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Pyridylacetic acids and related systems as alkylheteroarene surrogates in the asymmetric decarboxylative Michael addition

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Contents

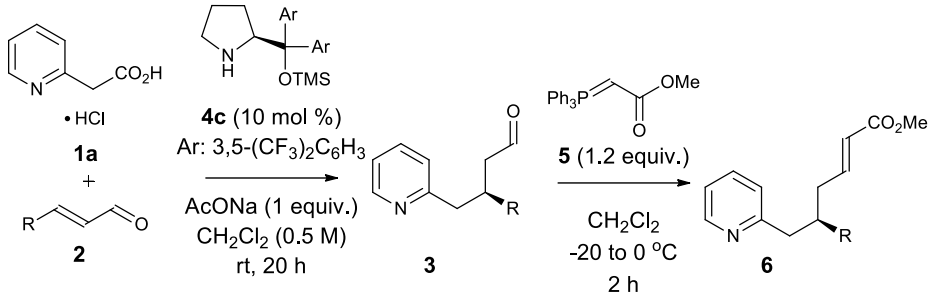
1. General methods

NMR spectra were acquired on a Bruker Ultra Shield 700 instrument, running at 700 MHz for ^{1}H and 176 MHz for ^{13}C, respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$: 7.26 ppm for ^{1}H NMR, 77.16 ppm for ^{13}C NMR). Mass spectra were recorded on a Bruker Maxis Impact spectrometer using electrospray (ES+) ionization (referenced to the mass of the charged species). Analytical thin layer chromatography (TLC) was performed using pre-coated aluminum-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or I_2 stain. Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification. For flash chromatography (FC) silica gel (Silica gel 60, 230-400 mesh, Fluka). The enantiomeric ratio (er) of the products were determined by Ultra Performance Convergence Chromatography (UPC[2]) or HPLC using Daicel Chiralpak IA, IB, IC and IG columns as chiral stationary phases. Aldehyde **2i** was synthetized according to the literature procedure.[1] Pyridine and heterocyclic derivatives **9**, **11a**, **11b** were prepared from the corresponding starting materials following the literature procedure.[2]

[1] G. Sirasani, T. Paul Rodrigo and B. Andrade, *Tetrahedron* 2011, **67***,* 2197-2205.

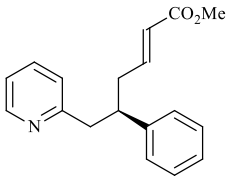
[2] (*a*) T. L. Gilchrist and A. Rahman, *J. Chem. Soc., Perkin Trans. 1*, 1998, ***7***, 1203-1208; (*b*) R. Shang, Z.-W. Yang, Y. Wang, S.-L. Zhang and L. Liu, *J. Am. Chem. Soc.* 2010, ***132***, 14391-14393.

2. Asymmetric decarboxylative Michael addition – general procedure



In an ordinary 4 mL glass vial equipped with a magnetic stirring bar, 2-pyridylacetic acid hydrochloride **1a** (17.3 mg; 0.1 mmol), α,β-unsaturated aldehyde **2** (0.1 mmol) and catalyst **4c** (6.0 mg, 0.01 mmol) were placed. Subsequently, dichloromethane (0.2 mL) and sodium acetate (8.2 mg, 0.1 mmol) were added. The progress of the reaction was controlled by ^{1}H NMR spectroscopy. After full conversion of the starting material **2**, the reaction mixture was diluted with dichloromethane (1 mL) and cooled to -20 °C. Then (methoxycarbonylmethylene)triphenylphosphorane **5** (40 mg; 0.12 mmol) was added to the vial and stirred at 0 °C for 2 hours. Subsequently, the solvent was removed under reduced pressure and the obtained residue was directly subjected to flash chromatography on silica gel to afford pure product **6**.

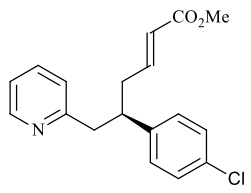
Methyl (*R*,*E*)-5-phenyl-6-(pyridin-2-yl)hex-2-enoate (6a)



Compound **6a** was obtained according to general procedure from (*E*)-3-phenylprop-2-enal **2a** in 67% yield (18.9 mg) after purification by FC (*n*-hexane:ethyl acetate; gradient from 3:1 to 1:1). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.51 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 7.44 (td, *J* = 7.6, 1.8 Hz, 1H), 7.24 – 7.20 (m, 2H), 7.17 – 7.13 (m, 1H), 7.12 – 7.09 (m, 2H), 7.04 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 6.85 (dt, *J* = 7.8, 1.1 Hz, 1H), 6.80 (dt, *J* = 15.6, 7.3 Hz, 1H), 5.72 (dt, *J* = 15.6, 1.5 Hz, 1H), 3.64 (s, 3H), 3.38 – 3.34 (m, *J* = 7.4 Hz, 1H), 3.12 (dd, *J* = 13.6, 7.1 Hz, 1H), 3.08 – 3.03 (m, 1H), 2.58 (td, *J* = 7.4, 1.5 Hz, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 166.7, 159.7, 149.2, 147.0, 143.2, 136.0, 128.4 (2C), 127.5 (2C), 126.5, 123.6, 122.4, 121.1, 51.2, 45.2, 45.1, 38.4. HRMS calculated for $C_{18}H_{20}NO_2^+$ [M+H]+ m/z: 282.1489, found: 282.1496. The er was determined by HPLC using a chiral Chiralpack IG

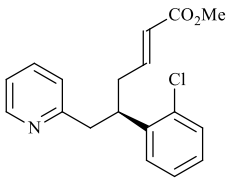
column [hexane:*i*-PrOH, 95:5]; flow rate 1.0 mL/min; τ_{major} = 22.6 min; τ_{minor} = 26.0min, (er 99:1); $[\alpha]_L^{20}$ = -30.4; (*c* = 1.05; $CHCl_3$).

Methyl (*R*,*E*)-5-(4-chlorophenyl)-6-(pyridin-2-yl)hex-2-enoate (6b)



Compound **6b** was obtained according to general procedure from (*E*)-3-(4-chlorophenyl)prop-2-enal **2b** in 79% yield (25.0 mg) after purification by FC (*n*-hexane:ethyl acetate; gradient from 3:1 to 1:1). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.51 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 7.46 (td, *J* = 7.6, 1.9 Hz, 1H), 7.21 – 7.18 (m, 2H), 7.06 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 7.04 – 7.02 (m, 2H), 6.85 (dt, *J* = 7.8, 1.1 Hz, 1H), 6.77 (dt, *J* = 15.6, 7.3 Hz, 1H), 5.72 (dt, *J* = 15.6, 1.4 Hz, 1H), 3.66 (s, 3H), 3.35 (tdd, *J* = 8.5, 6.7, 5.7 Hz, 1H), 3.11 (dd, *J* = 13.6, 6.9 Hz, 1H), 2.99 (dd, *J* = 13.6, 8.3 Hz, 1H), 2.63 – 2.50 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 166.7, 159.5, 149.5, 146.6, 141.9, 136.3, 132.3, 129.0 (2C), 128.7 (2C), 123.8, 122.9, 121.5, 51.5, 45.1, 44.8, 38.5. HRMS calculated for $C_{18}H_{19}ClNO_2^+$ [M+H]+ m/z: 316.1099, found: 316.1104. The er was determined by UPC^2 using a chiral Chiralpack IA gradient from 100% CO_2 up to 40%; *i*-PrOH, 2.2 mL/min; τ_{major} = 2.96 min, τ_{minor} = 3.12 min, (98:2 er); $[\alpha]_L^{20}$ = -43.9; (*c* = 0.88; $CHCl_3$).

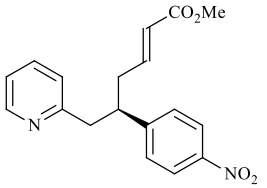
Methyl (*R*,*E*)-5-(3-chlorophenyl)-6-(pyridin-2-yl)hex-2-enoate (6c)



Compound **6c** was obtained according to general procedure from (*E*)-3-(3-chlorophenyl)prop-2-enal **2c** in 73% yield (23.0 mg) after purification by FC (*n*-hexane:ethyl acetate; gradient from 3:1 to 1:1). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.53 (ddd, *J* = 5.0, 1.9, 0.9 Hz, 1H), 7.48 (td, *J* = 7.7, 1.9 Hz, 1H), 7.18 – 7.10 (m, 3H), 7.07 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 6.99 (dt, *J* = 7.4, 1.6 Hz, 1H), 6.87 (dt, *J* = 7.8, 1.2 Hz, 1H), 6.78 (dt, *J* = 15.6, 7.3 Hz, 1H), 5.74 (dt, *J* = 15.5, 1.4 Hz, 1H), 3.67 (s, 3H), 3.35 (tt, *J* = 8.2, 6.3 Hz, 1H), 3.11 (dd, *J* = 13.6, 7.0 Hz, 1H), 3.01 (dd, *J* = 13.6, 8.0 Hz, 1H), 2.63 – 2.53 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 166.8, 159.4, 149.6, 146.5, 145.6, 136.3, 134.4, 129.9, 127.8, 126.9, 126.1, 123.9, 123.0, 121.5, 51.5, 45.1, 45.1, 38.4HRMS calculated for $C_{18}H_{19}ClNO_2^+$ [M+H]+ m/z: 316.1099, found: 316.11014. The er was determined by HPLC using a chiral Chiralpack IC column

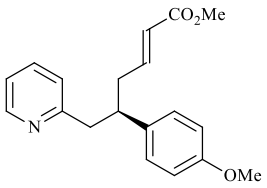
[hexane:*i*-PrOH, 80:20]; flow rate 1.0 mL/min; τ_{major} = 9.2 min; τ_{minor} = 8.5 min, (er 97.5:2.5); $[\alpha]_L^{20}$ = -49.0; (*c* = 0.45; CH_3OH).

Methyl (*R*,*E*)-5-(4-nitrophenyl)-6-(pyridin-2-yl)hex-2-enoate (6d)



Compound **6d** was obtained according to general procedure from (*E*)-3-(4-nitrophenyl)prop-2-enal **2d** in 91% yield (30.0 mg) after purification by FC (*n*-hexane:ethyl acetate; gradient from 3:1 to 1:1). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.50 (ddd, *J* = 4.9, 1.9, 0.9 Hz, 1H), 8.14 – 8.06 (m, 2H), 7.47 (td, *J* = 7.6, 1.9 Hz, 1H), 7.33 – 7.24 (m, 2H), 7.07 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 6.87 (dt, *J* = 7.8, 1.1 Hz, 1H), 6.76 (dt, *J* = 15.4, 7.3 Hz, 1H), 5.74 (dt, *J* = 15.6, 1.5 Hz, 1H), 3.66 (d, *J* = 0.7 Hz, 3H), 3.55 (ddd, *J* = 8.6, 6.3, 2.4 Hz, 1H), 3.19 (dd, *J* = 13.8, 6.8 Hz, 1H), 3.03 (dd, *J* = 13.8, 8.5 Hz, 1H), 2.71 – 2.53 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 166.5, 158.7, 151.2, 149.6, 146.9, 145.7, 136.5, 128.6 (2C), 123.9 (2C), 123.8, 123.4, 121.7, 51.6, 45.2, 44.7, 38.2. HRMS calculated for $C_{18}H_{19}N_2O_4^+$ [M+H]+ m/z: 327.1339, found: 327.1339. The er was determined by UPC^2 using a chiral Chiralpack IA gradient from 100% CO_2 up to 40%; *i*-PrOH, 2.2 mL/min τ_{major} = 3.33 min; τ_{minor} = 3.63 min, (97:3 er); $[\alpha]_L^{20}$ = -38.8; (*c* = 1.00; $CHCl_3$).

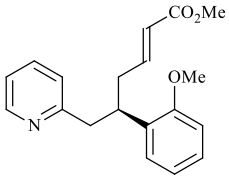
Methyl (*R*,*E*)-5-(4-methoxyphenyl)-6-(pyridin-2-yl)hex-2-enoate (6e)



Compound **6e** was obtained according to general procedure from (*E*)-3-(4-methoxyphenyl)prop-2-enal **2e** in 69% yield (21.5 mg) after purification by FC (*n*-hexane:ethyl acetate; gradient from 3:1 to 1:1).**^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.54 – 8.49 (m, 1H), 7.46 (td, J = 7.6, 1.9 Hz, 1H), 7.05 (ddd, J = 7.5, 5.0, 1.3 Hz, 1H), 7.04 – 7.00 (m, 2H), 6.86 (d, J = 7.8 Hz, 1H), 6.83 – 6.76 (m, 3H), 5.72 (dt, J = 15.6, 1.4 Hz, 1H), 3.76 (s, 3H), 3.66 (s, 3H), 3.29 (ddd, J = 14.8, 8.2, 6.5 Hz, 1H), 3.10 (dd, J = 13.5, 7.1 Hz, 1H), 3.01 (dd, J = 13.5, 8.2 Hz, 1H), 2.59 – 2.51 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 166.9, 160.0, 158.3, 149.4, 147.4, 136.2, 135.4, 128.6 (2C), 123.9, 122.6, 121.3, 114.0 (2C), 55.3, 51.4, 45.5, 44.7, 38.8. HRMS calculated for $C_{19}H_{22}NO_3^+$ [M+H]+ m/z: 312.1594, found: 312.1600. The er

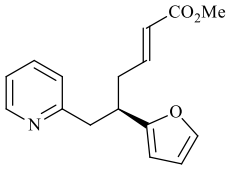
was determined by UPC^2 using a chiral Chiralpack IA gradient from 100% CO_2 up to 40%; *i*-PrOH, 2.2 mL/min; τ_{major} = 2.98 min, τ_{minor} = 3.08 min, (97:3 er); $[\alpha]_L^{20}$ = -43.9; (*c* = 0.70; $CHCl_3$).

Methyl (*R*,*E*)-5-(2-methoxyphenyl)-6-(pyridin-2-yl)hex-2-enoate (6f)



Compound **6f** was obtained according to general procedure from (*E*)-3-(2-methoxyphenyl)prop-2-enal **2f** in 65% yield (20.3 mg) after purification by FC (*n*-hexane:ethyl acetate; gradient from 3:1 to 1:1). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.53 – 8.48 (m, 1H), 7.46 (td, *J* = 7.6, 1.8 Hz, 1H), 7.14 (ddd, *J* = 8.1, 7.3, 1.7 Hz, 1H), 7.10 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.04 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 6.93 (dt, *J* = 7.7, 1.1 Hz, 1H), 6.86 (td, *J* = 7.5, 1.1 Hz, 1H), 6.84 – 6.79 (m, 2H), 5.71 (dt, *J* = 15.6, 1.5 Hz, 1H), 3.79 – 3.75 (m, 1H), 3.75 (s, 3H), 3.64 (s, 3H), 3.11 (dd, *J* = 7.6, 5.2 Hz, 2H), 2.64 – 2.54 (m, 2H).**^{13}C NMR** (176 MHz, $CDCl_3$) δ 167.0, 160.5, 157.4, 149.2, 148.0, 136.0, 131.5, 128.1, 127.5, 123.6, 122.0, 121.2, 120.7, 110.8, 55.4, 51.4, 43.5, 38.8, 37.2. HRMS calculated for $C_{19}H_{22}NO_3^+$ [M+H]+ m/z: 312.1594, found: 312.1604. The er was determined by UPC^2 using a chiral Chiralpack IB gradient from 100% CO_2 up to 40%; *i*-PrOH, 2.2 mL/min; τ_{major} = 2.87 min, τ_{minor} = 3.02 min, (97.5:2.5 er); $[\alpha]_L^{20}$ = -30.6; (*c* = 1.00; $CHCl_3$).

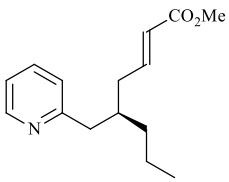
Methyl (*R*,*E*)-5-(furan-2-yl)-6-(pyridin-2-yl)hex-2-enoate (6g)



Compound **6g** was obtained according to general procedure from (*E*)-3-(furan-2-ylo)prop-2-enal **2g** in 85% yield (23.1 mg) after purification by FC (*n*-hexane:ethyl acetate; gradient from 3:1 to 1:1).**^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.54 – 8.51 (m, 1H), 7.51 (td, *J* = 7.6, 1.8 Hz, 1H), 7.31 (dd, *J* = 1.9, 0.8 Hz, 1H), 7.09 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 6.93 (dt, *J* = 7.9, 1.1 Hz, 1H), 6.86 (dt, *J* = 15.6, 7.3 Hz, 1H), 6.21 (dd, *J* = 3.1, 1.8 Hz, 1H), 5.92 – 5.90 (m, 1H), 5.77 (dt, *J* = 15.6, 1.5 Hz, 1H), 3.69 (s, 3H), 3.49 (qd, *J* = 7.7, 5.8 Hz, 1H), 3.14 (dd, *J* = 13.6, 8.0 Hz, 1H), 3.05 (dd, *J* = 13.6, 7.1 Hz, 1H), 2.61 – 2.52 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 166.9, 159.5, 156.3, 149.5, 146.7, 141.4, 136.3, 123.7, 122.8, 121.5, 110.1, 106.2, 51.5, 42.4, 38.7, 36.3. HRMS calculated for $C_{16}H_{18}NO_3^+$ [M+H]+ m/z: 272.1281, found: 272.1284. The er was determined by UPC^2 using a chiral Chiralpack IA gradient

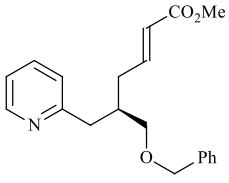
from 100% CO_2 up to 40%; *i*-PrOH, 2.2 mL/min; τ_{major} = 2.43 min, τ_{minor} = 2.53 min, (97:3 er); $[\alpha]_L^{20}$ = -20.6; (*c* = 1.07; $CHCl_3$).

Methyl (*R*,*E*)-5-(pyridin-2-ylmethyl)oct-2-enoate (6h)



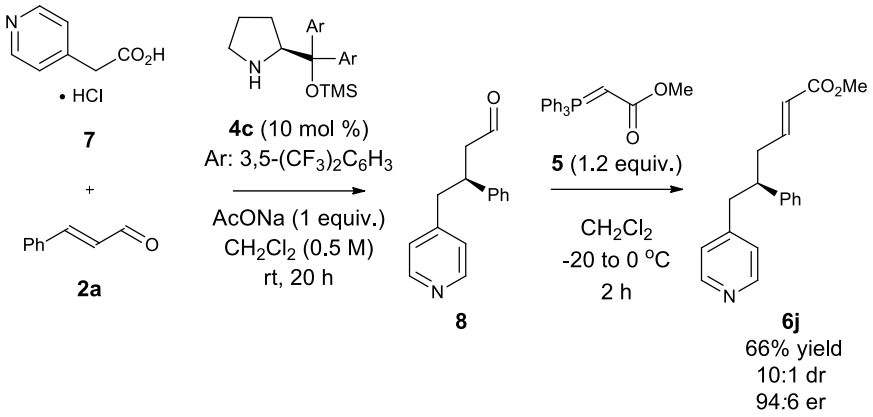
Compound **6h** was obtained according to general procedure from (*E*)-hex-2-enal **2h** in 47% yield (9.2 mg) after purification by FC (*n*-hexane:ethyl acetate; gradient from 3:1 to 1:1). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.56 – 8.52 (m, 1H), 7.57 (td, *J* = 7.6, 1.9 Hz, 1H), 7.12 – 7.08 (m, 2H), 6.94 (dt, *J* = 15.6, 7.4 Hz, 1H), 5.80 (dt, *J* = 15.6, 1.4 Hz, 1H), 3.72 (s, 3H), 2.78 (dd, *J* = 13.6, 6.5 Hz, 1H), 2.68 (dd, *J* = 13.6, 7.6 Hz, 1H), 2.25 – 2.09 (m, 3H), 1.42 – 1.23 (m, 4H), 0.90 – 0.84 (m, 3H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 167.0, 161.0, 149.5, 148.1, 136.3, 123.8, 122.6, 121.2, 51.5, 42.9, 38.1, 36.3, 35.9, 20.0, 14.4. HRMS calculated for $C_{15}H_{22}NO_2^+$ [M+H]+ m/z: 248.1645, found: 248.1637. The er was determined by HPLC using a chiral Chiralpack IC column [hexane:*i*-PrOH, 80:20]; flow rate 1.0 mL/min; τ_{major} = 7.7 min; τ_{minor} = 7.3 min, (er 96:4); $[\alpha]_L^{20}$ = 14,4; (*c* = 0.36; CH_3OH).

Methyl (*R*,*E*)-6-(benzyloxy)-5-(pyridin-2-ylmethyl)hex-2-enoate (6i)



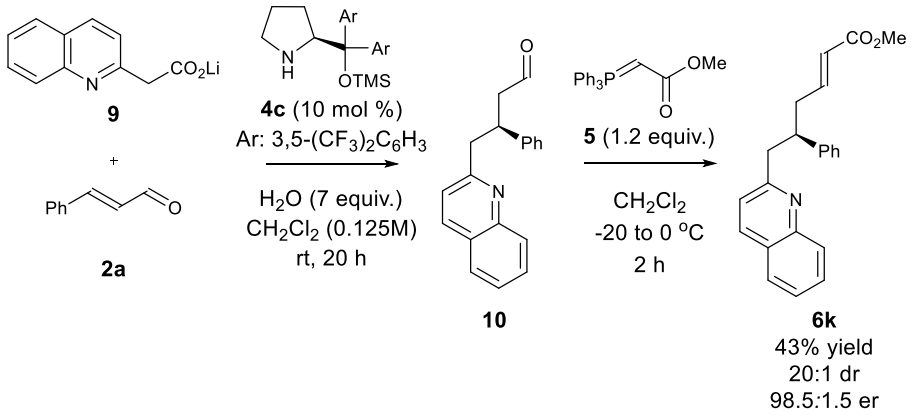
Compound **6i** was obtained according to general procedure from (*E*)-4-(benzyloxy)but-2-enal **2i** in 85% yield (24.5 mg) after purification by FC (*n*-hexane:ethyl acetate; gradient from 3:1 to 1:1). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.53 (dt, *J* = 4.3, 1.7 Hz, 1H), 7.55 (td, *J* = 7.6, 1.9 Hz, 1H), 7.35 – 7.27 (m, 5H), 7.12 – 7.08 (m, 2H), 6.95 (dt, *J* = 15.6, 7.4 Hz, 1H), 5.82 (dt, *J* = 15.6, 1.3 Hz, 1H), 4.46 (d, *J* = 2.4 Hz, 2H), 3.71 (s, 3H), 3.40 (dd, *J* = 9.3, 4.6 Hz, 1H), 3.34 (dd, *J* = 9.3, 5.3 Hz, 1H), 2.89 (dd, *J* = 13.7, 7.2 Hz, 1H), 2.78 (dd, *J* = 13.7, 6.8 Hz, 1H), 2.45 – 2.36 (m, 2H), 2.32 – 2.28 (m, 1H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 167.0, 160.4, 149.5, 147.7, 138.6, 136.3, 128.5 (2C), 127.7 (2C), 127.7, 123.9, 122.7, 121.3, 73.2, 71.8, 51.5, 40.1, 39.0, 34.3. HRMS calculated for $C_{20}H_{24}NO_3^+$ [M+H]+ m/z: 326.1751, found: 326.1754. The er was determined by HPLC using a chiral Chiralpack IC column [hexane:*i*-PrOH, 95:5]; flow rate 1.0 mL/min; τ_{major} = 26.8 min; τ_{minor} = 28.3 min, (er = 95:5); $[\alpha]_L^{20}$ = -5.7; (*c* = 0.65; $CHCl_3$).

Synthesis of methyl (*R*,*E*)-5-phenyl-6-(pyridin-4-yl)hex-2-enoate (6j)



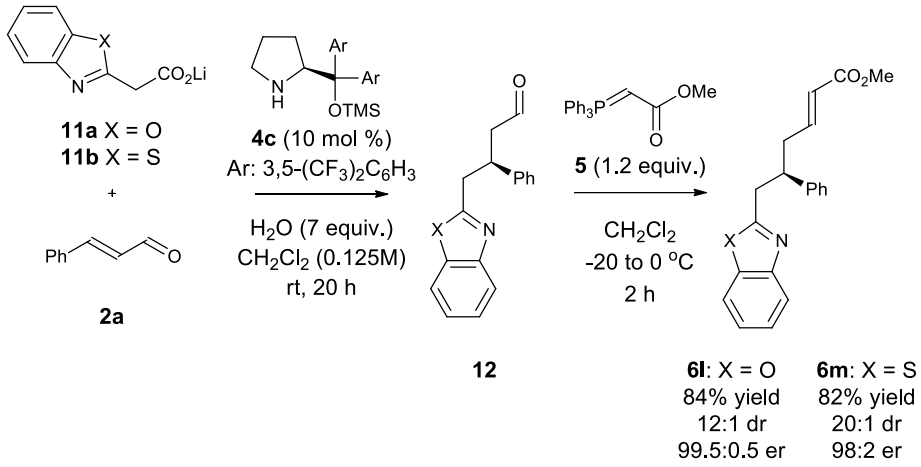
In an ordinary 4 mL glass vial equipped with a magnetic stirring bar, 4-pyridylacetic acid hydrochloride **7** (17.3 mg; 0.1 mmol), cinnamaldehyde **2a** (13.2 mg; 0.1 mmol) and catalyst **4c** (6.0 mg, 0.01 mmol) were placed. Subsequently, dichloromethane (0.2 mL) and sodium acetate (8.2 mg, 0.1 mmol) were added. After 72 hours, the reaction mixture was diluted with dichloromethane (1 mL) and cooled to -20 °C. Then (methoxycarbonylmethylene)triphenylphosphorane **5** (40 mg; 0.12 mmol) was added to the vial and stirred at 0 °C for 2 hours. Subsequently, the solvent was removed under reduced pressure and the obtained residue was directly subjected to flash chromatography on silica gel to afford pure products. Pure product was isolated by FC (*n*-hexane:ethyl acetate; gradient from 3:1 to 1:1) to give **6i** in 66% yield (18.6 mg). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.54 – 8.22 (m, 2H), 7.29 – 7.23 (m, 2H), 7.21 – 7.17 (m, 1H), 7.07 – 7.04 (m, 2H), 6.91 – 6.88 (m, 2H), 6.82 (dt, *J* = 15.6, 7.3 Hz, 1H), 5.78 (dt, *J* = 15.6, 1.5 Hz, 1H), 3.68 (s, 3H), 3.09 – 2.99 (m, 1H), 2.95 (dd, *J* = 13.6, 6.3 Hz, 1H), 2.87 (dd, *J* = 13.6, 8.7 Hz, 1H), 2.63 – 2.49 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 166.6, 149.5 (2C), 148.7, 146.4 (2C), 142.3, 128.6 (2C), 127.5 (2C), 126.9, 124.5, 122.9, 51.4, 46.2, 42.0, 38.5. HRMS calculated for $C_{18}H_{20}NO_2^+$ [M+H]+ m/z: 282.1489, found: 282.1495. The er was determined by HPLC using a chiral Chiralpack IC column [hexane:*i*-PrOH, 98:2]; flow rate 1.0 mL/min; τ_{major} = 17.3 min, τ_{minor} = 16.2 min, (94:6 er); $[\alpha]_L^{20}$ = -21.9; (*c* = 0.34; $CHCl_3$).

Synthesis of methyl (*R*,*E*)-5-phenyl-6-(quinolin-2-yl)hex-2-enoate (6k)

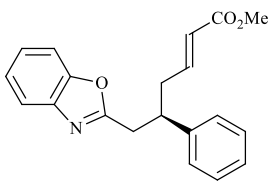


In an ordinary 4 mL glass vial equipped with a magnetic stirring bar, lithium 2-(quinolin-2-yl)acetate **9** (38.0 mg; 0.2 mmol), cinnamaldehyde **2a** (13.2 mg; 0.1 mmol) and catalyst **4c** (6.0 mg; 0.01 mmol) were placed. Then dichloromethane (0.8 mL) and H_2O (13 µL; 0.7 mmol) were added. The reaction mixture was stirred for 20 hours at room temperature. After full conversion of the starting material **2a**, the reaction mixture was diluted with dichloromethane (1 mL) and cooled to -20 °C. Then (methoxycarbonylmethylene)triphenylphosphorane **5** (40 mg; 0.12 mmol) was added to the vial and stirred at 0 °C for 2 hours. Subsequently, the solvent was removed under reduced pressure and the obtained residue was directly subjected to flash chromatography on silica gel (*n*-hexane:ethyl acetate; gradient from 5:1 to 3:1) to afford pure product **6k** in 43% yield (14.3 mg). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.07 – 8.01 (m, 2H), 7.94-7.93 (d, *J* = 8.4 Hz, 1H), 7.74 – 7.72 (m, 1H), 7.70 – 7.67 (m, 1H), 7.49 – 7.48 (m, 2H), 7.25 – 7.23 (m, 1H), 7.19 – 7.16 (m, 2H), 7.01 (d, *J* = 8.4 Hz, 1H), 6.81 (dt, *J* = 15.7, 7.3 Hz, 1H), 5.73 (dt, *J* = 15.6, 1.4 Hz, 1H), 3.63 (s, 3H), 3.51 – 3.42 (m, 1H), 3.37 – 3.21 (m, 2H), 2.70 – 2.59 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 166.7, 160.3, 147.9, 147.0, 143.2, 135.9, 129.3, 128.9, 128.5 (2C), 127.6 (2C), 127.5, 126.7, 126.6, 125.8, 122.5, 121.9, 51.3, 45.8, 45.3, 38.6. HRMS calculated for $C_{22}H_{22}NO_2^+$ $[M+H]^+$ m/z: 332.1645, found: 332.1643. The er was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 95:5]; flow rate 1.0 mL/min; τ_{major} = 10.8 min, τ_{minor} = 11.8 min, (98.5:1.5 er); $[\alpha]_L^{20}$ = -86.2; (*c* = 0.77; $CHCl_3$).

Synthesis of methyl (*R*,*E*)-6-(benzo[*d*]oxazol-2-yl)-5-phenylhex-2-enoate (6l) and methyl (*R*,*E*)-6-(benzo[*d*]thiazol-2-yl)-5-phenylhex-2-enoate (6m)

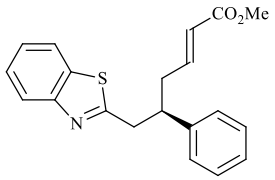


In an ordinary 4 mL glass vial equipped with a magnetic stirring bar, lithium 2-(benzo[*d*]oxaz-2-yl)acetate **11a** (73.2 mg; 0.4 mmol) or lithium 2-(benzo[*d*]thiazol-2-yl)acetate **11b** (79.7 mg; 0.4 mmol), cinnamaldehyde **2a** (13.2 mg; 0.1 mmol) and catalyst **6c** (6.0 mg; 0.01 mmol) were placed. Then dichloromethane (0.8 mL) and H_2O (13 µL; 0.7 mmol) were subsequently added. The reaction mixture was stirred for 20 hours at room temperature. After full conversion of the starting material **2a**, the reaction mixture was diluted with dichloromethane (1 mL) and cooled to -20 °C. Then (methoxycarbonylmethylene)triphenylphosphorane **5** (40 mg; 0.12 mmol) was added to the vial and stirred at 0 °C for 2 hours. Subsequently, the solvent was removed under reduced pressure and the obtained residue was directly subjected to flash chromatography on silica gel (*n*-hexane:ethyl acetate; gradient from 5:1 to 3:1) to give to afford pure products.



Methyl (*R*,*E*)-6-(benzo[d]oxazol-2-yl)-5-phenylhex-2-enoate (6l) was obtained in 84% yield (27 mg). **^{1}H NMR** (700 MHz, Chloroform-*d*) δ 8.52 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 7.45 (td, *J* = 7.6, 1.8 Hz, 1H), 7.26 – 7.21 (m, 2H), 7.16 (ddt, *J* = 7.9, 6.8, 1.3 Hz, 1H), 7.13 – 7.10 (m, 2H), 7.06 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 6.86 (dt, *J* = 7.8, 1.1 Hz, 1H), 6.81 (dt, *J* = 15.6, 7.3 Hz, 1H), 5.73 (dt, *J* = 15.6, 1.5 Hz, 1H), 3.65 (s, 3H), 3.34 (p, *J* = 7.4 Hz, 1H), 3.13 (dd, *J* = 13.6, 7.2 Hz, 1H), 3.05 (dd, *J* = 13.6, 8.1 Hz, 1H), 2.59 (td, *J* = 7.3, 1.5 Hz, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 166.5, 164.9, 150.7, 145.9, 142.2, 141.2, 128.8 (2C), 127.2 (2C), 127.1, 124.6, 124.2, 123.0, 119.7, 110.3, 51.4, 43.0, 38.4,

35.4. HRMS calculated for $C_{20}H_{20}NO_2^+$ $[M+H]^+$ m/z: 322.1438, found: 322.1437. The er was determined by UPC^2 using a chiral Chiralpack IA gradient from 100% CO_2 up to 40%; *i*-PrOH, 2.2 mL/min; τ_{major} = 2.86 min, τ_{minor} = 3.06 min, (99.5:0.5 er); $[\alpha]_L^{20}$ = -45.8; (*c* = 0.67; $CHCl_3$).



Methyl (*R*,*E*)-6-(benzo[*d*]thiazol-2-yl)-5-phenylhex-2-enoate (6m) was obtained followed in 82% yield (27.7 mg). **^{1}H NMR** (700 MHz, $CDCl_3$) δ 7.99 – 7.98 (m, 1H), 7.79 – 7.78 (m, 1H), 7.47 – 7.45 (m 1H), 7.37 – 7.35 (m, 1H), 7.34 – 7.25 (m, 2H), 7.24 – 7.20 (m, 3H), 6.82 (dt, *J* = 15.6, 7.3 Hz, 1H), 5.77 (dt, *J* = 15.6, 1.5 Hz, 1H), 3.65 (s, 3H), 3.51 – 3.36 (m, 3H), 2.73 – 2.61 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 169.3, 166.6, 153.1, 146.1, 142.2, 135.2, 128.8 (2C), 127.5 (2C), 127.1, 125.9, 124.8, 123.0, 122.7, 121.5, 51.4, 45.3, 40.7, 38.6. HRMS calculated for $C_{20}H_{20}NO_2S^+$ $[M+H]+$ m/z: 338.1209, found: 338.1212. The er was determined by UPC^2 using a chiral Chiralpack IA gradient from 100% CO_2 up to 40%; *i*-PrOH, 2.2 mL/min; τ_{major} = 3.33 min, τ_{minor} = 3.45 min, (98:2 er); $[\alpha]_L^{20}$ = -43.1; (*c* = 0.45; $CHCl_3$).

3. Crystal and X-ray data for 6a

The single crystal X-ray diffraction study at 100 K revealed that compound **6a** ($C_{18}H_{19}NO_2$) crystallizes in the non-centrosymmetric orthorhombic space group $P2_12_12_1$ (Z = 4) and the crystal structure consists of one crystallographically independent formula unit in the unit cell (Figure 1).

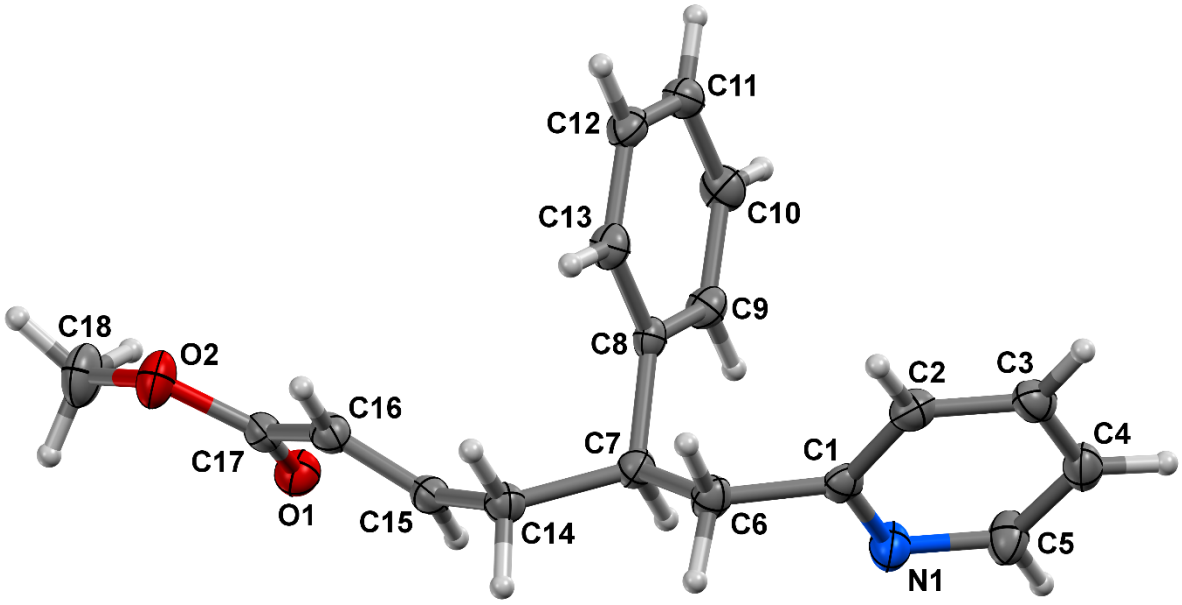


Figure 1. The molecular structure of the compound **6a** at 100 K, showing 50% probability displacement ellipsoids. Hydrogen atoms are drawn with an arbitrary radius.

Single crystal X-ray diffraction data were collected at 100 K by the ω-scan technique using a RIGAKU XtaLAB Synergy, Dualflex, Pilatus 300K diffractometer with PhotonJet micro-focus X-ray Source Cu-Kα (λ = 1.54184 Å).[3] Data collection, cell refinement, data reduction and absorption correction were performed using CrysAlis PRO software.[3] The crystal structure was solved by using direct methods with the SHELXT 2018/2 program.[4] Atomic scattering factors were taken from the International Tables for X-ray Crystallography. Positional parameters of non-H-atoms were refined by a full-matrix least-squares method on F^2 with anisotropic thermal parameters by

[3] Rigaku OD. CrysAlis PRO. Rigaku Oxford Diffraction Ltd, Yarnton, Oxfordshire, England, **2020**.
[4] G.M. Sheldrick, *Acta Cryst.* 2015, **A71**, 3-8.

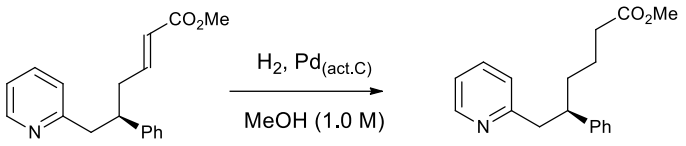
using the SHELXL 2018/3 program.[5] All hydrogen atoms were found from the difference Fourier maps and for further calculations they were positioned geometrically in calculated positions (C–H = 0.95–1.00 Å) and constrained to ride on their parent atoms with isotropic displacement parameters set to 1.2-1.5 times the U_{eq} of the parent atom.

Methyl (*R*,*E*)-5-phenyl-6-(pyridin-2-yl)hex-2-enoate (6a): Formula $C_{18}H_{19}NO_2$, monoclinic, space group $P2_12_12_1$, Z = 4, unit cell constants a = 5.7216(1), b = 15.4964(1), c = 17.3718(1) Å, V = 1540.26(3) Å^3. The integration of the data yielded a total of 41794 reflections with θ angles in the range of 3.82 to 66.60°, of which 2719 were independent (R_{int} = 2.42%), and 2694 were greater than 2σ(F^2). The final anisotropic full-matrix least-squares refinement on F^2 with 192 parameters converged at R_1 = 2.19% and wR_2 = 5.41% for all data. The largest peak in the final difference electron density synthesis was 0.118 e Å^{-3} and the largest hole was -0.104 e Å^{-3}. The goodness-of-fit was 1.067. The absolute configuration was unambiguously determined from anomalous scattering, by calculating the *x* Flack parameter of -0.04(3) using 1105 quotients.[6]

CCDC 2046872 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

[5] G.M. Sheldrick, *Acta Cryst.* 2015, **C71**, 3-8.
[6] S. Parsons, H.D. Flack and T. Wagner, *Acta Cryst.* 2013, **B69**, 249-259.

4. Synthesis of methyl (*R*)-5-phenyl-6-(pyridin-2-yl)hexanoate 13

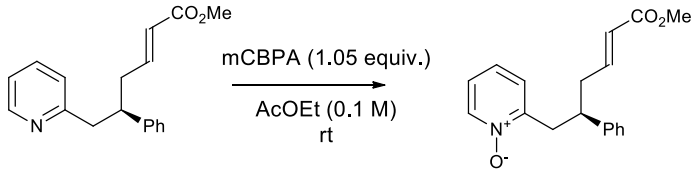


6a **13** >95% yield 97:3 er

Pd-C (5 mg) was added to a stirred solution of olefin **6a** (28.1 mg, 0.1 mmol) in methanol (3 mL).[7] The resulting mixture was vigorously stirred for 20 h at room temperature under a H_2 atmosphere. The mixture was then filtered through Celite, the filtercake was washed with methanol (5 mL) and the combined filtrates were concentrated in vacuo to give the desired product **13** with 95 % yield (27.3 mg) as a colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.52 – 8.47 (m, 1H), 7.47 – 7.38 (m, 1H), 7.24 – 7.21 (m, 2H), 7.17 – 7.13 (m, 1H), 7.13 – 7.07 (m, 2H), 7.03 (ddd, J = 7.5, 4.9, 1.1 Hz, 1H), 6.83 (dt, J = 7.8, 1.1 Hz, 1H), 3.59 (s, 3H), 3.15 – 3.05 (m, 2H), 3.05 – 2.97 (m, 1H), 2.28 – 2.14 (m, 2H), 1.76 – 1.66 (m, 2H), 1.54 – 1.41 (m, 2H). **^{13}C NMR** (176 MHz, $CDCl_3$) δ 173.9, 160.3, 149.2, 144.2, 135.9, 128.3 (2C), 127.6 (2C), 126.2, 123.7, 121.0, 51.4, 46.2, 46.0, 35.2, 34.0, 22.9. HRMS calculated for $C_{18}H_{22}NO_2^+$ [M+H]+ m/z: 284.1645, found: 284.1649. The er was determined by UPC[2] using a chiral Chiralpack IB gradient from 100% CO_2 up to 40%; *i*-PrOH, 2.5 mL/min; τ_{major} = 2.69 min, τ_{minor} = 2.84 min, (97:3 er); $[\alpha]_L^{20}$ = -50.6; (*c* = 1.00; $CHCl_3$).

[7] J. P. Mukherjee, S. Sil, A. K. Pahari and S. K. Chattopadhyay, *Synthesis* 2016, ***48***, 1181-1190.

5. Synthesis of (*R*,*E*)-2-(6-methoxy-6-oxo-2-phenylhex-4-en-1-yl)pyridine 1-oxide 14

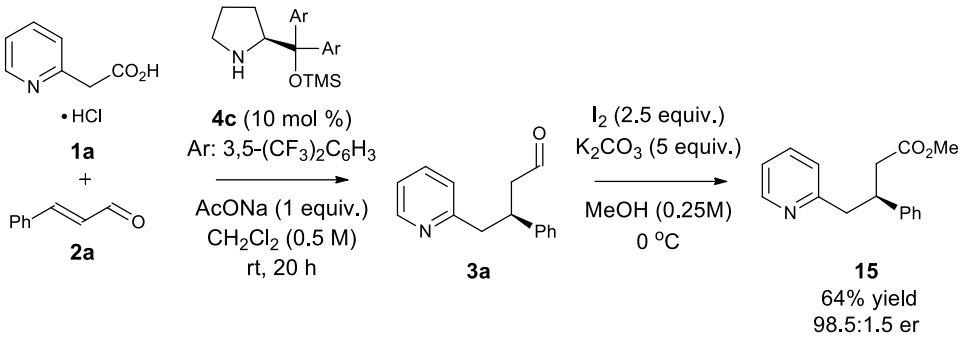


6a **14** 88% yield 97.5:2.5 er

To a stirred solution of olefin **6a** (25.5 mg, 0.1 mmol,) in ethyl acetate (1mL) 77% *m*CBPA (23.4 mg, 0.105 mmol,) was added.[8] After stirring for 20 h in room temperature, reaction mixture was directly subjected to flash chromatography (ethyl acetate: methanol eluent gradient from 98:2 to 90:10 (*v/v*)) to obtain pure product **14** in 88% yield (26.2 mg) as a yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.30 (d, *J* = 6.4 Hz, 1H), 7.21 – 7.19 (m, 2H), 7.14 – 7.12 (m, 1H), 7.09 – 7.05 (m, 3H), 7.03 – 6.95 (m, 1H), 6.82 (dt, *J* = 14.9, 7.1 Hz, 1H), 6.79 – 6.73 (m, 1H), 5.80 (d, *J* = 15.6 Hz, 1H), 3.63 (s, 3H), 3.53 – 3.46 (m, 2H), 2.97 (dd, *J* = 13.7, 9.6 Hz, 1H), 2.63 (t, *J* = 7.3 Hz, 2H).**^{13}C NMR** (176 MHz, $CDCl_3$) δ 166.80, 150.4, 146.5, 142.6, 139.9, 128.7 (2C), 127.5 (2C), 127.0, 126.9, 126.1, 123.9, 122.8, 51.4, 41.3, 39.0, 38.0. HRMS calculated for $C_{18}H_{20}NO_3^+$[M+H]+ m/z: 298.1438, found: 298.1442. The er was determined by UPC[2] using a chiral Chiralpack IA gradient from 100% CO_2 up to 40%; *i*-PrOH, 2.2 mL/min; τ_{major} = 4.27 min, τ_{minor} = 4.13 min, (97.5:2.5 er); $[\alpha]_L^{20}$ = -100.4; (*c* =1.00; MeOH).

[8] G. Li, S. Yang, B. Lv, Q. Han, X. Ma, K. Sun, Z. Wang, F. Zhao, Y. Lva and H. Wu, *Org. Biomol. Chem*. 2015, **13**, 11184-11188.

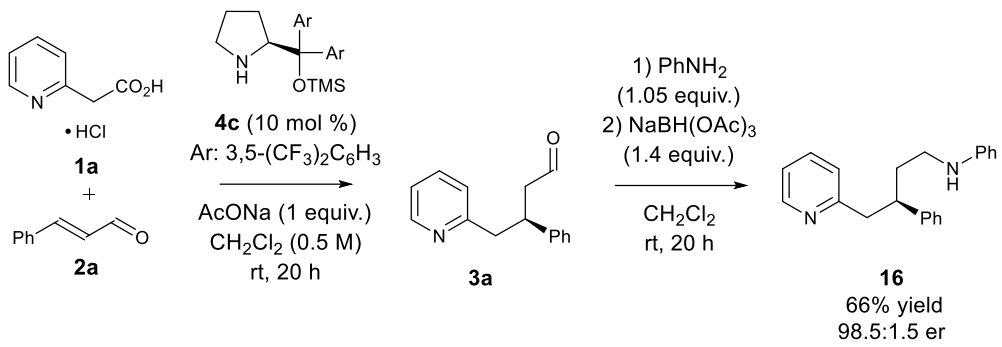
6. Synthesis of methyl (*S*)-3-phenyl-4-(pyridin-2-yl)butanoate 15



In an ordinary 4 mL glass vial equipped with a magnetic stirring bar, 2-pyridylacetic acid hydrochloride **1a** (17.3 mg; 0.1 mmol), α,β-unsaturated aldehyde **2a** (0.1 mmol) and catalyst **4c** (6.0 mg, 0.01 mmol) were placed. Subsequently, dichloromethane (0.2 mL) and sodium acetate (8.2 mg, 0.1 mmol) were added. After full conversion of starting material **2a** the mixture was cooled to 0 °C and methanol (0.2 mL), K_2CO_3 (69 mg, 0.5 mmol) were added.[9] After 5 minutes solution of iodine (63 mg, 0.25 mmol,) in methanol (0.4 mL) was added at 0 °C and the reaction mixture was stirred in this temperature for 1 h. Next, the reaction was quenched with saturated solution of $Na_2S_2O_5$ (5 mL) and extracted with ethyl acetate (3 x 5 mL). Combined organic layers were washed with water (5 mL) and brine (5 mL) and dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. Crude product was purified by flash chromatography (eluent: *n*-hexane:ethyl acetate 60:40 (*v/v*)) to yield ester **13** in 64 % yield (16.3 mg) as a yellow oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.65 – 8.46 (m, 1H), 7.51 – 7.49 (m, 1H), 7.33 – 7.23 (m, 2H), 7.23 – 7.12 (m, 3H), 7.09 – 7.07 (m, 1H), 6.98 – 6.96 (m, 1H), 3.71 (tdd, *J* = 9.0, 7.4, 4.1 Hz, 1H), 3.53 (s, 3H), 3.19 – 3.02 (m, 2H), 2.87 – 2.61 (m, 2H).**^{13}C NMR** (176 MHz, $CDCl_3$) δ 172.6, 159.7, 149.4, 143.4, 136.2, 128.5 (2C), 127.5 (2C), 126.7, 123.8, 121.4, 51.5, 45.1, 42.5, 40.4. HRMS calculated for $C_{16}H_{18}NO_2^+$ $[M+H]^+$ m/z: 256.1332, found: 256.1333. The er was determined by HPLC using a chiral Chiralpack IA column [hexane:*i*-PrOH, 98:2]; flow rate 1.0 mL/min; τ_{major} = 17.9 min, τ_{minor} = 19.8 min, (98.5:1.5 er); $[\alpha]_L^{20}$ = 48.5; (*c* = 1.00; $CHCl_3$).

[9] G. L. Bundy, L. S. Banitt, P. J. Dobrowolski, J. R. Palmer, T. M. Schwartz, D. C. Zimmermann, M. F. Lipton, M. A. Mauragis, M. F. Veley, R. B. Appell, R. C. Clouse and E. D. Daugs, *Org. Process Res. Dev.* 2001, ***5***, 144-151.

7. Synthesis of (*R*)-*N*-(3-phenyl-4-(pyridin-2-yl)butyl)aniline 16



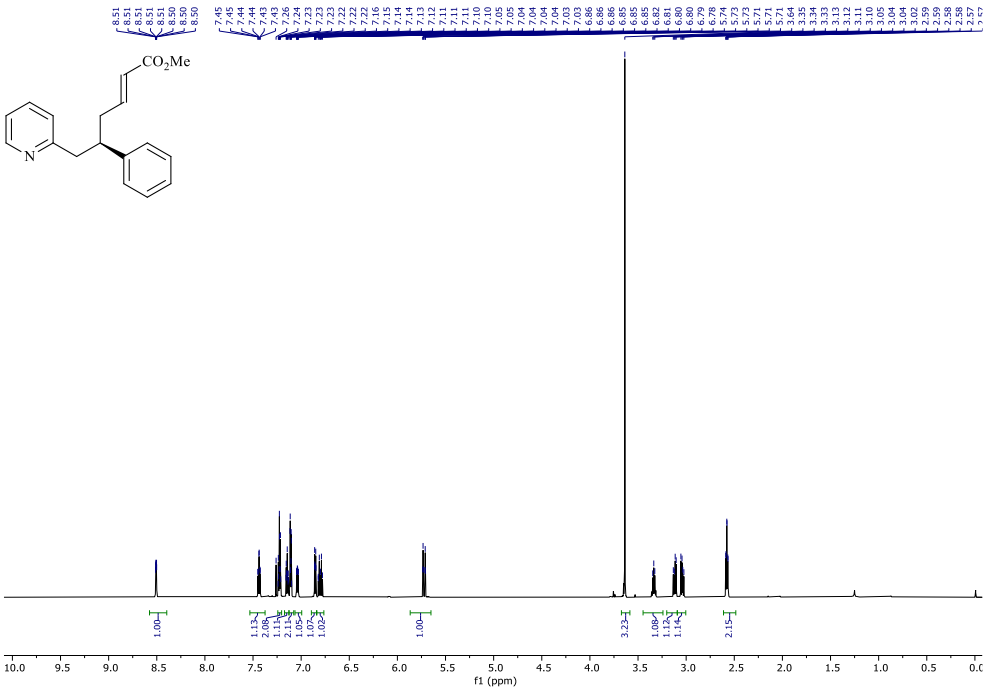
In an ordinary 4 mL glass vial equipped with a magnetic stirring bar, 2-pyridylacetic acid hydrochloride **1a** (17.3 mg; 0.1 mmol), α,β-unsaturated aldehyde **2a** (0.1 mmol) and catalyst **4c** (6.0 mg, 0.01 mmol) were placed. Subsequently, dichloromethane (0.2 mL) and sodium acetate (8.2 mg, 0.1 mmol) were added. After full conversion of starting material **2a** the reaction mixture was diluted with dichloromethane (0.5 mL) and aniline (8.3 mg, 0.105 mmol)was added.[10] After stirring for 5 minutes sodium triacetoxyborohydride (24.9 mg, 0.14 mmol) was added portion-wise to a reaction mixture. After stirring at room temperature for 20 h saturated solution of sodium hydrogen carbonate and dichloromethane were added. The organic layer was separated and washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (*n*-hexane/ethyl acetate gradient from 3:1 to 1:1) to give **16** in 66% yield (19.9 mg) as a colorless oil. **^{1}H NMR** (700 MHz, $CDCl_3$) δ 8.54 – 8.53 (m, 1H), 7.46 – 7.45 (m, 1H), 7.31 – 7.23 (m, 2H), 7.20 – 7.12 (m, 3H), 7.12 – 7.03 (m, 3H), 6.87 (dt, J = 7.8, 1.0 Hz, 1H), 6.64 (tt, J = 7.3, 1.1 Hz, 1H), 6.56 – 6.39 (m, 2H), 3.36 – 3.22 (m, 1H), 3.25 – 3.00 (m, 2H), 3.00 – 2.91 (m, 2H), 2.09 – 1.85 (m, 2H).**^{13}C NMR** (176 MHz, $CDCl_3$) δ 160.2, 149.4, 148.4, 144.2, 136.2, 129.2 (2C), 128.6 (2C), 127.8 (2C), 126.6, 123.9, 121.3, 117.2, 112.8 (2C), 46.0, 44.4, 42.3, 35.5. HRMS calculated for $C_{21}H_{23}N_2^+$ [M+H]+ m/z: 303.1856, found: 303.1862. The er was determined by UPC[2] using a chiral Chiralpack IC gradient from 100% CO_2 up to 40%; *i*-PrOH, 2.2 mL/min; τ_{major} = 3.91 min, τ_{minor} = 3.70 min, (98.5:1.5 er); $[\alpha]_L^{20}$ = -27.9; (*c* = 0.50; $CHCl_3$).

[10] R. Tedesco, A. N. Shaw, R. Bambal, D. Chai, N.O. Concha, M.G. Darcy, D. Dhanak, D. M. Fitch, A. Gates, W. G. Gerhardt, D. L. Halegoua, C. Han, G. A. Hofmann, V.K. Johnston, A. C. Kaura, N. Liu, R. M. Keenan, J. Lin-Goerke, R. T. Sarisky, K. J. Wiggall, M. N. Zimmerman and K. J. Duffy, *J. Med. Chem,* 2006, ***49***, 971-983.

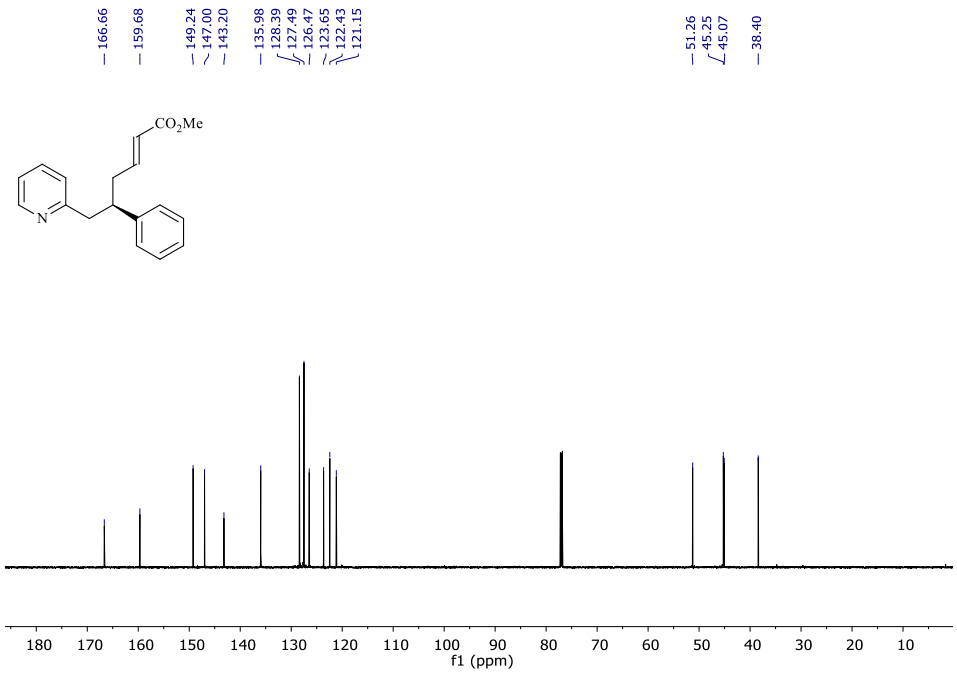
8. NMR Data

Methyl (*R*,*E*)-5-phenyl-6-(pyridin-2-yl)hex-2-enoate (6a)

^{1}H NMR

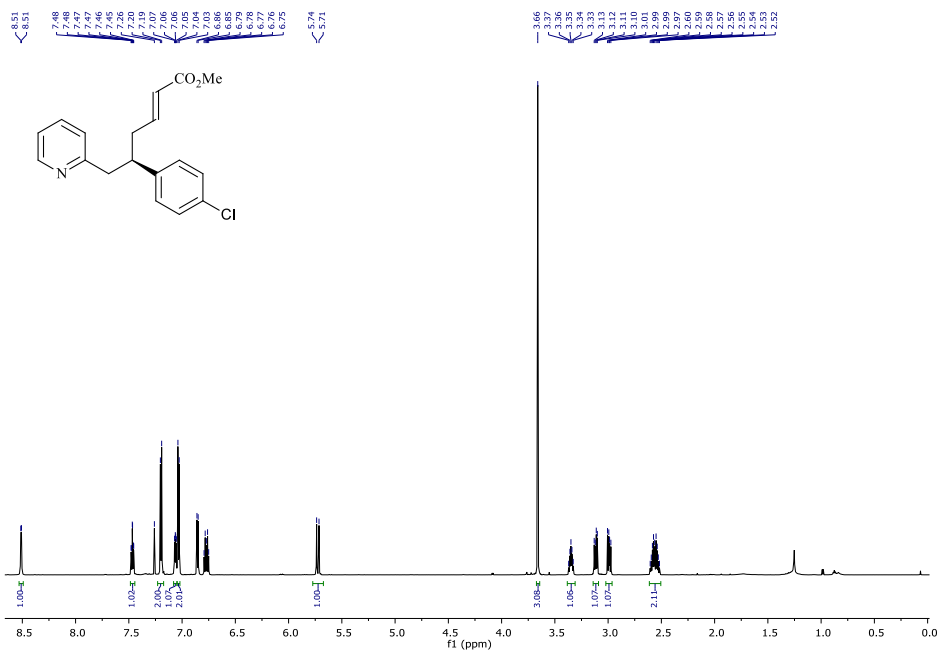


^{13}C NMR

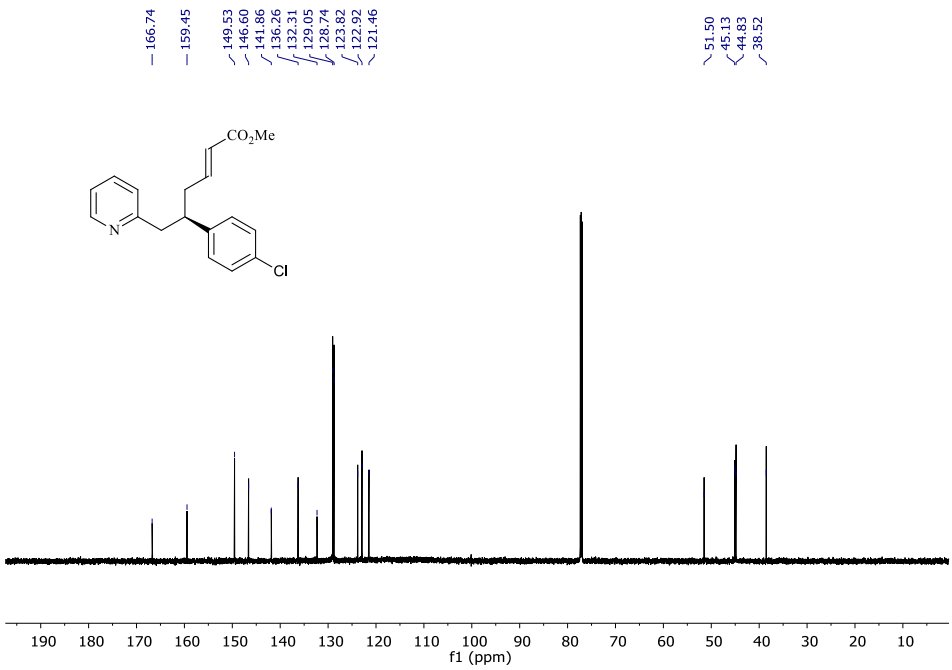


Methyl (*R*,*E*)-5-(4-chlorophenyl)-6-(pyridin-2-yl)hex-2-enoate (6b)

^{1}H NMR

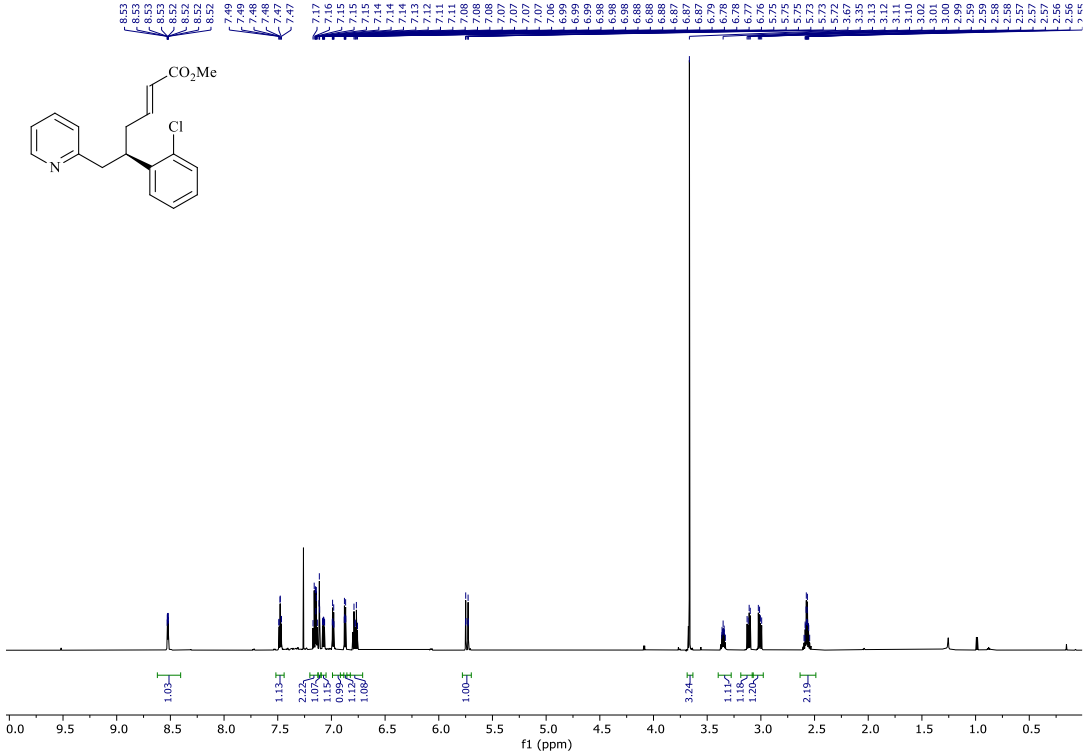


^{13}C NMR

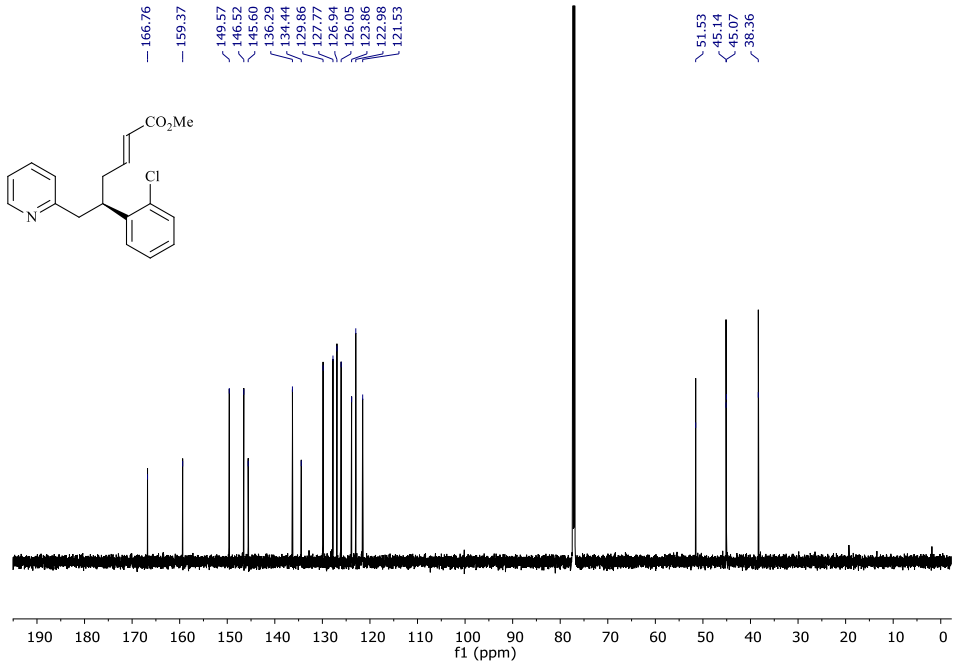


Methyl (*R*,*E*)-5-(3-chlorophenyl)-6-(pyridin-2-yl)hex-2-enoate (6c)

^{1}H NMR

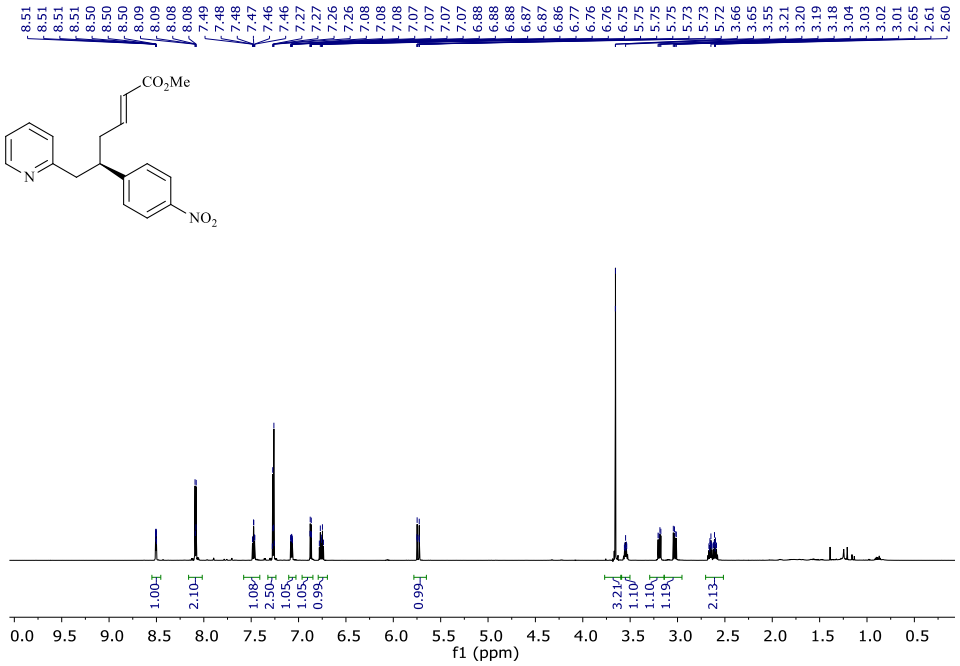


^{13}C NMR

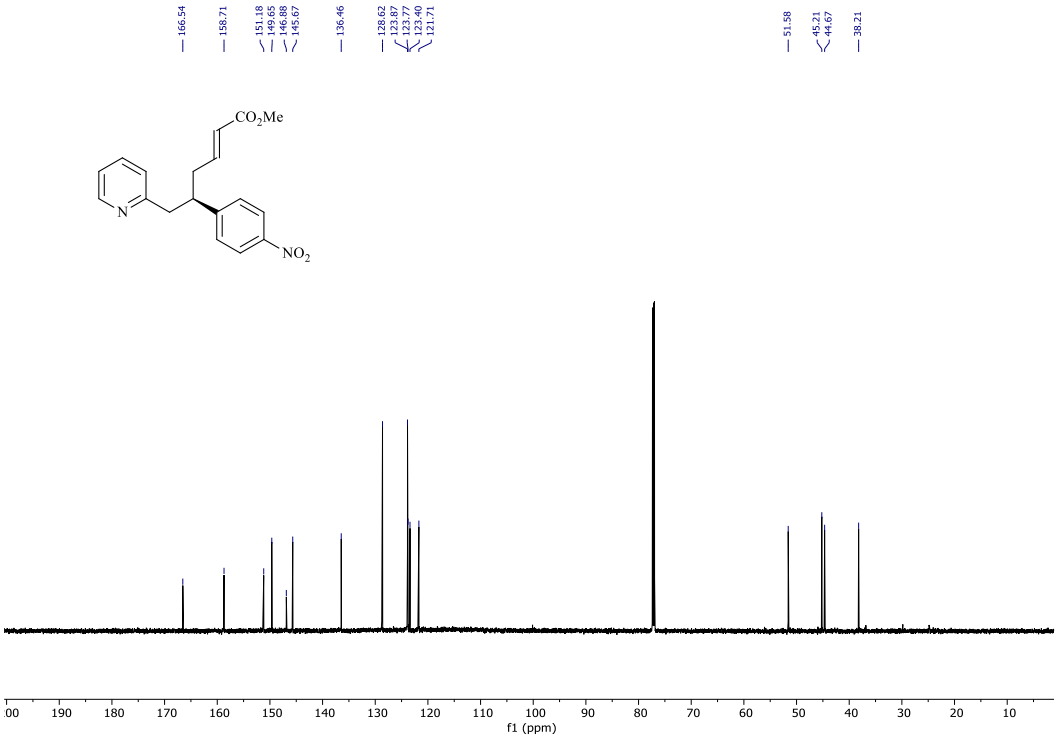


Methyl (*R*,*E*)-5-(4-nitrophenyl)-6-(pyridin-2-yl)hex-2-enoate (6d)

^{1}H NMR

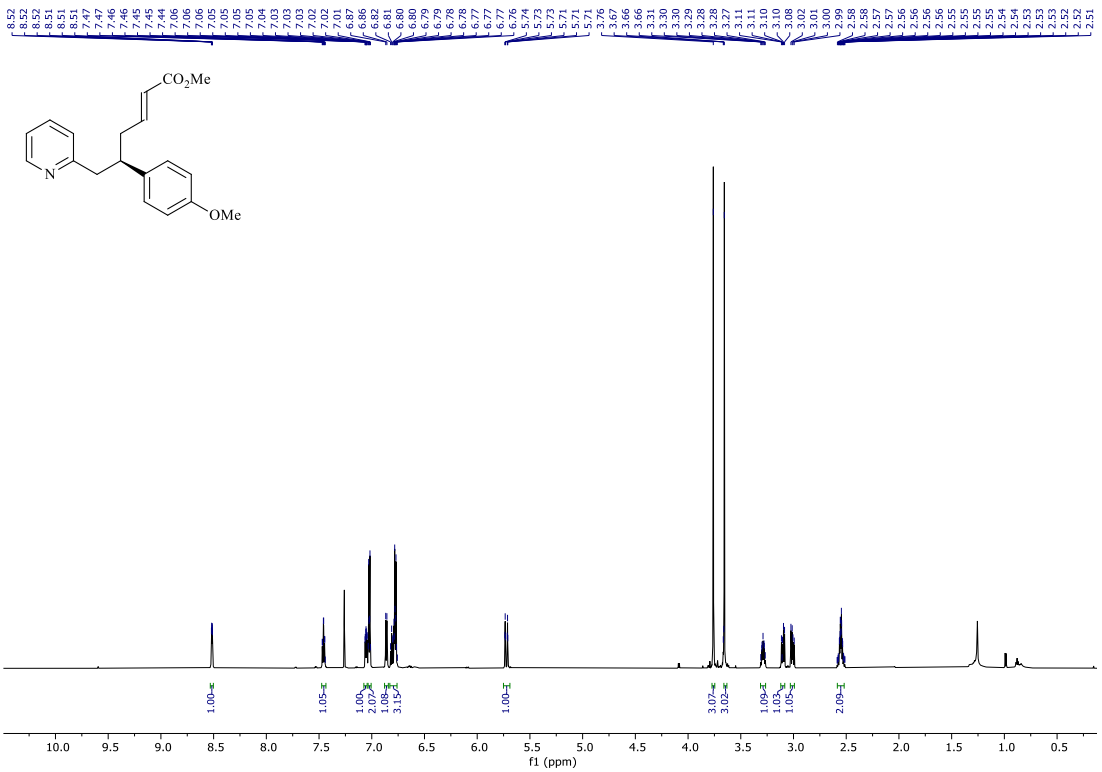


^{13}C NMR

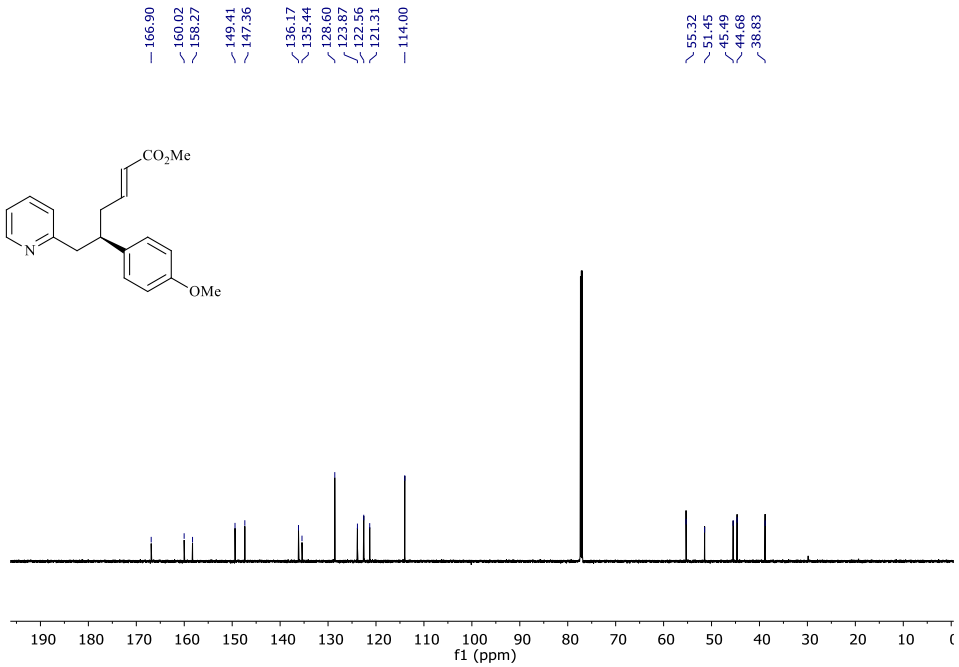


Methyl (*R*,*E*)-5-(4-methoxyphenyl)-6-(pyridin-2-yl)hex-2-enoate (6e)

^{1}H NMR

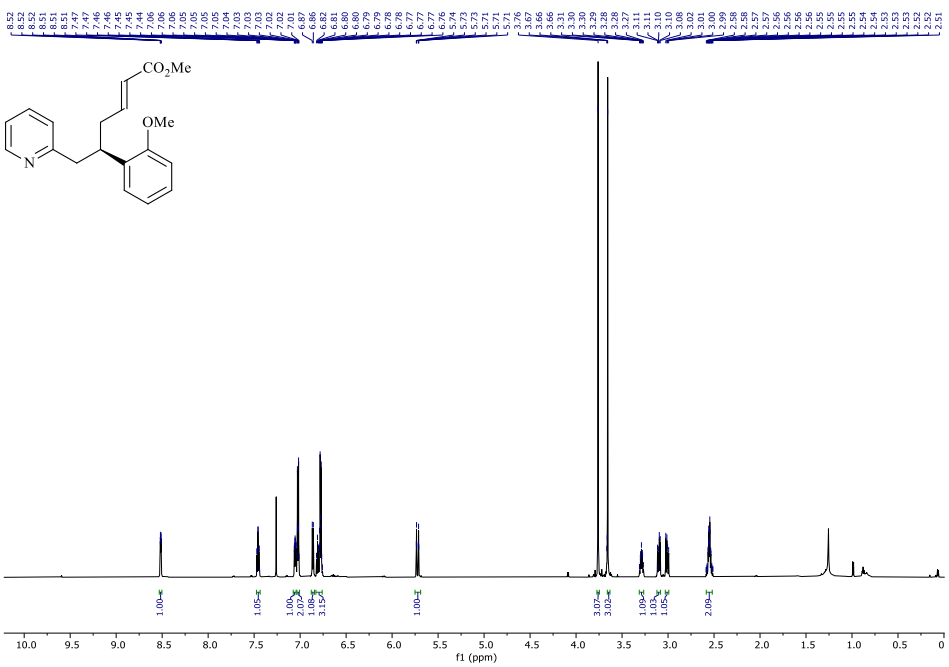


^{13}C NMR

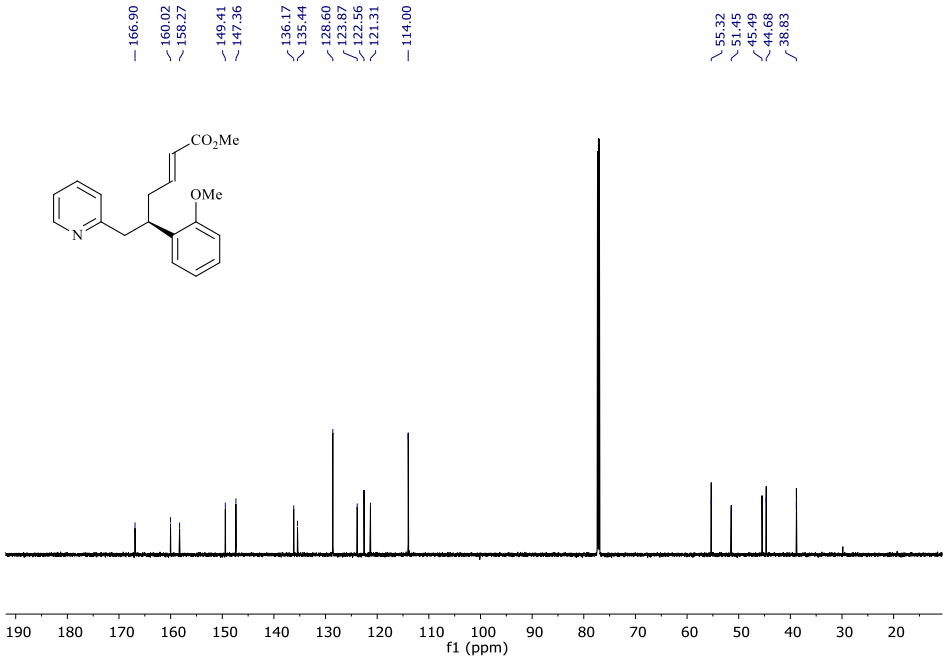


Methyl (*R*,*E*)-5-(2-methoxyphenyl)-6-(pyridin-2-yl)hex-2-enoate (6f)

^{1}H NMR

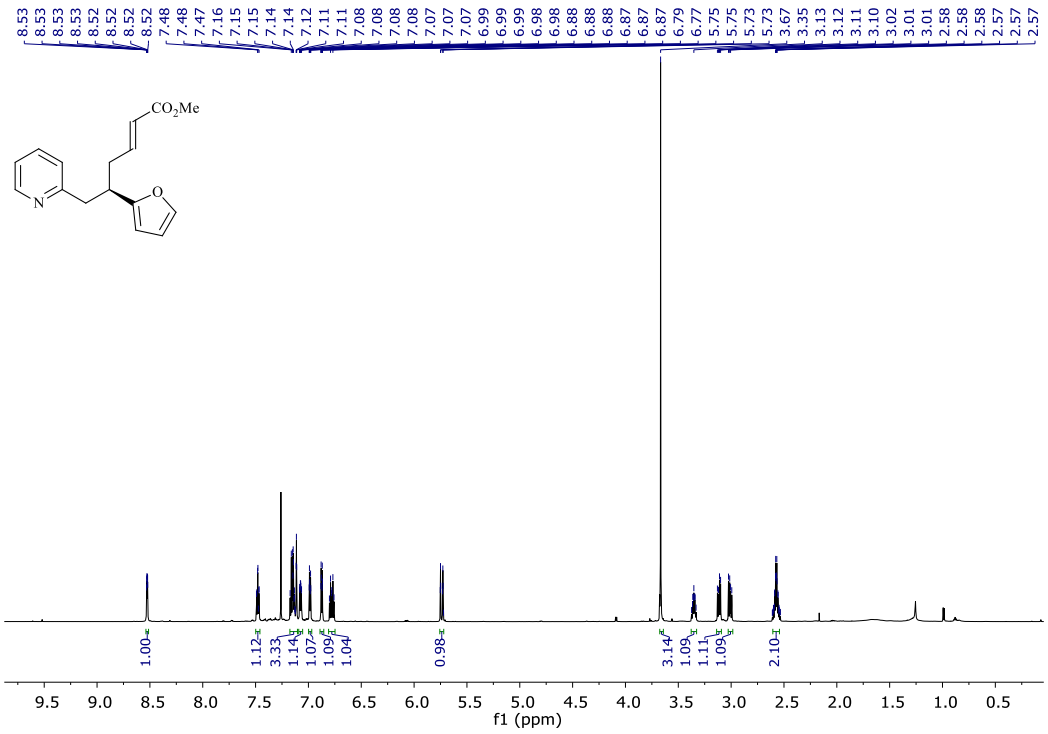


^{13}C NMR

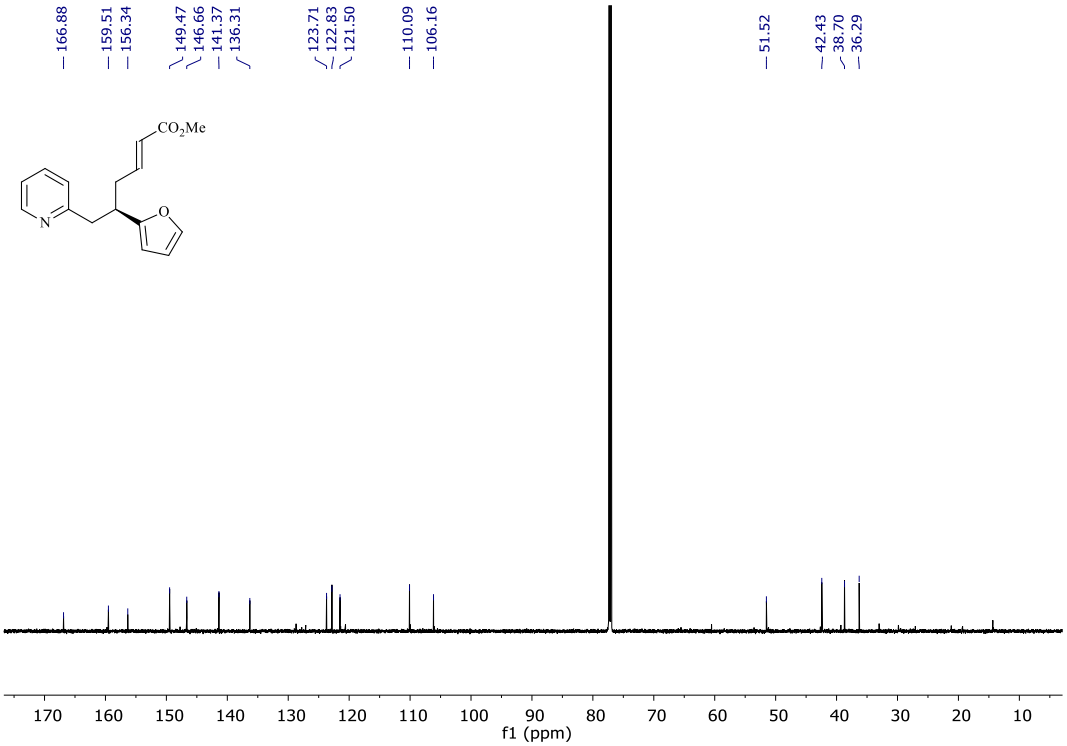


Methyl (*R*,*E*)-5-(furan-2-yl)-6-(pyridin-2-yl)hex-2-enoate (6g)

^{1}H NMR

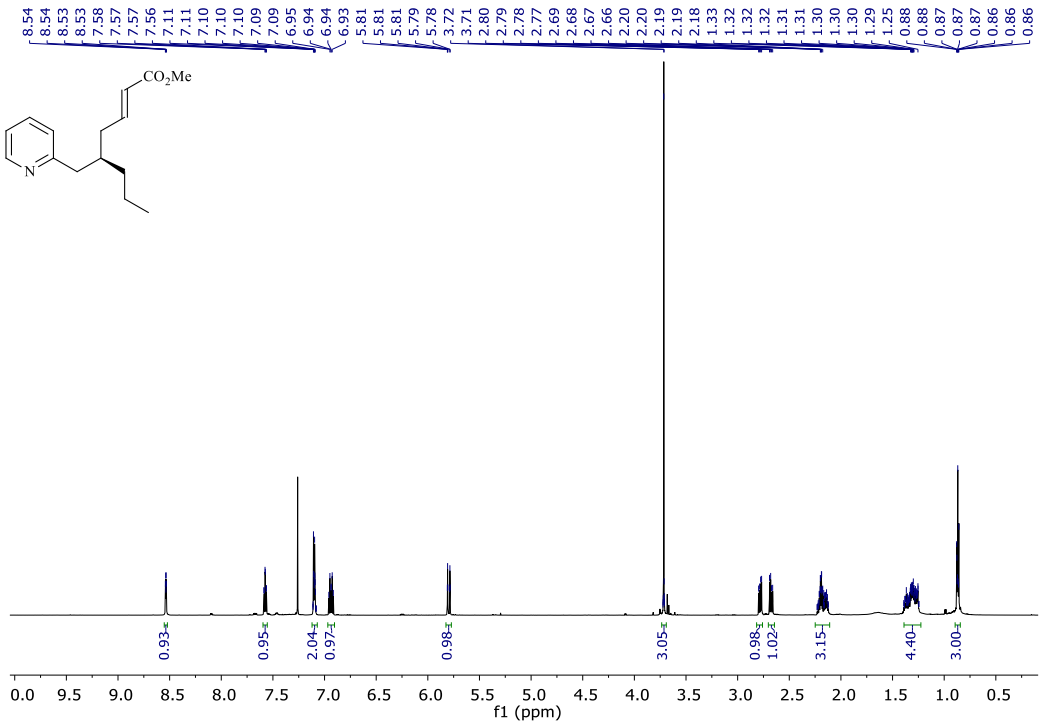


^{13}C NMR

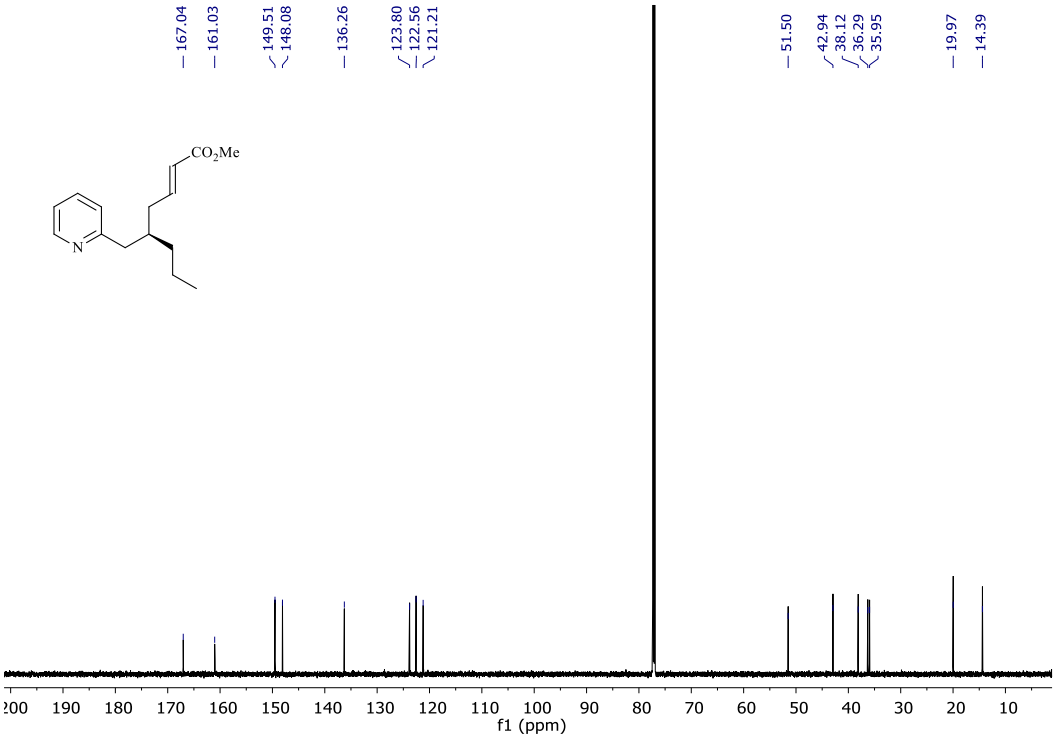


Methyl (*R*,*E*)-5-(pyridin-2-ylmethyl)oct-2-enoate (6h)

^{1}H NMR

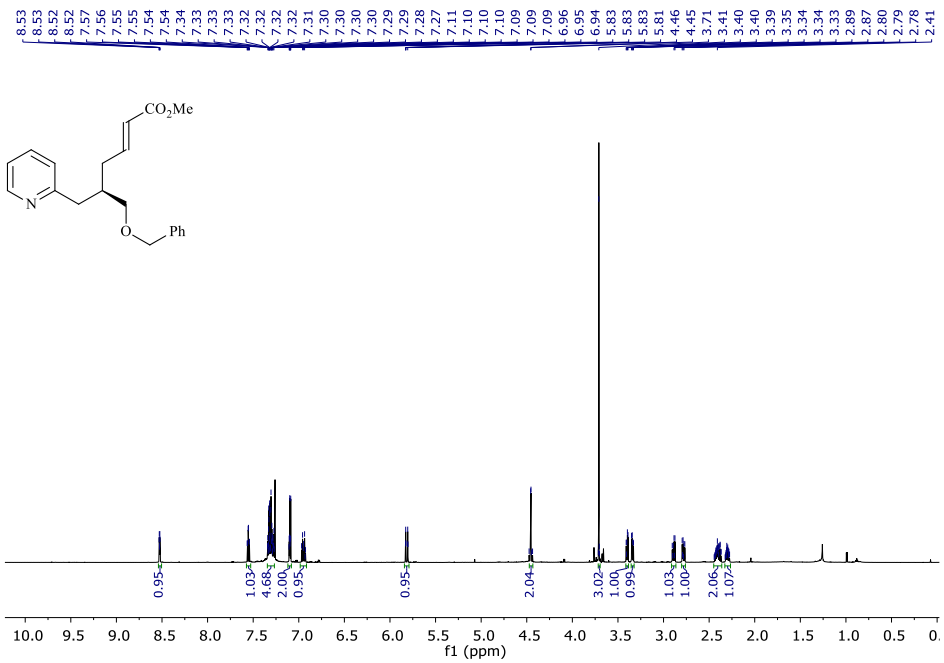


^{13}C NMR

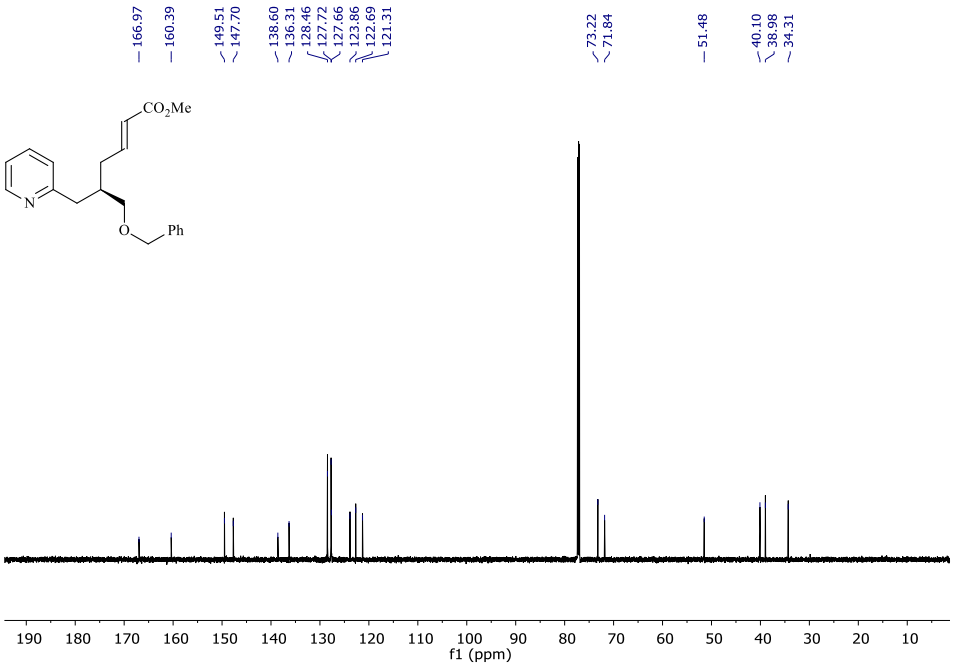


Methyl (*R*,*E*)-6-(benzyloxy)-5-(pyridin-2-ylmethyl)hex-2-enoate (6i)

^{1}H NMR

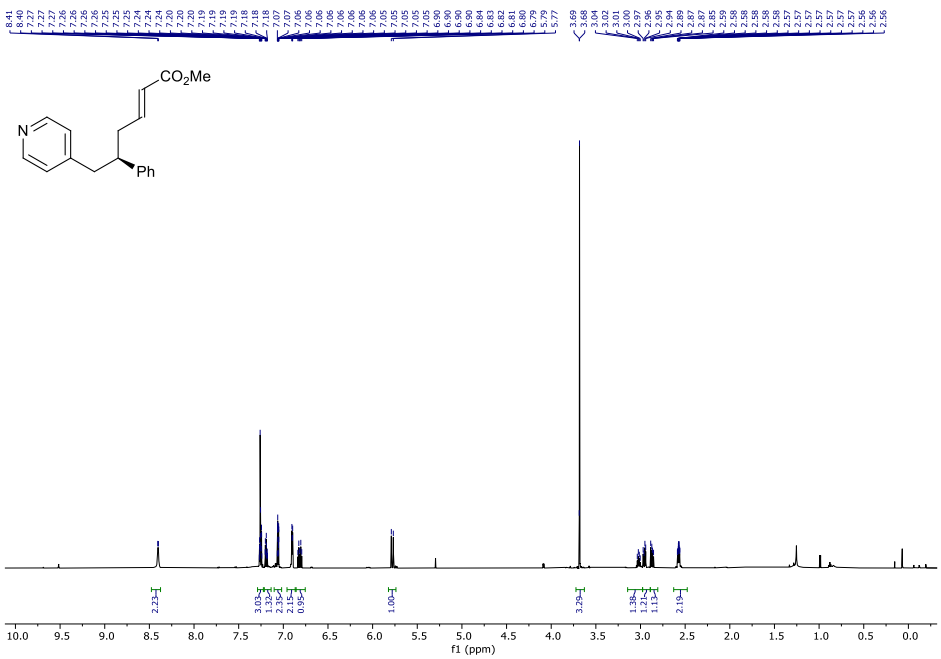


^{13}C NMR

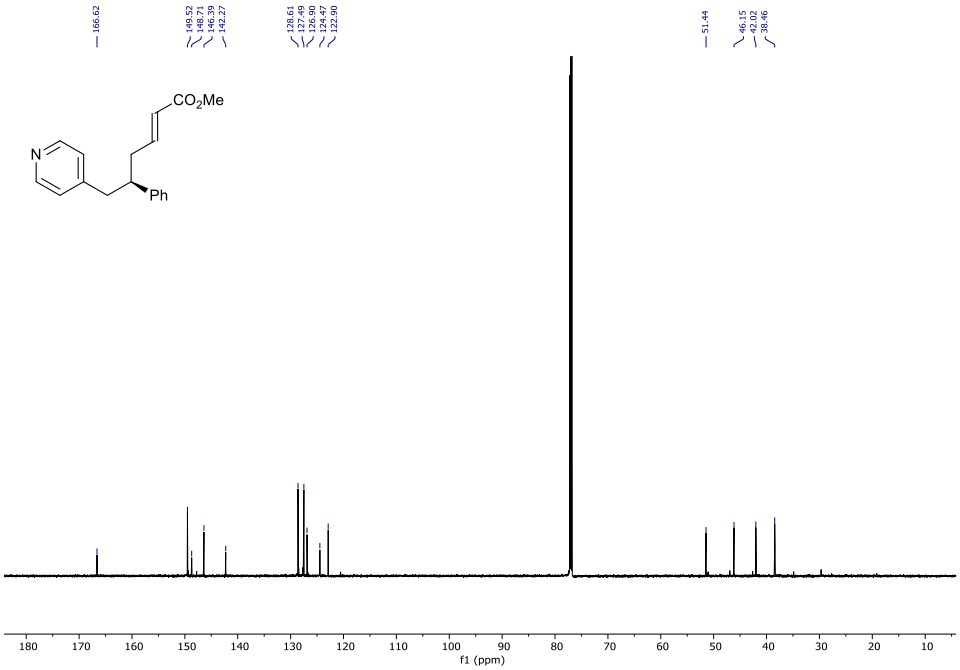


Methyl (*R*,*E*)-5-phenyl-6-(pyridin-4-yl)hex-2-enoate (6j)

^{1}H NMR

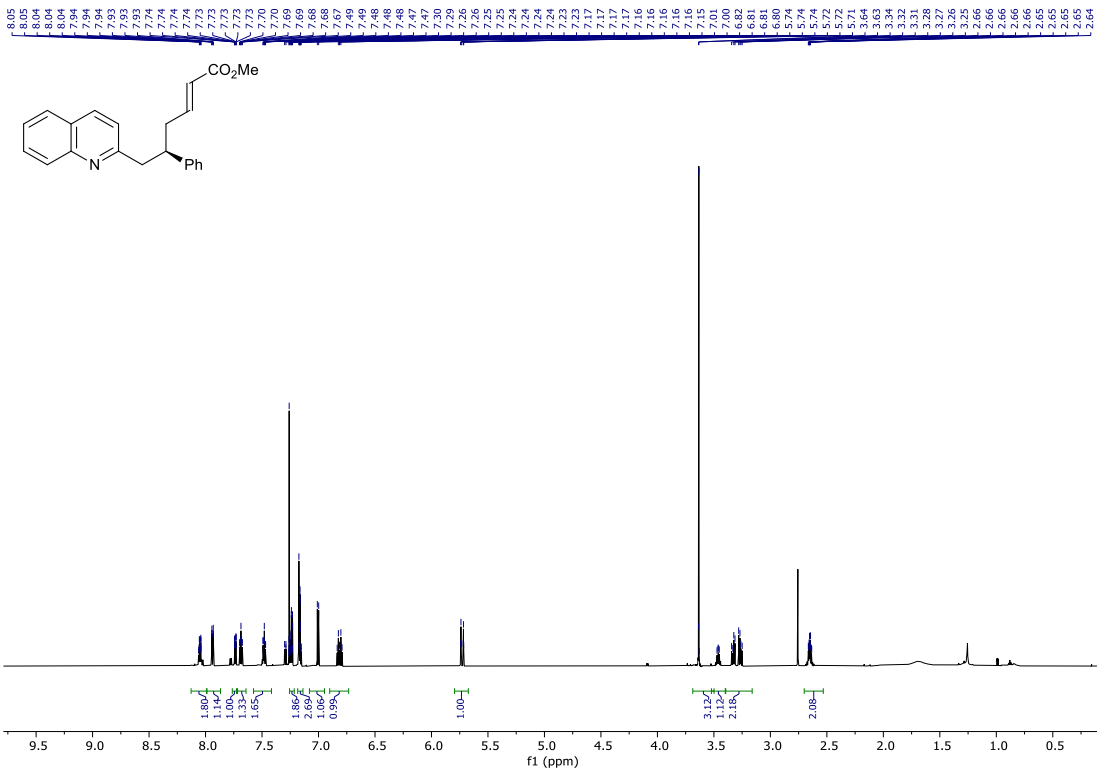


^{13}C NMR

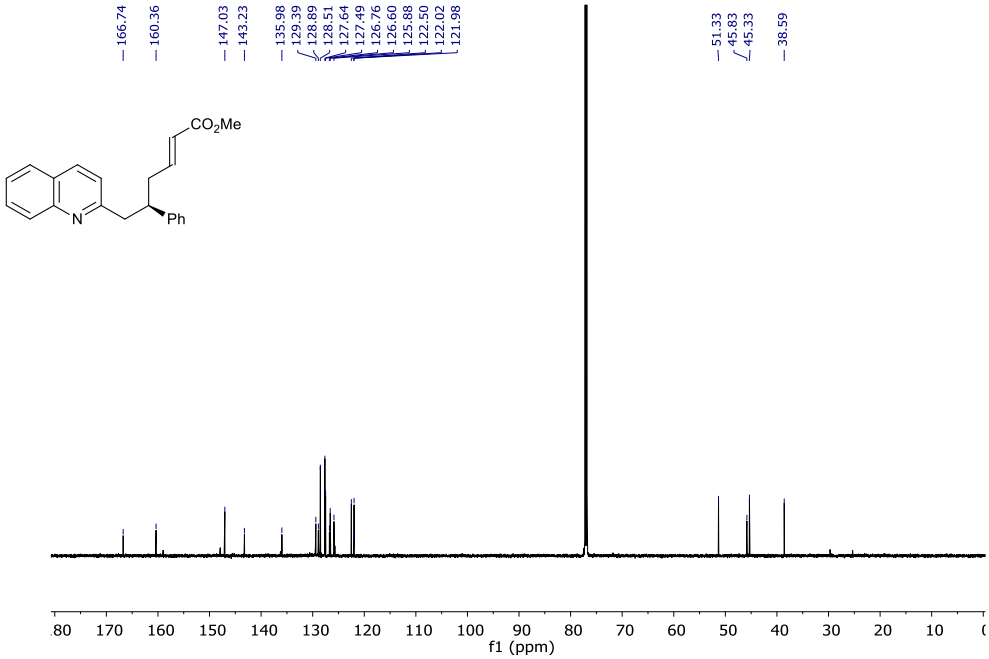


Methyl (*R*,*E*)-5-phenyl-6-(quinolin-2-yl)hex-2-enoate (6k)

1H NMR

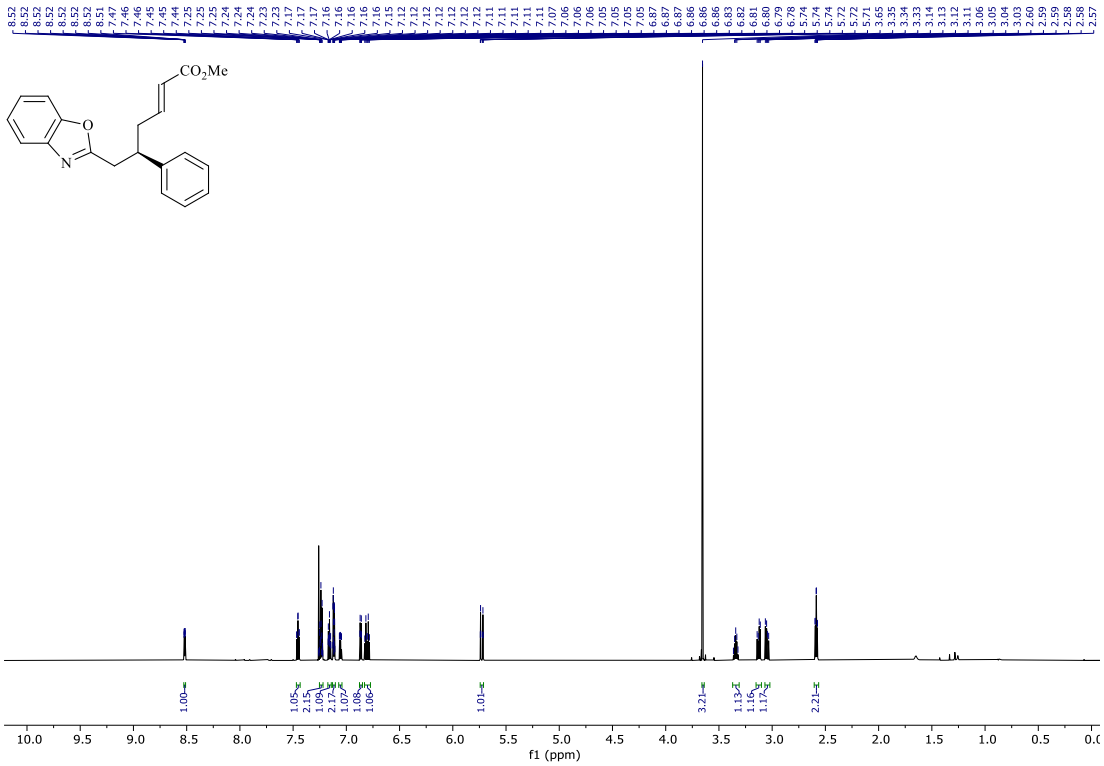


13C NMR

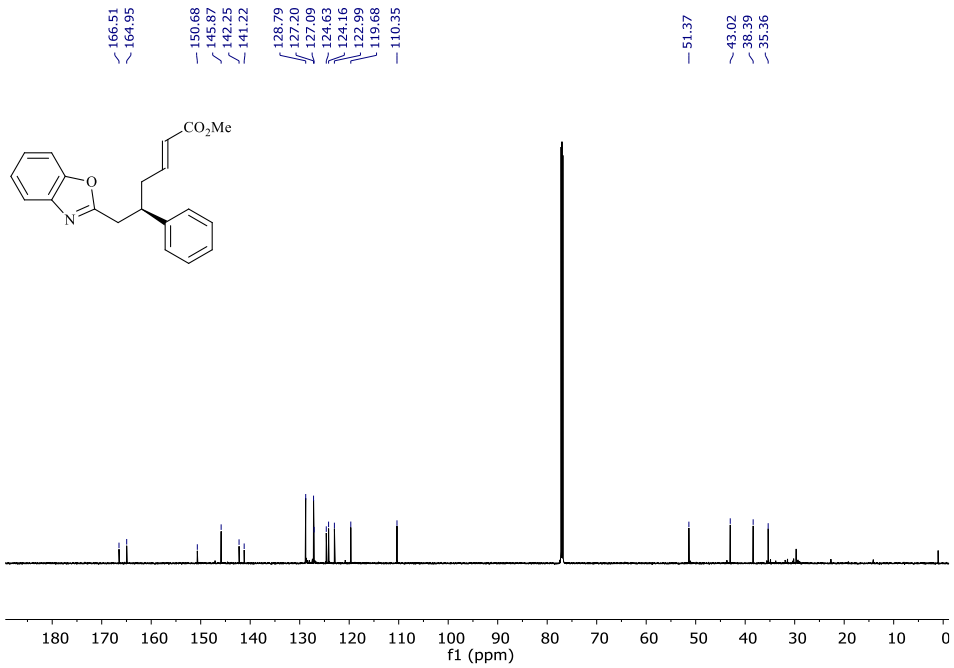


Methyl (*R*,*E*)-6-(benzo[d]oxazol-2-yl)-5-phenylhex-2-enoate (6l)

^{1}H NMR

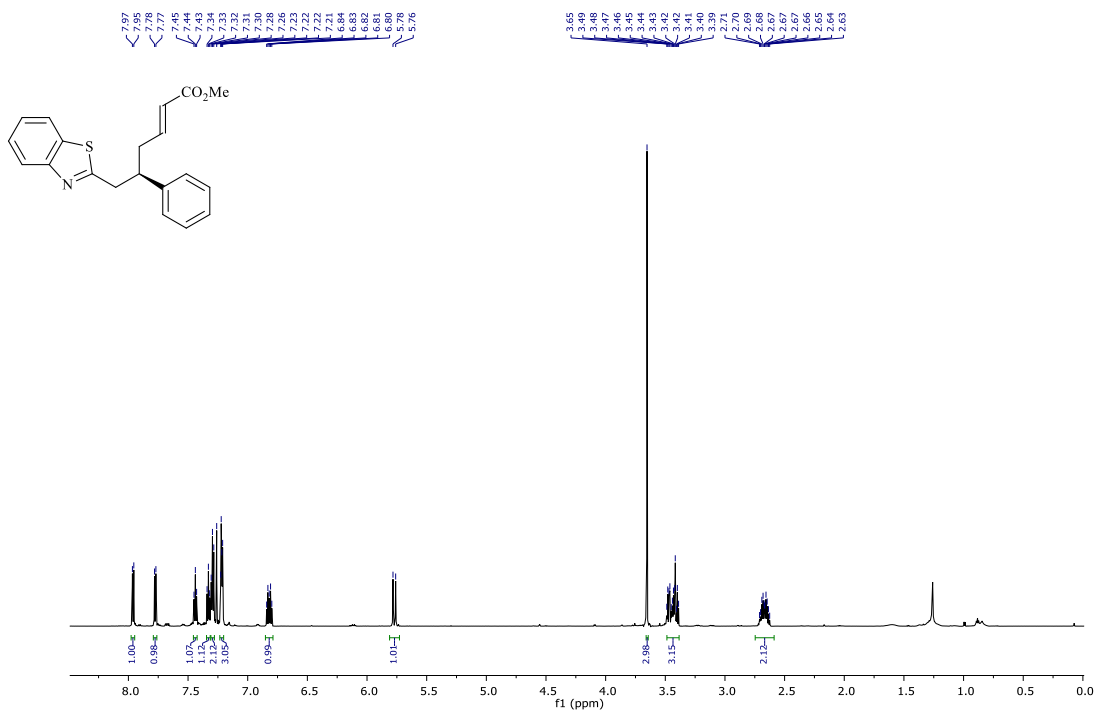


^{13}C NMR

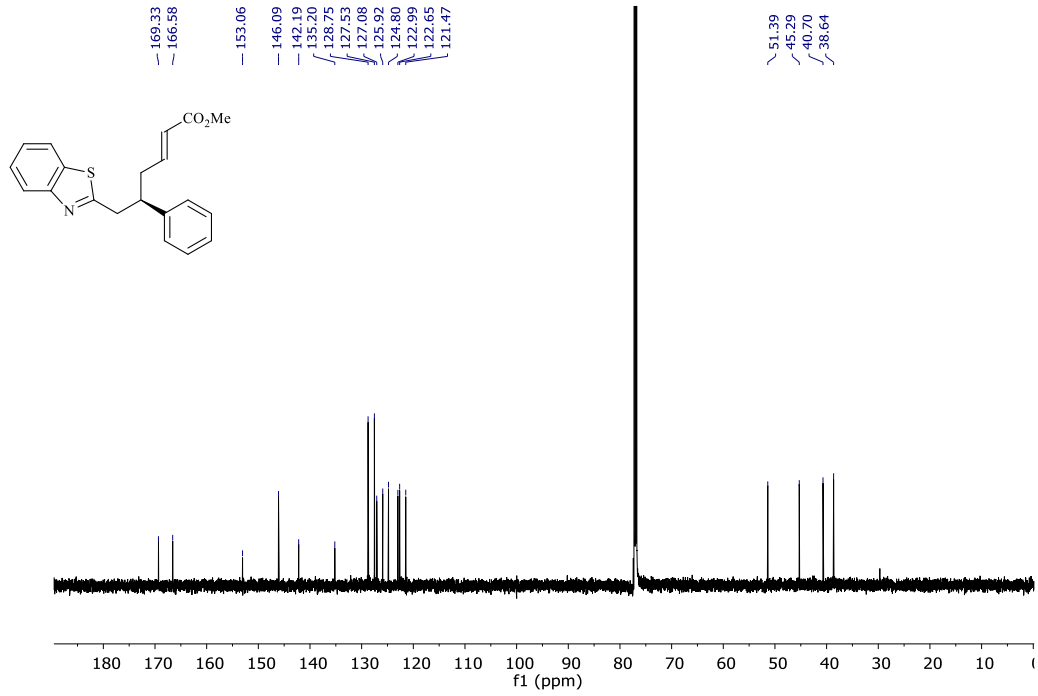


Methyl (*R*,*E*)-6-(benzo[*d*]thiazol-2-yl)-5-phenylhex-2-enoate (6m)

^{1}H NMR

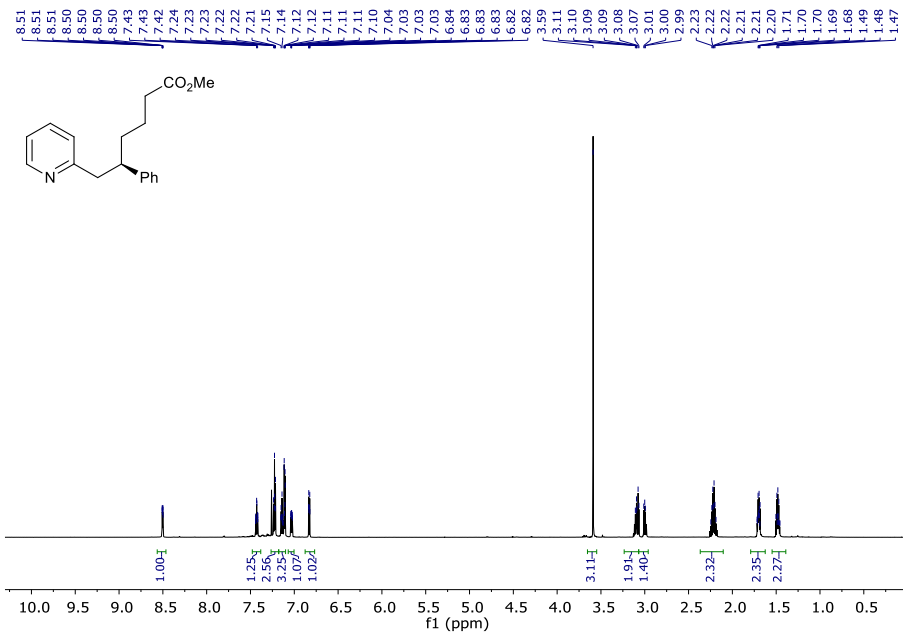


^{13}C NMR

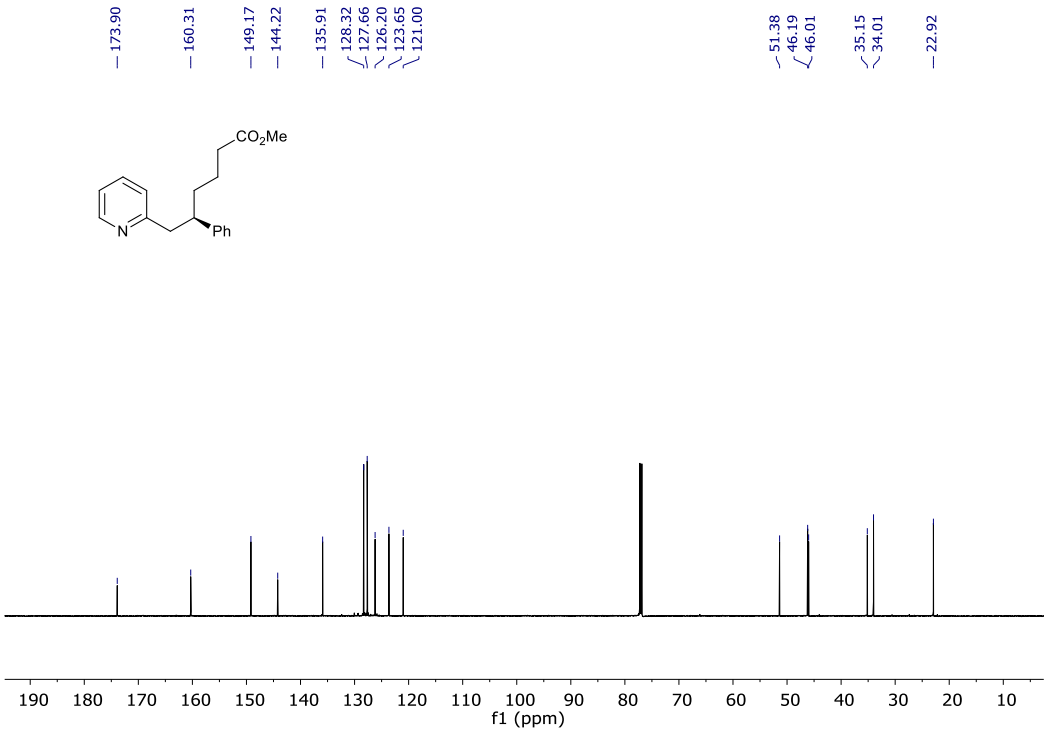


Methyl (*R*)-5-phenyl-6-(pyridin-2-yl)hexanoate 13

^{1}H NMR

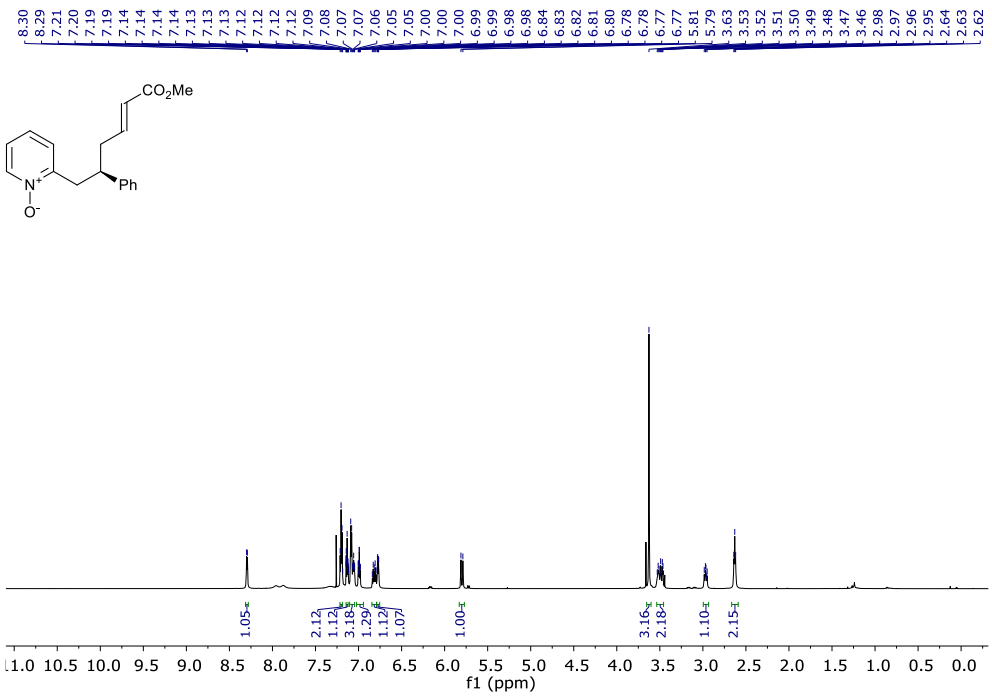


^{13}C NMR

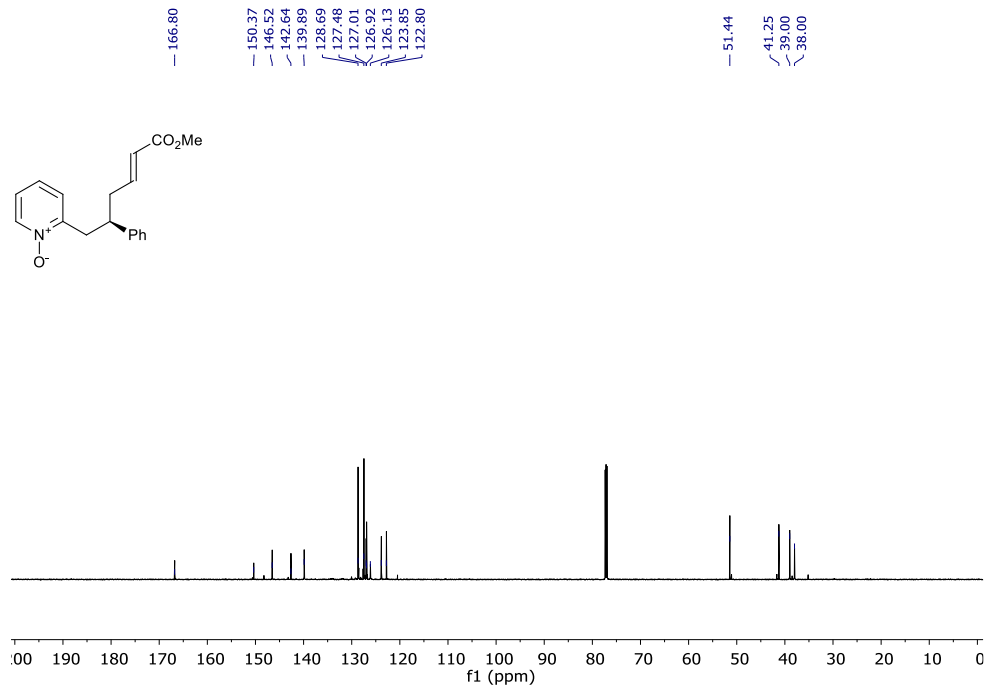


(*R*,*E*)-2-(6-Methoxy-6-oxo-2-phenylhex-4-en-1-yl)pyridine 1-oxide 14

^{1}H NMR

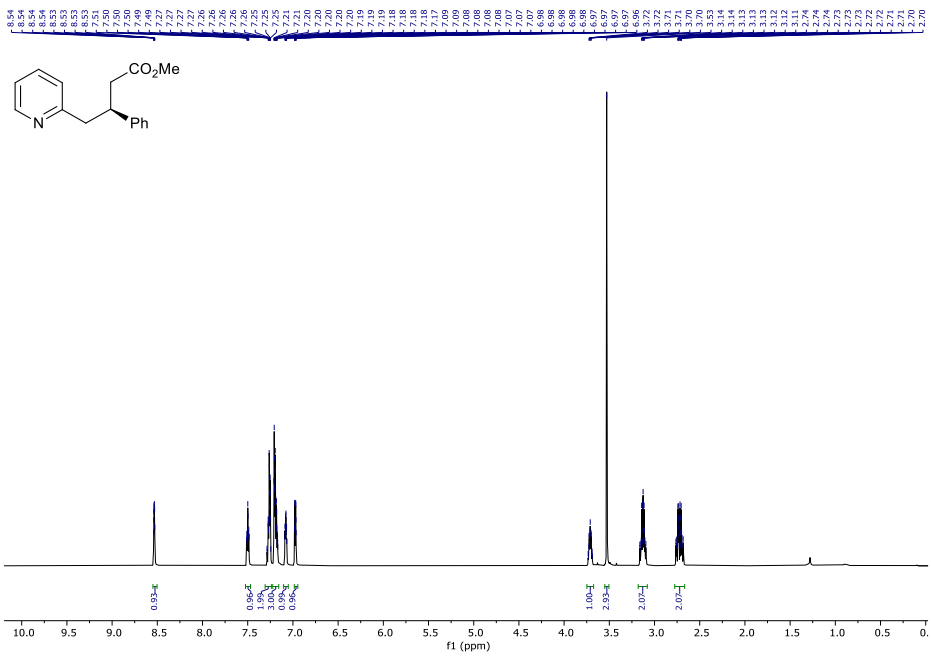


^{13} C NMR

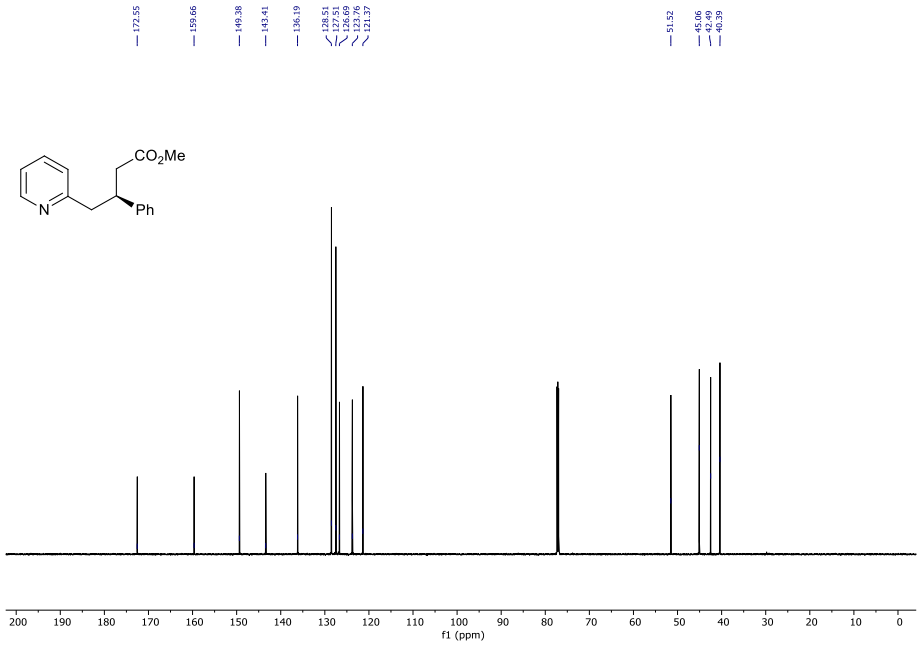


Methyl (*S*)-3-phenyl-4-(pyridin-2-yl)butanoate 15

^{1}H NMR

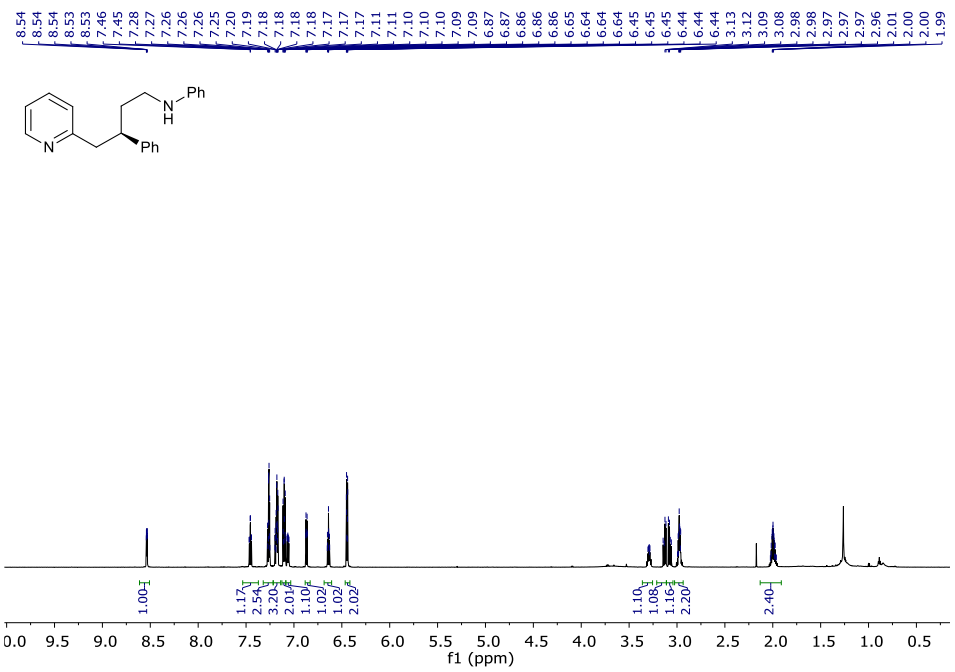


^{13}C NMR

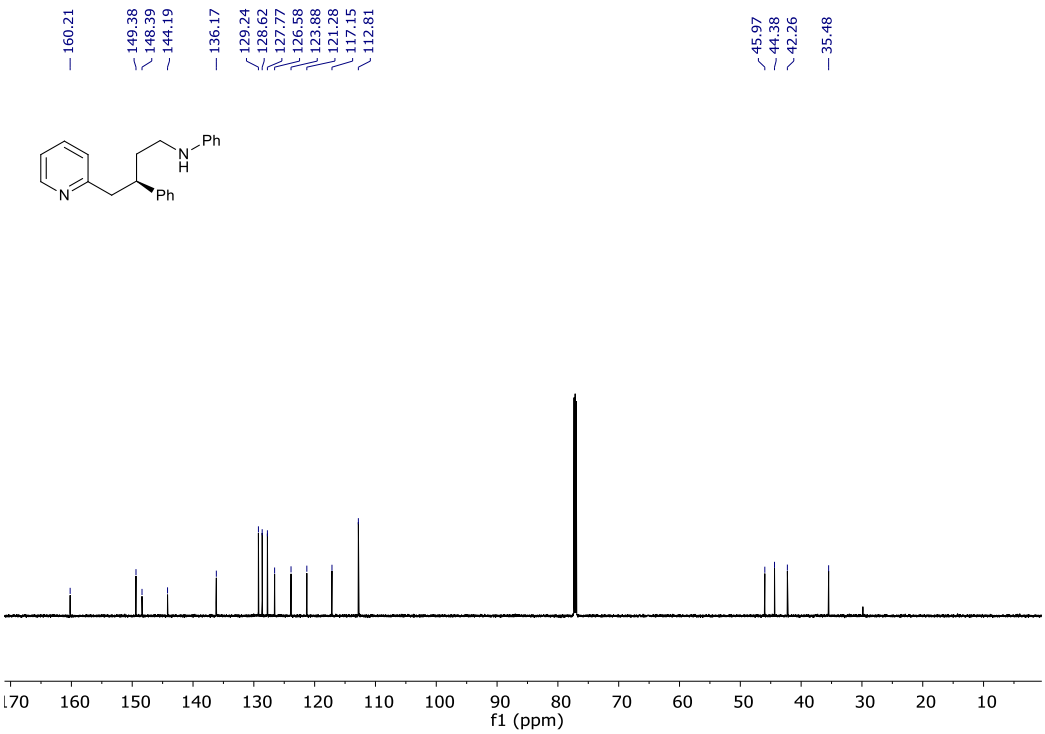


(*R*)-*N*-(3-Phenyl-4-(pyridin-2-yl)butyl)aniline 16

^{1}H NMR



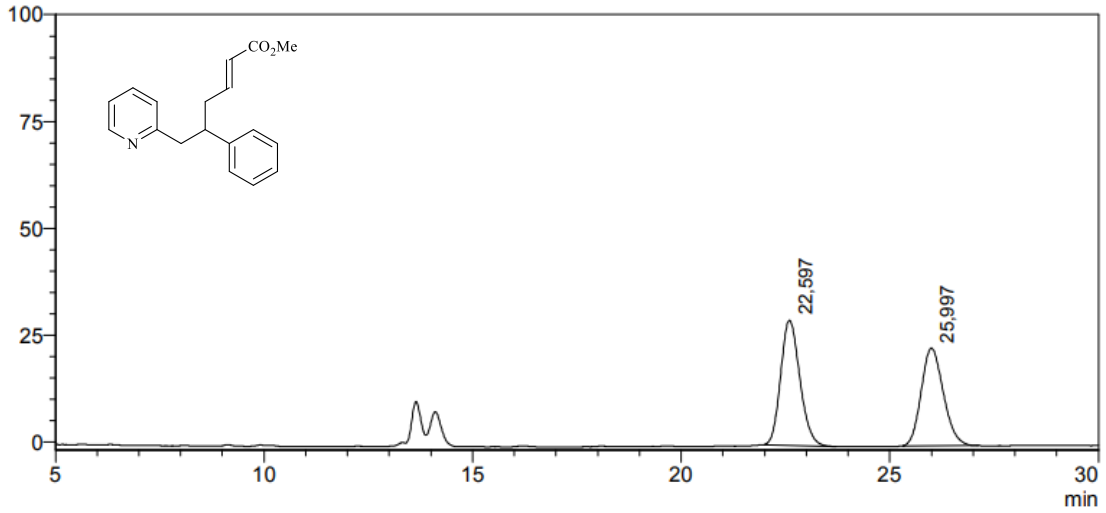
^{13}C NMR



9. HPLC Data

Methyl (*R*,*E*)-5-phenyl-6-(pyridin-2-yl)hex-2-enoate (6a)

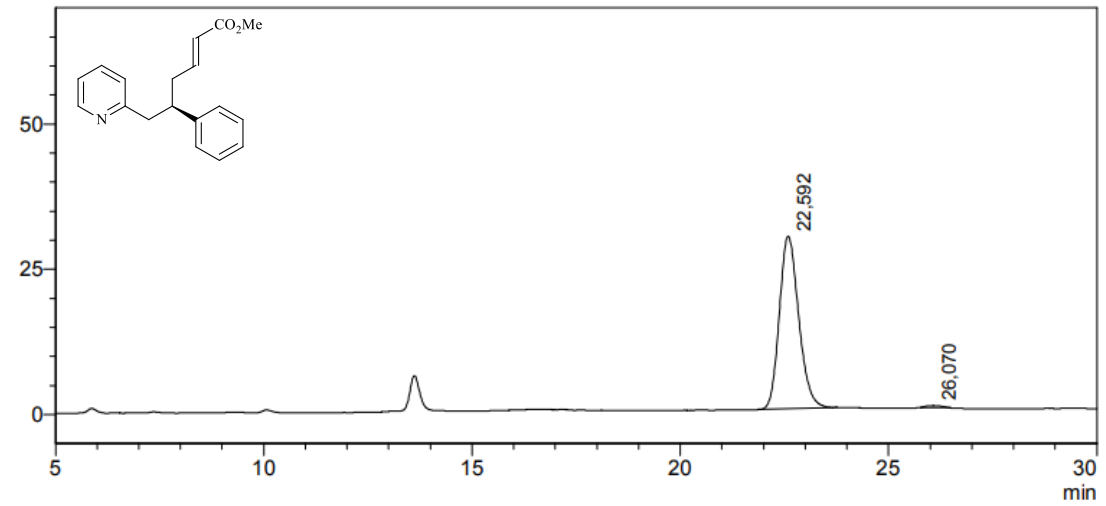
Racemic sample



PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	22,597	52,565
2	25,997	47,435
Total		100,000

Enantioenriched sample

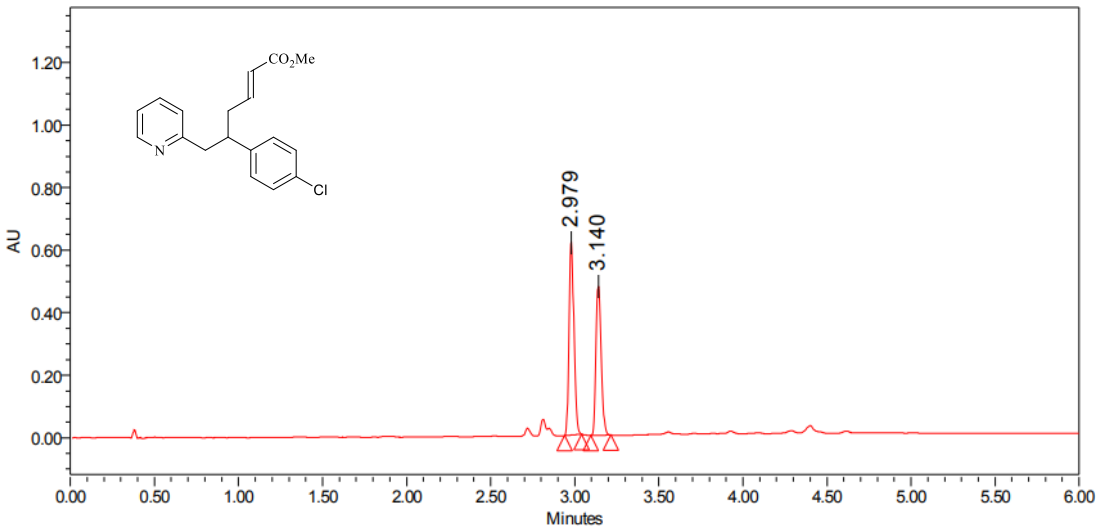


PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	22,592	99,090
2	26,070	0,910
Total		100,000

Methyl (*R*,*E*)-5-(4-chlorophenyl)-6-(pyridin-2-yl)hex-2-enoate (6b)

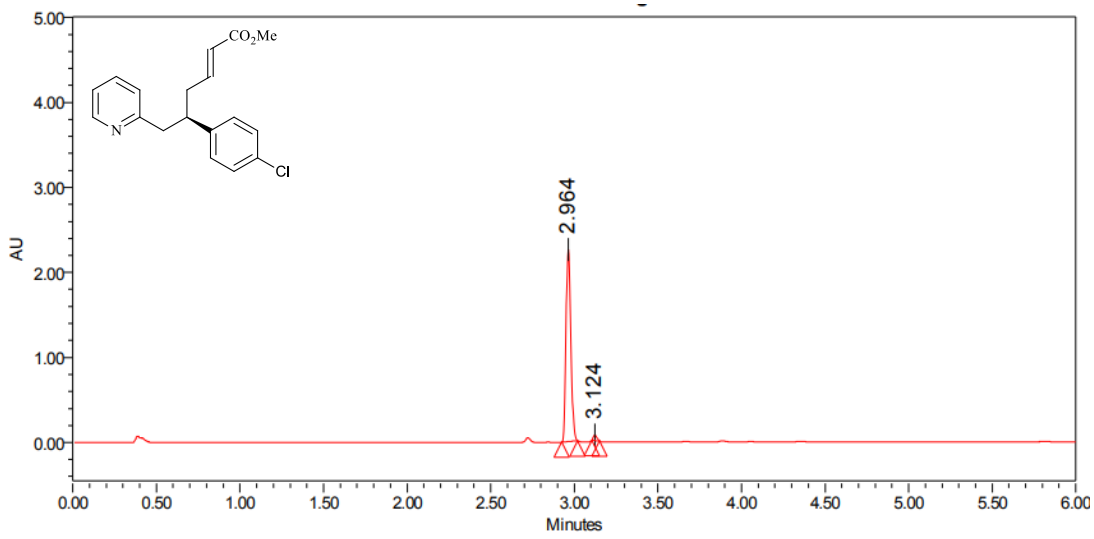
Racemic sample



Peak Results

	RT	% Area
1	2.979	55.02
2	3.140	44.98

Enantioenriched sample

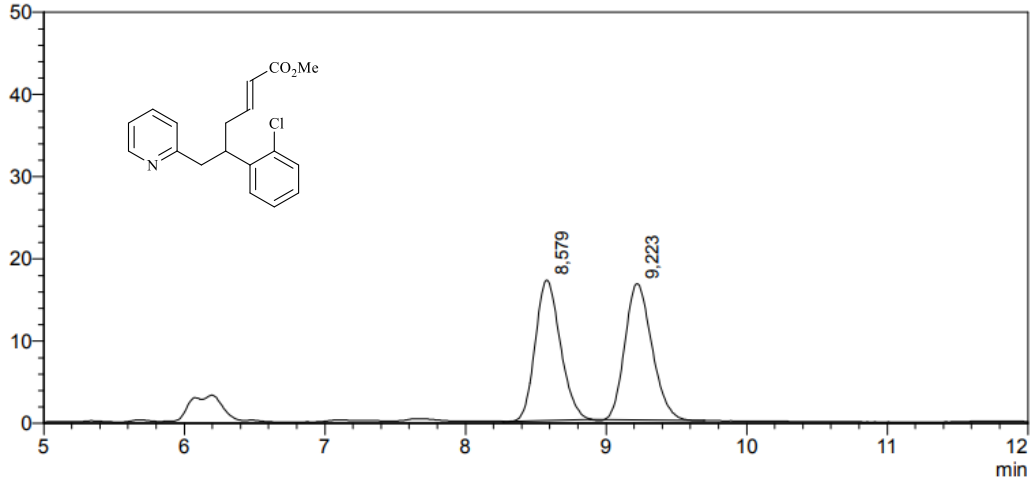


Peak Results

	RT	% Area
1	2.964	97.83
2	3.124	2.17

Methyl (*R*,*E*)-5-(3-chlorophenyl)-6-(pyridin-2-yl)hex-2-enoate (6c)

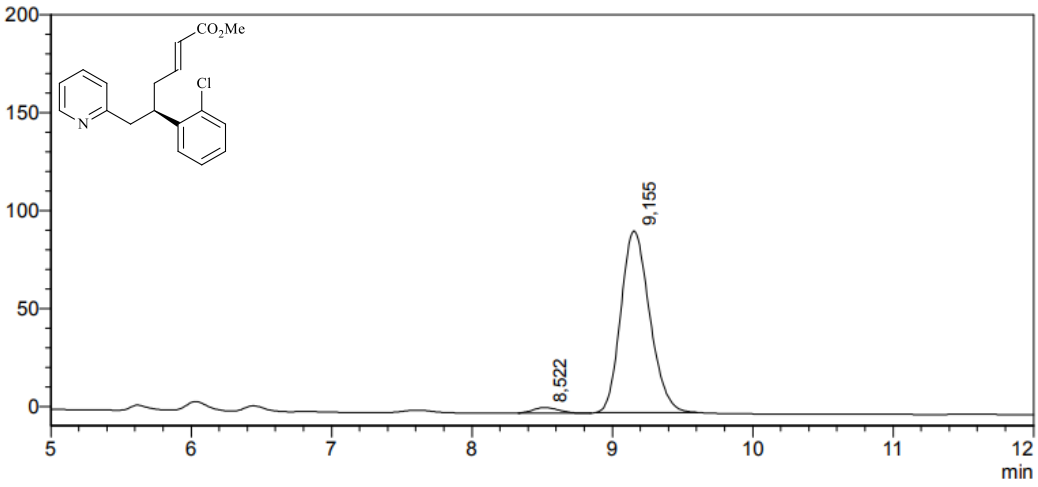
Racemic sample



PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8,579	48,957
2	9,223	51,043
Total		100,000

Enantioenriched sample

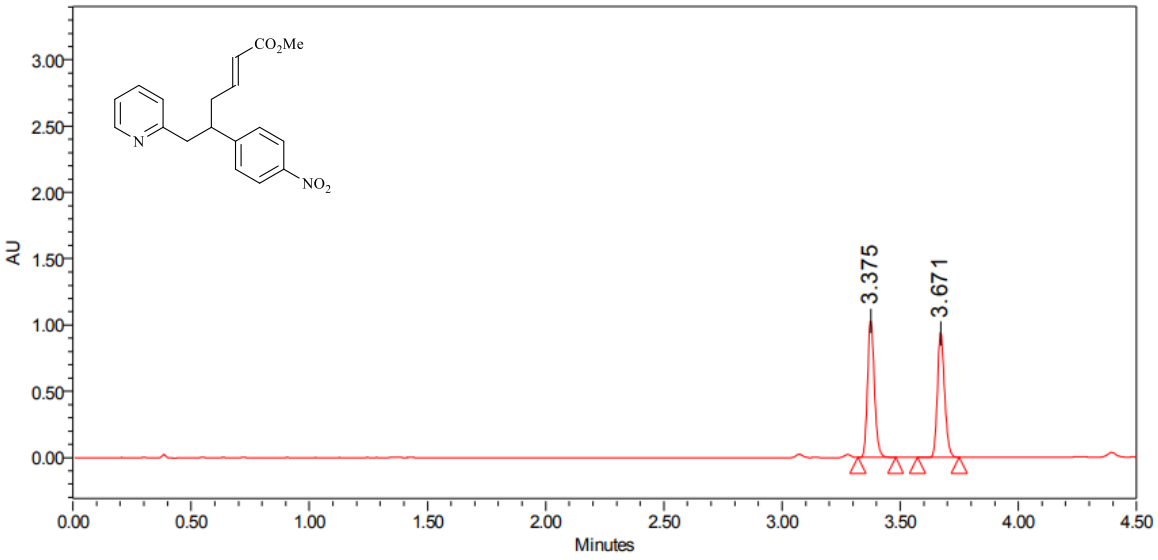


PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	8,522	2,533
2	9,155	97,467
Total		100,000

Methyl (*R*,*E*)-5-(4-nitrophenyl)-6-(pyridin-2-yl)hex-2-enoate (6d)

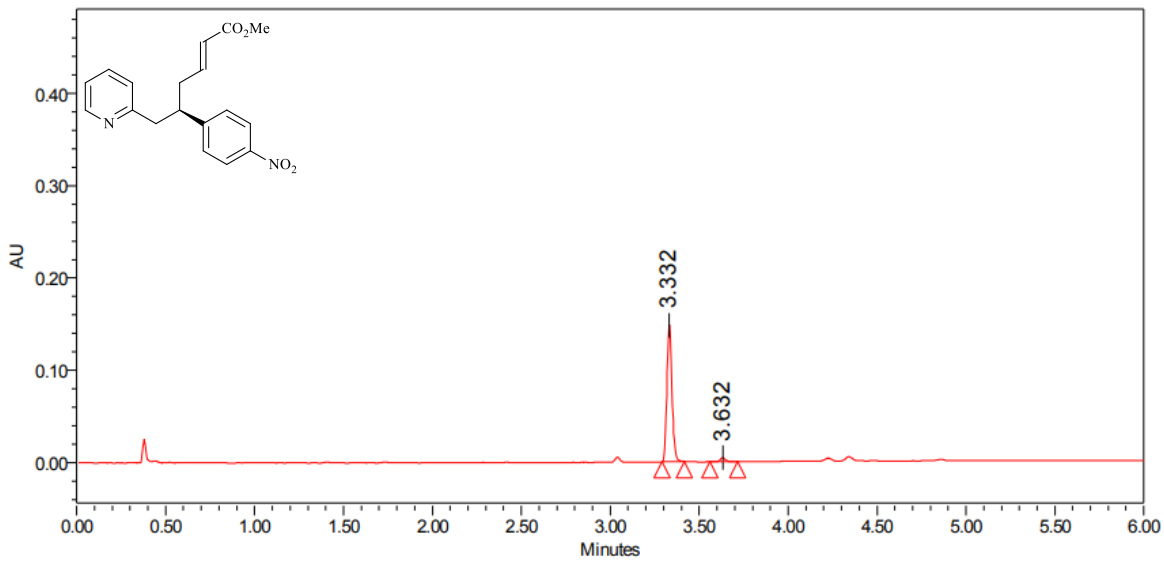
Racemic sample



Peak Results

	RT	% Area
1	3.375	51.27
2	3.671	48.73

Enantioenriched sample

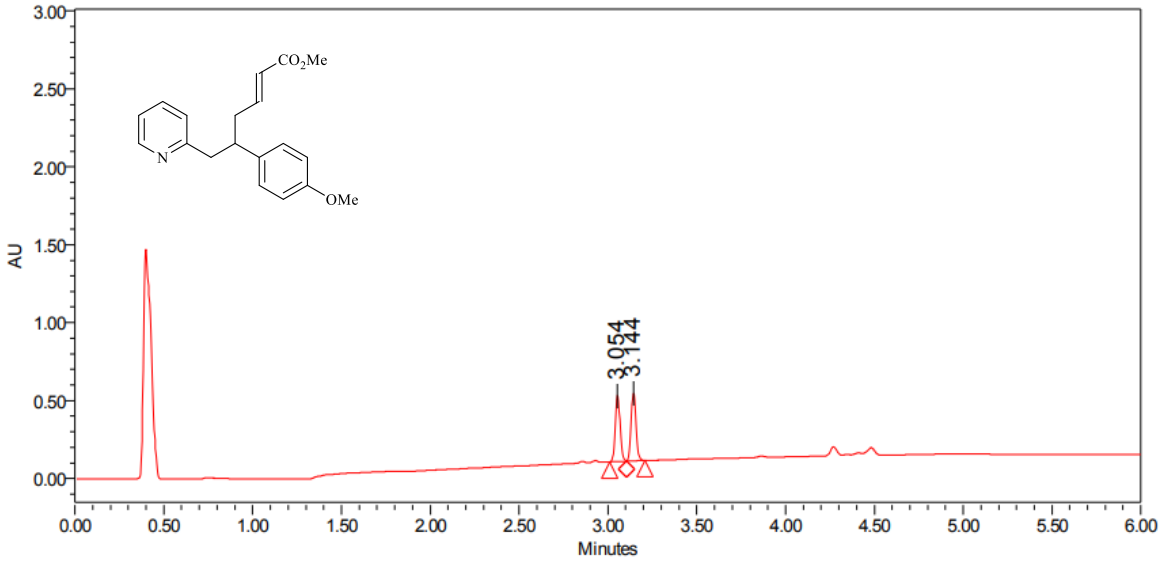


Peak Results

	RT	% Area
1	3.332	97.10
2	3.632	2.90

Methyl (*R*,*E*)-5-(4-methoxyphenyl)-6-(pyridin-2-yl)hex-2-enoate (6e)

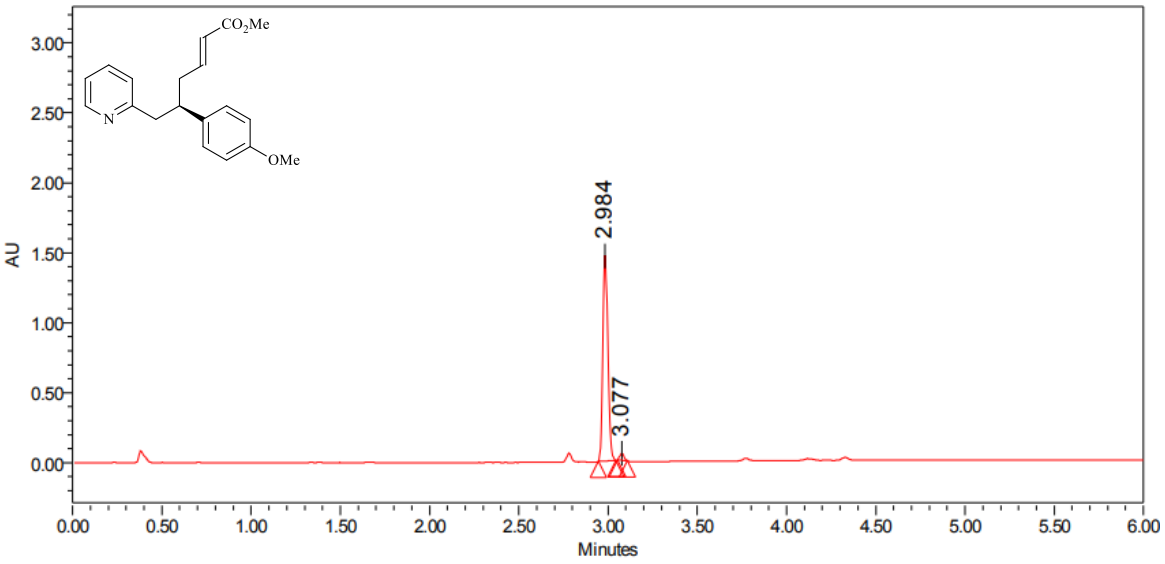
Racemic sample



Peak Results

	RT	% Area
1	3.054	48.98
2	3.144	51.02

Enantioenriched sample

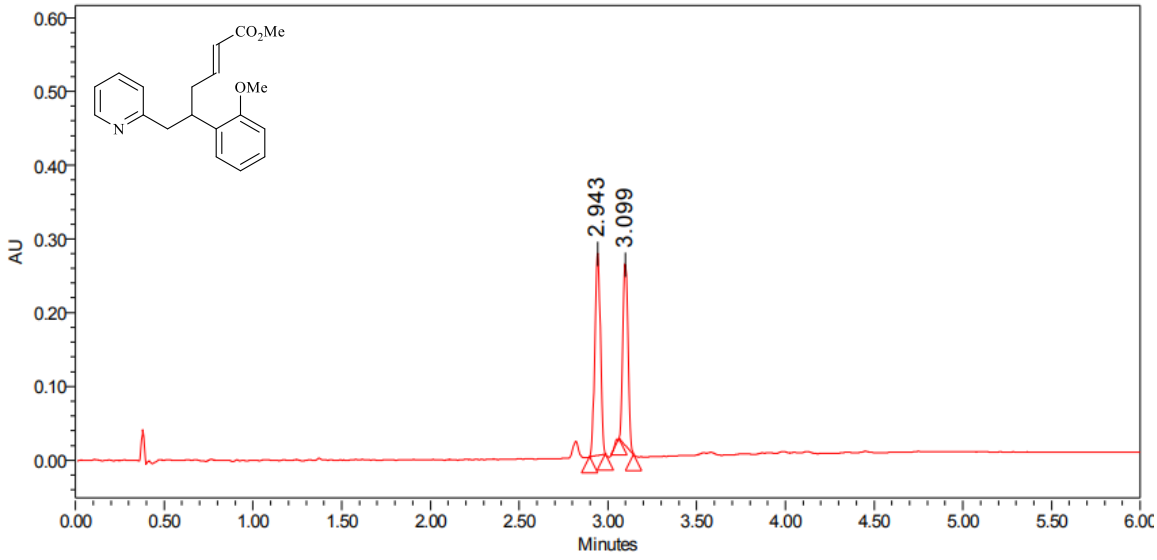


Peak Results

	RT	% Area
1	2.984	97.25
2	3.077	2.75

Methyl (*R*,*E*)-5-(2-methoxyphenyl)-6-(pyridin-2-yl)hex-2-enoate (6f)

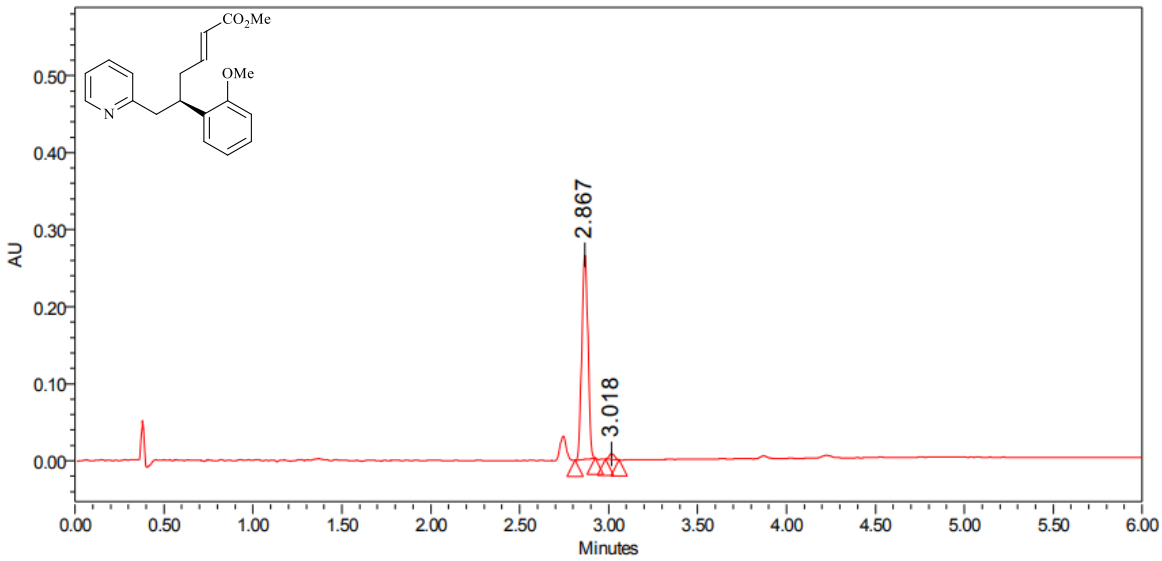
Racemic sample



Peak Results

	RT	% Area
1	2.943	54.46
2	3.099	45.54

Enantioenriched sample

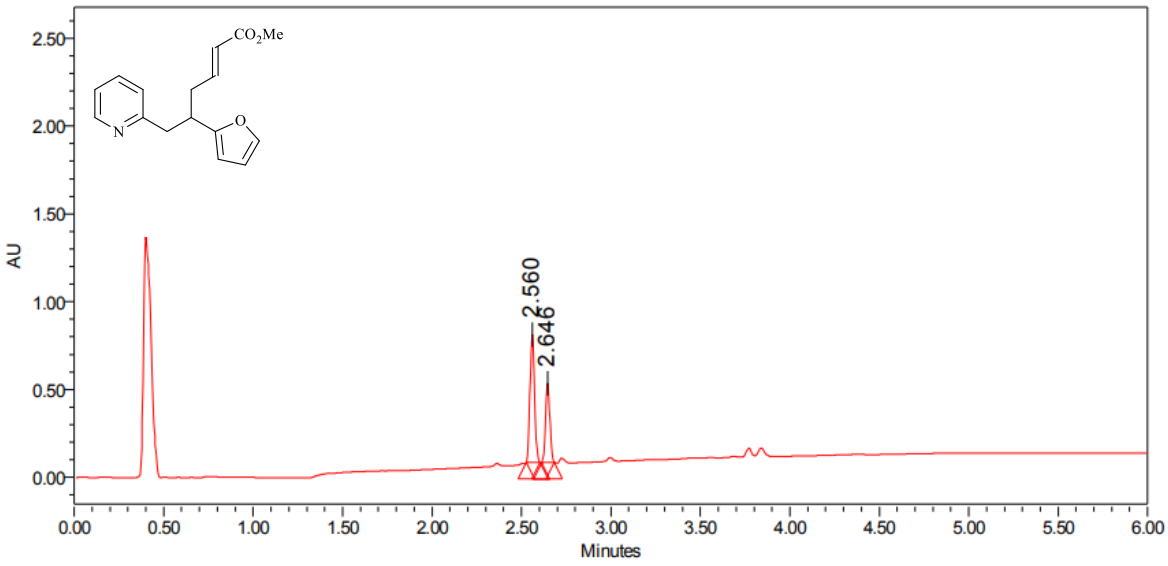


Peak Results

	RT	% Area
1	2.867	97.57
2	3.018	2.43

Methyl (*R*,*E*)-5-(furan-2-yl)-6-(pyridin-2-yl)hex-2-enoate (6g)

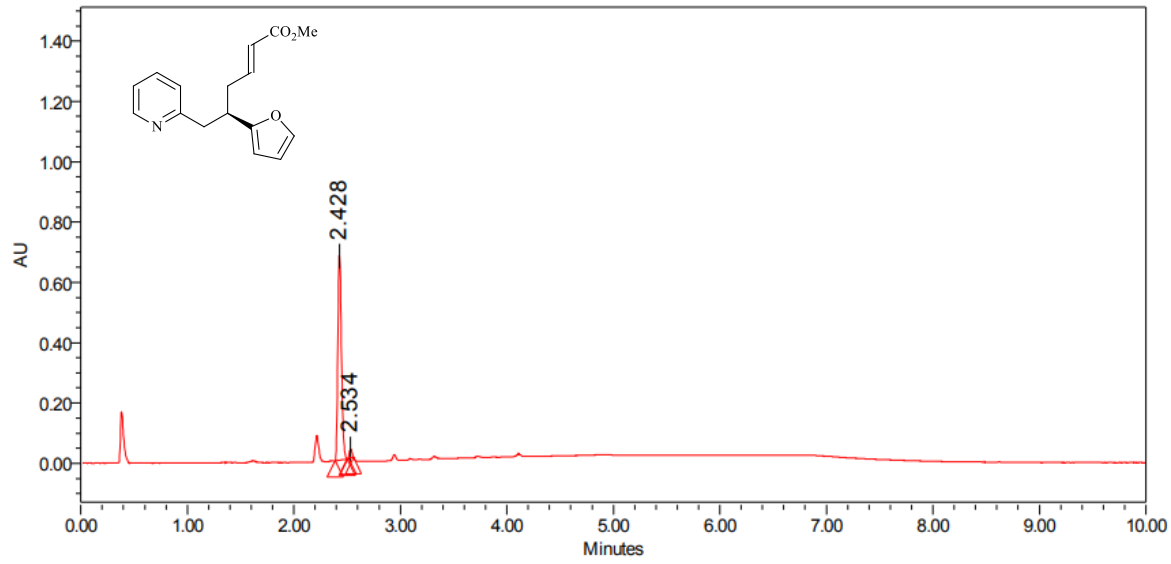
Racemic sample



Peak Results

	RT	% Area
1	2.560	62.93
2	2.646	37.07

Enantioenriched sample

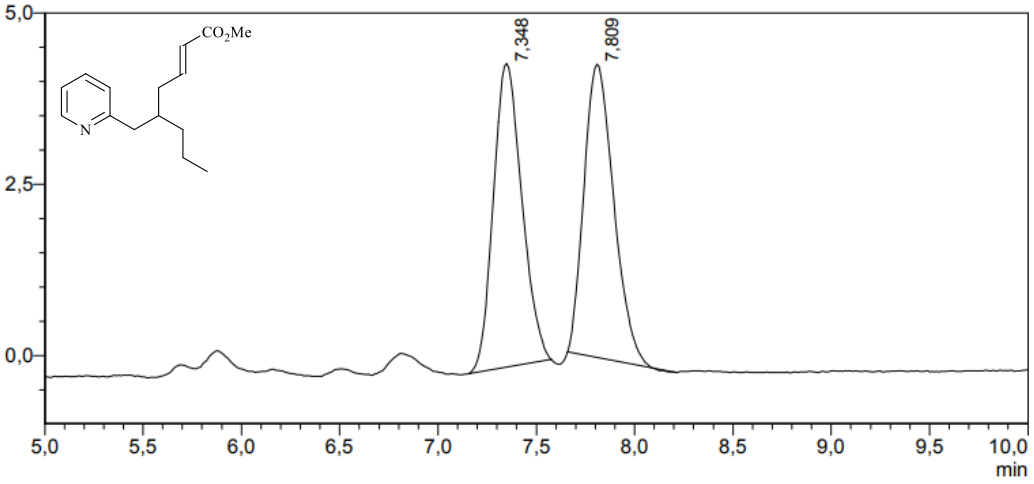


Peak Results

	RT	% Area
1	2.428	97.11
2	2.534	2.89

Methyl (*R*,*E*)-5-(pyridin-2-ylmethyl)oct-2-enoate (6h)

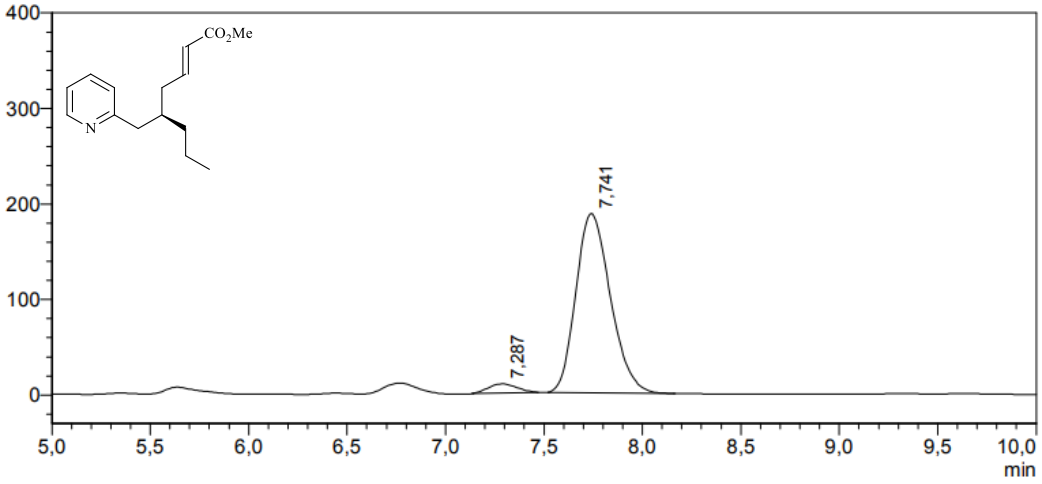
Racemic sample



PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7,348	49,986
2	7,809	50,014
Total		100,000

Enantioenriched sample

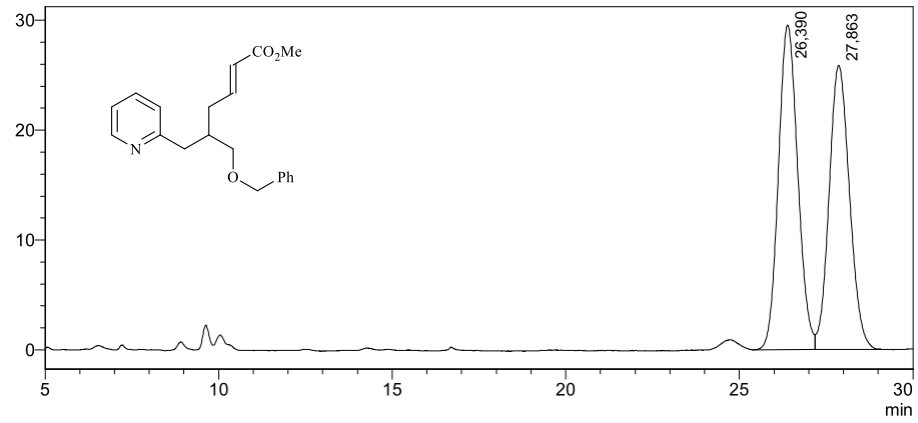


PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	7,287	4,058
2	7,741	95,942
Total		100,000

Methyl (*R*,*E*)-6-(benzyloxy)-5-(pyridin-2-ylmethyl)hex-2-enoate (6i)

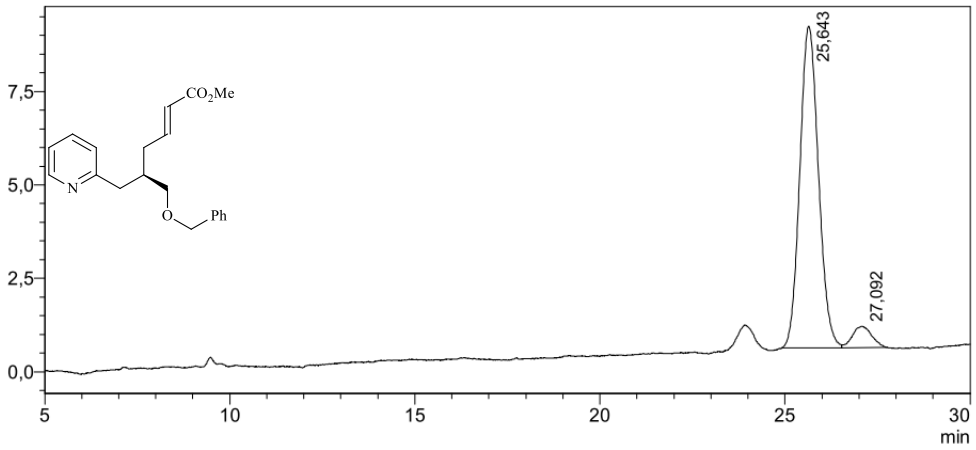
Racemic sample



PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	26,390	52,031
2	27,863	47,969
Total		100,000

Enantioenriched sample

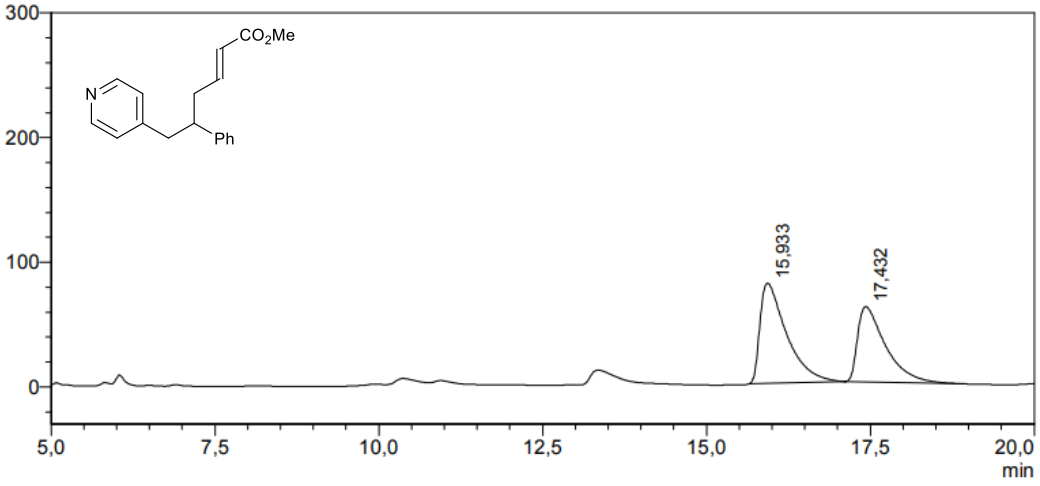


PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	25,643	93,544
2	27,092	6,456
Total		100,000

Methyl (*R*,*E*)-5-phenyl-6-(pyridin-4-yl)hex-2-enoate (6j)

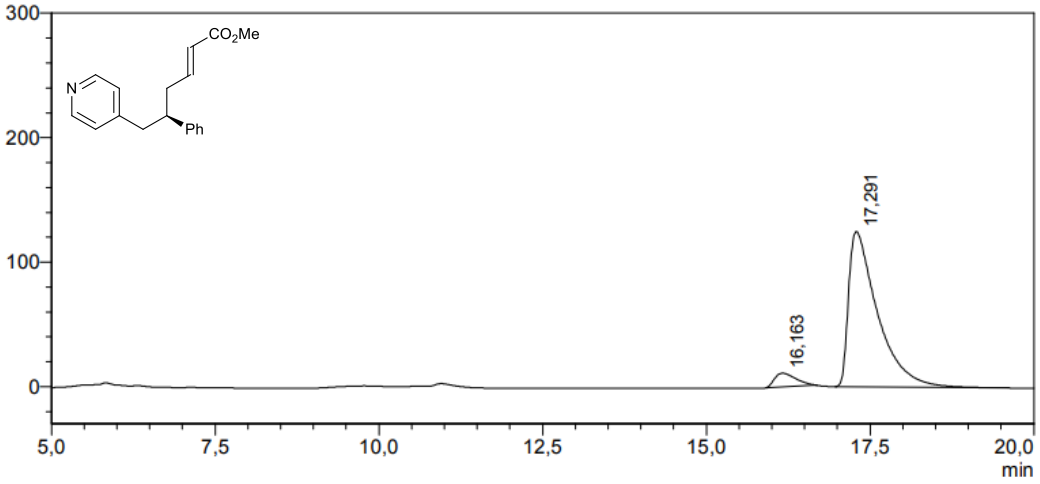
Racemic sample



PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	15,933	55,797
2	17,432	44,203
Total		100,000

Enantioenriched sample

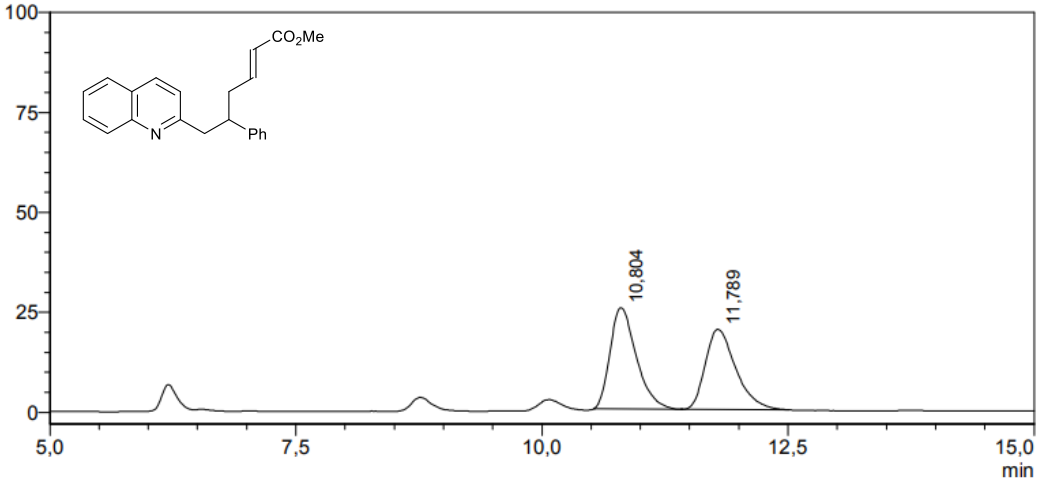


PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	16,163	6,039
2	17,291	93,961
Total		100,000

Methyl (*R*,*E*)-5-phenyl-6-(quinolin-2-yl)hex-2-enoate (6k)

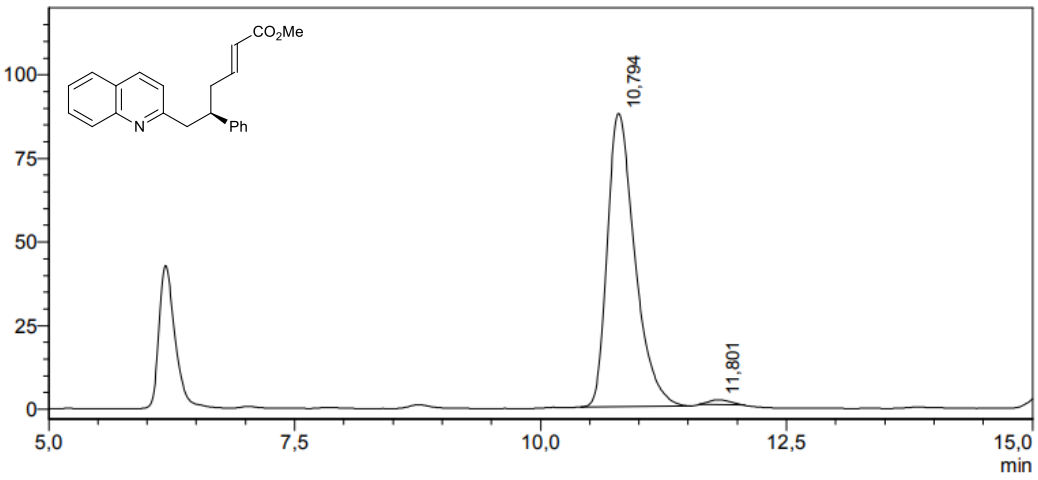
Racemic sample



PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	10,804	52,013
2	11,789	47,987
Total		100,000

Enantioenriched sample

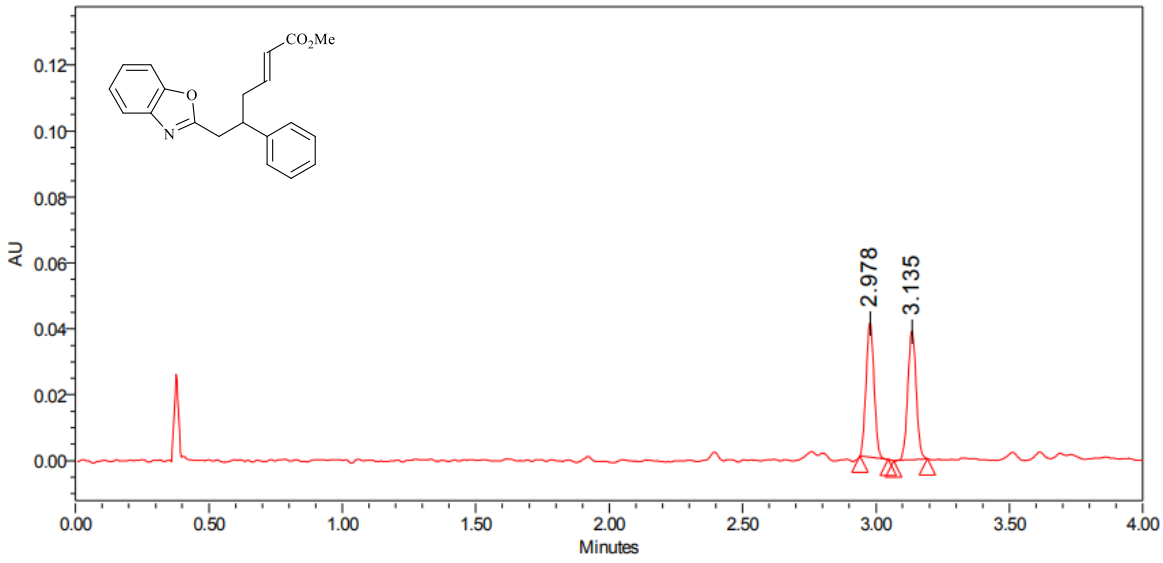


PDA Ch1 254nm

Peak#	Ret. Time	Area%
1	10,794	98,680
2	11,801	1,320
Total		100,000

Methyl (*R*,*E*)-6-(benzo[d]oxazol-2-yl)-5-phenylhex-2-enoate (6l)

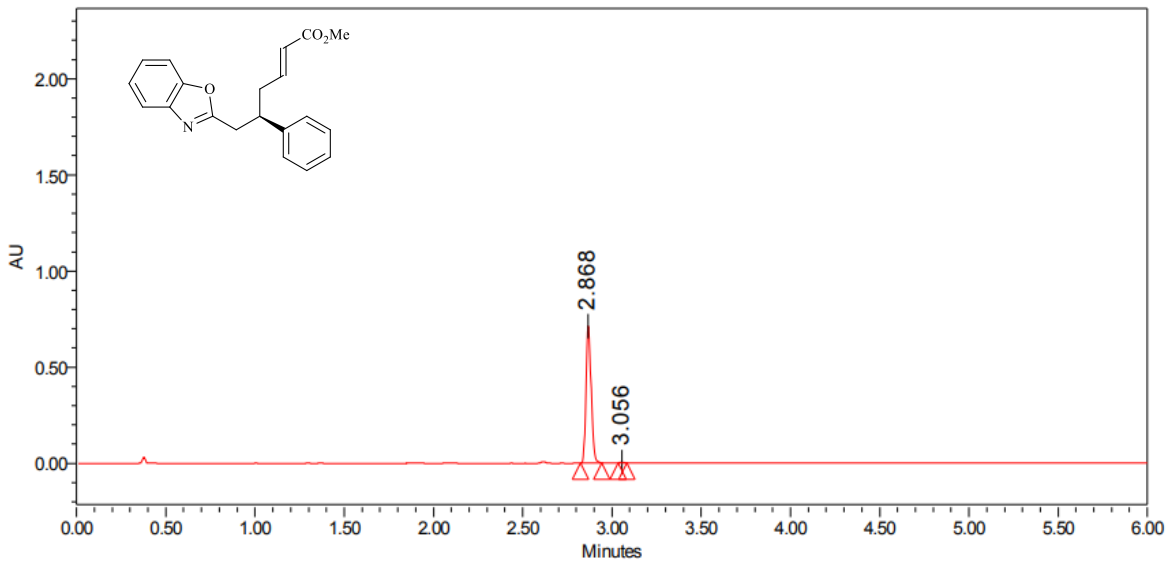
Racemic sample



Peak Results

	RT	% Area
1	2.978	49.80
2	3.135	50.20

Enantioenriched sample

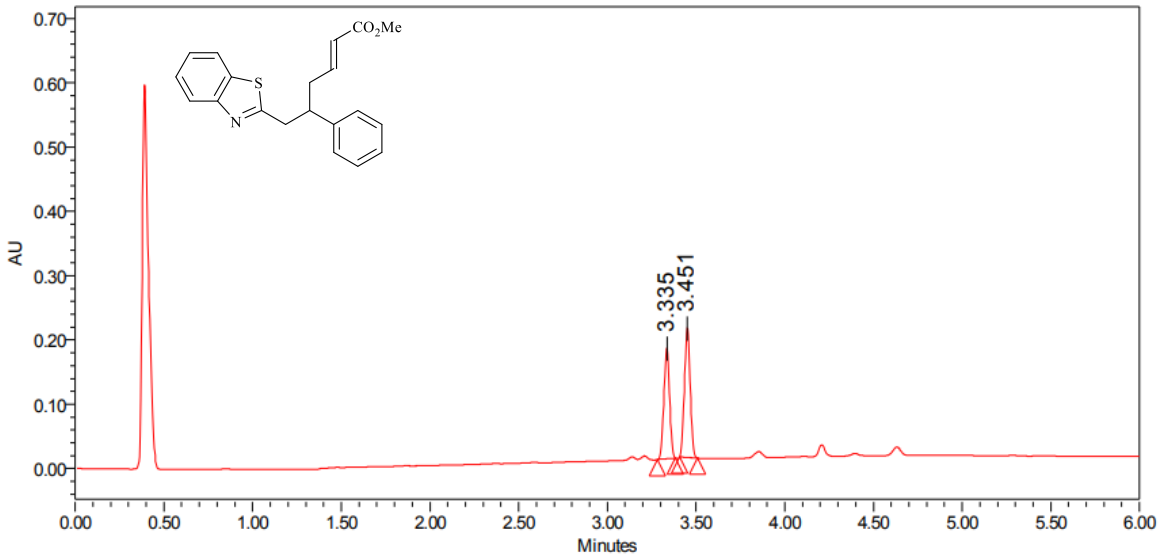


Peak Results

	RT	% Area
1	2.868	99.57
2	3.056	0.43

Methyl (*R*,*E*)-6-(benzo[*d*]thiazol-2-yl)-5-phenylhex-2-enoate (6m)

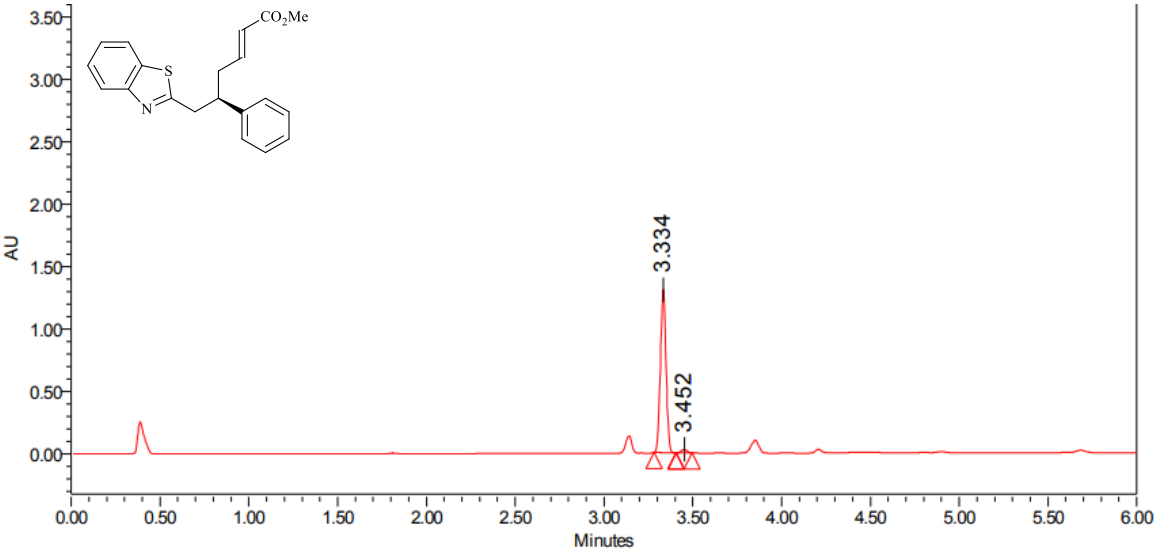
Racemic sample



Peak Results

	RT	% Area
1	3.335	45.70
2	3.451	54.30

Enantioenriched sample

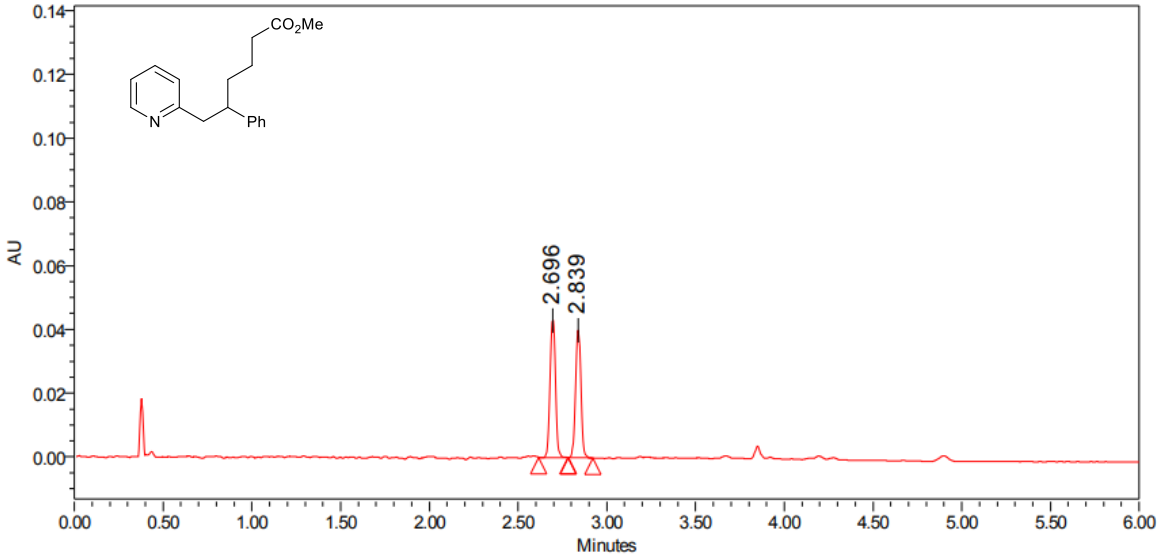


Peak Results

	RT	% Area
1	3.334	97.84
2	3.452	2.16

Methyl (*R*)-5-phenyl-6-(pyridin-2-yl)hexanoate 13

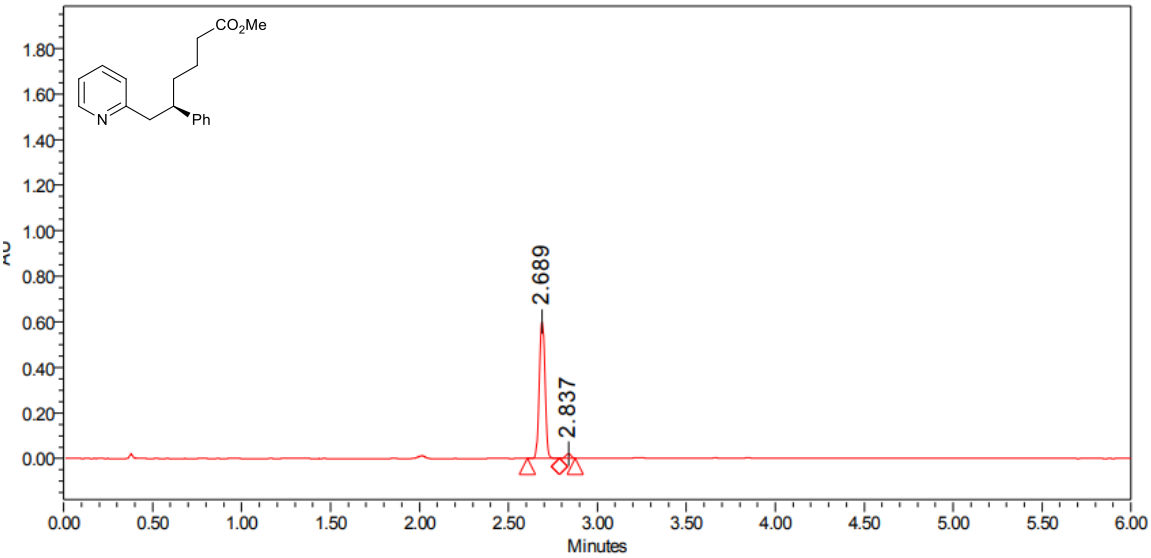
Racemic sample



Peak Results

	RT	% Area
1	2.696	52.11
2	2.839	47.89

Enantioenriched sample

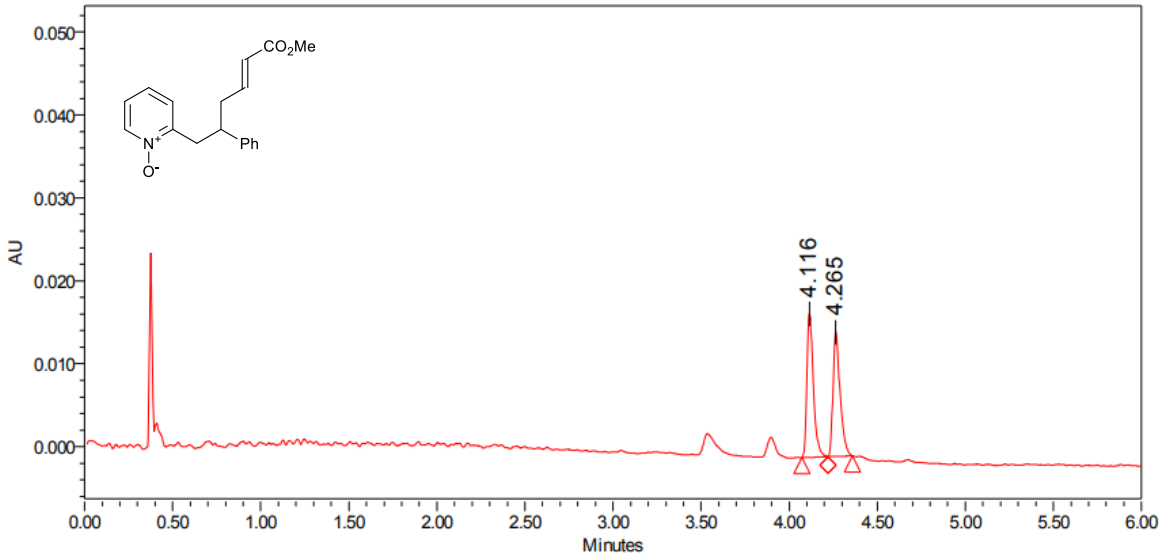


Peak Results

	RT	% Area
1	2.689	96.91
2	2.837	3.09

(*R*,*E*)-2-(6-Methoxy-6-oxo-2-phenylhex-4-en-1-yl)pyridine 1-oxide 14

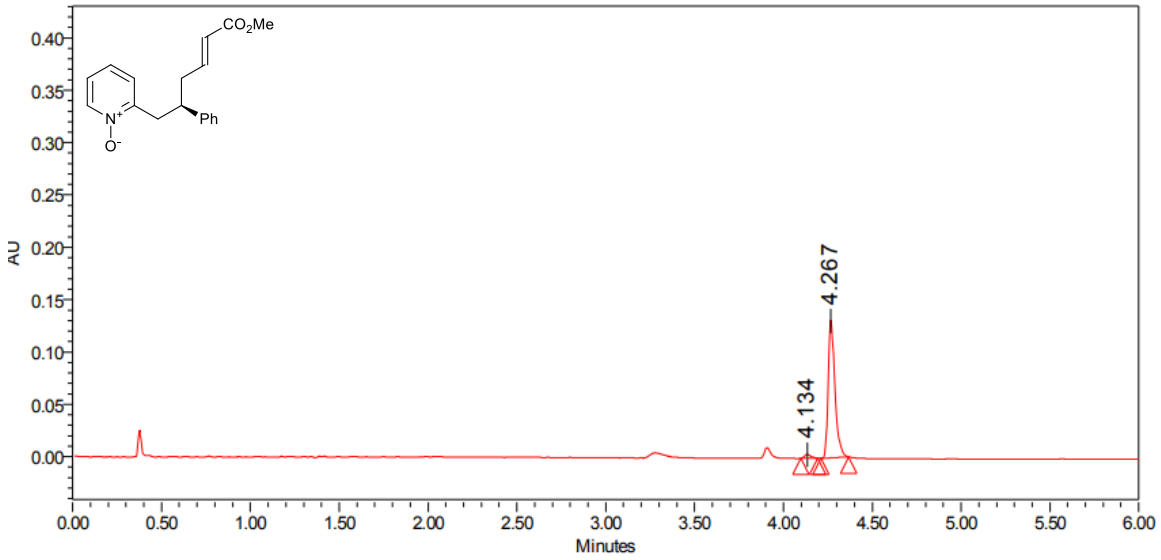
Racemic sample



Peak Results

	RT	% Area
1	4.116	51.32
2	4.265	48.68

Enantioenriched sample

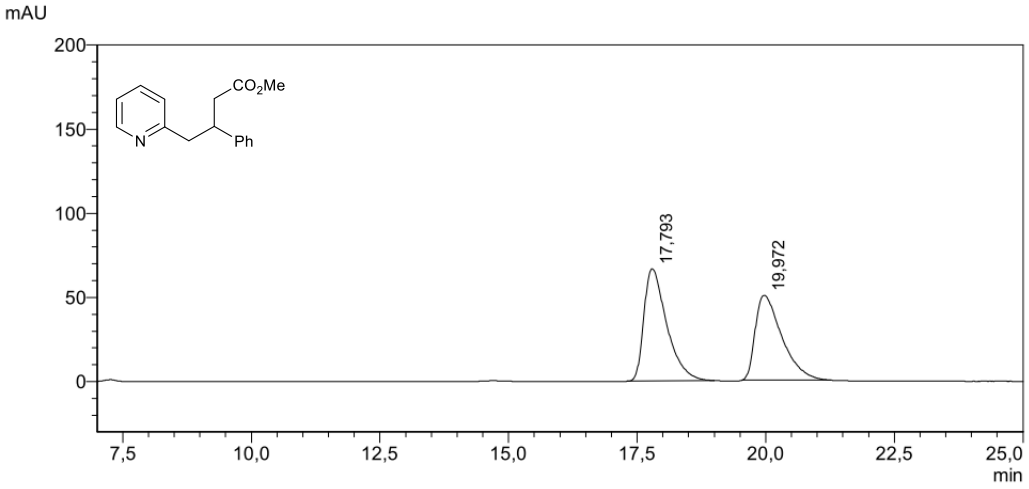


Peak Results

	RT	% Area
1	4.134	2.54
2	4.267	97.46

Methyl (*S*)-3-phenyl-4-(pyridin-2-yl)butanoate 15

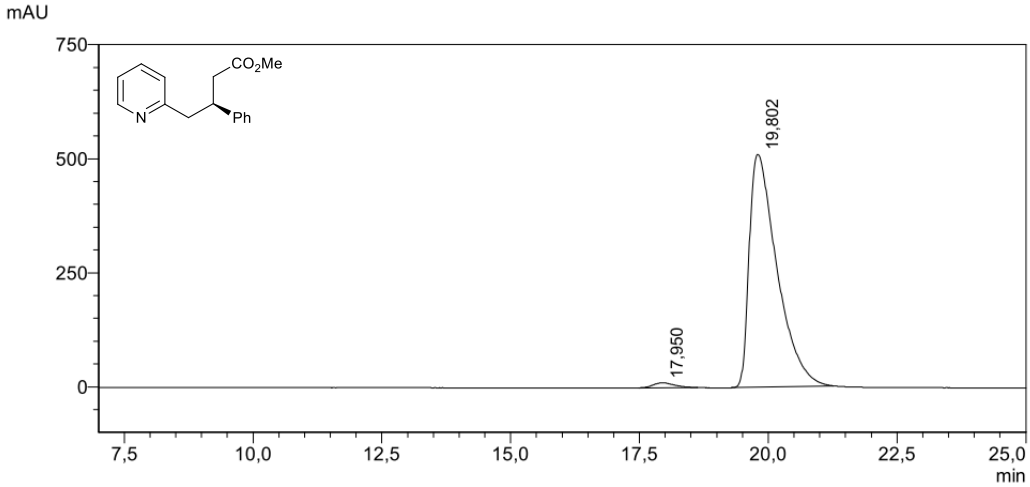
Racemic sample



PDA Ch2 266nm

Peak#	Ret. Time	Area%
1	17,793	53,189
2	19,972	46,811
Total		100,000

Enantioenriched sample

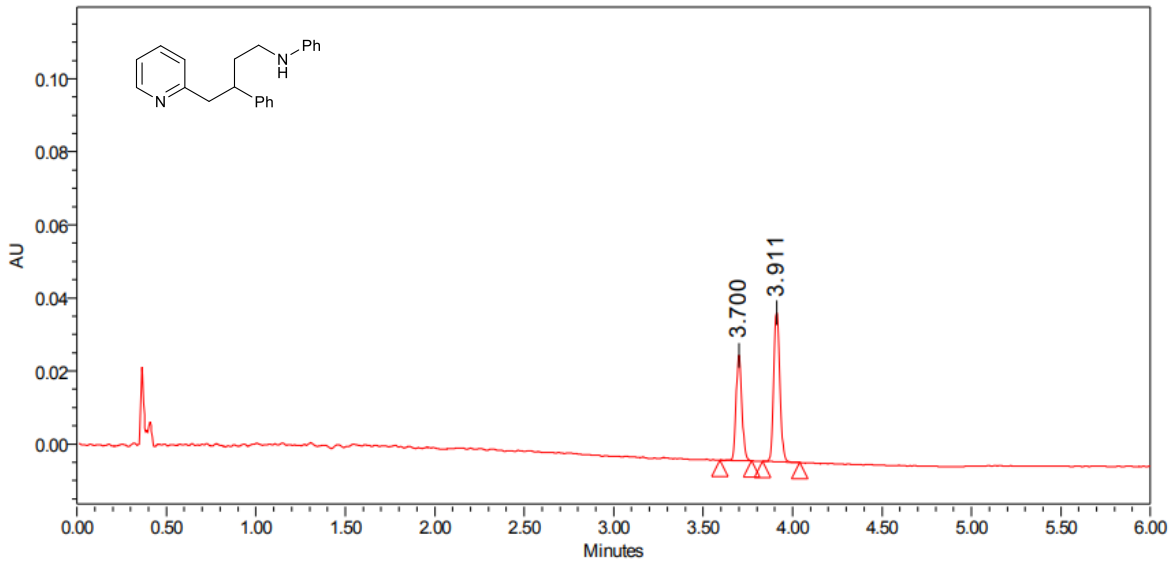


PDA Ch2 200nm

Peak#	Ret. Time	Area%
1	17,950	1,590
2	19,802	98,410
Total		100,000

(*R*)-*N*-(3-Phenyl-4-(pyridin-2-yl)butyl)aniline 16

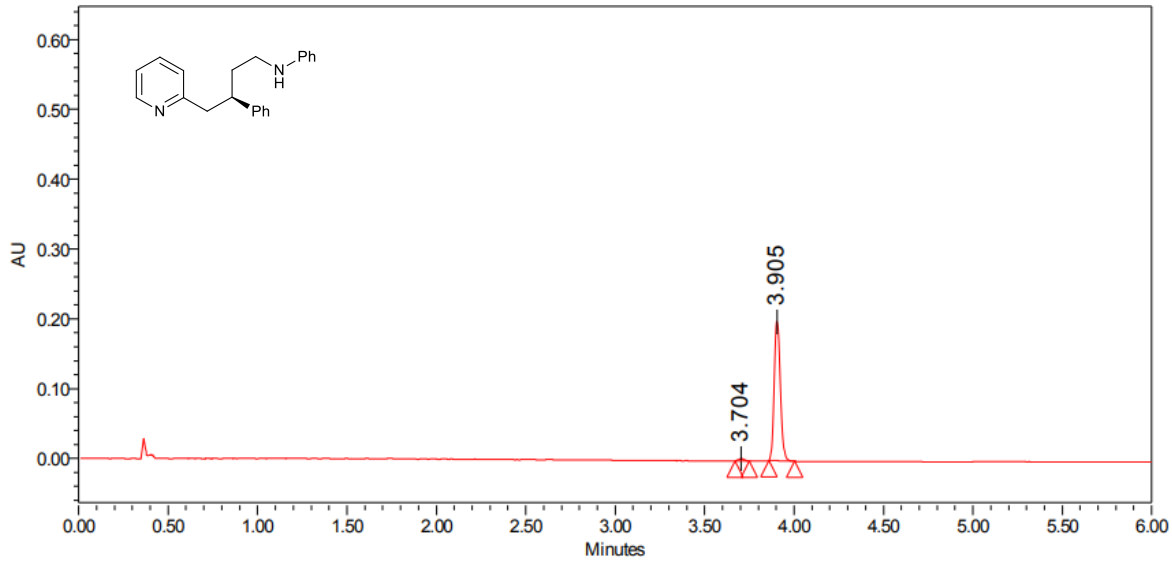
Racemic sample



Peak Results

	RT	% Area
1	3.700	39.97
2	3.911	60.03

Enantioenriched sample

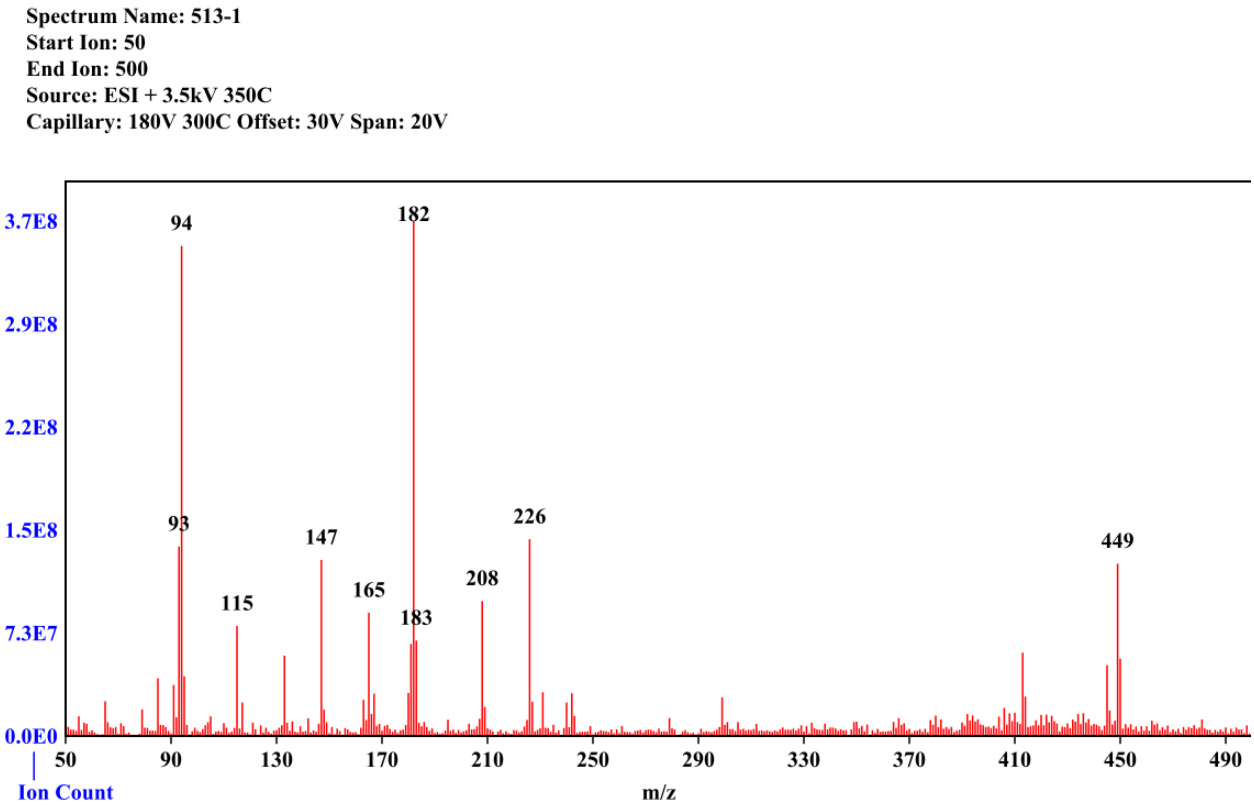


Peak Results

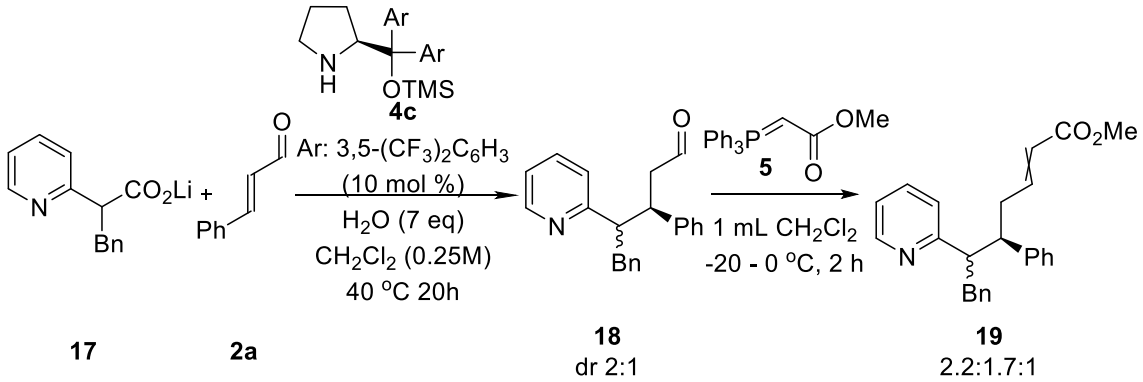
	RT	% Area
1	3.704	1.50
2	3.905	98.50

10. Mechanistic considerations using MS analysis

In order to clarify the assumed reaction mechanism, MS analysis was performed. An In an ordinary 4 mL glass vial equipped with a magnetic stirring bar, 2-pyridylacetic acid hydrochloride **1a** (17.3 mg; 0.1 mmol), α,β-unsaturated aldehyde **2** (0.1 mmol) and catalyst **4c** (6.0 mg, 0.01 mmol) were placed. Subsequently, dichloromethane (0.2 mL) and sodium acetate (8.2 mg, 0.1 mmol) were added. The resulting mixture was stirred at room temperature for 2 hours, the sample was taken (10 µL), diluted with MeOH (1 mL) and subjected to MS analysis [cationic mode, calculated for C_6H_7N (**+H**): 94, found: 94].



11. Additional scope experiment



17 **2a** **18** dr 2:1 **19** 2.2:1.7:1