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Si-Directed regiocontrol in asymmetric Pd-catalyzed allylic alkylations using C1-ammonium enolate nucleophiles

James W. B. Fyfe, Omaru M. Kabia, Colin M. Pearson, and Thomas N. Snaddon

Department of Chemistry, Indiana University, 800 E. Kirkwood Ave., Bloomington, Indiana 47405, United States

Abstract

Cooperative catalysis enables the direct enantioselective α -allylation of linear prochiral esters using Si-substituted allyl electrophiles. The Si-substituent directs the regioselectivity of enantioselective bond formation and provides products containing synthetically versatile pentafluorophenyl ester and vinylsilane moieties. Critical to the efficacy of this process was the recognition that the ancillary ligand on palladium could be altered to prevent formation of a deleterious ether by-product, whilst retaining enantioselectivity through the Lewis base catalyst. Flexibility such as this is unique to cooperative catalysis events and provides efficient access to an array of enantioenriched products that are orthogonally functionalized and easily modified.

Graphical Abstract

Keywords

Cooperative catalysis; Allylic alkylation; Silicon; Palladium; Ammonium enolate

1. Introduction

Transition metal-catalyzed asymmetric allylic alkylation is a mainstay of organic synthesis. Vast quantities of research in this field have led to the development of catalysis by numerous transition metals and the further development of versatile ligand classes to control chemo-, regio- and stereo-selectivity.¹ The versatility of this general class of reactions is now such that C(sp³)–carbon bonds can be forged efficiently and in highly enantioselective fashion

Supporting Information

The supporting information related to this article, including full experimental details, characterization data and associated spectra can be found at

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using a wide range of nucleophiles. However, challenges remain, and premier amongst these is the direct employment of linear, prochiral esters as partner nucleophiles.²

A major focus of our laboratory concerns the union of C1-ammonium enolates with transition metal electrophiles *via* cooperative catalysis.³ C1-Ammonium enolates are stereodefined ester enolate equivalents that are accessible from simple activated carboxylic acid derivatives.^{4,5} Within the sphere of transition metal-catalyzed allylic alkylation reactions, their use addresses many of the difficulties encountered when using linear, prochiral esters as partner nucleophiles, where control over enolate geometry, enantiofacial selectivity, and deleterious product racemization are prevalent.^{3,6} Through this manifold, enantioselectivity is governed by the Lewis base catalyst, while linear and branched products are accessible through judicious choice of the transition metal catalyst.

In this Article, we demonstrate the union of C1-ammonium enolates with silicon-substituted π -(allyl)Pd(II) electrophiles. Here, regiocontrol is directed by the silicon substituent (Figure 1, top) and provides the means to form synthetically versatile vinylsilanes in concert with catalytic asymmetric C(sp³)–C(sp³) bond formation (Figure 1, bottom). The incorporation of both an electrophilic pentafluorophenyl (Pfp) ester and a nucleophilic vinylsilane in the enantioenriched products provides the opportunity for orthogonal diversification.

Silicon-substituted electrophiles have been extensively investigated in transition metal-catalyzed allylic alkylation reactions.⁷ Silicon-substituents have demonstrated a remarkable capacity to direct nucleophilic attack to the distal carbon in the π -(allyl)Pd(II) complexes, through both steric and electronic factors,^{7g} even when the distal carbon bears a substituent.^{7a} Although subsequent protodesilylation would provide the corresponding branched products; however, our interest in Si-based regiocontrol concerns the synthetic utility of vinylsilanes.⁸ These are remarkably diverse synthetic handles that provide a convenient platform for further functionalization, for example *via* oxidation,⁹ or Hiyama–Denmark cross coupling.¹⁰ In addition, there is significant pharmaceutical interest in using silicon as a bioisostere for carbon.¹¹ Although encouraging, a lack of diverse methods for the incorporation of silicon into relevant molecular scaffolds has been cited as a significant limitation.¹¹

2. Results and Discussion

Our investigations began by assessing the reaction of phenyl acetic acid pentafluorophenyl ester and (*E*)-3- (dimethyl(phenyl)silyl)allyl methanesulfonate. Our previously optimized cooperative catalysis conditions^{3a} utilizing Buchwald's XantphosPd G3 precatalyst and Birman's (*R*)-benzotetramisole (BTM)¹² gave the desired (*R*)-configured allylated product¹³ in 51% yield and 93:7 er as the alkene (*E*)-isomer (Table 1, entry 1). Generating the catalyst *in situ* from Pd₂dba₃ precatalyst and Xantphos gave the product in an improved 77% yield and with comparable enantioselectivity (Table 1, entry 2). Thereafter, a short survey of phosphine ligands possessing different steric and electronic profiles revealed that a wide range of catalyst systems were capable of effectively catalyzing the reaction, albeit with slightly lower levels of enantioselection (entries 3–8). Returning to Xantphos, a solvent screen revealed comparable results in 1,4-dioxane; however, the reaction could not be

pushed beyond ~75% conversion (entry 9). Interrogation of the ^1H NMR spectra of the crude material determined this was due to competing attack of the pentafluorophenolate anion on the electrophilic allyl mesylate, thus preventing turnover of the Lewis base catalyst and regeneration of the Pfp ester. Competing pentafluorophenolate attack was suppressed when $\text{P}(2\text{-furyl})_3$ was used as the ligand and gave the product in 87% yield and 93:7 er (entry 10). Finally, increasing the Hünig's base stoichiometry to 1.25 equivalents gave 97% yield with no loss of enantioselectivity (entry 11). Notably, the reaction proceeds with exclusive formation of the *E*-isomer, regardless of the geometry of the starting silyl-substituted allyl mesylate (*vide infra*). As expected, performing the reaction in the absence of either catalyst did not provide the desired product.

With optimized conditions in hand, we then sought to evaluate the scope of the reaction with respect to both the aryl acetic acid ester and three commonly encountered silicon substituents **A–C** (Scheme 1), each of which provides opportunity for further functionalization of the products. A range of aryl substituents could be incorporated, encompassing a variety of electronic demands. Although nucleophiles bearing electron-donating groups performed well, the electron-withdrawing CF_3 group provided the products **5A–C** with lower enantioenrichment. We considered this was due to racemization of the products over time (due to the enhanced acidity of the stereogenic proton in the products). Running these reactions for a shorter time period (6 h vs. 24 h) restored the level of enantioenrichment with no loss in yield. The reaction could also be performed on preparative scale, with **2A** and **2C** synthesized on gram scale in comparable yield and enantioselectivity (see Supporting Information for details). Overall, the reaction was tolerant to variation of both the aryl and silyl substituents, and provides the desired products in good yields and useful levels of enantioselection.

Next, we turned our attention to the derivatization of the Pfp ester (Scheme 2). Here, the (*Z*)-isomer of the allyl mesylate was employed as a demonstration of the energetic preference for exclusive formation of the (*E*)-isomer products. A range of nucleophilic quenches were then employed, successfully affording amide **10**, ester **11** and carboxylic acid **12** in good yields and enantioselectivity without the need for any intermediate purification.

To demonstrate the chemical utility of the installed silyl functional groups, each of the three silicon substituents was subjected to a different transformation. The phenyldimethylsilyl group underwent facile halogenation with NIS giving **13** in excellent yield (Scheme 3). Although use of MeCN as the reaction solvent formed a 1:1 mixture of alkene isomers, performing the reaction in hexafluoroisopropanol (HFIP) afforded the (*Z*)-alkene isomer preferentially. This is an interesting observation that differs from the expected retention of stereochemistry reported by Zakarian and coworkers,^{14a} who utilized HFIP to suppress alkene isomerization. We speculate that participation of the proximal Pfp-ester leads to the observed stereodivergence in a manner described by Kishi and coworkers.^{14b} Hiyama–Denmark cross-coupling^{10,15} of the benzyldimethylsilane afforded compound **14** in excellent yield and enantioselectivity. This is complementary to our previously reported work with cinnamyl carbonate electrophiles, as it enables the bulk synthesis of the silylated intermediate which can then be differentially modified *via* cross-coupling with a range of aryl halides, allowing the type of late stage derivatization ideally suited to the development

of compound libraries. Finally, the trimethylsilyl moiety could be converted to the corresponding aldehyde *via* the intermediate silylated oxirane.^{9,16}

3. Conclusions

In summary, we have developed a cooperative catalysis process that permits the direct, enantioselective α -allylation of linear, prochiral esters using Si-substituted allyl electrophiles. The Si-substituent directs the regioselectivity of the enantioselective bond formation and provides products containing synthetically versatile pentafluorophenyl ester and vinylsilane moieties. This procedure is general across a range of pentafluorophenyl acetic ester nucleophiles along with three differentially Si-substituted allyl electrophiles. *In situ* quenching of the reaction allowed efficient derivatization of the Pfp ester group without the need for additional isolation/purification. We have also demonstrated chemical transformations of the three silyl moieties through halogenation, cross-coupling, and oxidation protocols, thus emphasizing the versatility of the reaction products for the efficient synthesis of enantioenriched molecular scaffolds.

4. Experimental

4.1. General Information

¹H and ¹³C NMR spectra were recorded at room temperature on Varian Inova-instrumentation: Varian I400 (¹H NMR at 400 MHz and ¹³C NMR at 100 MHz), Varian VXR400 (¹H NMR at 400 MHz and ¹³C NMR at 100 MHz), and Varian I500 (¹H NMR at 500 MHz and ¹³C NMR at 125 MHz) using deuterium lock. Data for ¹H NMR spectra are quoted relative to chloroform as an internal standard (7.26 ppm) and data for ¹³C NMR spectra are quoted relative to CDCl₃ as an internal standard (77.16 ppm) and are reported in terms of chemical shift (δ ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). In all cases ¹³C signals for pentafluorophenyl were not observed due to splitting. Infrared spectra (IR) were obtained on a Bruker Tensor II FT-IR Spectrometer and recorded in wavenumbers (cm⁻¹). High Resolution Mass (HRMS) analysis was obtained using Electron Impact Ionization (EI) or Chemical Ionization (CI) and reported as m/z (relative intensity) for the [M]⁺ or [M+H]⁺ molecular ion. GC-MS data was acquired using an Agilent 6890N Gas Chromatograph and 5973 Inert Mass Selective Detector. Chiral HPLC analyses were performed on an Agilent 1200 Series system. All [α]_D²³ values were obtained in CHCl₃ at c = 1.0.

4.2. General Procedure for synthesis of compounds 1A – 9C

To an oven dried 1 dram vial equipped with stirrer bar was added Pd₂dba₃ (4.5 mg, 0.005 mmol, 5 mol%), P(2-furyl)₃ (2.3 mg, 0.01 mmol, 10 mol%) and aryl acetic acid pentafluorophenyl ester (0.1 mmol, 1 equiv). The vial was then sealed with a PTFE lined cap and purged with nitrogen ($\times$ 3) before the addition of 1,4-dioxane (0.8 mL, 0.1 M). *i*Pr₂NEt (22 μ L, 0.125 mmol, 1.25 equiv) was then added *via* a microsyringe and the reaction was stirred at rt for 1 h before the addition of (+)-BTM (0.1 mL, 0.2 M, 0.02 mmol, 20 mol%) and the appropriate (silyl)allyl methanesulfonate (0.1 mL, 1.25 M, 0.125 mmol, 1.25 equiv)

as a solution in 1,4-dioxane. The reaction was then allowed to stir at rt for a further 24 h before being quenched with petroleum ether (4 mL). The resulting solution was then passed through a plug of acidic alumina, washing the vial and alumina plug with Et₂O (2 × 4 mL). The solution was then concentrated under vacuum and purified by column chromatography (silica gel, 100:1 pentane:Et₂O) to afford the desired product.

Pentafluorophenyl (*E*)-2-phenyl-5-(trimethylsilyl)pent-4-enoate, 1A—White solid (28 mg, 68% yield, 91:9 er). **IR** (film): 2958, 1775, 1516, 1242, 1096, 985, 839, 747, 697, 511. **¹H NMR** (CDCl₃, 400 MHz): δ 7.41 – 7.35 (m, 4H), 7.35 – 7.30 (m, 1H), 6.00 (dt, *J* = 18.6, 6.3 Hz, 1H), 5.80 (dt, *J* = 18.6, 1.4 Hz, 1H), 4.03 (dd, *J* = 9.3, 6.1 Hz, 1H), 2.99 (dd, *J* = 7.9, 1.4 Hz, 1H), 2.64 (dtd, *J* = 14.5, 6.1, 1.5 Hz, 1H), 0.02 (s, 9H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.7, 141.8, 137.1, 134.2, 129.1, 128.1, 128.0, 50.9, 40.2, –1.3. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –150.26 – –153.51 (m, 2F), –158.07 (t, *J* = 21.7 Hz, 1F), –162.49 (dd, *J* = 22.0, 17.0 Hz, 2F). **HRMS**: exact mass calculated for [M+H]⁺ C₂₀H₂₀F₅O₂Si requires *m/z* 415.1147, found *m/z* 415.1158. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.75 mL/min, 98:2 Hexane:Isopropanol, 210 nm, *t*_{minor} = 14.381 min, *t*_{major} = 14.832 min). [α]_D²³: –67.9.

Pentafluorophenyl (*E*)-5-(dimethyl(phenyl)silyl)-2-phenylpent-4-enoate, 1B—Colorless oil (45 mg, 95% yield, 94:6 er). **IR** (film): 2956, 1781, 1518, 1248, 1098, 991, 820, 731, 697. **¹H NMR** (CDCl₃, 400 MHz): δ 7.45 (dd, *J* = 7.6, 1.8 Hz, 2H), 7.41 – 7.29 (m, 7H), 6.08 (dt, *J* = 18.6, 6.3 Hz, 1H), 5.93 (dt, *J* = 18.6, 1.4 Hz, 1H), 4.06 (dd, *J* = 8.8, 6.6 Hz, 1H), 3.05 (dddd, *J* = 14.8, 8.7, 6.2, 1.3 Hz, 1H), 2.72 (dtd, *J* = 14.4, 6.5, 1.4 Hz, 1H), 0.31 (d, *J* = 1.7 Hz, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.6, 143.7, 138.6, 136.9, 133.2, 132.1, 129.09, 129.07, 128.09, 128.06, 127.9, 50.8, 40.3, –2.58, –2.61. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –149.99 – –153.78 (m, 2F), –158.03 (t, *J* = 21.6 Hz, 1F), –160.34 – –164.20 (m, 2F). **HRMS**: exact mass calculated for [M+Na]⁺ C₂₅H₂₁F₅O₂SiNa requires *m/z* 499.1129, found *m/z* 499.1120. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.5 mL/min, 600:1 Hexane:Isopropanol, 210 nm, *t*_{minor} = 12.108 min, *t*_{major} = 13.456 min). [α]_D²³: –34.3.

Pentafluorophenyl (*E*)-5-(benzyl dimethylsilyl)-2-phenylpent-4-enoate, 1C—Colorless oil (47 mg, 95% yield, 93:7 er). **IR** (film): 3026, 2955, 1781, 1518, 1493, 1248, 1096, 1028, 991, 831, 736, 697. **¹H NMR** (CDCl₃, 400 MHz): δ 7.47 – 7.28 (m, 5H), 7.20 (t, *J* = 7.5 Hz, 2H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 6.7 Hz, 2H), 5.99 (dt, *J* = 18.7, 6.2 Hz, 1H), 5.77 (dt, *J* = 18.6, 1.4 Hz, 1H), 4.02 (dd, *J* = 8.8, 6.5 Hz, 1H), 3.10 – 2.90 (m, 1H), 2.76 – 2.55 (m, 1H), 2.10 (s, 2H), 0.02 (s, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.6, 143.1, 140.0, 137.0, 132.2, 129.1, 128.4, 128.2, 128.1, 128.0, 124.1, 50.8, 40.2, 26.1, –3.4. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –147.22 – –156.01 (m, 2F), –158.00 (t, *J* = 21.7 Hz, 1F), –162.40 (dd, *J* = 21.8, 17.2 Hz, 2F). **HRMS**: exact mass calculated for [M+Na]⁺ C₂₆H₂₃F₅O₂Si requires *m/z* 513.1285, found *m/z* 513.1276. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 1.00 mL/min, 800:1 Hexane:Isopropanol, 210 nm, *t*_{major} = 6.955 min, *t*_{minor} = 7.61 min). [α]_D²³: –33.9.

Pentafluorophenyl (*E*)-2-(4-methoxyphenyl)-5-(trimethylsilyl)pent-4-enoate, 2A

—White solid (39 mg, 86% yield, 88:12 er). **IR** (film): 2956, 1775, 1518, 1247, 1093, 1028, 1002, 985, 871, 838. **¹H NMR** (CDCl₃, 400 MHz): δ 7.28 (d, *J* = 8.7 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.00 (dt, *J* = 18.6, 6.2 Hz, 1H), 5.80 (dt, *J* = 18.6, 1.4 Hz, 1H), 3.98 (dd, *J* = 9.3, 6.1 Hz, 1H), 3.81 (s, 3H), 3.02 – 2.87 (m, 1H), 2.69 – 2.56 (m, 1H), 0.02 (s, 9H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.9, 159.4, 141.9, 134.1, 129.1, 114.4, 55.4, 50.1, 40.3, –1.3. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –151.04 – –153.93 (m, 2F), –158.15 (t, *J* = 21.6 Hz, 1F), –162.35 – –162.77 (m, 2F). **HRMS**: exact mass calculated for [M+H]⁺ C₂₁H₂₂F₅O₃Si requires *m/z* 445.1253, found *m/z* 445.1241. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, *t*_{minor} = 4.913 min, *t*_{major} = 5.143 min). [α]_D²³: –77.1.

Pentafluorophenyl (*E*)-5-(dimethyl(phenyl)silyl)-2-(4-methoxyphenyl)pent-4-enoate, 2B

—Colorless oil (45 mg, 89% yield, 92:8 er). **IR** (film): 2956, 1780, 1612, 1517, 1427, 1249, 1180, 1093, 1034, 991, 822, 786, 731, 699. **¹H NMR** (CDCl₃, 400 MHz): δ 7.46 – 7.40 (m, 2H), 7.37 – 7.30 (m, 3H), 7.29 – 7.22 (m, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 6.06 (dt, *J* = 18.6, 6.3 Hz, 1H), 5.93 – 5.88 (m, 1H), 3.99 (dd, *J* = 8.7, 6.7 Hz, 1H), 3.81 (s, 3H), 3.13 – 2.91 (m, 1H), 2.84 – 2.60 (m, 1H), 0.29 (d, *J* = 2.1 Hz, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.8, 159.4, 143.9, 138.7, 133.9, 132.0, 129.14, 129.09, 128.9, 127.8, 114.4, 55.4, 49.9, 40.3, –2.6. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –148.37 – –154.93 (m, 2F), –158.11 (t, *J* = 21.6 Hz, 1F), –160.95 – –164.74 (m, 2F). **HRMS**: exact mass calculated for [M+Na]⁺ C₂₆H₂₃F₅O₃SiNa requires *m/z* 529.1234, found *m/z* 529.1215. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, = *t*_{major} 18.248 min, *t*_{minor} = 22.005 min). [α]_D²³: –50.3.

Pentafluorophenyl (*E*)-5-(benzyl(dimethyl)silyl)-2-(4-methoxyphenyl)pent-4-enoate, 2C

—Colorless oil (45 mg, 87% yield, 93:7 er). **IR** (film): 2956, 1780, 1517, 1493, 1249, 1180, 1092, 1034, 992, 907, 830, 732, 699, 553. **¹H NMR** (CDCl₃, 400 MHz): δ 7.22 (d, *J* = 7.8 Hz, 2H), 7.14 (t, *J* = 7.6 Hz, 2H), 7.01 (t, *J* = 7.3 Hz, 1H), 6.90 (d, *J* = 7.6 Hz, 2H), 6.86 (d, *J* = 8.4 Hz, 2H), 5.92 (dt, *J* = 18.7, 6.3 Hz, 1H), 5.71 (d, *J* = 18.6 Hz, 1H), 3.90 (dd, *J* = 8.8, 6.6 Hz, 1H), 3.77 (s, 3H), 2.91 (dt, *J* = 15.2, 7.8 Hz, 1H), 2.58 (dt, *J* = 13.9, 6.5 Hz, 1H), 2.04 (s, 2H), –0.05 (d, *J* = 1.7 Hz, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.8, 159.4, 143.2, 140.0, 132.1, 129.1, 128.9, 128.4, 128.2, 124.1, 114.4, 55.4, 50.0, 40.3, 26.1, –3.4. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –149.4 – –154.0 (m, 2F), –158.1 (t, *J* = 21.7 Hz, 1F), –161.2 – –165.0 (m, 2F). **HRMS**: exact mass calculated for [M+Na]⁺ C₂₇H₂₅F₅O₃SiNa requires *m/z* 543.1391, found *m/z* 543.1367. HPLC analysis using a chiral column (Chiralpak IB 3μ column, 22 °C, 1.00 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = *t*_{major} 13.793 min, *t*_{minor} = 20.379 min). [α]_D²³: –36.7.

Pentafluorophenyl (*E*)-2-(naphthalen-2-yl)-5-(trimethylsilyl)pent-4-enoate, 3A

—White solid (34 mg, 72% yield, 89:11 er). **IR** (film): 1775, 1517, 1248, 1100, 988, 862, 839, 751, 481, 420. **¹H NMR** (CDCl₃, 400 MHz): δ 7.96 – 7.67 (m, 4H), 7.54 – 7.45 (m, 3H), 6.05 (dt, *J* = 18.6, 6.3 Hz, 1H), 5.84 (dt, *J* = 18.7, 1.4 Hz, 1H), 4.21 (dd, *J* = 9.2, 6.1 Hz, 1H), 3.09 (dddd, *J* = 14.6, 9.3, 6.5, 1.4 Hz, 1H), 2.82 – 2.63 (m, 1H), 0.02 (s, 9H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.7, 141.7, 134.5, 134.4, 133.6, 133.0, 128.9, 128.0, 127.8, 127.1,

126.6, 125.6, 51.0, 40.3, -1.3. **¹⁹F NMR** (CDCl₃, 376 MHz): δ -151.95 – -152.66 (m, 2F), -157.99 (t, *J* = 21.7 Hz, 1F), -162.42 (dd, *J* = 21.9, 17.1 Hz, 2F). **HRMS**: exact mass calculated for [M+H]⁺ C₂₄H₂₂F₅O₂Si requires *m/z* 465.1304, found *m/z* 465.1291. HPLC analysis using a chiral column (Chiralpak IB 3μ column, 22 °C, 1.00 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = *t*_{major} 8.292 min, *t*_{minor} = 8.941 min). [α]_D²³: -81.9.

Pentafluorophenyl (*E*)-5-(dimethyl(phenyl)silyl)-2-(naphthalen-2-yl)pent-4-

enoate, 3B—Colorless oil (48 mg, 90% yield, 88:12 er). **IR** (film): 3054, 2956, 1781, 1518, 1248, 1096, 991, 839, 818, 786, 730, 699, 475. **¹H NMR** (CDCl₃, 400 MHz): δ 7.80 – 7.42 (m, 4H), 7.34 – 6.81 (m, 8H), 5.88 – 5.74 (m, 1H), 5.71 – 5.53 (m, 1H), 3.94 (t, *J* = 7.8 Hz, 1H), 2.84 (dt, *J* = 14.9, 7.4 Hz, 1H), 2.65 – 2.39 (m, 1H), -0.00 (d, *J* = 1.8 Hz, 4H). **¹³C NMR** (CDCl₃, 101 MHz): δ 143.7, 134.3, 133.9, 133.0, 132.3, 129.1, 128.9, 128.1, 127.9, 127.8, 127.3, 126.6, 126.4, 125.6, 50.9, 40.3, -2.6. **¹⁹F NMR** (CDCl₃, 376 MHz): δ -152.20 – -152.50 (m, 2F), -157.94 (t, *J* = 21.6 Hz, 1F), -162.36 (dd, *J* = 21.9, 17.3 Hz, 2F). **HRMS**: exact mass calculated for [M+Na]⁺ C₂₉H₂₃F₅O₂SiNa requires *m/z* 549.1285, found *m/z* 549.1307. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.5 mL/min, 99:1 Hexane:Isopropanol, 210 nm, = *t*_{major} 8.710 min, *t*_{minor} = 10.080 min). [α]_D²³: -50.2.

Pentafluorophenyl (*E*)-5-(benzyl(dimethyl)silyl)-2-(naphthalen-2-yl)pent-4-

enoate, 3C—Colorless oil (50 mg, 92% yield, 91:9 er). **IR** (film): 3059, 3024, 2955, 1780, 1518, 1493, 1248, 1095, 992, 831, 816, 733, 698, 475. **¹H NMR** (CDCl₃, 400 MHz): δ 7.96 – 7.76 (m, 4H), 7.57 – 7.44 (m, 3H), 7.15 (t, *J* = 7.5 Hz, 2H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.92 (d, *J* = 7.0 Hz, 2H), 6.02 (dt, *J* = 18.6, 6.2 Hz, 1H), 5.79 (d, *J* = 18.6 Hz, 1H), 4.18 (dd, *J* = 8.7, 6.5 Hz, 1H), 3.27 – 2.97 (m, 1H), 2.76 (dtd, *J* = 14.4, 6.3, 1.4 Hz, 1H), 2.08 (s, 2H), 0.00 (s, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.6, 143.0, 140.0, 134.3, 133.6, 133.0, 132.3, 128.9, 128.3, 128.2, 128.0, 127.9, 127.2, 126.6, 126.4, 125.6, 124.1, 50.9, 40.3, 26.1, -3.4. **¹⁹F NMR** (CDCl₃, 376 MHz): δ -152.36 (d, *J* = 17.5 Hz, 2F), -157.91 (t, *J* = 21.7 Hz, 1F), -162.32 (dd, *J* = 21.8, 17.3 Hz, 2F). **HRMS**: exact mass calculated for [M+Na]⁺ C₃₀H₂₅F₅O₂SiNa requires *m/z* 563.1442, found *m/z* 563.1437. **HPLC** analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.5 mL/min, 99:1 Hexane:Isopropanol, 210 nm, = *t*_{minor} 7.544 min, *t*_{major} = 8.355 min). [α]_D²³: -51.2.

Pentafluorophenyl (*E*)-2-(4-chlorophenyl)-5-(trimethylsilyl)pent-4-enoate, 4A—

White solid (33 mg, 72% yield, 88:12 er). **IR** (film): 2956, 1774, 1517, 1248, 1097, 985, 870, 838, 525. **¹H NMR** (CDCl₃, 400 MHz): δ 7.35 (d, *J* = 8.6 Hz, 2H), 7.30 (d, *J* = 8.5 Hz, 2H), 5.97 (dt, *J* = 18.6, 6.2 Hz, 1H), 5.85 – 5.72 (m, 1H), 4.01 (dd, *J* = 9.0, 6.4 Hz, 1H), 2.97 (dddd, *J* = 14.4, 9.0, 6.4, 1.3 Hz, 1H), 2.63 (dtd, *J* = 14.3, 6.2, 1.4 Hz, 1H), 0.03 (s, 9H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.3, 141.2, 135.5, 134.7, 134.1, 129.4, 129.2, 50.2, 40.2, -1.3. **¹⁹F NMR** (CDCl₃, 376 MHz): δ -149.99 – -154.32 (m, 2F), -157.78 (t, *J* = 21.7 Hz, 1F), -162.30 (dd, *J* = 21.8, 17.2 Hz, 2F). **HRMS**: exact mass calculated for [M+H]⁺ C₂₀H₁₉ClF₅O₂Si requires *m/z* 449.0758, found *m/z* 449.0751. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.5 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = *t*_{major} 13.671 min, *t*_{minor} = 17.323 min). [α]_D²³: -72.4.

Pentafluorophenyl (E)-5-(dimethyl(phenyl)silyl)-2-(4-chlorophenyl)pent-4-enoate, 4B—Colorless oil (45 mg, 88% yield, 92:8 er). **IR** (film): 2957, 1781, 1518, 1492, 1248, 1092, 992, 908, 821, 730, 699. **¹H NMR** (CDCl₃, 400 MHz): δ 7.43 – 7.38 (m, 2H), 7.37 – 7.30 (m, 5H), 7.28 (d, *J* = 8.5 Hz, 2H), 6.02 (dt, *J* = 18.6, 6.3 Hz, 1H), 5.94 – 5.86 (m, 1H), 4.02 (dd, *J* = 8.4, 7.0 Hz, 1H), 3.01 (dddd, *J* = 14.6, 8.5, 6.2, 1.3 Hz, 1H), 2.68 (dtd, *J* = 14.7, 6.6, 1.4 Hz, 1H), 0.29 (d, *J* = 1.8 Hz, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.3, 143.2, 138.5, 135.3, 134.1, 133.9, 132.7, 129.5, 129.3, 129.2, 127.9, 50.1, 40.2, –2.6. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –148.37 – –154.93 (m, 2F), –157.70 (t, *J* = 21.6 Hz, 1F), –162.21 (dd, *J* = 21.7, 17.2 Hz, 2F). **HRMS**: exact mass calculated for [M+Na]⁺ C₂₅H₂₀ClF₅O₂SiNa requires *m/z* 533.0739, found *m/z* 533.0744. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.75 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = *t*_{minor} 17.075 min, *t*_{major} = 21.525 min). [α]_D²³: –38.6.

Pentafluorophenyl (E)-5-(benzylidimethylsilyl)-2-(4-chlorophenyl)pent-4-enoate, 4C—Colorless oil (49 mg, 93% yield, 89:11 er). **IR** (film): 2955, 1781, 1518, 1492, 1248, 1092, 992, 830, 761, 733, 698, 476. **¹H NMR** (CDCl₃, 400 MHz): δ 7.36 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.20 (t, *J* = 7.5 Hz, 2H), 7.07 (t, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 6.9 Hz, 2H), 5.94 (dt, *J* = 18.6, 6.2 Hz, 1H), 5.76 (dt, *J* = 18.6, 1.4 Hz, 1H), 3.98 (dd, *J* = 8.6, 6.8 Hz, 1H), 3.07 – 2.90 (m, 1H), 2.64 (dtd, *J* = 12.9, 6.8, 1.4 Hz, 1H), 2.10 (s, 2H), 0.02 (s, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.3, 142.5, 139.9, 135.4, 134.1, 132.7, 129.4, 129.2, 128.3, 128.2, 124.1, 50.1, 40.1, 26.0, –3.4. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –148.03 – –153.51 (m, 2F), –157.68 (t, *J* = 21.6 Hz, 1F), –162.19 (dd, *J* = 21.8, 17.3 Hz, 2F). **HRMS**: exact mass calculated for [M]⁺ C₂₆H₂₂ClF₅O₂Si requires *m/z* 524.0992, found *m/z* 524.0975. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.4 mL/min, 600:1 Hexane:Isopropanol, 210 nm, = *t*_{major} 22.250 min, *t*_{minor} = 27.271 min). [α]_D²³: –38.8.

Pentafluorophenyl (E)-2-(4-(trifluoromethyl)phenyl)-5-(trimethylsilyl)pent-4-enoate, 5A—White solid (33 mg, 69% yield, 89:11 er). **IR** (film): 2957, 1783, 1519, 1325, 1168, 1129, 1100, 1069, 993, 863, 837, 734. **¹H NMR** (CDCl₃, 400 MHz): δ 7.65 (d, *J* = 7.9 Hz, 2H), 7.49 (d, *J* = 7.9 Hz, 2H), 6.04 – 5.90 (m, 1H), 5.86 – 5.73 (m, 1H), 4.11 (dd, *J* = 8.9, 6.3 Hz, 1H), 3.01 (ddd, *J* = 15.1, 8.5, 6.1 Hz, 1H), 2.75 – 2.60 (m, 1H), 0.03 (s, 9H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.1, 141.0, 140.9, 135.1, 130.5 (q, ²*J*_{C-F} = 32.7 Hz), 128.5, 126.0 (q, ³*J*_{C-F} = 3.8 Hz), 124.1 (q, ¹*J*_{C-F} = 272.0 Hz), 50.7, 40.2, –1.3. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –62.74 (s, 3F), –150.26 – –154.66 (m, 2F), –157.56 (t, *J* = 21.7 Hz, 1F), –162.17 (dd, *J* = 21.7, 17.2 Hz, 2F). **HRMS**: exact mass calculated for [M-CH₃]⁺ C₂₀H₁₅F₈O₂Si requires *m/z* 476.0708, found *m/z* 467.0718. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 1.0 mL/min, 98:2 Hexane:Isopropanol, 210 nm, = *t*_{major} 10.524 min, *t*_{minor} = 13.282 min). [α]_D²³: –46.3.

Pentafluorophenyl (E)-5-(dimethyl(phenyl)silyl)-2-(4-(trifluoromethyl)phenyl)pent-4-enoate, 5B—Colorless oil (45 mg, 81% yield, 86:14 er). **IR** (film): 2958, 1782, 1619, 1519, 1324, 1167, 1127, 1111, 1068, 992, 838, 820, 731, 699. **¹H NMR** (CDCl₃, 400 MHz): δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.39 (m, 2H), 7.37 – 7.29 (m, 3H), 6.12 – 5.95 (m, 1H), 5.95 – 5.86 (m, 1H), 4.12 (t, *J* =

7.7 Hz, 1H), 3.10 – 2.98 (m, 1H), 2.78 – 2.65 (m, 1H), 0.30 (s, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.0, 142.8, 139.6 (d, ¹J_{C-F} = 245.4 Hz), 133.9, 133.0, 130.5 (d, ²J_{C-F} = 32.9 Hz), 129.2, 128.6, 127.9, 126.0 (d, ³J_{C-F} = 3.8 Hz), 50.5, 40.2, –2.7. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –62.69 (s, 3F), –152.25 – –152.76 (m, 2F), –157.55 (t, *J* = 21.7 Hz, 1F), –161.78 – –162.39 (m, 2F). **HRMS**: exact mass calculated for [M+H]⁺ C₂₆H₂₁F₈O₂Si requires *m/z* 545.1178, found *m/z* 545.1159. HPLC analysis using a chiral column (Chiralpak IB 3μ column, 22 °C, 1.0 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = *t*_{minor} 9.576 min, *t*_{major} = 10.205 min). [α]_D²³: –19.2.

Pentafluorophenyl (*E*)-5-(benzyltrimethylsilyl)-2-(4-

(trifluoromethyl)phenyl)pent-4-enoate, 5C—Colorless oil (43 mg, 79% yield, 89:11 er). **IR** (film): 2957, 1783, 1519, 1493, 1324, 1127, 1068, 993, 831, 733, 699. **¹H NMR** (CDCl₃, 400 MHz): δ 7.66 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.20 (t, *J* = 7.6 Hz, 2H), 7.07 (t, *J* = 7.4 Hz, 1H), 6.96 (d, *J* = 6.7 Hz, 2H), 5.95 (dt, *J* = 18.6, 6.2 Hz, 1H), 5.84 – 5.73 (m, 1H), 4.09 (dd, *J* = 8.6, 6.7 Hz, 1H), 3.10 – 2.97 (m, 1H), 2.74 – 2.61 (m, 1H), 2.10 (s, 2H), 0.02 (s, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.0, 142.2, 140.8, 139.9, 133.0, 130.5 (d, ²J_{C-F} = 32.6 Hz), 128.5, 128.3 (d, ³J_{C-F} = 10.2 Hz), 126.0 (q, ⁴J_{C-F} = 3.7 Hz), 124.2, 50.6, 40.2, 26.0, –3.4. CF₃ carbon not observed. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –62.70 (s, 3F), –152.56 (d, *J* = 17.3 Hz, 2F), –157.49 (t, *J* = 21.7 Hz, 1F), –162.08 (dd, *J* = 21.7, 17.2 Hz, 2F). **HRMS**: exact mass calculated for [M+H]⁺ C₂₇H₂₃F₈O₂Si requires *m/z* 559.1334, found *m/z* 559.1308. HPLC analysis using a chiral column (Chiralpak IB 3μ column, 22 °C, 1.0 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = *t*_{major} 8.383 min, *t*_{minor} = 9.898 min). [α]_D²³: –18.4.

Pentafluorophenyl (*E*)-2-(4-tolyl)-5-(trimethylsilyl)pent-4-enoate, 6A—White solid

(39 mg, 90% yield, 91:9 er). **IR** (film): 2961, 1775, 1517, 1243, 1097, 1003, 986, 872, 839, 820, 544. **¹H NMR** (CDCl₃, 400 MHz): δ 7.27 (d, *J* = 9.1 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 6.03 (dt, *J* = 18.6, 6.2 Hz, 1H), 5.91 – 5.76 (m, 1H), 4.02 (dd, *J* = 9.4, 6.0 Hz, 1H), 3.09 – 2.91 (m, 1H), 2.71 – 2.55 (m, 1H), 2.38 (s, 3H), 0.06 (s, 9H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.8, 141.9, 137.8, 134.1, 134.1, 129.7, 127.8, 50.5, 40.3, 21.3, –1.3. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –152.42 (d, *J* = 17.3 Hz, 2F), –158.16 (t, *J* = 21.7 Hz, 1F), –162.55 (dd, *J* = 21.7, 17.3 Hz, 2F). **HRMS**: exact mass calculated for [M+H]⁺ C₂₁H₂₂F₅O₂Si requires *m/z* 429.1304, found *m/z* 429.1287. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 1.0 mL/min, 98:2 Hexane:Isopropanol, 210 nm, = *t*_{major} 8.818 min, *t*_{minor} = 9.590 min). [α]_D²³: –65.9.

Pentafluorophenyl (*E*)-5-(dimethyl(phenyl)silyl)-2-(4-tolyl)pent-4-enoate, 6B—

Colorless oil (45 mg, 91% yield, 92:8 er). **IR** (film): 2957, 1783, 1520, 1100, 1002, 822, 700. **¹H NMR** (CDCl₃, 400 MHz): δ 7.39 – 7.33 (m, 2H), 7.29 – 7.21 (m, 3H), 7.16 (dd, *J* = 8.5, 1.7 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 6.11 – 5.93 (m, 1H), 5.83 (d, *J* = 18.6 Hz, 1H), 3.94 (dd, *J* = 8.8, 6.5 Hz, 1H), 3.03 – 2.86 (m, 1H), 2.60 (dt, *J* = 13.8, 6.4 Hz, 1H), 2.28 (s, 3H), 0.23 (s, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.7, 143.9, 138.7, 137.8, 133.9, 131.9, 129.7, 129.1, 127.9, 127.8, 50.4, 40.3, –2.6. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –151.00 – –153.65 (m, 2F), –158.13 (t, *J* = 21.7 Hz, 1F), –162.51 (dd, *J* = 21.9, 17.2 Hz, 2F). **HRMS**: exact mass calculated for [M+Na]⁺ C₂₆H₂₃F₅O₂SiNa requires *m/z* 513.1285, found *m/z*

513.1263. HPLC analysis using a chiral column (Chiralpak IA 3 μ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, = t_{major} 12.367 min, t_{minor} = 14.733 min). $[\alpha]_{\text{D}}^{23}$: -41.8.

Pentafluorophenyl (E)-5-(benzyltrimethylsilyl)-2-(4-tolyl)pent-4-enoate, 6C—

Colorless oil (46 mg, 91% yield, 93:7 er). **IR** (film): 2955, 1781, 1518, 1493, 1248, 1093, 992, 830, 699, 476. **^1H NMR** (CDCl_3 , 400 MHz): δ 7.29 – 7.19 (m, 6H), 7.09 (t, J = 7.4 Hz, 1H), 6.98 (d, J = 6.6 Hz, 2H), 6.02 (dt, J = 18.6, 6.2 Hz, 1H), 5.85 – 5.72 (m, 1H), 4.01 (dd, J = 8.9, 6.4 Hz, 1H), 3.09 – 2.94 (m, 1H), 2.67 (dtd, J = 14.3, 6.3, 1.4 Hz, 1H), 2.40 (s, 3H), 2.13 (s, 2H), 0.05 (s, 6H). **^{13}C NMR** (CDCl_3 , 101 MHz): δ 169.8, 143.2, 140.0, 137.8, 134.0, 132.1, 129.7, 128.4, 128.2, 127.9, 124.1, 50.4, 40.3, 26.1, 21.3, -3.4. **^{19}F NMR** (CDCl_3 , 376 MHz): δ -151.79 – -152.94 (m, 2F), -158.08 (t, J = 21.7 Hz, 1F), -162.46 (dd, J = 21.6, 17.2 Hz, 2F). **HRMS**: exact mass calculated for $[\text{M}+\text{Na}]^+$ $\text{C}_{27}\text{H}_{25}\text{F}_5\text{O}_2\text{SiNa}$ requires m/z 527.1442, found m/z 527.1427. HPLC analysis using a chiral column (Chiralpak IB 3 μ column, 22 °C, 1.0 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = t_{major} 6.925 min, t_{minor} = 9.236 min). $[\alpha]_{\text{D}}^{23}$: -44.4.

Pentafluorophenyl (E)-2-(2-fluorophenyl)-5-(trimethylsilyl)pent-4-enoate, 7A—

Colorless oil (33 mg, 76% yield, 90:10 er). **IR** (film): 2956, 1784, 1518, 1493, 1248, 1102, 990, 863, 836, 754. **^1H NMR** (CDCl_3 , 400 MHz): δ 7.40 – 7.28 (m, 2H), 7.17 (td, J = 7.6, 1.3 Hz, 1H), 7.15 – 7.06 (m, 1H), 5.99 (dt, J = 18.6, 6.3 Hz, 1H), 5.86 – 5.61 (m, 1H), 4.40 (t, J = 7.6 Hz, 1H), 2.99 (dddd, J = 14.3, 7.9, 6.3, 1.3 Hz, 1H), 2.78 – 2.59 (m, 1H), 0.01 (s, 9H). **^{13}C NMR** (CDCl_3 , 101 MHz): δ 169.1, 160.5 (d, $^1J_{\text{C-F}}$ = 247.0 Hz), 141.3, 134.7, 129.7 (d, $^3J_{\text{C-F}}$ = 8.4 Hz), 129.1 (d, $J_{\text{C-F}}$ = 3.4 Hz), 124.6 (d, $J_{\text{C-F}}$ = 3.6 Hz), 124.4 (d, $^2J_{\text{C-F}}$ = 14.6 Hz), 115.8 (d, $^2J_{\text{C-F}}$ = 22.2 Hz), 43.4 (d, $^3J_{\text{C-F}}$ = 2.5 Hz), 39.2, -1.3. **^{19}F NMR** (CDCl_3 , 376 MHz): δ -117.55 – -117.66 (m, 1F), -152.54 (dd, J = 20.4, 3.6 Hz, 2F), -157.97 (t, J = 21.6 Hz, 1F), -162.45 (dd, J = 21.8, 17.2 Hz, 2F). **HRMS**: exact mass calculated for $[\text{M}+\text{H}]^+$ $\text{C}_{20}\text{H}_{19}\text{F}_6\text{O}_2\text{Si}$ requires m/z 433.1053, found m/z 433.1045. HPLC analysis using a chiral column (Chiralpak IA 3 μ column, 22 °C, 1.0 mL/min, 98:2 Hexane:Isopropanol, 210 nm, = t_{minor} 9.993 min, t_{major} = 10.413 min). $[\alpha]_{\text{D}}^{23}$: -75.2.

Pentafluorophenyl (E)-5-(dimethyl(phenyl)silyl)-2-(2-fluorophenyl)pent-4-enoate, 7B—

Colorless oil (35 mg, 71% yield, 88:12 er). **IR** (film): 2957, 1783, 1518, 1493, 1248, 1108, 991, 820, 755, 731, 699, 469. **^1H NMR** (CDCl_3 , 400 MHz): δ 7.47 – 7.42 (m, 2H), 7.40 – 7.29 (m, 5H), 7.18 (td, J = 7.6, 1.2 Hz, 1H), 7.12 (ddd, J = 9.7, 8.3, 1.2 Hz, 1H), 6.08 (dt, J = 18.5, 6.4 Hz, 1H), 5.90 (dt, J = 18.5, 1.4 Hz, 1H), 4.43 (t, J = 7.6 Hz, 1H), 3.05 (dddd, J = 14.1, 7.6, 6.2, 1.4 Hz, 1H), 2.80 – 2.72 (m, 1H), 0.30 (d, J = 3.6 Hz, 6H). **^{13}C NMR** (CDCl_3 , 101 MHz): δ 169.0, 160.6 (d, $^1J_{\text{C-F}}$ = 246.8 Hz), 143.3, 138.5, 133.9, 132.5, 129.7 (d, $^3J_{\text{C-F}}$ = 8.2 Hz), 129.2 (d, $J_{\text{C-F}}$ = 3.6 Hz), 129.1, 127.8, 124.7 (d, $J_{\text{C-F}}$ = 3.7 Hz), 124.2 (d, $^2J_{\text{C-F}}$ = 14.9 Hz), 115.9 (d, $^2J_{\text{C-F}}$ = 22.2 Hz), 43.3 (d, $^3J_{\text{C-F}}$ = 2.4 Hz), 39.2, -2.6. **^{19}F NMR** (CDCl_3 , 376 MHz): δ -116.03 – -119.61 (m, 1F), -151.07 – -153.51 (m, 2F), -157.88 (t, J = 21.7 Hz, 1F), -162.37 (dd, J = 21.8, 17.1 Hz, 2F). **HRMS**: exact mass calculated for $[\text{M}+\text{Na}]^+$ $\text{C}_{25}\text{H}_{20}\text{F}_6\text{O}_2\text{SiNa}$ requires m/z 517.1035, found m/z 517.1017. HPLC analysis using a chiral column (Chiralpak IA 3 μ column, 22 °C, 0.25 mL/min, 600:1 Hexane:Isopropanol, 210 nm, = t_{minor} 23.334 min, t_{major} = 26.967 min). $[\alpha]_{\text{D}}^{23}$: -36.3.

Pentafluorophenyl (*E*)-5-(benzyltrimethylsilyl)-2-(2-fluorophenyl)pent-4-enoate, 7C—Colorless oil (43 mg, 85% yield, 90:10 er). **IR** (film): 2957, 1785, 1521, 1493, 1107, 1004, 995, 833, 757. **¹H NMR** (CDCl₃, 400 MHz): δ 7.38 – 7.29 (m, 2H), 7.22 – 7.14 (m, 3H), 7.12 (ddd, *J* = 9.7, 8.2, 1.2 Hz, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.96 – 6.90 (m, 2H), 5.98 (dt, *J* = 18.6, 6.4 Hz, 1H), 5.83 – 5.66 (m, 1H), 4.38 (t, *J* = 7.6 Hz, 1H), 3.00 (dddd, *J* = 14.2, 7.7, 6.2, 1.4 Hz, 1H), 2.79 – 2.59 (m, 1H), 2.07 (s, 2H), 0.00 (d, *J* = 1.3 Hz, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.1, 160.6 (d, ¹*J*_{C-F} = 247.0 Hz), 142.6, 140.0, 132.6, 129.7 (d, ³*J*_{C-F} = 8.4 Hz), 129.2 (d, *J*_{C-F} = 3.4 Hz), 128.3, 128.2, 124.7 (d, *J*_{C-F} = 3.6 Hz), 124.3 (d, ²*J*_{C-F} = 14.7 Hz), 124.1, 115.8 (d, ²*J*_{C-F} = 22.2 Hz), 43.3 (d, ³*J*_{C-F} = 2.4 Hz), 39.2, 26.0, –3.4. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –117.47 (dd, *J* = 10.7, 5.6 Hz, 1F), –151.61 – –154.93 (m, 2F), –157.87 (t, *J* = 21.7 Hz, 1F), –162.36 (dd, *J* = 21.9, 17.3 Hz, 2F). **HRMS**: exact mass calculated for [M+Na]⁺ C₂₆H₂₂F₆O₂SiNa requires *m/z* 531.1191, found *m/z* 531.1189. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.75 mL/min, 98:2 Hexane:Isopropanol, 210 nm, = *t*_{minor} 18.069 min, *t*_{major} = 18.811 min). [α]_D²³: –33.7.

Pentafluorophenyl (*E*)-2-(3-bromophenyl)-5-(trimethylsilyl)pent-4-enoate, 8A—Colorless oil. (37 mg, 75% yield, 86:14 er) **IR** (film): 2955, 1783, 1518, 1248, 1091, 991, 836, 690. **¹H NMR** (CDCl₃, 400 MHz): δ 7.55 (t, *J* = 1.8 Hz, 1H), 7.49 (dt, *J* = 7.7, 1.7 Hz, 1H), 7.33 (dt, *J* = 7.8, 1.5 Hz, 1H), 7.32 – 7.25 (m, 1H), 6.00 (dt, *J* = 18.5, 6.2 Hz, 1H), 5.82 (dt, *J* = 18.5, 1.3 Hz, 1H), 4.03 (dd, *J* = 9.0, 6.3 Hz, 1H), 3.06 – 2.92 (m, 1H), 2.73 – 2.60 (m, 1H), 0.07 (s, 9H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.1, 141.1, 139.2, 134.9, 131.3, 130.5, 126.6, 123.0, 50.4, 40.1, –1.3. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –148.91 – –154.39 (m, 2F), –157.71 (t, *J* = 21.7 Hz, 1F), –162.23 (dd, *J* = 21.6, 17.2 Hz, 2F). **HRMS**: exact mass calculated for [M-CH₃] C₁₉H₁₅BrF₅O₂Si requires *m/z* 476.9939, found *m/z* 476.9934. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.5 mL/min, 1600:1 Hexane:Isopropanol, 210 nm, = *t*_{minor} 14.278 min, *t*_{major} = 16.110 min). [α]_D²³: –50.4

Pentafluorophenyl (*E*)-5-(dimethyl(phenyl)silyl)-2-(3-bromophenyl)pent-4-enoate, 8B—Colorless oil (47 mg, 84% yield, 87:13 er). **IR** (film): 2956, 1782, 1518, 1427, 1248, 1108, 1092, 991, 820, 731, 698. **¹H NMR** (CDCl₃, 400 MHz): δ 7.51 (d, *J* = 1.8 Hz, 1H), 7.47 (dt, *J* = 7.4, 1.7 Hz, 1H), 7.47 – 7.39 (m, 2H), 7.36 – 7.31 (m, 2H), 7.30 – 7.20 (m, 3H), 6.02 (dt, *J* = 18.5, 6.0 Hz, 1H), 5.94 – 5.87 (m, 1H), 4.01 (dd, *J* = 8.5, 6.8 Hz, 1H), 3.01 (dddd, *J* = 14.6, 8.5, 6.0, 1.1 Hz, 1H), 2.76 – 2.63 (m, 1H), 0.30 (s, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 169.1, 143.1, 139.0, 133.9, 132.8, 131.3, 130.6, 129.2, 127.9, 126.7, 123.0, 50.3, 40.1, –2.6. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –152.23 – –152.66 (m, 2F), –157.65 (t, *J* = 21.7 Hz, 1F), –162.17 (dd, *J* = 21.8, 17.3 Hz, 2F). **HRMS**: exact mass calculated for [M+Na]⁺ C₂₅H₂₀BrF₅O₂SiNa requires *m/z* 577.0234, found *m/z* 577.0259. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 1.00 mL/min, 600:1 Hexane:Isopropanol, 210 nm, = *t*_{minor} 6.372 min, *t*_{major} = 7.963 min). [α]_D²³: –31.2.

Pentafluorophenyl (*E*)-5-(benzyltrimethylsilyl)-2-(3-bromophenyl)pent-4-enoate, 8C—Colorless oil (51 mg, 89% yield, 88:12 er). **IR** (film): 2955, 1782, 1518, 1493, 1248, 1091, 991, 831, 733, 698. **¹H NMR** (CDCl₃, 400 MHz): δ 7.58 (d, *J* = 1.9 Hz, 1H), 7.54 (dt, *J* = 7.5, 1.7 Hz, 1H), 7.37 – 7.30 (m, 2H), 7.26 (t, *J* = 7.7 Hz, 2H), 7.16 – 7.10

(m, 1H), 7.04 – 6.99 (m, 2H), 6.00 (dt, $J = 18.6, 6.3$ Hz, 1H), 5.82 (dt, $J = 18.7, 1.4$ Hz, 1H), 4.03 (dd, $J = 8.7, 6.7$ Hz, 1H), 3.10 – 2.94 (m, 1H), 2.72 – 2.62 (m, 1H), 2.15 (s, 2H), 0.07 (d, $J = 1.4$ Hz, 6H). **^{13}C NMR** (CDCl_3 , 101 MHz): δ 169.1, 142.4, 139.9, 139.0, 132.8, 131.31, 131.27, 130.6, 128.3, 128.2, 126.7, 124.1, 123.0, 50.4, 40.1, 26.0, –3.3. **^{19}F NMR** (CDCl_3 , 376 MHz): δ –149.96 – –154.90 (m, 2F), –157.63 (t, $J = 21.7$ Hz, 1F), –162.14 (dd, $J = 21.8, 17.3$ Hz, 2F). **HRMS**: exact mass calculated for $[\text{M}+\text{Na}]^+ \text{C}_{26}\text{H}_{22}\text{BrF}_5\text{O}_2\text{SiNa}$ requires m/z 591.0390, found m/z 591.0414. HPLC analysis using a chiral column (Chiralpak IB 3μ column, 22 °C, 1.00 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = t_{major} 9.700 min, $t_{\text{minor}} = 13.405$ min). $[\alpha]_{\text{D}}^{23}$: –72.1.

Pentafluorophenyl (*E*)-2-(3-chlorophenyl)-5-(trimethylsilyl)pent-4-enoate, 9A—Colorless oil (30 mg, 67% yield, 85:15 er). **IR** (film): 2955, 1783, 1518, 1248, 1094, 991, 860, 836, 690. **^1H NMR** (CDCl_3 , 400 MHz): δ 7.35 – 7.30 (m, 1H), 7.30 – 7.25 (m, 2H), 7.24 – 7.18 (m, 1H), 5.94 (dt, $J = 18.6, 6.2$ Hz, 1H), 5.76 (dt, $J = 18.5, 1.4$ Hz, 1H), 3.97 (dd, $J = 9.0, 6.3$ Hz, 1H), 2.94 (dddd, $J = 14.4, 9.0, 6.4, 1.3$ Hz, 1H), 2.61 (dtd, $J = 14.3, 6.2, 1.4$ Hz, 1H), 0.00 (s, 9H). **^{13}C NMR** (CDCl_3 , 101 MHz): δ 169.1, 141.1, 138.9, 134.9, 130.3, 128.4, 128.3, 126.2, 50.5, 40.1, –1.3. **^{19}F NMR** (CDCl_3 , 376 MHz): δ –150.53 – –155.20 (m, 2F), –157.75 (t, $J = 21.7$ Hz, 1F), –162.27 (dd, $J = 21.8, 17.2$ Hz, 2F). **HRMS**: exact mass calculated for $[\text{M}-\text{CH}_3]^+ \text{C}_{19}\text{H}_{15}\text{ClF}_5\text{O}_2\text{Si}$ requires m/z 433.0445, found m/z 433.0443. HPLC analysis using a chiral column (Chiralpak IB 3μ column, 22 °C, 1.00 mL/min, 1600:1 Hexane:Isopropanol, 210 nm, = t_{minor} 6.751 min, $t_{\text{major}} = 7.726$ min). $[\alpha]_{\text{D}}^{23}$: –47.8.

Pentafluorophenyl (*E*)-5-(dimethyl(phenyl)silyl)-2-(3-chlorophenyl)pent-4-enoate, 9B—Colorless oil (45 mg, 88% yield, 88:12 er). **IR** (film): 2956, 1782, 1518, 1428, 1248, 1094, 1025, 991, 838, 820, 783, 731, 698. **^1H NMR** (CDCl_3 , 400 MHz): δ 7.43 – 7.36 (m, 2H), 7.35 – 7.23 (m, 6H), 7.23 – 7.16 (m, 1H), 6.04 – 5.94 (m, 1H), 5.87 (dt, $J = 18.5, 1.2$ Hz, 1H), 3.98 (dd, $J = 8.5, 6.8$ Hz, 1H), 2.98 (dddd, $J = 14.6, 8.6, 6.0, 1.1$ Hz, 1H), 2.73 – 2.60 (m, 1H), 0.27 (s, 6H). **^{13}C NMR** (CDCl_3 , 101 MHz): δ 169.1, 143.1, 138.8, 138.4, 134.9, 133.9, 132.8, 130.3, 129.2, 128.4, 128.4, 127.9, 126.2, 50.3, 40.1, –2.6. **^{19}F NMR** (CDCl_3 , 376 MHz): δ –150.53 – –153.58 (m, 2F), –157.67 (t, $J = 21.7$ Hz, 1F), –162.19 (dd, $J = 21.9, 17.2$ Hz, 2F). **HRMS**: exact mass calculated for $[\text{M}+\text{Na}]^+ \text{C}_{25}\text{H}_{20}\text{ClF}_5\text{O}_2\text{SiNa}$ requires m/z 533.0739, found m/z 533.0714. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.75 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = t_{minor} 11.206 min, $t_{\text{major}} = 16.342$ min). $[\alpha]_{\text{D}}^{23}$: –32.6.

Pentafluorophenyl (*E*)-5-(benzyl(dimethyl)silyl)-2-(3-chlorophenyl)pent-4-enoate, 9C—Colorless oil (44 mg, 84% yield, 87:13 er). **IR** (film): 2955, 1782, 1598, 1518, 1493, 1248, 1094, 991, 831, 733, 698. **^1H NMR** (CDCl_3 , 400 MHz): δ 7.35 (d, $J = 2.6$ Hz, 1H), 7.34 – 7.30 (m, 2H), 7.26 – 7.20 (m, 1H), 7.19 (t, $J = 7.7$ Hz, 2H), 7.11 – 7.01 (m, 1H), 6.98 – 6.91 (m, 2H), 5.94 (dt, $J = 18.6, 6.3$ Hz, 1H), 5.75 (dt, $J = 18.6, 1.4$ Hz, 1H), 3.97 (dd, $J = 8.7, 6.7$ Hz, 1H), 2.97 (dddd, $J = 14.9, 8.6, 6.4, 1.4$ Hz, 1H), 2.64 (dtd, $J = 14.5, 6.5, 1.5$ Hz, 1H), 2.08 (s, 2H), 0.00 (d, $J = 1.1$ Hz, 6H). **^{13}C NMR** (CDCl_3 , 101 MHz): δ 169.1, 142.4, 139.9, 138.8, 134.9, 132.8, 130.3, 128.4, 128.3, 128.2, 126.2, 124.1, 50.4, 40.1, 26.0, –3.3. **^{19}F NMR** (CDCl_3 , 376 MHz): δ –151.04 – –154.09 (m, 2F), –157.65 (t, J

= 21.6 Hz, 1F), -161.25 – -165.38 (m, 2F). **HRMS**: exact mass calculated for $[M+Na]^+$ $C_{26}H_{22}ClF_5O_2SiNa$ requires m/z 547.0985, found m/z 547.0908. HPLC analysis using a chiral column (Chiralpak IB 3 μ column, 22 °C, 1.00 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = t_{major} 8.900 min, t_{minor} = 10.485 min). $[\alpha]_D^{23}$: -34.5.

4.3. Synthesis of compounds from Scheme 2

(*R,E*)-*N*-benzyl-5-(benzyltrimethylsilyl)-2-(4-methoxyphenyl)pent-4-enamide, 10

—Prepared according to the General Procedure using 4-methoxyphenyl acetic acid pentafluorophenyl ester (33 mg, 0.1 mmol, 1 equiv) and (*Z*)-3-(benzyltrimethylsilyl)allyl methanesulfonate (0.1 mL, 1.25 M, 0.125 mmol, 1.25 equiv). After stirring for 24 h at rt, benzylamine (14 μ L, 0.13 mmol, 1.3 equiv) and DIPEA (26 μ L, 0.15 mmol, 1.5 equiv) were added and the reaction mixture continued stirring at rt for a further 18 h. The reaction was then subjected to the workup described in the General Procedure and purified by column chromatography (silica gel, 10–30% Et₂O/petroleum ether) to afford the desired product as a colorless oil (34 mg, 77% yield, 94:6 er). **IR** (film): 3292, 3026, 2953, 1645, 1611, 1510, 1453, 1248, 1179, 1035, 831, 699. **¹H NMR** (CDCl₃, 400 MHz): δ 7.32 – 7.22 (m, 3H), 7.22 – 7.13 (m, 5H), 7.04 (t, J = 7.3 Hz, 1H), 6.91 (d, J = 7.5 Hz, 2H), 6.86 (d, J = 8.6 Hz, 2H), 5.90 (dt, J = 18.6, 6.4 Hz, 1H), 5.74 – 5.51 (m, 2H), 4.51 – 4.24 (m, 2H), 3.80 (s, 3H), 3.35 (t, J = 7.5 Hz, 1H), 2.99 (dt, J = 13.8, 6.8 Hz, 1H), 2.53 (dt, J = 14.4, 7.3 Hz, 1H), 2.04 (s, 2H), -0.04 (s, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 173.2, 159.0, 145.3, 140.2, 138.4, 131.6, 130.7, 129.2, 128.8, 128.4, 128.2, 127.7, 127.5, 124.0, 114.3, 55.4, 52.4, 43.7, 40.6, 26.2, -3.3. **HRMS**: exact mass calculated for $[M]^+$ $C_{28}H_{33}O_2NSi$ requires m/z 443.2275, found m/z 443.2260. HPLC analysis using a chiral column (Chiralpak IA 3 μ column, 22 °C, 1.00 mL/min, 90:10 Hexane:Isopropanol, 210 nm, = t_{minor} 10.588 min, t_{major} = 17.343 min). $[\alpha]_D^{23}$: -45.6.

Methyl (*R,E*)-5-(benzyltrimethylsilyl)-2-(4-methoxyphenyl)pent-4-enoate, 11—

Prepared according to the General Procedure using 4-methoxyphenyl acetic acid pentafluorophenyl ester (33 mg, 0.1 mmol, 1 equiv) and (*Z*)-3-(benzyltrimethylsilyl)allyl methanesulfonate (0.1 mL, 1.25 M, 0.125 mmol, 1.25 equiv). After stirring for 24 h at rt methanol (0.5 mL) and Et₃N (70 μ L, 0.5 mmol, 5 equiv) and DMAP (2.4 mg, 0.02 mmol, 0.2 equiv) were added and the reaction mixture was heated to 65 °C for 18 h. The reaction was then subjected to the workup described in the General Procedure and purified by column chromatography (silica gel, 10–30% Et₂O/petroleum ether) to afford the desired product as a colorless oil (32 mg, 86% yield, 91:9 er). **IR** (film): 2951, 2836, 1734, 1612, 1510, 1247, 1151, 1034, 829, 794, 698. **¹H NMR** (CDCl₃, 400 MHz): δ 7.23 – 7.15 (m, 4H), 7.06 (t, J = 7.4 Hz, 1H), 6.95 – 6.90 (m, 2H), 6.89 – 6.79 (m, 2H), 5.89 (dt, J = 18.7, 6.4 Hz, 1H), 5.64 (dt, J = 18.6, 1.4 Hz, 1H), 3.78 (s, 3H), 3.64 (s, 3H), 3.59 (dd, J = 8.5, 7.0 Hz, 1H), 2.83 (dddd, J = 15.2, 8.3, 6.5, 1.4 Hz, 1H), 2.58 – 2.46 (m, 1H), 2.05 (s, 2H), -0.04 (d, J = 2.6 Hz, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 174.3, 158.9, 144.5, 140.1, 130.9, 130.8, 129.0, 128.3, 128.2, 124.0, 114.1, 55.4, 52.0, 50.4, 40.7, 26.2, -3.3. **HRMS**: exact mass calculated for $[M]^+$ $C_{22}H_{28}O_3Si$ requires m/z 368.1802, found m/z 368.1807. HPLC analysis using a chiral column (Chiralpak IA 3 μ column, 22 °C, 0.5 mL/min, 98:2 Hexane:Isopropanol, 210 nm, = t_{minor} 11.436 min, t_{major} = 12.024 min). $[\alpha]_D^{23}$: -65.7.

(*R,E*)-5-(Benzyldimethylsilyl)-2-(4-methoxyphenyl)pent-4-enoic acid, 12—

Prepared according to the General Procedure using 4-methoxyphenyl acetic acid pentafluorophenyl ester (33 mg, 0.1 mmol, 1 equiv) and (*Z*)-3-(benzyldimethylsilyl)allyl methanesulfonate (0.1 mL, 1.25 M, 0.125 mmol, 1.25 equiv). After stirring for 24 h at rt H₂O (0.5 mL) and Et₃N (70 μ L, 0.5 mmol, 5 equiv) and DMAP (2.4 mg, 0.02 mmol, 0.2 equiv) were added and the reaction mixture was heated to 65 °C for 18 h. The reaction was then acidified with 1 M HCl (3 mL) and extracted with Et₂O (4 mL). The organics were dried and concentrated under vacuum before being purified by column chromatography (silica gel, 10–30% Et₂O/petroleum ether) to afford the desired product as a colorless oil (25 mg, 70% yield, 85:15 er). **IR** (film): 2954, 1703, 1612, 1511, 1248, 1206, 1179, 1035, 830, 795, 699. **¹H NMR** (CDCl₃, 400 MHz): δ 7.23 – 7.19 (m, 2H), 7.17 (t, *J* = 7.6 Hz, 2H), 7.10 – 7.01 (m, 1H), 6.94 – 6.89 (m, 2H), 6.87 – 6.82 (m, 2H), 5.88 (dt, *J* = 18.6, 6.3 Hz, 1H), 5.65 (dt, *J* = 18.6, 1.4 Hz, 1H), 3.78 (s, 3H), 3.59 (t, *J* = 7.7 Hz, 1H), 2.87 – 2.75 (m, 1H), 2.59 – 2.48 (m, 1H), 2.03 (s, 2H), –0.05 (d, *J* = 2.3 Hz, 6H). **¹³C NMR** (CDCl₃, 101 MHz): δ 179.8, 159.1, 144.1, 140.1, 131.3, 130.1, 129.2, 128.3, 128.2, 124.0, 114.2, 55.4, 50.3, 40.1, 26.1, –3.3. **HRMS**: exact mass calculated for [M]⁺ C₂₁H₂₆O₃Si requires *m/z* 354.1646, found *m/z* 354.1650. HPLC analysis using a chiral column (Chiralpak IB 3 μ column, 22 °C, 1.00 mL/min, 98:2 Hexane:Isopropanol, 210 nm, = *t*_{major} 10.249 min, *t*_{minor} = 12.010 min). [α]_D²³: –57.6.

4.4. Synthesis of compounds from Scheme 3

Pentafluorophenyl (*R,Z*)-2-(4-chlorophenyl)-5-iodopent-4-enoate, 13—To an oven dried 1 dram vial equipped with stirrer bar was added pentafluorophenyl (*R,E*)-2-(4-chlorophenyl)-5-(dimethyl(phenyl)silyl)pent-4-enoate (60 mg, 0.12 mmol, 1 equiv) and HFIP (0.4 mL, 0.3 M) and cooled to 0 °C. *N*-iodosuccinimide (41 mg, 0.18 mmol, 1.5 equiv) was then added and stirred for 20 minutes. The reaction mixture was then quenched with H₂O (2 mL) and extracted with DCM (3 mL). The organic phase was then washed with sat. sodium thiosulfate, dried and concentrated under vacuum before being purified by column chromatography (silica gel, 1% Et₂O/petroleum ether) to afford the desired product as a colorless oil (55 mg, 92% yield, 89:11 er, 4:1 *Z:E*). **IR** (film): 2924, 1782, 1520, 1493, 1103, 1095, 1049, 997, 760. **¹H NMR** (CDCl₃, 400 MHz, *Z* isomer): δ 7.56 – 7.45 (m, 4H), 6.55 – 6.50 (m, 1H), 6.29 (q, *J* = 7.0 Hz, 1H), 4.42 (t, *J* = 7.7 Hz, 1H), 3.07 – 2.96 (m, 1H), 2.86 – 2.78 (m, 1H). **¹³C NMR** (CDCl₃, 101 MHz, *Z* isomer): δ 169.9, 137.9, 136.5, 134.4, 130.8, 129.9, 86.4, 49.2, 38.9. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –154.75 (d, *J* = 17.0 Hz, 2F), –160.07 (t, *J* = 21.1 Hz, 1F), –164.68 (dd, *J* = 21.4, 17.0 Hz, 2F). **HRMS**: exact mass calculated for [M]⁺ C₁₇H₁₀ClF₅O₂I requires *m/z* 502.9329, found *m/z* 502.9347. HPLC analysis using a chiral column (Chiralpak IA 3 μ column, 22 °C, 0.75 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = *t*_{minor} 25.856 min, *t*_{major} = 31.111 min). [α]_D²³: –41.8.

Methyl (*R,E*)-2-(4-methoxyphenyl)-5-(4-(trifluoromethyl)phenyl)pent-4-enoate, 14—To an oven dried 1 dram vial equipped with stirrer bar was added methyl (*R,E*)-5-(benzyldimethylsilyl)-2-(4-methoxyphenyl)pent-4-enoate (104 mg, 0.2 mmol, 1 equiv). The vial was then capped and purged with N₂ before adding THF (0.36 mL, 0.56 M) and H₂O (11 μ L, 0.6 mmol, 3 equiv) and cooling to 0 °C. Tetrabutylammonium fluoride (0.44 mL, 1 M in THF, 0.44 mmol, 2.2 equiv,) was then added and the reaction mixture was stirred at

0 °C for 5 minutes before the addition of 4-iodobenzotrifluoride (44 μ L, 0.3 mmol, 1.5 equiv) and Pd₂dba₃ (4.5 mg, 0.005 mmol, 2.5 mol%). The reaction mixture was then warmed to rt and stirred for 24 h before being quenched with H₂O (2 mL) and extracted with Et₂O (4 mL). The organics were then dried and concentrated under vacuum before being purified by column chromatography (silica gel, 10% Et₂O/petroleum ether) to afford the desired product as a yellow oil which crystallized on standing (61 mg, 84% yield, 91:9 er). **IR** (film): 2957, 1733, 1613, 1512, 1327, 1254, 1156, 1106, 1068, 1032, 975, 832, 800, 535. **¹H NMR** (CDCl₃, 400 MHz): δ 7.52 (d, J = 8.1 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.25 (d, J = 8.7 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 6.45 (d, J = 15.8 Hz, 1H), 6.19 (dt, J = 15.6, 7.1 Hz, 1H), 3.79 (s, 3H), 3.68 – 3.64 (m, 4H), 3.00 – 2.87 (m, 1H), 2.70 – 2.50 (m, 1H). **¹³C NMR** (CDCl₃, 101 MHz): δ 174.1, 159.1, 140.9, 131.1, 130.5, 130.0, 129.2 (d, $^2J_{C-F}$ = 17.0 Hz), 129.0, 126.3, 125.5 (d, $^3J_{C-F}$ = 3.9 Hz), 124.3 (d, $^1J_{C-F}$ = 271.8 Hz), 114.3, 55.3, 52.2, 50.8, 37.1. **¹⁹F NMR** (CDCl₃, 376 MHz): δ –62.47 (s, 3F). **HRMS**: exact mass calculated for [M]⁺ C₂₀H₁₉F₃O₃ requires m/z 364.1281, found m/z 364.1285. HPLC analysis using a chiral column (Chiralpak IA 3 μ column, 22 °C, 1.00 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = t_{minor} 19.925 min, t_{major} = 22.425 min). [α]_D²³: –88.2.

Methyl (*R*)-2-(4-methoxyphenyl)-5-oxopentanoate 15—To an oven dried 2 dram vial equipped with stirrer bar was added methyl (*R,E*)-2-(4-methoxyphenyl)-5-(trimethylsilyl)pent-4-enoate (146 mg, 0.5 mmol, 1 equiv) and DCM (2.5 mL, 0.2M). *m*CPBA (140 mg, 0.6 mmol, 1.2 equiv) was then added and the reaction mixture was stirred at rt for 18 h. The reaction mixture was then quenched with sat. sodium sulfite (2 mL) diluted with DCM (10 mL) and washed with sat. sodium bicarbonate (10 mL). The organics were then dried and concentrated under vacuum before being dissolved in THF (2 mL) and stirred with aq. H₂SO₄ (2 mL, 3.6 M) for 1 h at rt. The reaction mixture was then diluted with H₂O (5 mL), extracted with Et₂O (10 mL), washed with sat. sodium bicarbonate (10 mL) and brine (10 mL). The organics were then dried and concentrated under vacuum to afford the desired product as a colorless oil (72 mg, 61% yield). **IR** (film): 3018, 2954, 2932, 2838, 1730, 1611, 1513, 1249, 1215, 1164, 1034, 753. **¹H NMR** (CDCl₃, 400 MHz): δ 9.70 (t, J = 1.3 Hz, 1H), 7.19 (d, J = 8.7 Hz, 2H), 6.86 (d, J = 8.7 Hz, 2H), 3.79 (s, 3H), 3.65 (s, 3H), 3.55 (t, J = 7.5 Hz, 1H), 2.43 – 2.36 (m, 2H), 2.35 – 2.26 (m, 1H), 2.14 – 2.03 (m, 1H). **¹³C NMR** (CDCl₃, 101 MHz): δ 201.4, 174.2, 159.1, 130.2, 129.1, 114.3, 55.4, 52.2, 49.6, 41.6, 25.8. **HRMS**: exact mass calculated for [M]⁺ C₁₃H₁₆O₄ requires m/z 236.1043, found m/z 236.1048. [α]_D²³: –34.6.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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13. Running the reaction with (*S*)-BTM afforded the (*S*) configured product. In order to rule out an asymmetric protonation process, the (*R*) product was resubmitted to the reaction conditions with the opposite (*S*)-enantiomer of BTM. No change in er was observed by HPLC analysis.
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16. The er of product 15 could not be determined due to degradation under HPLC conditions.

(a) Si-directed nucleophilic attack:

(b) This work:

Figure 1.

Si-based regiocontrol in Pd-catalyzed allylic allylation. (a) Attack of nucleophile at carbon distal to silicon; (b) Attack of C1- ammonium enolate at carbon distal to silicon.

Scheme 1.

Evaluation of substrate scope^d

^aIsolated yields after silica gel chromatography. Enantiomeric ratio determined by chiral HPLC in comparison to the racemate. ^bEnantiomeric ratio determined following reduction to the corresponding alcohol. ^cEnantiomeric ratio after 6 h reaction time.

Scheme 2.*In situ* functionalization of the ester moiety.

Scheme 3.
Functionalization of vinyl silanes.

Table 1

Ligand evaluation and reaction optimization.

entry			yield [%] ^a	<i>er</i> ^b
1 ^c	XantphosPd G3 (5)	THF	51	93:7
2	Xantphos (10)	THF	77	94:6
3	DPEphos (10)	THF	76	91:9
4	dppf (10)	THF	39	88:12
5	dppe (10)	THF	-	-
6	PPh ₃ (20)	THF	74	82:18
7	PCy ₃ (20)	THF	-	-
8	P(2-furyl) ₃ (20)	THF	71	90:10
9	Xantphos (10)	1,4-dioxane	74	94:6
10	P(2-furyl) ₃ (10)	1,4-dioxane	87	93:7
11 ^d	P(2-furyl) ₃ (10)	1,4-dioxane	97	94:6

^aYields determined by ¹H-NMR comparison with an internal standard (1,2,4,5-tetramethylbenzene).^bDetermined by chiral HPLC analysis in comparison to the racemate.^cOnly XantphosPd G3 precatalyst was used, Pd₂dba₃ was omitted.^d1.25 equiv *i*Pr₂NEt used.