Supporting Information

Biocatalytic asymmetric radical alkene hydration

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1. General aspects

1.1 Materials and methods

All commercially available chemicals and solvents were purchased from Sigma-Aldrich, ABCR, TCI Europe, Acros Organics, Alfa Aesar, Fluka, Fluorochem, Merck or Ukrorgsyntez Ltd. and used without further purification. Dry solvents were purchased from Acros Organics and used without further purification. Flash chromatography was carried out on silica gel (Silicycle SiliaFlash P60(230-400 mesh)).

All catalytic experiments were performed in 2.0 mL glass vials in air using non-degassed solvents unless otherwise stated.

The water used for all biological and catalytic experiments was purified with a Milli-Q Advantage system. All enzymes used for PCRs and cloning were purchased from New England Biolabs (NEB). 1000x Trace Element Solution: 0.5 g L^{-1} $CaCl_2 \cdot 2H_2O$, 0.18 g L^{-1} $ZnSO_4 \cdot 7H_2O$, 0.1 g L^{-1} $MnSO_4 \cdot H_2O$, 20.1 g L^{-1} Na_2EDTA, 16.7 g L^{-1} $FeCl_3 \cdot 6H_2O$, 0.16 g L^{-1} $CuSO_4 \cdot 5H_2O$ dissolved in Milli-Q H_2O.

Primers for mutagenesis were ordered from Swiss Microsynth company.

1.2 Instrumentation

NMR spectra were recorded on a Bruker 500 MHz or 600 MHz spectrometer. The spectra were referenced using the undeuterated residual solvent peak (for ^{1}H NMR) and deuterated solvents (for ^{13}C NMR) as internal standard: chloroform (δH = 7.26 ppm) and $CDCl_3$ (δC = 77.16 ppm), dichloromethane (δH = 5.32 ppm) and CD_2Cl_2 (δC = 53.84 ppm), dimethyl sulfoxide (δH = 2.50 ppm) and DMSO-d_6 (δC = 39.52 ppm), acetonitrile (δH = 1.94 ppm) and CD_3CN (δC = 118.26 ppm), methanol (δH = 3.31 ppm) and MeOD-d_4 (δC = 49.00 ppm). The following abbreviations are used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad.

Electron-Spray Ionization Mass Spectra (ESI-MS) were recorded on a Bruker FTMS 4.7T bioAPEX II. High-resolution mass spectra (HRMS) were measured on a Bruker maXis 4G QTOF ESI mass spectrometer.

The catalytic experiments were analyzed using either supercritical fluid chromatography (SFC) on a Waters Acquity UPC^2 or gas chromatography (GC) on an Agilent GC 6890N. In both cases, 1,3,5-trimethoxybenzene was used as internal standard.

An EvoluChem 18 W blue LED was used for photochemical reaction.

An Agilent GC 7890B was used for the GC-MS analysis.

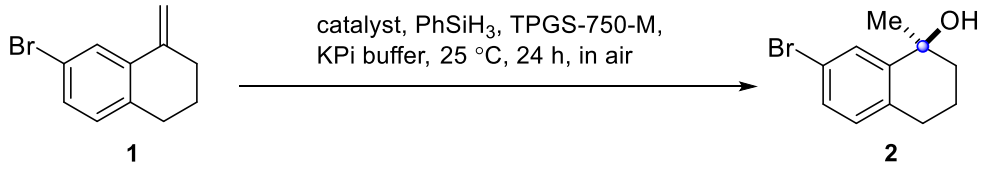
Sonication was performed using Fisher Scientific FB705 instrument, with 6.3 mm microtip.

Polymerase chain reactions (PCR) were carried out using BioRad C1000 thermal cycler.

2. Investigation of the biocatalytic asymmetric radical alkene hydration

2.1 Optimization of the biocatalytic asymmetric radical alkene hydration

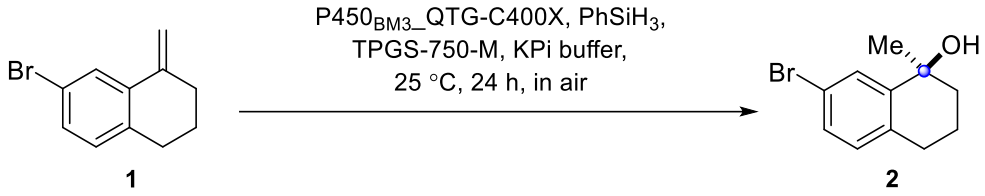
Supplementary Table 1. Directed evolution of P450$_{BM3}$ for asymmetric radical hydration of alkene 1



Entry[a]	catalyst	Yield (%)	e.e. (%)
1[b]	haemin chloride	20±1	*rac*
2	P450$_{BM3}$_WT	24±1	16±1
3	P450$_{BM3}$_T268G	19±1	–26±2
4	P450$_{BM3}$_F87T-T268G	26±1	88±0
5	P450$_{BM3}$_A74Q-F87T-T268G	23±0	93±2

[a]Unless otherwise stated, the standard conditions are: alkene **1** (1.0 mM), enzyme (1 μM, 0.1 mol % catalytic loading), KPi buffer (50 mM, pH 7.0), $PhSiH_3$ (2 μL of 50 % v/v in DMSO, 20 equiv. compared with alkene **1**), TPGS-750-M (40 μL, from 2 wt. % in H_2O stock solution), V_{tot} 400 μL, 25 °C in air for 24 h; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yields and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed. [b]haemin chloride (50 μM, 5.0 mol % catalytic loading).

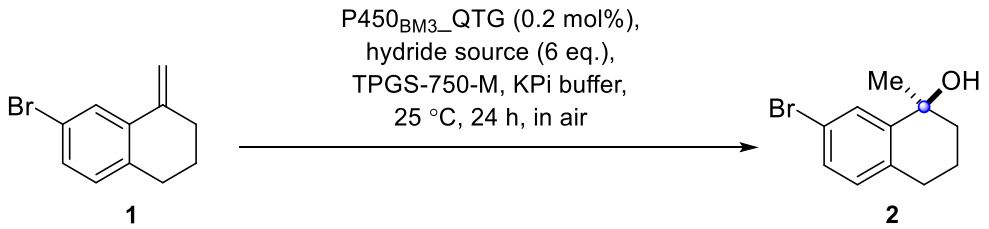
Supplementary Table 2. Influence of mutations at $P450_{BM3}$_C400 on the biocatalytic asymmetric radical alkene hydration



Entry[a]	Variants	Yield (%)	e.e. (%)
1	$P450_{BM3}$_QTG[b]	23±0	93±2
2	$P450_{BM3}$_QTG-C400M	5±1	-6±1
3	$P450_{BM3}$_QTG-C400S	6±2	23±3
4[c]	$P450_{BM3}$_QTG-C400A	5±1	11±1
5	$P450_{BM3}$_QTG-C400H	4±1	12±2

[a]Unless otherwise stated, the standard conditions are: alkene **1** (1.0 mM), $P450_{BM3}$ variant (1 μM, 0.1 mol % catalytic loading), KPi buffer (50 mM, pH 7.0), $PhSiH_3$ (2 μL of 50 % v/v in DMSO, 20 equiv. compared with alkene **1**), TPGS-750-M (40 μL, from 2 wt. % in H_2O stock solution), V_{tot} 400 μL, 25 °C in air for 24 h; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yield and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed. [b]$P450_{BM3}$_QTG is abbreviation for $P450_{BM3}$_A74Q-F87T-T268G. [c]$P450_{BM3}$_QTG-C400A (0.5 μM, 0.05 mol % catalytic loading).

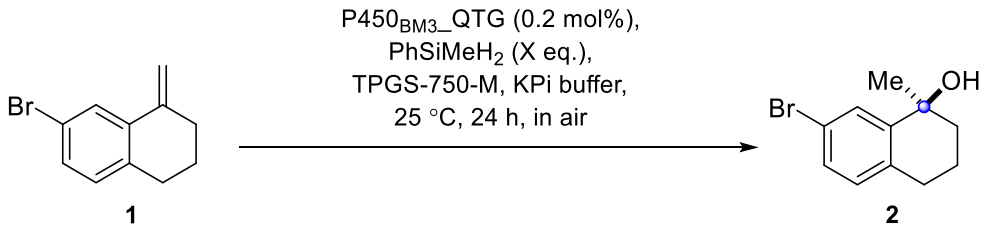
Supplementary Table 3. Influence of the hydride source on the P450$_{BM3}$_QTG catalyzed asymmetric radical alkene hydration



Entry[a]	Hydride source	Yield (%)	e.e. (%)
1	$PhSiH_3$	9±1	91±2
2	$PhMeSiH_2$	59±1	92±1
3	$PhMe_2SiH$	1±1	-
4	1,1,3,3-Tetramethyldisiloxane	4±0	-
5	Et_3SiH	0	-
6	$NaBH_4$	0	-

[a]Unless otherwise stated, the standard conditions are: alkene **1** (1.0 mM), P450$_{BM3}$_QTG (2 μM, 0.2 mol % catalytic loading), KPi buffer (50 mM, pH 7.0), hydride source (6.0 mM, 6 equiv. compared with alkene **1**), TPGS-750-M (40 μL, from 4 wt. % in H_2O stock solution), V_{tot} 400 μL, 25 °C in air for 24 h; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yield and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed.

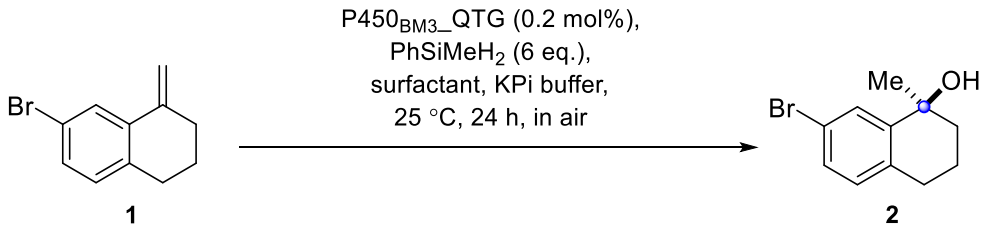
Supplementary Table 4. Influence of the $PhSiMeH_2$ concentration on the $P450_{BM3}$_QTG catalyzed asymmetric radical alkene hydration



Entry[a]	$PhSiMeH_2$ (eq.)	Yield (%)	e.e. (%)
1	2 eq.	26±1	92±0
2	3 eq.	40±2	91±1
3	4 eq.	49±1	91±1
4	5 eq.	53±0	91±1
5	6 eq.	61±0	92±1
6	8 eq.	66±0	90±1
7	10 eq.	65±2	89±1

[a]Unless otherwise stated, the standard conditions are: alkene **1** (1.0 mM), $P450_{BM3}$_QTG (2 μM, 0.2 mol % catalytic loading), KPi buffer (50 mM, pH 7.0), $PhSiMeH_2$ (equivalents indicated in the table), TPGS-750-M (40 μL, from 4 wt. % in H_2O stock solution), V_{tot} 400 μL, 25 °C in air for 24 h; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yield and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed.

Supplementary Table 5. Influence of non-ionic surfactant additives on the biocatalytic asymmetric radical alkene hydration

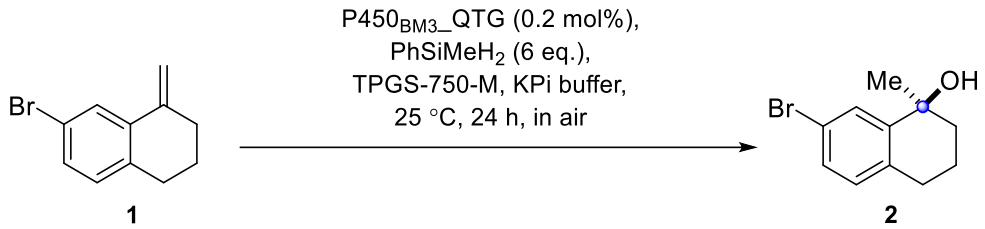


1 2

Entry[a]	Non-ionic surfactant	Yield (%)	e.e. (%)
1	TPGS-750-M	59±1	92±1
2	TPGS-1000-M	52±3	90±0
3	Milli-Q water	33±1	88±0
4	TWEEN 80	35±1	82±2
5	Triton X-100	56±1	88±1
6	SPGS-550M	43±6	88±1

[a]Unless otherwise stated, the standard conditions are: alkene **1** (1.0 mM), $P450_{BM3}$_QTG (2 μM, 0.2 mol % catalytic loading), KPi buffer (50 mM, pH 7.0), $PhSiMeH_2$ (2 μL of 25 % v/v in DMSO, 6 equiv. compared with alkene **1**), surfactant (40 μL, from 2 wt. % in H_2O stock solution), V_{tot} 400 μL, 25 °C in air for 24 h; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yield and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed.

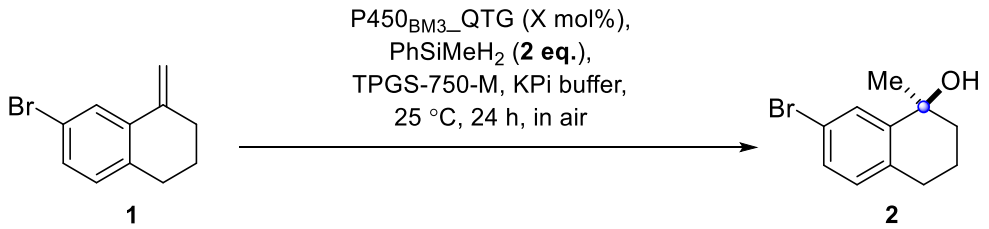
Supplementary Table 6. Influence of TPGS-750-M surfactant content on the biocatalytic asymmetric radical alkene hydration



Entry[a]	Final weight percent of TPGS-750-M (%)	Yield (%)	e.e. (%)
1	0.2	52±1	91±1
2	0.4	62±2	92±1
3	0.6	57±1	91±0
4	0.8	53±0	90±0
5	1.0	48±1	89±1

[a]Unless otherwise stated, the standard conditions are: alkene **1** (1.0 mM), $P450_{BM3}$_QTG (2 μM, 0.2 mol % catalytic loading), KPi buffer (50 mM, pH 7.0), $PhSiMeH_2$ (2 μL of 25 % v/v in DMSO, 6 equiv. compared with alkene **1**), TPGS-750-M (final weight percent indicated in the table), V_{tot} 400 μL, 25 °C in air for 24 h; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yield and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed.

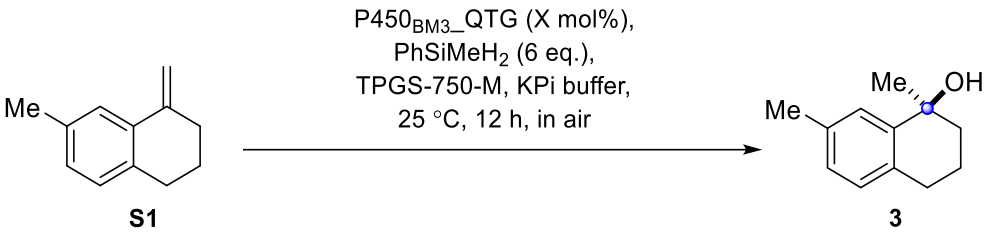
Supplementary Table 7. Influence of biocatalyst loading on the biocatalytic asymmetric radical hydration of alkene 1



Entry[a]	Biocatalyst loading (mol%)	Yield (%)	e.e. (%)
1	0.1	28±1	85±2
2	0.2	31±1	90±1
3	0.4	35±1	93±2
4	0.6	33±2	94±2
5	0.8	32±1	94±1
6	1.0	32±1	93±1

[a]Unless otherwise stated, the standard conditions are: alkene **1** (1.0 mM), $P450_{BM3}$_QTG (biocatalytic loading indicated in the table), KPi buffer (50 mM, pH 7.0), $PhSiMeH_2$ (2 μL of 8.3 % v/v in DMSO, 2 equiv. compared with alkene **1**), TPGS-750-M (40 μL, from 2 wt. % in H_2O stock solution), V_{tot} 400 μL, 25 °C in air for 24 h; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yield and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed.

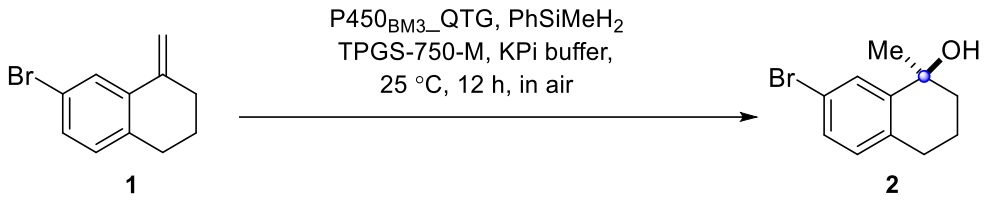
Supplementary Table 8. Influence of biocatalyst loading on the biocatalytic asymmetric radical hydration of alkene S1



Entry[a]	Biocatalyst loading (mol%)	Yield (%)	e.e. (%)
1	0.1	21±1	87±1
2	0.2	24±1	91±0
3	0.4	17±1	89±2
4	0.8	16±1	83±1

[a]Unless otherwise stated, the standard conditions are: alkene **S1** (1.0 mM), $P450_{BM3}$_QTG (biocatalytic loading indicated in the table), KPi buffer (50 mM, pH 7.0), $PhSiMeH_2$ (2 μL of 25 % v/v in DMSO, 6 equiv. compared with alkene **S1**), TPGS-750-M (40 μL, from 4 wt. % in H_2O stock solution), V_{tot} 400 μL, 25 °C in air for 12 h; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yield and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed.

Supplementary Table 9. Reaction optimization of the P450$_{BM3}$_QTG catalyzed asymmetric radical hydration of alkene 1

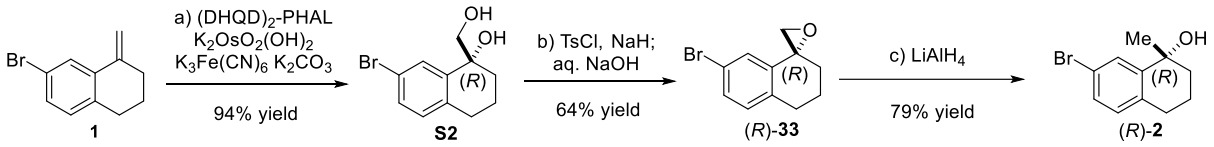


Entry[a]	Variations	Yield (%)	e.e. (%)
1	Standard conditions	66±3	92±0
2[b]	w/o TPGS-750-M	33±1	88±0
3[c]	w/ $PhSiH_3$ (6 eq.)	9±1	91±2
4[d]	w/o P450$_{BM3}$_QTG	0	-
5[e]	w/o $PhSiMeH_2$	0	-

[a]Unless otherwise stated, the standard conditions are: alkene **1** (1.0 mM), P450$_{BM3}$_QTG (2 μM, 0.2 mol % catalytic loading), KPi buffer (50 mM, pH 7.0), $PhSiMeH_2$ (2 μL of 25 % v/v in DMSO, 6 equiv. compared with alkene **1**), TPGS-750-M (40 μL, from 4 wt. % in H_2O stock solution), V_{tot} 400 μL, 25 °C in air for 12 h; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yield and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed. [b]Milli-Q water (40 μL) was used instead of surfactant. [c]$PhSiH_3$ (2 μL of 15 % v/v in DMSO, 6 equiv. compared with alkene **1**) instead of $PhSiMeH_2$. [d]No P450$_{BM3}$_QTG added. [e]No $PhSiMeH_2$ added.

2.2 Determination of the absolute configuration of tetralol 2

(1) Synthetic procedure for the synthesis of the reference sample (*R*)-2



Supplementary Fig. 1. Synthetic route for enantiopure (*R*)-2.

The synthesis of alkene **1** was performed according to the general procedure **A** (see below).

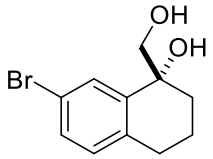
Diol S2: The synthesis was carried out according to a modified procedure[1]. To a stirred solution of $(DHQD)_2$-PHAL (7.8 mg, 0.01 mmol), $K_2OsO_2(OH)_4$ (1.8 mg, 0.005 mmol), $K_3Fe(CN)_6$ (988 mg, 3.0 mmol) and K_2CO_3 (414 mg, 3.0 mmol) in *t*-BuOH/H_2O (20 mL, 1:1 v./v.) was added alkene **1** (223 mg, 1.0 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 12 h before quenching with saturated aq. $Na_2S_2O_3$ (10 mL). The resulting mixture was gradually thawed to 22 °C, and stirred at that temperature for 2 h before diluting with ethyl acetate (60 mL). The mixture was extracted with ethyl acetate, and the combined organic extracts were sequentially washed with aq. H_2SO_4 (5 wt.%), saturated aq. $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$ and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using ethyl acetate/petroleum ether (1:3) to afford the diol **S2** (234 mg, 94% yield) as a pale yellow oil. The absolute configuration of major enantiomer was determined to be (*R*)-**S2** according to the reported literature[2].

Epoxide (*R*)-33: To a stirred solution of diol **S2** (77.1 mg, 0.3 mmol) in THF (5.0 mL) was added NaH (30 mg, 60% in mineral oil, 0.75 mmol) at 0 °C. The reaction mixture was stirred at that 0 °C for 5 min, followed by the addition TsCl (74.3 mg, 0.39 mmol) in a single portion. The reaction mixture was stirred at that temperature for 3 h before adding aq. NaOH (1.0 M), followed by stirring at 0 °C for 5 min. The mixture was extracted with CH_2Cl_2, and the combined organic phases were dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using ethyl acetate/petroleum ether (1:10) to afford the epoxide (*R*)-**33** (46 mg, 64% yield) as a pale yellow oil.

Tetralol (*R*)-2: To a stirred solution of epoxide (*R*)-**33** (47.8 mg, 0.2 mmol) in diethyl ether (2 mL) was added $LiAlH_4$ (0.2 mL, 1.0 M in Et_2O, 0.2 mmol) at 0 °C. The resulting mixture was stirred at that temperature for 30 min before quenching with aq. NaOH (15 wt.%). The resulting mixture was extracted with diethyl ether, and the combined organic phases were dried over anhydrous $MgSO_4$ and filtered. The solvent was evaporated under vacuum, and the residue was

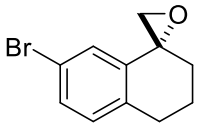
subjected to flash chromatography using ethyl acetate/petroleum ether (1:5) to afford the tetralol (*R*)-**2** (38 mg, 79% yield) as white solid.

(2) Characterization of the synthesized compounds



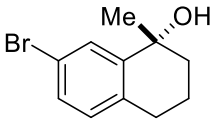
S2

Diol S2: ^{1}H NMR (600 MHz, CD_3CN) δ 7.64 (d, J = 2.2 Hz, 1H), 7.30 (dd, J = 8.2, 2.2 Hz, 1H), 7.07–6.96 (m, 1H), 3.56 (dd, J = 11.3, 6.6 Hz, 1H), 3.44 (ddd, J = 11.3, 5.8, 0.8 Hz, 1H), 3.31 (s, 1H), 3.05 (dd, J = 6.7, 5.8 Hz, 1H), 2.78–2.64 (m, 2H), 2.13 (dddd, J = 13.1, 6.9, 3.2, 0.8 Hz, 1H), 1.87–1.73 (m, 2H), 1.68–1.61 (m, 1H) ppm; ^{13}C NMR (151 MHz, CD_3CN) δ 143.8, 137.8, 131.5, 130.8, 130.7, 119.6, 73.1, 69.4, 33.5, 29.7, 20.4 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{11}H_{13}BrO_2Na^+$ 278.9991, found 278.9991.



33

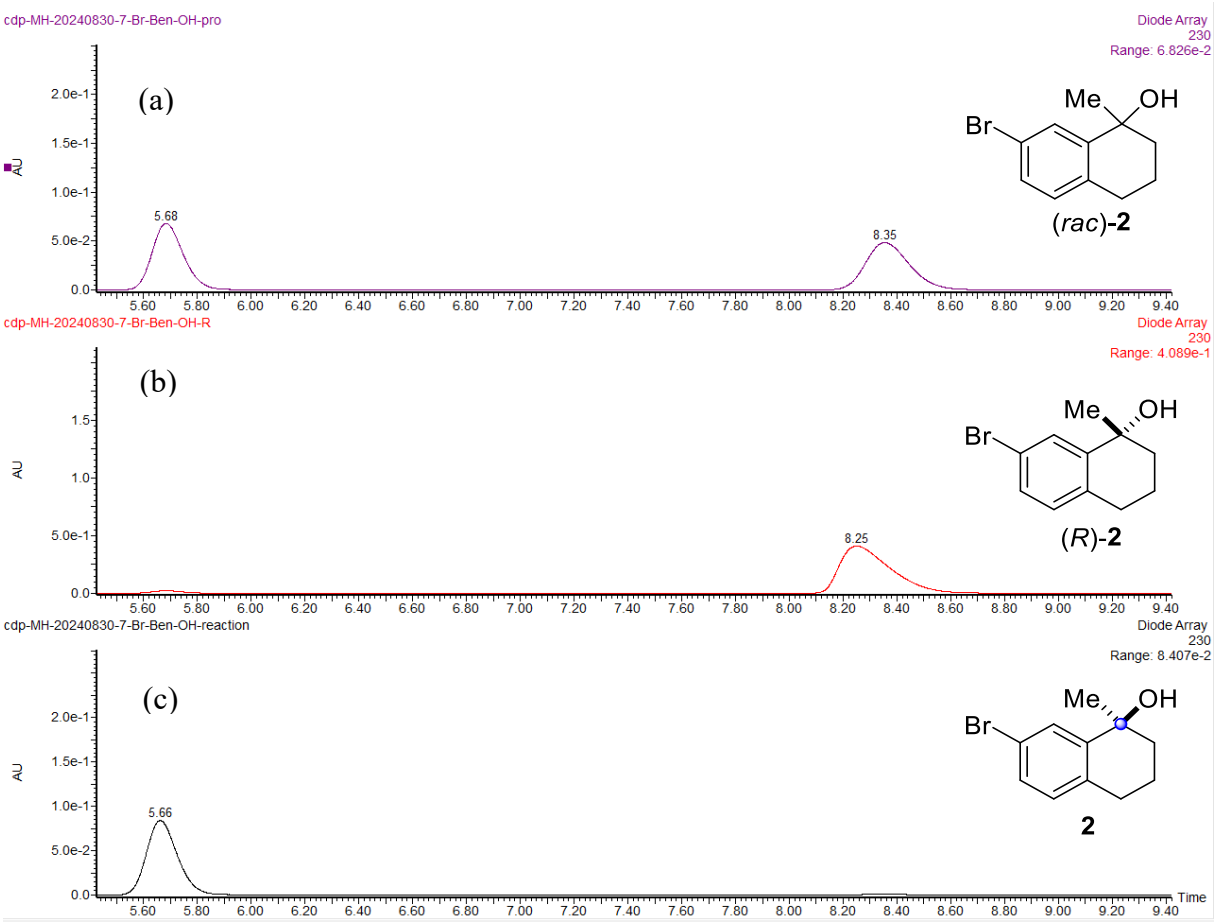
Epoxide 33: ^{1}H NMR (600 MHz, CD_3CN) δ 7.31 (dd, J = 8.2, 2.2 Hz, 1H), 7.14 (d, J = 2.2 Hz, 1H), 7.07–7.02 (m, 1H), 2.95–2.90 (m, 2H), 2.82–2.76 (m, 2H), 2.02–1.89 (m, 3H), 1.79–1.70 (m, 1H) ppm. ^{13}C NMR (151 MHz, CD_3CN) δ 139.9, 139.6, 131.6, 131.2, 127.1, 120.2, 59.4, 56.7, 31.9, 29.6, 22.4. HRMS (m/z): $[M+H]^+$ calcd for $C_{11}H_{12}BrO^+$ 239.0066, found 239.0065.



2

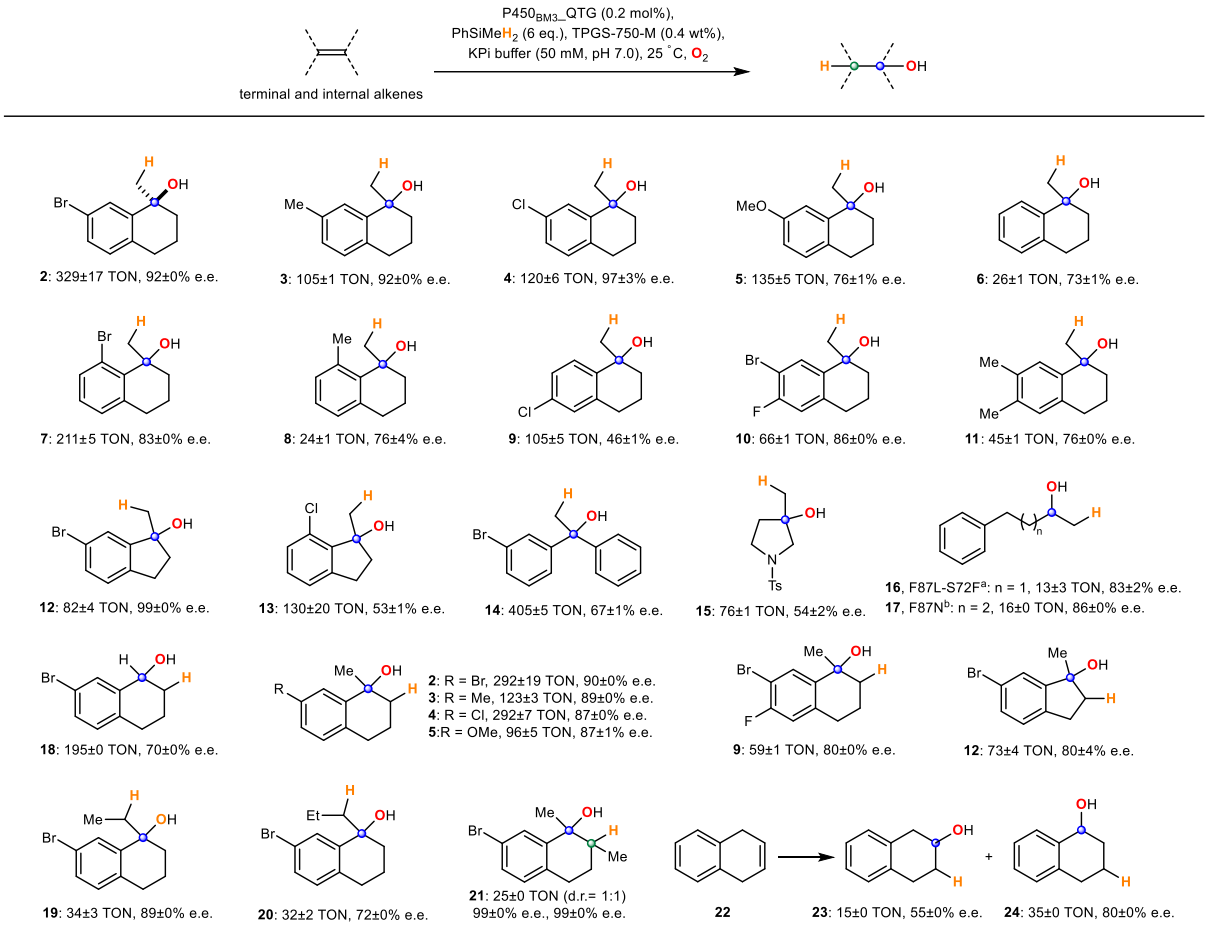
Tetralol 2: ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.70 (d, J = 2.3 Hz, 1H), 7.26 (dd, J = 8.2, 2.2 Hz, 1H), 7.01–6.93 (m, 1H), 2.80–2.64 (m, 2H), 1.98–1.73 (m, 5H), 1.50 (s, 3H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2) δ 145.9, 135.8, 131.0, 130.3, 129.7, 119.9, 70.7, 39.8, 31.1, 29.6, 20.7. HRMS (m/z): $[M+H]^+$ calcd for $C_{11}H_{14}BrO^+$ 241.0223, found 241.0223.

(3) SFC traces used to assign absolute configuration of tetralol 2 resulting from enzymatic alkene hydration of alkene 1



Supplementary Fig. 2. SFC traces of tetralol 2. (a) Synthesized racemic tetralol **2**. (b) Synthesized tetralol (*R*)-**2**. (c) Biocatalytic reaction of alkene **1** catalyzed by P450$_{BM3}$_QTG and $PhSiMeH_2$. **The absolute configuration of the major enantiomer for the biocatalytic asymmetric alkene hydration was determined to be (*S*)-2**.

2.3 Summary of the substrate scope for the P450$_{BM3}$-catalyzed alkene hydration

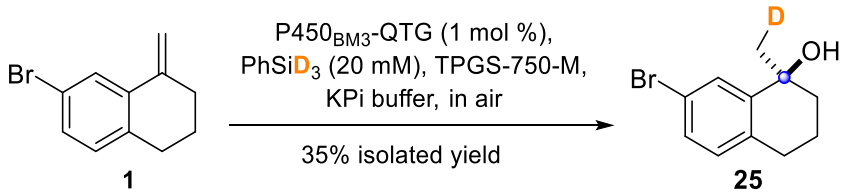


Supplementary Fig. 3. Substrate scope for the asymmetric radical alkene hydration catalyzed by the evolved radical hydratase. General procedure, unless otherwise stated: alkene substrate (1.0 mM), purified P450$_{BM3}$_QTG (2 μM, 0.2 mol % catalytic loading), KPi buffer (50 mM, pH 7.0), $PhSiMeH_2$ (2 μL of 25 % v/v in DMSO, 6 equiv. compared with alkene substrate), TPGS-750-M (40 μL, from 4 wt. % in H_2O stock solution), V_{tot} 400 μL, 25 °C in air for 12 h; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yield and e.e. were determined by SFC, using 1,3,5-trimethoxylbenzene as an internal standard. Reactions were performed in duplicate, and the standard deviations are listed. [a]alkene substrate (1.25 mM), purified P450$_{BM3}$_QTG (12.5 μM, 1 mol % catalytic loading), $PhSiH_3$ (2 μL of 50 % v/v in DMSO, 16 equiv. compared with alkene substrate), TPGS-1000-M (40 μL, from 2 wt. % in H_2O stock solution), 25 °C in air for 24 h. [b]alkene substrate (0.625 mM), purified P450$_{BM3}$_QTG (5 μM, 0.8 mol % catalytic loading), $PhSiH_3$ (2 μL of 50 % v/v in DMSO, 32 equiv. compared with alkene substrate), TPGS-1000-M (40 μL, from 2 wt. % in H_2O stock solution), 25 °C in air for 24 h.

3. Mechanistic studies

3.1 Deuterium-labeling experiments

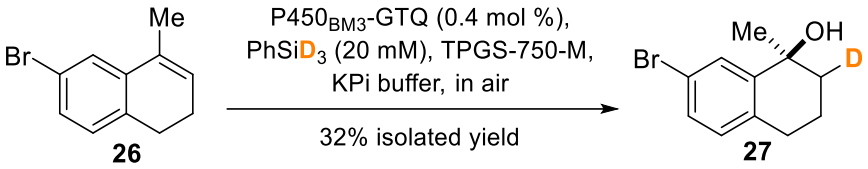
(1) Deuterium-labeling experiment with alkene 1 using $PhSiD_3$



Supplementary Fig. 4. Determining the D-incorporation using $PhSiD_3$ for the $P450_{BM3}$_QTG-catalyzed radical hydration of alkene 1.

Experimental procedure: Phenylsilane-d_3 was prepared following a reported procedure[3]. An Erlenmeyer flask (100 mL) was charged successively with purified $P450_{BM3}$_QTG (40 mL, KPi buffer (50 mM, pH 7.0), 1.0 mol% biocatalyst loading), TPGS-750-M surfactant (4.5 mL, from 2 wt% in H_2O stock solution) and alkene **1** (10 mg in 200 μL DMSO). The reaction was placed in a thermoshaker (5 min, 25 ºC, shaken at 260 rpm). Afterwards, $PhSiD_3$ (110 μL in 110 μL DMSO) was added. The reaction was placed in a thermoshaker (24 h, 25 ºC, shaken at 260 rpm). The reaction was quenched by adding $Na_2S_2O_4$ (50 mg) and stirred at that temperature for 10 min. The resulting mixture was diluted with ethyl acetate (50 mL). The aqueous phase was extracted with ether acetate (50 mL × 2), and the combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash column using dichloromethane to afford tetralol **25** (3.8 mg, 35% yield) as a colorless oil. The e.e. of isolated tetralol **25** was determined to be 96% e.e. by SFC analysis.

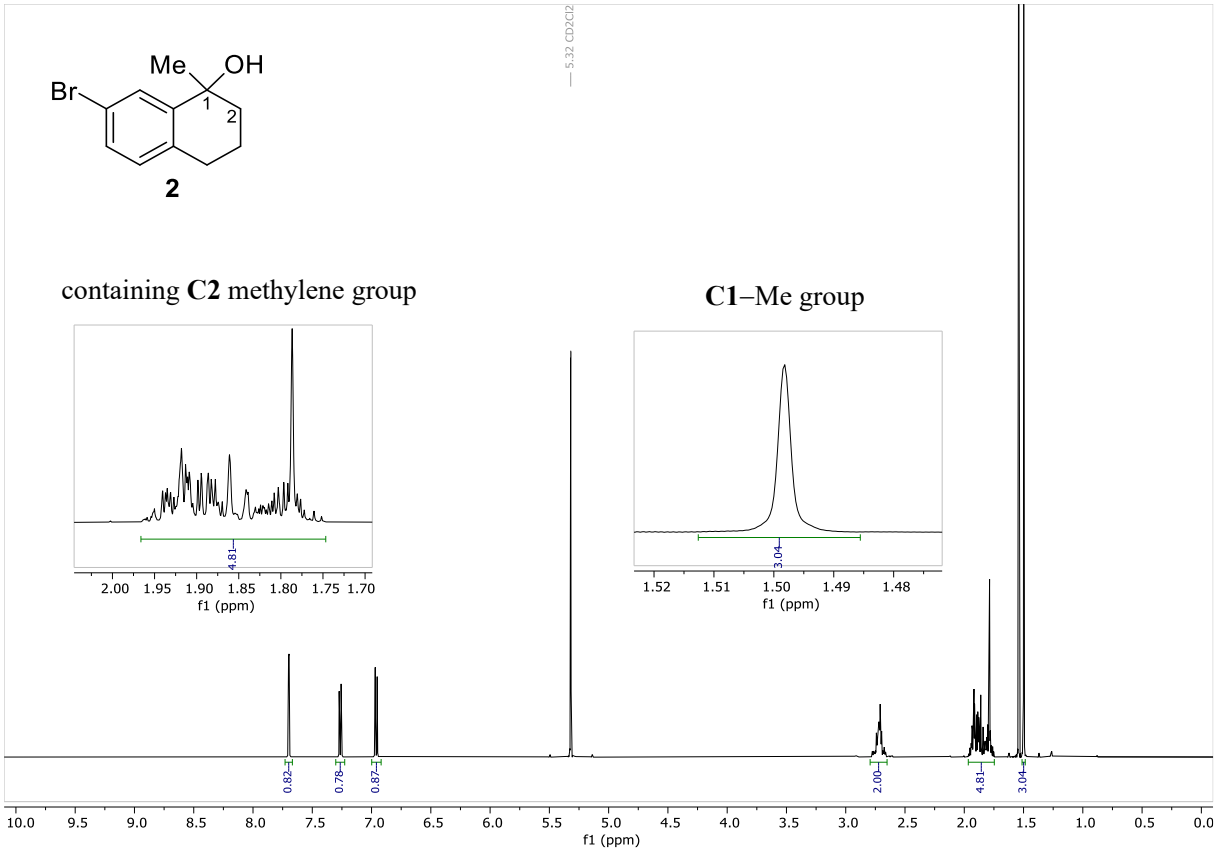
(2) Deuterium-labeling experiment with alkene 26 using $PhSiD_3$



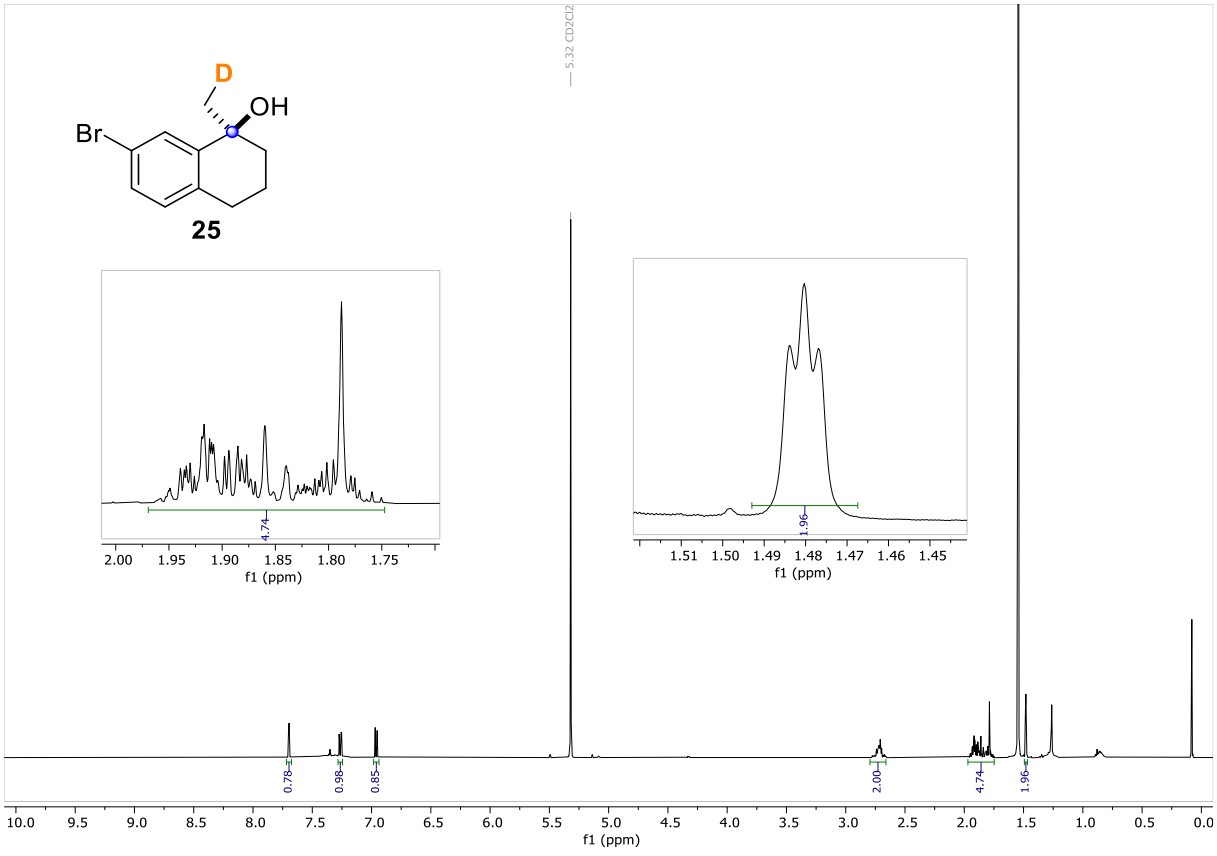
Supplementary Fig. 5. Determining the D-incorporation using $PhSiD_3$ for the $P450_{BM3}$_QTG-catalyzed radical hydration of alkene 26.

Experimental procedure: The biocatalytic radical cyclization was performed using the following procedure: An Erlenmeyer flask (100 mL) was charged successively with purified $P450_{BM3}$_QTG (40 mL, KPi buffer (50 mM, pH 7.0), 0.4 mol% biocatalyst loading), TPGS-750-M surfactant (4.5 mL, from 2 wt% in H_2O stock solution) and alkene **26** (10 mg in 200 μL DMSO). The reaction was placed in a thermoshaker (5 min, 25 °C, shaken at 260 rpm). Next, $PhSiD_3$ (110 μL in 110 μL DMSO) was added. The reaction was placed in a thermoshaker (24 h, 25 °C, shaken at 260 rpm). The reaction was quenched by adding $Na_2S_2O_4$ (50 mg) and stirred at that temperature for 10 min. The resulting mixture was diluted with ethyl acetate (50 mL). The aqueous phase was extracted with ether acetate (50 mL × 2), and the combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash column using dichloromethane to afford tetralol **27** (3.5 mg, 32% yield) as a colorless oil. The e.e. of isolated tetralol **27** was determined to be 95% e.e. by SFC analysis.

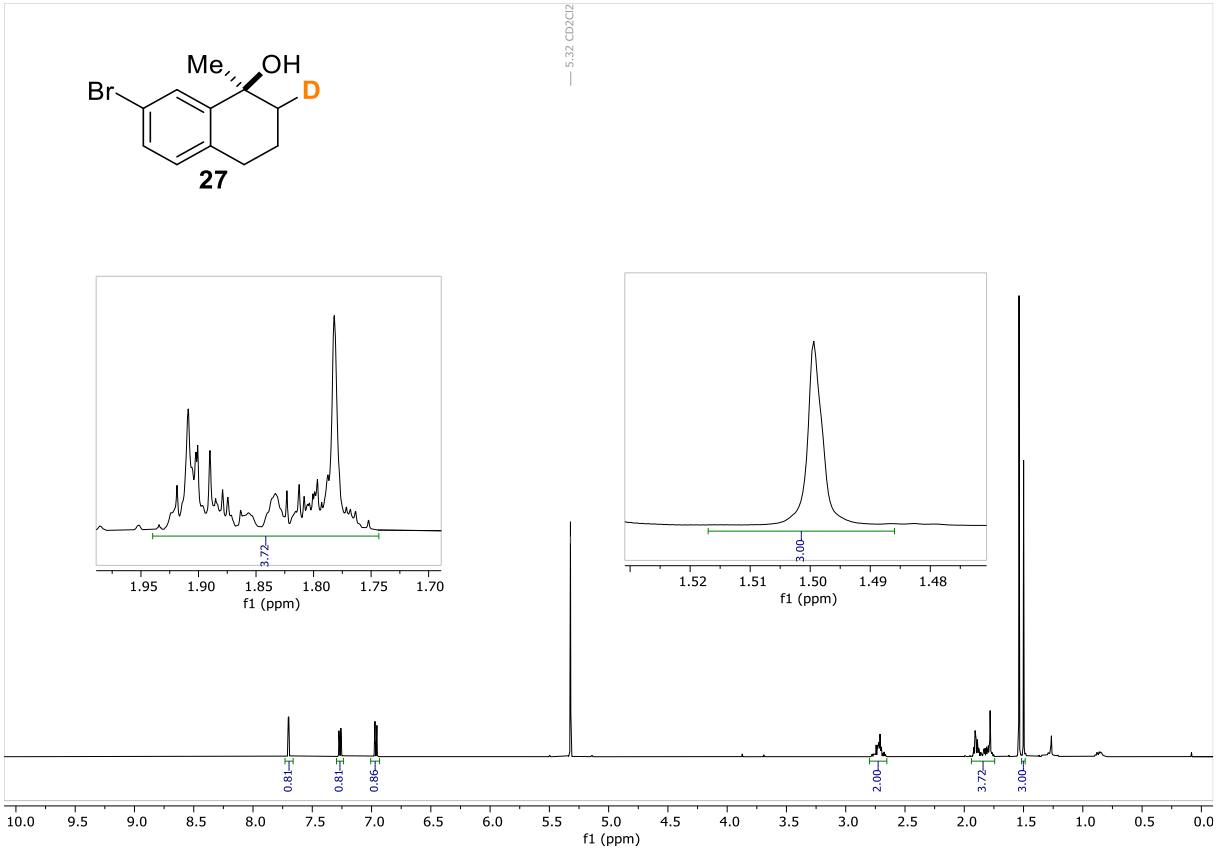
(3) ^{1}H NMR spectra



Supplementary Fig. 6. ^{1}H NMR spectrum of tetralol 2 (CD_2Cl_2, 500 MHz, 20 °C).



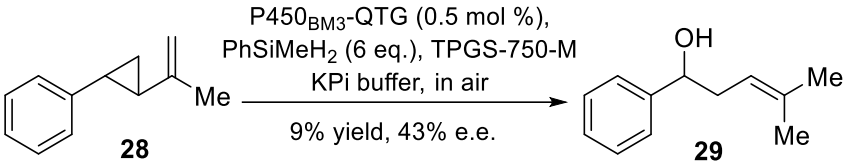
Supplementary Fig. 7. ^{1}H NMR spectrum of *D*$_1$-tetralol 25 (CD_2Cl_2, 500 MHz, 20 °C).



Supplementary Fig. 8. ^{1}H NMR spectrum of *D*$_1$-tetralol 27 (CD_2Cl_2, 500 MHz, 20 °C).

3.2 Radical-clock experiment

(1) Biocatalytic reaction with radical-clock substrate 28

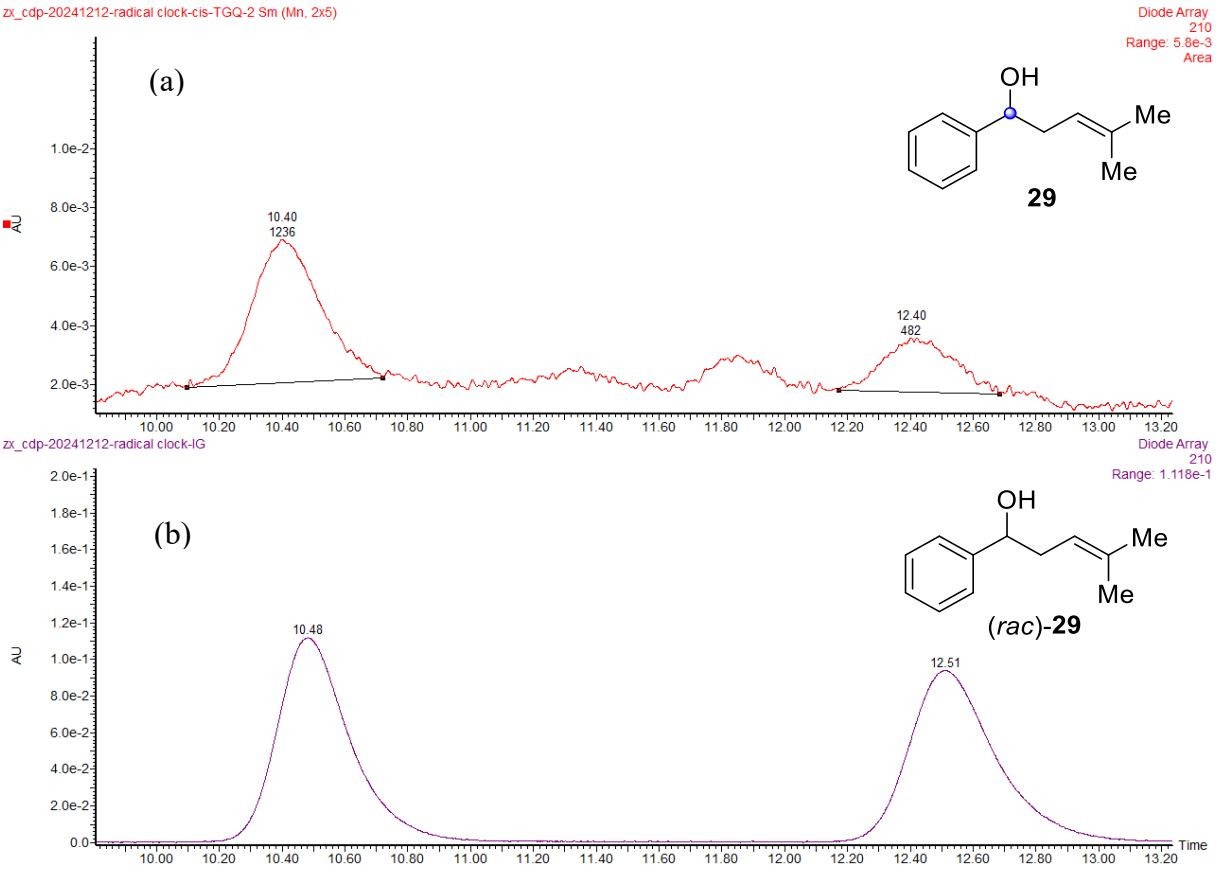


Supplementary Fig. 9. Radical-clock experiment with alkene 28 in the presence of $P450_{BM3}$_QTG and $PhSiMeH_2$.

Alkene **28**[4] and alcohol **29**[5] were prepared according to reported procedures, and their spectra are identical to the reported data.

Experimental procedure: A glass vial (2 mL) was charged successively with purified $P450_{BM3}$_QTG (356 μL, KPi buffer (50 mM, pH 7.0), 0.5 mol% biocatalyst loading), TPGS-750-M (40 μL, from 4 wt% in H_2O stock solution) and the alkene substrate **28** (2.0 μL of 200 mM in DMSO). The vial was incubated in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Next, $PhSiMeH_2$ (2 μL of 25% v/v in DMSO) was added, and the reaction was placed in a thermoshaker (12 h, 25 °C, shaken at 600 rpm). The reaction mixture was quenched by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution) and stirred at that temperature for 10 min. The resulting mixture was diluted with ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 μL), followed by adding ethyl acetate (320 μL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 μL) was transferred into a vial for SFC analysis. The yield and e.e. of alcohol **29** were 9% and 43% e.e, respectively.

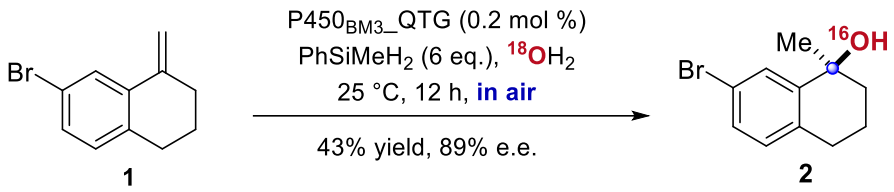
(2) SFC traces of reactions in the presence of alkene 28



Supplementary Fig. 10. SFC traces for radical-clock experiment. (a) Biocatalytic reaction of alkene **28** catalyzed by P450$_{BM3}$_QTG and $PhSiMeH_2$. (b) Synthesized racemic alcohol **29**. Chiral SFC separation conditions: Chiralpak IG, 4.6 × 250 mm; isocratic, 3% MeOH in CO_2, 2.5 mL/min, 210 nm; retention time: 10.48 min, 12.51 min. 1,3,5-trimethoxybenzene was used as internal standard (4.59 min).

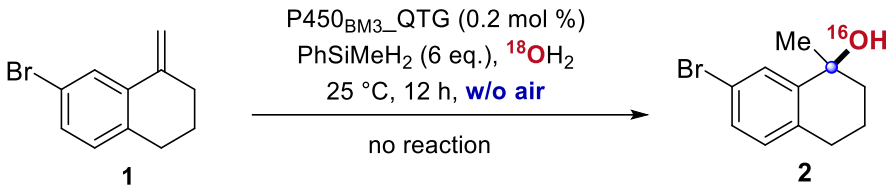
3.3 Determination of the oxygen source by ^{18}O-labeling experiments

(1) Biocatalytic reaction of alkene 1 with $^{18}OH_2$



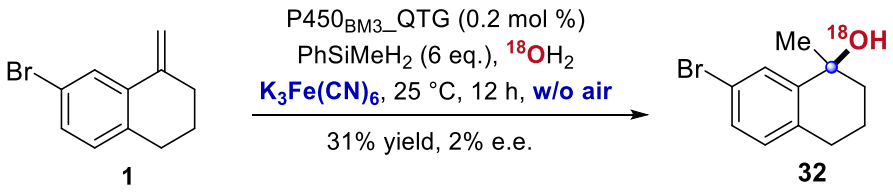
Supplementary Fig. 11. ^{18}O-labeling of alkene 1 with $^{18}OH_2$ under aerobic conditions.

Experimental procedure: A glass vial (2 mL) was charged successively with purified P450$_{BM3}$_QTG (388 µL, $^{18}OH_2$, 0.2 mol% biocatalyst loading) and the alkene **1** (2.0 µL of 200 mM in DMSO). The vial was incubated in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Next, $PhSiMeH_2$ (2 µL of 25% v/v in DMSO) was added, and the reaction was placed in a thermoshaker (12 h, 25 ºC, shaken at 600 rpm). The reaction mixture was quenched by adding aq. $Na_2S_2O_4$ (10 µL, from 0.5 M in $^{18}OH_2$ stock solution), stirred at that temperature for 10 min. The resulting mixture was diluted with ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 µL), followed by addition of ethyl acetate (320 µL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 µL) was transferred into two vials for SFC and GC-MS analyses. The yield and e.e. of tetralol **2** were determined by SFC analysis to be 43% yield and 89% e.e. The isotopic identity of tetralol **2** was verified by GC-MS, confirming that no ^{18}O-incorporation results from the use of $^{18}OH_2$.



Supplementary Fig. 12. ^{18}O-labeling experiment with alkene 1 and $^{18}OH_2$ under anaerobic conditions.

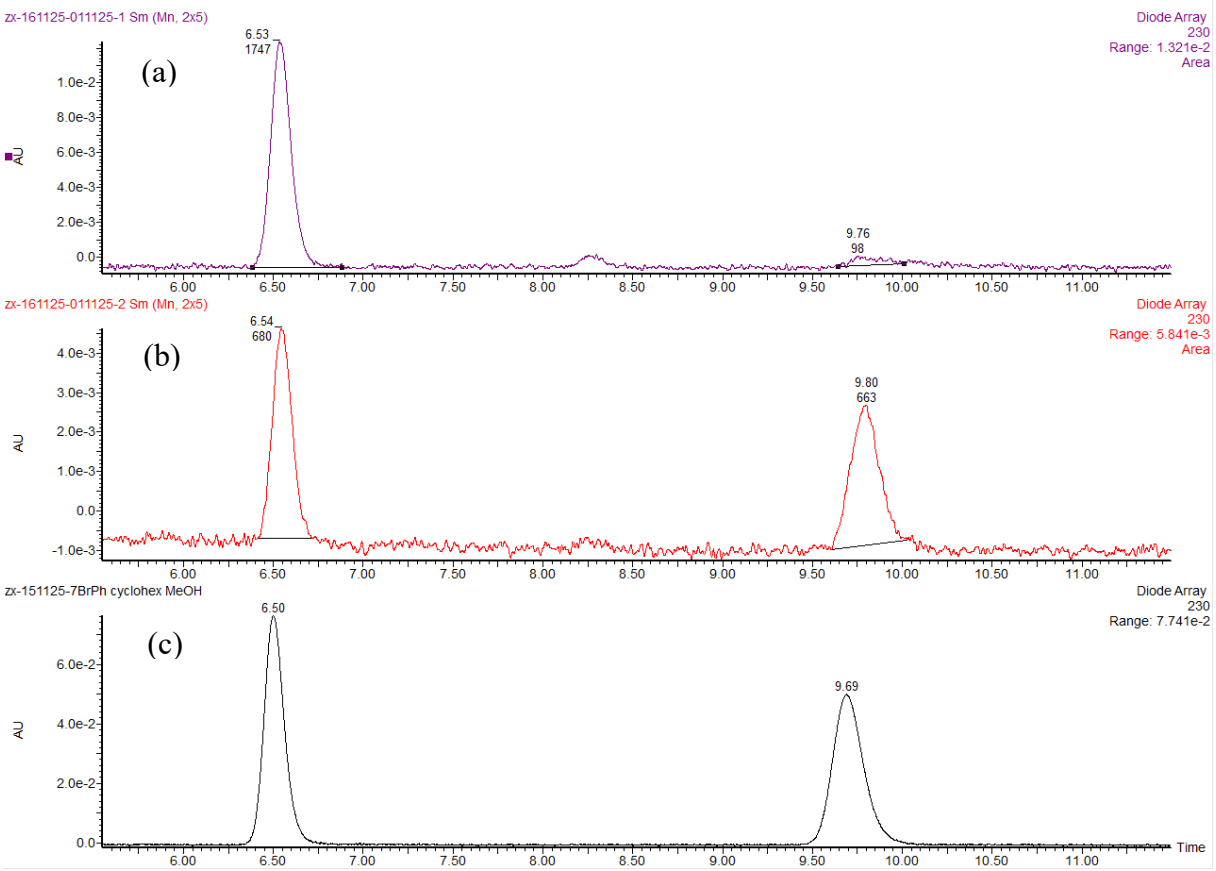
Experimental procedure: All reagents, samples and solvents were degassed and transferred into a glove box. A glass vial (2 mL) was charged successively with purified $P450_{BM3}$_QTG (388 µL, $^{18}OH_2$, 0.2 mol% biocatalyst loading) and the alkene **1** (2.0 µL of 200 mM in DMSO). The vial was incubated in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Afterwards, $PhSiMeH_2$ (2 µL of 25% v/v in DMSO) was added, and the reaction was placed in a thermoshaker (12 h, 25 °C, shaken at 600 rpm). The reaction mixture was quenched by a spatula tip of $Na_2S_2O_4$, and stirred at that temperature for 10 min. The resulting mixture was diluted with ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 µL), followed by addition of ethyl acetate (320 µL). After vortexing, the vial was removed from the glove box and the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 µL) was transferred into two vials for separate SFC and GC-MS analyses. No reaction was observed according to SFC and GC-MS analyses.



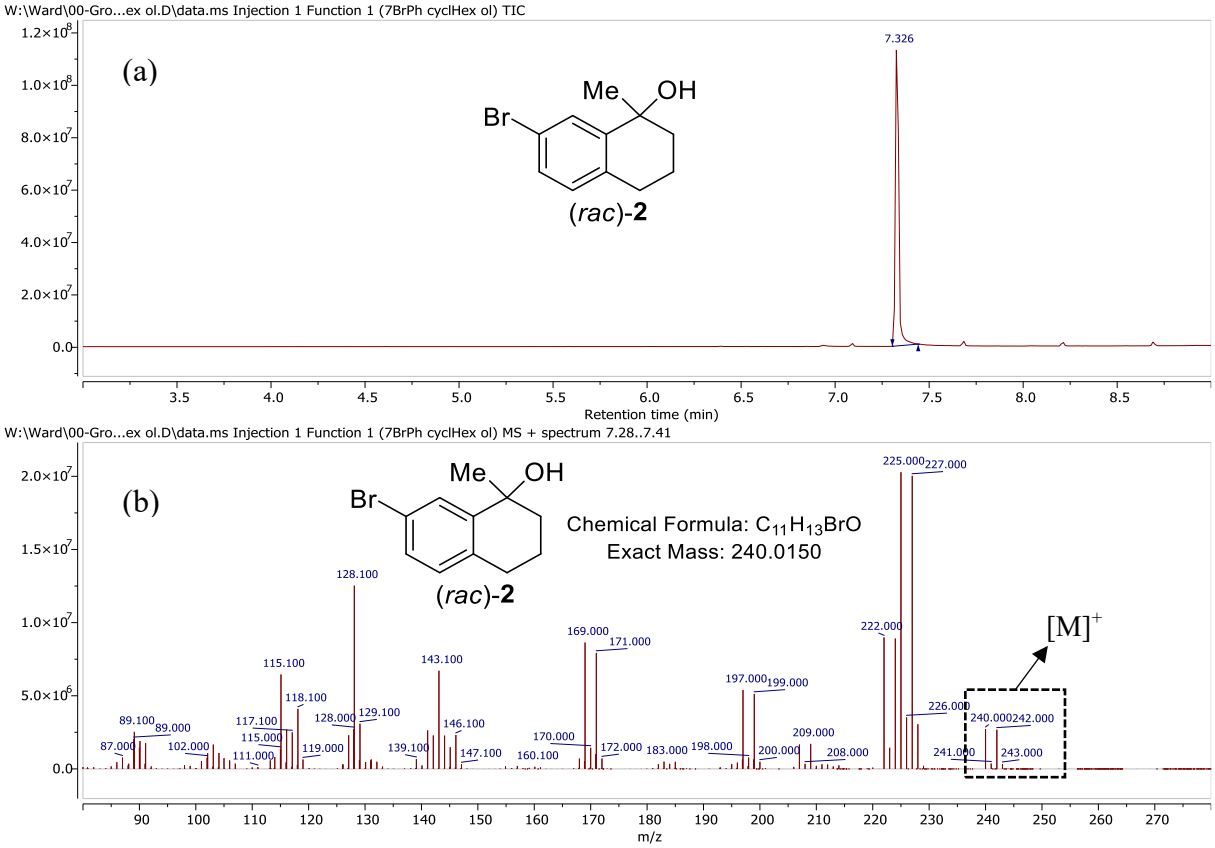
Supplementary Fig. 13. ^{18}O-labeling experiment with alkene 1 and $^{18}OH_2$ under anaerobic conditions in the presence of $K_3Fe(CN)_6$ as oxidant.

Experimental procedure: All reagents, samples and solvents were degassed and transferred into a glove box. A glass vial (2 mL) was charged successively with purified $P450_{BM3}$_QTG (378 µL, $^{18}OH_2$, 0.2 mol% biocatalyst loading), the alkene **1** (2.0 µL of 200 mM in DMSO) and $K_3Fe(CN)_6$ (10.0 µL, from 200 mM in $^{18}OH_2$ stock solution). The vial was incubated in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Next, $PhSiMeH_2$ (2 µL of 25% v/v in DMSO) was added, and the reaction was placed in a thermoshaker (12 h, 25 °C, shaken at 600 rpm). The reaction mixture was quenched by adding a spatula tip of $Na_2S_2O_4$ and stirred at that temperature for 10 min. The resulting mixture was diluted with ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 µL), followed by additional ethyl acetate (320 µL). After vortexing, the vial was removed from the glove box, and the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 µL) was transferred into two vials for SFC and GC-MS analyses. The yield (31 %) and e.e. (2 % ee) of tetralol **32** were determined by SFC. The isotopic identity of tetralol **32** was verified by GC-MS to confirm the incorporation of ^{18}O.

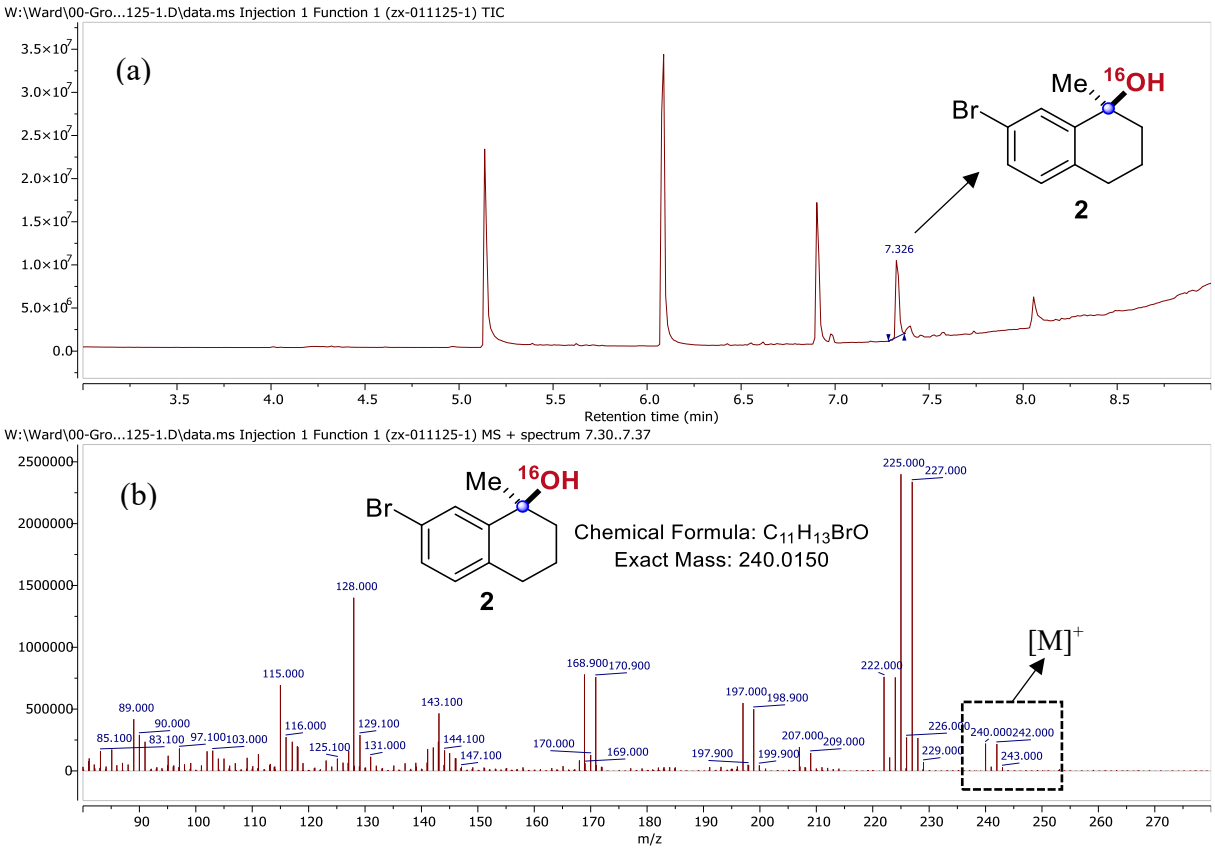
(2) Chromatograms of SFC and GC-MS



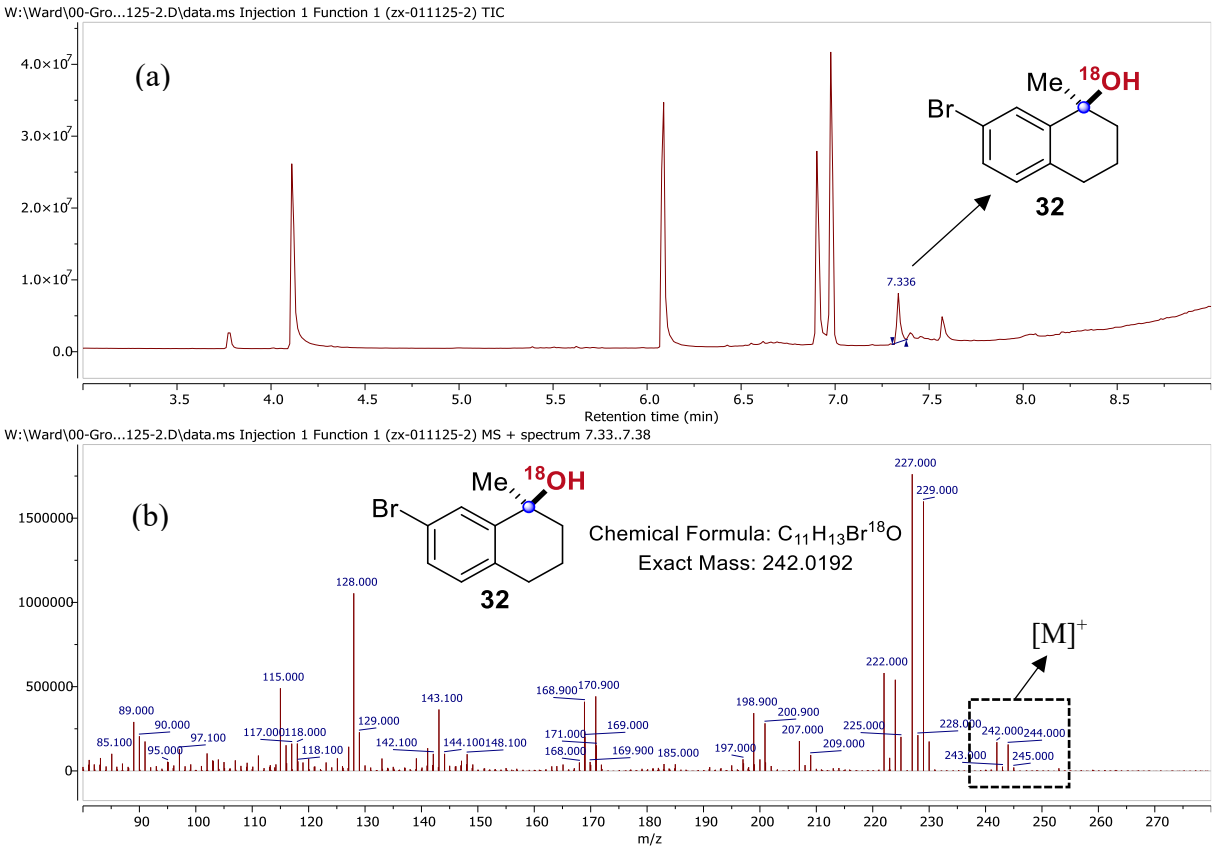
Supplementary Fig. 14. SFC traces for ^{18}O-labeling experiments. (a) Biocatalytic reaction of alkene **1** with $^{18}OH_2$ under aerobic conditions. (b) Biocatalytic reaction of alkene **1** with $^{18}OH_2$ under anaerobic conditions in the presence of $K_3Fe(CN)_6$. (c) Synthesized racemic tetralol **2**.



Supplementary Fig. 15. GC-MS traces of racemic tetralol 2. (a) GC chromatogram of synthesized racemic tetralol **2**. (b) Mass spectrum extracted at 7.326 min retention time (corresponding to tetralol **2**) in the GC-MS chromatogram.



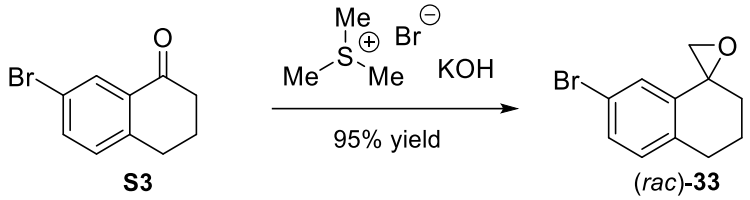
Supplementary Fig. 16. GC-MS traces of aerobic ^{18}O-labeling experiment. (a) GC chromatogram of biocatalytic reaction of alkene **1** with $^{18}OH_2$ under aerobic conditions. (b) Mass spectrum extracted at 7.326 min retention time (corresponding to tetralol **2**) in the GC-MS chromatogram, **confirming no incorporation of ^{18}O** (compare to **Supplementary Fig 15 b**).



Supplementary Fig. 17. GC-MS traces of anaerobic ^{18}O-labeling experiment in the presence of $K_3Fe(CN)_6$. (a) GC chromatogram of the biocatalytic reaction of alkene **1** with $^{18}OH_2$ under anaerobic conditions in the presence of $K_3Fe(CN)_6$ as oxidant. (b) Mass spectrum extracted at 7.336 min retention time (corresponding to tetralol **32**) in the GC-MS chromatogram, **confirming the incorporation of ^{18}O** (compare to **Supplementary Fig 15 b**).

3.4 Biocatalytic reaction with epoxide

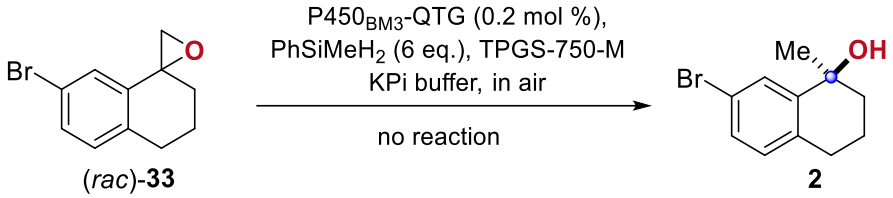
(1) Synthesis of (*rac*)-epoxide 33



Supplementary Fig. 18. Synthesis of racemic epoxide 33.

Racemic epoxide 33: To a stirred solution of trimethylsulfonium bromide (3.06 g, 15 mmol) in MeCN (15 mL) potassium hydroxide (4.21 g, 75 mmol) and water (0.05 mL) were added at 22 ºC. The reaction mixture was warmed to 60 ºC and stirred for 5 min. Next, a solution of commercially available ketone **S3** (2.25 g, 10 mmol, in 3.0 mL MeCN) was added, and the reaction mixture was stirred at 60 ºC for 3 h before cooling to 22 ºC. The resulting mixture was diluted with diethyl ether (75 mL) and filtered to remove insoluble salts. The filtrate was diluted with hexane and extracted with water. The organic phases were dried over anhydrous $MgSO_4$ and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using diethyl ether/petroleum ether (1:4) containing triethyl amine (0.1% v/v) to afford the epoxide (*rac*)-**33** (2.27 g, 95% yield) as a yellow oil (see characterization data of epoxide **33** in **Section 2.2**)

(2) Biocatalytic reaction with the racemic epoxide 33

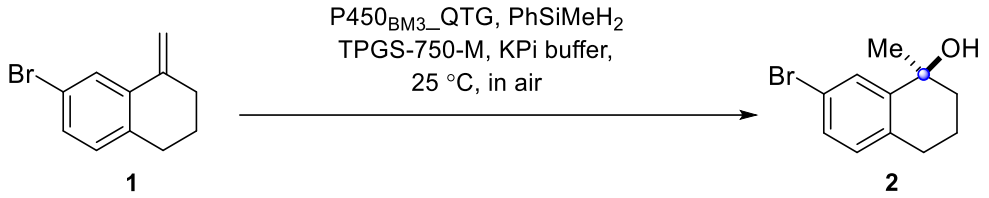


Supplementary Fig. 19. Biocatalytic reaction with epoxide (*rac*)-33 in the presence of P450$_{BM3}$_QTG and PhSiMeH$_2$.

Experimental procedure: A glass vial (2 mL) was charged successively with purified P450$_{BM3}$_QTG (356 µL, KPi buffer (50 mM, pH 7.0), 0.2 mol% biocatalyst loading), TPGS-750-M (40 µL, from 4 wt% in H_2O stock solution) and the epoxide (*rac*)-**33** (2.0 µL of 200 mM in DMSO). The vial was incubated in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Next, $PhSiMeH_2$ (2 µL of 25% v/v in DMSO) was added, and the reaction was placed in a thermoshaker (12 h, 25 °C, shaken at 600 rpm). The reaction mixture was quenched by adding aq. $Na_2S_2O_4$ (10 µL, from 0.5 M in H_2O stock solution) and stirred for 10 min. The resulting mixture was diluted with ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 µL), followed by additional ethyl acetate (320 µL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 µL) was transferred into a vial for SFC analysis. No tetralol **2** was detected by SFC, suggesting that the epoxide is not an intermediate in the biocatalytic cycle.

3.5 Time-course monitoring experiments

Supplementary Table 10. Time-course monitoring of the biocatalytic asymmetric alkene hydration reaction



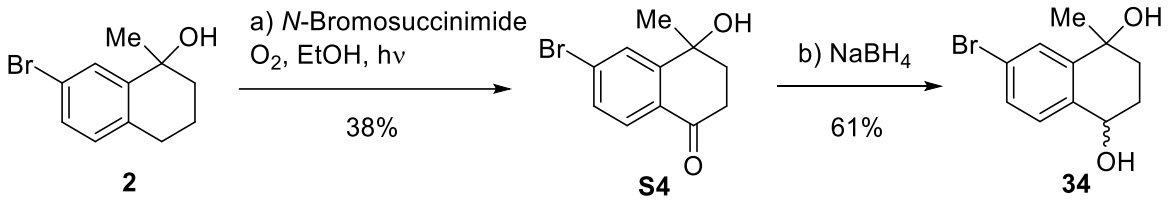
1 2

Entry[a]	Reaction time	Yield of **2** (%)	e.e. of **2** (%)	Recovery of **1** (%)	Mass balance
1	10 min	19±1	68±1	78±2	98±1
2	30 min	26±1	75±1	65±0	91±1
3	1 h	34±1	77±0	52±1	86±3
4	2 h	36±1	80±1	46±0	82±1
5	4 h	46±1	86±0	29±2	75±3
6	6.5 h	52±1	90±1	19±0	71±2
7	12 h	66±3	92±0	9±1	74±3
8	24 h	56±2	92±1	9±1	64±3
9	42 h	56±1	91±1	8±1	64±2

[a]Unless otherwise stated, the standard conditions are: alkene **1** (1.0 mM), $P450_{BM3}$_QTG (2 μM, 0.2 mol % catalytic loading), KPi buffer (50 mM, pH 7.0), $PhSiMeH_2$ (2 μL of 25 % v/v in DMSO, 6 equiv. compared with alkene **1**), TPGS-750-M (40 μL, from 4 wt. % in H_2O stock solution), V_{tot} 400 μL, 25 °C in air, reaction time was indicated in the table; workup by adding aq. $Na_2S_2O_4$ (10 μL, from 0.5 M in H_2O stock solution). Yield and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed.

3.6 Detection and characterization of the diol 34

(1) Synthesis of diol 34



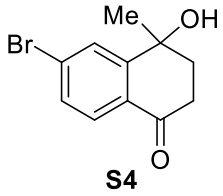
Supplementary Fig. 20. Synthesis of diol 34.

The synthesis of racemic tetralol **2** was performed according to the general procedure **D** (see below).

Ketone S4: The synthesis was carried out according to a modified procedure[6]. To a stirred solution of tetralol **2** (100 mg, 0.41 mmol) in EtOH (10 mL) was added *N*-Bromosuccinimide (7.1 mg, 0.04 mmol) at 22 ºC. The reaction mixture was stirred in air under light irradiation with an 18 W blue LED (405 nm) at 22 ºC for 48 h. The reaction mixture was concentrated *in vacuo*, and the product was purified by flash column using ethyl acetate/petroleum ether (1:1) to afford ketone **S4** (40.2 mg, 38% yield) as white solid.

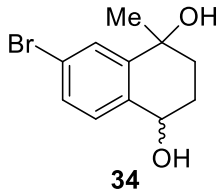
Diol 34: To a stirred solution of ketone **S4** (40.2 mg, 0.16 mmol) in MeOH (1.0 mL), $NaBH_4$ (18.1 mg, 0.48 mmol) was added at 0 ºC. The reaction mixture was stirred for 30 min, before quenching with saturated aq. NH_4Cl. The mixture was extracted with diethyl ether, and the combined organic phases were dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using acetone/petroleum ether (1:2) to afford the diol **34** (24.7 mg, 61% yield) as a mixture of diastereomers (d.r. = 2:1).

(2) Characterization of the synthesized compounds



S4

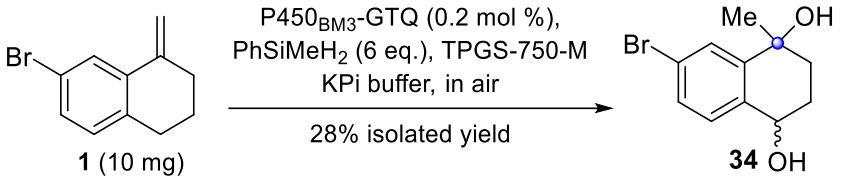
Ketone S4: ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.89 (d, J = 2.0 Hz, 1H), 7.80 (d, J = 8.4 Hz, 1H), 7.52 (dd, J = 8.4, 2.0 Hz, 1H), 2.80 (ddd, J = 17.9, 4.9, 4.9 Hz, 1H), 2.67 (ddd, J = 18.0, 9.7, 7.5 Hz, 1H), 2.28–2.24 (m, 2H), 1.60 (s, 3H) ppm; ^{13}C NMR (126 MHz, CD_2Cl_2) δ 196.4, 152.0, 131.5, 129.8, 129.6, 129.1, 129.0, 70.4, 38.6, 36.1, 29.3 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{11}H_{12}BrO_2^+$ 255.0015, found 255.0016.



34

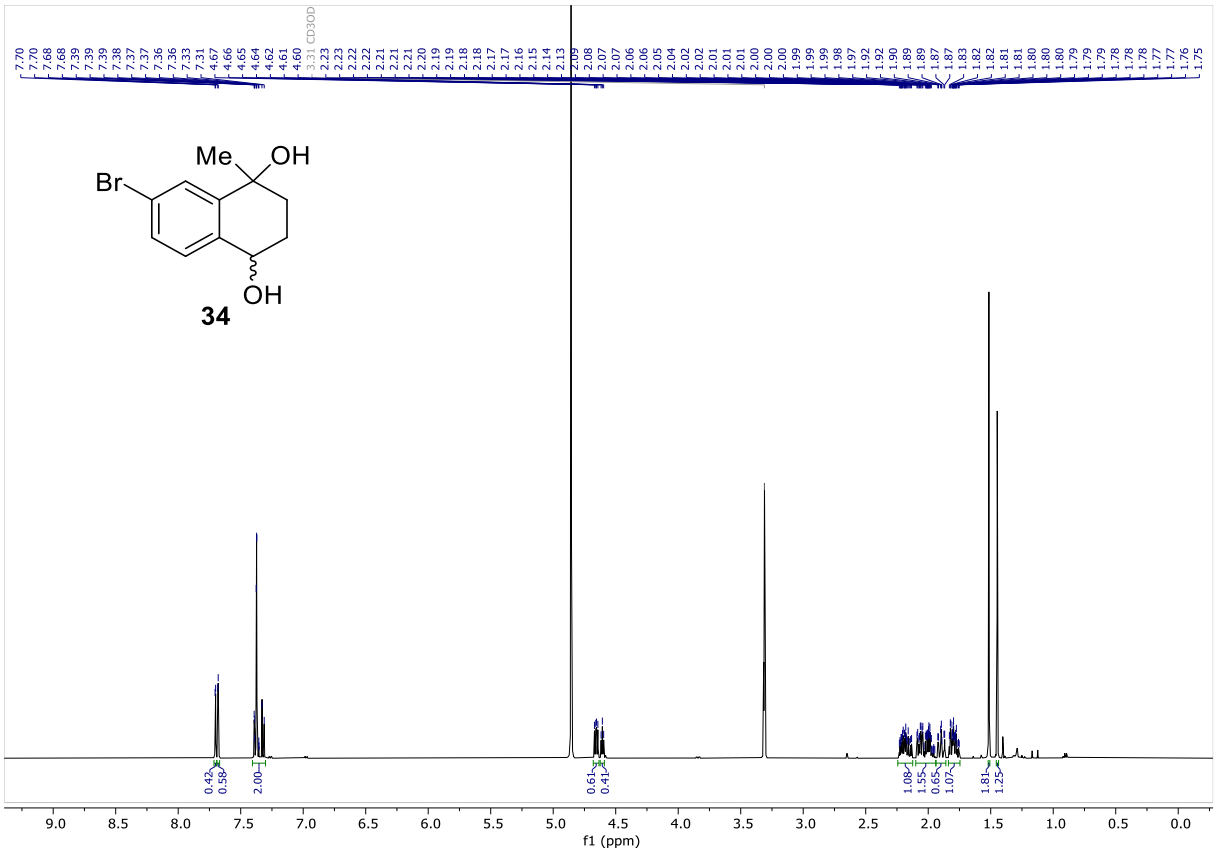
Diol 34: ^{1}H NMR (600 MHz, MeOD-d_4) δ 7.70 (s, 0.34H), 7.68 (s, 0.66H), 7.40-7.30 (m, 2H), 4.66 (dd, J = 8.8, 5.0 Hz, 0.66H), 4.63–4.58 (m, 0.34H), 2.24–2.13 (m, 1H), 2.09–1.87 (m, 2H), 1.84–1.75 (m, 1H), 1.52 (s, 2H), 1.45 (s, 1H) ppm; ^{13}C NMR (151 MHz, MeOD-d_4) δ 146.8, 139.0, 138.5, 131.5, 131.3, 131.2, 130.8, 130.5, 130.4, 122.6, 122.3, 71.1, 70.9, 68.9, 68.0, 37.2, 35.5, 31.2, 30.8, 30.3 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{11}H_{14}BrO_2^+$ 257.0172, found 257.0172. The NMR analyses confirm the structure of diol **34** (**Supplementary Figs. 79-83**)
Chiral SFC separation conditions: Chiralpak IH, 4.6 × 250 mm; isocratic, 8% MeOH in CO_2, 2.5 mL/min, 230 nm; retention time: 9.63 min and 10.06 min, 11.88 min and 12.35 min. 1,3,5-trimethoxybenzene was used as internal standard (1.53 min).

(3) Biocatalytic reaction of alkene 1 with $P450_{BM3}$_QTG and $PhSiMeH_2$



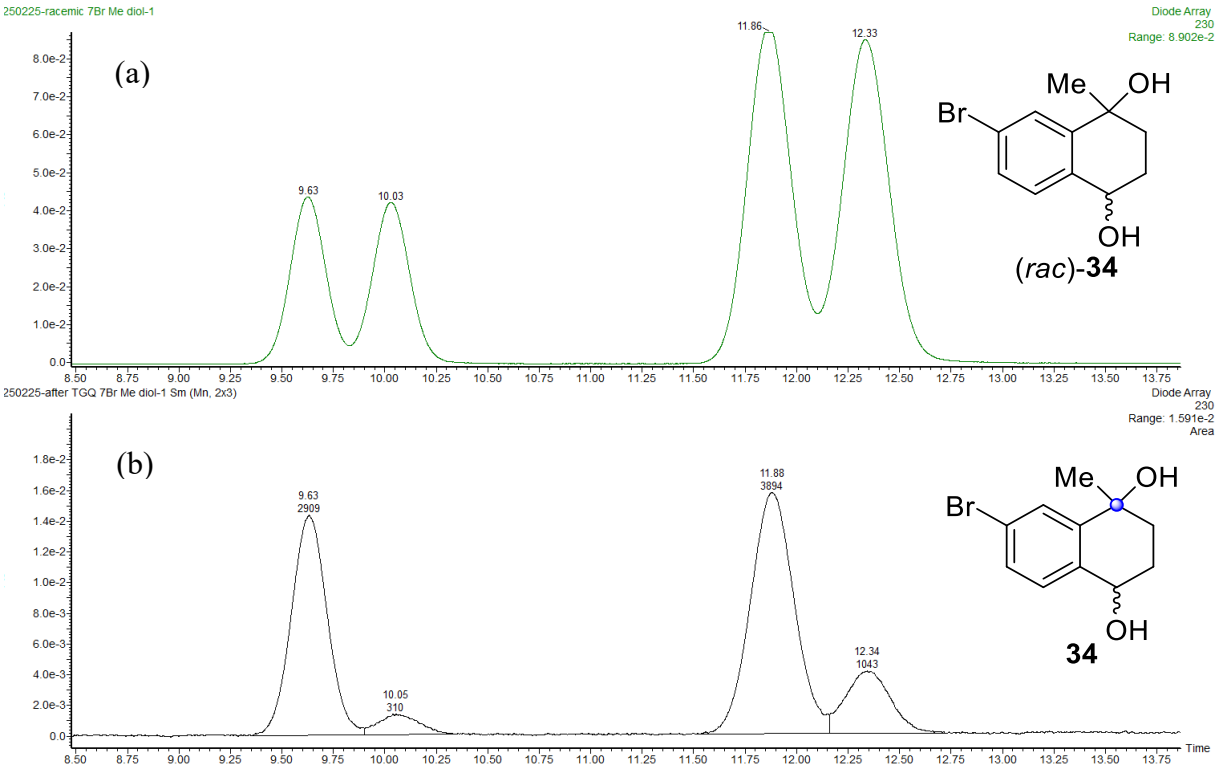
Supplementary Fig. 21. Biocatalytic reaction of alkene 1 with $P450_{BM3}$_QTG and $PhSiMeH_2$

Experimental procedure: An Erlenmeyer flask (100 mL) was charged successively with purified $P450_{BM3}$_QTG (40 mL, KPi buffer (50 mM, pH 7.0), 0.2 mol% biocatalyst loading), TPGS-750-M surfactant (4.5 mL, from 2 wt% in H_2O stock solution) and alkene **1** (10 mg in 200 μL DMSO). The reaction was placed in a thermoshaker (5 min, 25 °C, shaken at 260 rpm). Afterwards, $PhSiD_3$ (110 μL in 110 μL DMSO) was added. The reaction was placed in a thermoshaker (24 h, 25 °C, shaken at 260 rpm). The reaction was quenched by adding $Na_2S_2O_4$ (50 mg) and stirred at that temperature for 10 min. The resulting mixture was diluted with ethyl acetate (50 mL). The aqueous phase was extracted with ether acetate (50 mL × 2), and the combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromotography using acetone/petroleum ether (1:2) to afford the diol **34** (3.2 mg, 28% yield) as a mixture of diastereomers (d.r. = 1.5:1, 58% e.e. for major diastereomer and 81% e.e. for minor diastereomer). The proton NMR of the isolated diol **34** proved to be identical to that of independently-synthesized sample (**Supplementary Figs. 22 and 79**), confirming that diol **34** is a byproduct formed in the biocatalytic radical alkene hydration.

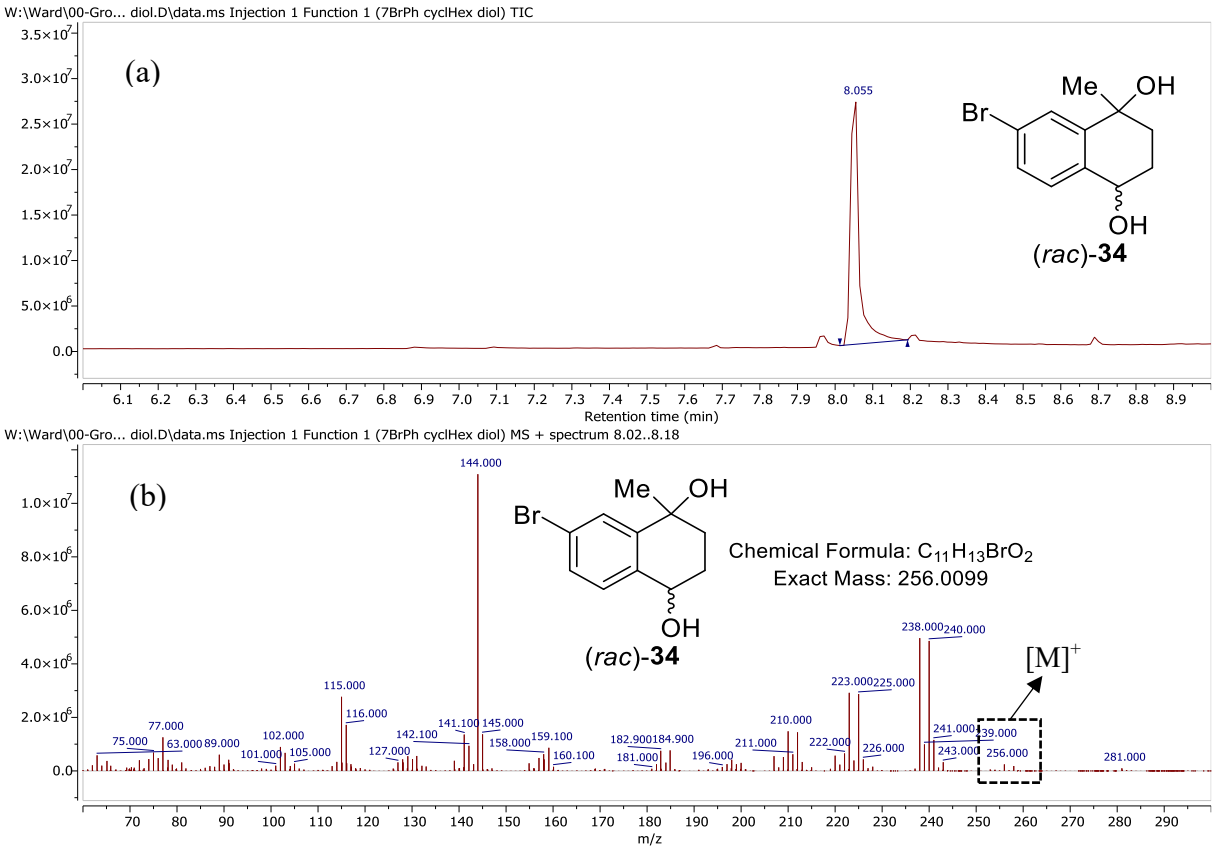


Supplementary Fig. 22. ^{1}H NMR spectrum of diol 34 obtained from the biocatalytic reaction of alkene 1 with P450$_{BM3}$_QTG and PhSiMeH$_2$. (MeOD-d$_4$, 500 MHz, 20 °C).

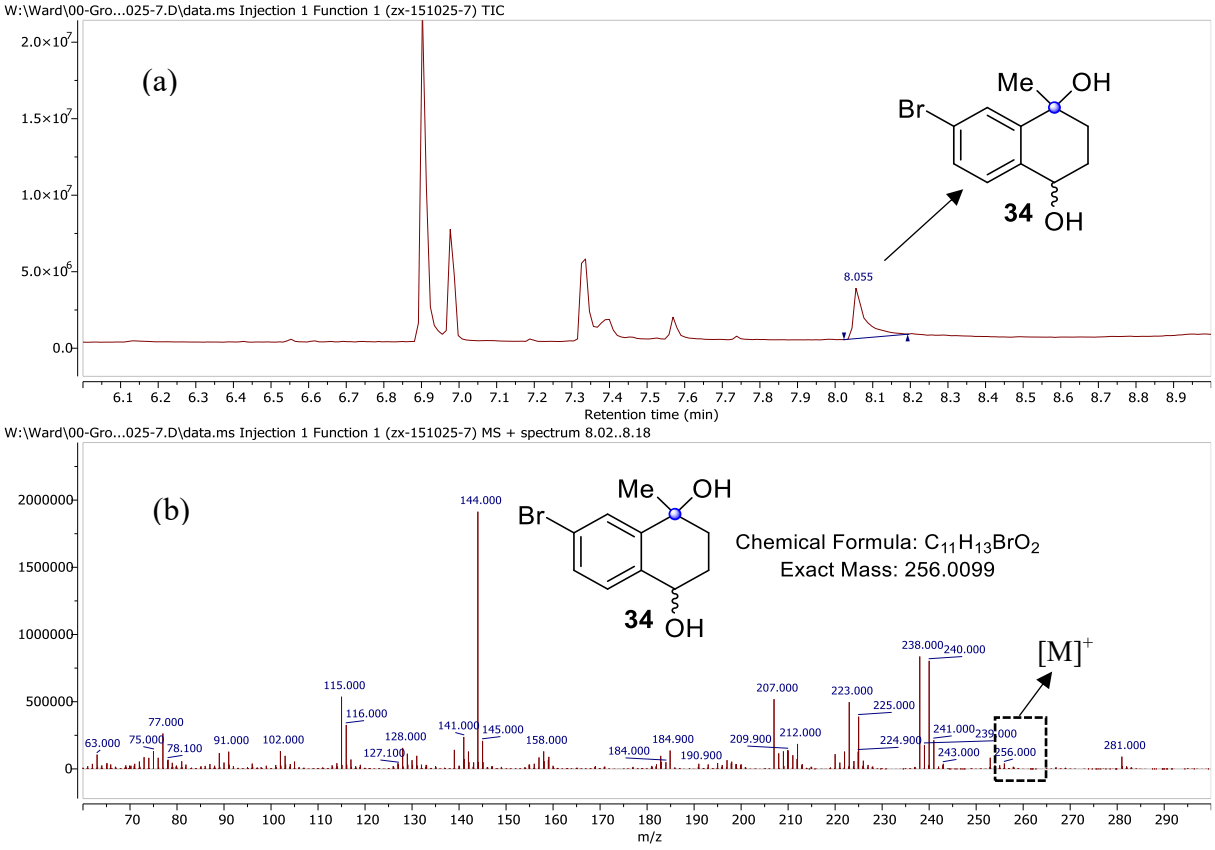
(4) Chromatograms of SFC and GC-MS



Supplementary Fig. 23. SFC traces of diol 34. (a) Diastereomeric mixture of the synthesized racemic diol **34**. (b) Biocatalytic reaction of alkene **1** with $P450_{BM3}$_QTG and $PhSiMeH_2$, revealing a 1.5:1 diastereomeric ratio.

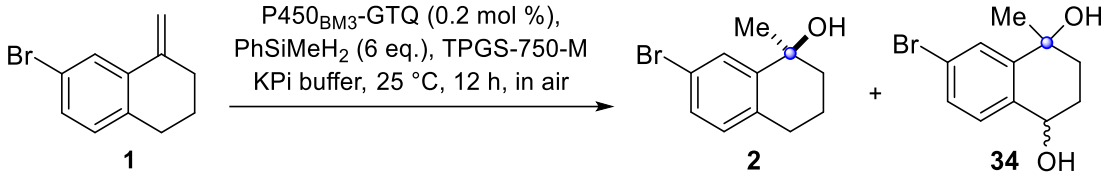


Supplementary Fig. 24. GC-MS traces of racemic diol 34. (a) GC chromatogram of independently-synthesized diol **34**. (b) Mass spectrum extracted at 8.055 min retention time (corresponding to diol **34**) in the GC-MS chromatogram.



Supplementary Fig. 25. GC-MS traces of the biocatalytic radical alkene hydration. (a) GC chromatogram of biocatalytic reaction of alkene **1** with P450$_{BM3}$_QTG and $PhSiMeH_2$. (b) Mass spectrum extracted at 8.055 min retention time (corresponding to diol **34**) in the GC-MS chromatogram. **Both the retention time and mass spectrum of the unknown compound match that of the independently-synthesized diol 34, confirming that diol 34 is the byproduct in the biocatalytic radical alkene hydration.**

(5) Mass balance analysis of the biocatalytic hydration of alkene 1 with $P450_{BM3}$_QTG and $PhSiMeH_2$



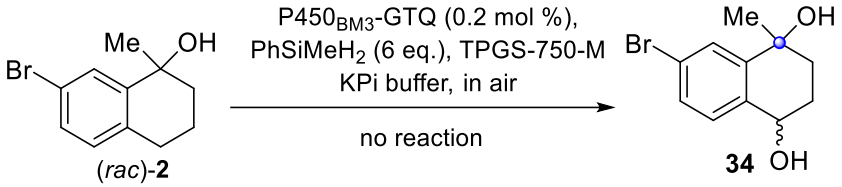
1 2 34

yield of **2** (%)	e.e. of **2** (%)	recovery of **1** (%)	yield of **34** (%)	mas balance (%)
66±3	92±0	9±1	23±3	97±1

Supplementary Fig. 26. Mass balance of the biocatalytic radical hydration with alkene 1 determined by SFC and GC-MS analysis of the reaction mixture.

Experimental procedure: A glass vial (2 mL) was charged successively with purified $P450_{BM3}$_QTG (356 µL, KPi buffer (50 mM, pH 7.0), 0.2 mol% biocatalyst loading), TPGS-750-M (40 µL, from 4 wt% in H_2O stock solution) and the alkene **1** (2.0 µL of 200 mM in DMSO). The vial was incubated in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Afterwards, $PhSiMeH_2$ (2 µL of 25% v/v in DMSO) was added, and the reaction was placed in a thermoshaker (12 h, 25 °C, shaken at 600 rpm). The reaction mixture was quenched by adding aq. $Na_2S_2O_4$ (10 µL, from 0.5 M in H_2O stock solution) and stirred at that temperature for 10 min. The resulting mixture was diluted with ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 µL), followed by addition of ethyl acetate (320 µL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 µL) was transferred into a vial for SFC analysis. The yield and e.e. of tetralol **2**, and the recovery of alkene **1** and the yield of diol **34** were determined by SFC analysis and are displayed in the **Supplementary Fig. 26**. The corrected mass balance, determined as the sum of the yields of tetralol **2**, diol **34** and recovered alkene **1** proved to be excellent, confirming that diol **34** is the main byproduct in the biocatalytic radical alkene hydration (see **Supplementary Table 10, Entry 7** for comparison).

3.7 Investigation of the formation of diol 34

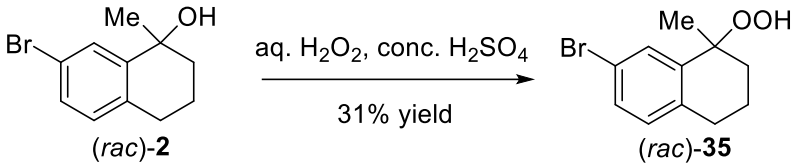


Supplementary Fig. 27. Biocatalytic reaction using racemic tatralol 2 as substrate

Experimental procedure: A glass vial (2 mL) was charged successively with purified $P450_{BM3}$_QTG (356 µL, KPi buffer (50 mM, pH 7.0), 0.2 mol% biocatalyst loading), TPGS-750-M (40 µL, from 4 wt% in H_2O stock solution), and the racemic tetralol **2** (2.0 µL of 200 mM in DMSO). The vial was incubated in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Afterwards, $PhSiMeH_2$ (2 µL of 25% v/v in DMSO) was added, and the reaction was placed in a thermoshaker (12 h, 25 ºC, shaken at 600 rpm). The reaction mixture was quenched by adding aq. $Na_2S_2O_4$ (10 µL, from 0.5 M in H_2O stock solution), and stirred at that temperature for 10 min. The resiulting mixture was diluted with ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 µL), followed by addition of ethyl acetate (320 µL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 µL) was transferred into a vial for SFC analysis. No diol **34** was detected and the tetalol **2** was fully recovered in the biocatalytic reaction according to the SFC analysis, suggesting that diol **34** is not directly produced from tetralol **2** under the biocatalytic conditions.

3.8 Detection of the hydroperoxide intermediate 35

(1) Synthesis of hydroperoxide 35



Supplementary Fig. 28. Synthesis of racemic hydroperoxide 35.

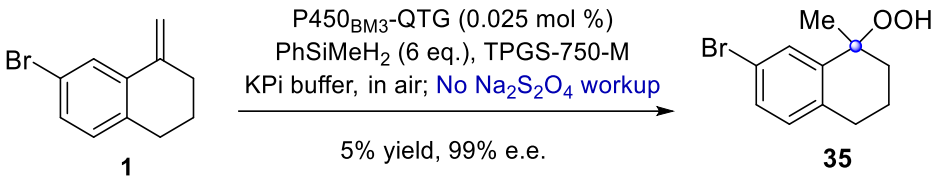
The synthesis of racemic tetralol **2** was performed according to the general procedure **D** (see below).

Hydroperoxide 35: The synthesis was carried out according to a modified procedure[7]. To a stirred solution of tetralol **2** (100 mg, 0.41 mmol) in diethyl ether (2.0 mL), aq. H_2O_2 (0.5 mL, 30 wt% in H_2O, 4.9 mmol), and conc. H_2SO_4 (10 μL, 0.19 mmol) were successively added at 0 °C. The reaction mixture was stirred for 1 h. The mixture was then warmed to 22 °C and stirred for 5 h before quenching with saturated aq. $NaHCO_3$. The mixture was extracted with diethyl ether, and the combined organic phases were dried over anhydrous Na_2SO_4, and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using dichloromethane to afford the (*rac*)-hydroperoxide **35** (33 mg, 31% yield) as a colorless oil.

Hydroperoxide 35: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 (d, J = 2.6 Hz, 1H), 7.31 (dd, J = 8.2, 2.9 Hz, 1H), 6.99 (d, J = 8.2 Hz, 1H), 2.79–2.65 (m, 2H), 2.45–2.37 (m, 1H), 2.02–1.94 (m, 1H), 1.85–1.74 (m, 2H), 1.58 (s, 1H), 1.50 (s, 3H) ppm; ^{13}C NMR (151 MHz, $CDCl_3$) δ 140.8, 137.5, 131.0, 130.8, 129.5, 120.0, 82.9, 33.0, 29.5, 27.0, 20.4 ppm; HRMS (m/z): $[M+Na]^+$ calcd for $C_{11}H_{13}BrO_2Na^+$ 278.9991, found 278.9991.

Chiral SFC separation conditions: Chiralpak IA, 4.6 × 250 mm; gradient, 10% *i*-PrOH (14 min)–10% to 30% *i*-PrOH (1 min)–30% *i*-PrOH (3 min)–30% to 10% *i*-PrOH (1 min)–10% *i*-PrOH (1 min), 2.5 mL/min, 230 nm; retention time: 7.61 min, 10.80 min. 1,3,5-trimethoxybenzene was used as internal standard (1.83 min).

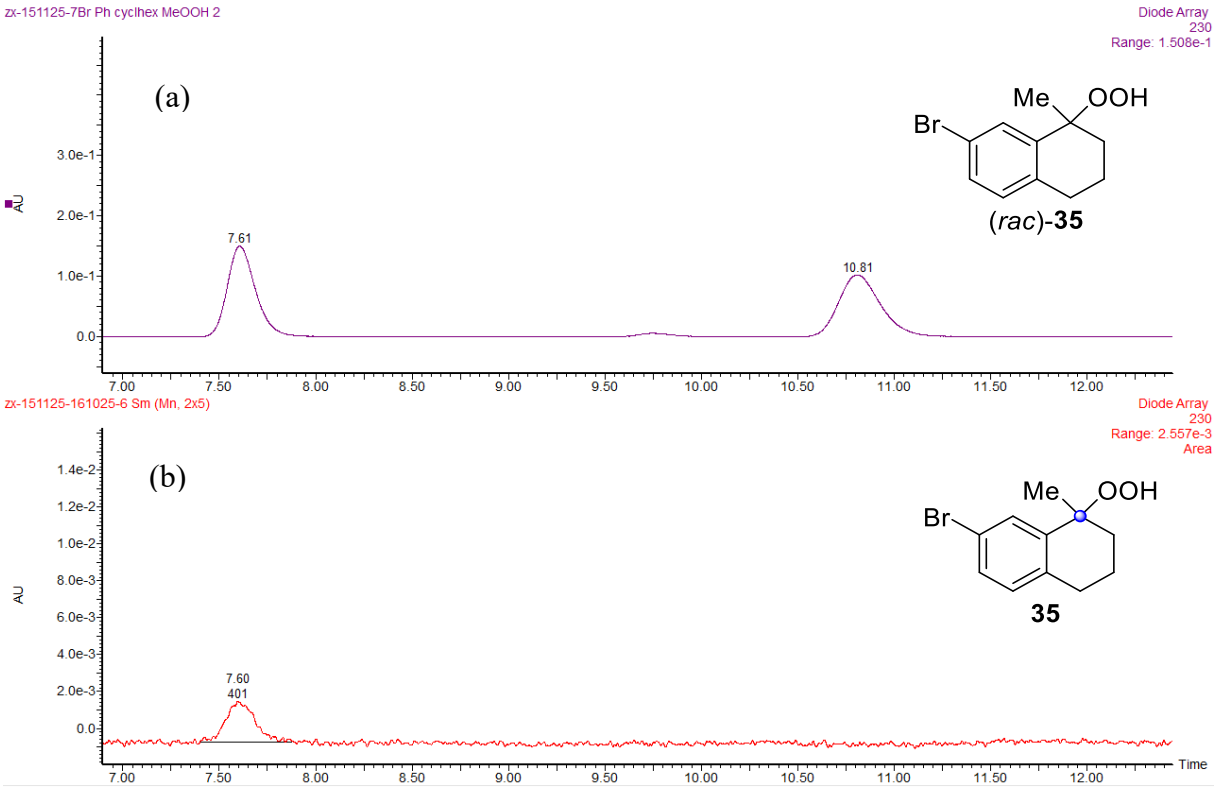
(2) Detection of the hydroperoxide 35 in the biocatalytic asymmetric radical hydration of alkene 1



Supplementary Fig. 29. Biocatalytic radical hydration of alkene 1.

Experimental procedure: A glass vial (2 mL) was charged successively with purified $P450_{BM3}$_QTG (356 μL, KPi buffer (50 mM, pH 7.0), 0.025 mol% biocatalyst loading), TPGS-750-M (40 μL, from 4 wt% in H_2O stock solution) and the racemic tetralol **2** (2.0 μL of 200 mM in DMSO). The vial was incubated in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Next, $PhSiMeH_2$ (2 μL of 25% v/v in DMSO) was added, and the reaction was placed in a thermoshaker (12 h, 25 ºC, shaken at 600 rpm). The reaction mixture was quenched by adding ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 μL), followed by additional ethyl acetate (320 μL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 μL) was transferred into a vial for SFC analysis. The yield and e.e. of hydroperoxide **35** were determined to be 5% yield and 99% e.e. according to SFC analysis.

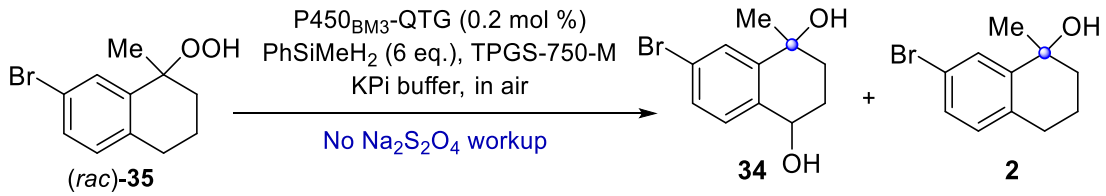
(3) Chromatograms of SFC



Supplementary Fig. 30. SFC traces of hydroperoxide 35. (a) Authentic sample of (*rac*)-hydroperoxide **35**. (b) Biocatalytic reaction of alkene **1** with $P450_{BM3}$_QTG and $PhSiMeH_2$.

3.9 Biocatalytic reaction of hydroperoxide 35

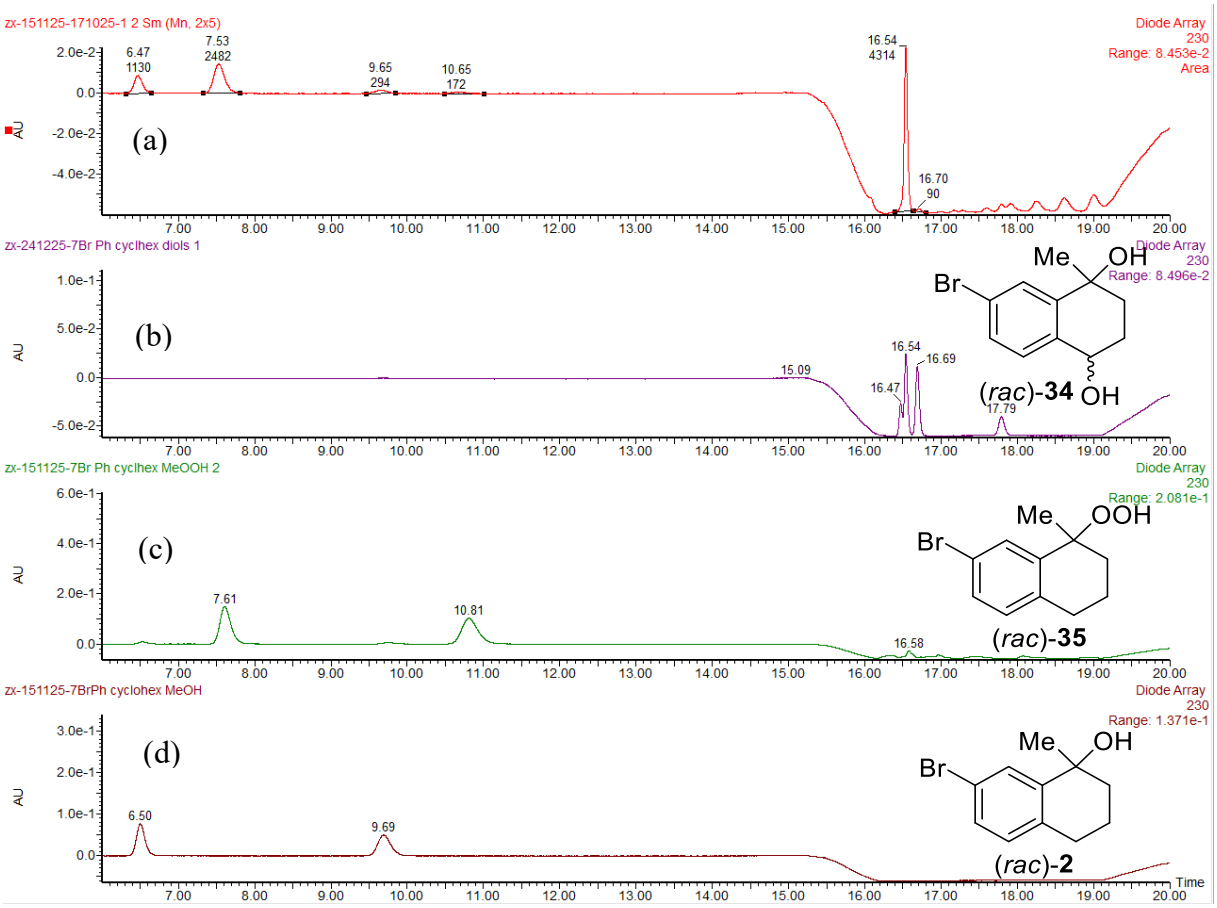
(1) Biocatalytic reaction using hydroperoxide 35 as substrate with $P450_{BM3}$_QTG and $PhSiMeH_2$



recovery of **35** (%)	e.e. of **35** (%)	yield of **34** (%)	yield of **2** (%)	e.e. of **2** (%)
37±2	88±0	30±0	32±2	56±2

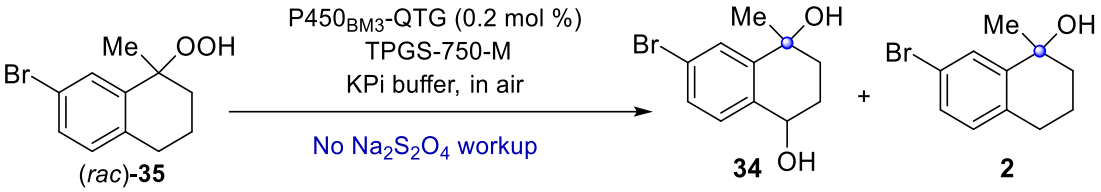
Supplementary Fig. 31. Biocatalytic reaction of racemic hydroperoxide 35 with $P450_{BM3}$_QTG and $PhSiMeH_2$

Experimental procedure: A glass vial (2 mL) was charged successively with purified $P450_{BM3}$_QTG (356 µL, KPi buffer (50 mM, pH 7.0), 0.2 mol% biocatalyst loading), TPGS-750-M (40 µL, from 4 wt% in H_2O stock solution) and the racemic hydroperoxide **35** (2.0 µL of 200 mM in DMSO). The vial was incubated in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Next, $PhSiMeH_2$ (2 µL of 25% v/v in DMSO) was added, and the reaction was placed in a thermoshaker (12 h, 25 °C, shaken at 600 rpm). The reaction mixture was quenched by adding ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 µL), followed by additional ethyl acetate (320 µL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 µL) was transferred into a vial for SFC analysis. The recovery yield and e.e. of hydroperoxide **35**, and the yield of diol **34**, and the yield and e.e. of tetralol **2** were determined by SFC analysis and collected in the **Supplementary Fig. 31**. This result confirms the occurrence of a kinetic resolution process of hydroperoxide **35** in the biocatalytic radical alkene hydration, resulting in the formation of diol **34** and the enantioenrichment of tetralol **2**.



Supplementary Fig. 32. SFC traces. (a) Biocatalytic reaction of (*rac*)-hydroperoxide **35** with $P450_{BM3}$_QTG and $PhSiMeH_2$. (b) Authentic sample of (*rac*)-diol **34**. (c) Synthesized (*rac*)-hydroperoxide **35**. (d) Synthesized (*rac*)-tetralol **2**.

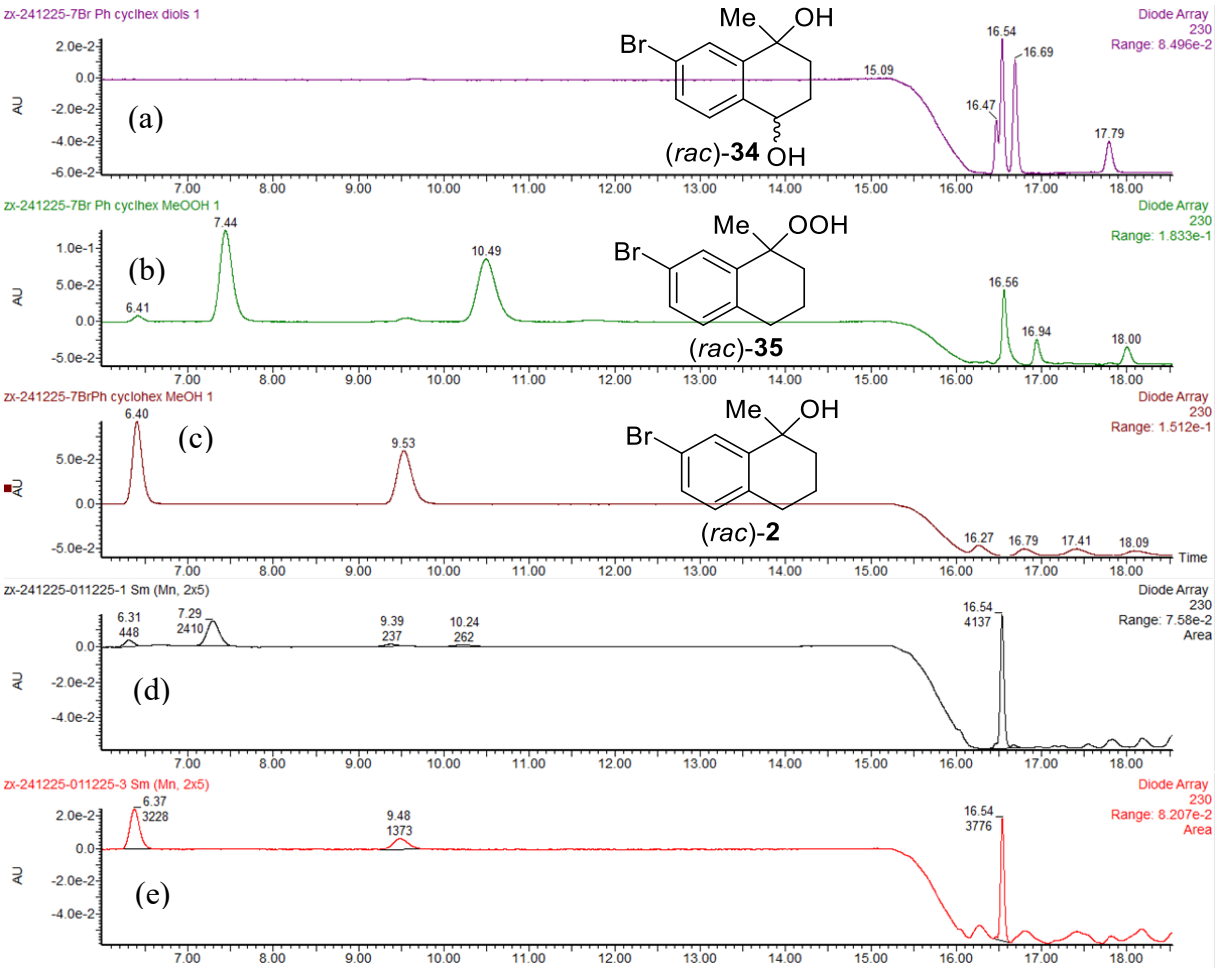
(2) Biocatalytic reaction using hydroperoxide 35 as substrate with P450$_{BM3}$_QTG alone



recovery of **35** (%)	e.e. of **35** (%)	yield of **34** (%)	yield of **2** (%)	e.e. of **2** (%)
41±2	81±1	28±1	16±0	25±6

Supplementary Fig. 33. Biocatalytic reaction of racemic hydroperoxide 35 with P450$_{BM3}$_QTG alone

Experimental procedure: A glass vial (2 mL) was charged successively with purified P450$_{BM3}$_QTG (356 µL, KPi buffer (50 mM, pH 7.0), 0.2 mol% biocatalyst loading), TPGS-750-M (40 µL, from 4 wt% in H_2O stock solution) and the (*rac*)-hydroperoxide **35** (2.0 µL of 200 mM in DMSO). The vial was incubated in a thermoshaker (12 h, 25 °C, shaken at 600 rpm). The reaction mixture was quenched by adding ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 µL), followed by additional ethyl acetate (320 µL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 µL) was transferred into a vial for SFC analysis. The recovery yield and e.e. of hydroperoxide **35**, and the yield of diol **34**, and the yield and e.e. of tetralol **2** were determined by SFC analysis and collected in the **Supplementary Fig. 33**. This result confirms the Fe–H species is *not* involved in the hydroxylation process and the P450$_{BM3}$_QTG can function as a peroxygenase in the presence of the hydroperoxide **35** which is formed during the biocatalytic alkene hydration of substrate **1**.



Supplementary Fig. 34. SFC traces. (a) Authentic sample of (*rac*)-diol **34**. (b) Synthesized (*rac*)-peroxide **34**. (c) Synthesized (*rac*)-tetralol **2**. (d) Biocatalytic reaction of (*rac*)-hydroperoxide **35** with P450$_{BM3}$_QTG in the absence of added $Na_2S_2O_4$ prior to workup. (e) Biocatalytic reaction of (*rac*)-hydroperoxide **35** with P450$_{BM3}$_QTG with $Na_2S_2O_4$ during workup, **suggesting the preferred hydroxylation of (*R*)-35 in the kinetic resolution process leading to the enrichment of (*S*)-2**.

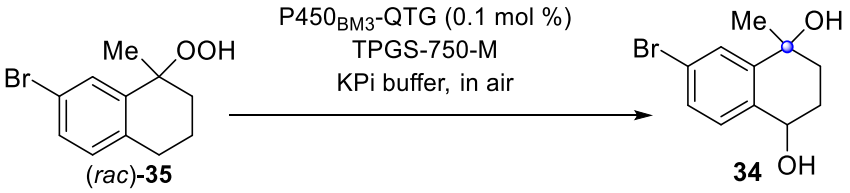
(3) Determination of (*s*)-factor for the kinetic resolution in the intramolecular hydroxylation of hydroperoxide 35 catalyzed by P450$_{BM3}$_QTG alone

Experimental procedure: To determine the selectivity factor *s*, we set out a time course reaction using (*rac*)-hydroperoxide **35** as substrate. The reaction was set up as follows: A glass vial (2 mL) was charged successively with purified P450$_{BM3}$_QTG (356 μL, KPi buffer (50 mM, pH 7.0, 0.1 mol% biocatalyst loading), TPGS-750-M (40 μL, from 4 wt% in H_2O stock solution) and the (*rac*)-hydroperoxide **35** (2.0 μL of 200 mM in DMSO). The reaction was performed by incubation (25 °C, shaken at 600 rpm) during the specified time. The reaction mixture was quenched by adding ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 μL), followed by additional ethyl acetate (320 μL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 μL) was transferred into a vial for SFC analysis. The selectivity factor (*s*), determined based on conversion and e.e. of hydroperoxide **35**, was (*s*) = 45 for P450$_{BM3}$_QTG alone (i.e. with no silane present)[8].

The selectivity factor (*s*) was determined based on conversion of hydroperoxide **35** (c) and e.e. of hydroperoxide **35** (ee) using the following equation:

$$s = \frac{\ln\left[(1-\mathrm{c})(1-\mathrm{ee})\right]}{\ln[(1-c)(1+\mathrm{ee})]}$$

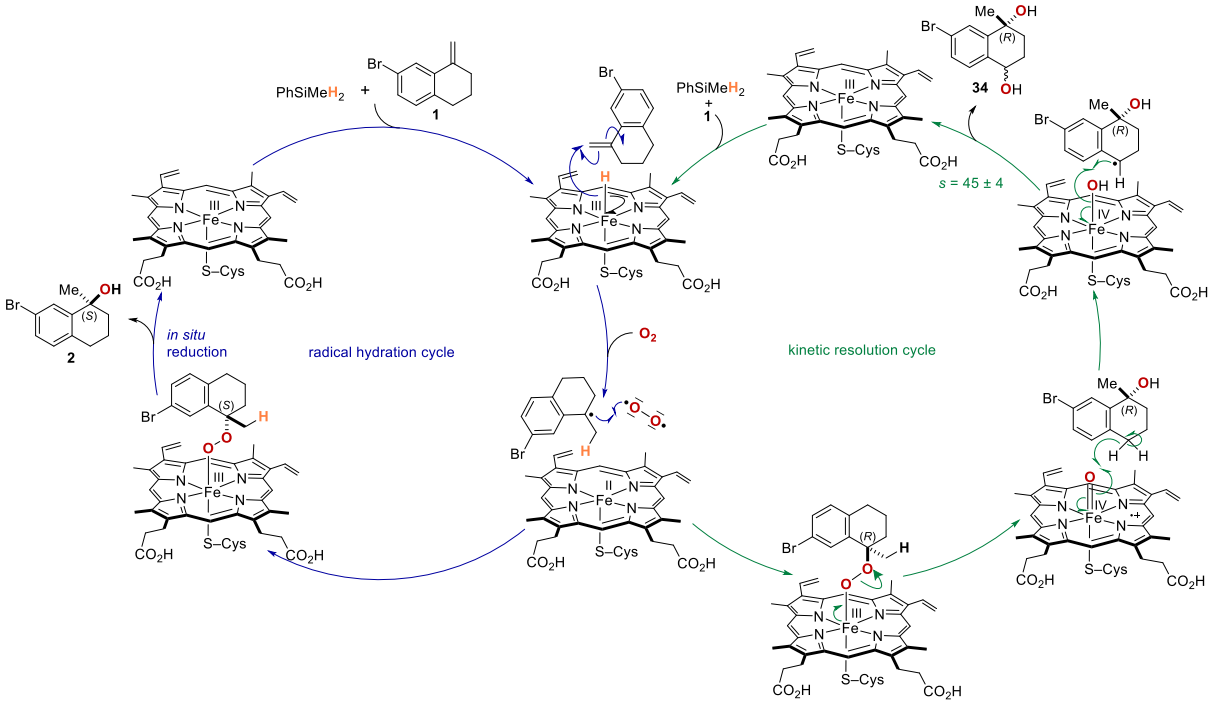
Supplementary Table 11. Determination of *s* factor for the kinetic resolution



Entry [a]	Reaction time	conversion of **35** (%)	e.e. of **35** (%)	average of calculated *s*
1	15 min	21±2	25±3	
2	20 min	23±0	28±0	45±4
3	60 min	27±3	35±2	

[a]Reaction conditions: (*rac*)-hydroperoxide **35** (1.0 mM), P450$_{BM3}$_QTG (1 μM, 0.1 mol % catalytic loading), KPi buffer (50 mM, pH 7.0), TPGS-750-M (40 μL, 4 wt. % in H_2O), V_{tot} 400 μL, 25 °C in air, reaction time was indicated in the table. Yield and e.e. were determined by SFC using 1,3,5-trimethoxylbenzene as internal standard. Reactions were performed in duplicate, and the standard deviations are listed.

(4) Proposed mechanism for the biocatalytic radical alkene hydration



Supplementary Fig. 35. Proposed catalytic cycle for the P450$_{BM3}$ asymmetric radical hydratase. Mechanistic investigation reveals that the haemoprotein functions as a bifunctional enzyme acting both as a radical hydratase featuring an Fe–H species and as a peroxygenase involving an Fe=O ferryl species.

4. Genetic Information

Cloning: pET24a (+) was used as a cloning and expression vector for all enzymes described in this study. The gene fragment for $P450_{BM3}$ (with its reductase-domain delected)[9] was cloned into the pET24a (+) vector using Gibson assembly. The cloned products were transformed into *E. coli* DH5α competent cells (NEB). The assembly was confirmed by Sanger sequencing (Microsynth). The assembled plasmid was isolated and transformed into *E. coli* BL21 (DE3) competent cells for protein expression. Mutagenesis libraries (**Supplementary Table 12**) were constructed using QuikChange with designed primers following the standard protocol provided by NEB.

Supplementary Table 12. Primer sequences with introduced mutations highlighted in red.

Primer Name	5'to 3' DNA Sequences
Fw G.A. backbone	GTATTCCTTCACCTAGCTAATAATAGGGATCCGAATTCG
Rev G.A. backbone	GGCATTTCTTTAATTGTCGCATTGGATTGGAAGTACA
Fw Insert	TGTACTTCCAATCCAATGCGACAATTAAAGAAATGCC
Rev Insert	CGAATTCGGATCCCTATTATTAGCTAGGTGAAGGAATAC
Fw F87NNK	GAGACGGGTTANNKACAAGCTGGACGCATG
Rev F87MNN	CAGCTTGTMNNTAACCCGTCTCCTGCAAAATC
Fw T268NNK	GGACACGAANNKACAAGTGGTCTTTTATCATTTGC
Rev T268MNN	CCACTTGTMNNTTCGTGTCCCGCAATTAAG
Fw A74NNK	AGTCAANNKCTTAAATTTGTACGTGATTTTGC
Rev A74MNN	TTAAGMNNTTGACTTAAGTTTTTATCAAAGCG
Fw I263NNK	TTCTTANNKGCGGGACACGAAAC
Rev I263MNN	GCMNNTAAGAATGTAATAATTTGATAGCG

Plate screening: The obtained DNA product was transformed into *E. coli* BL21 (DE3) competent cells for protein expression in 96 deep-well plate. The single colonies were cultured in LB media (supplemented with 50 μg/mL kanamycin) (37 °C, 300 rpm, overnight). The overnight culture (10 μL) was used to inoculate a 1 mL main culture (ZYP auto-induction medium, supplemented with 200 μg/mL kanamycin, 100 μL trace element (1000X stock solution), 0.5 mM 5'-aminolevulinic acid and 1 μg/mL thiamine pyrophosphate) in 96 deep-well plates (20 °C, 300 rpm for 24 h). The cells were harvested by centrifugation (4 °C, 4400 rpm, 20 min) and the medium was discarded. The cell pellet was immediately used for catalysis.

Transformation and expression: The top hits were verified by Sanger sequencing (Microsynth) and transformed into *E. coli* BL21 (DE3) competent cells for protein expression. The single colonies were cultured in LB media (supplemented with 50 μg/mL kanamycin) (37 °C, 300 rpm, overnight). The overnight culture (1.0 mL) was used to inoculate a 100 mL

main culture (ZYP auto-induction medium, supplemented with 200 µg/mL kanamycin, 100 µL of trace element (1000X stock solution), 0.5 mM 5'-aminolevulinic acid and 1 µg/mL thiamine pyrophosphate) in a 500 mL baffled flask (20 °C, 180 rpm for 36 h). The cells were harvested by centrifugation (4 ºC, 4400 rpm, 20 min) and the supernatant was discarded. The cells were frozen at −20 ºC for long term storage and purification.

Protein purification: The isolated cell pellets were thawed and resuspended in the loading buffer (50 mM NaPi, 250 mM NaCl, 10 mM imidazole, pH 8.0). The resuspended solution was lysed on ice by sonication (5 min, amplitude 50, 5 seconds on, 10 seconds off). The cell-free extract (CFE) was obtained by centrifugation (4 ºC, 8000 rpm, 30 min). The column packed with the Ni-NTA beads was washed with MQ water (5X column volume), and then equilibrated with the loading buffer (5X column volume). The cell-free-extract was then loaded onto the column and washed with the loading buffer (30X column volume). The protein was eluted with the elution buffer (50 mM NaPi, 250 mM NaCl, 250 mM imidazole, pH 8.0) (4X column volume). The eluted protein solution was buffer-exchanged into KPi buffer (pH 7.0, 50 mM) by PD-10 column. The desalted protein solution was divided into 1 mL aliquots and flash-frozen with liquid nitrogen for storage. The concentration of variants was determined by the haemchrome assay using UV-Vis spectroscopy[10,11].

Supplementary Table 13. Amino acid and DNA sequences of the evolved P450BM3_QTG (haem domain) variant with mutations (i.e. A74Q, F87T and T268G) highlighted in red.

Amino acid sequence
MGSHHHHHHGSGSGENLYFQSNATIKEMPQPKTFGELKNLPLLNTDKPVQALMKI ADELGEIFKFEAPGRVTRYLSSQRLIKEACDESRFDKNLSQQLKFVRDFAGDGLTTS WTHEKNWKKAHNILLPSFSQQAMKGYHAMMVDIAVQLVQKWERLNADEHIEVP EDMTRLTLDTIGLCGFNYRFNSFYRDQPHPFITSMVRALDEAMNKLQRANPDDPA YDENKRQFQEDIKVMNDLVDKIIADRKASGEQSDDLLTHMLNGKDPETGEPLDDE NIRYQIITFLIAGHEGTSGLLSFALYFLVKNPHVLQKAAEEAARVLVDPVPSYKQVK QLKYVGMVLNEALRLWPTAPAFSLYAKEDTVLGGEYPLEKGDELMVLIPQLHRD KTIWGDDVEEFRPERFENPSAIPQHAFKPFGNGQRACIGQQFALHEATLVLGMMLK HFDFEDHTNYELDIKETLTLKPEGFVVKAKSKKIPLGGIPSPS
DNA sequence
ATGGGTAGCCACCATCACCATCACCATGGGAGTGGTTCTGGTGAAAACCTGTA CTTCCAATCCAATGCGACAATTAAAGAAATGCCTCAGCCAAAAACGTTTGGAG AGCTTAAAAATTTACCGTTATTAAACACAGATAAACCGGTTCAAGCTTTGATGA

AAATTGCGGATGAATTAGGAGAAATCTTTAAATTCGAGGCGCCTGGTCGTGTA
ACGCGCTACTTATCAAGTCAGCGTCTAATTAAAGAAGCATGCGATGAATCACG
CTTTGATAAAAACTTAAGTCAAAACCTTAAATTTGTACGTGATTTTGCAGGAGA
CGGGTTAACTACAAGCTGGACGCATGAAAAAAATTGGAAAAAAGCGCATAATA
TCTTACTTCCAAGCTTCAGTCAGCAGGCAATGAAAGGCTATCATGCGATGATGG
TCGATATCGCCGTGCAGCTTGTTCAAAAGTGGGAGCGTCTAAATGCAGATGAG
CATATTGAAGTACCGGAAGACATGACACGTTTAACGCTTGATACAATTGGTCTT
TGCGGCTTTAACTATCGCTTTAACAGCTTTTACCGAGATCAGCCTCATCCATTTA
TTACAAGTATGGTCCGTGCACTGGATGAAGCAATGAACAAGCTGCAGCGAGCA
AATCCAGACGACCCAGCTTATGATGAAAACAAGCGCCAGTTTCAAGAAGATAT
CAAGGTGATGAACGACCTAGTAGATAAAATTATTGCAGATCGCAAAGCAAGCG
GTGAACAAAGCGATGATTTATTAACGCATATGCTAAACGGAAAAGATCCAGAA
ACGGGTGAGCCGCTTGATGACGAGAACATTCGCTATCAAATTATTACATTCTTA
ATTGCGGGACACGAAGGGACAAGTGGTCTTTTATCATTTGCGCTGTATTTCTTA
GTGAAAAATCCACATGTATTACAAAAAGCAGCAGAAGAAGCAGCACGAGTTCT
AGTAGATCCTGTTCCAAGCTACAAACAAGTCAAACAGCTTAAATATGTCGGCA
TGGTCTTAAACGAAGCGCTGCGCTTATGGCCAACTGCTCCTGCGTTTTCCCTAT
ATGCAAAAGAAGATACGGTGCTTGGAGGAGAATATCCTTTAGAAAAAGGCGAC
GAACTAATGGTTCTGATTCCTCAGCTTCACCGTGATAAAACAATTTGGGGAGAC
GATGTGGAAGAGTTCCGTCCAGAGCGTTTTGAAAATCCAAGTGCGATTCCGCA
GCATGCGTTTAAACCGTTTGGAAACGGTCAGCGTGCGTGTATCGGTCAGCAGTT
CGCTCTTCATGAAGCAACGCTGGTACTTGGTATGATGCTAAAACACTTTGACTT
TGAAGATCATACAAACTACGAGCTCGATATTAAAGAAACTTTAACGTTAAAAC
CTGAAGGCTTTGTGGTAAAAGCAAAATCGAAAAAAATTCCGCTTGGCGGTATT
CCTTCACCTAGCTAA

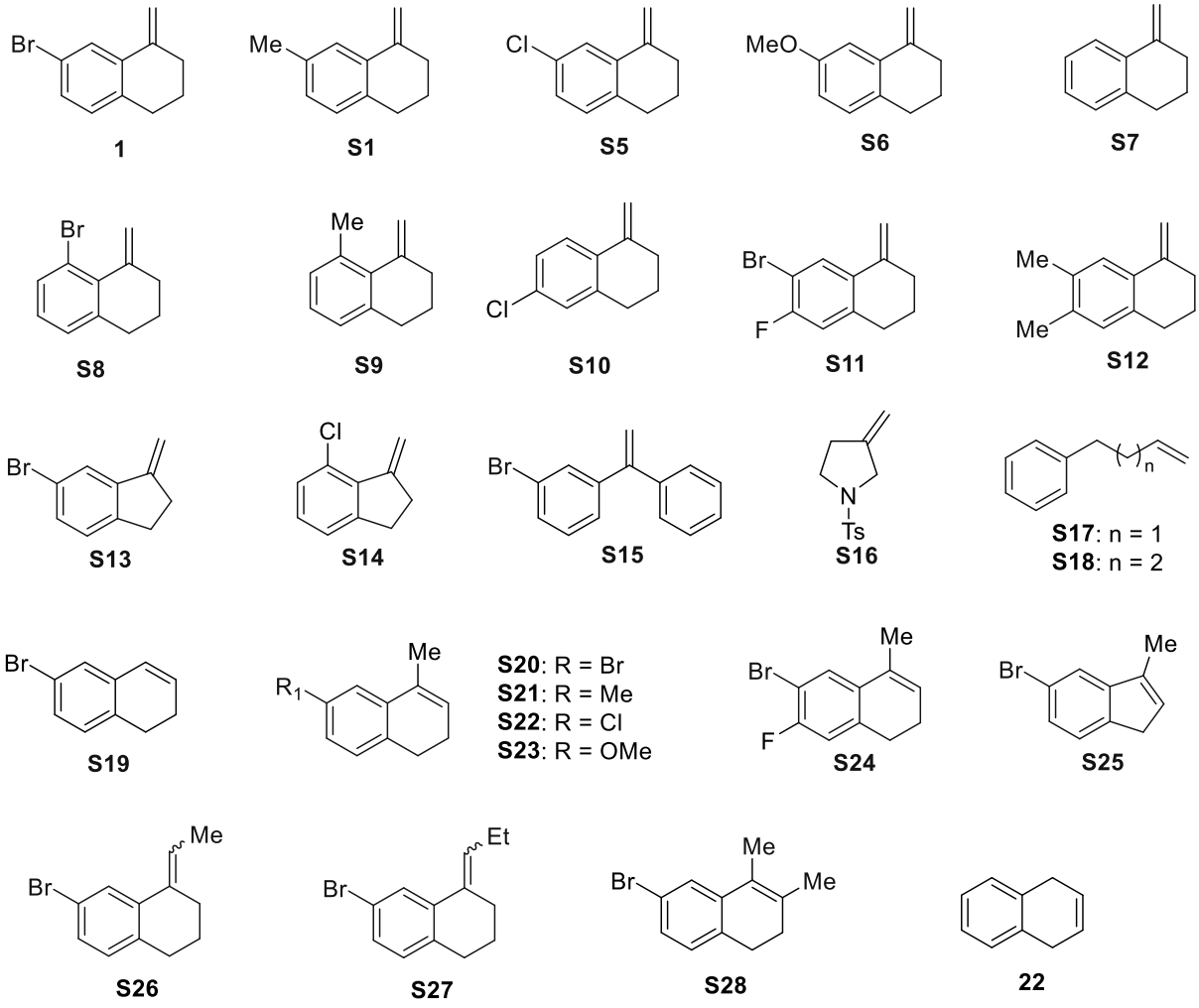
5. General catalytic procedures

General procedure for the biocatalytic radical alkene hydration with whole cells used during the directed evolution campaign: The cell pellet was resuspended in KPi buffer (400 µL, pH 7.0, 50 mM). The resulting whole-cell solution (354 µL) was transferred in a glass-coated 96 deep-well plate, followed by successive addition of TPGS-750-M (40 µL, from 2 wt% in H_2O as stock solution) and the alkene **1** (2.0 µL of 200 mM in DMSO). The plate was sealed and incubated in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Next, $PhSiH_3$ (2 µL of 50% v/v in DMSO, 20 equivalents vs. alkene **1**) was added and the plate was sealed. The reaction was placed in a thermoshaker (24 h, 25 ºC, shaken at 600 rpm). The reaction was quenched by adding ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 µL), followed by additional ethyl acetate (320 µL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 10 min). The clear supernatant (100 µL) was transferred into a vial for SFC analysis. The yield and e.r. were determined by SFC analysis.

General procedure for the biocatalytic radical alkene hydration using purified protein under standard conditions: A glass vial (2 mL) was charged successively with purified $P450_{BM3}$_QTG (0.2 mol% biocatalyst loading, in KPi buffer (pH 7.0, 50 mM), 354 µL), TPGS-750-M (40 µL, from 4 wt% in H_2O stock solution) and the alkene substrate (2.0 µL of 200 mM in DMSO). The vial was placed in a thermoshaker (5 min, 25 °C, shaken at 600 rpm). Next, $PhSiMeH_2$ (2 µL of 25% v/v in DMSO, 6 equivalents vs. alkene substrate) was added and the vial was sealed. The reaction was carried out in a thermoshaker (12 h, 25 ºC, shaken at 600 rpm). The reaction mixture was quenched by adding aq. $Na_2S_2O_4$ (10 µL, from 0.5 M in H_2O stock solution), and was further incubated in a thermoshaker (10 min, 25 °C, shaken at 600 rpm). The resulting mixture was diluted with ethyl acetate (containing 5 mM 1,3,5-trimethoxybenzene as internal standard, 80 µL), followed by addition of ethyl acetate (320 µL). After vortexing, the mixture was centrifuged (4 °C, 17000 g, 2 min). The clear supernatant (100 µL) was transferred into a vial for SFC analysis. The yield and e.r. were determined by SFC analysis.

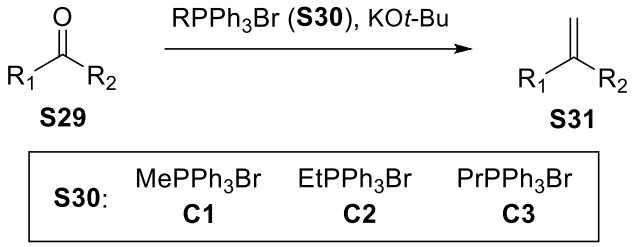
6. Synthesis and characterization of substrates and products

6.1 Synthesis and characterization of alkene substrates



Supplementary Fig. 36. Substrates evaluated in the biocatalytic radical alkene hydration.

(1) General synthetic procedure A for the synthesis of the alkene substrates synthesis (1, S1, S5-16 and S26-27)

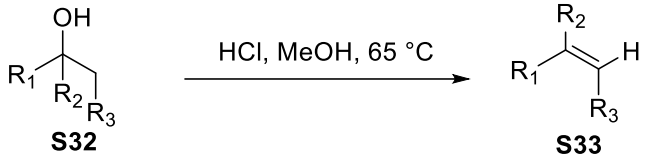


Supplementary Fig. 37. General synthetic route A.

The ketone compounds used for the synthesis of the corresponding akenes are all commercially available.

General synthetic procedure A: To a stirred solution of bromide **S30** (1.1 eq.) in dry THF (0.2 M), KO^{t}Bu (1.1 eq.) was slowly added at 22 °C. The reaction mixture was stirred for 30 min, before slowly adding the ketone **S29** (1.0 eq., 0.5 M in THF) at 22 °C. The reaction mixture was stirred for 2 h, before quenching with saturated $NaHCO_3$. The mixture was extracted with diethyl ether, and the combined organic phases were dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using diethyl ether /petroleum ether to afford the alkene **S31**.

(2) General synthetic procedure B for the synthesis of alkene substrates (S20-25)

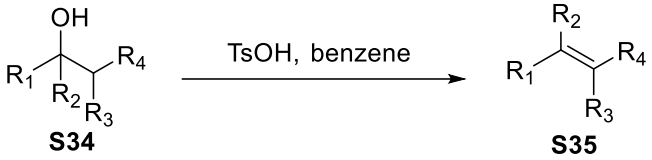


Supplementary Fig. 38. General synthetic route B.

The corresponding alcohol compounds used in the synthesis were prepared according to general procedure **D** (see below).

General synthetic procedure B: The synthesis was carried out according to a reported procedure[12]. To a stirred solution of alcohol **S32** (1.0 eq.) in THF (0.2 M), conc. HCl (2.0 eq.) was added at 22 °C. The reaction mixture was refluxed for 3 h before quenching with saturated $NaHCO_3$. The mixture was extracted with diethyl ether, and the combined organic phases were dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using diethyl ether /petroleum ether to afford the alkene **S33**.

(3) General synthetic procedure C for the synthesis of alkene substrates (S19 and S28)



S34 **S35**

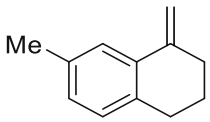
Supplementary Fig. 39. General synthetic route C.

The corresponding alcohol compound used in the synthesis was either commercially available (for **S19**) or prepared according to the synthetic procedure listed in **Supplementary Fig. 42** (for **S28**).

General synthetic procedure C: The synthesis was carried out according to a modified procedure[13]. To a stirred solution of alcohol **S34** (1.0 eq.) in benzene (0.2 M), *p*-toluenesulfonic acid (0.1 eq.) was added at 22 °C. The reaction mixture was refluxed for 12 h before quenching with saturated $NaHCO_3$. The mixture was extracted with diethyl ether, and the combined organic phases were dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using petroleum ether to afford the alkene **S35**.

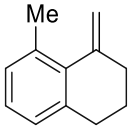
(4) Characterization of the alkene substrates

The spectral of the synthesized alkene substrates **1** and **S13**[14], **S5**[15], **S6** and **S7**[16], **S8** and **S10**[17], **S15**[18], **S16**[19], **S19**[13], **S20**[20], **S23**[21] and **S25**[22] are identical to the reported data. Alkenes **S17**, **S18** and **22** are commercially available and were used without further purification.



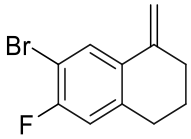
S1

The alkene **S1** was prepared according to the general procedure **A**, 86% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.01–6.97 (m, 2H), 5.49–5.43 (m, 1H), 4.95–4.91 (m, 1H), 2.81 (t, J = 6.3 Hz, 2H), 2.56–2.50 (m, 2H), 2.32 (s, 3H), 1.90–1.83 (m, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 135.3, 134.6, 134.5, 129.2, 128.7, 124.7, 107.7, 33.5, 30.2, 24.1, 21.3 ppm; HRMS (m/z): $[M+H]^+$ calcd for $C_{12}H_{15}^+$ 159.1168, found 159.1168.



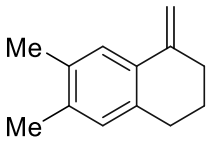
S9

The alkene **S9** was prepared according to the general procedure **A**, 82% yield. ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.09–7.00 (m, 2H), 6.98–6.92 (m, 1H), 5.28 (q, J = 1.5 Hz, 1H), 5.11–5.08 (m, 1H), 2.72 (t, J = 6.6 Hz, 2H), 2.48 (tt, J = 6.9, 1.2 Hz, 2H), 2.45 (s, 3H), 1.89–1.81 (m, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.1, 139.7, 137.0, 135.1, 129.3, 126.7, 126.1, 114.0, 34.1, 30.5, 24.2, 22.0 ppm; GCMS (m/z): $[M]^+$ calcd for $C_{12}H_{14}^+$ 158.109, found 158.100.



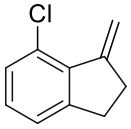
S11

The alkene **S11** was prepared according to the general procedure **A**, 84% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 7.0 Hz, 1H), 6.85 (dt, J = 9.2, 1.0 Hz, 1H), 5.38 (s, 1H), 5.00–4.93 (m, 1H), 2.81–2.72 (m, 2H), 2.54–2.47 (m, 2H), 1.91–1.81 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.26 (d, J = 248.0 Hz), 141.55 (d, J = 1.6 Hz), 138.83 (d, J = 6.6 Hz), 132.69 (d, J = 3.6 Hz), 129.45 (d, J = 1.0 Hz), 116.45 (d, J = 21.6 Hz), 108.89 (d, J = 2.2 Hz), 106.47 (d, J = 21.4 Hz), 32.81, 30.33 (d, J = 1.5 Hz), 23.40 ppm. GCMS (m/z): $[M]^+$ calcd for $C_{11}H_{10}BrF^+$ 239.994, found 240.000.



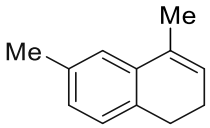
S12

The alkene **S12** was prepared according to the general procedure **A**, 80% yield. ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.40 (s, 1H), 6.87 (s, 1H), 5.41 (s, 1H), 4.86 (s, 1H), 2.75 (t, J = 6.3 Hz, 2H), 2.57–2.44 (m, 2H), 2.22 (s, 3H), 2.21 (s, 3H), 1.86–1.78 (m, 2H) ppm. ^{13}C NMR (151 MHz, CD_2Cl_2) δ 144.1, 136.7, 135.2, 134.4, 132.3, 130.5, 125.3, 106.5, 33.8, 30.3, 24.5, 19.6, 19.5 ppm. GCMS (m/z): $[M]^+$ calcd for $C_{13}H_{16}^+$ 172.125, found 172.100.



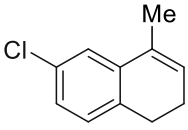
S14

The alkene **S14** was prepared according to the general procedure **A**, 87% yield. ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.22–7.09 (m, 3H), 6.12–6.06 (m, 1H), 5.31–5.28 (m, 1H), 2.99–2.94 (m, 2H), 2.86–2.80 (m, 2H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2) δ 150.7, 149.4, 137.1, 130.5, 129.2, 128.7, 124.2, 109.4, 33.3, 30.5 ppm. GCMS (m/z): $[M]^+$ calcd for $C_{10}H_9^+$ 164.039, found 164.000.



S21

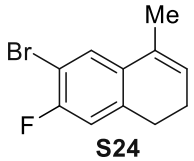
The alkene **S21** was prepared according to the general procedure **B**, 85% yield. ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.08–7.04 (m, 1H), 7.02 (d, J = 7.5 Hz, 1H), 6.96 (dd, J = 7.5, 1.1 Hz, 1H), 5.86 (tq, J = 4.6, 1.5 Hz, 1H), 2.71 (t, J = 8.2 Hz, 2H), 2.33 (s, 3H), 2.25–2.20 (m, 2H), 2.05 (q, J = 1.8 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2) δ 136.05, 136.03, 133.67, 132.64, 127.52, 127.49, 125.75, 123.98, 28.30, 23.81, 21.40, 19.49 ppm. GCMS (m/z): $[M]^+$ calcd for $C_{12}H_{14}^+$ 158.109, found 158.100.



S22

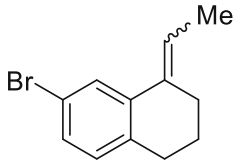
The alkene **S22** was prepared according to the general procedure **B**, 90% yield. ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.19 (d, J = 2.5 Hz, 1H), 7.10 (dd, J = 7.9, 2.4 Hz, 1H), 7.07 (d, J = 8.0 Hz, 1H), 5.95–5.90 (m, 1H), 2.71 (t, J = 8.1 Hz, 2H), 2.29–2.19 (m, 2H), 2.07–1.98 (m, 3H) ppm.

^{13}C NMR (151 MHz, CD_2Cl_2) δ 138.0, 135.2, 132.1, 131.7, 128.9, 127.3, 126.6, 123.2, 27.9, 23.5, 19.3 ppm. GCMS (m/z): $[M]^+$ calcd for $C_{11}H_{11}^+$ 178.054, found 178.000.



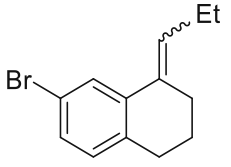
S24

The alkene **S24** was prepared according to the general procedure **B**, 88% yield. ^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.36 (d, J = 7.0 Hz, 1H), 6.92 (d, J = 9.0 Hz, 1H), 5.90–5.84 (m, 1H), 2.70 (t, J = 8.1 Hz, 2H), 2.29–2.18 (m, 2H), 2.01 (s, 3H) ppm. ^{13}C NMR (151 MHz, CD_2Cl_2) δ 157.8 (d, J = 245.7 Hz), 138.7 (d, J = 6.6 Hz), 134.1 (d, J = 3.6 Hz), 130.9 (d, J = 1.9 Hz), 127.8, 126.3 (d, J = 2.2 Hz), 115.8 (d, J = 22.4 Hz), 105.8 (d, J = 20.7 Hz), 28.3 (d, J = 1.7 Hz), 23.1, 19.4 ppm. GCMS (m/z): $[M]^+$ calcd for $C_{11}H_{10}BrF^+$ 239.994, found 240.000.



S26

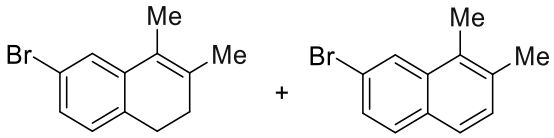
The alkene **S26** was prepared according to the general procedure **A**, 86% yield, along with a pair of inseparable Z/E isomers (ratio = 3:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, J = 2.0 Hz, 0.75H), 7.52 (d, J = 2.1 Hz, 0.25H), 7.26 (dd, J = 8.1, 2.1 Hz, 0.25H), 7.20 (dd, J = 8.1, 2.1 Hz, 0.75H), 7.00 (dt, J = 8.1, 1.0 Hz, 0.25H), 6.94 (dt, J = 8.1, 0.9 Hz, 0.75H), 6.09 (qt, J = 7.0, 2.0 Hz, 0.75H), 5.60 (qt, J = 7.2, 1.3 Hz, 0.25H), 2.75 (td, J = 6.7, 0.9 Hz, 0.5H), 2.68 (t, J = 6.2 Hz, 1.5H), 2.49–2.43 (m, 1.5H), 2.40–2.34 (m, 0.5H), 1.93–1.77 (m, 5H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.7, 138.0, 137.5, 136.1, 135.3, 134.0, 131.0, 130.5, 130.4, 129.5, 129.1, 126.6, 121.6, 120.2, 119.9, 118.6, 34.3, 30.3, 29.4, 26.1, 24.2, 22.9, 15.6, 13.9 ppm. GCMS (m/z): $[M]^+$ calcd for $C_{12}H_{13}Br^+$ 236.020, found 236.000.



S27

The alkene **S27** was prepared according to the general procedure **A**, 88% yield, along with a pair of inseparable Z/E isomers (ratio = 6.1:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, J = 2.1 Hz, 0.86H), 7.45 (d, J = 2.1 Hz, 0.14H), 7.26 (dd, J = 8.1, 2.1 Hz, 0.14H), 7.20 (dd, J = 8.1, 2.1 Hz, 0.86H), 7.00–6.97 (m, 0.14H), 6.96–6.90 (m, 0.86H), 5.98 (tt, J = 7.2, 2.0 Hz, 0.86H), 5.43 (tt, J = 7.0, 1.3 Hz, 0.14H), 2.76–2.72 (m, 0.28H), 2.69 (t, J = 6.2 Hz, 1.72H), 2.50–2.43 (m,

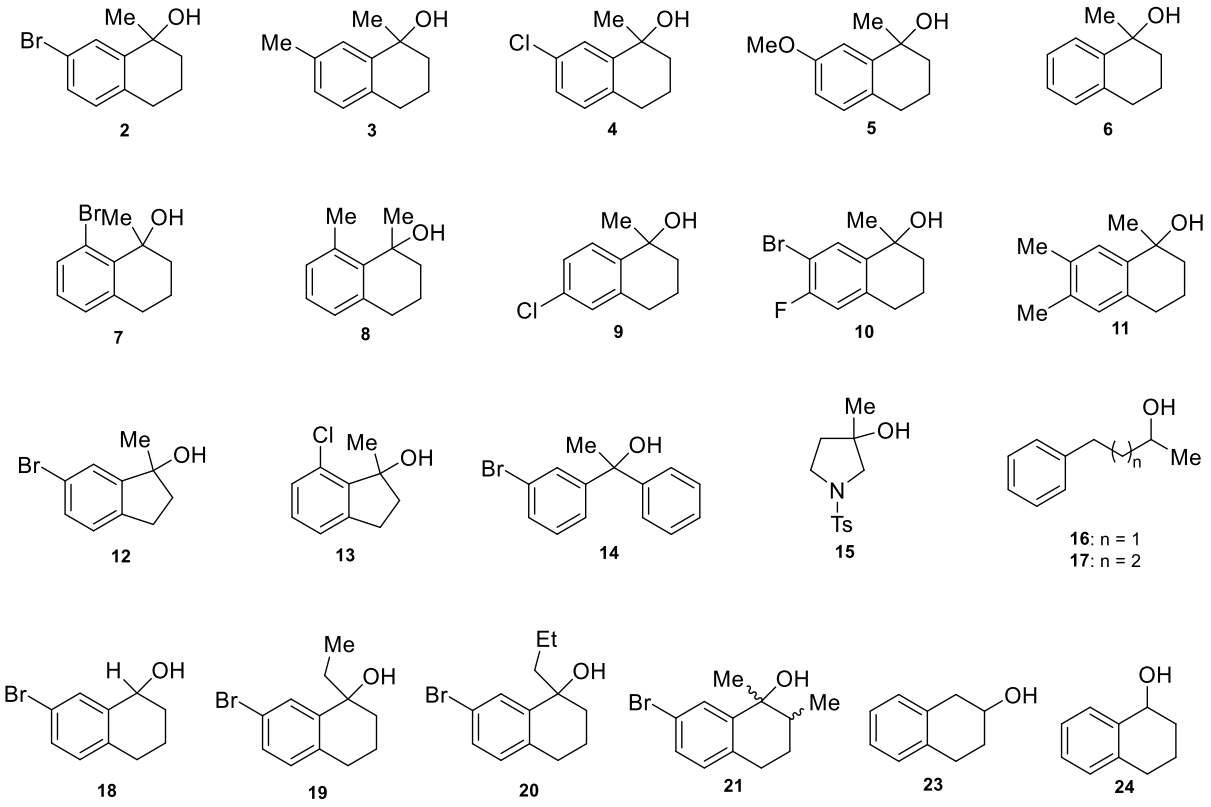
1.72H), 2.39–2.31 (m, 0.56H), 2.24–2.15 (m, 1.72H), 1.90–1.84 (m, 0.28H), 1.83–1.75 (m, 1.72H), 1.10–1.03 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.7, 137.5, 136.2, 132.7, 130.8, 130.5, 130.3, 129.9, 129.6, 129.2, 127.9, 126.6, 119.9, 34.2, 30.2, 29.4, 26.2, 24.3, 23.1, 22.8, 21.6, 15.1, 14.1 ppm. GCMS (m/z): $[M]^+$ calcd for $C_{13}H_{15}Br^+$ 250.035, found 250.000.



S28 (major) **S28a** (minor)

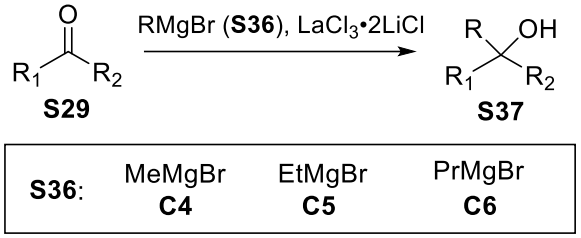
The alkene **S28** was prepared according to the general procedure **C**, 72% yield, along with the inseparable oxidized byproduct naphtalene **S28a** (**S28**:**S28a** = 6.3:1). ^{1}H NMR (600 MHz, CD_2Cl_2) δ 8.21 (s, 0.16H), 7.68 (d, J = 8.7 Hz, 0.16H), 7.59 (d, J = 8.3 Hz, 0.16H), 7.49 (dd, J = 8.7, 2.1 Hz, 0.16H), 7.37–7.29 (m, 1.16H), 7.19 (dd, J = 7.9, 2.3 Hz, 1H), 6.97 (d, J = 7.9 Hz, 1H), 2.66 (t, J = 8.0 Hz, 2H), 2.55 (s, 0.48H), 2.48 (s, 0.48H), 2.21 (t, J = 7.4 Hz, 2H), 1.98 (s, 3H), 1.92 (s, 3H) ppm. ^{13}C NMR (151 MHz, CD_2Cl_2) δ 139.80, 135.00, 134.77, 134.66, 134.41, 131.03, 130.96, 130.44, 129.90, 128.81, 128.33, 128.02, 126.60, 125.84, 125.71, 124.49, 120.23, 120.22, 30.75, 28.15, 20.95, 20.54, 14.70, 14.28 ppm. GCMS (m/z): $[M]^+$ calcd for $C_{12}H_{13}Br^+$ 236.020, found 236.000.

6.2 Synthesis and characterization of products



Supplementary Fig. 40. Alcohol products resulting from the biocatalytic radical alkene hydration.

(1) General procedure D for the synthesis of the alcohol products (2-5, 7-15 and 19-20)



Supplementary Fig. 41. General synthetic route D.

General synthetic procedure D: The synthesis was carried out according to a reported procedure[23]. To a stirred solution of ketone **S29** (1.0 eq.) in THF (0.3 M), $LaCl_3$·2LiCl (0.6 M in THF, 1.0 eq.) was added at 22 °C. The reaction mixture was stirred at that temperature for 1 h. The mixture was cooled to 0 °C, and the Grignard reagent **S36** in THF (1.1 eq.) was added. The resulting mixture was warmed to 22 °C and stirred for 12 h, before quenching with saturated NH_4Cl. The mixture was extracted with diethyl ether, and the combined organic phases were dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using diethyl ether/petroleum ether to afford the alcohol **S37**.

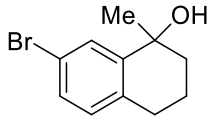
(2) Synthetic procedure for the synthesis of tetralol 21

Supplementary Fig. 42. Synthetic route for the racemic tetralol 21.

Tetralol 21: To a stirred solution of ketone **S38** (1.0 g, 4.44 mmol) in THF (10 mL), a lithium diisopropylamide solution (4.4 mL, 2.0 M in THF, 4.4 mmol) was added at −78 °C. The reaction mixture was stirred at that temperature for 1 h, before adding MeI (276 μL, 4.4 mmol). The mixture was stirred at −78 °C for 30 min, before warming to 22 °C. The reaction mixture was stirred for 12 h, before quenching with saturated NH_4Cl. The resulting mixture was extracted with diethyl ether, and the combined organic phases were dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using dichloromethane/petroleum ether (1:1) to afford the monomethylated ketone product (446 mg, 42% yield). To a stirred solution of the obtained ketone (185 mg, 0.77 mmol) in THF (2.0 mL), MeMgBr (0.4 mL, 3.0 M in diethyl ether, 1.2 mmol) was added at 0 °C. The reaction mixture was warmed to 22 °C and stirred for 12 h before quenching with saturated NH_4Cl. The resulting mixture was extracted with diethyl ether, and the combined organic phases were dried over anhydrous Na_2SO_4 and filtered. The solvent was evaporated under vacuum, and the residue was subjected to flash chromatography using diethyl ether /petroleum ether (1:5) to afford the **tetralol 21** as a racemic mixture of diastereomers (173 mg, 88% yield, 1.14:1 d.r.).

(3) Characterization of the alcohol products

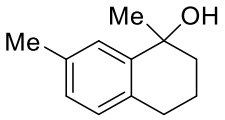
The spectral of synthesized alcohol products **2**[24], **5**[25], **7**[26], **9**[27], **12**[28] and **14**[29] are identical to the reported data. Alcohols **6, 16, 17, 18**, **23** and **24** are commercially available, and used without further purification.



2

The tetralol **2** was prepared according to the general procedure **D**, 94% yield.

Chiral SFC separation conditions: Chiralpak IA, 4.6 × 250 mm; gradient, 10% *i*-PrOH (14 min)–10% to 30% *i*-PrOH (1 min)–30% *i*-PrOH (3 min)–30% to 10% *i*-PrOH (1 min)– 10% *i*-PrOH (1 min), 2.5 mL/min, 230 nm; retention time: 6.50 min, 9.71 min. 1,3,5-trimethoxybenzene was used as internal standard (1.85 min).

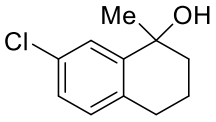


3

The tetralol **3** was prepared according to the general procedure **D**, 92% yield.

^{1}H NMR (500 MHz, DMSO-d$_6$) δ 7.34–7.31 (m, 1H), 6.93–6.86 (m, 2H), 4.77 (s, 1H), 2.70–2.57 (m, 2H), 2.28–2.21 (m, 3H), 1.88–1.61 (m, 4H), 1.36 (s, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-d$_6$) δ 144.1, 134.3, 132.4, 128.1, 127.0, 68.7, 31.5, 29.1, 20.9, 20.2 ppm. HRMS (m/z): $[M+H]^+$ calcd for $C_{11}H_{14}BrO^+$ 241.0223, found 241.0223.

Chiral SFC separation conditions: Chiralpak IA, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 210 nm; retention time: 3.86 min, 5.01 min. 1,3,5-trimethoxybenzene was used as internal standard (1.84 min).

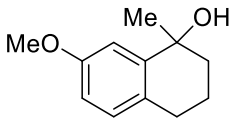


4

The tetralol **4** was prepared according to the general procedure **D**, 90% yield.

^{1}H NMR (500 MHz, DMSO-d$_6$) δ 7.51 (d, J = 2.4 Hz, 1H), 7.15 (dd, J = 8.2, 2.4 Hz, 1H), 7.06 (dt, J = 8.2, 1.1 Hz, 1H), 5.02 (s, 1H), 2.70–2.63 (m, 2H), 1.89–1.64 (m, 4H), 1.36 (s, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-d$_6$) δ 146.8, 134.5, 130.2, 130.1, 126.2, 126.1, 68.8, 38.6, 31.3, 28.7, 19.8 ppm. HRMS (m/z): $[M+H]^+$ calcd for $C_{11}H_{14}ClO^+$ 197.0728, found 197.0728.

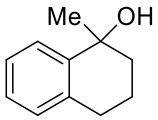
Chiral SFC separation conditions: Chiralpak IE, 4.6 × 250 mm; isocratic, 8% *i*-PrOH in CO_2, 2.5 mL/min, 220 nm; retention time: 5.62 min, 8.05 min. 1,3,5-trimethoxybenzene was used as internal standard (1.93 min).



5

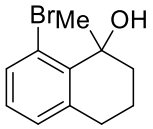
The tetralol **5** was prepared according to the general procedure **D**, 88% yield.

Chiral SFC separation conditions: Chiralpak IA, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 210 nm; retention time: 4.90 min, 5.76 min. 1,3,5-trimethoxybenzene was used as internal standard (2.09 min).



6

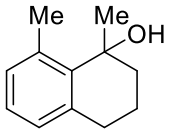
Chiral SFC separation conditions: Chiralpak IE, 4.6 × 250 mm; isocratic, 8% *i*-PrOH in CO_2, 2.5 mL/min, 210 nm; retention time: 4.78 min, 5.26 min. 1,3,5-trimethoxybenzene was used as internal standard (1.92 min).



7

The tetralol **7** was prepared according to the general procedure **D**, 91% yield.

Chiral SFC separation conditions: Chiralpak IH, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 210 nm; retention time: 3.44 min, 3.81 min. 1,3,5-trimethoxybenzene was used as internal standard (1.57 min).

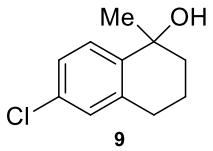


8

The tetralol **8** was prepared according to the general procedure **D**, 90% yield.

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.05–6.93 (m, 2H), 6.92–6.86 (m, 1H), 2.88–2.79 (m, 1H), 2.79–2.71 (m, 1H), 2.60 (s, 3H), 1.99 (dddd, J = 12.4, 5.7, 2.7, 1.5 Hz, 1H), 1.90–1.73 (m, 3H), 1.67 (s, 1H), 1.57 (s, 3H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2) δ 141.0, 138.0, 137.5, 130.8, 127.4, 126.9, 72.9, 43.9, 31.7, 28.6, 22.3, 21.3 ppm. HRMS (m/z): $[M+H]^+$ calcd for $C_{12}H_{17}O^+$ 177.1274, found 177.1274.

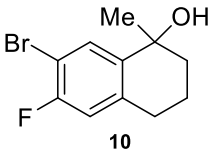
Chiral SFC separation conditions: Chiralpak IG, 4.6 × 250 mm; isocratic, 5% *i*-PrOH in CO_2, 2.5 mL/min, 220 nm; retention time: 8.22 min, 9.84 min. 1,3,5-trimethoxybenzene was used as internal standard (3.21 min).



9

The tetralol **9** was prepared according to the general procedure **D**, 92% yield.

Chiral SFC separation conditions: Chiralpak IA, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 220 nm; retention time: 5.36 min, 7.01 min. 1,3,5-trimethoxybenzene was used as internal standard (1.77 min).

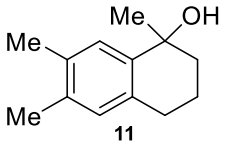


10

The tetralol **10** was prepared according to the general procedure **D**, 88% yield.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 7.1 Hz, 1H), 6.82 (dt, J = 9.2, 1.0 Hz, 1H), 2.83–2.57 (m, 2H), 1.97–1.77 (m, 4H), 1.69 (s, 1H), 1.53 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9 (d, J = 247.0 Hz), 140.6 (d, J = 3.4 Hz), 138.0 (d, J = 6.7 Hz), 131.8 (d, J = 1.1 Hz), 116.1 (d, J = 21.2 Hz), 106.6 (d, J = 21.0 Hz), 70.4, 39.6, 31.1, 29.7 (d, J = 1.4 Hz), 20.3 ppm. HRMS (m/z): $[M+H]^+$ calcd for $C_{11}H_{13}OBrF^+$ 259.0128, found 259.0128.

Chiral SFC separation conditions: Chiralpak IA, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 230 nm; retention time: 5.41 min, 7.59 min. 1,3,5-trimethoxybenzene was used as internal standard (1.79 min).

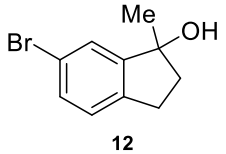


11

The tetralol **11** was prepared according to the general procedure **D**, 92% yield.

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.34 (s, 1H), 6.86 (s, 1H), 2.79–2.63 (m, 2H), 2.27 (d, J = 2.2 Hz, 3H), 2.24 (d, J = 1.9 Hz, 3H), 1.94–1.74 (m, 4H), 1.52 (s, 3H) ppm. ^{13}C NMR (151 MHz, CD_2Cl_2) δ 140.8, 135.7, 134.7, 134.0, 130.1, 127.6, 70.5, 40.3, 31.0, 29.8, 21.0, 19.6, 19.4 ppm. HRMS (m/z): $[M+H]^+$ calcd for $C_{13}H_{19}O^+$ 191.1430, found 191.1430.

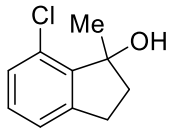
Chiral SFC separation conditions: Chiralpak ID, 4.6 × 250 mm; isocratic, 6% *i*-PrOH in CO_2, 2.5 mL/min, 210 nm; retention time: 5.03 min, 6.06 min. 1,3,5-trimethoxybenzene was used as internal standard (1.87 min).



12

The indanol **12** was prepared according to the general procedure **D**, 93% yield.

Chiral SFC separation conditions: Chiralpak IA, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 272 nm; retention time: 4.97 min, 7.33 min. 1,3,5-trimethoxybenzene was used as internal standard (1.80 min).

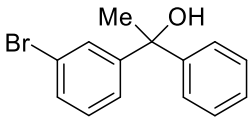


13

The indanol **13** was prepared according to the general procedure **D**, 94% yield.

^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.20–7.10 (m, 3H), 2.98–2.89 (m, 1H), 2.85–2.76 (m, 1H), 2.64 (s, 1H), 2.26–2.17 (m, 2H), 1.62 (s, 3H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2) δ 145.6, 144.3, 130.1, 129.7, 128.2, 124.2, 82.9, 42.4, 29.5, 26.9 ppm. HRMS (m/z): $[M+H]^+$ calcd for $C_{10}H_{12}ClO^+$ 183.0571, found 183.0571.

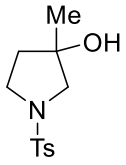
Chiral SFC separation conditions: Chiralpak IE, 4.6 × 250 mm; isocratic, 5% *i*-PrOH in CO_2, 2.5 mL/min, 220 nm; retention time: 5.36 min, 5.75 min. 1,3,5-trimethoxybenzene was used as internal standard (2.24 min).



14

The acyclic alcohol **14** was prepared according to the general procedure **D**, 91% yield.

Chiral SFC separation conditions: Chiralpak IF, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 230 nm; retention time: 4.64 min, 5.50 min. 1,3,5-trimethoxybenzene was used as internal standard (1.61 min).

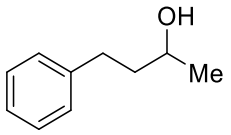


15

The pyrrolidinol **15** was prepared according to the general procedure **D**, 87% yield.

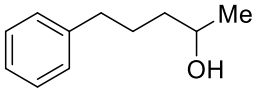
^{1}H NMR (600 MHz, CD_2Cl_2) δ 7.69 (d, J = 6.6 Hz, 2H), 7.35 (d, J = 8.0 Hz, 2H), 3.38–3.33 (m, 2H), 3.21 (d, J = 10.6 Hz, 1H), 3.10 (d, J = 10.5 Hz, 1H), 2.43 (s, 3H), 1.85–1.72 (m, 2H), 1.48 (s, 1H), 1.28 (s, 3H) ppm. ^{13}C NMR (151 MHz, CD_2Cl_2) δ 144.1, 134.1, 130.0, 127.9, 77.4, 60.7, 47.3, 39.9, 25.3, 21.6 ppm. HRMS (m/z): $[M+Na]^+$ calcd for $C_{12}H_{17}NO_3SNa^+$ 278.0821, found 278.0825.

Chiral SFC separation conditions: Chiralpak IG, 4.6 × 250 mm; isocratic, 25% *i*-PrOH in CO_2, 2.5 mL/min, 230 nm; retention time: 7.97 min, 9.54 min. 1,3,5-trimethoxybenzene was used as internal standard (1.52 min).



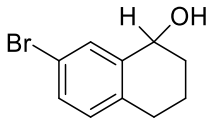
16

Chiral SFC separation conditions: Chiralpak ID, 4.6 × 250 mm; isocratic, 5% MeCN in CO_2, 2.5 mL/min, 210 nm; retention time: 5.58 min, 7.20 min. 1,3,5-trimethoxybenzene was used as internal standard (2.78 min).



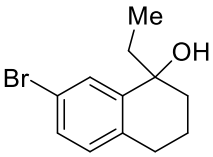
17

Chiral SFC separation conditions: Chiralpak ID, 4.6 × 250 mm; isocratic, 5% MeCN in CO_2, 2.5 mL/min, 210 nm; retention time: 6.85 min, 7.52 min. 1,3,5-trimethoxybenzene was used as internal standard (2.88 min).



18

Chiral SFC separation conditions: Chiralpak IE, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 230 nm; retention time: 7.27 min, 8.25 min. 1,3,5-trimethoxybenzene was used as internal standard (1.76 min).

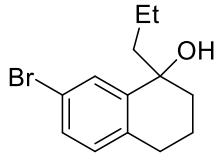


19

The tetralol **19** was prepared according to the general procedure **D**, 89% yield.

^{1}H NMR (500 MHz, CD_3CN) δ 7.56 (d, J = 2.1 Hz, 1H), 7.21 (dd, J = 8.2, 2.2 Hz, 1H), 6.94 (dt, J = 8.1, 1.0 Hz, 1H), 2.94 (s, 1H), 2.72–2.55 (m, 2H), 1.93–1.87 (m, 1H), 1.81–1.59 (m, 5H), 0.77 (t, J = 7.4 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CD_3CN) δ 146.94, 136.99, 131.64, 130.32, 130.26, 119.76, 72.70, 35.74, 35.30, 29.76, 20.18, 8.60 ppm. HRMS (m/z): $[M+H]^+$ calcd for $C_{12}H_{16}OBr^+$ 255.0379, found 255.0379.

Chiral SFC separation conditions: Chiralpak IH, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 230 nm; retention time: 3.25 min, 4.08 min. 1,3,5-trimethoxybenzene was used as internal standard (1.81 min).

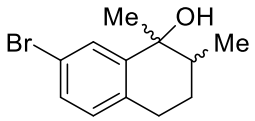


20

The tetralol **20** was prepared according to the general procedure **D**, 90% yield.

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.59 (d, J = 2.2 Hz, 1H), 7.27 (dd, J = 8.2, 2.2 Hz, 1H), 7.04–6.98 (m, 1H), 4.90 (s, 1H), 2.71–2.57 (m, 2H), 1.91–1.50 (m, 6H), 1.38–1.27 (m, 1H), 1.27–1.13 (m, 1H), 0.84 (t, J = 7.3 Hz, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6) δ 147.1, 135.2, 130.6, 129.1, 128.9, 118.4, 70.6, 44.8, 34.8, 28.5, 19.1, 16.6, 14.4 ppm. HRMS (m/z): $[M+H]^+$ calcd for $C_{13}H_{18}OBr^+$ 269.0536, found 269.0536.

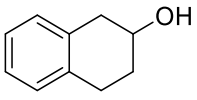
Chiral SFC separation conditions: Chiralpak IA, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 230 nm; retention time: 6.33 min, 8.95 min. 1,3,5-trimethoxybenzene was used as internal standard (1.87 min).



21

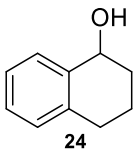
Tetralol **21**: ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.75 (d, J = 2.1 Hz, 0.53H), 7.74 (d, J = 2.1 Hz, 0.47H), 7.30–7.22 (m, 1H), 6.96 (dt, J = 8.1, 1.0 Hz, 0.47H), 6.93 (dt, J = 8.1, 1.1 Hz, 0.53H), 2.85–2.62 (m, 2H), 1.94–1.80 (m, 2H), 1.73–1.55 (m, 2H), 1.51 (s, 1.4H), 1.30 (s, 1.6H), 1.07 (d, J = 6.6 Hz, 1.6H), 1.04 (d, J = 6.9 Hz, 1.4H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2) δ 147.78, 145.46, 135.48, 135.26, 130.90, 130.70, 130.24, 130.14, 130.03, 129.75, 119.95, 119.85, 74.05, 72.51, 41.09, 39.50, 30.10, 28.71, 28.68, 27.32, 27.29, 25.08, 15.45, 14.68 ppm. HRMS (m/z): $[M+H]^+$ calcd for $C_{12}H_{16}OBr^+$ 255.0397, found 255.0397.

Chiral SFC separation conditions: Chiralpak IA, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 230 nm; retention time: 6.84 min and 10.48 min, 7.54 min and 9.87 min. 1,3,5-trimethoxybenzene was used as internal standard (1.76 min).



23

Chiral SFC separation conditions: Chiralpak IG, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 210 nm; retention time: 6.60 min and 7.17 min. 1,3,5-trimethoxybenzene was used as internal standard (2.30 min).



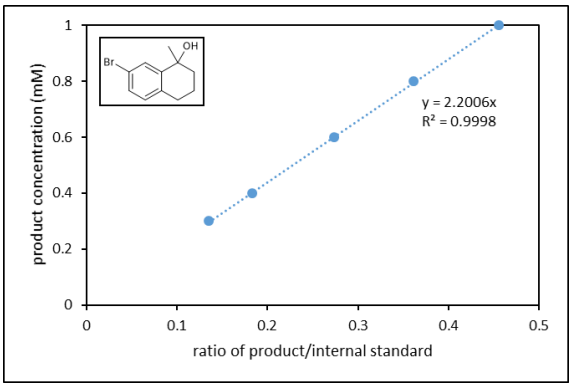
24

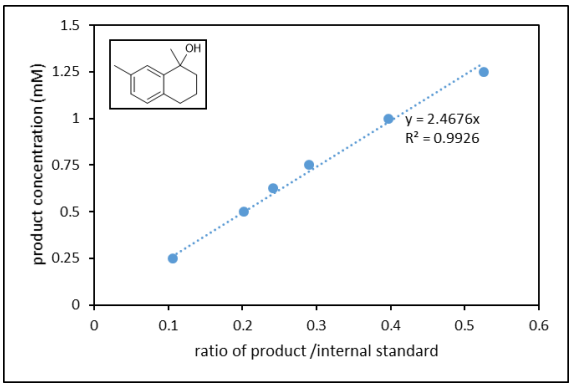
Chiral SFC separation conditions: Chiralpak IG, 4.6 × 250 mm; isocratic, 10% *i*-PrOH in CO_2, 2.5 mL/min, 210 nm; retention time: 6.26 min and 6.89 min. 1,3,5-trimethoxybenzene was used as internal standard (2.30 min).

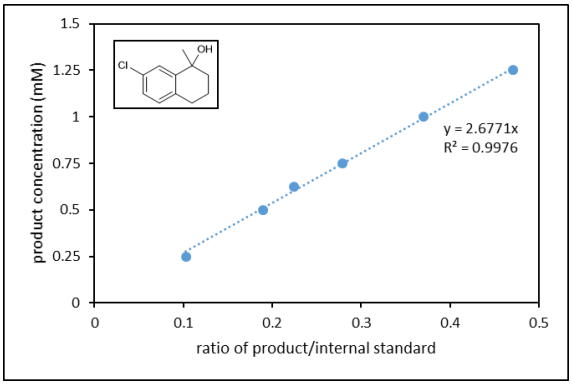
Chiral GC separation conditions: CP-Chiralsil-Dex-CB, 25 m × 0.25 mm × 0.25 μm film thickness, gradient method, temperature program: 50 °C (2 min)–10 °C/min–190 °C (4 min); retention time: 14.854 min, 14.905 min. 1,3,5-trimethoxybenzene was used as internal standard (13.634 min).

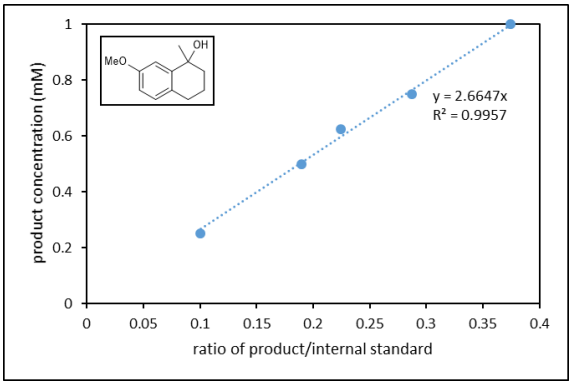
7. Supporting Figures

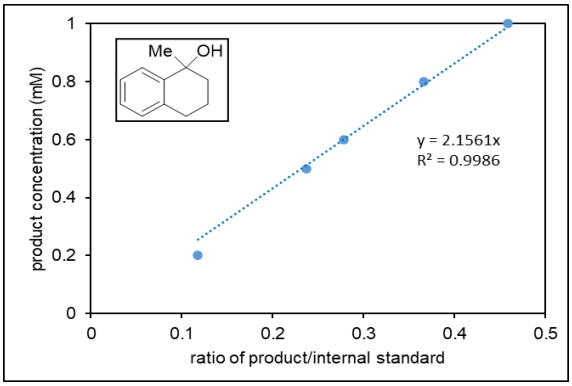
7.1 Calibration Curves

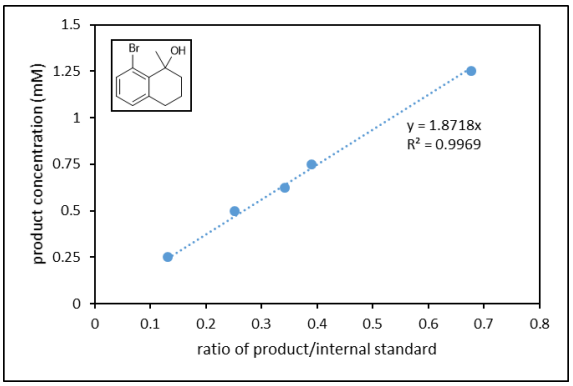


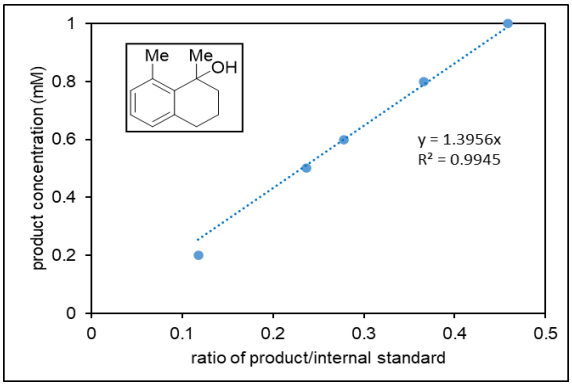


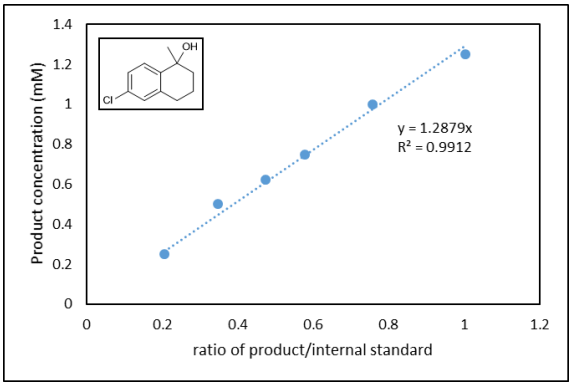


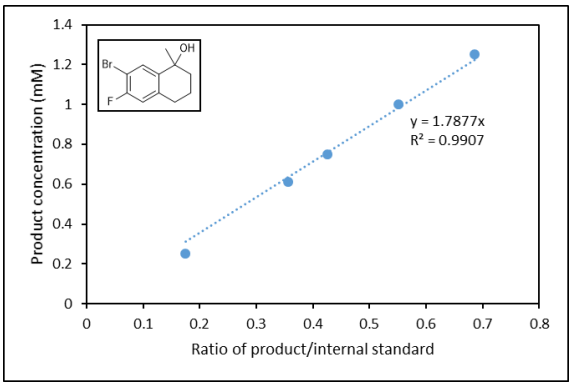


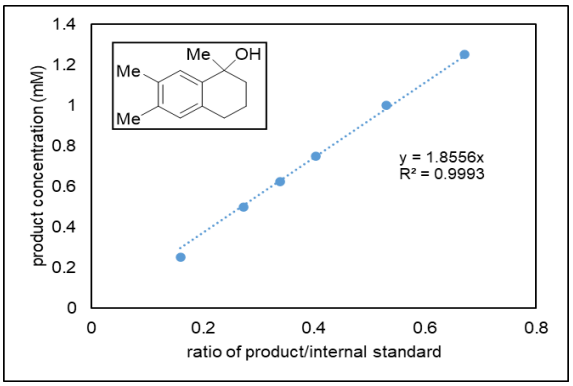









Product concentration (mM)
Ratio of product/internal standard
y = 1.7877x
R² = 0.9907
Br
F
OH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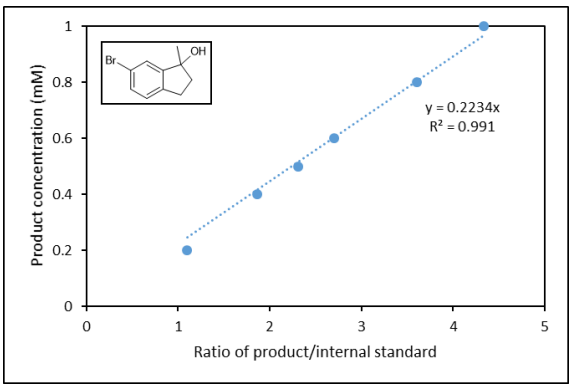
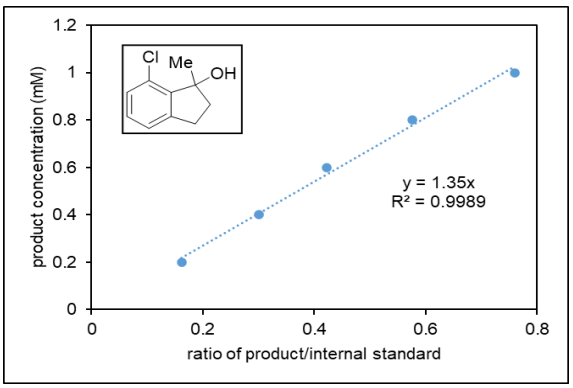
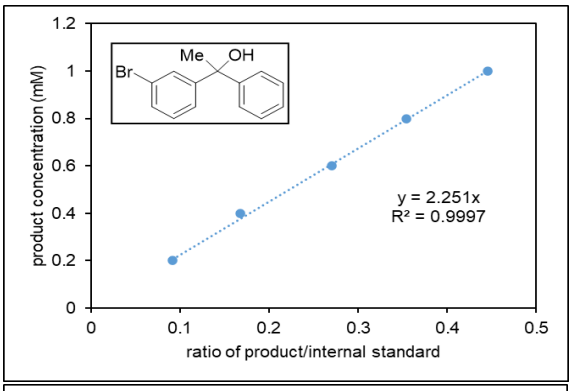
R² = 0.9993
Me
OH
Me
Me


Product concentration (mM)
Ratio of product/internal standard
y = 0.2234x
R² = 0.991
Br
OH


product concentration (mM)
ratio of product/internal standard
y = 1.35x
R² = 0.9989
Cl
Me
OH


product concentration (mM)
ratio of product/internal standard
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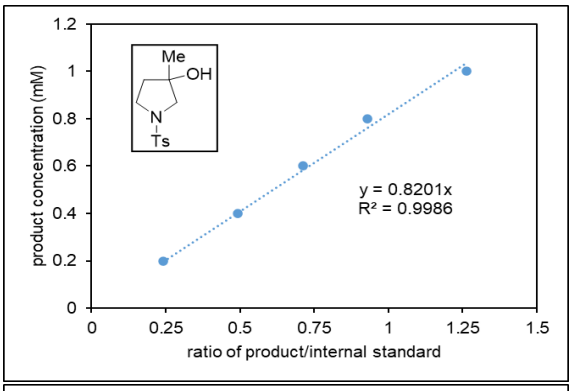
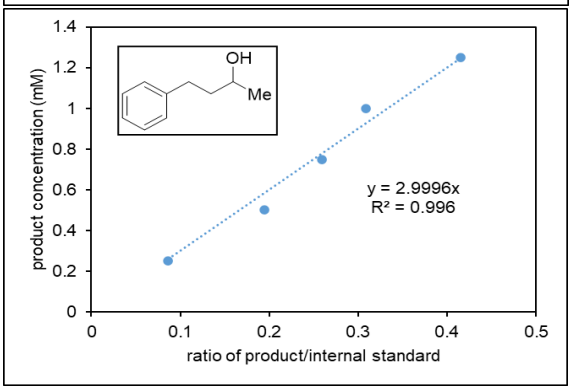
Br
Me
OH


product concentration (mM)
ratio of product/internal standard
y = 0.8201x
R² = 0.9986
Me
OH
N
Ts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ratio of product/internal standard
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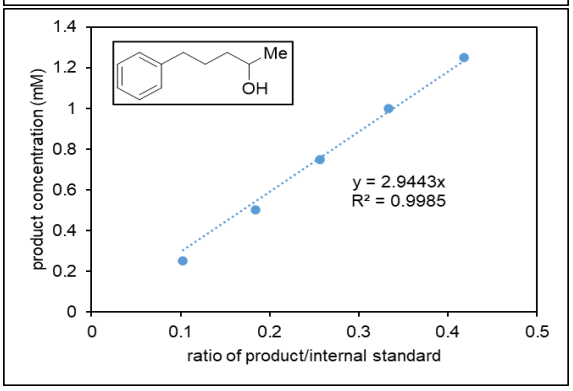
R² = 0.996
OH
Me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ratio of product/internal standard
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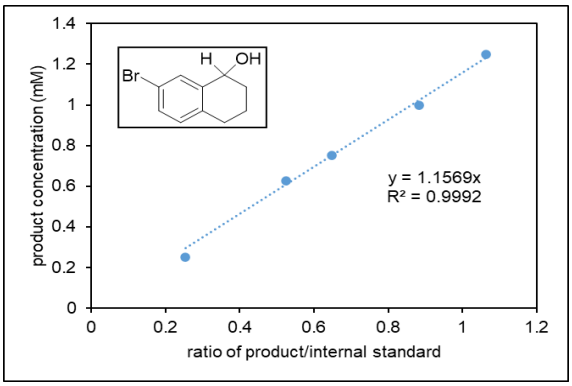
Me
OH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ratio of product/internal standard
y = 1.1569x
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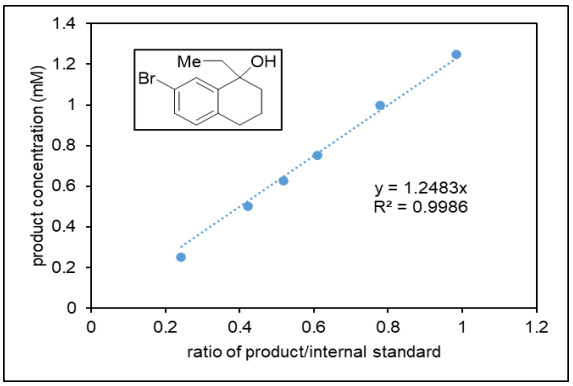
H
OH
Br


product concentration (mM)
ratio of product/internal standard
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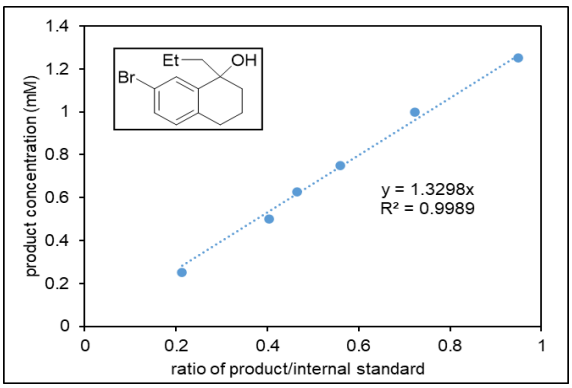
Me
OH
Br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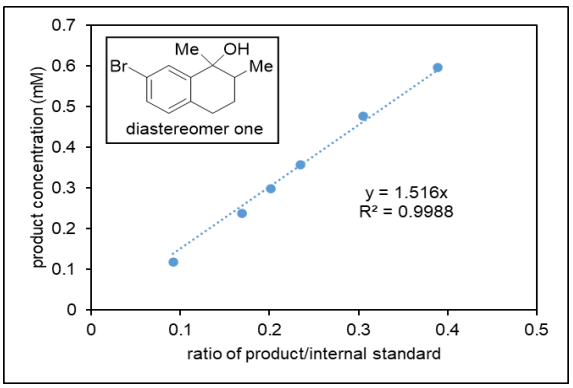
Et
OH
Br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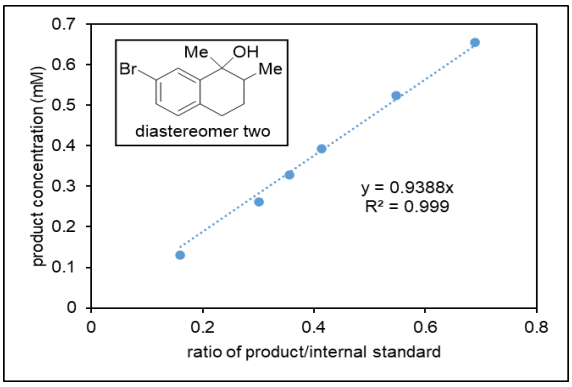
OH
Me
Br
diastereomer one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ratio of product/internal standard
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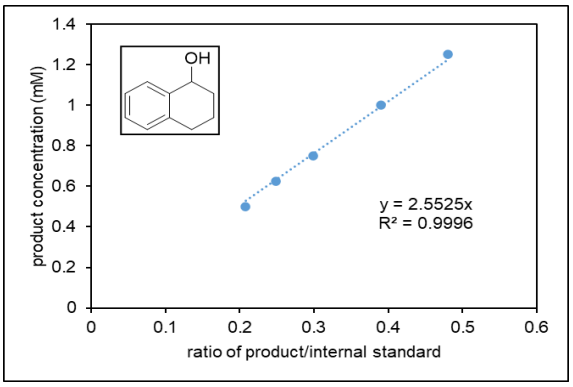
R² = 0.999
Me
OH
Me
Br
diastereomer two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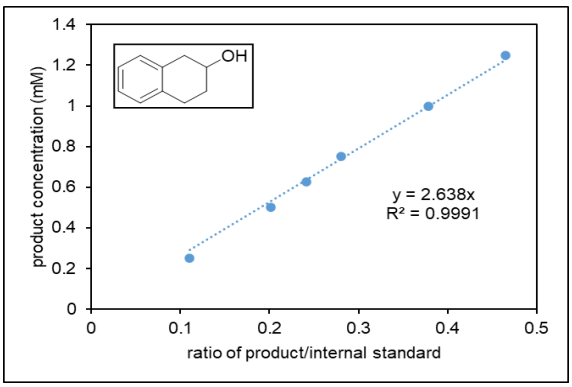
OH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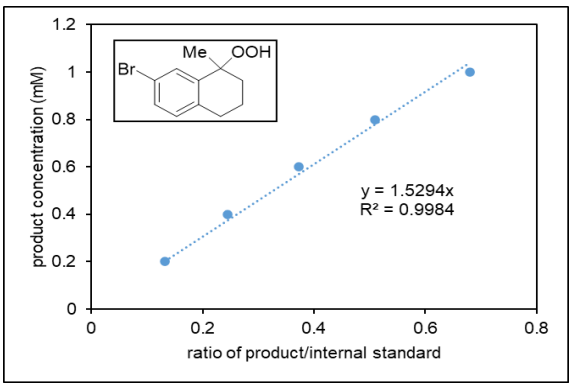
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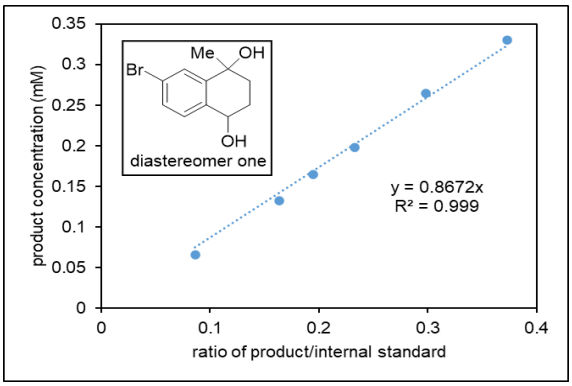
R² = 0.9984
Me
OOH
Br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ratio of product/internal standard
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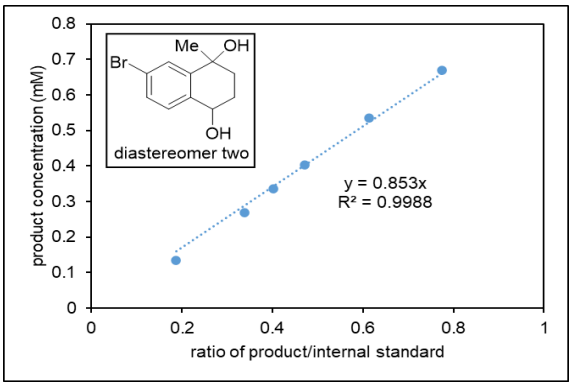
R² = 0.999
Me
OH
Br
OH
diastereomer one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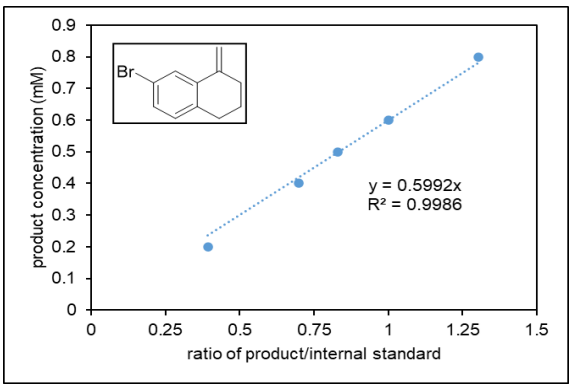
R² = 0.9988
Me
OH
Br
OH
diastereomer two


product concentration (mM)
ratio of product/internal standard
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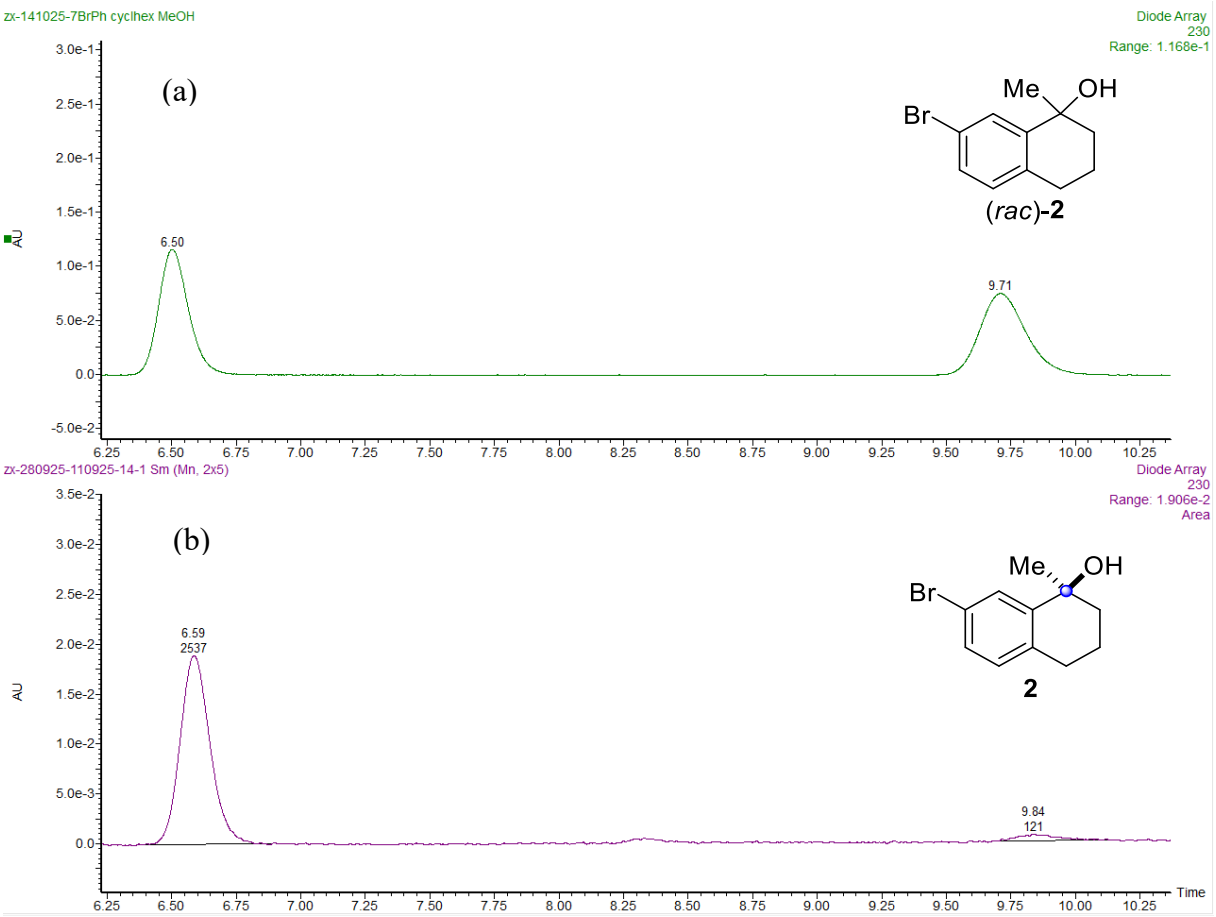
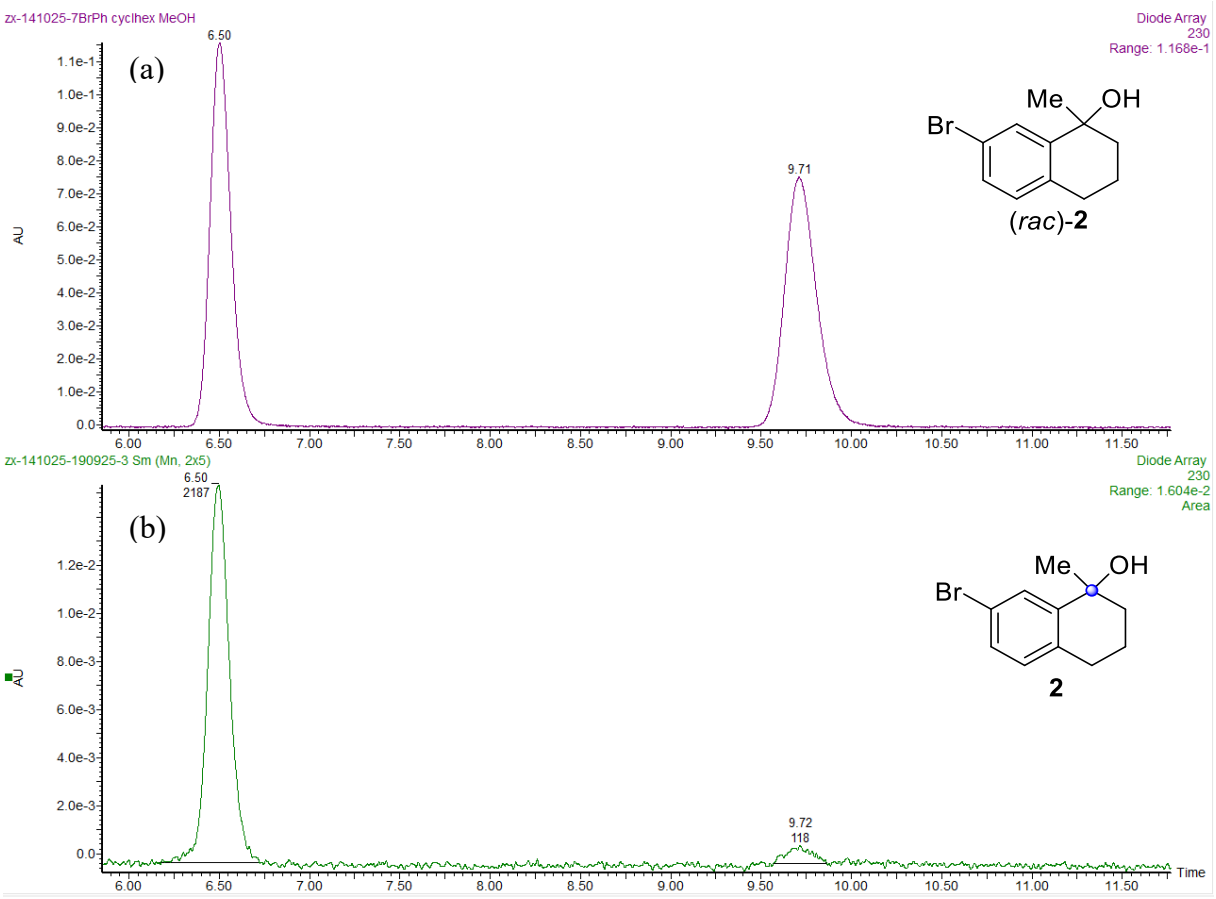
Br

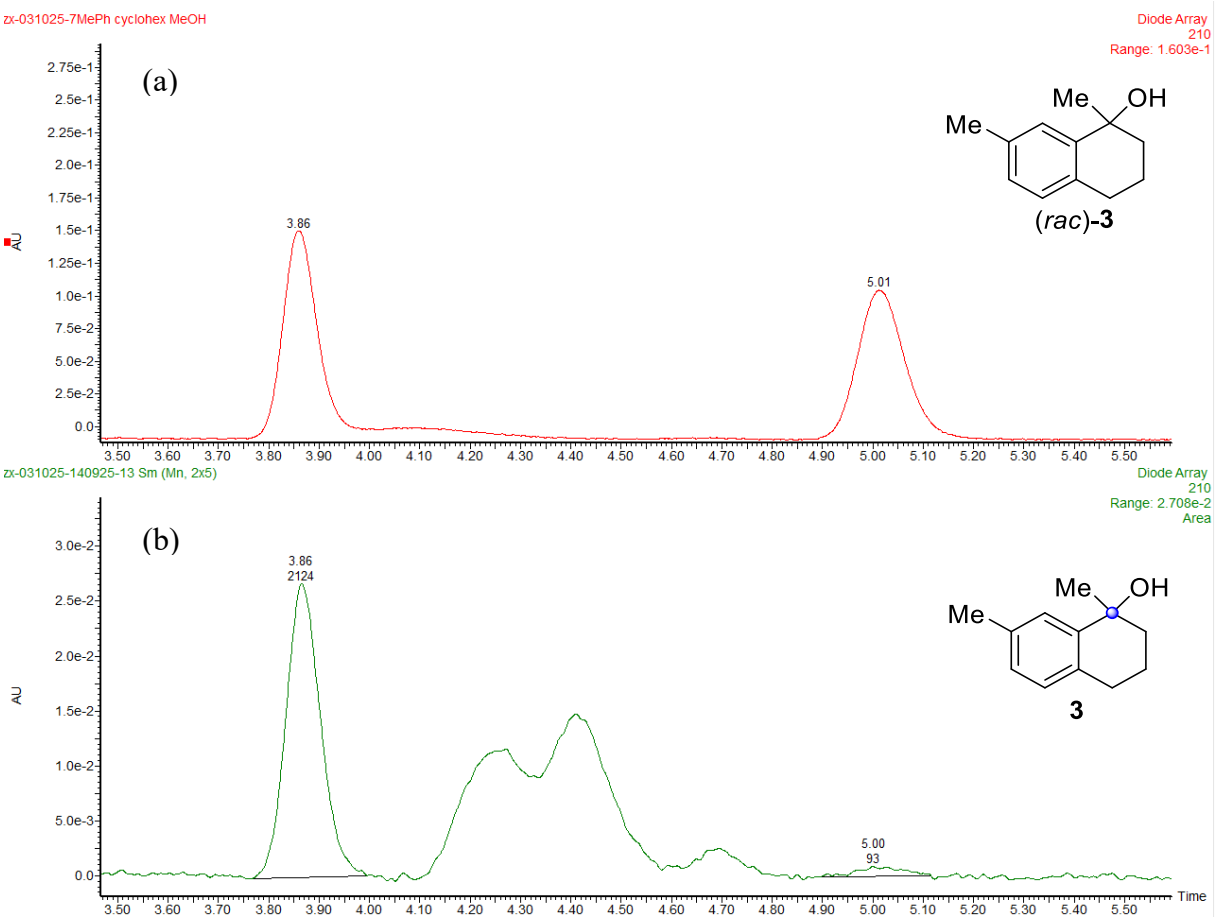
7.2 SFC traces



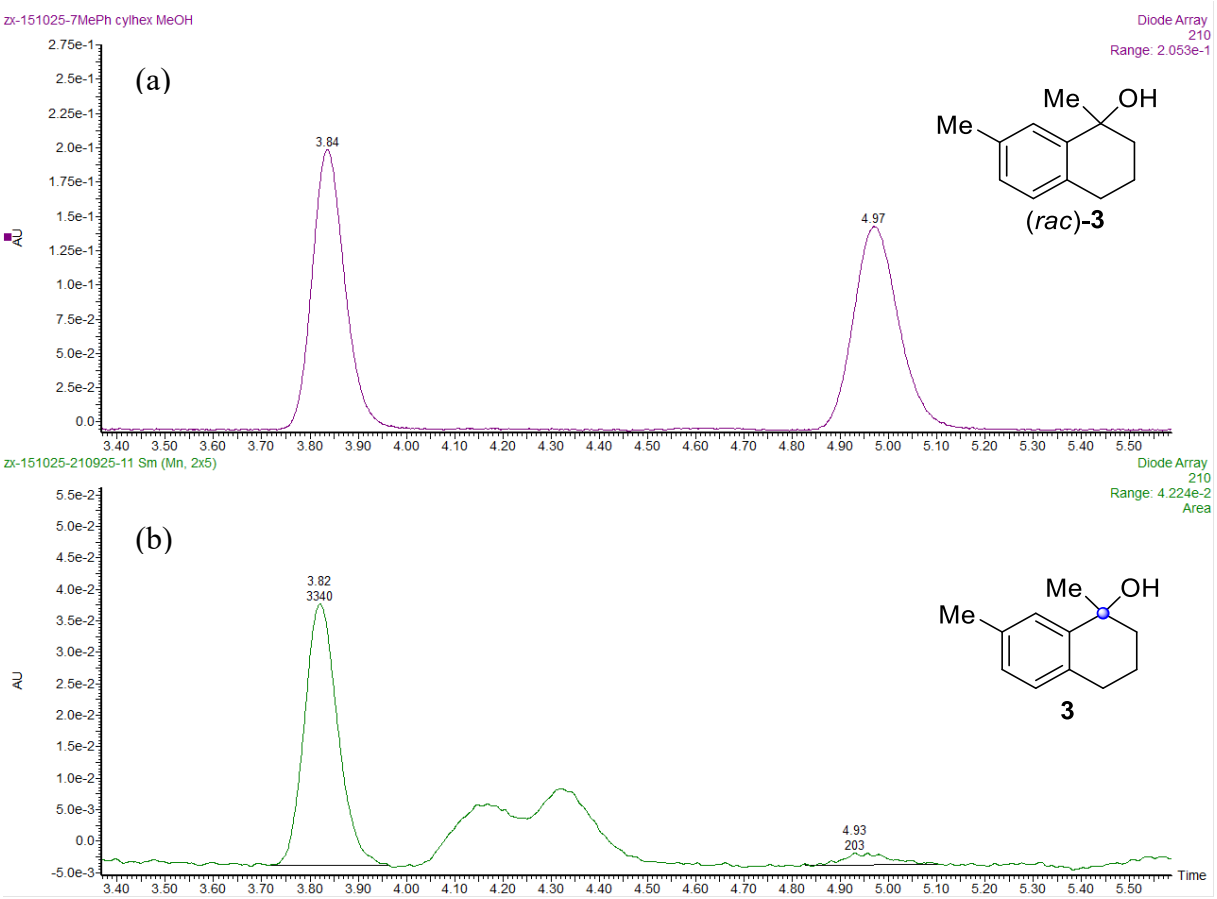
Supplementary Fig. 43. SFC traces of the radical hydration product tetralol 2. (a) Racemic tetralol **2**. (b) Biocatalytic radical hydration of alkene **1** with P450$_{BM3}$_QTG and $PhSiMeH_2$.



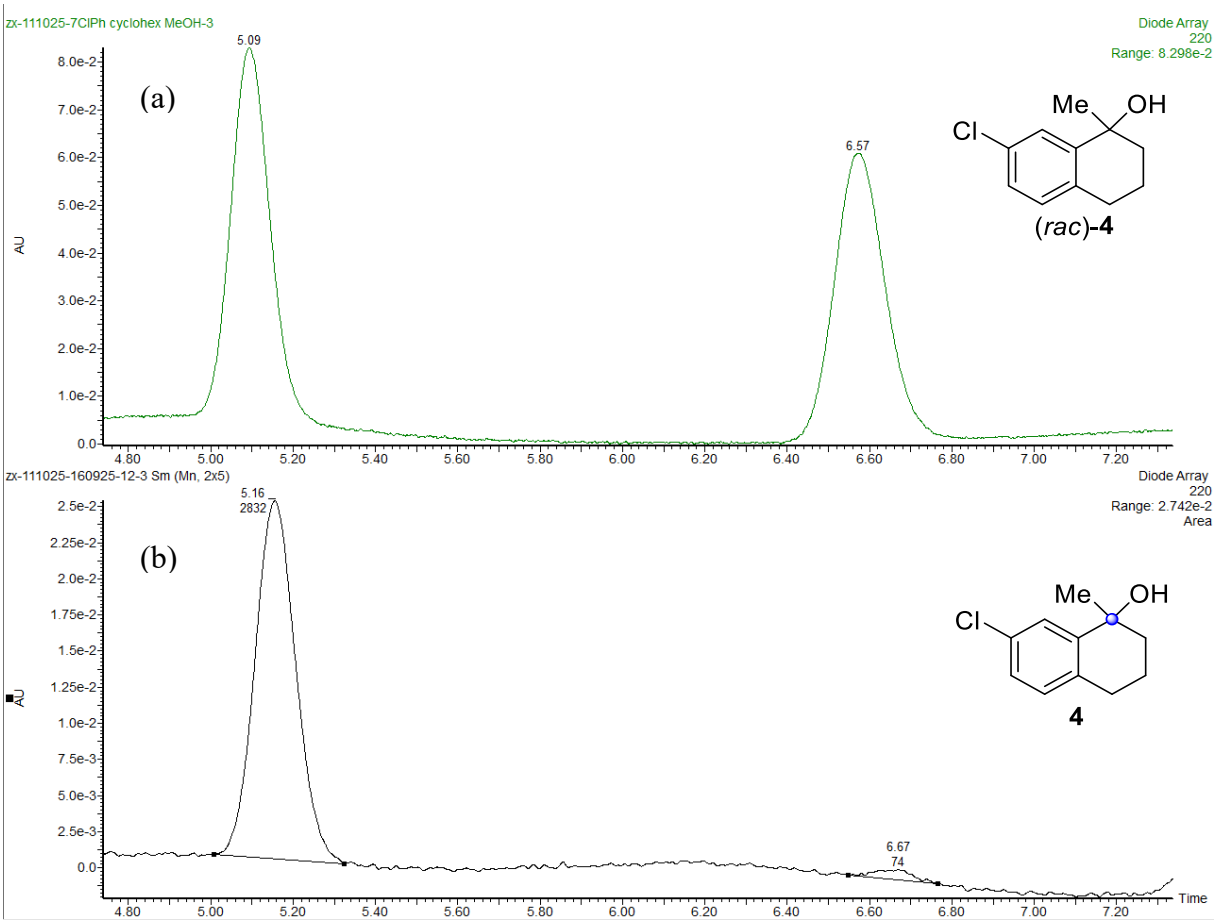
Supplementary Fig. 44. SFC traces of the radical hydration product tetralol 2. (a) Racemic tetralol **2**. (b) Biocatalytic radical hydration of alkene **S20** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



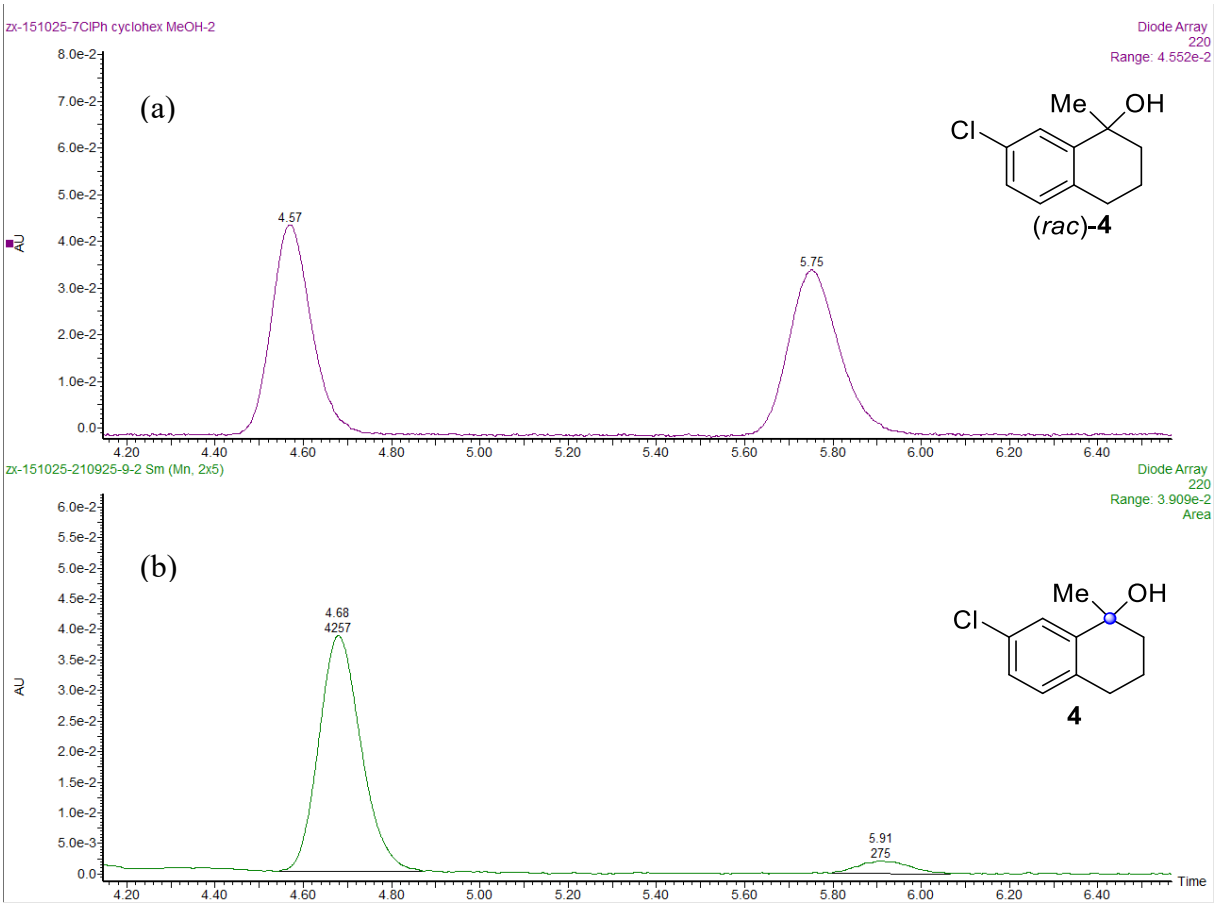
Supplementary Fig. 45. SFC traces of the radical hydration product tetralol 3. (a) Racemic tetralol **3**. (b) Biocatalytic radical hydration of alkene **S1** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



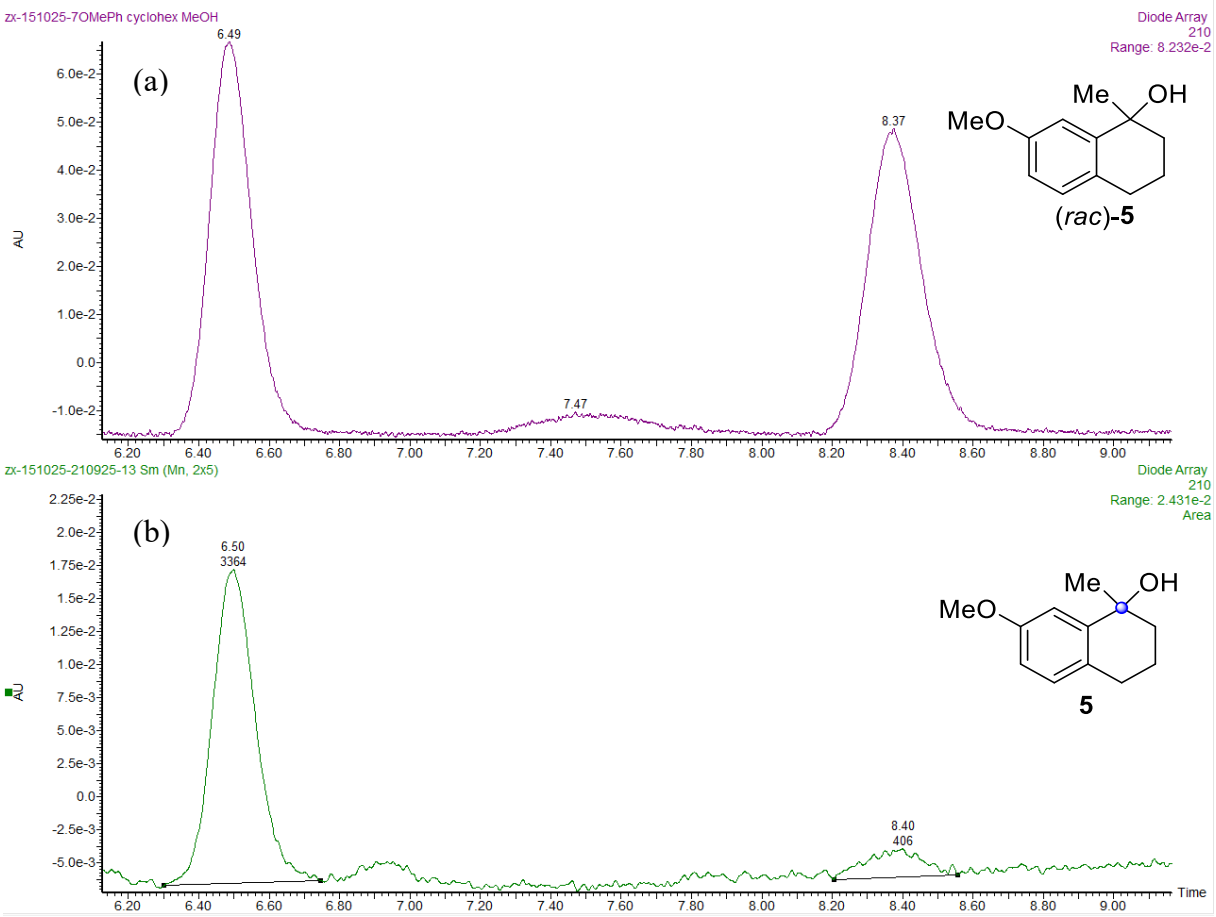
Supplementary Fig. 46. SFC traces of the radical hydration product tetralol 3. (a) Racemic tetralol **3**. (b) Biocatalytic radical hydration of alkene **S21** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



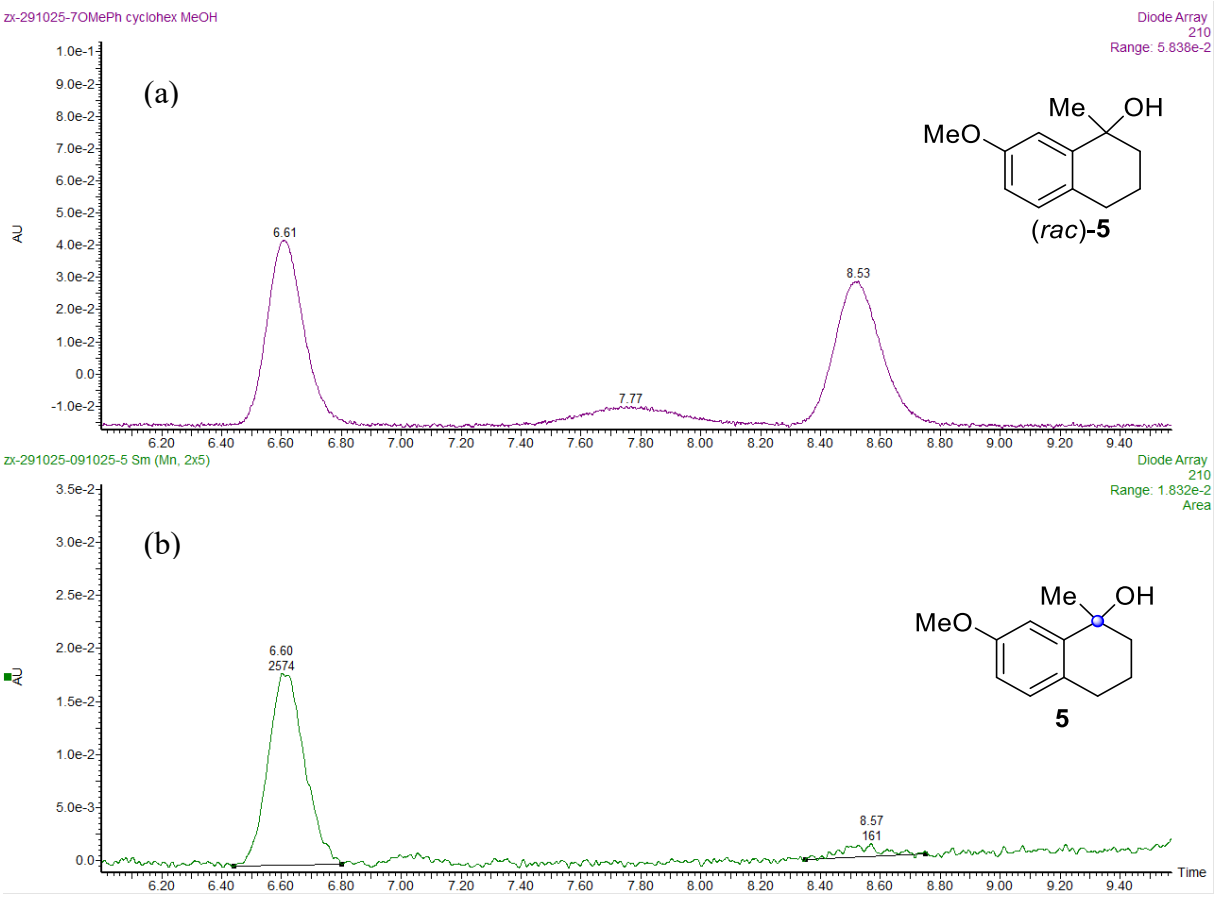
Supplementary Fig. 47. SFC traces of the radical hydration product tetralol 4. (a) Racemic tetralol **4**. (b) Biocatalytic radical hydration of alkene **S5** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



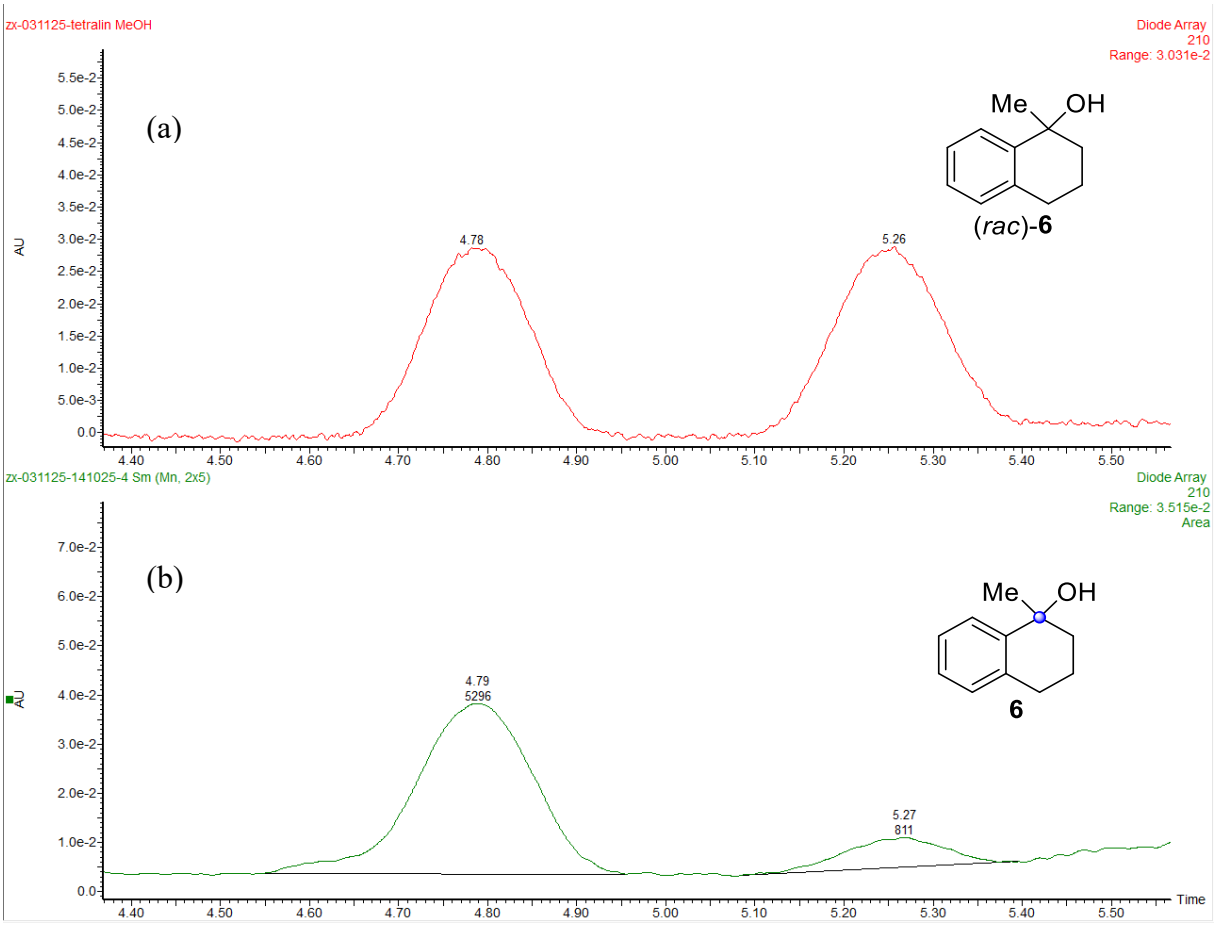
Supplementary Fig. 48. SFC traces of the radical hydration product tetralol 4. (a) Racemic tetralol **4**. (b) Biocatalytic radical hydration of alkene **S22** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



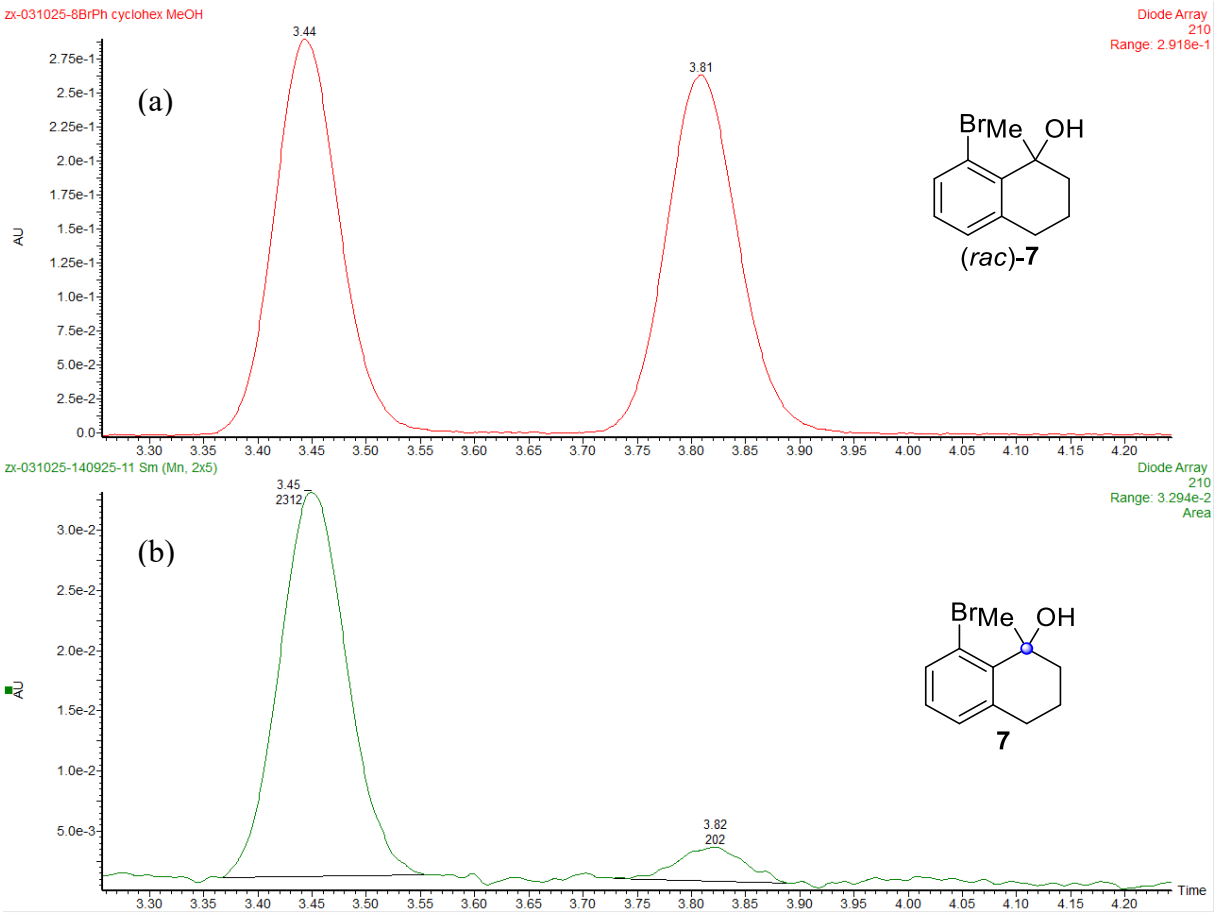
Supplementary Fig. 49. SFC traces of the radical hydration product tetralol 5. (a) Racemic tetralol **5**. (b) Biocatalytic radical hydration of alkene **S6** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



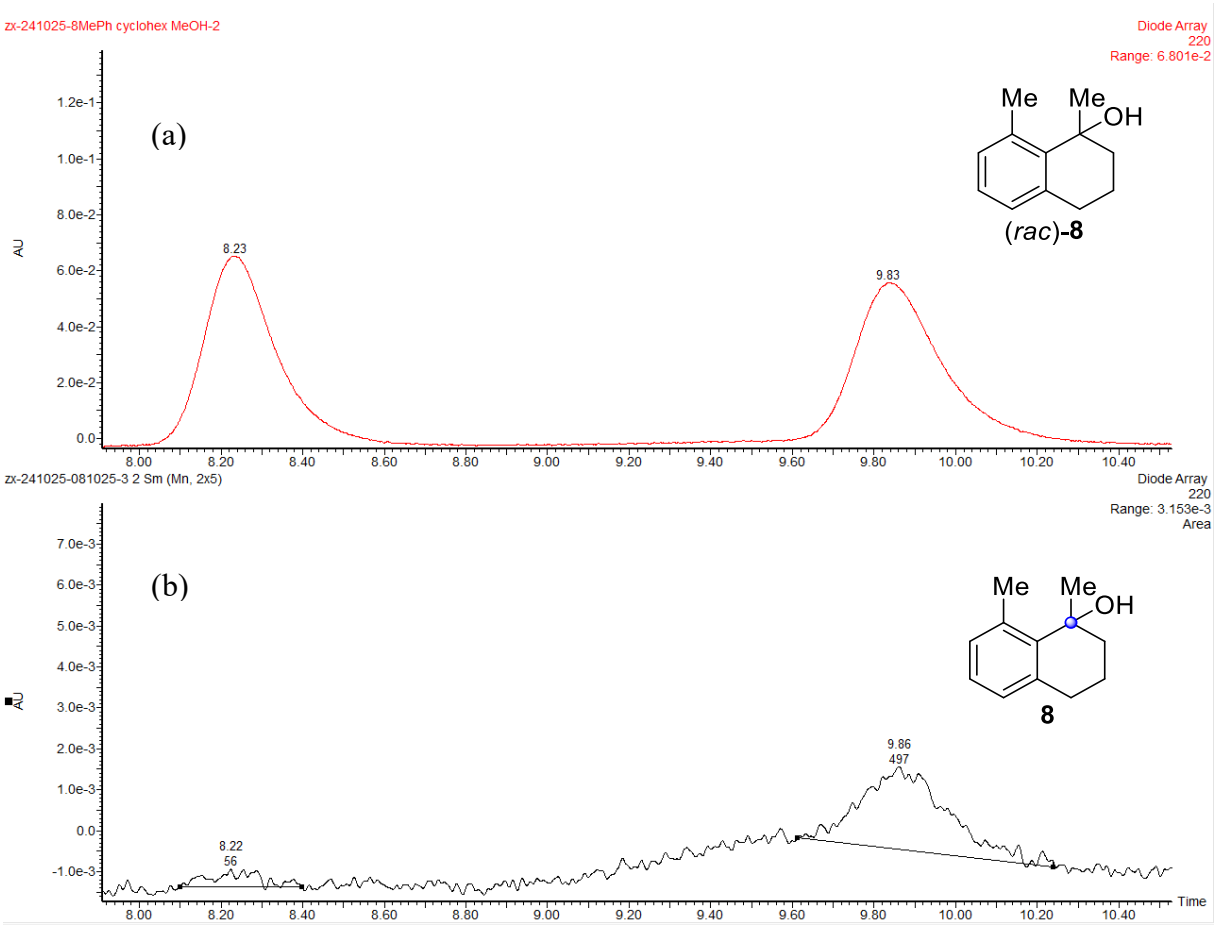
Supplementary Fig. 50. SFC traces of the radical hydration product tetralol 5. (a) Racemic tetralol **5**. (b) Biocatalytic radical hydration of alkene **S23** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



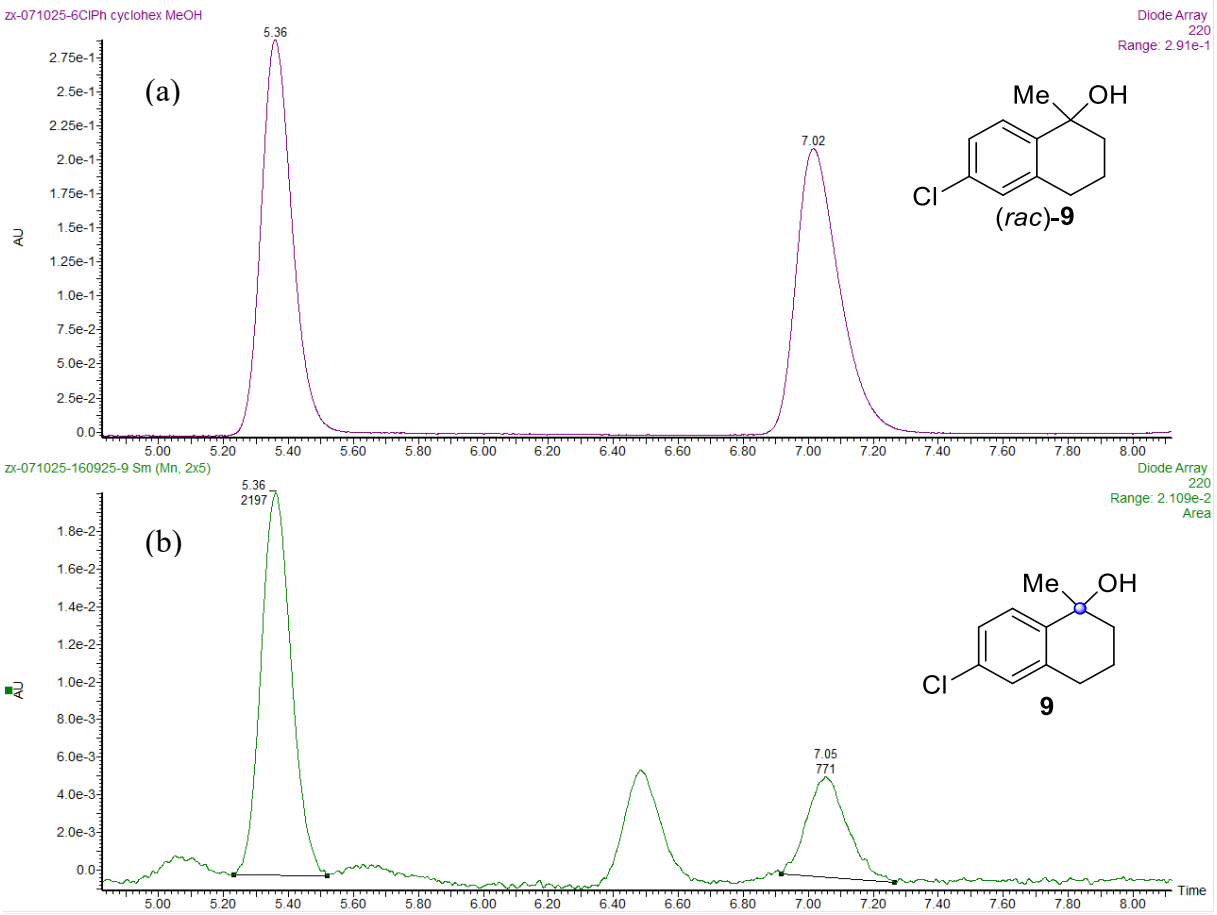
Supplementary Fig. 51. SFC traces of the radical hydration product tetralol 6. (a) Synthesized racemic tetralol **6**. (b) Biocatalytic radical hydration of alkene **S7** with P450$_{BM3}$_QTG and $PhSiMeH_2$.



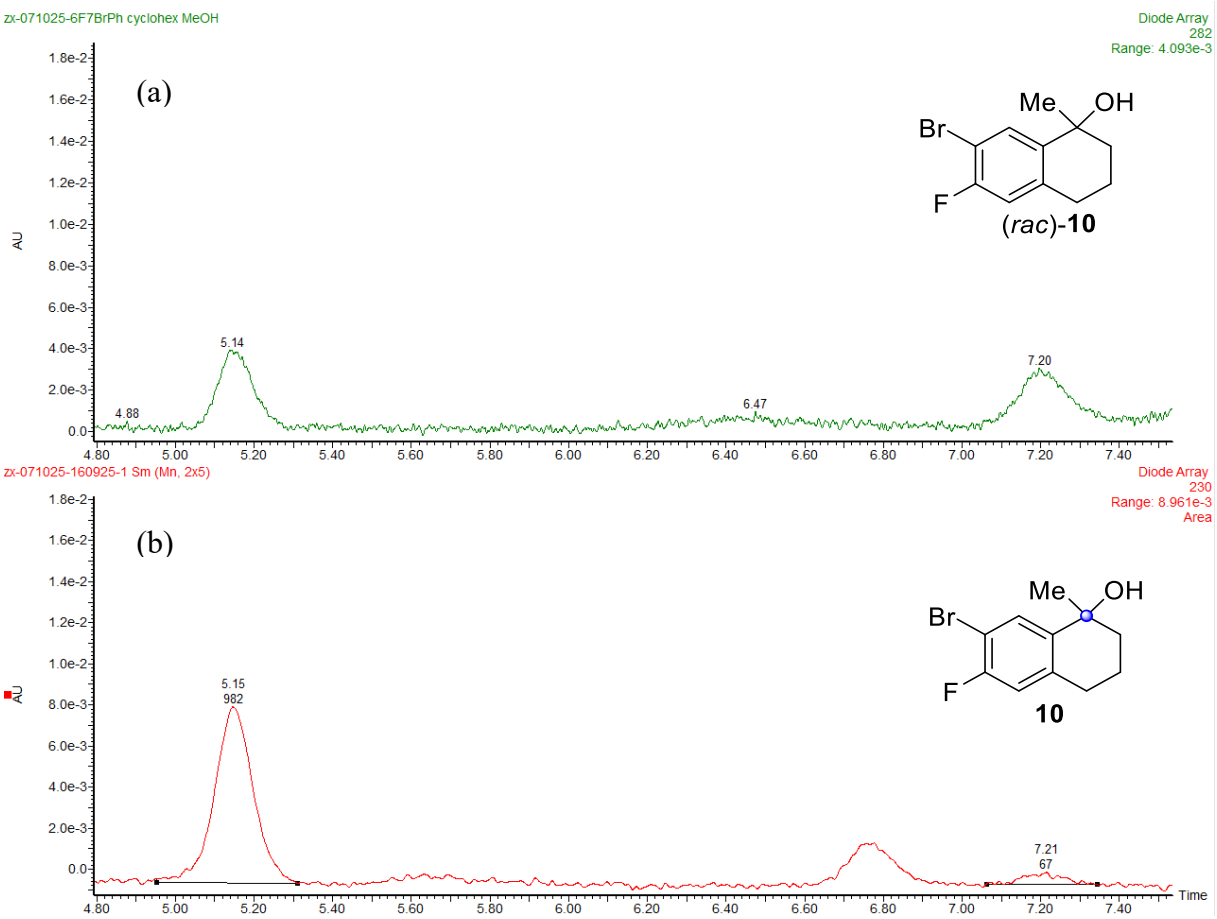
Supplementary Fig. 52. SFC traces of the radical hydration product tetralol 7. (a) Racemic tetralol **7**. (b) Biocatalytic radical hydration of alkene **S8** with P450$_{BM3}$_QTG and $PhSiMeH_2$.



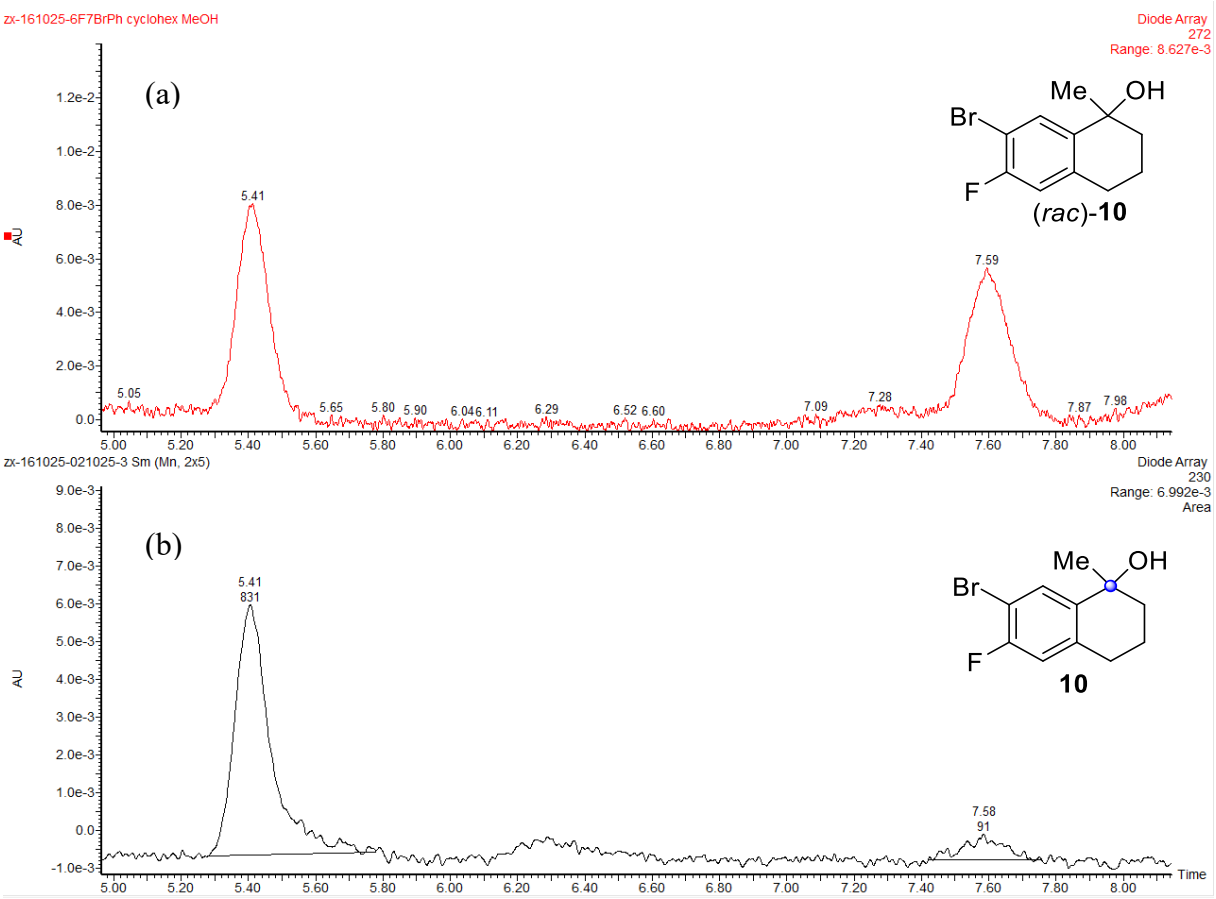
Supplementary Fig. 53. SFC traces of the radical hydration product tetralol 8. (a) Racemic tetralol **8**. (b) Biocatalytic radical hydration of alkene **S9** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



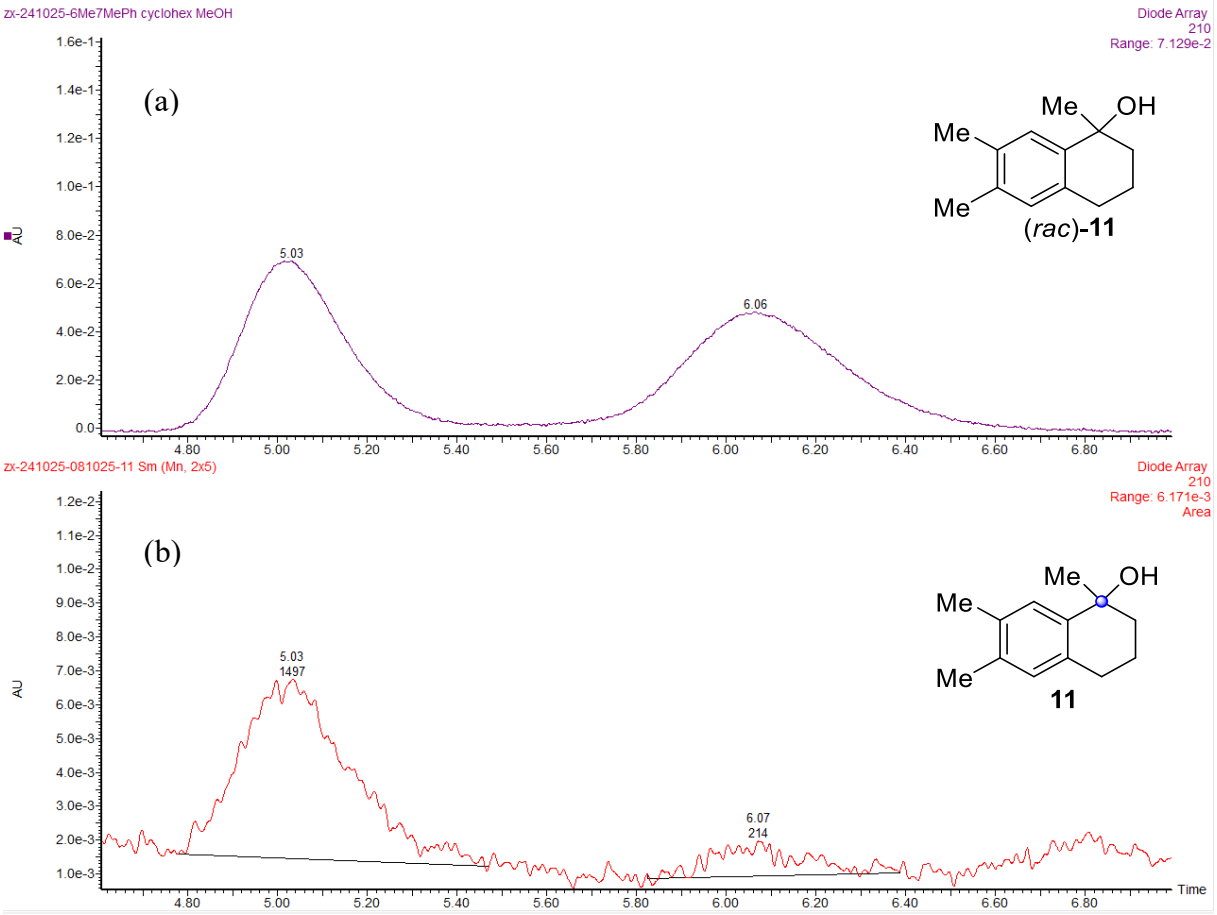
Supplementary Fig. 54. SFC traces of the radical hydration product tetralol 9. (a) Racemic tetralol **9**. (b) Biocatalytic radical hydration of alkene **S10** with P450$_{BM3}$_QTG and $PhSiMeH_2$.



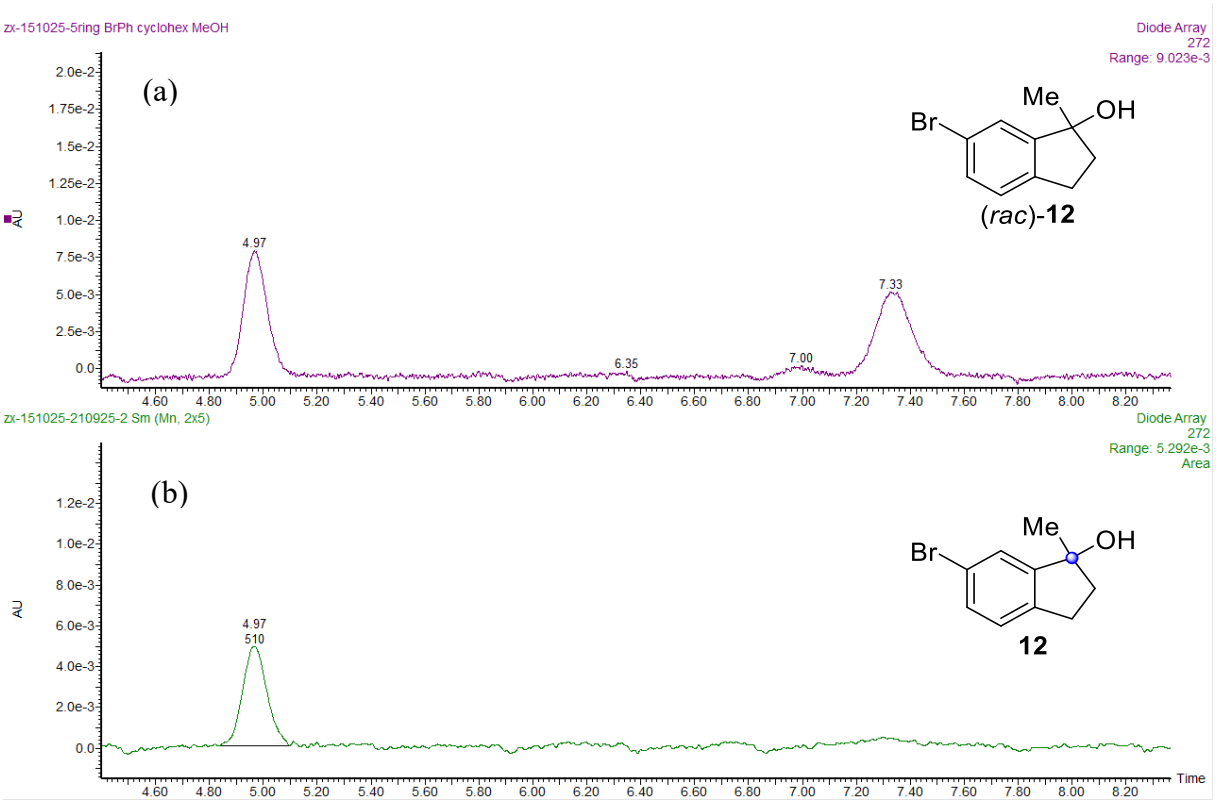
Supplementary Fig. 55. SFC traces of the radical hydration product tetralol 10. (a) Racemic tetralol **10**. (b) Biocatalytic radical hydration of alkene **S11** with P450$_{BM3}$_QTG and $PhSiMeH_2$.



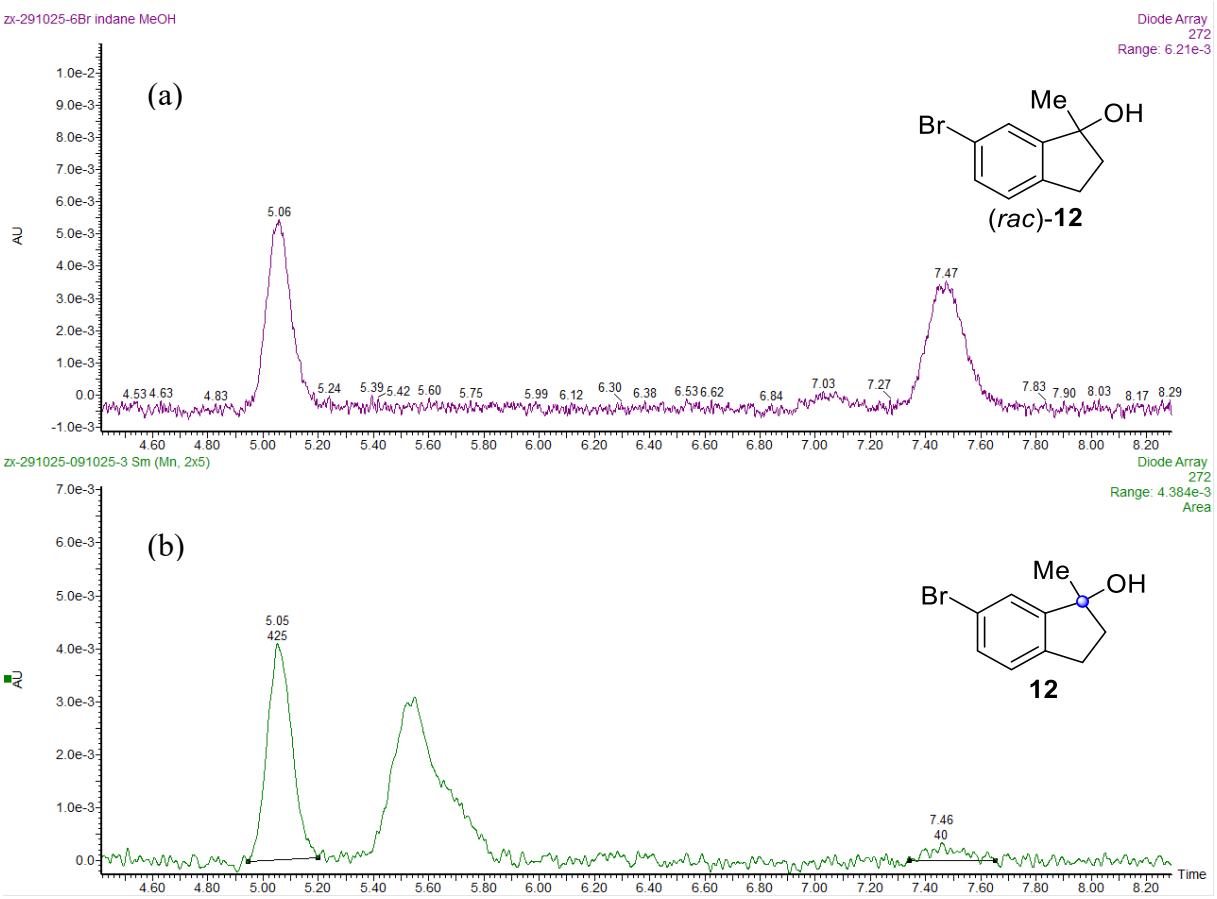
Supplementary Fig. 56. SFC traces of the radical hydration product tetralol 10. (a) Racemic tetralol **10**. (b) Biocatalytic radical hydration of alkene **S24** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



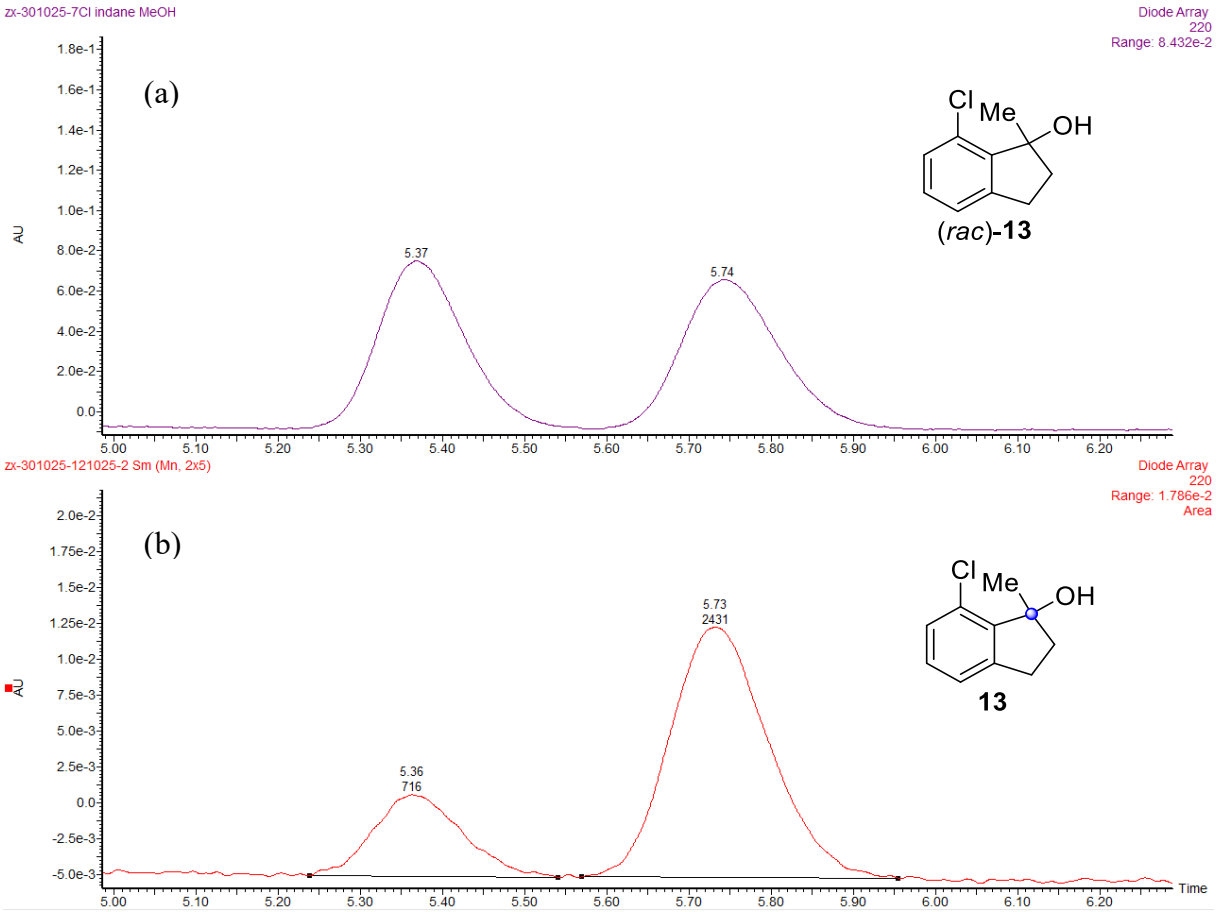
Supplementary Fig. 57. SFC traces of the radical hydration product tetralol 11. (a) Racemic tetralol **11**. (b) Biocatalytic radical hydration of alkene **S12** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



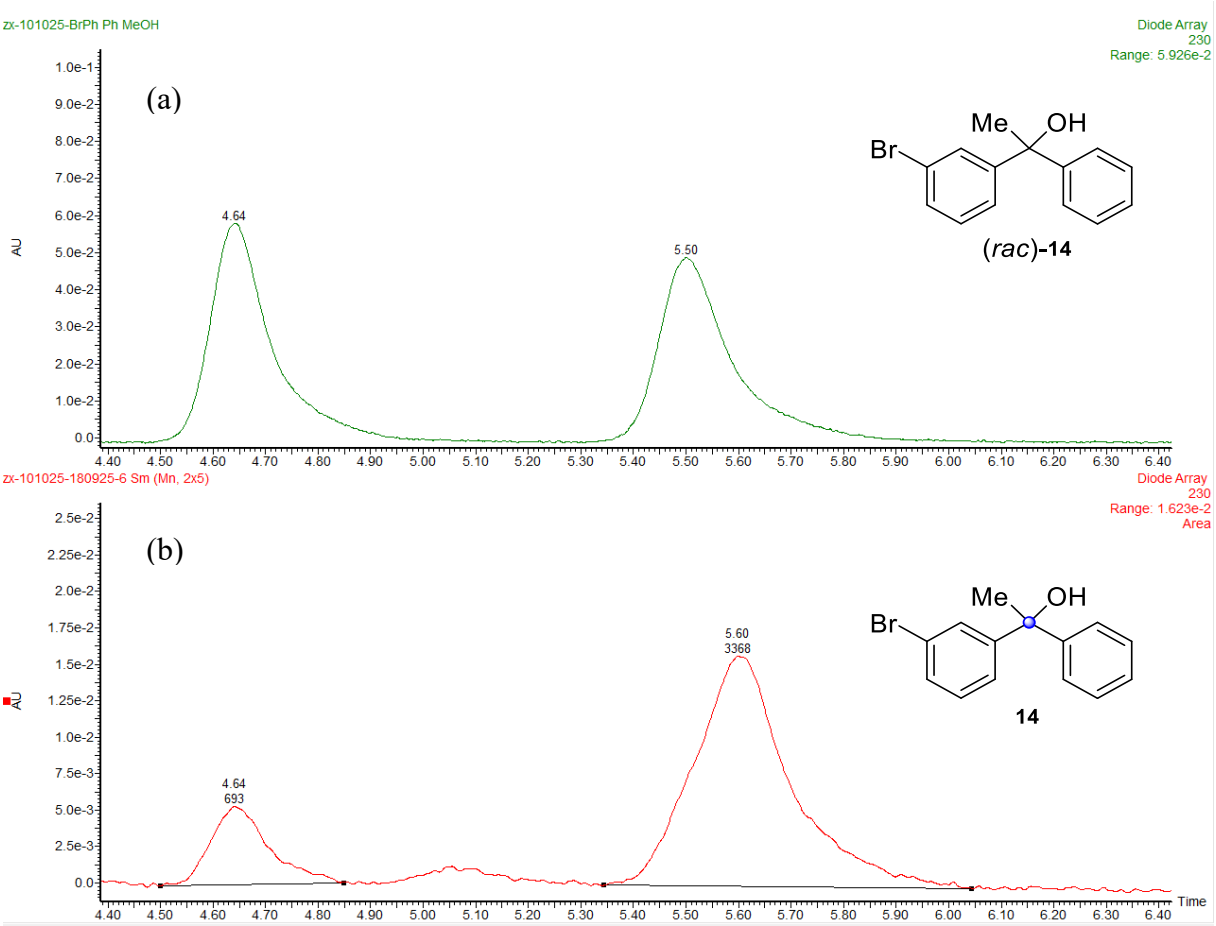
Supplementary Fig. 58. SFC traces of the radical hydration product indanol 12. (a) Racemic indanol **12**. (b) Biocatalytic radical hydration of alkene **S13** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



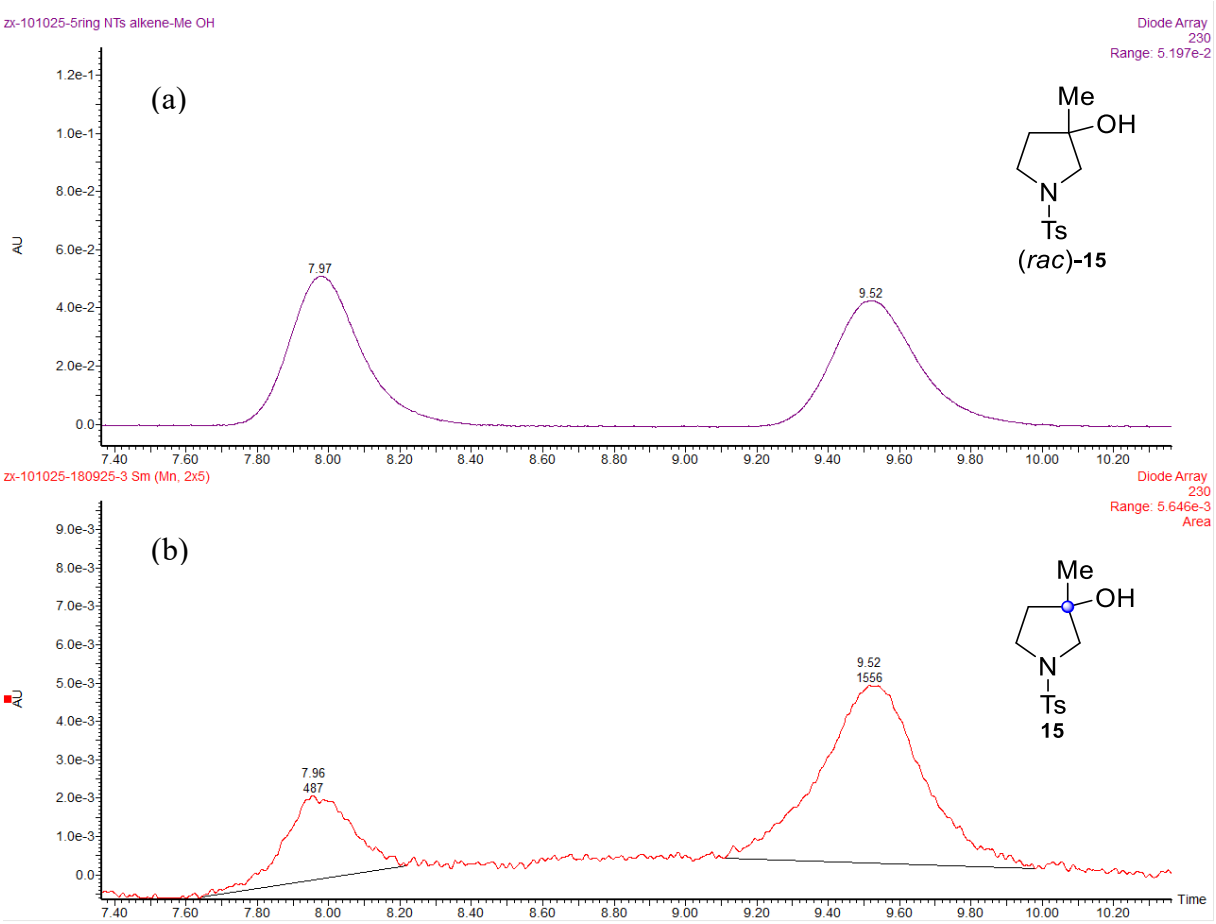
Supplementary Fig. 59. SFC traces of the radical hydration product indanol 12. (a) Racemic indanol **12**. (b) Biocatalytic radical hydration of alkene **S25** with P450$_{BM3}$_QTG and $PhSiMeH_2$.



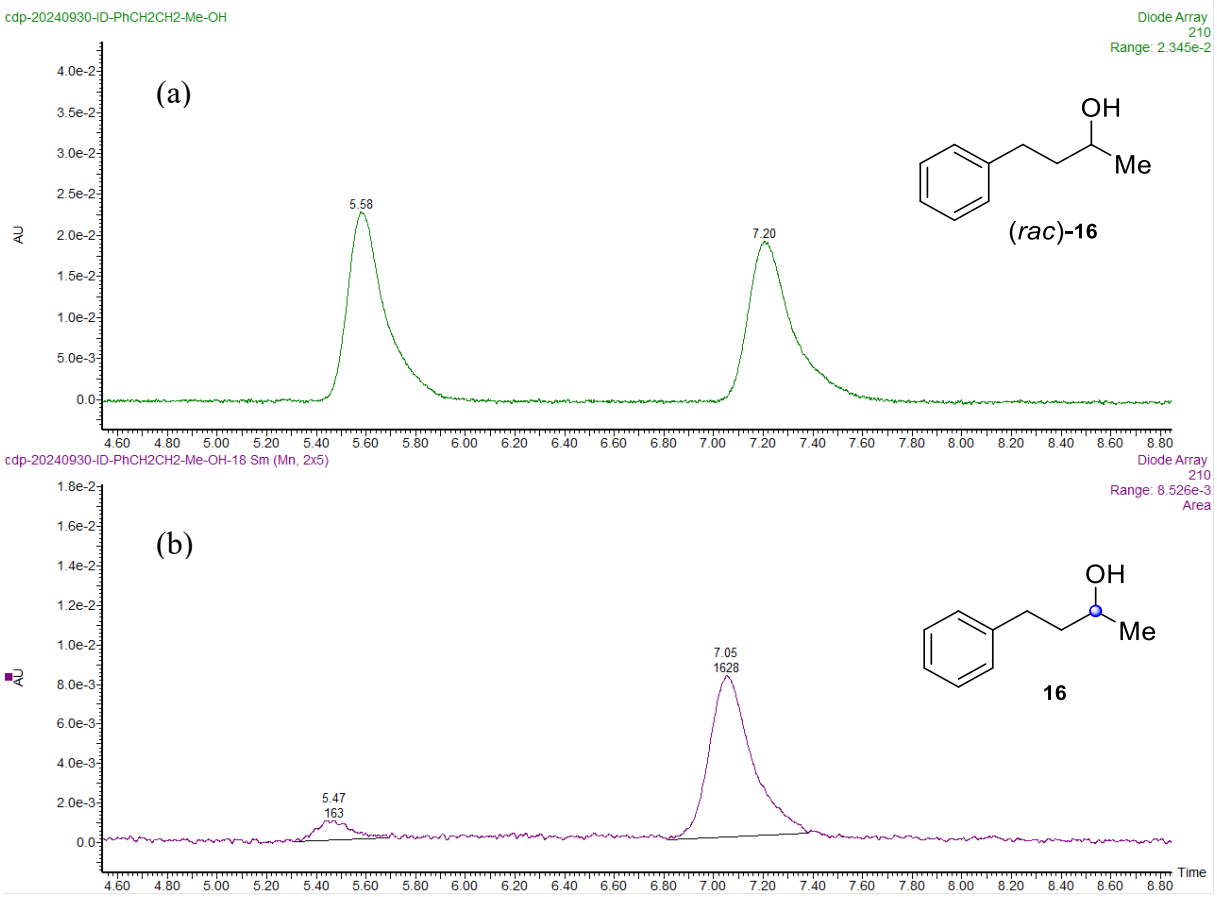
Supplementary Fig. 60. SFC traces of the radical hydration product indanol 13. (a) Racemic indanol **13**. (b) Biocatalytic radical hydration of alkene **S14** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



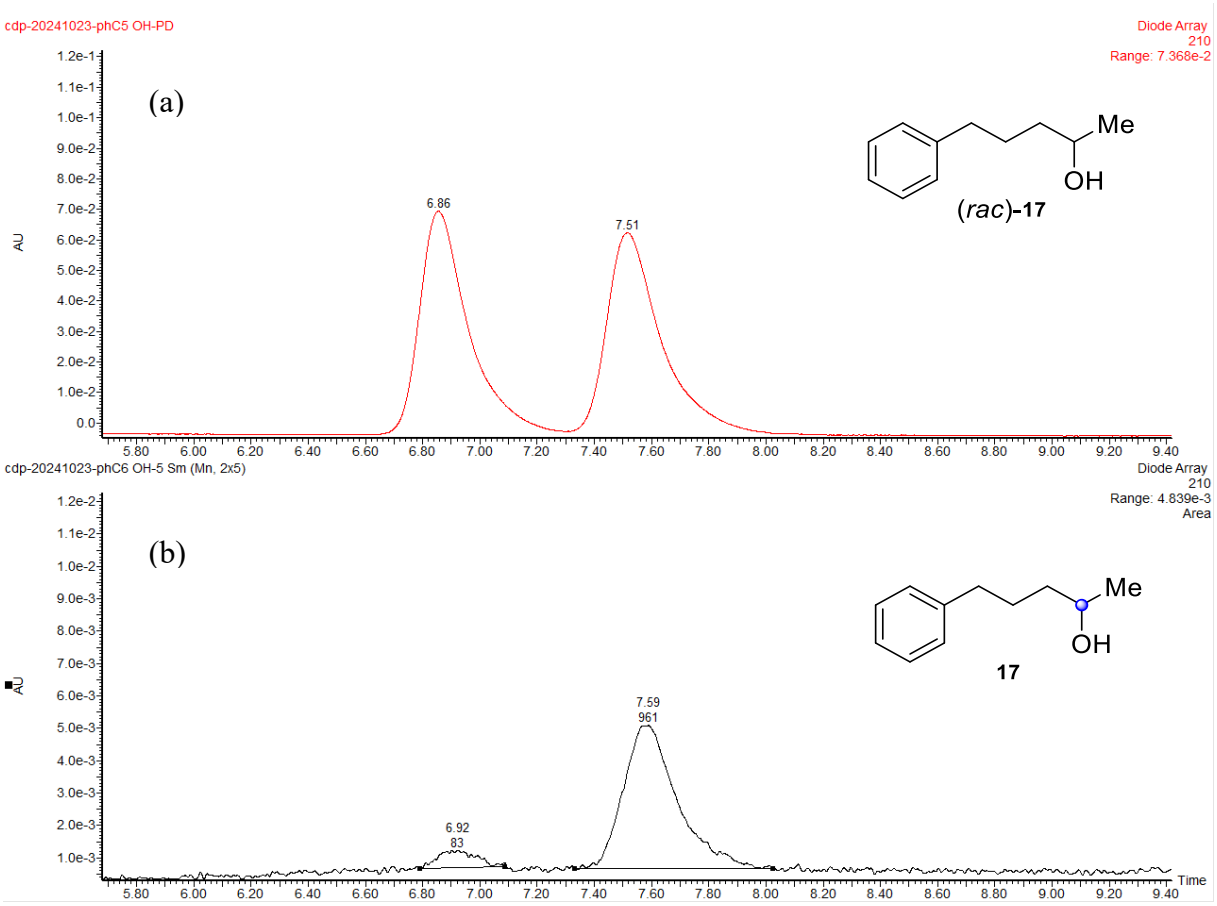
Supplementary Fig. 61. SFC traces of the radical hydration product acyclic alcohol 14. (a) Racemic acyclic alcohol **14**. (b) Biocatalytic radical hydration of alkene **S15** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



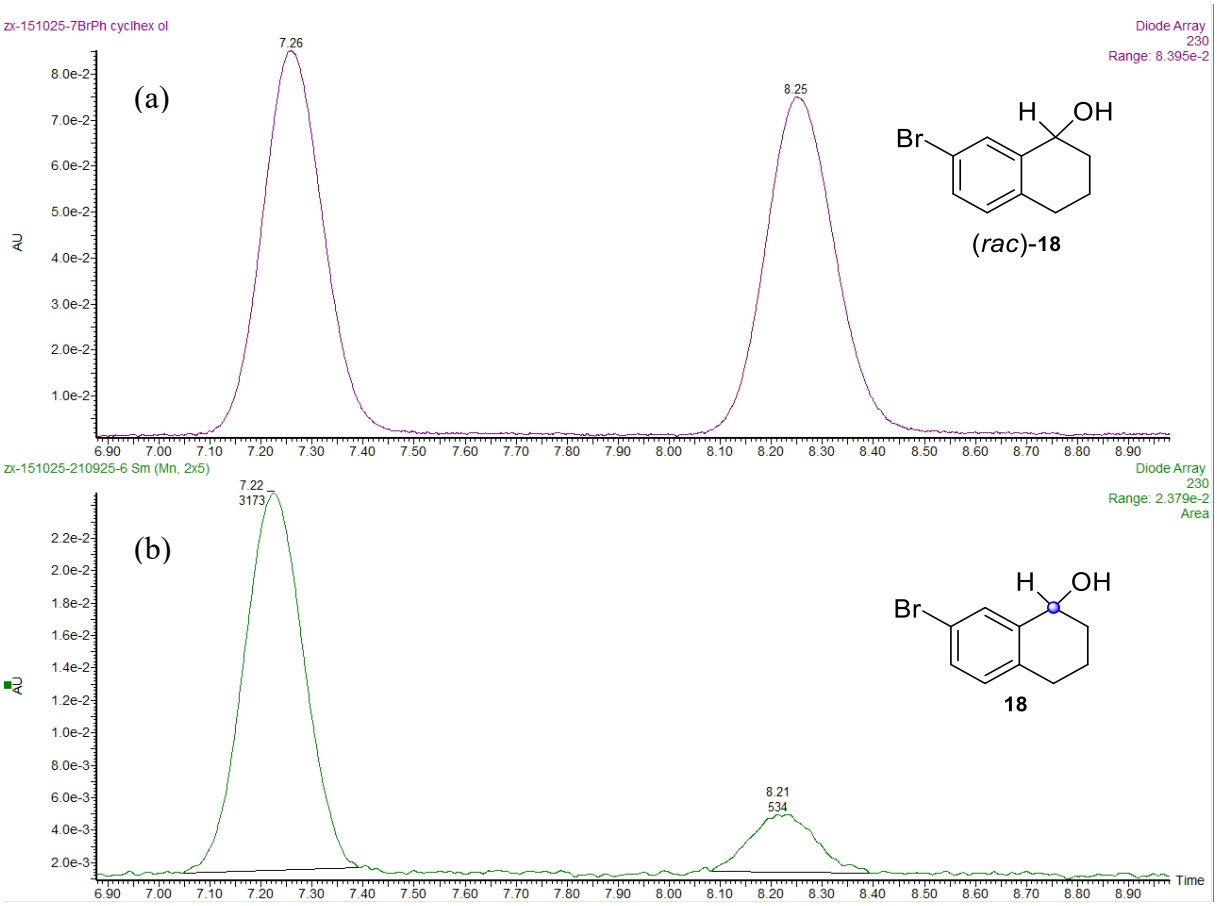
Supplementary Fig. 62. SFC traces of the radical hydration product pyrrolidinol 15. (a) Racemic pyrrolidinol **15**. (b) Biocatalytic radical hydration of alkene **S16** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



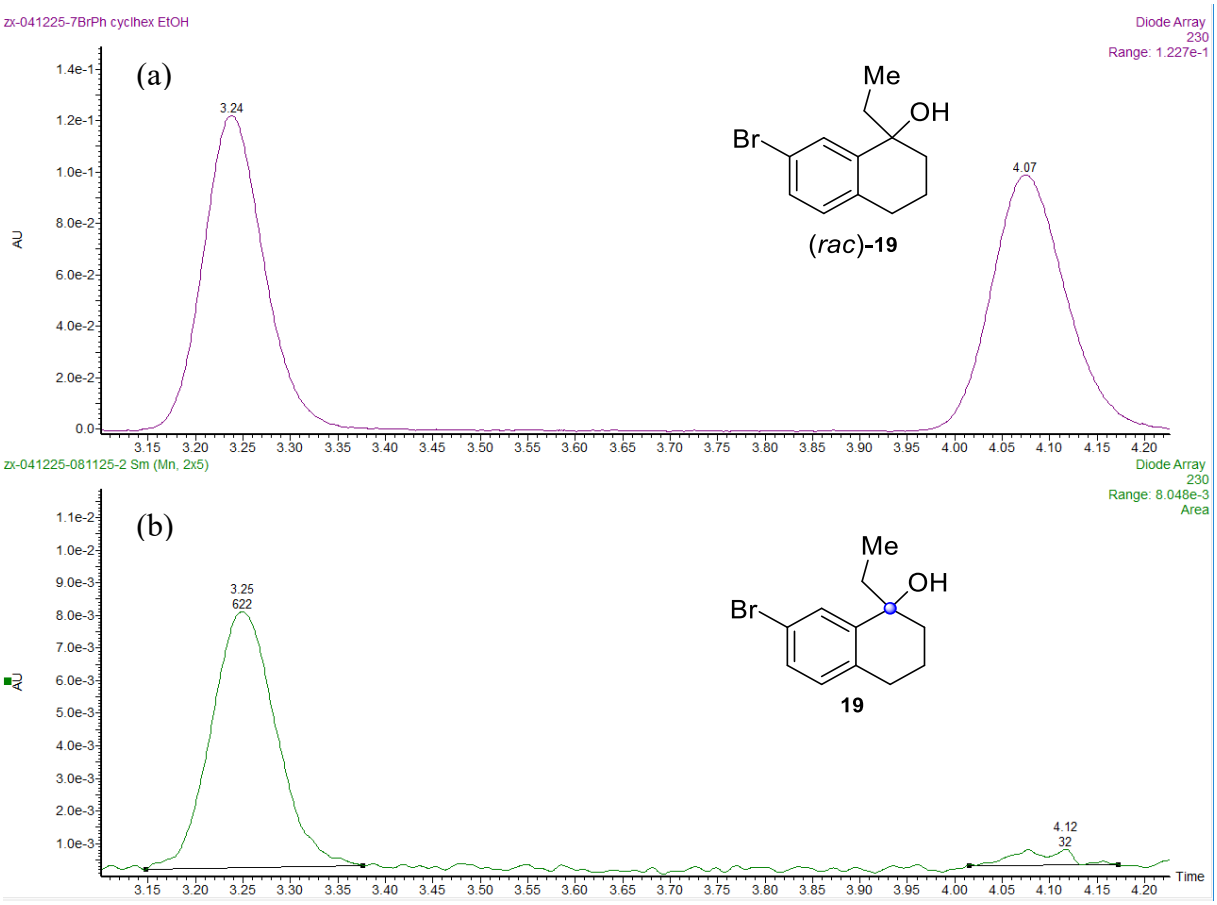
Supplementary Fig. 63. SFC traces of the radical hydration product aliphatic alcohol 16. (a) Racemic aliphatic alcohol **16**. (b) Biocatalytic radical hydration of alkene **S17** with $P450_{BM3}$_F87L-S72F and $PhSiH_3$.



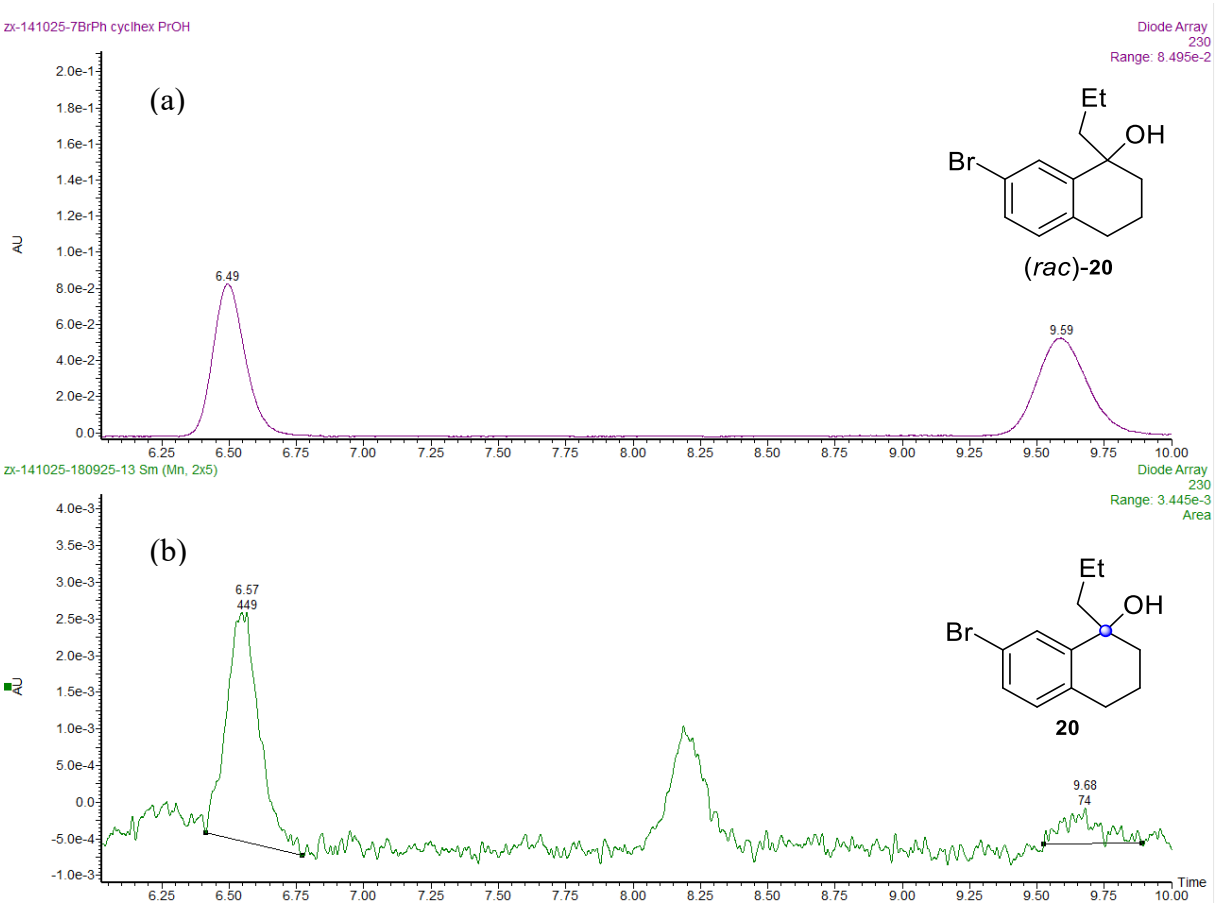
Supplementary Fig. 64. SFC traces of the radical hydration product aliphatic alcohol 17. (a) Racemic aliphatic alcohol **17**. (b) Biocatalytic radical hydration of alkene **S18** with $P450_{BM3}$_F87N and $PhSiH_3$.



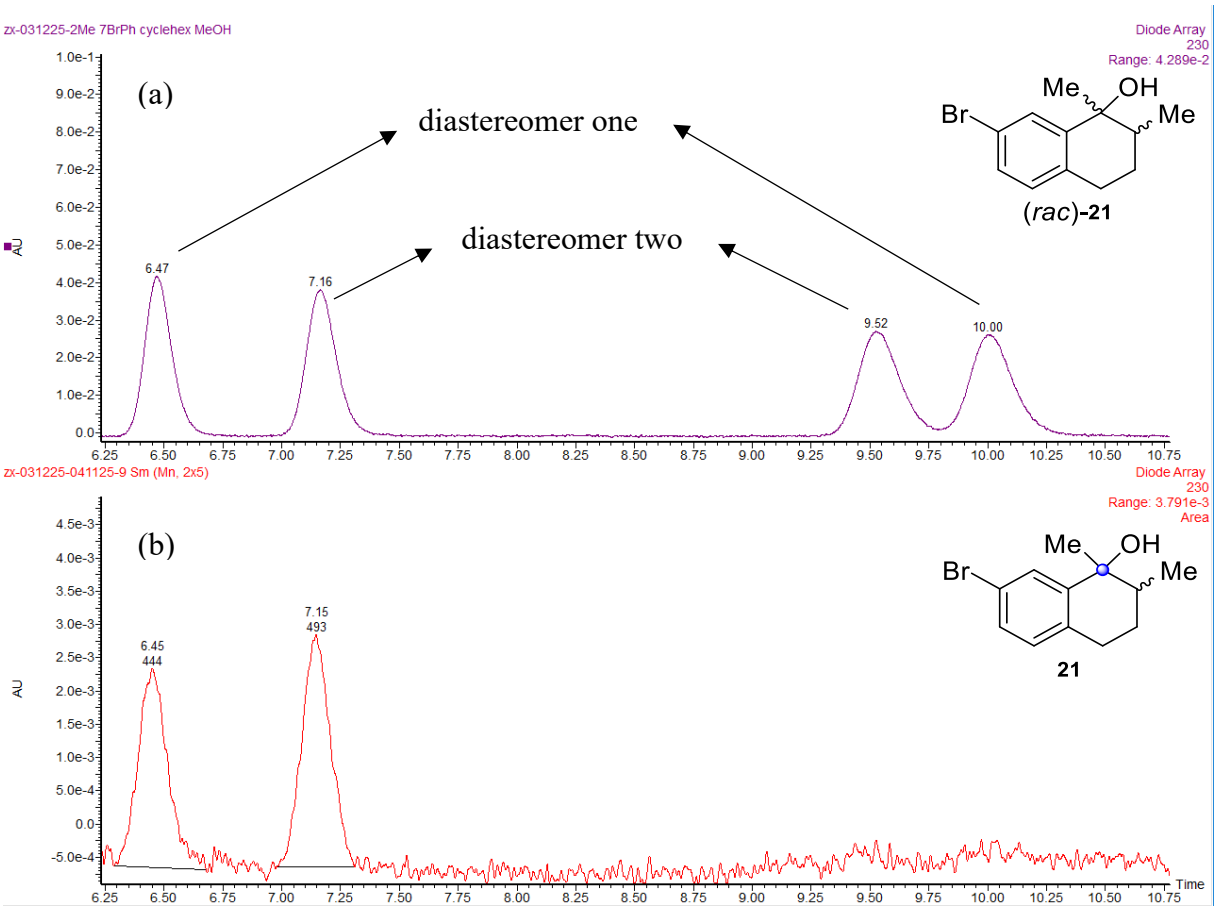
Supplementary Fig. 65. SFC traces of the radical hydration product tetralol 18. (a) Racemic tetralol **18**. (b) Biocatalytic radical hydration of alkene **S19** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



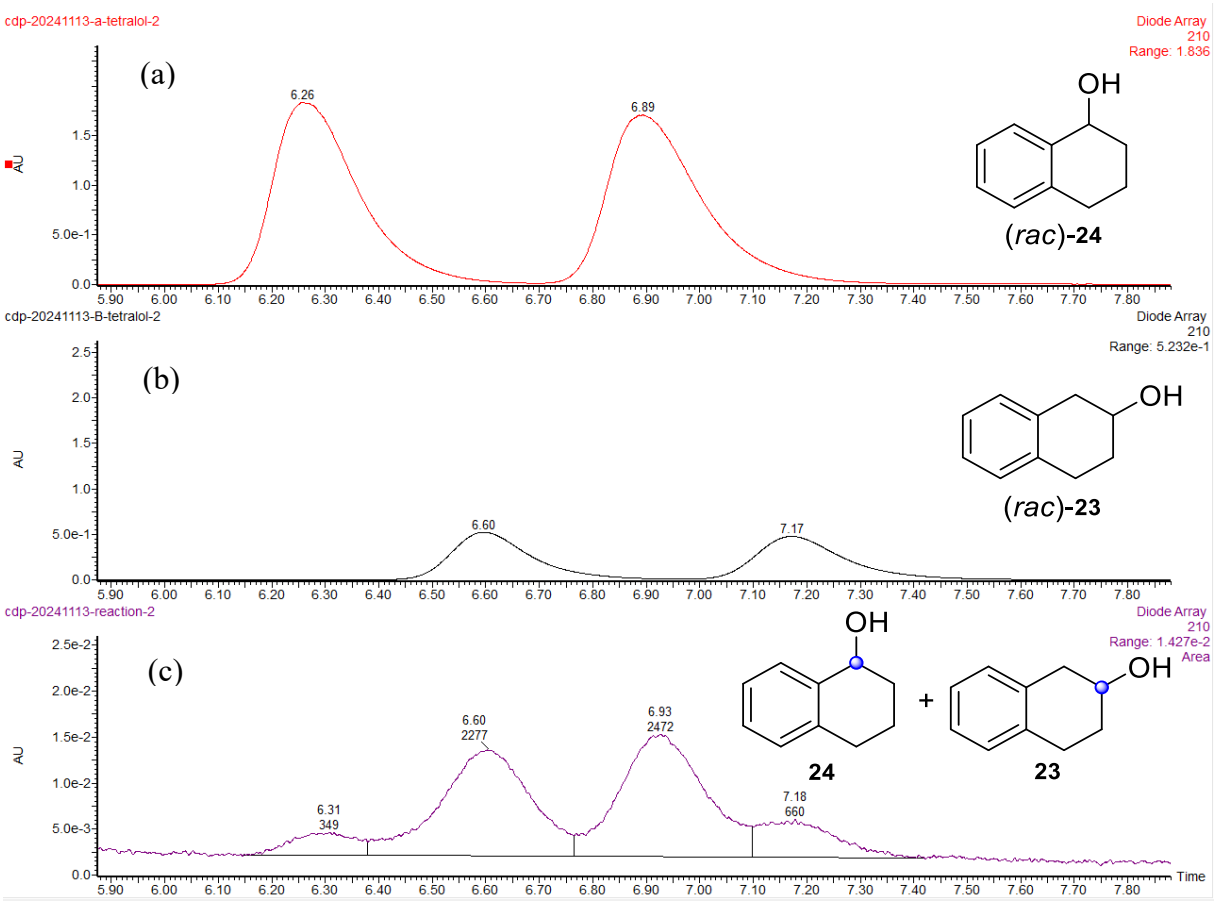
Supplementary Fig. 66. SFC traces of the radical hydration product tetralol 19. (a) Racemic tetralol **19**. (b) Biocatalytic radical hydration of alkene **S26** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



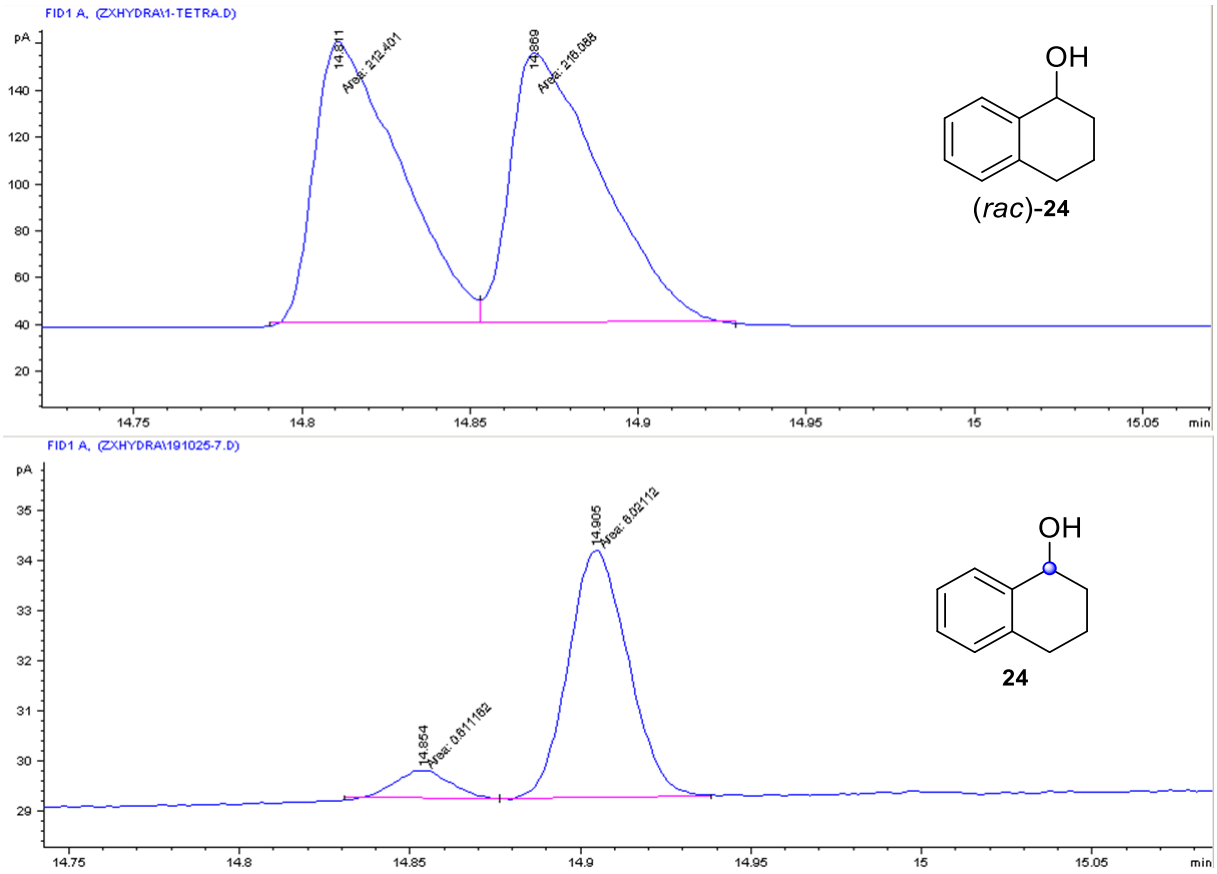
Supplementary Fig. 67. SFC traces of the radical hydration product tetralol 20. (a) Synthesized racemic tetralol **20**. (b) Biocatalytic radical hydration of alkene **S27** with $P450_{BM3}$_QTG and $PhSiMeH_2$.



Supplementary Fig. 68. SFC traces of the radical hydration product tetralol 21. (a) Racemic tetralol **21**. (b) Biocatalytic radical hydration of alkene **S28** with P450$_{BM3}$_QTG and $PhSiMeH_2$.

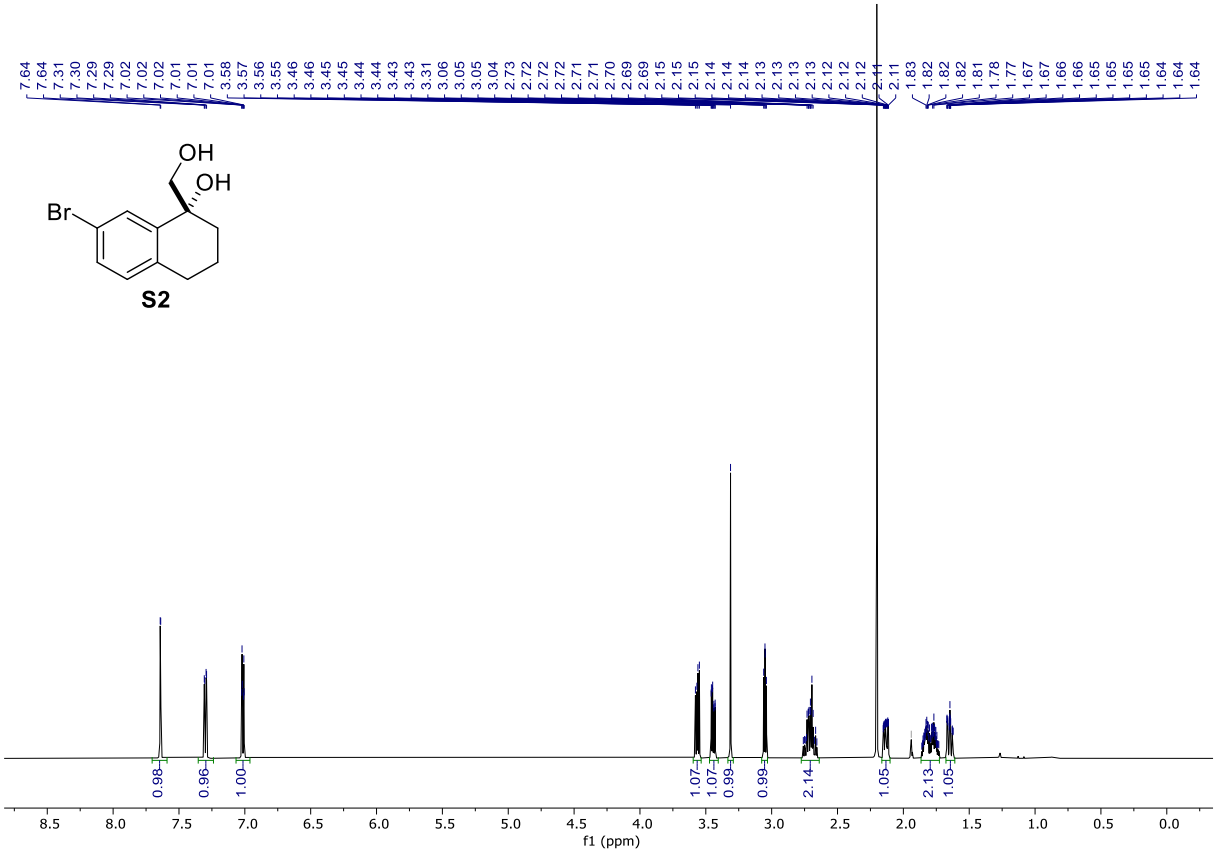


Supplementary Fig. 69. SFC traces of the radical hydration product tetralols 23 and 24. (a) Racemic tetralol **24**. (b) Racemic tetralol **23**. (c) Biocatalytic reaction of alkene **22** with P450$_{BM3}$_QTG and $PhSiMeH_2$, highlighting the formation of a mixture of regioisomers **24** and **23** (**24**:**23** = 2.3:1), which result from a radical migration following radical addition of dioxygen.

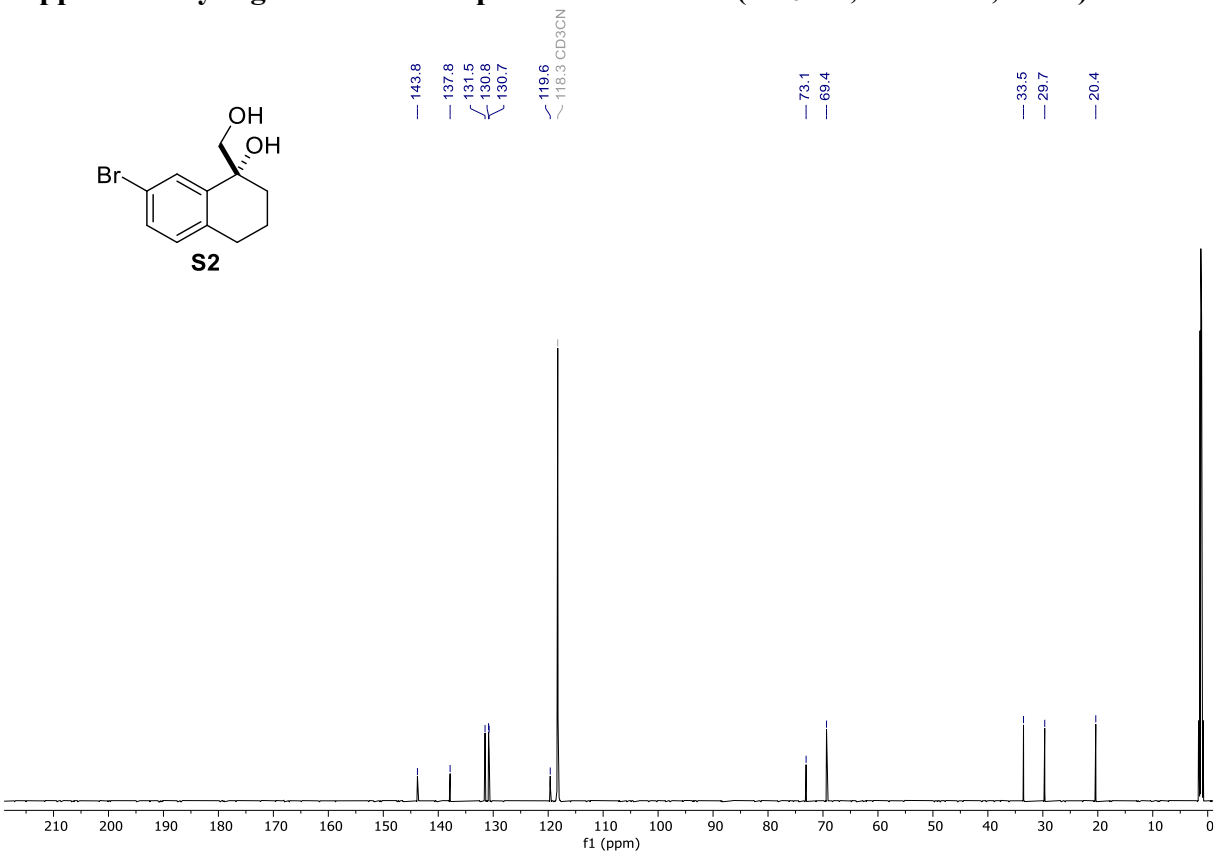


Supplementary Fig. 70. GC traces of the radical hydration product tetralol 24. (a) Racemic tetralol **24**. (b) Biocatalytic radical hydration of alkene **22** with P450$_{BM3}$_QTG and $PhSiMeH_2$.

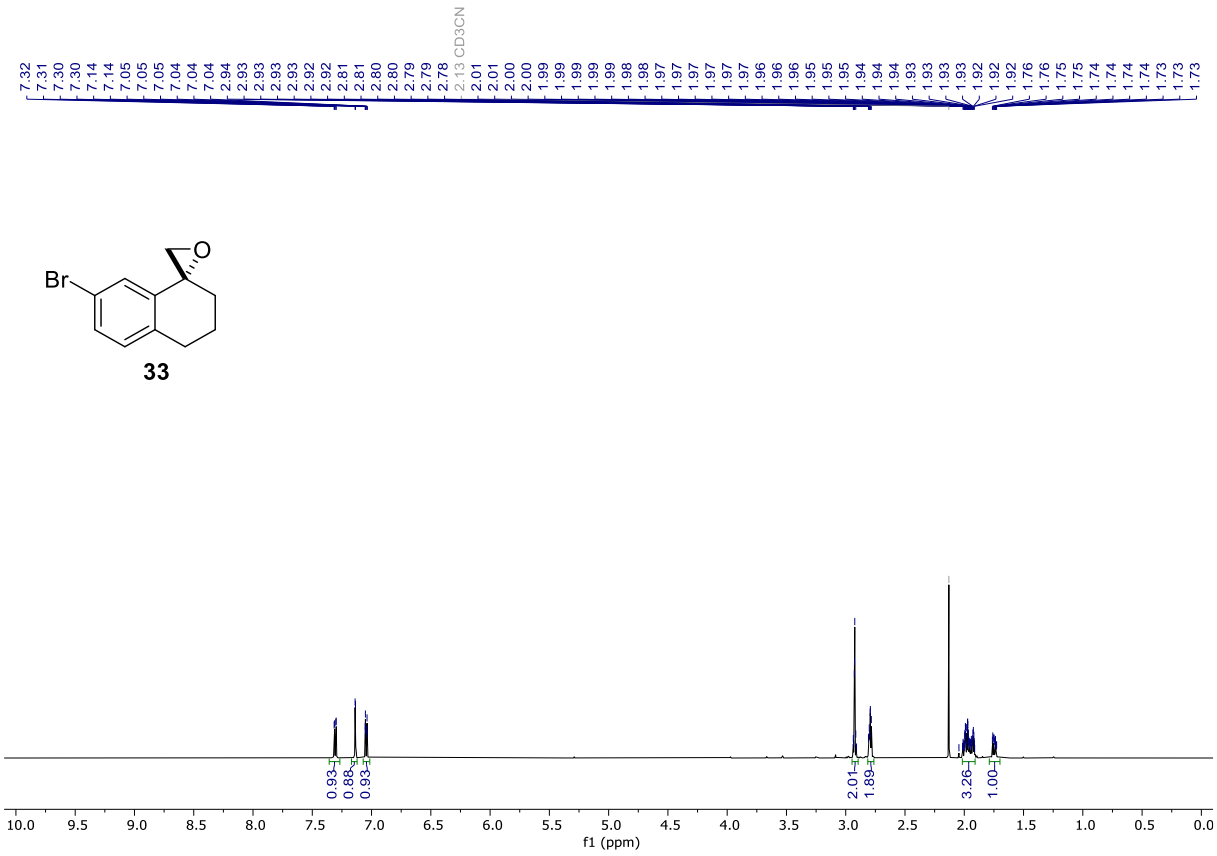
8. NMR spectra



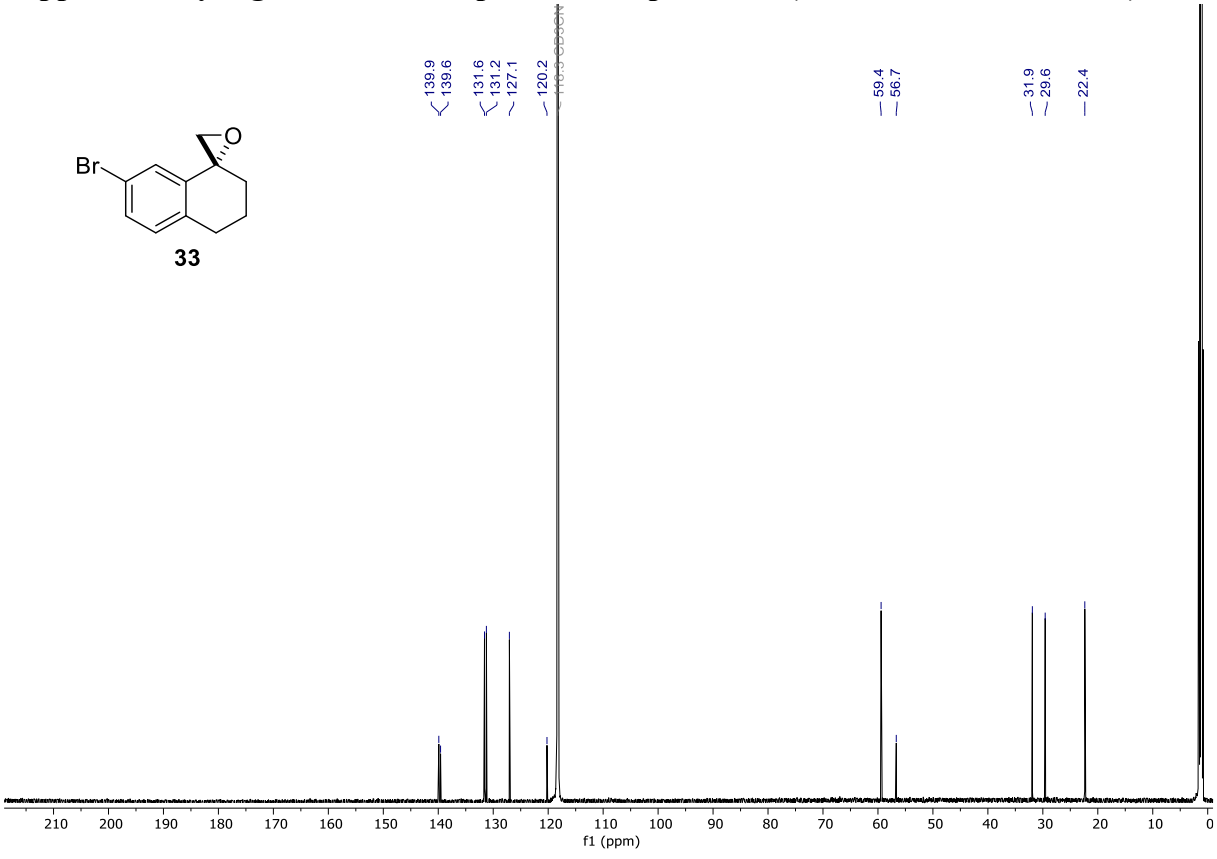
Supplementary Fig. 71. ^{1}H NMR Spectrum of diol S2 (CD_3CN, 600 MHz, 20 °C)



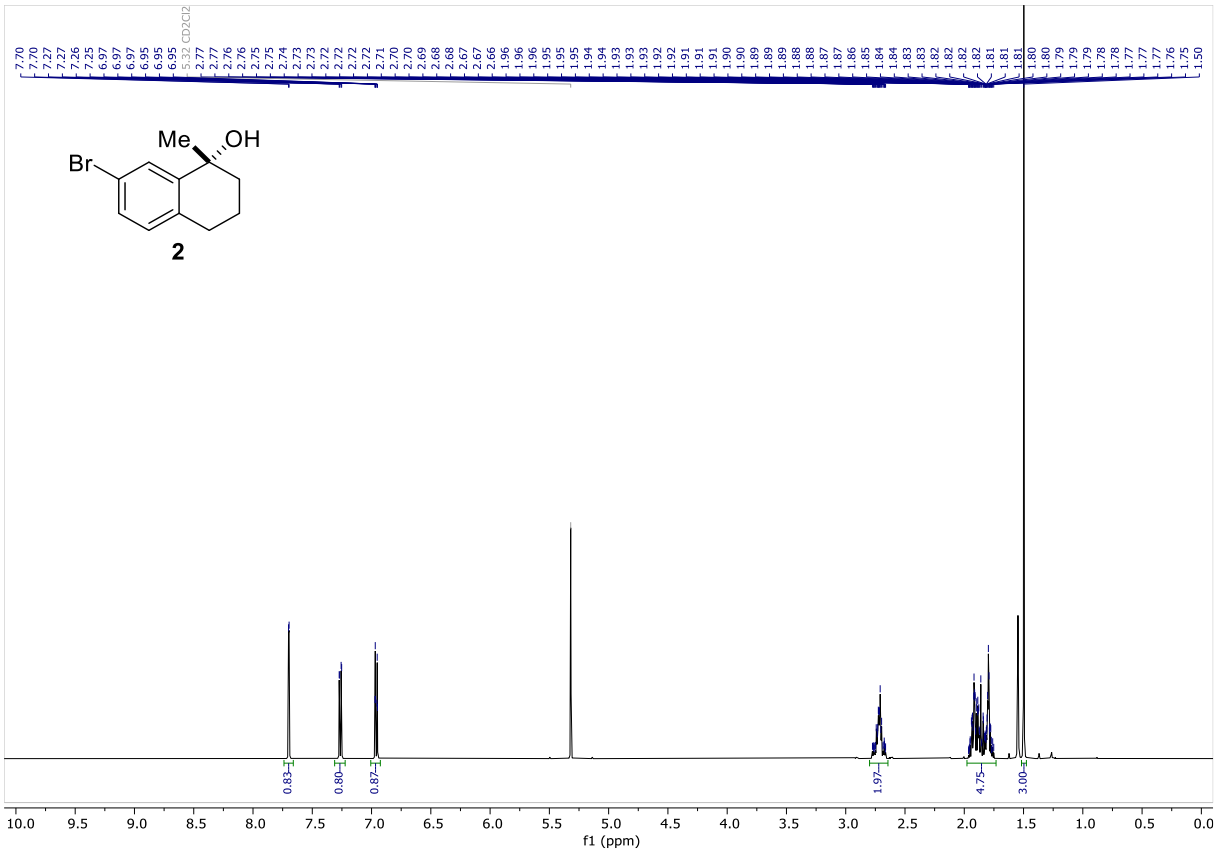
Supplementary Fig. 72. ^{13}C NMR Spectrum of diol S2 (CD_3CN, 151 MHz, 20 °C)



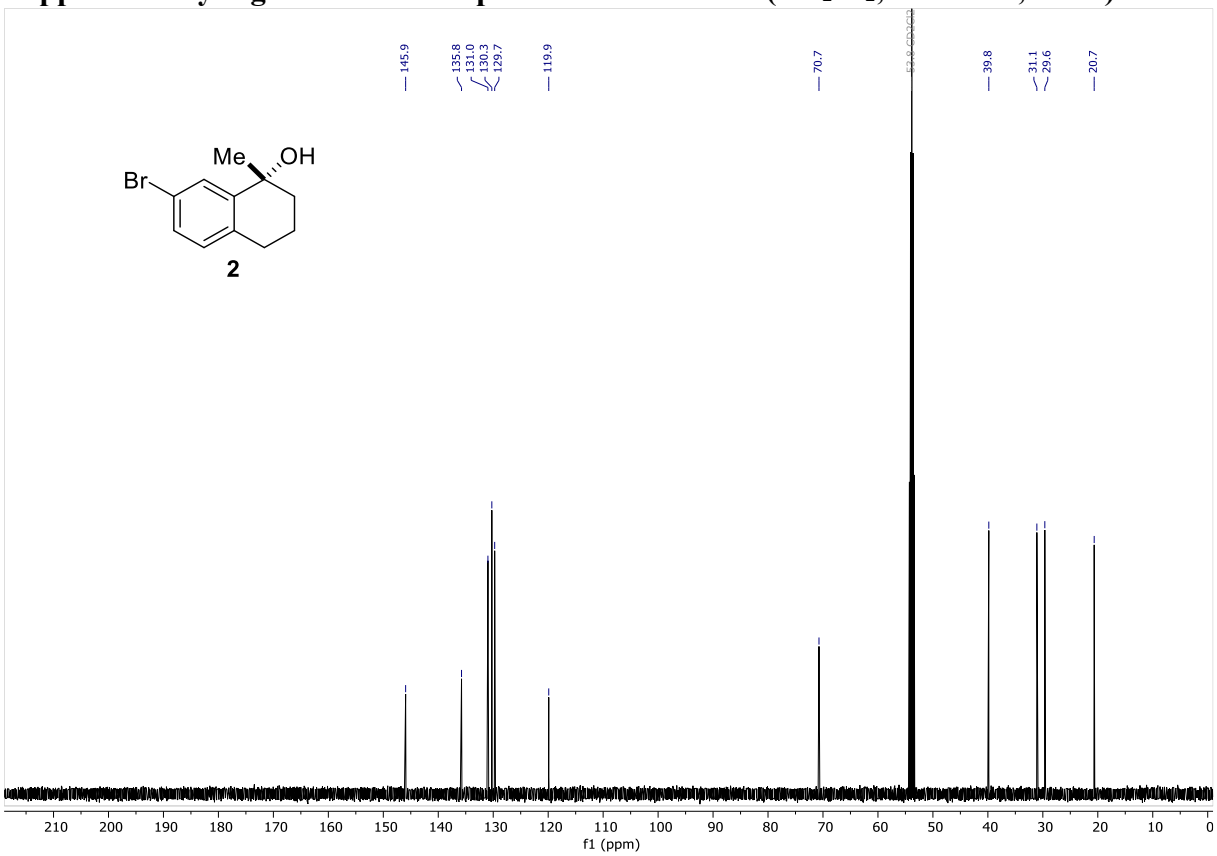
Supplementary Fig. 73. ^{1}H NMR Spectrum of epoxide 33 (CD_3CN, 600 MHz, 20 °C)



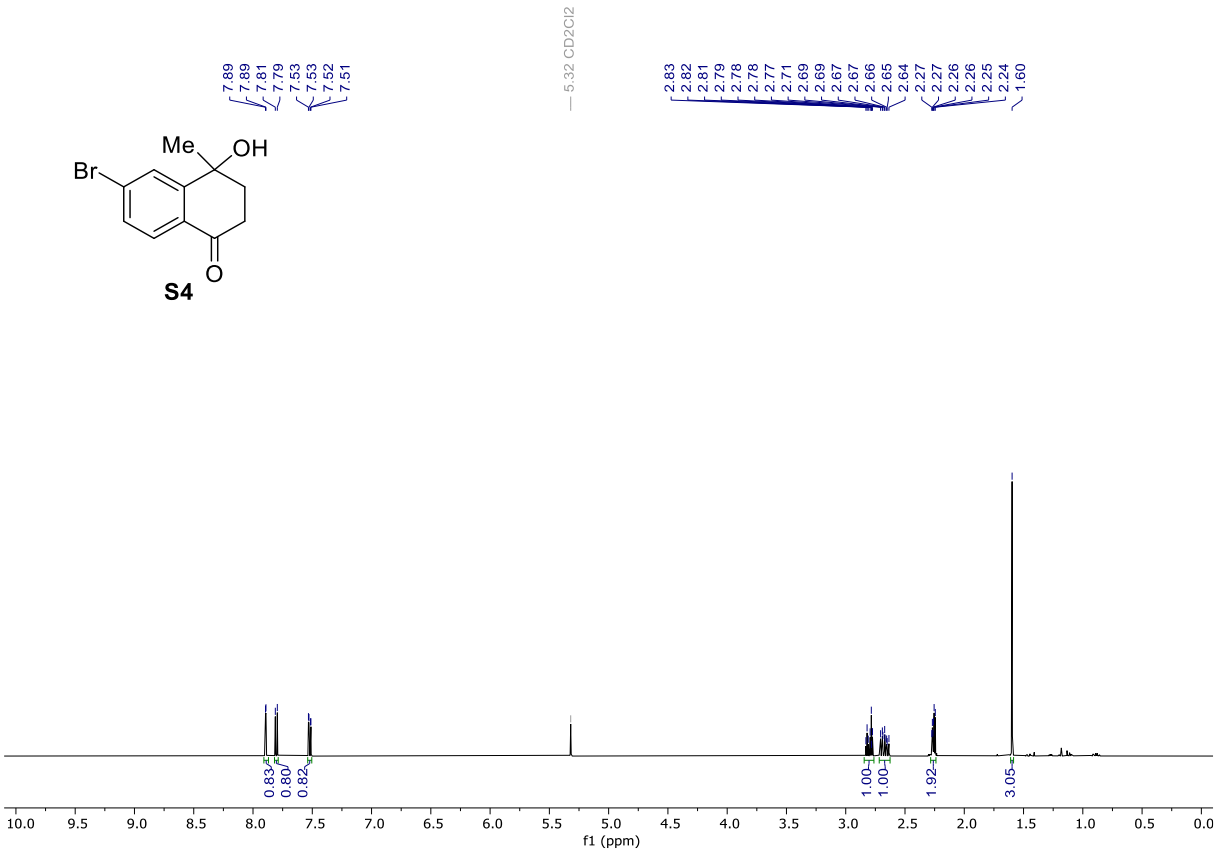
Supplementary Fig. 74. ^{13}C NMR Spectrum of epoxide 33 (CD_3CN, 151 MHz, 20 °C)



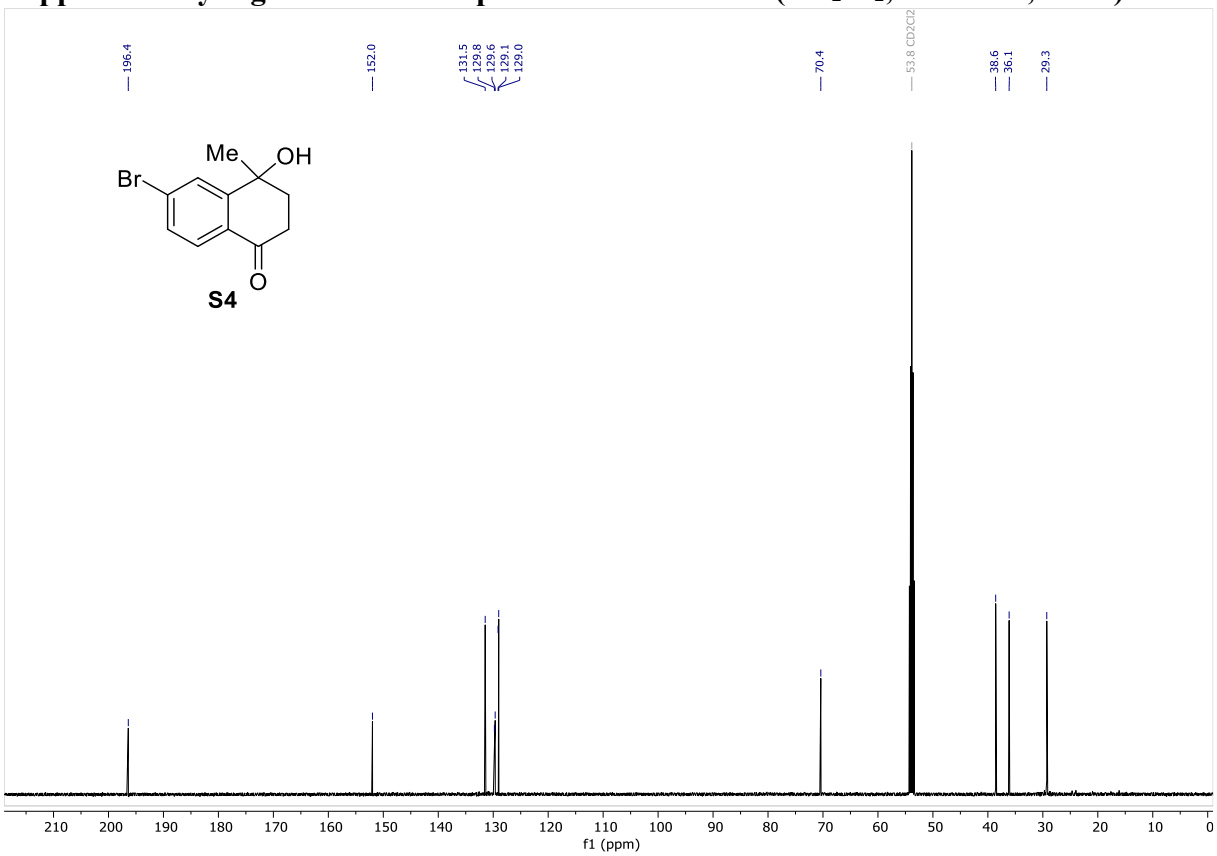
Supplementary Fig. 75. ^{1}H NMR Spectrum of tetralol 2 (CD_2Cl_2, 500 MHz, 20 °C)



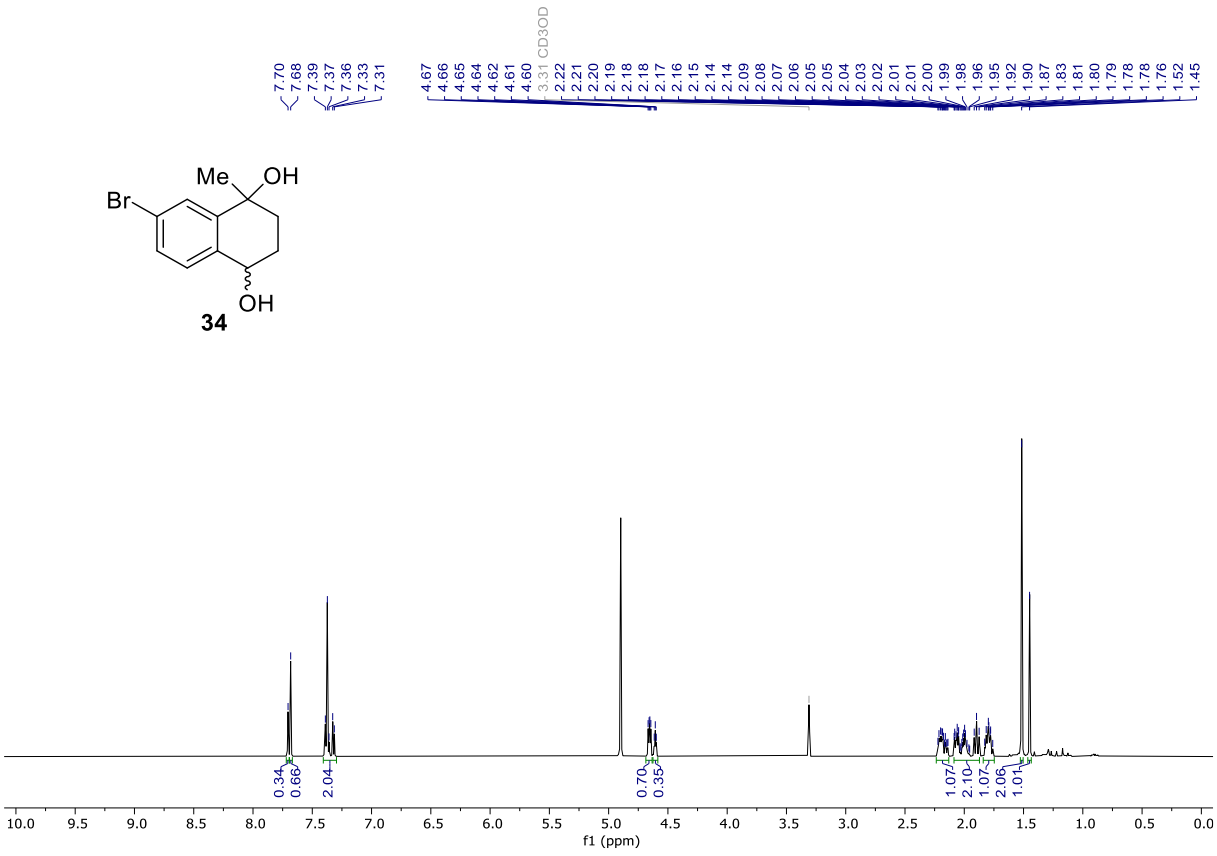
Supplementary Fig. 76. ^{13}C NMR Spectrum of tetralol 2 (CD_2Cl_2, 126 MHz, 20 °C)



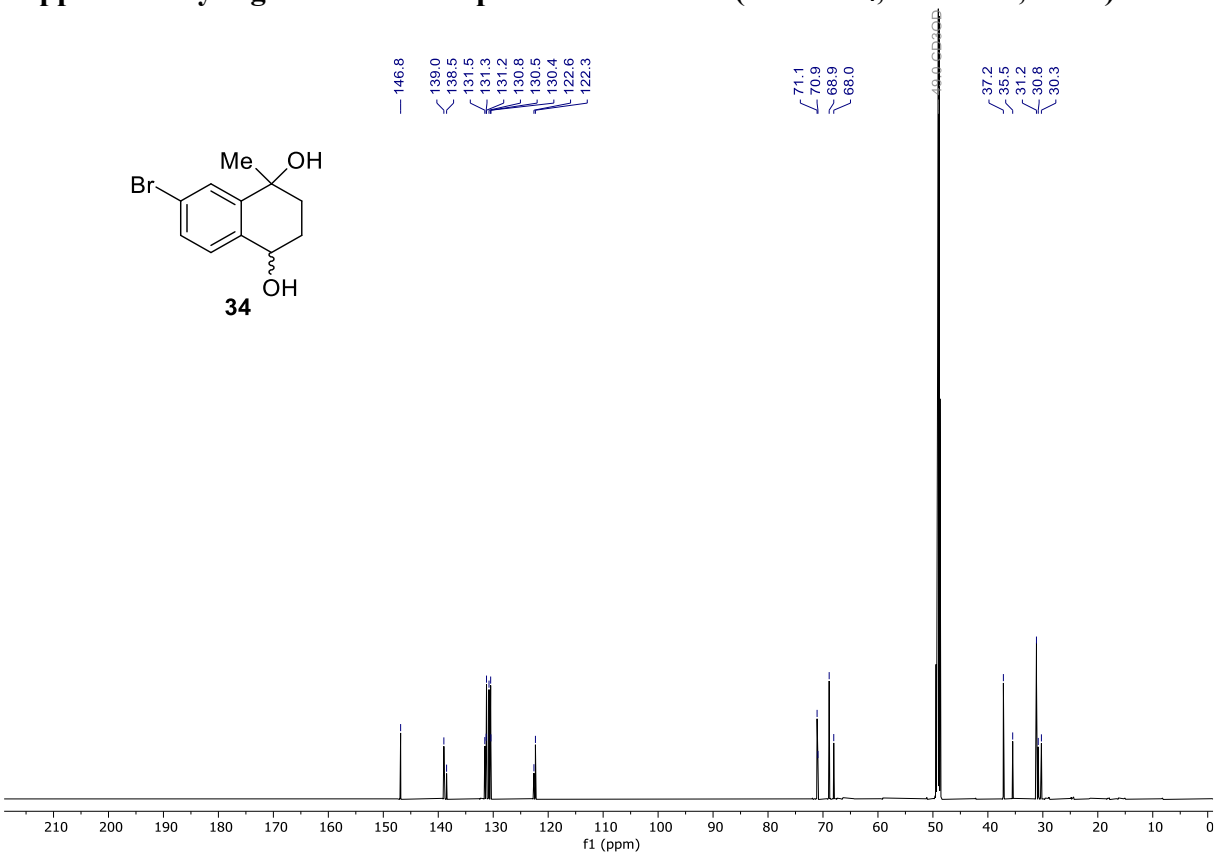
Supplementary Fig. 77. ^{1}H NMR Spectrum of ketone S4 (CD_2Cl_2, 500 MHz, 20 °C)



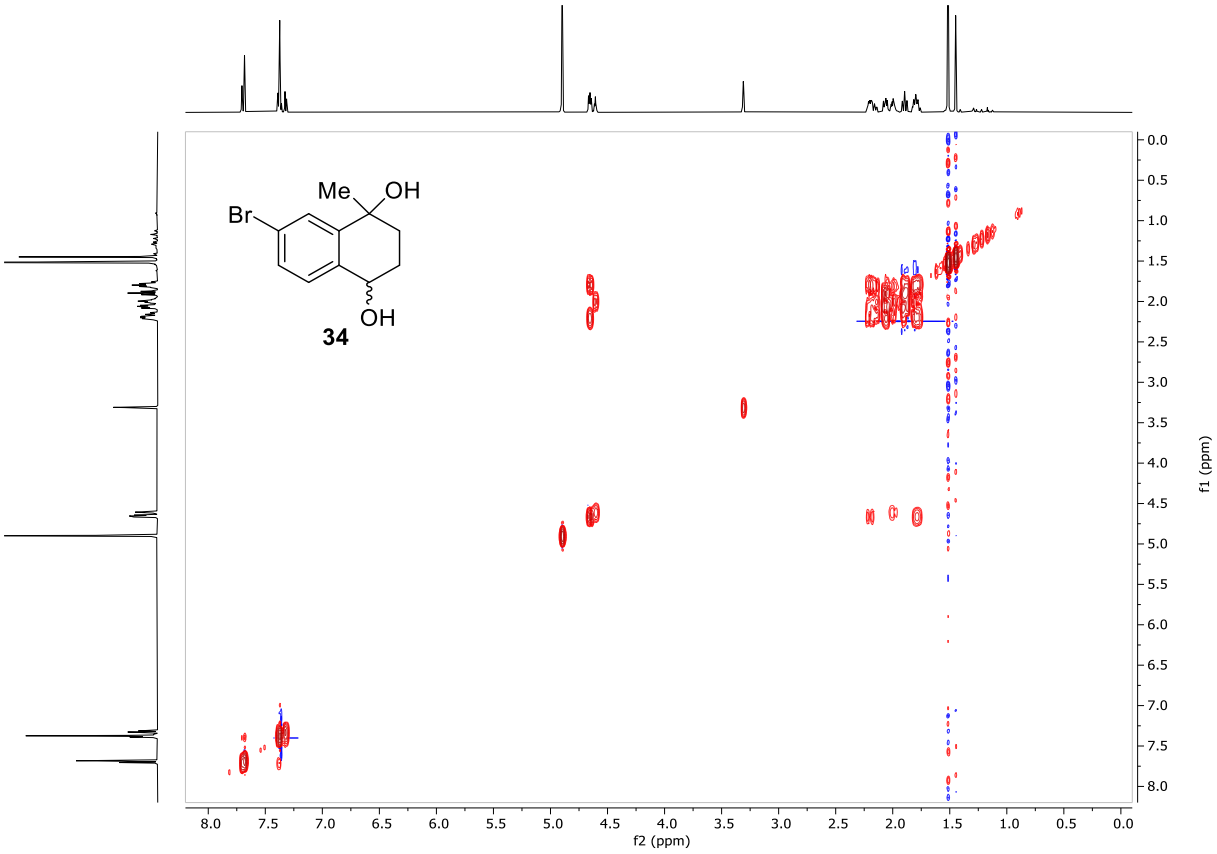
Supplementary Fig. 78. ^{13}C NMR Spectrum of ketone S4 (CD_2Cl_2, 126 MHz, 20 °C)



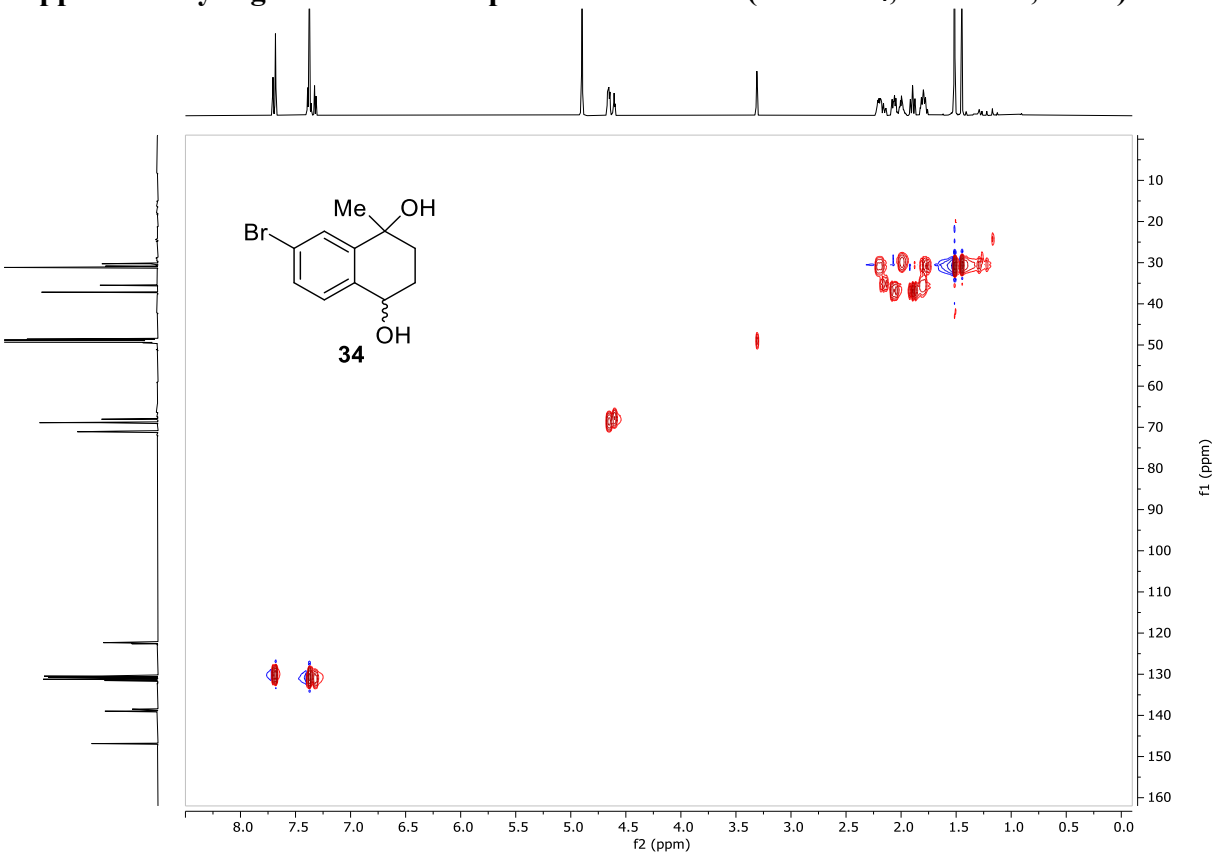
Supplementary Fig. 79. ^{1}H NMR Spectrum of diol 34 (MeOD-d$_4$, 600 MHz, 20 °C)



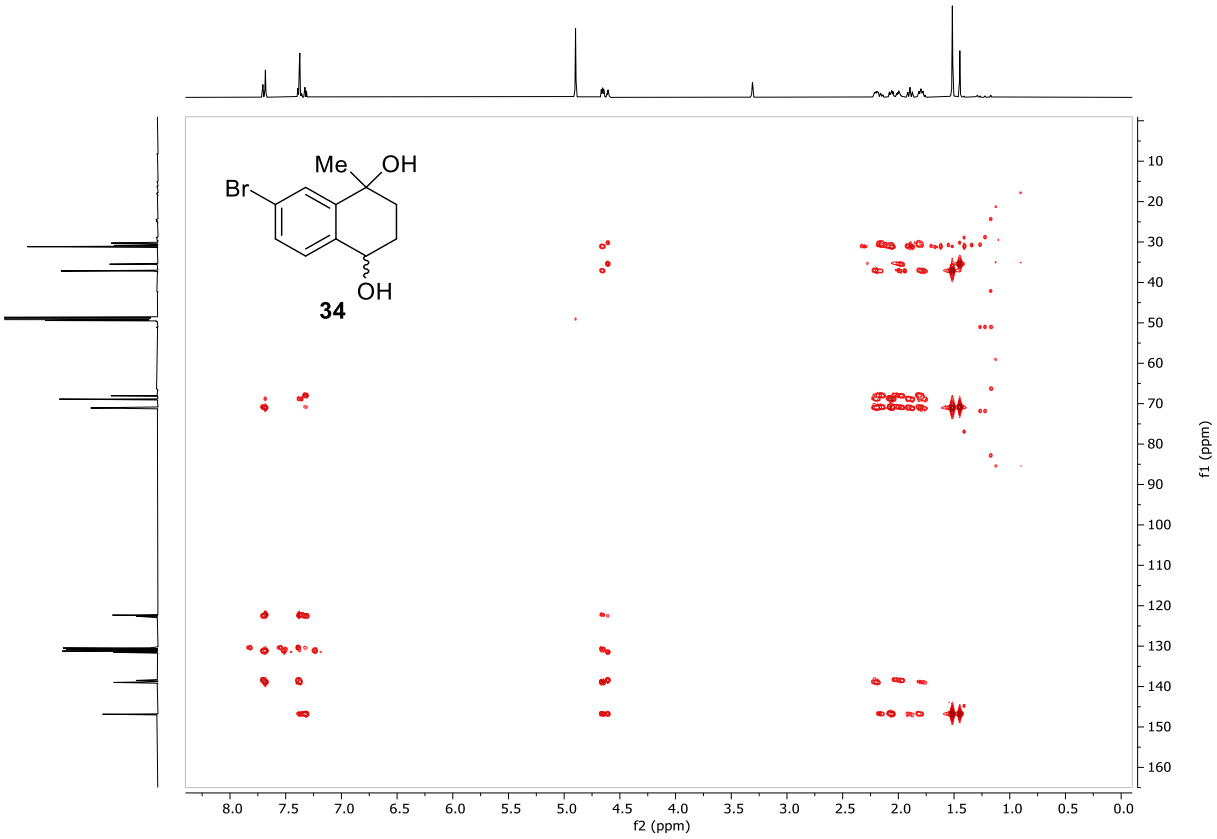
Supplementary Fig. 80. ^{13}C NMR Spectrum of diol 34 (MeOD-d$_4$, 151 MHz, 20 °C)



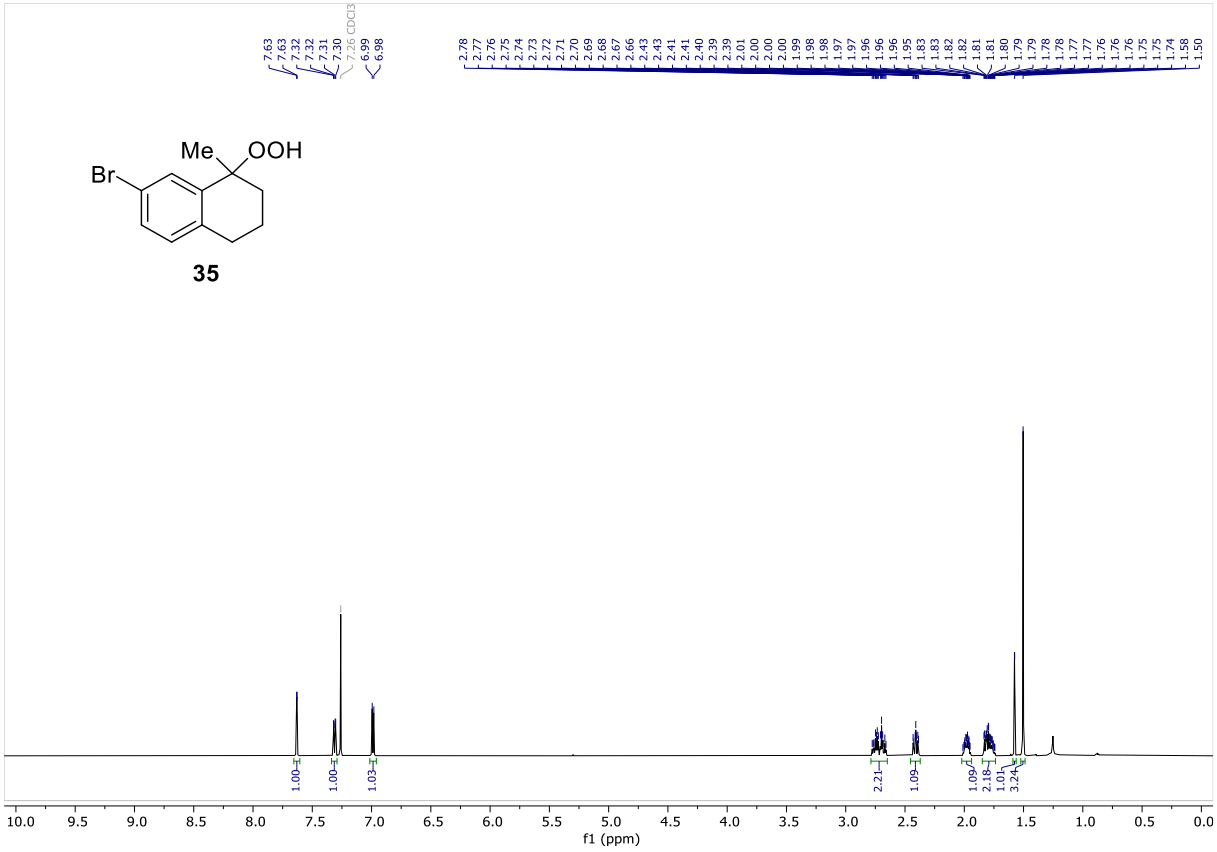
Supplementary Fig. 81. ^{1}H COSY Spectrum of diol 34 (MeOD-d$_4$, 600 MHz, 20 °C)



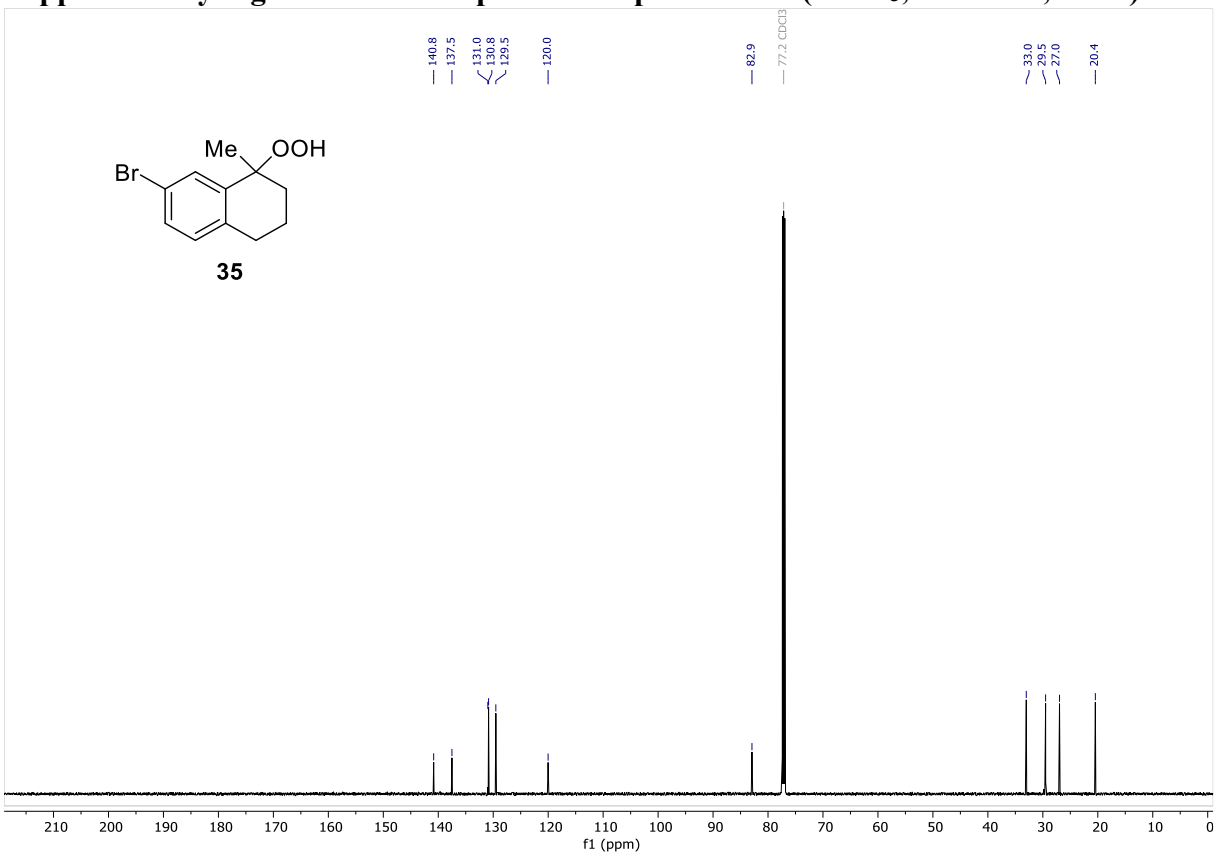
Supplementary Fig. 82. HMQC Spectrum of diol 34 (MeOD-d$_4$, 600 MHz, 20 °C)



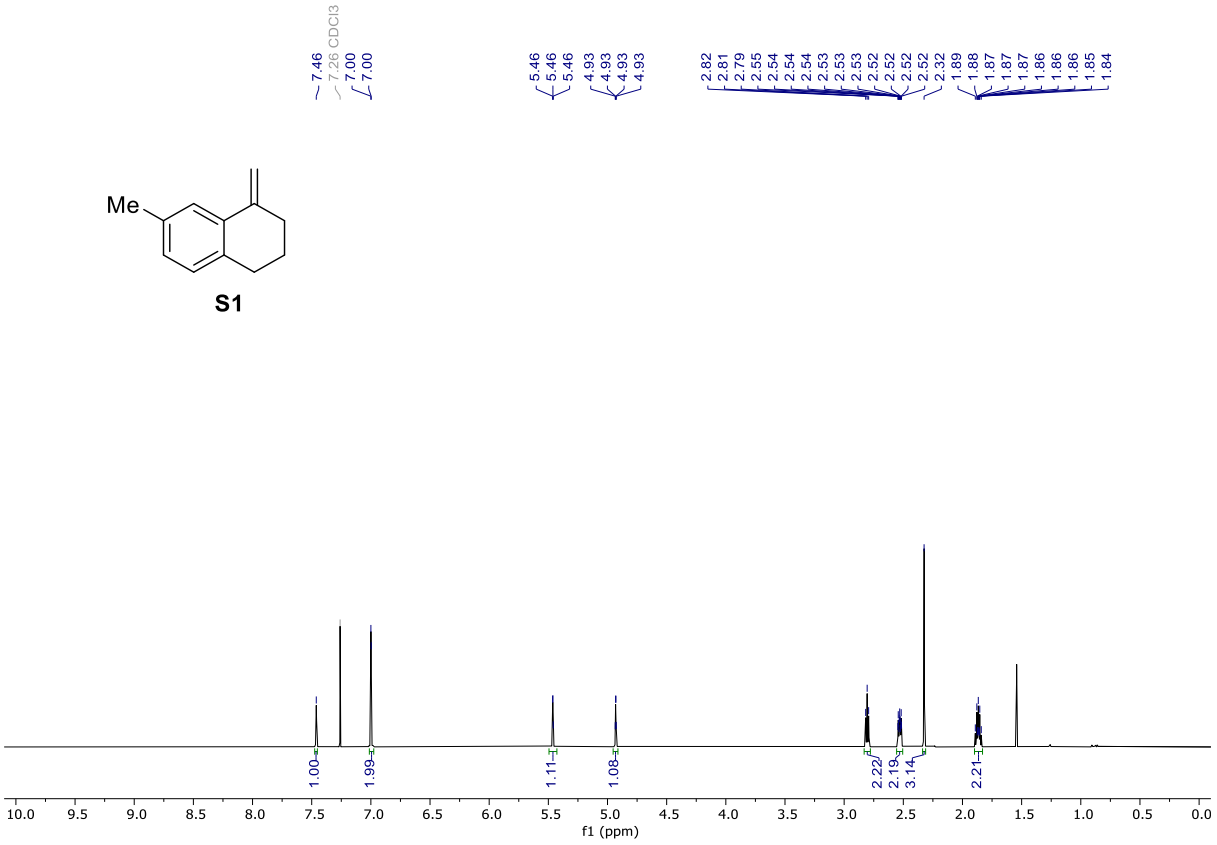
Supplementary Fig. 83. HMBC Spectrum of diol 34 (MeOD-d_4, 600 MHz, 20 °C)



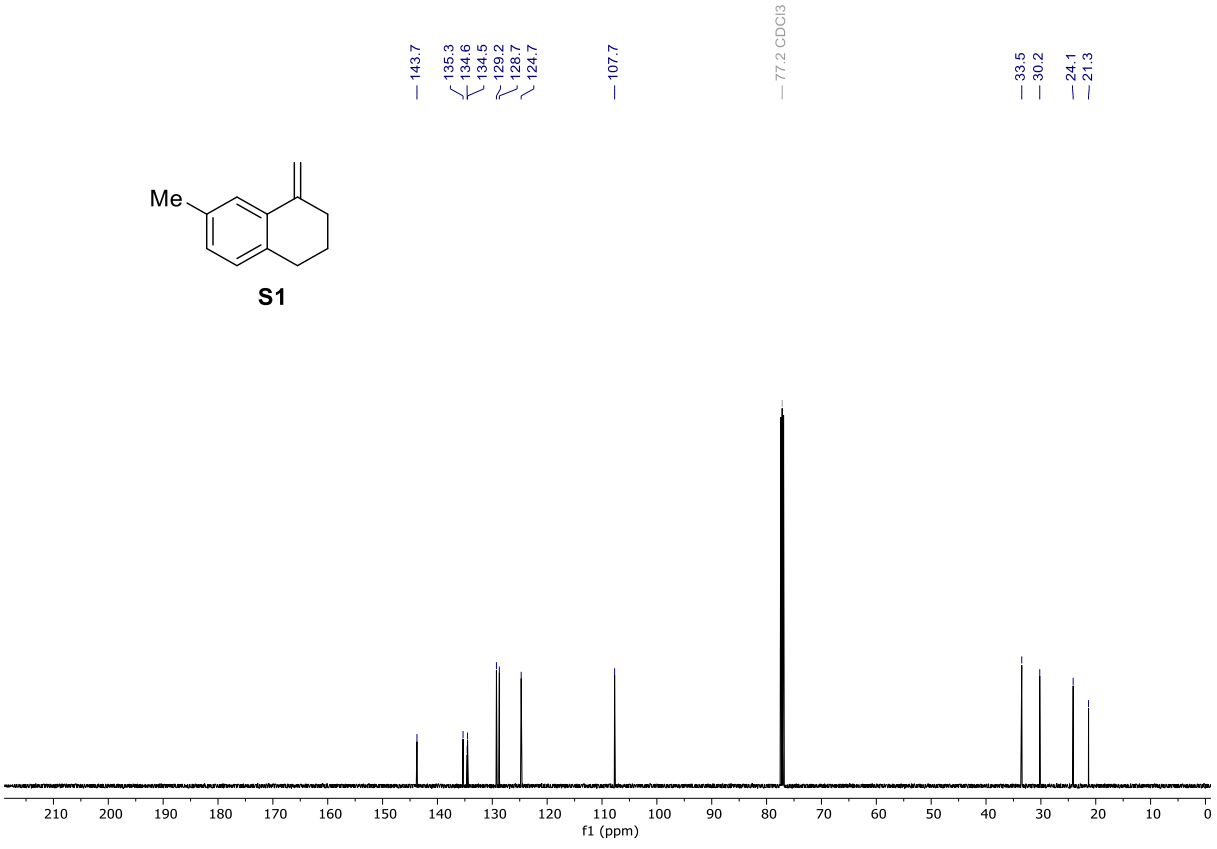
Supplementary Fig. 84. ^{1}H NMR Spectrum of peroxide 35 ($CDCl_3$, 600 MHz, 20 °C)



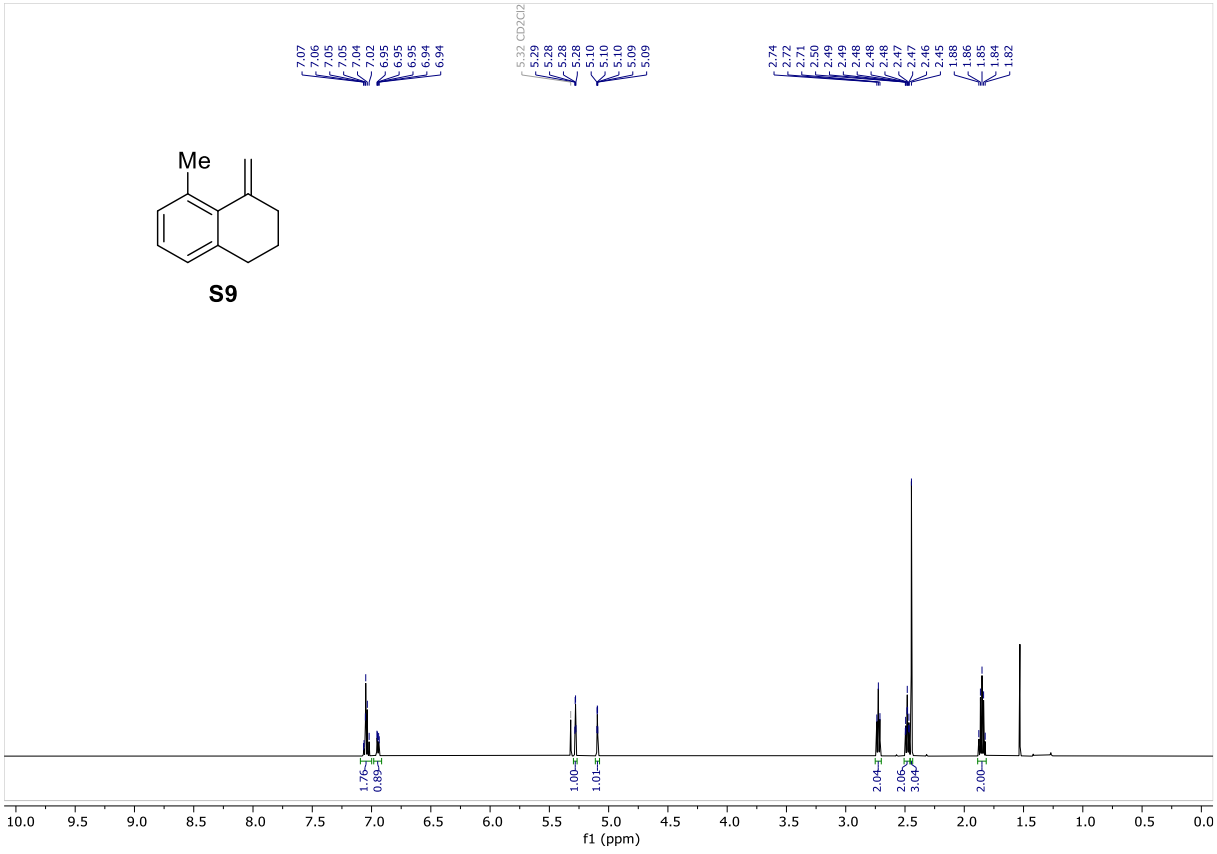
Supplementary Fig. 85. ^{13}C NMR Spectrum of peroxide 35 ($CDCl_3$, 151 MHz, 20 °C)



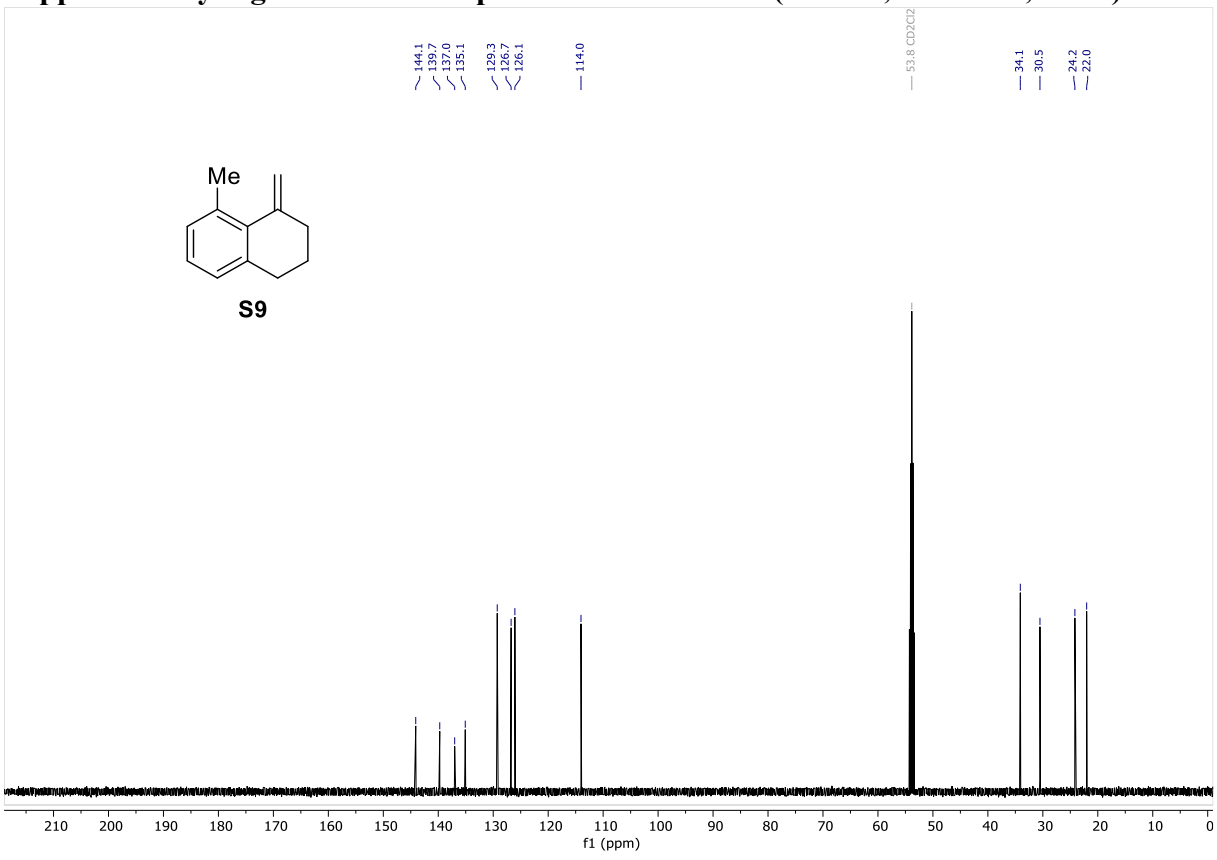
Supplementary Fig. 86. ^{1}H NMR Spectrum of alkene S1 ($CDCl_3$, 500 MHz, 20 °C)



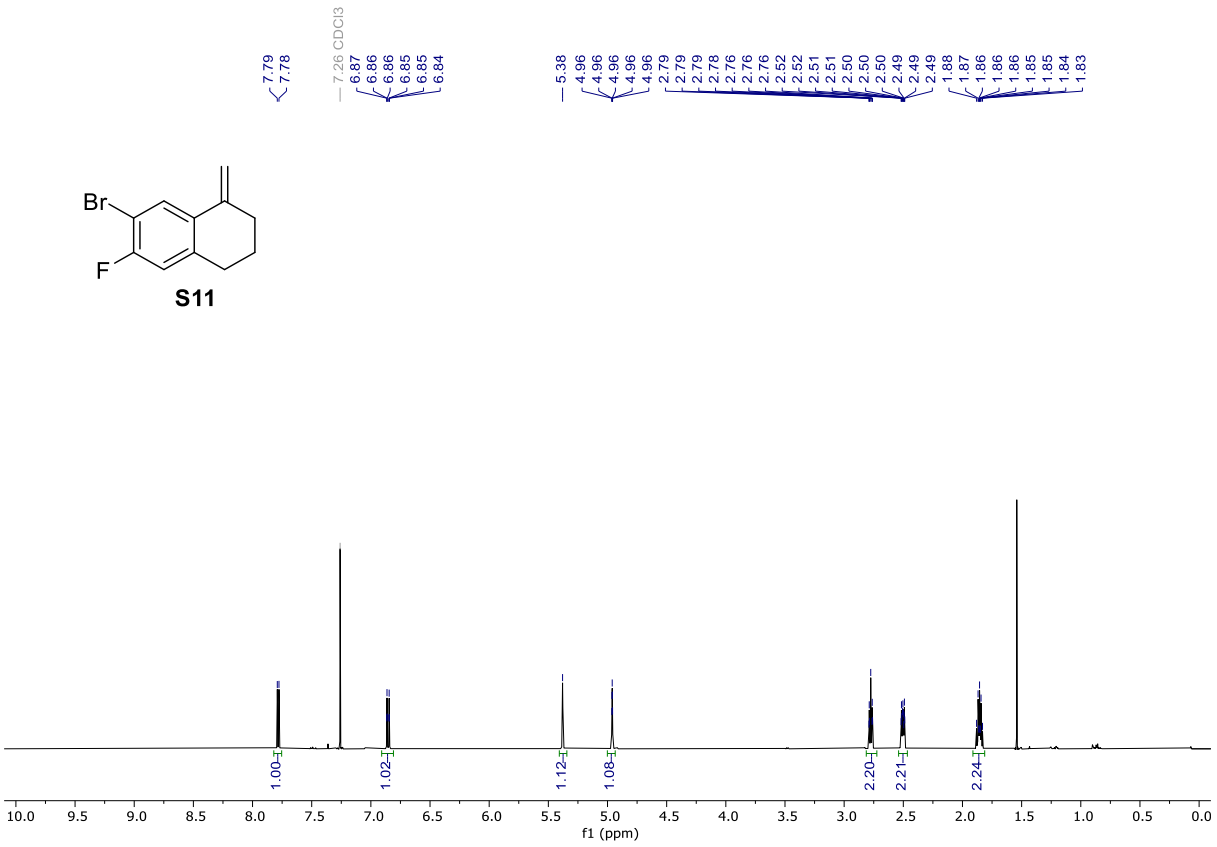
Supplementary Fig. 87. ^{13}C NMR Spectrum of alkene S1 ($CDCl_3$, 126 MHz, 20 °C)



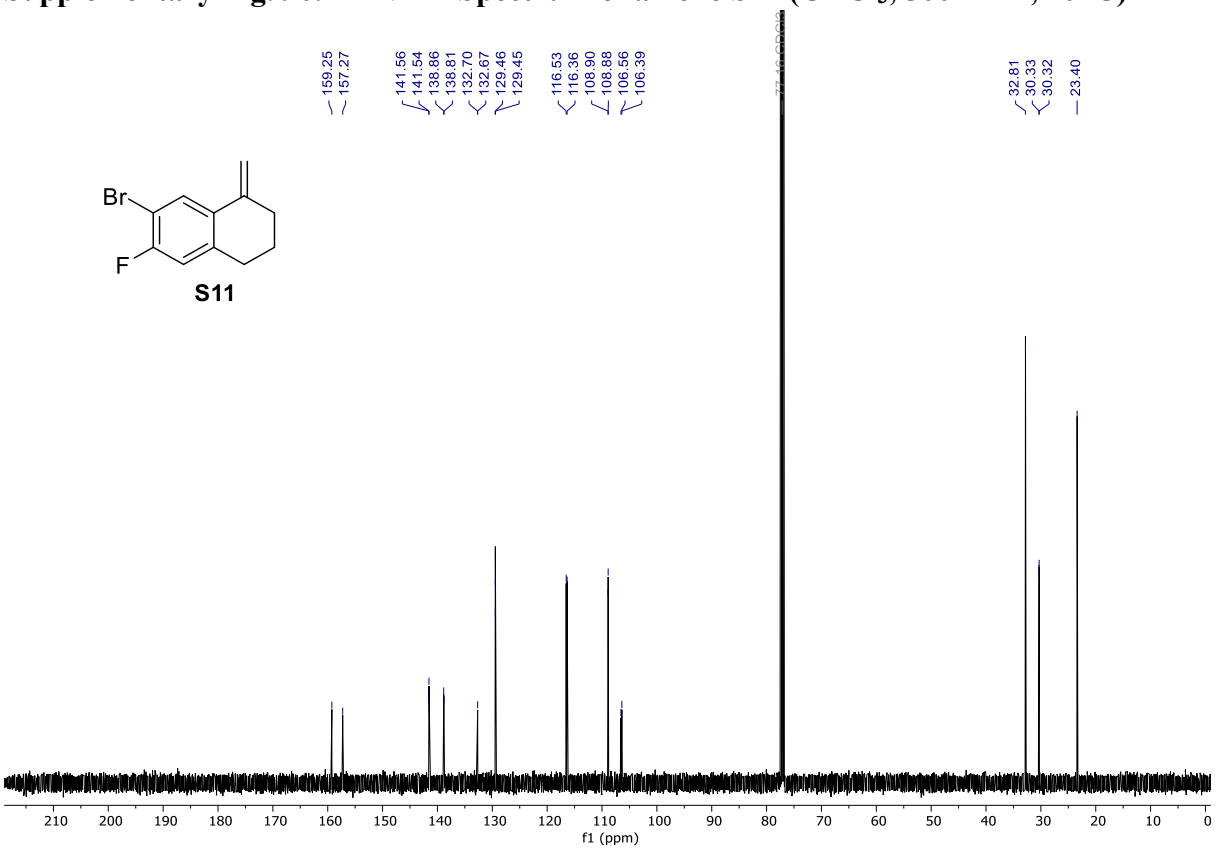
Supplementary Fig. 88. ^{1}H NMR Spectrum of alkene S9 (CD_2Cl_2, 500 MHz, 20 °C)



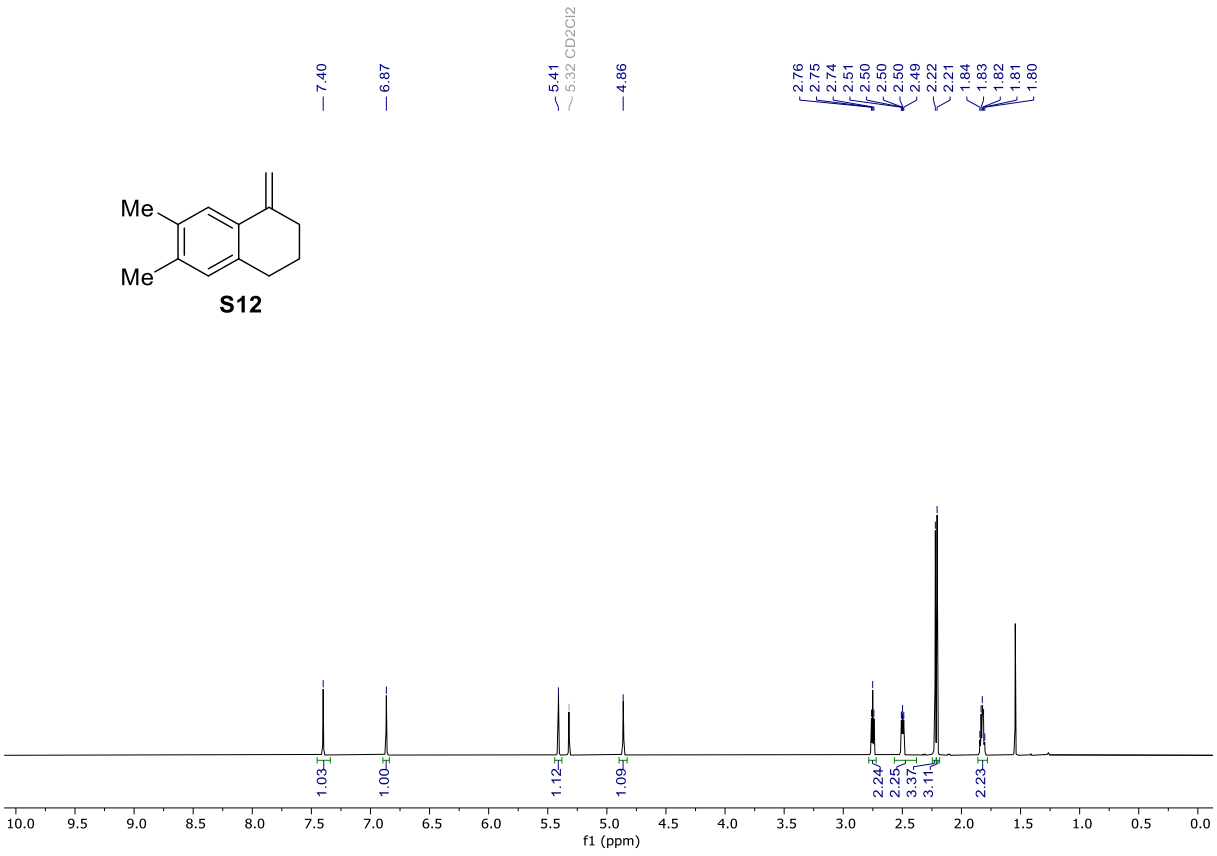
Supplementary Fig. 89. ^{13}C NMR Spectrum of alkene S9 (CD_2Cl_2, 126 MHz, 20 °C)



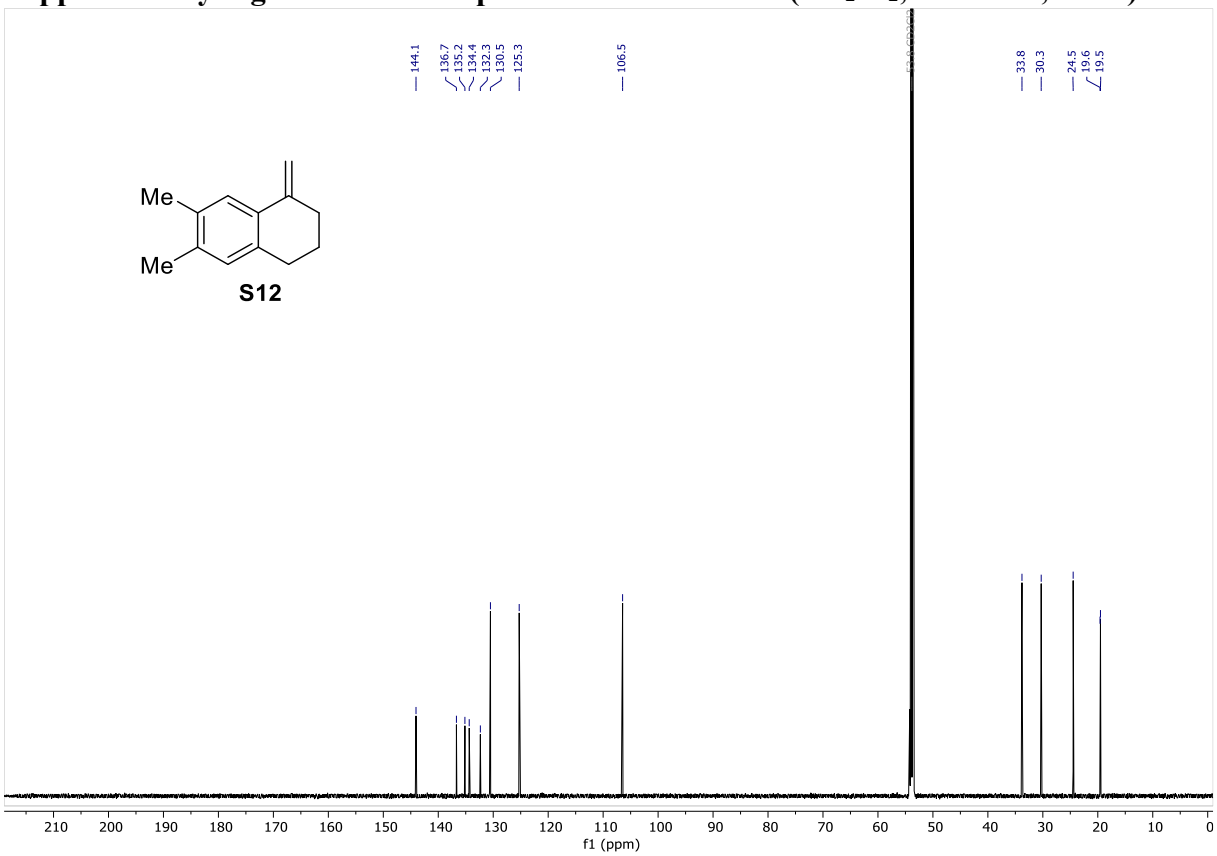
Supplementary Fig. 90. ^{1}H NMR Spectrum of alkene S11 ($CDCl_3$, 500 MHz, 20 °C)



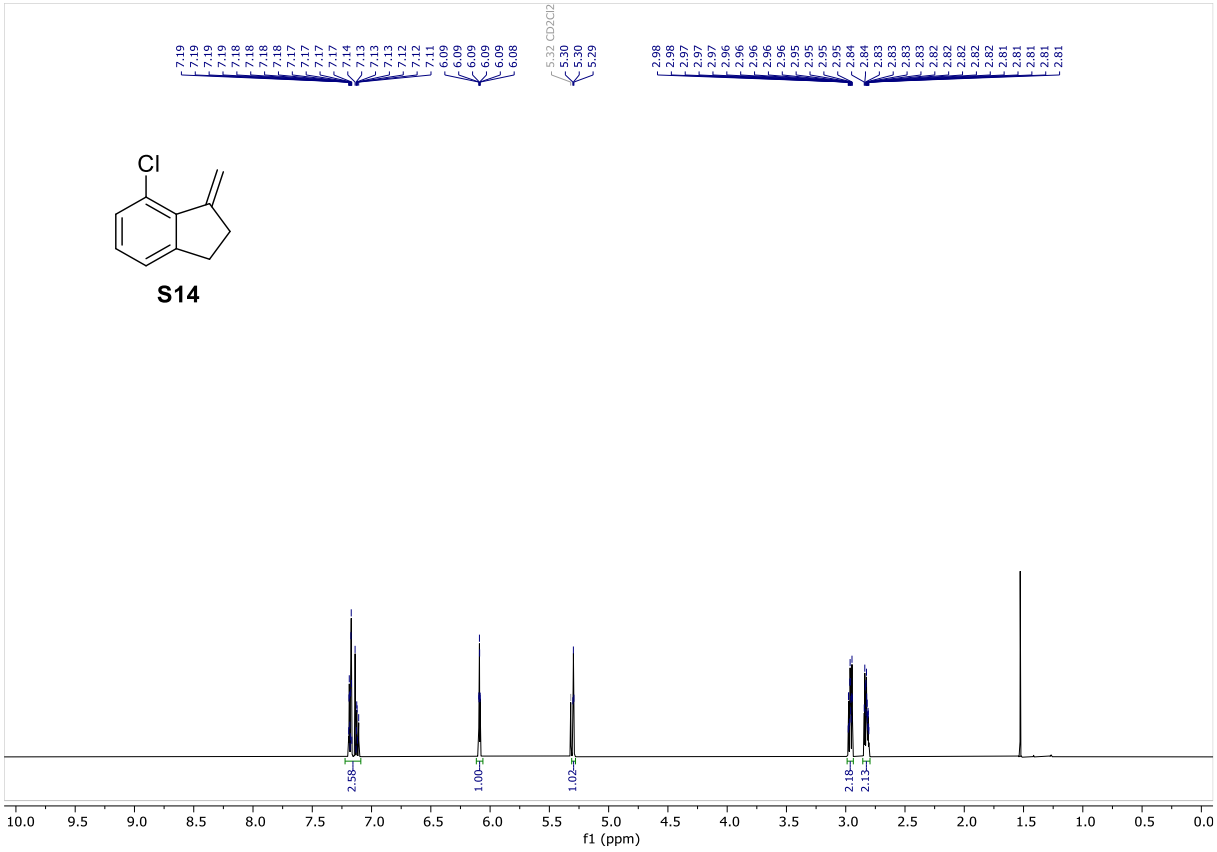
Supplementary Fig. 91. ^{13}C NMR Spectrum of alkene S11 ($CDCl_3$, 126 MHz, 20 °C)



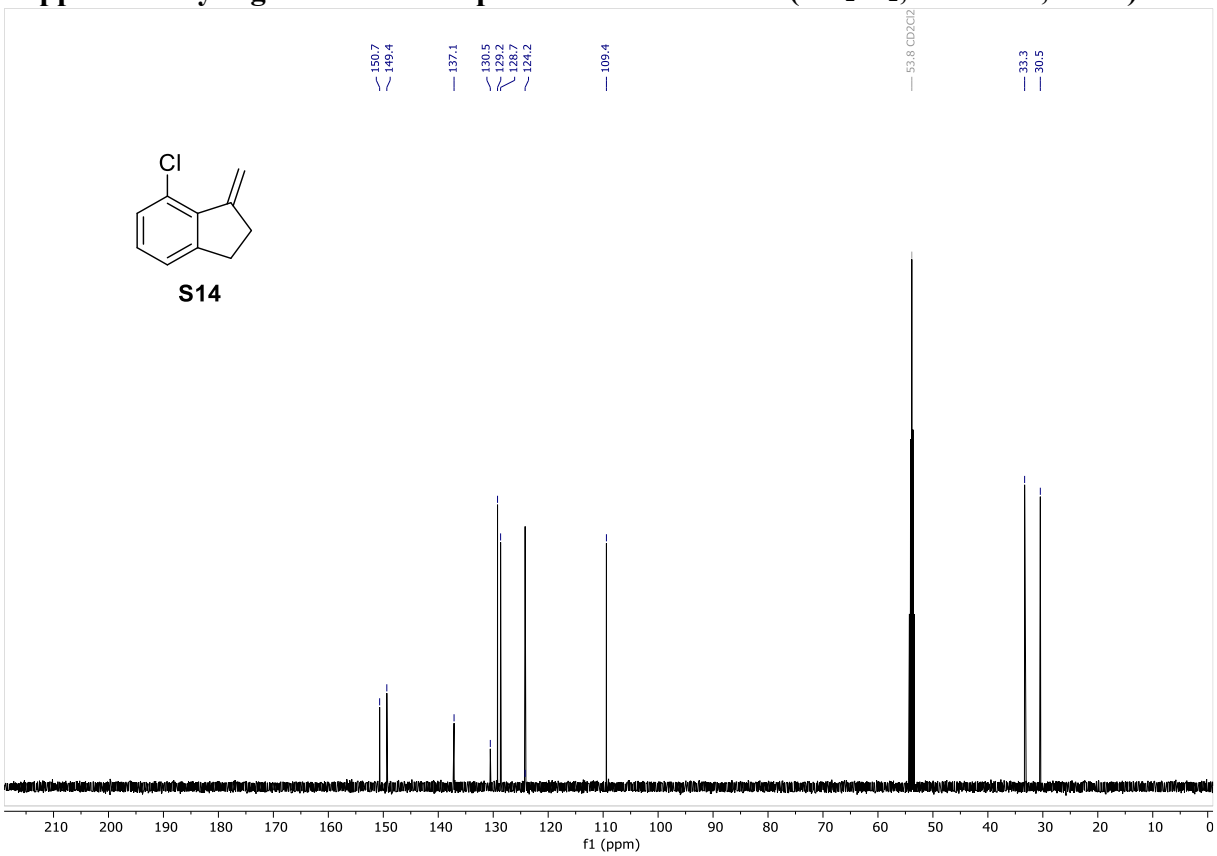
Supplementary Fig. 92. ^{1}H NMR Spectrum of alkene S12 (CD_2Cl_2, 600 MHz, 20 °C)



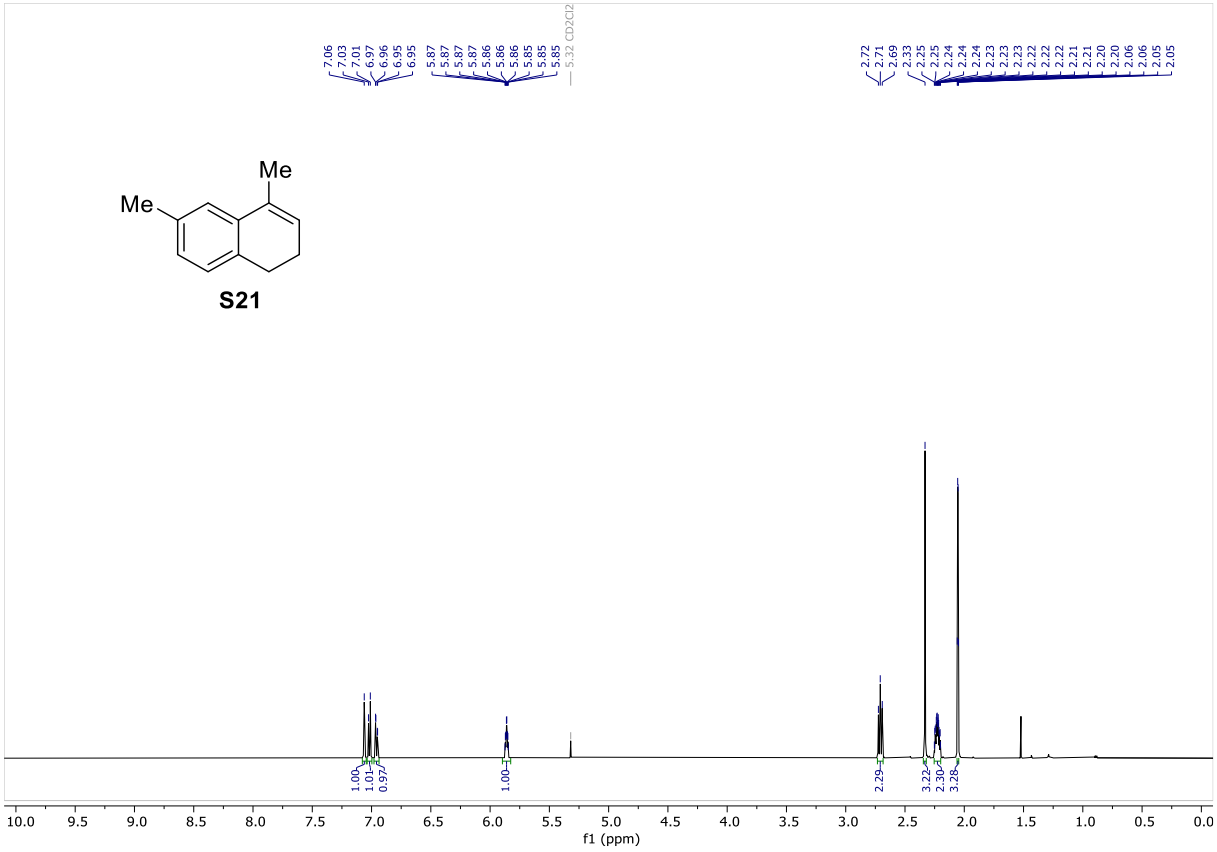
Supplementary Fig. 93. ^{13}C NMR Spectrum of alkene S12 (CD_2Cl_2, 151 MHz, 20 °C)



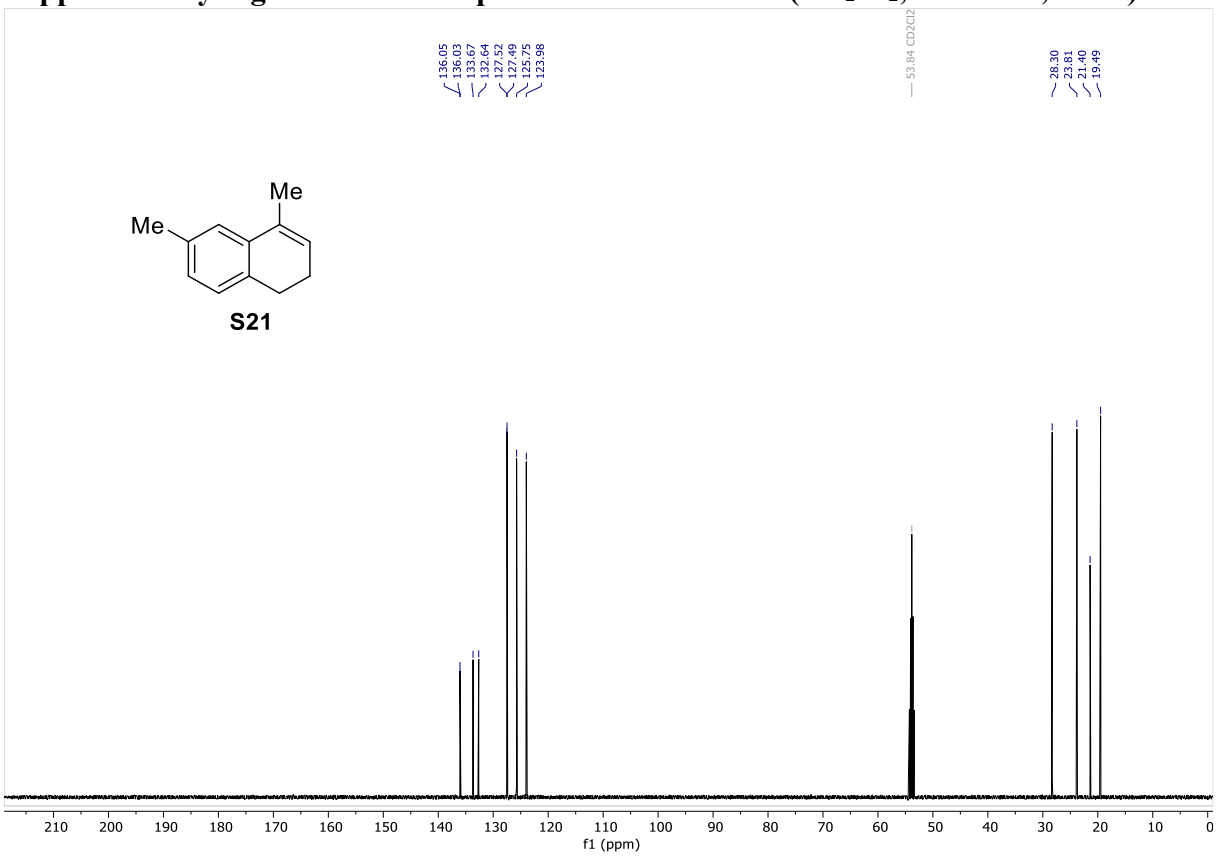
Supplementary Fig. 94. ^{1}H NMR Spectrum of alkene S14 (CD_2Cl_2, 500 MHz, 20 °C)



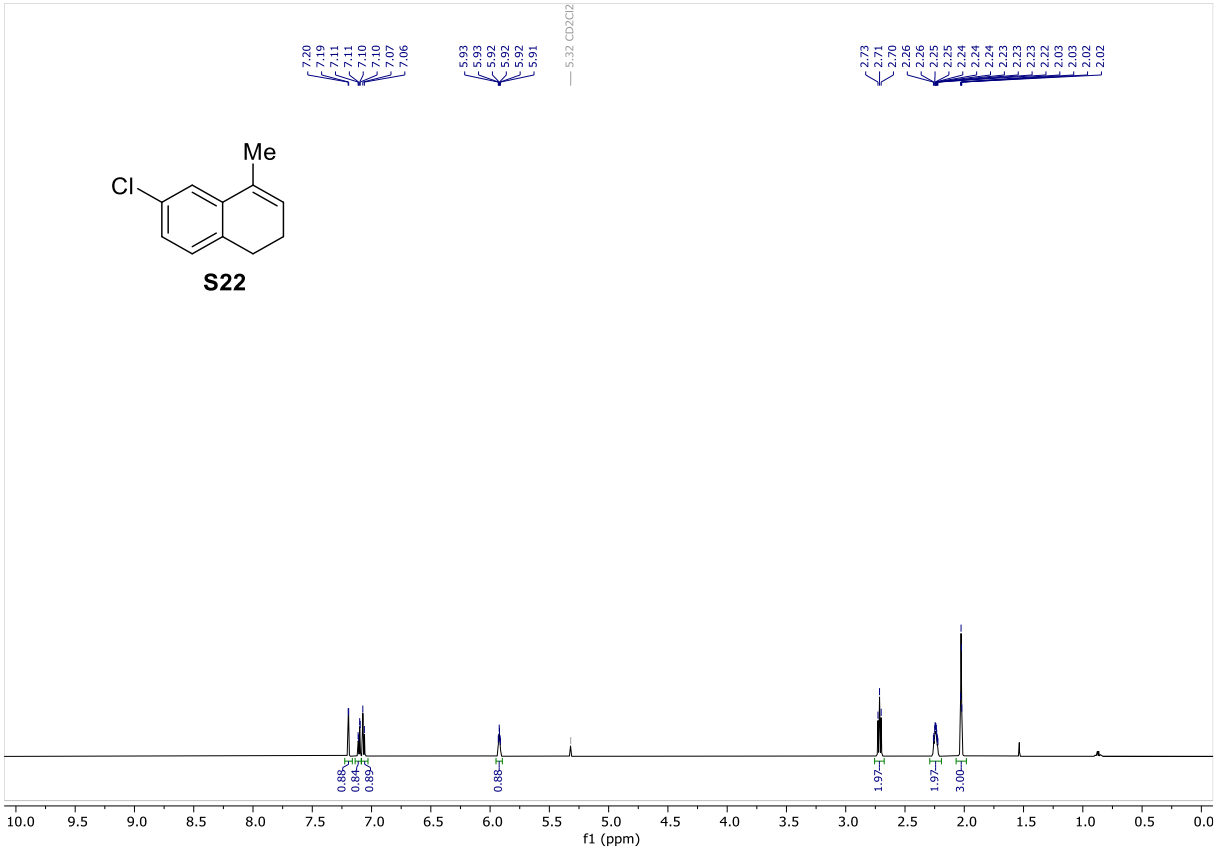
Supplementary Fig. 95. ^{13}C NMR Spectrum of alkene S14 (CD_2Cl_2, 126 MHz, 20 °C)



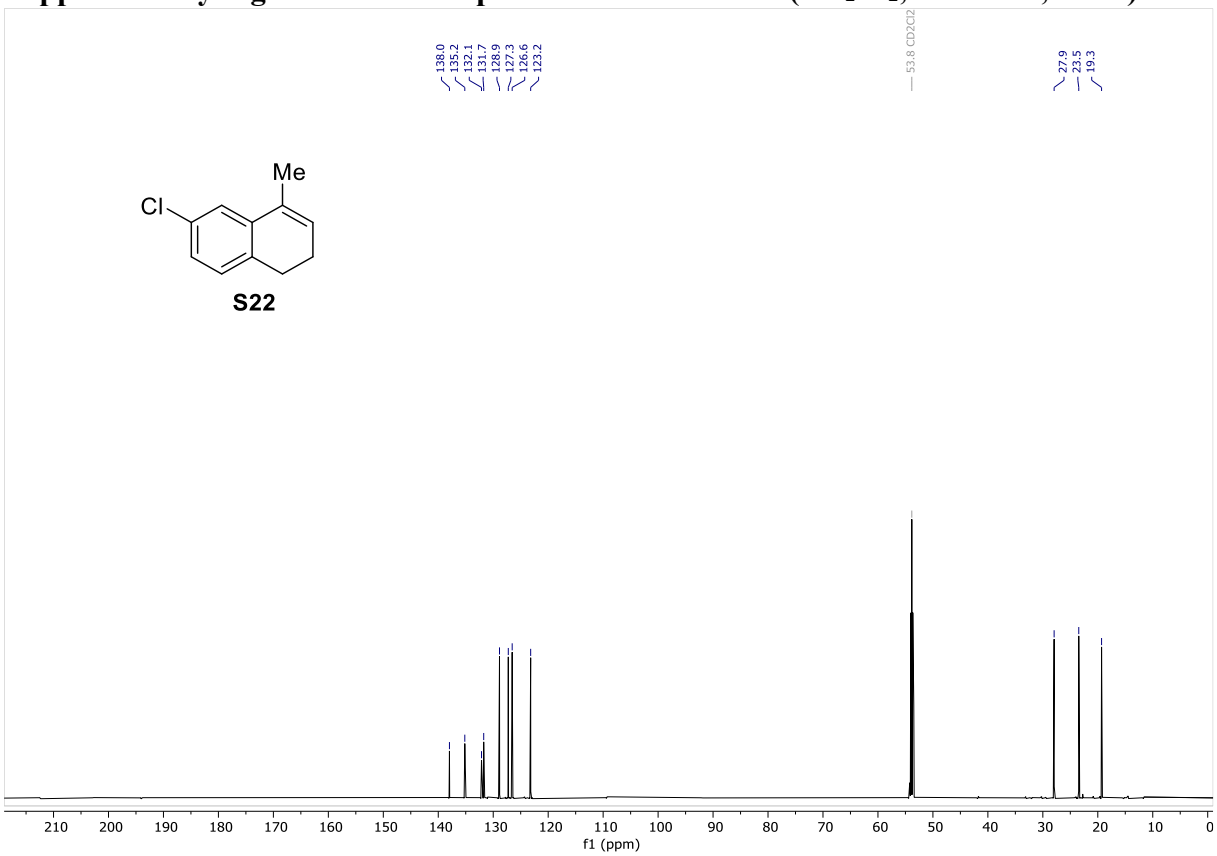
Supplementary Fig. 96. ^{1}H NMR Spectrum of alkene S21 (CD_2Cl_2, 500 MHz, 20 °C)



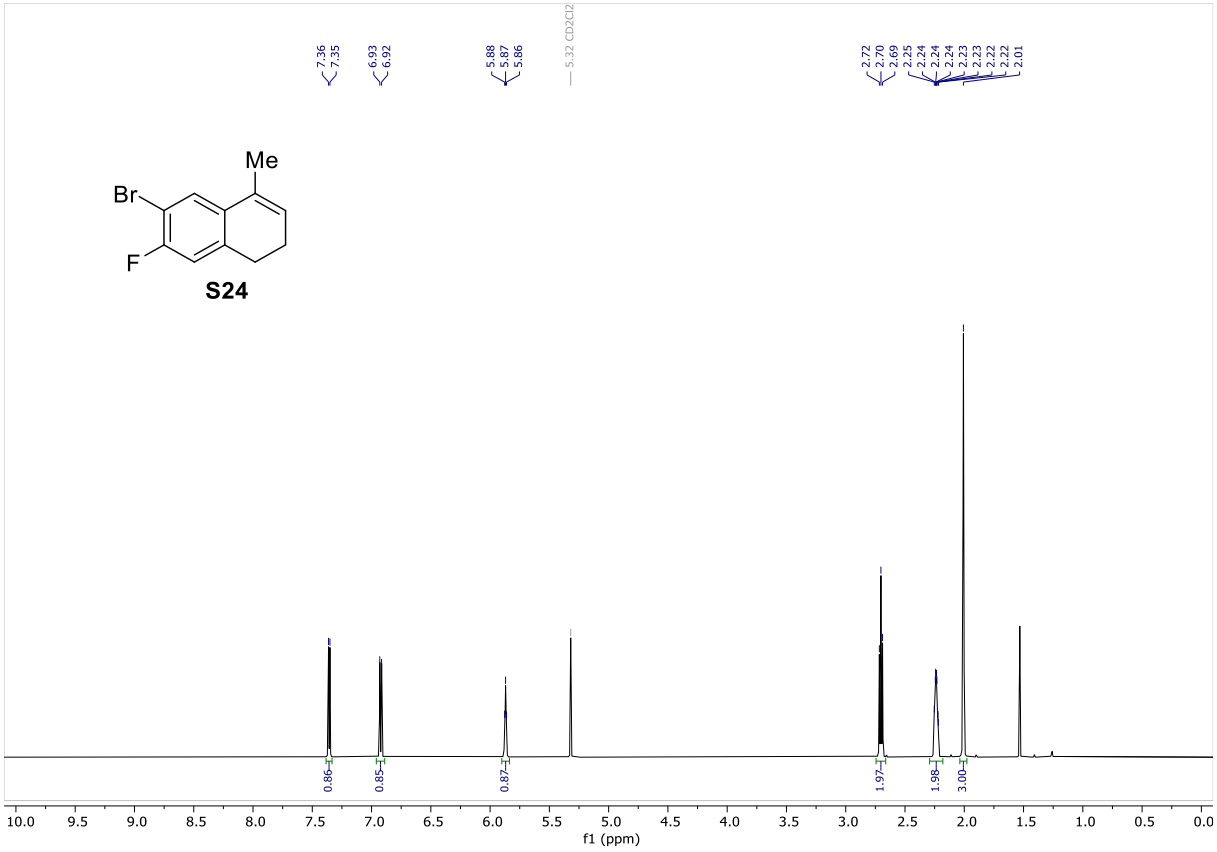
Supplementary Fig. 97. ^{13}C NMR Spectrum of alkene S21 (CD_2Cl_2, 126 MHz, 20 °C)



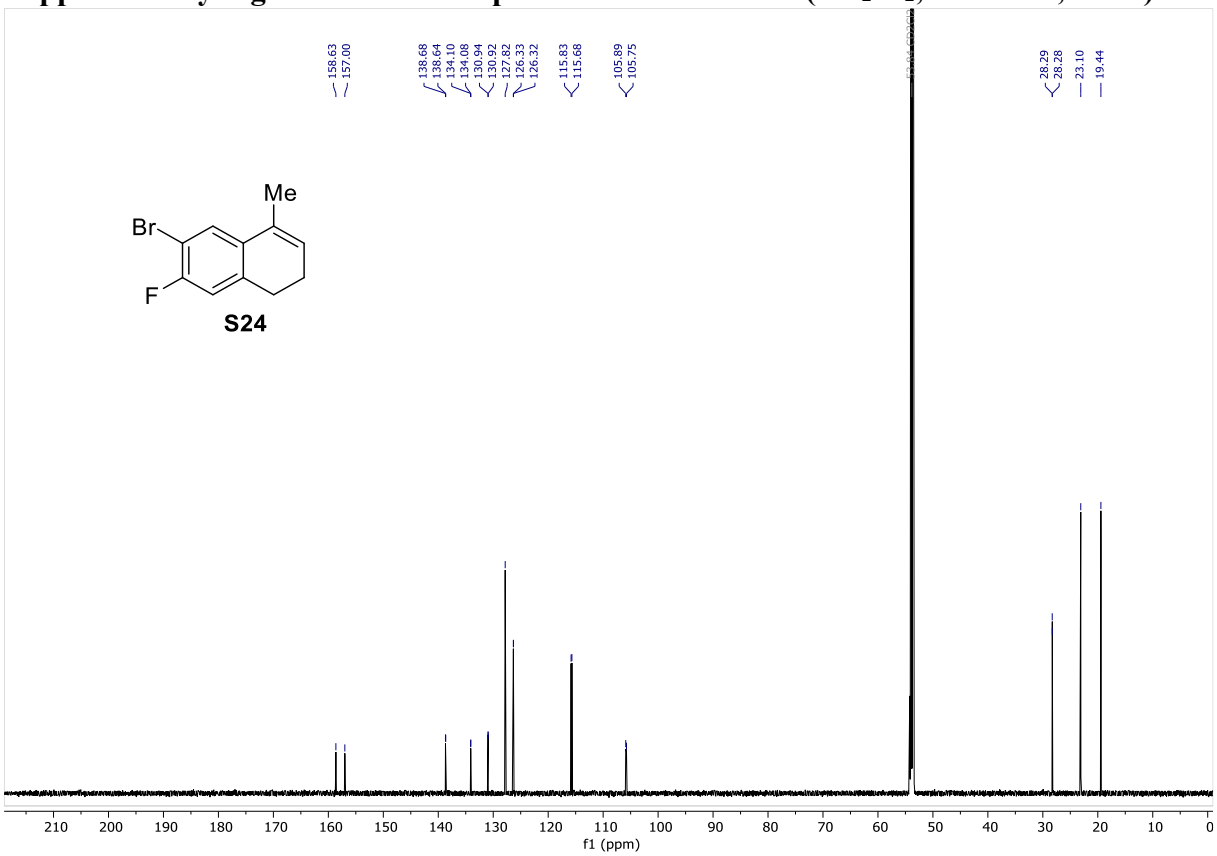
Supplementary Fig. 98. ^{1}H NMR Spectrum of alkene S22 (CD_2Cl_2, 600 MHz, 20 °C)



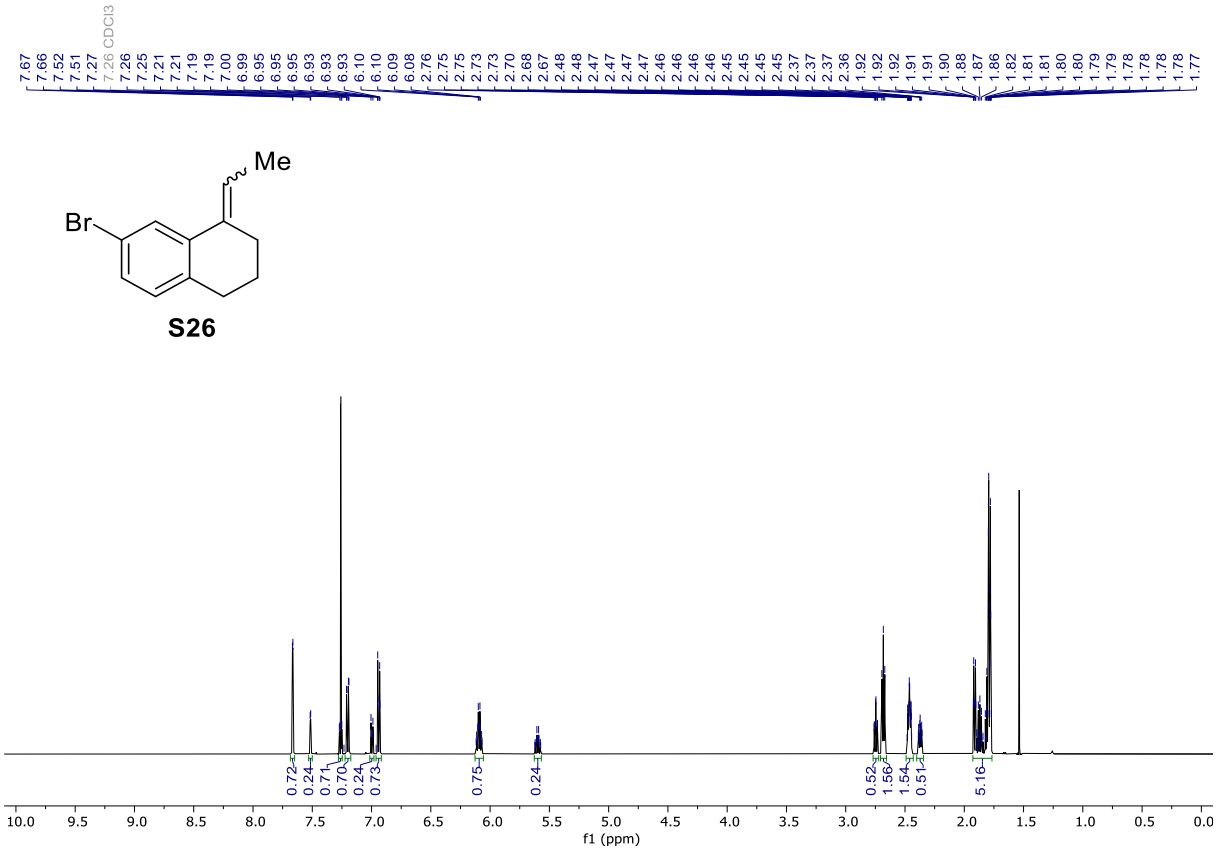
Supplementary Fig. 99. ^{13}C NMR Spectrum of alkene S22 (CD_2Cl_2, 151 MHz, 20 °C)



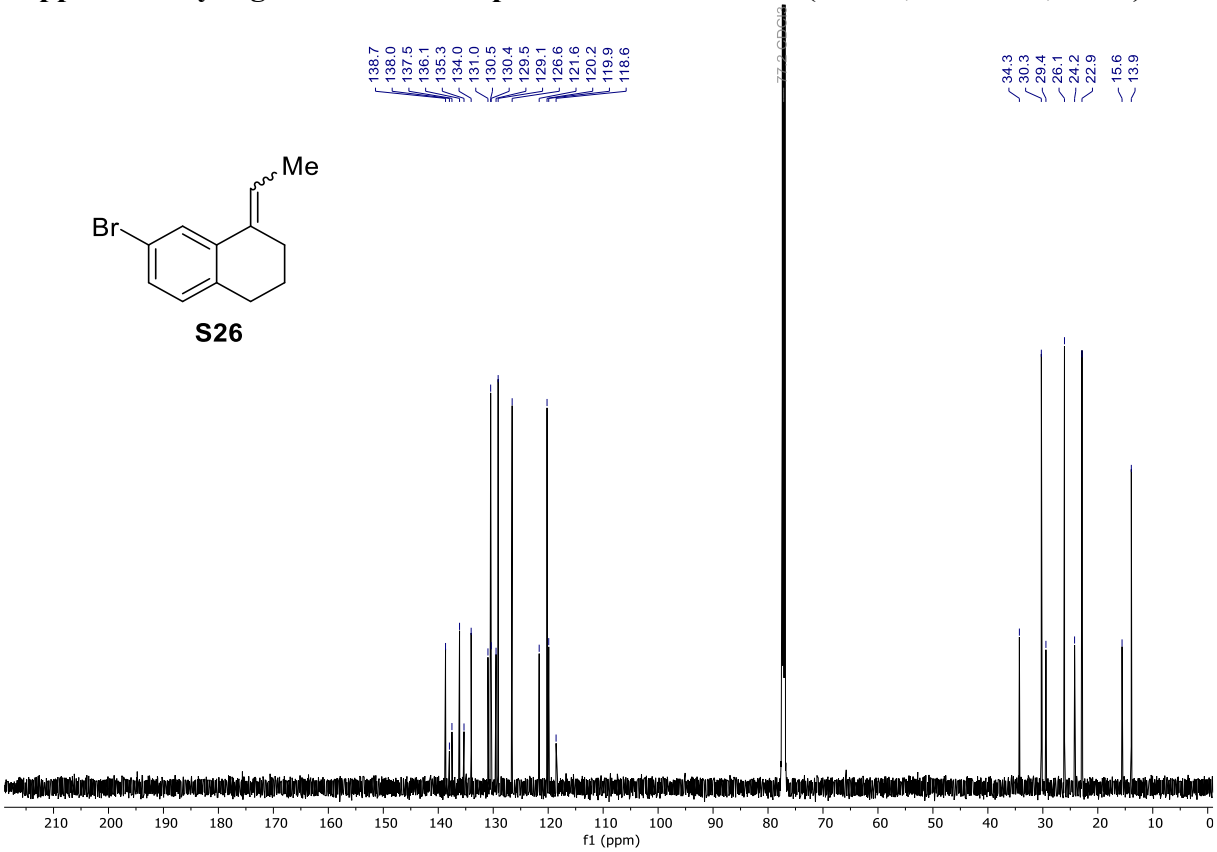
Supplementary Fig. 100. ^{1}H NMR Spectrum of alkene S24 (CD_2Cl_2, 600 MHz, 20 °C)



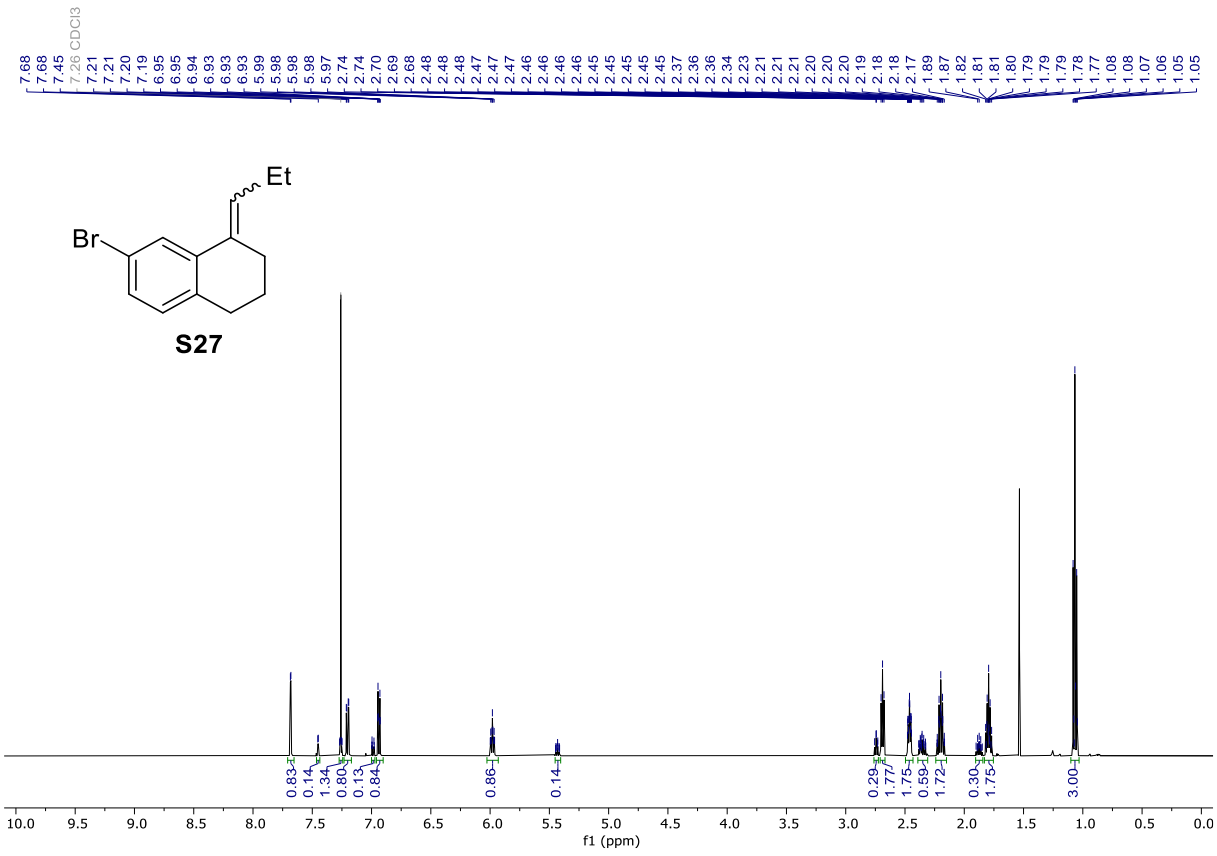
Supplementary Fig. 101. ^{13}C NMR Spectrum of alkene S24 (CD_2Cl_2, 151 MHz, 20 °C)



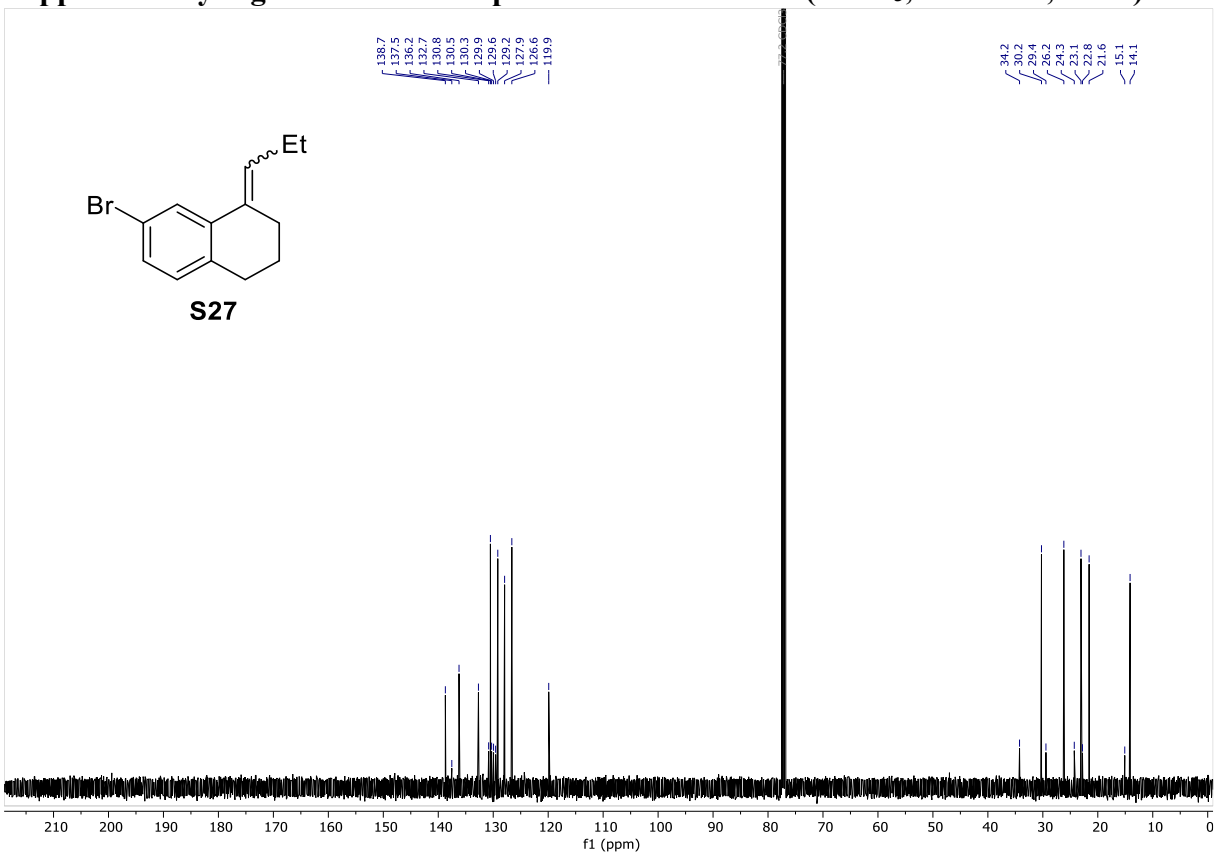
Supplementary Fig. 102. ^{1}H NMR Spectrum of alkene S26 ($CDCl_3$, 500 MHz, 20 °C)



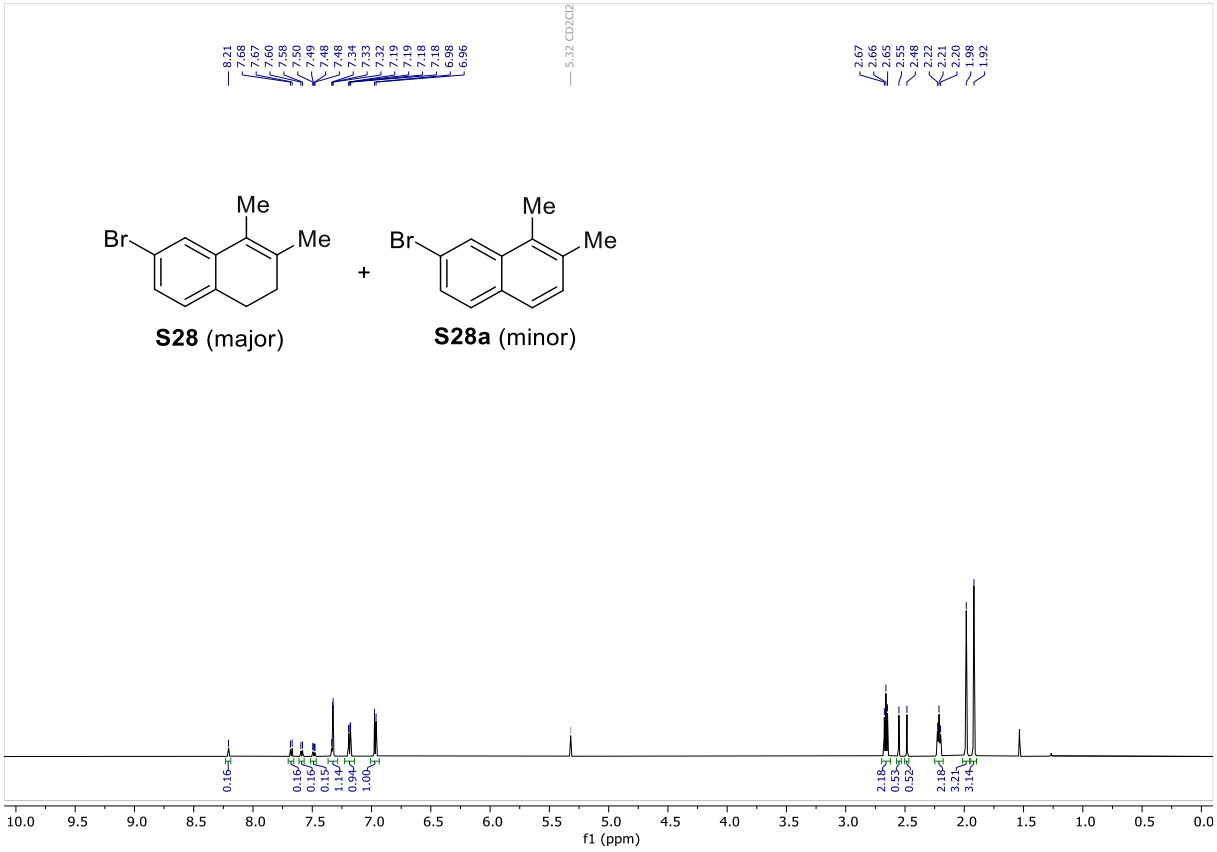
Supplementary Fig. 103. ^{13}C NMR Spectrum of alkene S26 ($CDCl_3$, 151 MHz, 20 °C)



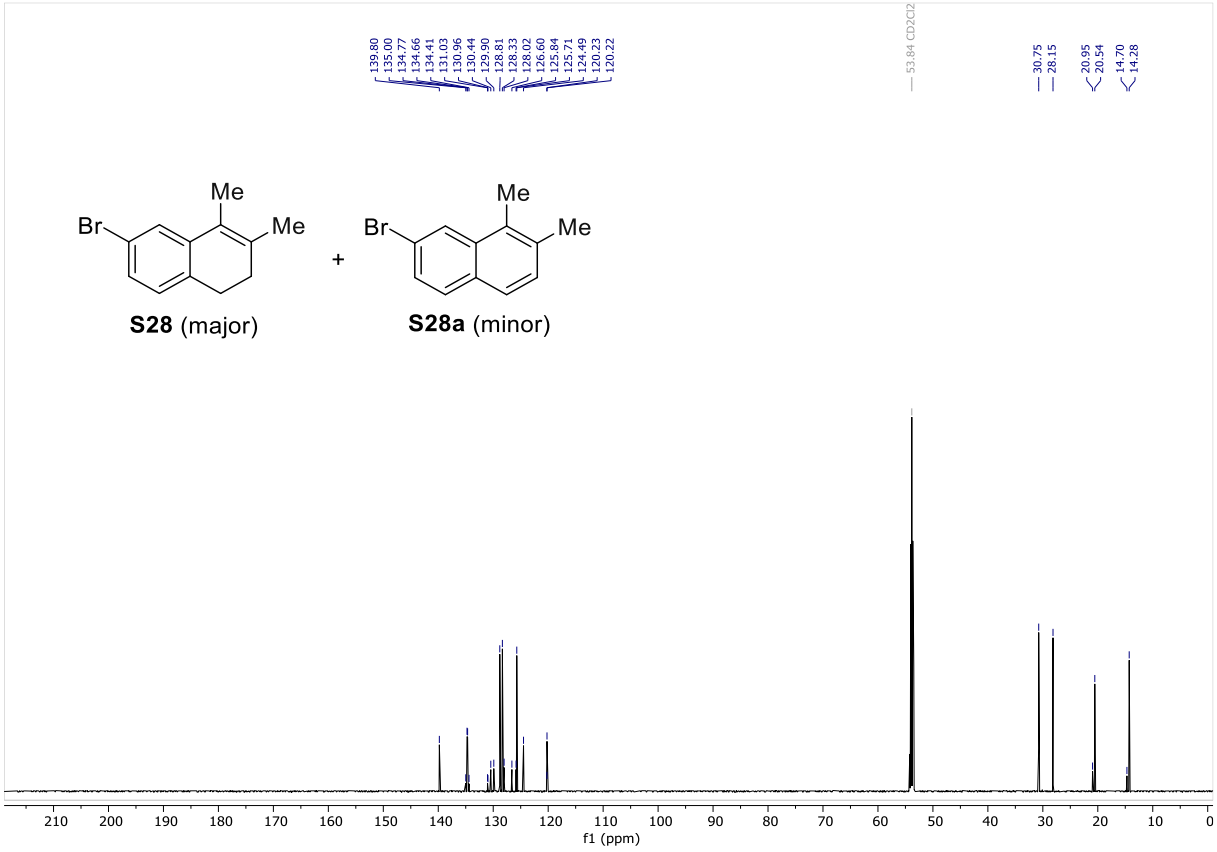
Supplementary Fig. 104. ^{1}H NMR Spectrum of alkene S27 ($CDCl_3$, 500 MHz, 20 °C)



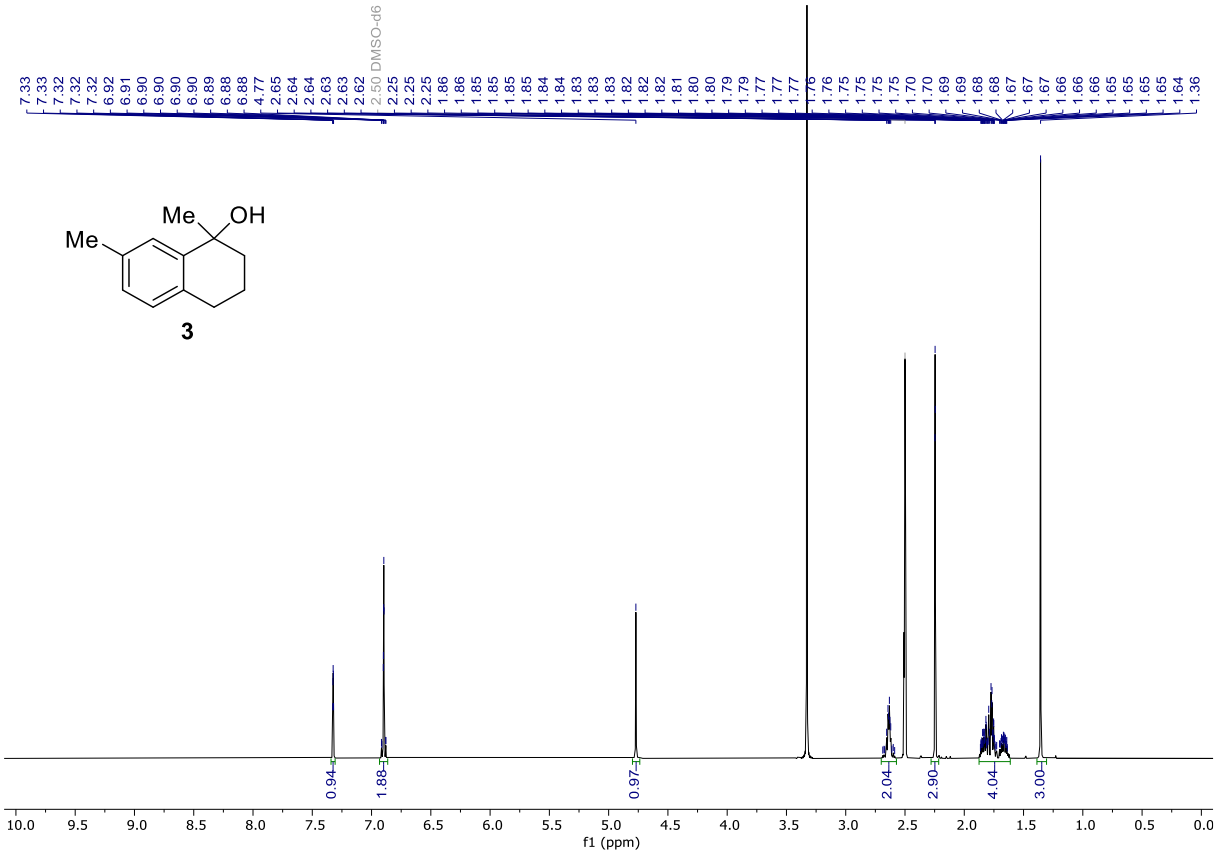
Supplementary Fig. 105. ^{13}C NMR Spectrum of alkene S27 ($CDCl_3$, 126 MHz, 20 °C)



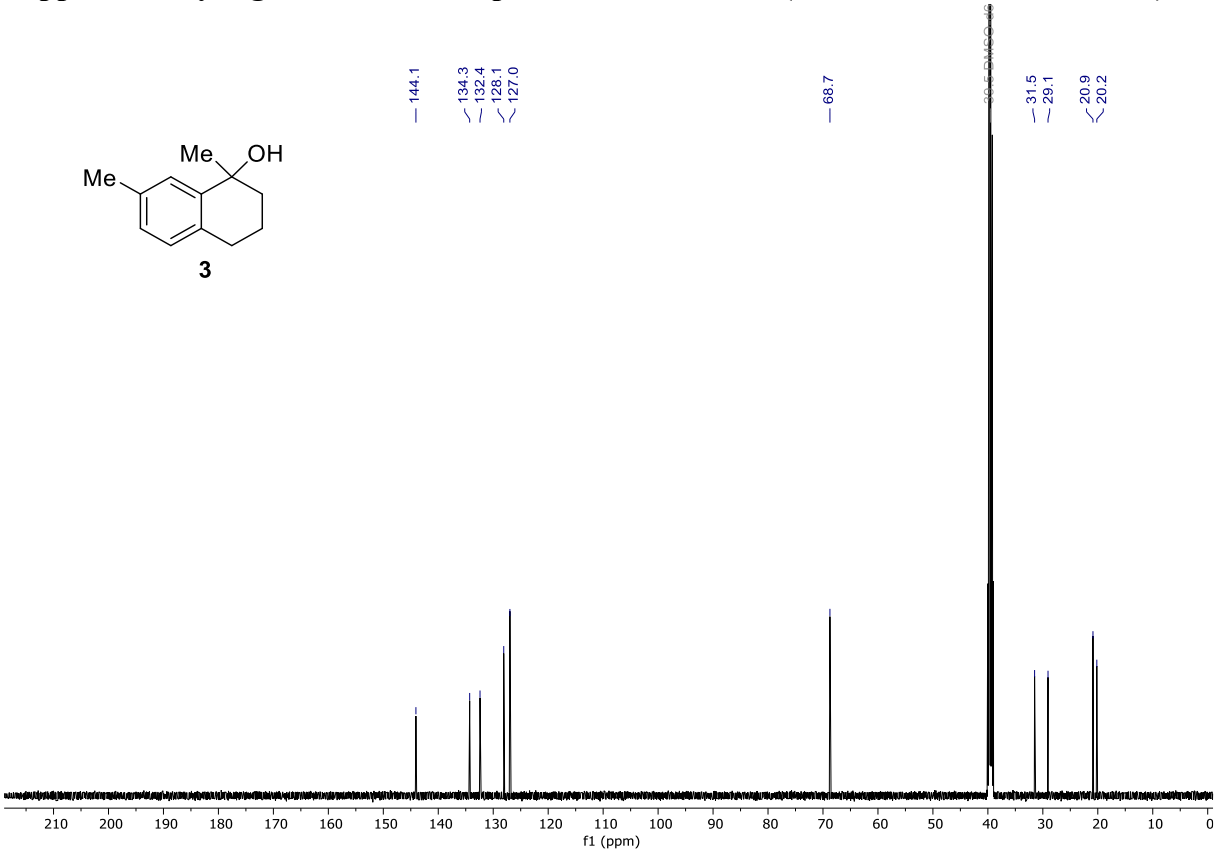
Supplementary Fig. 106. ^{1}H NMR Spectrum of alkene S28 and byproduct S28a (CD_2Cl_2, 600 MHz, 20 °C)



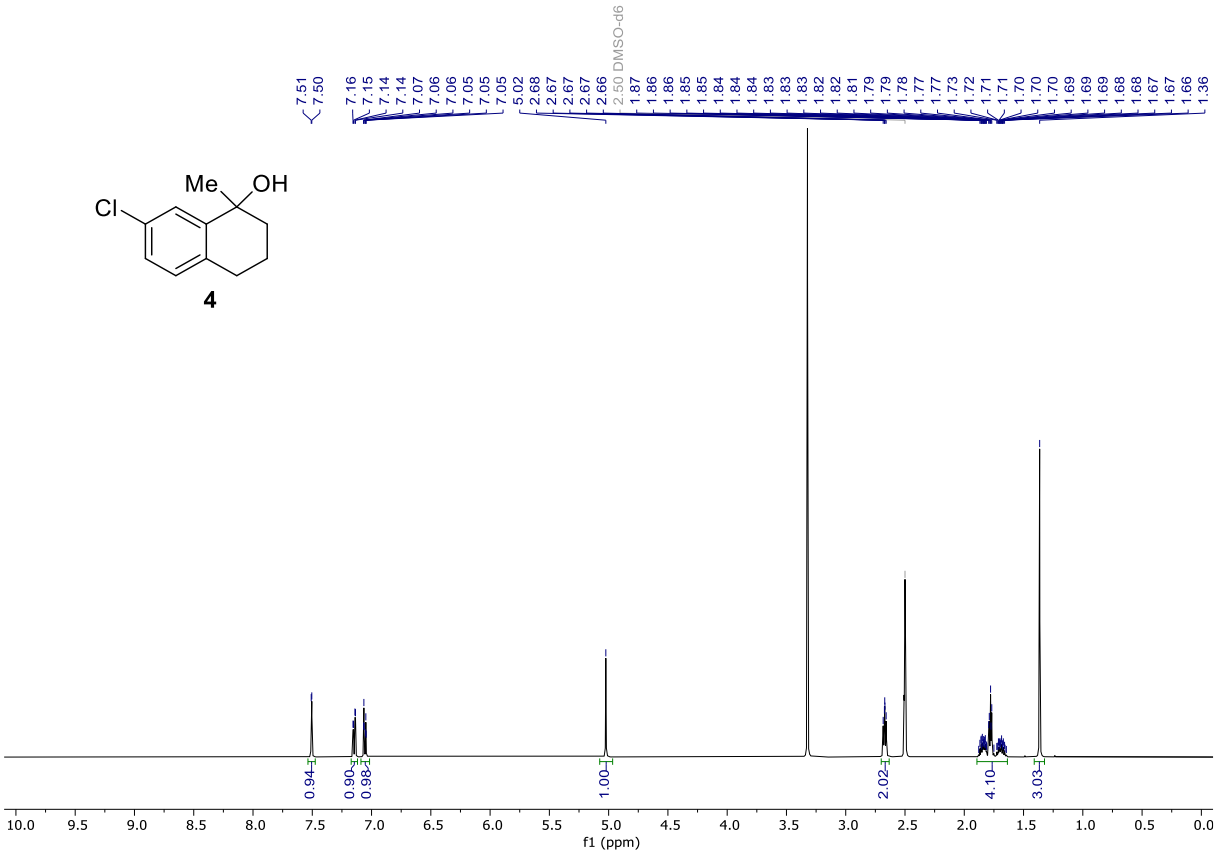
Supplementary Fig. 107. ^{13}C NMR Spectrum of alkene S28 and byproduct S28a (CD_2Cl_2, 151 MHz, 20 °C)



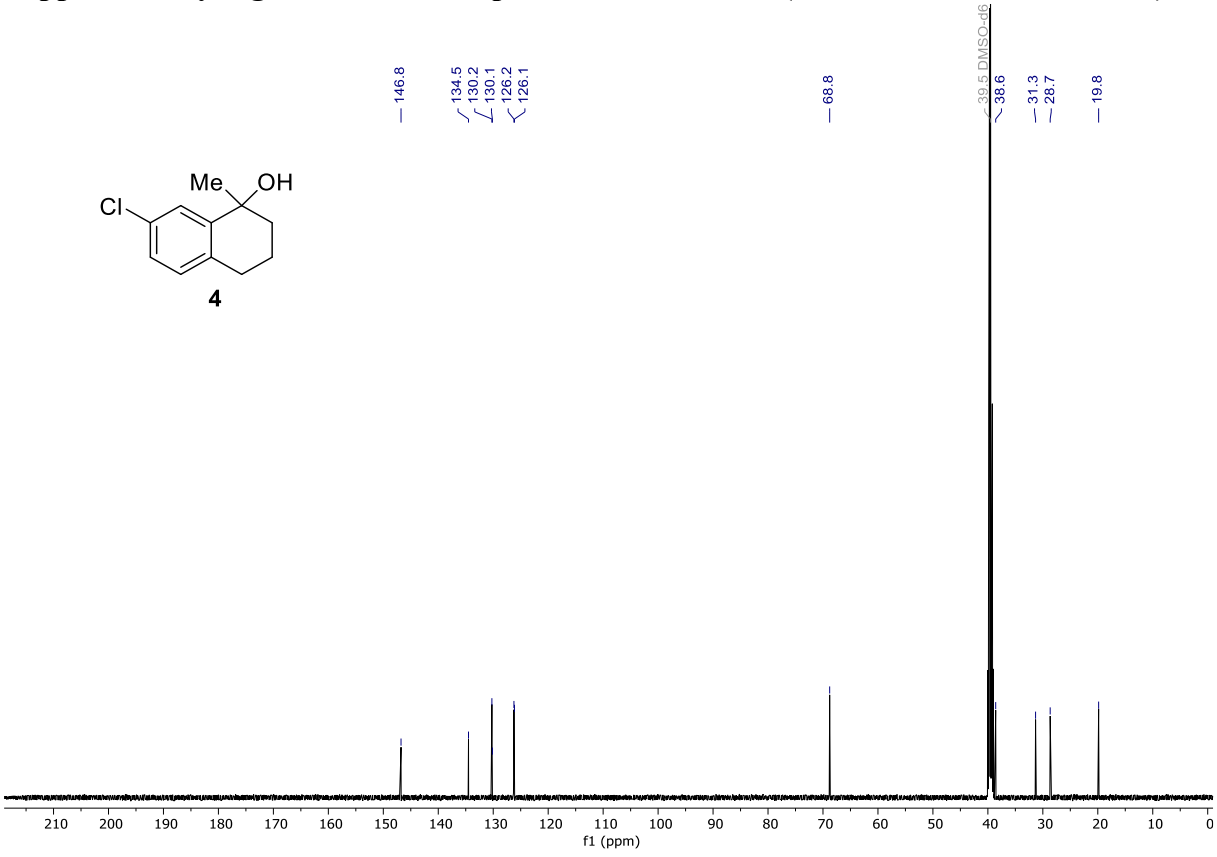
Supplementary Fig. 108. ^{1}H NMR Spectrum of tetralol 3 (DMSO-d$_6$, 500 MHz, 20 °C)



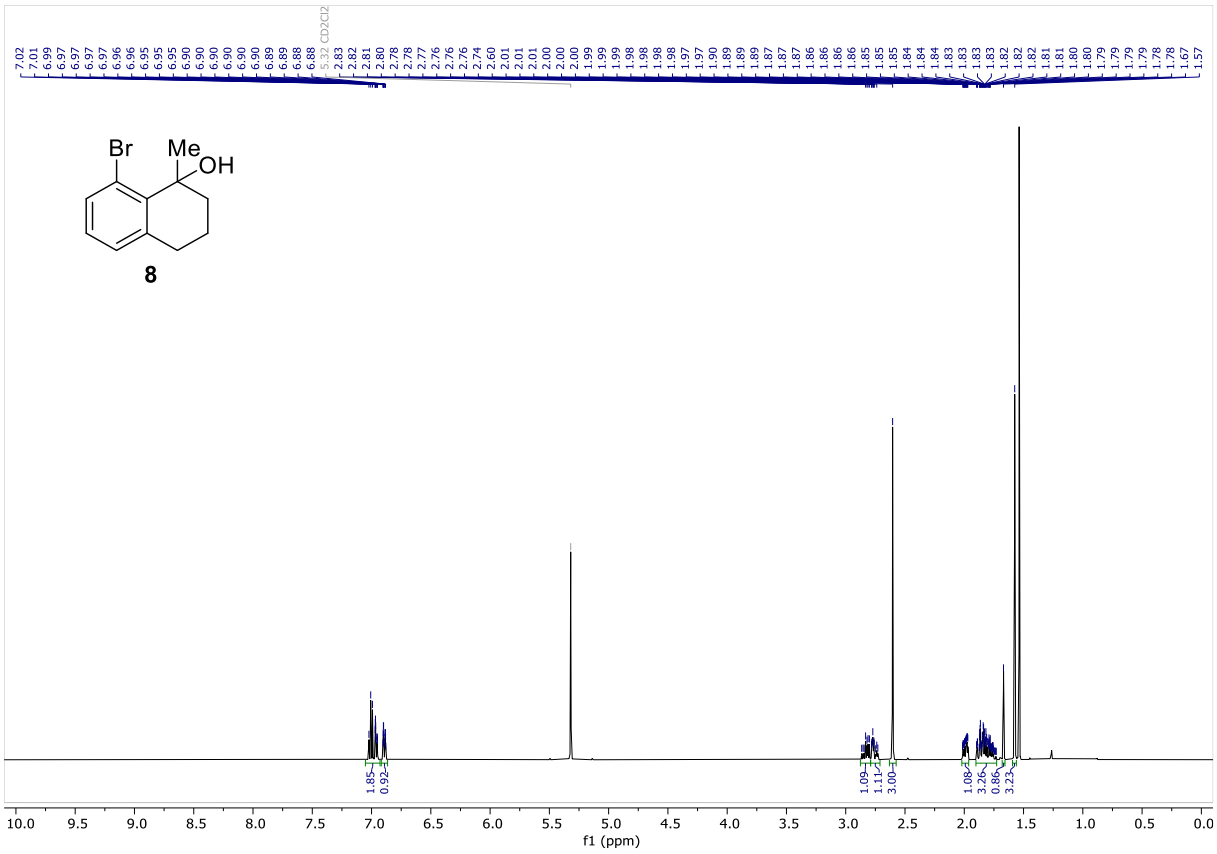
Supplementary Fig. 109. ^{13}C NMR Spectrum of tetralol 3 (DMSO-d$_6$, 126 MHz, 20 °C)



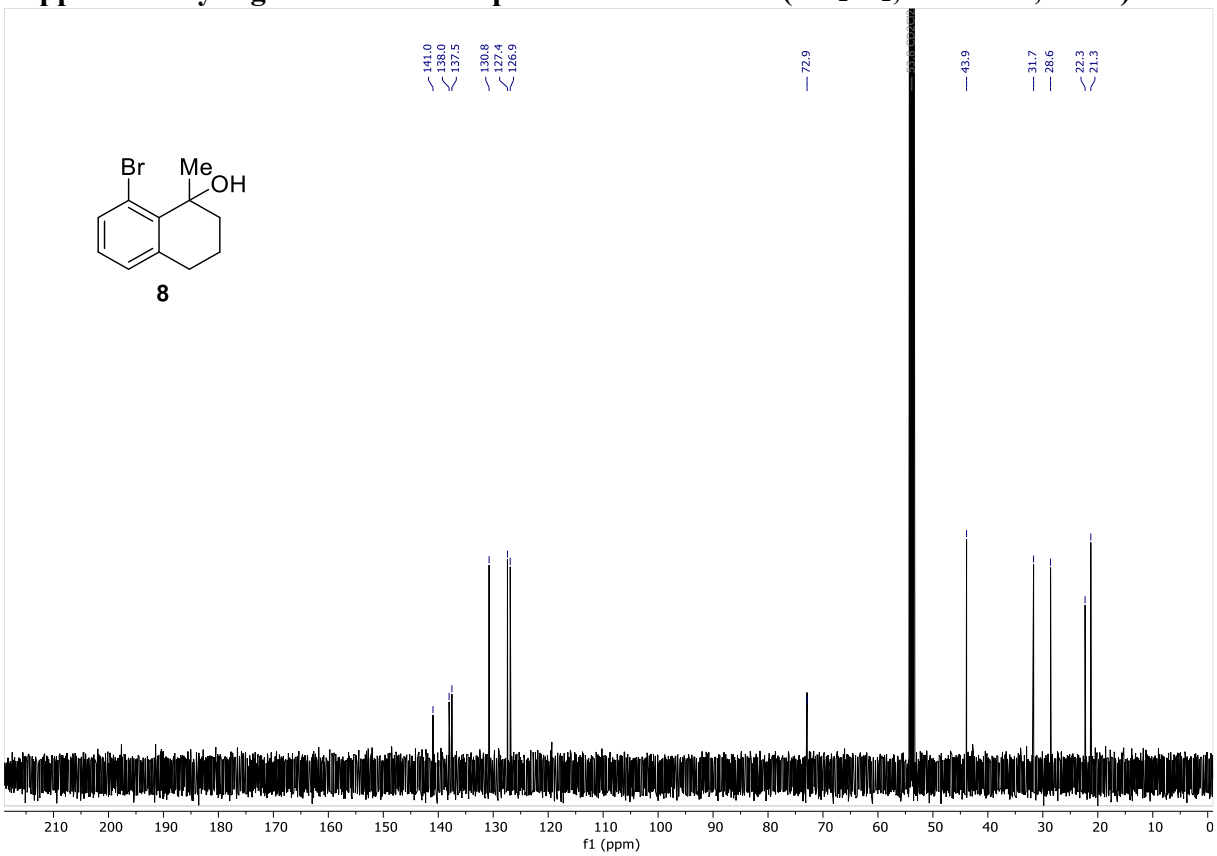
Supplementary Fig. 110. ^{1}H NMR Spectrum of tetralol 4 (DMSO-d$_6$, 500 MHz, 20 °C)



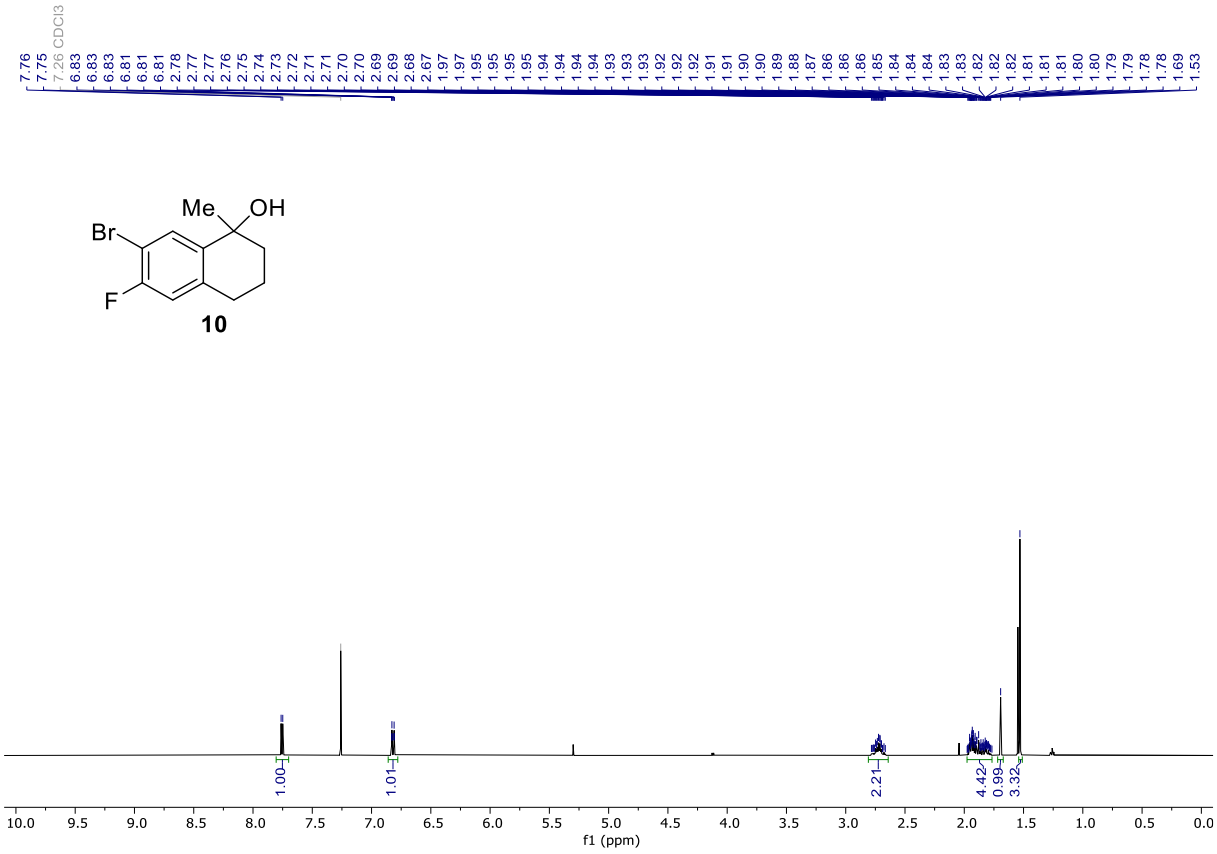
Supplementary Fig. 111. ^{13}C NMR Spectrum of tetralol 4 (DMSO-d$_6$, 126 MHz, 20 °C)



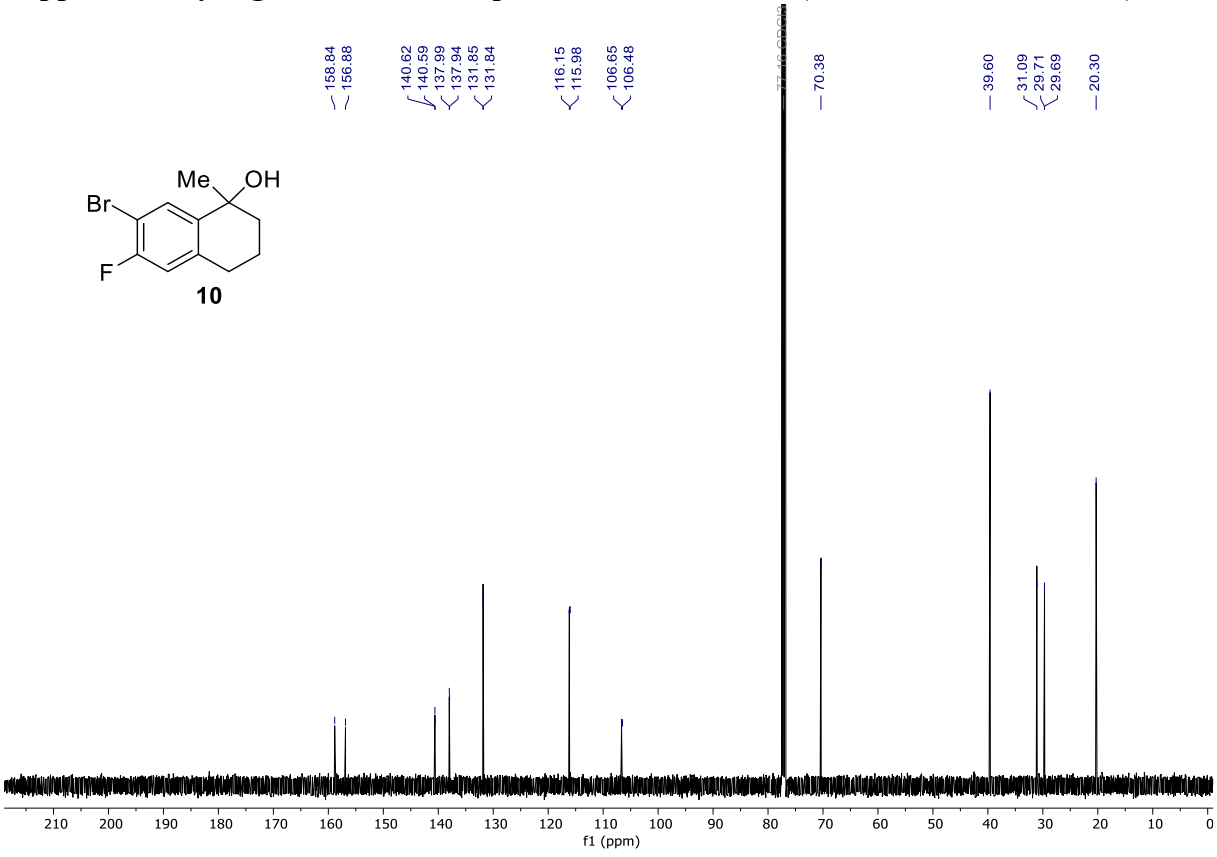
Supplementary Fig. 112. ^{1}H NMR Spectrum of tetralol 8 (CD_2Cl_2, 500 MHz, 20 °C)



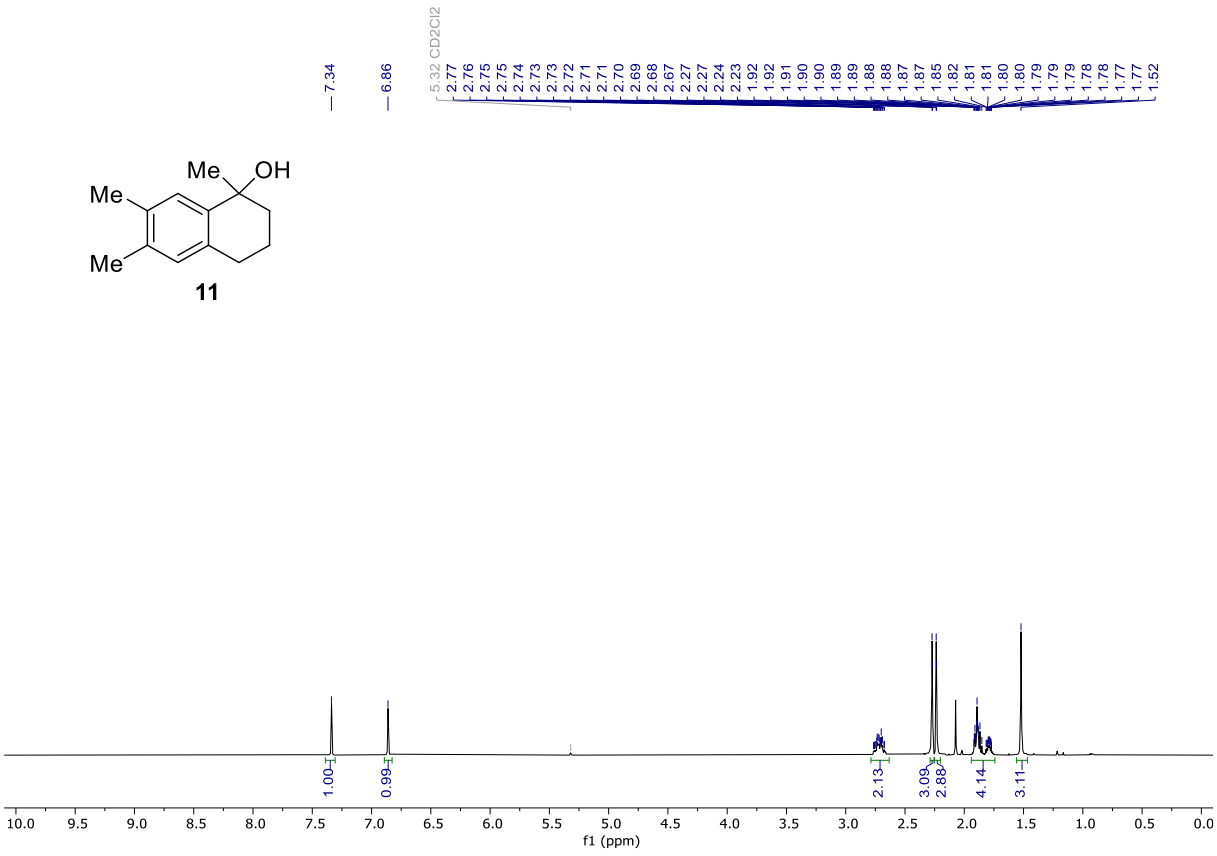
Supplementary Fig. 113. ^{13}C NMR Spectrum of tetralol 8 (CD_2Cl_2, 126 MHz, 20 °C)



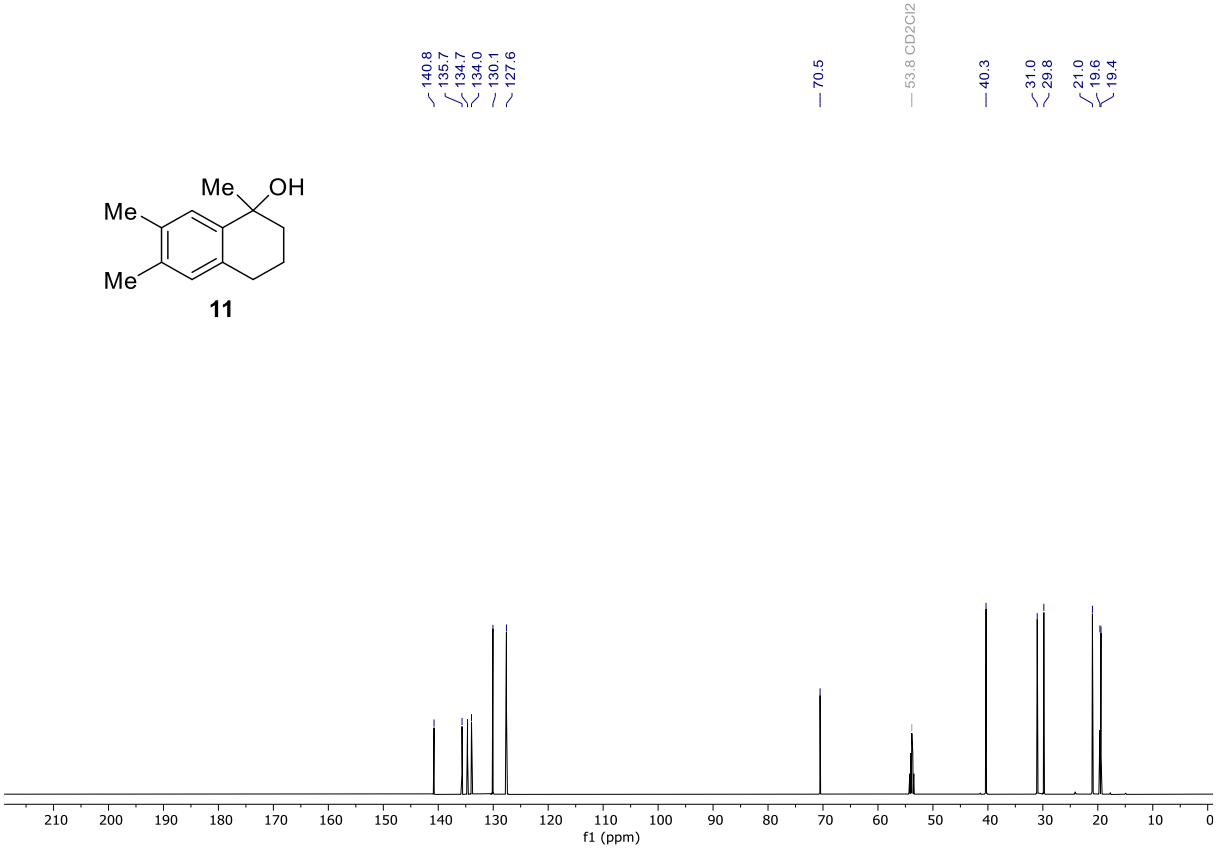
Supplementary Fig. 114. ^{1}H NMR Spectrum of tetralol 10 ($CDCl_3$, 500 MHz, 20 °C)



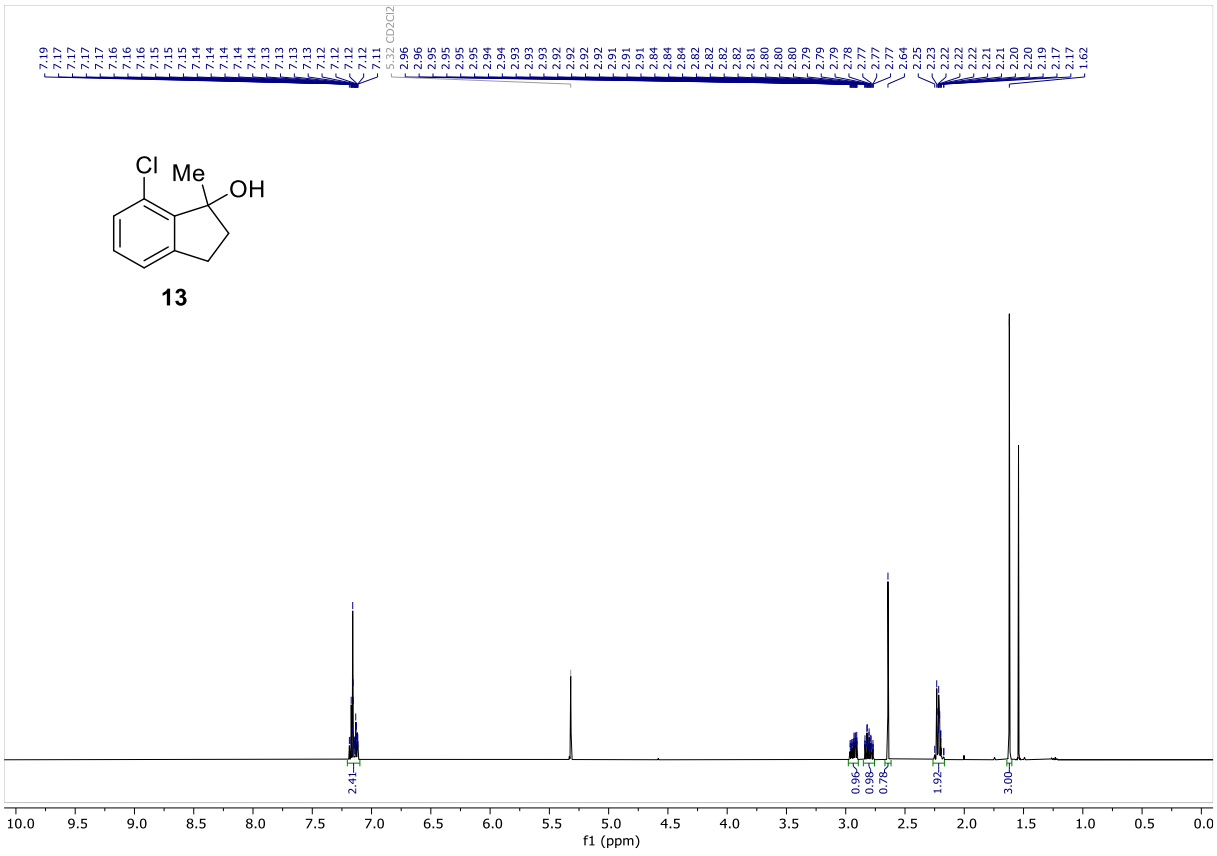
Supplementary Fig. 115. ^{13}C NMR Spectrum of tetralol 10 ($CDCl_3$, 126 MHz, 20 °C)



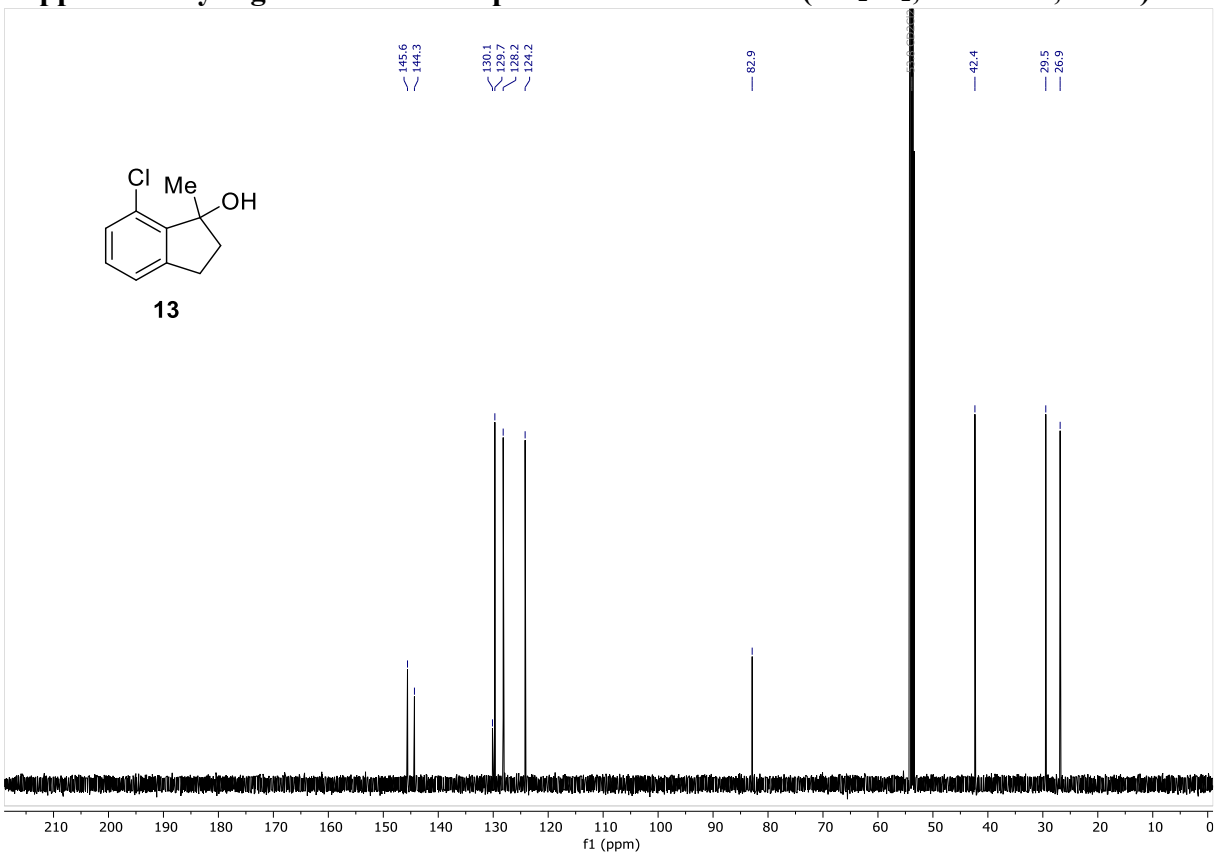
Supplementary Fig. 116. ^{1}H NMR Spectrum of tetralol 11 (CD_2Cl_2, 600 MHz, 20 °C)



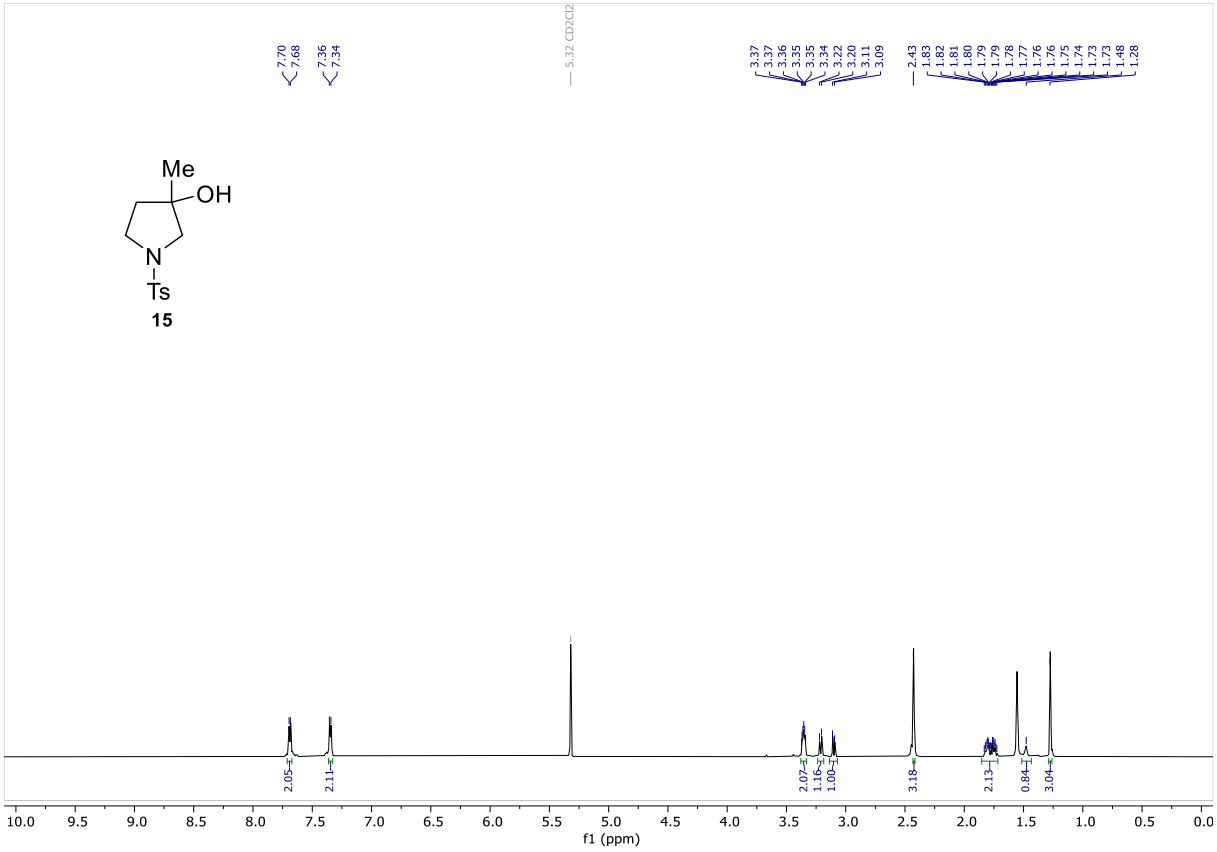
Supplementary Fig. 117. ^{13}C NMR Spectrum of tetralol 11 (CD_2Cl_2, 151 MHz, 20 °C)



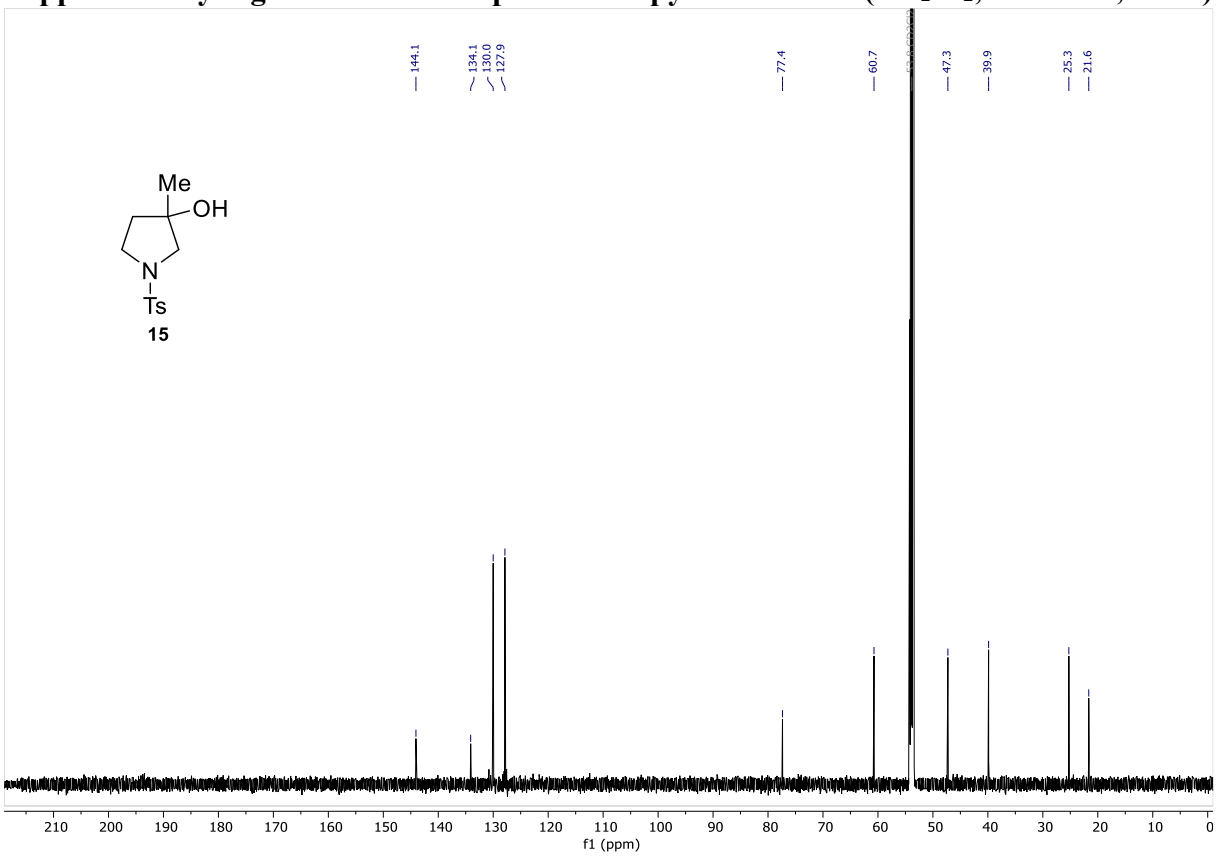
Supplementary Fig. 118. ^{1}H NMR Spectrum of indanol 13 (CD_2Cl_2, 500 MHz, 20 °C)



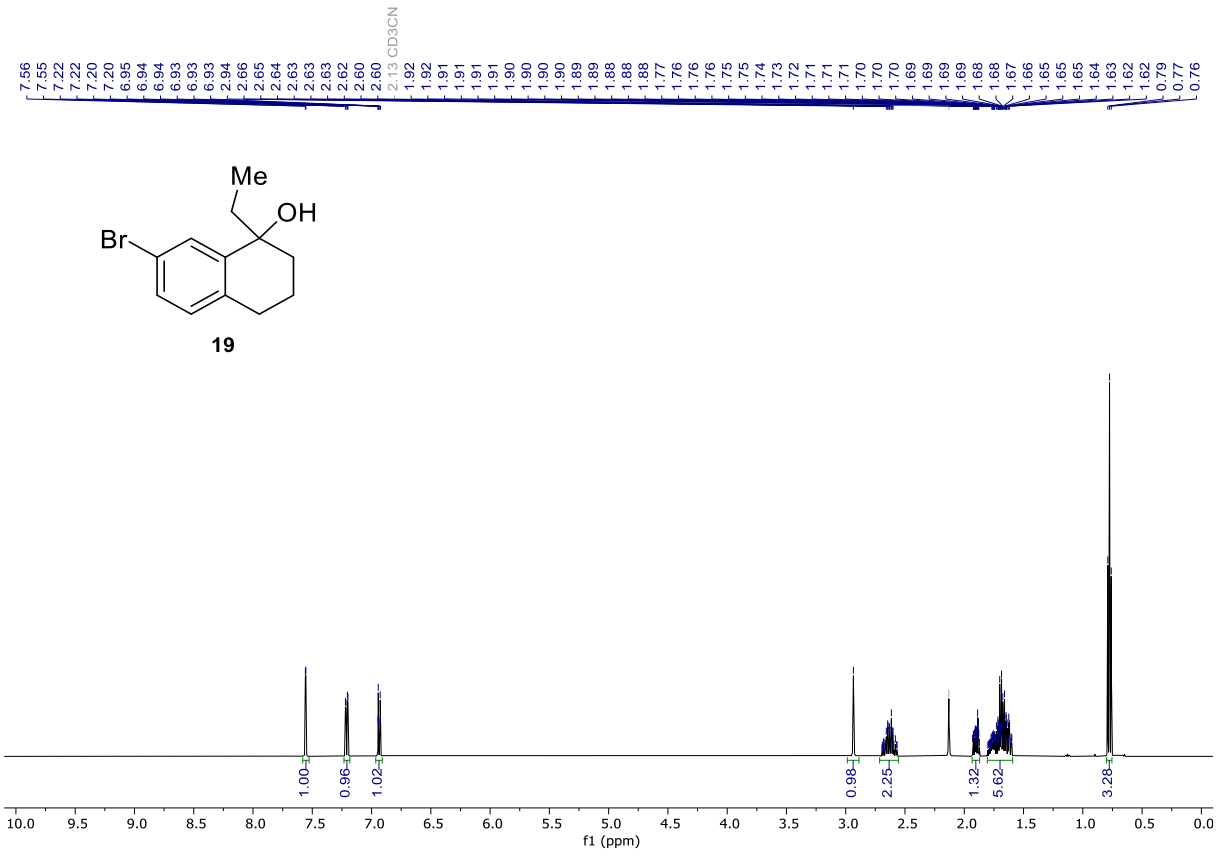
Supplementary Fig. 119. ^{13}C NMR Spectrum of indanol 13 (CD_2Cl_2, 126 MHz, 20 °C)



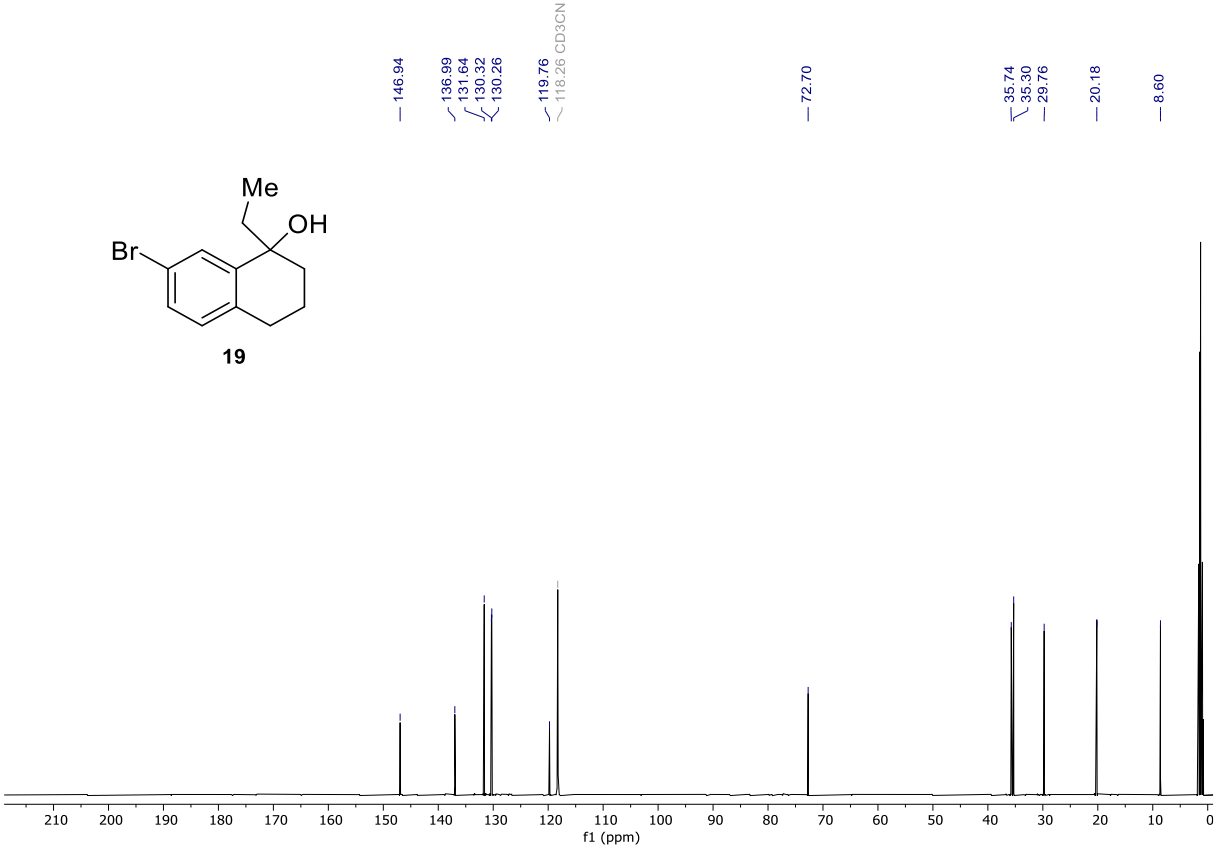
Supplementary Fig. 120. ^{1}H NMR Spectrum of pyrrolidinol 15 (CD_2Cl_2, 600 MHz, 20 °C)



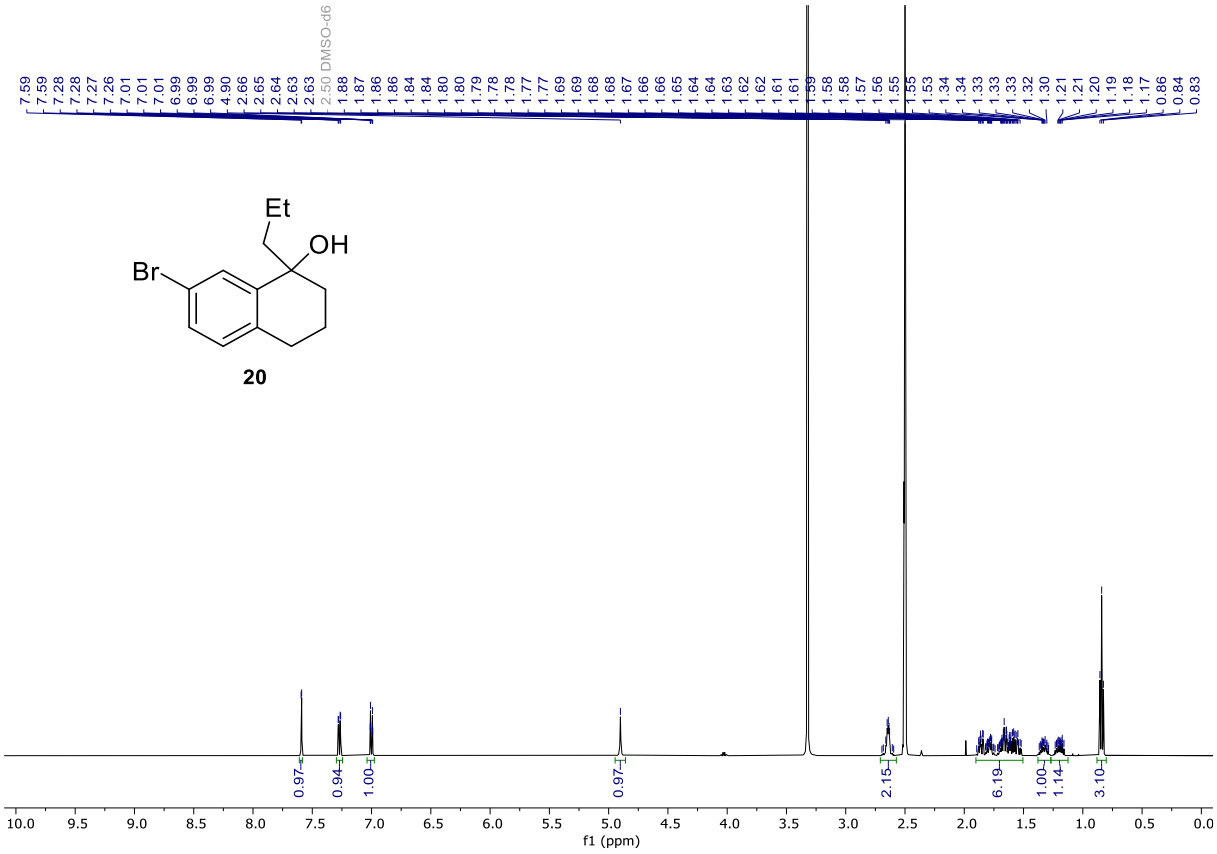
Supplementary Fig. 121. ^{13}C NMR Spectrum of pyrrolidinol 15 (CD_2Cl_2, 151 MHz, 20 °C)



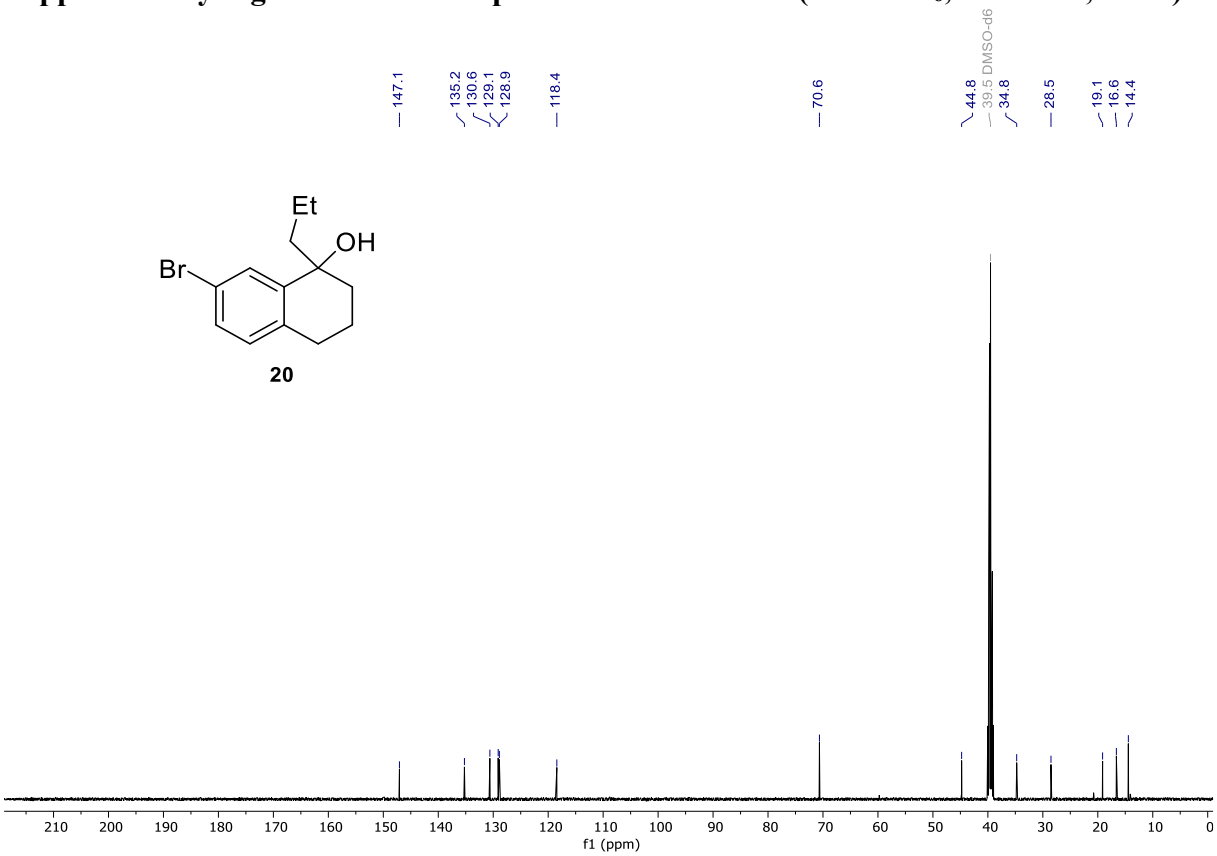
Supplementary Fig. 122. ^{1}H NMR Spectrum of tetralol 19 (CD_3CN, 500 MHz, 20 °C)



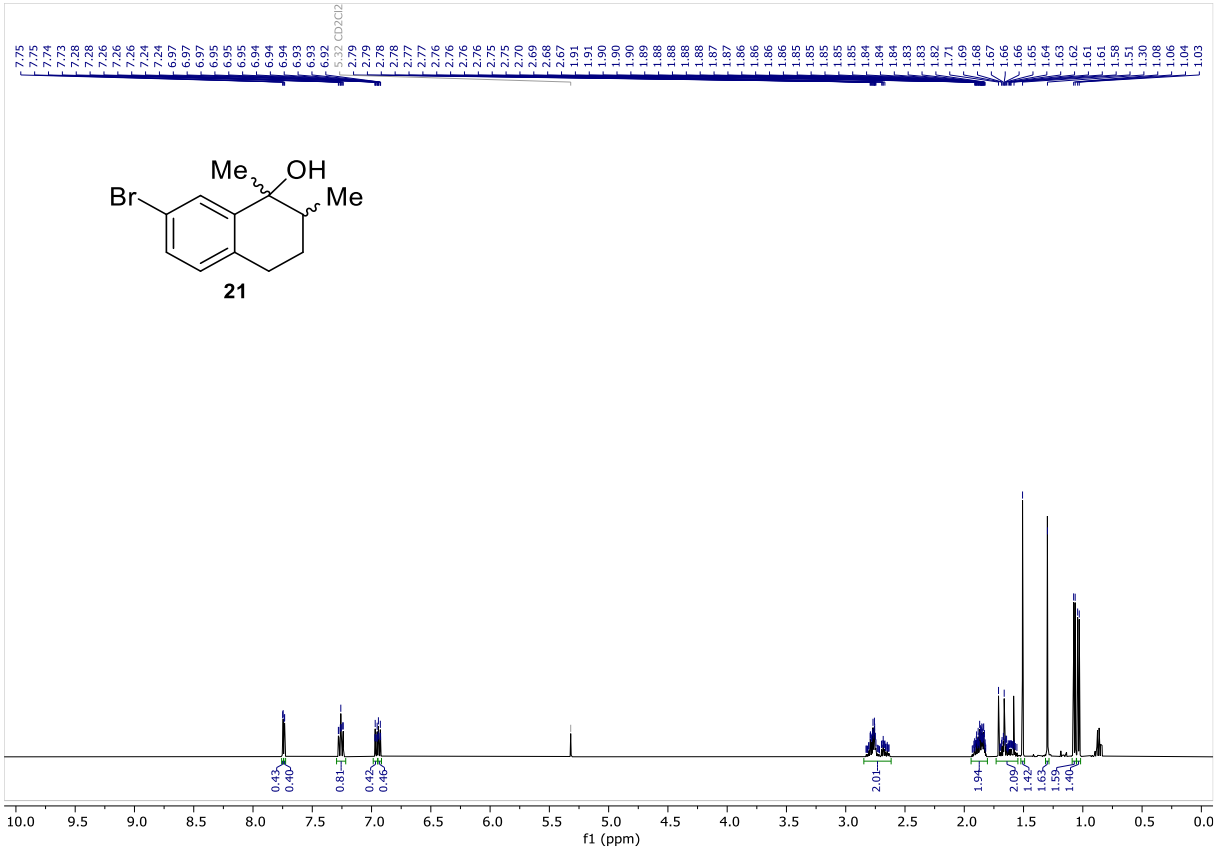
Supplementary Fig. 123. ^{13}C NMR Spectrum of tetralol 19 (CD_3CN, 126 MHz, 20 °C)



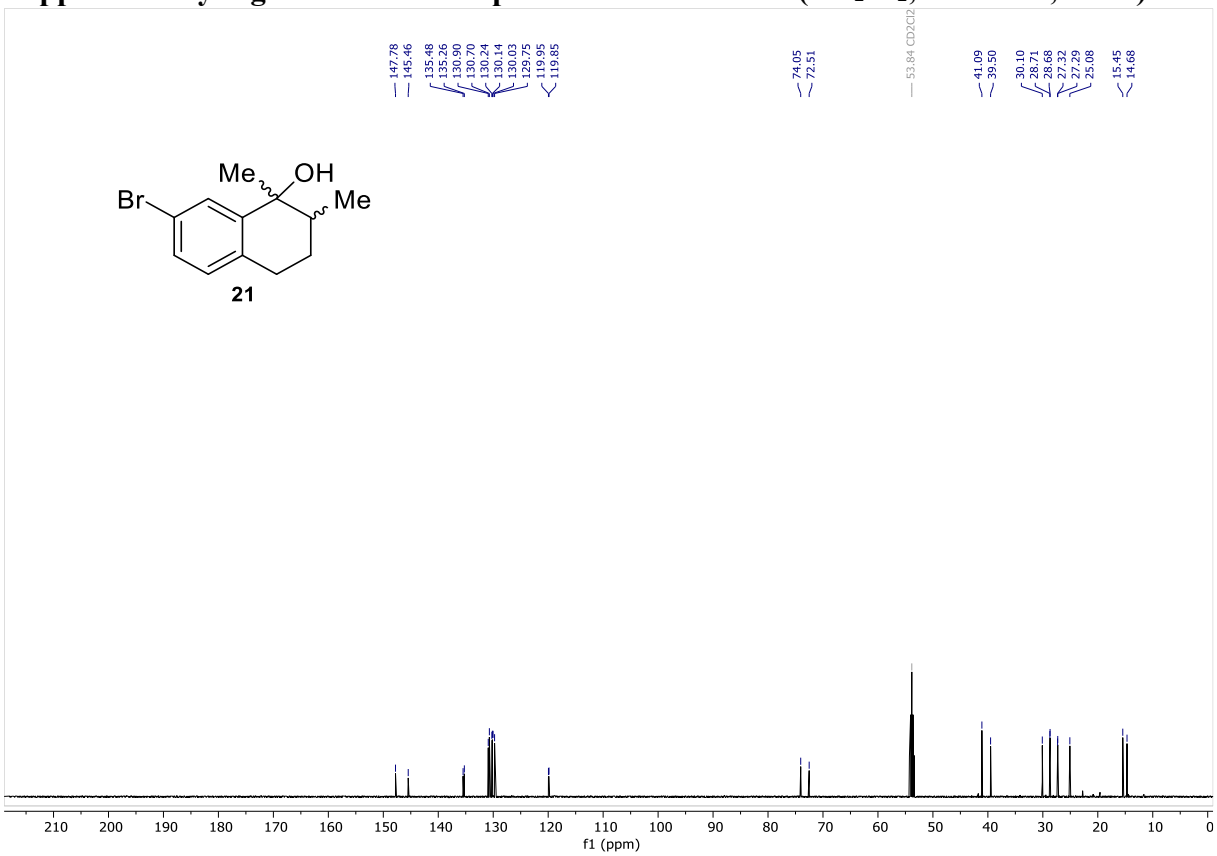
Supplementary Fig. 124. ^{1}H NMR Spectrum of tetralol 20 (DMSO-d$_6$, 500 MHz, 20 °C)



Supplementary Fig. 125. ^{13}C NMR Spectrum of tetralol 20 (DMSO-d$_6$, 126 MHz, 20 °C)



Supplementary Fig. 126. ^{1}H NMR Spectrum of tetralol 21 (CD_2Cl_2, 500 MHz, 20 °C)



Supplementary Fig. 127. ^{13}C NMR Spectrum of tetralol 21 (CD_2Cl_2, 126 MHz, 20 °C)

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