

Supplementary Information

Biocatalytic enantioselective formation and ring-opening of oxetanes

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1. Materials and methods

General.

¹H-NMR (400 MHz) and ¹³C-NMR (100 MHz) were recorded on Agilent Technologies 400 MR. Chemical shifts were reported in parts per million (ppm) relative to residual signals of the solvent. The following abbreviations are used to indicate multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double of doublets, td = triple of doublets, tt = triple of triplets, dt = double of triplets, ddd = double of double of doublets. High-resolution mass spectra (HRMS) was recorded by ESI ionization sources. Flash column chromatography was carried out with 200-400 mesh silica gel. Melting point was uncorrected.

Chemicals (*rac*)-**1a**, (*R*)-**1a**, (*S*)-**1a**, (*rac*)-**1f**, (*rac*)-**1da**, and (*rac*)-**1ea** were obtained from commercial suppliers. Other racemic γ -haloalcohols (*rac*)-**a**, oxetanes (*rac*)-**b**, γ -azidoalcohols (*rac*)-**c**, γ -cyanohydrin (*rac*)-**1d**, and γ -nitroalcohol **1e** were obtained by chemical synthesis. Isopropyl- β -D-thiogalactopyranoside (IPTG) and kanamycin sulfate (Kan) were purchased from Solarbio (Beijing, China). PrimeSTAR DNA polymerase and *DpnI* endonuclease were purchased from Takara. Cells were grown using or terrific broth (TB) medium. Phosphate buffer (PB, KH₂PO₄-Na₂HPO₄) was used as a buffering system for whole cell biotransformations, unless otherwise specified. Unless otherwise noted, all the other reagents and solvents were purchased from commercial sources and used as such without further purification.

Safety concerning statements

Organic azides are potentially explosive substances that can decompose with minimal energy input from external sources. When preparing and using organic azides, we diligently apply a specific calculation to account for all nitrogen atoms in the compound, not just those in the azido group. Handling both organic azides and sodium azide with care is essential. We have implemented strict safety protocols and have not experienced any safety incidents during these experiments.

$$\frac{n(C)+n(O)}{n(N)} \geq 3, \text{ n signifies the number of atoms.}$$

Chromatography.

The enantiomeric excess (*ee*) values of chiral compounds and analytic yields were determined by chiral HPLC or GC analysis. The chiral HPLC was performed on Shimadzu LC-20A, equipped with Chiralcel AD-H chiral column (4.6 mm Φ $\times$ 250 mmL, particle size 5 μ m), Chiralcel OJ-H

chiral column (4.6 mm Φ $\times$ 250 mmL, particle size 5 μ m), Chiralpak OB-H chiral column (4.6 mm Φ $\times$ 250 mmL, particle size 5 μ m), Chiralcel OD-H chiral column (4.6 mm Φ $\times$ 250 mmL, particle size 5 μ m), Chiralcel OX-3 chiral column (4.6 mm Φ $\times$ 250 mmL, particle size 3 μ m), Chiralcel IA-3 chiral column (4.6 mm Φ $\times$ 250 mmL, particle size 3 μ m), Chiralcel IH chiral column (4.6 mm Φ $\times$ 250 mmL, particle size 5 μ m), Chiralcel IC-3 chiral column (4.6 mm Φ $\times$ 250 mmL, particle size 3 μ m). Chiral GC analysis was performed on Agilent 7890B gas chromatograph equipped with a flame ionization detector (FID) using Rt-bDEXcst column or CYCLODEX-B column with nitrogen as the carrier gas.

Preparation and screening of HHDH.

The recombinant *E. coli* (HHDH) strains were constructed to express the corresponding halohydrin dehalogenase (HHDH) genes, which have been preserved in our laboratory^{1,2}. All variants described in this paper were cloned and expressed using plasmid pET-28b(+) as the vector and *Escherichia coli* BL21 (DE3) as the host. *E. coli* (HHDH) cells were cultured in TB medium containing 50 μ g/mL kanamycin at 37 $^{\circ}$ C until the optical density at 600 nm (OD₆₀₀) reached a range of 0.6-0.8. IPTG was then added to a final concentration of 0.2 mM to induce enzyme expression. The culture was then further incubated at 28 $^{\circ}$ C for an additional 12-14 h. Recombinant *E. coli* (HHDH) cells expressing the target HHDH were harvested by centrifugation at 8800 $\times$ g for 3 min at 4 $^{\circ}$ C. The collected cell pellet was resuspended in phosphate buffer (PB, KH₂PO₄-Na₂HPO₄) to reach the desired cell density for the biotransformation reactions. The model dehalogenation reaction was carried out with 10 mM (*rac*)-**1a** and 10 g dcw/L (about OD₆₀₀= 20) *E. coli* (HHDH) cells in 5 mL PB buffer (50 mM, pH 8.5) at 30 $^{\circ}$ C for 8 h. The model ring-opening reaction was carried out with 10 mM (*rac*)-**1b**, 10 mM NaN₃ and 10 g dcw/L (about OD₆₀₀= 20) *E. coli* (HHDH) cells in 5 mL PB buffer (50 mM, pH 7.5) at 30 $^{\circ}$ C for 10 h. After the reactions were completed, the reaction mixtures were extracted using 5 mL of ethyl acetate. The organic phases were separated, dried over anhydrous Na₂SO₄, and analyzed by chiral HPLC. Chiral analysis of **1a**: Chiralpak OX-3, *n*-hexane/*i*PrOH = 99/1, flow rate = 0.5 mL/min, λ = 210 nm, $t_{(S)-1a}$ = 44.8 min, $t_{(R)-1a}$ = 48.7 min. Chiral analysis of **1b** and **1c**: Chiralpak OX-3, *n*-hexane/*i*PrOH = 97/3, flow rate = 0.7 mL/min, λ = 210 nm, $t_{(S)-1b}$ = 10.1 min, $t_{(R)-1b}$ = 11.3 min; $t_{(S)-1c}$ = 15.3 min, $t_{(R)-1c}$ = 16.6 min.

Docking study.

The predicted structure model (AFDB code: AF-N6YXW4-F1) of the wild type HheD8 (HheD8-WT) was obtained AlphaFold Protein Structure Database (<https://alphafold.ebi.ac.uk>). Docking studies of (*R*)-**1b** in the active site of enzyme HheD8-WT/AF model was carried out using AutoDock 4.0 software³. The docking study was performed using “Genetic Algorithm” search parameters and default docking parameters. The possible docking pose with hydrogen bonds between oxetane ring of substrate (*R*)-**1b** and S117-OH, Y130-OH was chosen for further analysis with the PyMOL software⁴. Residues F19, A69, Y168, M124, R127, Q160, N161 and R182 were identified as hot-spots for site saturation mutagenesis study. In addition, the docking of (*R*)-**1b** in the crystal structure of the mutant HheD8-M3 was performed using analogous methods.

Directed evolution of HheD8.

Mutagenesis and cultivation: Site-saturation mutagenesis experiments of HheD8-WT were carried out using QuickChange PCR methods with degenerate codons. The resulting PCR products were purified, digested with *DpnI* and directly transformed into *E. coli* BL21(DE3) competent cells via the heat-shock method. Single colonies of *E. coli* cells were picked and cultured in 2-mL 96-deep-well plates containing TB-Kan medium (300 μ L per well, 50 μ g/mL kanamycin) at 37°C for 5 h. Subsequently, 900 μ L of TB-Kan medium with IPTG (to achieve a final concentration of 0.2 mM) was added to each well, and the plates were shaken at 28°C and 900 rpm for 12 h. Induced cells were harvested by centrifugation at $1600 \times g$ for 15 min at 4 °C and subsequently utilized for biotransformations.

Screening for dehalogenation reaction: To resuspend the *E. coli* (HheD8) cells, 500 μ L of PB buffer (50 mM, pH 8.5) containing 10 mM (*rac*)-**1a** was added. The plates containing the cell and substrate suspensions were shaken at 30 °C and 900 rpm for 8 h. After completion of the incubation, the reaction mixtures were extracted using 700 μ L of ethyl acetate. The organic phases were separated, dried over anhydrous Na₂SO₄, and analyzed by chiral HPLC.

Screening for ring-opening reaction: To resuspend the *E. coli* (HheD8) cells, 500 μ L of PB buffer (50 mM, pH 7.5) containing 10 mM (*rac*)-**1b** and 10 mM NaN₃ were added. The plates containing the cell and substrate suspensions were shaken at 30 °C and 900 rpm for 10 h. After completion of the incubation, the reaction mixtures were extracted using 700 μ L of ethyl acetate. The organic phases were separated, dried over anhydrous Na₂SO₄, and analyzed by chiral HPLC.

The mutants demonstrating improved catalytic activity and/or enantioselectivity were further verified using 5 mL biotransformation reactions, followed by preservation and gene sequencing analysis. The reaction conditions were consistent with those described for the earlier enzyme screening reactions.

The site-directed mutagenesis study focused on the catalytic triad S117-Y130-R134 of HheD8-M3, and the site-saturation mutagenesis study of HheD8-M4 for the reversal of enantioselectivity were conducted using analogous procedures.

Primers for site-saturation mutagenesis used in this work

Mutation site	Primer	Primer sequence
F19	F19-F	5'-GGCAGATGCANNKATGGGTCCTGCAC-3'
	F19-R	5'-CAGGACCCATMNNNTGCATCTGCCTGG-3'
A69	A69-F	5'-CTGGCAATTCCGNNKCCGAGCACACCG-3'
	A69-R	5'-ACCGGTGTGCTCGGMNNCGGAATTGCC-3'
M124 for M2	M124-M2-F	5'-CAGCAGCACTGCGTGGTNNKGCACTGCTGAGCAGC-3'
	M124-M2-R	5'-CTGCTCAGCAGTGCMNNACCACGCAGTGCTGCTGC-3'
M124 for M5	M124-M5-F	5'-CAGCAGCACTGCGTGGTNNKGCACTGGGGAGCAGC-3'
	M124-M5-R	5'-CTGCTCCCCAGTGCMNNACCACGCAGTGCTGCTGC-3'
R127	R127-F	5'-GGTATGGCACTGNNKAGCAGCTATGCAG-3'
	R127-R	5'-GCTGCATAGCTGCTMNNCAGTGCCATAC-3'
Q160	Q160-F	5'-GGTTAATGCAATTGCCNNKAATTTTGTGAAAACC-3'
	Q160-R	5'-GGGTTTTCAACAAAATTMNNNGGCAATTGCATTAAC-3'
N161	N161-F	5'-GCAATTGCCCAGNNKTTTGTGAAAAC-3'
	N161-R	5'-GGTTTTCAACAAAMNNCTGGGCAATTG-3'
Y168	Y168-F	5'-TTGAAAACCCGACCNNKTTTCCGCCAG-3'
	Y168-R	5'-TGAATTCTGGCGGAAAMNNGGTCGGG-3'
R182	R182-F	5'-CGGCATTTAAGATNNKCTGAAATGGCAGG-3'
	R182-R	5'-CCTGCCATTTTCAGMNNATCTTTAAATGCCGG-3'
A119	A119-F	5'-GGTAGCGCANNKGCACTGCGTG-3'
	A119-R	5'-ACGCAGTGCMNNNTGCGCTACCC-3'
G127 for M9	G127-F	5'-GGTCCGGCACTGMNNAGCAGCTATGCAG-3'
	G127-R	5'-GCTGCATAGCTGCTNNKCAGTGCCGGAC-3'
P124 for M10	P124-F	5'-GCACTGCGTGGTNNKGCACTGACTAGC-3'
	P124-R	5'-TGCTAGTCAGTGCMNNACCACGCAGTG-3'
S71	S71-F	5'-ATTCCGAATCCGNNKACACCGGTTTCATC-3'
	S71-R	5'-GAACCGGTGTMNNCGGATTCGGAATTGCC-3'

Enzyme expression and purification.

To purify the HheD8-M3 mutant, we introduced a 6×His tag at its *N*-terminus to construct the recombinant strain *E. coli* (HheD8-M3-His). A single colony from this strain was used to inoculate 100 mL of LB medium supplemented with 50 µg/mL kanamycin. The culture was incubated overnight at 37 °C and 220 rpm. Subsequently, 4 liters of LB medium, also containing 50 µg/mL kanamycin, were inoculated with a 1:100 dilution of the overnight culture. This larger culture was then incubated at 37 °C and 220 rpm until the OD₆₀₀ reached approximately 0.8 (3-5 h). To induce the expression of the recombinant protein, IPTG was added to the culture to achieve a final concentration of 0.5 mM, followed by further incubation at 16 °C and 220 rpm for another overnight. The cells were pelleted by centrifugation (8800×g, at 4 °C for 4 min), resuspended in lysis buffer A (25 mM Tris, pH 8.0, 350 mM NaCl), and lysed by sonication. Cell debris was removed by centrifugation (11000×g and 4 °C for 15 min) to obtain a clarified supernatant. The resulting supernatant harboring HheD8-M3 with *N*-terminal 6×His-tag was subsequently loaded onto a Ni-NTA affinity column (GE Healthcare) that had been pre-equilibrated with buffer A. To remove nonspecifically bound proteins, the column was washed with 20 column volumes of buffer B (25 mM Tris, 350 mM NaCl, 20 mM imidazole, pH 8.0). The bound target protein was then eluted using elution buffer C (25 mM Tris, 300 mM NaCl, 200 mM imidazole, pH 8.0) and the eluate was collected. The fractions were pooled and subsequently concentrated using a 10 kDa ultrafiltration cube (Amicon® Ultra-15, Millipore). The concentrated protein sample was filtered through a 0.2 µm filter and further purified with an anion exchange Q Sepharose column (HiTrap Q HP, GE Healthcare) eluting with buffer D (10 mM Tris, pH 8.0, 500 mM NaCl, 1 mM DTT) at a flow rate of 1 mL/min. Protein-containing fractions were collected and then concentrated to a final concentration of 20 mg/mL, in preparation for the subsequent crystallization experiments.

Crystallization and structure determination.

The crystallization experiment for HheD8-M3 was conducted at 18 °C using 96-well sitting-drop vapor diffusion plates in combination with commercial crystallization screen kits. In general, each drop was set up with 100 nL of the protein sample at a concentration of either 10 or 20 mg/mL, mixed with 100 nL of crystallization reagent, and the mixture was then equilibrated against 100 µL of reservoir solution. Crystals of HheD8-M3 were successfully grown in conditions containing 1.8 M ammonium sulfate. The crystals were rapidly soaked in the reservoir solution containing

20% (v/v) glycerol as cryo-protectant, mounted on loops, and flash-cooled at 100 K in a nitrogen gas cryo-stream. Crystal diffraction data were collected from a single crystal at the Shanghai Synchrotron Radiation Facility (SSRF, Shanghai, China) in BL02U beamline with a wavelength of 0.9791 Å at 100 K. The diffraction data obtained from the HheD8-M3 crystals were processed and scaled using the X-ray Diffraction Software (XDS) ⁵. The structure of HheD8-M3 was then solved by the molecular replacement method using the predicted HheD8 structure (with an accession number AF-N6YXW4-F1 from the AlphaFold Protein Structure Database, <https://alphafold.ebi.ac.uk>) as the initial search model⁶. The initial model was built using PHENIX autobuild ⁷, and manual adjustment of the model was carried out using the program COOT⁸. Afterward, the models were refined by PHENIX refinement⁷ and Refmac5⁹. Finally, the stereochemical quality of the refined structure was checked using¹⁰. The final validation of the HheD8-M3/Cl⁻ crystal structure was performed with Protein Data Bank ADIT Servers. The Ramachandran plot for HheD8-M3/Cl⁻ showed 95.51% of residues to be situated in the most favoured regions, 4.09% in additional allowed and 0.00% residues in outlier regions. Diffraction data and coordinates were deposited in the Protein Data Bank (PDB) with the accession number 8XXB (2.40 Å). All crystallographic figures were prepared using the PyMOL molecular graphics software package (Schrodinger, LLC)¹¹.

Kinetic measurements

To purify the HheD8-WT and mutants (M1, M3, M5, and M6), we introduced a 6×His tag at its *N*-terminus to these enzymes. The corresponding strains were cultured to purify the enzymes according to the analogous methods mentioned above. Kinetic parameters of HheD8-WT, M1, M3, M5, and M6 for the ring-opening of (*rac*)-**1b** were determined in PB buffer (200 mM, pH 7.5) at 30°C using purified enzymes. The reaction system is 800 µL, and the reaction was initiated by the addition of 20 mM NaN₃ and 10-20 µL of enzyme by varying the concentration of the substrate (*rac*)-**1b** (0.2-20 mM). Reaction samples in each moment were taken, extracted using 800 µL of ethyl acetate, and analyzed by chiral HPLC. Conversions were calculated from the *ee* values of the substrates and products, which were then used to determine reaction rates. Kinetic data were fitted with the Michaelis-Menten equation using the Origin software program to obtain the kinetic parameters. The enzyme concentrations were measured by BCA protein assay kit (Beyotime, China). All *k*_{cat} values are defined as per monomer.

Molecular dynamics simulations

Molecular dynamics (MD) simulations were performed using the GPU code (pmemd) of the AMBER 22 package¹². The restrained electrostatic potential (RESP) charges for substrates (*R*)-**1b** were calculated at the HF/6-31G(d) level¹³ using the Gaussian 16(C.01)¹⁴. The protonation states of enzymes' residues were determined using the H++ server (<http://biophysics.cs.vt.edu/H++>)¹⁵. The general AMBER force field (GAFF)¹⁶ and Amber 99 force field (ff99SBildn)¹⁷ were employed for the substrates and the proteins, respectively. Each enzyme was immersed in a pre-equilibrated truncated hexagonal box with a 10 Å buffer of TIP3P¹⁸ water molecules using the leap module, resulting in approximately 9,000 solvent molecules surrounding the enzyme. The systems were neutralized by addition of ions Na⁺ and Cl⁻. Then, two-stage geometry minimization was performed before the MD simulation. The first stage minimizes water molecules and ions imposing positional restraints on the solute with a force constant of 500 kcal/mol·Å², and the second stage minimizes the whole system. The systems were gently heated from 0 to 300 K under the NVT ensemble using six 50 ps steps, incrementing the temperature by 50 K for each step with a weak restraint of 10 kcal/mol·Å² and an 8 Å cutoff. The time step was kept at 1 fs during the heating stages. Each system was then equilibrated for 2 ns with a 2 fs time step under the NPT ensemble. Production trajectories were then run for an additional 150 ns in duplicate under the same simulation conditions.

2. Supplementary Tables 1-13

Supplementary Table 1. Recombinant *E. coli* (HHDH) strains used in this study.

HHDHs	Source	Accession	Identified in Ref.
HheA2	<i>Arthrobacter</i> sp. AD2	AAK92100	19
HheA5	<i>Tistrella mobilis</i> KA081020-065	WP_014743557	20
HheA8	alpha proteobacterium Mf 1.05b.01	WP_051402546	21
HheA10	<i>Tsukamurella</i> sp. 1534	WP_019201195	21
HheA11	<i>Reyranella massiliensis</i> 521	WP_020698933	21
HheA13	<i>Pseudomonas</i> sp. G5(2012)	WP_042955870	21
HheB3	marine metagenome	EBL02020	20
HheB4	marine metagenome	EBP61646	20
HheB6	marine metagenome	EDB56284	20
HheC	<i>Agrobacterium tumefaciens</i> AD1	AAK92099	19
HheD	<i>Dechloromonas aromatica</i> RCB	WP_011285856	20
HheD2	gamma proteobacterium HTCC2207	WP_007233072	20
HheD6	<i>Marinobacter nanhaiticus</i> D15-8W	WP_004579485	21
HheD7	<i>Thauera</i> sp. 27	WP_002926105	21
HheD8	<i>Thauera aminoaromatica</i> S2	WP_004302136	21
HheD14	<i>Gammaproteobacteria</i> bacterium MOLA455	WP_035490777	21
HheD15	<i>Candidatus Competibacter denitrificans</i> Run_A_D11	WP_048670059	21
HheD16	<i>Methylibium</i> sp. T29	WP_036236554	21
HheE	marine metagenome	EBP63112	20
HheE5	marine metagenome	WP_009577001	20
HheF	uncultured bacterium	BAH89601	20
HheG	<i>Ilumatobacter coccineus</i> YM16-304	WP_015443096	20
HheG2	<i>Ilumatobacter nonamiensis</i> YM16-303	WP_040495182	21
HHDHn1	<i>Rhodobiaceae</i> bacterium	PCJ71437.1	22
HHDHn2	<i>Alphaproteobacteria</i> bacterium HGW-Alphaproteobacteria-3	YJ5359PY013	22
HHDHn3	<i>Alphaproteobacteria</i> bacterium 46_93_T64	OUR79898	22
HHDHn4	<i>Reyranella massiliensis</i>	WP_020698933.1	22
HHDHn5	<i>Alphaproteobacteria</i> bacterium 65-37	OJU34764.1	22
HHDHn6	<i>Rhodospirillales</i> bacterium URHD0017	WP_092824593.1	22
HHDHn7	<i>Alphaproteobacteria</i> bacterium RIFCSPHIGHO2_12_FULL_66_14	OFW98094.1	22
HHDHn8	<i>Enhydrobacter aerosaccus</i>	WP_085934632.1	22
HHDHn9	<i>Rhodospirillaceae</i> bacterium TMED8	OUT52242.1	22
HHDHn10	<i>Rhodomicrobium</i>	WP_088343515.1	22
HHDHn11	<i>Aurantiochytrium</i> sp. FCC1311	GBG24028.1	22
HHDHamb	<i>Acidimicrobiia</i> bacterium	MSO17354.1	23
HHDHapb	<i>Alphaproteobacteria</i> bacterium 32-64-14	OYX46376.1	23
HHDHabb	<i>Actinobacteria</i> bacterium IMCC26256	AKL74579.1	23
HHDHnsr	<i>Novosphingobium resinovorum</i>	WP_069709913.1	23

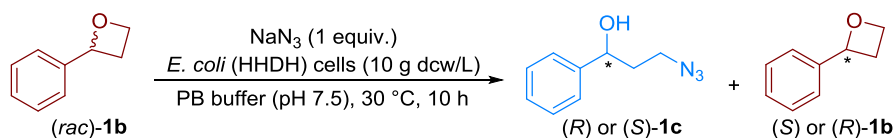
Supplementary Table 2. Screening of HDDHs for the dehalogenation reaction of (*rac*)-1a.^a

(*rac*)-1a $\xrightarrow[\text{PB buffer (pH 8.5), 30 }^{\circ}\text{C, 8 h}]{E. coli \text{ (HDDH) cells (10 g dcw/L)}}$ (*R*) or (*S*)-1b + (*S*) or (*R*)-1a

entry	biocatalyst	yield 1b (%) ^b	<i>ee</i> 1b (%) ^b	<i>ee</i> 1a (%) ^b	<i>E</i> ^c
1	-	NR	ND	<5	ND
2	<i>E. coli</i>	NR	ND	<5	ND
3	<i>E. coli</i> (HheA2)	NR	ND	<5	ND
4	<i>E. coli</i> (HheA5)	14	97 (<i>R</i>)	15 (<i>S</i>)	76
5	<i>E. coli</i> (HheA8)	trace	>99 (<i>R</i>)	<5	ND
6	<i>E. coli</i> (HheA10)	NR	ND	<5	ND
7	<i>E. coli</i> (HheA11)	NR	ND	<5	ND
8	<i>E. coli</i> (HheA13)	NR	ND	<5	ND
9	<i>E. coli</i> (HheB3)	trace	>99 (<i>R</i>)	<5	ND
10	<i>E. coli</i> (HheB4)	trace	>99 (<i>R</i>)	<5	ND
11	<i>E. coli</i> (HheB6)	9	89 (<i>R</i>)	8 (<i>S</i>)	18
12	<i>E. coli</i> (HheC)	26	86 (<i>S</i>)	38 (<i>R</i>)	19
13	<i>E. coli</i> (HheD)	7	35 (<i>R</i>)	<5	ND
14	<i>E. coli</i> (HheD2)	17	33 (<i>R</i>)	7 (<i>S</i>)	2
15	<i>E. coli</i> (HheD6)	29	38 (<i>R</i>)	17 (<i>S</i>)	3
16	<i>E. coli</i> (HheD7)	6	14 (<i>S</i>)	<5	ND
17	<i>E. coli</i> (HheD8)	19	83 (<i>R</i>)	21 (<i>S</i>)	13
18	<i>E. coli</i> (HheD14)	14	31 (<i>R</i>)	<5	ND
19	<i>E. coli</i> (HheD15)	29	30 (<i>R</i>)	13 (<i>S</i>)	2
20	<i>E. coli</i> (HheD16)	29	53 (<i>R</i>)	23 (<i>S</i>)	4
21	<i>E. coli</i> (HheE)	trace	90 (<i>R</i>)	<5	ND
22	<i>E. coli</i> (HheE5)	6	86 (<i>R</i>)	<5	ND
23	<i>E. coli</i> (HheF)	NR	ND	<5	ND
24	<i>E. coli</i> (HheG)	NR	ND	<5	ND
25	<i>E. coli</i> (HheG2)	NR	ND	<5	ND
26	<i>E. coli</i> (HDDHn1)	trace	98 (<i>R</i>)	<5	ND
27	<i>E. coli</i> (HDDHn2)	NR	ND	<5	ND
28	<i>E. coli</i> (HDDHn3)	trace	44 (<i>R</i>)	<5	ND
29	<i>E. coli</i> (HDDHn4)	trace	87 (<i>R</i>)	<5	ND
30	<i>E. coli</i> (HDDHn5)	trace	78 (<i>R</i>)	<5	ND
31	<i>E. coli</i> (HDDHn6)	trace	55 (<i>R</i>)	<5	ND
32	<i>E. coli</i> (HDDHn7)	trace	92 (<i>R</i>)	<5	ND
33	<i>E. coli</i> (HDDHn8)	trace	93 (<i>R</i>)	<5	ND
34	<i>E. coli</i> (HDDHn9)	NR	ND	<5	ND
35	<i>E. coli</i> (HDDHn10)	NR	ND	<5	ND
36	<i>E. coli</i> (HDDHn11)	NR	ND	<5	ND
37	<i>E. coli</i> ((HDDHamb)	NR	ND	<5	ND
38	<i>E. coli</i> (HDDHapb)	8	68 (<i>R</i>)	<5	ND
39	<i>E. coli</i> (HDDHabb)	NR	ND	<5	ND
40	<i>E. coli</i> (HDDHnsr)	NR	ND	<5	ND

^aThe reactions were carried out in triplicate with 10 mM (*rac*)-1a and 10 g dcw/L *E. coli* (HDDH) cells in 5 mL PB buffer (50 mM, pH 8.5) at 30 °C for 8 h. ^bThe yields and *ee* values were determined by chiral HPLC. ^cCalculated enantioselectivity: $E = \ln[(1-ee_{1a})/(1+ee_{1a}/ee_{1b})]/\ln[(1+ee_{1a})/(1+ee_{1a}/ee_{1b})]$. NR= no reaction. ND= not detected. The e.e. values and yields were calculated from the average of triplicate experiments ($n = 3$). Data are presented as mean values.

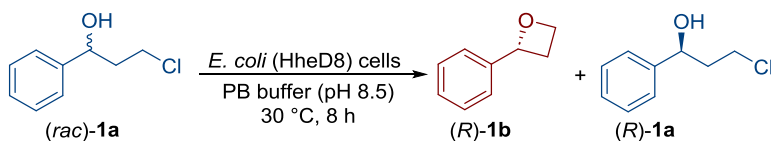
Supplementary Table 3. Screening of HDDHs for the ring-opening reaction of (*rac*)-1b.



entry	biocatalyst	yield 1c (%) ^b	ee 1c (%) ^b	ee 1b (%) ^b	<i>E</i> ^c
1	-	NR	ND	<5	ND
2	<i>E. coli</i>	NR	ND	<5	ND
3	<i>E. coli</i> (HheA5)	trace	<5	<5	ND
4	<i>E. coli</i> (HheA8)	trace	25 (<i>R</i>)	<5	ND
5	<i>E. coli</i> (HheB3)	trace	55 (<i>R</i>)	<5	ND
6	<i>E. coli</i> (HheB4)	trace	57 (<i>R</i>)	<5	ND
7	<i>E. coli</i> (HheB6)	trace	56 (<i>R</i>)	<5	ND
8	<i>E. coli</i> (HheC)	trace	>99 (<i>S</i>)	<5	ND
9	<i>E. coli</i> (HheD)	6	31 (<i>R</i>)	<5	ND
10	<i>E. coli</i> (HheD2)	trace	<5	<5	ND
11	<i>E. coli</i> (HheD6)	trace	16 (<i>R</i>)	<5	ND
12	<i>E. coli</i> (HheD7)	5	18 (<i>S</i>)	<5	ND
13	<i>E. coli</i> (HheD8)	18	74 (<i>R</i>)	18 (<i>S</i>)	8
14	<i>E. coli</i> (HheD14)	trace	6 (<i>R</i>)	<5	ND
15	<i>E. coli</i> (HheD15)	7	24 (<i>R</i>)	<5	ND
16	<i>E. coli</i> (HheD16)	trace	37 (<i>R</i>)	<5	ND
17	<i>E. coli</i> (HheE)	trace	46 (<i>R</i>)	<5	ND
18	<i>E. coli</i> (HheE5)	trace	45 (<i>R</i>)	<5	ND
19	<i>E. coli</i> (HDDHn1)	trace	29 (<i>S</i>)	<5	ND
20	<i>E. coli</i> (HDDHn3)	trace	49 (<i>S</i>)	<5	ND
21	<i>E. coli</i> (HDDHn4)	trace	45 (<i>R</i>)	<5	ND
22	<i>E. coli</i> (HDDHn5)	trace	41 (<i>R</i>)	<5	ND
23	<i>E. coli</i> (HDDHn6)	trace	34 (<i>R</i>)	<5	ND
24	<i>E. coli</i> (HDDHn7)	trace	<5	<5	ND
25	<i>E. coli</i> (HDDHn8)	trace	69 (<i>R</i>)	<5	ND
26	<i>E. coli</i> (HDDHapb)	trace	11 (<i>R</i>)	<5	ND

^aThe reactions were carried out in triplicate with 10 mM (*rac*)-1b, 10 mM NaN₃ and 10 g dcw/L *E. coli* (HDDH) cells in 5 mL PB buffer (50 mM, pH 7.5) at 30 °C for 10 h. ^bThe yields and *ee* values were determined by chiral HPLC. ^cCalculated enantioselectivity: $E = \ln[(1-ee_{1b})/(1+ee_{1b}/ee_{1c})]/\ln[(1+ee_{1b})/(1+ee_{1b}/ee_{1c})]$. NR= no reaction. ND= not detected. The e.e. values and yields were calculated from the average of triplicate experiments (*n* = 3). Data are presented as mean values.

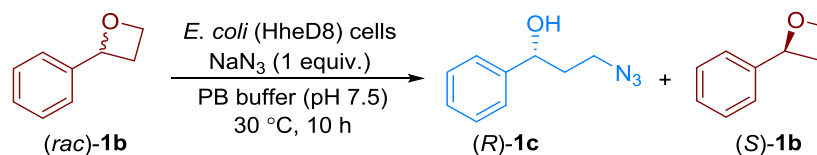
Supplementary Table 4. Directed evolution of HheD8 for enantioselective dehalogenation of γ -haloalcohol (*rac*)-1a**.^a**



entry	HheD8	mutation	conc. 1a (mM)	<i>ee</i> (<i>R</i>)- 1b (%) ^b	<i>ee</i> (<i>S</i>)- 1a (%) ^b	conv. 1a (%) ^c	<i>E</i> ^d
1	WT	none	10	82	21	20.06±0.13	12
2	M1	A69F	10	98	22	18.47±0.05	123
3	M2	A69F/ <u>R127G</u>	10	98	54	35.50±0.20	170
4	M3	A69F/R127G/ <u>M124P</u>	10	98	96	49.53±0.07	>200
5	M3	A69F/R127G/M124P	20	>99	76	43.52±0.23	>200
6	M4	A69F/R127G/M124P/ <u>R182W</u>	20	>99	94	48.64±0.07	>200
7	M5	A69F/R127L	10	91	5	5.47±0.16	22
8	M6	A69F/R127L/M124P	10	99	38	27.73±0.25	>200
9	M7	A69F/R127L/M124P/R182W	20	>99	36	26.66±0.18	>200

^aThe reactions were carried out in triplicate with 10-20 mM (*rac*)-**1a** and 10 g dcw/L *E. coli* (HheD8) cells in 5 mL PB buffer (50 mM, pH 8.5) at 30 °C for 8 h. ^bThe *ee* values were determined by chiral HPLC. ^cCalculated conversion: $conv. = ee_{1a}/(ee_{1a}+ee_{1b})$. ^dCalculated enantioselectivity: $E = \ln[(1-ee_{1a})/(1+ee_{1a}/ee_{1b})]/\ln[(1+ee_{1a})/(1+ee_{1a}/ee_{1b})]$. The e.e. values and conversions were calculated from the average of triplicate experiments ($n = 3$). Data are presented as mean values $\pm$ SD.

Supplementary Table 5. Directed evolution of HheD8 for enantioselective ring-opening of oxetane (*rac*)-1b** with azide.^a**



entry	HheD8	mutation	conc. 1b (mM)	<i>ee</i> (<i>R</i>)- 1c (%) ^b	<i>ee</i> (<i>S</i>)- 1b (%) ^b	conv. 1b (%) ^c	<i>E</i> ^d
1	WT	none	10	75	21	21.81±0.62	9
2	M1	A69F	10	>99	17	14.55±0.18	>200
3	M5	A69F/ <u>R127L</u>	10	99	31	24.03±0.03	>200
4	M6	A69F/R127L/ <u>M124P</u>	10	>99	75	42.82±0.51	>200
5	M6	A69F/R127L/M124P	20	>99	64	39.01±0.12	>200
6	M7	A69F/R127L/M124P/ <u>R182W</u>	20	>99	84	45.68±0.15	>200
7	M2	A69F/R127G	10	>99	19	16.02±0.20	>200
8	M3	A69F/R127G/M124P	20	99	82	45.16±0.20	>200
9	M4	A69F/R127G/M124P/R182W	20	99	>99	50.14±0.04	>200

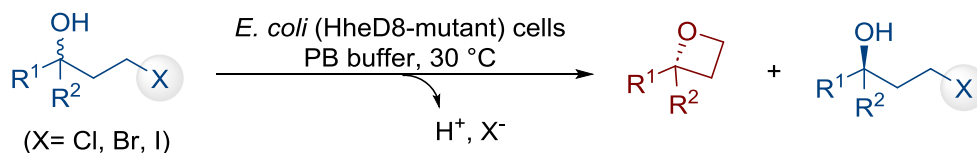
^aThe reactions were carried out in triplicate with 10-20 mM (*rac*)-**1b**, 1.0 equivalent of NaN₃ and 10 g dcw/L *E. coli* (HheD8) cells in 5 mL PB buffer (50 mM, pH 7.5) at 30 °C for 10 h. ^bThe *ee* values were determined by chiral HPLC. ^cCalculated conversion: $conv. = ee_{1b}/(ee_{1b}+ee_{1c})$. ^dCalculated enantioselectivity: $E = \ln[(1-ee_{1b})/(1+ee_{1b}/ee_{1c})]/\ln[(1+ee_{1b})/(1+ee_{1b}/ee_{1c})]$. The e.e. values and conversions were calculated from the average of triplicate experiments ($n = 3$). Data are presented as mean values ± SD.

Supplementary Table 6. Data collection and refinement statistics.

	HheD8-M3/Cl ⁻
Data collection	
Space group	P 62 2 2
Cell dimensions	
<i>a</i> , <i>b</i> , <i>c</i> (Å)	138.56, 138.56, 66.82
α , β , γ (°)	90.00, 90.00, 90.00
Resolution (Å)	40-2.4 (2.486-2.4)
<i>R</i> _{sym} or <i>R</i> _{merge}	0.09077 (0.616)
<i>I</i> / σI	38.88 (9.21)
Completeness (%)	99.75 (99.39)
Redundancy	37.5 (39.0)
Refinement	
Resolution (Å)	2.40
No. reflections	15241 (1477)
<i>R</i> _{work} / <i>R</i> _{free}	0.185 / 0.190
No. atoms	
Protein	1652
Ligand (Cl ⁻)	1
Water	39
<i>B</i> -factors	
Protein	51.44
Ligand/ion	53.18
Water	50.26
R.m.s. deviations	
Bond lengths (Å)	0.007
Bond angles (°)	1.25

One crystal was used to obtain this dataset. The values in parentheses are for the highest-resolution shell.

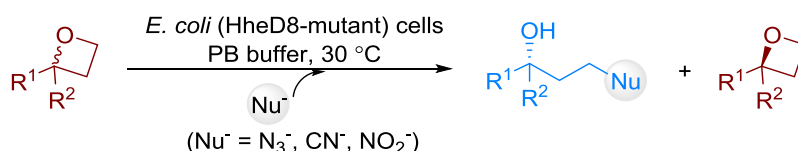
Supplementary Table 7. Scope of the biocatalytic enantioselective dehalogenation of γ -haloalcohols.^a



Substrate	Product	T (h)	yield b (%) ^b	<i>ee</i> (<i>R</i>)- b (%) ^c	yield a (%) ^b	<i>ee</i> (<i>S</i>)- a (%) ^c	conv. a (%) ^d	<i>E</i> ^e
1a	1b	8	41	98	50	>99	50	>200
2a	2b	6	39	98	49	98	50	>200
3a	3b	24	43	97	51	94	49	>200
4a	4b	24	46	96	50	93	49	168
5a	5b	24	33	99	50	93	48	>200
6a	6b	12	36	>99	47	94	49	>200
7a	7b	48	45	98	48	93	49	>200
8a	8b	48	43	95	50	92	49	129
9a	9b	24	34	99	51	91	48	>200
10a	10b	48	43	97	51	91	48	>200
11a	11b	12	34	>99	52	93	48	>200
12a	12b	48	37	>99	50	93	48	>200
13a	13b	48	42	98	50	92	48	>200
14a^f	14b	82	37	93	53	86	48	77
15a	15b	12	32	98	51	92	48	>200
16a^g	16b	82	37	>99	50	96	49	>200
17a	17b	1.5	36	>99	49	>99	50	>200
18a	18b	77	42	97	50	89	48	198
19a^f	19b	48	44	96	48	97	50	>200
20a	20b	12	NI	ND	50	>99	ND	ND
21a^f	21b	60	35	>99	48	98	49	>200
22a	22b	36	NI	ND	41	93	ND	ND
23a	1b	6	30	92	50	>99	50	126
24a	1b	1.5	39	93	48	>99	50	145

^aThe reactions were carried out with 20 mM (*rac*)-**a** and 10 g dcw/L *E. coli* (HheD8-M4) cells in 100 mL PB buffer (50 mM, pH 8.5) at 30 °C. ^bThe isolated yield were obtained by silica gel chromatography. ^cThe *ee* values were determined by chiral HPLC/GC. ^dCalculated conversion: $\text{conv.} = ee_a / (ee_a + ee_b)$. ^eCalculated enantioselectivity: $E = \ln[(1 - ee_a) / (1 + ee_a / ee_b)] / \ln[(1 + ee_a) / (1 + ee_a / ee_b)]$. ^fReactions were carried out at the substrate concentration of 10 mM. ^gReaction was carried out with *E. coli* (HheD8-M3) cells. NI= not isolated (oxetanes **20b** and **22b** were not isolated due to its unstable properties). ND= not detected. The e.e. values and isolated yields were determined from the single preparative experiment ($n = 1$).

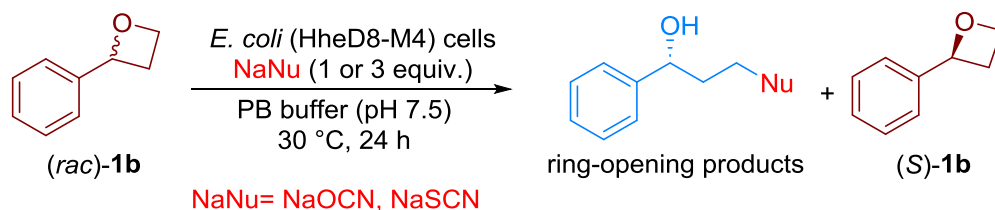
Supplementary Table 8. Scope of the biocatalytic enantioselective ring-opening of oxetanes.^a



Substrate	Product	T (h)	yield c/d/e/f (%) ^b	<i>ee</i> (<i>R</i>)- c/d/e/f (%) ^c	yield b (%) ^b	<i>ee</i> (<i>S</i>)- b (%) ^c	conv. b (%) ^d	<i>E</i> ^e
1b	1c	10	47	97	33	>99	51	>200
2b	2c	10	48	98	35	>99	50	>200
3b	3c	37	48	94	42	92	49	106
4b	4c	60	44	91	48	93	51	72
5b	5c	33	44	97	30	97	50	>200
6b	6c	12	47	>99	38	>99	50	>200
7b	7c	24	47	97	46	94	49	>200
8b	8c	23	48	95	48	95	50	146
9b	9c	24	48	98	37	94	49	>200
10b	10c	24	43	95	42	95	50	146
11b	11c	16	50	98	36	>99	50	>200
12b	12c	11	48	99	45	97	49	>200
13b	13c	26	47	98	42	98	50	>200
14b^f	14c	45	41	94	49	86	48	90
15b	15c	16	43	>99	42	>99	50	>200
16b^g	16c	45	43	95	35	98	51	180
17b^h	17c	14	39	>99	27	85	46	>200
18bⁱ	18c	26	48	98	45	99	50	>200
19b^j	19c	30	49	>99	46	95	49	>200
21b^k	21c	96	43	97	32	89	48	198
1b^l	1d	22	46	>99	37	97	49	>200
1b^m	1e	24	23	>99	43	>99	50	>200
	1f		19	88				82

^aThe reactions were carried out with 20 mM (*rac*)-**b**, 20 mM NaN₃ and 10 g dcw/L *E. coli* (HheD8-M4) cells in 100 mL PB buffer (50 mM, pH 7.5) at 30 °C. ^bThe isolated yield were obtained by silica gel chromatography. ^cThe *ee* values were determined by chiral HPLC/GC. ^dCalculated conversion: *conv.* = *ee*_b/(*ee*_b+*ee*_c). ^eCalculated enantioselectivity: *E* = ln[(1-*ee*_b)/(1+*ee*_b/*ee*_c)]/ln[(1+*ee*_b)/(1+*ee*_b/*ee*_c)]. ^fThe reaction was carried out with 5 mM (*rac*)-**14b**, 5 mM NaN₃ and 10 g dcw/L *E. coli* (HheD8-M4) cells. ^gThe reaction was carried out with 5 mM (*rac*)-**16b**, 5 mM NaN₃ and 10 g dcw/L *E. coli* (HheD8-M3). ^hThe reaction was carried with 5 mM (*rac*)-**17b**, 15 mM NaN₃ and 30 g dcw/L *E. coli* (HheD8-M7) cells in 100 mL Gly-NaOH buffer (300 mM, pH 9.5). ⁱThe reaction was carried out with 20 mM (*rac*)-**18b**, 20 mM NaN₃ and 10 g dcw/L *E. coli* (HheD8-M4) cells in 100 mL PB buffer (50 mM, pH 6.5). ^jThe reaction was carried out with 10 mM (*rac*)-**19b**, 10 mM NaN₃ and 10 g dcw/L *E. coli* (HheD8-M4) cells in 100 mL PB buffer (50 mM, pH 6.5). ^kThe reaction was carried out in 200 mL round-bottom flask with 5 mM (*rac*)-**21b**, 15 mM NaN₃ and 30 g dcw/L *E. coli* (HheD8-M4) cells. ^lThe reaction was carried with 20 mM (*rac*)-**1b**, 40 mM mandelonitrile and 10 g dcw/L *E. coli* (HheD8-M4) cells. ^mThe reaction was carried out with 40 mM (*rac*)-**1b**, 40 mM NaNO₂ and 10 g dcw/L *E. coli* (HheD8-M4) cells in 200 mL PB buffer (50 mM, pH 7.5). The e.e. values and isolated yields were determined from the single preparative experiment (*n* = 1).

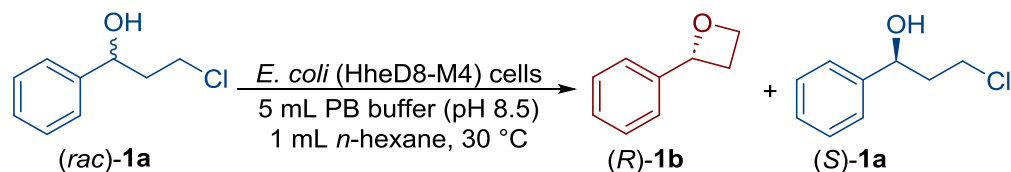
Supplementary Table 9. Ring-opening of (*rac*)-1b** with cyanate and thiocyanate.^a**



entry	Nucleophile (NaNu)	NaNu: 1b	Conversion 1b (%) ^b	<i>ee</i> (<i>S</i>)- 1b (%) ^b	<i>E</i> ^c
1	NaOCN	1:1	28	8	2
2	NaOCN	1:3	29	8	2
3	NaSCN	1:1	29	7	2
4	NaSCN	1:3	32	11	2

^aThe reactions were carried out in triplicate with 5 mM (*rac*)-**1b**, 5 or 15 mM NaNu and 20 g dcw/L *E. coli* (HheD8-M4) cells in 5 mL PB buffer (50 mM, pH 7.5) at 30 °C for 24 h. ^bThe conversion and *ee* values of **1b** were determined by chiral HPLC. ^cCalculated enantioselectivity: $E = \ln[(1-c)/(1-ee_s)]/\ln[(1-c)/(1+ee_s)]$, *c*= conversion of **1b**; *ee_s*= *ee* values of (*S*)-**1b**. The e.e. values and conversions were calculated from the single analytic experiment (*n* = 1).

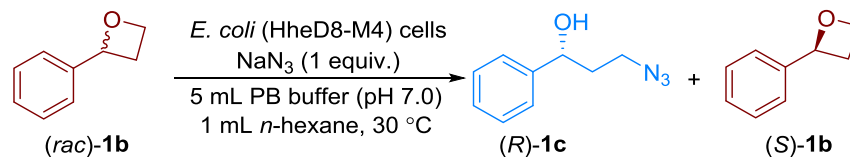
Supplementary Table 10. Time-course studies of the enantioselective dehalogenation reaction of (*rac*)-1a** at different substrate concentrations.^a**



Concentration 1a (mM)	T (h)	<i>ee</i> (<i>R</i>)- 1b (%) ^b	<i>ee</i> (<i>S</i>)- 1a (%) ^b	Conversion (%) ^c	<i>E</i> ^d
40	3	>99	96	49	>200
	6	>99	>99	50	>200
	12	>99	>99	50	>200
	24	>99	>99	50	>200
80	3	>99	44	31	>200
	6	>99	80	44	>200
	12	>99	92	48	>200
	24	>99	96	49	>200
	36	>99	98	49	>200
	48	>99	97	49	>200
100	3	>99	32	24	>200
	6	>99	57	36	>200
	12	>99	79	44	>200
	24	>99	92	48	>200
	36	>99	94	48	>200
	48	>99	96	49	>200
120	3	>99	26	21	>200
	6	>99	44	31	>200
	12	>99	67	40	>200
	24	>99	85	46	>200
	36	>99	91	48	>200
	48	>99	92	48	>200
140	3	>99	22	18	>200
	6	>99	39	28	>200
	12	>99	57	36	>200
	24	>99	75	43	>200
	36	>99	84	46	>200
	48	>99	87	47	>200

^aThe reactions were carried out at 30 °C within a two-phase system (PB buffer, 5 mL, 200 mM, pH 8.5; *n*-hexane, 1 mL) containing 40-140 mM (*rac*)-**1a** and 10 g dcw/L *E. coli* (HheD8-M4) cells. ^bThe *ee* values were determined by chiral HPLC. ^cCalculated conversion: $conv. = ee_{1a}/(ee_{1a}+ee_{1b})$. ^dCalculated enantioselectivity: $E = \ln[(1-ee_{1a})/(1+ee_{1a}/ee_{1b})]/\ln[(1+ee_{1a})/(1+ee_{1a}/ee_{1b})]$. The e.e. values and conversions were calculated from the single analytic experiment ($n = 1$).

Supplementary Table 11. Time-course studies of the enantioselective azide-mediated ring-opening reaction of (*rac*)-1b** at different substrate concentrations.^a**



Concentration 1b (mM)	T (h)	<i>ee</i> (<i>R</i>)- 1c (%) ^b	<i>ee</i> (<i>S</i>)- 1b (%) ^b	Conversion (%) ^c	<i>E</i> ^e
40	3	>99	44	31	>200
	6	>99	81	45	>200
	12	>99	99	50	>200
	24	>99	>99	50	>200
	36	>99	>99	50	>200
80	3	>99	25	20	>200
	6	>99	51	34	>200
	12	>99	87	47	>200
	24	>99	>99	50	>200
	36	>99	>99	50	>200
120	3	>99	25	20	>200
	6	>99	46	32	>200
	12	>99	80	44	>200
	24	>99	>99	50	>200
	36	>99	>99	50	>200
160	3	>99	18	15	>200
	6	>99	33	25	>200
	12	>99	63	39	>200
	24	>99	96	49	>200
	36	>99	>99	50	>200
200	3	>99	14	12	>200
	6	>99	28	22	>200
	12	>99	51	34	>200
	24	>99	92	48	>200
	36	>99	99	50	>200

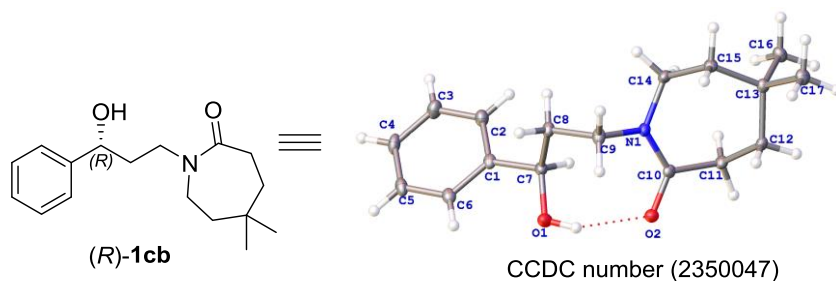
^aThe reactions were carried out at 30 °C within a two-phase system (PB buffer, 5 mL, 300 mM, pH 7.0; *n*-hexane, 1 mL) containing 40-200 mM (*rac*)-**1b**, 1 equivalent NaN₃, and 10 g dcw/L *E. coli* (HheD8-M4) cells. ^bThe *ee* values were determined by chiral HPLC. ^cCalculated conversion: $conv. = ee_{1b}/(ee_{1b}+ee_{1c})$. ^dCalculated enantioselectivity: $E = \ln[(1-ee_{1b})/(1+ee_{1b}/ee_{1c})]/\ln[(1+ee_{1b})/(1+ee_{1b}/ee_{1c})]$. The e.e. values and conversions were calculated from the single analytic experiment ($n = 1$).

Supplementary Table 12. Directed evolution of the mutant HheD8-M4 for the reversal of enantioselectivity.^a

<chem>ClCC(O)c1ccccc1</chem> $\xrightarrow[\text{30 } ^\circ\text{C, 8 h}]{\text{E. coli (HheD8) cells, PB buffer (pH 8.5)}}$ <chem>ClCC(O)[C@H](c1ccccc1)C2CCOC2</chem> + <chem>ClCC(O)[C@@H](c1ccccc1)C2CCOC2</chem> $(rac)\text{-1a}$ $(R) \text{ or } (S)\text{-1b}$ $(R) \text{ or } (S)\text{-1a}$					
entry	HheD8	mutation ^b	<i>ee</i> 1a (%) ^c	<i>ee</i> 1b (%) ^c	conv. 1a (%) ^d
1	M4	A69F/M124P/R127G/R182W	97 (<i>S</i>)	97 (<i>R</i>)	49.92 ± 0.16
2	M8	<u>A69N</u> /M124P/R127G/R182W	93 (<i>S</i>)	71 (<i>R</i>)	56.76 ± 1.10
3	M9	A69N/ <u>A119T</u> /M124P/R127G/R182W	<5	24 (<i>S</i>)	<5
4	M10	A69N/A119T/M124P/ <u>R127T</u> /R182W	7 (<i>R</i>)	56 (<i>S</i>)	10.63 ± 0.07
5	M11	A69N/A119T/ <u>M124W</u> /R127T/R182W	36 (<i>R</i>)	74 (<i>S</i>)	32.67 ± 0.12
9	M12	A69N/ <u>S71P</u> /A119T/M124W/R127T/R182W	41 (<i>R</i>)	92 (<i>S</i>)	30.63 ± 0.04

^aThe reactions were carried out in triplicate with 10 mM (*rac*)-**1a** and 10 g dcw/L *E. coli* (HHDH) cells in 5 mL PB buffer (50 mM, pH 8.5) at 30 °C for 8 h. ^bMutation are compared to the HheD8-WT. ^cThe *ee* values were determined by chiral HPLC. ^dCalculated conversion: $conv. = ee_{1a}/(ee_{1a}+ee_{1b})$. The e.e. values and conversion were calculated from the average of triplicate experiments ($n = 3$). Data are presented as mean values ± SD.

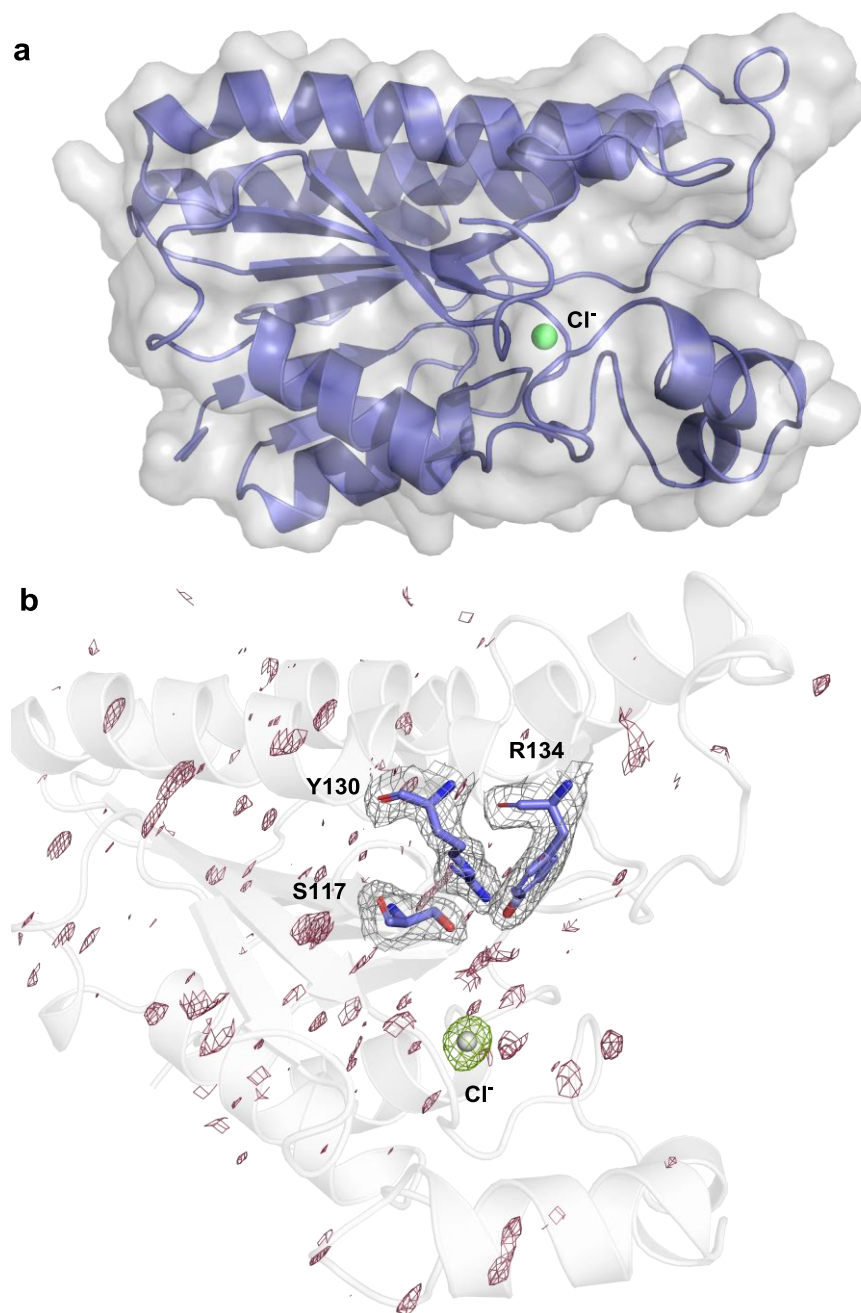
Supplementary Table 13. Crystal data and structure refinement for (*R*)-1cb.



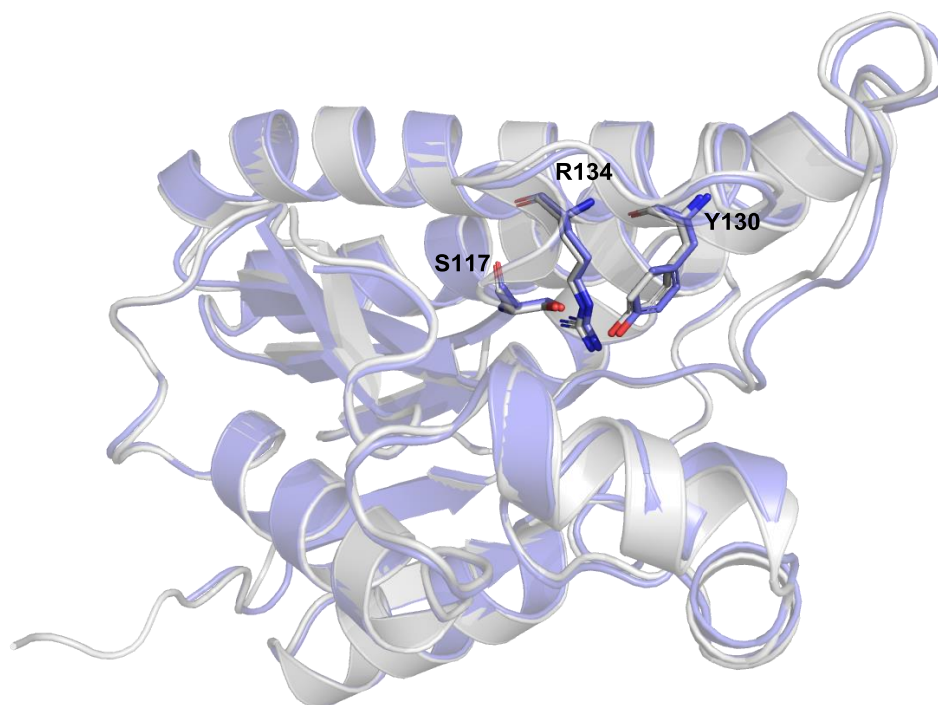
Identification code	(<i>R</i>)-1cb
Empirical formula	C ₁₇ H ₂₅ NO ₂
Formula weight	275.38
Temperature/K	99.98(11)
Crystal system	monoclinic
Space group	P2 ₁
a/Å	6.0384(3)
b/Å	7.4549(4)
c/Å	17.5882(11)
α/°	90
β/°	99.789(6)
γ/°	90
Volume/Å ³	780.22(8)
Z	2
ρ _{calc} /cm ³	1.172
μ/mm ⁻¹	0.596
F(000)	300.0
Crystal size/mm ³	0.14 × 0.12 × 0.11
Radiation	Cu Kα (λ = 1.54184)
2θ range for data collection/°	5.098 to 148.018
Index ranges	-7 ≤ h ≤ 6, -9 ≤ k ≤ 6, -21 ≤ l ≤ 21
Reflections collected	7816
Independent reflections	2532 [R _{int} = 0.0232, R _{sigma} = 0.0154]
Data/restraints/parameters	2532/1/185
Goodness-of-fit on F ²	1.042
Final R indexes [I > 2σ (I)]	R ₁ = 0.0266, wR ₂ = 0.0675
Final R indexes [all data]	R ₁ = 0.0268, wR ₂ = 0.0676
Largest diff. peak/hole / e Å ⁻³	0.20/-0.12
Flack/Hoof parameter	0.08(9)/0.09(6)

3. Supplementary Figures 1-11

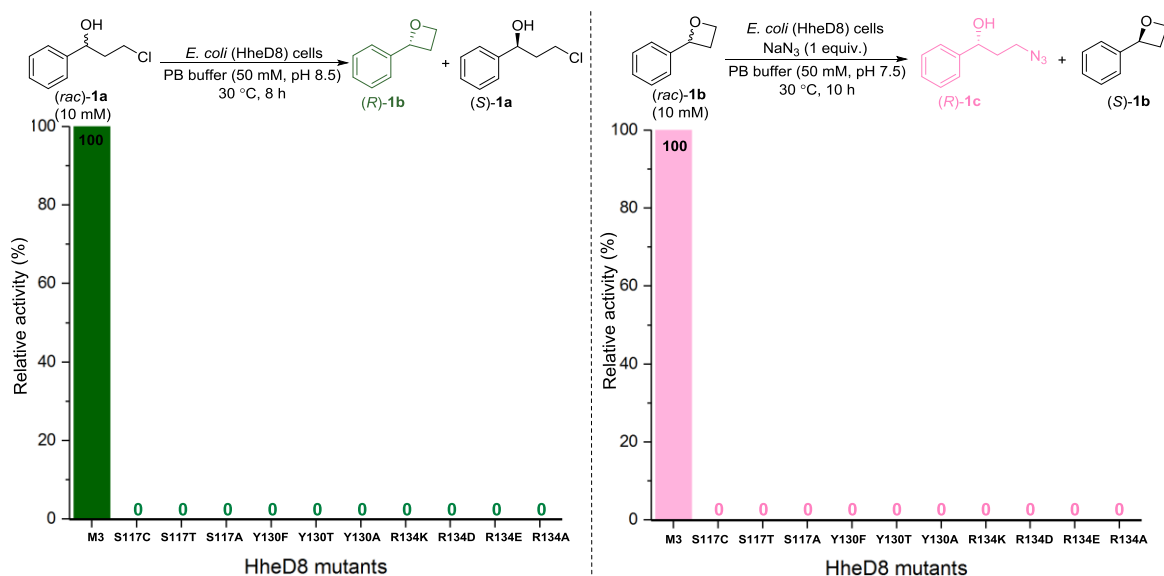
Supplementary Fig. 1 | Crystal structure of the HheD8-M3 complex with chloride. **a**, Cartoon and surface representation of the mutant HheD8-M3 complex with chloride. **b**, Electron density maps. 2Fo-Fc map, $\sigma=1$, Fo-Fc map, $\sigma=3$. The ligand Cl⁻ is highlighted in sphere.



Supplementary Fig. 2 | Overlap structure analysis of the mutant HheD8-M3 with HheD8-WT/AF. HheD8-M3 (PDB code: 8XXB) is shown as blue cartoon. HheD8-WT/AF (AFDB code: AF-N6YXW4-F1) is shown as gray cartoon. Catalytic triad S117-Y130-R134 are highlighted in sticks.



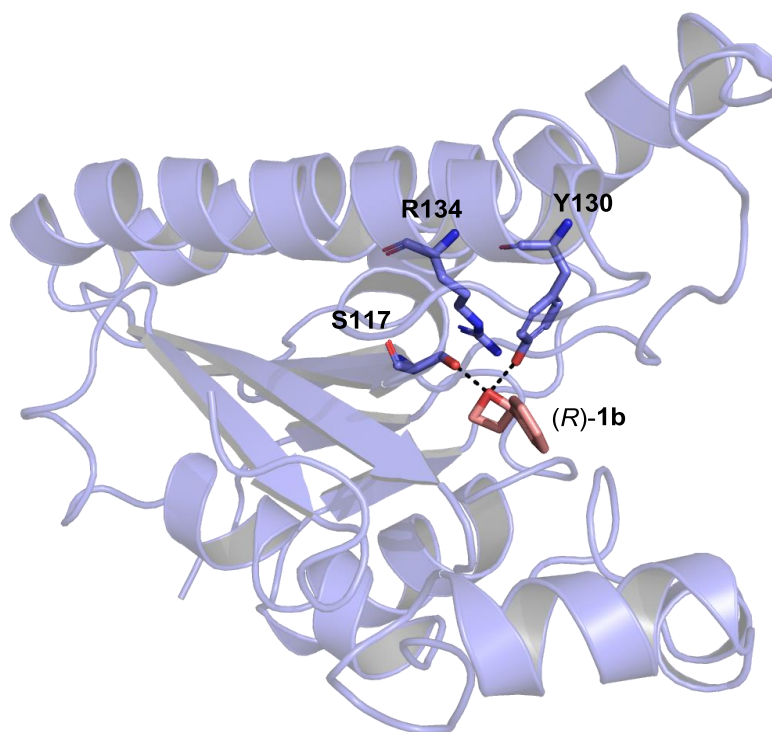
Supplementary Fig. 3 | Evaluation of the catalytic activity of the mutants obtained by performing site-directed mutagenesis at the catalytic triad S117-Y130-R134 of HheD8-M3. The relative activities were calculated from the single analytic experiment ($n = 1$). Bar charts: the relative activities (%).



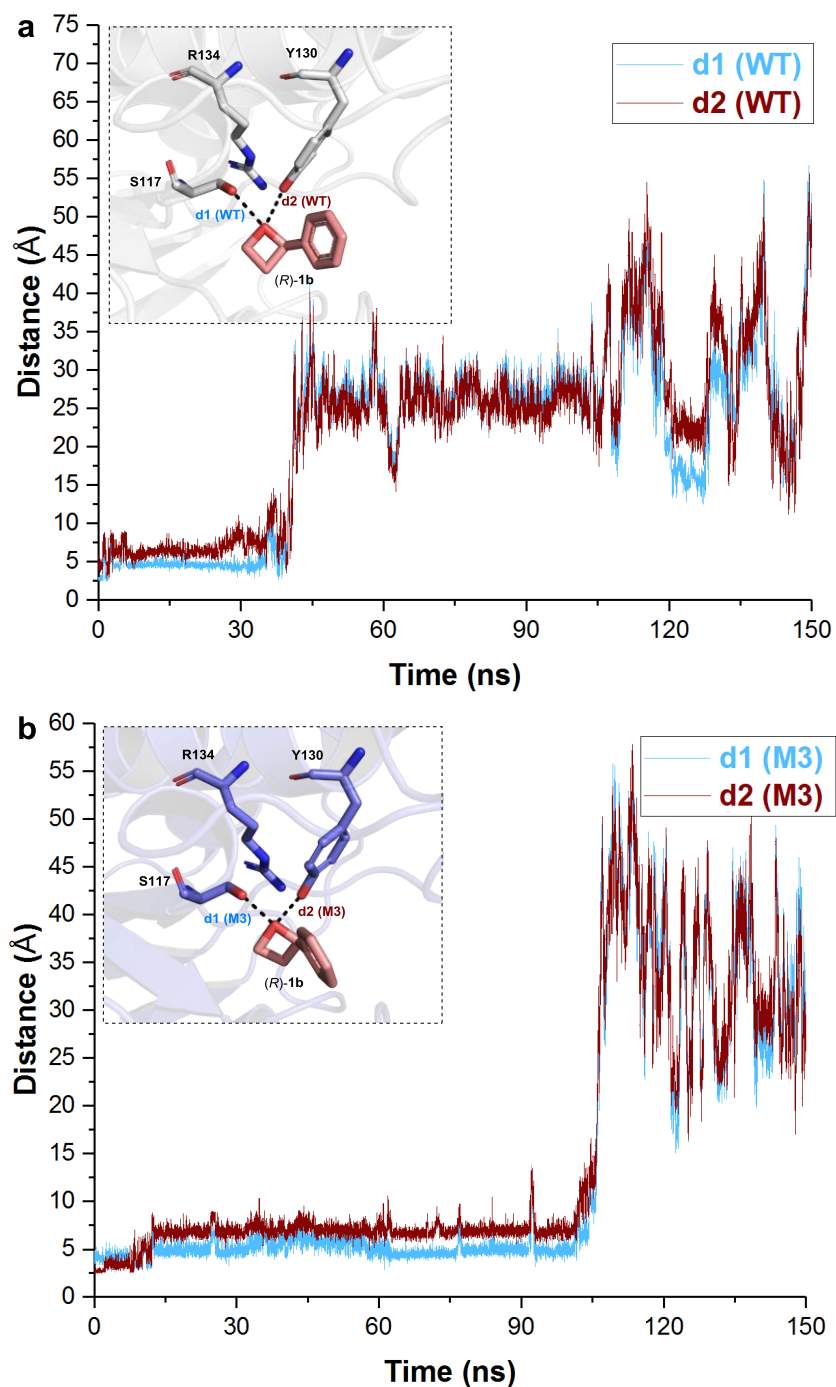
Primers for site-directed mutagenesis (mutants were obtained using methods analogous to the above-mentioned site-saturation mutagenesis experiments)

Mutation site	Primer	Primer sequence
S117C	S117C-F	5'-TCTGCTGATGGGT <u>TGCG</u> CAGCAGCACTGCGT-3'
	S117C-R	5'-ACCACGCAGTGCTGCTGCG <u>CA</u> ACCCATCAG-3'
S117T	S117T-F	5'-TCTGCTGATGGGT <u>ACCG</u> CAGCAGCACTGCGT-3'
	S117T-R	5'-ACCACGCAGTGCTGCTGCG <u>GT</u> ACCCATCAG-3'
S117A	S117A-F	5'-TCTGCTGATGGGT <u>GCCG</u> CAGCAGCACTGCGT-3'
	S117A-R	5'-CAGTGCTGCTGCG <u>GC</u> ACCGATCAGCAGAATT-3'
Y130F	Y130F-F	5'-ACTGGGGAGCAGC <u>TTT</u> GCAGCAGCCCGT-3'
	Y130F-R	5'-ACCACGGGCTGCTGC <u>AA</u> AGCTGCTCCCC-3'
Y130T	Y130T-F	5'-ACTGGGGAGCAGC <u>ACCG</u> CAGCAGCCCGT-3'
	Y130T-R	5'-ACCACGGGCTGCTGCG <u>GT</u> GCTGCTCCCC-3'
Y130A	Y130A-F	5'-ACTGGGGAGCAGC <u>GCG</u> CAGCAGCAGCCCGT-3'
	Y130A-R	5'-ACCACGGGCTGCTGCT <u>GCG</u> GCTGCTCCCC-3'
R134K	R134K-F	5'-TATGCAGCAGCC <u>AA</u> AGGTGCACAGCTG-3'
	R134K-R	5'-CTGTGCACCT <u>TTT</u> GGCTGCTGCATAGCT-3'
R134D	R134D-F	5'-TATGCAGCAGCC <u>GAT</u> GGTGCACAGCTG-3'
	R134D-R	5'-CTGTGCACCA <u>T</u> CGGCTGCTGCATAGCT-3'
R134E	R134E-F	5'-TATGCAGCAGCC <u>GA</u> AGGTGCACAGCTG-3'
	R134E-R	5'-CTGTGCACCT <u>TC</u> GGCTGCTGCATAGCT-3'
R134A	R134A-F	5'-TATGCAGCAGCC <u>GCA</u> GGTGCACAGCTG-3'
	R134A-R	5'-CTGTGCACCT <u>GCG</u> GCTGCTGCATAGCT-3'

Supplementary Fig. 4 | Possible docking pose of (*R*)-1b in the active site of the crystal structure of HheD8-M3. Catalytic triad S117-Y130-R134 and (*R*)-1b are highlighted in sticks. H-bonds are displayed in dashed lines.

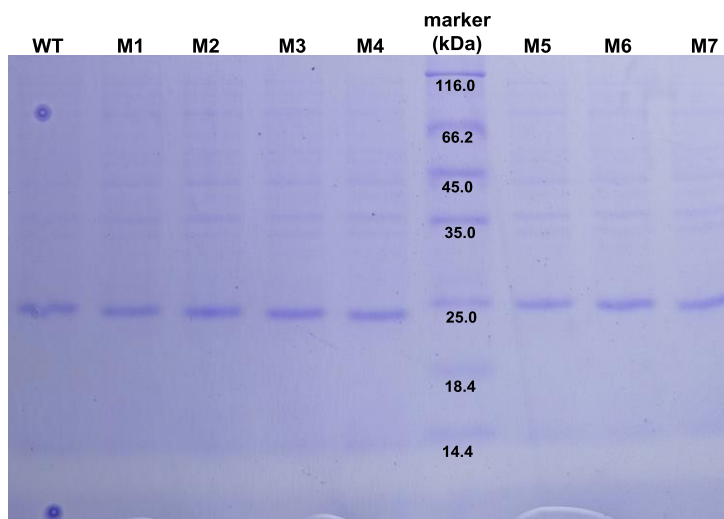


Supplementary Fig. 5 | Supplemental molecular dynamics simulation of HheD8-WT/(*R*)-1b and HheD8-M3/(*R*)-1b. a, The fluctuation of the distances of the **1b**-O between S117-O (d1) and Y130-O (d2) during the MD simulations of HheD8-WT/(*R*)-1b. **b,** The fluctuation of the distance of the **1b**-O between S117-O (d1) and Y130-O (d2) during the MD simulations of HheD8-M3/(*R*)-1b. Catalytic triad S117-Y130-R134, and (*R*)-1b are highlighted in sticks. Distances are displayed in dashed lines.

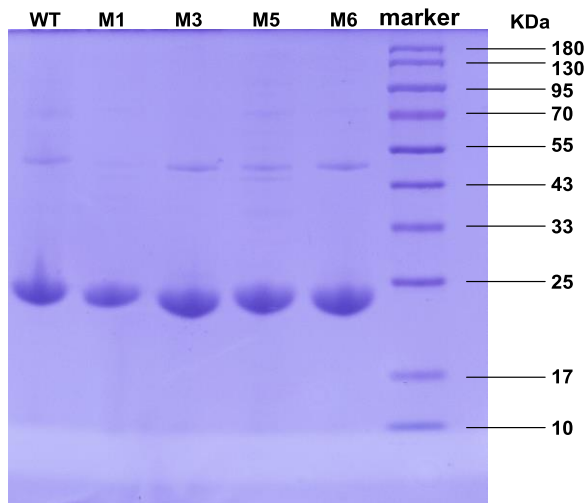


Supplementary Fig. 6 | Purification and kinetic characterization of HheD8 enzymes for the enantioselective ring-opening of (*rac*)-1b with azide. The kinetic parameters were calculated from the average of triplicate experiments ($n = 3$). Data are presented as mean values $\pm$ SD.

a Comparison of the expression levels of HheD8 enzymes in *E. coli* cells



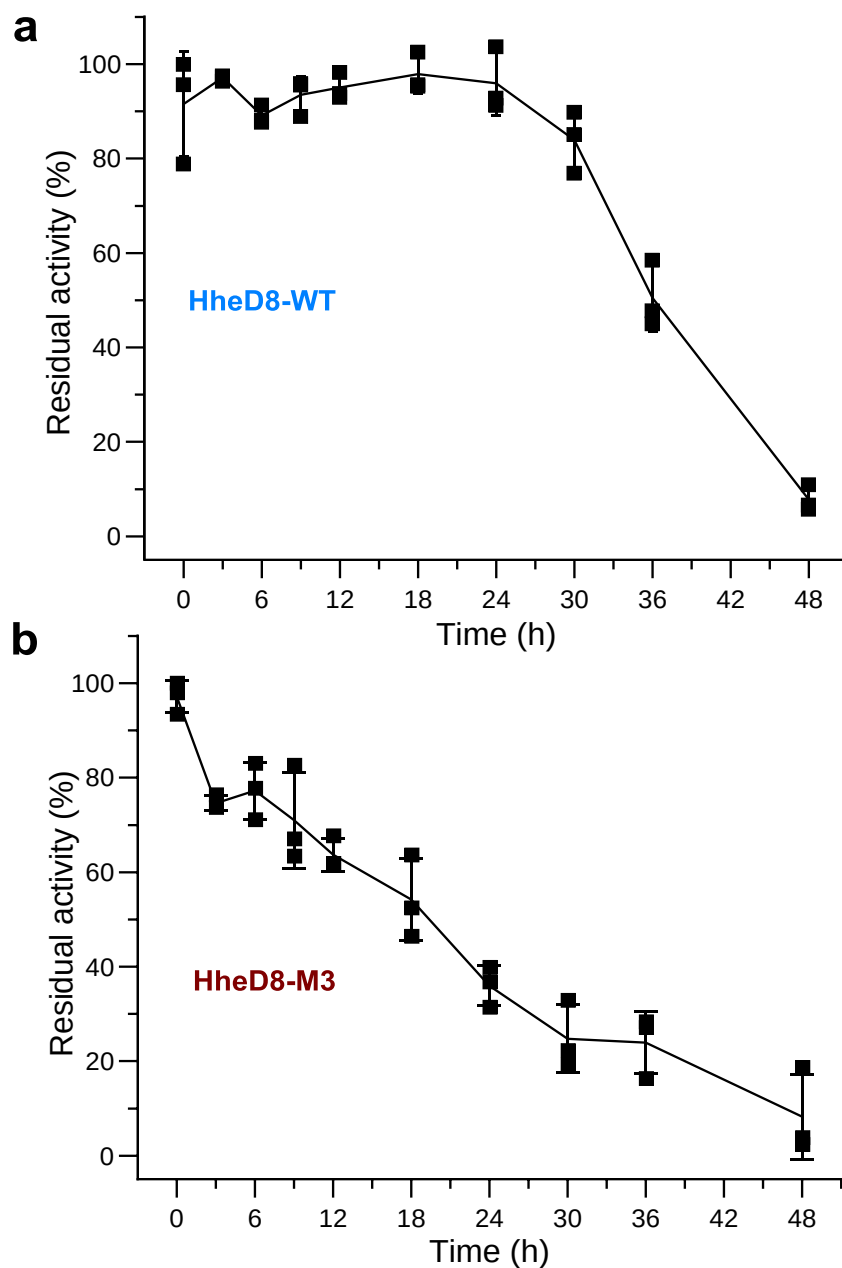
b SDS-PAGE analysis of the purified HheD8 enzymes



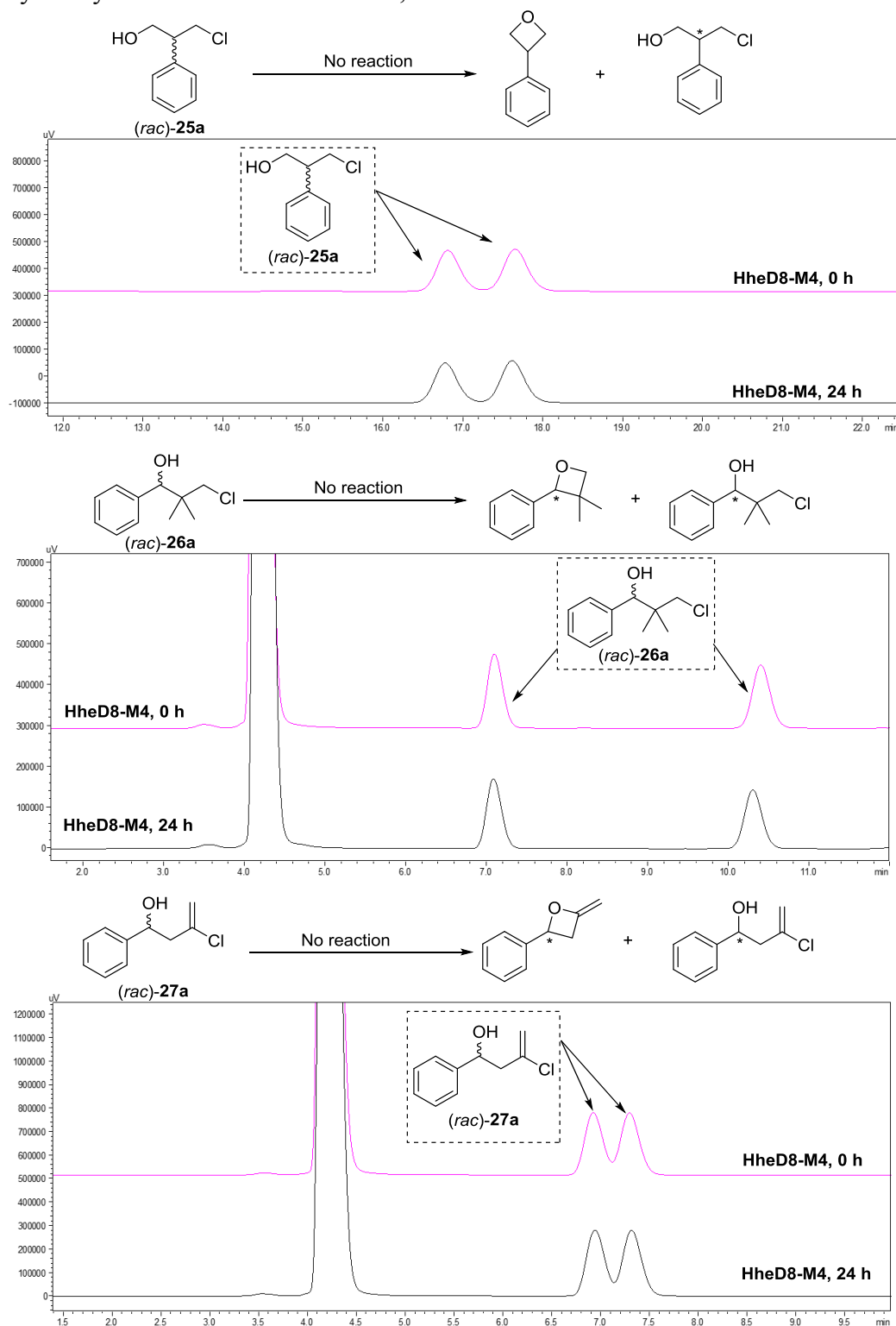
c The Michaelis-Menten kinetics of the HheD8 enzymes

Entry	Enzyme	K_m (mM)	v_{max} (mM/min)	k_{cat} (min^{-1})
1	HheD8-WT	18.85 ± 1.81	0.72 ± 0.04	11.30
2	HheD8-M1	11.70 ± 1.48	0.57 ± 0.04	10.20
3	HheD8-M3	11.93 ± 1.02	2.13 ± 0.10	83.77
4	HheD8-M5	11.32 ± 1.27	0.64 ± 0.04	11.68
5	HheD8-M6	5.46 ± 0.36	0.95 ± 0.03	41.18

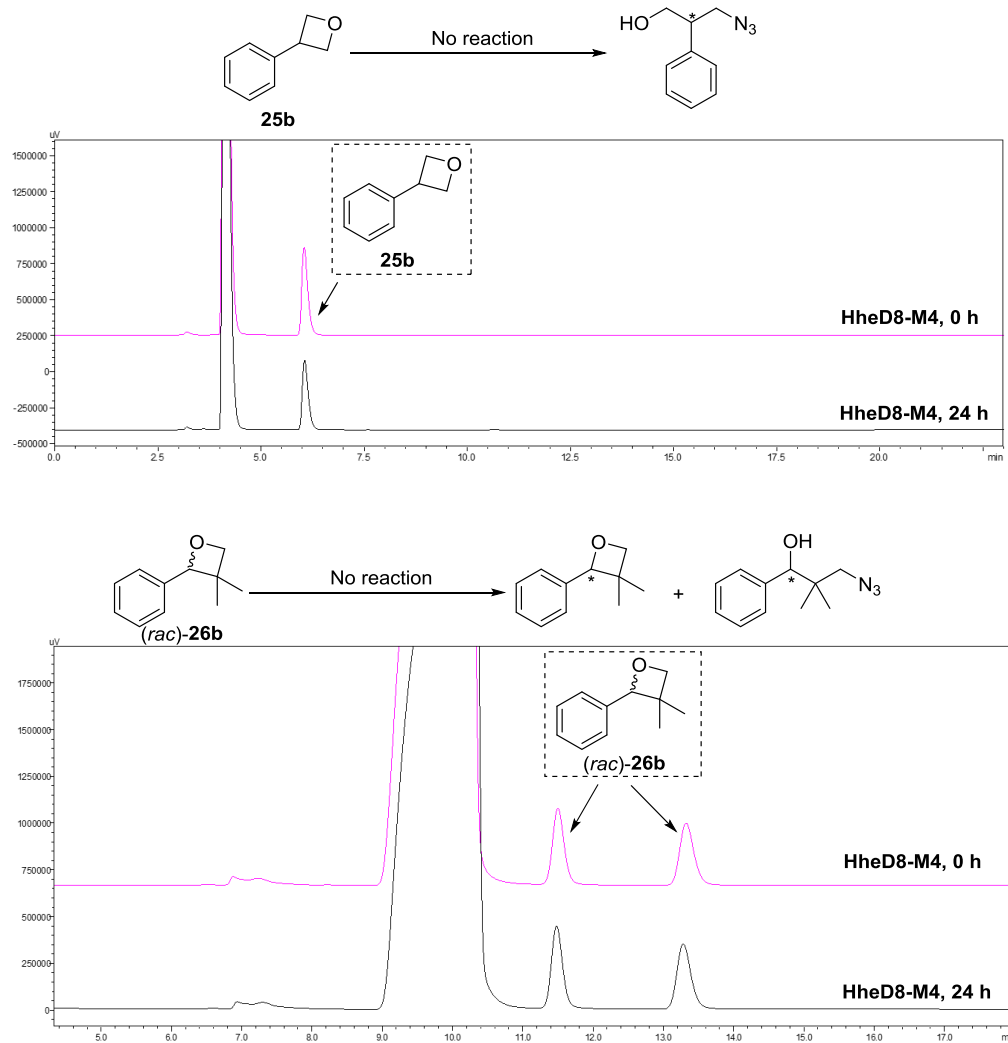
Supplementary Fig. 7 | Evaluation of the thermostability of the HheD8-WT (a) and the mutant HheD8-M3 (b). The reactions were carried out in the 800 μ L PB buffer (200 mM, pH 8.5) containing 1.5 mM (*rac*)-**1a** and 10 μ L of purified enzymes at 30 $^{\circ}$ C for 3 h (HheD8-WT) or 1 h (HheD8-M3). The reactions were extracted using 800 μ L of ethyl acetate, and analyzed by chiral HPLC. The highest activity at 0 h for each enzyme was set to 100%. The residual activities were calculated from the average of triplicate experiments ($n = 3$). Dots: residual activities (%).



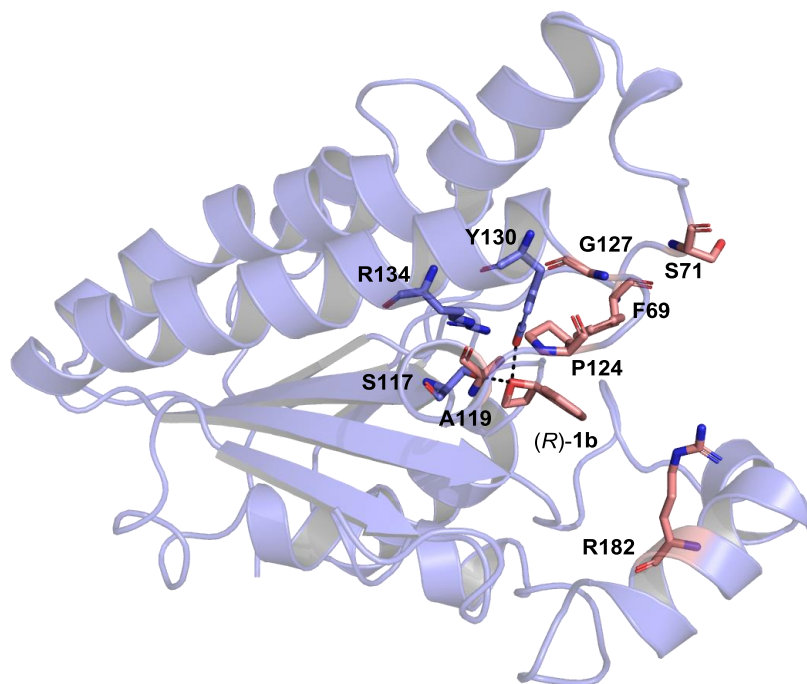
Supplementary Fig. 8 | Representative HPLC traces for the unsuccessful dehalogenation reactions of γ -haloalcohols. The reactions were carried out in 5 mL PB buffer (200 mM, pH 8.5) containing 5 mM (*rac*)-**a** and 10 g dcw/L *E. coli* (HheD8) cells at 30 °C for 24 h. All the reactions were analyzed by chiral HPLC. HheD8-WT, and the mutants M1-M7 were tested.



Supplementary Fig. 9 | Representative HPLC traces for the unsuccessful ring-opening reactions of oxetanes. The reactions were carried out in 5 mL PB buffer (200 mM, pH 7.5) containing 5 mM **b**, 5 mM NaN₃ and 10 g dcw/L *E. coli* (HheD8) cells at 30 °C for 24 h. All the reactions were analyzed by chiral HPLC. HheD8-WT, and the mutants M1-M7 were tested.

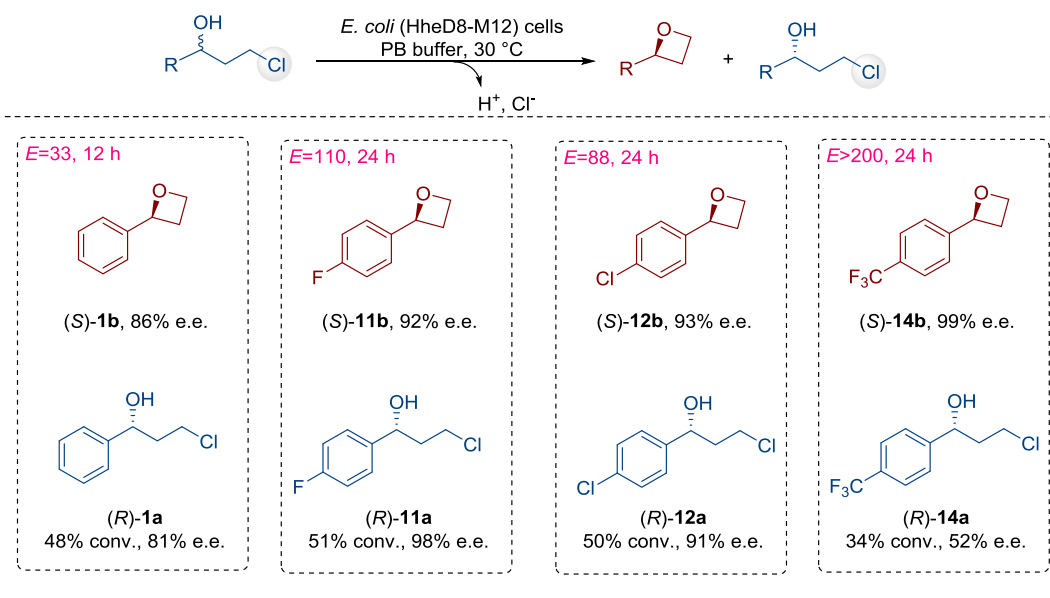


Supplementary Fig. 10 | Selected mutated residues based on the docking pose of HheD8-M3/(*R*)-1b. Catalytic triad S117-Y130-R134, (*R*)-1b, and selected residues (F69, S71, A119, P124, G127, and R182) are highlighted in sticks. H-bonds are displayed in dashed lines.

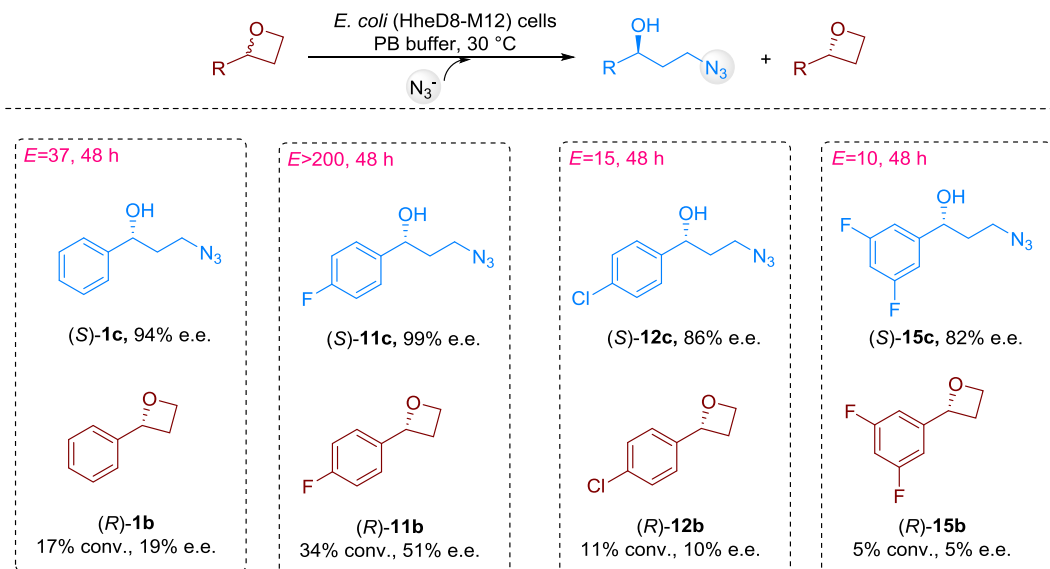


Supplementary Fig. 11 | Enantioselective formation and ring-opening of oxetanes catalyzed by the *S*-enantioselective mutant HheD8-M12. The dehalogenation reactions were carried out with 10 mM (*rac*)-**a** and 10 g dcw/L *E. coli* (HheD8-M12) cells in 5 mL PB buffer (200 mM, pH 8.5) at 30 °C. The *ee* values were determined by chiral HPLC. Calculated conversion: $conv. = ee_a/(ee_a+ee_b)$. Calculated enantioselectivity: $E = \ln[(1-ee_a)/(1+ee_a/ee_b)]/\ln[(1+ee_a)/(1+ee_a/ee_b)]$. The ring-opening reactions were carried out with 10 mM (*rac*)-**b**, 20 mM NaN₃ and 20 g dcw/L *E. coli* (HheD8-M12) cells in 5 mL PB buffer (200 mM, pH 6.5) at 30 °C. The *ee* values were determined by chiral HPLC. Calculated conversion: $conv. = ee_b/(ee_b+ee_c)$. Calculated enantioselectivity: $E = \ln[(1-ee_b)/(1+ee_b/ee_c)]/\ln[(1+ee_b)/(1+ee_b/ee_c)]$. The *e.e.* values and conversion were calculated from the single analytic experiment ($n = 1$).

● **Dehalogenation of γ -haloalcohols**



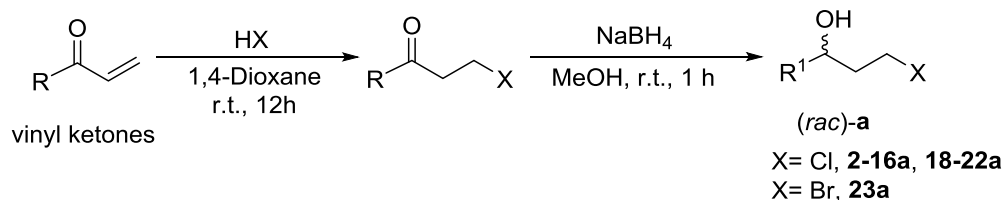
● **Ring-opening of oxetanes**



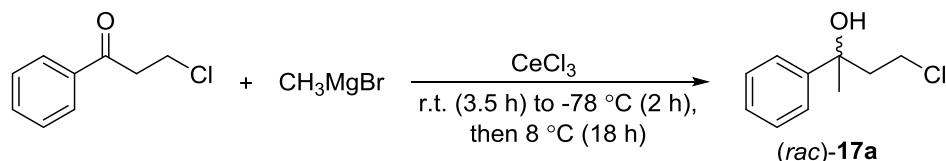
4. Chemical synthesis and characterization of racemic compounds

Synthesis of racemic γ -haloalcohols:

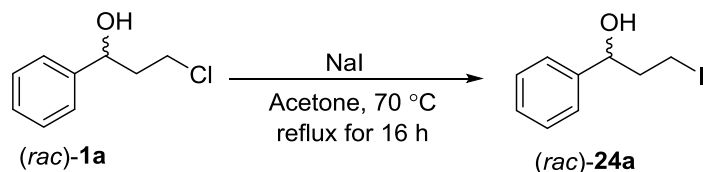
Method A



Method B



Method C

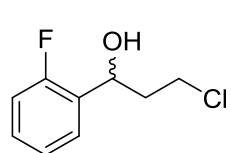


Racemic γ -haloalcohols **2-16a** and **18-23a** were synthesized from the corresponding vinyl ketones (Method A)^{24,25}. General procedure: To a 100-mL round-bottom flask, 20 mmol of vinyl ketone substrates was added, followed by the addition of 10 mL HCl (4 M in 1,4-dioxane). The reaction mixture was then stirred at room temperature for 12 h. Afterward, the reaction mixture was concentrated under reduced pressure to obtain the crude β -halo ketone intermediates. To a 100-mL round-bottom flask cooled with an ice bath, 15 mmol (1.0 eq.) crude β -halo ketones and 20 mL of methanol were added, followed by the addition of 18 mmol (1.2 eq.) NaBH₄. The reaction mixture was then stirred at room temperature for 1 h. Afterward, the methanol solvent was removed under reduced pressure, followed by the addition of 10 mL distilled water to the flask. The mixture was then extracted with ethyl acetate (3 $\times$ 10 mL) and saturated brine (twice). The organic layer was then dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to obtain the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 30:1 ~ 15:1; dichloromethane : ethyl acetate = 6:1 ~ 3:1) to afford the racemic γ -haloalcohols $(rac)\text{-a}$.

Racemic γ -chloroalcohol **17a** was synthesized from the corresponding β -halo ketone (Method B)²⁶. To a 200-mL round-bottom flask, 5.6 g (22.6 mmol) of anhydrous CeCl₃ and 40 mL of dry tetrahydrofuran (THF) were added under nitrogen atmosphere. The reaction mixture was then stirred at room temperature for 3.5 h and cooled to -78 °C, followed by the addition of 40 mL methylmagnesium bromide (1M in THF). The reaction was allowed to proceed at -78 °C for 2 h. Then, 3.4 g (20 mmol) 3-chloro-1-phenylpropan-1-one in 30 mL dry THF was added dropwise to the reaction mixture. The temperature was then gradually raised to 8 °C and the reaction was allowed to proceed for 18 h. Afterward, the reaction mixture was quenched with 15 mL of saturated NH₄Cl solution, extracted with ethyl acetate (3 $\times$ 20 mL), and washed with saturated brine. The organic layer was then dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to obtain the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 30:1~20:1) to afford the racemic γ -chloroalcohol (*rac*)-**17a**.

Racemic γ -iodoalcohol **24a** was synthesized from racemic **1a**²⁷. To a 100-mL round-bottom flask, 1.0 g (5.89 mmol) of (*rac*)-**1a** and 25 mL of acetone were added, followed by the addition of 1.5 g (9.96 mmol) sodium iodide. The temperature was then gradually raised to 70 °C and the reaction was refluxed for 16 h. Afterward, the acetone was removed under reduced pressure, followed by the addition of 10 mL distilled water to the flask. The mixture was then extracted with ethyl acetate (3 $\times$ 10 mL) and saturated brine (twice). The organic layer was then dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to afford the racemic γ -iodoalcohol (*rac*)-**24a**.

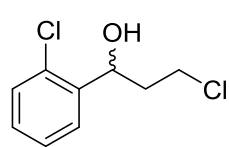
(*rac*)-3-chloro-1-(2-fluorophenyl)propan-1-ol [(*rac*)-2a]



¹H NMR (400 MHz, CDCl₃) δ 7.45 (td, J = 7.5, 1.8 Hz, 1H), 7.29 - 7.24 (m, 1H), 7.15 (t, J = 7.6 Hz, 1H), 7.05 - 7.00 (m, 1H), 5.22 (dd, J = 8.5, 4.3 Hz, 1H), 3.77 - 3.71 (m, 1H), 3.61 (dt, J = 11.0, 6.0 Hz, 1H), 2.27 - 2.11 (m, 3H).

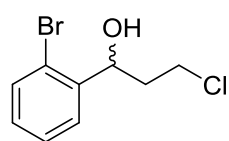
¹³C NMR (100 MHz, CDCl₃) δ 159.8 (d, J = 245.0 Hz), 130.6 (d, J = 13.0 Hz), 129.4 (d, J = 8.0 Hz), 127.4 (d, J = 5.0 Hz), 124.5 (d, J = 3.0 Hz), 115.6 (d, J = 22.0 Hz), 65.9, 41.6, 40.2 (d, J = 1.0 Hz).

(rac)-3-chloro-1-(2-chlorophenyl)propan-1-ol [(rac)-3a]



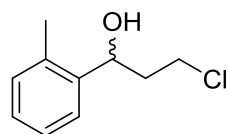
^1H NMR (400 MHz, CDCl_3) δ 7.56 (dd, $J = 7.6, 1.7$ Hz, 1H), 7.35 - 7.28 (m, 2H), 7.22 (td, $J = 7.7, 1.8$ Hz, 1H), 5.34 (dd, $J = 9.0, 3.3$ Hz, 1H), 3.83 - 3.76 (m, 1H), 3.71 - 3.65 (m, 1H), 2.25 - 2.17 (m, 2H), 2.14 - 2.05 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 141.2, 131.8, 129.7, 128.9, 127.4, 127.1, 68.1, 41.8, 39.8.

(rac)-1-(2-bromophenyl)-3-chloropropan-1-ol [(rac)-4a]



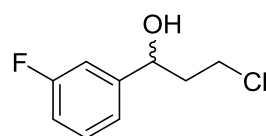
^1H NMR (400 MHz, CDCl_3) δ 7.54 (dd, $J = 11.8, 8.1$ Hz, 2H), 7.34 (t, $J = 7.5$ Hz, 1H), 7.15 (t, $J = 7.7$ Hz, 1H), 5.28 (d, $J = 9.3$ Hz, 1H), 3.83 - 3.77 (m, 1H), 3.71 - 3.66 (m, 1H), 2.41 (s, 1H), 2.25 - 2.17 (m, 1H), 2.10 - 2.01 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.8, 132.9, 129.2, 128.0, 127.3, 121.8, 70.3, 41.8, 39.8.

(rac)-3-chloro-1-(o-tolyl)propan-1-ol [(rac)-5a]



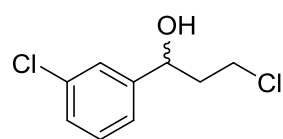
^1H NMR (400 MHz, CDCl_3) δ 7.48 (d, $J = 7.6$ Hz, 1H), 7.27 - 7.14 (m, 3H), 5.20 (dd, $J = 8.8, 3.7$ Hz, 1H), 3.86 - 3.79 (m, 1H), 3.68 - 3.62 (m, 1H), 2.36 (s, 3H), 2.17 - 2.04 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.1, 134.5, 130.6, 127.6, 126.5, 125.1, 67.6, 42.2, 40.6, 19.0.

(rac)-3-chloro-1-(3-fluorophenyl)propan-1-ol [(rac)-6a]



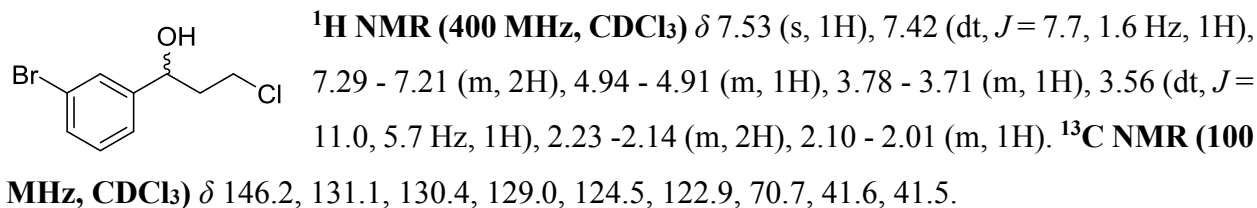
^1H NMR (400 MHz, CDCl_3) δ 7.32 (td, $J = 8.1, 6.2$ Hz, 1H), 7.13 - 7.06 (m, 2H), 6.98 (td, $J = 8.4, 2.6$ Hz, 1H), 4.94 (dd, $J = 8.8, 4.6$ Hz, 1H), 3.76 - 3.70 (m, 1H), 3.55 (dt, $J = 11.0, 5.8$ Hz, 1H), 2.31 (d, $J = 13.8$ Hz, 1H), 2.22 - 2.14 (m, 1H), 2.10 - 2.01 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 163.1 (d, $J = 245.0$ Hz), 146.5 (d, $J = 6.0$ Hz), 130.3 (d, $J = 7.0$ Hz), 121.4, 114.8 (d, $J = 21.0$ Hz), 112.8 (d, $J = 22.0$ Hz), 70.7 (d, $J = 11.0$ Hz), 41.6, 41.4.

(rac)-3-chloro-1-(3-chlorophenyl)propan-1-ol [(rac)-7a]

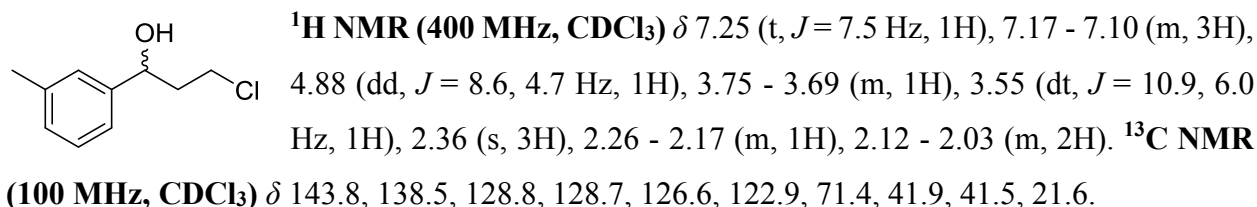


^1H NMR (400 MHz, CDCl_3) δ 7.37 (s, 1H), 7.32 - 7.22 (m, 3H), 4.93 (dd, $J = 8.3, 4.3$ Hz, 1H), 3.78 - 3.71 (m, 1H), 3.59 - 3.53 (m, 1H), 2.23 - 2.02 (m, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 145.9, 134.7, 130.1, 128.1, 126.1, 124.0, 70.8, 41.6, 41.2.

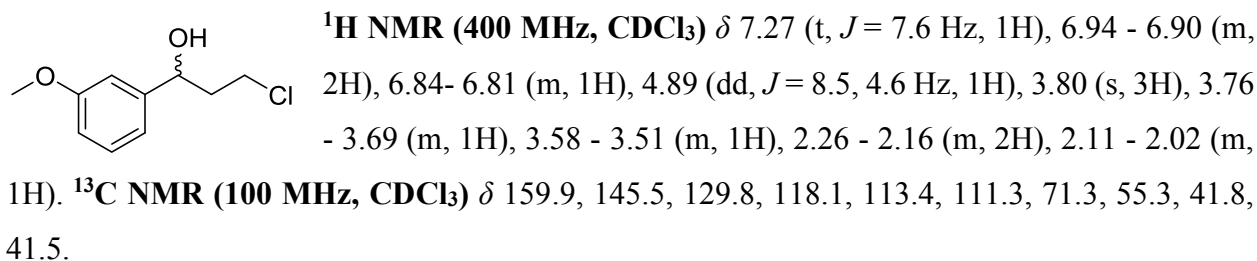
(rac)-1-(3-bromophenyl)-3-chloropropan-1-ol [(rac)-8a]



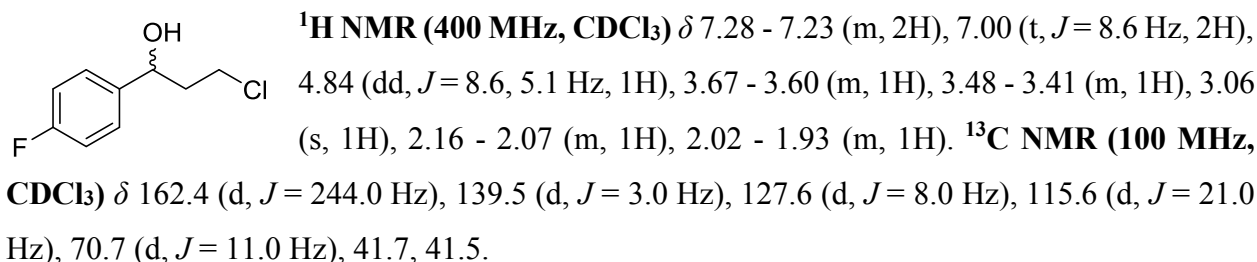
(rac)-3-chloro-1-(m-tolyl)propan-1-ol [(rac)-9a]



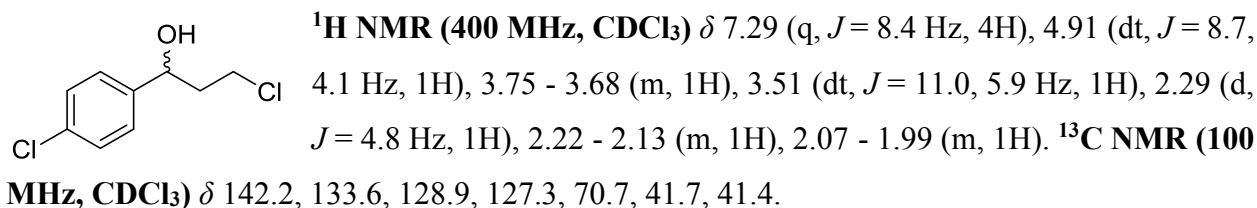
(rac)-3-chloro-1-(3-methoxyphenyl)propan-1-ol [(rac)-10a]



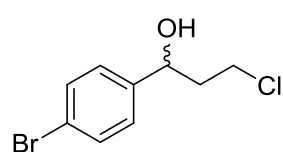
(rac)-3-chloro-1-(4-fluorophenyl)propan-1-ol [(rac)-11a]



(rac)-3-chloro-1-(4-chlorophenyl)propan-1-ol [(rac)-12a]

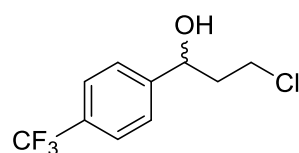


(rac)-1-(4-bromophenyl)-3-chloropropan-1-ol [(rac)-13a]



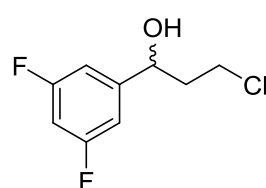
¹H NMR (400 MHz, CDCl₃) δ 7.48 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 4.90 (dd, *J* = 8.7, 4.7 Hz, 1H), 3.75 - 3.69 (m, 1H), 3.53 (dt, *J* = 12.6, 4.2 Hz, 1H), 2.22 - 2.13 (m, 2H), 2.07 - 1.99 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 142.8, 131.8, 127.6, 121.8, 70.7, 41.6, 41.4.

(rac)-3-chloro-1-(4-(trifluoromethyl)phenyl)propan-1-ol [(rac)-14a]



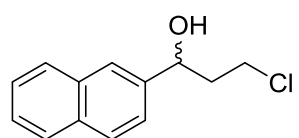
¹H NMR (400 MHz, CDCl₃) δ 7.62 (d, *J* = 8.1 Hz, 2H), 7.48 (d, *J* = 8.0 Hz, 2H), 5.02 (dd, *J* = 8.8, 4.4 Hz, 1H), 3.79 - 3.73 (m, 1H), 3.56 (dt, *J* = 11.0, 5.7 Hz, 1H), 2.39 (s, 1H), 2.22 - 2.15 (m, 1H), 2.11 - 2.02 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 147.8, 130.1 (d, *J* = 32.0 Hz), 127.2, 125.7 (q, *J* = 3.0 Hz), 125.5 (t, *J* = 270.0 Hz), 70.7, 41.6, 41.5.

(rac)-3-chloro-1-(3,5-difluorophenyl)propan-1-ol [(rac)-15a]



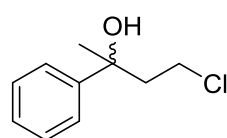
¹H NMR (400 MHz, CDCl₃) δ 6.89 (d, *J* = 6.0 Hz, 2H), 6.72 (tt, *J* = 8.8, 2.5 Hz, 1H), 4.94 (dd, *J* = 8.4, 4.0 Hz, 1H), 3.78 - 3.72 (m, 1H), 3.59 - 3.53 (m, 1H), 2.19 - 2.10 (m, 1H), 2.08 - 2.00 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) 163.3 (dd, *J* = 248.0, 13.0 Hz), 148.0 (t, *J* = 9.0 Hz), 108.7 (dd, *J* = 19.0, 7.0 Hz), 103.2 (t, *J* = 25.0 Hz), 70.4 (d, *J* = 12.0 Hz), 41.4 (d, *J* = 10.0 Hz).

(rac)-3-chloro-1-(naphthalen-2-yl)propan-1-ol [(rac)-16a]



¹H NMR (400 MHz, CDCl₃) δ 8.13 - 8.10 (m, 1H), 7.90 - 7.88 (m, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.66 (d, *J* = 7.2 Hz, 1H), 7.57 - 7.46 (m, 3H), 5.73 (dd, *J* = 8.9, 3.5 Hz, 1H), 3.94 - 3.88 (m, 1H), 3.68 (dt, *J* = 10.8, 4.8 Hz, 1H), 2.36 - 2.20 (m, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 139.7, 133.9, 130.2, 129.1, 128.4, 126.4, 125.8, 125.6, 123.0, 122.8, 68.0, 42.4, 40.8.

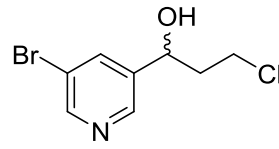
(rac)-4-chloro-2-phenylbutan-2-ol [(rac)-17a]



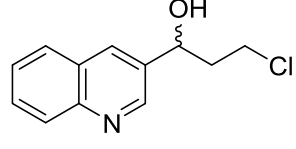
¹H NMR (400 MHz, CDCl₃) δ 7.44 - 7.41 (m, 2H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.29 - 7.25 (m, 1H), 3.58 - 3.51 (m, 1H), 3.37 - 3.31 (m, 1H), 2.37 - 2.26 (m,

2H), 1.61 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 146.5, 128.6, 127.1, 124.6, 74.4, 46.7, 40.6, 31.0.

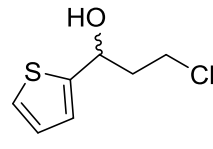
(rac)-1-(5-bromopyridin-3-yl)-3-chloropropan-1-ol [(rac)-18a]

 ^1H NMR (400 MHz, CDCl_3) δ 8.54 (d, $J = 2.2$ Hz, 1H), 8.45 (d, $J = 1.9$ Hz, 1H), 7.90 (t, $J = 2.0$ Hz, 1H), 5.01 (dd, $J = 9.1, 4.1$ Hz, 1H), 3.83 - 3.76 (m, 1H), 3.60 (dt, $J = 11.1, 5.4$ Hz, 1H), 2.24 - 2.15 (m, 1H), 2.10 - 2.02 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 150.2, 145.7, 141.5, 136.5, 121.2, 68.1, 41.4, 41.3.

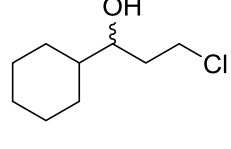
(rac)-3-chloro-1-(quinolin-3-yl)propan-1-ol [(rac)-19a]

 ^1H NMR (400 MHz, CDCl_3) δ 8.68 - 8.64 (m, 1H), 8.06 (s, 1H), 7.96 (d, $J = 8.7$ Hz, 1H), 7.70 (d, $J = 8.0$ Hz, 1H), 7.62 (t, $J = 7.3$ Hz, 1H), 7.49 (t, $J = 7.6$ Hz, 1H), 5.11 - 5.08 (m, 1H), 3.83 - 3.77 (m, 1H), 3.56 (dt, $J = 11.3, 5.4$ Hz, 1H), 2.28 - 2.20 (m, 1H), 2.12 - 2.02 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 149.0, 147.2, 137.1, 133.2, 129.7, 128.6, 127.9, 127.8, 127.1, 68.7, 41.6, 41.4.

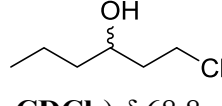
(rac)-3-chloro-1-(thiophen-2-yl)propan-1-ol [(rac)-20a]

 ^1H NMR (400 MHz, CDCl_3) δ 7.27 (dd, $J = 5.0, 1.4$ Hz, 1H), 7.02 - 6.96 (m, 2H), 5.20 (dd, $J = 8.5, 5.2$ Hz, 1H), 3.78 - 3.72 (m, 1H), 3.58 (dt, $J = 10.9, 5.9$ Hz, 1H), 2.37 - 2.28 (m, 2H), 2.24 - 2.15 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 147.6, 126.9, 125.1, 124.3, 67.2, 41.6.

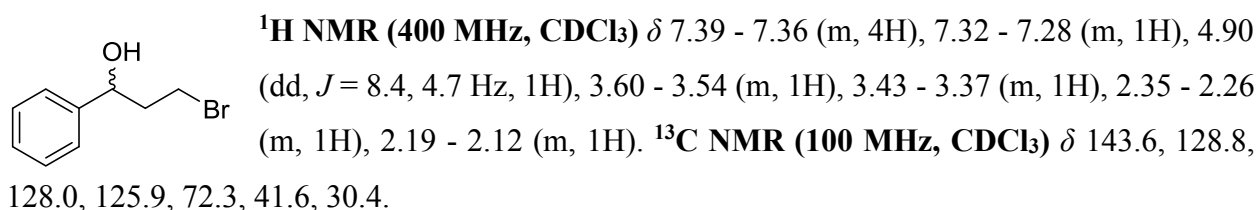
(rac)-3-chloro-1-cyclohexylpropan-1-ol [(rac)-21a]

 ^1H NMR (400 MHz, CDCl_3) δ 3.70 - 3.66 (m, 2H), 3.58 - 3.53 (m, 1H), 1.98 (s, 1H), 1.93 - 1.71 (m, 5H), 1.65 (d, $J = 10.7$ Hz, 1H), 1.35 - 0.90 (m, 6H). ^{13}C NMR (100 MHz, CDCl_3) δ 73.0, 43.8, 42.2, 36.8, 29.1, 28.0, 26.5, 26.3, 26.1.

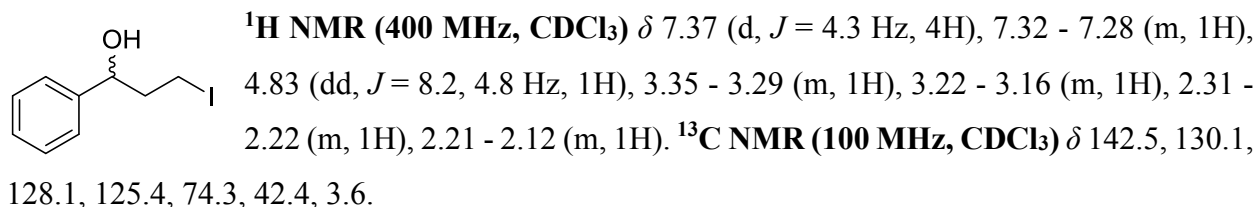
(rac)-1-chlorohexan-3-ol [(rac)-22a]

 ^1H NMR (400 MHz, CDCl_3) δ 3.86 - 3.80 (m, 1H), 3.74 - 3.62 (m, 2H), 1.93 - 1.78 (m, 3H), 1.48 - 1.33 (m, 4H), 0.94 - 0.91 (m, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 68.8, 42.1, 39.9, 39.8, 18.8, 14.1.

(rac)-3-bromo-1-phenylpropan-1-ol [(rac)-23a]

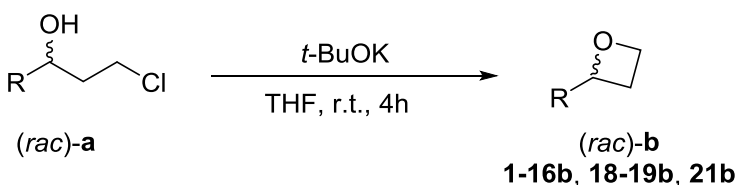


(rac)-3-iodo-1-phenylpropan-1-ol [(rac)-24a]

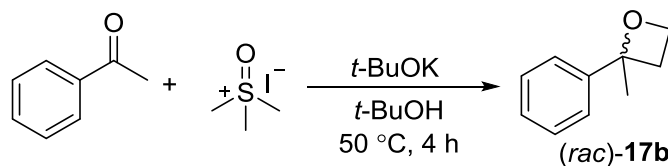


Synthesis of racemic oxetanes:

Method A



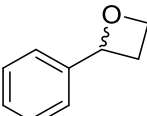
Method B



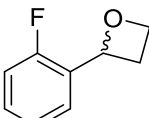
Racemic oxetanes **1-16b**, **18-19b**, and **21b** were synthesized from the corresponding γ -haloalcohols (Method A)²⁸. General procedure: To a 100-mL round-bottom flask, 10 mmol of γ -haloalcohols (*rac*)-**a** substrates and 20 mL THF were added, followed by the addition of 3.4 g (30 mmol) of potassium tert-butoxide (*t*-BuOK). The reaction mixture was then stirred at room temperature for 4 h. Afterward, the reaction mixture was quenched with 10 mL of distilled water, extracted with ethyl acetate (3 $\times$ 15 mL), and washed with saturated brine. The organic layer was then dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to obtain the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 50:1 ~ 10:1) to afford the racemic oxetanes (*rac*)-**b**.

Racemic oxetane **17b** was synthesized from acetophenone (Method B)²⁹. To a 200-mL round-bottom flask, 20 mmol of trimethylsulfoxonium iodide (4.4 g) and 20 mL of tertbutanol were added, followed by the addition of 2.2 g (20 mmol) of *t*-BuOK. The reaction mixture was then heated to 50 °C in an oil bath and stirred for 2 h. Afterwards, a solution of 10 mmol acetophenone in 10 mL tertbutanol was added dropwise to the reaction mixture. The reaction was allowed to proceed at 50 °C for 24 h. Water was added and the resulting layers were separated. The aqueous phase was extracted with hexane (thrice). The organic layers were then combined, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to obtain the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 80:1) to afford the racemic oxetane (*rac*)-**17b**.

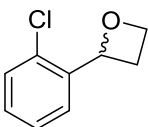
(*rac*)-2-phenyloxetane [(*rac*)-1b]

 ¹H NMR (400 MHz, CDCl₃) δ 7.48 - 7.46 (m, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.36 - 7.30 (m, 1H), 5.84 (t, *J* = 7.5 Hz, 1H), 4.85 (td, *J* = 8.0, 5.8 Hz, 1H), 4.68 (dt, *J* = 9.3, 5.8 Hz, 1H), 3.09 - 2.99 (m, 1H), 2.74 - 2.64 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 143.6, 128.5, 127.9, 125.3, 83.0, 68.3, 30.8.

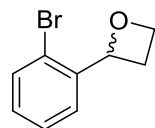
(*rac*)-2-(2-fluorophenyl)oxetane [(*rac*)-2b]

 ¹H NMR (400 MHz, CDCl₃) δ 7.67 (t, *J* = 7.5 Hz, 1H), 7.29 - 7.24 (m, 1H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.01 (t, *J* = 10.2 Hz, 1H), 6.05 (t, *J* = 7.6 Hz, 1H), 4.83 (td, *J* = 8.1, 6.2 Hz, 1H), 4.68 (dt, *J* = 9.2, 5.9 Hz, 1H), 3.12 - 3.04 (m, 1H), 2.70 - 2.61 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 159.3 (d, *J* = 245.0 Hz), 130.8 (d, *J* = 14.0 Hz), 129.2 (d, *J* = 8.0 Hz), 126.9 (d, *J* = 4.3 Hz), 124.3 (d, *J* = 3.5 Hz), 115.2 (d, *J* = 20.9 Hz), 77.7, 68.8, 29.9.

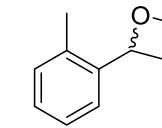
(*rac*)-2-(2-chlorophenyl)oxetane [(*rac*)-3b]

 ¹H NMR (400 MHz, CDCl₃) δ 7.75 (dt, *J* = 7.4, 1.4 Hz, 1H), 7.39 - 7.30 (m, 2H), 7.27 - 7.19 (m, 1H), 6.02 (t, *J* = 7.5 Hz, 1H), 4.84 (ddd, *J* = 8.4, 7.4, 5.8 Hz, 1H), 4.65 (dt, *J* = 9.1, 6.0 Hz, 1H), 3.24 - 3.13 (m, 1H), 2.58 - 2.45 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 141.4, 130.4, 129.2, 128.5, 127.0, 126.0, 80.4, 68.6, 30.0.

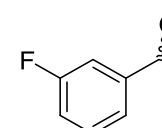
(rac)-2-(2-bromophenyl)oxetane [(rac)-4b]

**¹H NMR (400 MHz, CDCl₃)** δ 7.75 (ddd, J = 7.7, 1.8, 0.8 Hz, 1H), 7.51 (dd, J = 7.9, 1.2 Hz, 1H), 7.40 (td, J = 7.6, 1.2 Hz, 1H), 7.16 (td, J = 7.7, 1.7 Hz, 1H), 5.94 (t, J = 7.5 Hz, 1H), 4.83 (ddd, J = 8.4, 7.3, 5.8 Hz, 1H), 4.64 (dt, J = 9.1, 6.0 Hz, 1H), 3.27 - 3.17 (m, 1H), 2.53 - 2.43 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 142.9, 132.4, 128.8, 127.6, 126.3, 119.8, 82.2, 68.4, 30.1.

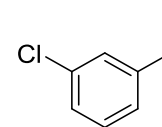
(rac)-2-(o-tolyl)oxetane [(rac)-5b]

**¹H NMR (400 MHz, CDCl₃)** δ 7.74 (d, J = 7.7 Hz, 1H), 7.33 (t, J = 7.5 Hz, 1H), 7.24 (t, J = 7.3 Hz, 1H), 7.17 (d, J = 7.5 Hz, 1H), 6.02 (t, J = 7.6 Hz, 1H), 4.88 (td, J = 8.0, 5.9 Hz, 1H), 4.68 (dt, J = 9.1, 5.8 Hz, 1H), 3.16 - 3.06 (m, 1H), 2.62 - 2.52 (m, 1H), 2.21 (s, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 141.7, 133.3, 130.0, 127.2, 126.1, 124.0, 80.6, 68.1, 29.7, 18.4.

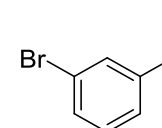
(rac)-2-(3-fluorophenyl)oxetane [(rac)-6b]

**¹H NMR (400 MHz, CDCl₃)** δ 7.34 (td, J = 7.8, 5.7 Hz, 1H), 7.20 - 7.15 (m, 2H), 6.98 (td, J = 8.4, 2.5 Hz, 1H), 5.79 (t, J = 7.5 Hz, 1H), 4.83 (td, J = 8.1, 6.2 Hz, 1H), 4.66 (dt, J = 9.3, 5.8 Hz, 1H), 3.09 - 3.00 (m, 1H), 2.66 - 2.57 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 163.2 (d, J = 246.0 Hz), 146.5 (d, J = 6.8 Hz), 130.2 (d, J = 8.2 Hz), 120.7 (d, J = 2.8 Hz), 114.7 (d, J = 21.1 Hz), 112.2 (d, J = 22.1 Hz), 82.2, 68.5, 30.7.

(rac)-2-(3-chlorophenyl)oxetane [(rac)-7b]

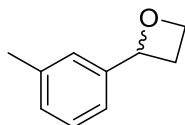
**¹H NMR (400 MHz, CDCl₃)** δ 7.45 (s, 1H), 7.34 - 7.24 (m, 3H), 5.77 (t, J = 7.5 Hz, 1H), 4.83 (td, J = 8.0, 5.9 Hz, 1H), 4.66 (dt, J = 9.2, 5.9 Hz, 1H), 3.08 - 2.99 (m, 1H), 2.67 - 2.56 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 145.8, 134.6, 129.9, 127.9, 125.4, 123.3, 82.2, 68.5, 30.7.

(rac)-2-(3-bromophenyl)oxetane [(rac)-8b]

**¹H NMR (400 MHz, CDCl₃)** δ 7.61 (s, 1H), 7.41 (d, J = 7.8 Hz, 1H), 7.32 (d, J = 7.7 Hz, 1H), 7.24 (t, J = 7.8 Hz, 1H), 5.75 (t, J = 7.5 Hz, 1H), 4.81 (td, J = 8.0, 6.0 Hz, 1H), 4.69 - 4.59 (m, 1H), 3.06 - 2.97 (m, 1H), 2.65 - 2.54 (m, 1H).

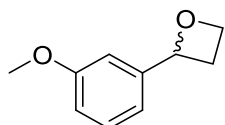
^{13}C NMR (100 MHz, CDCl_3) δ 146.0, 130.7, 130.1, 128.2, 123.7, 122.7, 82.0, 68.4, 30.7.

(rac)-2-(*m*-tolyl)oxetane [(rac)-9b]



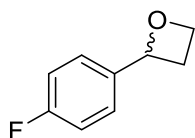
^1H NMR (400 MHz, CDCl_3) δ 7.37 - 7.24 (m, 3H), 7.16 (d, J = 7.4 Hz, 1H), 5.83 (t, J = 7.5 Hz, 1H), 4.86 (td, J = 8.1, 5.9 Hz, 1H), 4.69 (dt, J = 9.1, 5.7 Hz, 1H), 3.08 - 2.99 (m, 1H), 2.75 - 2.65 (m, 1H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.5, 138.1, 128.5, 128.4, 125.8, 122.3, 82.9, 68.2, 30.7, 21.4.

(rac)-2-(3-methoxyphenyl)oxetane [(rac)-10b]



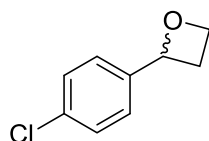
^1H NMR (400 MHz, CDCl_3) δ 7.31 (t, J = 7.9 Hz, 1H), 7.05 - 6.96 (m, 2H), 6.85 (ddd, J = 8.2, 2.6, 1.0 Hz, 1H), 5.80 (t, J = 7.5 Hz, 1H), 4.83 (td, J = 8.0, 5.8 Hz, 1H), 4.66 (dt, J = 9.2, 5.8 Hz, 1H), 3.84 (s, 3H), 3.07 - 2.98 (m, 1H), 2.70 - 2.60 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 159.9, 145.4, 129.7, 117.4, 113.4, 110.5, 82.8, 68.4, 55.3, 30.7.

(rac)-2-(4-fluorophenyl)oxetane [(rac)-11b]



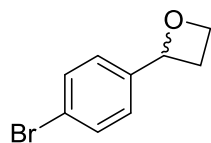
^1H NMR (400 MHz, CDCl_3) δ 7.42 (dd, J = 8.4, 5.6 Hz, 2H), 7.07 (t, J = 8.5 Hz, 2H), 5.78 (t, J = 7.5 Hz, 1H), 4.81 (td, J = 8.4, 6.4 Hz, 1H), 4.63 (dt, J = 9.0, 5.7 Hz, 1H), 3.04 - 2.96 (m, 1H), 2.68 - 2.59 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 162.4 (d, J = 245.7 Hz), 139.4 (d, J = 3.0 Hz), 127.2 (d, J = 8.2 Hz), 115.4 (d, J = 21.5 Hz), 82.4, 68.2, 30.9.

(rac)-2-(4-chlorophenyl)oxetane [(rac)-12b]



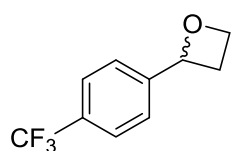
^1H NMR (400 MHz, CDCl_3) δ 7.39 - 7.31 (m, 4H), 5.76 (t, J = 7.5 Hz, 1H), 4.81 (td, J = 8.0, 5.9 Hz, 1H), 4.63 (dt, J = 9.2, 5.8 Hz, 1H), 3.05 - 2.96 (m, 1H), 2.64 - 2.54 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.1, 133.4, 128.6, 126.7, 82.1, 68.2, 30.8.

(rac)-2-(4-bromophenyl)oxetane [(rac)-13b]



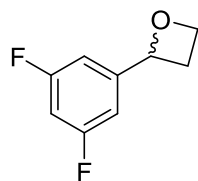
^1H NMR (400 MHz, CDCl_3) δ 7.55 - 7.44 (m, 2H), 7.33 - 7.27 (m, 2H), 5.74 (t, J = 7.6 Hz, 1H), 4.80 (td, J = 8.1, 5.9 Hz, 1H), 4.62 (dt, J = 9.3, 5.8 Hz, 1H), 3.04 - 2.94 (m, 1H), 2.62 - 2.52 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.6, 131.5, 126.9, 121.5, 82.1, 68.2, 30.6.

(rac)-2-(4-(trifluoromethyl)phenyl)oxetane [(rac)-14b]



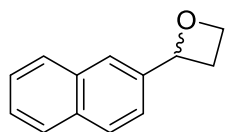
^1H NMR (400 MHz, CDCl_3) δ 7.64 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.1 Hz, 2H), 5.85 (t, J = 7.6 Hz, 1H), 4.84 (td, J = 8.0, 6.0 Hz, 1H), 4.66 (dt, J = 9.2, 5.9 Hz, 1H), 3.11 - 3.02 (m, 1H), 2.64 - 2.55 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 147.8, 129.9 (q, J = 32.0 Hz), 125.6 (q, J = 3.0 Hz), 125.4, 124.2 (q, J = 270.0 Hz), 82.5, 68.6, 30.7.

(rac)-2-(3,5-difluorophenyl)oxetane [(rac)-15b]



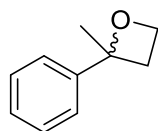
^1H NMR (400 MHz, CDCl_3) δ 6.93 - 6.87 (m, 2H), 6.66 (tt, J = 8.9, 2.4 Hz, 1H), 5.70 (t, J = 7.5 Hz, 1H), 4.76 (td, J = 8.2, 6.1 Hz, 1H), 4.59 (dt, J = 9.2, 6.1 Hz, 1H), 3.04 - 2.96 (m, 1H), 2.56 - 2.47 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 163.2 (dd, J = 247.0, 12.0 Hz), 148.0 (t, J = 8.0 Hz), 107.8 (dd, J = 19.0, 7.0 Hz), 103.0 (td, J = 26.0, 6.0 Hz), 81.7, 68.3, 30.6.

(rac)-2-(naphthalen-2-yl)oxetane [(rac)-16b]



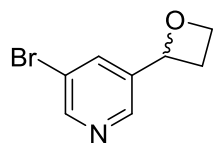
^1H NMR (400 MHz, CDCl_3) δ 8.06 - 7.98 (m, 2H), 7.89 (d, J = 8.4 Hz, 1H), 7.75 - 7.73 (m, 1H), 7.69 - 7.65 (m, 2H), 7.60 - 7.57 (m, 2H), 6.56 (t, J = 7.5 Hz, 1H), 5.02 - 4.95 (m, 1H), 4.80 - 4.74 (m, 1H), 3.27 - 3.16 (m, 1H), 2.75 - 2.64 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 139.1, 133.4, 128.8, 128.6, 127.4, 125.7, 125.4, 125.4, 122.5, 121.2, 80.3, 68.3, 29.8.

(rac)-2-methyl-2-phenyloxetane [(rac)-17b]



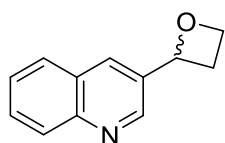
^1H NMR (400 MHz, CDCl_3) δ 7.45 - 7.38 (m, 4H), 7.30 - 7.26 (m, 1H), 4.66 (dt, J = 8.6, 6.3 Hz, 1H), 4.55 (dt, J = 9.1, 6.6 Hz, 1H), 2.86 - 2.73 (m, 1H), 1.77 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 148.2, 128.2, 126.6, 123.6, 86.5, 64.5, 35.5, 30.7.

(rac)-3-bromo-5-(oxetan-2-yl) pyridine [(rac)-18b]



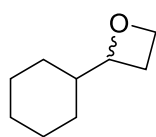
^1H NMR (400 MHz, CDCl_3) δ 8.59 (d, J = 2.3 Hz, 1H), 8.49 (d, J = 1.9 Hz, 1H), 7.96 (t, J = 2.1 Hz, 1H), 5.79 (t, J = 7.5 Hz, 1H), 4.83 (td, J = 8.0, 5.9 Hz, 1H), 4.66 (dt, J = 9.2, 5.9 Hz, 1H), 3.11 - 3.03 (m, 1H), 2.66 - 2.58 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 150.3, 145.2, 140.7, 135.7, 121.1, 79.8, 68.7, 30.5.

(rac)-3-(oxetan-2-yl)quinoline [(rac)-19b]



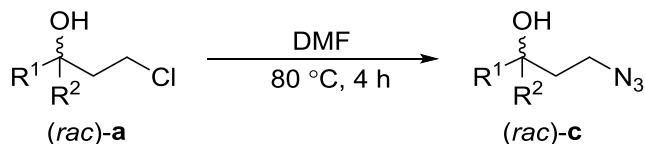
^1H NMR (400 MHz, CDCl_3) δ 8.94 (d, J = 2.2 Hz, 1H), 8.21 (s, 1H), 8.11 (d, J = 8.5 Hz, 1H), 7.83 (d, J = 8.2 Hz, 1H), 7.74 - 7.66 (m, 1H), 7.55 (td, J = 8.1, 1.2 Hz, 1H), 6.01 (t, J = 7.6 Hz, 1H), 4.90 (td, J = 8.0, 5.8 Hz, 1H), 4.75 (dt, J = 9.2, 5.8 Hz, 1H), 3.18 - 3.09 (m, 1H), 2.78 - 2.69 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 148.6, 147.9, 136.1, 132.3, 129.6, 129.3, 128.0, 127.8, 127.0, 81.0, 68.7, 30.7.

(rac)-2-cyclohexyloxetane [(rac)-21b]



^1H NMR (400 MHz, CDCl_3) δ 4.63 (td, J = 8.1, 5.9 Hz, 1H), 4.51 - 4.35 (m, 2H), 2.60 - 2.48 (m, 1H), 2.42 - 2.29 (m, 1H), 1.89 - 1.81 (m, 1H), 1.79 - 1.53 (m, 5H), 1.31 - 1.09 (m, 3H), 0.91 - 0.74 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 86.8, 68.2, 44.8, 27.6, 27.5, 26.6, 26.2, 25.8, 25.6.

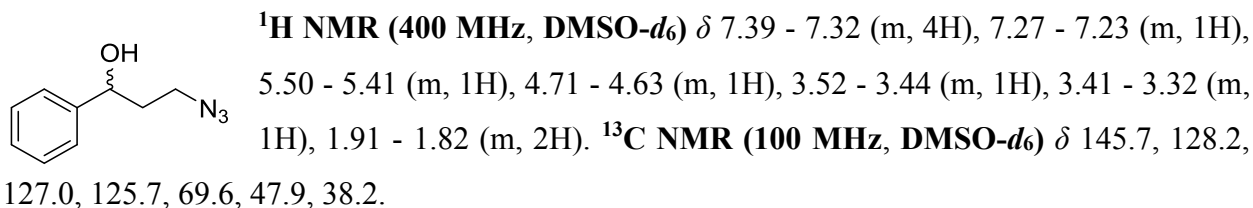
Synthesis of racemic γ -azidoalcohols³⁰:



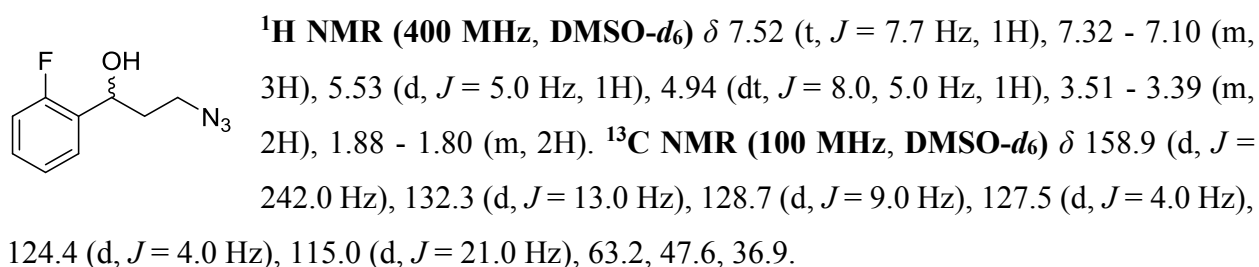
General procedure: To a 10-mL round-bottom flask, 1.0 mmol of racemic γ -haloalcohol substrates (*rac*)-**a** and 2 mL of *N,N*-dimethylformamide (DMF) were added, followed by the addition of 4.0 mmol 260.0 mg (4.0 mmol) NaN_3 . The reaction mixture was then stirred at room temperature for 15 min. The temperature was then gradually raised to 80 °C and the reaction was allowed to proceed for 4 h. Afterward, the reaction mixture was quenched with 10 mL of distilled water, extracted with ethyl acetate (3×5 mL), and washed with distilled water (twice) and saturated NH_4Cl solution (thrice). The organic layer was then dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to obtain the crude product. The resulting mixture was

purified by flash chromatography (petroleum ether: ethyl acetate = 10:1 ~ 3:1) to afford the racemic γ -azidoalcohols (*rac*)-**c**.

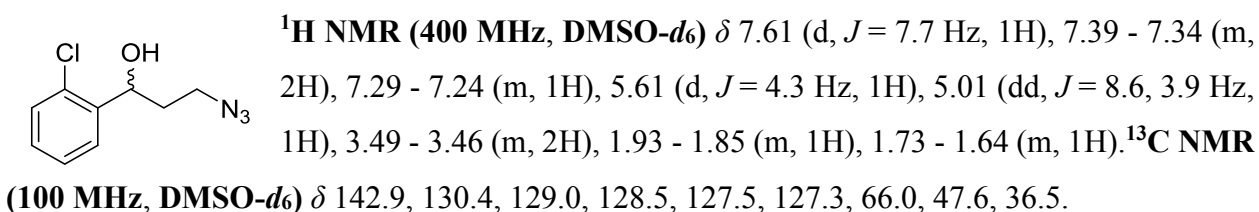
(*rac*)-3-azido-1-phenylpropan-1-ol [(*rac*)-1c]



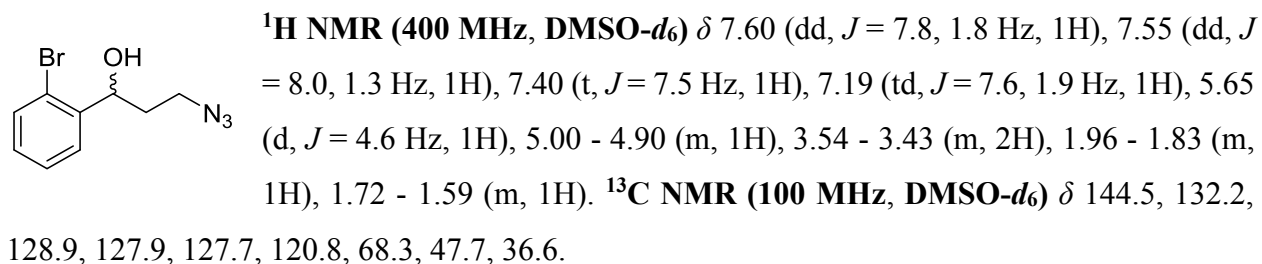
(*rac*)-3-azido-1-(2-fluorophenyl)propan-1-ol [(*rac*)-2c]



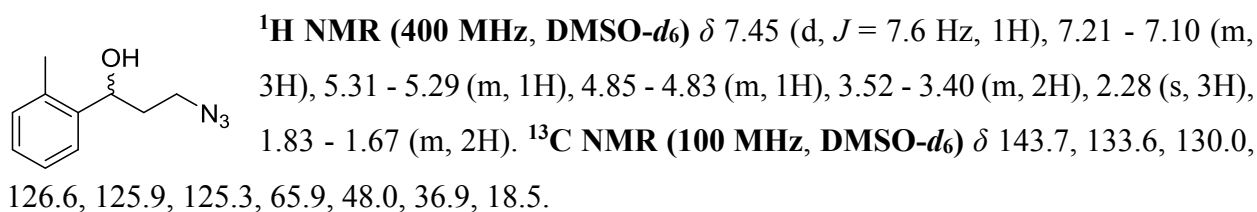
(*rac*)-3-azido-1-(2-chlorophenyl)propan-1-ol [(*rac*)-3c]



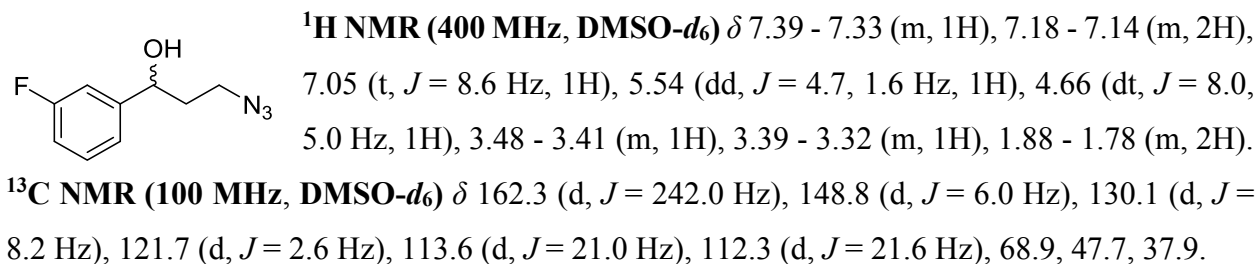
(*rac*)-3-azido-1-(2-bromophenyl)propan-1-ol [(*rac*)-4c]



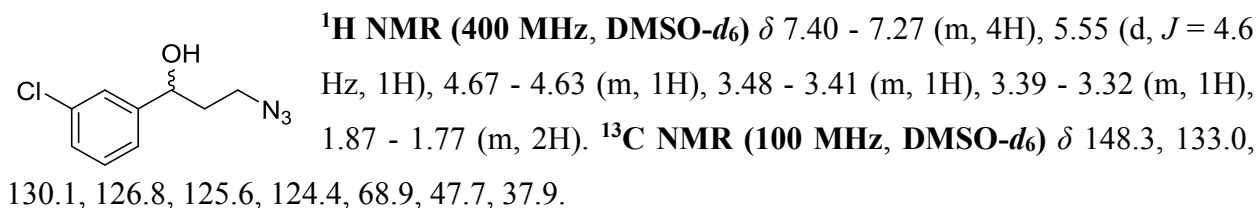
(rac)-3-azido-1-(o-tolyl)propan-1-ol [(rac)-5c]



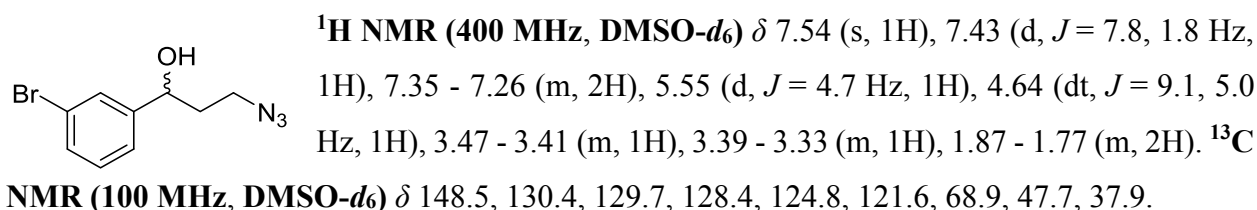
(rac)-3-azido-1-(3-fluorophenyl)propan-1-ol [(rac)-6c]



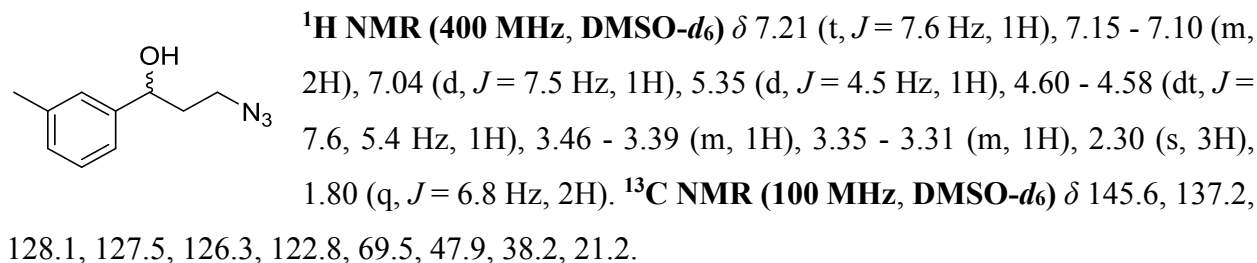
(rac)-3-azido-1-(3-chlorophenyl)propan-1-ol [(rac)-7c]



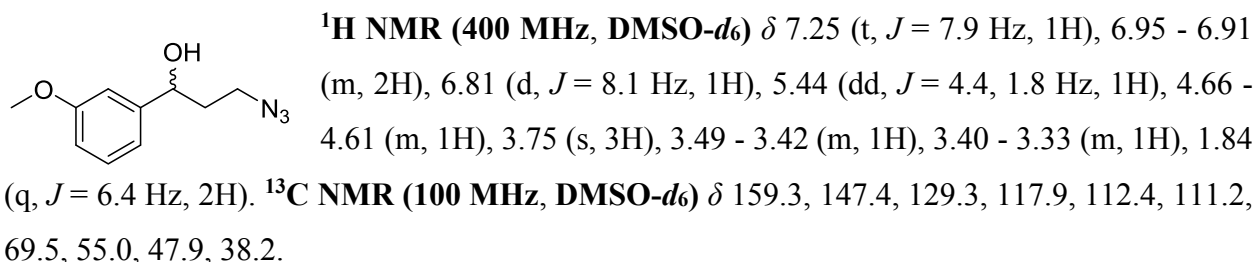
(rac)-3-azido-1-(3-bromophenyl)propan-1-ol [(rac)-8c]



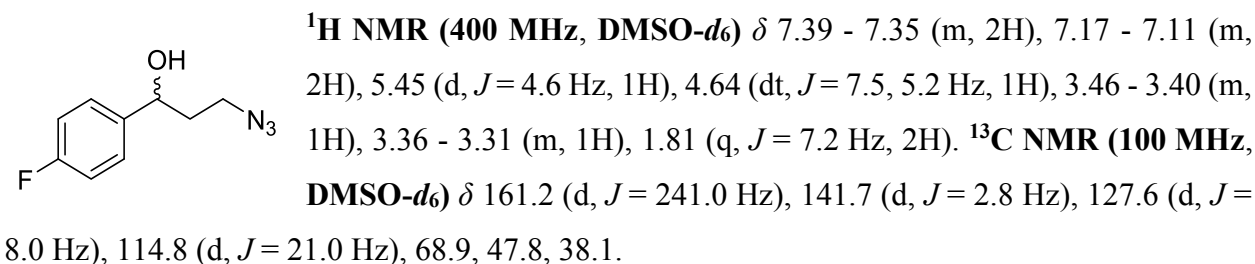
(rac)-3-azido-1-(*m*-tolyl)propan-1-ol [(rac)-9c]



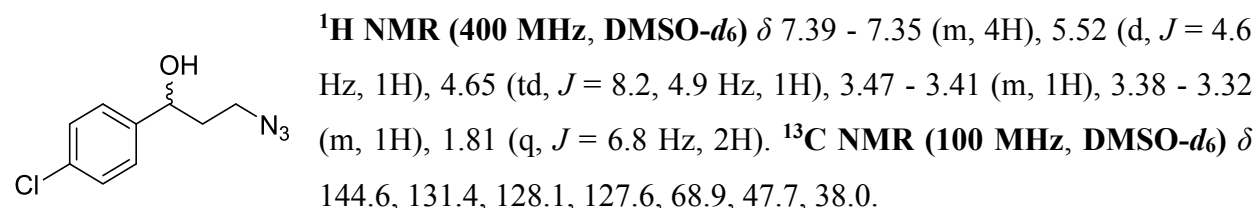
(rac)-3-azido-1-(3-methoxyphenyl)propan-1-ol [(rac)-10c]



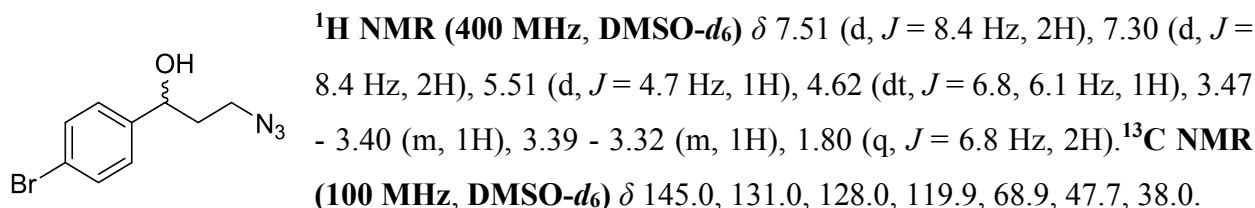
(rac)-3-azido-1-(4-fluorophenyl)propan-1-ol [(rac)-11c]



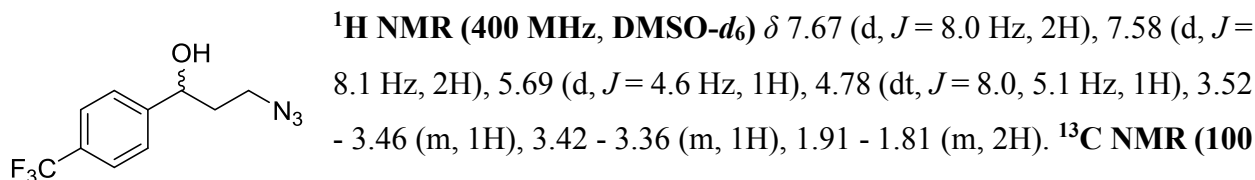
(rac)-3-azido-1-(4-chlorophenyl)propan-1-ol [(rac)-12c]



(rac)-3-azido-1-(4-bromophenyl)propan-1-ol [(rac)-13c]

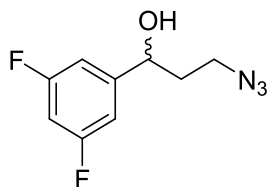


(rac)-3-azido-1-(4-(trifluoromethyl)phenyl)propan-1-ol [(rac)-14c]



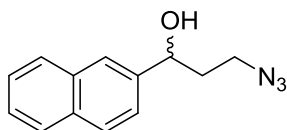
MHz, DMSO-*d*₆) δ 150.5, 127.9 (q, J = 31.0 Hz), 126.6 - 126.4 (m), 125.2 - 125.0 (m), 124.5 (q, J = 270.0 Hz), 69.2, 47.8, 38.1.

(*rac*)-3-azido-1-(3,5-difluorophenyl)propan-1-ol [(*rac*)-15c]



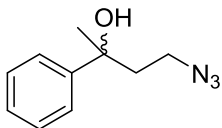
¹H NMR (400 MHz, DMSO-*d*₆) δ 7.09 - 7.04 (m, 3H), 5.66 (d, J = 4.9 Hz, 1H), 4.67 (dt, J = 8.7, 4.6 Hz, 1H), 3.47 - 3.42 (m, 1H), 3.40 - 3.37 (m, 1H), 1.90 - 1.74 (m, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 163.7 (d, J = 12.9 Hz), 161.2 (d, J = 13.0 Hz), 150.7 (t, J = 8.2 Hz), 108.8 (dd, J = 25.0, 7.0 Hz), 102.2 (t, J = 25.7 Hz), 68.7, 47.7, 37.7.

(*rac*)-3-azido-1-(naphthalen-2-yl)propan-1-ol [(*rac*)-16c]



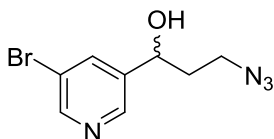
¹H NMR (400 MHz, DMSO-*d*₆) δ 8.19 - 8.13 (m, 1H), 7.95 - 7.68 (m, 3H), 7.58 - 7.48 (m, 3H), 5.67 - 5.60 (m, 1H), 5.49 - 5.41 (m, 1H), 3.70 - 3.59 (m, 1H), 3.46 - 3.41 (m, 1H), 2.09 - 1.85 (m, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 141.3, 133.4, 129.8, 128.8, 127.3, 126.0, 125.5, 123.2, 122.9, 66.4, 48.2, 37.7.

(*rac*)-4-azido-2-phenylbutan-2-ol [(*rac*)-17c]



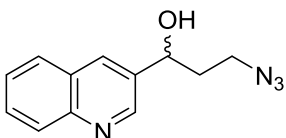
¹H NMR (400 MHz, DMSO-*d*₆) δ 7.46 - 7.44 (m, 2H), 7.31 (t, J = 7.4 Hz, 2H), 7.21 - 7.19 (m, 1H), 5.20 (s, 1H), 3.36 - 3.28 (m, 1H), 3.04 - 2.97 (m, 1H), 2.03 - 1.98 (m, 2H), 1.46 (s, 3H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 148.3, 127.9, 126.2, 124.8, 71.8, 46.9, 42.1, 30.5.

(*rac*)-3-azido-1-(5-bromopyridin-3-yl)propan-1-ol [(*rac*)-18c]



¹H NMR (400 MHz, DMSO-*d*₆) δ 8.56 (dd, J = 16.0, 2.3 Hz, 2H), 8.00 (t, J = 2.1 Hz, 1H), 5.72 (d, J = 4.8 Hz, 1H), 4.72 (dt, J = 7.9, 5.0 Hz, 1H), 3.50 - 3.45 (m, 1H), 3.43 - 3.38 (m, 1H), 1.90 - 1.85 (m, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 148.9, 146.2, 143.1, 136.0, 120.2, 67.0, 47.6, 37.5.

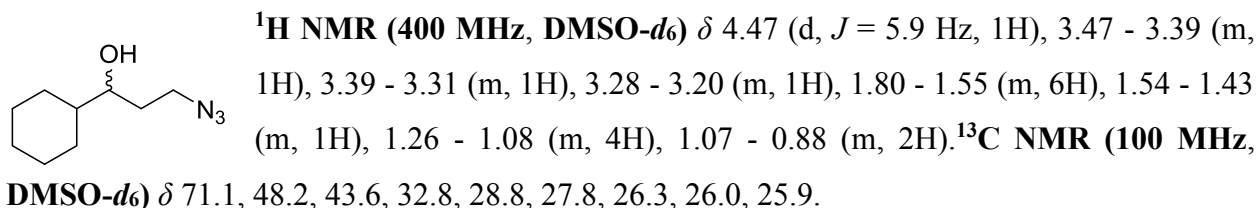
(*rac*)-3-azido-1-(quinolin-3-yl)propan-1-ol [(*rac*)-19c]



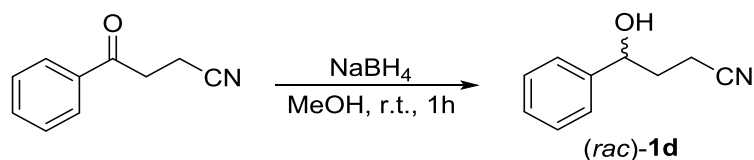
¹H NMR (400 MHz, DMSO-*d*₆) δ 8.95 (d, J = 2.2 Hz, 1H), 8.28 (d, J = 2.2 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.97 (dd, J = 8.2, 1.5 Hz, 1H), 7.71 (ddd, J = 8.4, 6.8, 1.5 Hz, 1H), 7.58 (ddd, J = 8.1, 6.8, 1.2 Hz, 1H), 5.80

(d, $J = 4.6$ Hz, 1H), 4.93 (dd, $J = 11.2, 6.8$ Hz, 1H), 3.58 - 3.50 (m, 1H), 3.47 - 3.41 (m, 1H), 2.00 (q, $J = 6.7$ Hz, 2H). ^{13}C NMR (100 MHz, DMSO- d_6) δ 149.7, 147.0, 138.1, 132.1, 129.1, 128.7, 128.1, 127.5, 126.7, 67.8, 47.7, 37.6.

(rac) 3-azido-1-cyclohexylpropan-1-ol [(rac)-21c]

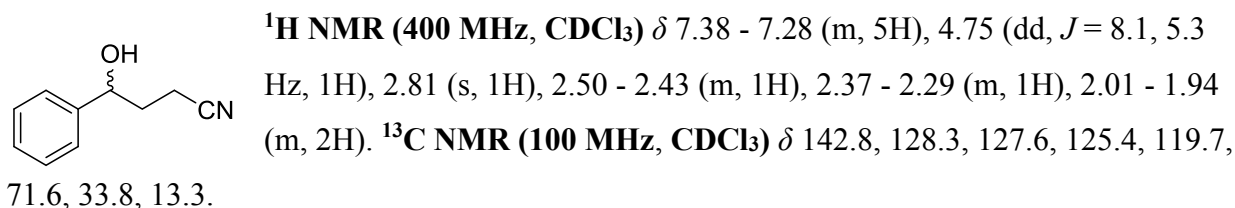


Synthesis of racemic γ -cyanohydrin³¹:

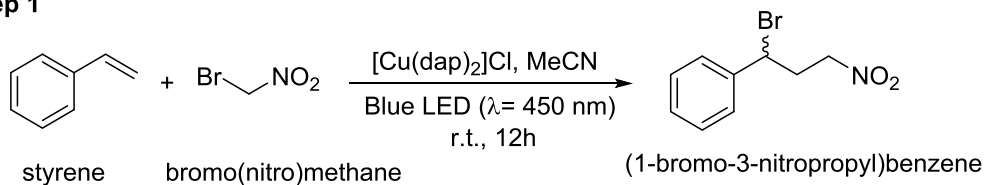
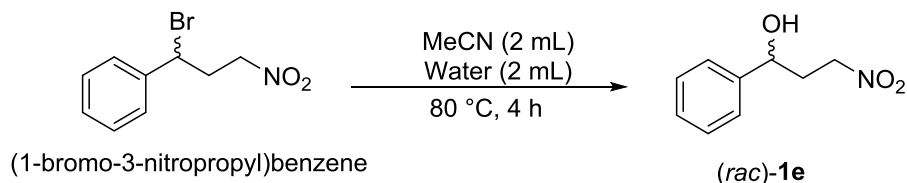


To a 10-mL round-bottom flask, 159.2 mg (1.0 mmol) of 4-oxo-4-phenylbutanenitrile and 2 mL of methanol were added. The flask was cooled to 0 °C, followed by the addition of 45.4 mg (1.2 mmol) of NaBH₄. The reaction mixture was then stirred at room temperature for 1 h. Afterward, the methanol solvent was removed under reduced pressure, followed by the addition of 5 mL distilled water to the flask. The mixture was then extracted with ethyl acetate (3×5 mL) and saturated brine (twice). The organic layer was then dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to obtain the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 2:1) to afford the racemic γ -cyanohydrin (rac)-**1d**.

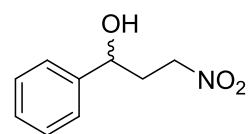
(rac)-4-hydroxy-4-phenylbutanenitrile [(rac)-1d]



Synthesis of racemic γ -nitroalcohol³²:

Step 1**Step 2**

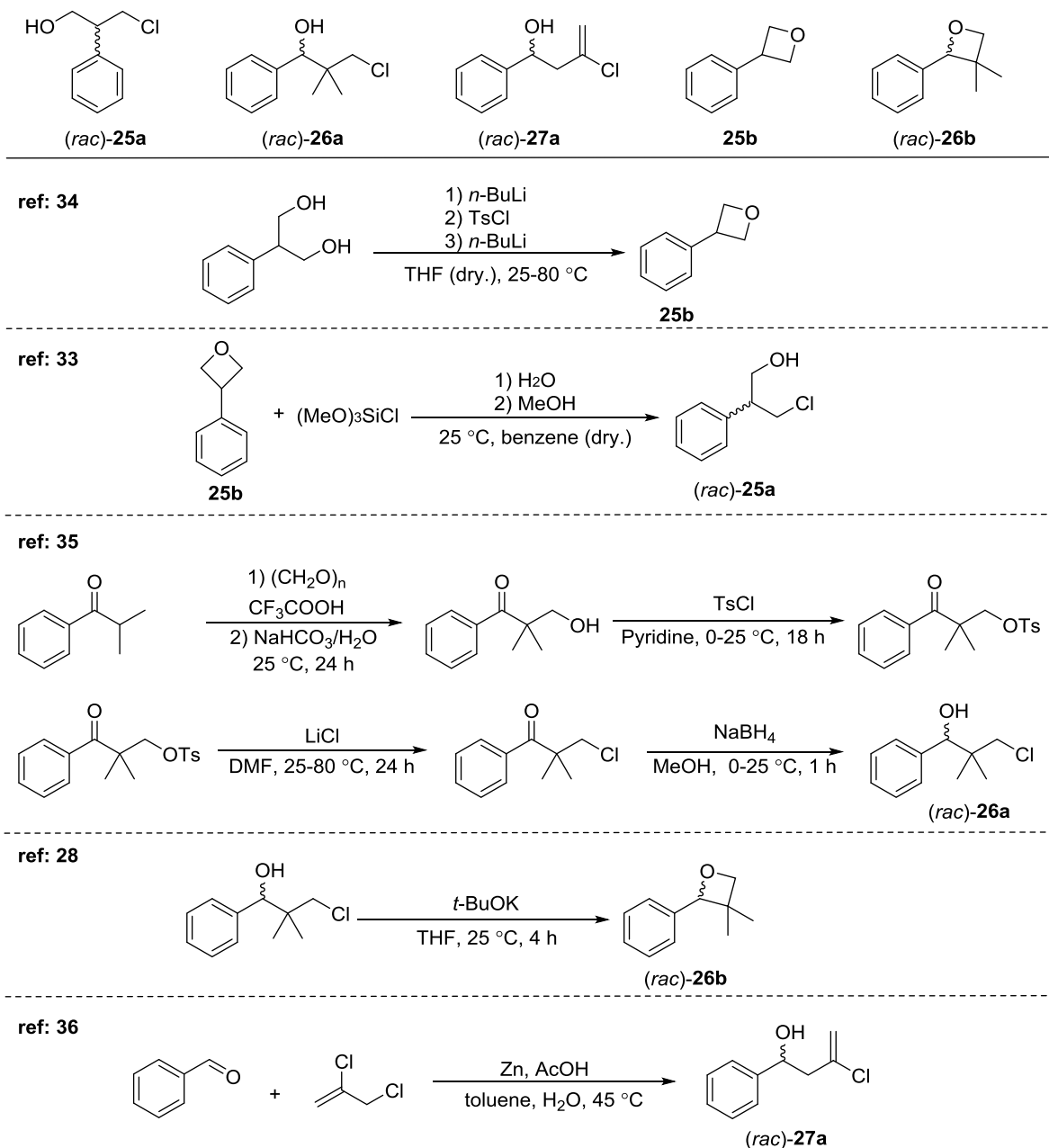
To a 10-mL round-bottom flask equipped with a magnetic stirring bar was charged with $[\text{Cu(dap)}_2]\text{Cl}$ (4.4 mg, 1 mol%, 0.01 equiv). Then dry MeCN (2 mL) was added under positive nitrogen atmosphere. Then 36 μL (0.5 mmol) of bromo(nitro)methane and 58 μL (0.5 mmol) styrene were added under nitrogen atmosphere. A Teflon sealed inlet for a glass rod was placed on the reaction tube, through which irradiation with $\text{LED}_{450 \text{ nm}}$ took place from above. The mixture was stirred in an aluminum block at room temperature for 12 h. Afterward, the reaction mixture was concentrated under reduced pressure to obtain the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 5:1) to afford the intermediate (1-bromo-3-nitropropyl)benzene. Then a 25-mL pressure tube equipped with a magnetic stirring bar was charged with 122.0 mg (0.50 mmol) of (1-bromo-3-nitropropyl)benzene and a mixture of MeCN and water (1:1, 4.0 mL) was added. The reaction mixture was then refluxed at 80 $^\circ\text{C}$ for 4 h. Afterward, the reaction mixture was concentrated under reduced pressure to obtain the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 2:1) to afford racemic γ -nitroalcohol (*rac*)-**1e**.

(*rac*)-3-nitro-1-phenylpropan-1-ol [(*rac*)-1e]

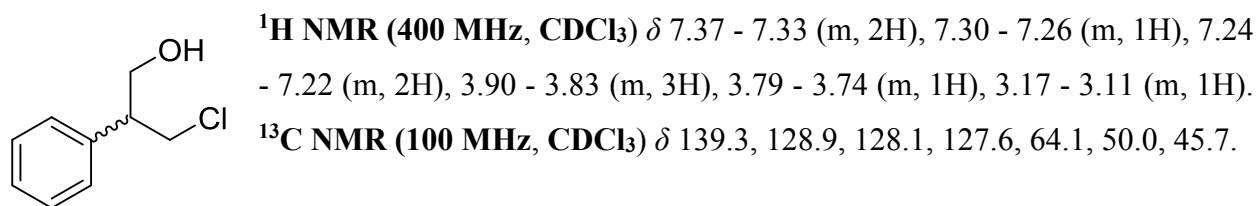
71.0, 35.8.

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.38 - 7.26 (m, 6H), 4.74 (dd, $J = 8.3, 4.6$ Hz, 1H), 4.54 - 4.48 (m, 1H), 4.41 - 4.36 (m, 1H), 3.42 (s, 1H), 2.37 - 2.27 (m, 2H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 142.8, 128.8, 128.2, 125.6, 72.3,

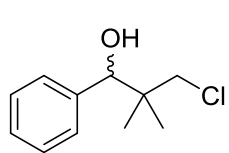
Synthesis of non-accepted racemic γ -haloalcohols and oxetanes:^{28,33-36}



(rac)-3-chloro-2-phenylpropan-1-ol [(rac)-25a]

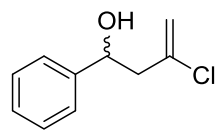


(rac)-3-chloro-2,2-dimethyl-1-phenylpropan-1-ol [(rac)-26a]



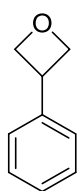
^1H NMR (400 MHz, CDCl_3) δ 7.36 - 7.27 (m, 5H), 4.76 (s, 1H), 3.72 (d, J = 10.6 Hz, 1H), 3.35 (d, J = 10.6 Hz, 1H), 1.01 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 141.2, 127.9, 127.8, 127.7, 77.4, 54.0, 40.3, 22.1, 20.5.

(rac)-3-chloro-1-phenylbut-3-en-1-ol [(rac)-27a]



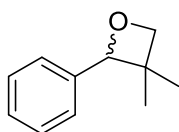
^1H NMR (400 MHz, CDCl_3) δ 7.39 - 7.28 (m, 5H), 5.29 (s, 1H), 5.23 (s, 1H), 5.05 - 5.02 (m, 1H), 2.80 - 2.74 (m, 1H), 2.68 - 2.64 (m, 1H), 2.22 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.1, 138.9, 128.6, 128.0, 125.9, 115.6, 71.3, 49.3.

3-phenyloxetane [25b]



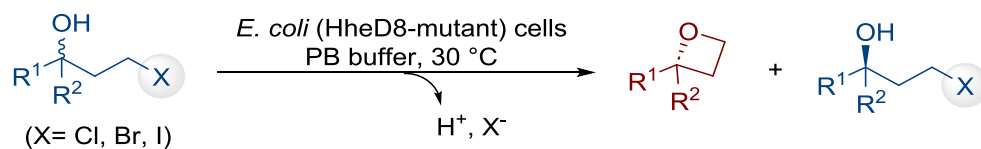
^1H NMR (400 MHz, CDCl_3) δ 7.32 - 7.25 (m, 4H), 7.19 - 7.15 (m, 1H), 5.00 - 4.96 (m, 2H), 4.69 (t, J = 6.4 Hz, 2H), 4.17 - 4.10 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 141.6, 128.9, 127.2, 126.9, 79.1, 40.4.

(rac)-3,3-dimethyl-2-phenyloxetane [(rac)-26b]



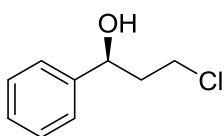
^1H NMR (400 MHz, CDCl_3) δ 7.39 - 7.28 (m, 5H), 5.52 (s, 1H), 4.54 (d, J = 5.4 Hz, 1H), 4.27 (d, J = 5.4 Hz, 1H), 1.41 (s, 3H), 0.80 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 140.3, 128.2, 127.4, 125.2, 91.9, 81.4, 40.6, 27.0, 22.6.

5. Biocatalytic enantioselective formation of oxetanes



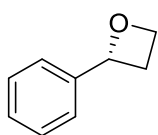
General procedure: In a 200 mL round-bottom flask, a resting cell suspension of *E. coli* (HheD8-M4) at a concentration of 10 g dcw/L was prepared in 100 mL of PB buffer (50 mM, pH 8.5). To this suspension, 2 mmol of γ -haloalcohol (*rac*)-**a** was added to a final concentration of 20 mM. The reaction mixture was then stirred at 30 °C. Upon completion of the enzymatic reaction, the mixture was subjected to extraction using ethyl acetate (3 $\times$ 70 mL). The organic phases were separated by centrifugation (8800 $\times$ g, 3 min), combined, dried over anhydrous Na₂SO₄, and evaporated at reduced pressure. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 50:1 ~ 20:1; dichloromethane: ethyl acetate = 6:1 ~ 3:1) on silica gel to afford the desired chiral oxetane (*R*)-**b** and γ -haloalcohol (*S*)-**a**.

(*S*)-3-chloro-1-phenylpropan-1-ol [(*S*)-**1a**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **1a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 8 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**1a** as a white solid in 50% yield (179.6 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.39 - 7.34 (m, 4H), 7.32 - 7.28 (m, 1H), 4.91 (dd, *J* = 8.5, 4.7 Hz, 1H), 3.75 - 3.69 (m, 1H), 3.54 (dt, *J* = 10.9, 5.9 Hz, 1H), 2.35 - 2.16 (m, 2H), 2.11 - 2.03 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 143.8, 128.7, 128.0, 125.9, 71.3, 41.8, 41.5. [α]_D²⁵ = -31.7 (*c* = 1.00, CH₂Cl₂). HPLC analysis (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated >99% *ee*: *t*_(S) (major) = 44.8 min, *t*_(R) (minor) = 48.7 min. HRMS (ESI) *m/z*: calculated for C₉H₁₂ClO [M+H]⁺: 171.0571, found: 171.0574. **m.p.**: 51.4-52.4 °C.

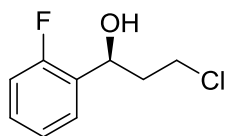
(*R*)-2-phenyloxetane [(*R*)-**1b**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **1a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 8 h. The crude product was purified by flash column chromatography

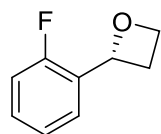
on silica gel (petroleum ether: ethyl acetate = 50:1 ~ 40:1) to provide **(R)-1b** as a light yellow liquid in 41% yield (117.0 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.48 - 7.45 (m, 2H), 7.41 (t, J = 7.2 Hz, 2H), 7.34 - 7.30 (m, 1H), 5.83 (t, J = 7.5 Hz, 1H), 4.85 (td, J = 8.0, 5.8 Hz, 1H), 4.68 (dt, J = 9.2, 5.8 Hz, 1H), 3.08 - 2.99 (m, 1H), 2.72 - 2.64 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 143.6, 128.6, 127.9, 125.3, 83.0, 68.4, 30.8. $[\alpha]_D^{25}$ = +174.91 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 98% *ee*: $t_{(S)}$ (minor) = 10.1 min, $t_{(R)}$ (major) = 11.3 min. **HRMS (ESI) m/z** : calculated for C₉H₁₀NaO [M+Na]⁺: 157.0624, found: 157.0632.

(S)-3-chloro-1-(2-fluorophenyl)propan-1-ol [(S)-2a]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **2a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 6 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide **(S)-2a** as a light yellow liquid in 49% yield (184.8 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.45 (t, J = 7.5 Hz, 1H), 7.27 (q, J = 5.8 Hz, 1H), 7.16 (t, J = 7.5 Hz, 1H), 7.03 (t, J = 11.1 Hz, 1H), 5.22 (dd, J = 8.6, 4.4 Hz, 1H), 3.78 - 3.71 (m, 1H), 3.61 (dt, J = 11.0, 5.9 Hz, 1H), 2.27 - 2.14 (m, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 159.8 (d, J = 245.0 Hz), 130.6 (d, J = 13.0 Hz), 129.4 (d, J = 8.0 Hz), 127.4 (d, J = 5.0 Hz), 124.6 (d, J = 3.0 Hz), 115.6 (d, J = 22.0 Hz), 65.9 (d, J = 3.0 Hz), 41.6, 40.2. $[\alpha]_D^{25}$ = -35.44 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OD-H, 10% IPA in *n*-hexane, 1.0 ml/min, λ = 210 nm) indicated 98% *ee*: $t_{(S)}$ (major) = 5.7 min, $t_{(R)}$ (minor) = 6.4 min. **HRMS (ESI) m/z** : calculated for C₉H₁₀ClFNaO [M+Na]⁺: 211.0296, found: 211.0300.

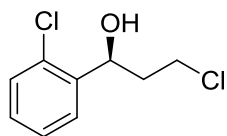
(R)-2-(2-fluorophenyl) oxetane [(R)-2b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **2a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 6 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 50:1 ~ 40:1) to provide **(R)-2b** as a light yellow liquid in 39% yield (118.4 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.66 (t, J = 7.5 Hz, 1H), 7.30 - 7.24 (m, 1H), 7.20 (t, J = 7.5 Hz, 1H), 6.05 (t, J = 7.6 Hz, 1H), 4.84 (td, J = 8.2, 6.3 Hz, 1H), 4.68 (dt, J = 9.2, 6.0 Hz, 1H), 3.13 - 3.05 (m, 1H), 2.70 - 2.61 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)**

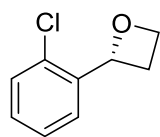
δ 159.3 (d, J = 244.0 Hz), 130.8 (d, J = 13.0 Hz), 129.2 (d, J = 8.0 Hz), 127.0 (d, J = 4.0 Hz), 124.3 (d, J = 4.0 Hz), 115.2 (d, J = 20.0 Hz), 77.8 (d, J = 4.0 Hz), 76.8, 30.0. $[\alpha]_D^{25}$ = + 148.42 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 98% *ee*: $t_{(S)}$ (minor) = 12.9 min, $t_{(R)}$ (major) = 15.3 min. **HRMS (ESI)** m/z : calculated for C₉H₁₀FO [M+H]⁺: 153.0710, found: 153.0715.

(*S*)-3-chloro-1-(2-chlorophenyl)propan-1-ol [(*S*)-3a]



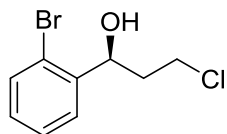
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **3a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**3a** as a light yellow liquid in 51% yield (212.1 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.57 (d, J = 7.7 Hz, 1H), 7.32 (q, J = 9.7 Hz, 2H), 7.23 (t, J = 7.5 Hz, 1H), 5.35 (d, J = 8.4 Hz, 1H), 3.84 - 3.77 (m, 1H), 3.69 (dt, J = 10.8, 5.2 Hz, 1H), 2.26 - 2.18 (m, 2H), 2.15 - 2.06 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 141.2, 131.8, 129.7, 128.9, 127.3, 127.1, 68.1, 41.8, 39.8. $[\alpha]_D^{25}$ = - 56.66 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 94% *ee*: $t_{(R)}$ (minor) = 34.7 min, $t_{(S)}$ (major) = 36.7 min. **HRMS (ESI)** m/z : calculated for C₉H₁₀Cl₂NaO [M+Na]⁺: 227.0001, found: 227.0000.

(*R*)-2-(2-chlorophenyl) oxetane[(*R*)-3b]



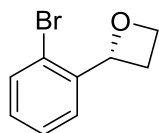
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **3a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 50:1 ~ 40:1) to provide (*R*)-**3b** as a colorless liquid in 43% yield (143.9 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.76 (d, J = 9.4 Hz, 1H), 7.37 - 7.31 (m, 2H), 7.23 (td, J = 7.6, 1.7 Hz, 1H), 6.02 (t, J = 7.5 Hz, 1H), 4.84 (td, J = 7.5, 6.0 Hz, 1H), 4.65 (dt, J = 9.1, 6.0 Hz, 1H), 3.23 - 3.15 (m, 1H), 2.55 - 2.45 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 141.4, 130.4, 129.2, 128.5, 127.0, 126.0, 80.3, 68.6, 30.0. $[\alpha]_D^{25}$ = + 193.99 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 97% *ee*: $t_{(S)}$ (minor) = 11.1 min, $t_{(R)}$ (major) = 12.0 min. **HRMS (ESI)** m/z : calculated for C₉H₉ClNaO [M+Na]⁺: 191.0234, found: 191.0233.

(S)-1-(2-bromophenyl)-3-chloropropan-1-ol [(S)-4a]



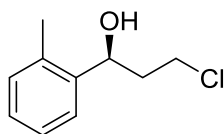
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **4a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide **(S)-4a** as a light yellow liquid in 50% yield (248.8 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.53 (dd, J = 11.6, 9.4 Hz, 2H), 7.34 (t, J = 7.9 Hz, 1H), 7.15 (t, J = 7.6 Hz, 1H), 5.28 (d, J = 7.6 Hz, 1H), 3.83 - 3.76 (m, 1H), 3.71 - 3.65 (m, 1H), 2.46 (s, 1H), 2.25 - 2.18 (m, 1H), 2.10 - 2.01 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** 142.8, 132.9, 129.2, 128.0, 127.3, 121.8, 70.3, 41.8, 39.8. **$[\alpha]_D^{25}$** = -53.76 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 93% *ee*: $t_{(R)}$ (minor) = 36.5 min, $t_{(S)}$ (major) = 39.5 min. **HRMS (ESI) m/z** : calculated for C₉H₁₁BrClO $[M+H]^+$: 248.9676, found: 248.9682.

(R)-2-(2-bromophenyl) oxetane [(R)-4b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **4a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 50:1 ~ 40:1) to provide **(R)-4b** as a colorless liquid in 46% yield (196.3 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.76 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 7.16 (t, J = 7.9 Hz, 1H), 5.94 (t, J = 7.5 Hz, 1H), 4.83 (td, J = 7.7, 6.0 Hz, 1H), 4.64 (dt, J = 9.1, 6.1 Hz, 1H), 3.26 - 3.18 (m, 1H), 2.52 - 2.44 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 142.7, 132.4, 128.8, 127.6, 126.3, 119.7, 82.2, 68.39, 30.1. **$[\alpha]_D^{25}$** = +192.79 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 96% *ee*: $t_{(S)}$ (minor) = 11.4 min, $t_{(R)}$ (major) = 12.3 min. **HRMS (ESI) m/z** : calculated for C₉H₉BrNaO $[M+Na]^+$: 234.9729, found: 234.9737.

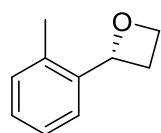
(S)-3-chloro-1-(o-tolyl)propan-1-ol [(S)-5a]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **5a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 20:1) to

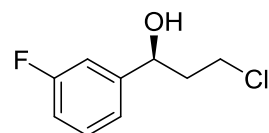
provide **(S)-5a** as a colorless liquid in 50% yield (185.6 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.46 (d, J = 7.5 Hz, 1H), 7.26 - 7.14 (m, 3H), 5.16 (dd, J = 8.8, 3.9 Hz, 1H), 3.83 - 3.76 (m, 1H), 3.62 (dt, J = 10.8, 5.3 Hz, 1H), 2.35 (s, 3H), 2.13 - 2.00 (m, 2H). **¹³C NMR (100 MHz, CDCl₃)** δ 142.0, 134.4, 130.6, 127.5, 126.4, 125.1, 67.4, 42.1, 40.5, 19.0. $[\alpha]_D^{25}$ = - 46.64 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 93% *ee*: $t_{(S)}$ (major) = 37.8 min, $t_{(R)}$ (minor) = 40.7 min. **HRMS (ESI)** m/z : calculated for C₁₀H₁₃ClNaO [M+Na]⁺: 207.0547, found: 207.0550.

(R)-2-(o-tolyl) oxetane [(R)-5b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **5a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide **(R)-5b** as a colorless liquid in 33% yield (98.7 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.70 (d, J = 7.7 Hz, 1H), 7.30 (t, J = 7.4 Hz, 1H), 7.21 (t, J = 5.9 Hz, 1H), 7.14 (d, J = 7.6 Hz, 1H), 6.00 (t, J = 7.6 Hz, 1H), 4.86 (td, J = 7.9, 5.8 Hz, 1H), 4.65 (dt, J = 9.2, 5.8 Hz, 1H), 3.13 - 2.05 (m, 1H), 2.59 - 2.51 (m, 1H), 2.19 (s, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 141.8, 133.4, 130.1, 127.3, 126.2, 124.1, 80.8, 68.2, 29.8, 18.5. $[\alpha]_D^{25}$ = + 224.21 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 99% *ee*: $t_{(R)}$ (major) = 15.0 min, $t_{(S)}$ (minor) = 15.9 min. **HRMS (ESI)** m/z : calculated for C₁₀H₁₂NaO [M+Na]⁺: 171.0780, found: 171.0783.

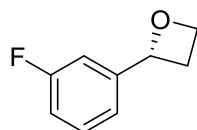
(S)-3-chloro-1-(3-fluorophenyl)propan-1-ol [(S)-6a]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **6a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 12 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 20:1) to provide **(S)-6a** as a light yellow liquid in 47% yield (179.4 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.32 (q, J = 8.2 Hz, 1H), 7.09 (dd, J = 15.7, 7.8 Hz, 2H), 6.98 (t, J = 8.4 Hz, 1H), 4.93 (dd, J = 8.8, 4.6 Hz, 1H), 3.76 - 3.70 (m, 1H), 3.54 (dt, J = 11.0, 5.8 Hz, 1H), 2.29 (s, 1H), 2.22 - 2.14 (m, 1H), 2.10 - 2.01 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 163.1 (d, J = 245.0 Hz), 146.5 (d, J = 6.0 Hz), 130.3 (d, J = 8.0 Hz), 121.4 (d, J = 3.0 Hz), 114.8 (d, J = 21.0 Hz), 112.8 (d, J = 22.0 Hz), 70.7, 41.6,

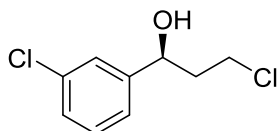
41.4. $[\alpha]_D^{25} = -14.79$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated 94% *ee*: $t_{(S)}$ (major) = 44.0 min, $t_{(R)}$ (minor) = 45.8 min. **HRMS (ESI) m/z** : calculated for $\text{C}_9\text{H}_{11}\text{ClFO}$ $[\text{M}+\text{H}]^+$: 189.0477, found: 189.0481.

(*R*)-2-(3-fluorophenyl) oxetane [(*R*)-6b]



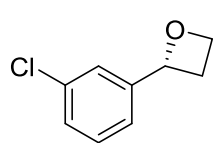
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **6a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 12 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide (*R*)-**6b** as a light yellow liquid in 36% yield (108.7 mg). **^1H NMR (400 MHz, CDCl_3)** δ 7.34 (td, $J = 7.8$, 5.6 Hz, 1H), 7.17 (t, $J = 8.2$ Hz, 2H), 7.01 - 6.96 (m, 1H), 5.79 (t, $J = 7.5$ Hz, 1H), 4.83 (td, $J = 8.0$, 6.0 Hz, 1H), 4.66 (dt, $J = 9.6$, 5.8 Hz, 1H), 3.09 - 3.00 (m, 1H), 2.66 - 2.58 (m, 1H). **^{13}C NMR (100 MHz, CDCl_3)** δ 163.2 (d, $J = 245.0$ Hz), 146.5 (d, $J = 7.0$ Hz), 130.2 (d, $J = 8.0$ Hz), 120.7 (d, $J = 3.0$ Hz), 114.6 (d, $J = 21.0$ Hz), 112.2 (d, $J = 22.0$ Hz), 82.2 (d, $J = 2.0$ Hz), 68.5, 30.7. $[\alpha]_D^{25} = +165.88$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated >99% *ee*: $t_{(S)}$ (minor) = 14.7 min, $t_{(R)}$ (major) = 15.8 min. **HRMS (ESI) m/z** : calculated for $\text{C}_9\text{H}_{10}\text{FO}$ $[\text{M}+\text{H}]^+$: 153.0710, found: 157.0712.

(*S*)-3-chloro-1-(3-chlorophenyl)propan-1-ol [(*S*)-7a]



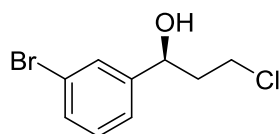
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **7a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 48 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**7a** as a light yellow liquid in 48% yield (196.0 mg). **^1H NMR (400 MHz, CDCl_3)** δ 7.35 (s, 1H), 7.30 - 7.24 (m, 2H), 7.21 (dd, $J = 6.6$, 2.1 Hz, 1H), 4.90 (dd, $J = 8.7$, 4.6 Hz, 1H), 3.74 - 3.68 (m, 1H), 3.53 (dt, $J = 11$, 5.7 Hz, 1H), 2.40 (s, 1H), 2.20 - 2.12 (m, 1H), 2.07 - 1.99 (m, 1H). **^{13}C NMR (100 MHz, CDCl_3)** δ 145.9, 134.6, 130.0, 128.1, 126.0, 124.0, 70.7, 41.6, 41.4. $[\alpha]_D^{25} = -21.68$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated 93% *ee*: $t_{(S)}$ (major) = 43.8 min, $t_{(R)}$ (minor) = 49.2 min. **HRMS (ESI) m/z** : calculated for $\text{C}_9\text{H}_{11}\text{Cl}_2\text{O}$ $[\text{M}+\text{H}]^+$: 205.0181, found: 205.0188.

(*R*)-2-(3-chlorophenyl) oxetane [(*R*)-7b]



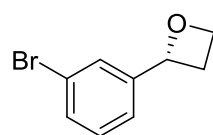
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **7a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 48 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide (*R*)-**7b** as a light yellow liquid in 45% yield (150.9 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.45 (s, 1H), 7.33 - 7.25 (m, 3H), 5.77 (t, *J* = 7.5 Hz, 1H), 4.83 (td, *J* = 7.9, 5.8 Hz, 1H), 4.66 (dt, *J* = 9.2, 5.8 Hz, 1H), 3.08 - 3.00 (m, 1H), 2.66 - 2.57 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 145.8, 134.6, 129.9, 127.9, 125.4, 123.3, 82.2, 68.5, 30.7. [α]_D²⁵ = + 137.77 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 98% *ee*: *t*_(S) (minor) = 14.4 min, *t*_(R) (major) = 16.9 min. **HRMS (ESI) *m/z***: calculated for C₉H₉ClNaO [M+Na]⁺: 191.0234, found: 191.0236.

(*S*)-1-(3-bromophenyl)-3-chloropropan-1-ol [(*S*)-8a]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **8a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 48 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**8a** as a light yellow liquid in 50% yield (251.1 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.52 (s, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 7.24 (dt, *J* = 16.1, 10.3 Hz, 2H), 4.91 (dd, *J* = 8.8, 4.6 Hz, 1H), 3.76 - 3.70 (m, 1H), 3.54 (dt, *J* = 11.0, 5.7 Hz, 1H), 2.26 (s, 1H), 2.20 - 2.13 (m, 1H), 2.09 - 2.00 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 146.2, 131.0, 130.4, 129.0, 124.5, 122.9, 70.7, 41.6, 41.4. [α]_D²⁵ = - 16.69 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 92% *ee*: *t*_(S) (major) = 48.0 min, *t*_(R) (minor) = 54.6 min. **HRMS (ESI) *m/z***: calculated for C₉H₁₀BrClNaO [M+Na]⁺: 270.9496, found: 270.9504.

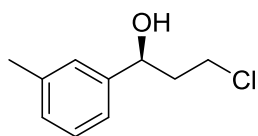
(*R*)-2-(3-bromophenyl)oxetane [(*R*)-8b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **8a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 48 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide (*R*)-**8b** as

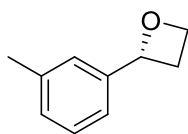
a light yellow liquid in 43% yield (182.5 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.61 (s, 1H), 7.42 (d, J = 7.8 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.25 (t, J = 7.8 Hz, 1H), 5.77 (t, J = 7.5 Hz, 1H), 4.83 (td, J = 8.1, 6.0 Hz, 1H), 4.66 (dt, J = 9.2, 5.8 Hz, 1H), 3.07 - 3.00 (m, 1H), 2.65 - 2.56 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 146.0, 130.8, 130.2, 128.3, 123.8, 122.8, 82.1, 68.4, 30.7. $[\alpha]_D^{25}$ = + 130.01 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 95% *ee*: $t_{(S)}$ (minor) = 14.8 min, $t_{(R)}$ (major) = 18.0 min. **HRMS (ESI)** m/z : calculated for C₉H₁₀BrO [M+H]⁺: 212.9910, found: 212.9911.

(*S*)-3-chloro-1-(*m*-tolyl)propan-1-ol [(*S*)-9a]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **9a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**9a** as a light yellow liquid in 51% yield (190.0 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.26 (t, J = 7.4 Hz, 1H), 7.18 - 7.15 (m, 2H), 7.12 (d, J = 7.6 Hz, 1H), 4.90 (dd, J = 8.6, 4.6 Hz, 1H), 3.77 - 3.71 (m, 1H), 3.59 - 3.54 (m, 1H), 2.37 (s, 3H), 2.28 - 2.19 (m, 1H), 2.12 - 2.04 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 143.8, 138.5, 128.8, 128.7, 126.6, 123.0, 71.4, 41.9, 41.5, 21.6. $[\alpha]_D^{25}$ = - 25.98 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 91% *ee*: $t_{(S)}$ (major) = 40.1 min, $t_{(R)}$ (minor) = 43.2 min. **HRMS (ESI)** m/z : calculated for C₁₀H₁₃ClNaO [M+Na]⁺: 207.0547, found: 207.0555.

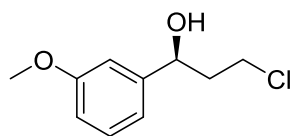
(*R*)-2-(*m*-tolyl)oxetane [(*R*)-9b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **9a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide (*R*)-**9b** as a light yellow liquid in 34% yield (102.5 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.29 (t, J = 7.7 Hz, 2H), 7.23 (d, J = 7.6 Hz, 1H), 7.13 (d, J = 7.4 Hz, 1H), 5.80 (t, J = 7.5 Hz, 1H), 4.84 (td, J = 8.4, 6.5 Hz, 1H), 4.67 (dt, J = 9.3, 5.8 Hz, 1H), 3.06 - 2.98 (m, 1H), 2.72 - 2.63 (m, 1H), 2.40 (s, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 143.6, 138.3, 128.7, 128.5, 126.0, 122.4, 83.1, 68.4, 30.8, 21.6. $[\alpha]_D^{25}$ = + 148.32 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ

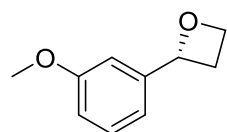
= 210 nm) indicated 99% *ee*: $t_{(S)}$ (minor) = 9.3 min, $t_{(R)}$ (major) = 10.8 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{13}O$ $[M+H]^+$: 149.0961, found: 149.0961.

(S)-3-chloro-1-(3-methoxyphenyl)propan-1-ol [(S)-10a]

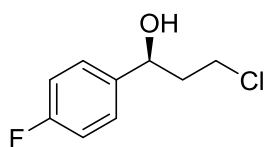


Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **10a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 48 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 20:1) to provide **(S)-10a** as a light yellow liquid in 51% yield (206.9 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.27 (t, J = 7.4 Hz, 1H), 6.92 (d, J = 8.8 Hz, 2H), 6.83 (d, J = 8.3 Hz, 1H), 4.90 (dd, J = 8.6, 4.8 Hz, 1H), 3.80 (s, 3H), 3.75 - 3.69 (m, 1H), 3.57 - 3.52 (m, 1H), 2.25 - 2.20 (m, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 159.9, 145.5, 129.8, 118.1, 113.4, 111.3, 71.3, 55.4, 41.8, 41.4. $[\alpha]_D^{25}$ = -19.79 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OD-H, 10% IPA in *n*-hexane, 1.0 ml/min, λ = 210 nm) indicated 91% *ee*: $t_{(S)}$ (major) = 11.9 min, $t_{(R)}$ (minor) = 13.8 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{14}ClO_2$ $[M+H]^+$: 201.0677, found: 201.0682.

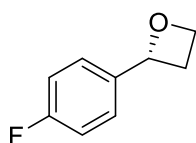
(R)-2-(3-methoxyphenyl)oxetane [(R)-10b]



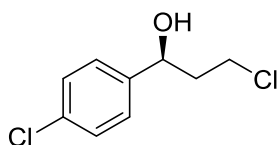
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **10a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 48 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide **(R)-10b** as a light yellow liquid in 43% yield (140.9 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.33 - 7.28 (m, 1H), 7.03 - 6.98 (m, 2H), 6.86 - 6.83 (m, 1H), 5.80 (t, J = 7.6 Hz, 1H), 4.86 - 4.80 (m, 1H), 4.69 - 4.64 (m, 1H), 3.84 (s, 1H), 3.07 - 2.98 (m, 1H), 2.70 - 2.61 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 159.9, 145.4, 129.7, 117.4, 113.5, 110.5, 82.9, 68.4, 55.4, 30.8. $[\alpha]_D^{25}$ = +133.21 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 97% *ee*: $t_{(S)}$ (minor) = 14.1 min, $t_{(R)}$ (major) = 20.5 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{12}NaO_2$ $[M+Na]^+$: 187.0730, found: 187.0734.

(S)-3-chloro-1-(4-fluorophenyl)propan-1-ol [(S)-11a]

Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **11a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 12 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide **(S)-11a** as a light yellow liquid in 52% yield (196.7 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.32 (dd, *J* = 8.6, 5.7 Hz, 2H), 7.04 (t, *J* = 8.6 Hz, 2H), 4.91 (dd, *J* = 8.6, 4.9 Hz, 1H), 3.74 - 3.68 (m, 1H), 3.52 (dt, *J* = 11.4, 5.8 Hz, 1H), 2.27 (s, 1H), 2.23 - 2.15 (m, 1H), 2.08 - 1.99 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 162.4 (d, *J* = 244.0 Hz), 139.5 (d, *J* = 3.0 Hz), 127.6 (d, *J* = 8.0 Hz), 115.6 (d, *J* = 22.0 Hz), 70.7, 41.7, 41.5. [α]_D²⁵ = - 32.31 (c = 1.00, CH₂Cl₂). HPLC analysis (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 93% *ee*: t_(S) (major) = 42.8 min, t_(R) (minor) = 47.9 min. HRMS (ESI) *m/z*: calculated for C₉H₁₀ClFNaO [M+Na]⁺: 211.0296, found: 211.0296.

(R)-2-(4-fluorophenyl) oxetane [(R)-11b]

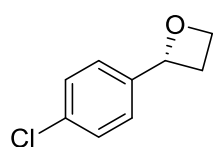
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **11a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 12 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 50:1 ~ 40:1) to provide **(R)-11b** as a light yellow liquid in 34% yield (103.7 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.42 (dd, *J* = 8.4, 5.6 Hz, 2H), 7.07 (t, *J* = 8.7 Hz, 2H), 5.78 (t, *J* = 7.5 Hz, 1H), 4.82 (td, *J* = 8.1, 6.0 Hz, 1H), 4.64 (dt, *J* = 9.3, 5.8 Hz, 1H), 3.05 - 2.97 (m, 1H), 2.69 - 2.60 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 162.5 (d, *J* = 244.0 Hz), 139.4 (d, *J* = 4.0 Hz), 127.2 (d, *J* = 8.0 Hz), 115.5 (d, *J* = 21.0 Hz), 82.5, 68.2, 31.0. [α]_D²⁵ = + 148.82 (c = 1.00, CH₂Cl₂). HPLC analysis (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated >99% *ee*: t_(S) (minor) = 15.3 min, t_(R) (major) = 17.2 min. HRMS (ESI) *m/z*: calculated for C₉H₁₀FO [M+H]⁺: 153.0710, found: 153.0720.

(S)-3-chloro-1-(4-chlorophenyl)propan-1-ol [(S)-12a]

Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **12a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide

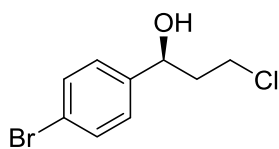
(S)-12a as a light yellow liquid in 50% yield (206.9 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.33 (q, $J = 8.6$ Hz, 4H), 4.94 (dd, $J = 8.6, 4.6$ Hz, 1H), 3.78 - 3.72 (m, 1H), 3.55 (dt, $J = 11.0, 5.8$ Hz, 1H), 2.37 (s, 1H), 2.25 - 2.16 (m, 1H), 2.10 - 2.02 (m, 1H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 141.6, 132.4, 128.9, 127.3, 70.1, 42.4, 41.0. $[\alpha]_{\text{D}}^{25} = -13.09$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated 93% *ee*: $t_{(\text{S})}$ (major) = 51.1 min, $t_{(\text{R})}$ (minor) = 54.3 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{11}\text{Cl}_2\text{O}$ $[\text{M}+\text{H}]^+$: 205.0181, found: 205.0186.

(R)-2-(4-chlorophenyl) oxetane [(R)-12b]



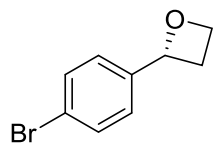
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **12a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 $^{\circ}\text{C}$, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 50:1 ~ 40:1) to provide **(R)-12b** as a light yellow liquid in 37% yield (126.2 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.36 (t, $J = 8.0$ Hz, 4H), 5.78 (t, $J = 7.5$ Hz, 1H), 4.82 (td, $J = 8.0, 5.9$ Hz, 1H), 4.64 (dt, $J = 9.2, 5.8$ Hz, 1H), 3.07 - 2.98 (m, 1H), 2.66 - 2.58 (m, 1H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 142.2, 133.6, 128.8, 126.8, 82.3, 68.4, 30.9. $[\alpha]_{\text{D}}^{25} = +160.69$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, $\lambda = 210$ nm) indicated >99% *ee*: $t_{(\text{S})}$ (minor) = 8.3 min, $t_{(\text{R})}$ (major) = 8.9 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{10}\text{ClO}$ $[\text{M}+\text{H}]^+$: 169.0415, found: 169.0419.

(S)-1-(4-bromophenyl)-3-chloropropan-1-ol [(S)-13a]



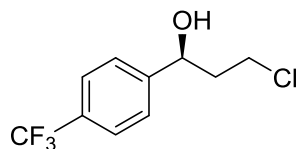
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **13a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 $^{\circ}\text{C}$, reaction for 48 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide **(S)-13a** as a light yellow liquid in 50% yield (249.3 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.48 (d, $J = 8.3$ Hz, 2H), 7.24 (d, $J = 8.2$ Hz, 2H), 4.92 (dd, $J = 8.7, 4.6$ Hz, 1H), 3.76 - 3.70 (m, 1H), 3.54 (dt, $J = 11.0, 5.8$ Hz, 1H), 2.22 - 1.99 (m, 3H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 142.8, 131.9, 127.6, 121.8, 70.5, 41.7, 41.4. $[\alpha]_{\text{D}}^{25} = -16.69$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OD-H, 10% IPA in *n*-hexane, 1.0 ml/min, $\lambda = 210$ nm) indicated 92% *ee*: $t_{(\text{S})}$ (major) = 7.1 min, $t_{(\text{R})}$ (minor) = 8.0 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{10}\text{BrClNaO}$ $[\text{M}+\text{Na}]^+$: 270.9496, found: 270.9495.

(*R*)-2-(4-bromophenyl) oxetane [(*R*)-13b]



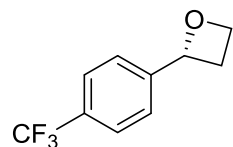
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **13a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 48 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide (*R*)-**13b** as a light yellow liquid in 42% yield (178.6 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.51 (d, J = 8.2 Hz, 2H), 7.31 (d, J = 8.1 Hz, 2H), 5.76 (t, J = 7.5 Hz, 1H), 4.82 (td, J = 8.1, 6.1 Hz, 1H), 4.64 (dt, J = 9.3, 5.8 Hz, 1H), 3.06 - 2.98 (m, 1H), 2.65 - 2.56 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 142.7, 131.7, 127.0, 121.7, 82.3, 68.4, 30.8. **$[\alpha]_D^{25}$** = + 129.74 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 98% *ee*: $t_{(S)}$ (minor) = 15.9 min, $t_{(R)}$ (major) = 17.7 min. **HRMS (ESI) m/z** : calculated for C₉H₉BrNaO [M+Na]⁺: 234.9729, found: 234.9733.

(*S*)-3-chloro-1-(4-(trifluoromethyl)phenyl)propan-1-ol [(*S*)-14a]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 10 mM **14a** (1 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 82 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**14a** as a light yellow liquid in 53% yield (125.6 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.62 (d, J = 8.0 Hz, 2H), 7.49 (d, J = 7.9 Hz, 2H), 5.04 (dd, J = 9.0, 4.2 Hz, 1H), 3.80 - 3.74 (m, 1H), 3.57 (dt, J = 11.1, 5.6 Hz, 1H), 2.25 - 2.03 (m, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 147.8, 130.2 (d, J = 32.0 Hz), 126.2, 125.7 (q, J = 4.0, Hz), 124.2 (d, J = 271.0 Hz), 70.8, 41.5 (d, J = 4.0 Hz). **$[\alpha]_D^{25}$** = - 10.39 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OJ-H, 5% IPA in *n*-hexane, 1.0 ml/min, λ = 210 nm) indicated 86% *ee*: $t_{(S)}$ (major) = 9.2 min, $t_{(R)}$ (minor) = 10.4 min. **HRMS (ESI) m/z** : calculated for C₁₀H₁₀ClF₃KO [M+K]⁺: 277.0004, found: 277.0006.

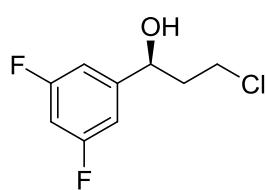
(*R*)-2-(4-(trifluoromethyl)phenyl)oxetane [(*R*)-14b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 10 mM **14a** (1 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 82 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1)

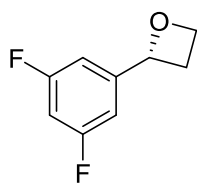
to provide **(R)-14b** as a light yellow liquid in 37% yield (74.1 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.65 (d, J = 8.1 Hz, 2H), 7.54 (d, J = 8.1 Hz, 2H), 5.86 (t, J = 7.6 Hz, 1H), 4.86 (td, J = 8.0, 6.0 Hz, 1H), 4.68 (dt, J = 9.2, 5.8 Hz, 1H), 3.13 - 3.04 (m, 1H), 2.65 - 2.57 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 147.7, 129.9 (q, J = 32.0 Hz), 125.6 (q, J = 3.0 Hz), 125.4, 124.2 (q, J = 256.0 Hz), 82.5, 68.6, 30.7. **$[\alpha]_D^{25}$** = + 99.32 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 93% *ee*: $t_{(S)}$ (minor) = 6.5 min, $t_{(R)}$ (major) = 7.0 min. **HRMS (ESI)** m/z : calculated for C₁₀H₁₀F₃O $[M+H]^+$: 203.0678, found: 203.0687.

(S)-3-chloro-1-(3,5-difluorophenyl)propan-1-ol [(S)-15a]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **15a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 12 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 20:1) to provide **(S)-15a** as a colorless liquid in 51% yield (211.6 mg). **¹H NMR (400 MHz, CDCl₃)** δ 6.89 (dd, J = 6.6, 2.2 Hz, 2H), 6.74 - 6.69 (m, 1H), 4.94 (dd, J = 8.8, 4.4 Hz, 1H), 3.77 - 3.71 (m, 1H), 3.56 (dt, J = 11.1, 5.6 Hz, 1H), 2.46 (s, 1H), 2.19 - 2.10 (m, 1H), 2.08 - 2.00 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** 163.3 (dd, J = 248.0, 12.0 Hz), 148.0 (t, J = 9.0 Hz), 108.7 (dd, J = 18.0, 7.0 Hz), 103.2 (t, J = 25.0 Hz), 70.4 (t, J = 2.0 Hz), 41.4 (d, J = 7.0 Hz). **$[\alpha]_D^{25}$** = - 10.79 (c = 1.00, CH₂Cl₂). **HPLC analysis** (AD-H, 5% IPA in *n*-hexane, 1.0 ml/min, λ = 210 nm) indicated 92% *ee*: $t_{(R)}$ (minor) = 9.3 min, $t_{(S)}$ (major) = 10.7 min. **HRMS (ESI)** m/z : calculated for C₉H₉ClF₂NaO $[M+Na]^+$: 229.0202, found: 229.0205.

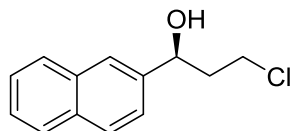
(R)-2-(3,5-difluorophenyl)oxetane [(R)-15b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **15a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 12 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide **(R)-15b** as a light yellow liquid in 32% yield (110.4 mg). **¹H NMR (400 MHz, CDCl₃)** δ 6.94 (dt, J = 6.3, 2.0 Hz, 2H), 6.72 (tt, J = 8.9, 2.4 Hz, 1H), 5.75 (t, J = 7.5 Hz, 1H), 4.82 (td, J = 8.0, 5.9 Hz, 1H), 4.65 (dt, J = 9.2, 5.9 Hz, 1H), 3.10 - 3.02 (m, 1H), 2.62 - 2.53 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 163.4 (dd, J = 247.0, 12.0 Hz), 148.0 (t, J = 9.0 Hz), 107.8 (dd, J = 19.0, 8.0

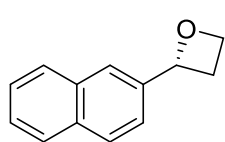
Hz), 103.0 (t, $J = 25.0$ Hz), 81.7, 68.6, 30.6. $[\alpha]_D^{25} = +153.59$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (IA-3, 1% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated 98% *ee*: $t_{(R)}$ (major) = 12.5 min, $t_{(S)}$ (minor) = 13.9 min. **HRMS (ESI) m/z** : calculated for $\text{C}_9\text{H}_9\text{F}_2\text{O}$ $[\text{M}+\text{H}]^+$: 171.0616, found: 171.0625.

(*S*)-3-chloro-1-(naphthalen-2-yl)propan-1-ol [(*S*)-16a]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **16a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M3) cells, 30 °C, reaction for 82 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 20:1) to provide (***S***)-**16a** as a light yellow liquid in 50% yield (219.5 mg). **^1H NMR (400 MHz, CDCl_3) δ** 8.13 (d, $J = 8.2$ Hz, 1H), 7.89 (d, $J = 7.3$ Hz, 1H), 7.81 (d, $J = 8.2$ Hz, 1H), 7.68 (d, $J = 7.1$ Hz, 1H), 7.52 (dt, $J = 24.7, 5.2$ Hz, 3H), 5.77 (dd, $J = 8.8, 3.5$ Hz, 1H), 3.94 (td, $J = 9.6, 5.1$ Hz, 1H), 3.70 (dt, $J = 15.7, 1.3$ Hz, 1H), 2.38 - 2.23 (m, 2H). **^{13}C NMR (100 MHz, CDCl_3) δ** 139.6, 133.9, 130.1, 129.1, 128., 126.4, 125.9, 125.6, 123.0, 122.8, 68.0, 42.4, 40.8. $[\alpha]_D^{25} = -51.66$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, $\lambda = 210$ nm) indicated 96% *ee*: $t_{(S)}$ (major) = 16.1 min, $t_{(R)}$ (minor) = 17.7 min. **HRMS (ESI) m/z** : calculated for $\text{C}_{13}\text{H}_{14}\text{ClO}$ $[\text{M}+\text{H}]^+$: 221.0728, found: 221.0735.

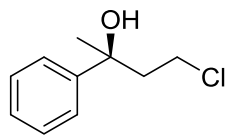
(*R*)-2-(naphthalen-2-yl)oxetane [(*R*)-16b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **16a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M3) cells, 30 °C, reaction for 82 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide (***R***)-**16b** as a light yellow solid in 37% yield (137.4 mg). **^1H NMR (400 MHz, CDCl_3) δ** 7.94 - 7.91 (m, 1H), 7.88 (d, $J = 7.1$ Hz, 1H), 7.83 (d, $J = 8.3$ Hz, 1H), 7.70 - 7.67 (m, 1H), 7.59 (t, $J = 7.7$ Hz, 1H), 7.54 - 7.51 (m, 2H), 6.51 (t, $J = 7.6$ Hz, 1H), 4.98 (td, $J = 7.9, 5.8$ Hz, 1H), 4.75 (dt, $J = 9.1, 5.9$ Hz, 1H), 3.34 - 3.26 (m, 1H), 2.74 - 2.66 (m, 1H). **^{13}C NMR (100 MHz, CDCl_3) δ** 139.2, 133.6, 129.0, 128.9, 127.7, 126.1, 125.7, 125.7, 122.8, 121.4, 80.8, 68.7, 30.1. $[\alpha]_D^{25} = +266.21$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, $\lambda = 210$ nm) indicated >99%

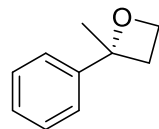
ee: $t_{(S)}$ (minor) = 9.7 min, $t_{(R)}$ (major) = 10.5 min. **HRMS (ESI)** m/z : calculated for $C_{13}H_{13}O$ $[M+H]^+$: 185.0961, found: 185.0970. **m.p.**: 65.5 - 66.7 °C.

(*S*)-4-chloro-2-phenylbutan-2-ol [(*S*)-17a]



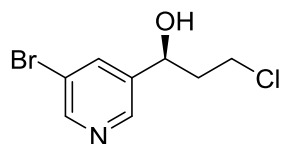
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **18a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 1.5 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**17a** as a light yellow liquid in 49% yield (179.5 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.42 (d, J = 7.0 Hz, 2H), 7.36 (t, J = 7.1 Hz, 2H), 7.27 (t, J = 7.3 Hz, 1H), 3.58 - 3.51 (m, 1H), 3.37 - 3.30 (m, 1H), 2.33 - 2.28 (m, 2H), 1.60 (s, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 146.4, 128.6, 127.2, 124.7, 74.5, 46.7, 40.6, 31.0. $[\alpha]_D^{25}$ = - 13.99 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated >99% *ee*: $t_{(S)}$ (major) = 30.4 min, $t_{(R)}$ (minor) = 33.8 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{13}ClKO$ $[M+K]^+$: 223.0287, found: 223.0290.

(*R*)-2-methyl-2-phenyloxetane [(*R*)-17b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **17a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 1.5 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide (*R*)-**17b** as a light yellow liquid in 36% yield (107.7 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.44 - 7.37 (m, 4H), 7.30 - 7.26 (m, 1H), 4.65 (dt, J = 8.6, 6.3 Hz, 1H), 4.55 (dt, J = 8.8, 6.5 Hz, 1H), 2.86 - 2.73 (m, 2H), 1.76 (s, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 148.2, 128.3, 126.7, 123.6, 86.6, 64.6, 35.6, 30.8. $[\alpha]_D^{25}$ = + 107.92 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated >99% *ee*: $t_{(S)}$ (minor) = 11.0 min, $t_{(R)}$ (major) = 13.8 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{13}O$ $[M+H]^+$: 149.0961, found: 149.0963.

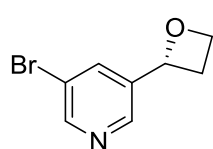
(*S*)-1-(5-bromopyridin-3-yl)-3-chloropropan-1-ol [(*S*)-18a]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **18a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 77 h. The crude product was purified by

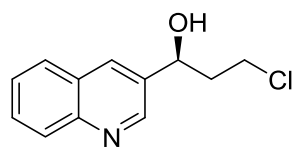
flash column chromatography on silica gel (dichloromethane : ethyl acetate = 6:1) to provide **(S)-18a** as a light yellow liquid in 50% yield (250.0 mg). **¹H NMR (400 MHz, CDCl₃)** δ 8.41 (d, J = 2.1 Hz, 1H), 8.32 (d, J = 1.9 Hz, 1H), 7.87 (t, J = 2.0 Hz, 1H), 4.94 (dd, J = 9.1, 4.0 Hz, 1H), 4.77 (s, 1H), 3.79 - 3.73 (m, 1H), 3.56 (dt, J = 11.1, 5.4 Hz, 1H), 2.18 - 2.09 (m, 1H), 2.05 - 1.96 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 149.5, 145.3, 142.0, 136.8, 121.2, 67.5, 41.4, 41.3. $[\alpha]_D^{25}$ = -12.09 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OJ-H, 5% IPA in *n*-hexane, 1.0 ml/min, λ = 210 nm) indicated 89% *ee*: $t_{(S)}$ (major) = 14.1 min, $t_{(R)}$ (minor) = 16.2 min. **HRMS (ESI)** m/z : calculated for C₈H₁₀BrClNO [M+H]⁺: 249.9629, found: 249.9636.

(R)-3-bromo-5-(oxetan-2-yl) pyridine [(R)-18b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **18a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 77 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 8:1 ~ 6:1) to provide **(R)-18b** as a light yellow liquid in 42% yield (178.5 mg). **¹H NMR (400 MHz, CDCl₃)** δ 8.59 (t, J = 1.8 Hz, 1H), 8.49 (s, 1H), 7.97 (q, J = 1.8 Hz, 1H), 5.80 (t, J = 7.0 Hz, 1H), 4.87 - 4.81 (m, 1H), 4.69 - 4.64 (m, 1H), 3.12 - 3.03 (m, 1H), 2.67 - 2.58 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** 150.3, 145.2, 140.8, 135.8, 121.1, 79.8, 68.8, 30.5. $[\alpha]_D^{25}$ = +104.03 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OB-H, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 97% *ee*: $t_{(S)}$ (minor) = 33.1 min, $t_{(R)}$ (major) = 35.8 min. **HRMS (ESI)** m/z : calculated for C₈H₉BrNO [M+H]⁺: 213.9862, found: 213.9864.

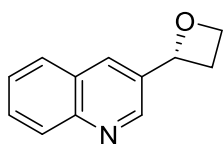
(S)-3-chloro-1-(quinolin-3-yl)propan-1-ol [(S)-19a]



Prepared according to the general procedure: 100 mL PB buffer (200 mM, pH 8.5) containing 10 mM **19a** (1 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 48 h. The crude product was purified by flash column chromatography on silica gel (dichloromethane: ethyl acetate = 4:1 ~ 3:1) to provide **(S)-19a** as a white solid in 48% yield (105.9 mg). **¹H NMR (400 MHz, CDCl₃)** δ 8.65 (d, J = 2.2 Hz, 1H), 8.05 (s, 1H), 7.96 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 8.2 Hz, 1H), 7.64 - 7.60 (m, 1H), 7.51 - 7.47 (m, 1H), 5.10 (dd, J = 8.9, 4.2 Hz, 1H), 3.83 - 3.77 (m, 1H), 3.56 (dt, J = 10.9, 5.6 Hz, 1H), 2.28 - 2.20 (m, 1H), 2.10 - 2.02 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 149.0, 147.2, 137.0, 133.2, 129.7, 128.6, 127.9, 127.8, 127.1, 68.6, 41.7, 41.4. $[\alpha]_D^{25}$ =

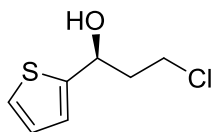
- 22.38 ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OD-H, 10% IPA in *n*-hexane, 1.0 ml/min, $\lambda = 210$ nm) indicated 97% *ee*: $t_{(S)}$ (major) = 16.3 min, $t_{(R)}$ (minor) = 17.8 min. **HRMS (ESI)** m/z : calculated for $\text{C}_{12}\text{H}_{13}\text{ClNO}$ $[\text{M}+\text{H}]^+$: 222.0680, found: 222.0690. **m.p.**: 70.2 - 72.3 °C .

(*R*)-3-(oxetan-2-yl)quinoline [(*R*)-19b]



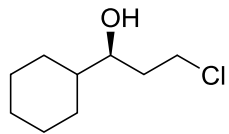
Prepared according to the general procedure: 100 mL PB buffer (200 mM, pH 8.5) containing 10 mM **19a** (1 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C , reaction for 48 h. The crude product was purified by flash column chromatography on silica gel (dichloromethane: ethyl acetate = 6:1 ~ 4:1) to provide (*R*)-**19b** as a light yellow in 44% yield (82.2 mg). **¹H NMR (400 MHz, CDCl₃)** δ 8.95 (d, $J = 2.2$ Hz, 1H), 8.22 (d, $J = 2.1$ Hz, 1H), 8.11 (d, $J = 8.5$ Hz, 1H), 7.83 (d, $J = 8.2$ Hz, 1H), 7.72 - 7.68 (m, 1H), 7.56 - 7.52 (m, 1H), 6.01 (t, $J = 7.5$ Hz, 1H), 4.90 (td, $J = 8.0, 5.9$ Hz, 1H), 4.74 (dt, $J = 9.3, 5.8$ Hz, 1H), 3.18 - 3.09 (m, 1H), 2.78 - 2.69 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 148.6, 147.8, 136.2, 132.4, 129.6, 129.3, 128.0, 127.8, 127.0, 81.0, 68.7, 30.7. $[\alpha]_{\text{D}}^{25} = +139.30$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (AD-H, 5% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated 96% *ee*: $t_{(S)}$ (minor) = 39.3 min, $t_{(R)}$ (major) = 41.3 min. **HRMS (ESI)** m/z : calculated for $\text{C}_{12}\text{H}_{12}\text{NO}$ $[\text{M}+\text{H}]^+$: 186.0913, found: 186.0921.

(*S*)-3-chloro-1-(thiophen-2-yl)propan-1-ol [(*S*)-20a]



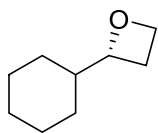
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **20a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C , reaction for 12 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**20a** as a light yellow liquid in 50% yield (179.0 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.27 (dd, $J = 4.9, 1.4$ Hz, 1H), 7.02 - 6.97 (m, 2H), 5.20 (dd, $J = 8.5, 5.1$ Hz, 1H), 3.77 - 3.71 (m, 1H), 3.58 (dt, $J = 16.9, 2.1$ Hz, 1H), 2.35 - 2.28 (m, 1H), 2.23 - 2.15 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 147.5, 126.9, 125.1, 124.2, 67.2, 41.6. $[\alpha]_{\text{D}}^{25} = -36.78$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 2% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated >99% *ee*: $t_{(S)}$ (major) = 28.1 min, $t_{(R)}$ (minor) = 30.2 min. **HRMS (ESI)** m/z : calculated for $\text{C}_7\text{H}_{10}\text{ClOS}$ $[\text{M}+\text{H}]^+$: 177.0135, found: 177.0138.

(*S*)-3-chloro-1-cyclohexylpropan-1-ol [(*S*)-21a]



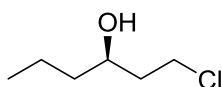
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 10 mM **21a** (1 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 60 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**21a** as a light yellow liquid in 48% yield (85.4 mg). ¹H NMR (400 MHz, CDCl₃) δ 3.72 - 3.68 (m, 2H), 3.61 - 3.56 (m, 1H), 1.96 - 1.74 (m, 5H), 1.69 - 1.63 (m, 2H), 1.61 (s, 1H), 1.37 - 0.95 (m, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 73.1, 43.5, 42.6, 36.9, 29.7, 28.4, 27.0, 26.3, 25.4. [α]_D²⁵ = - 17.60 (c = 1.00, CH₂Cl₂). GC analysis (CYCLODEX-B, 110 °C for 85 min) indicated 98% *ee*: t_(S) (major) = 50.9 min, t_(R) (minor) = 53.8 min. HRMS (ESI) *m/z*: calculated for C₉H₁₇ClNaO [M+Na]⁺: 199.0860, found: 199.0866.

(*R*)-2-cyclohexyloxetane [(*R*)-21b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 10 mM **21a** (1 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 60 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 50:1 ~ 40:1) to provide the (*R*)-**21b** as a light yellow liquid in 35% yield (48.9 mg). ¹H NMR (400 MHz, CDCl₃) δ 4.67 - 4.61 (m, 1H), 4.49 - 4.40 (m, 2H), 2.59 - 2.50 (m, 1H), 2.41 - 2.32 (m, 1H), 1.88 - 1.83 (m, 1H), 1.76 - 1.57 (m, 5H), 1.27 - 1.20 (m, 3H), 0.90 - 0.78 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 86.8, 68.2, 44.8, 27.6, 26.6, 26.2, 25.8, 25.7. [α]_D²⁵ = + 11.30 (c = 1.00, CH₂Cl₂). GC analysis (Rt-bDEXcst, 80 °C for 45 min) indicated >99% *ee*: t_(S) (minor) = 32.9 min, t_(R) (major) = 35.8 min. HRMS (ESI) *m/z*: calculated for C₉H₁₇O [M+H]⁺: 141.1274, found: 141.1281.

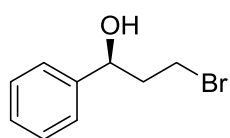
(*R*)-1-chlorohexan-3-ol [(*R*)-22a]



Prepared according to the general procedure: 100 mL PB buffer (200 mM, pH 8.5) containing 20 mM **22a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 36 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 60:1) to provide (*R*)-**22a** as a light yellow liquid in 41% yield (112.6 mg). ¹H NMR (400 MHz, CDCl₃) δ 3.84 - 3.78 (m, 1H), 3.72 - 3.61 (m, 2H), 2.15 (s, 1H), 1.91 - 1.76 (m, 2H), 1.48 - 1.30 (m, 4H), 0.93 - 0.89 (m, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 68.6,

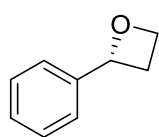
42.1, 39.8, 39.7, 18.8, 14.1. $[\alpha]_D^{25} = -27.30$ ($c = 1.00$, CH_2Cl_2). **GC analysis** (R_t -bDEXest, 90°C for 90 min) indicated 93% *ee*: $t_{(S)}$ (minor) = 74.1 min, $t_{(R)}$ (major) = 75.9 min. **HRMS (ESI) m/z** : calculated for $\text{C}_6\text{H}_{14}\text{ClO}$ $[\text{M}+\text{H}]^+$: 137.0728, found: 137.0728.

(*S*)-3-bromo-1-phenylpropan-1-ol [(*S*)-23a]



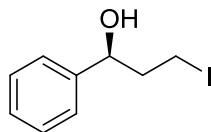
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **23a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30°C , reaction for 6 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**23a** as a white solid in 50% yield (212.4 mg). **^1H NMR (400 MHz, CDCl_3)** δ 7.37 (d, $J = 4.3$ Hz, 4H), 7.33 - 7.28 (m, 1H), 4.93 (dd, $J = 8.3, 4.6$ Hz, 1H), 3.62 - 3.56 (m, 1H), 3.42 (dt, $J = 10.0, 6.1$ Hz, 1H), 2.37 - 2.28 (m, 1H), 2.22 - 2.13 (m, 1H). **^{13}C NMR (100 MHz, CDCl_3)** δ 143.7, 128.8, 128.1, 125.9, 72.4, 41.7, 30.4. $[\alpha]_D^{25} = -9.59$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OD-H, 10% IPA in *n*-hexane, 1.0 ml/min, $\lambda = 210$ nm) indicated >99% *ee*: $t_{(S)}$ (major) = 7.5 min, $t_{(R)}$ (minor) = 8.9 min. **HRMS (ESI) m/z** : calculated for $\text{C}_9\text{H}_{11}\text{BrNaO}$ $[\text{M}+\text{Na}]^+$: 236.9885, found: 236.9891. **m.p.**: $55.5 - 56.2^\circ\text{C}$.

(*R*)-2-phenyloxetane [(*R*)-1b] from 23a



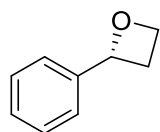
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 8.5) containing 20 mM **23a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30°C , reaction for 6 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 40:1) to provide (*R*)-**1b** as a light yellow liquid in 30% yield (80.9 mg). **^1H NMR (400 MHz, CDCl_3)** δ 7.46 (d, $J = 6.9$ Hz, 2H), 7.40 (t, $J = 7.4$ Hz, 2H), 7.31 (t, $J = 7.2$ Hz, 1H), 5.83 (t, $J = 7.5$ Hz, 1H), 4.85 (td, $J = 8.0, 5.8$ Hz, 1H), 4.67 (dt, $J = 9.3, 5.8$ Hz, 1H), 3.08 - 2.99 (m, 1H), 2.72 - 2.64 (m, 1H). **^{13}C NMR (100 MHz, CDCl_3)** δ 143.6, 128.5, 127.8, 125.3, 83.0, 68.3, 30.8. $[\alpha]_D^{25} = +161.58$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, $\lambda = 210$ nm) indicated 92% *ee*: $t_{(S)}$ (minor) = 10.0 min, $t_{(R)}$ (major) = 11.2 min. **HRMS (ESI) m/z** : calculated for $\text{C}_9\text{H}_{10}\text{NaO}$ $[\text{M}+\text{Na}]^+$: 157.0624, found: 157.0629.

(*S*)-3-iodo-1-phenylpropan-1-ol [(*S*)-24a]



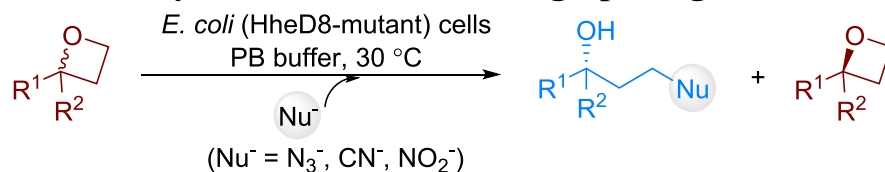
Prepared according to the general procedure: 100 mL Gly-NaOH buffer (300 mM, pH 9.5) containing 20 mM **24a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 1.5 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 40:1 ~ 20:1) to provide (*S*)-**24a** as a white solid in 47.9% yield (251.3 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.39 - 7.34 (m, 4H), 7.32 - 7.29 (m, 1H), 4.79 (dd, J = 8.1, 4.9 Hz, 1H), 3.32 - 3.26 (m, 1H), 3.19 - 3.14 (m, 1H), 2.29 - 2.10 (m, 2H). **¹³C NMR (100 MHz, CDCl₃)** δ 143.5, 128.8, 128.0, 125.9, 74.2, 42.3, 2.9. $[\alpha]_D^{25}$ = - 0.20 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OD-H, 10% IPA in *n*-hexane, 1.0 ml/min, λ = 210 nm) indicated >99% *ee*: $t_{(S)}$ (major) = 7.6 min, $t_{(R)}$ (minor) = 9.3 min. **HRMS (ESI)** m/z : calculated for C₉H₁₁INaO $[M+Na]^+$: 284.9747, found: 284.9743. **m.p.**: 44.6 - 45.3 °C.

(*R*)-2-phenyloxetane [(*R*)-1b] from 24a



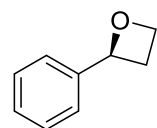
Prepared according to the general procedure: 100 mL Gly-NaOH buffer (300 mM, pH 9.5) containing 20 mM **24a** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 1.5 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 50:1 ~ 40:1) to provide (*R*)-**1b** as a light yellow liquid in 39% yield (107.1 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.48 - 7.45 (m, 2H), 7.43 - 7.39 (m, 2H), 7.34 - 7.30 (m, 1H), 5.83 (t, J = 7.5 Hz, 1H), 4.85 (td, J = 8.0, 5.8 Hz, 1H), 4.68 (dt, J = 9.2, 5.8 Hz, 1H), 3.08 - 3.00 (m, 1H), 2.73 - 2.64 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 143.6, 128.6, 127.9, 125.3, 83.0, 68.3, 30.8. $[\alpha]_D^{25}$ = + 173.18 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 93% *ee*: $t_{(S)}$ (minor) = 11.0 min, $t_{(R)}$ (major) = 12.2 min. **HRMS (ESI)** m/z : calculated for C₉H₁₁O $[M+H]^+$: 135.0804, found: 135.0812.

6. Biocatalytic enantioselective ring-opening of oxetanes



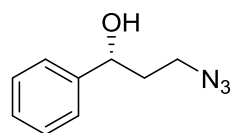
General procedure: In a 200 mL round-bottom flask, a resting cell suspension of *E. coli* (HheD8-M4) at a concentration of 10 g dcw/L was prepared in 100 mL of PB buffer (50 mM, pH 7.5). To this suspension, 2 mmol of oxetane (*rac*)-**b** and 2 mmol of NaN₃ were added to a final concentration of 20 mM. The reaction mixture was then stirred at 30 °C. Upon completion of the enzymatic reaction, the mixture was subjected to extraction using ethyl acetate (3 × 70 mL). The organic phases were separated by centrifugation (8800 × *g*, 3 min), combined, dried over anhydrous Na₂SO₄, and evaporated at reduced pressure. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 50:1 ~ 1:1) on silica gel to afford the desired chiral oxetane (*S*)-**b** and γ -azidoalcohol (*R*)-**c**.

(*S*)-2-phenyloxetane [(*S*)-**1b**] (Ring opening by azide)



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **1b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 10 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**1b** as a light yellow liquid in 33% yield (88.1 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.50 - 7.45 (m, 2H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.36 - 7.30 (m, 1H), 5.84 (t, *J* = 7.5 Hz, 1H), 4.85 (td, *J* = 8.0, 5.9 Hz, 1H), 4.68 (dt, *J* = 9.3, 5.7 Hz, 1H), 3.08 - 2.99 (m, 1H), 2.74 - 2.64 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 143.6, 128.5, 127.9, 125.3, 82.9, 68.3, 30.8. [α]_D²⁵ = -173.88 (*c* = 1.00, CH₂Cl₂). HPLC analysis (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated >99% *ee*: *t*_(*S*) (major) = 10.0 min, *t*_(*R*) (minor) = 11.3 min. HRMS (ESI) *m/z*: calculated for C₉H₁₁O [M+H]⁺: 135.0804, found: 135.0806.

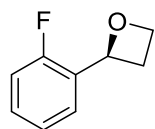
(*R*)-3-azido-1-phenylpropan-1-ol [(*R*)-**1c**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **1b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 10 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~

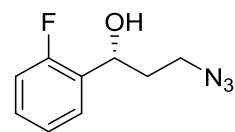
10:1) to provide (*R*)-**1c** as a light yellow liquid in 47% yield (165.1 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.40 - 7.31 (m, 4H), 7.30 - 7.20 (m, 1H), 5.45 (d, *J* = 4.4 Hz, 1H), 4.66 (q, *J* = 5.9 Hz, 1H), 3.51 - 3.41 (m, 1H), 3.41 - 3.32 (m, 1H), 1.85 (q, *J* = 7.5 Hz, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 145.7, 128.2, 127.0, 125.8, 69.6, 47.9, 38.2. $[\alpha]_D^{25} = +26.68$ (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 97% *ee*: *t*_(S) (minor) = 15.3 min, *t*_(R) (major) = 16.6 min. **HRMS (ESI)** *m/z*: calculated for C₉H₁₁N₃NaO [M+Na]⁺: 200.0794, found: 200.0803.

(*S*)-2-(2-fluorophenyl)oxetane [(*S*)-**2b**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **2b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 10 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1) to provide (*S*)-**2b** as a light yellow liquid in 35% yield (106.8 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.67 (td, *J* = 7.5, 2.0 Hz, 1H), 7.32 - 7.18 (m, 2H), 7.07 - 6.99 (m, 1H), 6.06 (t, *J* = 7.6 Hz, 1H), 4.85 (td, *J* = 7.8, 5.8 Hz, 1H), 4.69 (dt, *J* = 9.2, 5.9 Hz, 1H), 3.15 - 3.04 (m, 1H), 2.72 - 2.62 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 159.3 (d, *J* = 246.3 Hz), 130.8 (d, *J* = 13.6 Hz), 129.2 (d, *J* = 8.0 Hz), 126.9 (d, *J* = 4.5 Hz), 124.3 (d, *J* = 3.5 Hz), 115.2 (d, *J* = 20.7 Hz), 77.7, 68.9, 29.9. $[\alpha]_D^{25} = -135.20$ (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated >99% *ee*: *t*_(S) (major) = 12.9 min, *t*_(R) (minor) = 16.5 min. **HRMS (ESI)** *m/z*: calculated for C₉H₁₀FO [M+H]⁺: 153.0710, found: 153.0712.

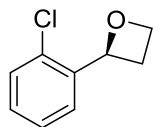
(*R*)-3-azido-1-(2-fluorophenyl)propan-1-ol [(*R*)-**2c**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **2b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 10 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 10:1) to provide (*R*)-**2c** as a light yellow liquid in 48% yield (186.4 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.52 (td, *J* = 7.6, 1.8 Hz, 1H), 7.32 - 7.27 (m, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 10.5 Hz, 1H), 5.54 (d, *J* = 4.8 Hz, 1H), 4.95 (dt, *J* = 8.1, 4.9 Hz, 1H), 3.53 - 3.37 (m, 2H), 1.92 - 1.74 (m, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 158.9 (d, *J* = 243.3 Hz), 132.3 (d, *J* = 13.7 Hz),

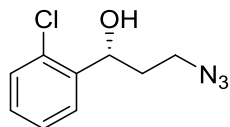
128.8 (d, $J = 8.2$ Hz), 127.5 (d, $J = 4.7$ Hz), 124.5 (d, $J = 3.3$ Hz), 115.0 (d, $J = 21.7$ Hz), 63.2, 47.6, 36.9. $[\alpha]_D^{25} = +68.15$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (IH, 3% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated 98% *ee*: $t_{(R)}$ (major) = 26.9 min, $t_{(S)}$ (minor) = 28.1 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{10}\text{FN}_3\text{NaO}$ $[\text{M}+\text{Na}]^+$: 218.0700, found: 218.0701.

(*S*)-2-(2-chlorophenyl)oxetane [(*S*)-3b]



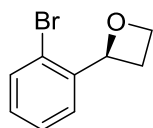
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **3b** (2 mmol), 20 mM NaN_3 (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 37 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1) to provide (*S*)-**3b** as a yellow liquid in 42% yield (141.7 mg). **^1H NMR (400 MHz, CDCl_3)** δ 7.77 (d, $J = 7.6$ Hz, 1H), 7.38 - 7.30 (m, 2H), 7.23 (td, $J = 6.4, 1.0$ Hz, 1H), 6.02 (t, $J = 7.5$ Hz, 1H), 4.84 (td, $J = 6.4, 5.2$ Hz, 1H), 4.65 (dt, $J = 9.2, 6.1$ Hz, 1H), 3.24 - 3.14 (m, 1H), 2.56 - 2.46 (m, 1H). **^{13}C NMR (100 MHz, CDCl_3)** δ 141.3, 130.3, 129.1, 128.4, 126.9, 125.9, 80.2, 68.5, 29.9. $[\alpha]_D^{25} = -207.95$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated 92% *ee*: $t_{(S)}$ (major) = 11.1 min, $t_{(R)}$ (minor) = 11.9 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_9\text{ClNaO}$ $[\text{M}+\text{Na}]^+$: 191.0234, found: 191.0234.

(*R*)-3-azido-1-(2-chlorophenyl)propan-1-ol [(*R*)-3c]



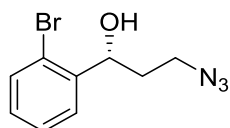
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **3b** (2 mmol), 20 mM NaN_3 (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 37 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 10:1) to provide (*R*)-**3c** as a light yellow liquid in 48% yield (204.9 mg). **^1H NMR (400 MHz, $\text{DMSO}-d_6$)** δ 7.62 (d, $J = 7.5$ Hz, 1H), 7.39 - 7.34 (m, 2H), 7.29 - 7.24 (m, 1H), 5.61 (d, $J = 4.3$ Hz, 1H), 5.02 (dt, $J = 9.6, 3.8$ Hz, 1H), 3.53 - 3.42 (m, 2H), 1.95 - 1.84 (m, 1H), 1.74 - 1.64 (m, 1H). **^{13}C NMR (100 MHz, $\text{DMSO}-d_6$)** δ 143.0, 130.4, 129.0, 128.6, 127.5, 127.4, 66.0, 47.7, 36.6. $[\alpha]_D^{25} = +78.34$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated 94% *ee*: $t_{(R)}$ (major) = 43.1 min, $t_{(S)}$ (minor) = 45.6 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{10}\text{ClN}_3\text{NaO}$ $[\text{M}+\text{Na}]^+$: 234.0405, found: 234.0409.

(*S*)-2-(2-bromophenyl)oxetane [(*S*)-4b]



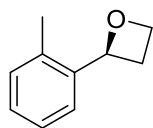
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **4b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 60 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1) to provide (*S*)-**4b** as a light yellow liquid in 48% yield (204.8 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.76 (d, J = 7.7 Hz, 1H), 7.51 (d, J = 7.9 Hz, 1H), 7.40 (t, J = 7.5 Hz, 1H), 7.16 (t, J = 7.8 Hz, 1H), 5.94 (t, J = 7.5 Hz, 1H), 4.83 (td, J = 8.5, 6.6 Hz, 1H), 4.64 (dt, J = 9.1, 6.1 Hz, 1H), 3.27 - 3.17 (m, 1H), 2.53 - 2.43 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 142.9, 132.4, 128.8, 127.6, 126.3, 119.7, 82.1, 68.4, 30.1. $[\alpha]_D^{25}$ = -169.48 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 93% *ee*: $t_{(S)}$ (major) = 11.5 min, $t_{(R)}$ (minor) = 12.3 min. **HRMS (ESI) m/z** : calculated for C₉H₉BrNaO [M+Na]⁺: 234.9729, found: 234.9729.

(*R*)-3-azido-1-(2-bromophenyl)propan-1-ol [(*R*)-4c]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **4b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 60 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 10:1) to provide (*R*)-**4c** as a light yellow liquid in 44% yield (222.8 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.58 (dd, J = 28.3, 9.6 Hz, 2H), 7.40 (t, J = 7.5 Hz, 1H), 7.19 (t, J = 7.8 Hz, 1H), 5.67 (d, J = 4.8 Hz, 1H), 4.97 (dt, J = 9.8, 3.6 Hz, 1H), 3.55 - 3.43 (m, 2H), 1.97 - 1.85 (m, 1H), 1.73 - 1.62 (m, 1H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 144.5, 132.3, 128.9, 127.9, 127.8, 120.9, 68.3, 47.7, 36.7. $[\alpha]_D^{25}$ = +84.24 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 91% *ee*: $t_{(R)}$ (major) = 12.7 min, $t_{(S)}$ (minor) = 13.7 min. **HRMS (ESI) m/z** : calculated for C₉H₁₀BrN₃NaO [M+Na]⁺: 277.9899, found: 277.9904.

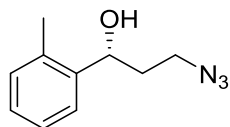
(*S*)-2-(*o*-tolyl)oxetane [(*S*)-5b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **5b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 33 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1) to

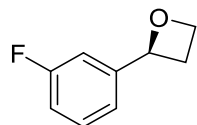
provide (*S*)-**5b** as a yellow liquid in 30% yield (91.5 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.72 (d, J = 7.6 Hz, 1H), 7.32 (t, J = 7.9 Hz, 1H), 7.22 (t, J = 7.4 Hz, 1H), 7.16 (d, J = 7.5 Hz, 1H), 6.01 (t, J = 7.6 Hz, 1H), 4.87 (td, J = 8.1, 6.4 Hz, 1H), 4.66 (dt, J = 9.3, 5.8 Hz, 1H), 3.15 - 3.06 (m, 1H), 2.61 - 2.51 (m, 1H), 2.20 (s, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 141.7, 133.3, 130.0, 127.2, 126.1, 124.0, 80.6, 68.1, 29.7, 18.4. $[\alpha]_D^{25}$ = -173.68 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 97% *ee*: $t_{(R)}$ (minor) = 14.4 min, $t_{(S)}$ (major) = 15.1 min. **HRMS (ESI)** m/z : calculated for C₁₀H₁₃O [M+H]⁺: 149.0961, found: 149.0968.

(*R*)-3-azido-1-(*o*-tolyl)propan-1-ol [(*R*)-**5c**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **5b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 33 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 10:1) to provide (*R*)-**5c** as a light yellow liquid in 44% yield (173.3 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.47 (d, J = 7.6 Hz, 1H), 7.22 - 7.18 (m, 1H), 7.16 - 7.10 (m, 2H), 5.32 (d, J = 4.5 Hz, 1H), 4.87 (dt, J = 8.7, 4.2 Hz, 1H), 3.57 - 3.40 (m, 2H), 2.30 (s, 3H), 1.86 - 1.69 (m, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 143.8, 133.7, 130.0, 126.6, 126.0, 125.4, 66.0, 48.1, 37.0, 18.6. $[\alpha]_D^{25}$ = +40.97 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 97% *ee*: $t_{(S)}$ (minor) = 13.0 min, $t_{(R)}$ (major) = 14.1 min. **HRMS (ESI)** m/z : calculated for C₁₀H₁₃N₃NaO [M+Na]⁺: 214.0951, found: 214.0949.

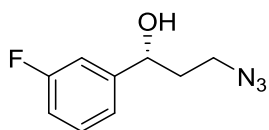
(*S*)-2-(3-fluorophenyl)oxetane [(*S*)-**6b**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **6b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 12 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**6b** as a light yellow liquid in 38% yield (115.7 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.34 (td, J = 7.9, 5.9 Hz, 1H), 7.20 - 7.15 (m, 2H), 6.98 (td, J = 8.2, 2.6 Hz, 1H), 5.79 (t, J = 7.5 Hz, 1H), 4.83 (td, J = 8.2, 6.2 Hz, 1H), 4.66 (dt, J = 9.3, 5.8 Hz, 1H), 3.08 - 3.00 (m, 1H), 2.66 - 2.57 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 163.2 (d, J = 246.0 Hz), 146.5 (d, J = 6.9 Hz), 130.2 (d, J = 8.1 Hz), 120.7 (d, J = 2.9 Hz), 114.6 (d, J = 21.3 Hz), 112.2 (d, J = 21.8 Hz), 82.2, 68.4, 30.7. $[\alpha]_D^{25}$ = -

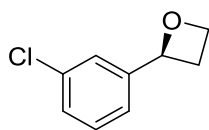
169.88 ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated 99% *ee*: $t_{(S)}$ (major) = 14.4 min, $t_{(R)}$ (minor) = 15.2 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{10}\text{FO}$ $[\text{M}+\text{H}]^+$: 153.0710, found: 153.0718.

(*R*)-3-azido-1-(3-fluorophenyl)propan-1-ol [(*R*)-6c]



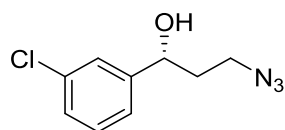
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **6b** (2 mmol), 20 mM NaN_3 (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 $^{\circ}\text{C}$, reaction for 12 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 10:1) to provide (*R*)-**6c** as a light yellow liquid in 47% yield (183.6 mg). **^1H NMR (400 MHz, $\text{DMSO}-d_6$)** δ 7.37 (dd, $J = 14.2, 8.2$ Hz, 1H), 7.20 - 7.12 (m, 2H), 7.05 (td, $J = 8.8, 2.6$ Hz, 1H), 5.54 (d, $J = 4.8$ Hz, 1H), 4.66 (dt, $J = 8.9, 5.0$ Hz, 1H), 3.49 - 3.40 (m, 1H), 3.39 - 3.33 (m, 1H), 1.90 - 1.75 (m, 2H). **^{13}C NMR (100 MHz, $\text{DMSO}-d_6$)** δ 162.3 (d, $J = 243.2$ Hz), 148.8 (d, $J = 6.6$ Hz), 130.1 (d, $J = 8.1$ Hz), 121.7 (d, $J = 2.6$ Hz), 113.6 (d, $J = 21.0$ Hz), 112.3 (d, $J = 21.6$ Hz), 68.9, 47.7, 37.9. $[\alpha]_D^{25} = +28.98$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated >99% *ee*: $t_{(S)}$ (minor) = 52.4 min, $t_{(R)}$ (major) = 58.7 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{10}\text{FN}_3\text{NaO}$ $[\text{M}+\text{Na}]^+$: 218.0700, found: 218.0711.

(*S*)-2-(3-chlorophenyl)oxetane [(*S*)-7b]



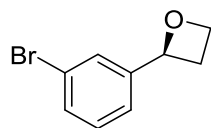
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **7b** (2 mmol), 20 mM NaN_3 (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 $^{\circ}\text{C}$, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**7b** as a light yellow liquid in 46% yield (167.2 mg). **^1H NMR (400 MHz, CDCl_3)** δ 7.46 (s, 1H), 7.33 - 7.23 (m, 3H), 5.76 (t, $J = 7.5$ Hz, 1H), 4.81 (td, $J = 8.2, 6.1$ Hz, 1H), 4.64 (dt, $J = 9.2, 6.0$ Hz, 1H), 3.07 - 2.97 (m, 1H), 2.65 - 2.54 (m, 1H). **^{13}C NMR (100 MHz, CDCl_3)** δ 145.8, 134.4, 129.8, 127.8, 125.3, 123.2, 82.0, 68.3, 30.6. $[\alpha]_D^{25} = -151.90$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 1% IPA in *n*-hexanes, 0.5 ml/min, $\lambda = 210$ nm) indicated 94% *ee*: $t_{(S)}$ (major) = 14.2 min, $t_{(R)}$ (minor) = 16.6 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{10}\text{ClO}$ $[\text{M}+\text{H}]^+$: 169.0415, found: 169.0419.

(*R*)-3-azido-1-(3-chlorophenyl)propan-1-ol [(*R*)-7c]



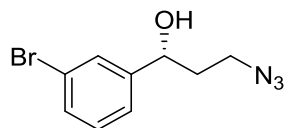
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **7b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 10:1) to provide (*R*)-**7c** as a light yellow liquid in 47% yield (212.0 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.39 - 7.34 (m, 2H), 7.31 - 7.28 (m, 2H), 5.54 (d, *J* = 4.7 Hz, 1H), 4.64 (dt, *J* = 8.8, 4.8 Hz, 1H), 3.50 - 3.38 (m, 1H), 3.40 - 3.30 (m, 2H), 1.89 - 1.74 (m, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 148.3, 133.1, 130.0, 126.8, 125.6, 124.4, 69.0, 47.8, 38.0. **$[\alpha]_D^{25}$** = + 26.08 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 97% *ee*: *t*_(S) (minor) = 13.7 min, *t*_(R) (major) = 14.8 min. **HRMS (ESI)** *m/z*: calculated for C₉H₁₁ClN₃O [M+H]⁺: 212.0585, found: 212.0589.

(*S*)-2-(3-bromophenyl)oxetane [(*S*)-8b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **8b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 23 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**8b** as a light yellow liquid in 48% yield (204.1 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.60 (s, 1H), 7.40 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.22 (t, *J* = 7.8 Hz, 1H), 5.74 (t, *J* = 7.5 Hz, 1H), 4.80 (td, *J* = 7.0, 5.4 Hz, 1H), 4.62 (dt, *J* = 9.3, 5.8 Hz, 1H), 3.07 - 2.94 (m, 1H), 2.65 - 2.51 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 146.0, 130.7, 130.1, 128.2, 123.7, 122.7, 81.9, 68.3, 30.6. **$[\alpha]_D^{25}$** = -121.31 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 95% *ee*: *t*_(S) (major) = 14.7 min, *t*_(R) (minor) = 17.9 min. **HRMS (ESI)** *m/z*: calculated for C₉H₉BrNaO [M+Na]⁺: 234.9729, found: 234.9728.

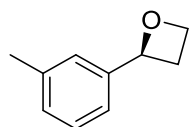
(*R*)-3-azido-1-(3-bromophenyl)propan-1-ol [(*R*)-8c]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **8b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 23 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate

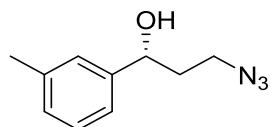
= 30:1 ~ 10:1) to provide (*R*)-**8c** as a light yellow liquid in 48% yield (245.1 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.53 (s, 1H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.35 - 7.26 (m, 2H), 5.54 (d, *J* = 4.7 Hz, 1H), 4.63 (dt, *J* = 8.8, 4.9 Hz, 1H), 3.49 - 3.39 (m, 1H), 3.39 - 3.31 (m, 1H), 1.88 - 1.74 (m, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 148.5, 130.4, 129.7, 128.4, 124.8, 121.6, 68.9, 47.7, 37.9. **$[\alpha]_D^{25}$** = + 22.78 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 95% *ee*: *t*_(S) (minor) = 13.9 min, *t*_(R) (major) = 15.2 min. **HRMS (ESI) *m/z***: calculated for C₉H₁₀BrN₃NaO [M+Na]⁺: 277.9899, found: 277.9906.

(*S*)-2-(*m*-tolyl)oxetane [(*S*)-**9b**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **9b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**9b** as a light yellow liquid in 37% yield (114.2 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.39 - 7.35 (m, 2H), 7.31 (d, *J* = 7.7 Hz, 1H), 7.20 (d, *J* = 7.4 Hz, 1H), 5.87 (t, *J* = 7.6 Hz, 1H), 4.91 (td, *J* = 8.2, 6.0 Hz, 1H), 4.74 (dt, *J* = 9.3, 5.7 Hz, 1H), 3.12 - 3.04 (m, 1H), 2.78 - 2.70 (m, 1H), 2.47 (s, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 143.5, 138.2, 128.6, 128.4, 125.9, 122.3, 83.0, 68.2, 30.7, 21.5. **$[\alpha]_D^{25}$** = -118.21 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 94% *ee*: *t*_(S) (major) = 9.1 min, *t*_(R) (minor) = 10.6 min. **HRMS (ESI) *m/z***: calculated for C₁₀H₁₂NaO [M+Na]⁺: 171.0780, found: 171.0785.

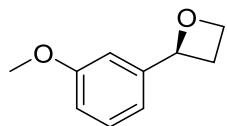
(*R*)-3-azido-1-(*m*-tolyl)propan-1-ol [(*R*)-**9c**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **9b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 10:1) to provide (*R*)-**9c** as a yellow liquid in 48% yield (190.4 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.21 (t, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 10.5 Hz, 2H), 7.05 (d, *J* = 7.4 Hz, 1H), 5.36 (d, *J* = 4.5 Hz, 1H), 4.59 (dt, *J* = 7.1, 5.6 Hz, 1H), 3.48 - 3.39 (m, 1H), 3.37 - 3.31 (m, 1H), 2.30 (s, 3H), 1.81 (q, *J* = 6.9 Hz, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 145.6, 137.2, 128.1, 127.6, 126.3, 122.8, 69.5, 47.9, 38.2, 21.2. **$[\alpha]_D^{25}$** = + 22.78 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3,

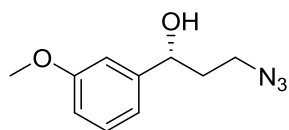
3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 98% *ee*: $t_{(S)}$ (minor) = 14.0 min, $t_{(R)}$ (major) = 15.2 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{13}N_3NaO$ $[M+Na]^+$: 214.0951, found: 214.0952.

(*S*)-2-(3-methoxyphenyl)oxetane [(*S*)-10b]



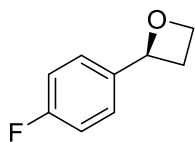
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **10b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**10b** as a colorless liquid in 42% yield (136.8 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.31 (t, J = 7.9 Hz, 1H), 7.06 - 6.97 (m, 2H), 6.85 (ddd, J = 8.2, 2.7, 1.1 Hz, 1H), 5.80 (t, J = 7.5 Hz, 1H), 4.83 (td, J = 8.1, 6.0 Hz, 1H), 4.66 (dt, J = 9.2, 5.8 Hz, 1H), 3.84 (s, 3H), 3.07 - 2.97 (m, 1H), 2.70 - 2.60 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 159.9, 145.4, 129.6, 117.3, 113.4, 110.5, 82.8, 68.3, 55.3, 30.7. $[\alpha]_D^{25}$ = -120.02 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 95% *ee*: $t_{(S)}$ (major) = 14.2 min, $t_{(R)}$ (minor) = 20.6 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{12}NaO_2$ $[M+Na]^+$: 187.0730, found: 187.0739.

(*R*)-3-azido-1-(3-methoxyphenyl)propan-1-ol [(*R*)-10c]



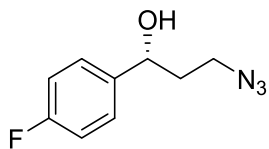
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **10b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 10:1) to provide (*R*)-**10c** as a light yellow liquid in 43% yield (178.5 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.25 (t, J = 7.8 Hz, 1H), 6.98 - 6.87 (m, 2H), 6.81 (dd, J = 8.2, 2.7 Hz, 1H), 5.44 (d, J = 4.5 Hz, 1H), 4.63 (q, J = 5.7 Hz, 1H), 3.75 (s, 3H), 3.49 - 3.41 (m, 1H), 3.40 - 3.31 (m, 1H), 1.84 (q, J = 6.8 Hz, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 159.3, 147.4, 129.3, 117.9, 112.4, 111.2, 69.5, 55.0, 47.9, 38.2. $[\alpha]_D^{25}$ = + 30.79 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 95% *ee*: $t_{(S)}$ (minor) = 26.4 min, $t_{(R)}$ (major) = 28.3 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{13}N_3NaO_2$ $[M+Na]^+$: 230.0900, found: 230.0907.

(*S*)-2-(4-fluorophenyl)oxetane [(*S*)-11b]



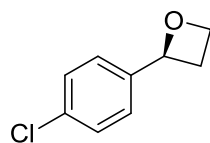
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **11b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 16 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**11b** as a yellow liquid in 36% yield (109.9 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.48 - 7.36 (m, 2H), 7.07 (t, J = 8.7 Hz, 2H), 5.78 (t, J = 7.5 Hz, 1H), 4.82 (td, J = 8.0, 6.2 Hz, 1H), 4.64 (dt, J = 9.3, 5.7 Hz, 1H), 3.07 - 2.94 (m, 1H), 2.70 - 2.57 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 162.5 (d, J = 245.9 Hz), 139.4 (d, J = 3.1 Hz), 127.2 (d, J = 8.1 Hz), 115.4 (d, J = 21.4 Hz), 82.4, 68.2, 30.9. $[\alpha]_D^{25}$ = -148.89 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 99% *ee*: $t_{(S)}$ (major) = 15.2 min, $t_{(R)}$ (minor) = 17.2 min. **HRMS (ESI)** m/z : calculated for C₉H₁₀FO [M+H]⁺: 153.0710, found: 153.0712.

(*R*)-3-azido-1-(4-fluorophenyl)propan-1-ol [(*R*)-11c]



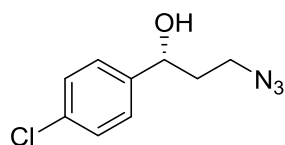
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **11b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 16 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 10:1) to provide (*R*)-**11c** as a light yellow liquid in 50% yield (194.1 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.37 (dd, J = 8.4, 5.7 Hz, 2H), 7.14 (t, J = 8.8 Hz, 2H), 5.46 (d, J = 4.5 Hz, 1H), 4.64 (q, J = 6.5 Hz, 1H), 3.48 - 3.39 (m, 1H), 3.39 - 3.30 (m, 1H), 1.81 (q, J = 6.7 Hz, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 161.2 (d, J = 242.2 Hz), 141.8 (d, J = 3.0 Hz), 127.6 (d, J = 8.0 Hz), 114.8 (d, J = 21.0 Hz), 68.9, 47.8, 38.1. $[\alpha]_D^{25}$ = + 31.28 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 98% *ee*: $t_{(S)}$ (minor) = 13.9 min, $t_{(R)}$ (major) = 15.3 min. **HRMS (ESI)** m/z : calculated for C₉H₁₁FN₃O [M+H]⁺: 196.0881, found: 196.0885.

(S)-2-(4-chlorophenyl)oxetane [(S)-12b]



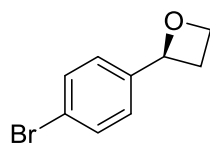
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **12b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 11 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (S)-**12b** as a light yellow liquid in 45% yield (164.4 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.39 - 7.29 (m, 4H), 5.76 (t, J = 7.5 Hz, 1H), 4.80 (td, J = 8.0, 5.8 Hz, 1H), 4.62 (dt, J = 9.2, 5.8 Hz, 1H), 3.04 - 2.95 (m, 1H), 2.63 - 2.54 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 142.1, 133.4, 128.6, 126.6, 82.1, 68.2, 30.7. **$[\alpha]_D^{25}$** = -144.40 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 97% *ee*: $t_{(S)}$ (major) = 8.3 min, $t_{(R)}$ (minor) = 8.9 min. **HRMS (ESI) m/z** : calculated for C₉H₉ClNaO $[M+Na]^+$: 191.0234, found: 191.0241.

(R)-3-azido-1-(4-chlorophenyl)propan-1-ol [(R)-12c]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **12b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 11 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 10:1) to provide (R)-**12c** as a light yellow liquid in 48% yield (216.7 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.37 (d, J = 2.2 Hz, 4H), 5.54 (d, J = 4.7 Hz, 1H), 4.67 (q, J = 6.2 Hz, 1H), 3.51 - 3.41 (m, 1H), 3.41 - 3.30 (m, 1H), 1.83 (q, J = 6.4 Hz, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 144.6, 131.5, 128.1, 127.6, 68.9, 47.8, 38.1. **$[\alpha]_D^{25}$** = + 21.69 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 99% *ee*: $t_{(S)}$ (minor) = 15.2 min, $t_{(R)}$ (major) = 16.5 min. **HRMS (ESI) m/z** : calculated for C₉H₁₁ClN₃O $[M+H]^+$: 212.0585, found: 212.0594.

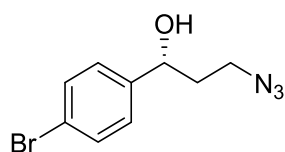
(S)-2-(4-bromophenyl)oxetane [(S)-13b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **13b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 26 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl

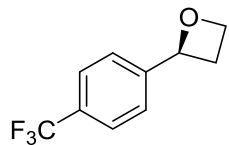
acetate = 30:1) to provide (*S*)-**13b** as a light yellow liquid in 42% yield (177.9mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.55 - 7.47 (m, 2H), 7.35 - 7.27 (m, 2H), 5.75 (t, *J* = 7.5 Hz, 1H), 4.82 (td, *J* = 8.0, 5.8 Hz, 1H), 4.64 (dt, *J* = 9.3, 5.8 Hz, 1H), 3.08 - 2.95 (m, 1H), 2.66 - 2.53 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 142.7, 131.6, 127.0, 121.6, 82.2, 68.3, 30.8. $[\alpha]_D^{25} = -129.83$ (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 98% *ee*: *t*_(S) (major) = 16.0 min, *t*_(R) (minor) = 17.8 min. **HRMS (ESI)** *m/z*: calculated for C₉H₁₀BrO [M+H]⁺: 212.9910, found: 212.9915.

(*R*)-3-azido-1-(4-bromophenyl)propan-1-ol [(*R*)-**13c**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **13b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 26 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 10:1) to provide (*R*)-**13c** as a light yellow liquid in 47% yield (240.0 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.51 (dd, *J* = 8.4, 1.5 Hz, 2H), 7.31 (d, *J* = 7.6 Hz, 2H), 5.52 (d, *J* = 4.6 Hz, 1H), 4.64 (q, *J* = 5.9 Hz, 1H), 3.49 - 3.40 (m, 1H), 3.40 - 3.31 (m, 1H), 1.81 (q, *J* = 6.8 Hz, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 145.0, 131.0, 128.0, 119.9, 68.9, 47.7, 38.0. $[\alpha]_D^{25} = +28.68$ (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 98% *ee*: *t*_(S) (minor) = 17.2 min, *t*_(R) (major) = 18.3 min. **HRMS (ESI)** *m/z*: calculated for C₉H₁₁BrN₃O [M+H]⁺: 256.0080, found: 256.0080.

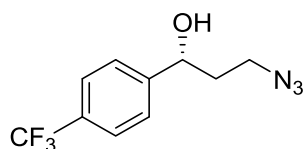
(*S*)-2-(4-(trifluoromethyl)phenyl)oxetane [(*S*)-**14b**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 5 mM **14b** (0.5 mmol), 5 mM NaN₃ (0.5 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 45 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**14b** as a light yellow liquid in 49% yield (52.0 mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H), 5.86 (t, *J* = 7.6 Hz, 1H), 4.85 (td, *J* = 8.0, 6.0 Hz, 1H), 4.67 (dt, *J* = 9.2, 5.5 Hz, 1H), 3.13 - 3.02 (m, 1H), 2.66 - 2.55 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 147.8, 129.9 (q, *J* = 32.0 Hz), 125.6 (q, *J* = 4.0 Hz), 125.3, 124.3 (q, *J* = 270.0 Hz), 82.1, 68.5, 30.7. $[\alpha]_D^{25} = -94.33$ (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3%

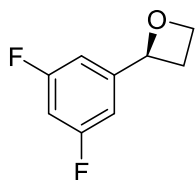
IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 86% *ee*: $t_{(S)}$ (major) = 6.6 min, $t_{(R)}$ (minor) = 7.0 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{10}F_3O$ $[M+H]^+$: 203.0678, found: 203.0683.

(*R*)-3-azido-1-(4-(trifluoromethyl)phenyl)propan-1-ol [(*R*)-14c]



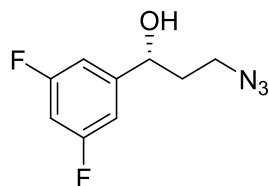
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 5 mM **14b** (0.5 mmol), 5 mM **NaN₃** (0.5 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 45 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 10:1) to provide (*R*)-**14c** as a light yellow liquid in 41% yield (53.5 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.69 (d, J = 8.1 Hz, 2H), 7.57 (d, J = 8.0 Hz, 2H), 5.63 (d, J = 3.8 Hz, 1H), 4.73 (t, J = 6.7 Hz, 1H), 3.51 - 3.42 (m, 1H), 3.40 - 3.35 (m, 1H), 1.89 - 1.78 (m, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 150.4, 127.6 (q, J = 32.0 Hz), 126.5, 125.0 (q, J = 4.0 Hz), 124.4 (d, J = 270.0 Hz), 69.0, 47.7, 37.9. $[\alpha]_D^{25}$ = +17.49 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 94% *ee*: $t_{(S)}$ (minor) = 10.5 min, $t_{(R)}$ (major) = 11.3 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{10}F_3N_3NaO$ $[M+Na]^+$: 268.0688, found: 268.0679.

(*S*)-2-(3,5-difluorophenyl)oxetane [(*S*)-15b]



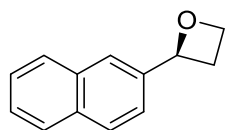
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **15b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 16 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**15b** as a light yellow liquid in 42% yield (158.7mg). **¹H NMR (400 MHz, CDCl₃)** δ 6.94 (dd, J = 8.6, 2.2 Hz, 2H), 6.71 (td, J = 8.9, 2.2 Hz, 1H), 5.75 (t, J = 7.5 Hz, 1H), 4.82 (td, J = 8.2, 6.0 Hz, 1H), 4.65 (dt, J = 9.3, 6.0 Hz, 1H), 3.10 - 3.02 (m, 1H), 2.61 - 2.53 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 163.3 (dd, J = 247.0, 12.0 Hz), 148.0 (t, J = 8.0 Hz), 107.8 (dd, J = 27.0, 4.0 Hz), 103.0 (td, J = 25.0, 6.0 Hz), 81.7, 68.6, 30.6. $[\alpha]_D^{25}$ = -142.89 (c = 1.00, CH₂Cl₂). **HPLC analysis** (IA-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated >99% *ee*: $t_{(R)}$ (minor) = 13.0 min, $t_{(S)}$ (major) = 13.8 min. **HRMS (ESI)** m/z : calculated for $C_9H_8F_2NaO$ $[M+Na]^+$: 193.0435, found: 193.0444.

(*R*)-3-azido-1-(3,5-difluorophenyl)propan-1-ol [(*R*)-15c]



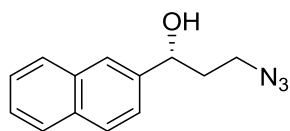
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **15b** (2 mmol), 20 mM **NaN₃** (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 16 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 15:1) to provide (*R*)-**15c** as a light yellow liquid in 43% yield (203.5 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.14 - 6.95 (m, 3H), 5.68 (d, *J* = 4.8 Hz, 1H), 4.67 (dt, *J* = 8.9, 4.6 Hz, 1H), 3.49- 3.41 (m, 1H), 3.40 - 3.32 (m, 1H), 1.91 - 1.73 (m, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 162.4 (dd, *J* = 246.0, 13.0 Hz), 150.7 (t, *J* = 8.2 Hz), 108.7 (dd, *J* = 18.0, 6.0 Hz), 102.2 (t, *J* = 25.9 Hz), 68.6 (t, *J* = 2.2 Hz), 47.6, 37.6. **[α]_D²⁵** = + 27.28 (c = 1.00, CH₂Cl₂). **HPLC analysis** (IC-3, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated >99% *ee*: *t*_(S) (minor) = 31.6 min, *t*_(R) (major) = 35.1 min. **HRMS (ESI) *m/z***: calculated for C₉H₉F₂N₃NaO [**M**+Na]⁺: 236.0606, found: 236.0612.

(*S*)-2-(naphthalen-2-yl)oxetane [(*S*)-16b]



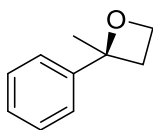
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 5 mM **16b** (0.5 mmol), 5 mM **NaN₃** (0.5 mmol) and 10 g dcw/L *E. coli* (HheD8-M3) cells, 30 °C, reaction for 45 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1) to provide (*S*)-**16b** as a light yellow liquid in 35% yield (31.9mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.95 - 7.89 (m, 1H), 7.86 (dt, *J* = 7.0, 1.3 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.70 - 7.64 (m, 1H), 7.60 - 7.55 (m, 1H), 7.54 - 7.49 (m, 2H), 6.50 (t, *J* = 7.6 Hz, 1H), 4.97 (td, *J* = 8.1, 6.0 Hz, 1H), 4.74 (dt, *J* = 9.0, 6.0 Hz, 1H), 3.35 - 3.25 (m, 1H), 2.75 - 2.64 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 139.2, 133.7, 129.1, 129.0, 127.7, 126.1, 125.8, 125.7, 122.8, 121.5, 80.9, 68.8, 30.2. **[α]_D²⁵** = -288.19 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 98% *ee*: *t*_(S) (major) = 9.7 min, *t*_(R) (minor) = 10.5 min. **HRMS (ESI) *m/z***: calculated for C₁₃H₁₃O [**M**+H]⁺: 185.0961, found: 185.0966.

(*R*)-3-azido-1-(naphthalen-2-yl)propan-1-ol [(*R*)-16c]



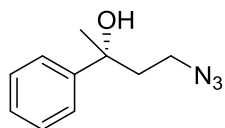
Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 5 mM **16b** (0.5 mmol), 5 mM **NaN₃** (0.5 mmol) and 10 g dcw/L *E. coli* (HheD8-M3) cells, 30 °C, reaction for 45 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 40:1 ~ 15:1) to provide (*R*)-**16c** as a light yellow liquid in 43% yield (49.3 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 8.13 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 7.5 Hz, 1H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.67 (d, *J* = 7.0 Hz, 1H), 7.59 - 7.47 (m, 3H), 5.60 (t, *J* = 3.1 Hz, 1H), 5.42 (dd, *J* = 8.6, 4.0 Hz, 1H), 3.68 - 3.58 (m, 1H), 3.55 - 3.45 (m, 1H), 2.06 - 1.96 (m, 1H), 1.94 - 1.82 (m, 1H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 141.3, 133.3, 129.8, 128.7, 127.3, 126.0, 125.5, 123.1, 122.8, 66.4, 48.2, 37.6. **[α]_D²⁵** = + 54.46 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 95% *ee*: *t*_(S) (minor) = 18.6 min, *t*_(R) (major) = 21.2 min. **HRMS (ESI)** *m/z*: calculated for C₁₃H₁₄N₃O [M+H]⁺: 228.1131, found: 228.1135.

(*S*)-2-methyl-2-phenyloxetane [(*S*)-17b]



Prepared according to the general procedure: 100 mL Gly-NaOH buffer (300 mM, pH 9.5) containing 5 mM **17b** (0.5 mmol), 15 mM **NaN₃** (1.5 mmol) and 30 g dcw/L *E. coli* (HheD8-M7) cells, 30 °C, reaction for 14 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 80:1) to provide (*S*)-**17b** as a light yellow liquid in 27% yield (21.8mg). **¹H NMR (400 MHz, CDCl₃)** δ 7.44 - 7.37 (m, 4H), 7.30 - 7.26 (m, 1H), 4.65 (ddd, *J* = 12.5, 6.6, 5.9 Hz, 1H), 4.55 (ddd, *J* = 12.8, 6.8, 5.8 Hz, 1H), 2.86 - 2.73 (m, 2H), 1.76 (s, 3H). **¹³C NMR (100 MHz, CDCl₃)** δ 148.3, 128.3, 126.7, 123.7, 86.7, 64.6, 35.6, 30.8. **[α]_D²⁵** = -99.54 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 85% *ee*: *t*_(S) (major) = 6.7 min, *t*_(R) (minor) = 7.7 min. **HRMS (ESI)** *m/z*: calculated for C₁₀H₁₃O [M+H]⁺: 149.0961, found: 149.0964.

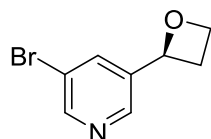
(*R*)-4-azido-2-phenylbutan-2-ol [(*R*)-17c]



Prepared according to the general procedure: 100 mL Gly-NaOH buffer (300 mM, pH 9.5) containing 5 mM **17b** (0.5 mmol), 15 mM **NaN₃** (1.5 mmol) and 30 g dcw/L *E. coli* (HheD8-M7) cells, 30 °C, reaction for 14 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate

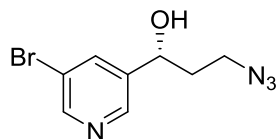
= 80:1 ~ 15:1) to provide (*R*)-**17c** as a light yellow liquid in 39% yield (39.8 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 7.46 - 7.44 (m, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.21 - 7.19 (m, 1H), 5.20 (s, 1H), 3.36 - 3.28 (m, 1H), 3.04 - 2.97 (m, 1H), 2.03 - 1.98 (m, 2H), 1.46 (s, 3H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 148.3, 127.9, 126.2, 124.8, 71.8, 46.9, 42.1, 30.5. **$[\alpha]_D^{25}$** = + 8.79 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated >99% *ee*: *t*_(S) (minor) = 11.3 min, *t*_(R) (major) = 11.8 min. **HRMS (ESI)** *m/z*: calculated for C₁₃H₁₄N₃NaO [M+Na]⁺: 214.0951, found: 214.0952.

(*S*)-3-bromo-5-(oxetan-2-yl)pyridine [(*S*)-**18b**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 6.5) containing 20 mM **18b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 26 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 10:1) to provide (*S*)-**18b** as a light yellow liquid in 45% yield (190.6mg). **¹H NMR (400 MHz, CDCl₃)** δ 8.58 (d, *J* = 2.2 Hz, 1H), 8.48 (d, *J* = 1.8 Hz, 1H), 7.95 (t, *J* = 2.0 Hz, 1H), 5.79 (t, *J* = 7.5 Hz, 1H), 4.83 (td, *J* = 8.0, 6.0 Hz, 1H), 4.65 (dt, *J* = 9.2, 5.9 Hz, 1H), 3.10 - 3.02 (m, 1H), 2.66 - 2.57 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 150.3, 145.2, 140.7, 135.7, 121.1, 79.8, 68.7, 30.5. **$[\alpha]_D^{25}$** = -99.15 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OB-H, 1% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 99% *ee*: *t*_(S) (major) = 33.0 min, *t*_(R) (minor) = 36.2 min. **HRMS (ESI)** *m/z*: calculated for C₈H₉BrNO [M+H]⁺: 213.9862, found: 213.9871.

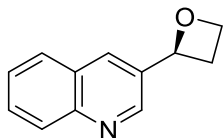
(*R*)-3-azido-1-(5-bromopyridin-3-yl)propan-1-ol [(*R*)-**18c**]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 6.5) containing 20 mM **18b** (2 mmol), 20 mM NaN₃ (2 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 26 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 10:1 ~ 3:1) to provide (*R*)-**18c** as a light yellow liquid in 48% yield (246.0 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 8.56 (dd, *J* = 16.0, 2.3 Hz, 2H), 8.00 (t, *J* = 2.1 Hz, 1H), 5.72 (d, *J* = 4.8 Hz, 1H), 4.72 (dt, *J* = 7.9, 5.0 Hz, 1H), 3.50 - 3.45 (m, 1H), 3.43 - 3.38 (m, 1H), 1.90 - 1.85 (m, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 148.9, 146.2, 143.1, 136.0, 120.2, 67.0, 47.6, 37.5. **$[\alpha]_D^{25}$** = + 20.79 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (AD-H, 3% IPA in

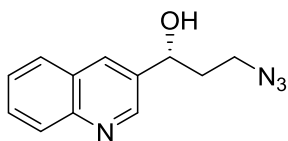
n-hexane, 0.5 ml/min, λ = 210 nm) indicated 98% *ee*: $t_{(R)}$ (major) = 69.0 min, $t_{(S)}$ (minor) = 97.9 min. **HRMS (ESI)** m/z : calculated for $C_8H_{10}N_4BrO$ $[M+H]^+$: 257.0033, found: 257.0042

(*S*)-3-(oxetan-2-yl)quinoline [(*S*)-19b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 6.5) containing 10 mM **19b** (1 mmol), 10 mM **NaN₃** (1 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 30 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 10:1) to provide (*S*)-**19b** as a light yellow liquid in 46% yield (81.5mg). **¹H NMR (400 MHz, CDCl₃)** δ 8.94 (d, J = 2.2 Hz, 1H), 8.21 (d, J = 2.1 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 7.83 (dd, J = 8.2, 1.5 Hz, 1H), 7.70 (ddd, J = 8.4, 6.8, 1.4 Hz, 1H), 7.54 (ddd, J = 8.2, 6.9, 1.3 Hz, 1H), 6.01 (t, J = 7.5 Hz, 1H), 4.90 (td, J = 7.9, 5.8 Hz, 1H), 4.74 (dt, J = 9.2, 5.9 Hz, 1H), 3.17 - 3.09 (m, 1H), 2.78 - 2.69 (m, 1H). **¹³C NMR (100 MHz, CDCl₃)** δ 148.7, 148.0, 136.2, 132.3, 129.5, 129.4, 128.0, 127.8, 127.0, 81.0, 68.7, 30.7. $[\alpha]_D^{25}$ = -158.32 (c = 1.00, CH₂Cl₂). **HPLC analysis** (AD-H, 5% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated 95% *ee*: $t_{(S)}$ (major) = 39.0 min, $t_{(R)}$ (minor) = 41.6 min. **HRMS (ESI)** m/z : calculated for $C_{12}H_{12}NO$ $[M+H]^+$: 186.0913, found: 186.0920.

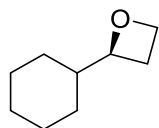
(*R*)-3-azido-1-(quinolin-3-yl)propan-1-ol [(*R*)-19c]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 6.5) containing 10 mM **19b** (1 mmol), 10 mM **NaN₃** (1 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 30 h. The crude product was purified by flash column chromatography on silica gel (dichloromethane : ethyl acetate = 10:1 ~ 3:1) to provide (*R*)-**19c** as a light yellow liquid in 49% yield (107.0 mg). **¹H NMR (400 MHz, DMSO-*d*₆)** δ 8.95 (d, J = 2.2 Hz, 1H), 8.28 (d, J = 2.2 Hz, 1H), 8.03 (d, J = 8.4 Hz, 1H), 7.97 (dd, J = 8.2, 1.5 Hz, 1H), 7.71 (ddd, J = 8.4, 6.8, 1.5 Hz, 1H), 7.58 (ddd, J = 8.1, 6.8, 1.2 Hz, 1H), 5.80 (d, J = 4.6 Hz, 1H), 4.93 (dd, J = 11.2, 6.8 Hz, 1H), 3.58 - 3.50 (m, 1H), 3.47 - 3.41 (m, 1H), 2.00 (q, J = 6.7 Hz, 2H). **¹³C NMR (100 MHz, DMSO-*d*₆)** δ 149.8, 147.1, 138.2, 132.1, 129.1, 128.7, 128.1, 127.6, 126.7, 67.8, 47.8, 37.7. $[\alpha]_D^{25}$ = +23.70 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OJ-H, 10% IPA in *n*-hexane, 1.0 ml/min, λ = 210 nm)

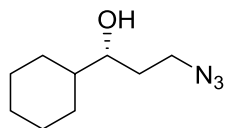
indicated >99% *ee*: $t_{(R)}$ (major) = 15.7 min, $t_{(S)}$ (minor) = 18.6 min. **HRMS (ESI)** m/z : calculated for $C_{12}H_{12}N_4NaO$ $[M+Na]^+$: 251.0903, found: 251.0911.

(*S*)-2-cyclohexyloxetane [(*S*)-21b]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 6.0) containing 5 mM **21b** (0.5 mmol), 15 mM NaN_3 (1.5 mmol) and 30 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 96 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether: ethyl acetate = 50 : 1) to provide (*S*)-**21b** as a light yellow liquid in 32% yield (23.1 mg). **1H NMR (400 MHz, $CDCl_3$)** δ 4.65 (td, J = 7.9, 5.7 Hz, 1H), 4.54 - 4.37 (m, 2H), 2.62 - 2.50 (m, 1H), 2.45 - 2.32 (m, 1H), 1.94 - 1.82 (m, 1H), 1.78 - 1.56 (m, 5H), 1.31 - 1.11 (m, 3H), 0.92 - 0.77 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ 86.8, 68.3, 44.8, 27.6, 26.6, 26.2, 25.8, 25.6. $[\alpha]_D^{25}$ = -10.80 (c = 1.00, CH_2Cl_2). **GC analysis** (Rt-bDEXcst, 80 °C for 45 min) indicated 89% *ee*: $t_{(S)}$ (major) = 33.0 min, $t_{(R)}$ (minor) = 36.0 min. **HRMS (ESI)** m/z : calculated for $C_9H_{16}NaO$ $[M+Na]^+$: 163.1093, found: 163.1096.

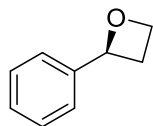
(*R*)-3-azido-1-cyclohexylpropan-1-ol [(*R*)-21c]



Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 6.0) containing 5 mM **21b** (0.5 mmol), 15 mM NaN_3 (1.5 mmol) and 30 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 96 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 50:1 ~ 15:1) to provide (*R*)-**21c** as a colorless liquid in 43% yield (39.7 mg). **1H NMR (400 MHz, $DMSO-d_6$)** δ 4.47 (d, J = 5.9 Hz, 1H), 3.46 - 3.39 (m, 1H), 3.37 - 3.34 (m, 1H), 3.27 - 3.21 (m, 1H), 1.78 - 1.57 (m, 6H), 1.52 - 1.48 (m, 1H), 1.26 - 1.07 (m, 4H), 1.05 - 0.87 (m, 2H). **^{13}C NMR (100 MHz, $DMSO-d_6$)** δ 71.1, 48.2, 43.6, 32.7, 28.7, 27.7, 26.3, 26.0, 25.9. $[\alpha]_D^{25}$ = -20.00 (c = 0.5, CH_2Cl_2). **GC analysis** (Rt-bDEXcst, 140 °C for 60 min) indicated 97% *ee*: $t_{(S)}$ (minor) = 49.3 min, $t_{(R)}$ (major) = 50.5 min. **HRMS (ESI)** m/z : calculated for $C_9H_{17}N_3NaO$ $[M+Na]^+$: 206.1264, found: 206.1264.

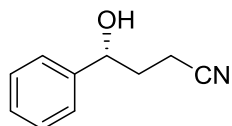
(*S*)-2-phenyloxetane [(*S*)-1b] (Ring opening by cyanide)

Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **1b** (2 mmol), 40 mM **mandelonitrile** (4 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 22 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**1b** as a light yellow liquid in 37% yield (98.1 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.50 - 7.45 (m, 2H), 7.42 (t, *J* = 7.7 Hz, 2H), 7.36 - 7.30 (m, 1H), 5.84 (t, *J* = 7.5 Hz, 1H), 4.85 (td, *J* = 8.1, 5.9 Hz, 1H), 4.68 (dt, *J* = 9.3, 5.8 Hz, 1H), 3.09 - 2.99 (m, 1H), 2.74 - 2.64 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 143.6, 128.6, 127.9, 125.3, 83.0, 68.3, 30.8. [α]_D²⁵ = -167.16 (c = 1.00, CH₂Cl₂). HPLC analysis (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 97% *ee*: t_(S) (major) = 9.8 min, t_(R) (minor) = 11.0 min. HRMS (ESI) *m/z*: calculated for C₉H₁₁O [M+H]⁺: 135.0804, found: 135.0811.



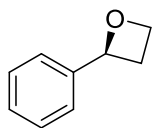
(*R*)-4-hydroxy-4-phenylbutanenitrile [(*R*)-1d]

Prepared according to the general procedure: 100 mL PB buffer (50 mM, pH 7.5) containing 20 mM **1b** (2 mmol), 40 mM **mandelonitrile** (4 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 22 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 2:1) to provide (*R*)-**1d** as a light yellow liquid in 46% yield (147.6 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.38 - 7.28 (m, 5H), 4.75 (dd, *J* = 8.1, 5.3 Hz, 1H), 2.81 (s, 1H), 2.50 - 2.43 (m, 1H), 2.37 - 2.29 (m, 1H), 2.01 - 1.94 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 143.0, 128.7, 128.1, 125.7, 119.8, 72.1, 34.2, 13.7. [α]_D²⁵ = + 12.79 (c = 1.00, CH₂Cl₂). HPLC analysis (IH, 5% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated >99% *ee*: t_(S) (minor) = 58.5 min, t_(R) (major) = 61.6 min. HRMS (ESI) *m/z*: calculated for C₁₀H₁₁NNaO [M+Na]⁺: 184.0733, found: 184.0740.



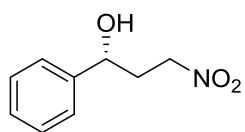
(*S*)-2-phenyloxetane [(*S*)-1b] (Ring opening by nitrite)

Prepared according to the general procedure: 200 mL PB buffer (50 mM, pH 7.5) containing 40 mM **1b** (8 mmol), 40 mM NaNO₂ (8 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 °C, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1) to provide (*S*)-**1b** as a light yellow liquid in 43% yield (459.1 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.51 - 7.45 (m, 2H),



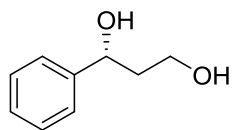
7.42 (t, $J = 7.6$ Hz, 2H), 7.36 - 7.30 (m, 1H), 5.84 (t, $J = 7.5$ Hz, 1H), 4.85 (td, $J = 8.0, 5.8$ Hz, 1H), 4.68 (dt, $J = 9.2, 5.8$ Hz, 1H), 3.09 - 2.99 (m, 1H), 2.74 - 2.63 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 143.6, 128.5, 127.9, 125.3, 83.0, 68.3, 30.8. $[\alpha]_{\text{D}}^{25} = -161.94$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, $\lambda = 210$ nm) indicated >99% *ee*: t_{S} (major) = 10.1 min, t_{R} (minor) = 11.4 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{11}\text{O}$ $[\text{M}+\text{H}]^+$: 135.0804, found: 135.0810.

(*R*)-3-nitro-1-phenylpropan-1-ol [(*R*)-1e]



Prepared according to the general procedure: 200 mL PB buffer (50 mM, pH 7.5) containing 40 mM **1b** (8 mmol), 40 mM NaNO_2 (8 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 $^{\circ}\text{C}$, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 2:1) to provide (*R*)-**1e** as a yellow liquid in 23% yield (327.2 mg). ^1H NMR (400 MHz, CDCl_3) δ 7.38 - 7.26 (m, 5H), 4.74 (dd, $J = 8.3, 4.6$ Hz, 1H), 4.54 - 4.48 (m, 1H), 4.41 - 4.36 (m, 1H), 3.42 (s, 1H), 2.37 - 2.27 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 142.9, 128.9, 128.3, 125.6, 72.4, 71.1, 35.9. $[\alpha]_{\text{D}}^{25} = +50.78$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (OD-H, 10% IPA in *n*-hexane, 0.5 ml/min, $\lambda = 210$ nm) indicated >99% *ee*: t_{S} (minor) = 29.0 min, t_{R} (major) = 39.8 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{11}\text{NNaO}_3$ $[\text{M}+\text{Na}]^+$: 204.0631, found: 204.0634.

(*R*)-1-phenylpropane-1,3-diol [(*R*)-1f]



Prepared according to the general procedure: 200 mL PB buffer (50 mM, pH 7.5) containing 40 mM **1b** (8 mmol), 40 mM NaNO_2 (8 mmol) and 10 g dcw/L *E. coli* (HheD8-M4) cells, 30 $^{\circ}\text{C}$, reaction for 24 h. The crude product was purified by flash column chromatography on silica gel (petroleum ether : ethyl acetate = 30:1 ~ 0:1) to provide (*R*)-**1f** as a light yellow liquid in 19% yield (232.1 mg). ^1H NMR (400 MHz, CDCl_3) δ 7.37 - 7.23 (m, 5H), 4.85 (dd, $J = 8.7, 3.9$ Hz, 1H), 3.70 - 3.77 (m, 2H), 3.64 (s, 2H), 1.93 - 1.83 (m, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 144.4, 128.5, 127.5, 125.7, 73.6, 60.9, 40.4. $[\alpha]_{\text{D}}^{25} = +43.09$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (IH, 12% IPA in *n*-hexane, 0.8 ml/min, $\lambda = 210$ nm) indicated 88% *ee*: t_{S} (minor) = 11.9 min, t_{R} (major) = 13.4 min. **HRMS (ESI)** m/z : calculated for $\text{C}_9\text{H}_{12}\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 175.0730, found: 175.0732.

7. Large-scale reactions

Large-scale reaction for the enantioselective dehalogenation of (*rac*)-**1a**:

In a 250 mL round-bottom flask, a resting cell suspension of *E. coli* (HheD8-M4) at a concentration of 10 g dcw/L was prepared in 100 mL of PB buffer (200 mM, pH 8.5). To the suspension, 20 mL of *n*-hexane was added, followed by 3.412 g (20 mmol) of γ -haloalcohol (*rac*)-**1a** dissolved in 2 mL of DMSO to achieve a final concentration of 200 mM. The reaction mixture was then stirred at 30 °C, and the pH was adjusted at 8.5 $\pm$ 0.1 using a pH stat and 5 M NaOH as the alkaline solution. Upon completion of the enzymatic reaction after 33 h, the reaction mixture was subjected to extraction with ethyl acetate (3 $\times$ 90 mL). The organic phases were separated by centrifugation (8800 $\times$ g, 3 min), combined, dried over anhydrous Na₂SO₄, and evaporated at reduced pressure. The resulting mixture was purified by flash chromatography (petroleum ether : ethyl acetate = 50:1 ~ 20:1) on silica gel to afford the desired chiral oxetane (*R*)-**1b** with 1.183 g (44% yield, >99% *ee*) and chiral γ -haloalcohol (*S*)-**1a** with 1.700 g (49% yield, 97% *ee*).

Large-scale reaction for the enantioselective ring-opening of (*rac*)-**1b**:

In a 250 mL round-bottom flask, a resting cell suspension of *E. coli* (HheD8-M4) at a concentration of 10 g dcw/L was prepared in 100 mL of PB buffer (300 mM, pH 7.0). To the suspension, 20 mL of *n*-hexane was added, followed by 2.683 g (20 mmol) of oxetane (*rac*)-**1b** dissolved in 2 mL of DMSO and 1.302 g (20 mmol) of NaN₃. The reaction mixture was then stirred at 30 °C for 39 h. Upon completion of the enzymatic reaction, the reaction mixture was subjected to extraction with ethyl acetate (3 $\times$ 90 mL). The organic phases were separated by centrifugation (8800 $\times$ g, 3 min), combined, dried over anhydrous Na₂SO₄, and evaporated at reduced pressure. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 50:1 ~ 15:1) on silica gel to afford the desired chiral γ -azidoalcohol (*R*)-**1c** with 1.597 g (45% yield, >99% *ee*) and chiral oxetane (*S*)-**1b** with 1.046 g (39% yield, 97% *ee*).

8. Biocatalytic cascades

General procedure: In a 200 mL round-bottom flask, a resting cell suspension of *E. coli* (HheD8-M4) at a concentration of 10 g dcw/L was prepared in 100 mL of PB buffer (50 mM, pH 7.5). To this suspension, 2 mmol of oxetane (*rac*)-**a** and 2 mmol of NaN₃ were added to a final concentration of 20 mM. The reaction mixture was then stirred at 30 °C. Upon completion of the

enzymatic reaction, the mixture was subjected to extraction using ethyl acetate (3 × 70 mL). The organic phases were separated by centrifugation (8800 × g, 3 min), combined, dried over anhydrous Na₂SO₄, and evaporated at reduced pressure. The resulting mixture was purified by flash chromatography (*n*-hexane: dichloromethane: ethyl acetate = 6:2:1) on silica gel to afford the desired chiral γ -azidoalcohol (*R*)-**c** and γ -haloalcohol (*S*)-**a**.

Substrate	T (h)	Isolated products	
(<i>rac</i>)- 1a	8	(<i>R</i>)- 1c (167.4 mg) (47% yield, >99% <i>ee</i>)	(<i>S</i>)- 1a (171.0 mg) (50% yield, >99% <i>ee</i>)
(<i>rac</i>)- 6a	12	(<i>R</i>)- 6c (184.3 mg) (47% yield, >99% <i>ee</i>)	(<i>S</i>)- 6a (187.2 mg) (49% yield, >99% <i>ee</i>)
(<i>rac</i>)- 7a	48	(<i>R</i>)- 7c (200.3 mg) (47% yield, >99% <i>ee</i>)	(<i>S</i>)- 7a (204.1 mg) (50% yield, >99% <i>ee</i>)

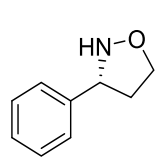
9. Transformations of chiral products

Synthesis of (*R*)-**1aa** from (*S*)-**1a**:

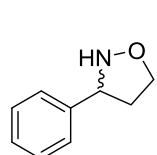
To a 50-mL round-bottom flask cooled with an ice bath, 264.2 mg (2.0 mmol) of tert-butyl *N*-hydroxycarbamate was added, followed by the addition of 5 mL of anhydrous *N,N*-dimethylformamide (DMF). Then, 88.0 mg (2.2 mmol) of NaH was added, and the mixture was stirred for 30 min. Subsequently, 0.5 mL of anhydrous DMF containing 170.6 mg (1.0 mmol) of (*S*)-**1a** was added dropwise to the reaction mixture. The temperature was then gradually raised to 25 °C and the reaction was allowed to proceed for 72 h. Upon completion, the reaction mixture was quenched with saturated NH₄Cl solution and extracted thrice with ethyl acetate 3 × 5 mL. The organic layers were then separated, combined, and washed thrice with saturated brine. The organic phase was then dried over anhydrous Na₂SO₄, concentrated under vacuum, and purified by flash chromatography (petroleum ether: ethyl acetate = 15:1) to give the intermediate. Next, the intermediate was dissolved in 20 mL of dichloromethane (DCM) while cooling in an ice bath. Then, 208.5 μ L (1.5 mmol) of triethylamine (Et₃N) was added, and the mixture was stirred for 10 min. Subsequently, 68 μ L (0.87 mmol) of methanesulfonyl chloride was added dropwise, and the reaction was continued for 2 h. Following the reaction, the mixture was diluted with 10 mL of DCM and washed three times with saturated brine. The organic phases were then separated and concentrated under reduced pressure to yield a crude intermediate product. Finally, the crude

intermediate was dissolved in 20 mL of DCM at room temperature (25 °C). To this, 2.2 mL of trifluoroacetic acid (TFA) was added, and the mixture was stirred for 1 h. The reaction mixture was concentrated under reduced pressure, and the residue was redissolved in 10 mL of DCM. The solution was then washed three times with saturated NaHCO₃ aqueous solution, dried over anhydrous Na₂SO₄, and then concentrated again under reduced pressure. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 15:1) on silica gel to afford the desired chiral product (*R*)-**1aa** as light yellow solid. The (*rac*)-**1aa** was synthesized from (*rac*)-**1a** according to the same procedures and used as a standard for chiral HPLC analysis.

(*R*)-3-phenylisoxazolidine [(*R*)-**1aa**]

 Light yellow solid in 64% yield (96.4 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.39 - 7.32 (m, 4H), 7.30 - 7.25 (m, 1H), 5.32 (s, 1H), 4.50 - 4.45 (m, 1H), 4.10 - 3.99 (m, 2H), 2.72 - 2.62 (m, 1H), 2.34 - 2.24 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 140.0, 128.8, 127.7, 127.0, 70.8, 63.5, 37.8. [α]_D²⁵ = - 12.59 (c = 1.00, CH₂Cl₂). HPLC analysis (OJ-H, 10% IPA in *n*-hexane, 1.0 ml/min, 210 nm) indicated 92% *ee*: t_(S) (minor) = 15.0 min, t_(R) (major) = 17.5 min. HRMS (ESI) *m/z*: calculated for C₉H₁₂NO [M+H]⁺: 159.0913, found: 159.0917. **m.p.**: 31.3 - 32.7 °C .

(*rac*)-3-phenylisoxazolidine [(*rac*)-**1aa**]

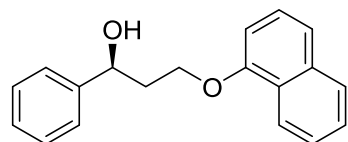
 ¹H NMR (400 MHz, CDCl₃) δ 7.40 - 7.33 (m, 4H), 7.30 - 7.26 (m, 1H), 5.10 (s, 1H), 4.47 (t, *J* = 6.3 Hz, 1H), 4.08 - 4.00 (m, 2H), 2.71 - 2.62 (m, 1H), 2.33 - 2.24 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 140.1, 128.7, 127.8, 126.9, 70.8, 63.5, 37.7.

Synthesis of (*S*)-**1ab** from (*S*)-**1a**:

To a 10-mL round-bottom flask, 82.9 mg (0.60 mmol) of anhydrous K₂CO₃ was added, followed by the addition of 1 mL of anhydrous DMF and 72.3 mg (0.5 mmol) of 1-naphthol. Afterward, the reaction temperature was increased to 70 °C, followed by the dropwise addition of 85.3 mg (0.5 mmol) of (*S*)-**1a**. The reaction was stirred for 12 hours, and subsequently quenched by adding 1 mL of distilled water. Equal volume of ethyl acetate was used to extract the mixture three times. The organic layers were then separated, combined, and washed thrice with saturated brine. The organic phase was then dried over anhydrous Na₂SO₄, and concentrated under reduced pressure to

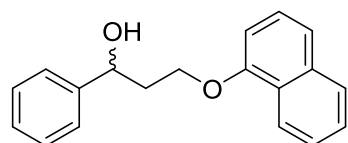
yield the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 15:1) on silica gel to afford the desired chiral product (*S*)-**1ab** as a light pink solid. The (*rac*)-**1ab** was synthesized from (*rac*)-**1a** according to the same procedures and used as a standard for chiral HPLC analysis.

(*S*)-3-(naphthalen-1-yloxy)-1-phenylpropan-1-ol [(*S*)-1ab**]**



Light pink solid in 78% yield (108.9 mg). **¹H NMR (400 MHz, CDCl₃)** δ 8.28 - 8.25 (m, 1H), 7.84 - 7.81 (m, 1H), 7.54 - 7.48 (m, 2H), 7.46 - 7.43 (m, 3H), 7.40 - 7.35 (m, 3H), 7.34 - 7.29 (m, 1H), 6.81 (d, J = 7.6 Hz, 1H), 5.15 (q, J = 4.9 Hz, 1H), 4.38 - 4.32 (m, 1H), 4.23 - 4.18 (m, 1H), 2.47 - 2.40 (m, 1H), 2.37 - 2.30 (m, 2H). **¹³C NMR (100 MHz, CDCl₃)** δ 154.5, 144.3, 134.6, 128.7, 127.8, 127.7, 126.5, 126.0, 126.0, 125.6, 125.4, 121.9, 120.5, 104.8, 72.3, 65.4, 38.6. **[α]_D²⁵** = +25.58 (c = 1.00, CH₂Cl₂). **HPLC analysis** (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, 210 nm) indicated 97% *ee*: $t_{(S)}$ (major) = 21.4 min, $t_{(R)}$ (minor) = 23.7 min. **HRMS (ESI) m/z** : calculated for C₁₉H₁₉O₂ [M+H]⁺: 279.1380, found: 279.1389. **m.p.**: 69.4 - 71.3 °C.

(*rac*)-3-(naphthalen-1-yloxy)-1-phenylpropan-1-ol [(*rac*)-1ab**]**



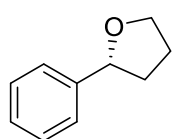
¹H NMR (400 MHz, CDCl₃) δ 8.34 - 8.32 (m, 1H), 7.88 - 7.86 (m, 1H), 7.59 - 7.53 (m, 2H), 7.50 (d, J = 8.2 Hz, 1H), 7.47 - 7.39 (m, 5H), 7.37 - 7.33 (m, 1H), 6.82 (d, J = 7.6 Hz, 1H), 5.13 (dd, J = 8.2, 5.0 Hz, 1H), 4.36 - 4.31 (m, 1H), 4.20 - 4.15 (m, 1H), 2.66 (s, 1H), 2.46 - 2.29 (m, 2H). **¹³C NMR (100 MHz, CDCl₃)** δ 154.5, 144.2, 134.5, 128.6, 127.7, 127.6, 126.5, 126.0, 125.9, 125.6, 125.3, 121.9, 120.4, 104.8, 72.0, 65.3, 38.5.

Synthesis of (*R*)-1ba** from (*R*)-**1b**:**

To a well-stirred suspension of 200.0 mg (5.0 mmol) of NaH in dry diglyme (1 mL) was added 660.0 mg (3.0 mmol) of trimethylsulfoxonium iodide at room temperature. The mixture was gently heated to 125 °C, and 67.2 mg (0.5 mmol) of chiral oxetane (*R*)-**1b** in diglyme (0.5 mL) was added dropwise to the reaction mixture. The reaction mixture was stirred at 125 °C for 0.5 h, cooled, carefully quenched with distilled water, and extracted four times with equal volume of *n*-hexane. The combined extracts were washed with saturated brine, dried over anhydrous Na₂SO₄ and

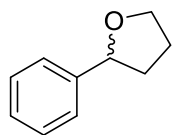
concentrated under reduced pressure to yield the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 50:1) on silica gel to afford the desired chiral product (*R*)-**1ba** as a light yellow liquid. The (*rac*)-**1ba** was synthesized from (*rac*)-**1b** according to the same procedures and used as a standard for chiral HPLC analysis.

(*R*)-2-phenyltetrahydrofuran [(*R*)-1ba**]**



Light yellow liquid in 73% yield (54.4 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.37 - 7.34 (m, 4H), 7.31 - 7.27 (m, 1H), 4.93 (t, *J* = 7.2 Hz, 1H), 4.13 (dt, *J* = 8.3, 6.9 Hz, 1H), 3.97 (td, *J* = 7.8, 6.4 Hz, 1H), 2.40 - 2.32 (m, 1H), 2.08 - 2.00 (m, 2H), 1.88 - 1.79 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 143.5, 128.4, 127.2, 125.7, 80.8, 68.8, 34.7, 26.1. [α]_D²⁵ = +34.27 (*c* = 1.00, CH₂Cl₂). HPLC analysis (OD-H, 8% IPA in *n*-hexane, 0.8 ml/min, 210 nm) indicated 92% *ee*: *t*_(*R*) (major) = 6.2 min, *t*_(*S*) (minor) = 8.0 min. HRMS (ESI) *m/z*: calculated for C₁₀H₁₃O [M+H]⁺: 149.0961, found: 149.0960.

(*rac*)-2-phenyltetrahydrofuran [(*rac*)-1ba**]**

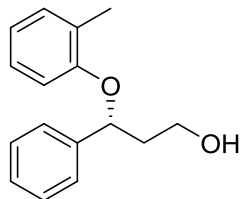


¹H NMR (400 MHz, CDCl₃) δ 7.35 (d, *J* = 4.3 Hz, 4H), 7.30 - 7.24 (m, 1H), 4.91 (t, *J* = 7.2 Hz, 1H), 4.12 (q, *J* = 7.4 Hz, 1H), 3.96 (q, *J* = 7.3 Hz, 1H), 2.38 - 2.30 (m, 1H), 2.08 - 1.97 (m, 2H), 1.86 - 1.77 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 143.5, 128.4, 127.2, 125.7, 80.8, 68.8, 34.7, 26.1.

Synthesis of (*R*)-1bb** from (*R*)-**1b**:**

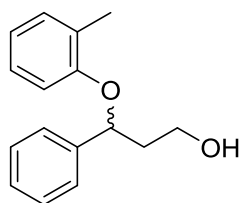
To a 10 mL round-bottom flask under argon, a solution of 149.5 mg (0.45 mmol) tris(2-methylphenyl)borate (CAS: 2665-12-5) in 1.0 mL of tetrahydrofuran (THF) was added, followed by the addition of 40.3 mg (0.3 mmol) oxetane (*R*)-**1b** in 0.5 mL of THF. The reaction mixture was stirred at 50 °C for 1 h. After evaporation of the solvent, the resulting mixture was then purified by flash chromatography (petroleum ether: ethyl acetate: DCM= 15:1:1) on silica gel, to give the desired chiral product (*R*)-**1bb** as a white solid. The (*rac*)-**1bb** was synthesized from (*rac*)-**1b** according to the same procedures and used as a standard for chiral HPLC analysis.

(*R*)-3-phenyl-3-(*o*-tolylloxy)propan-1-ol [(*R*)-1bb]



White solid in 54% yield (38.0 mg). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.37 - 7.31 (m, 4H), 7.27 - 7.23 (m, 1H), 7.13 (d, $J = 7.3$ Hz, 1H), 6.97 (t, $J = 7.8$ Hz, 0H), 6.79 (t, $J = 7.4$ Hz, 1H), 6.63 (d, $J = 8.2$ Hz, 0H), 5.40 (dd, $J = 8.6$, 4.2 Hz, 1H), 3.93 - 3.87 (m, 1H), 3.84 - 3.78 (m, 1H), 2.33 (s, 3H), 2.30 - 2.22 (m, 1H), 2.16 - 2.08 (m, 1H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 155.8, 141.7, 130.8, 128.8, 127.7, 126.9, 126.8, 125.8, 120.6, 112.9, 77.8, 60.0, 41.4, 16.8. $[\alpha]_{\text{D}}^{25} = -19.19$ ($c = 1.00$, CH_2Cl_2). **HPLC analysis** (AD-H, 5% IPA in *n*-hexane, 1.0 ml/min, 210 nm) indicated 83% *ee*: $t_{(R)}$ (major) = 9.0 min, $t_{(S)}$ (minor) = 13.5 min. **HRMS (ESI)** m/z : calculated for $\text{C}_{16}\text{H}_{18}\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 265.1199, found: 265.1205. **m.p.**: 49.7 - 51.4 $^{\circ}\text{C}$.

(*rac*)-3-phenyl-3-(*o*-tolylloxy)propan-1-ol [(*rac*)-1bb]



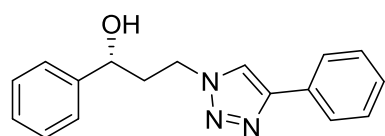
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.38 - 7.32 (m, 4H), 7.29 - 7.24 (m, 1H), 7.14 (d, $J = 7.3$ Hz, 1H), 6.98 (t, $J = 8.7$ Hz, 1H), 6.81 (t, $J = 7.3$ Hz, 1H), 6.65 (d, $J = 8.2$ Hz, 1H), 5.42 (dd, $J = 8.6$, 4.2 Hz, 1H), 3.93 - 3.88 (m, 1H), 3.84 - 3.79 (m, 1H), 2.35 (s, 3H), 2.31 - 2.23 (m, 1H), 2.18 - 2.09 (m, 1H). $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 155.8, 141.7, 130.8, 128.8, 127.7, 126.9, 126.7, 125.8, 120.6, 112.9, 77.7, 60.0, 41.4, 16.8.

Synthesis of (*R*)-1ca from (*R*)-1c:

To 50-mL round-bottom flask was added 181.1 mg (1.02 mmol) of γ -azidoalcohol (*R*)-1c and 225 μL (2.04 mmol) of ethynylbenzene. $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (3.7 mg, 0.01 mmol) was weighed into a 10-mL round-bottom flask along with sodium ascorbate (11.4 mg, 0.06 mmol) and dissolved in 5.0 mL distilled H_2O . To this solution was added MonoPhos (3.8 mg, 0.01 mmol) and the solution was stirred at room temperature for 15 min. The solution in the 10-mL round-bottom flask was added to the roundbottom flask (with stirring) and a further 10.0 mL of water was added to the mixture. The reaction mixture was stirred at room temperature overnight (approximately 14 h). Afterwards, 10.0 mL of ice-cold distilled water was added to the mixture, followed by extraction with equal volume of DCM for three times. The combined extracts were washed with saturated brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to yield the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl

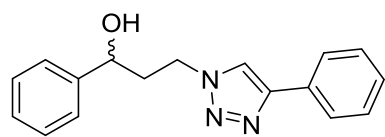
acetate= 2:1) on silica gel to afford the desired chiral product (*R*)-**1ca** as a white solid. The (*rac*)-**1ca** was synthesized from (*rac*)-**1c** according to the same procedures and used as a standard for chiral HPLC analysis.

(*R*)-1-phenyl-3-(4-phenyl-1H-1,2,3-triazol-1-yl)propan-1-ol [(*R*)-1ca**]**



White solid in 89% yield (255.1 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.76 - 7.74 (m, 3H), 7.39 - 7.23 (m, 8H), 4.66 (dd, *J* = 7.7, 5.7 Hz, 1H), 4.60 - 4.53 (m, 1H), 4.49 - 4.43 (m, 1H), 3.37 (s, 1H), 2.30 (dt, *J* = 7.7, 6.3 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 147.7, 143.6, 130.5, 128.9, 128.7, 128.3, 127.9, 125.8, 125.7, 120.4, 70.8, 47.3, 39.2. [α]_D²⁵ = + 7.10 (c = 1.00, CH₂Cl₂). HPLC analysis (OD-H, 20% IPA in *n*-hexane, 0.5 ml/min, λ = 210 nm) indicated >99% *ee*: t_(S) (minor) = 26.4 min, t_(R) (major) = 37.9 min. HRMS (ESI) *m/z*: calculated for C₁₇H₁₈N₃O [M+H]⁺: 280.1444, found: 280.1454. m.p.: 117.2 - 120.0 °C .

(*rac*)-1-phenyl-3-(4-phenyl-1H-1,2,3-triazol-1-yl)propan-1-ol [(*rac*)-1ca**]**



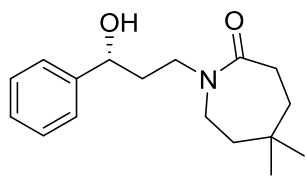
¹H NMR (400 MHz, CDCl₃) δ 7.76 - 7.74 (m, 3H), 7.39 - 7.24 (m, 8H), 4.67 (dd, *J* = 7.6, 5.6 Hz, 1H), 4.59 - 4.52 (m, 1H), 4.47 - 4.41 (m, 1H), 3.90 (s, 1H), 2.29 (q, *J* = 6.8 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 147.6, 143.7, 130.4, 128.9, 128.6, 128.2, 127.8, 125.7, 125.7, 120.4, 70.6, 47.2, 39.2.

Synthesis of (*R*)-**1cb** from (*R*)-**1c**:

To a 50-mL round-bottom flask, 104.2 mg (0.83 mmol) of 4,4-dimethylcyclohexan-1-one and 8 mL of anhydrous DCM were added. The flask was cooled to -78 °C, followed by the addition of 2 mL (16.21 mmol) of BF₃·OEt₂, and then stirred for 30 minutes. Subsequently, a solution of 186.6 mg (1.05 mmol) γ-azidoalcohol (*R*)-**1c** in 2.0 mL of anhydrous DCM was cooled to 0 °C and then added dropwise to the above round-bottom flask. The reaction temperature was then slowly increased to room temperature and allowed to proceed for 24 h. The reaction mixture was concentrated under vacuum to yield a viscous brown liquid. Next, 10 mL of 15% (w/v) aqueous KOH solution was added to the crude product, and the mixture was stirred for 1 h. Equal volume of DCM was used to extract the mixture three times. The organic layers were separated, combined,

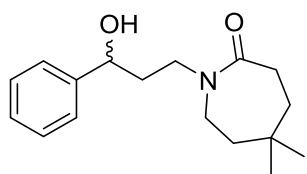
and washed with distilled water followed by saturated brine. The organic phase was dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The resultant mixture was further purified by flash chromatography (DCM: ethyl acetate = 2:1) on silica gel to afford the desired chiral product **(R)-1cb** as an orange liquid. The (rac)-1cb was synthesized from (rac)-1c according to the same procedures and used as a standard for chiral HPLC analysis.

(R)-1-(3-hydroxy-3-phenylpropyl)-5,5-dimethylazepan-2-one [(R)-1cb]



Yellow oil in 88% yield (256.3 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.35 - 7.29 (m, 4H), 7.23 (q, *J* = 6.3 Hz, 1H), 4.81 (d, *J* = 3.9 Hz, 1H), 4.54 (dt, *J* = 10.5, 3.4 Hz, 1H), 4.09 (ddd, *J* = 15.0, 11.3, 4.3 Hz, 1H), 3.28 (s, 2H), 3.05 (dt, *J* = 14.2, 4.5 Hz, 1H), 2.54 - 2.40 (m, 2H), 1.93 - 1.84 (m, 1H), 1.80 - 1.71 (m, 1H), 1.52 - 1.36 (m, 4H), 0.96 (d, *J* = 7.6 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 177.3, 144.2, 128.3, 127.1, 125.7, 69.8, 45.4, 45.3, 41.0, 37.6, 36.2, 32.5, 32.3. [α]_D²⁵ = -2.00 (*c* = 1.00, CH₂Cl₂). **HPLC analysis** (OJ-H, 10% IPA in *n*-hexane, 1.0 ml/min, λ = 214 nm) indicated >99% *ee*: *t*_(S) (minor) = 8.1 min, *t*_(R) (major) = 8.9 min. **HRMS (ESI)** *m/z*: calculated for C₁₇H₂₅NNaO₂ [M+Na]⁺: 298.1777, found: 298.1786. **m.p.**: 65.3 - 71.2 °C.

(rac)-1-(3-hydroxy-3-phenylpropyl)-5,5-dimethylazepan-2-one [(rac)-1cb]



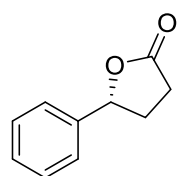
¹H NMR (400 MHz, CDCl₃) δ 7.35 - 7.28 (m, 4H), 7.23 - 7.19 (m, 1H), 4.87 (dt, *J* = 3.9 Hz, 1H), 4.53 (dt, *J* = 10.2, 3.4 Hz, 1H), 4.05 (ddd, *J* = 14.5, 10.8, 4.6 Hz, 1H), 3.27 (s, 2H), 3.05 (dt, *J* = 14.7, 4.0 Hz, 1H), 2.51 - 2.38 (m, 2H), 1.92 - 1.84 (m, 1H), 1.79 - 1.71 (m, 1H), 1.48 - 1.39 (m, 4H), 0.95 (d, *J* = 7.2 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 177.2, 144.1, 128.2, 127.0, 125.6, 69.7, 45.3, 45.2, 40.9, 37.6, 36.1, 32.4, 32.2.

Synthesis of (R)-1da from (R)-1d:

To a 10-mL round-bottom flask, 52.6 mg (0.33 mmol) γ-cyanoalcohol **(R)-1d** and 1.1 mL of 3 M aqueous NaOH solution were added. After the addition of 1.0 mL of 30% (w/v) H₂O₂, the solution was heated to 70 °C and allowed to proceed for 2 h. After cooling the flask to room temperature, 10.0 mL of distilled water was added to quench the reaction. The reaction mixture was extracted 20 mL of DCM. The aqueous phase was separated, followed by the addition of 6 M HCl solution

until the pH reached between 2-3. Then the reaction mixture was extracted with DCM (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to yield the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 2:1) on silica gel to afford the desired chiral product (*R*)-**1da** as a colorless liquid. The (*rac*)-**1da** was obtained from commercial suppliers and used as a standard for chiral HPLC analysis.

(*R*)-5-phenyldihydrofuran-2(3H)-one [(*R*)-**1da**]

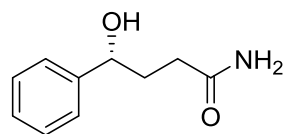


Colorless oil in 73% yield (38.8 mg). ^1H NMR (400 MHz, CDCl_3) δ 7.41 - 7.32 (m, 5H), 5.50 (dd, $J = 8.1, 5.8$ Hz, 1H), 2.69 - 2.62 (m, 3H), 2.22 - 2.15 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 177.1, 139.4, 128.8, 128.5, 125.4, 81.3, 31.1, 29.1. $[\alpha]_{\text{D}}^{25} = +17.19$ ($c = 1.00$, CH_2Cl_2). HPLC analysis (IH, 10% IPA in *n*-hexane, 1.0 ml/min, $\lambda = 210$ nm) indicated >99% *ee*: t_{S} (minor) = 24.5 min, t_{R} (major) = 28.3 min. HRMS (ESI) m/z : calculated for $\text{C}_{10}\text{H}_{10}\text{NaO}_2$ $[\text{M}+\text{Na}]^+$: 185.0573, found: 185.0581.

Synthesis of (*R*)-**1db** from (*R*)-**1d**:

To a 10-mL round-bottom flask, 71.8 mg (0.45 mmol) of γ -cyanoalcohol (*R*)-**1d**, 150 μL of 30% (w/v) H_2O_2 and 2.0 mL of 25% (w/v) $\text{NH}_3 \cdot \text{H}_2\text{O}$ were added. The reaction mixture was allowed to stir at room temperature for 12 h. Afterwards, 15 mL methanol was added to the reaction and dried over anhydrous Na_2SO_4 . Then the mixture were filtered and concentrated under reduced pressure to yield the crude product. The resulting mixture was purified by flash chromatography (methanol: ethyl acetate = 1:10) on silica gel to afford the desired chiral product (*R*)-**1db** as a colorless liquid. The (*rac*)-**1db** was synthesized from (*rac*)-**1d** according to the same procedures and used as a standard for chiral HPLC analysis.

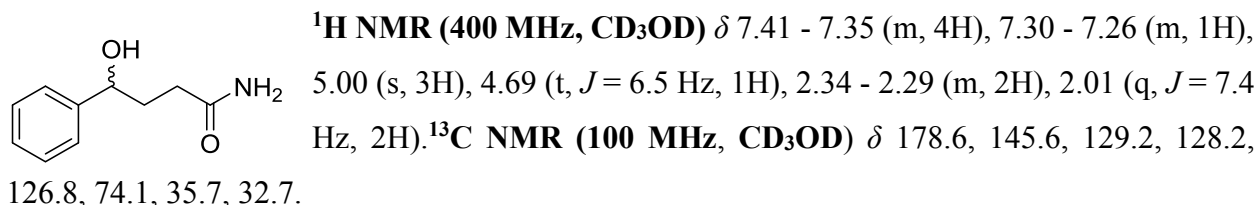
(*R*)-4-hydroxy-4-phenylbutanamide [(*R*)-**1db**]



Colorless liquid in 54% yield (42.9 mg). ^1H NMR (400 MHz, CD_3OD) δ 7.37 - 7.30 (m, 4H), 7.26 - 7.22 (m, 1H), 4.91 (s, 3H), 4.65 (t, $J = 6.6$ Hz, 1H), 2.30 - 2.22 (m, 2H), 2.03 - 1.96 (m, 2H). ^{13}C NMR (100 MHz, CD_3OD) δ 178.8, 145.9, 129.3, 128.3, 127.0, 74.3, 35.9, 32.8. $[\alpha]_{\text{D}}^{25} = +34.69$ ($c = 1.00$, CH_2Cl_2). HPLC analysis (OJ-H, 10% IPA in *n*-hexane, 1.0 ml/min, $\lambda = 210$ nm)

indicated >99% *ee*: $t_{(R)}$ (major) = 15.8 min, $t_{(S)}$ (minor) = 18.1 min. **HRMS (ESI)** m/z : calculated for $C_{10}H_{13}NNaO_2$ $[M+Na]^+$: 202.0838, found: 202.0846.

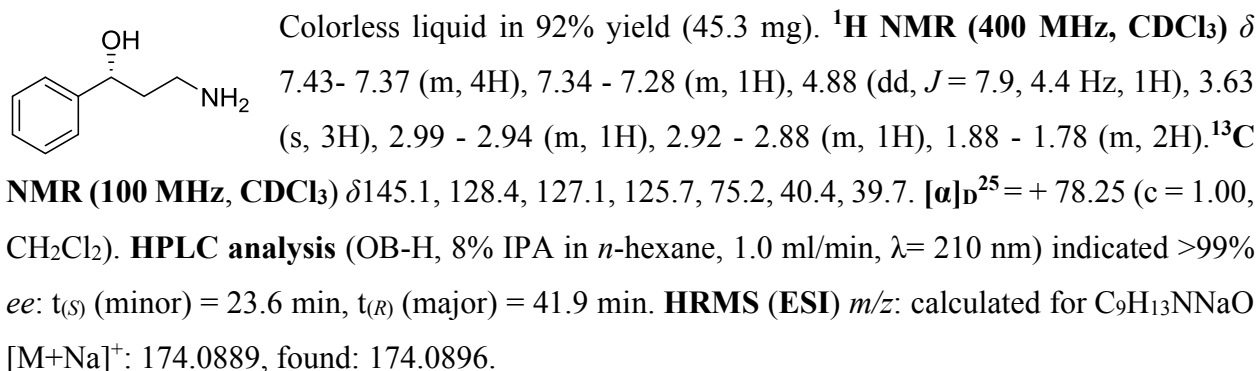
(rac)-4-hydroxy-4-phenylbutanamide [(rac)-1db]



Synthesis of (*R*)-1ea from (*R*)-1e:

To a stirred solution of γ -nitroalcohol (*R*)-1e (58.7 mg, 0.32 mmol) in MeOH (10 mL), 51.3 mg of Pd/C (10 mol%) was added. The mixture was stirred at room temperature for 6 h under a hydrogen balloon. Afterward, the reaction mixture was filtered through a pad of Celite, which was then washed with 30 mL of MeOH. The filtrate was dried over anhydrous Na_2SO_4 and concentrated, giving the desired chiral product (*R*)-1ea as a colorless liquid. The (*rac*)-1ea was obtained from commercial suppliers and used as a standard for chiral HPLC analysis.

(*R*)-3-amino-1-phenylpropan-1-ol [(*R*)-1ea]

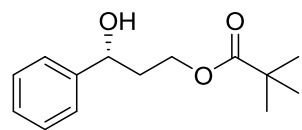


Synthesis of (*R*)-1fa from (*R*)-1f:

To a 10-mL round-bottom flask, 47.5 mg (0.31 mmol) of γ -diol (*R*)-1f, 1 mL of DCM, and 150 μ L (1.08 mmol) of Et_3N were added. The flask was cooled to 0 $^{\circ}C$, followed by dropwise addition of 50 μ L (0.41 mmol) of pivaloyl chloride. The reaction mixture was then stirred at room temperature for 6 h. Afterward, the reaction mixture was quenched with 2 mL of distilled water, extracted with

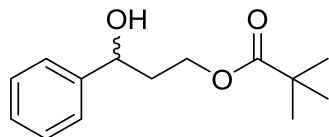
DCM (3 × 2 mL), and washed with saturated brine. The organic layer was then dried over anhydrous Na₂SO₄ and concentrated under reduced pressure to obtain the crude product. The resulting mixture was purified by flash chromatography (petroleum ether: ethyl acetate = 10:1) to afford the desired chiral product (*R*)-**1fa** as a colorless liquid. The (*rac*)-**1fa** was synthesized from (*rac*)-**1f** according to the same procedures and used as a standard for chiral HPLC analysis.

(*R*)-3-hydroxy-3-phenylpropyl pivalate [(*R*)-1fa]



Colorless liquid in 83% yield (61.4 mg). ¹H NMR (400 MHz, CDCl₃) δ 7.38 - 7.33 (m, 4H), 7.30 - 7.27 (m, 1H), 4.76 (dd, *J* = 8.3, 5.0 Hz, 1H), 4.30 (ddd, *J* = 13.1, 7.6, 5.5 Hz, 1H), 4.08 (dt, *J* = 11.2, 5.8 Hz, 1H), 2.59 (s, 1H), 2.12 - 1.98 (m, 2H), 1.21 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 178.9, 144.0, 128.7, 127.8, 125.8, 71.4, 61.6, 38.9, 38.2, 27.3. [α]_D²⁵ = +9.80 (*c* = 1.00, CH₂Cl₂). HPLC analysis (OX-3, 3% IPA in *n*-hexane, 0.7 ml/min, λ = 210 nm) indicated 87.8% *ee*: *t*_(S) (minor) = 24.1 min, *t*_(R) (major) = 25.4 min. HRMS (ESI) *m/z*: calculated for C₁₄H₂₀NaO₃ [M+Na]⁺: 259.1305, found: 259.1311.

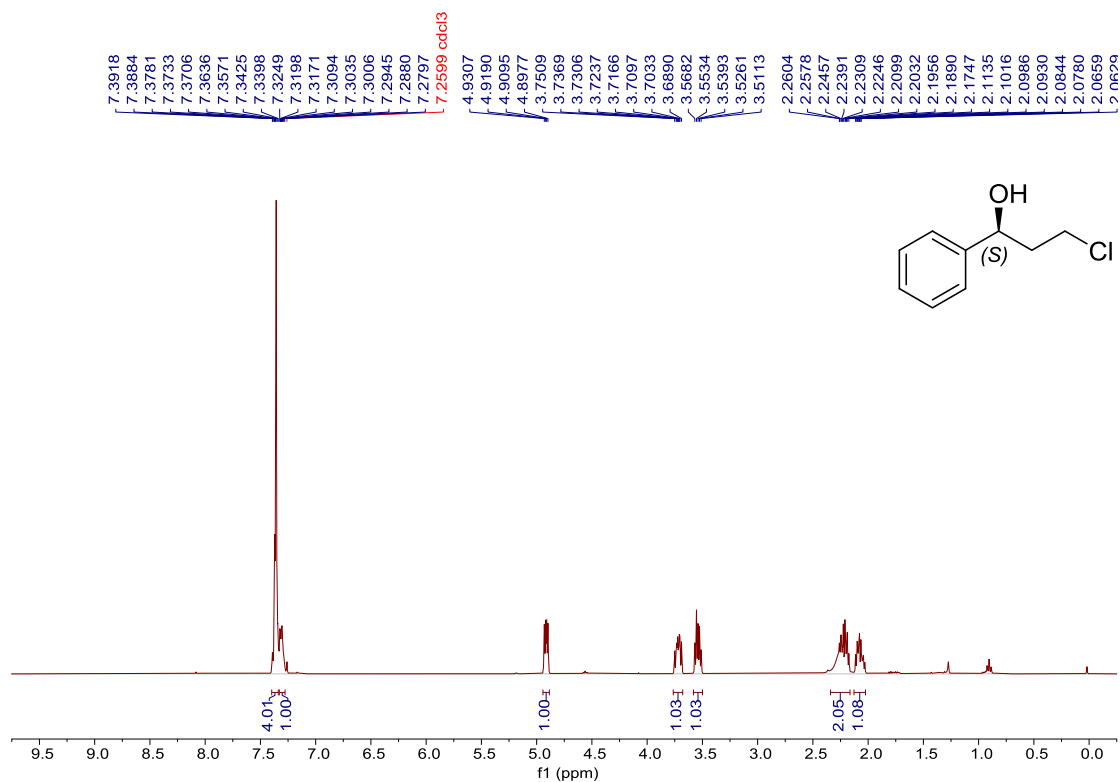
(*rac*)-3-hydroxy-3-phenylpropyl pivalate [(*rac*)-1fa]



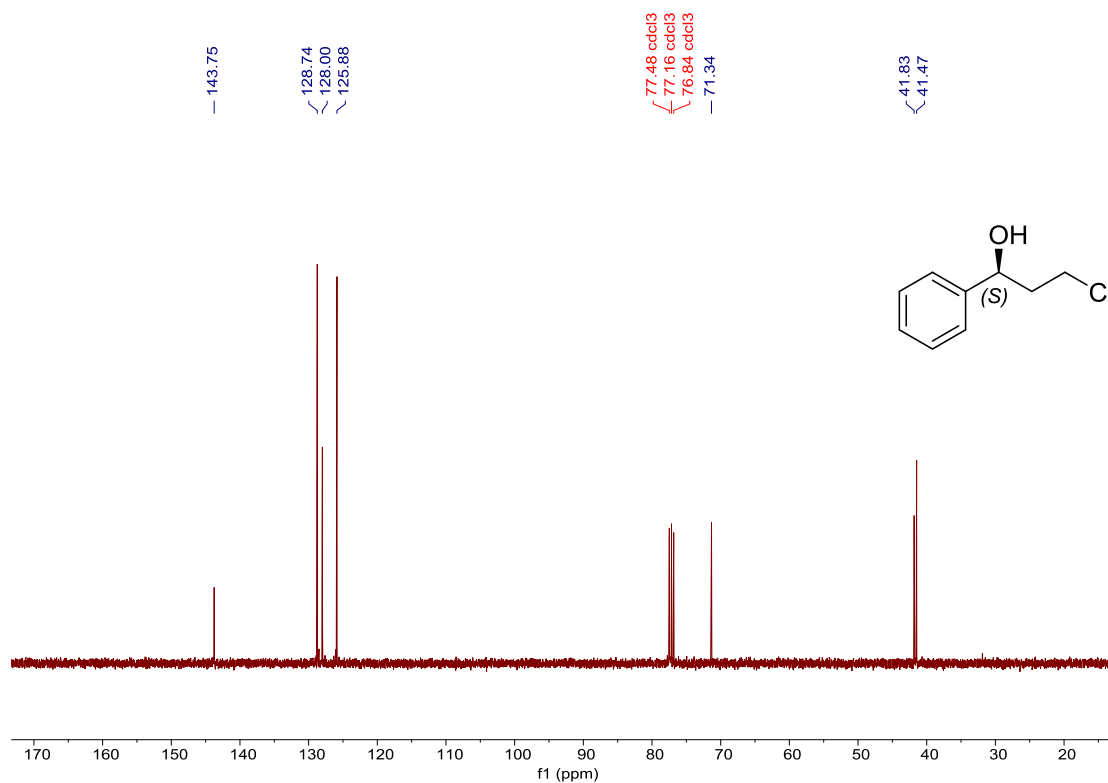
¹H NMR (400 MHz, CDCl₃) δ 7.37 - 7.27 (m, 5H), 4.76 (dd, *J* = 8.2, 5.0 Hz, 1H), 4.29 (ddd, *J* = 13.1, 7.6, 5.5 Hz, 1H), 4.07 (dt, *J* = 11.2, 5.9 Hz, 1H), 2.84 (s, 1H), 2.12 - 1.96 (m, 2H), 1.21 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 178.9, 144.0, 128.6, 127.7, 125.8, 71.3, 61.6, 38.8, 38.1, 27.2.

10. Copies of NMR spectra (Supplementary Figures 12-213)

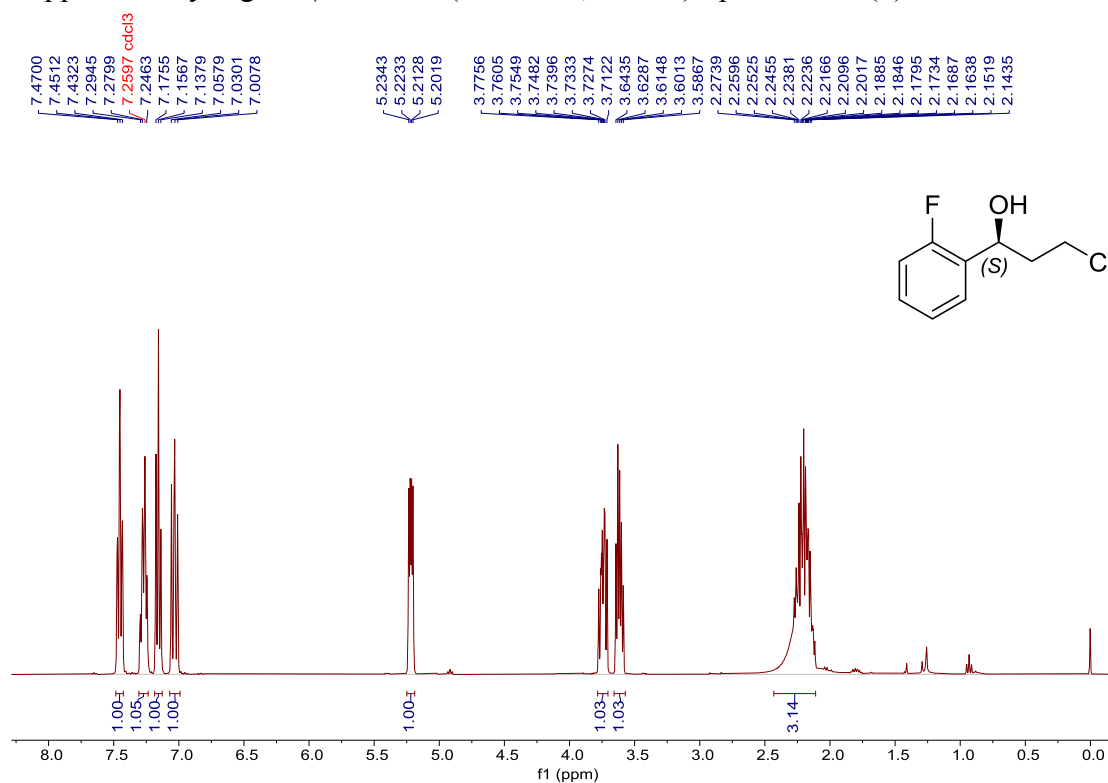
Supplementary Fig. 12 | ^1H NMR (400 MHz, CDCl_3) spectrum of (*S*)-**1a**.



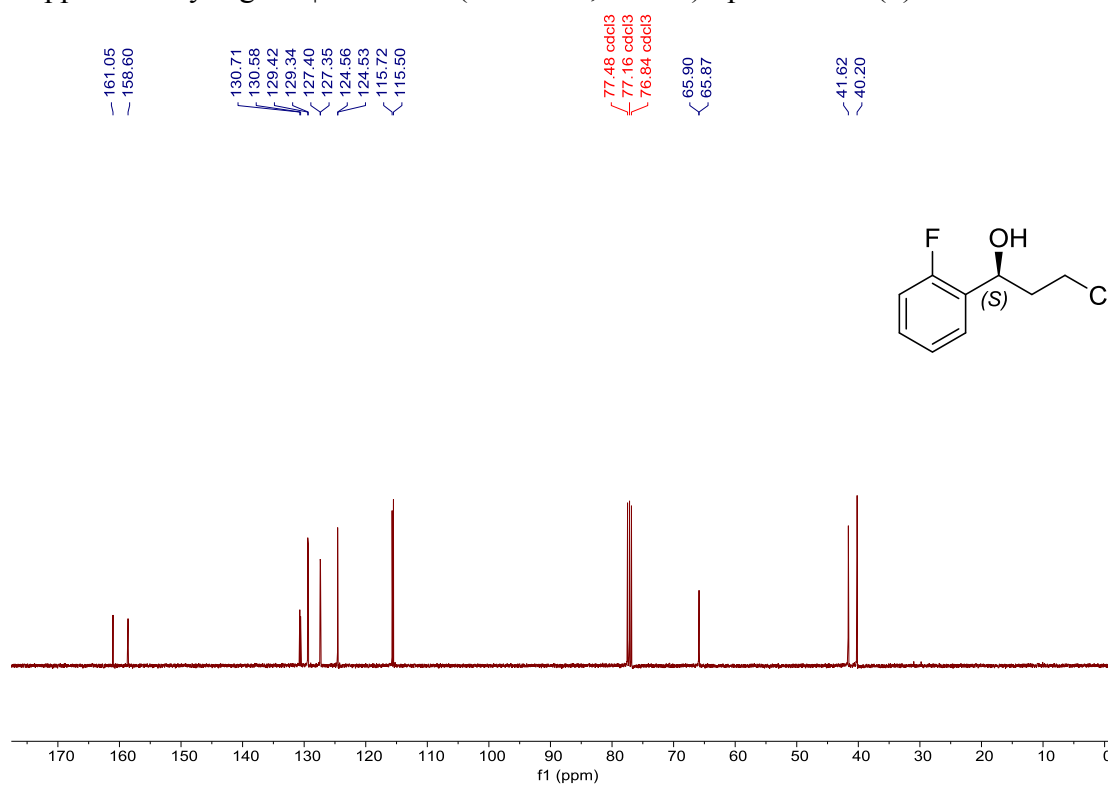
Supplementary Fig. 13 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**1a**.



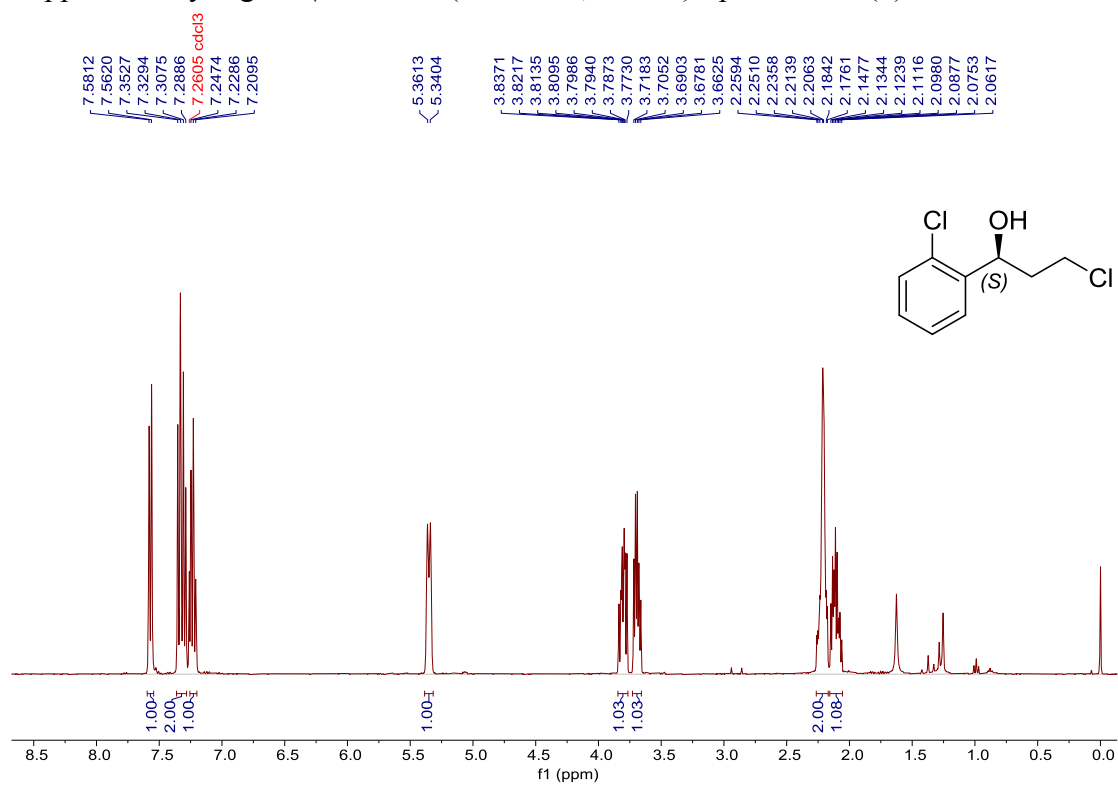
Supplementary Fig. 14 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**2a**.



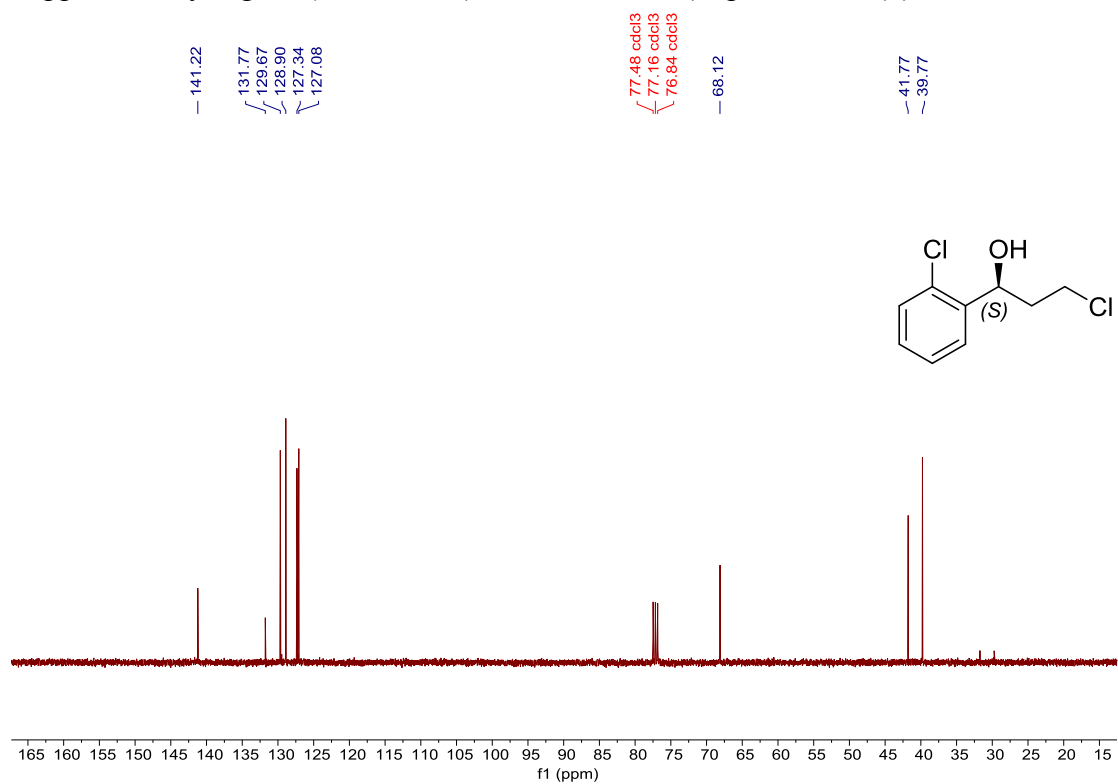
Supplementary Fig. 15 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**2a**.



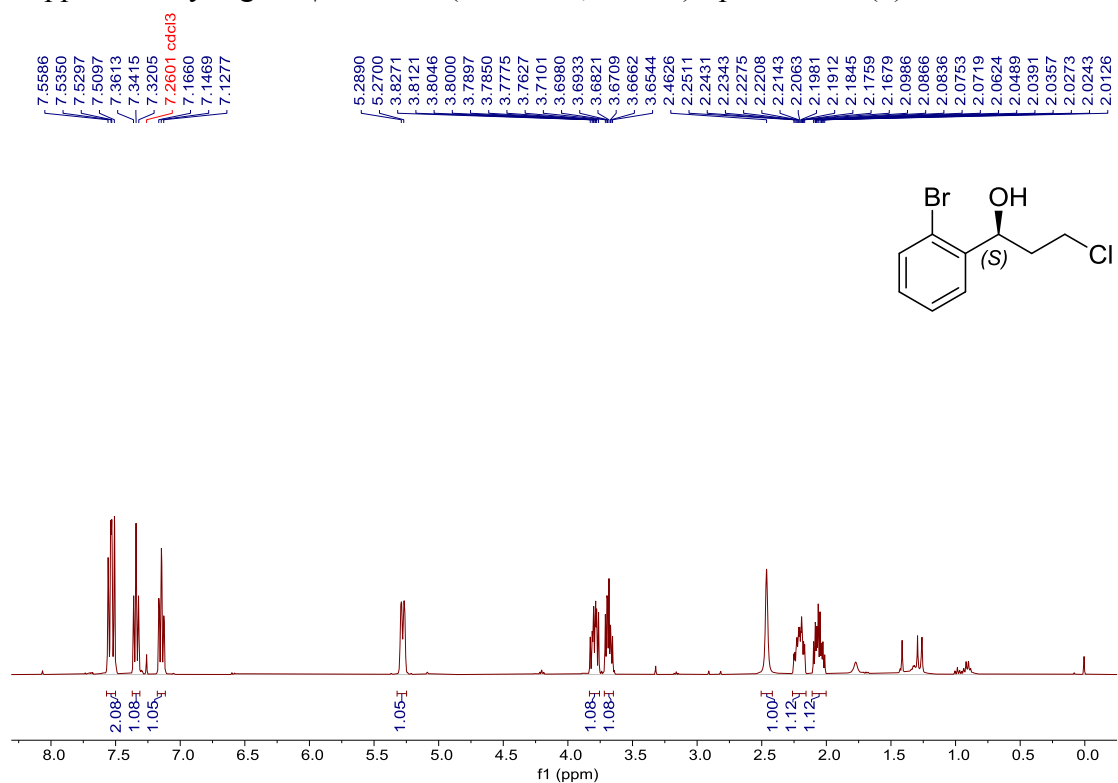
Supplementary Fig. 16 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**3a**.



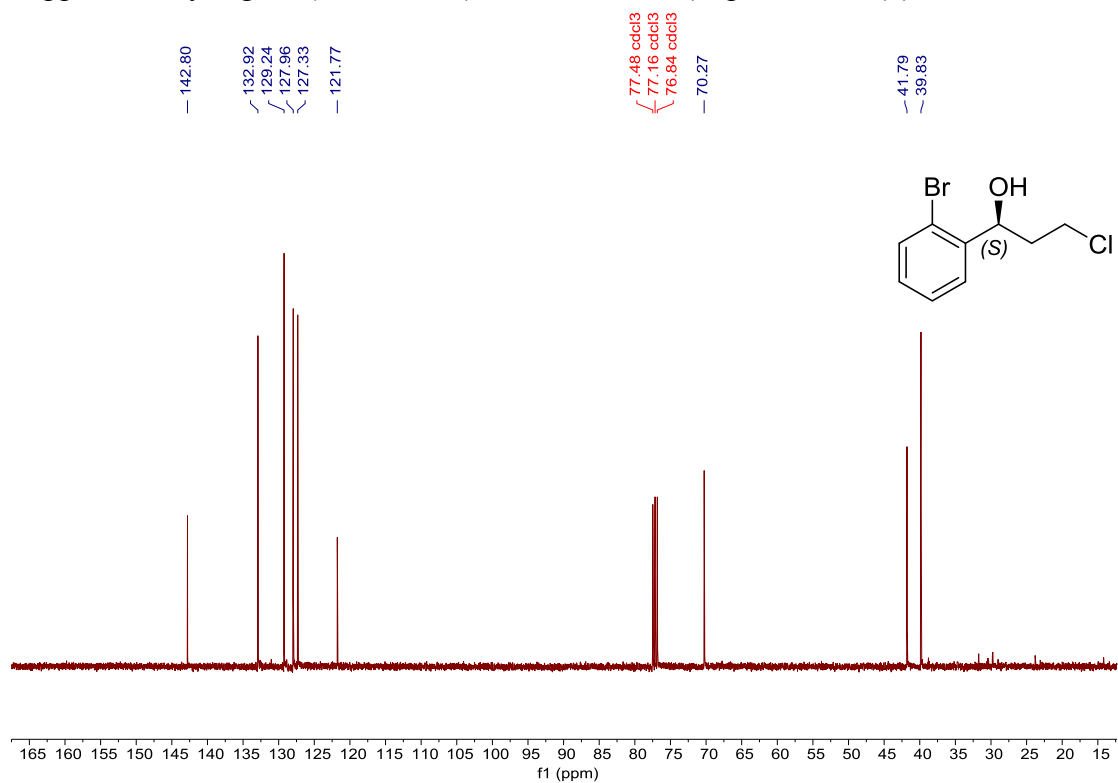
Supplementary Fig. 17 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**3a**.



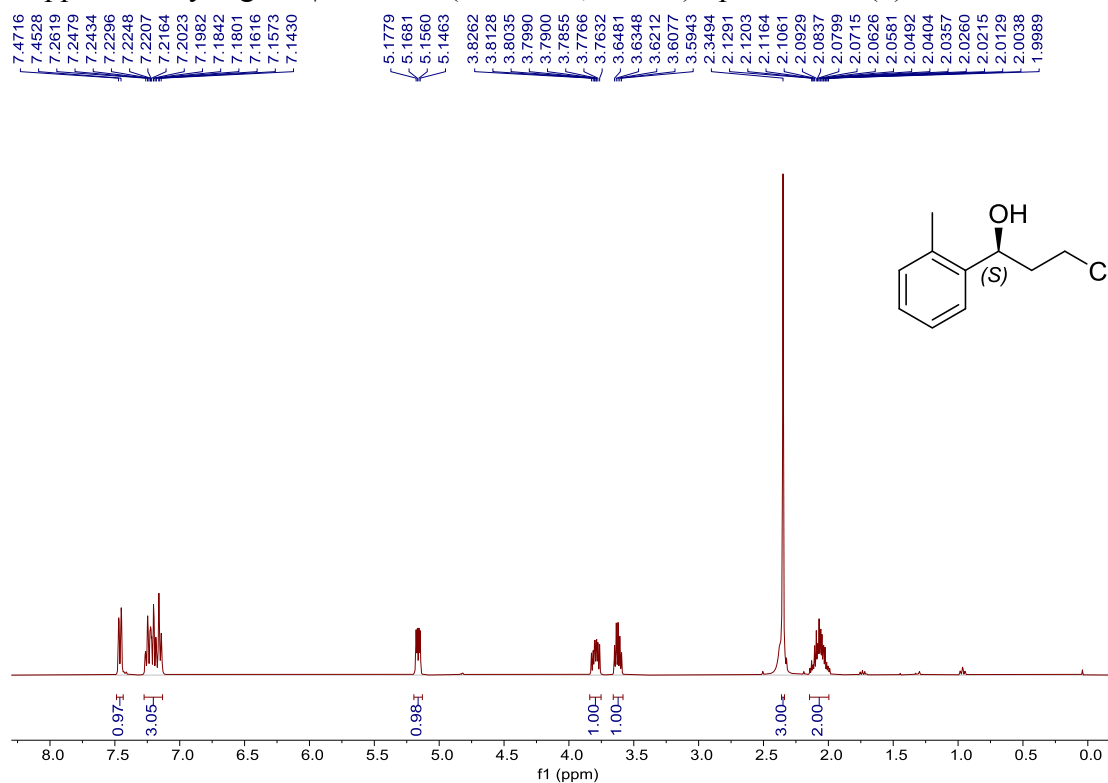
Supplementary Fig. 18 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**4a**.



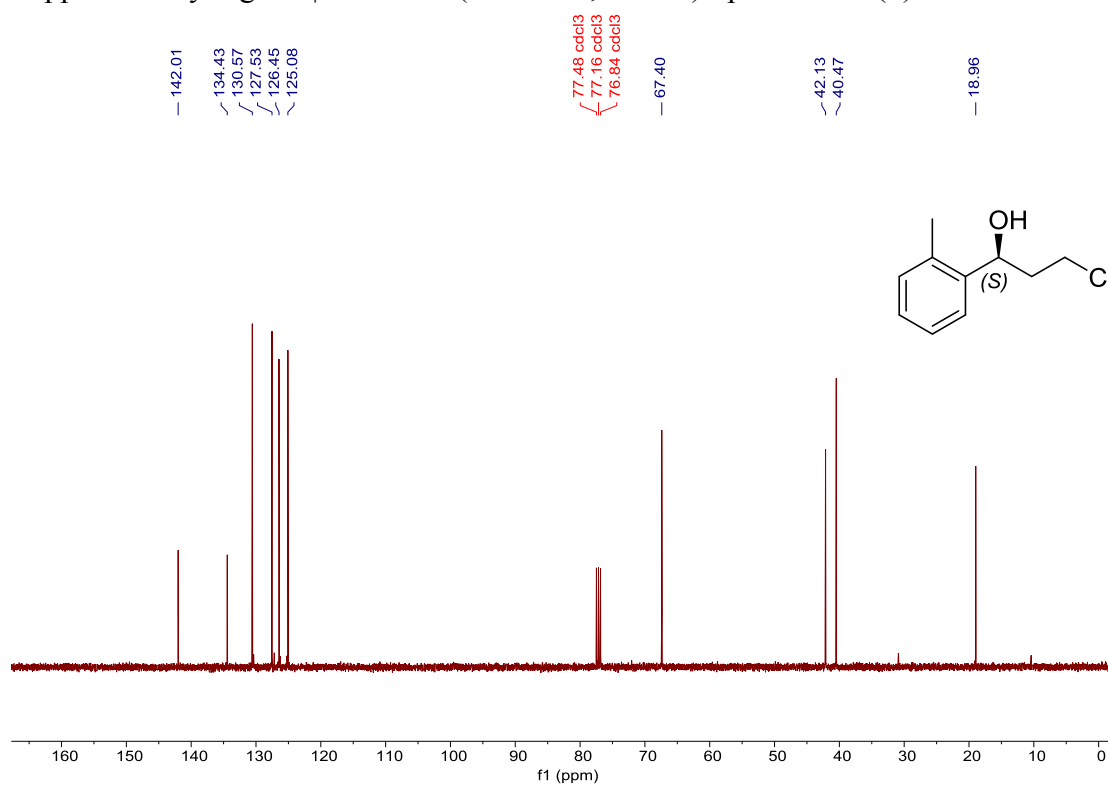
Supplementary Fig. 19 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**4a**.



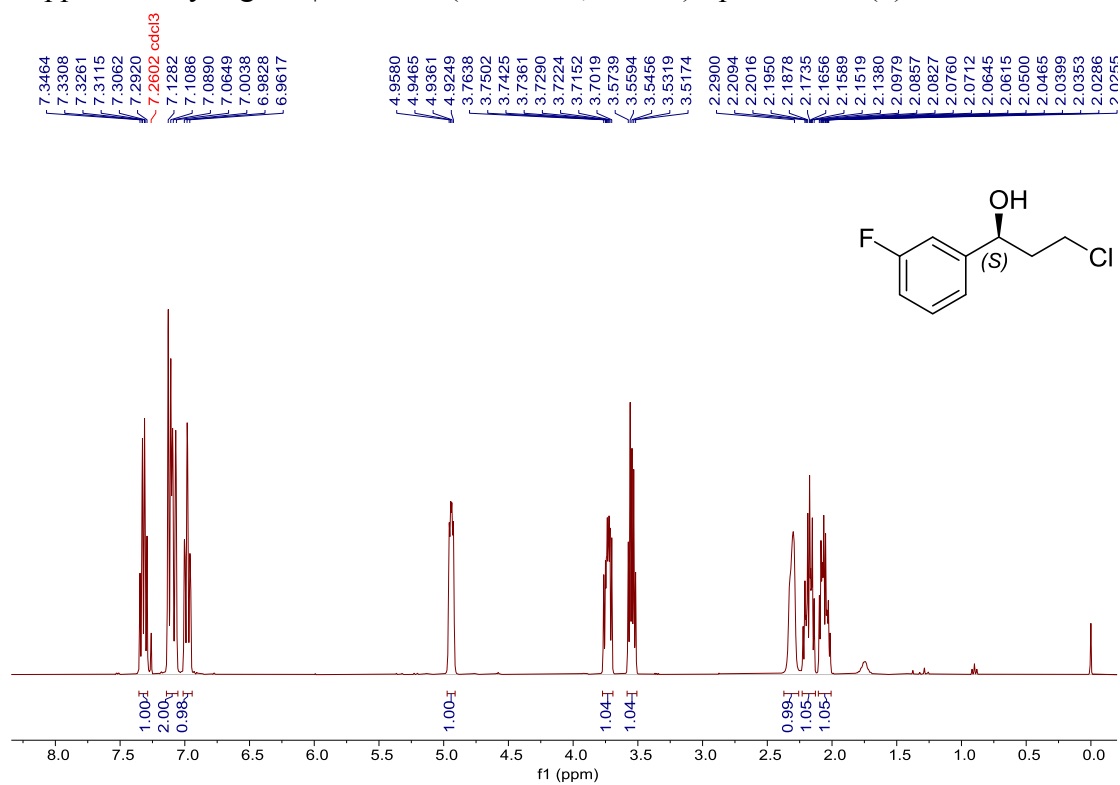
Supplementary Fig. 20 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**5a**.



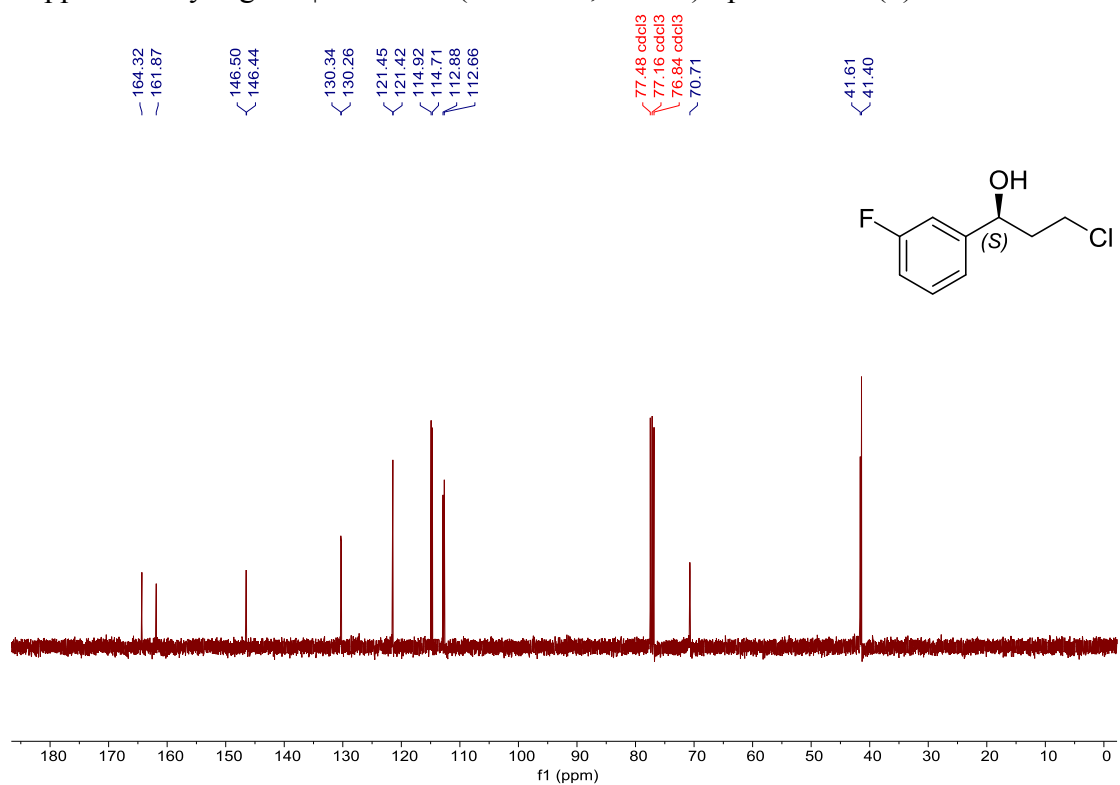
Supplementary Fig. 21 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**5a**.



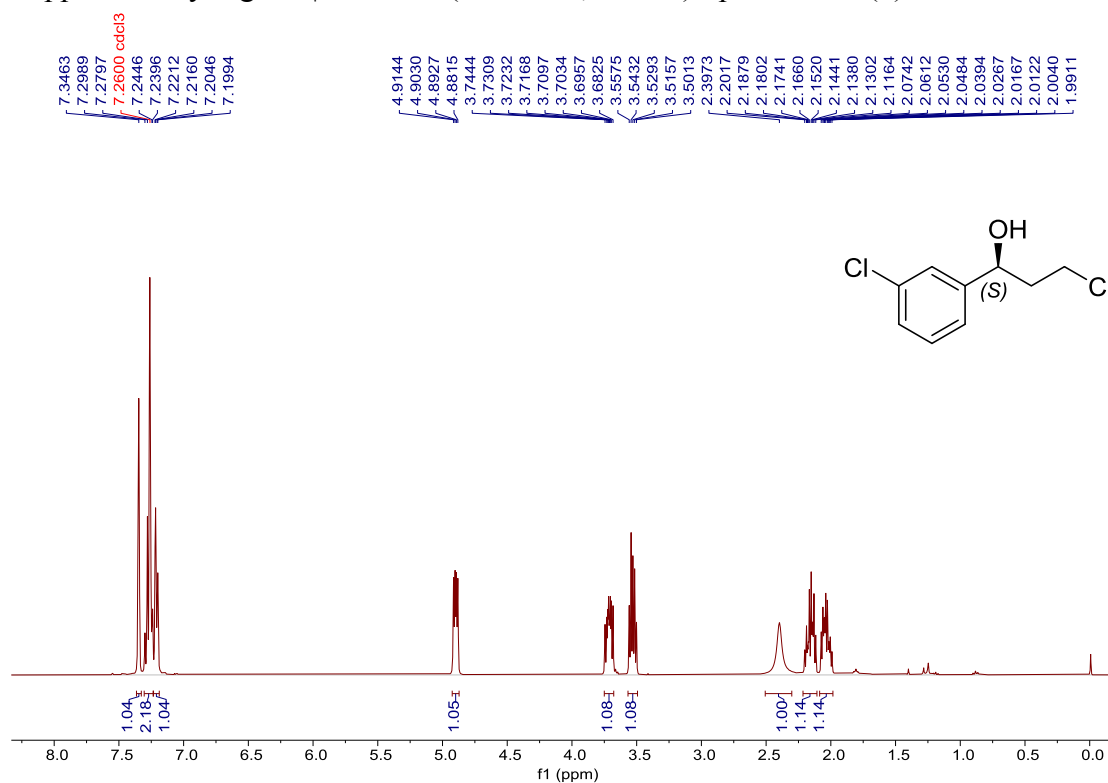
Supplementary Fig. 22 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**6a**.



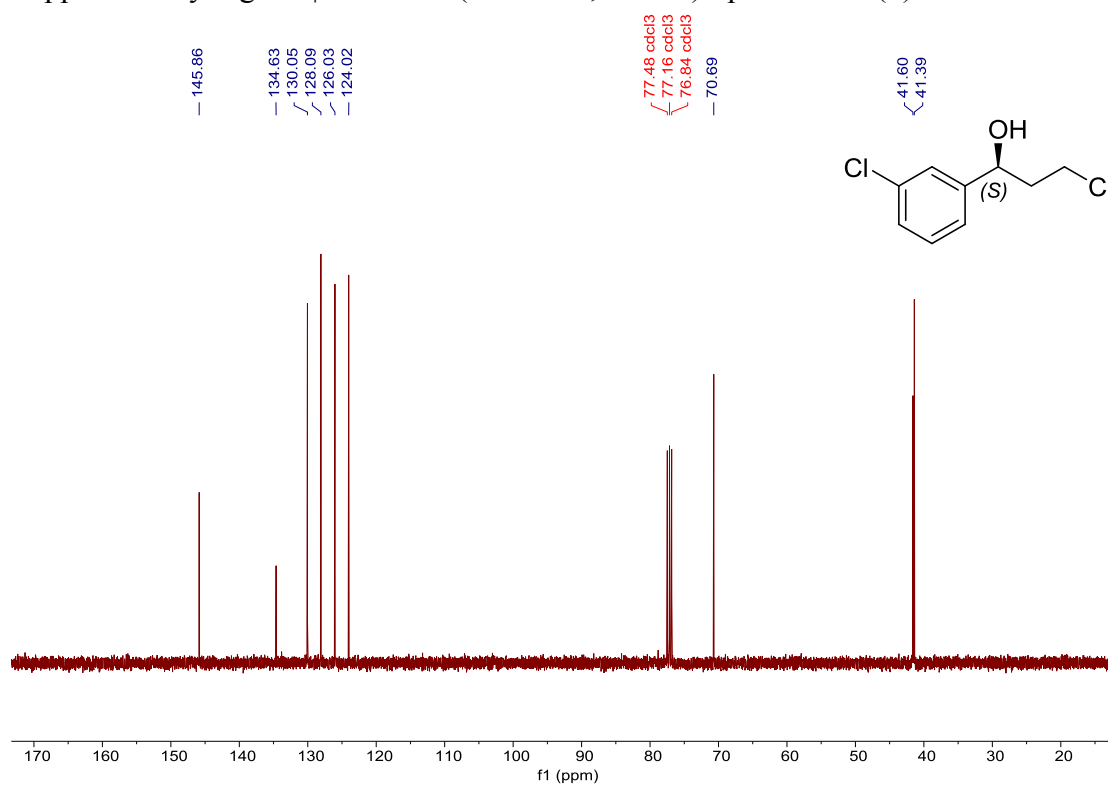
Supplementary Fig. 23 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**6a**.



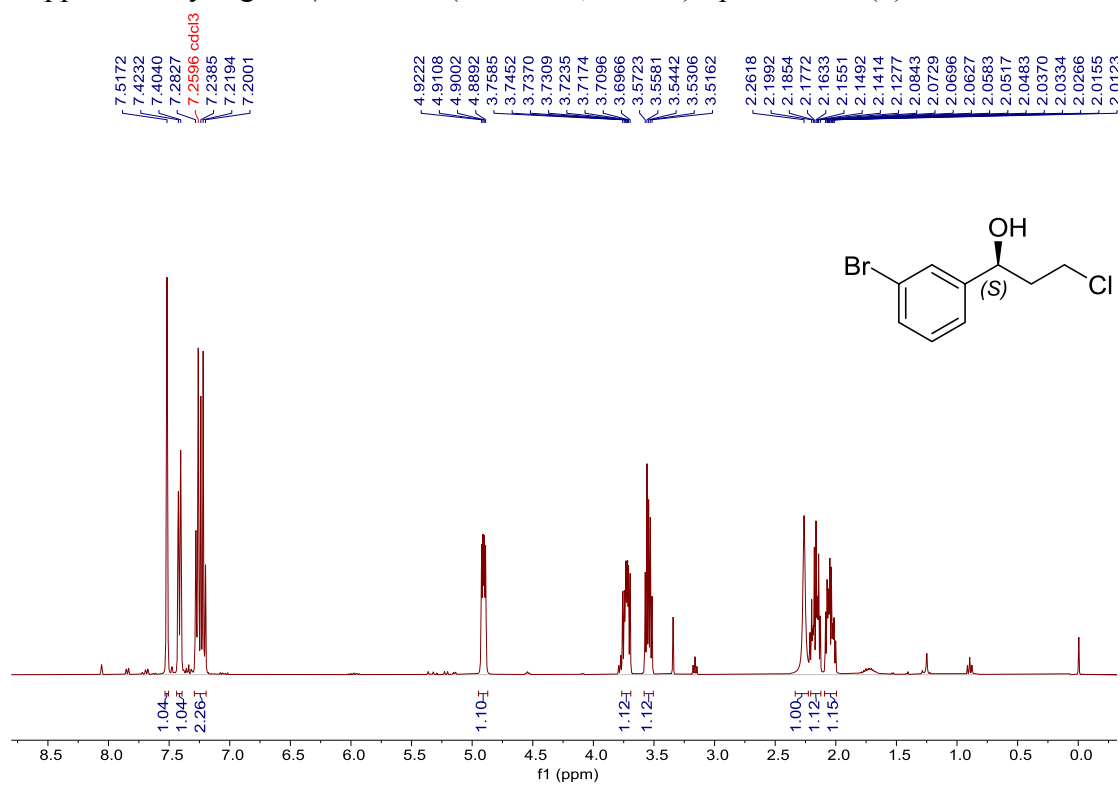
Supplementary Fig. 24 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**7a**.



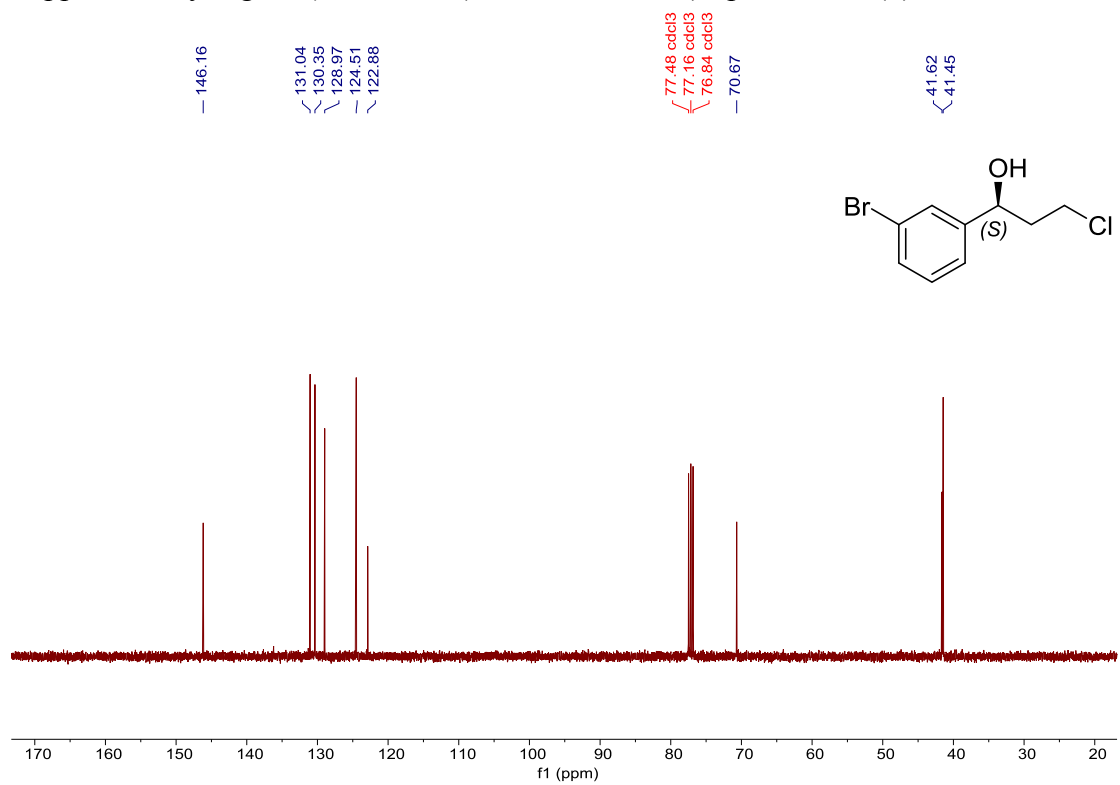
Supplementary Fig. 25 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**7a**.



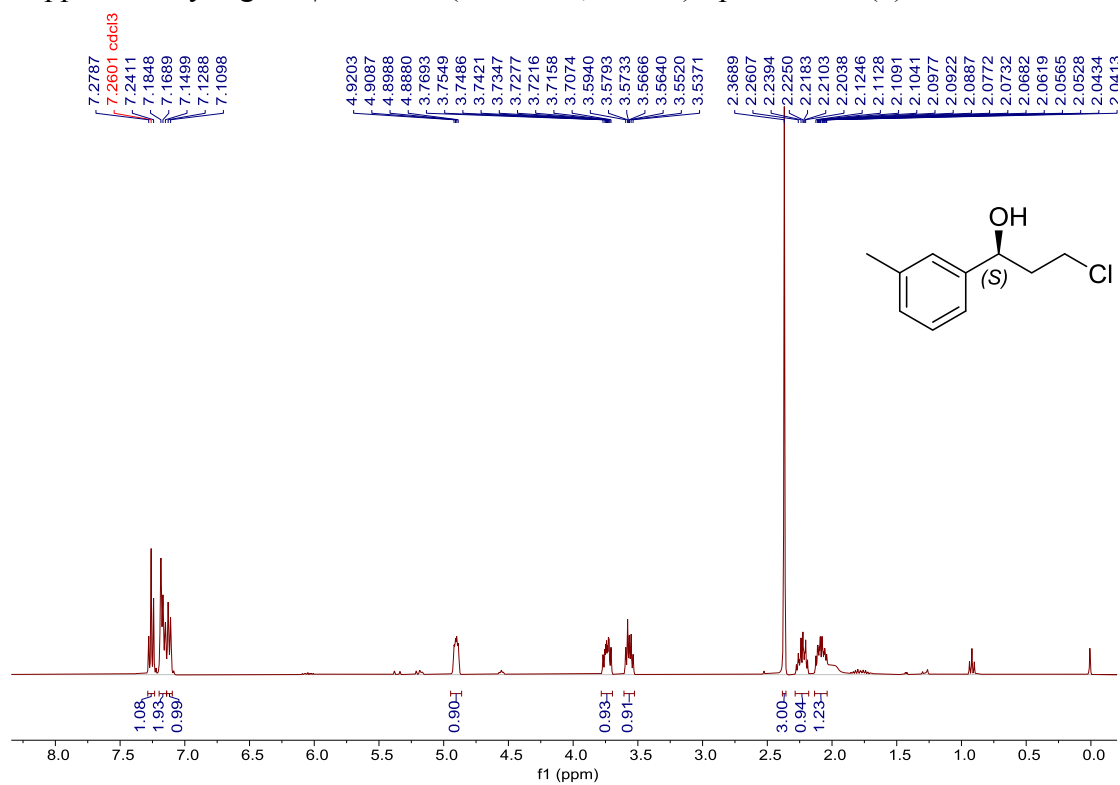
Supplementary Fig. 26 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**8a**.



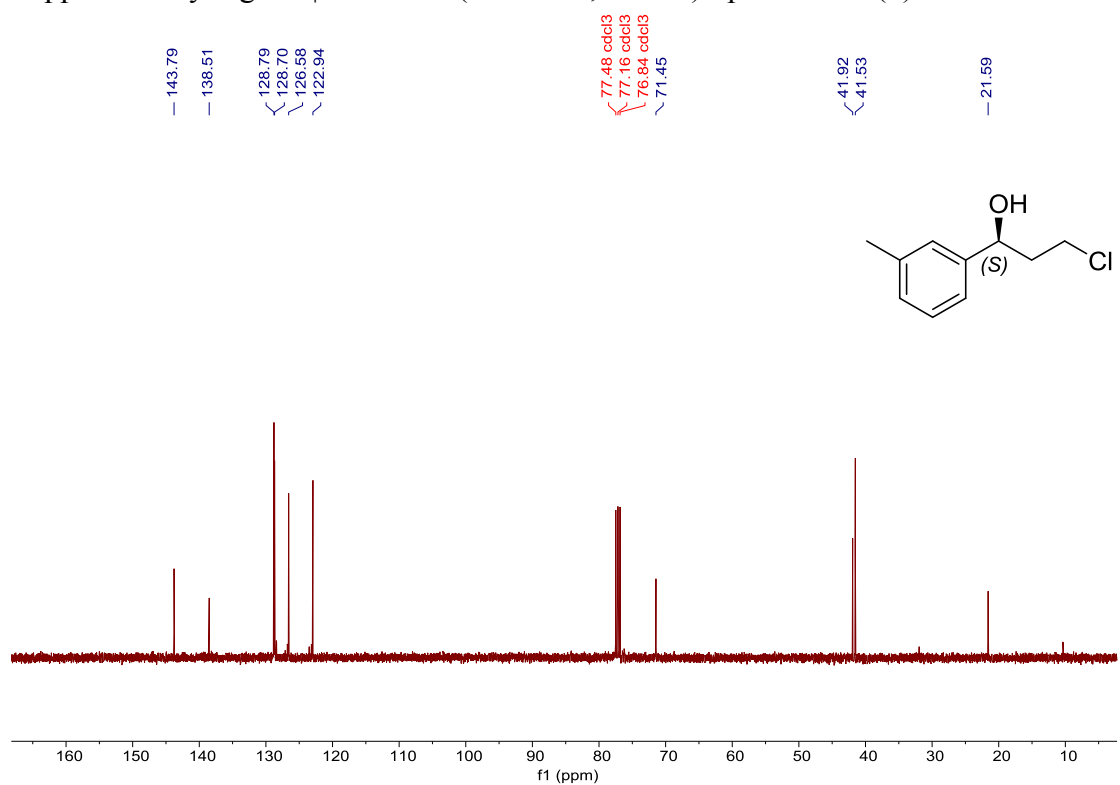
Supplementary Fig. 27 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**8a**.



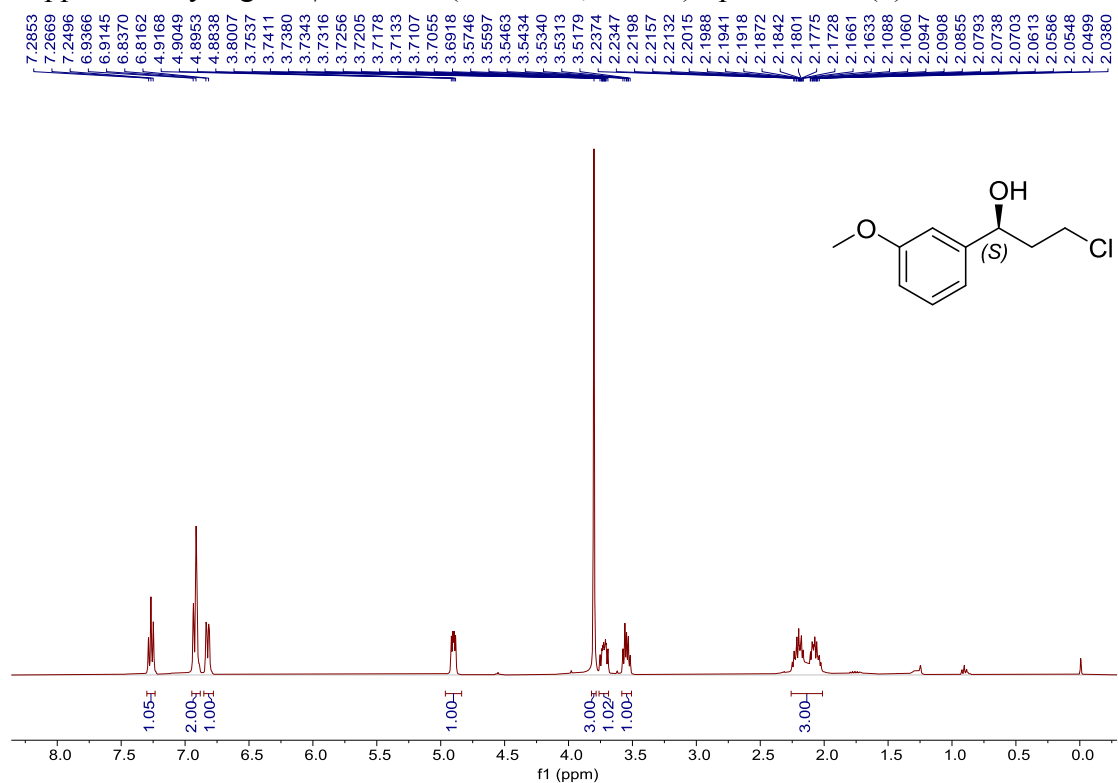
Supplementary Fig. 28 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**9a**.



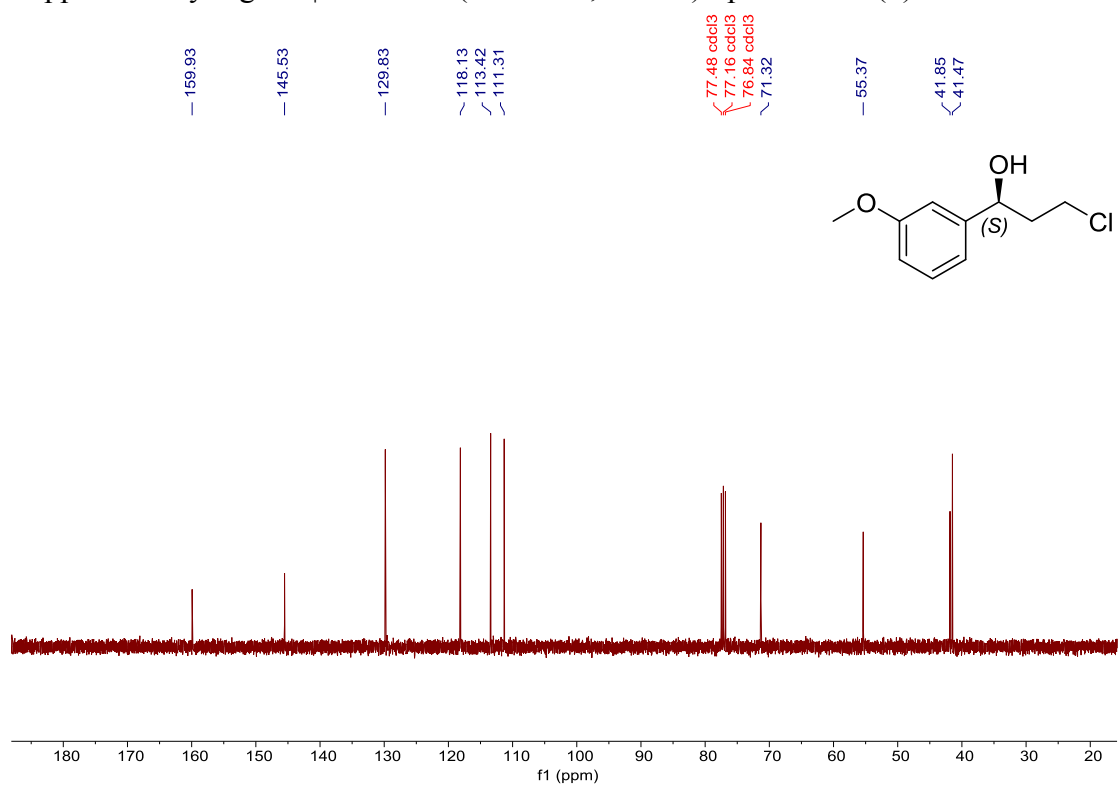
Supplementary Fig. 29 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**9a**.



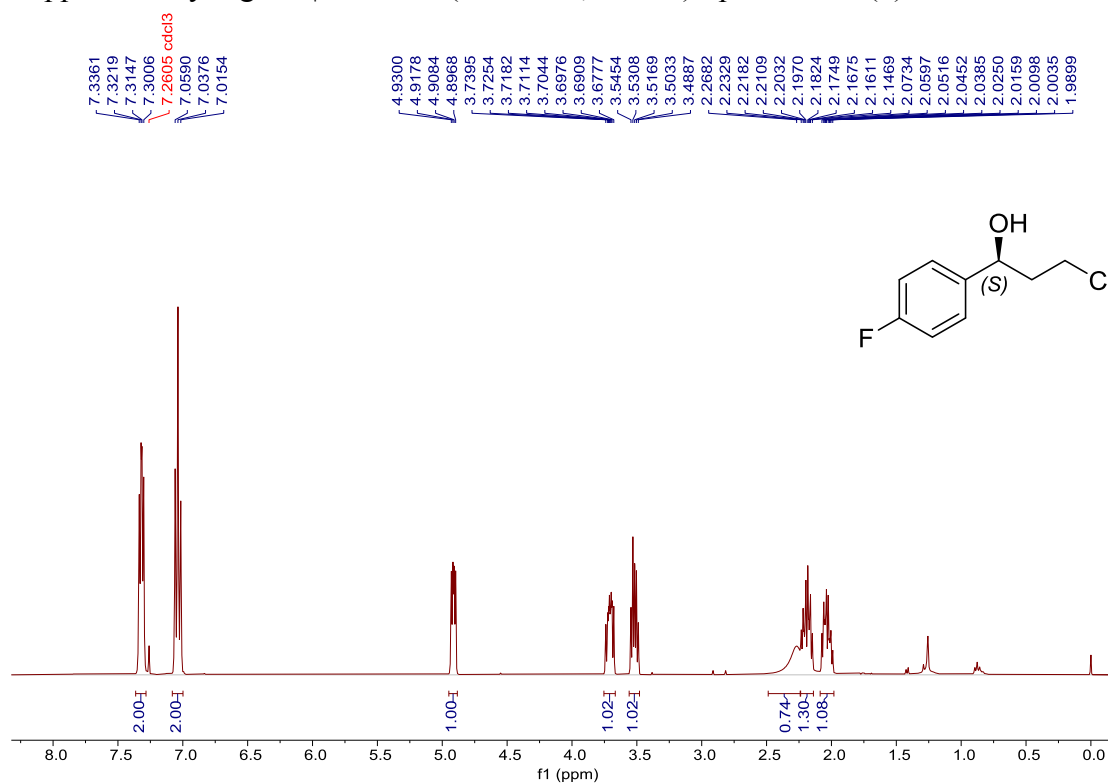
Supplementary Fig. 30 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**10a**.



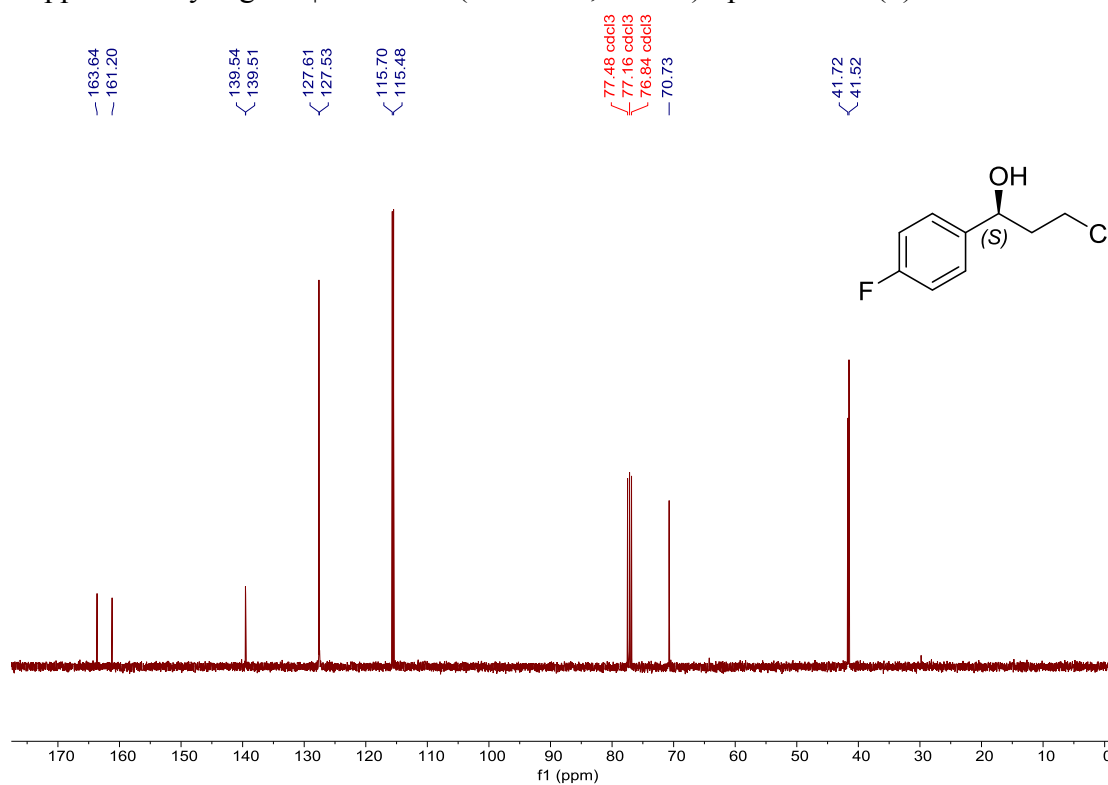
Supplementary Fig. 31 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**10a**.



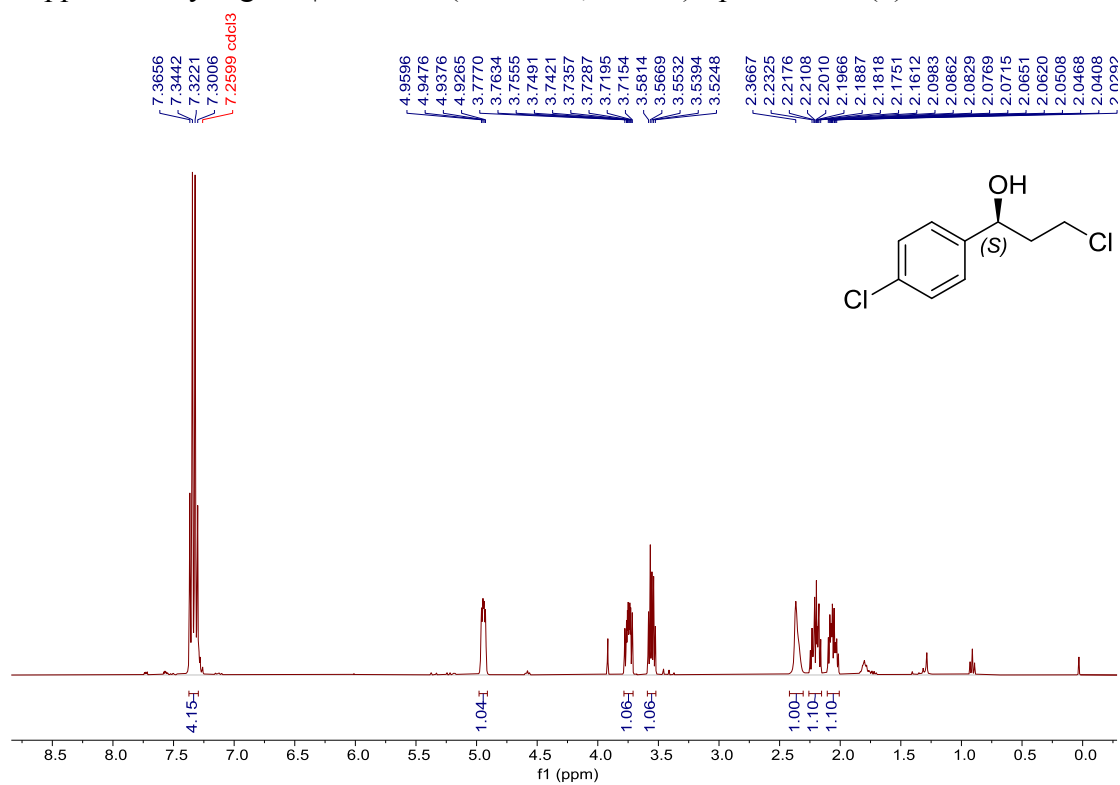
Supplementary Fig. 32 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**11a**.



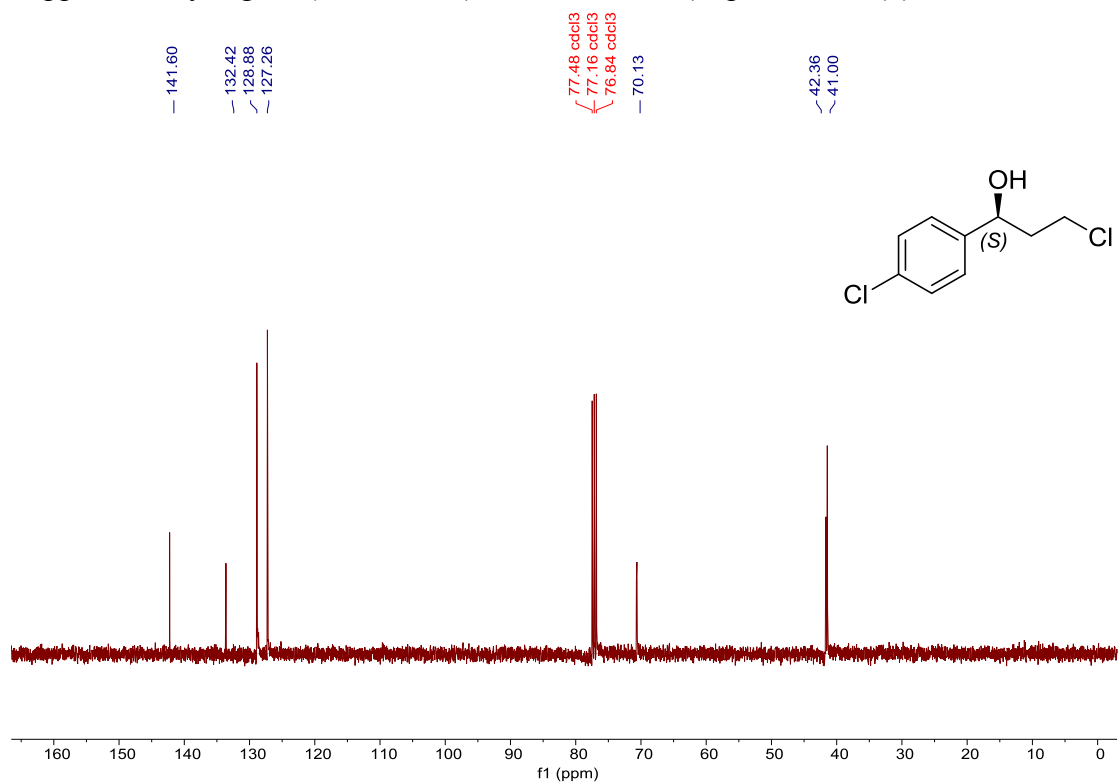
Supplementary Fig. 33 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**11a**.



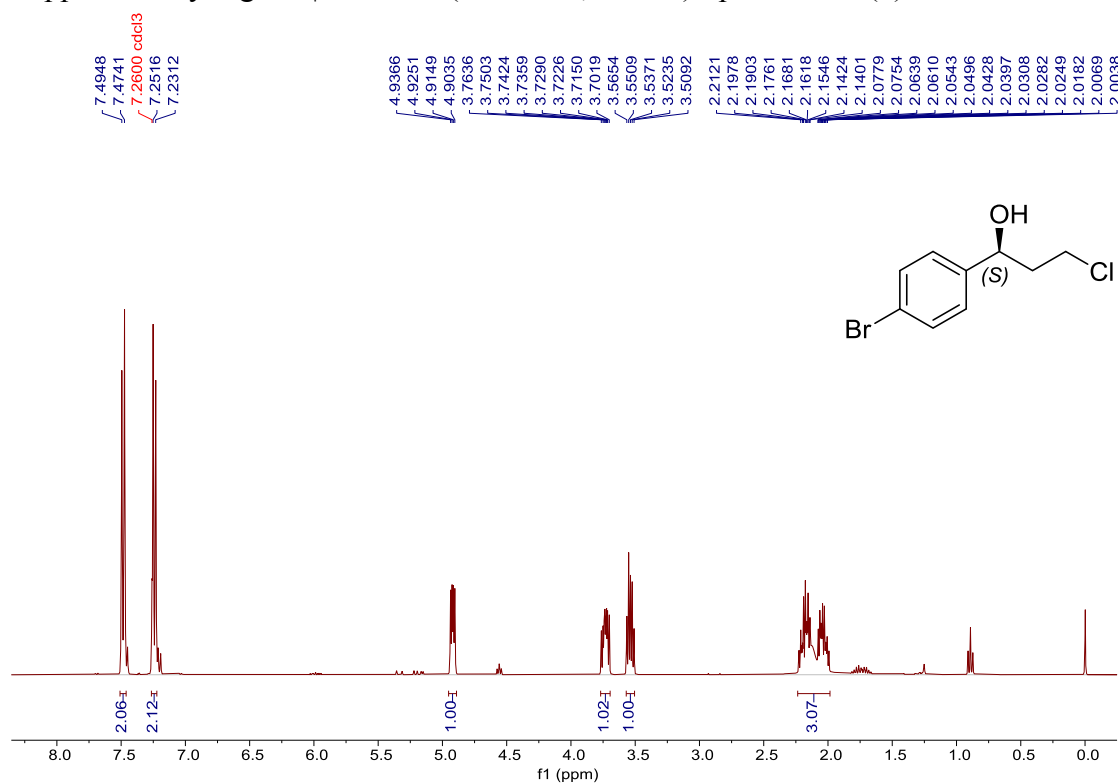
Supplementary Fig. 34 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**12a**.



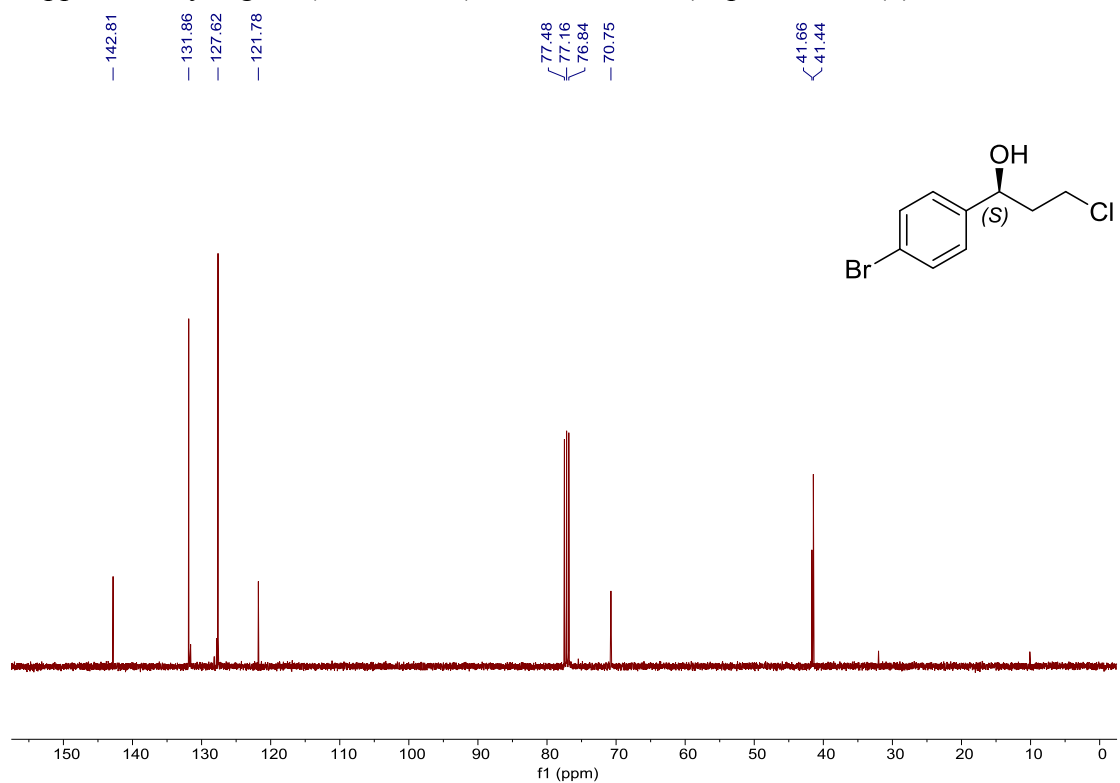
Supplementary Fig. 35 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**12a**.



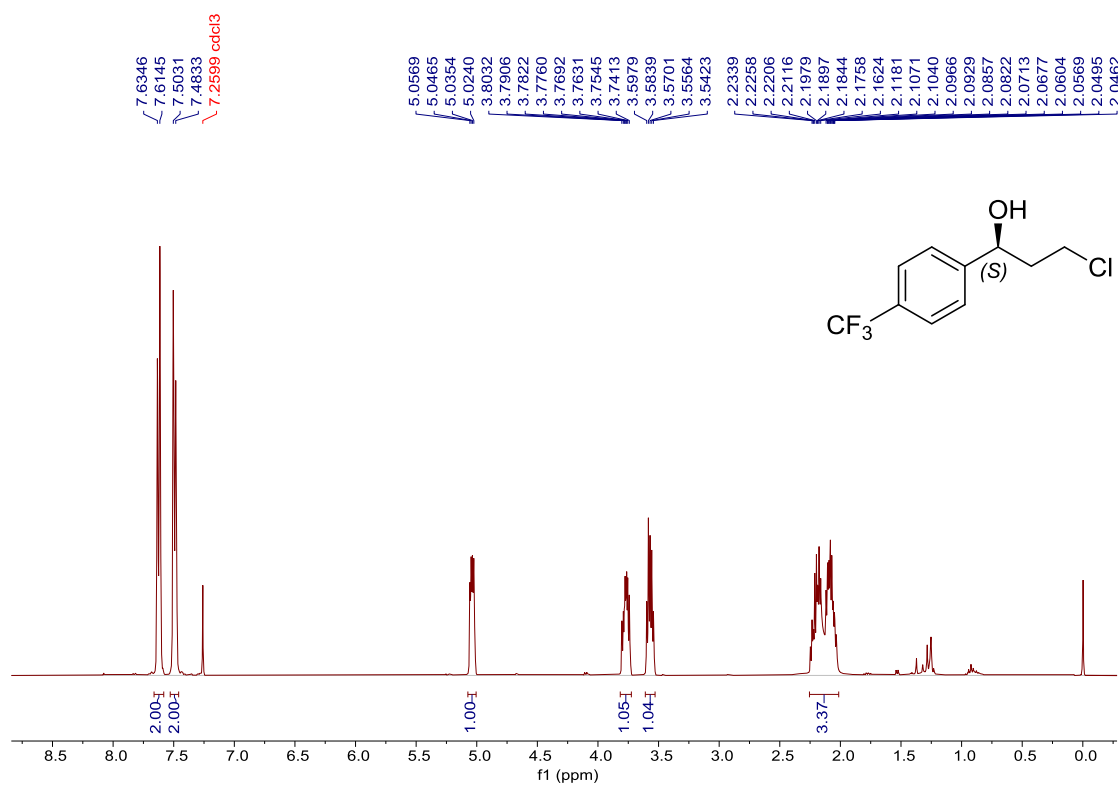
Supplementary Fig. 36 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**13a**.



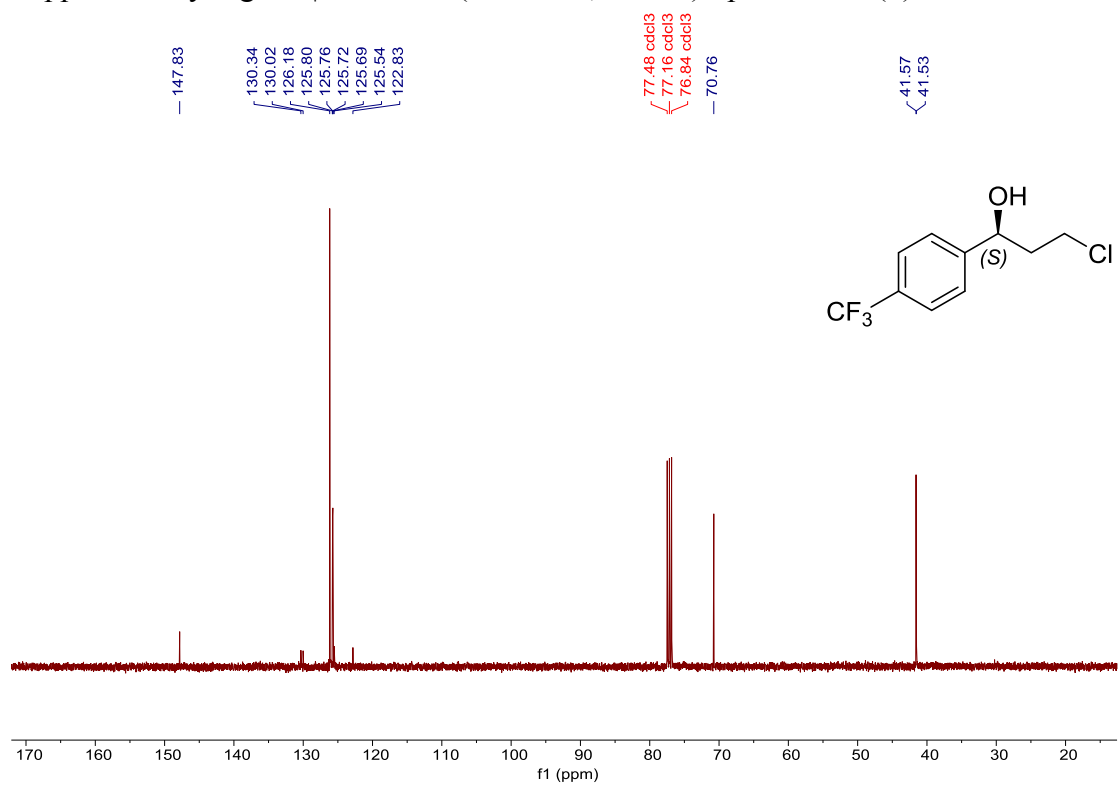
Supplementary Fig. 37 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**13a**.



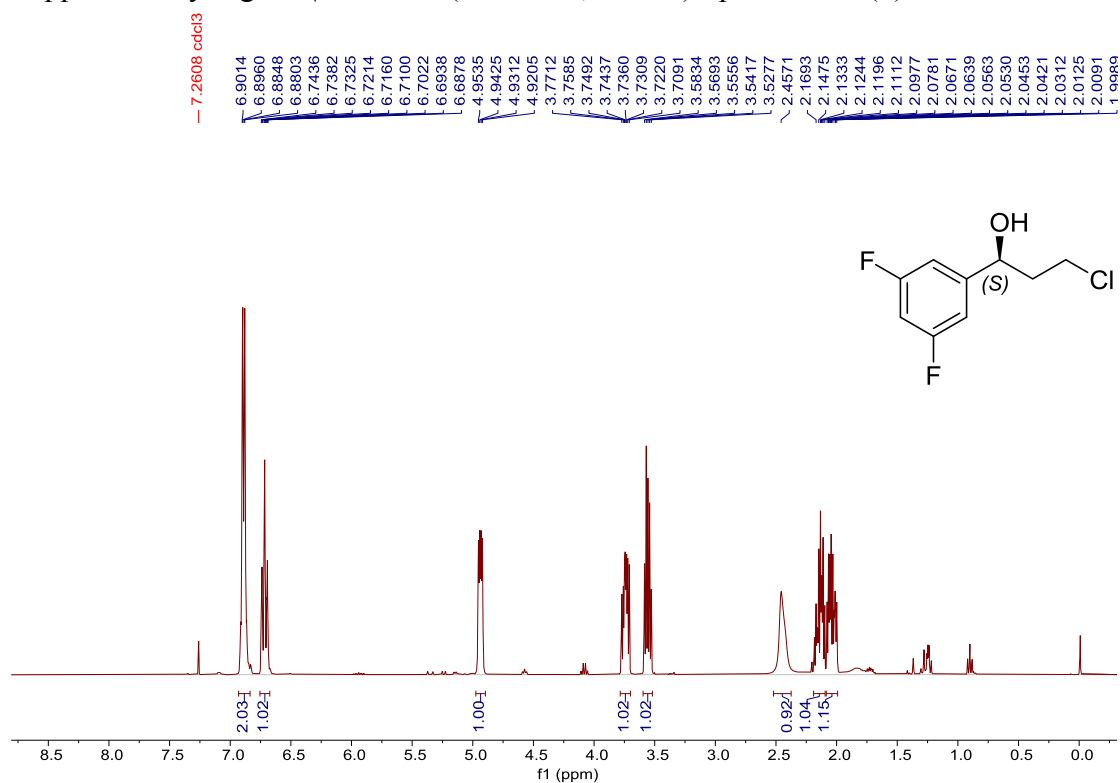
Supplementary Fig. 38 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**14a**.



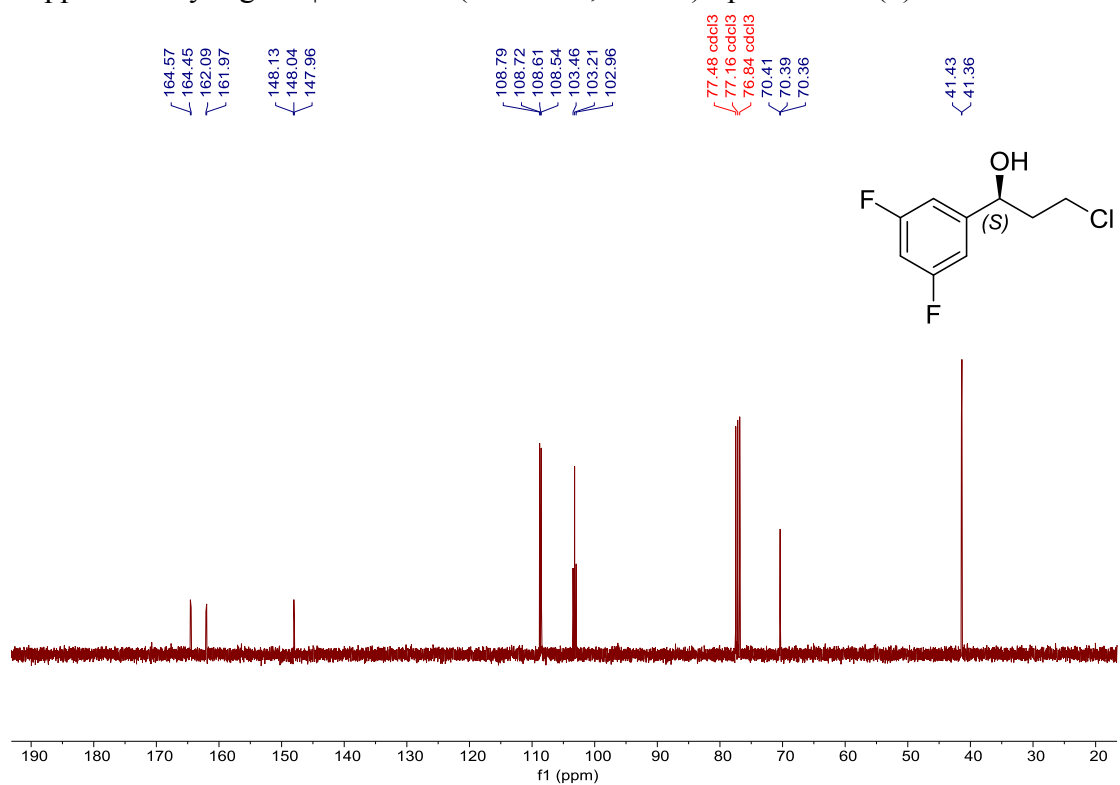
Supplementary Fig. 39 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**14a**.



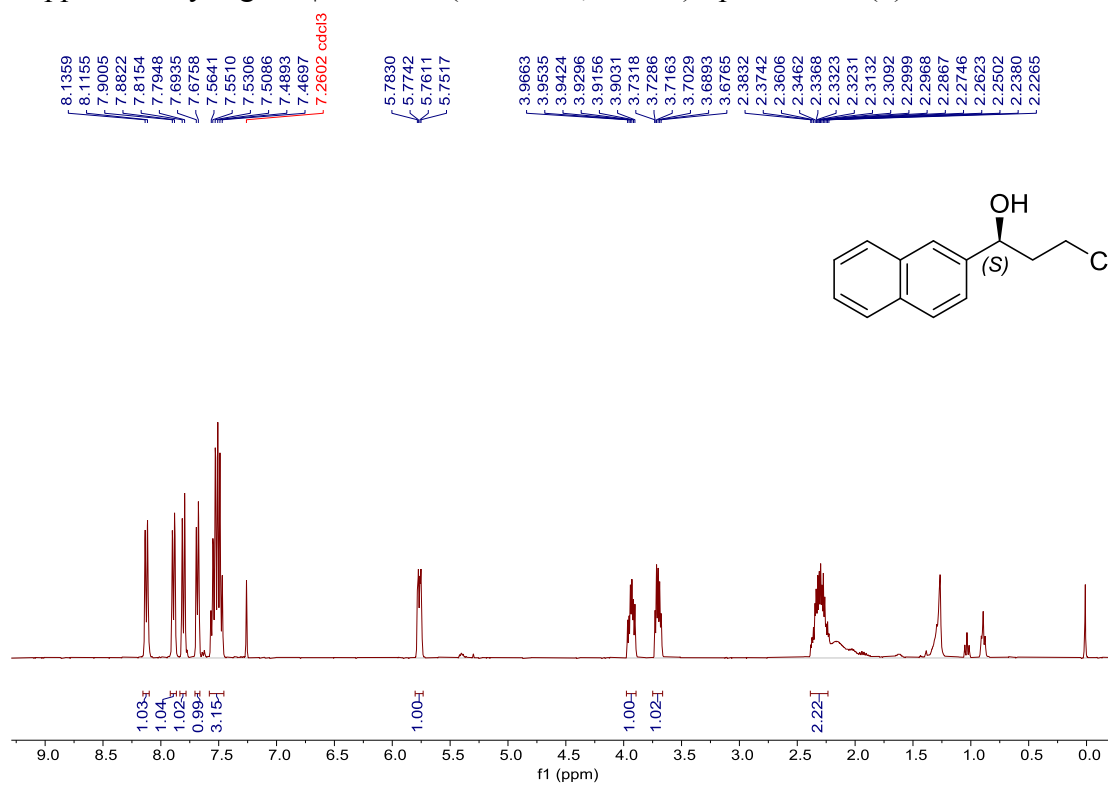
Supplementary Fig. 40 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**15a**.



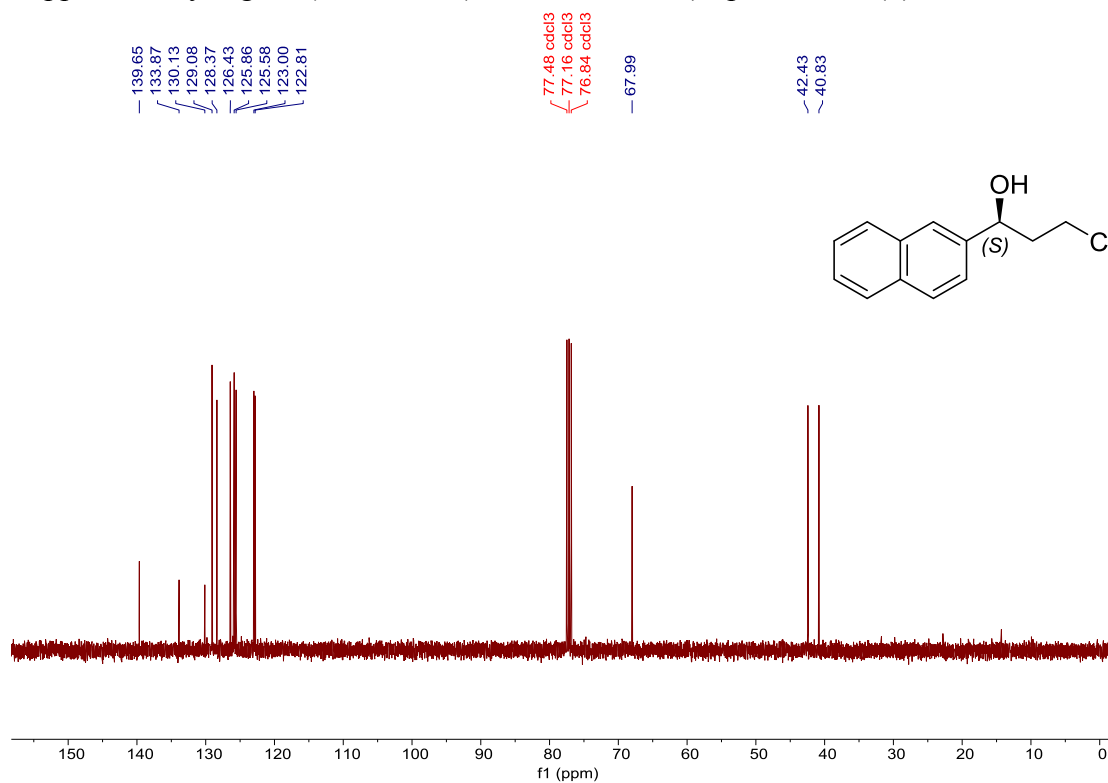
Supplementary Fig. 41 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**15a**.



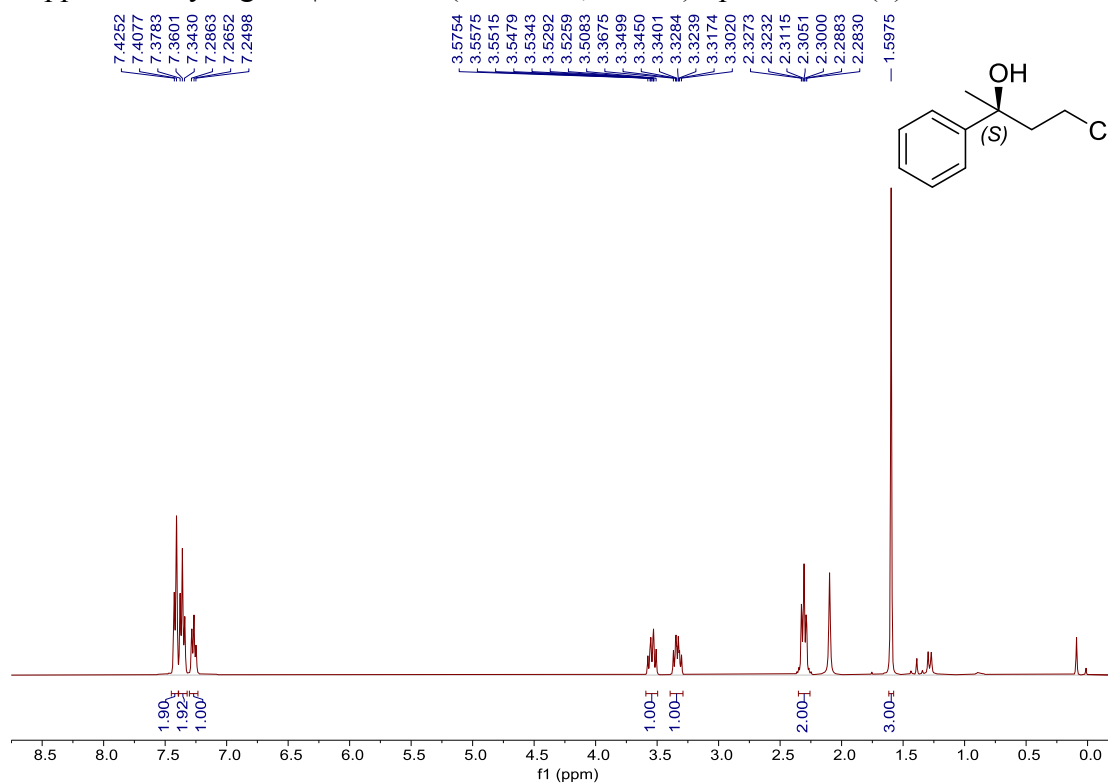
Supplementary Fig. 42 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**16a**.



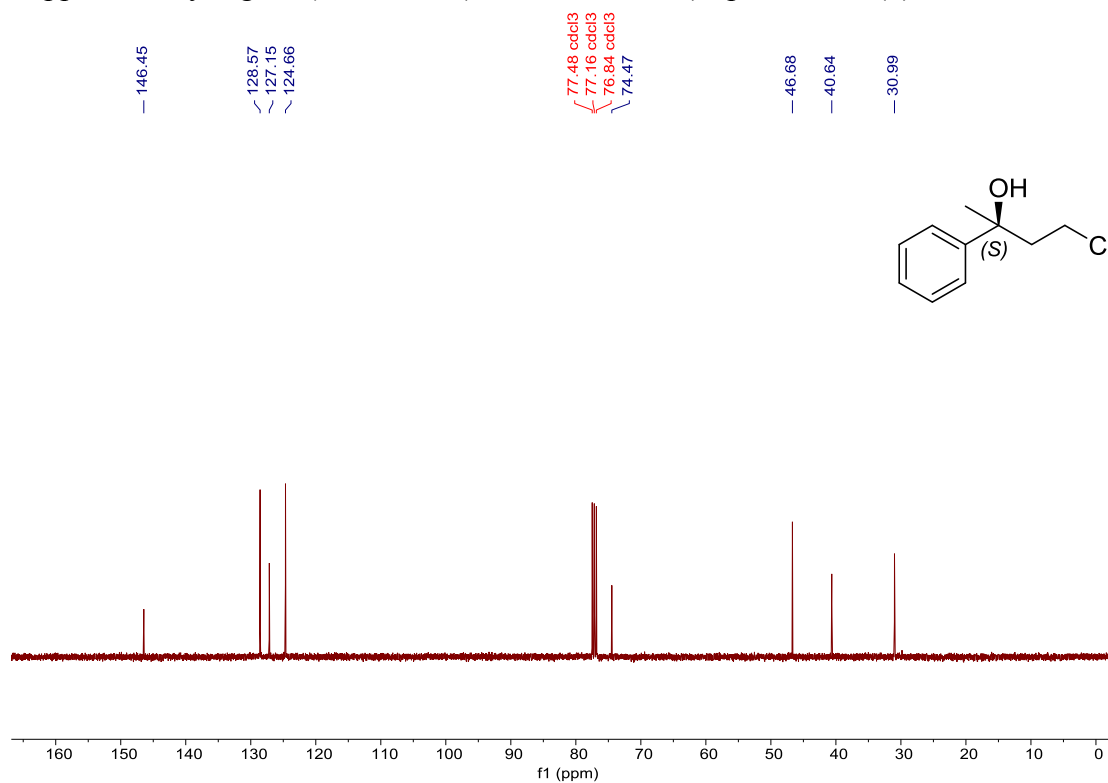
Supplementary Fig. 43 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**16a**.



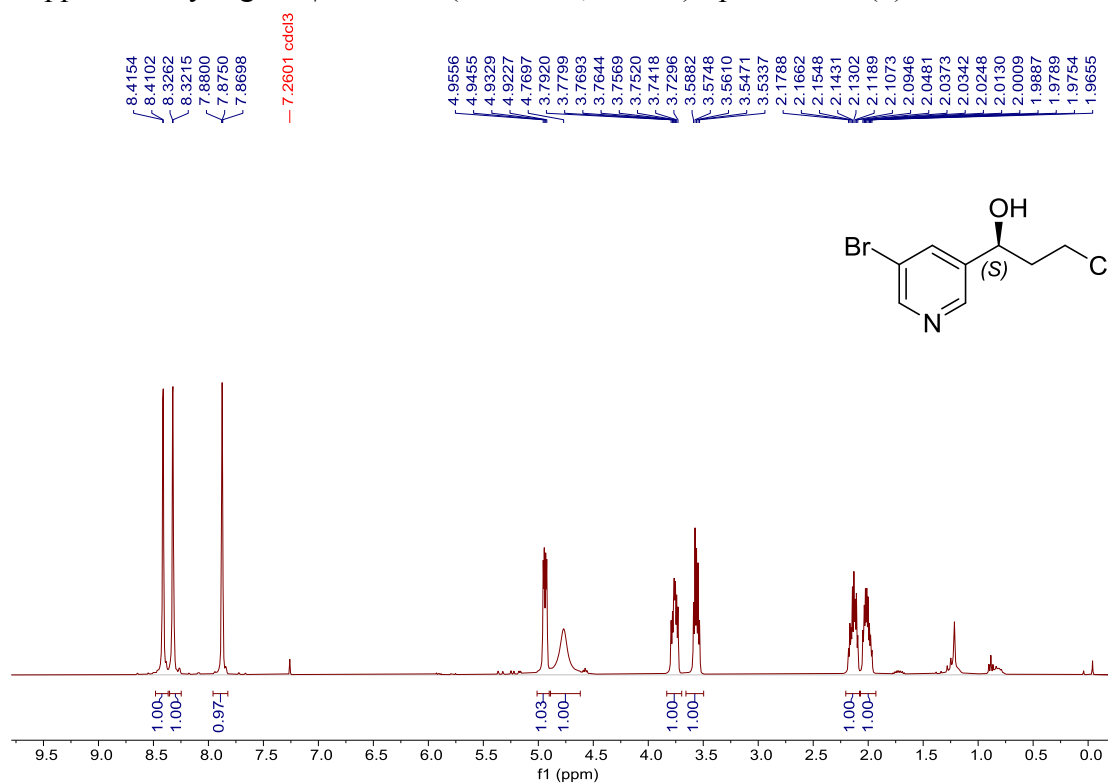
Supplementary Fig. 44 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**17a**.



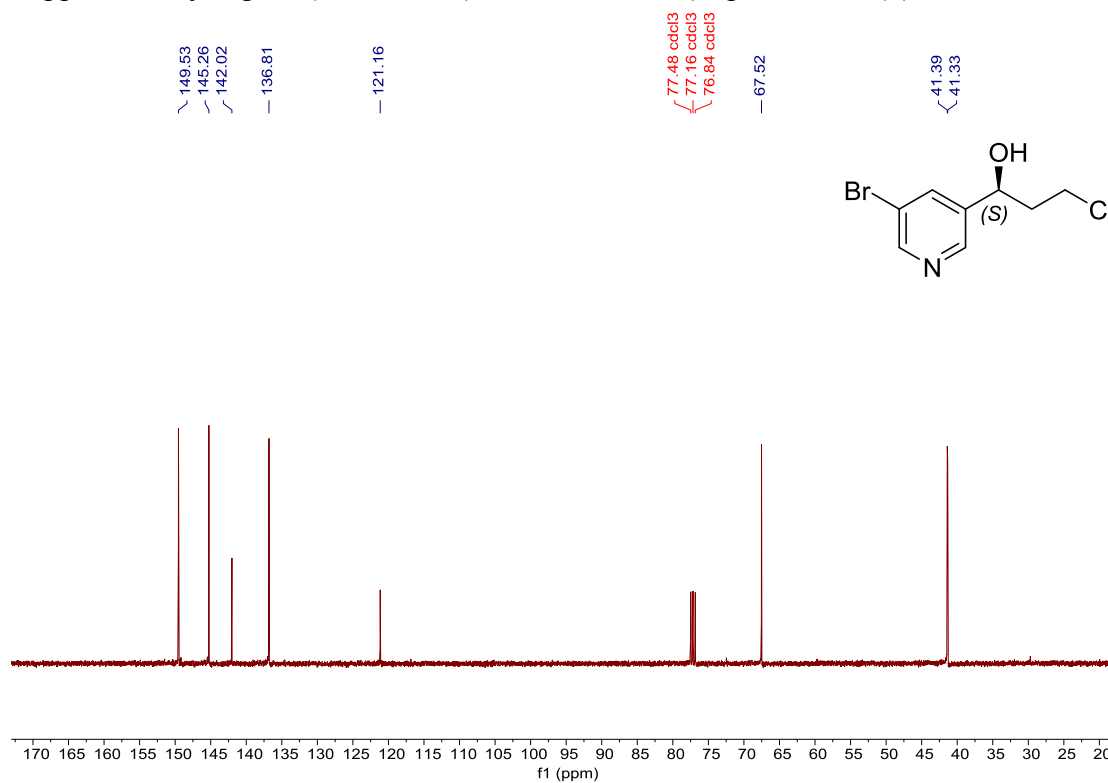
Supplementary Fig. 45 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**17a**.



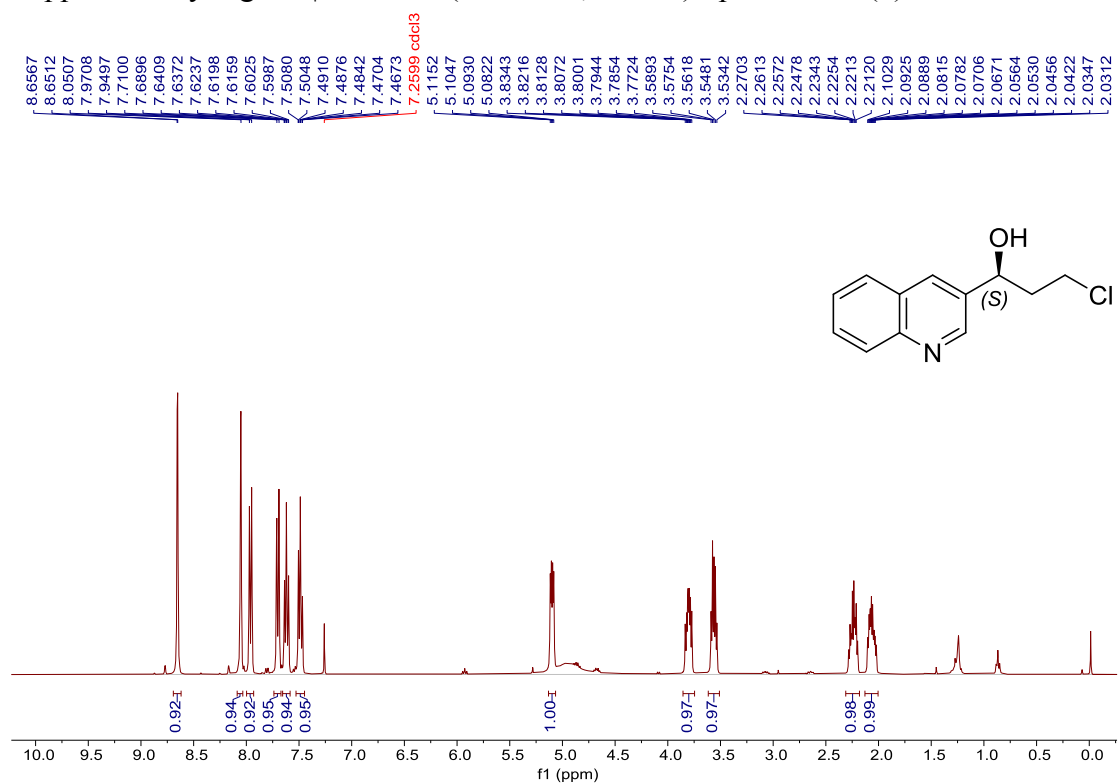
Supplementary Fig. 46 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**18a**.



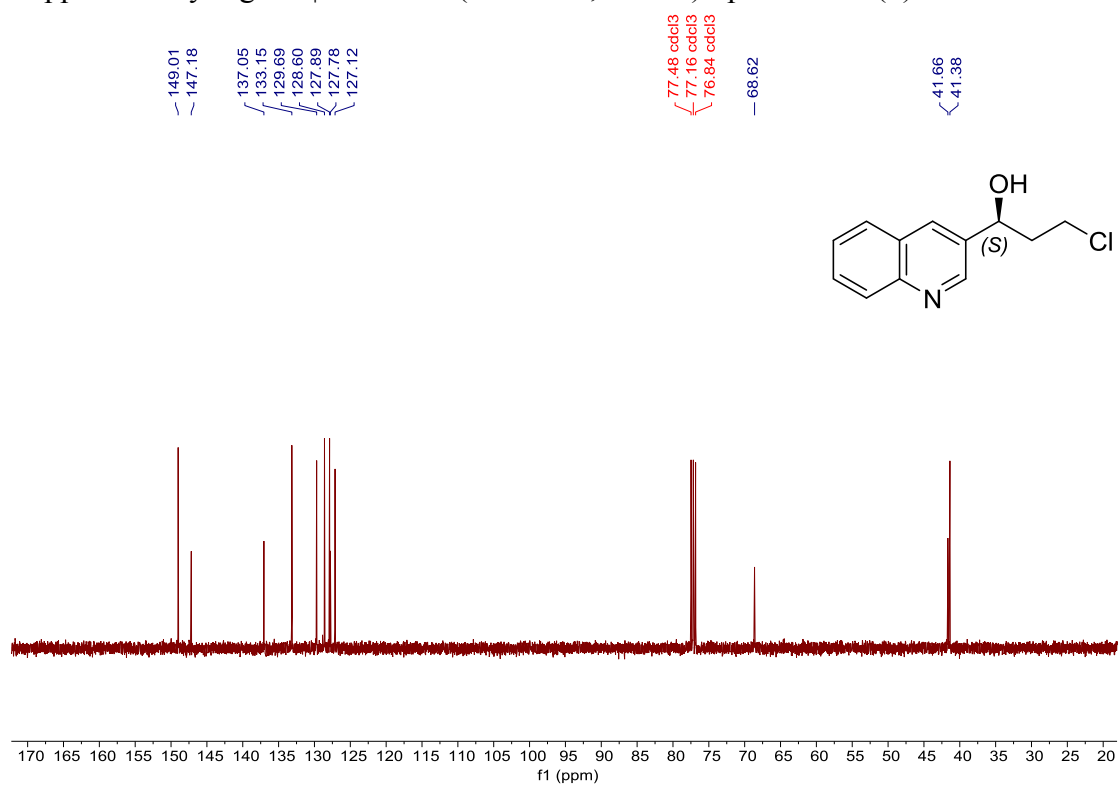
Supplementary Fig. 47 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**18a**.



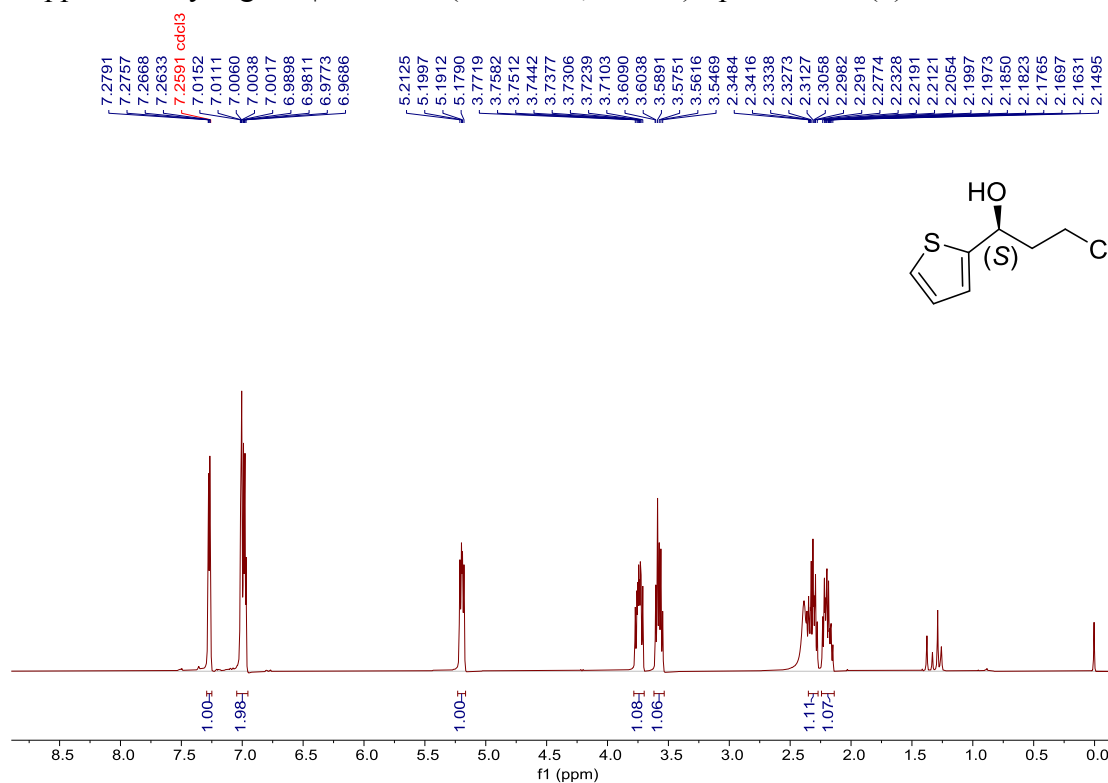
Supplementary Fig. 48 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**19a**.



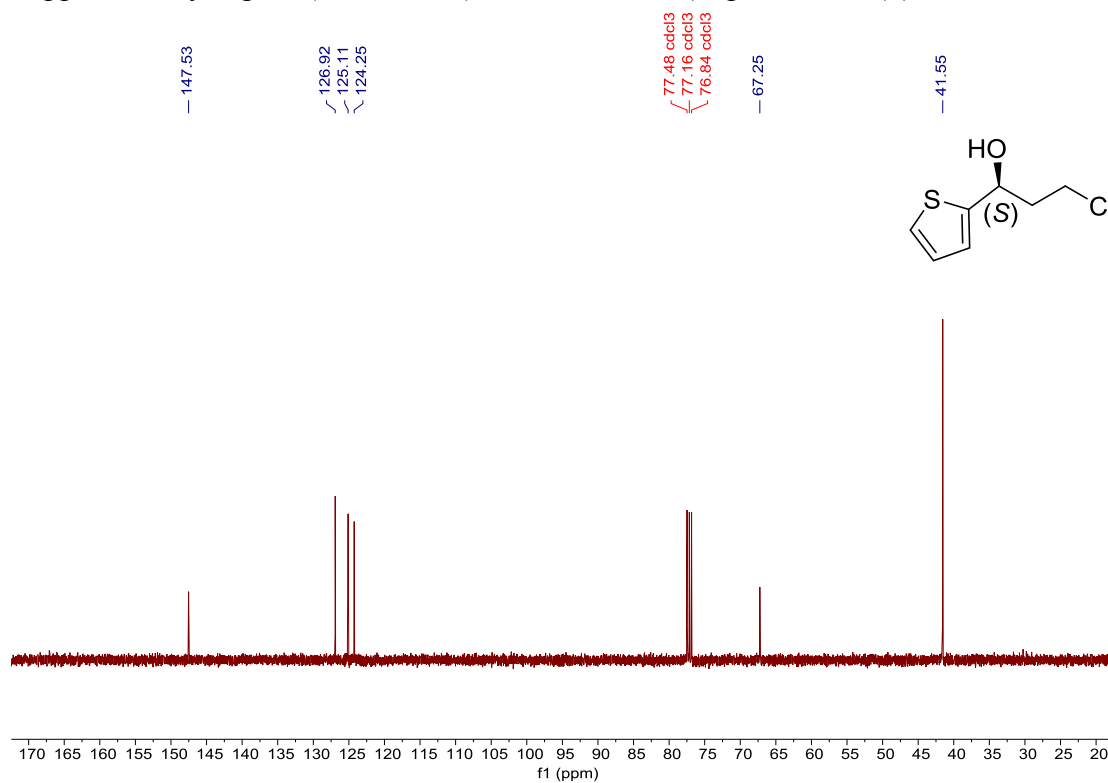
Supplementary Fig. 49 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**19a**.



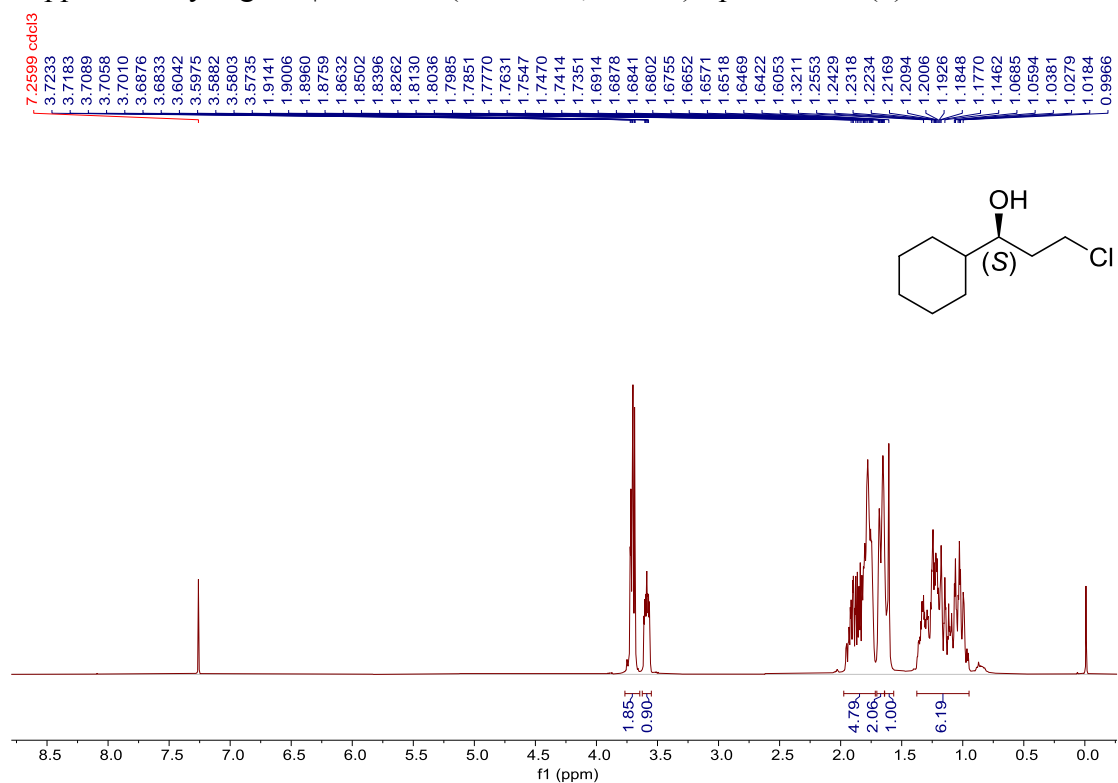
Supplementary Fig. 50 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**20a**.



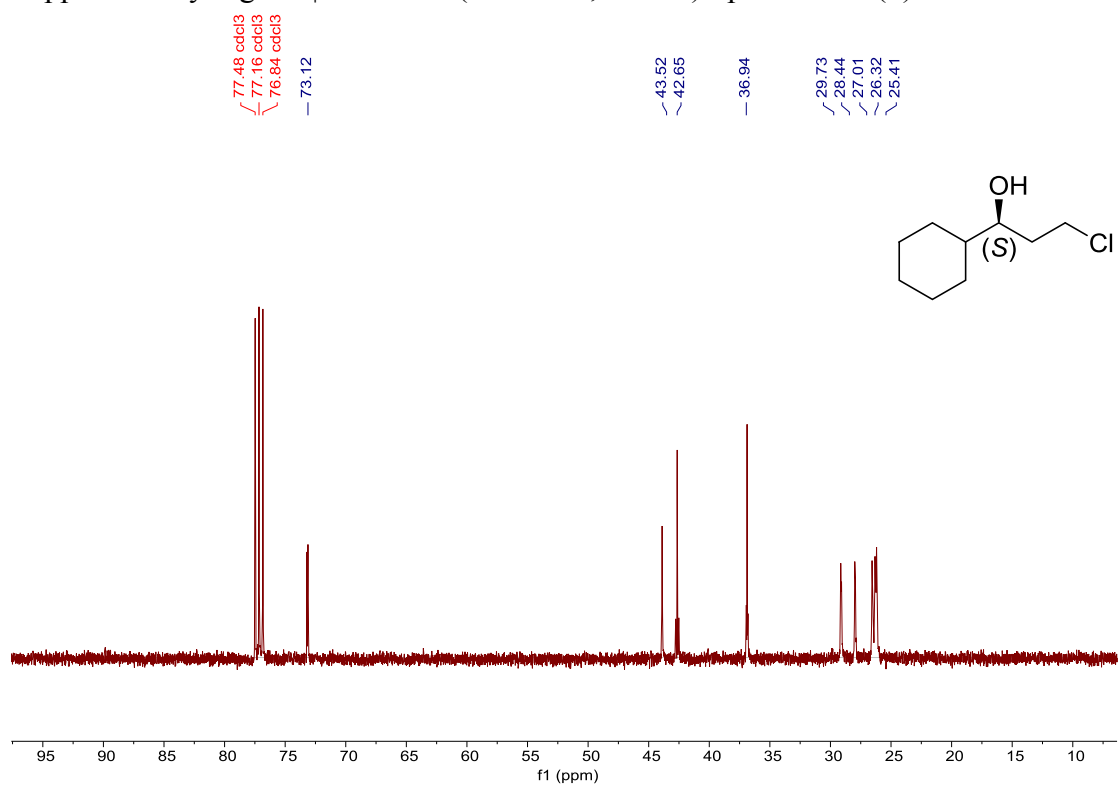
Supplementary Fig. 51 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**20a**.



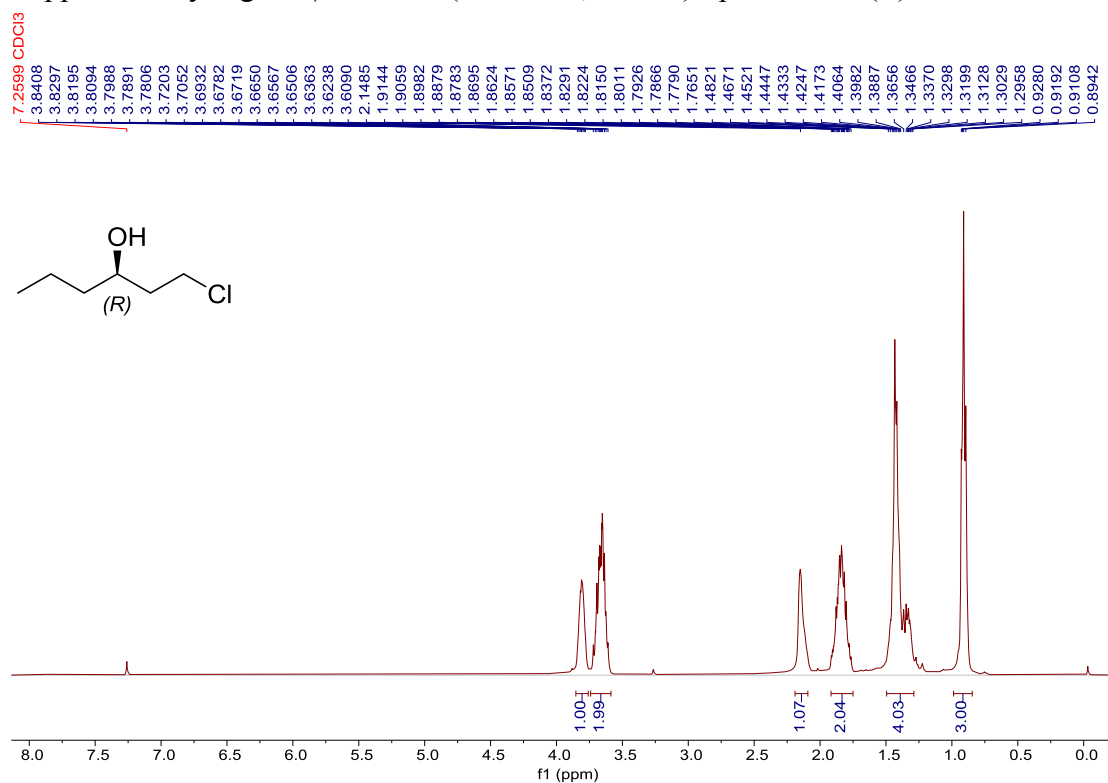
Supplementary Fig. 52 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**21a**.



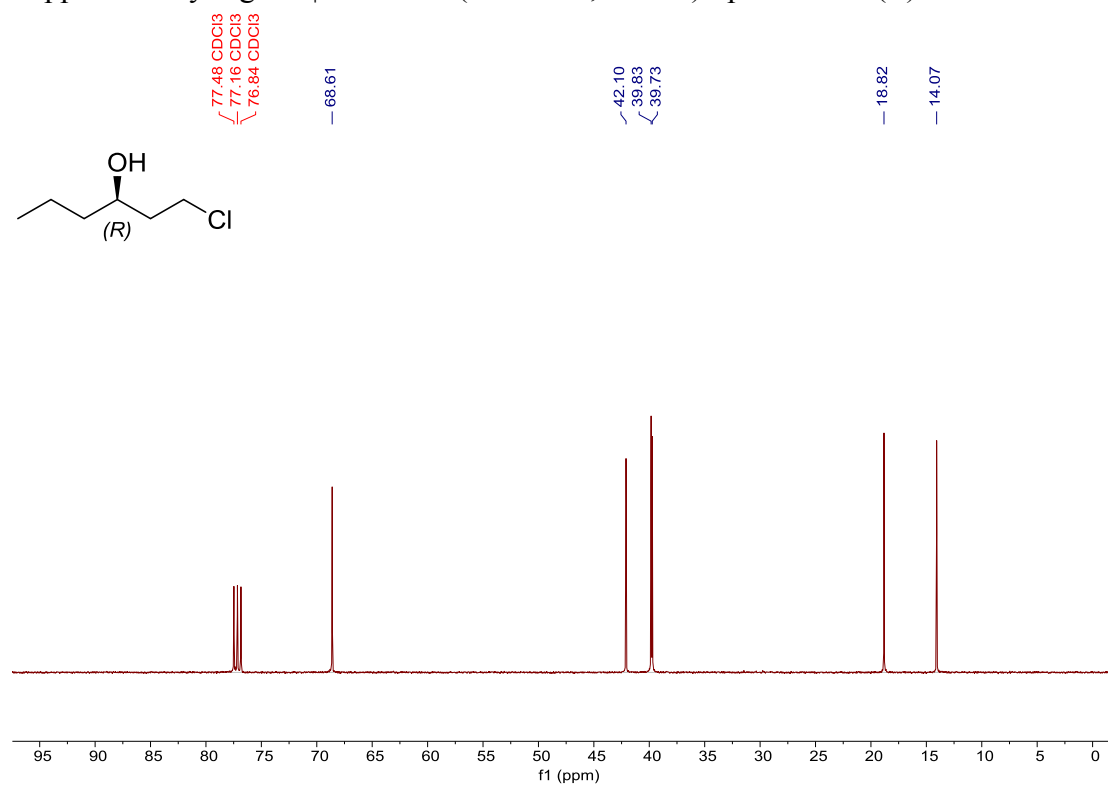
Supplementary Fig. 53 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**21a**.



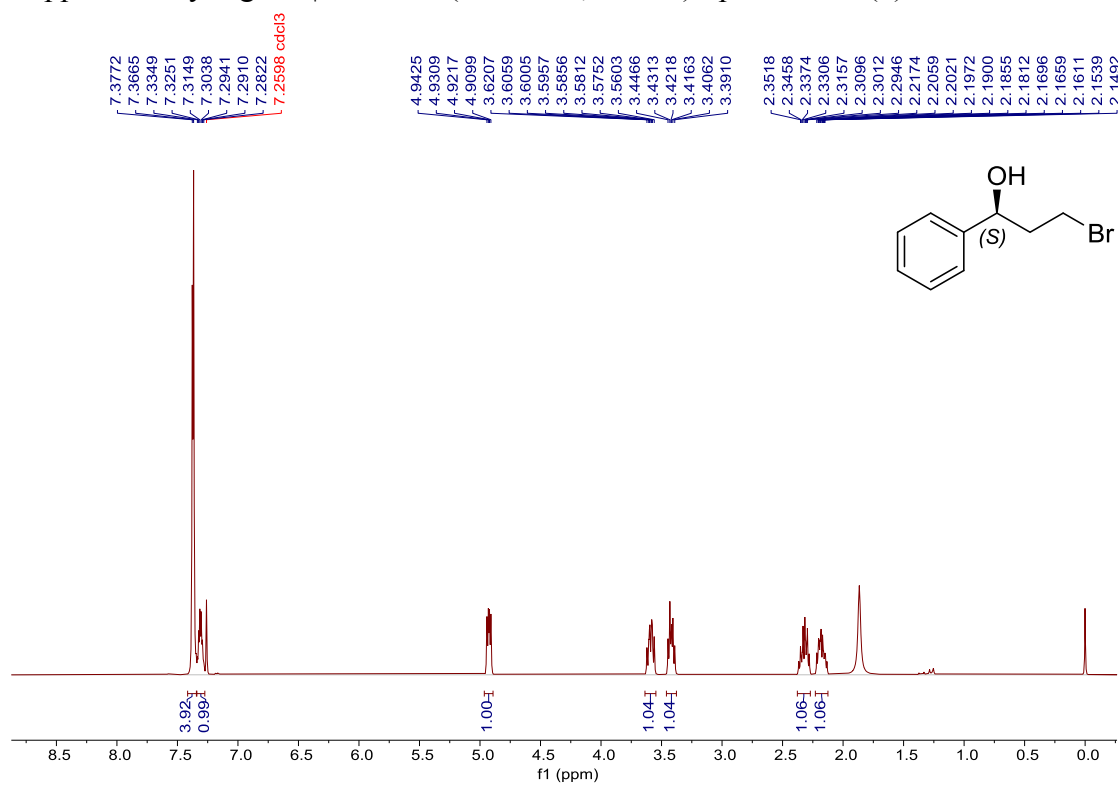
Supplementary Fig. 54 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**22a**.



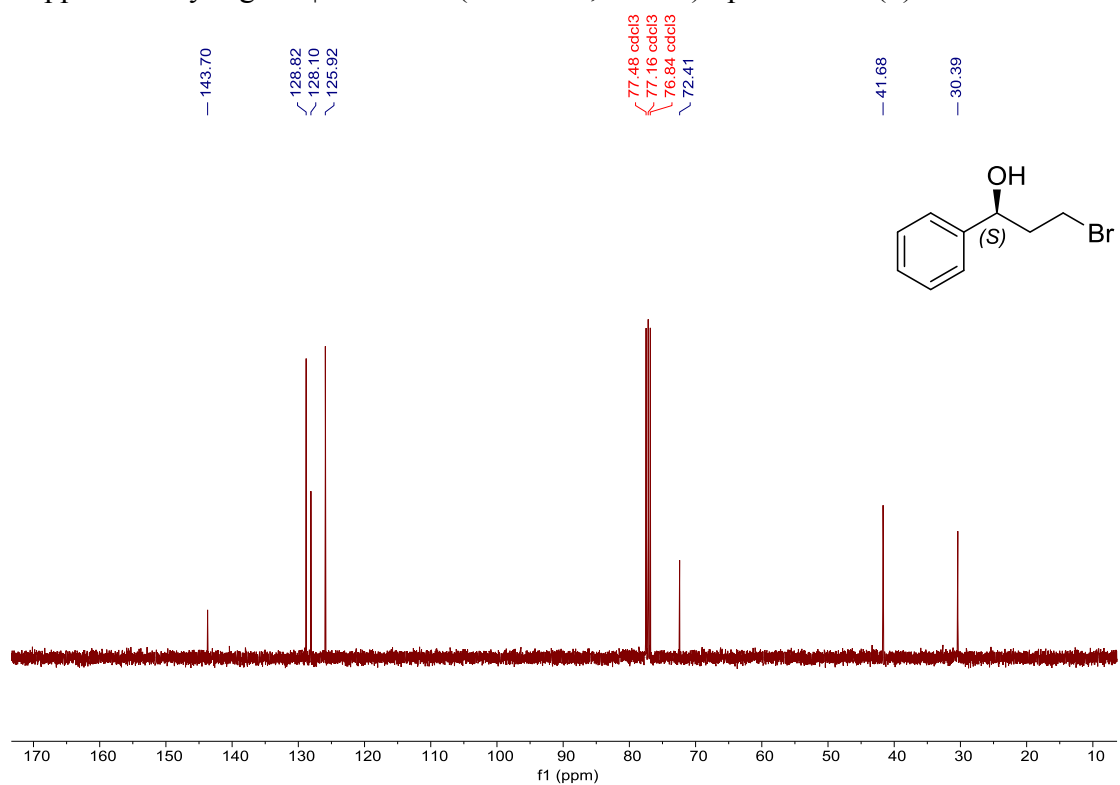
Supplementary Fig. 55 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**22a**.



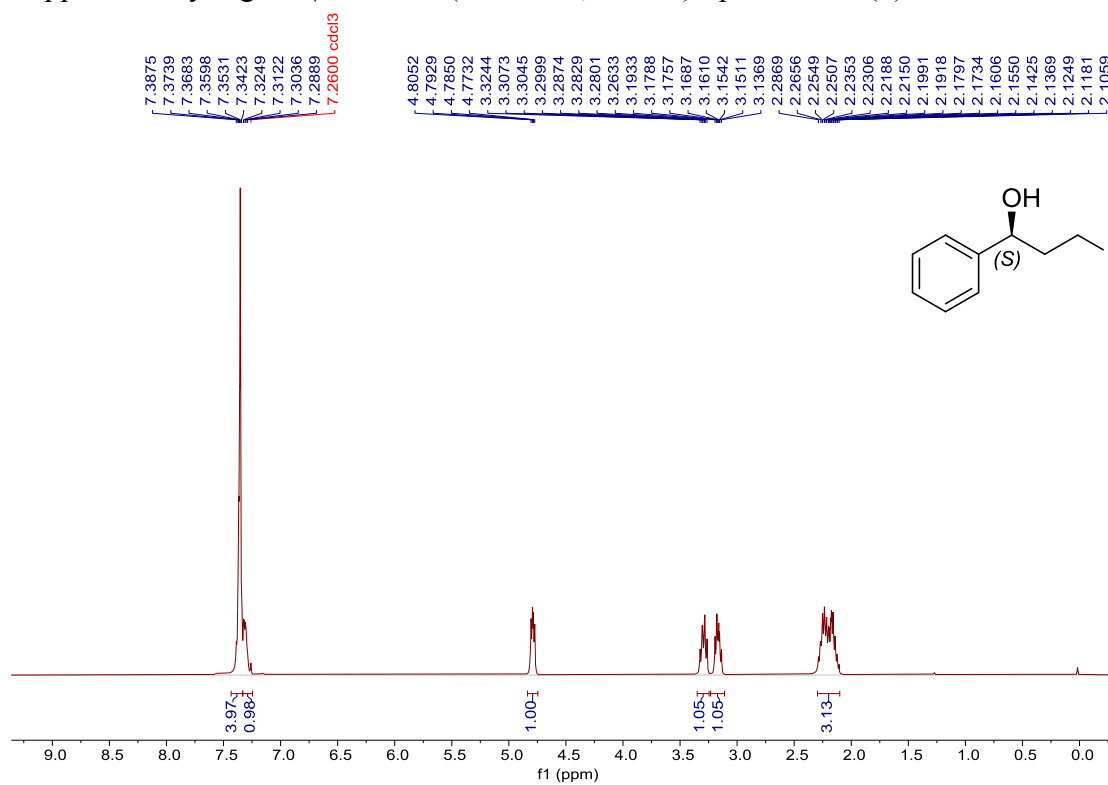
Supplementary Fig. 56 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**23a**.



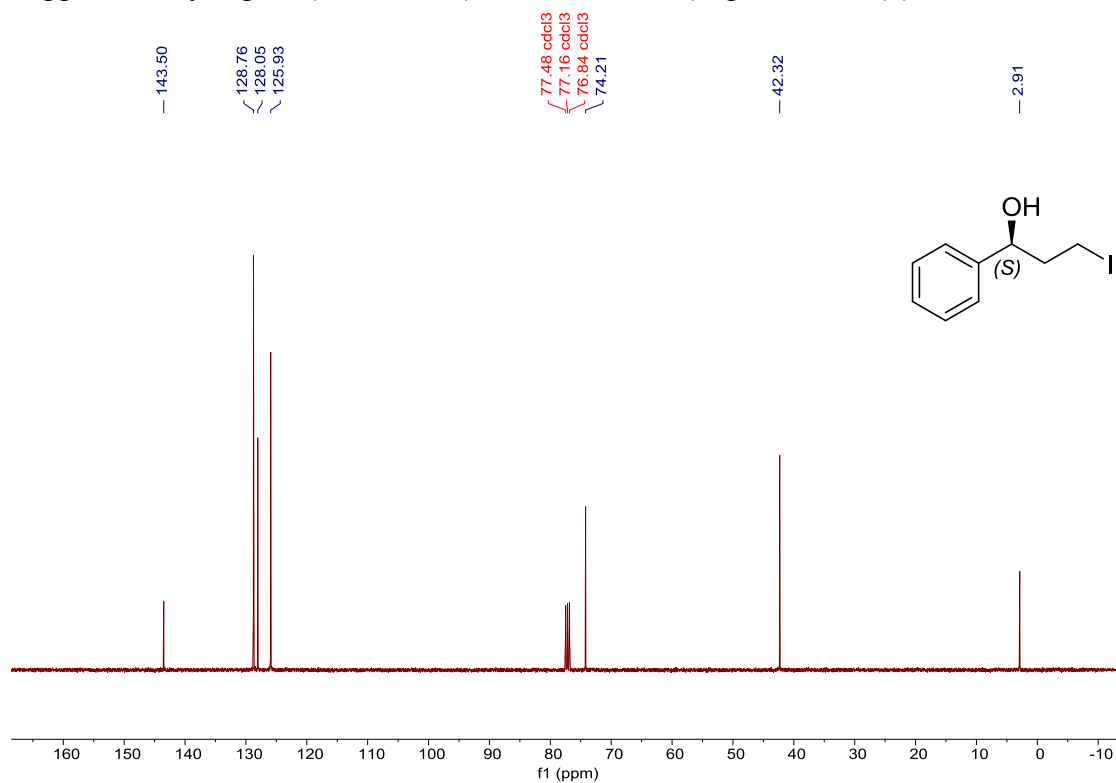
Supplementary Fig. 57 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**23a**.



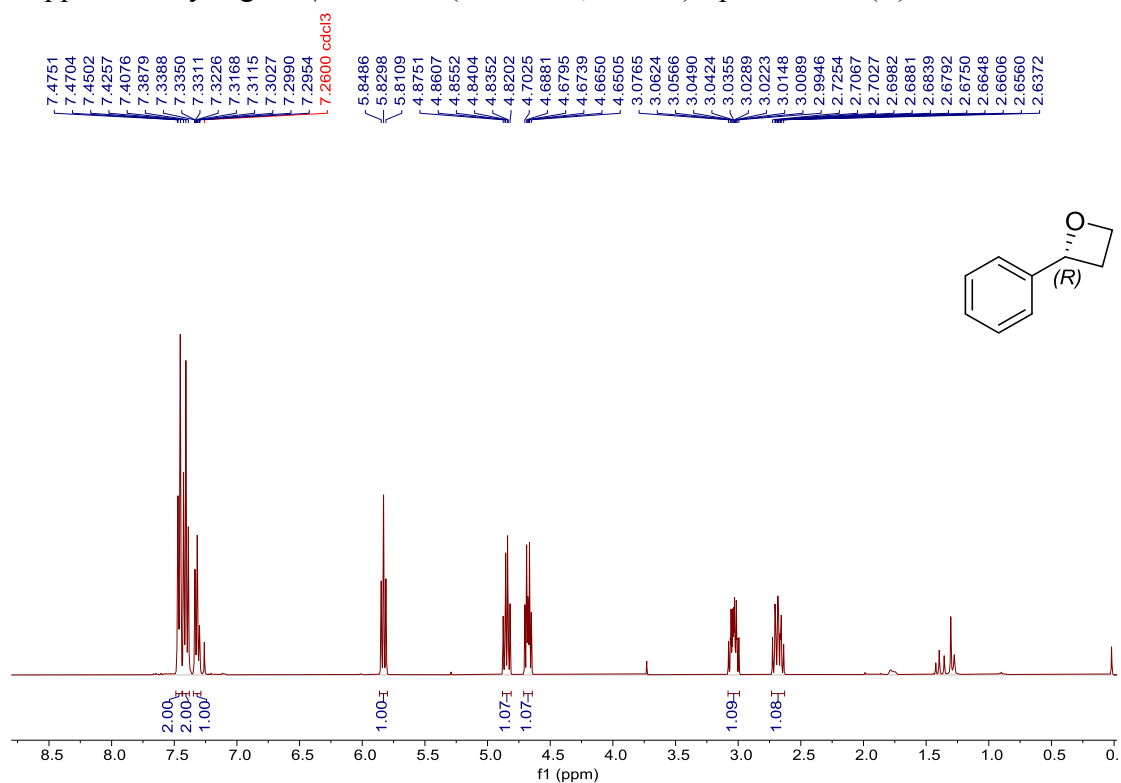
Supplementary Fig. 58 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**24a**.



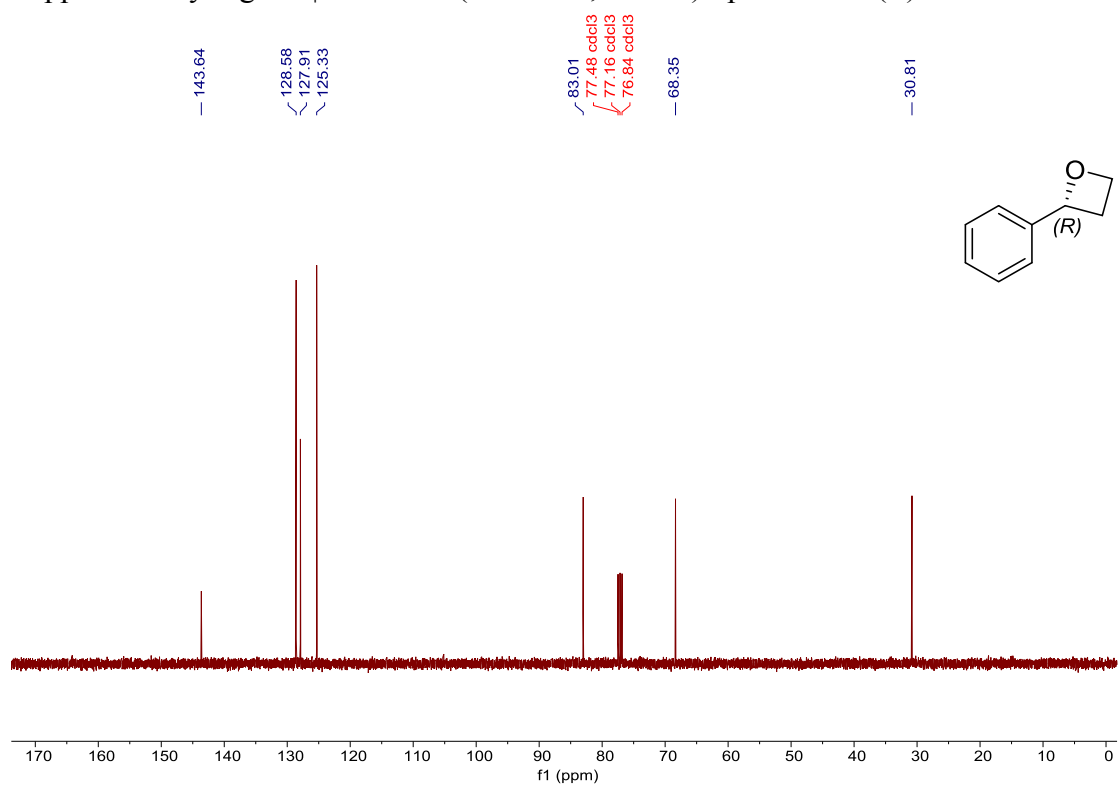
Supplementary Fig. 59 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**24a**.



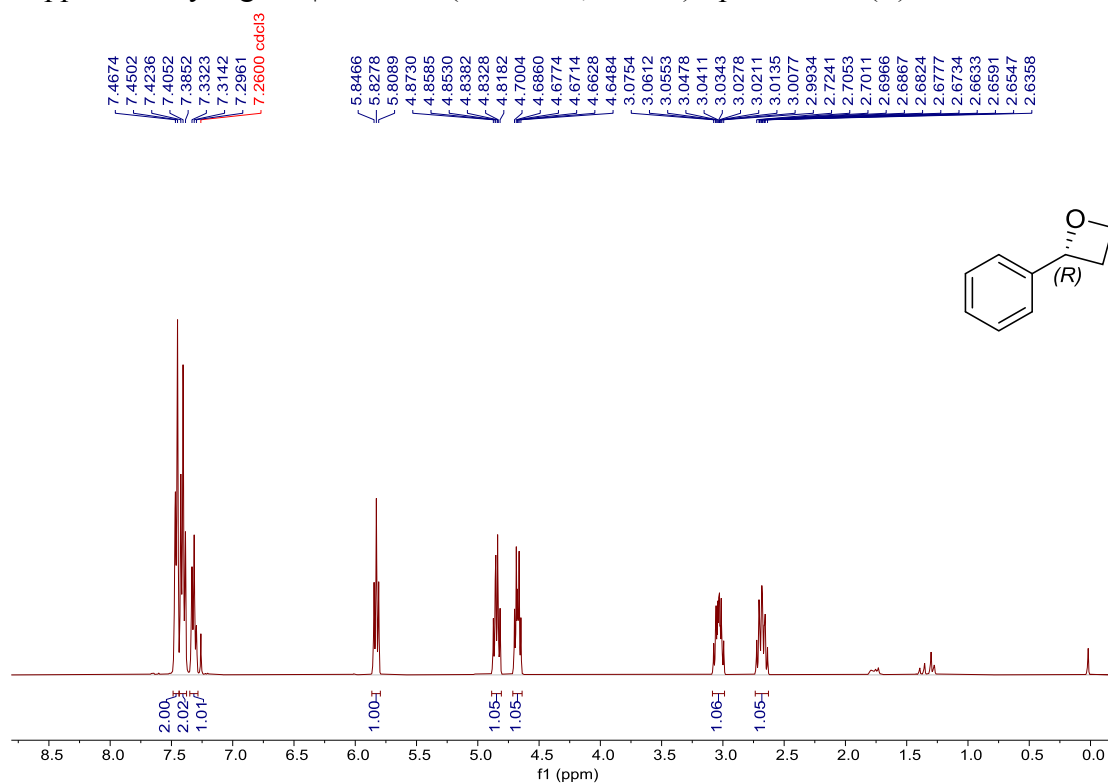
Supplementary Fig. 60 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1b** from **1a**.



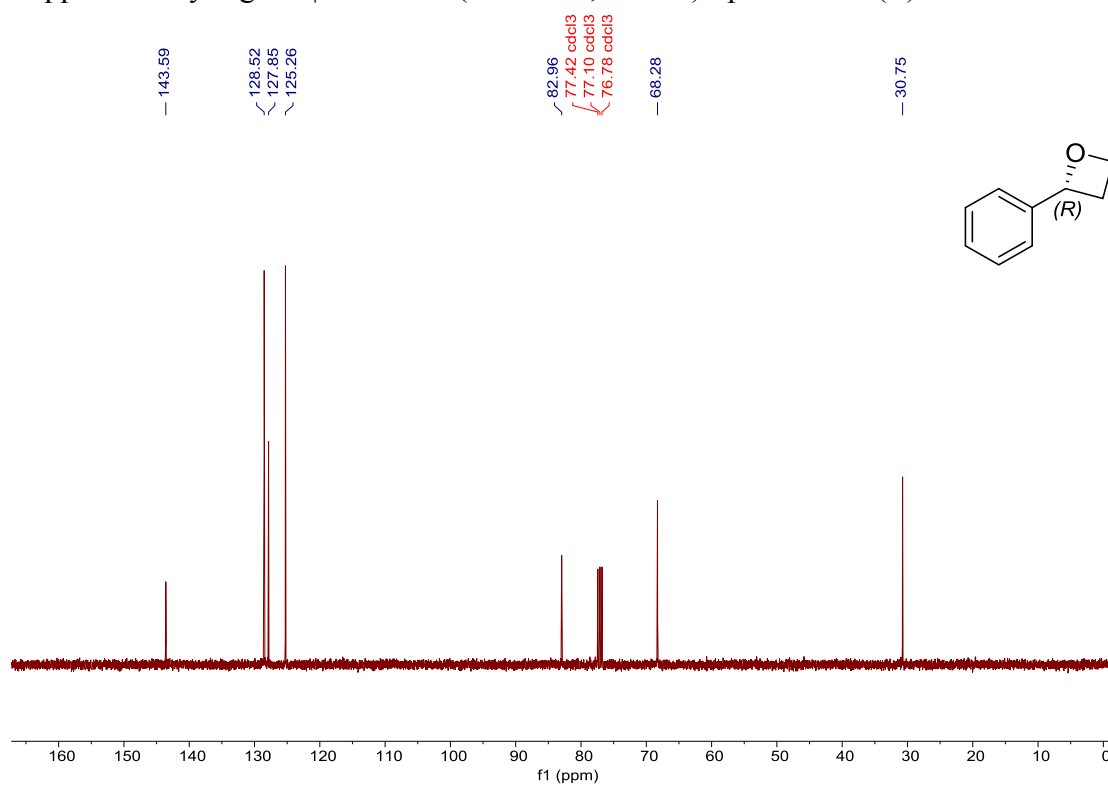
Supplementary Fig. 61 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1b** from **1a**.



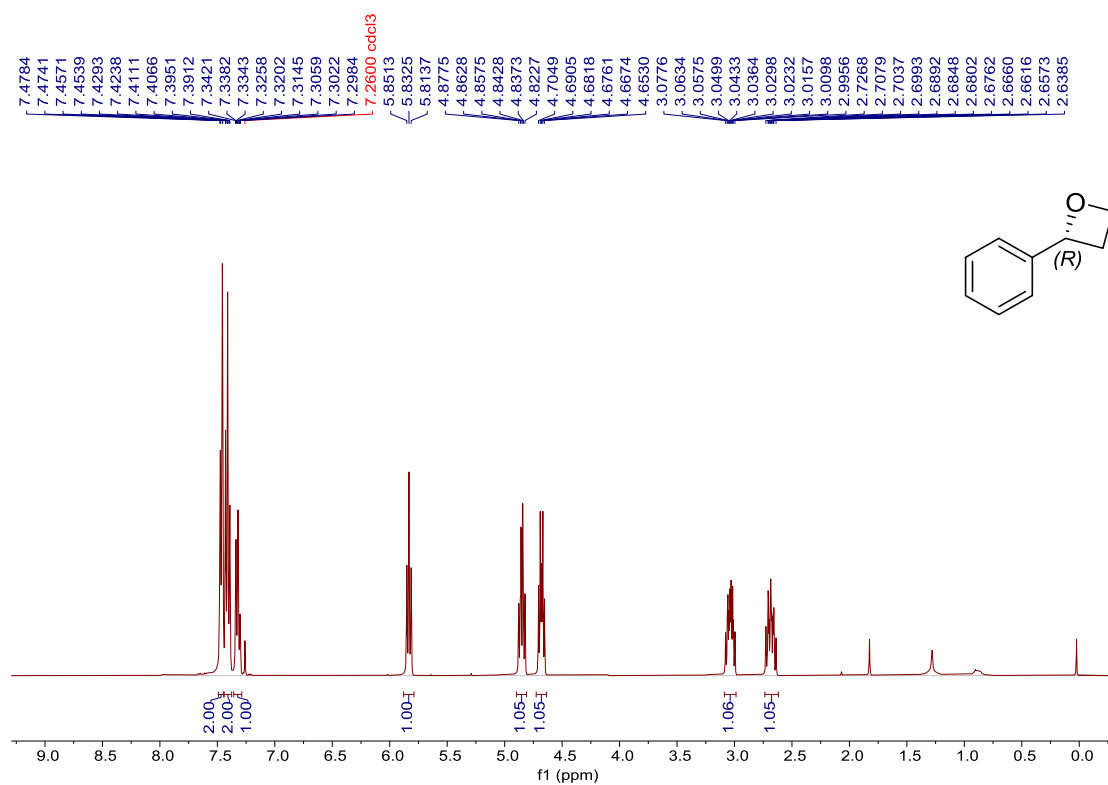
Supplementary Fig. 62 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1b** from **23a**.



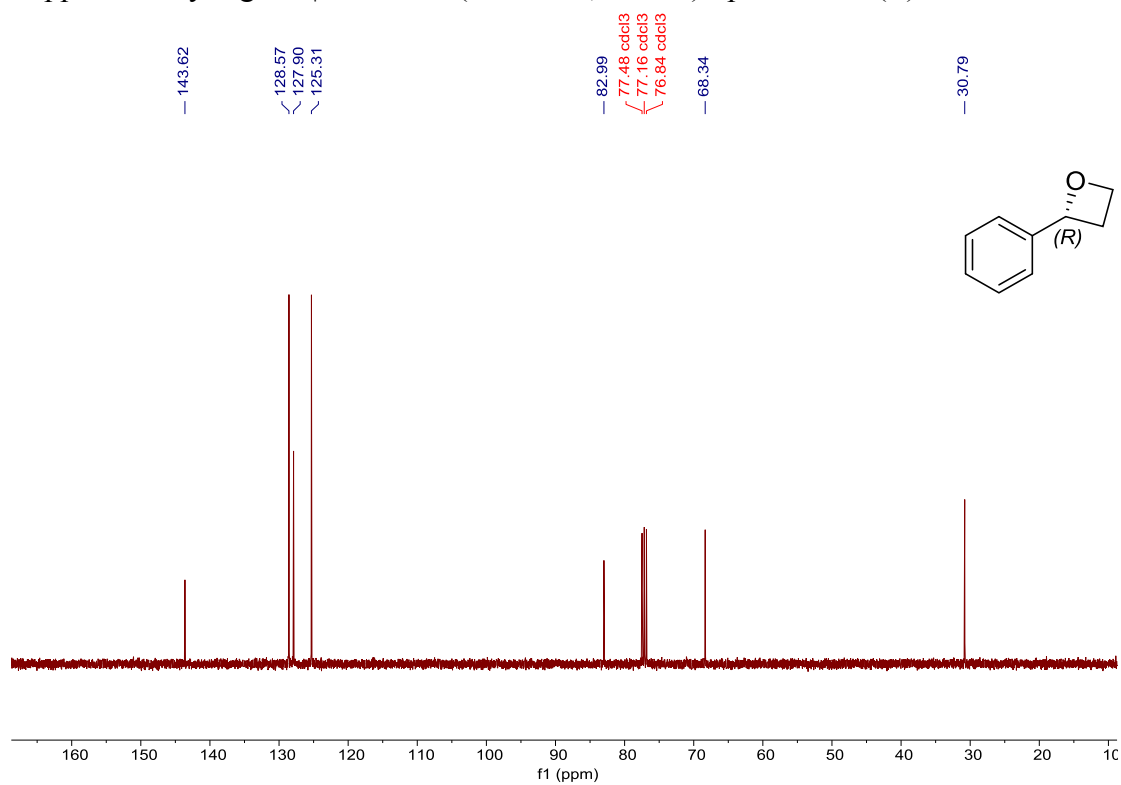
Supplementary Fig. 63 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1b** from **23a**.



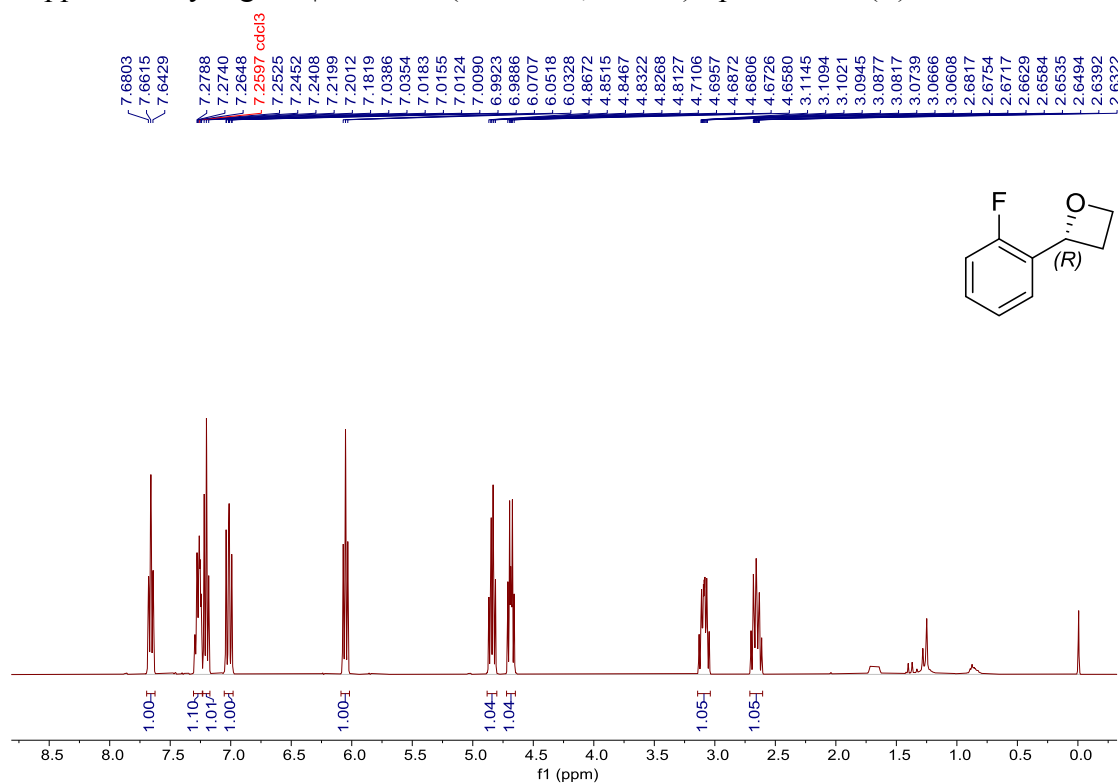
Supplementary Fig. 64 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1b** from **24a**.



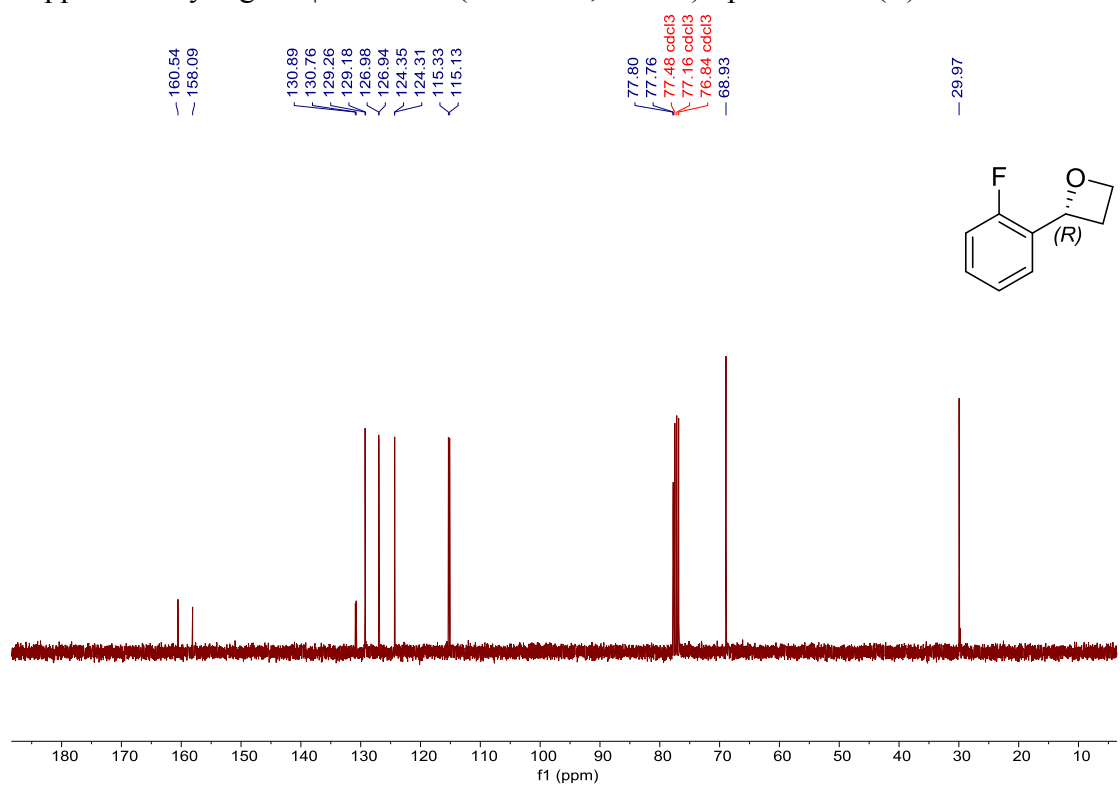
Supplementary Fig. 65 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1b** from **24a**.



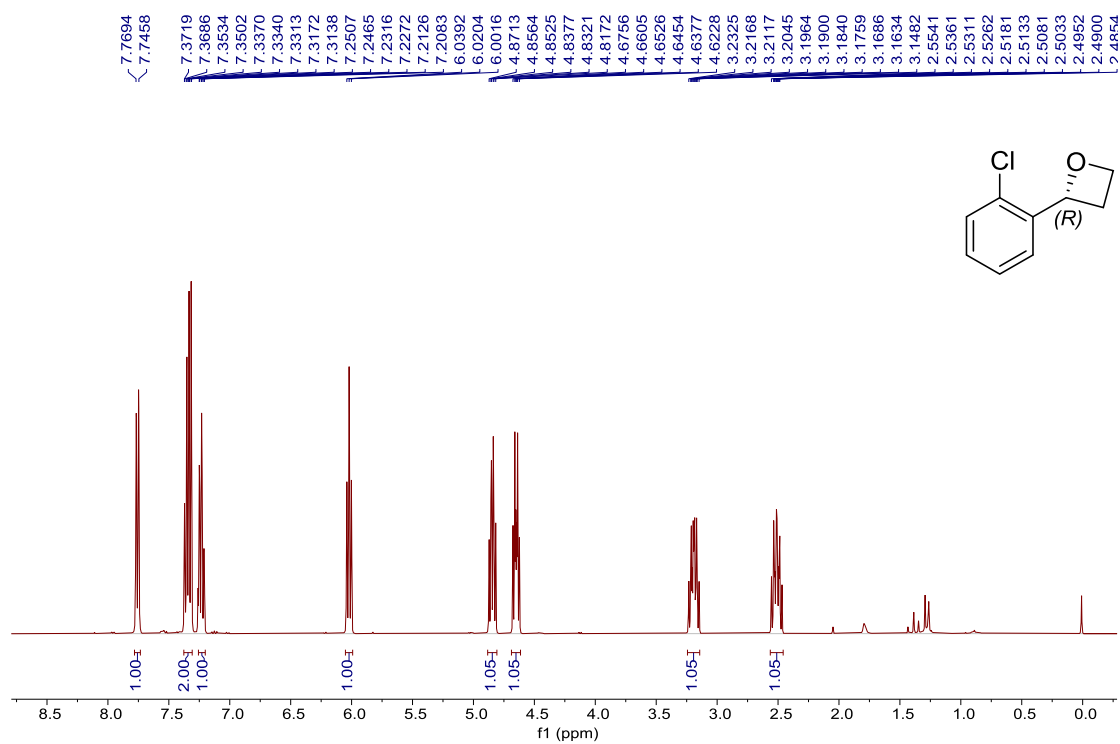
Supplementary Fig. 66 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**2b**.



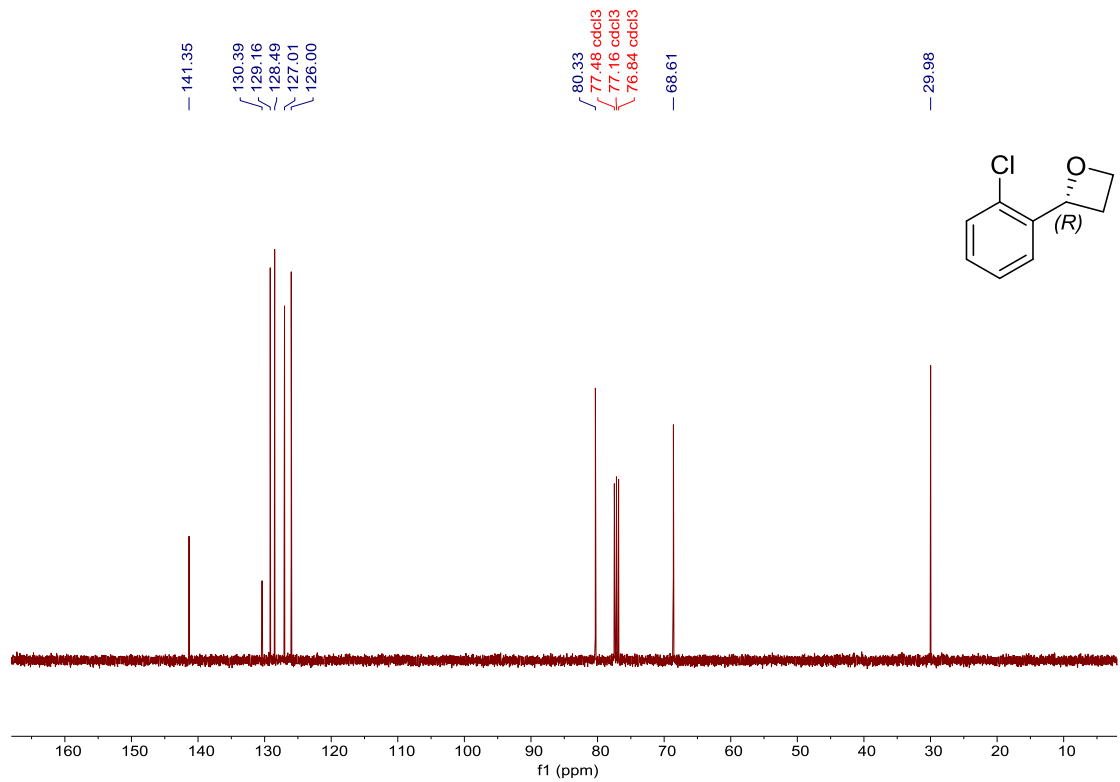
Supplementary Fig. 67 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**2b**.



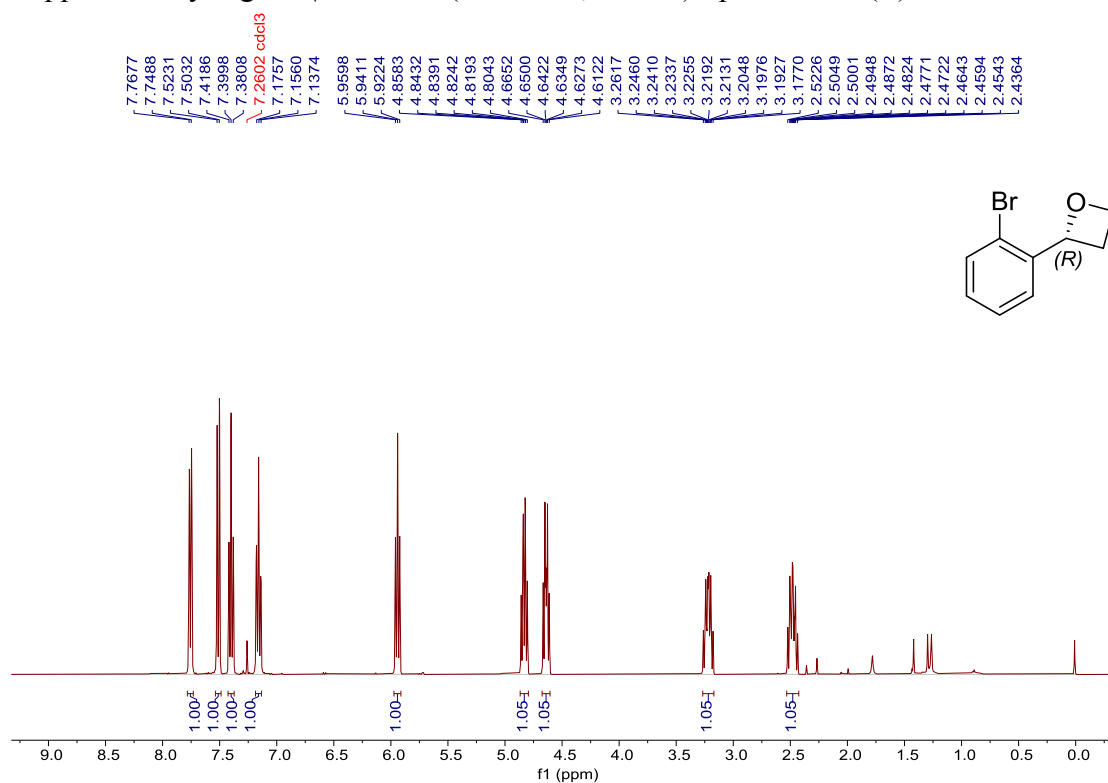
Supplementary Fig. 68 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**3b**.



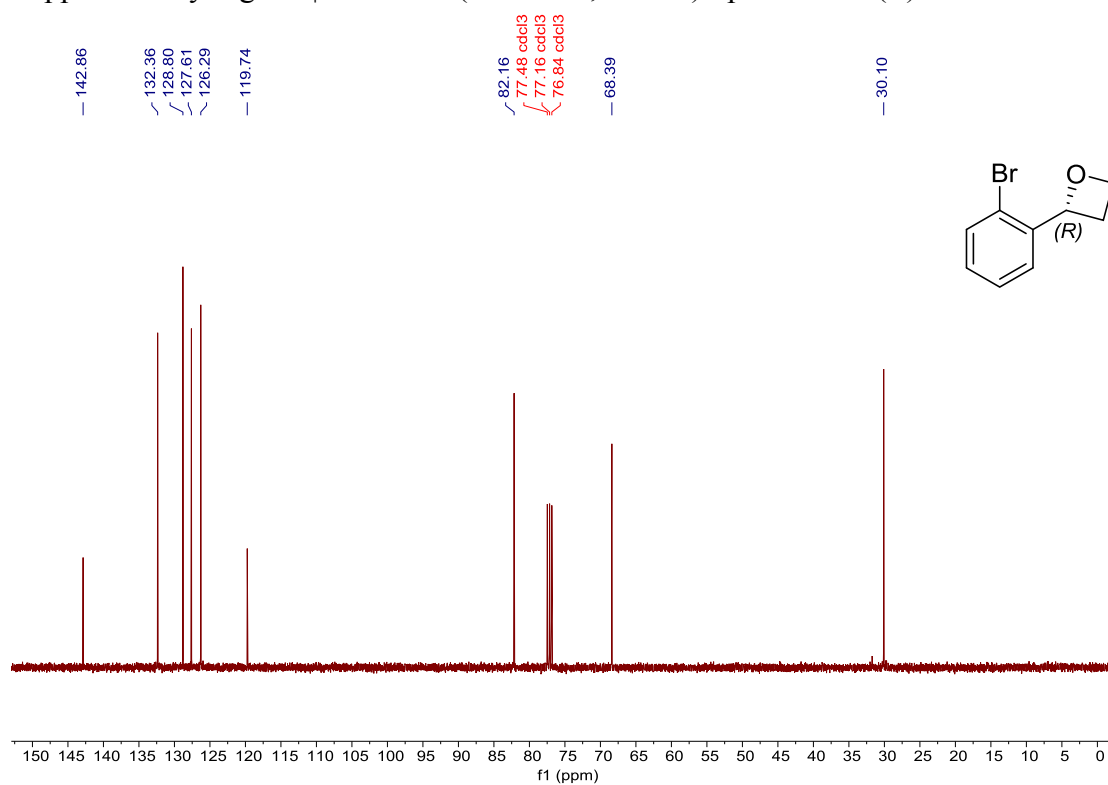
Supplementary Fig. 69 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**3b**.



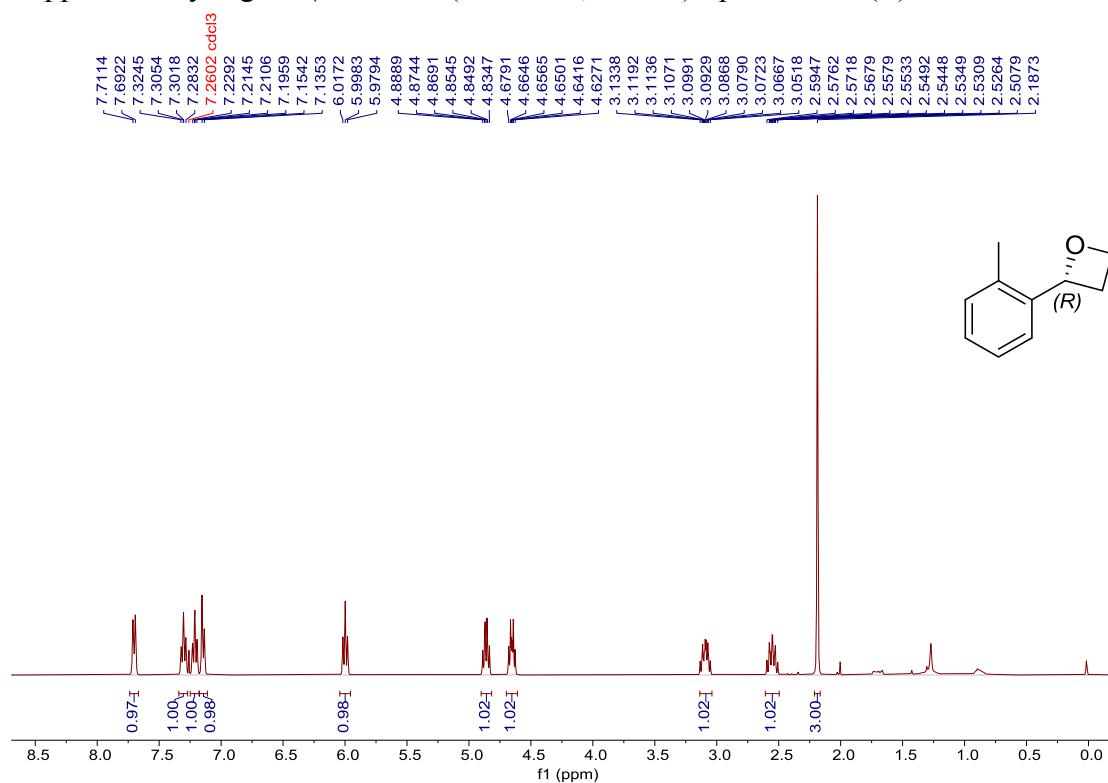
Supplementary Fig. 70 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**4b**.



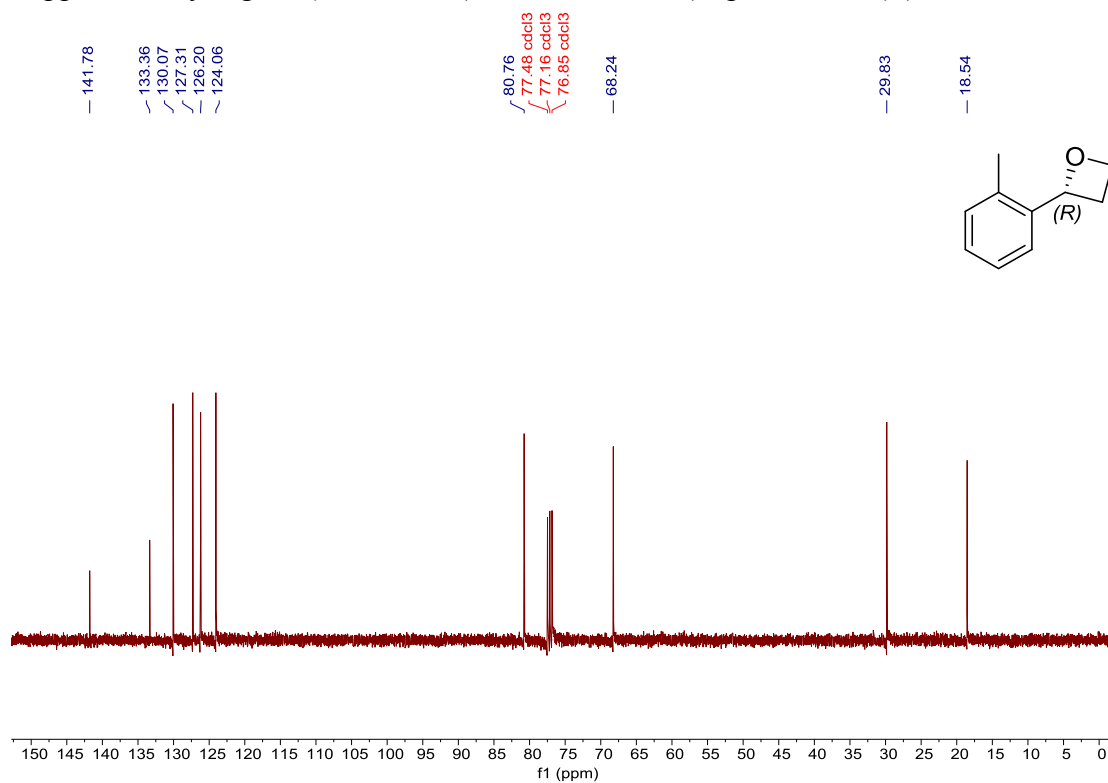
Supplementary Fig. 71 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**4b**.



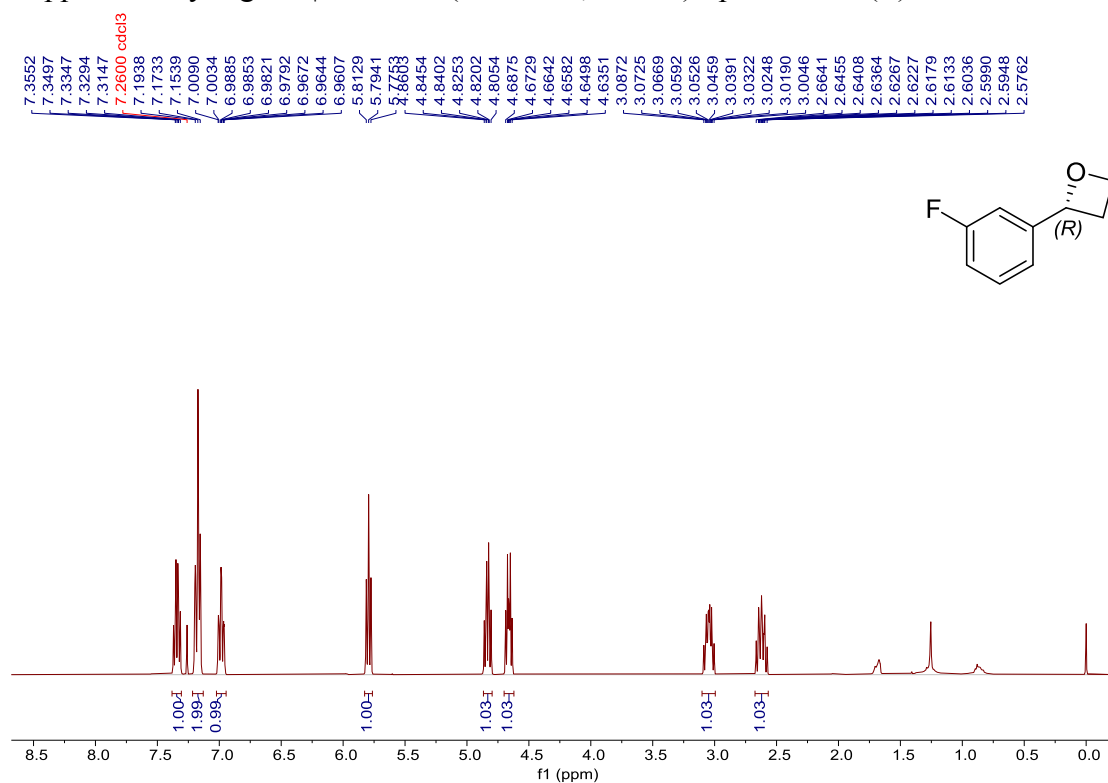
Supplementary Fig. 72 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**5b**.



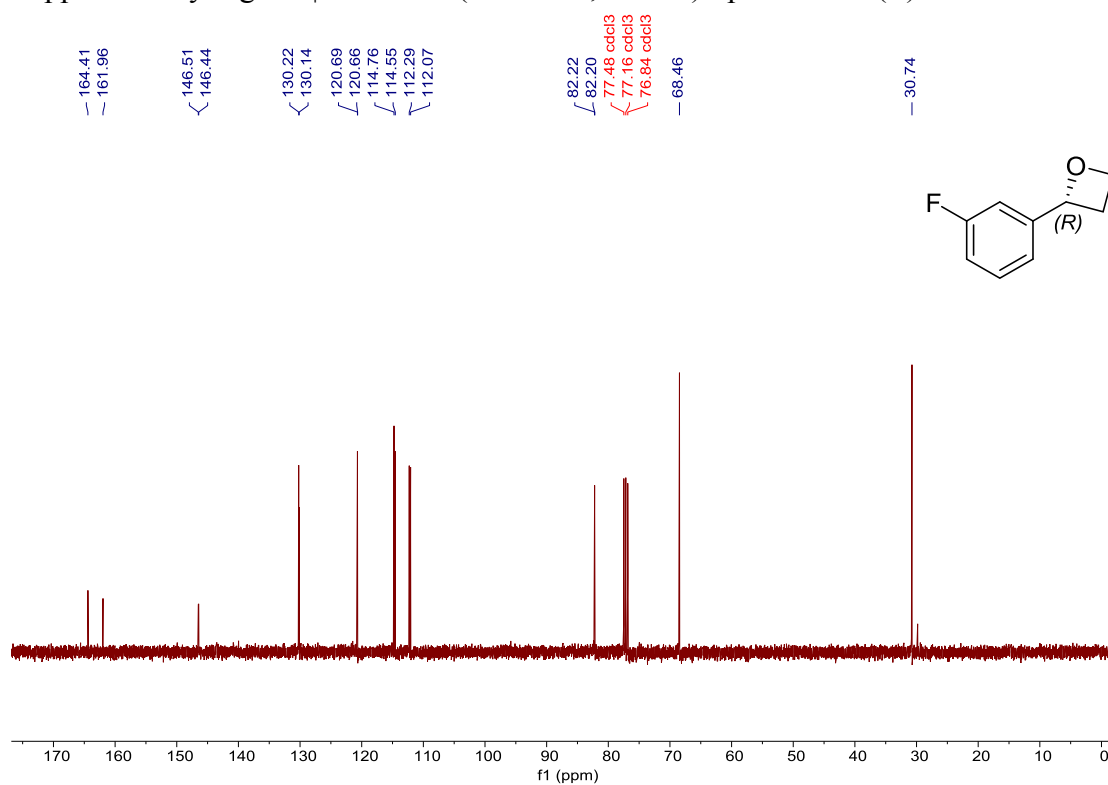
Supplementary Fig. 73 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**5b**.



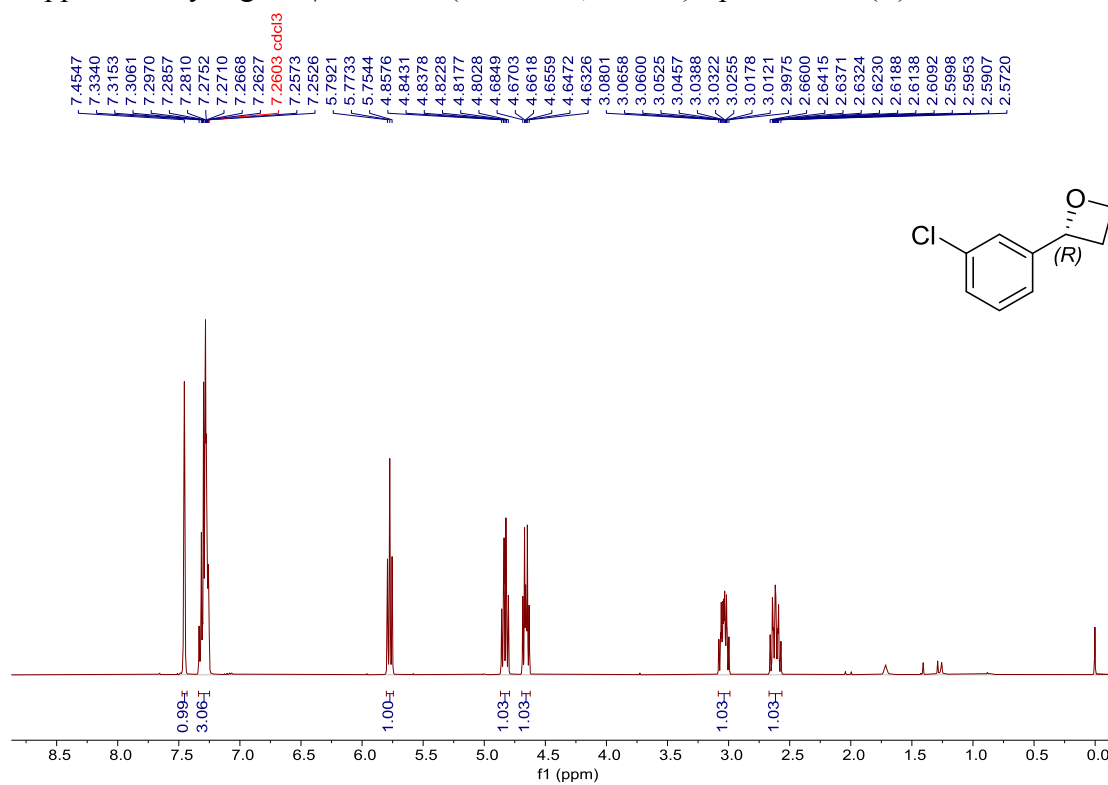
Supplementary Fig. 74 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**6b**.



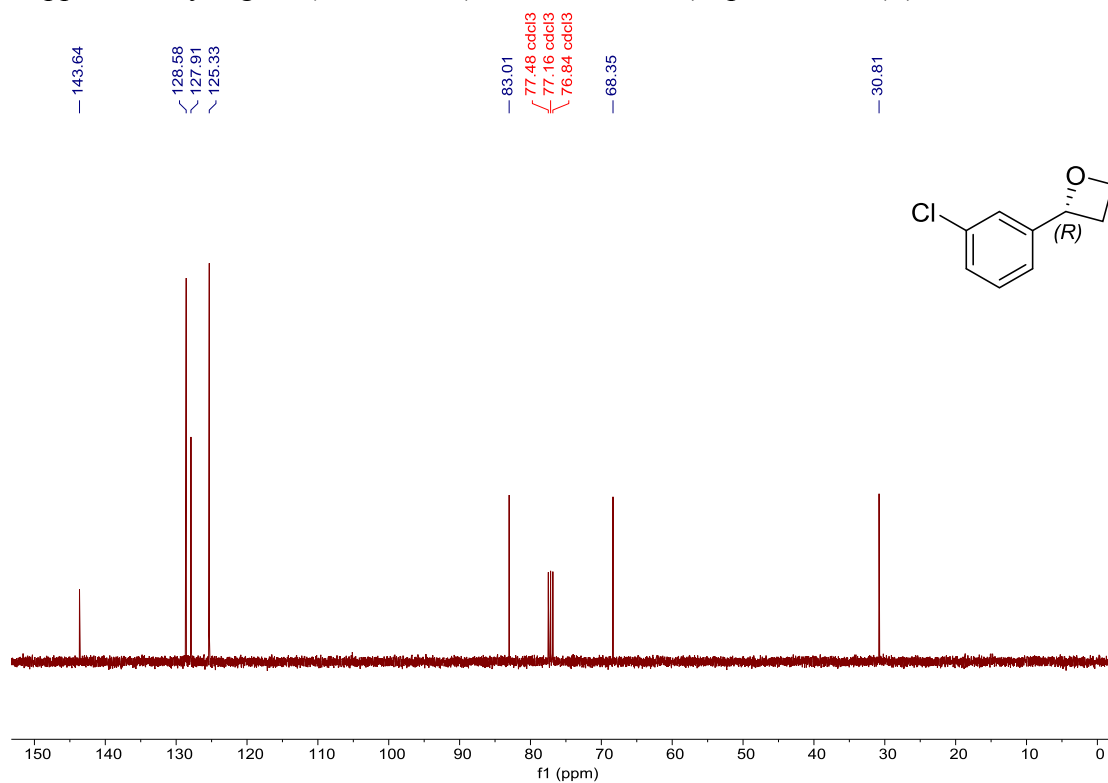
Supplementary Fig. 75 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**6b**.



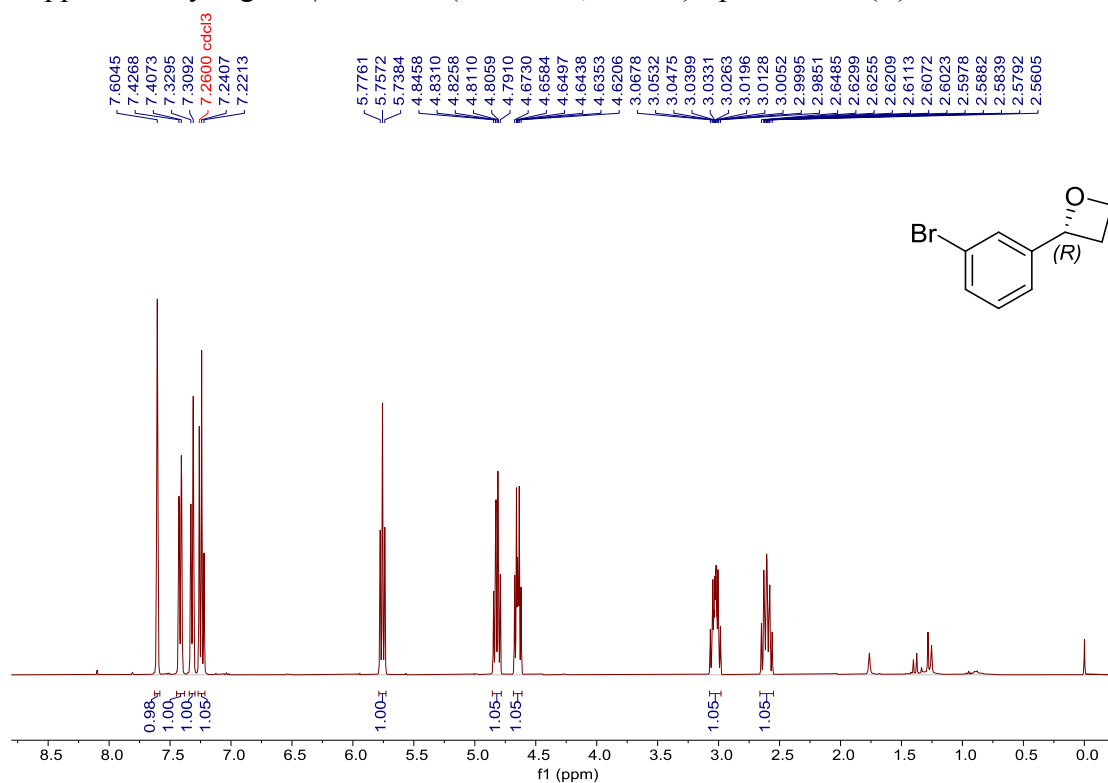
Supplementary Fig. 76 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**7b**.



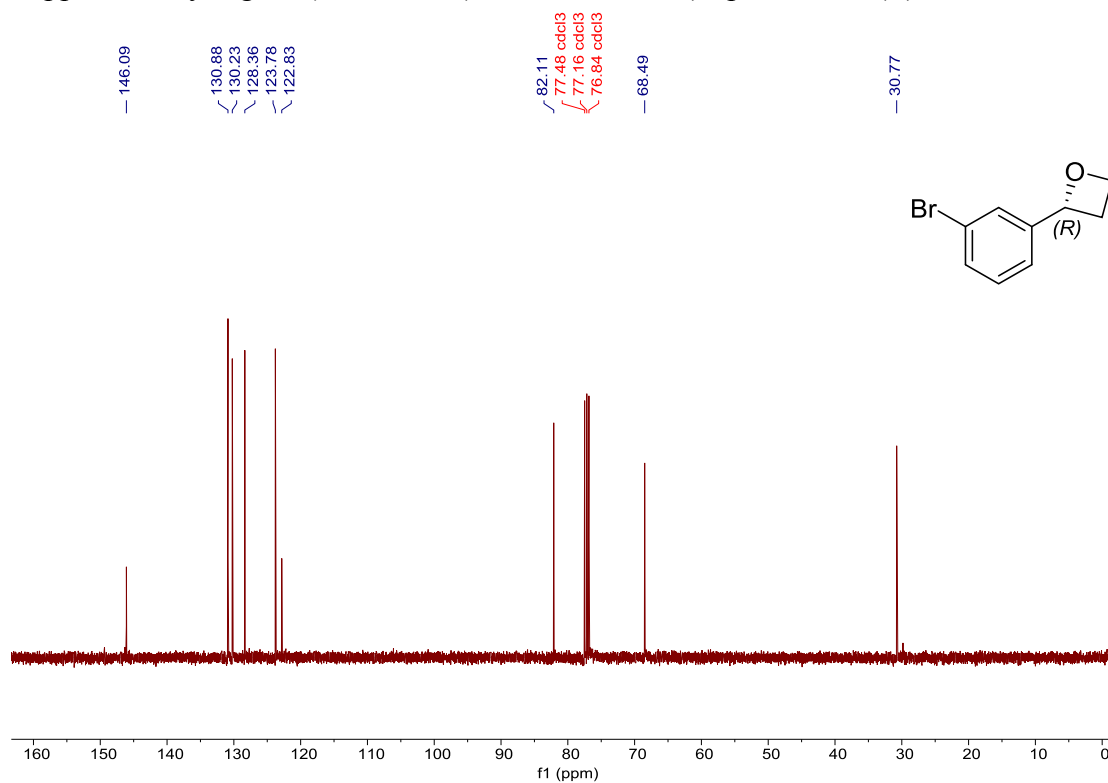
Supplementary Fig. 77 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**7b**.



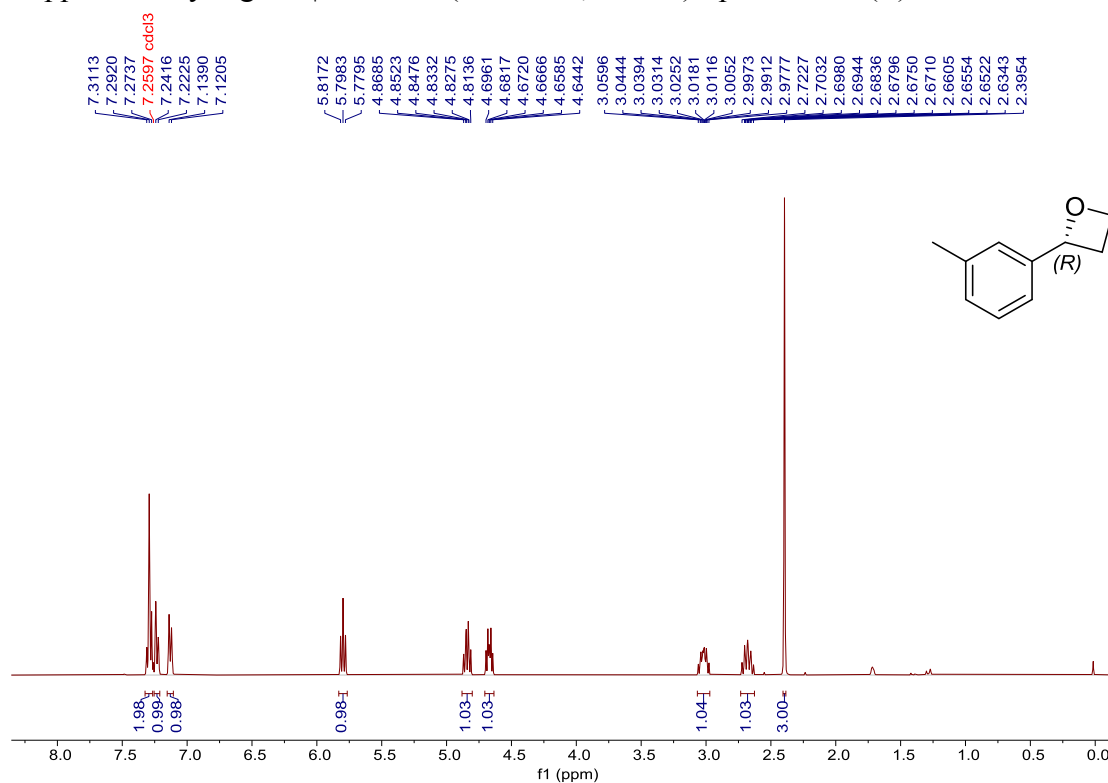
Supplementary Fig. 78 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**8b**.



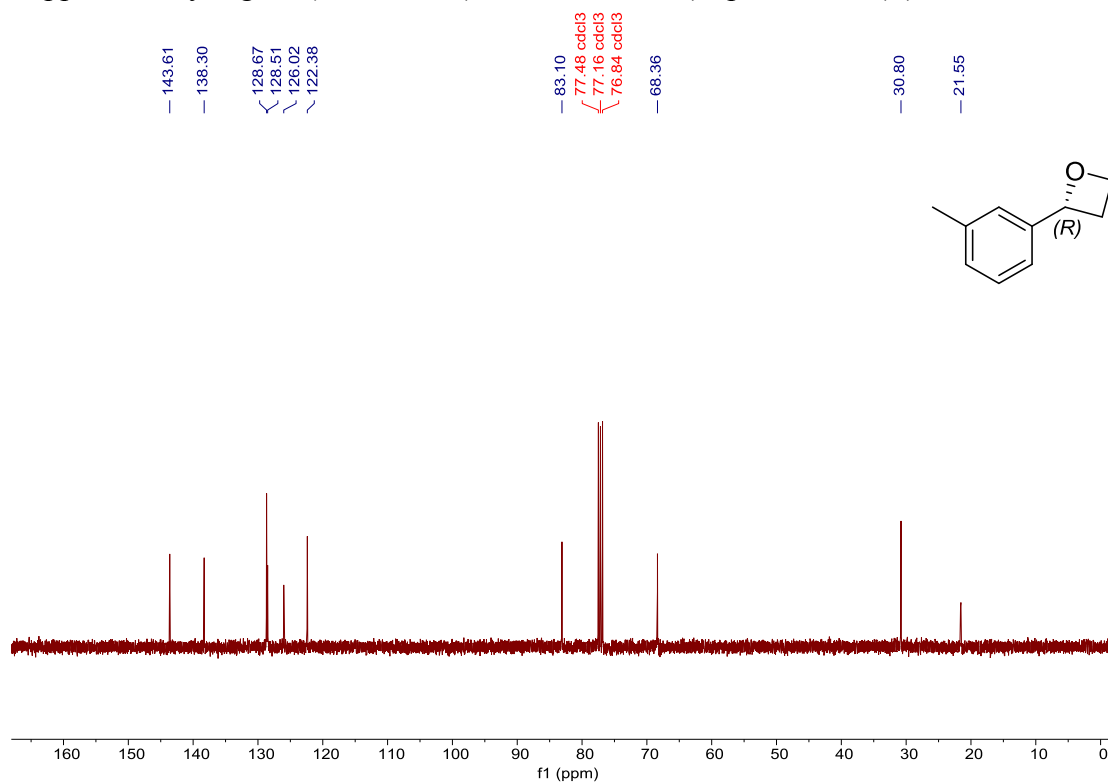
Supplementary Fig. 79 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**8b**.



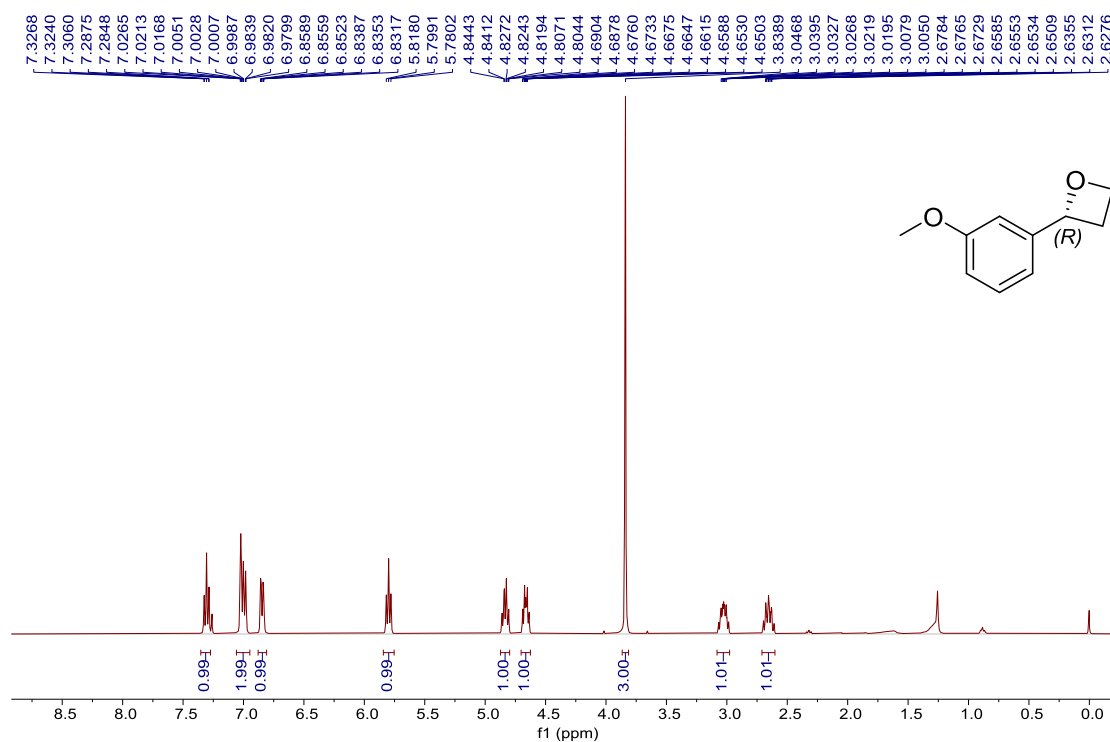
Supplementary Fig. 80 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**9b**.



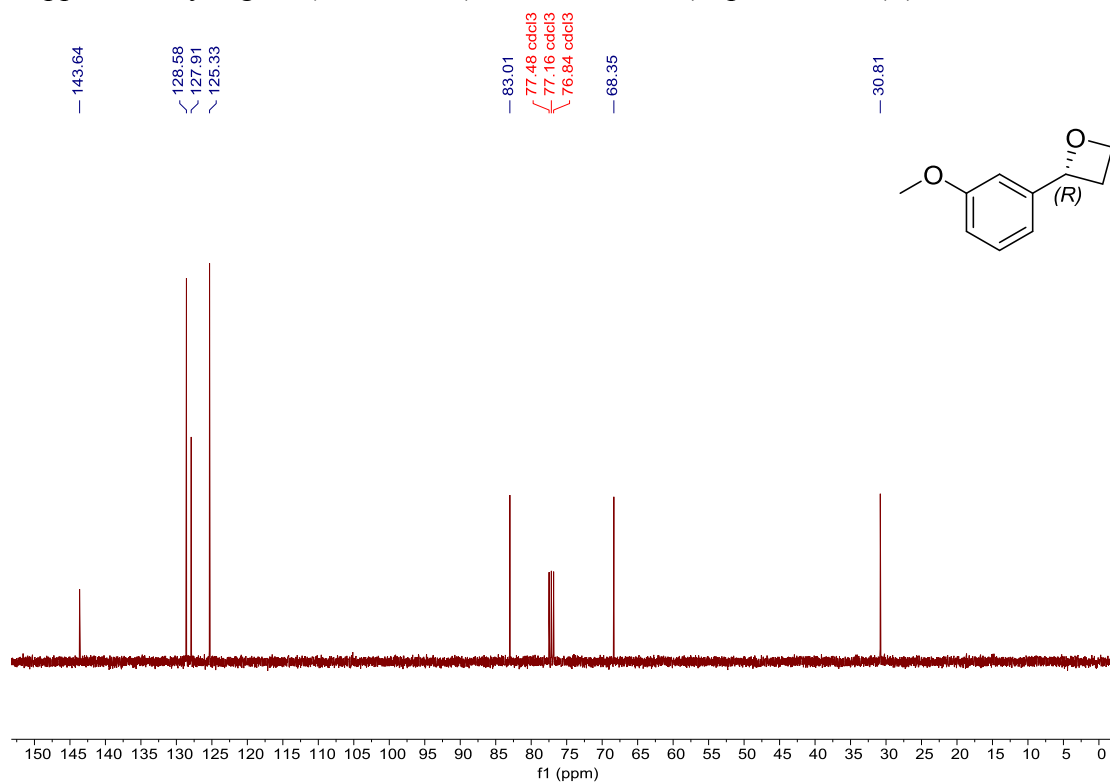
Supplementary Fig. 81 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**9b**.



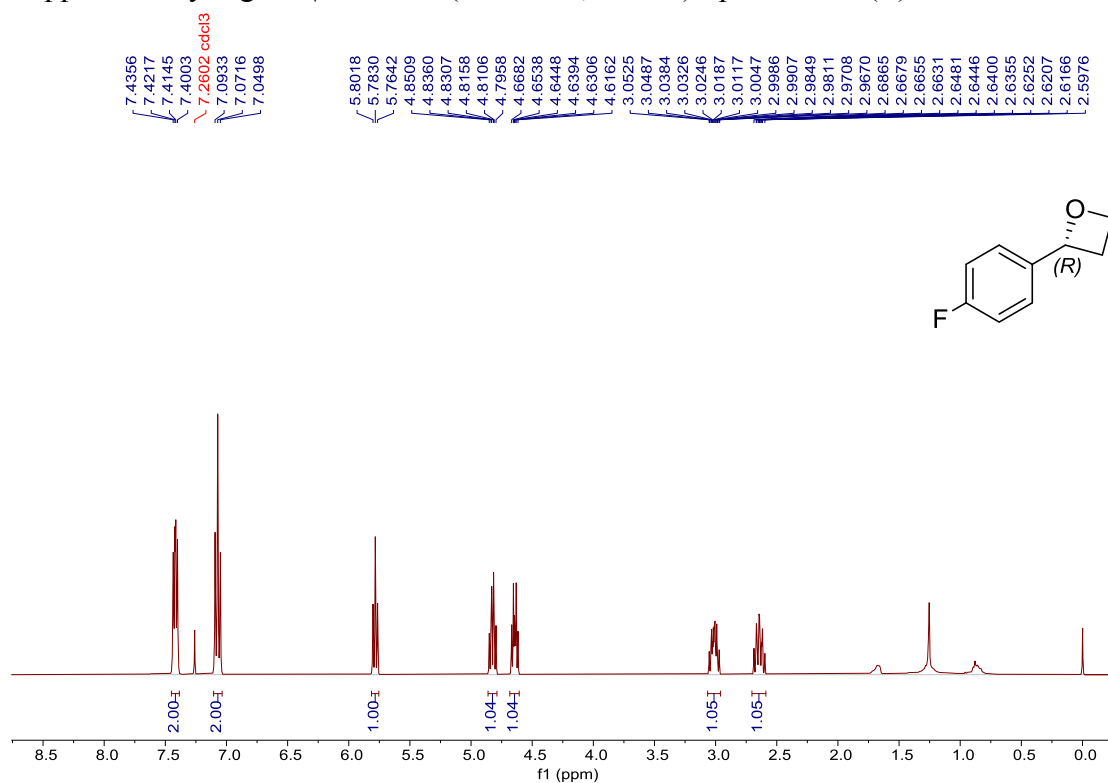
Supplementary Fig. 82 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**10b**.



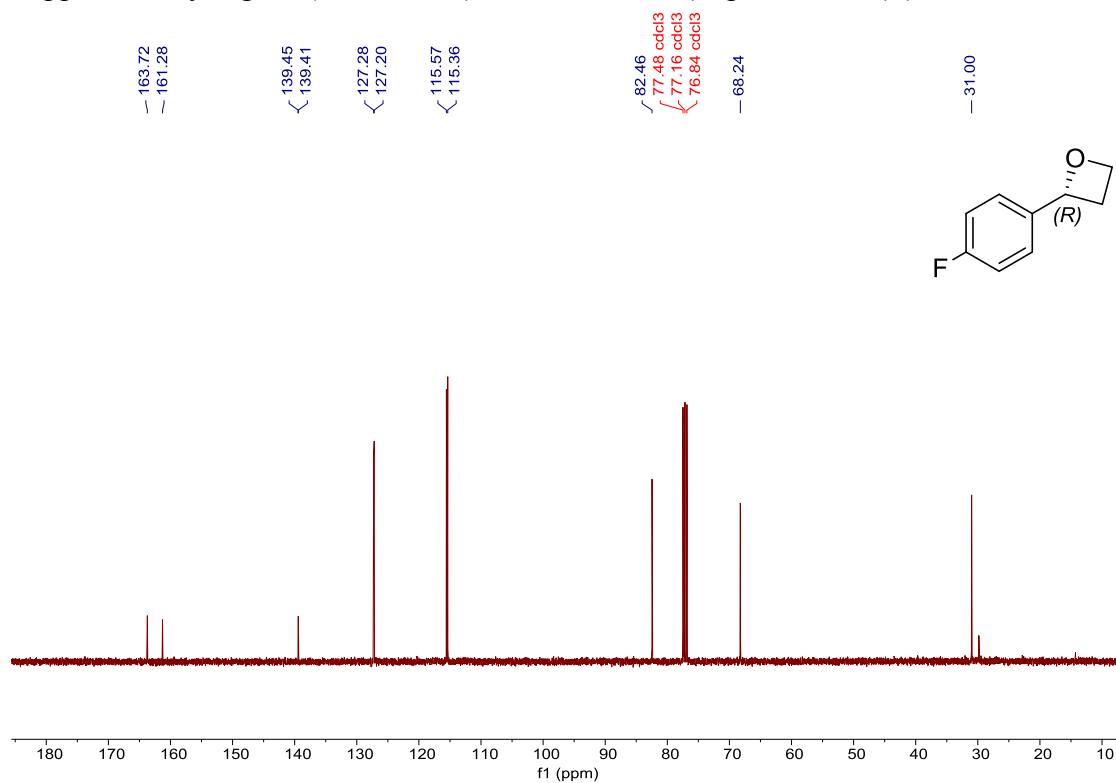
Supplementary Fig. 83 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**10b**.



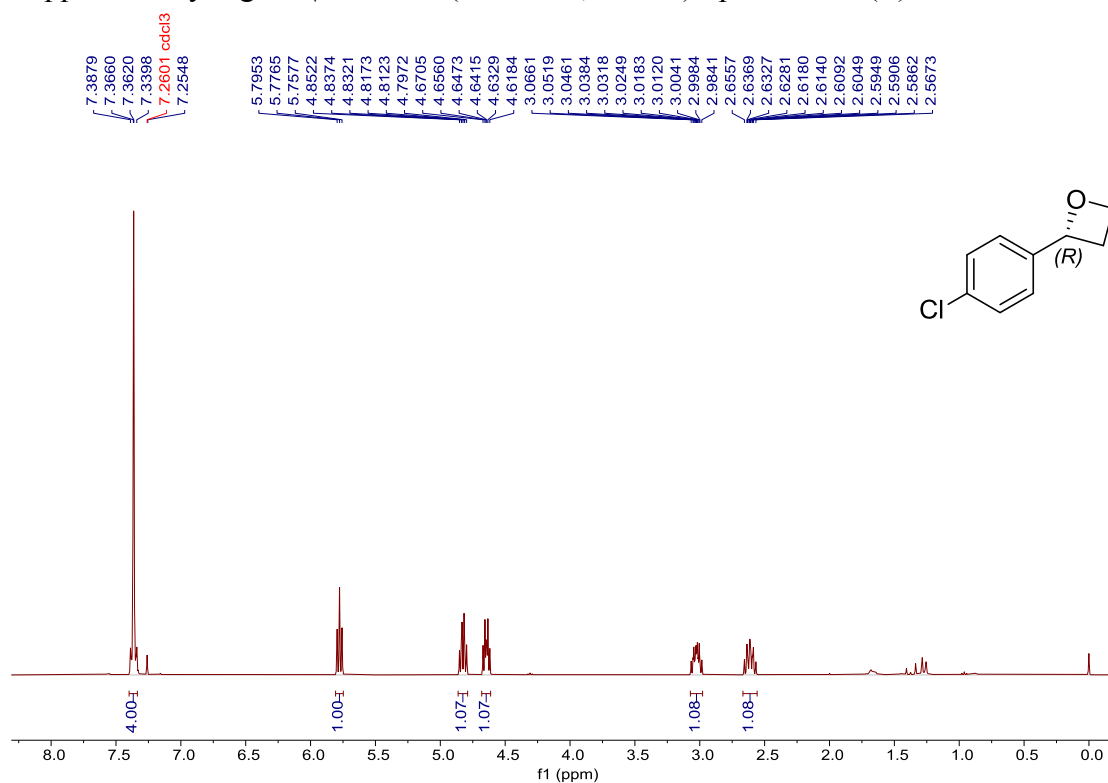
Supplementary Fig. 84 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**11b**.



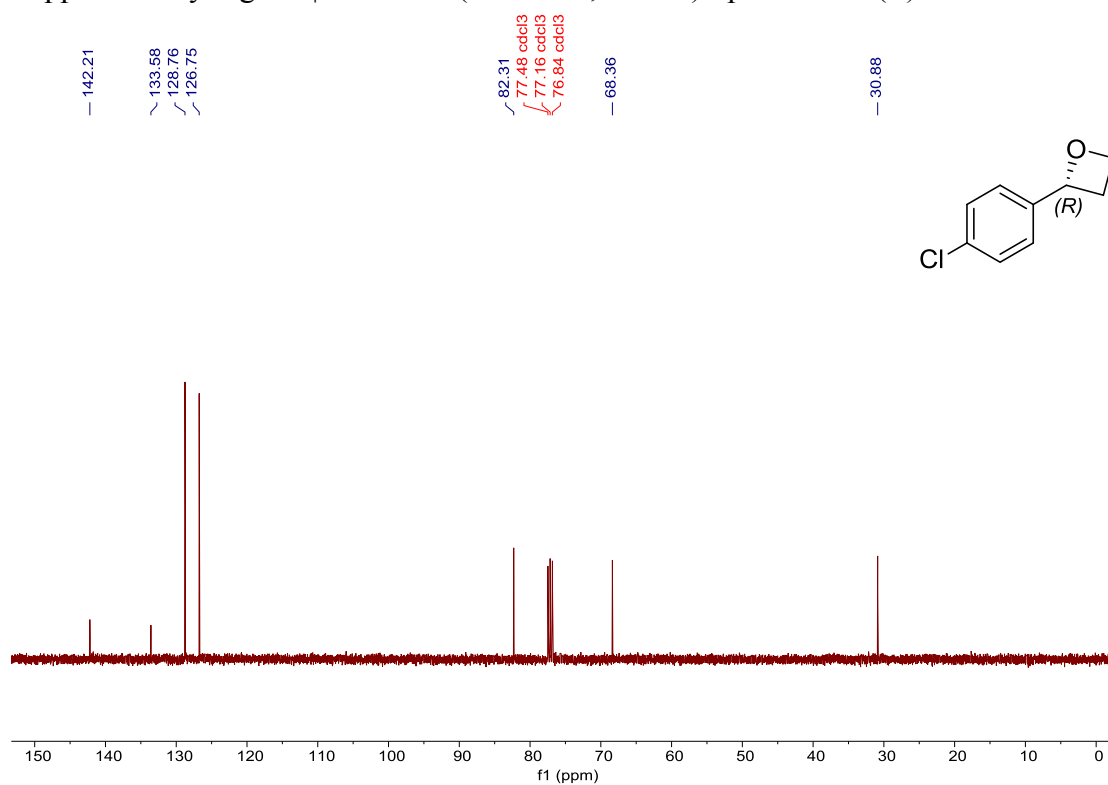
Supplementary Fig. 85 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**11b**.



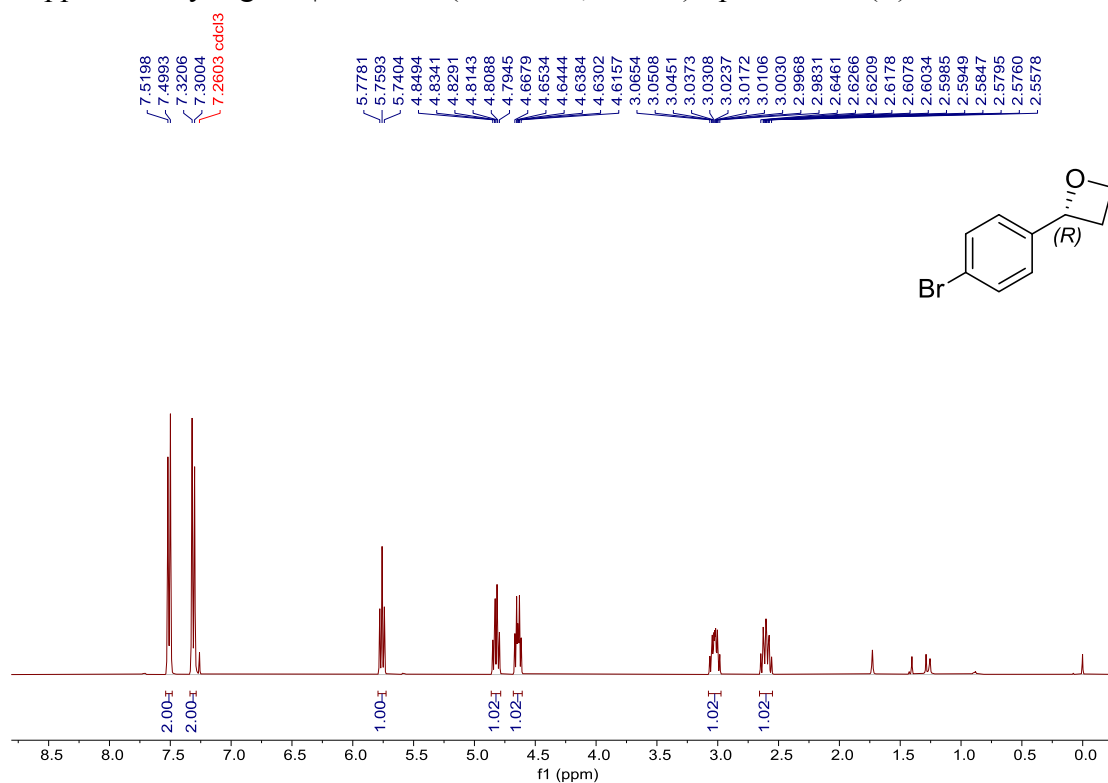
Supplementary Fig. 86 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**12b**.



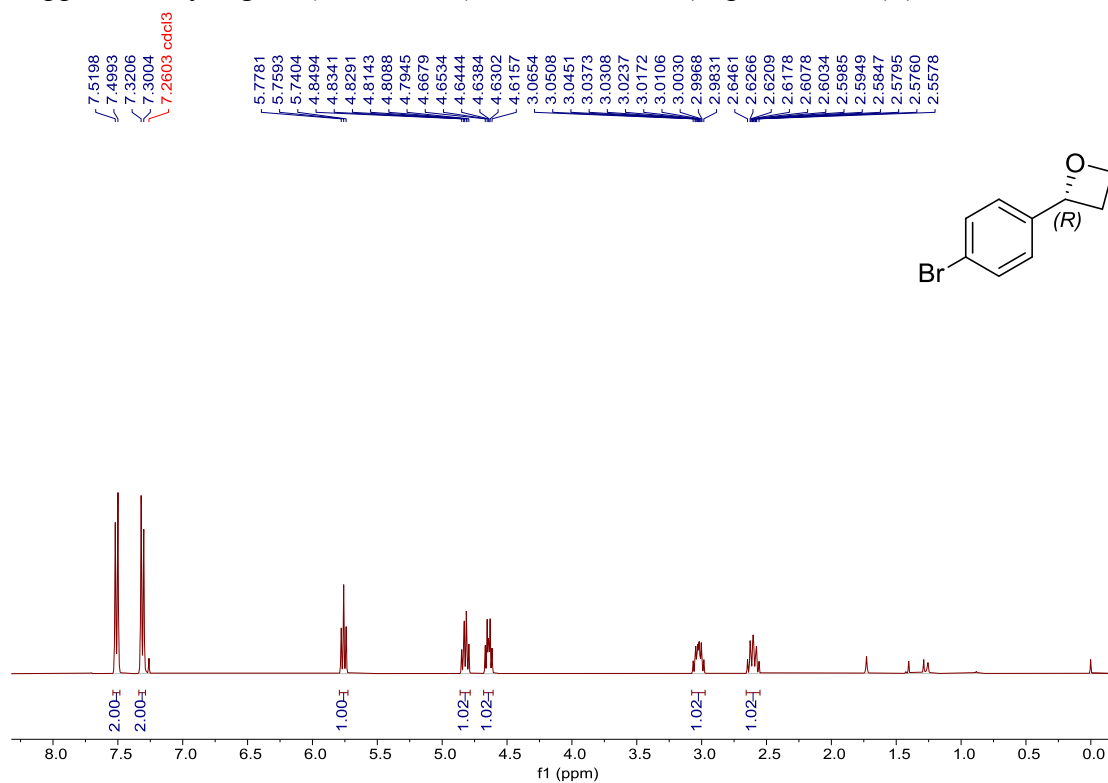
Supplementary Fig. 87 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**12b**.



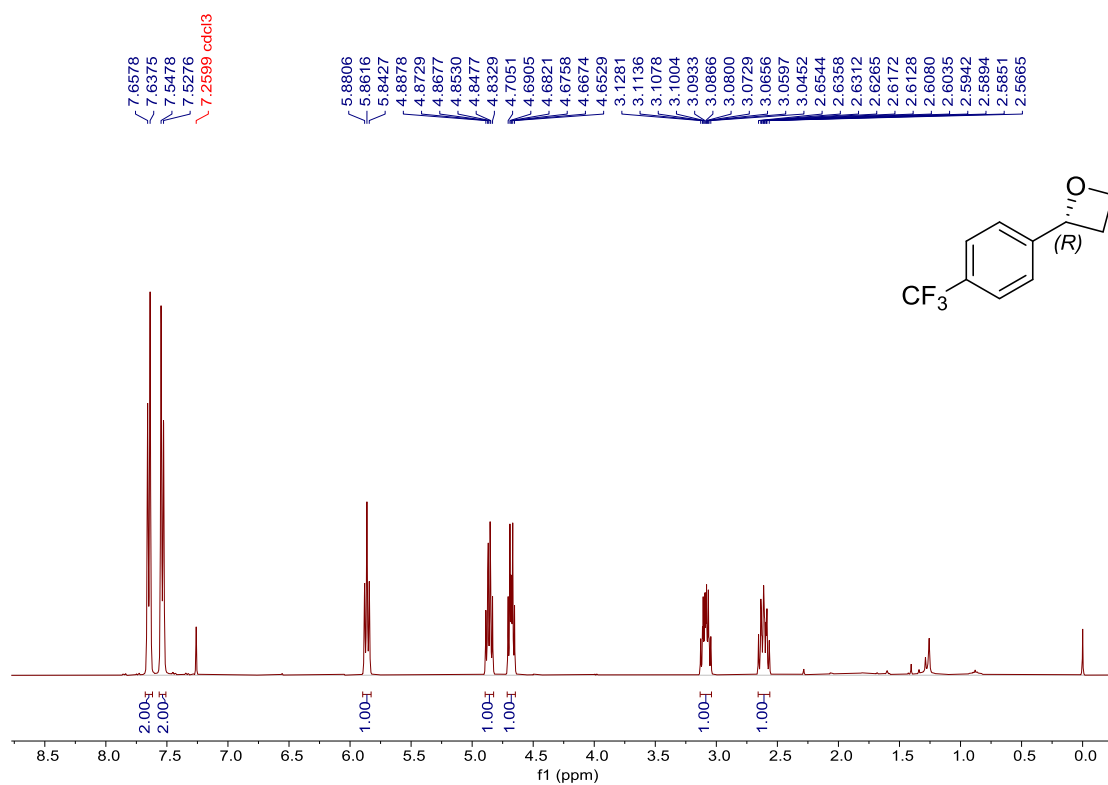
Supplementary Fig. 88 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**13b**.



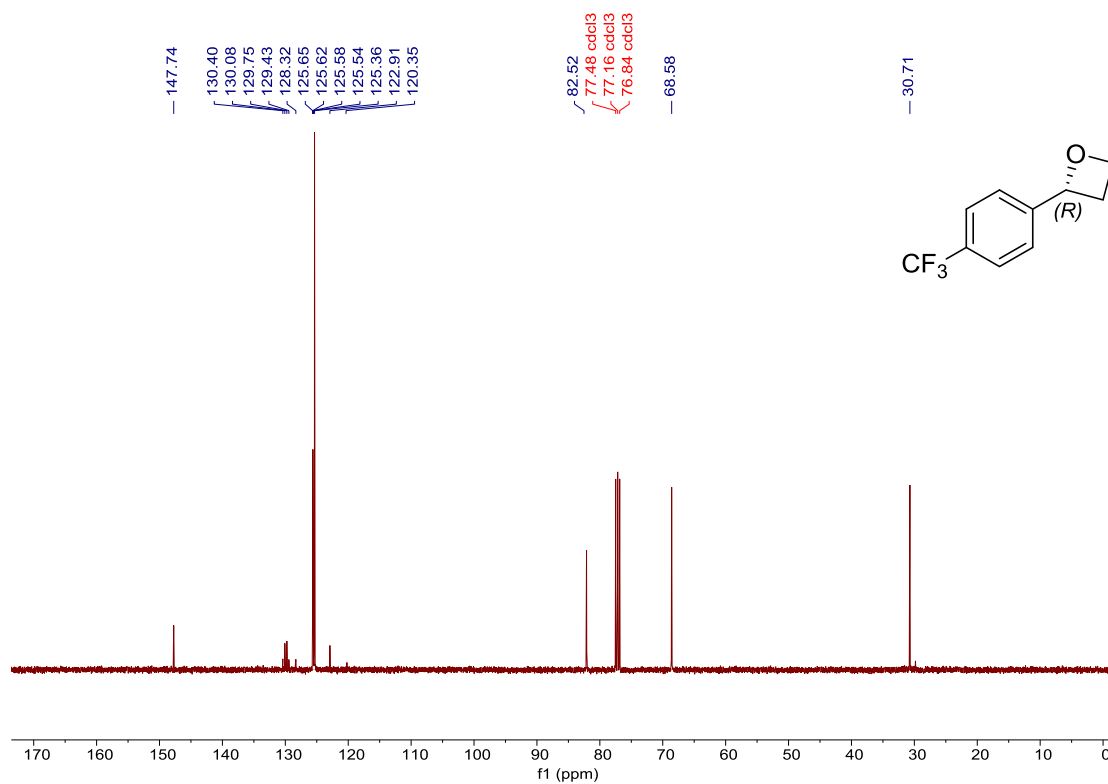
Supplementary Fig. 89 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**13b**.



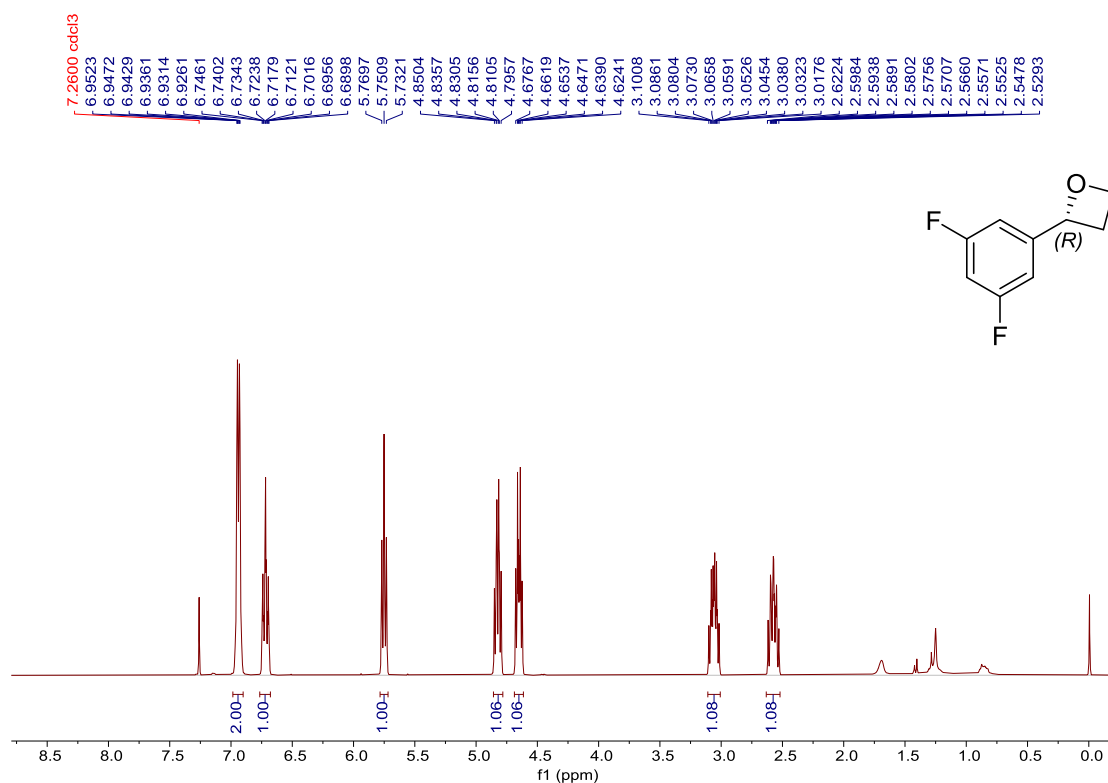
Supplementary Fig. 90 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**14b**.



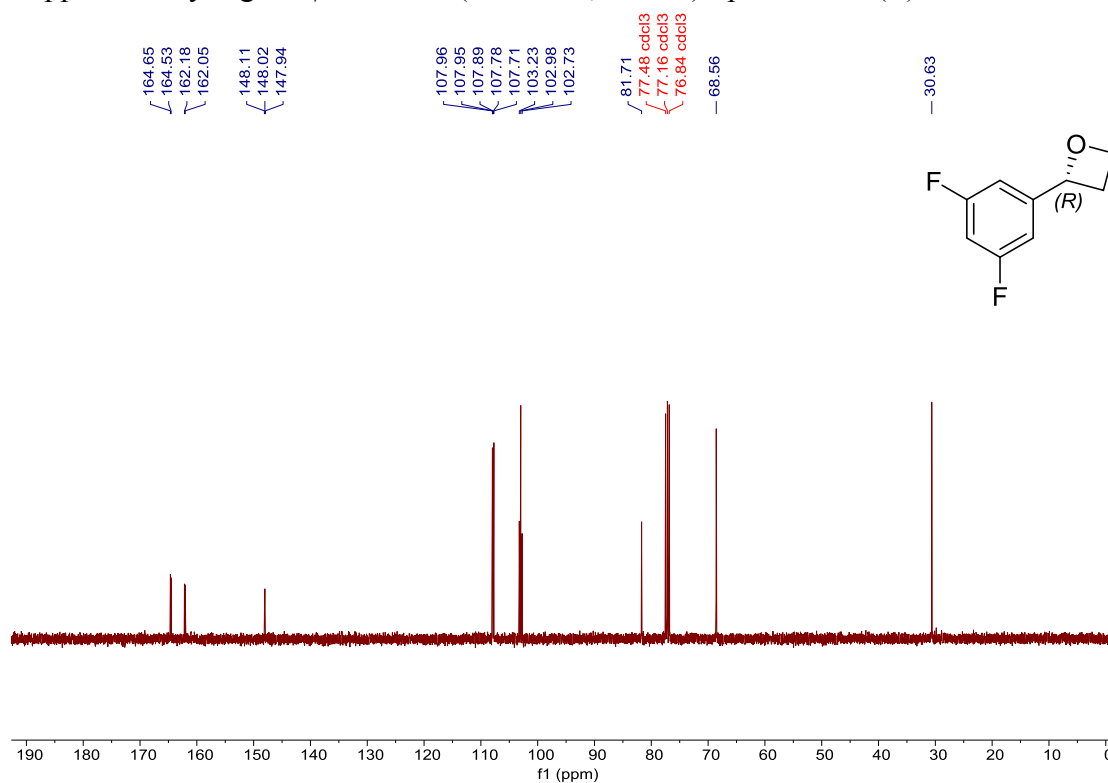
Supplementary Fig. 91 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**14b**.



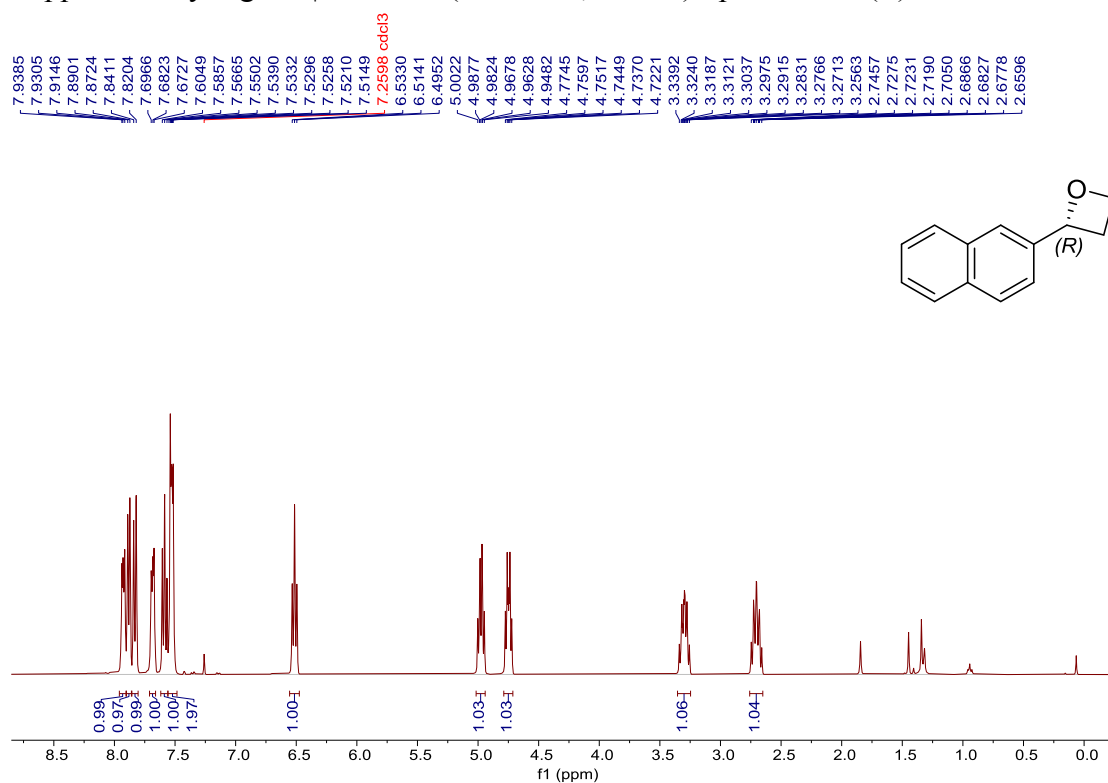
Supplementary Fig. 92 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**15b**.



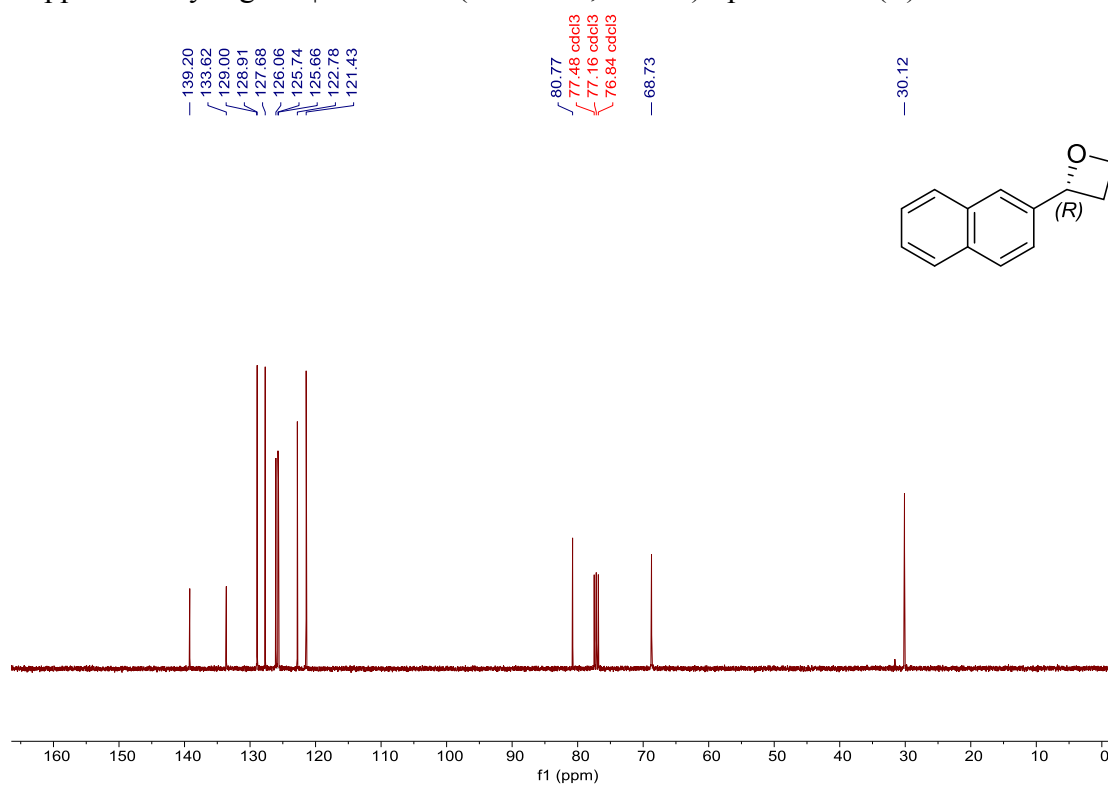
Supplementary Fig. 93 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**15b**.



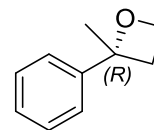
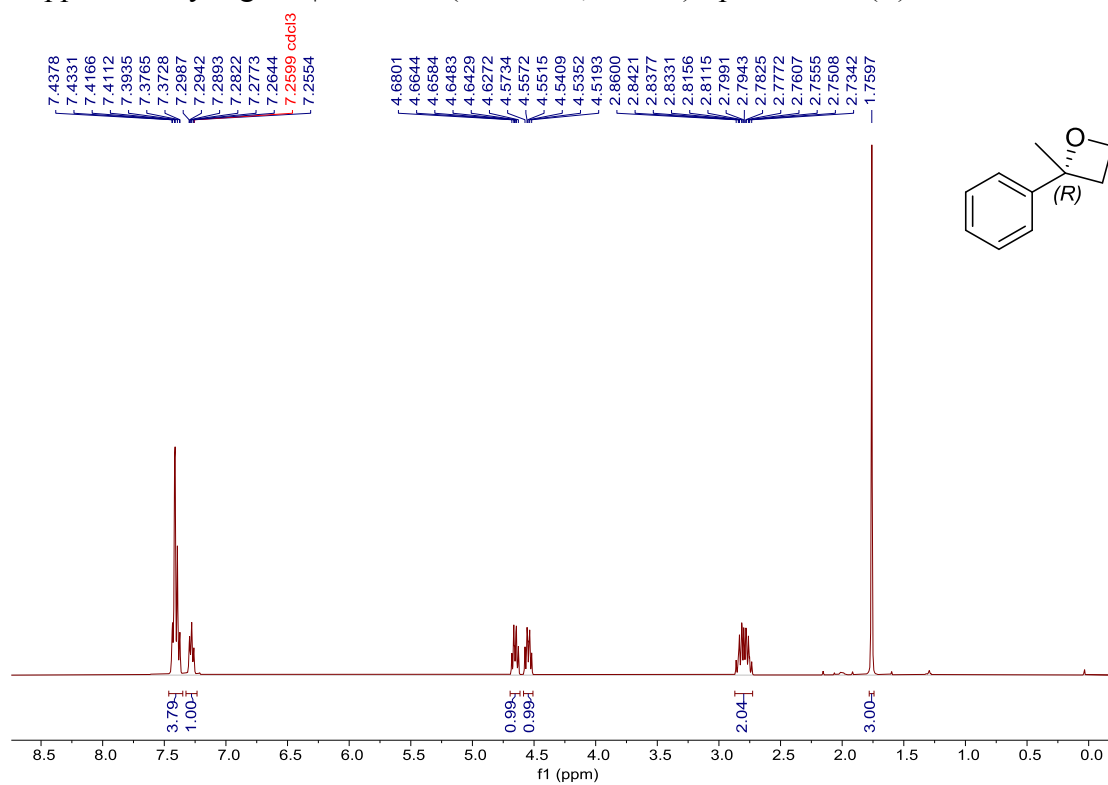
Supplementary Fig. 94 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**16b**.



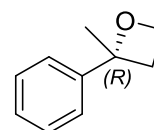
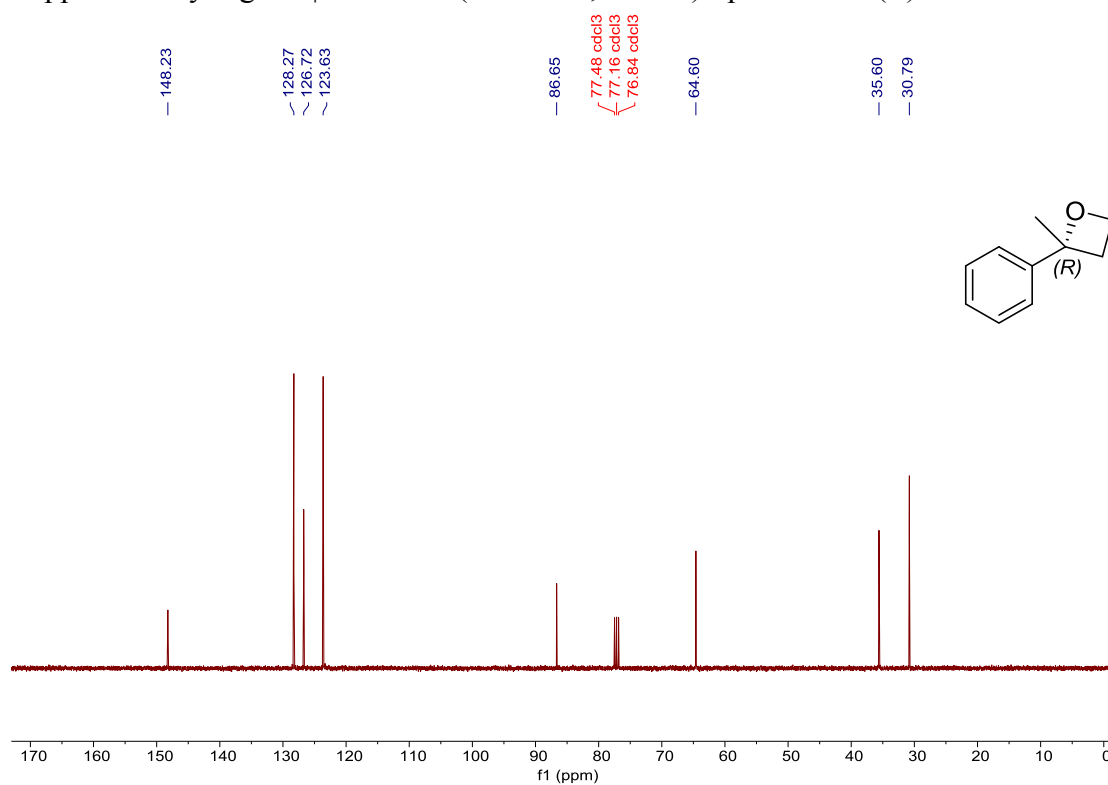
Supplementary Fig. 95 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**16b**.



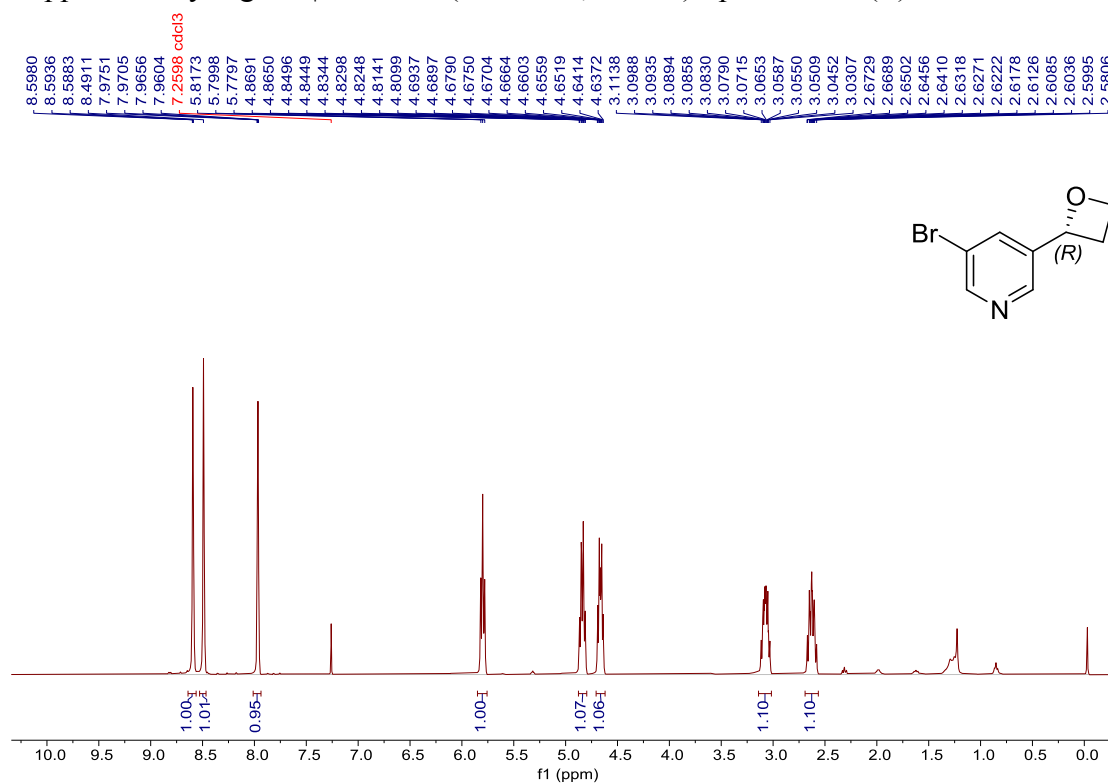
Supplementary Fig. 96 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**17b**.



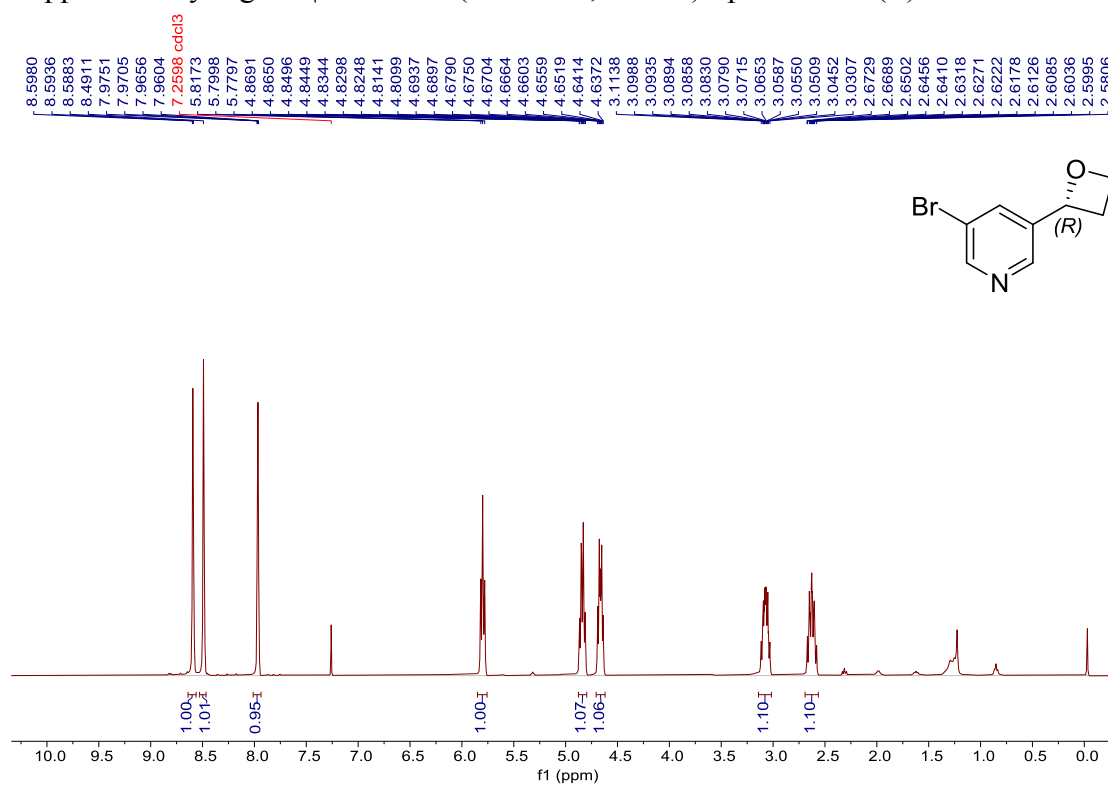
Supplementary Fig. 97 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**17b**.



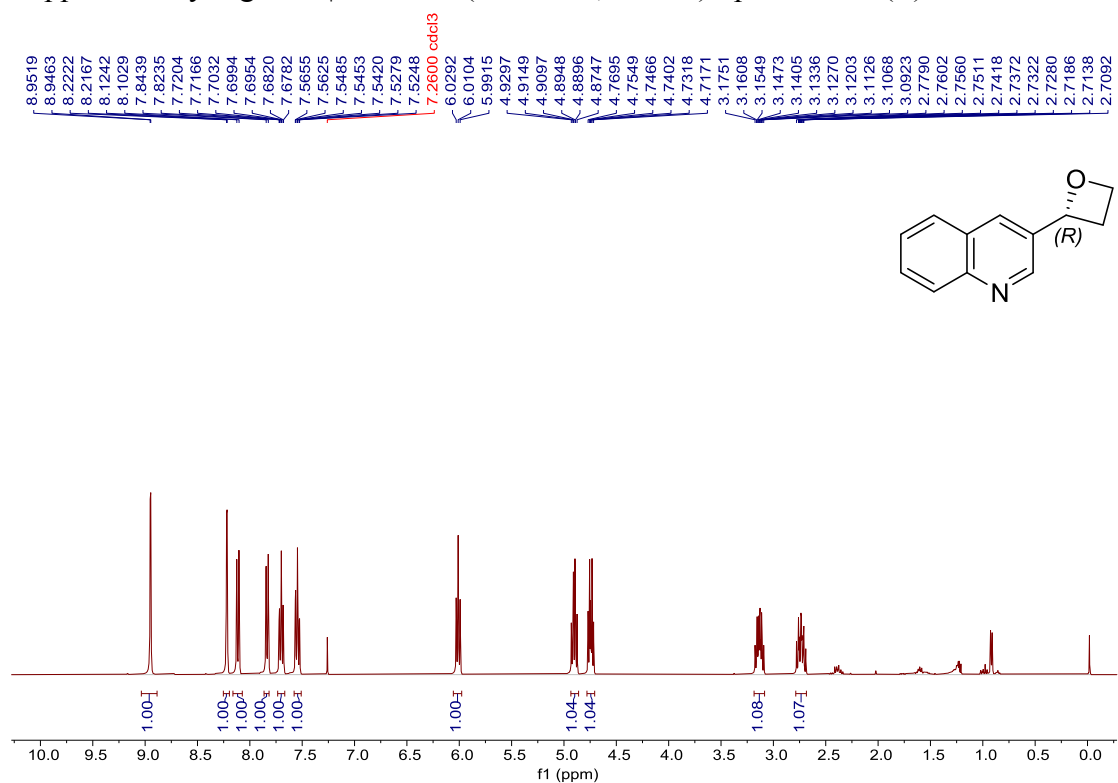
Supplementary Fig. 98 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**18b**.



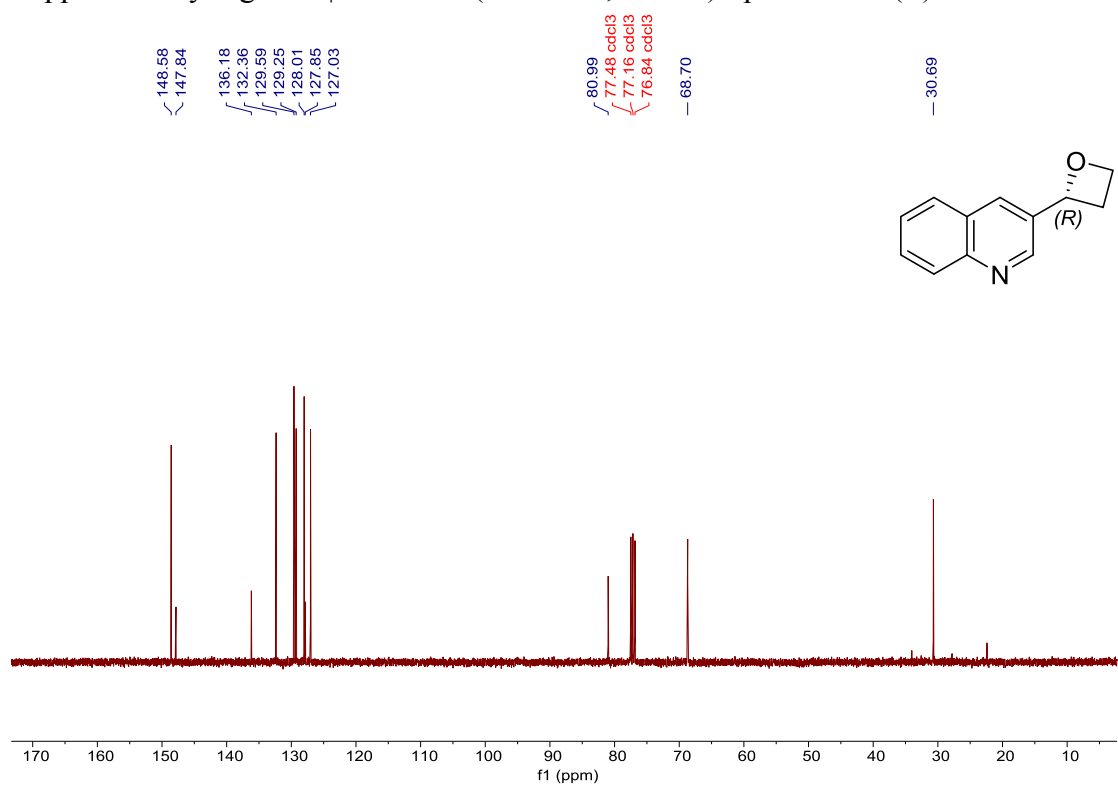
Supplementary Fig. 99 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**18b**.



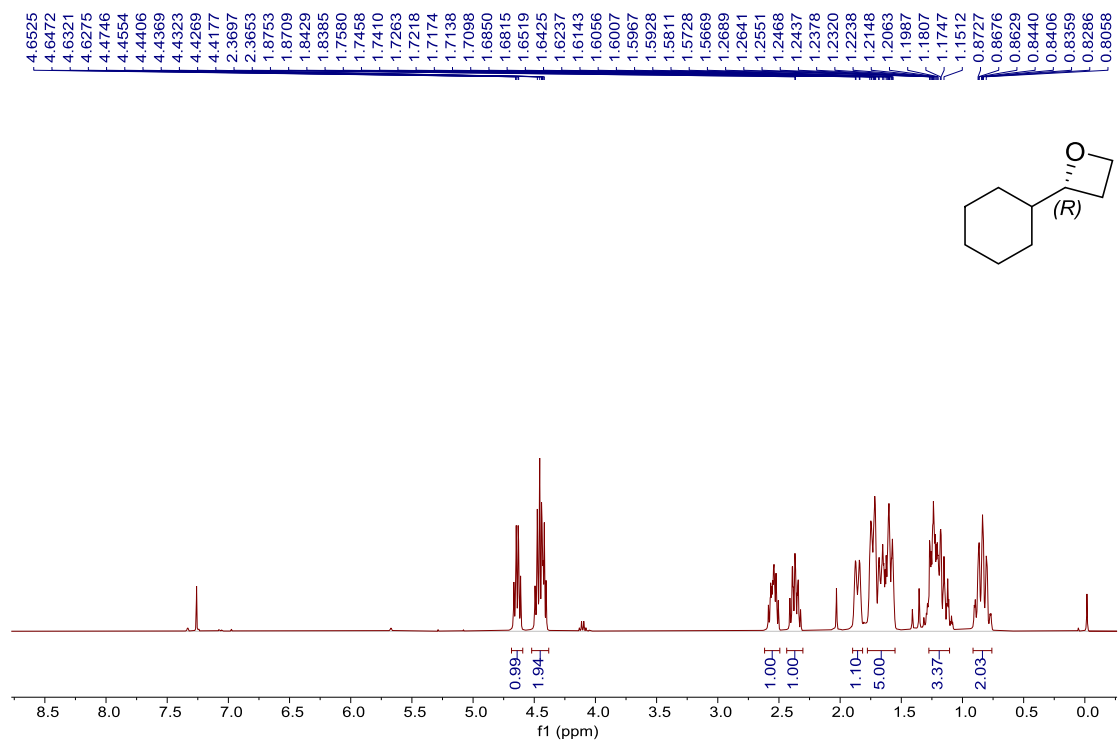
Supplementary Fig. 100 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**19b**.



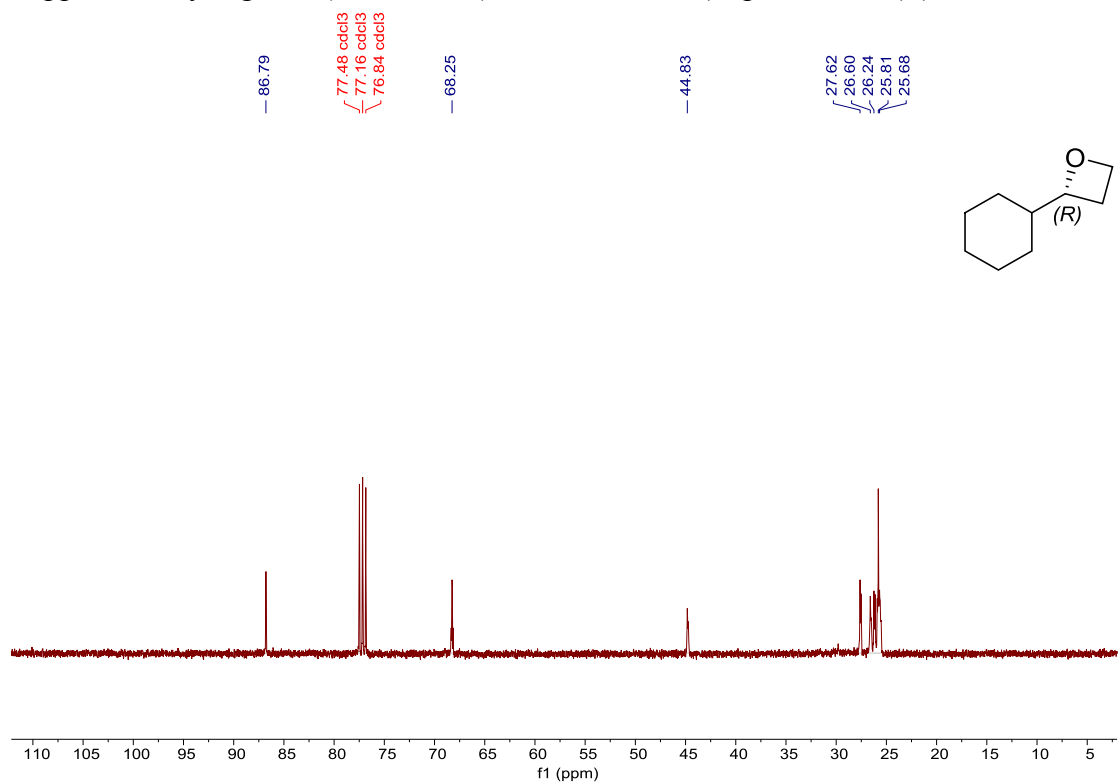
Supplementary Fig. 101 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**19b**.



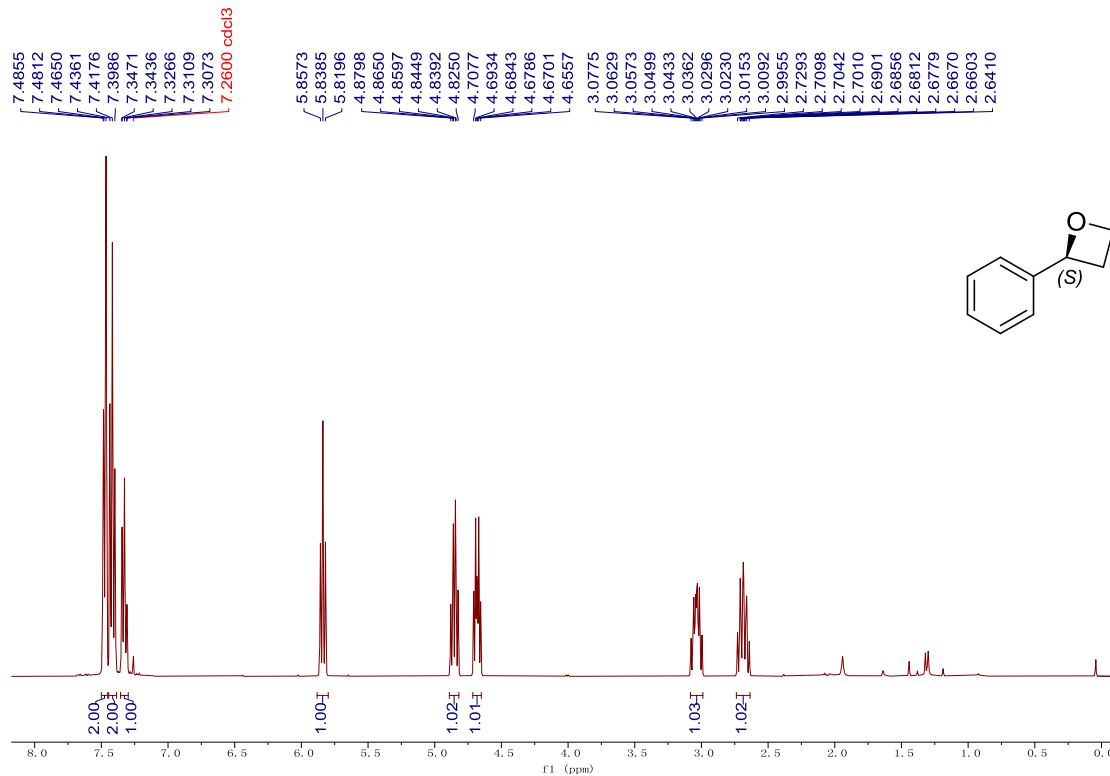
Supplementary Fig. 102 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**21b**.



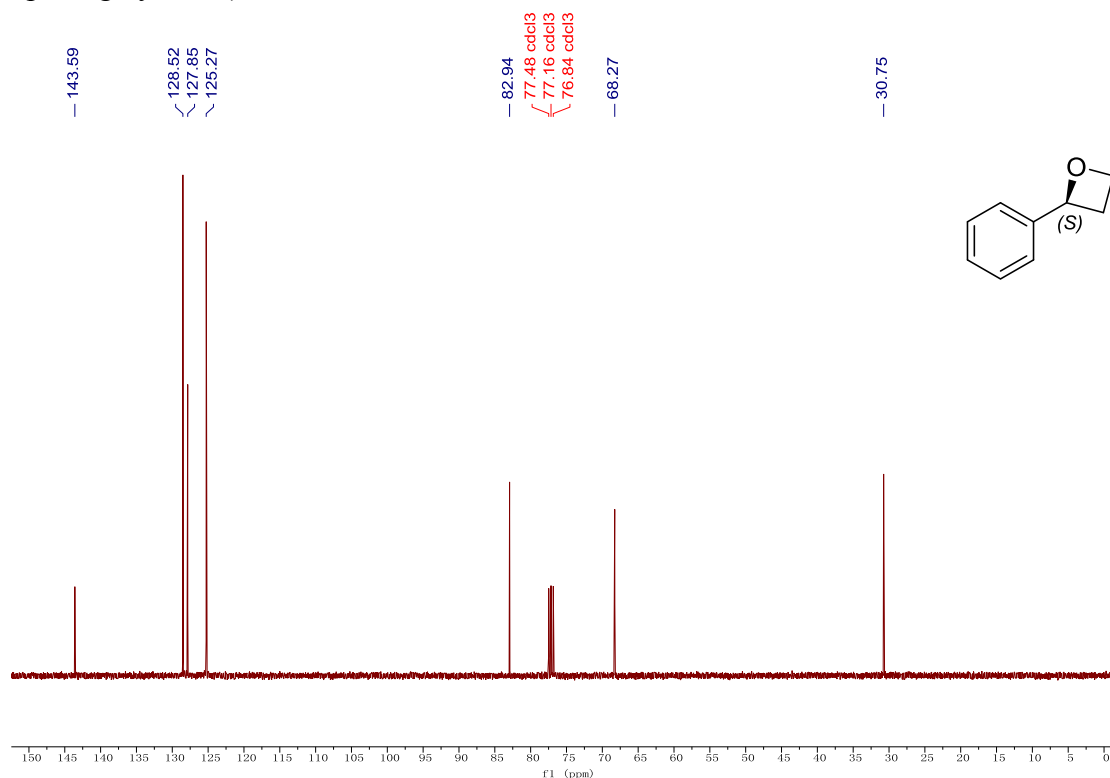
Supplementary Fig. 103 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**21b**.



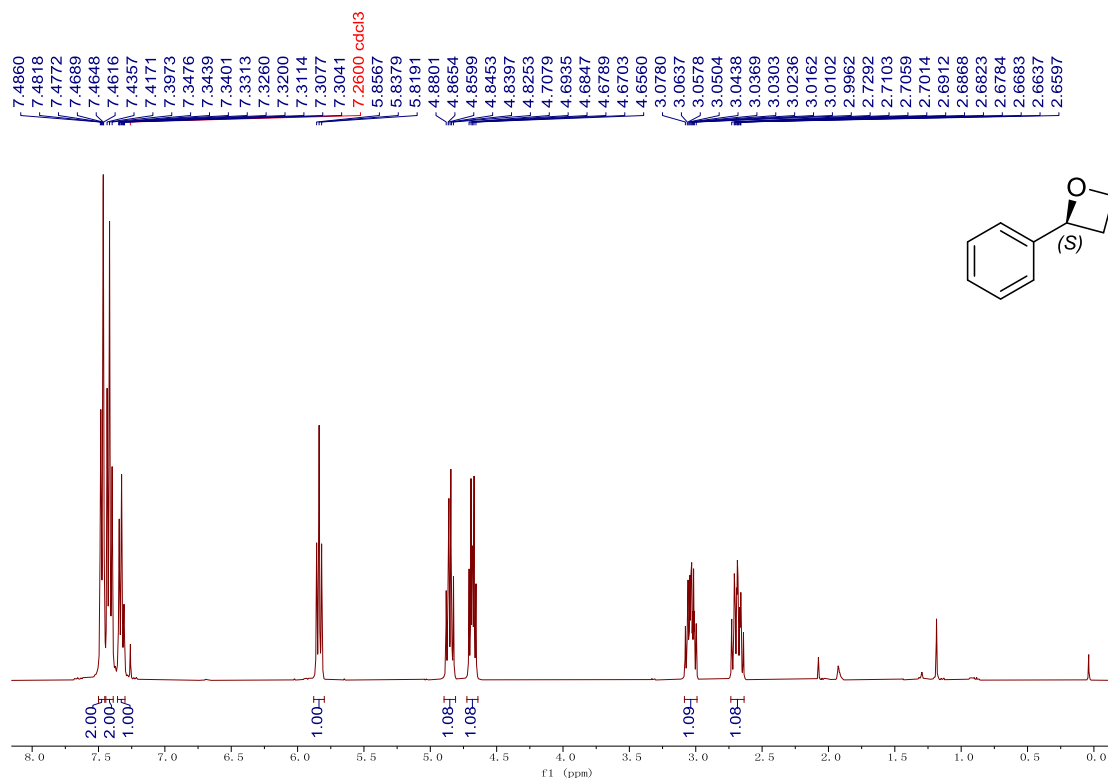
Supplementary Fig. 104 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**1b** (Ring opening by azide)



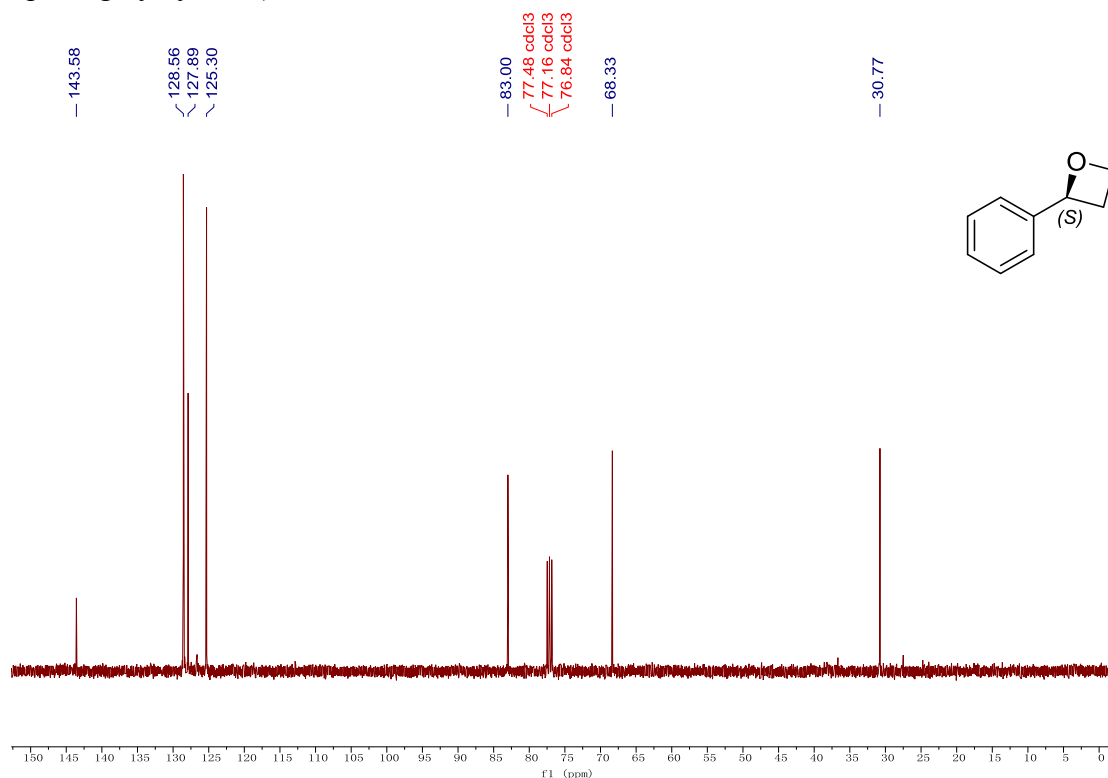
Supplementary Fig. 105 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**1b** (Ring opening by azide).



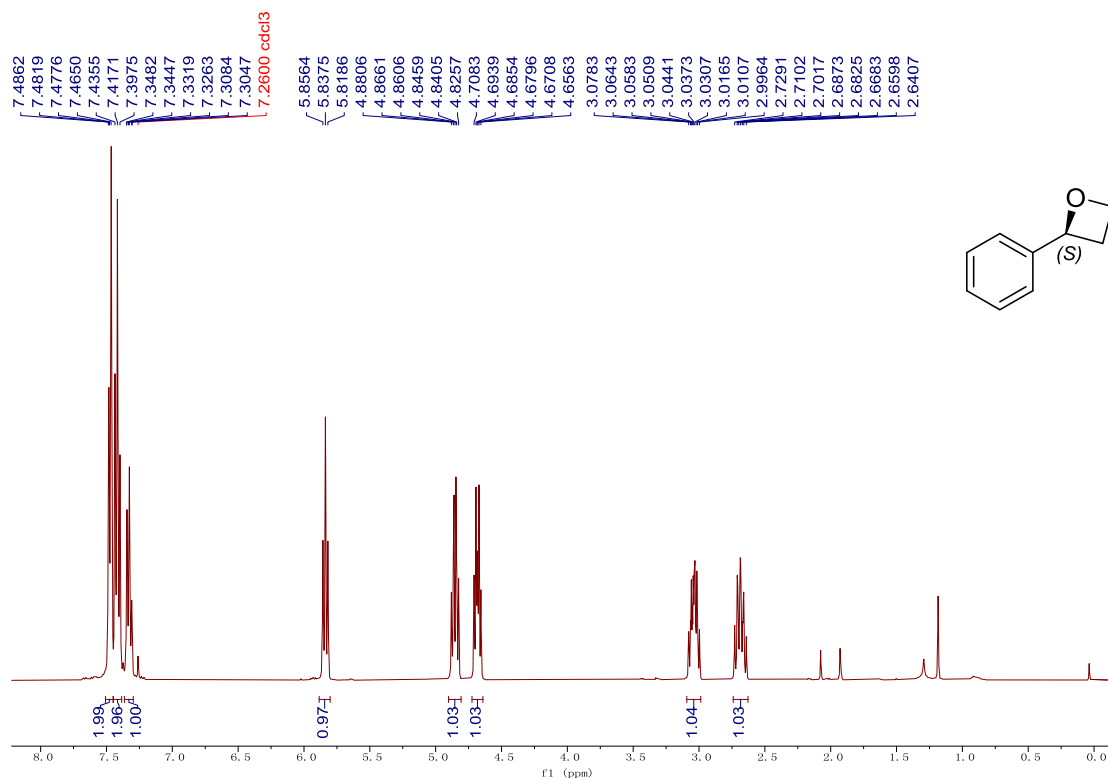
Supplementary Fig. 106 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**1b** (Ring opening by cyanide).



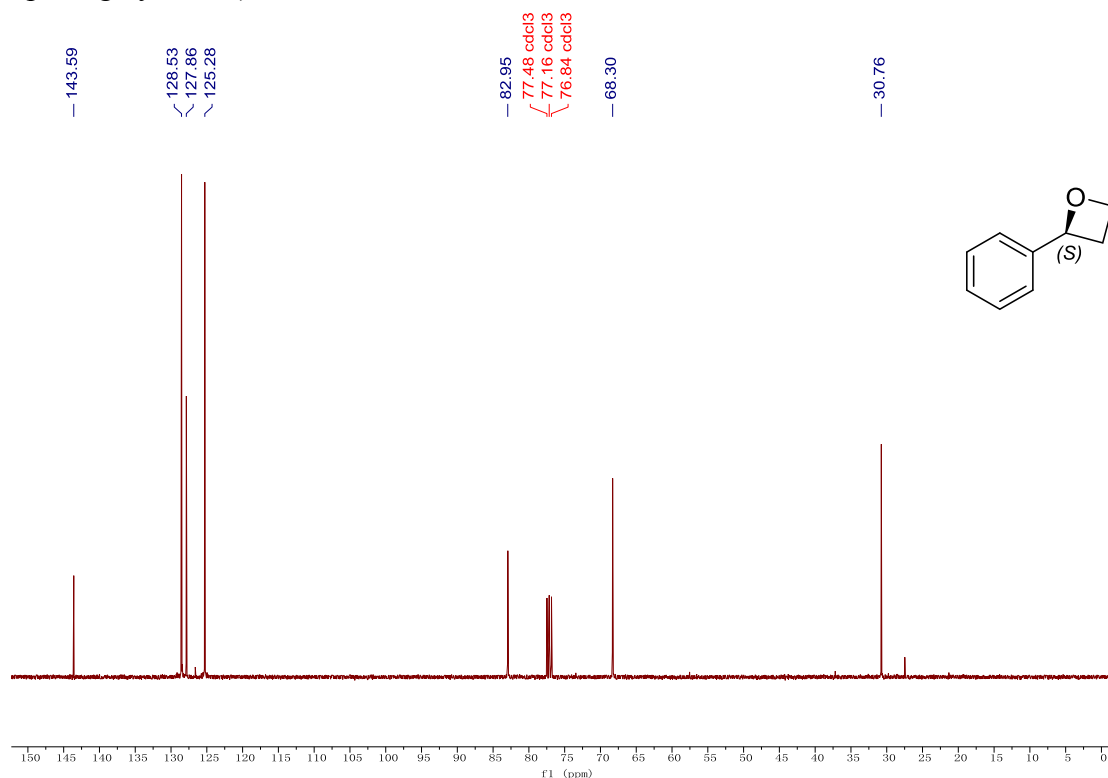
Supplementary Fig. 107 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**1b** (Ring opening by cyanide).



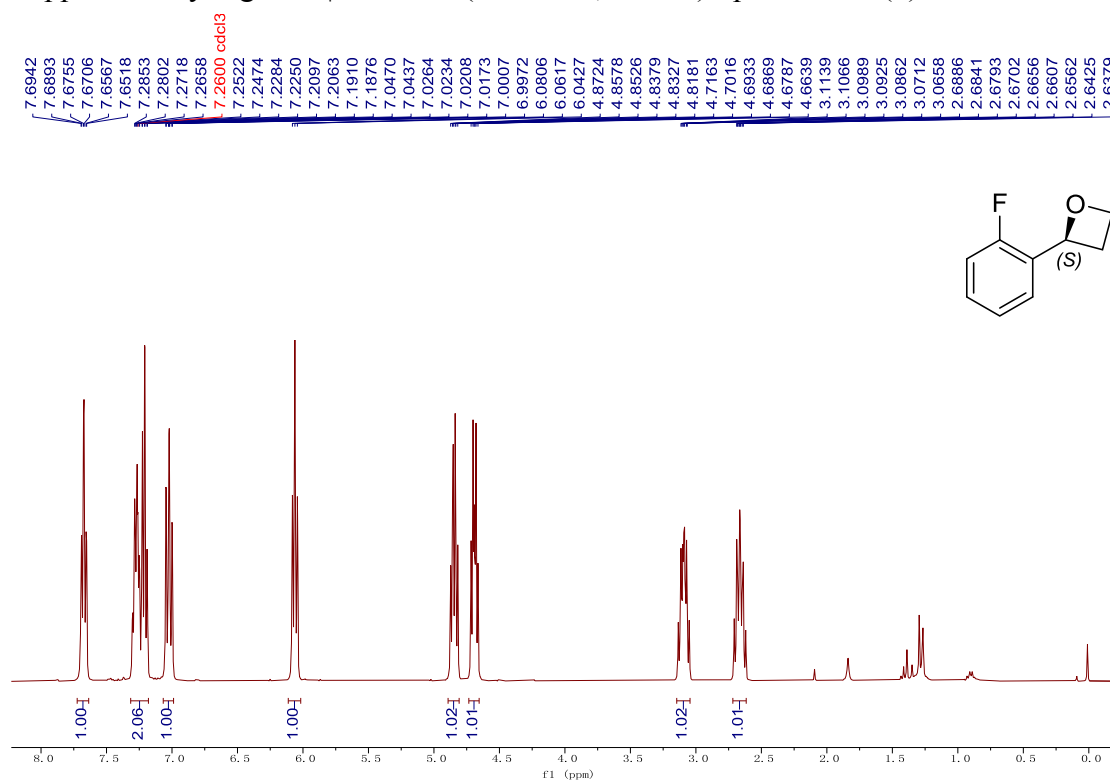
Supplementary Fig. 108 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**1b** (Ring opening by nitrite).



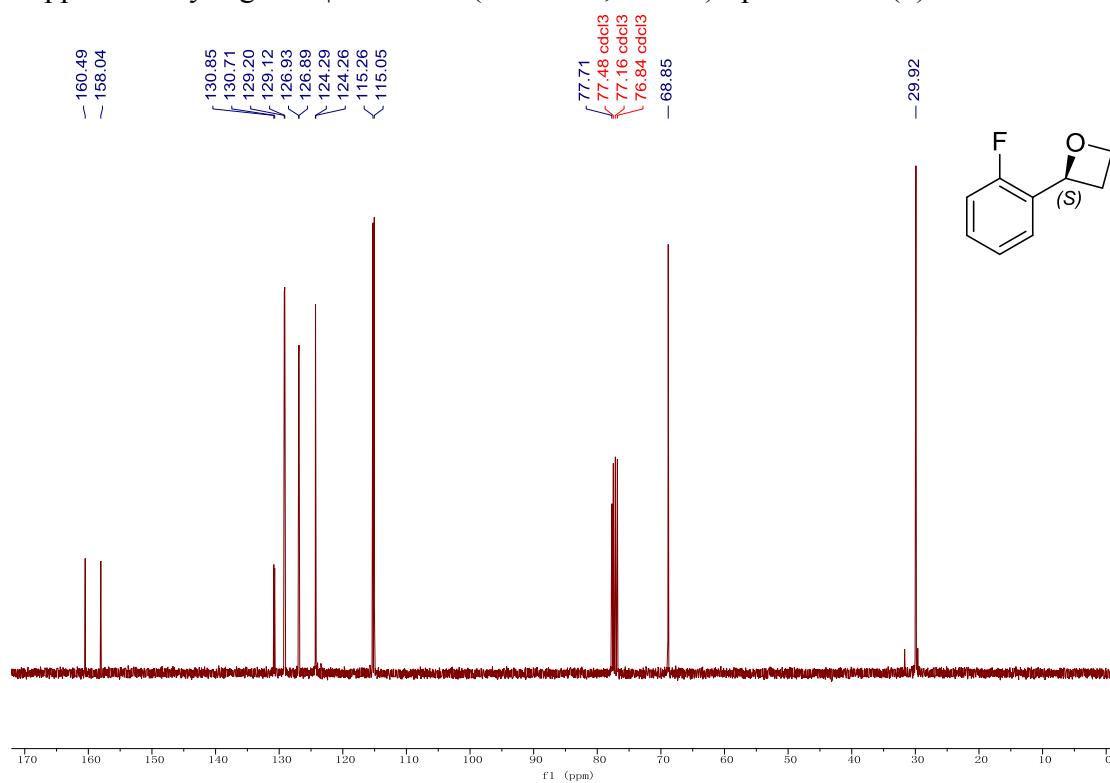
Supplementary Fig. 109 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**1b** (Ring opening by nitrite).



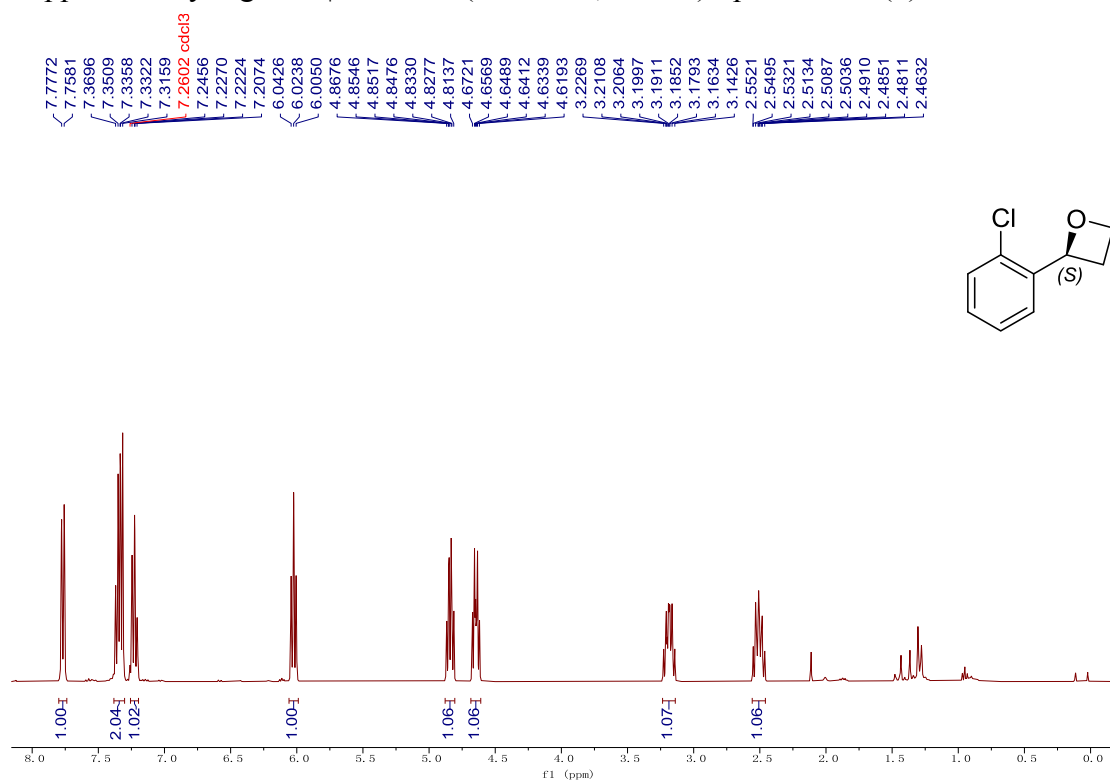
Supplementary Fig. 110 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**2b**.



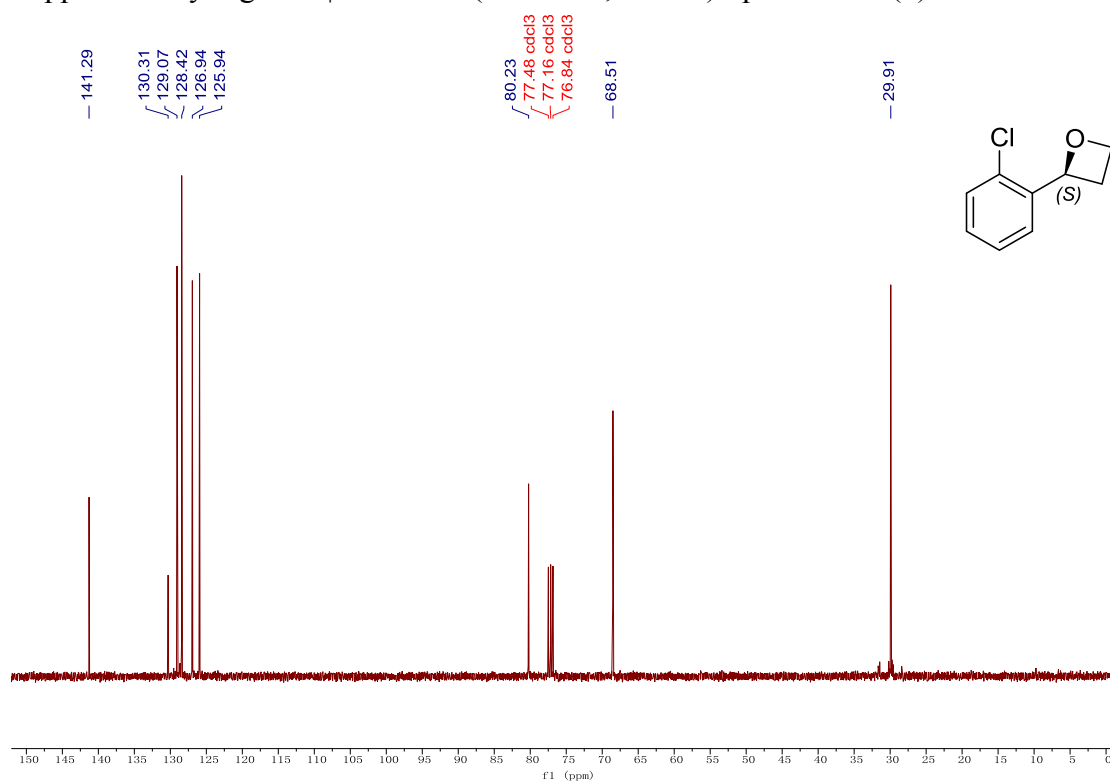
Supplementary Fig. 111 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**2b**.



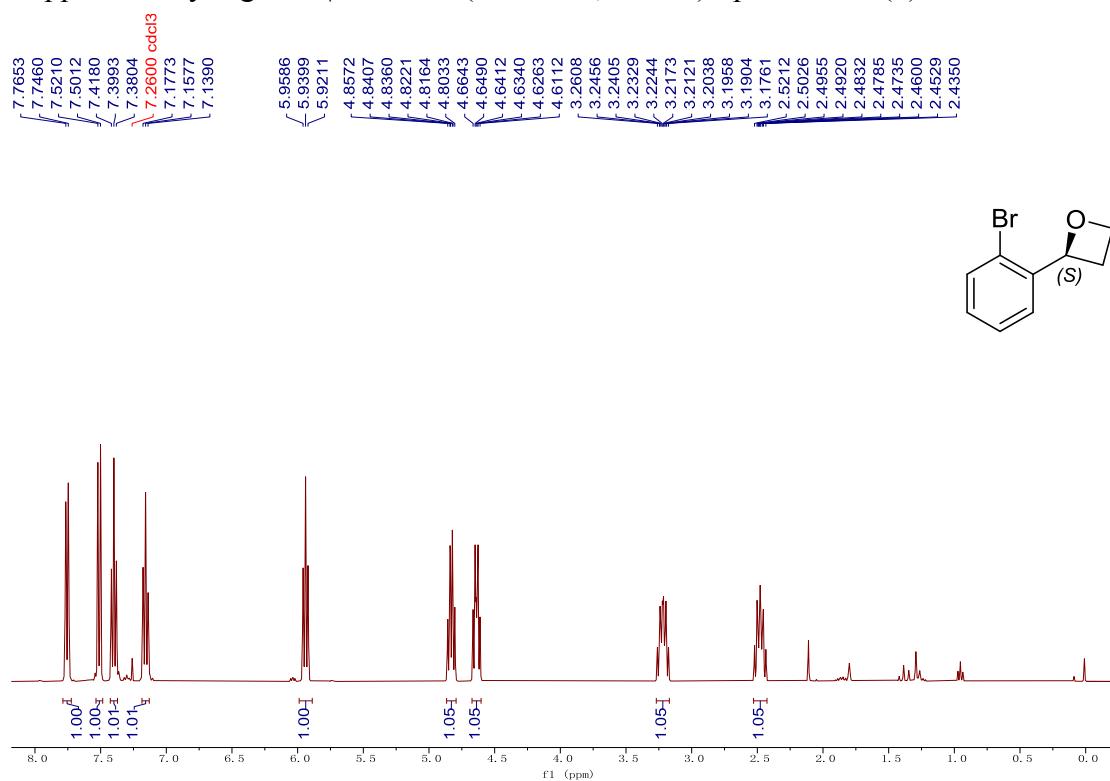
Supplementary Fig. 112 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**3b**.



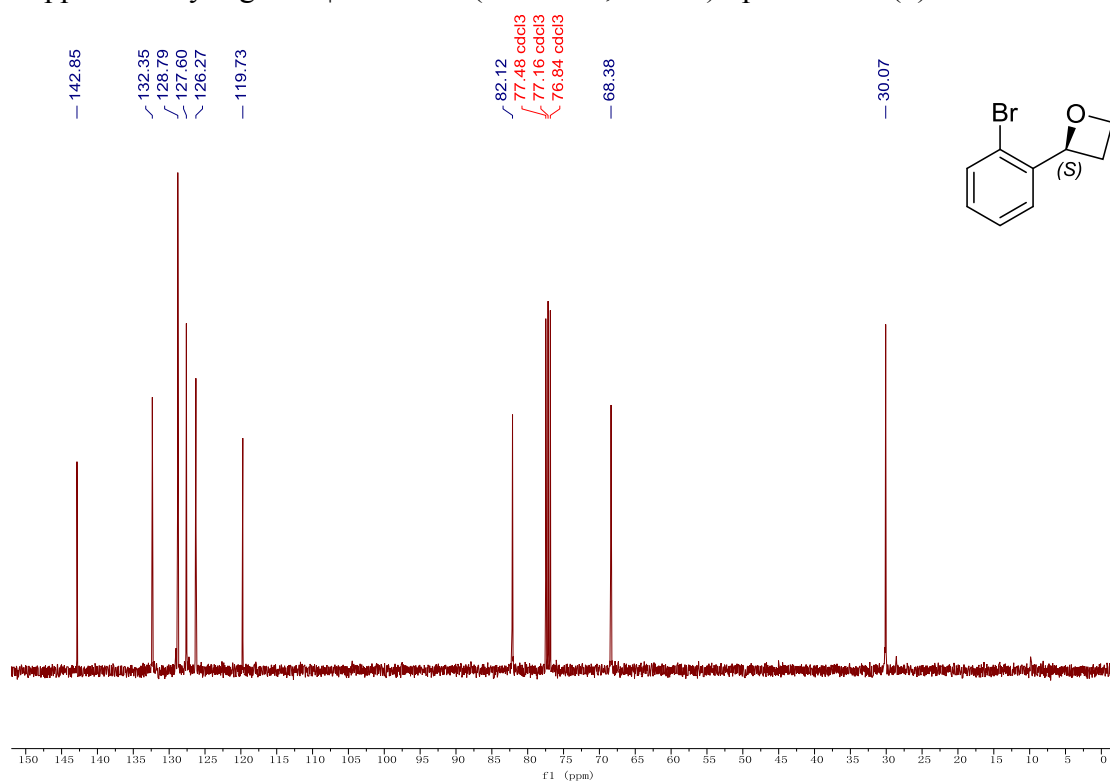
Supplementary Fig. 113 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**3b**.



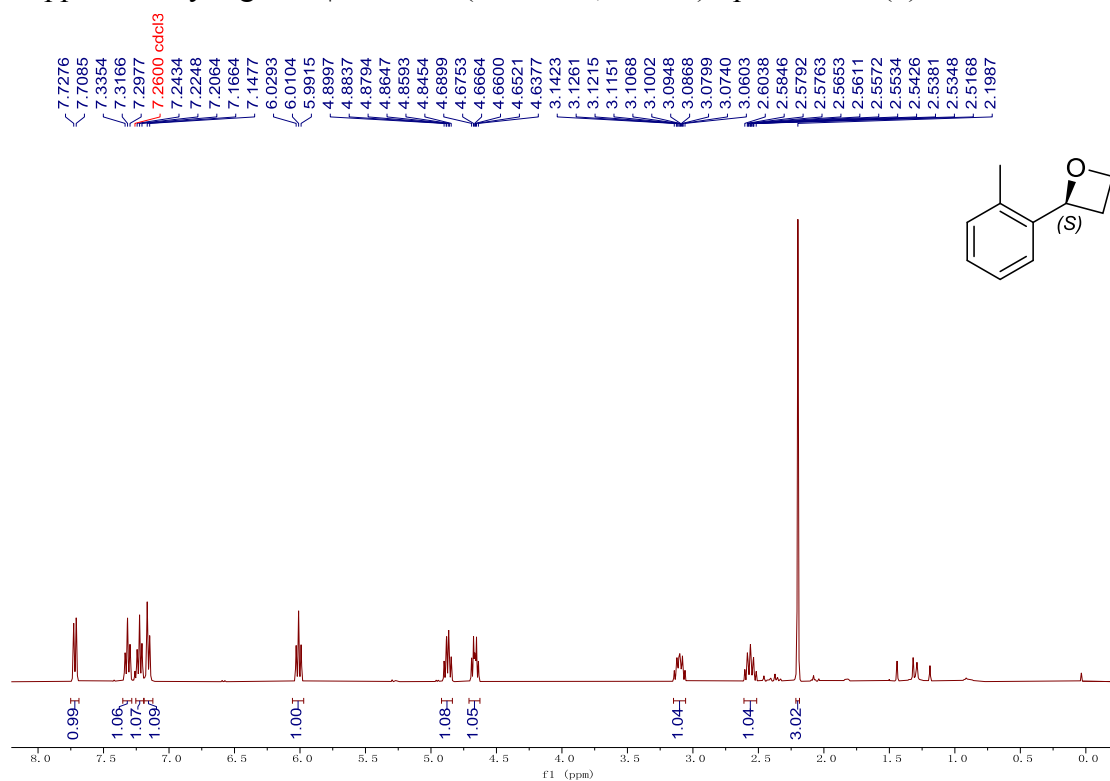
Supplementary Fig. 114 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**4b**.



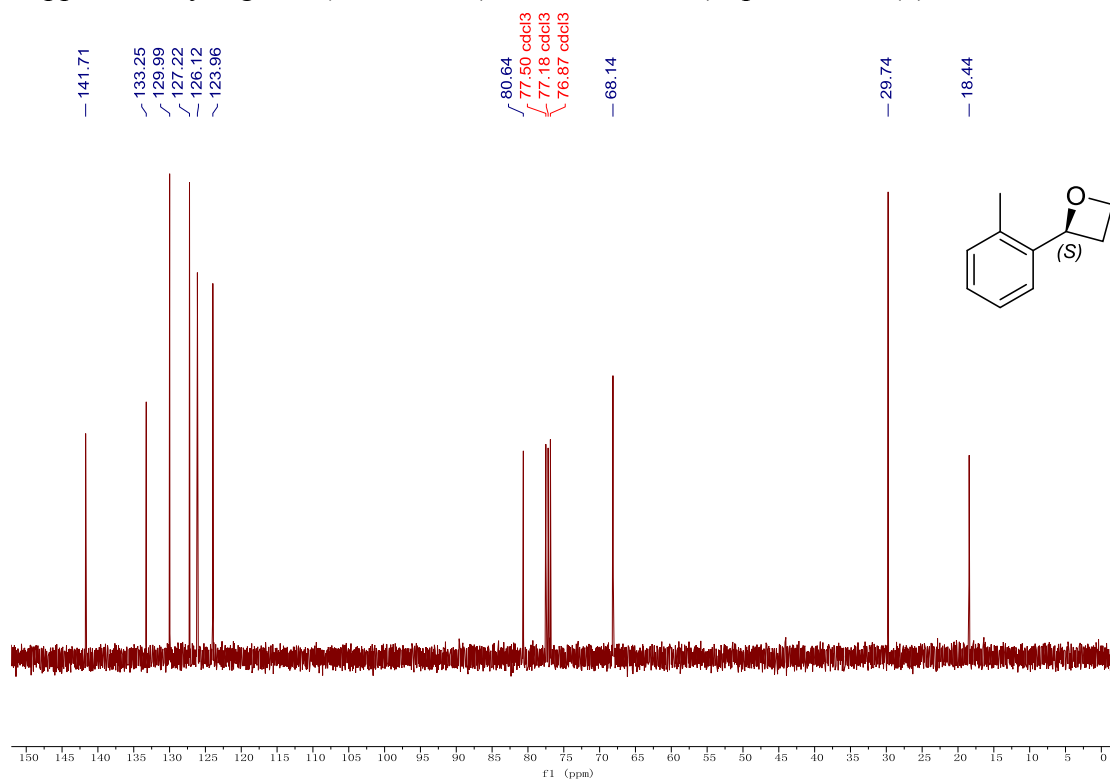
Supplementary Fig. 115 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**4b**.



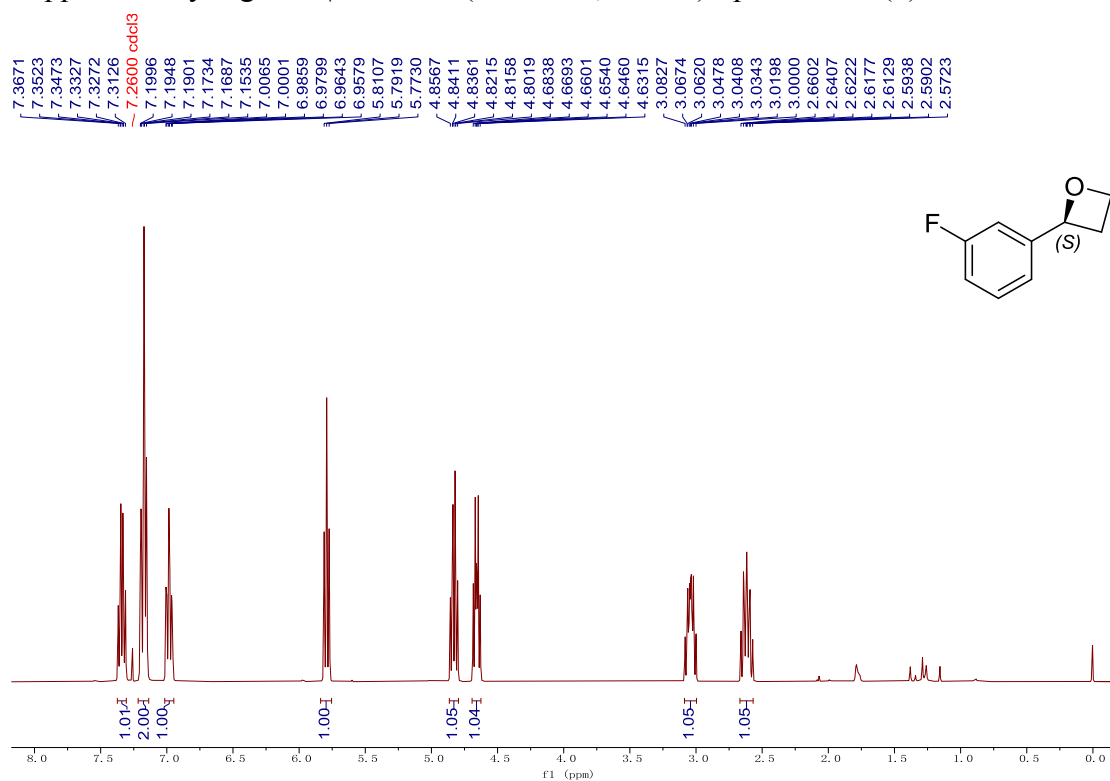
Supplementary Fig. 116 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**5b**.



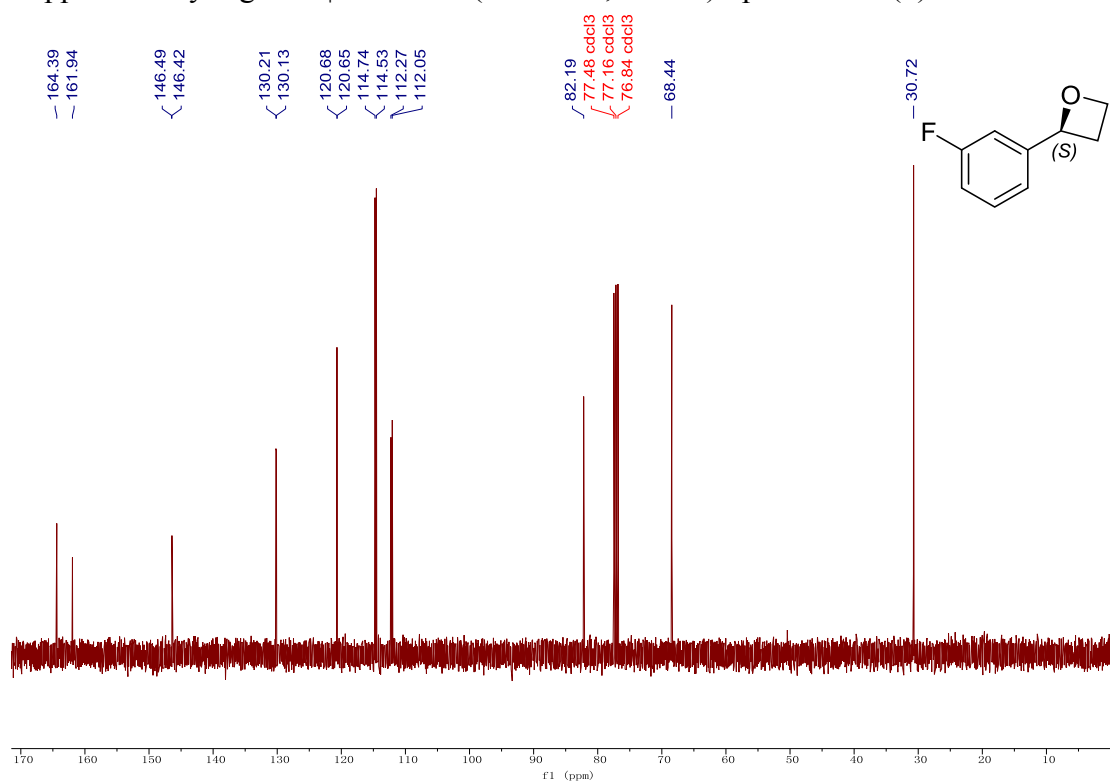
Supplementary Fig. 117 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**5b**.



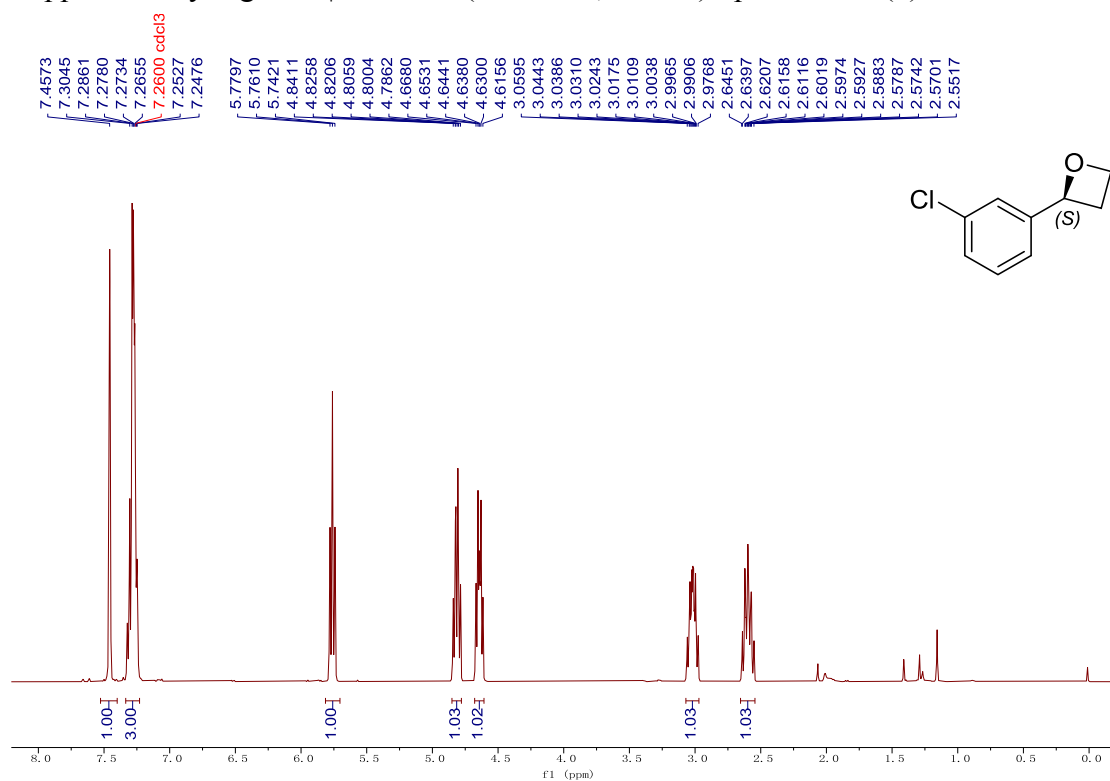
Supplementary Fig. 118 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**6b**.



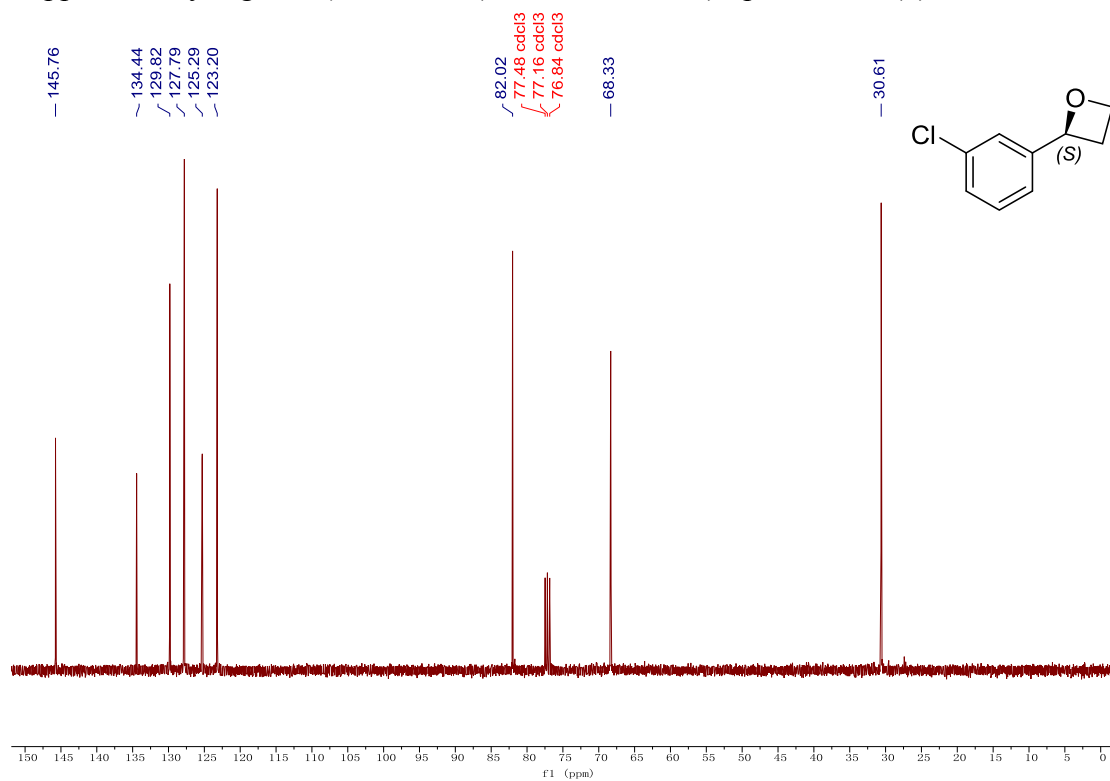
Supplementary Fig. 119 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**6b**.



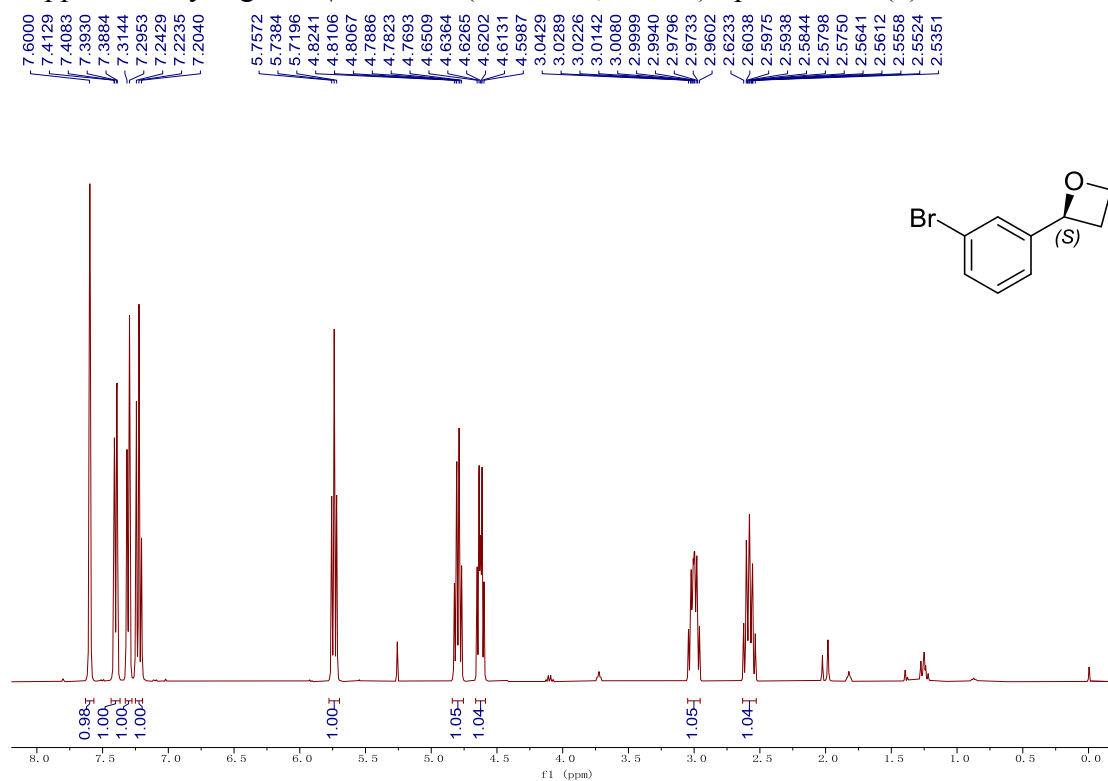
Supplementary Fig. 120 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**7b**.



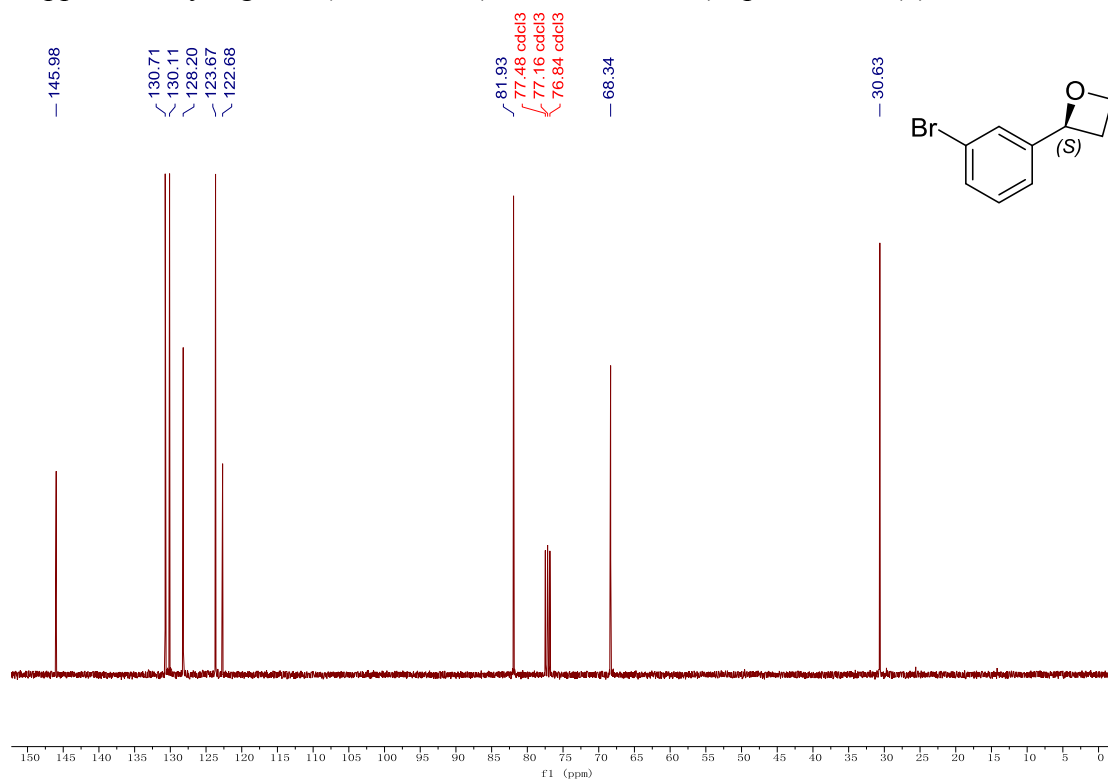
Supplementary Fig. 121 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**7b**.



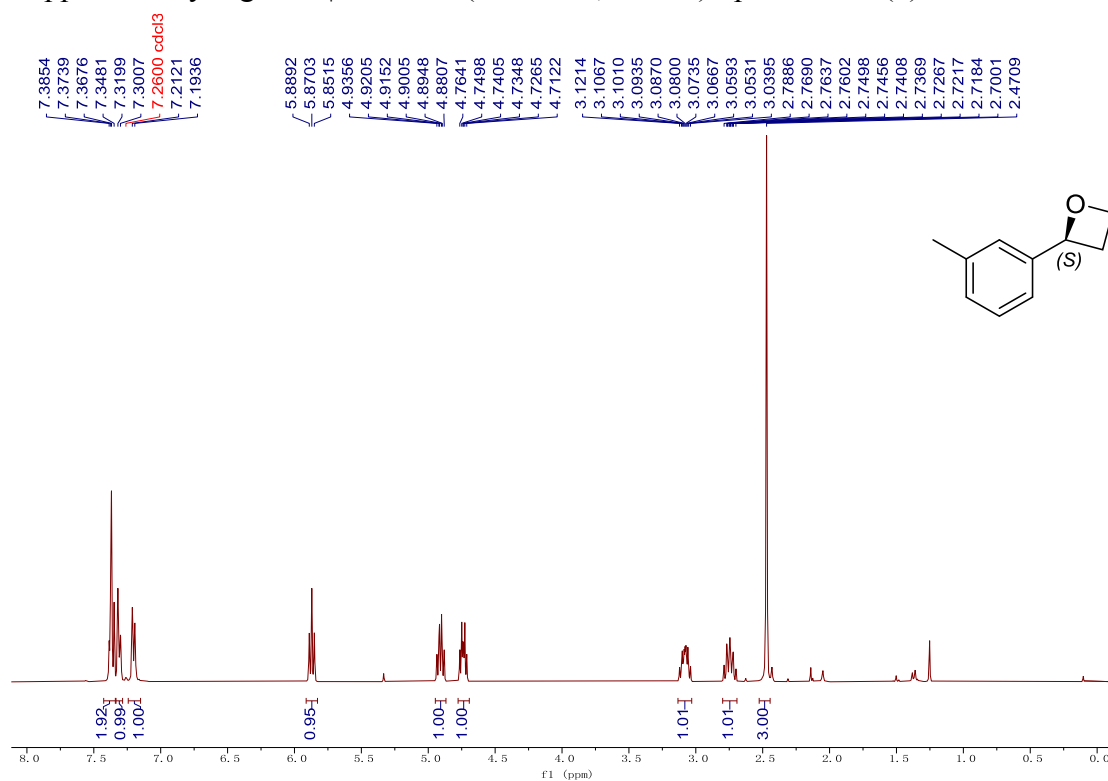
Supplementary Fig. 122 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**8b**.



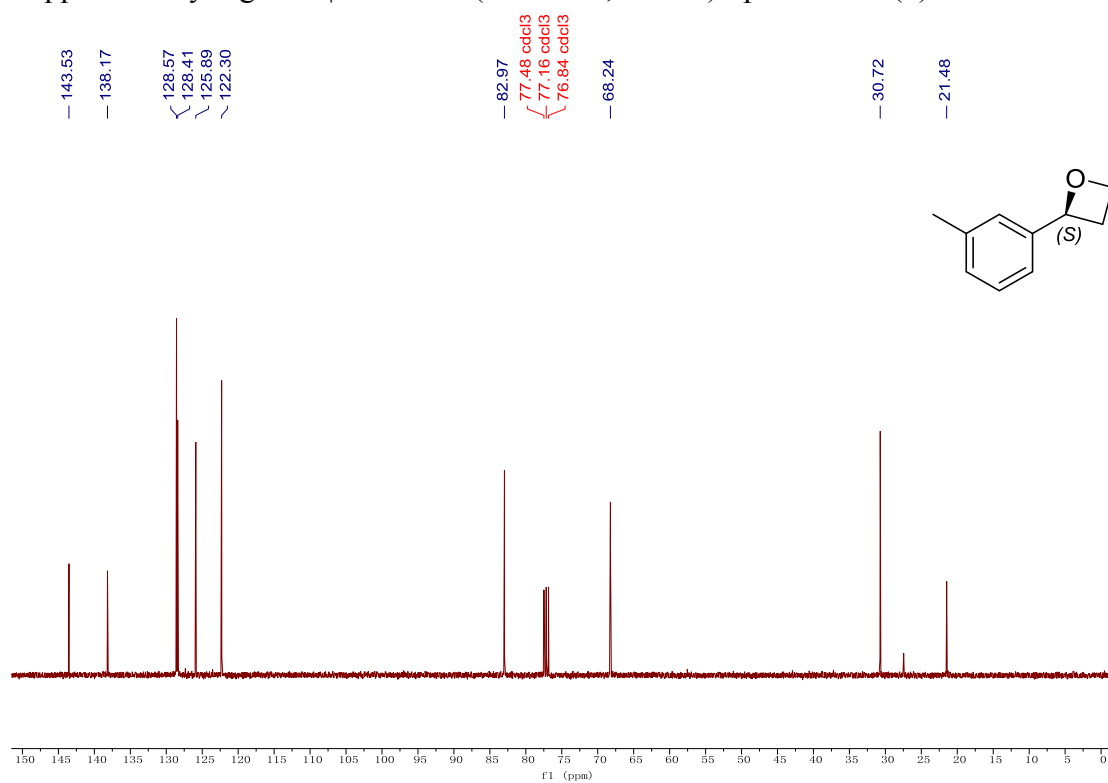
Supplementary Fig. 123 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**8b**.



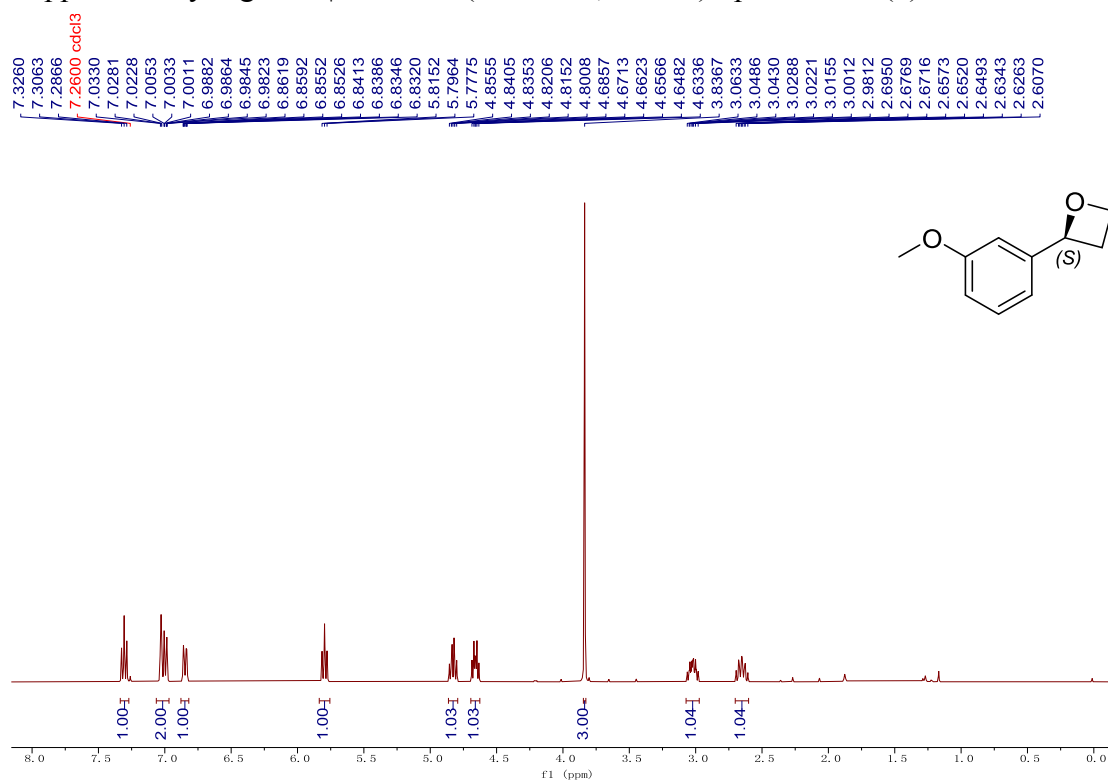
Supplementary Fig. 124 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**9b**.



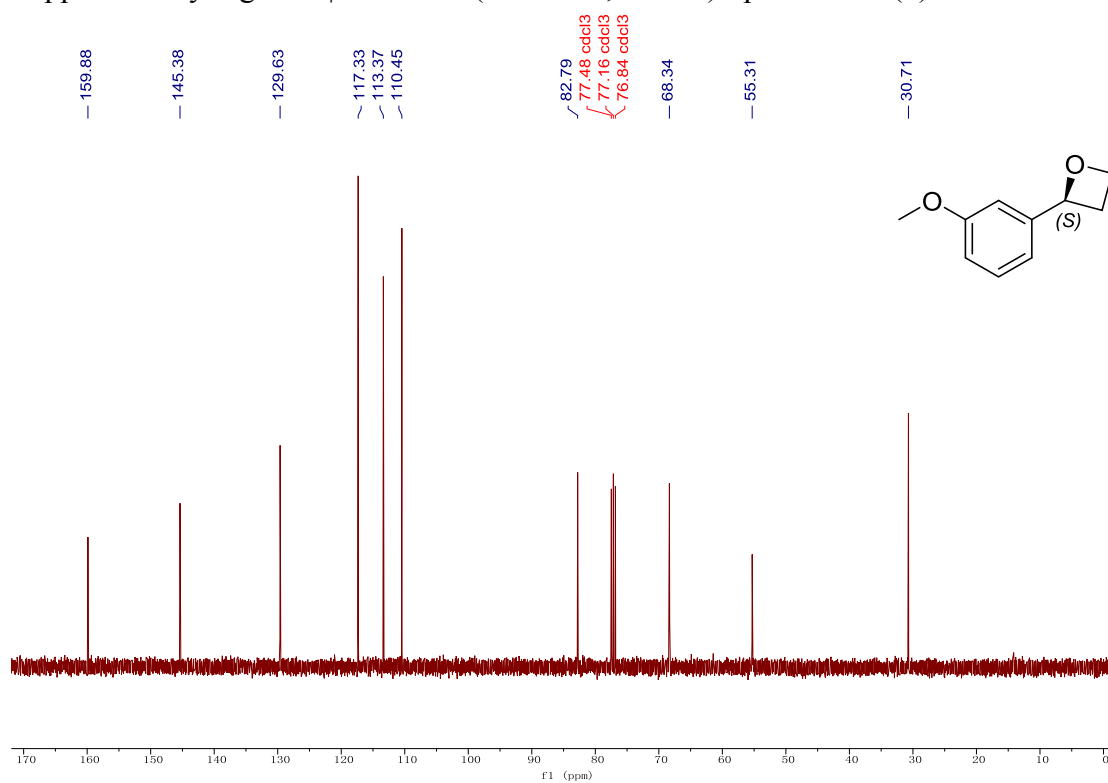
Supplementary Fig. 125 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**9b**.



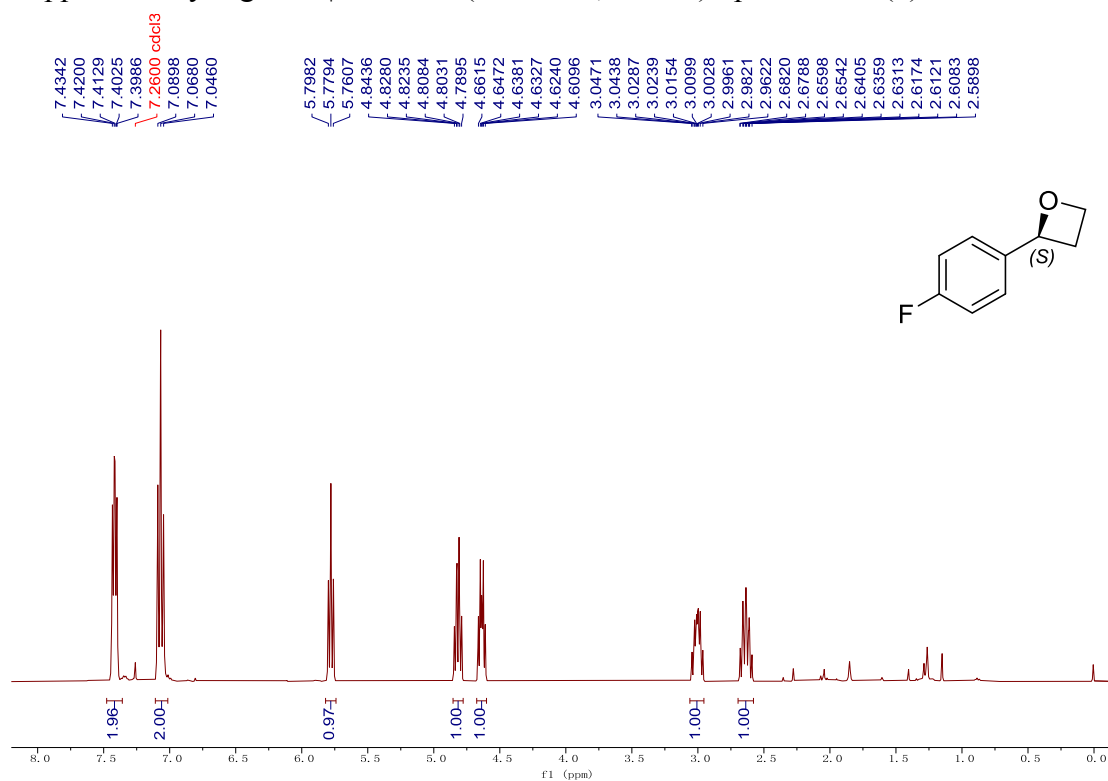
Supplementary Fig. 126 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**10b**.



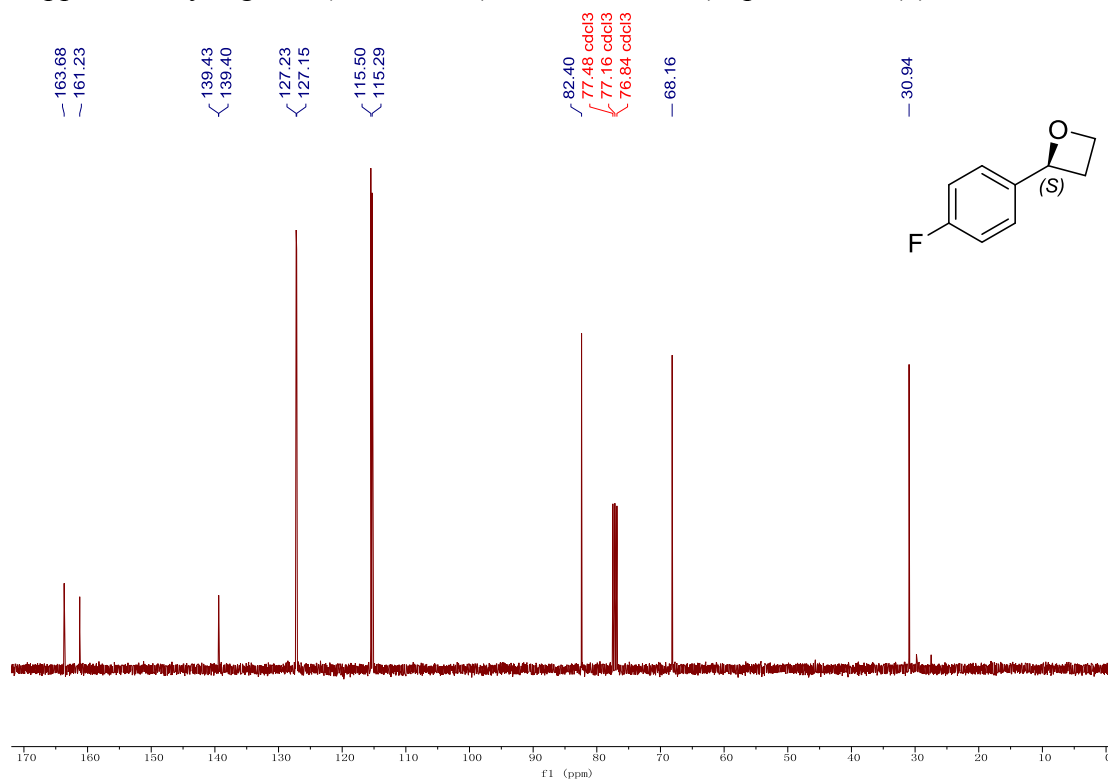
Supplementary Fig. 127 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**10b**.



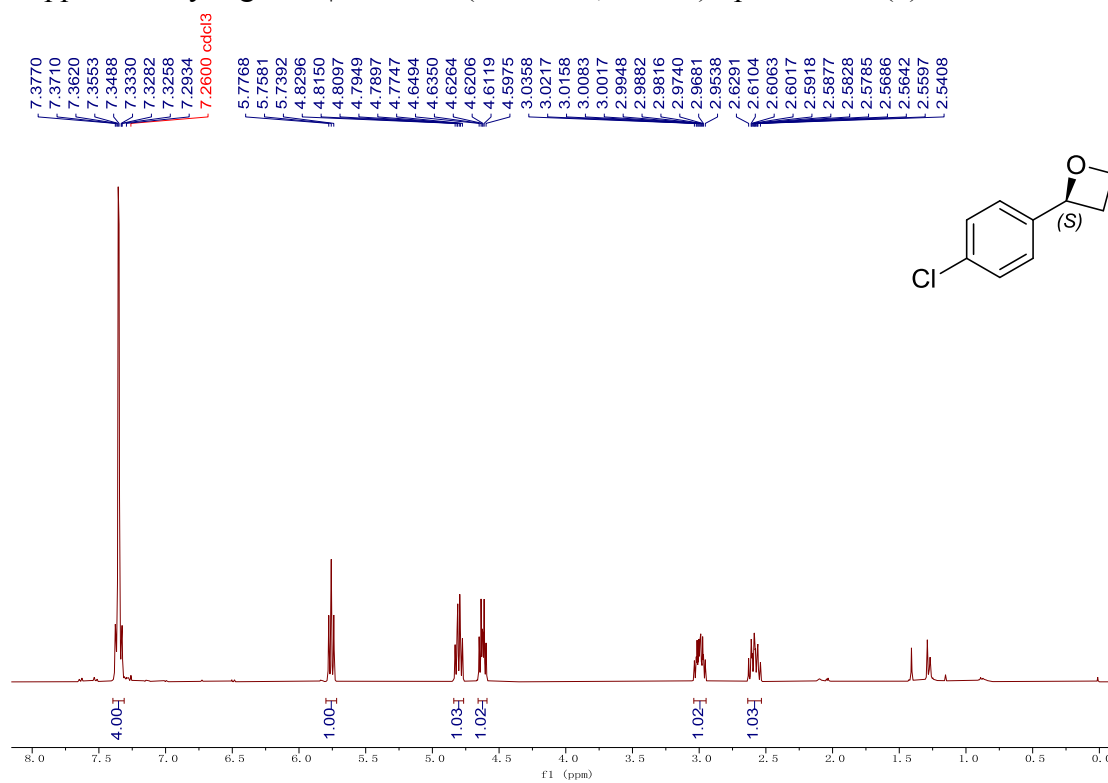
Supplementary Fig. 128 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**11b**.



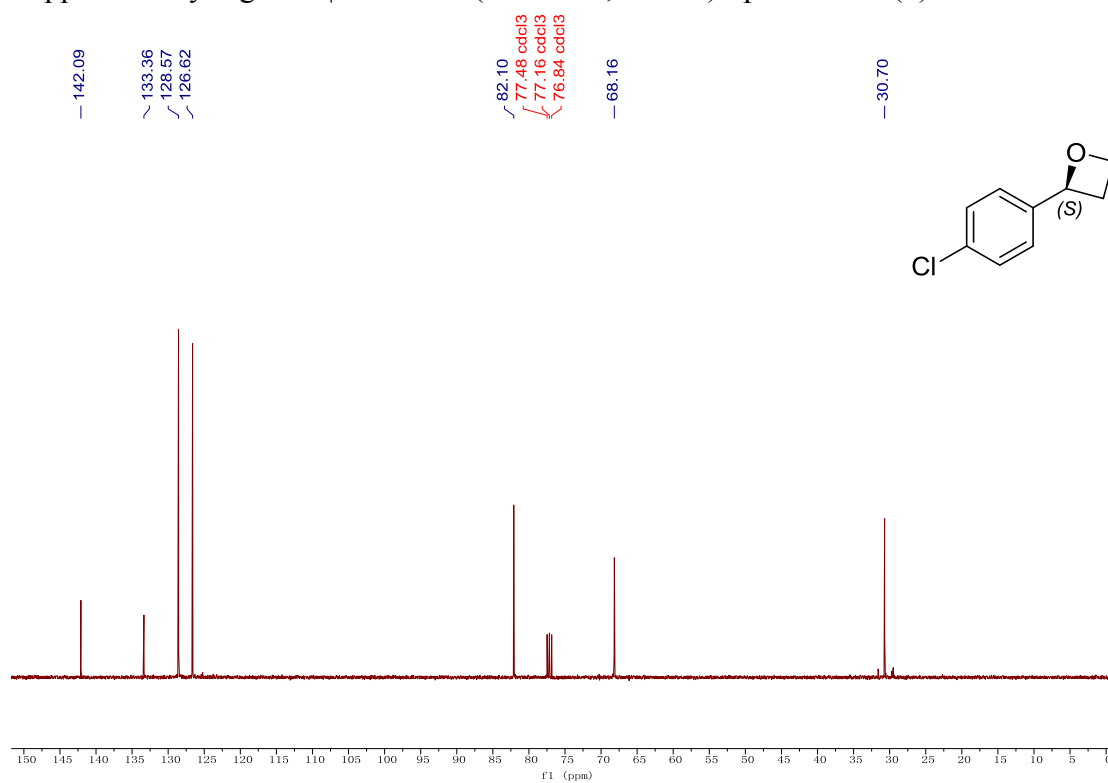
Supplementary Fig. 129 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**11b**.



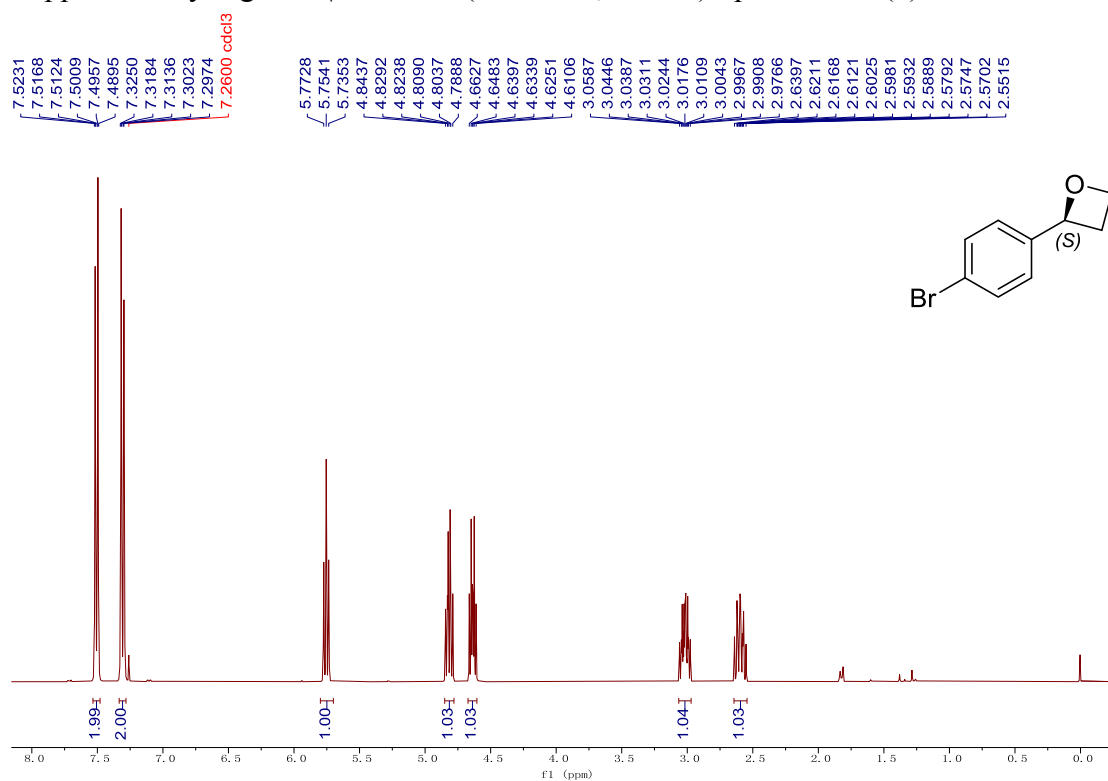
Supplementary Fig. 130 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**12b**.



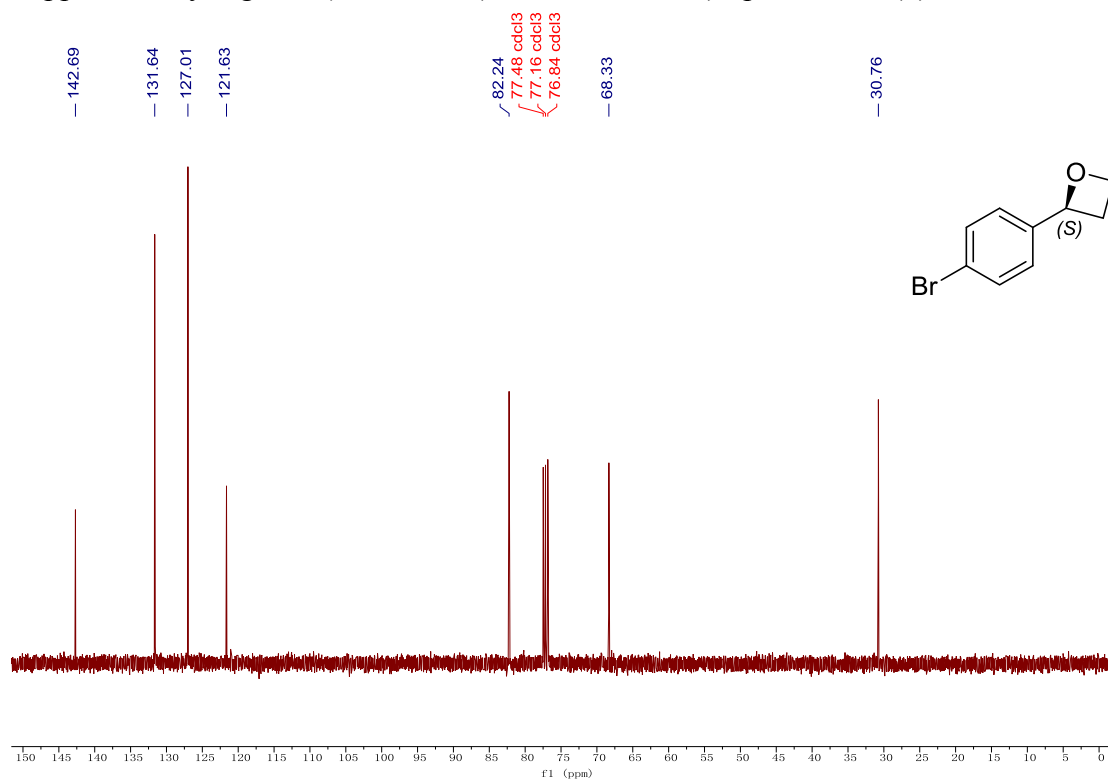
Supplementary Fig. 131 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**12b**.



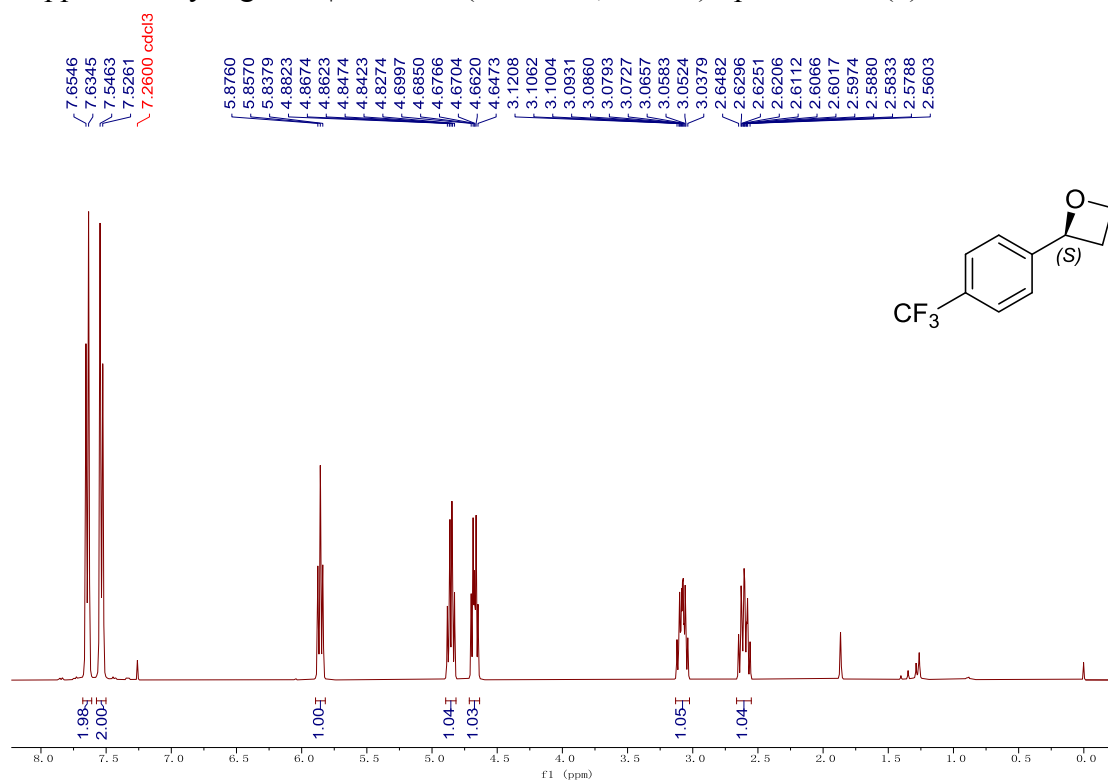
Supplementary Fig. 132 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**13b**.



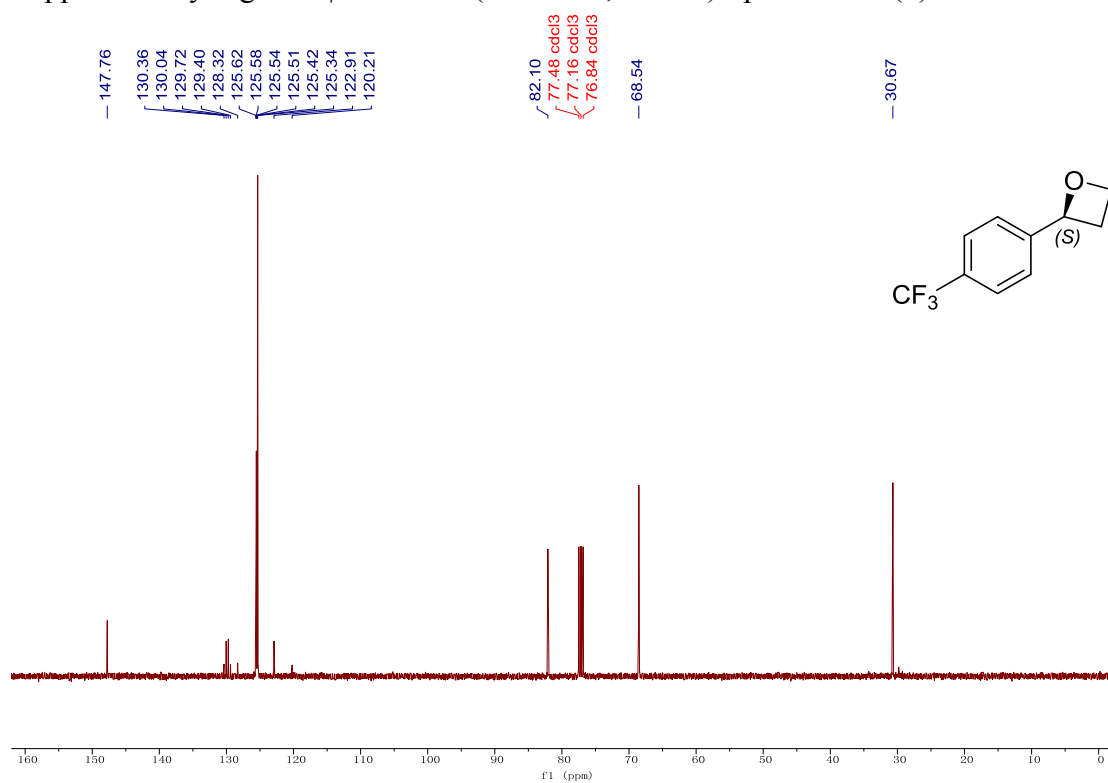
Supplementary Fig. 133 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**13b**.



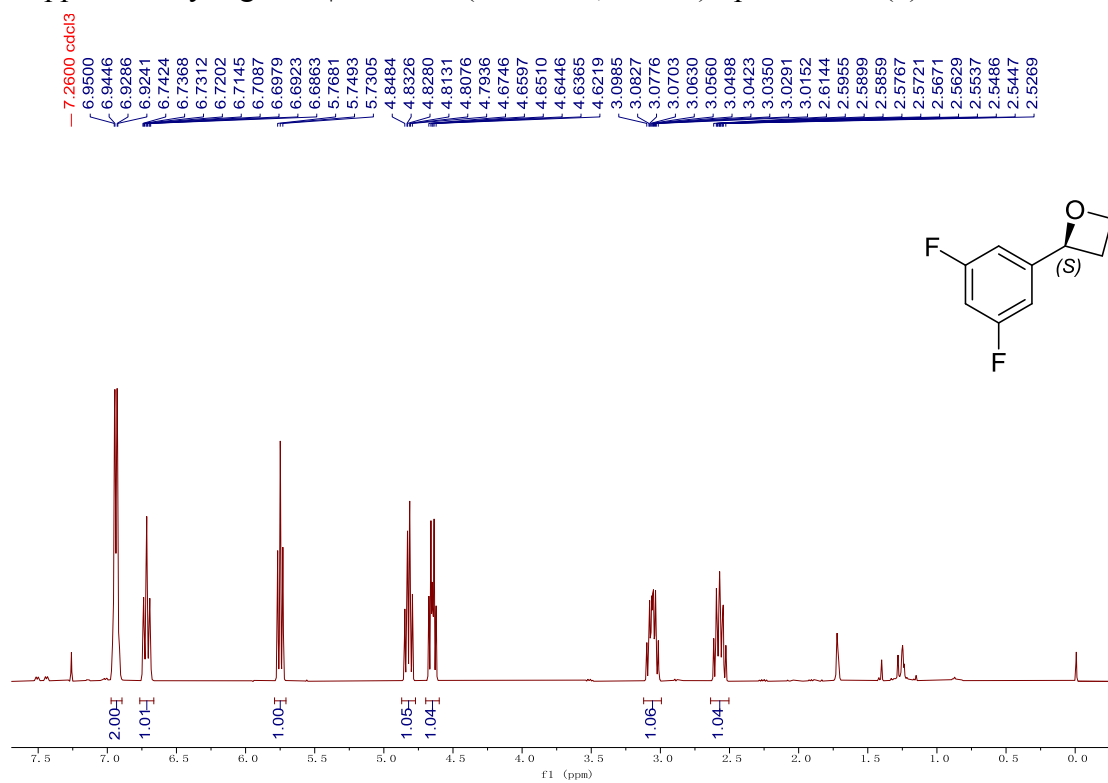
Supplementary Fig. 134 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**14b**.



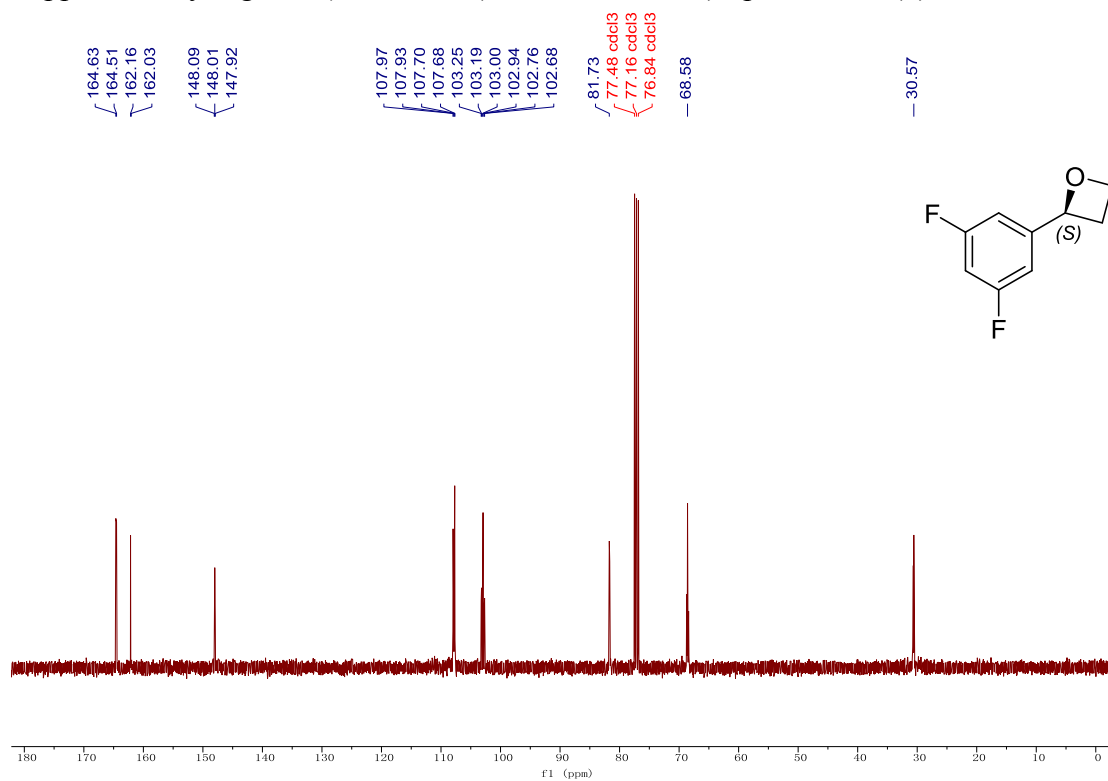
Supplementary Fig. 135 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**14b**.



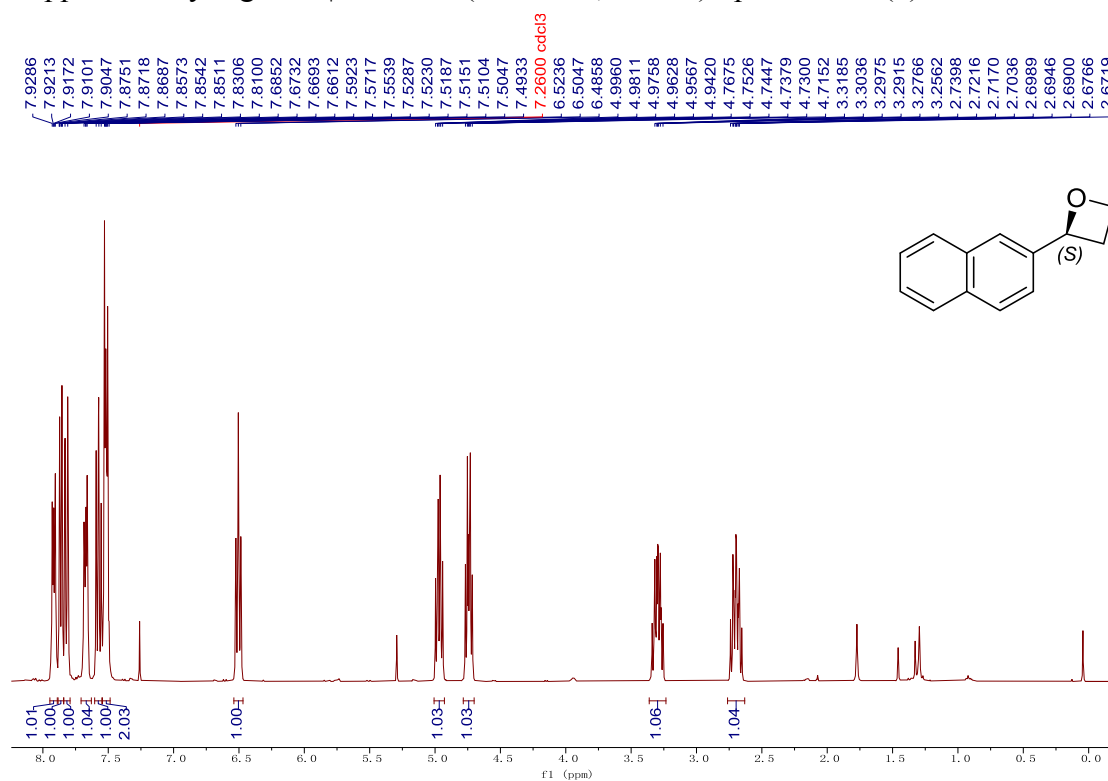
Supplementary Fig. 136 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**15b**.



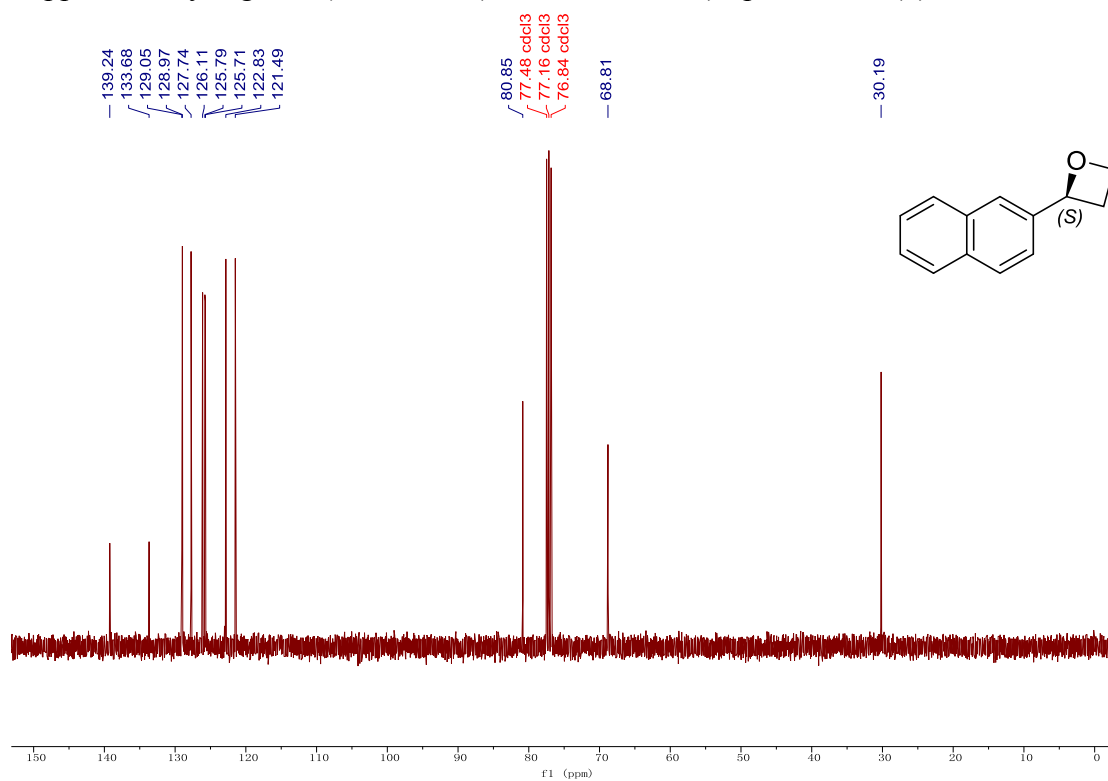
Supplementary Fig. 137 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**15b**.



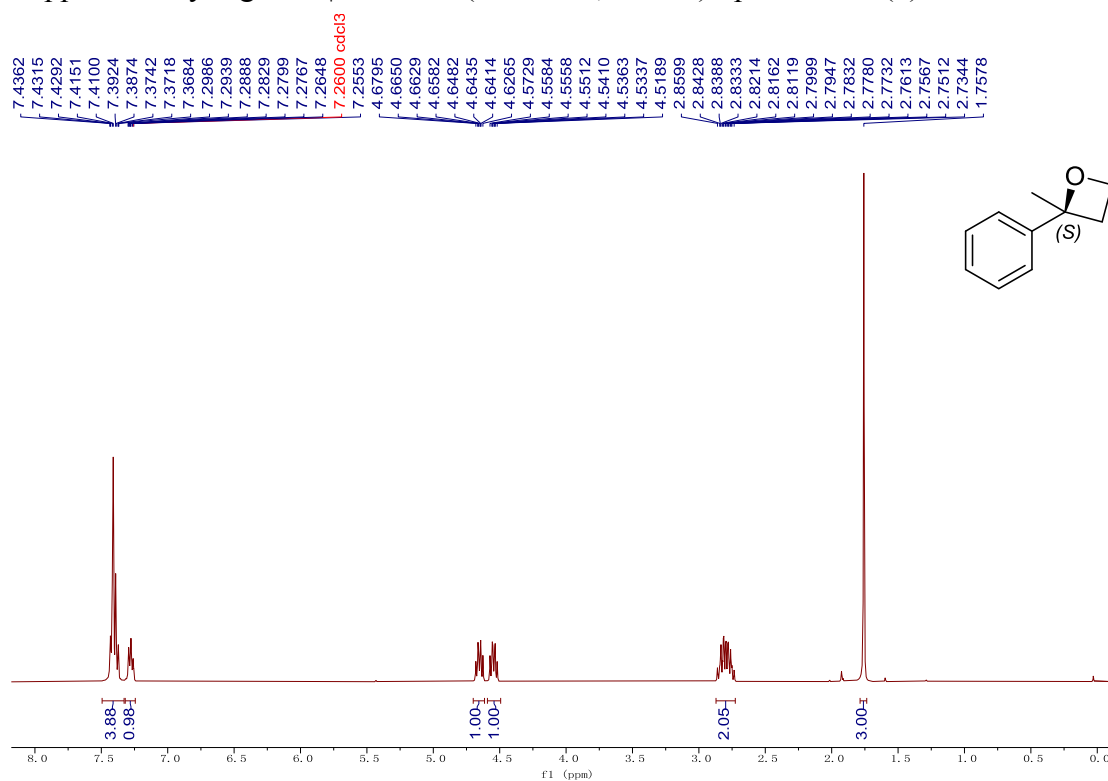
Supplementary Fig. 138 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**16b**.



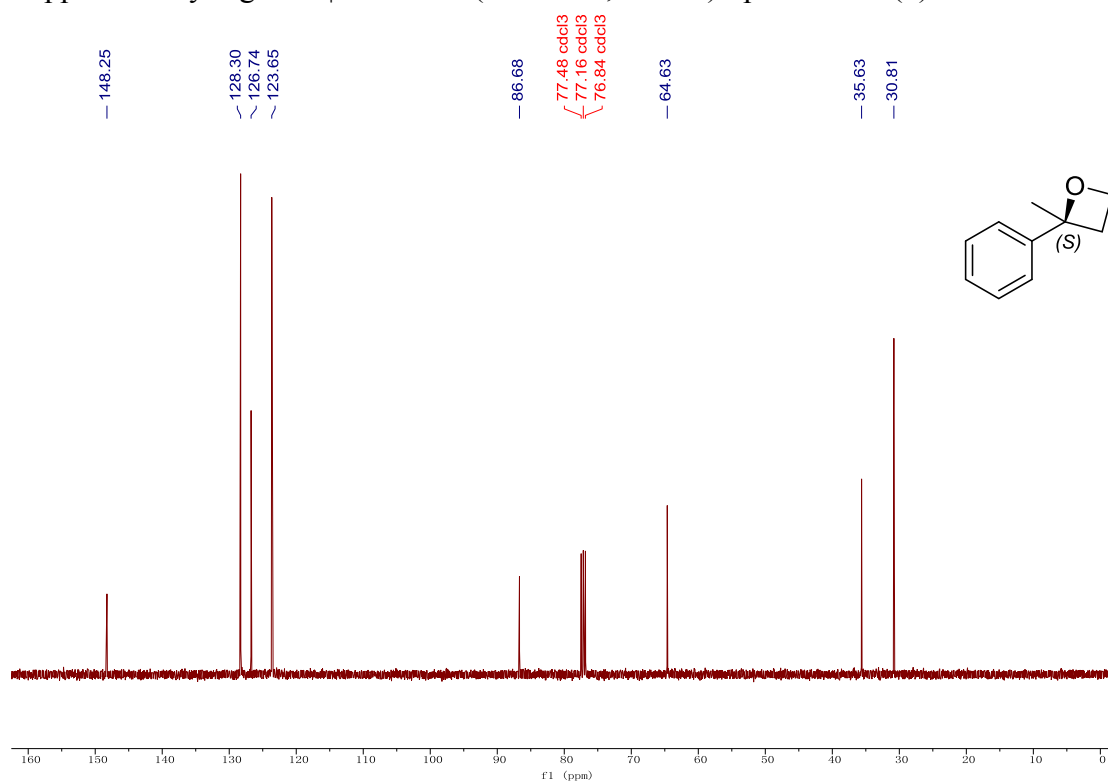
Supplementary Fig. 139 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**16b**.



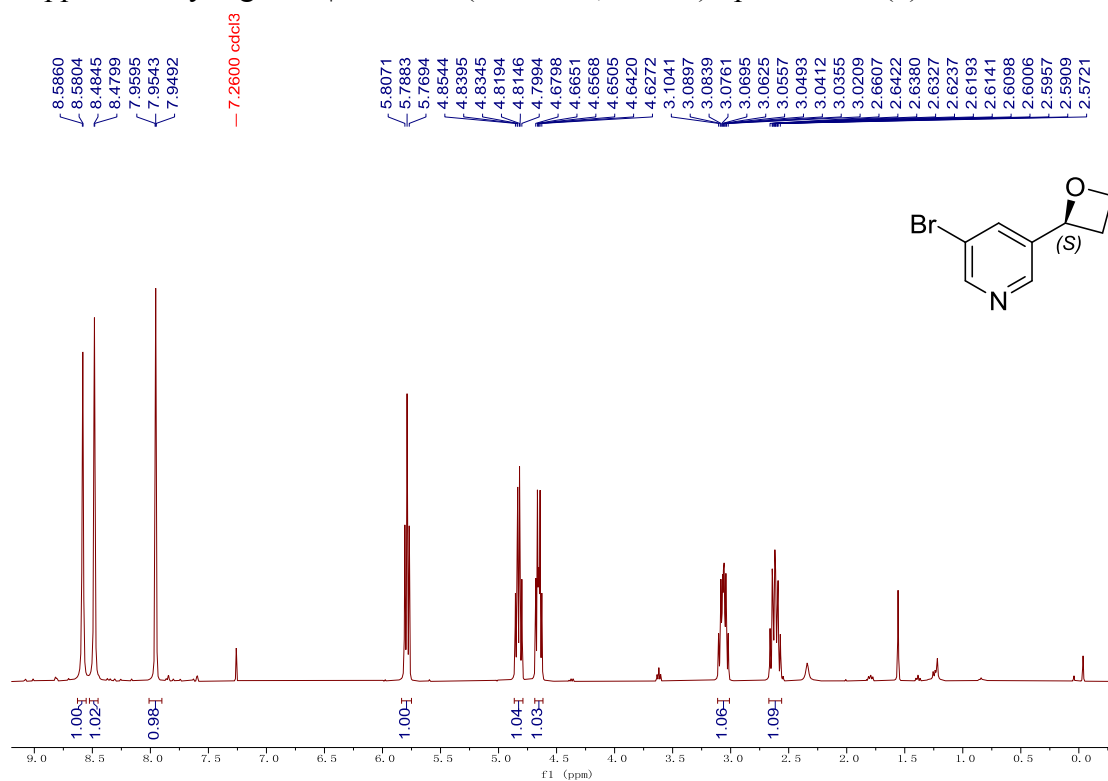
Supplementary Fig. 140 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**17b**.



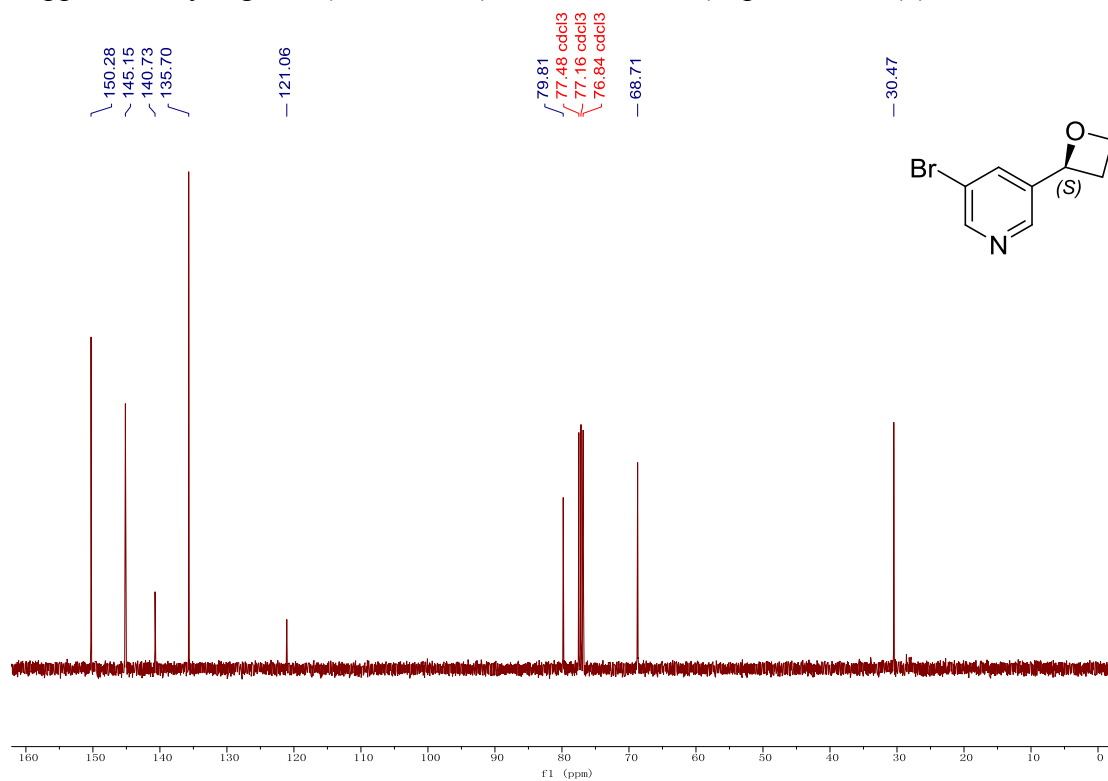
Supplementary Fig. 141 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**17b**.



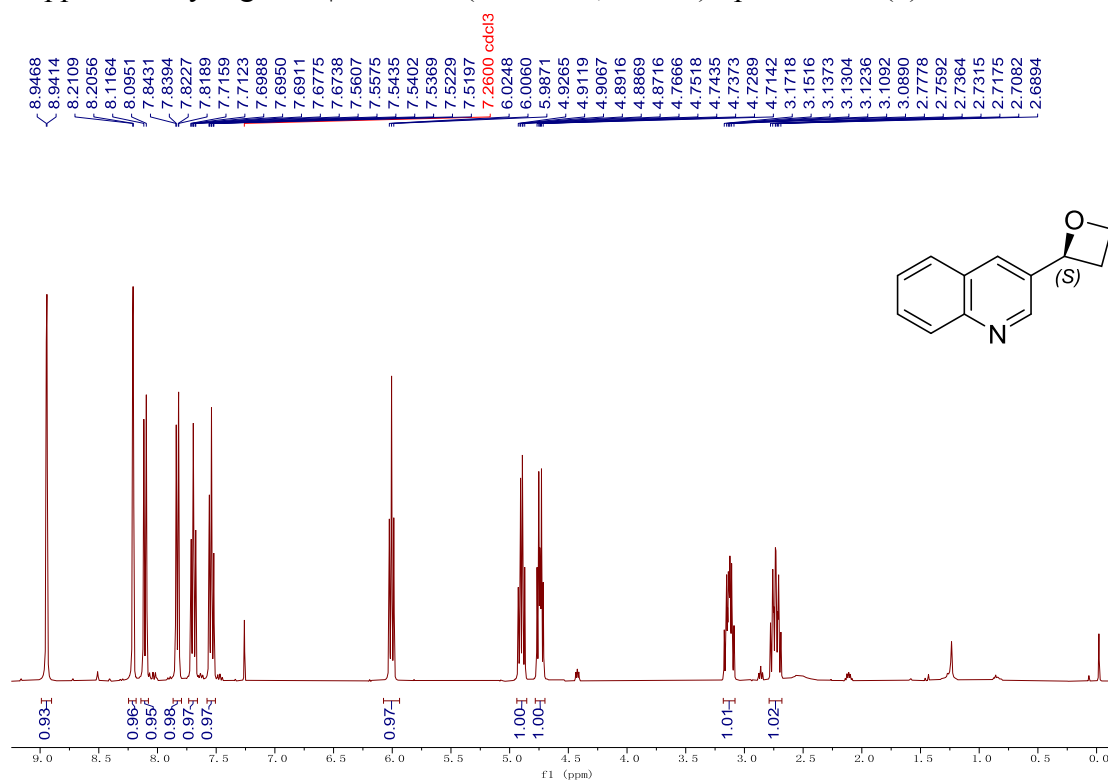
Supplementary Fig. 142 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**18b**.



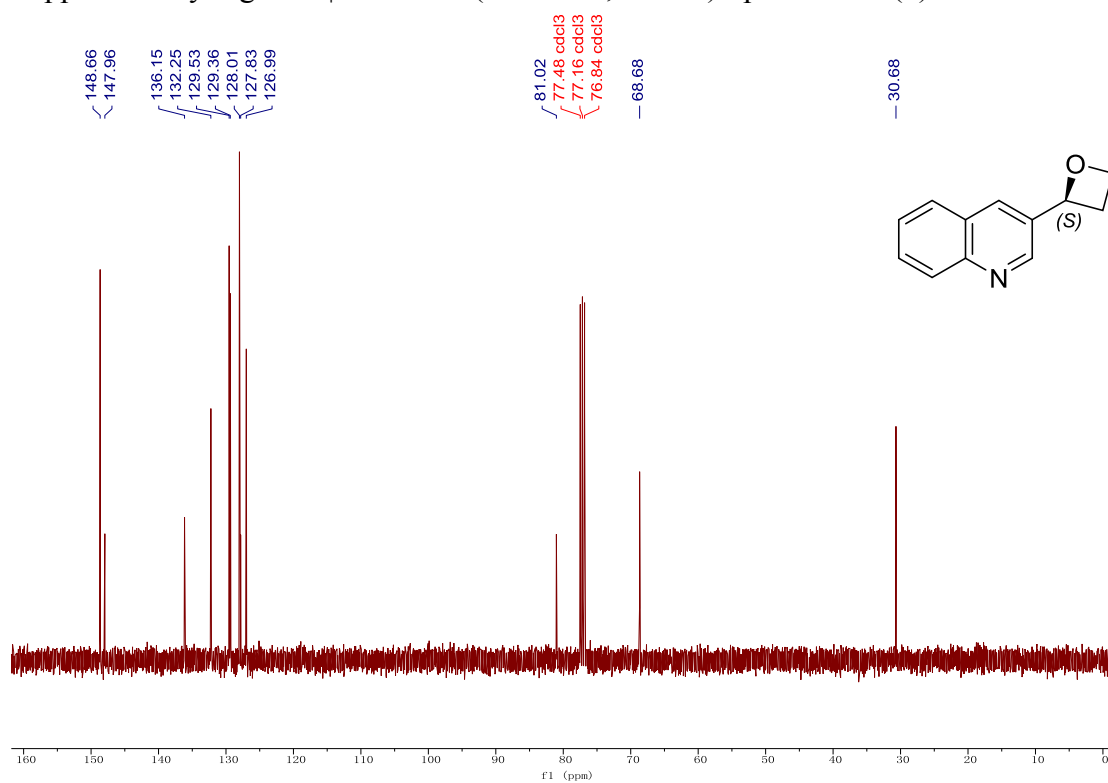
Supplementary Fig. 143 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**18b**.



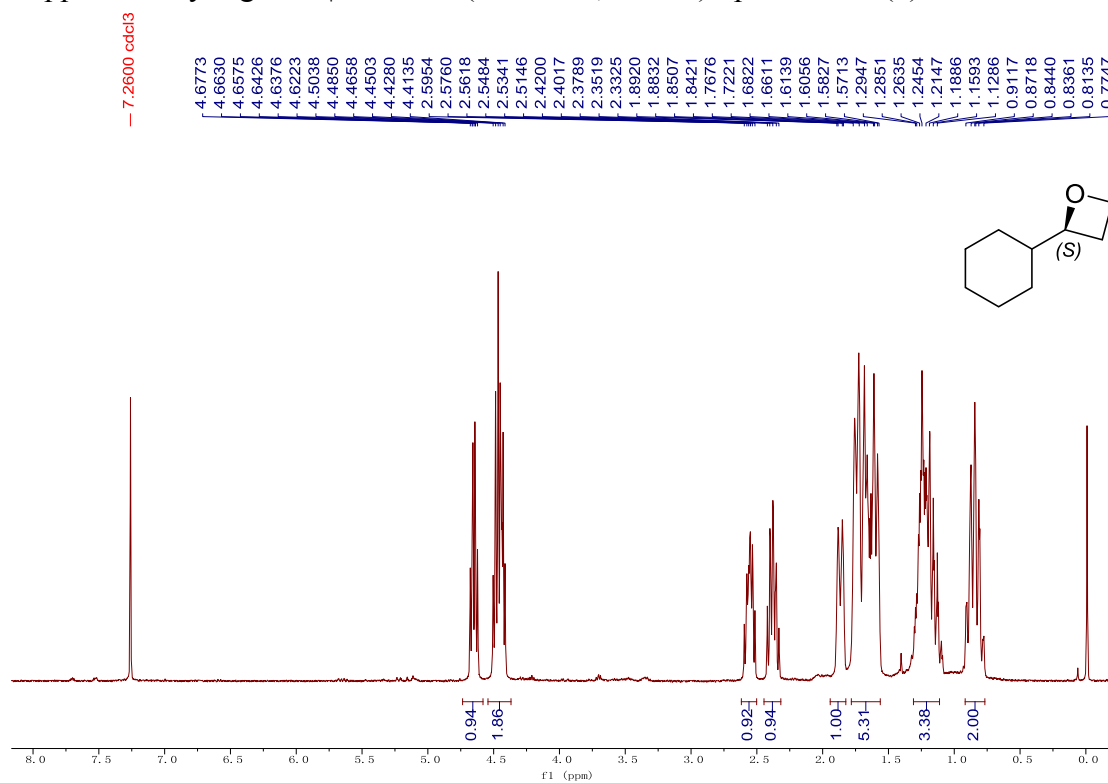
Supplementary Fig. 144 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**19b**.



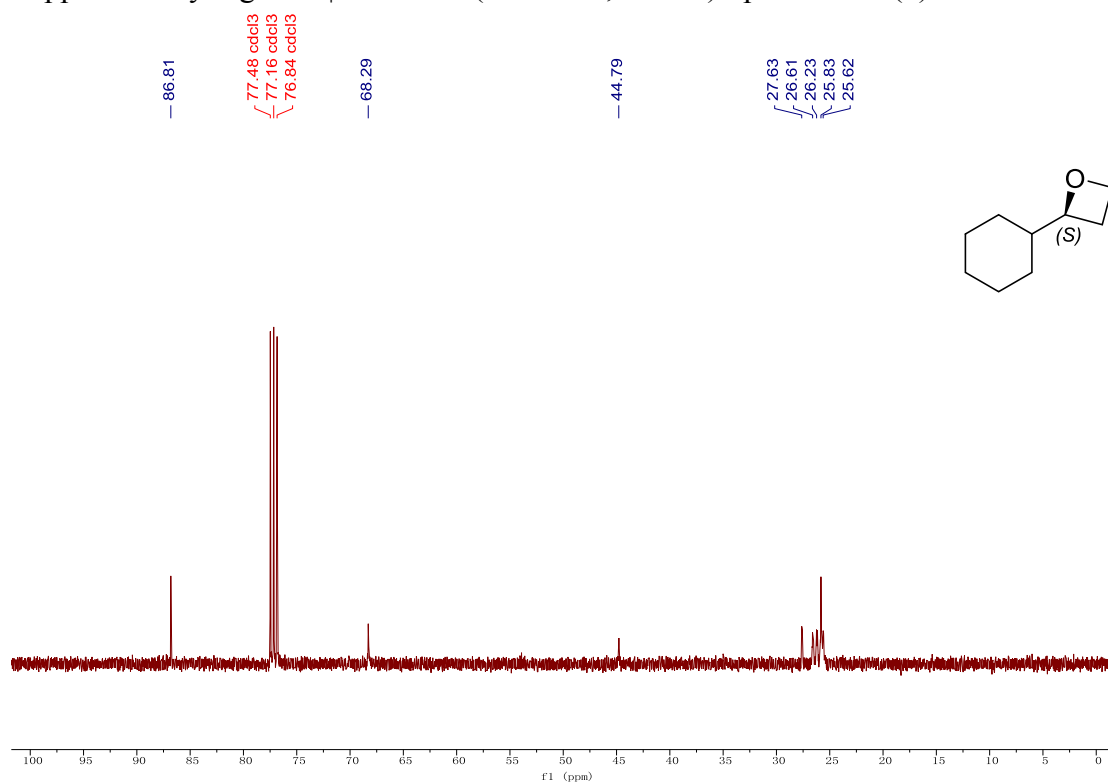
Supplementary Fig. 145 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**19b**.



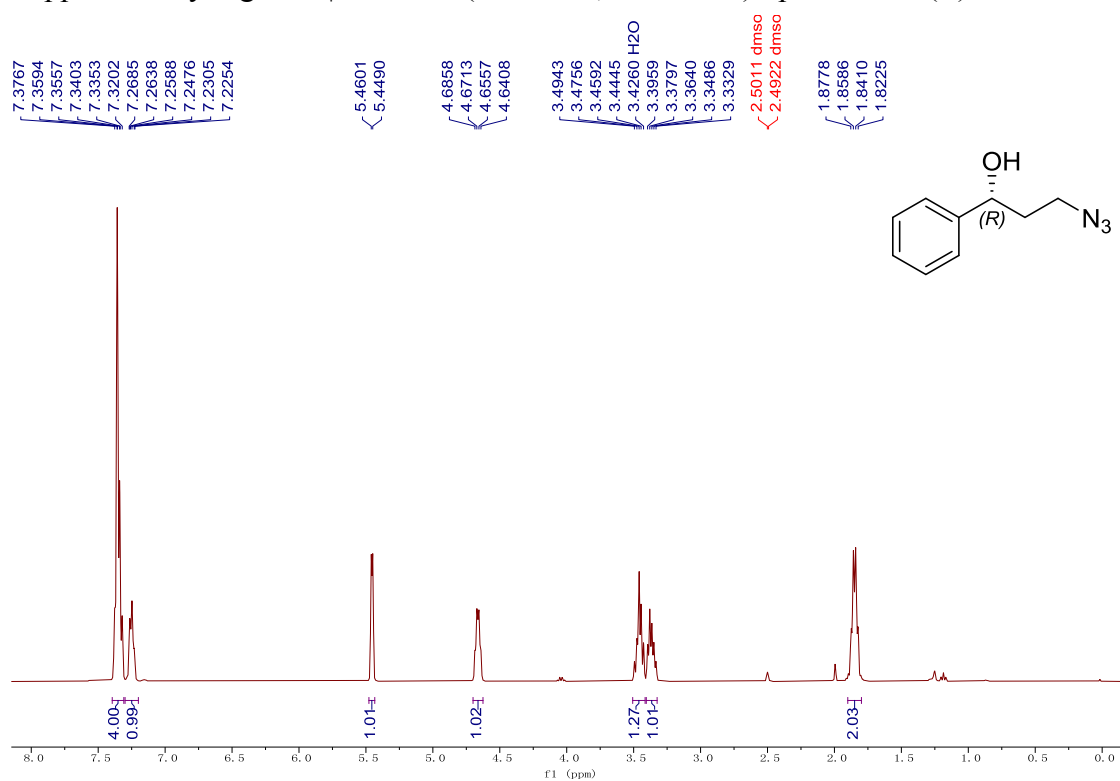
Supplementary Fig. 146 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**21b**.



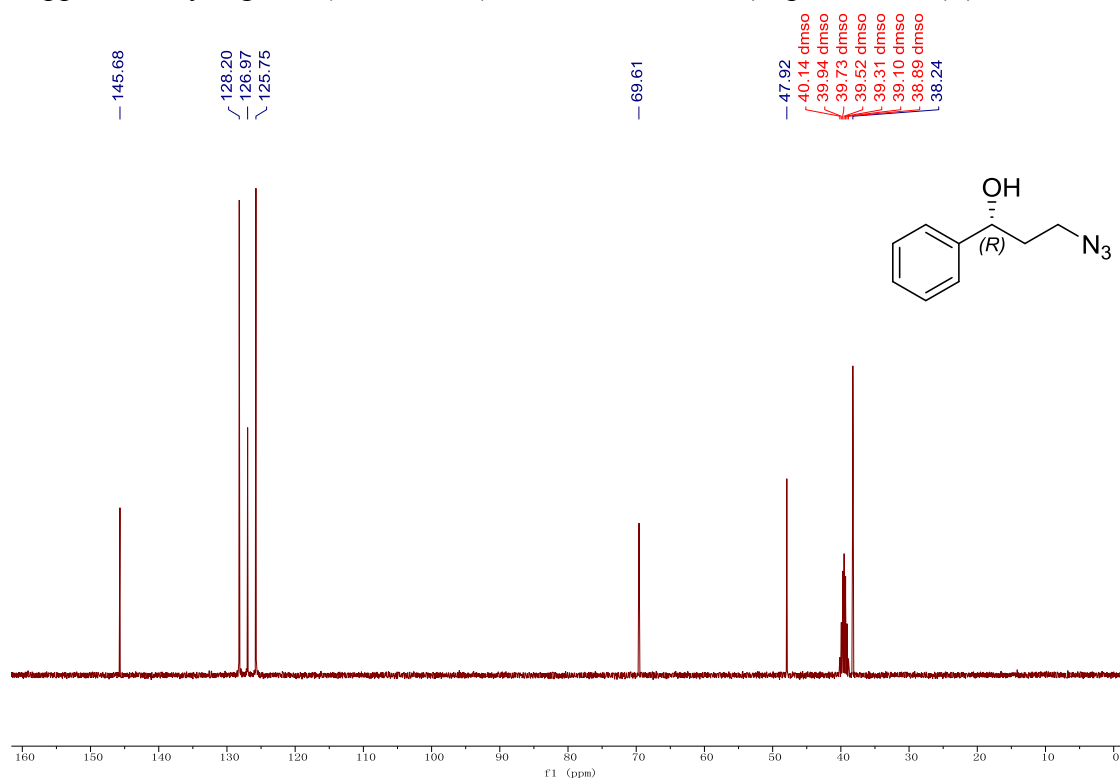
Supplementary Fig. 147 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**21b**.



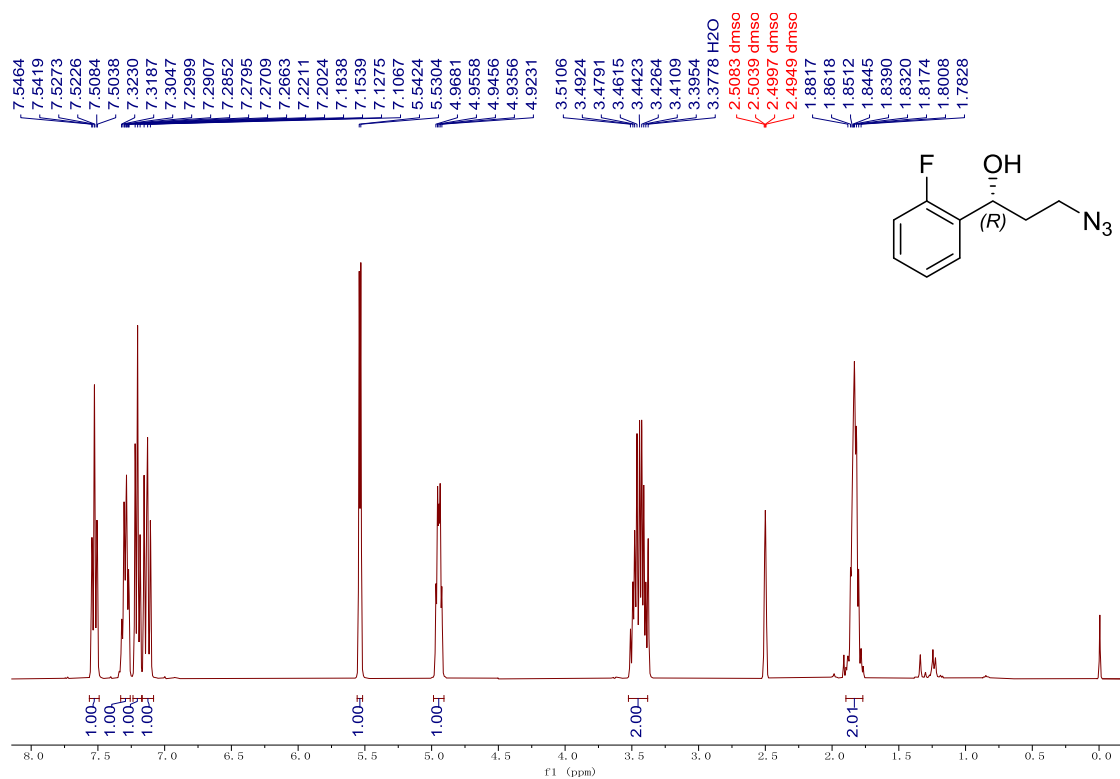
Supplementary Fig. 148 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**1c**.



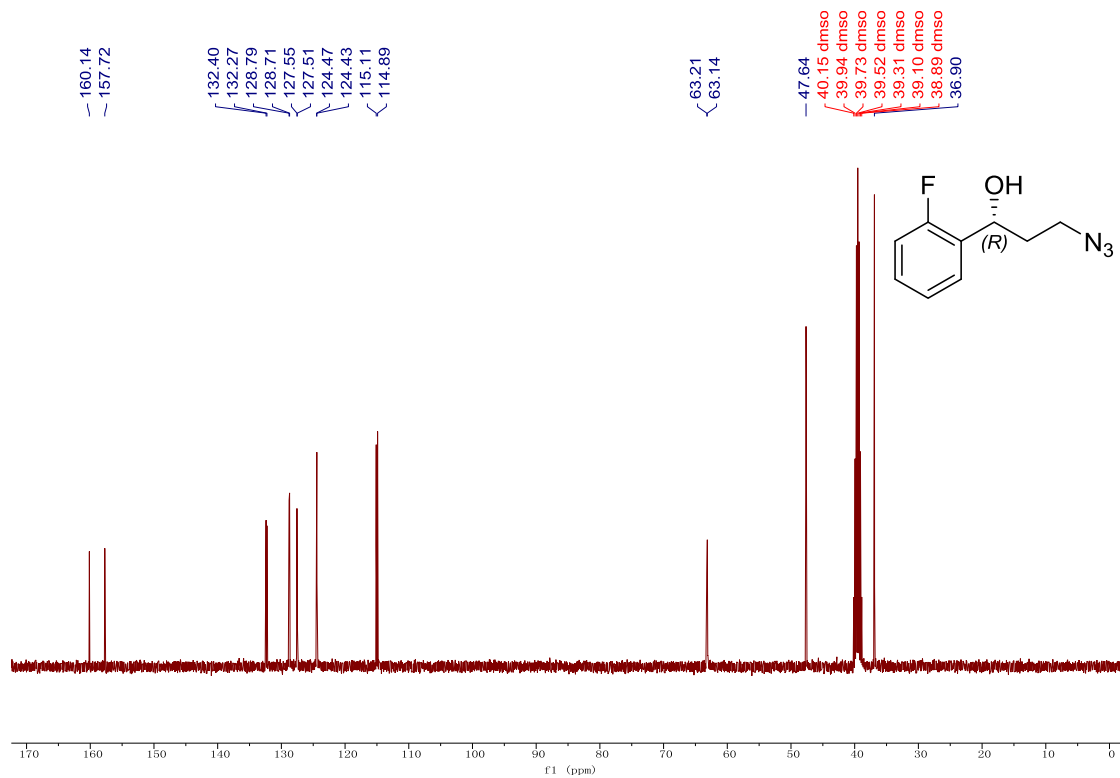
Supplementary Fig. 149 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**1c**.



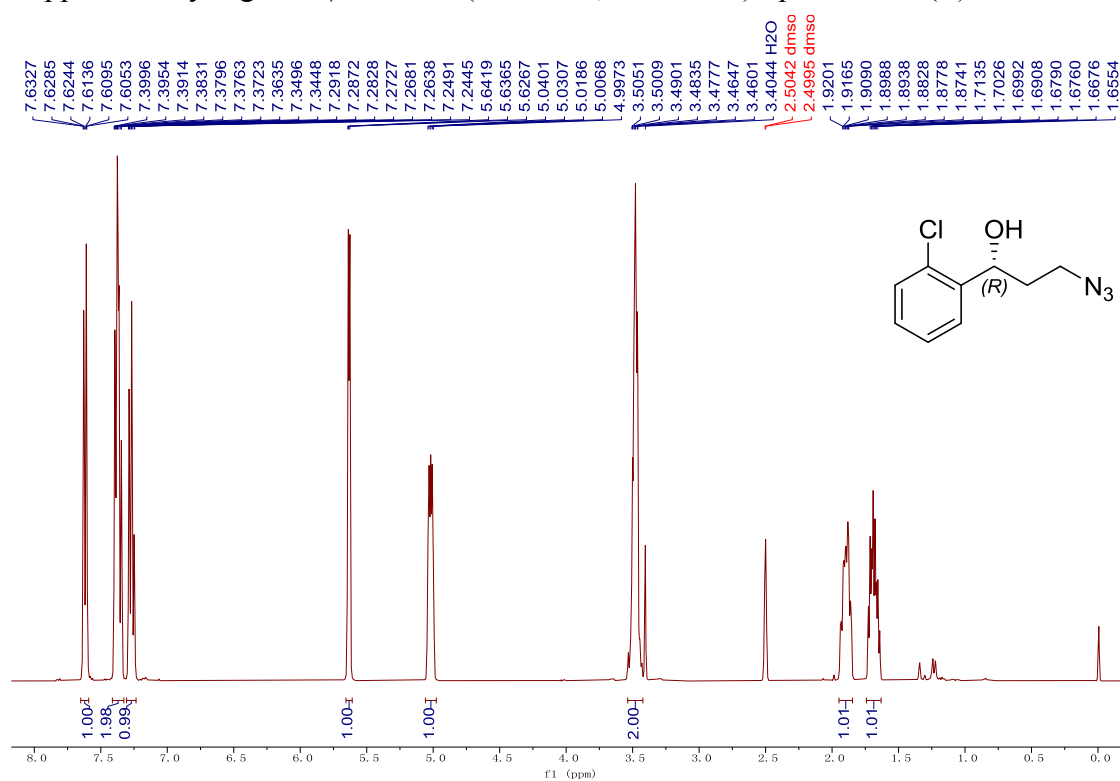
Supplementary Fig. 150 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**2c**.



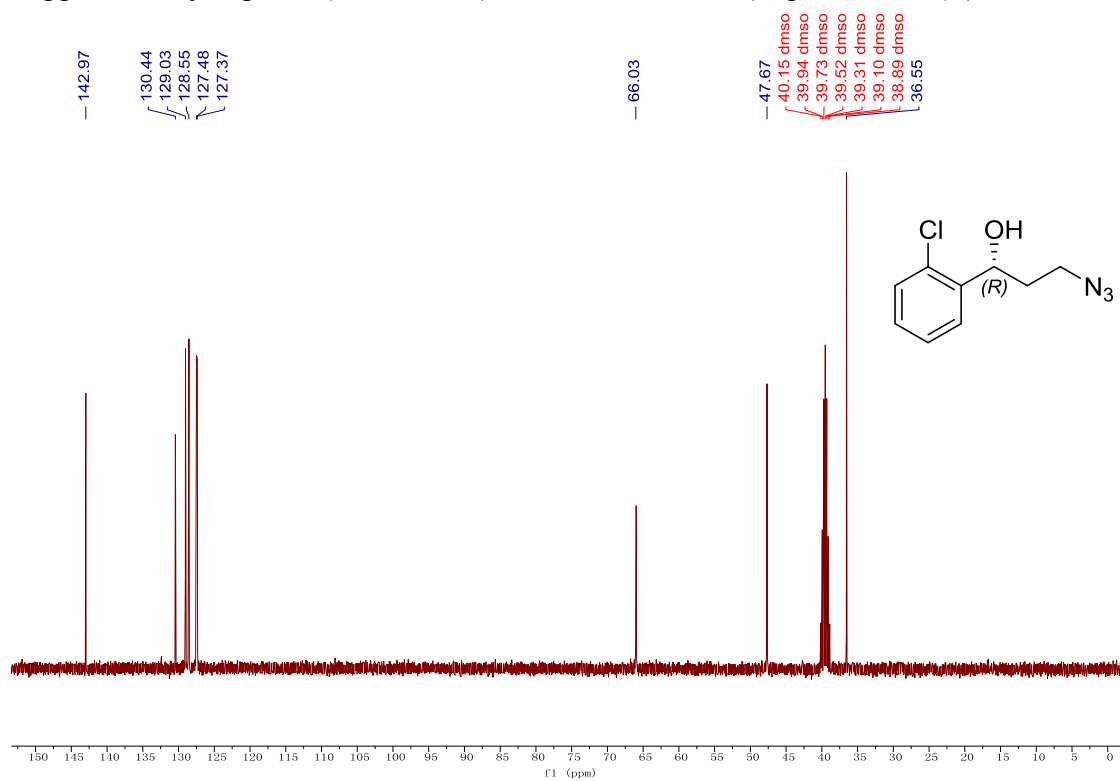
Supplementary Fig. 151 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**2c**.



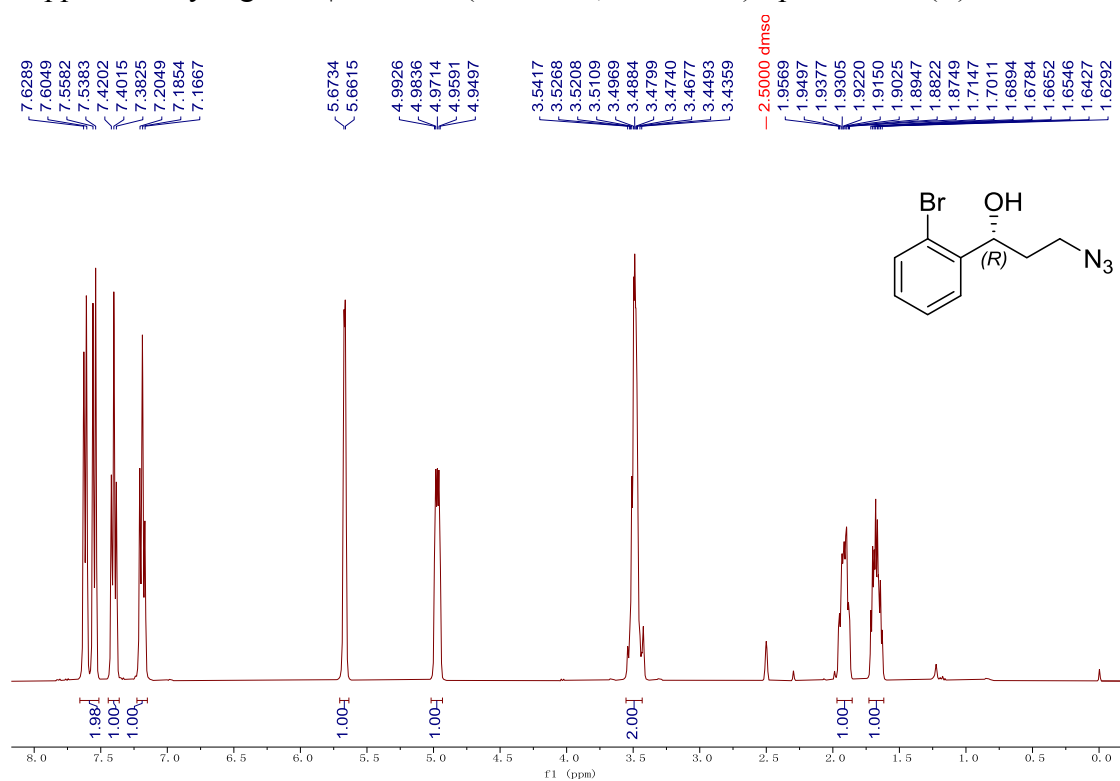
Supplementary Fig. 152 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**3c**.



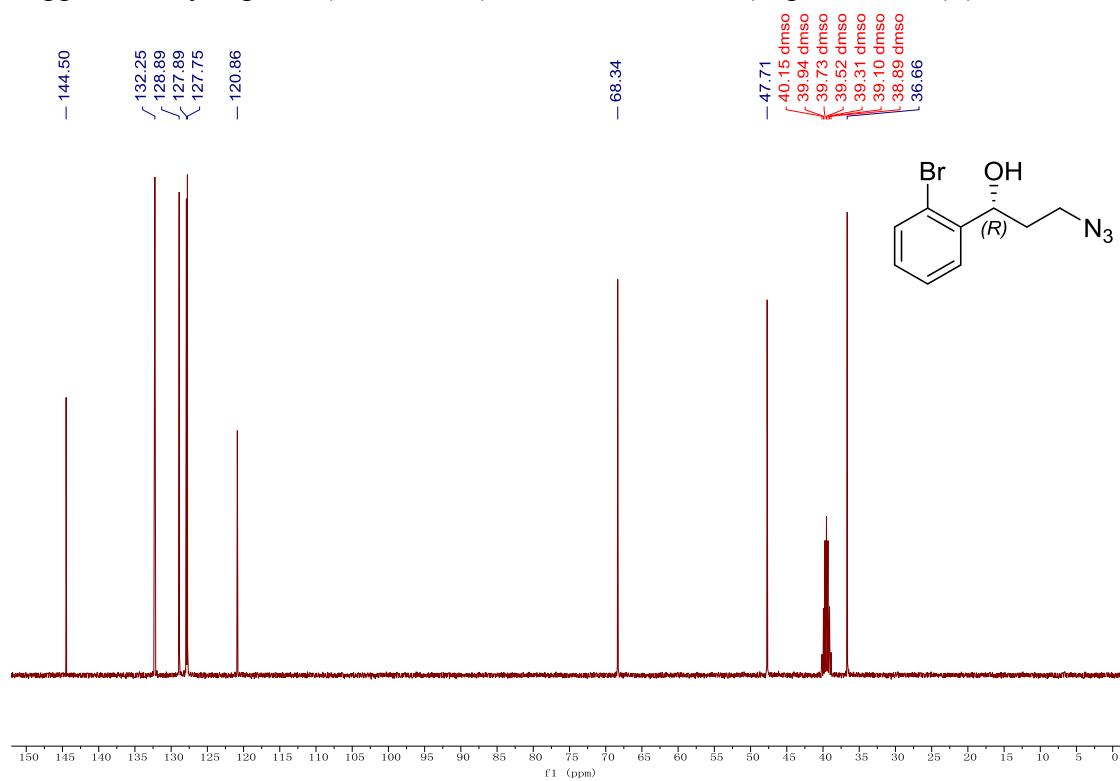
Supplementary Fig. 153 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**3c**.



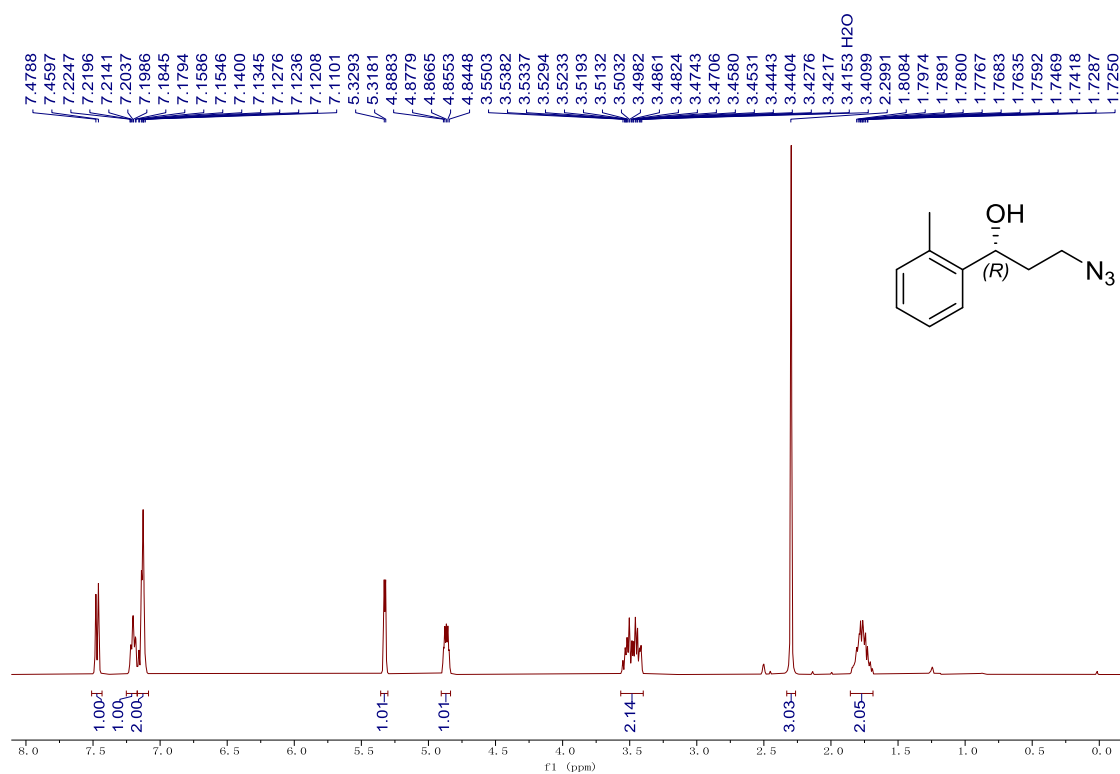
Supplementary Fig. 154 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**4c**.



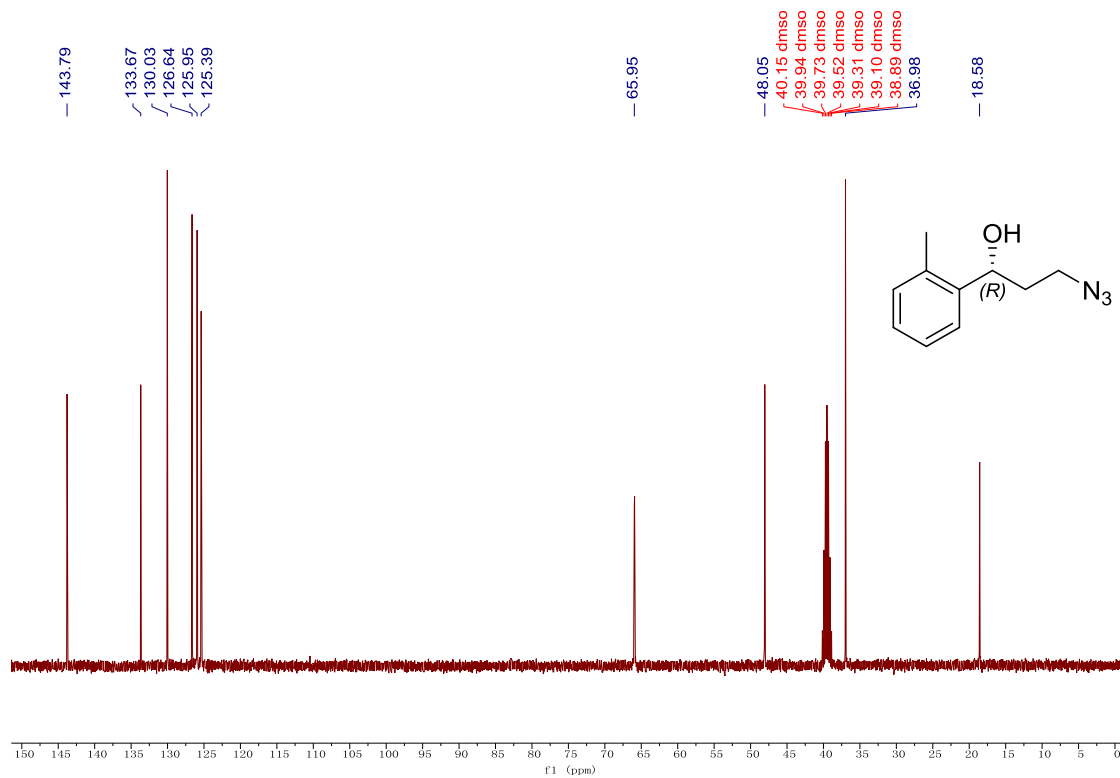
Supplementary Fig. 155 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**4c**.



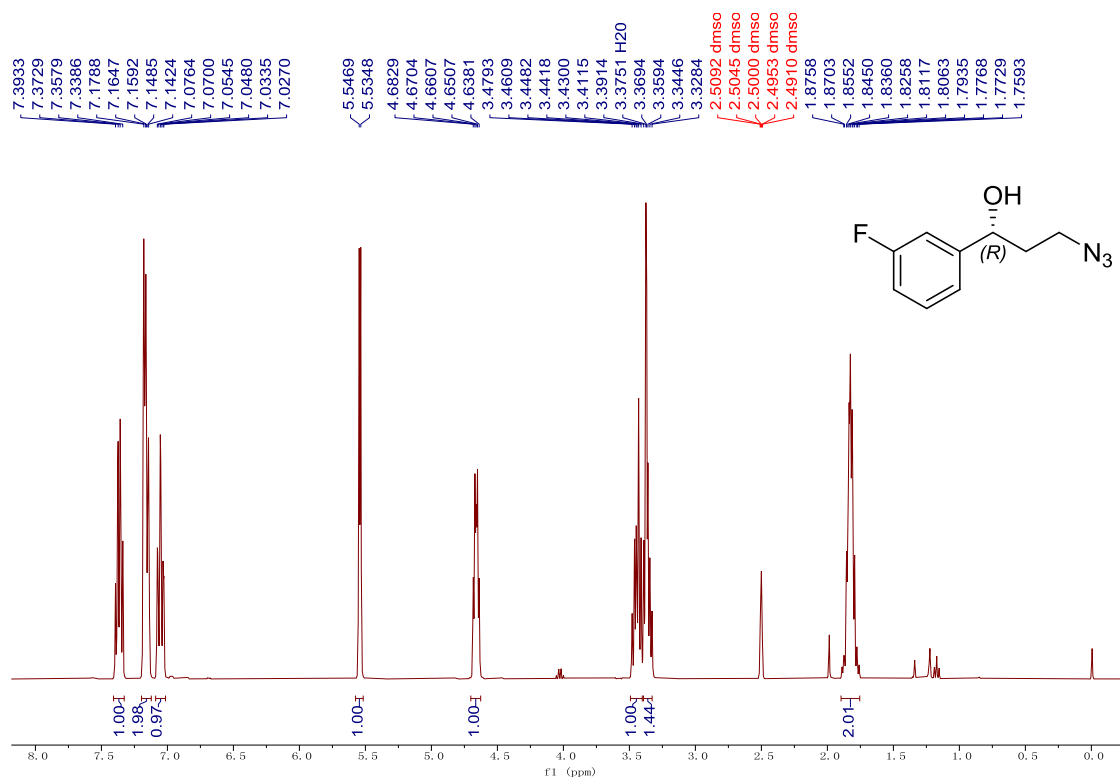
Supplementary Fig. 156 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**5c**.



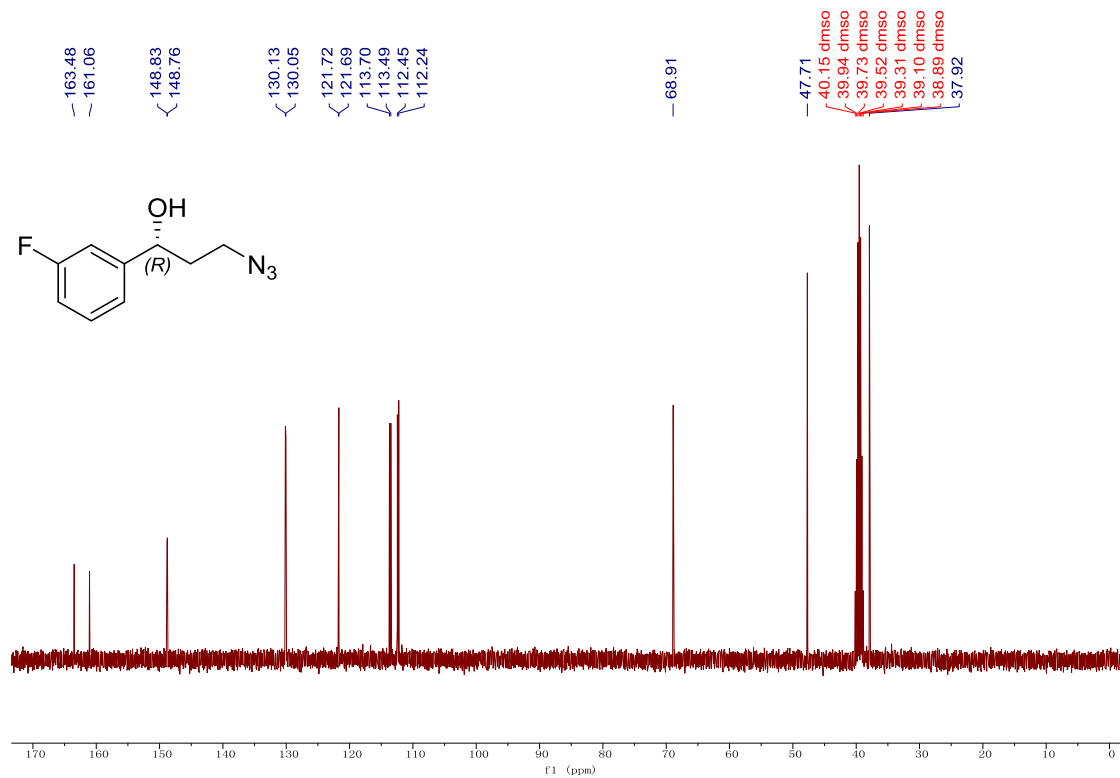
Supplementary Fig. 157 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**5c**.



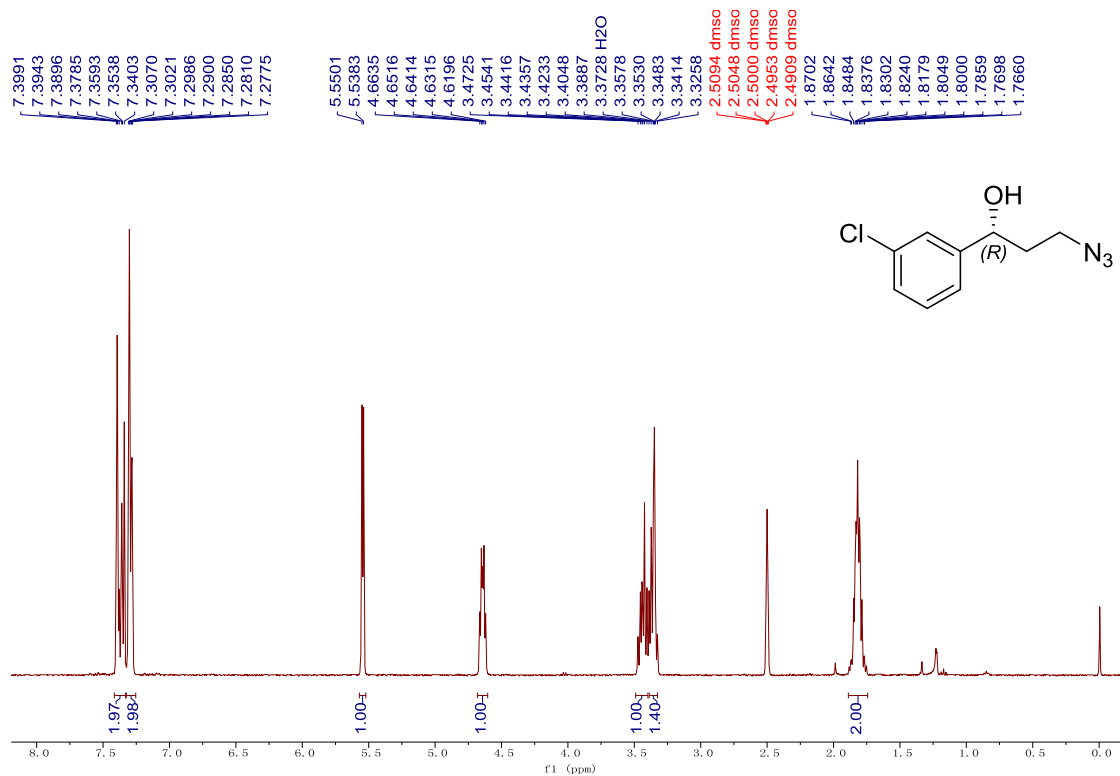
Supplementary Fig. 158 | ^1H NMR (400 MHz, DMSO-d_6) Spectrum of (*R*)-**6c**.



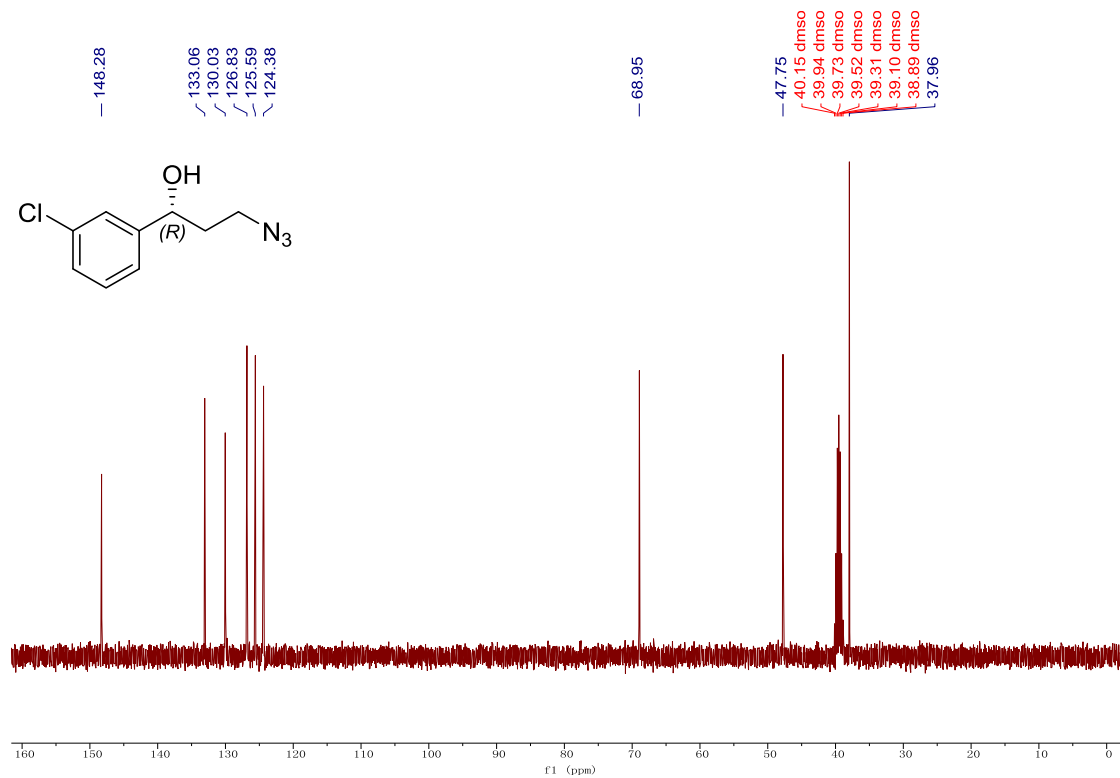
Supplementary Fig. 159 | ^{13}C NMR (100 MHz, DMSO-d_6) Spectrum of (*R*)-**6c**.



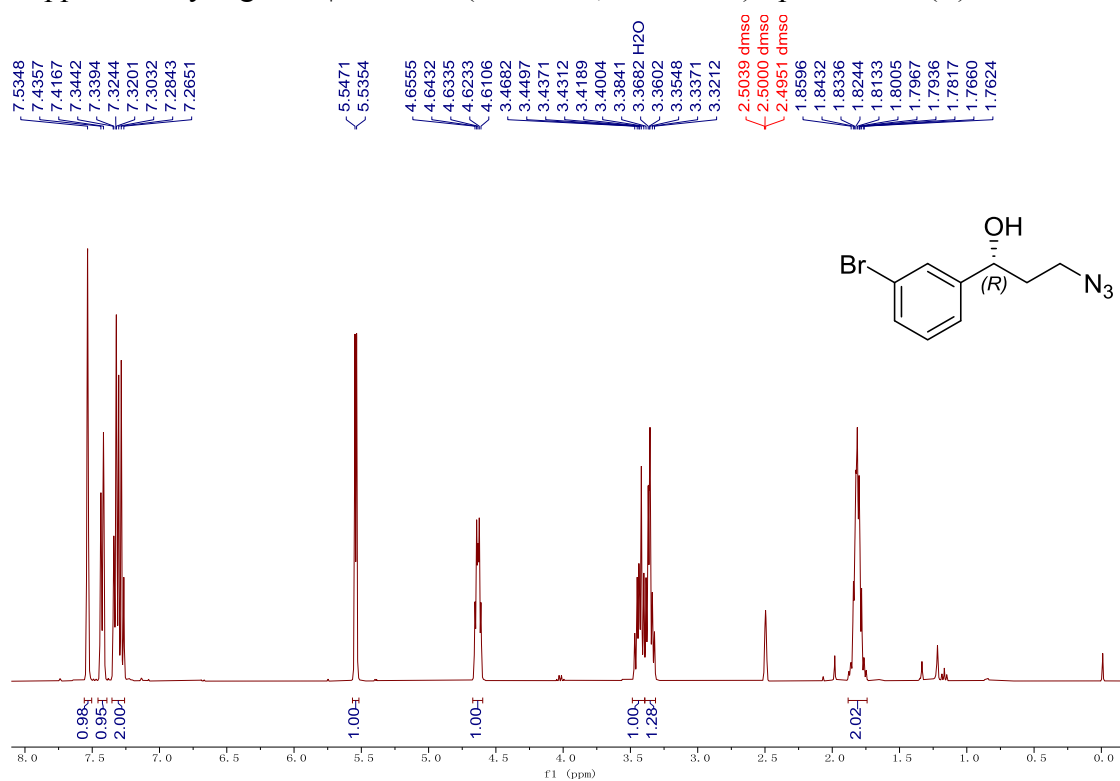
Supplementary Fig. 160 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**7c**.



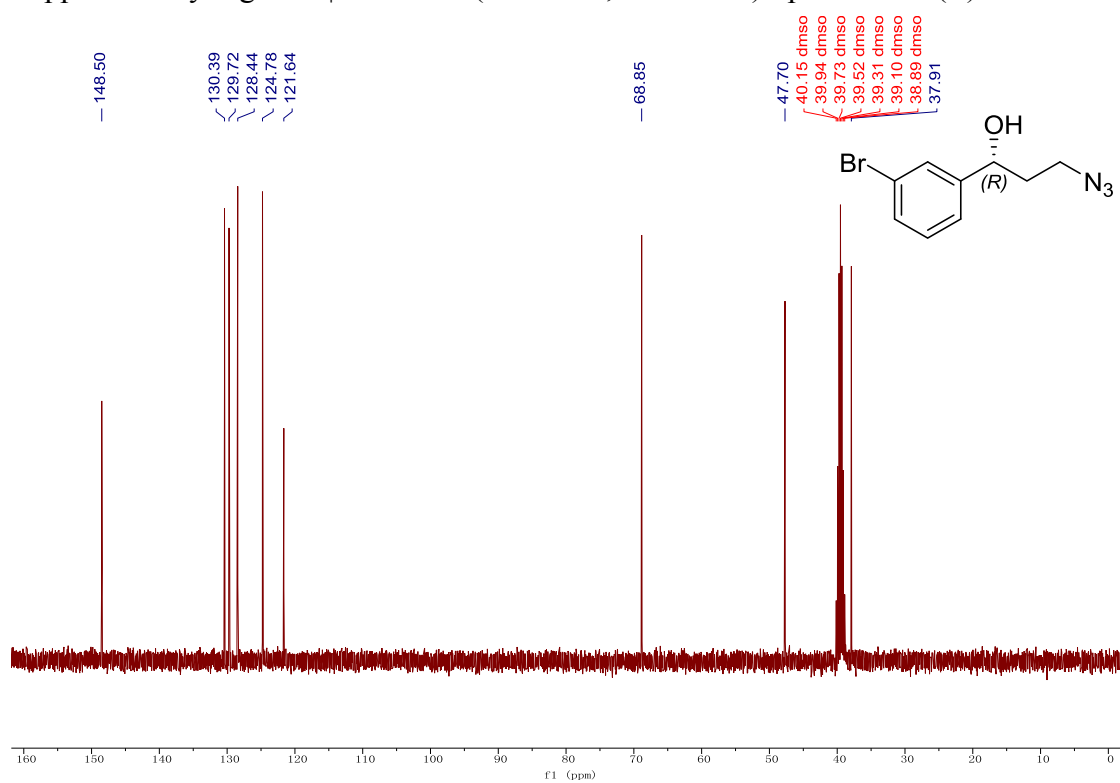
Supplementary Fig. 161 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**7c**.



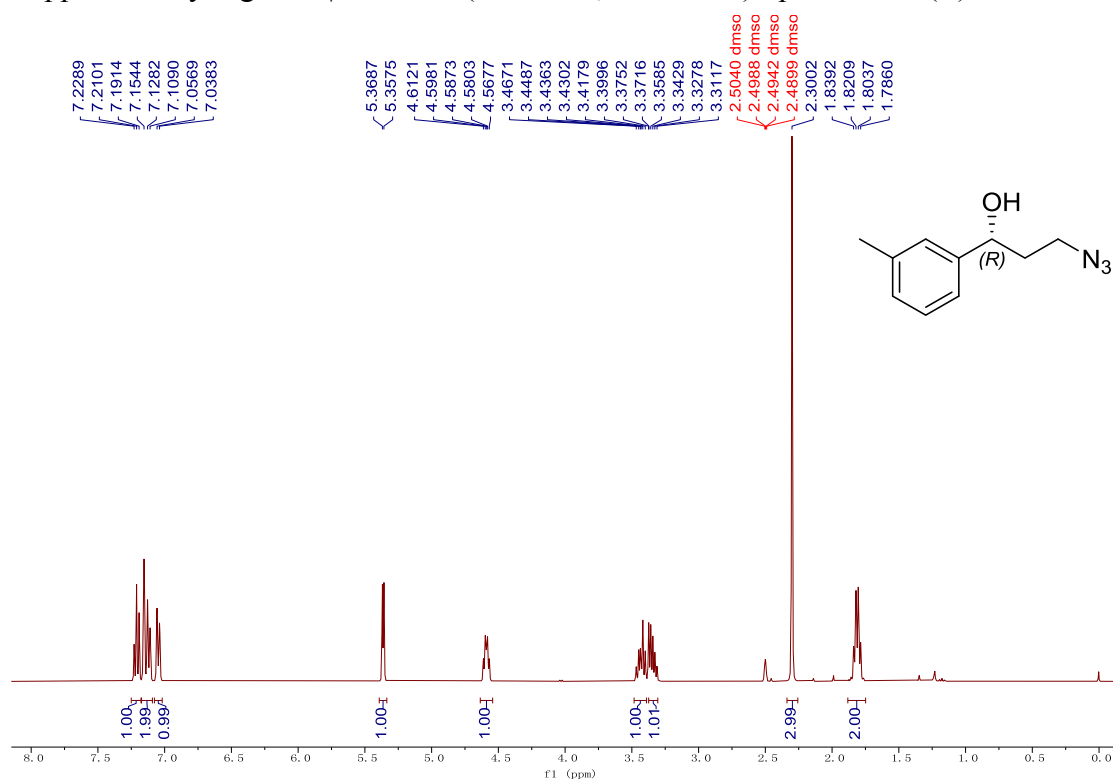
Supplementary Fig. 162 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**8c**.



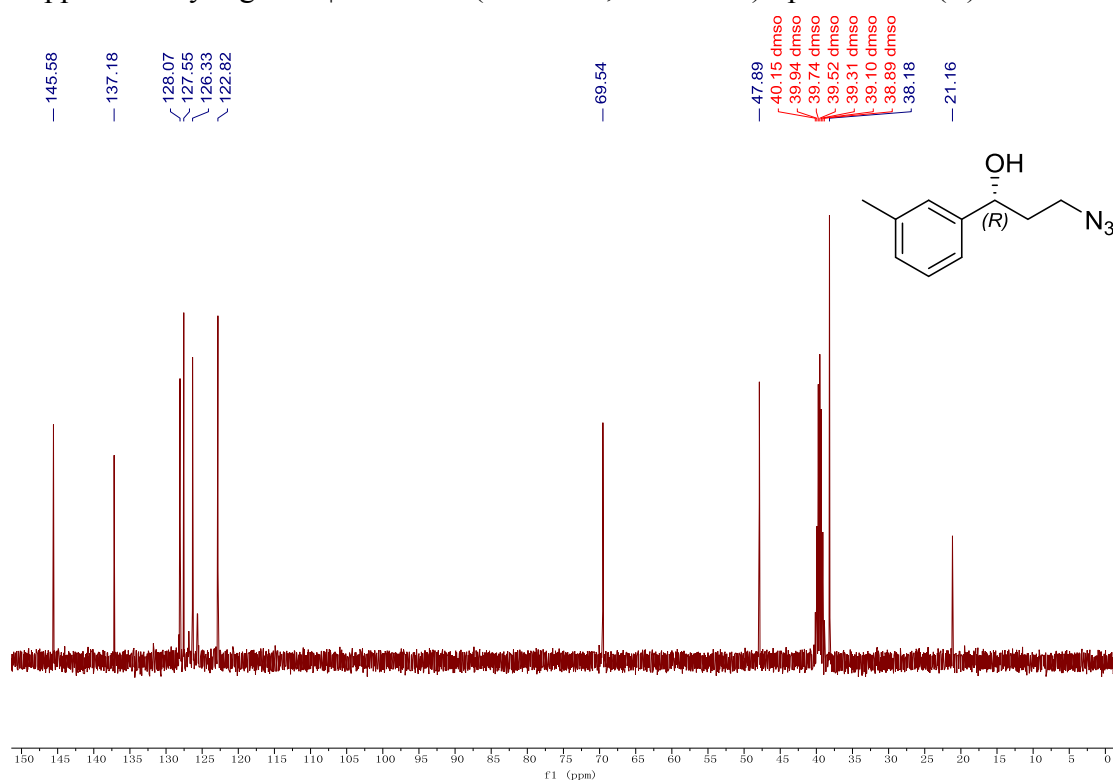
Supplementary Fig. 163 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**8c**.



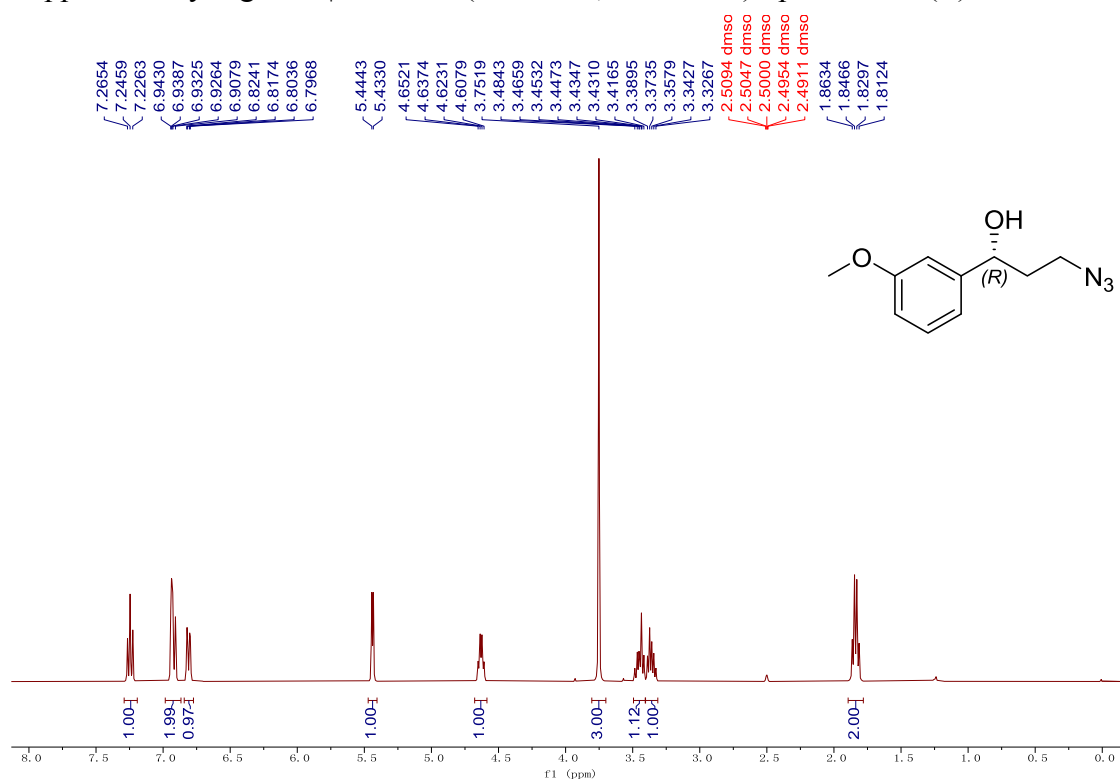
Supplementary Fig. 164 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**9c**.



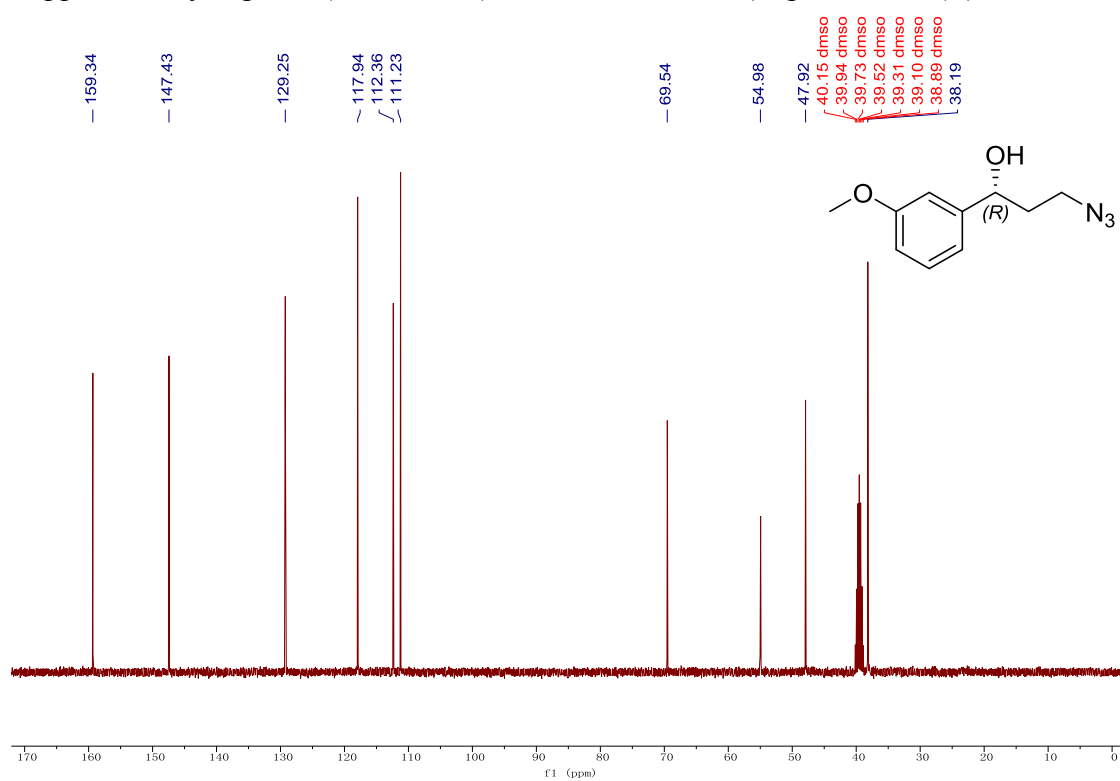
Supplementary Fig. 165 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**9c**.



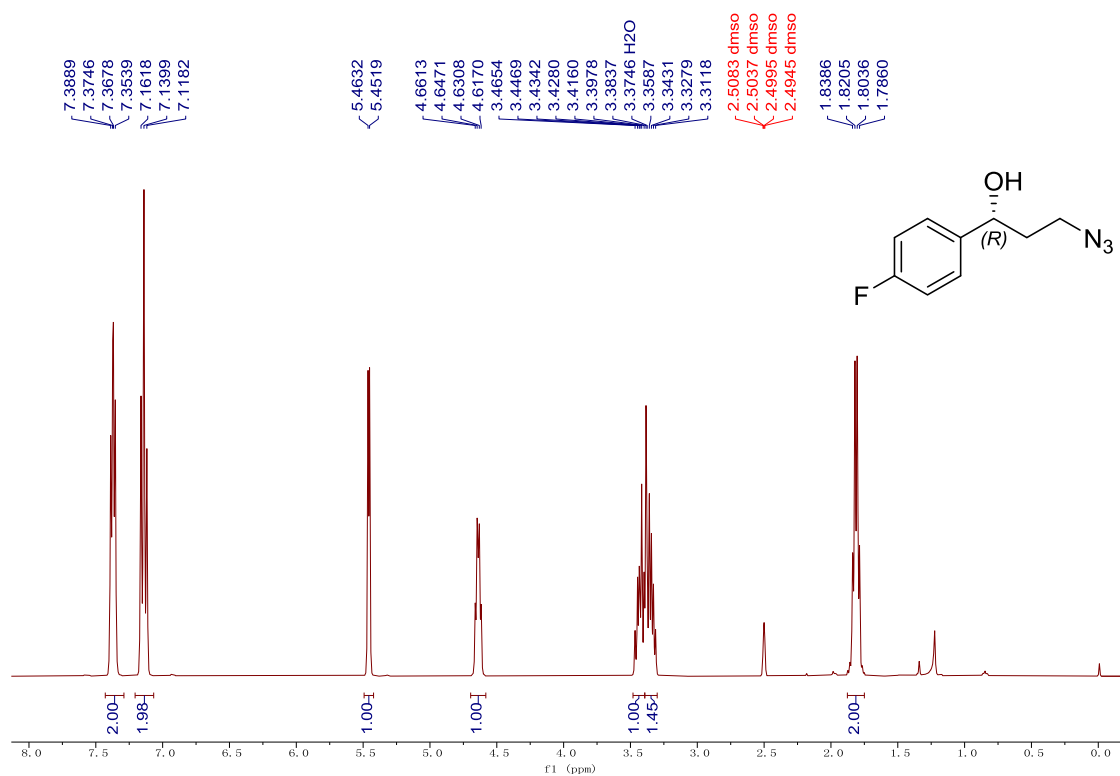
Supplementary Fig. 166 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**10c**.



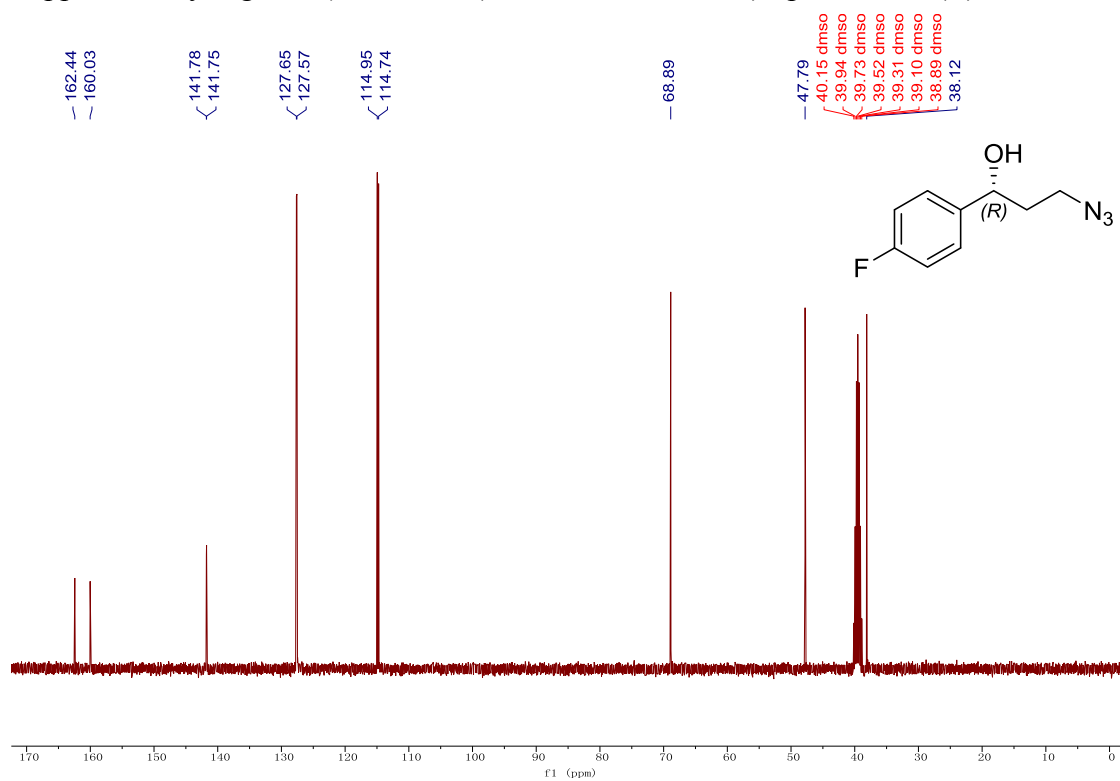
Supplementary Fig. 167 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**10c**.



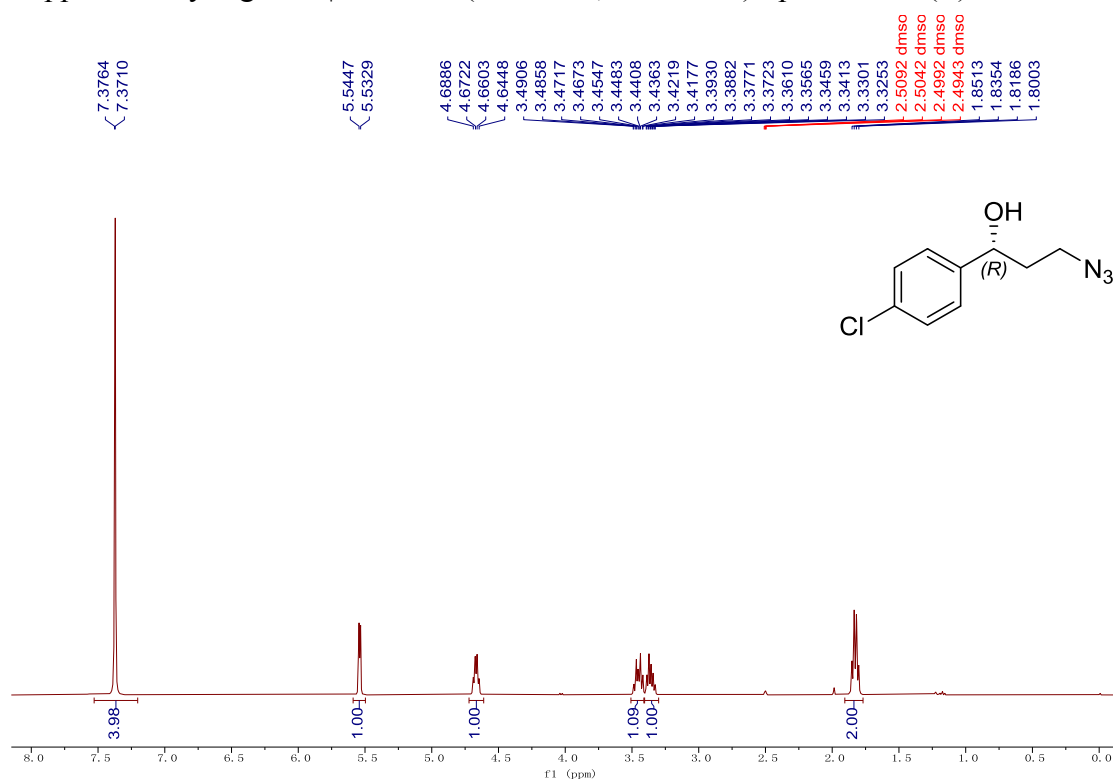
Supplementary Fig. 168 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**11c**.



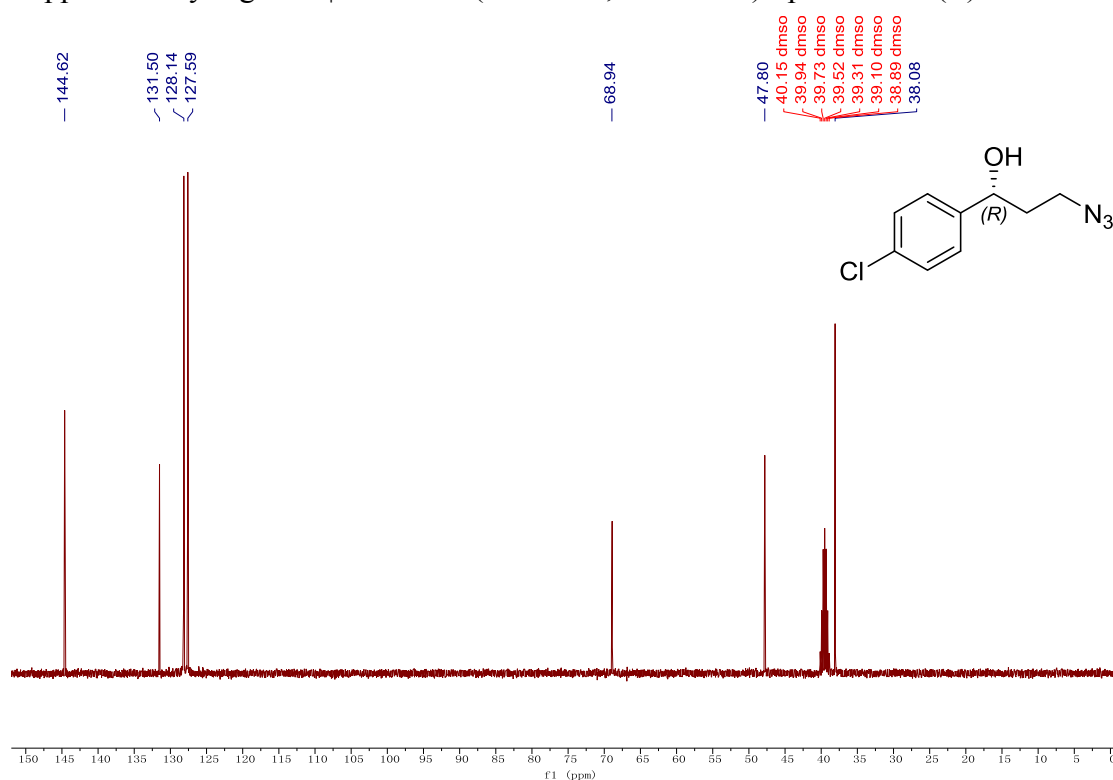
Supplementary Fig. 169 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**11c**.



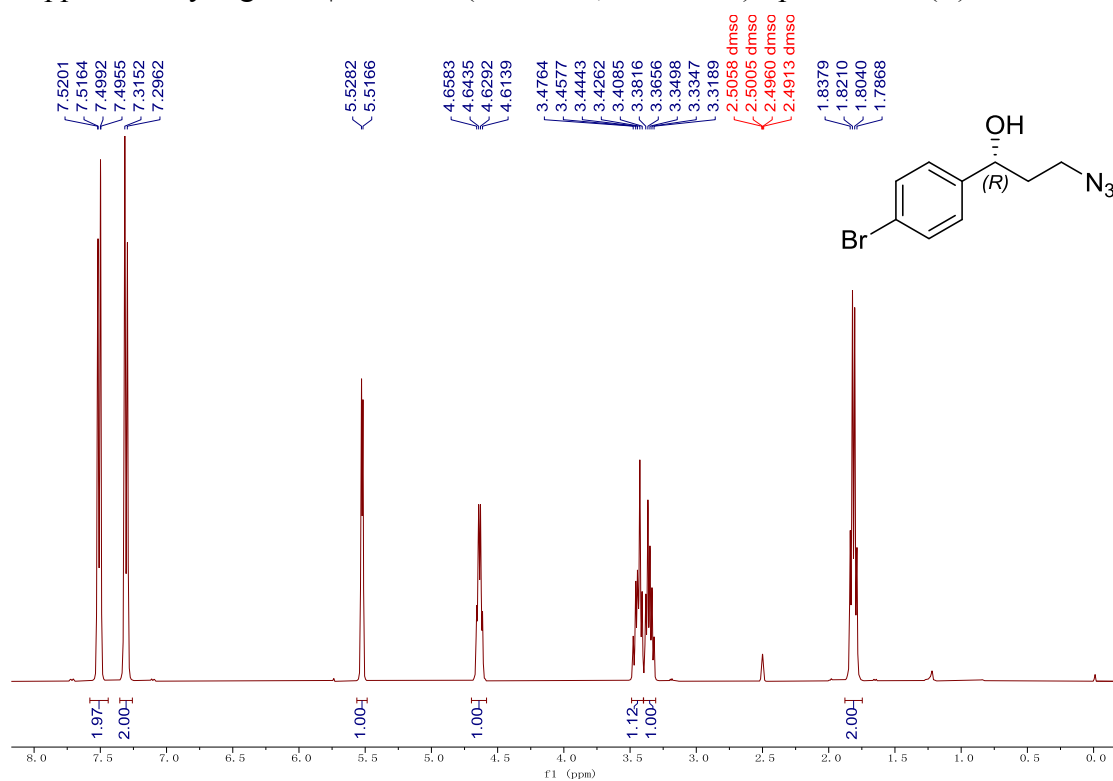
Supplementary Fig. 170 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**12c**.



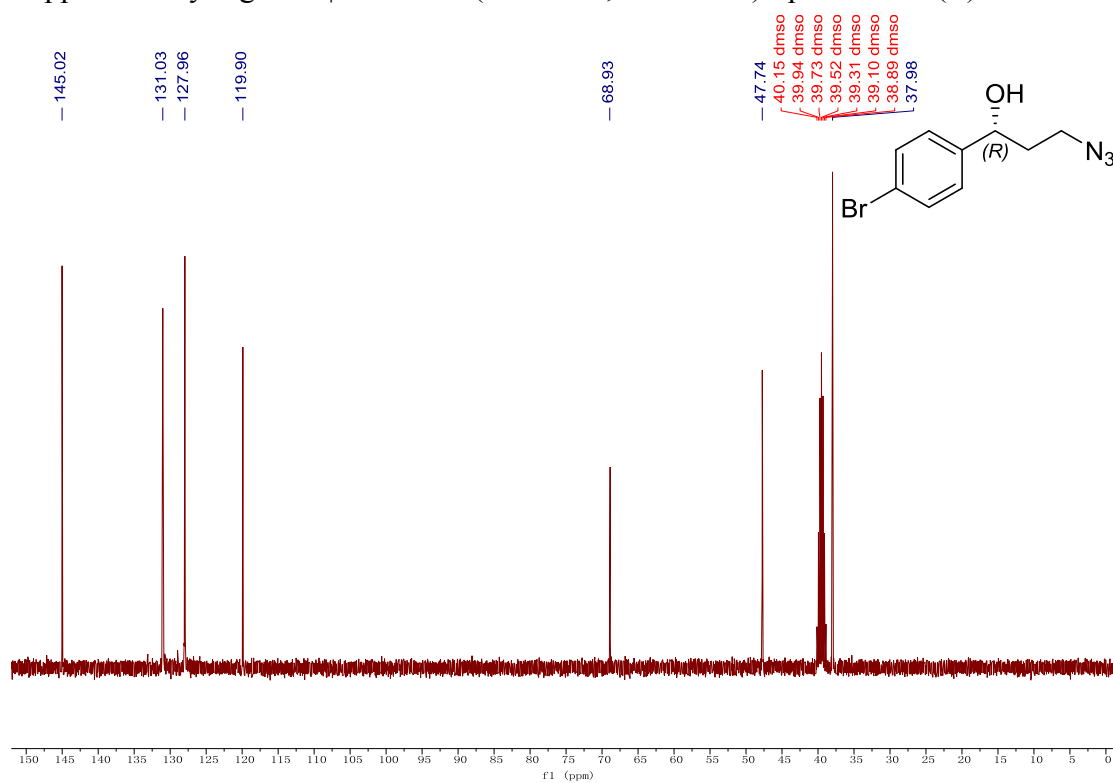
Supplementary Fig. 171 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**12c**.



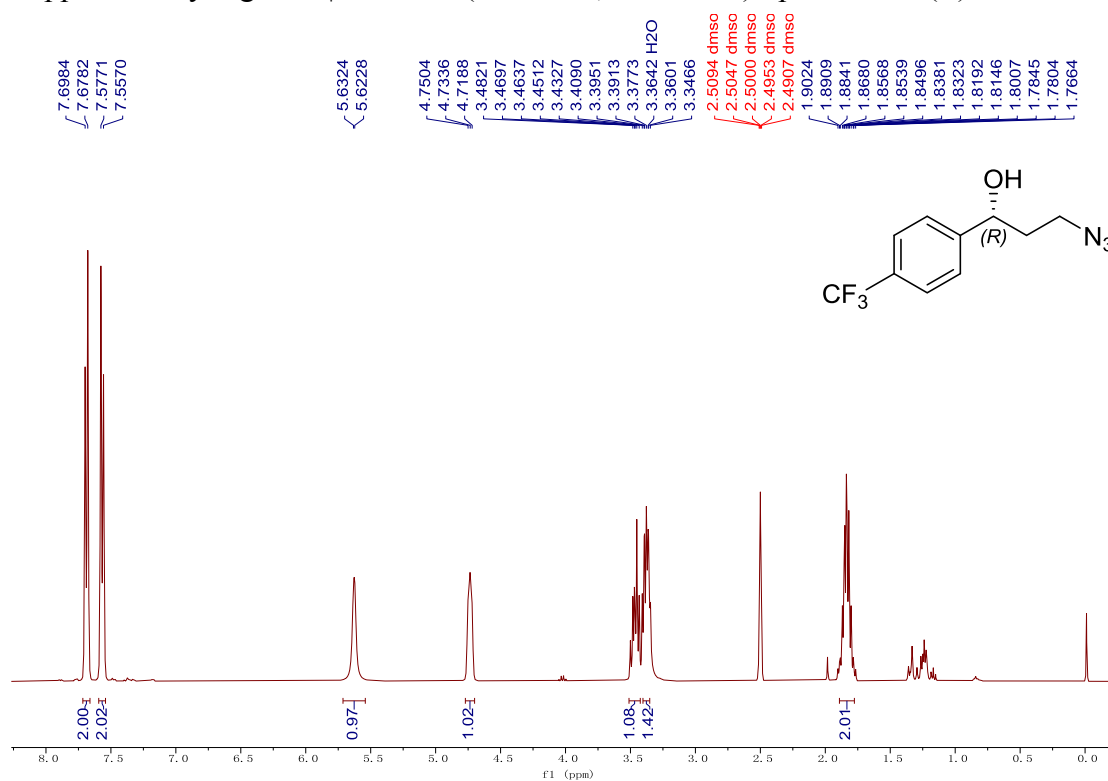
Supplementary Fig. 172 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**13c**.



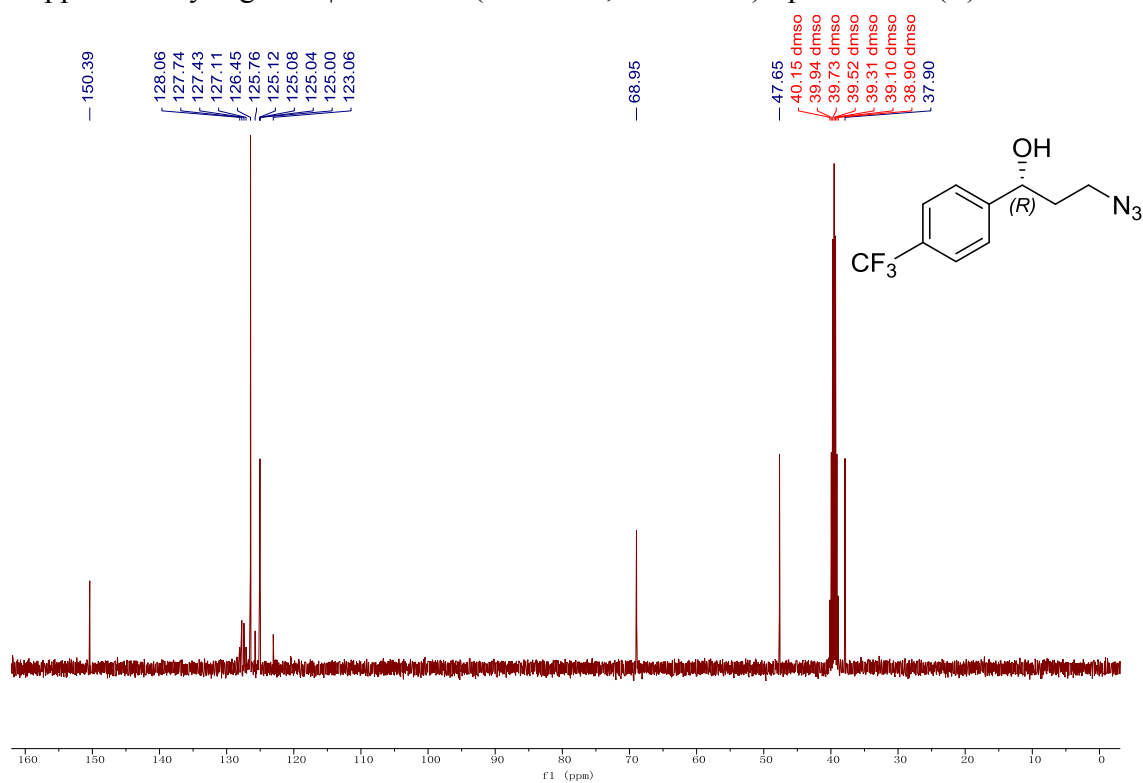
Supplementary Fig. 173 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**13c**.



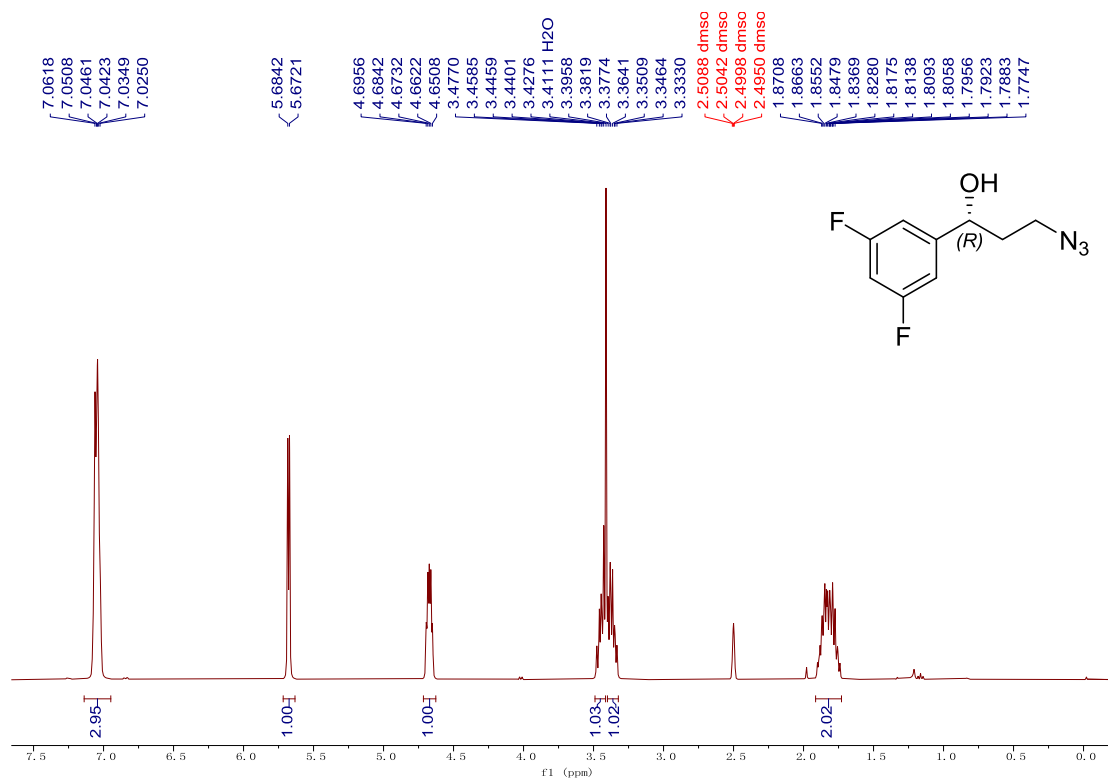
Supplementary Fig. 174 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**14c**.



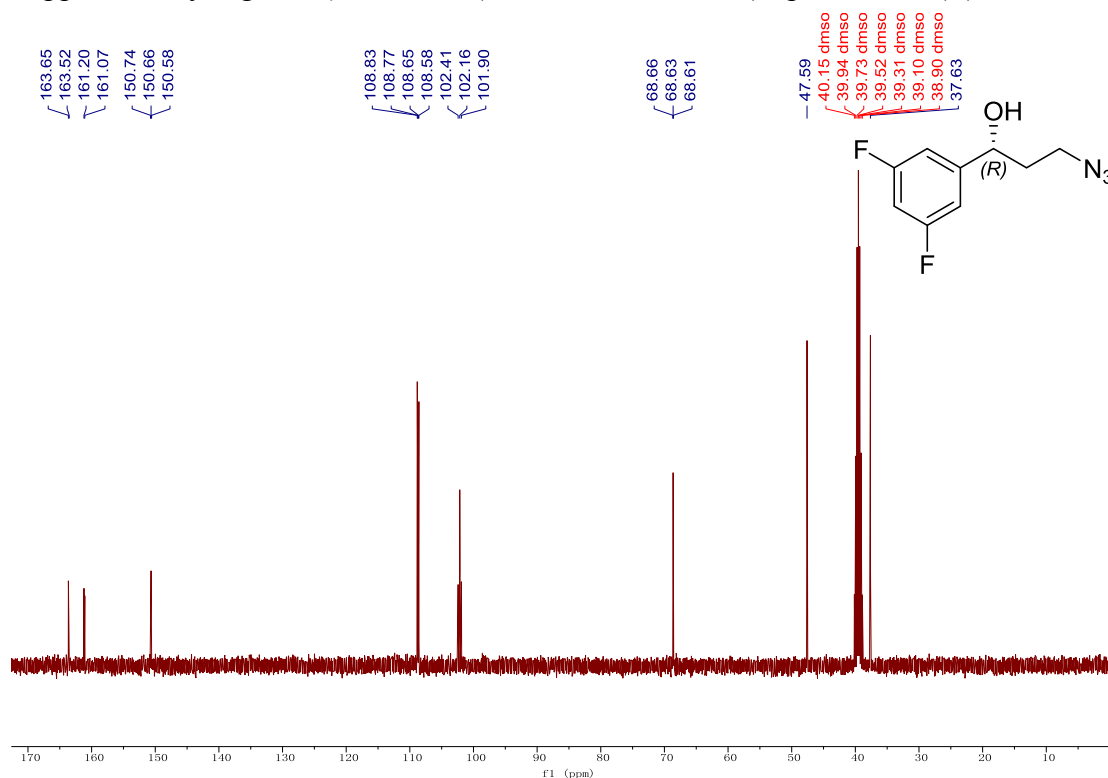
Supplementary Fig. 175 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**14c**.



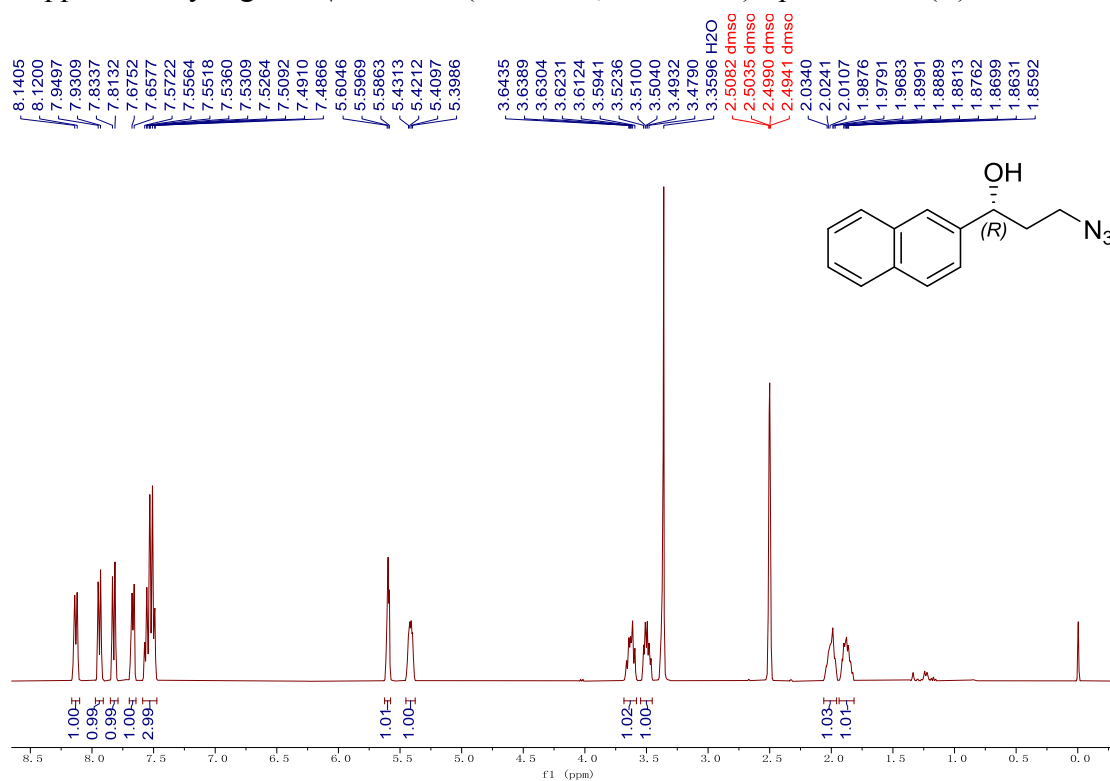
Supplementary Fig. 176 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**15c**.



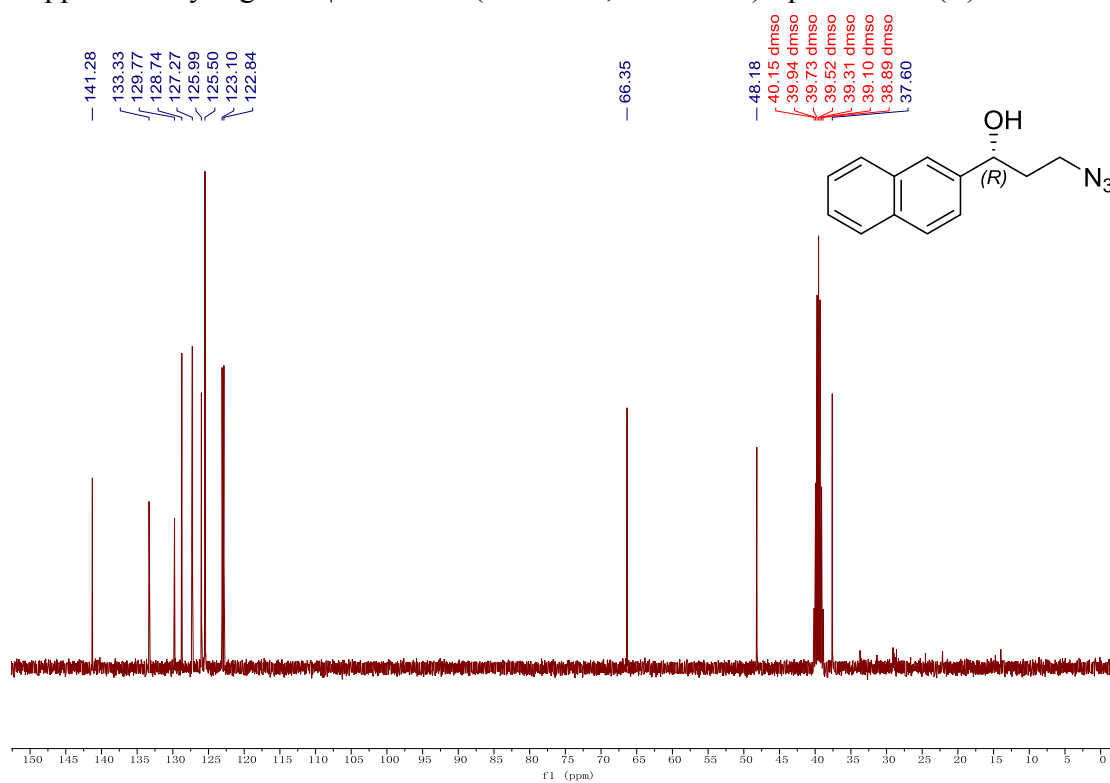
Supplementary Fig. 177 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**15c**.



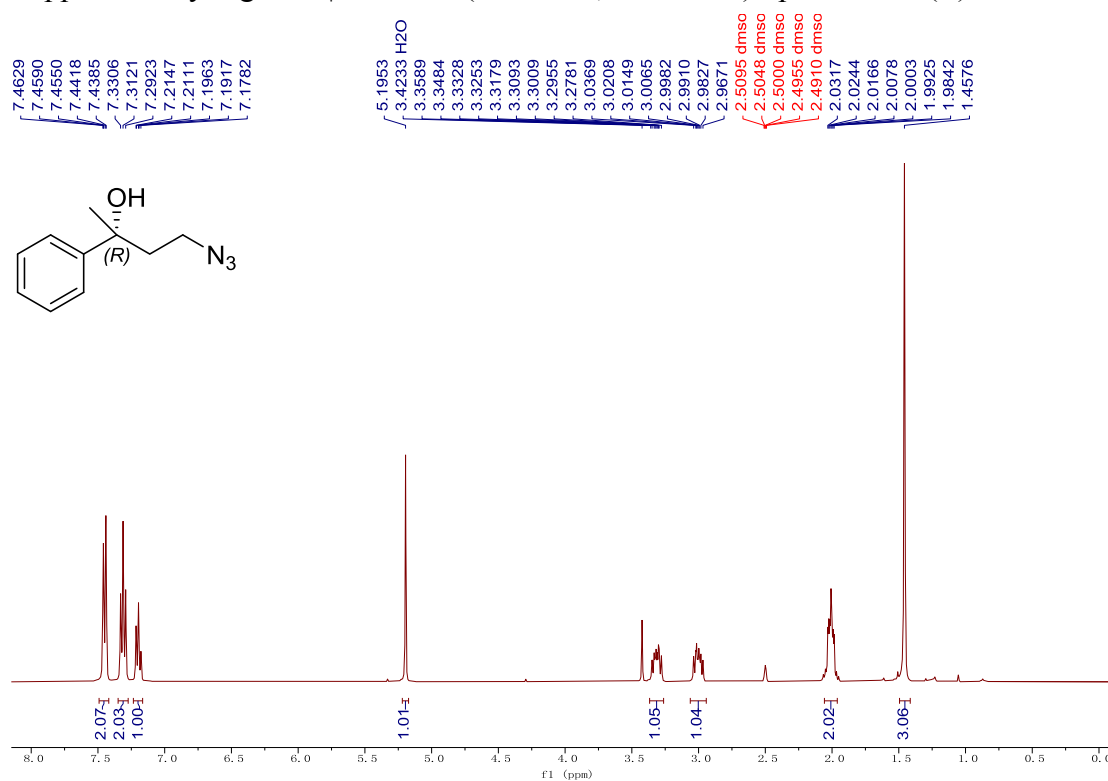
Supplementary Fig. 178 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**16c**.



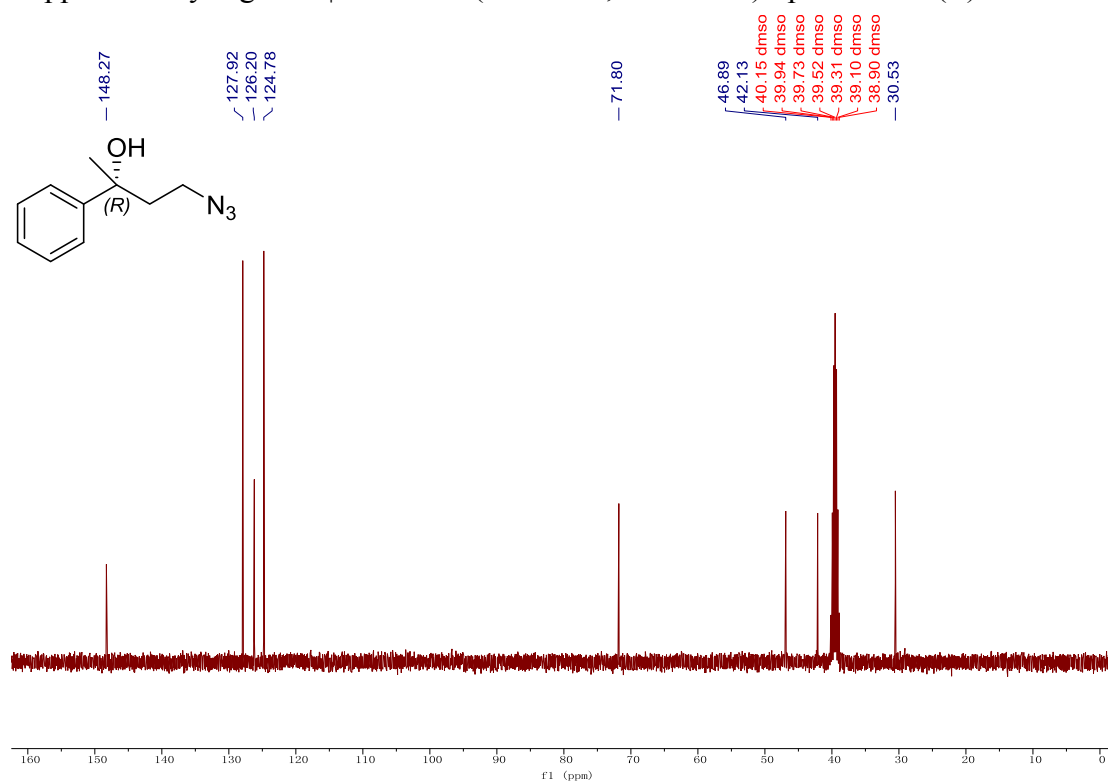
Supplementary Fig. 179 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**16c**.



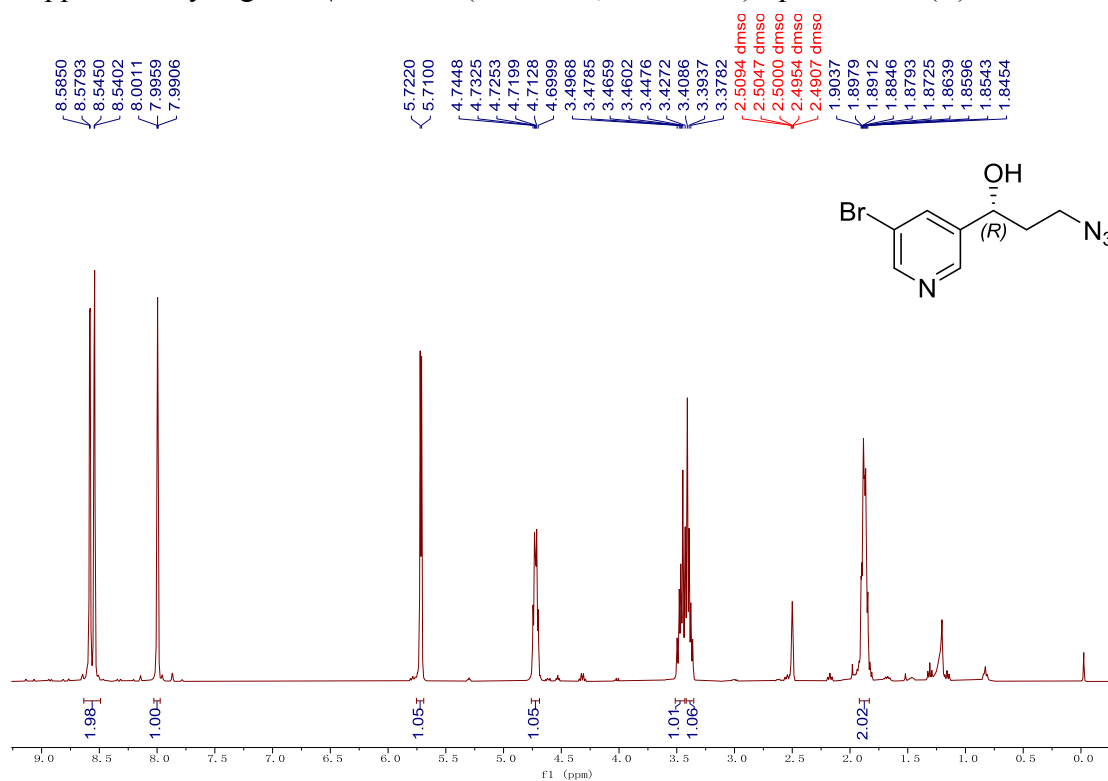
Supplementary Fig. 180 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**17c**.



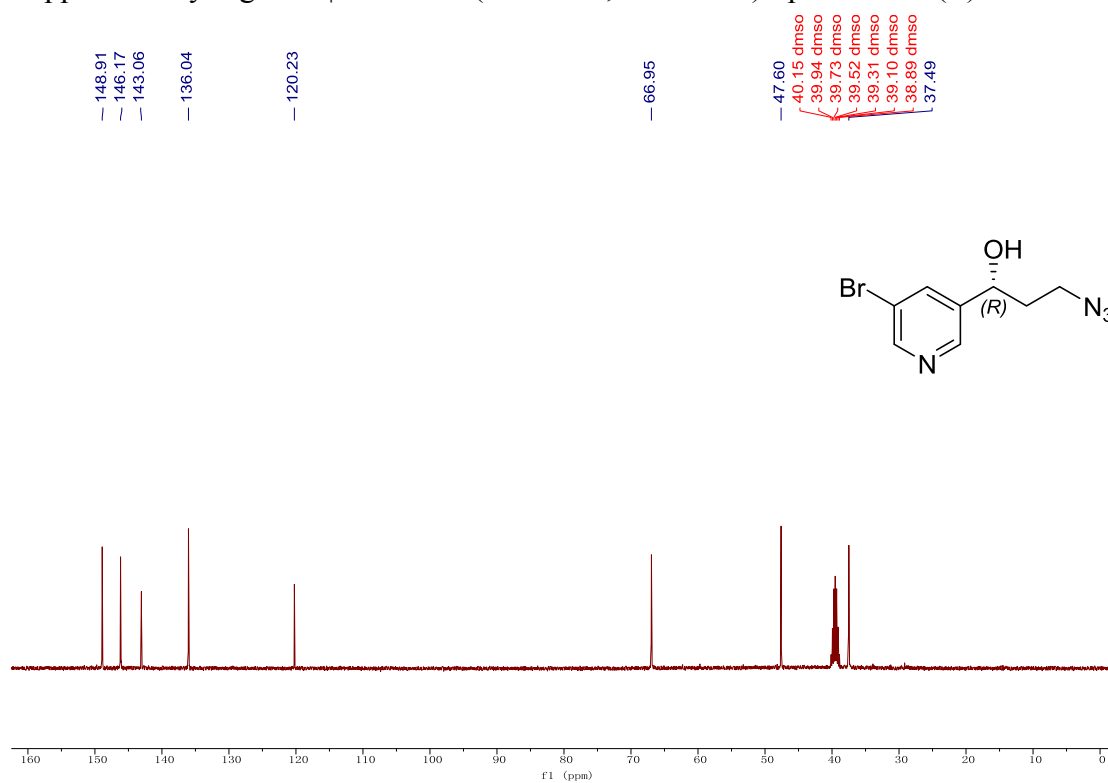
Supplementary Fig. 181 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**17c**.



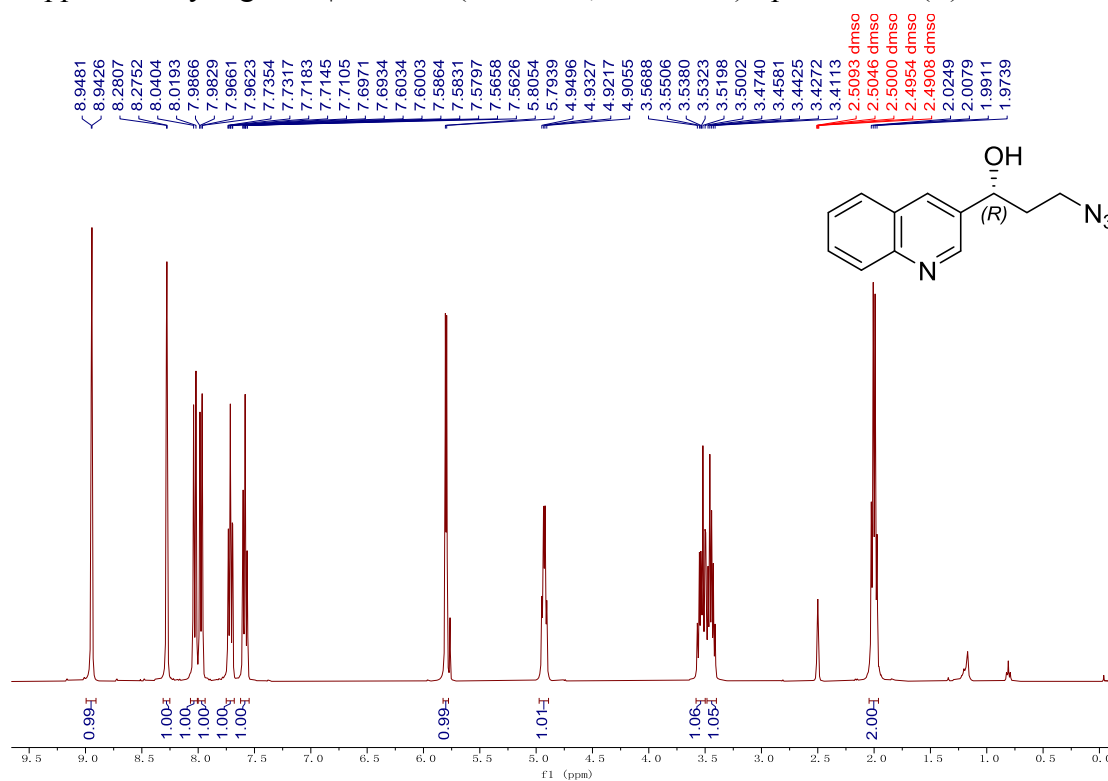
Supplementary Fig. 182 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**18c**.



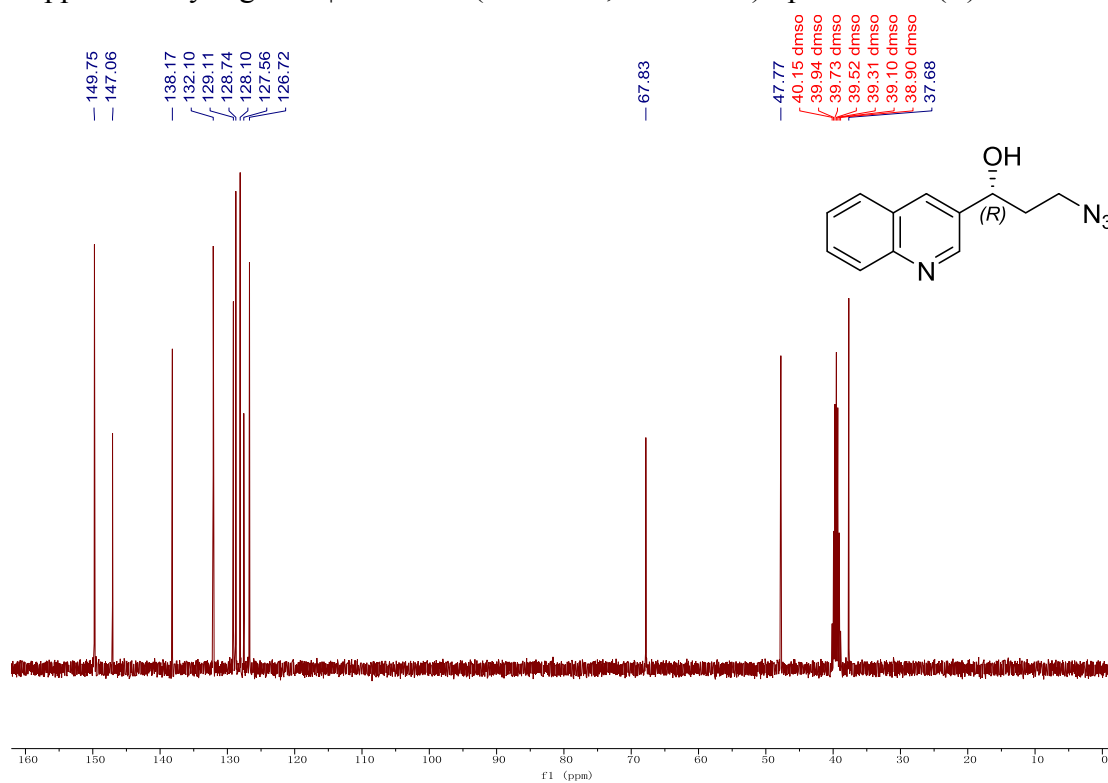
Supplementary Fig. 183 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**18c**.



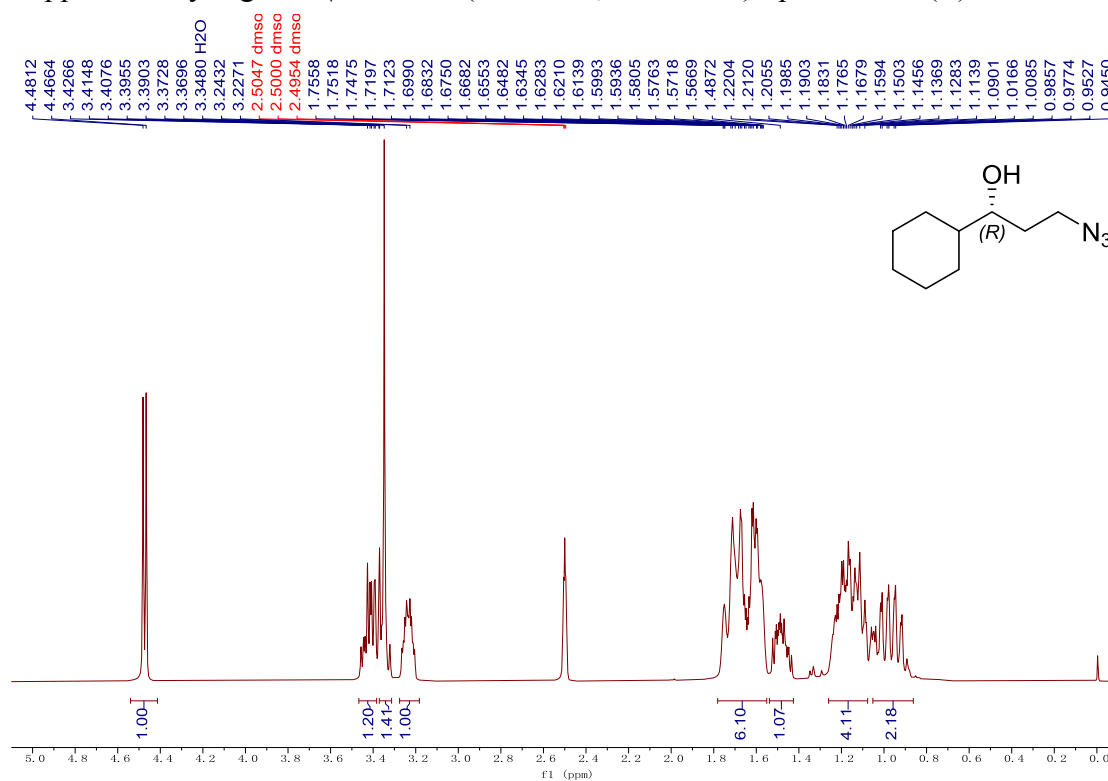
Supplementary Fig. 184 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**19c**.



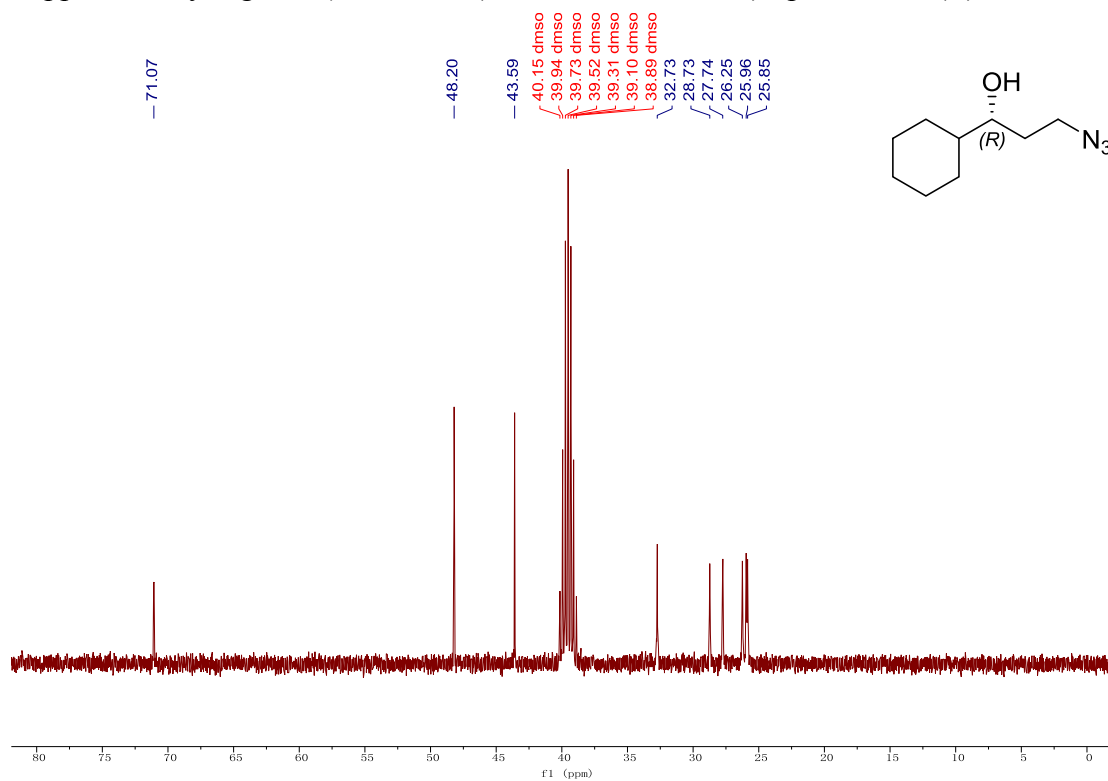
Supplementary Fig. 185 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**19c**.



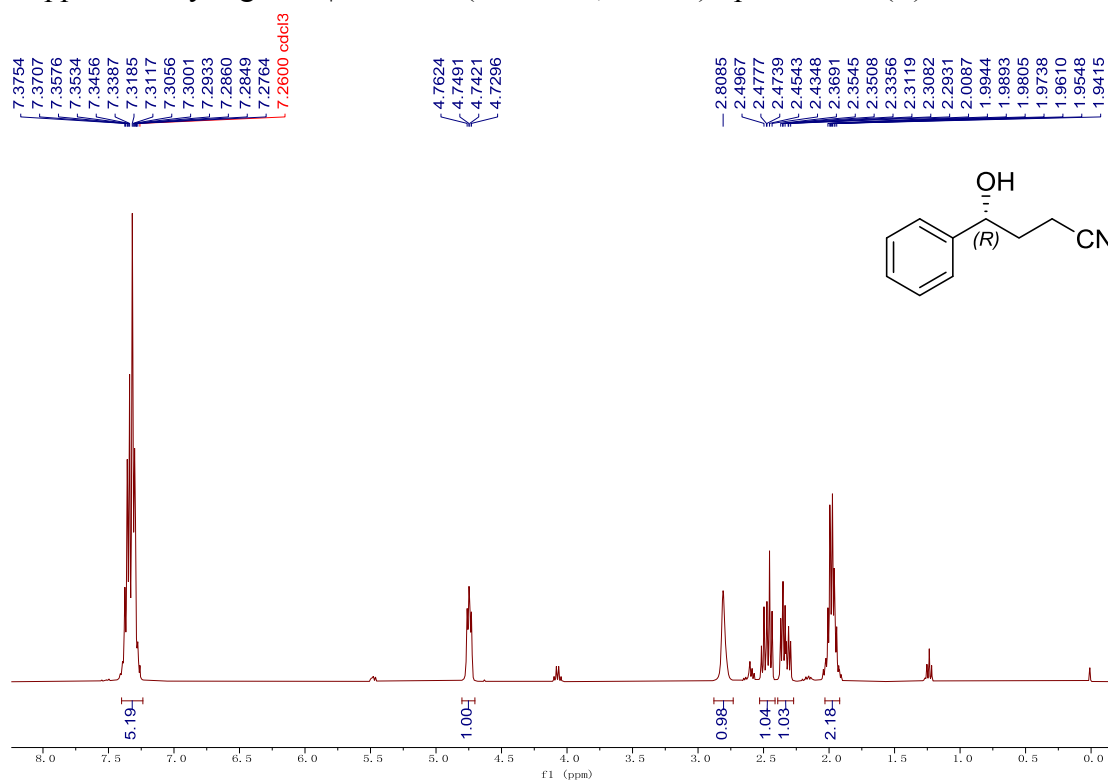
Supplementary Fig. 186 | ^1H NMR (400 MHz, DMSO- d_6) Spectrum of (*R*)-**21c**.



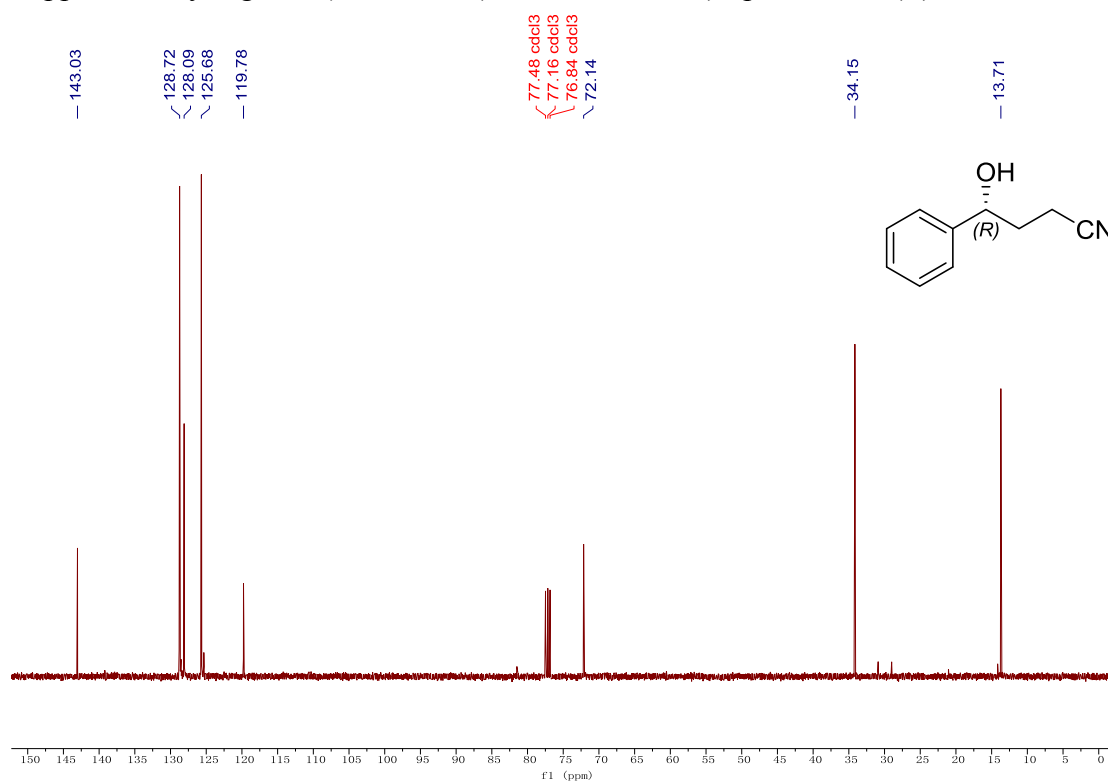
Supplementary Fig. 187 | ^{13}C NMR (100 MHz, DMSO- d_6) Spectrum of (*R*)-**21c**.



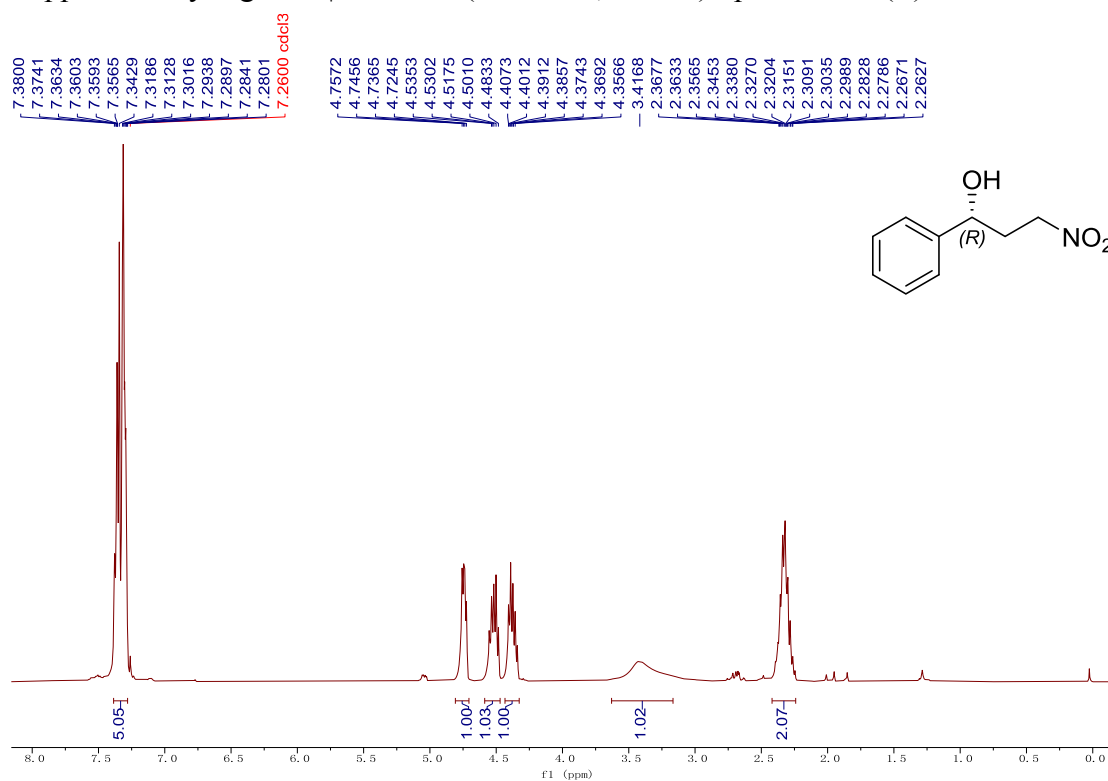
Supplementary Fig. 188 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1d**.



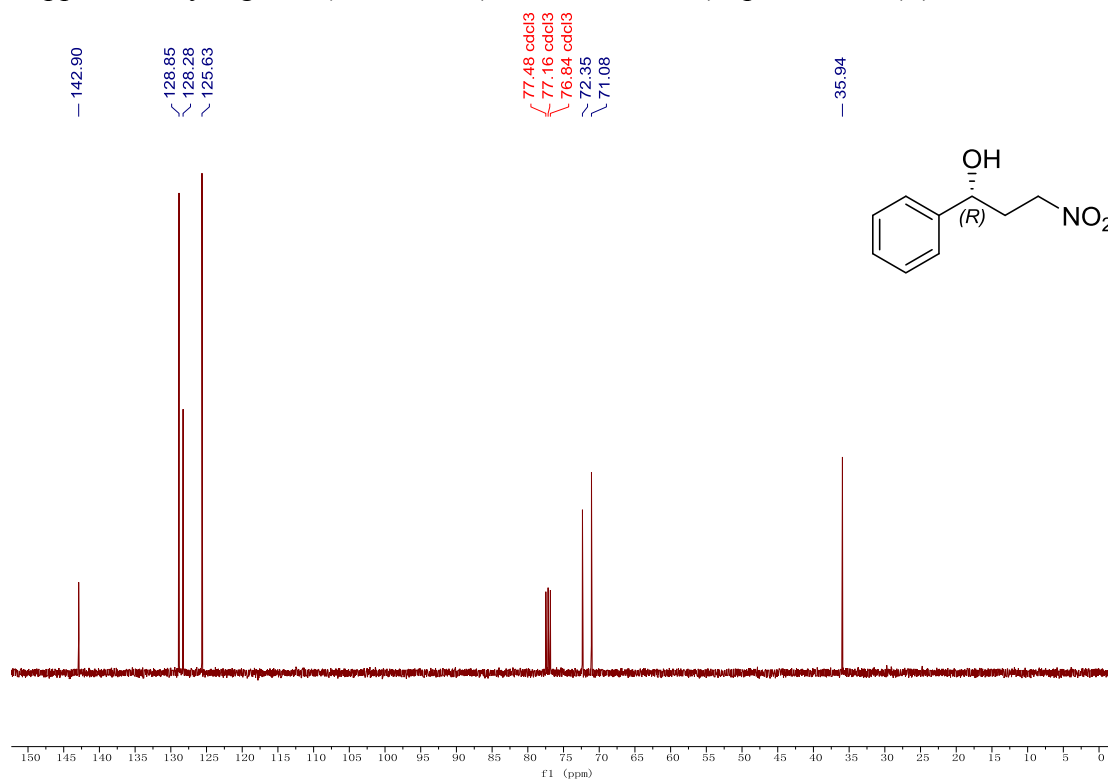
Supplementary Fig. 189 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1d**.



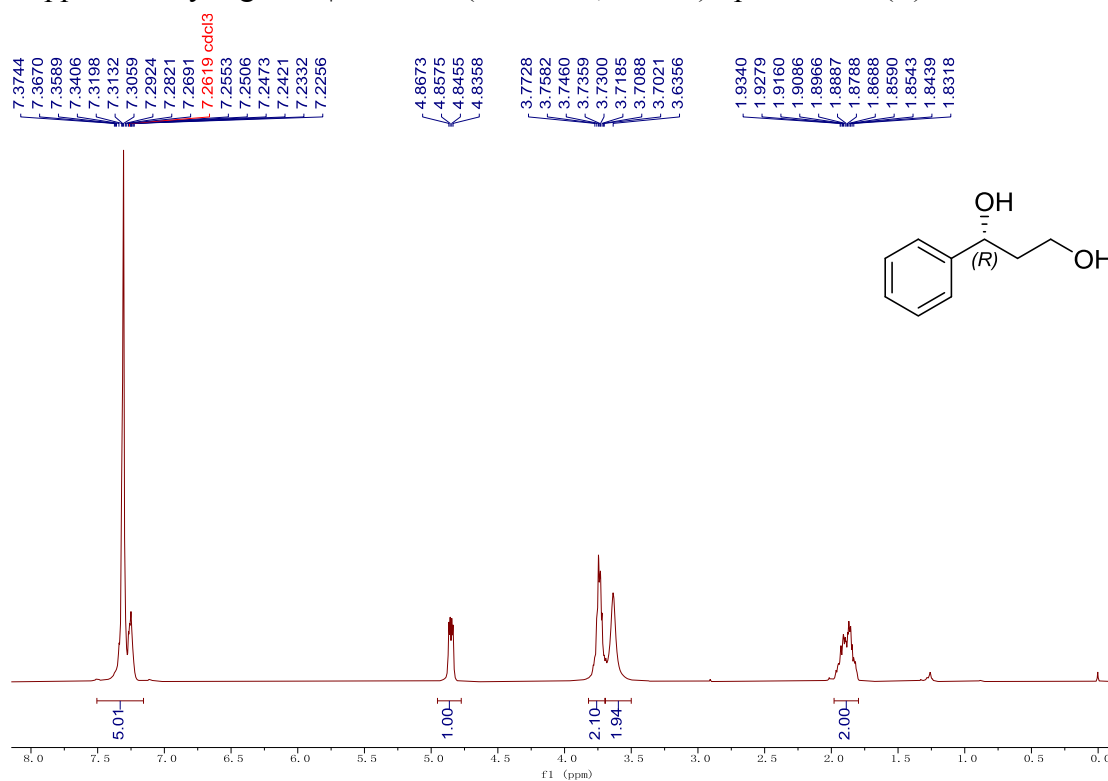
Supplementary Fig. 190 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1e**.



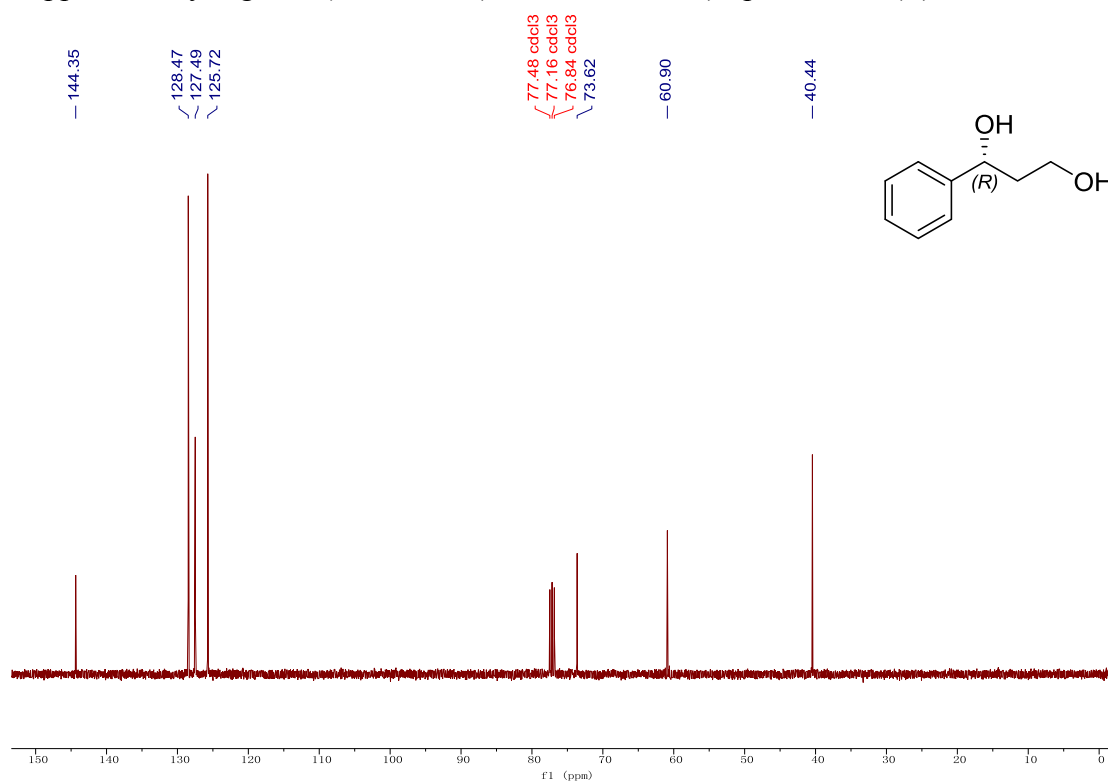
Supplementary Fig. 191 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1e**.



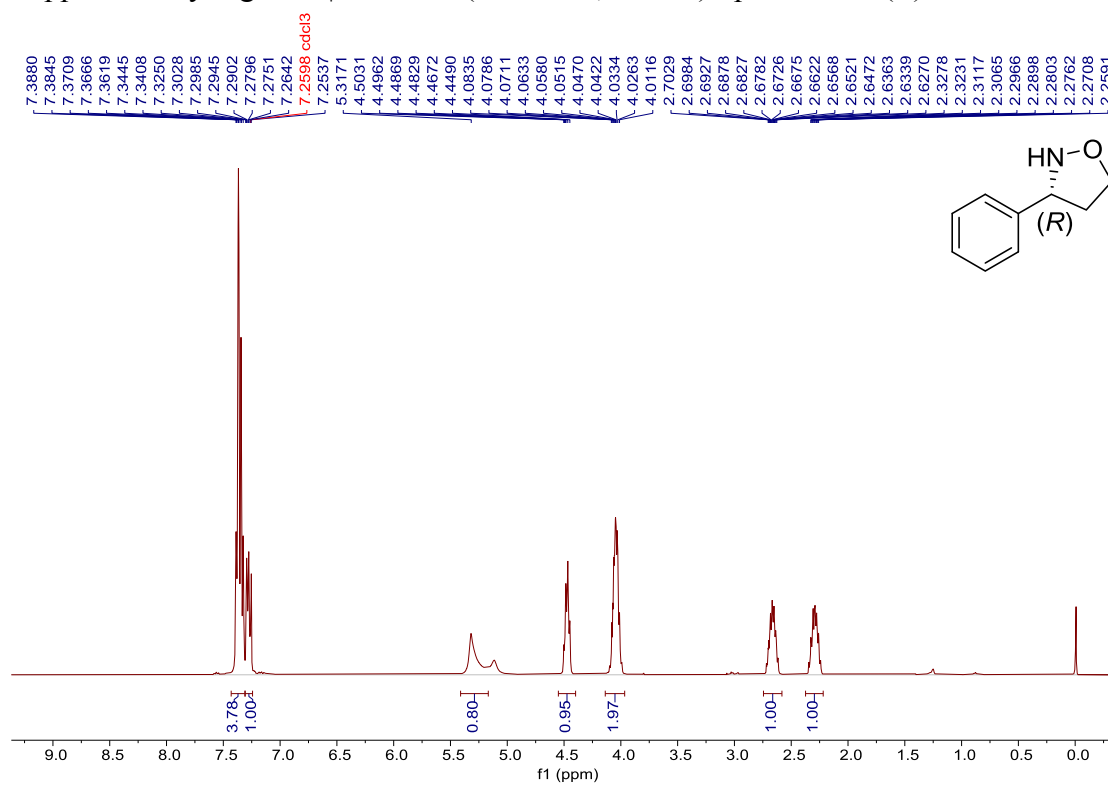
Supplementary Fig. 192 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1f**.



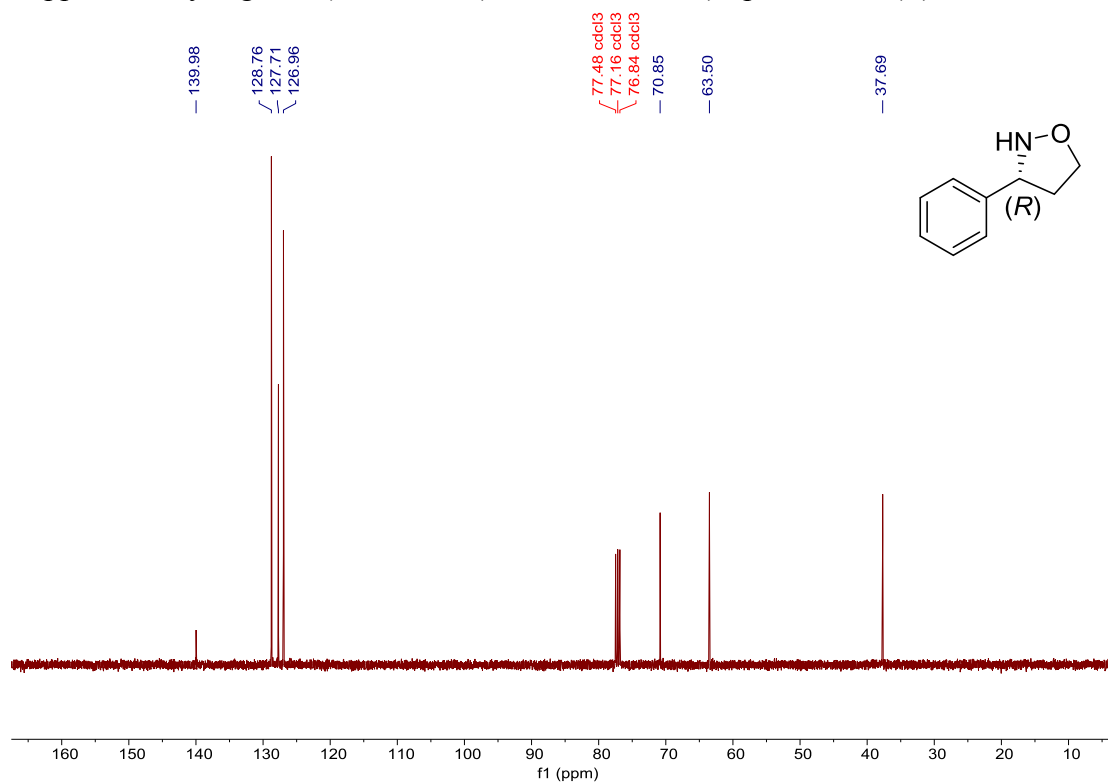
Supplementary Fig. 193 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1f**.



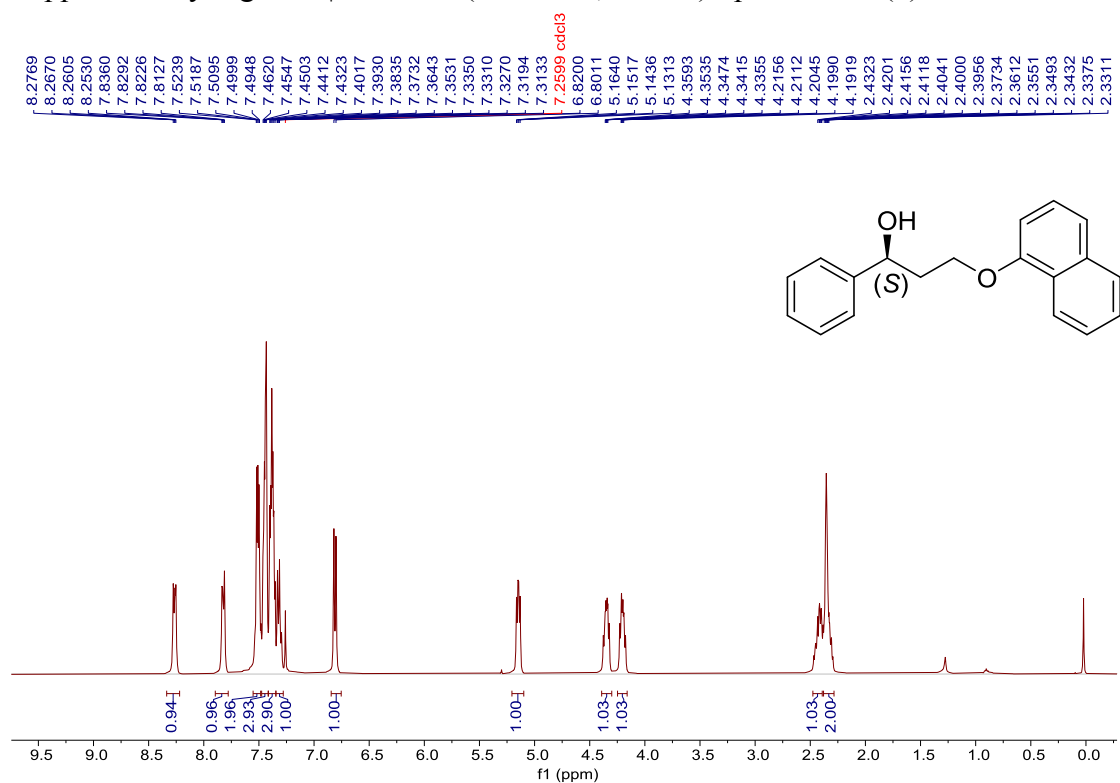
Supplementary Fig. 194 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1aa**.



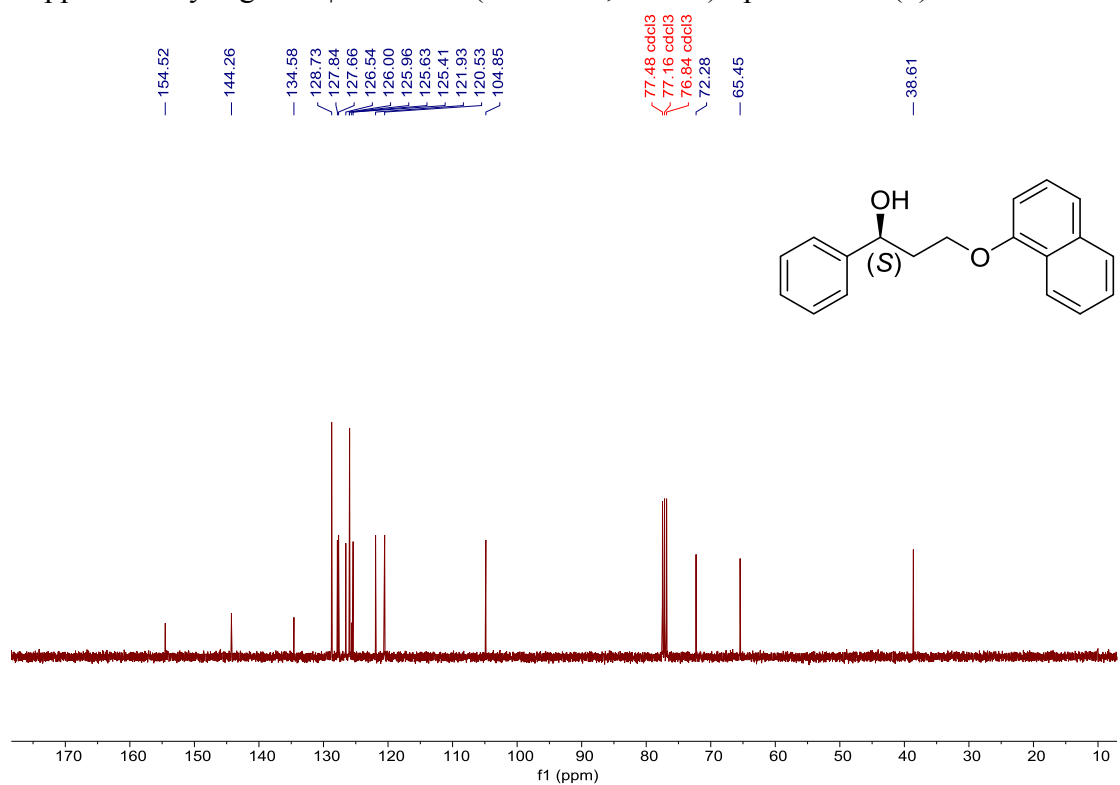
Supplementary Fig. 195 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1aa**.



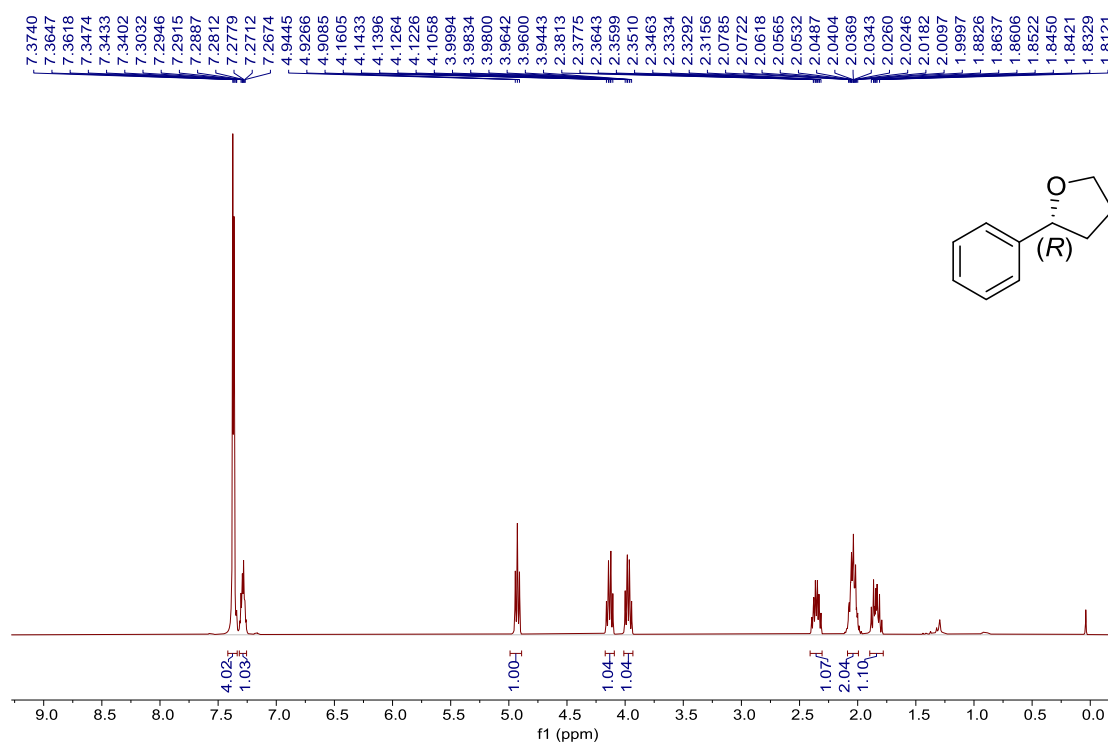
Supplementary Fig. 196 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*S*)-**1ab**.



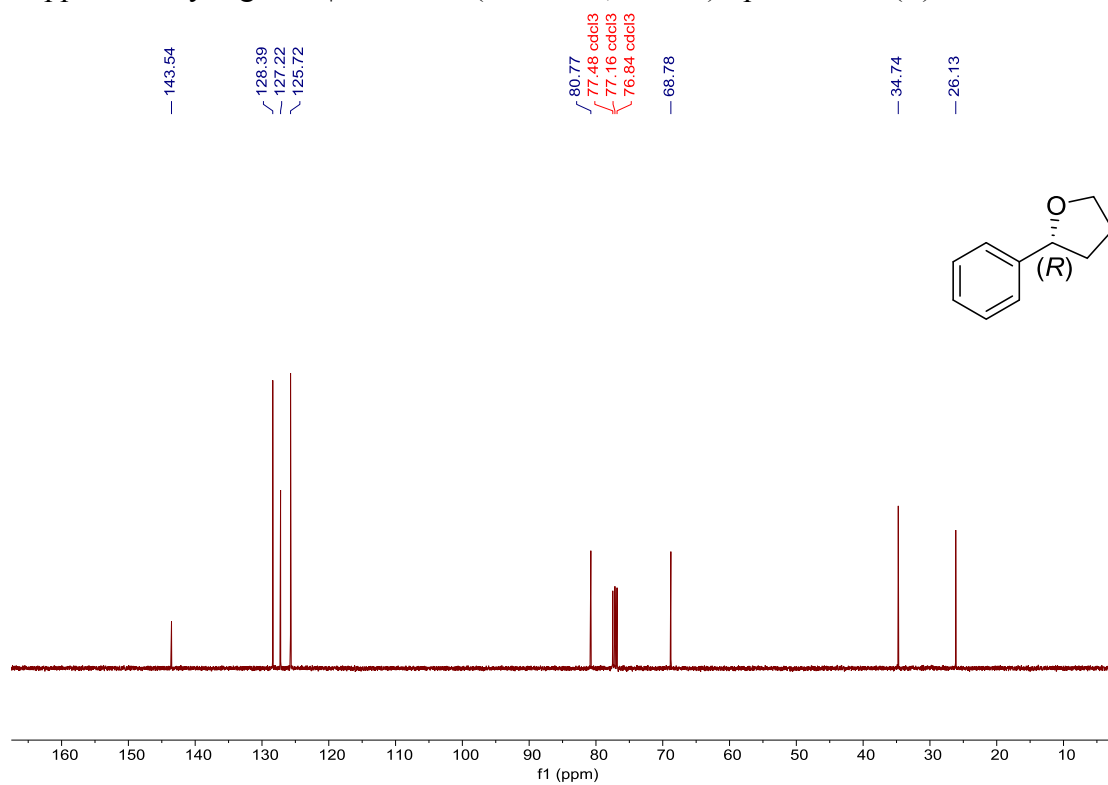
Supplementary Fig. 197 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*S*)-**1ab**.



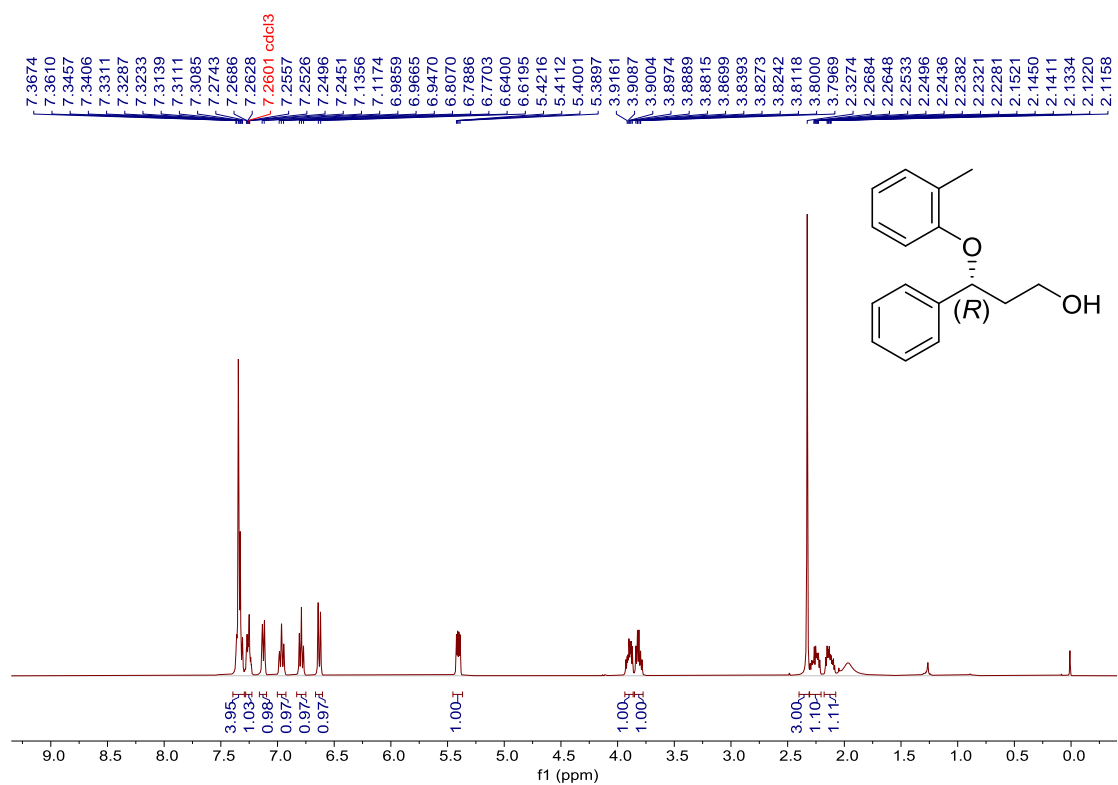
Supplementary Fig. 198 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1ba**.



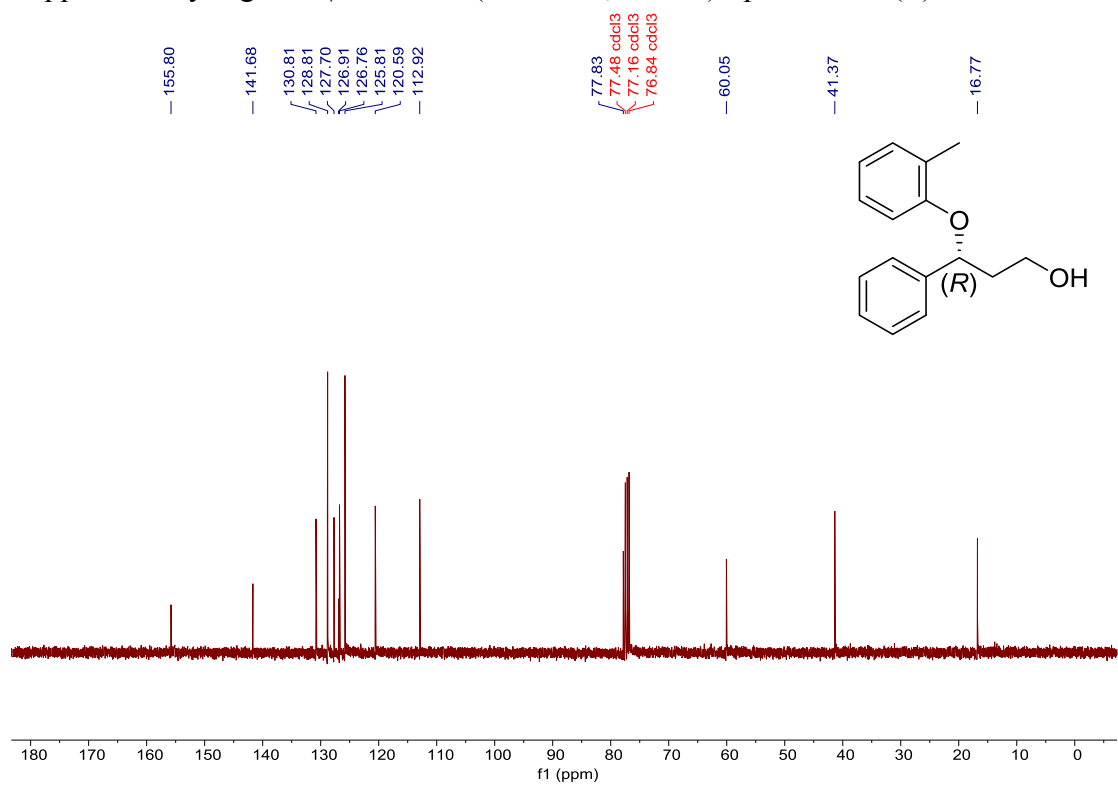
Supplementary Fig. 199 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1ba**.



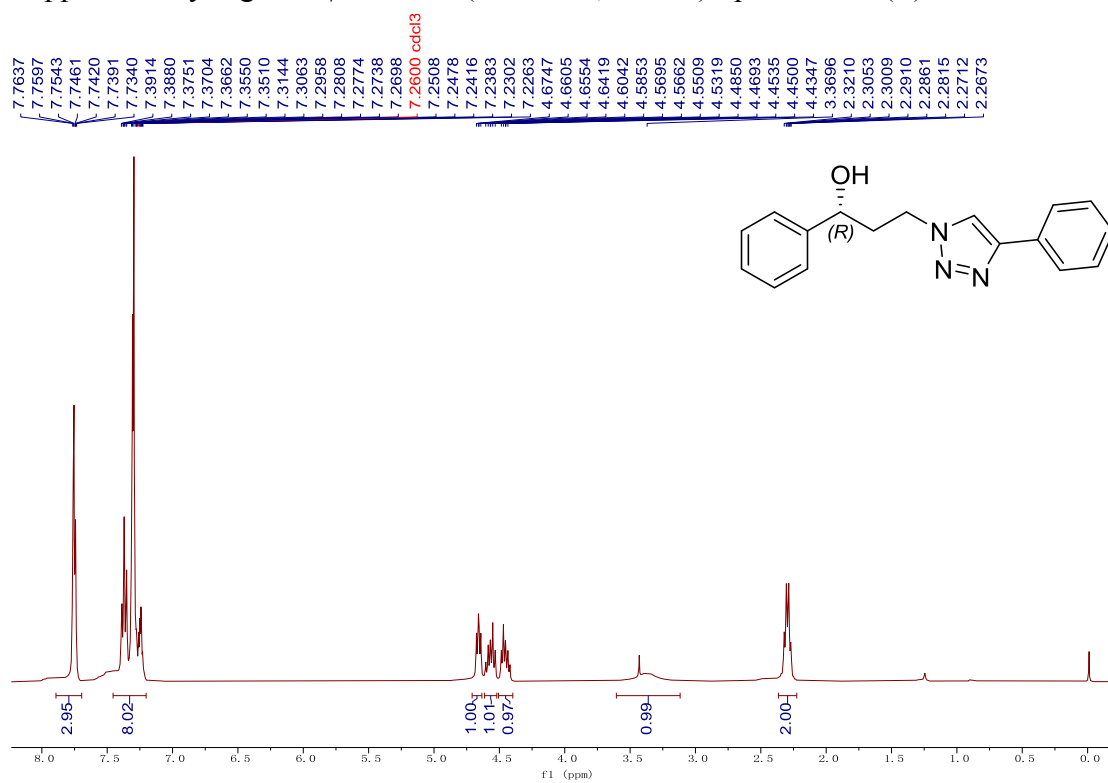
Supplementary Fig. 200 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1bb**.



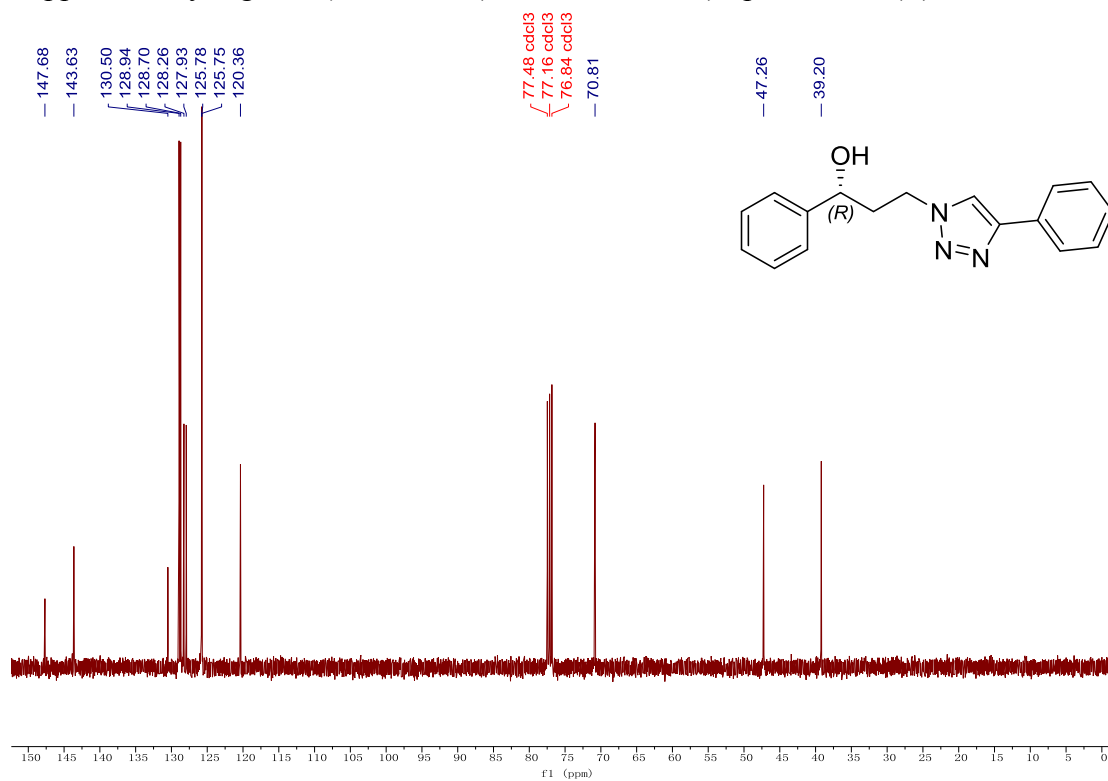
Supplementary Fig. 201 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1bb**.



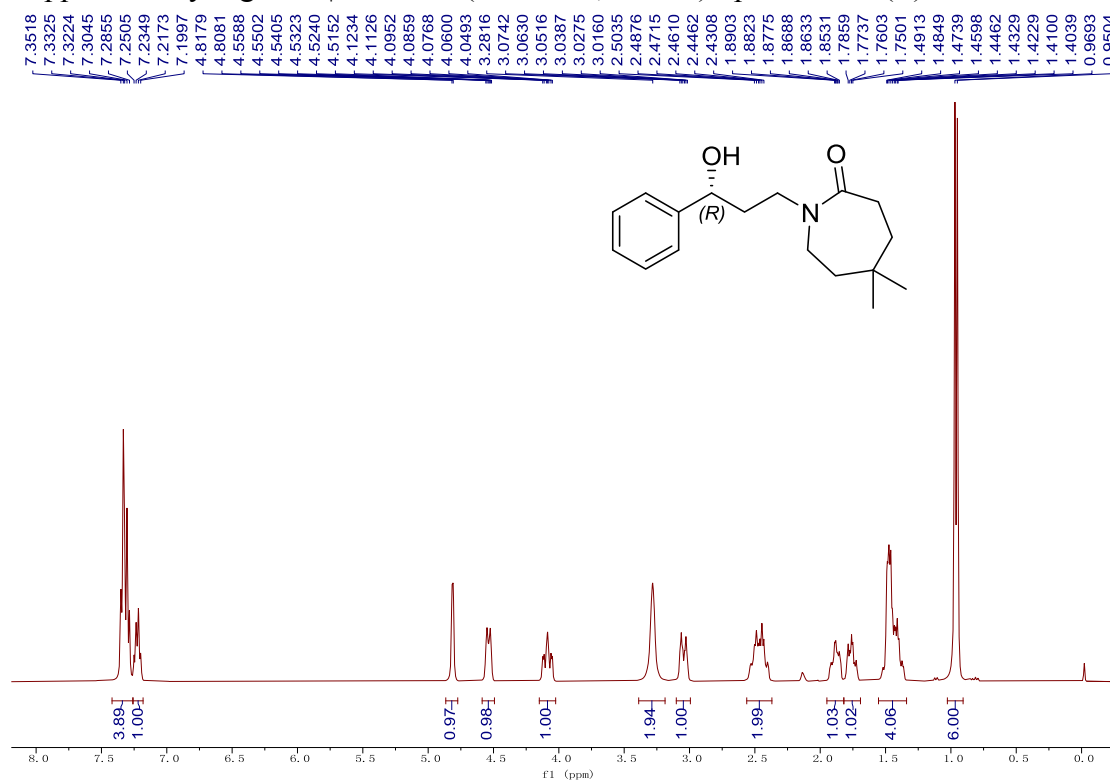
Supplementary Fig. 202 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1ca**.



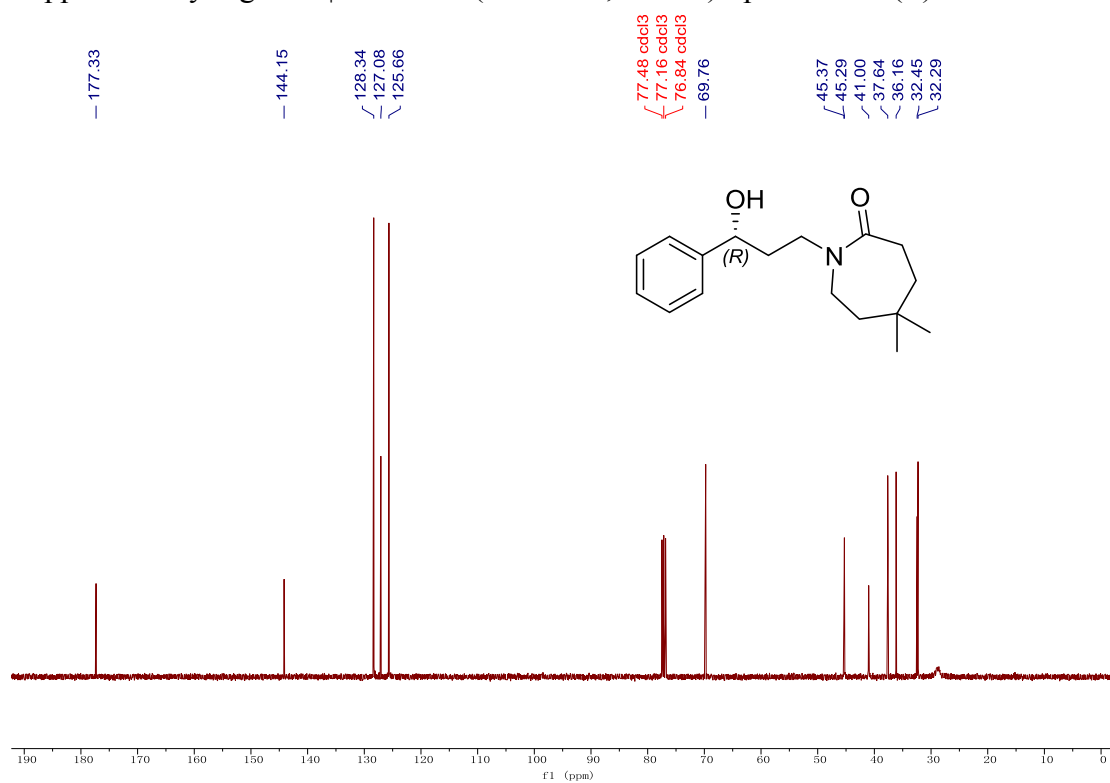
Supplementary Fig. 203 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1ca**.



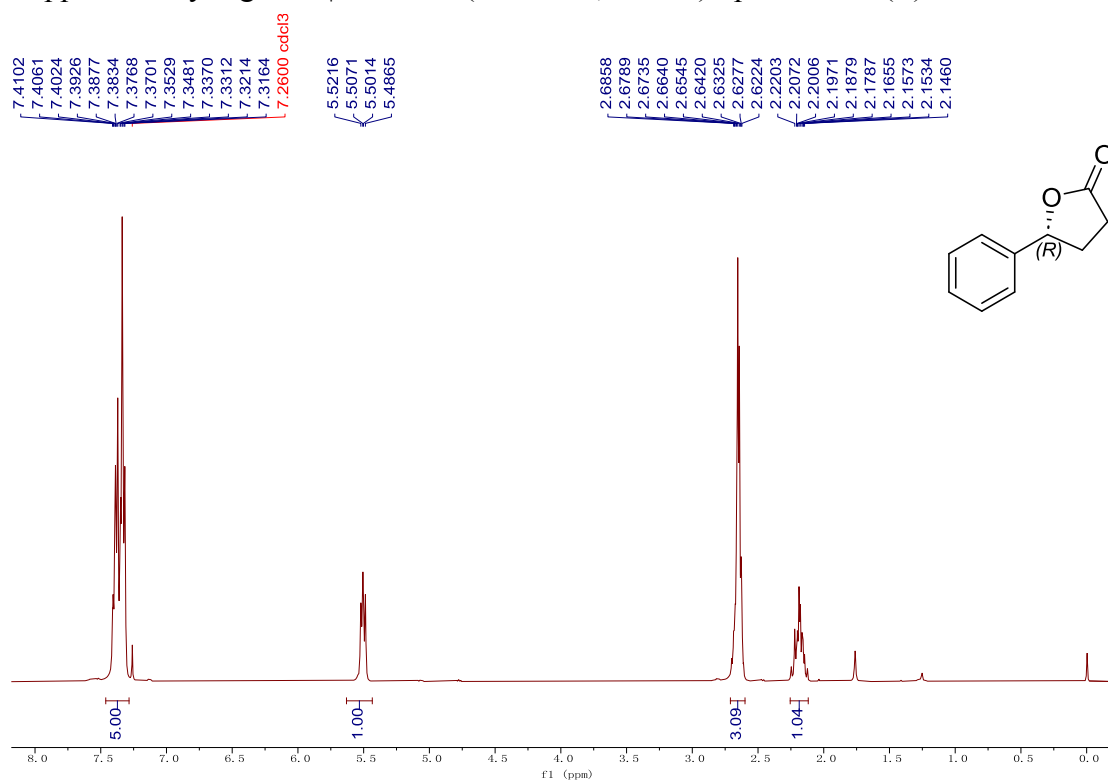
Supplementary Fig. 204 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1cb**.



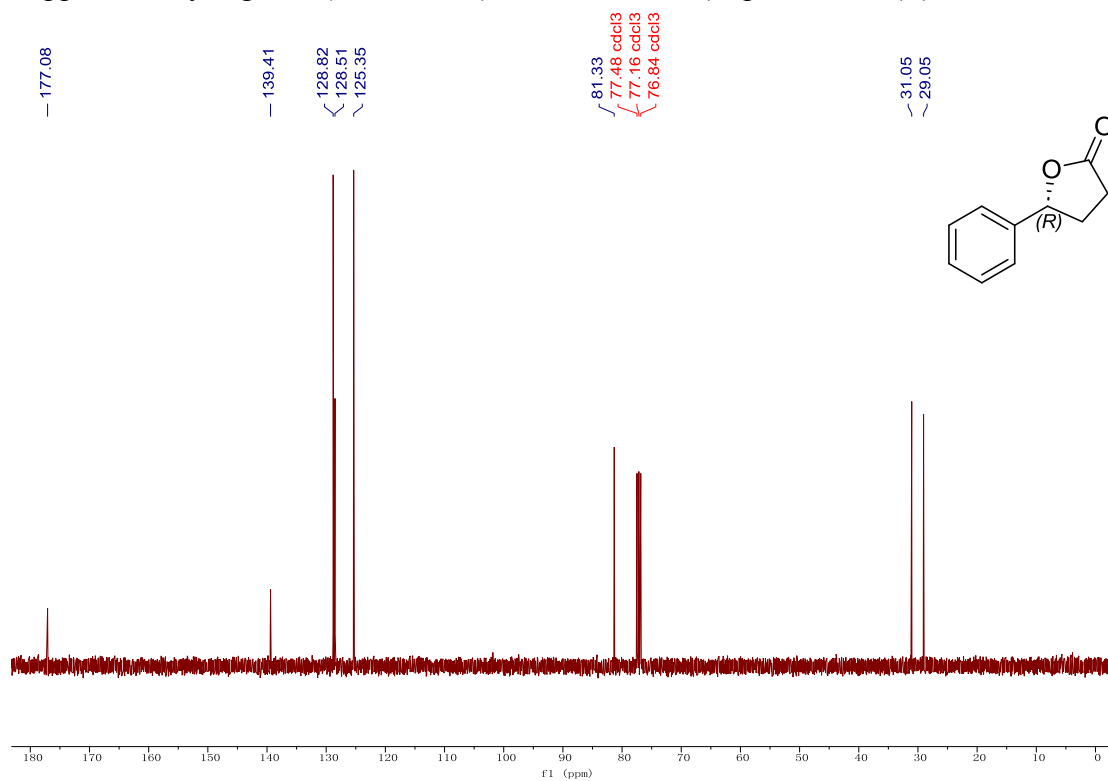
Supplementary Fig. 205 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1cb**.



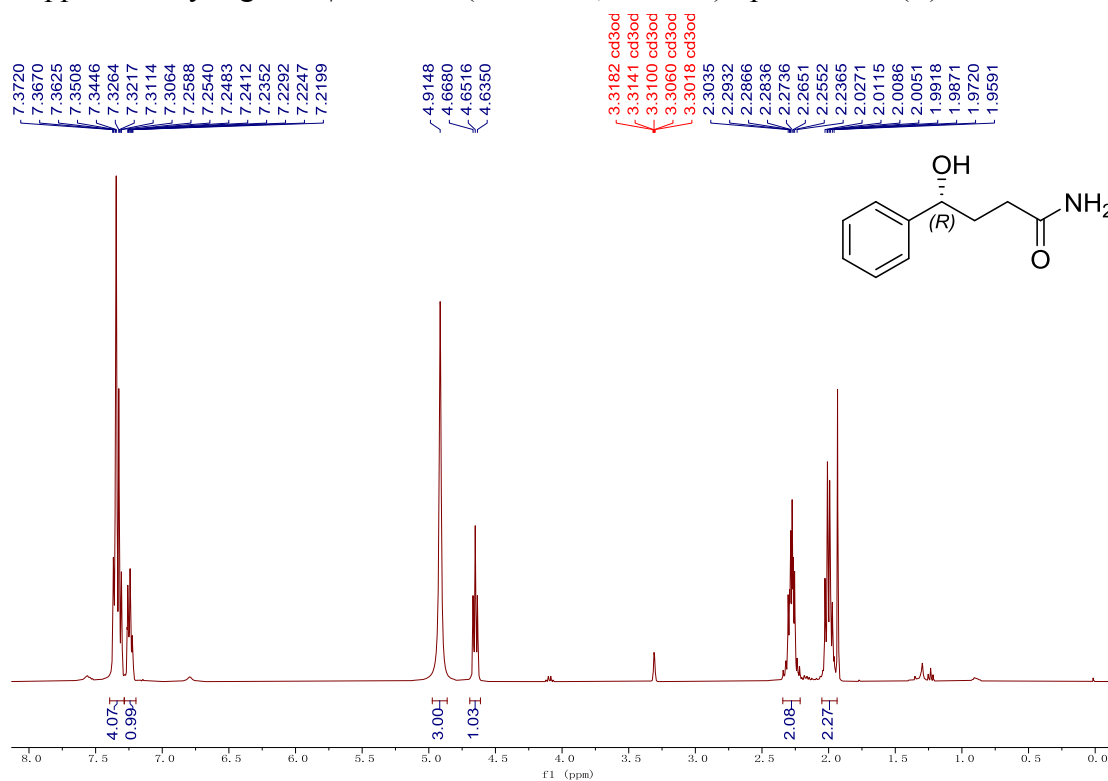
Supplementary Fig. 206 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1da**.



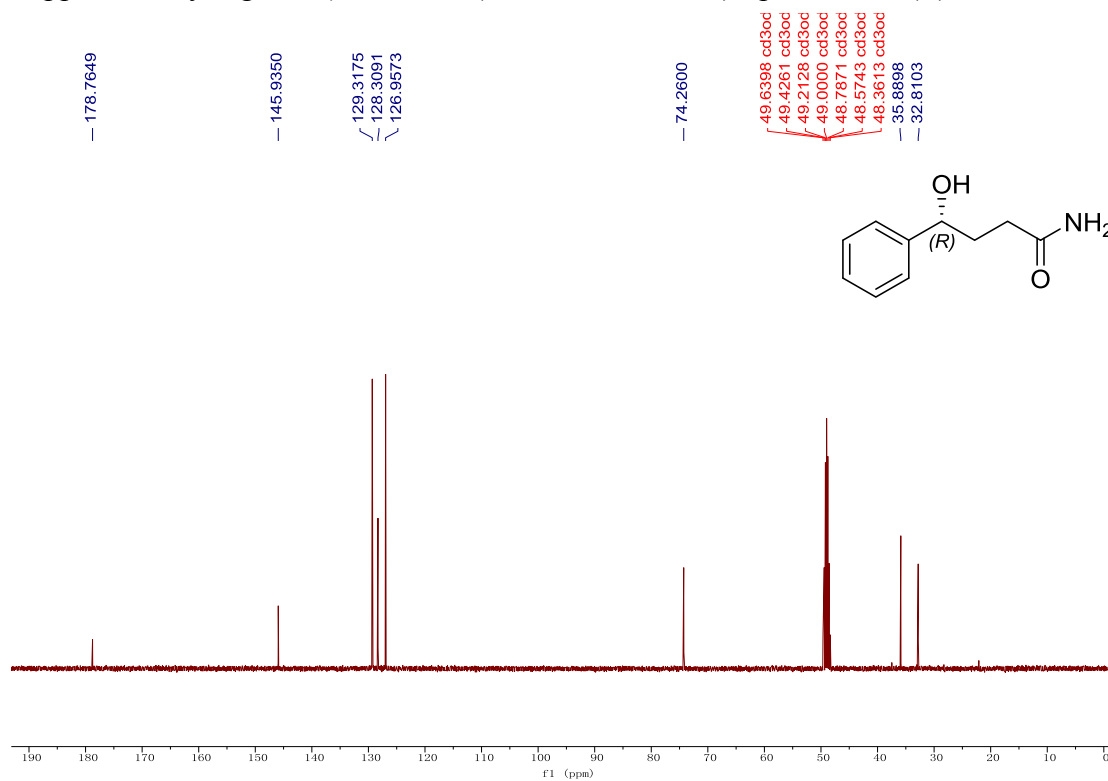
Supplementary Fig. 207 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1da**.



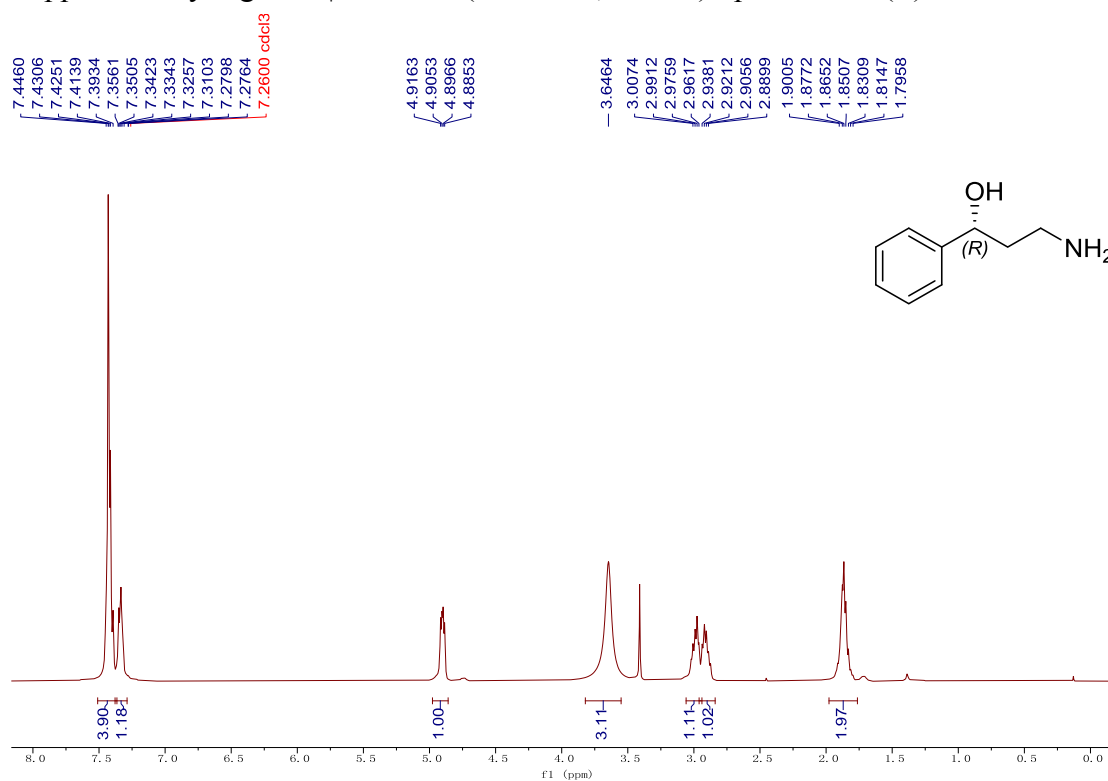
Supplementary Fig. 208 | ^1H NMR (400 MHz, CD_3OD) Spectrum of (*R*)-**1db**.



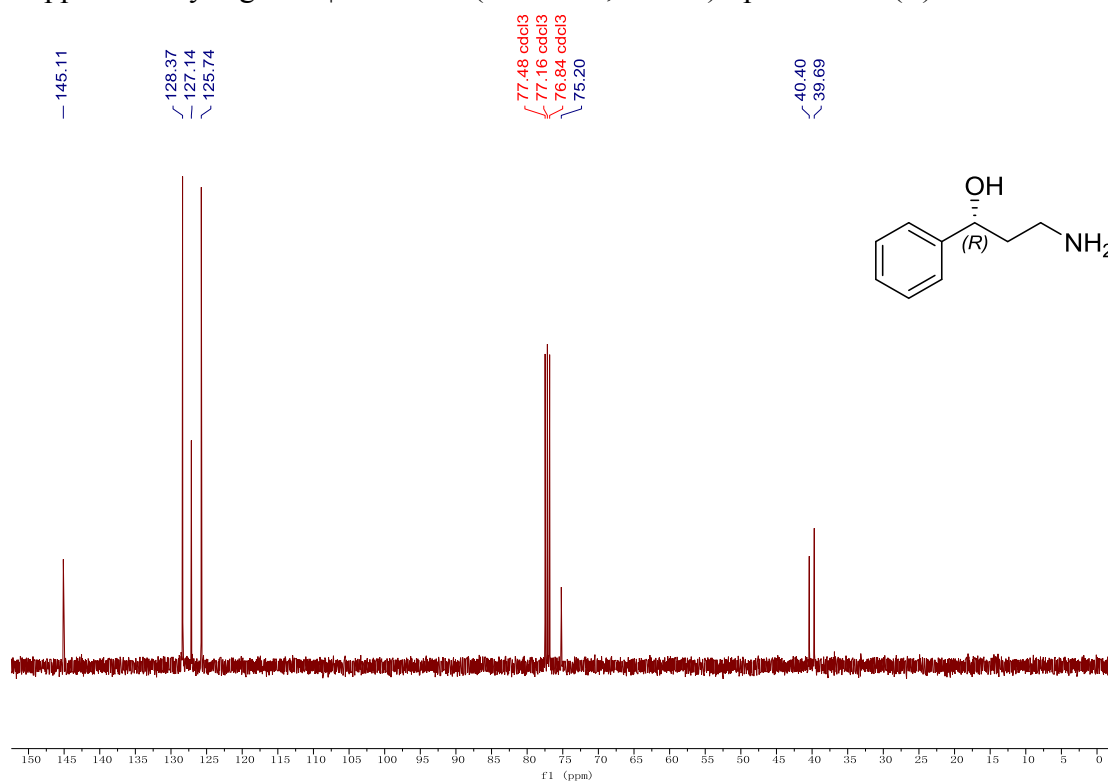
Supplementary Fig. 209 | ^{13}C NMR (100 MHz, CD_3OD) Spectrum of (*R*)-**1db**.



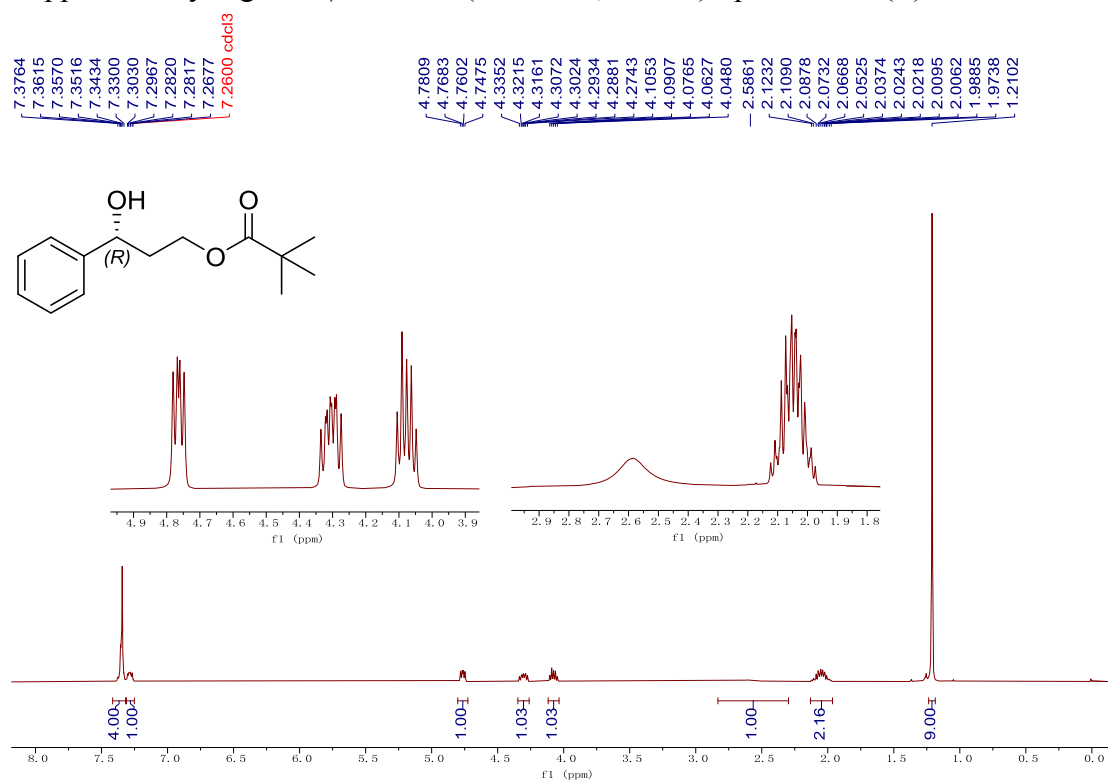
Supplementary Fig. 210 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1ea**.



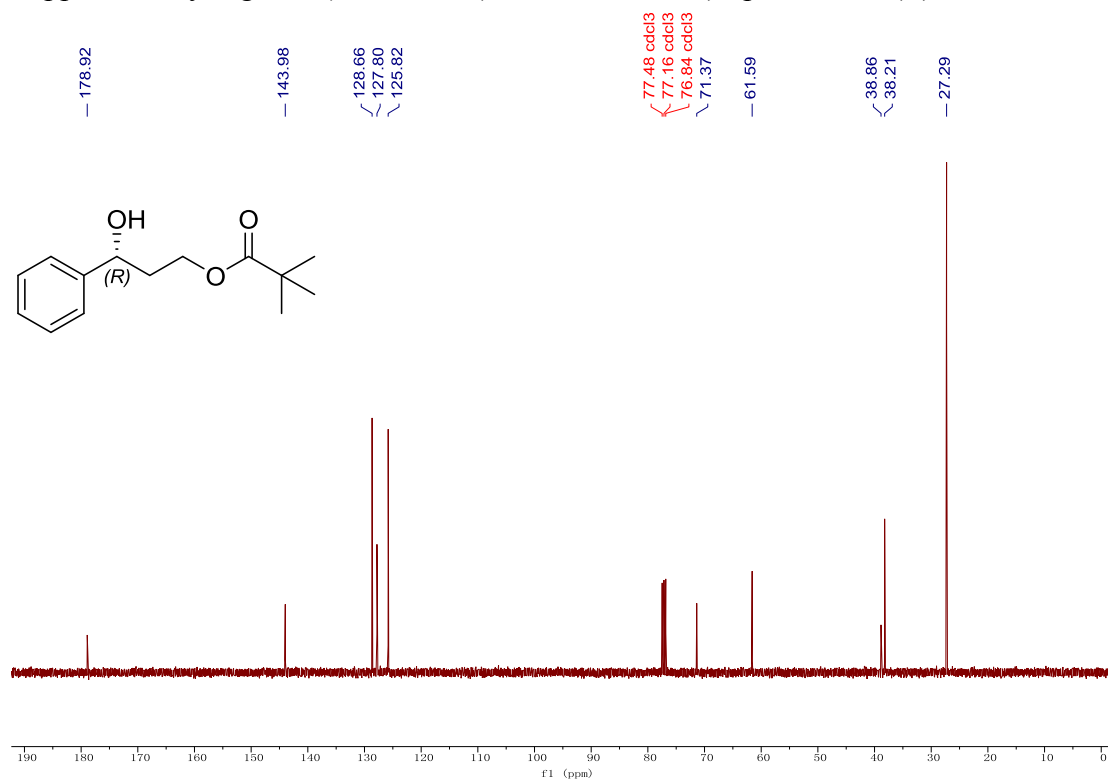
Supplementary Fig. 211 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1ea**.



Supplementary Fig. 212 | ^1H NMR (400 MHz, CDCl_3) Spectrum of (*R*)-**1fa**.



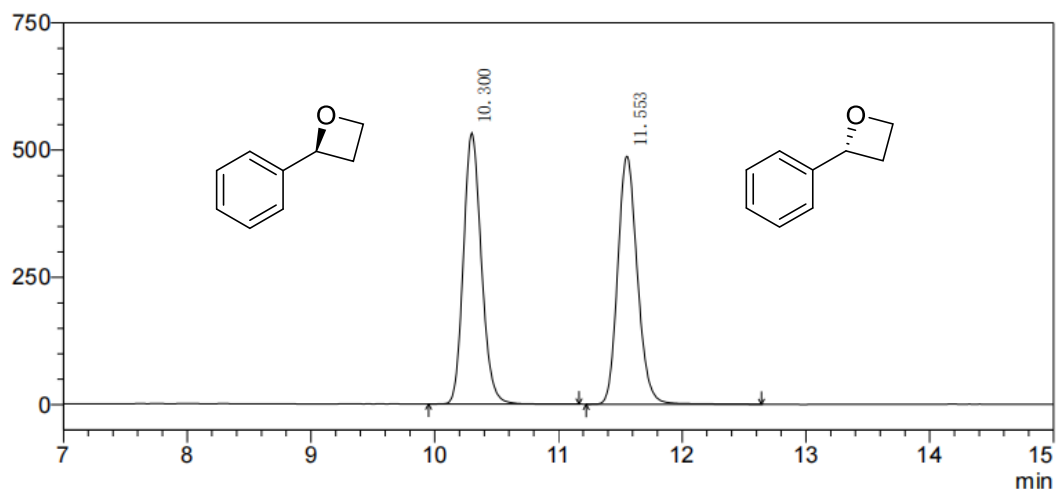
Supplementary Fig. 213 | ^{13}C NMR (100 MHz, CDCl_3) Spectrum of (*R*)-**1fa**.



11. Chiral HPLC/GC Traces (Supplementary Figures 214-425)

Supplementary Fig. 214 | HPLC trace for the chemical synthesized (*rac*)-**1b**.

mV

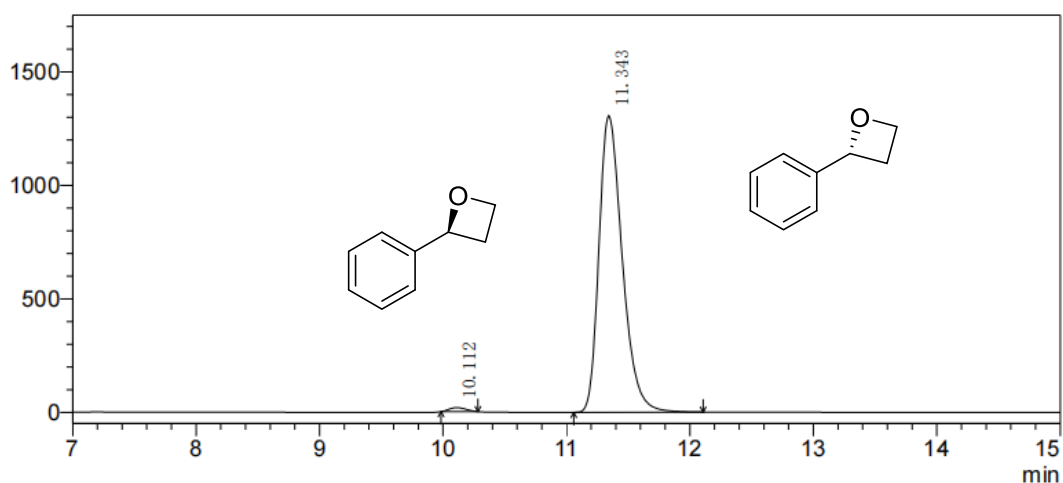


PDA 210nm

ID#	Rt. Time	Area	Height	Area %
1	10.300	5360586	532422	49.946
2	11.553	5372125	487092	50.054

Supplementary Fig. 215 | HPLC trace for the enzymatic synthesized (*R*)-**1b**.

mV

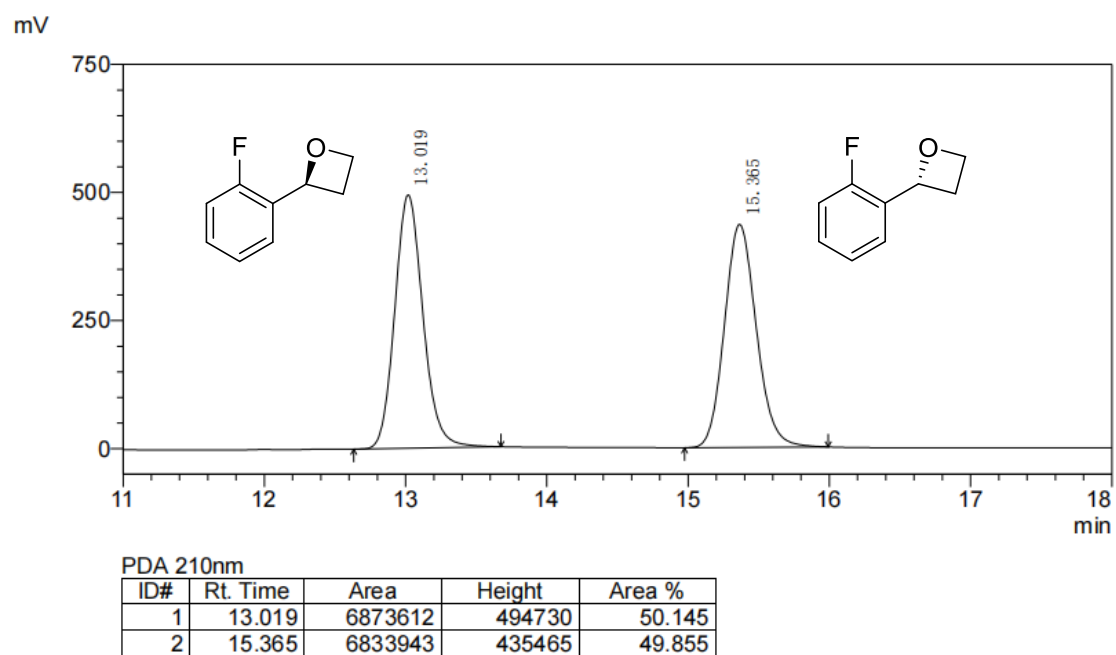


PDA 210nm

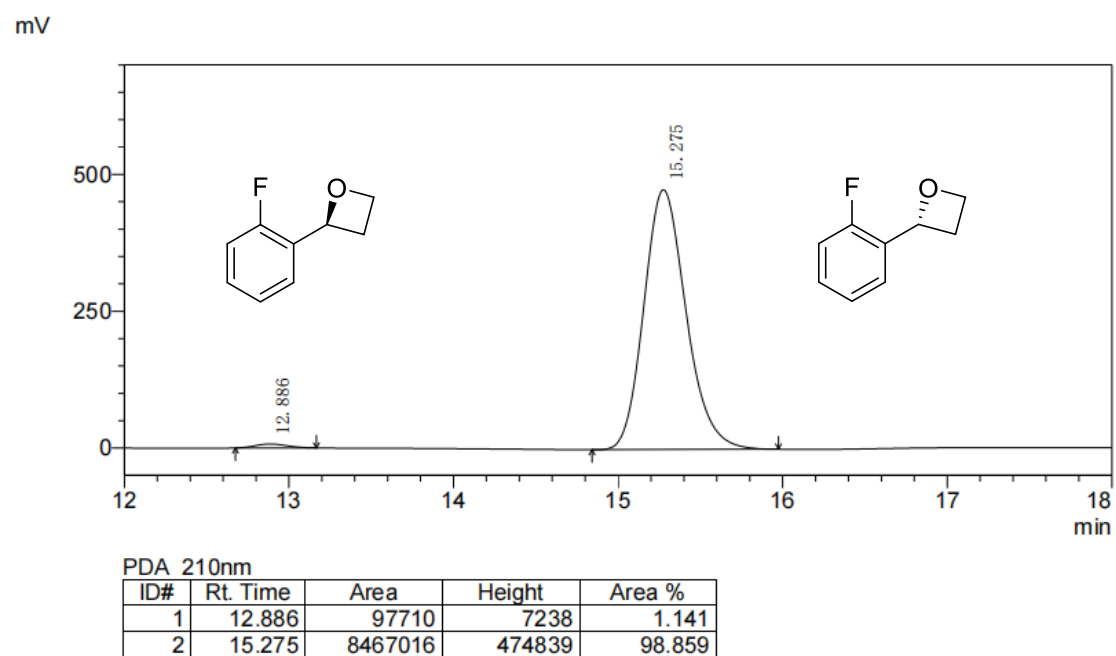
ID#	Rt. Time	Area	Height	Area %
1	10.112	167593	17743	0.969
2	11.343	17132548	1306991	99.031

Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, $\lambda = 210$ nm, $t_{(S)} = 10.1$ min, $t_{(R)} = 11.3$ min.

Supplementary Fig. 216 | HPLC trace for the chemical synthesized (*rac*)-**2b**.



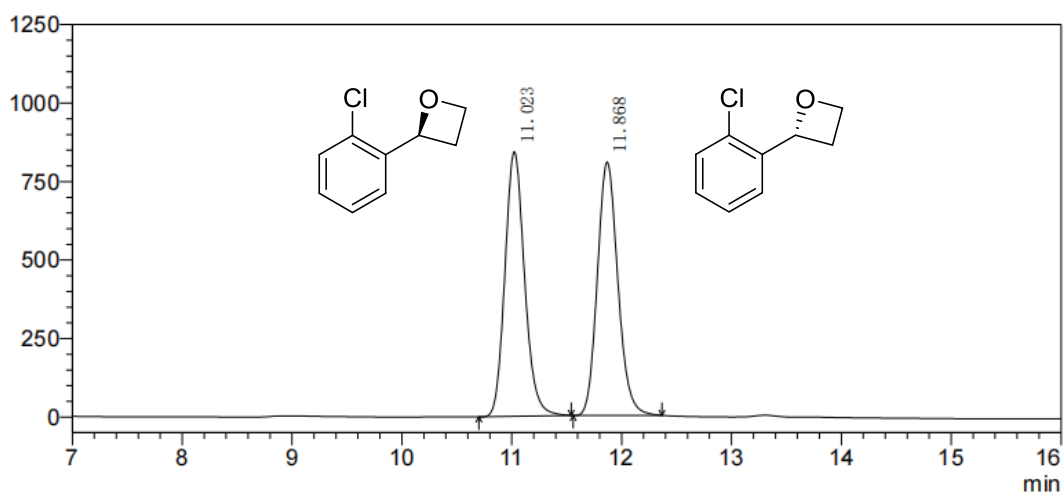
Supplementary Fig. 217 | HPLC trace for the enzymatic synthesized (*R*)-**2b**.



Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 12.9 min, $t_{(R)}$ = 15.3 min.

Supplementary Fig. 218 | HPLC trace for the chemical synthesized (*rac*)-**3b**.

mV

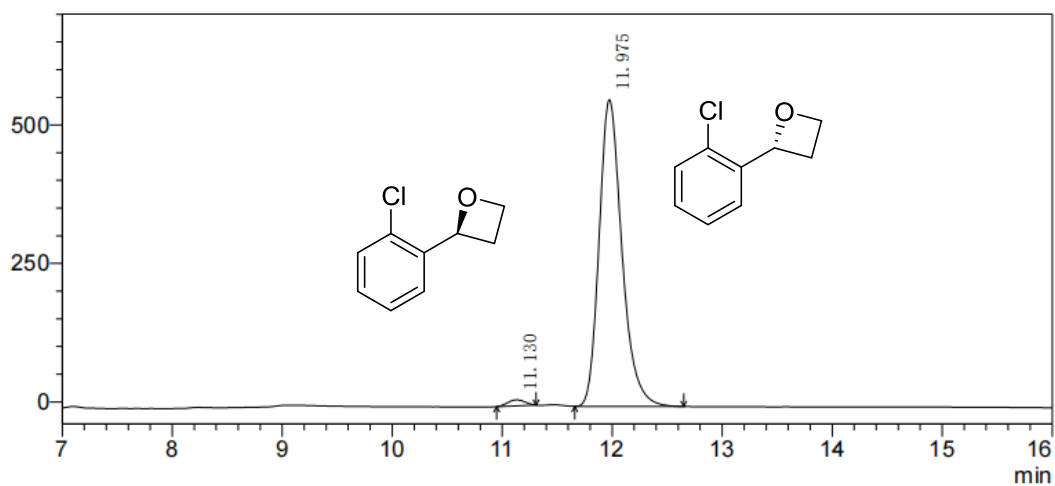


PDA 210nm

ID#	Rt. Time	Area	Height	Area %
1	11.023	10477966	842802	50.015
2	11.868	10471835	807073	49.985

Supplementary Fig. 219 | HPLC trace for the enzymatic synthesized (*R*)-**3b**.

mV

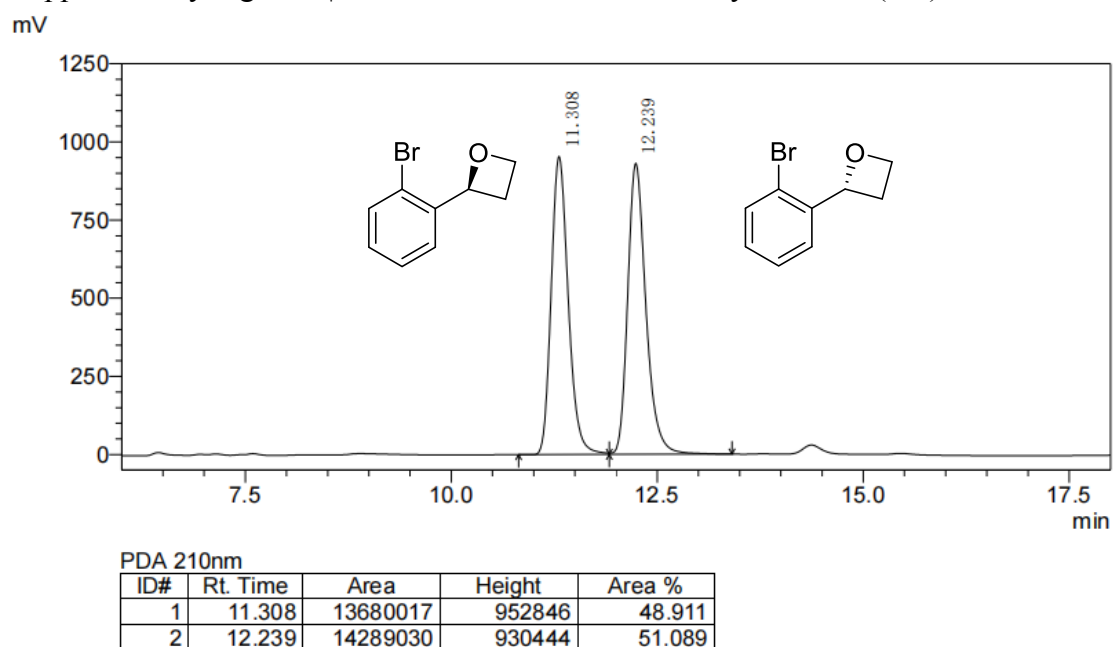


PDA 210nm

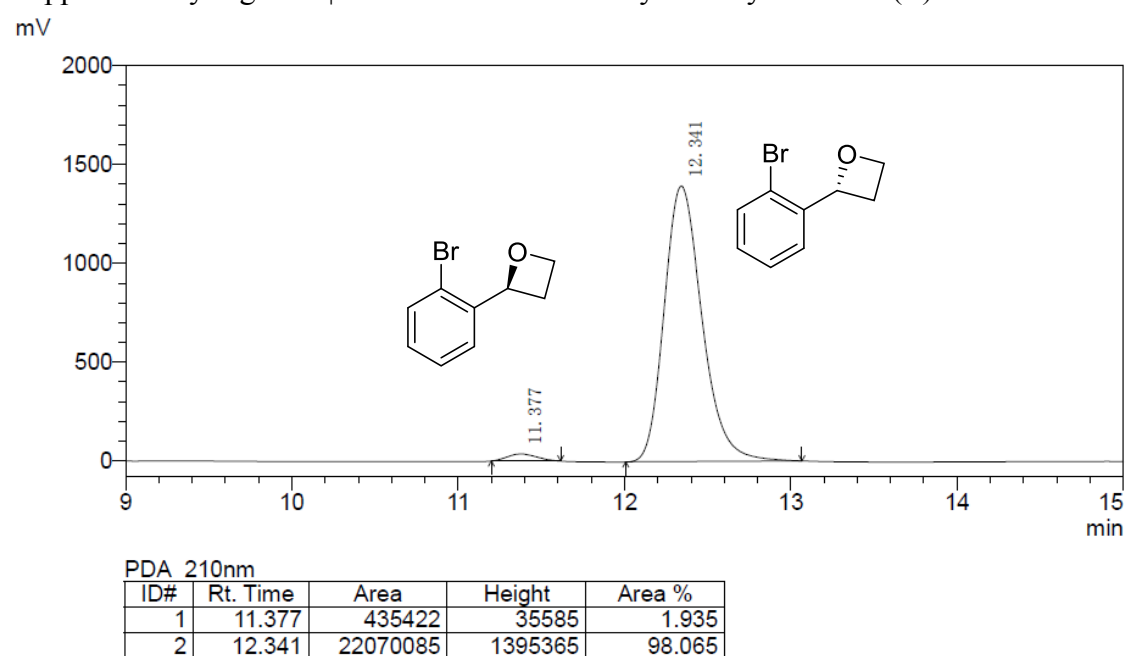
ID#	Rt. Time	Area	Height	Area %
1	11.130	118531	10775	1.463
2	11.975	7981297	553990	98.537

Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 11.1 min, $t_{(R)}$ = 12.0 min.

Supplementary Fig. 220 | HPLC trace for the chemical synthesized (*rac*)-**4b**.



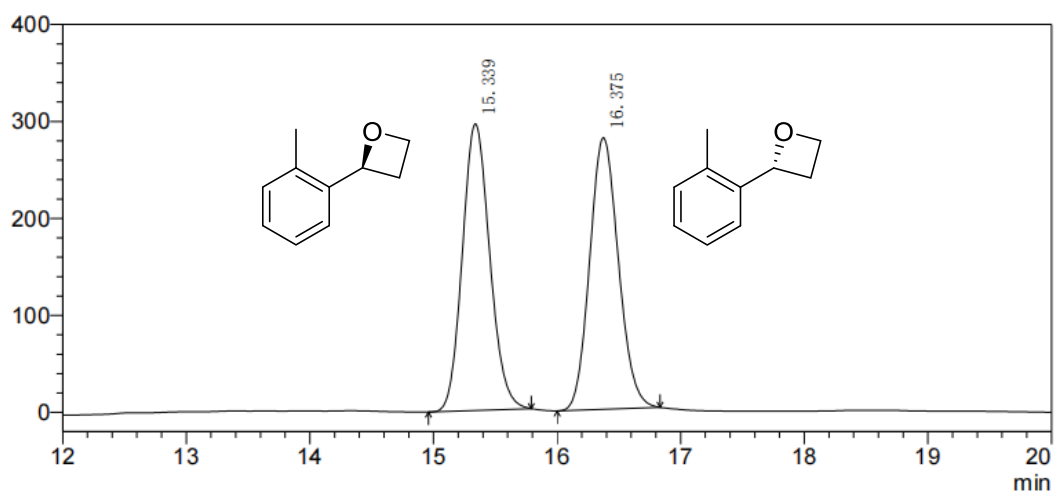
Supplementary Fig. 221 | HPLC trace for the enzymatic synthesized (*R*)-**4b**.



Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 11.4 min, $t_{(R)}$ = 12.3 min.

Supplementary Fig. 222 | HPLC trace for the chemical synthesized (*rac*)-**5b**.

mV

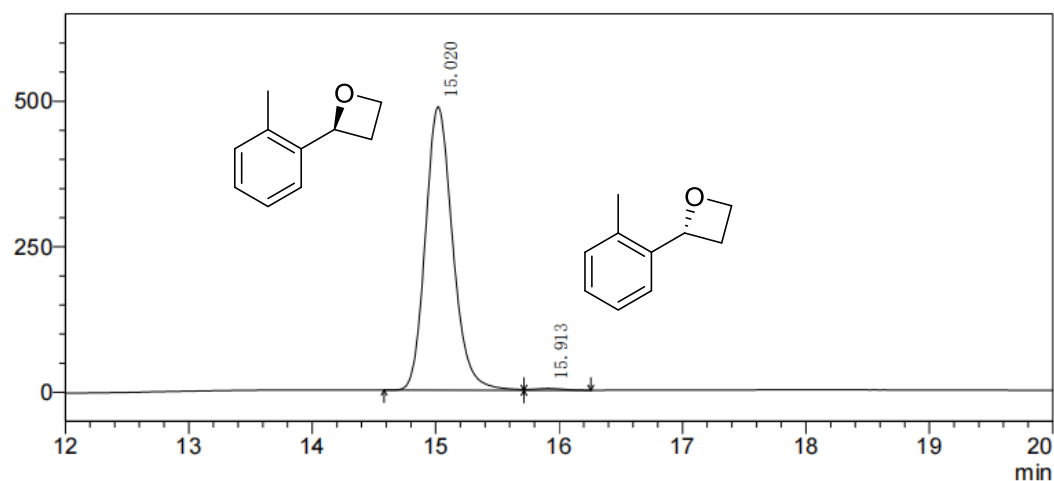


PDA 210nm

ID#	Rt. Time	Area	Height	Area %
1	15.339	4557692	295629	50.171
2	16.375	4526543	280296	49.829

Supplementary Fig. 223 | HPLC trace for the enzymatic synthesized (*R*)-**5b**.

mV

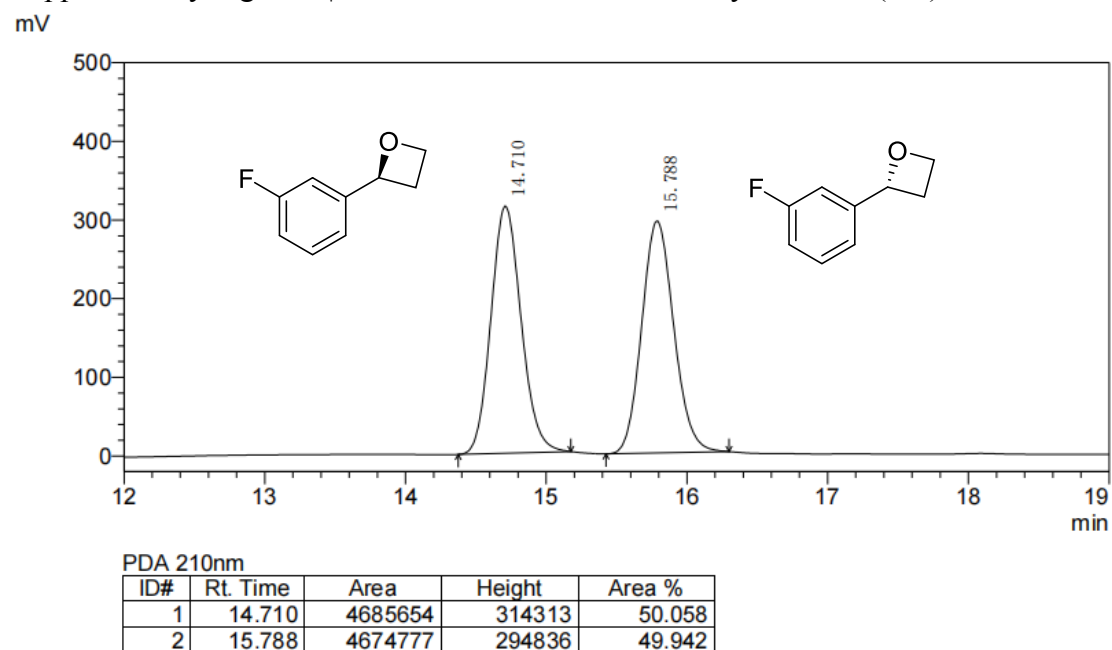


PDA 210nm

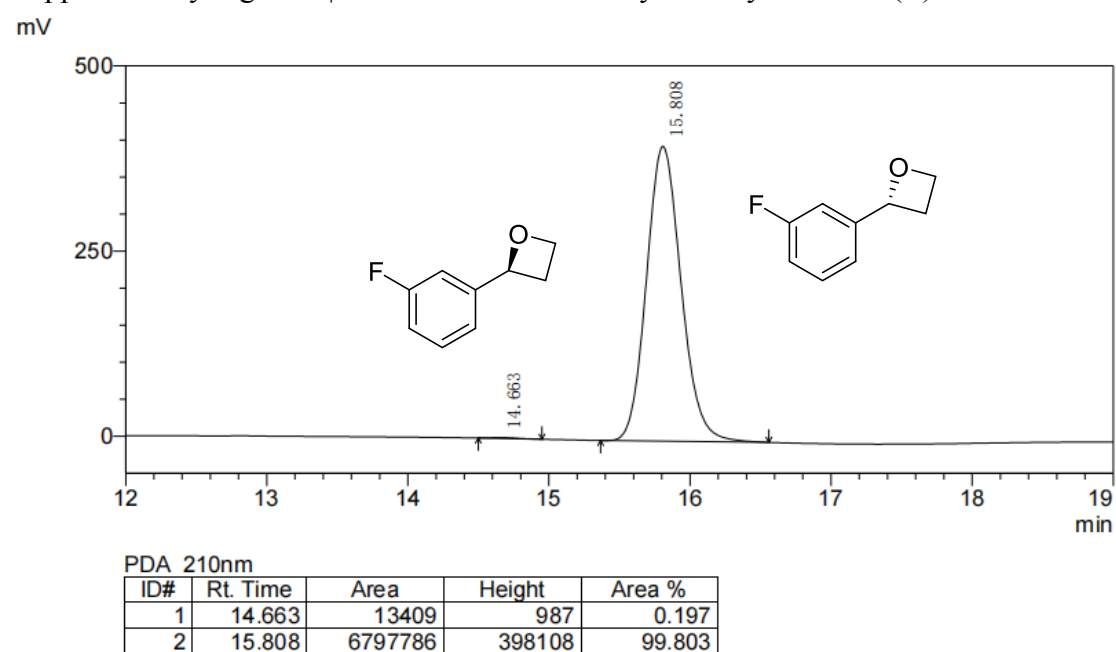
ID#	Rt. Time	Area	Height	Area %
1	15.020	7469458	486657	99.376
2	15.913	46869	2909	0.624

Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(R)}$ = 15.0 min, $t_{(S)}$ = 15.9 min.

Supplementary Fig. 224 | HPLC trace for the chemical synthesized (*rac*)-**6b**.

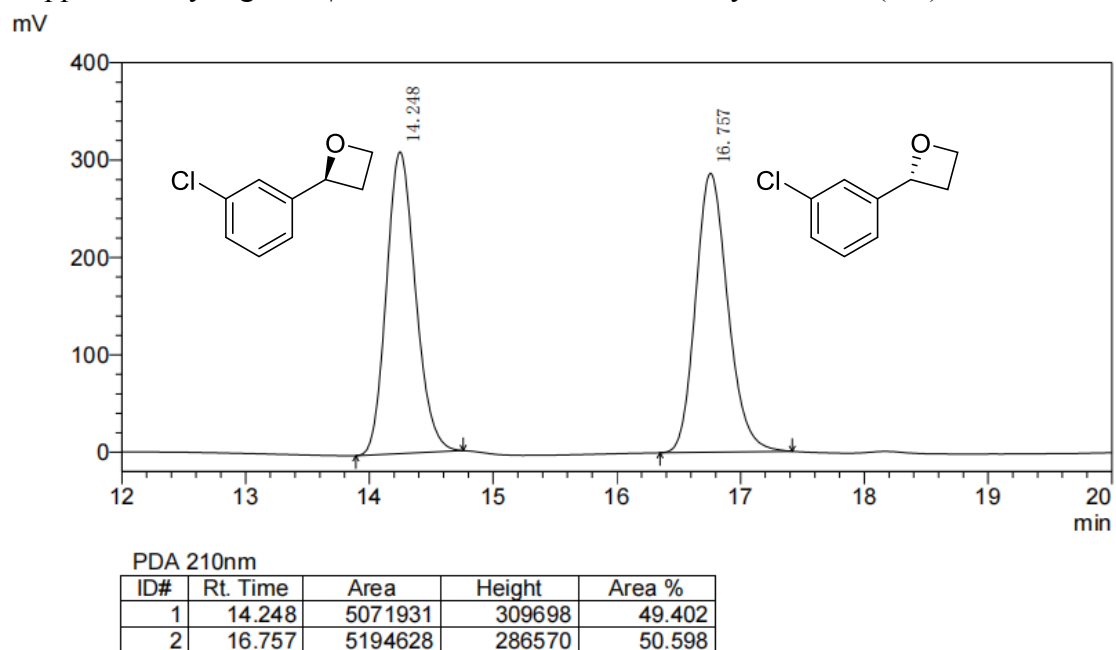


Supplementary Fig. 225 | HPLC trace for the enzymatic synthesized (*R*)-**6b**.

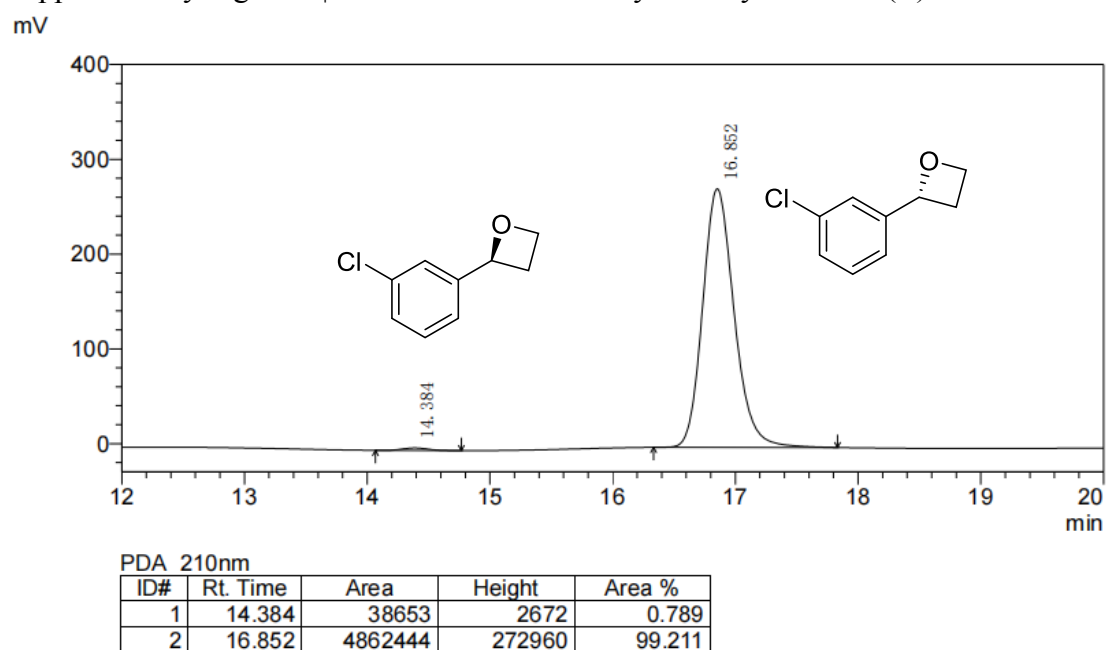


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, $\lambda = 210$ nm, $t_{(S)} = 14.7$ min, $t_{(R)} = 15.8$ min.

Supplementary Fig. 226 | HPLC trace for the chemical synthesized (*rac*)-**7b**.

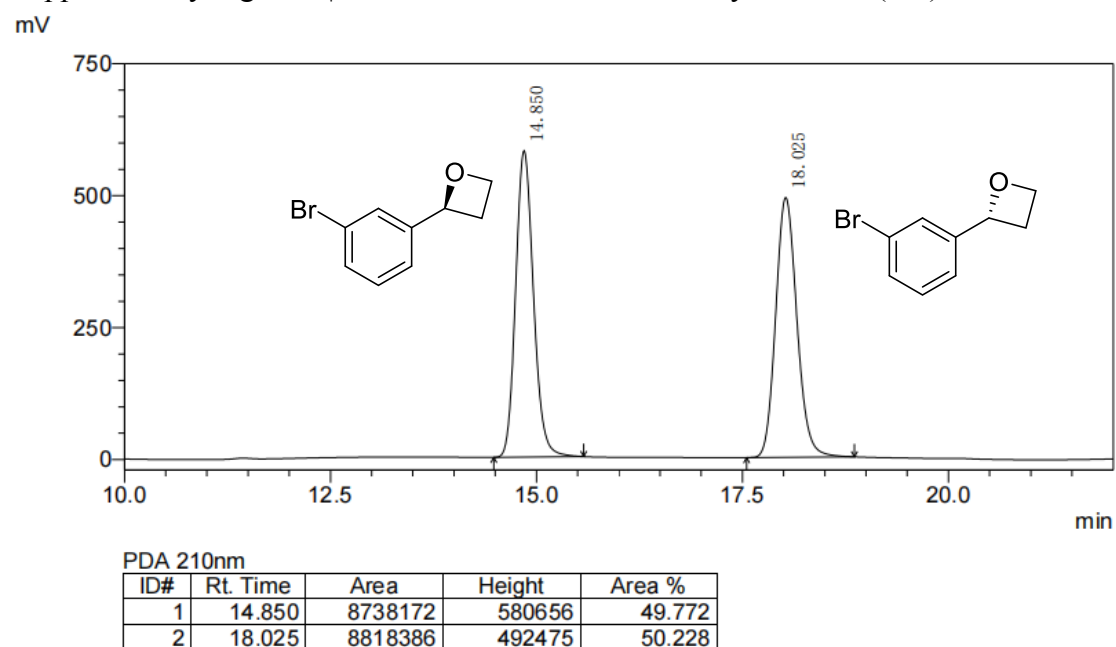


Supplementary Fig. 227 | HPLC trace for the enzymatic synthesized (*R*)-**7b**.

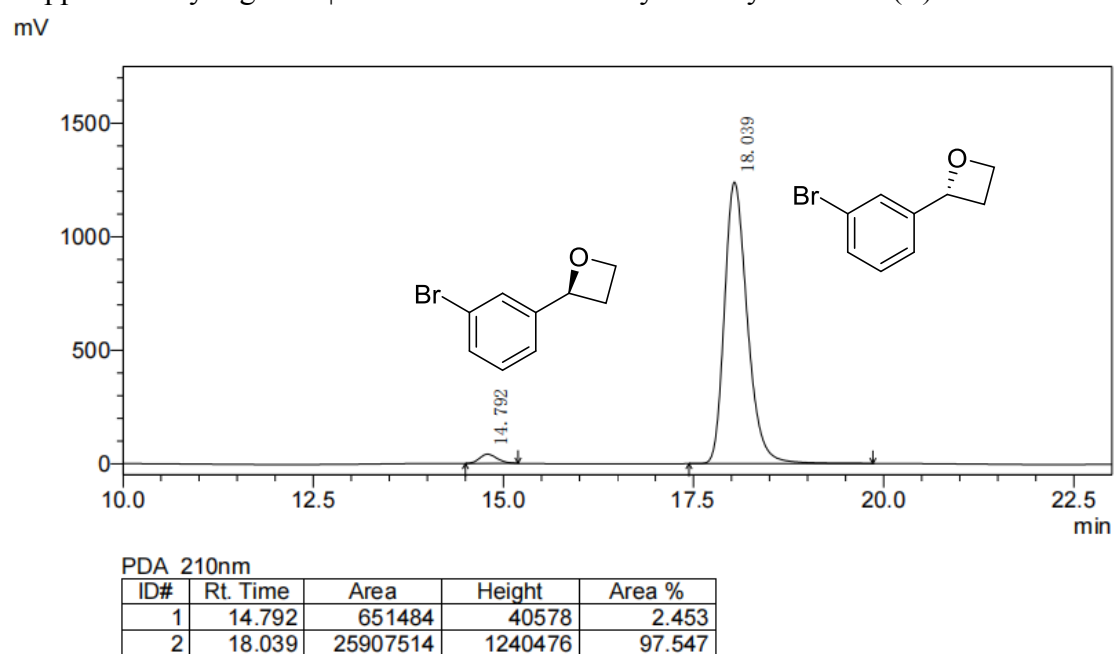


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, $\lambda = 210$ nm, $t_{(S)} = 14.4$ min, $t_{(R)} = 16.9$ min.

Supplementary Fig. 228 | HPLC trace for the chemical synthesized (*rac*)-**8b**.

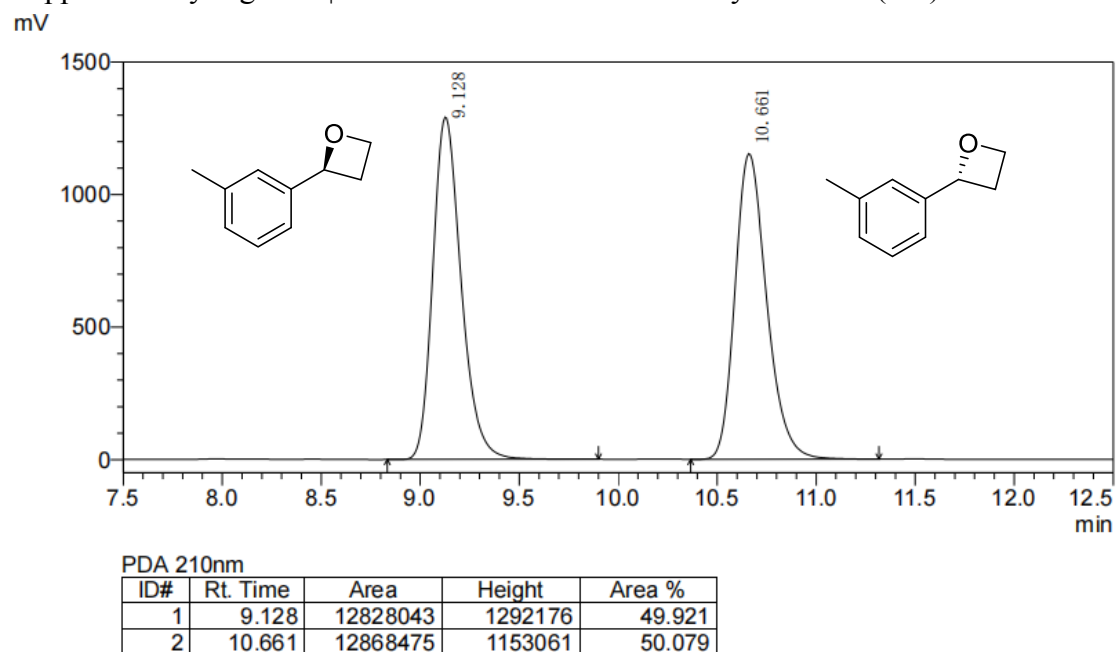


Supplementary Fig. 229 | HPLC trace for the enzymatic synthesized (*R*)-**8b**.

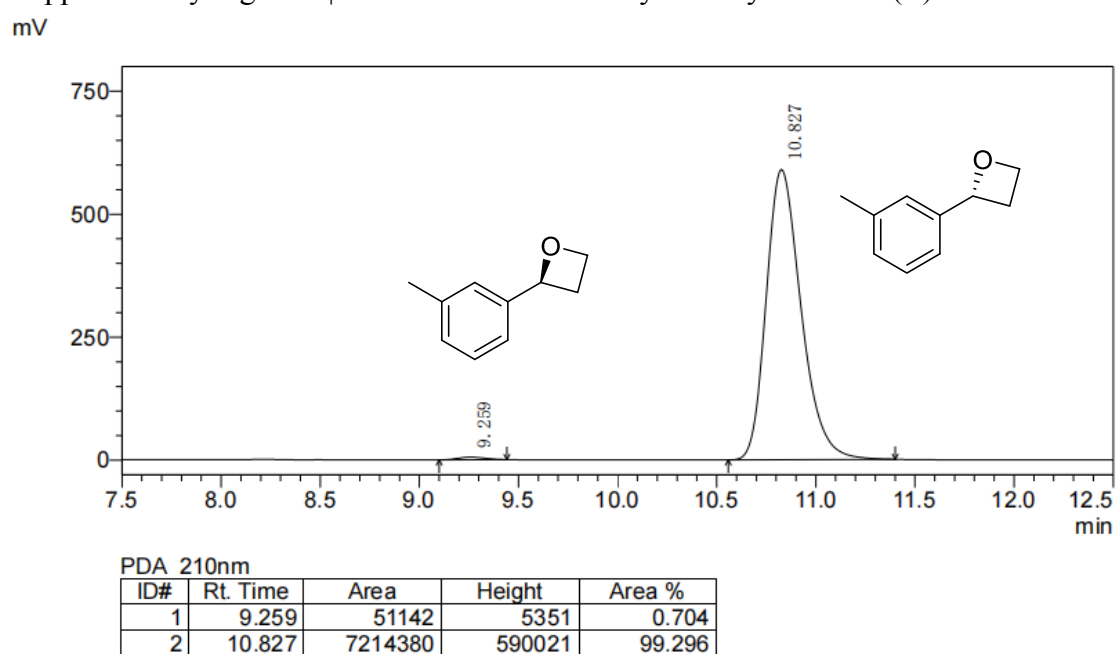


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 14.8 min, $t_{(R)}$ = 18.0 min.

Supplementary Fig. 230 | HPLC trace for the chemical synthesized (*rac*)-**9b**.

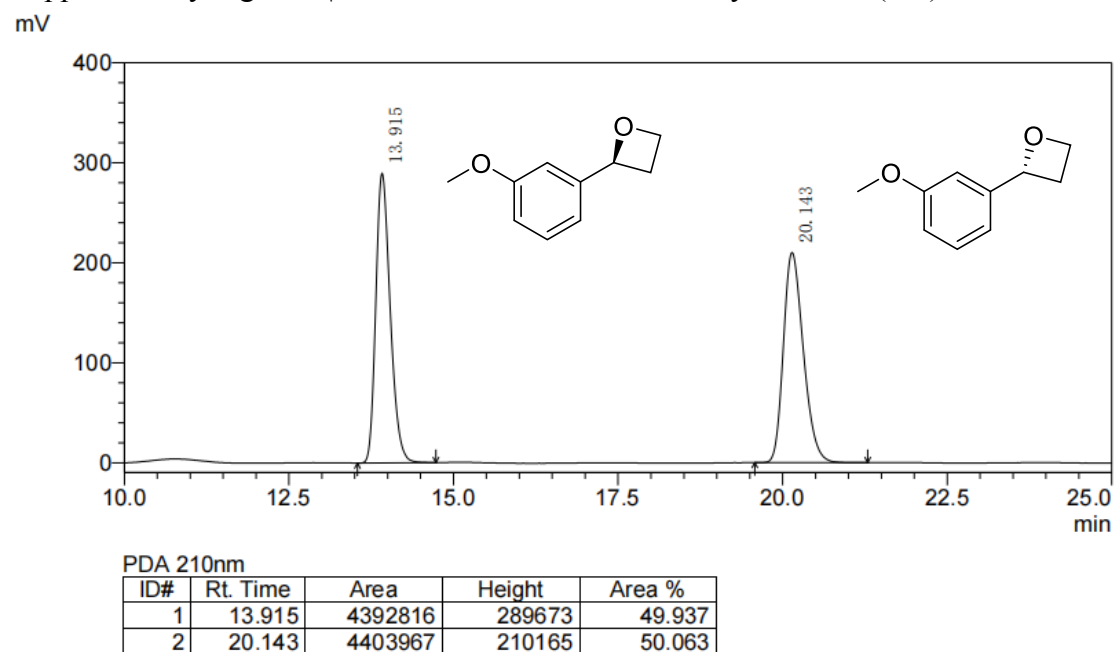


Supplementary Fig. 231 | HPLC trace for the enzymatic synthesized (*R*)-**9b**.

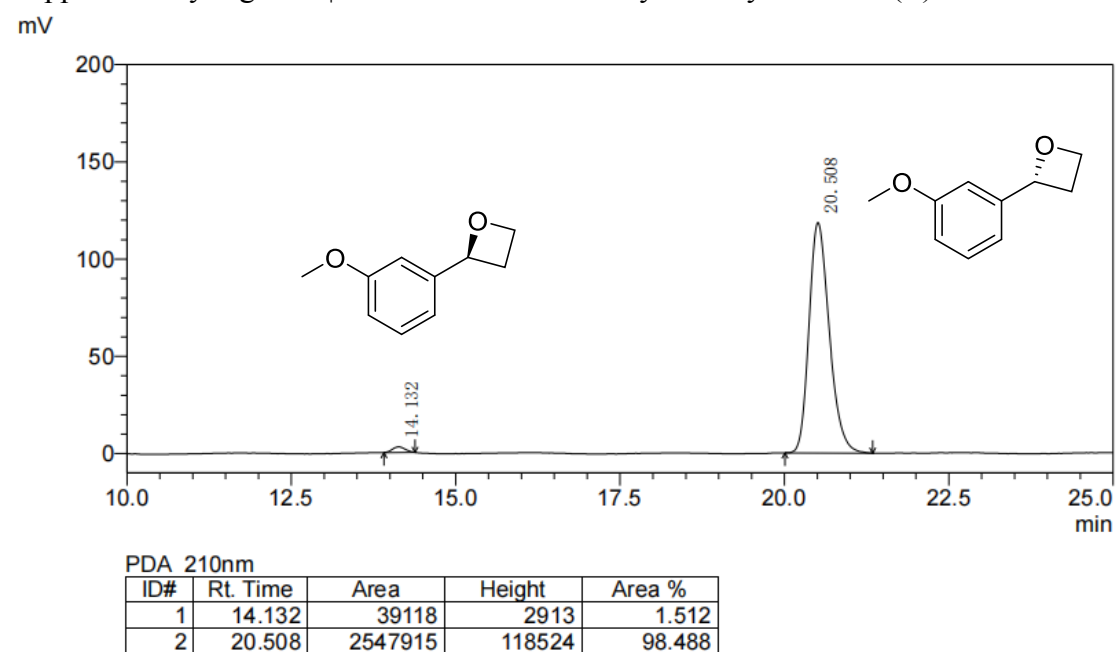


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 9.3 min, $t_{(R)}$ = 10.8 min.

Supplementary Fig. 232 | HPLC trace for the chemical synthesized (*rac*)-**10b**.

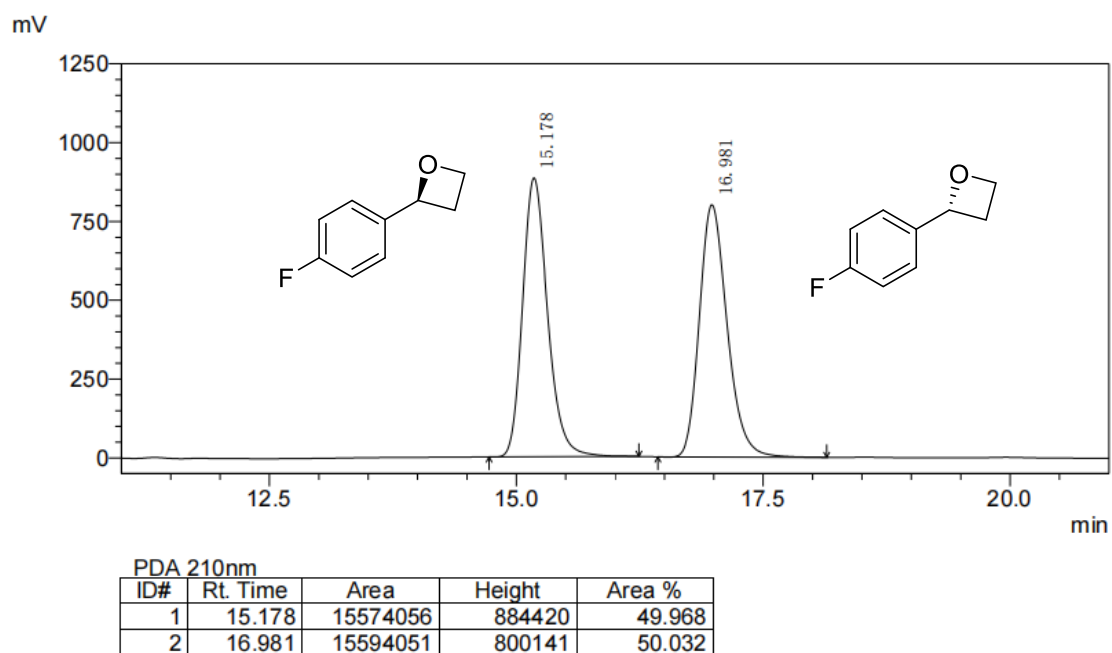


Supplementary Fig. 233 | HPLC trace for the enzymatic synthesized (*R*)-**10b**.

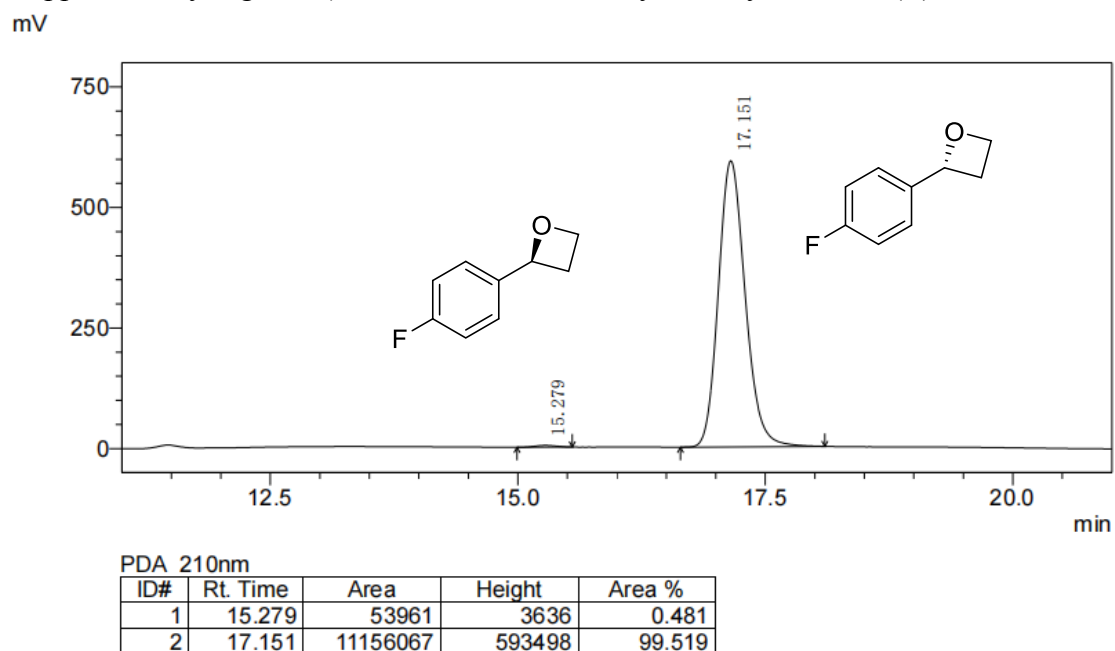


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 14.1 min, $t_{(R)}$ = 20.5 min.

Supplementary Fig. 234 | HPLC trace for the chemical synthesized (*rac*)-**11b**.

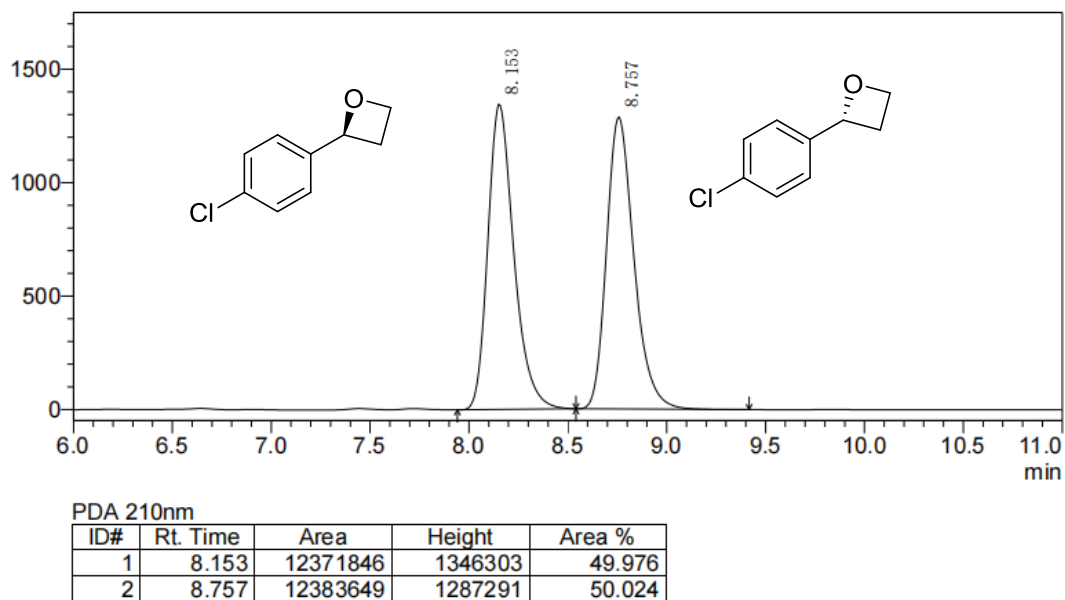


Supplementary Fig. 235 | HPLC trace for the enzymatic synthesized (*R*)-**11b**.

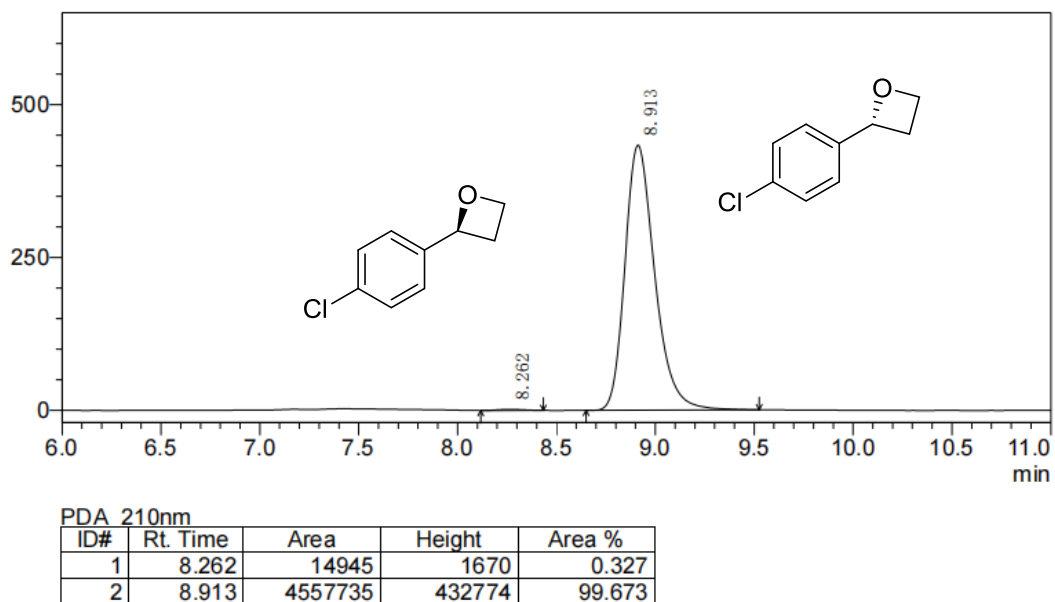


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, $\lambda = 210$ nm, $t_{(S)} = 15.3$ min, $t_{(R)} = 17.2$ min.

Supplementary Fig. 236 | HPLC trace for the chemical synthesized (*rac*)-**12b**.
mV

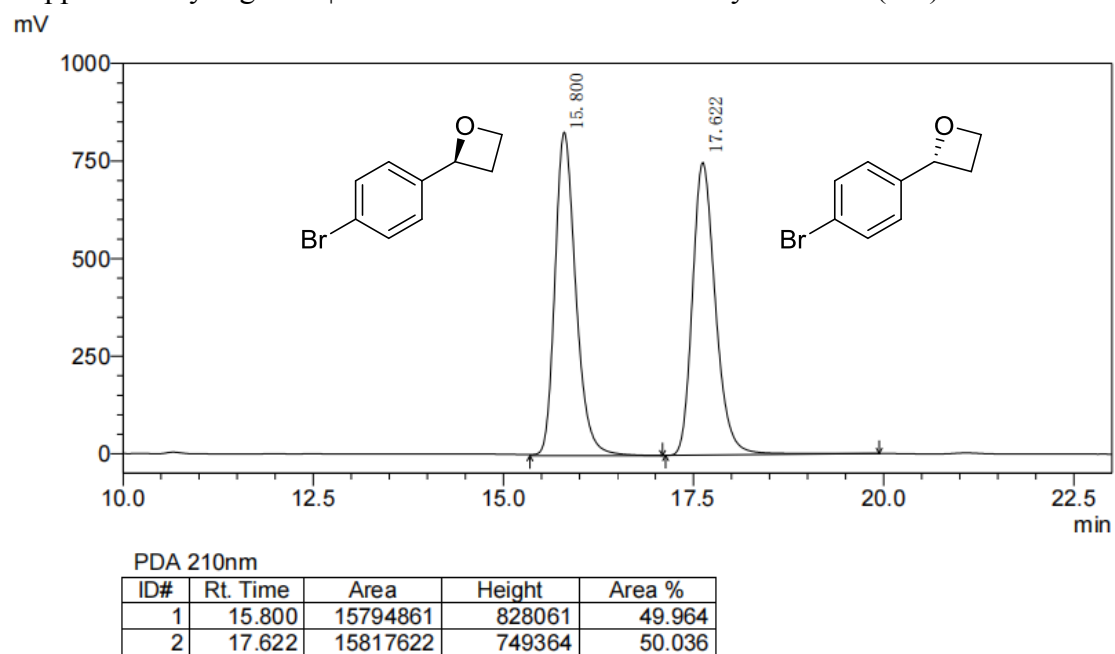


Supplementary Fig. 237 | HPLC trace for the enzymatic synthesized (*R*)-**12b**.
mV

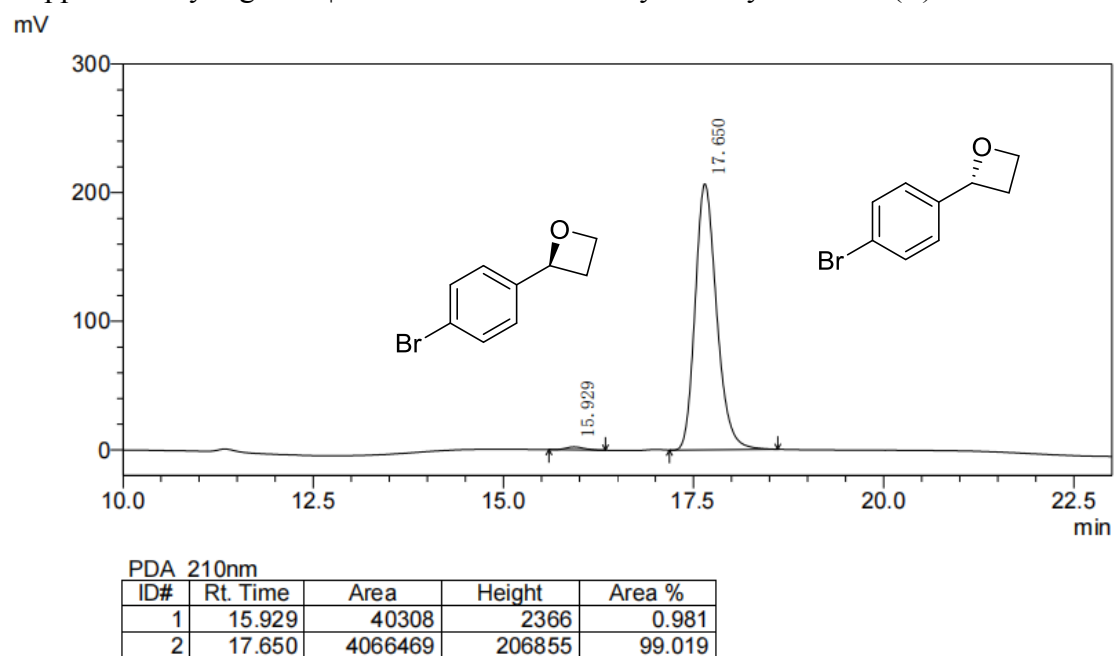


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, $\lambda = 210$ nm, $t_{(S)} = 8.3$ min, $t_{(R)} = 8.9$ min.

Supplementary Fig. 238 | HPLC trace for the chemical synthesized (*rac*)-**13b**.

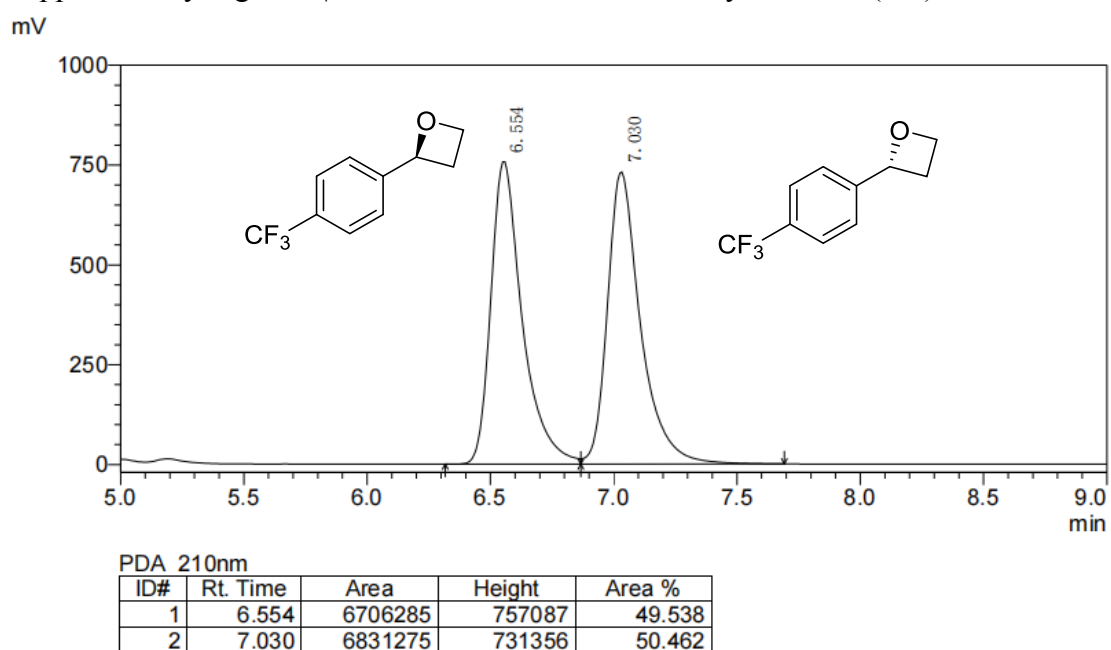


Supplementary Fig. 239 | HPLC trace for the enzymatic synthesized (*R*)-**13b**.

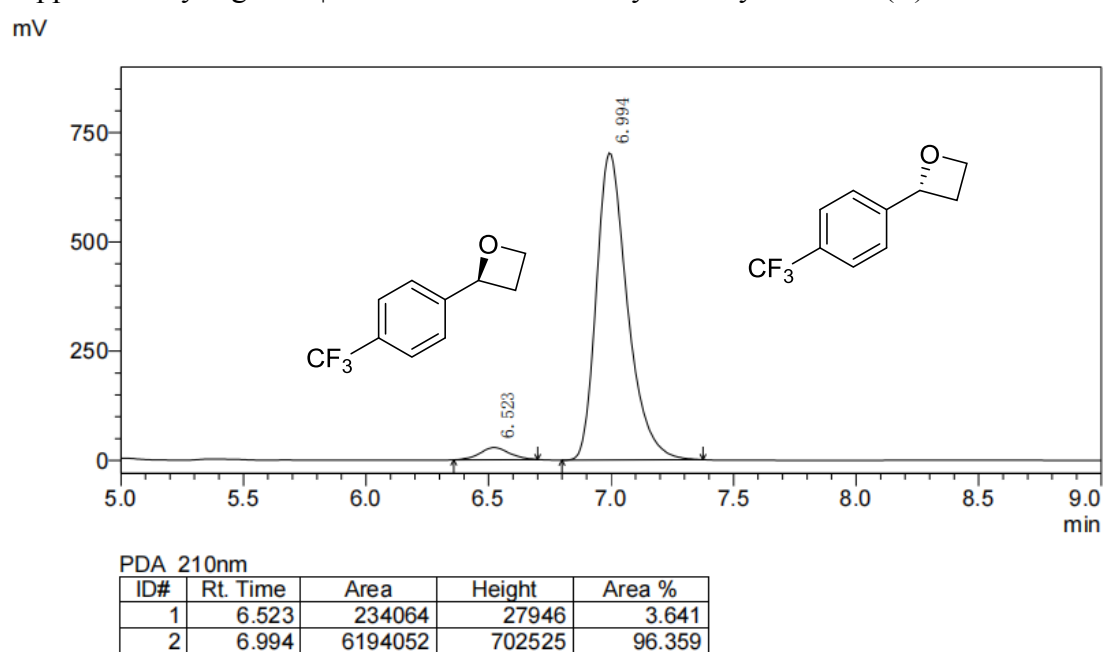


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 15.9 min, $t_{(R)}$ = 17.7 min.

Supplementary Fig. 240 | HPLC trace for the chemical synthesized (*rac*)-**14b**.

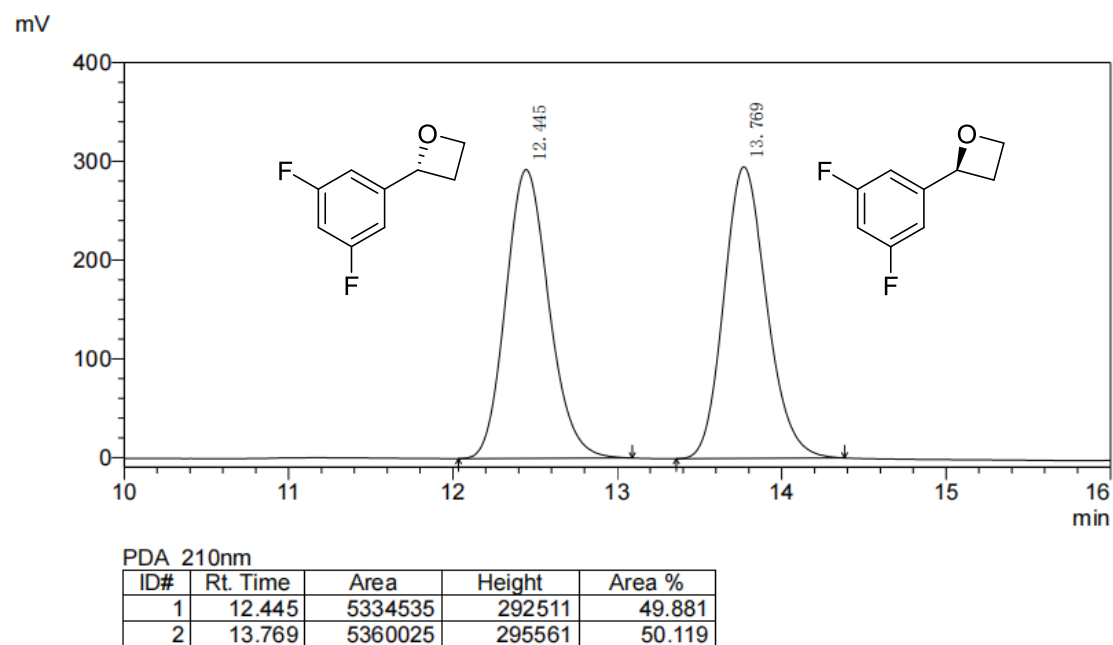


Supplementary Fig. 241 | HPLC trace for the enzymatic synthesized (*R*)-**14b**.

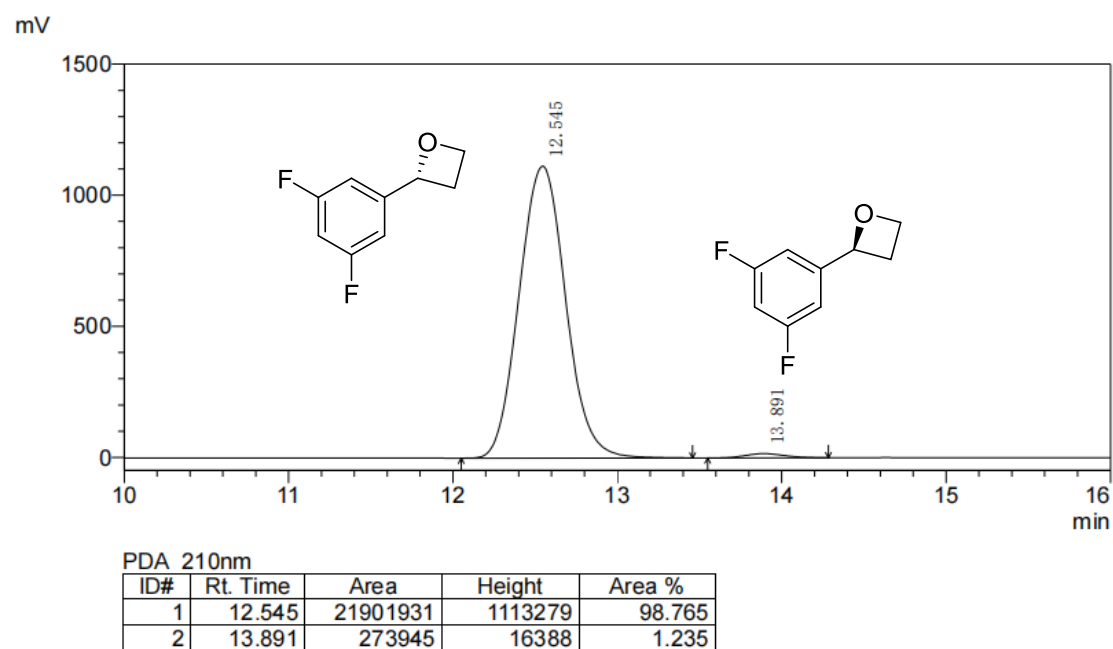


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm. $t_{(S)}$ = 6.5 min, $t_{(R)}$ = 7.0 min.

Supplementary Fig. 242 | HPLC trace for the chemical synthesized (*rac*)-**15b**.

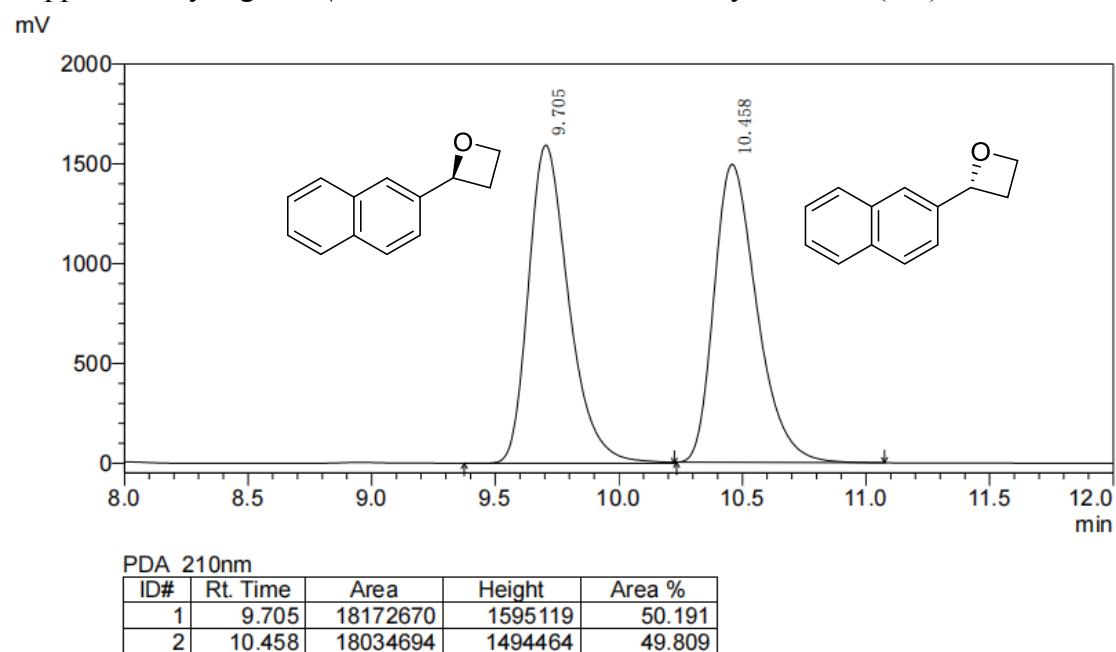


Supplementary Fig. 243 | HPLC trace for the enzymatic synthesized (*R*)-**15b**.

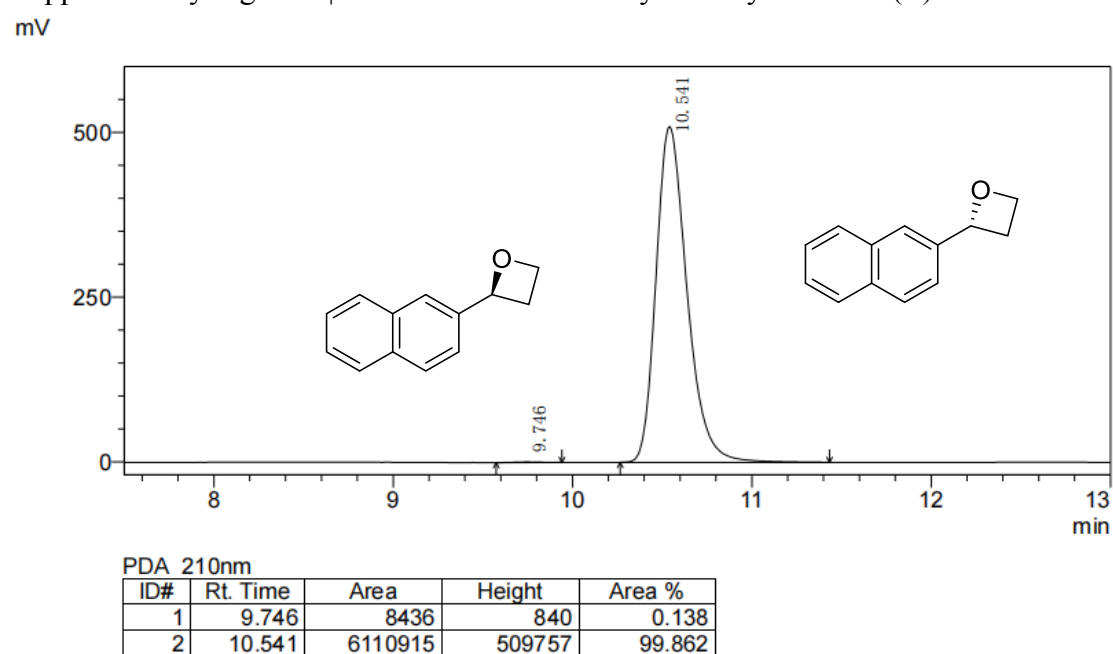


Chiral HPLC analysis: Diacel Chiralpak IA-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm. $t_{(R)}$ = 12.5 min, $t_{(S)}$ = 13.9 min.

Supplementary Fig. 244 | HPLC trace for the chemical synthesized (*rac*)-**16b**.

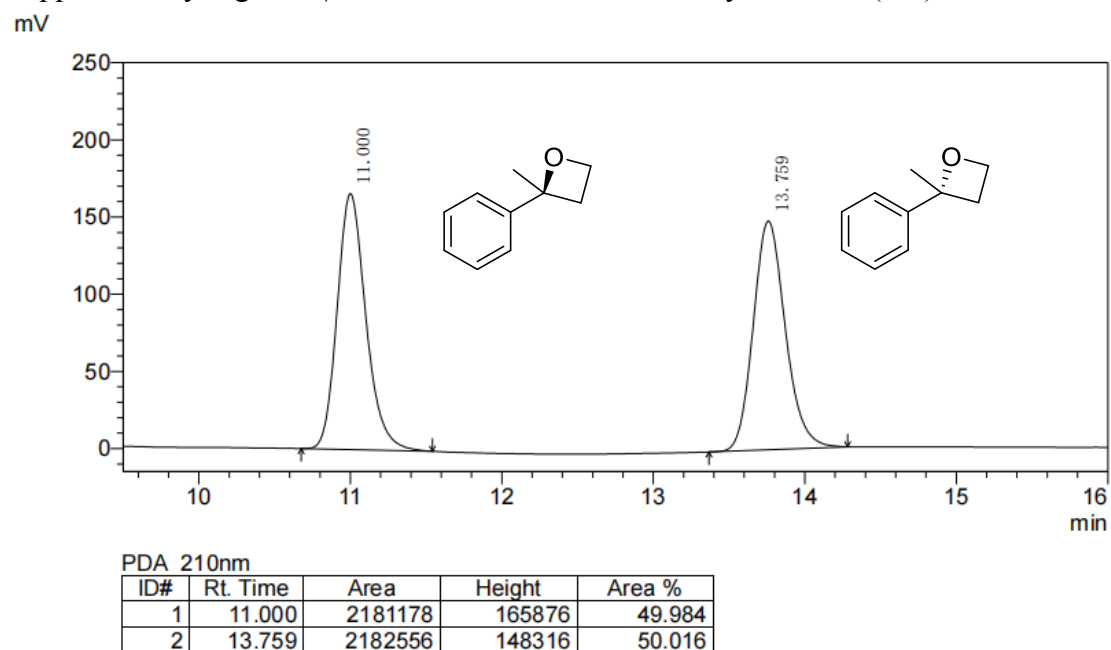


Supplementary Fig. 245 | HPLC trace for the enzymatic synthesized (*R*)-**16b**.

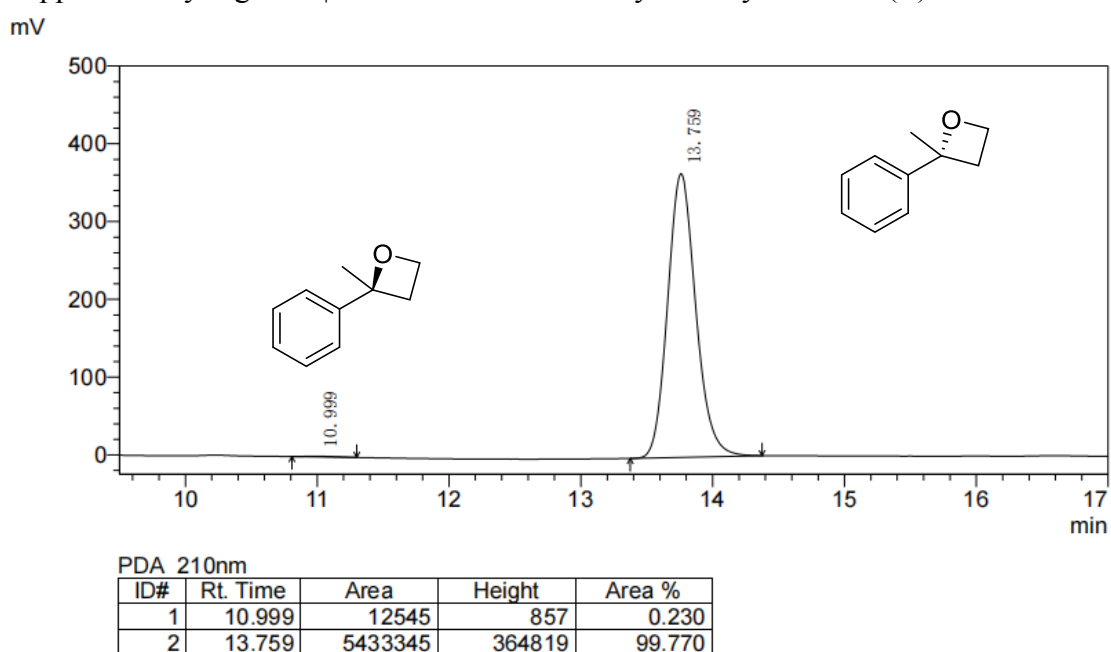


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm. $t_{(S)}$ = 9.7 min, $t_{(R)}$ = 10.5 min.

Supplementary Fig. 246 | HPLC trace for the chemical synthesized (*rac*)-**17b**.

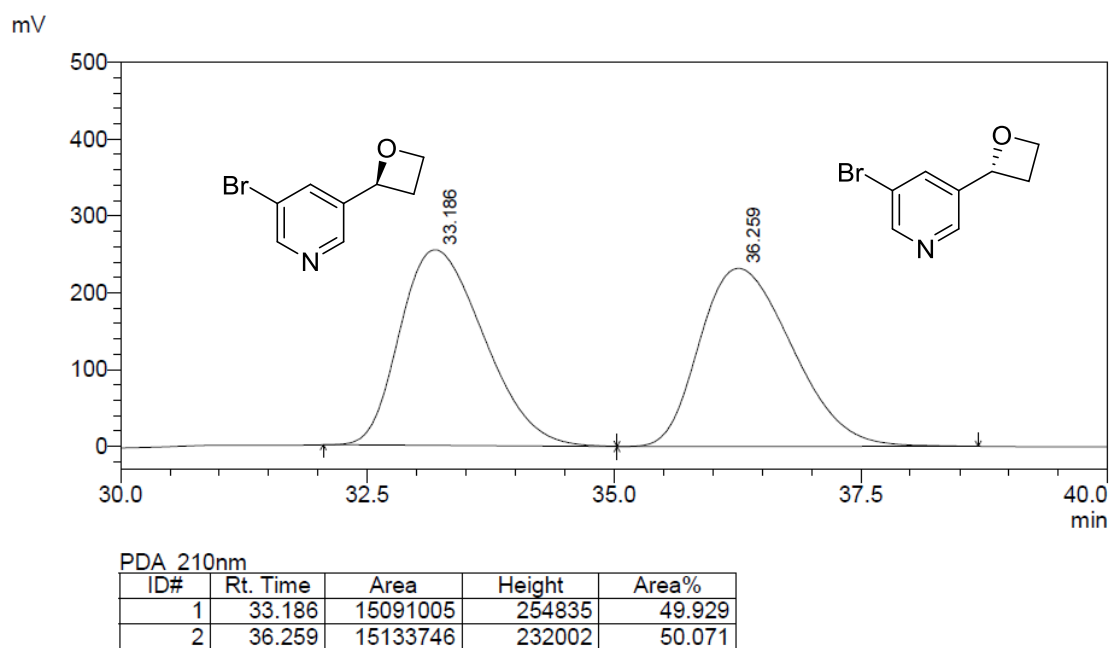


Supplementary Fig. 247 | HPLC trace for the enzymatic synthesized (*R*)-**17b**.

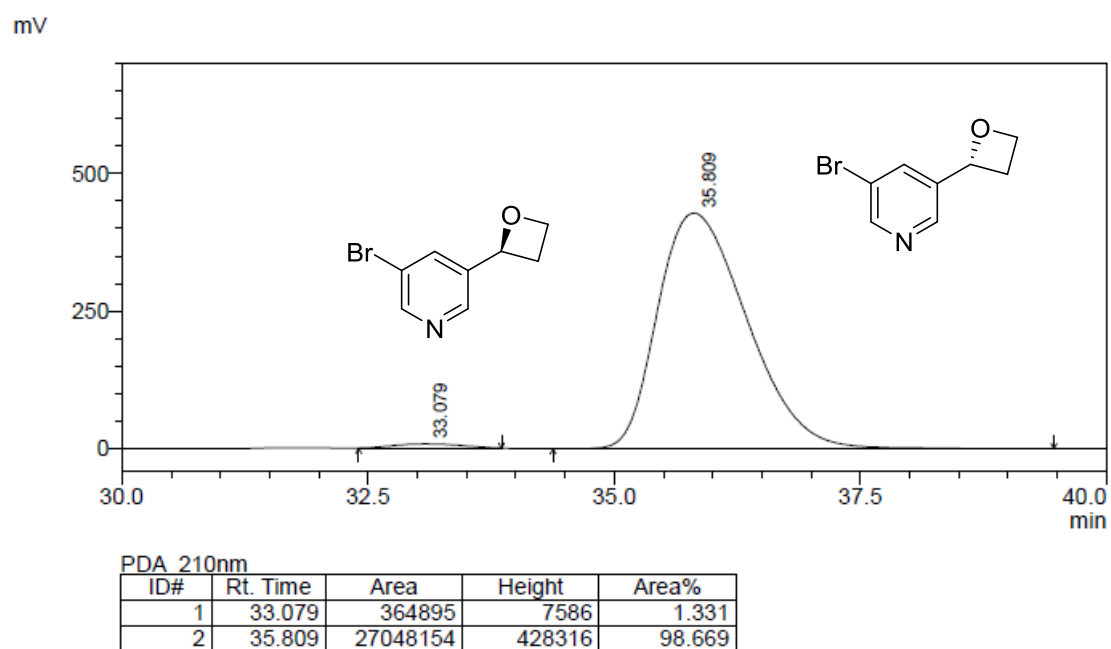


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, $\lambda = 210$ nm. $t_{(S)} = 11.0$ min, $t_{(R)} = 13.8$ min.

Supplementary Fig. 248 | HPLC trace for the chemical synthesized (*rac*)-**18b**.

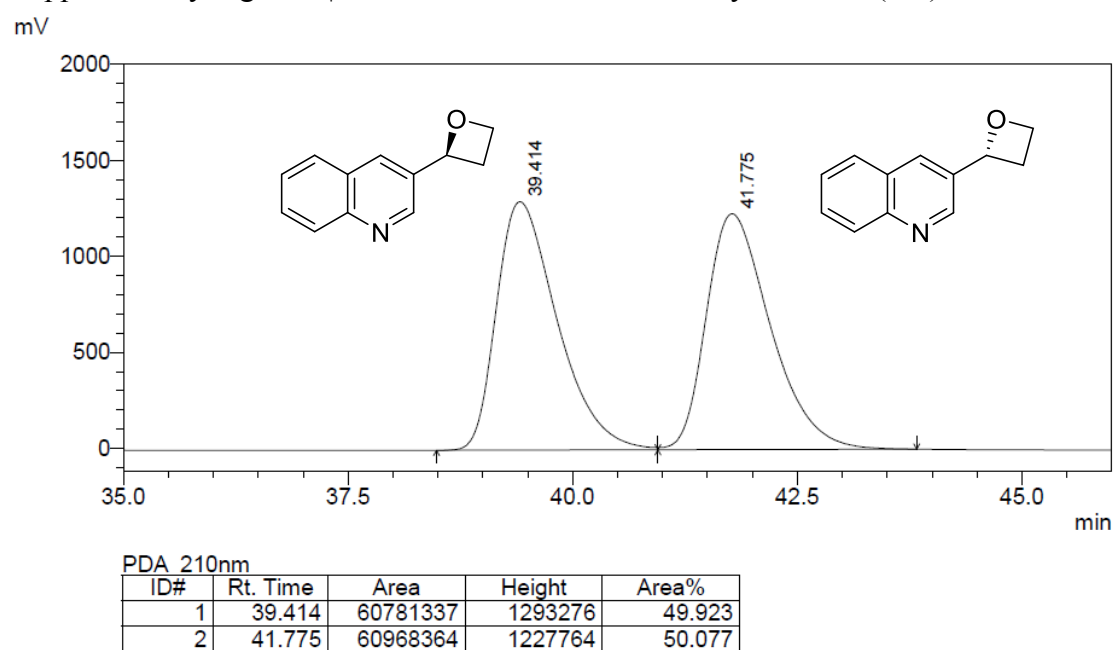


Supplementary Fig. 249 | HPLC trace for the enzymatic synthesized (*R*)-**18b**.

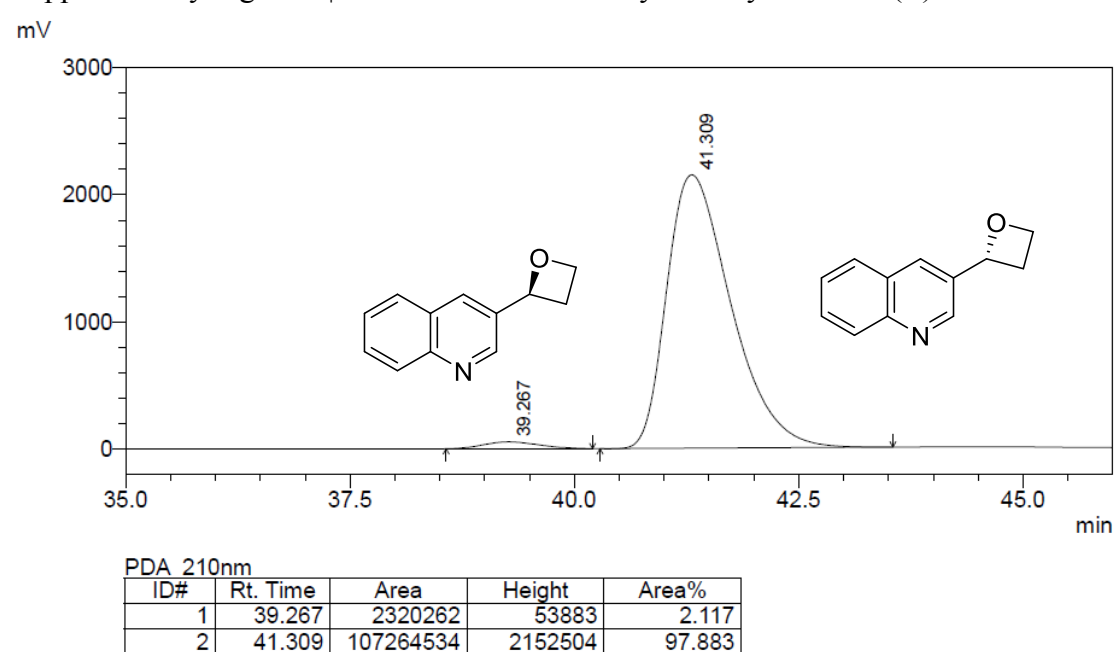


Chiral HPLC analysis: Diacel Chiralpak OB-H, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm. $t_{(S)}$ = 33.1 min, $t_{(R)}$ = 35.8 min.

Supplementary Fig. 250 | HPLC trace for the chemical synthesized (*rac*)-**19b**.

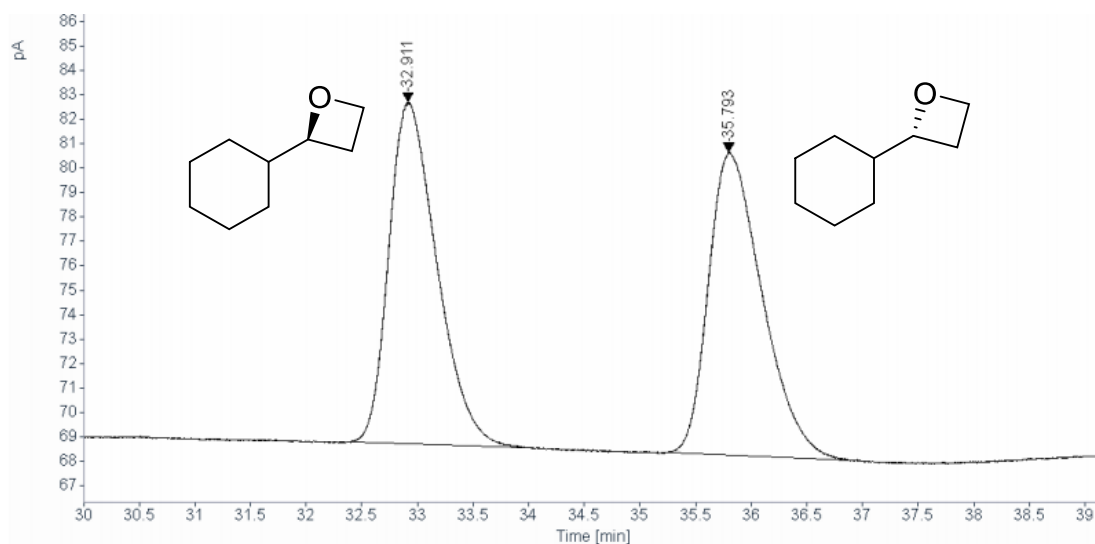


Supplementary Fig. 251 | HPLC trace for the enzymatic synthesized (*R*)-**19b**.



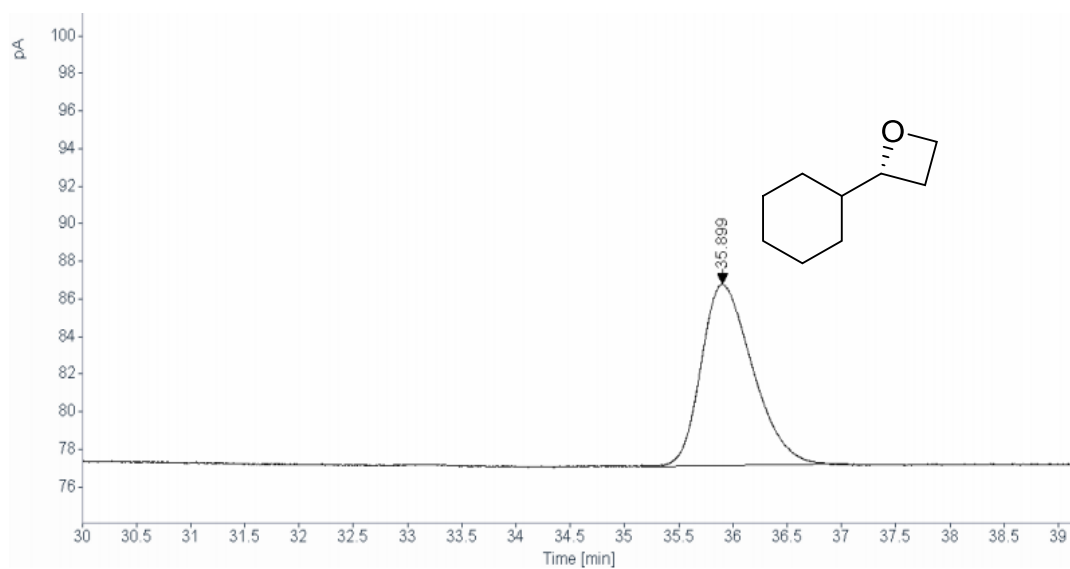
Chiral HPLC analysis: Diacel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 210 nm. $t_{(S)}$ = 39.3 min, $t_{(R)}$ = 41.3 min.

Supplementary Fig. 252 | GC trace for the chemical synthesized (*rac*)-**21b**.



ID#	Ret. Time	Area	Height	Area%	Resolution
1	32.911	420.903	14.020	50.148	
1	35.793	418.413	12.422	49.852	3.468

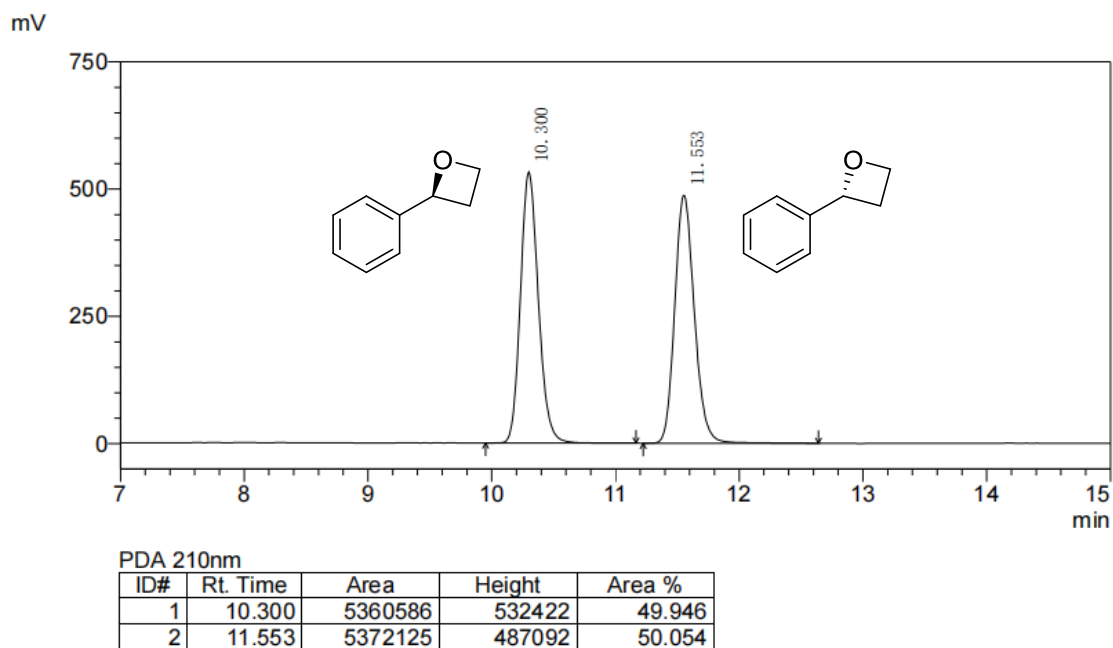
Supplementary Fig. 253 | GC trace for the enzymatic synthesized (*R*)-**21b**.



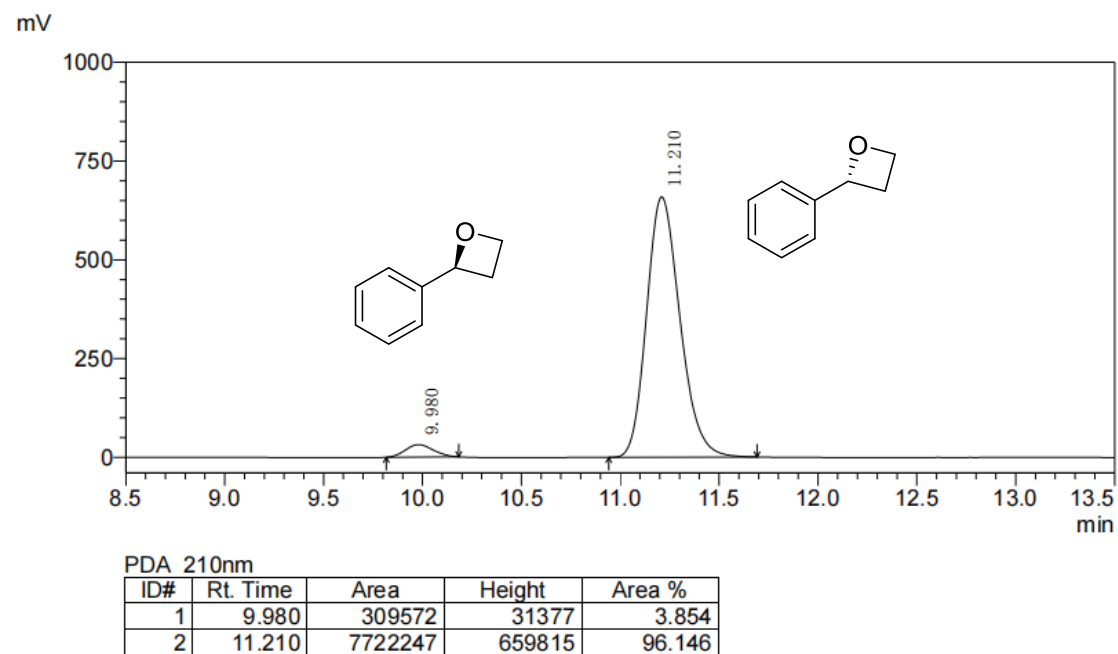
ID#	Ret. Time	Area	Height	Area%	Resolution
2	35.899	319.265	9.684	100.000	

Chiral GC analysis: Rt-bDEXcst (RESTEK), 80 °C for 45 min, $t_{(S)}$ = 32.9 min, $t_{(R)}$ = 35.8 min.

Supplementary Fig. 254 | HPLC trace for the chemical synthesized (*rac*)-**1b**.

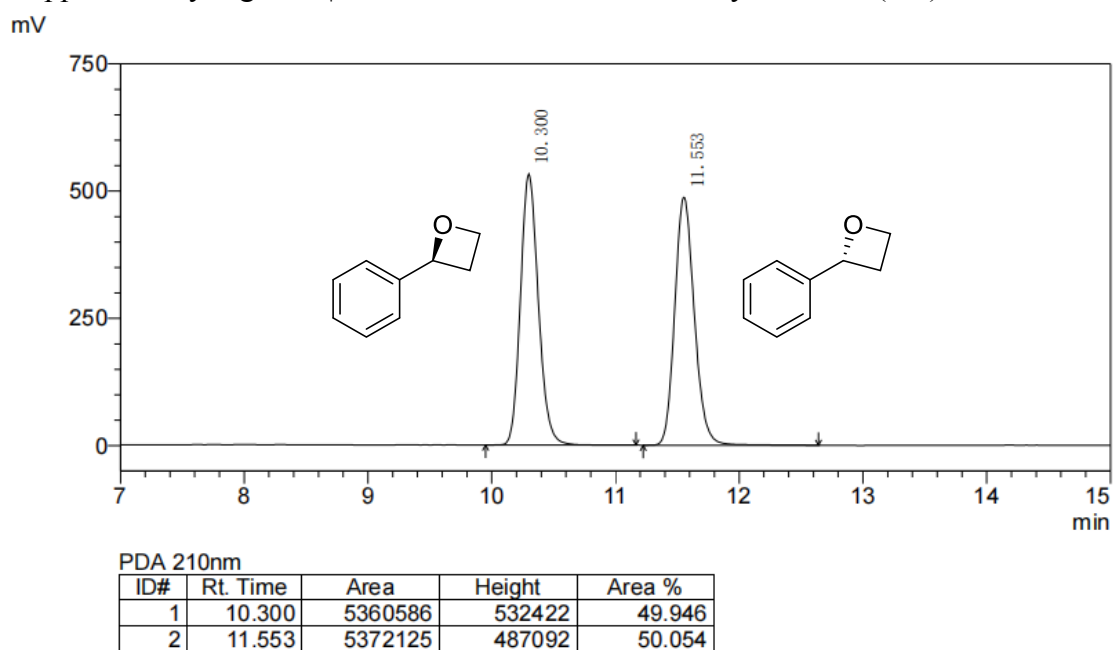


Supplementary Fig. 255 | HPLC trace for the enzymatic synthesized (*R*)-**1b** from **23a**.

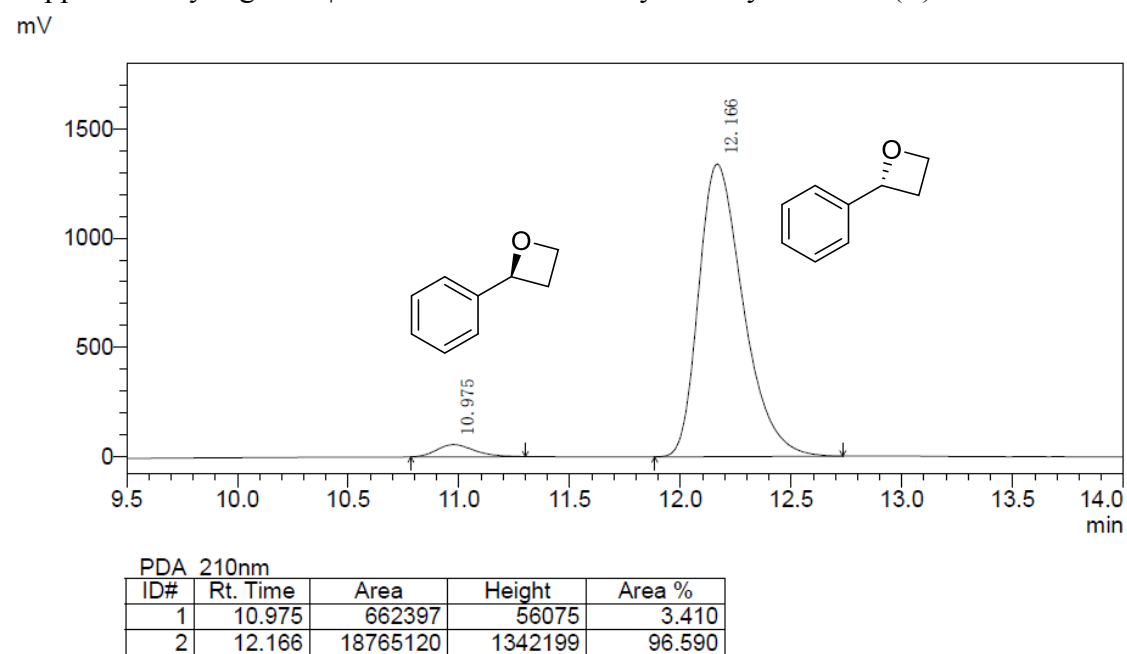


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, $\lambda = 210$ nm. $t_{(S)}$ = 10.0 min, $t_{(R)}$ = 11.2 min.

Supplementary Fig. 256 | HPLC trace for the chemical synthesized (*rac*)-**1b**.

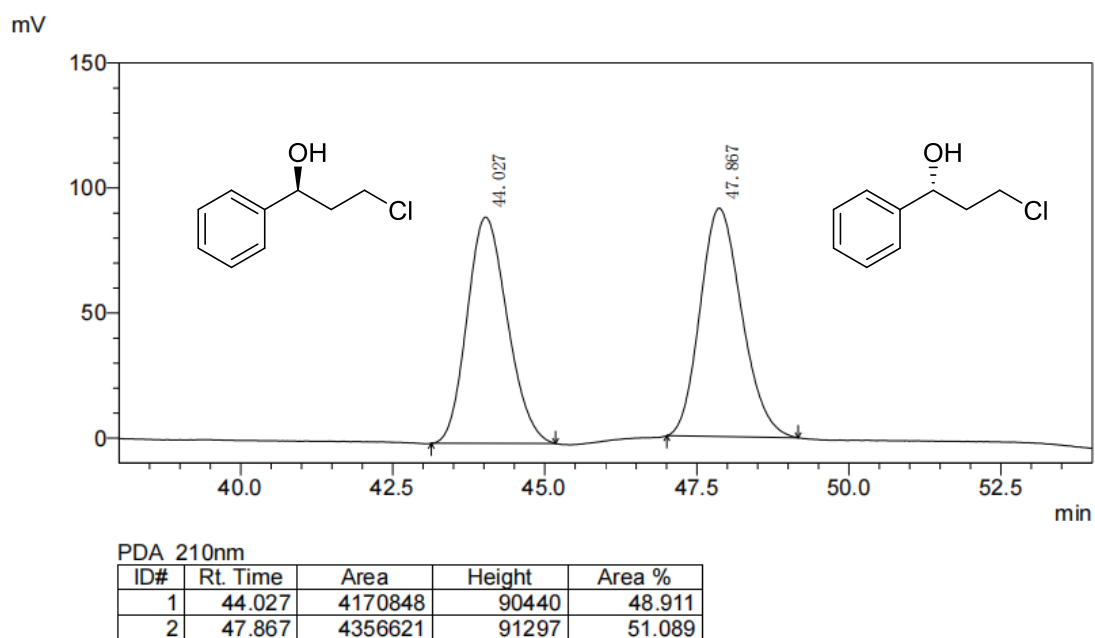


Supplementary Fig. 257 | HPLC trace for the enzymatic synthesized (*R*)-**1b** from **24a**.

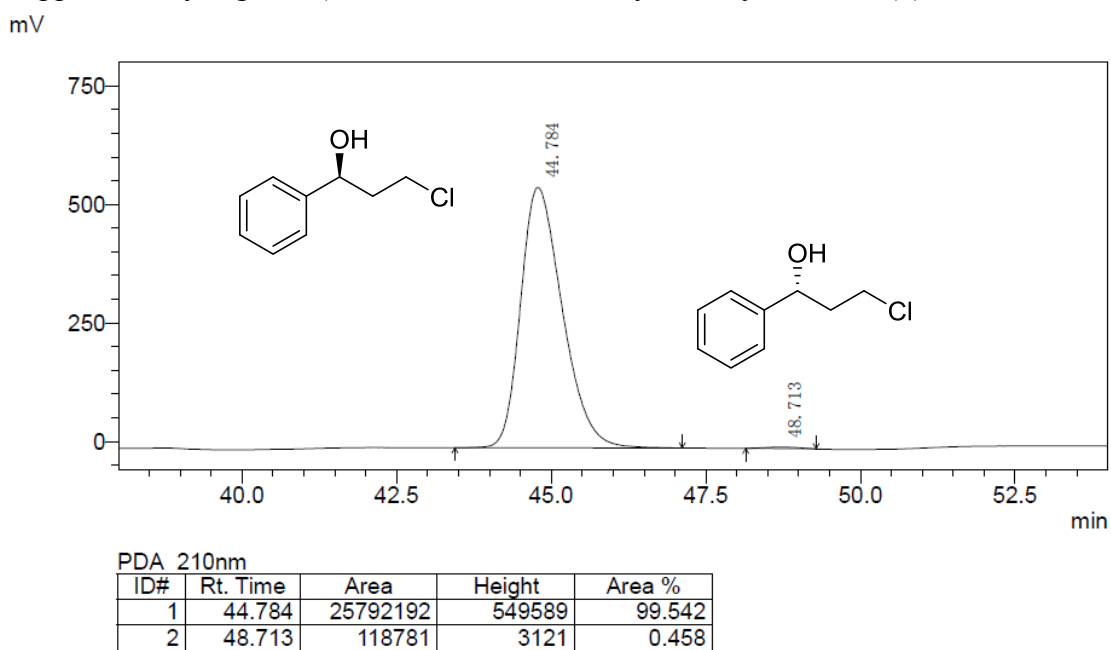


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm. $t_{(S)}$ = 11.0 min, $t_{(R)}$ = 12.2 min.

Supplementary Fig. 258 | HPLC trace for the chemical synthesized (*rac*)-**1a**.



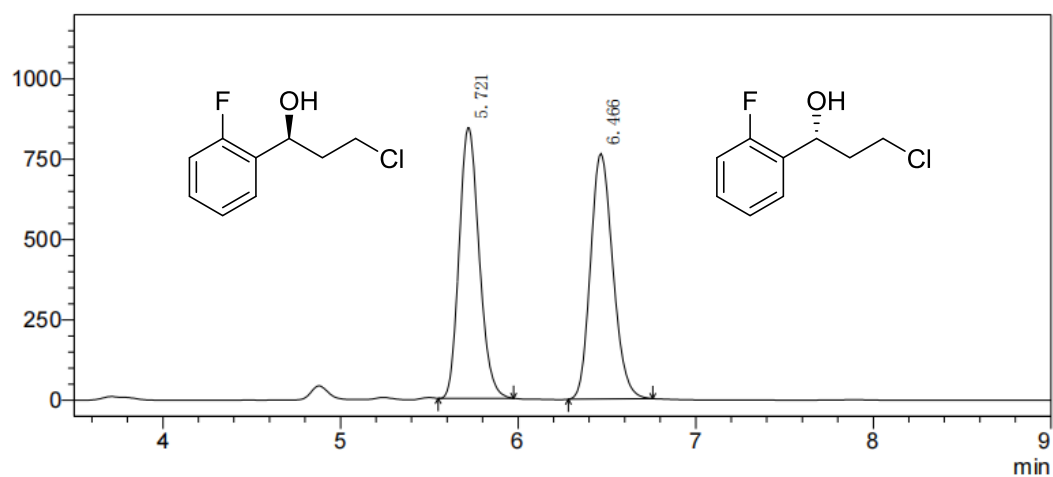
Supplementary Fig. 259 | HPLC trace for the enzymatic synthesized (*S*)-**1a**.



Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 44.8 min, $t_{(R)}$ = 48.7 min.

Supplementary Fig. 260 | HPLC trace for the chemical synthesized (*rac*)-**2a**.

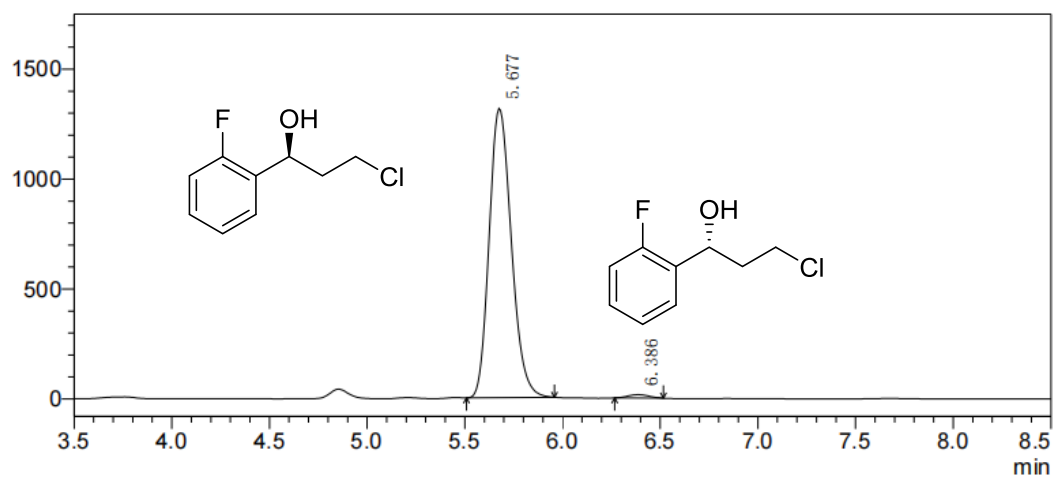
mV



PDA 210nm				
ID#	Rt. Time	Area	Height	Area %
1	5.721	6592144	842409	49.654
2	6.466	6684094	763639	50.346

Supplementary Fig. 261 | HPLC trace for the enzymatic synthesized (*S*)-**2a**.

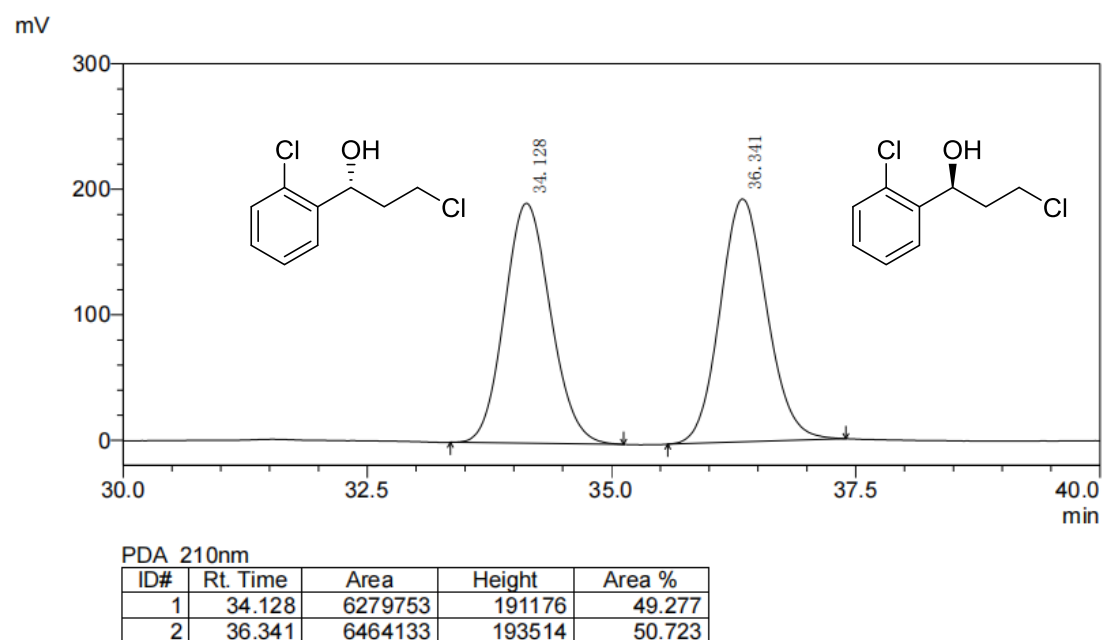
mV



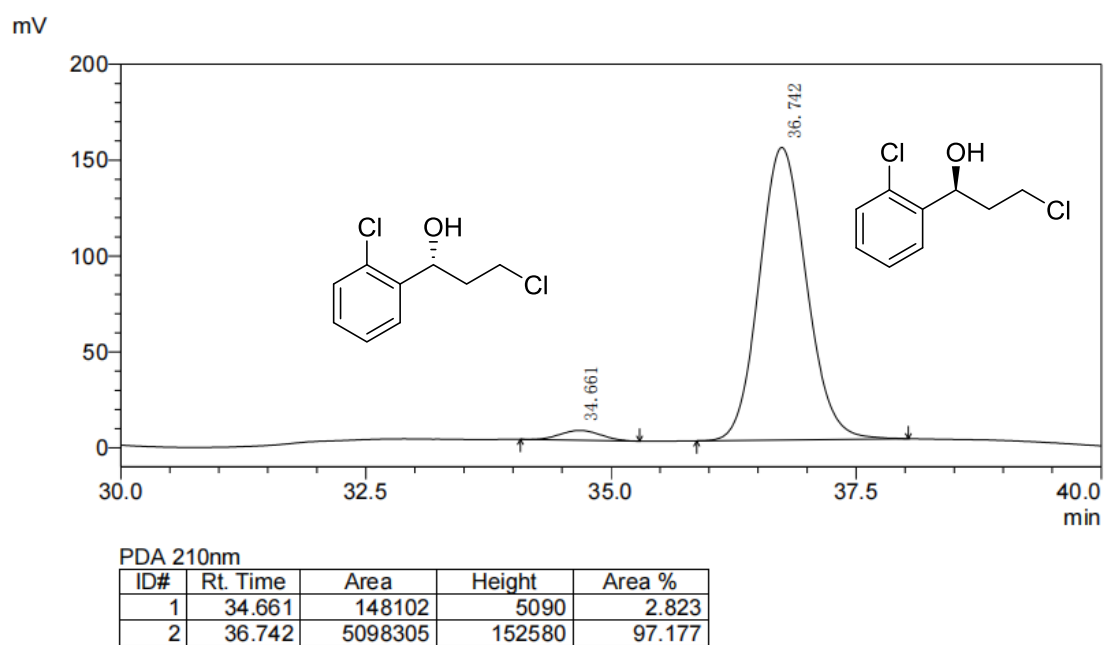
PDA 210nm				
ID#	Rt. Time	Area	Height	Area %
1	5.677	10452211	1315327	98.915
2	6.386	114640	15245	1.085

Chiral HPLC analysis: Diacel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 210 nm, $t_{(S)}$ = 5.7 min, $t_{(R)}$ = 6.4 min.

Supplementary Fig. 262 | HPLC trace for the chemical synthesized (*rac*)-**3a**.

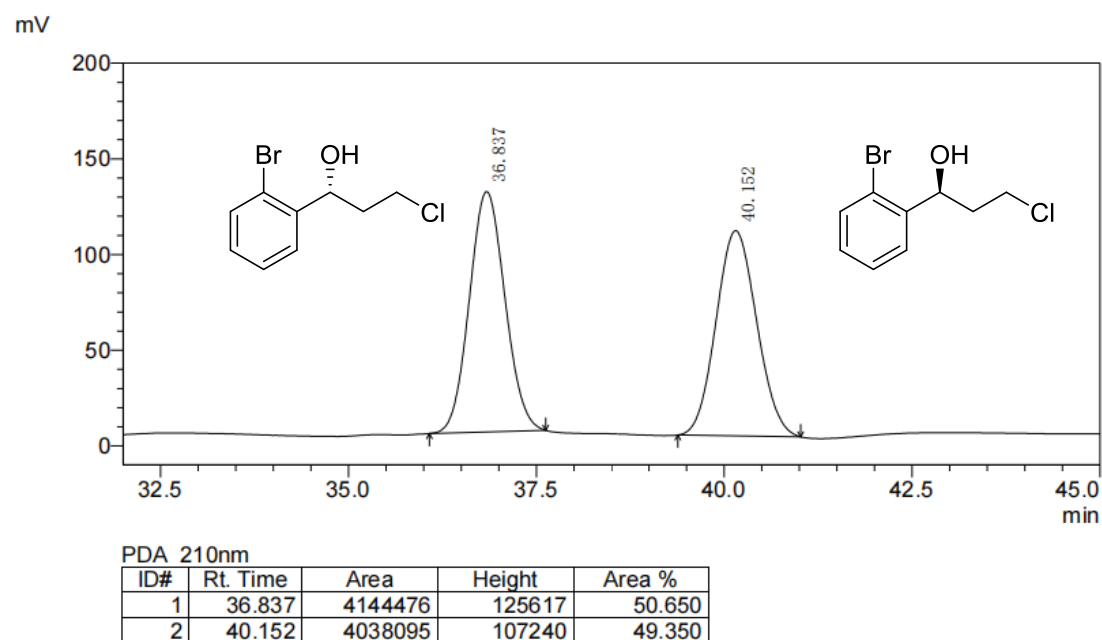


Supplementary Fig. 263 | HPLC trace for the enzymatic synthesized (*S*)-**3a**.

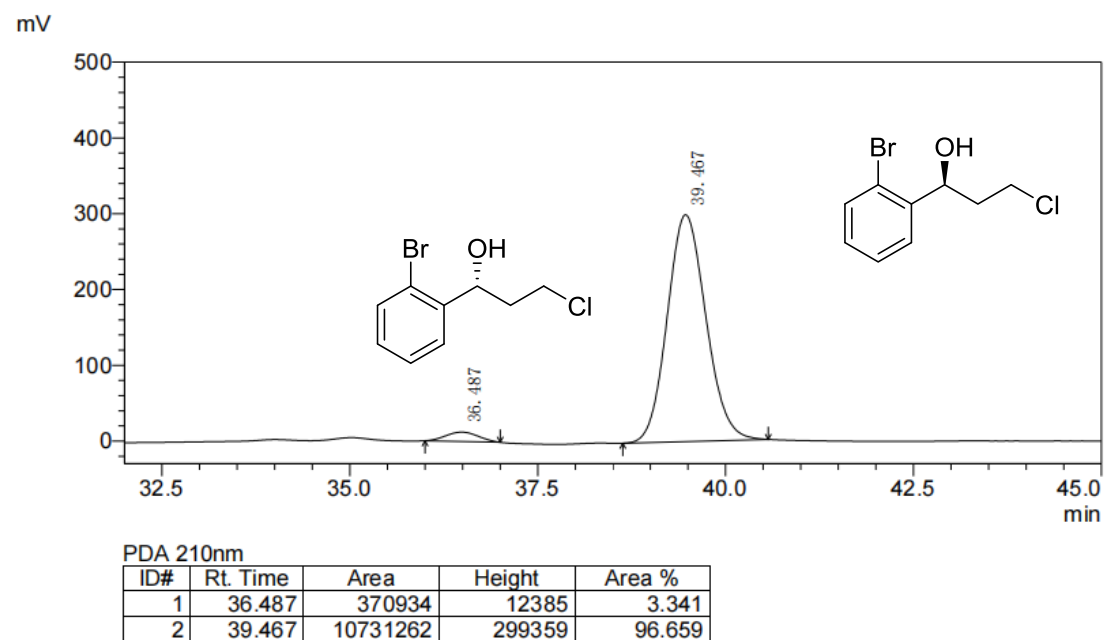


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(R)}$ = 34.7 min, $t_{(S)}$ = 36.7 min.

Supplementary Fig. 264 | HPLC trace for the chemical synthesized (*rac*)-**4a**.

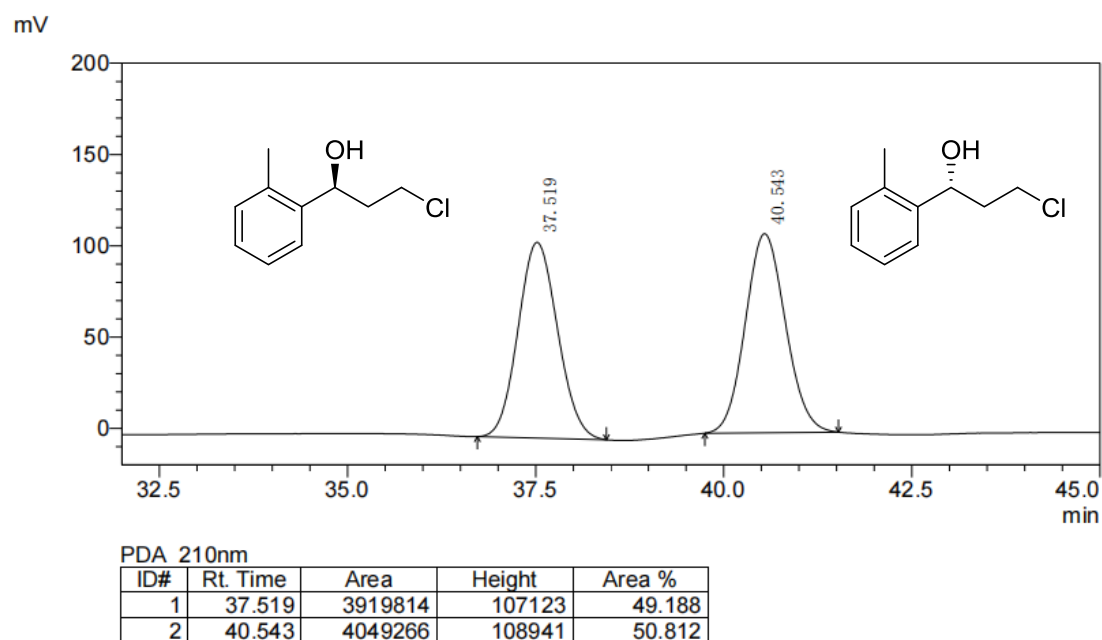


Supplementary Fig. 265 | HPLC trace for the enzymatic synthesized (*S*)-**4a**.

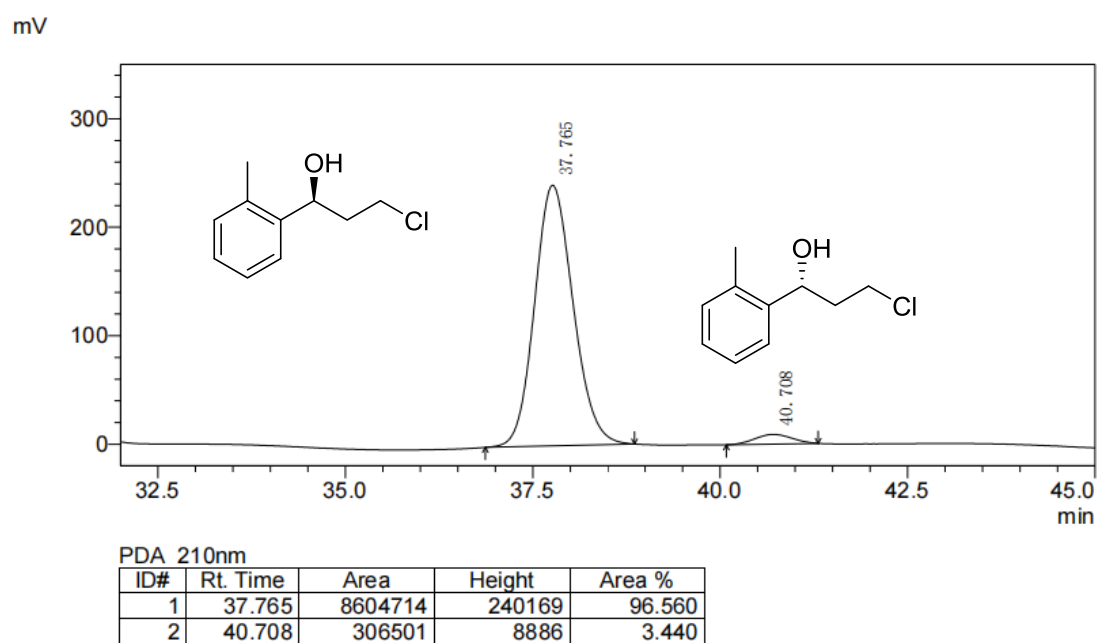


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(R)}$ = 36.5 min, $t_{(S)}$ = 39.5 min.

Supplementary Fig. 266 | HPLC trace for the chemical synthesized (*rac*)-**5a**.

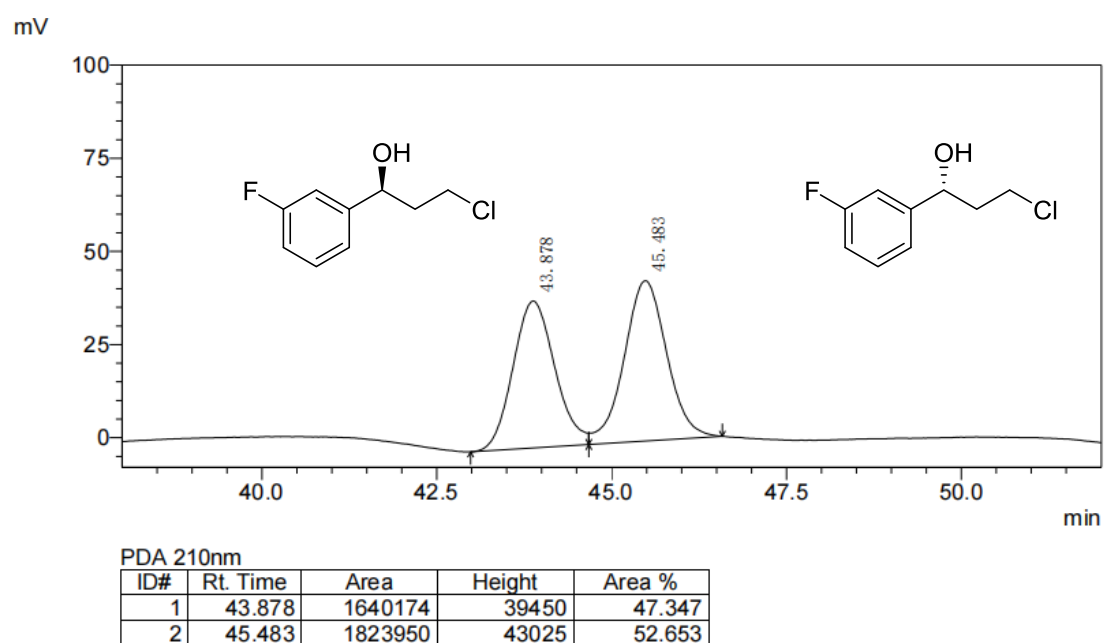


Supplementary Fig. 267 | HPLC trace for the enzymatic synthesized (*S*)-**5a**.

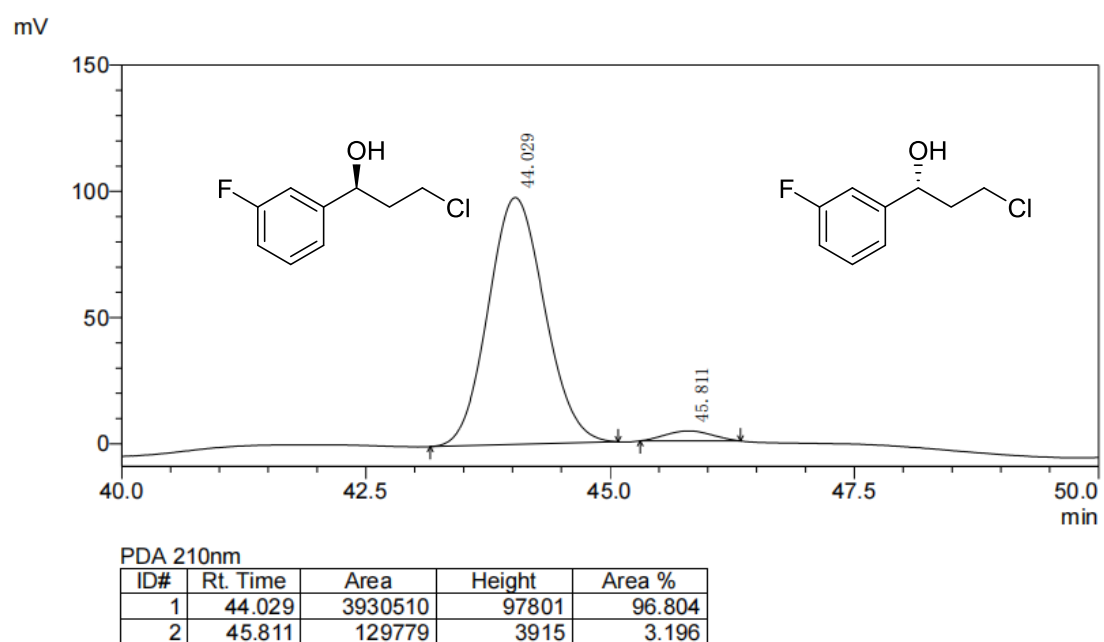


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 37.8 min, $t_{(R)}$ = 40.7 min.

Supplementary Fig. 268 | HPLC trace for the chemical synthesized (*rac*)-**6a**.



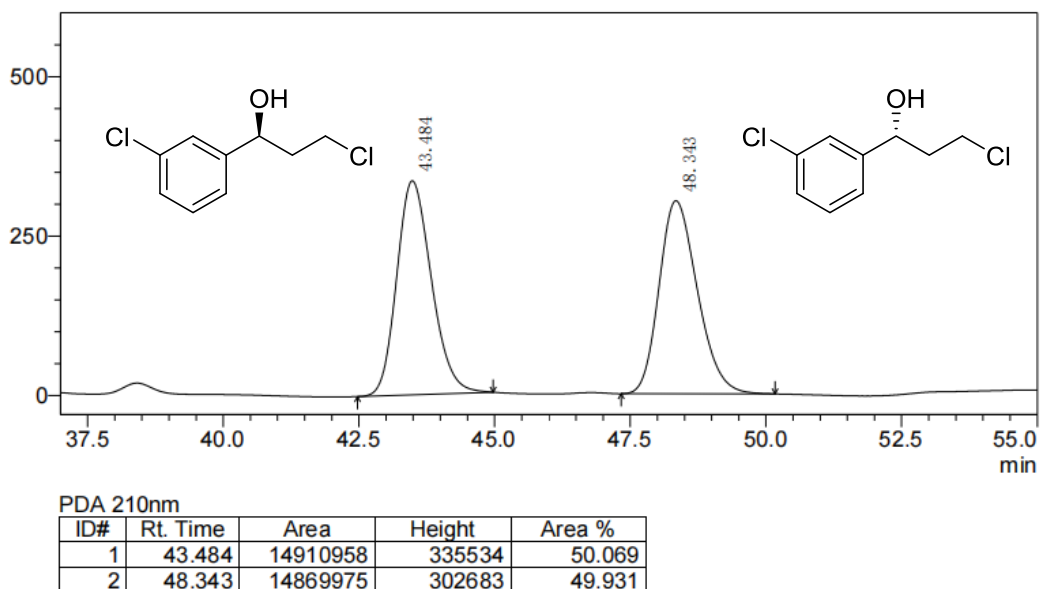
Supplementary Fig. 269 | HPLC trace for the enzymatic synthesized (*S*)-**6a**.



Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 44.0 min, $t_{(R)}$ = 45.8 min.

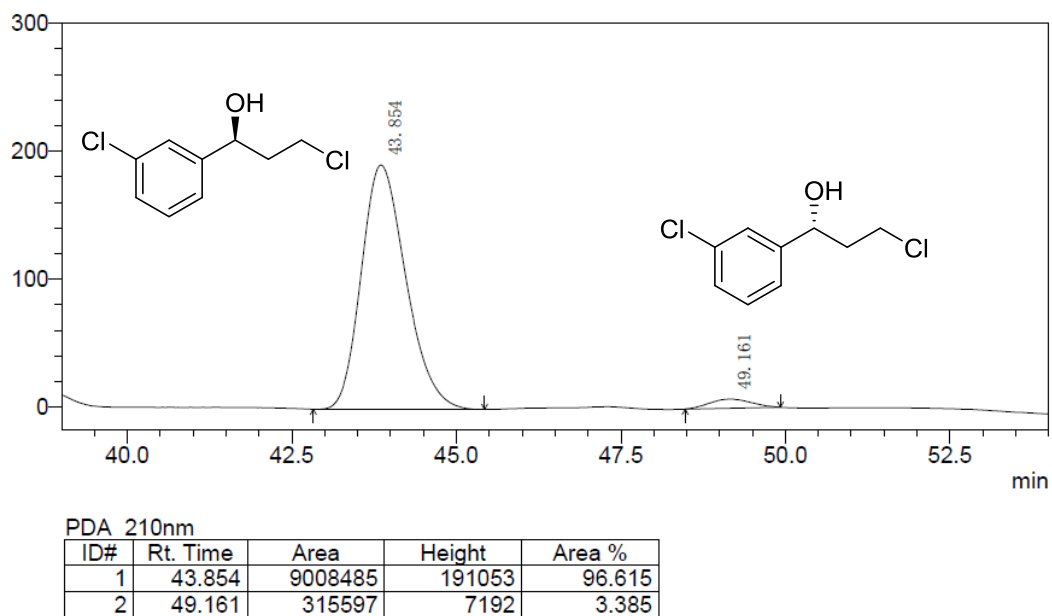
Supplementary Fig. 270 | HPLC trace for the chemical synthesized (*rac*)-**7a**.

mV



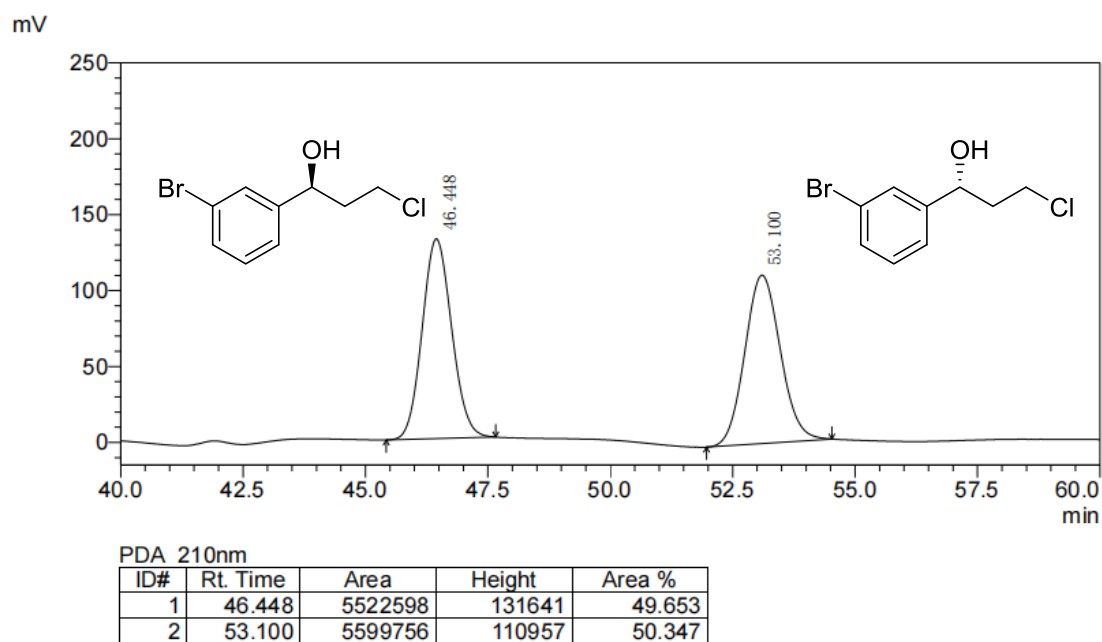
Supplementary Fig. 271 | HPLC trace for the enzymatic synthesized (*S*)-**7a**.

mV

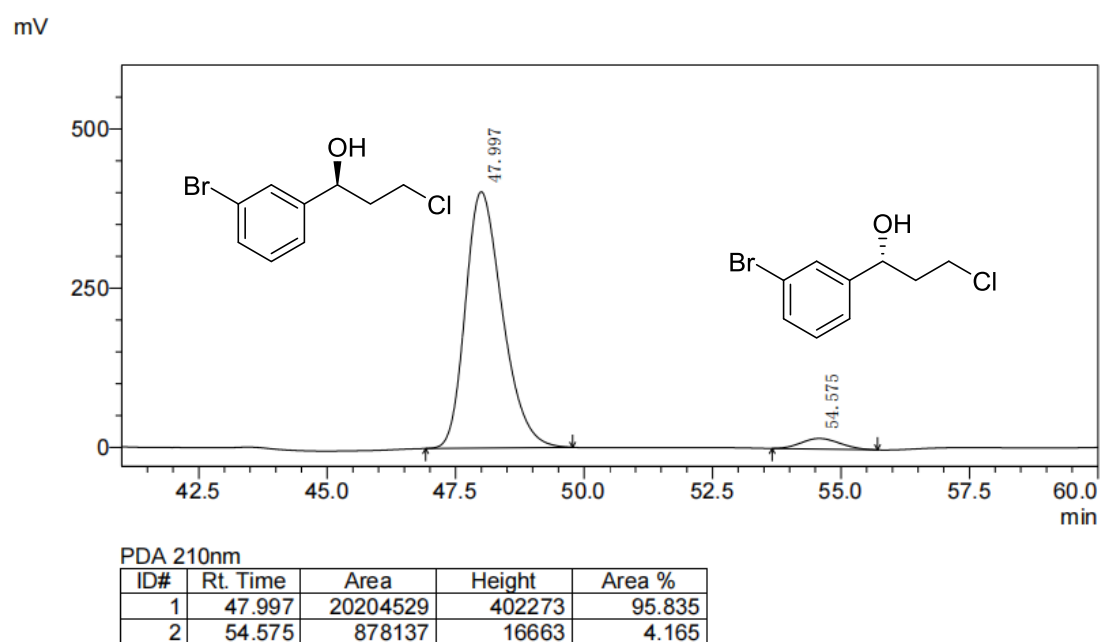


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 43.8 min, $t_{(R)}$ = 49.2 min.

Supplementary Fig. 272 | HPLC trace for the chemical synthesized (*rac*)-**8a**.

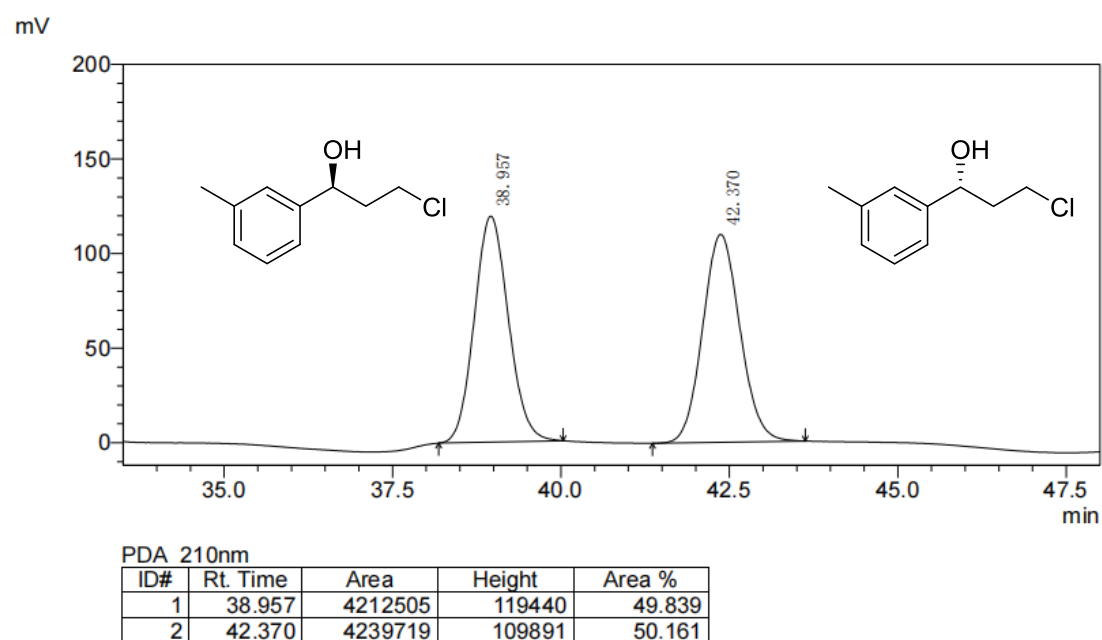


Supplementary Fig. 273 | HPLC trace for the enzymatic synthesized (*S*)-**8a**.

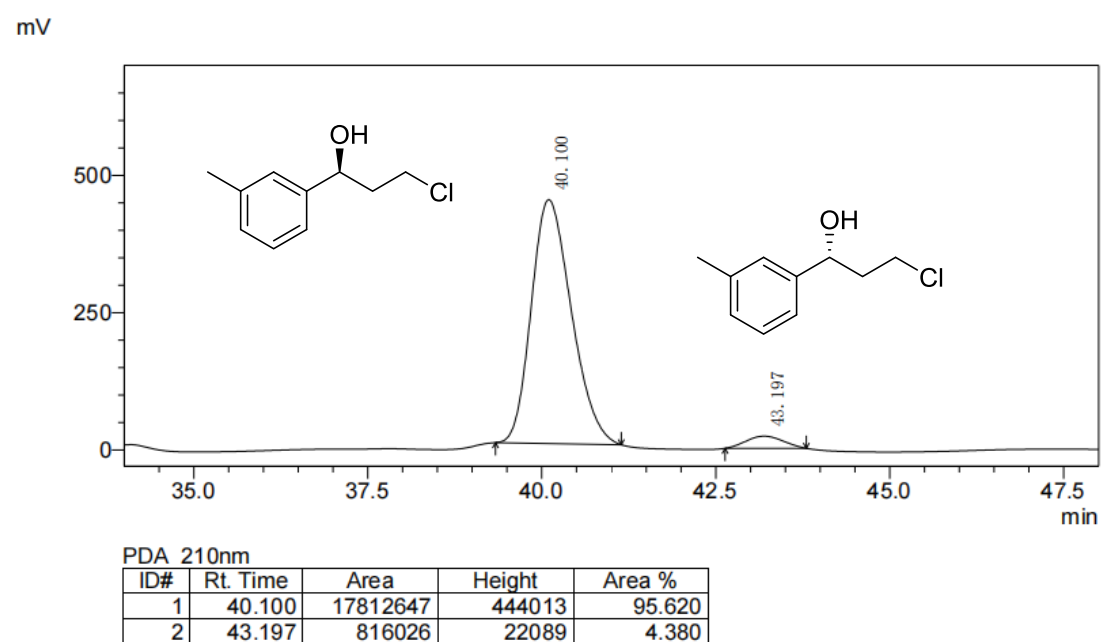


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, $\lambda = 210$ nm, $t_{(S)} = 48.0$ min, $t_{(R)} = 54.6$ min.

Supplementary Fig. 274 | HPLC trace for the chemical synthesized (*rac*)-**9a**.



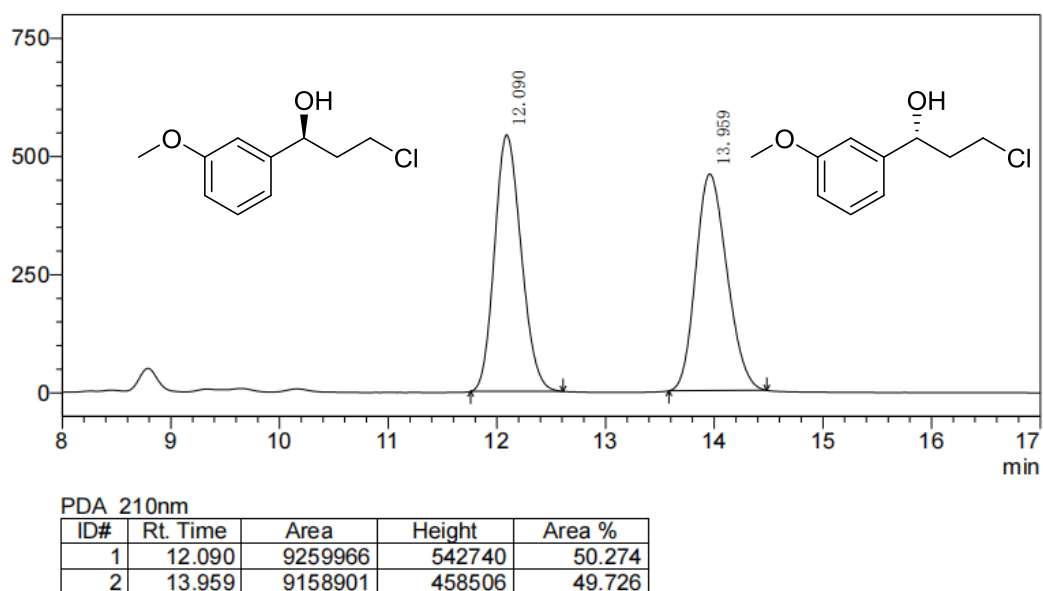
Supplementary Fig. 275 | HPLC trace for the enzymatic synthesized (*S*)-**9a**.



Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 40.1 min, $t_{(R)}$ = 43.2 min.

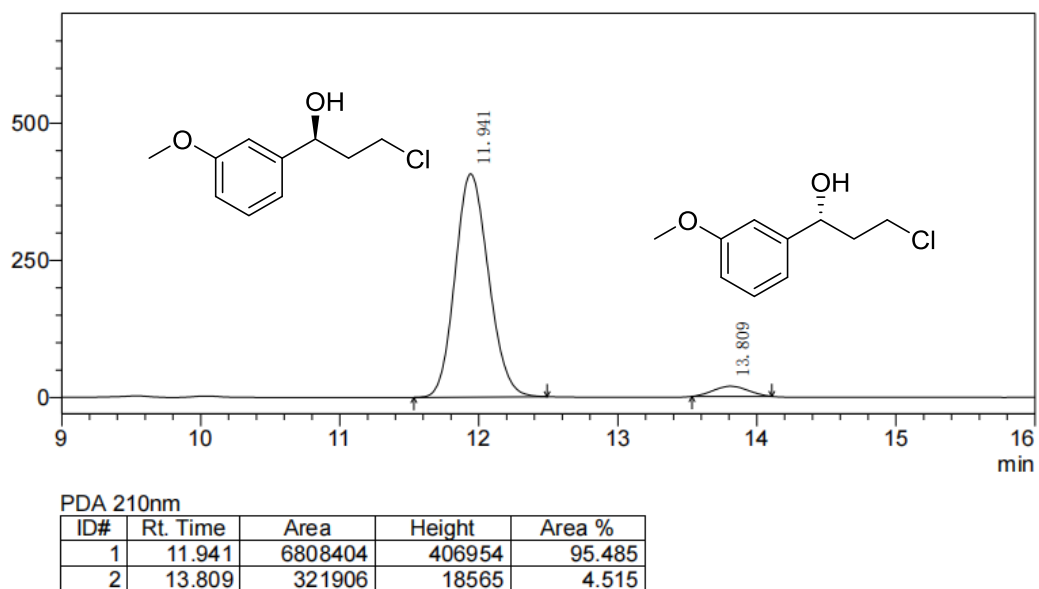
Supplementary Fig. 276 | HPLC trace for the chemical synthesized (*rac*)-**10a**.

mV



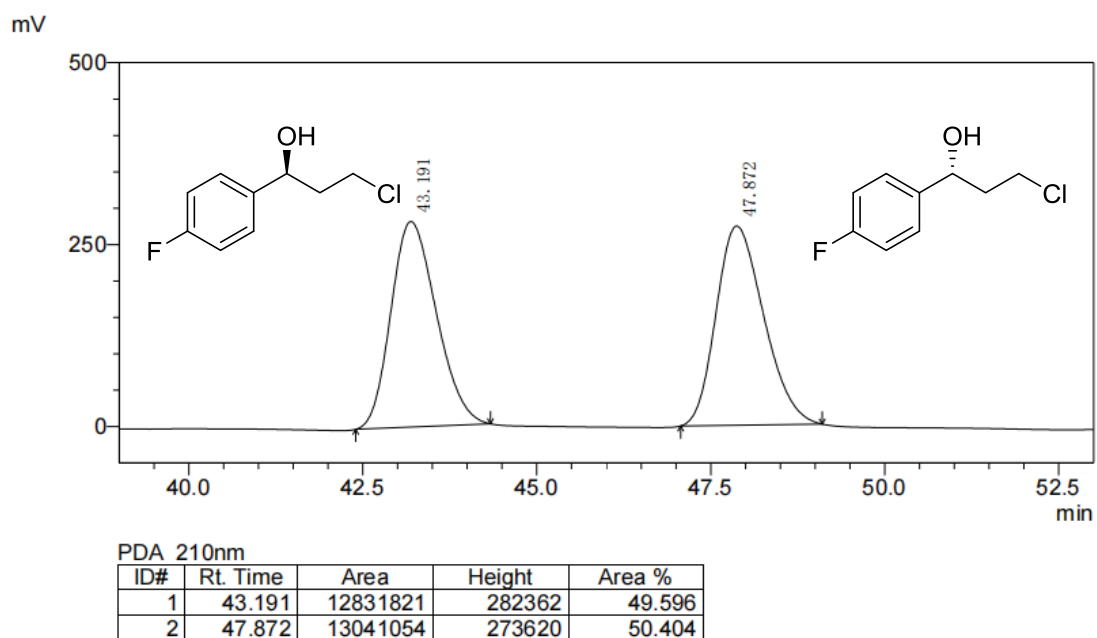
Supplementary Fig. 277 | HPLC trace for the enzymatic synthesized (*S*)-**10a**.

mV

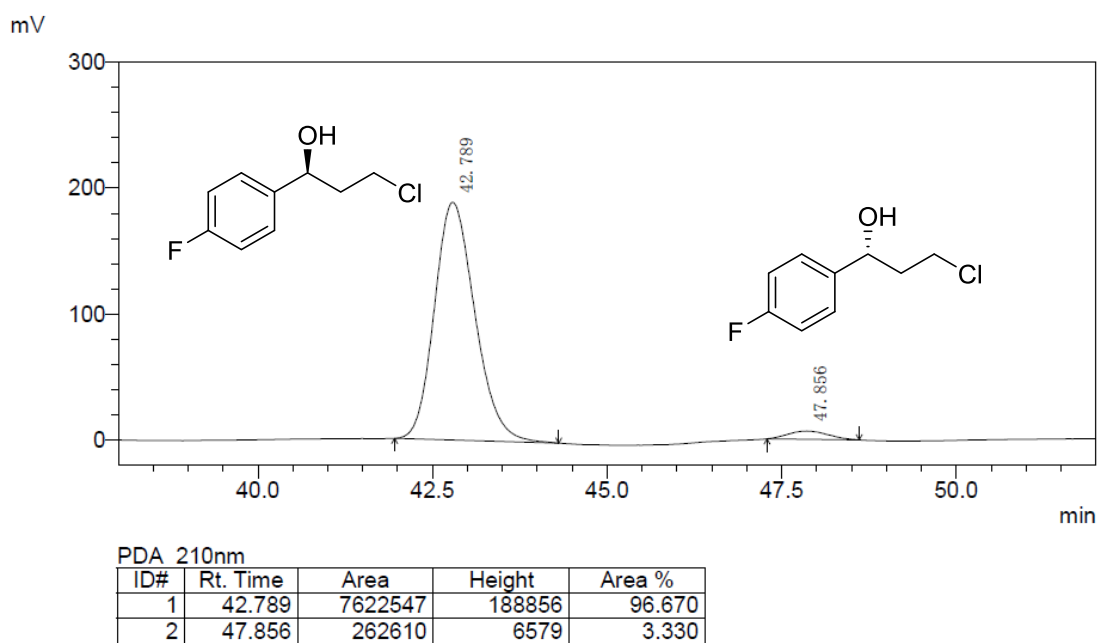


Chiral HPLC analysis: Diacel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 210 nm, $t_{(S)}$ = 11.9 min, $t_{(R)}$ = 13.8 min.

Supplementary Fig. 278 | HPLC trace for the chemical synthesized (*rac*)-**11a**.



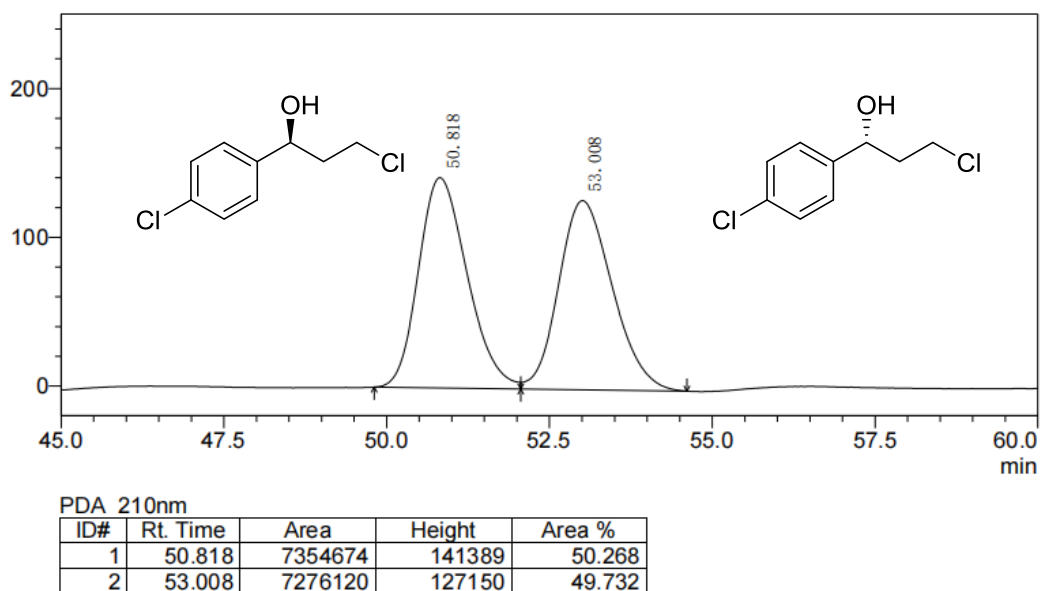
Supplementary Fig. 279 | HPLC trace for the enzymatic synthesized (*S*)-**11a**.



Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 42.8 min, $t_{(R)}$ = 47.9 min.

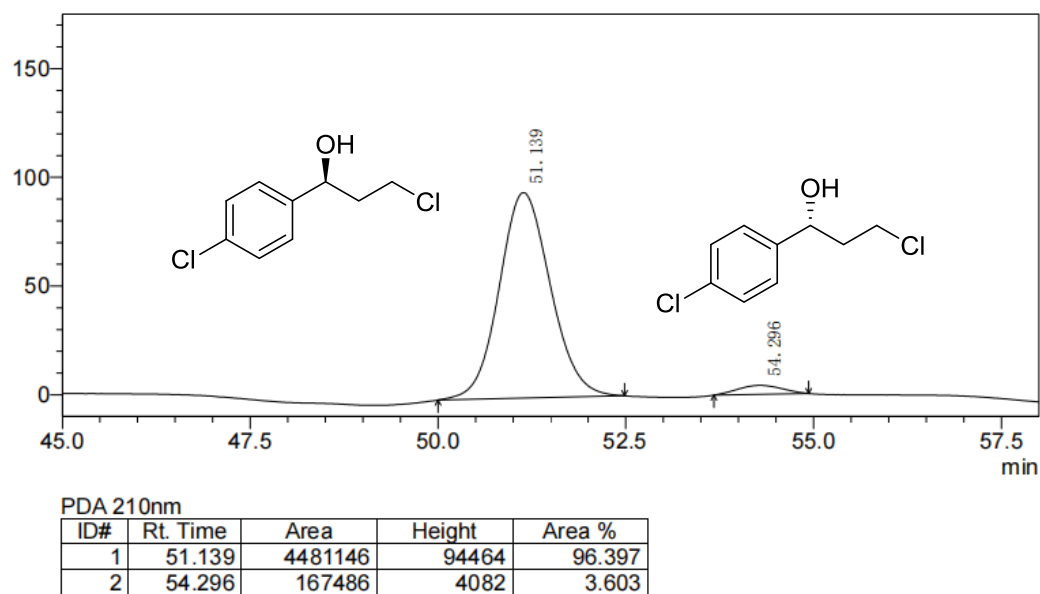
Supplementary Fig. 280 | HPLC trace for the chemical synthesized (*rac*)-**12a**.

mV



Supplementary Fig. 281 | HPLC trace for the enzymatic synthesized (*S*)-**12a**.

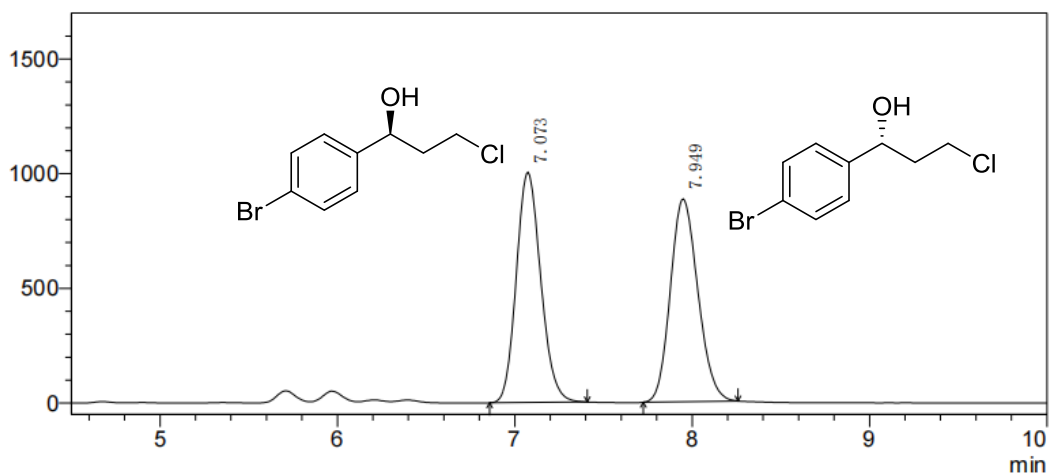
mV



Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 51.1 min, $t_{(R)}$ = 54.3 min.

Supplementary Fig. 282 | HPLC trace for the chemical synthesized (*rac*)-**13a**.

mV

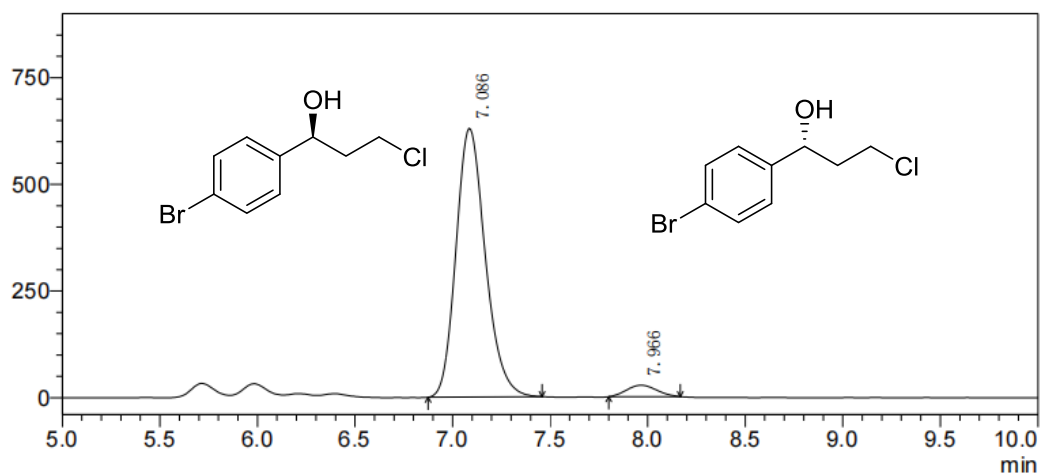


PDA 210nm

ID#	Rt. Time	Area	Height	Area %
1	7.073	9615969	1003581	50.201
2	7.949	9539085	884114	49.799

Supplementary Fig. 283 | HPLC trace for the enzymatic synthesized (*S*)-**13a**.

mV



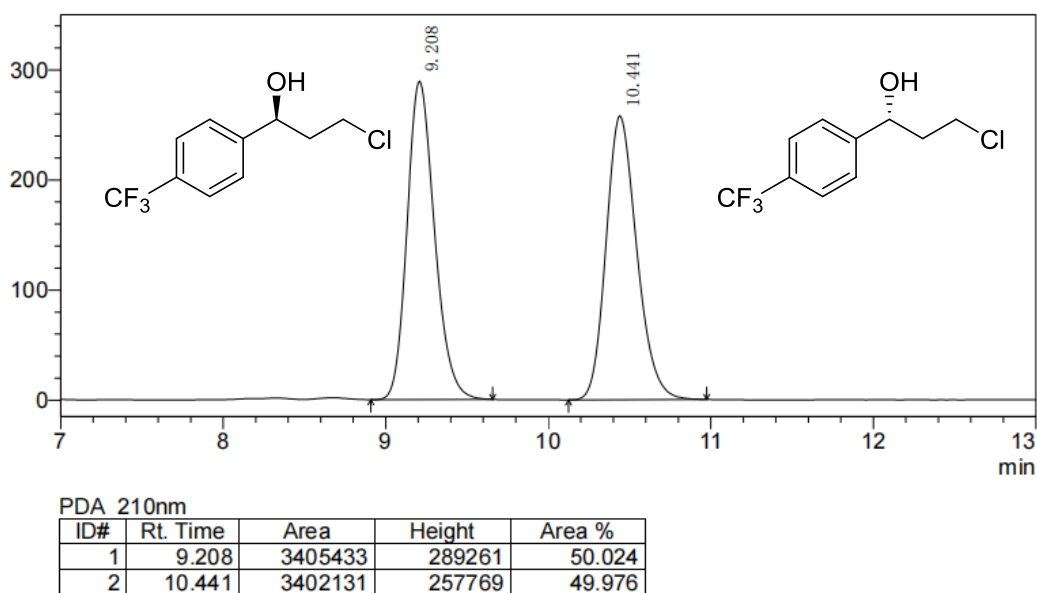
PDA 210nm

ID#	Rt. Time	Area	Height	Area %
1	7.086	6591918	629680	95.867
2	7.966	284204	26757	4.133

Chiral HPLC analysis: Diacel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 210 nm, $t_{(S)}$ = 7.1 min, $t_{(R)}$ = 8.0 min.

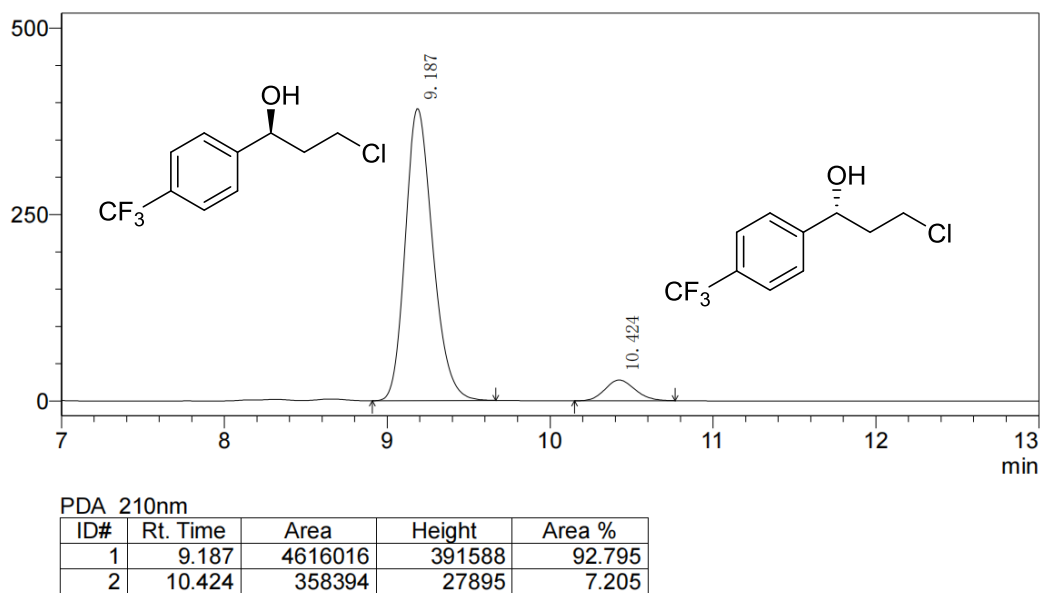
Supplementary Fig. 284 | HPLC trace for the chemical synthesized (*rac*)-**14a**.

mV



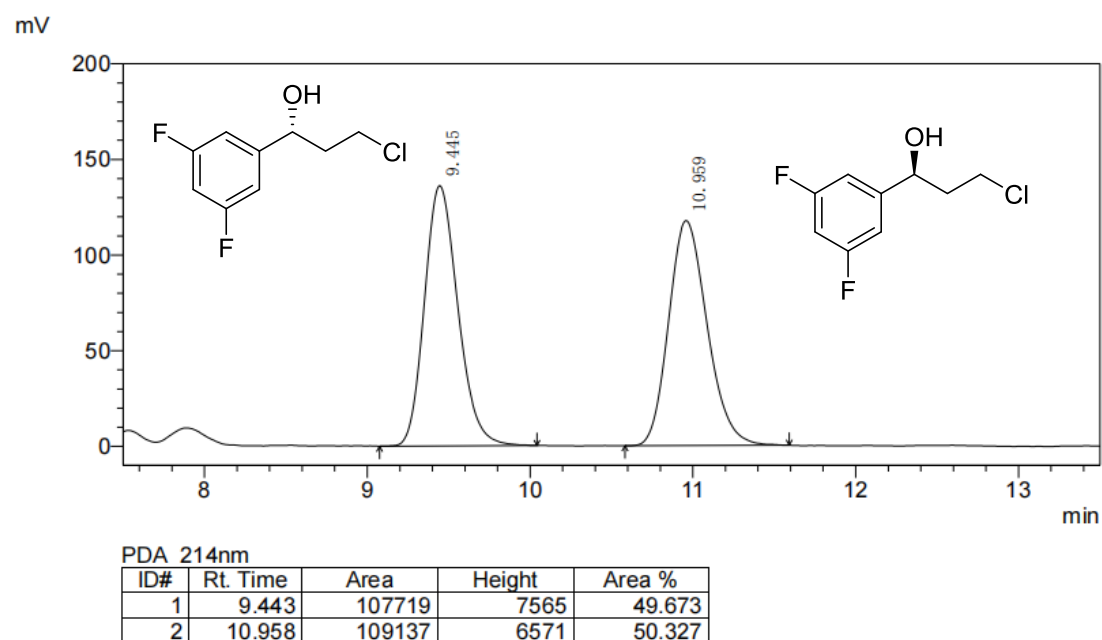
Supplementary Fig. 285 | HPLC trace for the enzymatic synthesized (*S*)-**14a**.

mV

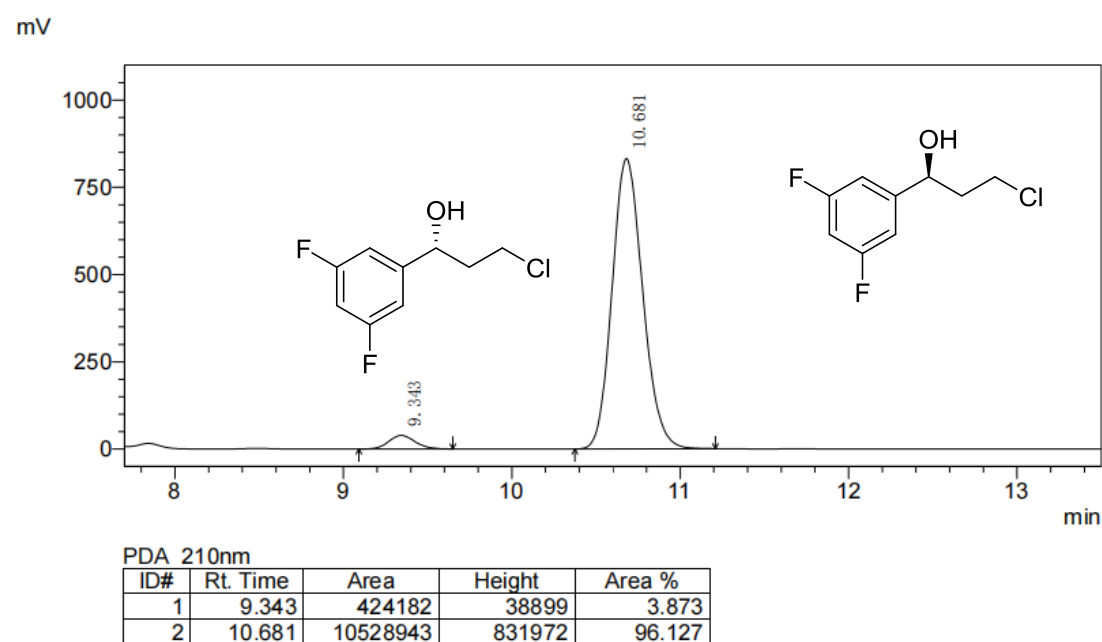


Chiral HPLC analysis: Diacel Chiralpak OJ-H, *n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 210 nm, $t_{(S)}$ = 9.2 min, $t_{(R)}$ = 10.4 min.

Supplementary Fig. 286 | HPLC trace for the chemical synthesized (*rac*)-**15a**.



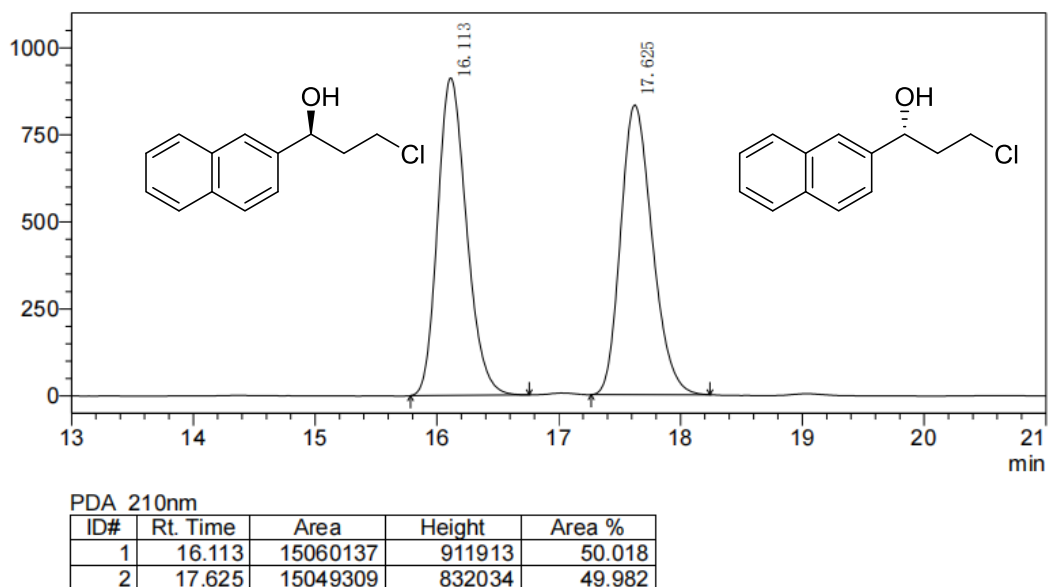
Supplementary Fig. 287 | HPLC trace for the enzymatic synthesized (*S*)-**15a**.



Chiral HPLC analysis: Diacel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 210 nm, $t_{(R)}$ = 9.3 min, $t_{(S)}$ = 10.7 min.

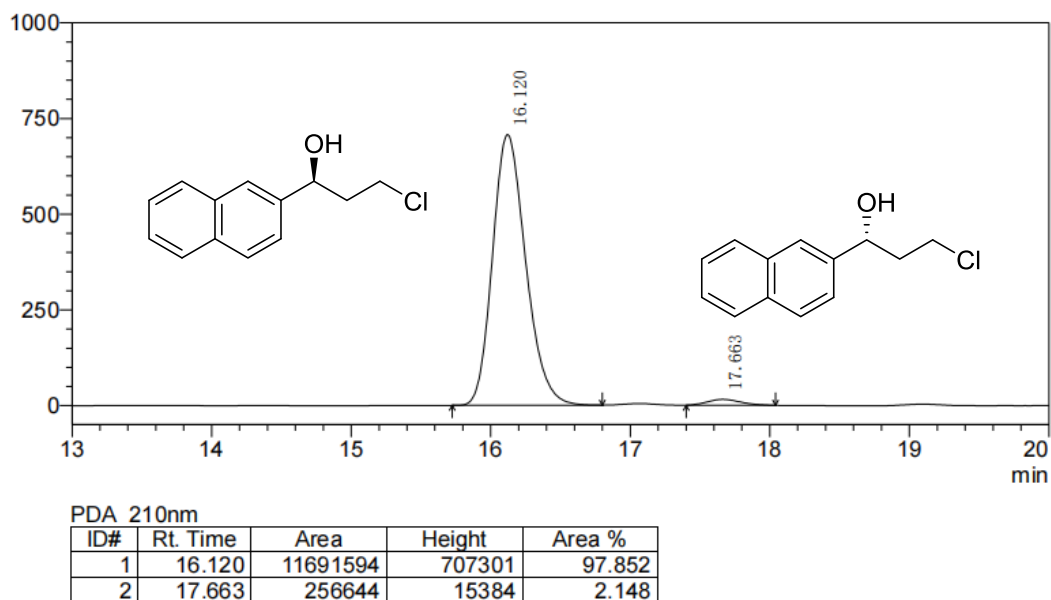
Supplementary Fig. 288 | HPLC trace for the chemical synthesized (*rac*)-**16a**.

mV



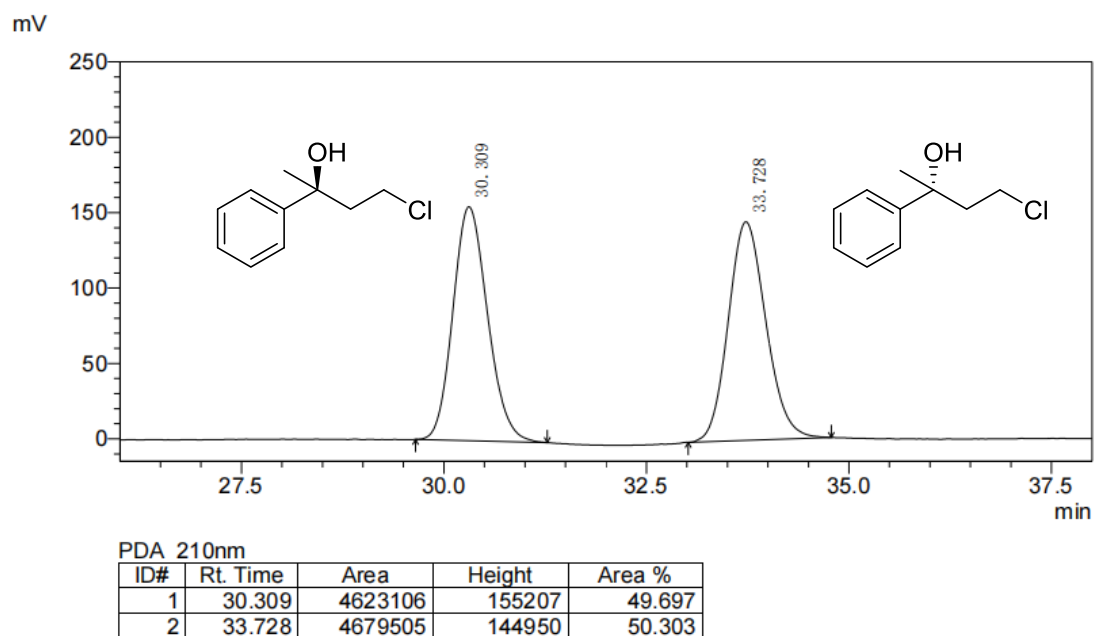
Supplementary Fig. 289 | HPLC trace for the enzymatic synthesized (*S*)-**16a**.

mV

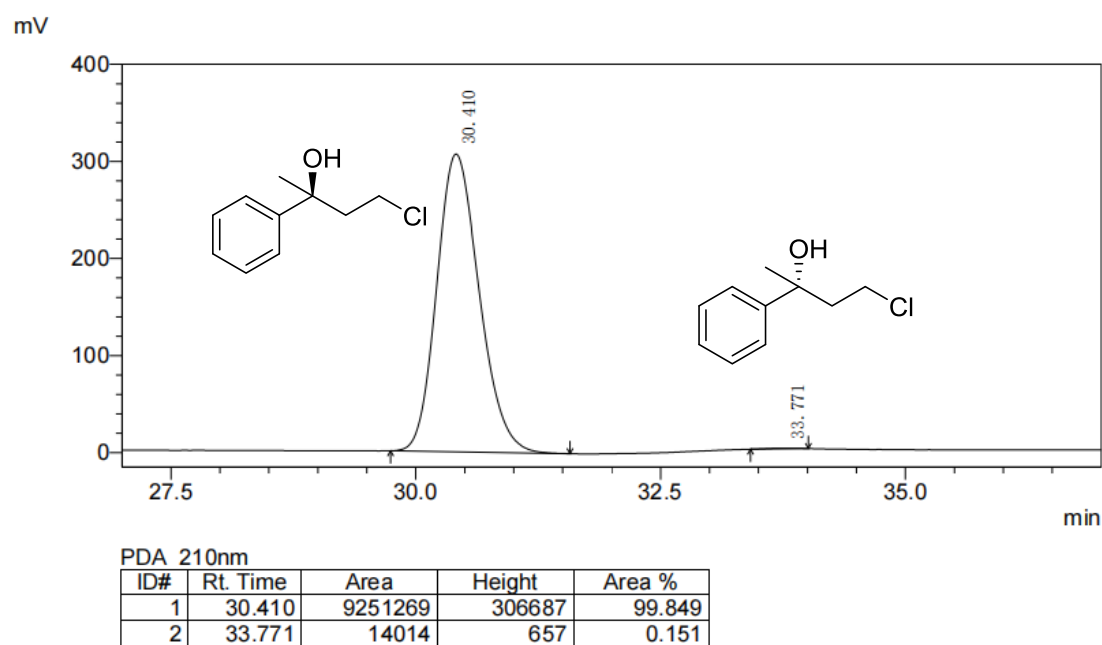


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 16.1 min, $t_{(R)}$ = 17.7 min.

Supplementary Fig. 290 | HPLC trace for the chemical synthesized (*rac*)-**17a**.



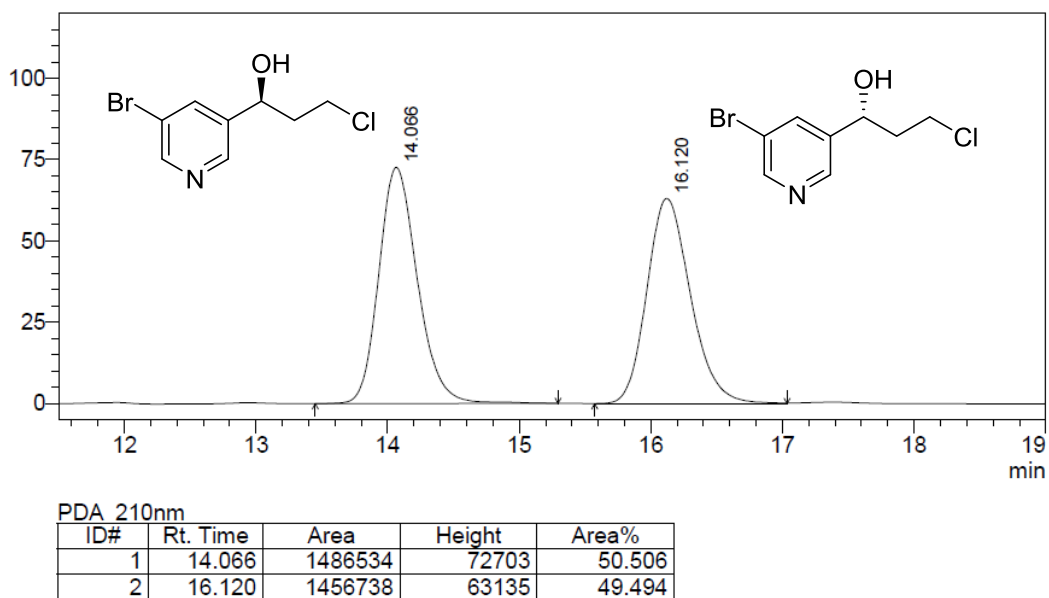
Supplementary Fig. 291 | HPLC trace for the enzymatic synthesized (*S*)-**17a**.



Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 30.4 min, $t_{(R)}$ = 33.8 min.

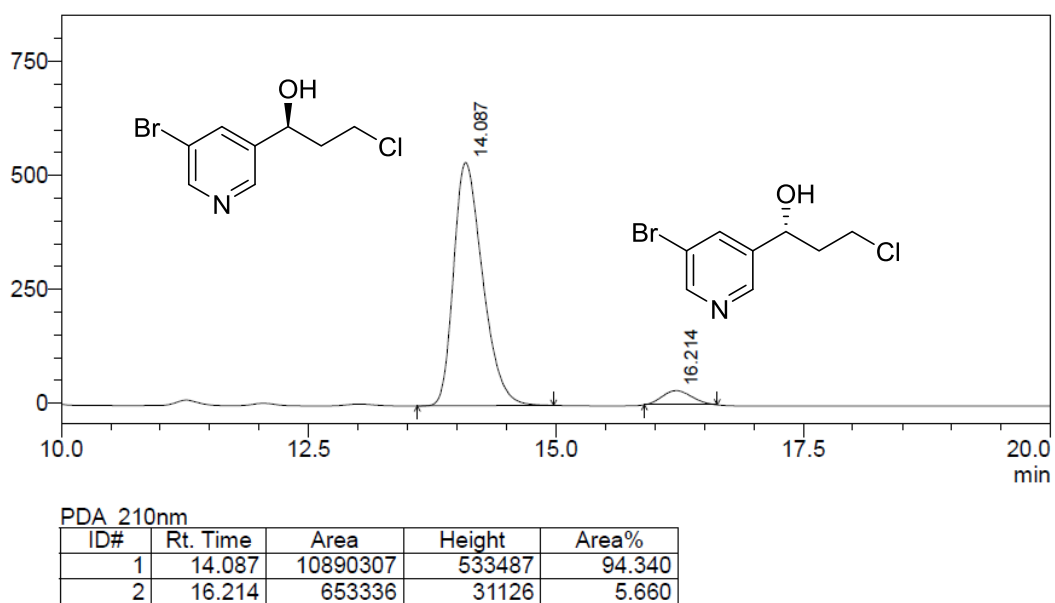
Supplementary Fig. 292 | HPLC trace for the chemical synthesized (*rac*)-**18a**.

mV



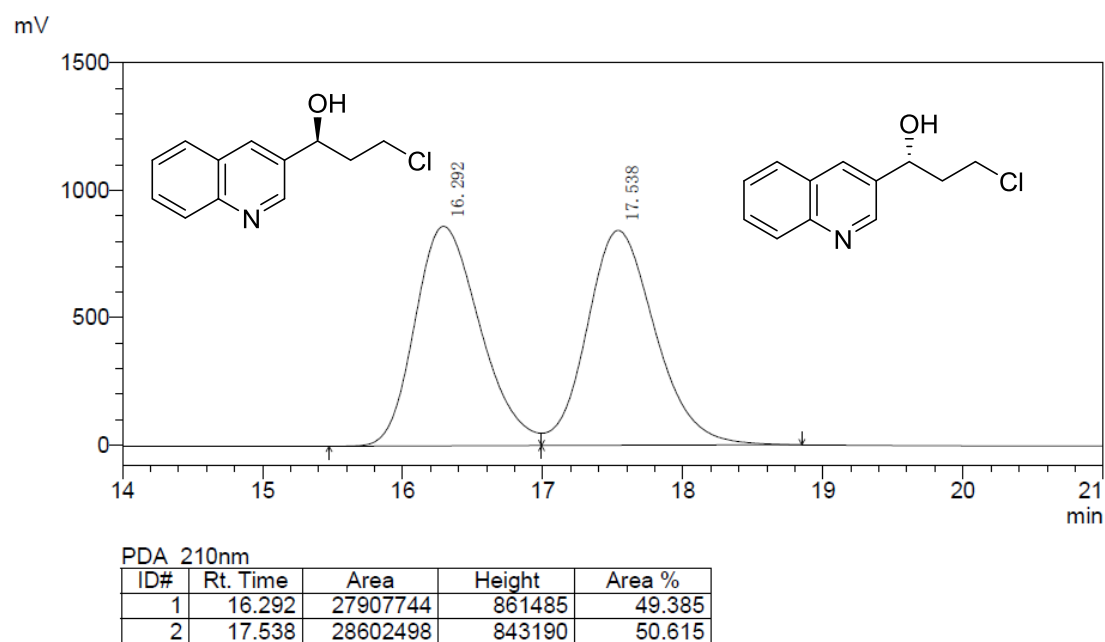
Supplementary Fig. 293 | HPLC trace for the enzymatic synthesized (*S*)-**18a**.

mV

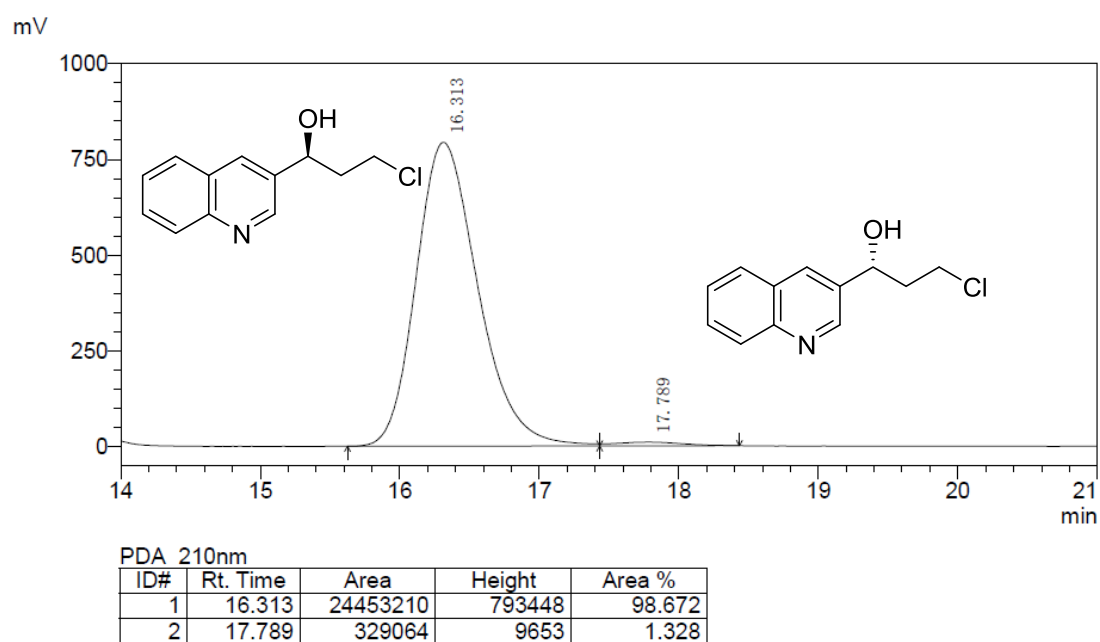


Chiral HPLC analysis: Diacel Chiralpak OJ-H, *n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 210 nm, $t_{(S)}$ = 14.1 min, $t_{(R)}$ = 16.2 min.

Supplementary Fig. 294 | HPLC trace for the chemical synthesized (*rac*)-**19a**.

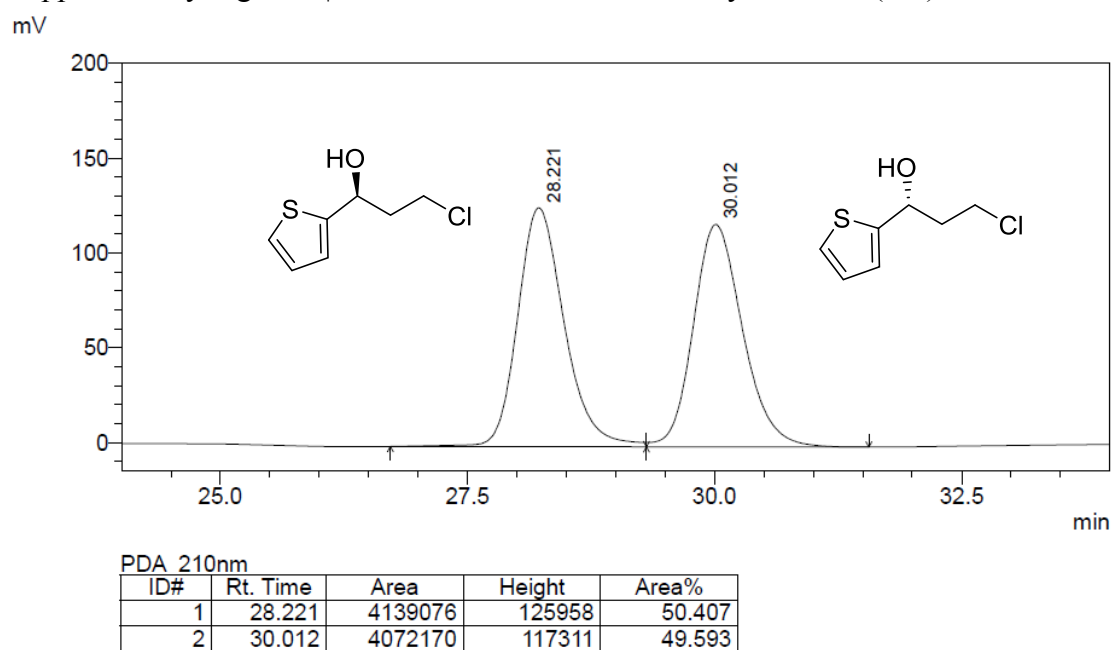


Supplementary Fig. 295 | HPLC trace for the enzymatic synthesized (*S*)-**19a**.

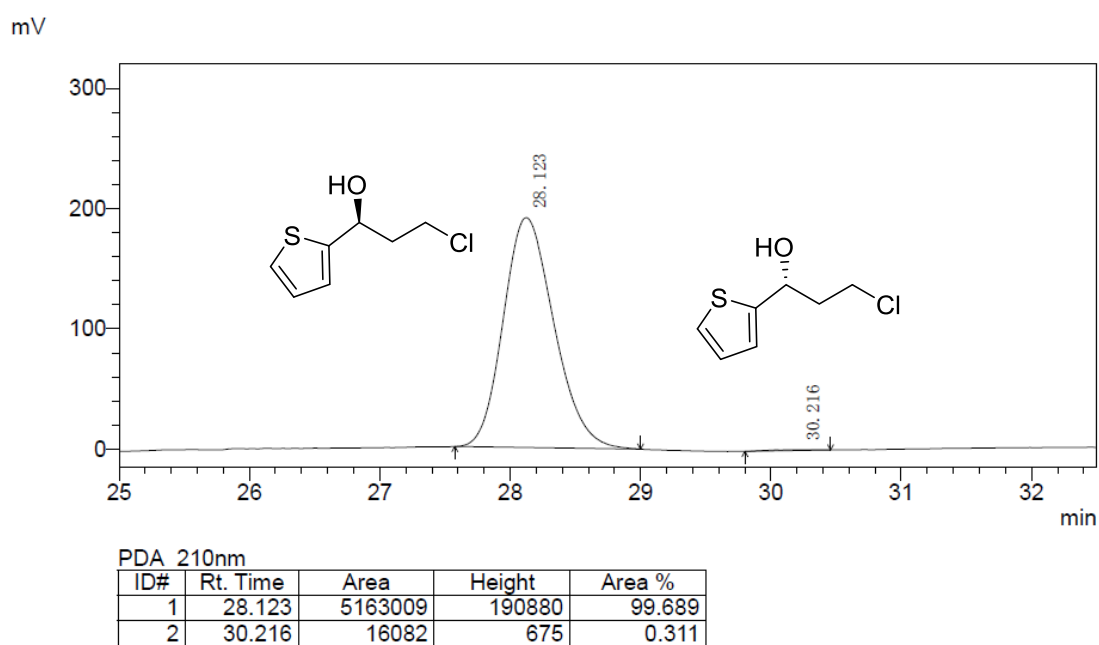


Chiral HPLC analysis: Diacel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 210 nm, $t_{(S)}$ = 16.3 min, $t_{(R)}$ = 17.8 min.

Supplementary Fig. 296 | HPLC trace for the chemical synthesized (*rac*)-**20a**.

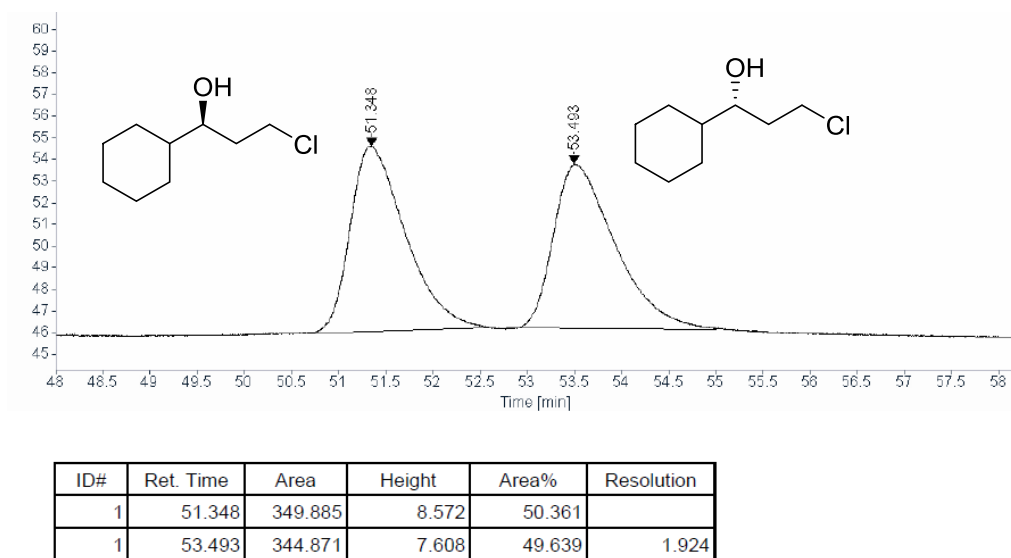


Supplementary Fig. 297 | HPLC trace for the enzymatic synthesized (*S*)-**20a**.

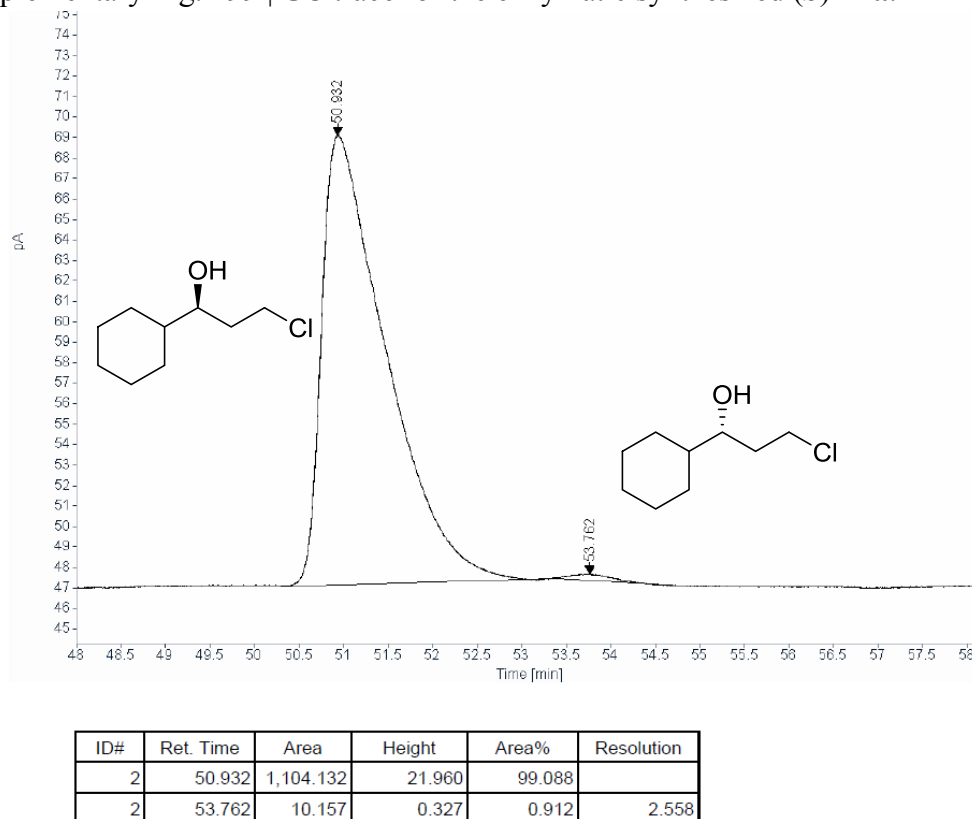


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 98/2, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 28.1 min, $t_{(R)}$ = 30.2 min.

Supplementary Fig. 298 | GC trace for the chemical synthesized (*rac*)-**21a**.

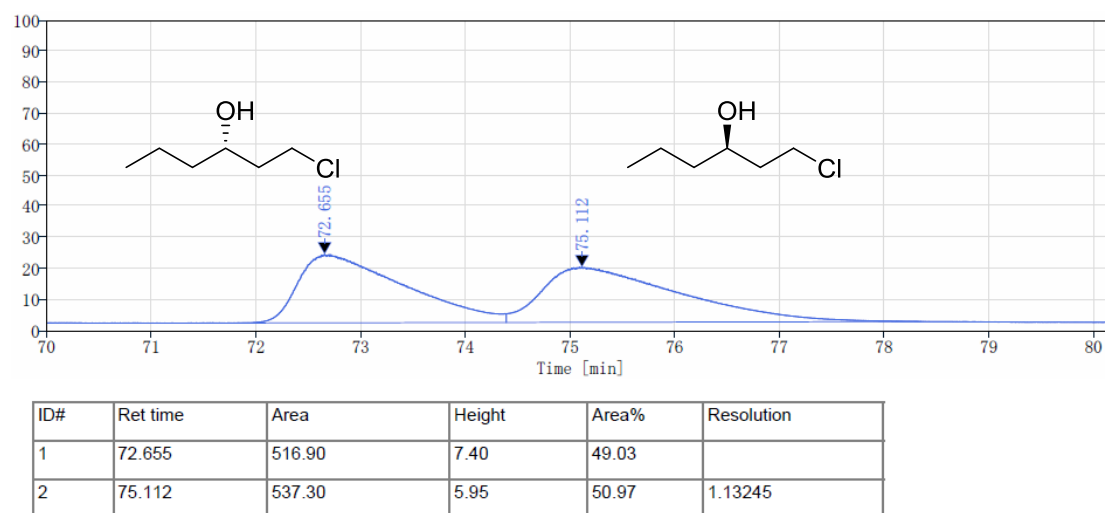


Supplementary Fig. 299 | GC trace for the enzymatic synthesized (*S*)-**21a**.

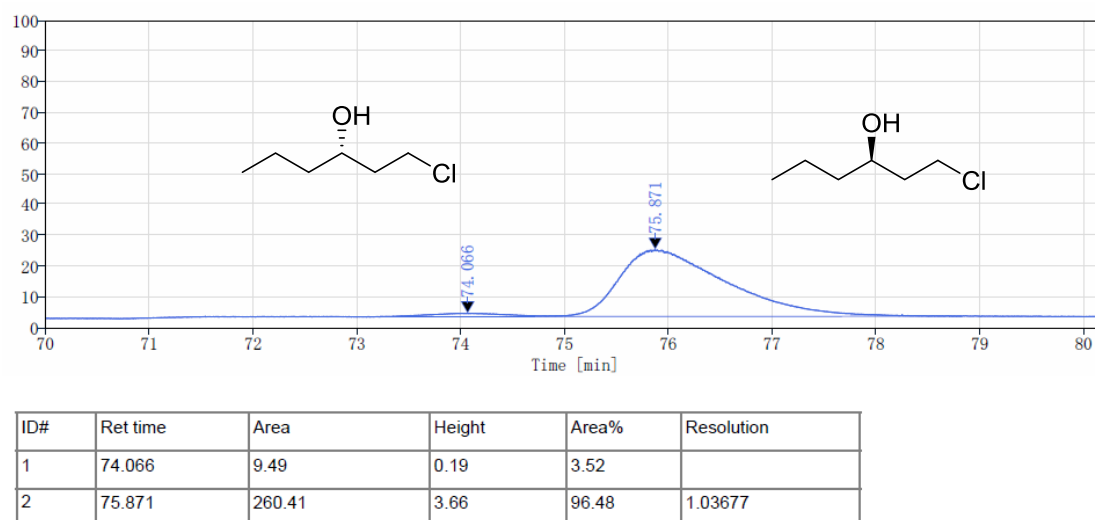


Chiral GC analysis: Chiral GC analysis: CYCLODEX-B, 110 °C for 85 min, $t_{(S)} = 50.9$ min, $t_{(R)} = 53.8$ min.

Supplementary Fig. 300 | GC trace for the chemical synthesized (*rac*)-**22a**.



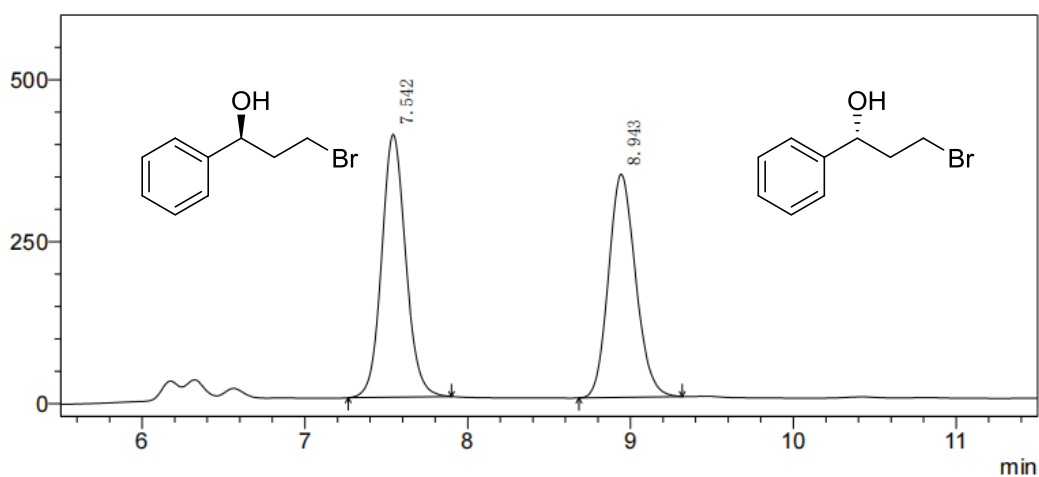
Supplementary Fig. 301 | GC trace for the enzymatic synthesized (*R*)-**22a**.



Chiral GC analysis: Rt-bDEXcst (RESTEK), 90 °C for 90 min, $t_{(S)} = 74.1$ min, $t_{(R)} = 75.9$ min.

Supplementary Fig. 302 | HPLC trace for the chemical synthesized (*rac*)-**23a**.

mV

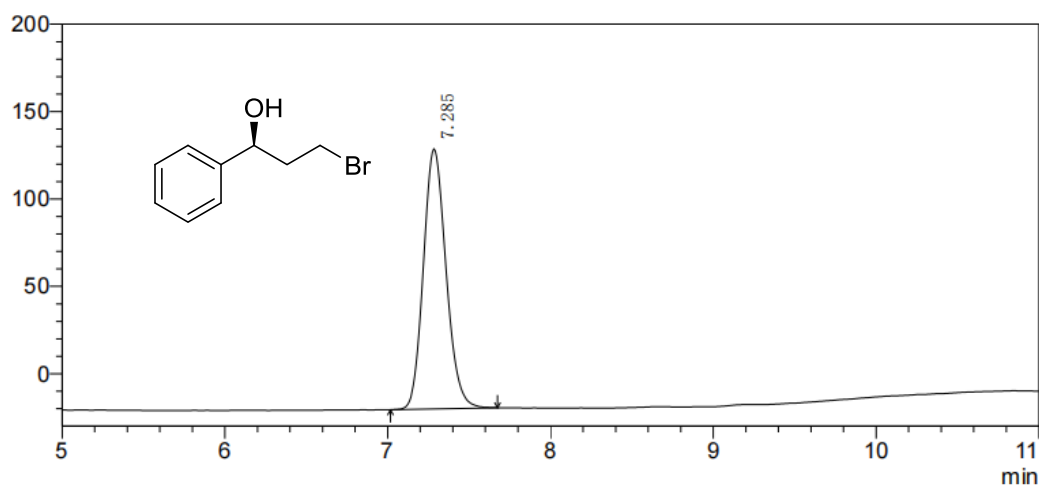


PDA 210nm

ID#	Rt. Time	Area	Height	Area %
1	7.542	4166331	405994	50.972
2	8.943	4007396	344770	49.028

Supplementary Fig. 303 | HPLC trace for the enzymatic synthesized (*S*)-**23a**.

mV

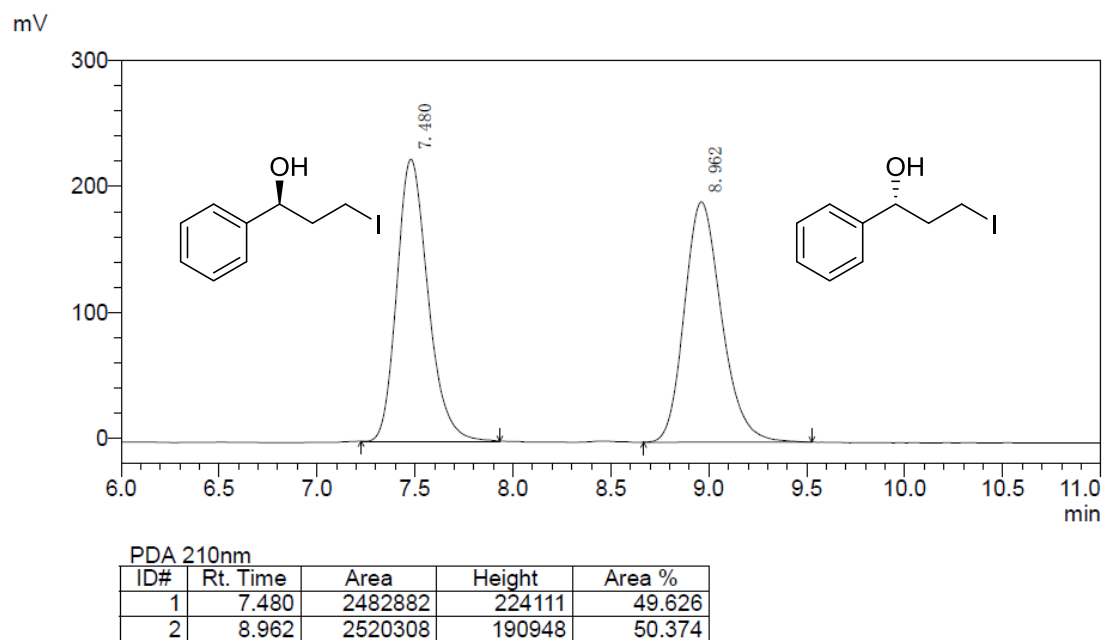


PDA 210nm

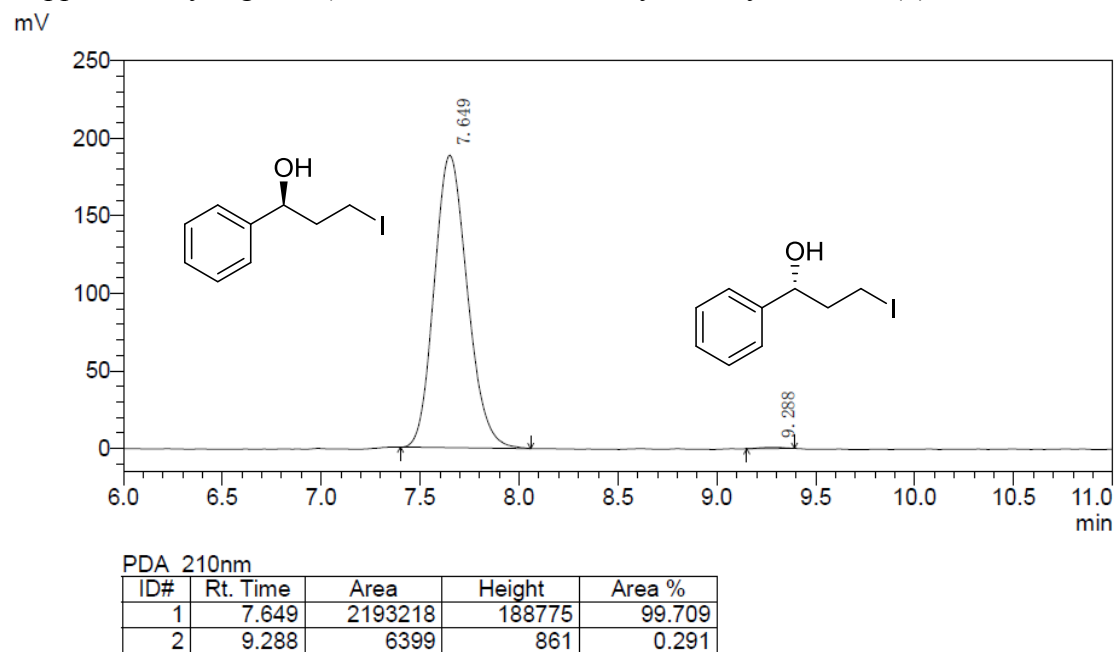
ID#	Rt. Time	Area	Height	Area %
1	7.285	1435713	148674	100.000

Chiral HPLC analysis: Diacel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, $\lambda = 210$ nm, $t_{(S)} = 7.5$ min, $t_{(R)} = 8.9$ min.

Supplementary Fig. 304 | HPLC trace for the chemical synthesized (*rac*)-**24a**.

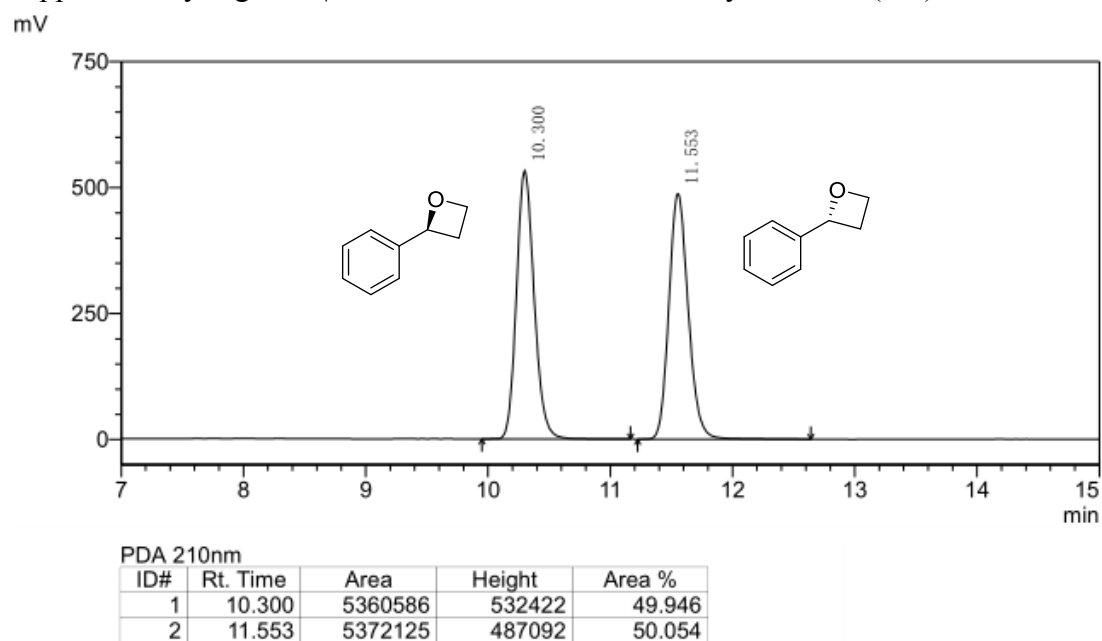


Supplementary Fig. 305 | HPLC trace for the enzymatic synthesized (*S*)-**24a**.

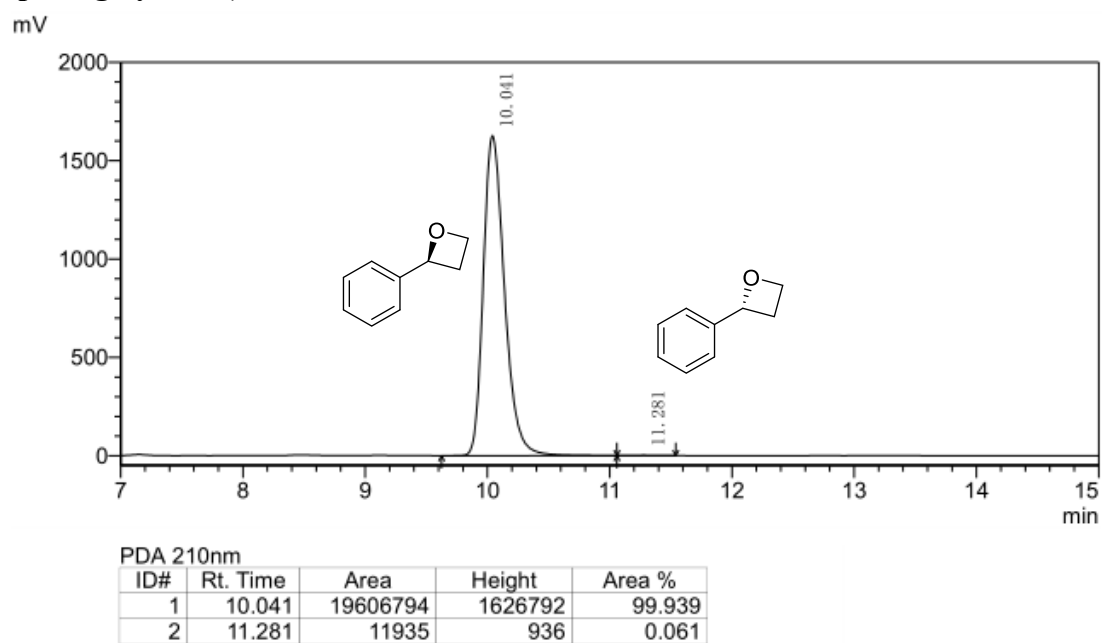


Chiral HPLC analysis: Diacel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 210 nm, $t_{(S)}$ = 7.6 min, $t_{(R)}$ = 9.3 min.

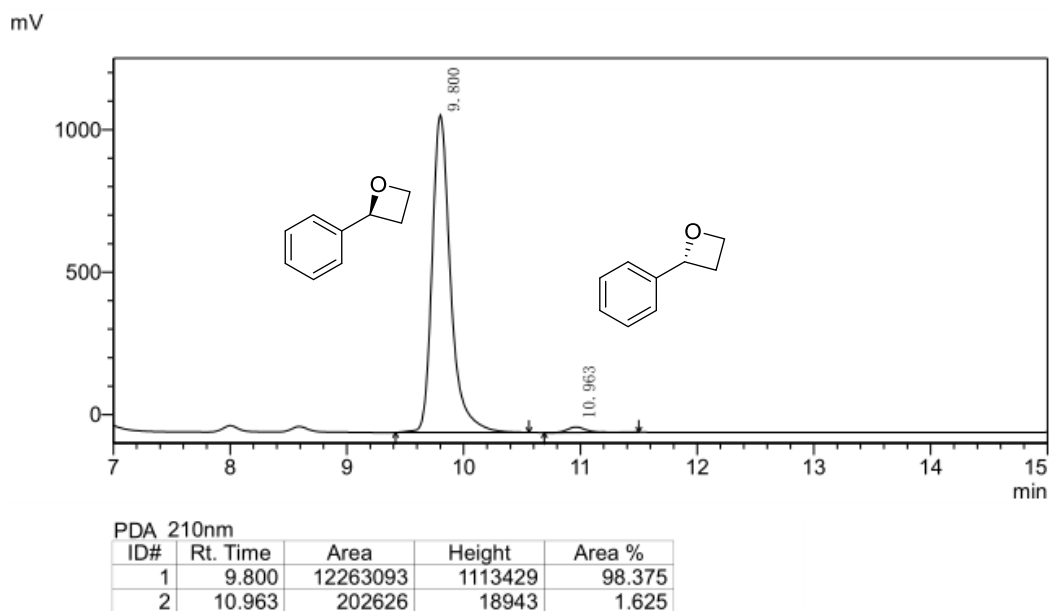
Supplementary Fig. 306 | HPLC trace for the chemical synthesized (*rac*)-**1b**.



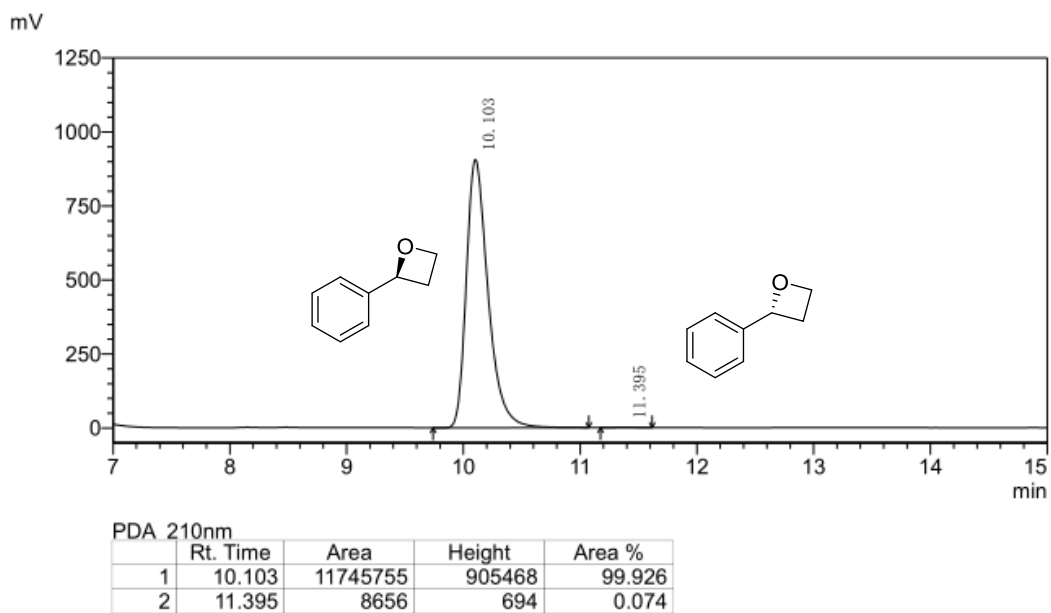
Supplementary Fig. 307 | HPLC trace for the enzymatic synthesized (*S*)-**1b** (Ring opening by azide).



Supplementary Fig. 308 | HPLC trace for the enzymatic synthesized (*S*)-**1b** (Ring opening by cyanide).

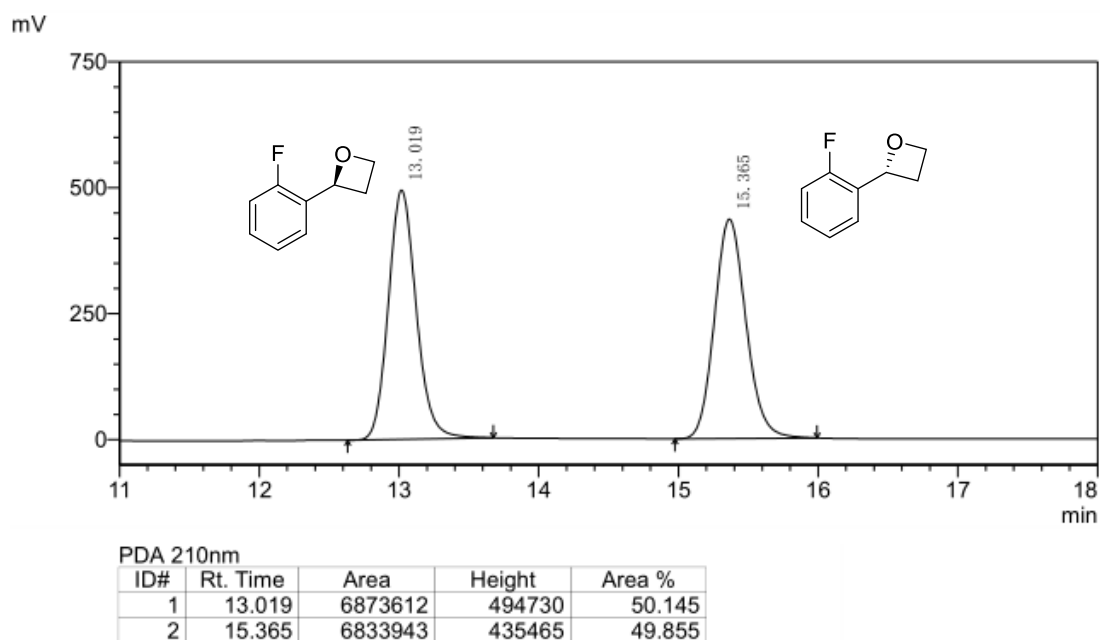


Supplementary Fig. 309 | HPLC trace for the enzymatic synthesized (*S*)-**1b** (Ring opening by nitrite).

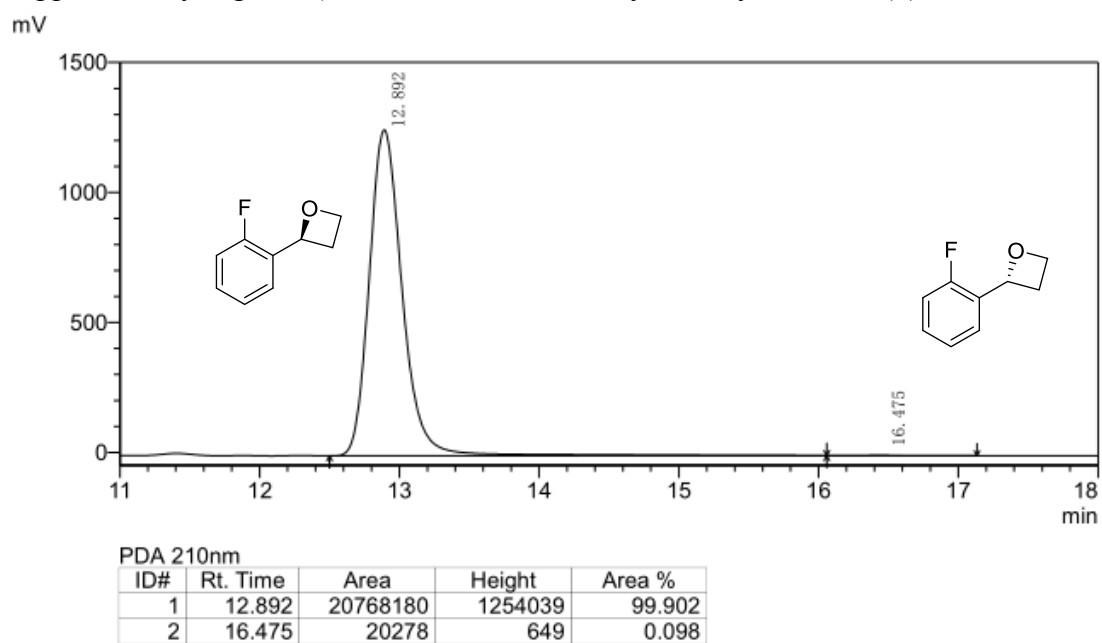


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, $\lambda = 210$ nm, $t_{(S)} = 10.3$ min, $t_{(R)} = 11.6$ min.

Supplementary Fig. 310 | HPLC trace for the chemical synthesized (*rac*)-**2b**.

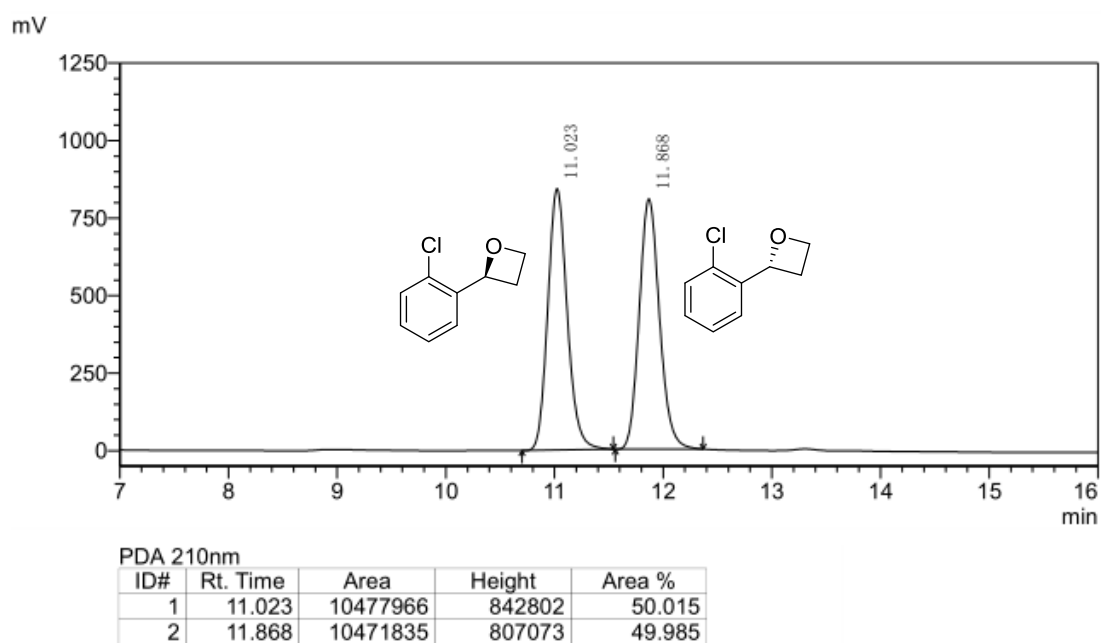


Supplementary Fig. 311 | HPLC trace for the enzymatic synthesized (*S*)-**2b**.

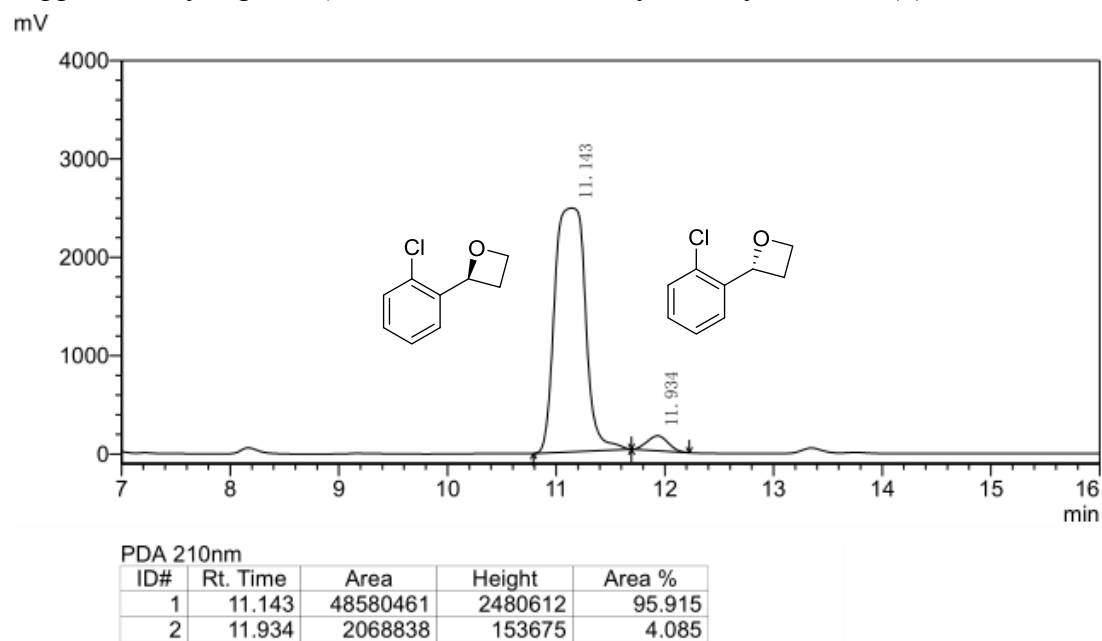


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 12.9 min, $t_{(R)}$ = 16.5 min.

Supplementary Fig. 312 | HPLC trace for the chemical synthesized (*rac*)-**3b**.

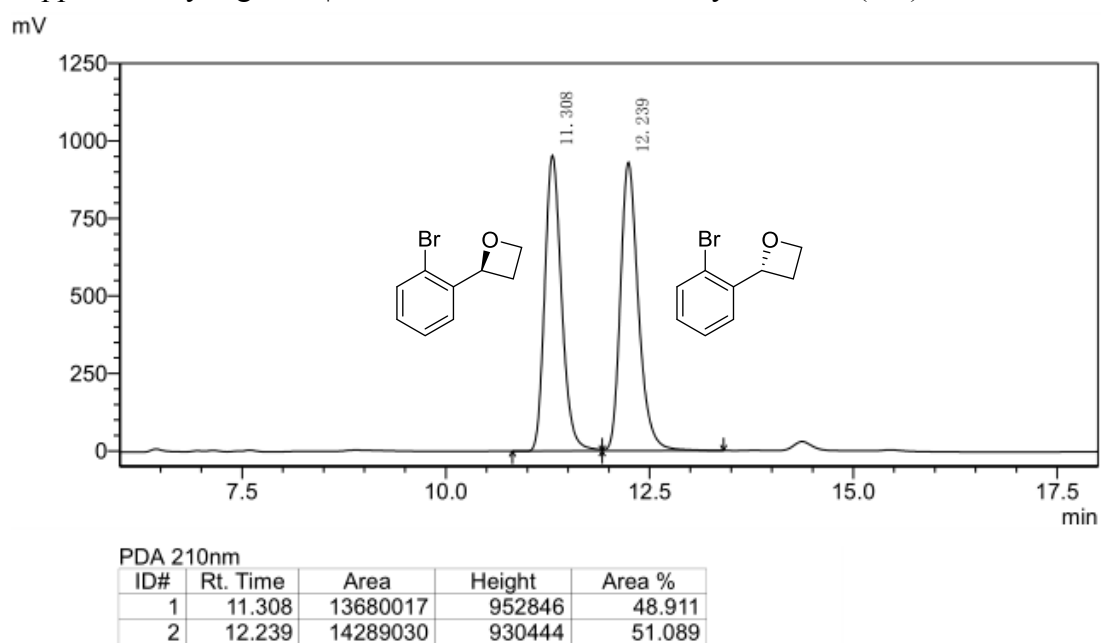


Supplementary Fig. 313 | HPLC trace for the enzymatic synthesized (*S*)-**3b**.

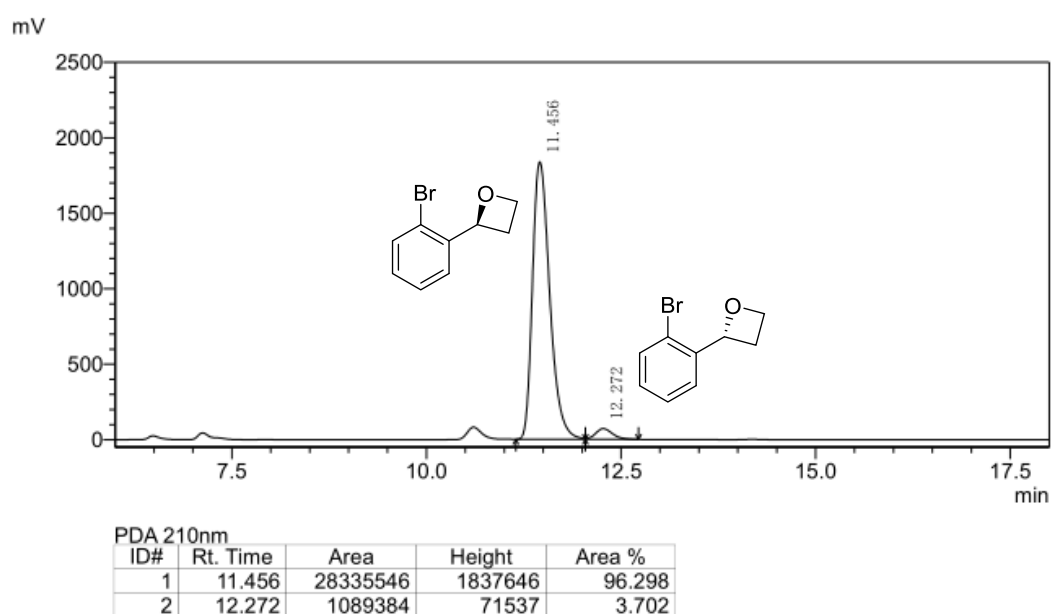


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 11.1 min, $t_{(R)}$ = 11.9 min.

Supplementary Fig. 314 | HPLC trace for the chemical synthesized (*rac*)-**4b**.

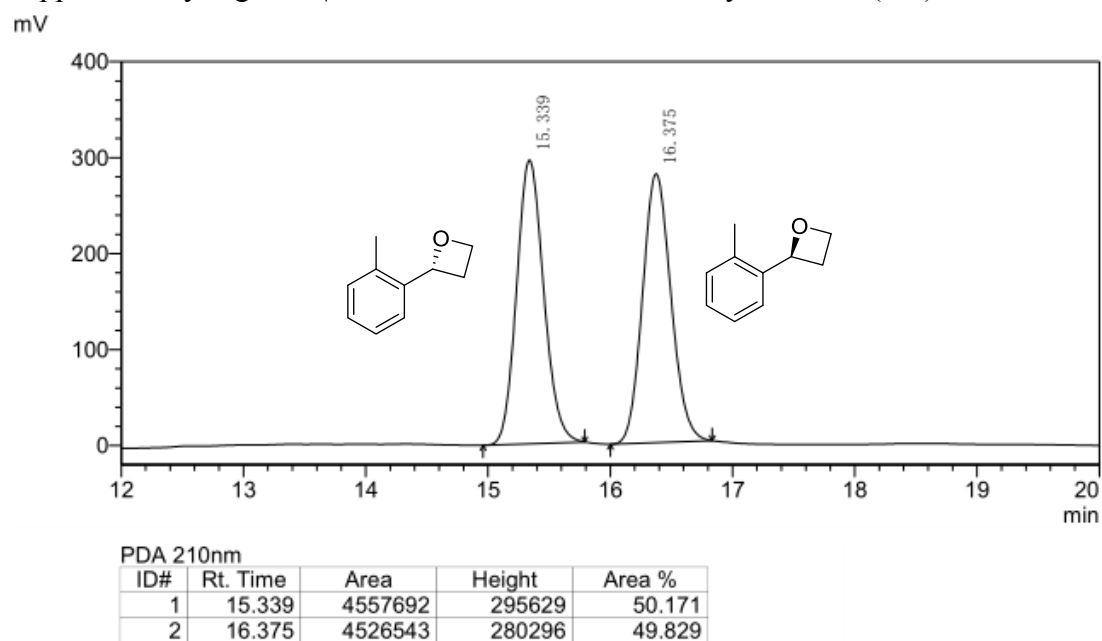


Supplementary Fig. 315 | HPLC trace for the enzymatic synthesized (*S*)-**4b**.

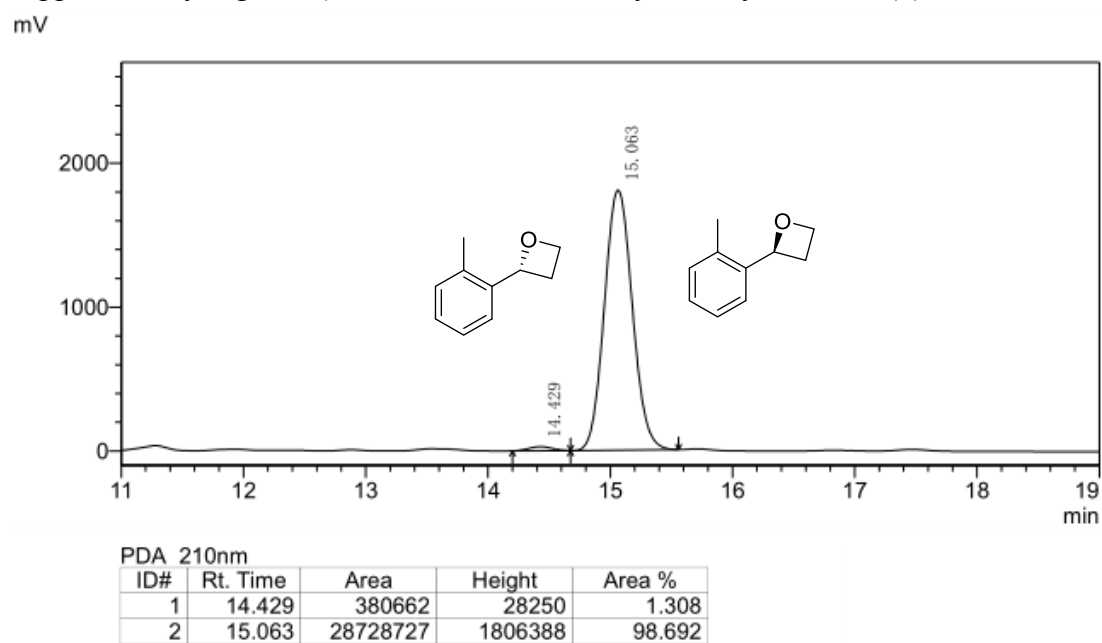


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 11.5 min, $t_{(R)}$ = 12.3 min.

Supplementary Fig. 316 | HPLC trace for the chemical synthesized (*rac*)-**5b**.

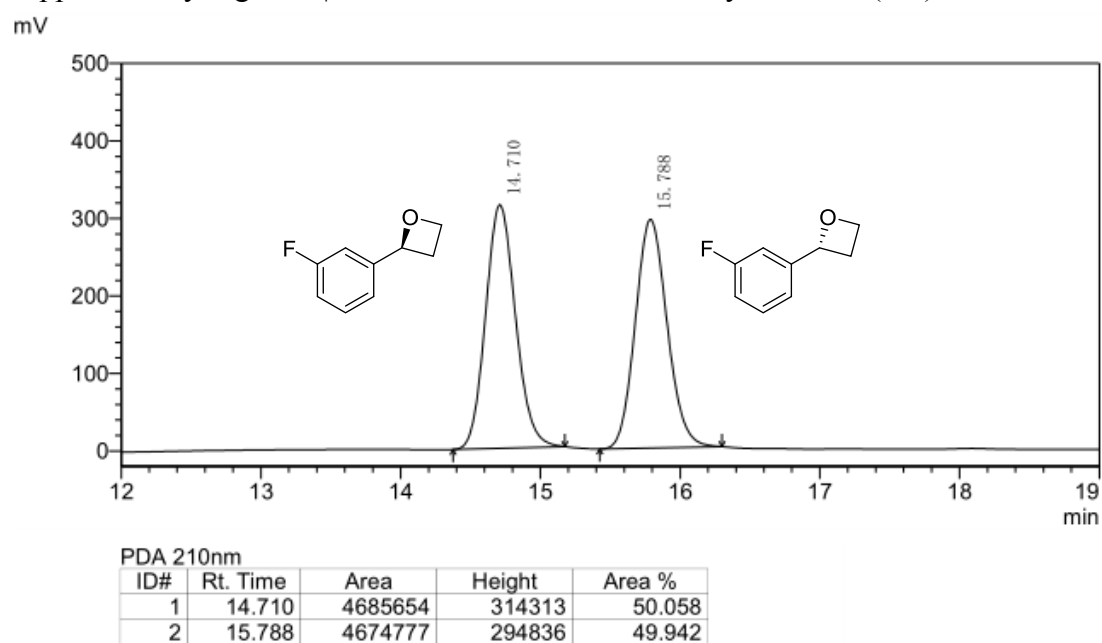


Supplementary Fig. 317 | HPLC trace for the enzymatic synthesized (*S*)-**5b**.

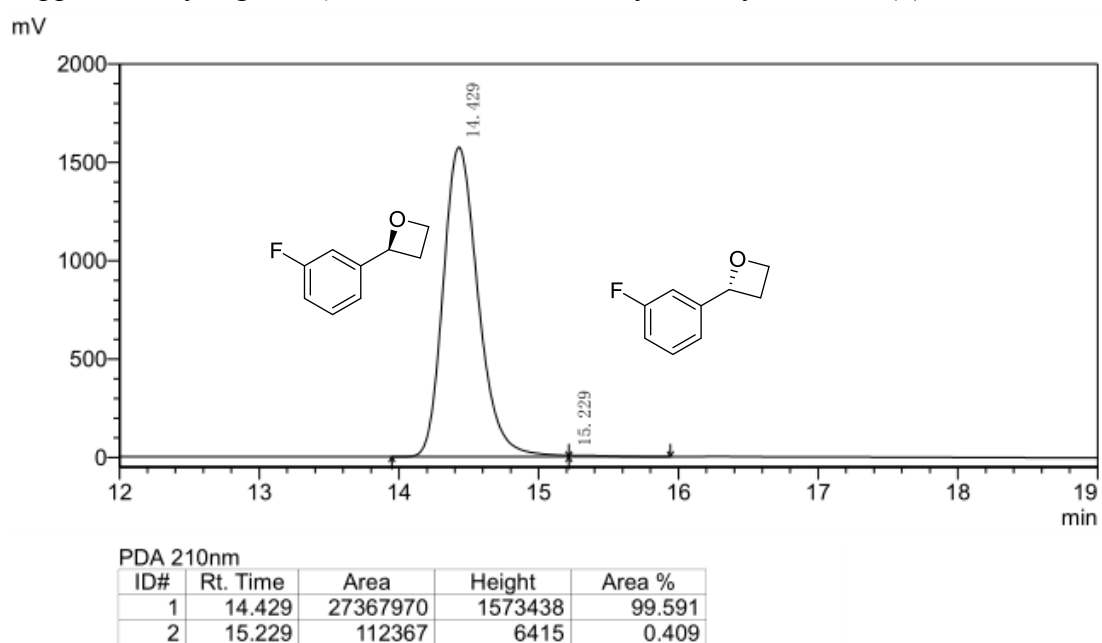


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(R)}$ = 14.4 min, $t_{(S)}$ = 15.1 min.

Supplementary Fig. 318 | HPLC trace for the chemical synthesized (*rac*)-**6b**.

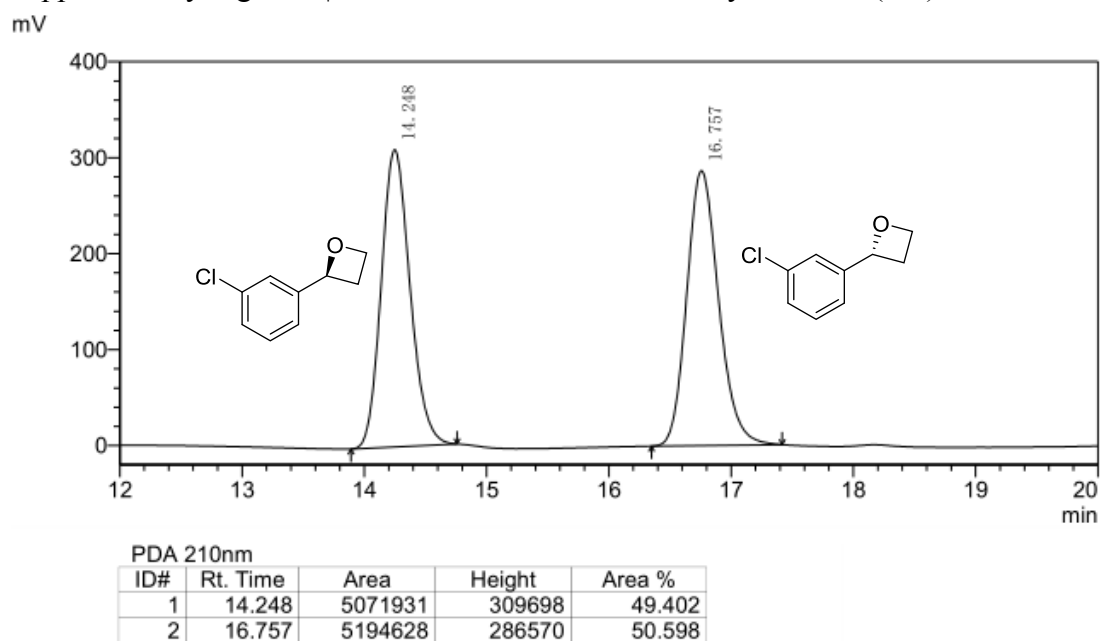


Supplementary Fig. 319 | HPLC trace for the enzymatic synthesized (*S*)-**6b**.

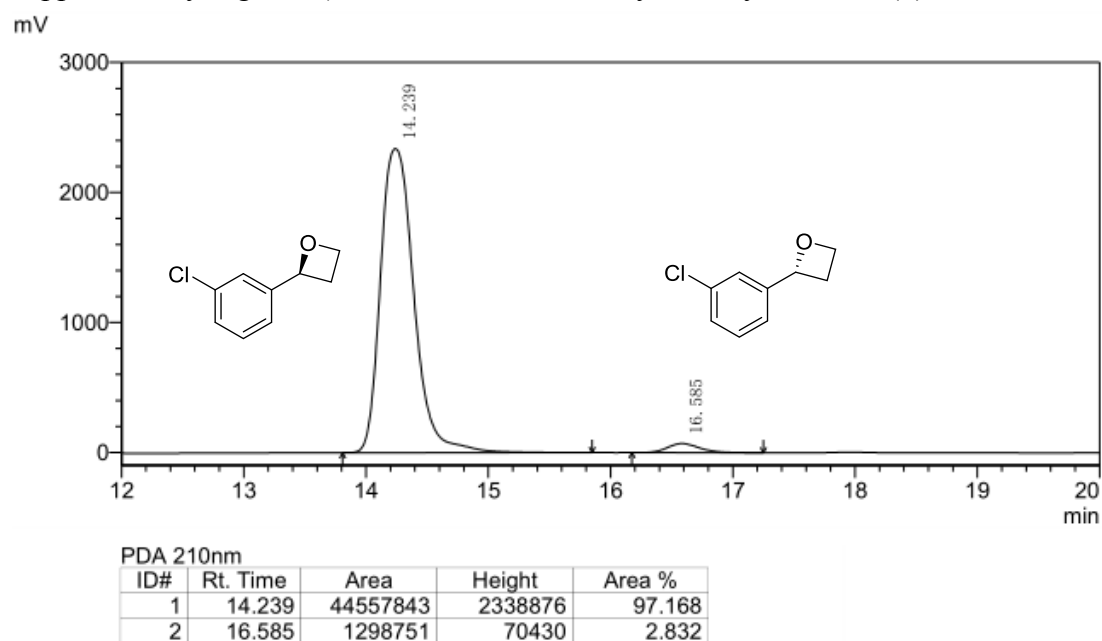


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 14.4 min, $t_{(R)}$ = 15.2 min.

Supplementary Fig. 320 | HPLC trace for the chemical synthesized (*rac*)-**7b**.

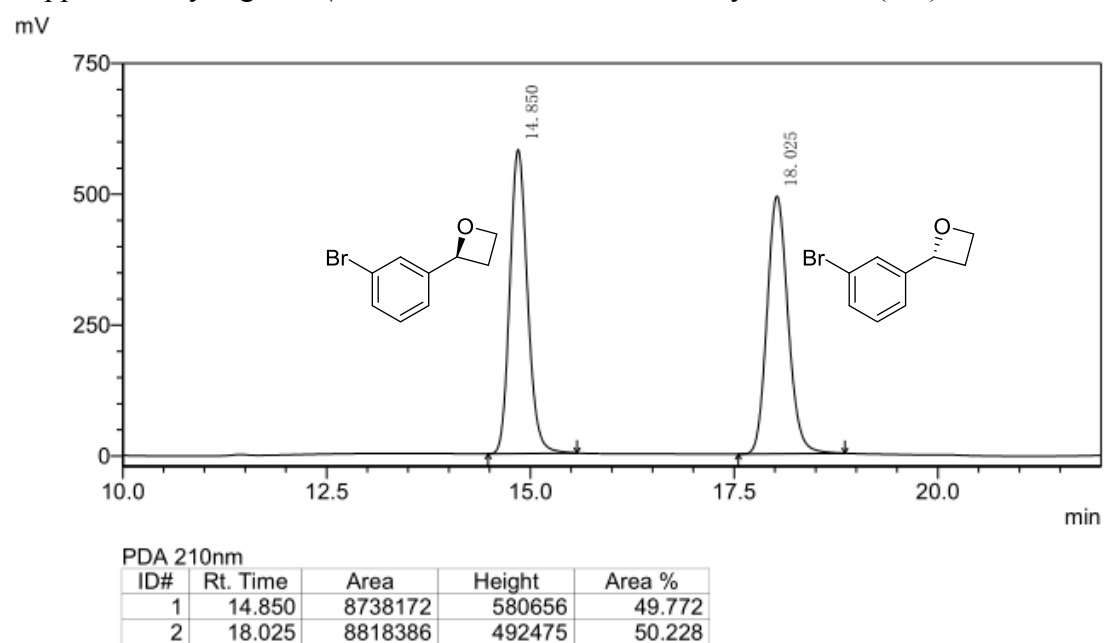


Supplementary Fig. 321 | HPLC trace for the enzymatic synthesized (*S*)-**7b**.

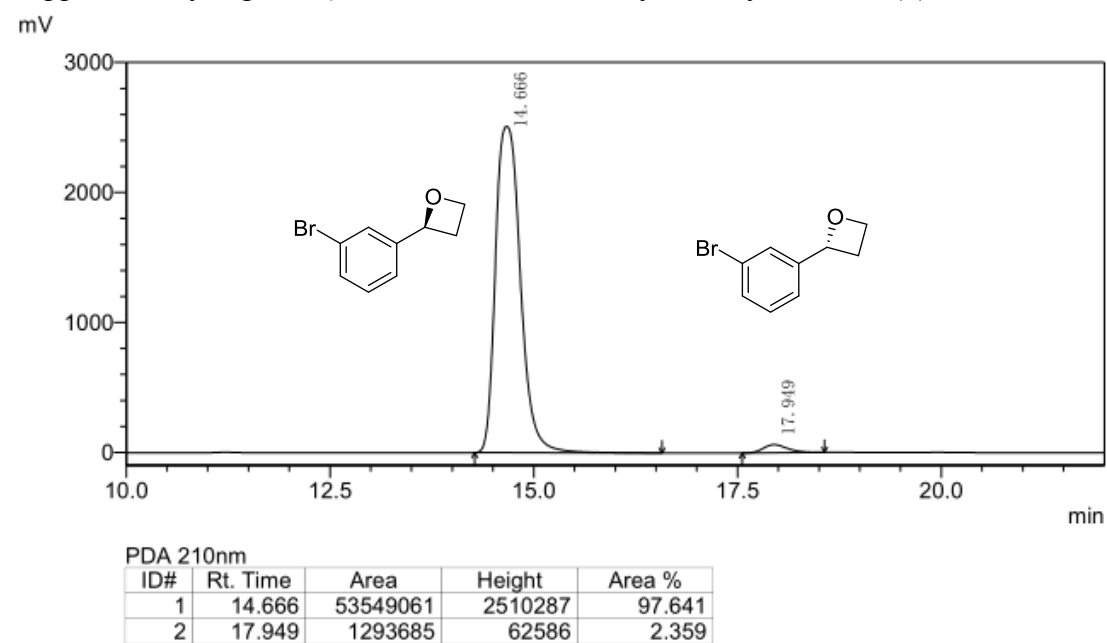


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 14.2 min, $t_{(R)}$ = 16.6 min.

Supplementary Fig. 322 | HPLC trace for the chemical synthesized (*rac*)-**8b**.

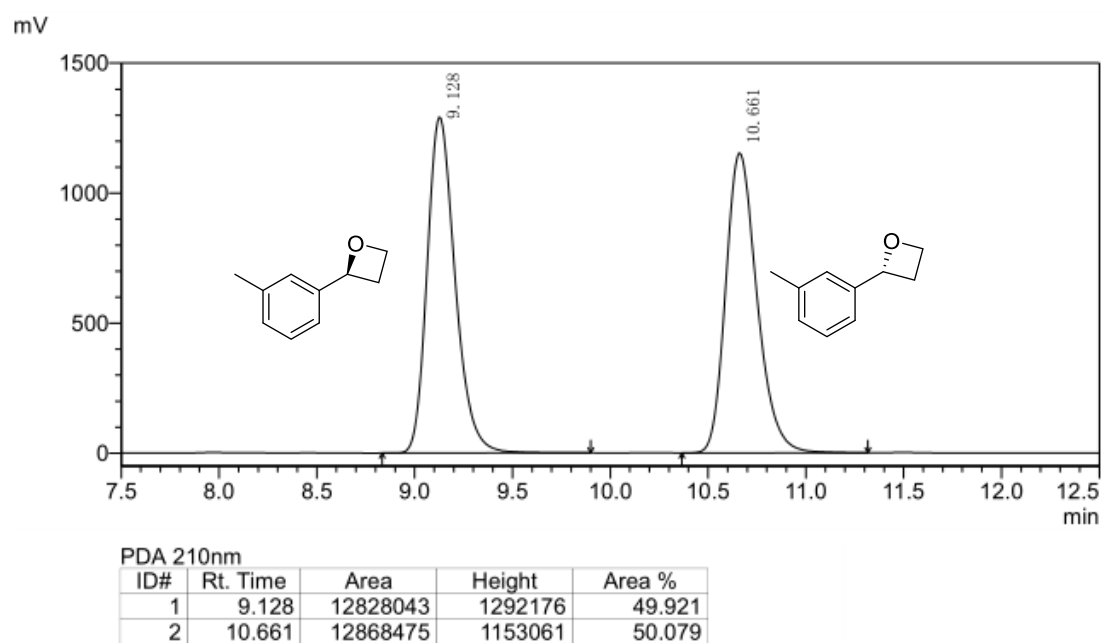


Supplementary Fig. 323 | HPLC trace for the enzymatic synthesized (*S*)-**8b**.

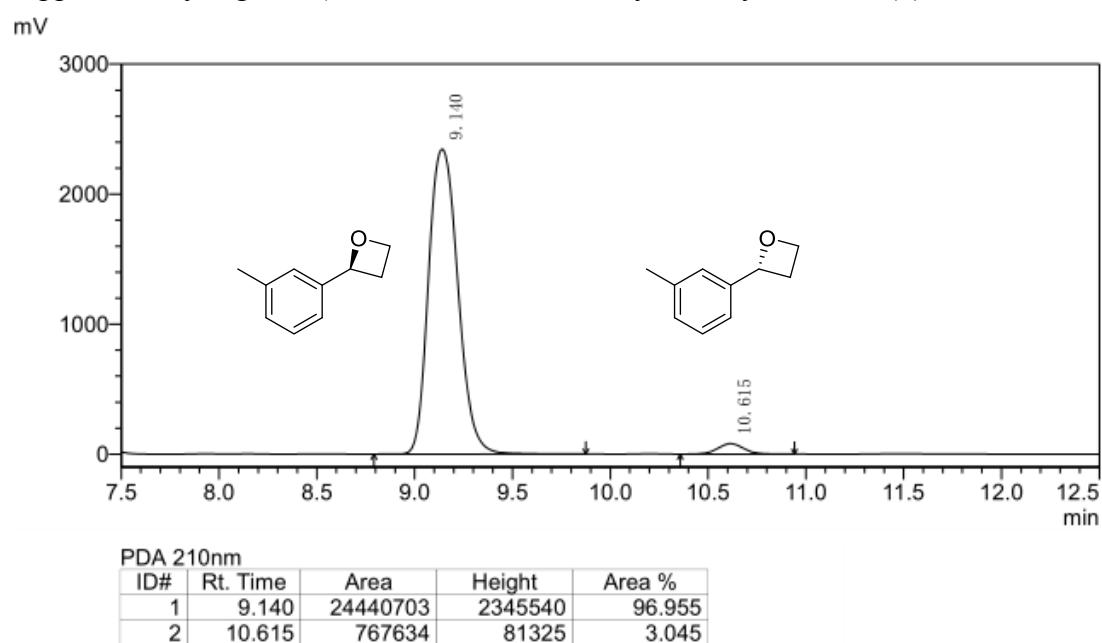


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 14.7 min, $t_{(R)}$ = 17.9 min.

Supplementary Fig. 324 | HPLC trace for the chemical synthesized (*rac*)-**9b**.

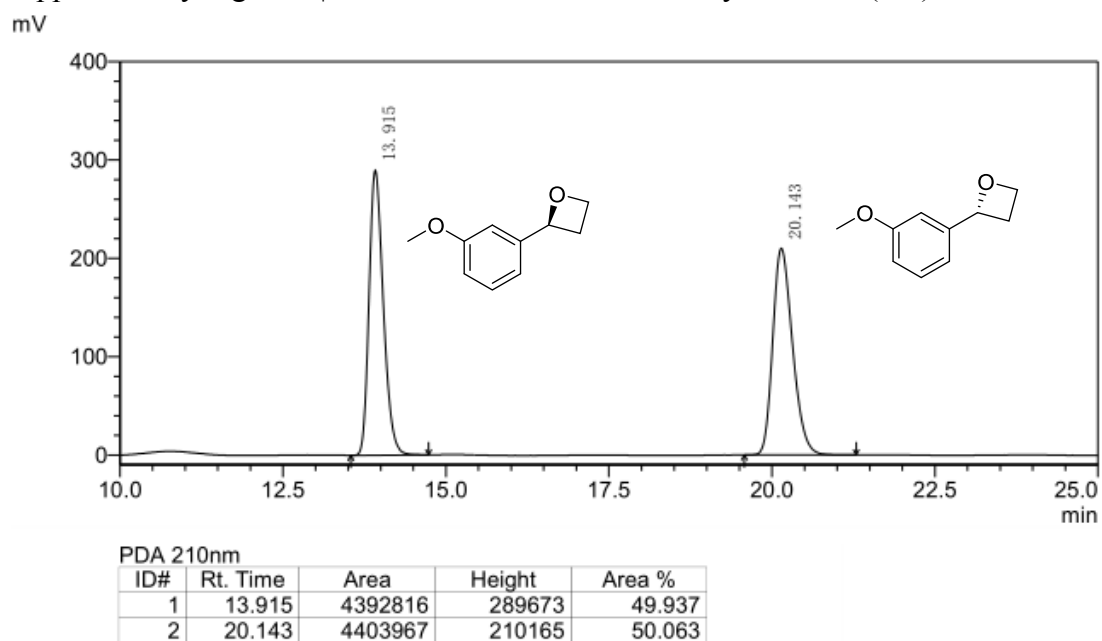


Supplementary Fig. 325 | HPLC trace for the enzymatic synthesized (*S*)-**9b**.

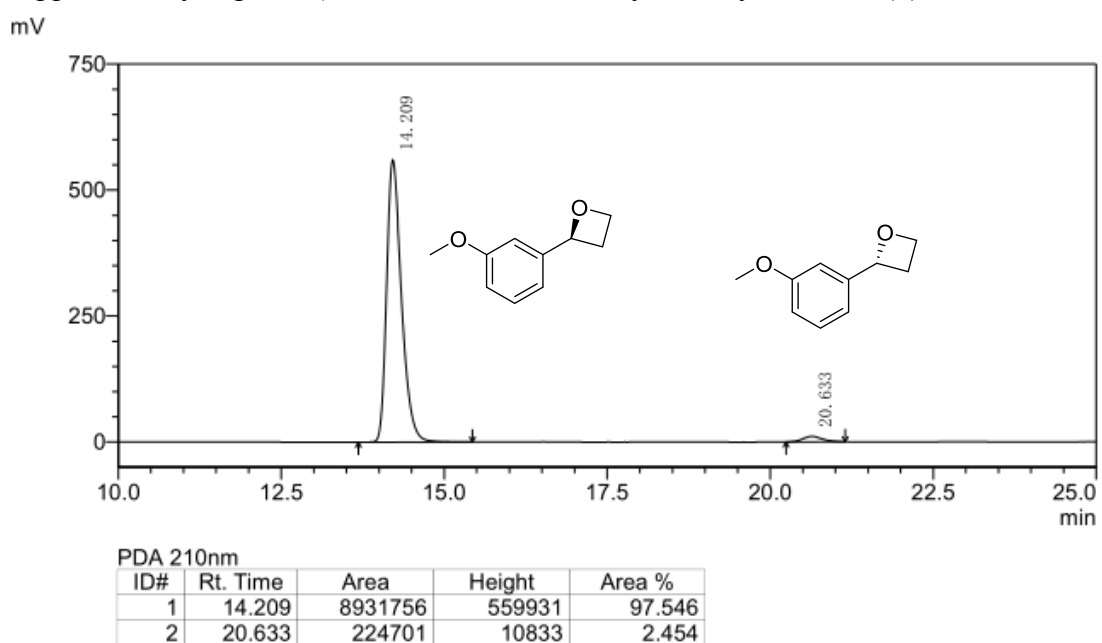


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 9.1 min, $t_{(R)}$ = 10.6 min.

Supplementary Fig. 326 | HPLC trace for the chemical synthesized (*rac*)-**10b**.

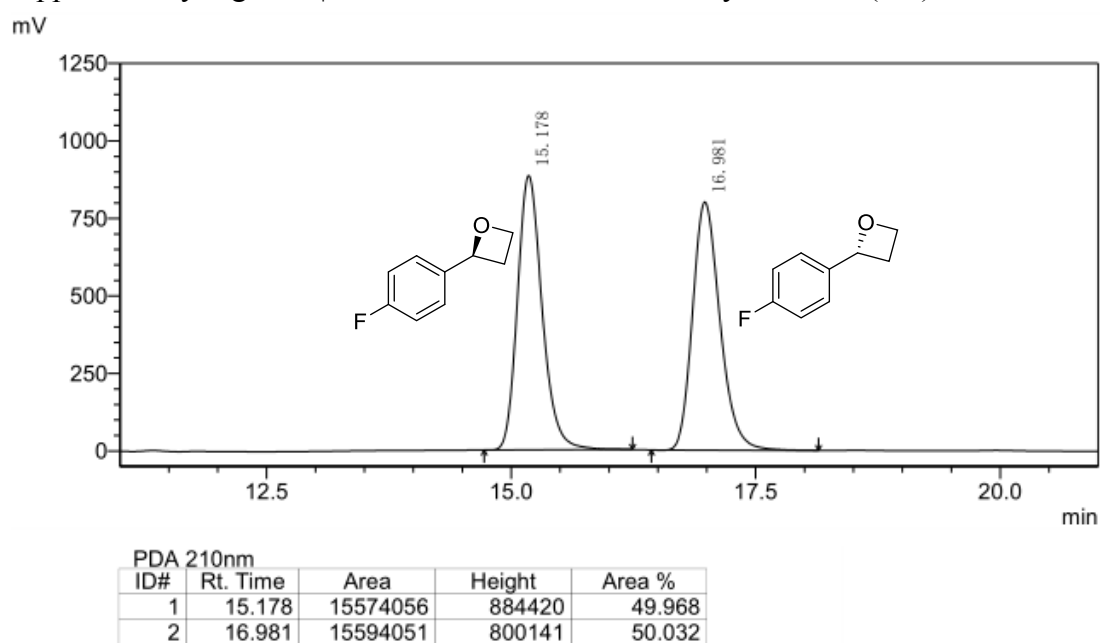


Supplementary Fig. 327 | HPLC trace for the enzymatic synthesized (*S*)-**10b**.

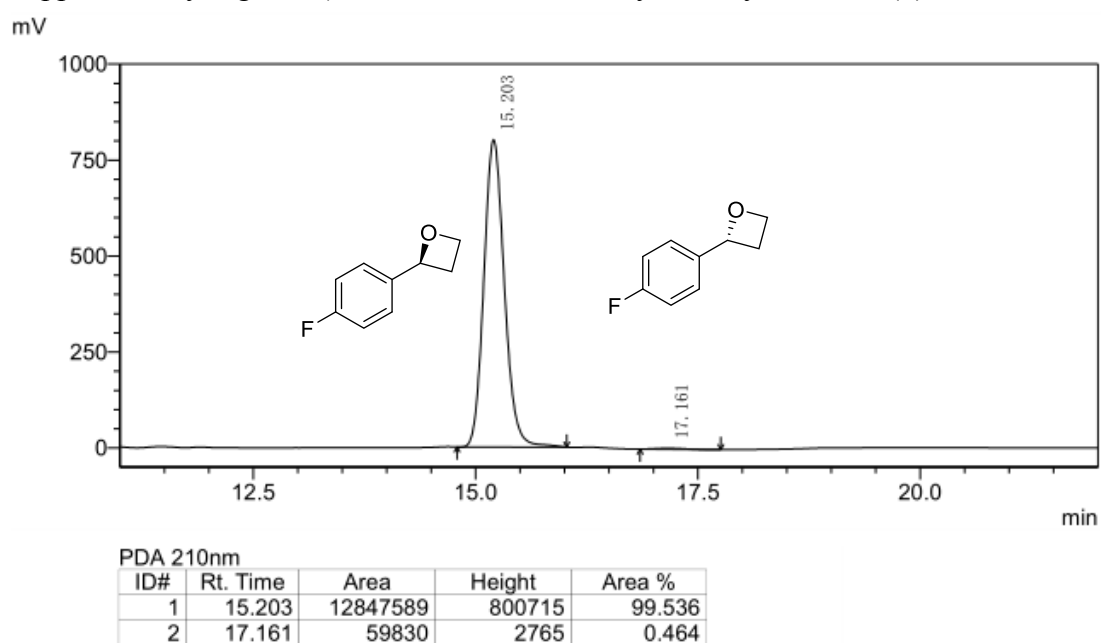


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 14.2 min, $t_{(R)}$ = 20.6 min.

Supplementary Fig. 328 | HPLC trace for the chemical synthesized (*rac*)-**11b**.

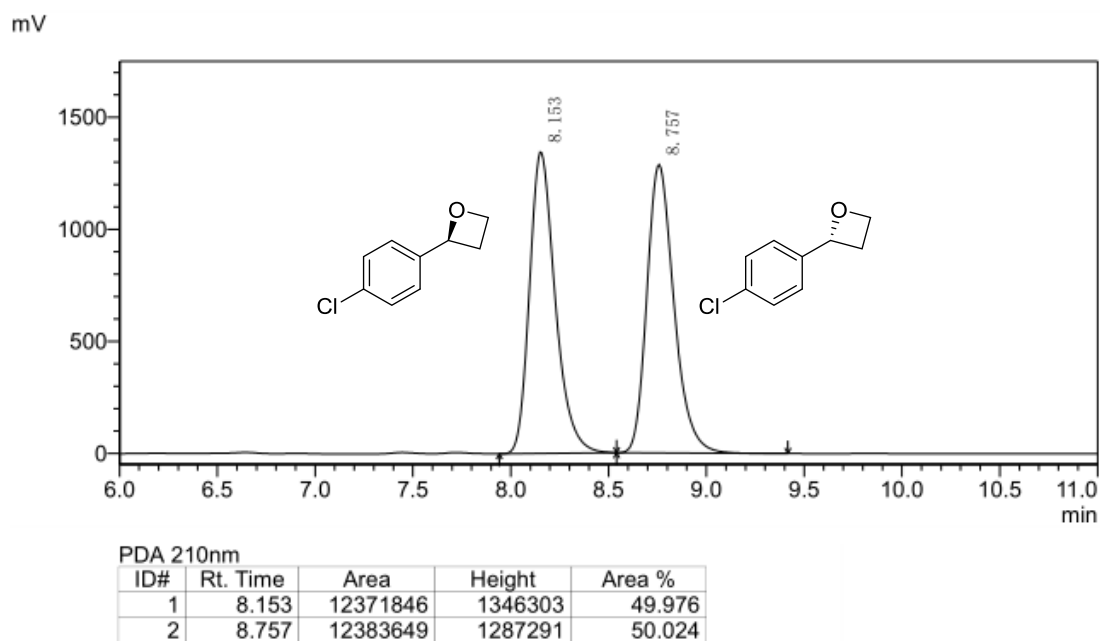


Supplementary Fig. 329 | HPLC trace for the enzymatic synthesized (*S*)-**11b**.

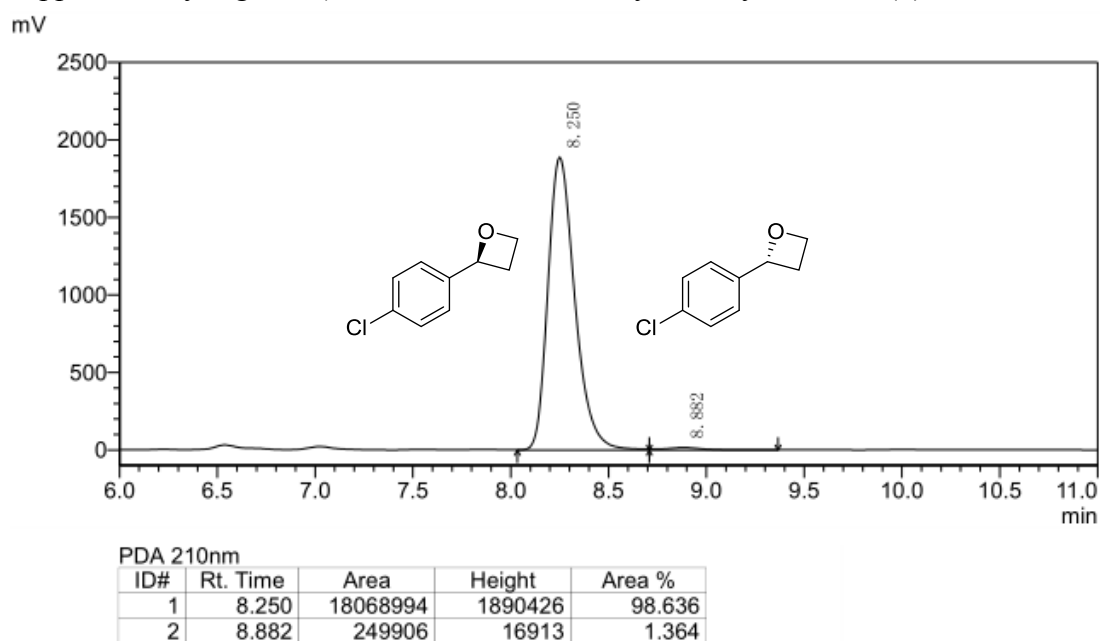


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 15.2 min, $t_{(R)}$ = 17.2 min.

Supplementary Fig. 330 | HPLC trace for the chemical synthesized (*rac*)-**12b**.

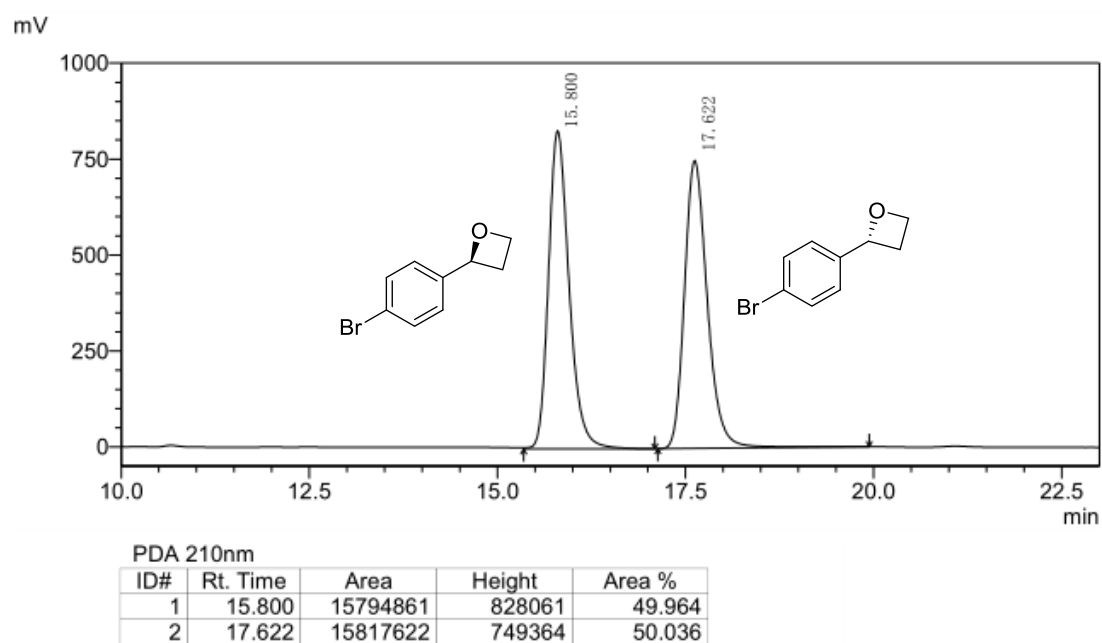


Supplementary Fig. 331 | HPLC trace for the enzymatic synthesized (*S*)-**12b**.

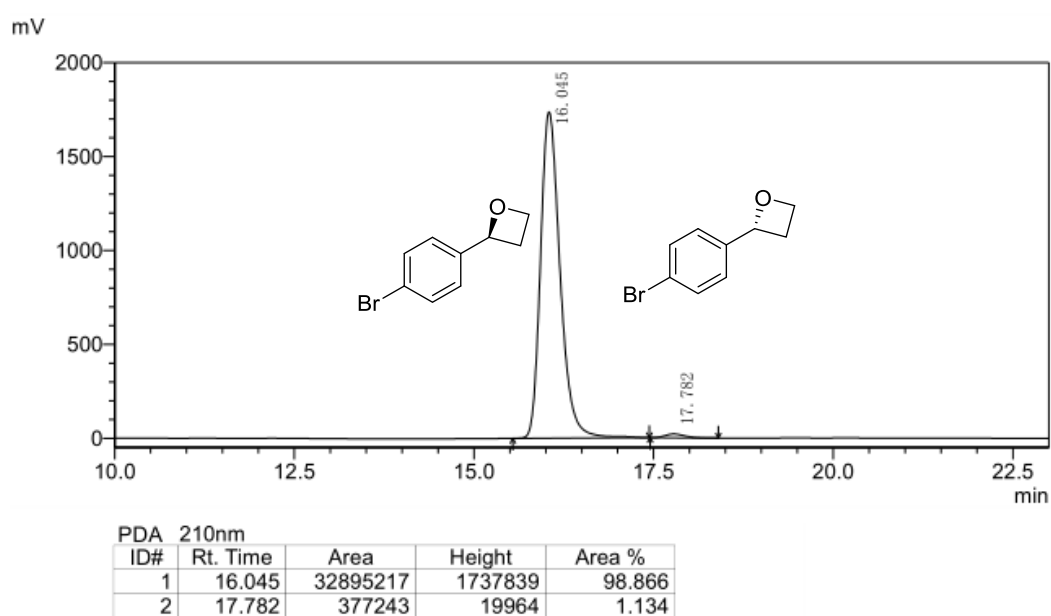


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 8.3 min, $t_{(R)}$ = 8.9 min.

Supplementary Fig. 332 | HPLC trace for the chemical synthesized (*rac*)-**13b**.

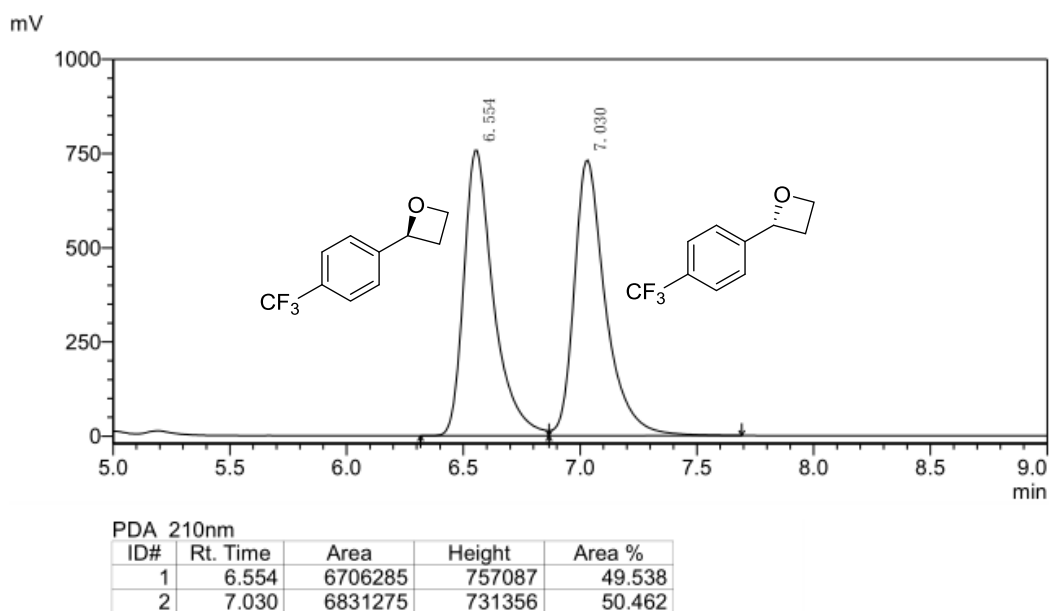


Supplementary Fig. 333 | HPLC trace for the enzymatic synthesized (*S*)-**13b**.

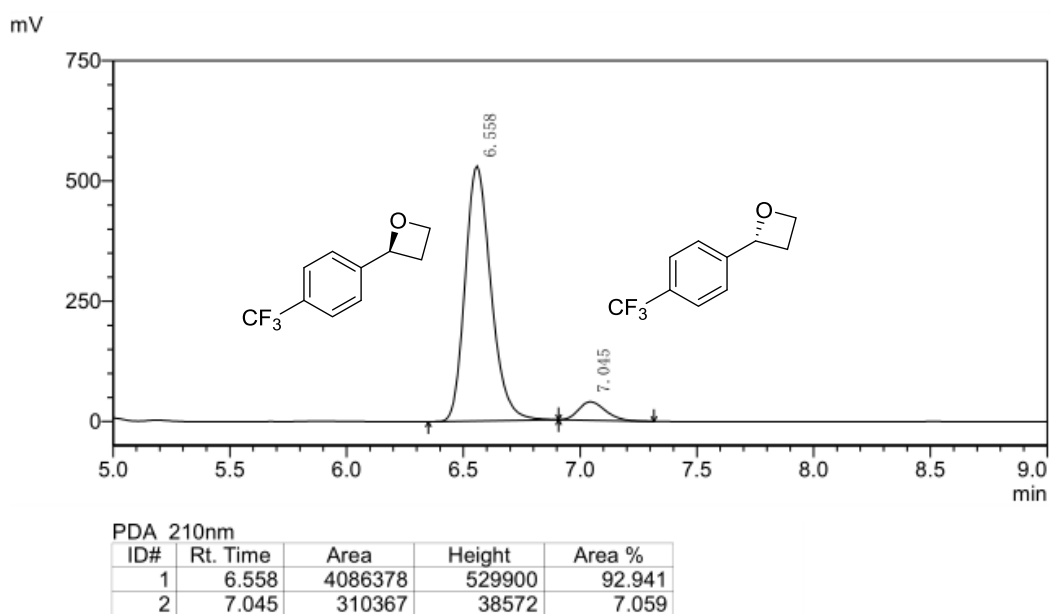


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 16.0 min, $t_{(R)}$ = 17.8 min.

Supplementary Fig. 334 | HPLC trace for the chemical synthesized (*rac*)-**14b**.

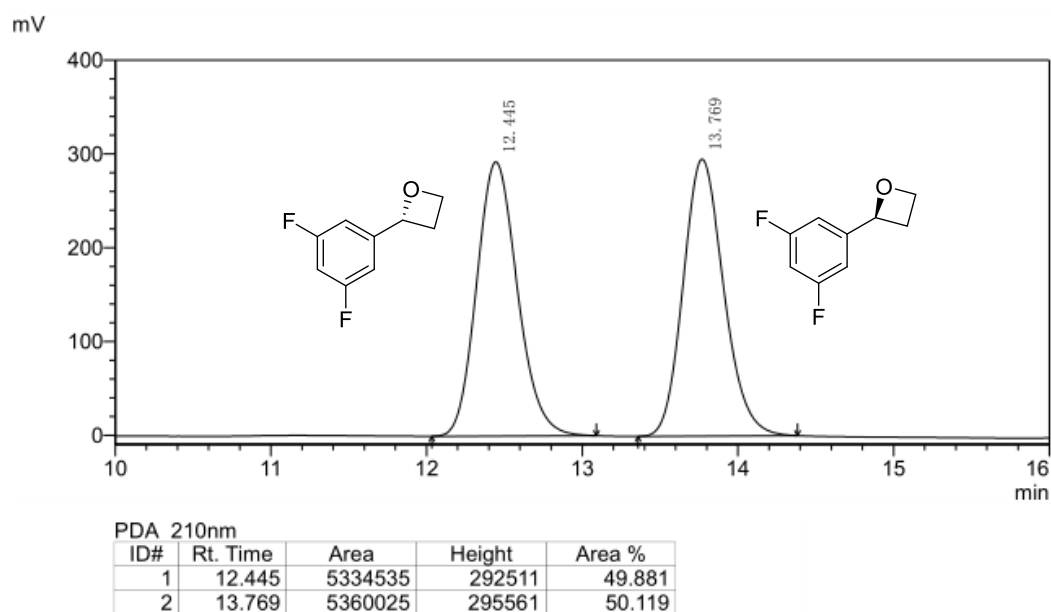


Supplementary Fig. 335 | HPLC trace for the enzymatic synthesized (*S*)-**14b**.

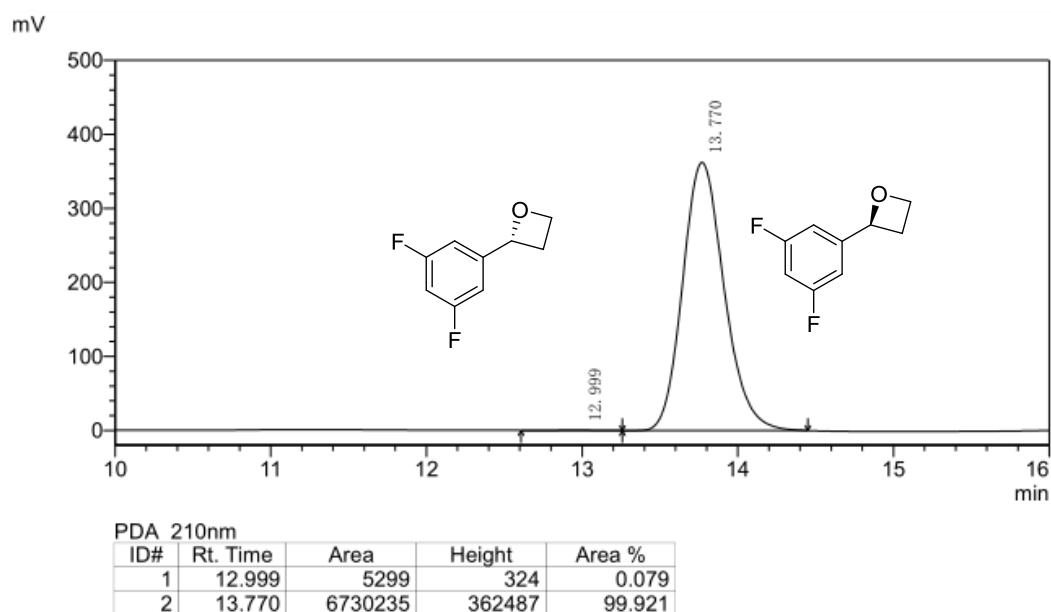


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 6.6 min, $t_{(R)}$ = 7.0 min.

Supplementary Fig. 336 | HPLC trace for the chemical synthesized (*rac*)-**15b**.

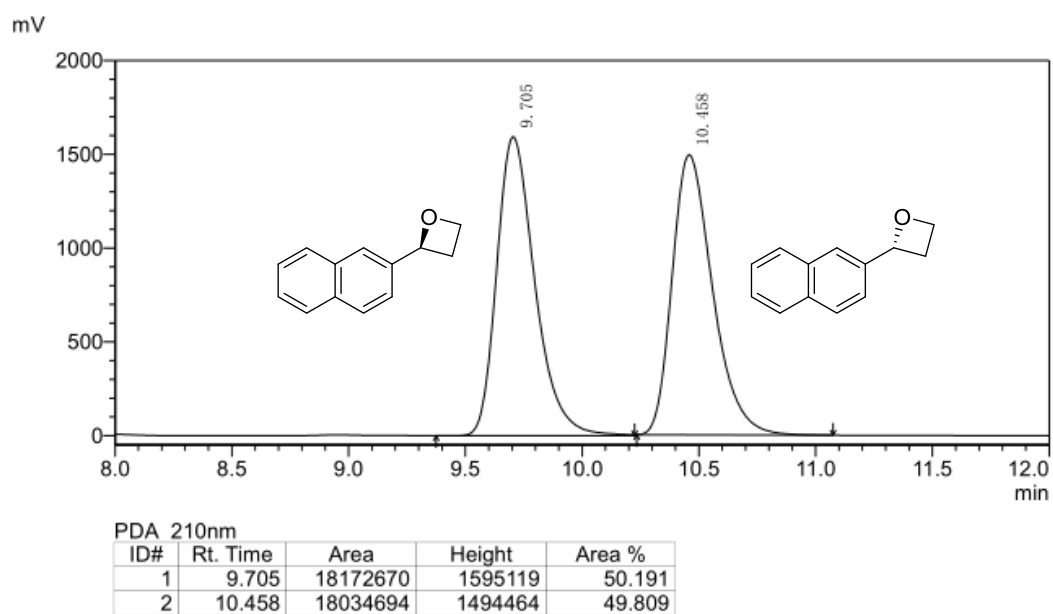


Supplementary Fig. 337 | HPLC trace for the enzymatic synthesized (*S*)-**15b**.

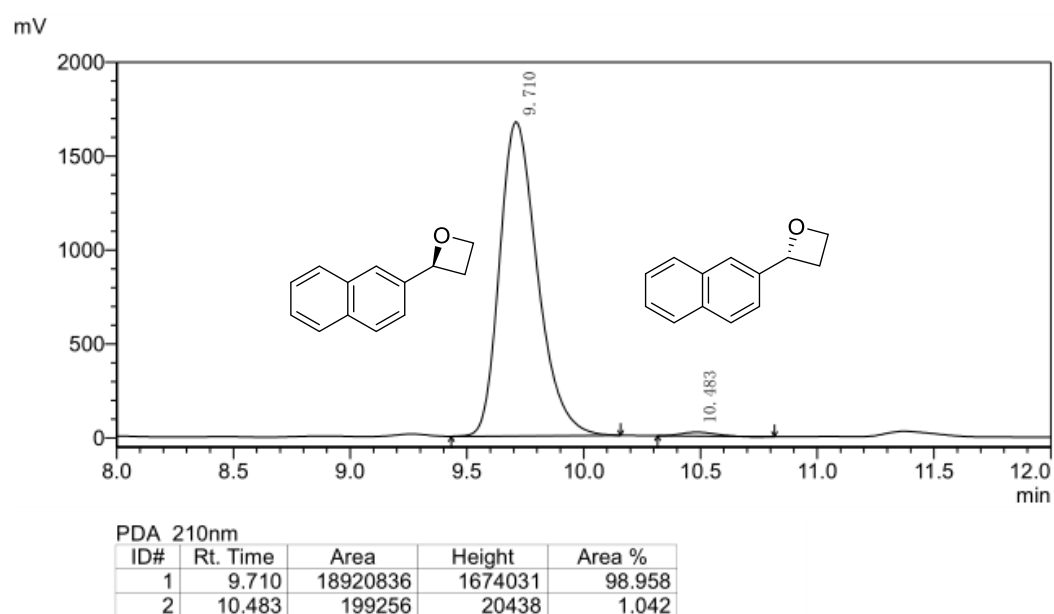


Chiral HPLC analysis: Diacel Chiralpak IA-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(R)}$ = 13.0 min, $t_{(S)}$ = 13.8 min.

Supplementary Fig. 338 | HPLC trace for the chemical synthesized (*rac*)-**16b**.

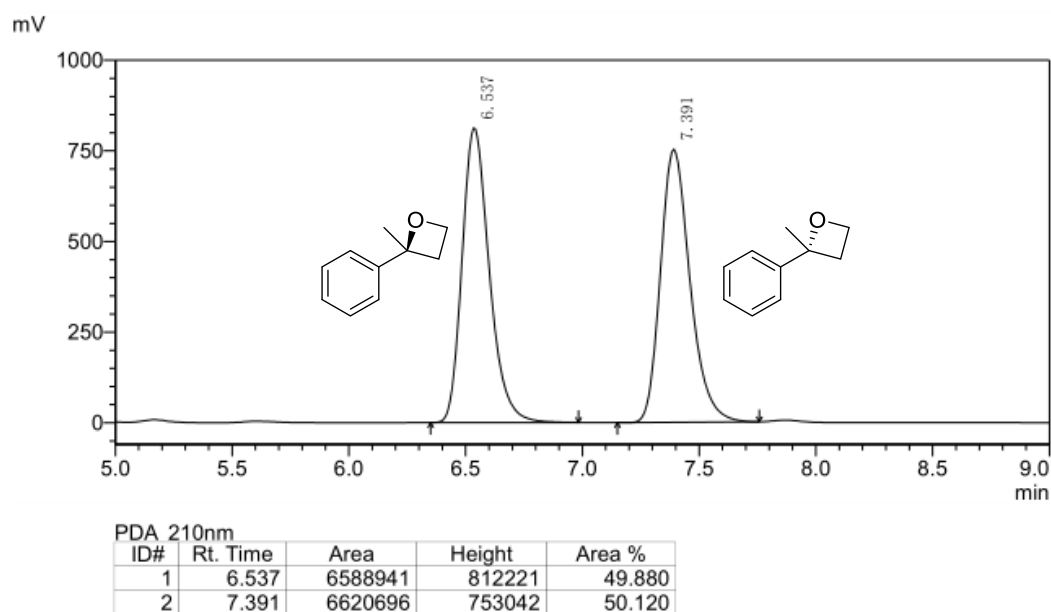


Supplementary Fig. 339 | HPLC trace for the enzymatic synthesized (*S*)-**16b**.

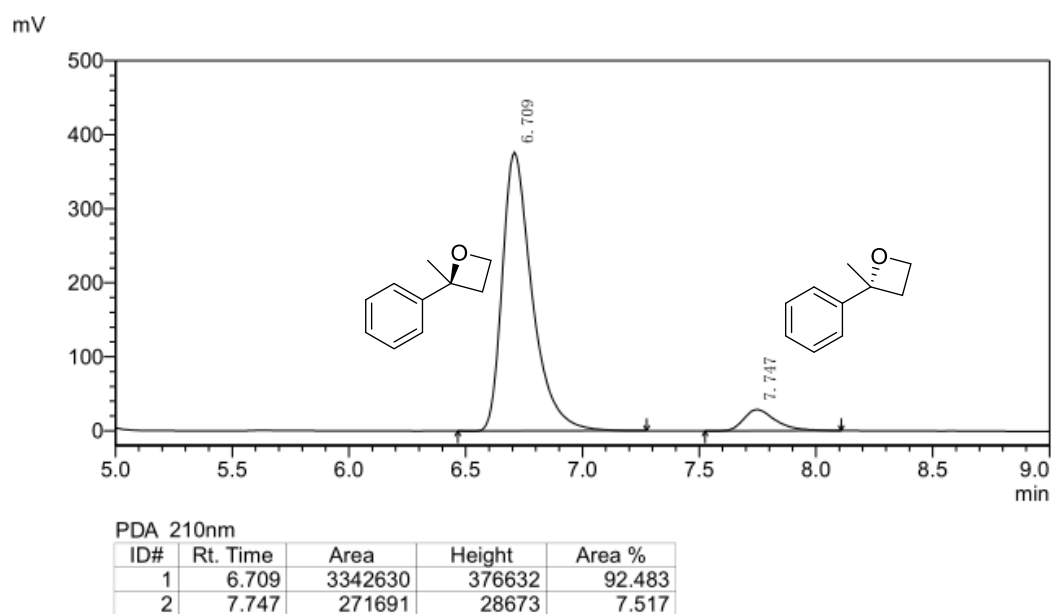


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 9.7min, $t_{(R)}$ = 10.5 min.

Supplementary Fig. 340 | HPLC trace for the chemical synthesized (*rac*)-**17b**.

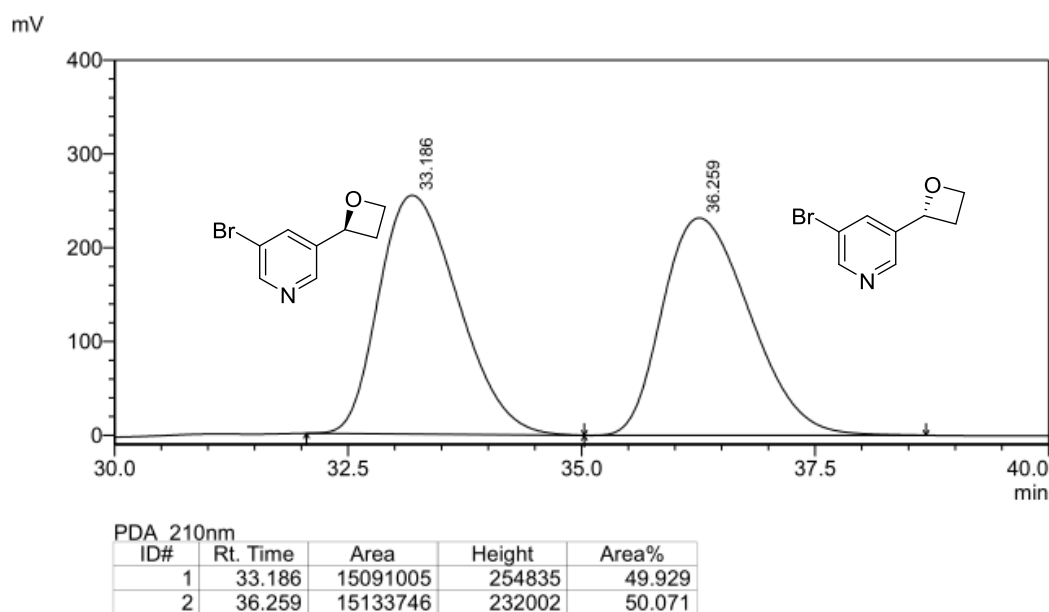


Supplementary Fig. 341 | HPLC trace for the enzymatic synthesized (*S*)-**17b**.

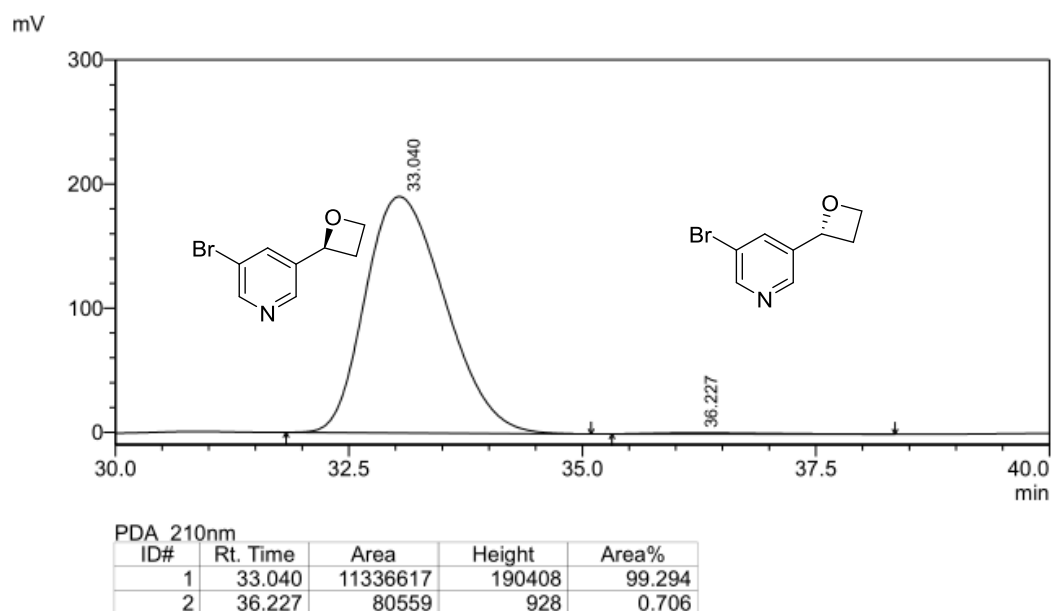


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 6.7min, $t_{(R)}$ = 7.7 min.

Supplementary Fig. 342 | HPLC trace for the chemical synthesized (*rac*)-**18b**.

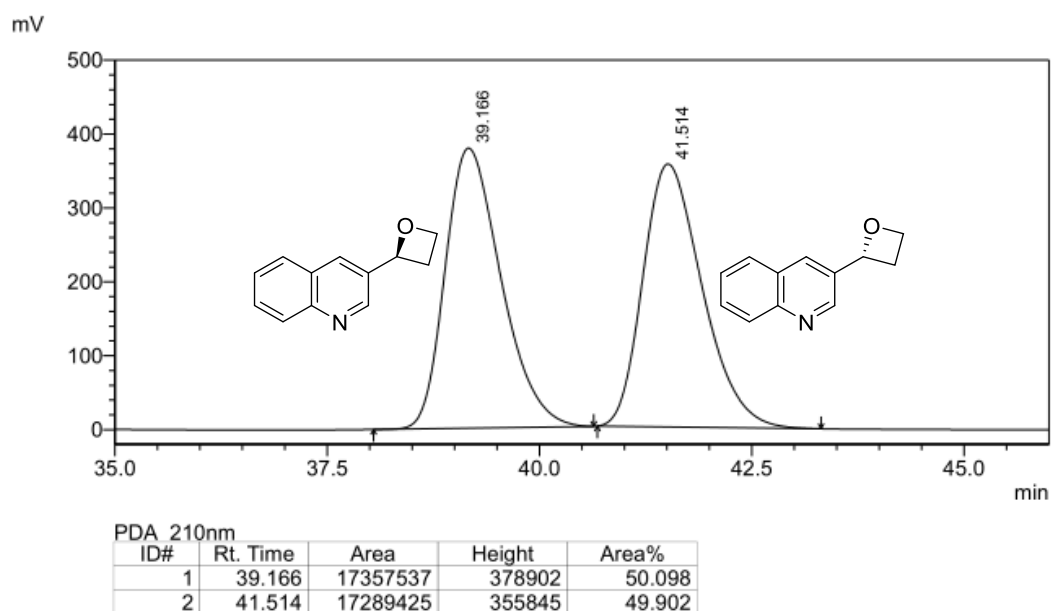


Supplementary Fig. 343 | HPLC trace for the enzymatic synthesized (*S*)-**18b**.

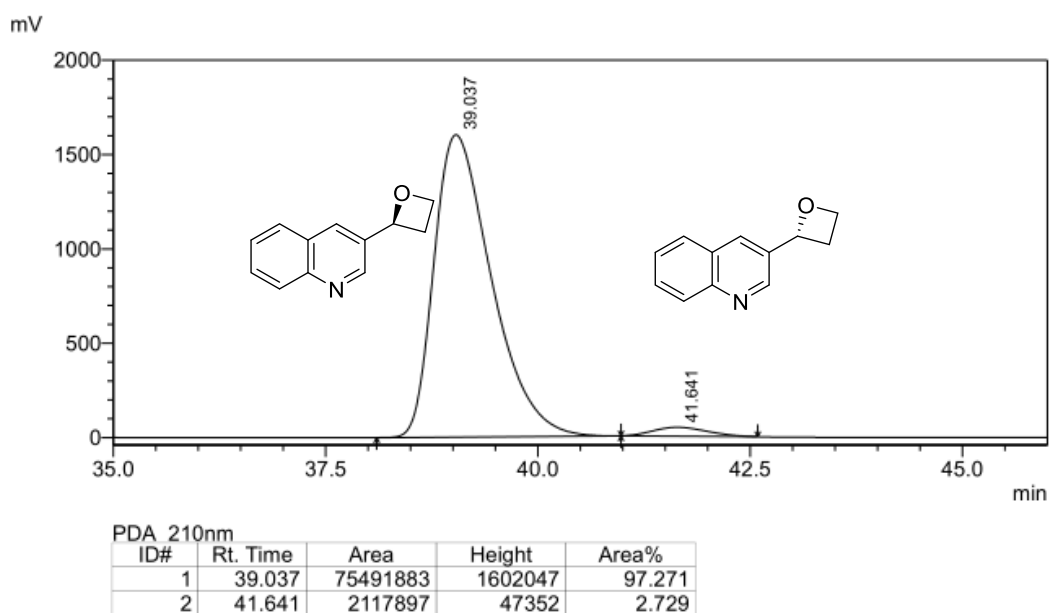


Chiral HPLC analysis: Diacel Chiralpak OB-H, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 33.0min, $t_{(R)}$ = 36.2 min.

Supplementary Fig. 344 | HPLC trace for the chemical synthesized (*rac*)-**19b**.

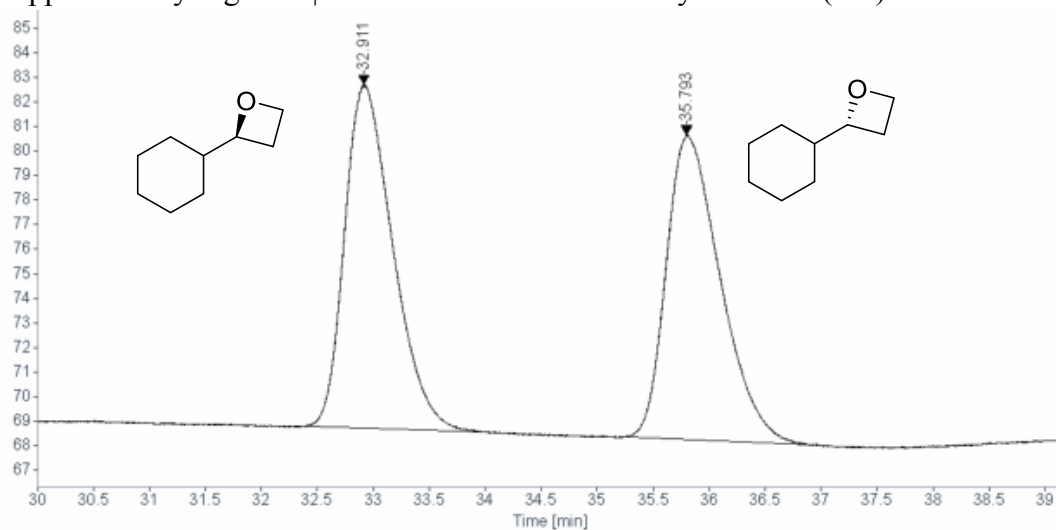


Supplementary Fig. 345 | HPLC trace for the enzymatic synthesized (*S*)-**19b**.



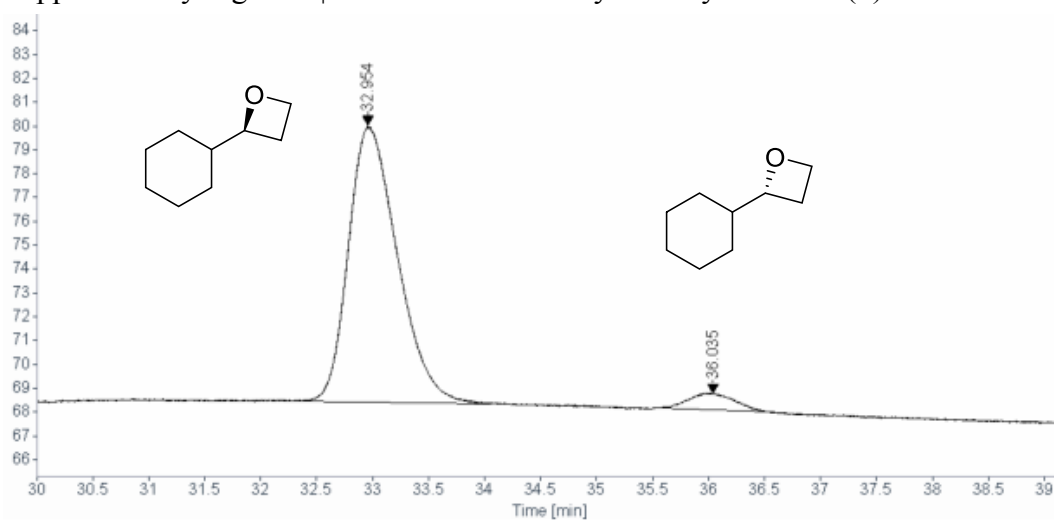
Chiral HPLC analysis: Diacel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 39.0 min, $t_{(R)}$ = 41.6 min.

Supplementary Fig. 346 | GC trace for the chemical synthesized (*rac*)-**21b**.



ID#	Ret. Time	Area	Height	Area%	Resolution
1	32.911	420.903	14.020	50.148	
1	35.793	418.413	12.422	49.852	3.468

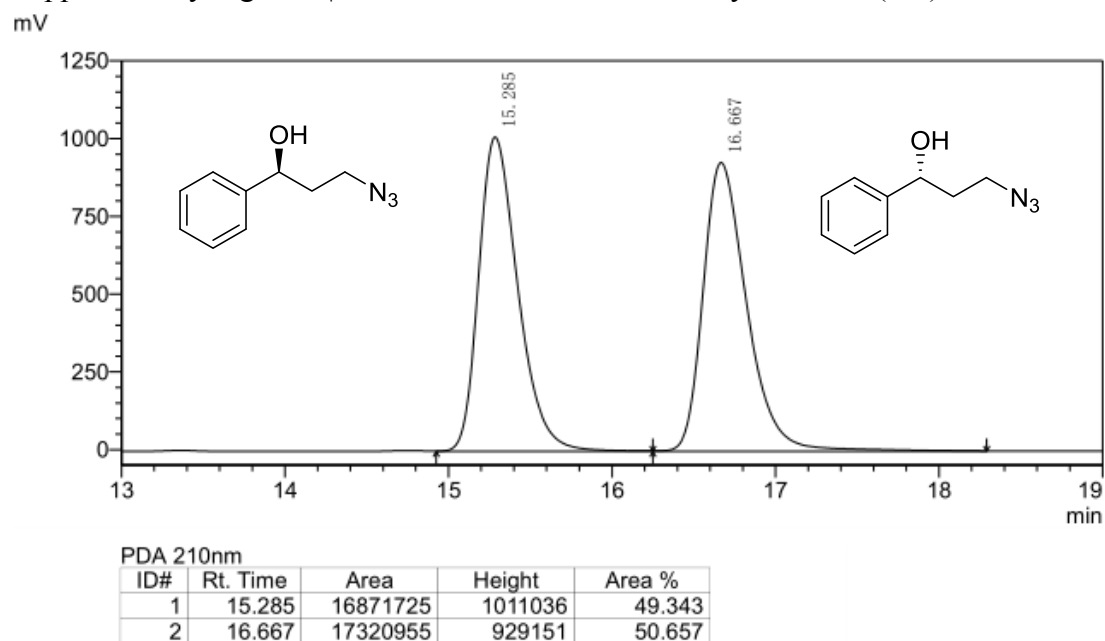
Supplementary Fig. 347 | GC trace for the enzymatic synthesized (*S*)-**21b**.



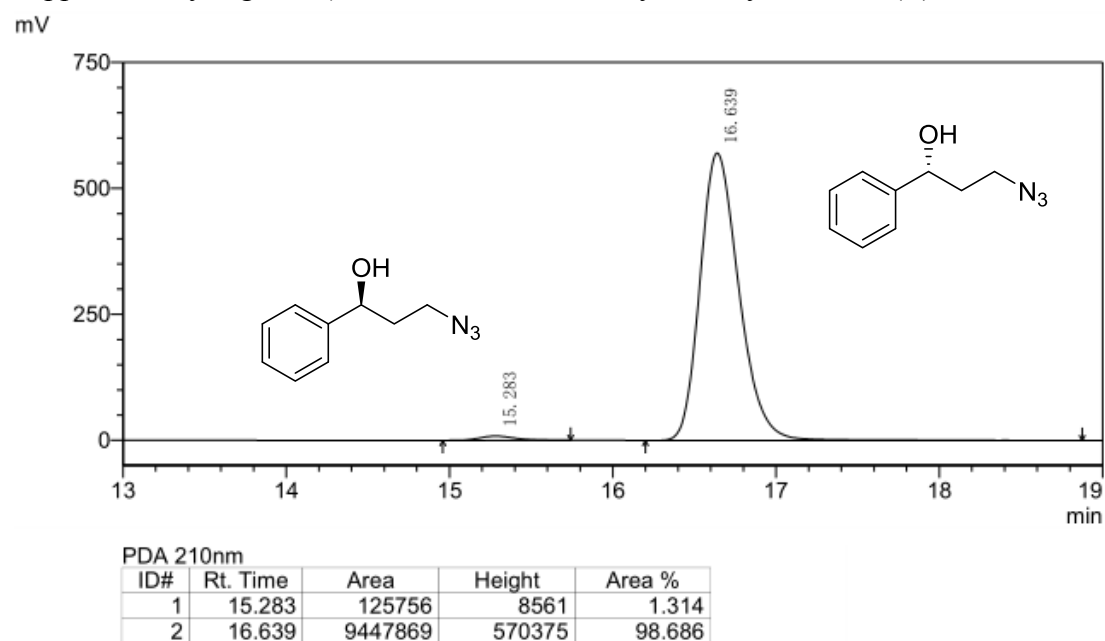
ID#	Ret. Time	Area	Height	Area%	Resolution
1	32.954	353.312	11.617	94.490	
1	36.035	20.602	0.709	5.510	3.879

Chiral GC analysis: Rt-bDEXcst (RESTEK), 80 °C for 45 min, $t_{(S)} = 33.0$ min, $t_{(R)} = 36.0$ min.

Supplementary Fig. 348 | HPLC trace for the chemical synthesized (*rac*)-**1c**.

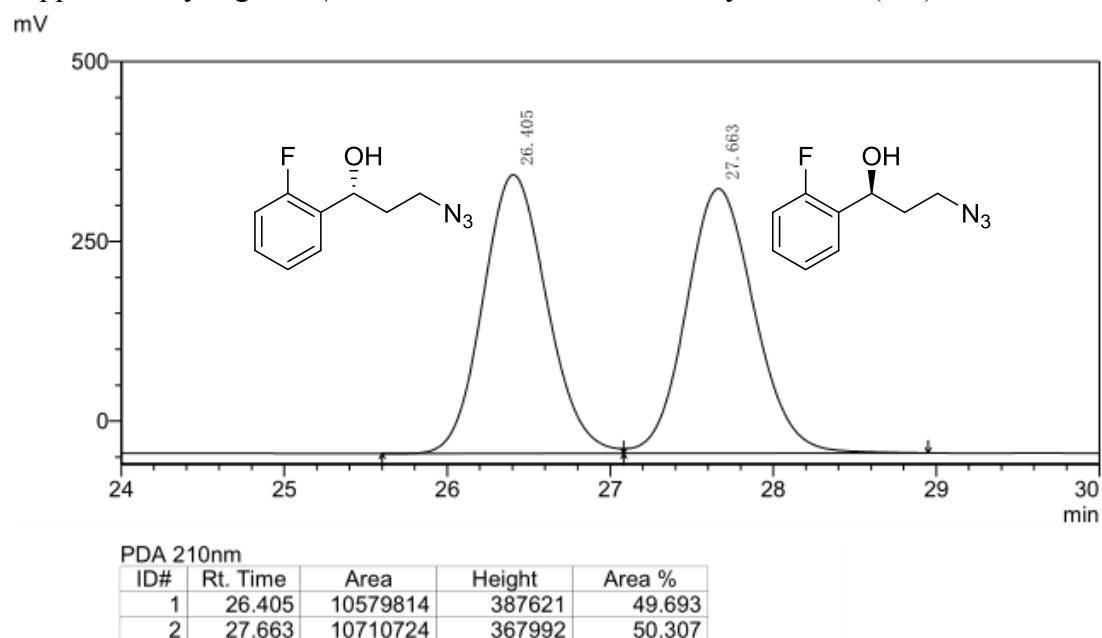


Supplementary Fig. 349 | HPLC trace for the enzymatic synthesized (*R*)-**1c**.

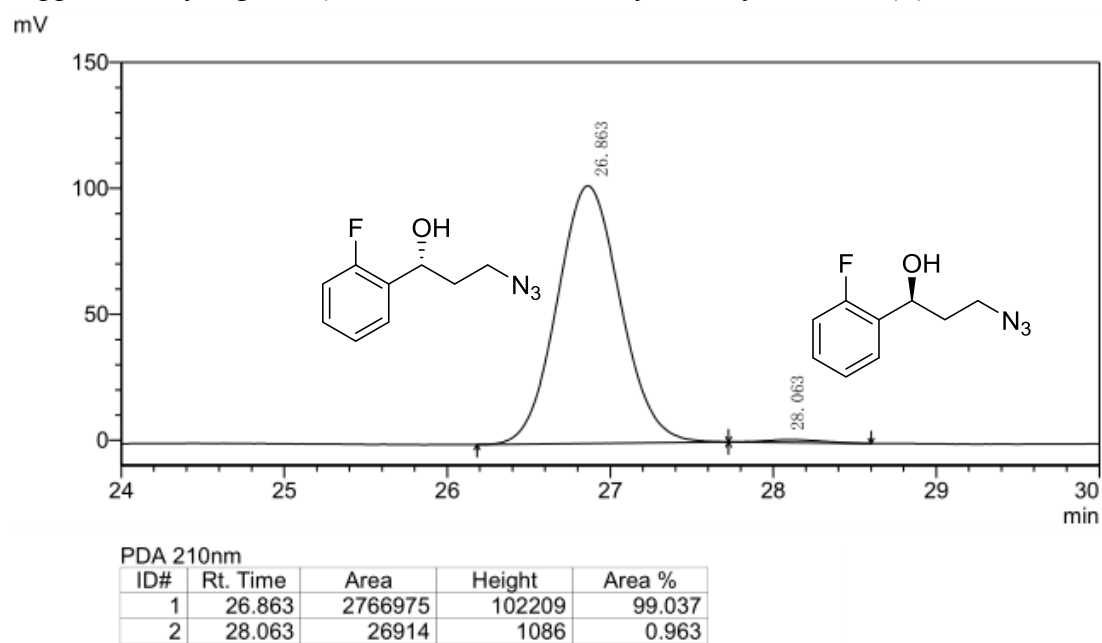


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 15.3 min, $t_{(R)}$ = 16.6 min.

Supplementary Fig. 350 | HPLC trace for the chemical synthesized (*rac*)-**2c**.

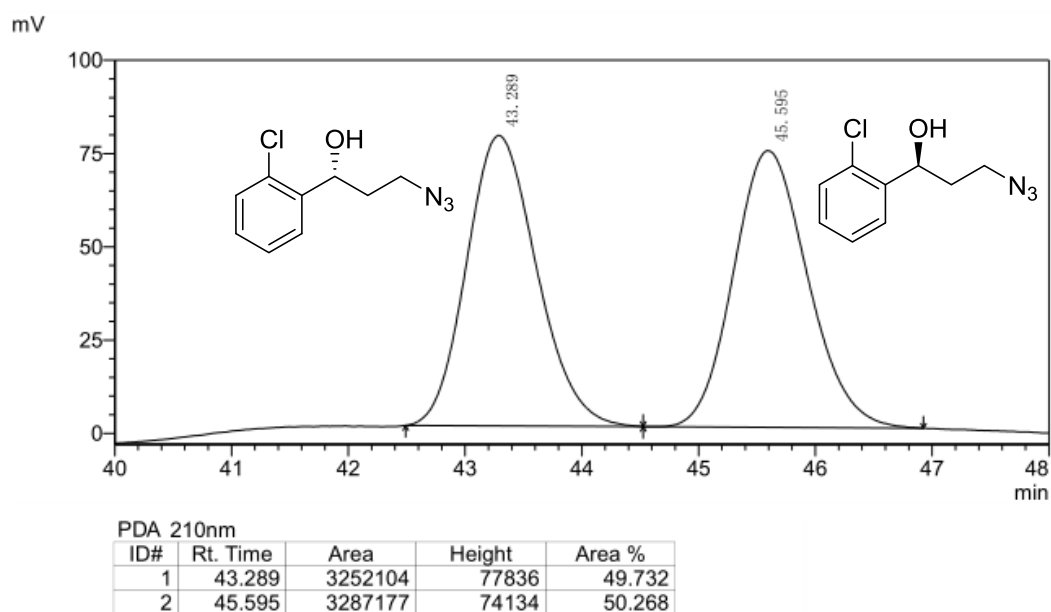


Supplementary Fig. 351 | HPLC trace for the enzymatic synthesized (*R*)-**2c**.

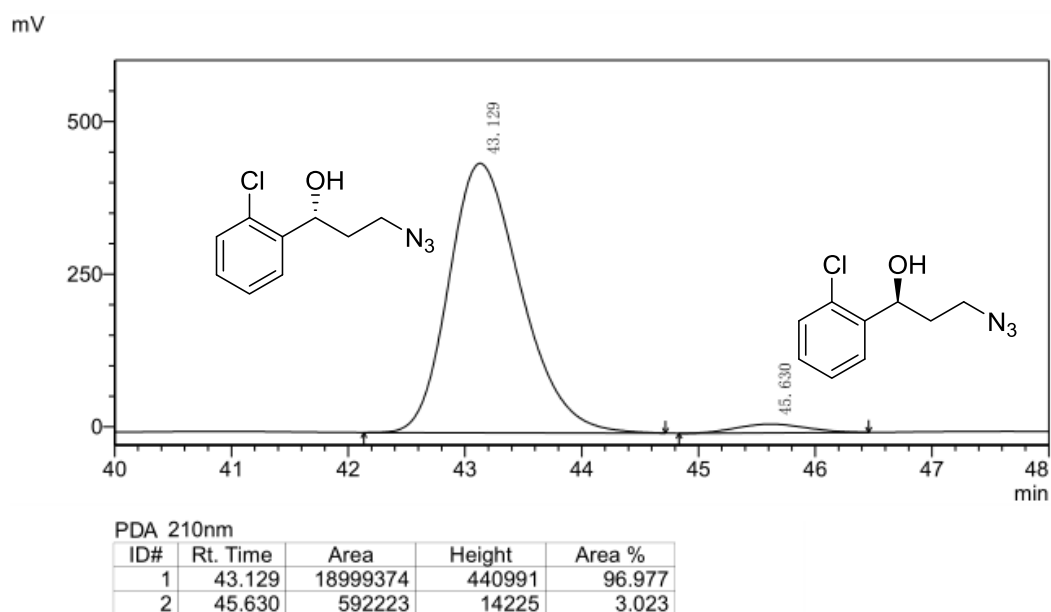


Chiral HPLC analysis: Diacel Chiralpak IH, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.5 mL/min, λ = 210 nm, $t_{(R)}$ = 26.9 min, $t_{(S)}$ = 28.1 min.

Supplementary Fig. 352 | HPLC trace for the chemical synthesized (*rac*)-**3c**.

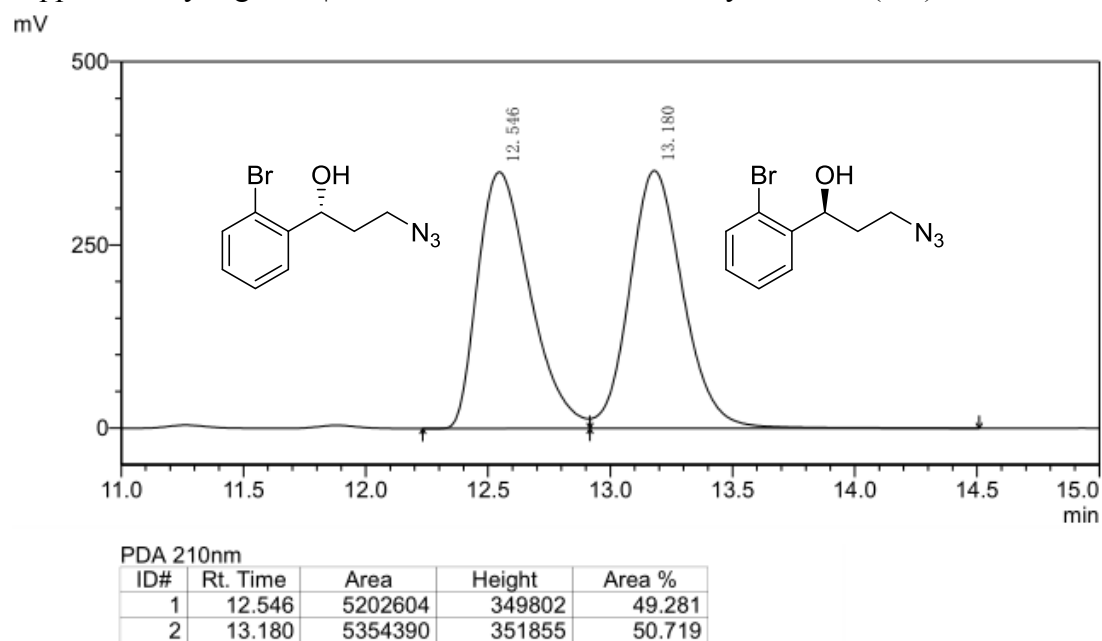


Supplementary Fig. 353 | HPLC trace for the enzymatic synthesized (*R*)-**3c**.

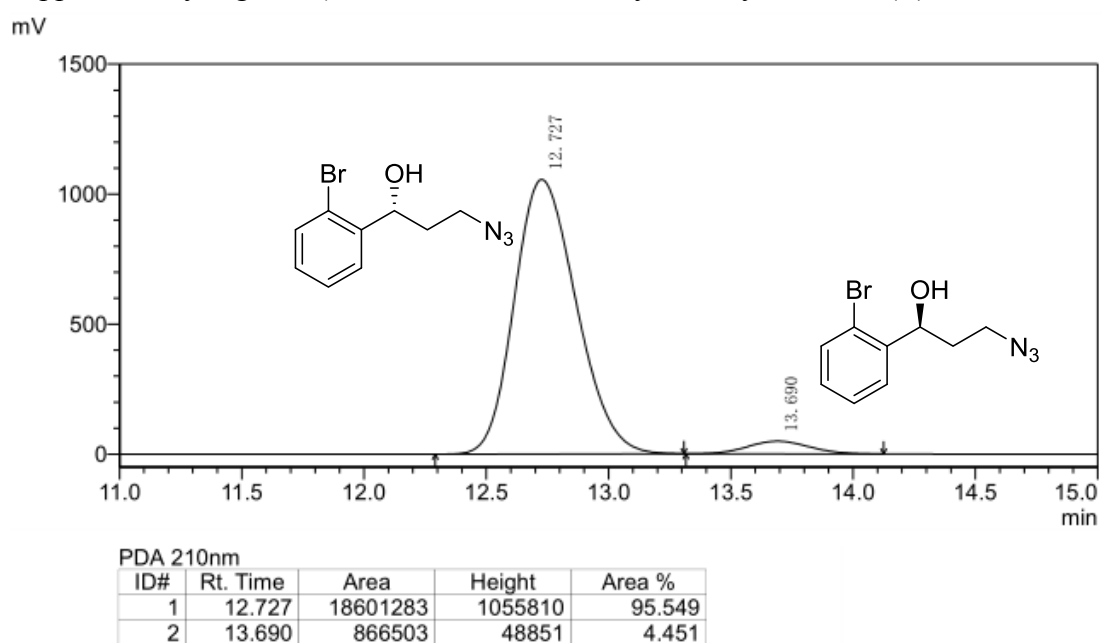


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(R)}$ = 43.1 min, $t_{(S)}$ = 45.6 min.

Supplementary Fig. 354 | HPLC trace for the chemical synthesized (*rac*)-**4c**.

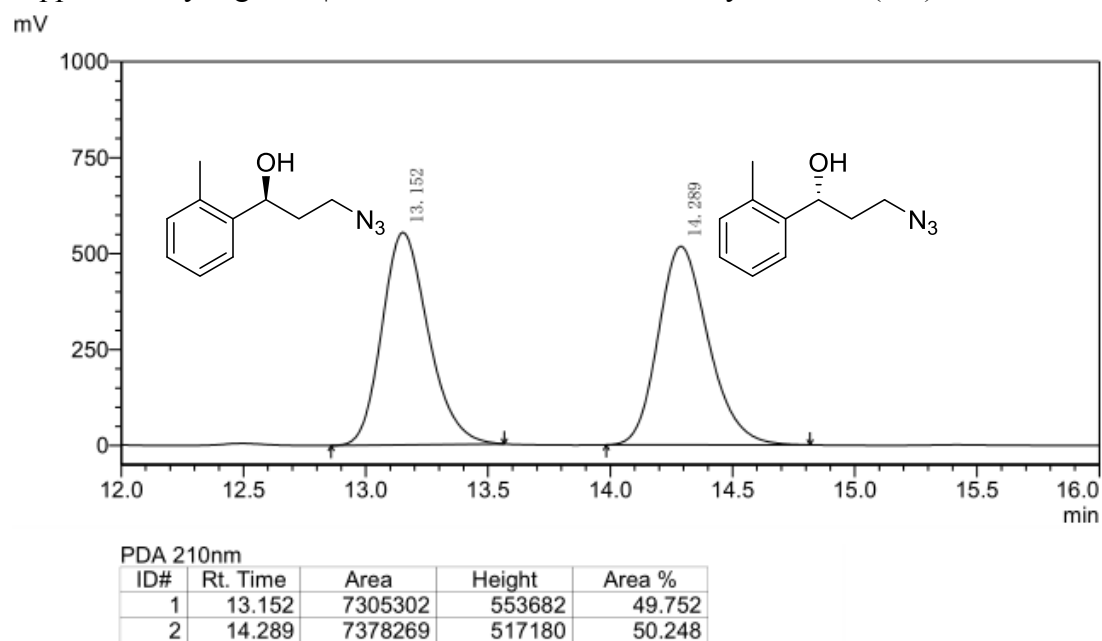


Supplementary Fig. 355 | HPLC trace for the enzymatic synthesized (*R*)-**4c**.

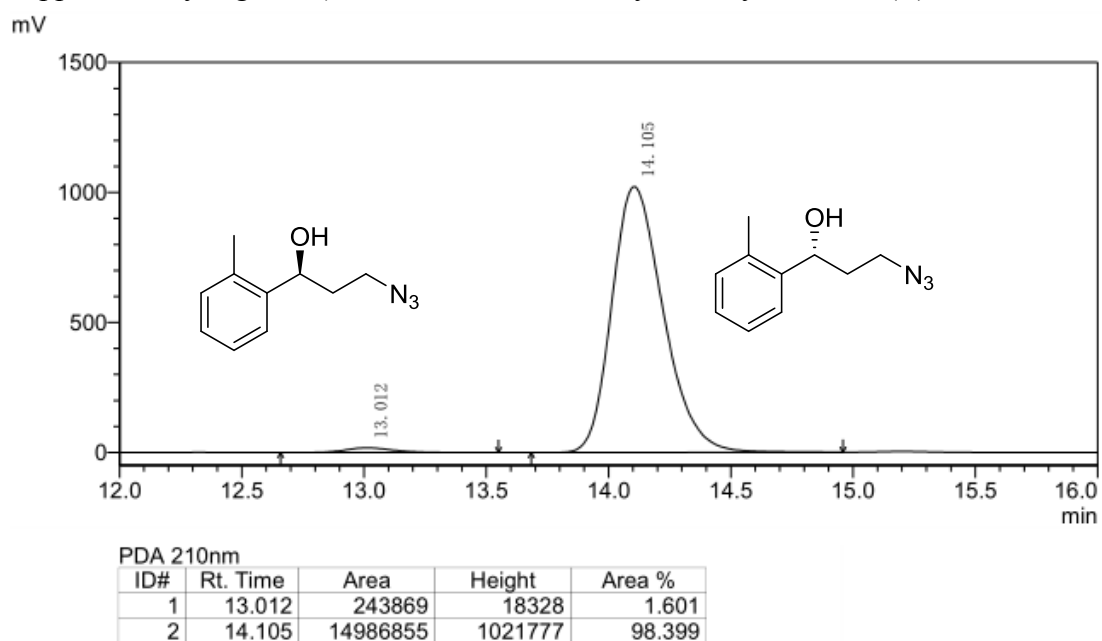


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(R)}$ = 12.7 min, $t_{(S)}$ = 13.7 min.

Supplementary Fig. 356 | HPLC trace for the chemical synthesized (*rac*)-**5c**.

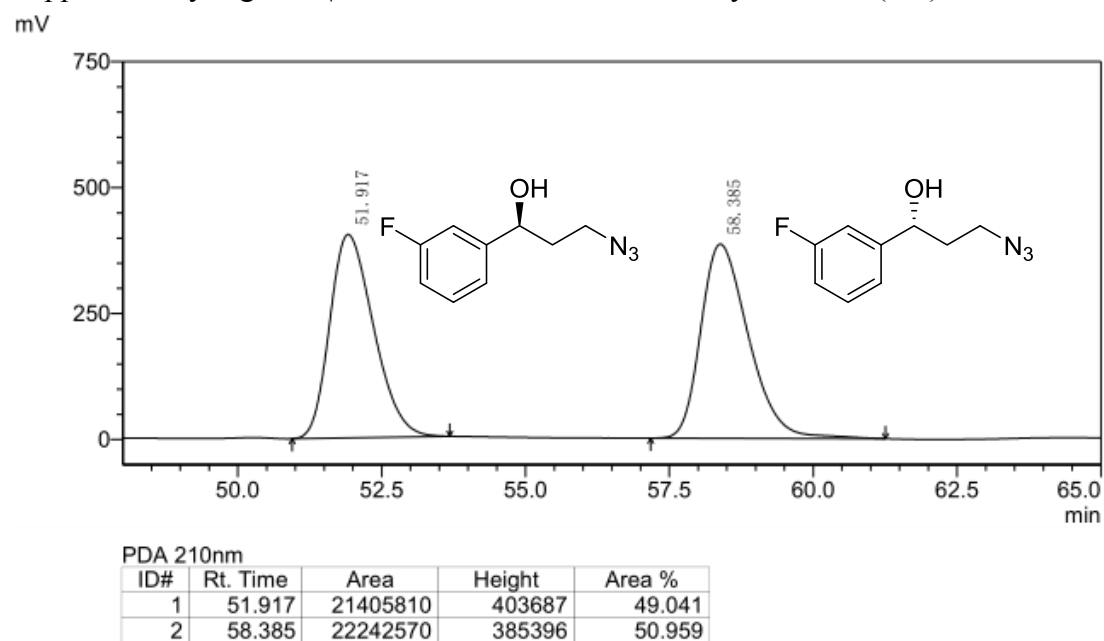


Supplementary Fig. 357 | HPLC trace for the enzymatic synthesized (*R*)-**5c**.

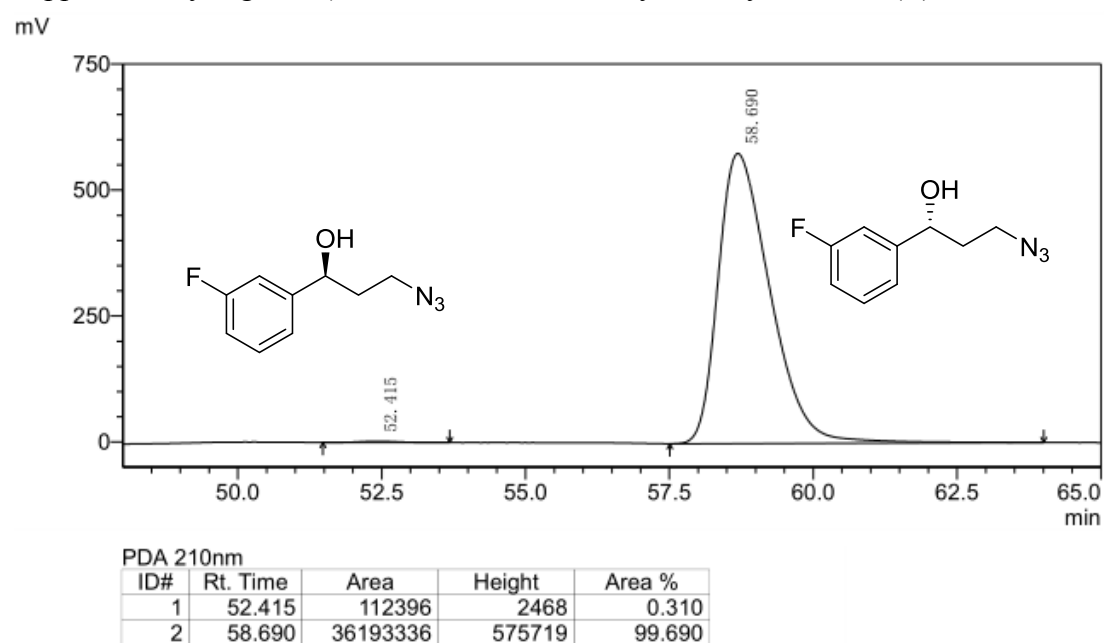


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 13.0 min, $t_{(R)}$ = 14.1 min.

Supplementary Fig. 358 | HPLC trace for the chemical synthesized (*rac*)-**6c**.

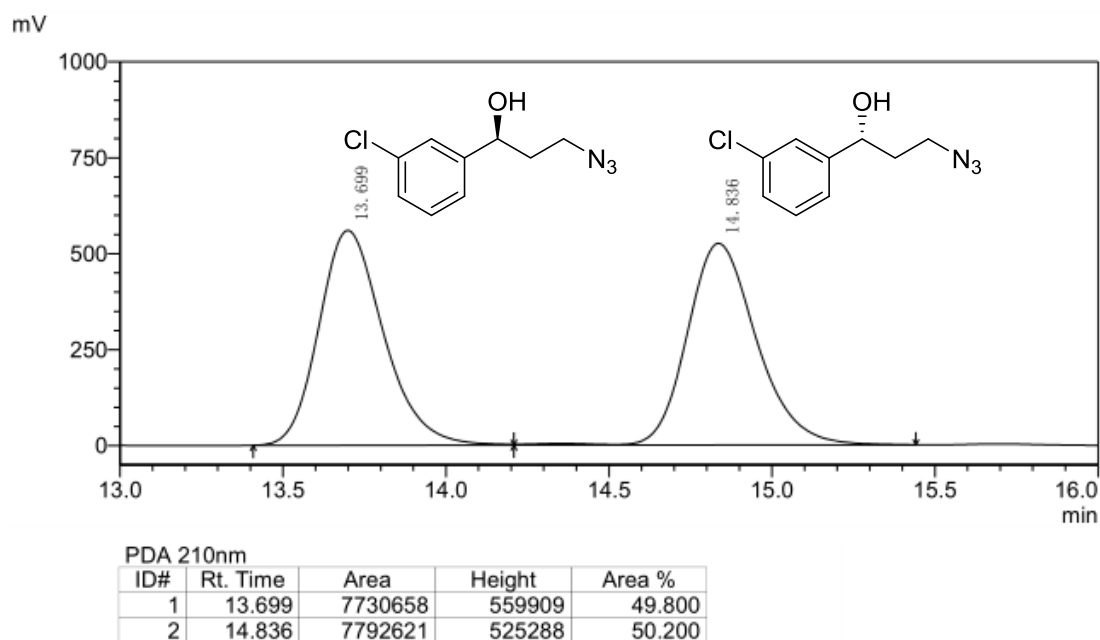


Supplementary Fig. 359 | HPLC trace for the enzymatic synthesized (*R*)-**6c**.

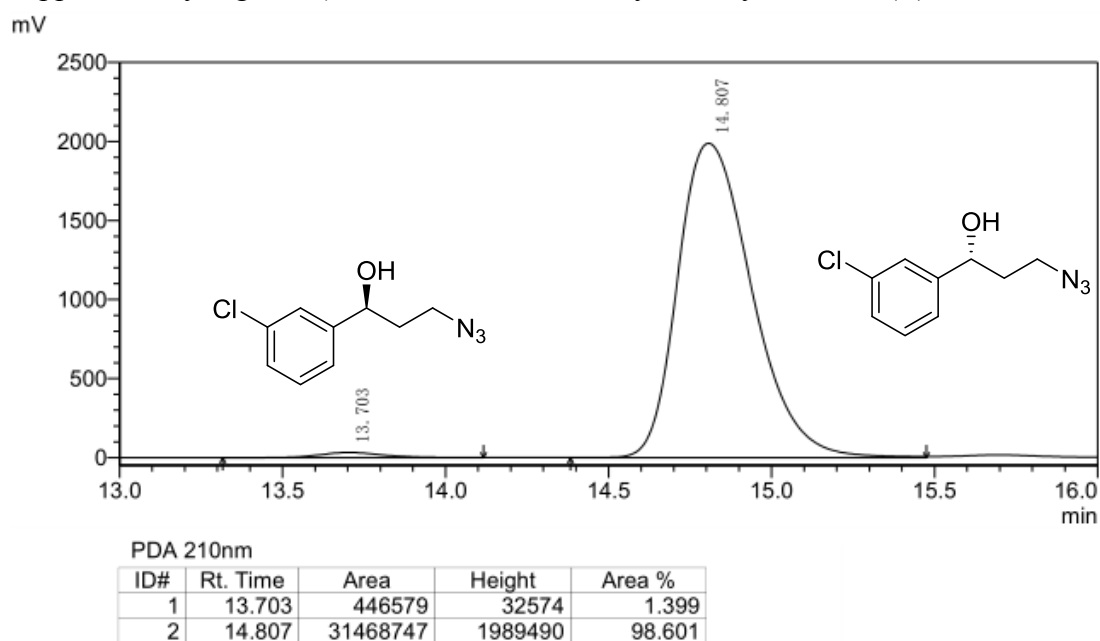


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 52.4 min, $t_{(R)}$ = 58.7 min.

Supplementary Fig. 360 | HPLC trace for the chemical synthesized (*rac*)-**7c**.

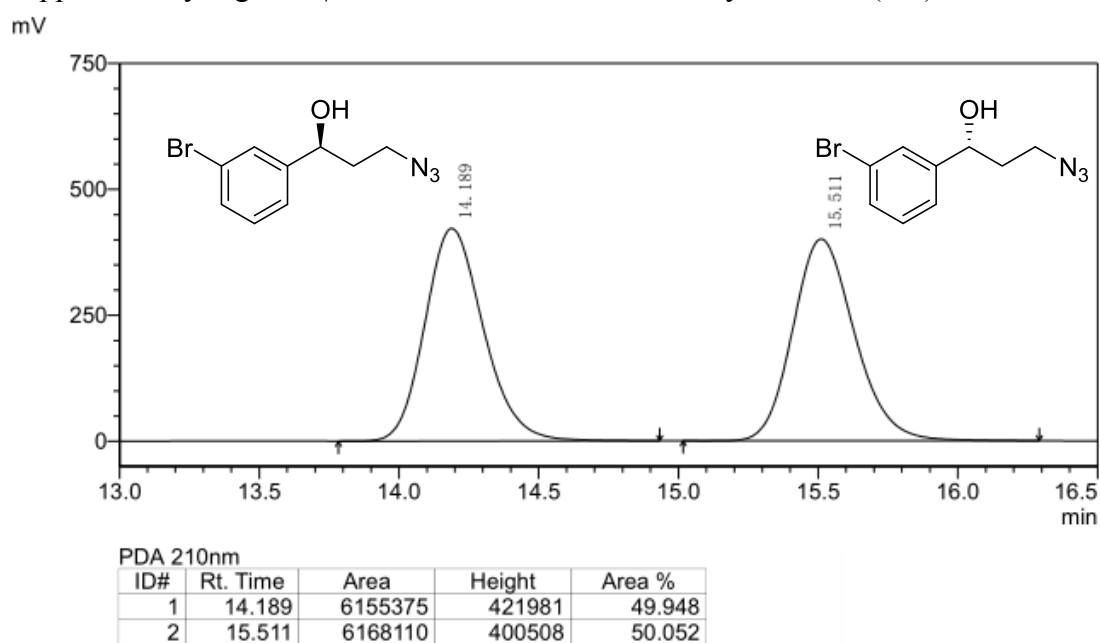


Supplementary Fig. 361 | HPLC trace for the enzymatic synthesized (*R*)-**7c**.

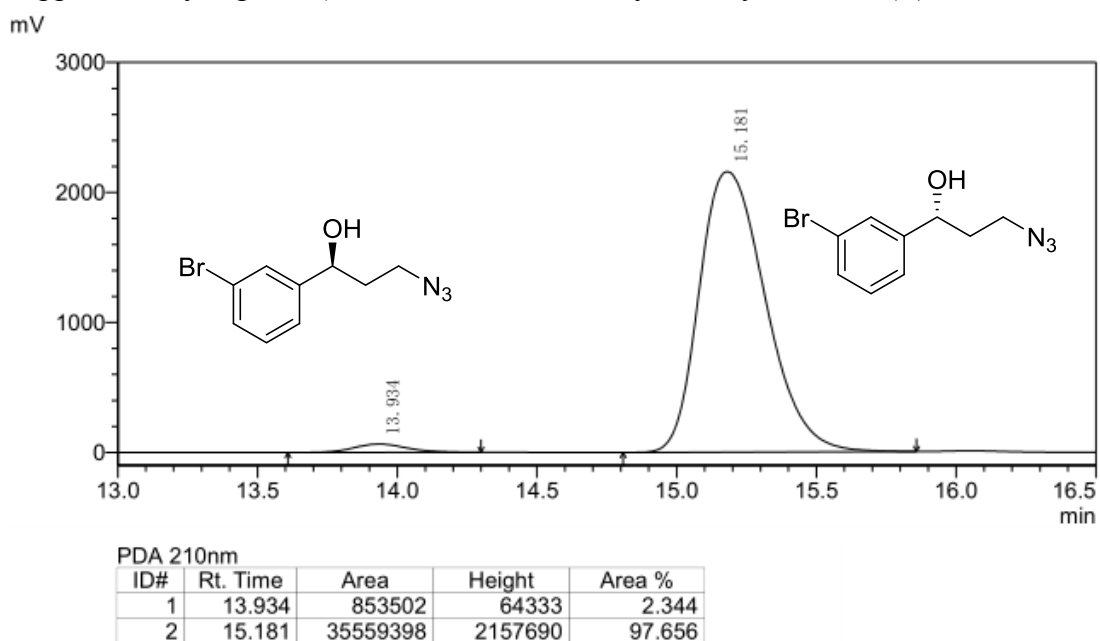


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 13.7 min, $t_{(R)}$ = 14.8 min.

Supplementary Fig. 362 | HPLC trace for the chemical synthesized (*rac*)-**8c**.

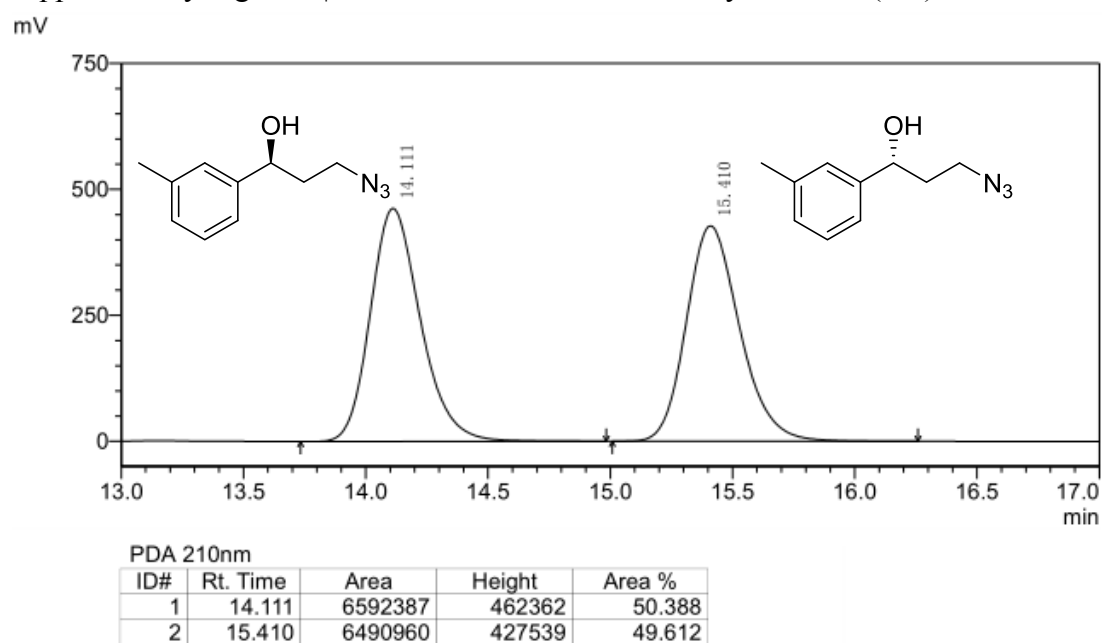


Supplementary Fig. 363 | HPLC trace for the enzymatic synthesized (*R*)-**8c**.

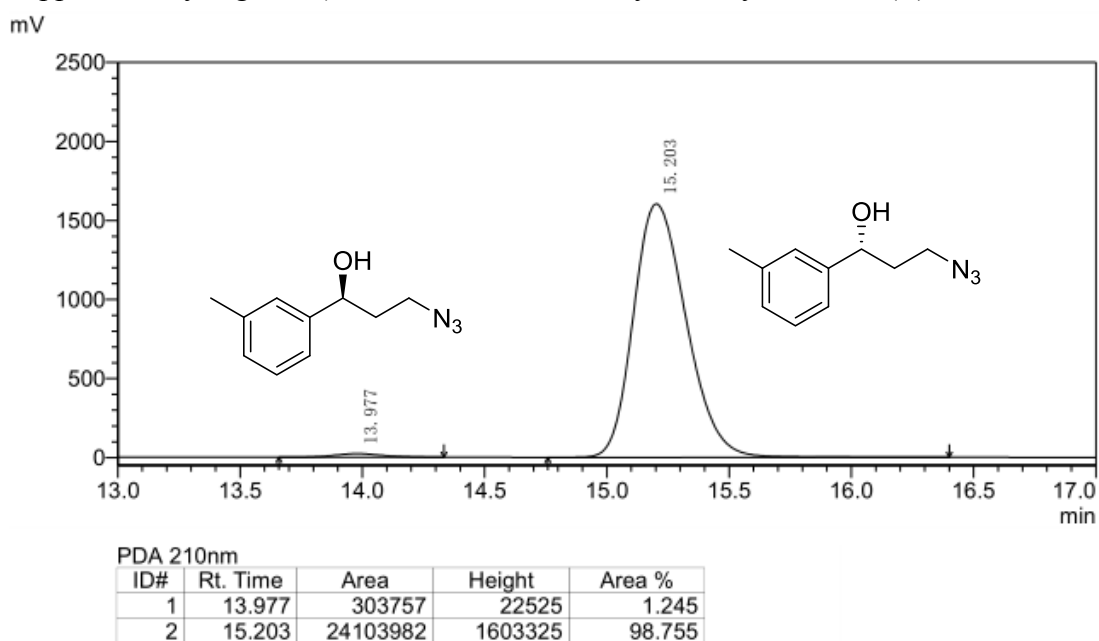


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 13.9 min, $t_{(R)}$ = 15.2 min.

Supplementary Fig. 364 | HPLC trace for the chemical synthesized (*rac*)-**9c**.

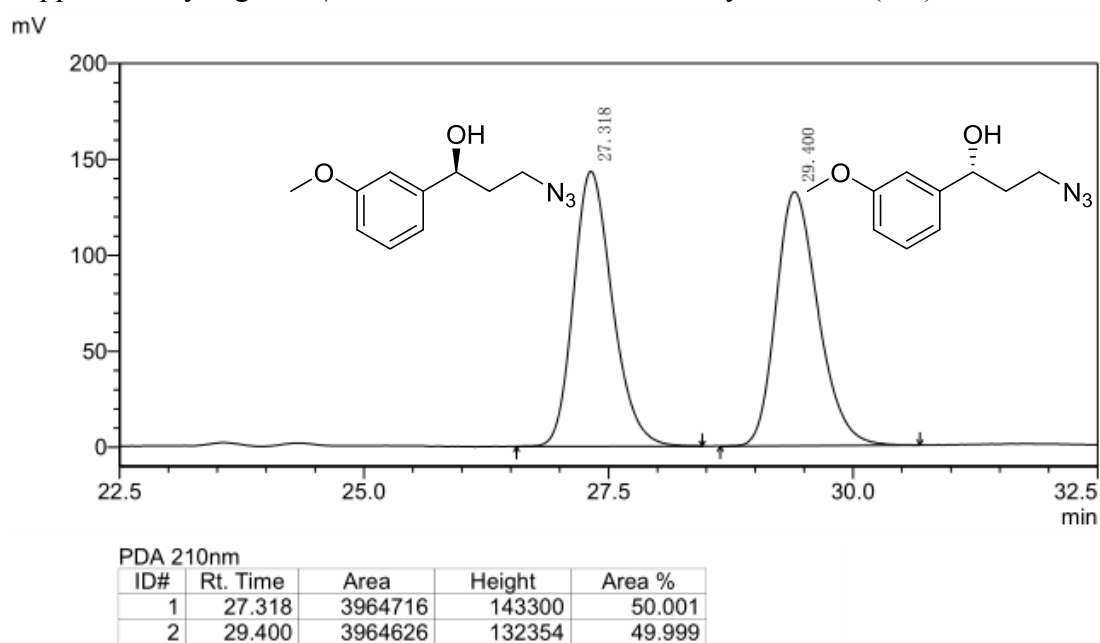


Supplementary Fig. 365 | HPLC trace for the enzymatic synthesized (*R*)-**9c**.

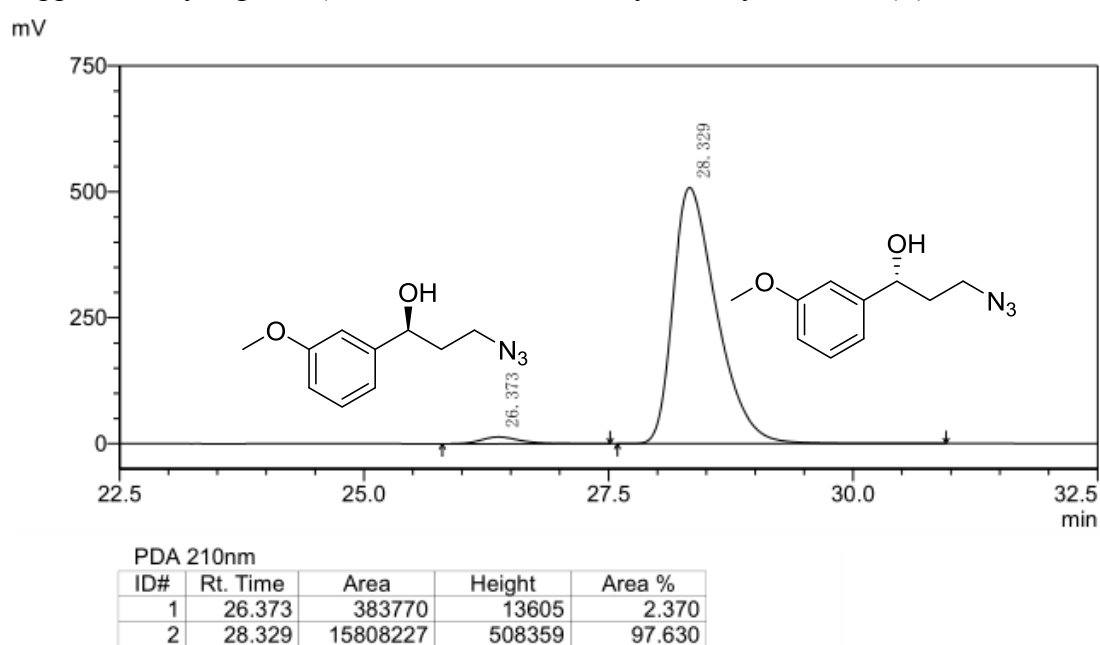


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 14.0 min, $t_{(R)}$ = 15.2 min.

Supplementary Fig. 366 | HPLC trace for the chemical synthesized (*rac*)-**10c**.

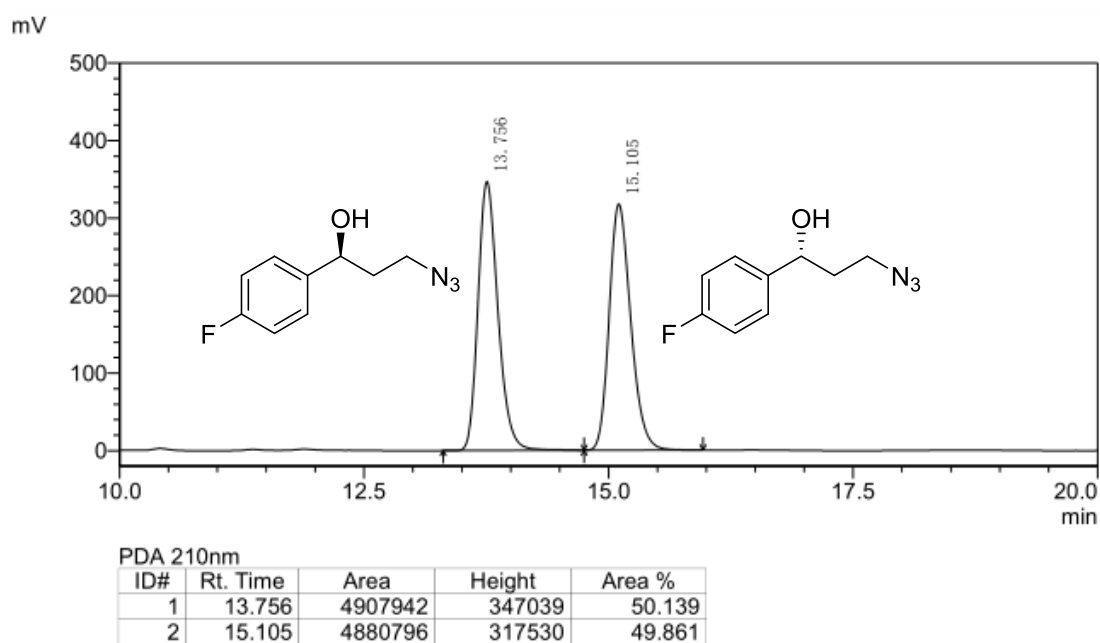


Supplementary Fig. 367 | HPLC trace for the enzymatic synthesized (*R*)-**10c**.

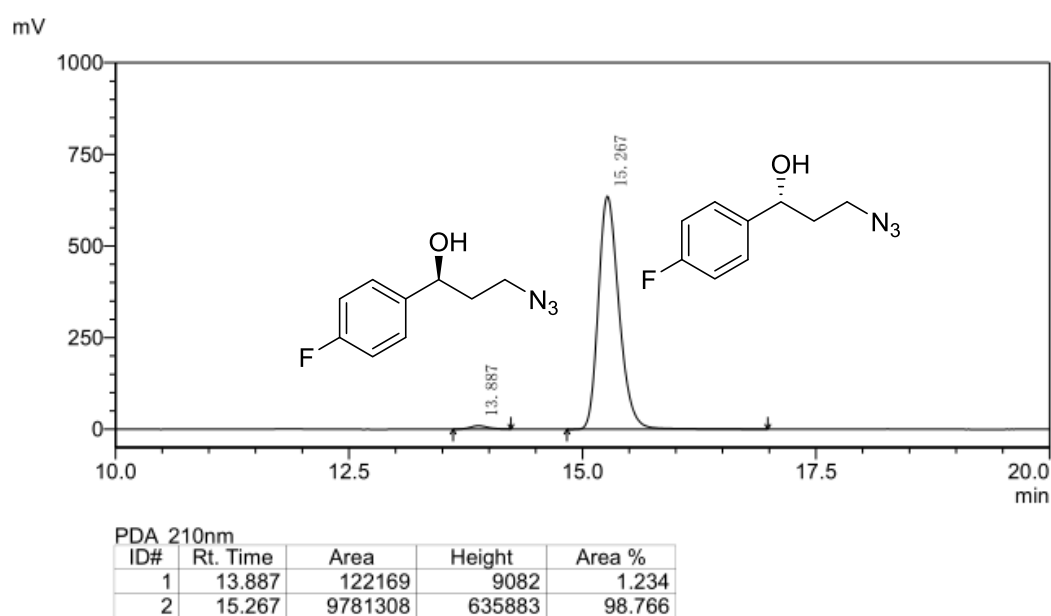


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 26.4 min, $t_{(R)}$ = 28.3 min.

Supplementary Fig. 368 | HPLC trace for the chemical synthesized (*rac*)-**11c**.

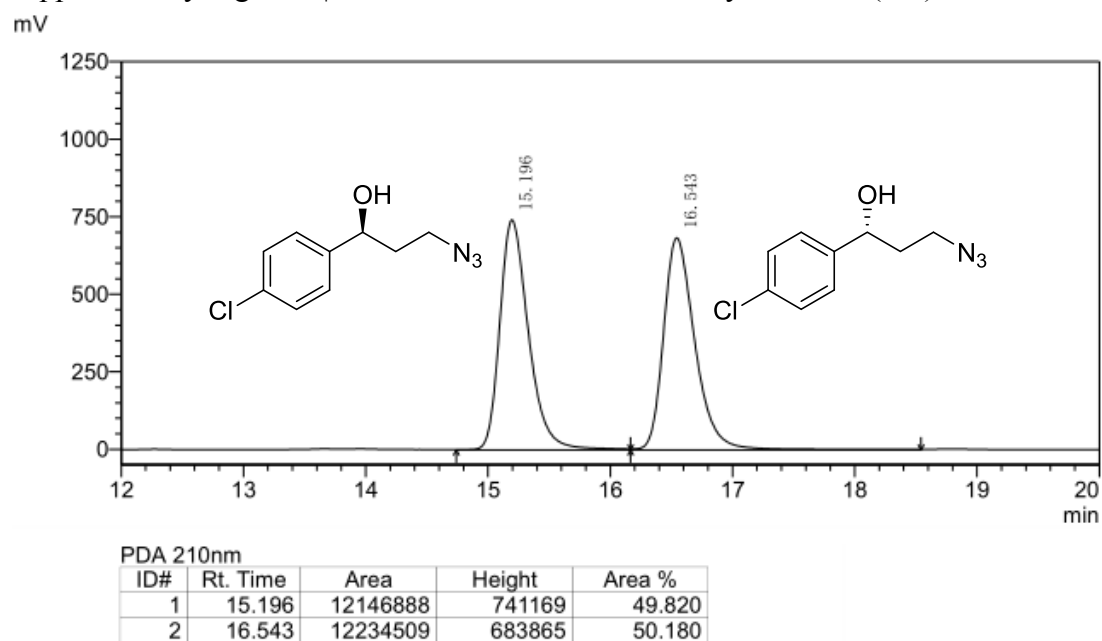


Supplementary Fig. 369 | HPLC trace for the enzymatic synthesized (*R*)-**11c**.

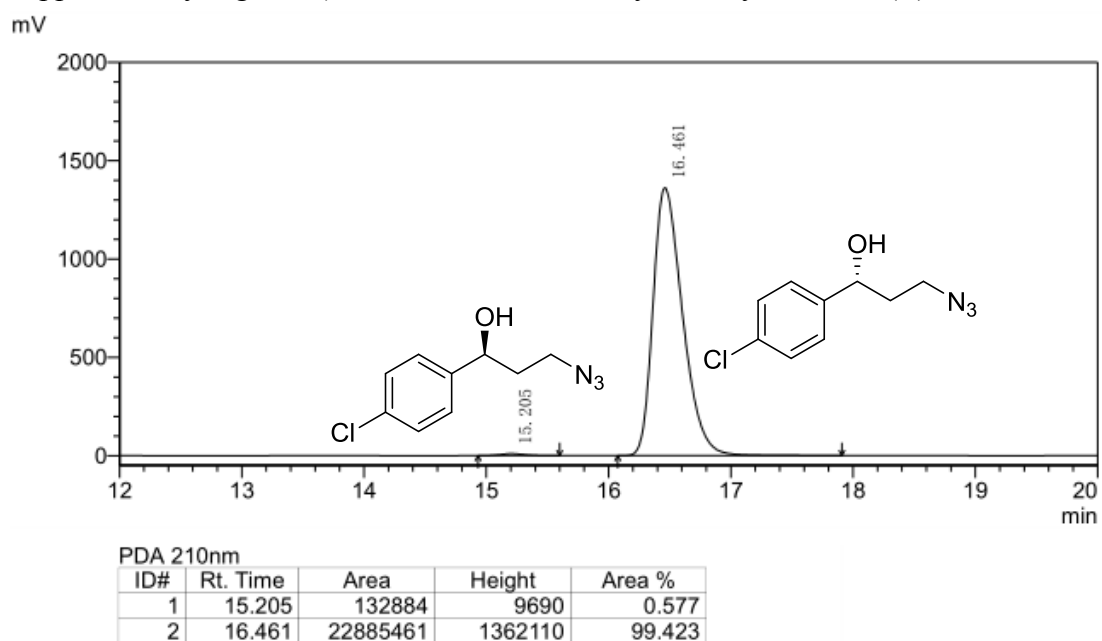


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 13.9 min, $t_{(R)}$ = 15.3 min.

Supplementary Fig. 370 | HPLC trace for the chemical synthesized (*rac*)-**12c**.

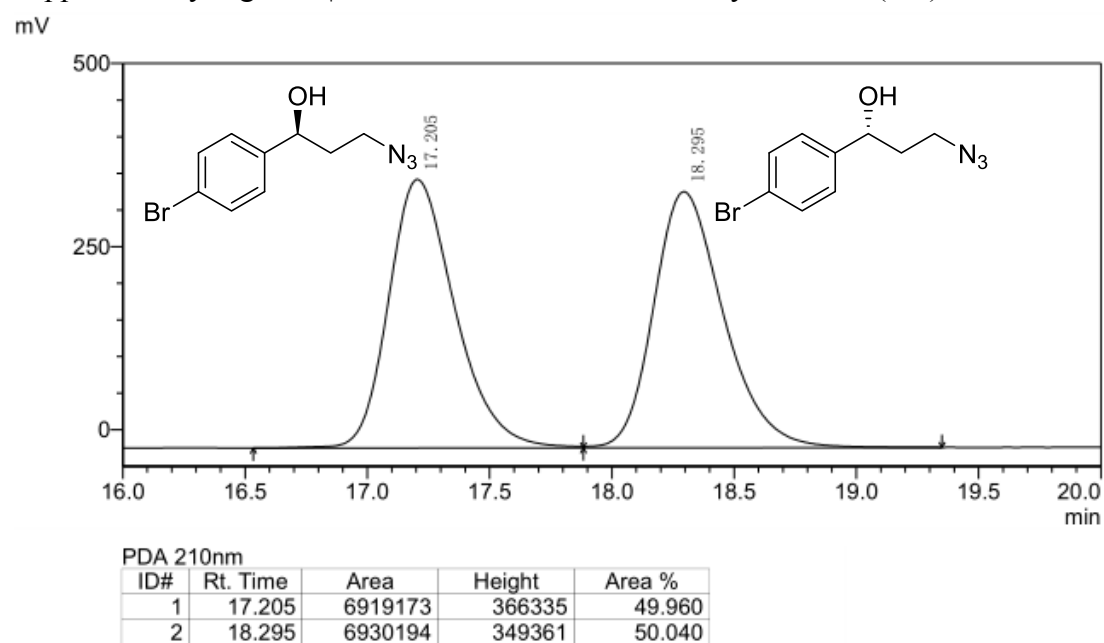


Supplementary Fig. 371 | HPLC trace for the enzymatic synthesized (*R*)-**12c**.

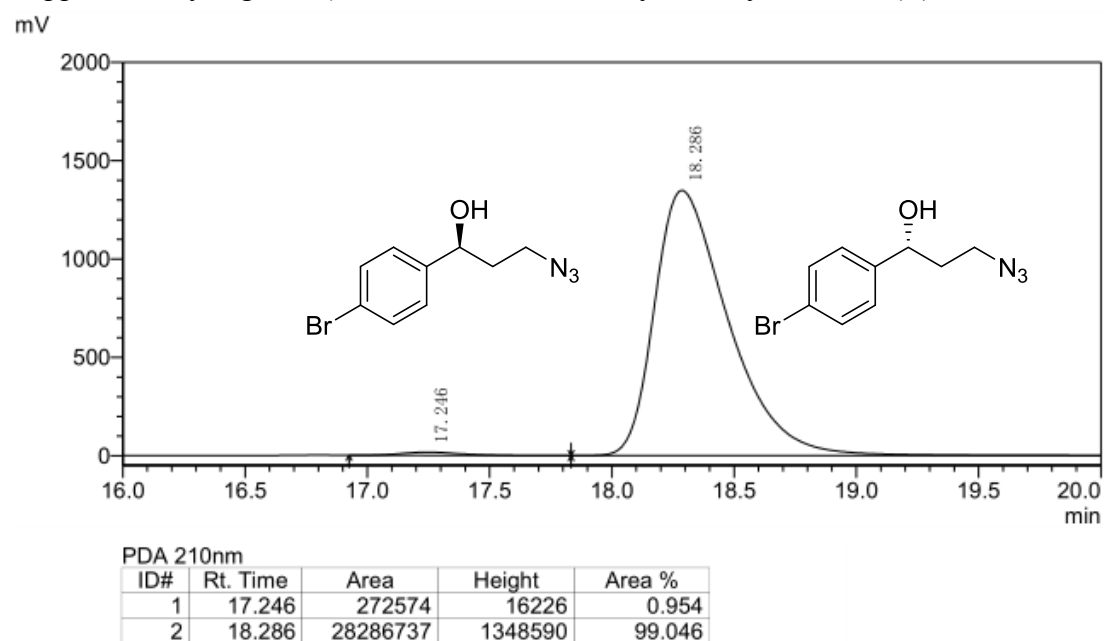


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 15.2 min, $t_{(R)}$ = 16.5 min

Supplementary Fig. 372 | HPLC trace for the chemical synthesized (*rac*)-**13c**.

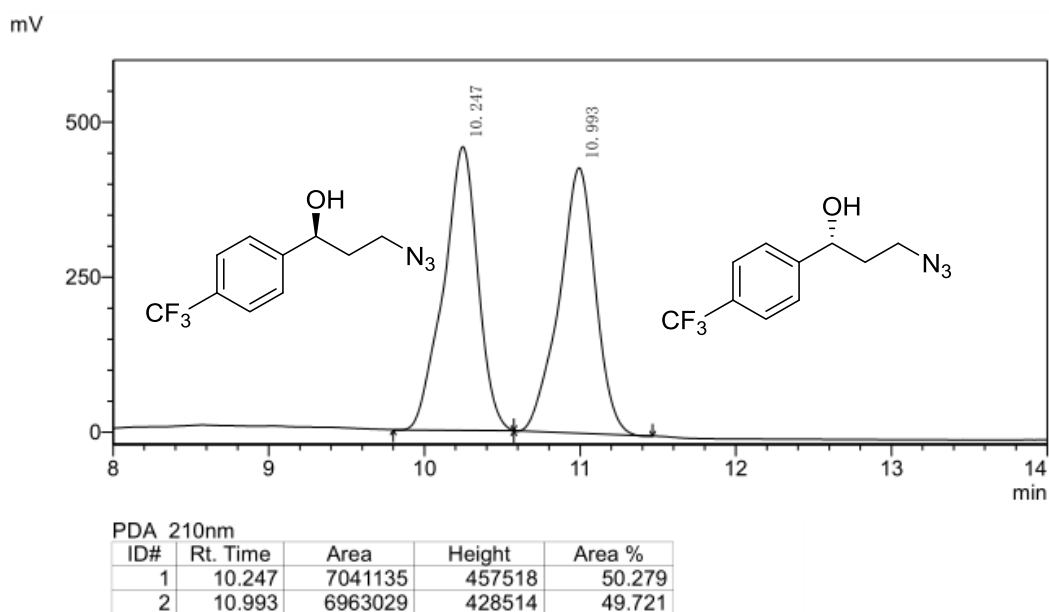


Supplementary Fig. 373 | HPLC trace for the enzymatic synthesized (*R*)-**13c**.

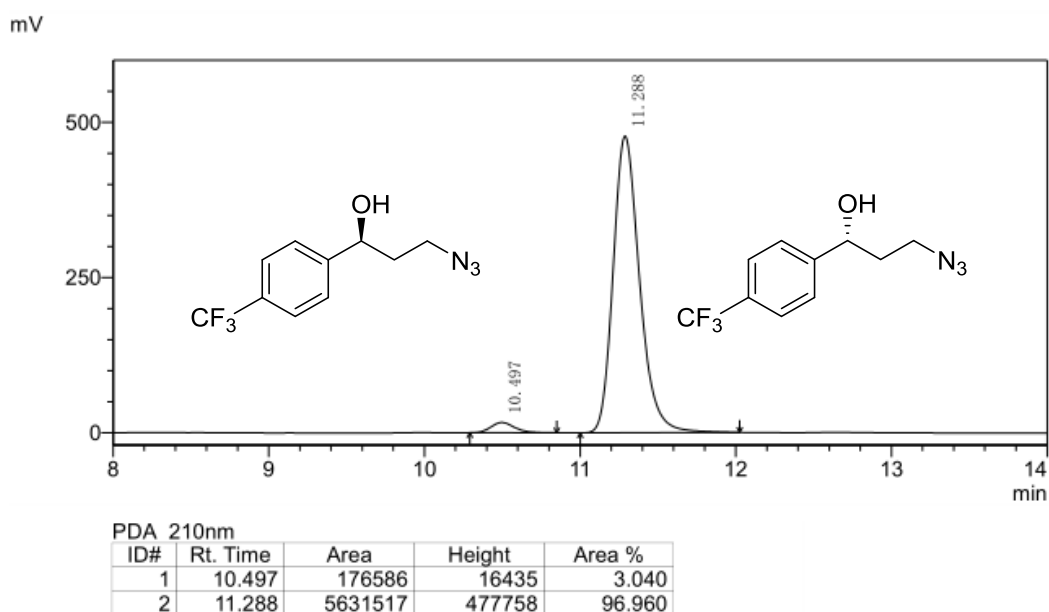


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 17.2 min, $t_{(R)}$ = 18.3 min.

Supplementary Fig. 374 | HPLC trace for the chemical synthesized (*rac*)-**14c**.

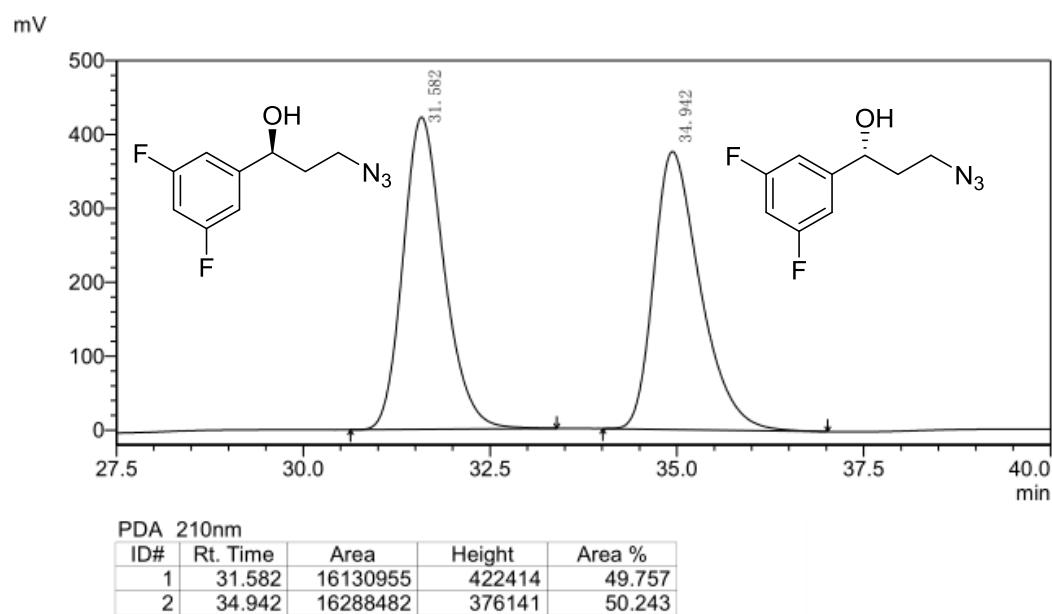


Supplementary Fig. 375 | HPLC trace for the enzymatic synthesized (*R*)-**14c**.

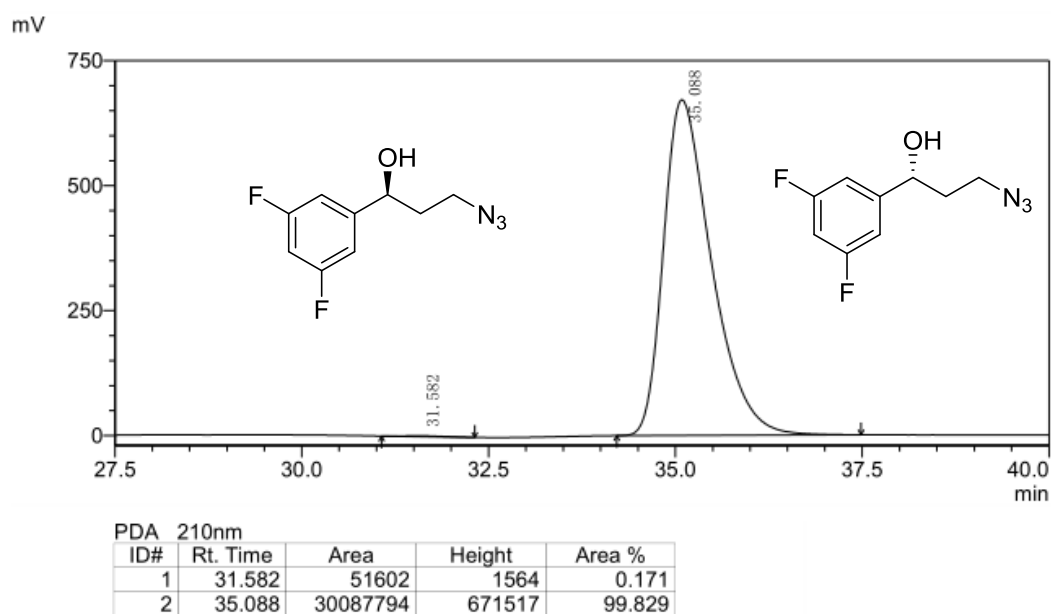


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 10.5 min, $t_{(R)}$ = 11.3 min.

Supplementary Fig. 376 | HPLC trace for the chemical synthesized (*rac*)-**15c**.

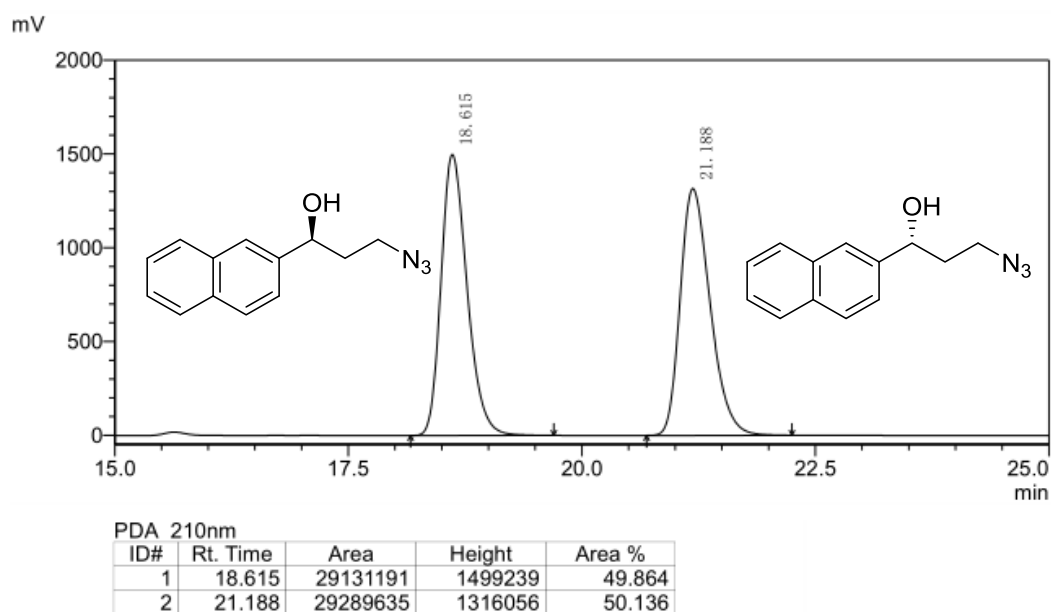


Supplementary Fig. 377 | HPLC trace for the enzymatic synthesized (*R*)-**15c**.

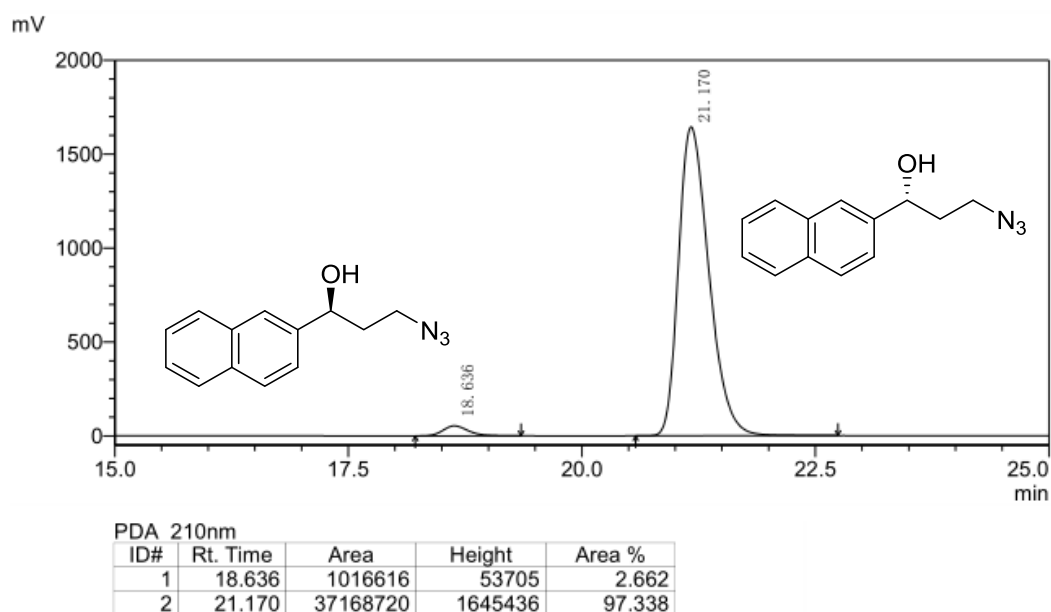


Chiral HPLC analysis: Diacel Chiralpak IC-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 31.6 min, $t_{(R)}$ = 35.1 min.

Supplementary Fig. 378 | HPLC trace for the chemical synthesized (*rac*)-**16c**.

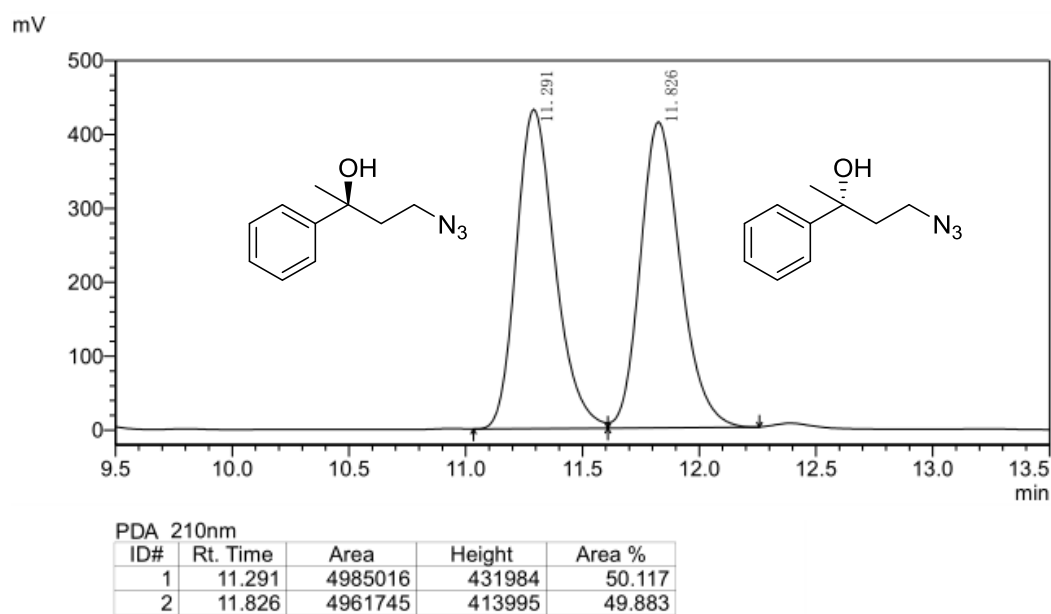


Supplementary Fig. 379 | HPLC trace for the enzymatic synthesized (*R*)-**16c**.

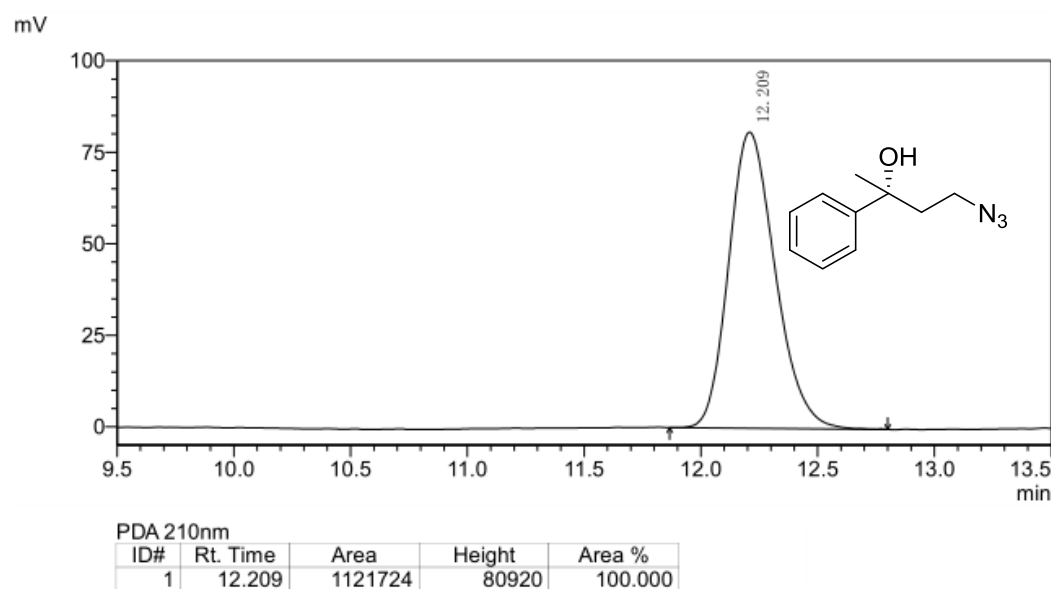


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 18.6 min, $t_{(R)}$ = 21.2 min.

Supplementary Fig. 380 | HPLC trace for the chemical synthesized (*rac*)-**17c**.

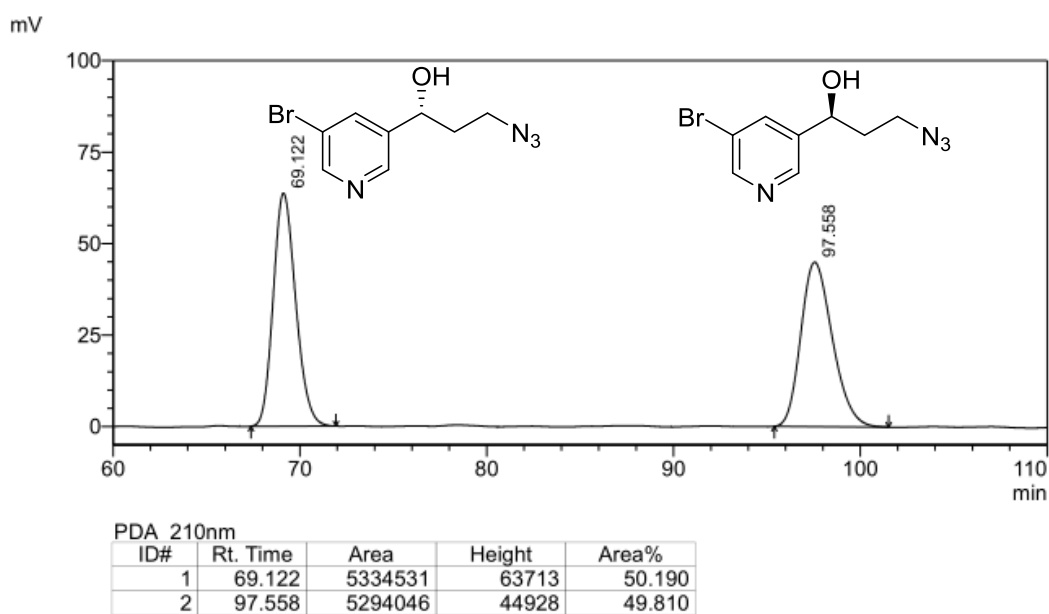


Supplementary Fig. 381 | HPLC trace for the enzymatic synthesized (*R*)-**17c**.

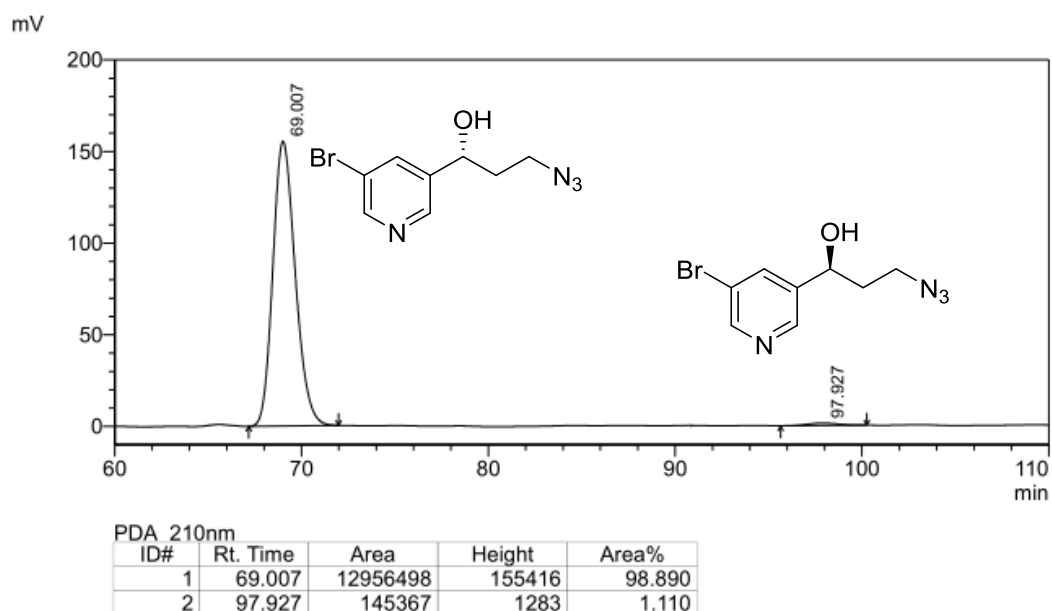


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 11.3 min, $t_{(R)}$ = 11.8 min.

Supplementary Fig. 382 | HPLC trace for the chemical synthesized (*rac*)-**18c**.

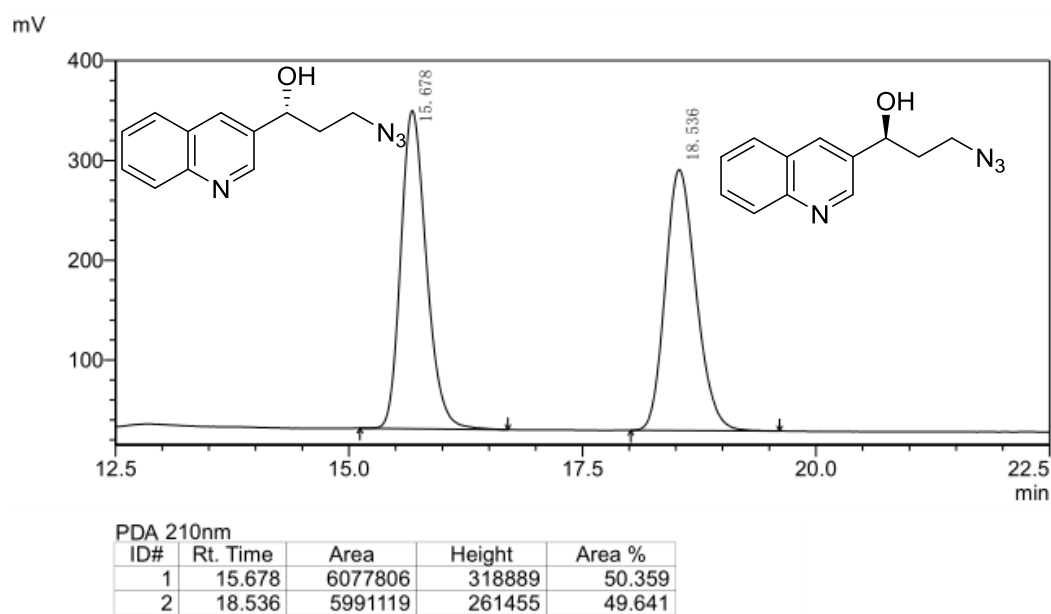


Supplementary Fig. 383 | HPLC trace for the enzymatic synthesized (*R*)-**18c**.

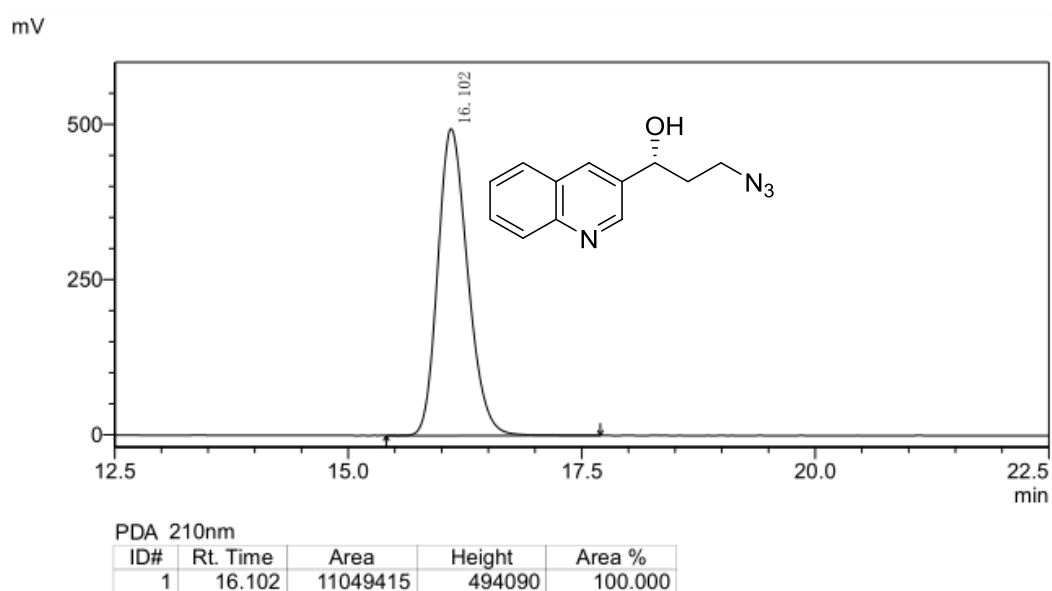


Chiral HPLC analysis: Diacel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.5 mL/min, λ = 210 nm, $t_{(R)}$ = 69.0 min, $t_{(S)}$ = 97.9 min.

Supplementary Fig. 384 | HPLC trace for the chemical synthesized (*rac*)-**19c**.

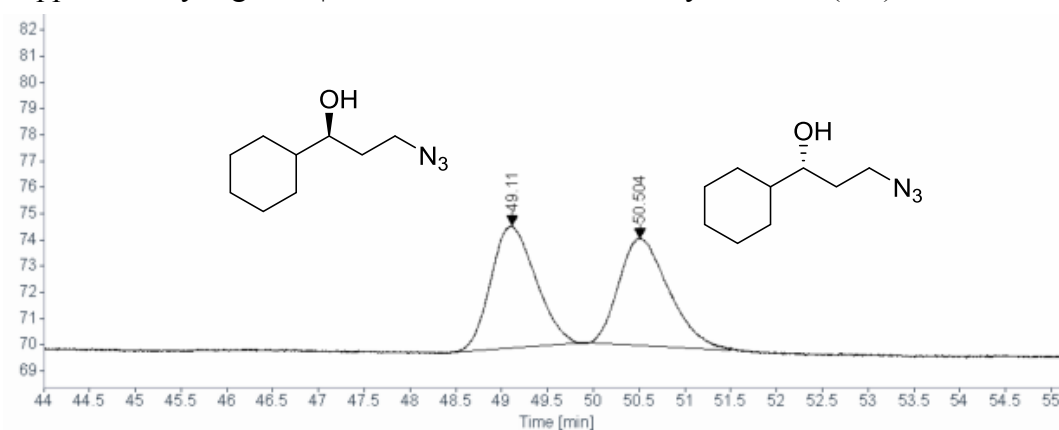


Supplementary Fig. 385 | HPLC trace for the enzymatic synthesized (*R*)-**19c**.



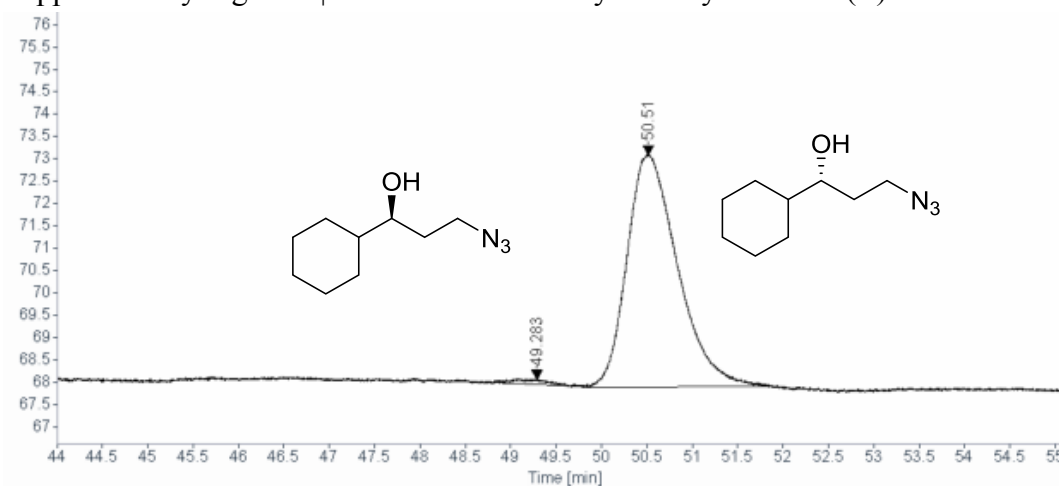
Chiral HPLC analysis: Diacel Chiralpak OJ-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 210 nm, $t_{(R)}$ = 15.7 min, $t_{(S)}$ = 18.6 min.

Supplementary Fig. 386 | GC trace for the chemical synthesized (*rac*)-**21c**.



ID#	Ret. Time	Area	Height	Area%	Resolution
1	49.110	161.409	4.702	50.686	
1	50.504	157.040	4.116	49.314	1.453

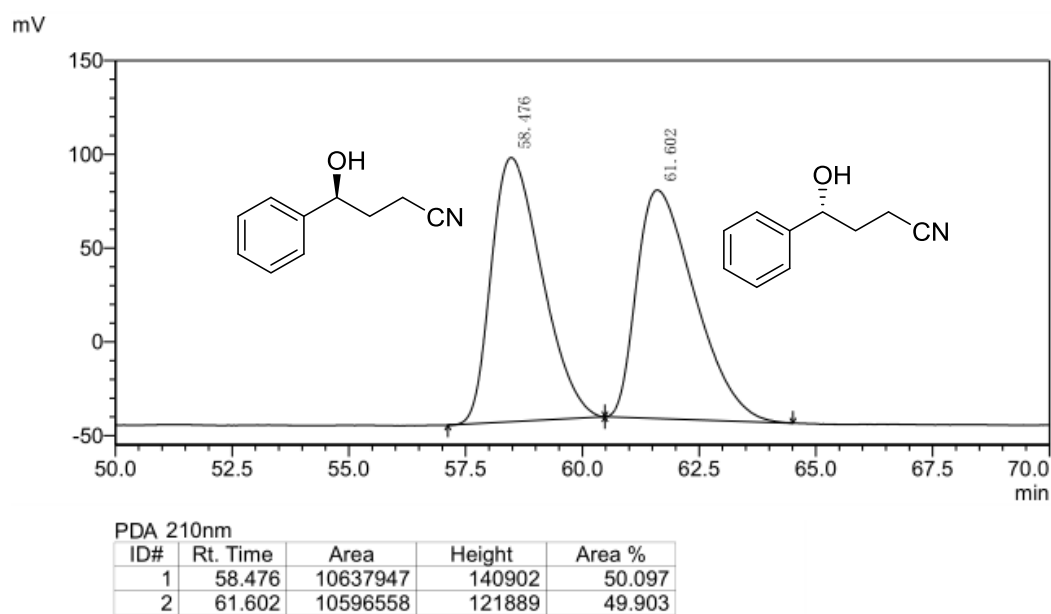
Supplementary Fig. 387 | GC trace for the enzymatic synthesized (*R*)-**21c**.



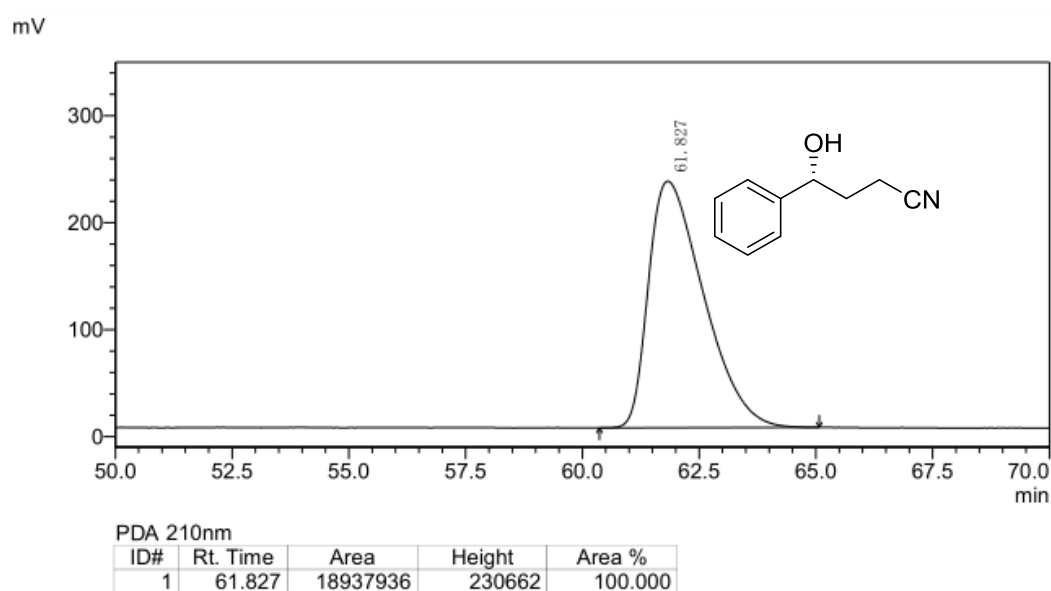
ID#	Ret. Time	Area	Height	Area%	Resolution
1	49.283	3.351	0.122	1.619	
1	50.510	203.651	5.209	98.381	2.011

Chiral GC analysis: Rt-bDEXcst (RESTEK), 140 °C for 60 min, $t_{(S)}$ = 49.3 min, $t_{(R)}$ = 50.5 min.

Supplementary Fig. 388 | HPLC trace for the chemical synthesized (*rac*)-**1d**.

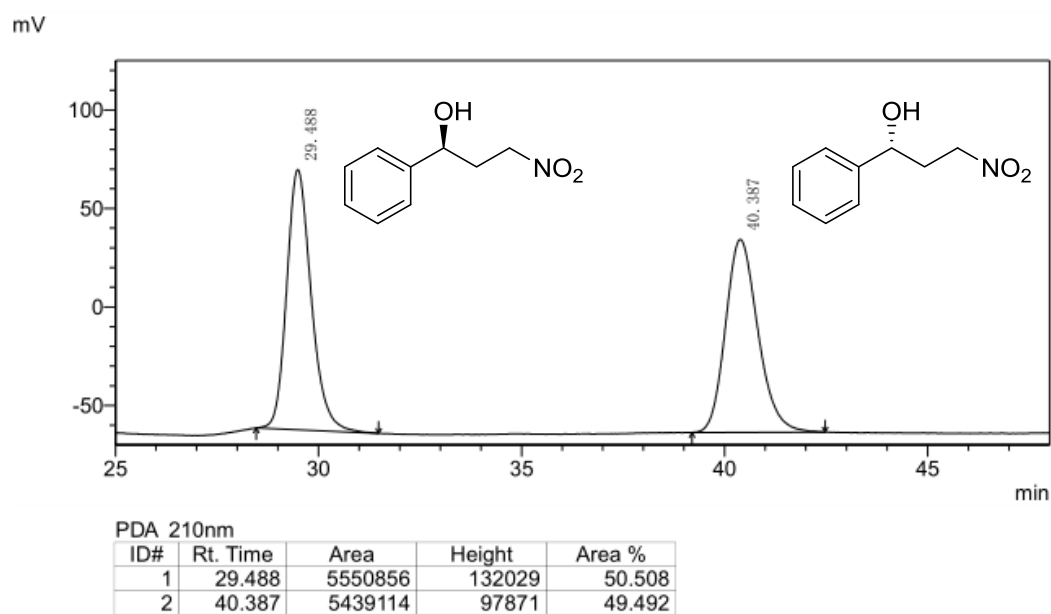


Supplementary Fig. 389 | HPLC trace for the enzymatic synthesized (*R*)-**1d**.

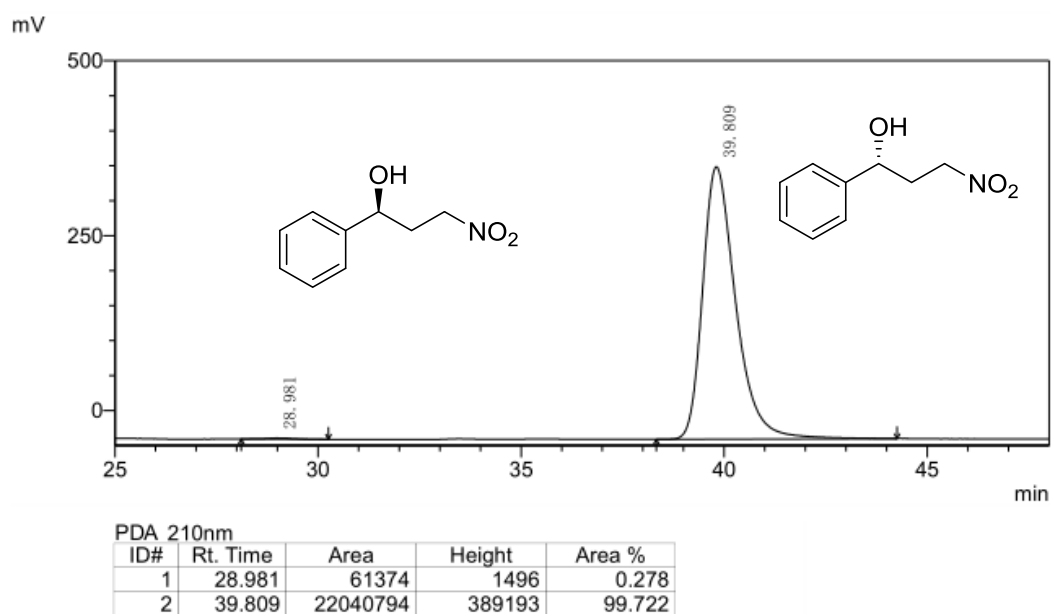


Chiral HPLC analysis: Diacel Chiralpak IH, *n*-hexane/*i*-PrOH = 95/5, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 58.5 min, $t_{(R)}$ = 61.6 min.

Supplementary Fig. 390| HPLC trace for the chemical synthesized (*rac*)-**1e**.

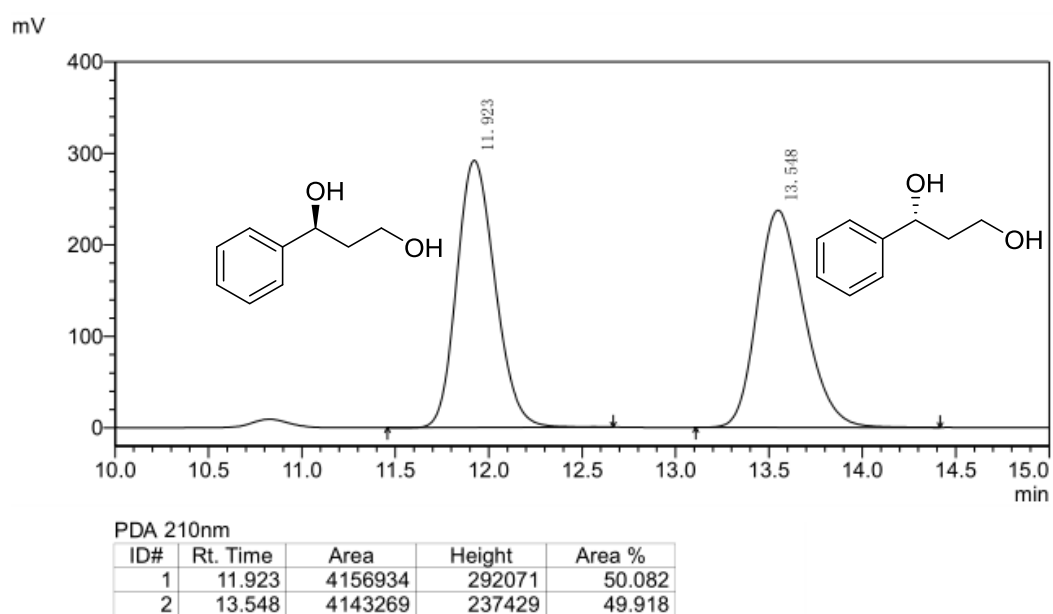


Supplementary Fig. 391 | HPLC trace for the enzymatic synthesized (*R*)-**1e**.

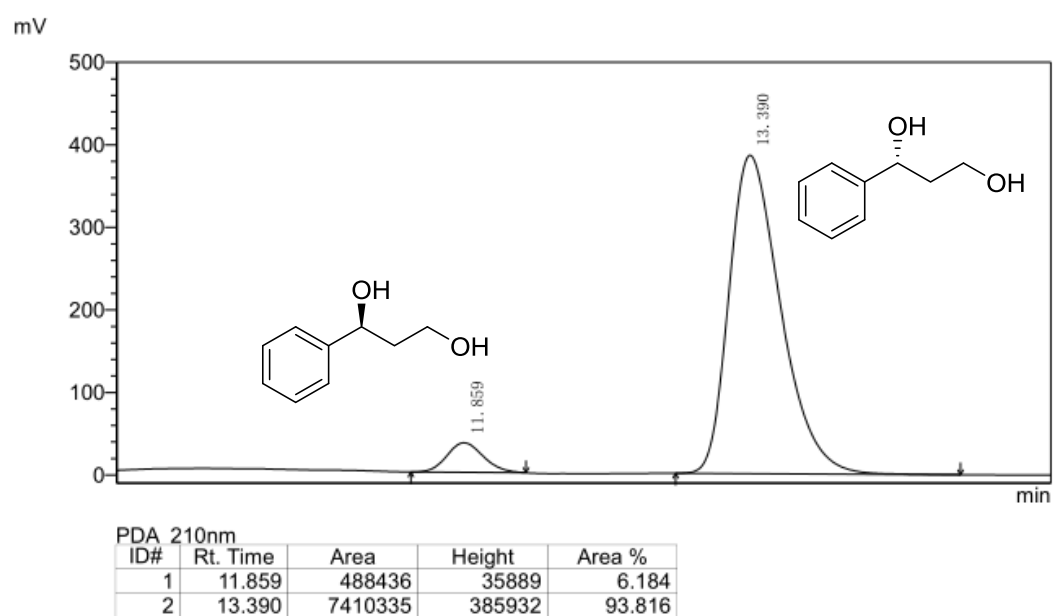


Chiral HPLC analysis: Diacel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 29.0 min, $t_{(R)}$ = 39.8 min.

Supplementary Fig. 392 | HPLC trace for the commercial (*rac*)-**1f**.

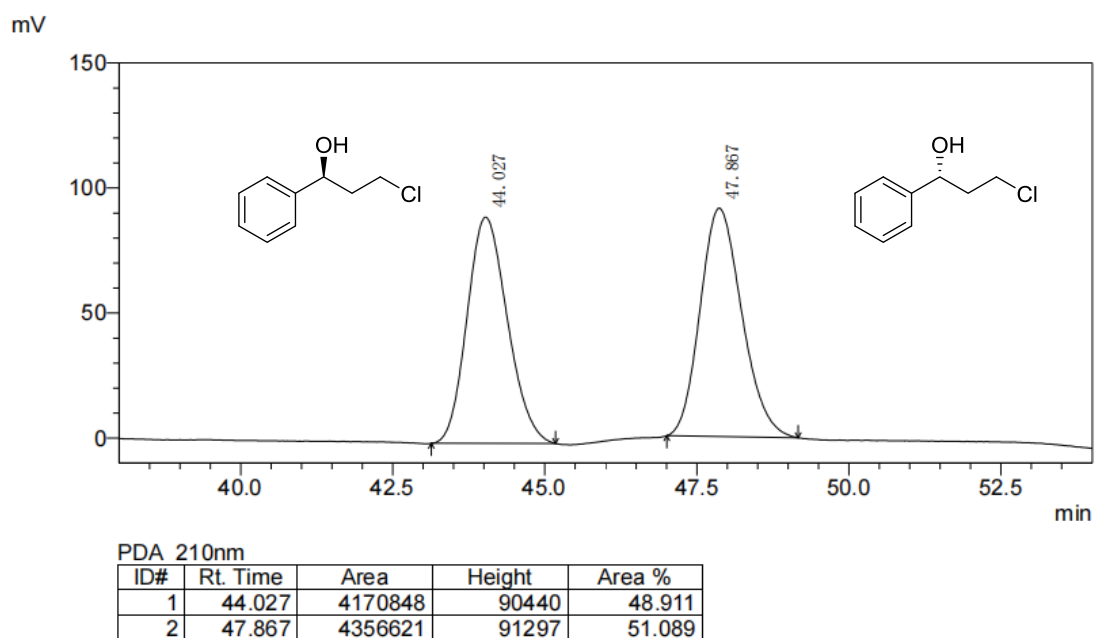


Supplementary Fig. 393 | HPLC trace for the enzymatic synthesized (*R*)-**1f**.

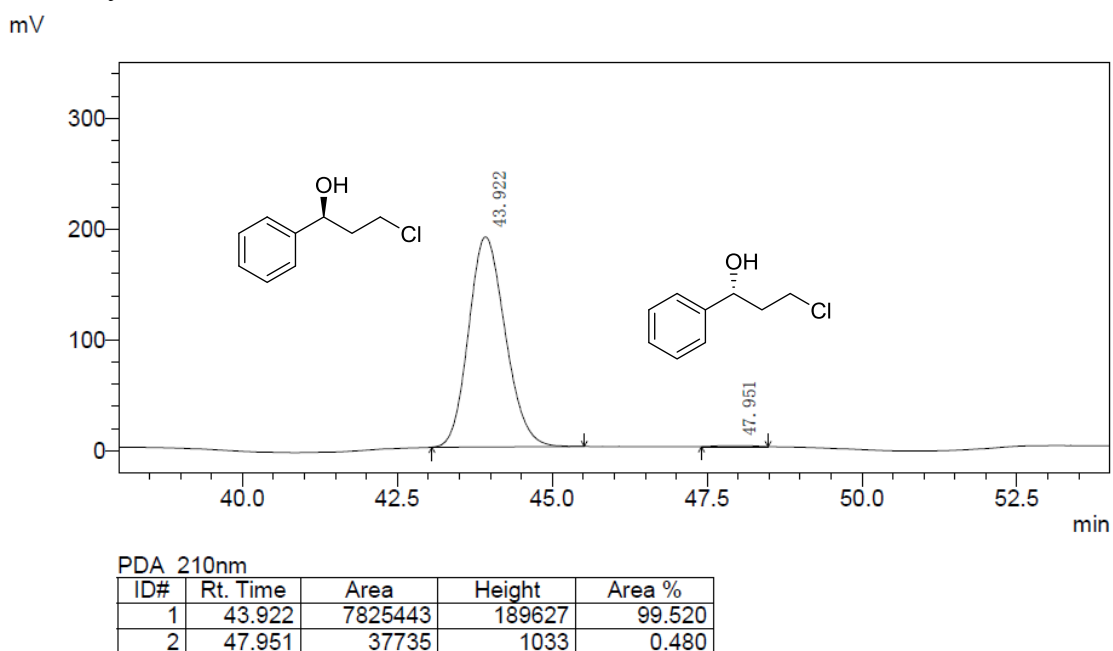


Chiral HPLC analysis: Diacel Chiralpak IH, *n*-hexane/*i*-PrOH = 88/12, flow rate 0.8 mL/min, λ = 210 nm, $t_{(S)}$ = 11.9 min, $t_{(R)}$ = 13.4 min.

Supplementary Fig. 394 | HPLC trace for the chemical synthesized (*rac*)-**1a**.

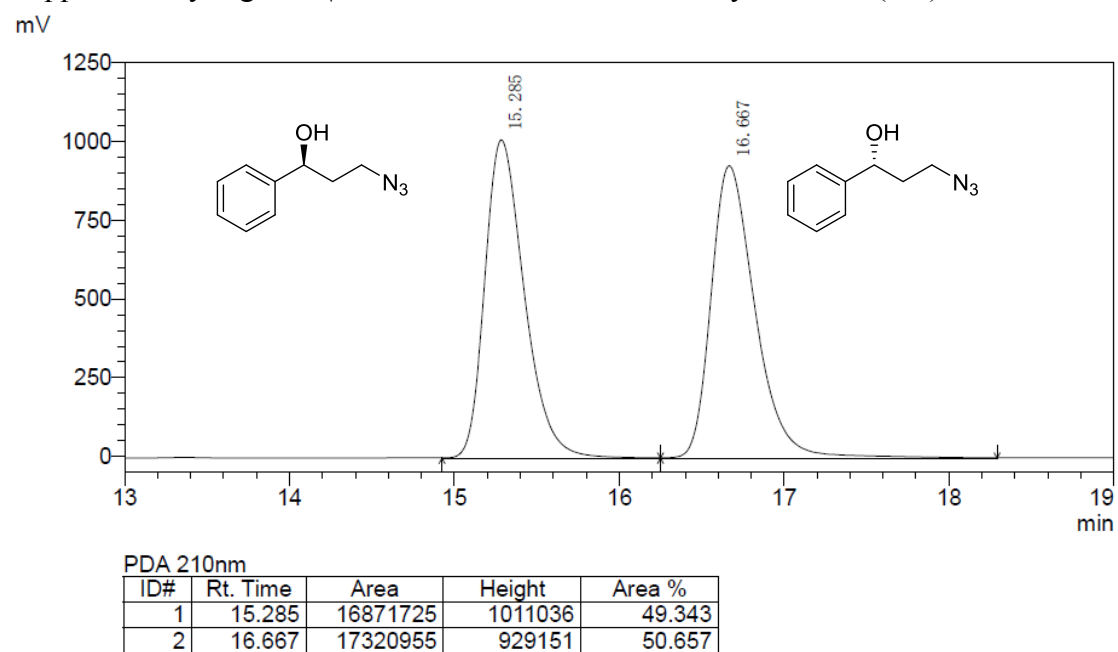


Supplementary Fig. 395 | HPLC trace for the enzymatic synthesized (*S*)-**1a** by biocatalytic cascade.

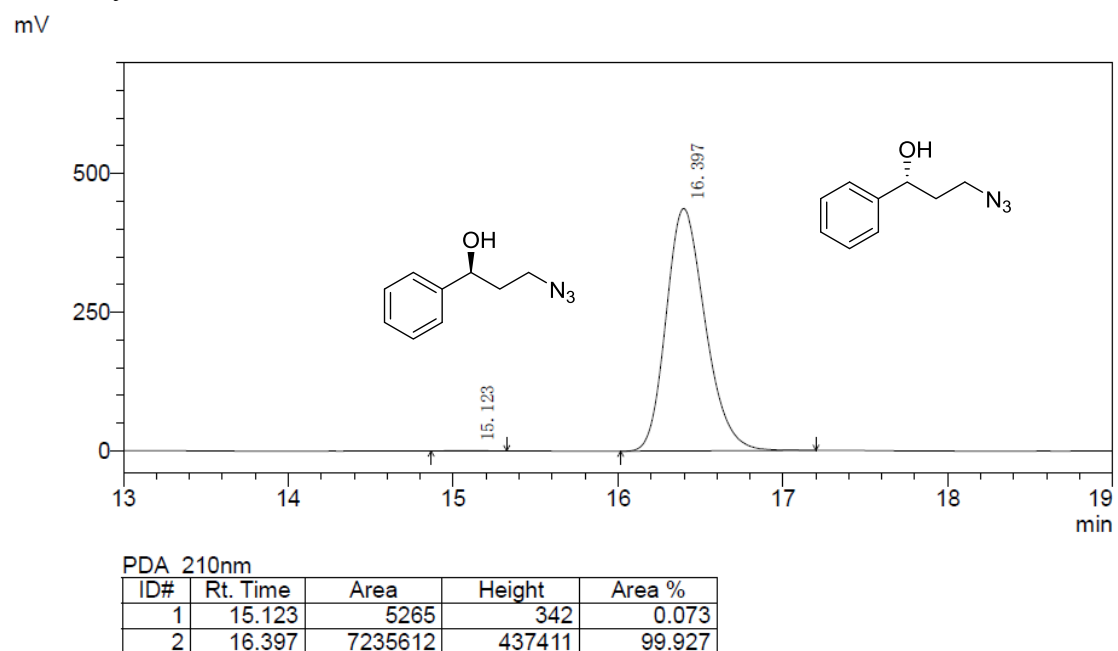


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(S)}$ = 43.9 min, $t_{(R)}$ = 48.0 min.

Supplementary Fig. 396 | HPLC trace for the chemical synthesized (*rac*)-**1c**.

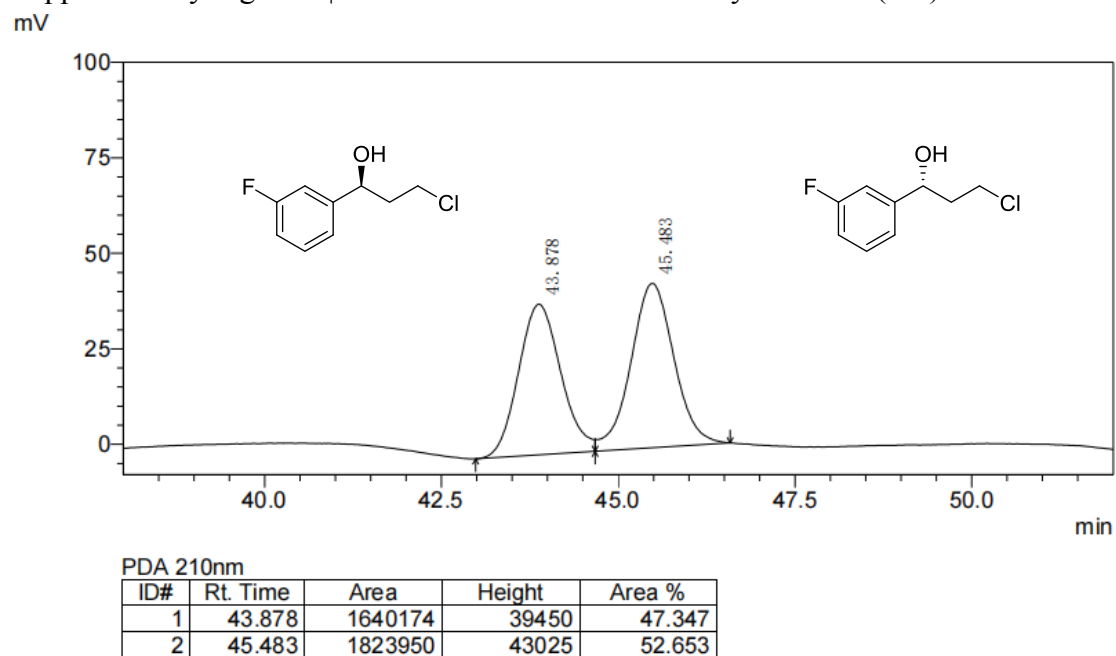


Supplementary Fig. 397 | HPLC trace for the enzymatic synthesized (*R*)-**1c** by biocatalytic cascade.

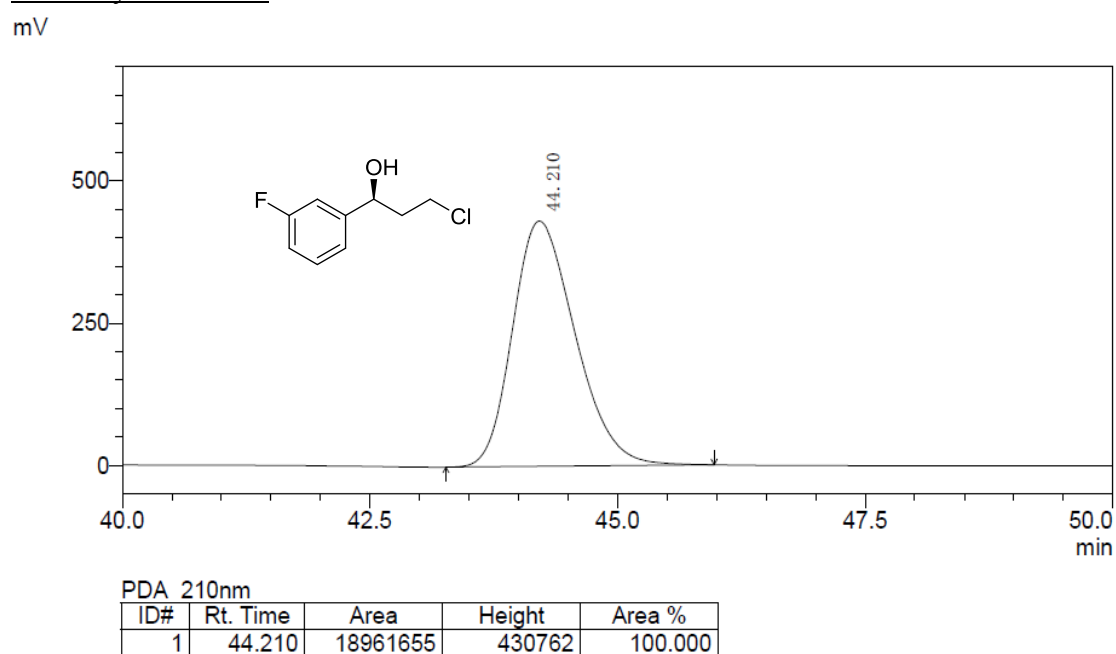


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 15.1 min, $t_{(R)}$ = 16.4 min.

Supplementary Fig. 398 | HPLC trace for the chemical synthesized (*rac*)-**6a**.

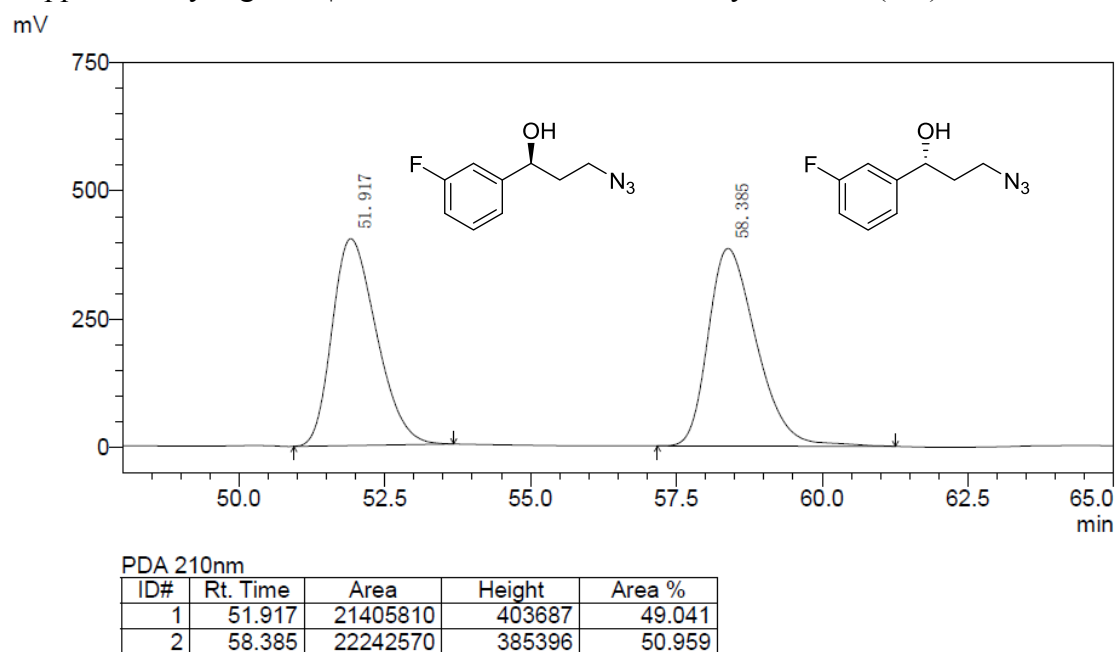


Supplementary Fig. 399 | HPLC trace for the enzymatic synthesized (*S*)-**6a** by biocatalytic cascade.

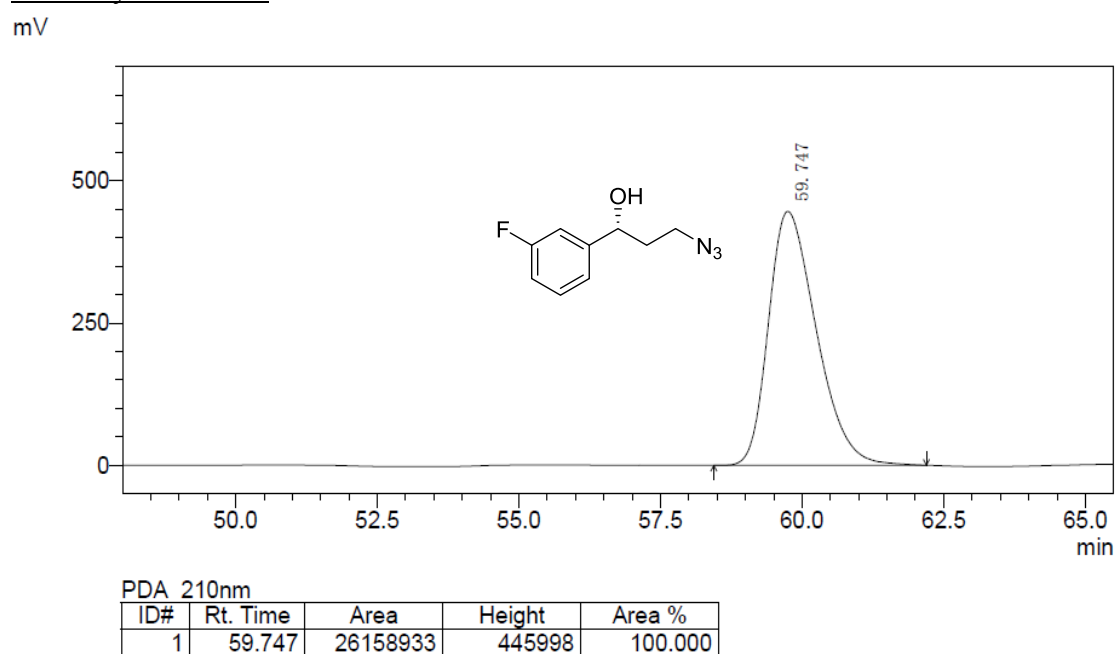


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, $\lambda = 210$ nm, $t_{(S)}$ = 44.2 min.

Supplementary Fig. 400 | HPLC trace for the chemical synthesized (*rac*)-**6c**.

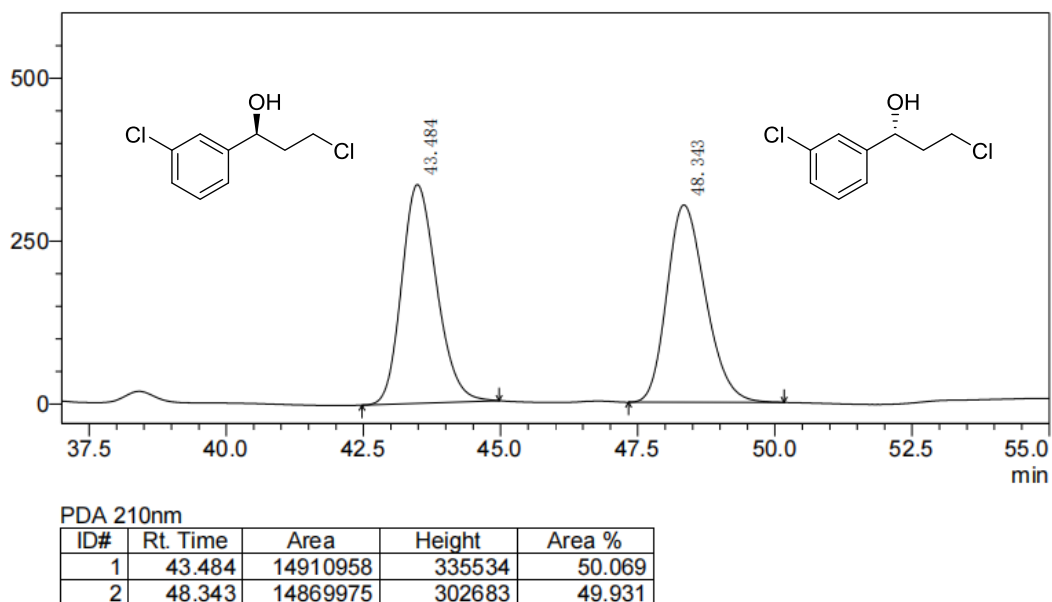


Supplementary Fig. 401 | HPLC trace for the enzymatic synthesized (*R*)-**6c** by biocatalytic cascade.

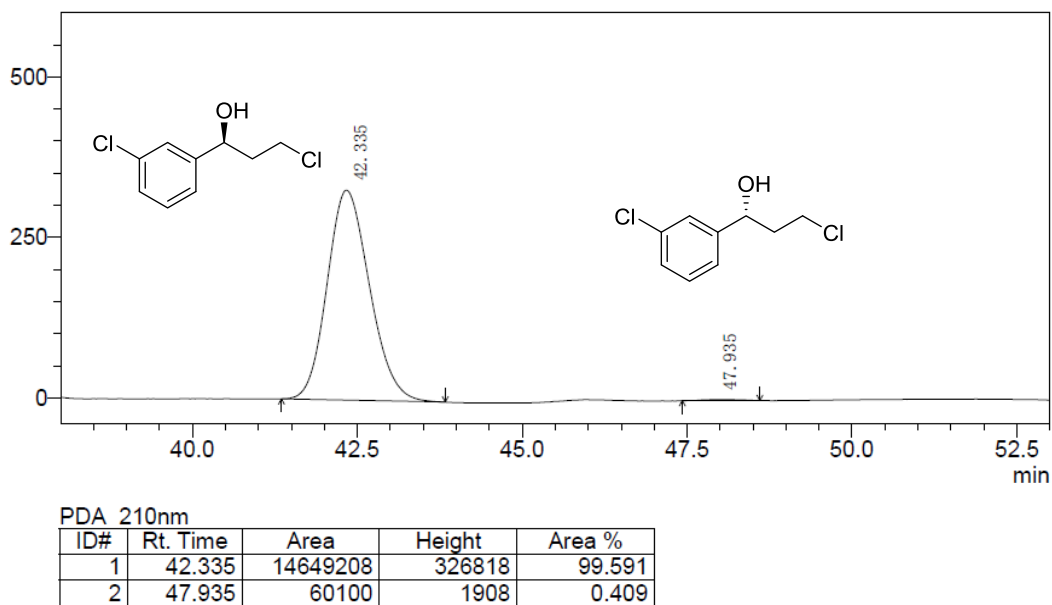


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, λ = 210 nm, $t_{(R)}$ = 59.7 min.

Supplementary Fig. 402 | HPLC trace for the chemical synthesized (*rac*)-**7a**.
mV

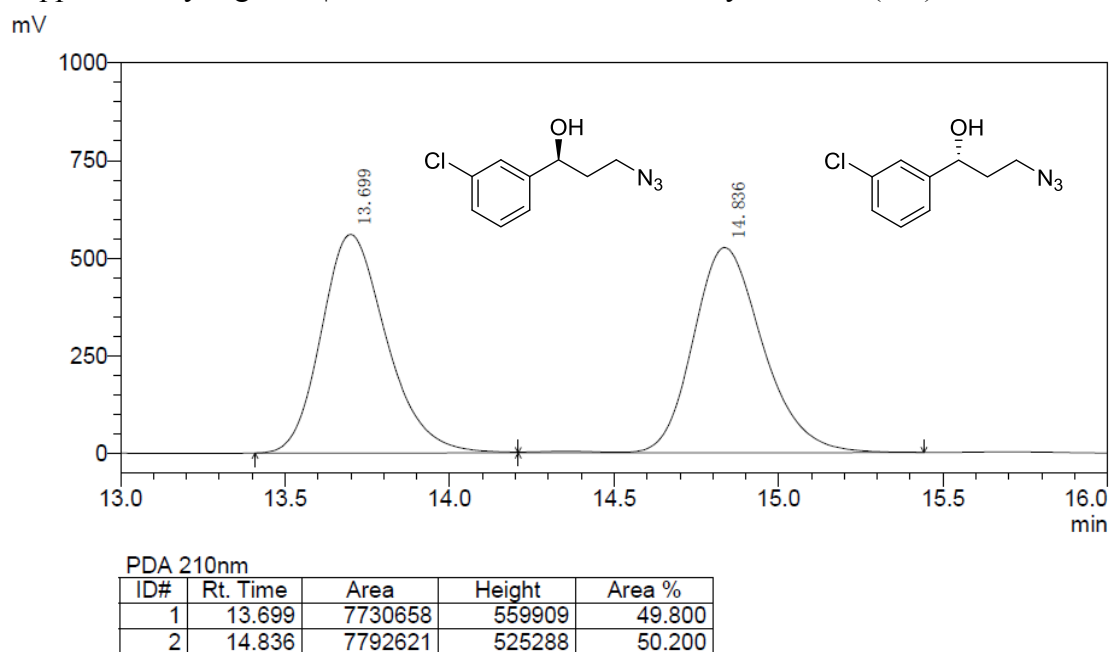


Supplementary Fig. 403 | HPLC trace for the enzymatic synthesized (*S*)-**7a** by biocatalytic cascade.
mV

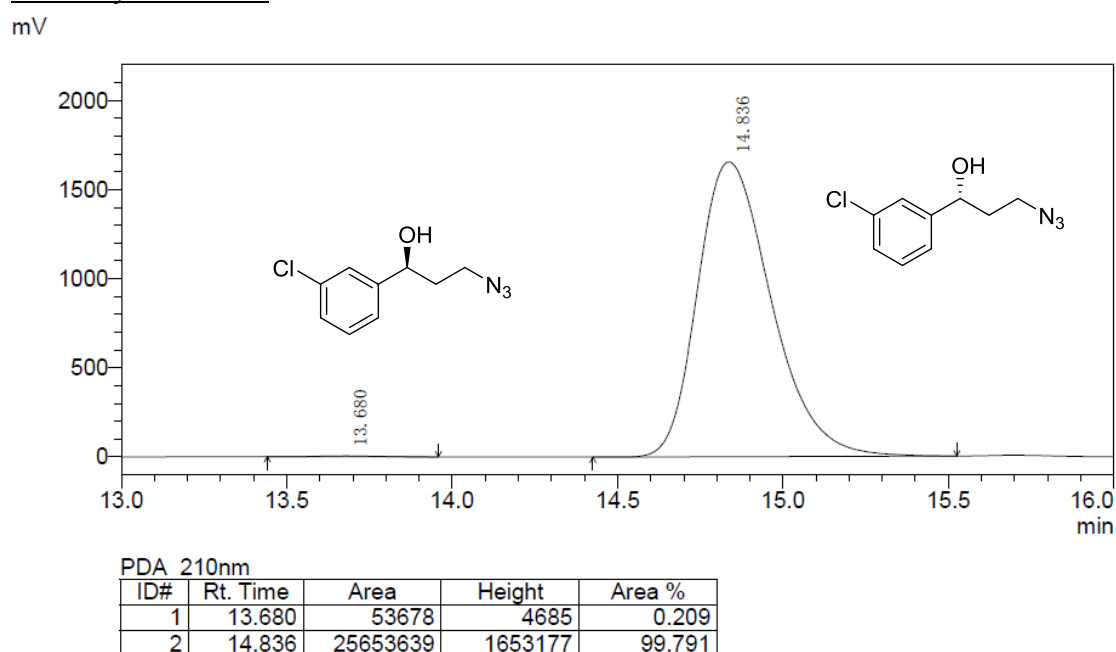


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 99/1, flow rate 0.5 mL/min, $\lambda = 210$ nm, $t_{(S)} = 42.3$ min, $t_{(R)} = 47.9$ min.

Supplementary Fig. 404 | HPLC trace for the chemical synthesized (*rac*)-**7c**.

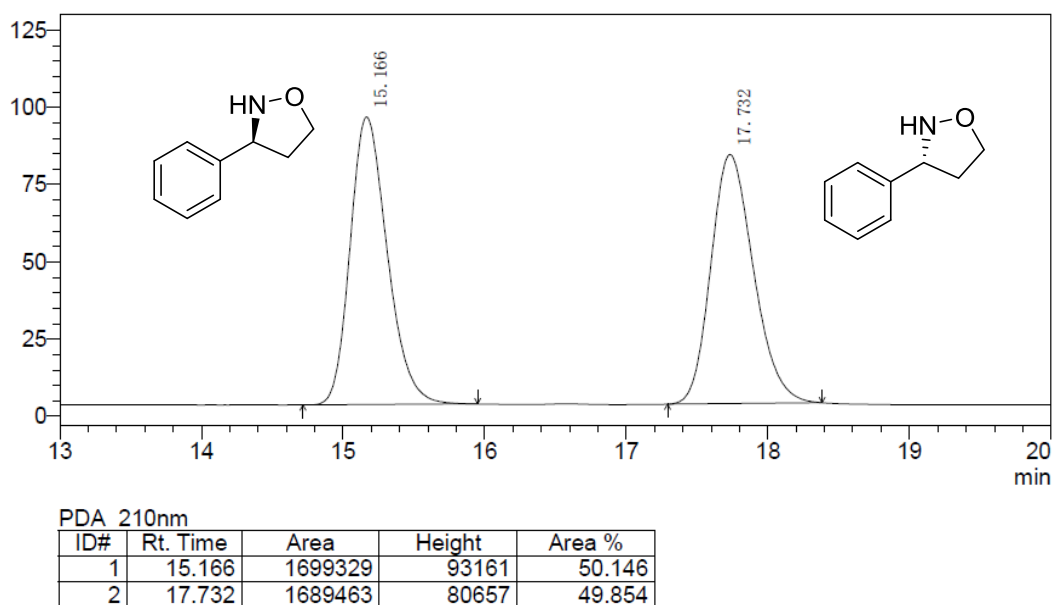


Supplementary Fig. 405 | HPLC trace for the enzymatic synthesized (*R*)-**7c** by biocatalytic cascade.

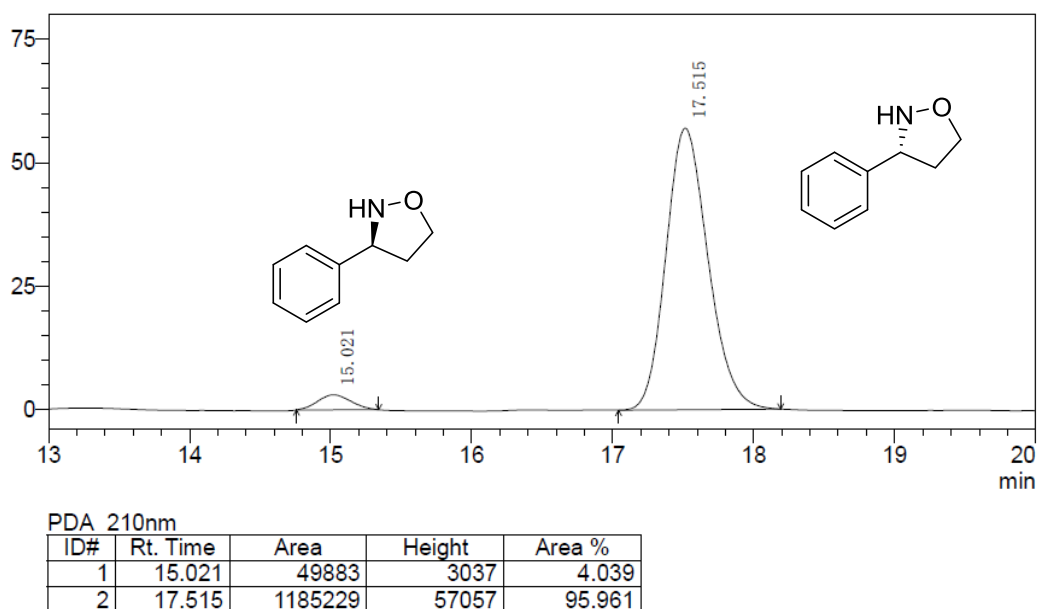


Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 13.7 min, $t_{(R)}$ = 14.8 min.

Supplementary Fig. 406 | HPLC trace for the chemical synthesized (*rac*)-**1aa**.
mV

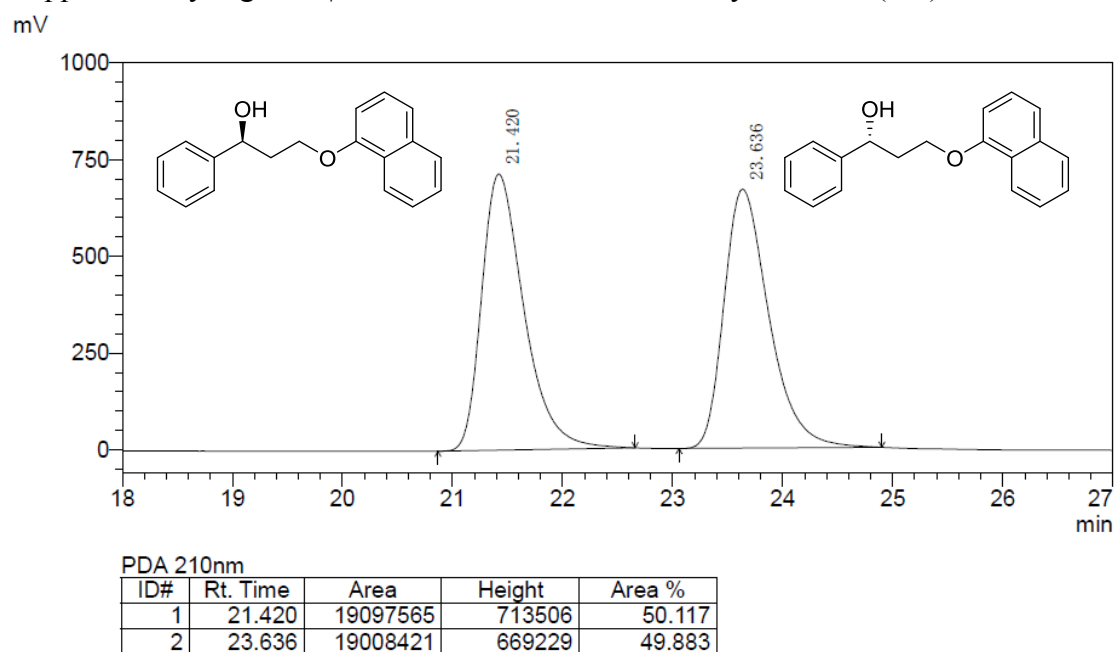


Supplementary Fig. 407 | HPLC trace for the enzymatic synthesized (*R*)-**1aa**.
mV

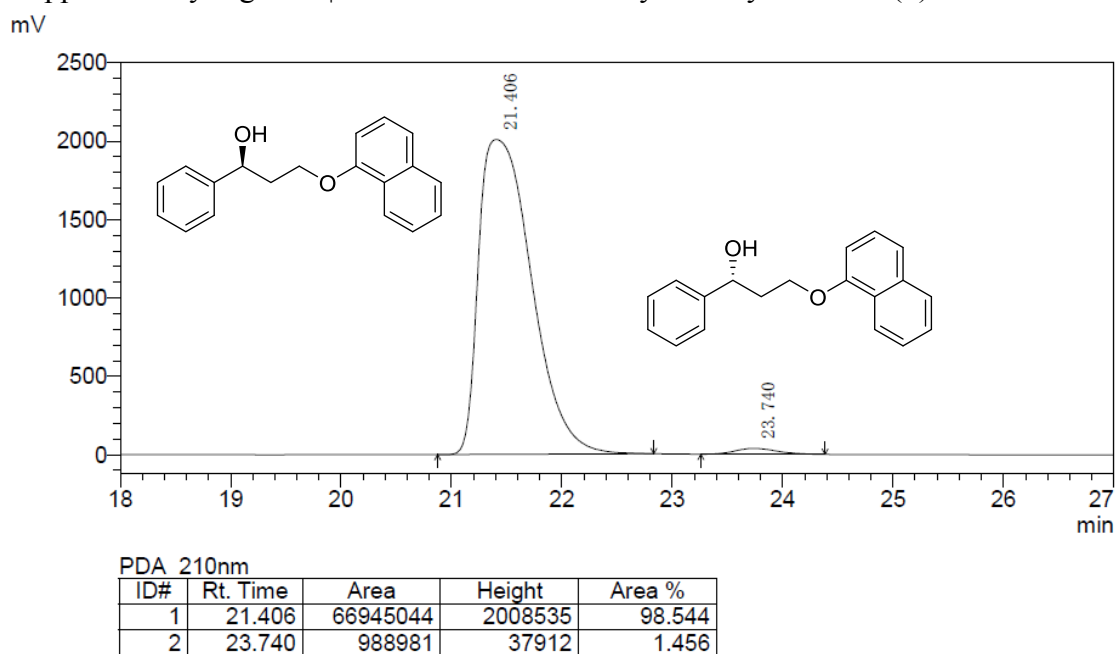


Chiral HPLC analysis: Diacel Chiralpak OJ-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 210 nm, $t_{(S)}$ = 15.0 min, $t_{(R)}$ = 17.5 min.

Supplementary Fig. 408 | HPLC trace for the chemical synthesized (*rac*)-**1ab**.



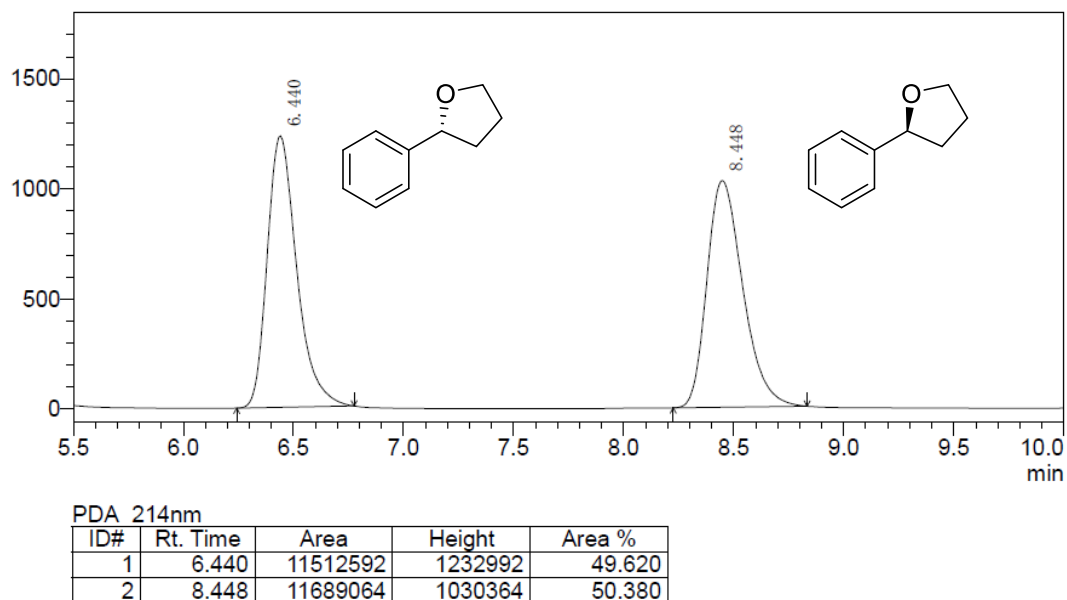
Supplementary Fig. 409 | HPLC trace for the enzymatic synthesized (*S*)-**1ab**.



Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 21.4 min, $t_{(R)}$ = 23.7 min.

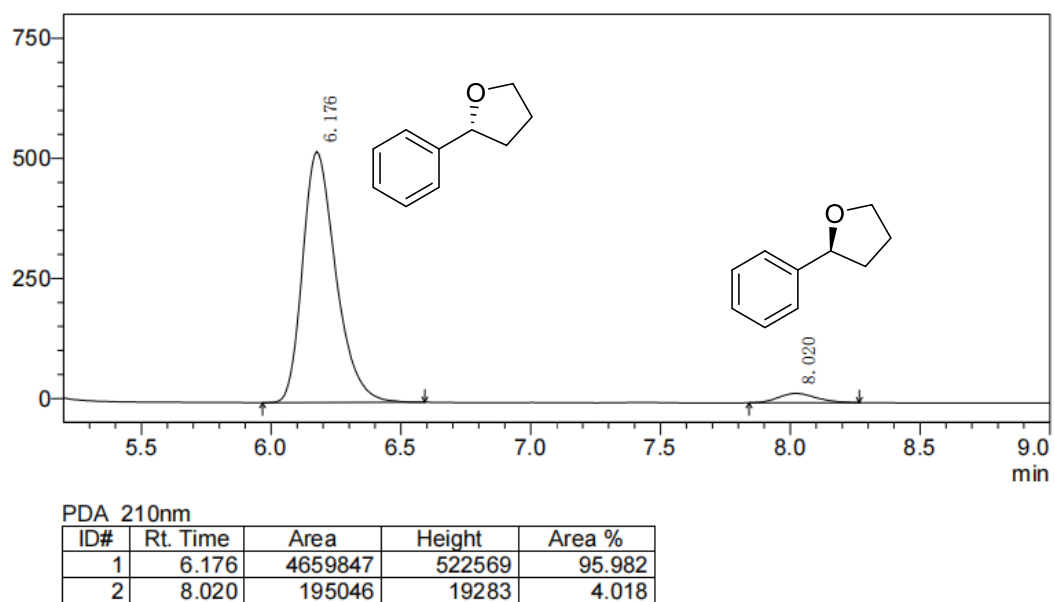
Supplementary Fig. 410 | HPLC trace for the chemical synthesized (*rac*)-**1ba**.

mV



Supplementary Fig. 411 | HPLC trace for the enzymatic synthesized (*R*)-**1ba**.

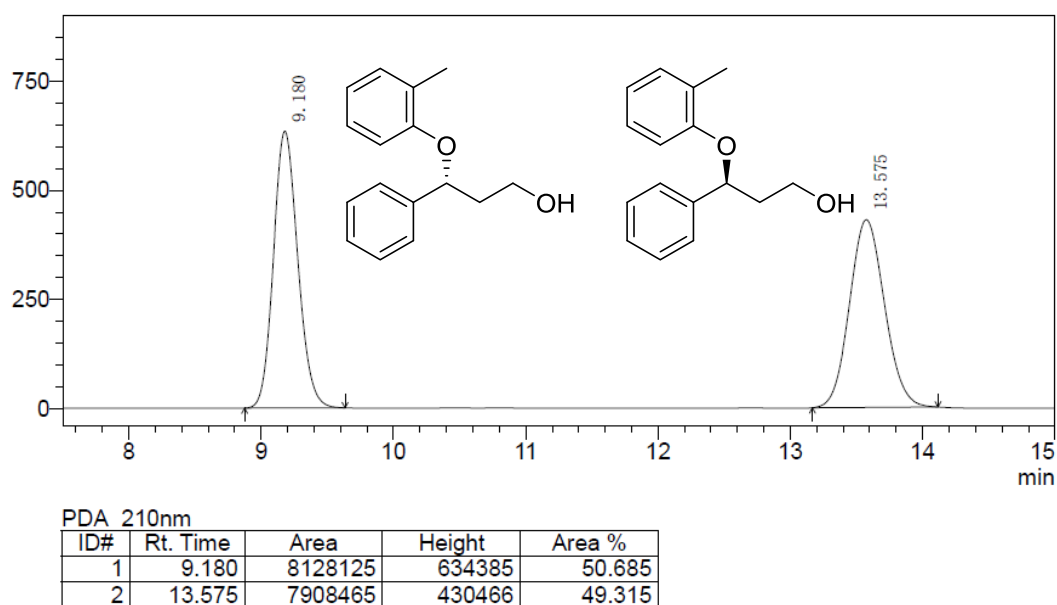
mV



Chiral HPLC analysis: Diacel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 92/8, flow rate 0.8 mL/min, λ = 210 nm, $t_{(R)}$ = 6.2 min, $t_{(S)}$ = 8.0 min.

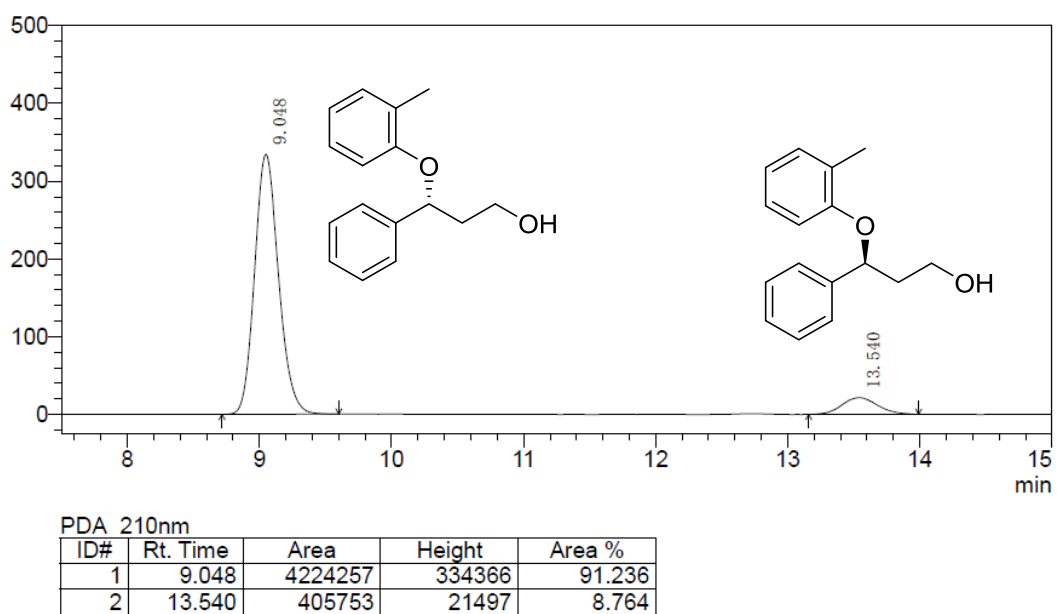
Supplementary Fig. 412 | HPLC trace for the chemical synthesized (*rac*)-**1bb**.

mV



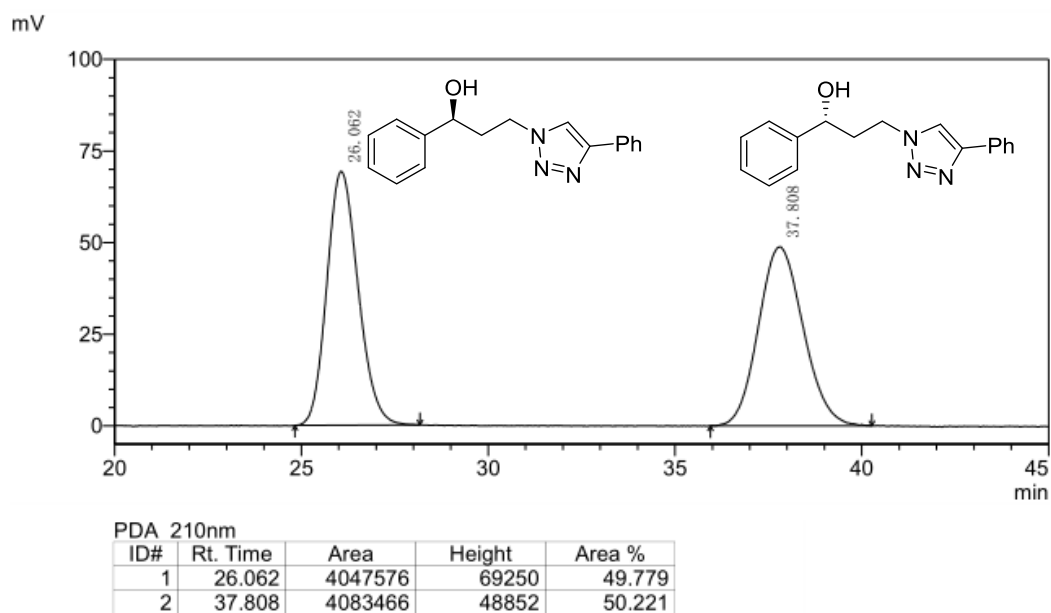
Supplementary Fig. 413 | HPLC trace for the enzymatic synthesized (*R*)-**1bb**.

mV

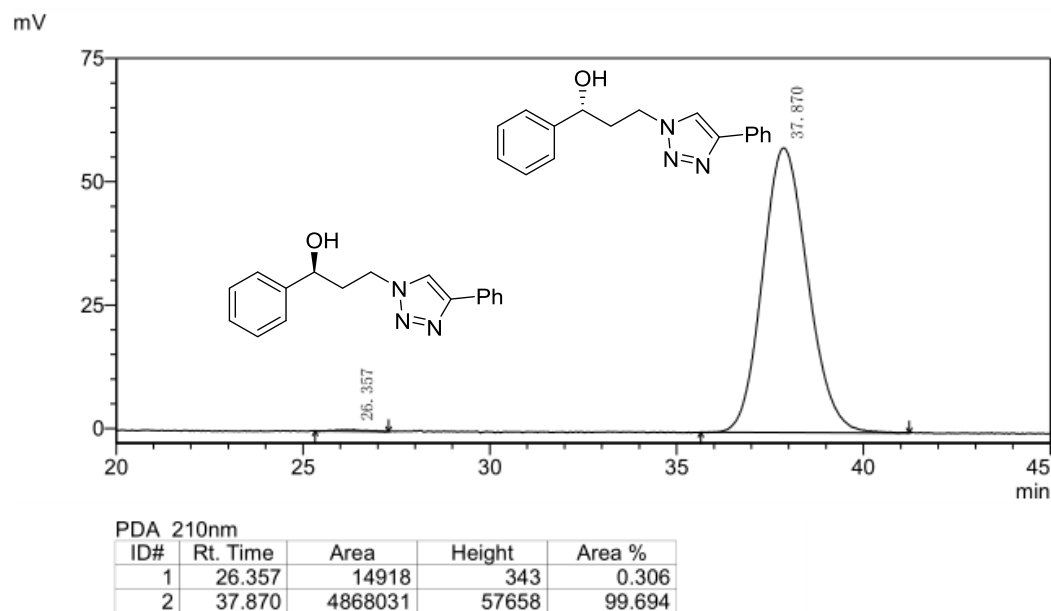


Chiral HPLC analysis: Diacel Chiralpak AD-H, *n*-hexane/*i*-PrOH = 95/5, flow rate 1.0 mL/min, λ = 210 nm, $t_{(R)}$ = 9.0 min, $t_{(S)}$ = 13.5 min.

Supplementary Fig. 414 | HPLC trace for the chemical synthesized (*rac*)-**1ca**.

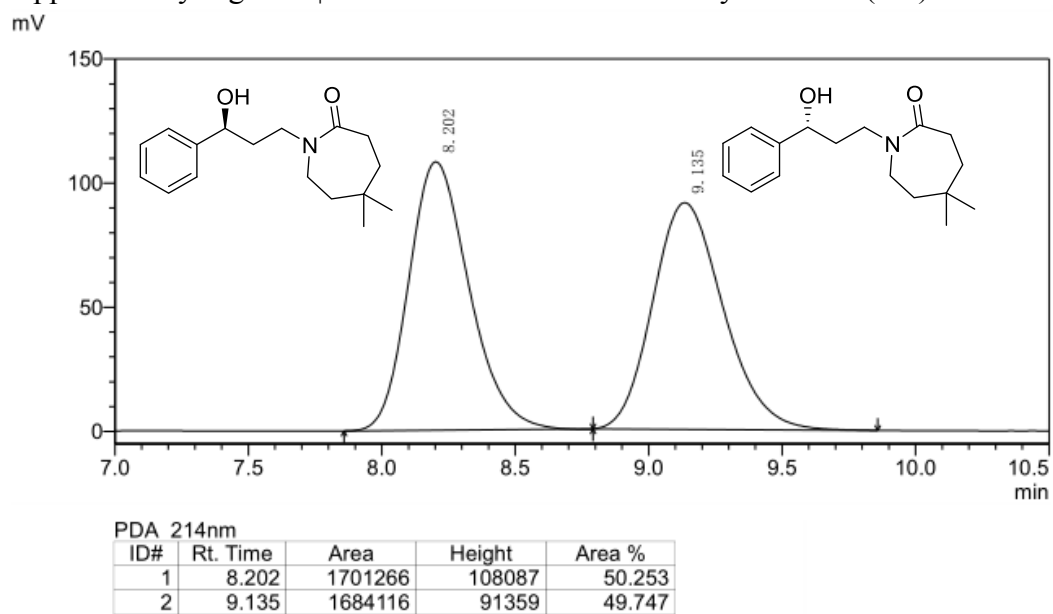


Supplementary Fig. 415 | HPLC trace for the enzymatic synthesized (*R*)-**1ca**.

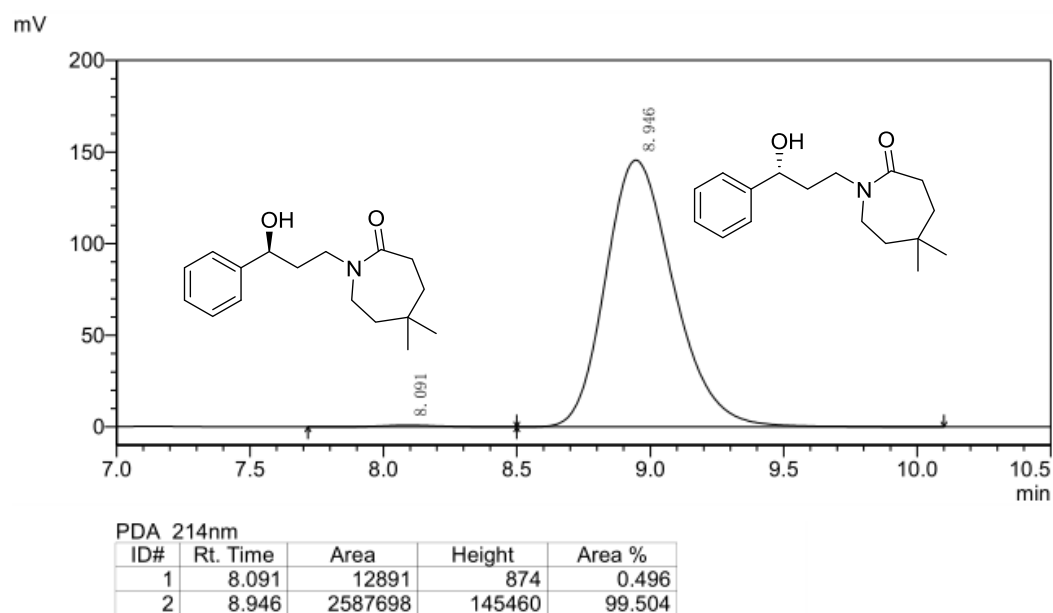


Chiral HPLC analysis: Diacel Chiralpak OD-H, *n*-hexane/*i*-PrOH = 80/20, flow rate 1.0 mL/min, λ = 210 nm, $t_{(S)}$ = 26.4 min, $t_{(R)}$ = 37.9 min.

Supplementary Fig. 416 | HPLC trace for the chemical synthesized (*rac*)-**1cb**.

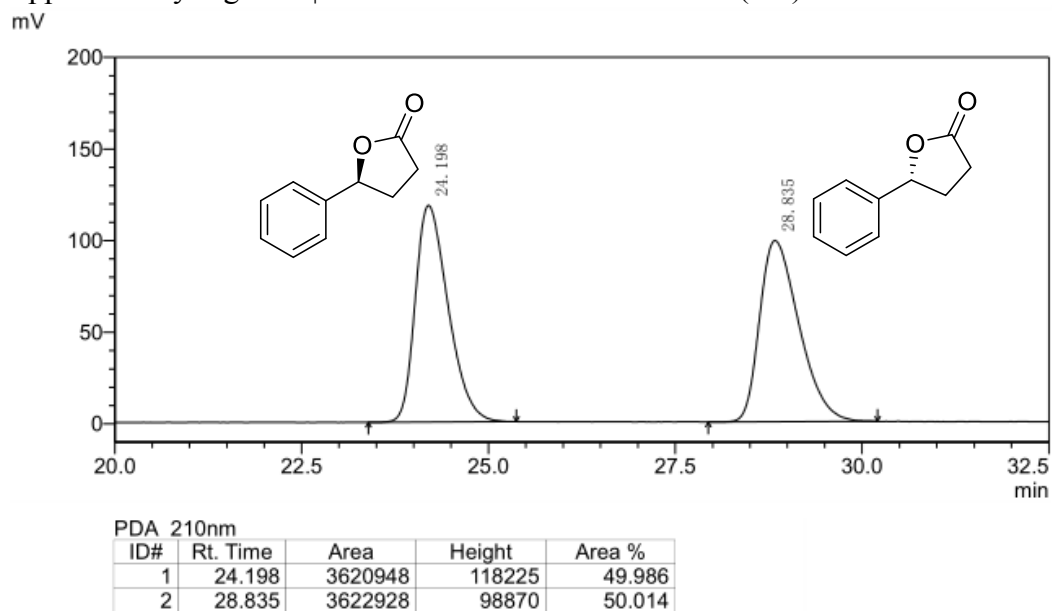


Supplementary Fig. 417 | HPLC trace for the enzymatic synthesized (*R*)-**1cb**.

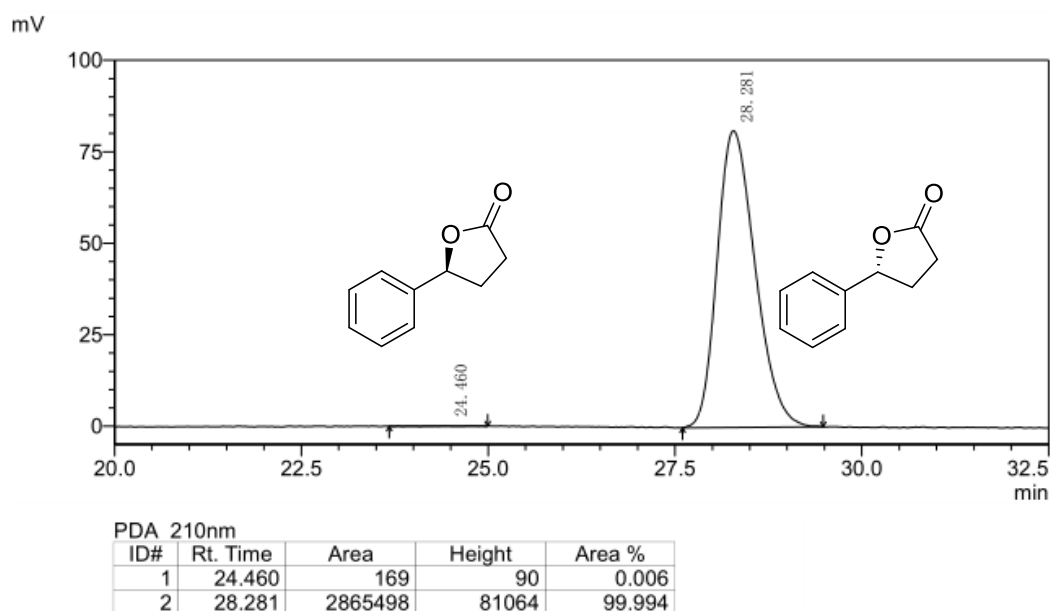


Chiral HPLC analysis: Diacel Chiralpak OJ-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 214 nm, $t_{(S)}$ = 8.1 min, $t_{(R)}$ = 8.9 min.

Supplementary Fig. 418 | HPLC trace for the commercial (*rac*)-**1da**.

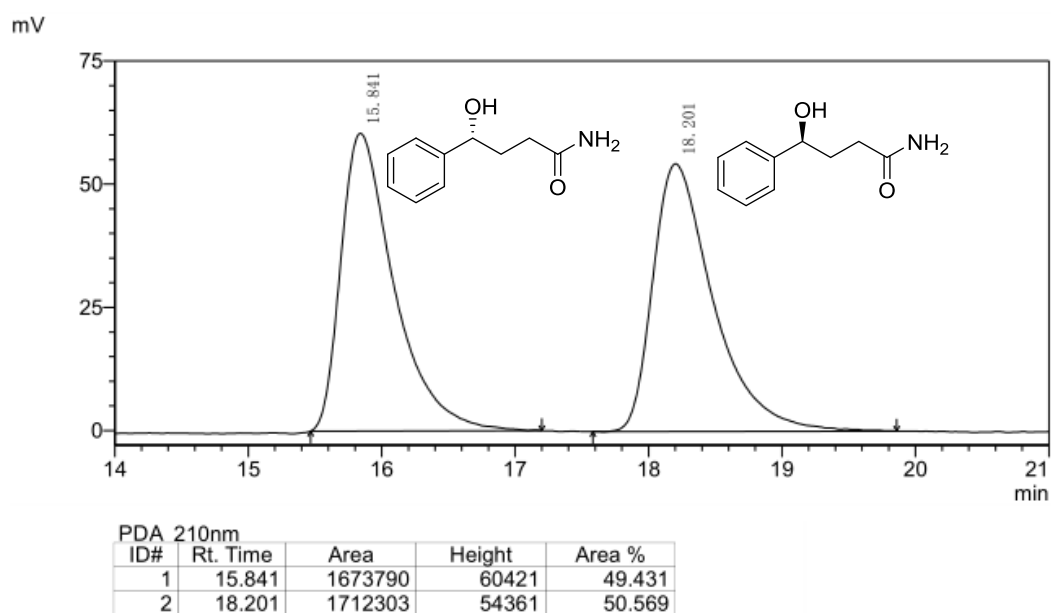


Supplementary Fig. 419 | HPLC trace for the enzymatic synthesized (*R*)-**1da**.

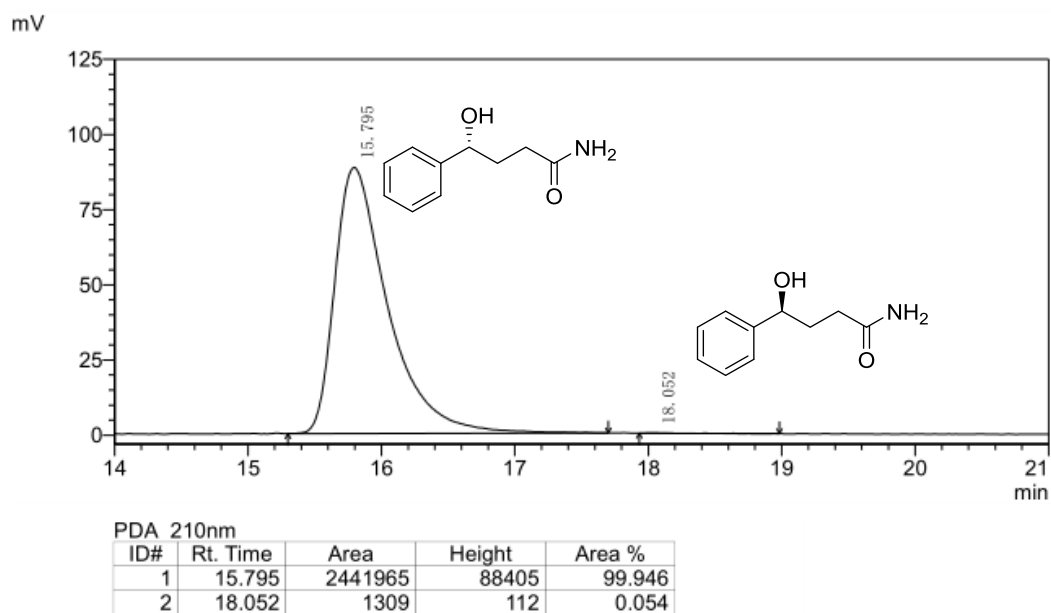


Chiral HPLC analysis: Diacel Chiralpak IH, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 210 nm, $t_{(S)}$ = 24.5 min, $t_{(R)}$ = 28.3 min.

Supplementary Fig. 420 | HPLC trace for the chemical synthesized (*rac*)-**1db**.

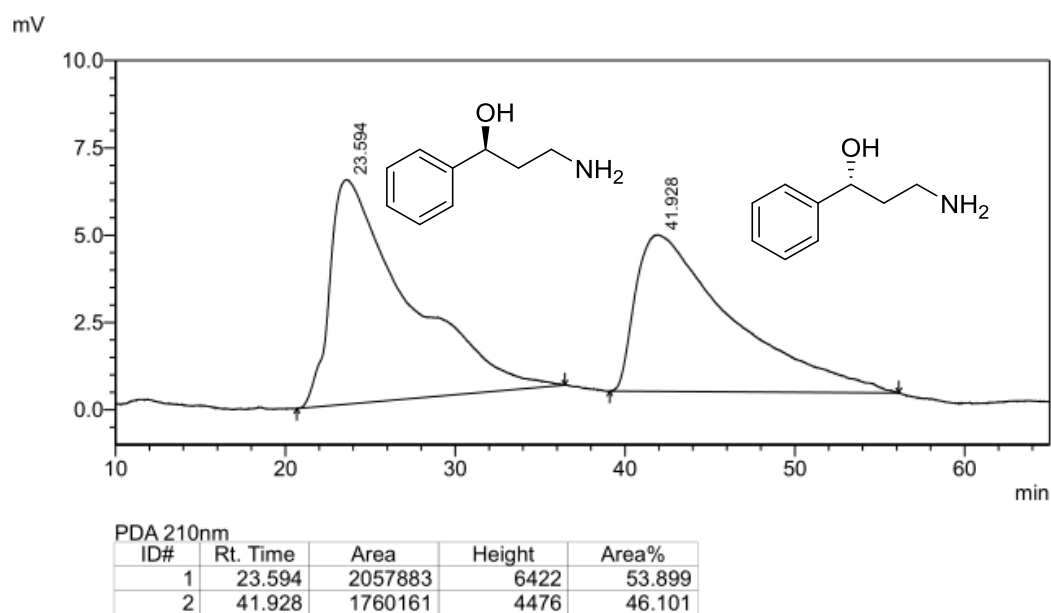


Supplementary Fig. 421 | HPLC trace for the enzymatic synthesized (*R*)-**1db**.

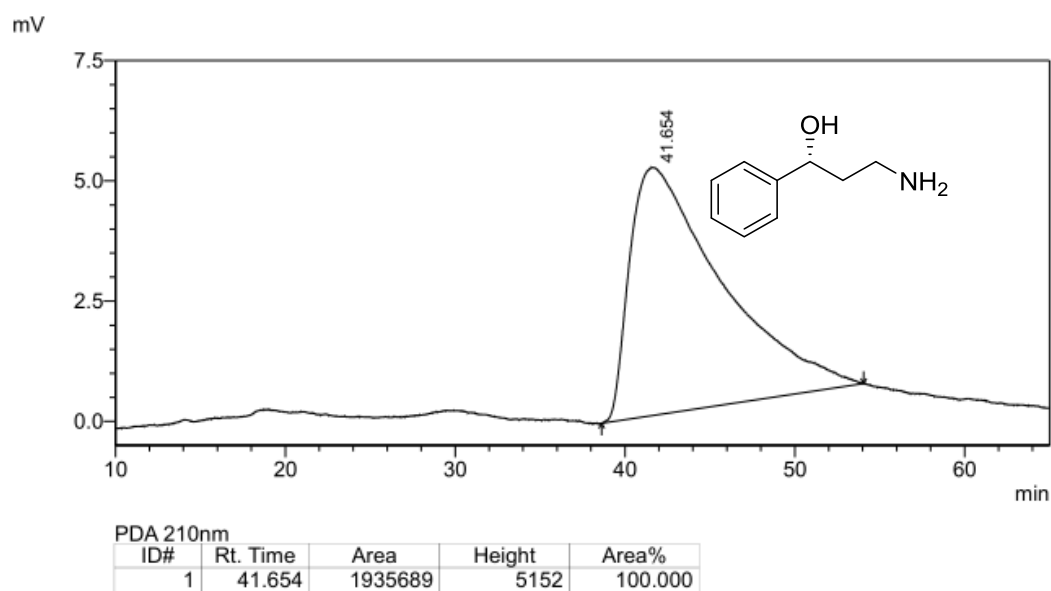


Chiral HPLC analysis: Diacel Chiralpak OJ-H, *n*-hexane/*i*-PrOH = 90/10, flow rate 1.0 mL/min, λ = 210 nm, $t_{(R)}$ = 15.8 min, $t_{(S)}$ = 18.1 min.

Supplementary Fig. 422 | HPLC trace for the commercial (*rac*)-**1ea**.

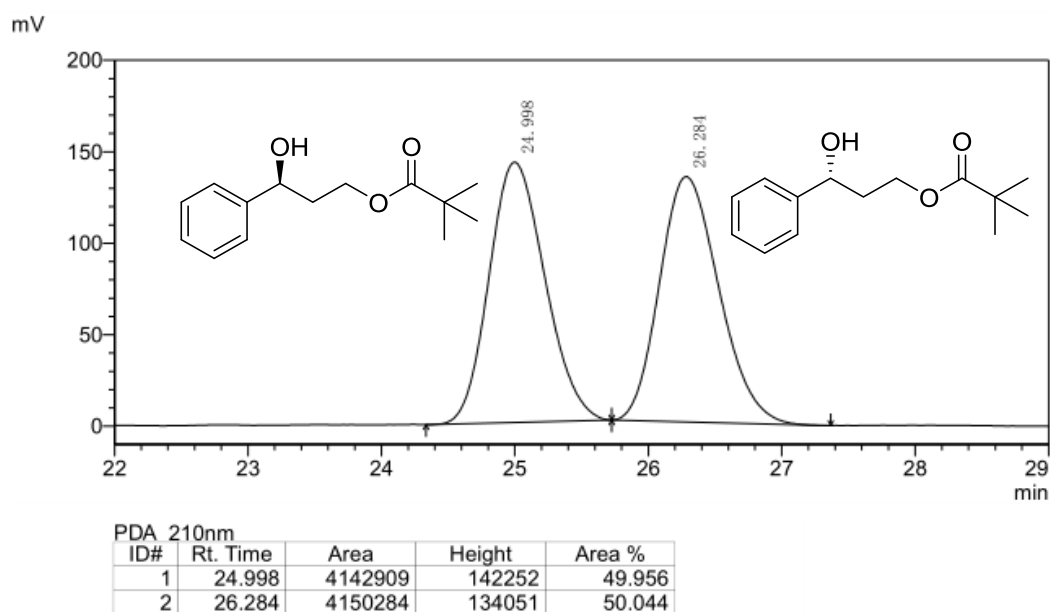


Supplementary Fig. 423 | HPLC trace for the enzymatic synthesized (*R*)-**1ea**.

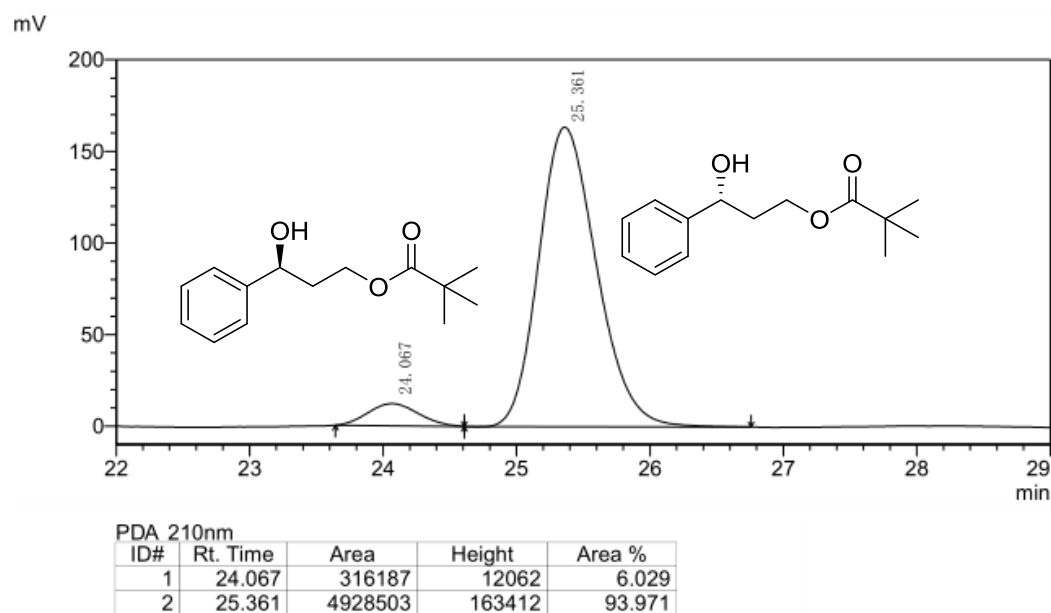


Chiral HPLC analysis: Diacel Chiralpak OB-H, *n*-hexane/*i*-PrOH = 92/8, flow rate 1.0 mL/min, $\lambda = 210$ nm, $t_{(S)} = 23.6$ min, $t_{(R)} = 41.9$ min.

Supplementary Fig. 424 | HPLC trace for the chemical synthesized (*rac*)-**1fa**.



Supplementary Fig. 425 | HPLC trace for the enzymatic synthesized (*R*)-**1fa**.



Chiral HPLC analysis: Diacel Chiralpak OX-3, *n*-hexane/*i*-PrOH = 97/3, flow rate 0.7 mL/min, λ = 210 nm, $t_{(S)}$ = 24.1 min, $t_{(R)}$ = 25.4 min.

12. HRMS spectra (Supplementary Figures 426-526)

Supplementary Fig. 426 | HRMS (ESI) of (*S*)-1a.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

96 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

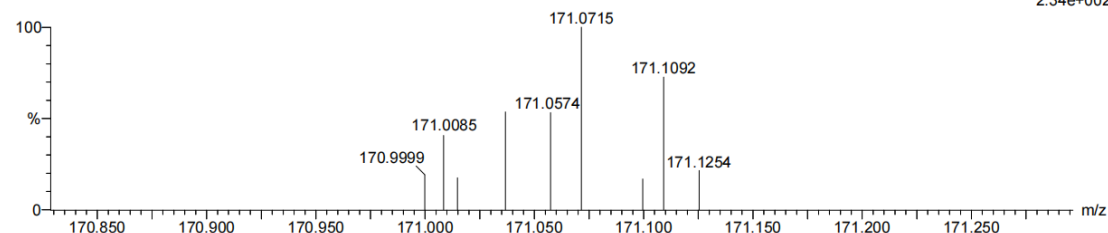
Elements Used:

C: 9-9 H: 12-12 N: 0-20 O: 0-37 Cl: 1-4

3

221127-1-263-2-1a 1 (0.030)

1: TOF MS ES+
2.34e+002



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
171.0574	171.0577	-0.3	-1.8	3.5	54.4	n/a	n/a	C9 H12 O Cl

Supplementary Fig. 427 | HRMS (ESI) of (*R*)-1b.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

175 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

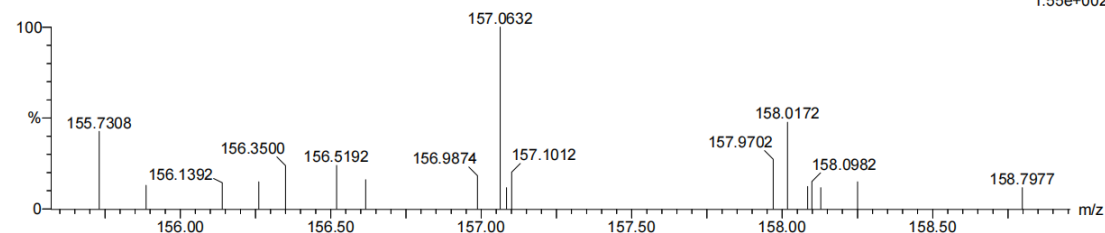
Elements Used:

C: 9-9 H: 10-10 N: 0-100 O: 0-100 Na: 0-4

37

240925-4-R-MB-HY 16 (0.121)

1: TOF MS ES+
1.55e+002



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
157.0632	157.0629	0.3	1.9	4.5	67.4	n/a	n/a	C9 H10 O Na

Supplementary Fig. 428 | HRMS (ESI) of (*S*)-**2a**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

617 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

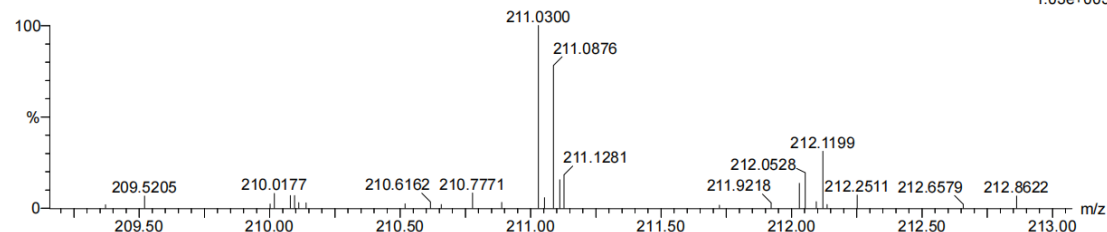
Elements Used:

C: 9-9 H: 10-10 N: 0-100 O: 0-100 Na: 0-4 Cl: 1-2 F: 1-3

37

240925-4-S-O-F 12 (0.100)

1: TOF MS ES+
1.03e+003



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
211.0300	211.0302	-0.2	-0.9	3.5	138.1	n/a	n/a	C9 H10 O Na Cl F

Supplementary Fig. 429 | HRMS (ESI) of (*R*)-**2b**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

21 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

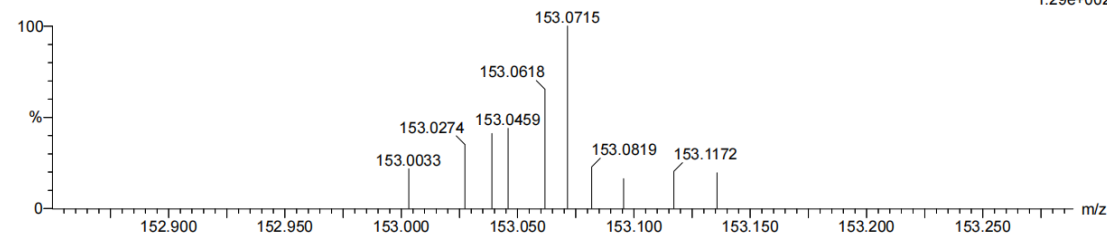
Elements Used:

C: 9-9 H: 10-10 O: 0-37 F: 1-3

3

221127-1-263-2-2b 45 (0.269)

1: TOF MS ES+
1.29e+002



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
153.0715	153.0716	-0.1	-0.7	4.5	42.0	n/a	n/a	C9 H10 O F

Supplementary Fig. 430 | HRMS (ESI) of (*S*)-**3a**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

443 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

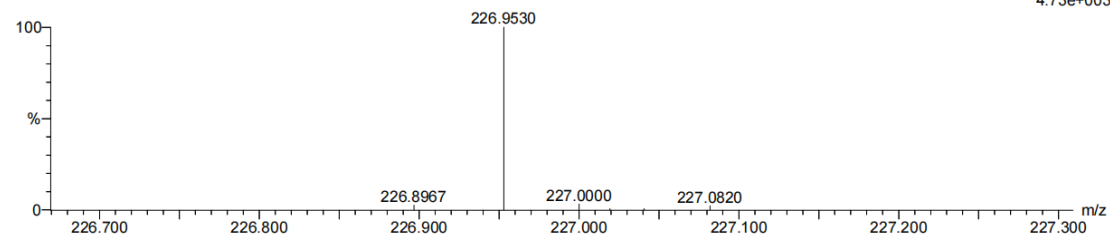
Elements Used:

C: 9-9 H: 10-10 N: 0-100 O: 0-100 Na: 0-4 Cl: 1-2

37

240925-4-S-O-Cl 20 (0.142)

1: TOF MS ES+
4.73e+003



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
227.0000	227.0006	-0.6	-2.6	3.5	41.2	n/a	n/a	C9 H10 O Na Cl2

Supplementary Fig. 431 | HRMS (ESI) of (*R*)-**3b**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

71 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

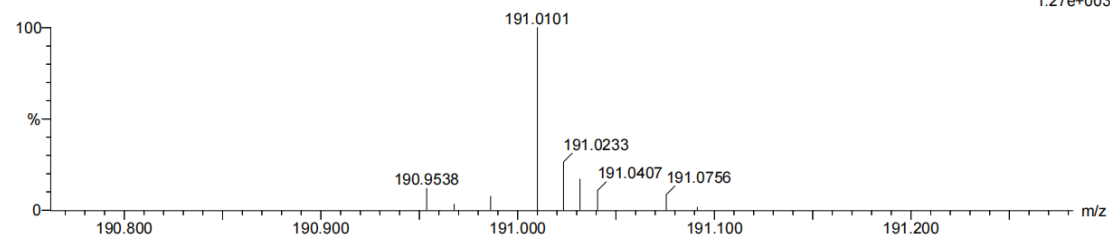
Elements Used:

C: 9-9 H: 9-9 O: 0-37 Cl: 1-4 Na: 0-3

3

221127-1-263-2-5b 30 (0.182)

1: TOF MS ES+
1.27e+003



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
191.0233	191.0240	-0.7	-3.7	4.5	56.7	n/a	n/a	C9 H9 O Cl Na

Supplementary Fig. 432 | HRMS (ESI) of (S)-4a.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

43 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

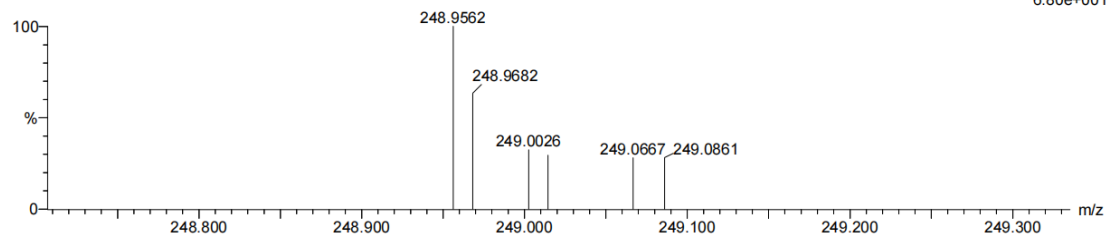
Elements Used:

C: 9-9 H: 11-11 O: 0-41 Na: 0-3 Cl: 1-2 Br: 1-1

8

230220-6-297-1-4a 43 (0.475)

1: TOF MS ES+
6.80e+001



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
248.9682	248.9682	0.0	0.0	3.5	41.0	n/a	n/a	C9 H11 O Cl Br

Supplementary Fig. 433 | HRMS (ESI) of (R)-4b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

39 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

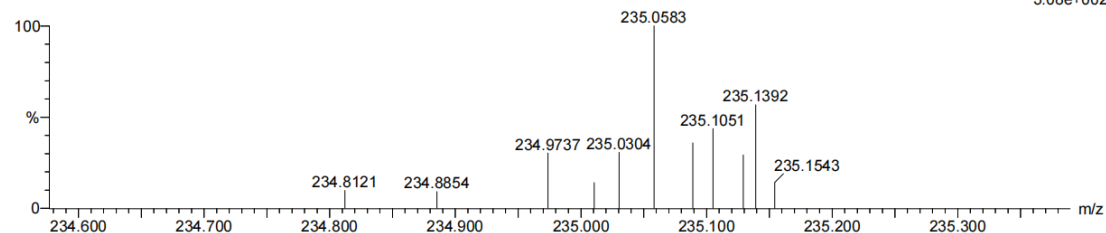
Elements Used:

C: 9-9 H: 9-9 O: 0-37 Br: 1-5 Na: 0-3

3

221127-1-263-2-8b 16 (0.109)

1: TOF MS ES+
3.08e+002



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
234.9737	234.9734	0.3	1.3	4.5	92.7	n/a	n/a	C9 H9 O Br Na

Supplementary Fig. 434 | HRMS (ESI) of (S)-5a.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

352 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

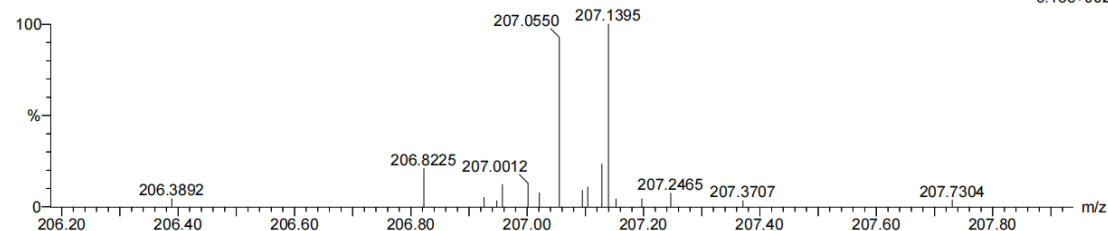
Elements Used:

C: 10-10 H: 13-13 N: 0-100 O: 0-100 Na: 0-4 Cl: 1-2

37

240925-4-S-O-Me 12 (0.100)

1: TOF MS ES+
5.18e+002



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
207.0550	207.0553	-0.3	-1.4	3.5	91.1	n/a	n/a	C10 H13 O Na Cl

Supplementary Fig. 435 | HRMS (ESI) of (R)-5b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

30 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

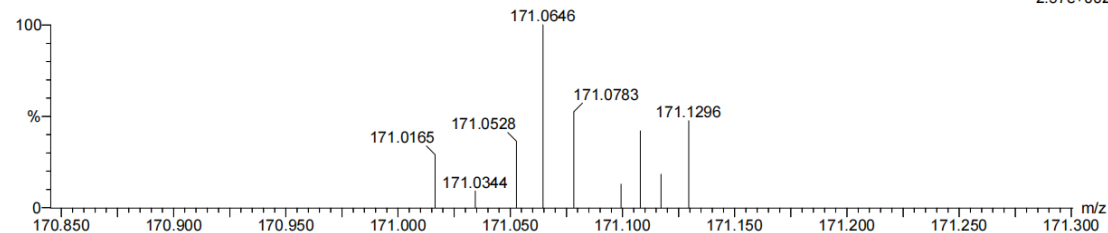
Elements Used:

C: 10-10 H: 12-12 O: 0-37 Na: 0-3

3

221127-1-263-2-11b 76 (0.440)

1: TOF MS ES+
2.57e+002



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
171.0783	171.0786	-0.3	-1.8	4.5	50.2	n/a	n/a	C10 H12 O Na

Supplementary Fig. 436 | HRMS (ESI) of (*S*)-6a.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

43 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

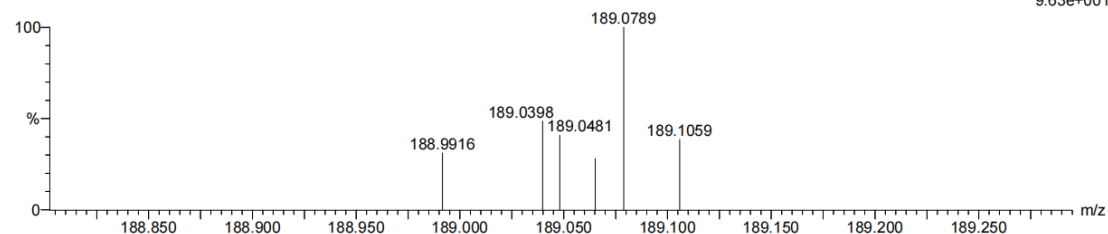
Elements Used:

C: 9-9 H: 11-11 O: 0-41 F: 1-1 Na: 0-3 Cl: 1-2

8

230220-6-297-1-6a 39 (0.433)

1: TOF MS ES+
9.63e+001



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
189.0481	189.0482	-0.1	-0.5	3.5	37.8	n/a	n/a	C9 H11 O F Cl

Supplementary Fig. 437 | HRMS (ESI) of (*R*)-6b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

21 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

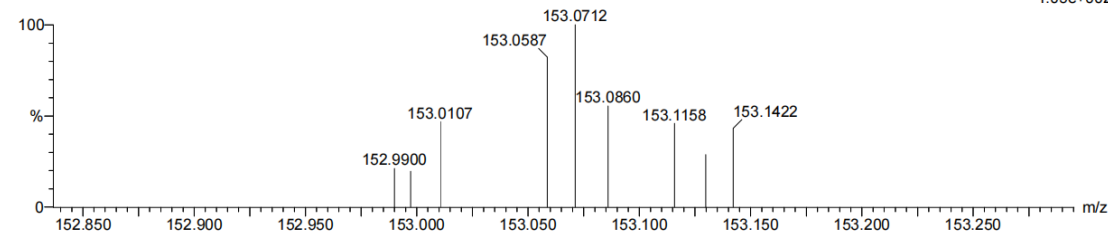
Elements Used:

C: 9-9 H: 10-10 O: 0-37 F: 1-3

3

221127-1-263-2-3b 80 (0.461)

1: TOF MS ES+
1.05e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
153.0712	153.0716	-0.4	-2.6	4.5	45.7	n/a	n/a	C9 H10 O F

Supplementary Fig. 438 | HRMS (ESI) of (S)-7a.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

305 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

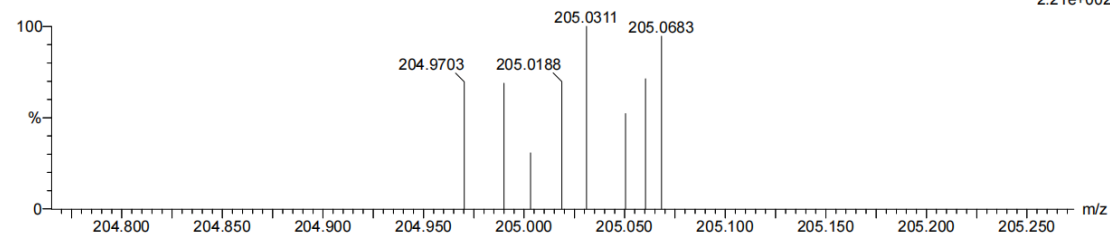
Elements Used:

C: 9-9 H: 11-11 N: 0-10 O: 0-17 Na: 0-3 Cl: 1-2

15

230210-3-291-1-7a 3 (0.051)

1: TOF MS ES+
2.21e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
205.0188	205.0187	0.1	0.5	3.5	60.3	n/a	n/a	C9 H11 O Cl2

Supplementary Fig. 439 | HRMS (ESI) of (R)-7b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

253 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

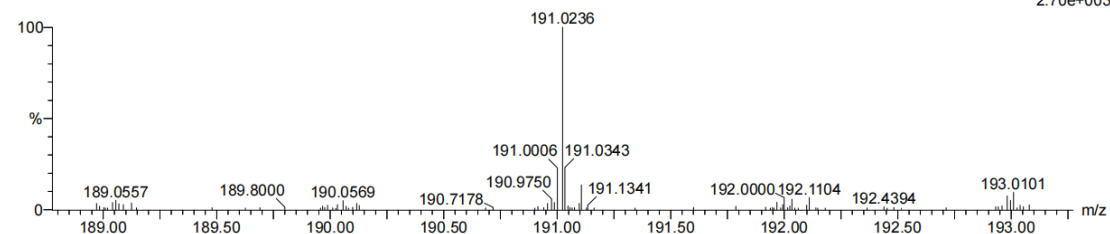
Elements Used:

C: 9-9 H: 9-9 N: 0-10 O: 0-17 Na: 0-3 Cl: 1-2

15

230210-3-291-1-7b 43 (0.475)

1: TOF MS ES+
2.70e+003



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
191.0236	191.0240	-0.4	-2.1	4.5	367.6	n/a	n/a	C9 H9 O Na Cl

Supplementary Fig. 440 | HRMS (ESI) of (*S*)-**8a**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

303 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

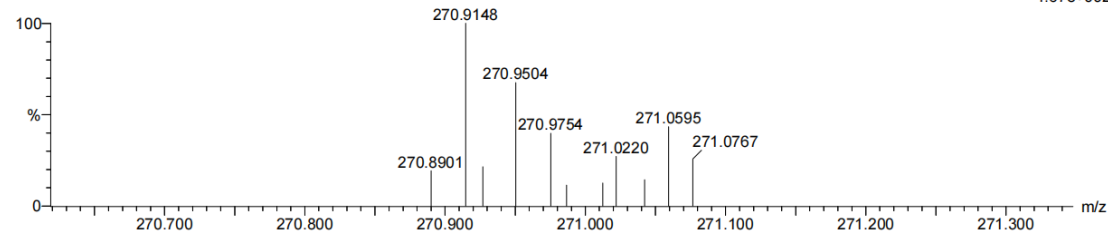
Elements Used:

C: 9-9 H: 10-10 N: 0-10 O: 0-17 Na: 0-3 Cl: 1-2 Br: 1-5

15

230210-3-291-1-8a 27 (0.305)

1: TOF MS ES+
1.67e+002



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
270.9504	270.9501	0.3	1.1	3.5	70.0	n/a	n/a	C9 H10 O Na Cl Br

Supplementary Fig. 441 | HRMS (ESI) of (*R*)-**8b**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

79 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

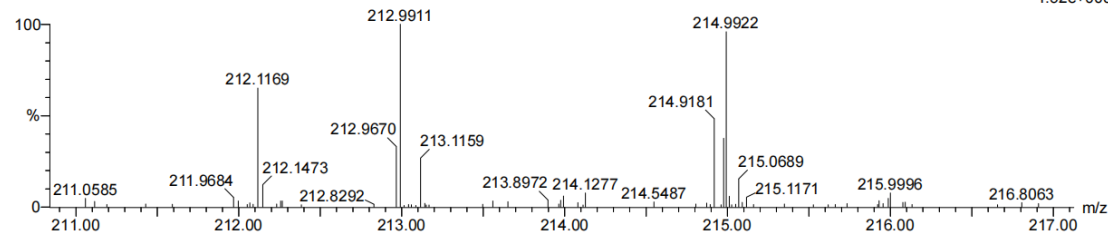
Elements Used:

C: 9-9 H: 10-10 N: 0-100 O: 0-100 Na: 0-1 Br: 1-1

37

240928-2-R-M-Br 8 (0.079)

1: TOF MS ES+
1.52e+003



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
212.9911	212.9915	-0.4	-1.9	4.5	253.6	n/a	n/a	C9 H10 O Br

Supplementary Fig. 442 | HRMS (ESI) of (*S*)-**9a**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

421 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

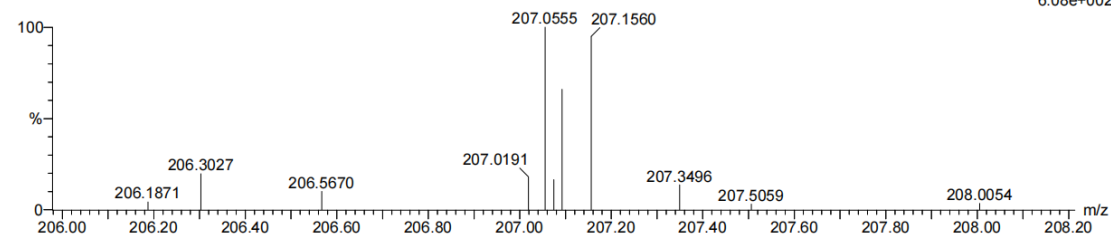
Elements Used:

C: 10-10 H: 13-13 N: 0-100 O: 0-100 Na: 0-4 Cl: 1-3

28

241229-2-S-3-ME-1 12 (0.060)

1: TOF MS ES+
6.08e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
207.0555	207.0553	0.2	1.0	3.5	76.9	n/a	n/a	C10 H13 O Na Cl

Supplementary Fig. 443 | HRMS (ESI) of (*R*)-**9b**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

151 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

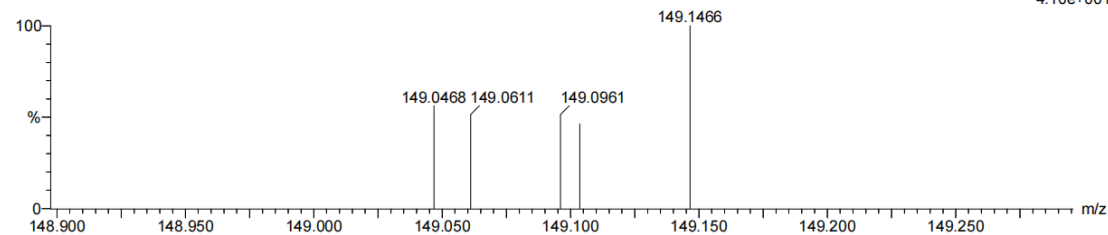
Elements Used:

C: 10-10 H: 13-13 N: 0-10 O: 0-17 Na: 0-3

15

230210-3-291-1-9b 22 (0.254)

1: TOF MS ES+
4.10e+001



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
149.0961	149.0966	-0.5	-3.4	4.5	23.8	n/a	n/a	C10 H13 O

Supplementary Fig. 444 | HRMS (ESI) of (S)-10a.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

299 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

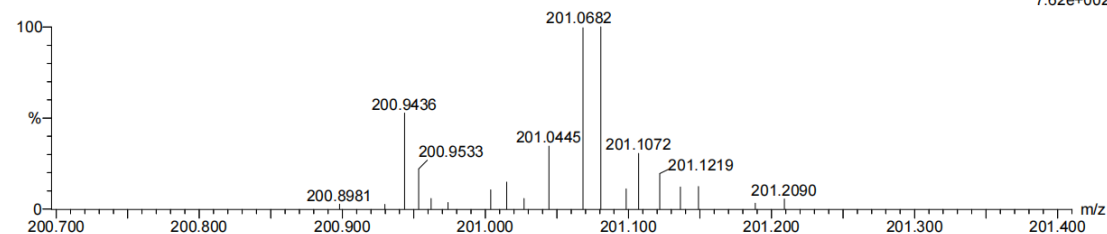
Elements Used:

C: 10-10 H: 14-14 N: 0-10 O: 0-17 Na: 0-3 Cl: 1-2

15

230210-3-291-1-10a 20 (0.229)

1: TOF MS ES+
7.62e+02



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
201.0682	201.0682	0.0	0.0	3.5	97.8	n/a	n/a	C10 H14 O2 Cl

Supplementary Fig. 445 | HRMS (ESI) of (R)-10b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

224 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

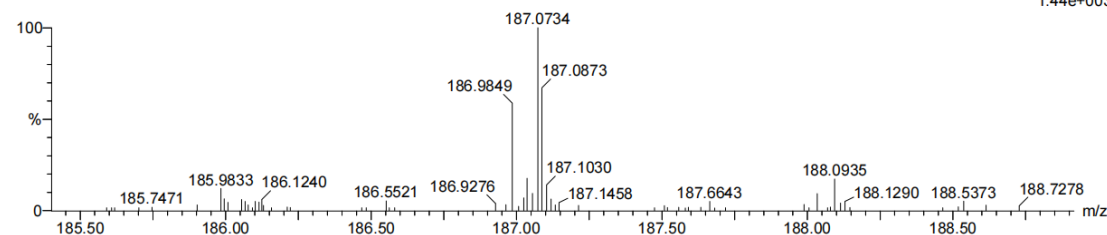
Elements Used:

C: 10-10 H: 12-12 N: 0-10 O: 0-17 Na: 0-3

15

230210-3-291-1-10b 7 (0.093)

1: TOF MS ES+
1.44e+03



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
187.0734	187.0735	-0.1	-0.5	4.5	239.0	n/a	n/a	C10 H12 O2 Na

Supplementary Fig. 446 | HRMS (ESI) of (*S*)-11a.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

501 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

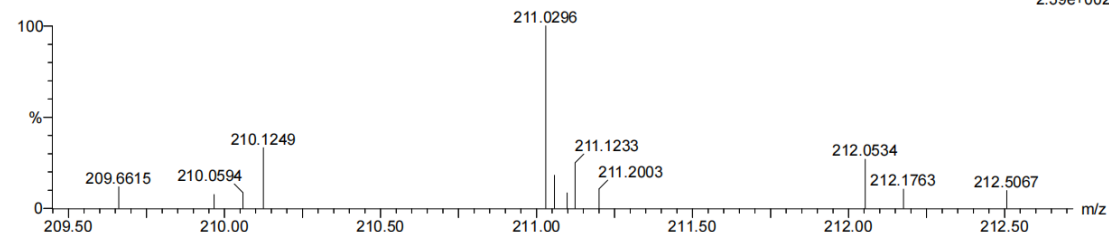
Elements Used:

C: 9-9 H: 10-10 N: 0-100 O: 0-100 Na: 0-1 Cl: 1-4 F: 1-3

37

240928-2-S-P-F 73 (0.459)

1: TOF MS ES+
2.39e+002



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
211.0296	211.0302	-0.6	-2.8	3.5	65.7	n/a	n/a	C ₉ H ₁₀ O Na Cl F

Supplementary Fig. 447 | HRMS (ESI) of (*R*)-11b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

21 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

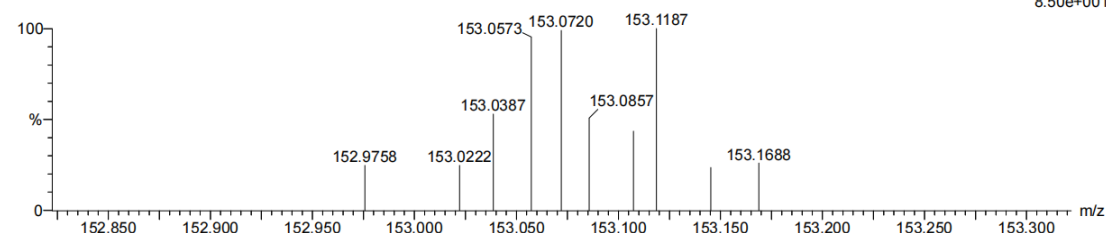
Elements Used:

C: 9-9 H: 10-10 O: 0-37 F: 1-3

3

221127-1-263-2-4b 17 (0.114)

1: TOF MS ES+
8.50e+001



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
153.0720	153.0716	0.4	2.6	4.5	50.6	n/a	n/a	C ₉ H ₁₀ O F

Supplementary Fig. 448 | HRMS (ESI) of (*S*)-12a.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

155 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

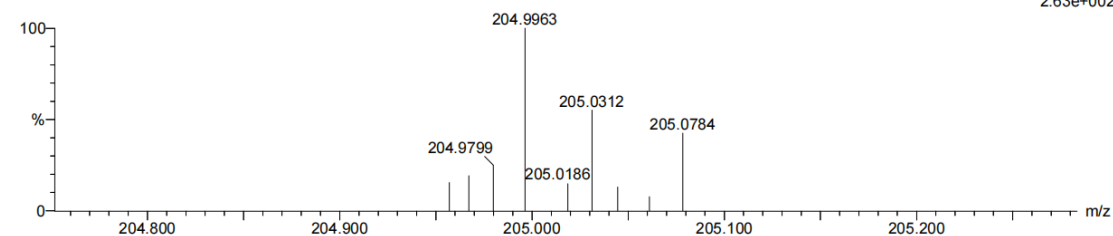
Elements Used:

C: 9-9 H: 11-11 N: 0-20 O: 0-37 Cl: 1-4

3

221127-1-263-2-7a 26 (0.161)

1: TOF MS ES+
2.63e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
205.0186	205.0187	-0.1	-0.5	3.5	48.3	n/a	n/a	C9 H11 O Cl2

Supplementary Fig. 449 | HRMS (ESI) of (*R*)-12b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

93 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

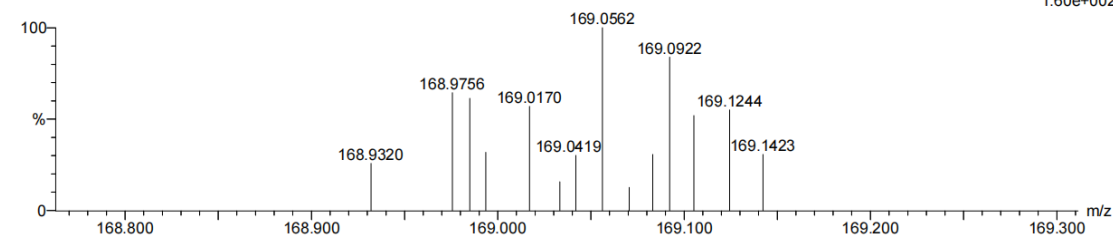
Elements Used:

C: 9-9 H: 10-10 N: 0-20 O: 0-37 Cl: 1-4

3

221127-1-263-2-7b 29 (0.177)

1: TOF MS ES+
1.60e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
169.0419	169.0420	-0.1	-0.6	4.5	74.8	n/a	n/a	C9 H10 O Cl

Supplementary Fig. 450 | HRMS (ESI) of (*S*)-**13a**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

303 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

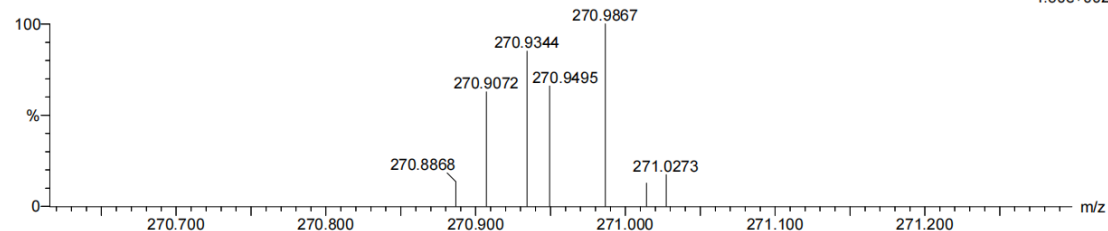
Elements Used:

C: 9-9 H: 10-10 N: 0-10 O: 0-17 Na: 0-3 Cl: 1-2 Br: 1-5

15

230210-3-291-1-13a 13 (0.161)

1: TOF MS ES+
1.50e+002



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
270.9495	270.9501	-0.6	-2.2	3.5	41.5	n/a	n/a	C ₉ H ₁₀ O Na Cl Br

Supplementary Fig. 451 | HRMS (ESI) of (*R*)-**13b**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

39 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

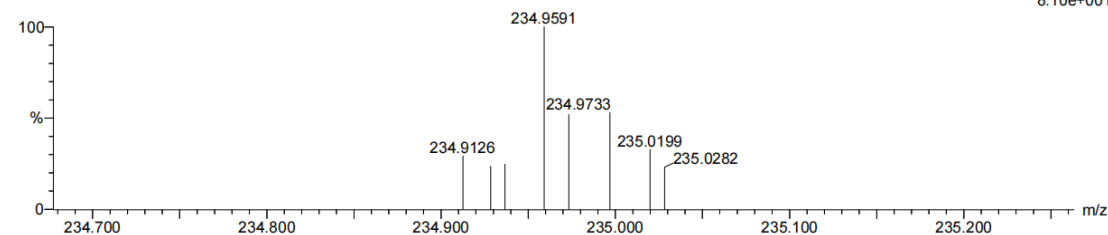
Elements Used:

C: 9-9 H: 9-9 O: 0-37 Na: 0-3 Br: 1-5

3

221127-1-263-2-10b 62 (0.366)

1: TOF MS ES+
8.10e+001



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
234.9733	234.9734	-0.1	-0.4	4.5	36.5	n/a	n/a	C ₉ H ₉ O Na Br

Supplementary Fig. 452 | HRMS (ESI) of (S)-14a.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

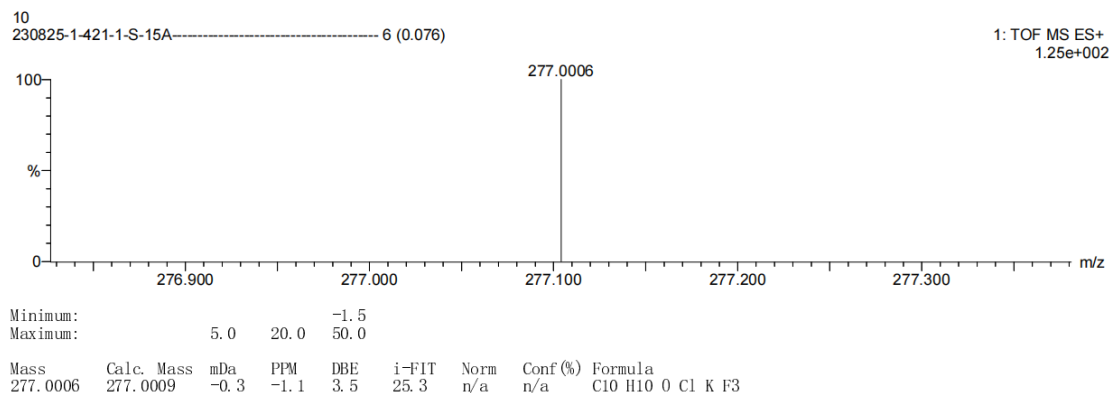
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

23 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 10-10 H: 10-10 O: 0-100 Cl: 1-4 K: 1-1 F: 3-3



Supplementary Fig. 453 | HRMS (ESI) of (R)-14b.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

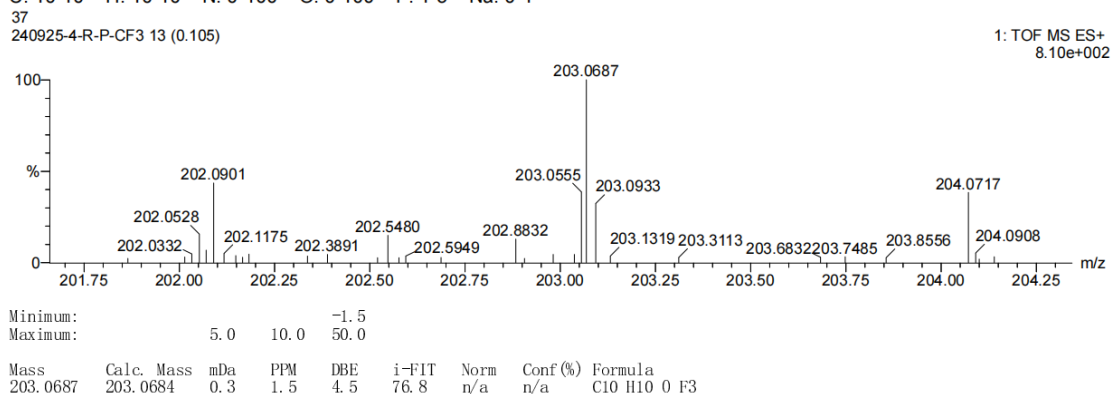
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

603 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 10-10 H: 10-10 N: 0-100 O: 0-100 F: 1-3 Na: 0-4



Supplementary Fig. 454 | HRMS (ESI) of (S)-15a.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

831 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

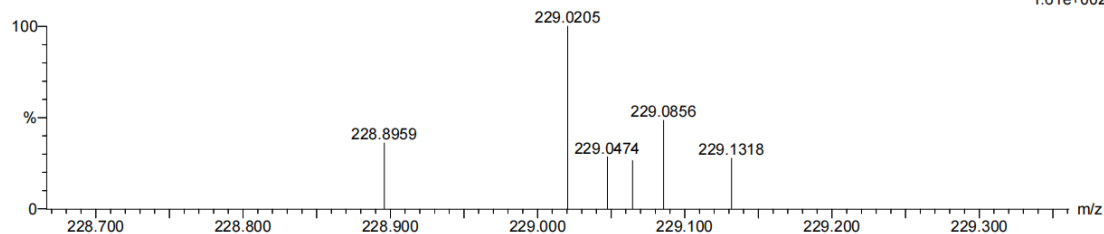
Elements Used:

C: 9-9 H: 9-9 N: 0-100 O: 0-100 F: 1-3 Na: 0-4 Cl: 1-2

37

240925-4-S-3-5-2F 72 (0.454)

1: TOF MS ES+
1.61e+002



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
229.0205	229.0208	-0.3	-1.3	3.5	50.5	n/a	n/a	C9 H9 O F2 Na Cl

Supplementary Fig. 455 | HRMS (ESI) of (R)-15b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

117 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

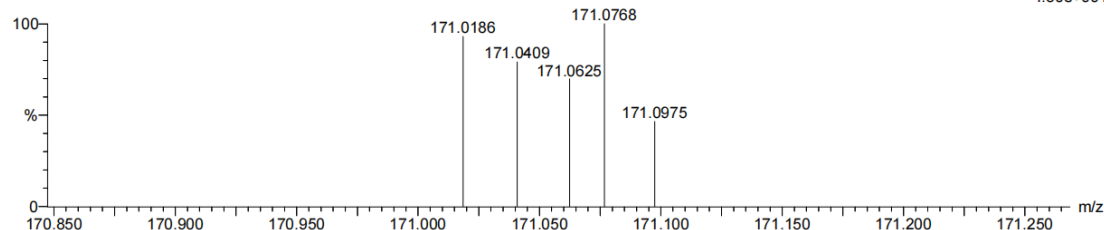
Elements Used:

C: 9-9 H: 9-9 N: 0-20 O: 0-20 F: 2-2 Na: 0-3

10

230416-8-337-3-14a 44 (0.483)

1: TOF MS ES+
4.30e+001



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
171.0625	171.0621	0.4	2.3	4.5	24.5	n/a	n/a	C9 H9 O F2

Supplementary Fig. 456 | HRMS (ESI) of (S)-16a.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

33 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

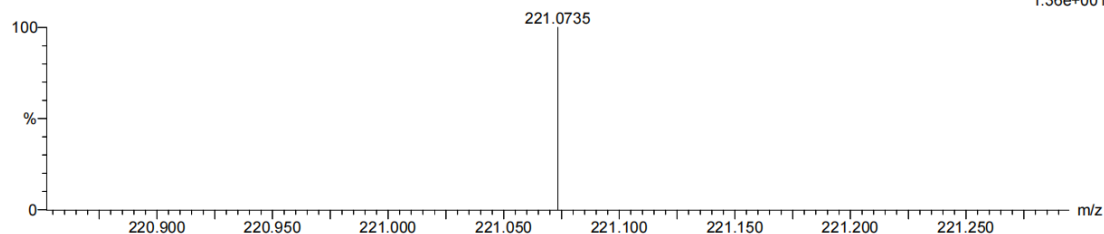
Elements Used:

C: 13-13 H: 14-14 O: 0-100 Cl: 1-4

10

230825-1-421-1-S-17A----- 15 (0.154)

1: TOF MS ES+
1.36e+001



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
221.0735	221.0733	0.2	0.9	6.5	11.6	n/a	n/a	C13 H14 O Cl

Supplementary Fig. 457 | HRMS (ESI) of (R)-16b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

154 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

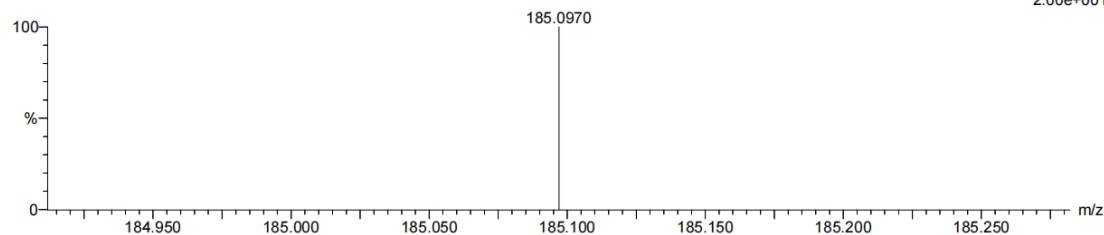
Elements Used:

C: 13-13 H: 13-13 N: 0-100 O: 0-100 Na: 0-1

10

230825-1-421-1-R-17B----- 27 (0.265)

1: TOF MS ES+
2.00e+001



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
185.0970	185.0966	0.4	2.2	7.5	10.8	n/a	n/a	C13 H13 O

Supplementary Fig. 458 | HRMS (ESI) of (S)-17a.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

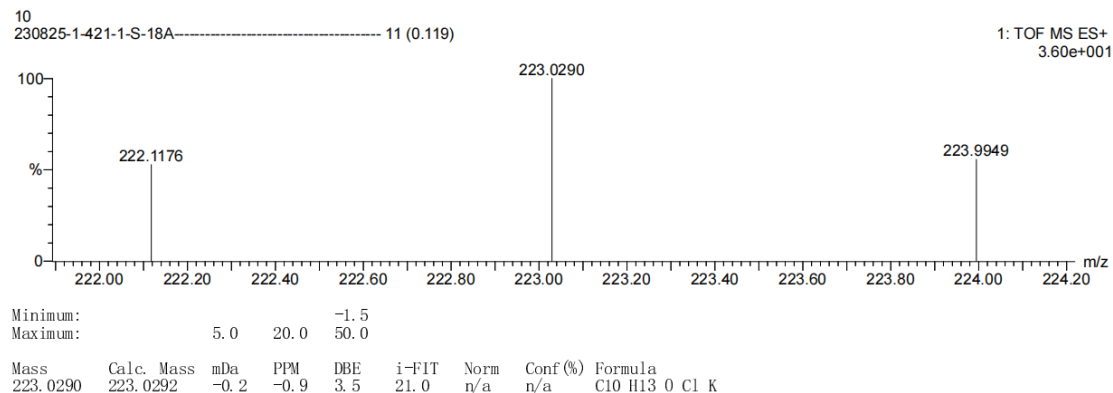
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

42 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 10-10 H: 13-13 O: 0-100 Cl: 1-4 K: 1-1 Na: 0-1



Supplementary Fig. 459 | HRMS (ESI) of (R)-17b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

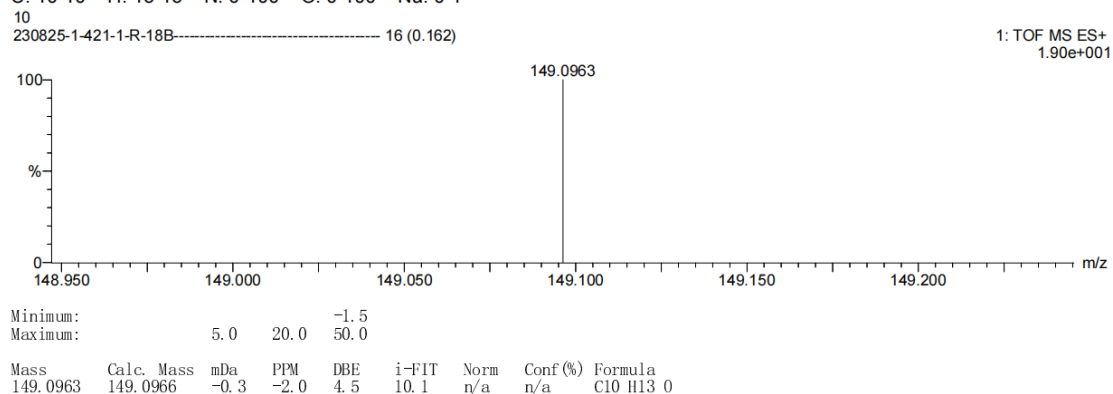
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

99 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 10-10 H: 13-13 N: 0-100 O: 0-100 Na: 0-1



Supplementary Fig. 460 | HRMS (ESI) of (S)-18a.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

212 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

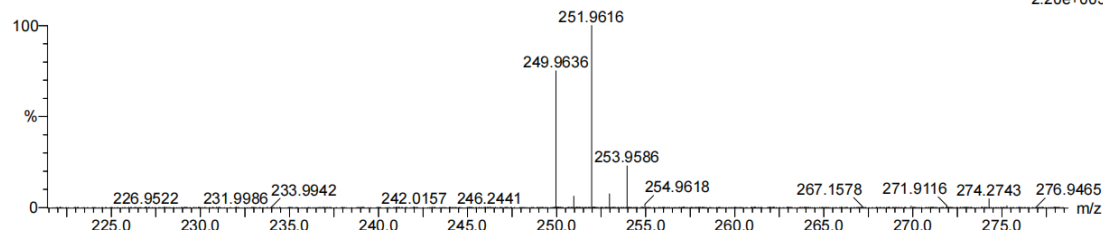
Elements Used:

C: 8-8 H: 10-10 N: 0-100 O: 0-100 Na: 0-4 Cl: 1-2 Br: 1-4

37

240925-4-S-3Brbd 12 (0.100)

1: TOF MS ES+
2.20e+005



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
249.9636	249.9634	0.2	0.8	3.5	658.2	n/a	n/a	C8 H10 N 0 Cl Br

Supplementary Fig. 461 | HRMS (ESI) of (R)-18b.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

142 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

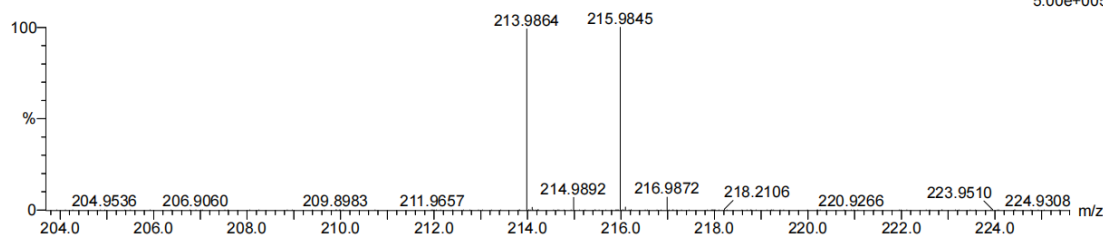
Elements Used:

C: 8-8 H: 9-9 N: 0-20 O: 0-100 Na: 0-4 Br: 1-4

32

240108-4-506-5-R-3-brbd 13 (0.070)

1: TOF MS ES+
5.00e+005



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
213.9864	213.9868	-0.4	-1.9	4.5	249.7	n/a	n/a	C8 H9 N 0 Br

Supplementary Fig. 462 | HRMS (ESI) of (*S*)-19a.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

181 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

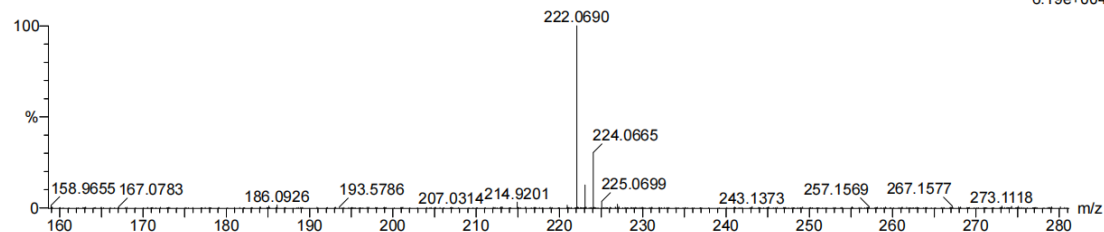
Elements Used:

C: 12-12 H: 13-13 N: 0-100 O: 0-100 Cl: 1-3

28

241229-2-S-3KL-1 50 (0.132)

1: TOF MS ES+
6.19e+004



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
222.0690	222.0686	0.4	1.8	6.5	275.7	n/a	n/a	Cl2 H13 N 0 Cl

Supplementary Fig. 463 | HRMS (ESI) of (*R*)-19b.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

150 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

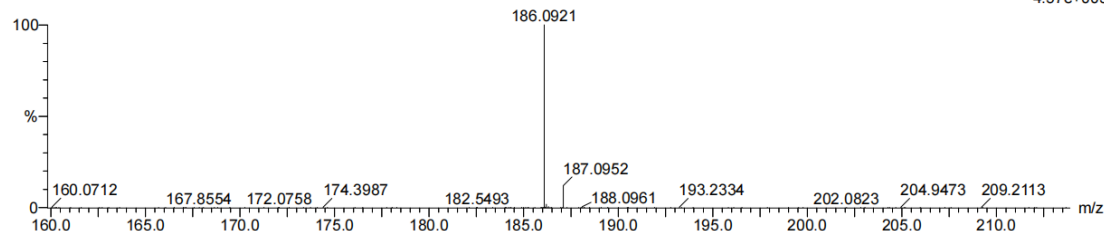
Elements Used:

C: 12-12 H: 12-12 N: 0-100 O: 0-100 Na: 0-1

30

240128-1-521-1-R-3-KL-HY 9 (0.069)

1: TOF MS ES+
4.57e+005



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
186.0921	186.0919	0.2	1.1	7.5	152.6	n/a	n/a	Cl2 H12 N 0

Supplementary Fig. 464 | HRMS (ESI) of (S)-20a.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

155 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

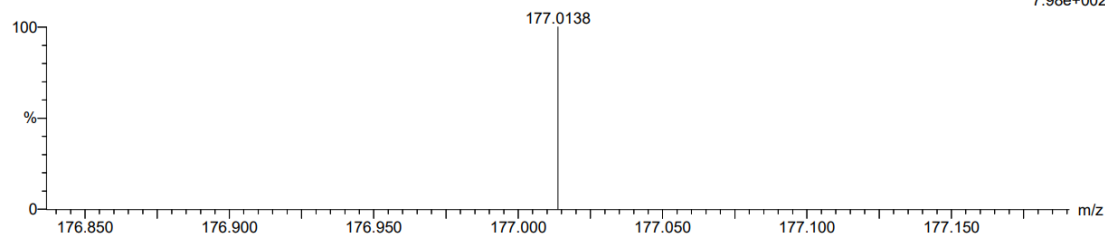
Elements Used:

C: 7-7 H: 10-10 N: 0-200 O: 0-200 Na: 0-2 S: 1-2 Cl: 1-4

8

231022-1-452-2-20A 17 (0.183)

1: TOF MS ES+
7.98e+002



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
177.0138	177.0141	-0.3	-1.7	2.5	22.8	n/a	n/a	C7 H10 O S Cl

Supplementary Fig. 465 | HRMS (ESI) of (S)-21a.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

245 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

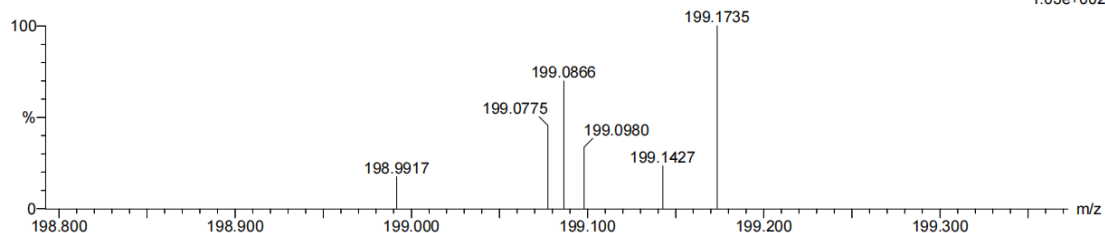
Elements Used:

C: 9-9 H: 17-17 N: 0-100 O: 0-100 Na: 0-1 Cl: 1-4

37

240928-2-S-HJJ 12 (0.100)

1: TOF MS ES+
1.03e+002



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
199.0866	199.0866	0.0	0.0	0.5	39.4	n/a	n/a	C9 H17 O Na Cl

Supplementary Fig. 466 | HRMS (ESI) of (R)-21b.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

86 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

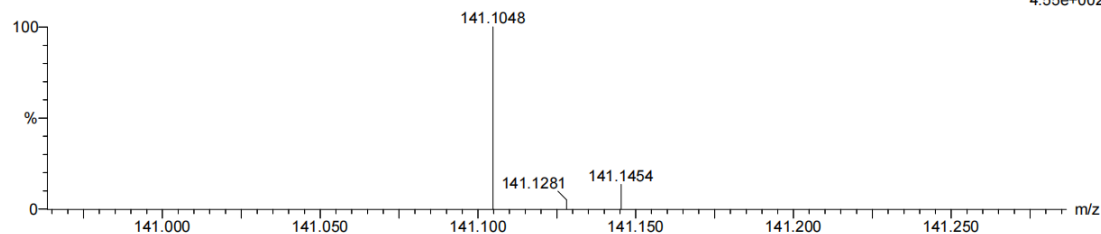
Elements Used:

C: 9-9 H: 17-17 N: 0-100 O: 0-100 Na: 0-1

28

240422-3-r-22b 19 (0.219)

1: TOF MS ES+
4.55e+002



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
141.1281	141.1279	0.2	1.4	1.5	18.2	n/a	n/a	C9 H17 O

Supplementary Fig. 467 | HRMS (ESI) of (R)-22a.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

74 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

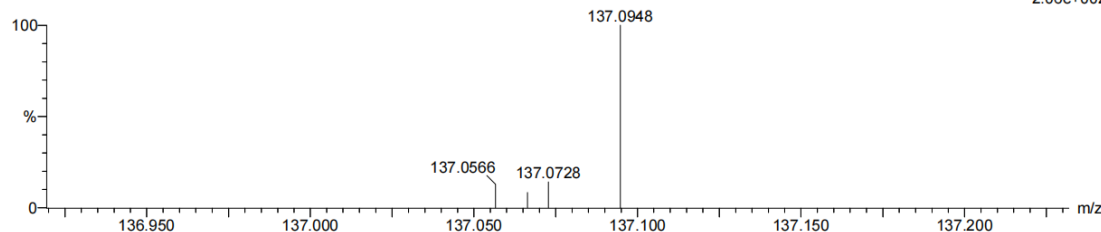
Elements Used:

C: 6-6 H: 14-14 N: 0-100 O: 0-100 Na: 0-1 Cl: 1-5

37

241001-10-S-ZBJ 9 (0.084)

1: TOF MS ES+
2.06e+002



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
137.0728	137.0733	-0.5	-3.6	-0.5	24.1	n/a	n/a	C6 H14 O Cl

Supplementary Fig. 468 | HRMS (ESI) of (*S*)-**23a**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

217 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

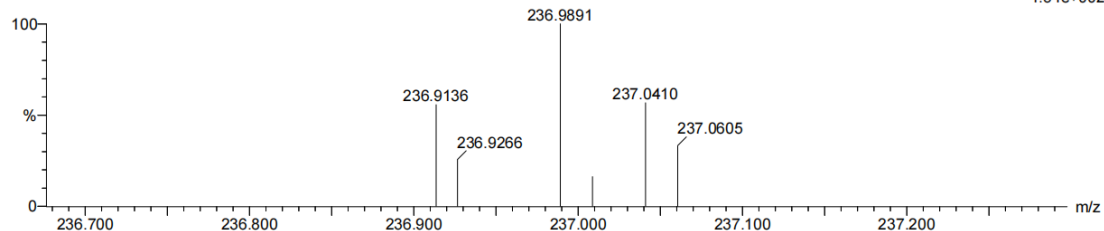
Elements Used:

C: 9-9 H: 11-11 N: 0-100 O: 0-100 Na: 0-4 Br: 1-4

37

240925-4-S-Br-OH-1 17 (0.126)

1: TOF MS ES+
1.54e+002



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
236.9891	236.9891	0.0	0.0	3.5	42.9	n/a	n/a	C9 H11 O Na Br

Supplementary Fig. 469 | HRMS (ESI) of (*R*)-**1b** from **23a**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

26 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

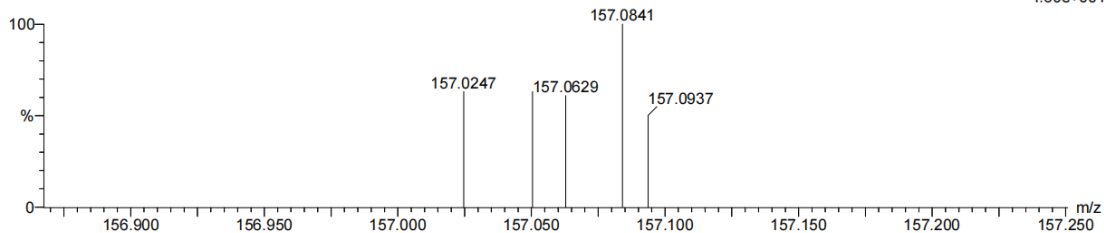
Elements Used:

C: 9-9 H: 10-10 O: 0-20 Na: 0-3

10

230416-8-337-3-15b 16 (0.187)

1: TOF MS ES+
4.60e+001



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
157.0629	157.0629	0.0	0.0	4.5	24.6	n/a	n/a	C9 H10 O Na

Supplementary Fig. 470 | HRMS (ESI) of (*S*)-**24a**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

35 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

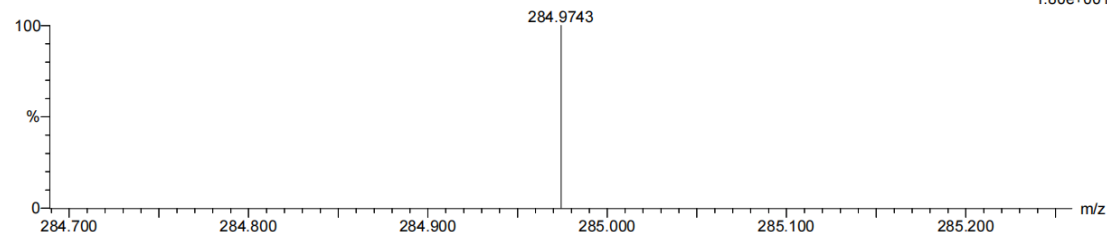
Elements Used:

C: 9-9 H: 11-11 O: 0-100 Na: 0-4 I: 1-2

32

240108-4-506-5-S-I-OH 11 (0.063)

1: TOF MS ES+
1.80e+001



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
284.9743	284.9752	-0.9	-3.2	3.5	10.7	n/a	n/a	C9 H11 O Na I

Supplementary Fig. 471 | HRMS (ESI) of (*R*)-**1b** from **24a**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

45 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

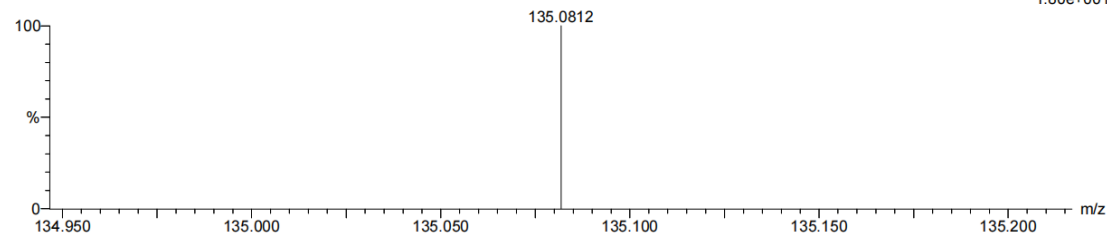
Elements Used:

C: 9-9 H: 11-11 N: 0-100 O: 0-100

30

240128-1-521-1-RI-I-OH-HY 16 (0.094)

1: TOF MS ES+
1.80e+001



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
135.0812	135.0810	0.2	1.5	4.5	9.8	n/a	n/a	C9 H11 O

Supplementary Fig. 472 | HRMS (ESI) of (S)-1b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

120 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

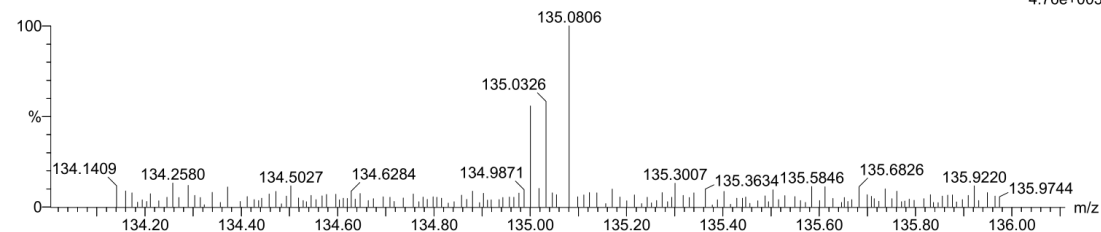
Elements Used:

C: 9-9 H: 11-11 N: 0-22 O: 0-47 Na: 0-3

3

221206-1-267-3-1b 20 (0.130)

1: TOF MS ES+
4.76e+003



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
135.0806	135.0810	-0.4	-3.0	4.5	818.7	n/a	n/a	C9 H11 O

Supplementary Fig. 473 | HRMS (ESI) of (R)-1c.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

243 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

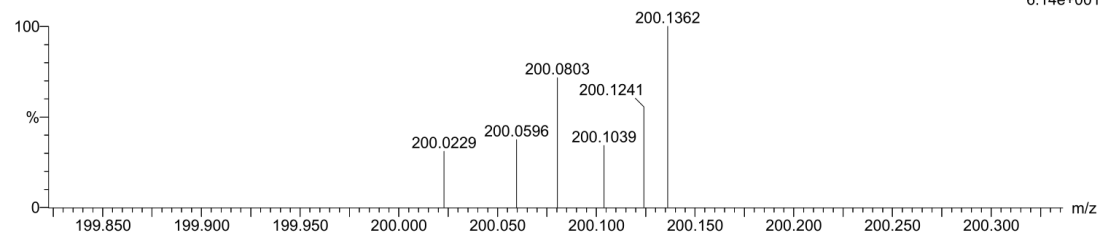
Elements Used:

C: 9-9 H: 11-11 N: 0-10 O: 0-17 Na: 0-3

15

230210-3-291-3-H-OH 21 (0.246)

1: TOF MS ES+
6.14e+001



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
200.0803	200.0800	0.3	1.5	5.5	34.0	n/a	n/a	C9 H11 N3 O Na

Supplementary Fig. 474 | HRMS (ESI) of (S)-2b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

118 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

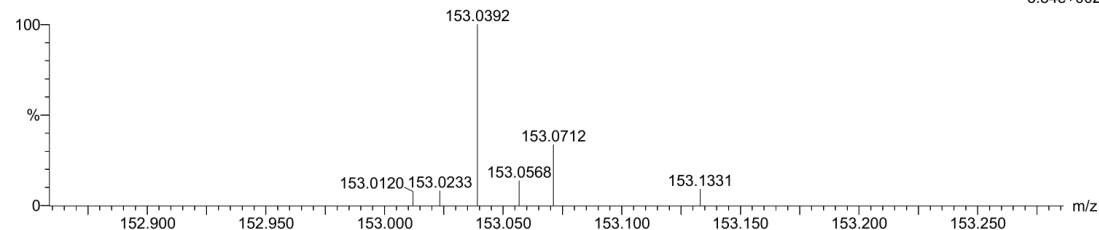
Elements Used:

C: 9-9 H: 10-10 N: 0-10 O: 0-23 Na: 0-3 F: 1-1

3

230215-2-294-1-2F-OXE 8 (0.102)

1: TOF MS ES+
3.84e+002



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
153.0712	153.0716	-0.4	-2.6	4.5	23.1	n/a	n/a	C9 H10 O F

Supplementary Fig. 475 | HRMS (ESI) of (R)-2c.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

235 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

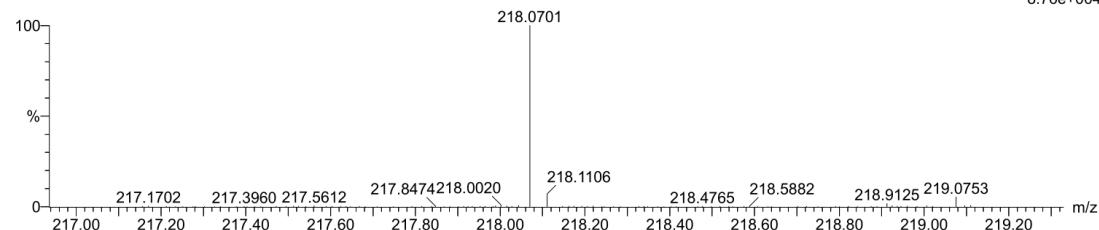
Elements Used:

C: 9-9 H: 0-100 N: 0-50 O: 0-50 Na: 1-1 F: 1-4

14

221119-2-160-4-2C 12 (0.088)

1: TOF MS ES+
8.76e+004



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
218.0701	218.0706	-0.5	-2.3	5.5	470.1	n/a	n/a	C9 H10 N3 O Na F

Supplementary Fig. 476 | HRMS (ESI) of (*S*)-**3b**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

273 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

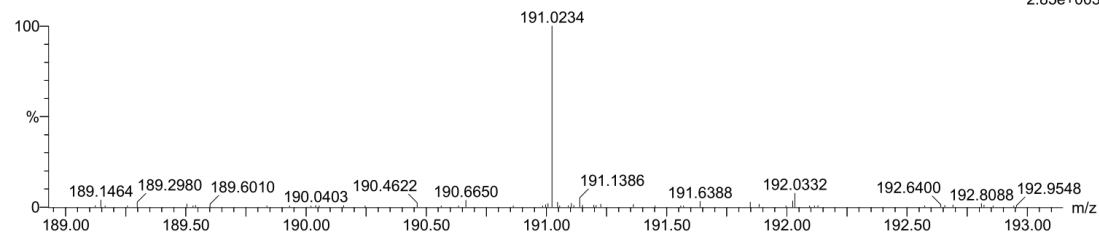
Elements Used:

C: 9-9 H: 9-9 N: 0-100 O: 0-100 Na: 0-4 Cl: 1-2

1

240924-3-S-3B 12 (0.100)

1: TOF MS ES+
2.85e+003



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
191.0234	191.0240	-0.6	-3.1	4.5	242.1	n/a	n/a	C9 H9 O Na Cl

Supplementary Fig. 477 | HRMS (ESI) of (*R*)-**3c**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

80 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

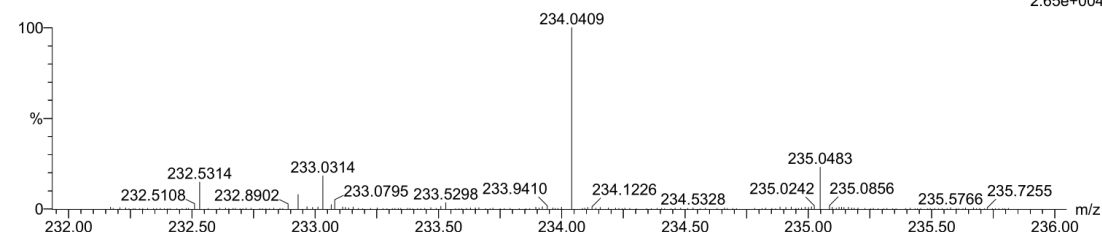
Elements Used:

C: 9-9 H: 0-100 N: 0-50 O: 0-50 Cl: 1-1 Na: 1-1

14

221119-2-160-4-6C 19 (0.125)

1: TOF MS ES+
2.65e+004



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
234.0409	234.0410	-0.1	-0.4	5.5	818.0	n/a	n/a	C9 H10 N3 O Cl Na

Supplementary Fig. 478 | HRMS (ESI) of (*S*)-4b.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

209 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

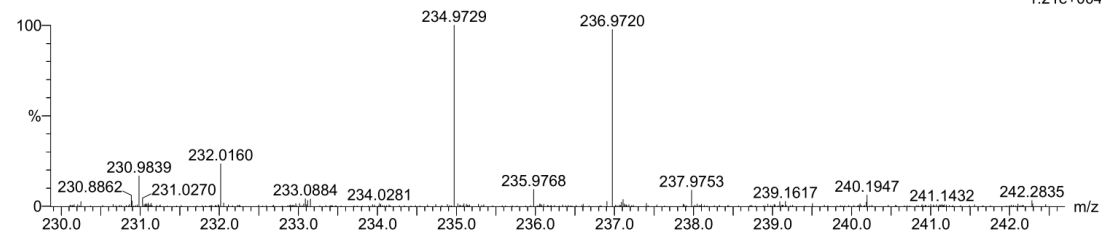
Elements Used:

C: 9-9 H: 9-9 N: 0-100 O: 0-100 Na: 0-4 Br: 1-4

1

240924-3-S-4B 12 (0.100)

1: TOF MS ES+
1.21e+004



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
234.9729	234.9734	-0.5	-2.1	4.5	470.7	n/a	n/a	C9 H9 O Na Br

Supplementary Fig. 479 | HRMS (ESI) of (*R*)-4c.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

392 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

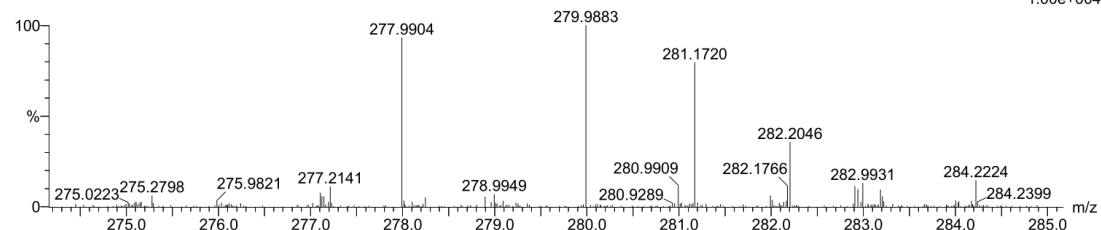
Elements Used:

C: 9-9 H: 10-10 N: 0-100 O: 0-100 Na: 0-4 Br: 1-4

1

240924-3-R-4C 12 (0.100)

1: TOF MS ES+
1.00e+004



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
277.9904	277.9905	-0.1	-0.4	5.5	515.7	n/a	n/a	C9 H10 N3 O Na Br

Supplementary Fig. 480 | HRMS (ESI) of (*S*)-**5b**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

151 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

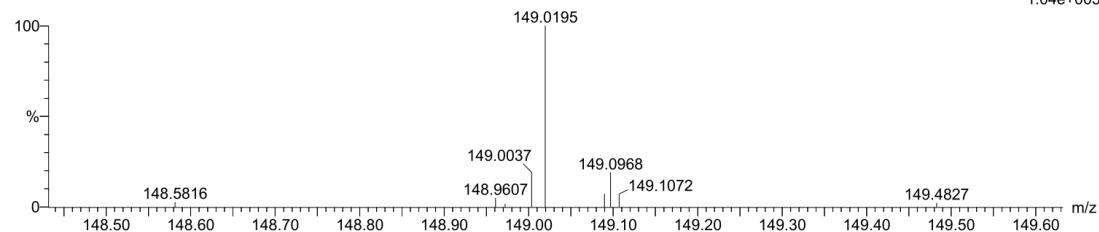
Elements Used:

C: 10-10 H: 13-13 N: 0-10 O: 0-23 Na: 0-3

3

230215-2-294-1-2me-oxe 9 (0.118)

1: TOF MS ES+
1.04e+003



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
149.0968	149.0966	0.2	1.3	4.5	32.2	n/a	n/a	C10 H13 O

Supplementary Fig. 481 | HRMS (ESI) of (*R*)-**5c**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

278 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

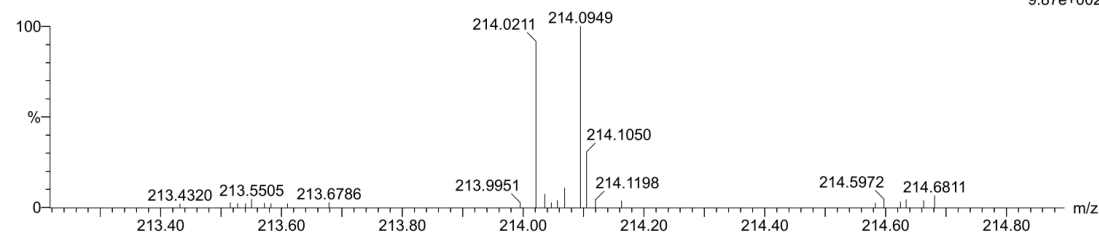
Elements Used:

C: 10-10 H: 13-13 N: 0-10 O: 0-17 Na: 0-3

15

230210-3-291-3-2me-OH 6 (0.085)

1: TOF MS ES+
9.87e+002



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
214.0949	214.0956	-0.7	-3.3	5.5	92.6	n/a	n/a	C10 H13 N3 O Na

Supplementary Fig. 482 | HRMS (ESI) of (*S*)-**6b**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

118 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

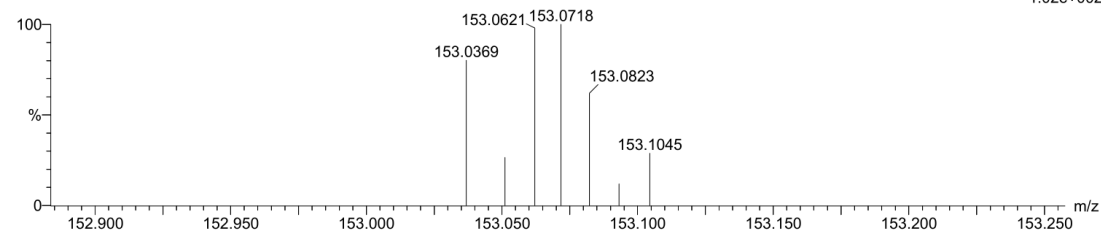
Elements Used:

C: 9-9 H: 10-10 N: 0-10 O: 0-23 F: 1-1 Na: 0-3

3

230215-2-294-1-3f-oxe 3 (0.051)

1: TOF MS ES+
1.02e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
153.0718	153.0716	0.2	1.3	4.5	35.4	n/a	n/a	C9 H10 O F

Supplementary Fig. 483 | HRMS (ESI) of (*R*)-**6c**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

517 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

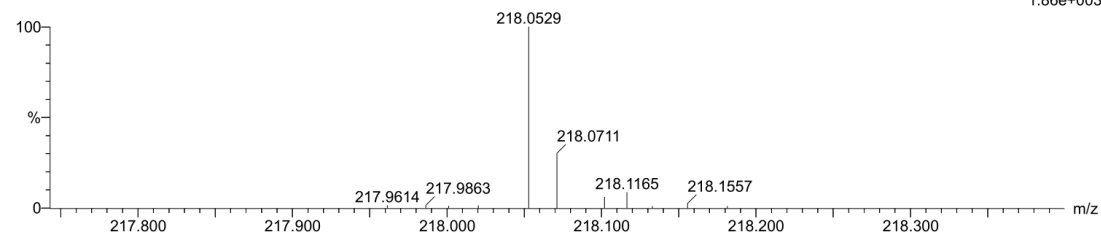
Elements Used:

C: 9-9 H: 10-10 N: 0-100 O: 0-100 F: 1-2 Na: 0-4

1

240924-3-R-6C 14 (0.110)

1: TOF MS ES+
1.86e+003



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
218.0711	218.0706	0.5	2.3	5.5	59.7	n/a	n/a	C9 H10 N3 O F Na

Supplementary Fig. 484 | HRMS (ESI) of (S)-7b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

93 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

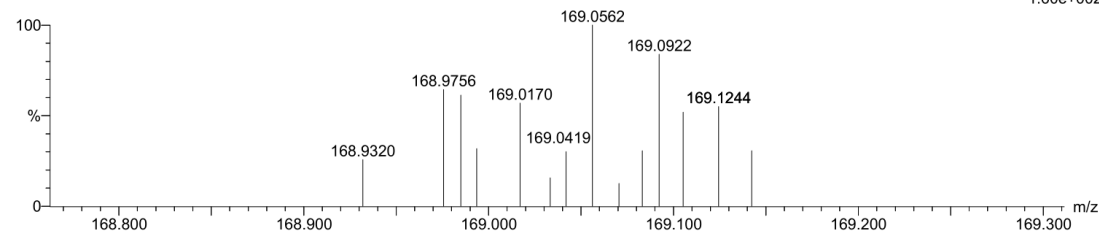
Elements Used:

C: 9-9 H: 10-10 N: 0-20 O: 0-37 Cl: 1-4

3

221127-1-263-2-7b 29 (0.177)

1: TOF MS ES+
1.60e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
169.0419	169.0420	-0.1	-0.6	4.5	74.8	n/a	n/a	C9 H10 O Cl

Supplementary Fig. 485 | HRMS (ESI) of (R)-7c.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

171 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

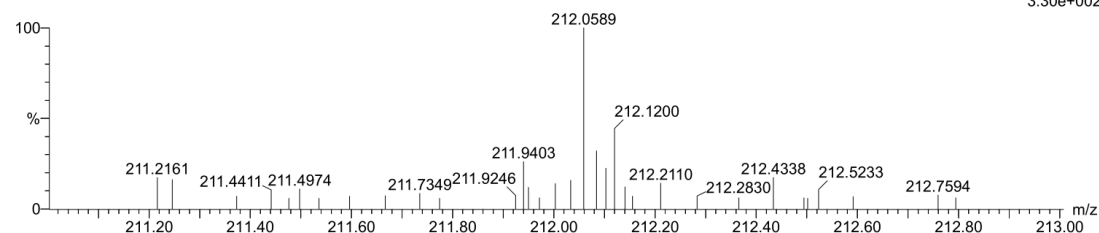
Elements Used:

C: 9-9 H: 11-11 N: 0-20 O: 0-37 Cl: 1-4

3

221127-1-263-2-7c 26 (0.161)

1: TOF MS ES+
3.30e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
212.0589	212.0591	-0.2	-0.9	5.5	128.8	n/a	n/a	C9 H11 N3 O Cl

Supplementary Fig. 486 | HRMS (ESI) of (*S*)-**8b**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

193 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

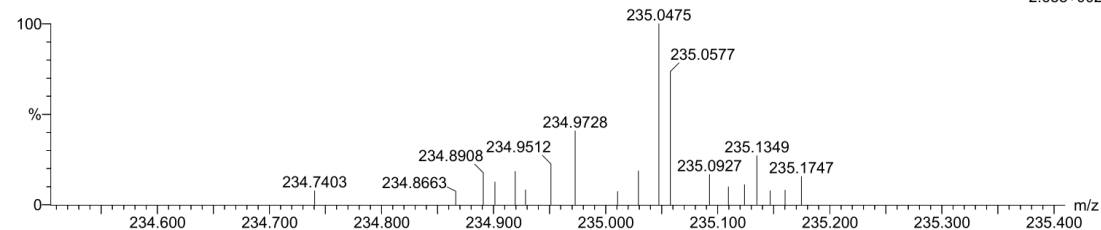
Elements Used:

C: 9-9 H: 9-9 N: 0-10 O: 0-17 Na: 0-3 Br: 1-5

15

230210-3-291-3-3Br-oxe 15 (0.178)

1: TOF MS ES+
2.65e+002



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
234.9728	234.9734	-0.6	-2.6	4.5	103.6	n/a	n/a	C9 H9 O Na Br

Supplementary Fig. 487 | HRMS (ESI) of (*R*)-**8c**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

108 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

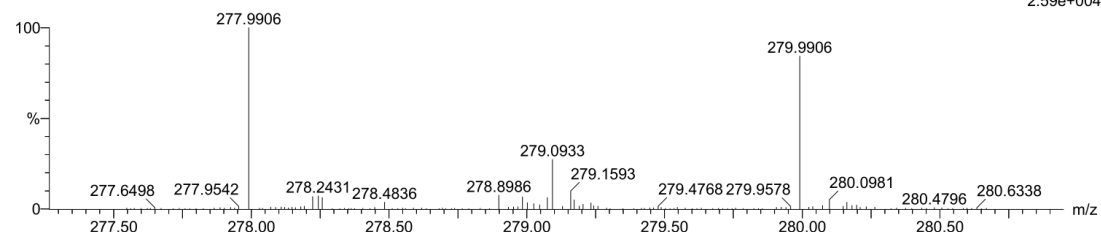
Elements Used:

C: 9-9 H: 0-100 N: 0-50 O: 0-50 Na: 1-1 Br: 1-2

14

221119-2-160-4-10C 12 (0.088)

1: TOF MS ES+
2.59e+004



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
277.9906	277.9905	0.1	0.4	5.5	1078.5	n/a	n/a	C9 H10 N3 O Na Br

Supplementary Fig. 488 | HRMS (ESI) of (*S*)-**9b**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

192 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

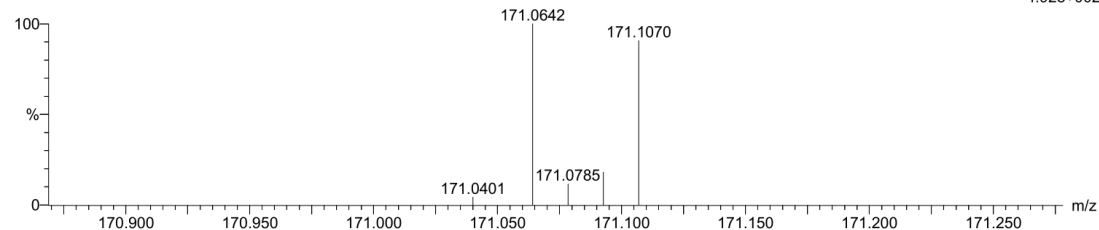
Elements Used:

C: 10-10 H: 12-12 N: 0-10 O: 0-17 Na: 0-3

15

230210-3-291-3-3me-oxe 2 (0.042)

1: TOF MS ES+
4.92e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
171.0785	171.0786	-0.1	-0.6	4.5	34.5	n/a	n/a	C10 H12 O Na

Supplementary Fig. 489 | HRMS (ESI) of (*R*)-**9c**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

340 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

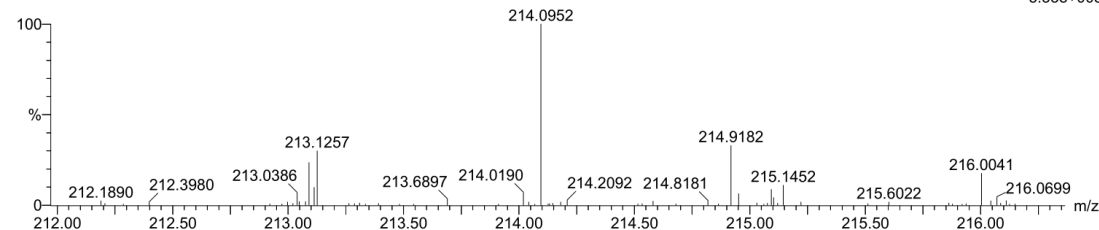
Elements Used:

C: 10-10 H: 13-13 N: 0-100 O: 0-100 Na: 0-4

1

240924-3-R-9C 12 (0.100)

1: TOF MS ES+
3.33e+003



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
214.0952	214.0956	-0.4	-1.9	5.5	272.0	n/a	n/a	C10 H13 N3 O Na

Supplementary Fig. 490 | HRMS (ESI) of (S)-10b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

224 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

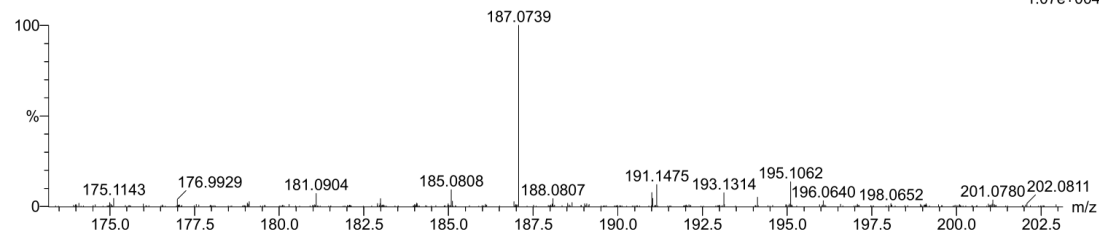
Elements Used:

C: 10-10 H: 12-12 N: 0-10 O: 0-23 Na: 0-3

3

230215-2-294-1-3ome-oxe 7 (0.093)

1: TOF MS ES+
1.07e+004



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
187.0739	187.0735	0.4	2.1	4.5	228.1	n/a	n/a	C10 H12 O2 Na

Supplementary Fig. 491 | HRMS (ESI) of (R)-10c.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

309 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

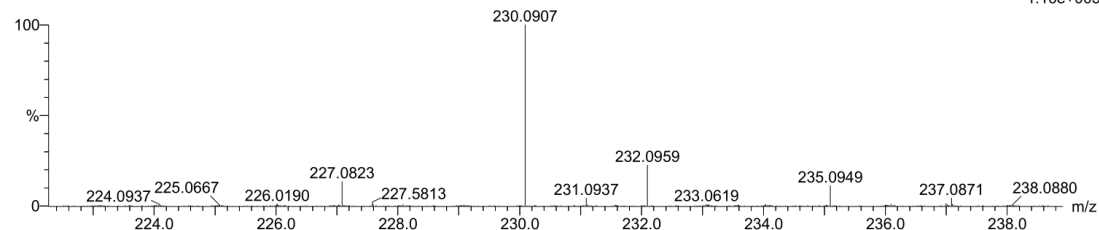
Elements Used:

C: 10-10 H: 13-13 N: 0-10 O: 0-17 Na: 0-3

15

230210-3-291-3-3ome-oh 5 (0.076)

1: TOF MS ES+
1.16e+005



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
230.0907	230.0905	0.2	0.9	5.5	513.9	n/a	n/a	C10 H13 N3 O2 Na

Supplementary Fig. 492 | HRMS (ESI) of (*S*)-**11b**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

263 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

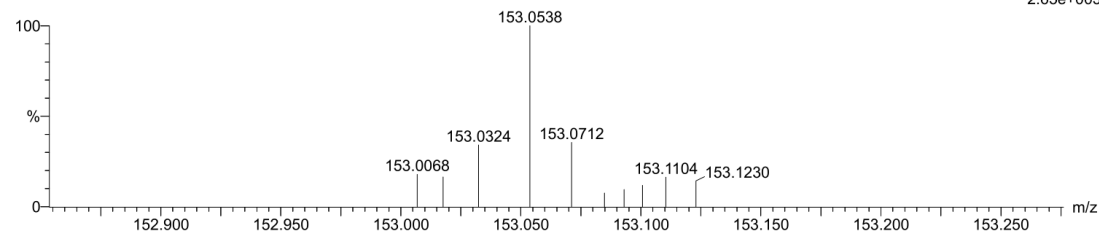
Elements Used:

C: 9-9 H: 10-10 N: 0-22 O: 0-47 Na: 0-3 F: 1-3

3

221206-1-267-3-4b 36 (0.225)

1: TOF MS ES+
2.65e+003



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
153.0712	153.0716	-0.4	-2.6	4.5	79.0	n/a	n/a	C9 H10 O F

Supplementary Fig. 493 | HRMS (ESI) of (*R*)-**11c**.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

176 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

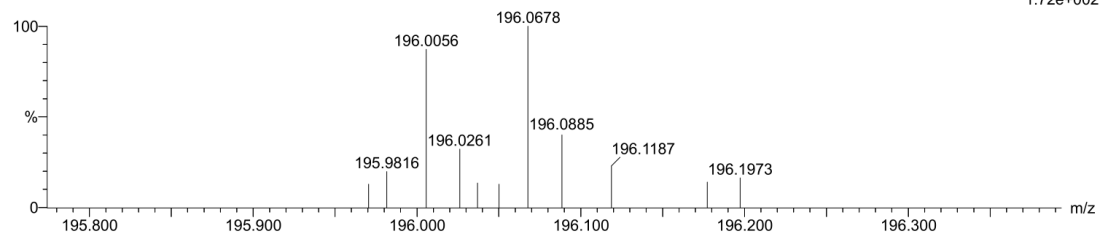
Elements Used:

C: 9-9 H: 11-11 N: 0-20 O: 0-37 F: 1-3

3

221127-1-263-2-4c 13 (0.093)

1: TOF MS ES+
1.72e+002



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
196.0885	196.0886	-0.1	-0.5	5.5	44.1	n/a	n/a	C9 H11 N3 O F

Supplementary Fig. 494 | HRMS (ESI) of (*S*)-12b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

49 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

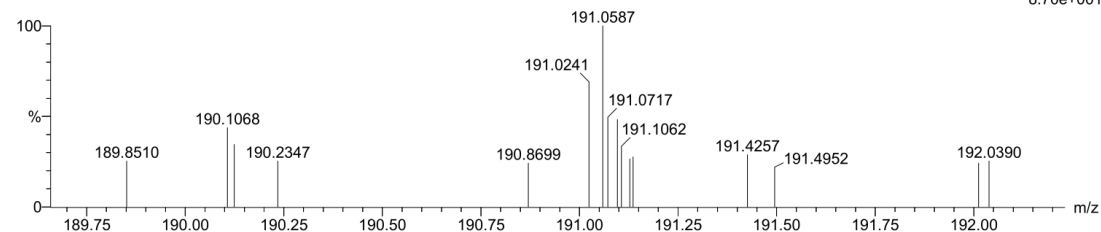
Elements Used:

C: 9-9 H: 9-9 O: 0-41 Na: 0-3 Cl: 1-2

8

230220-6-297-1-4cl-oxe 37 (0.415)

1: TOF MS ES+
8.70e+001



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
191.0241	191.0240	0.1	0.5	4.5	81.7	n/a	n/a	C9 H9 O Na Cl

Supplementary Fig. 495 | HRMS (ESI) of (*R*)-12c.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

333 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

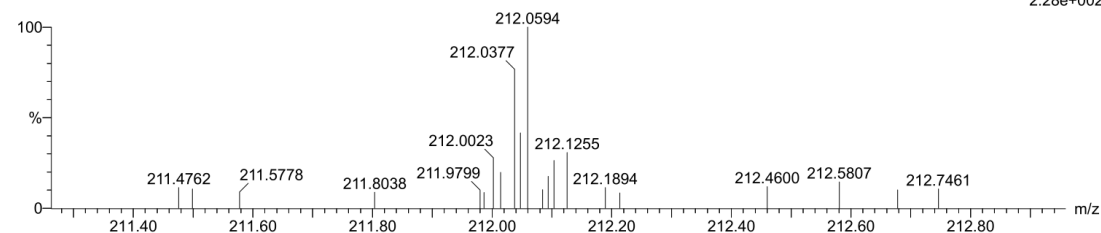
Elements Used:

C: 9-9 H: 11-11 N: 0-10 O: 0-17 Na: 0-3 Cl: 1-2

15

230210-3-291-3-4cl-oh 7 (0.093)

1: TOF MS ES+
2.28e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
212.0594	212.0591	0.3	1.4	5.5	89.4	n/a	n/a	C9 H11 N3 O Cl

Supplementary Fig. 496 | HRMS (ESI) of (*S*)-13b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

135 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

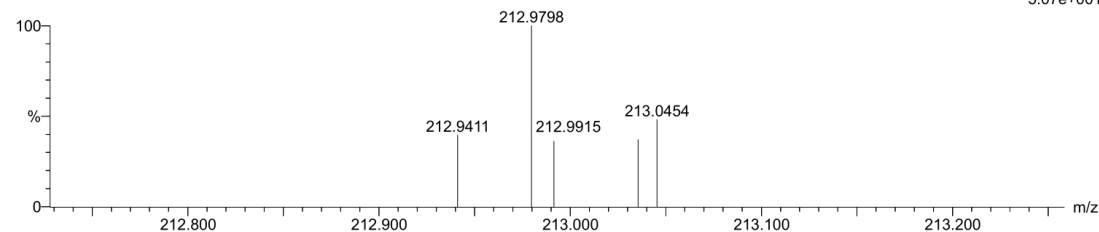
Elements Used:

C: 9-9 H: 10-10 N: 0-10 O: 0-23 Na: 0-3 Br: 1-5

3

230215-2-294-1-4br-oxe 42 (0.466)

1: TOF MS ES+
5.07e+001



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
212.9915	212.9915	0.0	0.0	4.5	34.4	n/a	n/a	C9 H10 O Br

Supplementary Fig. 497 | HRMS (ESI) of (*R*)-13c.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

264 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

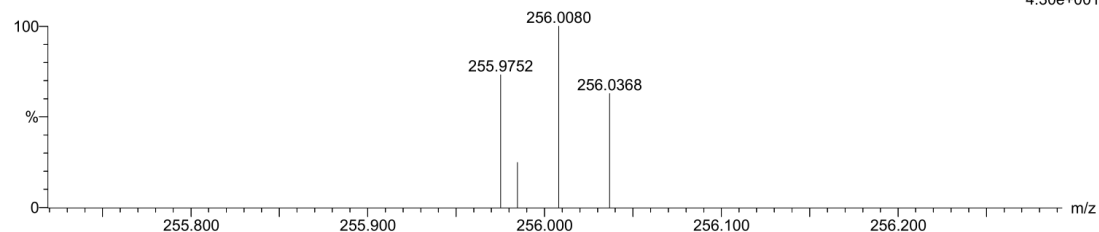
Elements Used:

C: 9-9 H: 11-11 N: 0-10 O: 0-23 Na: 0-3 Br: 1-5

3

230215-2-294-1-4Br-OH 40 (0.441)

1: TOF MS ES+
4.30e+001



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
256.0080	256.0085	-0.5	-2.0	5.5	23.2	n/a	n/a	C9 H11 N3 O Br

Supplementary Fig. 498 | HRMS (ESI) of (S)-14b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

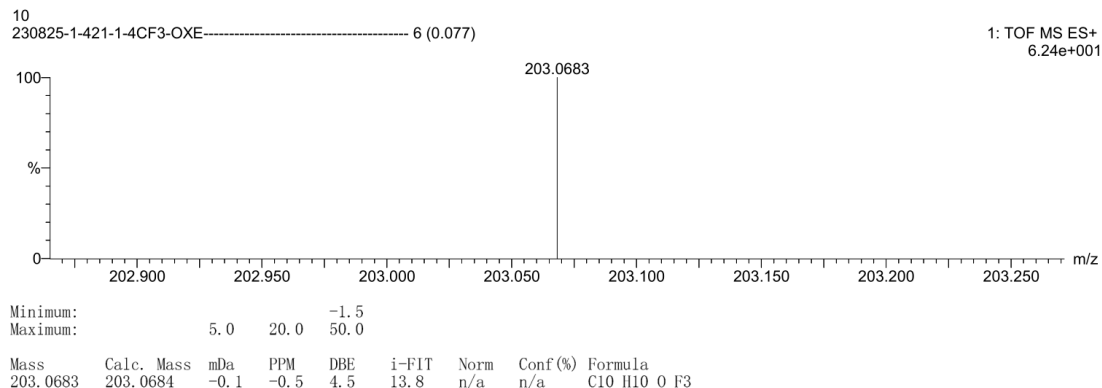
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

8 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

Elements Used:

C: 10-10 H: 10-10 O: 0-100 F: 3-3



Supplementary Fig. 499 | HRMS (ESI) of (R)-14c.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

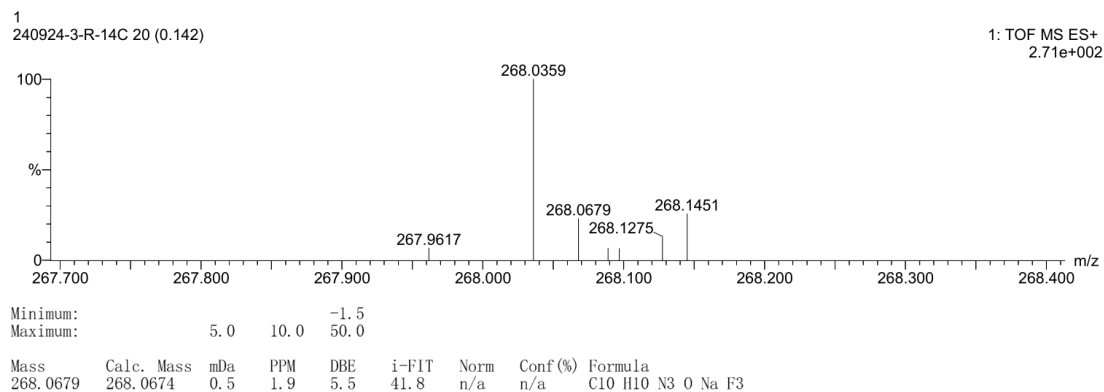
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

1857 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 10-10 H: 10-10 N: 0-100 O: 0-100 Na: 0-4 F: 1-6



Supplementary Fig. 500 | HRMS (ESI) of (*S*)-15b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

27 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

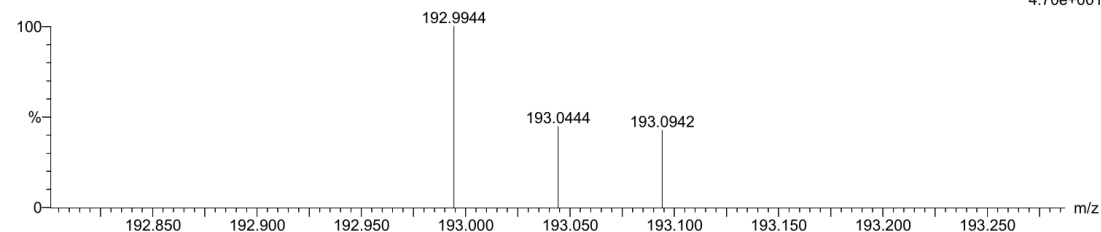
Elements Used:

C: 9-9 H: 8-8 O: 0-20 Na: 0-3 F: 2-2

4

230416-8-337-3-35-2f 21 (0.246)

1: TOF MS ES+
4.70e+001



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
193.0444	193.0441	0.3	1.6	4.5	16.5	n/a	n/a	C9 H8 O Na F2

Supplementary Fig. 501 | HRMS (ESI) of (*R*)-15c.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

290 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

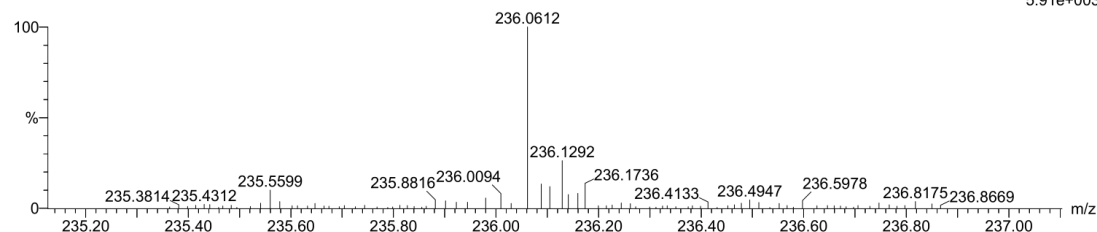
Elements Used:

C: 9-9 H: 0-100 N: 0-50 O: 0-50 Na: 1-1 F: 1-4

14

221119-2-160-4-18C 8 (0.067)

1: TOF MS ES+
5.91e+003



Minimum: -1.5
Maximum: 5.0 20.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
236.0612	236.0611	0.1	0.4	5.5	466.1	n/a	n/a	C9 H9 N3 O Na F2

Supplementary Fig. 502 | HRMS (ESI) of (*S*)-16b.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

20 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

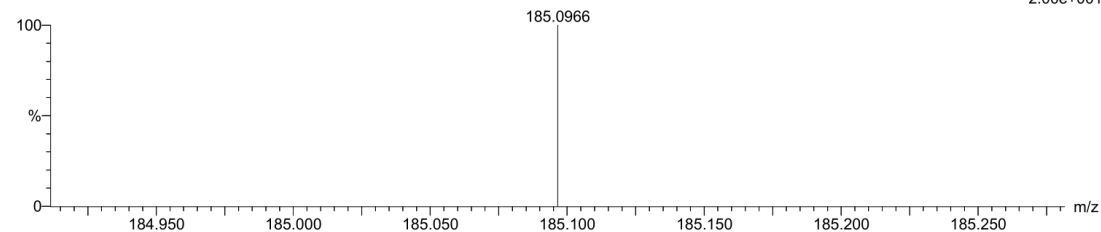
Elements Used:

C: 13-13 H: 13-13 O: 0-100 Na: 0-1

10

230825-1-421-1-HAPH-OXE----- 33 (0.316)

1: TOF MS ES+
2.00e+001



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
185.0966	185.0966	0.0	0.0	7.5	10.8	n/a	n/a	C13 H13 O

Supplementary Fig. 503 | HRMS (ESI) of (*R*)-16c.

Single Mass Analysis

Tolerance = 20.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

117 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)

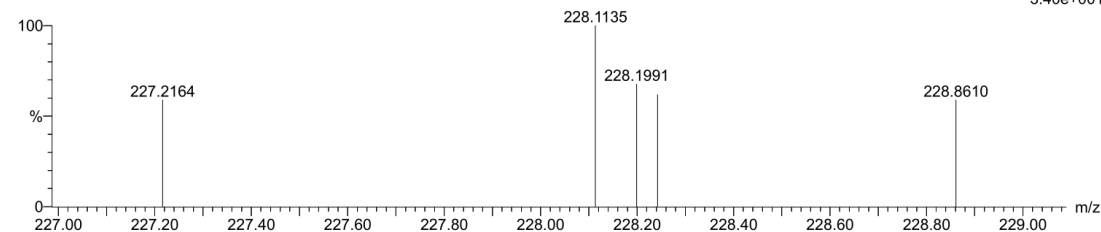
Elements Used:

C: 13-13 H: 14-14 N: 0-100 O: 0-100

10

230825-1-421-1-NAPH-N3OH----- 22 (0.222)

1: TOF MS ES+
3.40e+001



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
228.1135	228.1137	-0.2	-0.9	8.5	31.3	n/a	n/a	C13 H14 N3 O

Supplementary Fig. 504 | HRMS (ESI) of (*S*)-17b.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

130 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

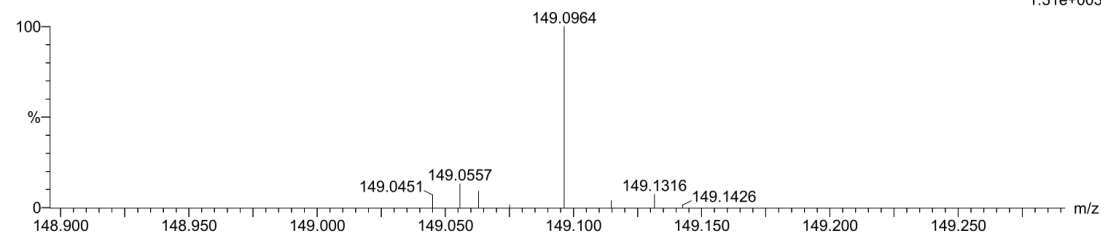
Elements Used:

C: 10-10 H: 13-13 N: 0-200 O: 0-200 Na: 0-2

8

231022-1-452-2-2-MEOXE 6 (0.088)

1: TOF MS ES+
1.31e+003



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
149.0964	149.0966	-0.2	-1.3	4.5	45.6	n/a	n/a	C10 H13 O

Supplementary Fig. 505 | HRMS (ESI) of (*R*)-17c.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

340 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

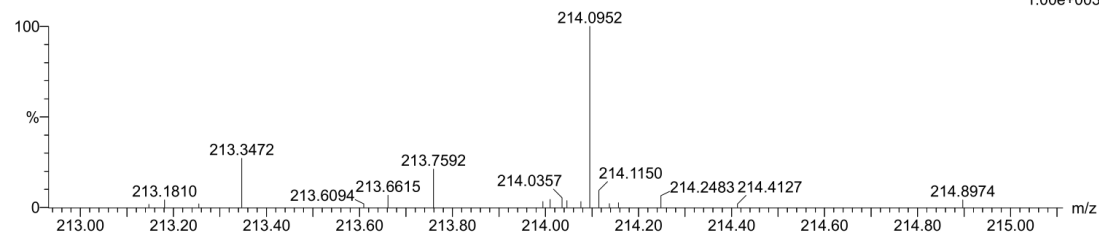
Elements Used:

C: 10-10 H: 13-13 N: 0-100 O: 0-100 Na: 0-4

1

240924-3-R-17C 27 (0.178)

1: TOF MS ES+
1.00e+003



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
214.0952	214.0956	-0.4	-1.9	5.5	66.1	n/a	n/a	C10 H13 N3 O Na

Supplementary Fig. 506 | HRMS (ESI) of (*S*)-**18b**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

95 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

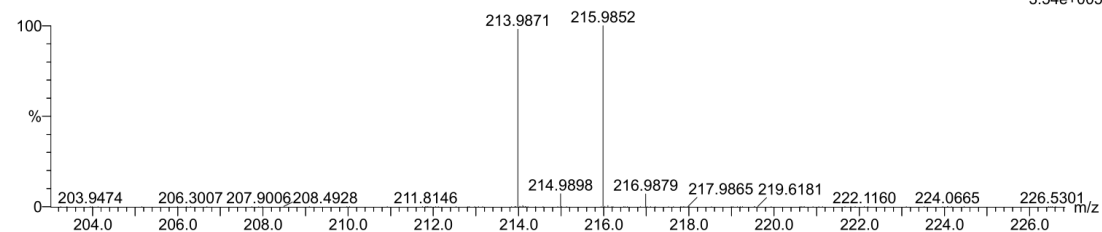
Elements Used:

C: 8-8 H: 9-9 N: 0-100 O: 0-100 Na: 0-1 Br: 1-4

30

240128-1-521-1-prdoxe 9 (0.069)

1: TOF MS ES+
3.54e+005



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
213.9871	213.9868	0.3	1.4	4.5	169.4	n/a	n/a	C8 H9 N 0 Br

Supplementary Fig. 507 | HRMS (ESI) of (*R*)-**18c**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

173 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

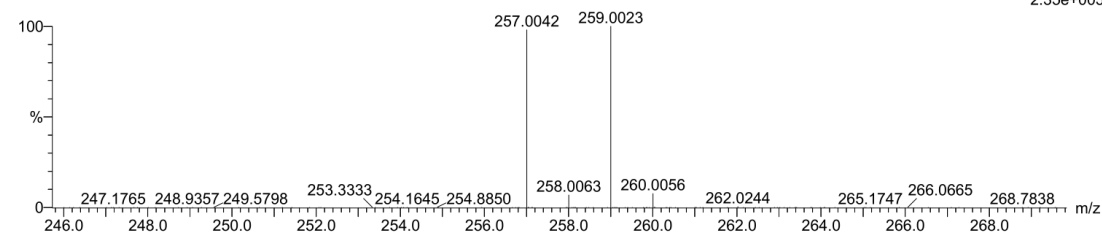
Elements Used:

C: 8-8 H: 10-10 N: 0-100 O: 0-100 Na: 0-1 Br: 1-4

30

240128-1-521-1-prdOH 10 (0.072)

1: TOF MS ES+
2.35e+005



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
257.0042	257.0038	0.4	1.6	5.5	161.0	n/a	n/a	C8 H10 N4 0 Br

Supplementary Fig. 508 | HRMS (ESI) of (*S*)-19b.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

150 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

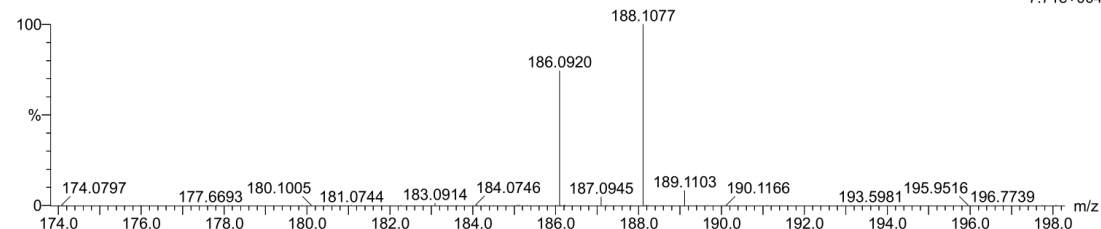
Elements Used:

C: 12-12 H: 12-12 N: 0-100 O: 0-100 Na: 0-1

13

230130-2-523-3-ql-oh 19 (0.105)

1: TOF MS ES+
7.71e+004



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
186.0920	186.0919	0.1	0.5	7.5	103.3	n/a	n/a	C12 H12 N 0

Supplementary Fig. 509 | HRMS (ESI) of (*R*)-19c.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

249 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

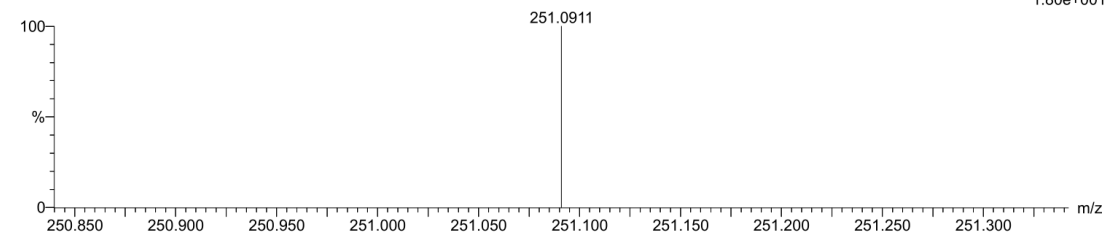
Elements Used:

C: 12-12 H: 12-12 N: 0-100 O: 0-100 Na: 0-1

13

230130-2-523-3-ql-oxe 5 (0.055)

1: TOF MS ES+
1.80e+001



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
251.0911	251.0909	0.2	0.8	8.5	10.9	n/a	n/a	C12 H12 N4 O Na

Supplementary Fig. 510 | HRMS (ESI) of (*S*)-**21b**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

108 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

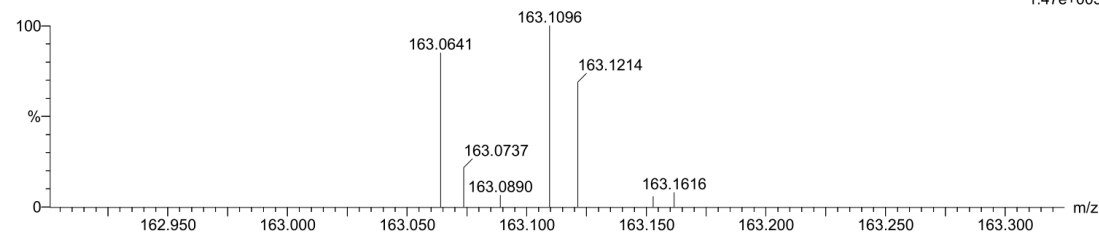
Elements Used:

C: 9-9 H: 16-16 N: 0-100 O: 0-100 Na: 0-1

28

240422-3-d-22b 27 (0.288)

1: TOF MS ES+
1.47e+003



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
163.1096	163.1099	-0.3	-1.8	1.5	55.3	n/a	n/a	C9 H16 O Na

Supplementary Fig. 511 | HRMS (ESI) of (*R*)-**21c**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

161 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

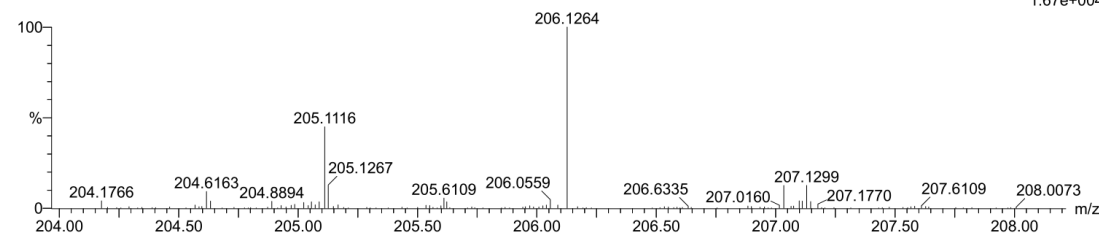
Elements Used:

C: 9-9 H: 17-17 N: 0-100 O: 0-100 Na: 0-1

28

240422-3-r-22c 19 (0.219)

1: TOF MS ES+
1.67e+004



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
206.1264	206.1269	-0.5	-2.4	2.5	457.6	n/a	n/a	C9 H17 N3 O Na

Supplementary Fig. 512 | HRMS (ESI) of (*S*)-**1b** (Ring opening by cyanide).

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

127 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

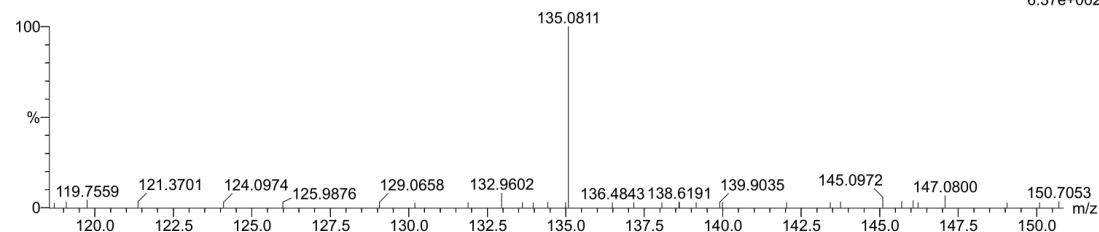
Elements Used:

C: 9-9 H: 11-11 N: 0-20 O: 0-100 Na: 0-4

32

240108-4-506-5-OXE 13 (0.070)

1: TOF MS ES+
6.37e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
135.0811	135.0810	0.1	0.7	4.5	32.4	n/a	n/a	C9 H11 O

Supplementary Fig. 513 | HRMS (ESI) of (*R*)-**1d**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

188 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

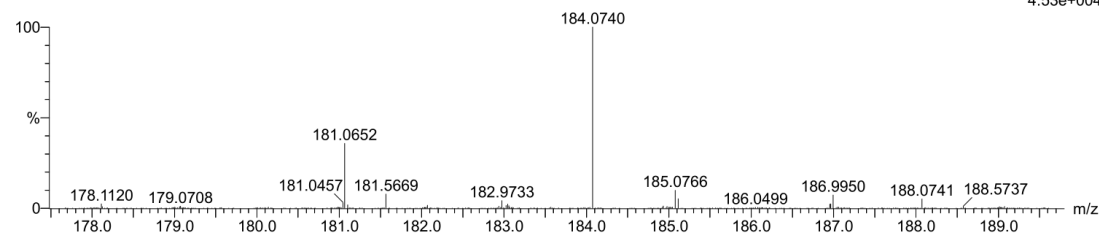
Elements Used:

C: 10-10 H: 11-11 N: 0-200 O: 0-200 Na: 0-2

8

231022-1-452-2-CN-OH 7 (0.097)

1: TOF MS ES+
4.53e+004



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
184.0740	184.0738	0.2	1.1	5.5	613.8	n/a	n/a	C10 H11 N O Na

Supplementary Fig. 514 | HRMS (ESI) of (*S*)-**1b** (Ring opening by nitrite).

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

127 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

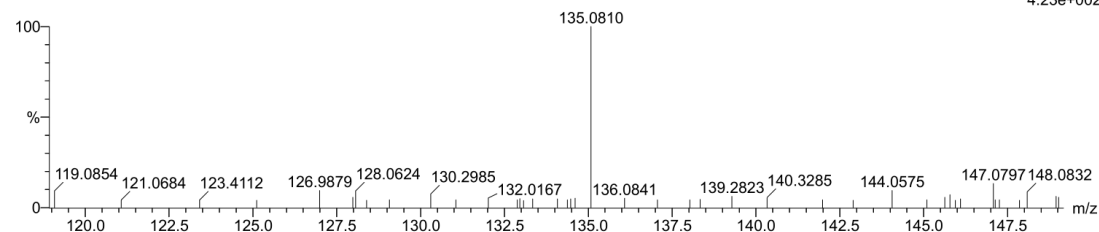
Elements Used:

C: 9-9 H: 11-11 N: 0-20 O: 0-100 Na: 0-4

32

240108-4-506-5-NO-OXE 15 (0.077)

1: TOF MS ES+
4.23e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
135.0810	135.0810	0.0	0.0	4.5	14.0	n/a	n/a	C9 H11 O

Supplementary Fig. 515 | HRMS (ESI) of (*R*)-**1e**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

300 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

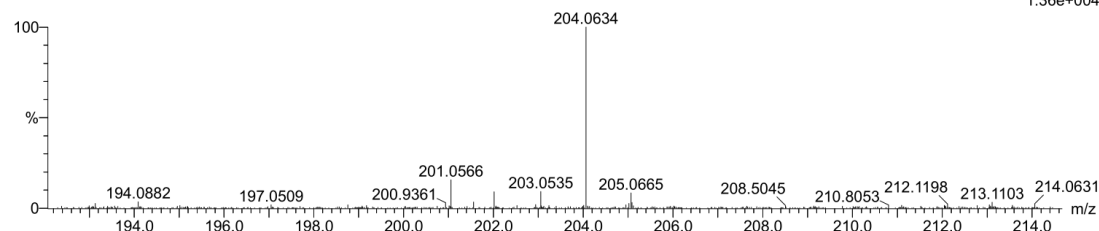
Elements Used:

C: 9-9 H: 11-11 N: 0-100 O: 0-100 Na: 0-4

1

240924-3-R-1E 11 (0.094)

1: TOF MS ES+
1.36e+004



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
204.0634	204.0637	-0.3	-1.5	4.5	491.9	n/a	n/a	C9 H11 N O3 Na

Supplementary Fig. 516 | HRMS (ESI) of (R)-1f.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

166 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

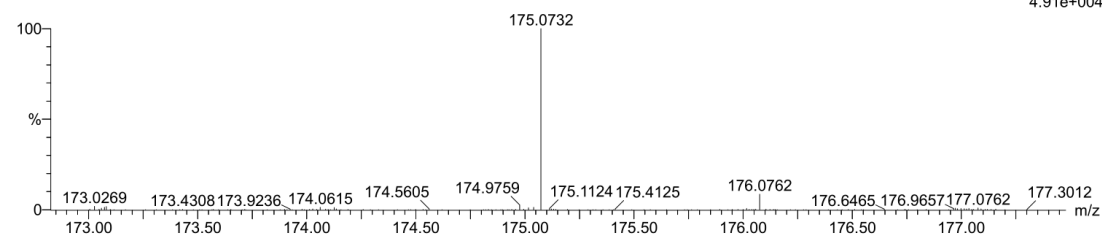
Elements Used:

C: 9-9 H: 12-12 N: 0-200 O: 0-200 Na: 0-2

8

231022-1-452-2-2OH 6 (0.088)

1: TOF MS ES+
4.91e+004



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
175.0732	175.0735	-0.3	-1.7	3.5	570.1	n/a	n/a	C9 H12 O2 Na

Supplementary Fig. 517 | HRMS (ESI) of (*R*)-**1aa**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

159 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

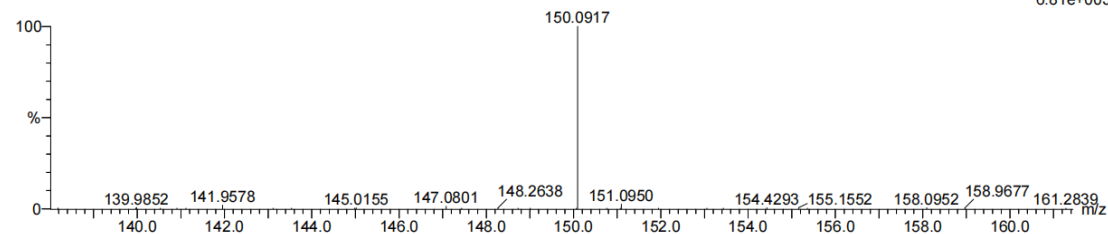
Elements Used:

C: 9-9 H: 12-12 N: 0-20 O: 0-100 Na: 0-4

32

240108-4-506-5-S-YEZ 35 (0.148)

1: TOF MS ES+
6.81e+003



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
150.0917	150.0919	-0.2	-1.3	4.5	36.0	n/a	n/a	C9 H12 N 0

Supplementary Fig. 518 | HRMS (ESI) of (*S*)-**1ab**.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

683 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

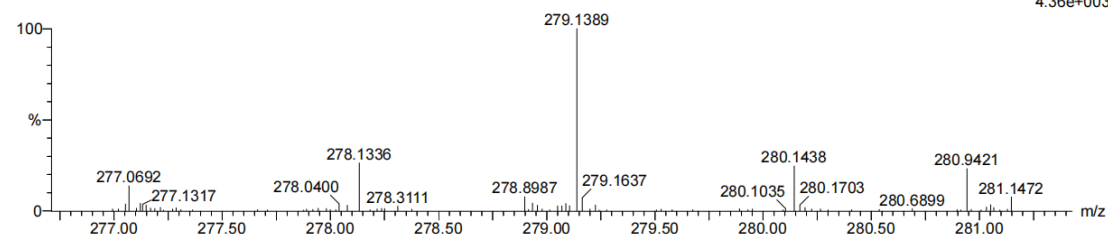
Elements Used:

C: 19-19 H: 19-19 N: 0-100 O: 0-100 Na: 0-4

37

240925-4-S-DPXT 11 (0.094)

1: TOF MS ES+
4.36e+003



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
279.1389	279.1385	0.4	1.4	10.5	254.4	n/a	n/a	C19 H19 O2

Supplementary Fig. 519 | HRMS (ESI) of (R)-1ba.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

32 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

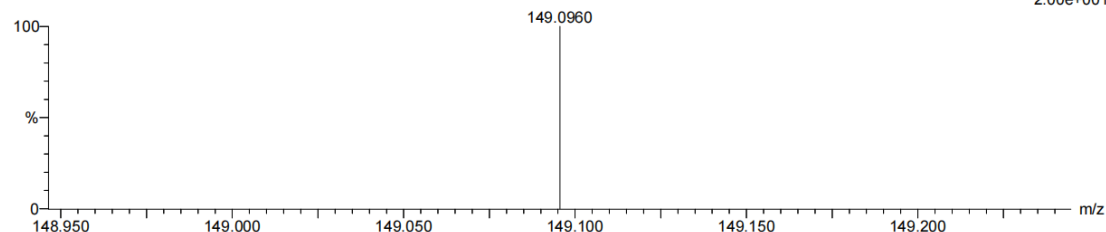
Elements Used:

C: 10-10 H: 13-13 O: 0-100 Na: 0-4

32

240108-4-506-5-R-5YH 119 (0.468)

1: TOF MS ES+
2.00e+001



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
149.0960	149.0966	-0.6	-4.0	4.5	10.2	n/a	n/a	C10 H13 O

Supplementary Fig. 520 | HRMS (ESI) of (R)-1bb.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

589 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

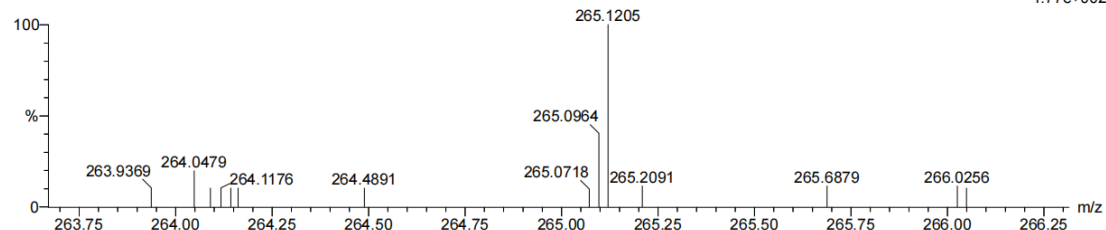
Elements Used:

C: 16-16 H: 18-18 N: 0-20 O: 0-100 Na: 0-4

32

240108-4-506-5-R-HYKH 14 (0.073)

1: TOF MS ES+
1.77e+002



Minimum: -1.5
Maximum: 5.0 10.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
265.1205	265.1204	0.1	0.4	7.5	38.5	n/a	n/a	C16 H18 O2 Na

Supplementary Fig. 521 | HRMS (ESI) of (R)-1ca.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

671 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

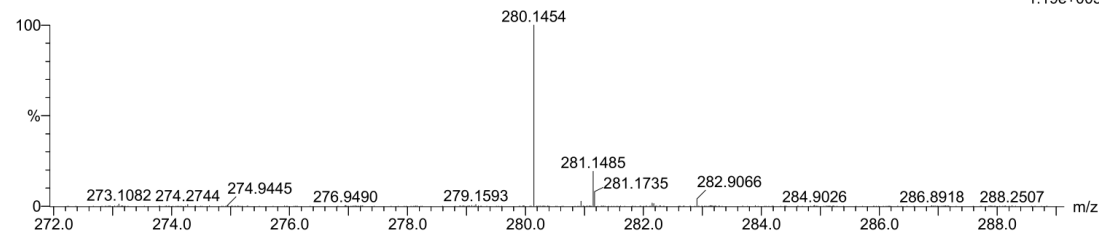
Elements Used:

C: 17-17 H: 18-18 N: 0-100 O: 0-100 Na: 0-4

1

240924-3-1CA 30 (0.194)

1: TOF MS ES+
1.19e+005



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
280.1454	280.1450	0.4	1.4	10.5	482.7	n/a	n/a	C17 H18 N3 O

Supplementary Fig. 522 | HRMS (ESI) of (R)-1cb.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

752 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

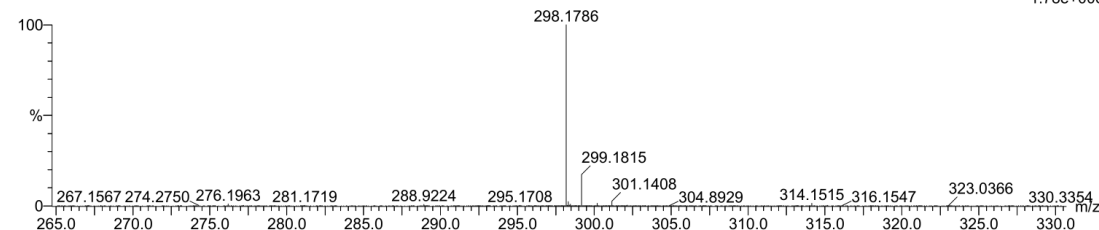
Elements Used:

C: 17-17 H: 25-25 N: 0-100 O: 0-100 Na: 0-4

1

240924-3-1CB 20 (0.142)

1: TOF MS ES+
1.78e+006



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
298.1786	298.1783	0.3	1.0	5.5	1069.5	n/a	n/a	C17 H25 N O2 Na

Supplementary Fig. 523 | HRMS (ESI) of (R)-1da.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

252 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

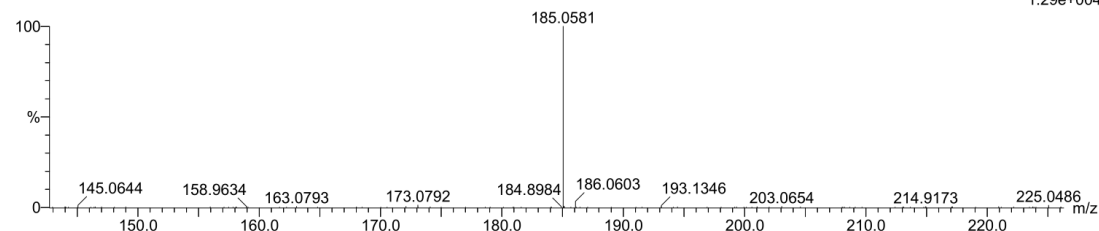
Elements Used:

C: 10-10 H: 10-10 N: 0-20 O: 0-100 Na: 0-4

32

240108-4-506-5-1DA 39 (0.169)

1: TOF MS ES+
1.29e+004



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
185.0581	185.0578	0.3	1.6	5.5	65.2	n/a	n/a	C10 H10 O2 Na

Supplementary Fig. 524 | HRMS (ESI) of (R)-1db.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

302 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

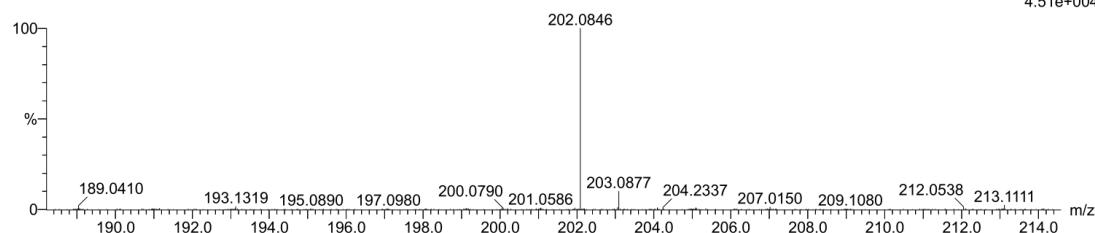
Elements Used:

C: 10-10 H: 13-13 N: 0-100 O: 0-100 Na: 0-4

1

240924-3-1DB 44 (0.287)

1: TOF MS ES+
4.51e+004



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
202.0846	202.0844	0.2	1.0	4.5	341.6	n/a	n/a	C10 H13 N O2 Na

Supplementary Fig. 525 | HRMS (ESI) of (R)-1ea.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

120 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

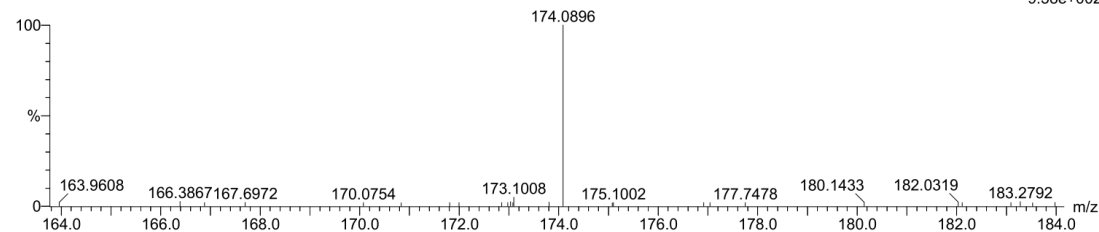
Elements Used:

C: 9-9 H: 13-13 N: 0-100 O: 0-100 Na: 0-1

30

240128-1-521-1-1EA 6 (0.058)

1: TOF MS ES+
9.58e+002



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
174.0896	174.0895	0.1	0.6	3.5	25.8	n/a	n/a	C9 H13 N 0 Na

Supplementary Fig. 526 | HRMS (ESI) of (R)-1fa.

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

540 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

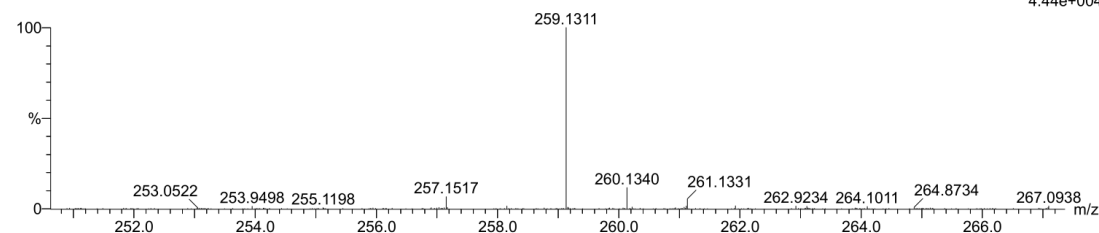
Elements Used:

C: 14-14 H: 20-20 N: 0-100 O: 0-100 Na: 0-4

1

240924-3-1FA 61 (0.396)

1: TOF MS ES+
4.44e+004



Minimum: -1.5
Maximum: 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
259.1311	259.1310	0.1	0.4	4.5	387.5	n/a	n/a	C14 H20 O3 Na

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