Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

An Enantioselective Synthesis of α-Alkylated Pyrroles via Cooperative Isothiourea/Palladium Catalysis

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General Information:

Commercial reagents were purified prior to use following the guidelines of Perrin and Armarego.[1] Unless otherwise noted, all reactions have been carried out with distilled and degassed solvents under an atmosphere of dry N_2 in flame or oven dried glassware with standard vacuum-line techniques. All reactions were carried out in Teflon screw cap reaction vials with magnetic stirring unless otherwise indicated. Tetrahydrofuran, diethyl ether, dichloromethane, and acetonitrile were dried under a positive pressure of dry argon by passage through two columns of activated alumina. Toluene was dried under a positive pressure of dry argon by passage through a column of activated alumina followed by a column Q5 (Grubbs apparatus). *N,N*-dimethylformamide was dried by passing through two columns of 5Å activated molecular sieves. Anhydrous 1,4-dioxane was purchase from Sigma-Aldrich and used without further drying. All workup and purification procedures were carried out with reagent grade solvents (purchased from Sigma-Aldrich) in air. Standard column chromatography techniques using ZEOprep 60/40-63 μm silica gel were used for purification. Liquids and solutions were transferred via syringe or cannula.

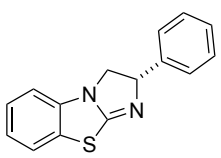
^{1}H and ^{13}C NMR spectra were recorded at 25 °C on Varian Inova-instrumentation: Varian I400 (^{1}H NMR at 400MHz and ^{13}C NMR at 101 MHz and ^{19}F NMR at 376 MHz), Varian VXR400 (^{1}H NMR at 400 MHz and ^{13}C NMR at 110 MHz and ^{19}F NMR at 376 MHz), and Varian I500 (^{1}H NMR at 500 MHz and ^{13}C NMR at 125 MHz and ^{19}F NMR at 470 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 chloroform as an internal standard (77.13 ppm) and are reported in terms of chemical shift (δ ppm). ^{19}F NMR were externally referenced using neat trifluoroacetic acid. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, b = broad, m = multiplet), coupling constants (Hz), and integration. Infrared spectra (IR) were obtained on an Avatar 360-FT IR E.S.P. on a diamond plate and recorded in wavenumbers (cm^{-1}). Melting points were obtained on a Thomas Hoover capillary melting point apparatus without correction. 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 $[M]^+$, $[M]^-$, $[M+H]^+$, or $[M+Na]^+$ molecular ion. Chiral HPLC analyses were performed on an Agilent 1200 Series system using the specified column.

[1] D. D. Perrin, W. L. F. Amarego, Purification of Laboratory Chemicals, Pergamon Press, Oxford, Ed. 3, 1988

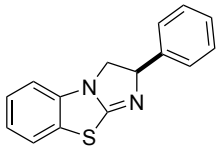
Experimental Section:

Catalysts/Ligands

(*R*)-(+)-Benzotetramisole [(+)-BTM, CAS: 885051-07-0], (*S*)-(–)-Benzotetramisol [(–)-BTM, CAS: 950194-37-3] and (*rac*)-Benzotetramisole were prepared from (+)-phenylglycinol, (–)-phenylglycinol, or (±)-phenylglycinol respectively according to a procedure by Smith and coworkers.[2]



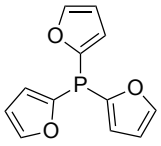
(*S*)-BTM



(*R*)-BTM

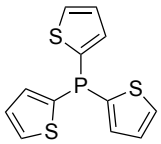
Ligands were purchased from the following vendors and used without further purification:

(tri(2-furyl))$_3$P:	Oakwood Chemicals
(tri(2-thienyl))$_3$P:	Alfa Aesar
XantPhos:	Strem
(*rac*)-BINAP:	Combi-Blocks
(+)-BINAP:	Combi-Blocks



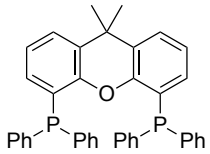
(tri-(2-furyl))$_3$P

Tri(2-furyl)phosphine
CAS: 5518–52-5



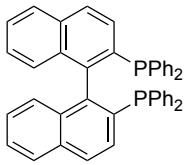
(tri-(2-thienyl))$_3$P

Tri(2-thienyl)phosphine
CAS: 24171-89-9



Xantphos

4,5-bis(diphenylphosphino-
9,9-dimethylxanthene
CAS: 161265-03-8



BINAP

(±)-2,2'-bis(diphenylphosphino)-
1,1'-dinaphthalene
CAS: 98327-87-8

$Pd_2(dba)_3$ was purchased from Oakwood Chemicals and used without further purification.

XantphosPd G3 was prepared using a known literature procedure.[3]

Palladium tris(2-thienyl)phosphine $Pd[(P\text{-}2Th)_3]_3$ was prepared using a known literature procedure.[4]

Grubbs II was purchased from ABPharmaTech and used without further purification.

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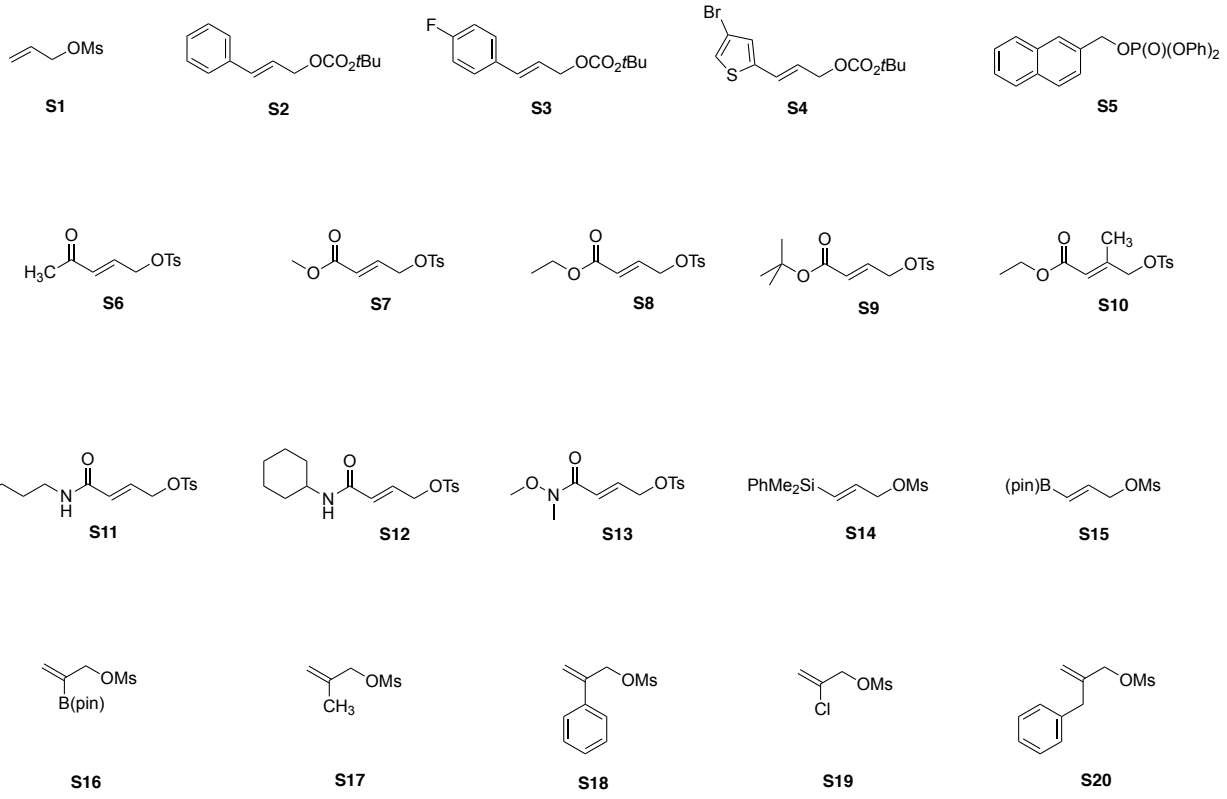
[2] D. S. B. Daniels; S. R. Smith; T. Lebl; P. Shapland; A. D. Smith *Synthesis* **2015**, *47*, 34
[3] N. C. Bruno; M. T. Tudge; S. L. Buchwald *Chem. Sci*, **2013**, *4*(3), 916
[4] W. Li; Y. Han; B. Li; C. Liu; Z. J. Bo *Polym. Sci. Part A Polym. Chem.* **2008**, *46*, 4556

Preparation of Electrophiles:

Electrophile **S1** was prepared using known literature procedure.[5] Electrophiles **S2 – S4** were prepared using a known literature procedure.[6] Electrophile **S5** was prepared using a known literature procedure.[7] Electrophiles **S6 – S13** were prepared using a known literature procedure.[8] Electrophile **S14** was prepared using a known literature procedure.[9] Electrophiles **S15** & **S16** were prepared using a known literature procedure.[10] Electrophiles **S17 – S20** were prepared using a known literature procedure.[11]



S1 S2 S3 S4 S5

S6 S7 S8 S9 S10

S11 S12 S13 S14 S15

S16 S17 S18 S19 S20

[5] K. J. Schwarz; J. L. Amos; J. C. Klein; D. T. Do; T. N. Snaddon *J. Am. Chem. Soc.*, **2016** *138*, 5214

[6] Q. Yuan; K. Yao; D. Liu; W. Zhang *Chem. Commun.* **2015**, *51*, 11834

[7] K. J. Schwarz; C. Yang; J. W. B. Fyfe; T. N. Snaddon *Angew. Chem. Int. Ed.* **2018***, 57,* 12102

[8] L. S. Hutchings-Goetz; C. Yang; T. N. Snaddon *ACS Catal.* **2018**, *8*, 10537

[9] J. W. B. Fyfe; O. M. Kabia; C. M. Pearson, T. N. Snaddon *Tetrahedron* **2018**, *74*, 5383

[10] W. R. Scaggs; T. N. Snaddon *Chem. Eur. J.* **2018**, *24*, 14378

[11] K. J. Schwarz; C. M. Pearson; G. A. Cintron-Rosado; P. Liu; T. N. Snaddon *Angew Chem. Int. Ed.* **2018**, *57*, 7800

Preparation of Nucleophiles:

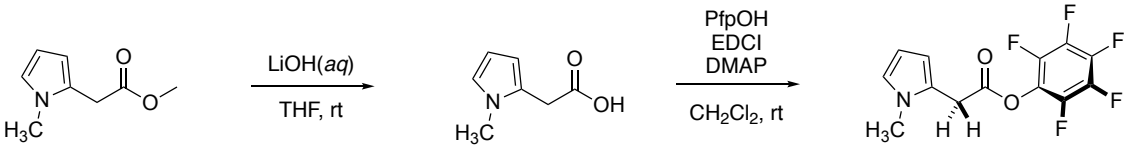
General Procedure A for PfpEster Formation from the Corresponding Carboxylic Acid: The starting pyrrole acetic acid (1.0 equiv) added to a dry RBF equipped with a stir bar and dissolved in dry CH_2Cl_2 (0.5 M). Pentafluorophenol (2.0 equiv), DMAP (20%), and EDCI (2.0 equiv) were added sequentially and the mixture stirred at room temperature for 16 hours. Upon completion by TLC, the mixture was transferred to a separatory funnel and diluted with Et_2O. The organic layer was washed with 1M HCl(*aq*) (2 ×) then saturated Na_2CO_3(*aq*) (3 ×) and dried over $MgSO_4$(*s*). The organic layer was removed under reduced pressure to afford a crude oil that was purified by column chromatography (SiO_2, specified eluent).

General Procedure B for the Hydrolysis of Ethyl and Methyl Esters to Carboxylic Acids: The starting pyrrole acetic acid ester (1.0 equiv) was added to a RBF equipped with stir bar and diluted in THF (0.34 M). 3M LiOH(*aq*) (0.67 M for ester) was then added in a single portion and the mixture stirred rapidly for 1.5 hours. Upon completion by TLC, the reaction was neutralized with 3M HCl(*aq*) (0.67 M for ester) and extracted with Et_2O (3 ×). The organic layer was dried over $MgSO_4$(*s*) and concentrated under reduced pressure to afford the pyrrole acetic acid that was used without further purification.

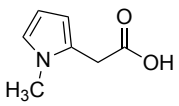
General Procedure C for the Formation of N-Substituted Pyrroles: DMSO (0.5 M) was added to a RBF, equipped with stir bar, containing freshly powdered KOH(*s*) (4.0 equiv). Pyrrole (1.0 equiv) was then added and the mixture stirred at ambient temperature for 30 min. The specified benzyl chloride or benzyl bromide (1.3 equiv) was then added and the mixture placed in an ice bath (*exotherm!*) and stirred for 45 min. The reaction mixture was then poured into a flask containing DI water (200 mL) and extracted with Et_2O (3 ×). The organic layers were combined and washed with 10% LiCl(*aq*) (3 ×) to remove DMSO then dried over $MgSO_4$(*s*). The organic layer was removed under reduced pressure and the crude oil purified by column chromatography (SiO_2, specified eluent).

General Procedure D for the Formation of N-Substituted Pyrrole Acetic Acids from N-Substituted Pyrroles: Oxalyl chloride (1.0 equiv) was added to a dried RBF containing a stir bar, diluted with CH_2Cl_2 (1.1 M) and cooled to –10 °C (ice/NaCl). The N-substituted pyrrole (1.0 equiv) in CH_2Cl_2 (3.3 M) was then added over 20 min by addition funnel (the reaction mixture will gradually darken and become black over the course of the addition). The reaction was stirred at –10 °C for 1 hour at which point 20% KOH(*aq*) was added and the reaction stirred for 30 min at room temperature. After 30 min, the reaction was transferred to a separatory funnel and the layers separated. The organic layer was dried over $MgSO_4$(*s*) and concentrated under reduced pressure to afford a dark oil.

The dark oil from the above reaction (assumed quantitative, 1.0 equiv) was dissolved in 20% KOH(*aq*) (0.6 M) then hydrazine monohydrate (1.7 equiv) was added. The reaction mixture was heated to reflux for 16 hours. Upon completion (TLC, pure EtOAc), the reaction was cooled to ambient temperature, taken to pH 1 with 3M HCl(*aq*), and extracted with EtOAc (3 ×). The organic layer was dried over $MgSO_4$(*s*) and concentrated under reduced pressure to afford the crude pyrrole acetic acid. This was assumed quantitative and taken through General Procedure A without purification.

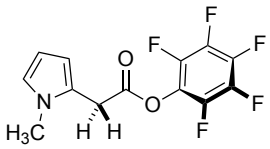


2-(1-methyl-1*H*-pyrrol-2-yl)acetic acid (S21): Prepared according to General Procedure B from the corresponding methyl ester in quantitative yield. Spectral data is consistent with previously reported.[12]



^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.58 (t, *J* = 2.4 Hz, 1H), 6.07 (d, *J* = 3.4 Hz, 1H), 6.05 (d, *J* = 3.4 Hz, 1H), 3.62 (s, 2H), 3.57 (s, 3H)

perfluorophenyl 2-(1-methyl-1*H*-pyrrol-2-yl)acetate (S22): Prepared according to General Procedure A. The title compound was obtained as a yellow solid (5.2 g, 17 mmol, 63% yield) following purification by column chromatography (SiO_2, 50:1 pentane:Et_2O)



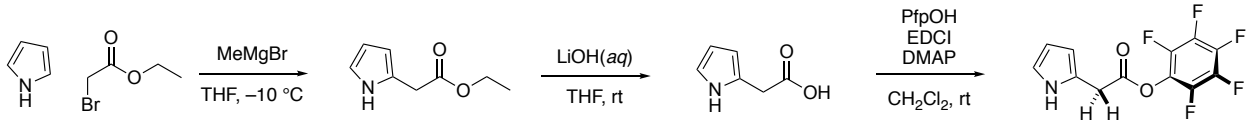
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.66 (dd, *J* = 2.7, 1.8 Hz, 1H), 6.17, (dd, *J* = 3.7, 1.8 Hz, 1H), 6.12 (dd, *J* = 3.7, 2.7 Hz, 1H), 3.99 (s, 2H), 3.63 (s, 3H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.7, 123.3, 122.7, 109.7, 107.4, 77.5, 77.2, 76.8, 33.8, 31.7

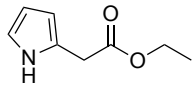
^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.19 – - 153.70 (m), -157.73 (t, *J* = 21.7 Hz), -162.22 (dd, *J* = 21.8, 17.2 Hz)

IR (ATR): 1786, 1514, 1330, 1296, 1228, 1103, 990, 870, 772, 725, 675, 605, 556, 468 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{13}H_9F_5NO_2^+$: 306.0548. Found: 306.0550



ethyl 2-(1*H*-pyrrol-2-yl)acetate (S23): Pyrrole (13.5 mL, 195 mmol, 3.9 equiv) was added to a flame dried, 2-neck, RBF containing a rubber septum and 125 mL dropping funnel under an atmosphere of nitrogen then dissolved in THF (130 mL, 1.5 M). Methylmagnesium chloride (2.5 M in THF, 74 mL, 185 mmol, 3.7 equiv) was transferred to the addition funnel *via* cannula. The system was cooled to –10 °C (ice/NaCl) and the MeMgCl added dropwise to the reaction over 30 min (*gas evolution!*). Once the addition was complete, the reaction was warmed to room temperature and stirred for 30 min more. The reaction was then cooled to 0 °C and ethyl bromoacetate (5.6 mL, 50 mmol, 1.0 equiv) was added in a single portion. The reaction was then warmed to room temperature and stirred for an hour then quenched with saturated $NH_4Cl(aq)$ and extracted with diethyl ether (2 ×). The organic layers were combined and dried over $MgSO_4(s)$ and concentrated under reduced pressure. The title compound



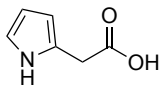
[12] L. A. Reddy; *et. al. Org. Process Res. Dev.*, **2010**, *14*, 362

was obtained by distillation of the crude oil (4.0 g, 26 mmol, 52% yield, b.p. = 85 °C, 1.040 torr) as a clear, colorless oil that darkens rapidly. Spectral data is consistent with previously reported.[13]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.70 (bs, 1 H), 6.75 (m, 1 H), 6.12 – 6.15 (m, 1 H), 6.02 (m, 1 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 3.67 (s, 2 H), 1.28 (t, *J* = 7.2 Hz, 3 H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.3, 123.6, 108.3, 107.3, 61.1, 33.2, 14.2

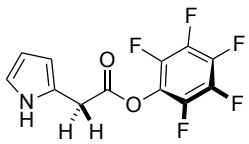
2-(1*H*-pyrrol-2-yl)acetic acid (S24): Prepared according to General Procedure B from the corresponding ethyl ester. The title compound was white solid (980 mg, 7.8 mmol, 81% yield) that darkens rapidly. Spectral data is consistent with previously reported.[14]



^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.91 (bs, 1H), 8.62 (bs, 1H), 6.80 (m, 1H), 6.25 (m, 1H), 6.10 (m, 1H), 3.72 (s, 2H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.2, 122.7, 118.5, 108.9, 108.3, 33.5

perfluorophenyl 2-(1*H*-pyrrol-2-yl)acetate (S25): Prepared according to General Procedure A. The title compound was obtained as a white solid (780 mg, 2.7 mmol, 79%) following purification by column chromatography (9:1 pentane:Et_2O)



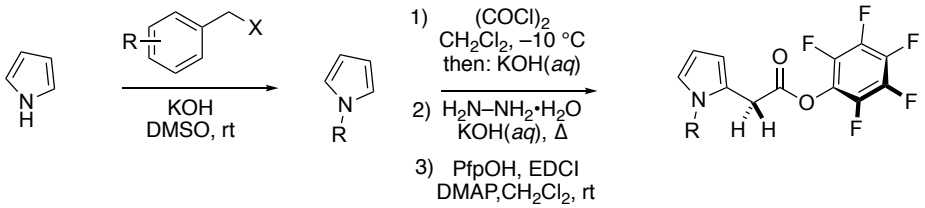
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (bs, 1H), 6.81 (dd, *J* = 2.7, 1.5 Hz, 1H), 6.20 (app q, *J* = 2.9 Hz, 1H), 6.18 – 6.15 (m, 1H), 4.05 (s, 2H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 167.1, 121.0, 118.7, 110.2, 108.9, 108.7, 32.5

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.58 (d, *J* = 17.2 Hz), -157.48 (t, *J* = 21.6 Hz), -162.07 (dd, *J* = 21.7, 17.0 Hz)

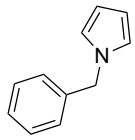
IR (ATR): 3418, 1781, 1518, 1390, 1367, 1213, 1132, 1092, 994, 910, 784, 649, 606, 566, 534 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{12}H_7F_5NO_2^+$: 292.0391. Found: 292.0393



[13] E. Bellur; H. Görls; P. Lander *J. Org. Chem.*, **2005**, *70*, 4751
[14] J. H. Byers; M. P. Duff; G. W. Woo *Tetrahedron Lett.*, **2003**, *44*, 6853

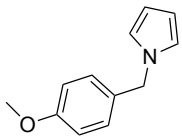
1-benzyl-1*H*-pyrrole (S26): Prepared according to General Procedure C using BnBr. The title compound was obtained as a clear, colorless oil (5.5 g, 35 mmol, 71% yield) following purification by column chromatography (40:1 pentane:Et_2O). Spectral data is consistent with previously reported.[15]



^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39- 7.27 (3H, m), 7.18-7.11 (2H, m), 6.72 (2H, app. t, *J* = 1.6 Hz), 6.22 (2H, app. t, *J* = 1.6 Hz), 5.09 (2H, s)

^{13}C NMR (75 MHz, $CDCl_3$): δ = 138.3, 128.8, 127.8, 127.1, 121.3, 108.6, 53.5

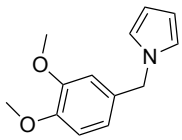
1-(4-methoxybenzyl)-1*H*-pyrrole (S27): Prepared according to General Procedure C using PMBCl. The title compound was obtained as a clear, yellow oil (5.5 g, 29 mmol, 89% yield) after column chromatography (30:1 pentane:Et_2O). Spectral data is consistent with previously reported.[16]



^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.08 (2H, d, *J* = 8.5 Hz), 6.86 (2H, d, *J* = 8.6 Hz), 6.68 (2H, t, *J* = 1.9 Hz), 6.18 (2H, t, *J* = 1.9 Hz), 5.01 (2H, s), 3.80 (3H, s)

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 130.3, 128.6, 121.1, 114.2, 108.5, 55.4, 53.0

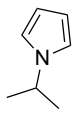
1-(3,4-dimethoxybenzyl)-1*H*-pyrrole (S28): Prepared according to General Procedure C using DMPCl. The title compound was obtained as a clear, yellow oil (5.5 g, 29 mmol, 89% yield) after column chromatography (30:1 pentane:Et_2O). Spectral data is consistent with previously reported.[17]



^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.81 (1H, d, *J* = 8.2 Hz), 6.71 (2H, t, *J* = 2.0 Hz), 6.46 (1H, d, *J* = 2.4 Hz), 6.41 (1H, dd, *J* = 8.3, 2.4 Hz), 6.15 (2H, t, *J* = 2.0 Hz), 5.00 (2H, s), 3.83 (3H, s), 3.79 (3H, s)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.7, 157.9, 129.5, 121.2, 119.3, 108.0, 104.2, 98.6, 55.6, 55.5, 48.0

1-isopropyl-1*H*-pyrrole (S29): Prepared according to General Procedure C using iPrCl. The title compound was obtained as a clear, colorless oil (2.0 g, 18 mmol, 37% yield) following purification by column chromatography (pentane). Spectral data is consistent with previously reported.[18]



^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.73 (2H, t, *J* = 1.7 Hz), 6.15 (2H, t, *J* = 1.7 Hz), 4.25 (1H, sept, *J* = 5.4 Hz), 1.45 (6H, d, *J* = 5.4 Hz)

^{13}C NMR (100 MHz, $CDCl_3$): δ = 118.1, 107.7, 50.7, 24.0

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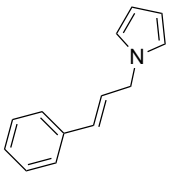
[15] J. E. Taylor; M. D. Jones; J. M. Williams J; S. D. Bull *Org. Lett.*, **2010**, *12*, 5740
[16] See reference 15
[17] See reference 15
[18] S. Nomiyama; T. Tsuchimoto *Adv. Synth. Catal*., **2014**, *356*, 3881

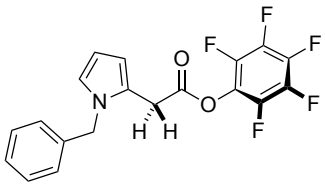
1-cinnamyl-1*H*-pyrrole (S30): Prepared according to General Procedure C using cinnamyl chloride. The title compound was obtained as a clear, yellow oil (6.7 g, 36 mmol, 73% yield) following purification by column chromatography (100:0 then 50:1 pentane:Et_2O). Spectral data is consistent with previously reported.[19]



^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35 (5H, m), 6.76 (2H, t, *J* = 2.0 Hz), 6.54 (1H, d, *J* = 15.7 Hz), 6.38 (1H, dt, *J* = 15.8, 6.2 Hz), 6.24 (2H, t, *J* = 2.0 Hz), 4.70 (2H, d, *J* = 6.1 Hz)

^{13}C NMR (125 MHz, $CDCl_3$): δ = 132.5, 128.7, 127.9, 127.0, 125.5, 120.6, 108.4, 51.6

perfluorophenyl 2-(1-benzyl-1*H*-pyrrol-2-yl)acetate (S31): Prepared according to General Procedure A. From the corresponding carboxylic acid (prepared according to General Procedure D). The product was obtained as a yellow solid (2.0 g, 5.2 mmol, 27% yield (3 steps)) following purification by column chromatography (9:1 pentane:Et_2O).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.4 – 7.3 (m, 3H), 7.1 – 7.0 (m, 2H), 6.8 (dd, *J* = 2.9, 1.7 Hz, 1H), 6.3 (dd, *J* = 3.6, 1.8 Hz, 1H), 6.2 – 6.2 (m, 1H), 5.1 (s, 2H), 3.8 (s, 2H)

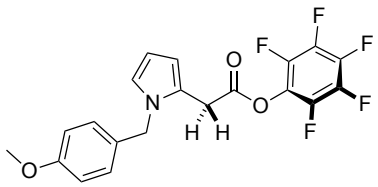
^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.7, 137.7, 129.0, 127.8, 126.6, 126.6, 123.3, 122.6, 110.5, 107.9, 51.0, 31.7

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.56 – -152.91 (m), -157.82 (tdd, *J* = 21.8, 10.0, 4.7 Hz), -162.35 (tdt, *J* = 18.7, 9.0, 5.1 Hz)

IR (ATR): 2924, 1786, 1518, 1453, 1298, 1217, 1145, 1089, 995, 714 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{19}H_{13}F_5NO_2^+$: 382.0861. Found: 382.0866

perfluorophenyl 2-(1-(4-methoxybenzyl)-1*H*-pyrrol-2-yl)acetate (S32): Prepared according to General Procedure A. From the corresponding carboxylic acid (prepared according to General Procedure D). The product was obtained as a clear, orange oil (4.6 g, 11 mmol, 40% yield (3 steps)) following purification by column chromatography (9:1 pentane:Et_2O).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.1 – 7.0 (m, 2H), 6.9 – 6.8 (m, 2H), 6.7 (dd, *J* = 2.8, 1.8 Hz, 1H), 6.3 (dd, *J* = 3.6, 1.8 Hz, 1H), 6.2 (dd, *J* = 3.6, 2.8 Hz, 1H), 5.1 (s, 2H), 3.9 (s, 2H), 3.8 (s, 3H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.7, 159.3, 129.5, 128.0, 123.2, 122.5, 114.4, 110.5, 107.7, 55.3, 50.5, 31.7

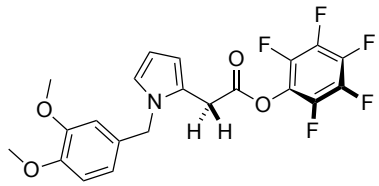
[19] N. K. Pahadi, M. Paley, R. Jana, S. R. Waetzig, J. A. Tunge *J. Am. Chem. Soc.*, **2009**, *131*, 16626

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.57 – -152.81 (m), -157.91 (td, *J* = 21.8, 4.4 Hz), -162.12 – -162.68 (m)

IR (ATR): 2938, 2839, 2668, 1784, 1587, 1514, 1292, 1246, 1087, 993, 823, 715 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{20}H_{15}F_5NO_3^+$: 412.0967. Found: 412.0971

perfluorophenyl 2-(1-(3,4-dimethoxybenzyl)-1*H*-pyrrol-2-yl)acetate (S33): Prepared according to General Procedure A. From the corresponding carboxylic acid (prepared according to General Procedure D). The product was obtained as an off white solid (2.3 g, 4.5 mmol, 41% yield (3 steps)) following purification by column chromatography (5:1 pentane:Et_2O).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.8 (d, *J* = 8.1 Hz, 1H), 6.7 (t, *J* = 2.3 Hz, 1H), 6.7 – 6.5 (m, 2H), 6.2 (dd, *J* = 3.6, 1.7 Hz, 1H), 6.2 (t, *J* = 3.2 Hz, 1H), 5.0 (s, 2H), 3.9 (d, *J* = 4.3 Hz, 5H), 3.8 (s, 3H)

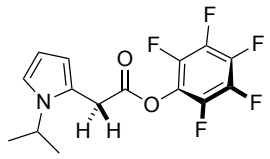
^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.8, 149.5, 148.7, 130.0, 123.2, 122.6, 119.0, 111.4, 110.6, 109.9, 107.8, 56.0, 55.9, 50.8, 31.7

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.55 – -152.91 (m), -157.72 (t, *J* = 21.7 Hz), -162.02 – -162.59 (m)

IR (ATR): 2940, 2838, 1786, 1593, 1518, 1467, 1260, 1238, 1140, 1090, 996, 716 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{21}H_{17}F_5NO_4^+$: 442.1072. Found: 442.1073

perfluorophenyl 2-(1-isopropyl-1*H*-pyrrol-2-yl)acetate (S34): Prepared according to General Procedure A. From the corresponding carboxylic acid (prepared according to General Procedure D). The product was obtained as a clear, orange oil (3.7 g, 11 mmol, 61% yield (3 steps)) following purification by column chromatography (30:1 pentane:Et_2O).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.91 – 6.85 (m, 1H), 6.32 – 6.22 (m, 1H), 6.22 – 6.15 (m, 1H), 4.51 – 4.23 (m, 1H), 4.11 (s, 2H), 1.56 (d, *J* = 6.7 Hz, 6H)

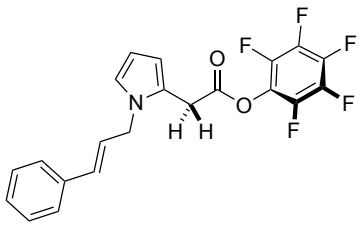
^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.8, 121.5, 117.3, 109.2, 107.9, 47.6, 31.7, 23.9

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.76 – -153.22 (m), -158.07 (tt, *J* = 21.6, 4.3 Hz), -162.42 (ddt, *J* = 26.6, 21.9, 5.7 Hz)

IR (ATR): 2981, 2939, 2669, 1785, 1516, 1470, 1281, 1135, 1082, 992, 709 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{15}H_{13}F_5NO_2^+$: 334.0861. Found: 334.0865

perfluorophenyl 2-(1-cinnamyl-1*H*-pyrrol-2-yl)acetate (S35): Prepared according to General Procedure A. From the corresponding carboxylic acid (prepared according to General Procedure D). The product was obtained as a light yellow solid (3.1 g, 7.7 mmol, 21% yield (3 steps)) following recrystallization (CH_2Cl_2/pentane).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 – 7.31 (m, 5H), 6.81 (dd, *J* = 2.9, 1.8 Hz, 1H), 6.45 (d, *J* = 15.7 Hz, 1H), 6.32 (dt, *J* = 15.9, 5.3 Hz, 1H), 6.25 (dd, *J* = 3.7, 1.8 Hz, 1H), 6.27 (t, *J* = 3.2 Hz, 1H), 4.77 (dd, *J* = 5.3, 1.3 Hz, 2H), 4.05 (s, 2H)

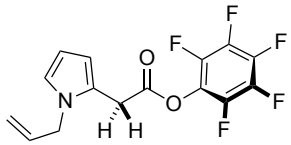
^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.7, 136.2, 132.4, 128.7, 128.1, 126.6, 125.2, 122.6, 122.5, 110.4, 107.9, 49.3, 31.8

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.28 – -152.92 (m), -157.84 (t, *J* = 21.7 Hz), -161.82 – -162.71 (m)

IR (ATR): 3028, 2917, 2668, 1785, 1519, 1214, 1089, 996, 714 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{21}H_{15}F_5NO_2^+$: 408.1017. Found: 408.1021

perfluorophenyl 2-(1-allyl-1*H*-pyrrol-2-yl)acetate (S36): Prepared according to General Procedure A. From the corresponding carboxylic acid (prepared according to General Procedure D). The product was obtained as an orange oil (1.2 g, 3.6 mmol, 12% yield (3 steps)) following purification by column chromatrography (SiO_2, 50:1 pentane:Et_2O).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.73 – 6.69 (m, 1H), 6.23 (dd, *J* = 3.7, 1.6 Hz, 1H), 6.20 – 6.17 (m, 1H), 5.99 (ddtd, *J* = 16.7, 10.3, 5.2, 1.4 Hz, 1H), 5.24 (dt, *J* = 10.3, 1.4 Hz, 1H), 5.04 (dt, *J* = 16.7, 1.4 Hz, 1H), 4.57 – 4.52 (m, 2H), 4.00 (s, 2H)

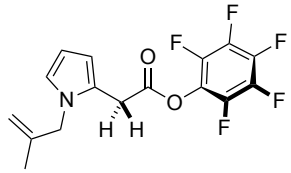
^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.7, 134.1, 122.5, 122.4, 117.2, 110.1, 107.8, 49.7, 31.6

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.76 (d, *J* = 18.1 Hz), -157.95 (td, *J* = 21.8, 5.2 Hz), -162.40 (dd, *J* = 21.8, 18.1 Hz)

IR (ATR): 2460, 1785, 1645, 1516, 1285, 1215, 1145, 1086, 991, 928, 712, 605, 551, 447 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{15}H_{11}F_5NO_2^+$: 332.0704. Found: 332.07

perfluorophenyl 2-(1-(2-methylallyl)-1*H*-pyrrol-2-yl)acetate (S37): Prepared according to General Procedure A. From the corresponding carboxylic acid (prepared according to General Procedure D). The product was obtained as a light yellow solid (1.6 g, 4.6 mmol, 10% yield (3 steps)) following purification by column chromatrography (SiO_2, 50:1 pentane:Et_2O).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.68 (dd, *J* = 2.8, 1.8 Hz, 1H), 6.21 (dd, *J* = 3.6, 1.7 Hz, 1H), 6.16 (app. t, *J* = 3.2, 1H), 4.93 (s, 1H), 4.61 (s, 1H), 4.43 (s, 2H), 3.96 (s, 2H), 1.72 (s, 3H)

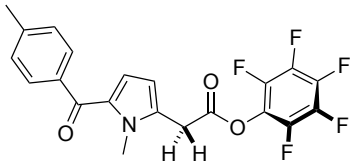
^{13}C NMR (101 MHz, $CDCl_3$): δ = 166.8, 141.8, 123.1, 122.6, 112.4, 110.2, 107.6, 53.3, 31.6, 19.8

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.48 – -152.85 (m), -157.68 – -158.19 (m), -162.05 – -162.65 (m)

IR (ATR): 1786, 1656, 1516, 1299, 1215, 1145, 1086, 993, 901, 712, 604, 551, 466 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{16}H_{13}F_5NO_2^+$: 346.0861. Found: 346.0863

perfluorophenyl 2-(1-methyl-5-(4-methylbenzoyl)-1*H*-pyrrol-2-yl)acetate (S38): Prepared according to General Procedure A. From the corresponding Tolmetin. The product was obtained as a light yellow solid (560 mg, 1.1 mmol, 65% yield) following purification by columun chromatography (SiO_2, 20:1 pentane:Et_2O).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 7.9, 3H), 6.71 (d, *J* = 4.1 Hz, 1H), 6.23 (d, *J* = 4.1 Hz, 1H), 4.08 (s, 2H), 4.00 (s, 3H), 2.43 (s, 3H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.2, 165.6, 142.3, 137.2, 132.1, 132.0, 129.6, 128.9, 122.2, 110.1, 33.3, 32.0, 21.7

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.60 (d, *J* = 17.3 Hz), –157.17 (t, *J* = 21.7 Hz), -161.86 (dd, *J* = 21.7, 17.3 Hz)

IR (ATR): 1788, 1626, 1519, 1483, 1456, 1376, 1264, 1093, 998, 883, 749 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{21}H_{15}F_5NO_2^+$: 424.0967. Found: 424.0970

Preparation of Products

General Procedure A:

$Pd(PTh_3)_3$ (3.8 mg, 2 mol%, 0.004 mmol), (*R*)-benzotetramisole (10 mg, 0.04 mmol, 20 mol%), N-methyl pyrrole pentafluorophenyl ester (118 mg, 0.36 mmol, 1.8 equiv), and the specified tosylate (0.20 mmol, 1 equiv) were added sequentially to an oven-dried 2-dram vial containing a magnetic stir bar and equipped with a Teflon insert screw cap. The vial was evacuated and backfilled with nitrogen (3 ×) then cooled to 0 °C. Anhydrous THF (2 mL, 0.1 M) was then added followed by *i*Pr$_2$NEt (44 µL, 0.25 mmol, 1.2 equiv). The reaction mixture was stirred at 0 °C for 24 hours and then diluted with 2.5 mL of petroleum ether (precipitation will occur) and passed through activated acidic Al_2O_3 (Brockmann I). The vial was washed with Et_2O (2.5 mL) and passed through the Al_2O_3. The alumina was then washed with Et_2O. The combined filtrates were concentrated and purified by column chromatography (SiO_2, specified eluent).

General Procedure B:

XantPhos PdG3 (9.5 mg, 5 mol%, 0.01 mmol), (*R*)-benzotetramisole (10 mg, 0.04 mmol, 20 mol%) and the specified pentafluorophenyl ester (0.20 mmol, 1 equiv) were added sequentially to an oven-dried 2-dram vial containing a magnetic stir bar and equipped with a Teflon insert screw cap. The vial was evacuated and backfilled with nitrogen (3 ×). Anhydrous THF (2 mL, 0.1 M) was then added followed by the specified electrophile (0.25 mmol, 1.25 equiv) and *i*Pr$_2$NEt (44 µL, 0.25 mmol, 1.2 equiv). The reaction mixture was stirred at room temperature for 24 hours and then diluted with 2.5 mL of petroleum ether (precipitation will occur) and passed through activated acidic Al_2O_3 (Brockmann I). The vial was washed with Et_2O (2.5 mL) and passed through the Al_2O_3. The alumina was then washed with Et_2O. The combined filtrates were concentrated and purified by column chromatography (SiO_2, specified eluent).

General Procedure C:

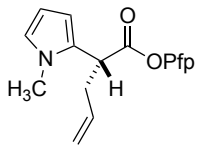
XantPhos PdG3 (9.5 mg, 5 mol%, 0.01 mmol), (*R*)-benzotetramisole (10 mg, 0.04 mmol, 20 mol%) and the specified pentafluorophenyl ester (0.25 mmol, 1.25 equiv) were added sequentially to an oven-dried 2-dram vial containing a magnetic stir bar and equipped with a Teflon insert screw cap. The vial was evacuated and backfilled with nitrogen (3 ×). Anhydrous THF (2 mL, 0.1 M) was then added followed by the specified tosylate (0.20 mmol, 1.00 equiv). The reaction mixture was cooled to 0 °C (cryocooler) and stirred for 20 mintures. *i*Pr$_2$NEt (44 µL, 0.25 mmol, 1.25 equiv) was then added. The temperature for 24 hours and then diluted with 2.5 mL of petroleum ether (precipitation will occur) and passed through activated acidic Al_2O_3 (Brockmann I). The vial was washed with Et_2O (2.5 mL) and passed through the Al_2O_3. The alumina was then washed with Et_2O. The combined filtrates were concentrated and purified by column chromatography (SiO_2, specified eluent).

General Procedure D:

$Pd(PTh_3)_3$ (3.8 mg, 2.5 mol%, 0.0050 mmol), (*R*)-benzotetramisole (10 mg, 0.040 mmol, 20 mol%), N-methyl pyrrole pentafluorophenyl ester (61 mg, 0.2 mmol, 1.0 equiv), and the specified

electrophoile (0.25 mmol, 1.3 equiv) were added sequentially to an oven-dried 2-dram vial containing a magnetic stir bar and equipped with a Teflon insert screw cap. The vial was evacuated and backfilled with nitrogen (3 ×) then cooled to 0 °C. Anhydrous 1,4-Dioxane (2 mL, 0.1 M) was then added followed by *i*Pr_2NEt (44 µL, 0.25 mmol, 1.2 equiv). The reaction mixture was stirred at 0 °C for 24 hours and then diluted with 2.5 mL of petroleum ether (precipitation will occur) and passed through activated acidic Al_2O_3 (Brockmann I). The vial was washed with Et_2O (2.5 mL) and passed through the Al_2O_3. The alumina was then washed with Et_2O. The combined filtrates were concentrated and purified by column chromatography (SiO_2, specified eluent).

perfluorophenyl (*R*)-2-(1-methyl-1*H*-pyrrol-2-yl)pent-4-enoate (17): Prepared according to general procedure B with **S1** as the electrophile. The title compound was obtained as a colorless oil (56 mg, 0.16 mmol, 81%) following purification by column (SiO_2: 50:1 pentane:Et_2O). The enantiomeric ratio (98:2) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -23.2$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.64 (dd, J = 2.8, 1.8 Hz, 1H), 6.20 (dd, *J* = 3.8, 1.8 Hz, 1H), 6.15 (dd, *J* = 3.8, 2.8 Hz, 1H), 5.95 – 5.79 (m, 1H), 5.23 (dd, *J* = 17.1, 1.6 Hz, 1H), 5.15 (dd, *J* = 10.2, 1.6 Hz, 1H), 4.04 (dd, *J* = 8.9, 6.4 Hz, 1H), 3.66 (s, 3H), 3.04 – 2.91 (m, 1H), 2.81 – 2.71 (m, 1H)

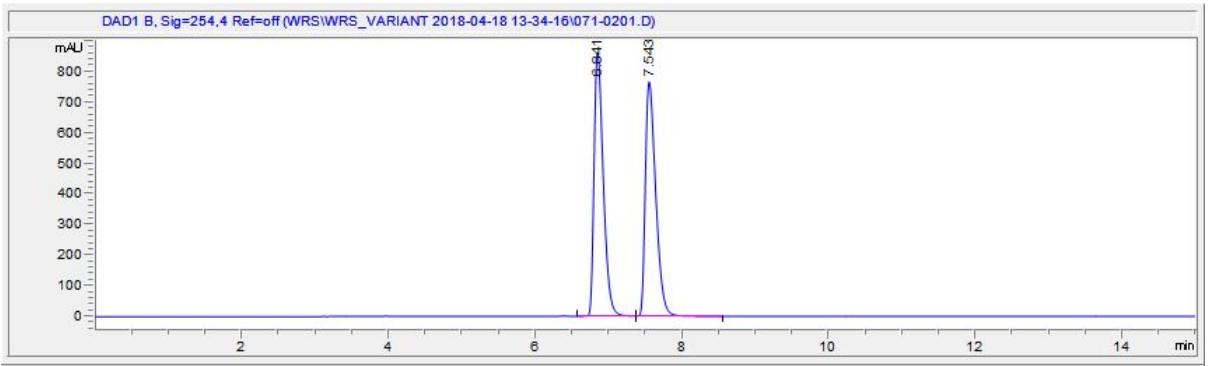
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 134.1, 127.4, 123.2, 118.3, 107.9, 107.6, 43.1, 36.1, 34.0

^{19}F NMR (376 MHz, $CDCl_3$): δ = -151.95 – -152.93 (m), -157.91 (t, *J* = 21.6 Hz), -162.37 (dd, *J* = 21.8, 17.3 Hz)

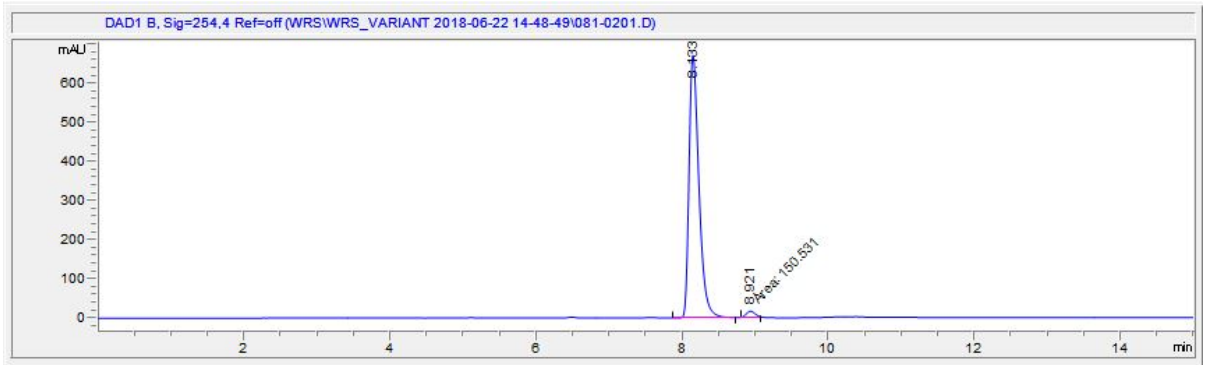
IR (ATR): 1783, 1520, 1089, 1004, 715 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{16}H_{13}F_5NO_2^+$: 346.0681. Found: 346.0684

HPLC analysis using chiral column (ChiralPak IA-3, 5µ column, 22 °C, 1.0 mL/min, 200:1 Hexanes:IPA, 254 nm, t_{major}: 8.1 min, t_{minor}: 8.6 min)

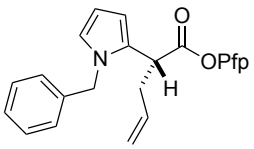


#	Time	Area	Height	Width	Area%	Symmetry
1	6.841	7494.8	858.6	0.1358	50.022	0.588
2	7.543	7488.3	762.1	0.1506	49.978	0.554



#	Time	Area	Height	Width	Area%	Symmetry
1	8.133	6309	671.7	0.1436	97.670	0.607
2	8.921	150.5	16.8	0.1496	2.330	0.822

perfluorophenyl (*R*)-2-(1-benzyl-1*H*-pyrrol-2-yl)pent-4-enoate (19): Prepared according to general procedure B with **S1** as the electrophile. The title compound was obtained as a yellow oil (69 mg, 0.16 mmol, 82%) following purification by column (SiO_2: 50:1 pentane:Et_2O). The enantiomeric ratio (97:3) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -71.8$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.23 (m, 3H), 7.12 – 7.06 (m, 2H), 6.74 (dd, *J* = 2.8, 1.7 Hz, 1H), 6.36 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.21 (t, *J* = 3.2 Hz, 1H), 5.73 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.32 – 5.08 (m, 4H), 3.91 (dd, *J* = 8.7, 6.5 Hz, 1H), 2.92 – 2.81 (m, 1H), 2.67 (dtt, *J* = 14.4, 6.5, 1.4 Hz, 1H)

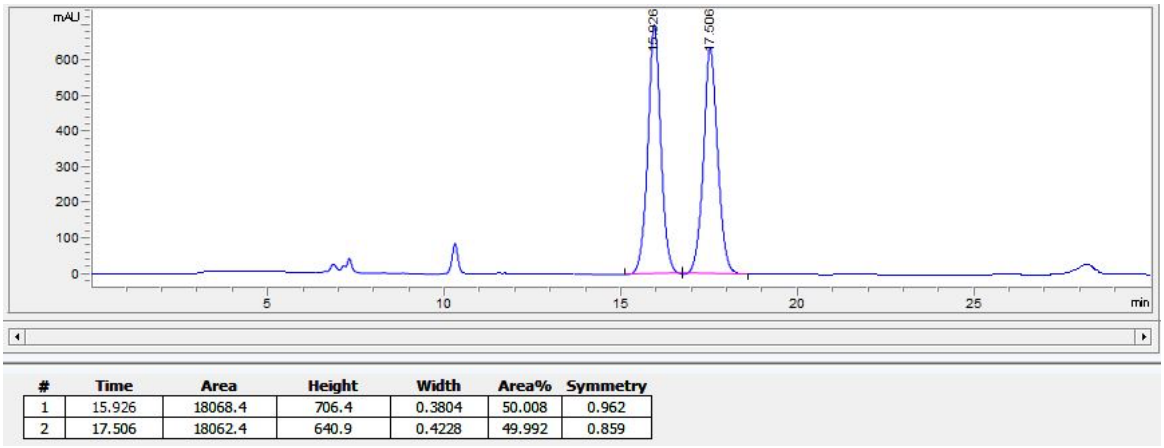
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.5, 137.9, 134.1, 129.0, 127.8, 127.4, 126.5, 123.1, 118.2, 108.6, 108.1, 50.8, 42.8, 36.5, 27.2

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.25 – -152.42 (m), -158.01 (t, *J* = 21.7 Hz), -162.44 (td, *J* = 21.7, 4.5 Hz)

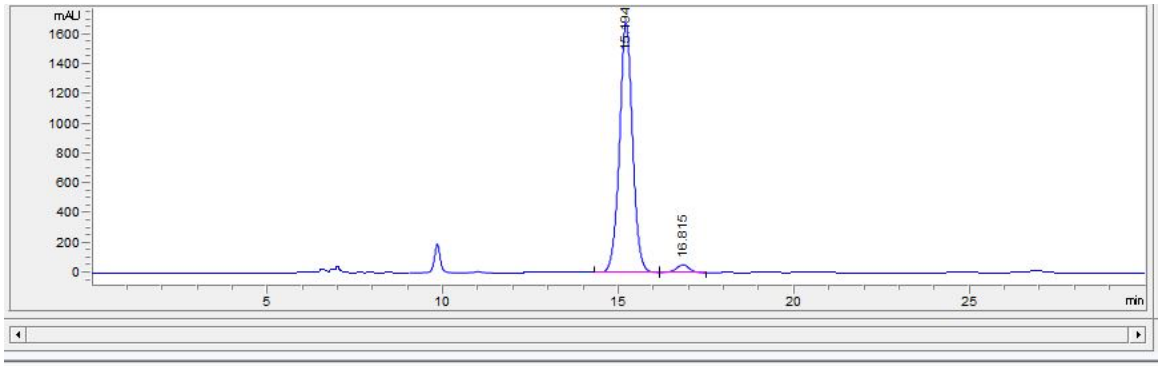
IR (ATR): 1784, 1520, 1297, 1705, 994, 717 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{22}H_{17}F_5NO_2^+$: 422.1176. Found: 422.1177

HPLC analysis using chiral column (ChiralPak IB, 5µ column, 22 °C, 1.0 mL/min, 200:1 Hexanes:IPA, 210 nm, t_{major}: 15.2 min, t_{minor}: 16.8 min)

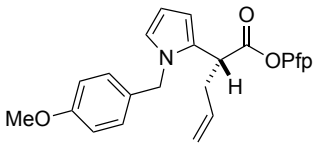


#	Time	Area	Height	Width	Area%	Symmetry
1	15.926	18068.4	706.4	0.3804	50.008	0.962
2	17.506	18062.4	640.9	0.4228	49.992	0.859



#	Time	Area	Height	Width	Area%	Symmetry
1	15.194	43693.2	1685.9	0.3924	96.924	0.942
2	16.815	1386.7	53.7	0.3931	3.076	1.044

perfluorophenyl (*R*)-2-(1-(4-methoxybenzyl)-1*H*-pyrrol-2-yl)pent-4-enoate (20): Prepared according to general procedure B with **S1** as the electrophile. The title compound was obtained as a yellow oil (76 mg, 0.17 mmol, 84%) following purification by column (SiO_2: 40:1 then 20:1 pentane:Et_2O). The enantiomeric ratio (98:2) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -70.5$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 8.3 Hz, 2H), 6.72 (dd, *J* = 2.8, 1.7 Hz, 1H), 6.32 (dd, *J* = 3.7, 1.8 Hz, 1H), 6.22 (t, *J* = 3.2 Hz, 1H), 5.72 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 3.97 (dd, *J* = 8.8, 6.5 Hz, 1H), 3.81 (s, 3H), 2.92 – 2.87 (m, 1H), 2.72 – 2.51 (m, 1H)

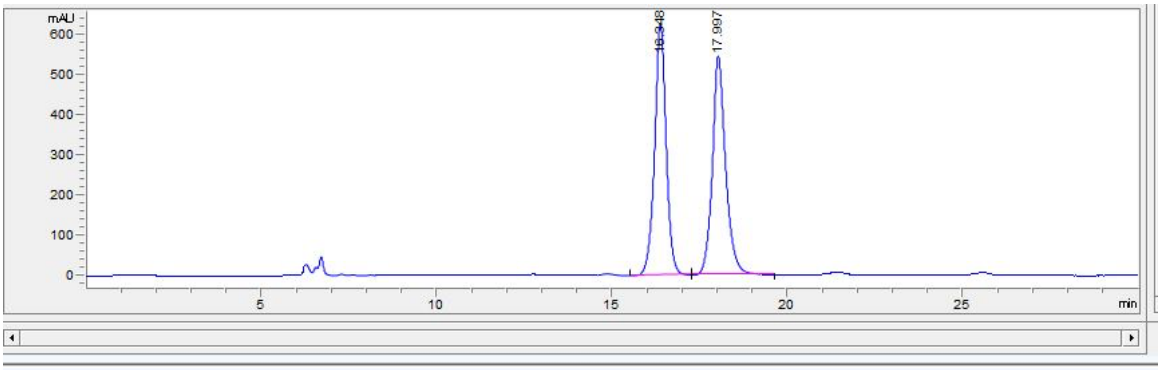
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 159.3, 134.1, 129.7, 127.9, 127.3, 122.9, 118.1, 114.3, 108.5, 108.0, 55.4, 50.3, 42.8, 36.5

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.18 – -152.42 (m), -158.03 (t, *J* = 21.7 Hz), -162.362 – 162.76 (m)

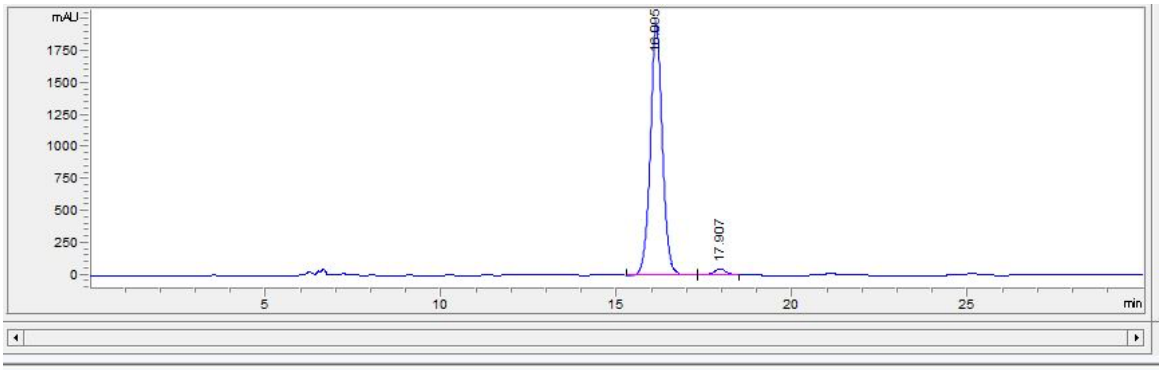
IR (ATR): 2931, 2839, 2668, 2458, 1781, 1613, 1515, 1292, 1247, 1075, 991, 923, 821, 714 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{23}H_{19}F_5NO_3^+$: 452.1280. Found: 452.1281

HPLC analysis using chiral column (ChiralPak IB, 5µ column, 22 °C, 1.0 mL/min, 200:1 Hexanes:IPA, 210 nm, t_{major}: 16.1 min, t_{minor}: 17.9 min)

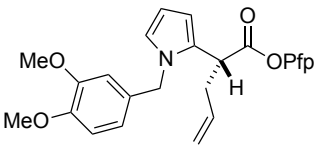


#	Time	Area	Height	Width	Area%	Symmetry
1	16.348	14311.1	627.5	0.3401	49.964	0.987
2	17.997	14331.5	546	0.3802	50.036	0.755



#	Time	Area	Height	Width	Area%	Symmetry
1	16.095	46978.1	1975.8	0.3574	97.678	0.91
2	17.907	1116.8	46.3	0.3595	2.322	0.944

perfluorophenyl (*R*)-2-(1-(3,4-dimethoxybenzyl)-1*H*-pyrrol-2-yl)pent-4-enoate (21): Prepared according to general procedure B with **S1** as the electrophile. The title compound was obtained as a yellow oil (80 mg, 0.17 mmol, 88%) following purification by column (SiO_2: 20:1 then 5:1 pentane:Et_2O). The enantiomeric ratio (97:3) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -65.8$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.82 (d, *J* = 8.2 Hz, 1H), 6.85 – 6.78 (m, 1H), 6.61 (dd, *J* = 8.2, 2.0 Hz, 1H), 6.52 (d, *J* = 2.0 Hz, 1H), 6.35 (dd, *J* = 3.7, 1.8 Hz, 1H), 6.28 (t, *J* = 3.2 Hz, 1H), 5.82 – 5.67 (m, 1H), 5.21 – 5.02 (m, 4H), 3.96 (dd, *J* = 8.7, 6.6 Hz, 1H), 3.92 (s, 3H), 3.81 (s, 3H), 2.92 – 2.86 (m, 1H), 2.71 – 2.52 (m, 1H)

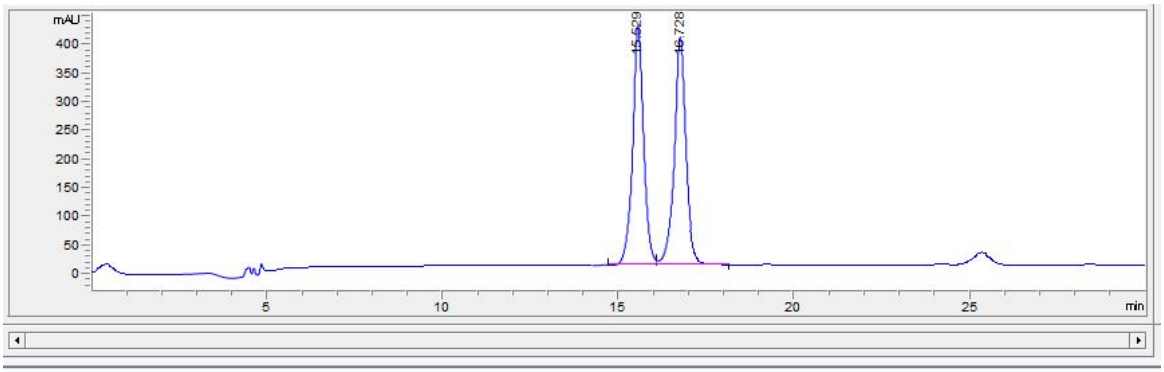
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.5, 149.5, 148.6, 134.1, 130.2, 127.3, 122.9, 118.9, 118.1, 111.3, 109.7, 108.5, 108.0, 56.0, 55.8, 50.5, 42.8, 36.4

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.26 – -152.62 (m), -158.05 (t, *J* = 21.7 Hz), -162.23 – -162.73 (m)

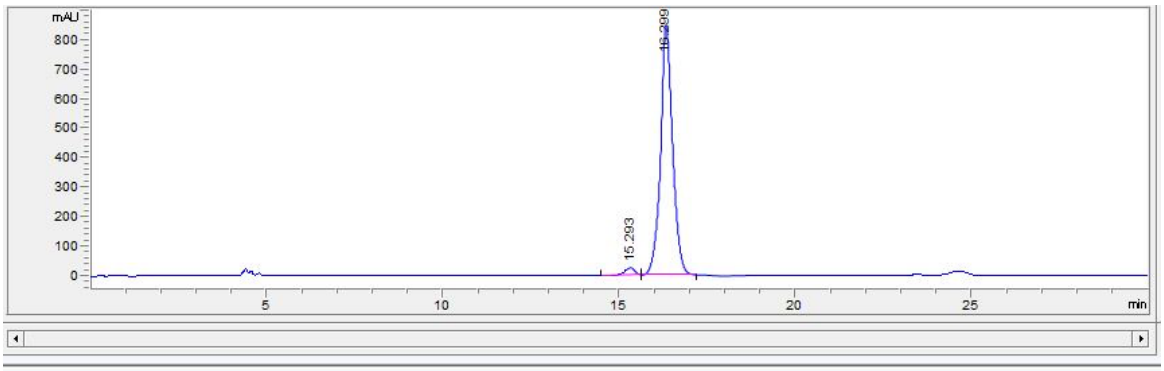
IR (ATR): 2936, 2838, 1781, 1593, 1516, 1466, 1419, 1260, 1237, 1139, 1075, 1025, 991, 919, 855, 713 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{24}H_{21}F_5NO_4^+$: 482.1385. Found: 482.1382

HPLC analysis using chiral column (ChiralPak IB, 5μ column, 22 °C, 1.5 mL/min, 99:1 Hexanes:IPA, 210 nm, t_{minor}: 15.3 min, t_{major}: 16.3 min)

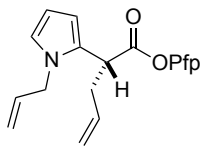


#	Time	Area	Height	Width	Area%	Symmetry
1	15.529	9118.4	418.2	0.3204	49.589	0.928
2	16.728	9269.5	397	0.3424	50.411	0.96



#	Time	Area	Height	Width	Area%	Symmetry
1	15.293	558.8	27.4	0.3063	2.684	1.244
2	16.299	20257.3	855.8	0.3462	97.316	0.818

perfluorophenyl (*R*)-2-(1-allyl-1*H*-pyrrol-2-yl)pent-4-enoate (22): Prepared according to general procedure B with **S1** as the electrophile. The title compound was obtained as a yellow oil (65 mg, 89%) following purification by column (SiO_2: 50:1 pentane:Et_2O). The enantiomeric ratio (98:2) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -62.6$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.64 (dd, *J* = 2.8, 1.8 Hz, 1H), 6.22 (dd, *J* = 3.8, 1.8 Hz, 1H), 6.16 (app. t, *J* = 3.3 Hz, 1H), 5.94 (ddt, *J* = 17.1, 10.2, 5.0 Hz, 1H), 5.83 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.21 (dd, *J* = 5.6, 1.5 Hz, 1H), 5.17 (d, *J* = 1.6 Hz, 1H), 5.12 (dd, *J* = 10.2, 1.4, 1H), 4.96 (dd, *J* = 17.1, 1.5 Hz, 1H), 4.64 – 4.47 (m, 2H), 3.99 (dd, *J* = 8.9, 6.4 Hz, 1H), 2.93 (dddd, *J* = 14.4, 8.6, 7.2, 1.2 Hz, 1H), 2.75 – 2.65 (m, 1H)

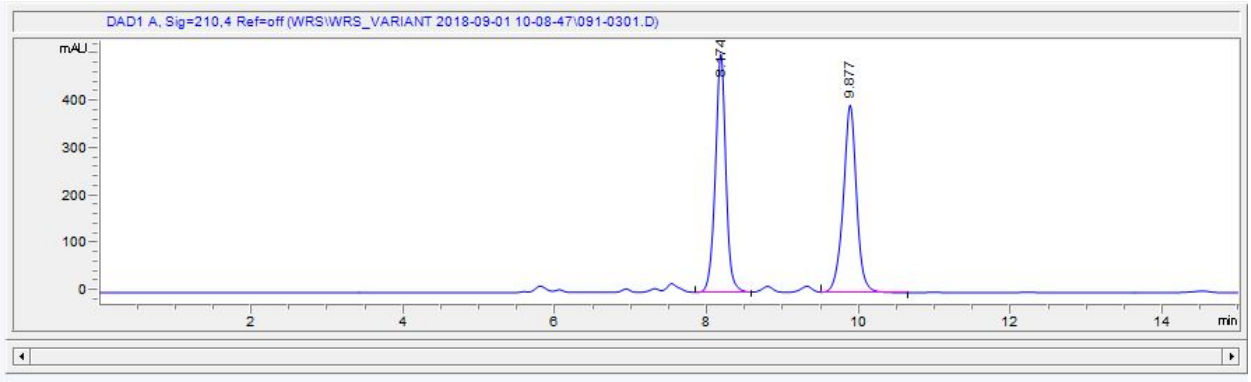
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 134.2, 127.2, 122.3, 118.2, 117.2, 108.2, 108.0, 49.4, 42.8, 36.6

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.32 (d, *J* = 17.3 Hz), -158.00 (t, *J* = 21.6 Hz), -162.43 (dd, *J* = 21.6, 17.3 Hz)

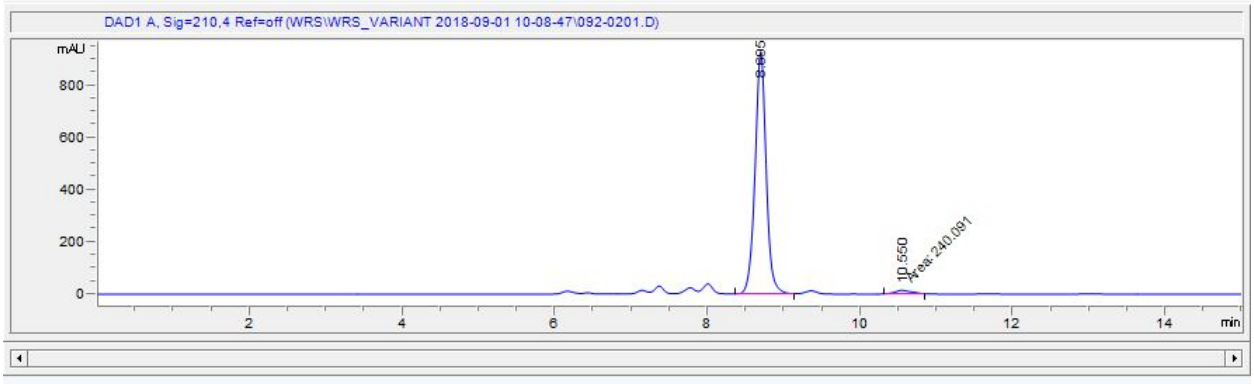
IR (ATR): 1781, 1644, 1516, 1478, 1284, 1143, 1077, 988, 923, 713, 615 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{18}H_{15}F_5NO_2^+$: 372.1017. Found: 372.1022

HPLC analysis using chiral column (ChiralPak IB, 5μ column, 22 °C, 1.0 mL/min, 200:1 Hexanes:IPA, 210 nm, t_{major}: 8.7 min, t_{minor}: 10.6 min)

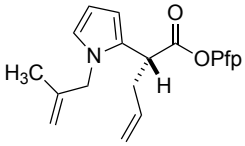


#	Time	Area	Height	Width	Area%	Symmetry
1	8.174	4857.7	505.6	0.1441	50.131	1.022
2	9.877	4832.4	397.5	0.1798	49.869	1.04



#	Time	Area	Height	Width	Area%	Symmetry
1	8.695	9362.6	922	0.1545	97.500	0.984
2	10.55	240.1	14.8	0.2707	2.500	0.769

perfluorophenyl (*R*)-2-(1-allyl-1*H*-pyrrol-2-yl)pent-4-enoate (23): Prepared according to general procedure B with **S1** as the electrophile. The title compound was obtained as a yellow oil (69 mg, 90%) following purification by column (SiO_2: 50:1 pentane:Et_2O). The enantiomeric ratio (98:2) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -56.9$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.64 (dd, *J* = 2.8, 1.8 Hz, 1H), 6.23 (dd, *J* = 3.7, 1.7 Hz, 1H), 6.21 – 6.13 (m, 1H), 5.84 (ddt, *J* = 17.1, 10.2, 6.8 Hz, 1H), 5.20 (dt, *J* = 17.1, 1.5 Hz, 1H), 5.13 (dd, *J* = 10.2, 1.4 Hz, 1H), 4.91 (s, 1H), 4.56 (s, 1H), 4.52 (d, *J* = 16.8 Hz, 1H), 4.41 (d, *J* = 16.7 Hz, 1H), 3.99 (dd, *J* = 8.7, 6.5 Hz, 1H), 2.99 – 2.88 (m, 1H), 2.76 – 2.66 (m, 1H), 1.71 (s, 3H)

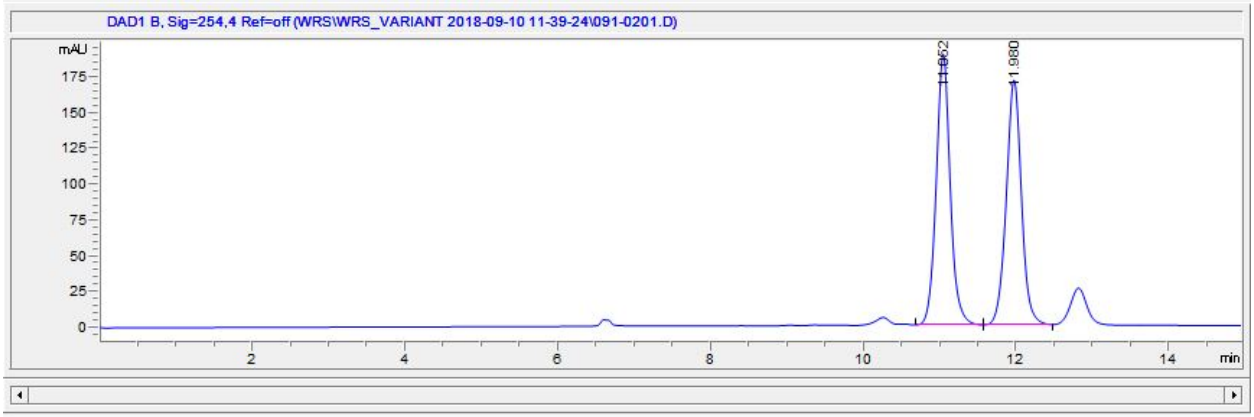
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.7, 141.9, 134.3, 127.4, 122.9, 118.2, 112.3, 108.2, 107.8, 53.0, 42.7, 36.6, 19.9

^{19}F NMR (376 MHz, $CDCl_3$): δ = -150.89 – -153.62 (m), -158.07 (t, *J* = 21.7 Hz), -162.47 (dd, *J* = 21.8, 17.2 Hz)

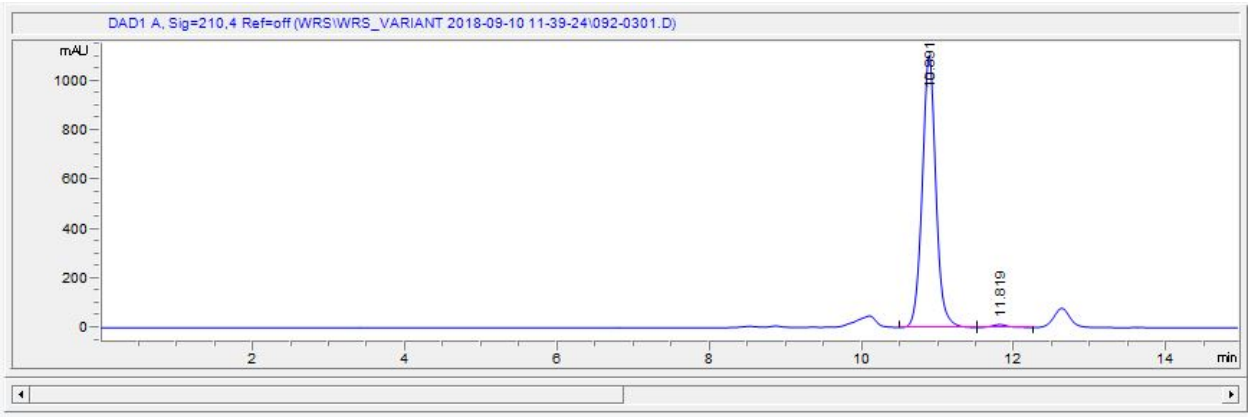
IR (ATR): 2923, 1783, 1642, 1517, 1479, 1445, 1298, 1142, 1076, 992, 904, 714, 615 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{19}H_{17}F_5NO_2^+$: 386.1174. Found: 386.1178

HPLC analysis using chiral column (ChiralPak IB, 5µ column, 22 °C, 1.0 mL/min, 200:1 Hexanes:IPA, 210 nm, t_{major}: 10.9 min, t_{minor}: 11.8 min)

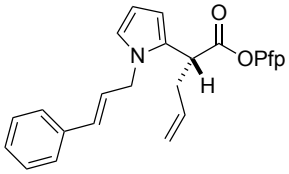


#	Time	Area	Height	Width	Area%	Symmetry
1	11.052	2412	188.5	0.1933	50.537	0.945
2	11.98	2360.7	170.4	0.2096	49.463	0.999



#	Time	Area	Height	Width	Area%	Symmetry
1	10.891	13698.1	1098.2	0.1895	98.654	0.955
2	11.819	186.8	12.2	0.2273	1.346	0.827

perfluorophenyl (*R*)-2-(1-cinnamyl-1*H*-pyrrol-2-yl)pent-4-enoate (24): Prepared according to general procedure B with **S1** as the electrophile. The title compound was obtained as a yellow oil (74 mg, 0.17 mmol, 83%) following purification by column (SiO_2: 40:1 pentane:Et_2O). The enantiomeric ratio (98:2) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -75.4$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (ddd, *J* = 23.6, 8.8, 6.8 Hz, 5H), 6.74 (dd, *J* = 2.8, 1.7 Hz, 1H), 6.32 – 6.16 (m, 4H), 5.84 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.22 – 5.01 (m, 2H), 4.87 – 4.52 (m, 2H), 4.07 (dd, *J* = 8.7, 6.6 Hz, 1H), 3.01 – 2.85 (m, 1H), 2.87 – 2.62 (m, 1H)

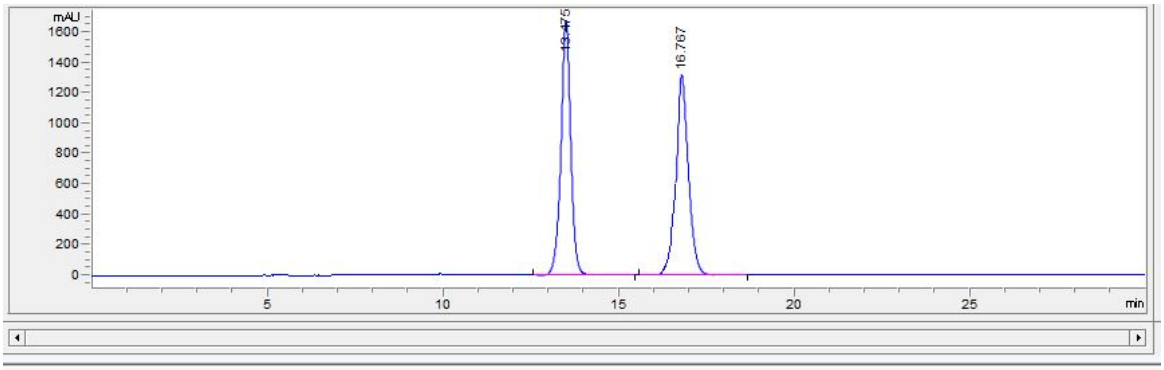
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 136.2, 134.2, 132.3, 128.7, 128.0, 127.2, 126.5, 125.4, 122.3, 118.3, 108.3, 108.1, 48.9, 42.9, 36.5, 27.2

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.09 – -152.42 (m), -158.03 (t, *J* = 21.7 Hz), -162.26 – -162.65 (m)

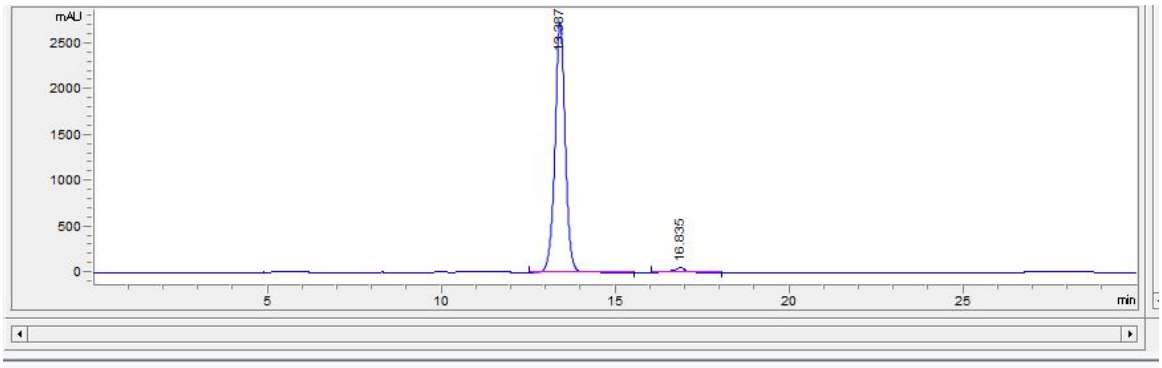
IR (ATR): 2923, 2856, 1780, 1643, 1517, 1478, 1447, 1289, 1141, 1075, 992, 923, 713, 691, 616 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{24}H_{19}F_5NO_2^+$: 448.1330. Found: 448.1334

HPLC analysis using chiral column (ChiralPak IB, 5µ column, 22 °C, 1.0 mL/min, 200:1 Hexanes:IPA, 254 nm, t_{major}: 13.4 min, t_{minor}: 16.8 min)



#	Time	Area	Height	Width	Area%	Symmetry
1	13.475	32167.9	1661.2	0.2879	49.965	0.994
2	16.767	32213.4	1310.4	0.3548	50.035	0.823



#	Time	Area	Height	Width	Area%	Symmetry
1	13.387	56094.1	2732.9	0.3075	98.033	0.939
2	16.835	1125.7	47.2	0.3522	1.967	1.205

perfluorophenyl (*R*)-2-(1-isopropyl-1*H*-pyrrol-2-yl)pent-4-enoate (25): Prepared according to general procedure B with **S1** as the electrophile. The title compound was obtained as a yellow oil (56 mg, 0.15 mmol, 74%) following purification by column (SiO_2: 40:1 pentane:Et_2O). The enantiomeric ratio (98:2) was determined by chiral HPLC in comparison with the racemate (see below).

$[\alpha]_D^{20} = -32.0$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95 – 6.72 (m, 1H), 6.37 – 6.12 (m, 2H), 5.98 (tt, *J* = 13.6, 5.2 Hz, 1H), 5.33 – 5.11 (m, 2H), 4.47 (p, *J* = 6.7 Hz, 1H), 4.13 (dd, *J* = 8.8, 6.5 Hz, 1H), 3.12 – 2.97 (m, 1H), 2.92 – 2.71 (m, 1H), 1.56 (d, *J* = 6.2 Hz, 6H)

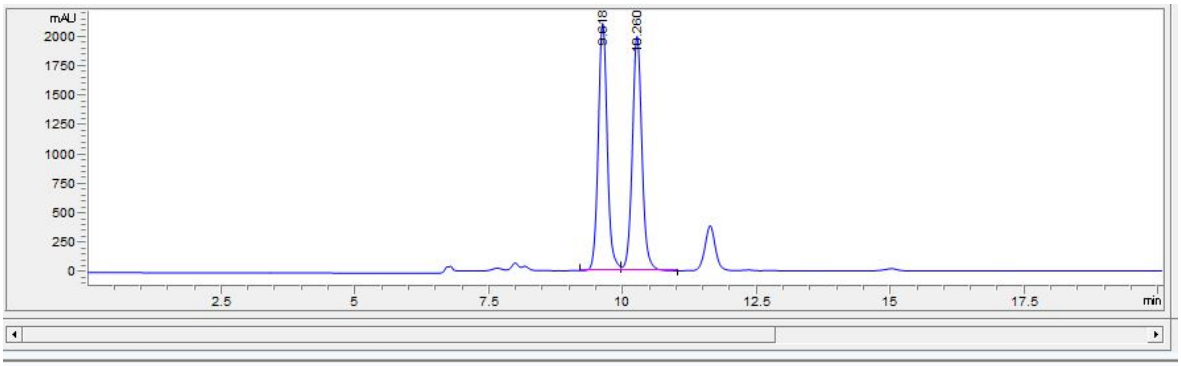
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.8, 134.3, 126.4, 118.2, 117.3, 108.1, 107.3, 47.2, 43.0, 36.6, 24.4, 23.7

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.16 – -152.62 (m), -158.06 (t, *J* = 21.7 Hz), -162.42 (td, *J* = 21.7, 4.9 Hz)

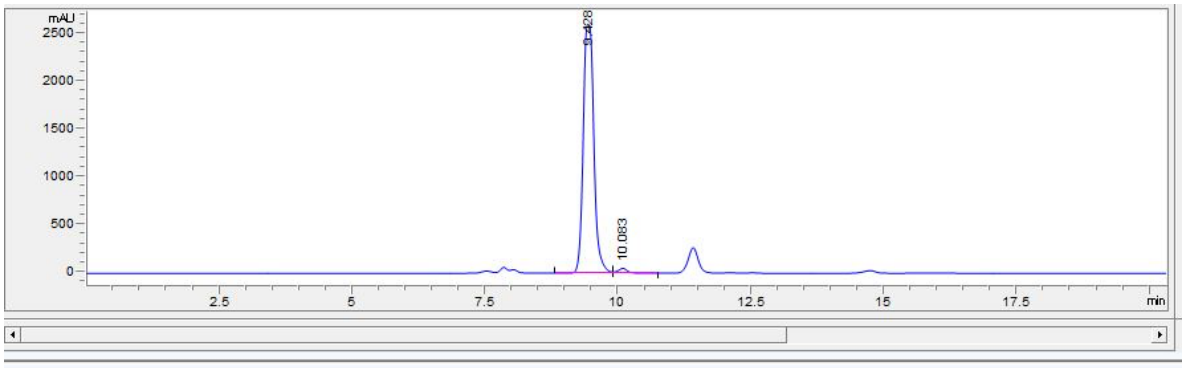
IR (ATR): 2981, 2932, 1781, 1517, 1471, 1282, 1232, 1137, 1081, 991, 923, 711, 621 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{18}H_{17}F_5NO_2^+$: 374.1174. Found: 374.1177

HPLC analysis using chiral column (ChiralPak IB, 5µ column, 22 °C, 1.0 mL/min, 200:1 Hexanes:IPA, 210 nm, t_{major}: 9.4 min, t_{minor}: 10.1 min)

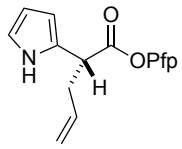


#	Time	Area	Height	Width	Area%	Symmetry
1	9.618	24617.7	2098.2	0.1809	49.730	0.914
2	10.26	24885.2	1987.9	0.192	50.270	0.902



#	Time	Area	Height	Width	Area%	Symmetry
1	9.428	36126	2609.7	0.2175	98.254	0.805
2	10.083	642	50.6	0.1879	1.746	0.973

perfluorophenyl (*R*)-2-(1*H*-pyrrol-2-yl)pent-4-enoate (26): Prepared according to general procedure B with **S1** as the electrophile. The title compound was obtained as a yellow oil (32 mg, 0.10 mmol, 49%) following purification by column (SiO_2: 50:1 pentane:Et_2O). The enantiomeric ratio (87:13) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -19.0$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.34 (bs, 1H), 6.71 (td, *J* = 2.6, 1.5 Hz, 1H), 6.15 – 6.05 (m, 2H), 5.76 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.13 (dd, *J* = 17.1, 1.2 Hz, 1H) 5.09 (dd, *J* = 10.4, 1.4 Hz, 1H), 4.06 (dd, *J* = 8.4, 6.5 Hz, 1H), 2.86 – 2.75 (m, 1H), 2.71 – 2.60 (m, 1H)

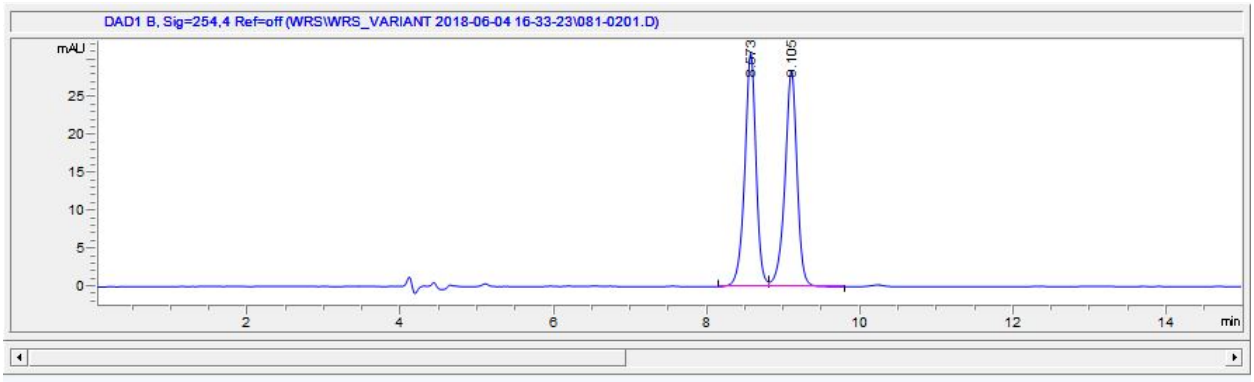
^{13}C NMR (101 MHz, $CDCl_3$): δ = 169.1, 133.8, 125.8, 118.6, 108.8, 107.7, 44.4, 37.3

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.27 (d, *J* = 17.4 Hz), -157.59 (t, *J* = 21.7 Hz), -162.16 (dd, *J* = 21.7, 17.3 Hz)

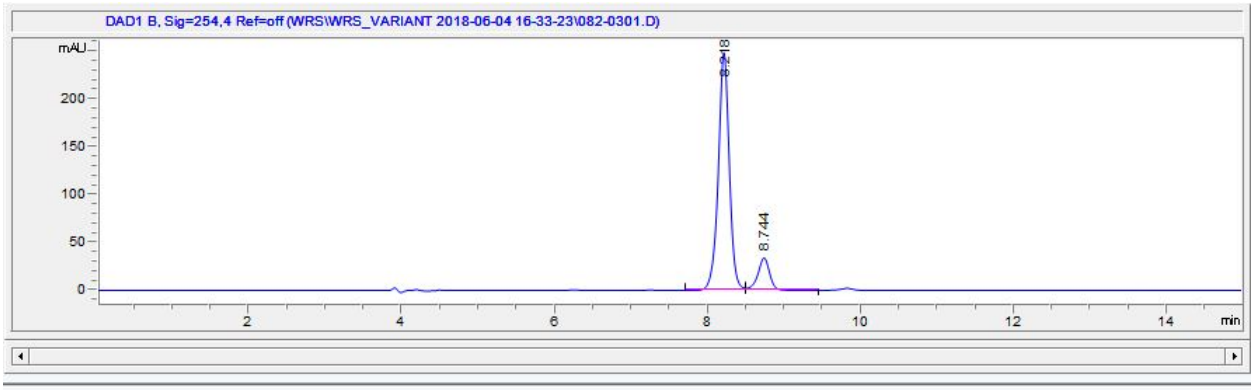
IR (ATR): 1777, 1520, 1093, 996, 723 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{15}H_{11}F_5NO_2^+$: 332.0704. Found: 332.0707

HPLC analysis using chiral column (ChiralPak IB-3, 5μ column, 22 °C, 1.0 mL/min, 99:1 Hexanes:IPA, 254 nm, t_{major}: 8.2 min, t_{minor}: 8.7 min)

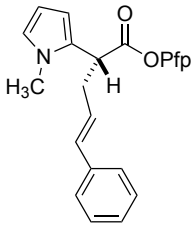


#	Time	Area	Height	Width	Area%	Symmetry
1	8.573	318.3	30.8	0.1564	50.221	1.089
2	9.105	315.5	28.5	0.167	49.779	1.11



#	Time	Area	Height	Width	Area%	Symmetry
1	8.218	2501.2	249.1	0.1512	87.212	1.008
2	8.744	366.7	34	0.1617	12.788	1.111

perfluorophenyl (*R*,*E*)-2-(1-methyl-1*H*-pyrrol-2-yl)-5-phenylpent-4-enoate (29): Prepared according to general procedure B with **S2** as the electrophile. The title compound was obtained as a colorless oil (71 mg, 0.17 mmol, 85%) following purification by column (SiO_2: 50:1 pentane:Et_2O). The enantiomeric ratio (91:9) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -12.4$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 – 7.28 (m, 4H), 7.28 – 7.20 (m, 1H), 6.65 (dd, *J* = 2.8, 1.8 Hz, 1H), 6.58 (d, *J* = 15.8 Hz, 1H), 6.31 – 6.20 (m, 2H), 6.16 (dd, *J* = 3.7, 2.7 Hz, 1H), 4.11 (dd, *J* = 8.8, 6.4 Hz, 1H), 3.72 (s, 3H), 3.13 (dddd, *J* = 14.4, 8.8, 7.6, 1.3 Hz, 1H), 2.91 (dtd, *J* = 14.4, 6.6, 1.5 Hz, 1)

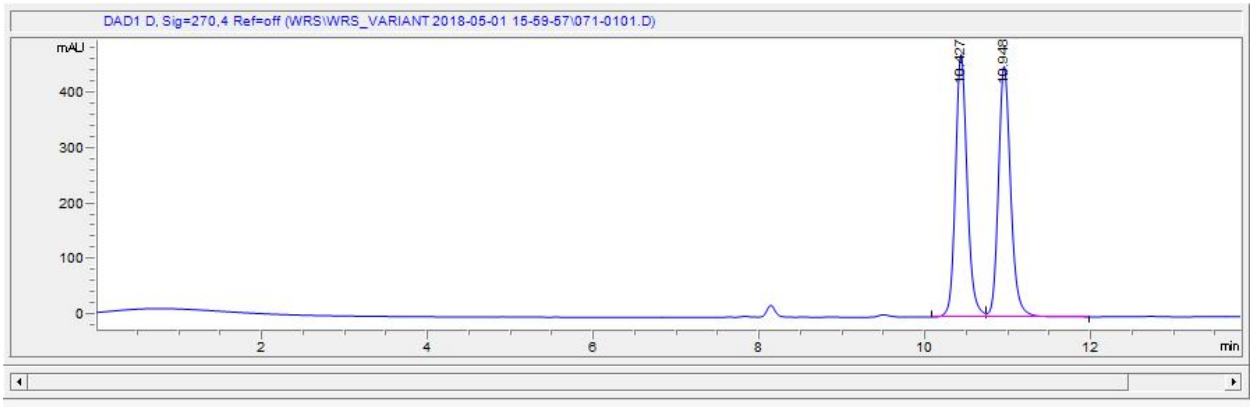
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 137.1, 133.5, 128.7, 127.7, 127.4, 126.4, 125.5, 123.3, 107.9, 107.4, 43.5, 35.6, 34.0, 27.2

^{19}F NMR (376 MHz, $CDCl_3$): δ = -151.54 – -153.39 (m), -157.80 (t, *J* = 21.6 Hz), -162.21 (dd, *J* = 21.6, 17.4 Hz)

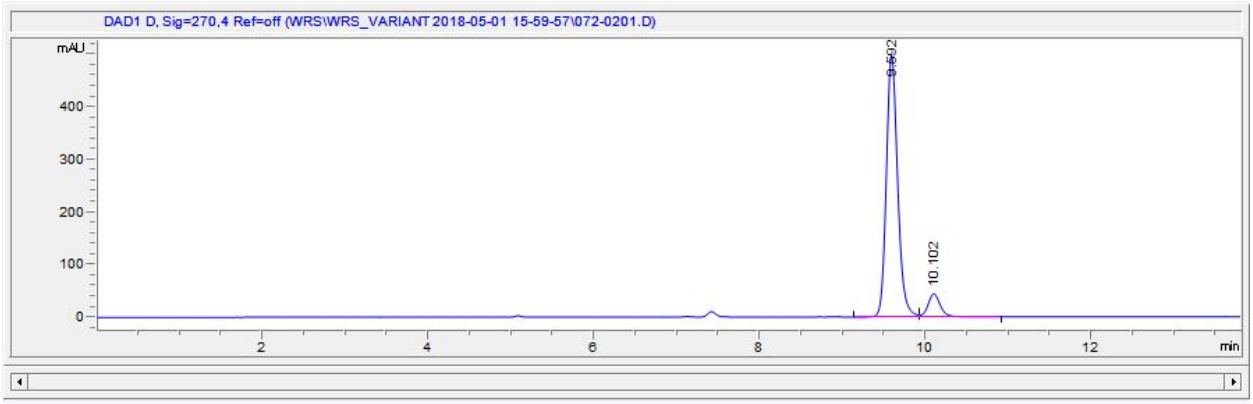
IR (ATR): 1782, 1520, 1089, 1003, 715 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{22}H_{17}F_5NO_4^+$: 422.1174. Found: 422.1179

HPLC analysis using chiral column (ChiralPak IA-3, 5µ column, 22 °C, 0.75 mL/min, 99:1 Hexanes:IPA, 270 nm, t_{major}: 9.6 min, t_{mior}: 10.1 min)

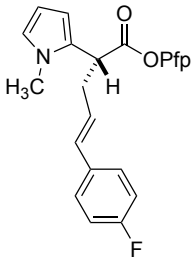


#	Time	Area	Height	Width	Area%	Symmetry
1	10.427	4659.5	475.4	0.1503	49.943	0.837
2	10.948	4670.2	453.8	0.1581	50.057	0.803



#	Time	Area	Height	Width	Area%	Symmetry
1	9.592	4726	500	0.1443	91.172	0.811
2	10.102	457.6	44.2	0.1568	8.828	0.837

perfluorophenyl (*R*,*E*)-5-(4-fluorophenyl)-2-(1-methyl-1*H*-pyrrol-2-yl)pent-4-enoate (30):



Prepared according to general procedure B with **S3** as the electrophile. The title compound was obtained as a yellow oil (58 mg, 0.13 mmol, 66%) following purification by column (SiO_2: 50:1 pentane:Et_2O). The enantiomeric ratio (93:7) was determined by chiral HPLC in comparison with the racemate (see below).

$[\alpha]_D^{20} = -10.8$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 –7.28 (m, 2H), 7.00 (t, *J* = 8.7 Hz, 2H), 6.65 (t, *J* = 2.3 Hz, 1H), 6.54 (d, *J* = 15.8 Hz, 1H), 6.24 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.21 – 6.10 (m, 2H), 4.10 (dd, *J* = 8.9, 6.3 Hz, 1H), 3.67 (s, 3H), 3.17 – 3.06 (m, 1H), 2.95 – 2.84 (m, 1H)

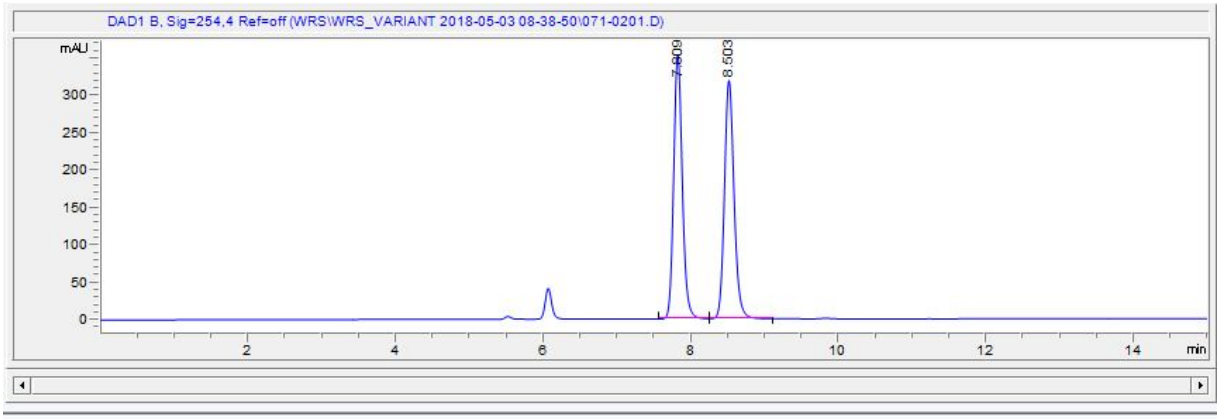
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 162.4 (d, *J* = 246.9 Hz), 133.23 (d, *J* = 3.4 Hz), 132.3, 127.85 (d, *J* = 8.1 Hz), 127.3, 125.2, 123.3, 115.6 (d, *J* = 21.6 Hz), 108.0, 107.7, 43.5, 35.5, 34.0, 27.9

^{19}F NMR (376 MHz, $CDCl_3$): δ = -114.61 – -114.71 (m), -152.46 (d, *J* = 17.4 Hz), -157.71 (t, *J* = 21.7 Hz), -162.16 (dd, 21.7, 17.4 Hz)

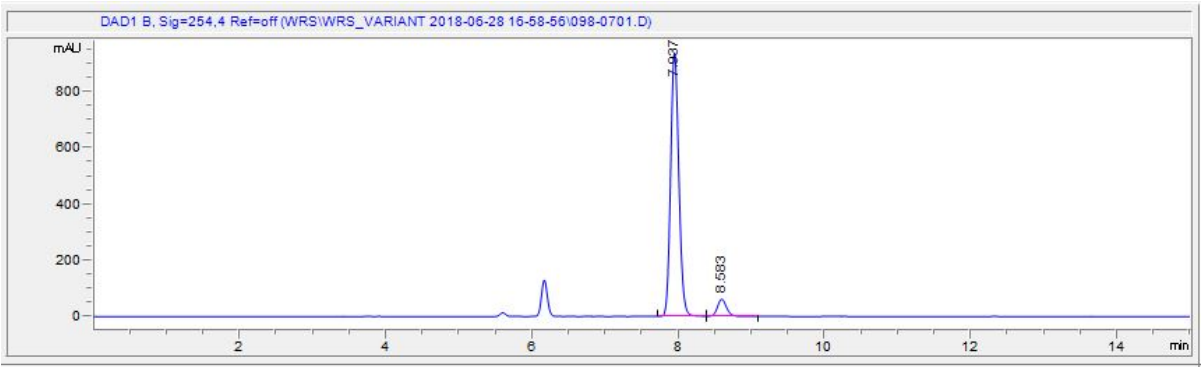
IR (ATR): 1783, 1520, 1231, 1158, 1093, 1003, 716 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{22}H_{16}F_6NO_2^+$: 440.1080. Found: 440.1803

HPLC analysis using chiral column (ChiralPak IA-3, 5µ column, 22 °C, 1.0 mL/min, 98:2 Hexanes:IPA, 254 nm, t_{minor}: 7.9 min, t_{major}: 8.6 min)

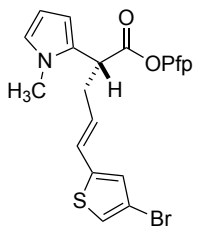


#	Time	Area	Height	Width	Area%	Symmetry
1	7.809	2877.4	354.5	0.1247	49.891	0.84
2	8.503	2889.9	319.5	0.1375	50.109	0.83



#	Time	Area	Height	Width	Area%	Symmetry
1	7.937	7304.2	935.6	0.1211	93.154	0.845
2	8.583	536.8	61.1	0.1364	6.846	0.849

perfluorophenyl (*R*,*E*)-5-(4-bromothiophen-2-yl)-2-(1-methyl-1*H*-pyrrol-2-yl)pent-4-enoate (31): Prepared according to general procedure B with **S4** as the electrophile. The title compound was obtained as a yellow oil (67 mg, 0.16 mmol, 78%) following purification by column (SiO_2: 50:1 pentane:Et_2O). The enantiomeric ratio (93:7) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -9.3$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.03 (d, *J* = 1.4 Hz, 1H), 6.84 (d, *J* = 1.4 Hz, 1H), 6.64 (t, *J* = 2.2 Hz, 1H), 6.60 (d, *J* = 15.7 Hz, 1H), 6.22 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.15 (d, *J* = 3.2 Hz, 1H), 6.15 – 6.03 (m, 1H), 4.09 (dd, *J* = 8.7, 6.4 Hz, 1H), 3.66 (s, 3H), 3.16 – 3.01 (m, 1H), 2.94 – 2.80 (m, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.4, 142.9, 127.6, 127.0, 126.7, 125.6, 123.4, 121.2, 110.1, 108.0, 107.8, 43.1, 35.3, 34.0, 27.2

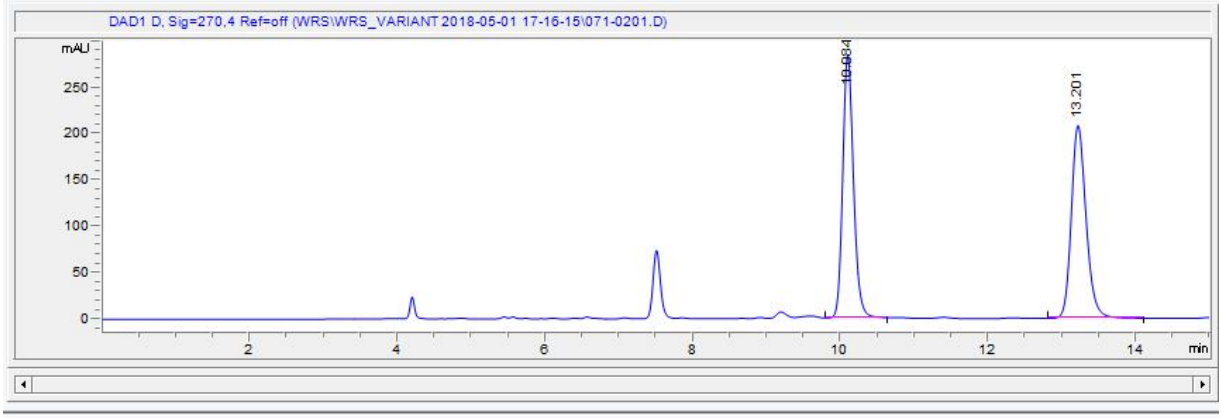
^{19}F NMR (376 MHz, $CDCl_3$): δ = -151.71 – -153.21 (m), -157.61 (t, *J* = 21.7 Hz), -162.08 (dd, *J* = 21.7, 17.3 Hz)

IR (ATR): 2923, 2360, 2341, 1781, 1520, 1090, 1003, 717 cm^{-1}

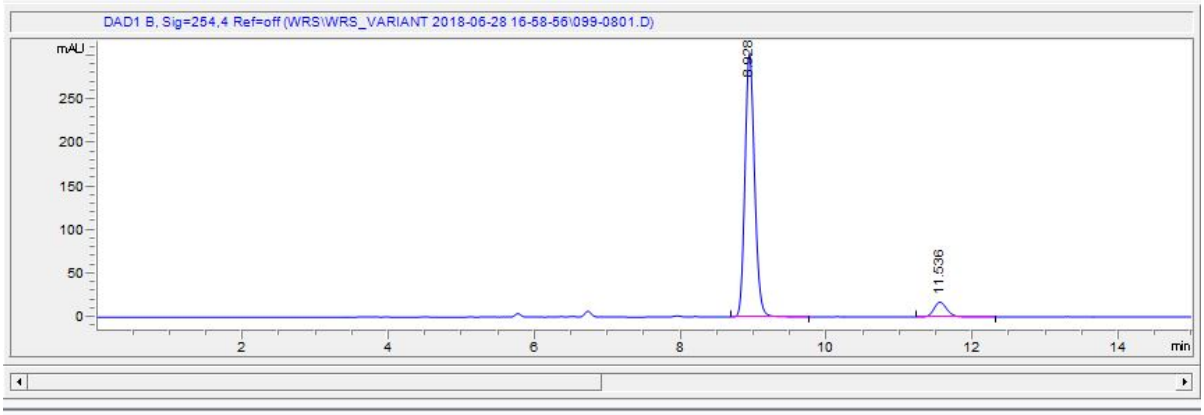
HRMS (APCI): *m/z* calc. for [M+H] $C_{20}H_{14}BrF_5NO_2S^+$: 505.9843. Found: 505.9849

HPLC analysis using chiral column (ChiralPak IA-3, 5μ column, 22 °C, 1.0 mL/min, 98:2 Hexanes:IPA, 254 nm, t_{major}: 8.9 min, t_{minor}: 11.5 min)

Note: There is a discrepancy in retention times between the racemic and enantioenriched traces. The cause is unknown; however, it is consistent across multiple runs.

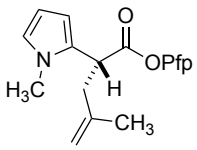


#	Time	Area	Height	Width	Area%	Symmetry
1	10.084	2882.8	284.2	0.1563	49.864	0.805
2	13.201	2898.6	208.6	0.2141	50.136	0.777



#	Time	Area	Height	Width	Area%	Symmetry
1	8.928	2764.1	302	0.1428	92.849	0.824
2	11.536	212.9	17	0.1938	7.151	0.82

perfluorophenyl (*R*)-4-methyl-2-(1-methyl-1*H*-pyrrol-2-yl)pent-4-enoate (32): Prepared according to general procedure D with **S17** as the electrophile. The title compound was obtained as a colorless oil (50. mg, 0.14 mmol, 70%) following purification by column (40:1 pentane:Et_2O). The enantiomeric ratio (95:5) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -5.8$ (c = 1.0, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.63 (dd, *J* = 2.7, 1.8 Hz, 1H), 6.20 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.13 (dd, *J* = 3.7, 2.7 Hz, 1H), 4.91 (s, 1H), 4.87 (s, 1H), 4.20 (dd, *J* = 9.8, 5.6 Hz, 1H), 3.68 (s, 3H), 2.99 (dd, *J* = 14.8, 9.8 Hz, 1H), 2.65 (dd, *J* = 14.8, 5.6 Hz, 1H), 1.82 (s, 3H)

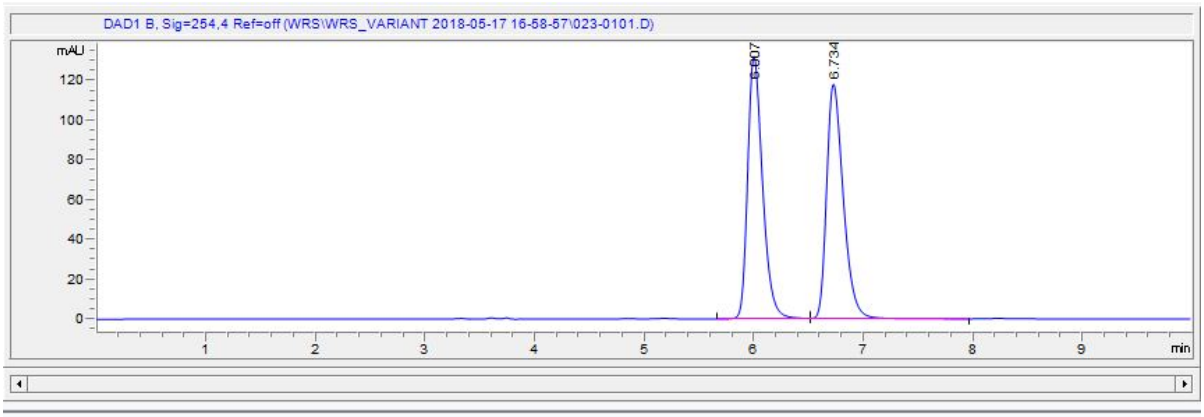
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 141.6, 127.7, 123.2, 113.2, 107.8, 107.7, 41.8, 39.9, 34.0, 22.6

^{19}F NMR (376 MHz, $CDCl_3$): δ = -149.56 – -153.84 (m), -157.98 (t, *J* = 21.7 Hz), -162.42 (dd, *J* = 21.7, 17.3 Hz)

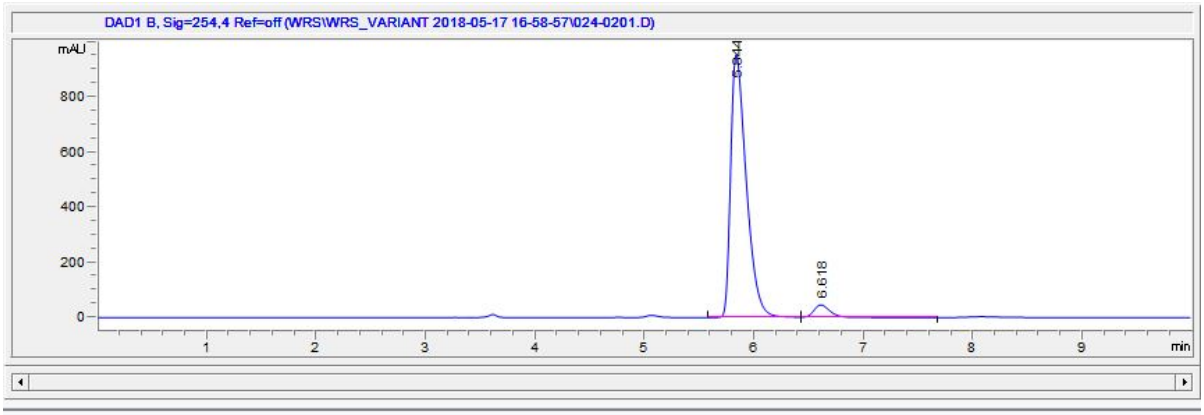
IR (ATR): 1786, 1653, 1520, 1302, 1091, 1004, 714 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{17}H_{15}F_5NO_2^+$: 360.1017. Found: 360.1019

HPLC analysis using chiral column (ChiralPak IA-3, 5µ column, 22 °C, 1.0 mL/min, 200:1 Hexanes:IPA, 254 nm, t_{major}: 5.8 min, t_{minor}: 6.6 min)

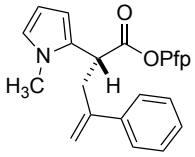


#	Time	Area	Height	Width	Area%	Symmetry
1	6.007	1250.6	132.1	0.1444	49.977	0.676
2	6.734	1251.7	118	0.1618	50.023	0.647



#	Time	Area	Height	Width	Area%	Symmetry
1	5.844	9448.9	952.8	0.1517	95.160	0.511
2	6.618	480.6	45.9	0.1602	4.840	0.7

perfluorophenyl (*R*)-2-(1-methyl-1*H*-pyrrol-2-yl)-4-phenylpent-4-enoate (33): Prepared according to general procedure D with **S18** as the electrophile. The title compound was obtained as a colorless oil (57 mg, 0.14 mmol, 68%) following purification by column (40:1 pentane:Et_2O). The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -54.9$ (c = 1.0, $CHCl_3$)

^1H NMR (400 MHz, $CDCl_3$): δ = 7.44 –7.30 (m, 5H), 6.59 (app. t, *J* = 2.3 Hz, 1H), 6.22 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.13 (app t, *J* = 3.2 Hz, 1H), 5.37 (s, 1H), 5.22 (s, 1H), 4.07 (dd, *J* = 9.6, 5.7 Hz, 1H), 3.48 (s, 3H), 3.41 (dd, *J* = 14.7, 9.7 Hz, 1H), 3.19 (dd, *J* = 14.6, 5.7 Hz, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.5, 144.6, 140.1, 128.8, 128.1, 127.5, 126.4, 123.2, 116.0, 107.9, 107.7, 41.8, 38.2, 33.9

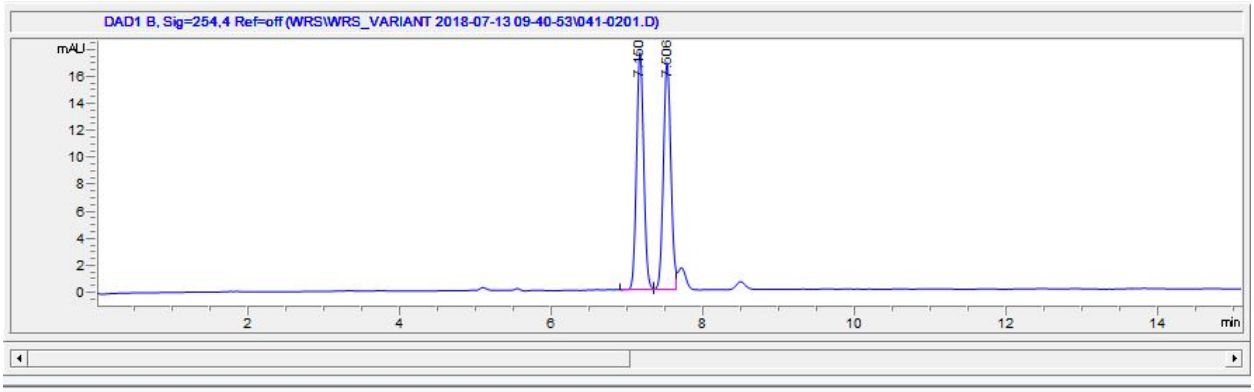
^{19}F NMR (376 MHz, $CDCl_3$): δ = -151.78 (m), -157.91 (t, *J* = 21.9 Hz), -162.35 (dd, *J* = 21.7, 17.4 Hz)

IR (ATR): 1785, 1520, 1302, 1091, 1004, 779, 711 cm^{-1}

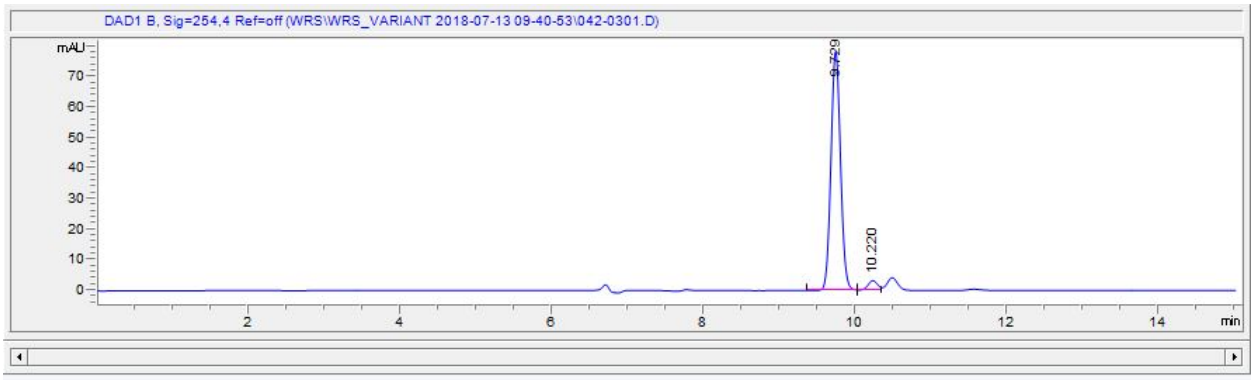
HRMS (APCI): *m/z* calc. for [M+H] $C_{22}H_{17}F_5NO_2^+$: 422.1174. Found: 442.1178

HPLC analysis using chiral column (ChiralPak IA-3, 5µ column, 22 °C, 1.0 mL/min, 99:1 Hexanes:IPA, 254 nm, t_{major}: 9.7 min, t_{minor}: 10.2 min).

Note: There is a discrepancy in retention times between the racemic and enantioenriched traces. The cause is unknown; however, it is consistent across multiple runs.

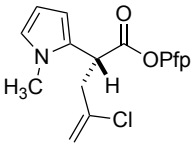


#	Time	Area	Height	Width	Area%	Symmetry
1	7.15	115.4	17.5	0.1028	49.764	0.918
2	7.506	116.5	16.8	0.107	50.236	0.917



#	Time	Area	Height	Width	Area%	Symmetry
1	9.729	684.5	78.1	0.1363	95.845	0.921
2	10.22	29.7	3.2	0.1415	4.155	1.018

perfluorophenyl (*R*)-4-chloro-2-(1-methyl-1*H*-pyrrol-2-yl)pent-4-enoate (34): Prepared according to general procedure D with **S19** as the electrophile. The title compound was obtained as a colorless oil (33 mg, 0.043 mmol, 37%) following purification by column (40:1 pentane:Et_2O). The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -64.5$ (c = 1.0, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.65 (dd, *J* = 2.7, 1.8 Hz, 1H), 6.18 (dd, *J* = 3.8, 1.8 Hz, 1H), 6.15 (dd, *J* = 3.7, 2.8 Hz, 1H), 5.32 (s, 2H), 4.46 (dd, *J* = 8.8, 6.2 Hz, 1H), 3.73 (s, 3H), 3.29 (dd, *J* = 14.3, 8.7 Hz, 1H), 2.94 (dd, *J* = 13.8, 6.0 Hz, 1H)

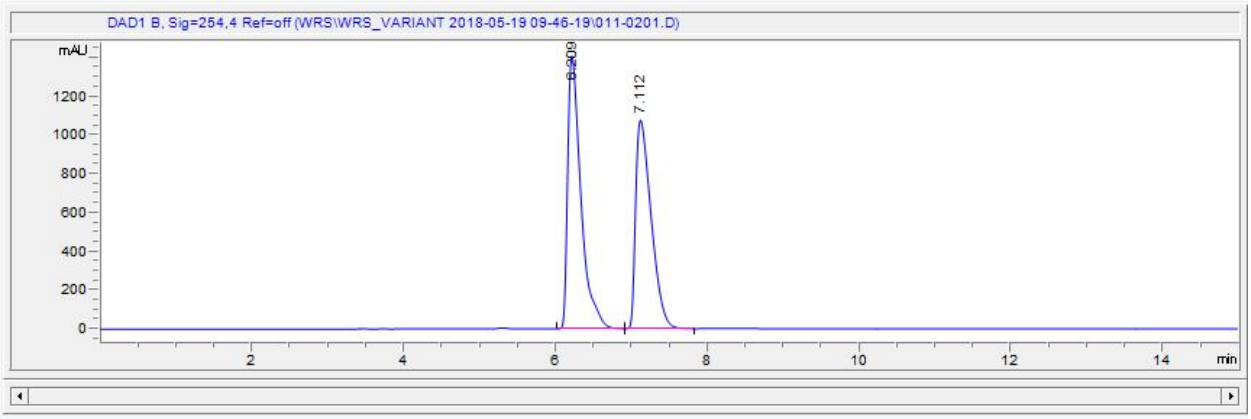
^{13}C NMR (126 MHz, $CDCl_3$): δ = 167.9, 138.1, 126.4, 123.5, 116.0, 107.9, 107.8, 41.8, 41.0, 34.0

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.27 (d, *J* = 17.4 Hz), -157.65 (t, *J* = 21.7 Hz), -162.21 (dd, *J* = 21.7, 17.4 Hz)

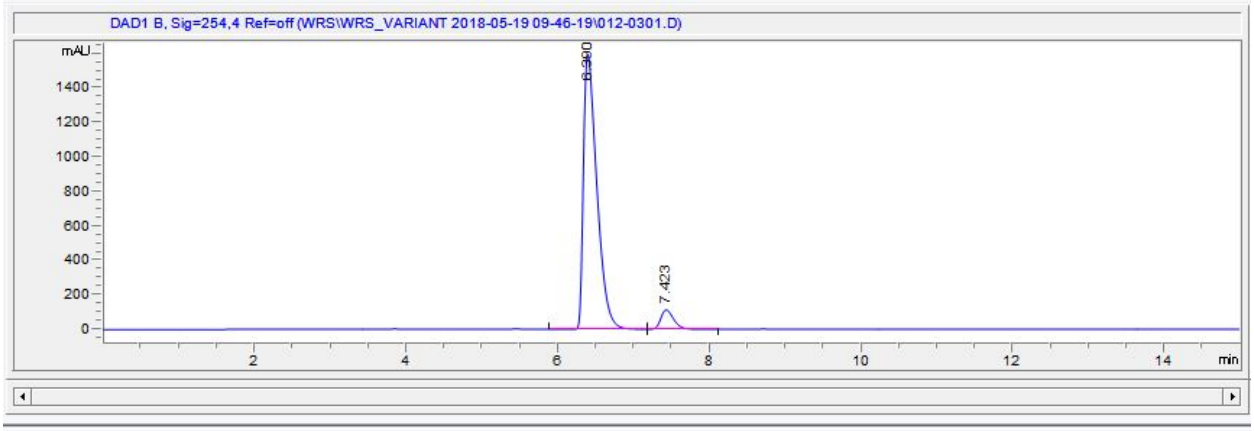
IR (ATR): 1785, 1520, 1092, 995, 895, 717 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{16}H_{12}ClF_5NO_2^+$: 380.0471. Found: 380.0474

HPLC analysis using chiral column (ChiralPak IA-3, 5μ column, 22 °C, 1.0 mL/min, 200:1 Hexanes:IPA, 254 nm, t_{major}: 6.4 min, t_{minor}: 7.4 min)

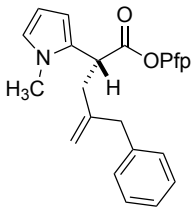


#	Time	Area	Height	Width	Area%	Symmetry
1	6.209	17026.3	1405.2	0.1834	52.802	0.434
2	7.112	15219.4	1074	0.2193	47.198	0.43



#	Time	Area	Height	Width	Area%	Symmetry
1	6.39	19424.2	1581.2	0.1853	93.592	0.445
2	7.423	1330	112.3	0.1822	6.408	0.678

perfluorophenyl (*R*)-4-benzyl-2-(1-methyl-1*H*-pyrrol-2-yl)pent-4-enoate (35): Prepared according to general procedure D with **S20** as the electrophile. The title compound was obtained as a colorless oil (74 mg, 0.17 mmol, 85%) following purification by column (40:1 pentane:Et_2O). The enantiomeric ratio (93:7) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -28.5$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 – 7.27 (m, 2H), 7.25 – 7.18 (m, 3H), 6.59 (dd, *J* = 2.8, 1.8 Hz, 1H), 6.14 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.11 (dd, *J* = 3.7, 2.7 Hz, 1H), 5.03 (s, 1H), 4.98 (s, 1H), 4.13 (dd, *J* = 10.0, 5.5 Hz, 1H), 3.56 (s, 3H), 3.42 (s, 2H), 2.95 (dd, *J* = 15.0, 10.1 Hz, 1H), 2.58 (dd, *J* = 15.0, 5.5 Hz, 1H)

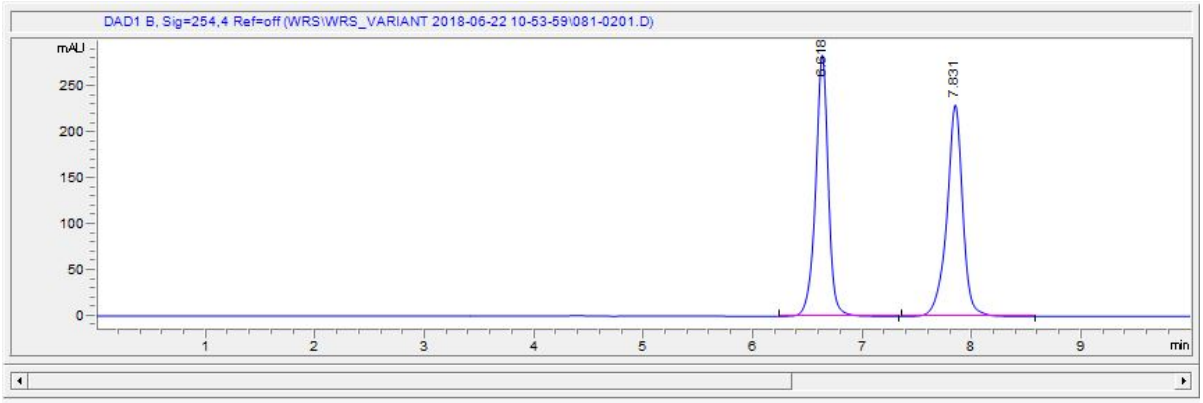
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.5, 144.8, 139.0, 129.1, 128.6, 127.5, 126.6, 123.2, 114.6, 107.8, 107.6, 43.3, 41.8, 37.7, 33.9

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.19 (d, *J* = 17.5 Hz), -157.93 (t, *J* = 21.9 Hz), -162.36 (dd, *J* = 21.7, 17.3 Hz)

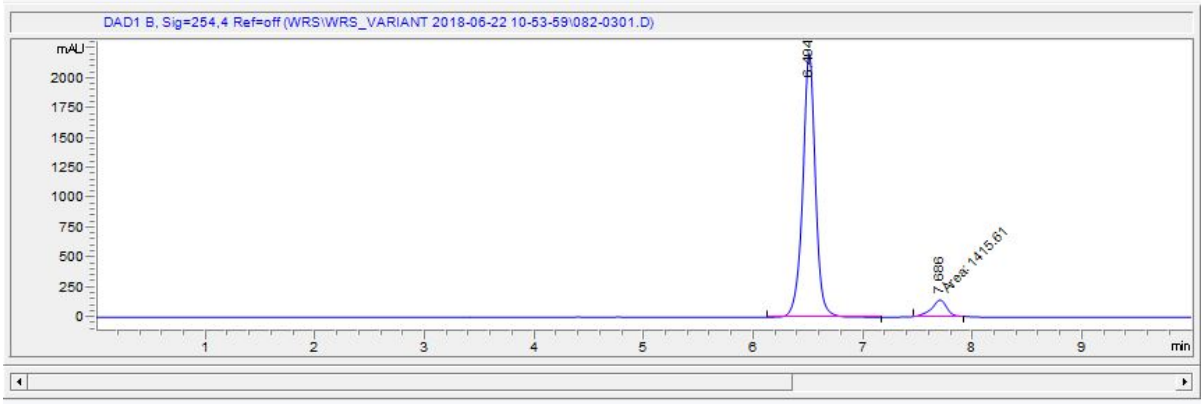
IR (ATR): 1786, 1520, 1091, 996, 702 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{23}H_{19}F_5NO_2^+$: 436.1330. Found: 436.1334

HPLC analysis using chiral column (ChiralPak IA-3, 5µ column, 22 °C, 1.0 mL/min, 99:1 Hexanes:IPA, 254 nm, t_{major}: 6.5 min, t_{minor}: 7.7 min)

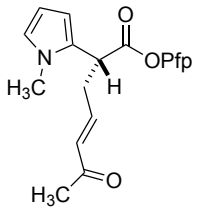


#	Time	Area	Height	Width	Area%	Symmetry
1	6.618	2293.5	286	0.1196	49.662	1.068
2	7.831	2324.7	231.2	0.1473	50.338	1.111



#	Time	Area	Height	Width	Area%	Symmetry
1	6.494	17637.8	2197.5	0.1196	92.570	1.001
2	7.686	1415.6	141.3	0.167	7.430	1.216

perfluorophenyl (*R*,*E*)-2-(1-methyl-1*H*-pyrrol-2-yl)-6-oxohept-4-enoate (36): XantPhos PdG3 (9.5 mg, 5 mol%, 0.01 mmol), (*R*)-benzotetramisole (10 mg, 0.04 mmol, 20 mol%), N-methyl pyrrole pentafluorophenyl ester (76 mg, 0.25 mmol, 1.25 equiv), and **S6** (0.20 mmol, 1 equiv) were added sequentially to an oven-dried 2-dram vial containing a magnetic stir bar and equipped with a Teflon insert screw cap. The vial was evacuated and backfilled with nitrogen (3 ×) then cooled to 0 °C. Anhydrous THF (2 mL, 0.1 M) was then added followed by *i*Pr$_2$NEt (44 µL, 0.25 mmol, 1.2 equiv). The reaction mixture was stirred at 0 °C for 24 hours and then diluted with 2.5 mL of petroleum ether (precipitation will occur) and passed through activated acidic Al_2O_3 (Brockmann I). The vial was washed with Et_2O (2.5 mL) and passed through the Al_2O_3. The alumina was then washed with Et_2O. The combined filtrates were concentrated to afford the title compound as yellow oil (56 mg, 0.14 mmol, 73%) following purification by column chromatography (SiO_2: 9:1 then 3:1 pentane:EtOAc). The enantiomeric ratio (93:7) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -9.3$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.82 (dt, *J* = 16.0, 7.0 Hz, 1H), 6.67 (dd, *J* = 2.8, 1.7 Hz, 1H), 6.32 – 6.14 (m, 3H), 4.17 (dd, *J* = 8.6, 6.5 Hz, 1H), 3.79 (s, 3H), 3.2 – 3.0 (m, 1H), 3.03 – 2.82 (m, 1H), 2.23 (s, 3H)

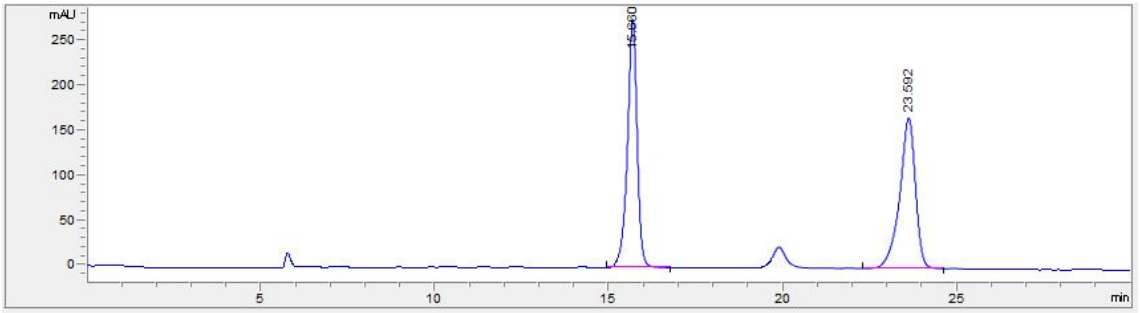
^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.0, 168.1, 142.3, 133.6, 126.4, 123.6, 108.1, 107.8, 42.0, 34.5, 33.9, 27.2

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.44 – -152.92 (m), -157.42 (t, *J* = 21.7 Hz), -162.01 (td, *J* = 21.7, 4.4 Hz)

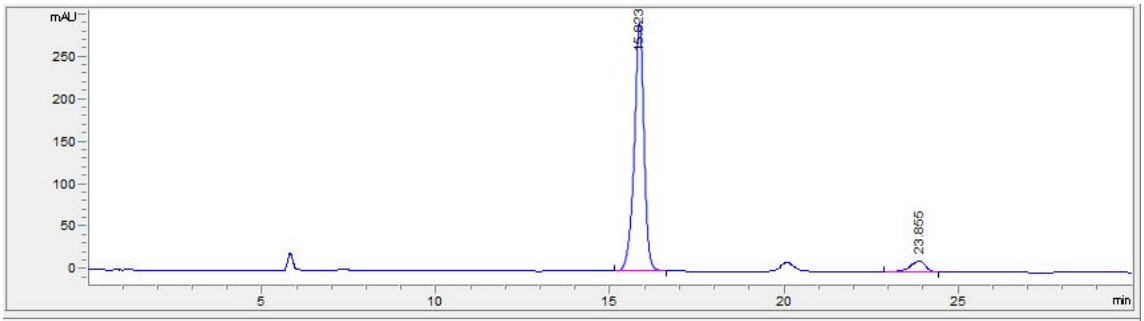
IR (ATR): 1782, 1678, 1521, 1256, 1090, 996, 719

HRMS (ESI): *m/z* calc. for [M+Na] $C_{18}H_{14}F_5NNaO_3^+$: 410.0786. Found: 410.0789

HPLC analysis using chiral column (ChiralPak IB, 5µ column, 22 °C, 1.0 mL/min, 85:15 Hexanes:IPA, 210 nm, t_{major}: 15.8 min, t_{minor}: 23.9 min)

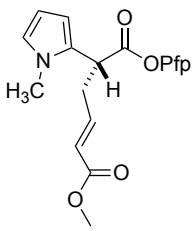


#	Time	Area	Height	Width	Area%	Symmetry
1	15.66	5330	275.2	0.2879	50.271	1.147
2	23.592	5272.5	167	0.4684	49.729	1.327



#	Time	Area	Height	Width	Area%	Symmetry
1	15.823	5708.1	292.8	0.2895	93.178	1.149
2	23.855	417.9	13.3	0.4537	6.822	1.414

1-methyl 6-(perfluorophenyl) (*R*,*E*)-5-(1-methyl-1*H*-pyrrol-2-yl)hex-2-enedioate (37):



Prepared according to general procedure C with **S7** as the electrophile. The title compound was obtained as a colorless oil (66 mg, 0.16 mmol, 81%) following purification by column (SiO_2: 4:1 pentane:Et_2O). The enantiomeric ratio (92:8) was determined by chiral HPLC in comparison with the racemate (see below).

$[\alpha]_D^{20} = -13.6$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.10 – 6.89 (m, 1H), 6.63 (t, *J* = 2.3 Hz, 1H), 6.18 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.16 – 6.12 (m, 1H), 5.98 (dt, *J* = 15.8, 1.5 Hz, 1H), 4.11 (t, *J* = 8.1, 7.1 Hz, 1H), 3.74 (s, 3H), 3.66 (s, 3H), 3.16 – 3.04 (m, 1H), 2.89 (dtd, *J* = 15.1, 6.8, 1.6 Hz, 1H)

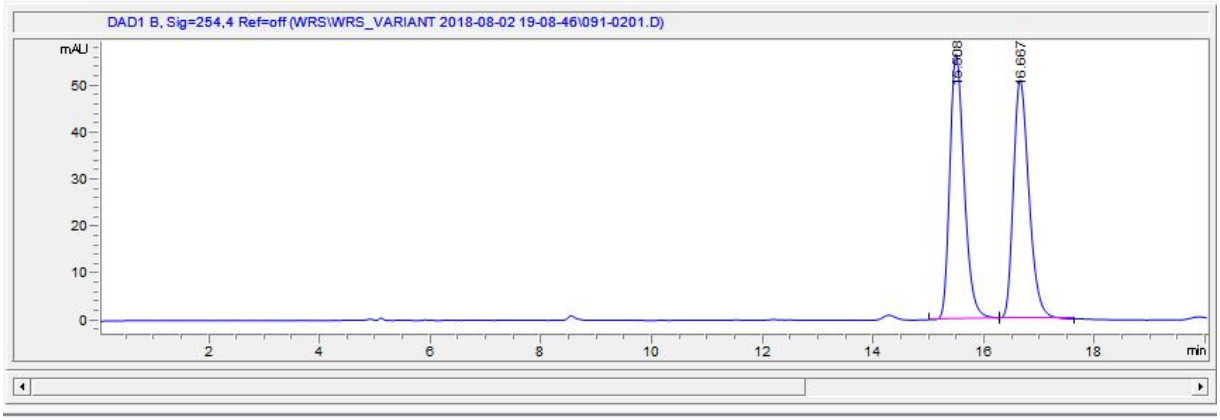
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.1, 166.5, 143.9, 126.4, 124.1, 123.6, 108.1, 107.8, 51.8, 42.0, 34.4, 34.0

^{19}F NMR (376 MHz, $CDCl_3$): δ = -151.80 – -153.16 (m), -157.53 (t, *J* = 21.7 Hz), -162.09 (dd, *J* = 21.7, 17.5 Hz)

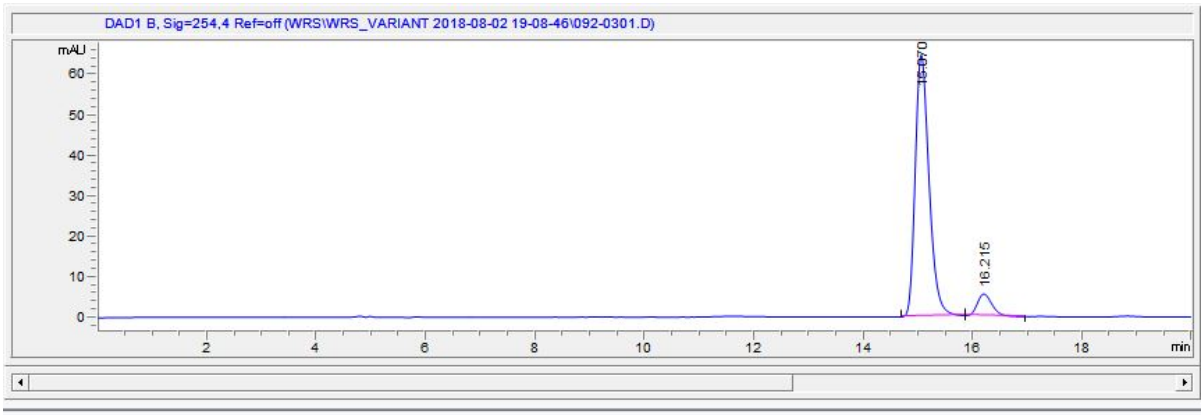
IR (ATR): 1783, 1245, 1520, 1300, 1090, 955, 718 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{18}H_{15}F_5NO_4^+$: 404.0916. Found: 404.0920

HPLC analysis using chiral column (ChiralPak IA-3, 5μ column, 22 °C, 1.0 mL/min, 98:2 Hexanes:IPA, 254 nm, t_{major}: 15.1 min, t_{major}: 16.2 min)

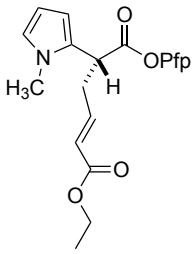


#	Time	Area	Height	Width	Area%	Symmetry
1	15.508	1013.7	56.3	0.2802	50.674	0.727
2	16.667	986.7	50.6	0.3016	49.326	0.708



#	Time	Area	Height	Width	Area%	Symmetry
1	15.07	1134.7	64.5	0.2713	91.789	0.711
2	16.215	101.5	5.4	0.2906	8.211	0.749

1-ethyl 6-(perfluorophenyl) (*R*,*E*)-5-(1-methyl-1*H*-pyrrol-2-yl)hex-2-enedioate (38): Prepared according to general procedure C with **S8** as the electrophile. The title compound was obtained as a colorless oil (71 mg, 0.17 mmol, 86%) following purification by column (SiO_2: 6:1 penatne:Et_2O). The enantiomeric ratio (94:6) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -19.9$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.95 (ddd, *J* = 15.6, 7.5, 6.7 Hz, 1H), 6.63 (dd, *J* = 2.8, 1.8 Hz, 1H), 6.18 (dd, *J* = 3.9, 1.7 Hz, 1H), 6.13 (dd, *J* = 3.7, 2.7 Hz, 1H), 5.98 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 4.11 (dd, *J* = 8.4, 6.7 Hz, 1H), 3.63 (s, 3H), 3.10 (dddd, *J* = 15.0, 8.7, 7.6, 1.4 Hz, 1H), 2.88 (app. dtd, *J* = 15.0, 6.7, 1.6 Hz, 1H), 1.29 (t, 7.1 Hz, 3H)

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 166.1, 143.5, 126.5, 124.6, 123.6, 108.1, 107.8, 60.6, 42.0, 34.4, 34.0, 14.3

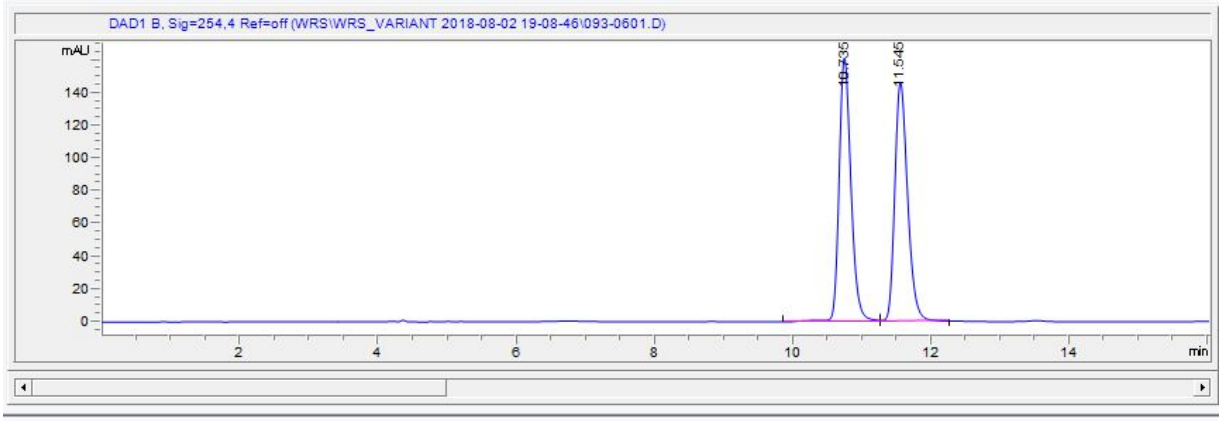
^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.43 (d, *J* = 17.4 Hz), -157.53 (t, *J* = 21.7 Hz), -162.11 (dd, *J* = 21.7, 17.4 Hz)

IR (ATR): 1783, 1719, 1657, 1519, 1302, 1172, 1090, 995, 716 cm^{-1}

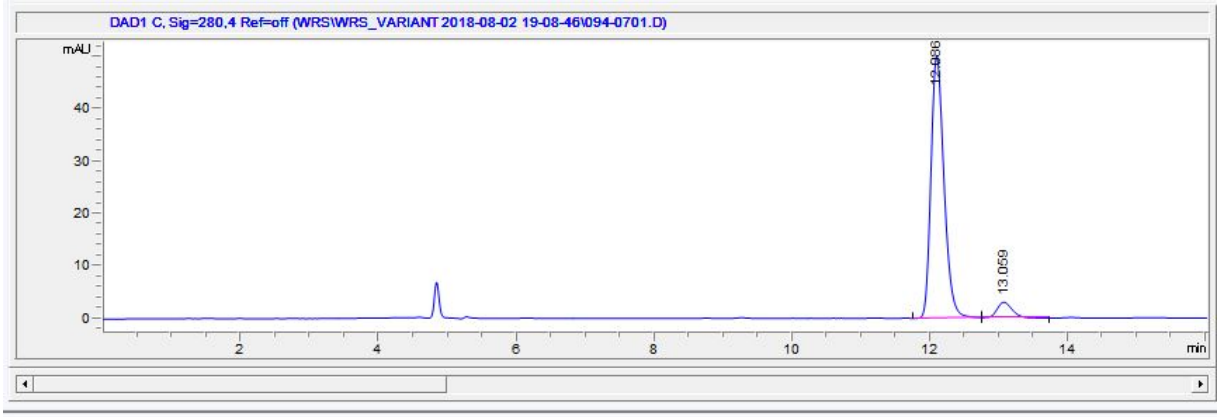
HRMS (APCI): *m/z* calc. for [M+H] $C_{19}H_{17}F_5NO_4^+$: 418.1072. Found: 418.1075

HPLC analysis using chiral column (ChiralPak IA-3, 5µ column, 22 °C, 1.0 mL/min, 99:1 Hexanes:IPA, 280 nm, t_{major}: 12.1 min, t_{minor}: 13.1 min)

Note: There is a discrepancy in retention times between the racemic and enantioenriched traces. The cause is unknown; however, it is consistent across multiple runs.

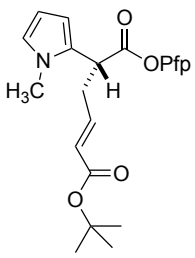


#	Time	Area	Height	Width	Area%	Symmetry
1	10.735	1936.4	162.1	0.1834	50.551	0.769
2	11.545	1894.2	146.8	0.1985	49.449	0.728



#	Time	Area	Height	Width	Area%	Symmetry
1	12.086	660.1	50.3	0.2012	93.547	0.728
2	13.059	45.5	3	0.2353	6.453	0.737

1-(*tert*-butyl) 6-(perfluorophenyl) (*R*,*E*)-5-(1-methyl-1*H*-pyrrol-2-yl)hex-2-enedioate (39):



Prepared according to general procedure C with **S9** as the electrophile. The title compound was obtained as a colorless oil (70 mg, 0.16 mmol, 78%) following purification by column (SiO_2: 6:1 penatne:Et_2O). The enantiomeric ratio (90:10) was determined by chiral HPLC in comparison with the racemate (see below).

$[\alpha]_D^{20} = -19.5$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.85 (ddd, *J* = 15.6, 7.5, 6.7 Hz, 1H), 6.63 (dd, *J* = 2.7, 1.8 Hz, 1H), 6.18 (dd, *J* = 3.8, 1.8 Hz, 1H), 6.13 (dd, *J* = 3.8, 2.7 Hz, 1H), 5.90 (dd, *J* = 15.5, 1.5 Hz, 1H), 4.10 (dd, *J* = 8.7, 6.4, 1H), 3.66 (s, 3H), 3.08 (dddd, *J* = 14.9, 8.8, 7.5, 1.4 Hz, 1H), 2.84 (dtd, *J* = 14.9, 6.6, 1.6 Hz, 1H), 1.48 (s, 9H)

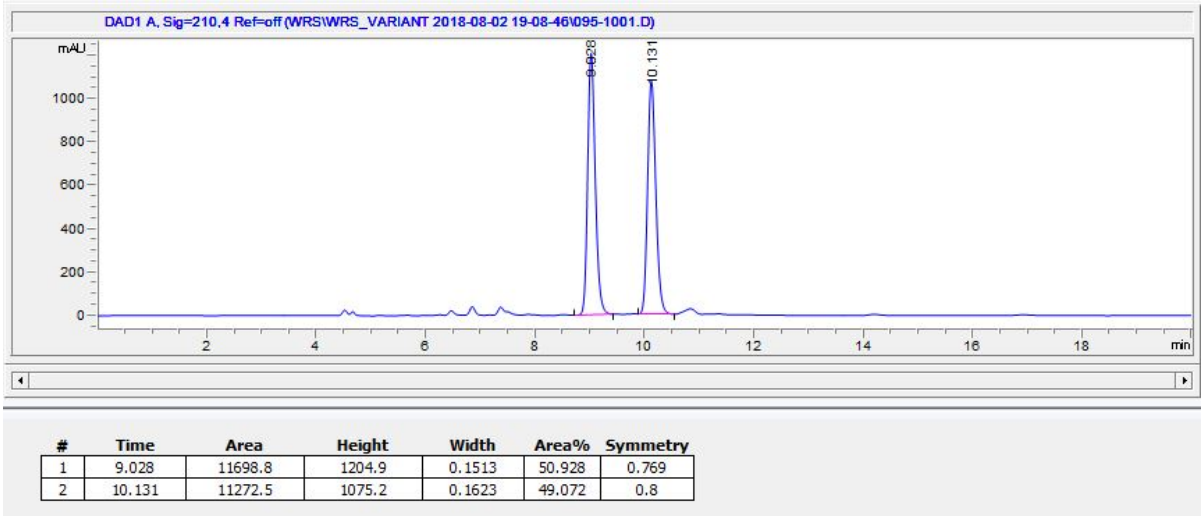
^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.2, 165.4, 142.2, 126.7, 126.3, 123.5, 108.1, 107.8, 80.7, 42.1, 34.4, 34.0, 28.2

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.39 (d, *J* = 17.3 Hz), -157.63 (t, *J* = 21.7 Hz), -162.22 (dd, *J* = 21.7, 17.3 Hz)

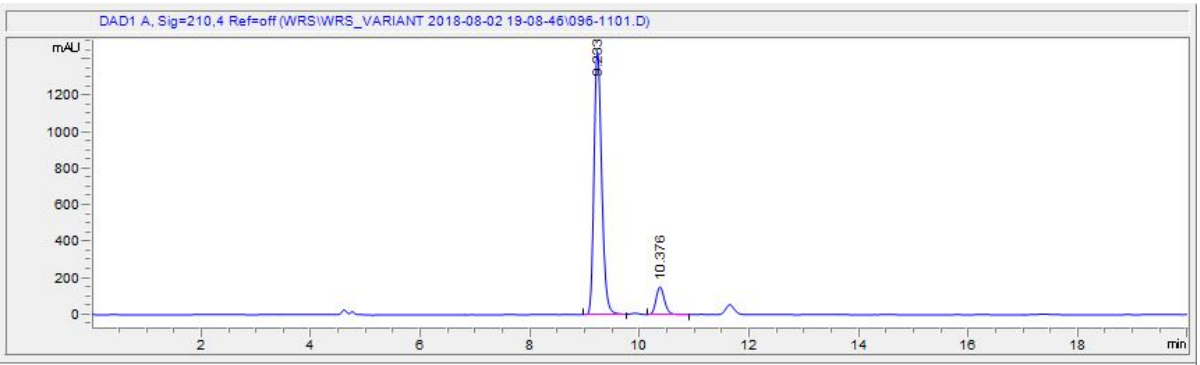
IR (ATR): 2980, 1784, 1714, 1520, 1368, 1301, 1158, 1089, 996, 715 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{21}H_{21}F_5NO_4^+$: 446.1385. Found: 446.1387

HPLC analysis using chiral column (ChiralPak IA-3, 5µ column, 22 °C, 1.0 mL/min, 99:1 Hexanes:IPA, 210 nm, t_{major}: 9.2 min, t_{major}: 10.4 min)

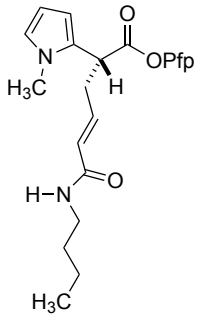


#	Time	Area	Height	Width	Area%	Symmetry
1	9.028	11698.8	1204.9	0.1513	50.928	0.769
2	10.131	11272.5	1075.2	0.1623	49.072	0.8



#	Time	Area	Height	Width	Area%	Symmetry
1	9.233	14046.7	1432.3	0.1524	89.681	0.747
2	10.376	1616.2	150.2	0.1655	10.319	0.82

perfluorophenyl (*R*,*E*)-6-(butylamino)-2-(1-methyl-1*H*-pyrrol-2-yl)-6-oxohex-4-enoate (40):



Prepared according to the general procedure A with **S11** as the electrophile. The title compound was obtained as a light yellow solid (55 mg, 0.12 mmol, 61%) following purification by column (SiO_2: 4:1 then 1:1 pentane:EtOAc). The enantiomeric ratio (92:8) was determined by chiral HPLC in comparison with the racemate (see below).

$[\alpha]_D^{20} = -18.3$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.85 (ddd, *J* = 14.8, 7.9, 6.5 Hz, 1H), 6.63 (dd, *J* = 2.7, 1.8 Hz, 1H), 6.25 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.18 (dd, *J* = 3.7, 2.7 Hz, 1H), 5.93 (dt, *J* = 15.2, 1.5 Hz, 1H), 5.66 (d, *J* = 6.1 Hz, 1H), 4.14 (dd, *J* = 8.5, 6.5 Hz, 1H), 3.65 (s, 3H), 3.47 – 3.23 (m, 2H), 3.16 – 3.09 (m, 1H), 2.95 – 2.84 (m, 1H), 1.66 – 1.44 (m, 2H), 1.42 – 1.37 (m, 2H), 0.92 (t, *J* = 7.3 Hz, 3H)

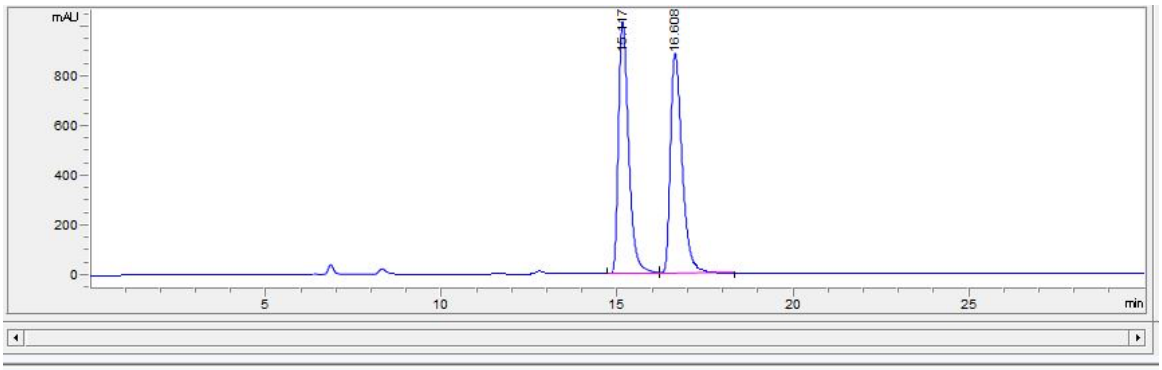
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.2, 165.2, 138.9, 126.9, 126.7, 123.4, 107.9, 107.7, 42.1, 39.4, 34.4, 33.9, 31.7, 20.1, 13.8

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.37 – -152.64 (m), -157.68 (t, *J* = 21.7 Hz), -162.11 (td, *J* = 21.7, 4.5 Hz)

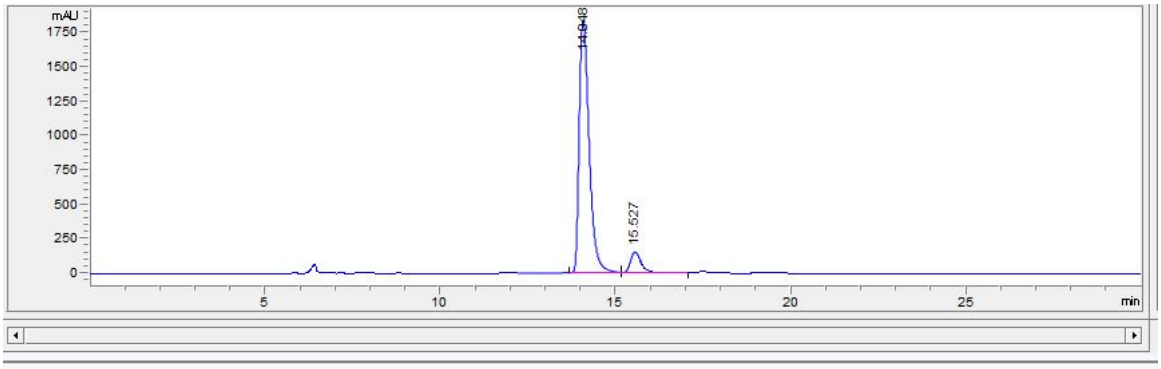
IR (ATR): 3328, 3082, 2961, 2935, 2874, 1781, 1672, 1631, 1520, 1302, 1091, 1003, 715 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{21}H_{22}F_5N_2O_3^+$: 445.1545. Found: 445.1547

HPLC analysis using chiral column (ChiralPak IA-3, 5μ column, 22 °C, 1.0 mL/min, 85:15 Hexanes:IPA, 210 nm, t_{major}: 14.0 min, t_{major}: 15.5 min)

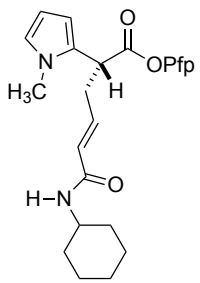


#	Time	Area	Height	Width	Area%	Symmetry
1	15.117	20321.2	1008.7	0.309	49.831	0.628
2	16.608	20458.8	880.6	0.3571	50.169	0.607



#	Time	Area	Height	Width	Area%	Symmetry
1	14.048	36316.3	1833.9	0.305	91.299	0.592
2	15.527	3461	153.3	0.3413	8.701	0.646

perfluorophenyl (*R*,*E*)-6-(cyclohexylamino)-2-(1-methyl-1*H*-pyrrol-2-yl)-6-oxohex-4-enoate (41): $Pd(PTh_3)_3$ (3.8 mg, 2 mol%, 0.004 mmol), (*R*)-benzotetramisole (10 mg, 0.04 mmol, 20 mol%), N-methyl pyrrole pentafluorophenyl ester (118 mg, 0.36 mmol, 1.8 equiv), and **S12** (0.20 mmol, 1 equiv) were added sequentially to an oven-dried 2-dram vial containing a magnetic stir bar and equipped with a Teflon insert screw cap. The vial was evacuated and backfilled with nitrogen (3 ×). Anhydrous 1,4-dioxane (2 mL, 0.1 M) was then added followed by *i*Pr_2NEt (44 µL, 0.25 mmol, 1.2 equiv). The reaction mixture was stirred at room temperature for 2 hours and then diluted with 2.5 mL of petroleum ether (precipitation will occur) and passed through activated acidic Al_2O_3 (Brockmann I). The vial was washed with Et_2O (2.5 mL) and passed through the Al_2O_3. The alumina was then washed with Et_2O. The combined filtrates were concentrated to afford the title compound as a light yellow solid (53 mg, 0.11 mmol, 57%) following purification by column chromatography (SiO_2: 4:1 then 1:1 pentane:EtOAc). The enantiomeric ratio (93:7) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -18.7$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.87 (ddd, *J* = 14.7, 7.8, 6.6 Hz, 1H), 6.68 (t, *J* = 2.2 Hz, 1H), 6.23 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.19 – 6.11 (m, 1H), 5.94 – 5.81 (m, 1H), 5.45 (d, *J* = 8.2 Hz, 1H),

4.12 (dd, *J* = 8.6, 6.4 Hz, 1H), 3.91 – 3.75 (m, 1H), 3.6 (s, 3H), 3.14 – 2.91 (m, 1H), 2.93 – 2.73 (m, 1H), 2.01 – 1.86 (m, 2H), 1.82 – 1.55 (m, 2H), 1.56 – 1.38 (m, 2H), 1.32 – 1.01 (m, 11H)

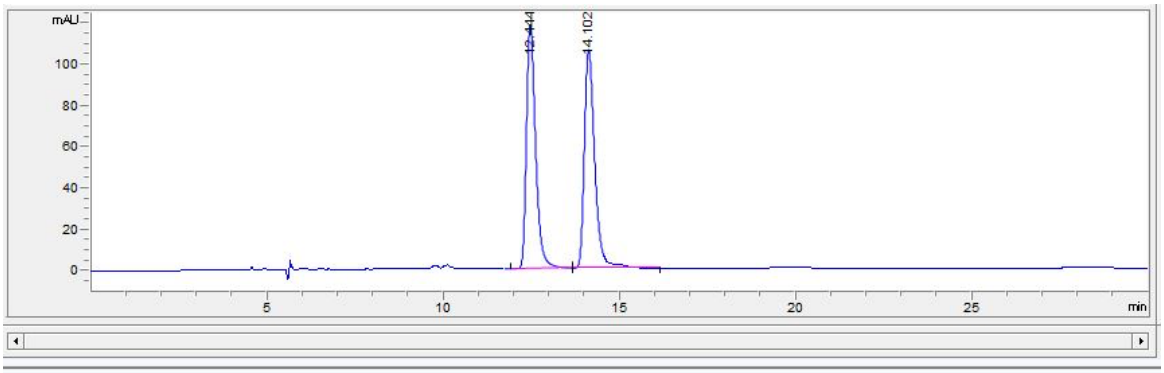
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.2, 164.2, 138.7, 127.2, 126.7, 123.4, 107.9, 107.7, 48.3, 42.1, 34.4, 33.9, 33.2, 27.2, 25.6, 24.9

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.12 – -152.66 (m), -157.62 (t, *J* = 21.6 Hz), -162.18 (td, *J* = 21.6, 4.2 Hz)

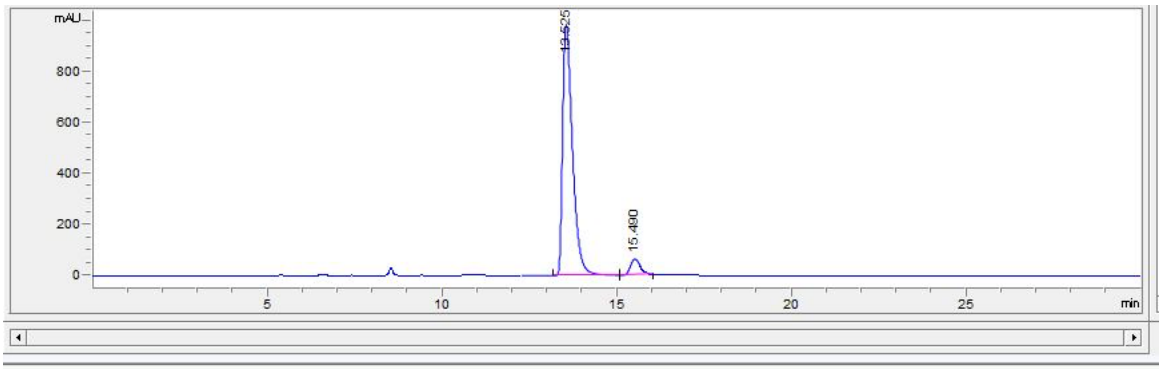
IR (ATR): 3285, 2935, 2856, 2360, 2341, 1778, 1668, 1630, 1520, 1303, 1091, 1003, 982, 705 cm^{-1}

HRMS (ESI): *m/z* calc. for [M+H] $C_{23}H_{24}F_5N_2O_3^+$: 471.1702. Found: 471.1704

HPLC analysis using chiral column (ChiralPak IA-3, 5µ column, 22 °C, 1.0 mL/min, 85:15 Hexanes:IPA, 210 nm, t_{major}: 13.5 min, t_{minor}: 15.5 min)

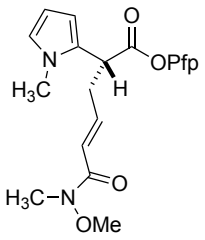


#	Time	Area	Height	Width	Area%	Symmetry
1	12.444	2128.3	117.9	0.2747	49.639	0.651
2	14.102	2159.3	105.7	0.3103	50.361	0.637



#	Time	Area	Height	Width	Area%	Symmetry
1	13.525	19252.1	988.2	0.2953	93.795	0.505
2	15.49	1273.6	63.1	0.3136	6.205	0.737

perfluorophenyl (*R*,*E*)-6-(methoxy(methyl)amino)-2-(1-methyl-1*H*-pyrrol-2-yl)-6-oxohex-4-enoate (42): Prepared according to general procedure A with **S13** as the electrophile. The title compound was obtained as a colorless oil (62 mg, 0.14 mmol, 72%) following purification by column (SiO_2: 5:1 then 2:1 pentane:EtOAc). The enantiomeric ratio (92:8) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -14.6$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.93 (dt, *J* = 14.8, 7.2 Hz, 1H), 6.71 – 6.47 (m, 2H), 6.32 – 6.01 (m, 2H), 4.16 (t, *J* = 7.5 Hz, 1H), 3.78 (d, *J* = 1.6 Hz, 6H), 3.22 (s, 3H), 3.17 (dt, *J* = 15.4, 7.9 Hz, 1H), 3.07 – 2.84 (m, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.2, 166.2, 141.9, 126.7, 123.4, 122.0, 108.0, 107.7, 61.8, 42.1, 34.7, 34.0, 32.4, 29.8, 27.2

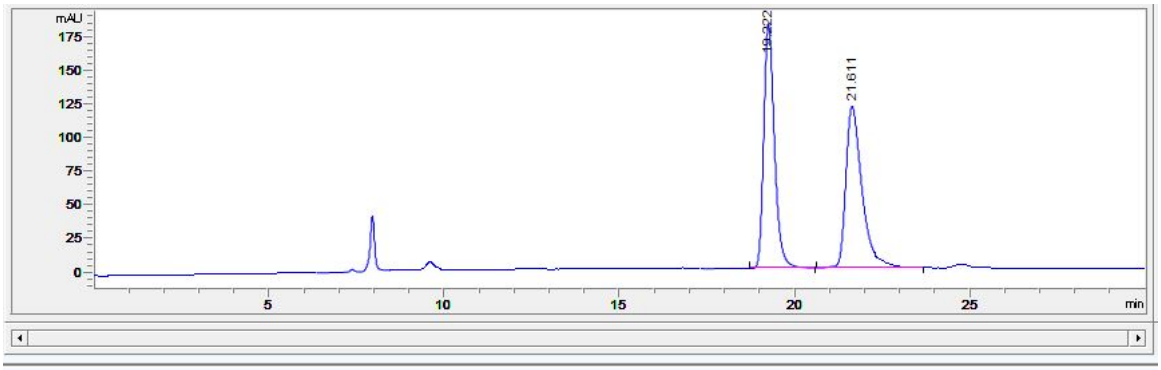
^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.12 – -152.85 (m), -157.72 (t, *J* = 21.7 Hz), -162.26 (td, *J* = 21.7, 4.4 Hz)

IR (ATR): 1782, 1666, 1634, 1520, 1384, 1093, 995, 717 cm^{-1}

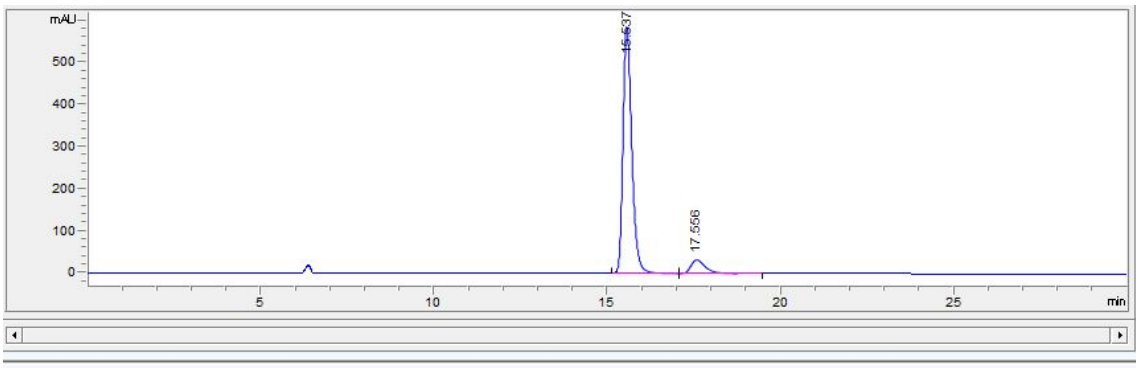
HRMS (APCI): *m/z* calc. for [M+H] $C_{19}H_{18}F_5N_2O_4^+$: 499.1710. Found: 499.1705

HPLC analysis using chiral column (ChiralPak IA-3, 5μ column, 22 °C, 1.0 mL/min, 85:15 Hexanes:IPA, 210 nm, t_{major}: 15.5 min, t_{minor}: 17.6 min)

Note: There is a discrepancy in retention times between the racemic and enantioenriched traces. The cause is unknown; however, it is consistent across multiple runs.



#	Time	Area	Height	Width	Area%	Symmetry
1	19.222	3848.5	181.3	0.3276	49.954	0.725
2	21.611	3855.6	119.7	0.4799	50.046	0.587



#	Time	Area	Height	Width	Area%	Symmetry
1	15.537	10422.5	591.3	0.2696	91.629	0.701
2	17.556	952.1	32.7	0.4354	8.371	0.608

perfluorophenyl (*R*)-2-(1-methyl-1*H*-pyrrol-2-yl)-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pent-4-enoate (43): Prepared according to general procedure D with **S16** as the electrophile. The title compound was obtained as a colorless oil (27 mg, 0.060 mmol, 37%) following purification by column (B-SiO_2, 40:1 pentane:Et_2O). The enantiomeric ratio (96:4) was determined by chiral HPLC in comparison with the racemate (see below).

$[\alpha]_D^{20} = -48.2$ (c = 1.0, $CHCl_3$)

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.61 (dd, *J* = 2.8, 1.8 Hz, 1H), 6.18 (dd, *J* = 3.8, 1.8 Hz, 1H), 6.11 (dd, *J* = 3.7, 2.8 Hz, 1H), 5.93 (s, 1H), 5.78 (s, 1H), 4.41 (dd, *J* = 9.9, 5.5 Hz, 1H), 3.67 (s, 3H), 2.96 (dd, *J* = 13.7, 10.0 Hz, 1H), 2.82 (dd, *J* = 13.6, 5.5 Hz, 1H), 1.28 (s, 6H), 1.27 (s, 6H)

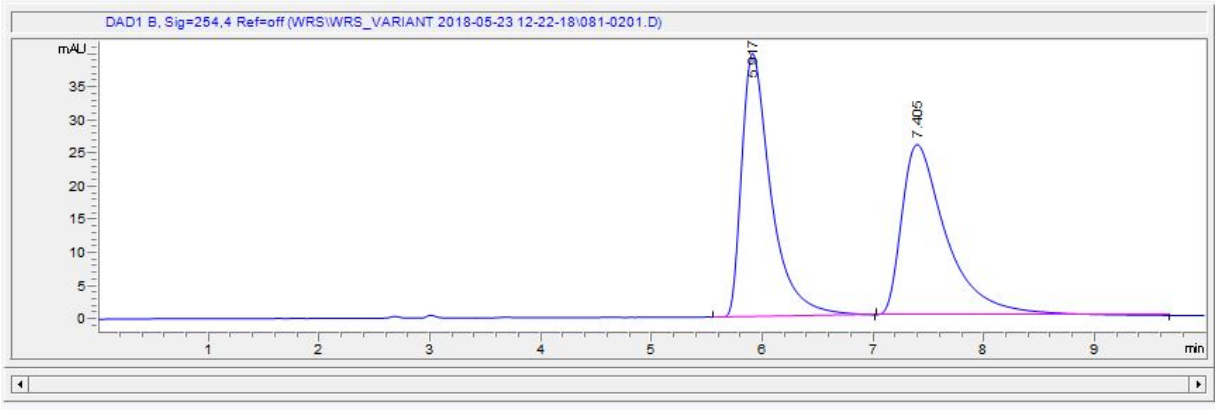
^{13}C NMR (126 MHz, $CDCl_3$): δ = 168.7, 133.3, 128.2, 122.9, 107.6, 107.5, 83.8, 42.9, 38.6, 33.9, 25.0, 24.9

^{19}F NMR (376 MHz, $CDCl_3$): δ = -151.89 (d, *J* = 17.5 Hz), -158.27 (t, *J* = 21.7 Hz), -162.58 (dd, *J* = 21.7, 17.5 Hz)

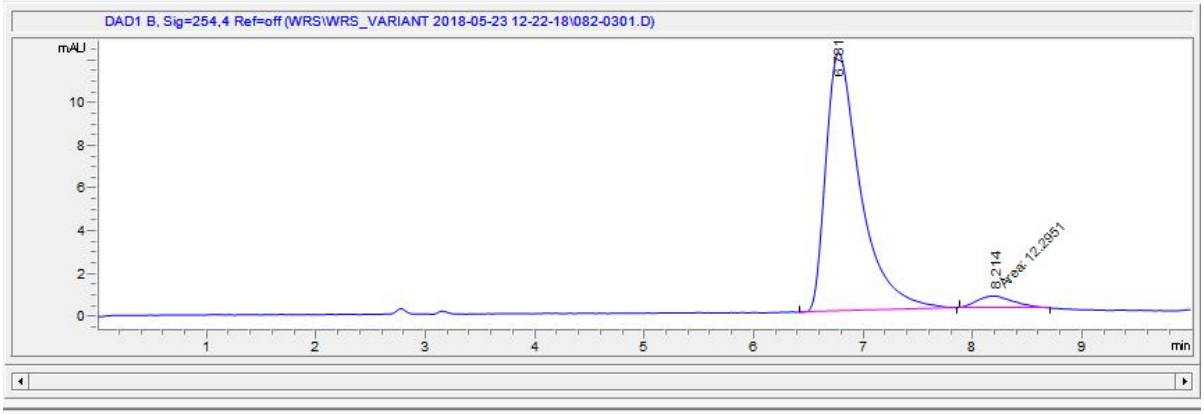
IR (ATR): 2979, 1788, 1521, 1371, 1312, 1214, 1143, 1004, 713 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{22}H_{24}BF_5NO_4^+$: 472.1713. Found: 472.1720

HPLC analysis using chiral column (ChiralPak IA-3, 5μ column, 22 °C, 1.0 mL/min, 800:1 Hexanes:IPA, 254 nm, t_{major}: 6.8 min, t_{major}: 8.2 min)



#	Time	Area	Height	Width	Area%	Symmetry
1	5.917	726.4	39.5	0.2766	50.078	0.537
2	7.405	724.2	25.6	0.4182	49.922	0.473



#	Time	Area	Height	Width	Area%	Symmetry
1	6.781	265	12	0.3288	95.566	0.529
2	8.214	12.3	5.3E-1	0.3881	4.434	0.909

perfluorophenyl (*R*,*E*)-5-(dimethyl(phenyl)silyl)-2-(1-methyl-1*H*-pyrrol-2-yl)pent-4-enoate (44): $Pd_2(dba)_3$ (5 mol%, 0.010 mmol, 4.6 mg), tri-(2-Furyl)phosphine (10 mol%, 0.020 mmol, 4.6 mg), and the N-Methylpyrrole acetic acid ester (0.20 mmol, 1.0 equiv) were added sequentially to an oven-dried 2-dram vial containing a magnetic stir bar and equipped with a Teflon insert screw cap. The vial was evacuated and backfilled with nitrogen (3 ×). Anhydrous 1,4-dioxane (2.0 mL, 0.1 M) and the mixture stirred for 1 hour. *i*Pr_2NEt (1.2 equiv, 0.25 mmol, 44 µL), **S14** (1.6 equiv, 0.32 mmol, 87 mg), and finally (*R*)-(–)-benzotetramisole (20 mol%, 0.04 mmol, 10. mg) were added sequentially to the stirring mixture. The solution was stirred at ambient temperature for 24 hours. The reaction was then diluted with 2.5 mL of petroleum ether (precipitation will occur) and passed through activated acidic Al_2O_3 (Brockmann I). The vial was washed with fresh Et_2O (2.5 mL) and passed through the Al_2O_3. The combined filtrates were concentrated and purified by column chromatography (SiO_2, 20:1 pentane:Et_2O). to give the title compound (65 mg, 0.14 mmol, 70%) as a colorless oil. The enantiomeric ratio (91:9) was determined by chiral HPLC in comparison with the racemate (see below).

$[\alpha]_D^{20} = -10.4$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 – 7.47 (m, 2H), 7.36 (dd, *J* = 5.6, 1.6 Hz, 3H), 6.64 (dd, *J* = 2.7, 1.8 Hz, 1H), 6.20 (dd, *J* = 3.7, 1.7 Hz, 1H), 6.17 – 6.11 (m, 2H), 6.03 (dt, *J* = 18.5, 1.1 Hz, 1H), 4.10 (dd, *J* = 9.3, 6.0 Hz, 1H), 3.65 (s, 3H), 3.08 (dddd, *J* = 14.5, 9.3, 6.5, 1.1 Hz, 1H), 2.83 (dtd, *J* = 14.6, 5.9, 1.4 Hz, 1H), 0.35 (s, 6H)

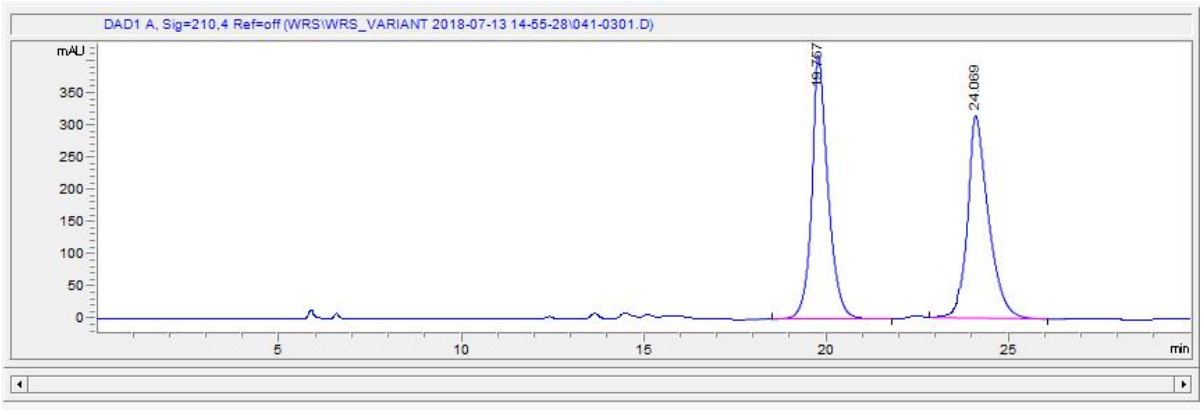
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.5, 143.5, 138.6, 133.9, 132.4, 129.1, 127.9, 127.4, 123.2, 108.0, 107.6, 42.8, 39.0, 34.0, -2.6

^{19}F NMR (376 MHz, $CDCl_3$): δ = -151.80 – -152.74 (m), -157.89 (t, *J* = 21.6 Hz), -162.32 (dd, *J* = 21.7, 17.2 Hz)

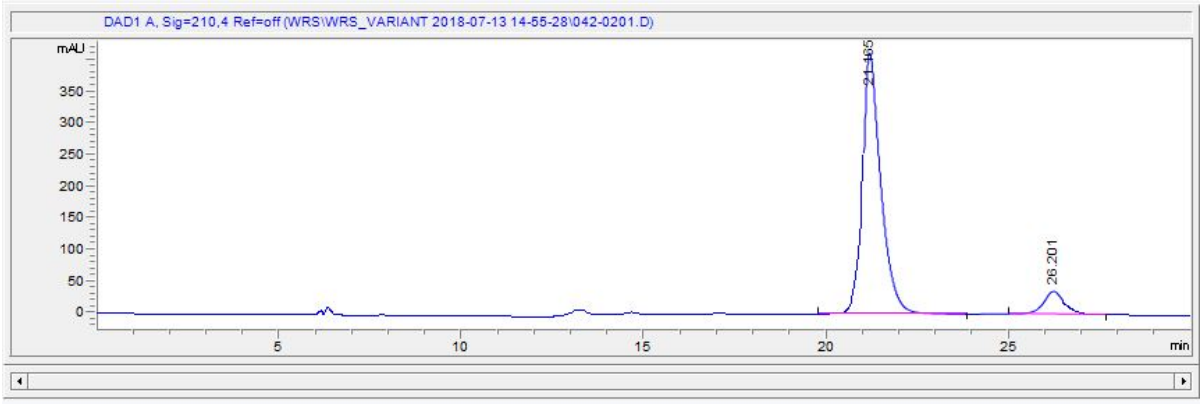
IR (ATR): 2957, 1784, 1520, 1249, 1091, 996, 822, 713 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{24}H_{22}F_5NO_4Si^+$: 480.1413. Found: 480.1416

HPLC analysis using chiral column (ChiralPak IB, 3µ column, 22 °C, 1.0 mL/min, 800:1 Hexanes:IPA, 210 nm, t_{major}: 21.7 min, t_{minor}: 26.2 min)

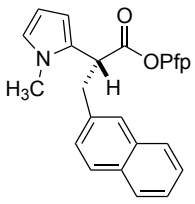


#	Time	Area	Height	Width	Area%	Symmetry
1	19.757	12544.5	407.2	0.4414	50.255	0.672
2	24.069	12417.4	312.4	0.5717	49.745	0.625



#	Time	Area	Height	Width	Area%	Symmetry
1	21.165	14381.2	410.7	0.5065	90.728	0.604
2	26.201	1469.7	36	0.5923	9.272	0.845

perfluorophenyl (*R*)-2-(1-methyl-1*H*-pyrrol-2-yl)-3-(naphthalen-2-yl)propanoate (45):



XantPhos PdG3 (9.5 mg, 5 mol%, 0.01 mmol), (*R*)-benzotetramisole (10 mg, 0.04 mmol, 20 mol%), N-methylpyrrole acetic acid ester (0.20 mmol, 1 equiv), and **S5** were added sequentially to an oven-dried 2-dram vial containing a magnetic stir bar and equipped with a Teflon insert screw cap. The vial was evacuated and backfilled with nitrogen (3 ×). Anhydrous Toluene (2 mL, 0.1 M) was then added followed by *i*Pr$_2$NEt (44 µL, 0.25 mmol, 1.2 equiv). The reaction mixture was stirred at room temperature for 24 hours and then diluted with 2.5 mL of petroleum ether (precipitation will occur) and passed through activated acidic Al_2O_3 (Brockmann I). The vial was washed with Et_2O (2.5 mL) and passed through the Al_2O_3. The alumina was then washed with Et_2O. The combined filtrates were concentrated and purified by column chromatography (SiO_2, 99:1 pentane:Et_2O) to afford the product (60 mg, 0.13 mmol, 67% yield) as a white solid. The enantiomeric ratio (98:2) was determined by chiral HPLC in comparison with the racemate (see below).

$[\alpha]_D^{20} = -12.8$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 –7.75 (m, 3H), 7.67 (d, *J* = 1.7 Hz, 1H), 7.52 – 7.42 (m, 2H), 7.30 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.59 (dd, *J* = 2.7, 1.8 Hz, 1H), 6.34 (dd, *J* = 3.7, 1.8 Hz, 1H), 6.18 (dd, *J* = 3.7, 2.7 Hz, 1H), 4.33 (dd, *J* = 8.4, 6.9 Hz, 1H), 3.69 (dd, *J* = 13.8, 8.4 Hz, 1H), 3.45 (s, 3H), 3.44 –3.36 (m, 1H)

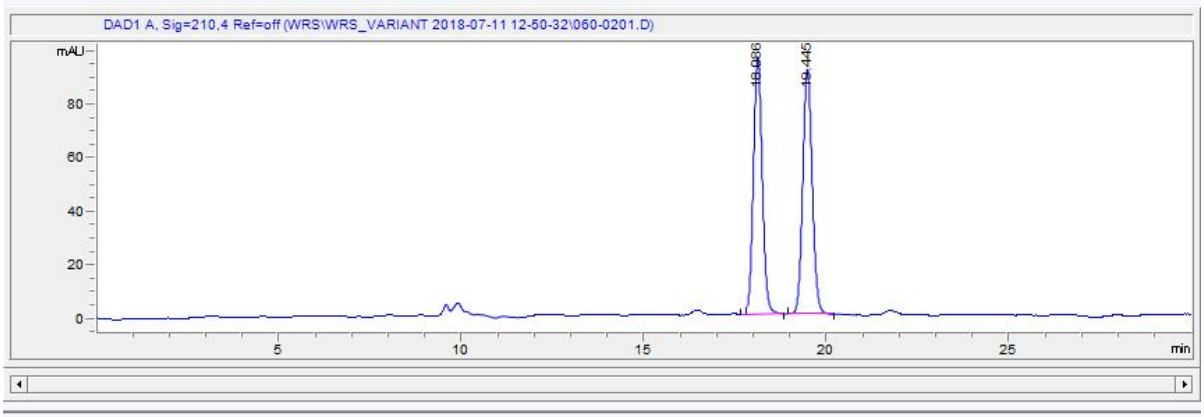
^{13}C NMR (101 MHz, $CDCl_3$): δ = 168.6, 135.5, 133.6, 132.5, 128.4, 127.8, 127.8, 127.7, 127.5, 127.2, 126.3, 125.9, 123.2, 108.0, 107.8, 45.0, 39.0, 33.9

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.17 (d, *J* = 17.5 Hz), -157.87 (t, *J* = 21.7 Hz), -162.29 (dd, *J* = 21.7, 17.5 Hz)

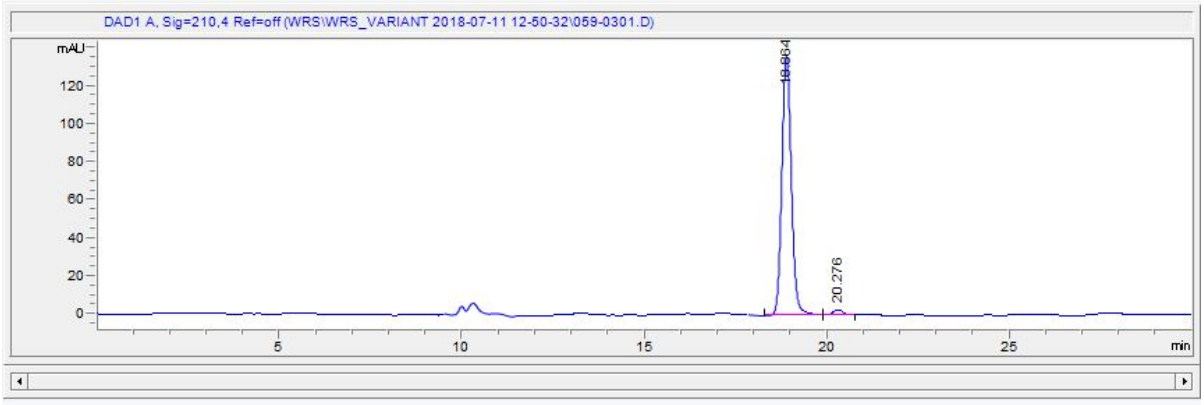
IR (ATR): 2927, 1781, 1519, 1302, 1091, 995, 815, 748, 715, 480 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{24}H_{17}F_5NO_2^+$: 446.1174. Found: 446.1179

HPLC analysis using chiral column (ChiralPak IA-3, 5µ column, 22 °C, 1.0 mL/min, 99:1 Hexanes:IPA, 210 nm, t_{major}: 18.9 min, t_{major}: 20.3 min)

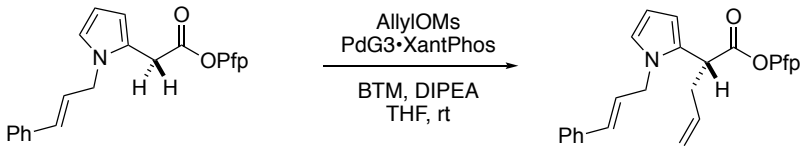


#	Time	Area	Height	Width	Area%	Symmetry
1	18.086	1625.3	96.2	0.2611	49.783	0.89
2	19.445	1639.5	91.3	0.2776	50.217	0.901



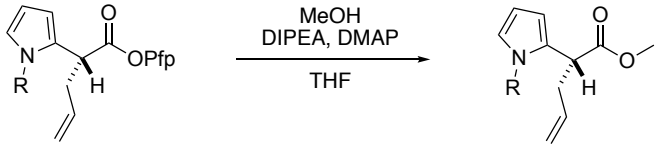
#	Time	Area	Height	Width	Area%	Symmetry
1	18.864	2468.1	137.2	0.2778	97.951	0.869
2	20.276	51.6	2.8	0.2716	2.049	0.908

Large Scale Allylations:



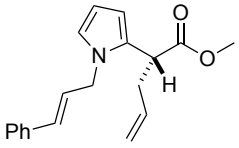
XantPhos PdG3 (119 mg, 5 mol%, 0.13 mmol), (*R*)-benzotetramisole (116 mg, 0.5 mmol, 20 mol%) and the *N*-cinnamylpyrrole pentafluorophenyl ester (1.0 g, 2.5 mmol, 1 equiv) were added sequentially to a flame-dried 100 mL RBF containing a magnetic stir bar. The vessel was evacuated and backfilled with nitrogen (3 ×). Anhydrous THF (25 mL, 0.1 M) was then added followed by allyl mesylate (420 mg, 3.1 mmol, 1.3 equiv) and *i*Pr_2NEt (0.54 mL, 3.1 mmol, 1.3 equiv). The reaction mixture was stirred at room temperature for 24 hours and then diluted with 25 mL of petroleum ether (precipitation will occur) and passed through activated acidic Al_2O_3 (Brockmann I). The vial was washed with Et_2O (25 mL) and passed through the Al_2O_3. The alumina was then washed with Et_2O (25 mL). The combined filtrates were concentrated and purified by column chromatography (SiO_2, 40:1 pentane:Et_2O) to give the product (0.9 g, 2.0 mmol, 80%) as a colorless oil. The enantiomeric ratio (98:2) was determined by chiral HPLC is comparison with a racemate. See above for characterization and HPLC traces.

Derivatizations:



General Procedure for the Formation of Methyl Esters from the Corresponding Pfp Esters: Starting pentaflurophenol ester (1.0 equiv) was dissolved in THF(0.1 M). Methanol (5.0 equiv), *N*,*N*-diisopropylethylamine (5.0 equiv), and *N*,*N*-dimethylaminopyridine (20%) were added and the solution stirred for 24 hours. After, the mixture was diluted with Et_2O and washed with 1M HCl(*aq*) (2 ×) then sat. Na_2CO_3(*aq*) (2 ×) and dried over $MgSO_4$(s). The solvent was removed under reduced pressure to afford the pure methyl ester as a liquid.

methyl (*R*)-2-(1-cinnamyl-1*H*-pyrrol-2-yl)pent-4-enoate (46): Prepared according to general procedure. The title compound was obtained as a colorless oil (0.18 g, 0.61 mmol, 95%). The enantiomeric ratio (98:2) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20} = -56.8$ (c = 1.0, $CHCl_3$)

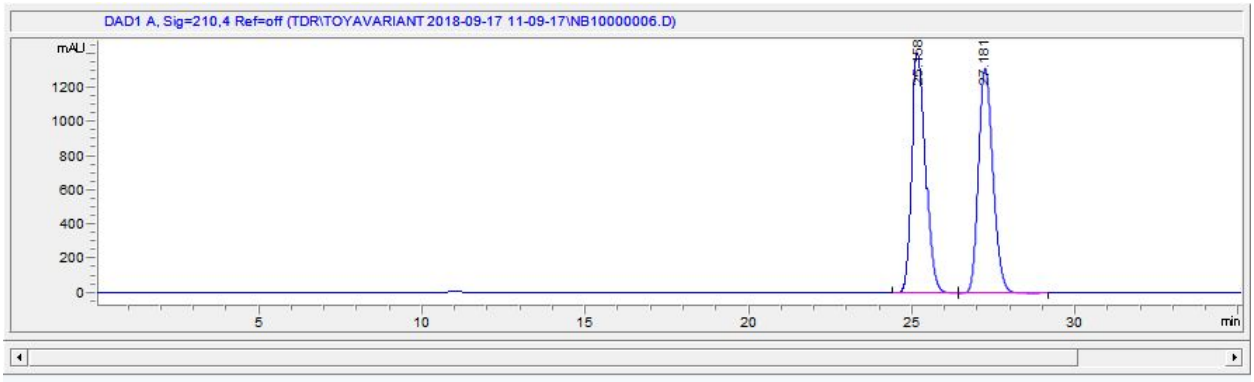
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 – 7.34 (m, 5H), 6.72 (t, *J* = 2.3 Hz, 1H), 6.33 (s, 2H), 6.37 – 6.23 (m, 2H), 5.91 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1H), 5.34 – 5.12 (m, 2H), 4.93 – 4.69 (m, 2H), 3.94 (dd, *J* = 8.6, 6.8 Hz, 1H), 3.72 (s, 3H), 3.03 – 2.81 (m, 1H), 2.87 – 2.62 (m, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.8, 136.2, 135.2, 131.5, 129.1, 128.5, 127.7, 126.3, 125.7, 121.4, 117.1, 107.6, 107.2, 52.0, 48.6, 43.0, 36.3

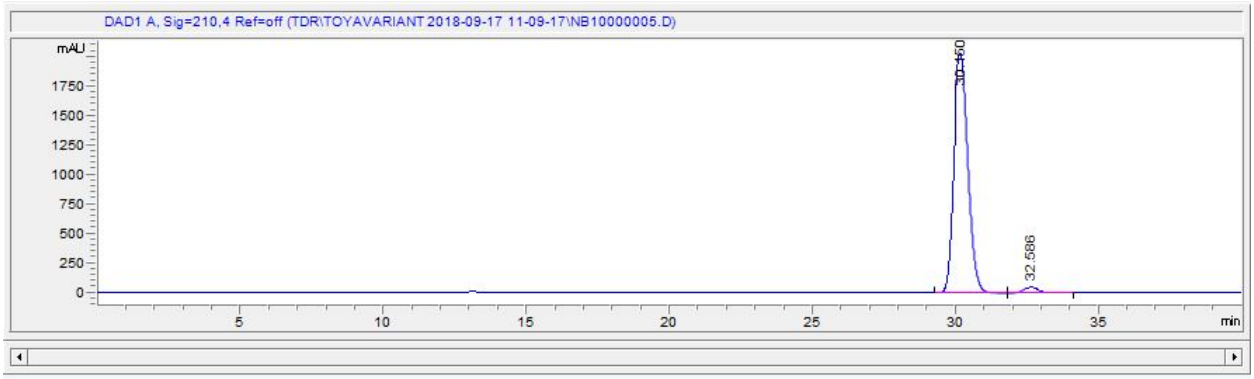
IR (ATR): 2950, 1738, 1642, 1479, 1442, 1288, 1233, 1166, 969, 919, 715 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{19}H_{22}NO_2^+$: 422.1174. Found: 442.1178

HPLC analysis using chiral column (Phenomenex Cellulose-1, 3µ column, 22 °C, 1.0 mL/min, 90:10 Hexanes:IPA, 210 nm, t_{minor}: 30.2 min, t_{major}: 32.5 min).

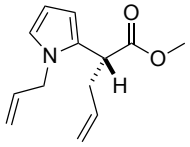


#	Time	Area	Height	Width	Area%	Symmetry
1	25.158	40162.2	1406.6	0.4431	49.920	0.782
2	27.181	40290.4	1308.3	0.4773	50.080	0.784



#	Time	Area	Height	Width	Area%	Symmetry
1	30.15	72486.6	2037.7	0.557	97.644	0.795
2	32.586	1749.2	47.9	0.562	2.356	0.826

methyl (*R*)-2-(1-allyl-1*H*-pyrrol-2-yl)pent-4-enoate (49): Prepared according to general procedure. The title compound was obtained as a colorless oil (180 mg, 0.82 mmol, 91%). The enantiomeric ratio (98:2) was determined by chiral HPLC in comparison with the racemate (see below).



$[\alpha]_D^{20}$ = (c = 1.0, $CHCl_3$)

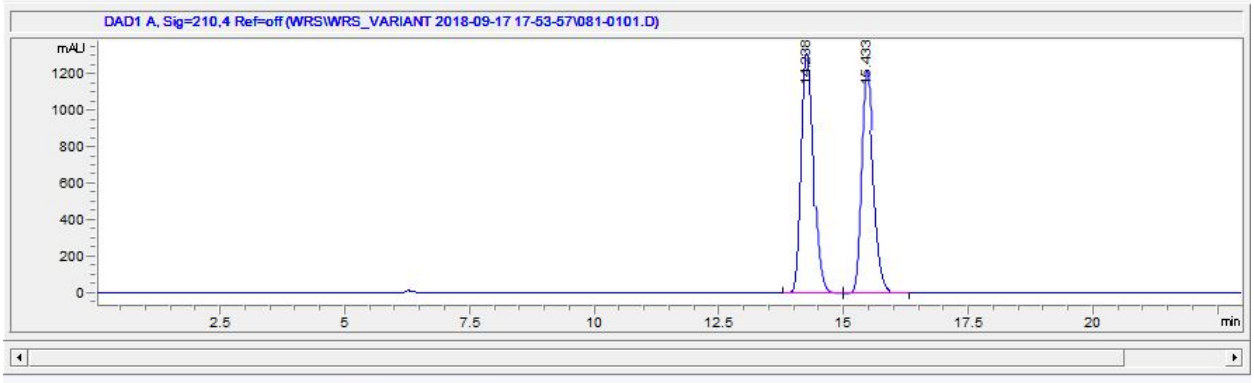
^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.59 (dd, *J* = 2.7, 1.9 Hz, 1H), 6.15 – 6.08 (m, 2H), 5.92 (ddt, *J* = 17.1, 10.2, 5.0 Hz, 1H), 5.82 – 5.69 (m, 1H), 5.19 – 5.07 (m, 2H), 5.03 (ddt, *J* = 10.2, 2.1, 1.1 Hz, 1H), 4.91 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.61 – 4.42 (m, 2H), 3.68 – 3.66 (m, 1H), 3.65 (s, 3H), 2.86 –2.76 (m, 1H), 2.60 – 2.51 (m, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.1, 135.4, 134.5, 129.2, 121.6, 117.2, 116.7, 107.6, 107.1, 52.2, 49.2, 43.1, 36.4

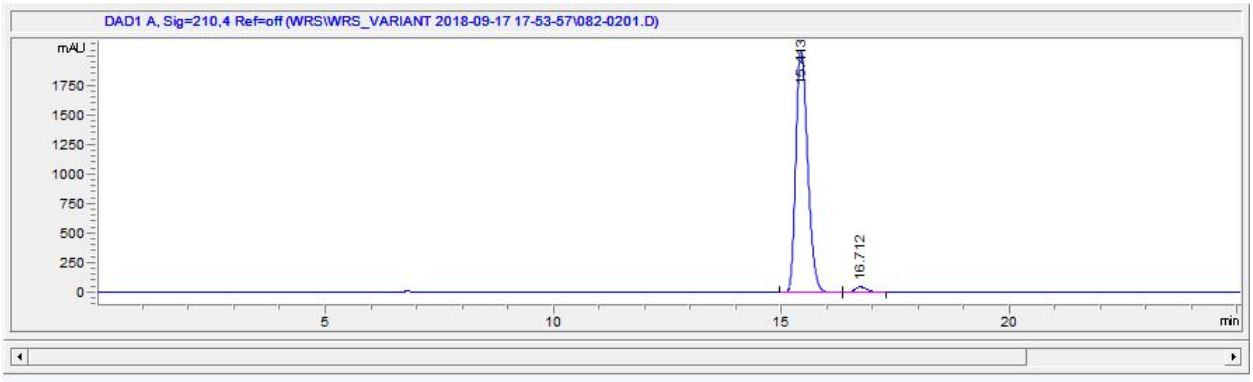
IR (ATR): 2951, 1732, 1642, 1479, 1435, 1283, 1250, 1165, 1073, 990, 917, 709, 614, 558 cm^{-1}

HRMS (ESI): *m/z* calc. for [M+H] $C_{13}H_{18}NO_2^+$: 220.1332. Found: 220.1336

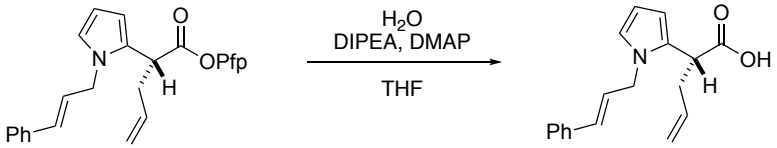
HPLC analysis using chiral column (Phenomenex Cellulose-1, 22 °C, 1.0 mL/min, 85:15 Hexanes:IPA, 210 nm, t_{major}: 15.4 min, t_{major}: 16.7 min)



#	Time	Area	Height	Width	Area%	Symmetry
1	14.238	21497.6	1319.7	0.2501	49.930	0.744
2	15.433	21558.3	1220.6	0.2701	50.070	0.745



#	Time	Area	Height	Width	Area%	Symmetry
1	15.413	37251.2	2044.8	0.2825	97.611	0.728
2	16.712	911.6	48.6	0.2869	2.389	0.767



(*R*)-2-(1-cinnamyl-1*H*-pyrrol-2-yl)pent-4-enoic acid (47): Starting pentaflurophenol ester (0.65 mmol, 1.0 equiv) was dissolved in THF (6.5 mL, 0.1 M). Methanol (3.3 mmol, 5.0 equiv), *N*,*N*-diisopropylethylamine (3.3 mmol, 5.0 equiv), and *N*,*N*-dimethylaminopyridine (0.13 mmol, 20. mol%) were added and the solution stirred for 24 hours. After, the mixture was diluted with Et_2O (15 mL) and washed with 1M HCl(*aq*) (2 × 15 mL) and dried over $MgSO_4$(s). The solvent was removed under reduced pressure and the crude mixture purified by column chromatography (SiO_2, 9:1 pentane:Et_2O then pure Et_2O) to afford the product (165 mg, 0.59 mmol, 90%) as a colorless solid. The enantiomeric excess (98:2) was determined by chiral HPLC in comparison with a racemate.[20]

$[\alpha]_D^{20} = -53.6$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.08 (br s, 1H), 7.39 – 7.30 (m, 4H), 7.30 – 7.23 (m, 1H), 7.71 (t, *J* = 2.3 Hz, 1H), 6.30 (d, *J* = 1.8 Hz, 2H), 6.24 – 6.19 (m, 2H), 5.78 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1H), 5.13 (dd, *J* = 17.1, 1.6 Hz, 1H), 5.05 (d, *J* = 10.2 Hz, 1H), 4.81 – 4.63 (m, 2H), 3.74 (dd, *J* = 8.1, 7.2 Hz, 1H), 2.90 – 2.77 (m, 1H), 2.69 – 2.55 (m, 1H)

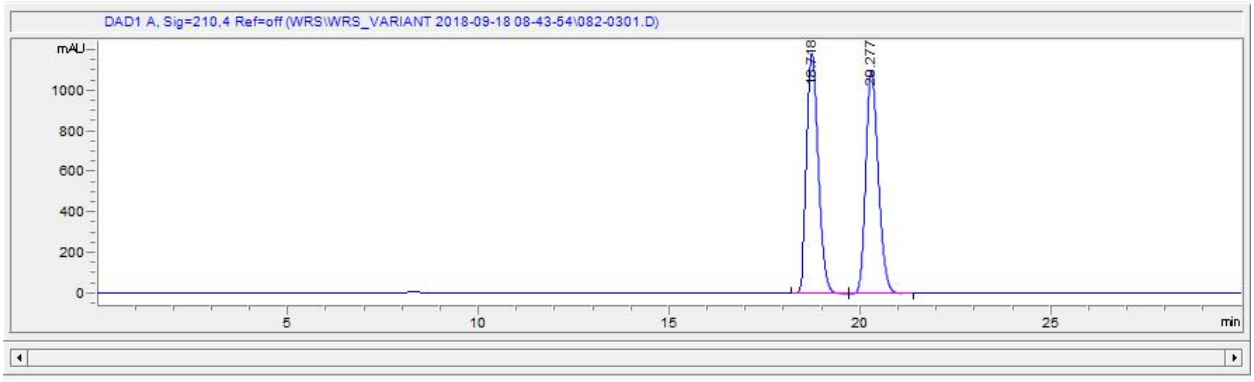
^{13}C NMR (101 MHz, $CDCl_3$): δ = 179.0, 136.4, 135.0, 131.9, 128.7, 128.5, 127.9, 126.6, 125.7, 121.8, 117.6, 107.8, 107.7, 48.9, 42.9, 35.9

IR (ATR): 3026, 1708, 1642, 1549, 1479, 1443, 1290, 968, 920, 715 cm^{-1}

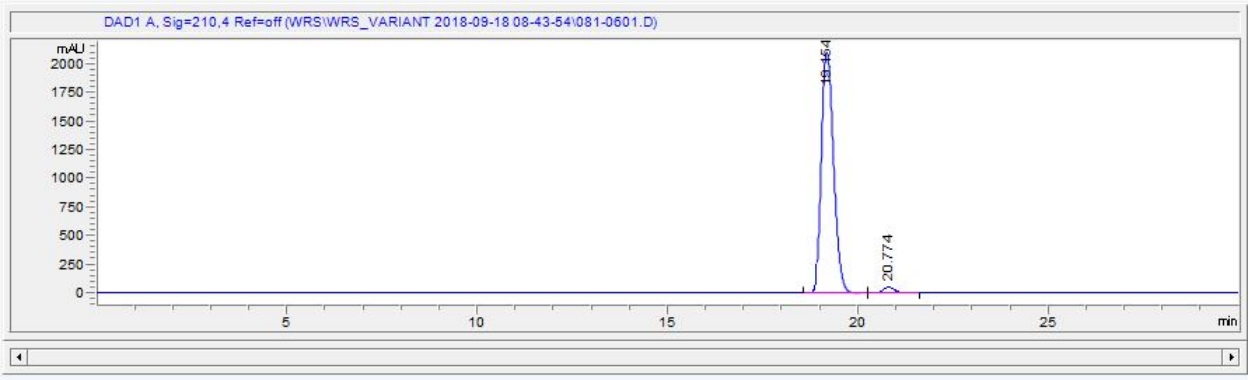
HRMS (ESI): *m/z* calc. for [M+Na] $C_{18}H_{19}NNaO_2^+$: 304.1308. Found: 304.1309

HPLC analysis using chiral column (Phenomenex Cellulose-1, 3μ column, 22 °C, 1.0 mL/min, 90:10 Hexanes:IPA, 210 nm, t_{major}: 19.1 min, t_{minor}: 20.8 min).

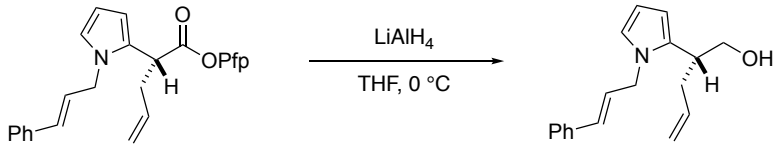
[20] The carboxylic acid was converted to the corresponding methyl ester by treatment with TMS diazomethane.



#	Time	Area	Height	Width	Area%	Symmetry
1	18.718	24906.8	1187.2	0.3228	49.973	0.763
2	20.277	24933.4	1097.7	0.351	50.027	0.764



#	Time	Area	Height	Width	Area%	Symmetry
1	19.154	47027.6	2094.2	0.352	97.622	0.747
2	20.774	1145.8	49.9	0.3536	2.378	0.782



(*R*)-2-(1-cinnamyl-1*H*-pyrrol-2-yl)pent-4-en-1-ol (48): Starting pentaflurophenol ester (0.63 mmol, 1.0 equiv) was dissolved in THF (6.5 mL, 0.1 M). The solution was cooled to 0 °C. $LiAlH_4$ (1M in THF, 0.69 mmol, 1.1 equiv) was added dropwise. The reaction was warmed to room temperature and stirred for 1 hour. Upon completion (TLC) the reaction was slowly quenched with 1M HCl(*aq*) (10 mL) (*gas evolution!*). The mixture was extracted with Et_2O (2 × 10 mL) and dried over $MgSO_4$(s). The solvent was removed under reduced pressure to afford the corresponding alcohol (0.15 g, 0.56 mmol, 89%) as a colorless oil. The enantiomeric ratio (98:2) was determined by chiral HPLC in comparison to a racemate.

$[\alpha]_D^{20} = -3.8$ (c = 1.0, $CHCl_3$)

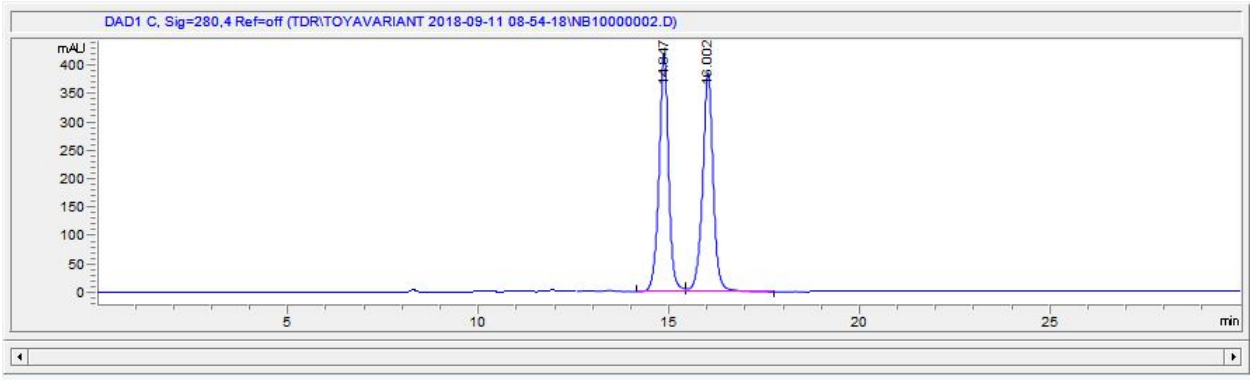
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 – 7.31 (m, 5H), 6.7 (dd, *J* = 2.8, 1.7 Hz, 1H), 6.32 (s, 2H), 6.26 (t, *J* = 3.2 Hz, 1H), 6.16 (dd, *J* = 3.6, 1.7 Hz, 1H), 5.81 (ddt, *J* = 17.2, 10.1, 7.1 Hz, 1H), 5.25 – 4.91 (m, 2H), 4.85 – 4.61 (m, 2H), 3.81 – 3.62 (m, 2H), 3.13 – 2.91 (m, 1H), 2.45 (q, *J* = 7.1 Hz, 2H), 2.01 (s, 1H)

^{13}C NMR (101 MHz, $CDCl_3$): δ = 136.3, 133.0, 131.7, 128.6, 127.8, 126.4, 126.0, 120.9, 116.6, 107.5, 105.5, 66.1, 48.5, 39.1, 36.7

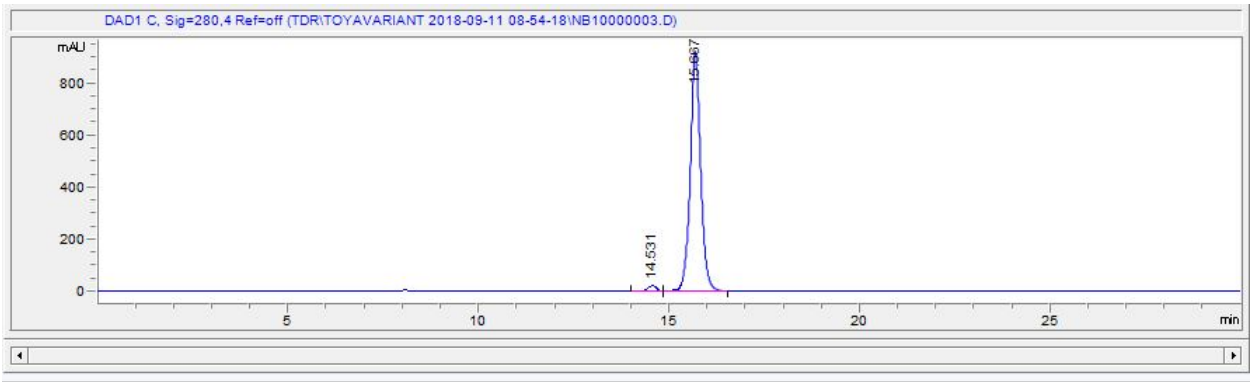
IR (ATR): 3406, 2924, 2869, 1599, 1478, 1443, 1357, 1287, 1064, 1025, 996, 913, 691 cm^{-1}

HRMS (ESI): *m/z* calc. for [M+Na] $C_{18}H_{21}NNaO^{+}$: 290.1515. Found: 290.1516

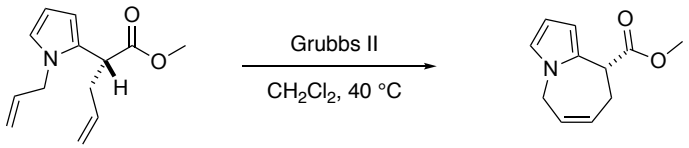
HPLC analysis using chiral column (ChiralPak IB, 5µ column, 22 °C, 1.0 mL/min, 85:15 Hexanes:IPA, 280 nm, t_{minor}: 14.5 min, t_{major}: 15.7 min).



#	Time	Area	Height	Width	Area%	Symmetry
1	14.847	7394.6	419.5	0.2657	49.715	1.035
2	16.002	7479.3	386	0.29	50.285	1.001



#	Time	Area	Height	Width	Area%	Symmetry
1	14.531	369.2	21.7	0.2548	2.053	1.079
2	15.667	17613.3	920.8	0.2832	97.947	0.901



methyl (*R*)-8,9-dihydro-5*H*-pyrrolo[1,2-*a*]azepine-9-carboxylate (50): Starting methyl ester (50. mg, 0.22 mmol, 1.0 equiv) was added to an oven-dried 2-dram vial with a magnetic stir bar equipped with a Teflon insert screw cap then diluted with CH_2Cl_2 (2.2 mL, 0.1 M). The solution was degassed for two minutes by bubbling argon through the mixture. Grubbs II (8.5 mg, 0.010 mmol, 5.0 mol%) was added and the mixture degassed with argon for two minutes. A vent needle was inserted into the Teflon septa and the mixture heated to 40 °C. Upon completion (TLC, *ca.* 1 hour), the solvent was removed under reduced pressure and the crude mixture purified by column chromatography (SiO_2, 9:1 pentane:Et_2O) to afford the *title compound* (34 mg, 0.18 mmol, 81%) as a colorless oil. The enantiomeric ratio (98:2) was determined by comparison to a racemate (see below).

$[\alpha]_D^{20} = -6.6$ (c = 1.0, $CHCl_3$)

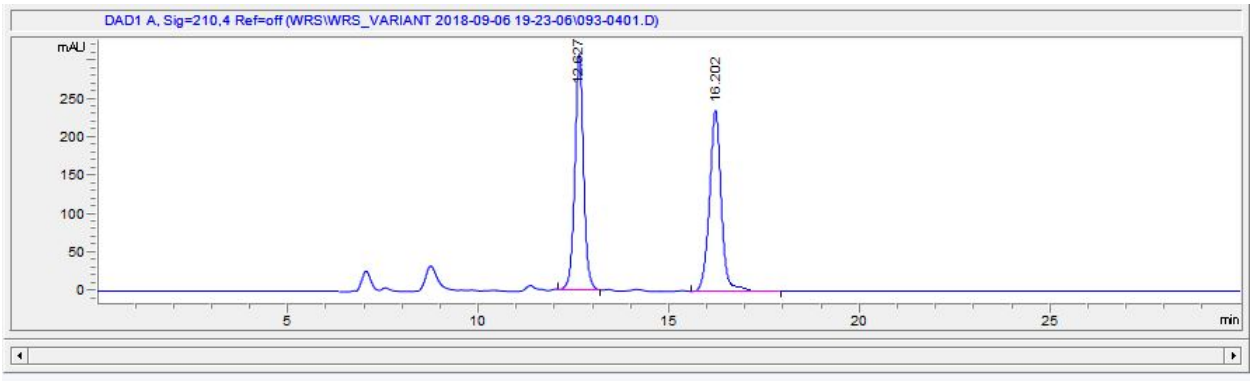
^{1}H NMR (600 MHz, $CDCl_3$): δ = 6.54 (app. q, *J* = 2.4 Hz, 1H), 6.02 (app. q, *J* = 2.9 Hz, 1H), 5.95 (dd, *J* = 2.9, 2.5 Hz, 1H), 5.73 (s, 2H), 4.51 (qt, *J* = 17.6, 2.8 Hz, 2H), 4.11 (dt, *J* = 6.3, 3.0 Hz, 1H), 3.76 (s, 3H), 2.78 (dd, *J* = 17.6, 8.3 Hz, 1H), 2.58 (d, *J* = 18.2 Hz, 1H)

^{13}C NMR (151 MHz, $CDCl_3$): δ = 173.1, 130.6, 129.4, 123.6, 122.4, 107.2, 106.4, 52.3, 47.1, 42.3, 32.1

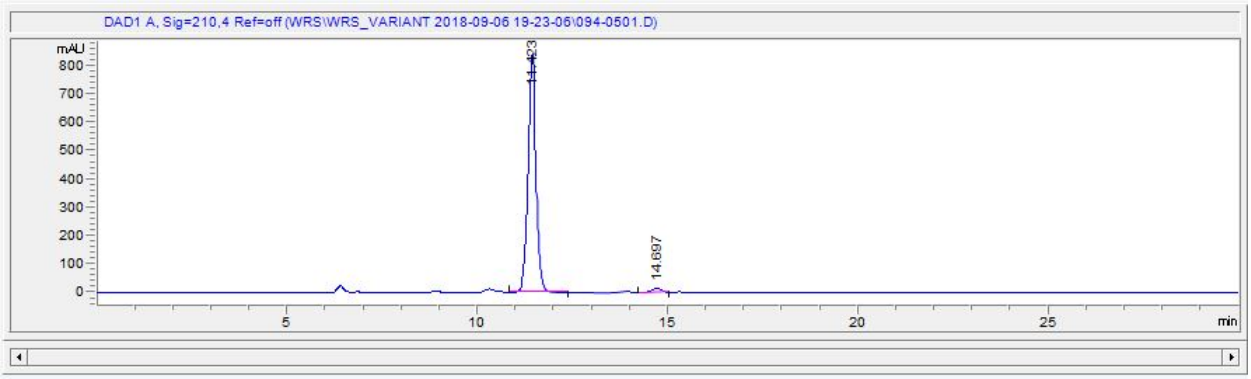
IR (ATR): 2952, 1736, 1487, 1439, 1211, 1167, 717 cm^{-1}

HRMS (GC/HRMS): *m/z* calc. for $[M–CH_3+H]^+$: 178.0863. Found: 178.0868

HPLC analysis using chiral column (ChiralPak IB, 5µ column, 22 °C, 1.0 mL/min, 85:15 Hexanes:IPA, 210 nm, t_{minor}: 11.4 min, t_{major}: 14.7 min).

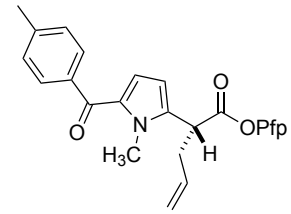


#	Time	Area	Height	Width	Area%	Symmetry
1	12.627	5057	311.8	0.2412	49.724	1.007
2	16.202	5113.1	237.6	0.321	50.276	0.978



#	Time	Area	Height	Width	Area%	Symmetry
1	11.423	12278	843.4	0.2158	97.877	0.965
2	14.697	266.3	15.2	0.2671	2.123	1.228

perfluorophenyl (*R*)-2-(1-methyl-5-(4-methylbenzoyl)-1*H*-pyrrol-2-yl)pent-4-enoate (53):



Prepared according to general procedure B with **S1** as the electrophile. The title compound was obtained as a yellow oil (83 mg, 90%) following purification by column (SiO_2: 50:1 pentane:Et_2O). The enantiomeric ratio (91:9) was determined by chiral HPLC in comparison with the racemate (see below).

$[\alpha]_D^{20} = -131.1$ (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.96 – 7.62 (m, 2H), 7.42 – 7.16 (m, 2H), 6.74 (d, *J* = 4.2 Hz, 1H), 6.32 (d, *J* = 4.2 Hz, 1H), 5.96 (ddt, *J* = 17.0, 10.2, 6.9 Hz, 1H), 5.33 – 5.12 (m, 2H), 4.25 (dd, *J* = 8.5, 6.7 Hz), 4.01 (s, 3H), 3.18 – 2.91 (m, 1H), 2.84 (dtt, *J* = 14.5, 6.6, 1.4 Hz, 1H), 2.44 (s, 3H)

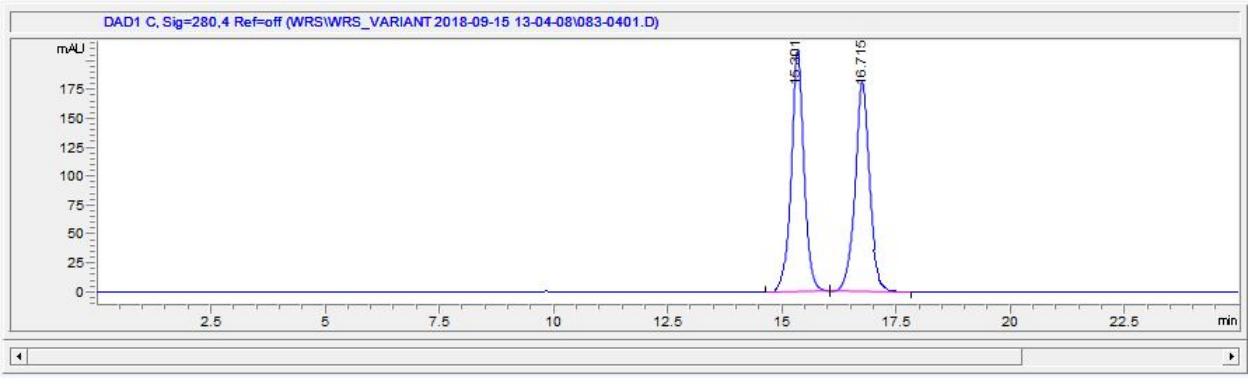
^{13}C NMR (101 MHz, $CDCl_3$): δ = 186.2, 167.8, 142.3, 137.2, 136.7, 133.4, 131.9, 129.6, 128.8, 122.4, 118.9, 108.1, 42.9, 36.1, 33.1, 21.6

^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.17 – -152.51 (m), -157.45 (t, *J* = 21.6 Hz), -161.82 – -162.38 (m)

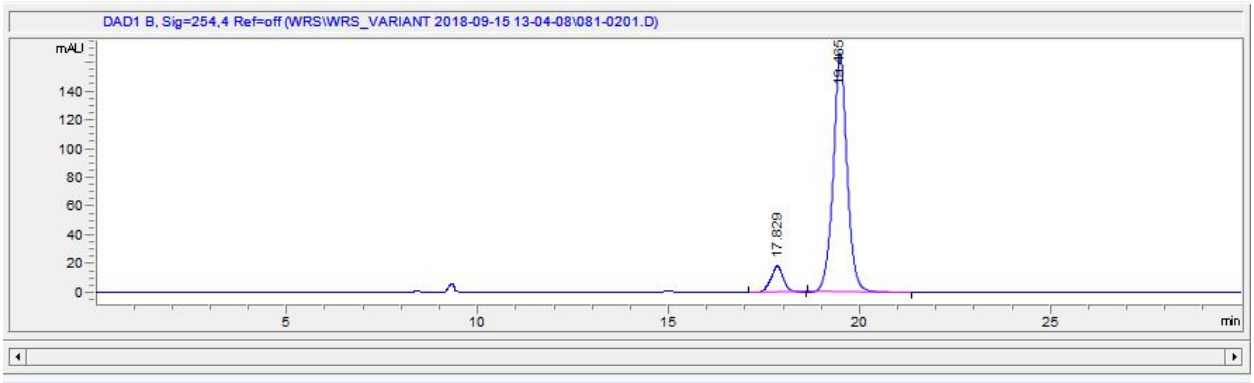
IR (ATR): 2855, 2669, 1782, 1606, 1518, 1476, 1373, 1262, 1154, 1084, 992, 834, 791, 747 cm^{-1}

HRMS (APCI): *m/z* calc. for [M+H] $C_{24}H_{19}F_5NO_2^+$: 464.1280. Found: 464.1279

HPLC analysis using chiral column (ChiralPak IB, 5μ column, 22 °C, 1.0 mL/min, 99:1 Hexanes:IPA, 210 nm, t_{minor}: 17.8 min, t_{major}: 19.5 min)



#	Time	Area	Height	Width	Area%	Symmetry
1	15.301	4010.2	206.3	0.2887	49.903	0.929
2	16.715	4025.9	180	0.331	50.097	0.924



#	Time	Area	Height	Width	Area%	Symmetry
1	17.829	426.1	18.8	0.3379	9.145	1.069
2	19.465	4233.5	166.5	0.3746	90.855	0.927