroacetimidate. The product was purified by flash chromatography (1% ether/pentane). Colorless oil (583 mg, 57% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 (dddd, 1H, J = 17.3, 14.1, 10.6, 6.0 Hz), 5.32 (ddt, 1H, J = 17.3, 3.5, 1.4 Hz), 5.23 (dt, 1H, J = 10.6, 1.3 Hz), 5.03–4.72 (m, 1H), 3.55 (t, 2H, J = 6.6 Hz), 1.93–1.43 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 136.7 (d, J = 18.9 Hz), 117.4 (d, J = 12.6 Hz), 93.7 (d, J = 167.6 Hz), 45.1, 34.7 (d, J = 22.7 Hz), 32.6, 22.4 (d, J = 5.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -177.21 – -177.68 (m).

MS (EI) *m/z* (M^+) calcd for $C_7H_{12}ClF$: 150.0612, found: 150.0659.



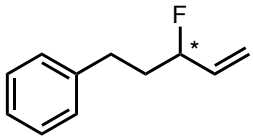
2-(2-fluorobut-3-en-1-yl)isoindoline-1,3-dione. The fluoride was prepared according to General Procedure A from the corresponding trichloroacetimidate, 1-(1,3-dioxoisoindolin-2-yl)but-3-en-2-yl 2,2,2-trichloroacetimidate. The product was purified by flash chromatography (20% Et_2O/pentane). White solid (173 mg, 65% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91–7.80 (m, 2H), 7.78–7.67 (m, 2H), 5.93 (dddd, 1H, *J* = 17.3, 14.5, 10.7, 6.0 Hz), 5.46 (ddt, 1H, *J* = 17.2, 3.3, 1.2 Hz), 5.34 (dt, 1H, *J* = 10.7, 1.2 Hz), 5.29–5.11 (m, 1H), 4.03 (ddd, 1H, *J* = 14.4, 13.7, 8.2 Hz), 3.82 (ddd, 1H, *J* = 26.4, 14.4, 4.0 Hz).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.3, 134.5, 133.3 (d, *J* = 17.6 Hz), 132.2, 123.8, 120.0 (d, *J* = 11.3 Hz), 90.4 (d, *J* = 173.9 Hz), 41.8 (d, *J* = 26.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -184.20 – -184.59 (m).

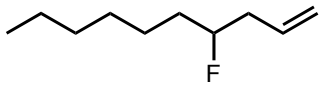
MS (FAB) *m/z* (M^++H) calcd for $C_{12}H_{11}FNO_2$: 220.0774, found: 220.0771.



(3-fluoropent-4-en-1-yl)benzene. The fluoride was prepared according to literature procedure[7h] from the corresponding trichloroacetimidate, 5-phenylpent-1-en-3-yl 2,2,2-trichloroacetimidate. The commercially available Lin diene ligand investigated by Nguyen (CAS# 940280-80-8, (*S*,*S*)-enantiomer) was used. The product was purified by flash chromatography (1% ether/pentane) followed by purification by preparative HPLC (Daicel CHIRALPAK® IC column, 2.0 cm X 25.0 cm, 0.5% 2-PrOH/hexanes). Colorless oil (37 mg, 30% yield, 90% ee).

HPLC analysis: Daicel CHIRALCEL® OD column; 0.5% 2-PrOH/hexanes; 0.8 mL/min; retention times: 8.5 min (minor), 9.1 min (major).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.27 (m, 2H), 7.25–7.18 (m, 3H), 5.92 (dddd, 1H, *J* = 17.3, 14.2, 10.7, 6.0 Hz), 5.34 (ddt, 1H, *J* = 17.2, 3.6, 1.4 Hz), 5.25 (dt, 1H, *J* = 10.6, 1.3 Hz), 5.03–4.77 (m, 1H), 2.88–2.64 (m, 2H), 2.15–1.84 (m, 2H).



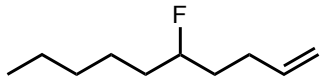
4-fluorodec-1-ene. The fluoride was prepared according to General Procedure B from the corresponding alcohol, dec-1-en-4-ol. The product was purified by flash chromatography (pentane). Colorless oil (374 mg, 37% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.83 (ddt, 1H, *J* = 17.2, 10.2, 7.0 Hz), 5.18–5.05 (m, 2H), 4.61–4.43 (m, 1H), 2.46–2.22 (m, 2H), 1.71–1.21 (m, 10H), 0.93–0.85 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 133.8 (d, *J* = 5.0 Hz), 118.0, 93.9 (d, *J* = 168.8 Hz), 39.9 (d, *J* = 21.4 Hz), 35.0 (d, *J* = 21.4 Hz), 32.1, 29.5, 25.3 (d, *J* = 5.0 Hz), 22.9, 14.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -179.49 – -180.17 (m).

MS (EI) *m/z* (M^+) calcd for $C_{10}H_{19}F$: 158.1471, found: 158.1478.



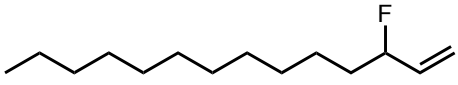
5-fluorodec-1-ene. The fluoride was prepared according to General Procedure B from the corresponding alcohol, dec-1-en-5-ol. The product was purified by flash chromatography (pentane). Colorless oil (495 mg, 49% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82 (ddt, 1H, *J* = 16.9, 10.2, 6.6 Hz), 5.12–4.90 (m, 2H), 4.63–4.34 (m, 1H), 2.33–2.03 (m, 2H), 1.83–1.17 (m, 10H), 0.94–0.83 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.2, 115.3, 94.1 (d, *J* = 167.6 Hz), 35.5 (d, *J* = 20.2 Hz), 34.7 (d, *J* = 20.2 Hz), 32.04, 29.7 (d, *J* = 5.0 Hz), 25.1 (d, *J* = 5.0 Hz), 22.9, 14.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -180.92 – -181.52 (m).

MS (EI) *m/z* (M^+) calcd for $C_{10}H_{19}F$: 158.1471, found: 158.1497.



3-fluorotetradec-1-ene. The fluoride was prepared according to General Procedure A from the corresponding trichloroacetimidate, tetradec-1-en-3-yl 2,2,2-

trichloroacetimidate. The product was purified by flash chromatography (pentane). Colorless oil (693 mg, 65% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.96–5.82 (m, 1H), 5.32 (ddt, 1H, *J* = 17.3, 3.6, 1.4 Hz), 5.22 (dt, 1H, *J* = 10.7, 1.3 Hz), 4.97–4.78 (m, 1H), 1.81–1.52 (m, 2H), 1.50–1.18 (m, 18H), 0.97–0.82 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 137.1 (d, *J* = 20.2 Hz), 117.1 (d, *J* = 12.6 Hz), 94.1 (d, *J* = 167.6 Hz), 35.6 (d, *J* = 22.7 Hz), 32.3, 30.00, 29.98, 29.91, 29.86, 29.74, 29.70, 25.0 (d, *J* = 5.0 Hz), 23.0, 14.5.

^{19}F NMR (376 MHz, $CDCl_3$) δ -176.52 – -177.01 (m).

MS (EI) *m/z* (M^+) calcd for $C_{14}H_{27}F$: 214.2097, found: 214.2095.

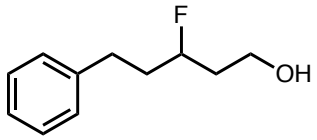
Wacker Oxidations of Allylic Fluorides (Table 3.1)

General Procedure C: Nitrite-Modified Wacker Oxidations of Allylic Fluorides. A 2-dram vial equipped with a septum cap and magnetic stir bar was charged with $CuCl_2$ (2.7 mg, 0.02 mmol, 0.05 equiv), $AgNO_2$ (3.1 mg, 0.02 mmol, 0.05 equiv), and $Pd(PhCN)_2Cl_2$ (7.7 mg, 0.02 mmol, 0.05 equiv). The atmosphere was then purged using an oxygen-filled balloon for ~30 seconds. *Tert*-butanol (3.5 mL) was then added via syringe, followed by nitromethane (0.7 mL). This mixture was sparged using an oxygen-filled balloon for ~60 seconds, and the balloon was left attached to the vial for the remainder of the reaction. The allylic fluoride (0.4 mmol) was injected via glass syringe, and the reaction mixture was stirred for 4 hours. Upon completion, the solvent was removed via rotary evaporation. The reaction crude was resuspended in ~2 mL dichloromethane and filtered through a glass pipet containing celite washed with dichloromethane into a round-bottom flask. Dichloromethane was removed via rotary evaporation. The crude aldehyde product was subjected to ^{1}H NMR analysis to determine regioselectivity of oxidation prior to reduction.

For solid substrates: The reaction set up was completed as described above, but the allylic fluoride was added as a solution in nitromethane, followed by final sparging with oxygen.

General Procedure D: Reduction of Aldehyde Products and Isolation. The flask containing crude aldehyde product was equipped with a large stir bar, closed with a septum, and purged using an argon-filled balloon, left attached for the course of the

reduction. Dichloromethane (14 mL) and ethanol (10 mL) were added via syringe, and the mixture was stirred and cooled to 0 °C. Sodium borohydride (22.7 mg, 0.6 mmol, 1.5 equiv) was then added and the atmosphere purged again using an argon-filled balloon. This mixture was allowed to warm to room temperature and stirred for 30 minutes. Following reduction of the aldehyde, the reaction mixture was cooled to 0 °C. Saturated NH_4Cl solution (~70 mL) was added slowly (over 5-10 minutes) through the septum via syringe with the argon-filled balloon left intact, followed by vigorous stirring for 30 minutes at 0 °C. The reaction mixture was then transferred to a separatory funnel and extracted 4 times with ether, without further dilution with water. The combined organic layers were washed twice with saturated sodium bicarbonate solution and once with brine, and then dried over Na_2SO_4. The solvent was removed by rotary evaporation and the residue purified by column chromatography (ether/pentane).



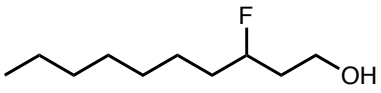
3-fluoro-5-phenylpentan-1-ol (Table 3.1, Entry 1). The title compound was synthesized according to General Procedures C and D from (3-fluoropent-4-en-1-yl)benzene (65.7 mg, 0.40 mmol). ^{1}H NMR analysis displayed 33:1 aldehyde selectivity. The product was purified by column chromatography on silica gel (40% ether/pentane). Pale yellow oil (60 mg, 82% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.27 (m, 2H), 7.24–7.16 (m, 3H), 4.72 (dtt, 1H, J = 49.7, 8.9, 3.4 Hz), 3.88–3.75 (m, 2H), 2.84 (ddd, 1H, J = 14.6, 9.9, 5.2 Hz), 2.72 (ddd, 1H, J = 13.8, 9.5, 7.0 Hz), 2.12–1.73 (m, 4H), 1.66 (br s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.6, 128.80, 128.77, 126.3, 91.9 (d, J = 166.3 Hz), 59.6 (d, J = 3.8 Hz), 38.2 (d, J = 20.2 Hz), 37.5 (d, J = 21.4 Hz), 31.6 (d, J = 5.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -184.22 (dtd, J = 65.9, 33.0, 16.1 Hz).

MS (FAB) *m/z* (M^++H) calcd for $C_{11}H_{16}FO$: 183.1185, found: 183.1204.



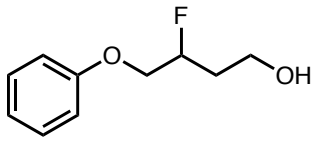
3-fluorodecan-1-ol (Table 3.1, Entry 2). The title compound was synthesized according to General Procedures C and D from 3-fluorodec-1-ene (63.3 mg, 0.40 mmol). ^{1}H NMR analysis displayed 29:1 aldehyde selectivity. The product was purified by column chromatography on silica gel (40% ether/pentane). Pale yellow solid (62 mg, 87% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 4.80–4.59 (m, 1H), 3.87–3.75 (m, 2H), 1.94–1.19 (m, 15H), 0.96–0.81 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 93.1 (d, J = 166.3 Hz), 59.9 (d, J = 3.8 Hz), 38.2 (d, J = 20.2 Hz), 35.7 (d, J = 21.4 Hz), 32.1, 29.7, 29.5, 25.4 (d, J = 3.8 Hz), 22.3, 14.4.

^{19}F NMR (376 MHz, $CDCl_3$) δ -182.30 (dddt, J = 50.6, 34.2, 29.6, 17.1 Hz).

MS (FAB) *m/z* (M^+–F) calcd for $C_{10}H_{21}O$: 157.1592, found: 157.1594.



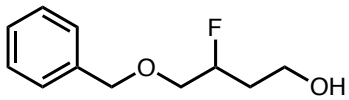
3-fluoro-4-phenoxybutan-1-ol (Table 3.1, Entry 3). The title compound was synthesized according to General Procedures C and D from ((2-fluorobut-3-en-1-yl)oxy)benzene (66.5 mg, 0.40 mmol). ^{1}H NMR analysis displayed ≥99:1 aldehyde selectivity. The product was purified by column chromatography on silica gel (50% ether/pentane). Pale yellow solid (69 mg, 94% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.27 (m, 2H), 6.98 (t, 1H, J = 7.4 Hz), 6.93 (d, 2H, J = 8.0 Hz), 5.17–4.95 (m, 1H), 4.19–4.09 (m, 2H), 3.92–3.82 (m, 2H), 2.16–1.85 (m, 2H), 1.76 (br s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.7, 129.9, 121.6, 114.9, 90.1 (d, J = 172.6 Hz), 69.9 (d, J = 23.9 Hz), 59.0 (d, J = 5.0 Hz), 34.6 (d, J = 20.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -189.32 (ddtd, J = 48.3, 31.6, 22.3, 16.3 Hz).

MS (EI) *m/z* (M^+) calcd for $C_{10}H_{13}FO_2$: 184.0900, found: 184.0912.



4-(benzyloxy)-3-fluorobutan-1-ol (Table 3.1, Entry 4). The title compound was synthesized according to General Procedures C and D from (((2-fluorobut-3-en-1-

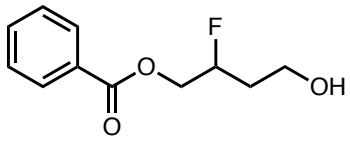
yl)oxy)methyl)benzene (72.1 mg, 0.40 mmol). ^{1}H NMR analysis displayed ≥99:1 aldehyde selectivity. The product was purified by column chromatography on silica gel (50% ether/pentane). Pale yellow oil (74 mg, 93% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H), 4.98–4.78 (m, 1H), 4.63–4.57 (m, 2H), 3.84–3.76 (m, 2H), 3.70–3.64 (m, 1H), 3.64–3.58 (m, 1H), 2.05–1.81 (m, 2H), 1.68 (br s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 138.0, 128.8, 128.2, 128.1, 91.2 (d, J = 171.4 Hz), 73.8, 72.1 (d, J = 22.7 Hz), 59.0 (d, J = 5.0 Hz), 34.8 (d, J = 21.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -188.08 – -188.66 (m).

MS (EI) *m/z* (M^+) calcd for $C_{11}H_{15}FO_2$: 198.1056, found: 198.1084.



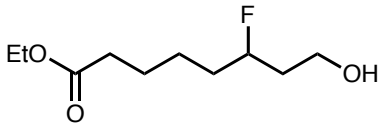
2-fluoro-4-hydroxybutyl benzoate (Table 3.1, Entry 5). The title compound was synthesized according to General Procedures C and D from 2-fluorobut-3-en-1-yl benzoate (77.7 mg, 0.40 mmol). ^{1}H NMR analysis displayed ≥99:1 aldehyde selectivity. The product was purified by column chromatography on silica gel (60% ether/pentane). White solid (79 mg, 93% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10–8.06 (m, 2H), 7.61–7.55 (m, 1H), 7.49–7.42 (m, 2H), 5.06 (ddddd, 1H, J = 49.2, 9.0, 6.4, 3.9, 2.7 Hz), 4.60–4.41 (m, 2H), 3.91–3.86 (m, 2H), 2.14–1.83 (m, 2H), 1.55 (br s, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.7, 133.6, 130.1, 129.9, 128.8, 89.6 (d, J = 172.6 Hz), 66.6 (d, J = 21.4 Hz), 58.8 (d, J = 5.0 Hz), 34.4 (d, J = 21.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -189.14 – -189.79 (m).

MS (FAB) *m/z* (M^++H) calcd for $C_{11}H_{14}FO_3$: 213.0927, found: 213.0938.



ethyl 6-fluoro-8-hydroxyoctanoate (Table 3.1, Entry 6). The title compound was synthesized according to General Procedures C and D from ethyl 6-fluorooct-7-enoate

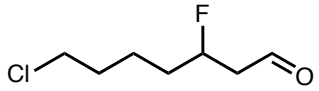
(75.3 mg, 0.40 mmol). ^{1}H NMR analysis displayed 29:1 aldehyde selectivity. The product was purified by column chromatography on silica gel (60% ether/pentane). Colorless oil (59 mg, 72% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.79–4.59 (m, 1H), 4.11 (q, 2H, J = 7.2 Hz), 3.83–3.74 (m, 2H), 2.30 (t, 2H, J = 7.4 Hz), 1.93–1.29 (m, 9H), 1.24 (t, 3H, J = 7.1 Hz).

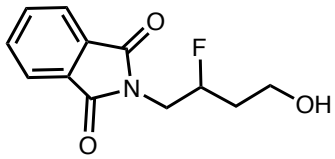
^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 92.5 (d, J = 166.3 Hz), 60.6, 59.6 (d, J = 3.8 Hz), 38.1 (d, J = 20.2 Hz), 35.3 (d, J = 21.4 Hz), 34.5, 25.0, 24.9 (d, J = 3.8 Hz), 14.6.

^{19}F NMR (376 MHz, $CDCl_3$) δ -182.90 (dddt, J = 50.2, 33.8, 29.7, 16.9 Hz).

MS (FAB) *m/z* (M^++H) calcd for $C_{10}H_{20}FO_3$: 207.1396, found: 207.1401.



7-chloro-3-fluoroheptanal (Table 3.1, Entry 7). The title compound was synthesized according to General Procedure C from 7-chloro-3-fluorohept-1-ene (60.4 mg, 0.40 mmol). Upon completion, nitrobenzene (0.40 mmol) was added as an NMR standard. ^{1}H NMR analysis of an aliquot of the crude reaction mixture (without any rotary evaporation step) displayed 42:1 aldehyde selectivity and 81% yield.



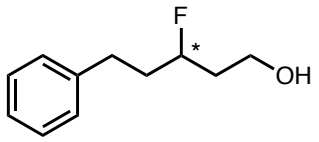
2-(2-fluoro-4-hydroxybutyl)isoindoline-1,3-dione (Table 1, Entry 8). The title compound was synthesized according to General Procedures C and D from 2-(2-fluorobut-3-en-1-yl)isoindoline-1,3-dione (87.7 mg, 0.40 mmol). ^{1}H NMR analysis displayed ≥99:1 aldehyde selectivity. The product was purified by column chromatography on silica gel (1:1:1 ether/DCM/pentane). Light yellow solid (73 mg, 77% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90–7.83 (m, 2H), 7.77–7.70 (m, 2H), 5.10–4.90 (m, 1H), 4.05 (ddd, 1H, J = 16.1, 14.5, 7.8 Hz), 3.92–3.78 (m, 3H), 2.02–1.86 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 134.5, 132.2, 123.8, 89.5 (d, J = 173.9 Hz), 59.0 (d, J = 5.0 Hz), 42.1 (d, J = 23.9 Hz), 35.7 (d, J = 20.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -188.23 – -188.74 (m).

MS (EI) *m/z* (M^+) calcd for $C_{12}H_{12}FNO_3$: 237.0801, found: 237.0797.



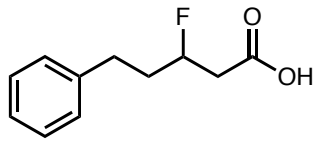
3-fluoro-5-phenylpentan-1-ol (Eq. 3.1). The title compound was synthesized according to General Procedures C and D from (3-fluoropent-4-en-1-yl)benzene (33 mg, 0.20 mmol). ^{1}H NMR analysis displayed 30:1 aldehyde selectivity. The product was purified by column chromatography on silica gel (25→75% ether/pentane). Colorless oil (30 mg, 82% yield, 90% ee).

HPLC analysis: Daicel CHIRALCEL® OD column; 15% 2-PrOH/hexanes; 0.9 mL/min; retention times: 7.3 min (minor), 8.7 min (major).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.27 (m, 2H), 7.24–7.16 (m, 3H), 4.72 (dtt, 1H, *J* = 49.7, 8.9, 3.4 Hz), 3.87–3.76 (m, 2H), 2.84 (ddd, 1H, *J* = 14.7, 9.9, 5.2 Hz, 1H), 2.72 (ddd, 1H, *J* = 13.8, 9.5, 7.0 Hz), 2.09–1.74 (m, 4H), 1.55 (br s, 1H).

Derivatizations of β-Fluorinated Aldehydes (Scheme 3.2)

All derivatizations were performed on crude aldehydes produced from (3-fluoropent-4-en-1-yl)benzene using General Procedure C. All yields reported over two steps.



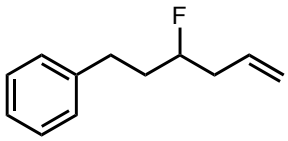
3-fluoro-5-phenylpentanoic acid (Scheme 3.2a). The title compound was synthesized from 3-fluoro-5-phenylpentanal (produced from 0.40 mmol (3-fluoropent-4-en-1-yl)benzene) using the "General Procedure for Oxidation of Aldehyde to Carboxylic Acid" reported by Borhan.[27] The product was purified by column chromatography on silica gel (5% MeOH/pentane). Clear crystals (71 mg, 90% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (br s, 1H), 7.35–7.27 (m, 2H), 7.24–7.15 (m, 3H), 4.95 (dtt, 1H, *J* = 48.1, 8.3, 4.0 Hz), 2.92–2.50 (m, 4H), 2.17–1.81 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 176.2 (d, *J* = 6.1 Hz), 141.1, 128.9, 128.8, 126.5, 89.5 (d, *J* = 170.7 Hz), 40.4 (d, *J* = 24.2 Hz), 36.9 (d, *J* = 21.2 Hz), 31.4 (d, *J* = 4.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -181.38 – -181.83 (m).

MS (FAB) *m/z* (M^++H) calcd for $C_{11}H_{14}O_2F$: 197.0978, found: 197.0980.



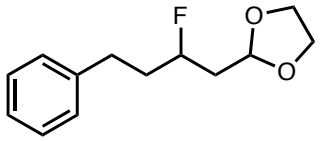
(3-fluorohex-5-en-1-yl)benzene (Scheme 3.2b). A 1-dram vial equipped with a septum cap and stir bar was charged with $MePPh_3Br$ (54 mg, 1.5 equiv, 0.15 mmol). The atmosphere was purged using an argon-filled balloon, and anhydrous THF was added via syringe (0.5 mL). The mixture was cooled to 0 °C with stirring, and *n*BuLi (2.5 M in hexanes, 1.4 equiv) was added via glass syringe. The mixture was allowed to stir for 30 minutes at 0 °C. 3-fluoro-5-phenylpentanal (produced from 0.10 mmol (3-fluoropent-4-en-1-yl)benzene) was dissolved in THF (0.2 mL) under argon atmosphere, and the solution was added via microsyringe to the reaction mixture. The reaction was allowed to warm to room temperature and stirred overnight. Saturated NH_4Cl solution was added to the crude mixture and extracted 3 times with ether. Following drying over Na_2SO_4, the solvent was removed by rotary evaporation. The residue was purified by preparative thin-layer chromatography on silica gel (2% ether/pentane). Pale yellow oil (12 mg, 65% yield).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35–7.24 (m, 2H), 7.24–7.15 (m, 3H), 5.91–5.73 (m, 1H), 5.18–5.05 (m, 2H), 4.69–4.39 (m, 1H), 2.83 (ddd, 1H, *J* = 14.9, 9.8, 5.3 Hz), 2.69 (ddd, 1H, *J* = 13.8, 9.4, 7.1 Hz), 2.54–2.24 (m, 2H), 2.08–1.71 (m, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.7, 133.4 (d, *J* = 6.3 Hz), 128.80, 128.79, 126.3, 118.3, 92.8 (d, *J* = 170.1 Hz), 39.9 (d, *J* = 22.7 Hz), 36.8 (d, *J* = 21.4 Hz), 31.6 (d, *J* = 3.8 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -181.34 – -181.99 (m).

MS (EI) *m/z* (M^+) calcd for $C_{12}H_{15}F$: 178.1158, found: 178.1158.



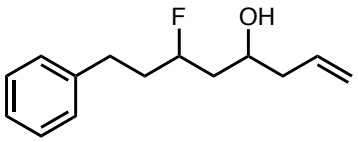
2-(2-fluoro-4-phenylbutyl)-1,3-dioxolane (Scheme 3.2d). 3-fluoro-5-phenylpentanal (produced from 0.40 mmol (3-fluoropent-4-en-1-yl)benzene) was dissolved in 2 mL ethylene glycol (0.2 M). Molecular sieves (4Å, 130 mg) were then added. *P*-toluenesulfonic acid (76.1 mg, 1 equiv, 0.40 mmol) was added, and the reaction was stirred for 6 hours at room temperature. The reaction was quenched with saturated $NaHCO_3$ solution, and extracted three times with ether. After drying over Na_2SO_4, the solvent was removed by rotary evaporation. The residue was purified by column chromatography on silica gel (20% Et_2O/pentane). Colorless oil (50 mg, 56% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.27 (m, 2H), 7.23–7.17 (m, 3H), 5.03 (dd, 1H, *J* = 6.4, 3.6 Hz), 4.75 (dtt, 1H, *J* = 49.4, 8.7, 3.6 Hz), 4.03–3.92 (m, 2H), 3.92–3.82 (m, 2H), 2.84 (ddd, 1H, *J* = 13.8, 10.1, 5.2 Hz), 2.71 (ddd, 1H, *J* = 13.9, 9.7, 6.8 Hz), 2.14 (dddd, 1H, *J* = 16.4, 14.5, 8.7, 3.6 Hz), 2.08–1.77 (m, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.6, 128.8, 126.3, 101.9 (d, *J* = 5.0 Hz), 90.5 (d, *J* = 167.6 Hz), 65.3, 65.1, 40.0 (d, *J* = 20.2 Hz), 37.7 (d, *J* = 20.2 Hz), 31.5 (d, *J* = 3.8 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -183.15 (dtt, *J* = 48.9, 32.5, 16.4 Hz).

MS (FAB) *m/z* (M^++H) calcd for $C_{13}H_{18}FO_2$: 225.1291, found: 225.1281.



6-fluoro-8-phenyloct-1-en-4-ol (Scheme 3.2e). A 20 mL vial containing 3-fluoro-5-phenylpentanal (produced from 0.40 mmol (3-fluoropent-4-en-1-yl)benzene) was purged using an argon-filled balloon. The aldehyde was dissolved in 3.3 mL anhydrous DCM (0.12 M) and the mixture cooled to -78 °C. Allylboronic acid pinacol ester (75 μL, 0.4 mmol, 1.0 equiv) was then added via glass syringe. The reaction mixture was then allowed to warm to room temperature and stirred overnight. Water was added to the crude mixture and extracted three times with ether. After drying over Na_2SO_4, the solvent was removed by rotary evaporation. The residue was purified by column chromatography on silica gel (30% Et_2O/pentane). ^{1}H NMR analysis displayed ~1:1 dr. Colorless oil (72 mg, 81% yield).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34–7.26 (m, 2H), 7.24–7.15 (m, 3H), 5.90–5.72 (m, 1H), 5.20–5.08 (m, 2H), 4.96–4.59 (m, 1H), 4.00–3.83 (m, 1H), 2.90–2.77 (m, 1H), 2.76–2.63 (m, 1H), 2.39–2.12 (m, 2H), 2.11–1.46 (m, 5H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 141.7, 141.6, 134.65, 134.61, 128.80, 128.77, 128.76, 128.75, 126.4, 126.3, 118.9, 118.7, 93.3 (d, J = 166.3 Hz), 91.1 (d, J = 166.3 Hz), 69.1 (d, J = 3.8 Hz), 67.1 (d, J = 2.5 Hz), 42.8, 42.4 (d, J = 20.2 Hz), 42.1, 41.9 (d, J = 18.9 Hz), 37.7 (d, J = 21.4 Hz), 37.5 (d, J = 20.2 Hz), 31.7 (d, J = 5.0 Hz), 31.5 (d, J = 5.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ -181.75 (dtt, J = 49.0, 32.5, 15.6 Hz), -183.91 – -184.74 (m).

MS (FAB) *m/z* (M^++H) calcd for $C_{14}H_{20}FO$: 223.1498, found: 223.1491.

Mechanistic Studies

General Procedure for Figure 3.2. A 1-dram vial equipped with a septum cap and magnetic stir bar was charged with $CuCl_2$ (0.7 mg, 0.005 mmol, 0.05 equiv), $AgNO_2$ (0.8 mg, 0.005 mmol, 0.05 equiv), and $Pd(PhCN)_2Cl_2$ (1.9 mg, 0.005 mmol, 0.05 equiv). The atmosphere was then purged using an oxygen-filled balloon for ~30 seconds. *Tert*-butanol (0.88 mL) was then added via syringe, followed by nitromethane (0.18 mL). This mixture was sparged using an oxygen-filled balloon for ~60 seconds. The olefin (0.1 mmol) was injected via glass syringe, the balloon was removed, and the septum cap was greased. The reaction mixture was stirred for 4 hours at room temperature. Upon completion, the solvent was removed via rotary evaporation. The reaction crude was resuspended in dichloromethane and filtered through a glass pipet containing celite, which was washed with dichloromethane. Dichloromethane was removed via rotary evaporation. Nitrobenzene (0.1 mmol, 10.3 μL) was added as a standard, and ^{1}H NMR analysis of the crude product was performed to determine yield and selectivity.

	Selectivity (%)		Oxidation Yield (%)	
	run 1	**run 2**	**run 1**	**run 2**
n=0	95	96	55	49
n=1	79	80	68	59
n=2	64	69	53	59
1-decene	54	61	54	51

General Procedure for Figure 3.3a: Individual rate comparison. A 4 mL vial with a stir bar was charged with $CuCl_2$ (2.7 mg, 0.020 mmol), $AgNO_2$ (3.1 mg, 0.020 mmol), and $Pd(PhCN)_2Cl_2$ (7.7 mg, 0.020 mmol). The vial was capped with a septum cap and purged with O_2 using an oxygen-filled balloon. Next, *tert*-BuOH (1.32 mL, anhydrous) and nitromethane (0.36 mL, anhydrous) were added via syringe, and the reaction mixture was stirred. In a separate vial, a solution of olefin (0.20 mmol) and diphenylmethane (16.7 μL, 0.10 mmol; internal standard) in *t*-BuOH (0.44 mL) was prepared. The olefin solution was added to the catalyst mixture via syringe, and an aliquot (0.3 mL) was immediately collected for a time = 0 data point. The aliquot was quenched with a solution of pyridine (6.0 μL) in DCM (0.2 mL). After quenching, the aliquot was concentrated, diluted with hexanes, and filtered through a plug of celite with hexanes. The filtrate was concentrated and analyzed by ^1H NMR. Aliquots were taken at time = 5, 10, 15, and 20 minutes following the same quenching procedure, and conversions were determined by ^1H NMR relative to the time = 0 data point.

Tetradecene

Time (min) Conversion (%)

	run 1	run 2	run 3	Average
0	0	0	0	0
5	7.7	6.7	8	7.5
10	12.1	11.9	11.6	11.9
15	17.2	13.7	15.7	15.5
20	19.9	16.9	19.6	18.8

Allylic Fluoride

Time (min) Conversion (%)

	run 1	run 2	Average
0	0	0	0
5	9.6	11.2	10.4
10	18.5	20.9	19.7
15	28.4	30.6	29.5
20	36.9	40.5	38.7

General Procedure for Figure 3.3b: Competition experiment. A 4 mL vial with a stir bar was charged with $CuCl_2$ (2.7 mg, 0.020 mmol), $AgNO_2$ (3.1 mg, 0.020 mmol), and $Pd(PhCN)_2Cl_2$ (7.7 mg, 0.020 mmol). The vial was capped with a septum cap and

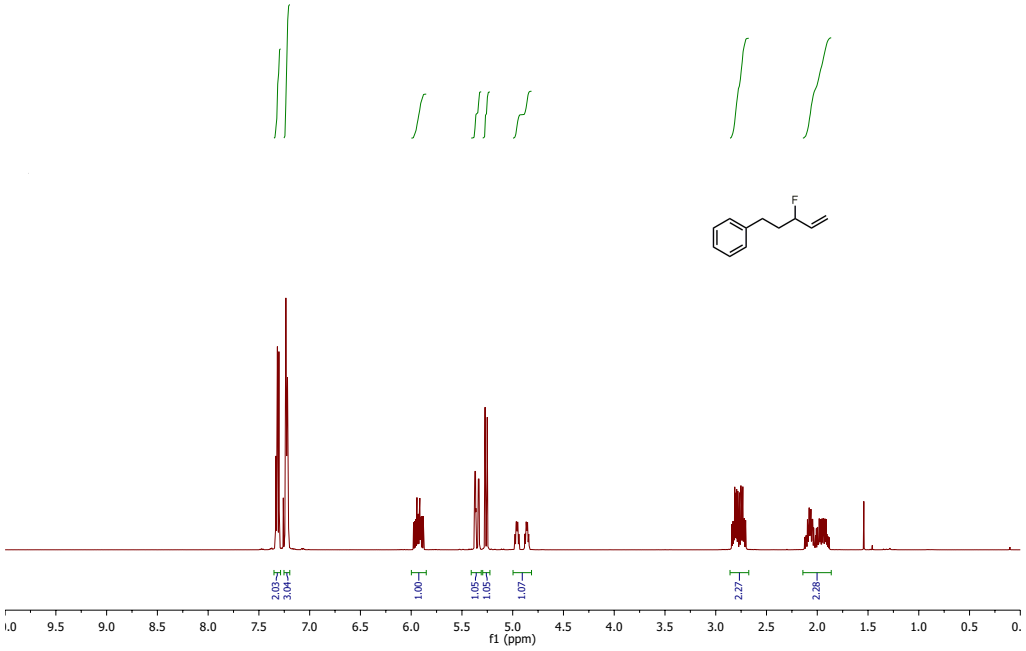
purged with O_2 using an oxygen-filled balloon. Next, *tert*-BuOH (1.32 mL, anhydrous) and nitromethane (0.36 mL, anhydrous) were added via syringe, and the reaction mixture was stirred. In a separate vial, a solution of tetradecene (19.6 mg, 0.10 mmol), 3-fluorotetradec-1-ene (21.4 mg, 0.10 mmol), and diphenylmethane (16.7 μL, 0.10 mmol; internal standard) in *t*-BuOH (0.44 mL) was prepared. The olefin solution was added to the catalyst mixture via syringe, and an aliquot (0.3 mL) was immediately collected for a time = 0 data point. The aliquot was quenched with a solution of pyridine (6.0 μL) in DCM (0.2 mL). After quenching, the aliquot was concentrated, diluted with hexanes, and filtered through a plug of celite with hexanes. The filtrate was concentrated and analyzed by ^{1}H NMR. A second aliquot was collected at time = 10 minutes following the same quenching procedure, and the conversion of each olefin was determined by ^{1}H NMR relative to the time = 0 data point.

Conversion (%)

	Tetradecene	**Allylic Fluoride**	**Selectivity**
run 1	11.2	5.0	2.2:1
run 2	11.1	4.6	2.4:1

^{1}H, ^{13}C, and ^{19}F NMR Spectra

293PROTON01
bc-I-28-C13_1H



293CARBON01
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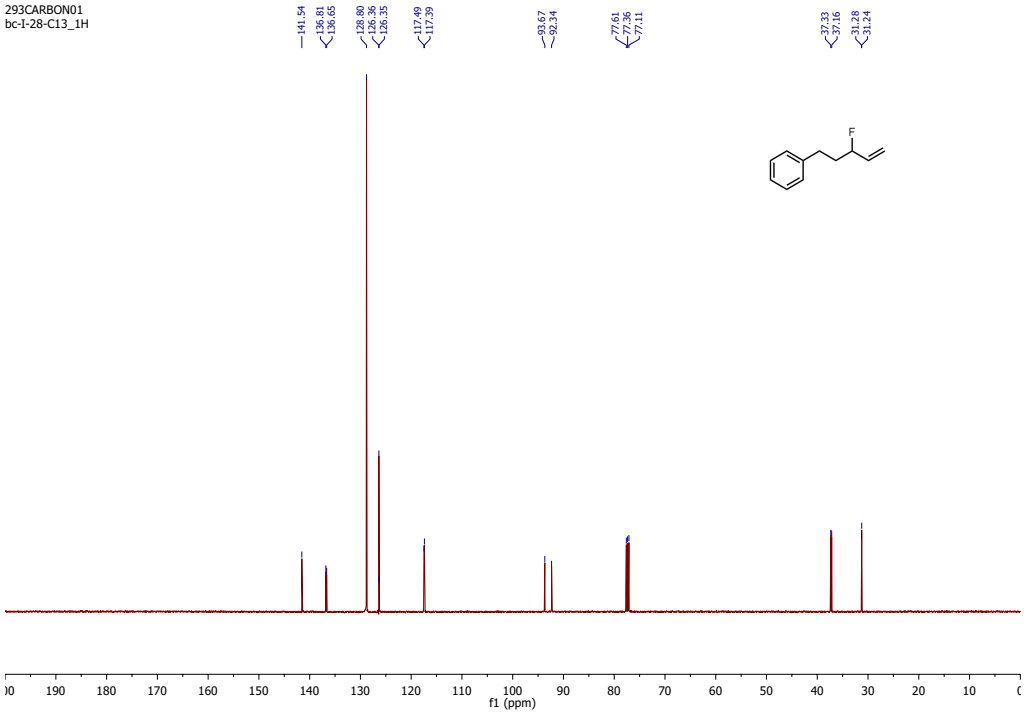
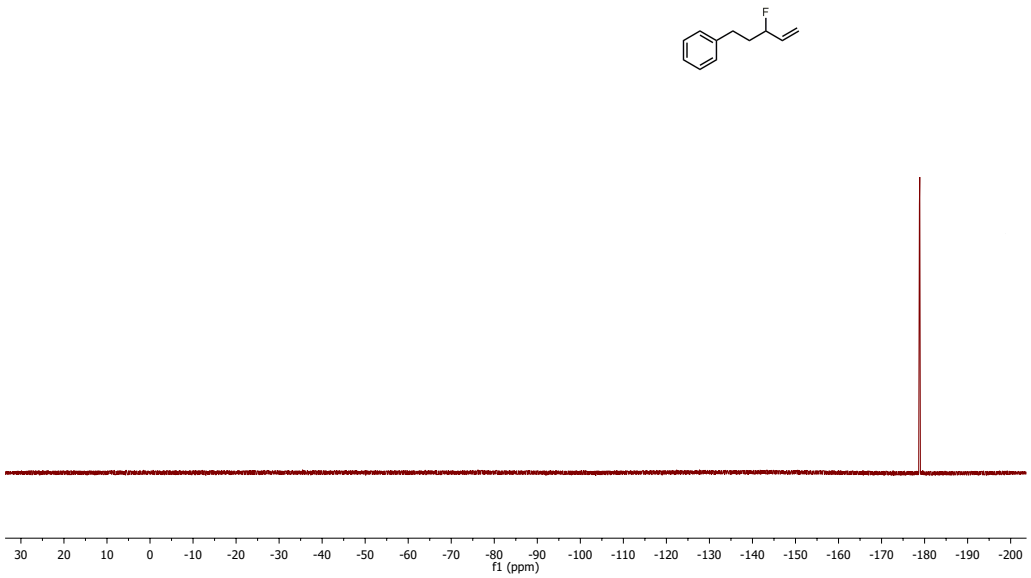
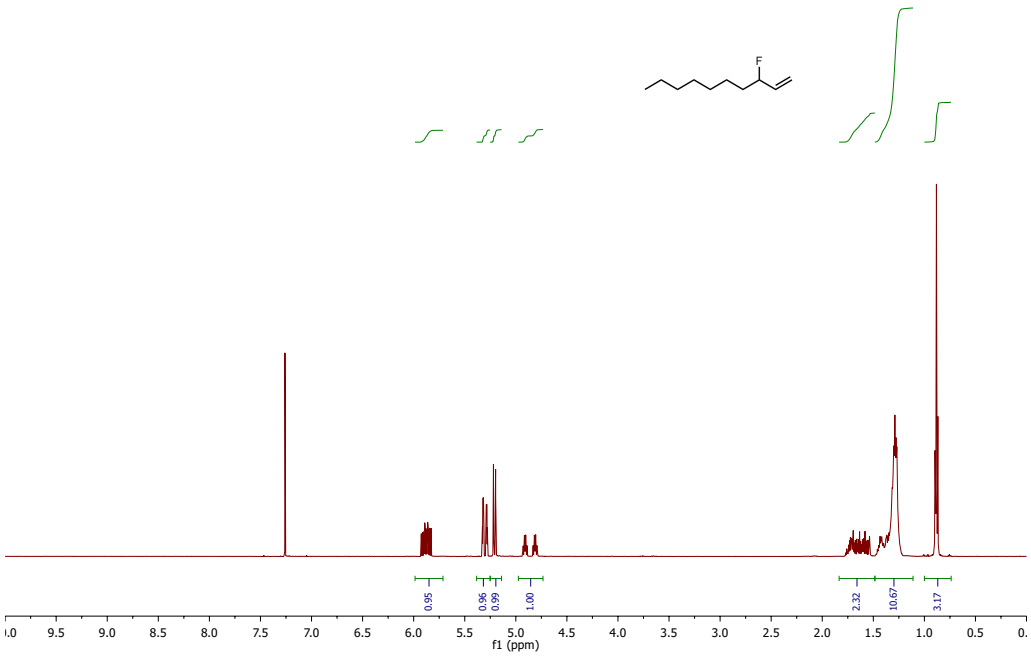


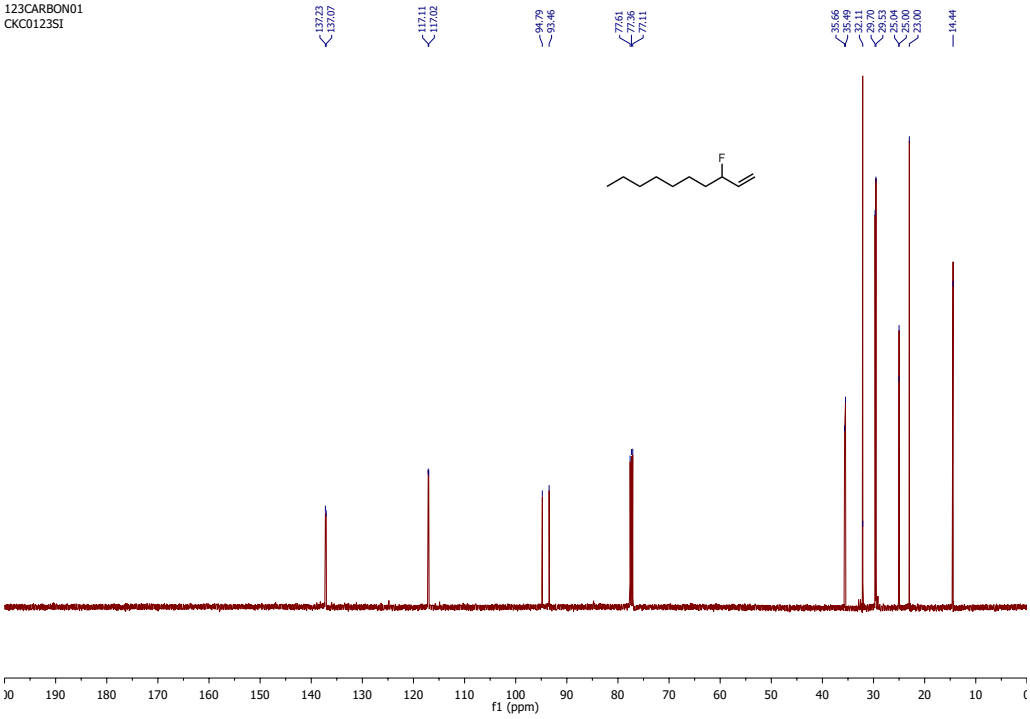
FLUORINE01
CKC0293siena



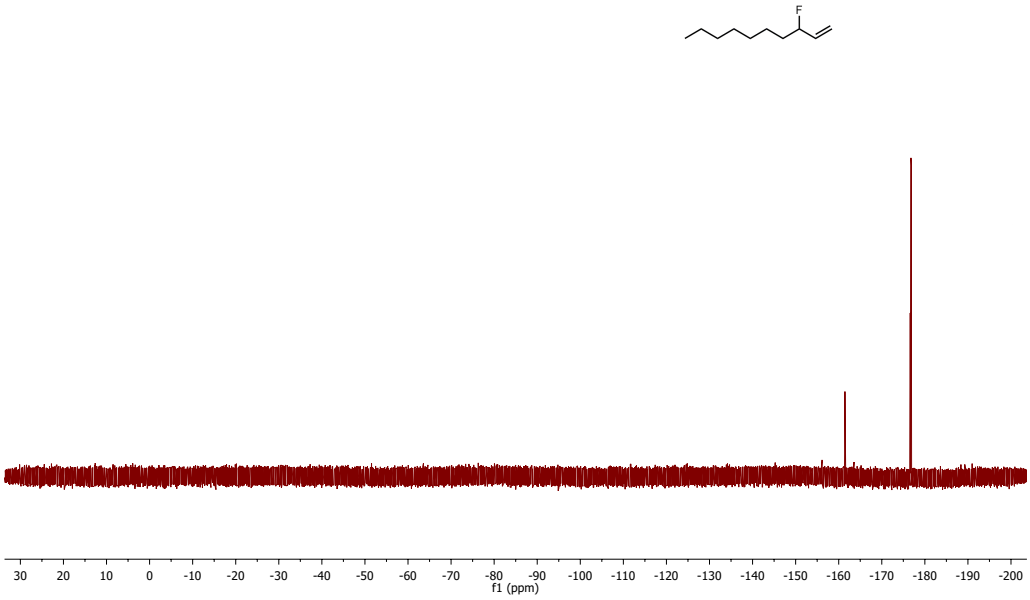
CKC0123SIr
CKC0123SIr



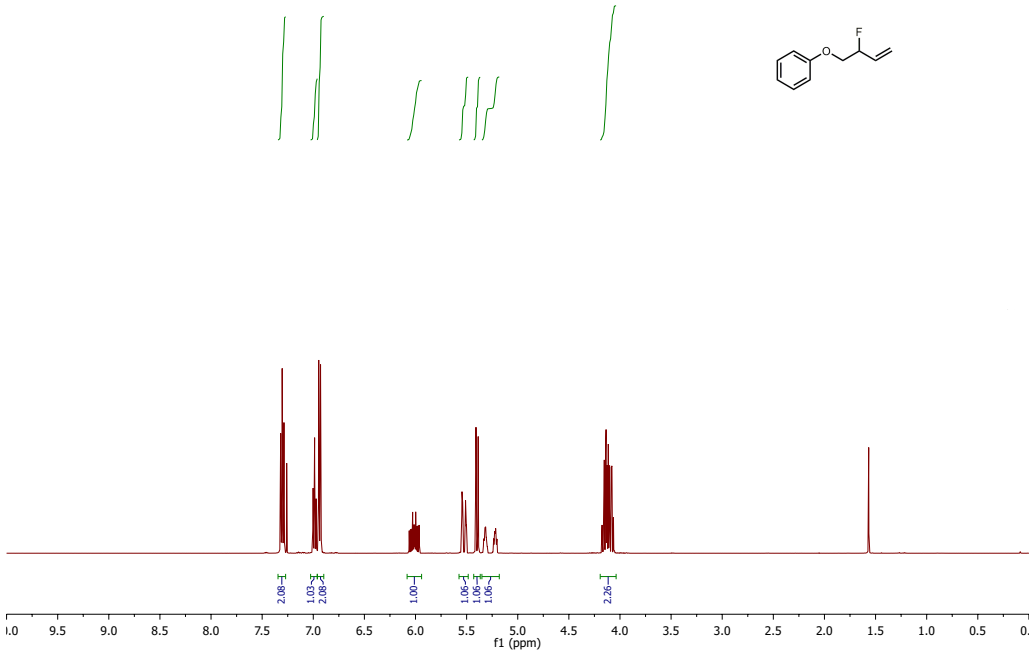
123CARBON01
CKC0123SI



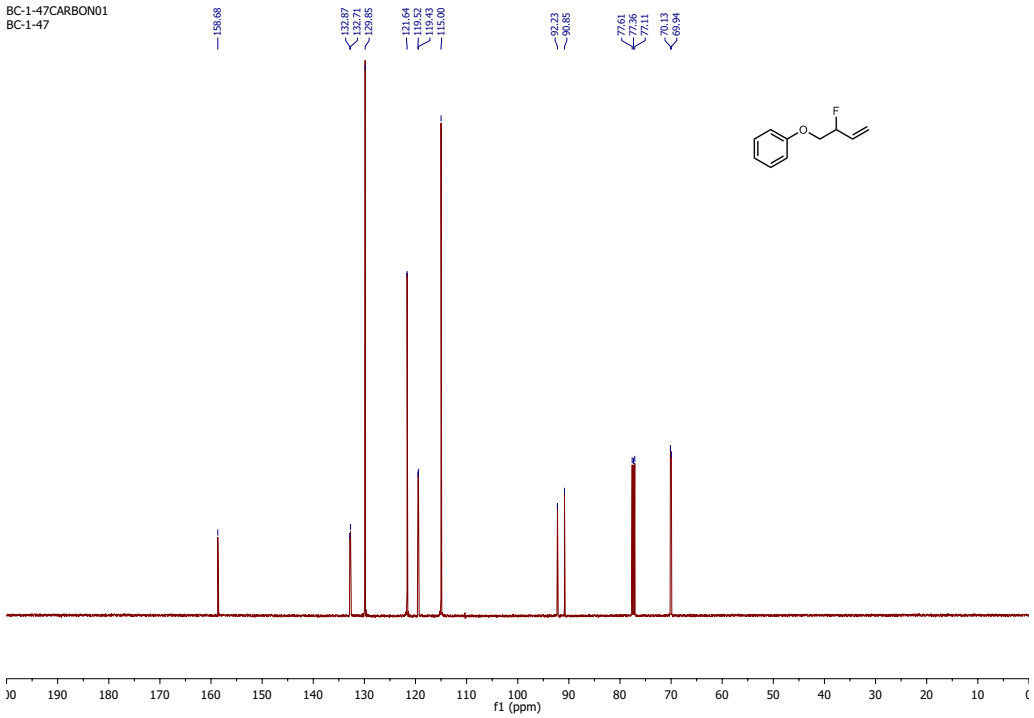
FLUORINE01
CKC0123siena



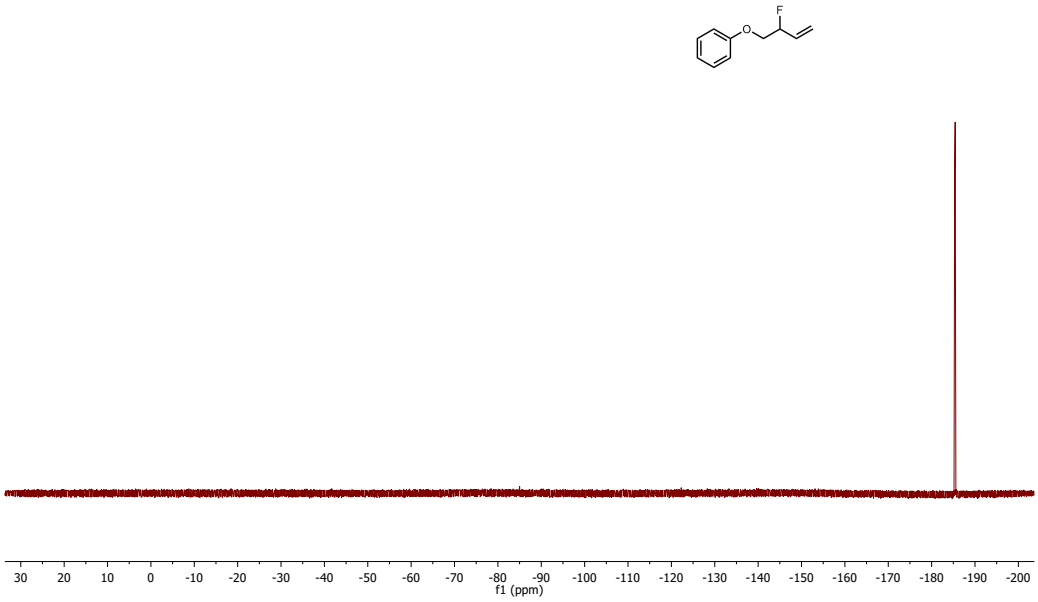
BC-1-47PROTON01
bc-I-47-13C_1H



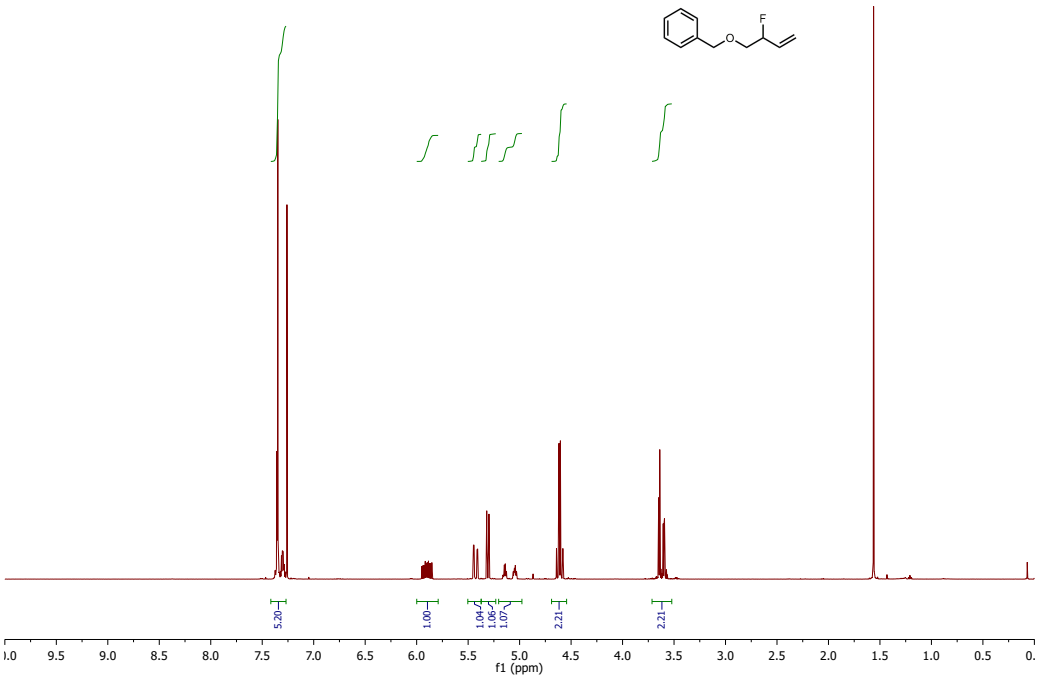
BC-1-47CARBON01
BC-1-47



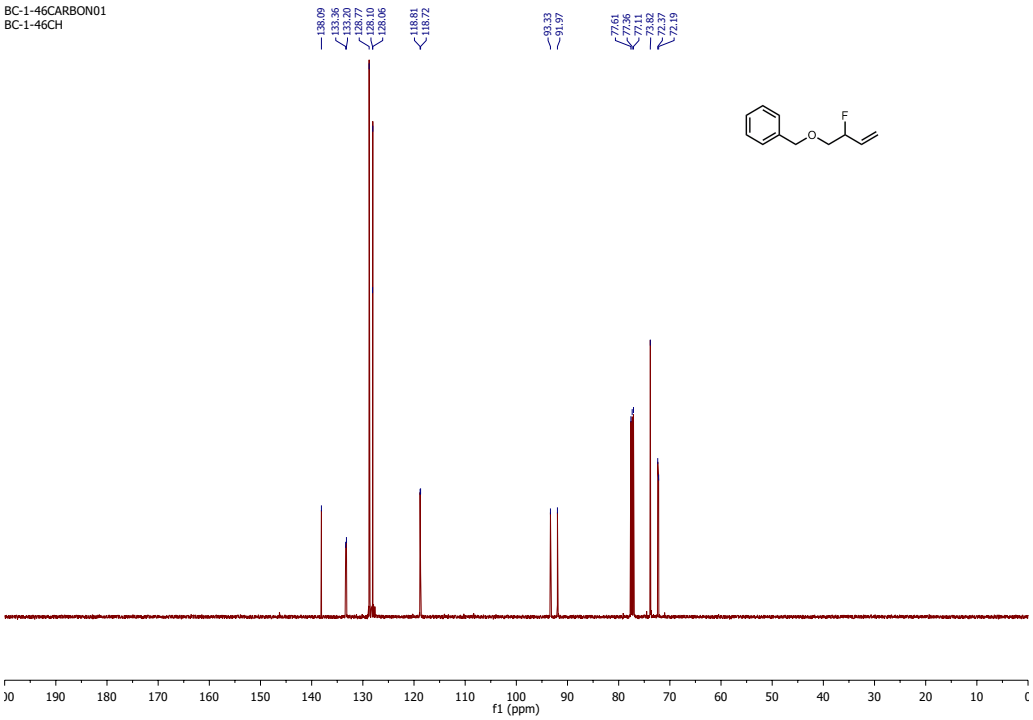
FLUORINE01
BC-1-47siena



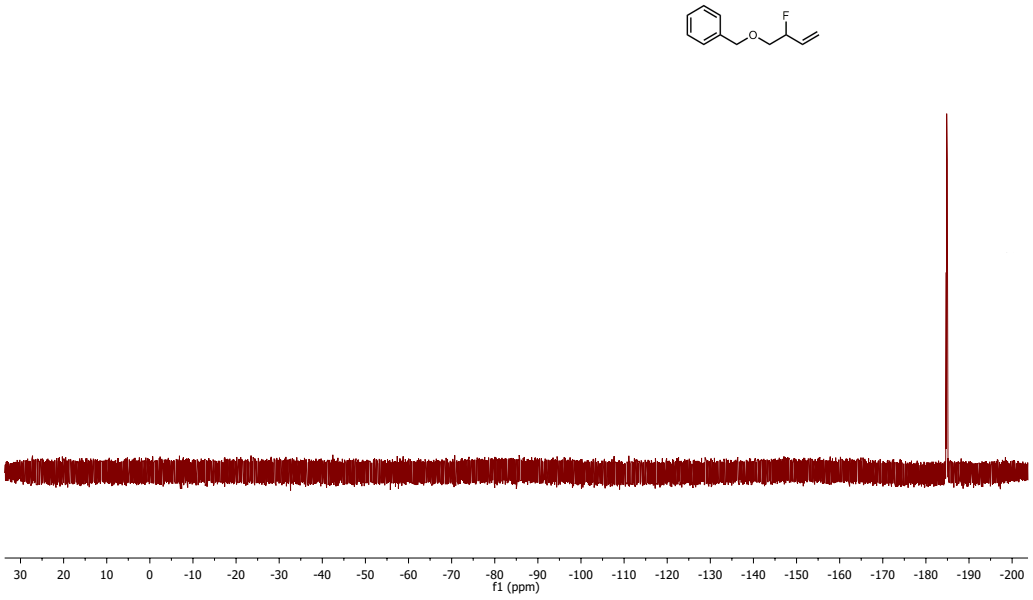
BC-1-46PROTON01
bc-I-46-H1



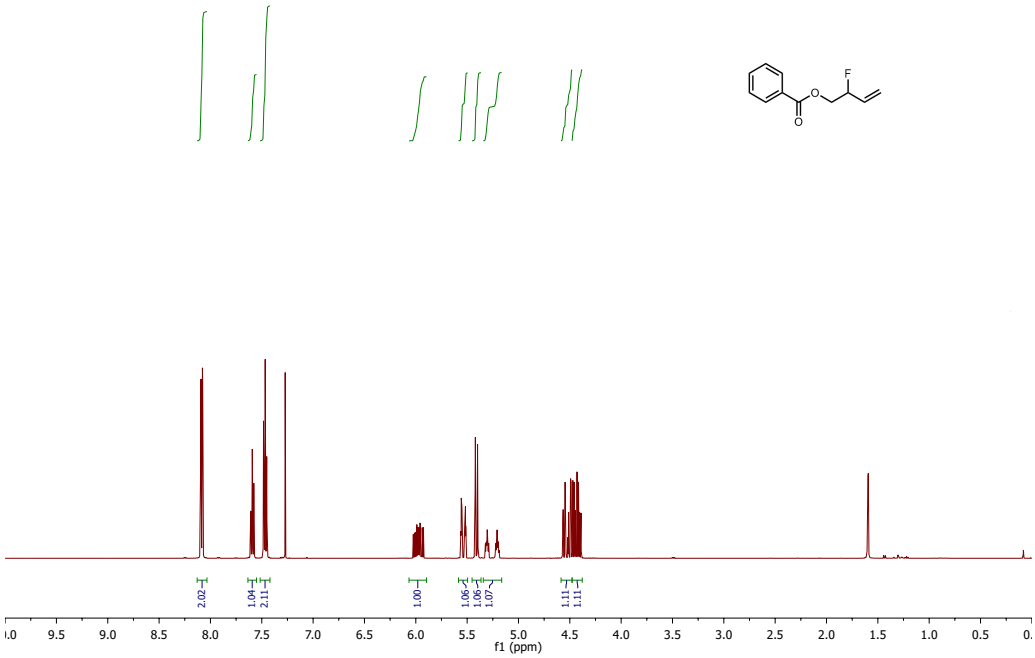
BC-1-46CARBON01
BC-1-46CH



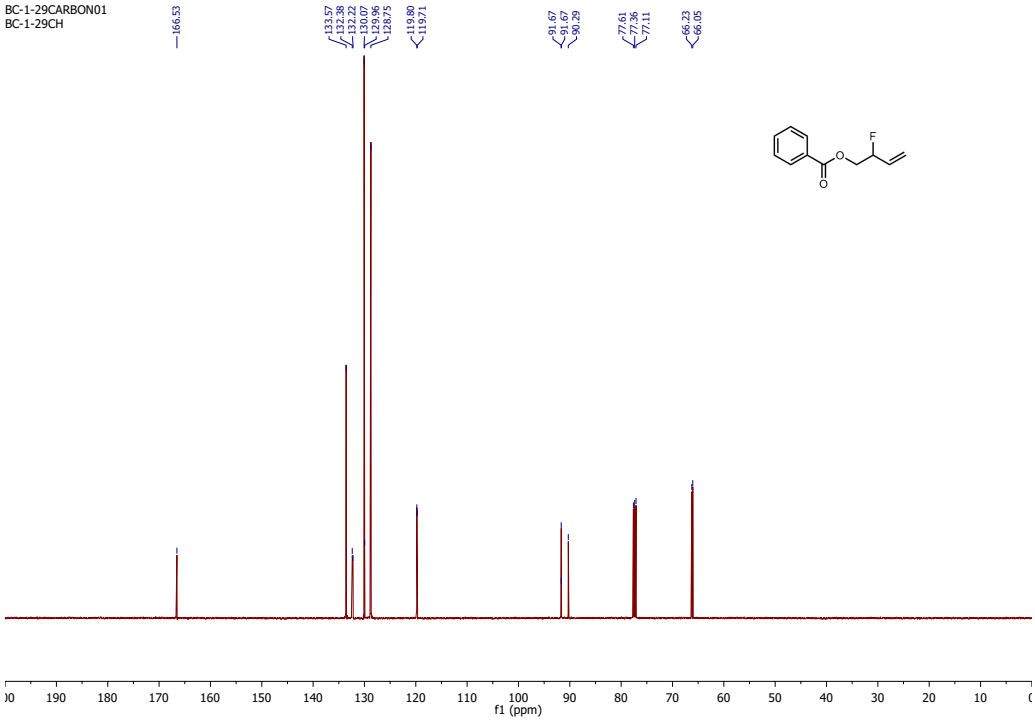
FLUORINE01
BC-1-46siena



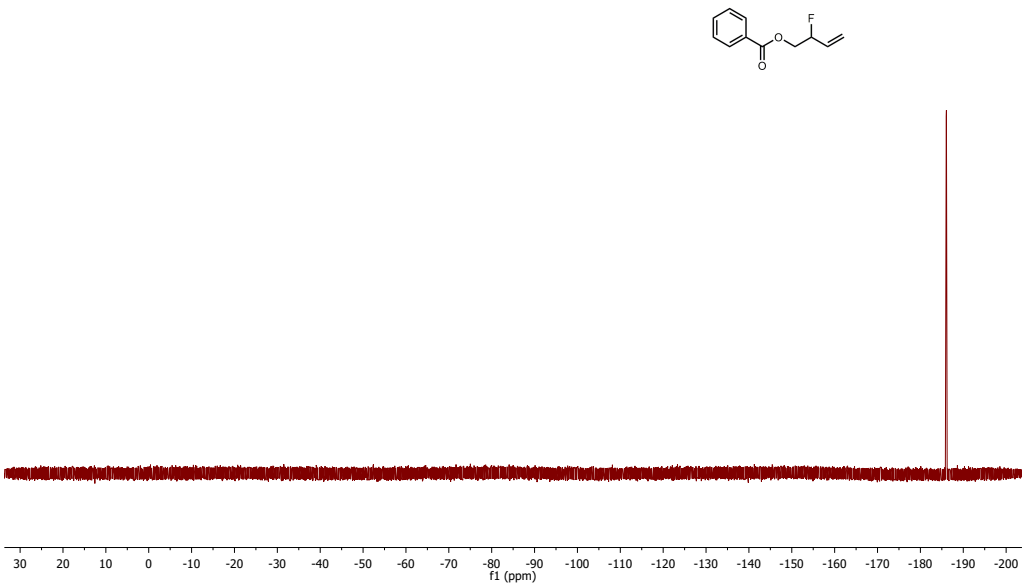
BC-1-29PROTON01
bc-I-29-H1



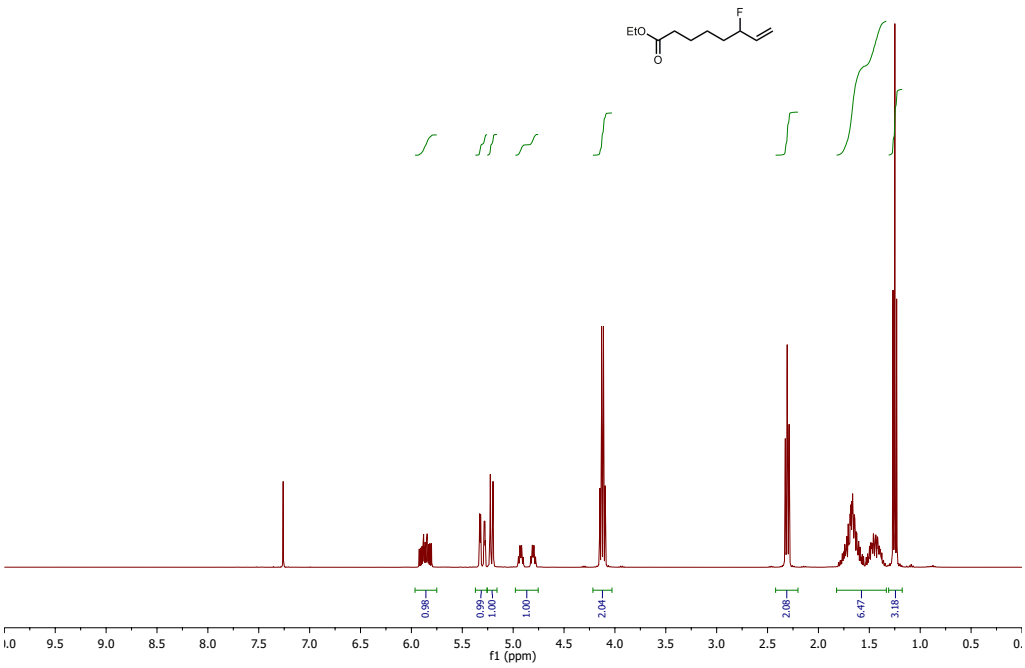
BC-1-29CARBON01
BC-1-29CH



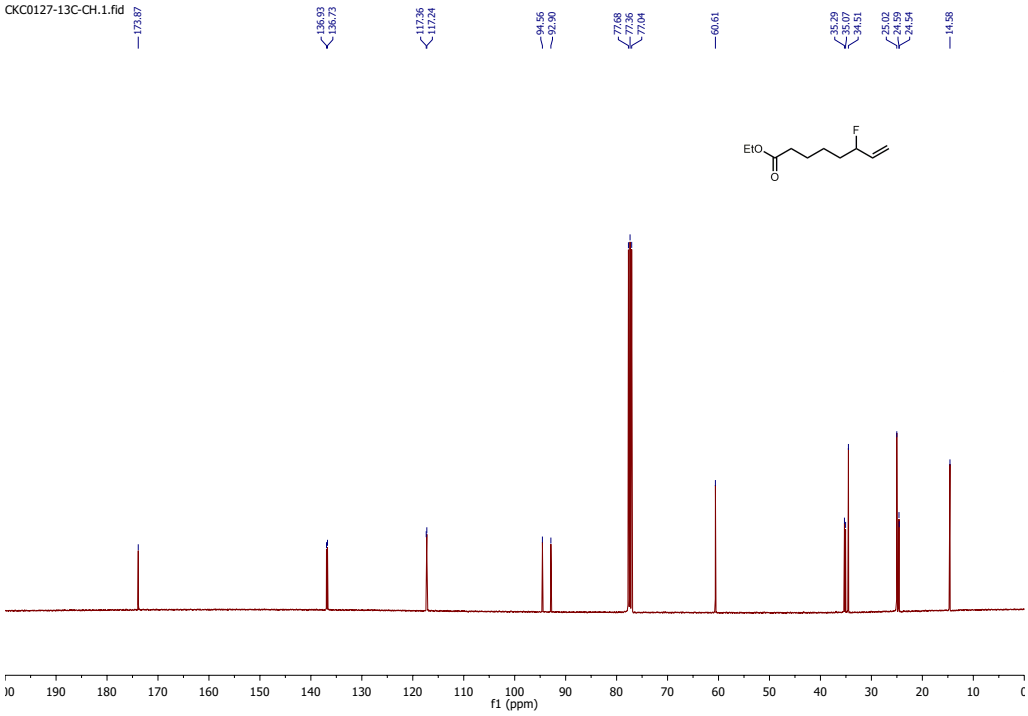
FLUORINE01
BC-1-29siena



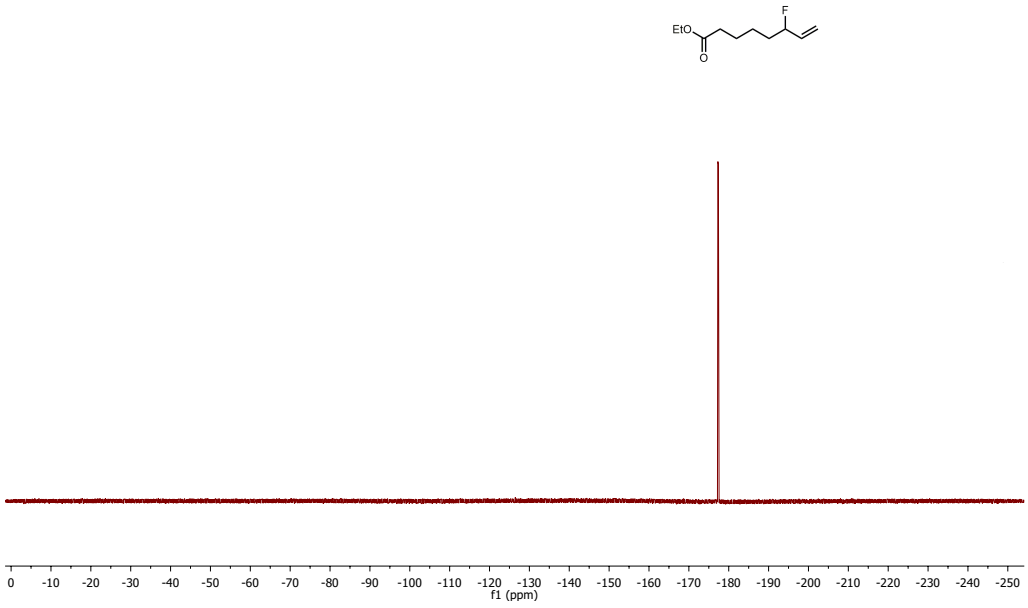
CKC0127-1H-CH.1.fid



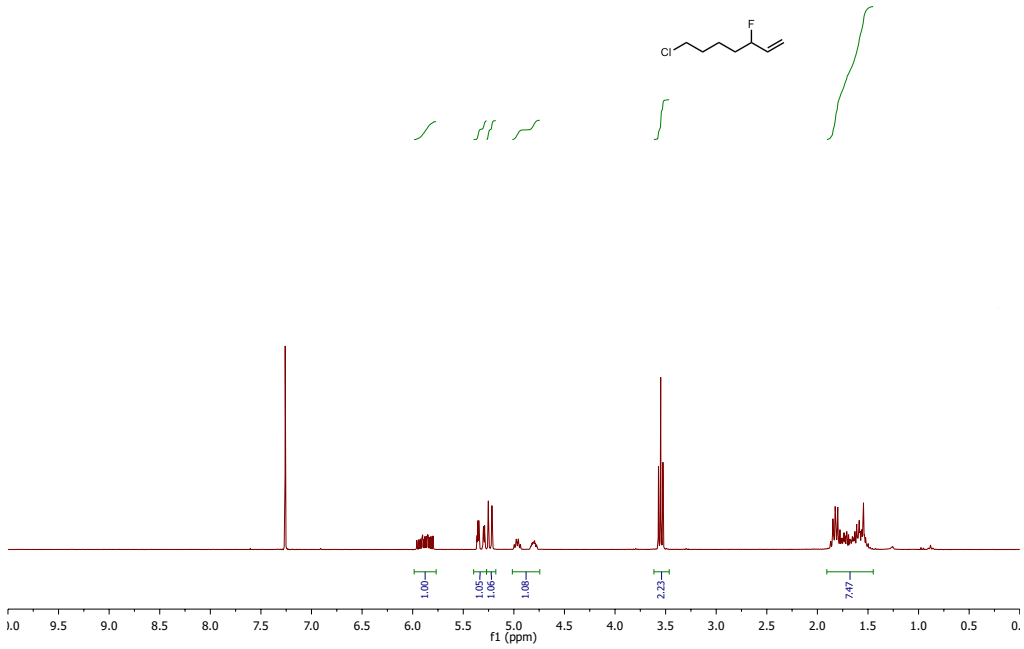
CKC0127-13C-CH.1.fid



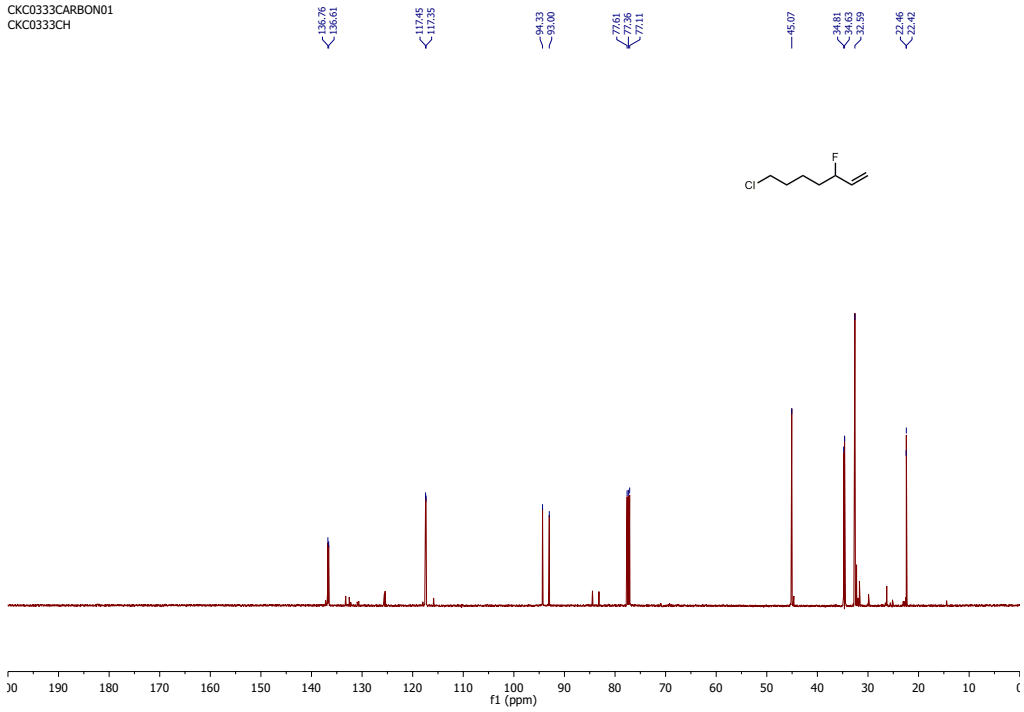
FLUORINE01
BC-1-29siena



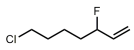
CKC0333PROTON01
CKC0333rota2

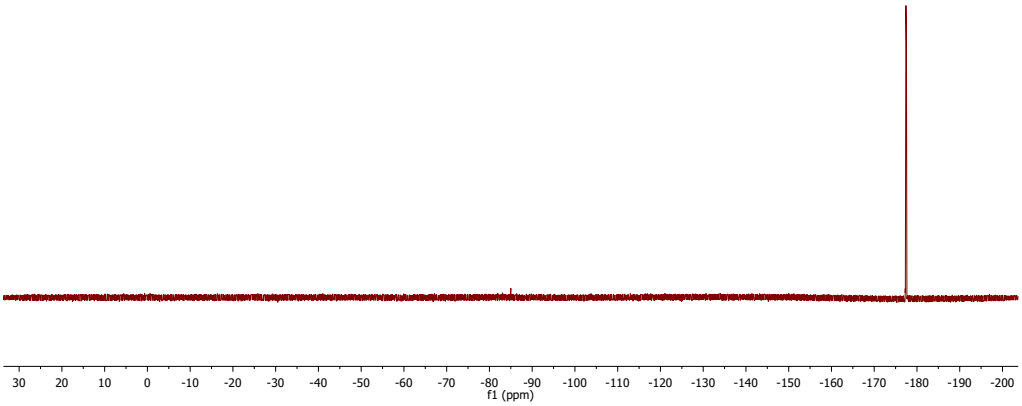


CKC0333CARBON01
CKC0333CH

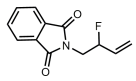


FLUORINE01
CKC0333siena

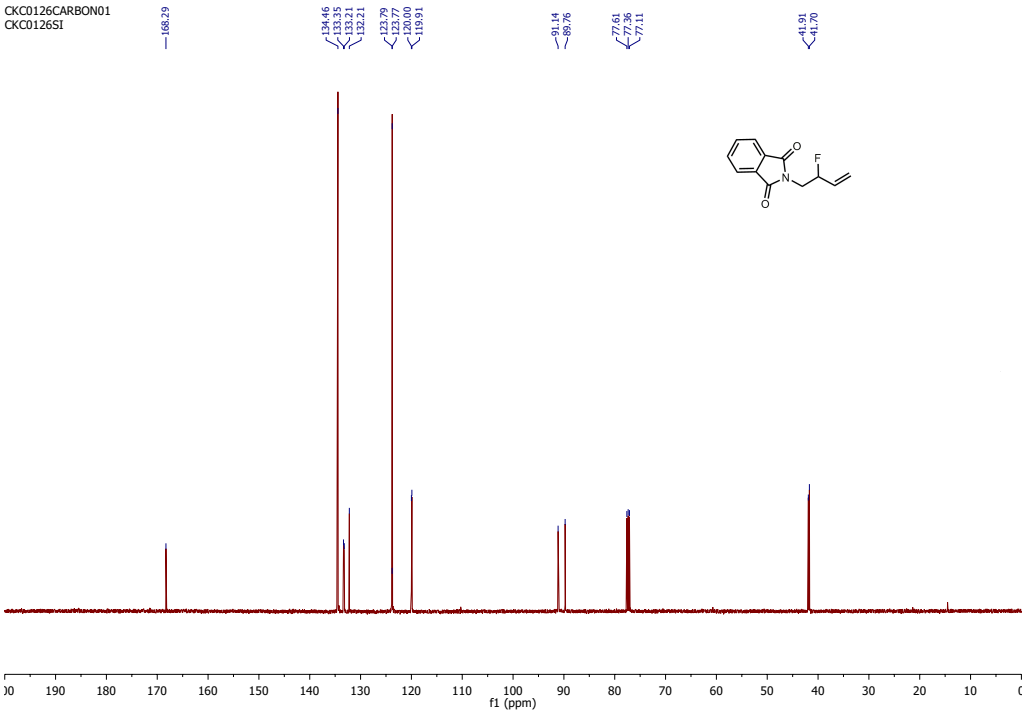




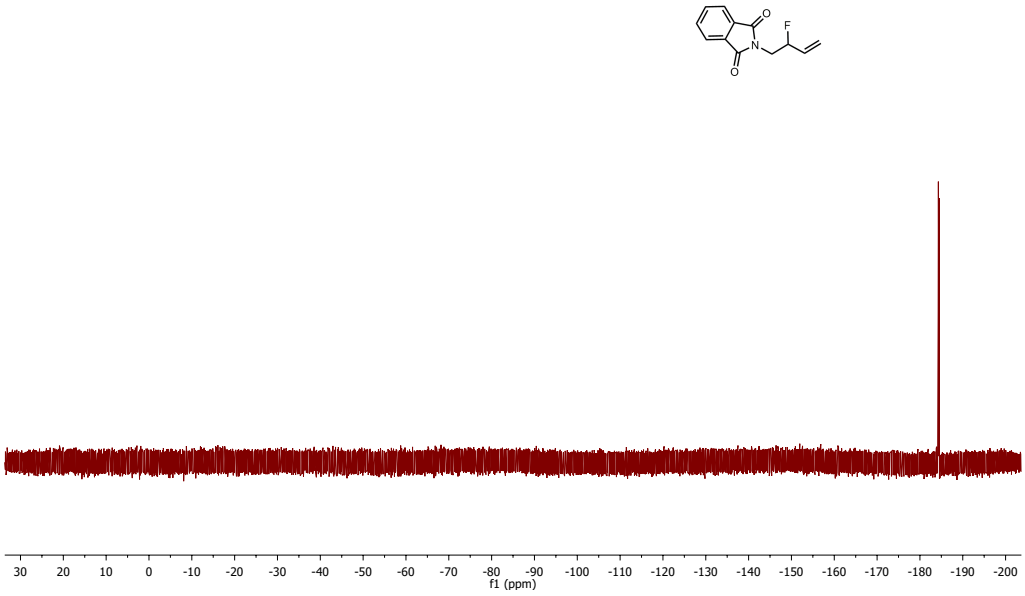
CKC0126PROTON01
CKC0126SIr



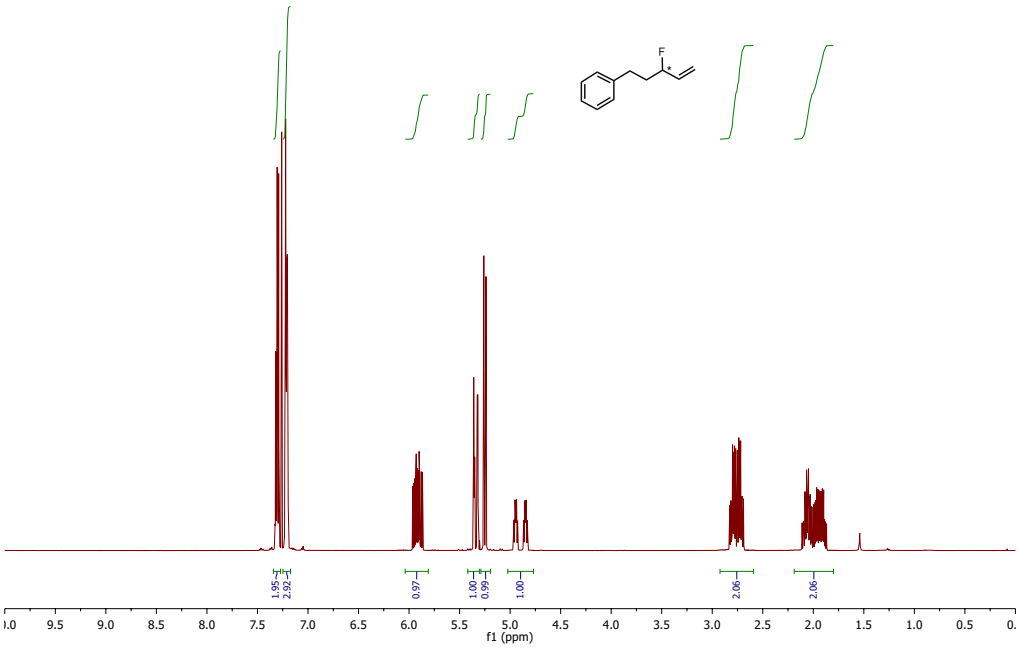
CKC0126CARBON01
CKC0126SI

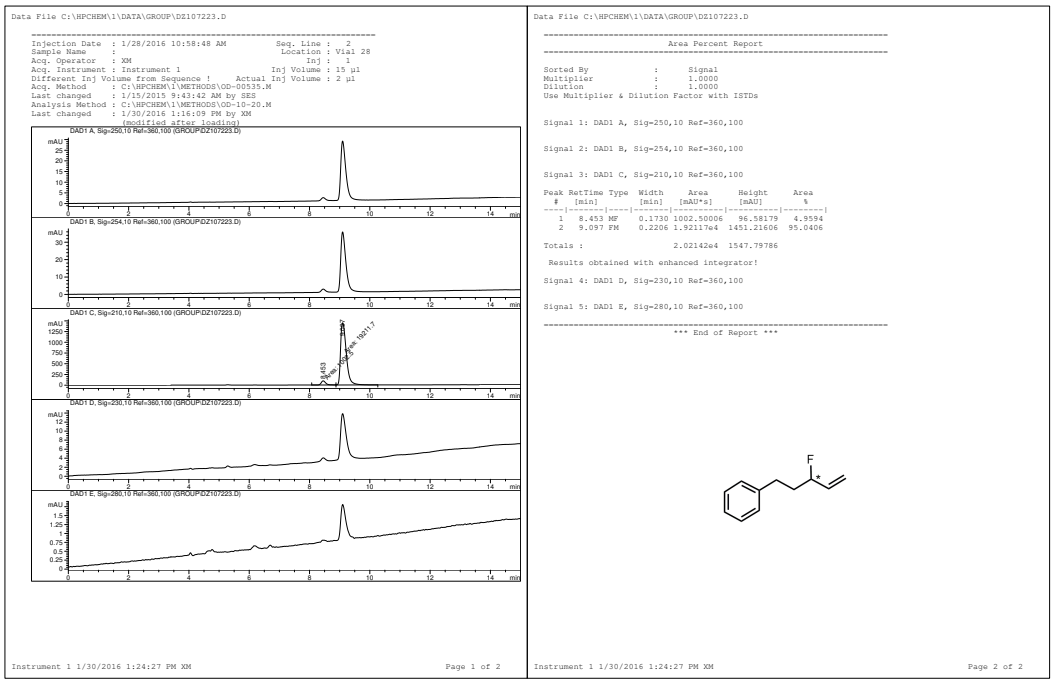


FLUORINE01
CKC0126siena



PROTON05
DZ-01-072-2-Purified





Data File C:\HPCHEM\1\DATA\GROUP\DZ107223.D

Injection Date : 1/28/2016 10:58:48 AM Seq. Line : 2
Sample Name : Location : Vial 28
Acq. Operator : XM Inj : 1
Acq. Instrument : Instrument 1 Inj Volume : 15 µl
Different Inj Volume from Sequence ! Actual Inj Volume : 2 µl
Acq. Method : C:\HPCHEM\1\METHODS\OD-00535.M
Last changed : 1/15/2015 9:43:42 AM by SES
Analysis Method : C:\HPCHEM\1\METHODS\OD-10-20.M
Last changed : 1/30/2016 1:16:09 PM by XM
(modified after loading)

DAD1 A, Sig=250,10 Ref=360,100 (GROUP\DZ107223.D)
DAD1 B, Sig=254,10 Ref=360,100 (GROUP\DZ107223.D)
DAD1 C, Sig=210,10 Ref=360,100 (GROUP\DZ107223.D)
8.453 MF 0.1730 1002.50006
9.097 FM 0.2206 1.92117e4
DAD1 D, Sig=230,10 Ref=360,100 (GROUP\DZ107223.D)
DAD1 E, Sig=280,10 Ref=360,100 (GROUP\DZ107223.D)

Instrument 1 1/30/2016 1:24:27 PM XM Page 1 of 2

Data File C:\HPCHEM\1\DATA\GROUP\DZ107223.D

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=250,10 Ref=360,100

Signal 2: DAD1 B, Sig=254,10 Ref=360,100

Signal 3: DAD1 C, Sig=210,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.453	MF	0.1730	1002.50006	96.58179	4.9594
2	9.097	FM	0.2206	1.92117e4	1451.21606	95.0406

Totals : 2.02142e4 1547.79786

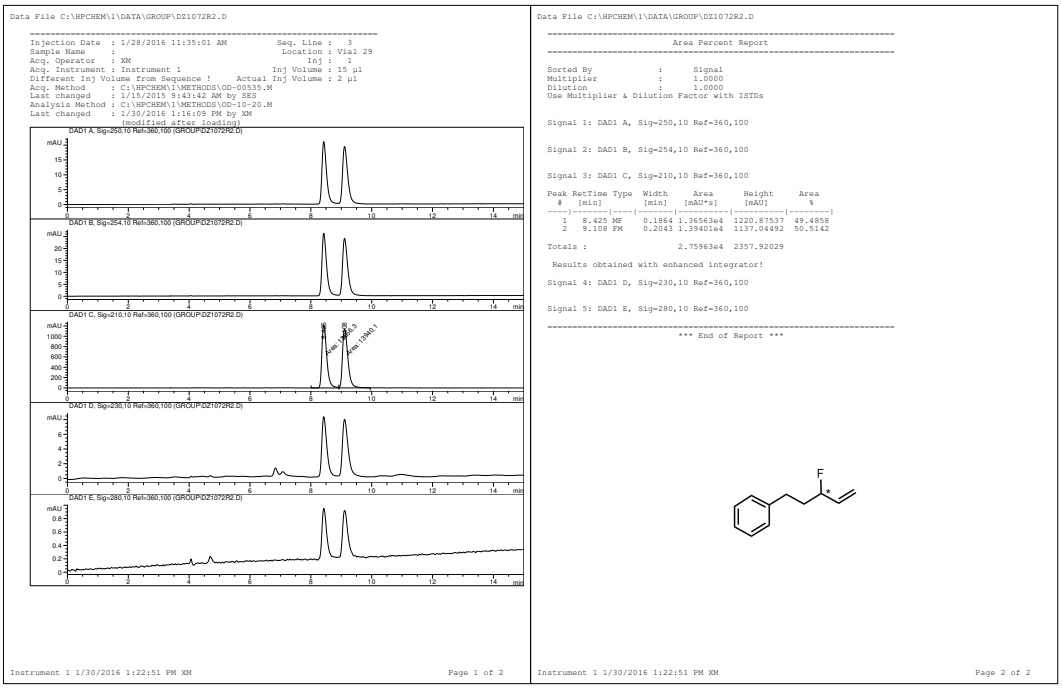
Results obtained with enhanced integrator!

Signal 4: DAD1 D, Sig=230,10 Ref=360,100

Signal 5: DAD1 E, Sig=280,10 Ref=360,100

*** End of Report ***

Instrument 1 1/30/2016 1:24:27 PM XM Page 2 of 2



Data File C:\HPCHEM\1\DATA\GROUP\DZ1072R2.D

Injection Date : 1/28/2016 11:35:01 AM Seq. Line : 3
Sample Name : Location : Vial 29
Acq. Operator : XM Inj : 1
Acq. Instrument : Instrument 1 Inj Volume : 15 µl
Different Inj Volume from Sequence ! Actual Inj Volume : 2 µl
Acq. Method : C:\HPCHEM\1\METHODS\OD-00535.M
Last changed : 1/15/2015 9:43:42 AM by SES
Analysis Method : C:\HPCHEM\1\METHODS\OD-10-20.M
Last changed : 1/30/2016 1:16:09 PM by XM
(modified after loading)

DAD1 A, Sig=250,10 Ref=360,100 (GROUP\DZ1072R2.D)
DAD1 B, Sig=254,10 Ref=360,100 (GROUP\DZ1072R2.D)
DAD1 C, Sig=210,10 Ref=360,100 (GROUP\DZ1072R2.D)
Area: 13563.9
Area: 13940.1
DAD1 D, Sig=230,10 Ref=360,100 (GROUP\DZ1072R2.D)
DAD1 E, Sig=280,10 Ref=360,100 (GROUP\DZ1072R2.D)

Instrument 1 1/30/2016 1:22:51 PM XM Page 1 of 2

Data File C:\HPCHEM\1\DATA\GROUP\DZ1072R2.D

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=250,10 Ref=360,100

Signal 2: DAD1 B, Sig=254,10 Ref=360,100

Signal 3: DAD1 C, Sig=210,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.425	MF	0.1864	1.36563e4	1220.87537	49.4858
2	9.108	FM	0.2043	1.39401e4	1137.04492	50.5142

Totals : 2.75963e4 2357.92029

Results obtained with enhanced integrator!

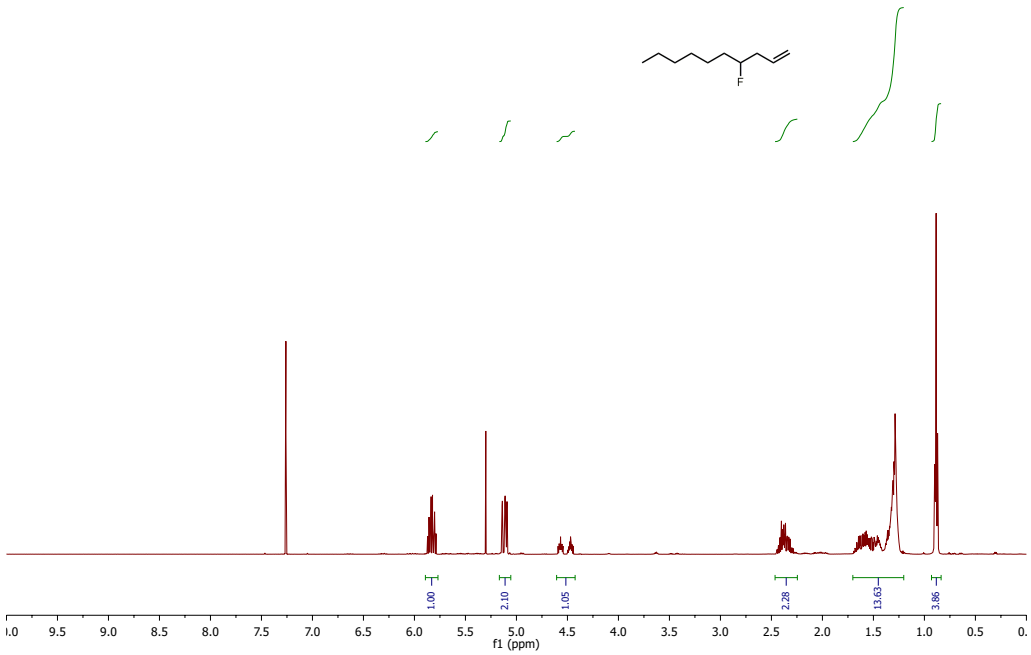
Signal 4: DAD1 D, Sig=230,10 Ref=360,100

Signal 5: DAD1 E, Sig=280,10 Ref=360,100

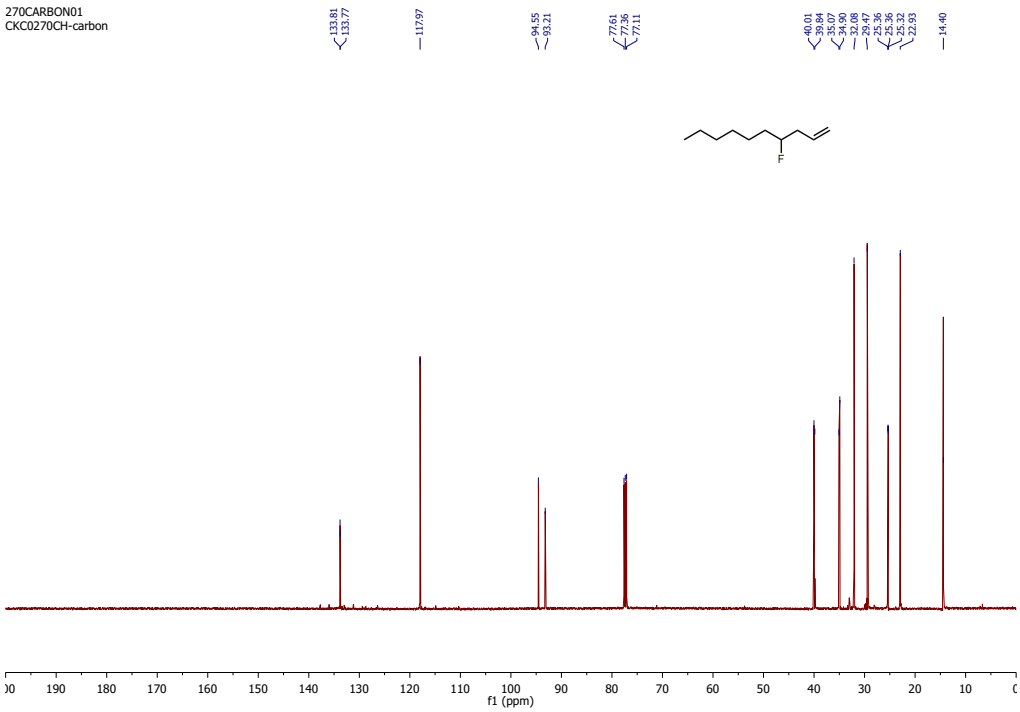
*** End of Report ***

Instrument 1 1/30/2016 1:22:51 PM XM Page 2 of 2

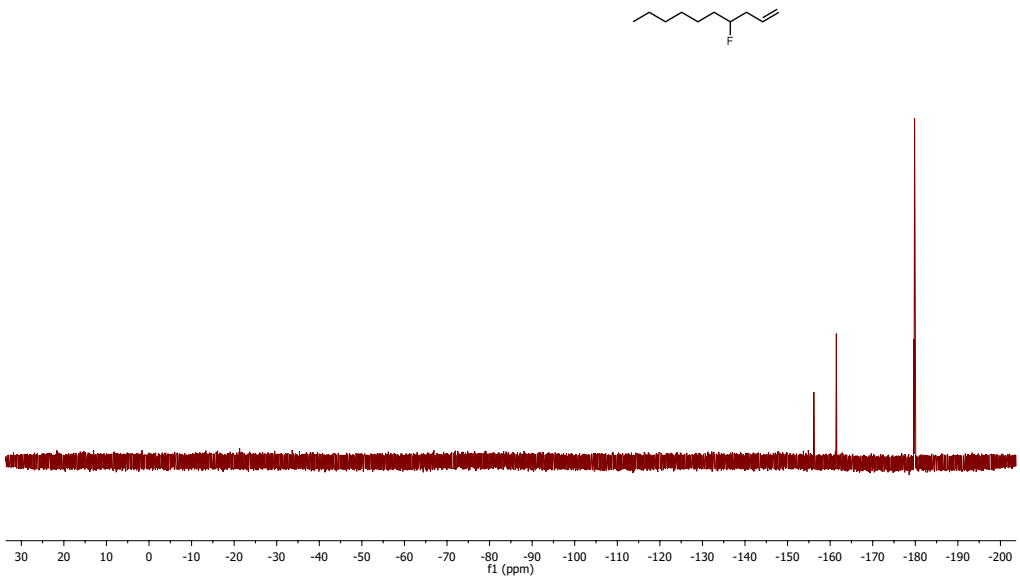
270PROTON01
CKC0270CH-proton



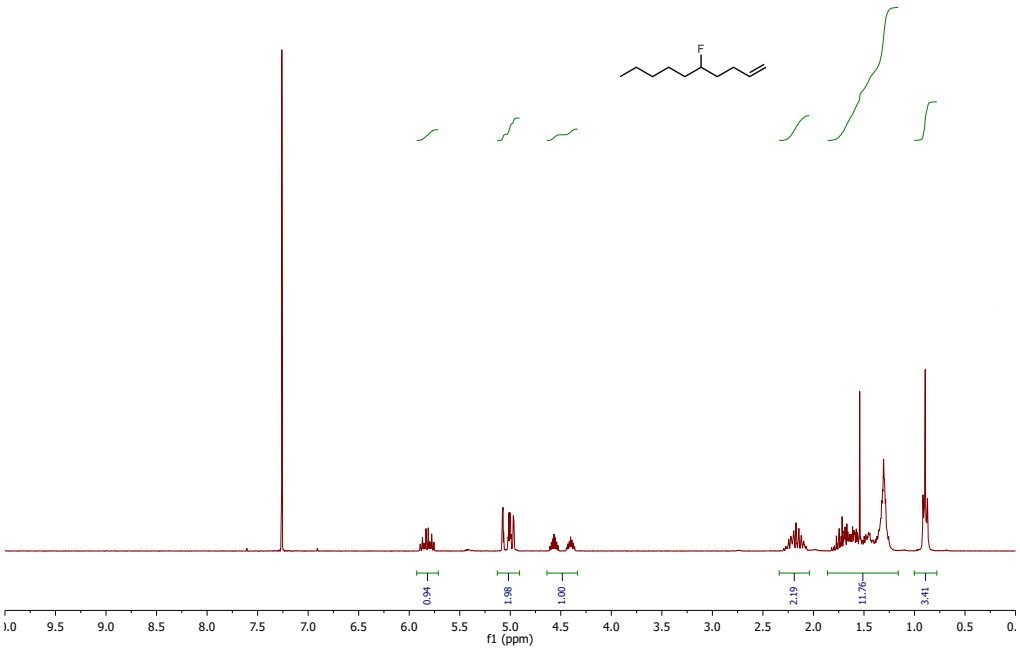
270CARBON01
CKC0270CH-carbon



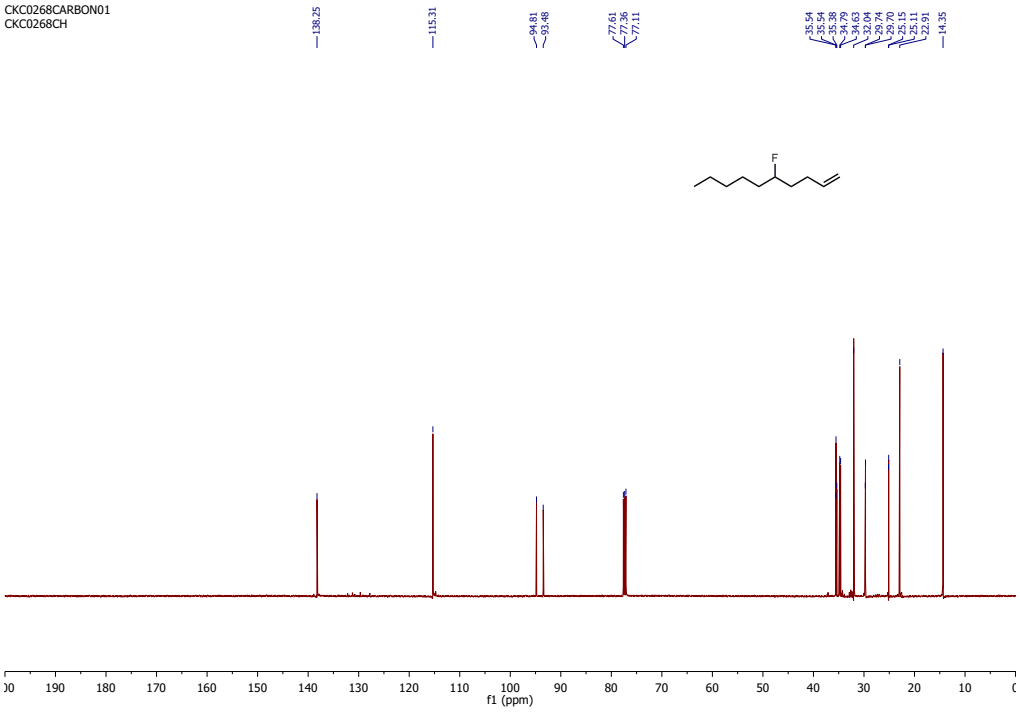
FLUORINE01
CKC0270sienaNo2



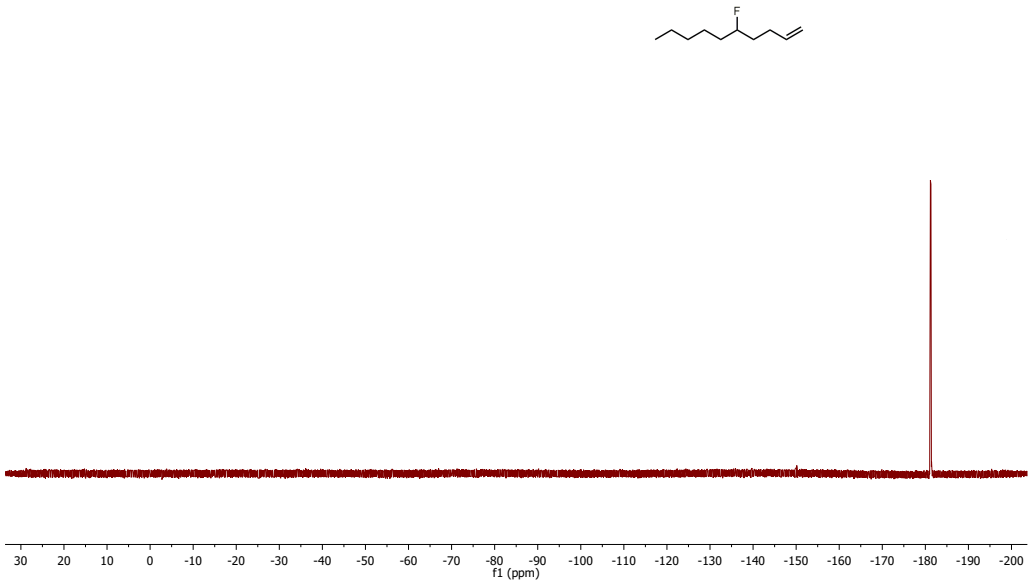
CKC0268nosolvent
CKC0268-7-8-15



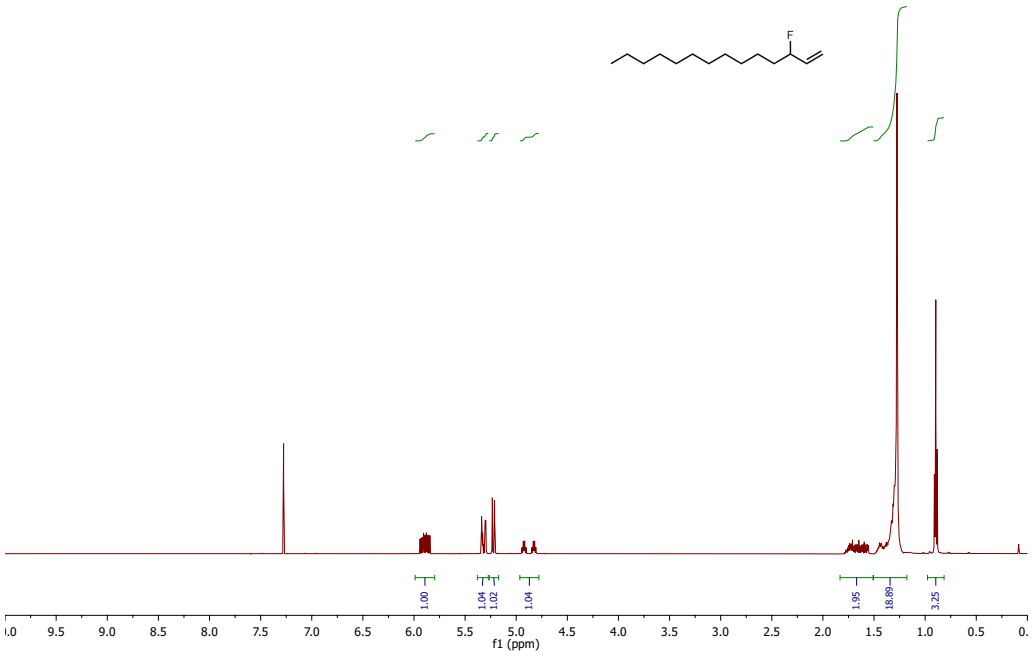
CKC0268CARBON01
CKC0268CH



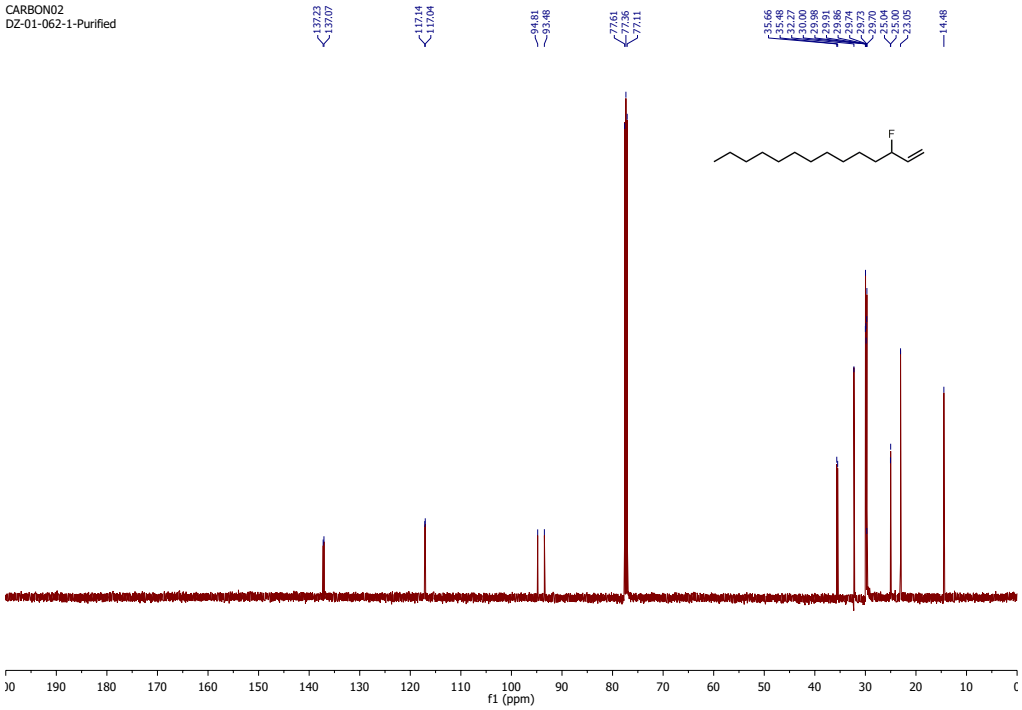
FLUORINE01
CKC0268siena



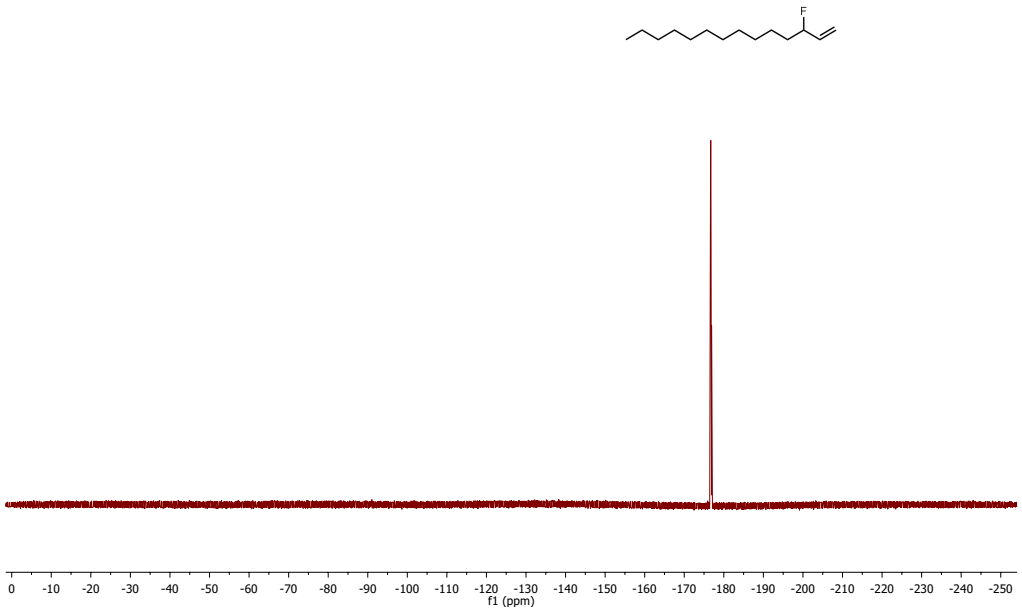
PROTON03
DZ-01-062-1-Purified



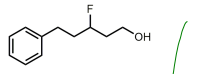
CARBON02
DZ-01-062-1-Purified



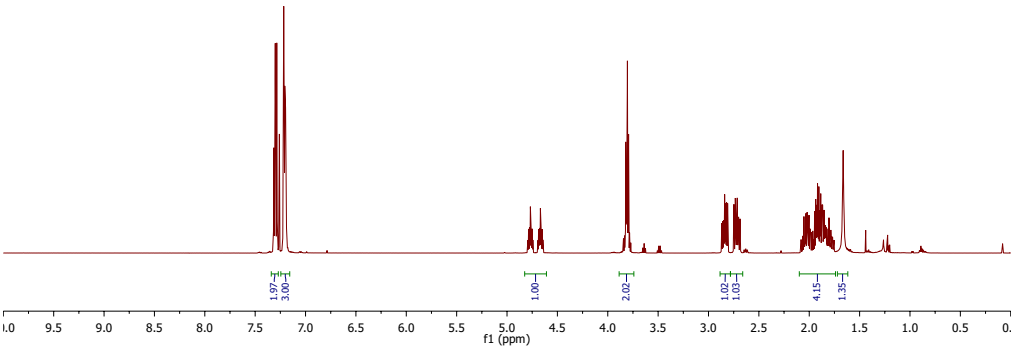
FLUORINE01
BC-1-29siena



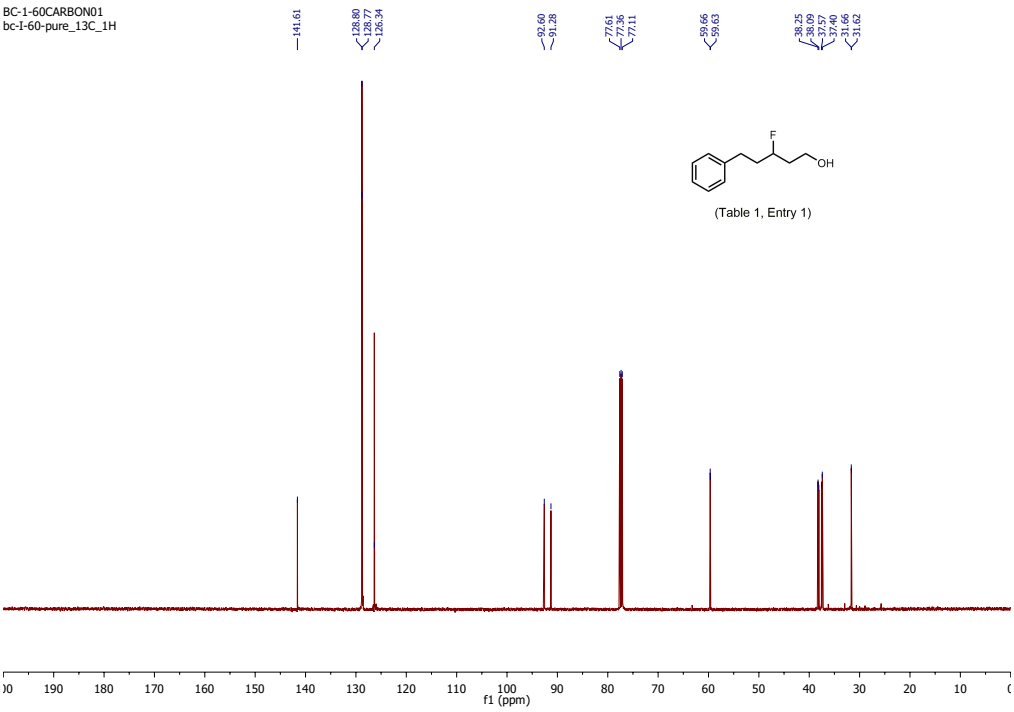
BC-1-60PROTON01
bc-I-60-pure_13C_1H



(Table 1, Entry 1)

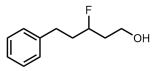


BC-1-60CARBON01
bc-I-60-pure_13C_1H

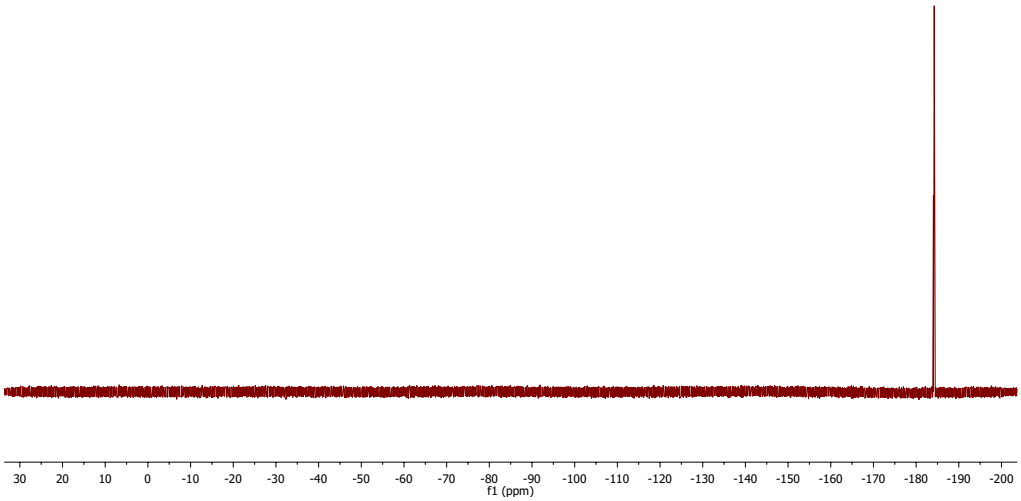


(Table 1, Entry 1)

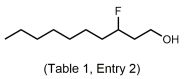
FLUORINE01
CKC0064siena



(Table 1, Entry 1)

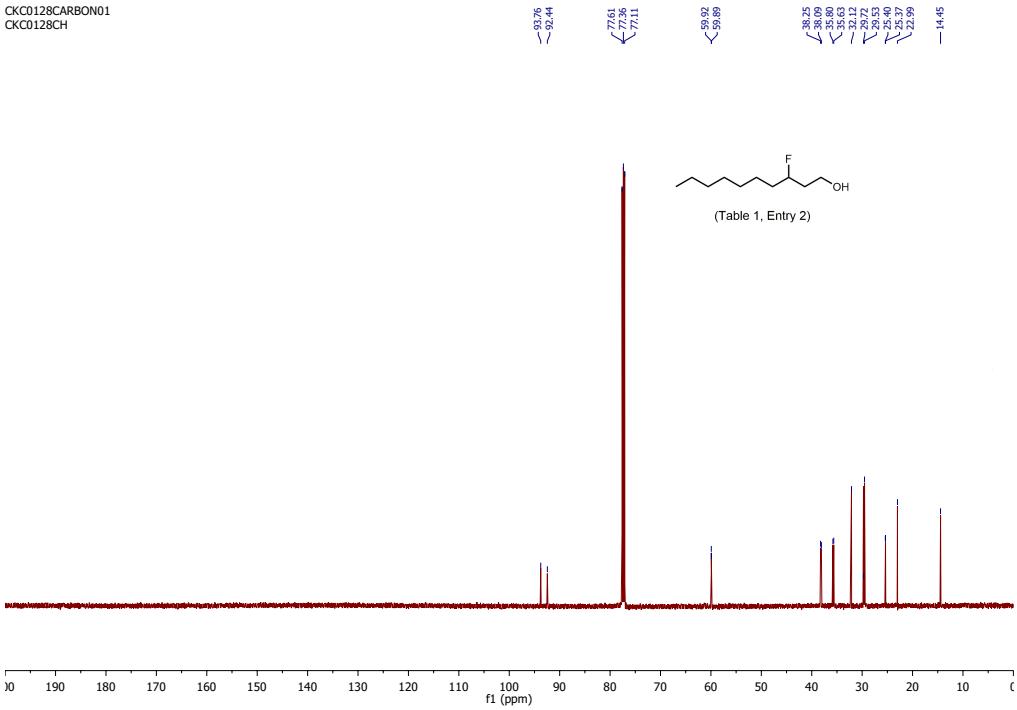


CKC0128PROTON01
CKC0128hivac

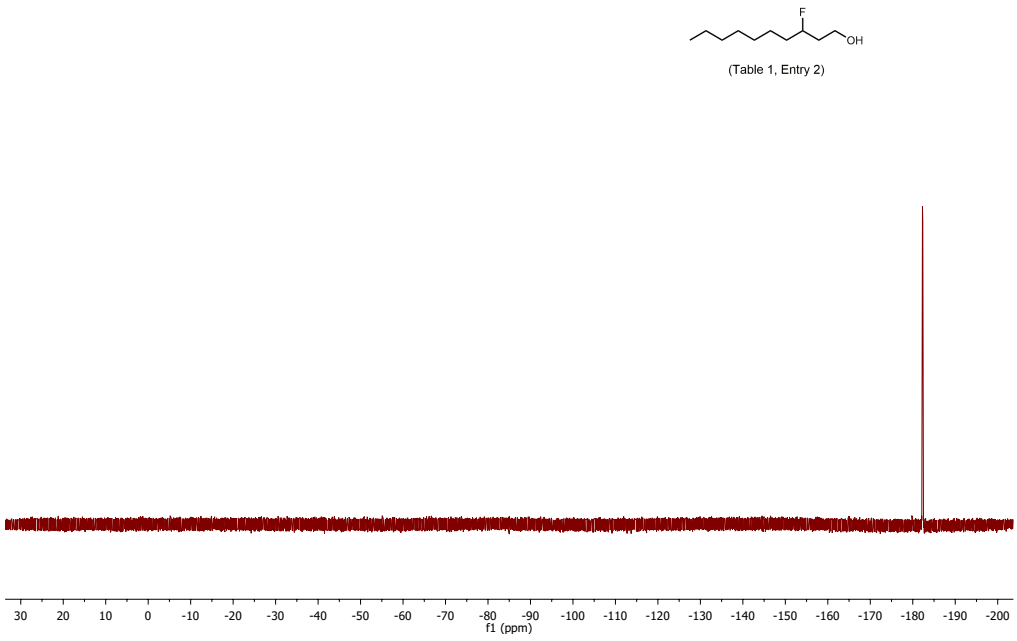


(Table 1, Entry 2)

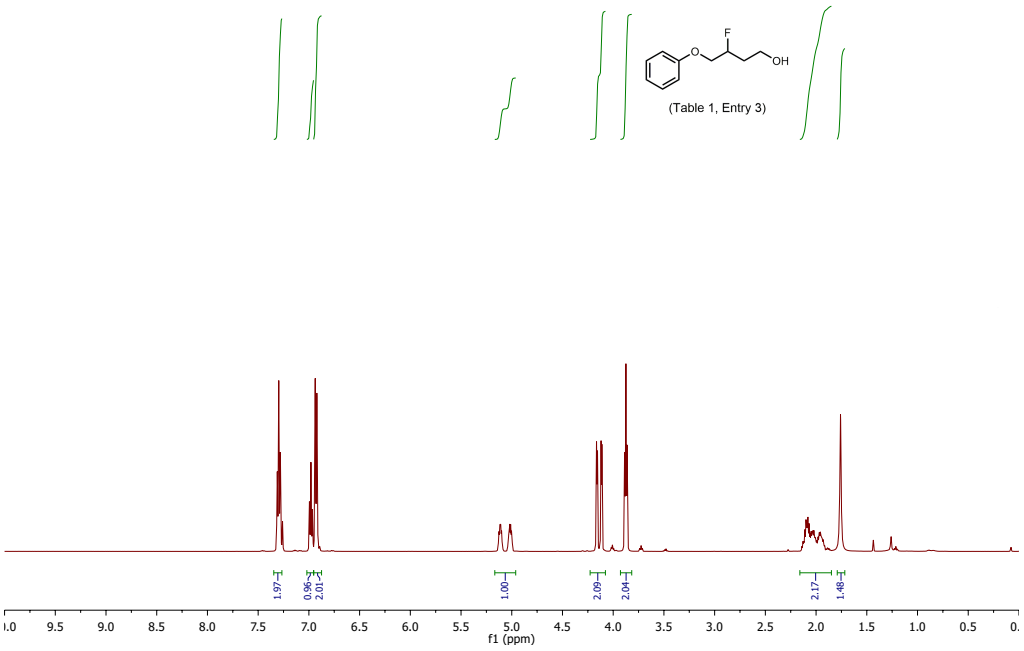
CKC0128CARBON01
CKC0128CH



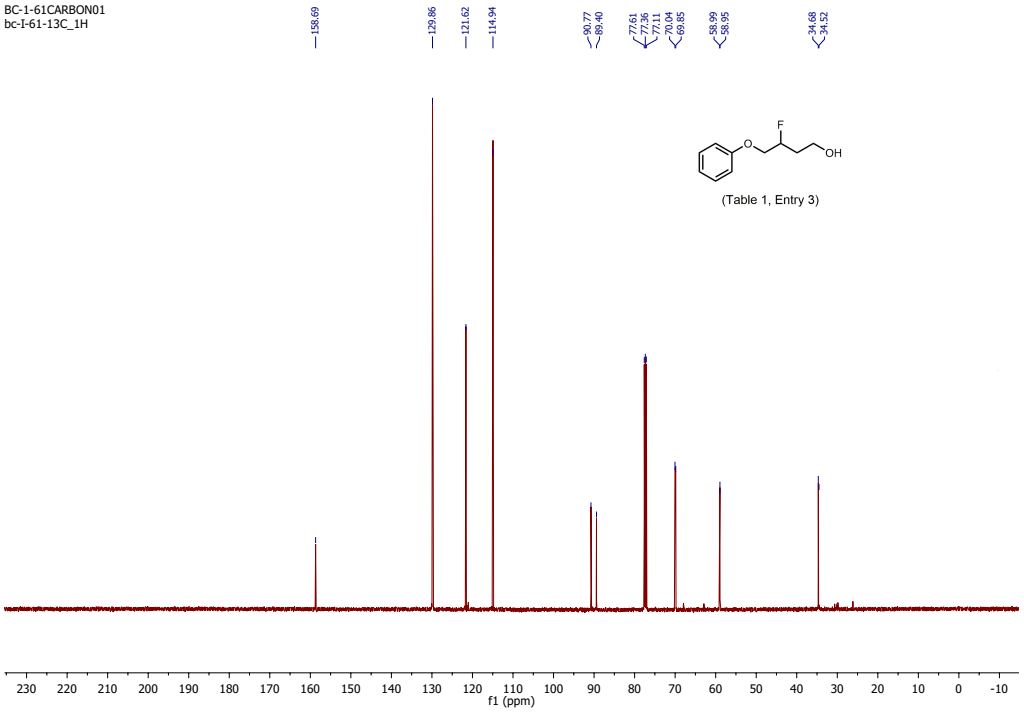
FLUORINE01
CKC0128siena



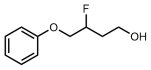
BC-1-61PROTON01
bc-I-61-13C_1H



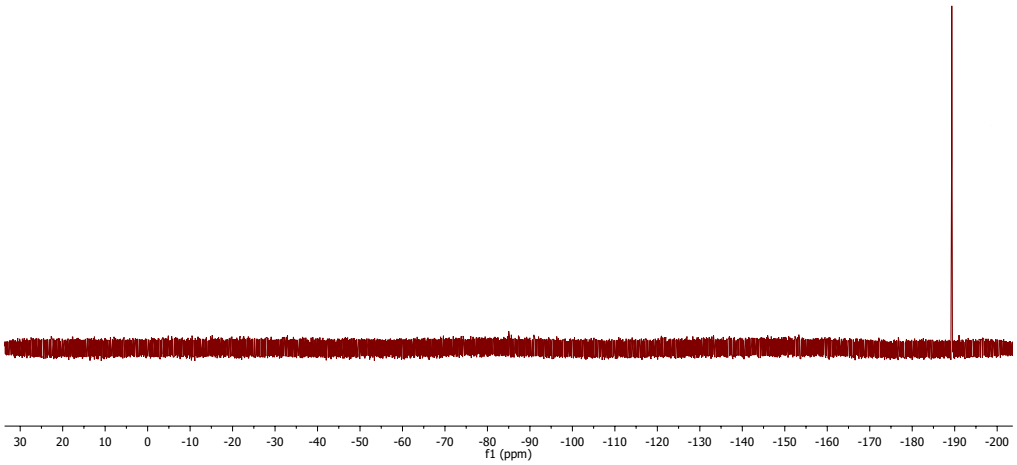
BC-1-61CARBON01
bc-I-61-13C_1H



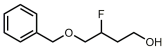
FLUORINE01
CKC0103siena



(Table 1, Entry 3)

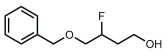


CKC0109CH-protonRE
CKC0109CH-protonRE

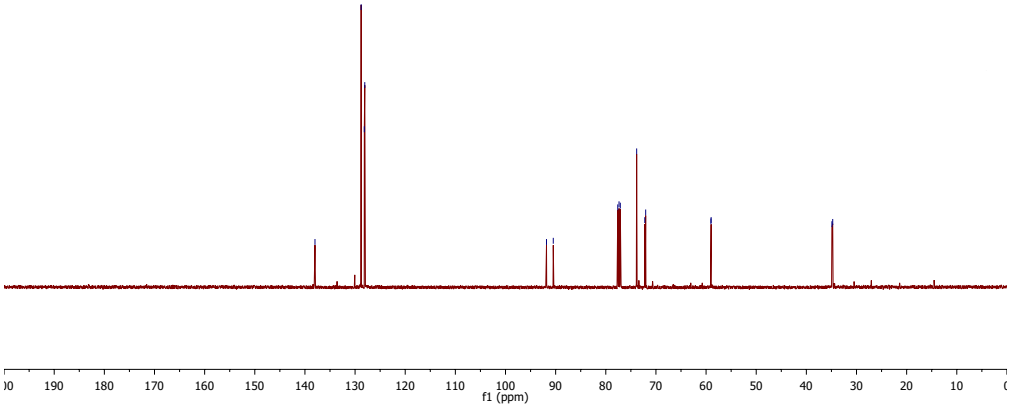


(Table 1, Entry 4)

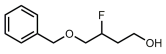
109CARBON01
CKC0109SI



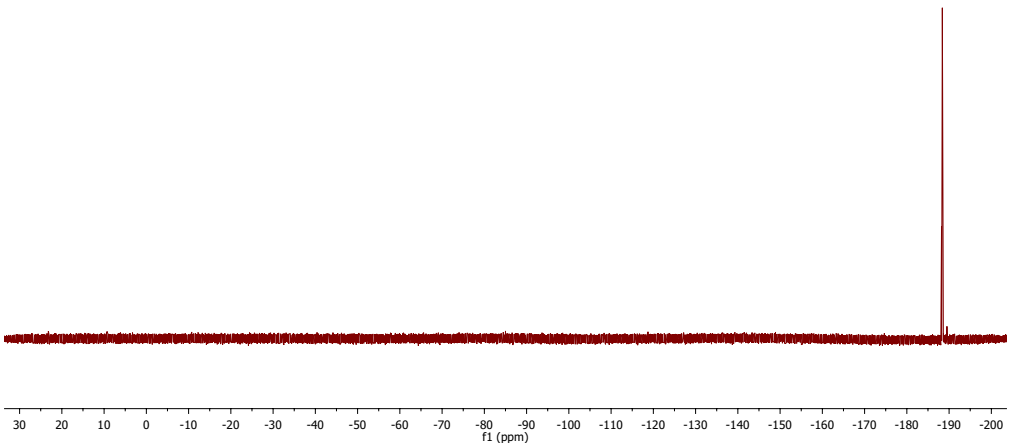
(Table 1, Entry 4)



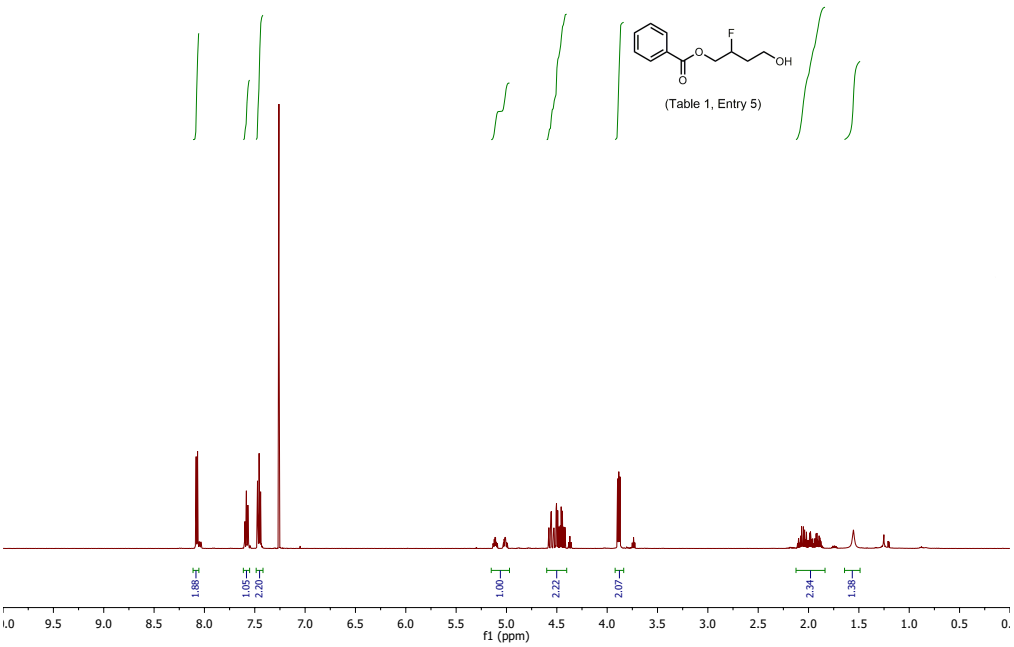
FLUORINE01
CKC0109siena



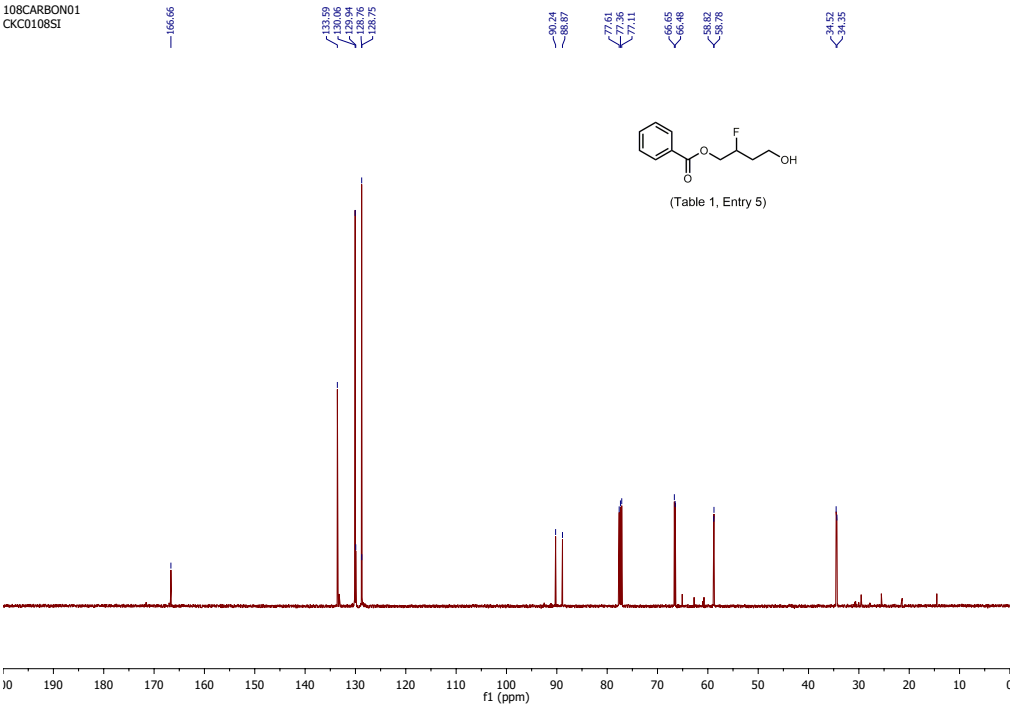
(Table 1, Entry 4)



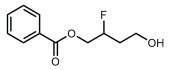
108PROTON01
CKC0108CH-proton



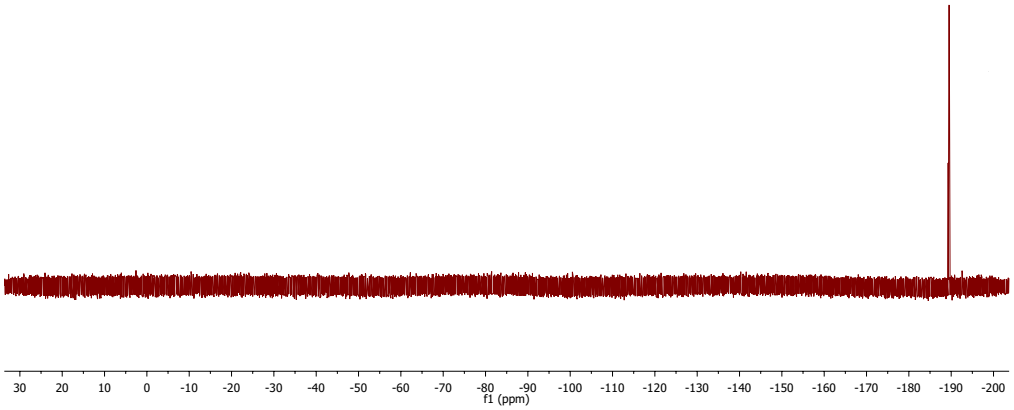
108CARBON01
CKC0108SI



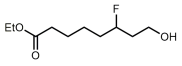
FLUORINE01
CKC0108siena



(Table 1, Entry 5)

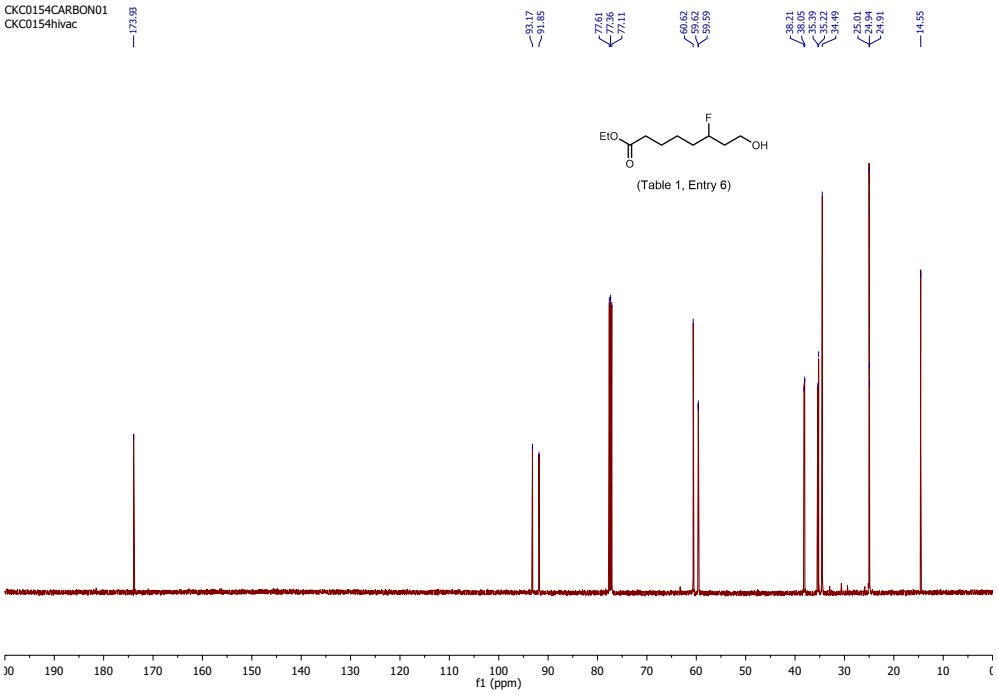


CKC0154PROTON01
CKC0154hivac

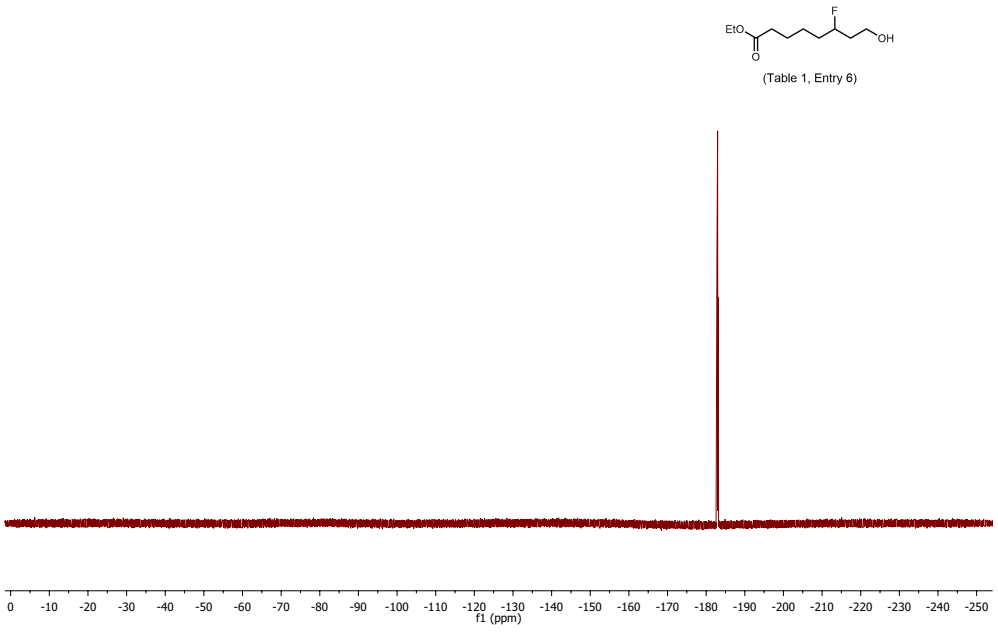


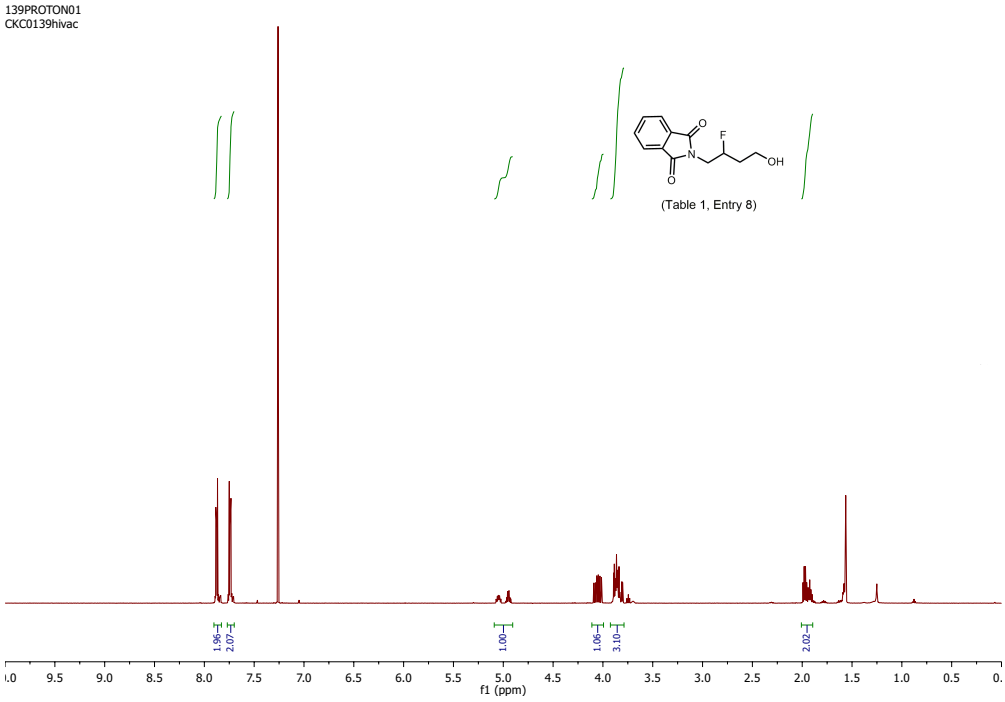
(Table 1, Entry 6)

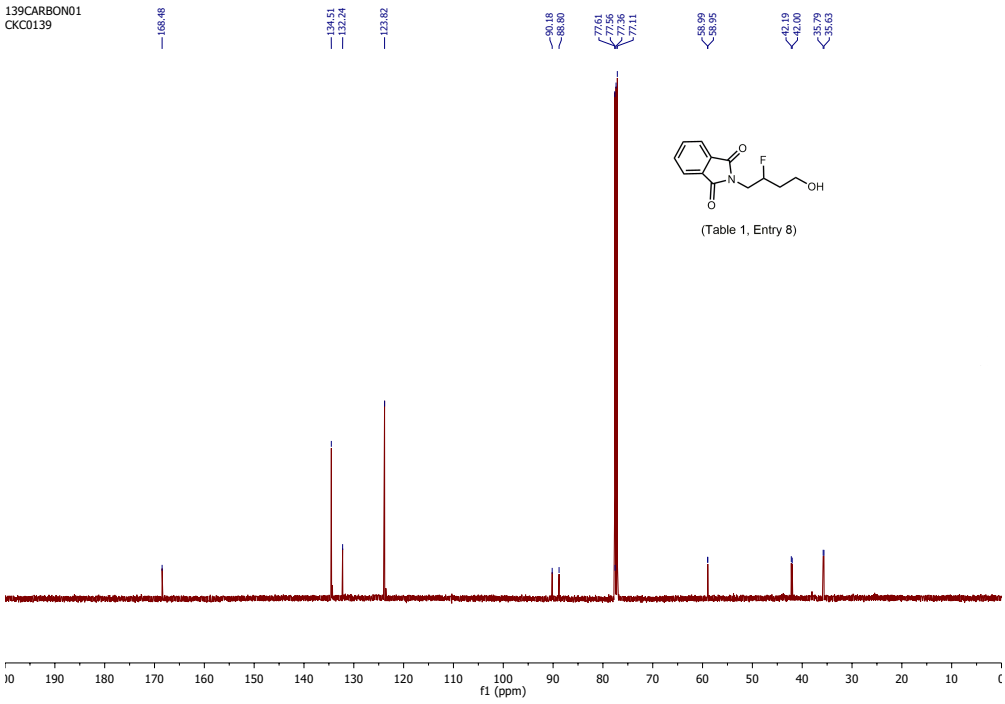
CKC0154CARBON01
CKC0154hivac



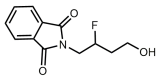
FLUORINE01
BC-1-29siena



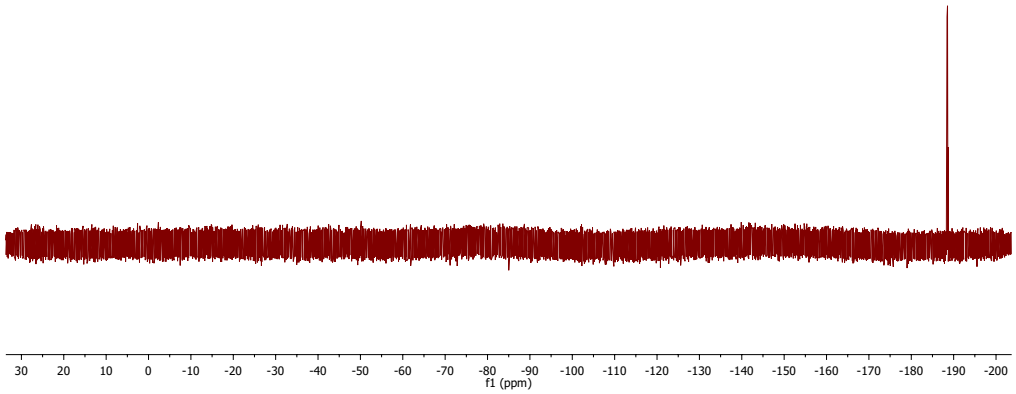

139PROTON01
CKC0139hivac
O
F
N
OH
O
(Table 1, Entry 8)
1.98
2.07
1.00
1.06
3.10
2.02
f1 (ppm)


139CARBON01
CKC0139
168.48
134.51
132.24
123.82
90.18
88.80
77.61
77.56
77.36
77.11
58.99
58.95
42.19
42.00
35.79
35.63
O
F
N
OH
O
(Table 1, Entry 8)
f1 (ppm)

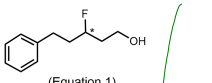
FLUORINE01
CKC0139siena



(Table 1, Entry 8)



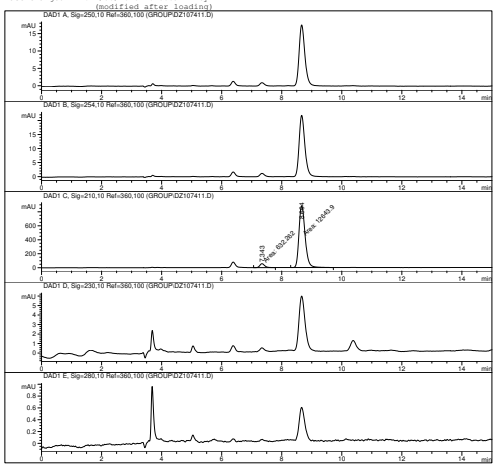
PROTON03
DZ-01-074-1-Purified



(Equation 1)

Data File C:\HPCHEM\1\DATA\GROUP\DZ107411.D

Injection Date : 1/30/2016 12:27:33 PM Seq. Line : 3
Sample Name : Location : Vial 2
Acq. Operator : XM Inj : 1
Acq. Instrument : Instrument 1 Inj Volume : 15 µl
Different Inj Volume from Sequence ! Actual Inj Volume : 2 µl
Acq. Method : C:\HPCHEM\1\METHODS\OD-15-20.M
Last changed : 5/19/2011 9:25:09 PM by NB
Analysis Method : C:\HPCHEM\1\METHODS\OD-10-20.M
Last changed : 1/30/2016 1:16:09 PM by XM
(modified after loading)



Data File C:\HPCHEM\1\DATA\GROUP\DZ107411.D

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=250,10 Ref=360,100

Signal 2: DAD1 B, Sig=254,10 Ref=360,100

Signal 3: DAD1 C, Sig=210,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.343	MM	0.1888	632.26190	55.80346	4.7624
2	8.664	MM	0.2383	1.26439e4	884.45312	95.2376

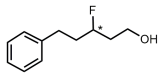
Totals : 1.32762e4 940.25658

Results obtained with enhanced integrator!

Signal 4: DAD1 D, Sig=230,10 Ref=360,100

Signal 5: DAD1 E, Sig=280,10 Ref=360,100

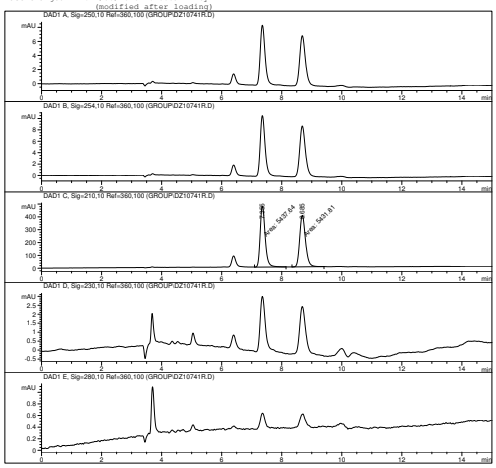
*** End of Report ***



(Equation 1)

Data File C:\HPCHEM\1\DATA\GROUP\DZ10741R.D

Injection Date : 1/30/2016 12:06:19 PM Seq. Line : 2
Sample Name : Location : Vial 1
Acq. Operator : XM Inj : 1
Acq. Instrument : Instrument 1 Inj Volume : 15 µl
Different Inj Volume from Sequence ! Actual Inj Volume : 2 µl
Acq. Method : C:\HPCHEM\1\METHODS\OD-15-20.M
Last changed : 5/19/2011 9:25:09 PM by NB
Analysis Method : C:\HPCHEM\1\METHODS\OD-10-20.M
Last changed : 1/30/2016 1:16:09 PM by XM
(modified after loading)



Data File C:\HPCHEM\1\DATA\GROUP\DZ10741R.D

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 A, Sig=250,10 Ref=360,100

Signal 2: DAD1 B, Sig=254,10 Ref=360,100

Signal 3: DAD1 C, Sig=210,10 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.355	MM	0.1907	5437.64014	475.33261	50.0268
2	8.685	MM	0.2258	5431.81152	400.93201	49.9732

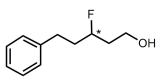
Totals : 1.08695e4 876.26462

Results obtained with enhanced integrator!

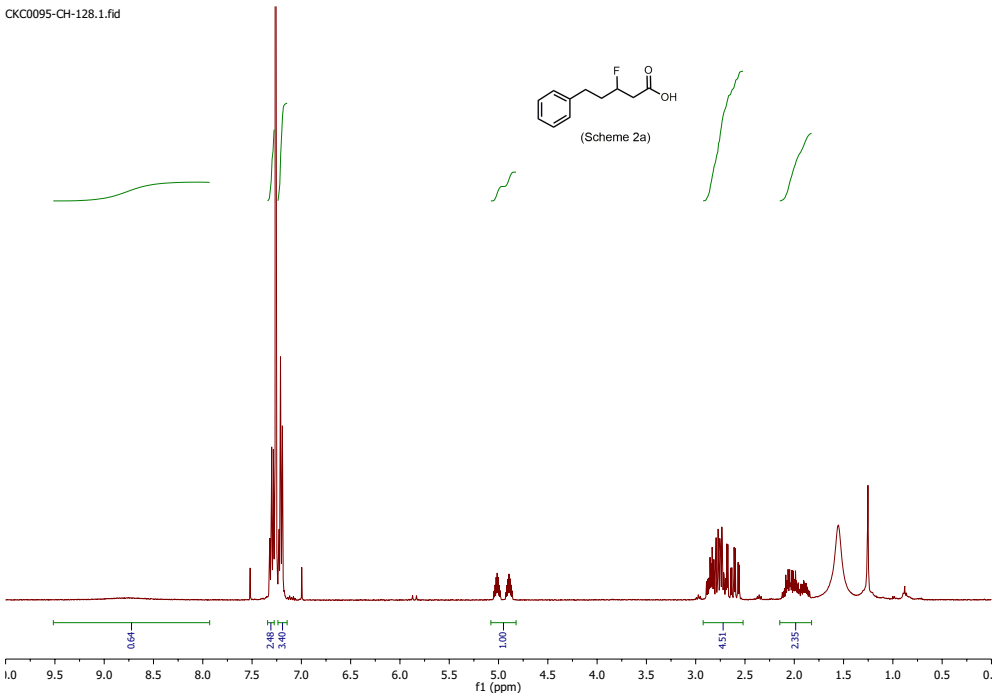
Signal 4: DAD1 D, Sig=230,10 Ref=360,100

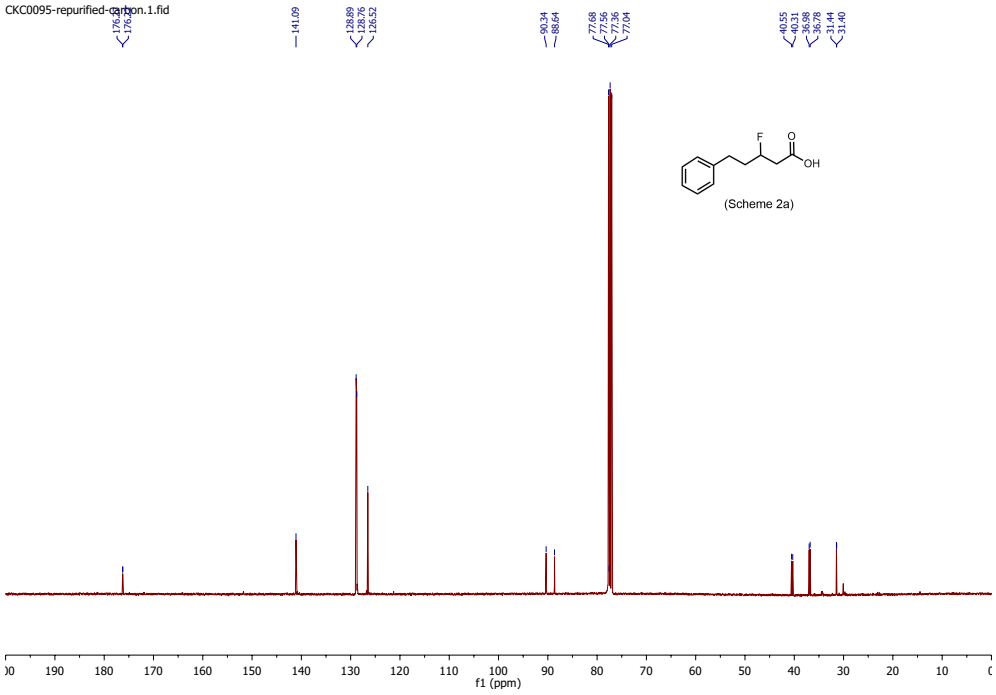
Signal 5: DAD1 E, Sig=280,10 Ref=360,100

*** End of Report ***

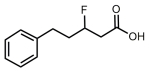


(Equation 1)

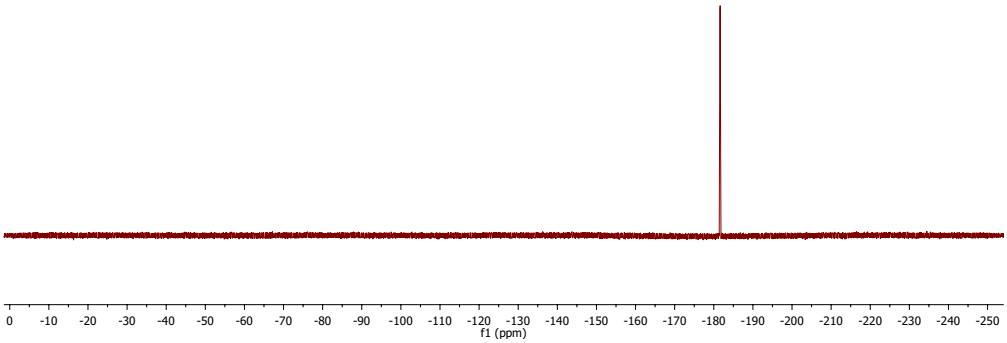

CKC0095-CH-128.1.fid
F
O
OH
(Scheme 2a)
0.64
2.48
3.40
1.00
4.51
2.35
f1 (ppm)


CKC0095-repurified-carbon.1.fid
176.29
176.52
141.09
128.89
128.76
126.52
90.34
88.64
77.68
77.56
77.36
77.04
40.55
40.31
36.98
36.78
31.44
31.40
F
O
OH
(Scheme 2a)
f1 (ppm)

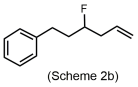
CKC0095FLUORINE
BC-1-29siena



(Scheme 2a)

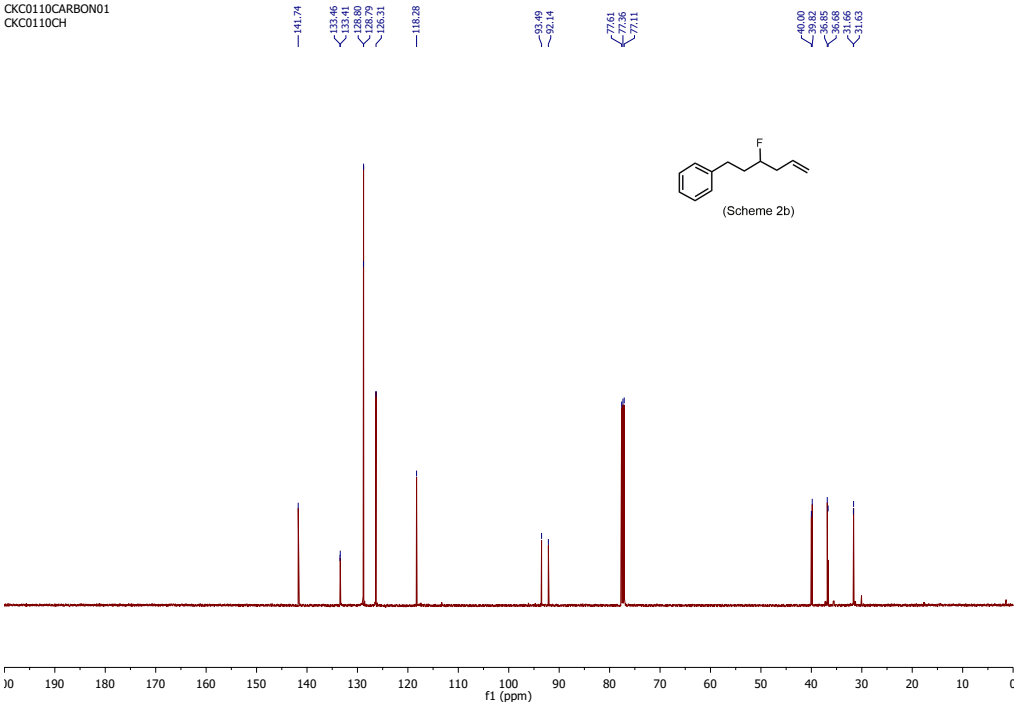


CKC0310cleanPROTON01
CKC0310prep

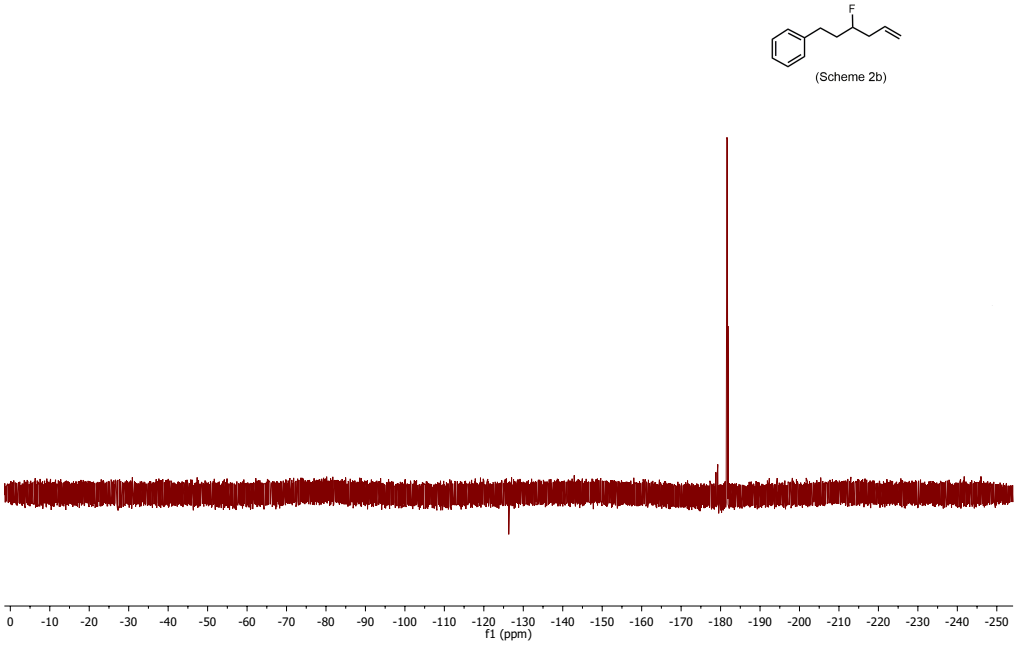


(Scheme 2b)

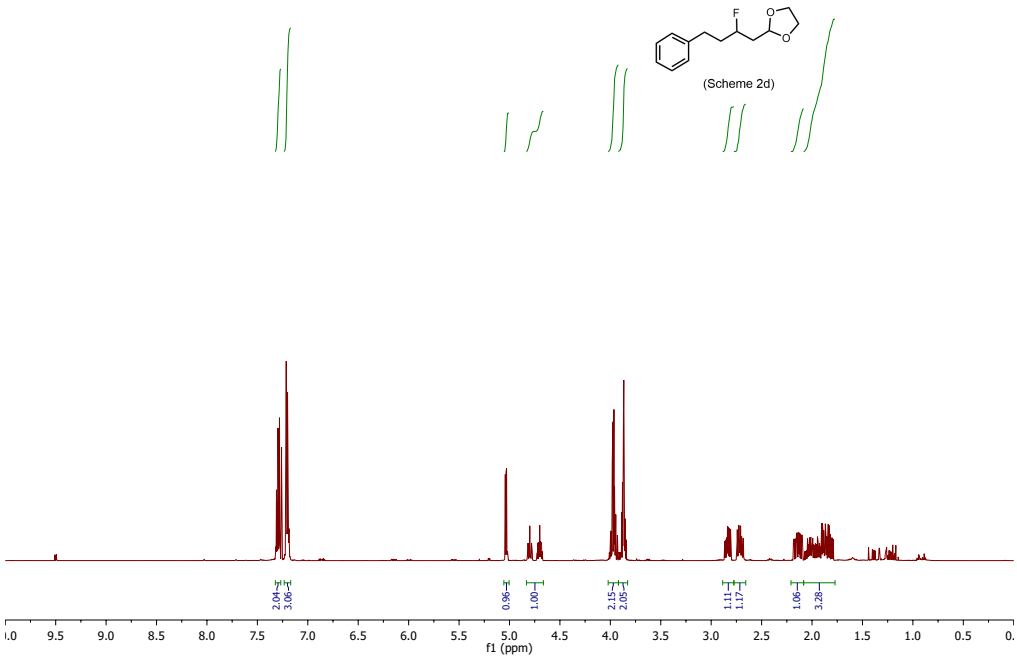
CKC0110CARBON01
CKC0110CH



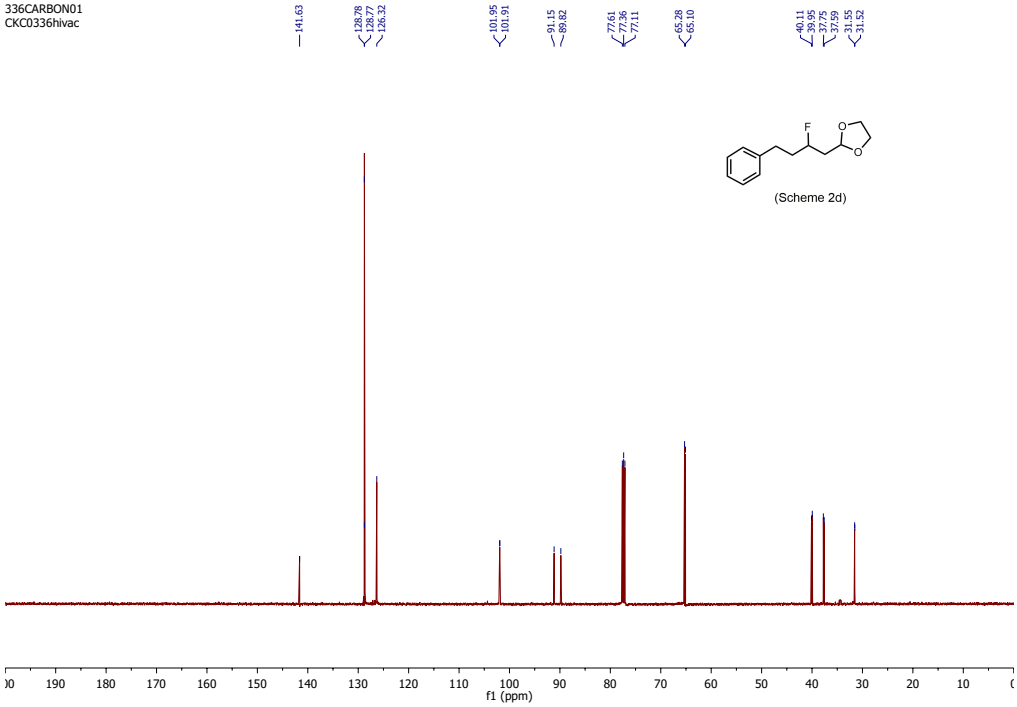
CKC0110FLUORINE01
BC-1-29siena



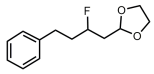
336PROTON01
CKC0336hivac



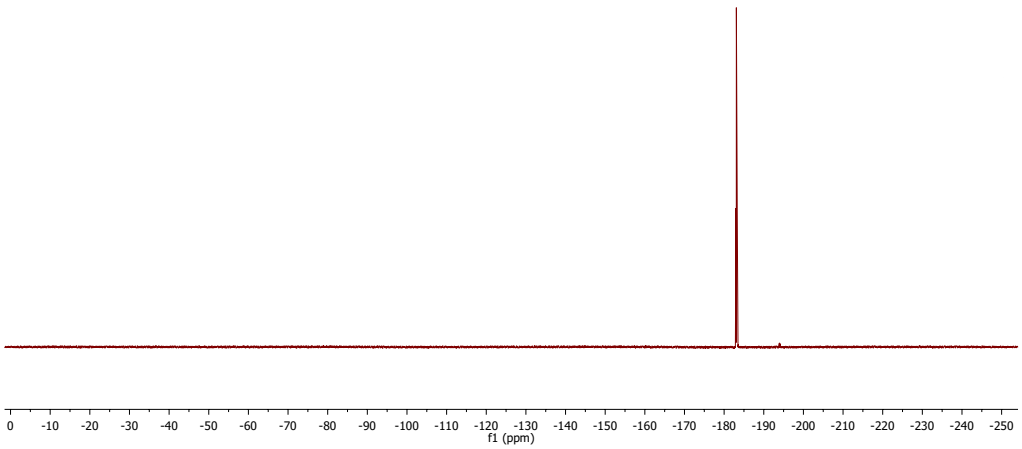
336CARBON01
CKC0336hivac



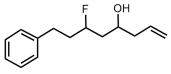
FLUORINE01
BC-1-29siena



(Scheme 2d)

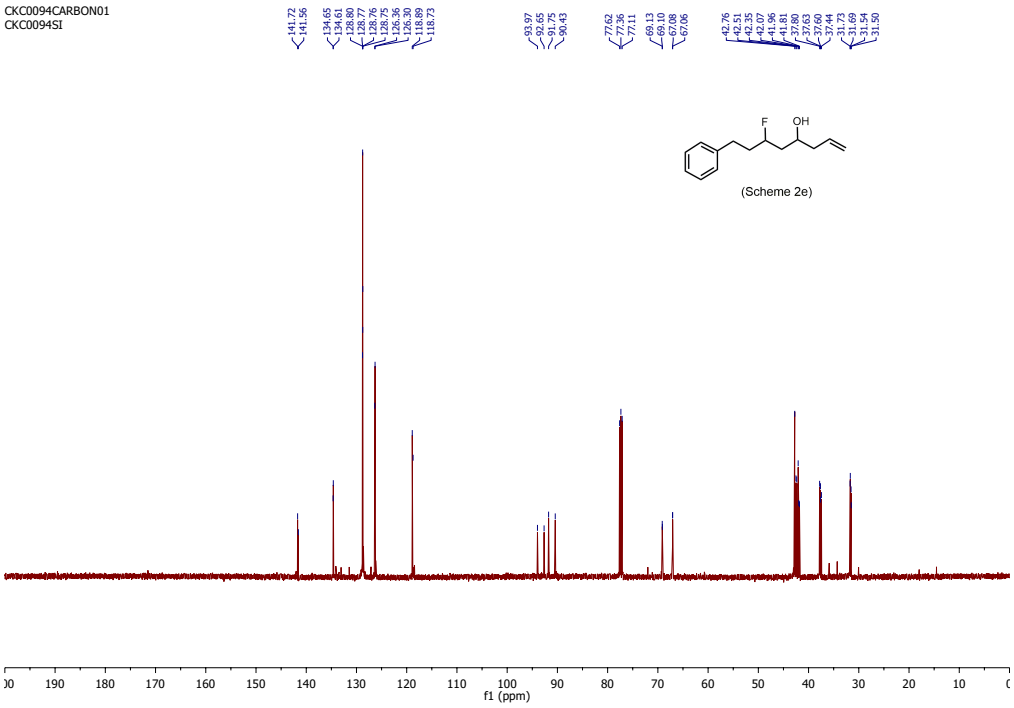


CKC0094pure2
CKC0094pure2

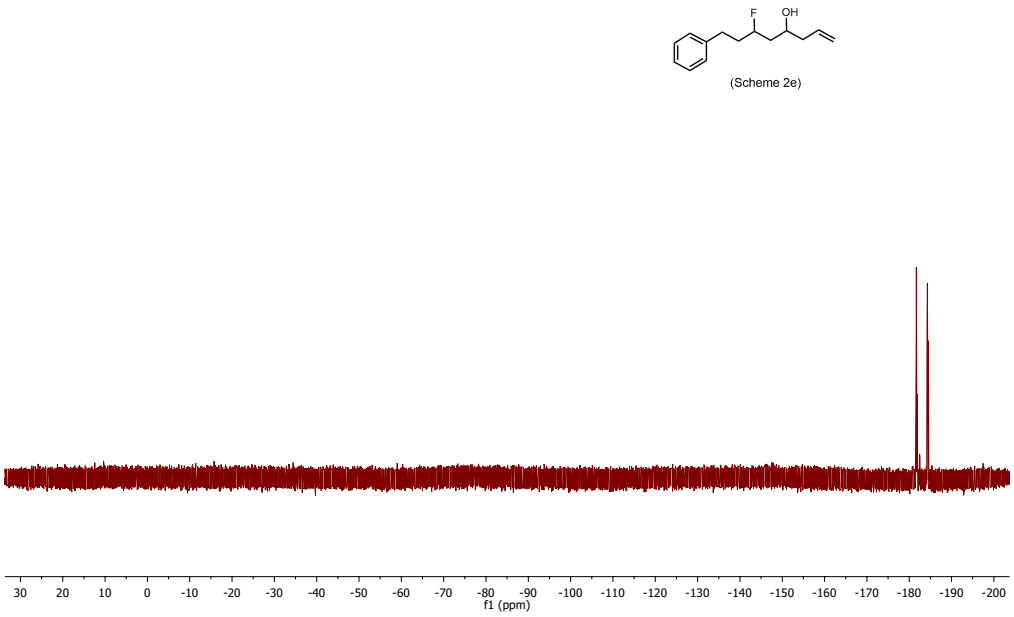


(Scheme 2e)

CKC0094CARBON01
CKC0094SI



FLUORINE01
CKC0094siena



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(24) Although β-fluorinated aldehydes are not stable to column chromatography, the crude products could be directly reduced to stable alcohol derivatives by treatment with $NaBH_4$.

(25) Studies by Feringa have shown retention of enantiopurity in allylic amides (Reference 21) and racemization in the case of allylic esters (Reference 22(e)).

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