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4Graphical Abstract

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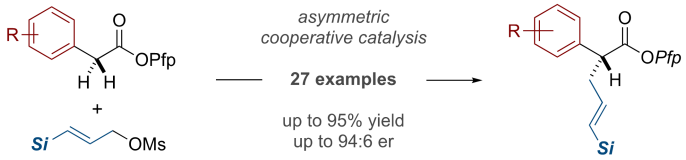

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Si-Directed regiocontrol in asymmetric Pd-catalyzed allylic alkylations using C1-ammonium enolate nucleophiles

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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.

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(sp^3)–carbon bonds can be forged efficiently and in highly enantioselective fashion 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(sp^3)–C(sp^3) 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.

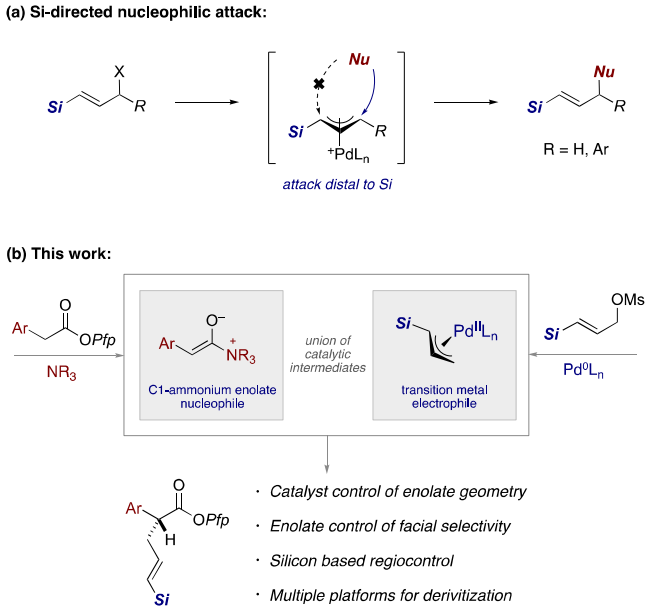


Figure 1. Si-based regiocontrol in Pd-catalyzed allylic allylation. (a) Attack of nucleophile at carbon distal to silicon; (b) Attack of C1-ammonium enolate at carbon distal to silicon.

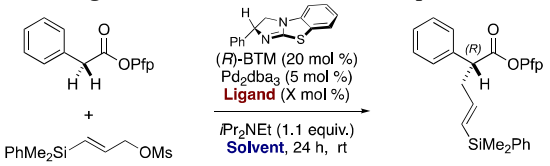
Silicon-substituted electrophiles have been extensively investigated in transition metal-catalyzed allylic alkylation

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 product[13] in 51% yield and 93:7 er as the alkene (*E*)-isomer (Table 1, entry 1).

Table 1. Ligand evaluation and reaction optimization.

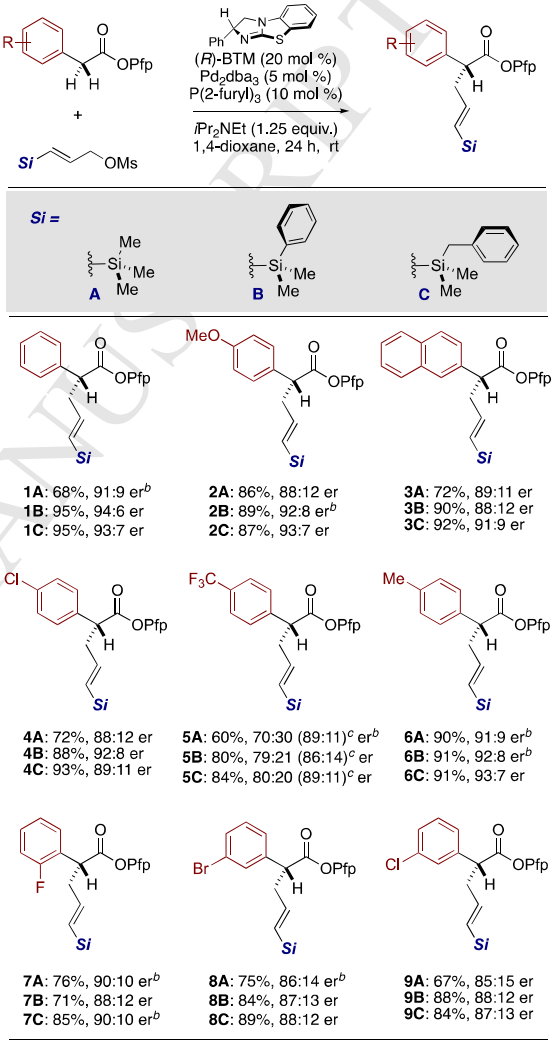


entry	ligand (mol %)	solvent	yield [%][a]	*er* [b]
1[c]	XantphosPd G3 (5)	THF	51	93:7
2	Xantphos (10)	THF	77	94:6
3	DPEphos (10)	THF	76	91:9
4	dppf (10)	THF	39	88:12
5	dppe (10)	THF	-	-
6	PPh_3 (20)	THF	74	82:18
7	PCy_3 (20)	THF	-	-
8	P(2-furyl)$_3$ (20)	THF	71	90:10
9	Xantphos (10)	1,4-dioxane	74	94:6
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

[a]Yields determined by ^{1}H-NMR comparison with an internal standard (1,2,4,5-tetramethylbenzene). [b]Determined by chiral HPLC analysis in comparison to the racemate. [c]Only XantphosPd G3 precatalyst was used, Pd_2dba_3 was omitted. [d]1.25 equiv *i*Pr_2NEt used.

Generating the catalyst *in situ* from Pd_2dba_3 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 ^{1}H 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 P(2-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.

Scheme 1. Evaluation of substrate scope[a]



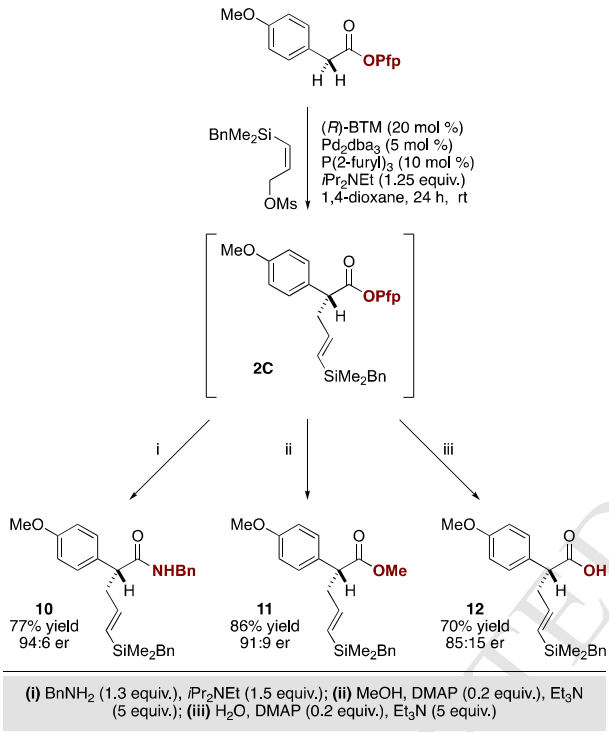
[a]Isolated yields after silica gel chromatography. Enantiomeric ratio determined by chiral HPLC in comparison to the racemate. [b]Enantiomeric ratio determined following reduction to the corresponding alcohol. [c]Enantiomeric ratio after 6 h reaction time.

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.

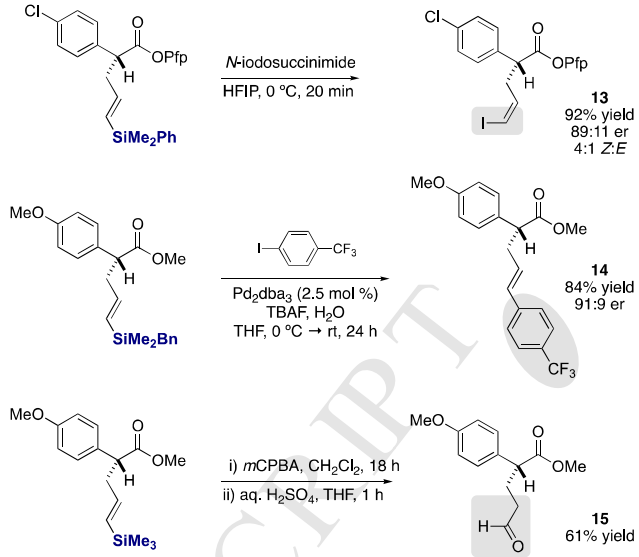
Next, we turned our attention to the derivatization of the Pfp ester (Scheme 2). Here, the (*Z*)-isomer of the allyl mesylate was employed as a demonstration of the energetic preference for exclusive formation of the (*E*)-isomer products. A range of nucleophilic quenches were then employed, successfully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

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



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 co-workers.[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]

Scheme 3. Functionalization of vinyl silanes.



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

^{1}H and ^{13}C NMR spectra were recorded at room temperature on Varian Inova-instrumentation: Varian I400 (^{1}H NMR at 400MHz and ^{13}C NMR at 100 MHz), Varian VXR400 (^{1}H NMR at 400 MHz and ^{13}C NMR at 100 MHz), and Varian I500 (^{1}H NMR at 500 MHz and ^{13}C NMR at 125 MHz) using deuterium lock. Data for ^{1}H NMR spectra are quoted relative to chloroform as an internal standard (7.26 ppm) and data for ^{13}C NMR spectra are quoted relative to $CDCl_3$ 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 ^{13}C signals for pentafluorophenyl were not observed due to splitting. Infrared spectra (IR) were obtained on an 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 $[\alpha]_D^{23}$ values were obtained in $CHCl_3$ 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 Pd_2dba_3 (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 (× 3) before the addition of 1,4-dioxane (0.8 mL, 0.1 M). *i*Pr$_2$NEt (22 µL, 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 Et$_2$O (2 × 4 mL). The solution was then concentrated under vacuum and purified by column chromatography (silica gel, 100:1 pentane:Et$_2$O) 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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 169.7, 141.8, 137.1, 134.2, 129.1, 128.1, 128.0, 50.9, 40.2, –1.3. **^{19}F NMR** ($CDCl_3$, 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 $[M+H]^+$ $C_{20}H_{20}F_5O_2Si$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. ^{19}F NMR ($CDCl_3$, 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 $[M+Na]^+$ $C_{25}H_{21}F_5O_2SiNa$ 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). $[\alpha]_D^{23}$: –34.3.

Pentafluorophenyl (*E*)-5-(benzyldimethylsilyl)-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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M+Na]^+$ $C_{26}H_{23}F_5O_2Si$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 169.9, 159.4, 141.9, 134.1, 129.1, 114.4, 55.4, 50.1, 40.3, –1.3. **^{19}F NMR** ($CDCl_3$, 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 $[M+H]^+$ $C_{21}H_{22}F_5O_3Si$ 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} = 4.913min, t_{major} = 5.143 min). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M+Na]^+$ $C_{26}H_{23}F_5O_3SiNa$ 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). $[\alpha]_D^{23}$: –50.3.

Pentafluorophenyl (*E*)-5-(benzyldimethylsilyl)-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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M+Na]^+$ $C_{27}H_{25}F_5O_3SiNa$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M+H]^+$ $C_{24}H_{22}F_5O_2Si$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M+Na]^+$ $C_{29}H_{23}F_5O_2SiNa$ 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). $[\alpha]_D^{23}$: –50.2.

Pentafluorophenyl (*E*)-5-(benzyldimethylsilyl)-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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M+Na]^+$ $C_{30}H_{25}F_5O_2SiNa$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 169.3, 141.2, 135.5, 134.7, 134.1, 129.4, 129.2, 50.2, 40.2, –1.3. **^{19}F NMR** ($CDCl_3$, 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 $[M+H]^+$ $C_{20}H_{19}ClF_5O_2Si$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M+Na]^+$ $C_{25}H_{20}ClF_5O_2SiNa$ 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). $[\alpha]_D^{23}$: –38.6.

Pentafluorophenyl (*E*)-5-(benzyldimethylsilyl)-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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M]^+$ $C_{26}H_{22}ClF_5O_2Si$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 169.1, 141.0, 140.9, 135.1, 130.5 (q, $^2J_{C\text{-}F}$ = 32.7 Hz), 128.5, 126.0 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 124.1 (q, $^1J_{C\text{-}F}$ = 272.0 Hz), 50.7, 40.2, –1.3. **^{19}F NMR** ($CDCl_3$, 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 $[M-CH_3]^+$ $C_{20}H_{15}F_8O_2Si$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 169.0, 142.8, 139.6 (d, $^1J_{C\text{-}F}$ = 245.4 Hz), 133.9, 133.0, 130.5 (d, $^2J_{C\text{-}F}$ = 32.9 Hz), 129.2, 128.6, 127.9, 126.0 (d, $^3J_{C\text{-}F}$ = 3.8 Hz), 50.5, 40.2, –2.7. **^{19}F NMR** ($CDCl_3$, 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 $[M+H]^+$ $C_{26}H_{21}F_8O_2Si$ 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). $[\alpha]_D^{23}$: –19.2.

Pentafluorophenyl (*E*)-5-(benzyldimethylsilyl)-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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 169.0, 142.2, 140.8, 139.9, 133.0, 130.5 (d, $^2J_{C\text{-}F}$ = 32.6 Hz), 128.5, 128.3 (d, $^3J_{C\text{-}F}$ = 10.2 Hz), 126.0 (q, $^4J_{C\text{-}F}$ = 3.7 Hz), 124.2, 50.6, 40.2, 26.0, –3.4. CF_3 carbon not observed. **^{19}F NMR** ($CDCl_3$, 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 $[M+H]^+$ $C_{27}H_{23}F_8O_2Si$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M+H]^+$ $C_{21}H_{22}F_5O_2Si$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M+Na]^+$ $C_{26}H_{23}F_5O_2SiNa$ requires m/z 513.1285, found m/z 513.1263. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.75 mL/min, 99:1 Hexane:Isopropanol, 210 nm, = t_{major} 12.367 min, t_{minor} = 14.733 min). $[\alpha]_D^{23}$: –41.8.

Pentafluorophenyl (*E*)-5-(benzyldimethylsilyl)-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. **^{1}H 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 $[M+Na]^+$ $C_{27}H_{25}F_5O_2SiNa$ requires m/z 527.1442, found m/z 527.1427. HPLC analysis using a chiral column (Chiralpak IB 3μ column, 22 °C, 1.0 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = t_{major} 6.925 min, t_{minor} = 9.236 min). $[\alpha]_D^{23}$: –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. **^{1}H 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, $^1J_{C\text{-}F}$ = 247.0 Hz), 141.3, 134.7, 129.7 (d, $^3J_{C\text{-}F}$ = 8.4 Hz), 129.1 (d, $J_{C\text{-}F}$ = 3.4 Hz), 124.6 (d, $J_{C\text{-}F}$ = 3.6 Hz), 124.4 (d, $^2J_{C\text{-}F}$ = 14.6 Hz), 115.8 (d, $^2J_{C\text{-}F}$ = 22.2 Hz), 43.4 (d, $^3J_{C\text{-}F}$ = 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 $[M+H]^+$ $C_{20}H_{19}F_6O_2Si$ requires m/z 433.1053, found m/z 433.1045. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 1.0 mL/min, 98:2 Hexane:Isopropanol, 210 nm, = t_{minor} 9.993 min, t_{major} = 10.413 min). $[\alpha]_D^{23}$: –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. **^{1}H 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, $^1J_{C\text{-}F}$ = 246.8 Hz), 143.3, 138.5, 133.9, 132.5, 129.7 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 129.2 (d, $J_{C\text{-}F}$ = 3.6 Hz), 129.1, 127.8, 124.7 (d, $J_{C\text{-}F}$ = 3.7 Hz), 124.2 (d, $^2J_{C\text{-}F}$ = 14.9 Hz), 115.9 (d, $^2J_{C\text{-}F}$ = 22.2 Hz), 43.3 (d, $^3J_{C\text{-}F}$ = 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 $[M+Na]^+$ $C_{25}H_{20}F_6O_2SiNa$ requires m/z 517.1035, found m/z 517.1017. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.25 mL/min, 600:1 Hexane:Isopropanol, 210 nm, = t_{minor} 23.334 min, t_{major} = 26.967 min). $[\alpha]_D^{23}$: –36.3.

Pentafluorophenyl (*E*)-5-(benzyldimethylsilyl)-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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 169.1, 160.6 (d, $^1J_{C\text{-}F}$ = 247.0 Hz), 142.6, 140.0, 132.6, 129.7 (d, $^3J_{C\text{-}F}$ = 8.4 Hz), 129.2 (d, $J_{C\text{-}F}$ = 3.4 Hz), 128.3, 128.2, 124.7 (d, $J_{C\text{-}F}$ = 3.6 Hz), 124.3 (d, $^2J_{C\text{-}F}$ = 14.7 Hz), 124.1, 115.8 (d, $^2J_{C\text{-}F}$ = 22.2 Hz), 43.3 (d, $^3J_{C\text{-}F}$ = 2.4 Hz), 39.2, 26.0, –3.4. **^{19}F NMR** ($CDCl_3$, 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 $[M+Na]^+$ $C_{26}H_{22}F_6O_2SiNa$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M\text{-}CH_3]$ $C_{19}H_{15}BrF_5O_2Si$ 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). $[\alpha]_D^{23}$: –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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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. **^{19}F NMR** ($CDCl_3$, 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 $[M+Na]^+$ $C_{25}H_{20}BrF_5O_2SiNa$ 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). $[\alpha]_D^{23}$: –31.2.

Pentafluorophenyl (*E*)-5-(benzyldimethylsilyl)-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. **^{1}H NMR** ($CDCl_3$, 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 $[M+Na]^+$ $C_{26}H_{22}BrF_5O_2SiNa$ 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_{minor} = 13.405 min). $[\alpha]_D^{23}$: –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. **^{1}H 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 $[M\text{-}CH_3]^+$ $C_{19}H_{15}ClF_5O_2Si$ 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_{major} = 7.726 min). $[\alpha]_D^{23}$: –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. **^{1}H 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 $[M+Na]^+$ $C_{25}H_{20}ClF_5O_2SiNa$ 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_{major} = 16.342 min). $[\alpha]_D^{23}$: –32.6.

Pentafluorophenyl (*E*)-5-(benzyldimethylsilyl)-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. **^{1}H 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 3μ 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-(benzyldimethylsilyl)-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-(benzyldimethylsilyl)allyl methanesulfonate (0.1 mL, 1.25 M, 0.125 mmol, 1.25 equiv). After stirring for 24 h at rt, benzylamine (14 μL, 0.13 mmol, 1.3 equiv) and DIPEA (26 μL, 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% Et_2O/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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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 3μ 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-(benzyldimethylsilyl)-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-(benzyldimethylsilyl)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 Et_3N (70 μL, 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% Et_2O/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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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 3μ 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 H_2O (0.5 mL) and Et_3N (70 μL, 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 Et_2O (4 mL). The organics were dried and concentrated under vacuum before being purified by column chromatography (silica gel, 10-30% Et_2O/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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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 $[M]^+$ $C_{21}H_{26}O_3Si$ requires m/z 354.1646, found m/z 354.1650. HPLC analysis using a chiral column (Chiralpak IB 3μ column, 22 °C, 1.00 mL/min, 98:2 Hexane:Isopropanol, 210 nm, = t_{major} 10.249 min, t_{minor} = 12.010 min). $[\alpha]_D^{23}$: –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 H_2O (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% Et_2O/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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 101 MHz, *Z* isomer): δ 169.9, 137.9, 136.5, 134.4, 130.8, 129.9, 86.4, 49.2, 38.9. **^{19}F NMR** ($CDCl_3$, 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 $[M]^+$ $C_{17}H_{10}ClF_5O_2I$ requires m/z 502.9329, found m/z 502.9347. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 0.75 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = t_{minor} 25.856 min, t_{major} = 31.111 min). $[\alpha]_D^{23}$: –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 N_2 before adding THF (0.36 mL, 0.56 M) and H_2O (11 μL, 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 μL, 0.3 mmol, 1.5 equiv) and Pd_2dba_3 (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 H_2O (2 mL) and extracted with Et_2O (4 mL). The organics were then dried and concentrated under vacuum before being purified

by column chromatography (silica gel, 10% Et_2O/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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 101 MHz): δ 174.1, 159.1, 140.9, 131.1, 130.5, 130.0, 129.2 (d, $^2J_{C\text{-}F}$ = 17.0 Hz), 129.0, 126.3, 125.5 (d, $^3J_{C\text{-}F}$ = 3.9 Hz), 124.3 (d, $^1J_{C\text{-}F}$ = 271.8 Hz), 114.3, 55.3, 52.2, 50.8, 37.1. **^{19}F NMR** ($CDCl_3$, 376 MHz): δ –62.47 (s, 3F). **HRMS**: exact mass calculated for $[M]^+$ $C_{20}H_{19}F_3O_3$ requires m/z 364.1281, found m/z 364.1285. HPLC analysis using a chiral column (Chiralpak IA 3μ column, 22 °C, 1.00 mL/min, 800:1 Hexane:Isopropanol, 210 nm, = t_{minor} 19.925 min, t_{major} = 22.425 min). $[\alpha]_D^{23}$: –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. H_2SO_4 (2 mL, 3.6 M) for 1 h at rt. The reaction mixture was then diluted with H_2O (5 mL), extracted with Et_2O (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. **^{1}H NMR** ($CDCl_3$, 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). **^{13}C NMR** ($CDCl_3$, 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 $[M]^+$ $C_{13}H_{16}O_4$ requires m/z 236.1043, found m/z 236.1048. $[\alpha]_D^{23}$: –34.6.

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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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