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Stereoselective conjugate cyanation of enals by combining photoredox and organocatalysis

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General Information

The NMR spectra were recorded at 300 MHz, 400 MHz and 500 MHz Bruker spectrometers for ^{1}H or at 75 MHz, 101 MHz and 126 MHz for ^{13}C or 376 MHz and 471 MHz for ^{19}F, respectively. The chemical shifts (δ) for ^{1}H and ^{13}C signals are given in ppm relative to residual signals of the solvents ($CHCl_3$ at 7.26 ppm in ^{1}H NMR and at 77.16 ppm in ^{13}C NMR spectra). Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), hept (heptet), m (multiplet), br (broad).

High-resolution mass spectra (HRMS) were obtained from the ICIQ High-Resolution Mass Spectrometry Unit on MicroTOF Focus and Maxis Impact (Bruker Daltonics) with electrospray ionization (EI) or atmospheric pressure chemical ionization (APCI). X-ray data were obtained from the ICIQ X-Ray Unit using a Bruker-Nonius diffractometer equipped with an APPEX 2 4K CCD area detector. Optical rotations were measured on a Polarimeter Jasco P-1030 and are reported as follows: $[\alpha]_D$ ambient temperature (c in g per 100 mL, solvent). Cyclic voltammetry studies were carried out on a Princeton Applied Research PARSTAT 2273 potentiostat, offering compliance voltage up to ± 100 V (available at the counter electrode), ± 10 V scan range and ±2 A current range. UV-Vis measurements were carried out on a Agilent Cary 60 spectrophotometer equipped with silicon diode detector, double beam optics and 80 Hz Xenon Flash Lamp as light source. Ozonolysis was carried out using a CMG 5-5 Ozone Generator and the OMG 200-2 Ozone Analyzer. Hydrogenation was carried out using a H-Cube Pro system using disposible CatCarts cartridges (30 mm, 10% Pd/C).

The authors are indebted to the team of the Research Support Area at ICIQ, particularly to the X-ray, the NMR, and the High-Resolution Mass Spectrometry Units.

General Procedures. All reactions were set up under an argon atmosphere in dry glassware using standard Schlenk techniques, unless otherwise stated. Synthesis grade solvents were used as purchased. Anhydrous solvents were taken from a commercial SPS solvent dispenser. Chromatographic purification of products was accomplished using flash column chromatography (FC) on silica gel (Merck, 230-400 mesh). For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used, using UV light as the visualizing agent and common laboratory stains (potassium permanganate ($KMnO_4$), vanillin, phosphomolybdic acid (PMA), bromocresol) as developing agents. For preparative thin layer chromatography (prepTLC) purification throughout this work, Uniplate precoated TLC plates (silica gel GF_{254}, 1000 micron) were used, using UV light as the visualizing agent. Organic solvents were removed under reduced pressure on a Büchi rotary evaporator.

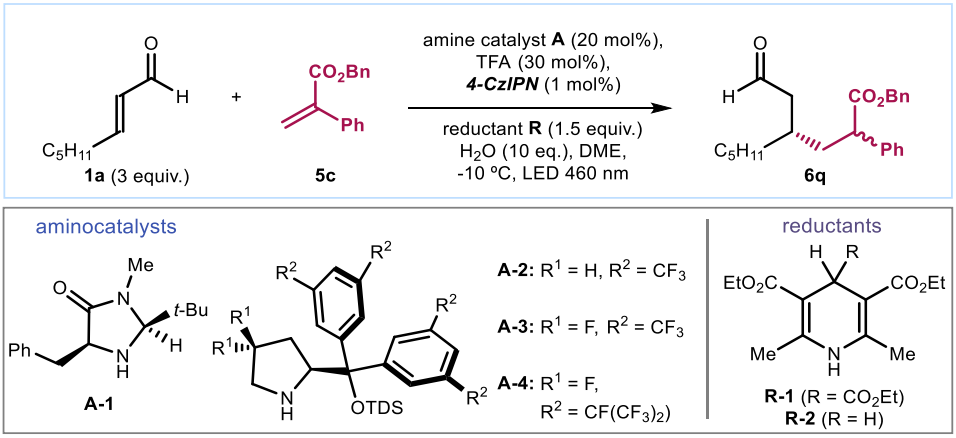
Determination of Enantiomeric Purity: UPC^2 analysis on chiral stationary phase was performed on a Waters ACQUITY® instrument using IA-3, IB-3, ID-3, IE-3, IG-3 and OJ-3 chiral columns. HPLC analysis on chiral stationary phase was performed on an Agilient 1200 series HPLC, using Daicel Chiralpak IC-3 column with n-hexane:iPrOH as the eluent. The exact conditions for the analyses are specified in the experimental section of the individual compounds. UPC^2 traces were compared to racemic samples prepared by running the reaction either in the presence of a catalytic amount (20 mol%) of racemic catalyst **A-3** (for the conjugate cyanation) or racemic catalyst **A-1** (for the cross electrophile coupling), the latter being commercially available from Sigma Aldrich.

Materials: Commercial grade reagents and solvents were purchased at the highest commercial quality from Sigma Aldrich, Fluka, Acros Organics, Fluorochem or Alfa Aesar and used as received unless otherwise stated. The photocatalyst 4-CzIPN is commercially available and was used as obtained. The chiral secondary amine catalysts **A-1** and **A-2** are commercially available, while amine catalysts **A-3** and **A-4** were prepared according to reported procedures.[1] Some of the enal substrates **1**, including octenal **1a**, crotonaldehyde, and enal **1k** are commercially available and were distilled prior to use. Other

enals or acrylates were prepared according to literature procedures or as detailed in the Supplementary Methods.

Optimisation Studies for the Cross-Electrophile Coupling

Supplementary Table 1. Optimisation studies.[a]

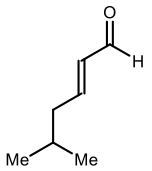


entry	amine A	reductant	notes	**6q** yield (%)	d.r.	e.r.[1], e.r.[2]
1	A-1	R-1	-	90	1.2:1	77.5:22.5, 60:40
2	A-2	R-1	-	29	2:1	78:22, 64:36
3	A-3	R-1	-	88	1.1:1	94:6, 88:12
4	A-4	R-1	-	90	1:1	94:6, 88:12
5	A-3	R-1	DME/H_2O (4:1)	19	1.1:1	94:6, 82.5:17.5
6	A-3	R-1	3 eq. H_2O	21	1:1	-
7	A-3	R-1	no PC or light	0	-	-
8	-	R-1	no amine	<15	1.5:1	-
9	A-3	R-2	-	0	-	-

[a] Reactions performed on a 0.1 mmol scale under illumination by a blue LED; yields determined by ^{1}H NMR analysis using trichloroethylene as the internal standard.

Preparation of Enals 1

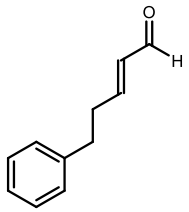
(*E*)-5-methylhex-2-enal (**1c**): prepared according to a procedure reported in the literature.[2]



Chemical Formula: $C_7H_{12}O$
Molecular Weight: 112,1720

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.52 (d, *J* = 7.9 Hz, 1H), 6.83 (dt, *J* = 15.5, 7.4 Hz, 1H), 6.12 (ddt, *J* = 15.6, 7.9, 1.4 Hz, 1H), 2.23 (td, *J* = 7.1, 1.4 Hz, 2H), 1.83 (hept, *J* = 6.6 Hz, 1H), 0.96 (d, *J* = 6.7 Hz, 6H).

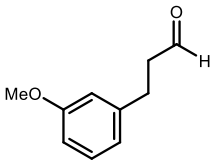
(*E*)-5-Phenylpent-2-enal (**1e**): prepared according to a procedure reported in the literature.[3] Spectral data are in agreement with the literature.



Chemical Formula: $C_{11}H_{12}O$
Molecular Weight: 160,2160

^{1}H NMR (500 MHz, $CDCl_3$) δ = 9.50 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.33 – 7.29 (m, 2H), 7.25 – 7.16 (m, 3H), 6.86 (dt, *J* = 15.7, 6.7 Hz, 1H), 6.14 (ddt, *J* = 15.6, 7.9, 1.5 Hz, 1H), 2.84 (t, *J* = 7.6 Hz, 2H), 2.70 – 2.65 (m, 2H).

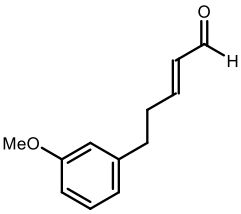
3-(3-Methoxyphenyl)propanal. 3-(3-methoxyphenyl)propan-1-ol (1.66 g, 10.0 mmol, 1.0 equiv.) was dissolved in DCM (50 mL). The mixture was cooled to 0 °C and Dess-Martin periodinane (5.09 g, 12.0 mmol, 1.2 equiv.) was added in portions over 10 minutes. The mixture was stirred for 16 h and quenched carefully with a mixture of aqueous $NaHCO_3$ (saturated, 100 mL) and aqueous NaS_2O_3 (10%, 100 mL) and stirred vigorously for 1 hour. The layers were separated and the aqueous layer was extracted with DCM (2 x 100 mL). The combined organic layers were dried with $MgSO_4$, concentrated and purified by column chromatography (silica gel, 10% EtOAc in hexanes) to afford 1.56 g (95%) of aldehyde. Analytical data is in agreement with the literature.[4]



Chemical Formula: $C_{10}H_{12}O_2$
Molecular Weight: 164,2040

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.82 (t, *J* = 1.4 Hz, 1H), 7.21 (td, *J* = 7.7, 0.8 Hz, 1H), 6.80 – 6.73 (m, 3H), 3.80 (s, 3H), 2.94 (t, *J* = 7.6 Hz, 2H), 2.78 (t, *J* = 7.7 Hz, 2H) ppm.

(*E*)-5-(3-Methoxyphenyl)pent-2-enal (**1f**). 3-(3-methoxyphenyl)propanal (1.56 g, 9.53 mmol, 1.0 equiv.) was dissolved in THF (anhydrous, 19 mL) under an argon atmosphere. (Triphenylphosphoranylidene)-acetaldehyde (3.48 g, 11.4 mmol, 1.2 equiv.) was added and the mixture was refluxed for 1 day. Upon concentration, the product was purified by column chromatography (silica gel, 5-10% EtOAc in hexanes). Clean fractions were combined to afford 751 mg (41%) of **1f** as yellow oil.

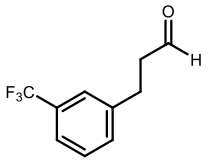


Chemical Formula: $C_{12}H_{14}O_2$
Molecular Weight: 190,2420

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.50 (d, *J* = 7.8 Hz, 1H), 7.23 (dd, *J* = 8.2, 7.5 Hz, 1H), 6.85 (dt, *J* = 15.6, 6.7 Hz, 1H), 6.80 – 6.73 (m, 3H), 6.14 (ddt, *J* = 15.7, 7.9, 1.5 Hz, 1H), 3.80 (s, 3H), 2.81 (t, *J* = 7.6 Hz, 2H), 2.71 – 2.63 (m, 2H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 194.1, 159.9, 157.4, 142.0, 133.6, 129.7, 120.8, 114.4, 111.6, 55.3, 34.2 (2C) ppm.

HRMS (ESI): m/z calculated for $[C_{12}H_{14}NaO_2]^+$ $[M+Na]^+$: 213.0886; found: 213.0889.

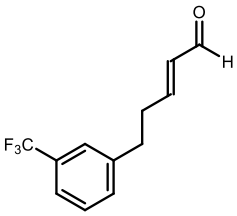
3-(3-(Trifluoromethyl)phenyl)propanal. 3-(3-(trifluoromethyl)phenyl)propan-1-ol (2.04 g, 10.0 mmol, 1.0 equiv.) was dissolved in DCM (50 mL). The mixture was cooled to 0 °C and Dess-Martin periodinane (5.09 g, 12.0 mmol, 1.2 equiv.) was added in portions over 10 minutes. The mixture was stirred for 16 h and quenched carefully with a mixture of aqueous $NaHCO_3$ (saturated, 100 mL) and aqueous NaS_2O_3 (10%, 100 mL) and stirred vigorously for 1 hour. The layers were separated and the aqueous layer was extracted with DCM (2 x 100 mL). The combined organic layers were dried with $MgSO_4$, concentrated and purified by column chromatography (silica gel, 10% EtOAc in hexanes) to afford 1.47 g (73%) of aldehyde. Analytical data is in agreement with the literature.[5]



Chemical Formula: $C_{10}H_9F_3O$
Molecular Weight: 202,1762

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.83 (t, *J* = 1.2 Hz, 1H), 7.50 – 7.36 (m, 4H), 3.02 (t, *J* = 7.5 Hz, 2H), 2.83 (td, *J* = 7.5, 0.9 Hz, 2H) ppm.

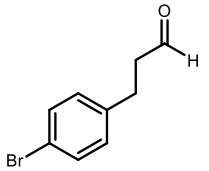
(*E*)-5-(3-(trifluoromethyl)phenyl)pent-2-enal (**1g**).
3-(3-(trifluoromethyl)phenyl)propanal (1.47 g, 7.28 mmol, 1.0 equiv.) was dissolved in THF (anhydrous, 15 mL) under an Argon atmosphere. (Triphenylphosphoranylidene)-acetaldehyde (2.22 g, 7.28 mmol, 1.0 equiv.) was added and the mixture was refluxed for 1 day. Upon concentration, the product was purified by column chromatography (silica gel, 5-10% EtOAc in hexanes). Clean fractions were combined to afford 545 mg (33%) of **1g** as yellow oil.



Chemical Formula: $C_{12}H_{11}F_3O$
Molecular Weight: 228,2142

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.51 (d, *J* = 7.8 Hz, 1H), 7.57 – 7.34 (m, 4H), 6.84 (dt, *J* = 15.7, 6.7 Hz, 1H), 6.14 (ddt, *J* = 15.7, 7.8, 1.5 Hz, 1H), 2.90 (d, *J* = 7.4 Hz, 2H), 2.74 – 2.64 (m, 2H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 193.8, 156.3, 141.3, 133.8, 131.9, 131.1 (q, *J* = 32.0 Hz), 129.2, 125.2 (q, *J* = 3.9 Hz) 124.2 (q, *J* = 271.8 Hz), 123.5 (q, *J* = 3.8 Hz), 34.1, 34.0 ppm. **^{19}F NMR (471 MHz, $CDCl_3$):** δ = -62.64 ppm.
HRMS (ESI): m/z calculated for $[C_{12}H_{11}F_3NaO]^+$ $[M+Na]^+$: 251.0654; found: 251.0653.

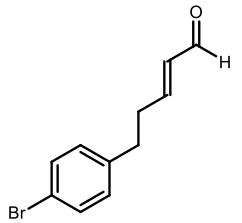
3-(4-Bromophenyl)propanal. 3-(4-bromophenyl)propan-1-ol (2.15 g, 10.0 mmol, 1.0 equiv.) was dissolved in DCM (50 mL). The mixture was cooled to 0 °C and Dess-Martin periodinane (5.09 g, 12.0 mmol, 1.2 equiv.) was added in portions over 10 minutes. The mixture was stirred for 16 h and quenched carefully with a mixture of aqueous $NaHCO_3$ (saturated, 100 mL) and aqueous NaS_2O_3 (10%, 100 mL) and stirred vigorously for 1 hour. The layers were separated and the aqueous layer was extracted with DCM (2 x 100 mL). The combined organic layers were dried with $MgSO_4$, concentrated and purified by column chromatography (silica gel, 10% EtOAc in hexanes) to afford 1.40 g (66%) of aldehyde as bright-yellow solid. Analytical data is in agreement with the literature.[6]



Chemical Formula: C_9H_9BrO
Molecular Weight: 213,0740

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.81 (s, 1H), 7.41 (d, *J* = 8.3 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 2H), 2.91 (t, *J* = 7.4 Hz, 2H), 2.77 (td, *J* = 7.5, 1.1 Hz, 3H) ppm.

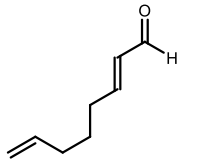
(*E*)-5-(4-Bromophenyl)pent-2-enal (**1h**). 3-(4-bromophenyl)propanal (1.40 g, 6.58 mmol, 1.0 equiv.) was dissolved in THF (anhydrous, 15 mL) under an Argon atmosphere. (Triphenylphosphoranylidene)-acetaldehyde (3.21 g, 10.5 mmol, 1.6 equiv.) was added and the mixture was refluxed for 1 day. Upon concentration, the product was purified by column chromatography (silica gel, 5-10% EtOAc in hexanes) to afford 970 mg (62%) of **1h**. Analytical data is in agreement with the literature.[7]



Chemical Formula: $C_{11}H_{11}BrO$
Molecular Weight: 239,1120

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.49 (d, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 6.82 (dt, *J* = 15.7, 6.7 Hz, 1H), 6.13 (ddt, *J* = 15.7, 7.8, 1.5 Hz, 1H), 2.79 (t, *J* = 7.6 Hz, 2H), 2.68 – 2.60 (m, 2H) ppm.

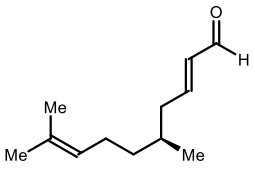
(E)-octa-2,7-dienal (**1i**). (E)-octa-2,7-dienal was prepared according to a previous report[8] and analytical data is in agreement with the literature.



Chemical Formula: $C_8H_{12}O$
Molecular Weight: 124,1830

^{1}H NMR (300 MHz, $CDCl_3$): δ 9.51 (d, *J* = 7.9 Hz, 1H), 6.85 (dt, *J* = 15.6, 6.8 Hz, 1H), 6.12 (ddt, *J* = 15.6, 7.9, 1.5 Hz, 1H), 5.79 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H), 5.09 – 4.96 (m, 2H), 2.35 (dtd, *J* = 8.1, 6.9, 1.5 Hz, 2H), 2.11 (dtt, *J* = 8.0, 6.8, 1.4 Hz, 2H), 1.62 (tt, *J* = 8.1, 6.9 Hz, 2H) ppm.

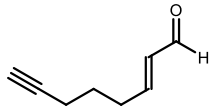
(*S*,*E*)-5,9-Dimethyldeca-2,8-dienal (**1j**). (S)-3,7-dimethyloct-6-enal (1.00 g, 6.48 mmol, 1.0 equiv.) was dissolved in THF (anhydrous, 13.0 mL) under an Argon atmosphere. (Triphenylphosphoranylidene)-acetaldehyde (2.37 g, 7.78 mmol, 1.2 equiv.) was added and the mixture was refluxed for 2 days. Upon concentration, the product was filtered through a pad of silica gel (eluting with DCM). The filtrate was concentrated and purified by column chromatography (silica gel, 1% EtOAc in hexanes) to afford afford 300 mg (26%) of **1j** as colorless oil. Analytical data is in agreement with the literature.[9]



Chemical Formula: $C_{12}H_{20}O$
Molecular Weight: 180,2910

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.51 (d, *J* = 7.9 Hz, 1H), 6.83 (dt, *J* = 15.0, 7.3 Hz, 1H), 6.12 (ddd, *J* = 15.5, 7.9, 1.4 Hz, 1H), 2.39 – 2.32 (m, 1H), 2.22 – 2.15 (m, 1H), 2.06 – 1.94 (m, 2H), 1.74 – 1.66 (m, 1H), 1,69 (s, 3H), 1.60 (s, 3H), 1.43 – 1.32 (m, 1H), 1.29 – 1.17 (m, 2H), 0.94 (d, *J* = 6.7 Hz, 3H) ppm.

(*E*)-Oct-2-en-7-ynal (**1l**). The product was synthesized by stirring hex-5-ynal (0.800 g, 8.32 mmol, 1.0 equiv.), which was synthesized from 5-hexyn-1-ol using reported procedure,[10] with (triphenylphosphoranylidene)-acetaldehyde (5.07 g, 2.0 equiv.) in dry CH_2Cl_2. The reaction was stirred at room temperature for 48 hours. The reaction mixture was carefully concentrated *in vacuo*, re-dissolved in 10% Et_2O in n-pentane and filtered through a pad of celite. The crude product was then purified by flash column chromatography (silica gel, 5% Et_2O in n-pentane) to afford **1l** as a colorless oil (562 mg, 55% yield). *Remarks: Product is highly volatile and would oxidise readily.*

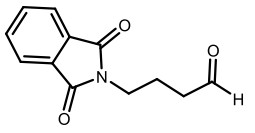


Chemical Formula: $C_8H_{10}O$
Molecular Formula: 112.0732

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.51 (d, *J* = 7.8 Hz, 1H), 6.84 (dt, *J* = 15.6, 6.7 Hz, 1H), 6.15 (ddt, *J* = 15.6, 7.8, 1.5 Hz, 1H), 2.48 (dtd, *J* = 7.6, 6.8, 1.5 Hz, 2H), 2.26 (td, *J* = 6.9, 2.6 Hz, 2H), 1.99 (t, *J* = 2.6 Hz, 1H), 1.75 (p, *J* = 7.2 Hz, 2H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 194.0, 157.3, 133.6, 83.3, 69.5, 31.6, 26.6, 18.0 ppm.

HRMS (APCI): m/z calculated for $[C_8H_{11}O]^+$ $[M+H]^+$: 123.0804, found: 123.0799.

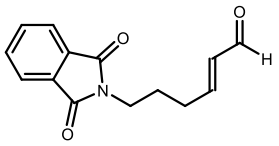
4-(1,3-Dioxoisoindolin-2-yl)butanal. The product was synthesized by stirring 2-(4-hydroxybutyl)isoindoline-1,3 dione (2.51 g, 11.4 mmol, 1.00 equiv.), which was prepared according to previous report,[11] with pyridinium chlorochromate (PCC, 2.95 g, 1.20 equiv.) in dry CH_2Cl_2 (15 mL) overnight. The crude product was filtered through a pad of celite, concentrated *in vacuo* and purified by flash column chromatography (silica, 25% EtOAc in n-hexanes) to afford the aldehyde as white solid (1.40 g, 56% yield).



Chemical Formula: $C_{12}H_{11}NO_3$
Molecular Formula: 217.0739

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.67 (t, *J* = 1.2 Hz, 1H), 7.75 – 7.65 (m, 2H), 7.65 – 7.58 (m, 2H), 3.60 (t, *J* = 6.9 Hz, 2H), 2.46 (td, *J* = 7.2, 1.2 Hz, 2H), 1.89 (p, *J* = 7.0 Hz, 2H) ppm. The spectroscopic data is consistent with previous report.[12]

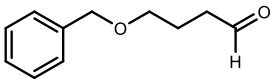
(*E*)-6-(1,3-Dioxoisoindolin-2-yl)hex-2-enal (**3m**). The product was synthesized by stirring 4-(1,3-dioxoisoindolin-2-yl)butanal (2.10 g, 9.67 mmol, 1.0 equiv.) with (triphenylphosphoranylidene)-acetaldehyde (3.53 g, 1.2 equiv.) in dry THF (21.0 mL). The reaction was heated under reflux for 24 hours. The reaction mixture was concentrated *in vacuo* and purified by flash column chromatography (silica, 25% EtOAc in n-hexanes). The crude product was then recrystallized from CH_2Cl_2/n-hexanes to afford **3m** as white solid. (582 mg, 25% yield).



Chemical Formula: $C_{14}H_{13}NO_3$
Molecular Formula: 243.0895

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.38 (d, *J* = 7.8 Hz, 1H), 7.74 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.64 (dd, *J* = 5.5, 3.1 Hz, 2H), 6.77 (dt, *J* = 15.6, 6.7 Hz, 1H), 6.05 (ddt, *J* = 15.7, 7.8, 1.6 Hz, 1H), 3.65 (t, *J* = 7.0 Hz, 2H), 2.38 – 2.29 (m, 2H), 1.84 (p, *J* = 7.4 Hz, 2H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 193.9, 168.5, 156.7, 134.2, 133.6, 132.1, 123.5, 37.4, 30.1, 26.9 ppm.
HRMS (ESI): m/z calculated for $[C_{14}H_{13}NO_3Na]^+$ $[M+Na]^+$: 266.0788, found: 266.0788.

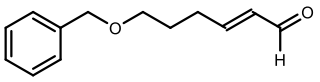
4-(Benzyloxy)butanal. Dess-martin periodinane (9.43 mmol, 4.00 g, 1.1 equiv.) was added portionwise to a mixture of 4-(benzyloxy)butan-1-ol (8.50 mmol, 1.5 mL, 1.0 equiv.) and water (8.93 mmol, 161 µL, 1.05 equiv.) in DCM (42 mL) previously cooled to 0 °C. The reaction mixture was allowed to warm to room temperature and further stirred for 2 h until completion of the reaction. The reaction mixture was then cooled to 0 °C and carefully quenched by a 1:1 mixture of 10% aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$ (75 mL) and let to stir until complete dissolution of the reaction mixture. The organic layer was further washed with a 1:1 mixture of 10% aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$ (3x 50 mL) and dried over $MgSO_4$. The volatiles were removed under reduced pressure and the crude was purified by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) to obtain 4-(benzyloxy)butanal (1.35 g, 89%) as a colorless oil. Spectroscopic data are consistent with those previously reported.[13]



Chemical Formula: $C_{11}H_{14}O_2$
Exact Mass: 178.10

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.78 (t, *J* = 1.6 Hz, 1H), 7.40 – 7.24 (m, 5H), 4.49 (s, 2H), 3.51 (t, *J* = 6.1 Hz, 2H), 2.55 (td, *J* = 7.1, 1.6 Hz, 2H), 1.95 (tt, *J* = 7.1, 6.0 Hz, 2H) ppm.

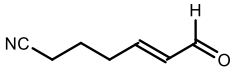
(*E*)-6-(Benzyloxy)hex-2-enal (**1n**). Under an argon atmosphere a solution of (triphenylphosphoranylidene)acetaldehyde (9.09 mmol, 2.77 g, 1.2 equiv.) and 4-(benzyloxy)butanal (7.57 mmol, 1.35 g, 1.0 equiv.) in anhydrous THF (15 mL) was stirred under reflux for 16 h. The reaction mixture was allowed to cool to room temperature and concentrated under reduced pressure. The crude was purified by flash column chromatography (silica gel, 10-15% EtOAc in hexanes) to obtain **1n** (654 mg, 42 %, *E*/*Z* = 9:1) as a colorless oil.



Chemical Formula: $C_{13}H_{16}O_2$
Exact Mass: 204.12

^{1}H NMR (500 MHz, $CDCl_3$, mixture of isomers): δ = 9.53 (d, *J* = 8.0 Hz, 1H, *Z*-isomer), 9.49 (d, *J* = 7.9 Hz, 1H, *E*-isomer), 7.37 – 7.29 (m, 5H), 7.10 – 7.02 (m, 1H, *Z*-isomer), 6.85 (dt, *J* = 15.7, 6.8 Hz, 1H, *E*-isomer), 6.31 – 6.25 (m, 1H, *Z*-isomer), 6.12 (ddt, *J* = 15.6, 7.9, 1.5 Hz, 1H, *E*-isomer), 4.50 (s, 2H), 3.51 (t, *J* = 6.1 Hz, 2H), 2.55 (td, *J* = 7.1, 1.6 Hz, 1H, *Z*-isomer), 2.49 – 2.42 (m, 2H, *E*-isomer), 1.98 – 1.93 (m, 1H, *Z*-isomer), 1.83 (tt, *J* = 7.4, 6.2 Hz, 2H, *E*-isomer) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, major isomer):** δ = 194.2, 158.3, 138.4, 133.3, 128.6, 127.8, 127.8, 73.2, 69.2, 29.7, 28.2 ppm.
HRMS (ESI): m/z calculated for $[C_{13}H_{16}O_2Na]^+$ $[M+Na]^+$: 227.1043; found: 227.1038.

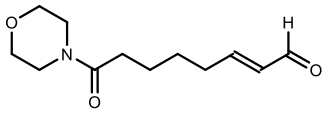
(*E*)-7-Oxohept-5-enenitrile (**1o**). Under an atmosphere of argon, a solution of hex-5-enenitrile (9.30 mmol, 1.0 mL, 1.0 equiv.), acrolein (45.0 mmol, 3.0 mL, 4.8 equiv.) and Hoveyda-Grubbs Catalyst 2nd Generation (186 µmol, 117 mg, 2 mol%) in anhydrous DCM (19 mL) was stirred under reflux for 16 h. The volatiles were removed under reduced pressure and the crude purified by flash column chromatography (silica



Chemical Formula: C_7H_9NO
Molecular Weight: 123.16

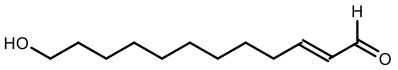
gel, 50% EtOAc in hexanes) to obtain **1o** (340 mg, 30%) as colorless oil. Spectroscopic data are consistent with those previously reported.[14]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.53 (d, *J* = 7.7 Hz, 1H), 6.80 (dt, *J* = 15.7, 6.7 Hz, 1H), 6.17 (ddt, *J* = 15.7, 7.7, 1.5 Hz, 1H), 2.57 – 2.48 (m, 2H), 2.46 – 2.36 (m, 2H), 1.95 – 1.86 (m, 2H).

(*E*)-8-Morpholino-8-oxooct-2-enal (**1p**). A solution of 1-morpholinohept-6-en-1-one (7.00 mol, 1.38 g, 1.0 equiv. previously prepared following a reported procedure[15] in anhydrous DCM (28 mL) was cooled to -78 °C and degassed with a stream of oxygen. Ozone was then bubbled through the reaction mixture until it turned blue. The reaction was then purged with oxygen to remove excess of ozone and quenched with excess dimethyl sulfide. The reaction mixture was then let to warm to room temperature, the organic layer was washed with brine (3 x 30 mL) and dried over $MgSO_4$. The volatiles were removed under reduced pressure to obtain crude 6-morpholino-6-oxohexanal (950 mg, 68%) which was engaged in the next step without further purification.


Chemical Formula: $C_{12}H_{19}NO_3$
Molecular Weight: 225.29

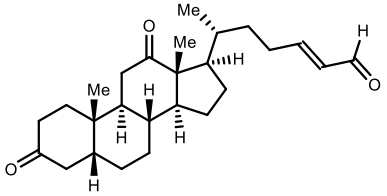
Under an atmosphere of argon, a solution of (triphenylphosphoranylidene)acetaldehyde (5.72 mmol, 1.74 g, 1.2 equiv.) and 6-Morpholino-6-oxohexanal (4.77 mmol, 950 mg, 1.0 equiv.) in anhydrous THF (10 mL) was stirred under reflux for 16 h. The reaction mixture was allowed to cool to room temperature and concentrated under reduced pressure. The crude was purified by flash column chromatography (silica gel, 2% MeOH in DCM) to obtain **1p** (219 mg, 20%) as a gum.
^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.50 (d, *J* = 7.8 Hz, 1H), 6.85 (dt, *J* = 15.6, 6.7 Hz, 1H), 6.12 (ddt, *J* = 15.6, 7.9, 1.5 Hz, 1H), 3.69 – 3.65 (m, 4H), 3.65 – 3.59 (m, 2H), 3.49 – 3.42 (m, 2H), 2.41 – 2.35 (m, 2H), 2.34 (t, *J* = 7.3 Hz, 2H), 1.74 – 1.67 (m, 2H), 1.60 – 1.53 (m, 2H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 194.1, 171.2, 158.2, 133.3, 67.1 (rotamer), 66.8 (rotamer), 46.1, 42.1, 32.7 (rotamer), 32.7 (rotamer), 27.8, 24.7 ppm.
HRMS (ESI): m/z calculated for $[C_{12}H_{19}NO_3Na]^+$ $[M+Na]^+$: 248.1257; found: 248.1261.

(*E*)-12-Hydroxydodec-2-enal (**1q**). Under an atmosphere of argon, a solution of undec-10-en-1-ol (5.12 mmol, 1.0 mL, 1.0 equiv.), acrolein (15.4 mmol, 1.0 mL, 3.0 equiv.) and Hoveyda-Grubbs Catalyst 2nd Generation (51.2 μmol, 32.2 mg, 1 mol%) in anhydrous DCM (10 mL) was stirred under reflux for 16 h. The volatiles were removed under reduced pressure and the crude purified by flash column chromatography (silica gel, 5-10% Et_2O in hexanes) to obtain **1q** (433 mg, 43%) as a colorless oil. Spectroscopic data are consistent with those previously reported.[16]


Chemical Formula: $C_{12}H_{22}O_2$
Molecular Weight: 198.31

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.50 (d, *J* = 7.9 Hz, 1H), 6.85 (dt, *J* = 15.6, 6.8 Hz, 1H), 6.11 (ddt, *J* = 15.6, 7.9, 1.5 Hz, 1H), 3.64 (t, *J* = 6.6 Hz, 2H), 2.36 – 2.29 (m, 2H), 1.60 – 1.54 (m, 2H), 1.53 – 1.48 (m, 2H), 1.35 – 1.29 (m, 10H).

(*R,E*)-6-((*5R,8R,9S,10S,13R,14S,17R*)-10,13-Dimethyl-3,12-dioxohexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)hept-2-enal (**1r**).
(*R*)-4-((5R,8R,9S,10S,13R,14S,17R)-10,13-dimethyl-3,12-dioxohexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)pentanal (600 mg, 1.61 mmol, 1.0 equiv., prepared according to a previous report[17]) was dissolved in THF (anhydrous, 10.0 mL) under an Argon atmosphere. (triphenylphosphoranylidene)-acetaldehyde (784 mg, 2.58 mmol, 1.6 equiv.) were added and the mixture was refluxed for 6 days. In order to achieve full conversion, another 0.4 equiv. of


Chemical Formula: $C_{26}H_{38}O_3$
Molecular Weight: 398,5870

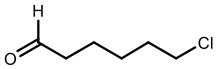
(triphenylphosphoranylidene)-acetaldehyde were added and the mixture was refluxed for 1 day. Upon concentration, the mixture was purified by column chromatography (silica gel, 15-20% EtOAc in hexanes). Fractions with minor impurities (< 20% by NMR) were combined, concentrated and purified again by column chromatography (silica gel, 1% MeOH in DCM) to afford 84.0 mg (13%) of **1r** as colorless foam.

$[\alpha]_D^{25}$ = +76.4 (c = 1.0, $CHCl_3$)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.49 (d, *J* = 7.9 Hz, 1H), 6.84 (ddd, *J* = 15.6, 7.2, 6.3 Hz, 1H), 6.11 (ddt, *J* = 15.6, 7.9, 1.5 Hz, 1H), 2.66 – 2.52 (m, 2H), 2.49 – 2.22 (m, 3H), 2.22 – 2.14 (m, 1H), 2.13 – 1.98 (m, 3H), 1.92 (dddd, *J* = 15.9, 8.3, 6.3, 3.4 Hz, 6H), 1.76 (ddt, *J* = 11.9, 7.1, 4.1 Hz, 2H), 1.67 – 1.56 (m, 2H), 1.50 – 1.38 (m, 2H), 1.37 – 1.26 (m, 4H), 1.18 – 1.07 (m, 1H), 1.10 (s, 3H), 1.05 (s, 3H), 0.88 (d, *J* = 6.2 Hz, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$)**: δ = 214.2, 212.2, 194.3, 159.4, 133.0, 58.7, 57.7, 46.7, 44.4, 43.8, 42.2, 38.5, 37.0, 36.9, 35.9, 35.7, 35.6, 33.7, 30.0, 27.8, 26.7, 25.6, 24.4, 22.3, 18.8, 11.8 ppm.

HRMS (ESI): m/z calculated for $[C_{27}H_{42}NaO_4]^+$ $[M+MeOH+Na]^+$: 453.2975; found: 453.2970.

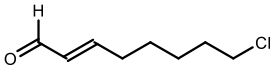
6-Chlorohexanal. Dess-martin periodinane (9.01 mmol, 3.82 g, 1.2 equiv.) was added portionwise to a mixture of 6-chlorohexan-1-ol (7.51 mmol, 1.0 mL, 1.0 equiv.) and water (8.26 mmol, 149 μL, 1.1 equiv.) in DCM (37 mL) previously cooled to 0 °C. The reaction mixture was let to warm to room temperature and further stirred for 2 h until completion of the reaction. The reaction mixture was then cooled to 0 °C and carefully quenched by a 1:1 mixture of 10% aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$ (50 mL) and let to stir until complete dissolution of the reaction mixture. The organic layer was further washed with a 1:1 mixture of 10% aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$ (3x 25 mL) and dried over $MgSO_4$. The volatiles were removed under reduced pressure and the crude was purified by flash column chromatography (silica gel, 25% Et_2O in hexanes) to obtain 6-chlorohexanal (1.01 g, quant.) as a colorless oil. Spectroscopic data are consistent with those previously reported.[18]



Chemical Formula: $C_6H_{11}ClO$
Molecular Weight: 134.60

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.78 (t, *J* = 1.6 Hz, 1H), 3.54 (t, *J* = 6.6 Hz, 2H), 2.47 (td, *J* = 7.3, 1.6 Hz, 2H), 1.88 – 1.75 (m, 2H), 1.71 – 1.60 (m, 2H), 1.53 – 1.39 (m, 2H) ppm.

(*E*)-8-Chlorooct-2-enal (**1s**). Under an atmosphere of argon, a solution of (triphenylphosphoranylidene)acetaldehyde (10.9 mmol, 3.32 g, 1.4 equiv.) and 6-chlorohexanal (7.80 mmol, 1.01 g, 1.0 equiv.) in anhydrous THF (16 mL) was stirred under reflux for 16 h. The reaction mixture was allowed to cool to room temperature and carefully (low boiling point) concentrated under reduced pressure. The crude was purified by flash column chromatography (silica gel, 20% Et_2O in hexanes) to obtain **1s** (324 mg, 26%, *E*/*Z* = 9:1) as a colorless oil. (NMR spectra contain solvent peaks from FCC due to low boiling point of product).

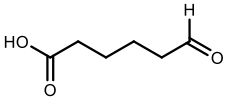


Chemical Formula: $C_8H_{13}ClO$
Molecular Weight: 160.64

^{1}H NMR (300 MHz, $CDCl_3$, mixture of isomers): δ = 9.51 (d, *J* = 7.9 Hz, 1H), 7.16 – 7.00 (m, 1H, *Z*-isomer), 6.84 (dt, *J* = 15.6, 6.8 Hz, 1H, *E*-isomer), 6.34 – 6.25 (m, 1H, *Z*-isomer), 6.12 (ddt, *J* = 15.6, 7.9, 1.5 Hz, 1H, *E*-isomer), 3.54 (t, *J* = 6.6 Hz, 3H) 2.43 – 2.31 (m, 2H), 1.93 – 1.72 (m, 2H), 1.63 – 1.45 (m, 4H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, major isomer):** δ = 194.1, 158.2, 133.4, 44.9, 32.6, 32.4, 27.3, 26.5 ppm.

HRMS (ESI): m/z calculated for $[C_8H_{13}ClONa]^+$ $[M+Na]^+$: 183.0547; found: 183.0543.

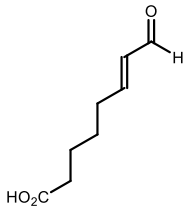
6-Oxohexanoic acid. A solution of 6-heptenoic acid (7.21 mol, 977 μL, 1.0 equiv.) in anhydrous DCM (29 mL) was cooled to -78 °C and degassed with a stream of oxygen. Ozone was then bubbled through the reaction mixture until it turned blue. The reaction was then purged with oxygen to remove excess of ozone and quenched with excess dimethyl sulfide. The reaction mixture was then



Chemical Formula: $C_6H_{10}O_3$
Molecular Weight: 130.14

lallowed to warm to room temperature, the organic layer was washed with sat. aq. NH_4Cl (3x 30 mL) and dried over $MgSO_4$. The volatiles were removed under reduced pressure to obtain crude 6-oxohexanoic acid (969 mg, quant.) which was engaged in the next step without further purification.

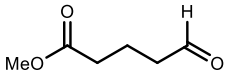
(*E*)-8-Oxooct-6-enoic enal (**1t**). 6-Oxohexanoic acid (937 mg, 7.20 mmol, 1.0 equiv.) was dissolved in THF (anhydrous, 14.4 mL) under an Argon atmosphere. (Triphenylphosphoranylidene)-acetaldehyde (2.894 g, 9.36 mmol, 1.3 equiv.) was added and the mixture was stirred for 6 days at room temperature. Upon concentration, the residue was purified by column chromatography (silica gel, EtOAc/hexanes/AcOH = 20:79:1) to afford 289 mg (26%) of **1t** as bright yellow solid.



Chemical Formula: $C_8H_{12}O_3$
Molecular Weight: 156,1810

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.51 (d, *J* = 7.9 Hz, 1H), 6.84 (dt, *J* = 15.6, 6.8 Hz, 1H), 6.14 (ddt, *J* = 15.6, 7.8, 1.5 Hz, 1H), 2.43 – 2.34 (m, 4H), 1.75 – 1.66 (m, 2H), 1.64 – 1.55 (m, 2H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 194.2, 178.5, 157.9, 133.4, 33.6, 32.4, 27.3, 24.2 ppm. **HRMS (ESI):** m/z calculated for $[C_8H_{11}O_3]^-$ [M-H]$^-$: 155.0714; found: 155.0714.

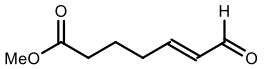
Methyl 5-oxopentanoate. A few drops of conc. sulfuric acid were added to a solution of δ-valerolactone (25.0 mmol, 2.50 g, 1.0 equiv.) in methanol (50 mL) and the reaction mixture was stirred under reflux for 2 h. The solvent was then removed under reduced pressure and the obtained crude was then dissolved in DCM (150 mL) and cooled to 0 °C. Dess-martin periodinane (30.0 mmol, 12.7 g, 1.2 equiv.) was added portionswise to the reaction mixture, followed by water (28.7 mmol, 518 µL, 1.15 equiv.). The reaction mixture was then let to warm to room temperature and further stirred for 2 h until completion of the reaction. The reaction mixture was then cooled to 0 °C and carefully quenched by a 1:1 mixture of 10% aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$ (150 mL) and let to stir until complete dissolution of the reaction mixture. The organic layer was further washed with a 1:1 mixture of 10% aq. $Na_2S_2O_3$ and sat. aq. $NaHCO_3$ (3x 100 mL) and dried over $MgSO_4$. The volatiles were removed under reduced pressure and the crude was purified by flash column chromatography (silica gel, 20% EtOAc in hexanes) to obtain methyl 5-oxopentanoate (2.00 g, 62%) as a colorless oil. Spectroscopic data are consistent with those previously reported.[19]



Chemical Formula: $C_6H_{10}O_3$
Molecular Weight: 130.14

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.74 (t, *J* = 1.3 Hz, 1H), 3.64 (s, 3H), 2.50 (td, *J* = 7.2, 1.3 Hz, 2H), 2.35 (t, *J* = 7.3 Hz, 2H), 1.93 (qq, *J* = 7.1 Hz, 2H) ppm.

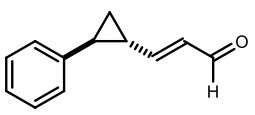
Methyl (*E*)-7-oxohept-5-enoate (**1u**). Under an atmosphere of argon, a solution of (triphenylphosphoranylidene)acetaldehyde (18.4 mmol, 5.61 g, 1.2 equiv.) and methyl 5-oxopentanoate (15.4 mmol, 2.00 g, 1.0 equiv.) in anhydrous THF (31 mL) was stirred under reflux for 16 h. The reaction mixture was allowed to cool to room temperature and concentrated under reduced pressure. The crude was purified by flash column chromatography (silica gel, 5-20% EtOAc in hexanes) to obtain **1u** as a colorless oil. Spectroscopic data are consistent with those previously reported.[20]



Chemical Formula: $C_8H_{12}O_3$
Molecular Weight: 156.18

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.50 (d, *J* = 7.8 Hz, 1H), 6.81 (dt, *J* = 15.7, 6.7 Hz, 1H), 6.12 (ddt, *J* = 15.7, 7.8, 1.5 Hz, 1H), 3.66 (s, 3H), 2.41 – 2.33 (m, 4H), 1.85 (qq, *J* = 7.4 Hz, 2H) ppm.

(*E*)-3-(*trans*-2-Phenylcyclopropyl)acrylaldehyde (**10**). Under an atmosphere of argon, a solution of (triphenylphosphoranylidene)acetaldehyde (8.28 mmol, 2.52 g, 1.4 equiv.) and (*trans*)-2-phenylcyclopropane-1-carbaldehyde (5.92 mmol, 865 mg, 1.0 equiv. prepared following a reported procedure[21]) in anhydrous THF (12 mL) was stirred under reflux for 16 h. The reaction mixture was allowed to cool to room temperature and concentrated under reduced pressure. The crude was



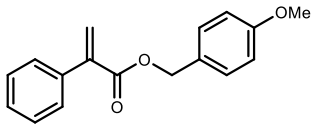
Chemical Formula: $C_{12}H_{12}O$
Molecular Weight: 172.23

purified by flash column chromatography (silica gel, 5-10% Et_2O in hexanes) to obtain **10** (621 mg, 61%) as an orange solid. Spectroscopic data are consistent with those previously reported.[22]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.47 (d, *J* = 7.8 Hz, 1H), 7.34 – 7.26 (m, 2H), 7.25 – 7.19 (m, 1H), 7.14 – 7.07 (m, 2H), 6.46 (dd, *J* = 15.4, 9.7 Hz, 1H), 6.21 (dd, *J* = 15.4, 7.8 Hz, 1H), 2.33 – 2.26 (m, 1H), 1.96 (dddd, *J* = 9.5, 8.3, 5.4, 4.0 Hz, 1H), 1.64 – 1.56 (m, 1H), 1.41 (ddd, *J* = 9.0, 5.3 Hz, 1H) ppm.

Synthesis of Acrylates 5

General procedure A for the synthesis of benzyl phenylacetate esters: To a 25 mL round bottom flask was added phenylacetic acid (1.05 equiv.), potassium carbonate (0.6 equiv.) and benzyl bromide (1.0 equiv.). DMF (5.0 mL) was added and the reaction stirred at room temperature for 6 hours. Then, water (10 mL) and Et_2O (10 mL) were added. The layers were separated and the organic layer was washed with water (5 x 10 mL), dried with $MgSO_4$, and concentrated *in vacuo* to afford desired ester product. The ester was used directly in the next step without further purification.

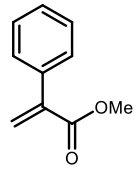
General procedure B for synthesis of benzyl acrylate esters: the procedure was adopted from a previous report.[23] To a 50 mL round bottom flask was added benzyl phenylacetate ester (1.0 equiv.), potassium carbonate (1.0 equiv.), paraformaldehyde (10.0 equiv.) and tetrabutylammonium iodide (1.0 equiv.). Toluene (30 mL) was added and the reaction was heated at 80 °C and stirred for 4 hours in the dark. The reaction mixture was then washed with water, the layers were separated, and the organic layer was dried with $MgSO_4$. The crude product was then concentrated, re-dissolved in 10% Et_2O in *n*-hexanes and purified by passing through a pad of silica.



Chemical Formula: $C_{17}H_{16}O_3$
Molecular Weight: 268.31

4-Methoxybenzyl 2-phenylacrylate (**5a**). Oxalyl chloride (11.4 mmol, 1.0 mL, 1.15 equiv.) was added to a solution of 2-phenylacrylic acid (10.0 mmol, 1.48 g, 1.0 equiv.) in anhydrous DCM (25 mL) under inert atmosphere at 0 °C, followed by a few drops of DMF. The reaction mixture was let to warm to room temperature and stirred until the bubbling ceased. The reaction mixture was concentrated under reduced pressure and placed under an inert atmosphere. The crude residue was dissolved in anhydrous DCM (25 mL) and (4-methoxyphenyl)methanol (11.4 mmol, 1.4 mL, 1.15 equiv.), pyridine (11.4 mmol, 922 μL, 1.15 equiv.) and *N*,*N*-dimethylpyridin-4-amine (1.00 mmol, 122 mg, 0.1 equiv.) were added to the reaction mixture, which was let to stir for 3 h. The reaction mixture was then quenched and washed with 1M HCl (3x 20 mL) and brine (20 mL) and the organic layer was dried over $MgSO_4$. The volatiles were removed under reduced pressure and the crude was purified by flash column chromatography (silica gel, 10% EtOAc in hexanes) to obtain **5**a (2.15 g, 80%) as a colorless oil. Spectroscopic data are consistent with those previously reported.[24]
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (dtd, *J* = 5.4, 3.1, 1.6 Hz, 2H), 7.38 – 7.33 (m, 5H), 6.94 – 6.88 (m, 2H), 6.37 (d, *J* = 1.2 Hz, 1H), 5.91 (d, *J* = 1.2 Hz, 1H), 5.23 (s, 2H), 3.82 (s, 3H) ppm.

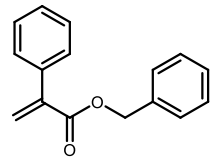
Methyl 2-phenylacrylate (**5b**). Procedure adapted from previous report.[25] To a 25 mL round bottom flask was added 2-phenylacrylic acid (500 mg, 3.37 mmol, 1.05 equiv.), potassium carbonate (267 mg, 0.6 equiv.) and methyl iodide (190 μL, 1.0 equiv.). DMF (5.0 mL) was added and reaction was stirred at room temperature for 6 hours. Upon completion of reaction water (10 mL) and Et_2O (10 mL) was added. The layers were separated in a separatory funnel. The organic layer was washed with water (5 x 10 mL), dried with $MgSO_4$ and concentrated *in vacuo* to afford desired **5b** as a light-yellow oil (497 mg, 95% yield). The spectroscopic data is consistent with previous report.[26]



Chemical Formula: $C_{10}H_{10}O_2$
Molecular Weight: 162,1880

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 – 7.39 (m, 2H), 7.37 – 7.28 (m, 3H), 6.36 (d, *J* = 1.2 Hz, 1H), 5.89 (d, *J* = 1.2 Hz, 1H), 3.82 (s, 3H) ppm.

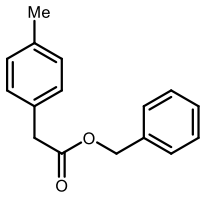
Benzyl 2-phenylacrylate (**5c**). Prepared according to reported procedure [25] using 2-phenylacrylic acid (500 mg, 3.37 mmol, 1.05 equiv.). The product was obtained as a colorless oil which solidifies upon storage at -20 °C (785 mg, 98% yield). The spectroscopic data is consistent with previous report.



Chemical Formula: $C_{16}H_{14}O_2$
Molecular Weight: 238,2860

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.29 (m, 10H), 6.39 (d, *J* = 1.0 Hz, 1H), 5.93 (d, *J* = 1.0 Hz, 1H), 5.29 (s, 2H) ppm.

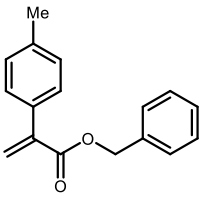
Benzyl 2-(p-tolyl)acetate. Prepared according to general procedure **A** using p-tolyl acetic acid (510 mg, 3.40 mmol). The product was obtained as a colorless oil (707 mg, 91% yield). The spectroscopic data is consistent with previous report.[23]



Chemical Formula: $C_{16}H_{16}O_2$
Molecular Weight: 240,3020

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 – 7.24 (m, 5H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 5.13 (s, 2H), 3.64 (s, 2H), 2.34 (s, 3H) ppm.

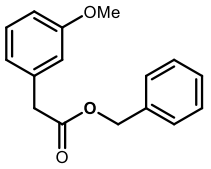
Benzyl 2-(p-tolyl)acrylate (**5d**). Prepared according to general procedure **B** using benzyl 2-(p-tolyl)acetate (707 mg, 2.94 mmol). The product was obtained as a colorless oil (390 mg, 55% yield).



Chemical Formula: $C_{17}H_{16}O_2$
Molecular Weight: 252,3130

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46 – 7.29 (m, 7H), 7.21 – 7.07 (m, 2H), 6.35 (d, *J* = 1.2 Hz, 1H), 5.89 (d, *J* = 1.2 Hz, 1H), 5.29 (s, 2H), 2.34 (s, 3H) ppm. The spectroscopic data is consistent with previous report.[23]

Benzyl 2-(3-methoxyphenyl)acetate. Prepared according to general procedure **A** using 3-methoxyphenyl acetic acid (500 mg, 3.01 mmol). The product was obtained as a colorless oil (713 mg, 96% yield).

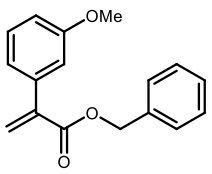


Chemical Formula: $C_{16}H_{16}O_3$
Molecular Weight: 256,3010

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.43 – 7.28 (m, 5H), 7.24 (t, *J* = 7.8 Hz, 1H), 6.90 – 6.79 (m, 3H), 5.14 (s, 2H), 3.78 (s, 3H), 3.65 (s, 2H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 171.4, 159.9, 136.0, 135.4, 129.7, 128.7, 128.4, 128.3, 121.8, 114.9, 113.0, 66.8, 55.3, 41.5 ppm.

HRMS (ESI): m/z calculated for $[C_{16}H_{16}O_3Na]^+$ $[M+Na]^+$: 279.0992, found: 279.0982.

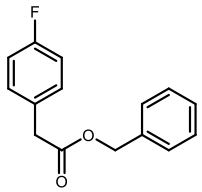
Benzyl 2-(3-methoxyphenyl)acrylate (**5e**). Prepared according to the general procedure **B** using benzyl 2-(3-methoxyphenyl)acetate (384 mg, 1.50 mmol). The product was obtained as a light yellow oil (150 mg, 37% yield).



Chemical Formula: $C_{17}H_{16}O_3$
Molecular Weight: 268,3120

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49 – 7.33 (m, 5H), 7.30 (dd, *J* = 8.2, 7.7 Hz, 1H), 7.05 (ddd, *J* = 7.6, 1.6, 1.0 Hz, 1H), 7.01 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.92 (ddd, *J* = 8.3, 2.6, 0.9 Hz, 1H), 6.42 (d, *J* = 1.2 Hz, 1H), 5.95 (d, *J* = 1.2 Hz, 1H), 5.31 (s, 2H), 3.81 (s, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 166.5, 159.4, 141.2, 138.0, 136.0, 129.2, 128.7, 128.3, 128.3, 127.2, 120.9, 114.0 (2C), 66.9, 55.3 ppm.
HRMS (ESI): m/z calculated for $[C_{17}H_{16}O_3Na]^+$ $[M+Na]^+$: 291.0992, found: 291.0978.

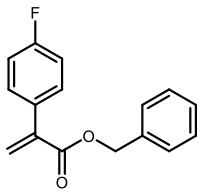
Benzyl 2-(4-fluorophenyl)acetate. Prepared according to the general procedure **A** using 4-fluorophenyl acetic acid (510 mg, 3.31 mmol). The product was obtained as a colorless oil, which solidifies upon storage at -20 °C (725 mg, 94% yield). The spectroscopic data is consistent with previous report.[27]



Chemical Formula: $C_{15}H_{13}FO_2$
Molecular Weight: 244,2654

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 –7.28 (m, 5H), 7.36 – 7.21 (m, 2H), 6.99 (t, *J* = 8.7 Hz, 2H), 5.13 (s, 2H), 3.63 (s, 2H) ppm.

Benzyl 2-(4-fluorophenyl)acrylate (**5f**). Prepared according to general procedure **B** using benzyl 2-(4-fluororophenyl)acetate (770 mg, 3.15 mmol). The product was obtained as a light-yellow oil which solidifies upon storage at -20 °C (561 mg, 69% yield).

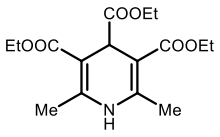


Chemical Formula: $C_{16}H_{13}FO_2$
Molecular Weight: 256,2764

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 – 7.30 (m, 7H), 7.09 – 7.00 (m, 2H), 6.40 (d, *J* = 1.1 Hz, 1H), 5.90 (d, *J* = 1.1 Hz, 1H), 5.27 (s, 2H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 166.5, 162.9 (d, J_{C-F} = 247.7 Hz), 140.3, 136.0, 132.8 (d, J_{C-F} = 3.3 Hz), 130.2 (d, J_{C-F} = 8.1 Hz), 128.7, 128.4, 128.3, 127.3, 115.2 (d, J_{C-F} = 21.6 Hz), 67.0 ppm. **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$):** δ = -113.79 ppm.
HRMS (ESI): m/z calculated $[C_{16}H_{13}FO_2Na]^+$ $[M+Na]^+$: 279.0792, found: 279.0787.

Preparation of Dihydropyridine R-1

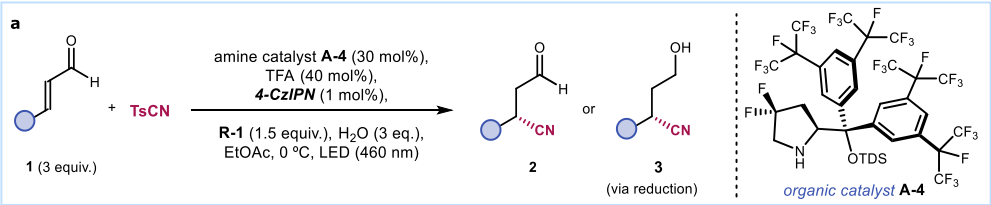
Triethyl 2,6-dimethyl-1,4-dihydropyridine-3,4,5-tricarboxylate (**R-1**). Ethyl glyoxylate (50 % by weight in PhMe, 11.0 mL, 1.0 equiv., 55.5 mmol) and ethyl (*Z*)-3-aminobut-2-enoate (14.0 mL, 2.0 equiv., 111 mmol) was stirred in glacial acetic acid (25 mL) for 16 hours. After removal of volatiles, the residue was transferred to a separation funnel containing aqueous $NaHCO_3$ (saturated, 100 mL) and the product was extracted with EtOAc (3 x 200 mL). After concentration of the combined organic layers, the product was purified by flash column chromatography (silica, 25% EtOAc in n-hexanes) to afford a bright yellow solid, which was then recrystallized from CH_2Cl_2/n-hexanes to afford **R-1** as a white crystalline solid. (7.27 g, 40% yield)



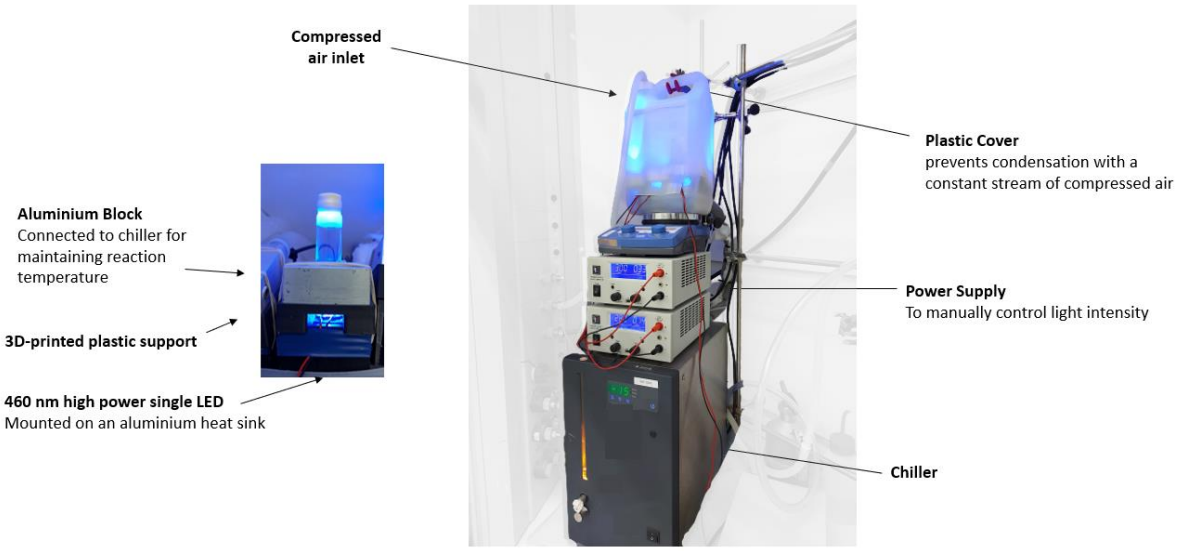
Chemical Formula: $C_{16}H_{23}NO_6$
Molecular Weight: 325,3610

^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.18 (br s, 1H), 4.82 (s, 1H), 4.28 – 4.11 (m, 4H), 4.07 (q, *J* = 7.1 Hz, 2H), 2.28 (s, 6H), 1.28 (t, *J* = 7.1 Hz, 6H), 1.20 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 174.4, 167.4, 145.6, 98.8, 60.8, 60.1, 40.7, 19.3, 14.5, 14.3 ppm.
HRMS (ESI): m/z calculated for $[C_{16}H_{23}NO_6Na]^+$ $[M+Na]^+$: 348.1418, found: 348.1412.

General Procedure for the Conjugate Cyanation of Enals

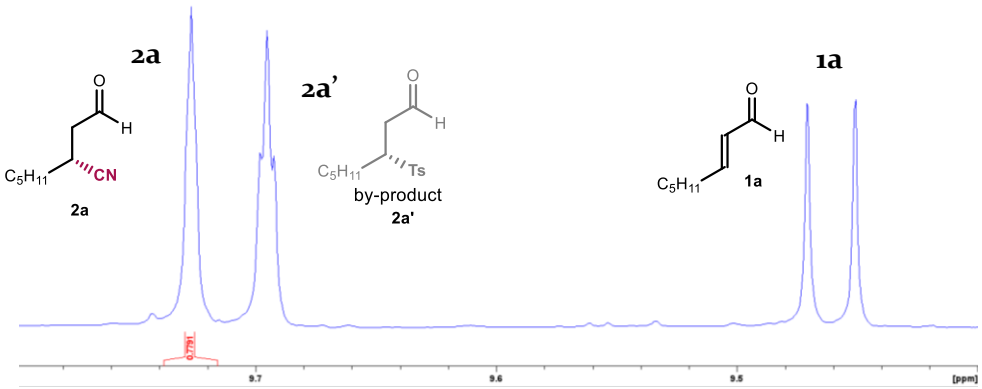


General procedure C (*for 0.25 mmol scale*): An 8.0 mL vial equipped with a stirring bar was charged with tosyl cyanide (48 mg, 250 µmol, 95% purity, 1.0 equiv.), the chiral amine catalyst **A-4** (83 mg, 75.0 µmol, 0.3 equiv.), **R-1** (122 mg, 375 µmol, 1.5 equiv.), 4-CzIPN (2 mg, 2.50 µmol, 1 mol%) and enal **1** (3.0 equiv.). The vial was sealed with a septum and purged with Argon. The reactants were suspended in EtOAc (500 µL, ensure that all compounds are suspended) and deionized water (13.5 µL, 3.0 equiv.) was added. Then, TFA (7.5 µL, 100 µmol, 0.4 eq) was added and the vial was instantly placed in a pre-cooled metal support (set for an internal temperature of 5 °C) mounted on an aluminum block fitted with a high-power single blue LED (λ_{max} = 460 nm, irradiance set at 90 mW/cm^2 as controlled by an external power supply). The set-up secured a reliable irradiation while keeping a distance of 1 cm between the reaction vessel and the light source (set-up detailed in **Supplementary Figure 1**). After 16 hours (unless otherwise stated), the mixture was concentrated under reduced pressure.



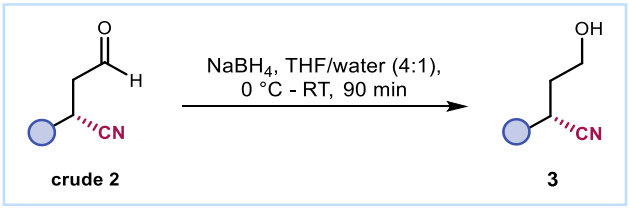
Supplementary Figure 1: Detailed set-up and illumination system used in these studies. The light source consisted of a single 460 nm high-power LED (LZ1-00DB00) purchased from LedEngin; distance between LED and reaction vessel = 1 cm.

Determination of analytical yields for the conjugate cyanation of enals. Analytical yields were determined by ^{1}H NMR analysis (400 MHz) of the crude reaction mixtures using trichloroethylene (TCE, 22.5 uL, 250 µmol, 1.0 equiv.) as the internal standard. For integration, aldehydic peaks have been used (d1 = 6 seconds). This analysis allowed to infer the analytic yields of both the target cyanation product **2** and the by-product **2'** (arising from the competitive addition of tosyl radical to enal **1**), which was typically formed in a similar amount as the target adduct **2**. *For each specific entry (see below), we report the analytical yields of products **2** and **2'**.* The aldehydic peaks typically appear in the following order from low to high field, as shown in **Supplementary Figure 2** (case example using octenal **1a**).



Supplementary Figure 2: Crude reaction mixture using **1a** (400 MHz), showing aldehydic products: β-cyanoaldehyde **2a** (br s, left); β-sulfone aldehyde **2a'** (t, *J* = 1.00 Hz), and octenal starting material **1a** (d, *J* = 8.0 Hz, right)

It was not always possible to isolate the cyanoaldehydes **2** because of a difficult separation from the β-sulfone aldehyde by-product **2'**. When the direct isolation of pure cyanoaldehydes was not feasible, they were isolated as cyano-alcohols **3** upon reduction of the crude reaction mixture according to **Supplementary Figure 3**. *Conversion to alcohols **3** allowed a simple separation from the sulfone by-product **2'**.*

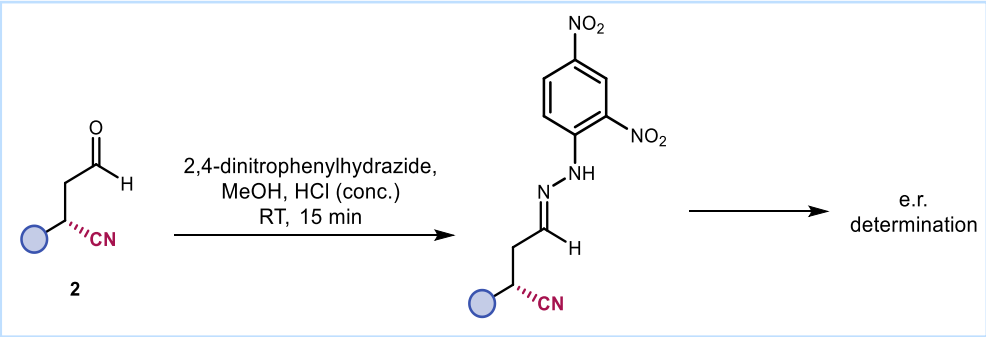


Supplementary Figure 3: Reduction of cyanoaldehydes **2** (crude mixture) to their corresponding cyanoalcohols **3**

Reduction to β-cyanoalcohols 3 (*one-pot*) - General procedure D: Upon completion of the organocatalytic conjugate cyanation, the solvent was evaporated and the crude reaction mixture containing **2** was dissolved in THF (2.0 mL); then water (0.5 mL) was added. After cooling to 0 °C with an ice bath, $NaBH_4$ (94.6 mg, 2.50 mmol, 10 equiv.) was added in a few portions under vigorous stirring. After 10 minutes, the ice bath was removed and the mixture was stirred for 90 minutes at ambient temperature. After cooling to 0 °C with an ice bath, the slurry was quenched dropwise with 1 N HCl until gas evolution ceased. The mixture was transferred to a separation funnel and extracted with DCM (3 x 20 mL). The combined organic layers were dried with $MgSO_4$ and concentrated. The β-cyano-alcohols **3** were isolated under conditions stated at the individual compounds below.

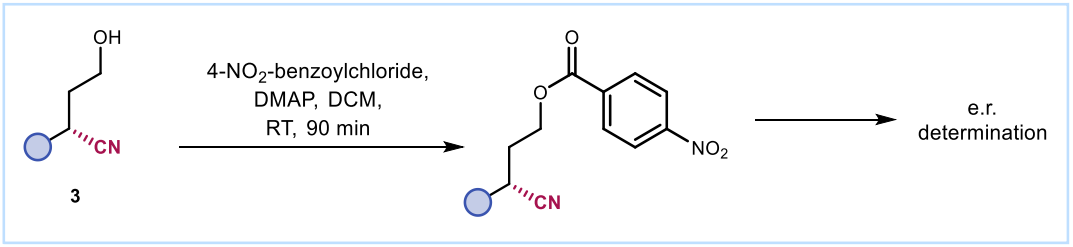
Derivatization of products 2 or 3 for determination of the enantiomeric ratio by UPC² analysis

In order to determine the enantiomeric ratio of the products, β-cyanoaldehydes **2** were converted into the corresponding 2,4-dinitrophenylhydrazones (see **Supplementary Figure 4**), while β-cyanoalcohols **3** were best analysed upon derivatisation into the corresponding nitrobenzoic esters (**Supplementary Figure 5**).



Supplementary Figure 4: Preparation of an analytical sample of 2,4-dinitrophenylhydrazones from β-cyanoaldehydes **2**

Procedure: A analytical sample of cyanoaldehyde **2** (1.00 mg) and 1 equiv. of 2,4-dinitrophenylhydrazine were dissolved in MeOH (0.3 mL). 1 drop of concentrated HCl was added and the solution was allowed to stand for 15 minutes and then concentrated under reduced pressure. The hydrazone was separated from unreacted hydrazine by preparative TLC and the enantiomeric ratio of the hydrazones was determined by UPC^2 analysis with conditions specified in the experimental section of the individual compounds.

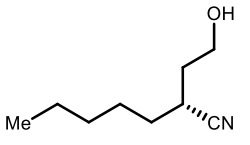


Supplementary Figure 5: Preparation of an analytical sample of 4-nitrobenzoic esters from β-cyanoalcohols **3**.

Procedure: An analytical sample of cyanoalcohol **3** (1.00 mg) and 1 equiv. of *p*-NO_2-benzoyl chloride were suspended in DCM (0.3 mL). 1 Equiv. of 4-dimethylaminopyridine (DMAP) was added and the solution was allowed to stir for 90 minutes. The ester was separated from unreacted reactands by preparative TLC and the enantiomeric ratio of the benzoic ester was determined by UPC^2 analysis with conditions specified in the experimental section of the individual compounds.

Characterization Data for the Conjugate Cyanation of Enals

(*R*)-2-(2-Hydroxyethyl)heptanenitrile (**3a**)



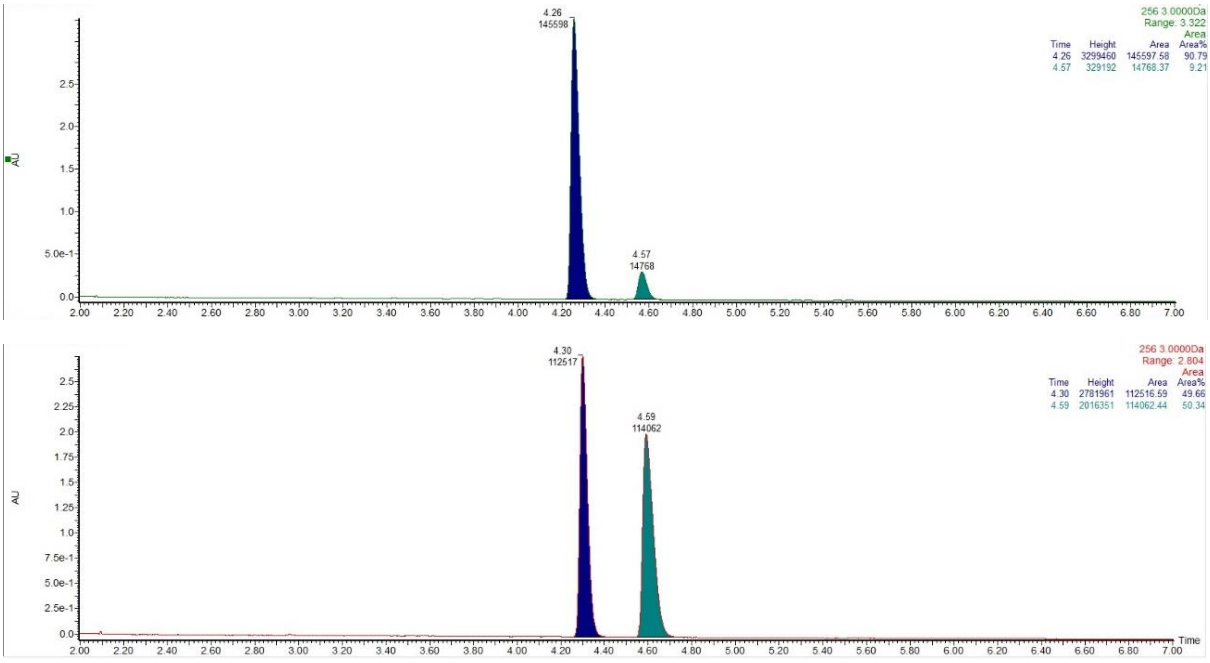
Chemical Formula: $C_9H_{17}NO$
Molecular Weight: 155,2410

Following the general procedure **C** using enal **1a** (750 µmol, 94.5 mg), a mixture containing the β-cyanoaldehyde **2a** (77% NMR yield) and the sulfone by-product **2a'** (45% NMR yield) was obtained. The crude target product **2a** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3a** as a pale-yellow oil (29.0 mg, 75% yield). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 90.5:9.5 by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 4.25 min, τ_{Minor} = 4.55 min.

$[\alpha]_D^{25}$ = -2.0 (c = 1.0, $CHCl_3$, 90.5:9.5 e.r.).

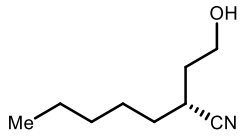
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.86-3.79 (m, 2H), 2.85-2.76 (m, 1H), 1.88-1.78 (m, 2H), 1.69-1.39 (m, 4H), 1.38-1.27 (m, 4H), 0.93-0.87 (t, *J* = 6.9 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 122.2, 59.9, 35.0, 32.3, 31.4, 28.3, 26.9, 22.5, 14.1 ppm.

HRMS (APCI): m/z calculated for $[C_9H_{18}NO]^+$ $[M+H]^+$: 156.1383; found: 156.1386.



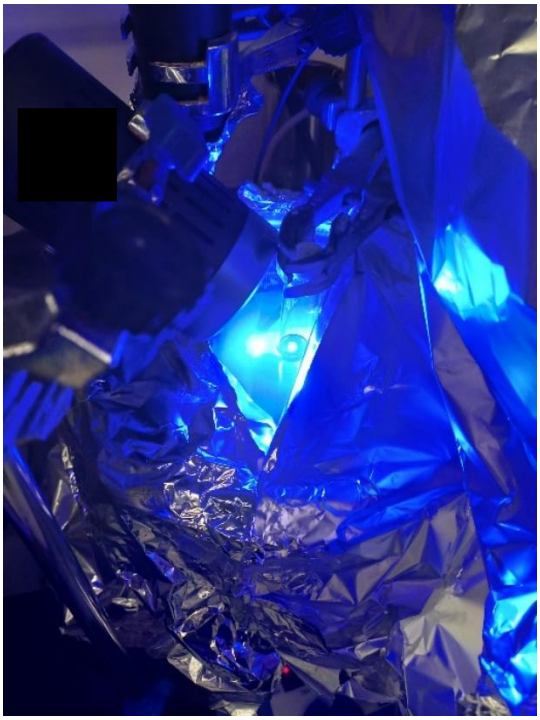
Supplementary Figure 6: UPC^2 traces of **3a**

(*R*)-2-(2-Hydroxyethyl)heptanenitrile (**3a**) (*Kessil Lamp Experiment*)



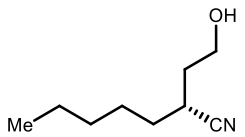
Chemical Formula: $C_9H_{17}NO$
Molecular Weight: 155,2410

The reaction mixture (0.25 mmol standard scale) was prepared as described above and the vial containing all reactants was instantly placed in a cooling bath (set to 5 °C) using a cryostat. The mixture was irradiated with a Kessil lamp (PR160L-456 nm, 40 W). After 40 hours, the mixture was concentrated under reduced pressure. A mixture containing the β-cyanoaldehyde **2a** (67% NMR yield) and the sulfone by-product **2a'** (73% NMR yield) was obtained. The crude target product **2a** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3a** as a pale-yellow oil (25.0 mg, 65% yield). Analytical data was in agreement with the product obtained from the single LED experiment as described above. The enantiomeric ratio was determined as described above to be 90:10 by UPC^2 analysis.



Supplementary Figure 7: Set-up for the conjugate cyanation of octenal **1a** using a Kessil lamp (456 nm, maximal intensity). The vial was placed in a cooling bath (Dewar containing toluene) which was cooled to 5 °C by use of a cryostat (Thermo Fisher Scientific - EK90 Immersion Cooler). Distance from the Kessil lamp to the bottom of the vial was approximately 5 cm.

(*R*)-2-(2-Hydroxyethyl)heptanenitrile (**3a**) (*1 mmol scale experiment*)

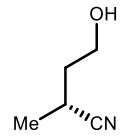


Chemical Formula: $C_9H_{17}NO$
Molecular Weight: 155,2410

An 8 mL vial equipped with a stirring bar was charged with tosyl cyanide (191 mg, 1.00 mmol, 95% purity, 1.0 equiv.), **A-4** (331 mg, 300 µmol, 0.3 equiv.), **R-1** (390 mg, 1.20 mmol, 1.2 equiv.), 4-CzIPN (8 mg, 10.0 µmol, 1 mol%) and **1a** (450 µL, 3.00 mmol, 3.0 equiv.). The vial was sealed with a septum and purged with Argon. The reactants were suspended in EtOAc (2.00 mL, ensure that all compounds are suspended) and deionized water (54.1 µL, 3.0 equiv.) was added. Then, TFA (30.0 µL, 400 µmol, 400 µmol) was added and the vial was instantly placed in a pre-cooled metal block (set for an internal temperature of 5 °C) and irradiated with a high-power single LED (460 nm, irradiance 150 mW/cm^2). After 40 hours, the mixture was concentrated under reduced pressure.

The crude reaction mixture containing the β-cyanoaldehyde **2a** (58% NMR yield) and the sulfone by-product **2a'** (68% NMR yield) was dissolved in THF (8.00 mL) and then water (2.00 mL) was added. After cooling 0 °C with an ice bath, $NaBH_4$ (380 mg, 10.0 mmol, 10 equiv.) was added in a few portions while rigorous stirring. After 10 minutes, the ice bath was removed and the mixture was stirred for 90 minutes at ambient temperature. After cooling to 0 °C with an ice bath, the slurry was quenched dropwise with 1 N HCl until gas evolution ceased. The mixture was transferred to a separation funnel and extracted with DCM (3 x 50 mL). The combined organic layers were dried with $MgSO_4$ and concentrated. A mixture containing the β-cyanoaldehyde with 58% NMR yield was obtained. The crude mixture was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3a** as a pale-yellow oil (86.0 mg, 55% yield). Analytical data was in agreement with the product obtained from the 0.25 mmol scale experiment as described above. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative (**Supplementary Figure 5**) was determined to be 90.5:9.5 by UPC^2 analysis on a Daicel Chiralpak IA-3 column as described for the 0.25 mmol scale experiment.

(*R*)-4-Hydroxy-2-methylbutanenitrile (**3b**)



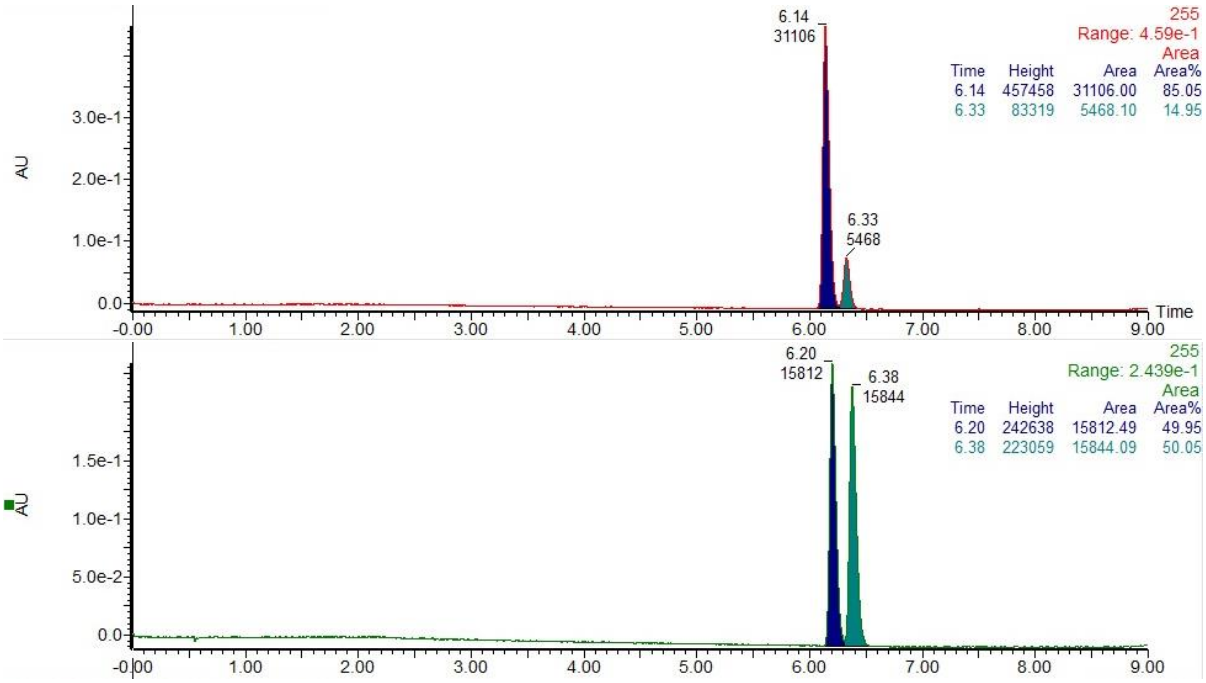
Chemical Formula: C_5H_9NO
Molecular Weight: 99,1330

Following the general procedure **C** using enal **1b** (750 μmol, 52.5 mg), a mixture containing the β-cyanoaldehyde **2b** (56% NMR yield) and the sulfone by-product **2b'** (45% NMR yield) was obtained. The crude target product **2b** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3b** as a pale-yellow oil (14.0 mg, 57% yield). *During all operations, low pressure was best avoided due to the high volatility of the compound.* The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 85:15 by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 90% CO_2 in CH_3CN for 5 min, 90% CO_2 in CH_3CN for 2 min, gradient 90% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 255 nm) τ_{Major} = 6.15 min, τ_{Minor} = 6.30 min.

$[\alpha]_D^{25}$ = -43.7 (c = 0.5, $CHCl_3$, 85:15 e.r.).

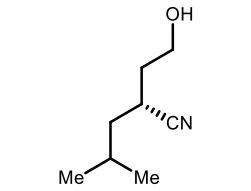
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (dd, *J* = 6.6, 5.4 Hz, 2H), 2.94-2.84 (m, 1H), 1.90-1.74 (m, 2H), 1.35 (d, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 123.0, 59.6, 36.6, 22.2, 18.0 ppm.

HRMS: not obtained due to volatility



Supplementary Figure 8: UPC^2 traces of **3b**.

(*R*)-2-(2-Hydroxyethyl)-4-methylpentanenitrile (**3c**)



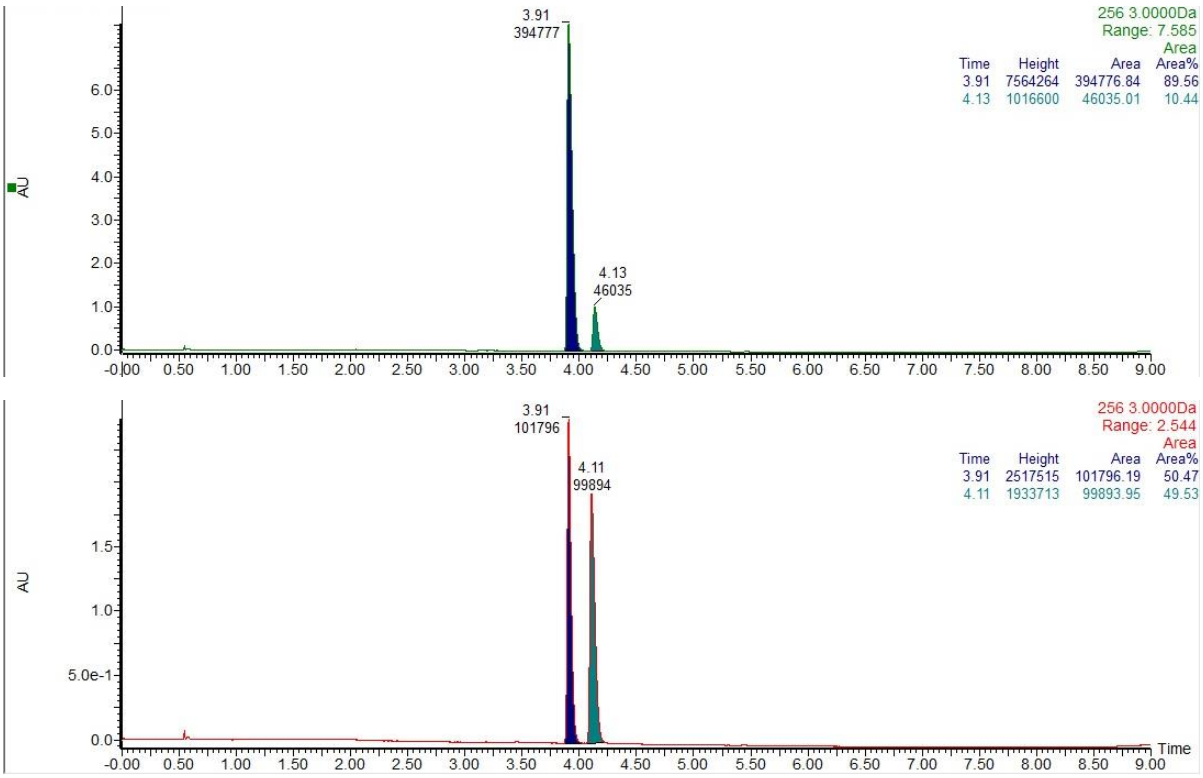
Chemical Formula: $C_8H_{15}NO$
Molecular Weight: 141,2140

Following the general procedure **C** using enal **1c** (750 µmol, 187 mg, 45 w% in hexanes), a mixture containing the β-cyanoaldehyde **2c** (60% NMR yield) and the sulfone by-product **2c'** (85% NMR yield) was obtained. The crude target product **2c** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3c** as a colorless oil (19.5 mg, 56% yield). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 89.5:10.5 by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 3.90 min, τ_{Minor} = 4.15 min.

$[\alpha]_D^{25}$ = -1.2 (c = 0.5, $CHCl_3$, 89.5:10.5 e.r.).

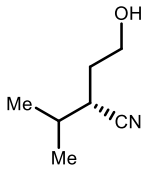
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.83 (t, *J* = 5.7 Hz, 2H), 2.92 – 2.78 (m, 1H), 1.94 – 1.74 (m, 3H), 1.72 (br s, OH), 1.63 (ddd, *J* = 13.5, 10.4, 5.0 Hz, 1H), 1.33 (ddd, *J* = 13.5, 9.3, 5.4 Hz, 1H), 0.97 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 122.2, 59.8, 41.3, 35.3, 26.4, 26.3, 23.0, 21.6 ppm.

HRMS (APCI): m/z calculated for $[C_8H_{16}NO]^+$ $[M+H]^+$: 142.1226; found: 142.1231.



Supplementary Figure 9: UPC^2 traces of **3c.**

***(S)*-4-Hydroxy-2-isopropylbutanenitrile** (**3d**)



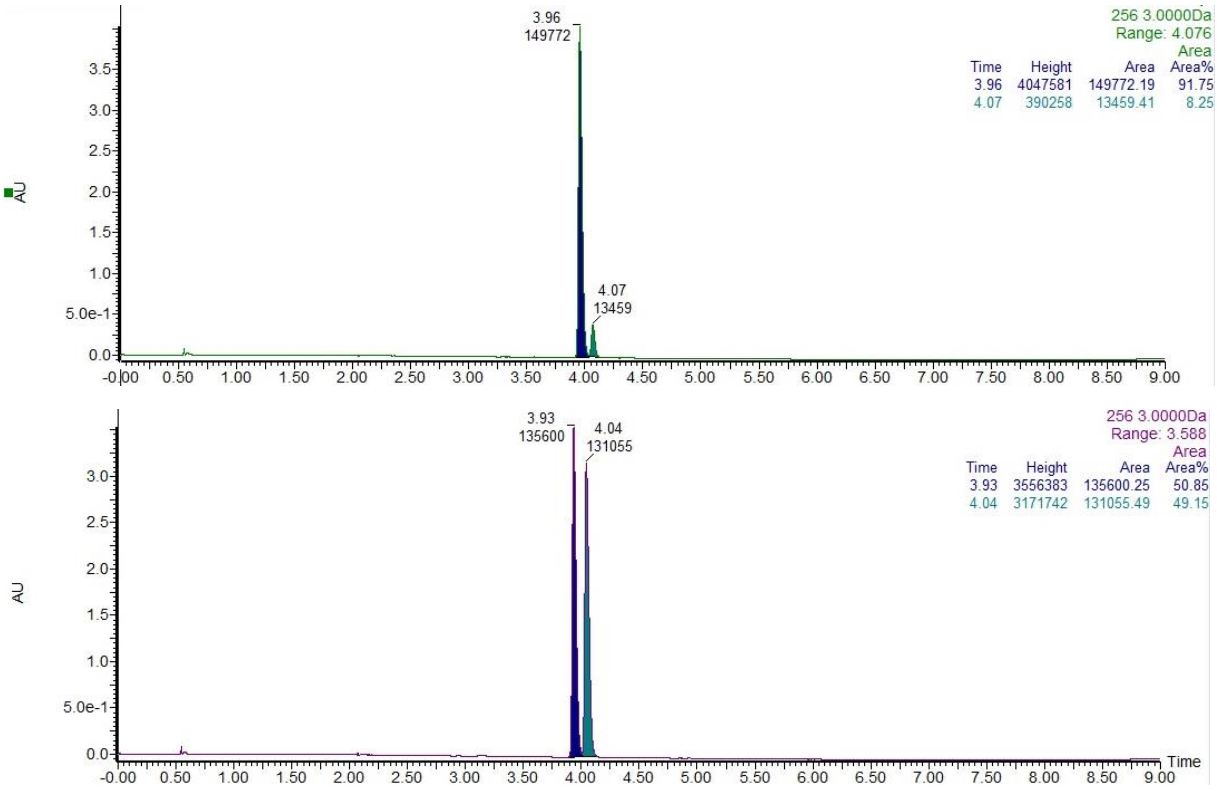
Chemical Formula: $C_7H_{13}NO$
Molecular Weight: 127,1870

Following the general procedure **C** using enal **1d** (750 μmol, 73.5 mg), a mixture containing the β-cyanoaldehyde **2d** (42% NMR yield) and the sulfone by-product **2d'** (> 95% NMR yield) was obtained. The crude target product **2d** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3d** as a pale-yellow oil (13.0 mg, 42% yield). *During all operations, low pressure was best avoided due to potential volatility.* The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 92:8 by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 3.95 min, τ_{Minor} = 4.05 min.

$[\alpha]_D^{25}$ = -20.9 (c = 0.5, $CHCl_3$, 92:8 e.r.).

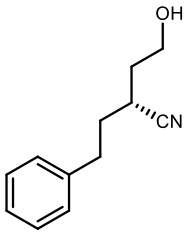
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.92-3.76 (m, 2H), 2.79-2.69 (m, 1H), 1.96-1.74 (m, 3H), 1.08 (dd, *J* = 7.9, 6.7 Hz, 6H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 121.0, 60.2, 35.5, 32.8, 30.2, 21.1, 18.7 ppm.

HRMS (APCI): m/z calculated for $[C_7H_{14}NO]^+$ $[M+H]^+$: 128.1070; found: 128.1071.



Supplementary Figure 10: UPC^2 traces of **3d**.

(*R*)-4-Hydroxy-2-phenethylbutanenitrile (**3e**)



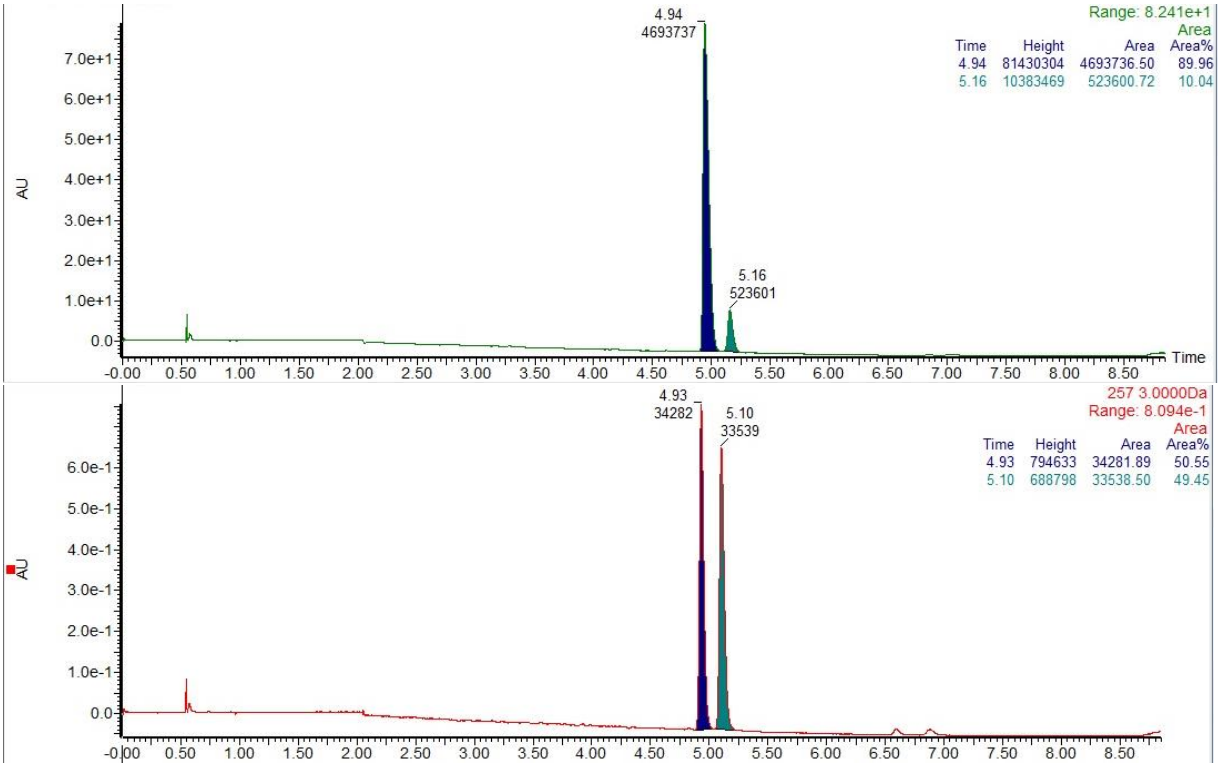
Chemical Formula: $C_{12}H_{15}NO$
Molecular Weight: 189,2580

Following the general procedure **C** using enal **1e** (750 μmol, 120 mg), a mixture containing the β-cyanoaldehyde **2e** (71% NMR yield) and the sulfone by-product **2e'** (73% NMR yield) was obtained. The crude target product **2e** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3e** as a colorless oil (35.0 mg, 74% yield). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 90:10 by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 257 nm) τ_{Major} = 4.95 min, τ_{Minor} = 5.10 min.

$[\alpha]_D^{25}$ = +30.1 (c = 1.0, $CHCl_3$, 90:10 e.r.).

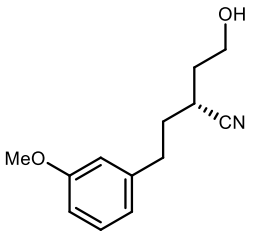
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 – 7.28 (m, 2H), 7.25 – 7.18 (m, 3H), 3.86 – 3.75 (m, 2H), 2.91 (ddd, *J* = 14.1, 9.0, 4.6 Hz, 1H), 2.86 – 2.71 (m, 2H), 2.04 – 1.80 (m, 4H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 140.2, 128.8 (2C), 128.5 (2C), 126.5, 121.9, 59.7, 34.9, 34.0, 33.4, 27.8 ppm.

HRMS (APCI): m/z calculated for $[C_{12}H_{16}NO]^+$ $[M+H]^+$: 190.1226; found: 190.1235.



Supplementary Figure 11: UPC^2 traces of **3e.**

(*R*)-4-Hydroxy-2-(3-methoxyphenethyl)butanenitrile (**3f**)



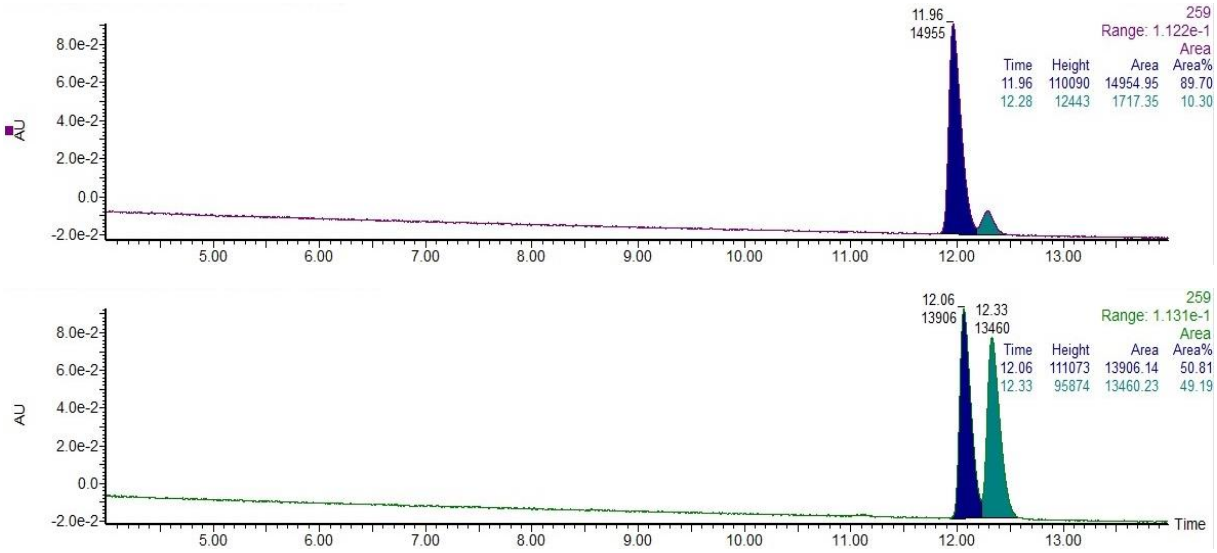
Chemical Formula: $C_{13}H_{17}NO_2$
Molecular Weight: 219,2840

Following the general procedure **C** using enal **1f** (750 μmol, 143 mg), a mixture containing the β-cyanoaldehyde **2f** (66% NMR yield) and the sulfone by-product **2f'** (64% NMR yield) was obtained. The crude target product **2f** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) followed by preparative TLC (silica gel, 60% ethylacetate in hexane) to afford product **3f** as a pale-yellow oil (32.0 mg, 58% yield). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 89.5:10.5 by UPC^2 analysis on a Daicel Chiralpak IE-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 70% CO_2 in CH_3CN for 12 min, 70% CO_2 in CH_3CN for 2 min, gradient 70% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 259 nm) τ_{Major} = 11.95 min, τ_{Minor} = 12.30 min.

$[\alpha]_D^{25}$ = +31.6 (c = 1.0, $CHCl_3$, 89.5:10.5 e.r.).

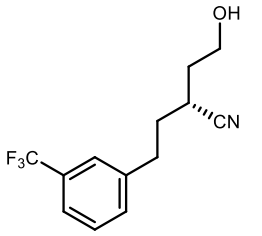
^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.22 (t, *J* = 7.7 Hz, 1H), 6.82 – 6.72 (m, 3H), 3.86 – 3.77 (m, 5H), 2.93 – 2.84 (m, 1H), 2.84 – 2.69 (m, 2H), 2.01 – 1.81 (m, 4H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 159.9, 141.8, 129.8, 121.9, 120.9, 114.3, 111.8, 59.8, 55.3, 34.9, 33.9, 33.5, 27.8 ppm.

HRMS (ESI): m/z calculated for $[C_{13}H_{17}NNaO_2]^+$ $[M+Na]^+$: 242.1151; found: 242.1146.



Supplementary Figure 12: UPC^2 traces of **3f.**

(*R*)-4-Hydroxy-2-(3-(trifluoromethyl)phenethyl)butanenitrile (**3g**)



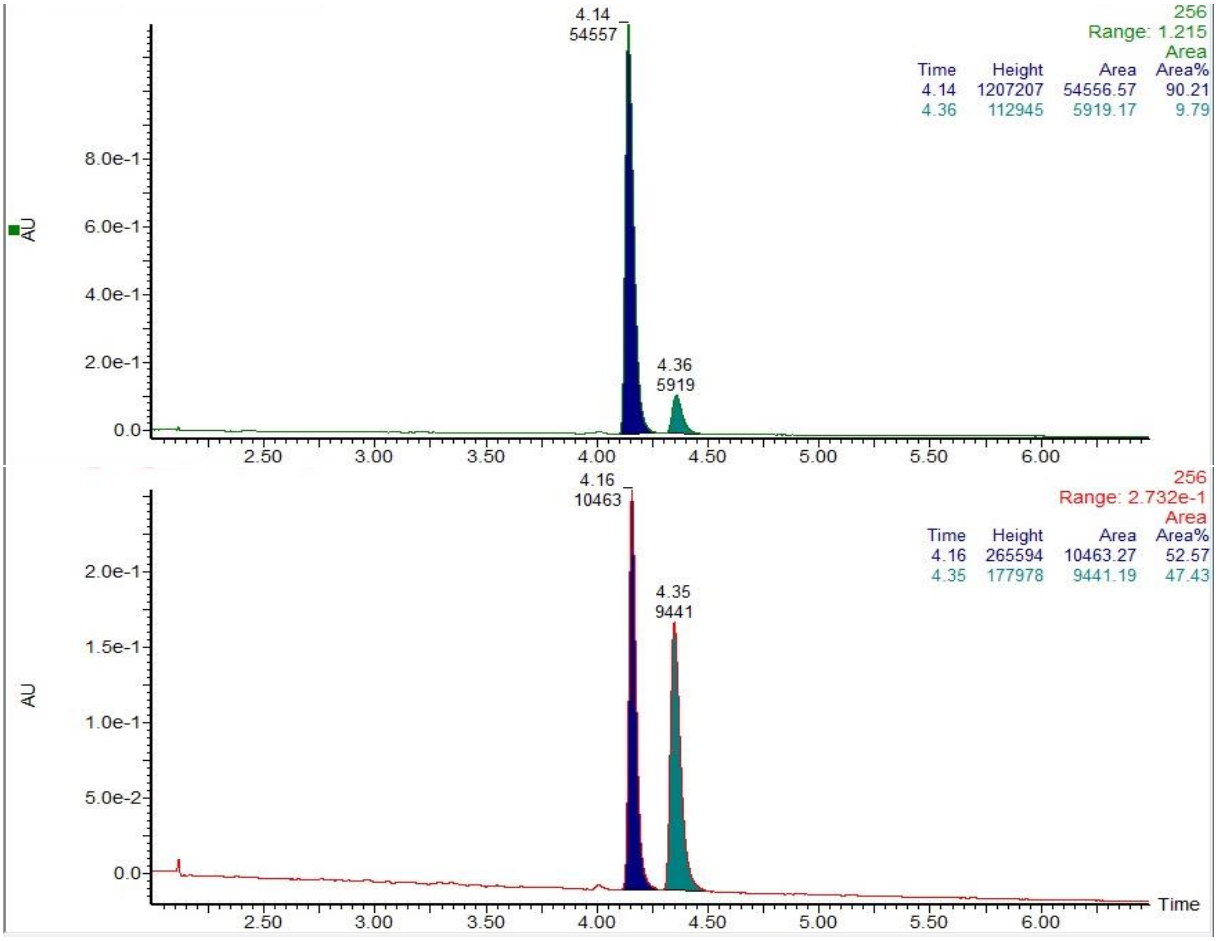
Chemical Formula: $C_{13}H_{14}F_3NO$
Molecular Weight: 257,2562

Following the general procedure **C** using enal **1g** (750 µmol, 171 mg), a mixture containing the β-cyanoaldehyde **2g** (78% NMR yield) and the sulfone by-product **2g'** (79% NMR yield) was obtained. The crude target product **2g** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3g** as a colorless oil (44.5 mg, 70% yield). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 90:10 by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 4.15 min, τ_{Minor} = 4.35 min.

$[\alpha]_D^{25}$ = +14.4 (c = 1.0, $CHCl_3$, 90:10 e.r.).

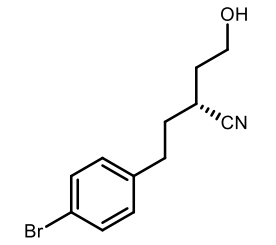
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 – 7.21 (m, 4H), 3.75 – 3.60 (m, 2H), 2.83 (ddd, *J* = 14.7, 9.6, 5.5 Hz, 1H), 2.75 – 2.61 (m, 2H), 1.91 – 1.65 (m, 4H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 141.2, 132.0 (q, *J* = 1.5 Hz), 131.1 (q, *J* = 32.2 Hz), 129.2, 125.2 (q, *J* = 3.6 Hz), 124.20 (q, *J* = 272.3 Hz), 123.5 (q, *J* = 3.9 Hz), 121.6, 59.6, 34.8, 33.8, 33.3, 27.9 ppm. **^{19}F NMR (376 MHz, $CDCl_3$):** δ = -62.7 ppm.

HRMS (ESI): m/z calculated for $[C_{13}H_{14}F_3NNaO]^+$ $[M+Na]^+$: 280.0920; found: 280.0919.



Supplementary Figure 13: UPC^2 traces of **3g**.

(*R*)-2-(4-Bromophenethyl)-4-hydroxybutanenitrile (**3h**)



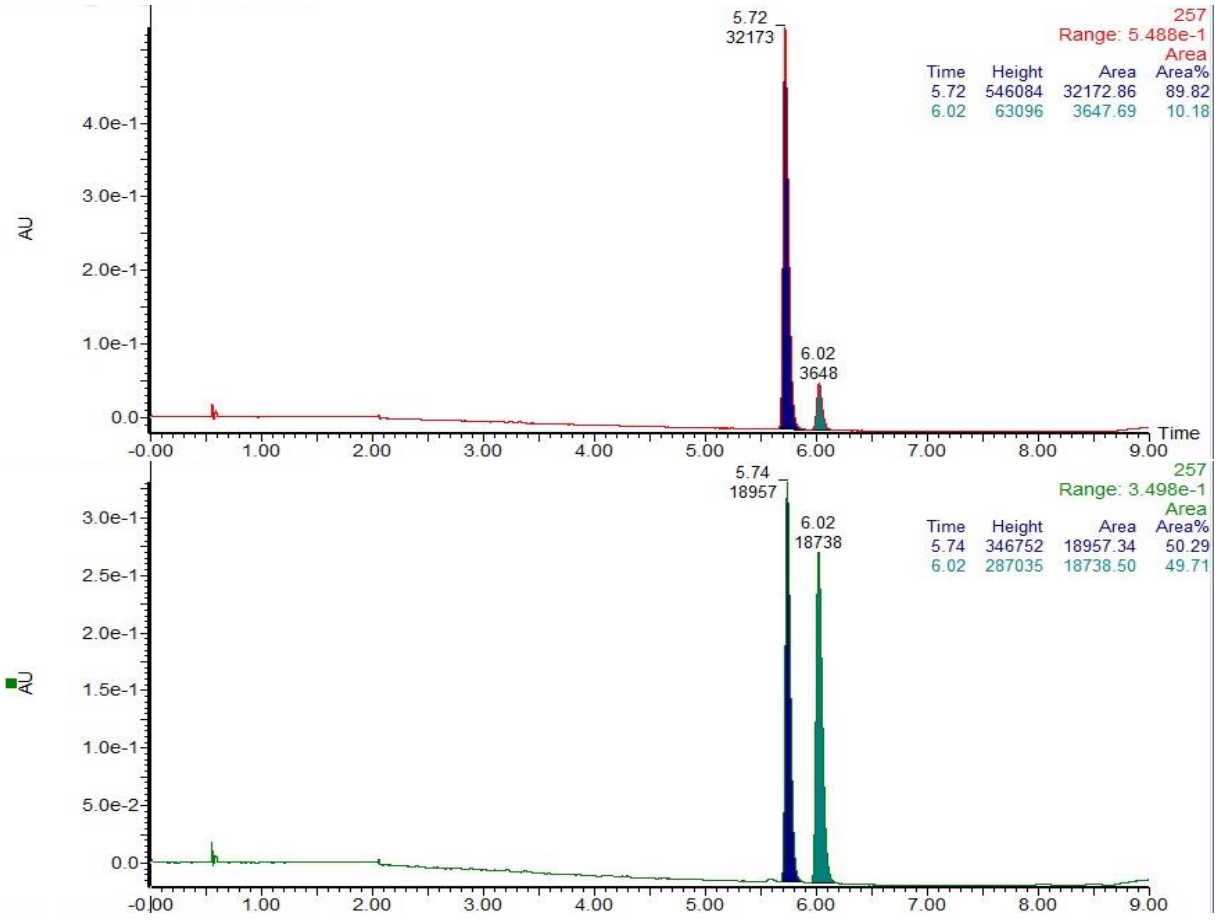
Chemical Formula: $C_{12}H_{14}BrNO$
Molecular Weight: 268,1540

Following the general procedure **C** using enal **1h** (750 µmol, 179 mg), a mixture containing the β-cyanoaldehyde **2h** (57% NMR yield) and the sulfone by-product **2h'** (61% NMR yield) was obtained. The crude target product **2h** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3h** as a pale yellow oil (34.5 mg, 52% yield). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 90:10 by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 257 nm) τ_{Major} = 5.70 min, τ_{Minor} = 6.00 min.

$[\alpha]_D^{25}$ = +26.1 (c = 1.0, $CHCl_3$, 90:10 e.r.).

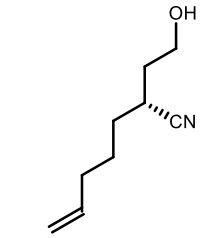
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.6 Hz, 2H), 3.82 (br t, *J* = 5.5 Hz, 2H), 2.92 – 2.66 (m, 3H), 2.01 – 1.76 (m, 4H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 139.2, 131.9 (2C), 130.3 (2C), 121.7, 120.4, 59.7, 34.9, 33.8, 32.9, 27.7 ppm.

HRMS (ESI): m/z calculated for $[C_{12}H_{14}BrNNaO]^+$ $[M+Na]^+$: 290.0151 found: 290.0155.



Supplementary Figure 14: UPC^2 traces of **3h.**

(*R*)-2-(2-Hydroxyethyl)hept-6-enenitrile (**3i**)



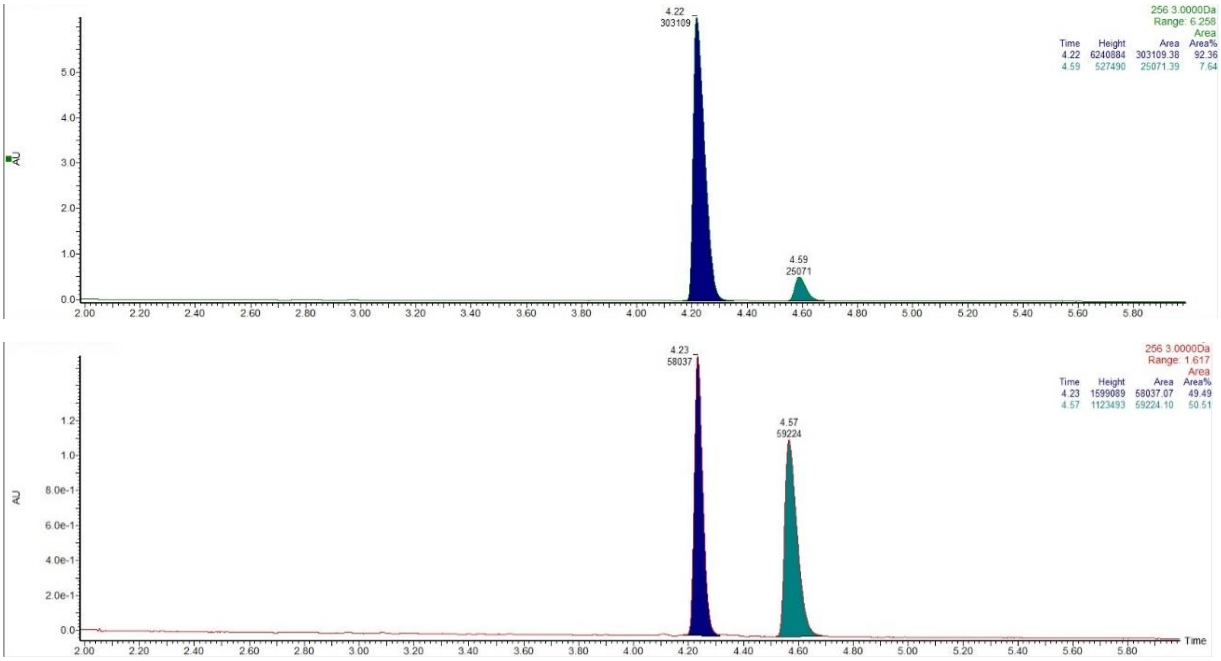
Chemical Formula: $C_9H_{15}NO$
Molecular Weight: 153,2250

Following the general procedure **C** using enal **1i** (750 µmol, 93.0 mg), a mixture containing the β-cyanoaldehyde **2i** (73% NMR yield) and the sulfone by-product **2i'** (< 10% NMR yield) was obtained. The crude target product **2i** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3i** as a pale yellow oil (27.5 mg, 72% yield). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 92.5:7.5 by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 4.20 min, τ_{Minor} = 4.60 min.

$[\alpha]_D^{25}$ = -4.9 (c = 1.0, $CHCl_3$, 92.5:7.5 e.r.).

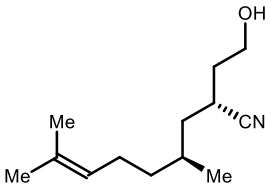
^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.78 (ddt, *J* = 17.0, 10.2, 6.7 Hz, 1H), 5.06 – 5.00 (m, 1H), 5.00 – 4.96 (m, 1H), 3.89 – 3.72 (m, 2H), 2.88 – 2.75 (m, 1H), 2.18 – 2.03 (m, 2H), 1.86 – 1.80 (m, 2H), 1.71 – 1.50 (m, 4H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 137.8, 122.1, 115.5, 59.7, 34.9, 33.2, 31.6, 28.1, 26.4 ppm.

HRMS (APCI): m/z calculated for $[C_9H_{16}NO]^+$ $[M+H]^+$: 154.1226; found: 154.1230.



Supplementary Figure 15: UPC^2 traces of **3i.**

(*2R,4S*)-2-(2-Hydroxyethyl)-4,8-dimethylnon-7-enenitrile (**3j**)



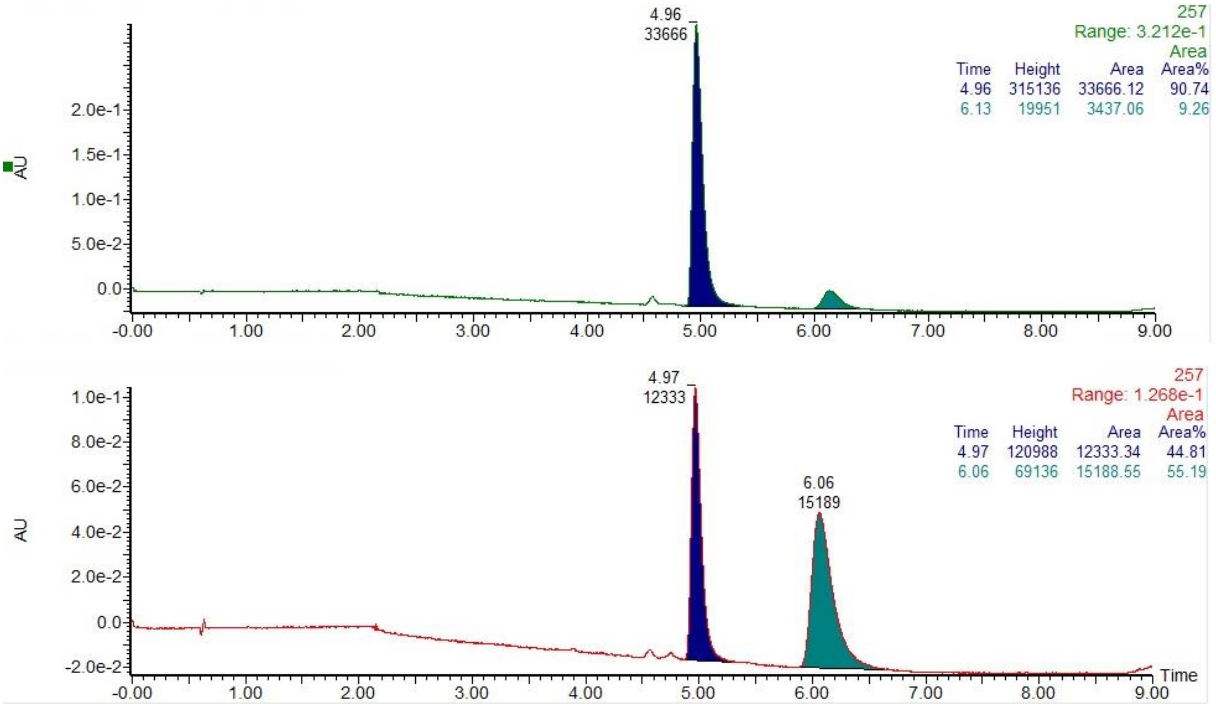
Chemical Formula: $C_{13}H_{23}NO$
Molecular Weight: 209,3330

Following the general procedure **C** using enal **1j** (750 μmol, 135 mg), a mixture containing the β-cyanoaldehyde **2j** (80% NMR yield) and the sulfone by-product **2j'** (> 95% NMR yield) was obtained. The crude target product **2j** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3j** as a pale yellow oil (35.5 mg, 68% yield). Since determination of the d.r. by NMR was not successful due to overlapping signals, the diastereomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 90.5:9.5 by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 257 nm) τ_{Major} = 4.95 min, τ_{Minor} = 6.05 min.

$[\alpha]_D^{25}$ = -4.7 (c = 1.0, $CHCl_3$, 90.5:9.5 d.r.).

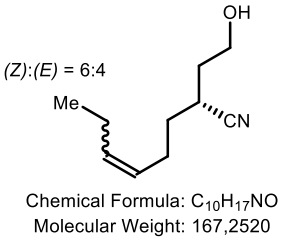
^{1}H NMR (400 MHz, $CDCl_3$, major diastereomer): δ = 5.12 – 5.05 (m, 1H), 3.83 (dd, *J* = 6.6, 5.4 Hz, 2H), 2.96 – 2.82 (m, 1H), 2.07-1.93 (m, 2H), 1.85-1.77 (m, 2H), 1.76 – 1.65 (m, 6H), 1.60 (s, 3H), 1.38 – 1.17 (m, 3H), 0.94 (d, *J* = 6.5 Hz, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, major diastereomer):** δ = 131.8, 124.3, 122.1, 59.8, 39.6, 37.5, 35.6, 30.8, 26.3, 25.8, 25.5, 18.9, 17.8 ppm.

HRMS (APCI): m/z calculated for $[C_{13}H_{24}NO]^+$ $[M+H]^+$: 210.1852; found: 210.1858.



Supplementary Figure 16: UPC^2 traces of **3j.**

(*R*)-2-(2-Hydroxyethyl)oct-5-enenitrile (**3k**)



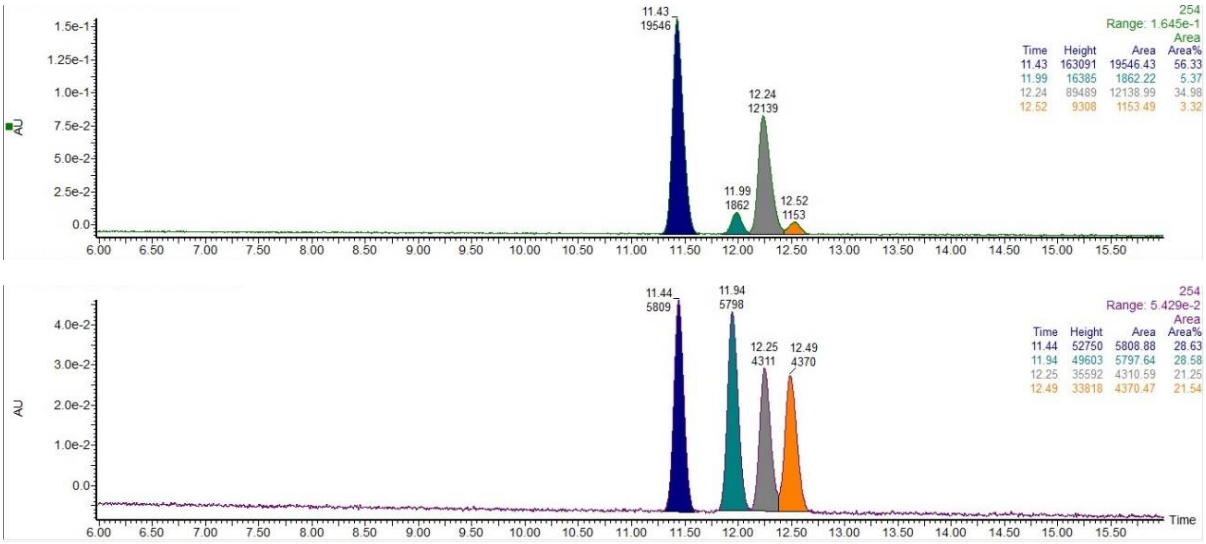
Chemical Formula: $C_{10}H_{17}NO$
Molecular Weight: 167,2520

Following the general procedure **C** using enal **1k** (750 µmol, 104 mg), a mixture containing the β-cyanoaldehyde **2k** (73% NMR yield) and the sulfone by-product **2k'** (32% NMR yield) was obtained. The crude target product **2k** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3k** as a pale yellow oil (21.0 mg, 69% yield, (*Z*):(*E*) = 60:40). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 91.5:8.5 for both double bond isomers by UPC^2 analysis on a Daicel Chiralpak IE-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in MeOH for 14 min, 60% CO_2 in MeOH for 2 min, gradient 60% - 100% CO_2 in MeOH for 1 min; flow rate 2.0 mL/min, λ = 254 nm) (*Z*)-isomer: τ_{Major} = 11.45 min, τ_{Minor} = 12.00 min; (*E*)-isomer: τ_{Major} = 12.25 min, τ_{Minor} = 12.50 min.

$[\alpha]_D^{25}$ = +6.2 (c = 1.0, $CHCl_3$, *E:Z* = 60:40, 91.5:8.5 e.r.).

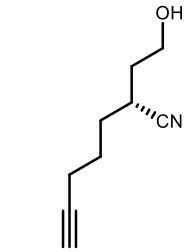
^{1}H NMR (500 MHz, $CDCl_3$, mixture of *E/Z*-isomers): δ = 5.60 – 5.50 (m, 1H, minor), 5.50 – 5.41 (m, 1H, major), 5.35 (td, *J* = 7.7, 6.1 Hz, 1H, minor), 5.30 – 5.22 (m, 1H, major), 3.87 – 3.77 (m, 4H, major & minor), 2.88 – 2.78 (m, 2H, major & minor), 2.32 – 1.93 (m, 8H, major & minor), 1.90-1.80 (m, 4H, major & minor), 1.78 – 1.58 (m, 6H, major and minor), 0.97 (t, *J* = 7.5, 3H, major), 0.96 (t, *J* = 7.5, 3H, minor). **^{13}C NMR (126 MHz, $CDCl_3$, mixture of *E/Z*-isomers):** δ = 134.3, 133.9, 126.7, 126.5, 122.1, 122.0, 59.8, 59.8, 34.9, 34.9, 32.3, 32.2, 30.1, 27.7, 27.6, 25.7, 24.8, 20.7, 14.4, 13.9 ppm.

HRMS (APCI): m/z calculated for $[C_{10}H_{18}NO]^+$ $[M+H]^+$: 168.1383; found: 168.1385.



Supplementary Figure 17: UPC^2 traces of **3k.**

(*R*)-2-(2-Hydroxyethyl)hept-6-ynenitrile (**3l**)



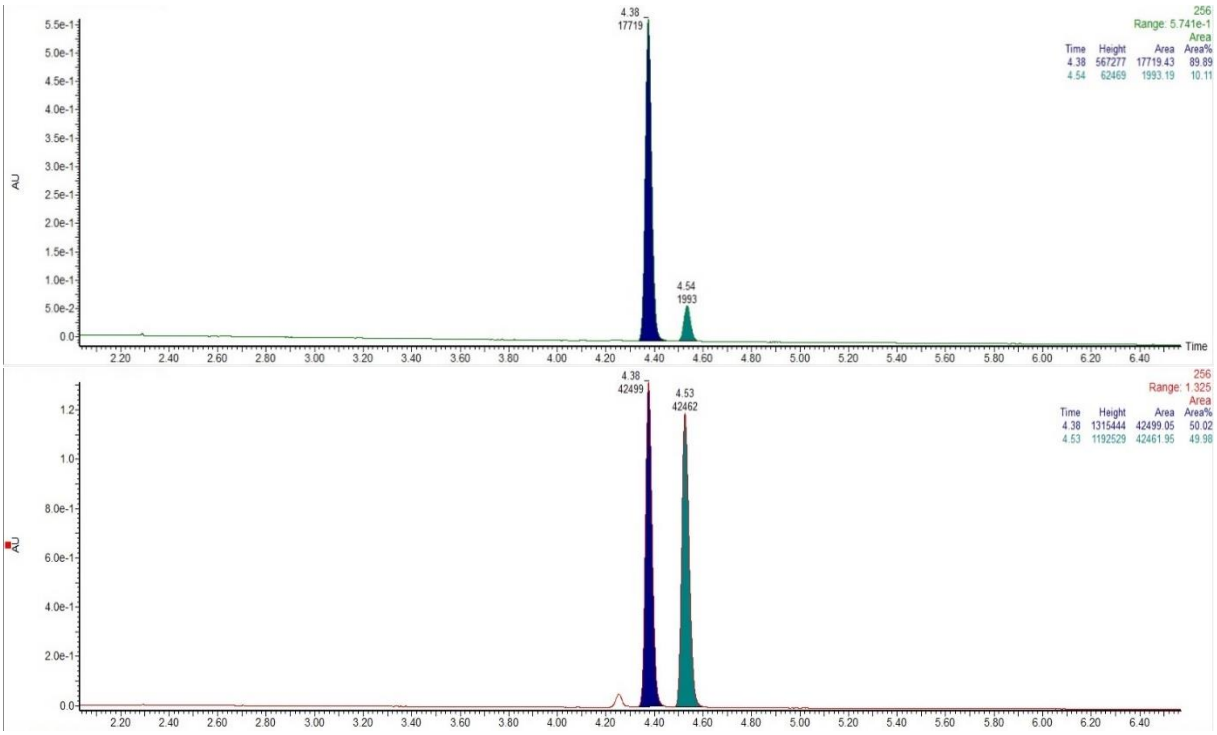
Chemical Formula: $C_9H_{13}NO$
Molecular Weight: 151,2090

Following the general procedure **C** using enal **1l** (750 μmol, 91.5 mg), a mixture containing the β-cyanoaldehyde **2l** (56% NMR yield) and the sulfone by-product **2l'** (41% NMR yield) was obtained. The crude target product **2l** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3l** as a pale yellow oil (21.0 mg, 56% yield). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 90:10 by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in i-PrOH for 5 min, 60% CO_2 in i-PrOH for 2 min, gradient 60% - 100% CO_2 in i-PrOH for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 4.40 min, τ_{Minor} = 4.55 min.

$[\alpha]_D^{25}$ = -51.3 (c = 1.0, $CHCl_3$, 90:10 e.r.).

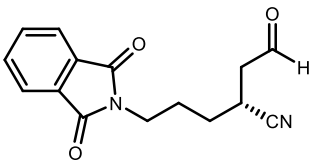
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 – 3.76 (m, 2H), 2.92 – 2.78 (m, 1H), 2.30 – 2.23 (m, 2H), 1.98 (t, *J* = 2.7 Hz, 1H), 1.89 – 1.63 (m, 6H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 121.8, 83.3, 69.4, 59.7, 34.9, 31.2, 27.9, 25.9, 18.1 ppm.

HRMS (APCI): m/z calculated for $[C_9H_{14}NO]^+$ $[M+H]^+$: 152.1070; found: 152.1069.



Supplementary Figure 18: UPC^2 traces of **3l.**

(*R*)-5-(1,3-Dioxoisoindolin-2-yl)-2-(2-oxoethyl)pentanenitrile (**2m**)



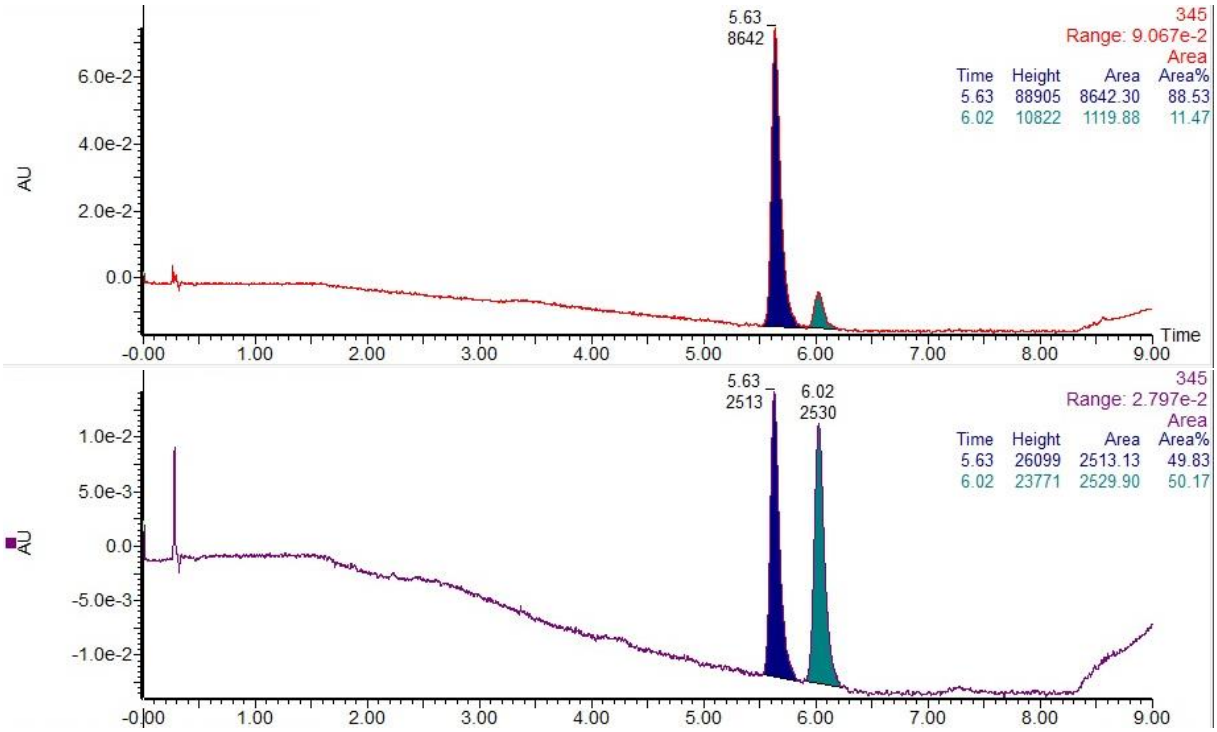
Chemical Formula: $C_{15}H_{14}N_2O_3$
Molecular Weight: 270,2880

Following the general procedure **C** using enal **1m** (750 μmol, 182 mg), a mixture containing the β-cyanoaldehyde **2m** (71% NMR yield) and the sulfone by-product **2m'** (78% NMR yield) was obtained. The crude target product **2m** was purified by flash column chromatography (silica gel, 20-30% ethyl acetate in hexanes). Product containing fractions were loaded on a pad of silica gel, kept to open air and eluted after 16 h with ethylacetate. The filtrate was concentrated and purified by preparative TLC (silica gel, 70% ethylacetate in hexanes) to afford the aldehyde product **2m** as a pale-yellow wax (53.5 mg, 79% yield). The enantiomeric ratio of the corresponding dinitrophenylhydrazone derivative (see **Supplementary Figure 4**) was determined to be 88.5:11.5 by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in i-PrOH for 5 min, 60% CO_2 in i-PrOH for 2 min, gradient 60% - 100% CO_2 in i-PrOH for 1 min; flow rate 2.0 mL/min) λ = 345 nm, τ_{Major} = 5.65 min, τ_{Minor} = 6.00 min.

$[\alpha]_D^{25}$ = +3.3 (c = 1.0, $CHCl_3$, 88.5:11.5 e.r.).

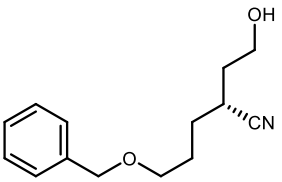
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.74 (s, 1H), 7.84 (dd, *J* = 5.5, 3.0 Hz, 2H), 7.72 (dd, *J* = 5.4, 3.1 Hz, 2H), 3.74 (t, *J* = 6.8 Hz, 2H), 3.22 – 3.12 (m, 1H), 2.90 (ddd, *J* = 18.6, 7.0, 0.7 Hz, 1H), 2.74 (ddd, *J* = 18.6, 6.4, 0.7 Hz, 1H), 2.03 – 1.90 (m, 1H), 1.90 – 1.79 (m, 1H), 1.76 – 1.58 (m, 2H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 196.9, 168.5 (2C), 134.2 (2C), 132.1 (2C), 123.5 (2C), 120.6, 45.5, 36.9, 29.2, 26.4, 24.5 ppm.

HRMS (ESI): m/z calculated for $[C_{15}H_{14}N_2NaO_3]^+$ [M+Na]$^+$: 293.0897; found: 293.0895.



Supplementary Figure 19: UPC^2 traces of **2m.**

(*R*)-5-(Benzyloxy)-2-(2-hydroxyethyl)pentanenitrile (**3n**)



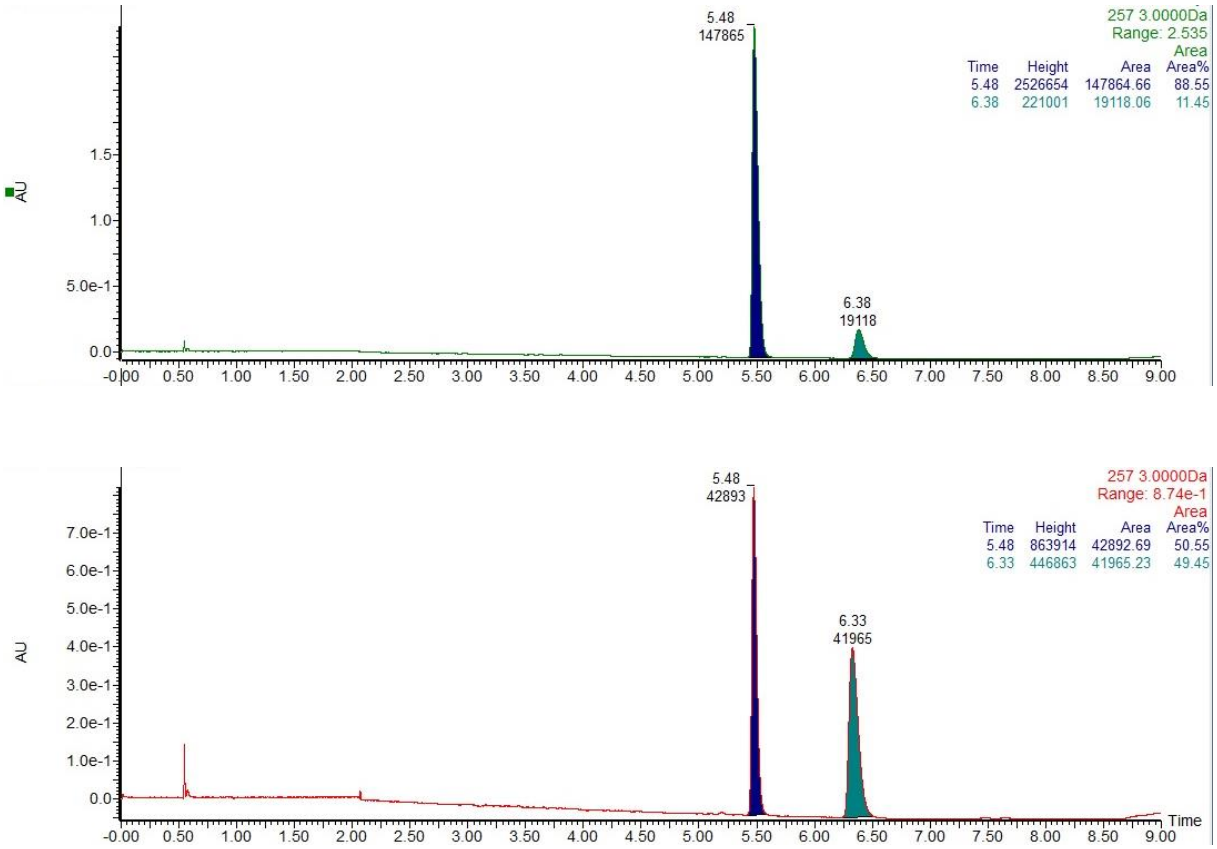
Chemical Formula: $C_{14}H_{19}NO_2$
Molecular Weight: 233,3110

Following the general procedure **C** using enal **1n** (750 μmol, 153 mg), a mixture containing the β-cyanoaldehyde **2n** (55% NMR yield) and the sulfone by-product **2n'** (72% NMR yield) was obtained. The crude target product **2n** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford product **3n** as a pale-yellow oil (30.0 mg, 52% yield). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 88.5:11.5 by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min) λ = 257 nm, τ_{Major} = 5.50 min, τ_{Minor} = 6.40 min.

$[\alpha]_D^{25}$ = +0.1 (c = 1.0, $CHCl_3$, 88.5:11.5 e.r.).

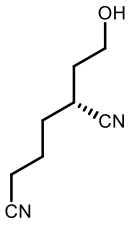
^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40 – 7.23 (m, 5H), 4.50 (s, 2H), 3.85 – 3.75 (m, 2H), 3.57 – 3.47 (m, 2H), 2.89 – 2.78 (m, 1H), 1.97 – 1.60 (m, 6H), 1.52 (t, *J* = 4.9 Hz, OH) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 138.4, 128.6 (2C), 127.8 (2C), 127.8, 122.1, 73.1, 69.3, 59.7, 34.9, 29.3, 28.0, 27.4 ppm.

HRMS (APCI): m/z calculated for $[C_{14}H_{20}NO_2]^+$ $[M+H]^+$: 234.1489; found: 234.1493.



Supplementary Figure 20: UPC^2 traces of **3n.**

(*R*)-2-(2-Hydroxyethyl)hexanedinitrile (**3o**)



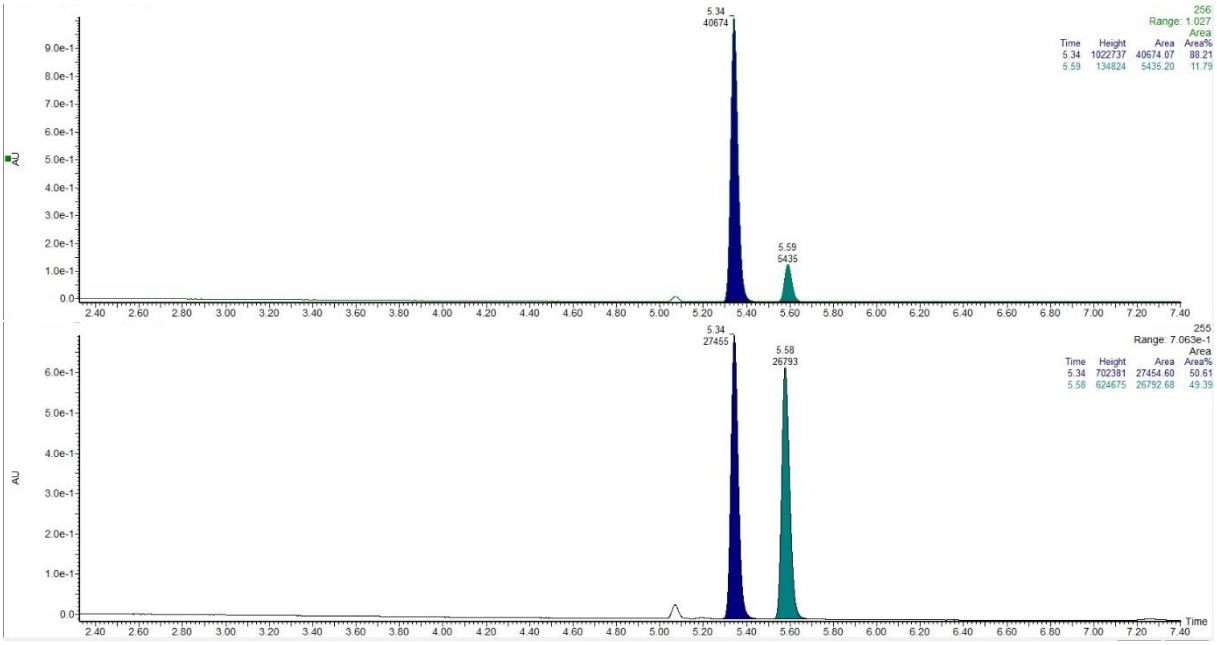
Chemical Formula: $C_8H_{12}N_2O$
Molecular Weight: 152,1970

Following the general procedure **C** using enal **1o** (750 µmol, 92.5 mg), a mixture containing the β-cyanoaldehyde **2o** (60% NMR yield) and the sulfone by-product **2o'** (75% NMR yield) was obtained. The crude target product **2o** was reduced according to the general procedure **D** and the desired alcohol was purified by flash column chromatography (silica gel, 40-50% ethyl acetate in hexanes). Product-containing fractions were combined and purified by preparative TLC (silica gel, 100% ethylacetate) to afford product **3o** as a pale yellow oil (17.0 mg, 44% yield). The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative was determined to be 88:12 by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in i-PrOH for 5 min, 60% CO_2 in i-PrOH for 2 min, gradient 60% - 100% CO_2 in i-PrOH for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 5.35 min, τ_{Minor} = 5.60 min.

$[\alpha]_D^{25}$ = -55.8 (c = 0.5, $CHCl_3$, 88:12 e.r.).

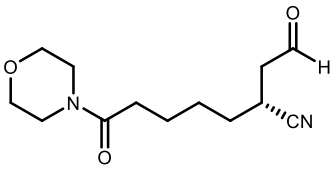
^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.91 – 3.76 (m, 2H), 2.96 – 2.84 (m, 1H), 2.51 – 2.41 (m, 2H), 1.97 – 1.74 (m, 6H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 121.3, 118.9, 59.4, 34.7, 31.1, 27.8, 23.2, 17.0 ppm.

HRMS (APCI): m/z calculated for $[C_8H_{13}N_2O]^+$ $[M+H]^+$: 153.1022; found: 153.1022.



Supplementary Figure 21: UPC^2 traces of **3o.**

(*R*)-7-Morpholino-7-oxo-2-(2-oxoethyl)heptanenitrile (**2p**)



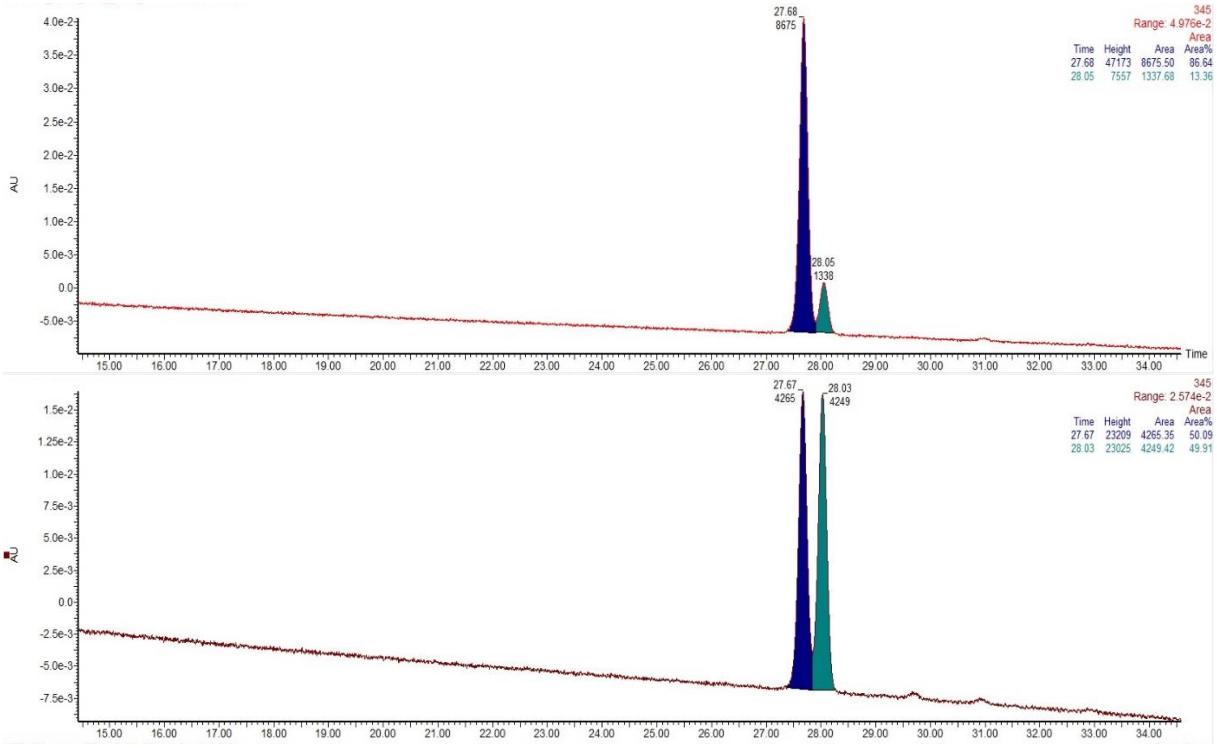
Chemical Formula: $C_{13}H_{20}N_2O_3$
Molecular Weight: 252,3140

Following the general procedure **C** using enal **1p** (750 µmol, 169 mg), a mixture containing the β-cyanoaldehyde **2p** (64% NMR yield) and the sulfone by-product **2p'** (86% NMR yield) was obtained. The crude target product **2p** was purified by flash column chromatography (silica gel, 1% MeOH in DCM). The product-containing fractions were combined and loaded on another column chromatography (silica gel, 100% ethylacetate). After 16 h, the product was eluted with ethylacetate to afford the aldehyde product **2p** as a pale yellow oil (41.0 mg, 65% yield). The enantiomeric ratio of the corresponding dinitrophenylhydrazone derivative (**Supplementary Figure 4**) was determined to be 86.5:13.5 by UPC^2 analysis on a Daicel Chiralpak IB-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 70% CO_2 in EtOH for 34 min, 70% CO_2 in EtOH for 2 min, gradient 70% - 100% CO_2 in EtOH for 1 min; flow rate 2.0 mL/min, λ = 345 nm) τ_{Major} = 27.70 min, τ_{Minor} = 28.05 min.

$[\alpha]_D^{25}$ = +2.4 (c = 1.0, $CHCl_3$, 86.5:13.5 e.r.).

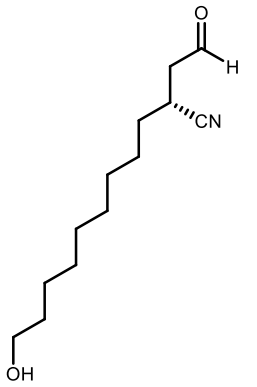
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.75 (s, 1H), 3.70 – 3.63 (m, 4H), 3.63 – 3.57 (m, 2H), 3.45 (t, *J* = 4.9 Hz, 2H), 3.14 – 3.04 (m, 1H), 2.90 (ddd, *J* = 18.6, 6.9, 0.7 Hz, 1H), 2.75 (ddd, *J* = 18.6, 6.5, 0.7 Hz, 1H), 2.33 (t, *J* = 7.2 Hz, 2H), 1.76 – 1.45 (m, 6H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 197.2, 171.1, 121.0, 67.0, 66.7, 46.0, 45.6, 42.1, 32.6, 31.7, 26.9, 24.7, 24.4 ppm.

HRMS (ESI): m/z calculated for $[C_{13}H_{20}N_2NaO_3]^+$ $[M+Na]^+$: 275.1366; found: 275.1365.



Supplementary Figure 22: UPC^2 traces of **2p.**

(*R*)-11-Hydroxy-2-(2-oxoethyl)undecanenitrile (**2q**)



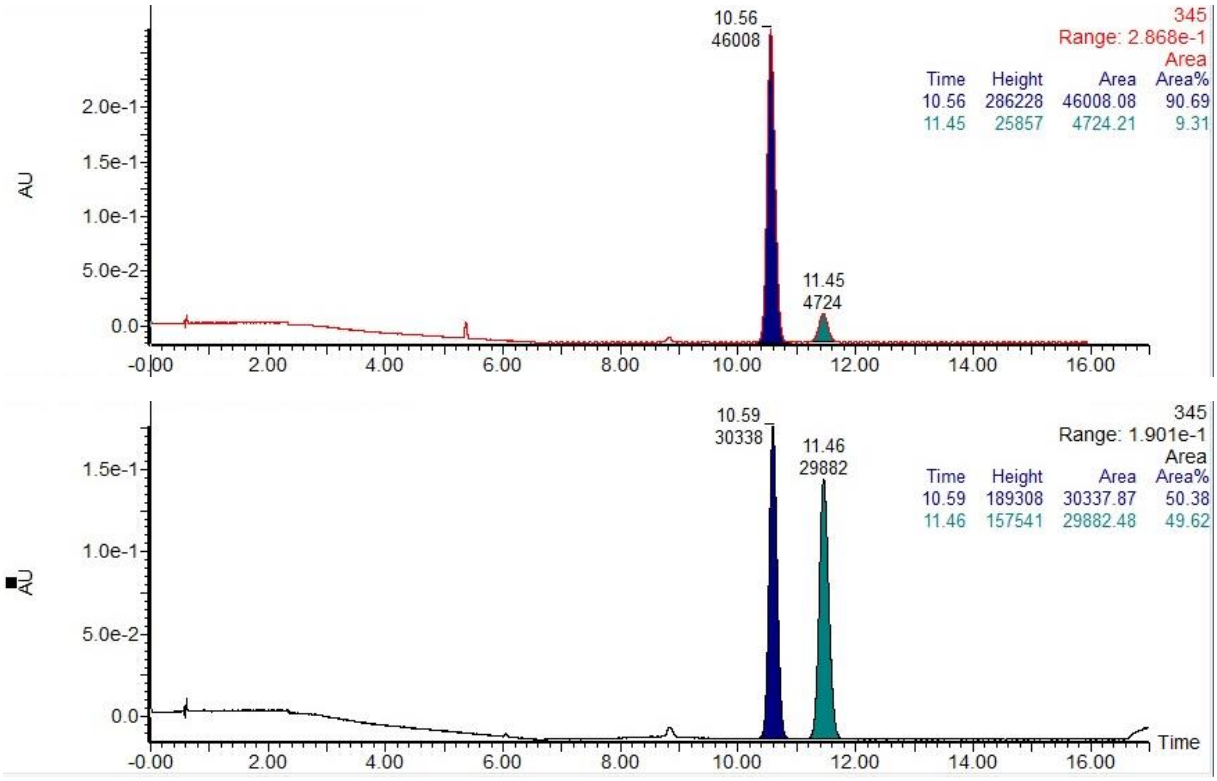
Chemical Formula: $C_{13}H_{23}NO_2$
Molecular Weight: 225,3320

Following the general procedure **C** using enal **1q** (750 μmol, 149 mg), a mixture containing the β-cyanoaldehyde **2q** (47% NMR yield) and the sulfone by-product **2q'** (75% NMR yield) was obtained. The crude target product **2q** was loaded on column chromatography (silica gel, 20% ethyl acetate in hexanes). After 3 days, the product was eluted (20-30% ethylacetate in hexanes). Product-containing fractions were combined, concentrated and purification by chromatography was repeated as described above to afford the aldehyde product **2q** as a pale yellow oil (25.5 mg, 46% yield). The enantiomeric ratio of the corresponding dinitrophenylhydrazone derivative (**Supplementary Figure 4**) was determined to be 90.5:9.5 by UPC^2 analysis on a Daicel Chiralpak IE-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in EtOH for 5 min, 60% CO_2 in EtOH for 10 min, gradient 60% - 100% CO_2 in EtOH for 1 min; flow rate 2.0 mL/min, λ = 345 nm) τ_{Major} = 10.55 min, τ_{Minor} = 11.45 min. Note: This compound was found unstable and decomposed upon storage at -20 °C for several months.

$[\alpha]_D^{25}$ = -32.4 (c = 0.5, $CHCl_3$, 90.5:9.5 e.r.).

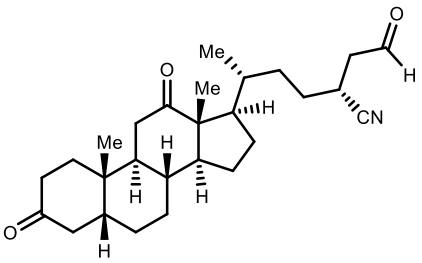
^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.77 (s, 1H), 3.63 (t, *J* = 6.6 Hz, 2H), 3.13 – 3.02 (m, 1H), 2.90 (dd, *J* = 18.5, 6.9 Hz, 1H), 2.73 (dd, *J* = 18.5, 6.5 Hz, 1H), 1.67 – 1.19 (m, 17H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 197.3, 121.2, 63.2, 45.7, 32.9, 31.9, 29.5, 29.4, 29.3, 29.0, 27.1, 25.8, 24.9 ppm.

HRMS (ESI): m/z calculated for $[C_{13}H_{23}NNaO_2]^+$ $[M+Na]^+$: 248.1621; found: 248.1624.



Supplementary Figure 23: UPC^2 traces of **2q**.

(*2R,5R*)-5-((*5R,8R,9S,10S,13R,14S,17R*)-10,13-Dimethyl-3,12-dioxohexadecahydro-1H-cyclopenta[a]phenanthren-17-yl)-2-(2-oxoethyl)hexanenitrile (**2r**)



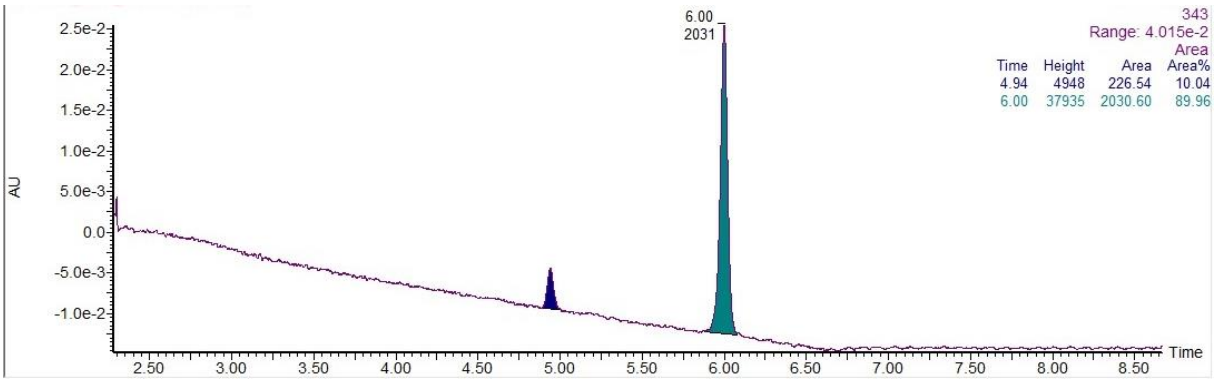
Chemical Formula: $C_{27}H_{39}NO_3$
Molecular Weight: 425,6130

Tosyl cyanide (1.0 equiv., 19.0 mg, 100 μmol, 95%), **2r** (2.0 equiv., 79.5 mg, 200 μmol), dihydropyridine **R-1** (1.2 eq, 39.0 mg, 120 μmol), aminocatalyst **A-4** (0.3 equiv., 31.1 mg, 30.0 μmol) and 4-CzlPN (1 mol%, 790 μg, 1.00 μmol) were loaded in a reaction vial and the vessel was sealed with a septum and flushed with argon. Then, ethylacetate (200 μL), water (3.0 equiv., 5.41 μL) and TFA (0.4 equiv., 2.97 μL, 40.0 μmol) was added and the vial was immediately placed in a cooling block (set to 5 °C internal temperature) and irradiated with 460 nm (90 mW/cm^2) for 16 hours. The crude mixture, containing β-cyanoaldehyde **2r** (44% NMRy) and sulfone by-product **2r'** (83% NMRy) was concentrated and loaded on column chromatography (silica gel, 15% ethyl acetate in hexanes). After 16 h being absorbed on the silica gel (in order to decompose unstable and inseparable sulfone by-product **2r'**), the product was eluted (15-30% ethylacetate in hexanes). The product-containing fractions were combined, concentrated and column chromatography was repeated as described above to afford the aldehyde product **2r** as a white solid (42.5 mg, 42% yield). Although no minor diaseteroisomer could be observed by NMR analysis, we conducted chiral chromatographic analysis of the the corresponding dinitrophenylhydrazone derivative to reveal a d.r. of 90:10 by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in MeOH for 5 min, 60% CO_2 in MeOH for 2 min, gradient 60% - 100% CO_2 in MeOH for 1 min; flow rate 2.0 mL/min, λ = 343 nm) τ_{Major} = 6.00 min, τ_{Minor} = 4.95 min.

$[\alpha]_D^{25}$ = +56.1 (c = 0.5, $CHCl_3$, 90:10 d.r.).

^{1}H NMR (400 MHz, $CDCl_3$, major diastereoisomer): δ = 9.77 (s, 1H), 3.13 – 3.01 (m, 1H), 2.92 (ddd, *J* = 18.6, 6.9, 0.7 Hz, 1H), 2.74 (ddd, *J* = 18.6, 6.6, 0.8 Hz, 1H), 2.67 – 2.52 (m, 2H), 2.34 (td, *J* = 14.6, 5.3 Hz, 1H), 2.23 – 2.14 (m, 1H), 2.13-1.27 (m, 21H), 1.19-1.07 (m, 1H), 1.11 (s, 3H), 1.06 (s, 3H), 0.86 (d, *J* = 7.3 Hz, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, major diastereoisomer):** δ = 214.3, 212.2, 197.3, 121.1, 58.7, 57.7, 46.4, 45.9, 44.4, 43.8, 42.3, 38.5, 37.1, 36.9, 35.8, 35.6, 35.3, 32.6, 28.7, 27.7, 26.7, 25.6, 24.9, 24.4, 22.3, 18.8, 11.9. ppm.

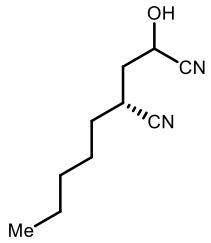
HRMS (ESI): m/z calculated for $[C_{28}H_{43}NNaO_4]^+$ [M+MeOH+Na]$^+$: 480.3084; found: 480.3093.



Supplementary Figure 24: UPC^2 trace of **2r** (diastereoisomer).

Further Derivatization of Cyanoaldehyde 2a

(*4R*)-2-Hydroxy-4-pentylpentanedinitrile (**4a**)



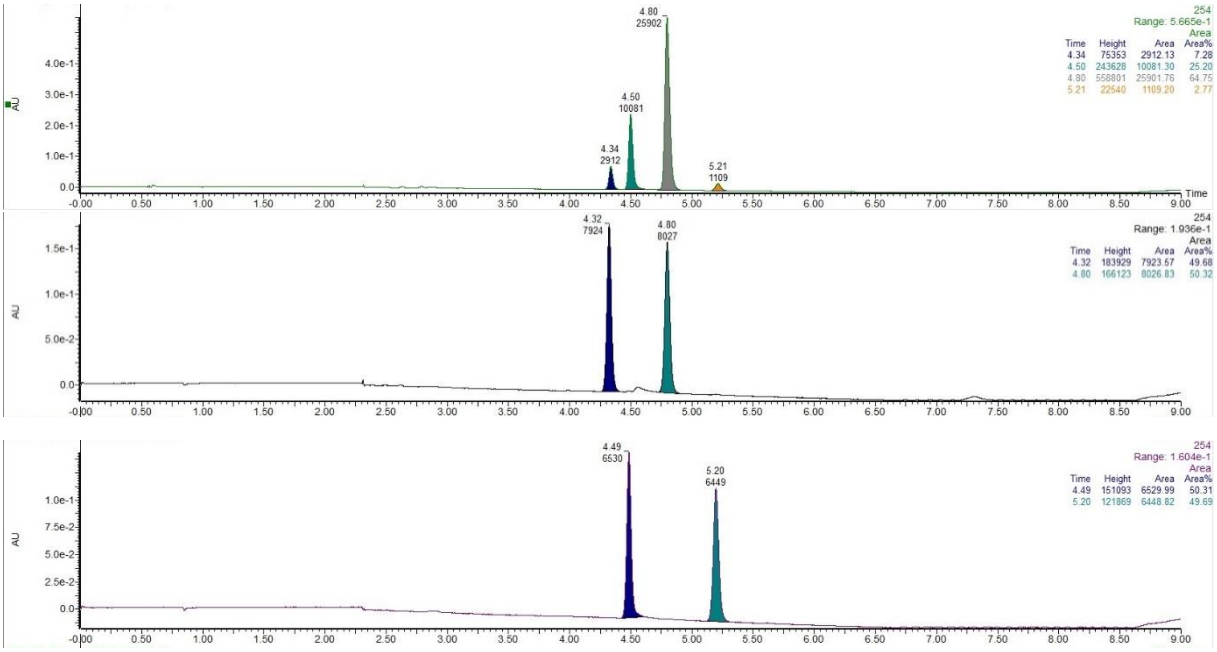
Chemical Formula: $C_{10}H_{16}N_2O$
Molecular Weight: 180,2510

Following the general procedure **C** using enal **1a** (750 µmol, 94.5 mg), the crude mixture containing cyanoaldehyde **2a** was used without purification (evaporation of the solvent, *one-pot approach*). A solution of $NaHSO_3$ (104 mg, 1.00 mmol, 4.0 equiv.) in water (0.5 mL) was added to the crude product and the mixture was cooled to 0 °C. Then, a solution of KCN (130 mg, 2.00 mmol, 8.0 equiv.) in water (1.0 mL) was added dropwise and stirred for 10 minutes at 0 °C. DCM (1.5 mL) was added and the mixture was stirred vigorously at room temperature under open air. The mixture was transferred to a separation funnel and extracted with DCM (3 x 20 mL). The combined layers were dried with $MgSO_4$ and concentrated. Column chromatography (silica gel, 5-8% ethyl acetate in hexanes) afforded 31.0 mg (69% yield over 2 steps) of cyanohydrine **4a** as a diastereomeric mixture of 66:34. The enantiomeric ratios of the corresponding 4-nitrobenzoate derivatives were determined to be 90:10 (for both diastereoisomers) by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in MeOH for 5 min, 60% CO_2 in MeOH for 2 min, gradient 60% - 100% CO_2 in MeOH for 1 min; flow rate 2.0 mL/min, λ = 254 nm) Major diastereoisomer: τ_{Major} = 4.80 min, τ_{Minor} = 4.35 min, Minor diastereoisomer: τ_{Major} = 4.50 min, τ_{Minor} = 5.20 min. Racemic material could be obtained as diastereopure samples (see UPC^2 traces below).

$[\alpha]_D^{25}$ = -143.2 (c = 0.5, $CHCl_3$, 66:34 d.r., 90:10 e.r.).

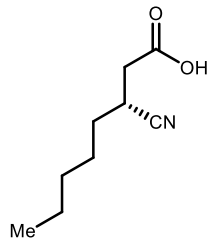
^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 4.78 – 4.64 (m, 2H, major & minor), 3.24 – 2.98 (br m, 2 OH, major & minor), 2.93 (ddt, *J* = 10.3, 8.9, 5.4 Hz, 1H, major), 2.86 – 2.70 (m, 1H, minor), 2.29 – 2.04 (m, 4H, major & minor), 1.75 – 1.28 (m, 16H, major & minor), 0.91 (t, *J* = 6.9 Hz, 6H, major & minor). **^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 120.8 (2C), 119.0, 118.8, 59.5, 58.5, 37.4, 37.4, 32.1, 32.1, 31.2 (2C), 27.9, 27.7, 26.8, 26.7, 22.5 (2C), 14.0 (2C) ppm.

HRMS (APCI): m/z calculated for $[C_{10}H_{17}N_2O]^+$ $[M+H]^+$: 181.1335; found: 181.1331.



Supplementary Figure 25: UPC^2 traces of **4a.**

(*R*)-3-Cyanooctanoic acid (**4b**)

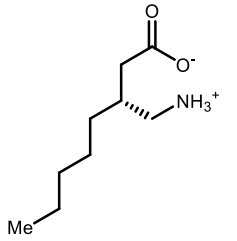


Chemical Formula: $C_9H_{15}NO_2$
Molecular Weight: 169,2240

Following the general procedure **C** using enal **1a** (750 µmol, 94.5 mg), the crude mixture containing cyanoaldehyde **2a** was used without purification (evaporation of the solvent, *one-pot approach*). The crude mixture was redissolved in t-BuOH (8.0 mL) and 2-methylbut-1-ene (808 µL, 7.50 mmol, 30 equiv.) was added. Then, a solution of $NaClO_2$ (271 mg, 3.00 mmol, 12 equiv.) and NaH_2PO_4 (300 mg, 2.50 mmol, 10 equiv.) in water (3.0 mL) was added dropwise and the mixture was stirred for 2 hours at room temperature. The mixture was diluted with water (30 mL), acidified to pH = 3 by use of aqueous HCl (1.0 M) and extracted with DCM (3 x 30 mL). The combined organic layers were dried with $MgSO_4$, concentrated and the product was purified by column chromatography (silica gel, 8-15% EtOAc in hexanes with 1% AcOH). The pyridine containing product was again separated by column chromatography (silica gel, 10-15% EtOAc in hexanes for elution of pyridine followed by 1% AcOH in EtOAc for elution of product) to obtain 26.0 mg (62%) of the desired cyanoacid **4b** as bright yellow oil. NMR data was found to be in agreement with the literature.[28]

^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.06 – 2.94 (m, 1H), 2.77 (dd, *J* = 17.1, 7.7 Hz, 1H), 2.62 (dd, *J* = 17.1, 6.6 Hz, 1H), 1.73 – 1.21 (m, 8H), 0.91 (t, *J* = 6.8 Hz, 3H) ppm.

(*R*)-3-(Aminomethyl)octanoic acid (**4c**)



Chemical Formula: $C_9H_{19}NO_2$
Molecular Weight: 173,2560

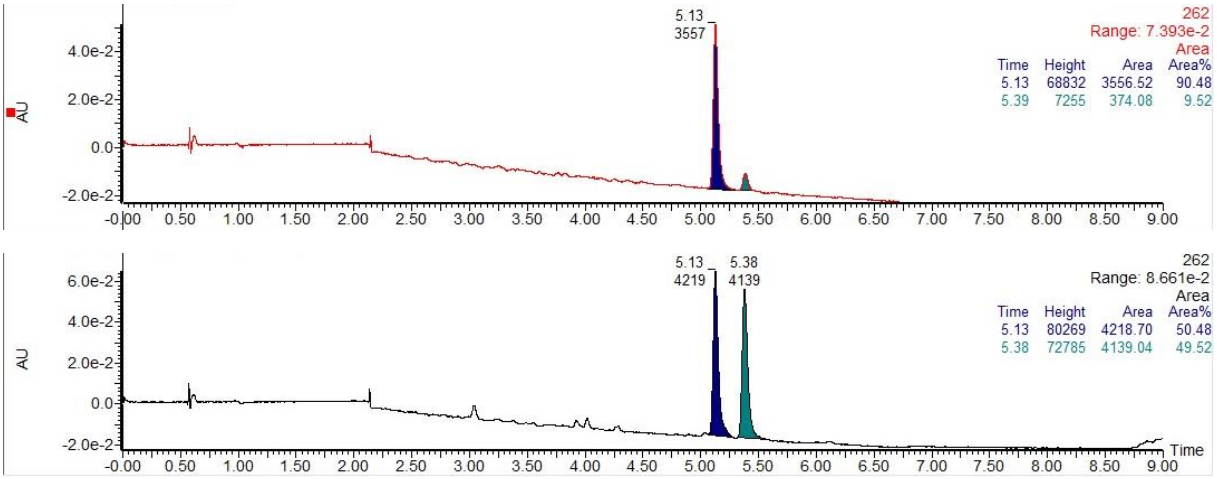
Cyanoacid **4b** (26.1 mg, 154 µmol) was dissolved in MeOH (100 mL, HPLC grade and the solution was subjected to hydrogenation using a H-Cube pro apparatus (conditions: new Pd/C cartridge, 70 °C, 50 bar H_2, 1.0 mL/min). The apparatus was flushed with MeOH (3 x 20 mL) and the combined fractions were concentrated to afford 24.5 mg (91%) of aminoacid **4c** as off-white semi-solid without need for further purification.

Determination of e.r.: 1.00 mg of **4c** was dissolved in MeOH (1 mL) and TMS-diazomethane (2M in diethylether, 0.3 mL) was added. After 5 minutes, the mixture was dried under reduced pressure, and the methylester was re-dissolved in $CHCl_3$ (0.2 mL) and 4-NO_2-benzoyl chloride (5.0 equiv.) and DMAP (5.0 equiv.) were added. After stirring for 1 h, the amide was isolated by preparative TLC (20% EtOAc in hexanes) and the enantiomeric ratio was determined to be 90.5:9.5 by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 262 nm, τ_{Major} = 5.15 min, τ_{Minor} = 5.40 min.

$[\alpha]_D^{25}$ = -97.6 (c = 0.5, MeOH, 90.5:9.5 e.r.).

^{1}H NMR (400 MHz, CD_3OD) δ = 2.98 (dd, *J* = 12.8, 4.7 Hz, 1H), 2.90 (dd, *J* = 12.8, 7.5 Hz, 1H), 2.45 (dd, *J* = 16.0, 4.4 Hz, 1H), 2.33 (dd, *J* = 16.0, 8.0 Hz, 1H), 2.08 – 1.98 (m, 1H), 1.43 – 1.26 (m, 8H), 0.92 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR (101 MHz, CD_3OD)** δ = 179.0, 45.1, 41.0, 35.3, 33.4, 33.0, 27.4, 23.6, 14.4 ppm.

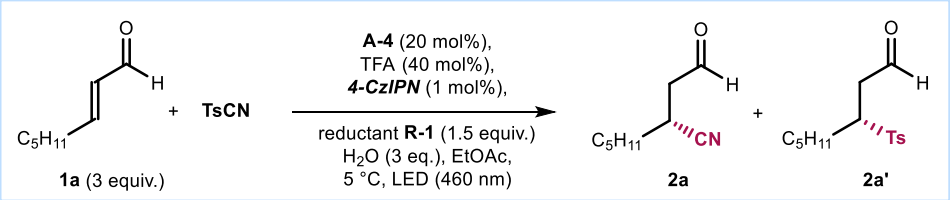
HRMS (ESI): m/z calculated for $[C_9H_{20}NO_2]^+$ $[M+H]^+$: 174.1489; found: 174.1496.



Supplementary Figure 26: UPC^2 traces of **4c.**

Characterization of the β-Sulfone Aldehyde 2a' (byproduct)

Due to the inseparability of the aldehydic reaction products **2a** and **2a'**, a clean mixture was obtained upon reduction to alcohols **3** and column chromatography purification, as described below.



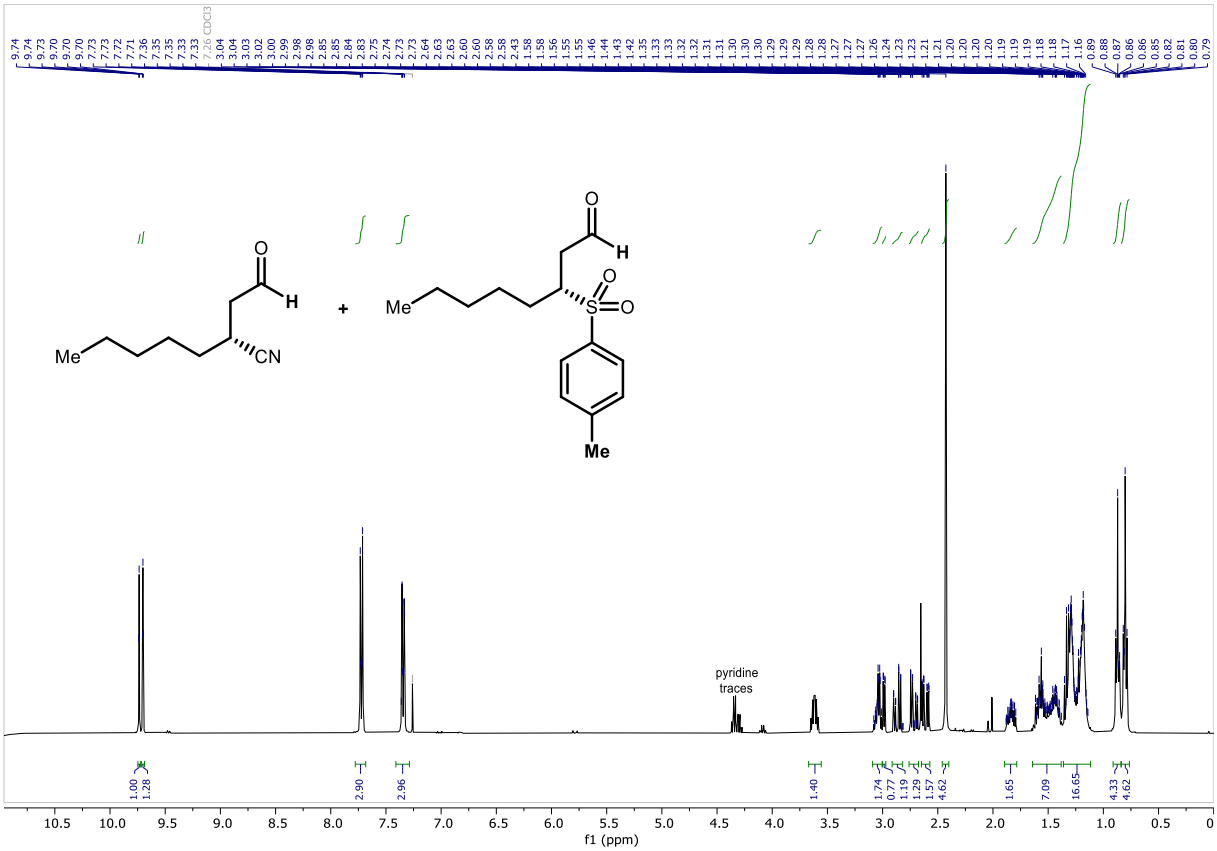
Following the general procedure **C** using enal **1a** (750 µmol, 94.5 mg), the crude product was purified by flash column chromatography (silica gel, $CHCl_3$) to afford 38.0 mg of an inseparable mixture of **2a** and **2a'** (and traces of pyridine byproduct). Isolated peaks in ^{1}H NMR are as following:

Characteristic peaks of **2a**:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.74 (bs, 1H), 3.08 – 3.01 (m, 1H), 2.87 (ddd, *J* = 18.5, 7.1, 0.7 Hz, 1H), 2.71 (ddd, *J* = 18.6, 6.4, 0.8 Hz, 1H), 0.87 (t, *J* = 7.0 Hz, 3H), ppm.

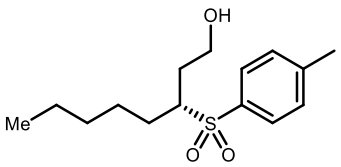
Characteristic peaks of **2a'**:

^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.70 (t, *J* = 1.2 Hz, 1H), 7.72 (d, *J* = 8.3 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 3.66-3.57 (m, 1H), 3.00 (ddd, *J* = 18.3, 5.9, 1.4 Hz, 1H), 2.61 (ddd, *J* = 18.3, 6.1, 0.9 Hz, 1H), 2.43 (s, 3H), 0.80 (t, *J* = 6.7 Hz, 3H) ppm.



Supplementary Figure 27: Mixture of β-cyano aldehyde **2a** and β-sulfone aldehyde **2a'** (400 MHz).

Upon reduction of the crude mixture obtained with enal **1a**, the alcohol derivatives of **2a** and **2a'** could be separated readily by column chromatography. This allowed us to isolate and characterise the sulfonyl-alcohol by-product **3a'**:



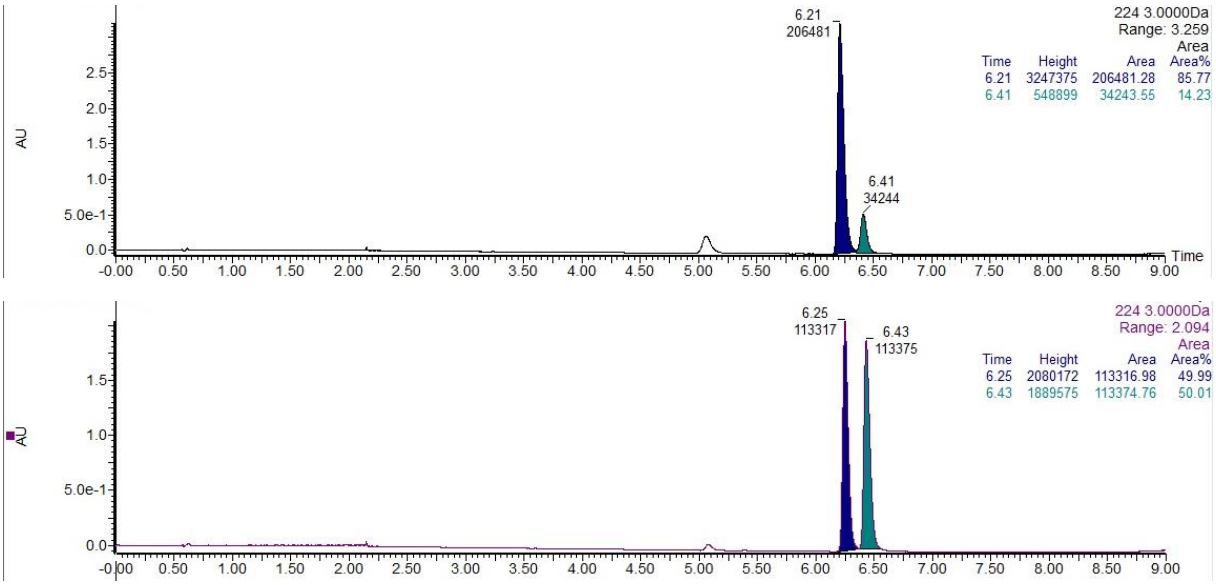
Chemical Formula: $C_{15}H_{24}O_3S$
Molecular Weight: 284,4140

3-Tosyloctan-1-ol (**3a'**). A 8.0 mL vial equipped with a stirring bar was charged with tosyl cyanide (19.1 mg, 100 µmol, 95% purity, 1.0 equiv.), **A-3** (14.0 mg, 20.0 µmol, 0.2 equiv.), **R-1** (49.0 mg, 150 µmol, 1.5 equiv.), 4-CzIPN (1.00 mg, 1.00 µmol, 1 mol%) and octenal **1a** (44.8 µL, 300 µmol, 3.0 equiv.). The vial was sealed with a septum and purged with Argon. The reactants were suspended in EtOAc (200 µL, ensure that all compounds are suspended) and deionized water (5.4 µL, 3.0 equiv.) was added. Then, TFA (2.23 µL, 30 µmol, 0.3 equiv.) was added and the vial was instantly placed in a pre-cooled metal block (set for an internal temperature of -10 °C) and irradiated with a high-power single LED (460 nm, irradiance 90 mW/cm^2). After 16 hours the mixture was concentrated under reduced pressure. The residue was dissolved in THF (0.40 mL) and then water (0.10 mL) was added. After cooling to 0 °C with an ice bath, $NaBH_4$ (37.8 mg, 1.00 mmol, 10 equiv.) was added in a few portions while rigorous stirring. After 10 minutes, the ice bath was removed and the mixture was stirred for 90 minutes at ambient temperature. After cooling to 0 °C with an ice bath, the slurry was quenched dropwise with 1 N HCl until gas evolution ceased. The mixture was transferred to a separation funnel and extracted with DCM (3 x 20 mL). The desired alcohol were purified by flash column chromatography (silica gel, 15-20% ethyl acetate in hexanes) to afford 20.0 mg (70%) of sulfone alcohol **3a'** as a pale-yellow oil. The enantiomeric ratio of the corresponding 4-nitrobenzoate (prepared in anaolgy to the general procedure for derivatization of β-cyanoalcohols) was determined to be 86:14 by UPC^2 analysis on a Daicel Chiralpak IE-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 224 nm) τ_{Major} = 6.20 min, τ_{Minor} = 6.40 min.

$[\alpha]_D^{25}$ = -3.2 (c = 1.0, $CHCl_3$, 86:14 e.r.).

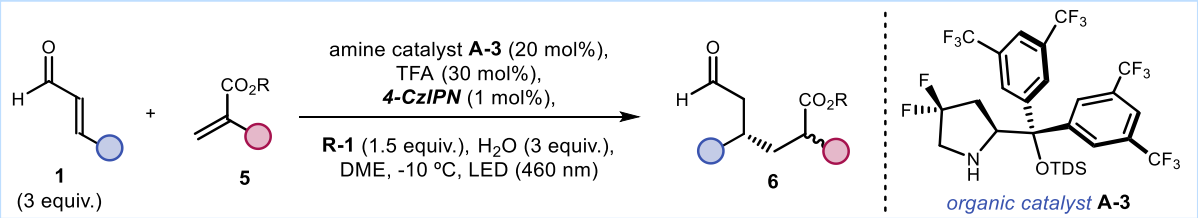
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 8.2 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 3.90 – 3.80 (m, 1H), 3.75 – 3.65 (m, 1H), 3.19 – 3.08 (m, 1H), 2.45 (s, 3H), 2.15 – 2.02 (m, 2H), 1.92 – 1.73 (m, 2H), 1.54 – 1.35 (m, 2H), 1.32 – 1.13 (m, 4H), 0.83 (t, *J* = 6.9 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$)** δ = 144.8, 134.7 (2C), 129.9 (2C), 129.1, 62.0, 60.0, 31.6, 31.0, 28.7, 26.4, 22.4, 21.8, 14.0 ppm.

HRMS (ESI): m/z calculated for $[C_{15}H_{25}O_3S]^+$ $[M+H]^+$: 285.1519; found: 285.1523.



Supplementary Figure 28: UPC^2 traces of **3a'**

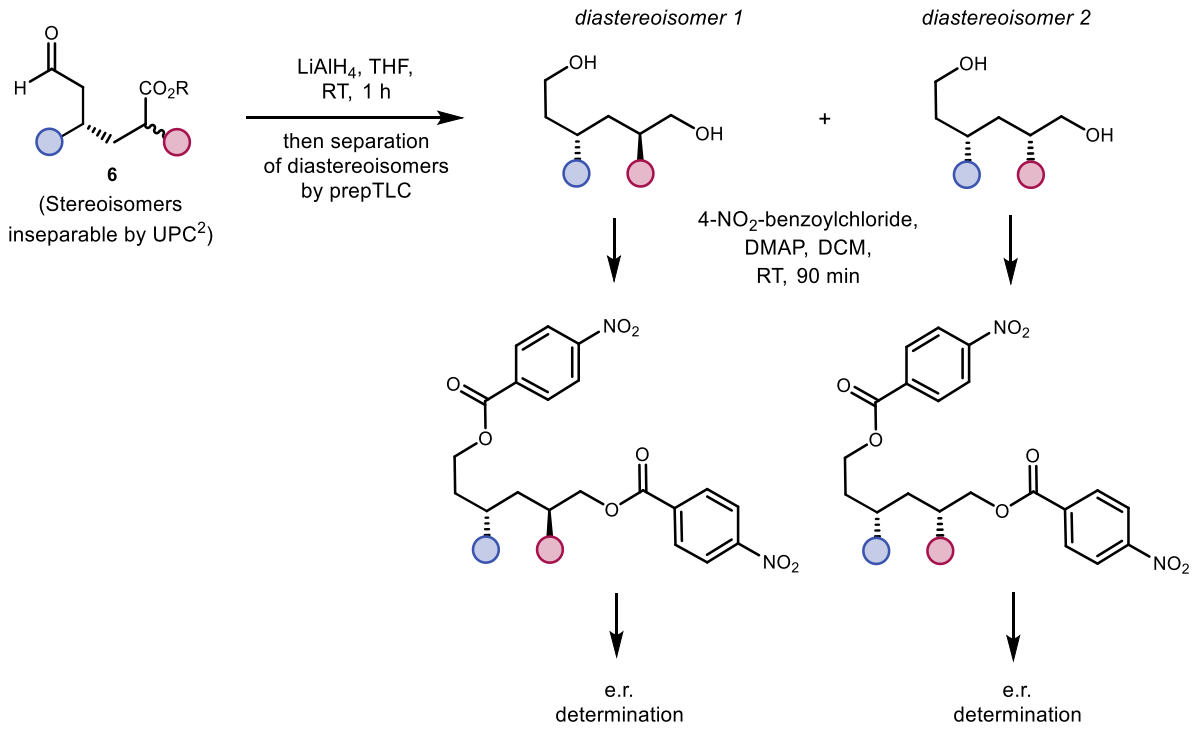
General Procedure for the Cross-Electrophile Coupling of Enals and Acrylates



General Procedure E (*for 0.25 mmol scale*): To a 8.0 mL argon-purged glass vial, containing the acrylate **5** (1.0 equiv.), enal **1** (3.0 equiv.), DHP **R-1** (375 µmol, 1.5 equiv.), 4-CzIPN (2.50 µmol, 1 mol%) and amine catalyst **A-3** (50.0 µmol, 20 mol%), was added 500 µL of dimethoxyethane, H_2O (2.50 mmol, 10 equiv.) and TFA (75.0 µmol, 30 mol%). The vial was sealed with Parafilm, and then placed into a cooled aluminium support mounted on an aluminium block fitted with a 460 nm high-power single LED (λ = 460 nm, irradiance = 90 mW/cm^2, as controlled by an external power supply; the set-up is detailed in **Supplementary Figure 1**). This set-up secured a reliable irradiation while keeping a constant distance of 1 cm between the reaction vessel and the light source. The reaction was stirred under visible light irradiation at -10 °C internal temperature for 16 hours. Then the solvent was evaporated, and the crude mixture was purified by column chromatography on silica gel to furnish product **6** in the stated yield and enantiomeric purity. Diastereomeric ratio was determined by ^{1}H NMR analysis of the crude mixture. The light source for illuminating the reaction vessel consisted in a 460 nm high-power single LED (OCU-440 UE460-X-T) purchased from OSA OPTO.

Derivatization of 6 for determination of enantiomeric ratio by UPC^2 analysis

Determination of enantiomeric ratios of the individual diastereoisomers of 1,6-dicarbonyls **6** failed in our hands due to inseparability of the 4 stereoisomers. Therefore, the following reaction sequence was performed for e.r. determination of the individual diastereoisomers (as outlined in **Supplementary Figure 29**). Upon global reduction of **6**, the diastereoisomeric mixture of the obtained diols could be separated by preparative TLC. Then, the individual diastereomeric diols were converted to their 4-nitrobenzoic esters by global acylation which could then be used for determination of the e.r. values by UPC^2 analysis.



Supplementary Figure 29: Reaction sequence to separate diastereoisomers and determine e.r. of **6**

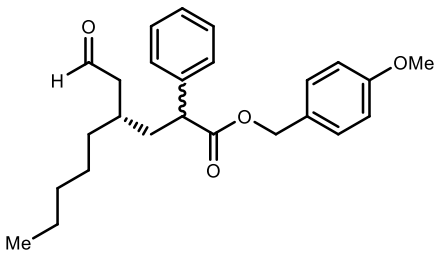
Procedure:

An analytical sample of 1,6-dicarbonyl product **6** (5.00 mg) was dissolved in 500 µL of THF. $LiAlH_4$ (5 equiv.) were added and the mixture was stirred for 1 h. The reaction mixture was diluted with Et_2O (2.0 mL), quenched with Glauber's salt ($NaSO_4 \cdot 10\ H_2O$) and then filtered over a pad of silica gel, which was subsequently rinsed with EtOAc. The volatiles were removed under reduced pressure and the two diastereomeric diols were separated by preparative TLC using EtOAc in hexanes (generally 75% EtOAc in hexanes).

The obtained diols were then further functionalized to the 4-nitrobenzoates as follows. The diol together with a slight excess of both *p*-NO_2-benzoyl chloride and 4-dimethylaminopyridine (DMAP) were suspended in DCM (0.5 mL) and the solution was allowed to stir for 90 minutes. The ester was separated by preparative TLC from unreacted starting material (generally 25% EtOAc in hexanes) and analyzed by UPC^2 analysis with conditions specified in the experimental section of the individual compounds.

Characterization Data of the Cross Electrophile Coupling Products 6

4-Methoxybenzyl (4*S*)-4-(2-oxoethyl)-2-phenylnonanoate (6a)



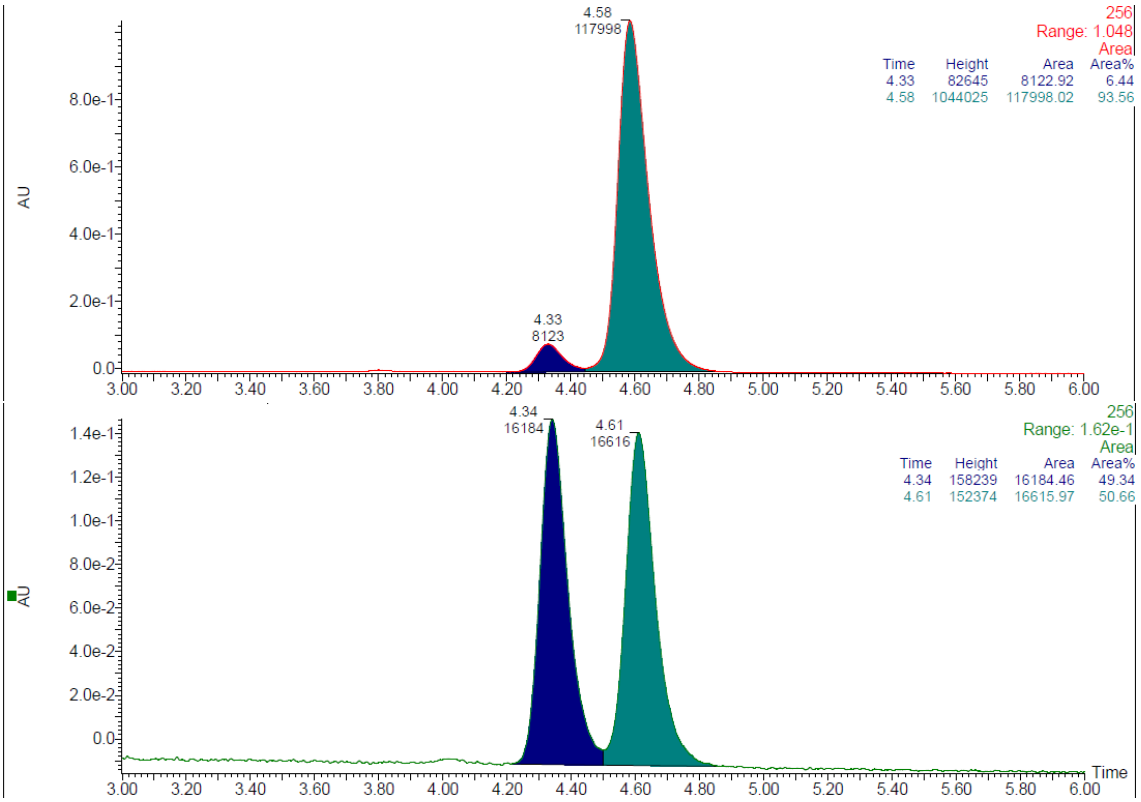
Chemical Formula: $C_{25}H_{32}O_4$
Molecular Weight: 396.53

Following the general procedure **E** using acrylate **5a** (250 μmol, 67.0 mg) and 2-octenal **1a** (750 μmol, 94.5 mg, 112 μL), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) afforded product **6a** as a pale yellow oil (91.0 mg, 92% yield) in a 1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 94:6 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 85% CO_2 in CH_3CN for 5 min, 85% CO_2 in CH_3CN for 2 min, gradient 85% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 4.60 min, τ_{Minor} = 4.35 min, and 87:13 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 80% CO_2 in CH_3CN for 5 min, 80% CO_2 in CH_3CN for 2 min, gradient 80% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 7.80 min, τ_{Minor} = 7.45 min.

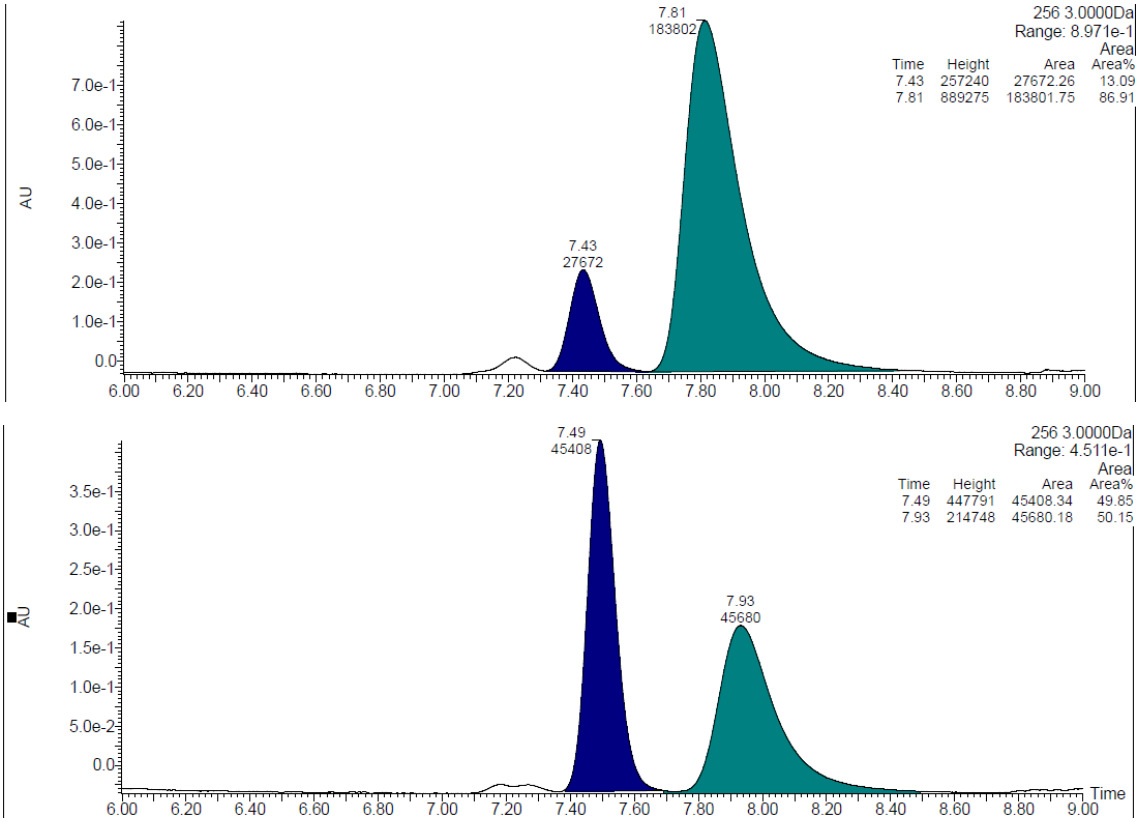
$[\alpha]_D^{26}$ = -6.5 (c = 1.0, $CHCl_3$, 1:1 d.r., 94:6 e.r.[1], 87:13 e.r.[2]).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.63 (t, *J* = 2.4 Hz, 1H), 9.60 (t, *J* = 2.2 Hz, 1H), 7.34 – 7.25 (m, 10H), 7.21 – 7.15 (m, 4H), 6.87 – 6.80 (m, 4H), 5.08 (d, *J* = 12.0 Hz, 2H), 4.98 (d, *J* = 12.1 Hz, 1H), 4.97 (d, *J* = 12.1 Hz, 1H), 3.80 (s, 6H), 3.66 (td, *J* = 7.8, 3.6 Hz, 2H), 2.30 (ddt, *J* = 4.5, 2.2, 1.0 Hz, 4H), 2.17 – 2.10 (m, 1H), 2.06 – 1.99 (m, 1H), 1.88 – 1.80 (m, 3H), 1.75 (dd, *J* = 13.7, 7.0 Hz, 1H), 1.30 – 1.15 (m, 16H), 0.88 – 0.82 (m, 6H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.7, 202.5, 173.7, 173.7, 159.7 (2C), 138.8, 138.8, 130.0, 130.02, 128.8, 128.8, 128.1, 128.1 (2C), 128.0, 127.5 (2C), 114.0 (2C), 66.6 (2C), 55.4 (2C), 49.4, 49.4, 48.3, 48.2, 38.0, 38.0, 34.0, 33.9, 32.0, 32.0, 31.1, 31.0, 26.1, 26.0, 22.6 (2C), 14.1, 14.1 ppm.

HRMS (ESI): m/z calculated for $[C_{25}H_{32}O_4Na]^+$ $[M+Na]^+$: 419.2193; found: 419.2193.

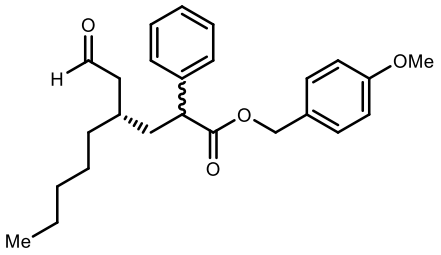


Supplementary Figure 30: UPC^2 traces of **6a**, diastereomer 1.



Supplementary Figure 31: UPC^2 traces of **6a**, diastereomer 2.

4-Methoxybenzyl (4*S*)-4-(2-oxoethyl)-2-phenylnonanoate (**6a**) (*1.00 mmol scale experiment*)



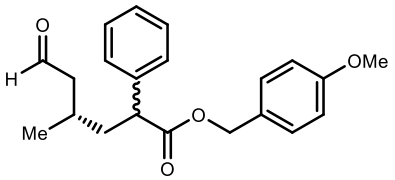
Chemical Formula: $C_{25}H_{32}O_4$
Molecular Weight: 396.53

To a 8.0 mL argon-purged glass vial, containing the acrylate **5a** (1.00 mmol, 268 mg, 1 equiv.), octenal **1a** (3.00 mmol, 379 mg, 448 µL), DHP **R-3*** (1.20 mmol, 532 mg 1.2 equiv.), 4-CzIPN (10.0 µmol, 7.9 mg, 1 mol%) and amine catalyst **A-3** (2.00 mmol, 141 mg, 20 mol%), was added 2.0 mL of dimethoxyethane, H_2O (10.0 mmol, 180 µL, 10 equiv.) and TFA (300 µmol, 23 µL, 30 mol%). The vial was sealed with Parafilm, and then placed into a cooled alluminium support mounted on an aluminium block fitted with a 460 nm high-power single LED (λ = 460 nm, irradiance = 90 mW/cm^2, as controlled by an external power supply; the set-up is detailed in **Supplementary Figure 1**). This set-up secured a reliable irradiation while keeping a constant distance of 1 cm between the reaction vessel and the light source. The reaction was stirred under visible light irradiation at -10 °C internal temperature for 72 hours. Then the solvent was evaporated, and the crude mixture was purified by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) to afford product **6a** as a pale yellow oil (258 mg, 65% yield) in a 1:1 diastereomeric ratio. The light source for illuminating the reaction vessel consisted in a 460 nm high-power single LED (OCU-440 UE460-X-T) purchased from OSA OPTO. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 93:7 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 85% CO_2 in CH_3CN for 5 min, 85% CO_2 in CH_3CN for 2 min, gradient 85% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 4.65 min, τ_{Minor} = 4.40 min, and 84:16 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 80% CO_2 in CH_3CN for 5 min, 80% CO_2 in CH_3CN for 2 min, gradient 80% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 8.00 min, τ_{Minor} = 7.55 min.

Spectroscopic data are consistent with those of the smaller scale reaction.

* Reductant **R-3** (**Supplementary Figure 83**) was used for enhanced solubility

4-Methoxybenzyl (*S*)-4-methyl-6-oxo-2-phenylhexanoate (**6b**)



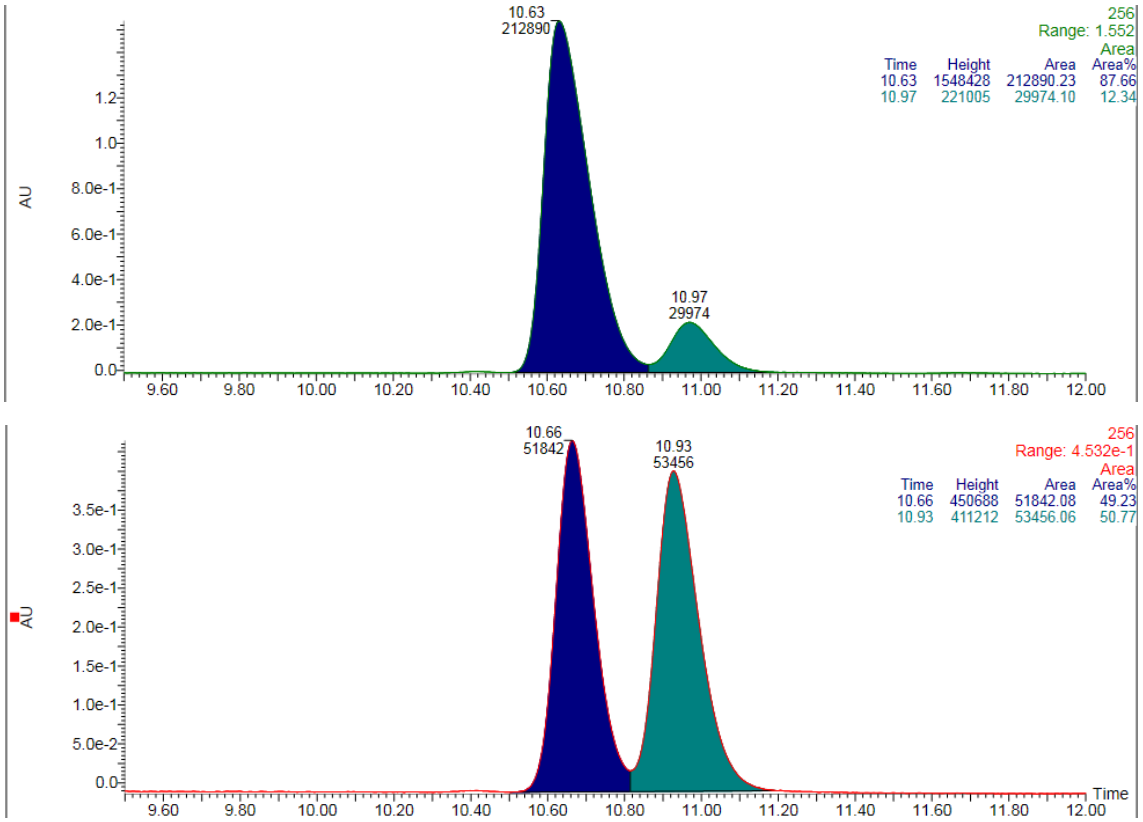
Chemical Formula: $C_{21}H_{24}O_4$
Molecular Weight: 340.42

Following the general procedure **E** using acrylate **5a** (250 μmol, 67.0 mg) and enal **1b** (750 μmol, 52.5 mg, 61.6 μL), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) afforded product **6b** as a pale yellow oil (60.0 mg, 71% yield) in a 1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 87:13 for *diastereomer 1* by UPC[2] analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 70% CO_2 in MeOH for 8 min, 70% CO_2 in MeOH for 4 min, gradient 70% - 100% CO_2 in MeOH for 2 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 10.65 min, τ_{Minor} = 10.95 min, and 76.5:23.5 for *diastereomer 2* by UPC[2] analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 6.10 min, τ_{Minor} = 5.65 min.

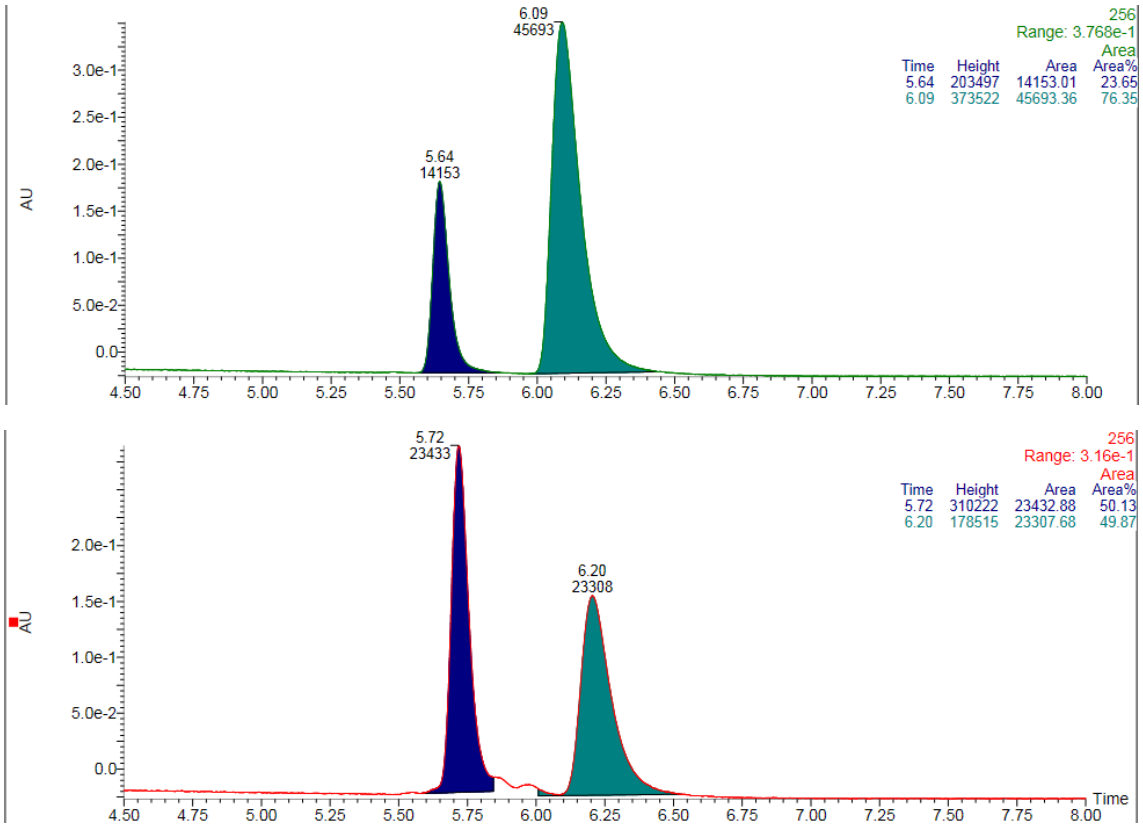
$[\alpha]_D^{26}$ = -11.2 (c = 1.0, $CHCl_3$, 1:1 d.r., 87:13 e.r.[1], 76.5:23.5 e.r.[2]).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.66 – 9.63 (m, 1H), 9.63 – 9.61 (m, 1H), 7.35 – 7.25 (m, 10H), 7.22 – 7.16 (m, 4H), 6.87 – 6.82 (m, 4H), 5.08 (d, *J* = 12.1 Hz, 2H), 5.00 (d, *J* = 12.0 Hz, 1H), 4.97 (d, *J* = 12.1 Hz, 1H), 3.79 (s, 6H), 3.73 – 3.65 (m, 2H), 2.42 – 2.34 (m, 2H), 2.24 – 2.13 (m, 3H), 2.02 – 1.87 (m, 4H), 1.68 – 1.63 (m, 1H), 0.98 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.2 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.3, 202.2, 173.8, 173.6, 159.7 (2C), 139.0, 138.4, 130.0, 130.0, 128.8 (2C), 128.2, 128.0 (2C), 128.0, 127.6, 127.5, 114.0 (2C), 66.6 (2C), 55.4 (2C), 51.0, 50.8, 49.4, 49.3, 40.7, 40.0, 26.5, 26.0, 19.9, 19.5 ppm.

HRMS (ESI): m/z calculated for $[C_{21}H_{24}O_4Na]^+$ $[M+Na]^+$: 363.1567; found: 363.1566.

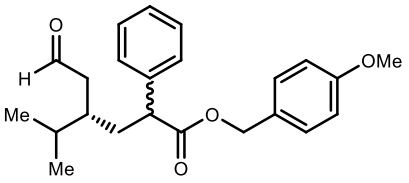


Supplementary Figure 32: UPC^2 traces of **6b**, diastereomer 1.



Supplementary Figure 33: UPC^2 traces of **6b**, diastereomer 2.

4-Methoxybenzyl (*S*)-4-isopropyl-6-oxo-2-phenylhexanoate (**6c**)



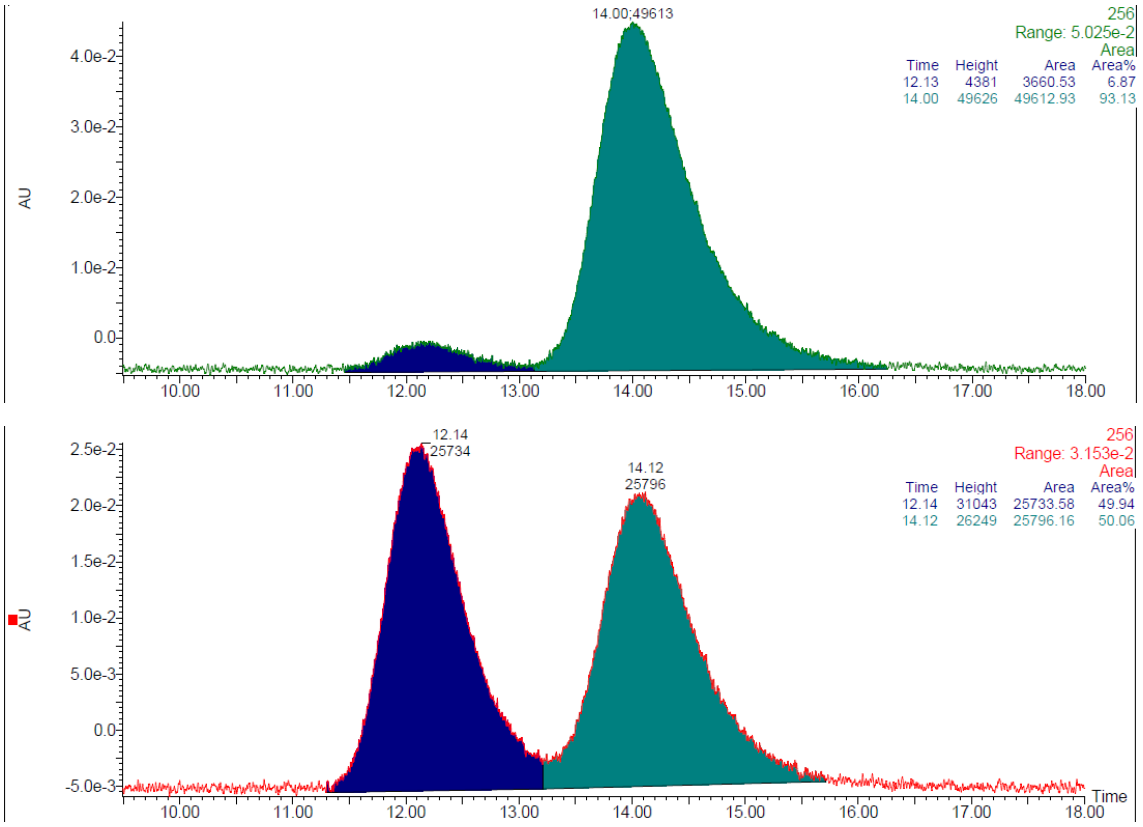
Chemical Formula: $C_{23}H_{28}O_4$
Molecular Weight: 368.47

Following the general procedure **E** using acrylate **5a** (250 μmol, 67.0 mg) and enal **1c** (750 μmol, 73.5 mg, 87.0 μL), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) afforded product **6c** as a pale yellow oil (42.0 mg, 46% yield) in a 1.1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 93:7 for *diastereomer 1* by UPC[2] analysis on a Daicel Chiralpak OJ-3 column (eluent: 99% CO_2 in CH_3CN for 20 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 14.0 min, τ_{Minor} = 12.15 min, and 89:11 for *diastereomer 2* by UPC[2] analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 258 nm) τ_{Major} = 5.60 min, τ_{Minor} = 5.35 min.

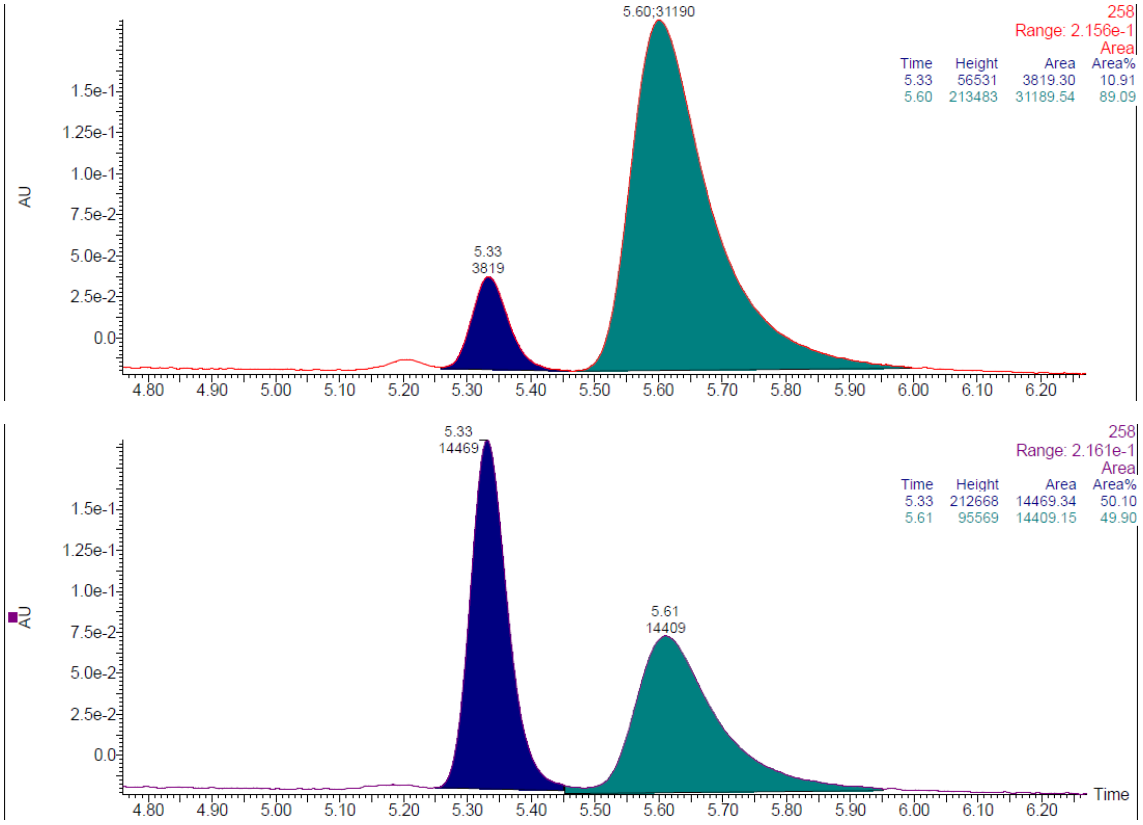
$[\alpha]_D^{26}$ = +2.4 (c = 0.5, $CHCl_3$, 1.1:1 d.r., 93:7 e.r.[1], 89:11 e.r.[2]).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.61 (t, *J* = 2.4 Hz, 1H), 9.58 (t, *J* = 2.2 Hz, 1H), 7.34 – 7.24 (m, 10H), 7.22 – 7.15 (m, 4H), 6.88 – 6.81 (m, 4H), 5.09 (d, *J* = 12.0 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.97 (d, *J* = 12.1 Hz, 1H), 3.79 (s, 6H), 3.65 – 3.59 (m, 2H), 2.39 – 2.29 (m, 2H), 2.26 – 2.15 (m, 3H), 1.95 – 1.90 (m, 1H), 1.85 – 1.70 (m, 4H), 1.69 – 1.58 (m, 2H), 0.84 (d, *J* = 6.8 Hz, 3H), 0.83 – 0.79 (m, 6H), 0.78 (d, *J* = 6.8 Hz, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 203.0, 202.8, 173.8, 173.7, 159.7 (2C), 138.9, 138.7, 130.1, 130.1, 128.9, 128.9, 128.2, 128.1, 128.1 (2C), 127.6, 127.6, 114.0 (2C), 66.6 (2C), 55.4 (2C), 49.7, 49.6, 45.3, 45.2, 36.4, 36.2, 35.6, 35.2, 30.1, 30.1, 19.5, 19.4, 18.4, 18.2 ppm.

HRMS (ESI): m/z calculated for $[C_{23}H_{28}O_4Na]^+$ $[M+Na]^+$: 391.1880; found: 391.1872.

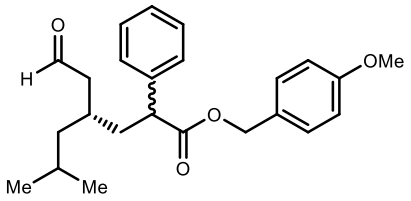


Supplementary Figure 34: UPC^2 traces of **6c**, diastereomer 1.



Supplementary Figure 35: UPC^2 traces of **6c**, diastereomer 2.

4-Methoxybenzyl (*S*)-6-methyl-4-(2-oxoethyl)-2-phenylheptanoate (**6d**)



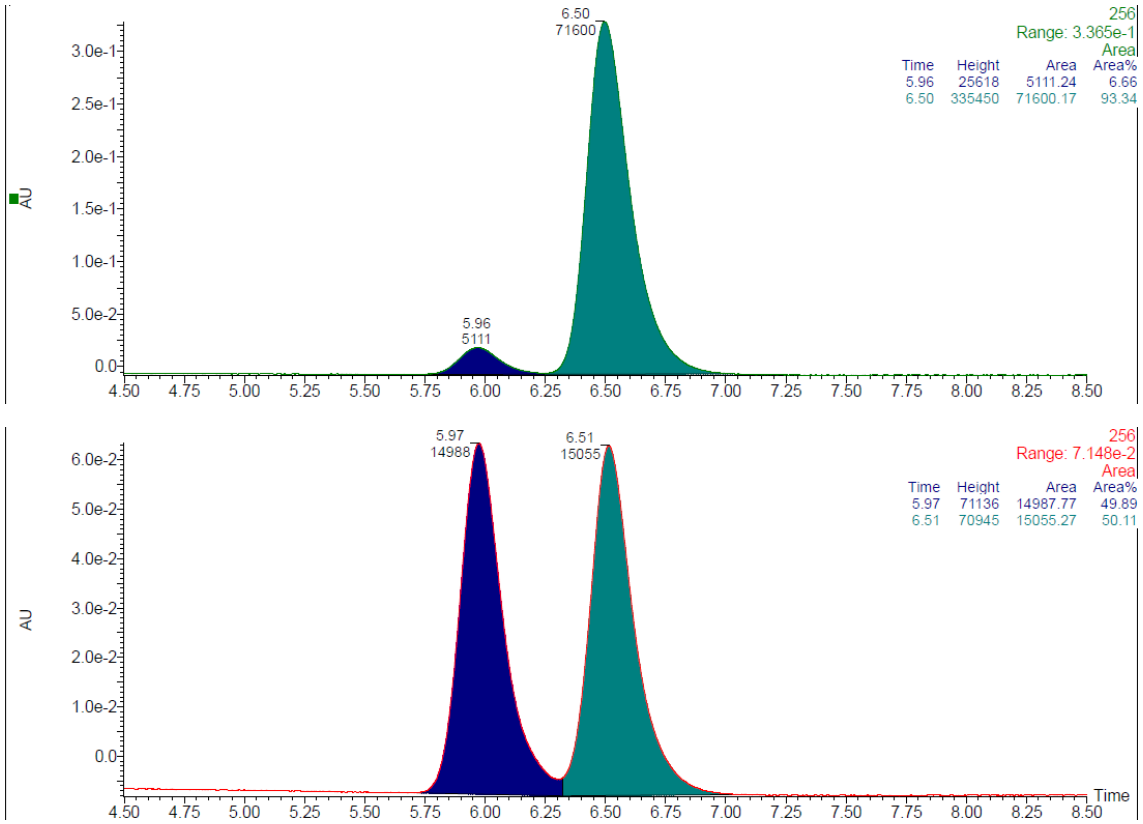
Chemical Formula: $C_{24}H_{30}O_4$
Molecular Weight: 382.50

Following the general procedure **E** using acrylate **5a** (250 μmol, 67.0 mg) and a solution of enal **1d** (750 μmol, 187 mg, 45 wt% in hexanes), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) afforded product **6d** as a pale yellow oil (54.0 mg, 56% yield) in a 1.1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 93.5:6.5 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 95% CO_2 in CH_3CN for 5 min, 95% CO_2 in CH_3CN for 2 min, gradient 95% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 6.50 min, τ_{Minor} = 5.95 min, and 89:11 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 5.40 min, τ_{Minor} = 5.20 min.

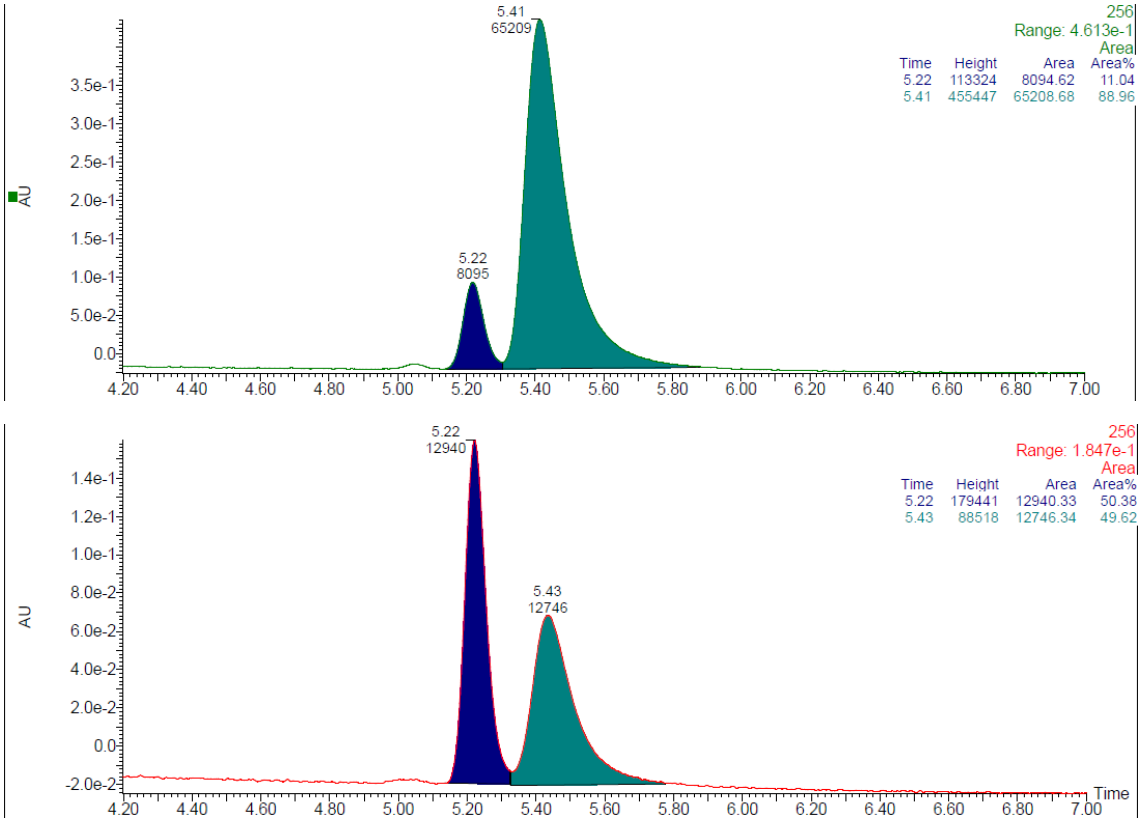
$[\alpha]_D^{26}$ = -1.1 (c = 1.0, $CHCl_3$, 1.1:1 d.r., 93.5:6.5 e.r.[1], 89:11 e.r.[2]).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.62 (t, *J* = 2.4 Hz, 1H), 9.60 (t, *J* = 2.3 Hz, 1H), 7.33 – 7.24 (m, 10H), 7.19 (dd, *J* = 8.7, 2.2 Hz, 4H), 6.86 – 6.81 (m, 4H), 5.10 (d, *J* = 12.0 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 2H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.96 (d, *J* = 12.0 Hz, 2H), 3.79 (s, 6H), 3.67 (t, *J* = 7.7 Hz, 2H), 2.37 – 2.23 (m, 4H), 2.18 – 2.10 (m, 1H), 2.07 – 1.98 (m, 1H), 1.92 – 1.79 (m, 3H), 1.75 – 1.68 (m, 1H), 1.62 – 1.54 (m, 2H), 1.22 – 1.05 (m, 6H), 0.85 (d, *J* = 6.6 Hz, 3H), 0.78 (d, *J* = 6.6 Hz, 3H), 0.76 (d, *J* = 6.6 Hz, 3H), 0.75 (d, *J* = 6.6 Hz, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.7, 202.6, 173.7, 173.7, 159.7 (2C), 138.8, 138.7, 130.1, 130.1, 128.9, 128.8, 128.1, 128.1 (2C), 128.1, 127.6, 127.5, 114.0, 114.0, 66.6 (2C), 55.4 (2C), 49.4, 49.3, 48.6, 48.5, 44.0, 43.9, 38.4, 38.3, 29.0, 29.0, 25.2 (2C), 23.0, 22.7, 22.6, 22.6 ppm.

HRMS (ESI): m/z calculated for $[C_{24}H_{30}O_4Na]^+$ $[M+Na]^+$: 405.2036; found: 405.2038.

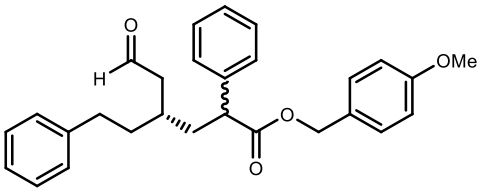


Supplementary Figure 36: UPC^2 traces of **6d**, diastereomer 1.



Supplementary Figure 37: UPC^2 traces of **6d**, diastereomer 2

4-Methoxybenzyl (*S*)-6-oxo-4-phenethyl-2-phenylhexanoate (**6e**)



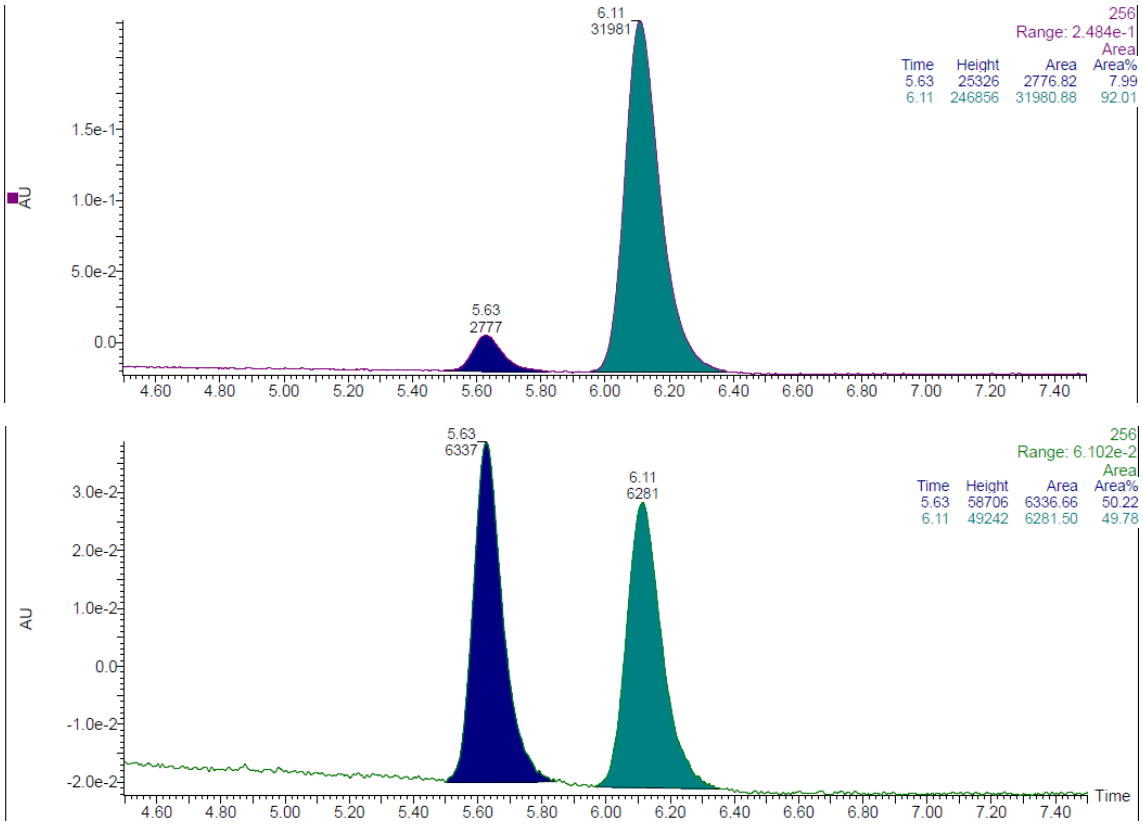
Chemical Formula: $C_{28}H_{30}O_4$
Molecular Weight: 430.54

Following the general procedure **E** using acrylate **5a** (250 μmol, 67.0 mg) and enal **1e** (750 μmol, 120 mg), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) and preparative thin layer chromatography (silica gel, DCM) afforded product **6e** as a pale yellow oil (84.0 mg, 78% yield) in a 1.1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 92:8 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 75% CO_2 in CH_3CN for 8 min, 75% CO_2 in CH_3CN for 4 min, gradient 75% - 100% CO_2 in CH_3CN for 2 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 6.10 min, τ_{Minor} = 5.65 min, and 84.5:15.5 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 85% CO_2 in CH_3CN for 20 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 12.75 min, τ_{Minor} = 11.60 min.

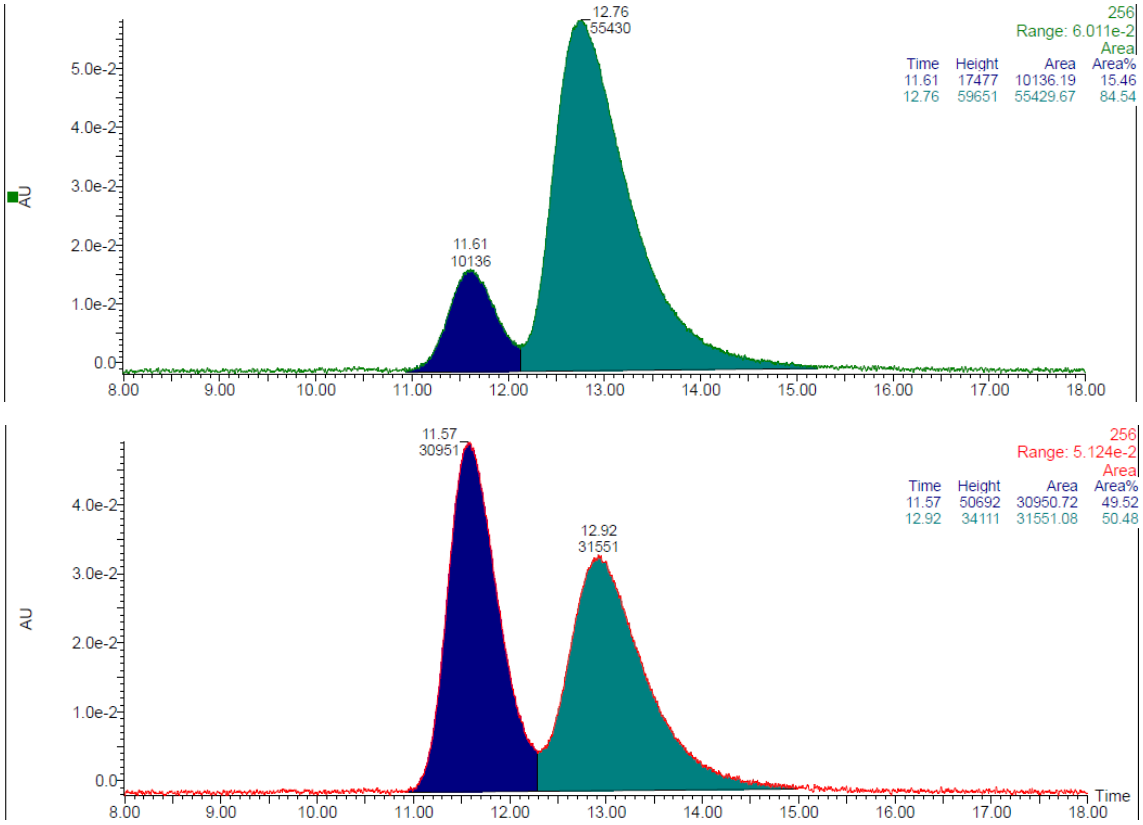
$[\alpha]_D^{26}$ = -4.6 (c =1.0 , $CHCl_3$, 1.1:1 d.r., 92:8 e.r.[1], 84.5:15.5 e.r.[2]).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.65 (t, *J* = 2.3 Hz, 1H), 9.62 (t, *J* = 2.1 Hz, 1H), 7.38 – 7.25 (m, 14H), 7.24 – 7.18 (m, 6H), 7.17 – 7.12 (m, 2H), 7.12 – 7.07 (m, 2H), 6.90 – 6.83 (m, 4H), 5.10 (d, *J* = 12.0 Hz, 1H), 5.10 (d, *J* = 12.0 Hz, 1H), 5.01 (d, *J* = 12.0 Hz, 1H), 5.00 (d, *J* = 12.0 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.74 – 3.65 (m, 2H), 2.62 – 2.52 (m, 4H), 2.44 – 2.37 (m, 4H), 2.29 – 2.23 (m, 1H), 2.17 – 2.11 (m, 1H), 2.01 – 1.92 (m, 3H), 1.86 – 1.81 (m, 1H), 1.76 – 1.68 (m, 2H), 1.68 – 1.60 (m, 2H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.3, 202.2, 173.7, 173.7, 159.8 (2C), 141.9, 141.8, 138.7, 138.7, 130.1, 130.1, 128.9, 128.9, 128.6, 128.6, 128.4, 128.4, 128.1, 128.1, 128.0, 128.0, 127.6, 127.6, 126.1 (2C), 114.0 (2C), 66.7 (2C), 55.4 (2C), 49.4, 49.4, 48.2, 48.2, 37.9, 37.9, 36.0, 35.8, 32.9, 32.8, 30.9, 30.8 ppm.

HRMS (ESI): m/z calculated for $[C_{28}H_{30}O_4Na]^+$ $[M+Na]^+$: 453.2036; found: 453.2041.

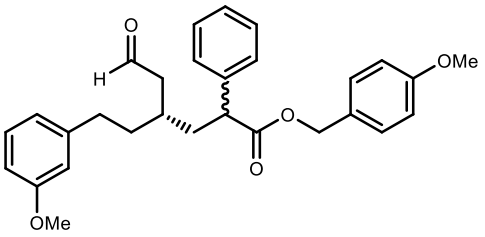


Supplementary Figure 38: UPC^2 traces of **6e**, diastereomer 1.



Supplementary Figure 39: UPC^2 traces of **6e**, diastereomer 2

4-Methoxybenzyl (*S*)-4-(3-methoxyphenethyl)-6-oxo-2-phenylhexanoate (**6f**)



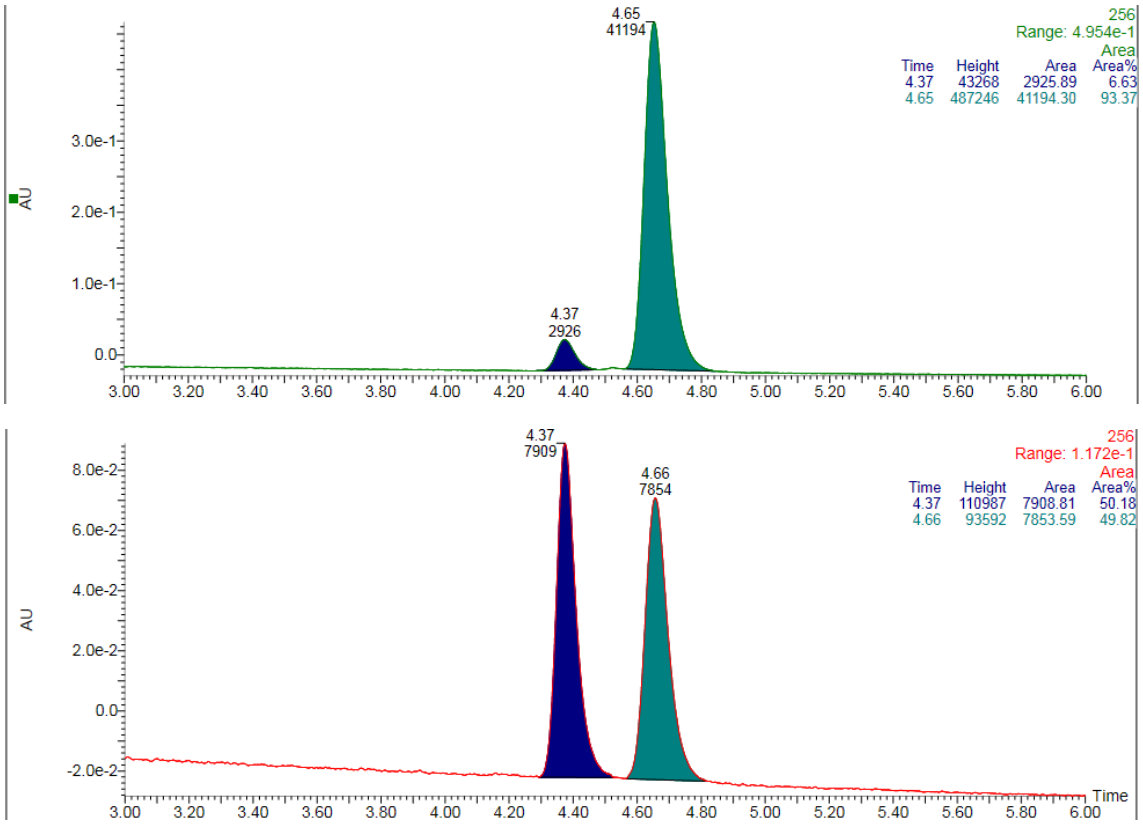
Chemical Formula: $C_{29}H_{32}O_5$
Molecular Weight: 460.57

Following the general procedure **E** using acrylate **5a** (250 μmol, 67.0 mg) and enal **1f** (750 μmol, 143 mg), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) and preparative thin layer chromatography (silica gel, DCM) afforded product **6f** as a pale yellow oil (62.0 mg, 54% yield) in a 1.1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 93.5:6.5 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 4.65 min, τ_{Minor} = 4.35 min, and 84.5:15.5 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak IC-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 65% CO_2 in CH_3CN for 5 min, 65% CO_2 in CH_3CN for 2 min, gradient 65% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 6.85 min, τ_{Minor} = 7.10 min.

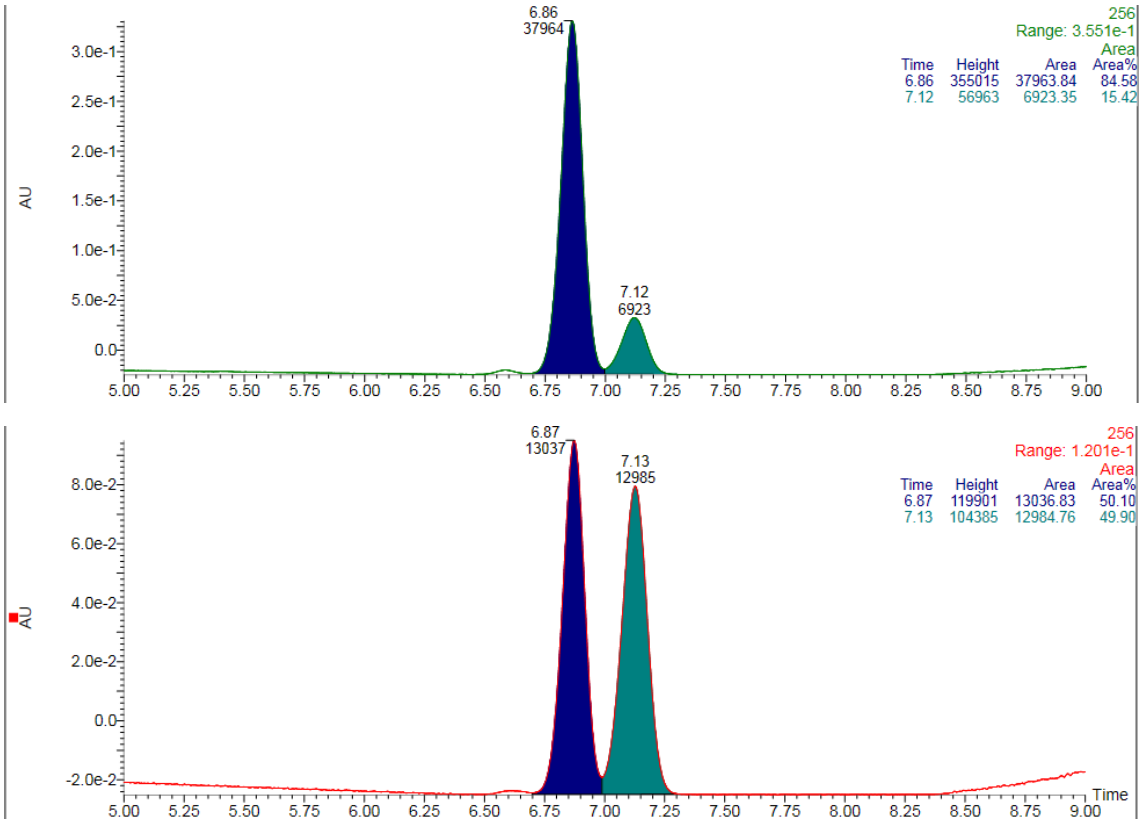
$[\alpha]_D^{26}$ = -6.0 (c = 1.0, $CHCl_3$, 1.1:1 d.r., 93.5:6.5 e.r.[1], 84.5:15.5 e.r.[2]).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.63 (t, *J* = 2.3 Hz, 1H), 9.60 (t, *J* = 2.1 Hz, 1H), 7.36 – 7.25 (m, 10H), 7.22 – 7.15 (m, 6H), 6.88 – 6.81 (m, 4H), 6.76 – 6.64 (m, 6H), 5.08 (d, *J* = 12.0 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 1H), 4.99 (d, *J* = 12.0 Hz, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 3.80 (s, 6H), 3.79 (s, 3H), 3.78 (s, 3H), 3.72 – 3.63 (m, 2H), 2.61 – 2.48 (m, 4H), 2.42 – 2.33 (m, 4H), 2.28 – 2.19 (m, 1H), 2.16 – 2.08 (m, 1H), 1.99 – 1.89 (m, 3H), 1.85 – 1.76 (m, 1H), 1.73 – 1.58 (m, 4H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.3, 202.1, 173.6, 173.6, 159.8 (2C), 159.7 (2C), 143.5, 143.4, 138.7 (2C), 130.1, 130.0, 129.5, 129.5, 128.9, 128.8, 128.1, 128.0, 128.0, 128.0, 127.6, 127.6, 120.8, 120.8, 114.2, 114.1, 114.0 (2C), 111.4, 111.3, 66.6 (2C), 55.4 (2C), 55.2 (2C), 49.4, 49.3, 48.1, 48.1, 37.9, 37.8, 35.8, 35.7, 32.9, 32.9, 30.9, 30.7 ppm.

HRMS (ESI): m/z calculated for $[C_{29}H_{32}O_5Na]^+$ $[M+Na]^+$: 483.2142; found: 483.2153.

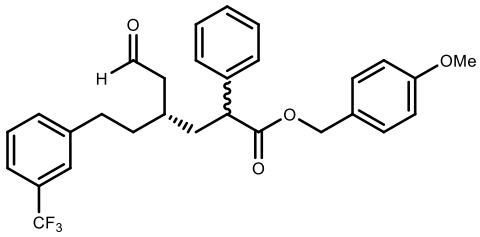


Supplementary Figure 40: UPC^2 traces of **6f**, diastereomer 1



Supplementary Figure 41: UPC^2 traces of **6f**, diastereomer 2

4-Methoxybenzyl (*S*)-6-oxo-2-phenyl-4-(3-(trifluoromethyl)phenethyl)hexanoate (**6g**)



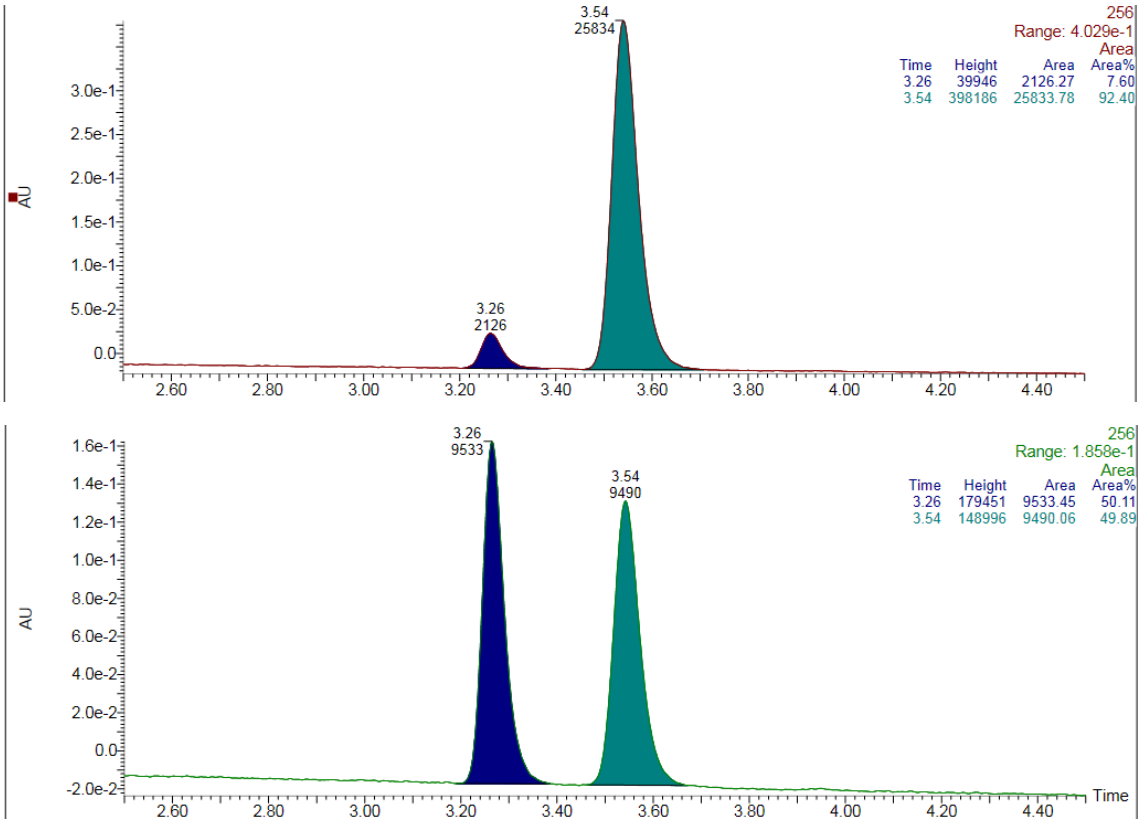
Chemical Formula: $C_{29}H_{29}F_3O_4$
Molecular Weight: 498.54

Following the general procedure **E** using acrylate **5a** (250 μmol, 67.0 mg) and enal **1g** (750 μmol, 171 mg), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) and preparative thin layer chromatography (silica gel, DCM) afforded product **6g** as a pale yellow oil (68.0 mg, 55% yield) in a 1.1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 92.5:7.5 for *diastereomer 1* by UPC[2] analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 3.55 min, τ_{Minor} = 3.25 min, and 83.5:16.5 for *diastereomer 2* by UPC[2] analysis on a Daicel Chiralpak IE-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 80% CO_2 in MeOH for 38 min, 80% CO_2 in MeOH for 5 min, gradient 80% - 100% CO_2 in MeOH for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 31.35 min, τ_{Minor} = 30.75 min.

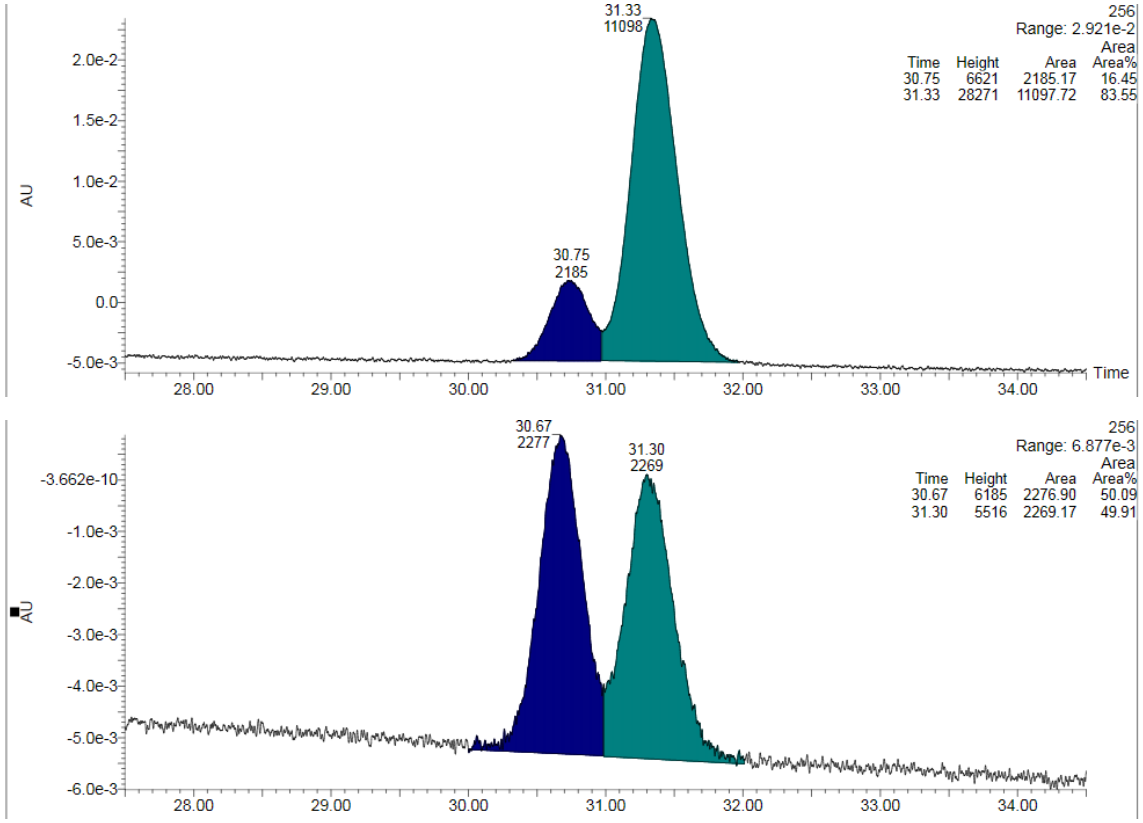
$[\alpha]_D^{26}$ = -4.6 (c = 1.0, $CHCl_3$, 1.1:1 d.r., 92.5:7.5 e.r.[1], 83.5:16.5 e.r.[2]).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.65 (t, *J* = 2.1 Hz, 1H), 9.63 (t, *J* = 2.0 Hz, 1H), 7.48 – 7.40 (m, 2H), 7.41 – 7.22 (m, 16H), 7.22 – 7.15 (m, 4H), 6.87 – 6.80 (m, 4H), 5.09 (d, *J* = 12.0 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 1H), 4.99 (d, *J* = 12.0 Hz, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.70 – 3.63 (m, 2H), 2.67 – 2.51 (m, 4H), 2.48 – 2.34 (m, 4H), 2.31 – 2.22 (m, 1H), 2.16 – 2.07 (m, 1H), 2.02 – 1.87 (m, 3H), 1.85 – 1.77 (m, 1H), 1.70 – 1.57 (m, 4H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 201.9, 201.8, 173.6, 173.5, 159.8 (2C), 142.8, 142.7, 138.6, 138.5, 131.8 (q, *J* = 1.1 Hz), 131.8 (q, *J* = 1.1 Hz), 130.8 (q, *J* = 31.9 Hz), 130.8 (q, *J* = 32.0 Hz), 130.1, 130.1, 129.0, 128.9, 128.9, 128.9, 128.0, 128.0, 128.0, 128.0, 127.7, 127.6, 125.1 (q, *J* = 3.7 Hz), 125.0 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 272.4 Hz, 2C), 123.0 (q, *J* = 3.9 Hz, 2C), 114.0 (2C), 66.7 (2C), 55.4, 55.4, 49.4, 49.4, 48.1 (2C), 37.8, 37.69, 35.8, 35.7, 32.7, 32.7, 30.8, 30.8 ppm. **^{19}F NMR (376 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = -62.59 ppm.

HRMS (ESI): m/z calculated for $[C_{29}H_{29}F_3O_4Na]^+$ $[M+Na]^+$: 521.1910; found: 521.1908.

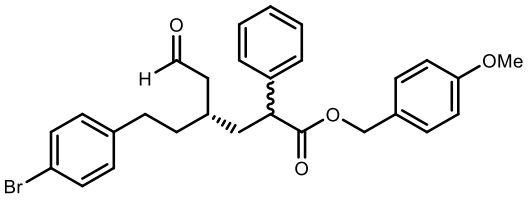


Supplementary Figure 42: UPC^2 traces of **6g**, diastereomer 1.



Supplementary Figure 43: UPC^2 traces of **6g**, diastereomer 2

4-Methoxybenzyl (*S*)-4-(4-bromophenethyl)-6-oxo-2-phenylhexanoate (**6h**)



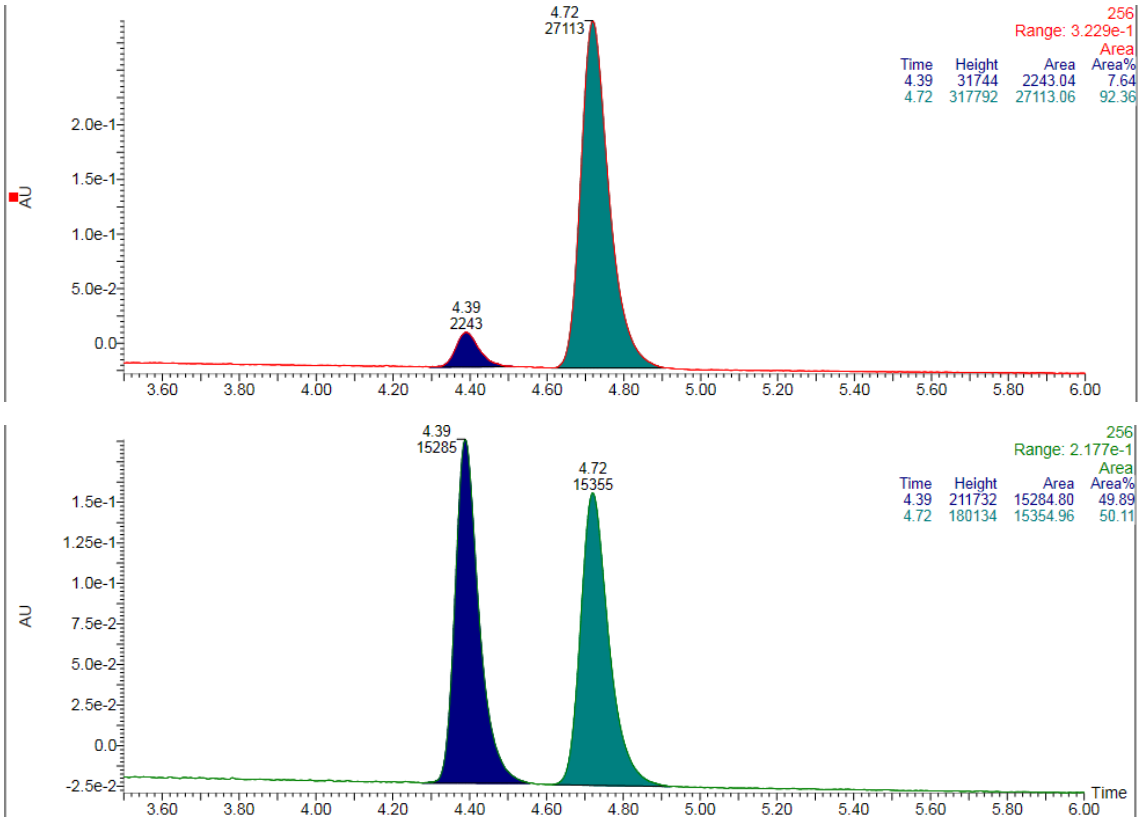
Chemical Formula: $C_{28}H_{29}BrO_4$
Molecular Weight: 509.44

Following the general procedure **E** using acrylate **5a** (250 μmol, 67.0 mg) and enal **1h** (750 μmol, 179 mg), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) and preparative thin layer chromatography (silica gel, DCM) afforded product **6h** as a pale yellow oil (68.0 mg, 53% yield) in a 1.1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 92.5:7.5 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 4.70 min, τ_{Minor} = 4.40 min, and 84:16 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak IC-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 70% CO_2 in CH_3CN for 5 min, 70% CO_2 in CH_3CN for 2 min, gradient 70% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 7.05 min, τ_{Minor} = 7.30 min.

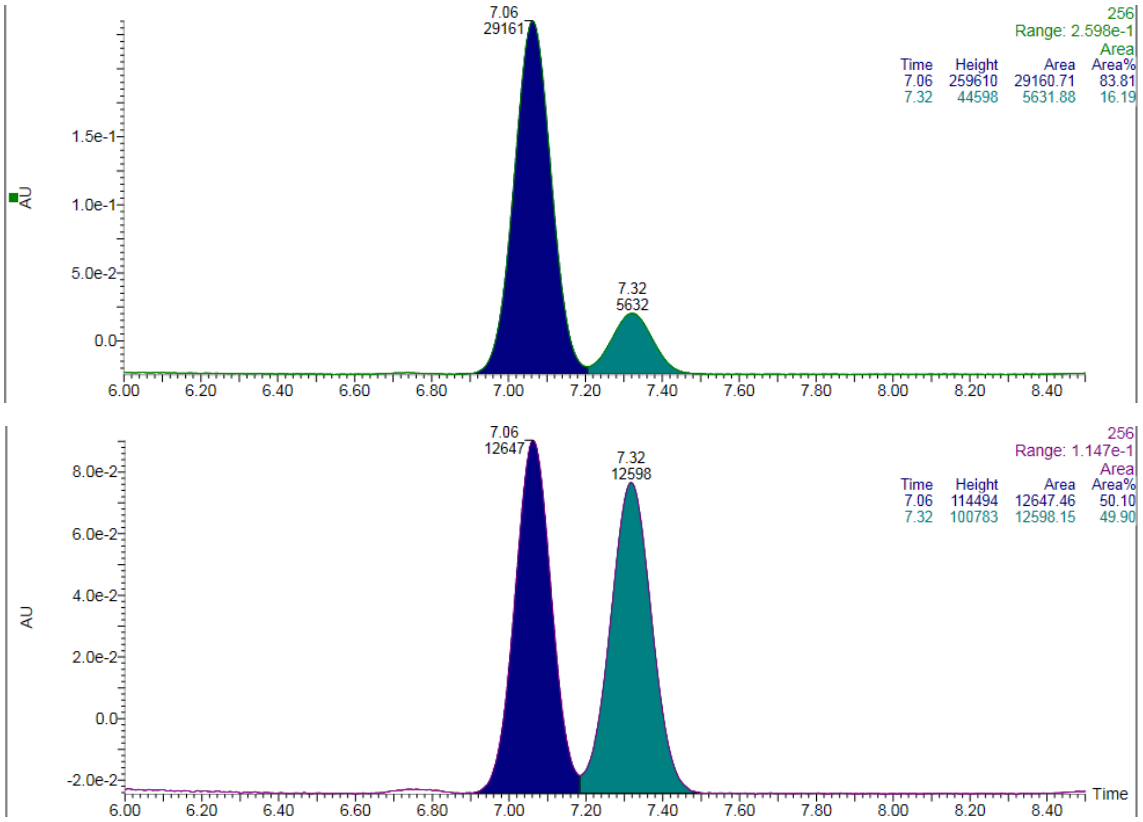
$[\alpha]_D^{26}$ = -9.0 (c = 1.0, $CHCl_3$, 1.1:1 d.r., 92.5:7.5 e.r.[1], 84:16 e.r.[2]).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.62 (t, *J* = 2.2 Hz, 1H), 9.59 (t, *J* = 2.1 Hz, 1H), 7.40 – 7.36 (m, 2H), 7.36 – 7.34 (m, 2H), 7.33 – 7.23 (m, 10H), 7.20 – 7.15 (m, 4H), 7.00 – 6.96 (m, 2H), 6.94 – 6.89 (m, 2H), 6.86 – 6.82 (m, 4H), 5.08 (d, *J* = 12.0 Hz, 1H), 5.07 (d, *J* = 12.0 Hz, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.97 (d, *J* = 12.0 Hz, 1H), 3.79 (s, 3H), 3.79 (s, 3H), 3.68 – 3.60 (m, 2H), 2.56 – 2.43 (m, 4H), 2.42 – 2.33 (m, 4H), 2.26 – 2.18 (m, 1H), 2.13 – 2.05 (m, 1H), 1.98 – 1.92 (m, 1H), 1.92 – 1.85 (m, 2H), 1.82 – 1.76 (m, 1H), 1.66 – 1.54 (m, 4H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.1, 202.0, 173.6, 173.6, 159.7 (2C), 140.8, 140.7, 138.6 (2C), 131.6, 131.5, 130.2, 130.1, 130.1, 130.1, 128.9, 128.9, 128.0, 128.0, 128.0, 127.9, 127.6, 127.6, 119.8, 119.7, 114.0 (2C), 66.7 (2C), 55.4 (2C), 49.4, 49.3, 48.1, 48.1, 37.8, 37.7, 35.7, 35.6, 32.2, 32.2, 30.6, 30.5 ppm.

HRMS (ESI): m/z calculated for $[C_{28}H_{29}BrO_4Na]^+$ $[M+Na]^+$: 531.1141; found: 531.1141.

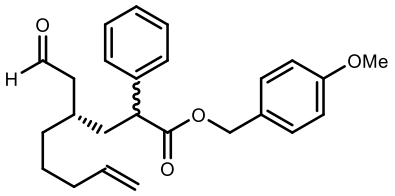


Supplementary Figure 44: UPC^2 traces of **6h**, diastereomer 1.



Supplementary Figure 45: UPC^2 traces of **6h**, diastereomer 2.

4-Methoxybenzyl (*S*)-4-(2-oxoethyl)-2-phenylnon-8-enoate (**6i**)



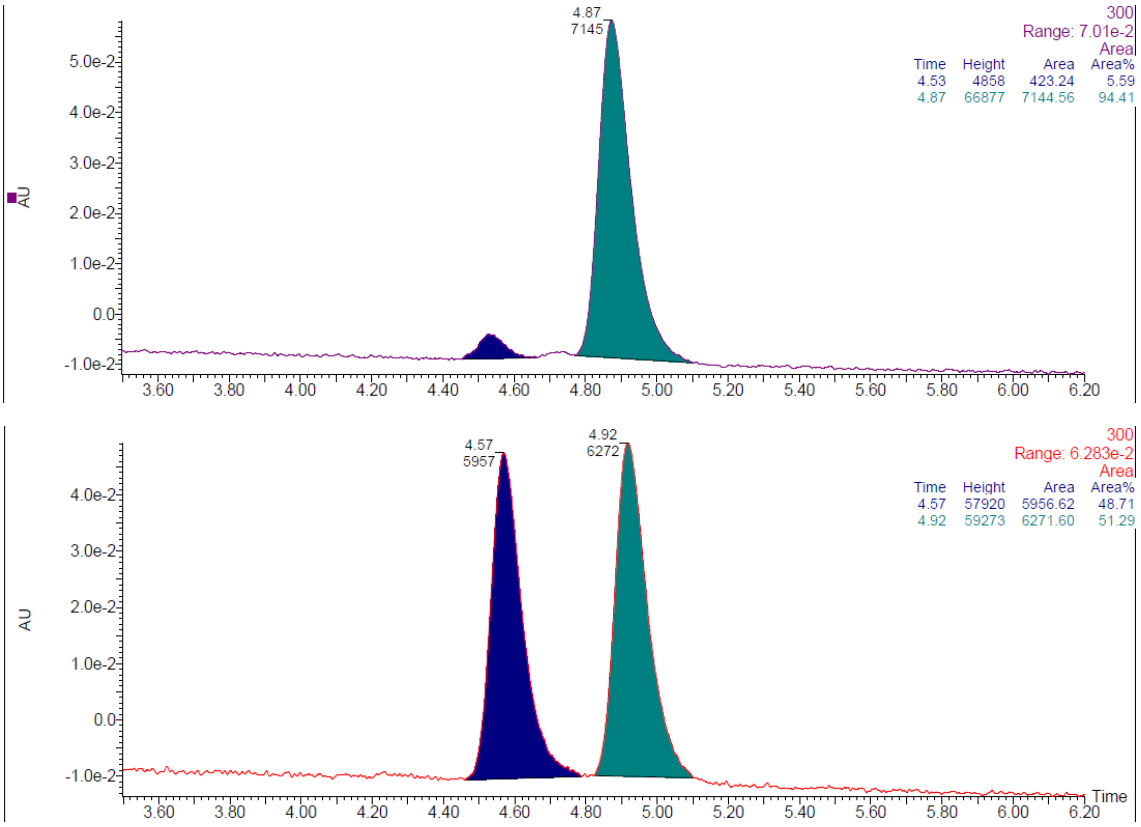
Chemical Formula: $C_{25}H_{30}O_4$
Molecular Weight: 394.51

Following the general procedure E using acrylate **5a** (250 μmol, 67.0 mg) and enal **1i** (750 μmol, 93.0 mg), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) afforded product **6i** as a pale yellow oil (81.0 mg, 82% yield) in a 1.2:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 94.5:5.5 for *diastereomer 1* by UPC[2] analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 85% CO_2 in CH_3CN for 8 min, 85% CO_2 in CH_3CN for 4 min, gradient 85% - 100% CO_2 in CH_3CN for 2 min; flow rate 2.0 mL/min, λ = 300 nm) τ_{Major} = 4.85 min, τ_{Minor} = 4.55 min, and 86.5:13.5 for *diastereomer 2* by UPC[2] analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 5.65 min, τ_{Minor} = 5.45 min.

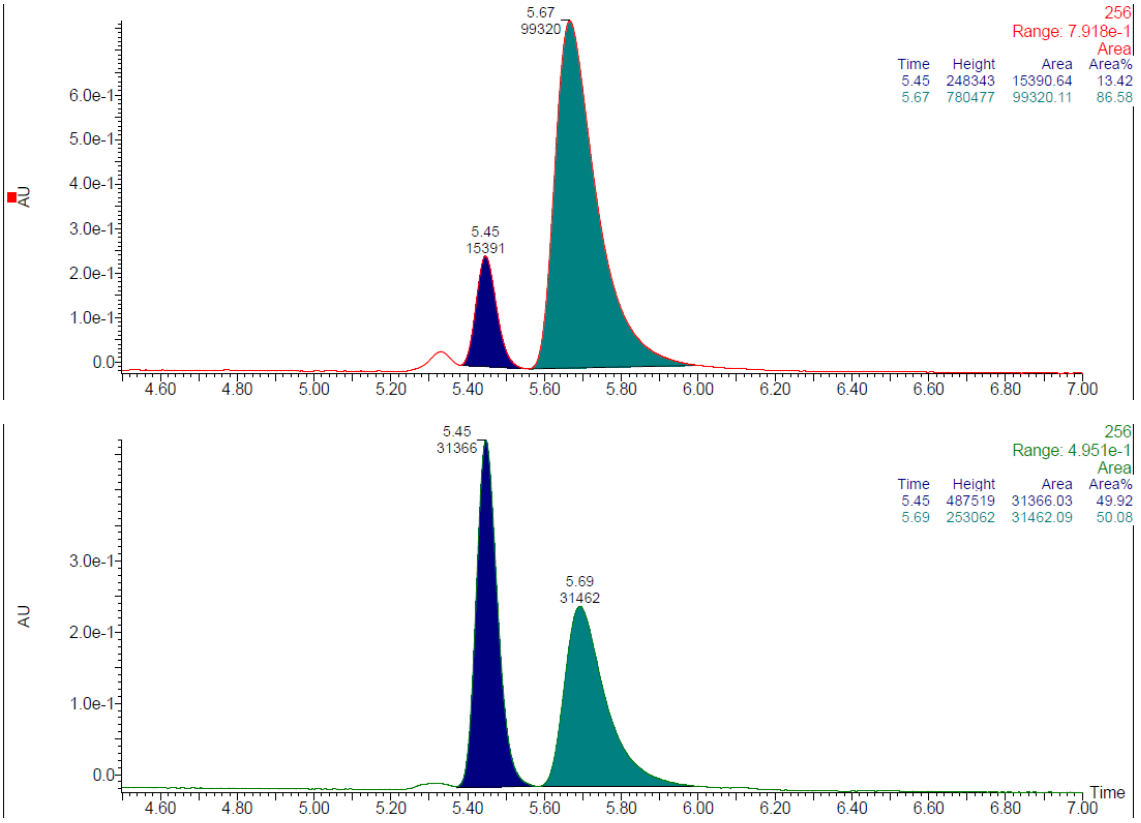
$[\alpha]_D^{26}$ = -7.4 (c = 1.0, $CHCl_3$, 1.2:1 d.r., 94.5:5.5 e.r.[1], 86.5:13.5 e.r.[2]).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.63 (t, *J* = 2.3 Hz, 1H), 9.61 (t, *J* = 2.2 Hz, 1H), 7.34 – 7.25 (m, 10H), 7.22 – 7.16 (m, 4H), 6.88 – 6.82 (m, 4H), 5.80 – 5.69 (m, 2H), 5.08 (d, *J* = 12.0 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 1H), 5.00 – 4.92 (m, 6H), 3.79 (s, 6H), 3.69 – 3.63 (m, 2H), 2.38 – 2.27 (m, 4H), 2.18 – 2.12 (m, 1H), 2.07 – 2.03 (m, 1H), 2.01 – 1.93 (m, 4H), 1.90 – 1.80 (m, 3H), 1.76 (dd, *J* = 13.9, 7.0 Hz, 1H), 1.37 – 1.27 (m, 8H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers)**: δ = 202.5, 202.4, 173.7, 173.7, 159.7 (2C), 138.8, 138.7, 138.5, 138.5, 130.1, 130.1, 128.9, 128.8, 128.1 (2C), 128.0 (2C), 127.6, 114.9, 114.0, 114.0, 66.6, 55.4, 49.4, 49.4, 48.2, 48.2, 37.9, 33.8, 33.8, 33.5, 33.3, 30.9, 30.9, 25.7, 25.6 ppm.

HRMS (ESI): m/z calculated for $[C_{25}H_{30}O_4Na]^+$ $[M+Na]^+$: 417.2036; found: 417.2034.

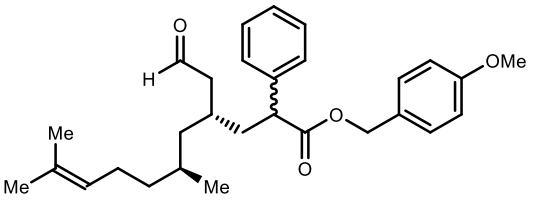


Supplementary Figure 46: UPC^2 traces of **6i**, diastereomer 1.



Supplementary Figure 47: UPC^2 traces of **6i**, diastereomer 2.

4-Methoxybenzyl (4*S*,6*S*)-6,10-dimethyl-4-(2-oxoethyl)-2-phenylundec-9-enoate (**6j**)



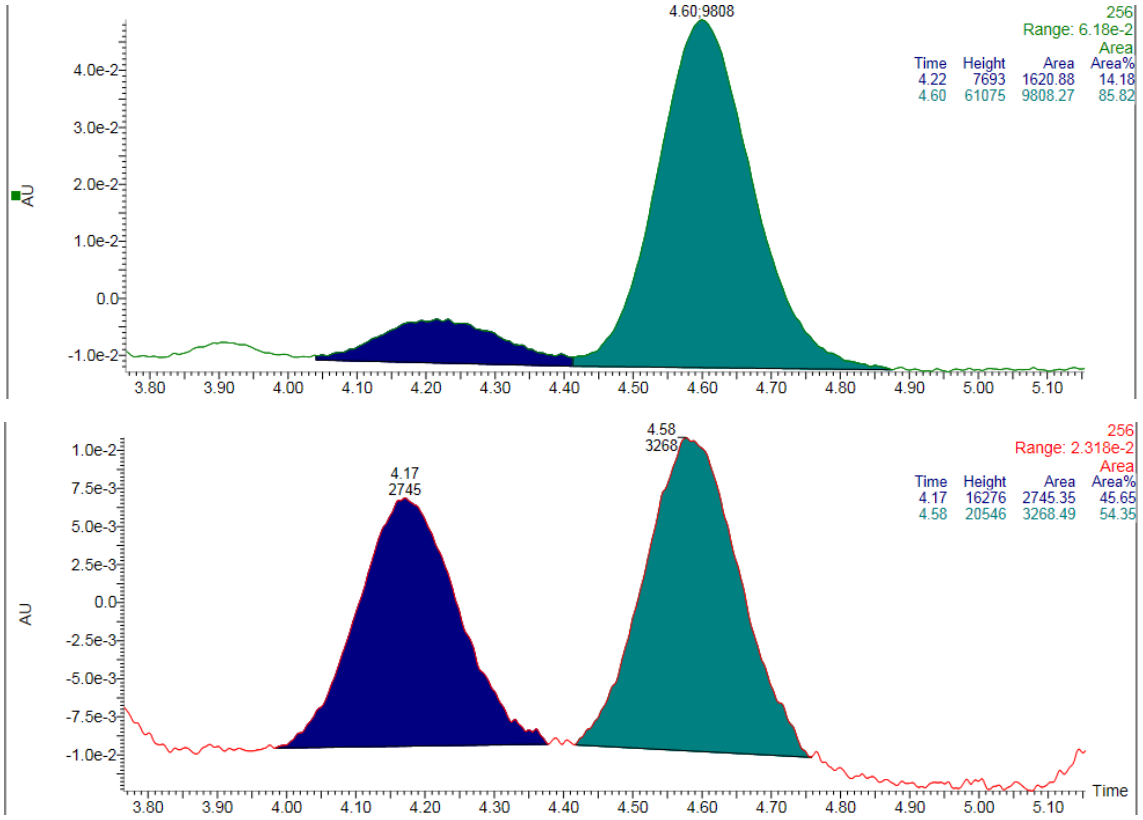
Chemical Formula: $C_{29}H_{38}O_4$
Molecular Weight: 450.62

Following the general procedure **E** using acrylate **5a** (250 μmol, 67.0 mg) and enal **1j** (750 μmol, 135 mg), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) afforded product **6j** as a pale yellow oil (75.0 mg, 67% yield) in a 1.6:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 86:14 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 80% CO_2 in iPrOH for 8 min, 80% CO_2 in iPrOH for 4 min, gradient 80% - 100% CO_2 in iPrOH for 2 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 4.60 min, τ_{Minor} = 4.20 min, and 88.5:11.5 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak IB-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 80% CO_2 in iPrOH for 8 min, 80% CO_2 in iPrOH for 4 min, gradient 80% - 100% CO_2 in iPrOH for 2 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 7.05 min, τ_{Minor} = 7.20 min.

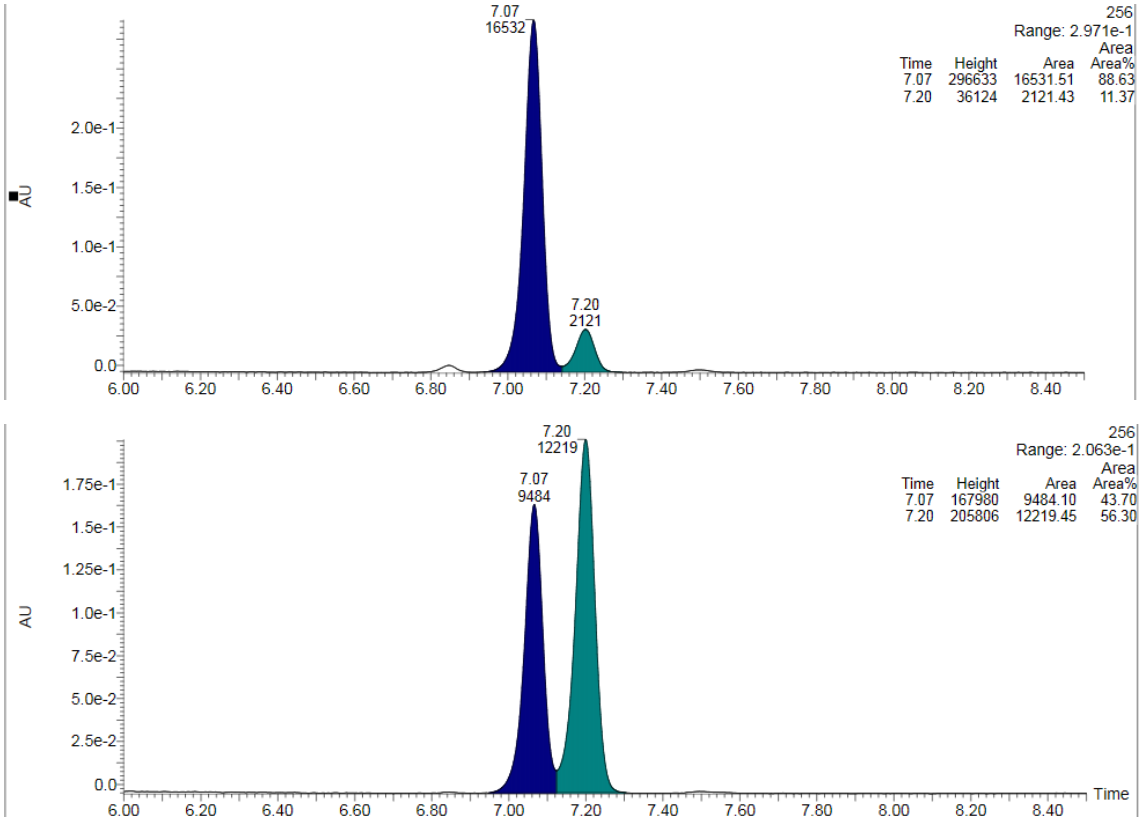
$[\alpha]_D^{26}$ = -2.3 (c = 1.0, $CHCl_3$, 1.6:1 d.r., 86:14 e.r.[1], 88.5:11.5 e.r.[2]).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.65 – 9.57 (m, 2H), 7.34 – 7.24 (m, 10H), 7.24 – 7.16 (m, 4H), 6.87 – 6.80 (m, 4H), 5.14 – 4.93 (m, 6H), 3.79 (s, 6H), 3.70 – 3.63 (m, 2H), 2.41 – 2.29 (m, 2H), 2.29 – 2.18 (m, 3H), 1.99 – 1.86 (m, 7H), 1.68 (dt, *J* = 4.3, 1.3 Hz, 6H), 1.67 – 1.61 (m, 2H), 1.59 (dd, *J* = 8.0, 1.3 Hz, 6H), 1.44 (dt, *J* = 9.5, 7.1 Hz, 2H), 1.36 – 1.28 (m, 2H), 1.22 – 1.16 (m, 2H), 1.11 – 0.97 (m, 4H), 0.85 (d, *J* = 6.5 Hz, 3H), 0.71 (d, *J* = 6.5 Hz, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.6, 202.5, 173.8, 173.6, 159.7, 159.7, 139.0, 138.6, 131.4, 131.4, 130.1, 130.0, 128.9, 128.8, 128.1, 128.0, 128.0 (2C), 127.6, 127.5, 124.8, 124.7, 114.0, 114.0, 66.6 (2C), 55.4, 55.4, 49.4, 49.3, 48.8, 48.7, 42.4, 42.3, 38.2, 37.8, 37.2, 37.2, 29.8, 29.7, 28.9, 28.6, 25.8, 25.8, 25.5, 25.5, 19.8, 19.6, 17.8, 17.8 ppm.

HRMS (ESI): m/z calculated for $[C_{29}H_{38}O_4Na]^+$ $[M+Na]^+$: 473.2662; found: 473.2660.

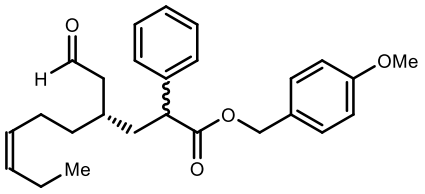


Supplementary Figure 48: UPC^2 traces of **6j**, diastereomer 1



Supplementary Figure 49: UPC^2 traces of **6j**, diastereomer 2

4-Methoxybenzyl (*S,Z*)-4-(2-oxoethyl)-2-phenyldec-7-enoate (**6k**)



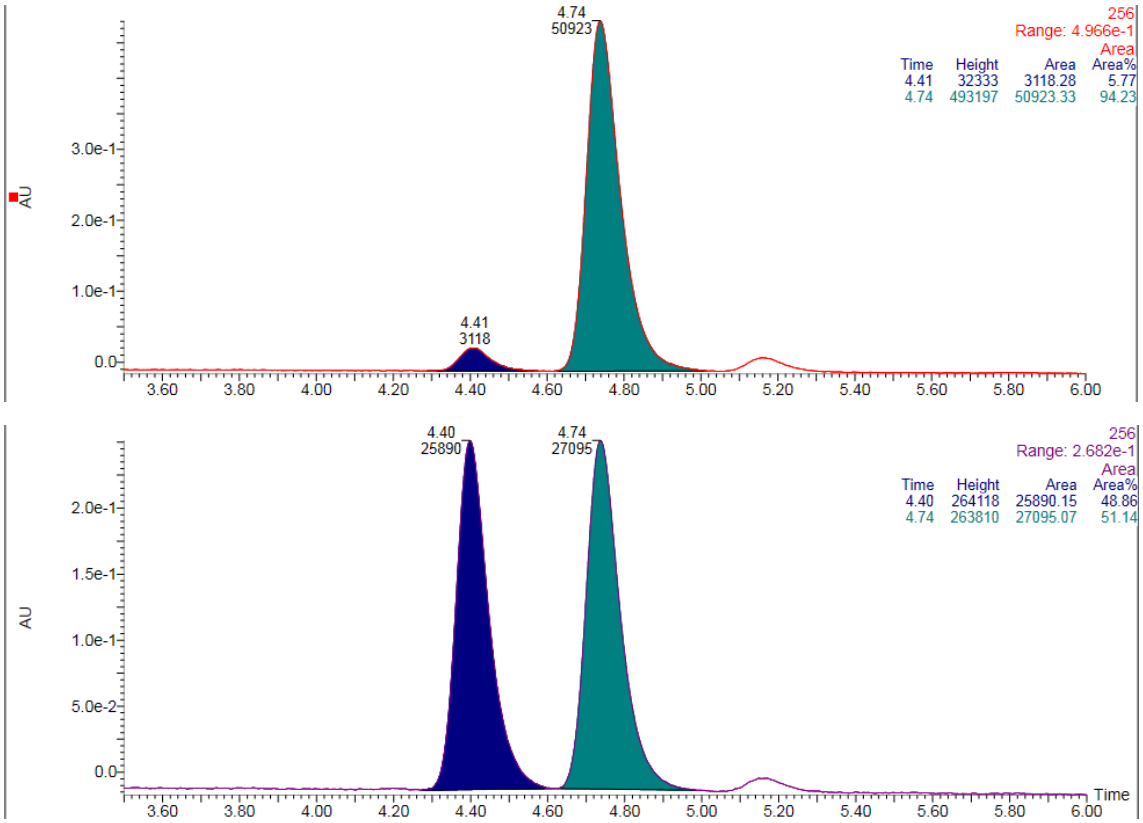
Chemical Formula: $C_{26}H_{32}O_4$
Molecular Weight: 408.54

Following the general procedure E using acrylate **5a** (250 μmol, 67.0 mg) and enal **1k** (750 μmol, 109 mg, 126 μL), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) afforded product **6k** as a pale yellow oil (87.0 mg, 85% yield) in a 1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 94:6 for *diastereomer 1* by UPC[2] analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 85% CO_2 in CH_3CN for 8 min, 85% CO_2 in CH_3CN for 4 min, gradient 85% - 100% CO_2 in CH_3CN for 2 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 4.75 min, τ_{Minor} = 4.40 min, and 88.5:11.5 for *diastereomer 2* by UPC[2] analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 80% CO_2 in CH_3CN for 5 min, 80% CO_2 in CH_3CN for 2 min, gradient 80% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 8.15 min, τ_{Minor} = 7.80 min.

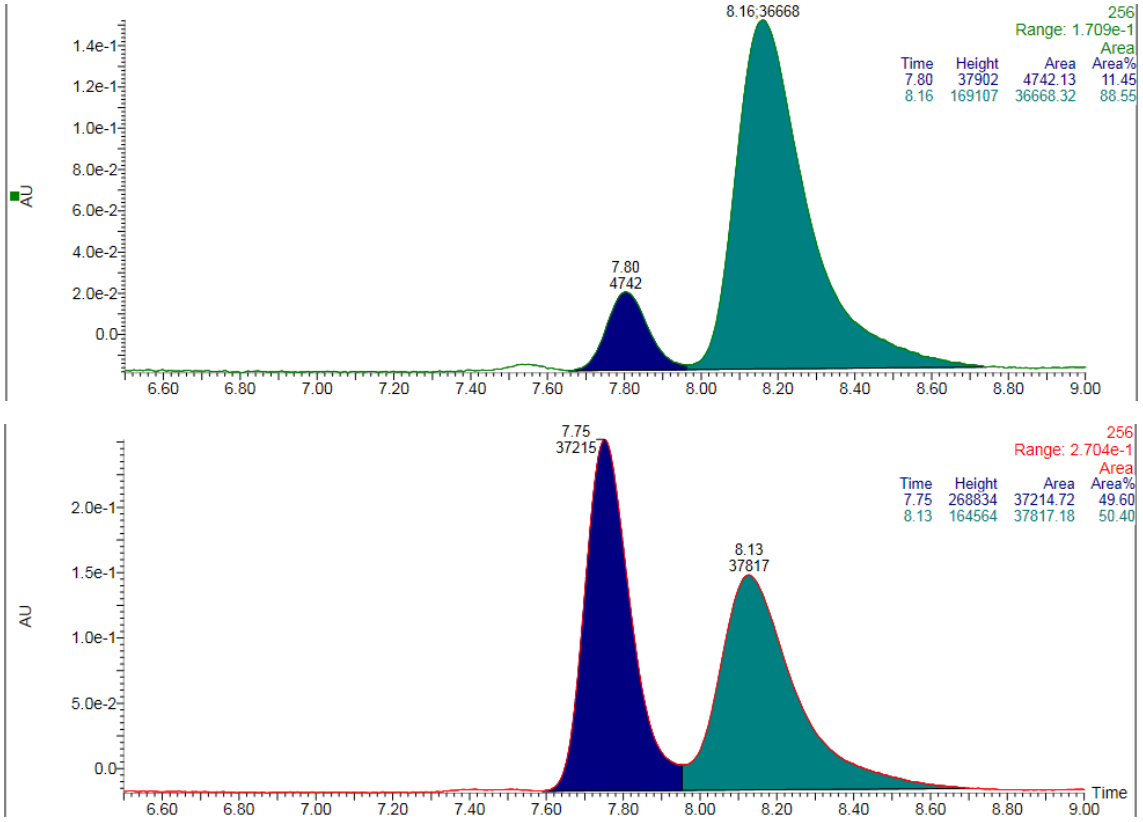
$[\alpha]_D^{26}$ = -5.6 (c = 1.0, $CHCl_3$, 1:1 d.r., 94:6 e.r.[1], 88.5:11.5 e.r.[2]).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.63 (t, *J* = 2.3 Hz, 1H), 9.60 (t, *J* = 2.2 Hz, 1H), 7.34 – 7.25 (m, 10H), 7.22 – 7.17 (m, 4H), 6.86 – 6.82 (m, 4H), 5.40 – 5.30 (m, 2H), 5.27 – 5.15 (m, 2H), 5.09 (d, *J* = 12.0 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.97 (d, *J* = 12.0 Hz, 1H), 3.79 (s, 6H), 3.70 – 3.64 (m, 2H), 2.37 – 2.27 (m, 4H), 2.20 – 2.14 (m, 1H), 2.09 – 2.05 (m, 1H), 2.01 – 1.93 (m, 8H), 1.90 – 1.84 (m, 3H), 1.81 – 1.75 (m, 1H), 1.45 – 1.38 (m, 2H), 1.37 – 1.30 (m, 2H), 0.94 (td, *J* = 7.5, 1.7 Hz, 6H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.5, 202.3, 173.7 (2C), 159.7 (2C), 138.8, 138.7, 132.4 (2C), 130.0, 130.0, 128.9, 128.8, 128.2, 128.2, 128.1 (2C), 128.0 (2C), 127.5 (2C), 114.0 (2C), 66.6 (2C), 55.4 (2C), 49.4, 49.3, 48.1, 48.1, 37.9, 37.9, 34.1, 33.9, 30.8, 30.7, 24.1, 24.0, 20.6 (2C), 14.4 (2C) ppm.

HRMS (ESI): m/z calculated for $[C_{26}H_{32}O_4Na]^+$ $[M+Na]^+$: 431.2193; found: 431.2192.

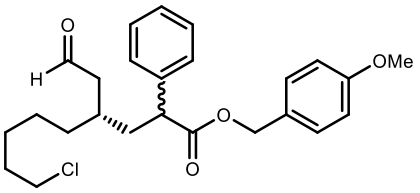


Supplementary Figure 50: UPC^2 traces of **6k**, diastereomer 1.



Supplementary Figure 51: UPC^2 traces of **6k**, diastereomer 2

4-Methoxybenzyl (*S*)-10-chloro-4-(2-oxoethyl)-2-phenyldecanoate (**6l**)



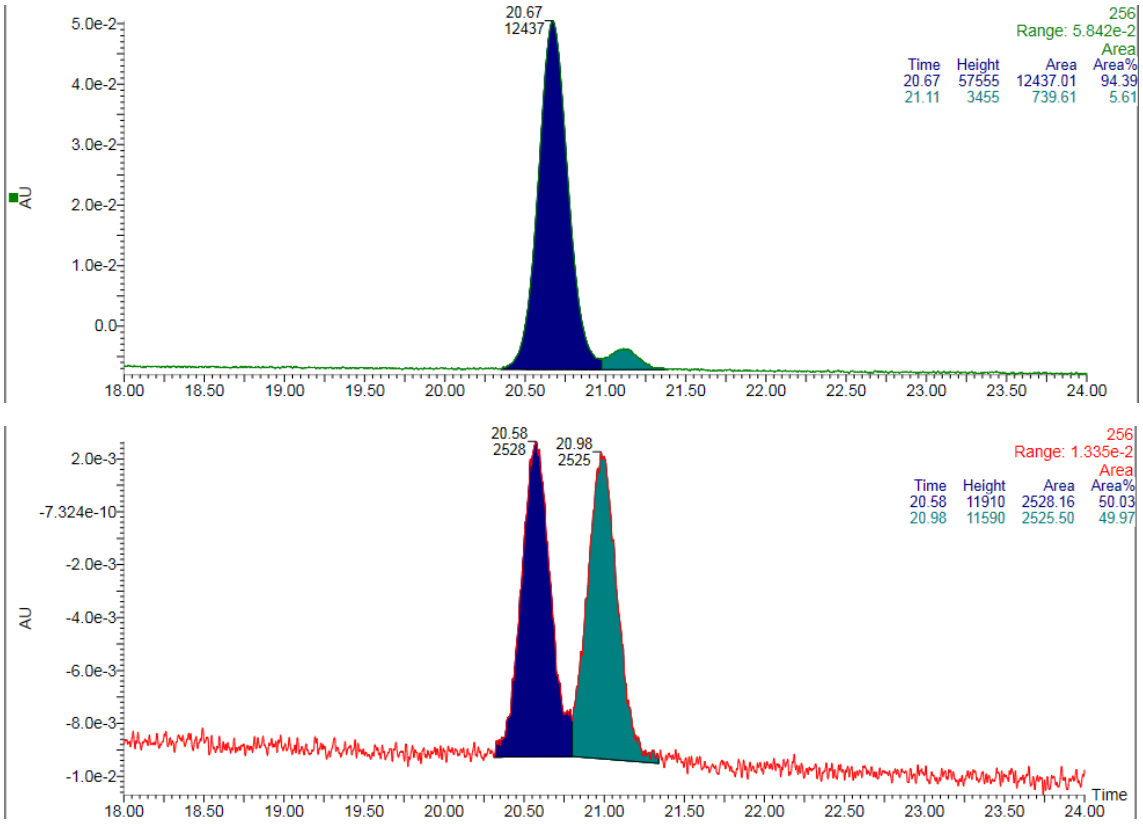
Chemical Formula: $C_{25}H_{31}ClO_4$
Molecular Weight: 430.97

Following the general procedure E using acrylate **5a** (250 μmol, 67.0 mg) and enal **1s** (750 μmol, 52.5 mg, 61.6 μL), purification of the crude product by flash column chromatography (silica gel, 10-20% EtOAc in hexanes) afforded product **6l** as a pale yellow oil (70.5 mg, 65% yield) in a 1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate drivative, prepared following the general procedure, was determined to be 94.5:5.5 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 80% CO_2 in MeOH for 20 min, 80% CO_2 in MeOH for 8 min, gradient 85% - 100% CO_2 in MeOH for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 20.65 min, τ_{Minor} = 21.10 min, and 86:14 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 90% CO_2 in CH_3CN for 5 min, 90% CO_2 in CH_3CN for 2 min, gradient 90% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 6.80 min, τ_{Minor} = 6.50 min.

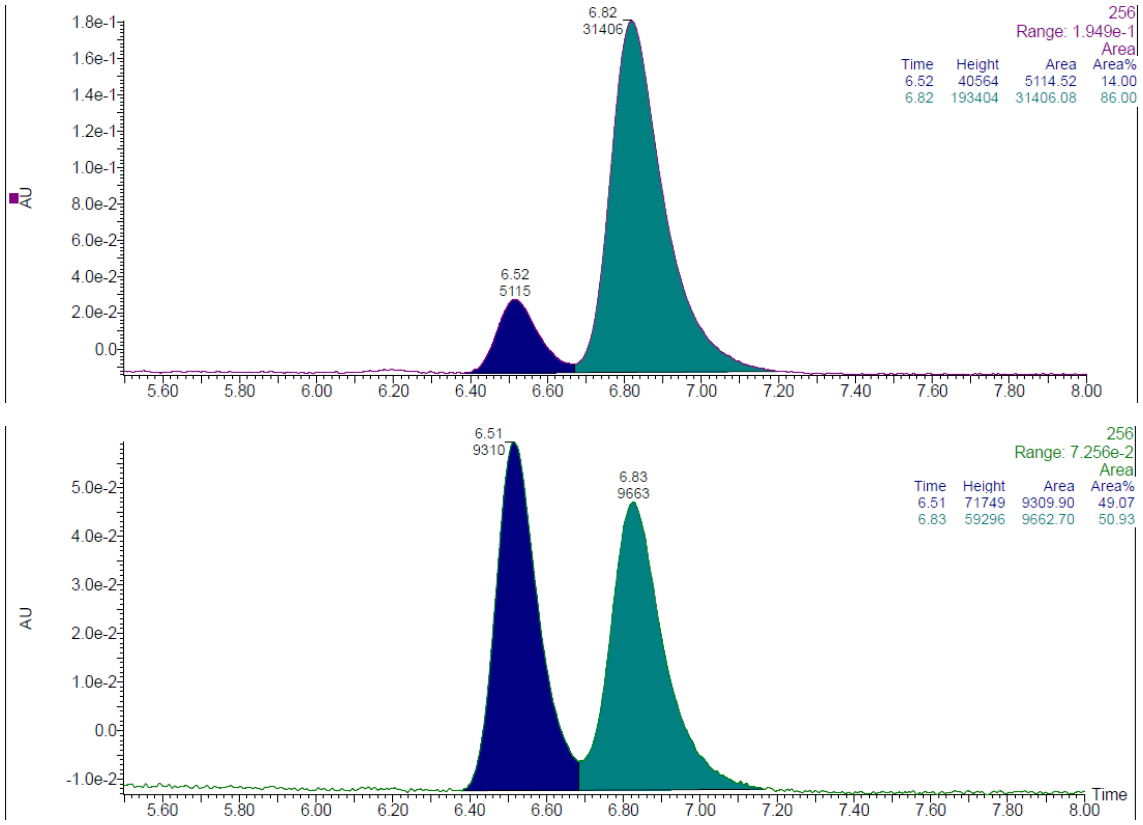
$[\alpha]_D^{26}$ = -3.6 (c = 1.0, $CHCl_3$, 1:1 d.r., 94.5:5.5 e.r.[1], 86:14 e.r.[2]).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.63 (t, *J* = 2.3 Hz, 1H), 9.61 (t, *J* = 2.1 Hz, 1H), 7.34 – 7.24 (m, 10H), 7.22 – 7.16 (m, 4H), 6.87 – 6.80 (m, 4H), 5.09 (d, *J* = 12.0 Hz, 1H), 5.08 (d, *J* = 12.0 Hz, 1H), 4.98 (d, *J* = 12.1 Hz, 2H), 3.79 (s, 6H), 3.69 – 3.61 (m, 2H), 3.50 (t, *J* = 6.7 Hz, 2H), 3.48 (t, *J* = 6.7 Hz, 2H), 2.38 – 2.26 (m, 4H), 2.16 (ddd, *J* = 13.7, 8.4, 6.4 Hz, 1H), 2.07 – 1.99 (m, 1H), 1.90 – 1.81 (m, 3H), 1.76 – 1.67 (m, 5H), 1.37 – 1.23 (m, 12H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.4, 202.3, 173.7, 173.6, 159.7 (2C), 138.7, 138.7, 130.1 (2C), 128.9, 128.9, 128.1, 128.0, 128.0 (2C), 127.6, 127.6, 114.0 (2C), 66.6 (2C), 55.4 (2C), 49.4, 49.4, 48.3, 48.2, 45.1, 45.0, 37.9 (2C), 33.9, 33.8, 32.5 (2C), 30.9 (2C), 27.1, 27.0, 25.7, 25.7 ppm.

HRMS (ESI): m/z calculated for $[C_{26}H_{31}ClO_4Na]^+$ $[M+Na]^+$: 453.1803; found: 453.1796.

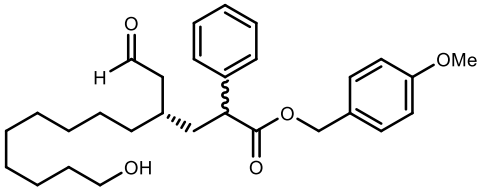


Supplementary Figure 52: UPC^2 traces of **6l**, diastereomer 1



Supplementary Figure 53: UPC^2 traces of **6l**, diastereomer 2

4-Methoxybenzyl (*S*)-13-hydroxy-4-(2-oxoethyl)-2-phenyltridecanoate (**6m**)



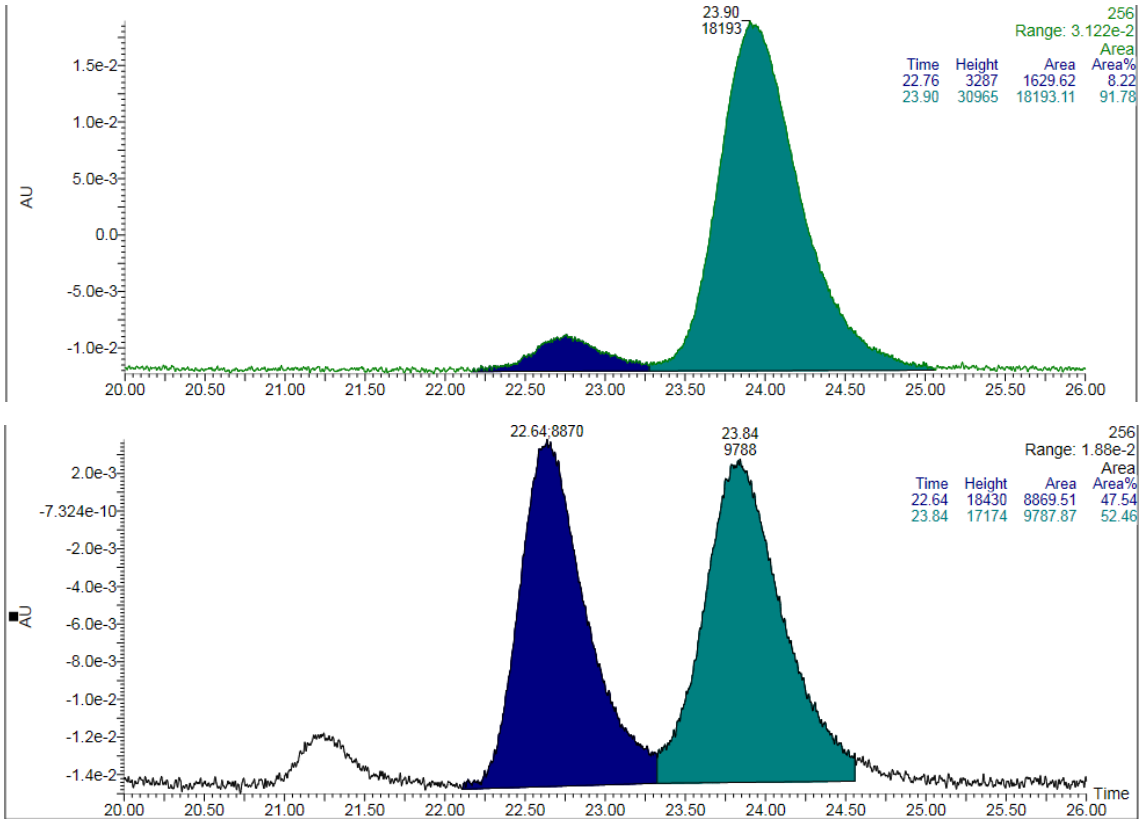
Chemical Formula: $C_{29}H_{40}O_5$
Molecular Weight: 468.63

Following the general procedure **E** using acrylate **5a** (250 μmol, 67.0 mg) and enal **1q** (750 μmol, 153 mg), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) afforded product **6m** as a pale yellow oil (84.0 mg, 71% yield) in a 1.1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 92:8 for *diastereomer 1* by UPC[2] analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 10% CO_2 in CH_3CN for 19 min, 10% CO_2 in CH_3CN for 6 min, gradient 10% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 23.90 min, τ_{Minor} = 22.75 min, and 81.5:18.5 for *diastereomer 2* by UPC[2] analysis on a Daicel Chiralpak OJ-3 column eluent: 100% CO_2 for 1 min, gradient 100% - 10% CO_2 in CH_3CN for 19 min, 10% CO_2 in CH_3CN for 6 min, gradient 10% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 25.60 min, τ_{Minor} = 23.80 min.

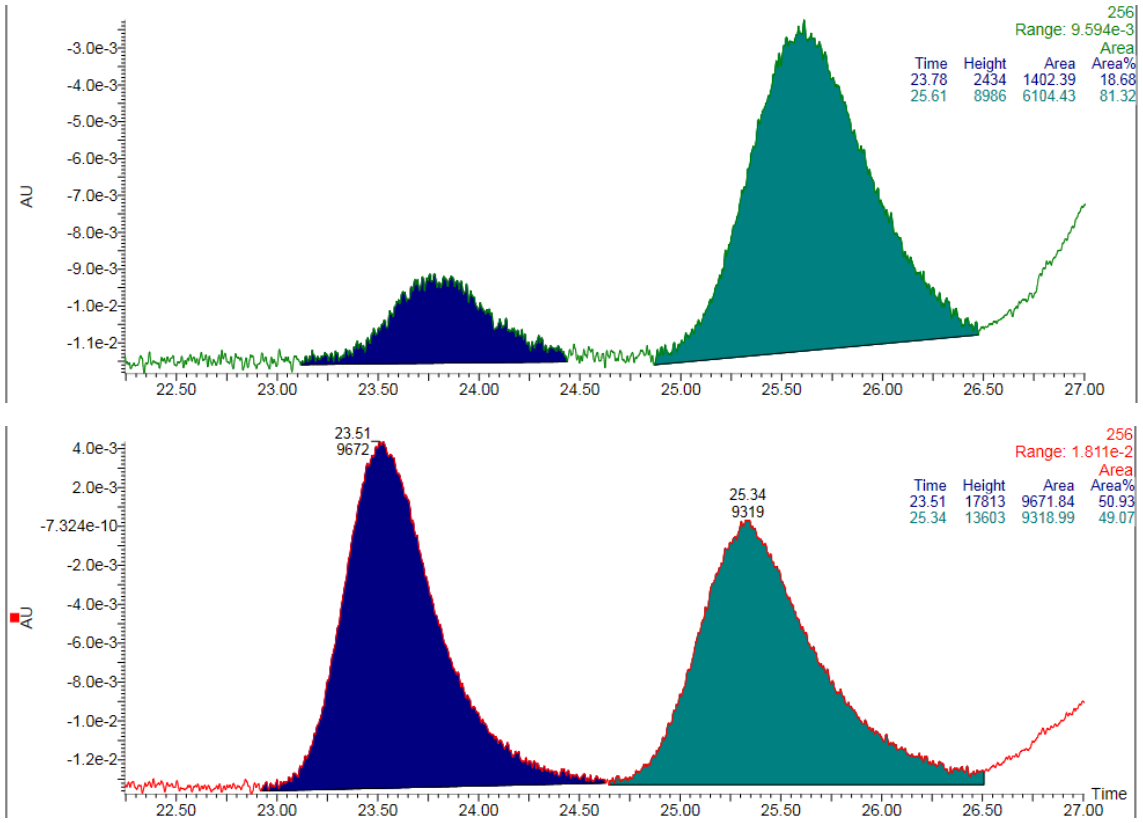
$[\alpha]_D^{26}$ = -4.8 (c = 1.0, $CHCl_3$, 1,1:1 d.r., 92:8 e.r.[1], 81.5:18.5 e.r.[2])

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.62 (t, *J* = 2.4 Hz, 1H), 9.60 (t, *J* = 2.2 Hz, 1H), 7.34 – 7.24 (m, 10H), 7.21 – 7.15 (m, 4H), 6.87 – 6.80 (m, 4H), 5.08 (d, *J* = 12.0 Hz, 2H), 4.98 (d, *J* = 12.1 Hz, 1H), 4.97 (d, *J* = 12.1 Hz, 1H), 3.79 (s, 6H), 3.69 – 3.63 (m, 2H), 3.63 (td, *J* = 6.7, 1.2 Hz, 4H), 2.35 – 2.26 (m, 4H), 2.19 – 2.10 (m, 1H), 2.06 – 2.01 (m, 1H), 1.89 – 1.80 (m, 3H), 1.77 – 1.71 (m, 1H), 1.60 (bs, 2H), 1.63 – 1.52 (m, 4H), 1.34 – 1.17 (m, 28H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.8, 202.6, 173.8, 173.7, 159.7 (2C), 138.8, 138.8, 130.0, 130.0, 128.9, 128.8, 128.1 (2C), 128.1 (2C), 127.5 (2C), 114.0, 113.9, 66.6 (2C), 63.2 (2C), 55.4 (2C), 49.4, 49.4, 48.3, 48.3, 38.0 (2C), 34.1, 33.9, 32.9 (2C), 31.1, 31.0, 29.8, 29.7, 29.6 (2C), 29.5 (2C), 29.5 (2C), 26.4, 26.3, 25.8 (2C) ppm.

HRMS (ESI): m/z calculated for $[C_{29}H_{40}O_5Na]^+$ $[M+Na]^+$: 491.2768; found: 491.2768.

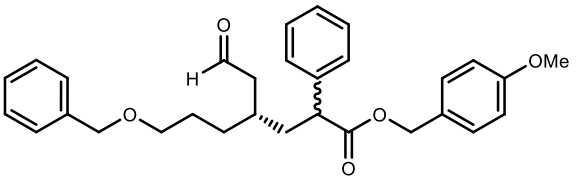


Supplementary Figure 54: UPC^2 traces of **6m**, diastereomer 1



Supplementary Figure 55: UPC^2 traces of **6m**, diastereomer 2.

4-Methoxybenzyl (*S*)-7-(benzyloxy)-4-(2-oxoethyl)-2-phenylheptanoate (**6n**)



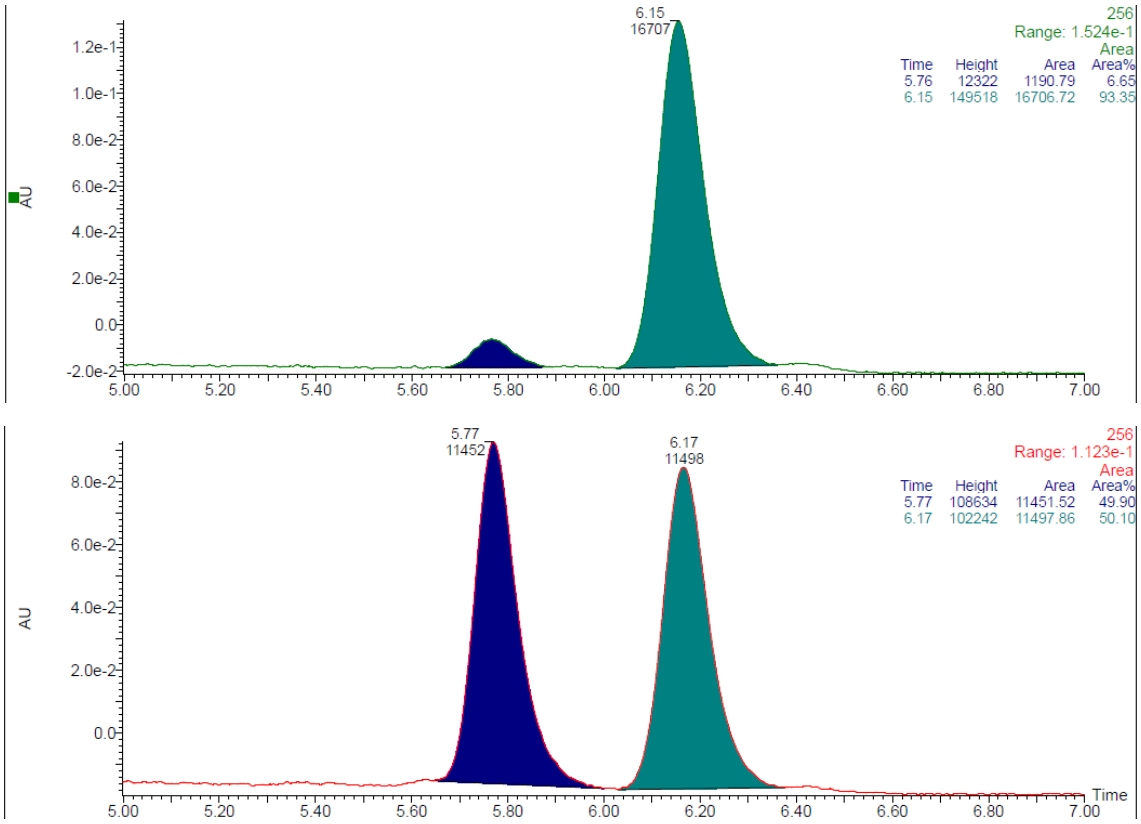
Chemical Formula: $C_{30}H_{34}O_5$
Molecular Weight: 474.60

Following the general procedure E using acrylate **5a** (250 μmol, 67.0 mg) and enal **1n** (750 μmol, 153 mg), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) afforded product **6n** as a pale yellow oil (84.0 mg, 71% yield) in a 1.1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 93.5:6.5 for *diastereomer 1* by UPC[2] analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 75% CO_2 in CH_3CN for 8 min, 75% CO_2 in CH_3CN for 4 min, gradient 75% - 100% CO_2 in CH_3CN for 2 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 6.15 min, τ_{Minor} = 5.75 min, and 83.5:16.5 for *diastereomer 2* by UPC[2] analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 6.95 min, τ_{Minor} = 6.70 min.

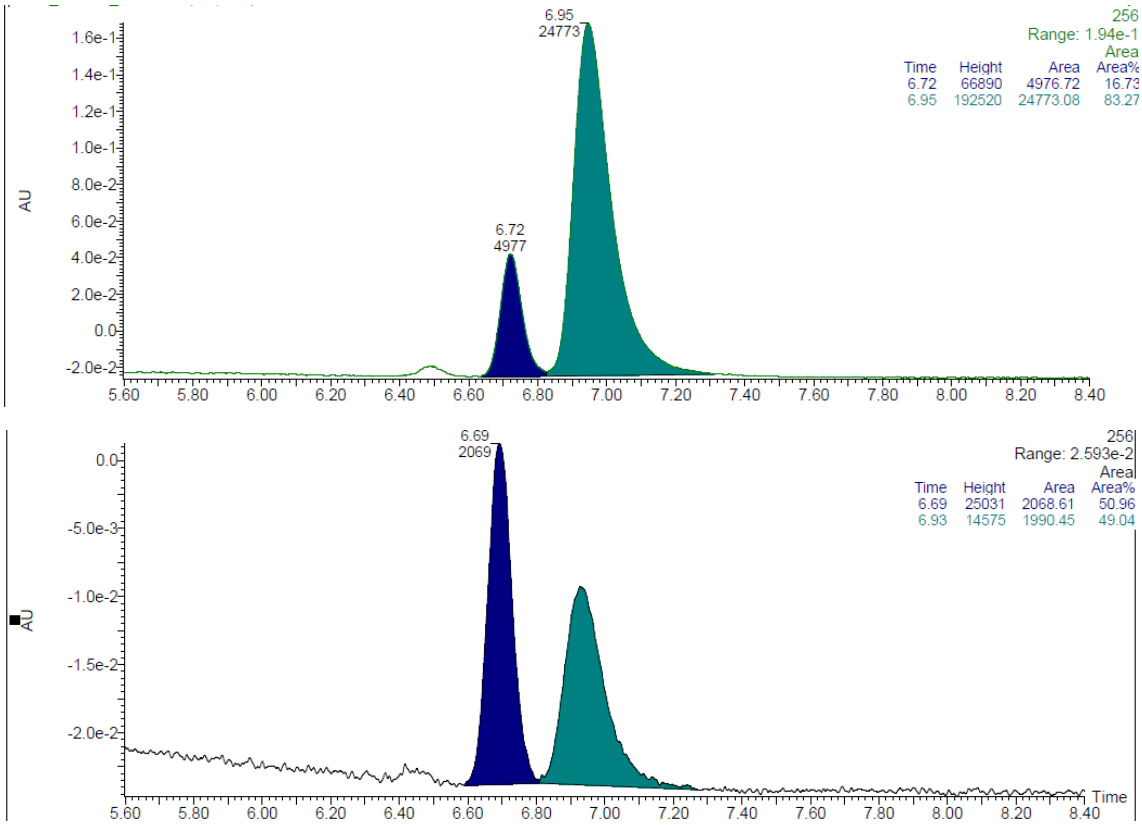
$[\alpha]_D^{26}$ = -3.2 (c = 1.0, $CHCl_3$, 1.1:1 d.r., 93.5:6.5 e.r.[1], 83.5:16.5 e.r.[2]).

^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.63 (t, *J* = 2.3 Hz, 1H), 9.61 (t, *J* = 2.1 Hz, 1H), 7.40 – 7.22 (m, 20H), 7.22 – 7.15 (m, 4H), 6.90 – 6.80 (m, 4H), 5.08 (d, *J* = 12.1 Hz, 1H), 5.08 (d, *J* = 12.1 Hz, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.98 (d, *J* = 12.0 Hz, 1H), 4.48 (s, 2H), 4.45 (s, 2H), 3.79 (s, 3H), 3.79 (s, 3H), 3.71 – 3.64 (m, 2H), 3.42 (t, *J* = 6.3 Hz, 2H), 3.38 (t, *J* = 6.3 Hz, 2H), 2.39 – 2.28 (m, 4H), 2.20 – 2.01 (m, 2H), 1.94 – 1.82 (m, 3H), 1.81 – 1.74 (m, 1H), 1.59 – 1.37 (m, 8H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.4, 202.3, 173.7, 173.7, 159.7 (2C), 138.7, 138.7, 138.6, 138.6, 130.0 (2C), 128.7, 128.8, 128.5 (2C), 128.1 (2C), 128.1 (2C), 127.8, 127.7, 127.7 (2C), 127.6 (2C), 114.0 (2C), 73.1, 73.0, 70.3, 70.3, 66.6 (2C), 55.4 (2C), 49.4, 49.3, 48.2 (2C), 37.8, 37.8, 30.9, 30.7, 30.6, 30.4, 26.7, 26.6 ppm.

HRMS (ESI): m/z calculated for $[C_{30}H_{34}O_5Na]^+$ $[M+Na]^+$: 497.2298; found: 497.2295.

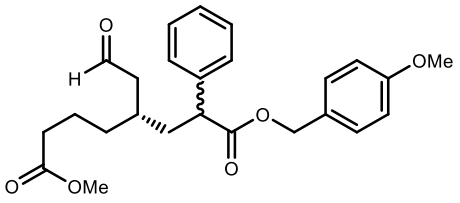


Supplementary Figure 56: UPC^2 traces of **6n**, diastereomer 1.



Supplementary Figure 57: UPC^2 traces of **6n**, diastereomer 2

1-(4-Methoxybenzyl) 8-methyl (*S*)-4-(2-oxoethyl)-2-phenyloctanedioate (6o)



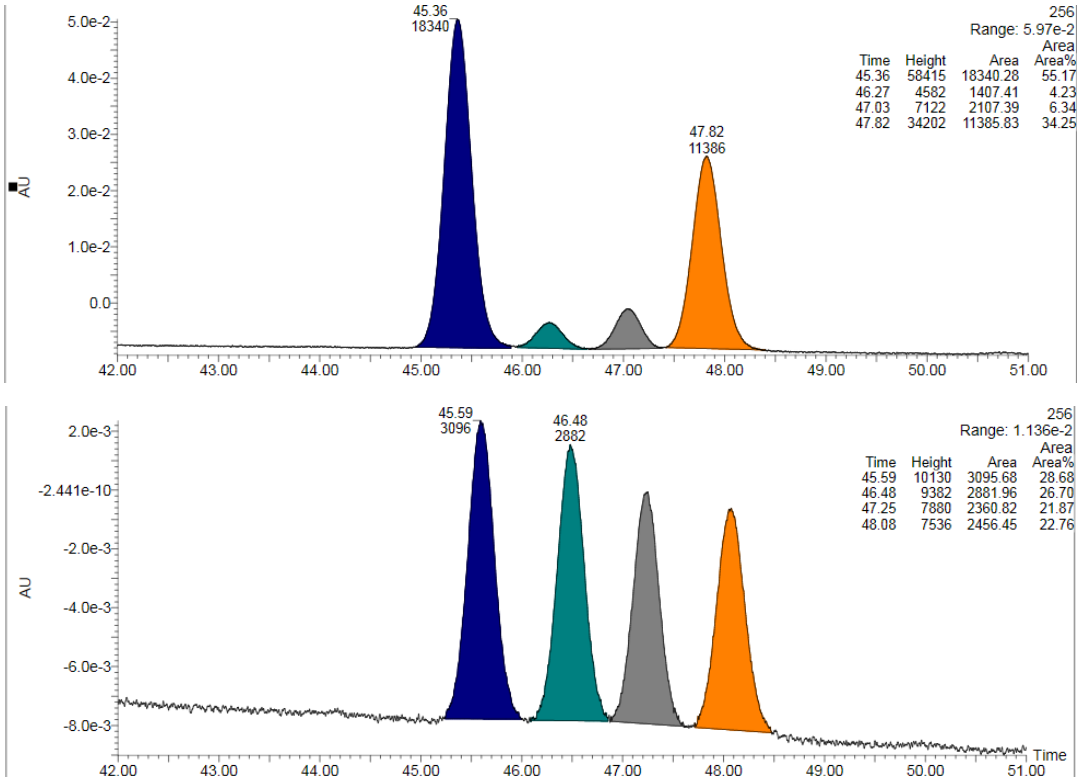
Chemical Formula: $C_{25}H_{30}O_6$
Molecular Weight: 426.51

Following the general procedure E using acrylate **5a** (250 µmol, 67.0 mg) and enal **1o** (750 µmol, 117 mg), purification of the crude product by flash column chromatography (silica gel, 5-10% EtOAc in hexanes) afforded product **6o** as a pale yellow oil (62.0 mg, 58% yield) in a 1.2:1 diastereomeric ratio. The enantiomeric ratio was determined to be 93:7 for *diastereomer 1* and 85:15 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak IA-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 75% CO_2 in iPrOH for 49 min, 75% CO_2 in iPrOH for 10 min, gradient 75% - 100% CO_2 in iPrOH for 1 min; flow rate 2.0 mL/min, λ = 256 nm) τ_{Major} = 45.35 min, τ_{Minor} = 46.25 min for *diastereomer 1*, and τ_{Major} = 47.80 min, τ_{Minor} = 47.05 min for *diastereomer 2*.

$[\alpha]_D^{26}$ = -4.8 (c = 1.0, $CHCl_3$, 1.2:1 d.r., 93:7 e.r.[1], 85:15 e.r.[2]).

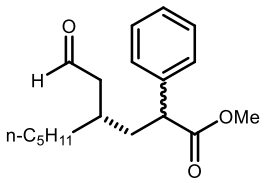
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.63 (t, J = 2.2 Hz, 1H), 9.61 (t, J = 2.0 Hz, 1H), 7.34 – 7.22 (m, 10H), 7.21 – 7.16 (m, 4H), 6.87 – 6.79 (m, 4H), 5.08 (d, J = 12.1 Hz, 2H), 4.97 (d, J = 12.0 Hz, 1H), 4.97 (d, J = 12.0 Hz, 1H), 3.79 (s, 6H), 3.67 – 3.62 (m, 8H), 2.37 – 2.30 (m, 4H), 2.27 – 2.18 (m, 4H), 2.16 – 2.11 (m, 1H), 2.07 – 2.03 (m, 1H), 1.90 – 1.82 (m, 3H), 1.79 – 1.73 (m, 1H), 1.60 – 1.50 (m, 4H), 1.37 – 1.27 (m, 4H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.2, 202.0, 173.8, 173.8, 173.6 (2C), 159.7 (2C), 138.7, 138.6, 130.1 (2C), 128.9, 128.9, 128.1, 128.0, 128.0 (2C), 127.6 (2C), 114.0 (2C), 66.6 (2C), 55.4 (2C), 51.6 (2C), 49.4, 49.3, 48.0 (2C), 37.7, 37.7, 34.0, 34.0, 33.4, 33.2, 30.8, 30.6, 21.7, 21.7 ppm.

HRMS (ESI): m/z calculated for $[C_{25}H_{30}O_6Na]^+$ $[M+Na]^+$: 449.1935; found: 449.1936.



Supplementary Figure 58: UPC^2 traces of **6o**, mixture of diastereomers.

Methyl (*4S*)-phenyl-4-(2-oxoethyl)nonanoate (**6p**)

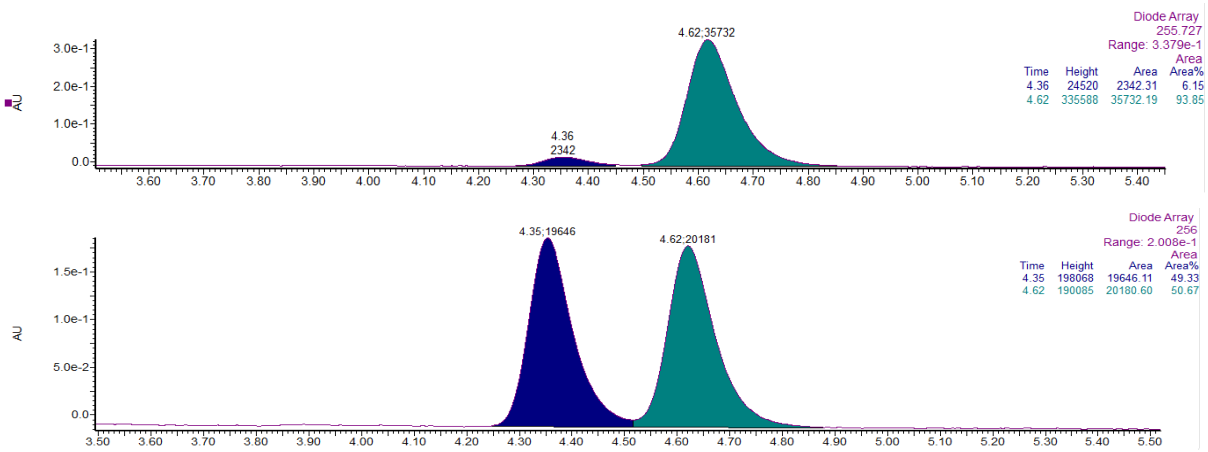


Chemical Formula: $C_{18}H_{26}O_3$
Molecular Weight: 290,4030

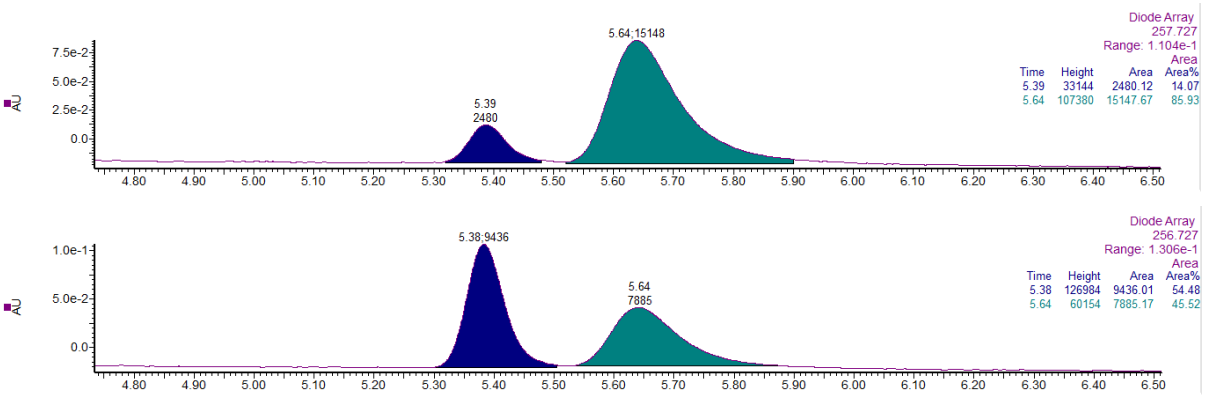
Prepared according to the general procedure **E** using octenal **1a** (112 µL, 750 µmol) and acrylate **5b** (40.5 mg, 250 µmol), the crude product was purified by flash column chromatography (silica, 5% EtOAc in n-hexanes) to obtain product **6p** as a colorless oil (54.0 mg, 75% yield) in a 1.2:1 diastereomeric ratio. Analytical data is in agreement with the literature.[29] The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 94:6 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 85% CO_2 in CH_3CN for 11 min, 85% CO_2 in CH_3CN for 2 min, gradient 85% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 258 nm, τ_{Major} = 4.60 min, τ_{Minor} = 4.35 min.), and 86.0:14.0 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm, τ_{Major} = 5.65 min, τ_{Minor} = 5.40 min)

$[\alpha]_D^{24}$ = -148.1 (c = 0.5, $CHCl_3$, 1.2:1 d.r., 94:6 e.r.[1], 86:14 e.r.[2]).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.72 (t, *J* = 2.3 Hz, 1H), 9.69 (t, *J* = 2.2 Hz, 1H), 7.47 – 7.18 (m, 10H), 3.68 (s, 6H), 2.40 – 2.34 (m, 4H), 2.19 – 2.14 (m, 2H), 2.07 – 2.02 (m, 2H), 1.94 – 1.84 (m, 4H), 1.81 – 1.75 (m, 2H), 1.47 – 1.09 (m, 14H), 0.98 – 0.76 (m, 6H) ppm.

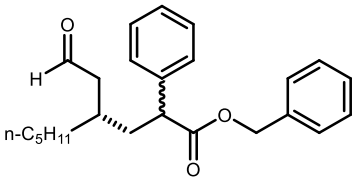


Supplementary Figure 59: UPC^2 Traces of **6p**, diastereomer 1.



Supplementary Figure 60: UPC^2 Traces of **6p**, diastereomer 2.

Benzyl (*4S*)-phenyl-4-(2-oxoethyl)nonanoate (6q)

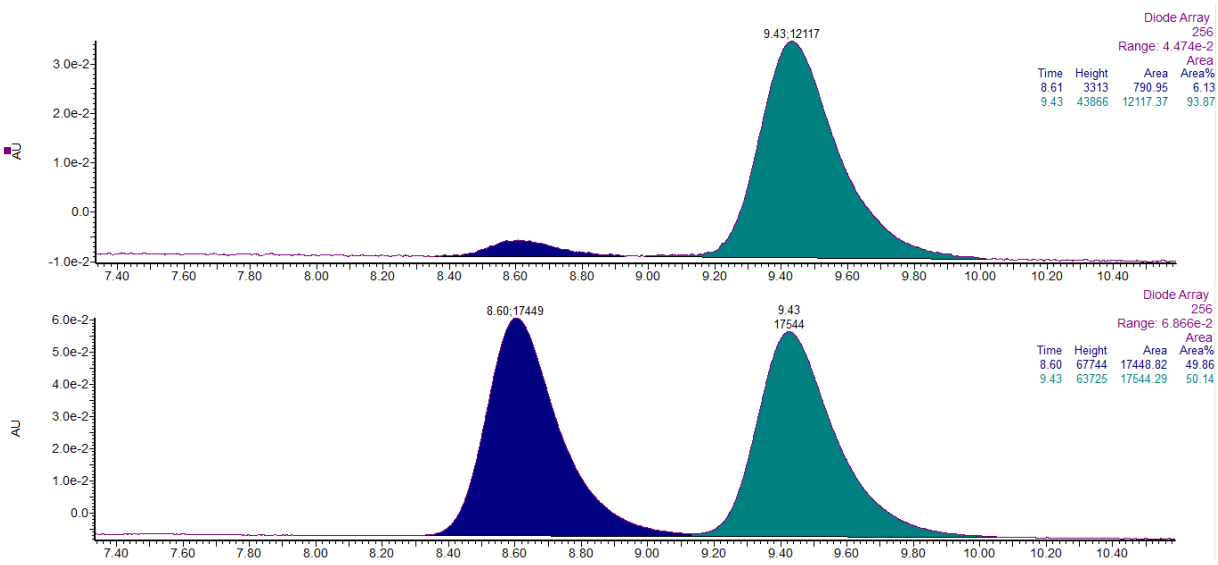


Chemical Formula: $C_{24}H_{30}O_3$
Molecular Weight: 366,5010

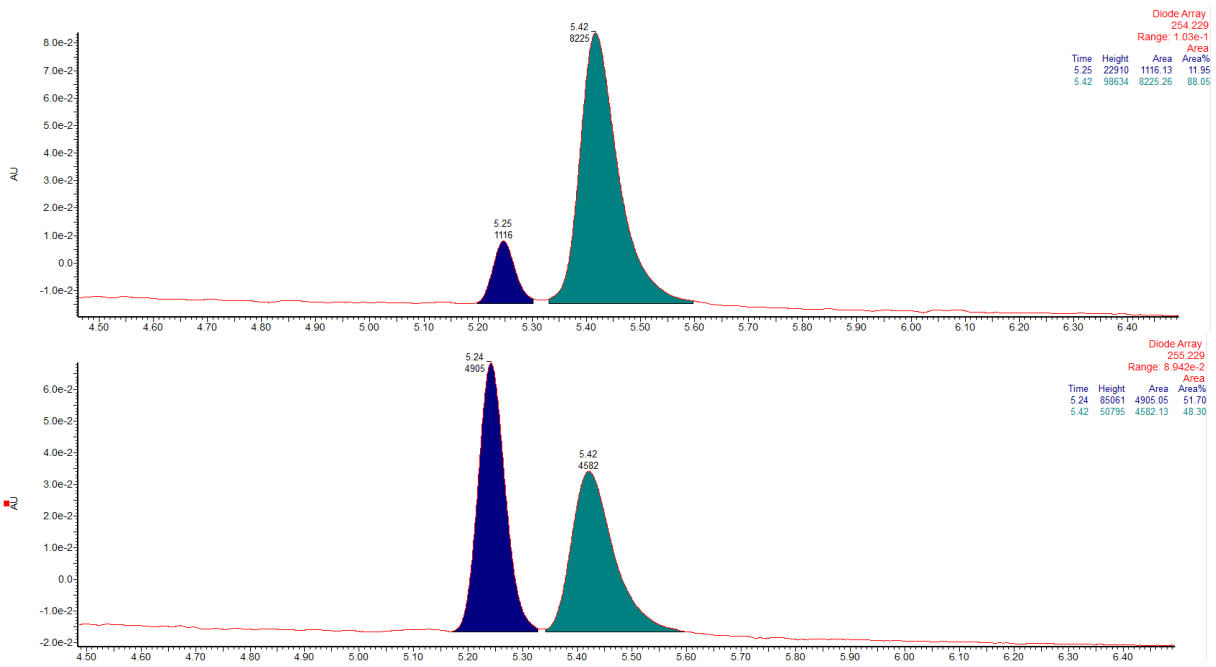
Prepared according to the general procedure **E** using octenal **1a** (46.0 µL, 300 µmol) and acrylate **5c** (23.8 mg, 100 µmol), the crude product was purified by flash column chromatography (silica, 5% EtOAc in n-hexanes) to obtain product **6q** as a colorless oil (33.0 mg, 89% yield) in a 1.1:1 diastereomeric ratio. Analytical data is in agreement with the literature.[29] The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 94:6 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 93% CO_2 in CH_3CN for 11 min, 93% CO_2 in CH_3CN for 2 min, gradient 93% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 254 nm, τ_{Major} = 9.40 min, τ_{Minor} = 8.60 min.), and 88:12 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in CH_3CN for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 254 nm, τ_{Major} = 5.40 min, τ_{Minor} = 5.25 min.)

$[\alpha]_D^{24}$ = -118.3 (c = 0.5, $CHCl_3$, 1.1:1 d.r., 94:6 e.r.[1], 88:12 e.r.[2]).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.66 (t, *J* = 2.3 Hz, 1H), 9.64 (t, *J* = 2.2 Hz, 1H), 7.35 – 7.29 (m, 14H), 7.27 – 7.24 (m, 6H), 5.16 (d, *J* = 12.4 Hz, 2H), 5.08 (dd, *J* = 12.4, 2.4 Hz, 2H), 3.74 – 3.70 (m, 2H), 2.36 – 2.33 (m, 4H), 2.22 – 2.16 (m, 2H), 2.13 – 2.02 (m, 1H), 1.86 – 1.73 (m, 1H), 1.50 – 1.13 (m, 18H), 0.91 – 0.87 (m, 6H) ppm.



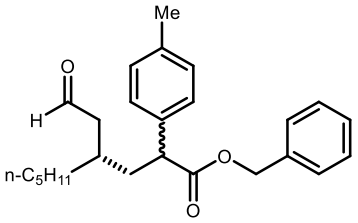
Supplementary Figure 61: UPC^2 Traces of **6q**, diastereomer 1.



Supplementary Figure 62: UPC^2 Traces of **6q**, diastereomer 2.

Benzyl (*4S*)-(4-methylphenyl)-4-(2-oxoethyl)nonanoate (**6r**)

Prepared according to the general procedure **E** using octenal **1a** (112 µL, 750 µmol) and acrylate **5d** (63.0 mg, 250 µmol), the crude product was purified by flash column chromatography (silica, 5% EtOAc in n-hexanes) to obtain product **6r** as a colorless oil (72.0 mg, 76% yield) in a 1.5:1 diastereomeric ratio. The enantiomeric ratio was determined to be 93.5:6.5 and 87.5:12.5 by HPLC analysis on a Daicel Chiralpak IC-3 column, isocratic 96:4 n-hexane: iPrOH, flow rate = 0.45 mL/min, 15 °C; λ = 215 nm. Diastereoisomer 1: τ_{Major} = 36.70 min, τ_{Minor} = 51.65 min. Diastereoisomer 2: τ_{Major} = 34.55 min, τ_{Minor} = 44.55 min.

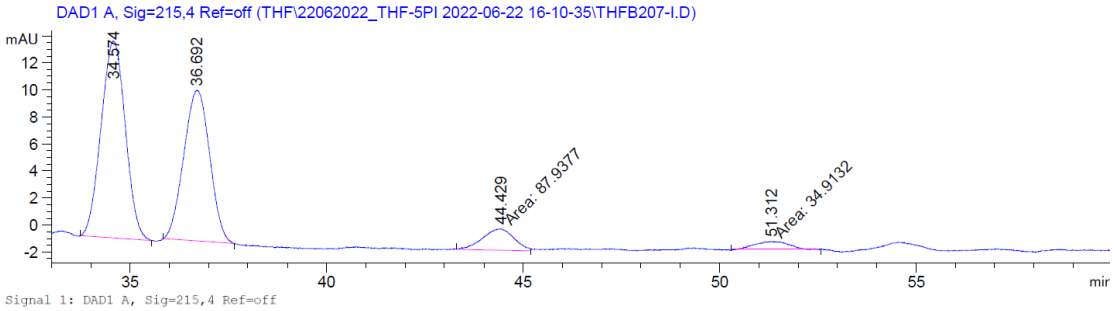


Chemical Formula: $C_{25}H_{32}O_3$
Molecular Weight: 380,5280

$[\alpha]_D^{25}$ = -4.5 (c = 0.5, $CHCl_3$, 1.5:1 d.r., 93.5:6.5 e.r.[1], 87.5:12.5 e.r.[2]).

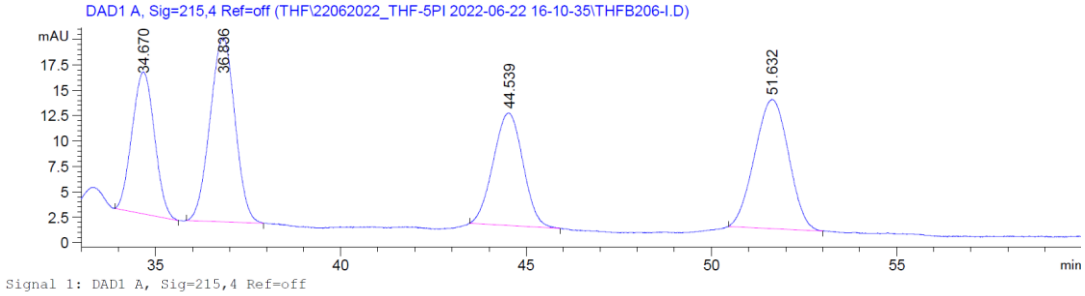
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.66 (t, *J* = 2.4 Hz, 1H), 9.63 (t, *J* = 2.2 Hz, 1H), 7.37 – 7.31 (m, 6H), 7.29 – 7.26 (m, 4H), 7.23 – 7.19 (m, 4H), 7.17 – 7.13 (m, 4H), 5.17 (d, *J* = 12.4 Hz, 2H), 5.07 (dd, *J* = 12.4, 2.0 Hz, 2H), 3.73 – 3.67 (m, 2H), 2.36 (s, 6H), 2.34 – 2.32 (m, 3H), 2.24 – 2.13 (m, 1H), 2.11 – 2.02 (m, 1H), 1.89 (m, 3H), 1.78 (dt, *J*=14.1, 7.1 Hz, 1H), 1.44 – 1.14 (m, 18H), 0.91 – 0.87 (m, 6H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.8, 202.7, 173.9, 173.8, 137.3 (2C), 136.0 (2C), 135.7 (2C), 129.6, 129.5, 128.6 (2C), 128.3, 128.2 (2C) 128.2, 128.0, 127.9, 66.7 (2C), 49.0 (2C), 48.3, 48.3 (2C), 37.9 (2C), 37.9, 34.1, 33.8, 32.1, 32.0, 31.1, 31.0, 26.1, 26.0, 22.87 (2C), 21.2 (2C), 14.2, 14.1 ppm.

HRMS (ESI): m/z calculated for $[C_{25}H_{32}O_3Na]^+$ $[M+Na]^+$: 403.2244, found: 403.2250.



Signal 1: DAD1 A, Sig=215,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.574	BB	0.5055	625.65411	14.58457	49.6997
2	36.692	BB	0.5425	510.36462	11.11967	40.5415
3	44.429	MM T	0.9238	87.93772	1.58644	6.9855
4	51.312	MM T	1.0061	34.91323	5.78369e-1	2.7734
Totals :				1258.86969	27.86904	

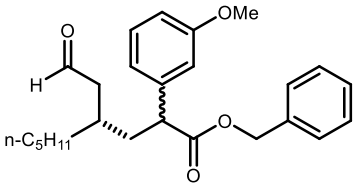


Signal 1: DAD1 A, Sig=215,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.670	BB	0.4946	586.74939	13.95324	20.4911
2	36.836	BB	0.5523	847.72852	18.10344	29.6052
3	44.539	BB	0.6597	617.29889	11.06796	21.5579
4	51.632	BB	0.7507	811.66351	12.71526	28.3457
Totals :				2863.44031	55.83989	

Supplementary Figure 63: HPLC Traces of **6r.**

Benzyl (*4S*)-(3-methoxyphenyl)-4-(2-oxoethyl)nonanoate (6s)



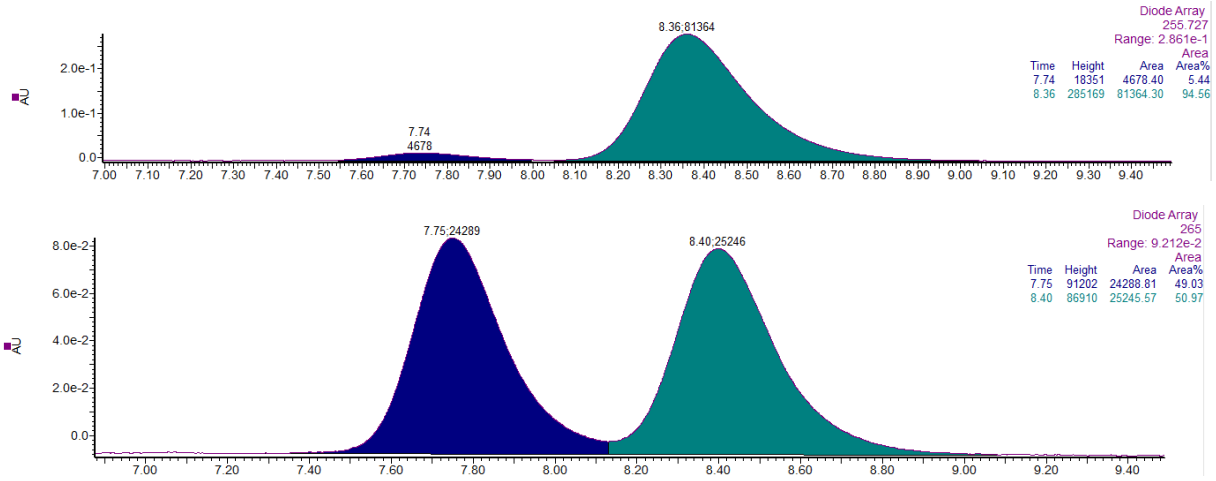
Chemical Formula: $C_{25}H_{32}O_4$
Molecular Weight: 396,5270

Prepared according to the general procedure E using octenal **1a** (112 µL, 750 µmol) and acrylate **5e** (67.0 mg, 250 µmol), the crude product was purified by flash column chromatography (silica, 5% EtOAc in n-hexanes) to obtain product **6s** as a colorless oil (83.5 mg, 85% yield) in a 1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 94.5:5.5 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 93% CO_2 in CH_3CN for 11 min, 93% CO_2 in CH_3CN for 2 min, gradient 93% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm, τ_{Major} = 8.35 min, τ_{Minor} = 7.75 min.), and 91:9 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 80% CO_2 in CH_3CN for 5 min, 80% CO_2 in CH_3CN for 2 min, gradient 80% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm, τ_{Major} = 8.20 min, τ_{Minor} = 7.85 min.)

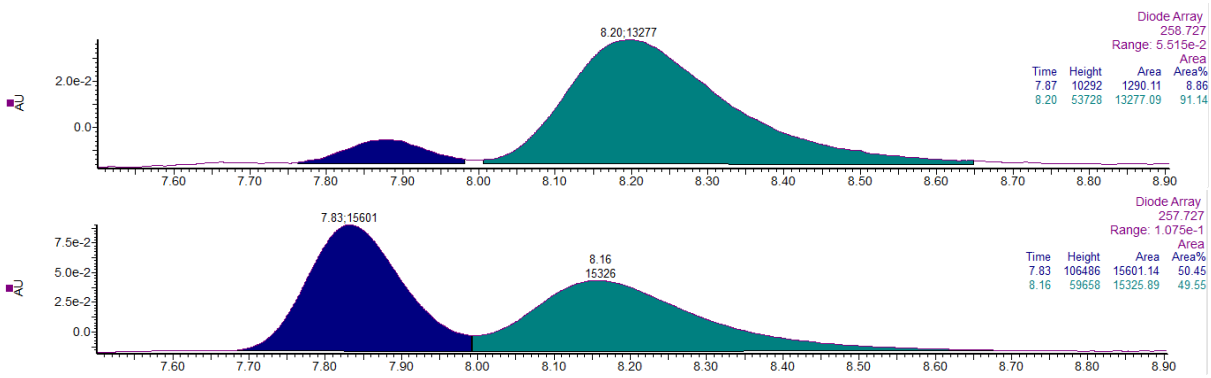
$[\alpha]_D^{24}$ = -83.1 (c = 1.0, $CHCl_3$, 1:1 d.r., 94.5:5.5 e.r.[1], 91:9 e.r.[2]).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.67 (t, *J* = 2.3 Hz, 1H), 9.64 (t, *J* = 2.2 Hz, 1H), 7.35 – 7.31 (m, 6H), 7.31 – 7.19 (m, 6H), 6.93 – 6.88 (m, 3H), 6.88 – 6.80 (m, 3H), 5.17 (d, *J* = 12.3 Hz, 2H), 5.09 (dd, *J* = 12.3, 2.3 Hz, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.75 – 3.65 (m, 2H), 2.39 – 2.30 (m, 4H), 2.17 (ddd, *J* = 13.7, 8.1, 6.7 Hz, 1H), 2.13 – 2.03 (m, 1H), 1.95 – 1.84 (m, 3H), 1.80 (dt, *J* = 14.0, 7.1 Hz, 1H), 1.47 – 1.15 (m, 18H), 0.92 – 0.86 (m, 6H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.7, 202.5, 173.5 (2C), 156.0, 159.9, 140.2, 140.2, 135.9 (2C), 129.8, 129.8, 128.6 (2C), 128.3 (2C), 128.2, 128.2, 120.5, 120.4, 113.6, 113.6, 113.1, 113.08, 66.7 (2C), 55.3 (2C), 49.4, 49.4, 48.3, 48.3, 37.9, 37.8, 34.0, 33.9, 32.0, 32.0, 31.1, 31.0, 26.1, 26.0, 22.6 (2C), 14.1, 14.1 ppm.

HRMS (ESI): m/z calculated for $[C_{25}H_{32}O_4Na]^+$ $[M+Na]^+$: 419.2193, found: 419.2181.

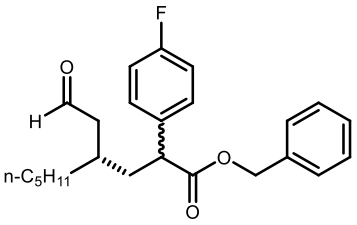


Supplementary Figure 64: UPC^2 Traces of **6s**, diastereomer 1.



Supplementary Figure 65: UPC^2 Traces of **6s**, diastereomer 2.

Benzyl (*4S*)-(4-fluorophenyl)-4-(2-oxoethyl)nonanoate (6t)



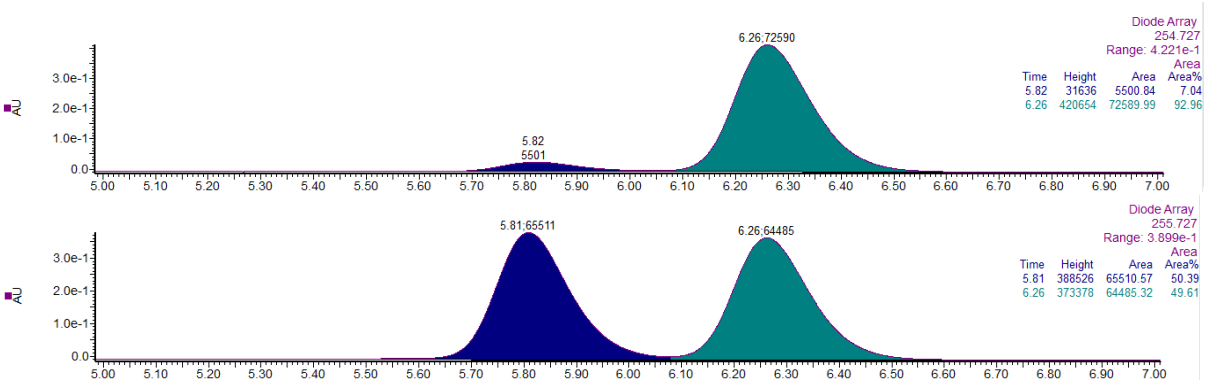
Chemical Formula: $C_{24}H_{29}FO_3$
Molecular Weight: 384,4914

Prepared according to the general procedure E using octenal **1a** (112 µL, 750 µmol) and acrylate **5f** (64.0 mg, 250 µmol), the crude product was purified by flash column chromatography (silica, 5% EtOAc in n-hexanes) to obtain **6t** as a colorless oil (85.0 mg, 89% yield) in a 1:1 diastereomeric ratio. The enantiomeric ratio of the corresponding 4-nitrobenzoate derivative, prepared following the general procedure, was determined to be 93:7 for *diastereomer 1* by UPC^2 analysis on a Daicel Chiralpak OJ-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 93% CO_2 in CH_3CN for 5 min, 93% CO_2 in CH_3CN for 2 min, gradient 93% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 255 nm, τ_{Major} = 6.25 min, τ_{Minor} = 5.80 min.), and 88:12 for *diastereomer 2* by UPC^2 analysis on a Daicel Chiralpak ID-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 80% CO_2 in CH_3CN for 5 min, 80% CO_2 in CH_3CN for 2 min, gradient 80% - 100% CO_2 in CH_3CN for 1 min; flow rate 2.0 mL/min, λ = 256 nm, τ_{Major} = 7.15 min, τ_{Minor} = 6.95 min).

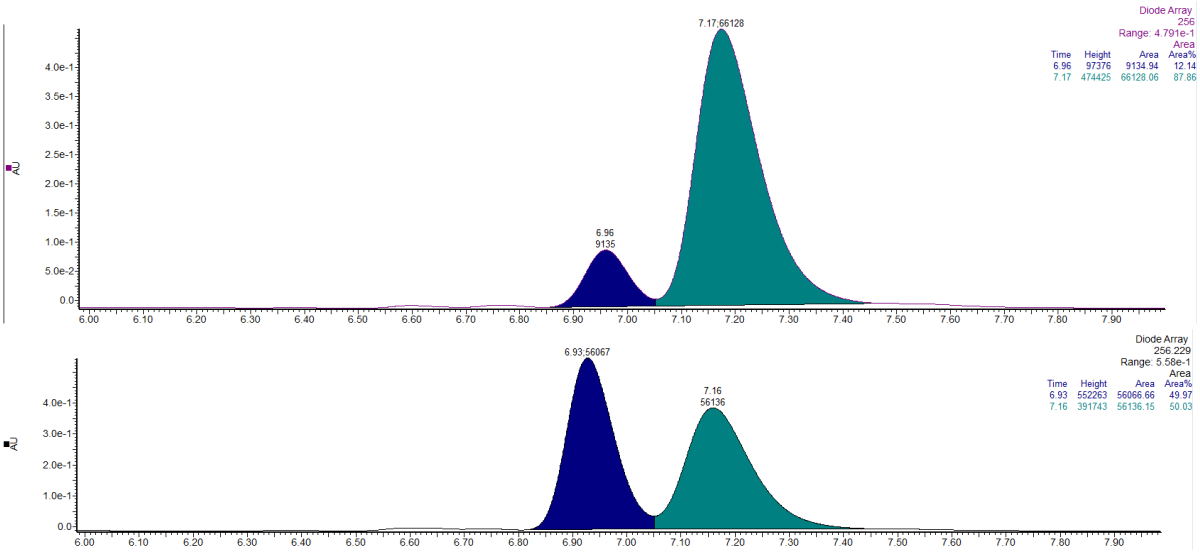
$[\alpha]_D^{24}$ = -87.9 (c = 1.0, $CHCl_3$, 1:1 d.r., 93:7 e.r.[1], 88:12 e.r.[2]).

^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers): δ = 9.67 (t, *J* = 2.3 Hz, 1H), 9.65 (t, *J* = 2.1 Hz, 1H), 7.35 – 7.21 (m, 14H), 7.03 (m, 4H), 5.16 (d, *J* = 12.3 Hz, 2H), 5.09 (dd, *J* = 12.3, 2.7 Hz, 2H), 3.76 – 3.69 (m, 2H), 2.37 – 2.28 (m, 4H), 2.20 – 2.09 (m, 1H), 2.10 – 2.00 (m, 1H), 1.89 – 1.82 (m, 3H), 1.77 (dt, *J*= 14.1, 7.1 Hz, 1H), 1.44 – 1.21 (m, 18H), 0.91 – 0.86 (m, 6H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = 202.5, 202.4, 173.7, 173.5, 162.3 (d, $J_{C\text{-}F}$ = 246.0 Hz, 2C), 135.8 (2C) 134.5 (d, $J_{C\text{-}F}$ = 3.3 Hz), 134.4 (d, $J_{C\text{-}F}$ = 3.2 Hz), 129.7 (d, $J_{C\text{-}F}$ = 7.8 Hz), 129.6 (d, $J_{C\text{-}F}$ = 7.8 Hz), 128.6 (2C), 128.4 (2C), 128.2, 128.2, 115.7 (d, $J_{C\text{-}F}$ = 21.5 Hz), 115.7 (d, $J_{C\text{-}F}$ = 21.3 Hz) 66.8 (2C), 48.6, 48.6, 48.3, 48.2, 38.1, 38.0, 34.1, 33.8, 32.0, 31.9, 31.0, 30.8, 26.1, 26.0, 22.6 (2C), 14.1, 14.1 ppm. **^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$, mixture of diastereoisomers):** δ = -115.04 (s), -115.07 (s) ppm.

HRMS (ESI): m/z calculated for $[C_{24}H_{29}FO_3Na]^+$ $[M+Na]^+$: 407.1993, found: 407.1997.



Supplementary Figure 66: UPC^2 Traces of **6t**, diastereomer 1.

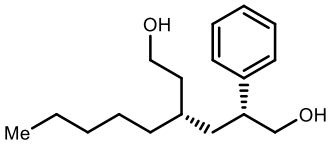


Supplementary Figure 67: UPC^2 Traces of **6t**, diastereomer 2.

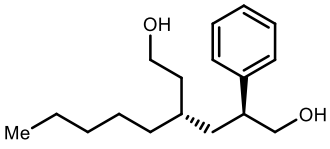
Derivatization of 1,6-Dicarbonyl Products

Separation of diastereomers

Lithium aluminium hydride (500 µmol, 19.0 mg, 2.0 equiv.) was added portion wise to a solution of **6a** (250 µmol, 99.0 mg, 1.0 equiv.) in anhydrous THF (1.0 mL) at 0 °C under an Argon atmosphere. The reaction mixture was allowed to warm to room temperature and was stirred for 3 h. The reaction mixture was then diluted with Et_2O (20 mL), cooled to 0 °C and carefully quenched by addition of Glauber's salt ($NaSO_4 \cdot 10\ H_2O$). After 10 min the solids were removed by filtration over a silica pad, which was thoroughly rinsed with EtOAc. The volatiles were removed under reduce pressure and the crude was purified by flash column chromatography (silica gel, 25-50% EtOAc in hexanes) to afford (2*R*,4*S*)-4-pentyl-2-phenylhexane-1,6-diol (**7a**, 25.0 mg, 38% yield, see x-ray analysis) and (2*S*,4*S*)-4-pentyl-2-phenylhexane-1,6-diol (**7b**, 21.0 mg, 32% yield) as colorless oils.



Chemical Formula: $C_{17}H_{28}O_2$
Molecular Weight: 264.41



Chemical Formula: $C_{17}H_{28}O_2$
Molecular Weight: 264.41

7a:

$[\alpha]_D^{26}$ = -34.1 (c = 1.0, $CHCl_3$, 93:7 e.r.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 – 7.28 (m, 2H), 7.25 – 7.17 (m, 3H), 3.75 – 3.64 (m, 2H), 3.59 – 3.51 (m, 2H), 2.93 – 2.84 (m, 1H), 1.62 – 1.56 (m, 2H), 1.56 – 1.47 (m, 2H), 1.47 – 1.37 (m, 2H), 1.32 – 1.15 (m, 7H), 0.87 (t, *J*=7.1 Hz, 3H) ppm. **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 142.6, 128.9, 128.2, 126.9, 68.1, 61.1, 46.4, 37.3, 36.5, 33.4, 32.4, 31.7, 25.7, 22.8, 14.2 ppm.

HRMS (ESI): m/z calculated for $[C_{17}H_{28}O_2Na]^+$ $[M+Na]^+$: 287.1982; found: 287.1972.

7b:

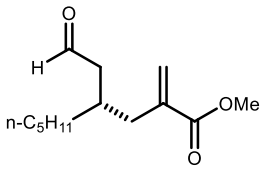
$[\alpha]_D^{26}$ = +6.6 (c = 1.0, $CHCl_3$, 84:16 e.r.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 – 7.28 (m, 2H), 7.27 – 7.17 (m, 3H), 3.71 (d, *J* = 6.6 Hz, 2H), 3.69 – 3.51 (m, 2H), 2.95 – 2.84 (m, 1H), 1.61 (t, *J* = 7.0 Hz, 2H), 1.59 – 1.45 (m, 2H), 1.39 – 1.09 (m, 9H), 0.85 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$):** δ = 142.8, 128.8, 128.2, 126.9, 68.0, 60.9, 46.2, 36.5, 36.3, 34.6, 32.2, 32.0, 26.2, 22.8, 14.2.

HRMS (ESI): m/z calculated for $[C_{17}H_{28}O_2Na]^+$ $[M+Na]^+$: 287.1982; found: 287.1973.

Organocatalytic Asymmetric Conjugate Allylation of Enals

Methyl (*S*)-2-methylene-4-(2-oxoethyl)nonanoate (9)



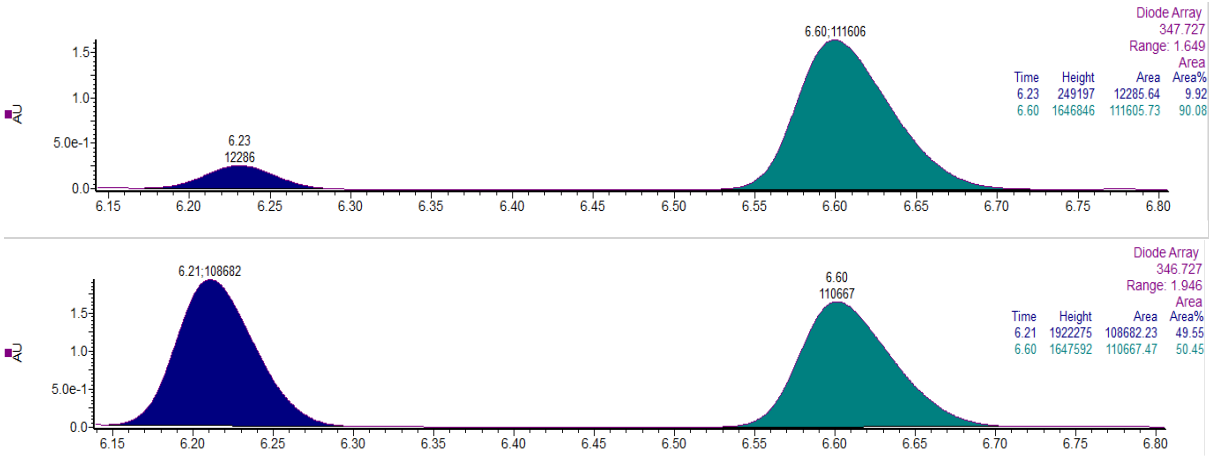
Chemical Formula: $C_{13}H_{22}O_3$
Molecular Weight: 226,3160

To a 8.0 mL argon-purged glass vial, containing acrylate **8** (24.0 mg, 100 µmol), octenal **1a** (59.6 µL, 400 µmol, 4.0 equiv.), DHP **R-1** (48.5 mg, 150 µmol, 1.5 equiv.), 4-CzIPN (1.0 mg, 1.0 µmol, 1 mol%) and amine catalyst **A-3** (14.0 mg, 20.0 µmol, 20 mol%), was added 200 µL of dimethoxyethane, H_2O (5.5 µL, 300 µmol, 3 equiv.) and trichloroacetic acid (3.0 µL 30.0 µmol, 30 mol%). The vial was sealed with Parafilm, and then placed into a cooled aluminium support mounted on an aluminium block fitted with a 460 nm high-power single LED (λ = 460 nm, irradiance = 90 mW/cm^2, as controlled by an external power supply; the set-up is detailed in **Supplementary Figure 1**). The reaction was stirred under visible light irradiation at 5 °C internal temperature for 16 hours. The product was purified by flash column chromatography (silica,5% EtOAc in n-hexanes) to obtain **9** as a colorless oil (13.5 mg, 60% yield). The enantiomeric ratio of the corresponding 2,4-dinitrophenylhydrazone derivative (prepared following the general procedure of β-cyanoaldehydes **2a**), was determined to be 90.0:10.0 by UPC^2 analysis on a Daicel Chiralpak IE-3 column (eluent: 100% CO_2 for 1 min, gradient 100% - 60% CO_2 in EtOH for 5 min, 60% CO_2 in CH_3CN for 2 min, gradient 60% - 100% CO_2 in EtOH for 1 min; flow rate 2.0 mL/min, λ = 348 nm, τ_{Major} = 6.60 min, τ_{Minor} = 6.25 min).

$[\alpha]_D^{25}$ = -0.9 (c = 0.1, $CHCl_3$, 90:10 e.r.).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.74 (t, *J* = 2.2 Hz, 1H), 6.22 (d, *J* = 1.5 Hz, 1H), 5.55 (d, *J* = 1.3 Hz, 1H), 3.76 (s, 3H), 2.50 – 2.42 (m, 1H), 2.40 – 2.27 (m, 2H), 2.25 – 2.20 (m, 1H), 2.18 – 2.16 (m, 1H), 1.39 – 1.23 (m, 8H), 0.88 (t, *J* = 7.1 Hz, 3H) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 203.0, 167.6, 138.9, 127.2, 52.1, 48.1, 37.2, 34.3, 32.3, 32.1, 26.4, 22.7, 14.2 ppm.

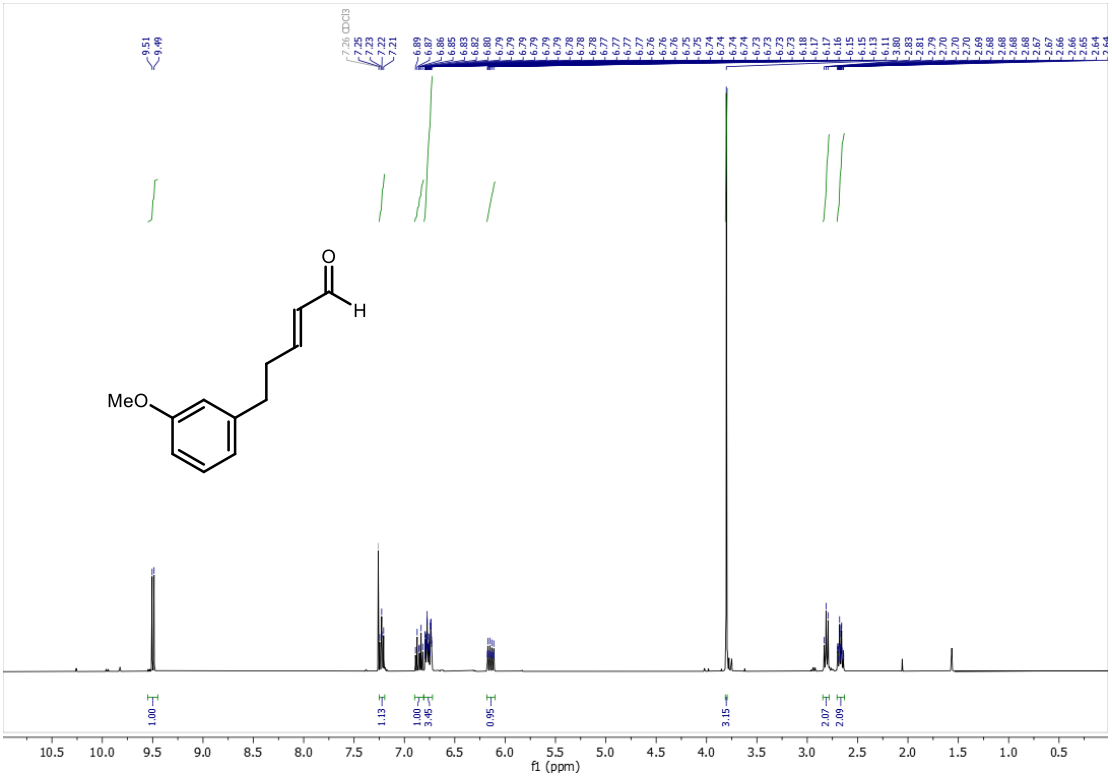
HRMS (ESI): m/z calculated for $[C_{13}H_{22}O_3Na]^+$ $[M+Na]^+$: 249.1461, found: 249.1452.



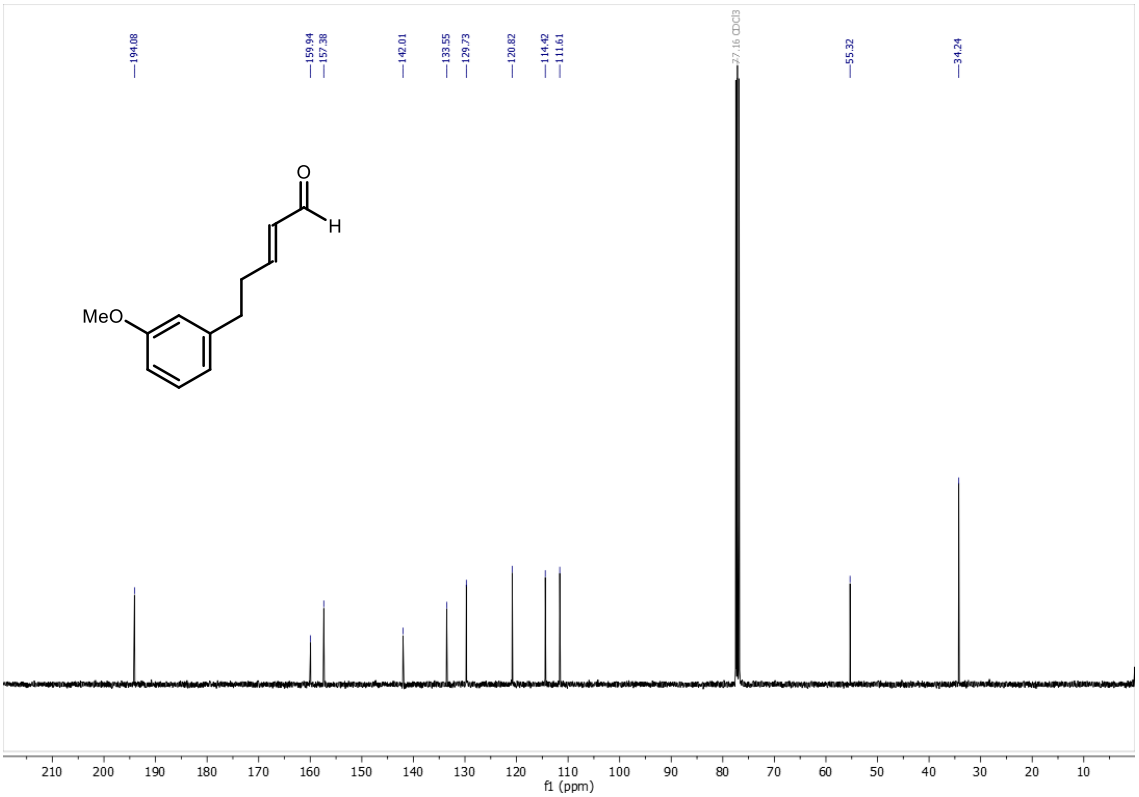
Supplementary Figure 68: UPC^2 Traces of **9.**

NMR Spectra

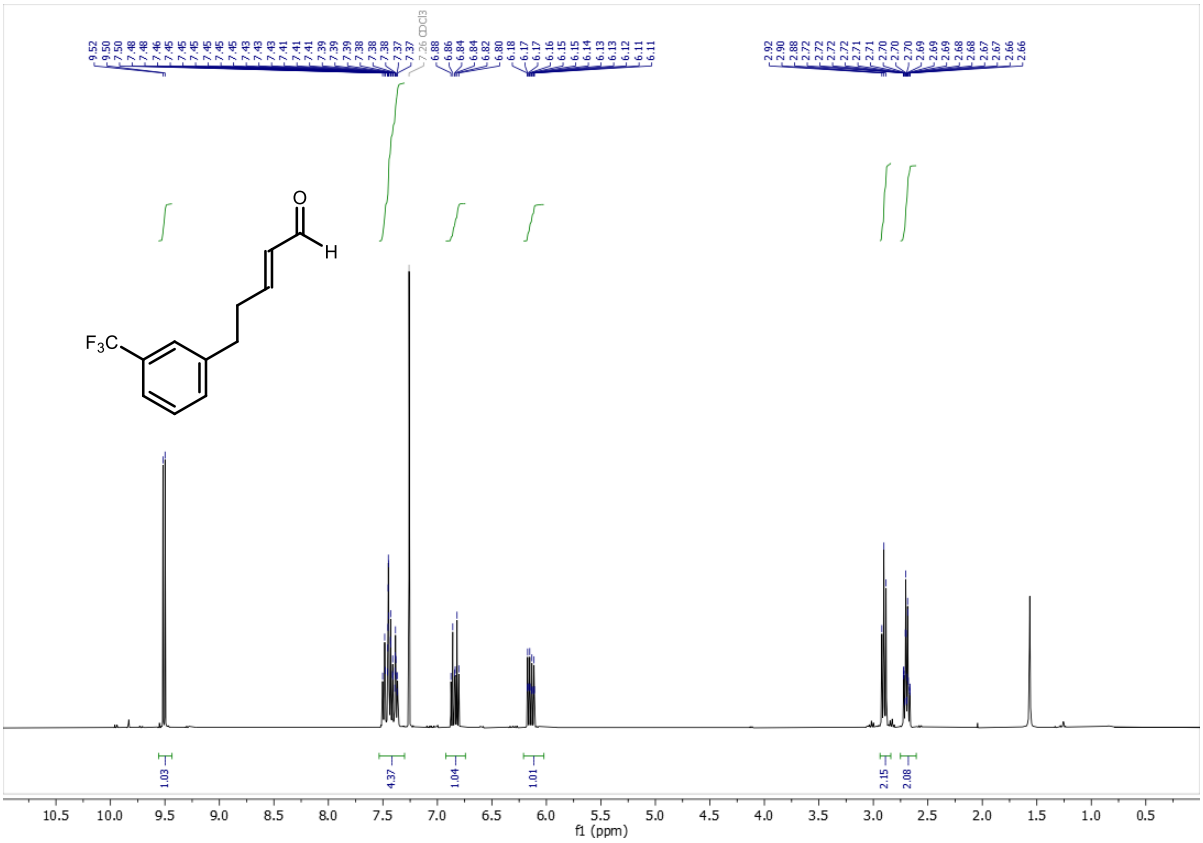
^{1}H NMR (400 MHz, $CDCl_3$) of **1f**:



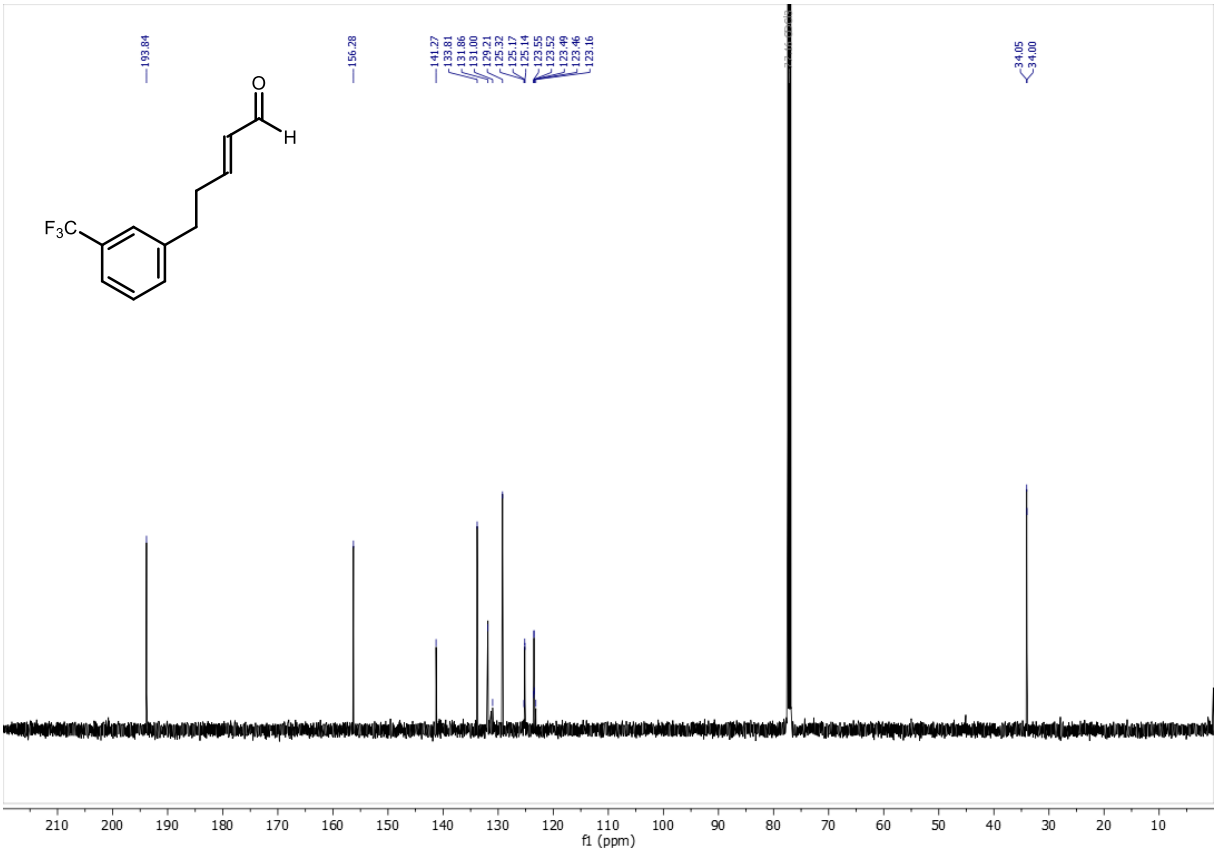
^{13}C NMR (126 MHz, $CDCl_3$) of **1f**:



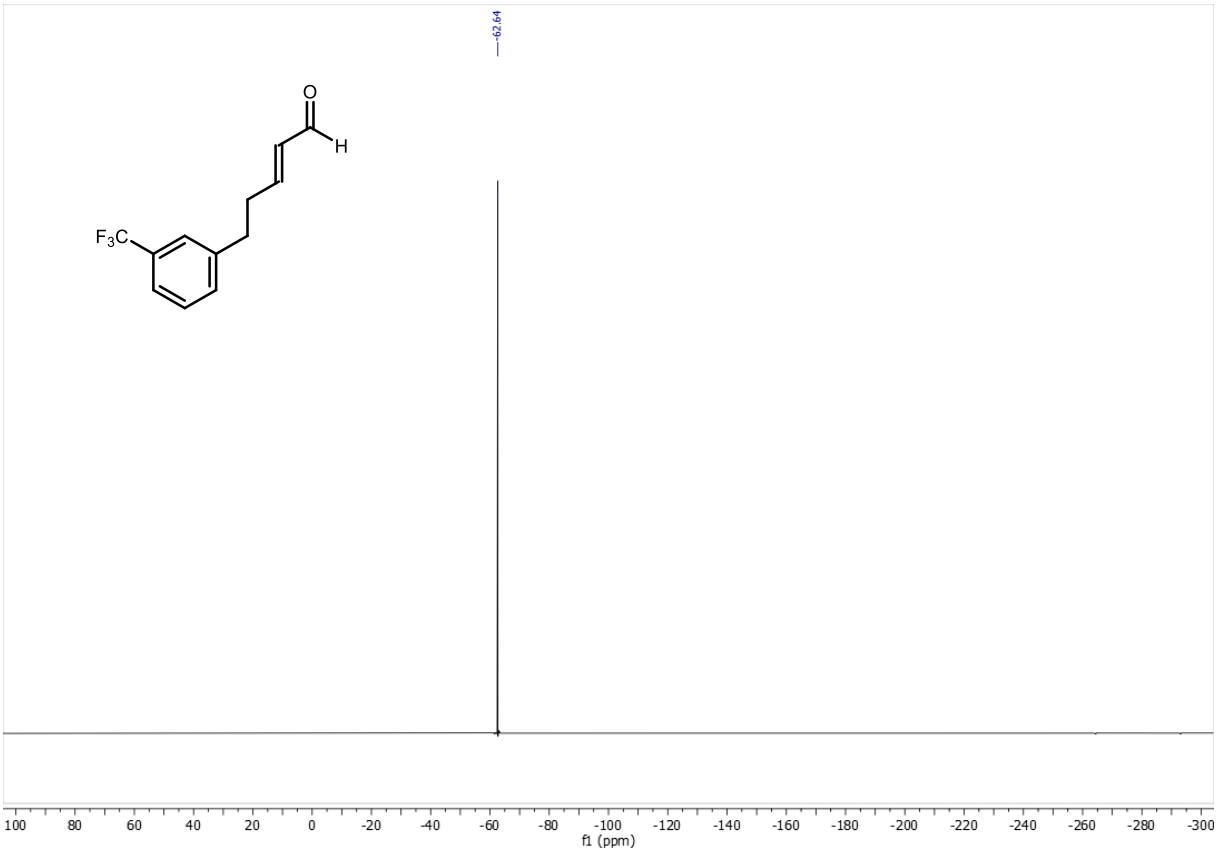
^{1}H NMR (400 MHz, $CDCl_3$) of **1g**:



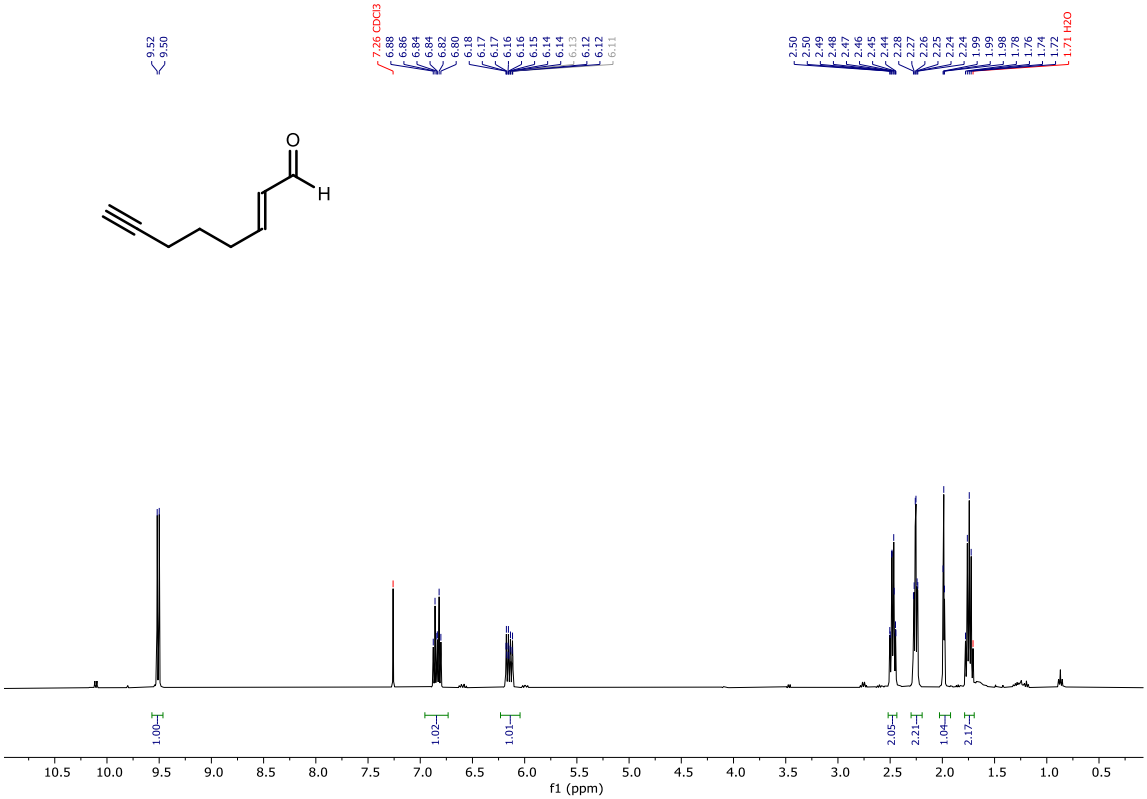
^{13}C NMR (126 MHz, $CDCl_3$) of **1g**:



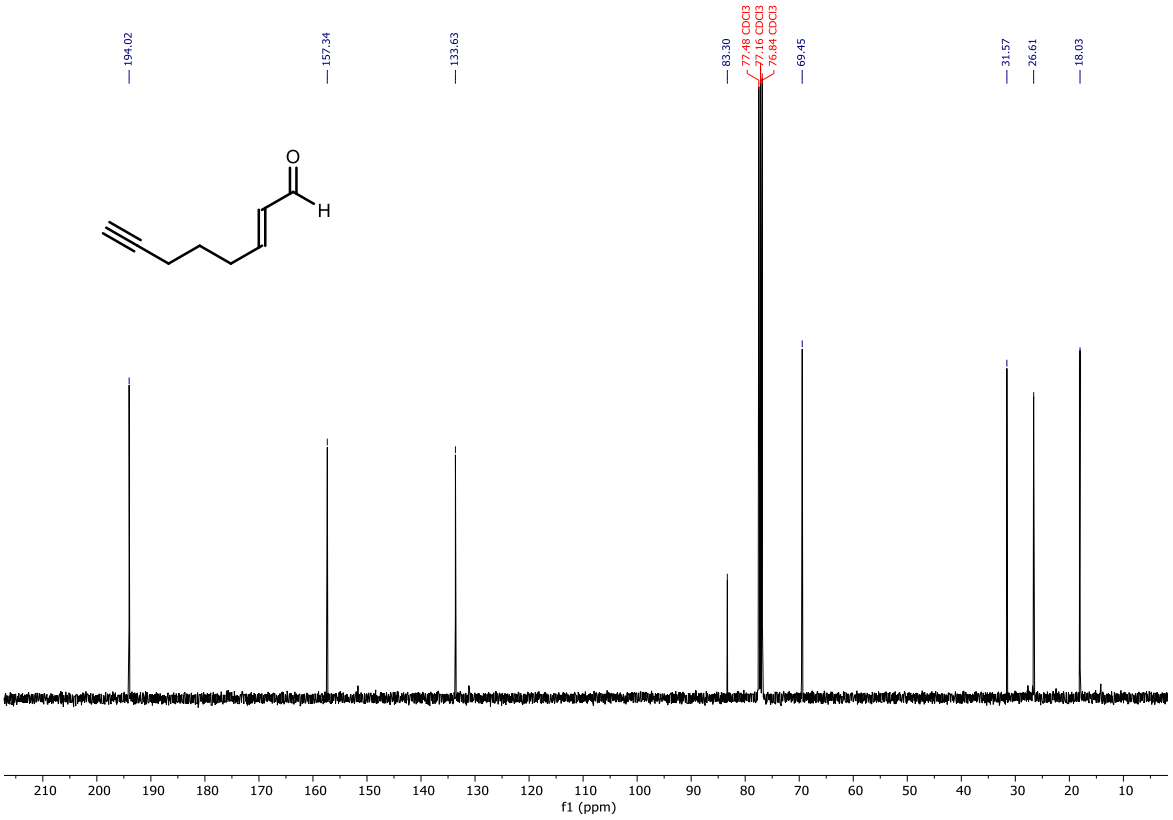
^{19}F NMR (471 MHz, $CDCl_3$) of **1g**:



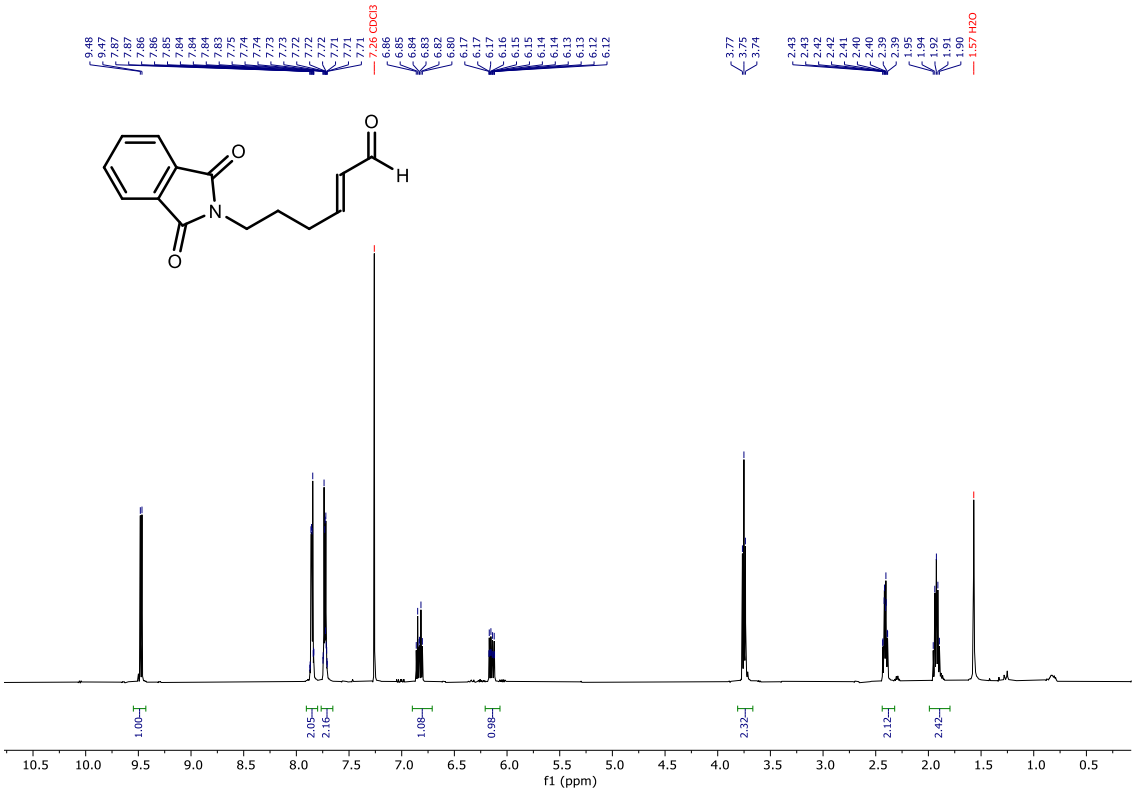
^{1}H NMR (400 MHz, $CDCl_3$) of **1l**:



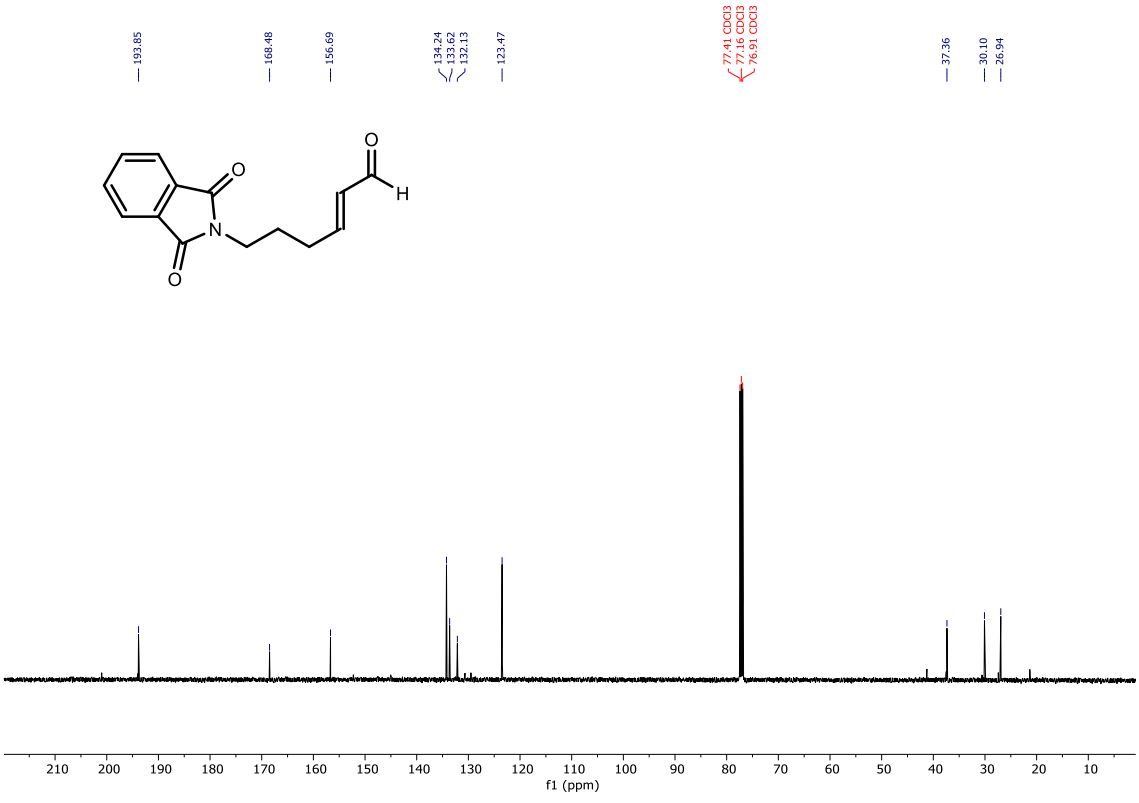
^{13}C NMR (101 MHz, $CDCl_3$) of **1l**:



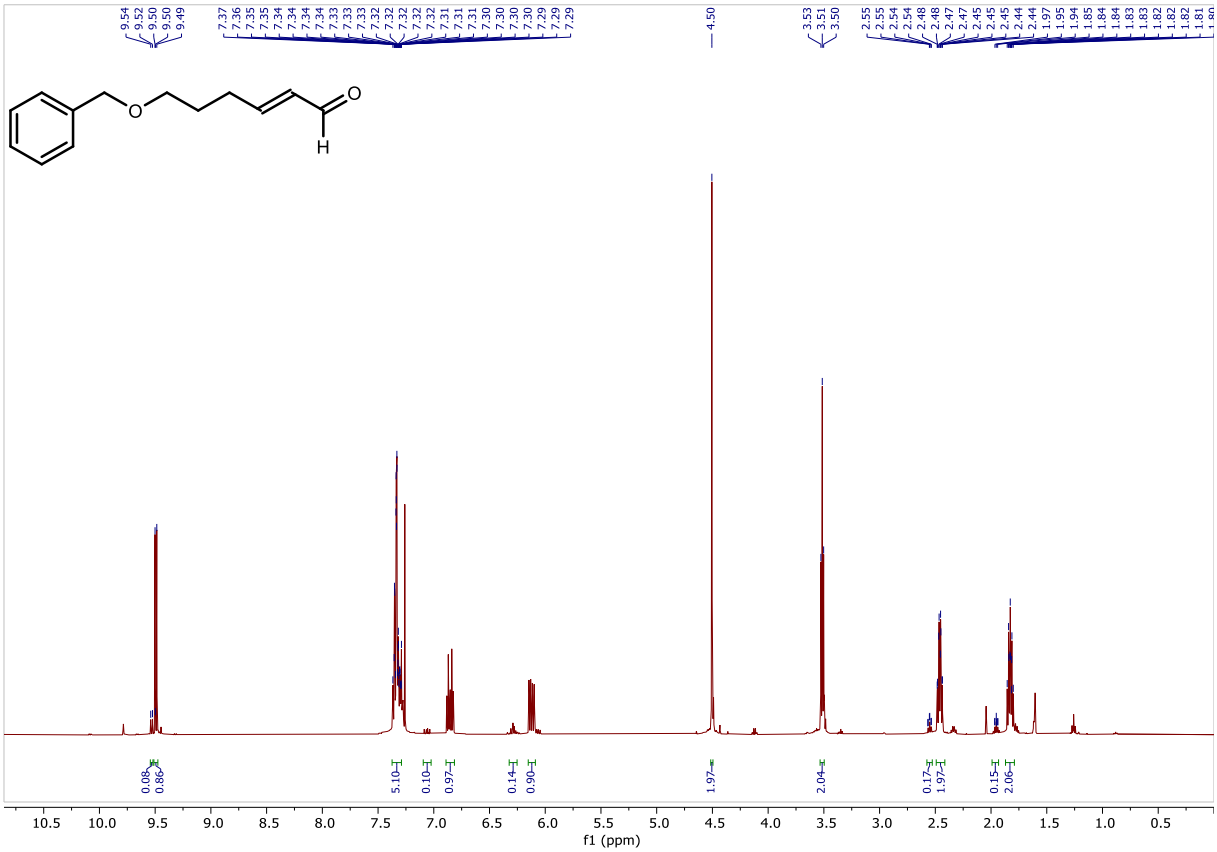
^{1}H NMR (500 MHz, $CDCl_3$) of **1m**:



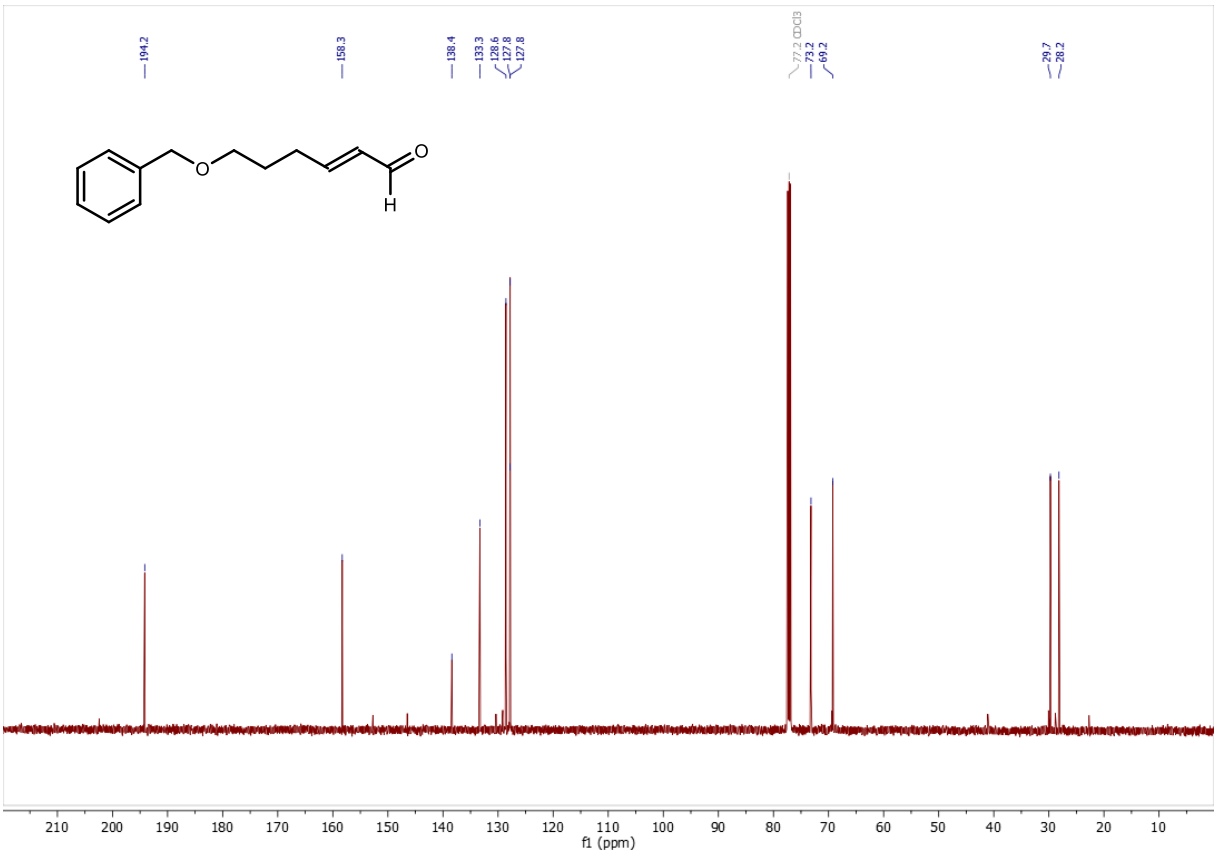
^{13}C NMR (126 MHz, $CDCl_3$) of **1m**:



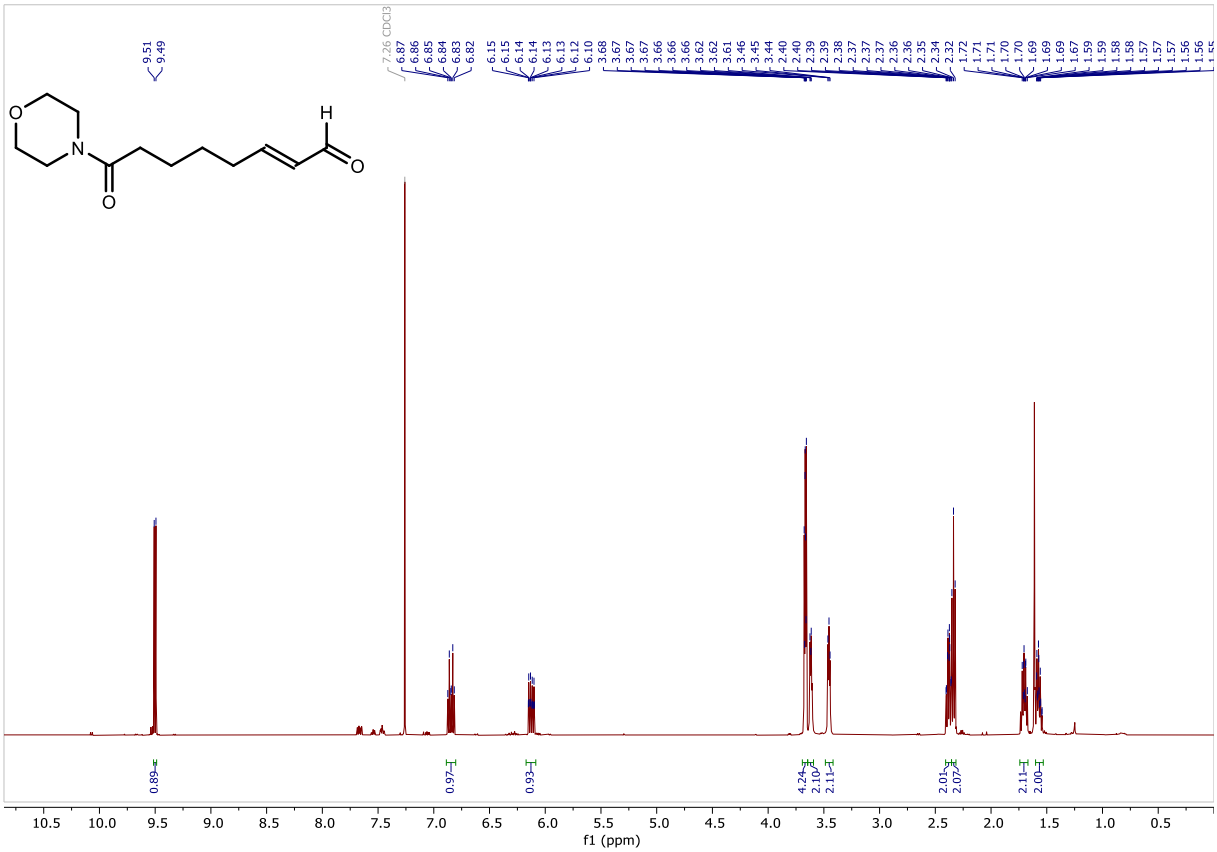
^{1}H NMR (500 MHz, $CDCl_3$, *E/Z* = 9:1) of **1n**:



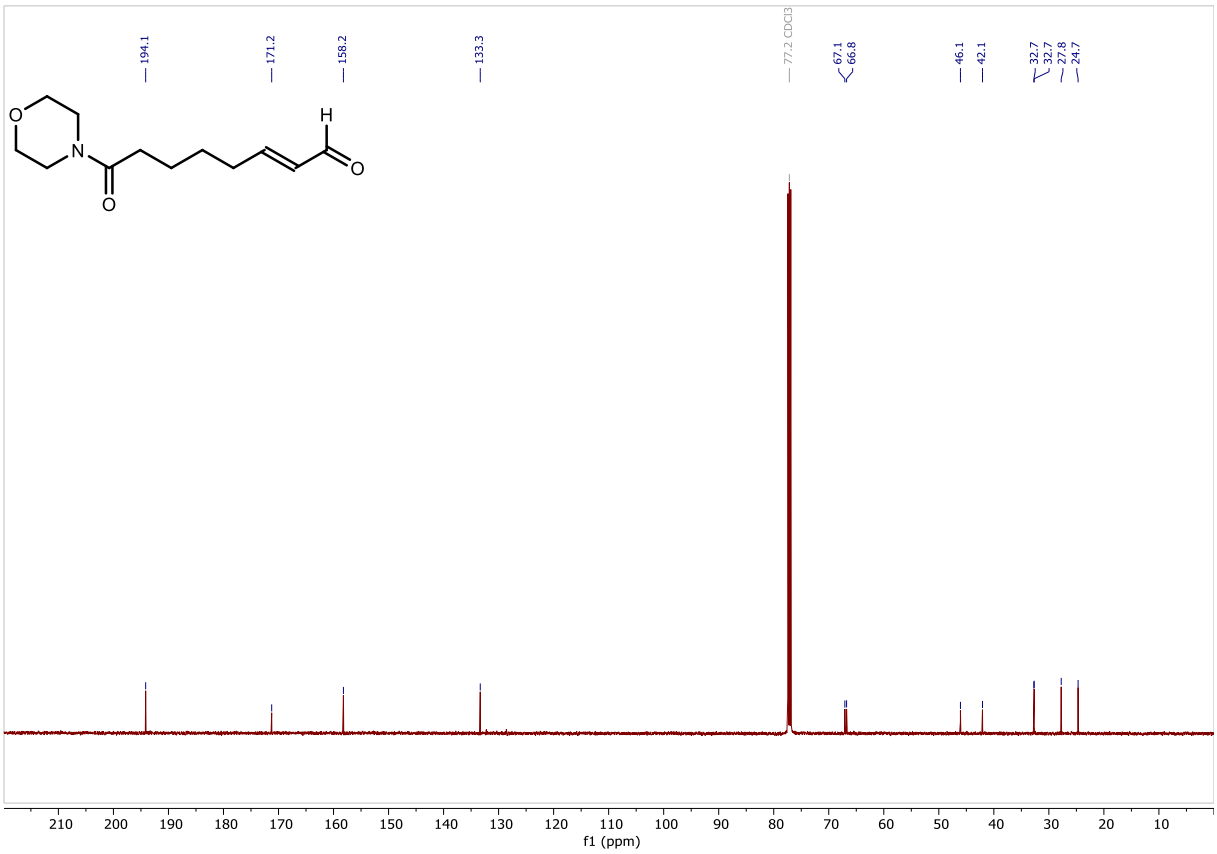
^{13}C NMR (126 MHz, $CDCl_3$, *E/Z* = 9:1) of **1n**:



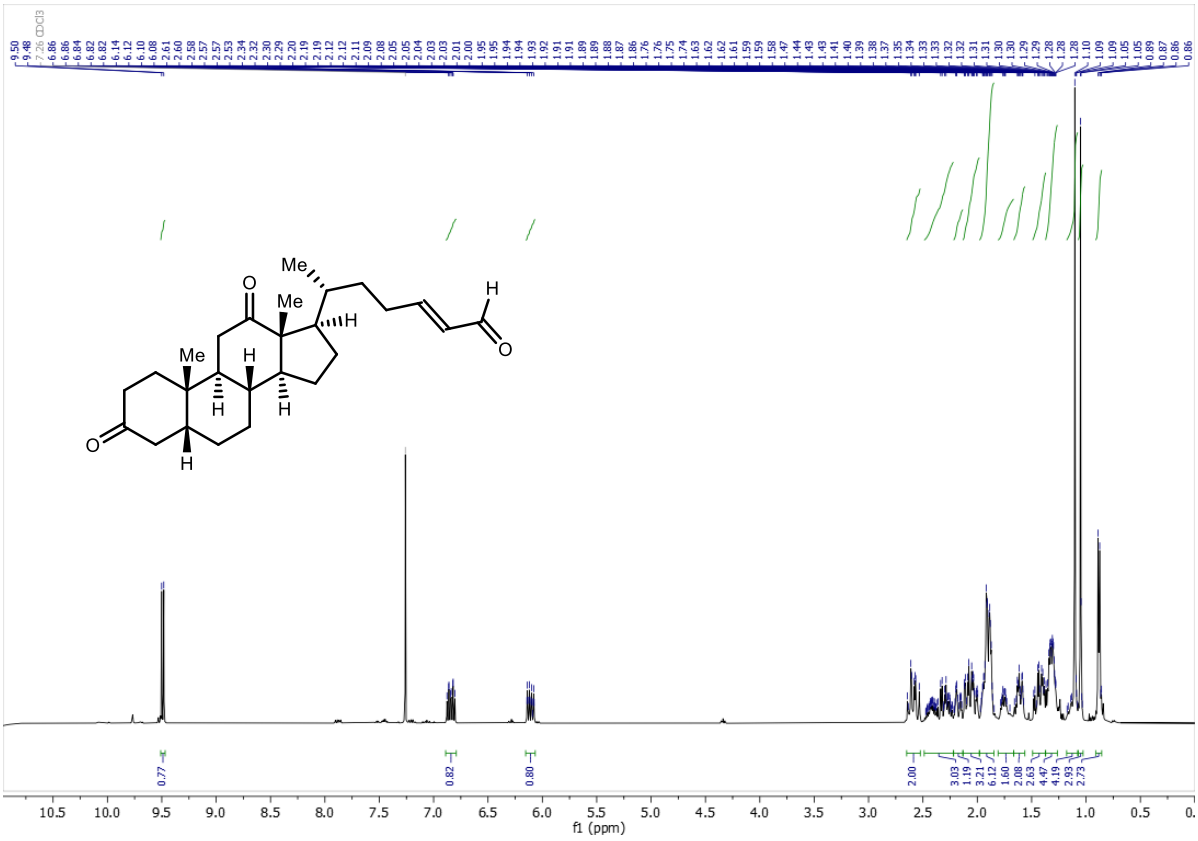
^{1}H NMR (500 MHz, $CDCl_3$) of **1p**:



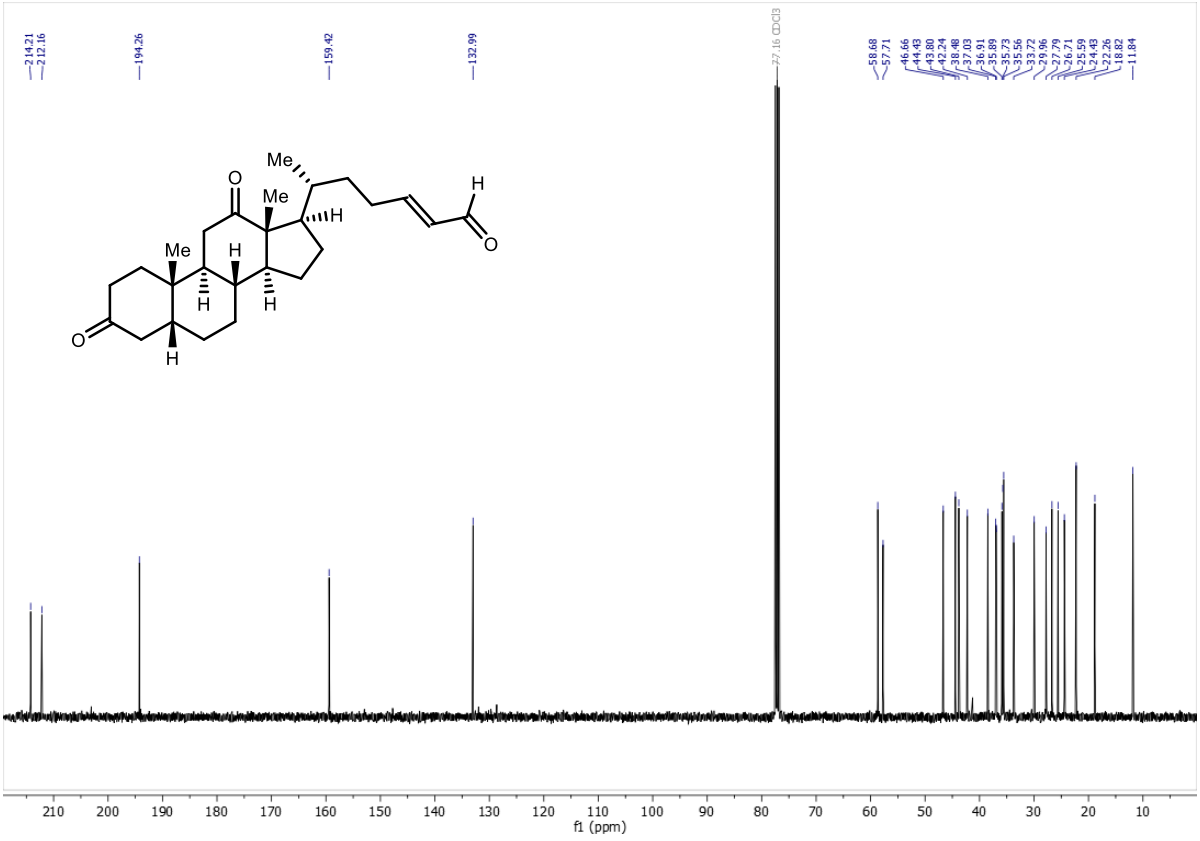
^{13}C NMR (126 MHz, $CDCl_3$) of **1p**:



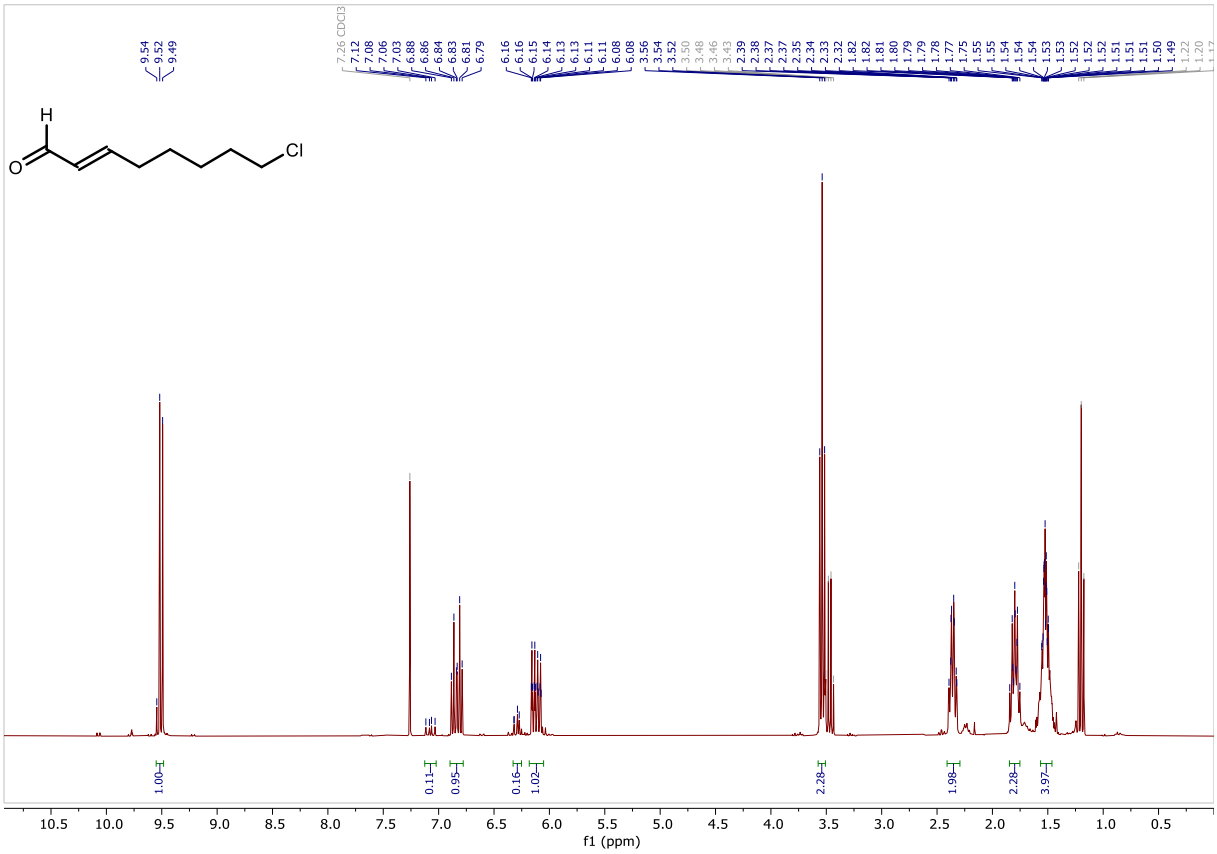
^{1}H NMR (400 MHz, $CDCl_3$) of **1r**:



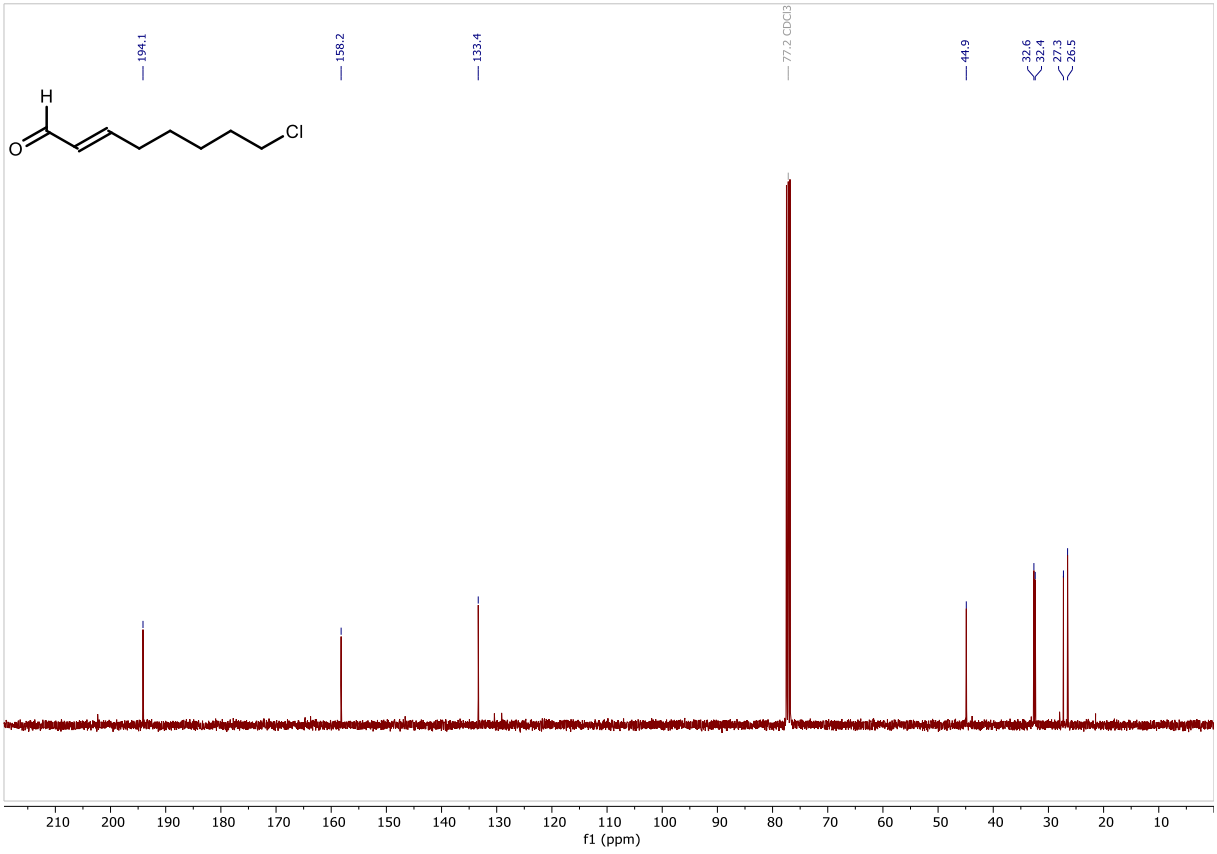
^{13}C NMR (101 MHz, $CDCl_3$) of **1r**:



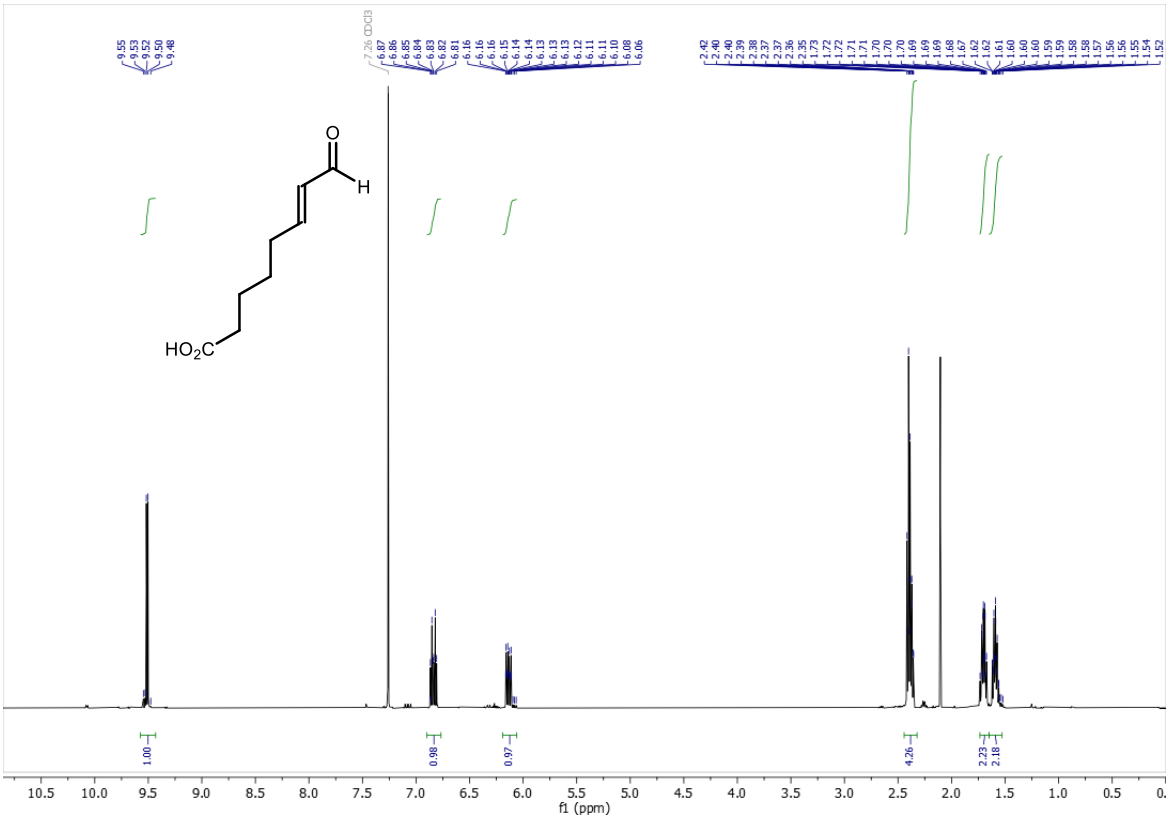
^{1}H NMR (300 MHz, $CDCl_3$) of **1s**:



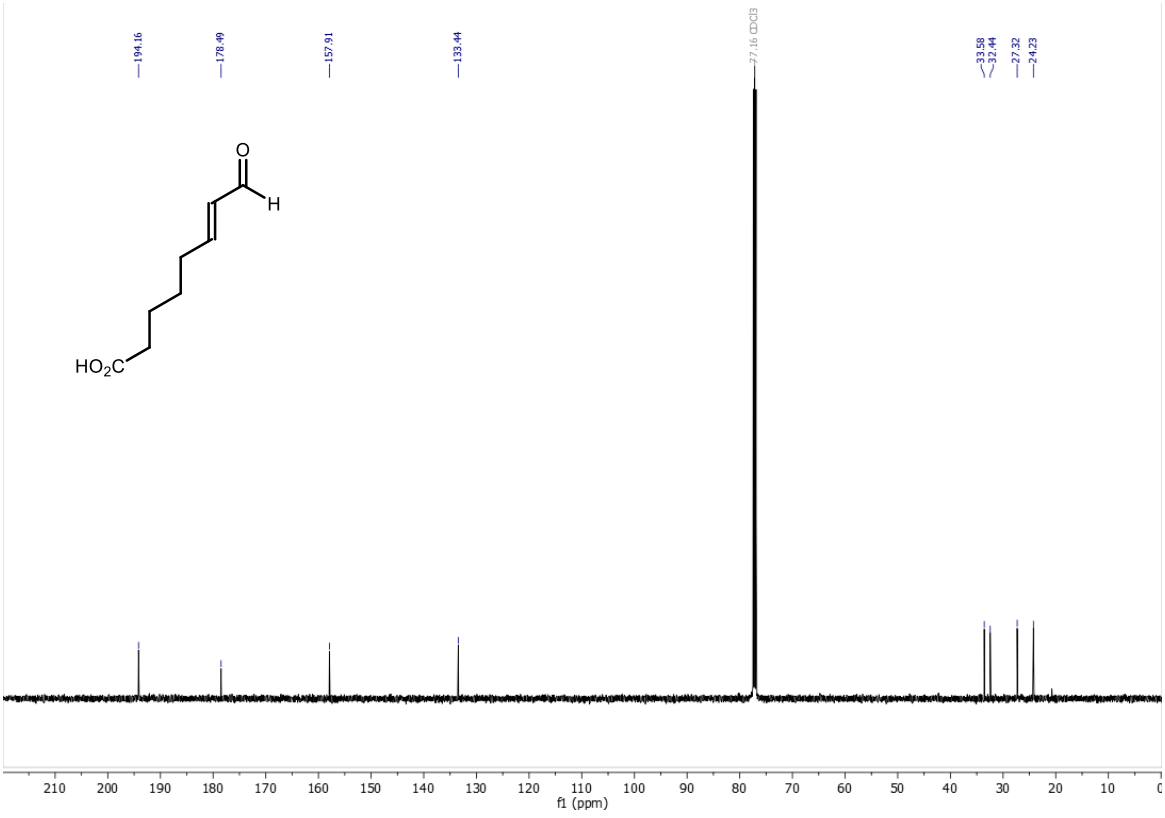
^{13}C NMR (101 MHz, $CDCl_3$) of **1s**:



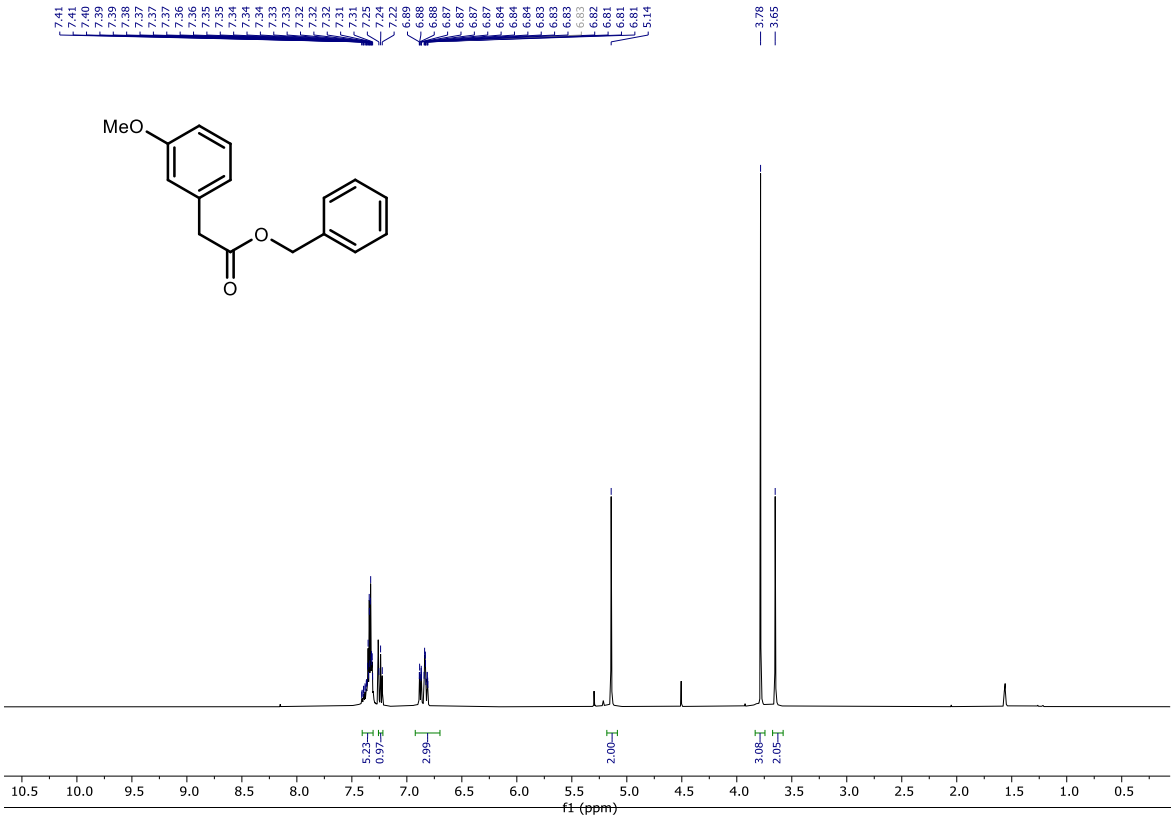
^{1}H NMR (500 MHz, $CDCl_3$) of **1t**:



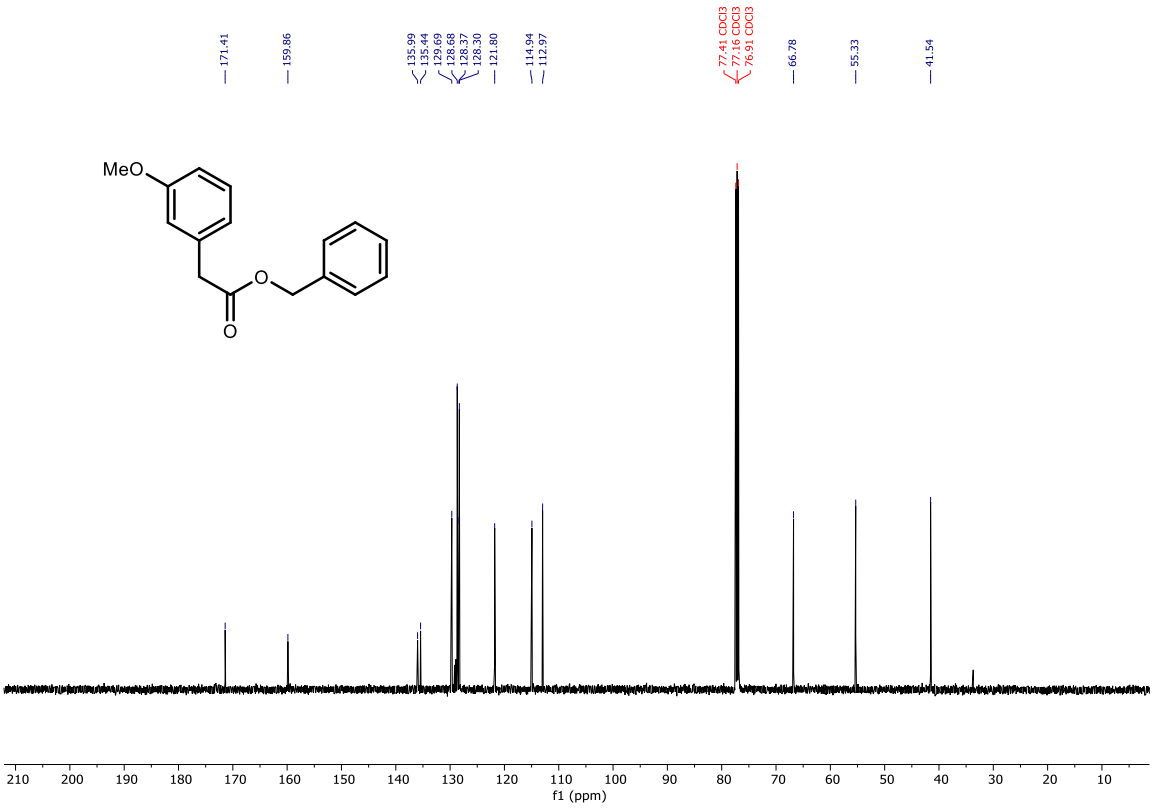
^{13}C NMR (126 MHz, $CDCl_3$) of **1t**:



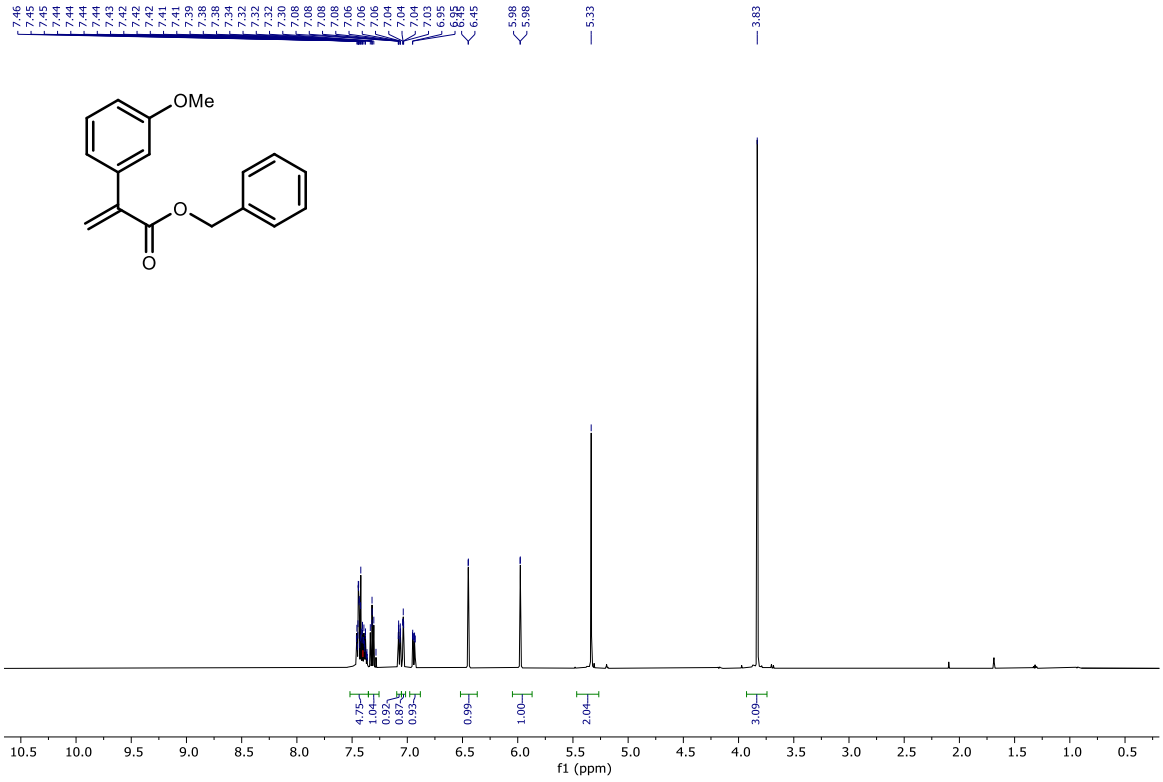
^{1}H NMR (500 MHz, $CDCl_3$) of precursor to **5e**:



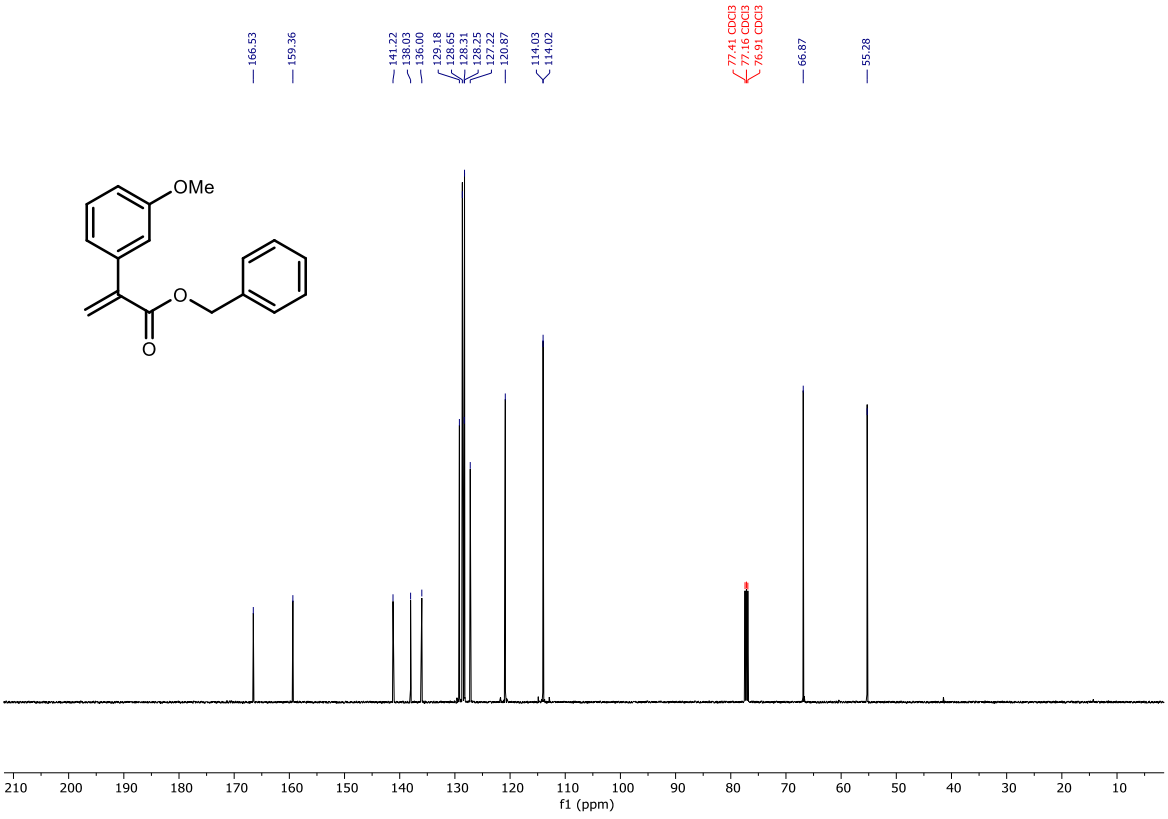
^{13}C NMR (126 MHz, $CDCl_3$) of precursor to **5e**:



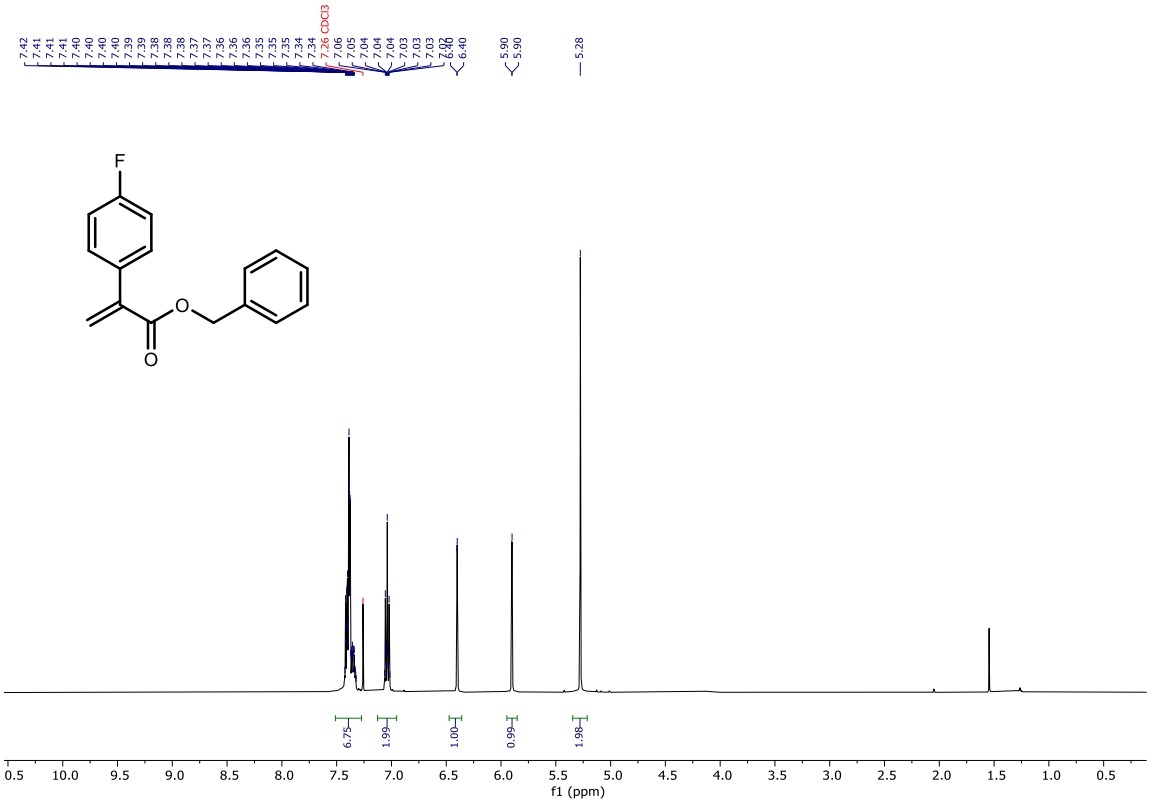
^{1}H NMR (500 MHz, $CDCl_3$) of **5e**:



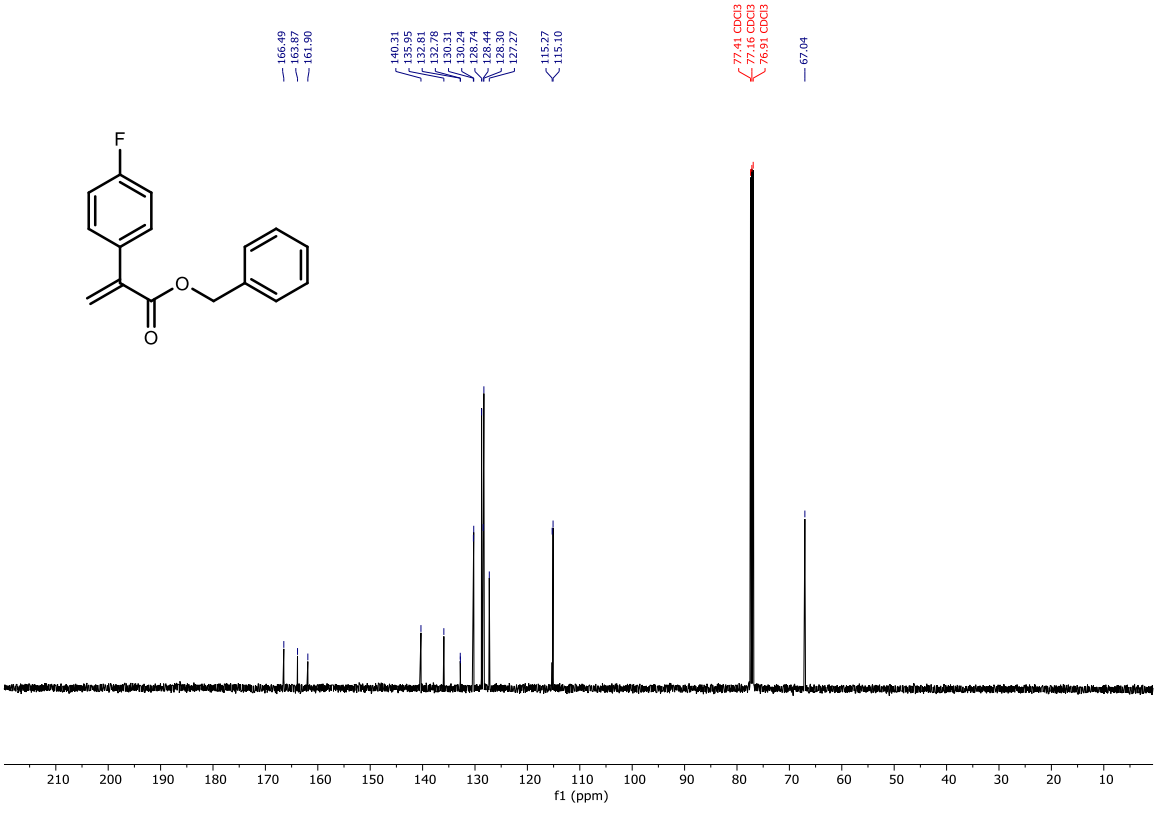
^{13}C NMR (126 MHz, $CDCl_3$) of **5e**:



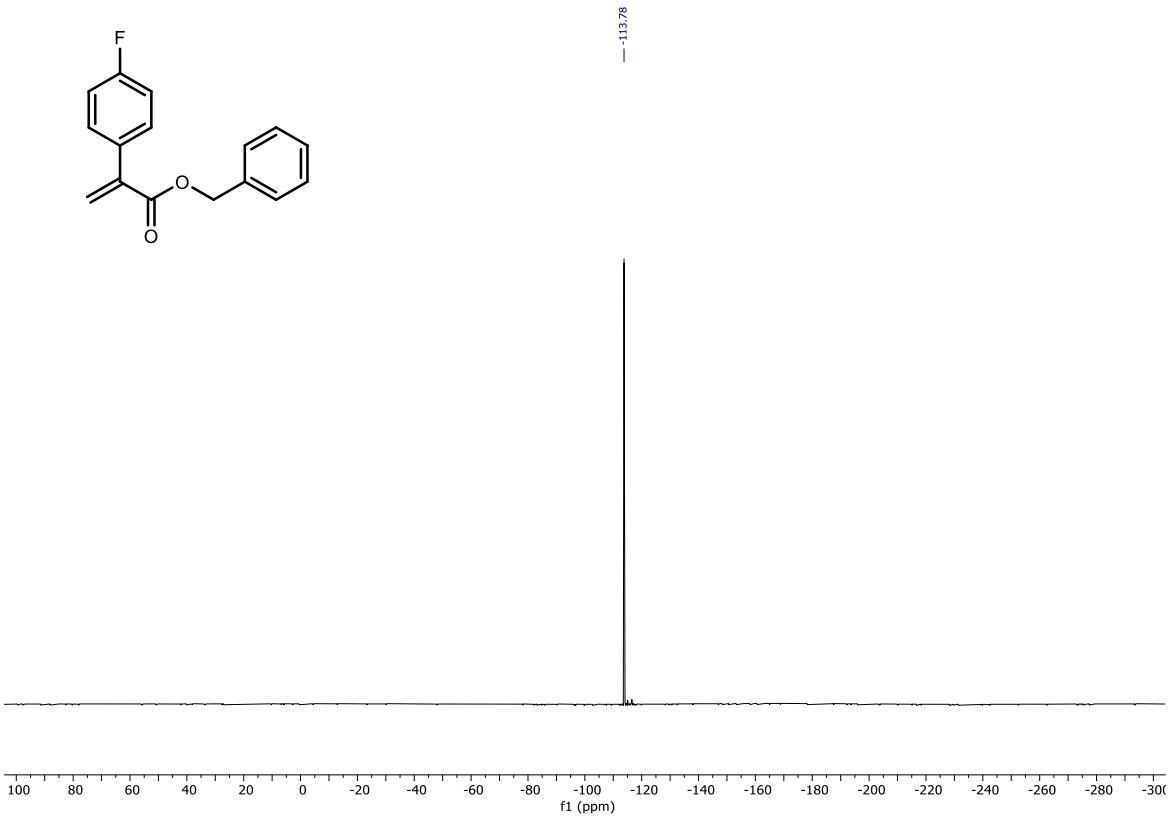
^{1}H NMR (500 MHz, $CDCl_3$) of **5f**:



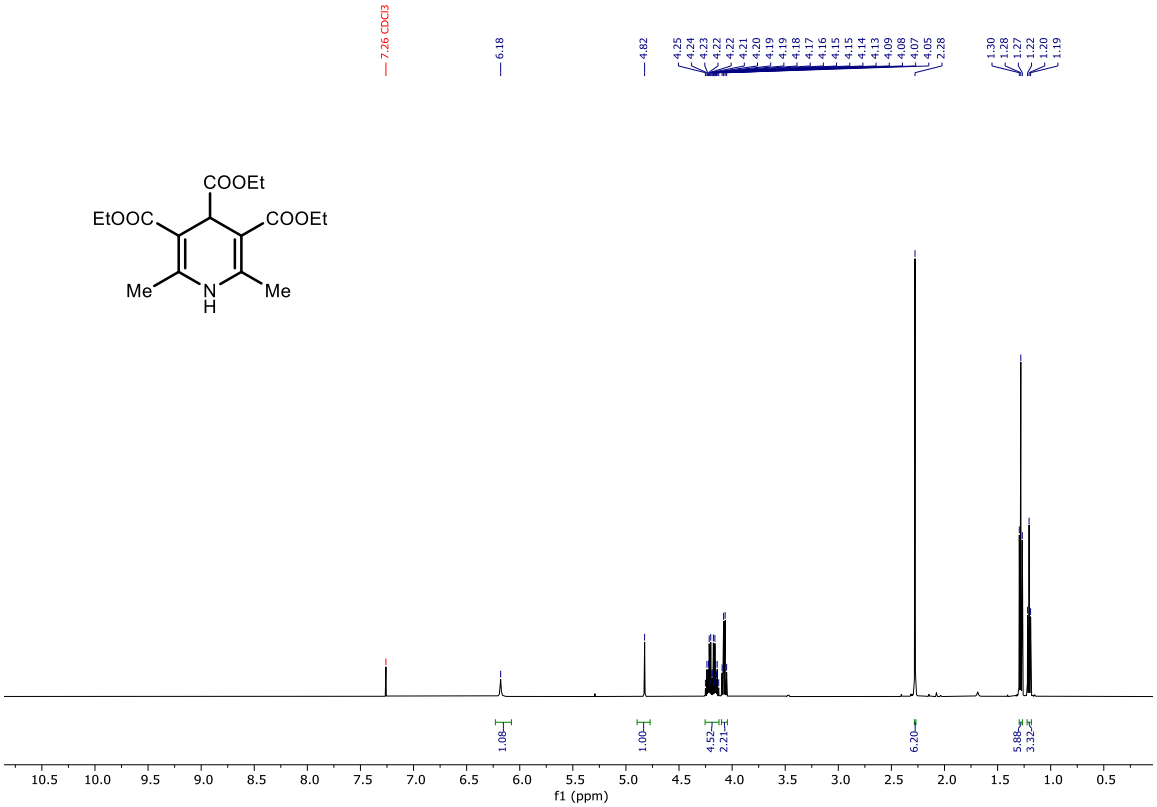
^{13}C NMR (126 MHz, $CDCl_3$) of **5f**:



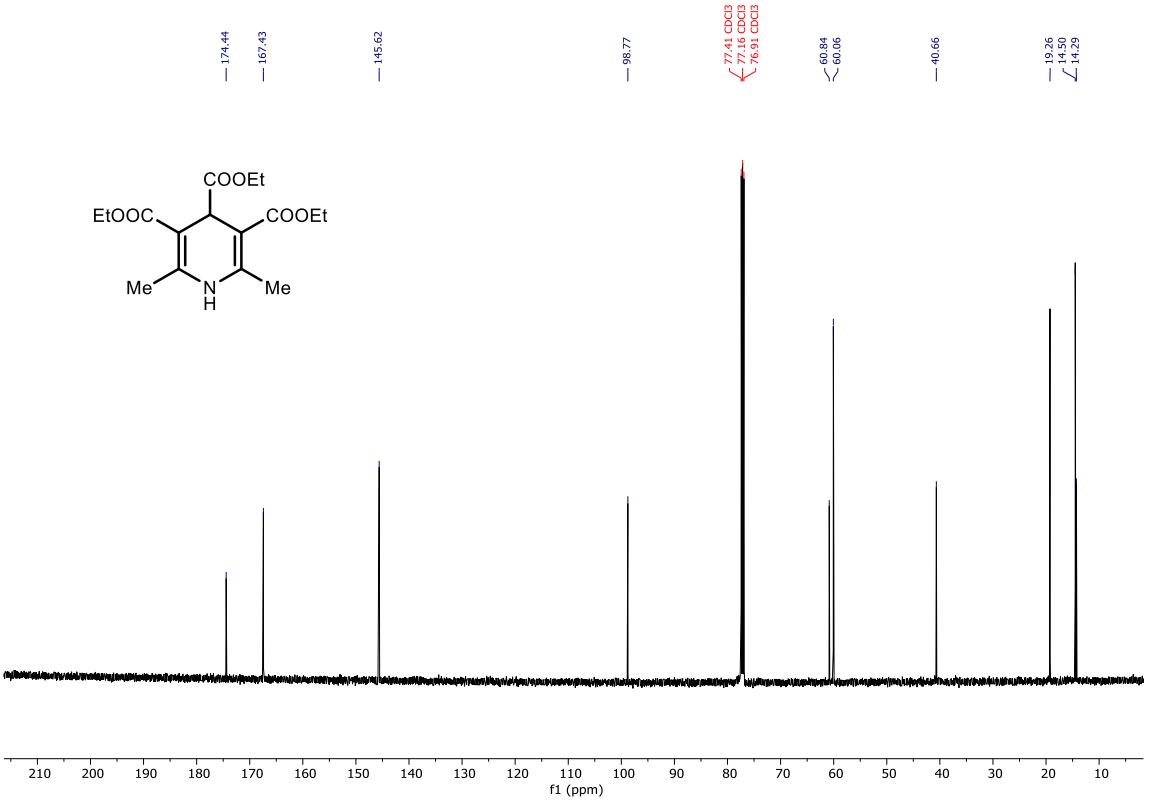
$^{19}F\{^{1}H\}$ NMR (471 MHz, $CDCl_3$) of **5f**:



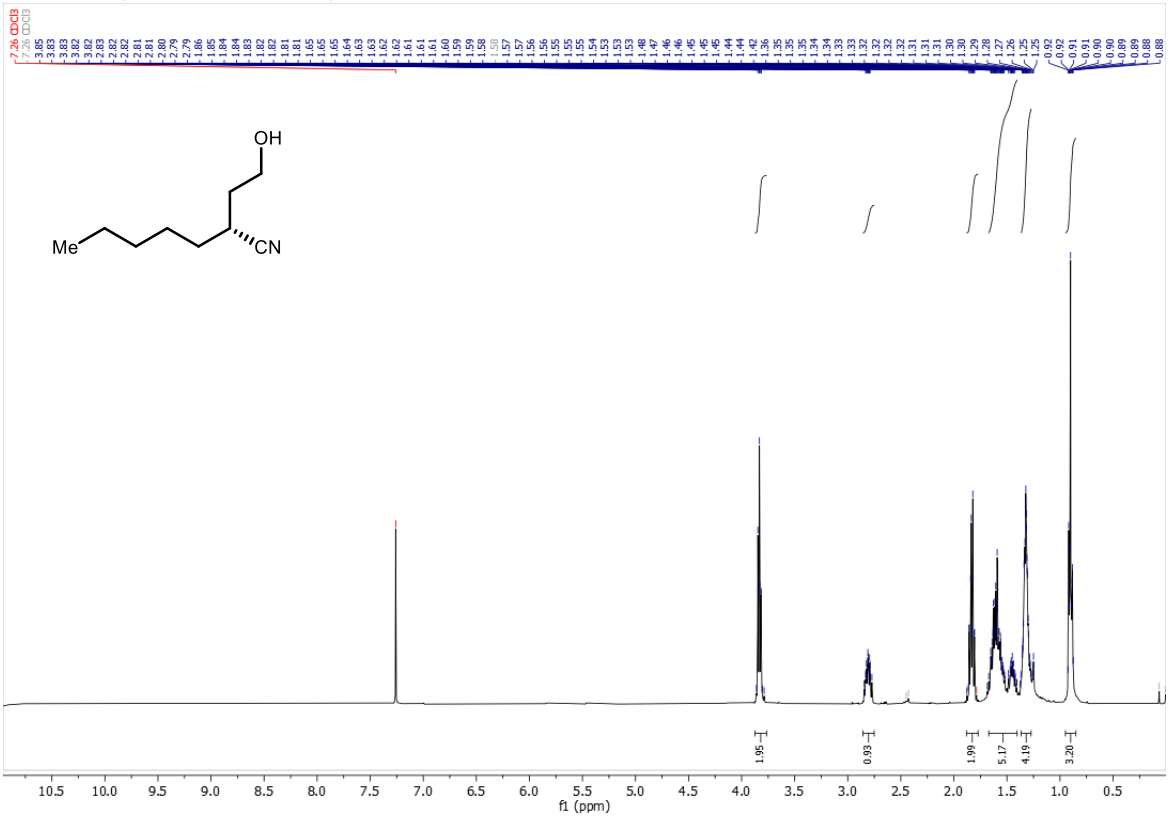
^{1}H NMR (500 MHz, $CDCl_3$) of **R-1**:



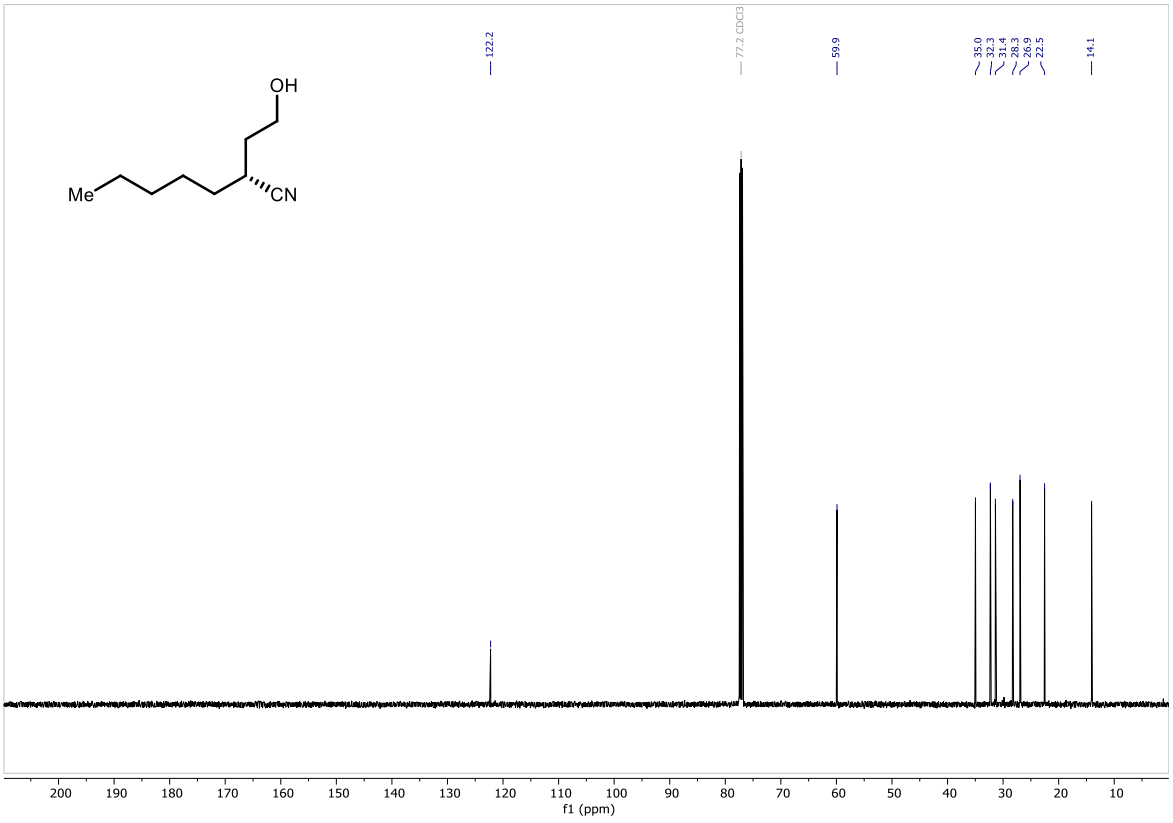
^{13}C NMR (126 MHz, $CDCl_3$) of **R-1**:



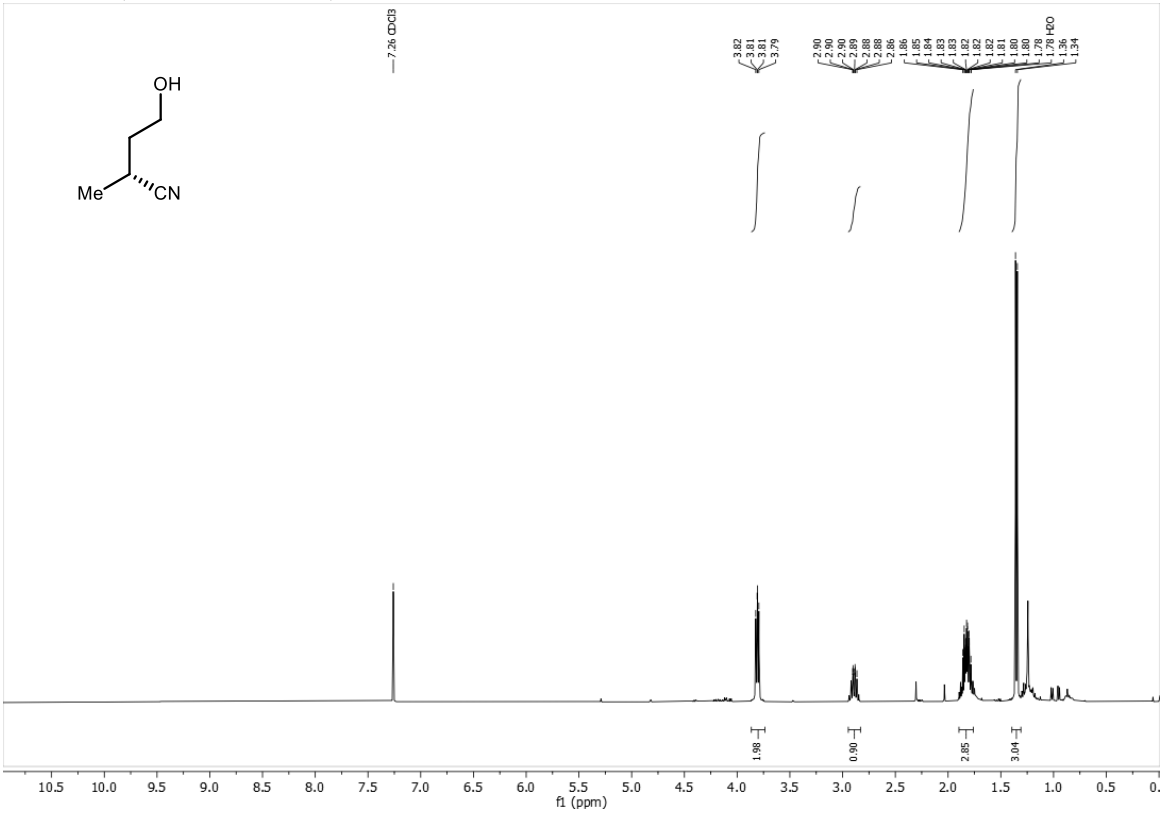
^{1}H NMR (400 MHz, $CDCl_3$) of **3a**:



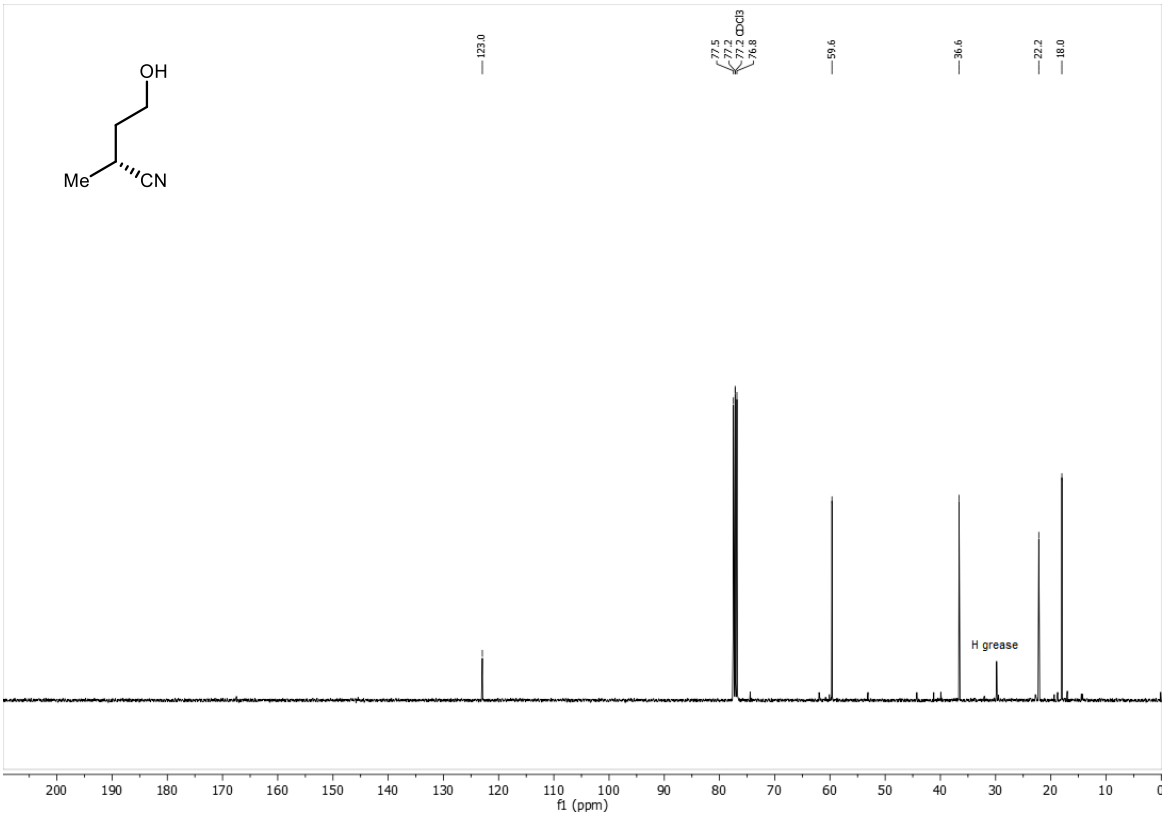
^{13}C NMR (126 MHz, $CDCl_3$) of **3a**:



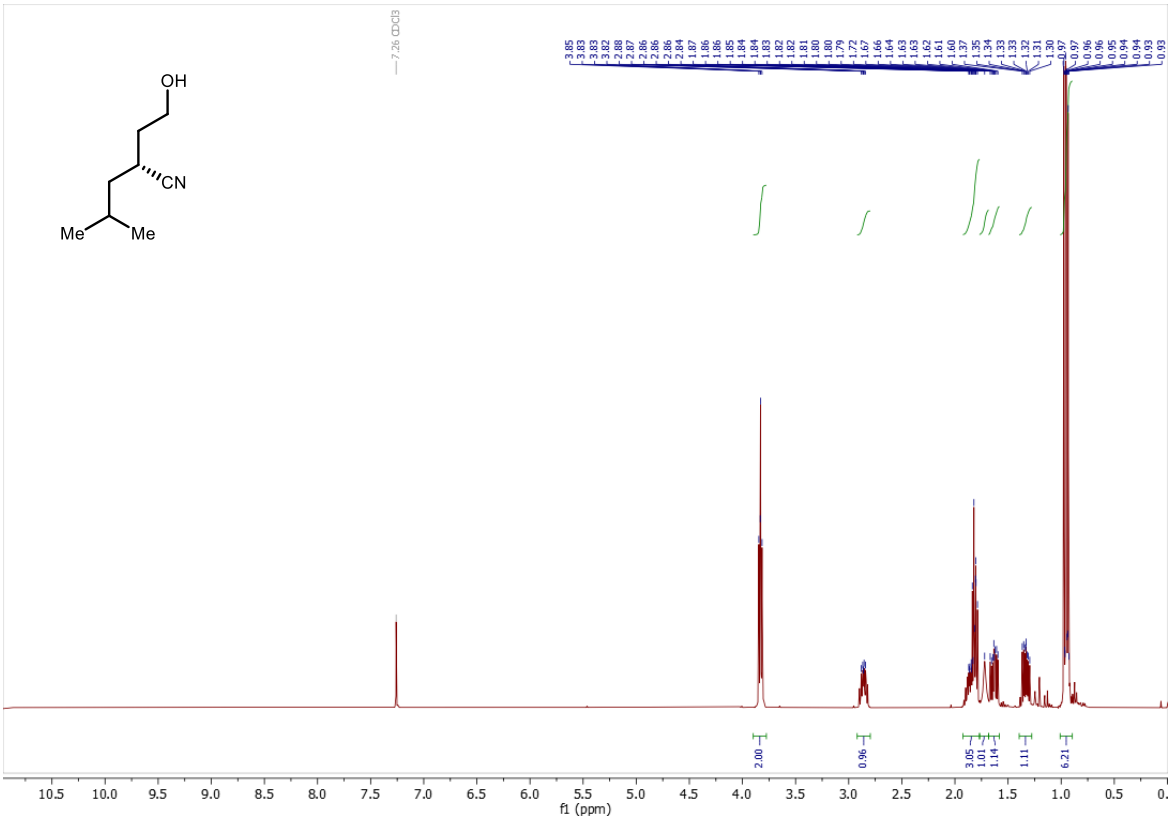
^{1}H NMR (400 MHz, $CDCl_3$) of **3b**:



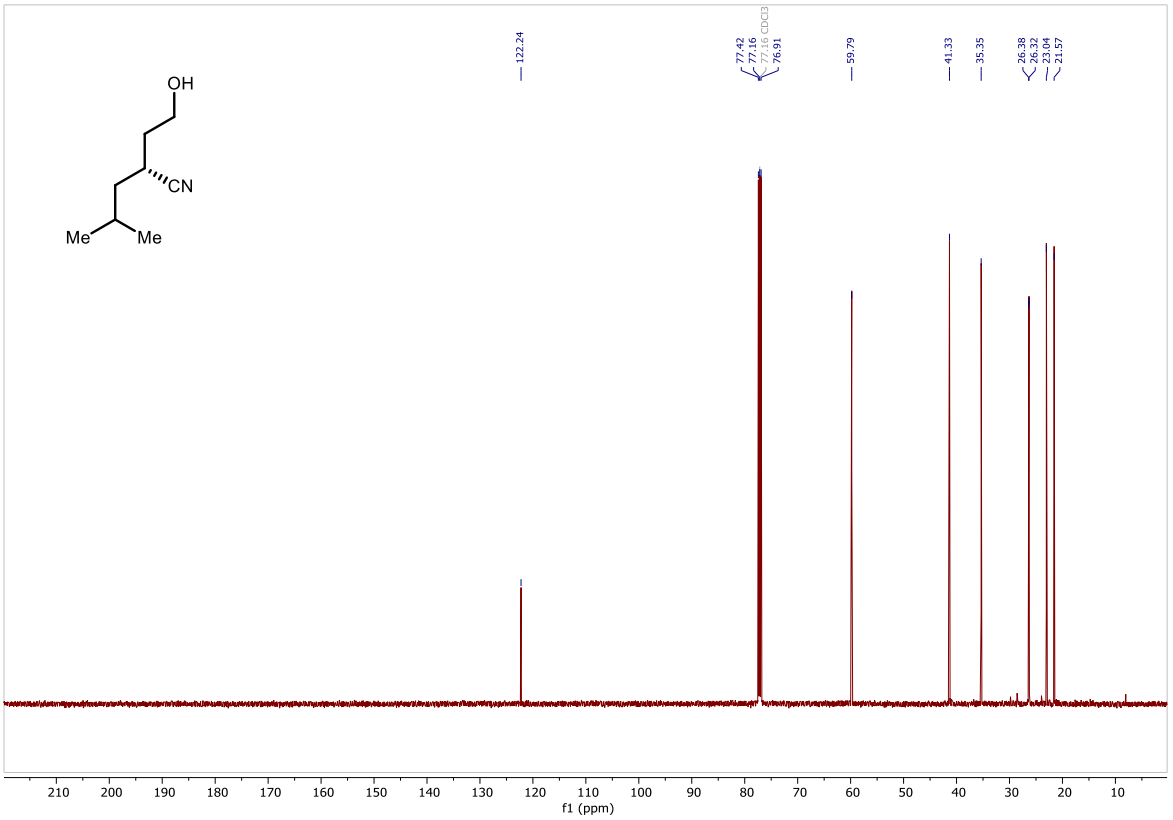
^{13}C NMR (100 MHz, $CDCl_3$) of **3b**:



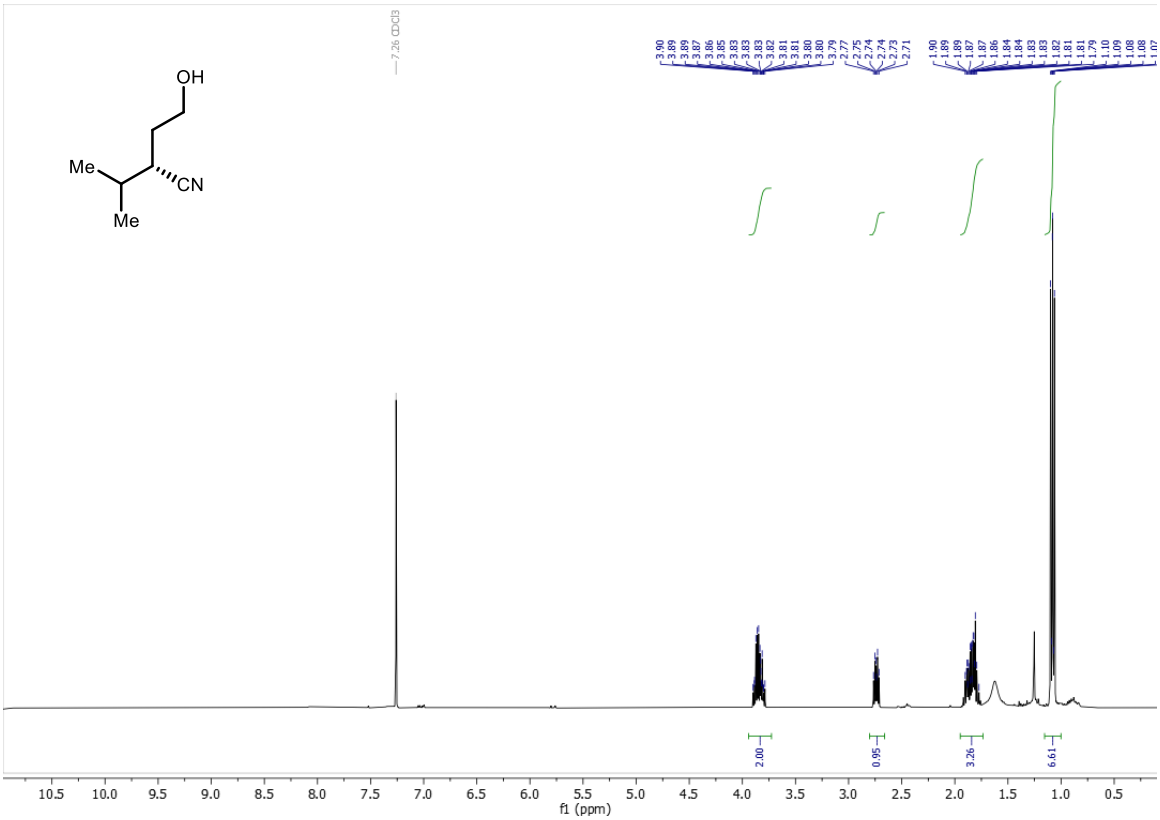
^{1}H NMR (400 MHz, $CDCl_3$) of **3c**:



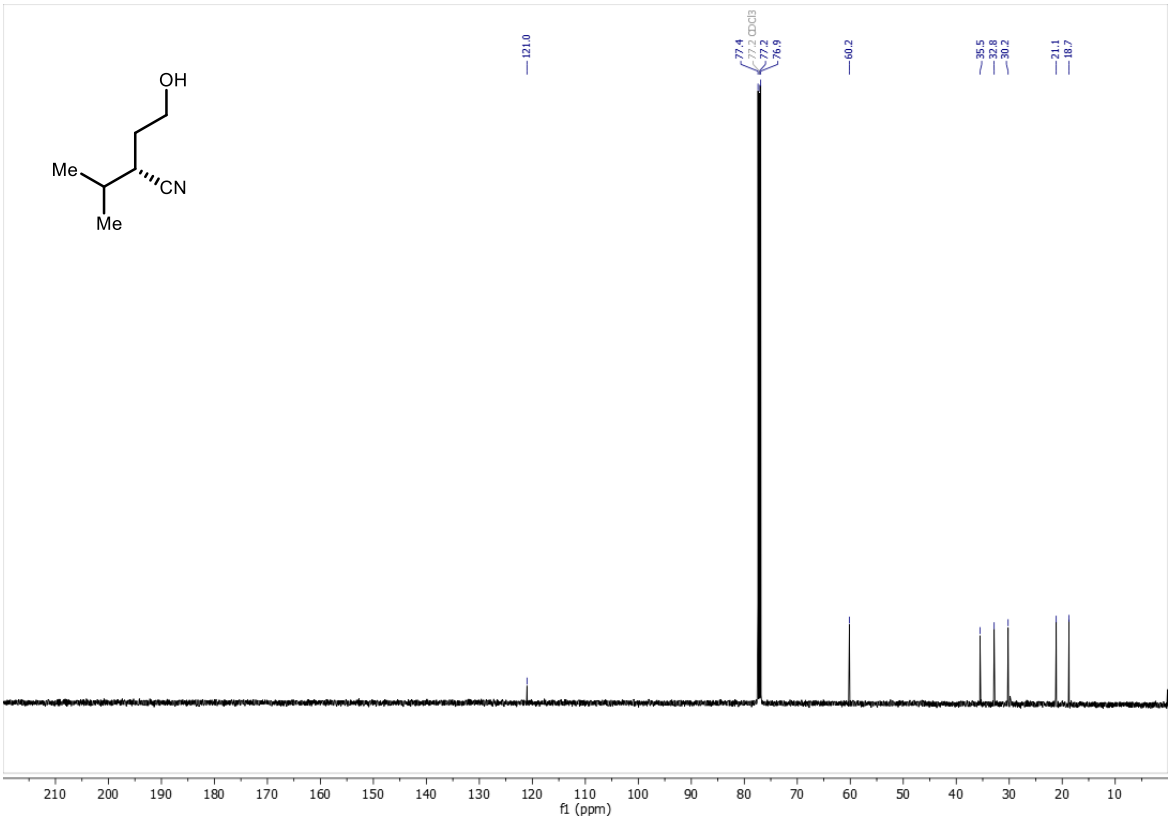
^{13}C NMR (126 MHz, $CDCl_3$) of **3c**:



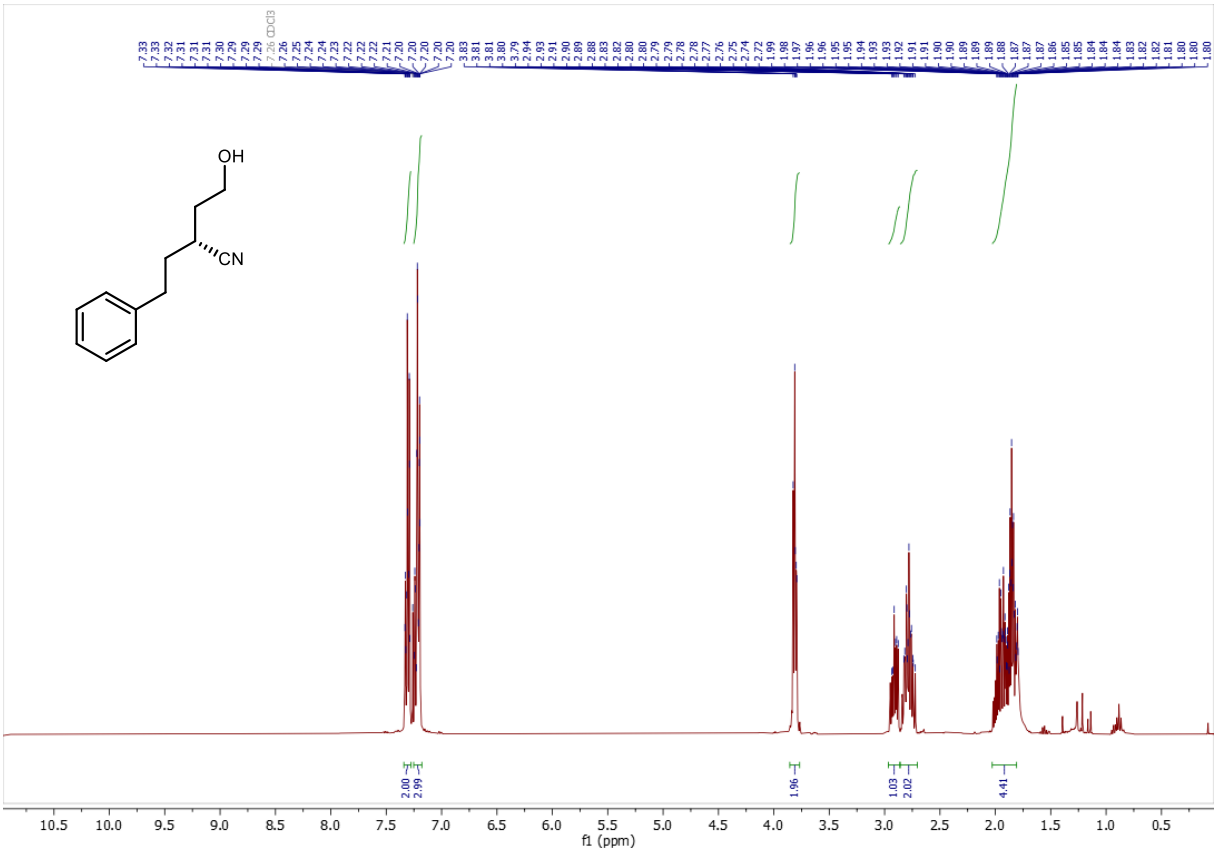
^{1}H NMR (400 MHz, $CDCl_3$) of **3d**:



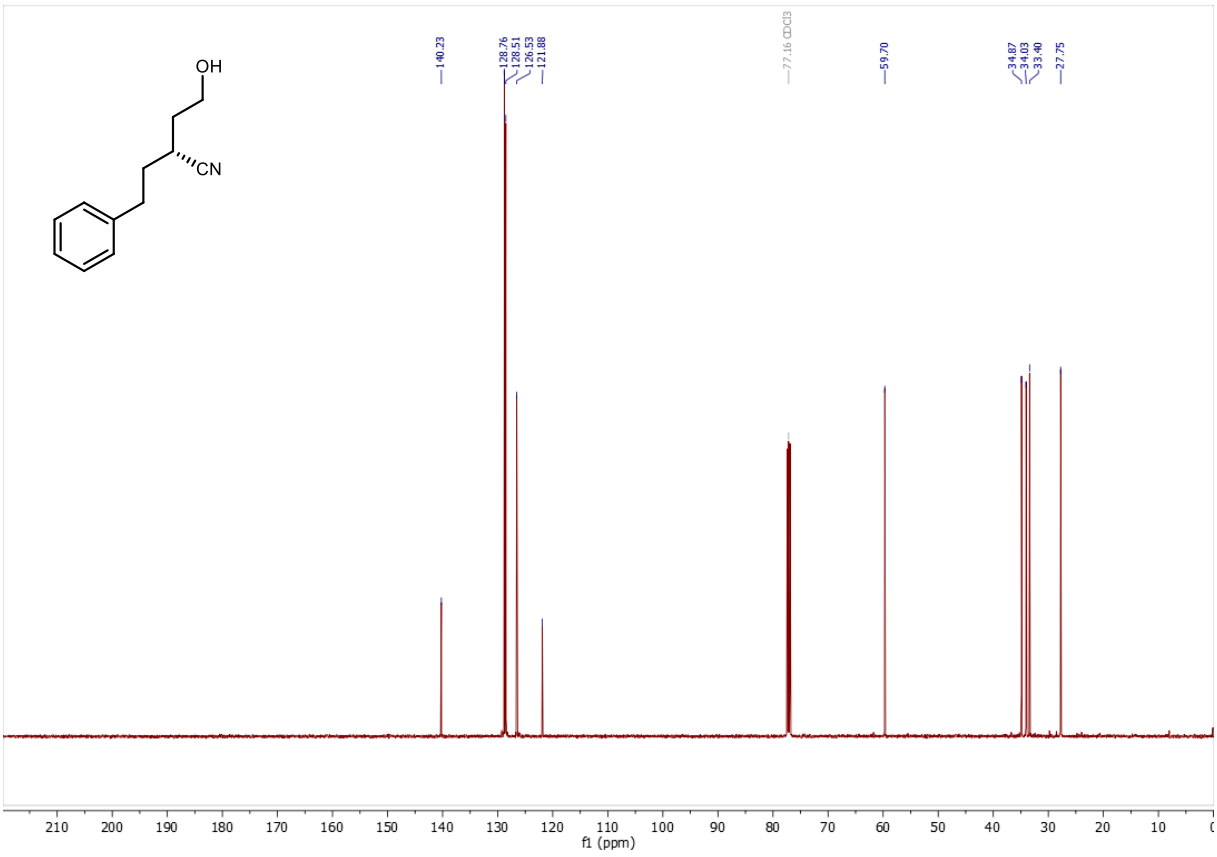
^{13}C NMR (126 MHz, $CDCl_3$) of **3d**:



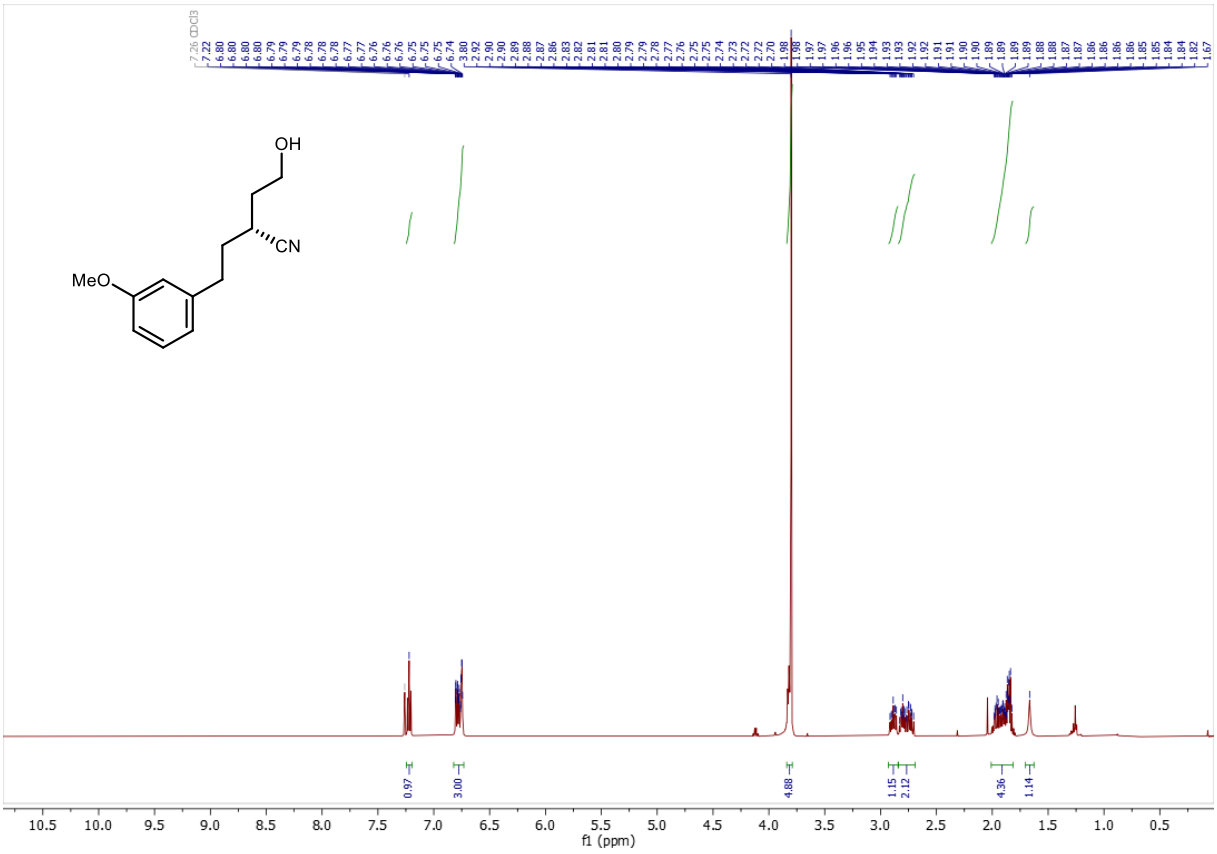
^{1}H NMR (400 MHz, $CDCl_3$) of **3e**:



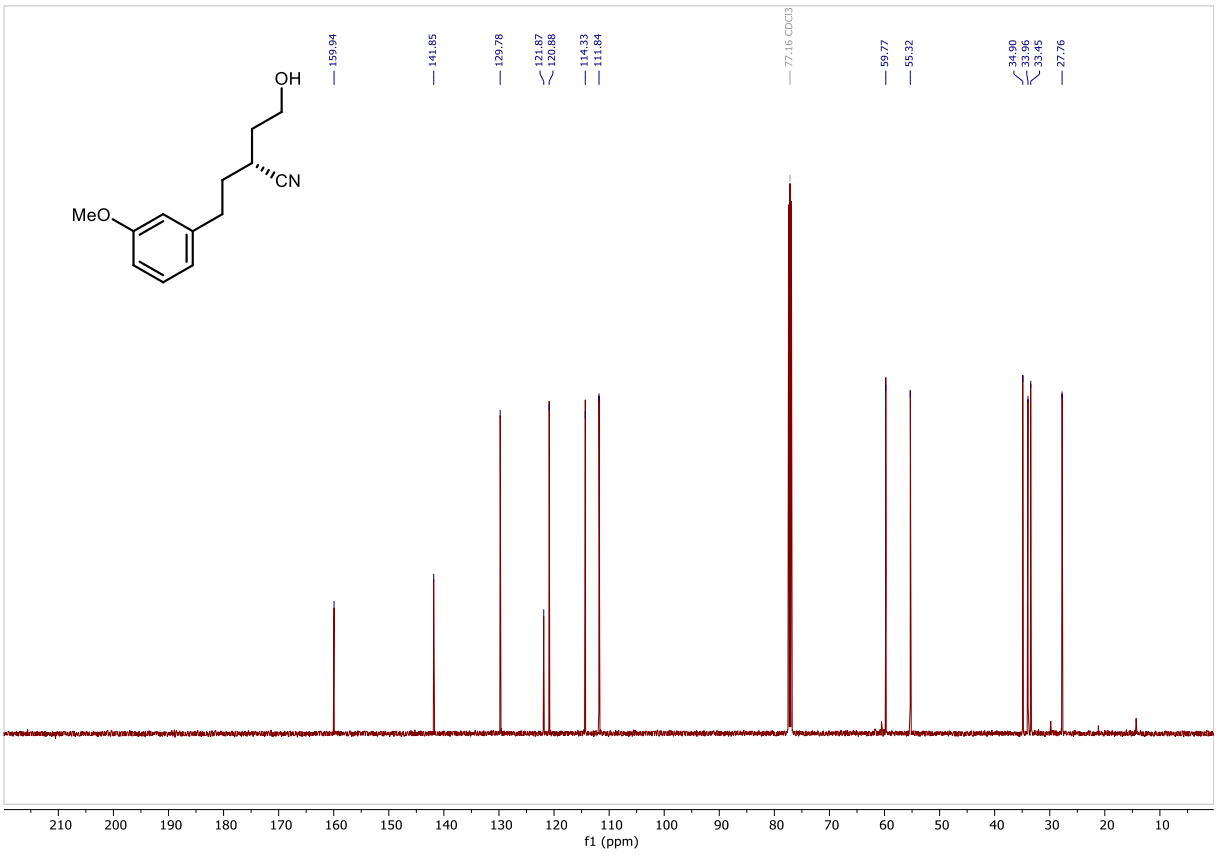
^{13}C NMR (126 MHz, $CDCl_3$) of **3e**:



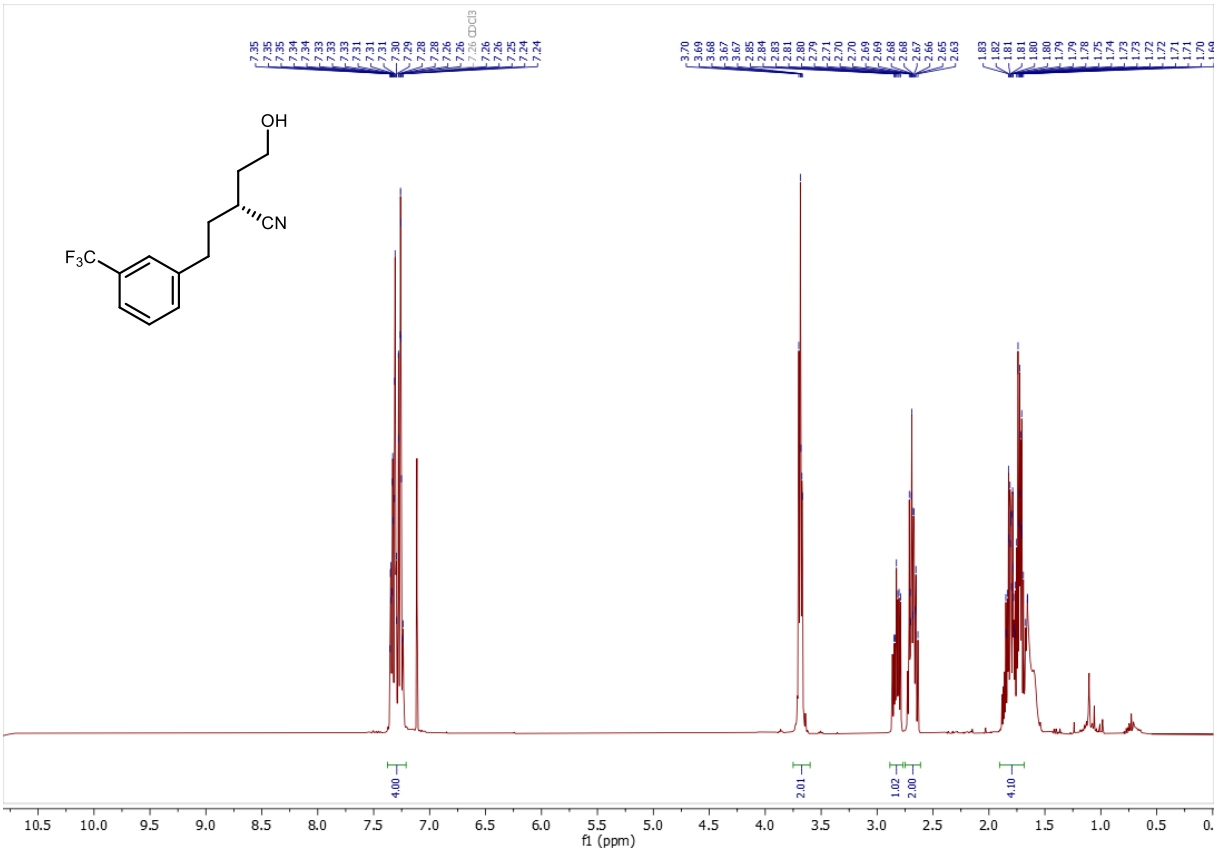
^{1}H NMR (500 MHz, $CDCl_3$) of **3f**:



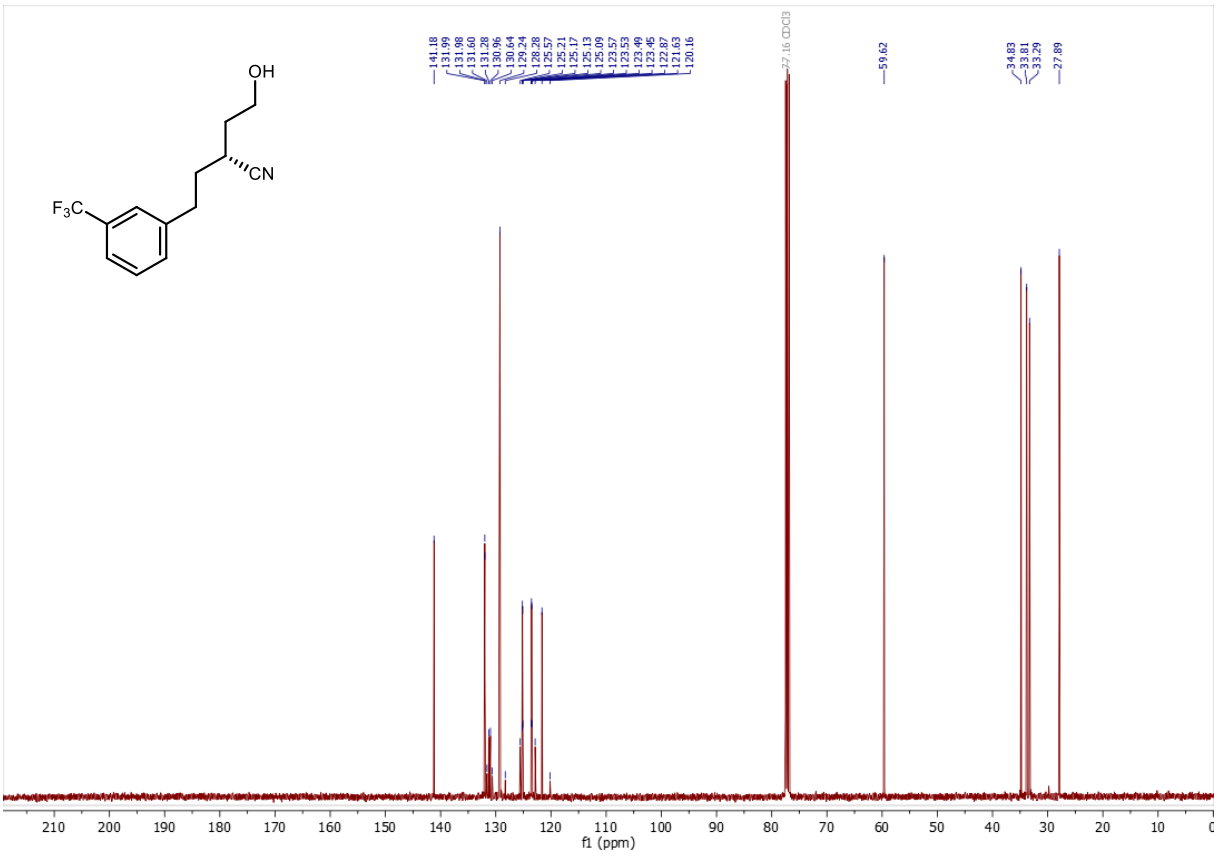
^{13}C NMR (126 MHz, $CDCl_3$) of **3f**:



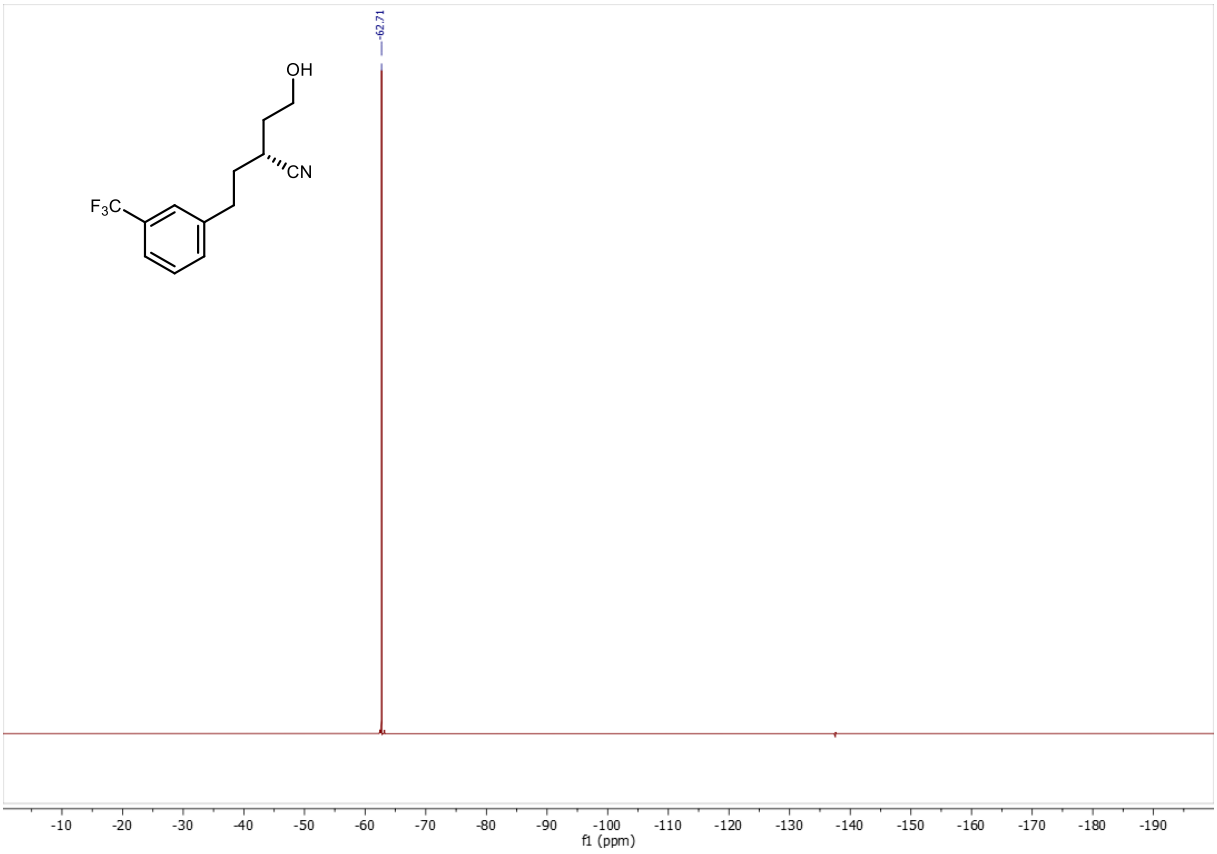
^{1}H NMR (400 MHz, $CDCl_3$) of **3g**:



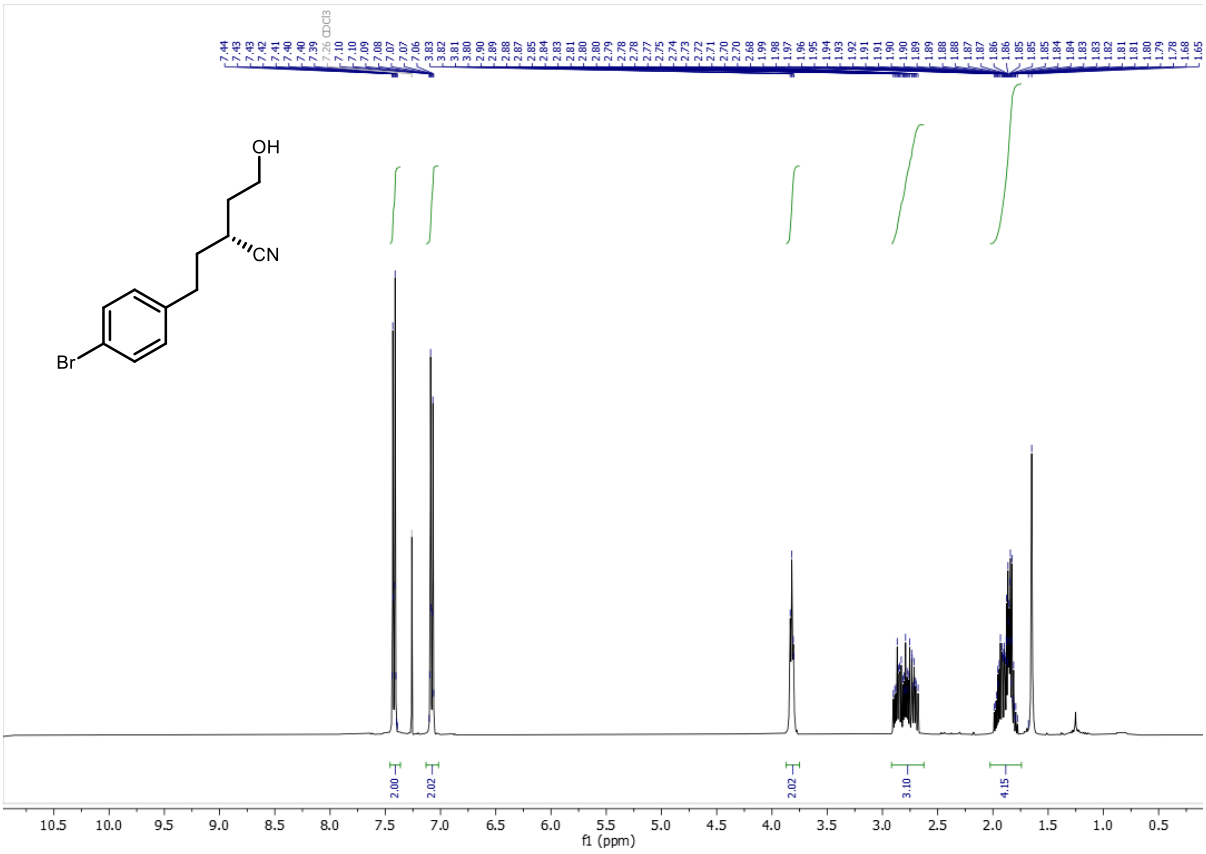
^{13}C NMR (101 MHz, $CDCl_3$) of **3g**:



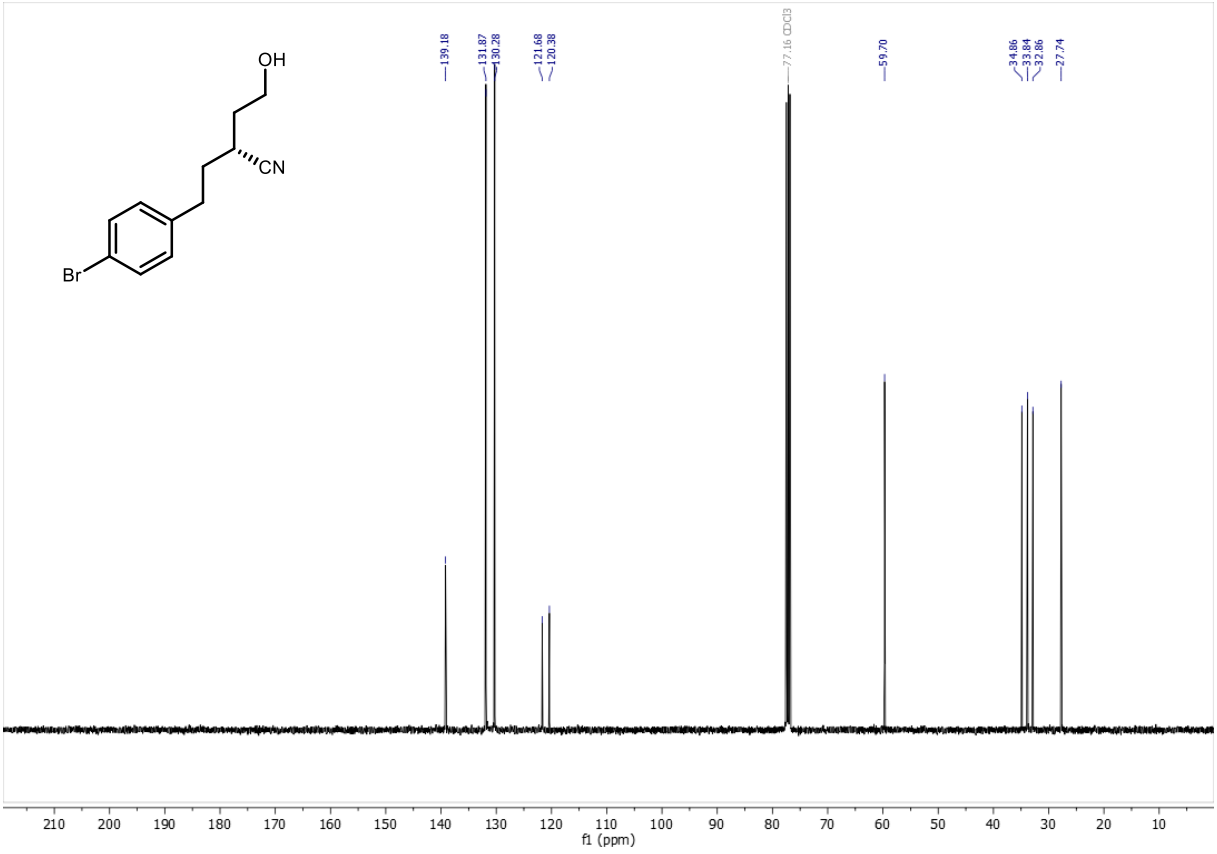
^{19}F NMR (376 MHz, $CDCl_3$) of **3g**:



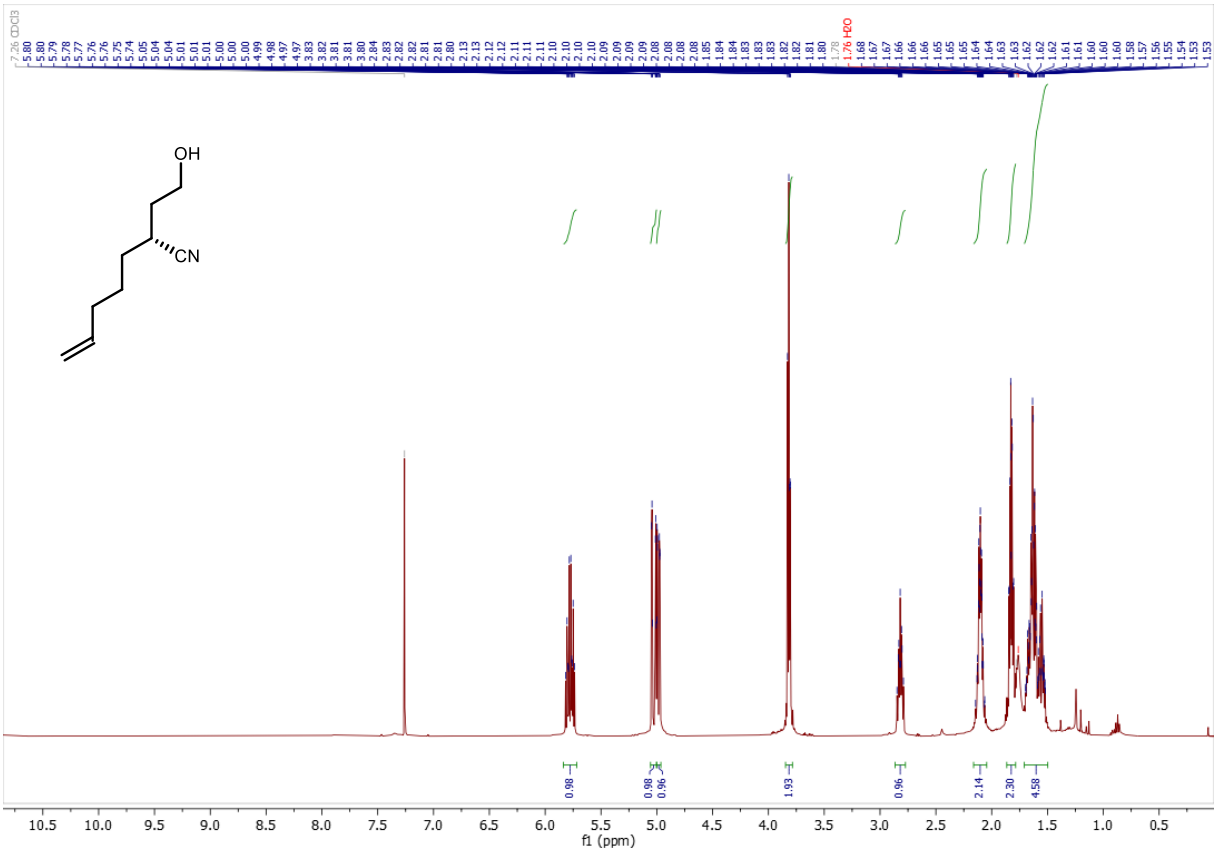
^{1}H NMR (400 MHz, $CDCl_3$) of **3h**:



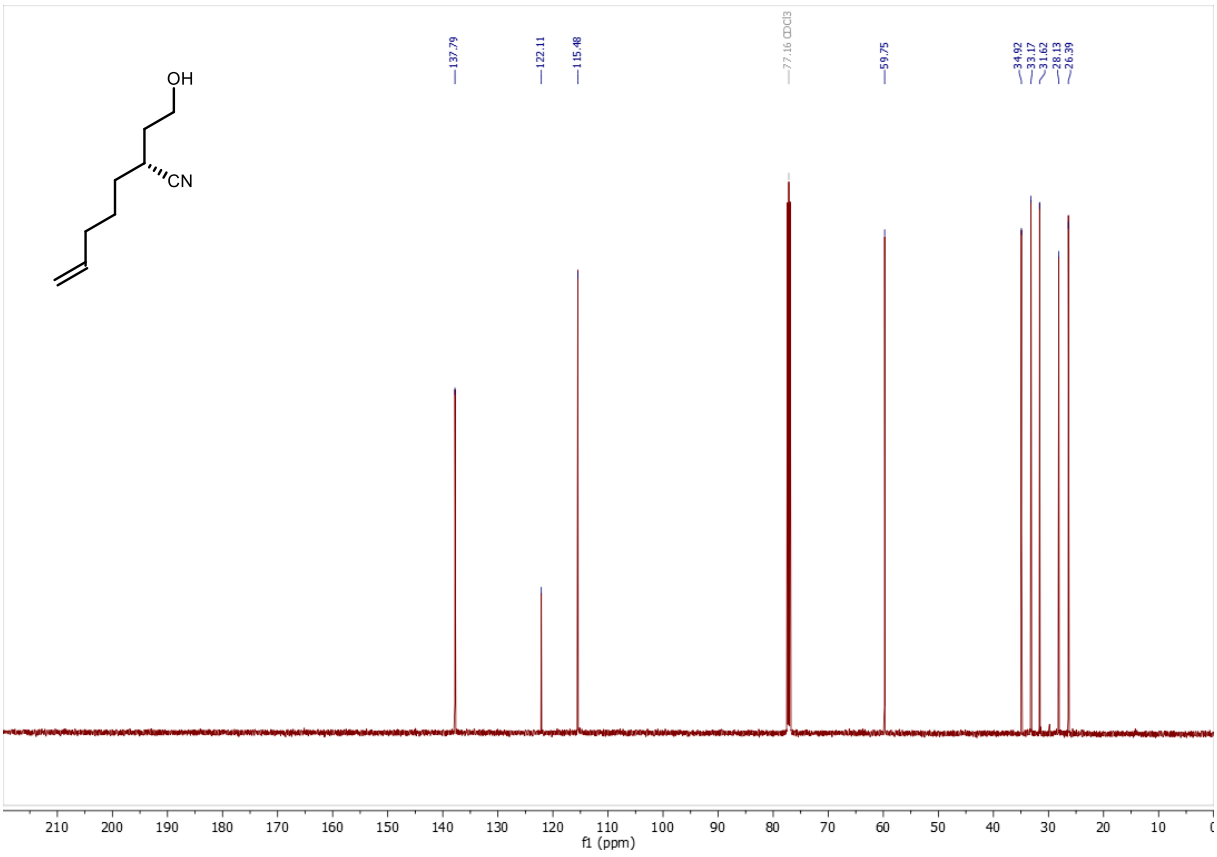
^{13}C NMR (101 MHz, $CDCl_3$) of **3h**:



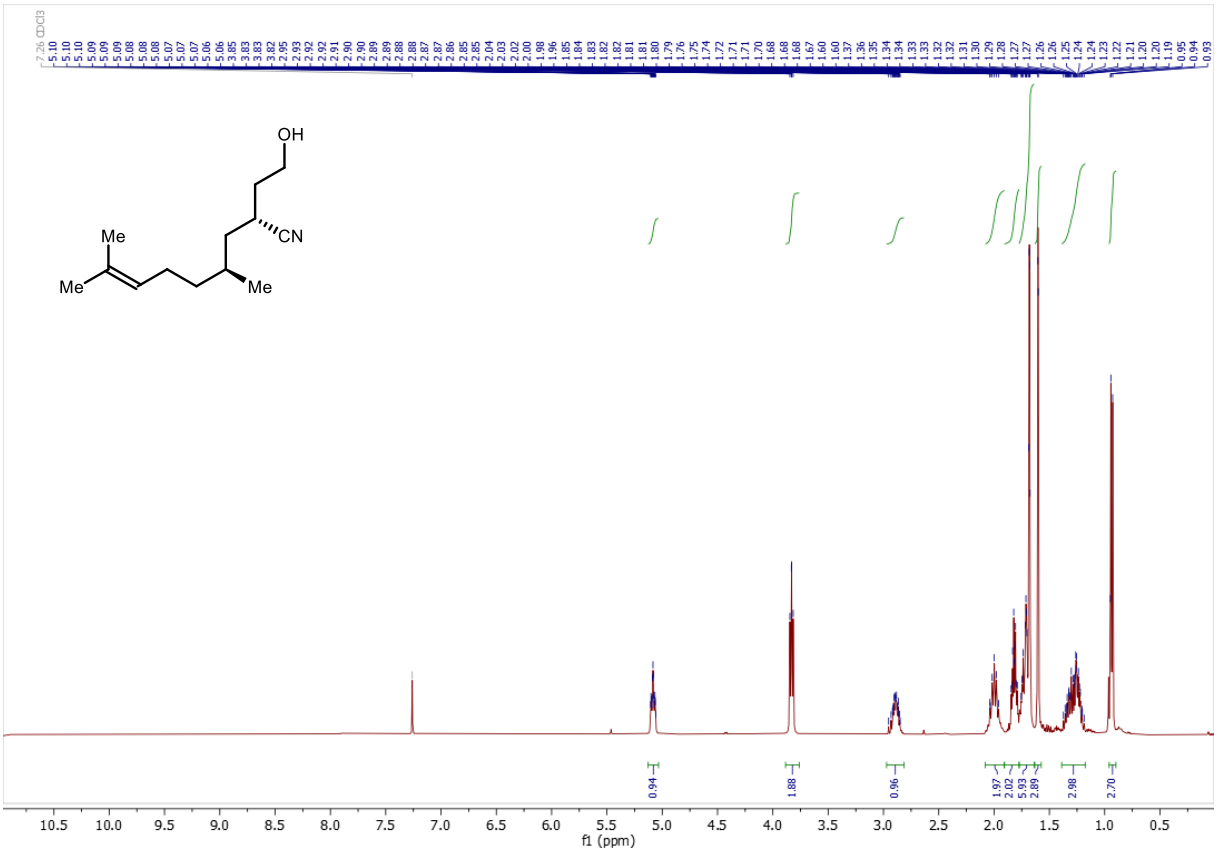
^{1}H NMR (500 MHz, $CDCl_3$) of **3i**:



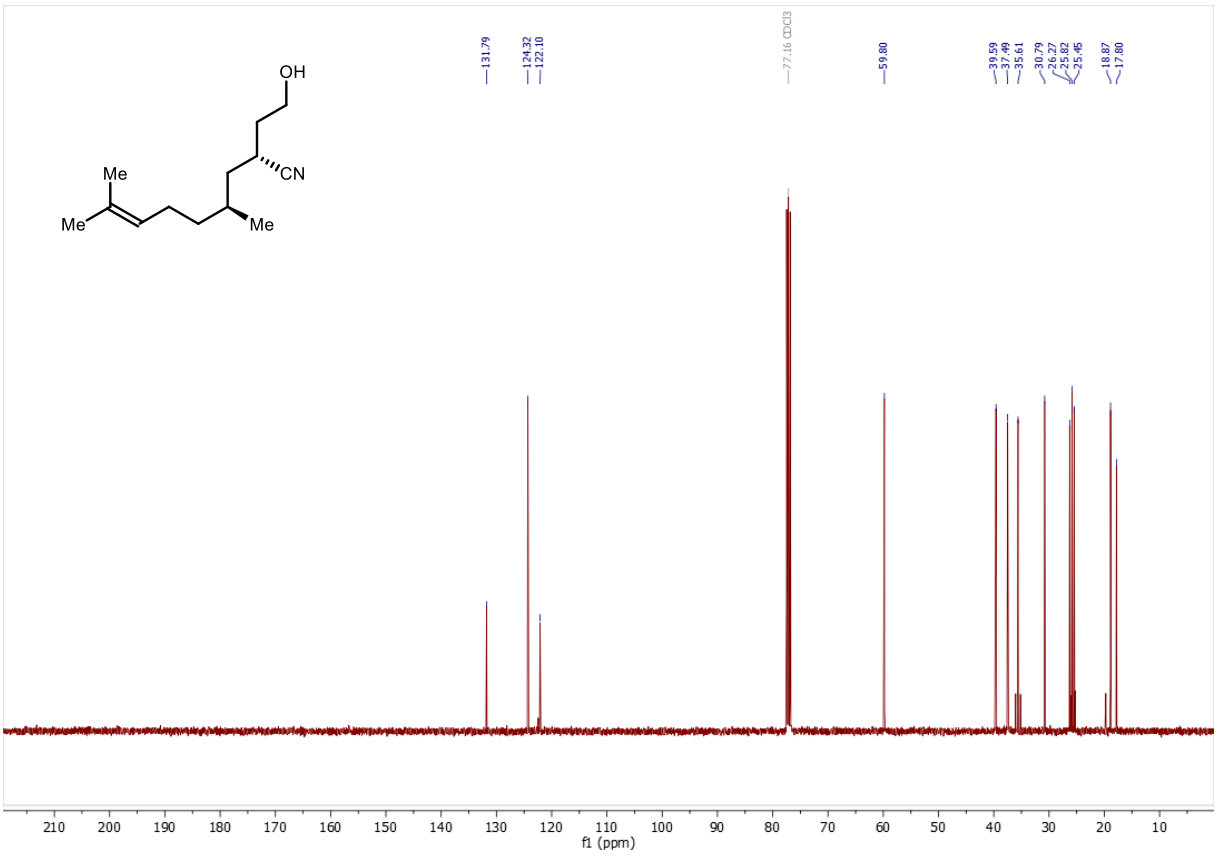
^{13}C NMR (126 MHz, $CDCl_3$) of **3i:**



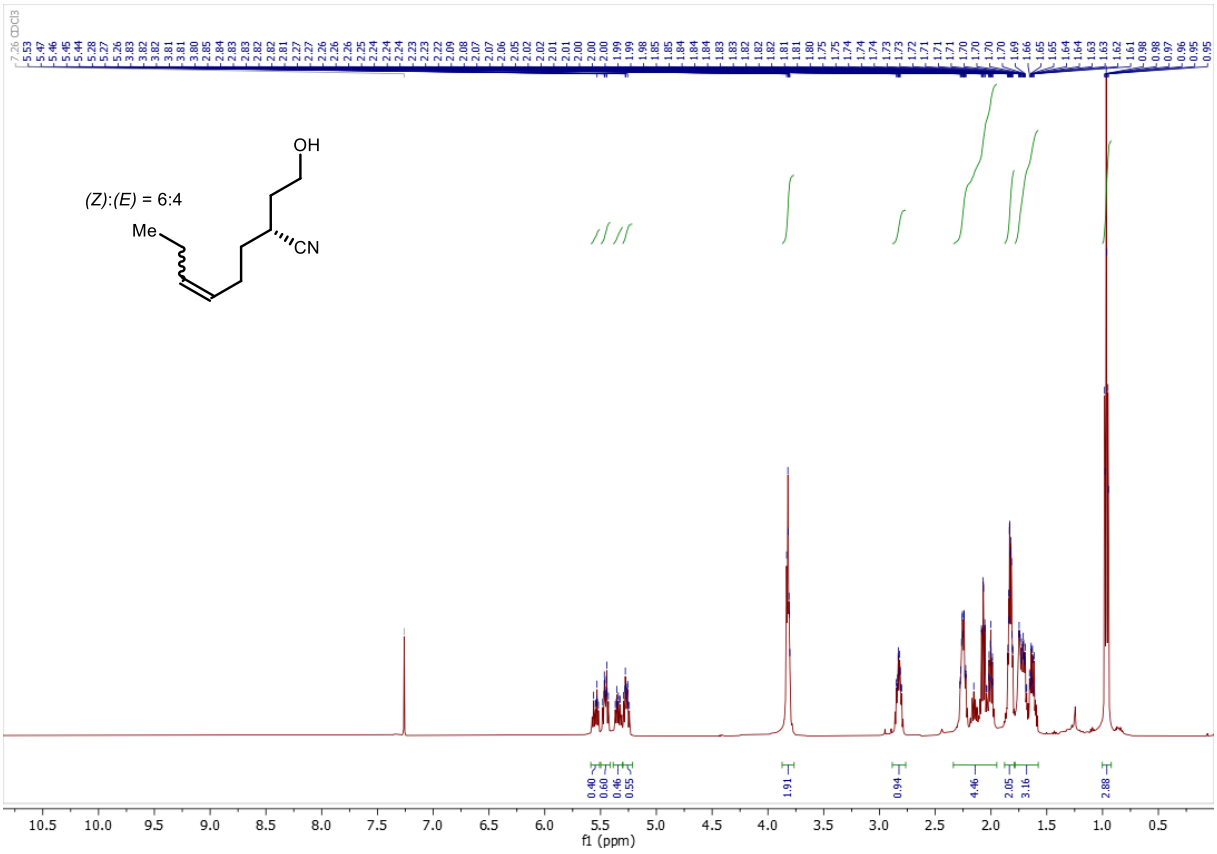
^{1}H NMR (400 MHz, $CDCl_3$, *90.5:9.5 d.r.*) of **3j**:



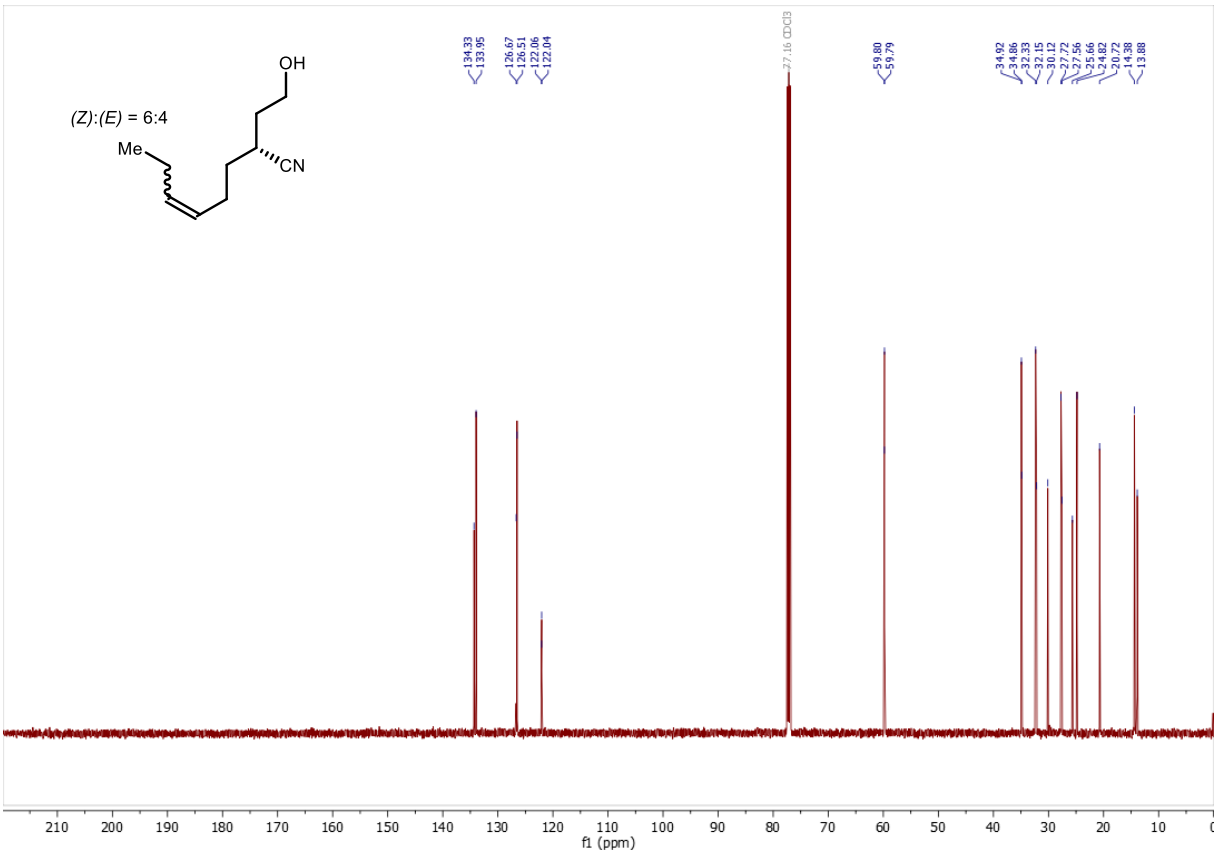
^{13}C NMR (101 MHz, $CDCl_3$, *90.5:9.5 d.r.*) of **3j**:



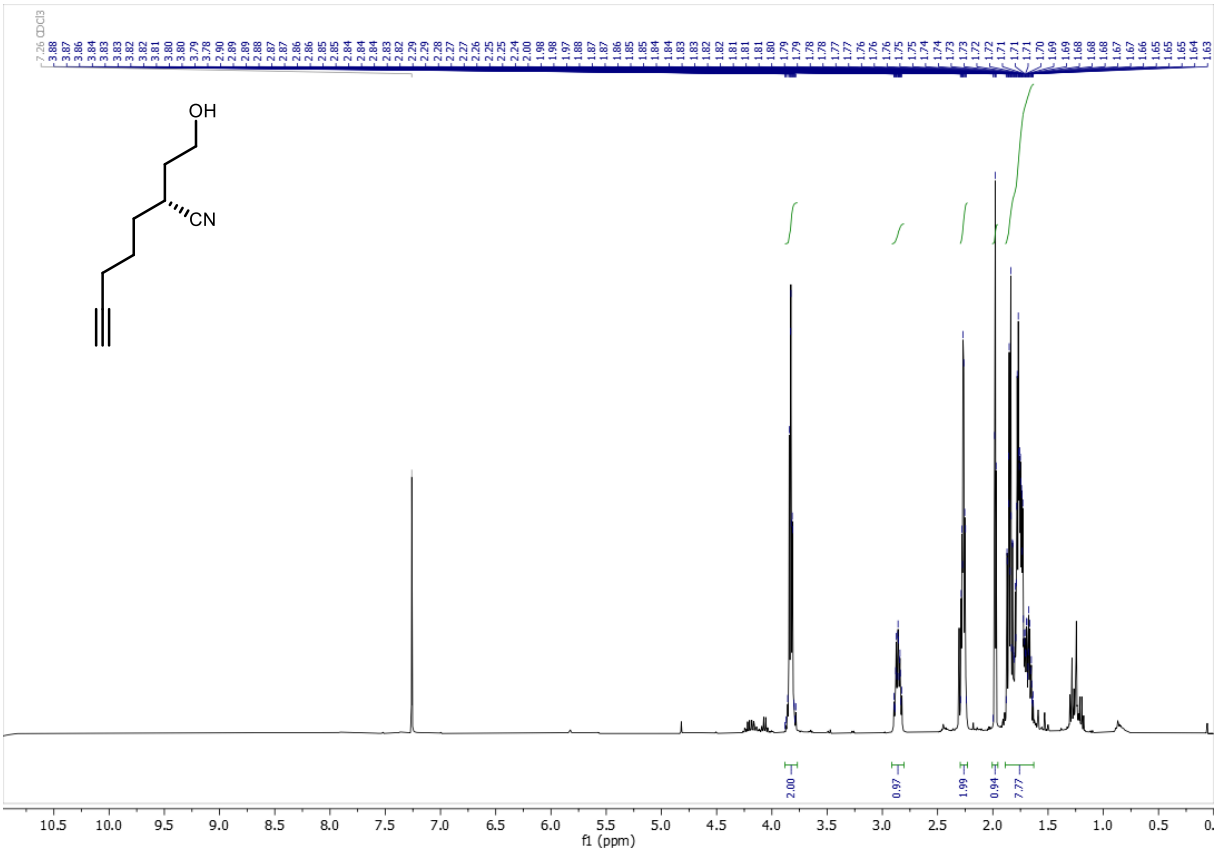
^{1}H NMR (500 MHz, $CDCl_3$, *E/Z* = 60:40) of **3k**:



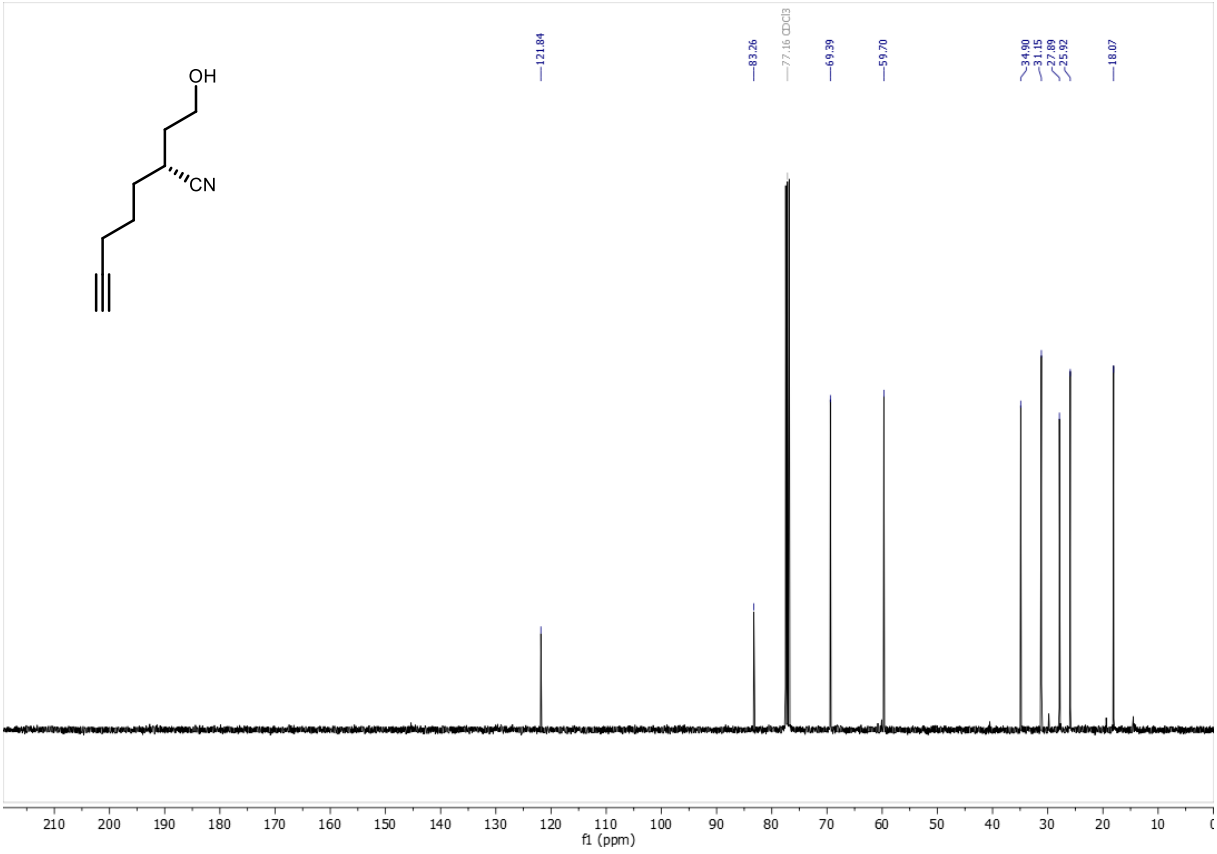
^{13}C NMR (126 MHz, $CDCl_3$, *E/Z* = 60:40) of **3k**:



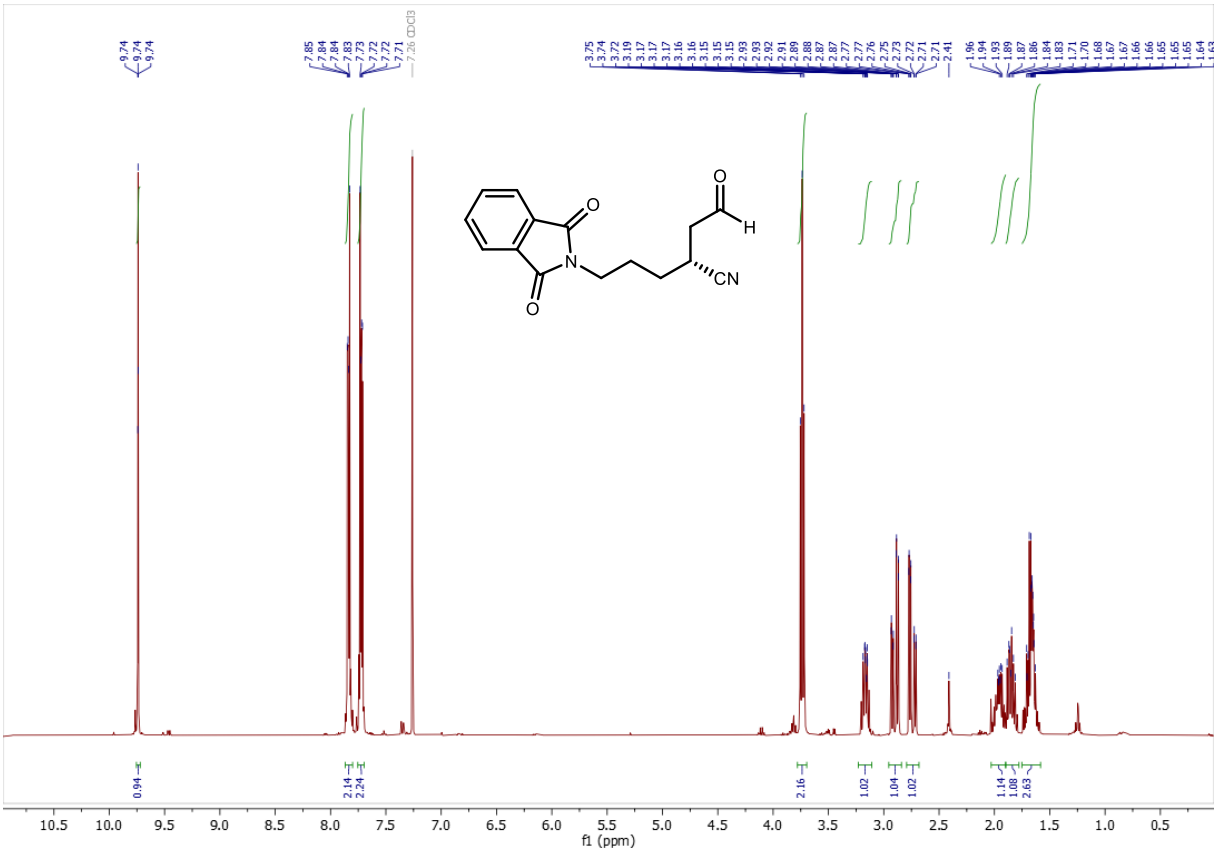
^{1}H NMR (400 MHz, $CDCl_3$) of **3l**:



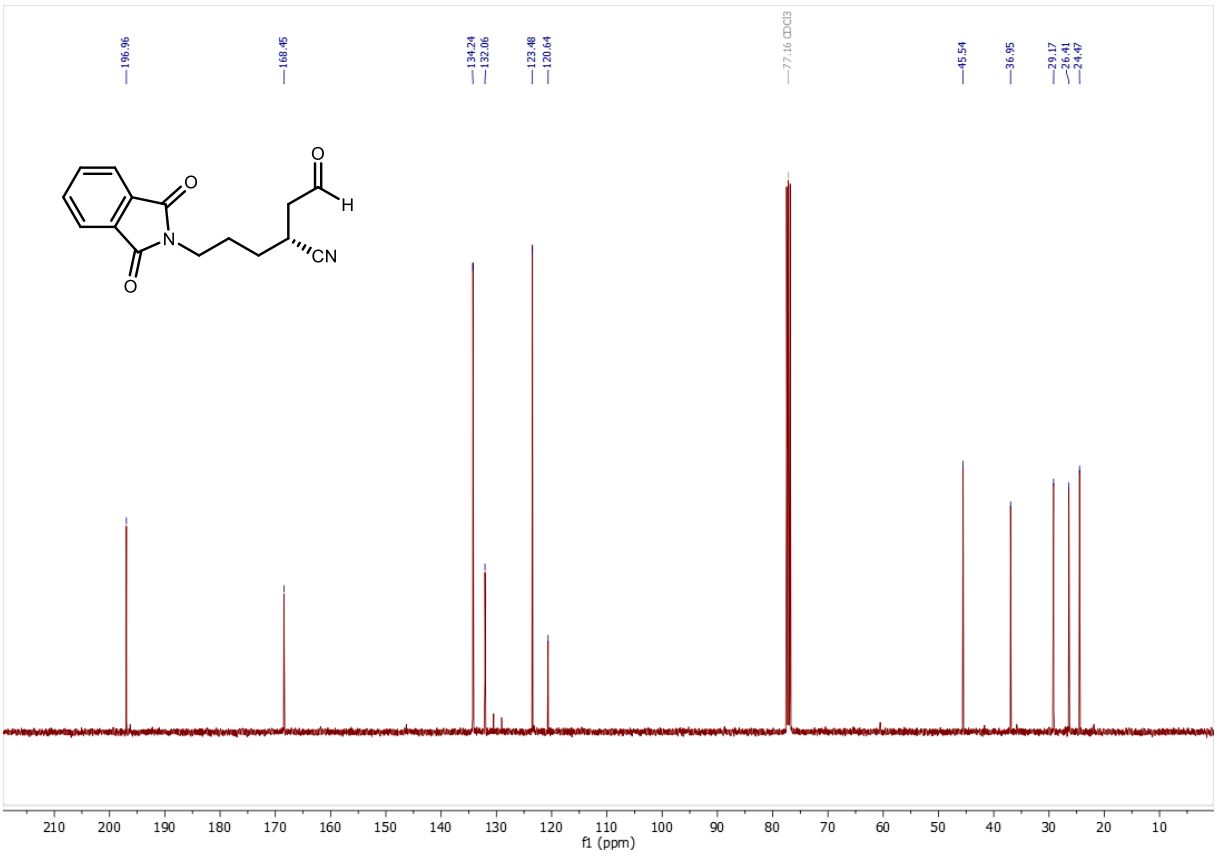
^{13}C NMR (101 MHz, $CDCl_3$) of **3l**:



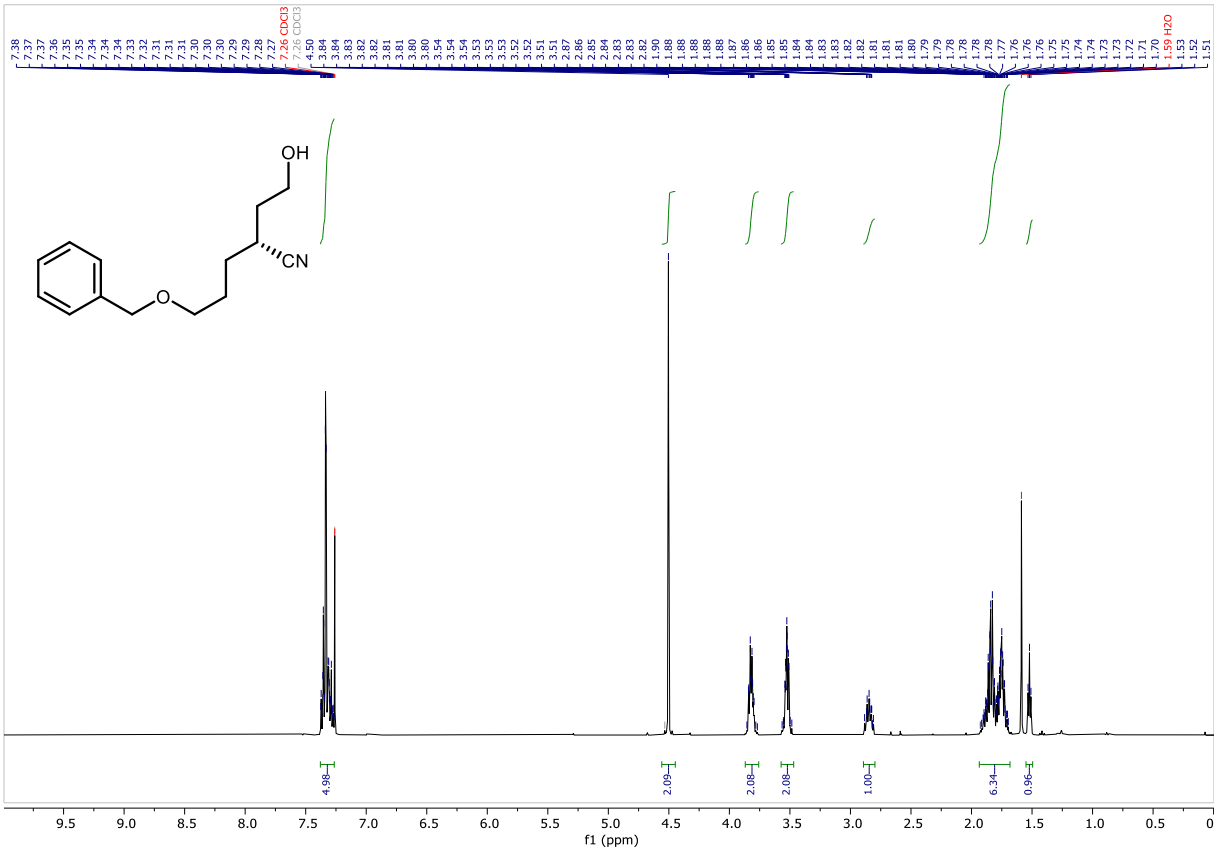
^{1}H NMR (400 MHz, $CDCl_3$) of **2m**:



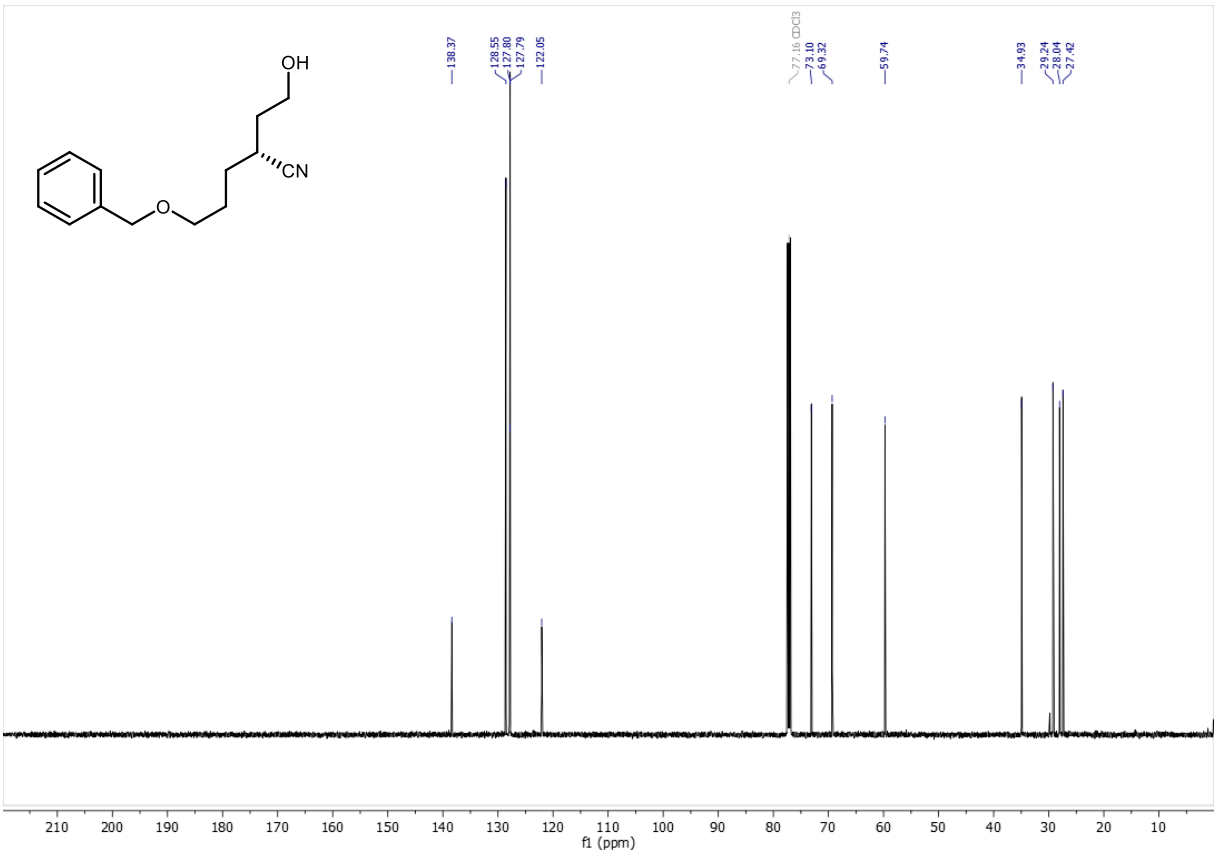
^{13}C NMR (101 MHz, $CDCl_3$) of **2m**:



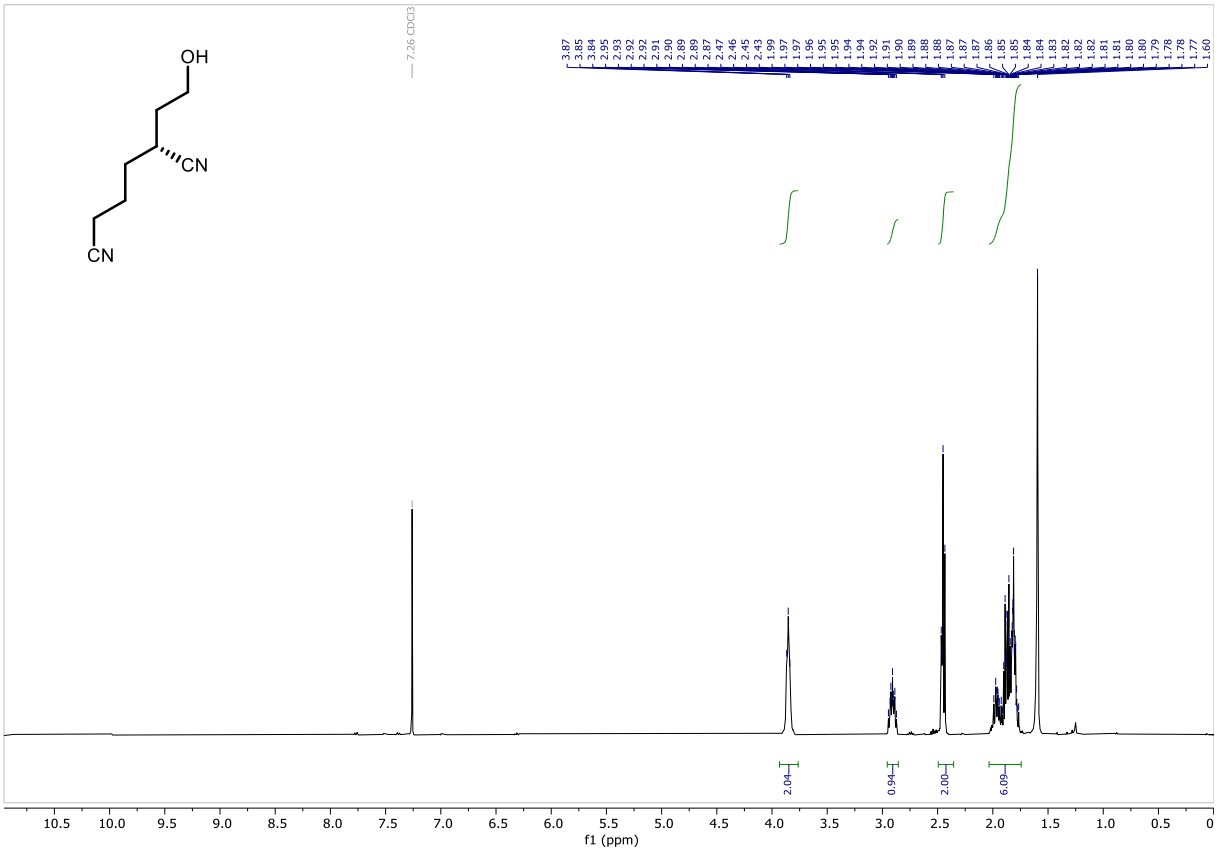
^{1}H NMR (500 MHz, $CDCl_3$) of **3n**:



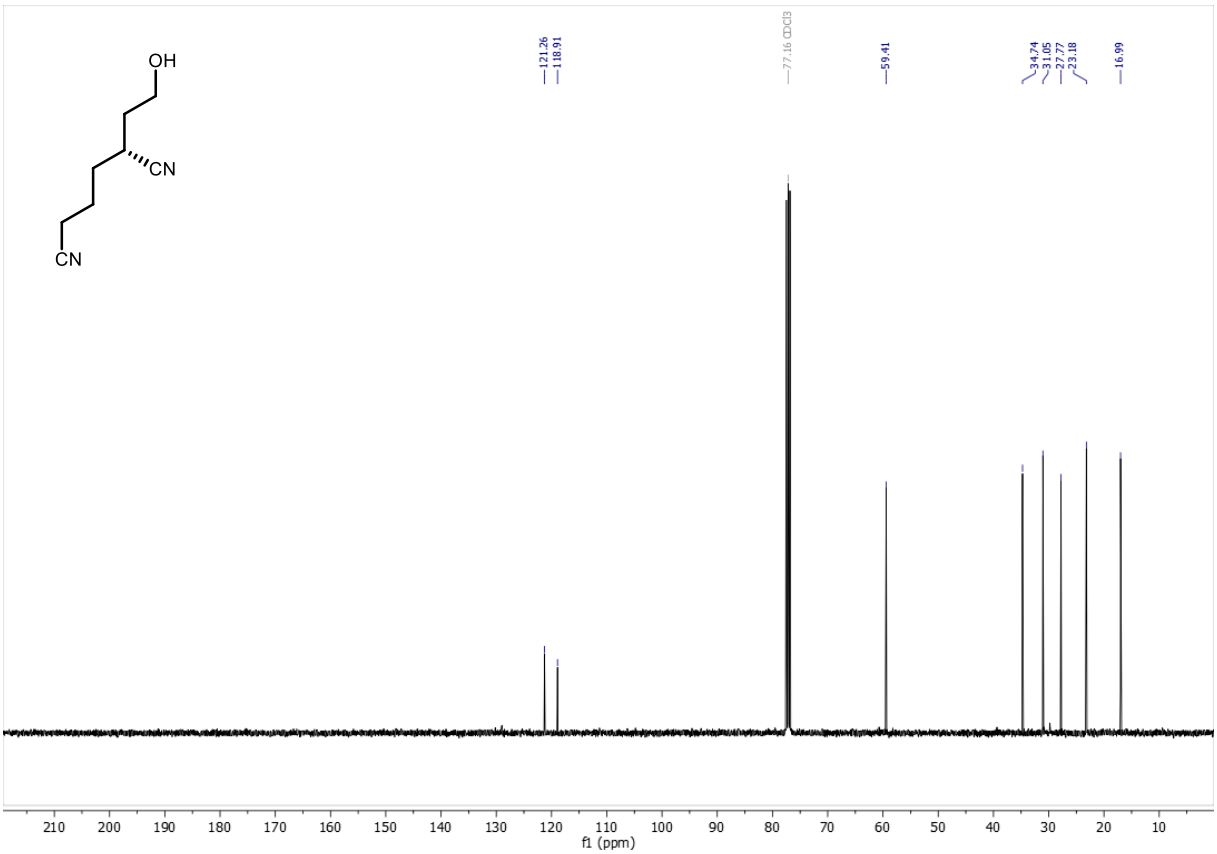
^{13}C NMR (126 MHz, $CDCl_3$) of **3n**:



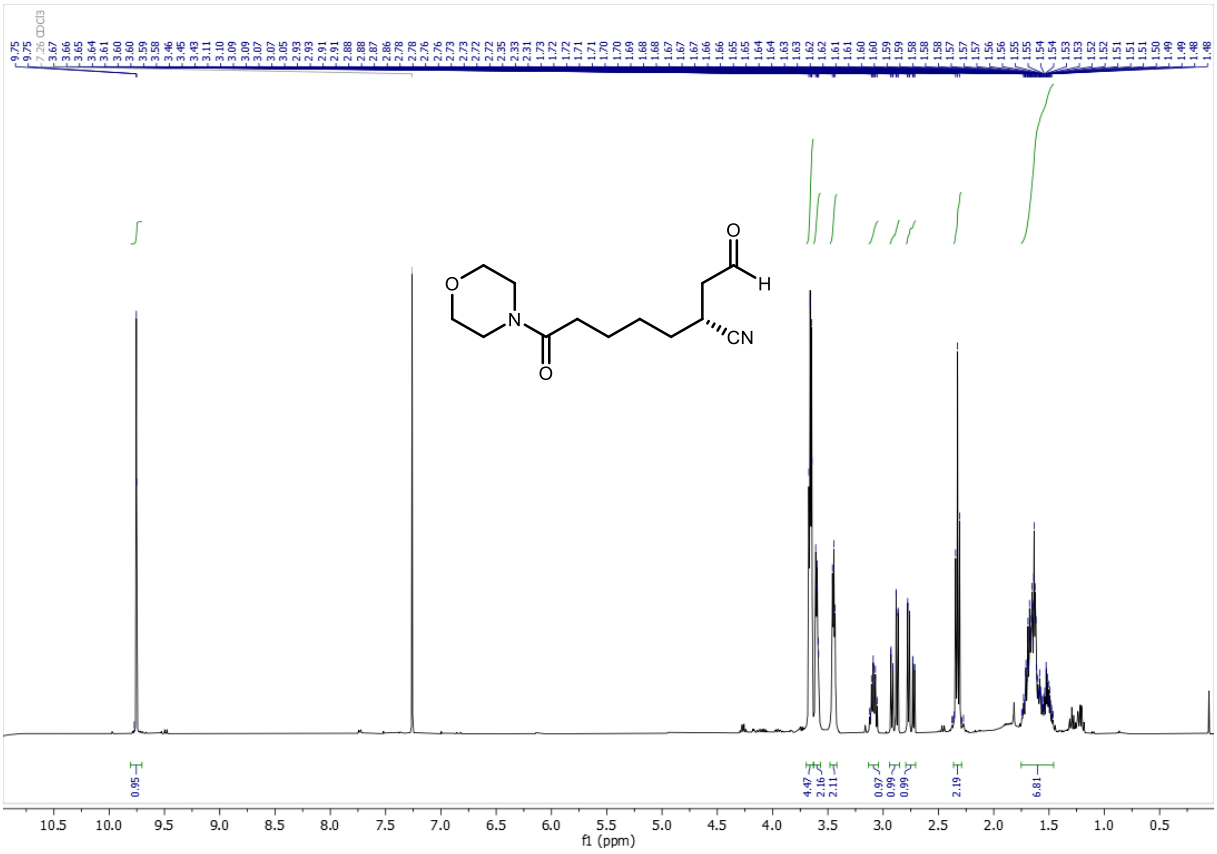
^{1}H NMR (400 MHz, $CDCl_3$) of **3o**:



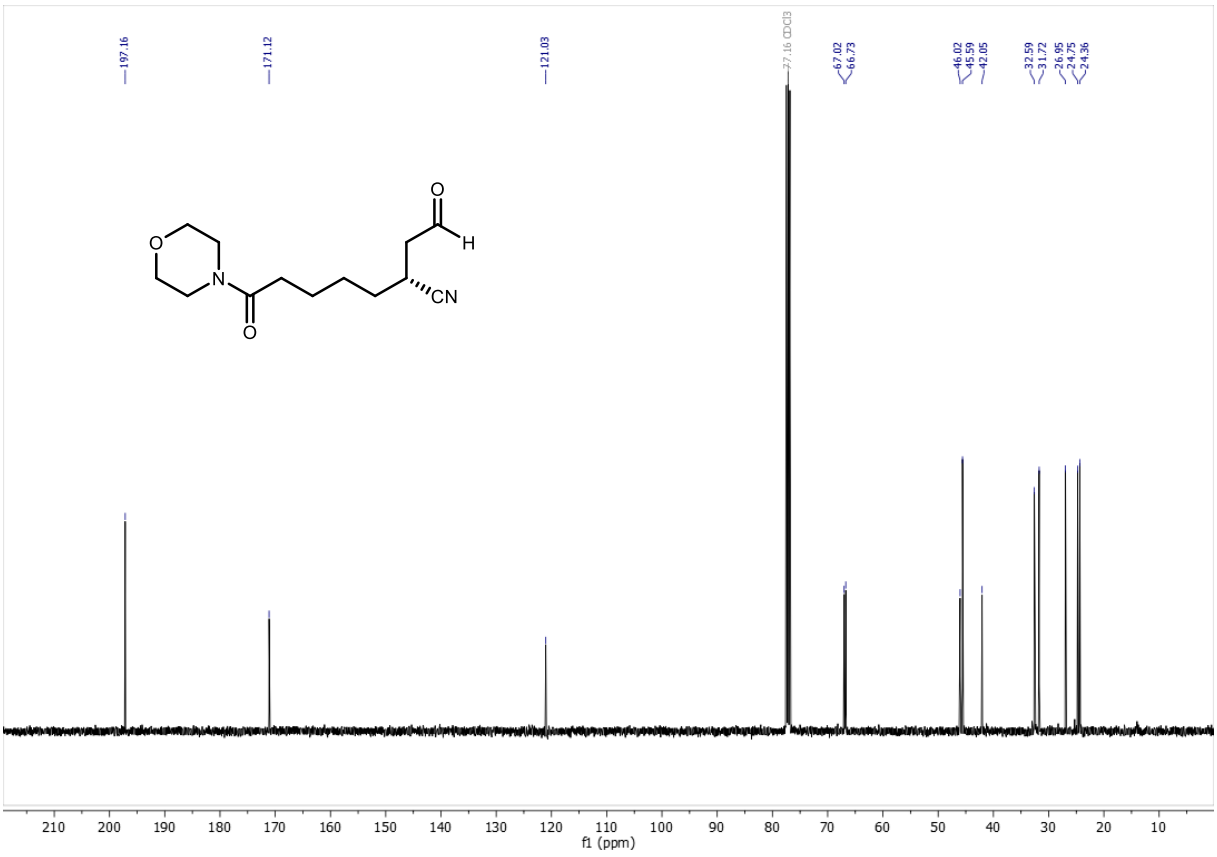
^{13}C NMR (101 MHz, $CDCl_3$) of **3o**:



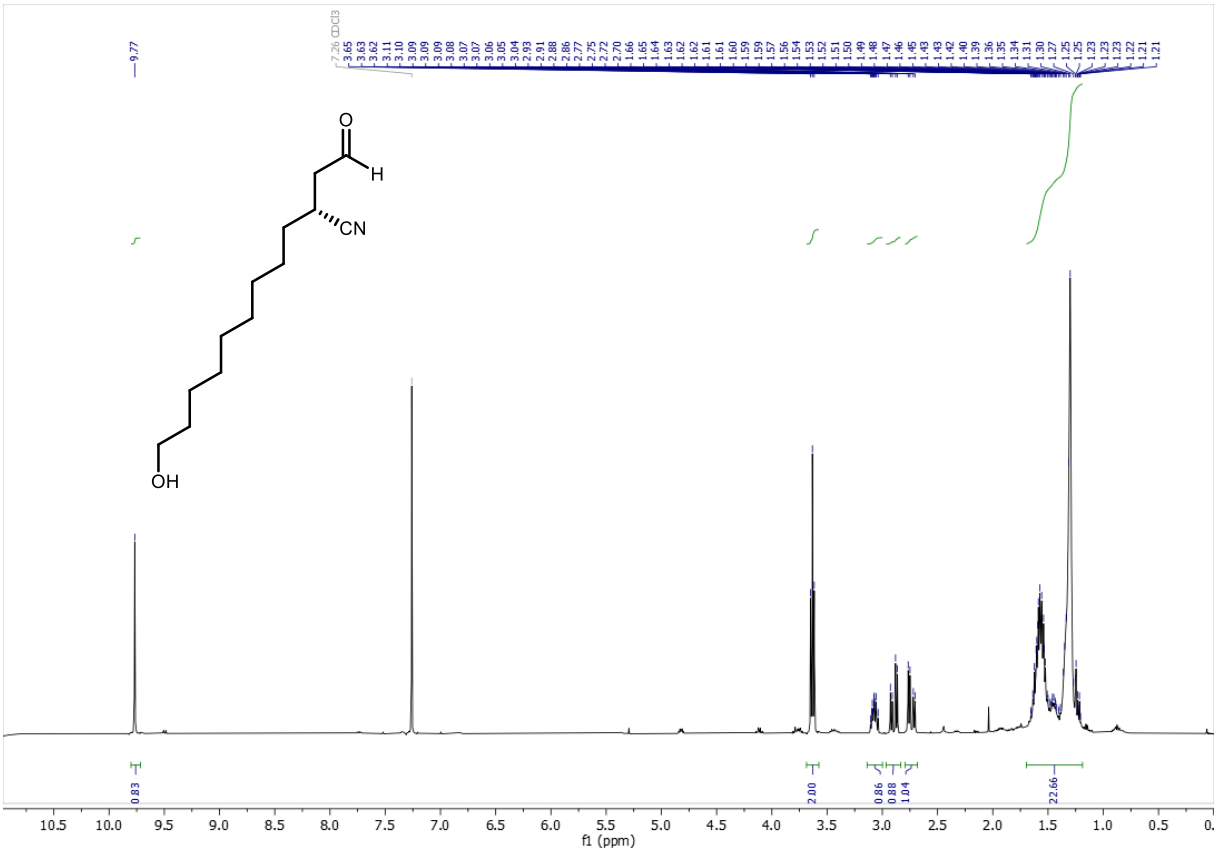
^{1}H NMR (400 MHz, $CDCl_3$) of **2p**:



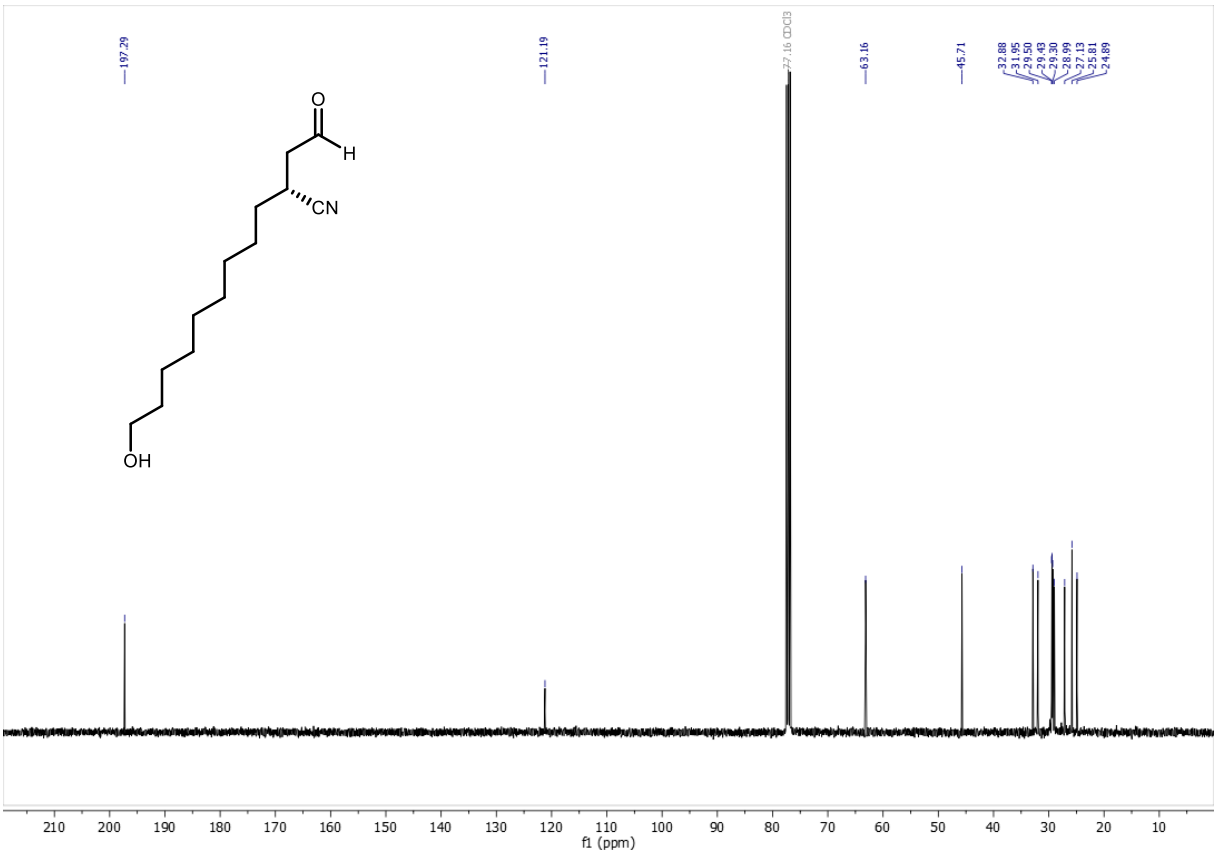
^{13}C NMR (101 MHz, $CDCl_3$) of **2p:**



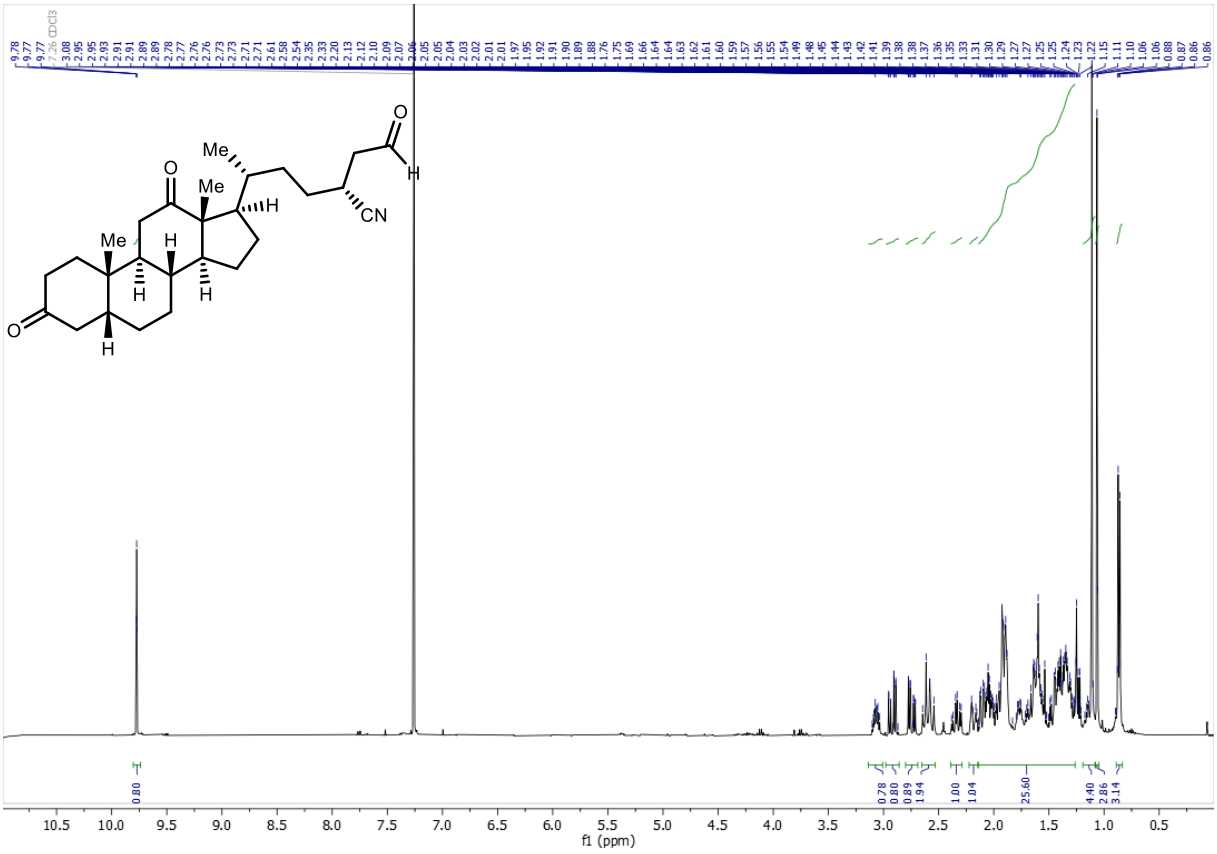
^{1}H NMR (400 MHz, $CDCl_3$) of **2q**:



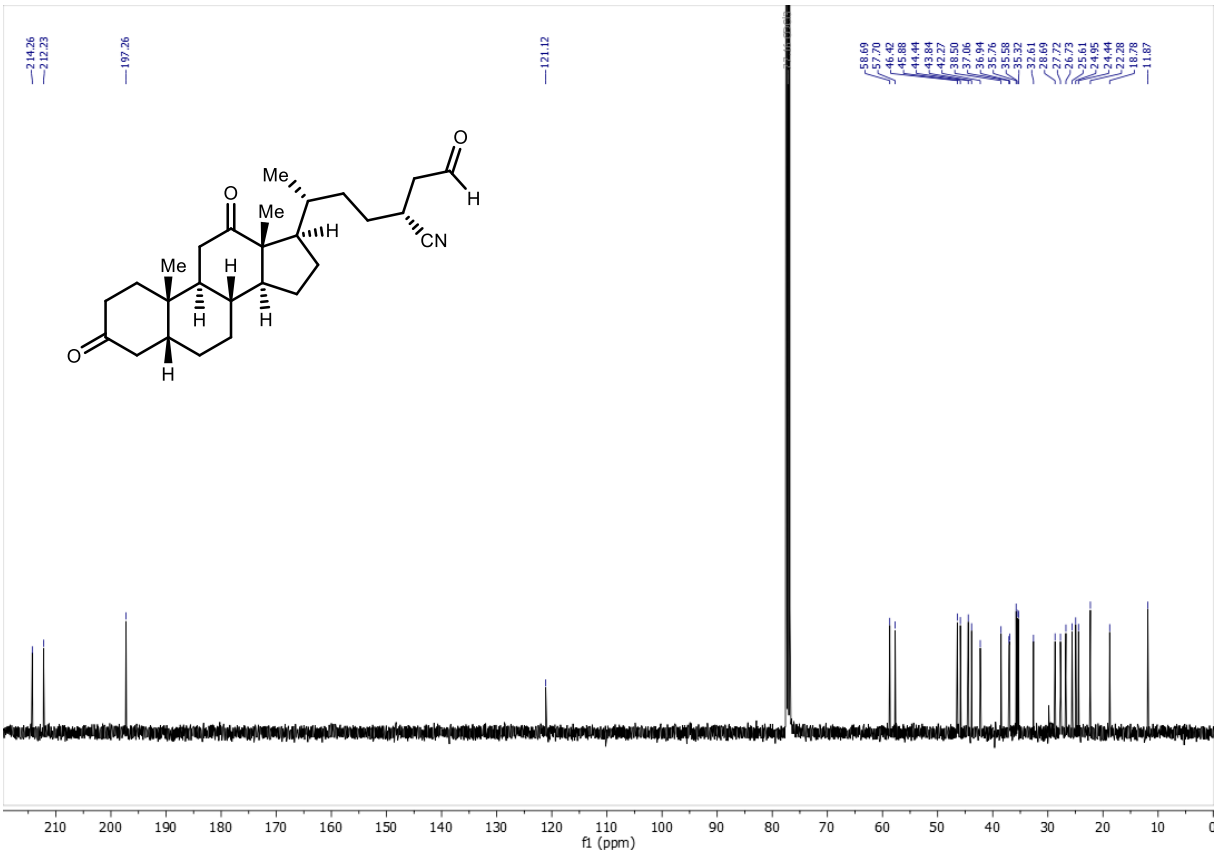
^{13}C NMR (101 MHz, $CDCl_3$) of **2q**:



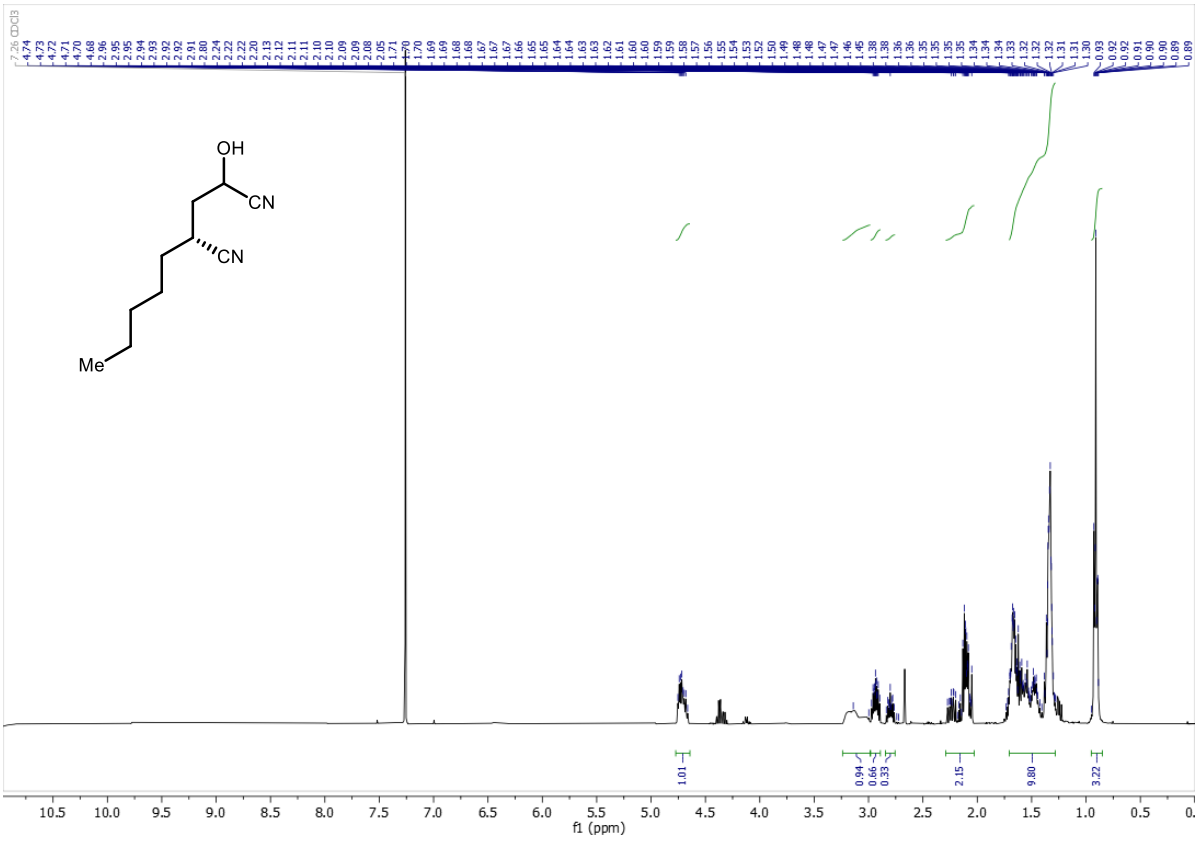
^{1}H NMR (400 MHz, $CDCl_3$) of **2r**:



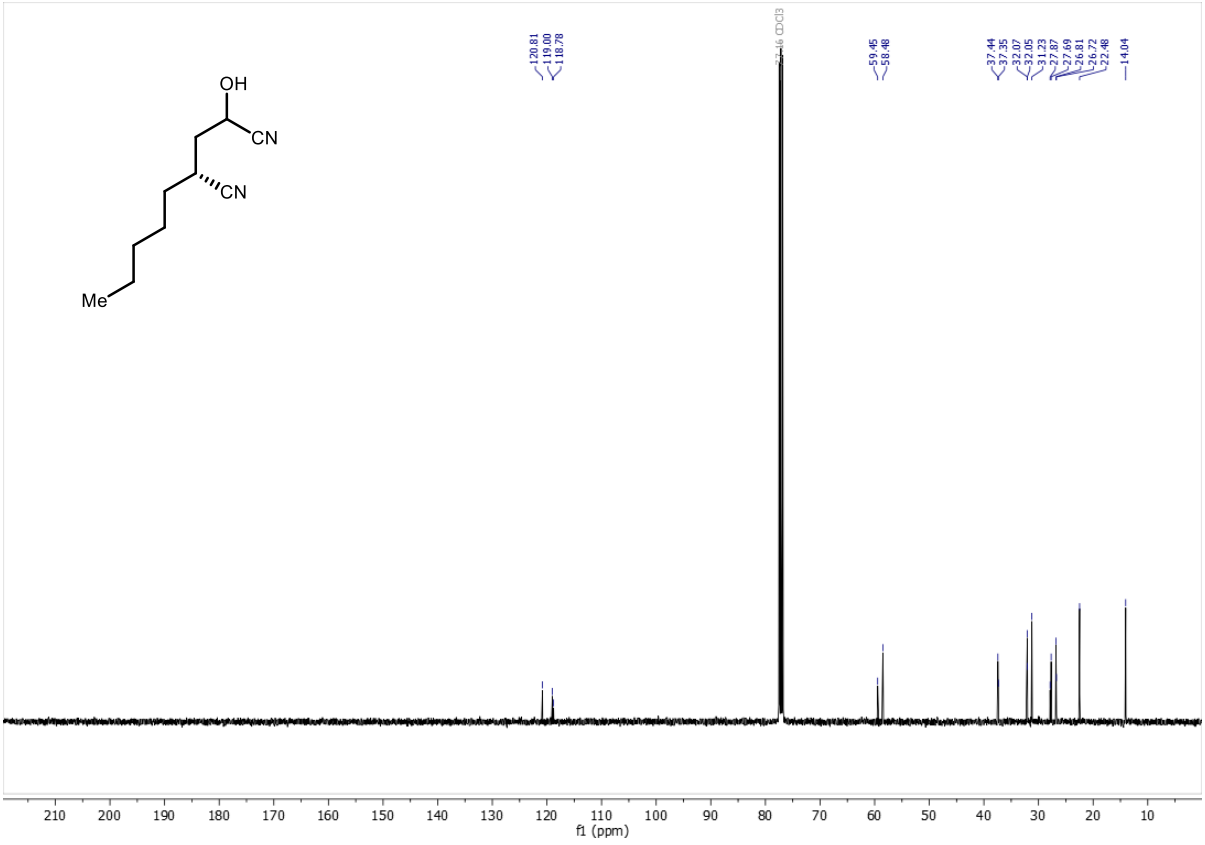
^{13}C NMR (101 MHz, $CDCl_3$) of **2r**:



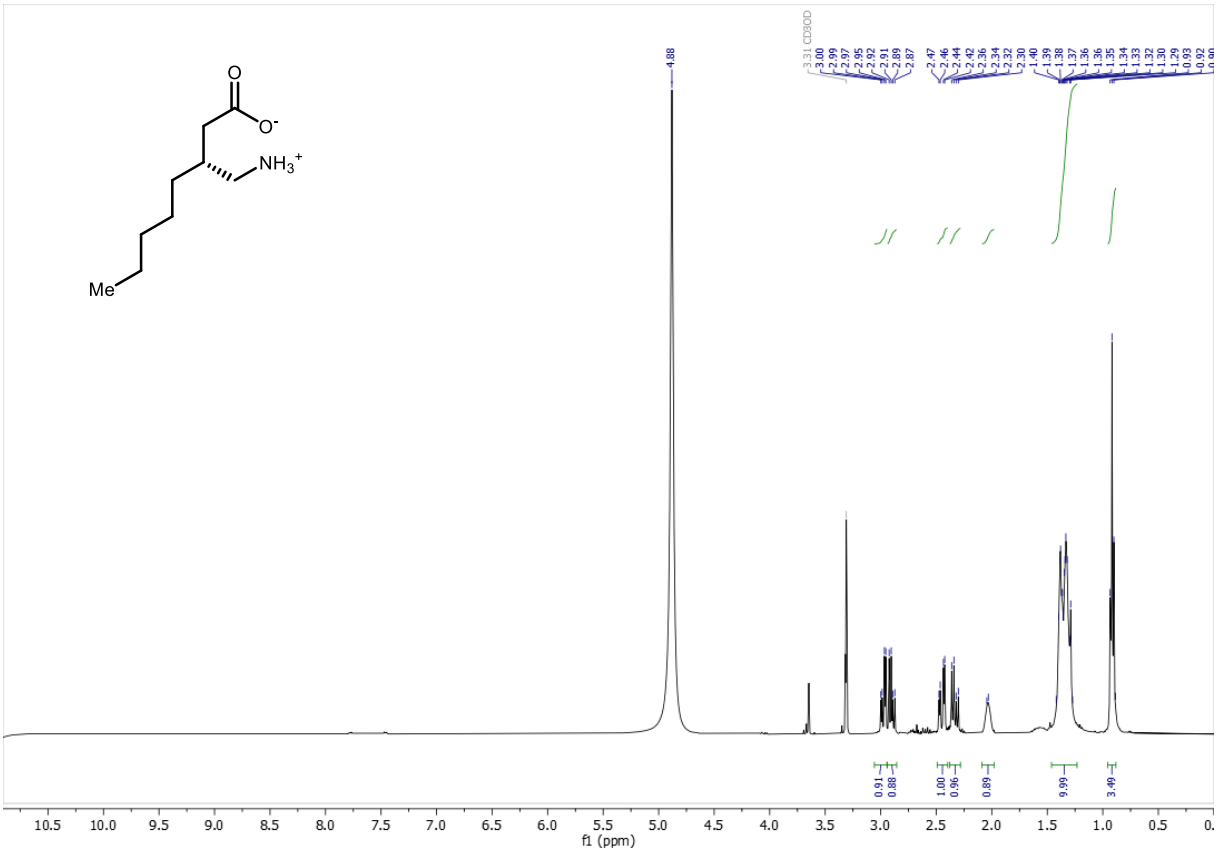
^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) of **4a**:



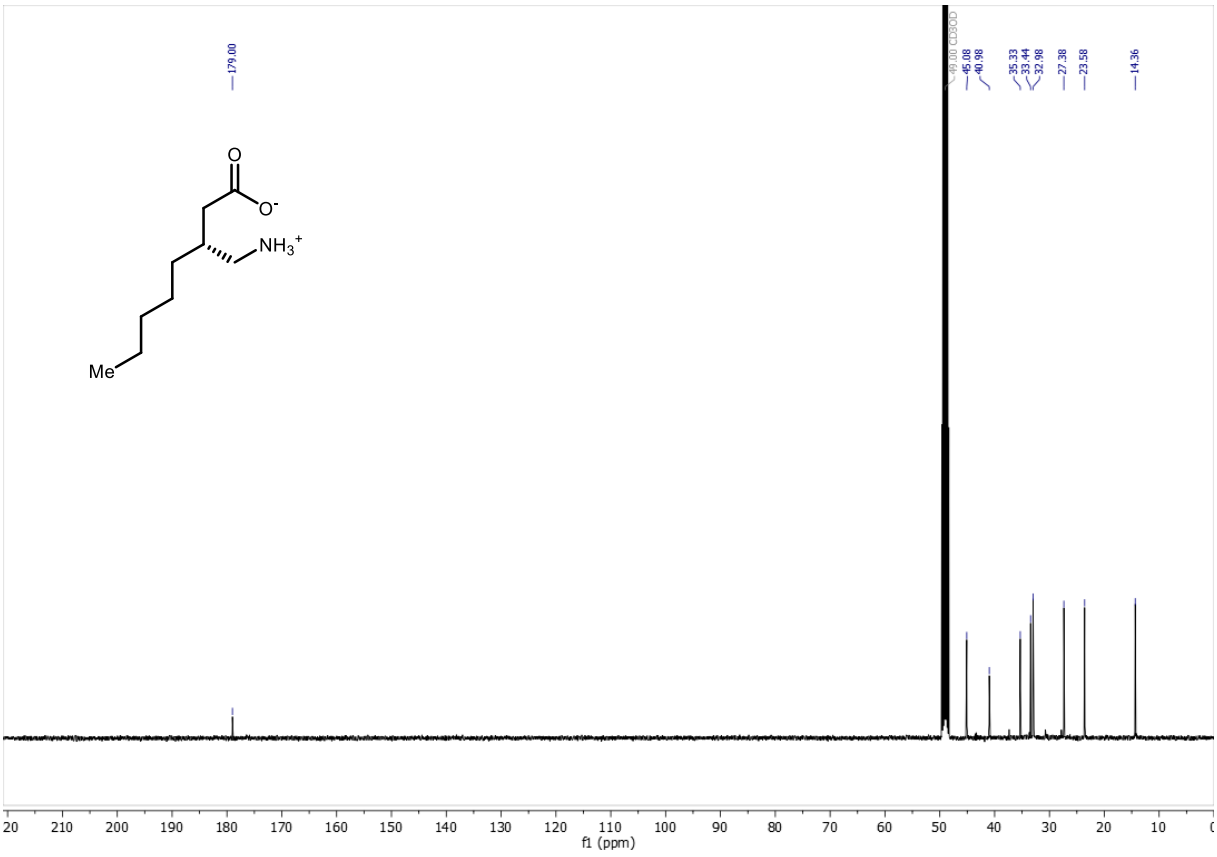
^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers) of **4a**:



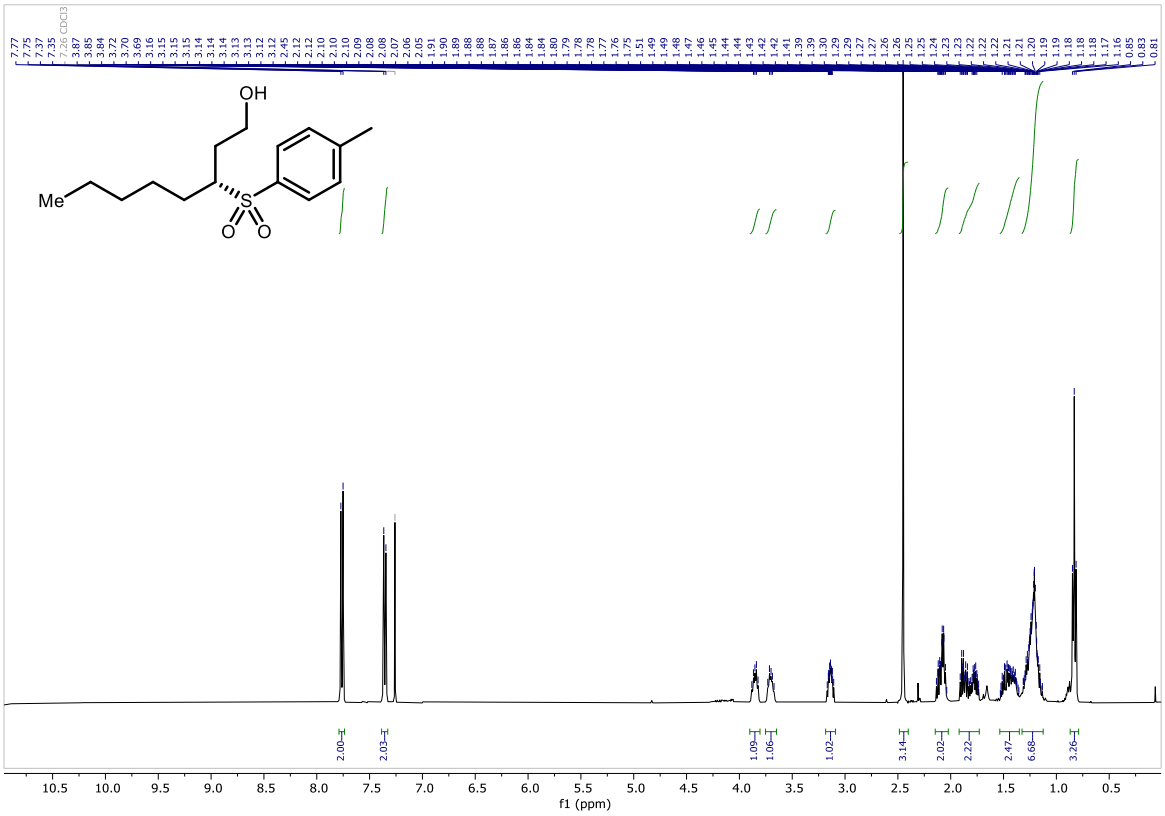
^{1}H NMR (400 MHz, CD_3OD) of **4c**:



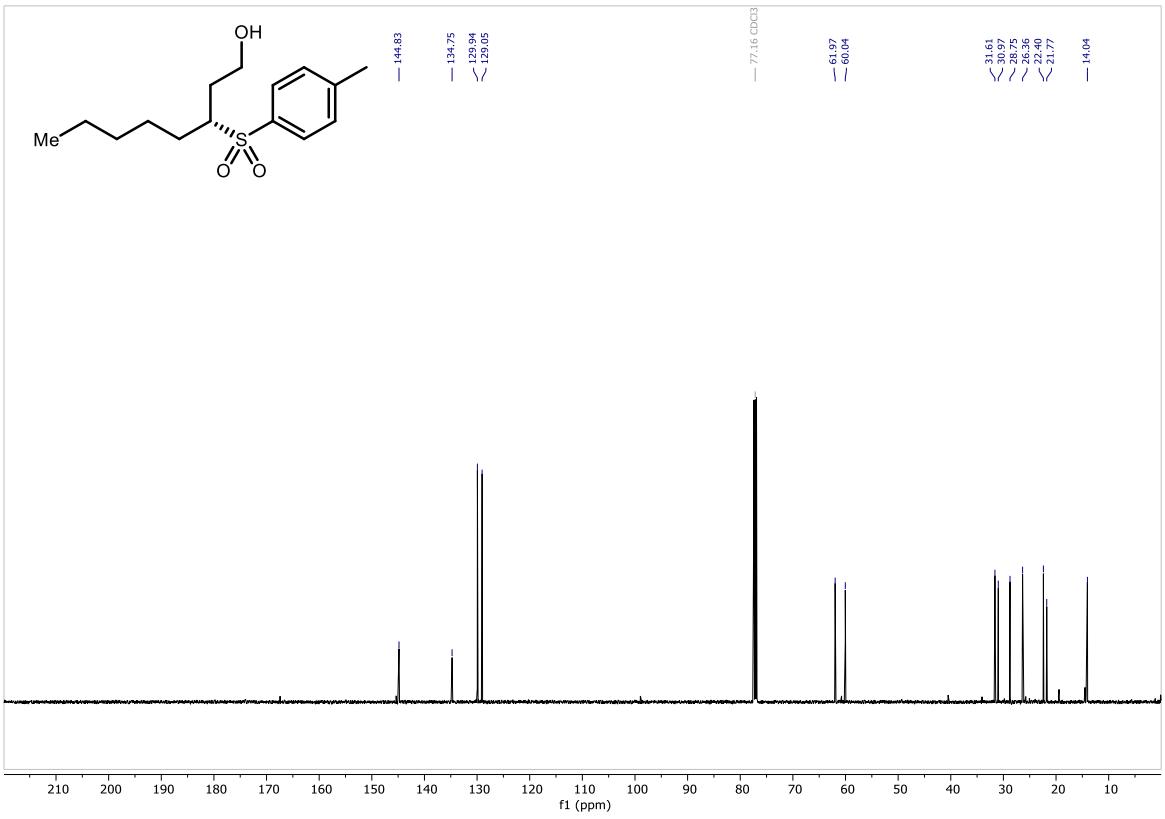
^{13}C NMR (101 MHz, CD_3OD) of **4c**:



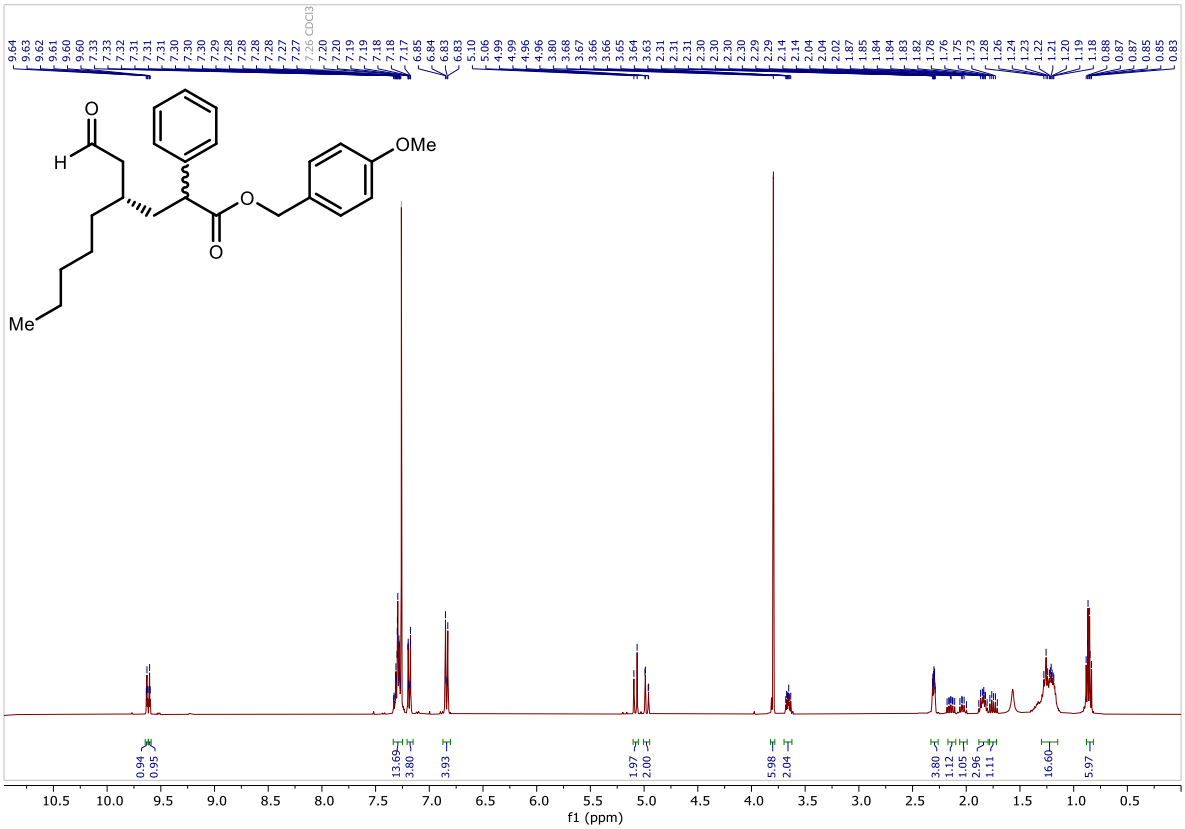
^{1}H NMR (400 MHz, $CDCl_3$) of **3a'**:



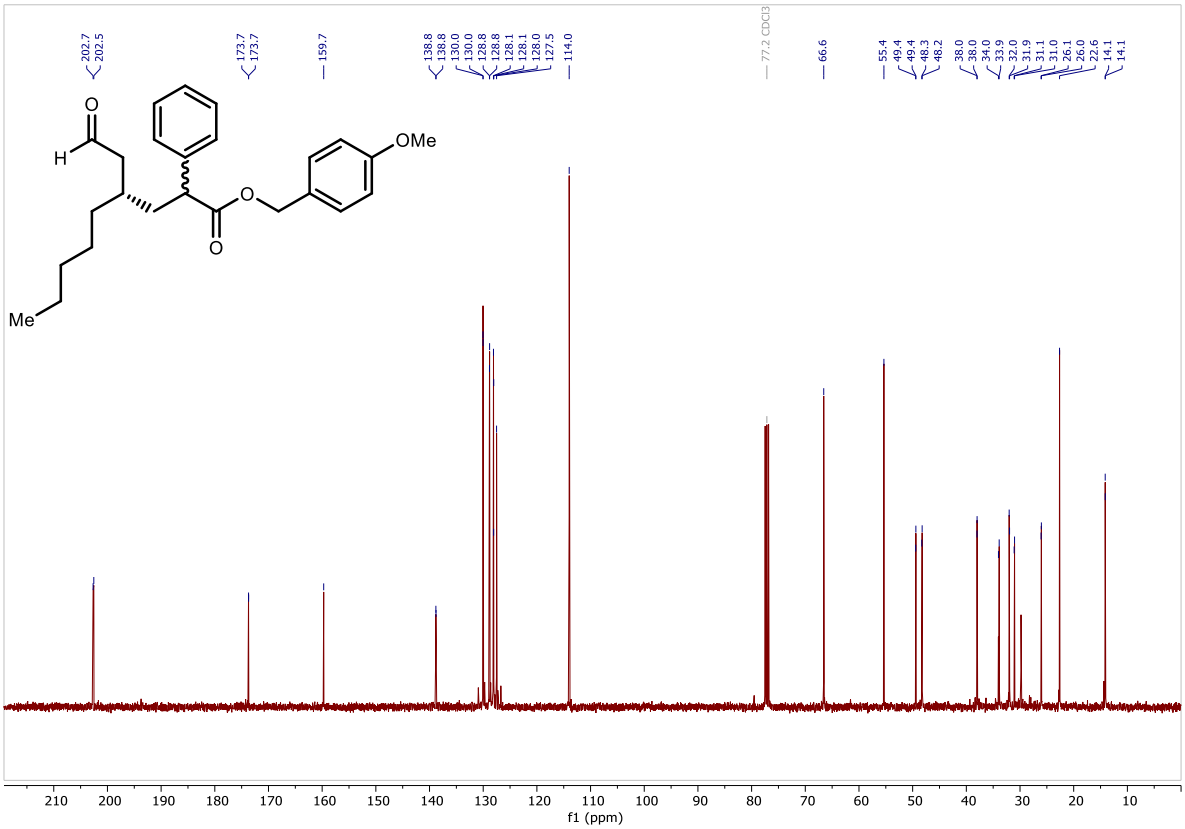
^{13}C NMR (126 MHz, $CDCl_3$) of 3**a'**:



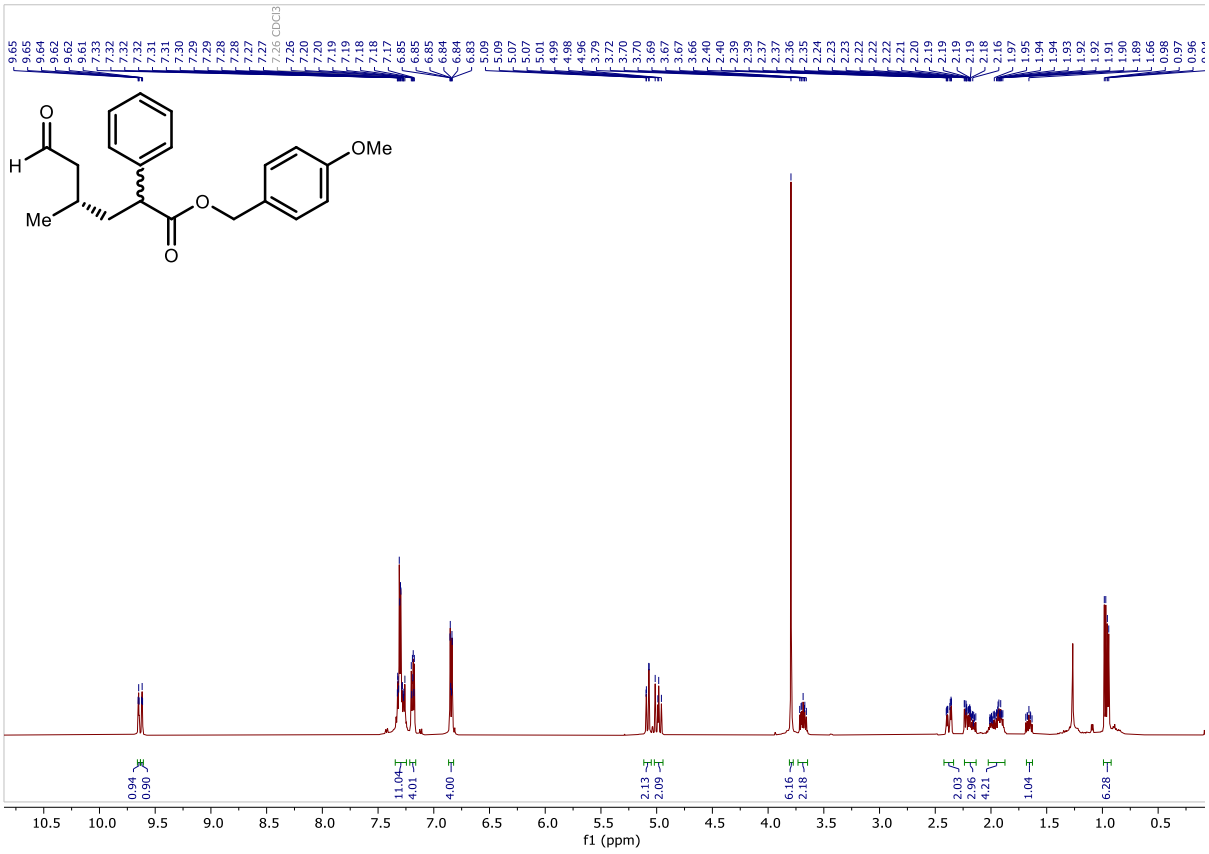
^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) of **6a**:



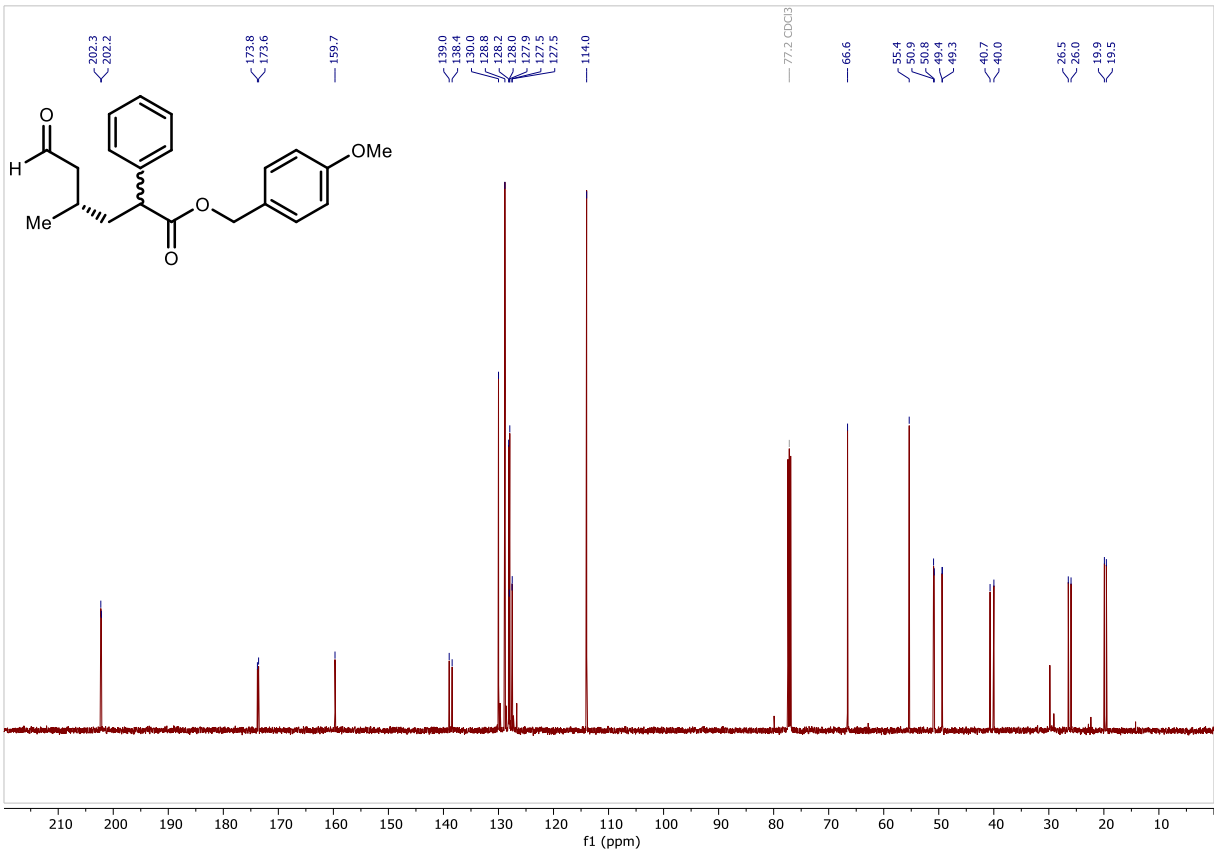
^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers) of **6a**:



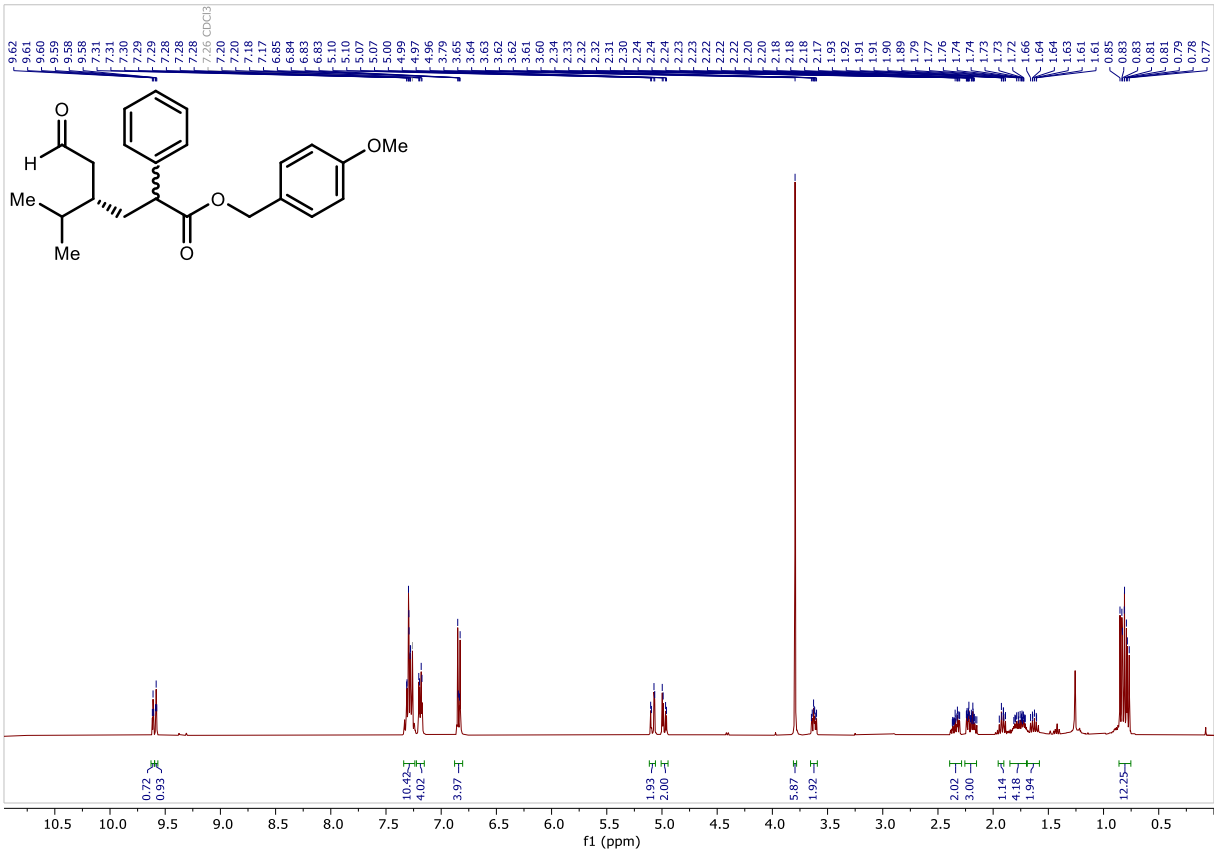
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6b**:



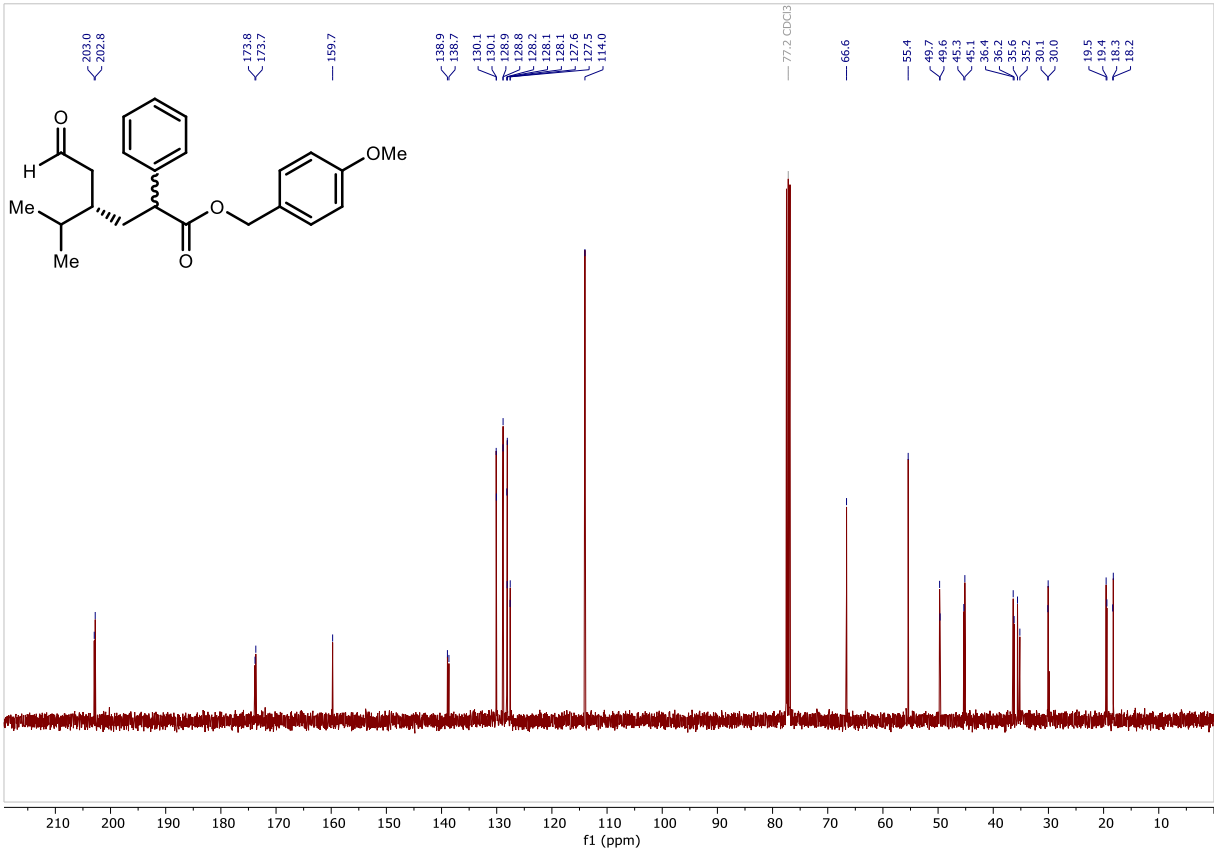
^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers) of **6b**:



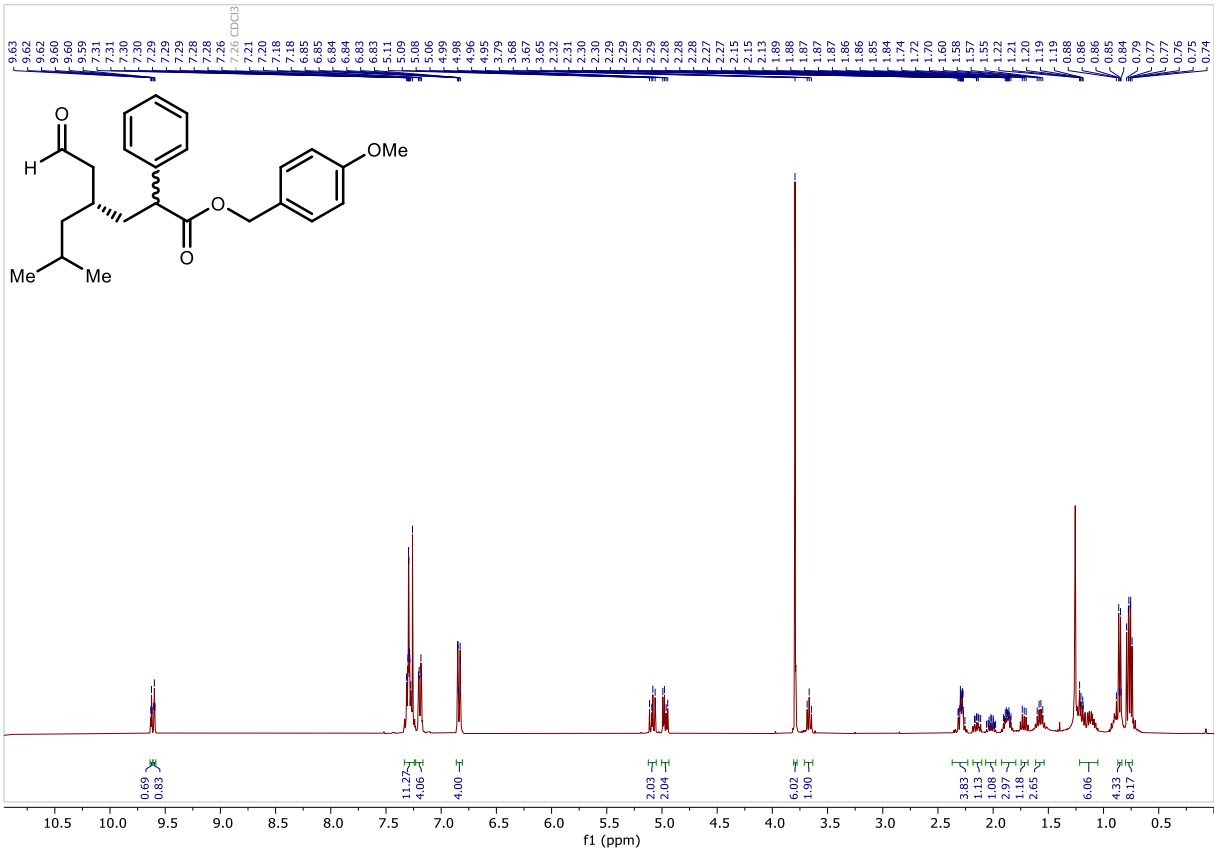
^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) of **6c**:



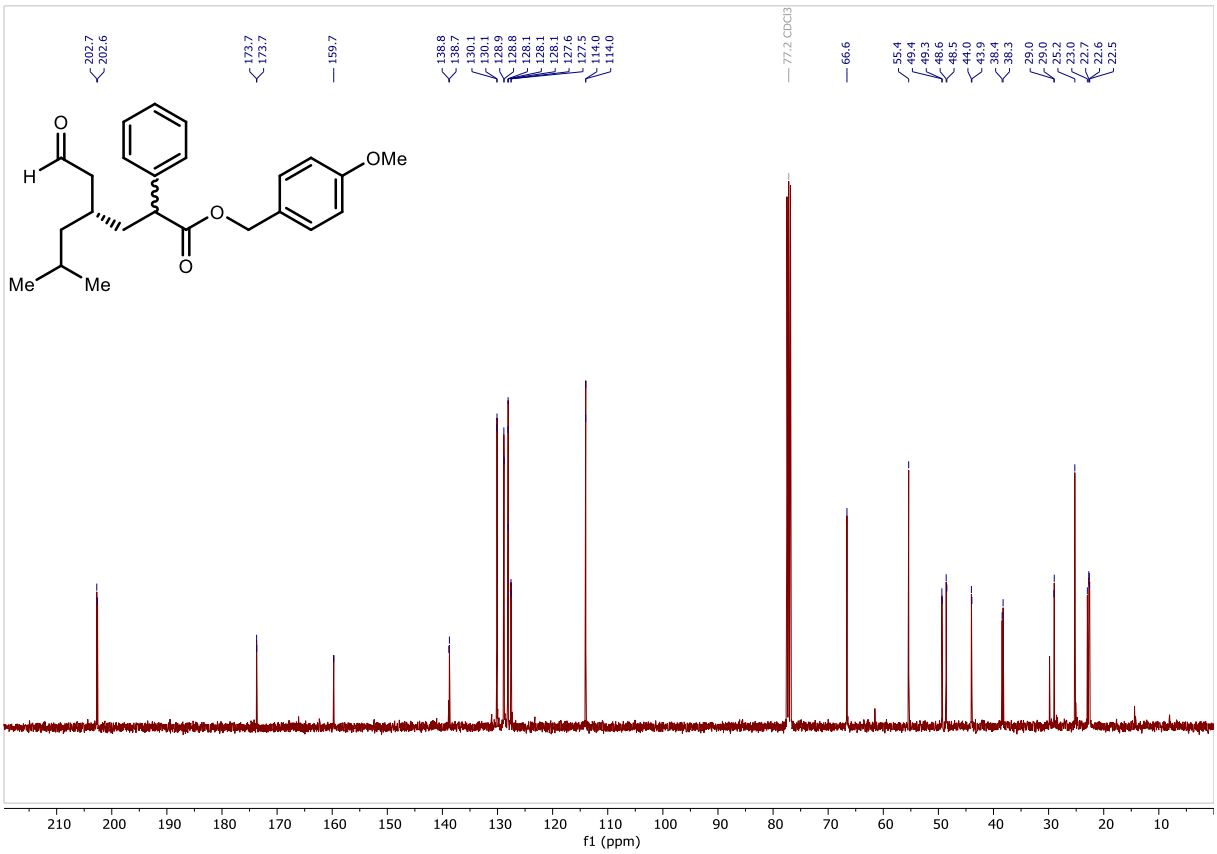
^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers) of **6c**:



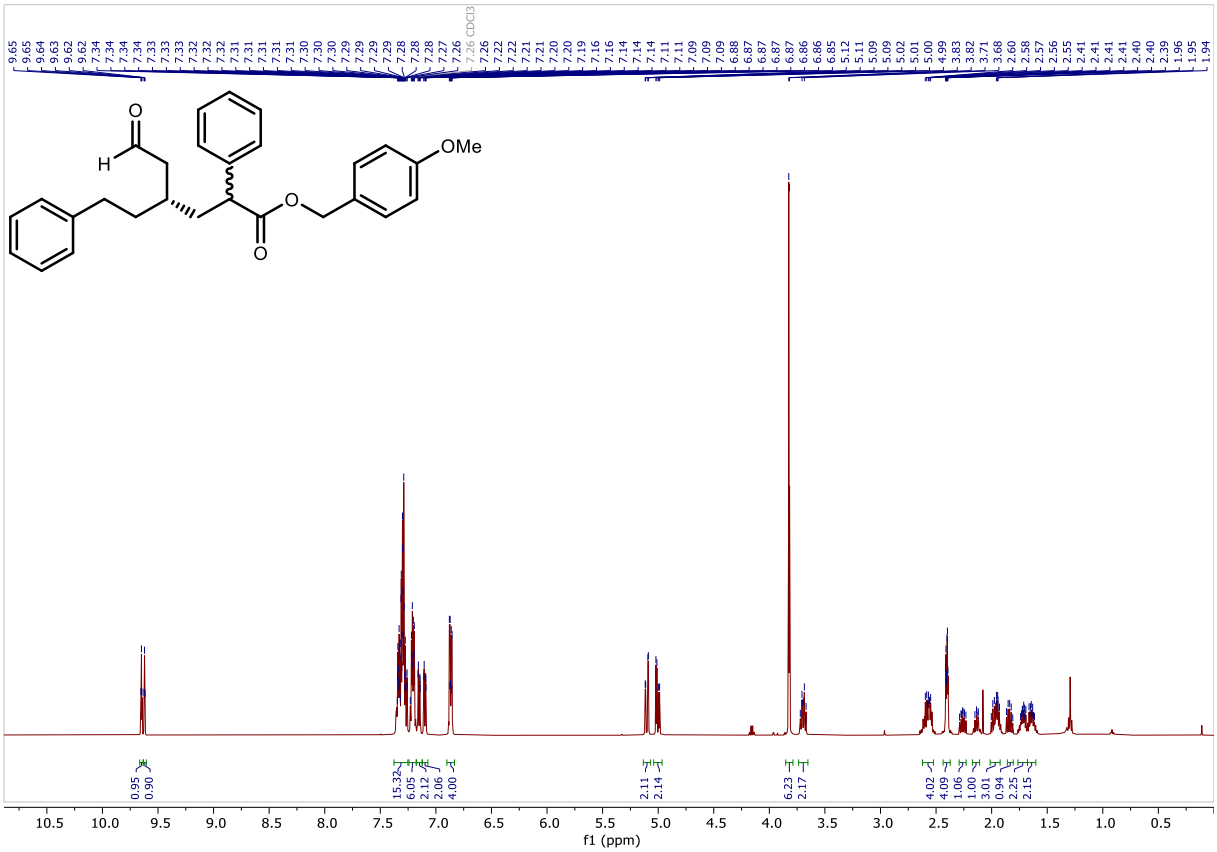
^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) of **6d**:



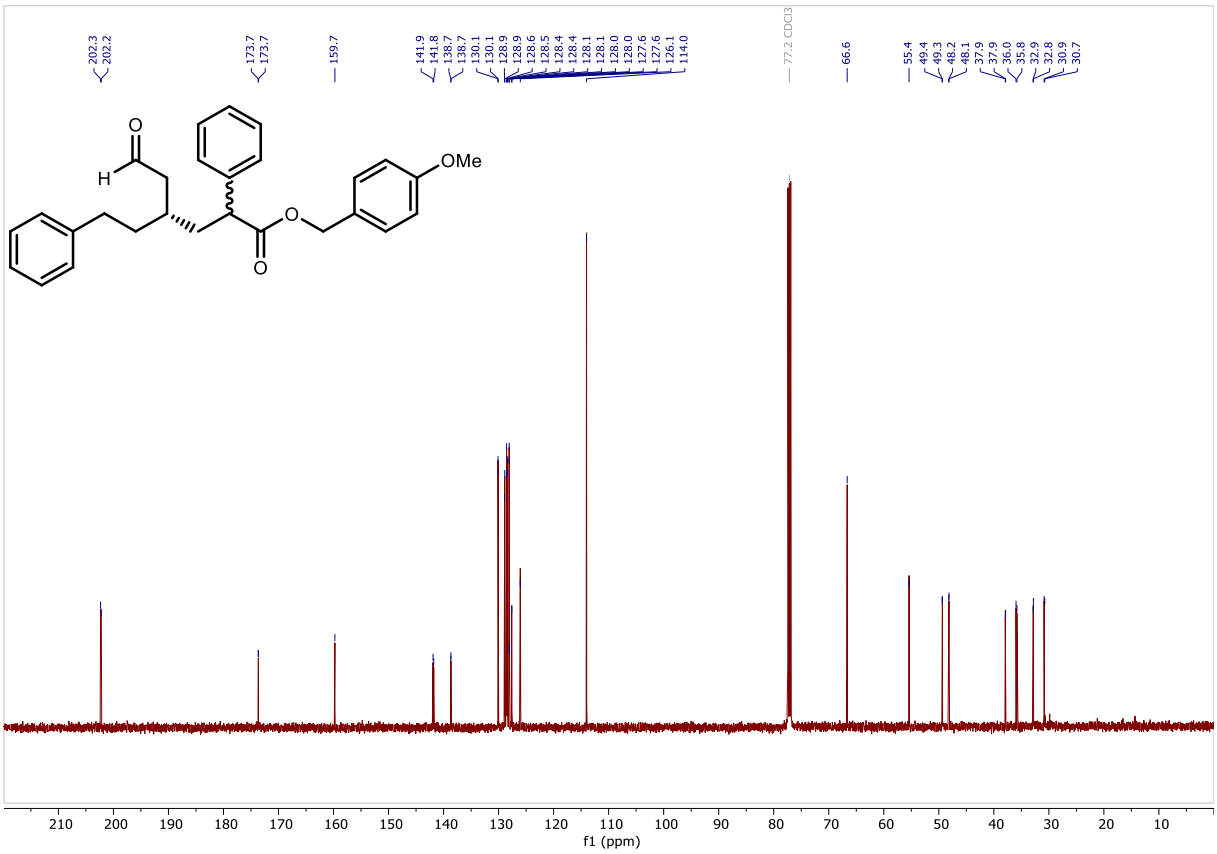
^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers) of **6d**:



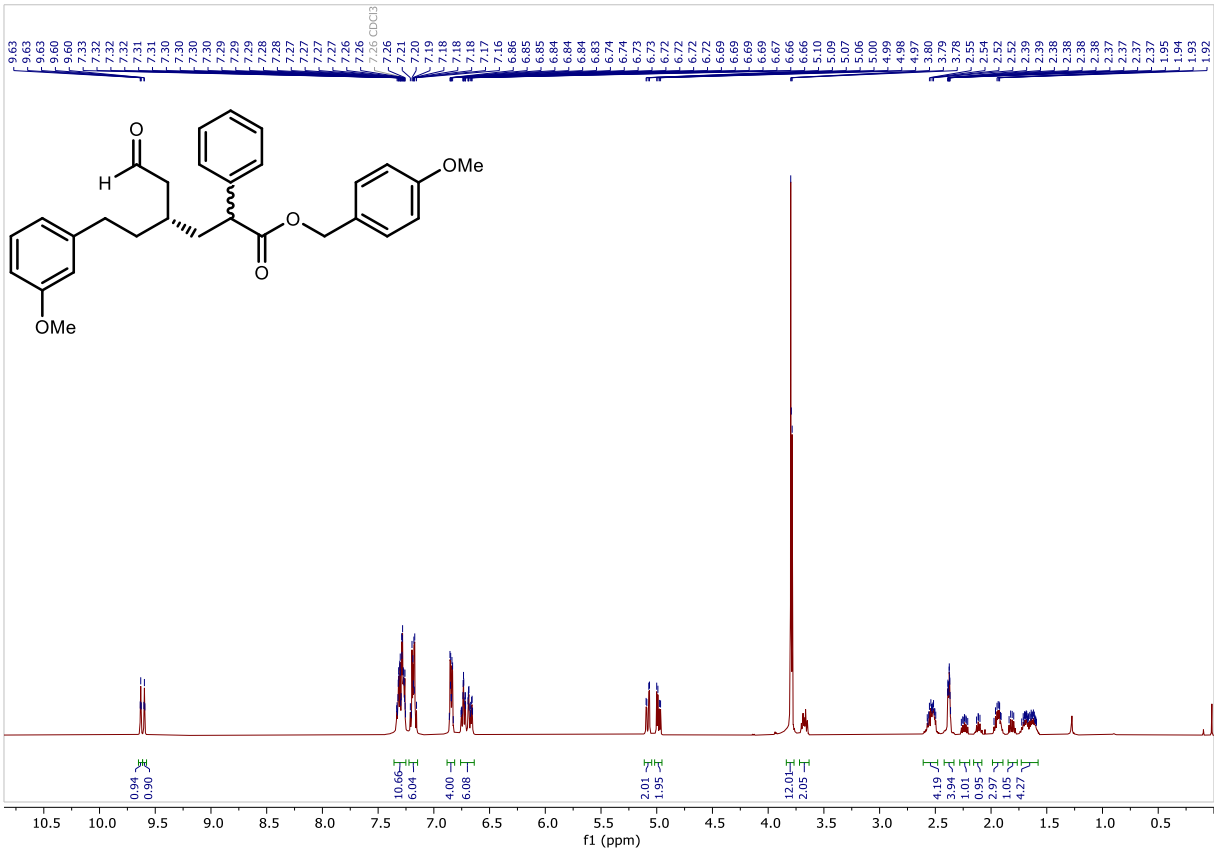
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6e**:



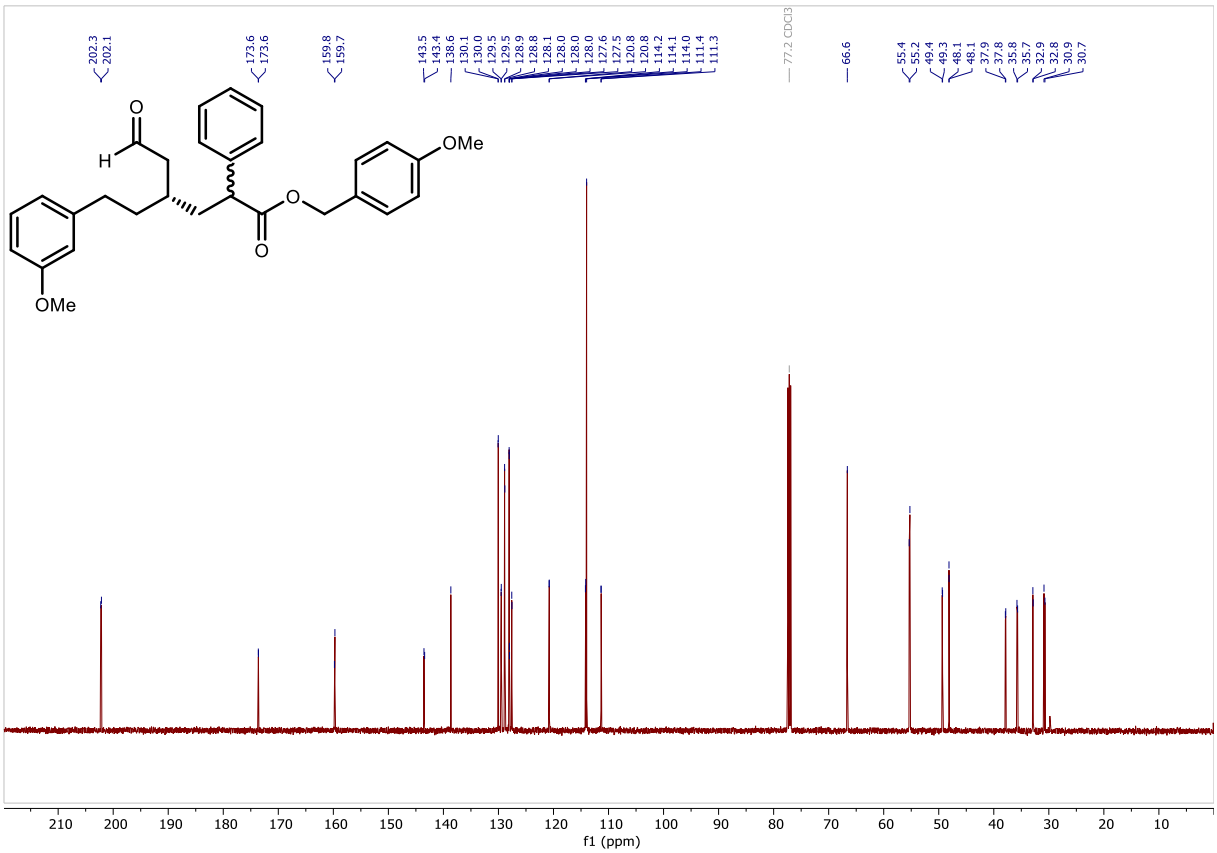
^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers) of **6e**:



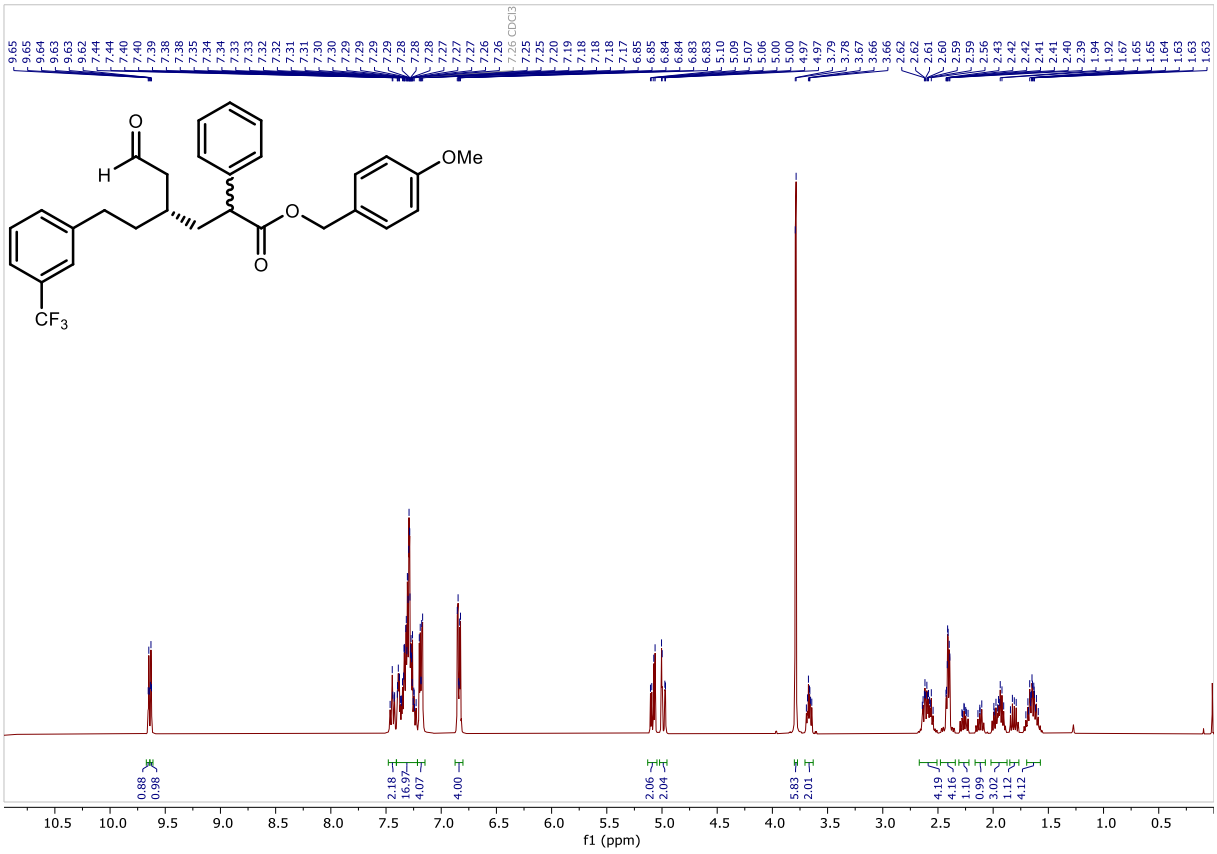
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6f**:



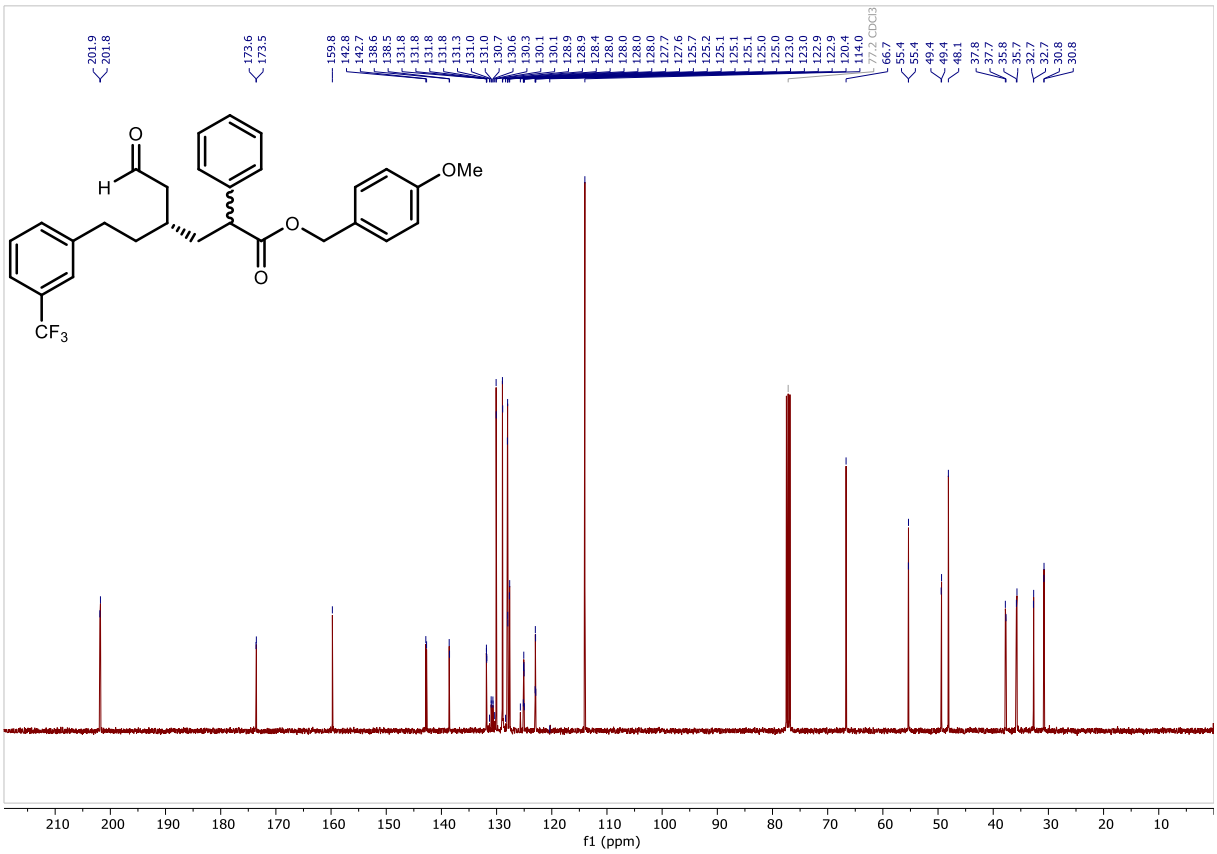
^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers) of **6f**:



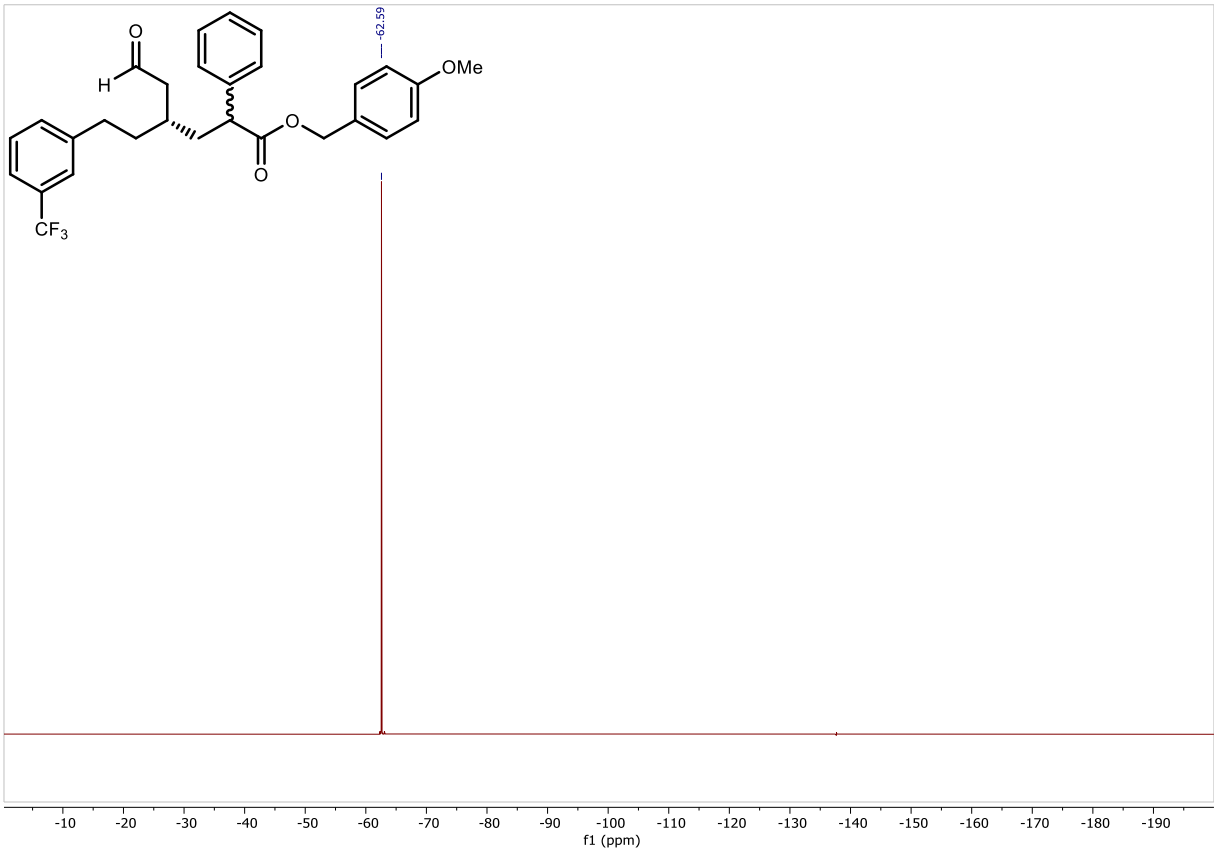
^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) of **6g**:



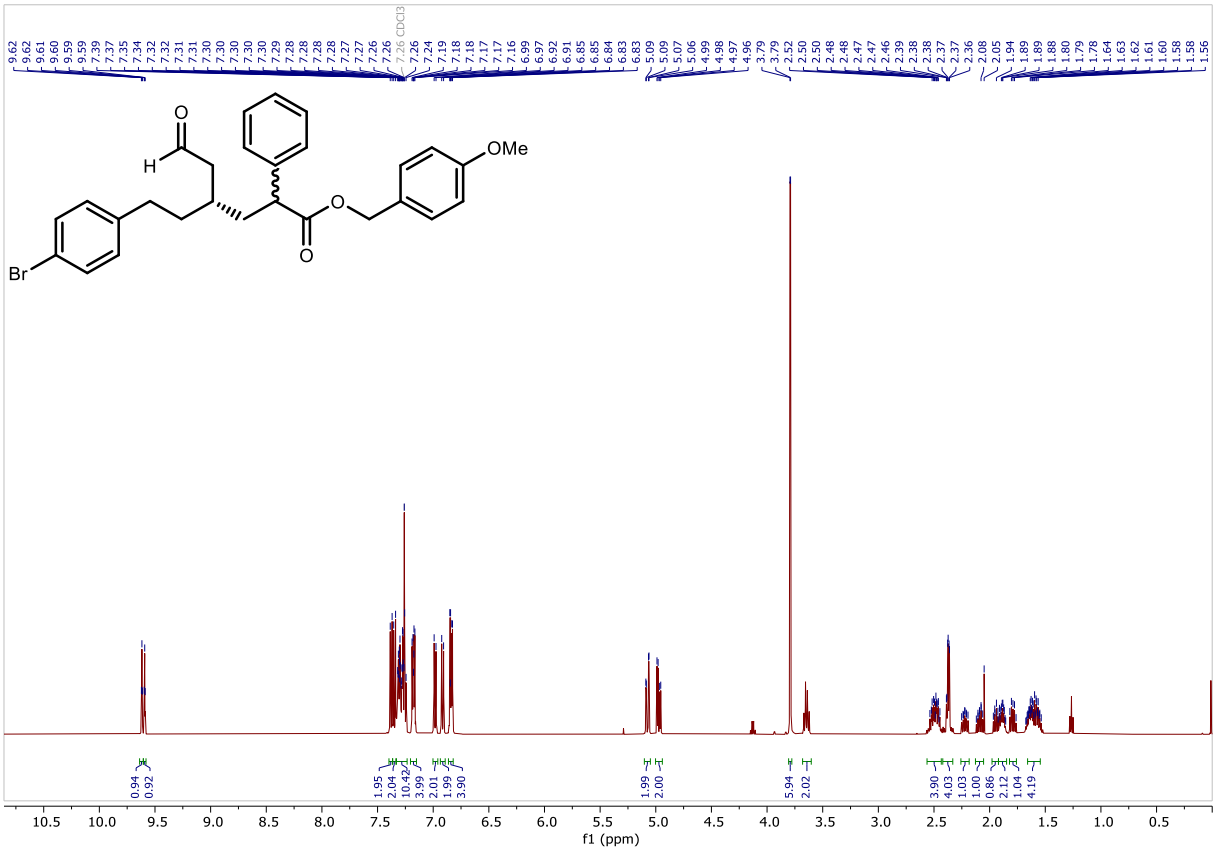
^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers) of **6g**:



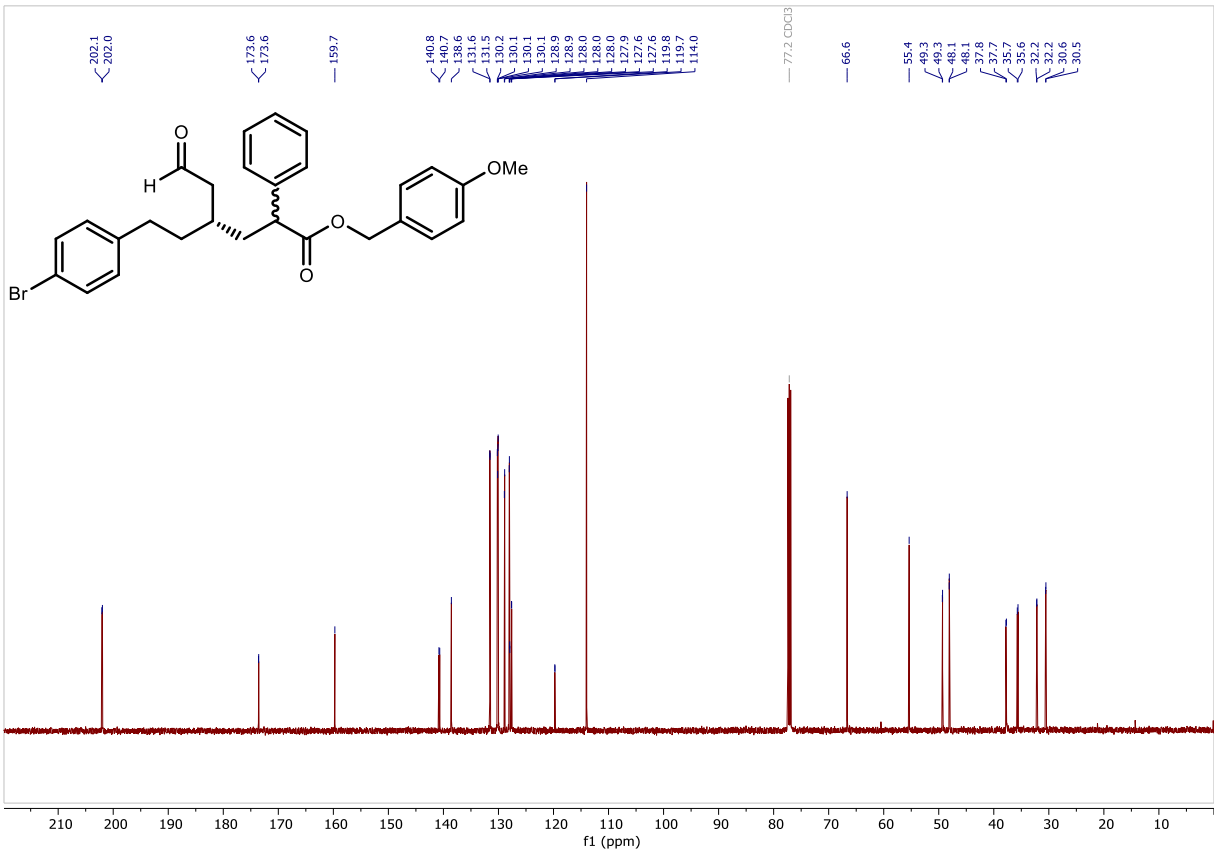
^{19}F NMR (376 MHz, $CDCl_3$, mixture of diastereoisomers) of **6g**:



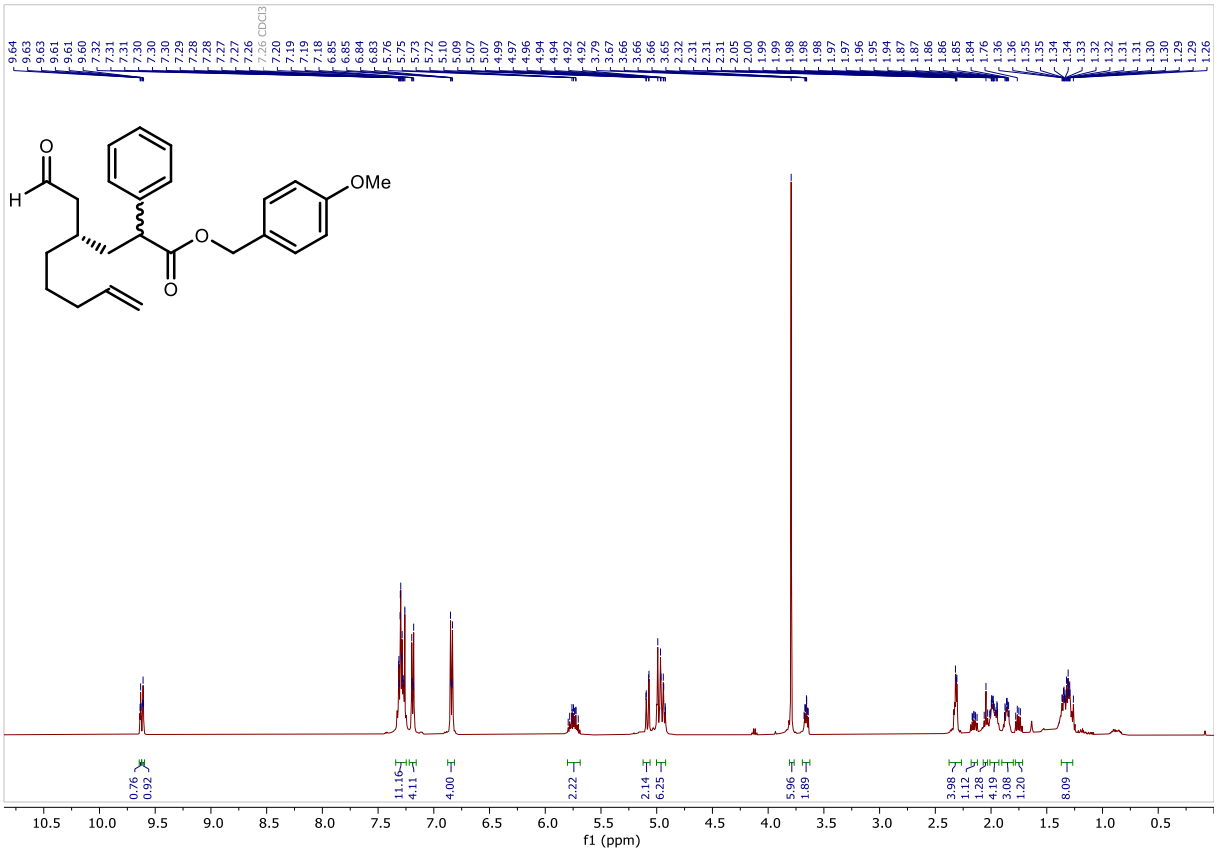
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6h**:



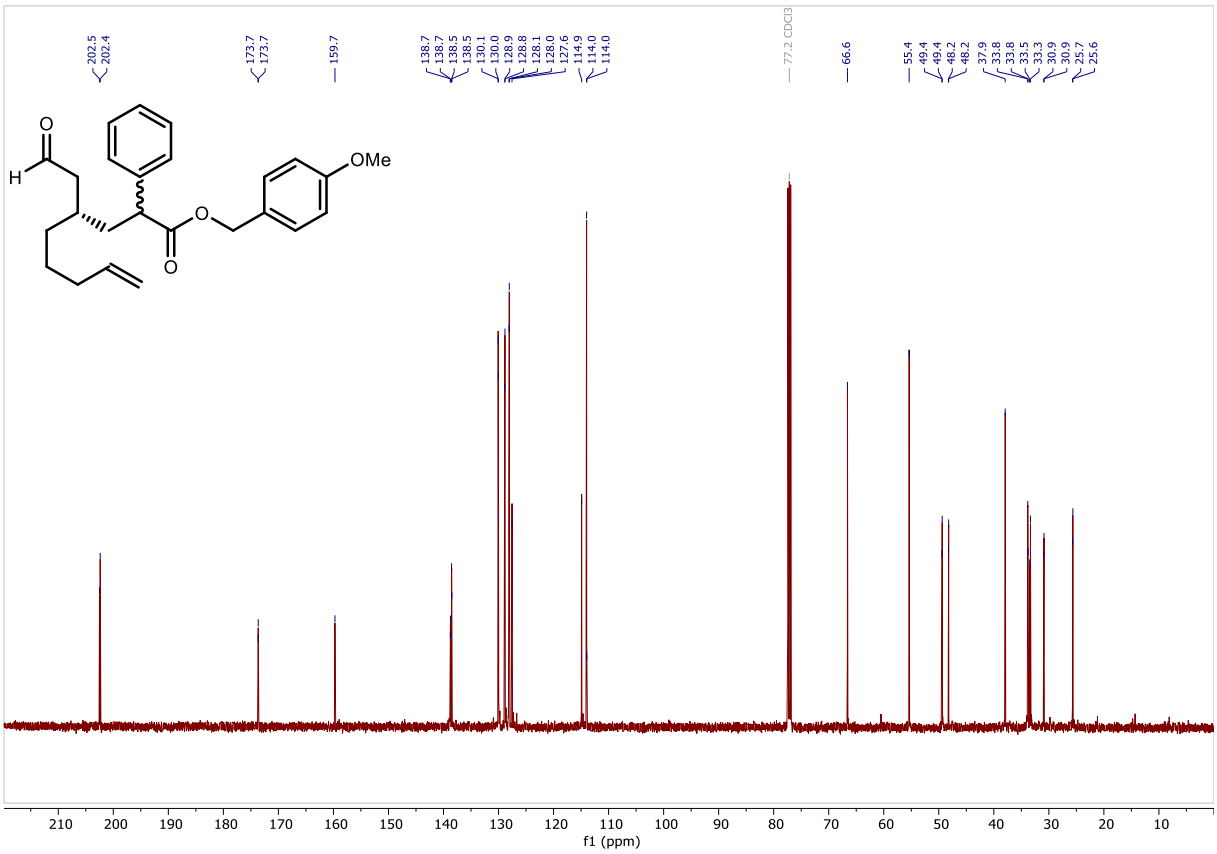
^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers) of **6h**:



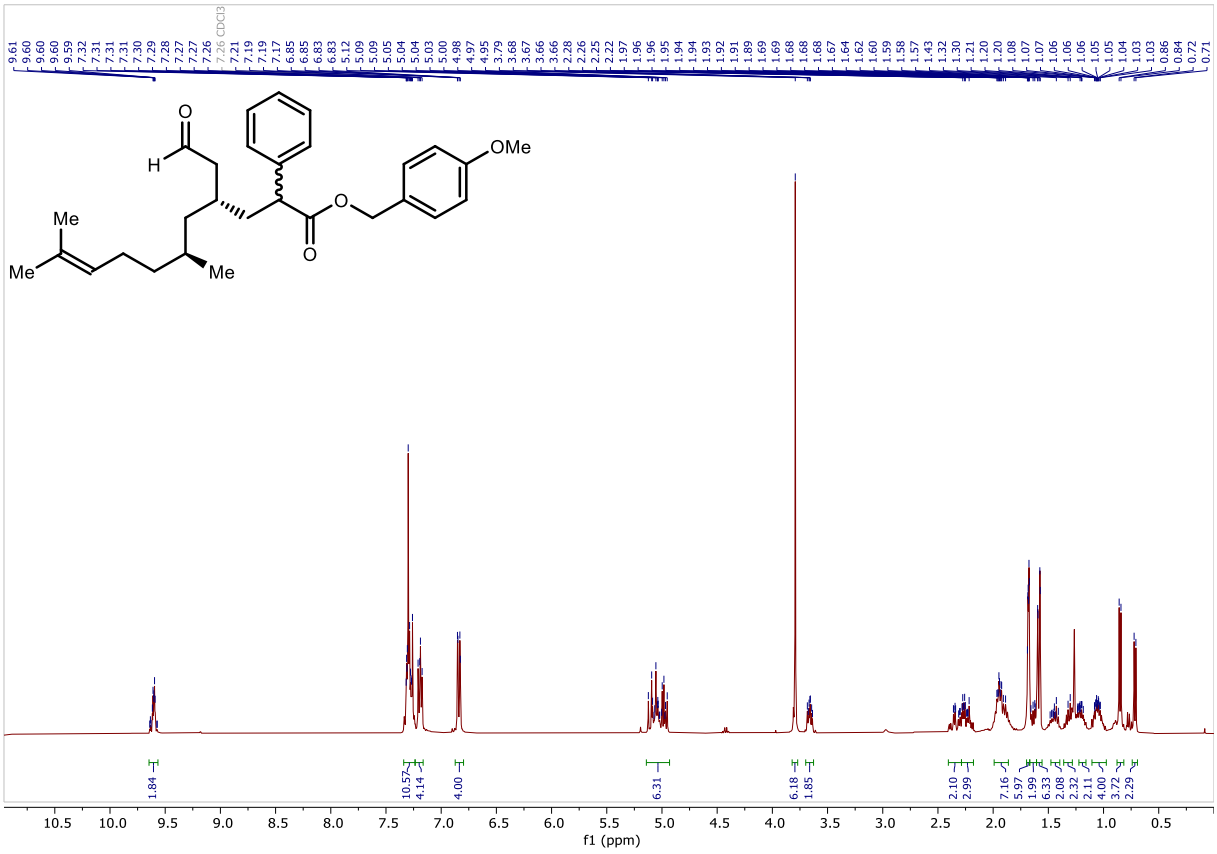
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6i**:



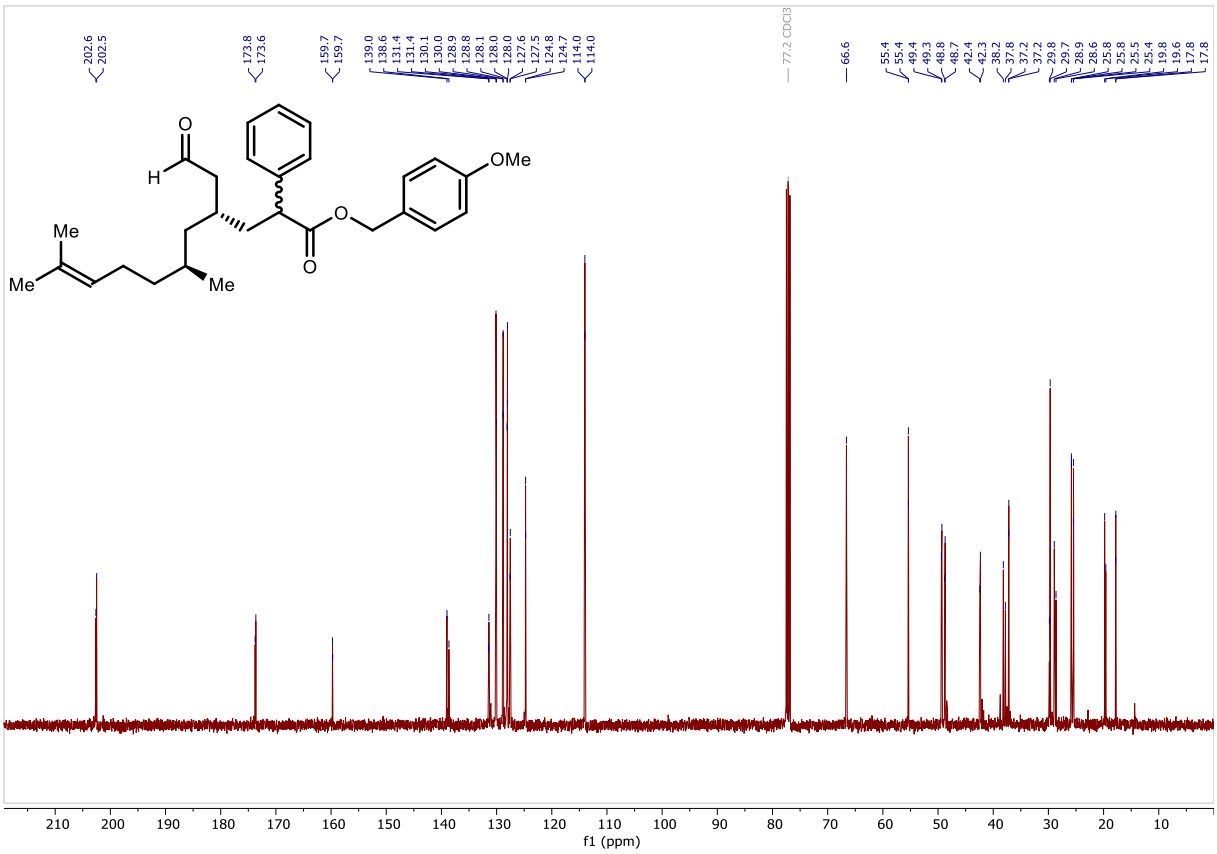
^{13}C NMR (126 MHz, CDCl3, mixture of diastereoisomers) of **6i**:



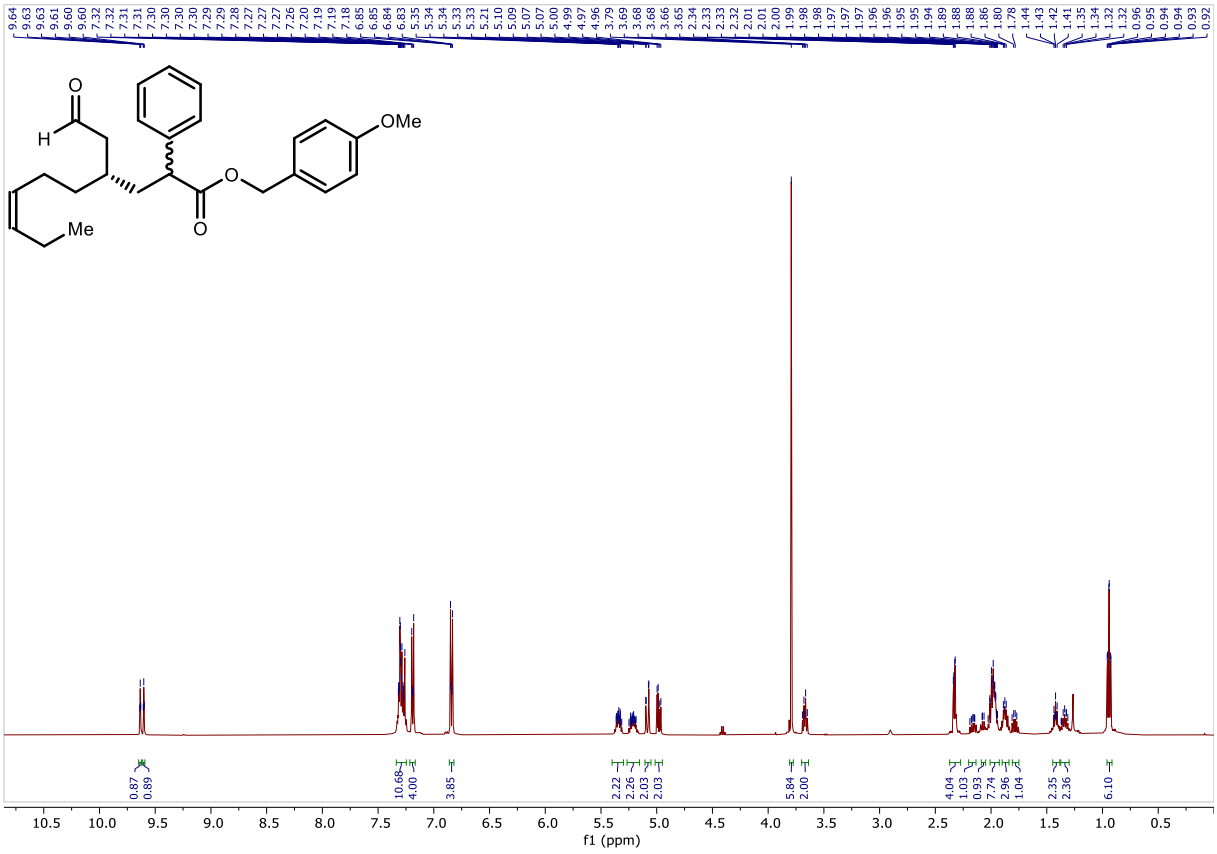
^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) of **6j**:



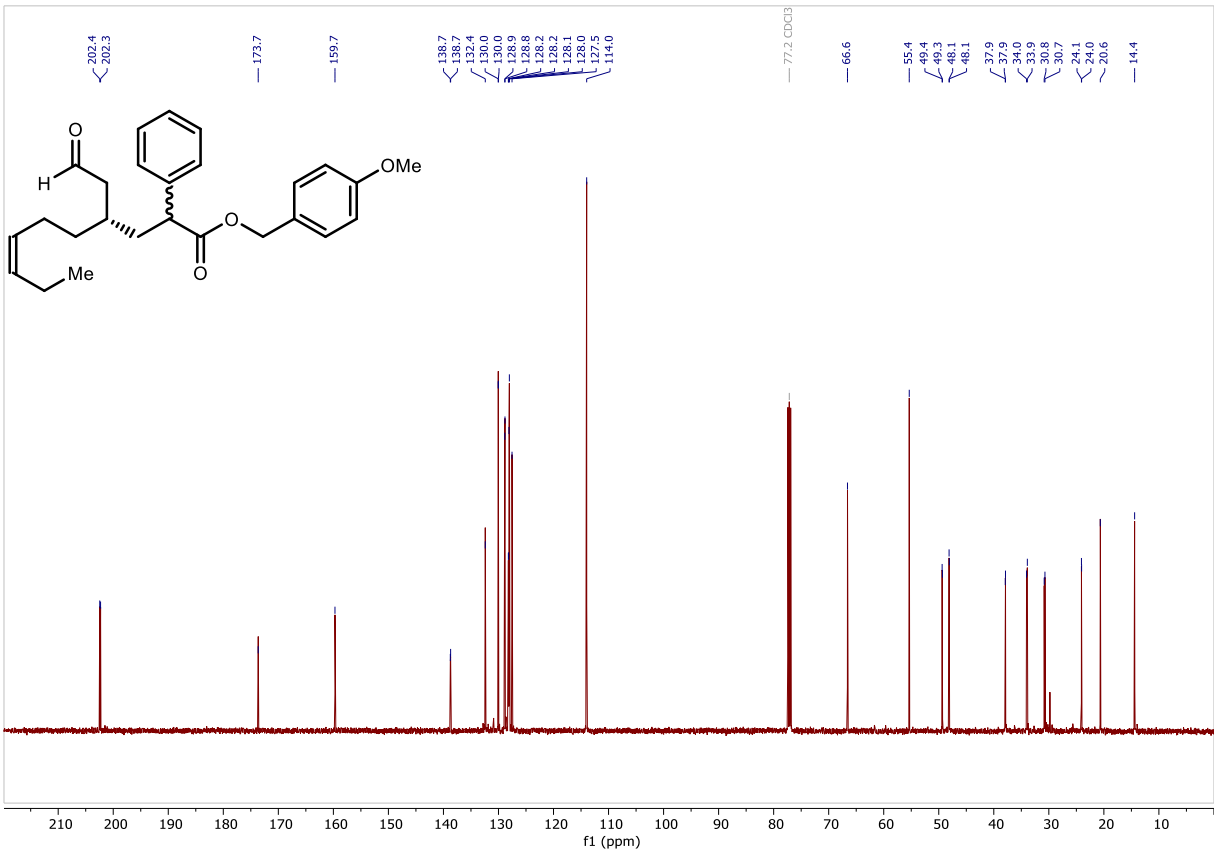
^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers) of **6j**:



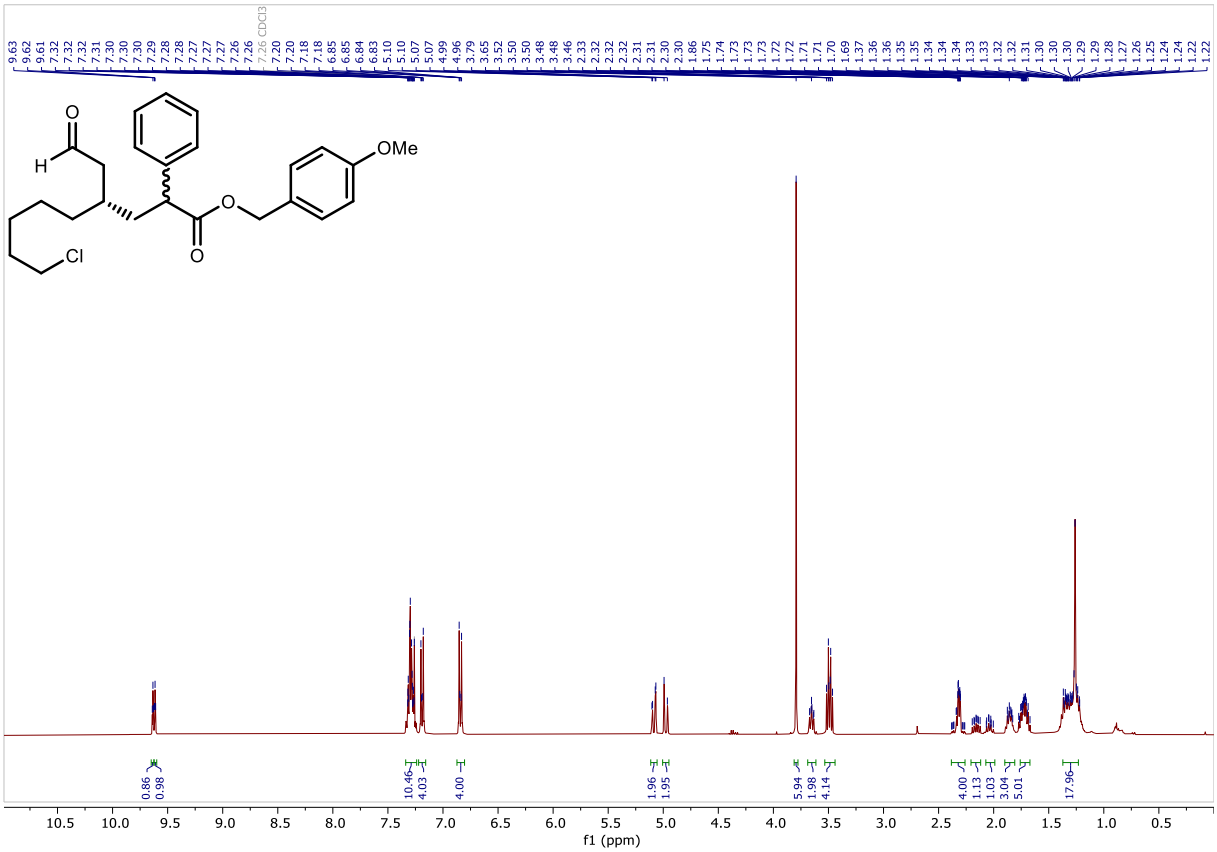
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6k**:



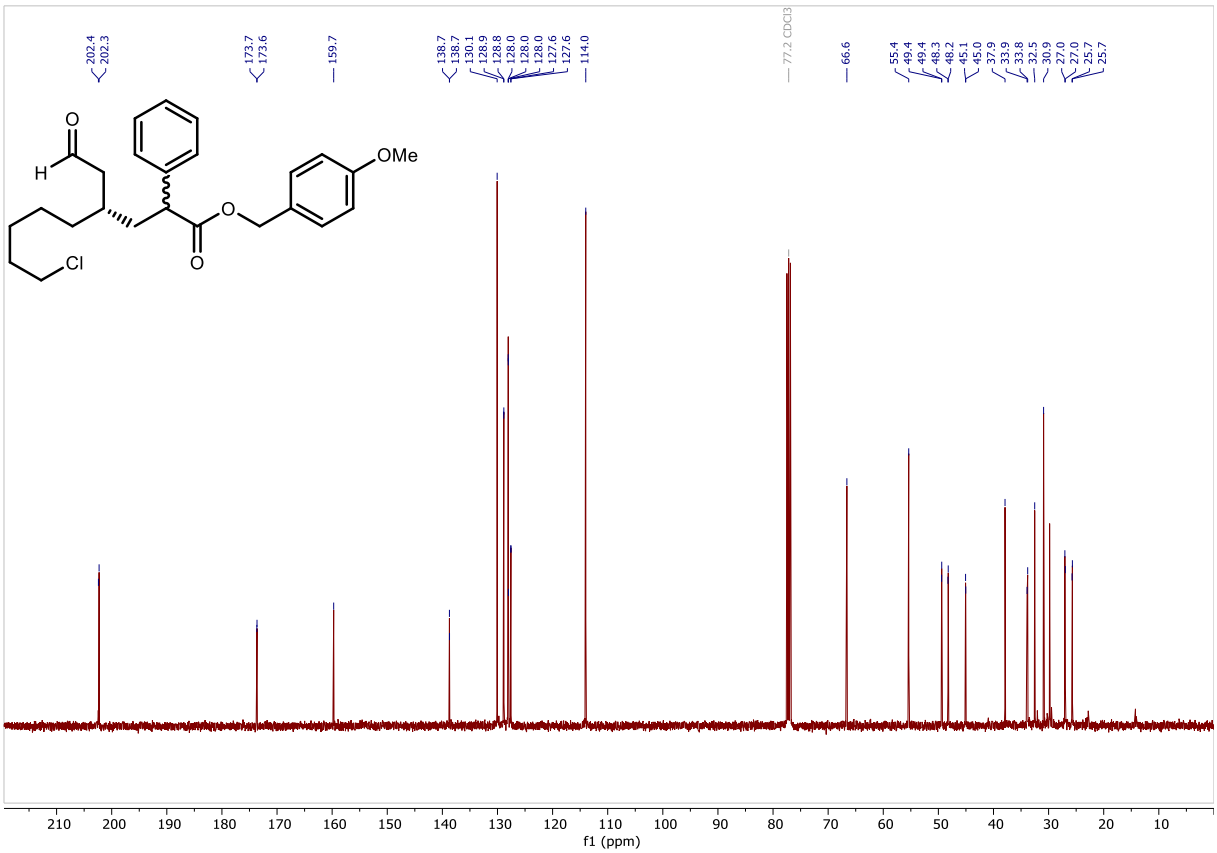
^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers) of **6k**:



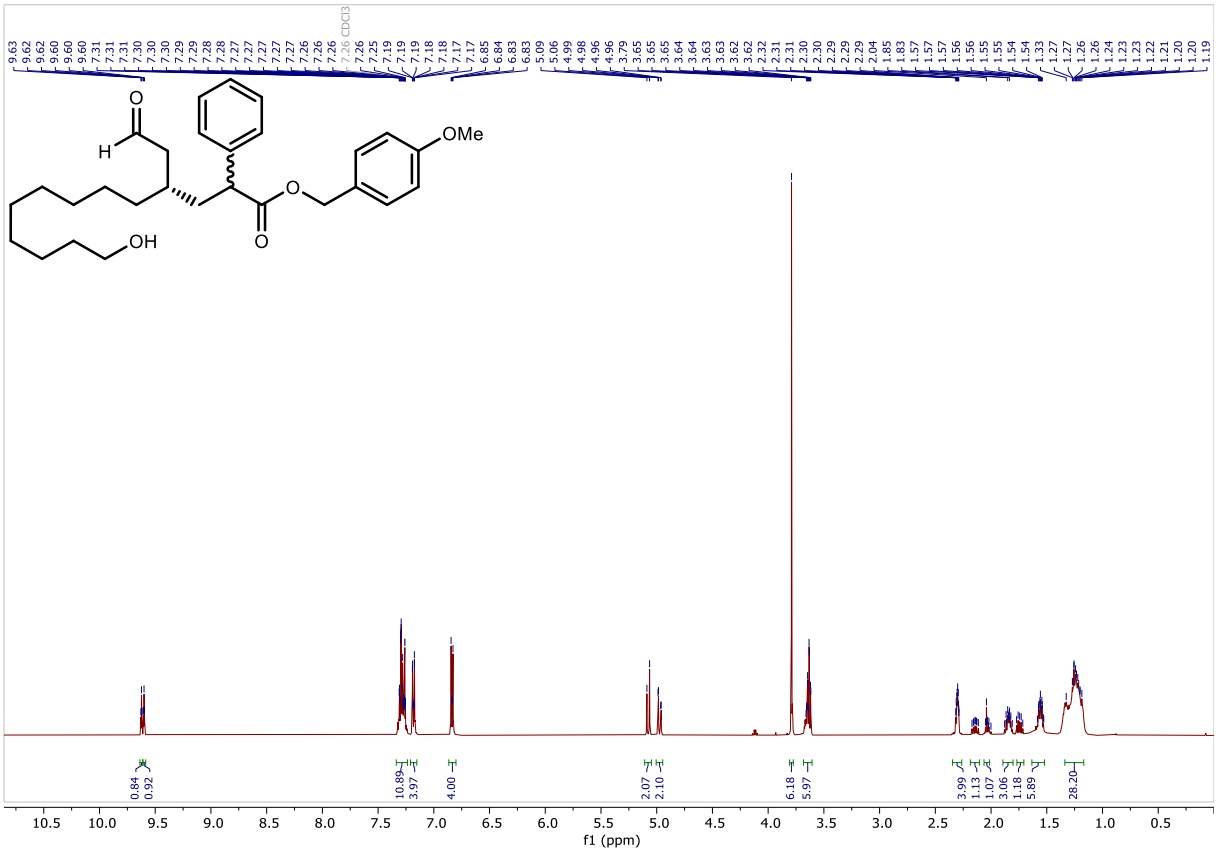
^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) of **6l**:



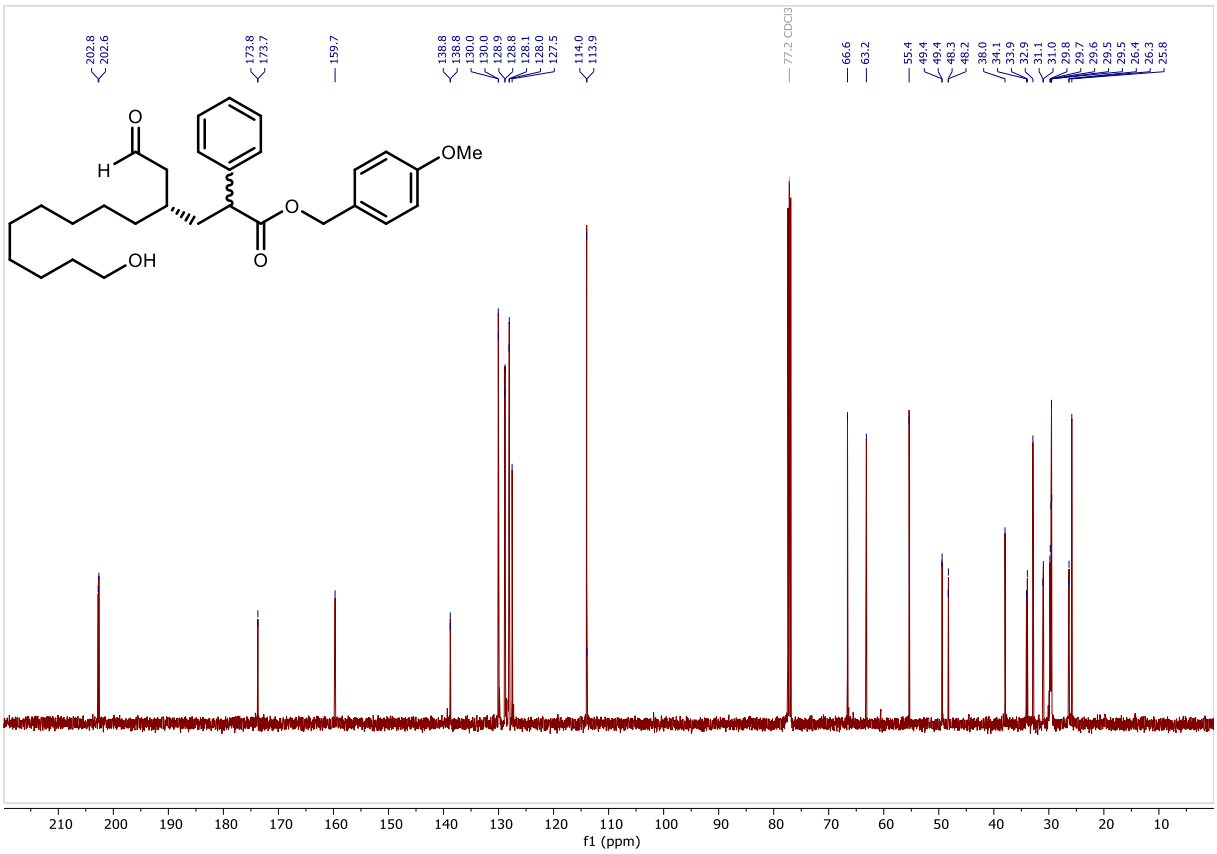
^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers) of **6l**:



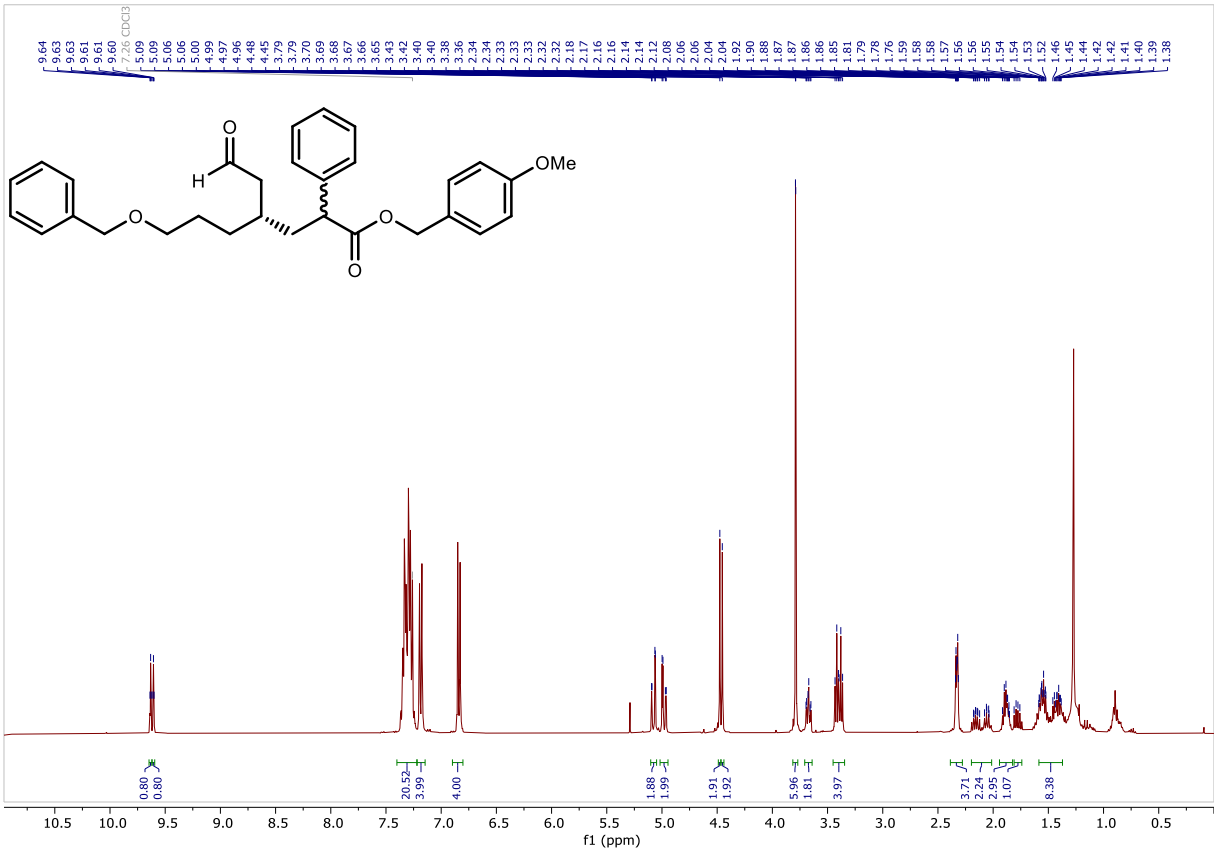
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6m**:



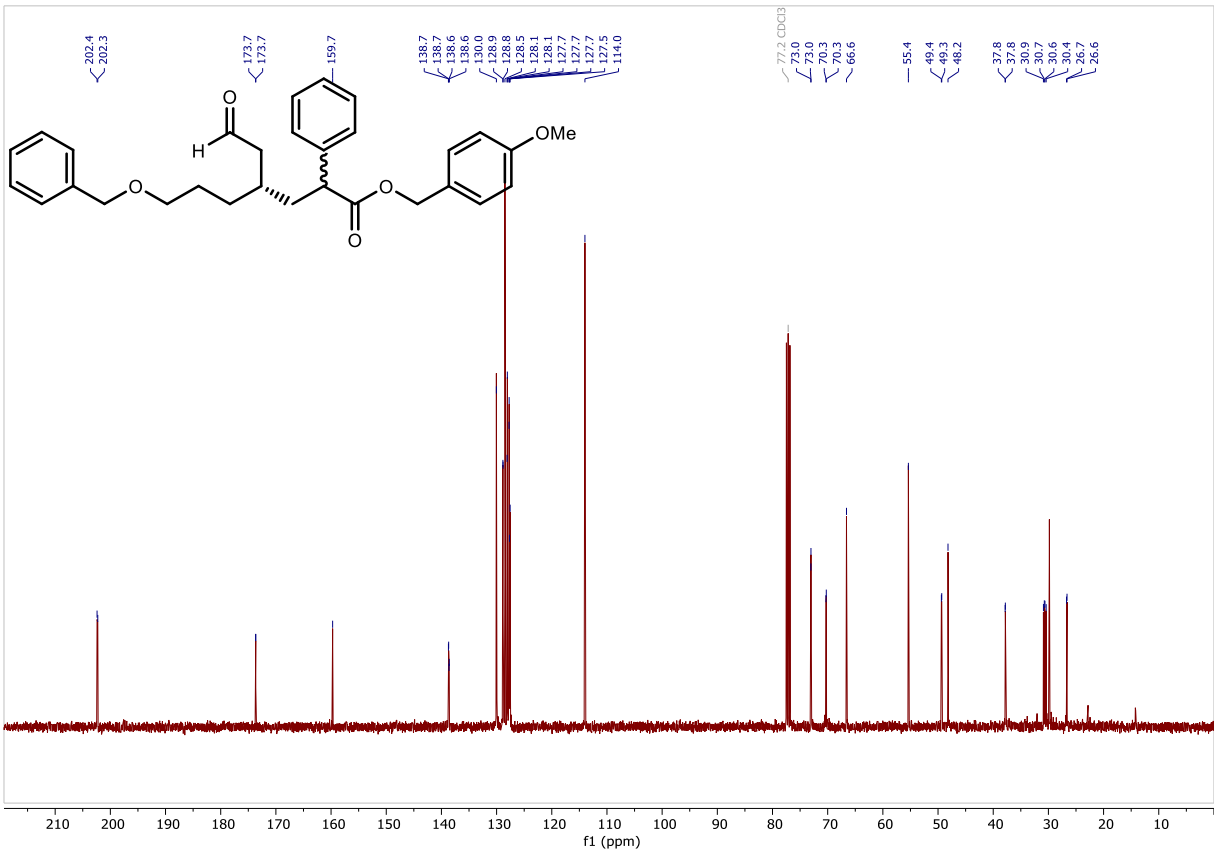
^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers) of **6m**:



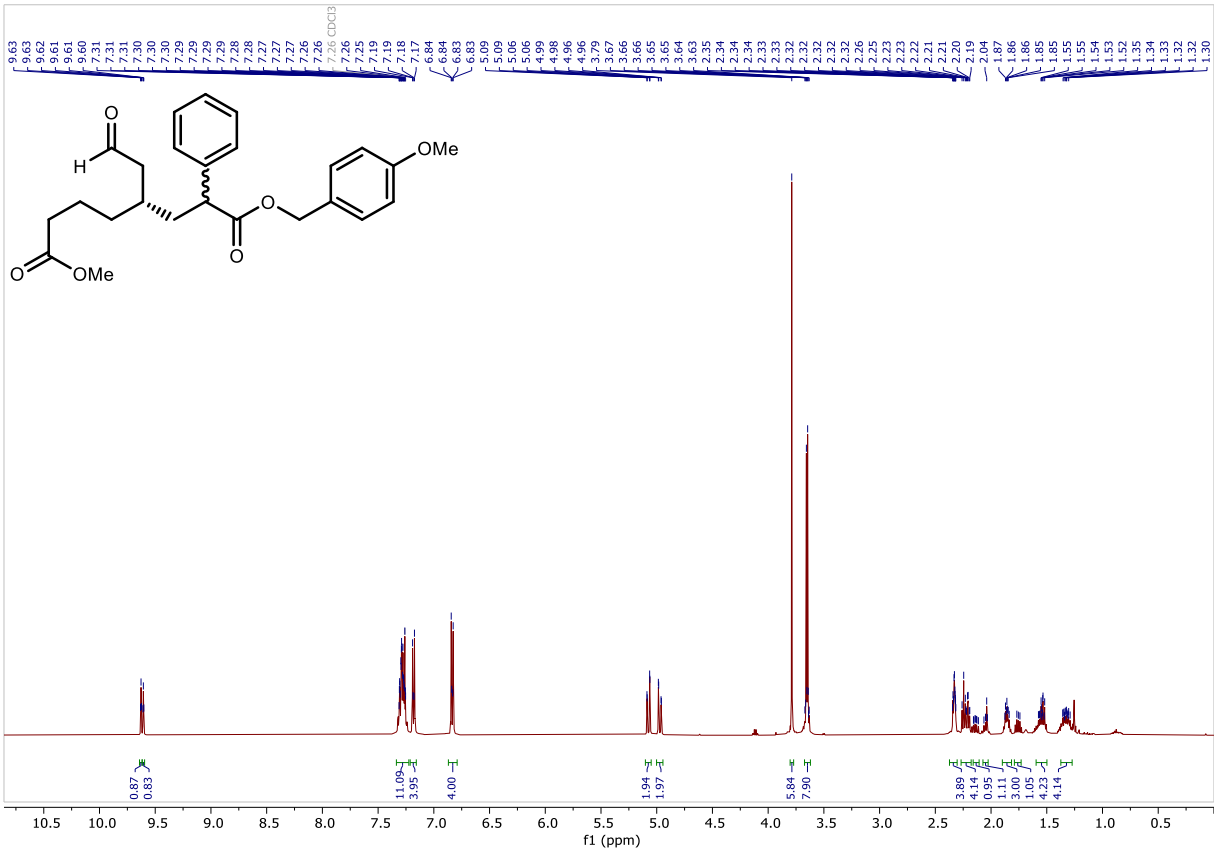
^{1}H NMR (400 MHz, $CDCl_3$, mixture of diastereoisomers) of **6n**:



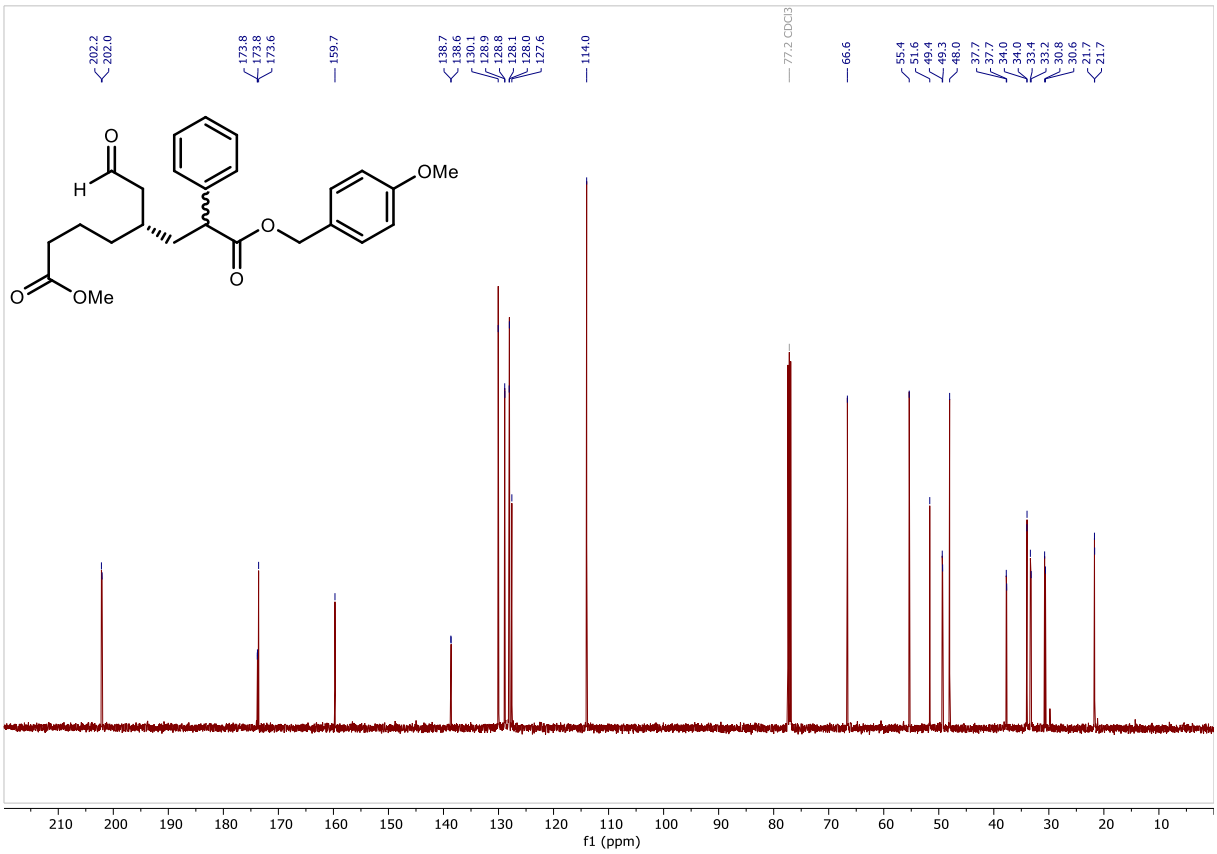
^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereoisomers) of **6n**:



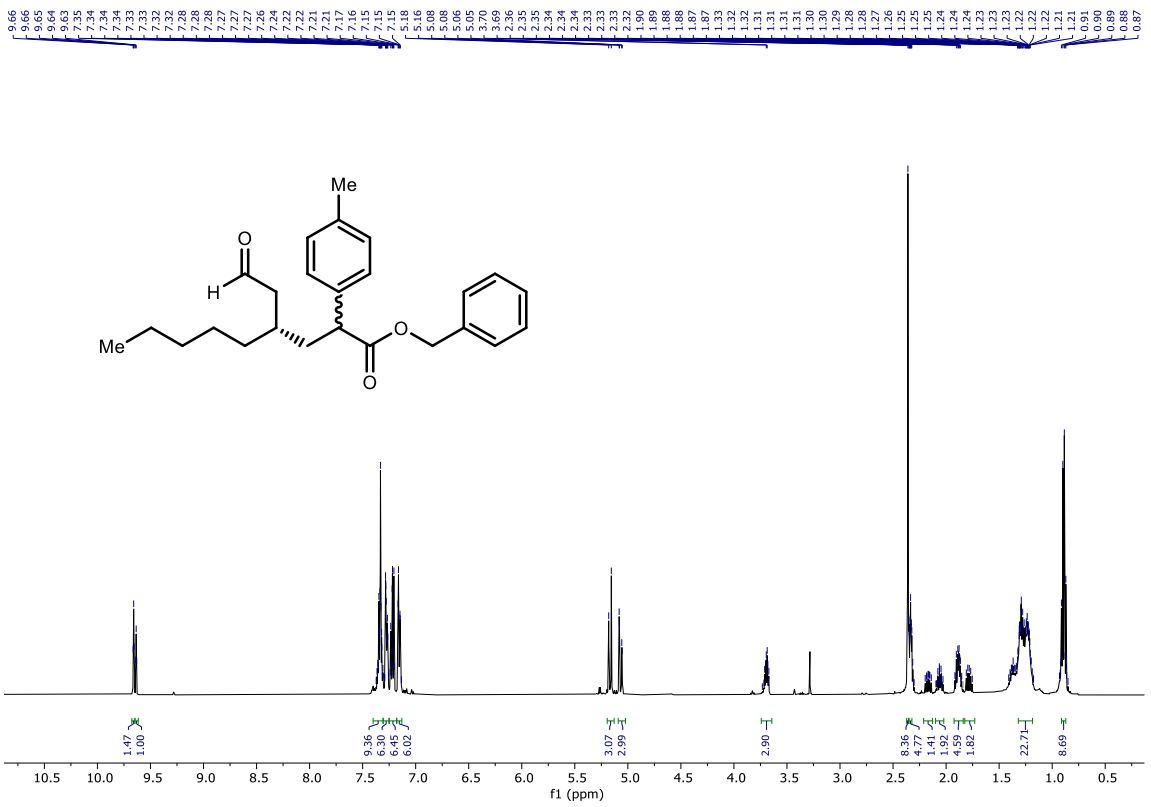
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6o:**



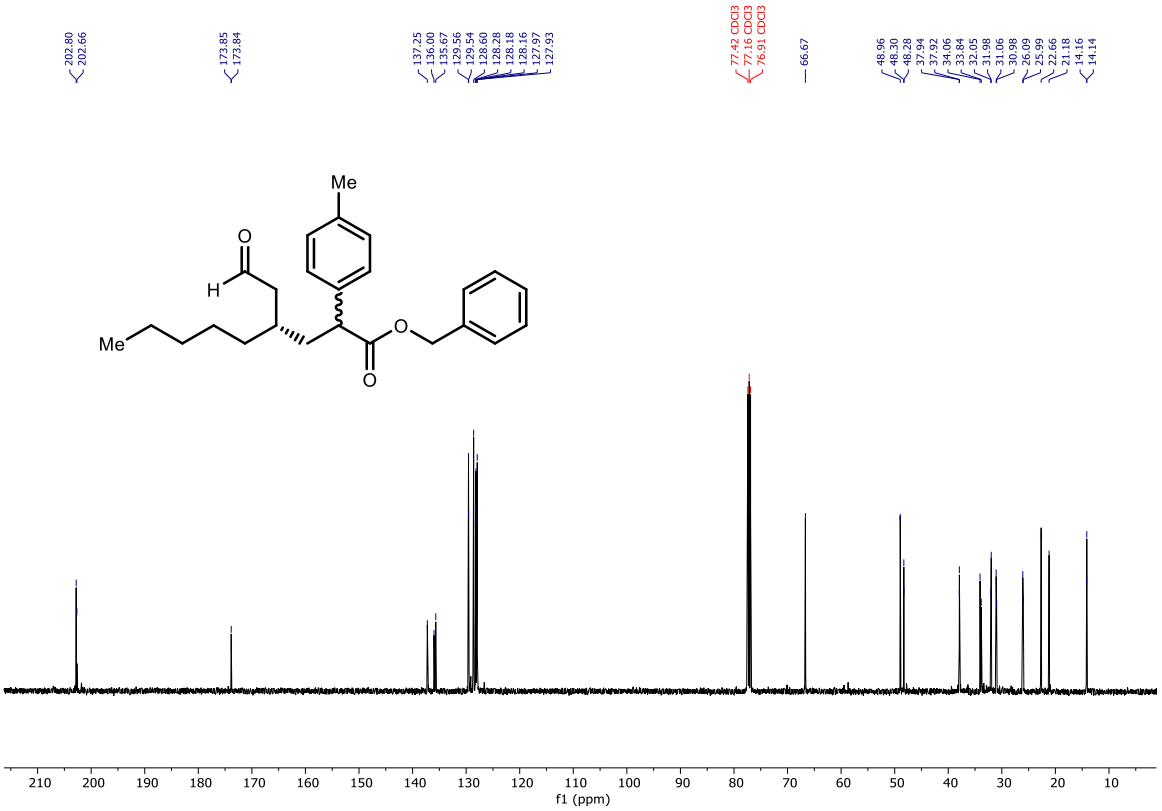
^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers) of **6o**:



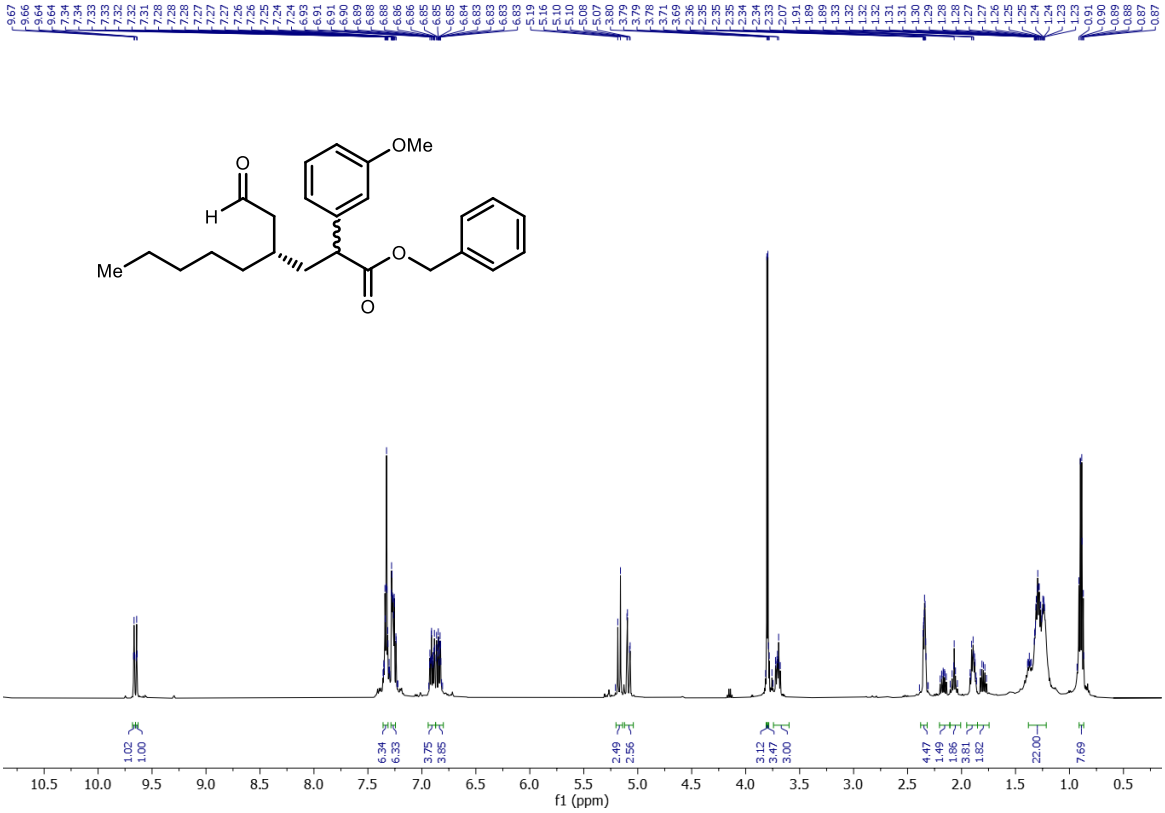
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6r**:



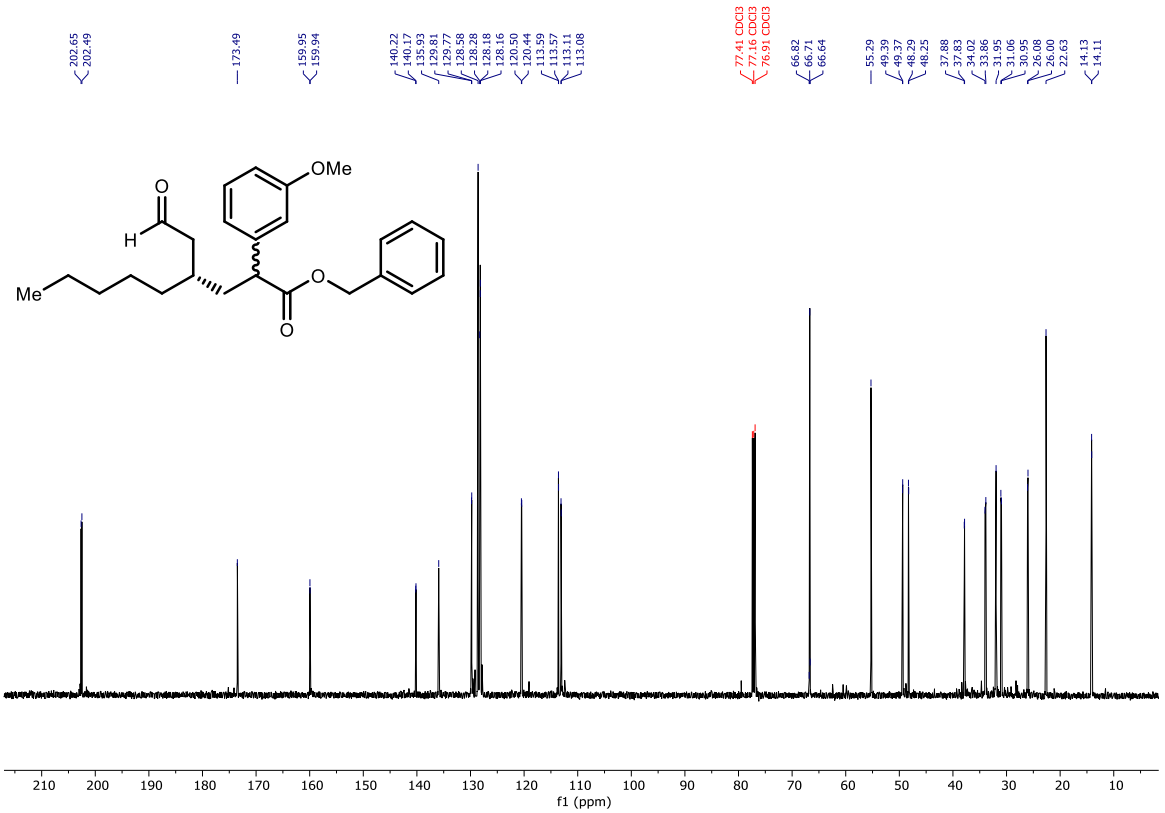
^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers) of **6r**:



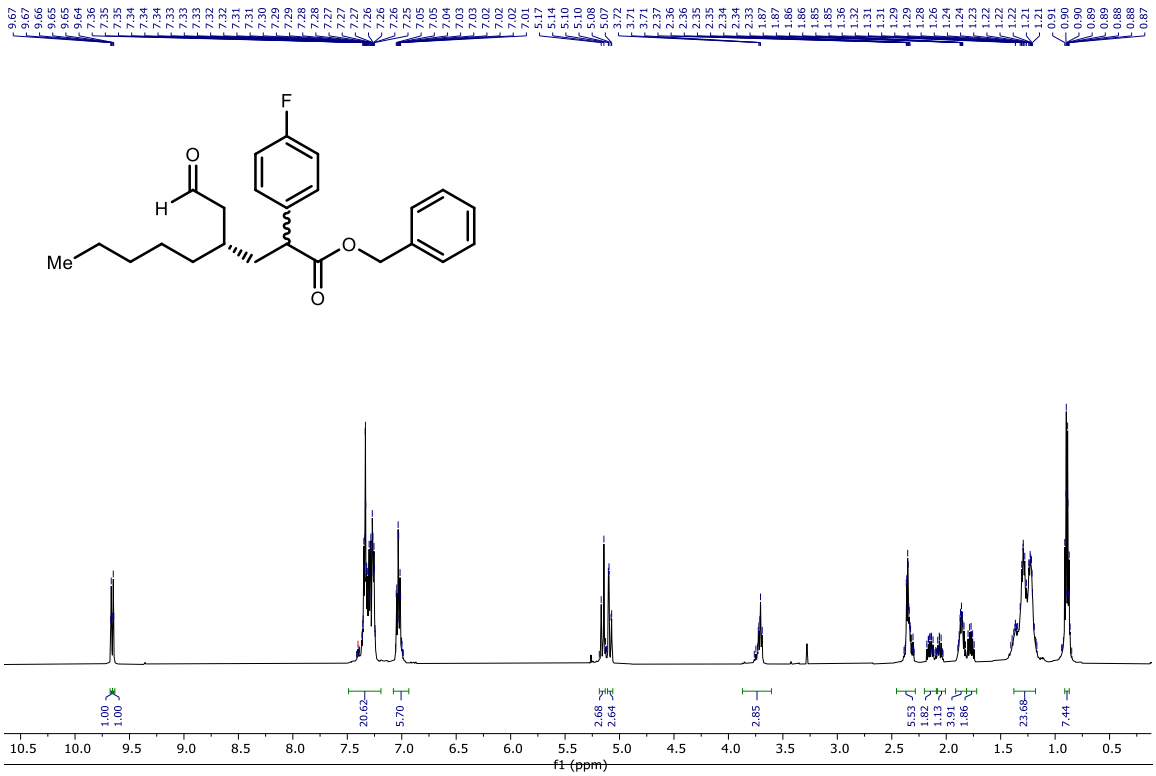
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6s**:



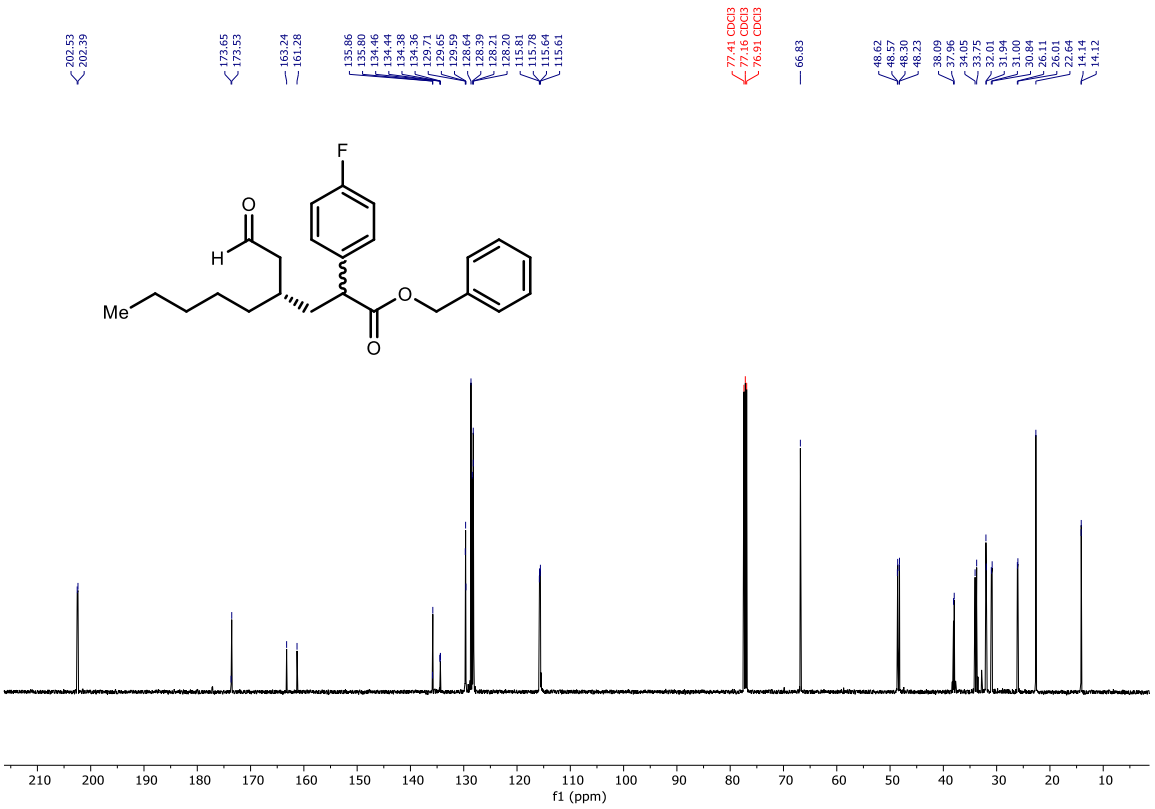
^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers) of **6s**:



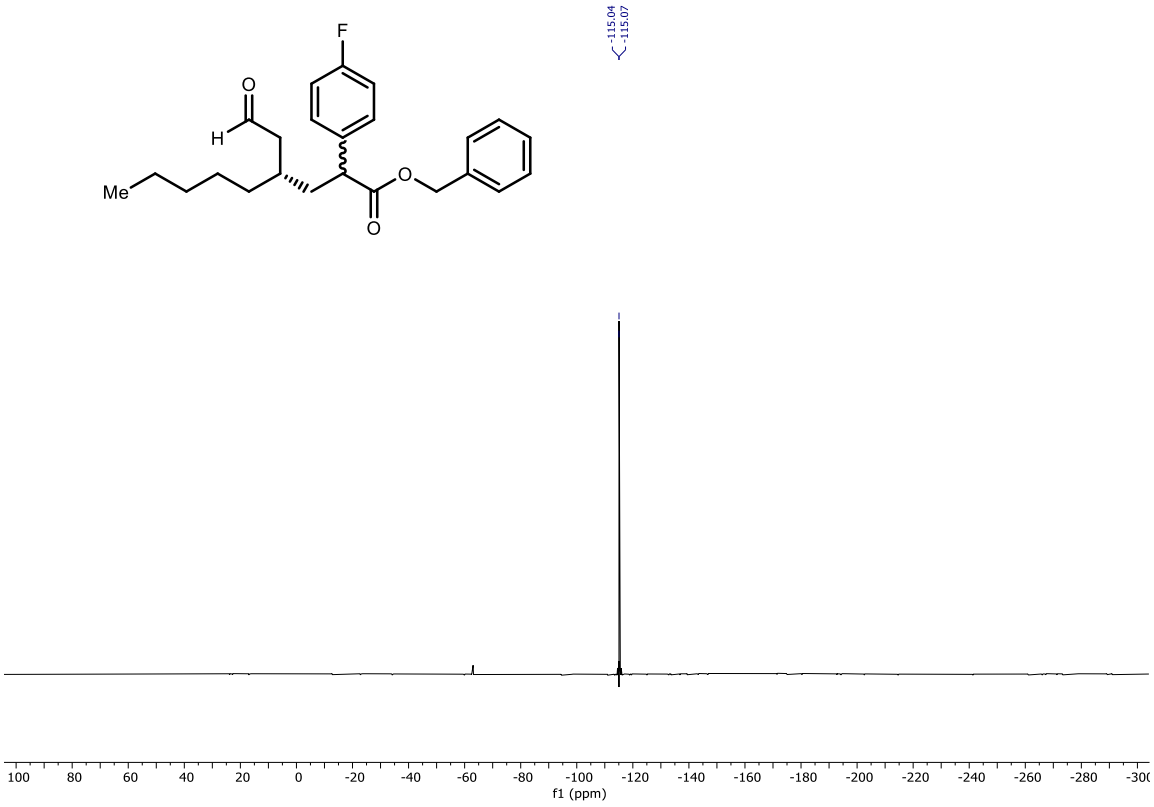
^{1}H NMR (500 MHz, $CDCl_3$, mixture of diastereoisomers) of **6t**:



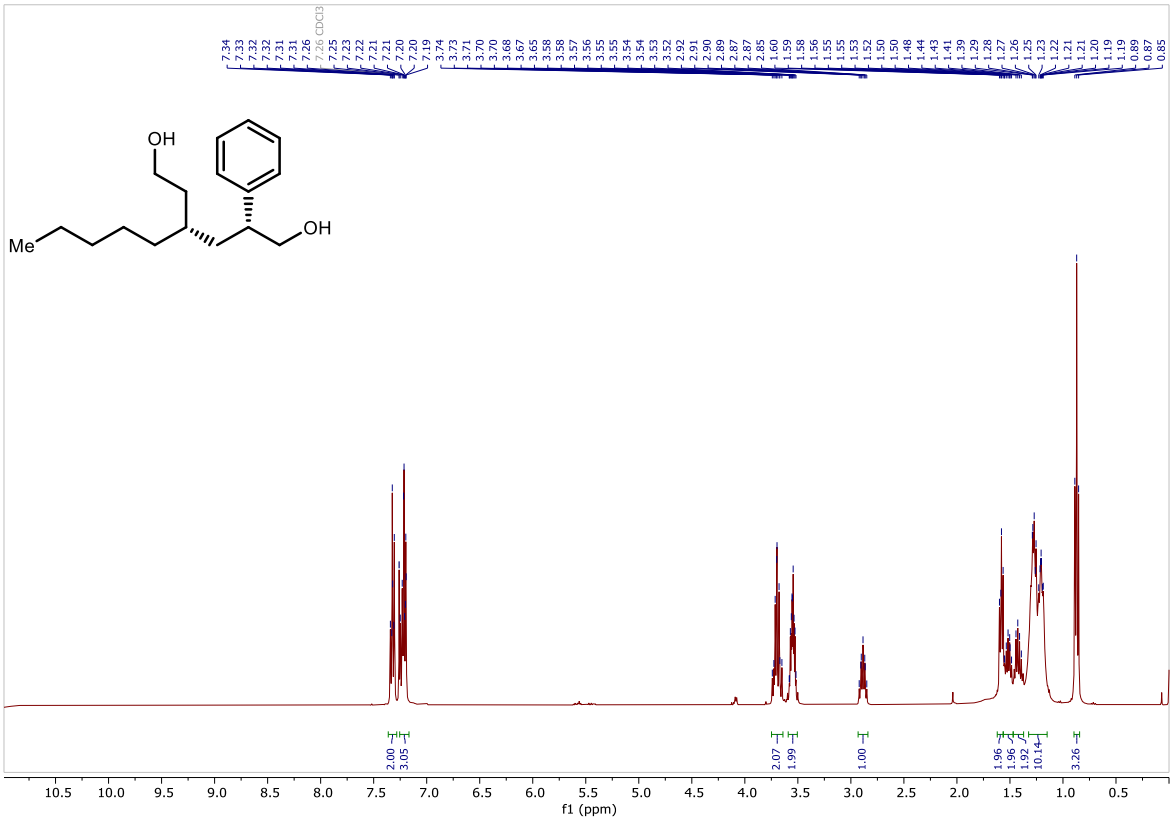
^{13}C NMR (126 MHz, $CDCl_3$, mixture of diastereoisomers) of **6t**



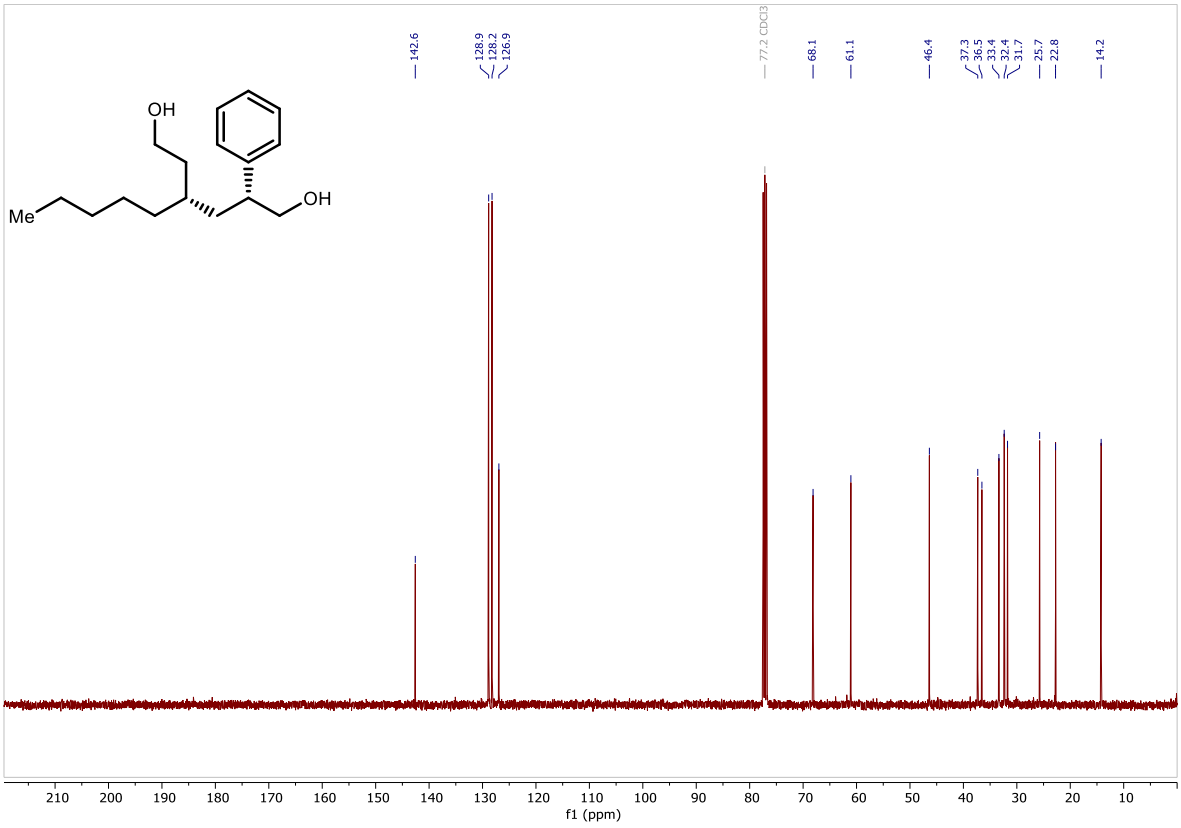
$^{19}F\{^{1}H\}$ NMR (471 MHz, $CDCl_3$, mixture of diastereoisomers) of **6t**:



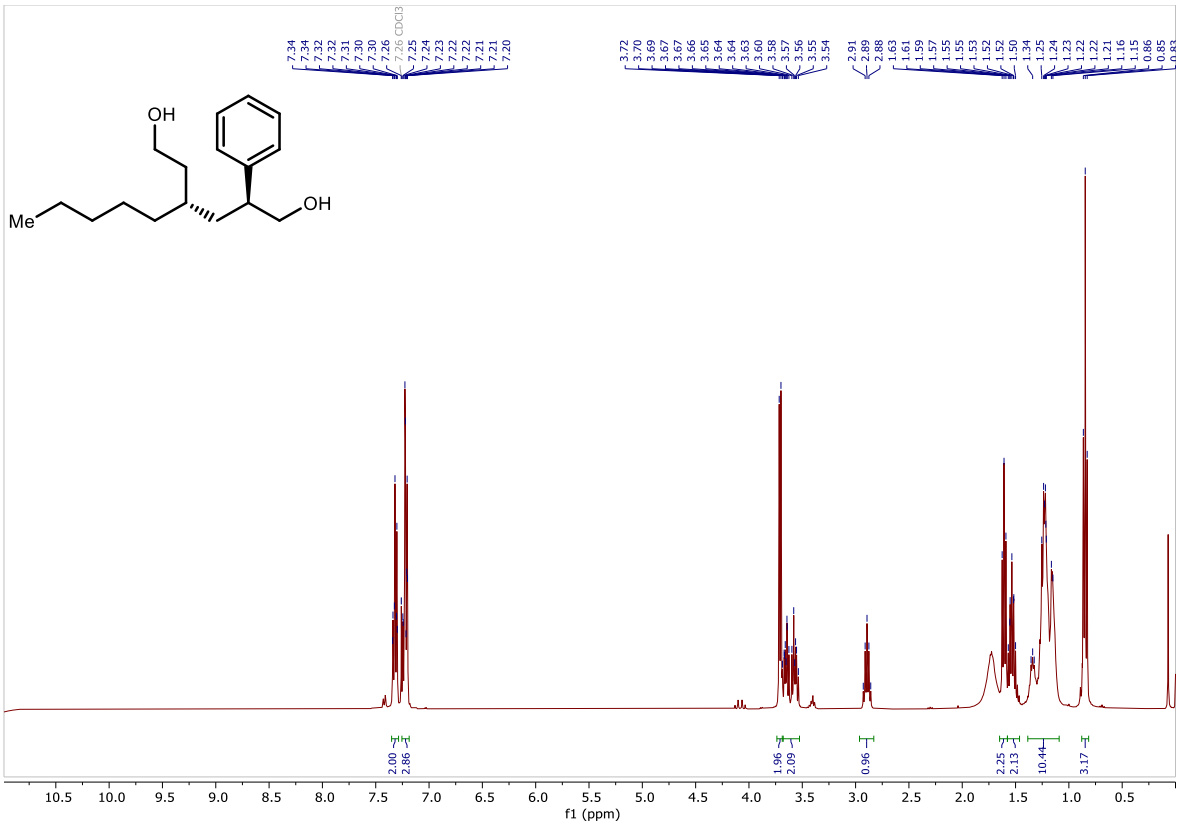
^{1}H NMR (400 MHz, $CDCl_3$) of **7a**:



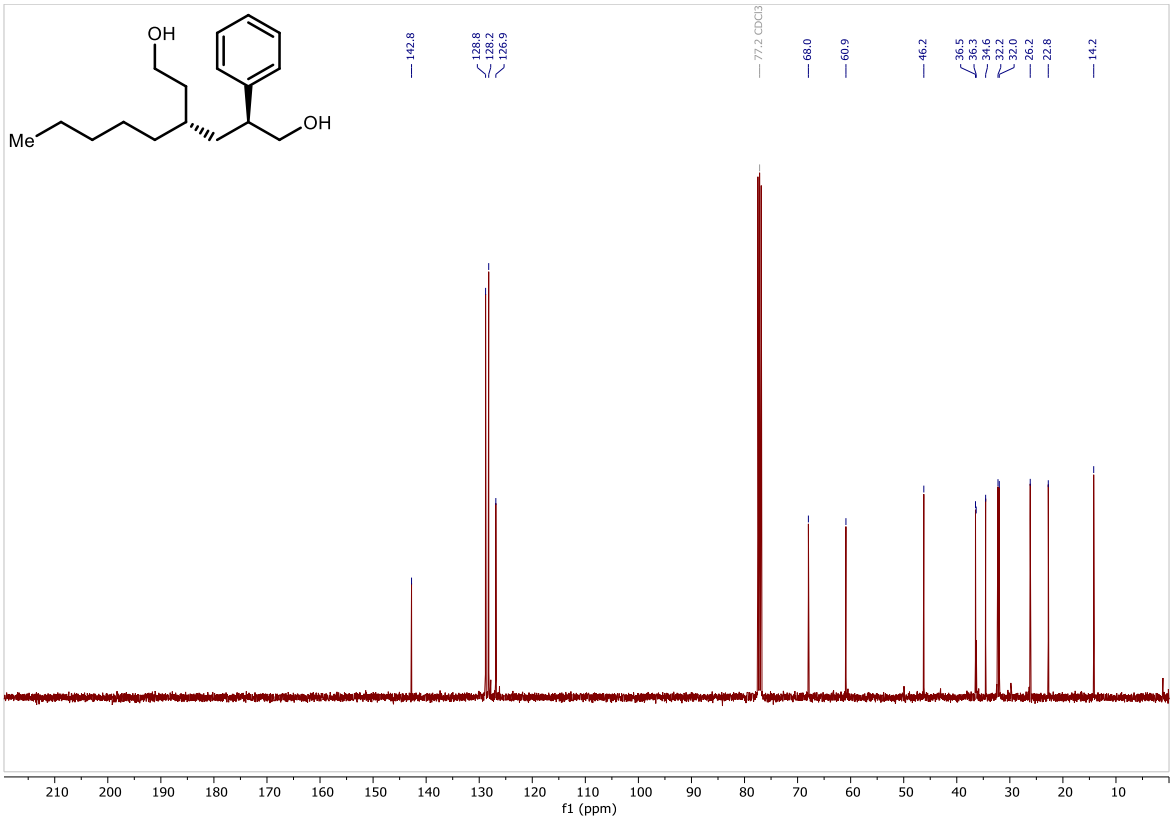
^{13}C NMR (101 MHz, $CDCl_3$) of **7a**:



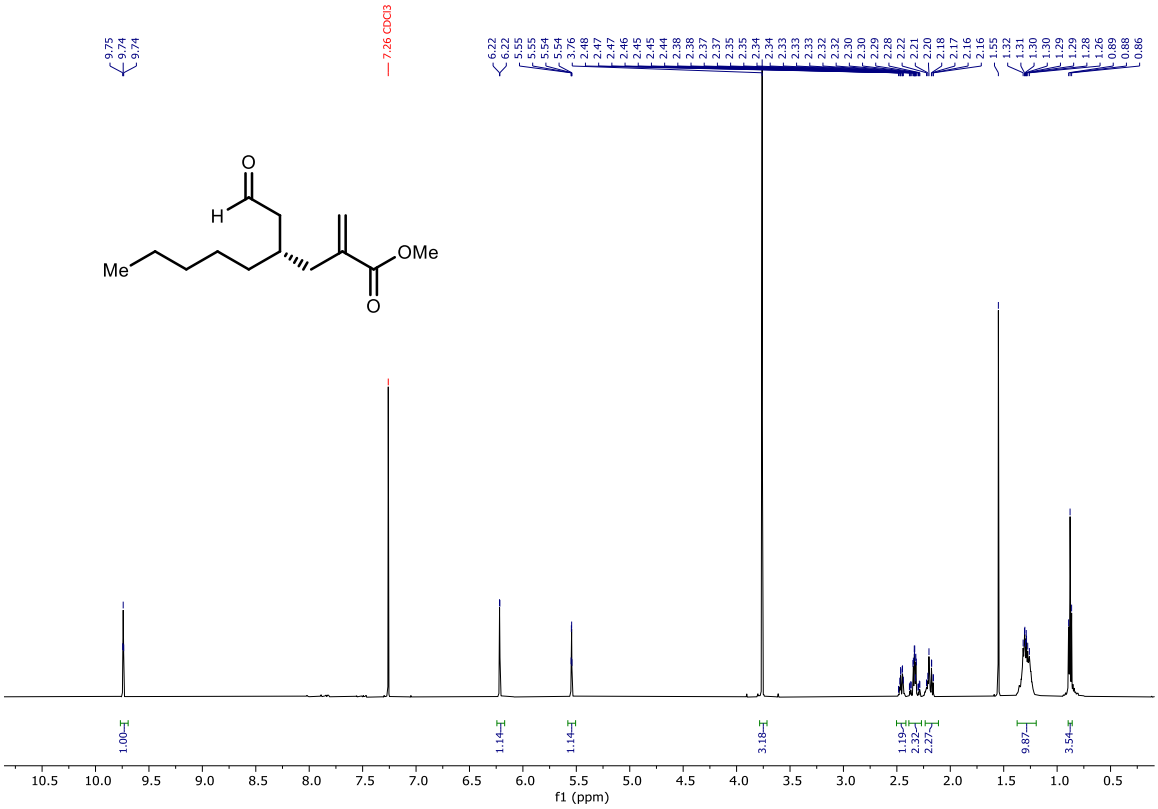
^{1}H NMR (400 MHz, $CDCl_3$) of **7b**:



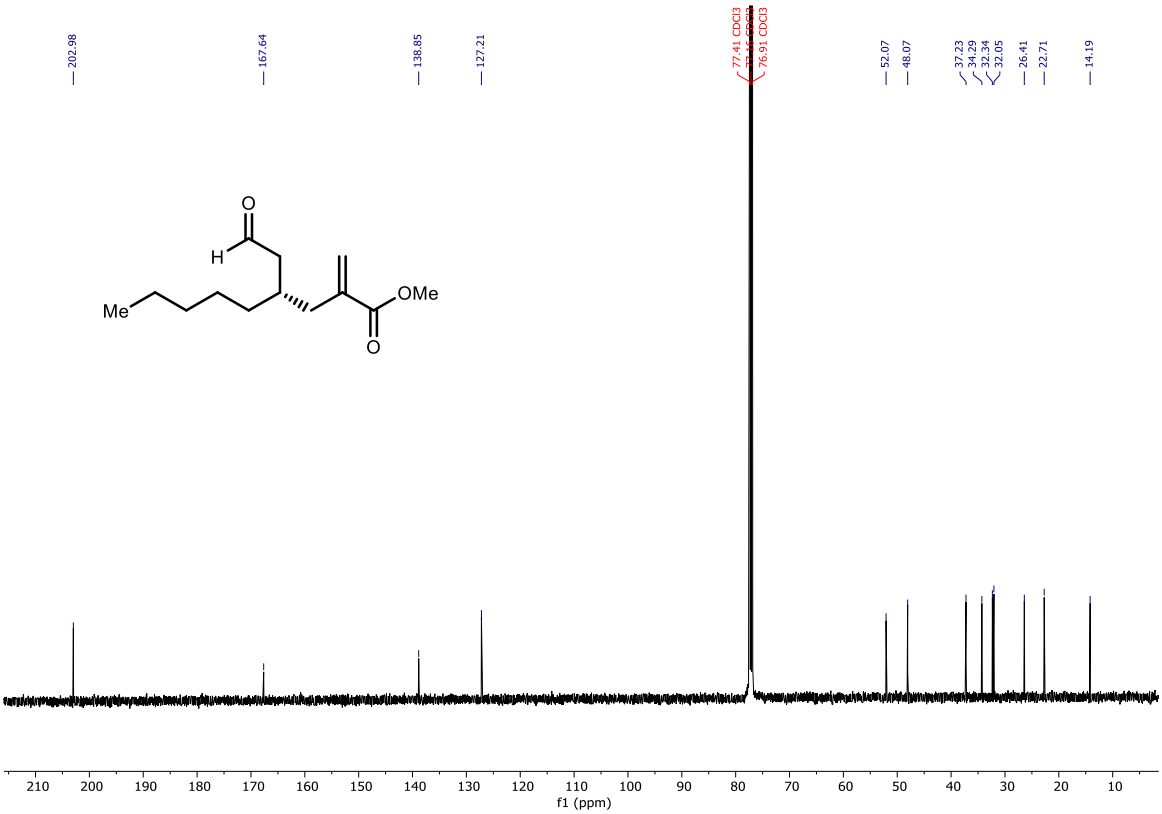
^{13}C NMR (101 MHz, $CDCl_3$) of **7b:**



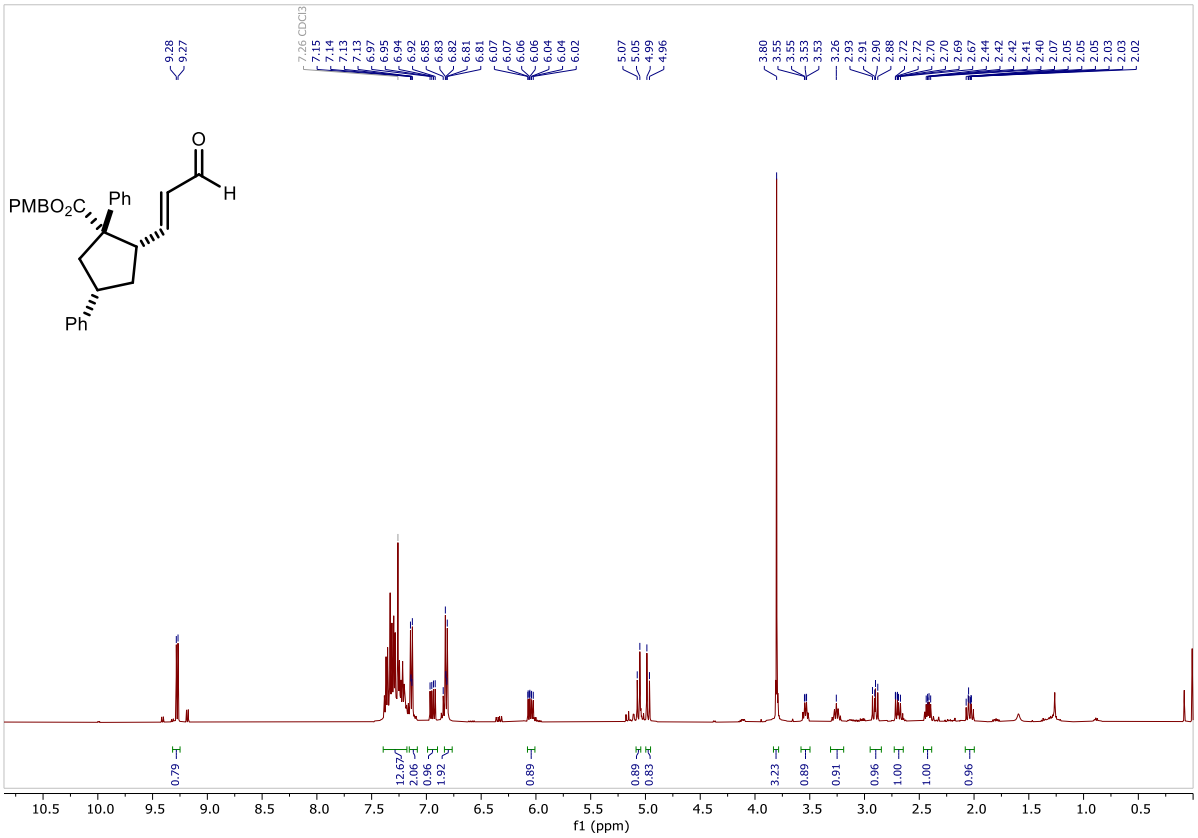
^{1}H NMR (500 MHz, $CDCl_3$) of **9**:



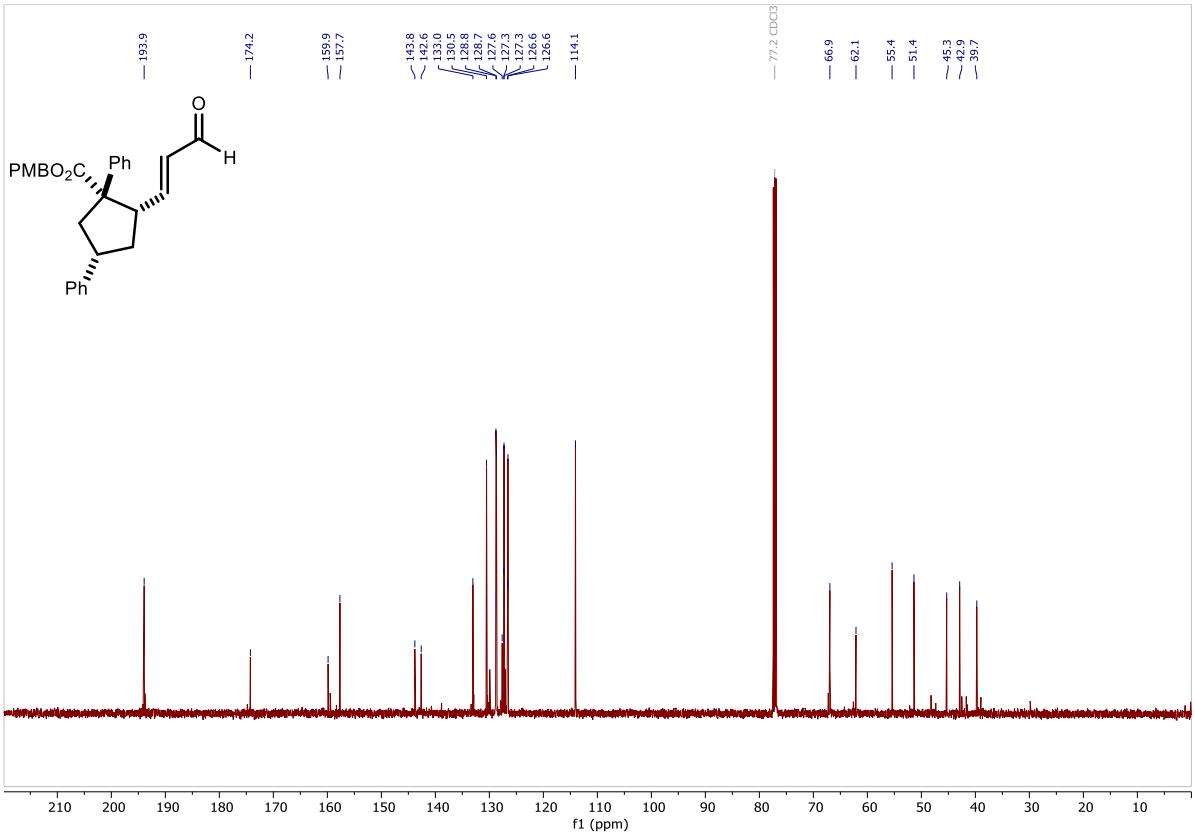
^{13}C NMR (126 MHz, $CDCl_3$) of **9**:



^{1}H NMR (500 MHz, $CDCl_3$) of **11**:

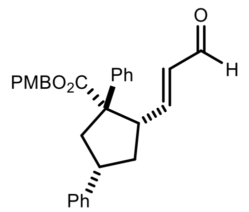


^{13}C NMR (126 MHz, $CDCl_3$) of **11**:



Radical Clock Experiment

4-Methoxybenzyl (*E*)-2-(3-oxoprop-1-en-1-yl)-1,4-diphenylcyclopentane-1-carboxylate (**11**)



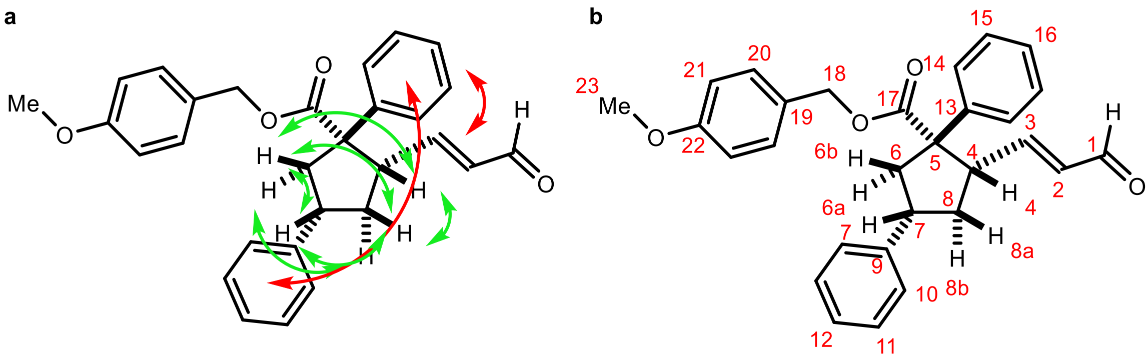
Chemical Formula: $C_{29}H_{28}O_4$
Molecular Weight: 440.54

Following the general procedure **E** using acrylate **5a** (250 µmol, 67.0 mg) and enal **10** (750 µmol, 129 mg), purification of the crude product by flash column chromatography (silica gel, 5-8% EtOAc in hexanes) afforded product **11** as a pale yellow oil (39.0 mg, 35% yield) in a 16.5:2.5:1:1 diastereomeric ratio.

NMR peaks of major diastereomer only:

^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.28 (d, *J* = 7.9 Hz, 1H, H1), 7.40 – 7.19 (m, 10H, H9-H16), 7.16 – 7.08 (m, 2H, H20), 6.94 (dd, *J* = 15.6, 7.8 Hz, 1H, H3), 6.84 – 6.76 (m, 2H, H21), 6.05 (ddd, *J* = 15.6, 7.9, 1.2 Hz, 1H, H2), 5.06 (d, *J* = 11.9 Hz, 1H, H18a), 4.98 (d, *J* = 11.9 Hz, 1H, H18b), 3.80 (s, 3H, H23), 3.58 – 3.50 (m, 1H, H4), 3.31 – 3.19 (m, 1H, H7), 2.90 (dd, *J* = 13.9, 10.3 Hz, 1H, H6a), 2.70 (dd, *J* = 14.6, 8.8 Hz, 1H, H6b), 2.46 – 2.39 (m, 1H, H8a), 2.08 – 2.00 (m, 1H, H8b) ppm. **^{13}C NMR (126 MHz, $CDCl_3$):** δ = 193.9 (C1), 174.3 (C17), 159.9 (C22), 157.7 (C3), 143.8 (C9), 142.6 (C13), 133.0 (C2), 130.5 (C20), 128.8 (C_{arom}), 128.7(C_{arom}), 127.6(C_{arom}), 127.3(C_{arom}), 127.3(C_{arom}), 126.6(C_{arom}), 126.6(C_{arom}), 114.1 (C21), 66.9 (C18), 62.1 (C5), 55.4 (C23), 51.4 (C4), 45.3 (C6), 42.9 (C7), 39.7 (C8) ppm.

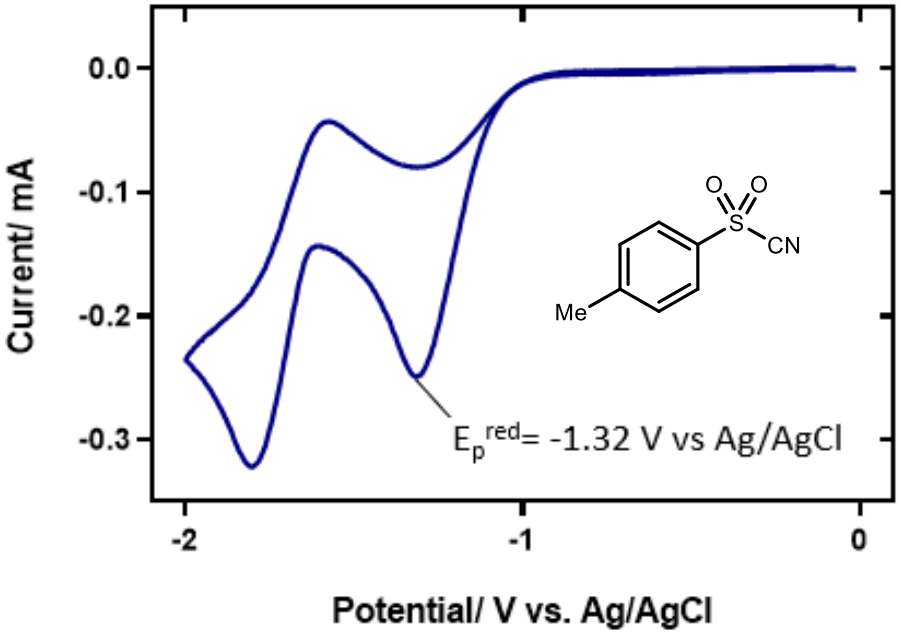
HRMS (ESI): m/z calculated for $[C_{29}H_{28}O_4Na]^+$ $[M+Na]^+$: 463.1880; found: 463.1877.



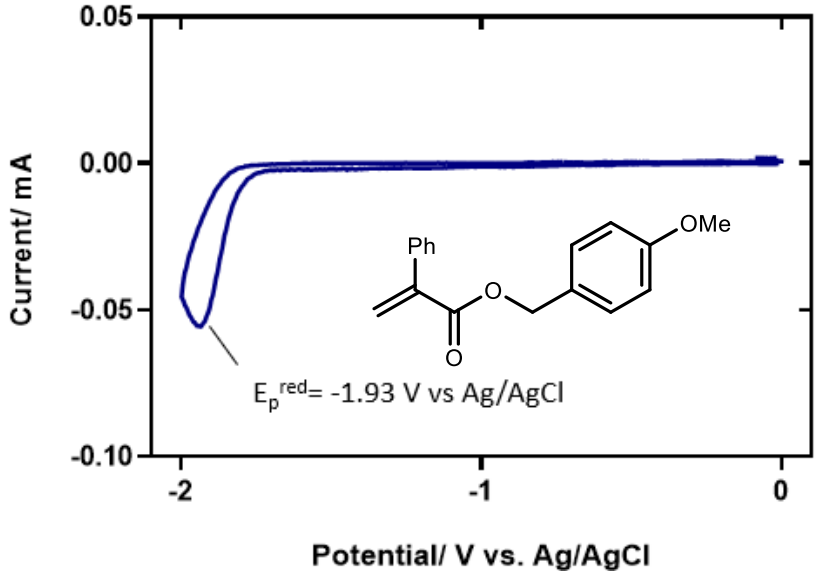
Supplementary Figure 69: Cross peaks (NOESY) (**a**) and numbering (**b**) for product **11**, which established the relative configuration of the major diastereomer; green: NOE signals; red: no NOE signals

Cyclic Voltammetric Studies

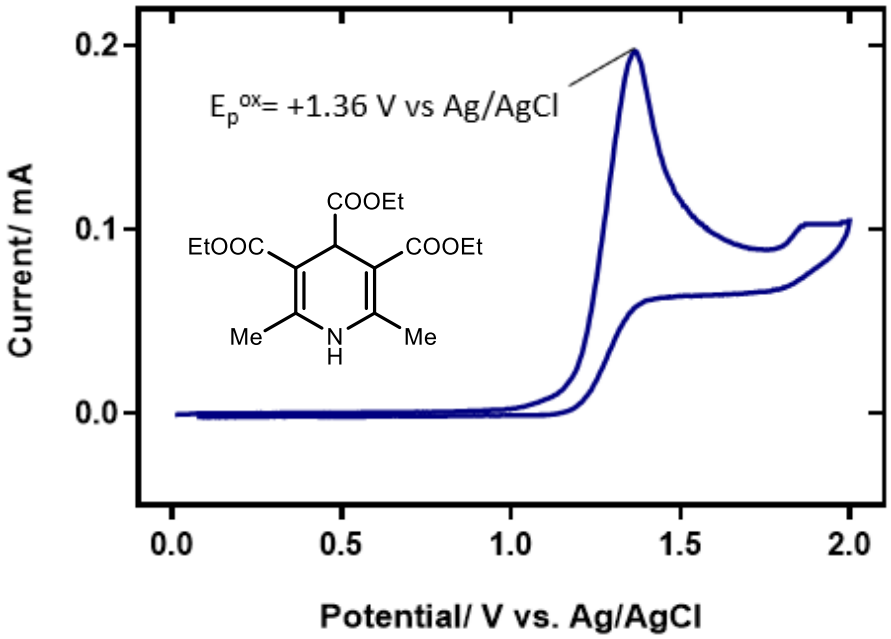
The following section details the cyclic voltammograms of the substrates (**TsCN** and **5a)** and the reductant (**R-1**) used in this study.



Supplementary Figure 70: Cyclic voltammogram of **TsCN** (5 mM) in 0.1 M [NBu_4PF_6] in MeCN. Sweep rate: 100 mV/s. Working electrode: Glassy carbon; reference electrode: Ag/AgCl (KCl sat.); Auxiliary electrode: Pt. Irreversible reduction. $E_p^A = E_p^{red}$ ($TsCN^{\bullet-}$/TsCN) = -1.32 V; E_p^A is the cathodic peak potential, while E_p^{red} value describes the electrochemical properties of **TsCN**.



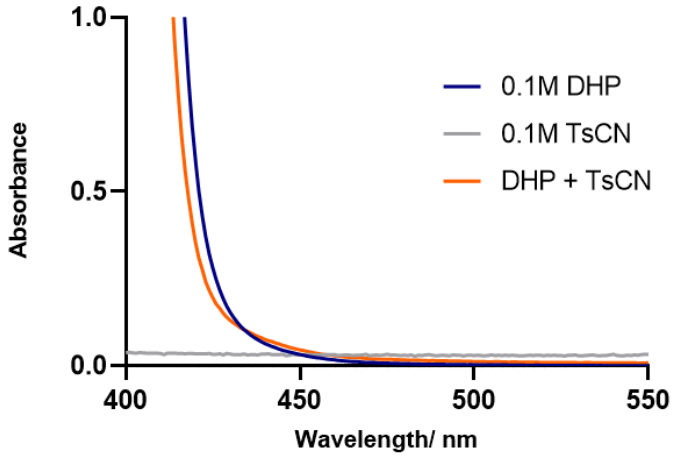
Supplementary Figure 71: Cyclic voltammogram of acrylate **5a** (1 mM) in 0.1 M [NBu_4PF_6] in MeCN. Sweep rate: 100 mV/s. Working electrode: Glassy carbon; reference electrode: Ag/AgCl (KCl sat.); Auxiliary electrode: Pt. Irreversible reduction. $E_p^A = E_p^{red}$ (**5a**$^{\bullet-}$/**5a**) = -1.93 V; E_p^A is the cathodic peak potential, while E_p^{red} value describes the electrochemical properties of **5a**.



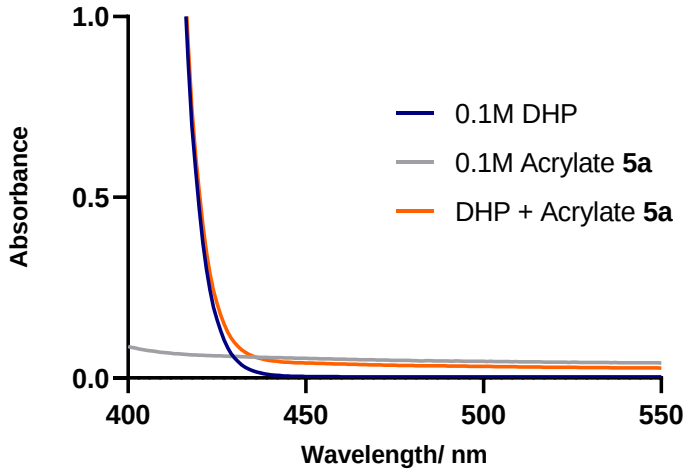
Supplementary Figure 72: Cyclic voltammogram of dihydropyridine **R-1** (5 mM) in 0.1 M [NBu_4PF_6] in MeCN. Sweep rate: 100 mV/s. Working electrode: Glassy carbon; reference electrode: Ag/AgCl (KCl sat.); Auxiliary electrode: Pt. Irreversible oxidation. $E_p^A = E_p^{ox}$ (**R-1**$^{\bullet+}$/ **R-1**) = +.1.36 V; E_p^A is the anodic peak potential, while E_p^{ox} value describes the electrochemical properties of **R-1**.

UV-Vis Spectroscopic Studies

The following section reports the UV/Vis spectra of substrates and reductant **R-1** used in this study. None of the substrates (alone or as mixture) can absorb significantly at 460 nm. The best absorbing species is the photoredox catalyst 4-CzIPN.



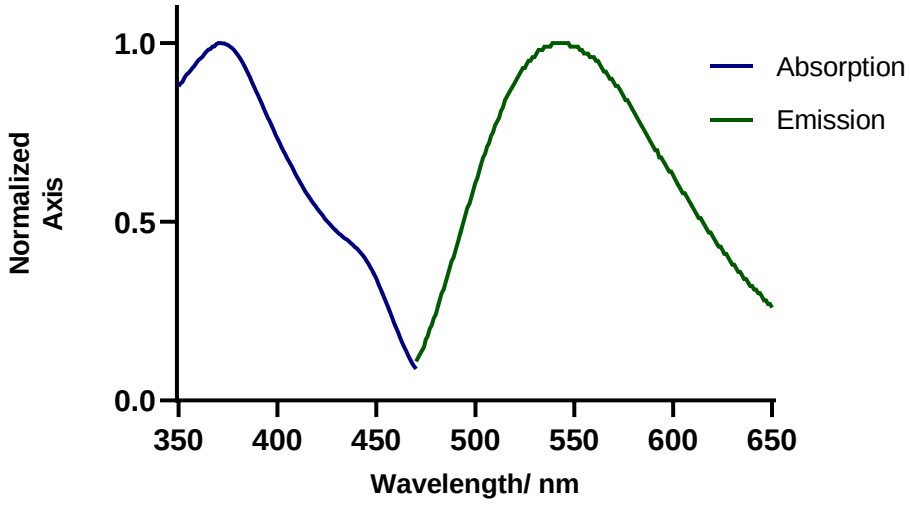
Supplementary Figure 73: UV-Vis absorption spectra, recorded in DME in 1 cm path quartz cuvettes using an Agilent Cary 60 spectrophotometer. DHP [**R-1**] = 0.10 M, [**TsCN**] = 0.10 M.



Supplementary Figure 74: UV-Vis absorption spectra, recorded in DME in 1 cm path quartz cuvettes using an Agilent Cary 60 spectrophotometer. DHP [**R-1**] = 0.10 M, [**5a**] = 0.10 M.

Stern-Volmer Quenching Studies

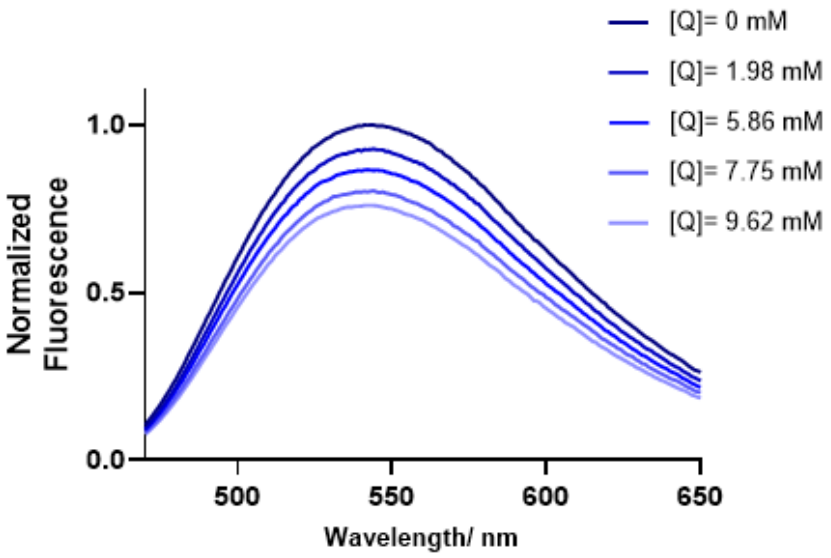
To evaluate the feasibility of the proposed reductive quenching of the excited photocatalyst **4-CzPIN** ($E_{1/2}(PC^*/PC^{\bullet-})$ = +1.35 V vs SCE) by dihydropyridine **R-1** (E^{ox} = +1.36 V vs. Ag/AgCl), we conducted Stern Volmer studies, which confirmed this mechanistic scenario. The emission spectra were recorded in a Fluorolog Horiba Jobin Yvon spectrofluorimeter equipped with a photomultiplier detector, a double monochromator, and a 450W xenon light source. 2.5 mL of HPLC grade DME, thoroughly degassed by freeze-pump-thaw, were placed in a 10 x 10 mm light path quartz fluorescence cuvette equipped with Silicone/PTFE 3.2 mm septum under an argon atmosphere. Then, 25 µL of a 1.5 mM solution of photocatalyst 4-CzIPN in DME was added to give a final concentration of 15 µM. To measure the emission spectrum, the excitation wavelength was fixed at 460 nm (incident light slit regulated to 3 nm).



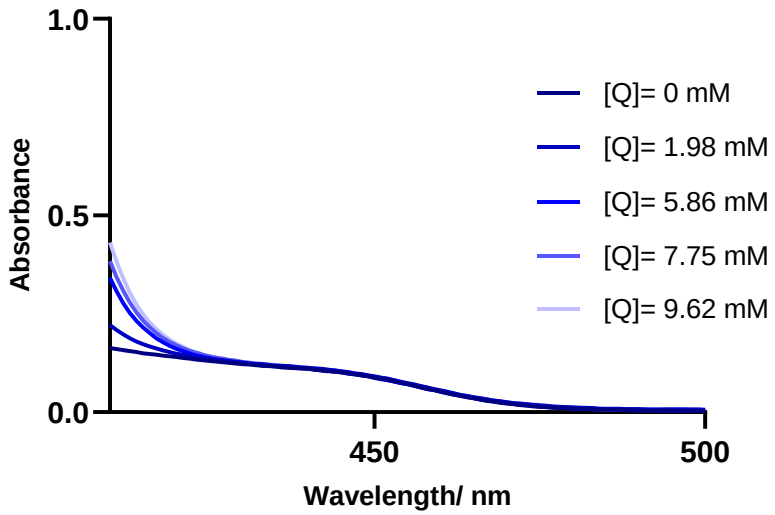
Supplementary Figure 75: Absorption and emission spectra of photocatalyst 4-CzIPN

Stern-Volmer quenching studies with dihydropyridine R-1

A 0.25 M solution of dihydropyridine **R-1** in DME was prepared, and 20 µL of this stock solution was added to the solution of photocatalyst 4-CzIPN, prepared as described above. The addition of **R-1** solution was repeated four consecutive times. After each addition, the solution was sparged with argon for 20 s. An absorption spectrum and an emission spectrum of the solution were then recorded. The excitation wavelength was fixed at 460 nm (incident light slit regulated to 3 nm); the emission light was acquired from 470 nm to 650 nm (emission light slit regulated to 3 nm). A solvent blank was subtracted from all the measurements. The excitation wavelength was chosen in order to avoid saturation of the emission detector. The results shown in **Supplementary Figure 76** indicate that **R-1** quenches the excited state of 4-CzIPN and its emission. No change in the relevant region of absorption spectra were observed during the addition of **R-1** (**Supplementary Figure 77**).



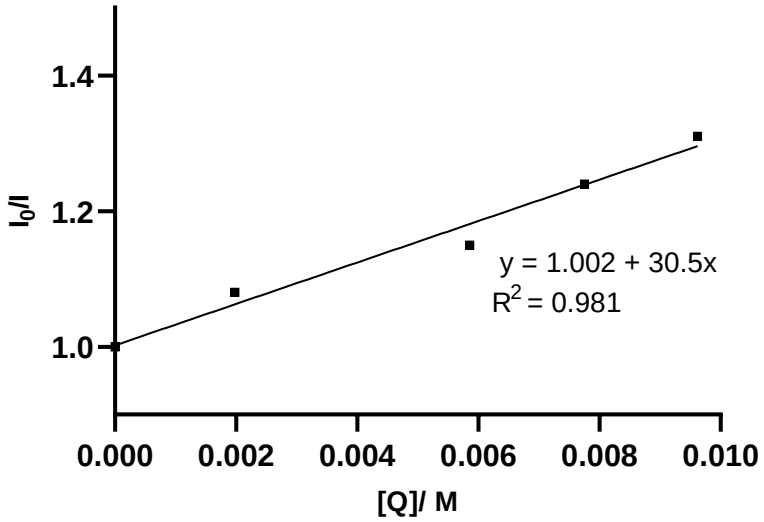
Supplementary Figure 76: Emission of the photocatalyst 4-CzIPN (15 µM in DME) in the presence of increasing amounts of dihydropyridine **R-1** [Q].



Supplementary Figure 77: UV-vis absorption spectra of 4-CzIPN (15 µM in DME) in the presence of increasing amounts of dihydropyridine **R-1** [Q].

The Stern-Volmer plot (**Supplementary Figure 78**), derived from the normalized emission intensity at 530 nm, shows a linear correlation between the amounts of **R-1** and the ratio I^0/I. Based on the following Equation 1, we calculated the Stern-Volmer constant $K_{SV\ 2}{}^{30}$ as 30.5 M^{-1}.

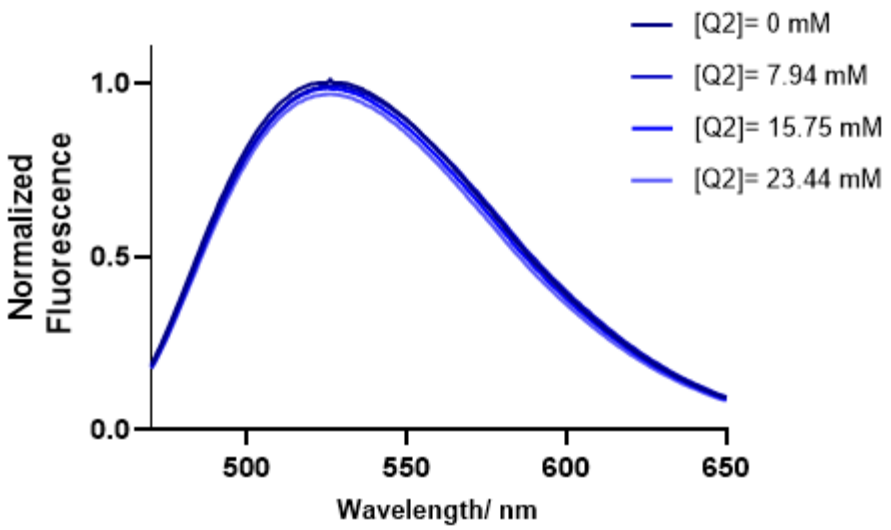
$$\frac{I^0}{I} = 1 + K_{SV}[Q] \ (1)$$



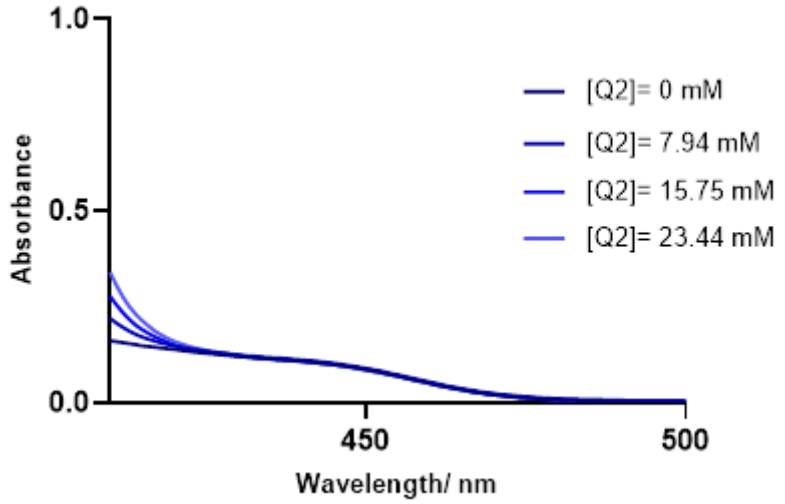
Supplementary Figure 78: Stern-Volmer quenching plot using **R-1** as the quencher.

Stern-Volmer quenching studies with TsCN

A 1.00 M solution of TsCN in DME was prepared, and 20 μL was added to the solution of photocatalyst 4-CzIPN, prepared as described above. The addition of TsCN solution was repeated three consecutive times. After each addition, the solution was sparged with argon for 20 s. An absorption spectrum and an emission spectrum of the solution were then recorded. The excitation wavelength was fixed at 460 nm (incident light slit regulated to 3 nm); the emission light was acquired from 470 nm to 650 nm (emission light slit regulated to 3 nm). A solvent blank was subtracted from all the measurements. The excitation wavelength was chosen in order to avoid saturation of the emission detector. The results shown in **Supplementary Figure 79** indicate that TsCN does not quench the excited state of 4-CzIPN and its emission significantly. No change in the relevant region of absorption spectra were observed during the addition of TsCN (**Supplementary Figure 80**).

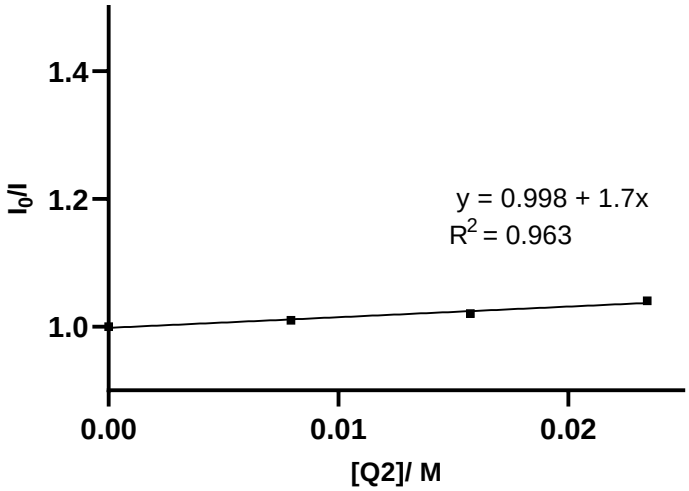


Supplementary Figure 79: Emission of the photocatalyst 4-CzIPN (15 µM in DME) in the presence of increasing amounts of TsCN [Q2].



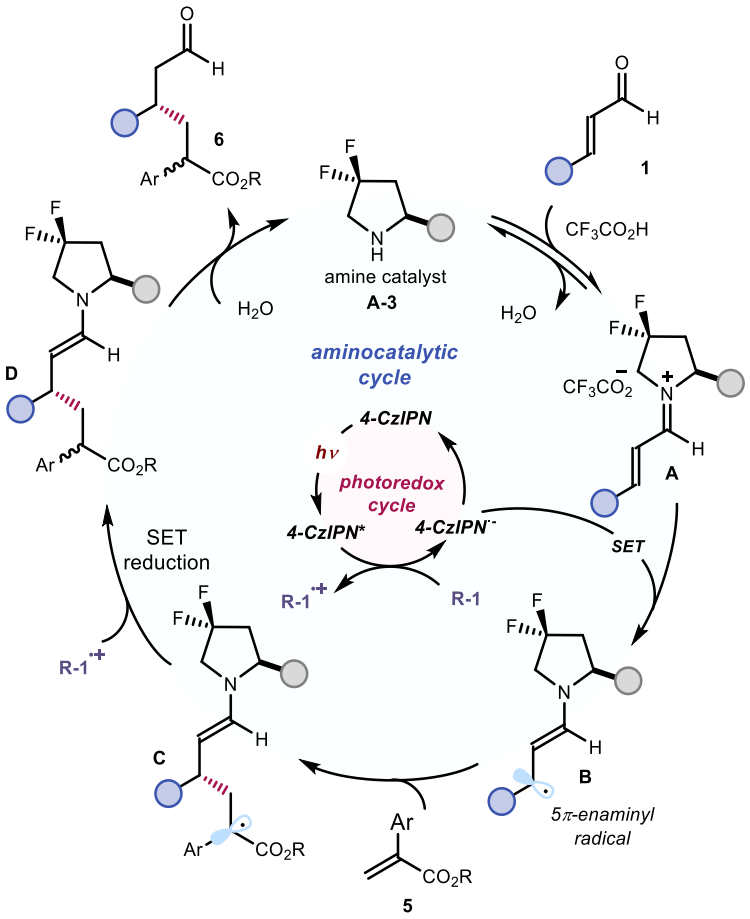
Supplementary Figure 80: UV-Vis absorption spectra of 4-CzIPN (15 µM in DME) in the presence of increasing amounts of TsCN [Q2].

The Stern-Volmer plot (**Supplementary Figure 81**), derived from the normalized emission intensity at 530 nm, shows a linear correlation between the amounts of TsCN and the ratio I^0/I. Based on equation 1, we calculated the Stern-Volmer constant $K_{SV\text{-}2}$[31] as 1.7 M^{-1}.



Supplementary Figure 81: Stern-Volmer quenching plot using TsCN as the quencher.

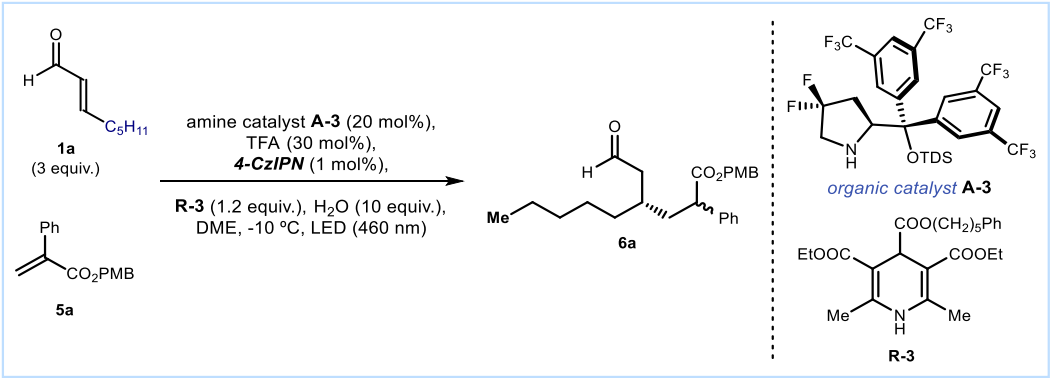
Proposed Catalytic Cycle for the Cross Electrophile Coupling



Supplementary Figure 82: Proposed mechanism for the cross electrophile coupling of enals **1** with acrylates **5** by merging the action of photocatalyst 4-CzIPN and chiral amine catalyst **A-3**.

Quantum Yield Determination

In order to confirm the proposed reaction mechanism for the cross-electrophile coupling proposed in **Supplementary Figure 82**, a quantum yield measurement was conducted on the reaction of **1a** and **5a** (**Supplementary Figure 83**).



Supplementary Figure 83: Conditions for the quantum yield determination of the cross electrophile coupling. In this case, reductant **R-3** was used to guarantee homogeneity of the reaction mixture due to improved solubility.

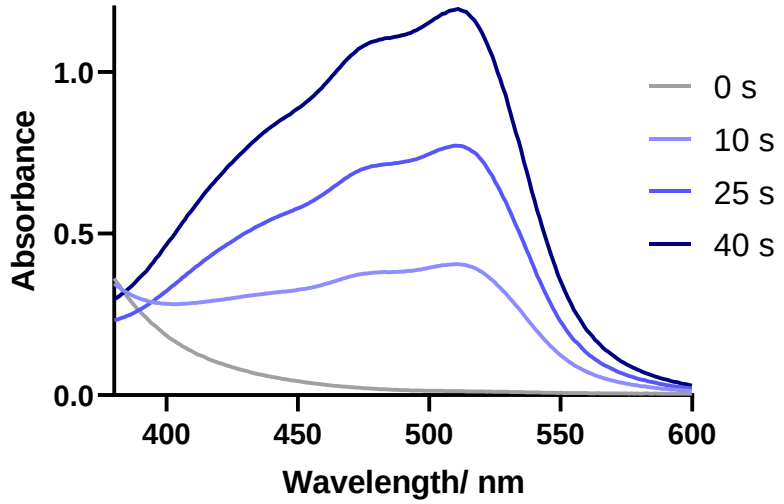
A ferrioxalate actinometer solution was prepared by following the Hammond variation of the Hatchard and Parker procedure[31] outlined in the *Handbook of Photochemistry*.[32] Ferrioxalate actinometer solution measures the decomposition of Fe(III) to Fe(II) ions, which are complexed by 1,10-phenanthroline and monitored by UV/Vis absorbance at 510 nm. The number of moles of Fe(II)-phenanthroline complex formed are directly proportional to moles of photons absorbed. The values of the quantum yield of potassium ferrioxalate are related to concentration and wavelength.

The solutions were prepared and stored in the dark (wrapped with aluminium foil, red light environment):
0.012M Potassium ferrioxalate solution: 147.4 mg of potassium ferrioxalate (commercially available from Alfa Aesar) and 69.5 μL of sulfuric acid (96%) were added to a 25 mL volumetric flask, and filled to the mark with HPLC grade water.
Phenanthroline solution: 100 mg of 1,10-phenanthroline in a 50 mL volumetric flask, filled to the mark with HPLC grade water (0.2% by weight).
Buffer solution: to a 100 mL volumetric flask 4.94 g of NaOAc and 1.0 mL of sulfuric acid (96%) were added and filled to the mark with HPLC grade water.
Internal standard solution: 1.261 g of 1,3,5-trimethoxybenzene was added to a 5 mL volumetric flask which was filled up with HPLC grade acetonitrile (1.50 M).

Reaction setup.

Reaction solution: A Schlenk flask was charged with amine catalyst **A-3** (14.1 mg, 0.2 equiv., 20 μmol), DHP **R-3** (53.2 mg, 1.2 equiv., 120 μmol), *which was chosen for its improved solubility*, unsaturated ester **1a** (26.8 mg, 1.0 eq., 100 μmol), photocatalyst 4-CzIPN (0.8 mg, 1 mol%, 1.00 μmol), *(E)*-oct-2-enal (44.8 μL, 3.0 eq., 300 μmol) and water (18 μL, 10 equiv., 1.00 mmol). After four cycles of freeze-pump-thaw (with septum), TFA (2.2 μL, 30.0 μmol) in DME (0.4 mL) and were added and the tube was sealed with parafilm and put in the HP-LED 460 nm at 1 cm distance at -10 ºC with irradiance of 90 mW/cm^2. Three different reactions were set up and irradiated for different times: 15 min, 30 min and 45 min. After each reaction was finished, internal standard solution (66 μL, 0.1 mmol) was added. This solution was diluted with 3 mL of acetone, from the solution was taken 1 mL to be analyzed by GC-FID.

Actinometer solutions: A Schlenk flask of the same dimensions as used for the reaction mixtures was loaded with 0.4 mL of actinometer solution and placed on the HP-LED the same light intensity as the reaction (without freeze-pump-thaw). Three different actinometer solutions were irradiated in sequence for 10 s, 25 s and 40 s. To irradiate the Schlenk tube, it was placed on the holder with the light off and the light was turned on for the desired time. After each irradiation the actinometer solutions were carefully transferred into a 10 mL volumetric flask, then 0.5 mL of phenanthroline solution and 2.0 mL of buffer solution were added and the flask was filled up with water. The mixture was then analyzed by UV-Vis absorption spectroscopy (**Supplementary Figure 84**).



Supplementary Figure 84: UV-Vis spectra of the actinometer solutions irradiated for different periods.

The moles of Fe(II) formed for each sample are determined using Beers' Law (**Supplementary Equation 2**):

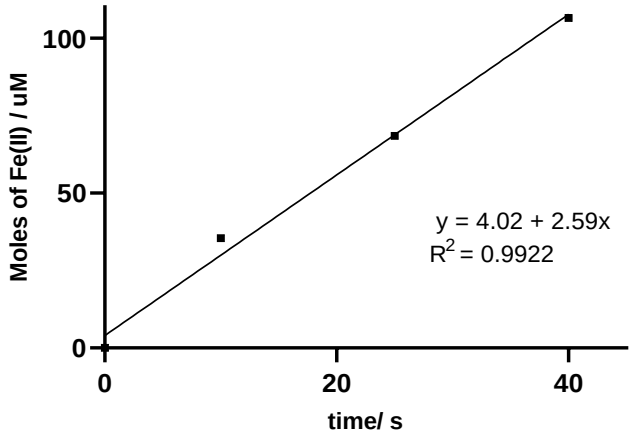
$$Moles\ of\ Fe(II) = \frac{V_1 V_3 \cdot \Delta A\ (510\ nm)}{10^3 V_2 l \cdot \varepsilon(510\ nm)} \quad (2)$$

where V_1 is the irradiated volume (0.4 mL), V_2 is the aliquot of the irradiated solution taken for the quantification of the Fe(II) complex (0.4 mL), V_3 is the final volume after complexation with phenanthroline (10 mL), l is the optical path-length of the irradiation cell (1 cm), ΔA (510 nm) is the optical difference in absorbance between the irradiated solution and the one stored in the dark, $\varepsilon_{510\ nm}$ is the extinction coefficient the complex $[Fe(phen)_3]^{2+}$ at 510 nm (11100 L mol^{-1} cm^1).

The moles of Fe(II) formed (x) are plotted as a function of time (t) (**Supplementary Figure 85**). The slope of this line was correlated to the moles of incident photons by unit of time ($q^0_{n,p}$) by the use of the following **Supplementary Equation 3**:

$$\Phi(\lambda) = \frac{dx/dt}{q^0_{n,p}[1 - 10^{-A(\lambda)}]} \quad (3)$$

where the quantum yield (Φ) for formation of Fe(II) at 458 nm is 1.11[33], dx/dt is the rate of change of a measurable quantity (spectral or any other property), $[1\text{-}10^{-A(\lambda)}]$ is the ratio of absorbed photons by the solution, and A(λ) is the absorbance of the actinometer at the wavelength used to carry out the experiments (460 nm). The absorbance at 460 nm was 0.03.



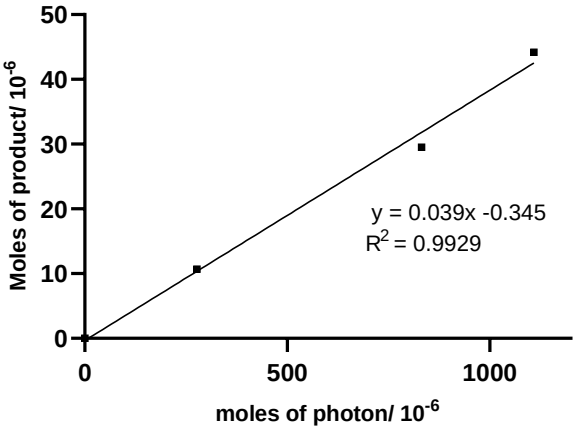
Supplementary Figure 85: Plot of the moles of Fe(II) generated from the irradiation of the actinometer solutions against time.

The photon flux, which is $q^0_{n,p}$, was determined to *3.08 x 10^{-7} einstein s^{-1}*.

The moles of product **6a** per unit of time are plotted against the number of photons absorbed (**Supplementary Figure 86**). The photons absorbed are correlated to the number of incident photons by the use of Equiv. 3. According to this, if we plot the moles of product (y-axis) versus the moles of incident photons ($q^0_{n,p}dt$, x-axis), the slope is equal to:

$$\text{slope} = \Phi\left[1 - 10^{-A(460\,nm)}\right] \quad (4)$$

where Φ is the quantum yield to be determined and $A_{460\,nm}$ is the absorption of the reaction under study. $A_{460\,nm}$ was measured to be of 0.12 for the model reaction mixture after 25-fold dilution.



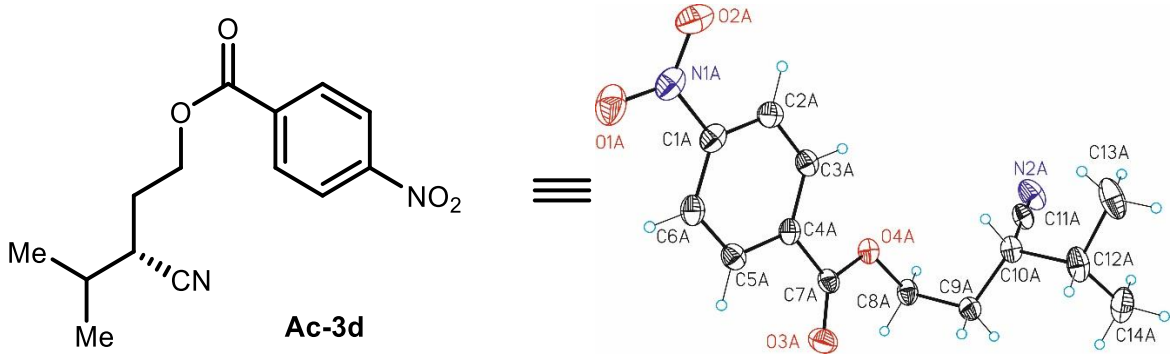
Supplementary Figure 86: Plot of the moles of products **6a** generated from the irradiation of the reaction solutions, against the moles of photons absorbed.

The quantum yield of the cross electrophile coupling process was calculated to be 0.04.

X-Ray Crystallography

Single Crystal X-ray Diffraction Data for the 4-nitrobenzoate derivative of β-cyano alcohol 3d (Ac-3d)

4-Nitrobenzoate derivative **Ac-3d** was obtained from an analytical sample prepared according to the general procedure as described in the Supplementray Figure 5 using β-cyano alcohol **3d**. Crystals of the compound **Ac-3d** were obtained by slow evaporation of a dichloromethane/hexane solution. *Data Collection*. Measurements were performed at 100 K on a Bruker Kappa Apex II DUO diffractometer equiped with a Cryostream 700 plus low temperature device, a microsource anode with Mo Kα (λ= 0.71073 Å).



Supplementary Figure 87: Structure of **Ac-3d.**

This chiral compound crystallizes in the space group P21 with two identical molecules (A and B) in the asymmetric unit. One of the molecules is disordered in two inverted orientations of the chiral center with a ratio 82:18. The absolute structure could be determined reliable with a Flack value based on Parsons' quotients of 0.02(8)[34-37] Flack X determined using 2186 quotients [(I+)-(I-)]/[(I+)+(I-)]. The Flack parameter value for the correct absolute structure determination should be 0; the inverted structure would give 1; always taking in account the standard deviation. For molecule A the absolute configuration was assigned with S(C10A). In molecule B the absolute configuration was assigned with 82% of configuration S(C10B) and 18% of configuration R(C10'). Adding the results, it was determined that the majoritarian part of the structure (91%) shows S configuration and a minoritarian part (9%) shows a R configuration in accordance with the e.r. value obtained in the preparation of the product. The structure is of excellent quality (no A- or B-alerts) and of publishable quality with a R1 value of 3.07%.

Crystal data and structure refinement for **Ac-3d**. ***CCDC2197381***

Identification code	cu_MBE389_0m
Empirical formula	C28 H32 N4 O8
Formula weight	552.57
Temperature	100(2)K
Wavelength	1.54178 Å
Crystal system	monoclinic
Space group	P 21
Unit cell dimensions	a = 7.2034(2)Å a= 90°. b = 18.8414(6)Å b = 91.8741(14)°. c = 10.3566(3)Å g = 90°.
Volume	1404.87(7) $Å^3$
Z	2
Density (calculated)	1.306 Mg/m^3

Absorption coefficient	0.806 mm^{-1}
F(000)	584
Crystal size	0.200 x 0.200 x 0.010 mm^3
Theta range for data collection	4.271 to 67.930°.
Index ranges	-8<=h<=8,-22<=k<=21,-8<=l<=12
Reflections collected	11462
Independent reflections	4916[R(int) = 0.0278]
Completeness to theta =67.930°	98.6%
Absorption correction	Multi-scan
Max. and min. transmission	0.75 and 0.65
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4916/ 99/ 432
Goodness-of-fit on F^2	1.058
Final R indices [I>2sigma(I)]	R1 = 0.0307, wR2 = 0.0814
R indices (all data)	R1 = 0.0315, wR2 = 0.0819
Flack parameter	x =0.02(8)
Largest diff. peak and hole	0.189 and -0.158 e.$Å^{-3}$

Bond lengths [Å] and angles [°] for **Ac-3d**. ***CCDC2197381***

Bond lengths		
O1A	N1A	1.225(3)
O2A	N1A	1.229(3)
O3A	C7A	1.203(3)
O4A	C7A	1.340(3)
O4A	C8A	1.454(3)
N1A	C1A	1.475(3)
N2A	C11A	1.145(3)
C1A	C2A	1.382(4)
C1A	C6A	1.385(4)
C2A	C3A	1.388(3)
C2A	H2A	0.9500
C3A	C4A	1.389(3)
C3A	H3A	0.9500
C4A	C5A	1.391(4)
C4A	C7A	1.496(3)
C5A	C6A	1.385(3)
C5A	H5A	0.9500
C6A	H6A	0.9500
C8A	C9A	1.517(3)
C8A	H8AA	0.9900
C8A	H8AB	0.9900
C9A	C10A	1.533(3)
C9A	H9AA	0.9900
C9A	H9AB	0.9900
C10A	C11A	1.470(3)
C10A	C12A	1.547(3)
C10A	H10A	1.0000
C12A	C14A	1.522(4)
C12A	C13A	1.530(4)
C12A	H12A	1.0000
C13A	H13A	0.9800
C13A	H13B	0.9800
C13A	H13C	0.9800
C14A	H14A	0.9800
C14A	H14B	0.9800
C14A	H14C	0.9800
O1B	N1B	1.224(3)
O2B	N1B	1.228(3)
O3B	C7B	1.204(3)

O4B C7B 1.338(3)
O4B C8B 1.449(3)
N1B C1B 1.472(3)
C1B C6B 1.381(4)
C1B C2B 1.385(3)
C2B C3B 1.386(3)
C2B H2B 0.9500
C3B C4B 1.389(4)
C3B H3B 0.9500
C4B C5B 1.399(3)
C4B C7B 1.494(3)
C5B C6B 1.382(3)
C5B H5B 0.9500
C6B H6B 0.9500
C8B C9' 1.322(17)
C8B C9B 1.550(4)
C8B H8BA 0.9900
C8B H8BB 0.9900
C8B H8BX 0.9900
C8B H8BY 0.9900
N2B C11B 1.145(4)
C9B C10B 1.536(4)
C9B H9BA 0.9900
C9B H9BB 0.9900
C10B C11B 1.470(4)
C10B C12B 1.548(4)
C10B H10B 1.0000
C12B C13B 1.527(6)
C12B C14B 1.534(5)
C12B H12B 1.0000
C13B H13D 0.9800
C13B H13E 0.9800
C13B H13F 0.9800
C14B H14D 0.9800
C14B H14E 0.9800
C14B H14F 0.9800
N2' C11' 1.11(2)
C9' C10' 1.46(3)
C9' H9BC 0.9900
C9' H9BD 0.9900
C10' C11' 1.52(2)
C10' C12' 1.59(2)
C10' H10' 1.0000
C12' C13' 1.45(3)
C12' C14' 1.52(3)
C12' H12' 1.0000
C13' H13G 0.9800
C13' H13H 0.9800
C13' H13I 0.9800
C14' H14G 0.9800
C14' H14H 0.9800
C14' H14I 0.9800

Angles
C7A O4A C8A 116.25(18)
O1A N1A O2A 124.1(2)
O1A N1A C1A 118.0(2)
O2A N1A C1A 117.9(2)
C2A C1A C6A 123.0(2)
C2A C1A N1A 118.7(2)
C6A C1A N1A 118.2(2)

C1A C2A C3A 118.2(2)
C1A C2A H2A 120.9
C3A C2A H2A 120.9
C2A C3A C4A 119.7(2)
C2A C3A H3A 120.1
C4A C3A H3A 120.1
C3A C4A C5A 121.0(2)
C3A C4A C7A 121.6(2)
C5A C4A C7A 117.4(2)
C6A C5A C4A 119.8(2)
C6A C5A H5A 120.1
C4A C5A H5A 120.1
C5A C6A C1A 118.2(2)
C5A C6A H6A 120.9
C1A C6A H6A 120.9
O3A C7A O4A 124.4(2)
O3A C7A C4A 123.5(2)
O4A C7A C4A 112.08(19)
O4A C8A C9A 109.83(18)
O4A C8A H8AA 109.7
C9A C8A H8AA 109.7
O4A C8A H8AB 109.7
C9A C8A H8AB 109.7
H8AA C8A H8AB 108.2
C8A C9A C10A 113.50(19)
C8A C9A H9AA 108.9
C10A C9A H9AA 108.9
C8A C9A H9AB 108.9
C10A C9A H9AB 108.9
H9AA C9A H9AB 107.7
C11A C10A C9A 109.66(18)
C11A C10A C12A 110.26(19)
C9A C10A C12A 114.1(2)
C11A C10A H10A 107.5
C9A C10A H10A 107.5
C12A C10A H10A 107.5
N2A C11A C10A 177.8(3)
C14A C12A C13A 111.5(2)
C14A C12A C10A 112.4(2)
C13A C12A C10A 109.9(2)
C14A C12A H12A 107.6
C13A C12A H12A 107.6
C10A C12A H12A 107.6
C12A C13A H13A 109.5
C12A C13A H13B 109.5
H13A C13A H13B 109.5
C12A C13A H13C 109.5
H13A C13A H13C 109.5
H13B C13A H13C 109.5
C12A C14A H14A 109.5
C12A C14A H14B 109.5
H14A C14A H14B 109.5
C12A C14A H14C 109.5
H14A C14A H14C 109.5
H14B C14A H14C 109.5
C7B O4B C8B 118.02(19)
O1B N1B O2B 123.8(2)
O1B N1B C1B 118.3(2)
O2B N1B C1B 117.9(2)
C6B C1B C2B 122.9(2)
C6B C1B N1B 118.4(2)

C2B C1B N1B 118.7(2)
C1B C2B C3B 118.1(2)
C1B C2B H2B 120.9
C3B C2B H2B 120.9
C2B C3B C4B 120.2(2)
C2B C3B H3B 119.9
C4B C3B H3B 119.9
C3B C4B C5B 120.4(2)
C3B C4B C7B 118.4(2)
C5B C4B C7B 121.2(2)
C6B C5B C4B 119.8(2)
C6B C5B H5B 120.1
C4B C5B H5B 120.1
C1B C6B C5B 118.6(2)
C1B C6B H6B 120.7
C5B C6B H6B 120.7
O3B C7B O4B 125.0(2)
O3B C7B C4B 123.6(2)
O4B C7B C4B 111.3(2)
C9' C8B O4B 128.7(9)
O4B C8B C9B 104.0(2)
O4B C8B H8BA 111.0
C9B C8B H8BA 111.0
O4B C8B H8BB 111.0
C9B C8B H8BB 111.0
H8BA C8B H8BB 109.0
C9' C8B H8BX 105.1
O4B C8B H8BX 105.1
C9' C8B H8BY 105.1
O4B C8B H8BY 105.1
H8BX C8B H8BY 105.9
C10B C9B C8B 113.6(2)
C10B C9B H9BA 108.9
C8B C9B H9BA 108.9
C10B C9B H9BB 108.9
C8B C9B H9BB 108.9
H9BA C9B H9BB 107.7
C11B C10B C9B 109.9(2)
C11B C10B C12B 110.2(2)
C9B C10B C12B 112.0(3)
C11B C10B H10B 108.2
C9B C10B H10B 108.2
C12B C10B H10B 108.2
N2B C11B C10B 179.3(4)
C13B C12B C14B 111.0(3)
C13B C12B C10B 112.9(4)
C14B C12B C10B 111.0(3)
C13B C12B H12B 107.2
C14B C12B H12B 107.2
C10B C12B H12B 107.2
C12B C13B H13D 109.5
C12B C13B H13E 109.5
H13D C13B H13E 109.5
C12B C13B H13F 109.5
H13D C13B H13F 109.5
H13E C13B H13F 109.5
C12B C14B H14D 109.5
C12B C14B H14E 109.5
H14D C14B H14E 109.5
C12B C14B H14F 109.5
H14D C14B H14F 109.5

H14E C14B H14F 109.5
C8B C9' C10' 105.2(16)
C8B C9' H9BC 110.7
C10' C9' H9BC 110.7
C8B C9' H9BD 110.7
C10' C9' H9BD 110.7
H9BC C9' H9BD 108.8
C9' C10' C11' 108.6(12)
C9' C10' C12' 117.6(14)
C11' C10' C12' 107.1(14)
C9' C10' H10' 107.7
C11' C10' H10' 107.7
C12' C10' H10' 107.7
N2' C11' C10' 179(2)
C13' C12' C14' 113.8(17)
C13' C12' C10' 110.6(18)
C14' C12' C10' 112.8(15)
C13' C12' H12' 106.3
C14' C12' H12' 106.3
C10' C12' H12' 106.3
C12' C13' H13G 109.5
C12' C13' H13H 109.5
H13G C13' H13H 109.5
C12' C13' H13I 109.5
H13G C13' H13I 109.5
H13H C13' H13I 109.5
C12' C14' H14G 109.5
C12' C14' H14H 109.5
H14G C14' H14H 109.5
C12' C14' H14I 109.5
H14G C14' H14I 109.5
H14H C14' H14I 109.5

Torsion angles [°] for **Ac-3d**. ***CCDC2197381***

O1A	N1A	C1A	C2A	175.8(2)
O2A	N1A	C1A	C2A	-6.0(3)
O1A	N1A	C1A	C6A	-6.6(3)
O2A	N1A	C1A	C6A	171.6(2)
C6A	C1A	C2A	C3A	-0.6(3)
N1A	C1A	C2A	C3A	176.77(18)
C1A	C2A	C3A	C4A	-0.9(3)
C2A	C3A	C4A	C5A	1.7(3)
C2A	C3A	C4A	C7A	-176.63(19)
C3A	C4A	C5A	C6A	-1.0(3)
C7A	C4A	C5A	C6A	177.41(18)
C4A	C5A	C6A	C1A	-0.5(3)
C2A	C1A	C6A	C5A	1.3(3)
N1A	C1A	C6A	C5A	-176.09(19)
C8A	O4A	C7A	O3A	-2.9(3)
C8A	O4A	C7A	C4A	175.97(16)
C3A	C4A	C7A	O3A	167.4(2)
C5A	C4A	C7A	O3A	-11.0(3)
C3A	C4A	C7A	O4A	-11.5(3)
C5A	C4A	C7A	O4A	170.11(18)
C7A	O4A	C8A	C9A	-85.8(2)
O4A	C8A	C9A	C10A	-59.7(3)
C8A	C9A	C10A	C11A	-59.9(3)
C8A	C9A	C10A	C12A	175.8(2)
C11A	C10A	C12A	C14A	-58.4(3)
C9A	C10A	C12A	C14A	65.5(3)

C11A C10A C12A C13A 66.4(3)
C9A C10A C12A C13A -169.7(2)
O1B N1B C1B C6B -177.3(2)
O2B N1B C1B C6B 3.3(3)
O1B N1B C1B C2B 4.4(3)
O2B N1B C1B C2B -175.0(2)
C6B C1B C2B C3B -0.5(3)
N1B C1B C2B C3B 177.75(18)
C1B C2B C3B C4B 1.0(3)
C2B C3B C4B C5B -0.7(3)
C2B C3B C4B C7B -179.16(18)
C3B C4B C5B C6B -0.2(3)
C7B C4B C5B C6B 178.18(18)
C2B C1B C6B C5B -0.4(3)
N1B C1B C6B C5B -178.67(18)
C4B C5B C6B C1B 0.8(3)
C8B O4B C7B O3B 13.7(3)
C8B O4B C7B C4B -165.90(17)
C3B C4B C7B O3B 9.7(3)
C5B C4B C7B O3B -168.7(2)
C3B C4B C7B O4B -170.65(18)
C5B C4B C7B O4B 10.9(3)
C7B O4B C8B C9' 73.3(12)
C7B O4B C8B C9B 93.9(3)
O4B C8B C9B C10B 166.1(2)
C8B C9B C10B C11B -63.2(3)
C8B C9B C10B C12B 174.0(3)
C11B C10B C12B C13B -66.3(4)
C9B C10B C12B C13B 56.3(4)
C11B C10B C12B C14B 59.1(4)
C9B C10B C12B C14B -178.3(3)
O4B C8B C9' C10' 67.6(13)
C8B C9' C10' C11' 65.3(16)
C8B C9' C10' C12' -173.0(12)
C9' C10' C12' C13' 167.4(18)
C11' C10' C12' C13' -70(2)
C9' C10' C12' C14' -63.8(19)
C11' C10' C12' C14' 58.7(19)

Symetry operations

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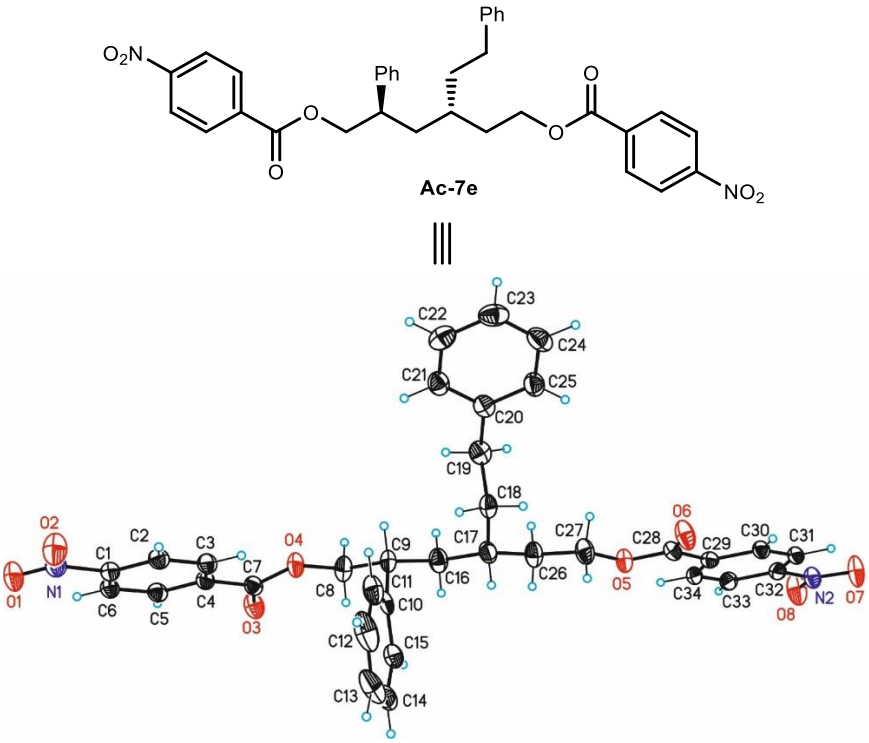
1 'x, y, z'
2 '-x, y+1/2, -z'

Single Crystal X-ray Diffraction Data for the 4-nitrobenzoate derivative of diol 7e (Ac-7e)

4-Nitrobenzoate derivative **Ac-7e** was obtained from an analytical sample prepared according to the general procedure as described in the Supplementray Figure 5 using diol **7e** obtained upon reduction of 1,6-dicarbonyl **6e**. Crystals of the compound **Ac-7e** were obtained by slow evaporation of a dichloromethane/hexane solution. *Data Collection*. Measurements were performed at 100 K on a Bruker Kappa Apex II DUO diffractometer equiped with a Cryostream 700 plus low temperature device, a microsource anode with Mo Kα (λ= 0.71073 Å).



Supplementary Figure 88: Structure of **Ac-7e.**

This chiral compound crystallizes in the space group P1 showing disorder in the group with the benzene ring (atoms C18 to C25) with a ratio of 75:25. Both disordered orientations show the same stereochemistry. The absolute structure could be determined reliable with a Flack value based on Parsons' quotients of -0.05(9) [34-37]. Flack X determined using 1202 quotients [(I+)-(I-)]/[(I+)+(I-)]. The Flack parameter value for the correct absolute structure determination should be 0; the inverted structure would give 1; always taking in account the standard deviation. The absolute configuration based on the absolute structure of the measured crystal was determined with S(C9), R(C17). The structure is of excellent quality (no A-alerts and ***one commented B-alerts related to the poor data to parameter ratio***, see CIF/checkCIF) and of publishable quality with a R1 value of 3.18%.

The B alert in the checkCIF file is due to formation of small chiral crystals of low symmetry (Space group P1) which were measured using CuKalfa radiation. Additionally, the structure showed disorder which enlarged the number of parameters. Maximum exposition time and intensity was used for the measurement. The data measured were considered of enough quality for publication.

Crystal data and structure refinement for **Ac-7e**. ***CCDC 2197380***

Identification code	cu_YBA203D1-c_0m
Empirical formula	C34 H32 N2 O8
Formula weight	596.61
Temperature	100(2)K
Wavelength	1.54178 Å
Crystal system	triclinic
Space group	P 1
Unit cell dimensions	a = 6.9484(2)Å a= 82.727(2)°. b = 7.1418(2)Å b = 86.432(2)°. c = 15.8024(5)Å g = 75.4121(19)°.
Volume	752.42(4) $Å^3$
Z	1
Density (calculated)	1.317 Mg/m^3
Absorption coefficient	0.778 mm^{-1}
F(000)	314
Crystal size	0.300 x 0.030 x 0.020 mm^3
Theta range for data collection	2.820 to 66.476°.
Index ranges	-8<=h<=8,-8<=k<=8,-16<=l<=18
Reflections collected	8999
Independent reflections	4737[R(int) = 0.0243]
Completeness to theta =66.476°	96.8%
Absorption correction	Multi-scan
Max. and min. transmission	0.75 and 0.52
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4737/ 150/ 469
Goodness-of-fit on F^2	1.046
Final R indices [I>2sigma(I)]	R1 = 0.0318, wR2 = 0.0823
R indices (all data)	R1 = 0.0356, wR2 = 0.0848
Flack parameter	x =-0.05(9)
Largest diff. peak and hole	0.116 and -0.193 e.$Å^{-3}$

Bond lengths [Å] and angles [°] for **Ac-7e**. ***CCDC 2197380***

Bond lengths----

O1	N1	1.229(3)
O2	N1	1.223(3)
O3	C7	1.206(3)
O4	C7	1.333(3)
O4	C8	1.450(3)
O5	C28	1.330(3)
O5	C27	1.461(3)
O6	C28	1.201(3)
O7	N2	1.223(3)
O8	N2	1.219(3)
N1	C1	1.473(3)
N2	C32	1.469(3)
C1	C2	1.386(4)
C1	C6	1.386(3)
C2	C3	1.380(4)
C2	H2	0.9500
C3	C4	1.402(3)
C3	H3	0.9500
C4	C5	1.388(4)
C4	C7	1.494(4)
C5	C6	1.382(4)
C5	H5	0.9500
C6	H6	0.9500

C8 C9 1.523(4)
C8 H8A 0.9900
C8 H8B 0.9900
C9 C10 1.510(3)
C9 C16 1.528(3)
C9 H9 1.0000
C10 C15 1.385(4)
C10 C11 1.393(3)
C11 C12 1.390(5)
C11 H11 0.9500
C12 C13 1.377(6)
C12 H12 0.9500
C13 C14 1.371(5)
C13 H13 0.9500
C14 C15 1.384(4)
C14 H14 0.9500
C15 H15 0.9500
C16 C17 1.528(4)
C16 H16A 0.9900
C16 H16B 0.9900
C17 C26 1.531(3)
C17 C18 1.563(4)
C17 C18' 1.586(10)
C17 H17 1.0000
C17 H17' 1.0000
C26 C27 1.487(4)
C26 H26A 0.9900
C26 H26B 0.9900
C27 H27A 0.9900
C27 H27B 0.9900
C28 C29 1.496(3)
C29 C30 1.392(4)
C29 C34 1.393(3)
C30 C31 1.382(3)
C30 H30 0.9500
C31 C32 1.386(3)
C31 H31 0.9500
C32 C33 1.383(4)
C33 C34 1.382(4)
C33 H33 0.9500
C34 H34 0.9500
C18 C19 1.532(5)
C18 H18A 0.9900
C18 H18B 0.9900
C19 C20 1.508(5)
C19 H19A 0.9900
C19 H19B 0.9900
C20 C25 1.386(6)
C20 C21 1.391(6)
C21 C22 1.394(8)
C21 H21 0.9500
C22 C23 1.379(7)
C22 H22 0.9500
C23 C24 1.370(7)
C23 H23 0.9500
C24 C25 1.391(7)
C24 H24 0.9500
C25 H25 0.9500
C18' C19' 1.541(10)
C18' H18C 0.9900
C18' H18D 0.9900

C19' C20' 1.508(10)
C19' H19C 0.9900
C19' H19D 0.9900
C20' C25' 1.379(11)
C20' C21' 1.391(11)
C21' C22' 1.397(13)
C21' H21' 0.9500
C22' C23' 1.377(12)
C22' H22' 0.9500
C23' C24' 1.369(12)
C23' H23' 0.9500
C24' C25' 1.393(12)
C24' H24' 0.9500
C25' H25' 0.9500

Angles
C7 O4 C8 117.3(2)
C28 O5 C27 114.90(19)
O2 N1 O1 123.8(2)
O2 N1 C1 118.4(2)
O1 N1 C1 117.8(2)
O8 N2 O7 123.6(2)
O8 N2 C32 118.7(2)
O7 N2 C32 117.8(2)
C2 C1 C6 122.9(2)
C2 C1 N1 118.8(2)
C6 C1 N1 118.4(2)
C3 C2 C1 118.2(2)
C3 C2 H2 120.9
C1 C2 H2 120.9
C2 C3 C4 120.0(2)
C2 C3 H3 120.0
C4 C3 H3 120.0
C5 C4 C3 120.4(2)
C5 C4 C7 117.9(2)
C3 C4 C7 121.8(2)
C6 C5 C4 120.1(2)
C6 C5 H5 119.9
C4 C5 H5 119.9
C5 C6 C1 118.3(2)
C5 C6 H6 120.8
C1 C6 H6 120.8
O3 C7 O4 124.0(2)
O3 C7 C4 124.2(2)
O4 C7 C4 111.8(2)
O4 C8 C9 106.59(19)
O4 C8 H8A 110.4
C9 C8 H8A 110.4
O4 C8 H8B 110.4
C9 C8 H8B 110.4
H8A C8 H8B 108.6
C10 C9 C8 109.8(2)
C10 C9 C16 114.1(2)
C8 C9 C16 109.4(2)
C10 C9 H9 107.8
C8 C9 H9 107.8
C16 C9 H9 107.8
C15 C10 C11 117.6(2)
C15 C10 C9 121.4(2)
C11 C10 C9 120.9(2)
C12 C11 C10 120.7(3)

C12 C11 H11 119.6
C10 C11 H11 119.6
C13 C12 C11 120.5(3)
C13 C12 H12 119.8
C11 C12 H12 119.8
C14 C13 C12 119.4(3)
C14 C13 H13 120.3
C12 C13 H13 120.3
C13 C14 C15 120.3(3)
C13 C14 H14 119.9
C15 C14 H14 119.9
C14 C15 C10 121.5(2)
C14 C15 H15 119.3
C10 C15 H15 119.3
C17 C16 C9 114.4(2)
C17 C16 H16A 108.7
C9 C16 H16A 108.7
C17 C16 H16B 108.7
C9 C16 H16B 108.7
H16A C16 H16B 107.6
C16 C17 C26 109.8(2)
C16 C17 C18 116.9(2)
C26 C17 C18 116.0(2)
C16 C17 C18' 99.0(4)
C26 C17 C18' 99.8(4)
C16 C17 H17 104.1
C26 C17 H17 104.1
C18 C17 H17 104.1
C16 C17 H17' 115.3
C26 C17 H17' 115.3
C18' C17 H17' 115.3
C27 C26 C17 112.2(2)
C27 C26 H26A 109.2
C17 C26 H26A 109.2
C27 C26 H26B 109.2
C17 C26 H26B 109.2
H26A C26 H26B 107.9
O5 C27 C26 108.65(19)
O5 C27 H27A 110.0
C26 C27 H27A 110.0
O5 C27 H27B 110.0
C26 C27 H27B 110.0
H27A C27 H27B 108.3
O6 C28 O5 123.7(2)
O6 C28 C29 123.2(2)
O5 C28 C29 113.12(19)
C30 C29 C34 120.3(2)
C30 C29 C28 117.0(2)
C34 C29 C28 122.7(2)
C31 C30 C29 120.5(2)
C31 C30 H30 119.7
C29 C30 H30 119.7
C30 C31 C32 117.8(2)
C30 C31 H31 121.1
C32 C31 H31 121.1
C33 C32 C31 123.0(2)
C33 C32 N2 118.7(2)
C31 C32 N2 118.3(2)
C34 C33 C32 118.4(2)
C34 C33 H33 120.8
C32 C33 H33 120.8

C33 C34 C29 119.9(2)
C33 C34 H34 120.0
C29 C34 H34 120.0
C19 C18 C17 112.9(3)
C19 C18 H18A 109.0
C17 C18 H18A 109.0
C19 C18 H18B 109.0
C17 C18 H18B 109.0
H18A C18 H18B 107.8
C20 C19 C18 112.0(3)
C20 C19 H19A 109.2
C18 C19 H19A 109.2
C20 C19 H19B 109.2
C18 C19 H19B 109.2
H19A C19 H19B 107.9
C25 C20 C21 118.1(4)
C25 C20 C19 120.3(4)
C21 C20 C19 121.6(4)
C20 C21 C22 120.9(5)
C20 C21 H21 119.6
C22 C21 H21 119.6
C23 C22 C21 119.7(6)
C23 C22 H22 120.1
C21 C22 H22 120.1
C24 C23 C22 120.1(5)
C24 C23 H23 120.0
C22 C23 H23 120.0
C23 C24 C25 120.2(6)
C23 C24 H24 119.9
C25 C24 H24 119.9
C20 C25 C24 120.9(5)
C20 C25 H25 119.5
C24 C25 H25 119.5
C19' C18' C17 106.2(7)
C19' C18' H18C 110.5
C17 C18' H18C 110.5
C19' C18' H18D 110.5
C17 C18' H18D 110.5
H18C C18' H18D 108.7
C20' C19' C18' 112.9(8)
C20' C19' H19C 109.0
C18' C19' H19C 109.0
C20' C19' H19D 109.0
C18' C19' H19D 109.0
H19C C19' H19D 107.8
C25' C20' C21' 118.6(9)
C25' C20' C19' 120.7(9)
C21' C20' C19' 120.6(9)
C20' C21' C22' 120.9(11)
C20' C21' H21' 119.6
C22' C21' H21' 119.6
C23' C22' C21' 119.0(12)
C23' C22' H22' 120.5
C21' C22' H22' 120.5
C24' C23' C22' 120.7(11)
C24' C23' H23' 119.7
C22' C23' H23' 119.7
C23' C24' C25' 119.9(13)
C23' C24' H24' 120.1
C25' C24' H24' 120.1
C20' C25' C24' 120.7(11)

C20'	C25'	H25'	119.7
C24'	C25'	H25'	119.7

Torsion angles [°] for **Ac-7e**. ***CCDC 2197380***

O2	N1	C1	C2	-0.5(3)
O1	N1	C1	C2	179.3(2)
O2	N1	C1	C6	-179.6(2)
O1	N1	C1	C6	0.2(3)
C6	C1	C2	C3	0.6(3)
N1	C1	C2	C3	-178.5(2)
C1	C2	C3	C4	0.0(4)
C2	C3	C4	C5	-0.7(4)
C2	C3	C4	C7	-179.6(2)
C3	C4	C5	C6	0.9(3)
C7	C4	C5	C6	179.8(2)
C4	C5	C6	C1	-0.3(3)
C2	C1	C6	C5	-0.4(3)
N1	C1	C6	C5	178.7(2)
C8	O4	C7	O3	-0.8(4)
C8	O4	C7	C4	178.87(19)
C5	C4	C7	O3	-10.5(4)
C3	C4	C7	O3	168.4(2)
C5	C4	C7	O4	169.8(2)
C3	C4	C7	O4	-11.3(3)
C7	O4	C8	C9	-159.8(2)
O4	C8	C9	C10	58.7(3)
O4	C8	C9	C16	-175.5(2)
C8	C9	C10	C15	65.6(3)
C16	C9	C10	C15	-57.6(3)
C8	C9	C10	C11	-109.8(3)
C16	C9	C10	C11	127.0(3)
C15	C10	C11	C12	-1.3(4)
C9	C10	C11	C12	174.3(3)
C10	C11	C12	C13	-0.8(5)
C11	C12	C13	C14	1.8(5)
C12	C13	C14	C15	-0.8(5)
C13	C14	C15	C10	-1.2(4)
C11	C10	C15	C14	2.3(4)
C9	C10	C15	C14	-173.2(2)
C10	C9	C16	C17	-57.1(3)
C8	C9	C16	C17	179.5(2)
C9	C16	C17	C26	177.9(2)
C9	C16	C17	C18	-47.3(3)
C9	C16	C17	C18'	-78.2(4)
C16	C17	C26	C27	-174.9(2)
C18	C17	C26	C27	49.8(3)
C18'	C17	C26	C27	81.7(4)
C28	O5	C27	C26	169.3(2)
C17	C26	C27	O5	172.3(2)
C27	O5	C28	O6	-0.2(4)
C27	O5	C28	C29	-178.8(2)
O6	C28	C29	C30	0.3(3)
O5	C28	C29	C30	179.0(2)
O6	C28	C29	C34	-178.1(2)
O5	C28	C29	C34	0.5(3)
C34	C29	C30	C31	0.6(3)
C28	C29	C30	C31	-177.9(2)
C29	C30	C31	C32	-0.6(3)
C30	C31	C32	C33	0.3(3)
C30	C31	C32	N2	-178.66(19)

O8	N2	C32	C33	2.5(3)
O7	N2	C32	C33	-176.2(2)
O8	N2	C32	C31	-178.5(2)
O7	N2	C32	C31	2.8(3)
C31	C32	C33	C34	0.0(4)
N2	C32	C33	C34	178.9(2)
C32	C33	C34	C29	0.1(3)
C30	C29	C34	C33	-0.4(3)
C28	C29	C34	C33	178.0(2)
C16	C17	C18	C19	-62.6(3)
C26	C17	C18	C19	69.5(3)
C17	C18	C19	C20	-176.2(3)
C18	C19	C20	C25	84.2(5)
C18	C19	C20	C21	-94.2(5)
C25	C20	C21	C22	1.3(9)
C19	C20	C21	C22	179.7(7)
C20	C21	C22	C23	0.1(14)
C21	C22	C23	C24	-2.0(14)
C22	C23	C24	C25	2.6(13)
C21	C20	C25	C24	-0.7(9)
C19	C20	C25	C24	-179.1(7)
C23	C24	C25	C20	-1.2(12)
C16	C17	C18'	C19'	129.9(6)
C26	C17	C18'	C19'	-118.0(6)
C17	C18'	C19'	C20'	175.7(7)
C18'	C19'	C20'	C25'	-92.9(14)
C18'	C19'	C20'	C21'	89.0(14)
C25'	C20'	C21'	C22'	1(3)
C19'	C20'	C21'	C22'	179(2)
C20'	C21'	C22'	C23'	-3(4)
C21'	C22'	C23'	C24'	5(4)
C22'	C23'	C24'	C25'	-6(4)
C21'	C20'	C25'	C24'	-2(3)
C19'	C20'	C25'	C24'	-179.8(19)
C23'	C24'	C25'	C20'	4(4)

Symetry operations

1	'x, y, z'

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