Supporting Information

Stereoselective Rh-catalyzed hydrogenative desymmetrization of achiral substituted 1,4-dienes

Héctor Fernández-Pérez,[†,§] Joan R. Lao,[†,§] and Anton Vidal-Ferran*[,†,‡,§]

[†]*Institute of Chemical Research of Catalonia (ICIQ), Av. Països Catalans, 16, 43007 Tarragona, Spain*

[‡]*Catalan Institution for Research and Advanced Studies (ICREA), P. Lluís Companys, 23, 08010 Barcelona, Spain*

[§]*The Barcelona Institute of Science and Technology, Av. Països Catalans, 16, 43007 Tarragona, Spain*

Table of Contents

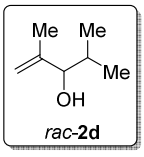
(A) General considerations

Air- and moisture-sensitive manipulations or reactions were carried out in an inert atmosphere using anhydrous solvents (Solvent Purification System), either in a glove box or with standard Schlenk techniques. Glassware was dried under vacuum and was heated with a hot air gun before use. Silica gel 60 (230–400 mesh) was used for column chromatography. NMR spectra were recorded on 400 MHz or 500 MHz spectrometers in $CDCl_3$, unless otherwise cited. ^{1}H NMR and $^{13}C\{^1H\}$ NMR chemical shifts are quoted in ppm relative to the residual solvent peaks. High-resolution mass spectra (HRMS) were recorded using the ESI or EI ionization method in positive mode, unless otherwise cited. HPLC analyses were performed using a chromatograph equipped with a diode array UV detector (DAD). Melting points were determined by DSC. IR spectra were recorded using Attenuated Total Reflection (ATR) technique. Optical rotations were measured on a polarimeter.

(B) Preparation of substrates 1b–f

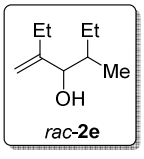
Dienes **1d**,[1] **1e**,[2] **1f**,[3] and silyl-ether derivatives **1b**[4] and **1c**[4] were prepared following an already reported synthetic methodology, which was efficiently reproduced. The spectroscopic data was consistent with the reported data.

General procedure for *rac*-2d and *rac*-2e: Products *rac*-**2d** and *rac*-**2e** were prepared following a method previously reported in the literature,[5] with the following modifications: Under inert conditions, the corresponding aldehyde (5.98 mmol) was added to a stirring solution of the organomagnesium bromide (*ca*. 7.18 mmol) in anhydrous THF (25 mL) at 0 °C. Stirring was continued for 1 h at 0 °C and the reaction mixture was then allowed to reach rt, and stirred for additional 18 h. The reaction was quenched at 0 °C by the slow addition of *ca*. 20 mL of a saturated aqueous solution of NH_4Cl. The resulting crude was then extracted with Et_2O (3 x 80 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo* to afford the crude as a yellowish oil. Further purification by silica gel column chromatography yielded the desired product as a colorless liquid.



rac-**2d**

***rac*-2,4-dimethylpenten-1-en-3-ol[5] (*rac*-2d):** The general procedure was efficiently applied starting from isopropylmagnesium bromide and methacrolein to afford the desired product as a colorless liquid (1.77 g, 22% isol. yield). The spectral data was consistent with that reported.[5]



rac-**2e**

***rac*-3-methyleneheptan-4-ol (*rac*-2e):** The general procedure was efficiently applied, starting from 2-butenyl-magnesium bromide [6] and 2-methylbutyraldehyde to afford the desired product (0.41 g, 40% isol. yield) as a colorless liquid. The isolated product was obtained as a mixture of *syn*-**2e** and *anti*-**2e** diastereoisomers in a *syn:anti* 60:40 ratio. ^{1}H NMR (400 MHz, $CDCl_3$) *syn*-**2e**: δ 5.01–5.00 (m, 1H, C*H*H), 4.90–4.89 (m, 1H, CH*H*), 3.94 (d, $J = 5.2$ Hz, 1H, CH), 2.17–1.89 (m,

2H, CH_2), 1.59–1.51 (m, 1H, CH), 1.47–1.37 (m, 1H, C*H*H), 1.25–1.14 (m, 1H, CH*H*), 1.07 (t, J = 7.4 Hz, 3H, CH_3), 0.92 (t, J = 7.4 Hz, 3H, CH_3), 0.86 (d, J = 6.7 Hz, 3H, CH_3); *anti*-**2e**: δ 4.98–4.97 (m, 1H, C*H*H), 4.89–4.88 (m, 1H, CH*H*), 3.82 (d, J = 7.3 Hz, 1H, CH), 2.17–1.89 (m, 2H, CH_2), 1.72–1.63 (m, 1H, C*H*H), 1.59–1.51 (m, 1H, CH), 1.14–1.10 (m, 1H, CH*H*), 1.07 (t, J = 7.4 Hz, 3H, CH_3), 0.90 (t, J = 7.4 Hz, 3H, CH_3), 0.82 (d, J = 6.8 Hz, 3H, CH_3); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) *syn*-**2e**: δ 152.7 (C), 108.7 (CH_2), 78.5 (CH), 37.5 (CH), 26.5 (CH_2), 24.5 (CH_2), 13.3 (CH_3), 12.2 (CH_3), 11.8 (CH_3); *anti*-**2e**: δ 152.6 (C), 109.7 (CH_2), 80.6 (CH), 37.7 (CH), 24.2 (CH_2), 23.6 (CH_2), 15.7 (CH_3), 12.1 (CH_3), 11.3 (CH_3); HRMS (EI^+) *m/z* calcd for C_9H_{17} $[M-OH]^+$ 125.1330, found 125.1331; IR (neat, cm^{-1}) υ 3392 ($O-H_{st}$), 1646 ($C=C_{st}$).

(C) General procedure for catalytic hydrogenative desymmetrizations

The following procedure was performed inside a nitrogen filled dry box: A solution of the Rh-precursor $[Rh(nbd)_2]BF_4$ (2 μmol), the P–OP ligand (2.2 μmol) and the 1,4-diene (0.2 mmol) in anhydrous and degassed CH_2Cl_2 were placed in a glass vessel. In all cases the molar concentration of a given substrate was adjusted to 0.1 M by adding the required amount of CH_2Cl_2. The reaction mixtures were loaded under N_2 into an autoclave reactor or in a sealed glass vessel equipped with septa. The autoclave was pressurized with N_2 gas (10 bar) without stirring, and the reaction mixtures were placed into a precooled bath (at the required temperature) and were allowed to equilibrate for *ca*. 20 min. In the case 1 bar experiments, an atmosphere of N_2 was maintained during the temperature equilibration. The autoclave was then slowly depressurized, purged three times with H_2 gas (3 bar) or with a balloon filled with H_2 (for low pressure experiments) and finally pressurized at the required pressure of H_2 gas. The general work-up was: rapid filtration on a short pad of silica gel, elution with EtOAc (1.5 mL) and solvent removal *in vacuo*. Conversions, chemo- and diastereo-selectivities were determined by ^1H NMR from the reaction crude. The enantiomeric excesses were determined by chiral HPLC after derivatization into the corresponding benzoate derivatives **4**.

(D) General procedure for derivatization of compounds 2 into benzoate ester derivatives 4

Reaction products bearing silyl-ether groups (**2b** and **2c**) were subjected to desilylation prior to the benzoylation step.[4]

Method A: Under inert conditions, Et_3N (3.92 mmol) was slowly added to a stirring solution of the corresponding alkene (3.27 mmol), DMAP (0.16 mmol) and Bz_2O (3.94 mmol) in anhydrous CH_2Cl_2 (20 mL). The resulting solution was stirred for 18 h under the same conditions. After that time, the reaction crude was directly concentrated *in vacuo* to afford the crude product as a yellowish oil. Further purification by silica gel column chromatography (using a solvent mixture of *n*-hexane:EtOAc or *n*-pentane:MTBE) yielded the desired product as a colorless liquid.

Method B: Under inert conditions, LiHMDS (2.94 mmol) was carefully added to a stirring solution of the corresponding alkene (1.96 mmol) in anhydrous THF (1.6 mL) at rt. The reaction mixture was stirred for 30 min and BzCl (2.94 mmol) was then added, and the resulting solution was stirred for 16 h under the same conditions. After that time, the reaction was quenched by the addition of water (5.0 mL) and extracted with EtOAc (3 x 5 mL), washed with brine (10 mL), dried over anhydrous $MgSO_4$, filtered and concentrated *in vacuo.* Further purification by silica gel column chromatography (using a solvent mixture of Cy:EtOAc) yielded the desired product.

The racemic and/or enantiopure benzoate ester derivatives **4a**, **4d**, and **4e** were prepared following *Method A*. On the other hand, the racemic and/or enantiopure benzoate ester derivative **4f** was prepared following *Method B*.

(E) Characterization and determination of the enantiomeric excess of reaction products 4

(*S*)-pent-1-en-3-yl benzoate[7] (**4a**; entries 1–3, Table 3): The spectral data was consistent with that reported. [Lit:[7] $[\alpha]^{27}_{D} = +43.8$ (*c* 1.5, $CHCl_3$) for 98% ee (*S*)]. Product **4a** (from **1a**; entry 1, Table 3): 84% ee (*S*), $[\alpha]^{27}_{D} = +31.8$ (*c* 0.28, $CHCl_3$); product **4a** (from **1b**; entry 2, Table 3): 87% ee (*S*); product **4a** (from **1c**; entry 3, Table 3): 80% ee (*S*). HPLC conditions for the enantiomers:[7] Daicel Chiralcel® (25 cm x 0.46 cm) OB-H, 99.5:0.5 *n*-heptane/2-propanol, 0.5 mL/min, 210 nm. Retention times for the enantiomers: 11.9 min (*S*)-**4a** and 13.3 min (*R*)-**4a**.

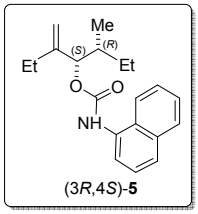
(*S*)-2,4-dimethylpent-1-en-3-yl benzoate (**4d**; entry 4, Table 3): 59% ee (*S*), $[\alpha]^{28}_{D} = +18.3$ (*c* 0.84, $CHCl_3$). HPLC conditions: Daicel Chiralpak® (25 cm x 0.46 cm) IA, 100% *n*-pentane, 1.0 mL/min, 210 nm. Retention times for the enantiomers: 10.0 min (*R*)-**4d** and 10.8 min (*S*)-**4d**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11–8.08 (m, 2H, CH), 7.60–7.56 (m, 1H, CH), 7.49–7.45 (m, 2H, CH), 5.18 (d, J = 7.2 Hz, 1H, CH), 5.03–5.02 (m, 1H, CH), 4.98–4.97 (m, 1H, CH), 2.15–2.07 (m, 1H, CH), 1.80–1.79 (m, 3H, CH_3), 1.00 (dd, J = 20.9 Hz, J = 6.7 Hz, 6H, CH_3); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.8 (C=O), 142.2 (C), 132.8 (CH), 130.6 (C), 129.5 (CH), 128.3 (CH), 113.7 (CH_2), 82.8 (CH–OBz), 29.9 (CH), 19.1 (CH_3), 18.5 (CH_3), 17.8 (CH_3); HRMS (ESI$^+$) *m/z* calcd for $C_{14}H_{18}NaO_2$ $[M+Na]^+$ 241.1199, found 241.1203; IR (neat, cm^{-1}) υ 1719 ($C{=}O_{st}$), 1286 ($C{-}O_{st}$).

(3*R*,4*S*)-3-methyl-5-methyleneheptan-4-yl benzoate (**4e**; entry 5, Table 3): 70% ee (+), $[\alpha]^{27}_{D} = +32.5$ (*c* 0.43, $CHCl_3$). HPLC conditions: Daicel Chiralcel® (25 cm x 0.46 cm) OD-H, 100% *n*-pentane, 1.0 mL/min, 210 nm. Retention times for the *syn*-enantiomers: 8.8 min (3*S*,4*R*)-**4e** and 9.4 min (3*R*,4*S*)-**4e**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09–8.06 (m, 2H, CH), 7.58–7.54 (m, 1H, CH), 7.47–7.43 (m, 2H, CH), 5.38 (d, J = 5.4 Hz, 1H, CH), 5.02–5.01 (m, 1H, C*H*H), 4.94–4.93 (m, 1H, CH*H*), 2.14–2.07 (m, 2H, CH_2), 1.91–1.77 (m, 1H, CH), 1.51–1.41 (m, 1H, C*H*H), 1.30–1.18 (m, 1H, CH*H*), 1.10 (t, J = 7.4 Hz, 3H, CH_3), 0.99 (d, J = 6.8 Hz, 3H, CH_3), 0.95 (t, J = 7.3 Hz, 3H, CH_3); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.79 (C=O), 148.1 (C), 132.82 (CH), 130.69 (C), 129.6 (CH), 128.38 (CH), 110.1 (CH_2), 80.0 (CH), 36.7 (CH), 26.3 (CH_2), 25.0 (CH_2), 14.0 (CH_3), 12.0 (CH_3), 11.7 (CH_3); HRMS (ESI$^+$) *m*/*z* calcd for $C_{16}H_{22}NaO_2$ $[M+Na]^+$ 269.1512, found 269.1500; IR (neat, cm^{-1}) υ 1718 ($C{=}O_{st}$), 1649 ($C{=}C_{st}$).

(*S*)-3-methylpent-1-en-3-yl benzoate (**4f**; entry 6, Table 3): 92% ee (*S*), $[\alpha]^{27}_{D} = +15.8$ (*c* 0.24, $CHCl_3$). HPLC conditions: Daicel Chiralcel® (25 cm x 0.46 cm) OD-H, 100% *n*-pentane, 1.0 mL/min, 210 nm. Retention times for the enantiomers: 14.4 min (*R*)-**4f** and 15.5 min (*S*)-**4f**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04–8.01 (m, 2H, CH), 7.56–7.52 (m, 1H, CH), 7.44–7.41 (m, 2H, CH), 6.08 (dd, J = 17.5 Hz, J = 11.0 Hz, 1H, CH), 5.26 (dd, J = 17.5 Hz, J = 0.9 Hz, 1H,

C*H*H), 5.19 (dd, *J* = 11.0 Hz, *J* = 0.9 Hz, 1H, CH*H*), 2.05–1.91 (m, 2H, CH_2), 1.67 (s, 3H, CH_3), 0.96 (t, *J* = 14.8 Hz, 3H, CH_3); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 165.3 (C=O), 141.7 (CH), 132.6 (CH), 131.7 (C), 129.5 (CH), 128.3 (CH), 113.4 (CH_2), 84.0 (C), 32.4 (CH_2), 23.2 (CH_3), 8.0 (CH_3); HRMS (ESI^+) *m/z* calcd for $C_{13}H_{16}NaO_2$ $[M+Na]^+$ 227.1043, found 227.1039; IR (neat, cm^{-1}) υ 1714 ($C=O_{st}$), 1644 ($C=C_{st}$).

(F) Preparation of 1-naphthyl urethane derivative 5



(3*R*,4*S*)-3-methyl-5-methyleneheptan-4-yl-1-naphthyl urethane (5): Under inert conditions, LiHMDS (117 μL, 1 M, 0.117 mmol) was carefully added to a stirring solution of the enantioenriched (70% ee; entry 5, Table 3) *syn*-**2e** (16.6 mg, 0.117 mmol) and 1-naphthyl isocyanate (18.8 μL, 98%, 0.129 mmol) in THF (1.5 mL), at rt. Stirring was continued for 2 h and the resulting suspension was evaporated under reduced pressure to yield a yellowish oil. Further purification by silica gel column chromatography (using a solvent mixture of *n*-pentane:MTBE) afforded the desired product as a white solid (22.6 mg, 62% isol. yield), mp = 56–57 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.92–7.87 (m, 3H, CH), 7.69–7.66 (m, 1H, CH), 7.58–7.45 (m, 3H, CH), 6.97 (bs, 1H, NH), 5.18 (d, *J* = 5.8 Hz, 1H, CH), 5.06 (s, 1H, C*H*H), 4.98 (s, 1H, CH*H*), 2.11–2.04 (m, 2H, CH_2), 1.76–1.72 (m, 1H, C*H*H), 1.50–1.43 (m, 1H, CH*H*), 1.28–1.09 (m, 5H, CH_2 and CH_3), 0.99–0.74 (m, 6H, CH_3); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 154.1 (C=O), 148.4 (C), 134.0 (C), 132.6 (C), 128.8 (CH), 126.1 (CH), 125.9 (CH), 125.8 (CH), 124.9 (C), 120.4 (C),110.2 (CH_2), 81.0 (CH), 36.6 (CH), 26.1 (CH_2), 24.9 (CH_2), 14.0 (CH_3), 11.9 (CH_3), 11.6 (CH_3); HRMS (ESI^+) *m/z* calcd for $C_{20}H_{25}NNaO_2$ $[M+Na]^+$ 334.1777, found 334.1771; $[\alpha]_{25}^{D}$ = +15.8 (*c* 0.03, $CHCl_3$); IR (neat, cm^{-1}) υ 3283 ($N–H_{st}$), 3053 ($C=–H_{st}$), 1693 ($C=O_{st}$), 1529 ($C_{Ar}–C_{Ar,st}$).

(G) Single crystal X-ray structure determination of product 5

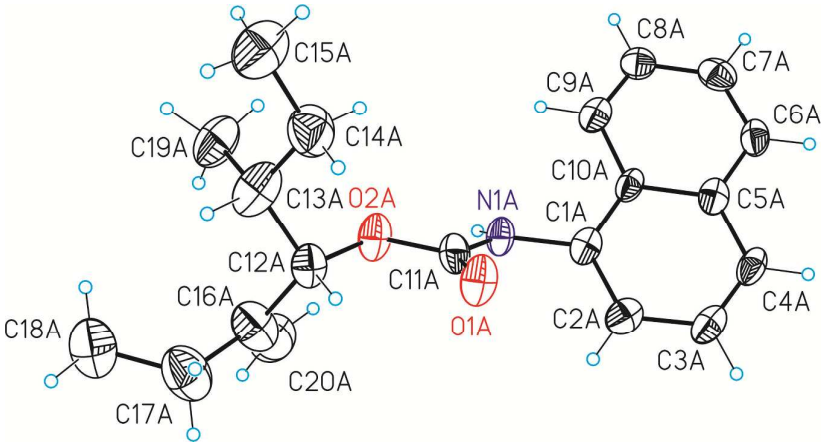


Figure SI1. ORTEP Plot (thermal ellipsoids shown 50% probability level) of **5**

Crystal preparation: Single crystals of compound **5** were grown by melting the product (50–60 °C) followed by seeding when cooled at 45 °C. The crystals were allowed to grow under these conditions for 18 h. The resulted crystals were immersed in perfluoropolyether oil for manipulation.

Data collection: Crystal structure determination for **5** was carried out using a Apex DUO diffractometer equipped with a Kappa 4-axis goniometer, an APEX II 4K CCD area detector, a Microfocus Source E025 IuS using MoK_α radiation, Quazar MX multilayer Optics as monochromator and an Oxford Cryosystems low temperature device Cryostream 700 plus (T = −173 °C). Full-sphere data collection was used with ω and φ scans. *Programs used:* Data collection APEX-2, [8] data reduction Bruker Saint [9] V/.60A and absorption correction SADABS.[10]

Structure Solution and Refinement: Crystal structure solution was achieved using the computer program SHELXTL.[11] Visualization was performed with the program SHELXle.[12] Missing atoms were subsequently located from difference Fourier synthesis and added to the atom list. Least-squares refinement on F^2 using all measured intensities was carried out using the program SHELXL 2015.[1113] All non-hydrogen atoms were refined including anisotropic displacement parameters.

Comments to the structure of 5: The asymmetric unit contains two independent molecules of the same compound with the same relative stereochemistry. Due to the low quality of the crystals obtained it was not possible to determine the absolute configuration of this molecule using anomalous dispersion effects.

Table SI1. Crystal data and structural parameters for 5

Compound		**5**	
Formula	$C_{20}H_{25}N_1O_2$	**Z**	4
Formula weight	311.41	**ρ (g/cm^3)**	1.189
Crystal size (mm^3)	0.25 x 0.06 x 0.02	**μ (mm^{-1})**	0.076
Crystal colour	colourless	**θ_{max} (°)**	26.15
Temp (K)	100	**Reflec. measured**	21143
Crystal system	Monoclinic	**Unique reflections**	4734 [R_{int} = 0.0796]
Space group	$P2_1$	**Absorpt. correct.**	SADABS
A (Å)	9.3889(11)	**Trans. min/max**	0.998/0.665
B (Å)	11.6277(14)	**Parameters/Restrains**	426/3
C (Å)	16.0269(18)	**R1/wR2 [I>2σ(I)]**	0.0903/0.2405
α (deg)	90	**R1/wR2 [all data]**	0.1277/0.2703
β (deg)	96.069(4)	**Goodness-of-fit (F^2)**	1.035
γ (deg)	90	**Peak/hole (e/Å^3)**	0.552/–0.320
V (Å^3)	1739.9(4)	**Absolute Structure Determination**	Not possible

(H) NMR spectra of desymmetrized products 2

H.1. Catalytic hydrogenative desymmetrization of substrate 1a

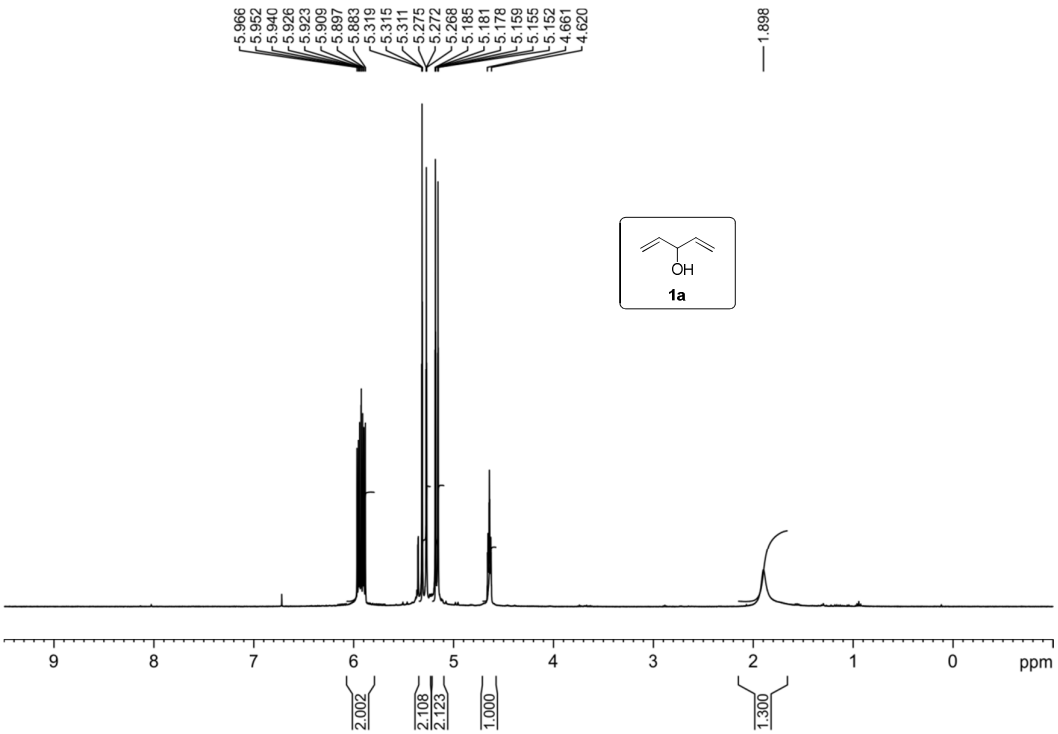


Figure SI2. ^{1}H NMR (400 MHz, CD_2Cl_2) of **1a**

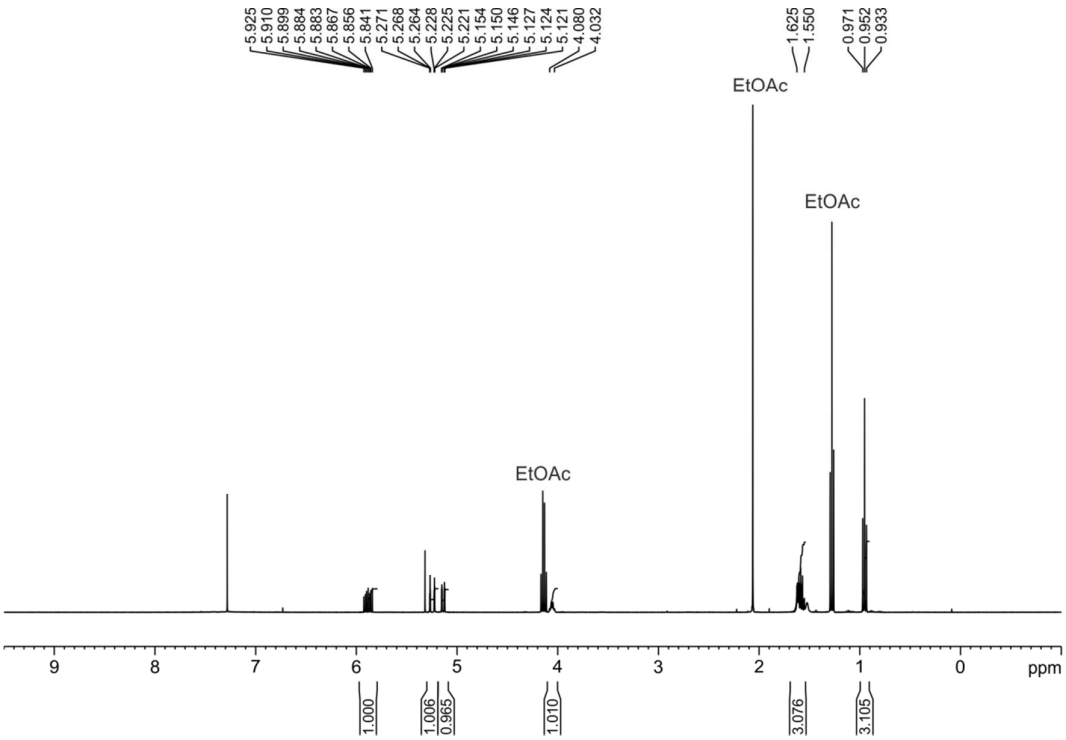


Figure SI3. ^{1}H NMR (400 MHz, $CDCl_3$) of the crude mixture for the desymmetrization of **1a** (Table 3, entry 1)

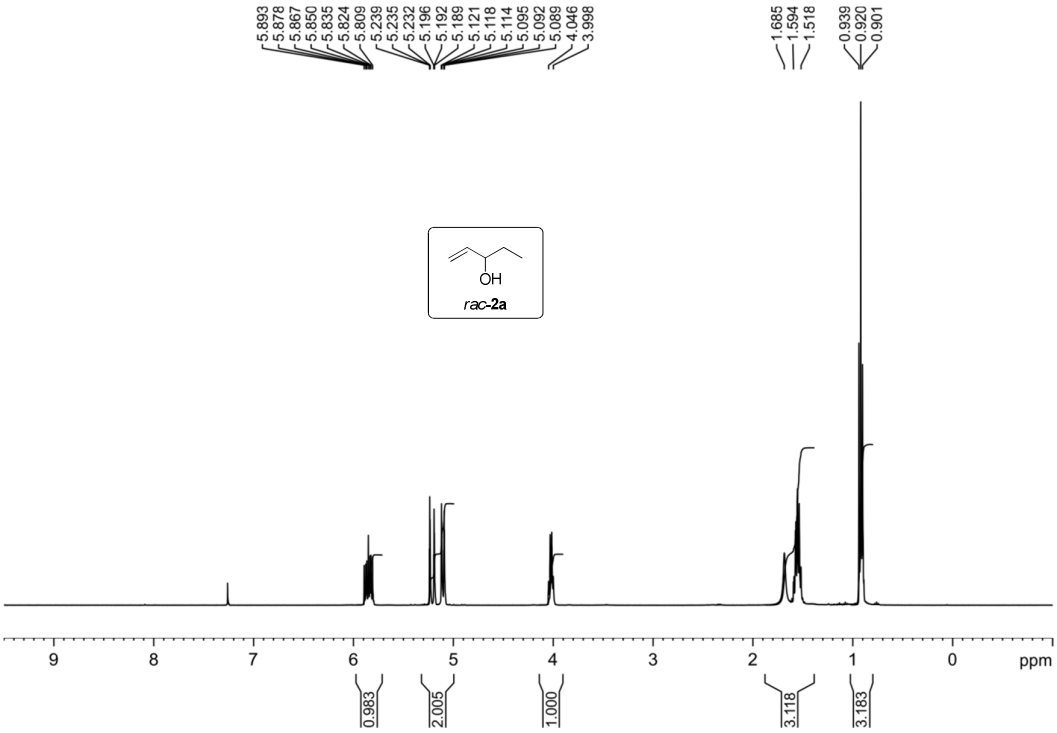


Figure SI4. ^{1}H NMR (400 MHz, $CDCl_3$) of *rac*-**2a**

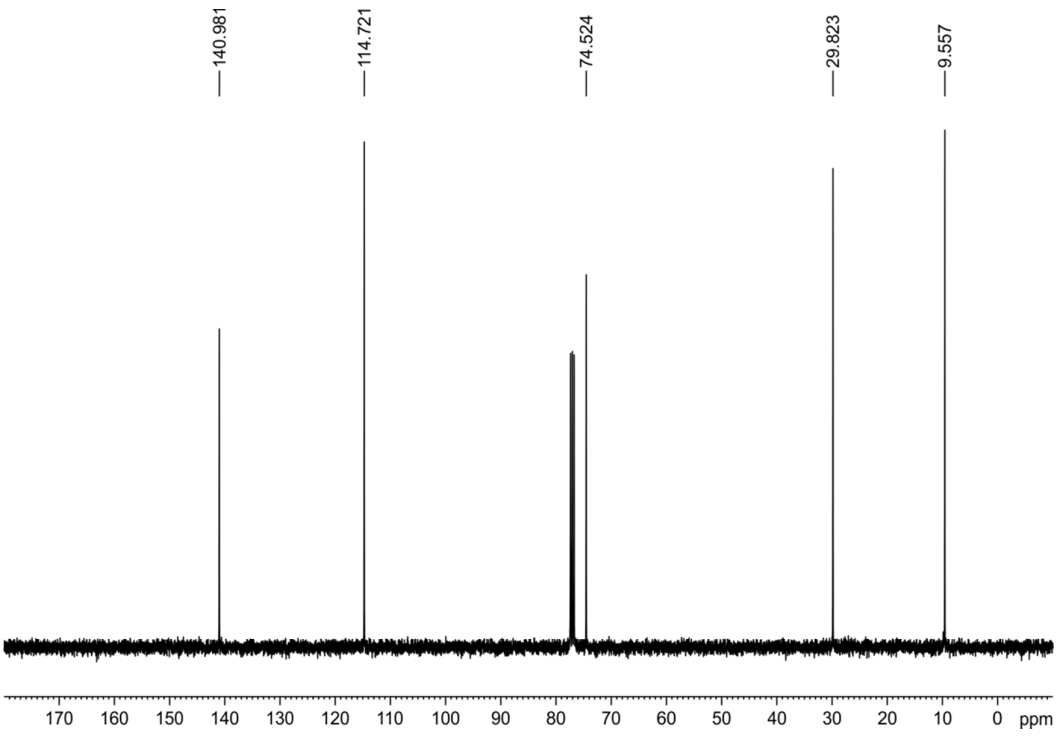


Figure SI5. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of *rac*-**2a**

H.2. Catalytic hydrogenative desymmetrization of substrate 1b

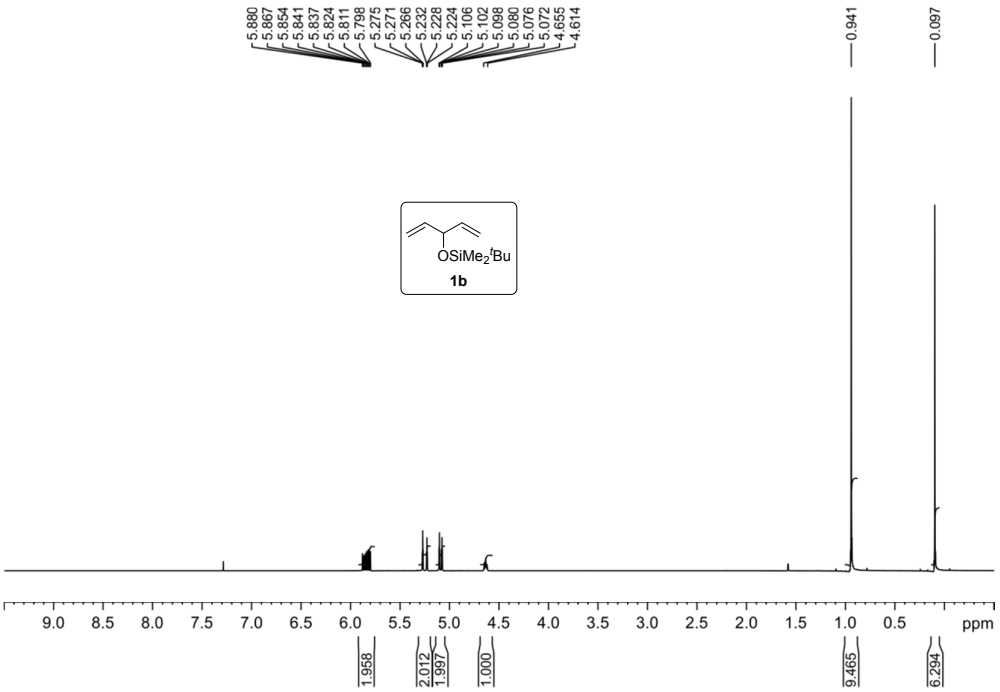


Figure SI6. ^{1}H NMR (400 MHz, $CDCl_3$) of **1b**

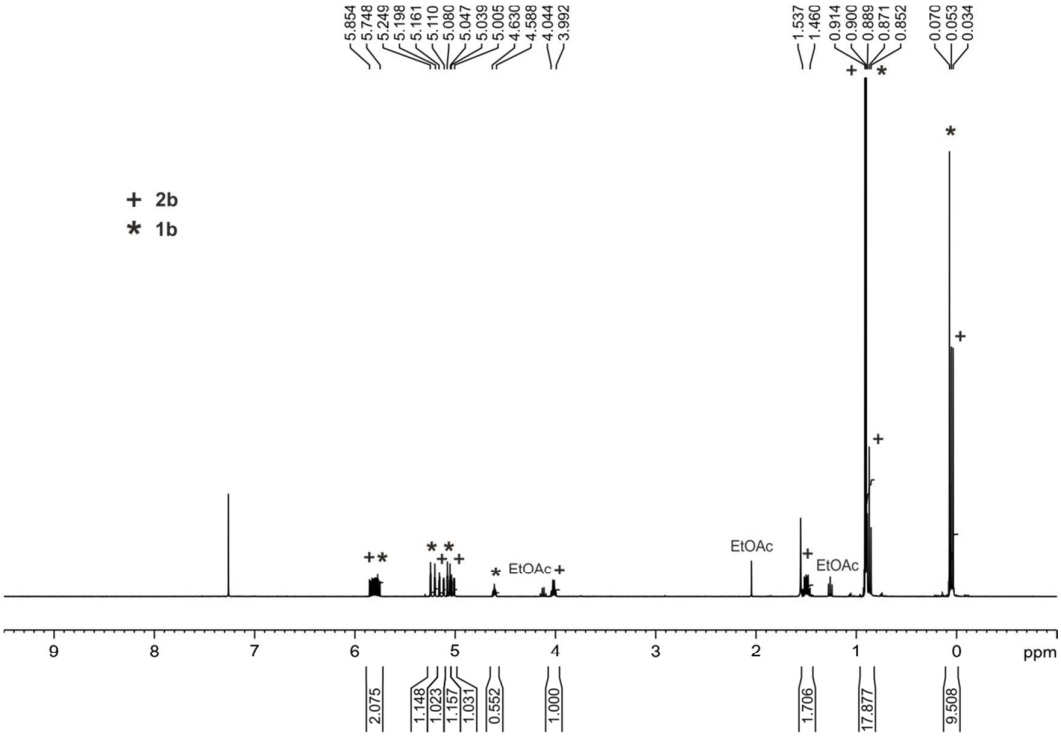


Figure SI7. ^{1}H NMR (400 MHz, $CDCl_3$) of the crude mixture for the desymmetrization of **1b** (Table 3, entry 2)

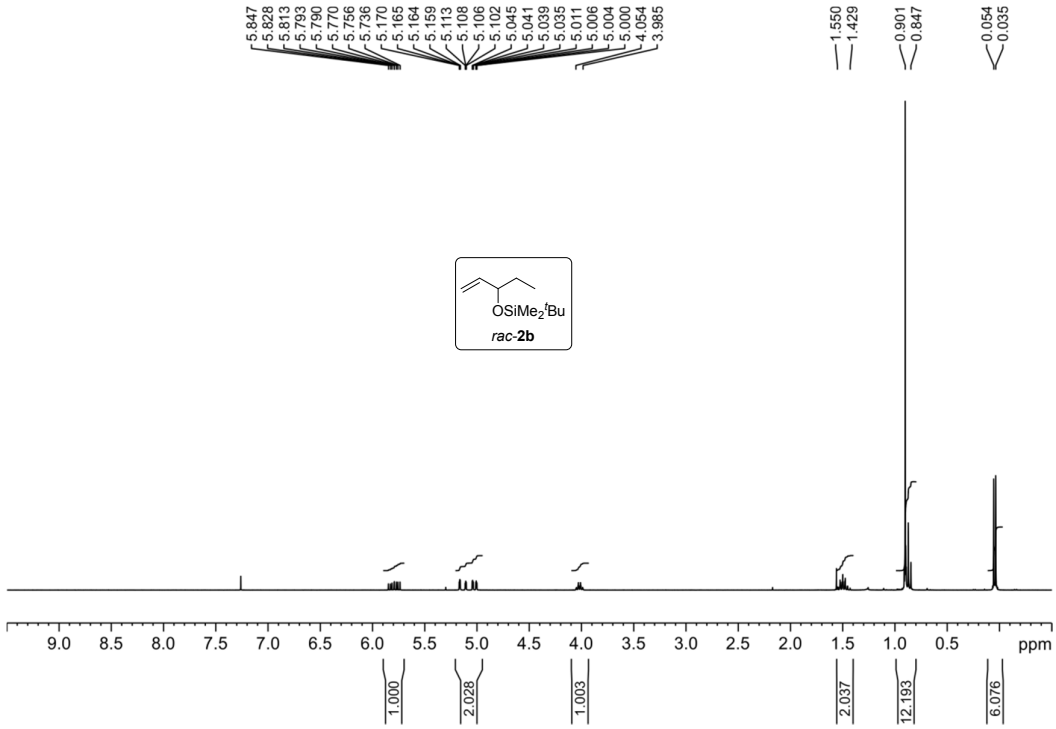


Figure SI8. ^{1}H NMR (300 MHz, $CDCl_3$) of *rac*-**2b**

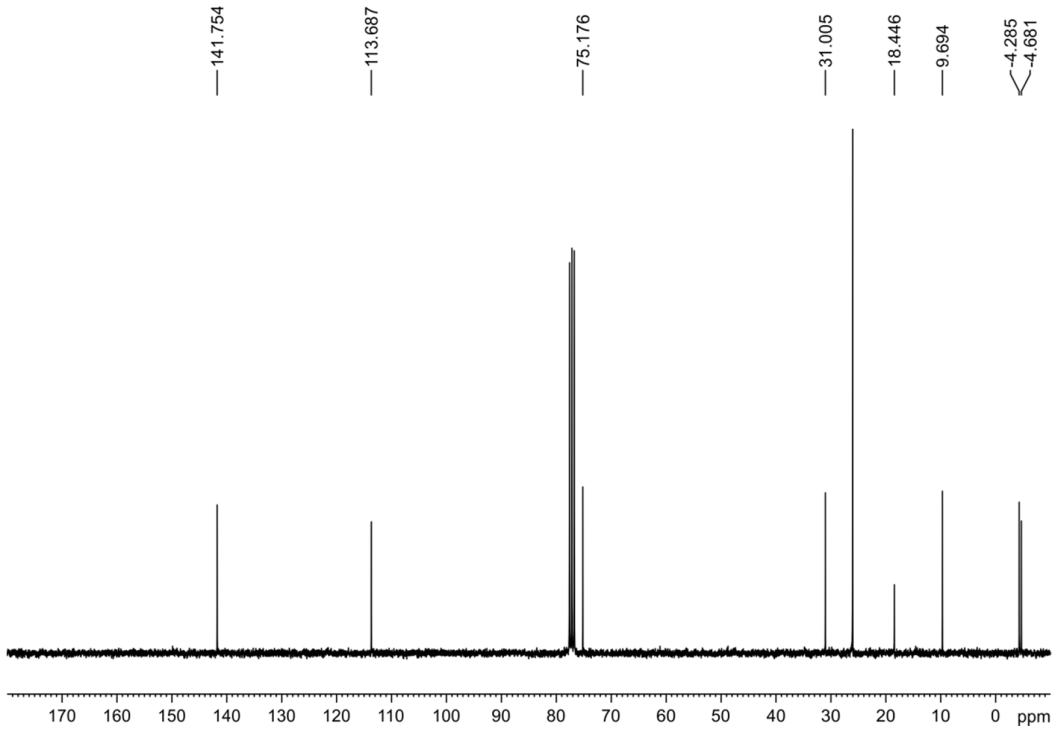


Figure SI9. $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of *rac*-**2b**

H.3. Catalytic hydrogenative desymmetrization of substrate 1c

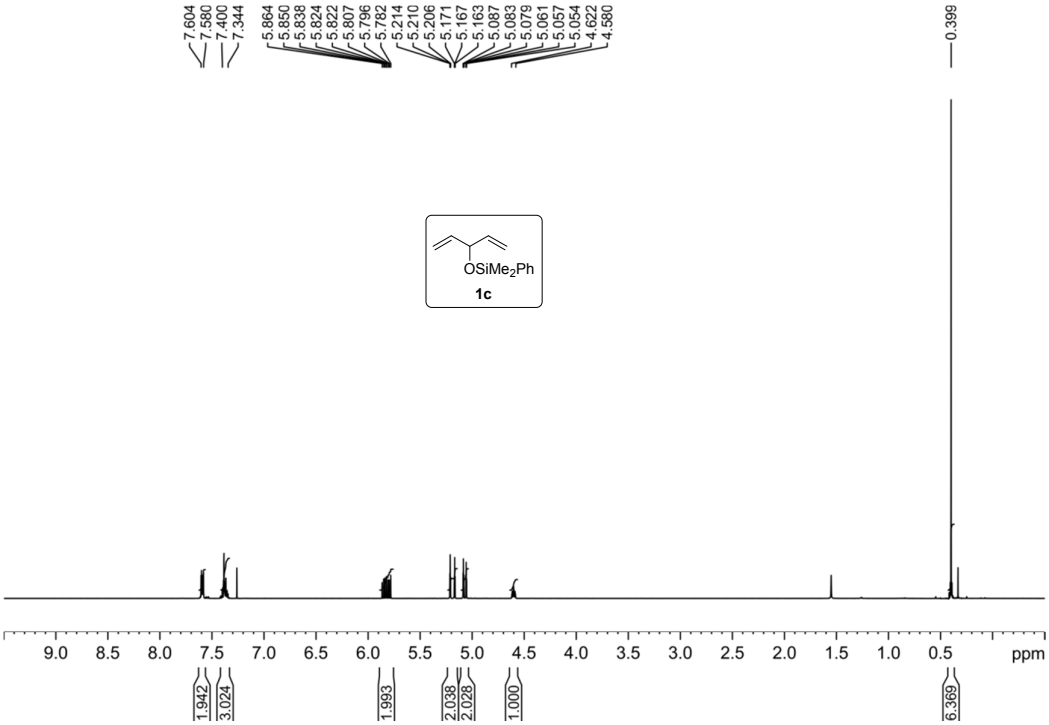


Figure SI10. ^{1}H NMR (400 MHz, $CDCl_3$) of **1c**

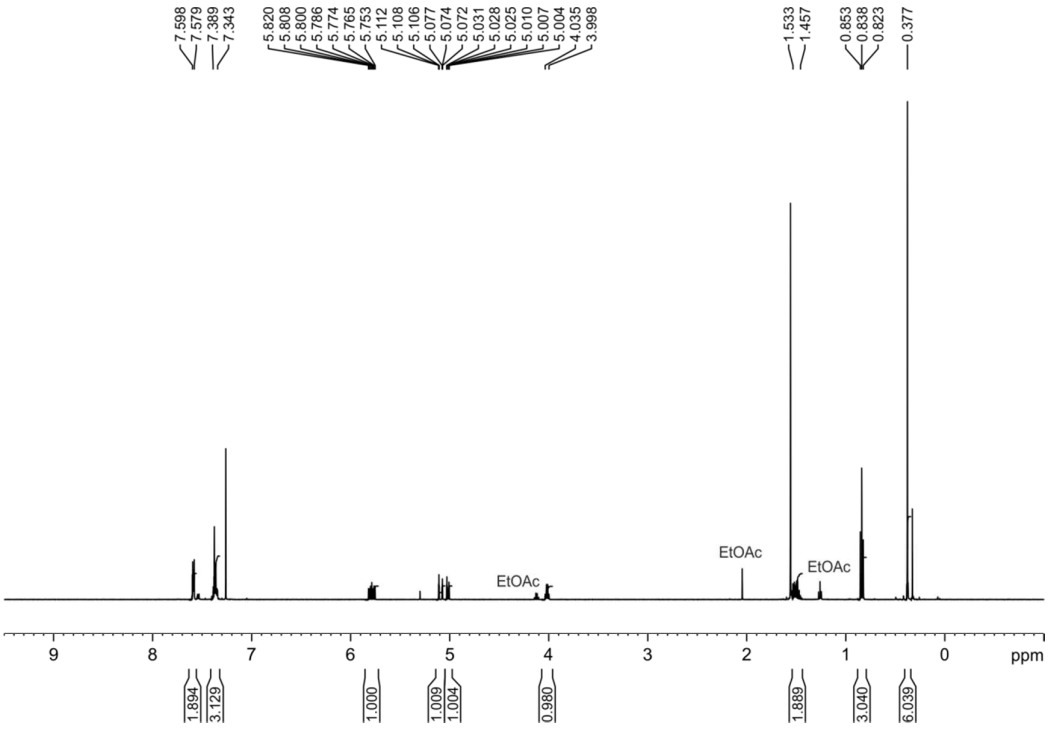


Figure SI11. ^{1}H NMR (400 MHz, $CDCl_3$) of the crude mixture for the desymmetrization of **1c** (Table 3, entry 3)

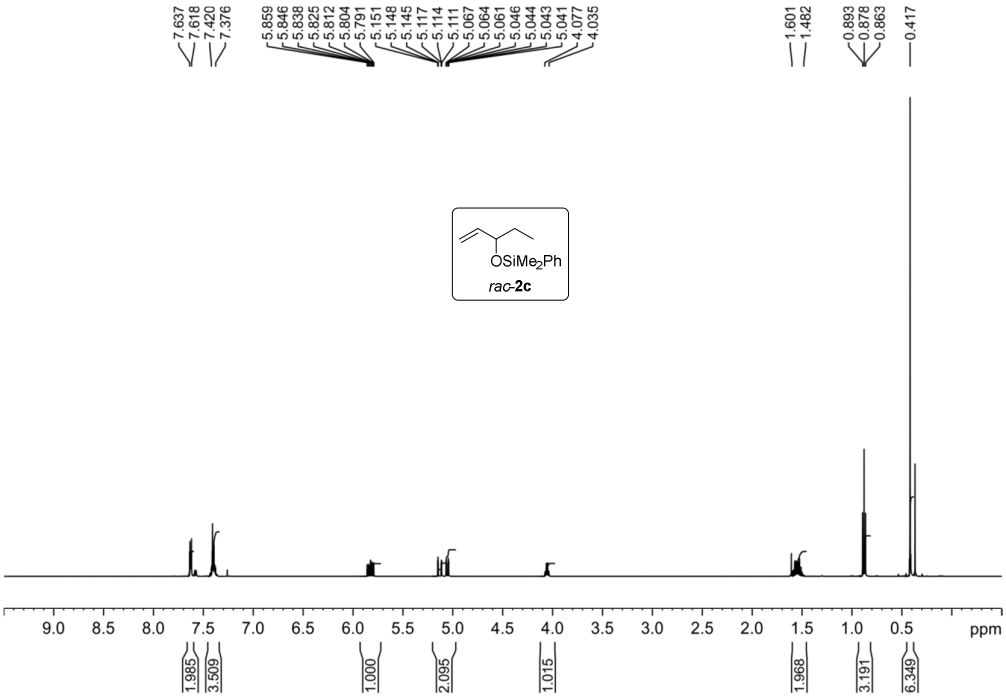


Figure SI12. ^{1}H NMR (500 MHz, $CDCl_3$) of *rac*-**2c**

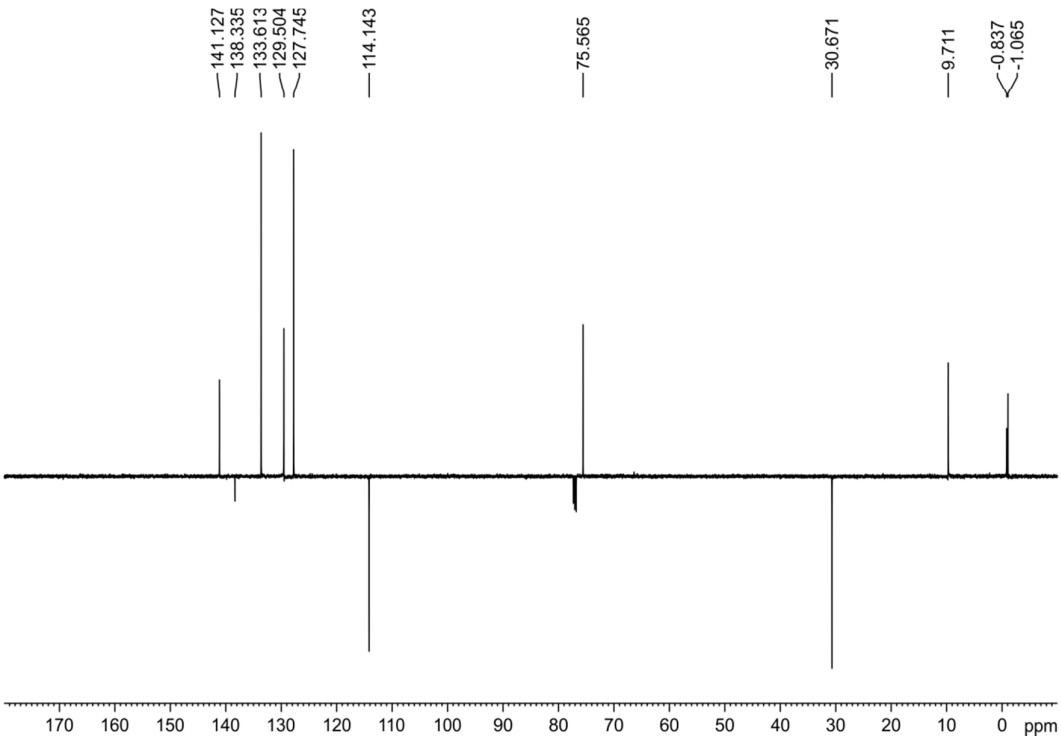


Figure SI13. $^{13}C\{^{1}H\}$ NMR as DEPTQ135 (125 MHz, $CDCl_3$) of *rac*-**2c**

H.4. Catalytic hydrogenative desymmetrization of substrate 1d

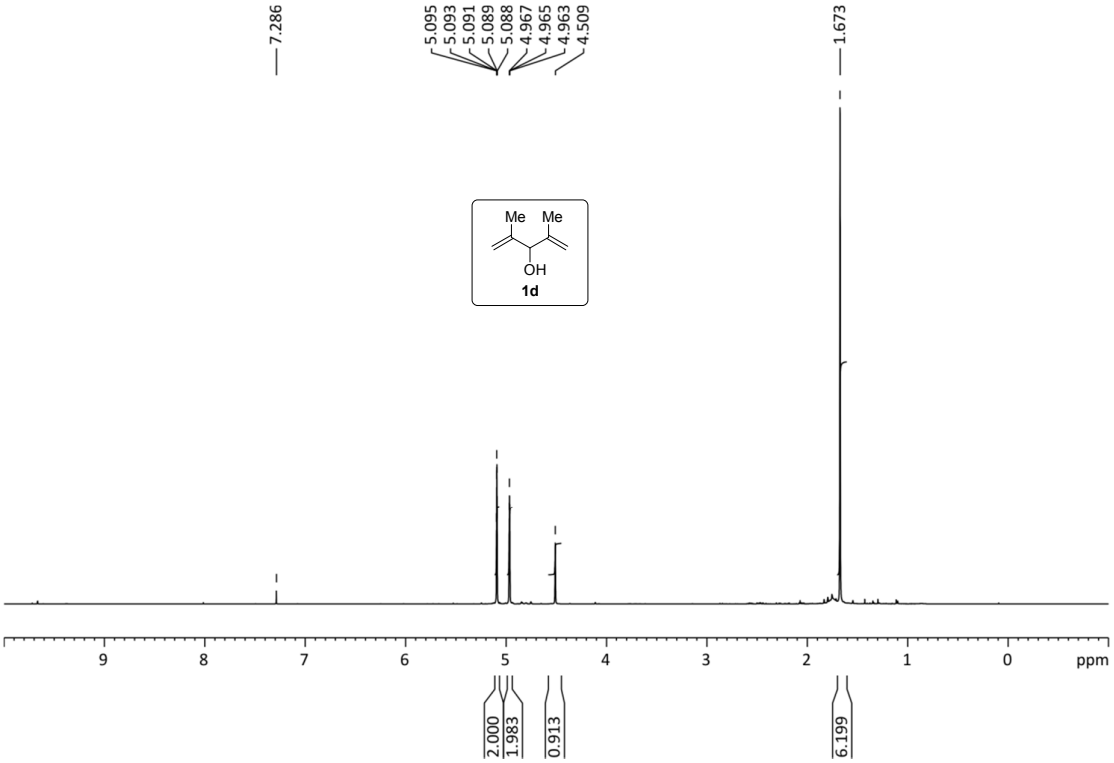


Figure SI14. ^{1}H NMR (500 MHz, $CDCl_3$) of **1d**

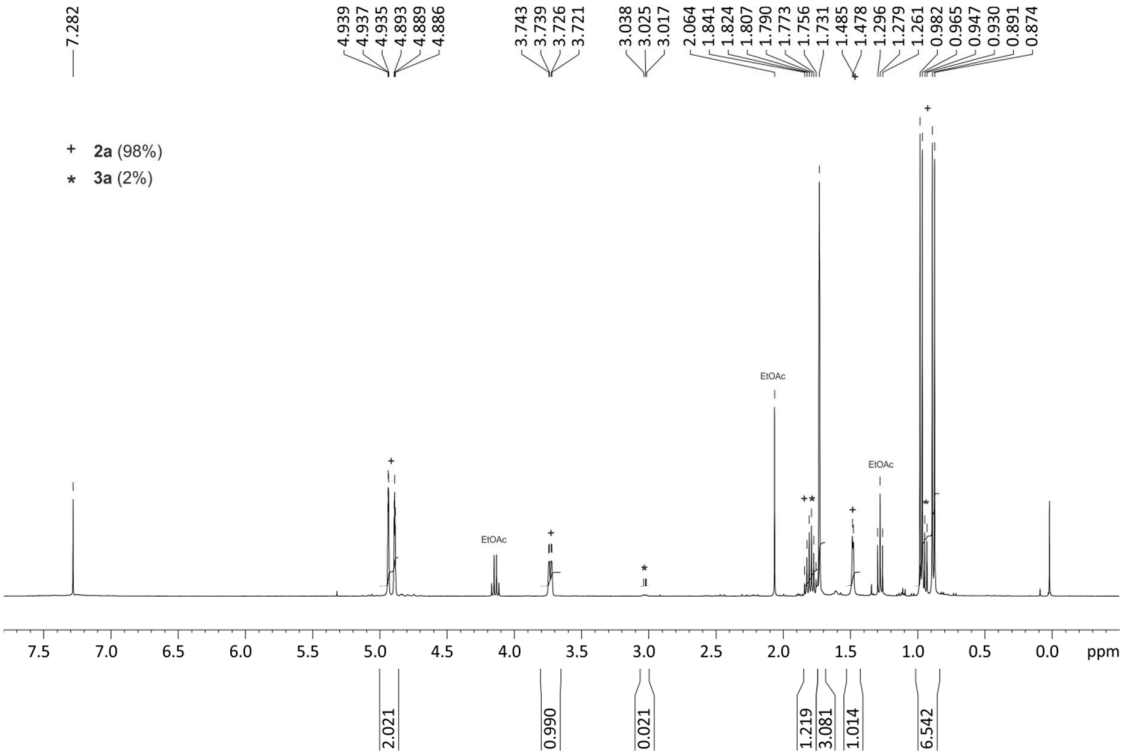


Figure SI15. ^{1}H NMR (400 MHz, $CDCl_3$) of the crude mixture for the desymmetrization of **1d** (Table 3, entry 4)

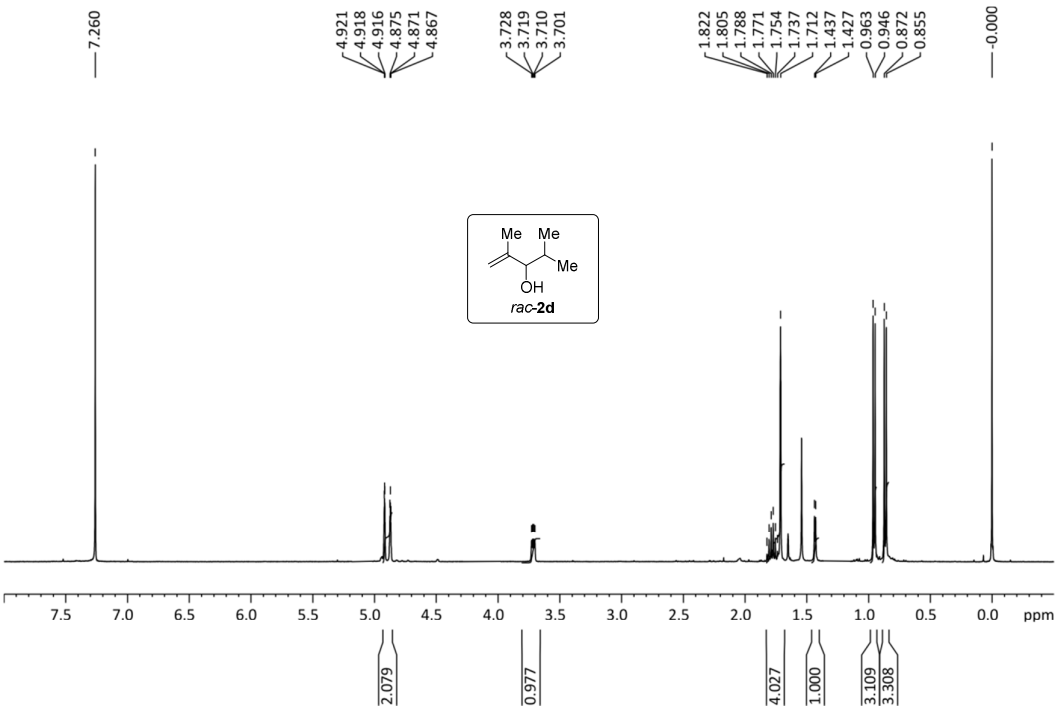


Figure SI16. ^{1}H NMR (400 MHz, $CDCl_3$) of *rac*-**2d**

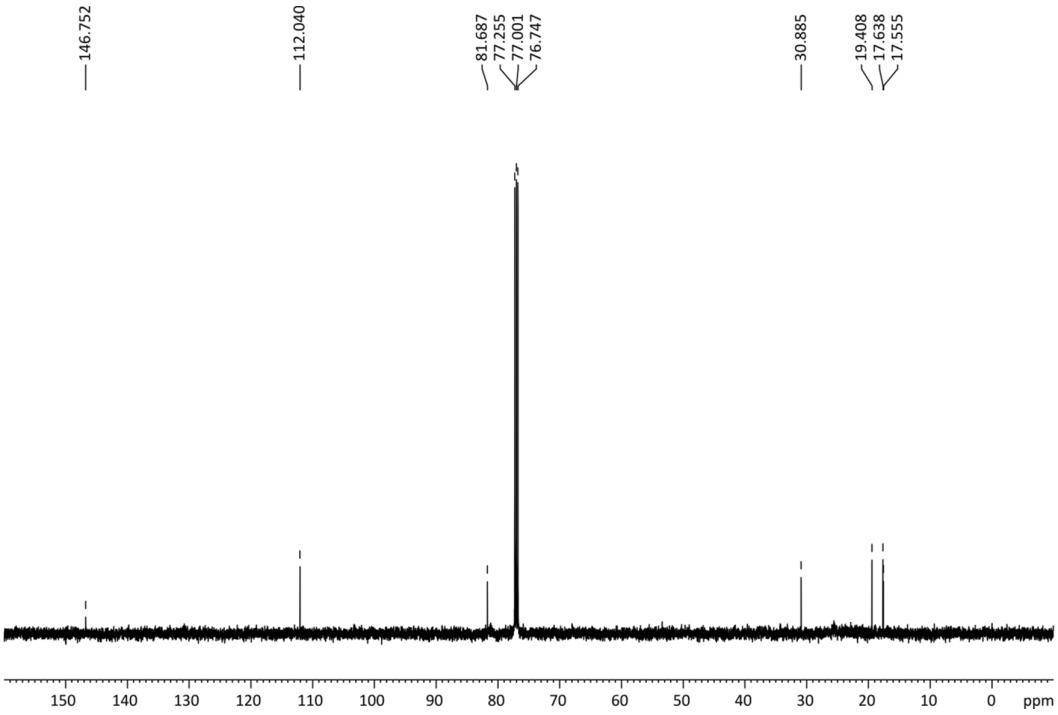


Figure SI17. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of *rac*-**2d**

H.5. Catalytic hydrogenative desymmetrization of substrate 1e

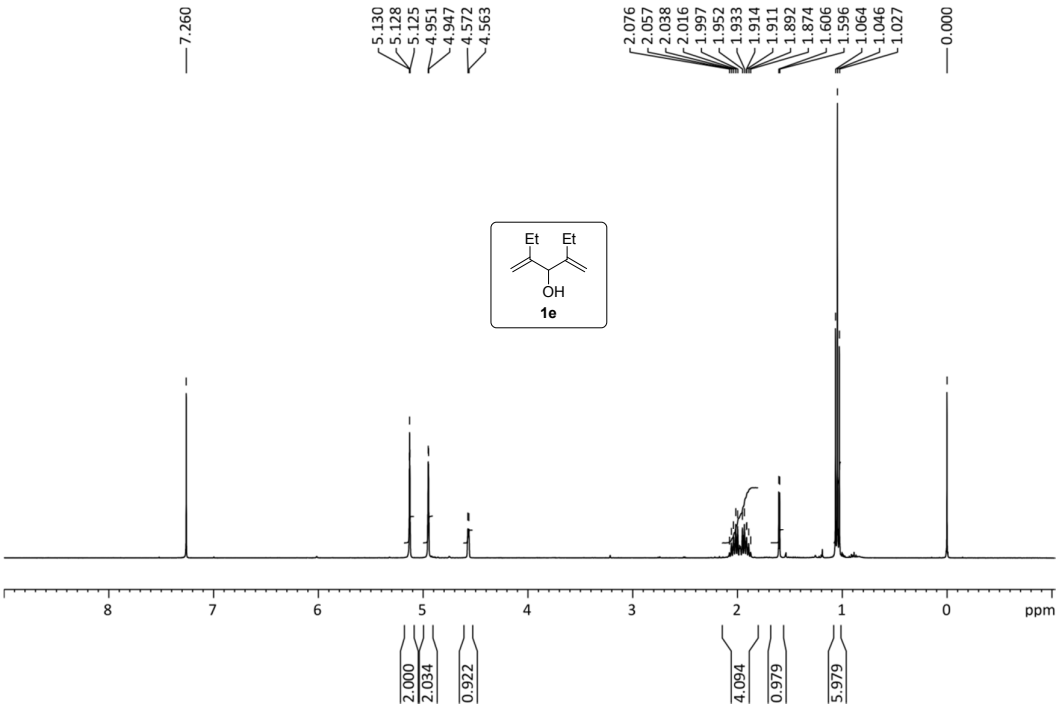


Figure SI18. ^{1}H NMR (400 MHz, $CDCl_3$) of **1e**

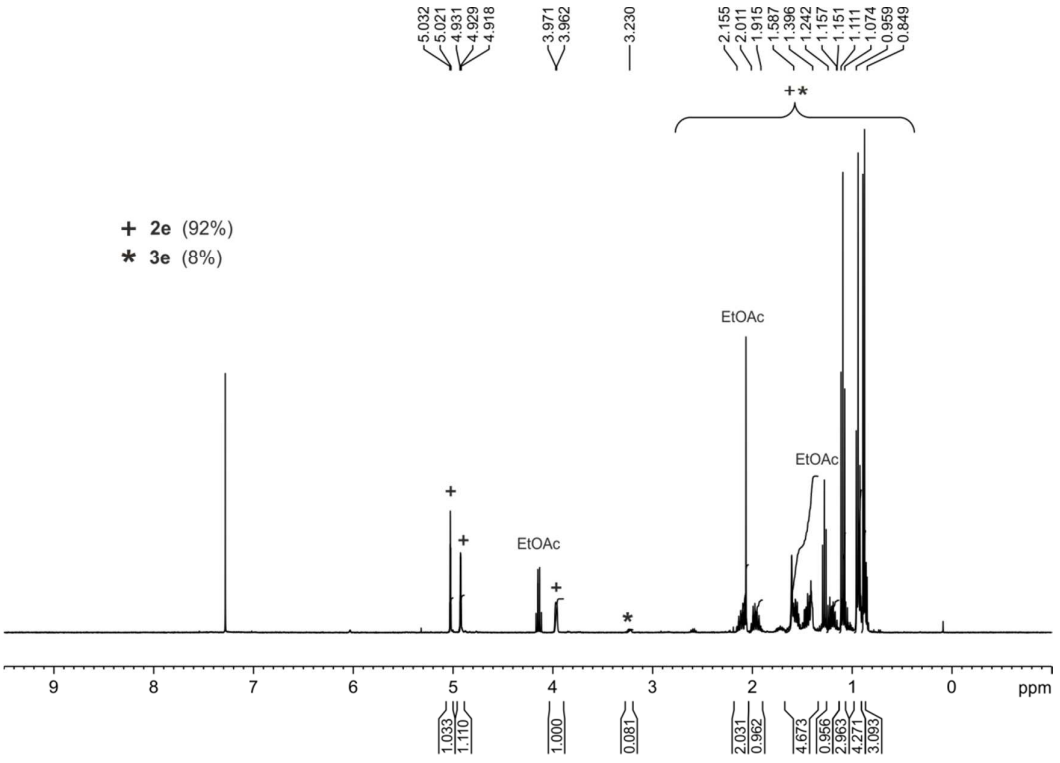


Figure SI19. ^{1}H NMR (400 MHz, $CDCl_3$) of the crude mixture for the desymmetrization of **1e** (Table 3, entry 5)

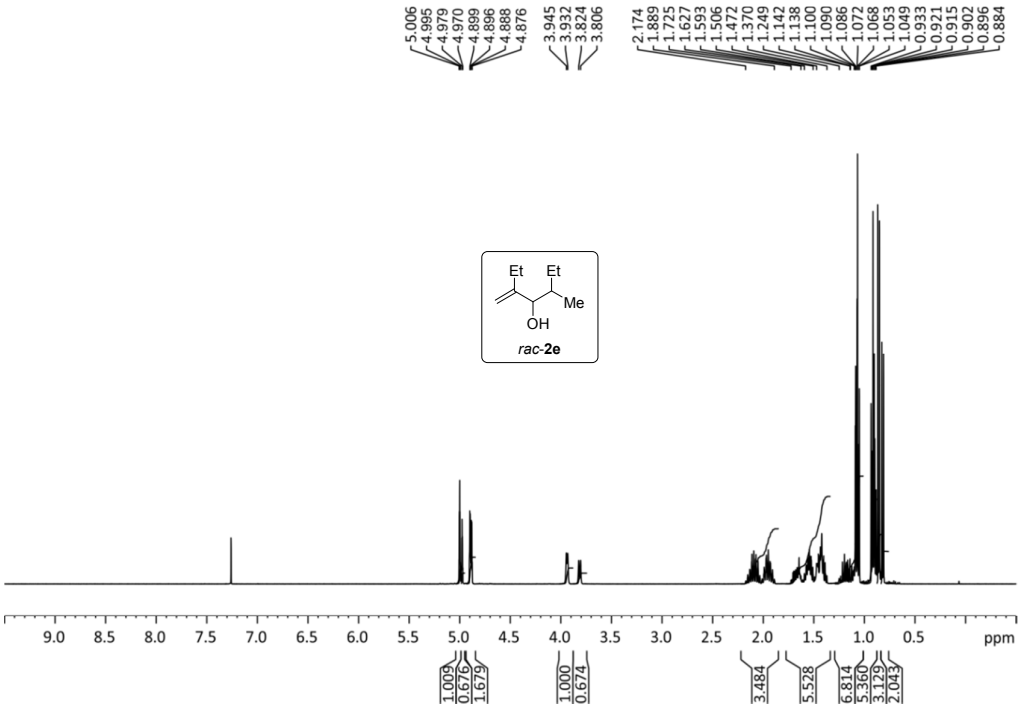


Figure SI20. ^{1}H NMR (400 MHz, $CDCl_3$) of *rac*-**2e**

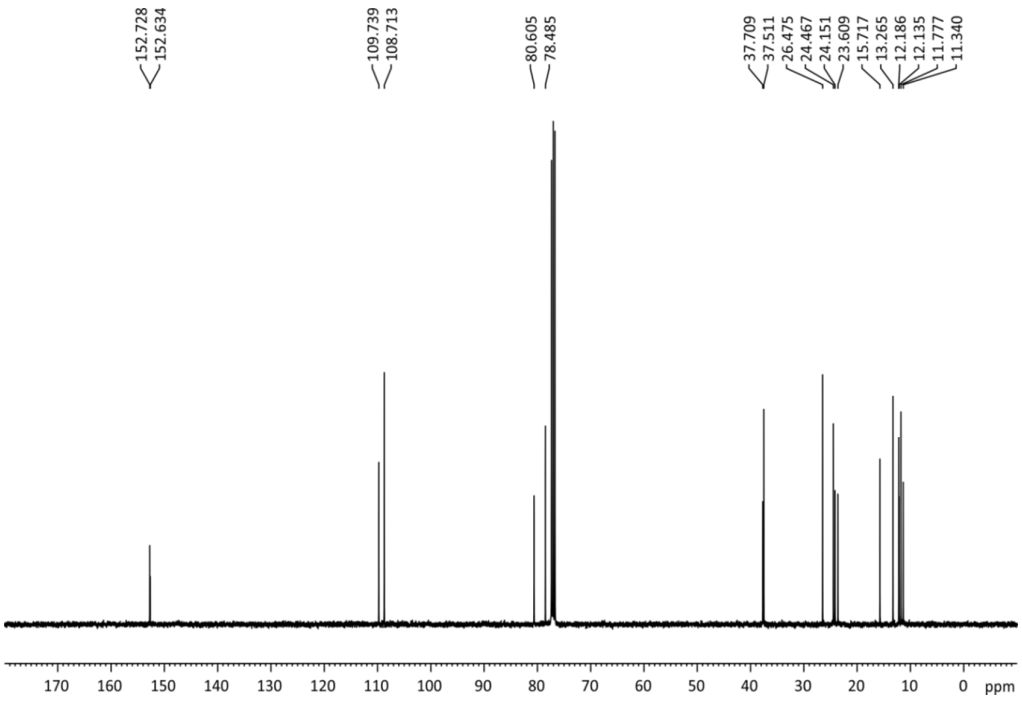


Figure SI21. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of *rac*-**2e**

H.6. Catalytic hydrogenative desymmetrization of substrate 1f

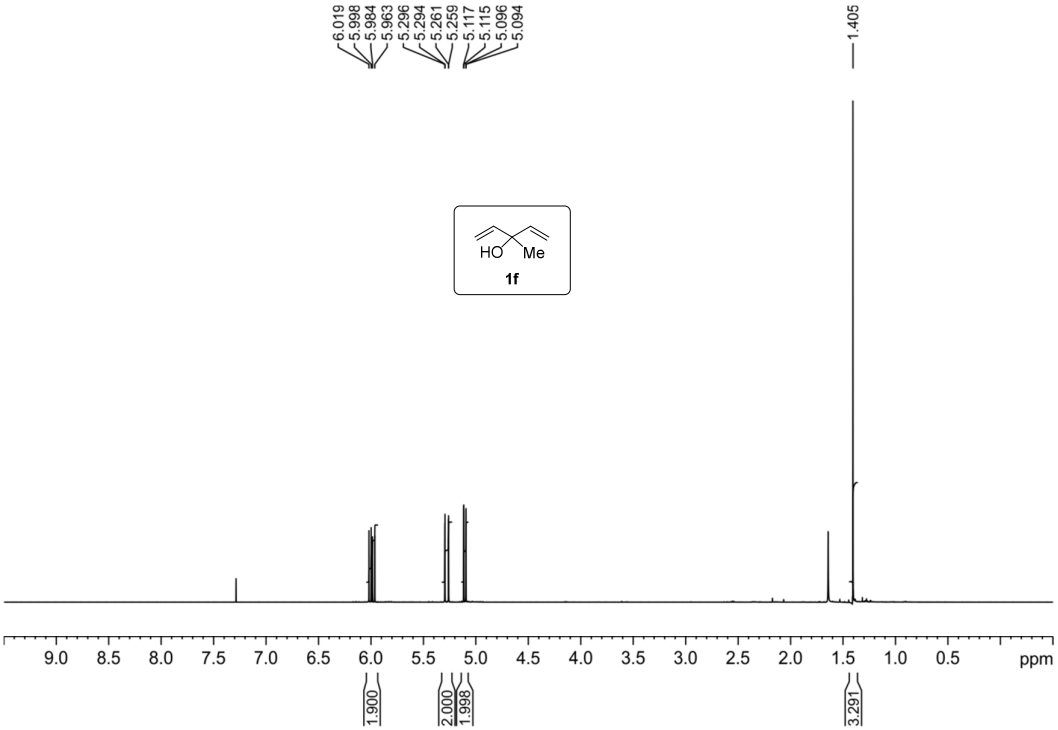


Figure SI22. ^{1}H NMR (500 MHz, $CDCl_3$) of **1f**

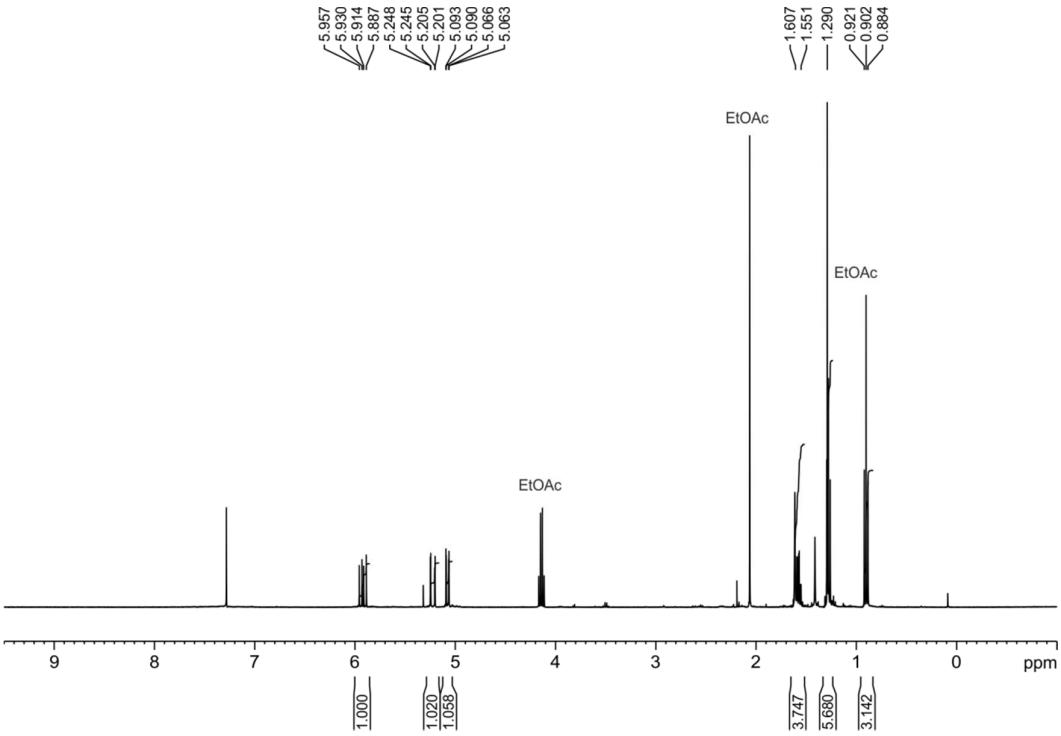


Figure SI23. ^{1}H NMR (400 MHz, $CDCl_3$) of the crude mixture for the desymmetrization of **1f** (Table 3, entry 6)

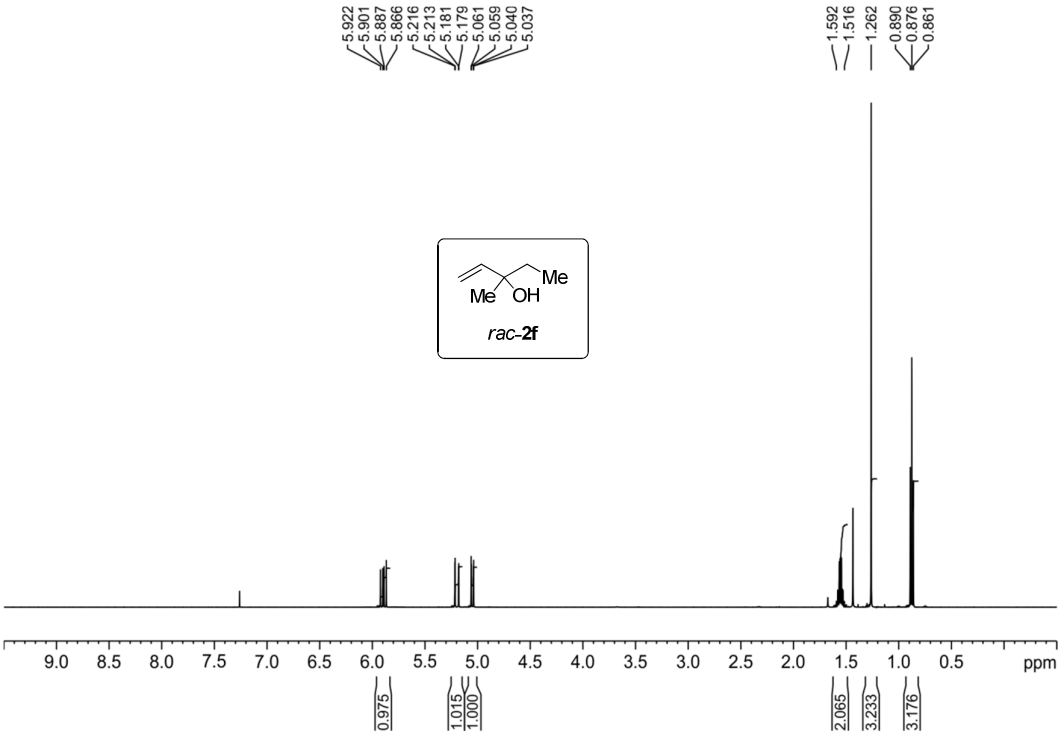


Figure SI24. ^{1}H NMR (500 MHz, $CDCl_3$) of *rac*-**2f**

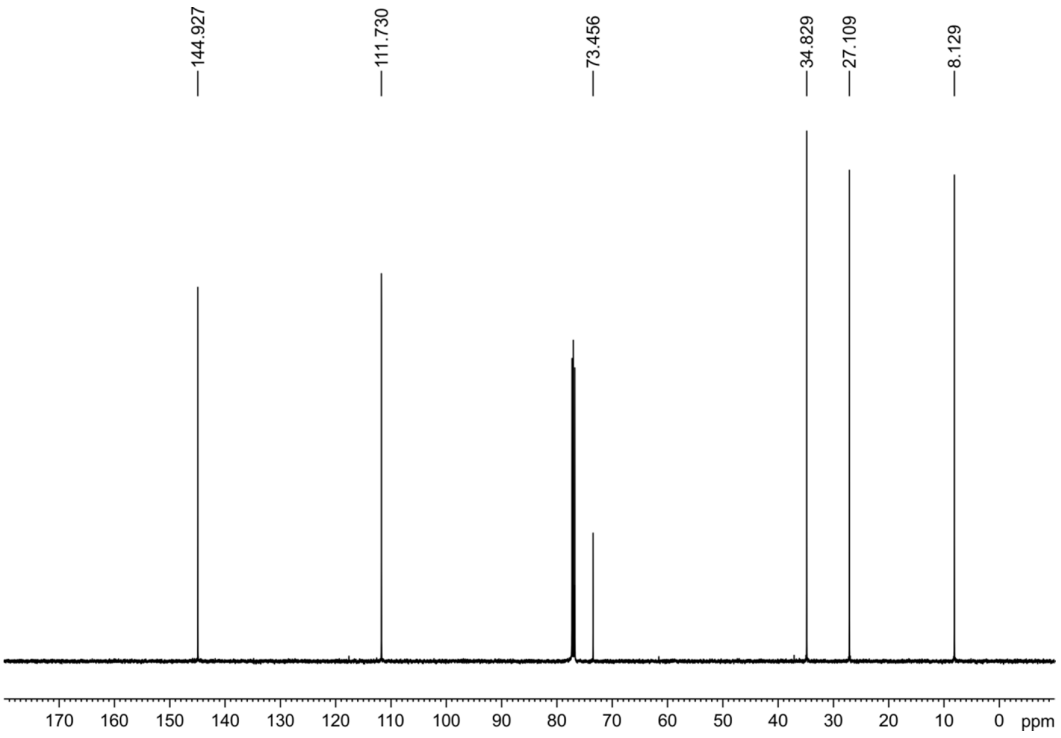


Figure SI25. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) of *rac*-**2f**

(I) NMR spectra of benzoate ester derivatives 4 and derivative 5

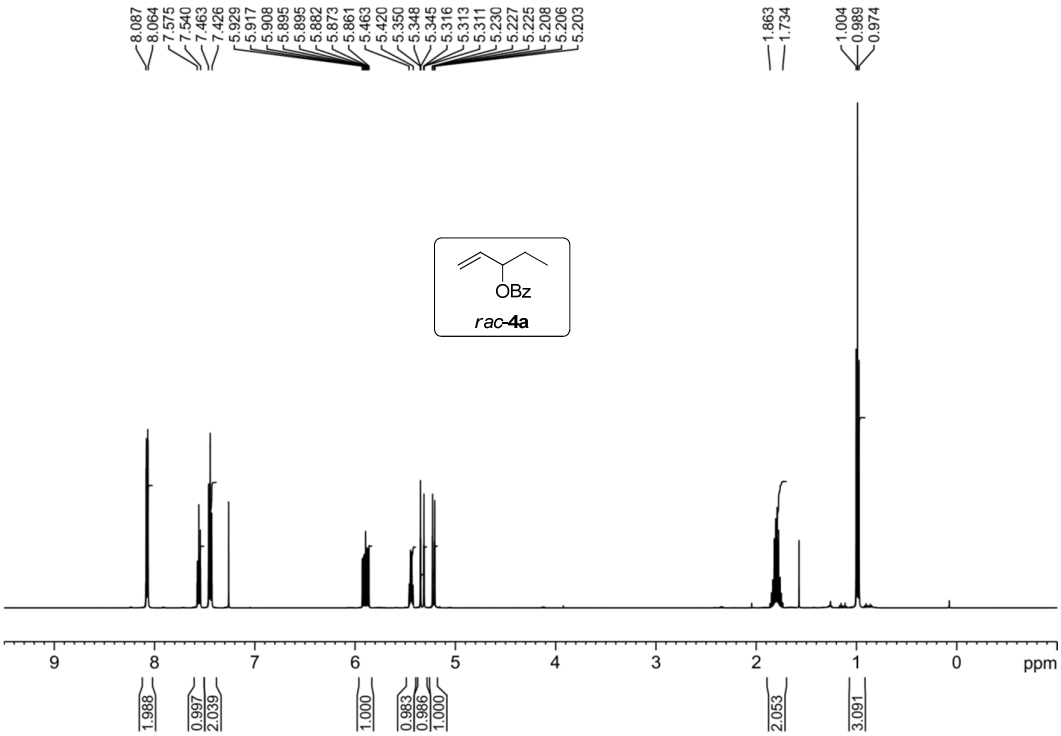


Figure SI26. ^{1}H NMR (500 MHz, $CDCl_3$) of *rac*-**4a**

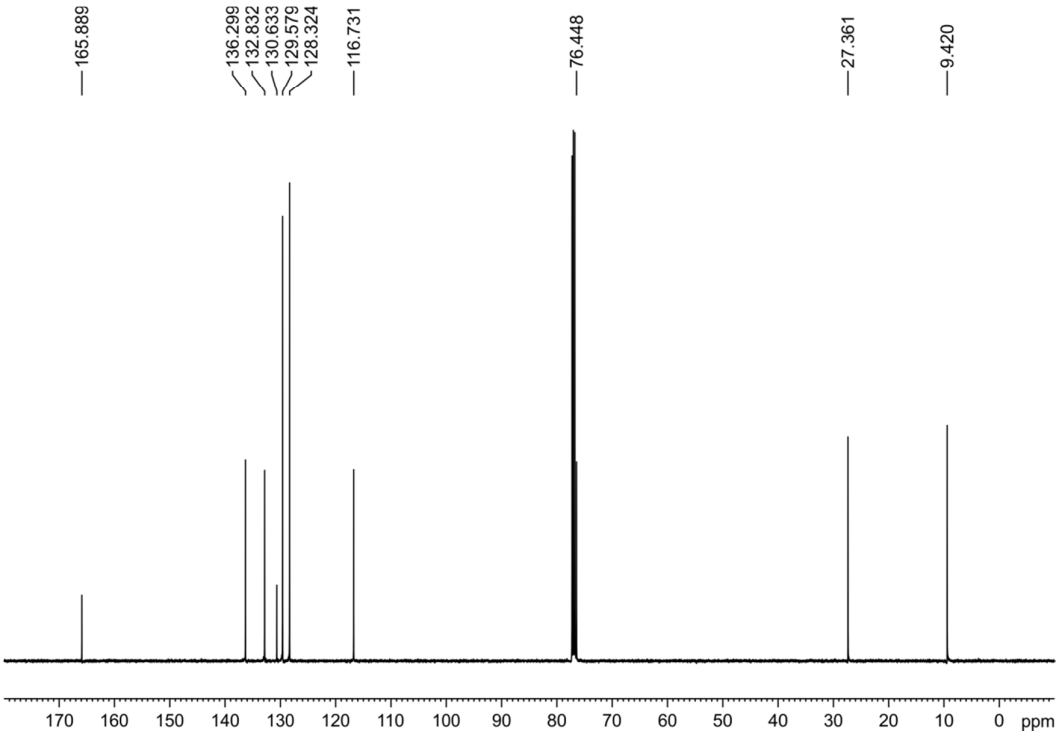


Figure SI27. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) of *rac*-**4a**

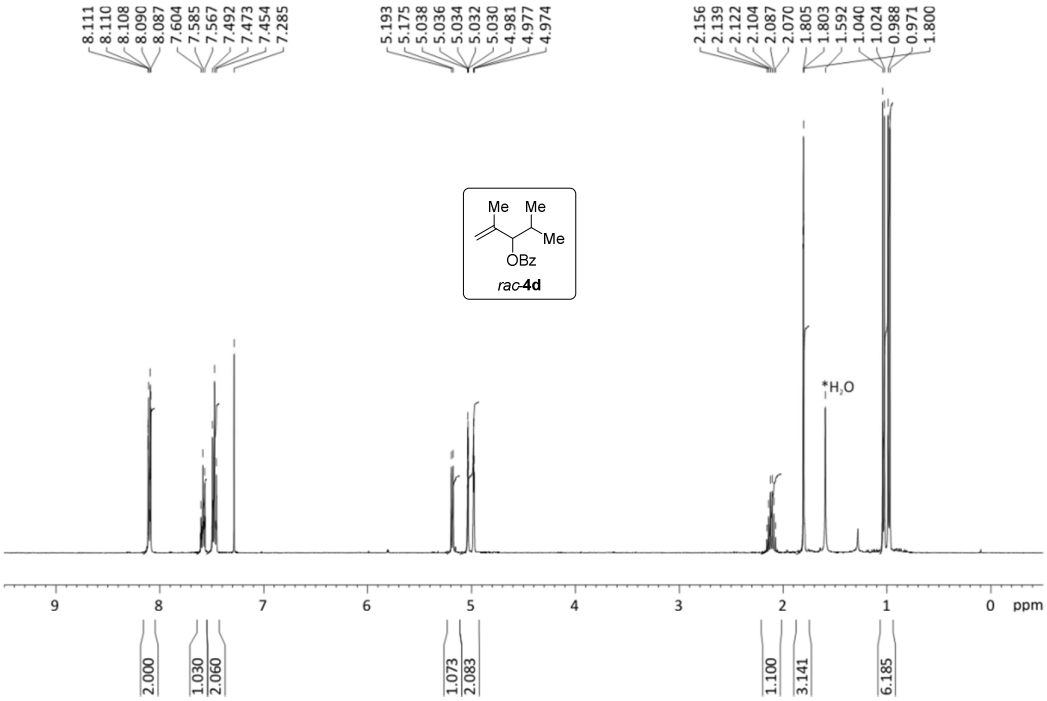


Figure SI28. ^{1}H NMR (400 MHz, $CDCl_3$) of *rac*-**4d**

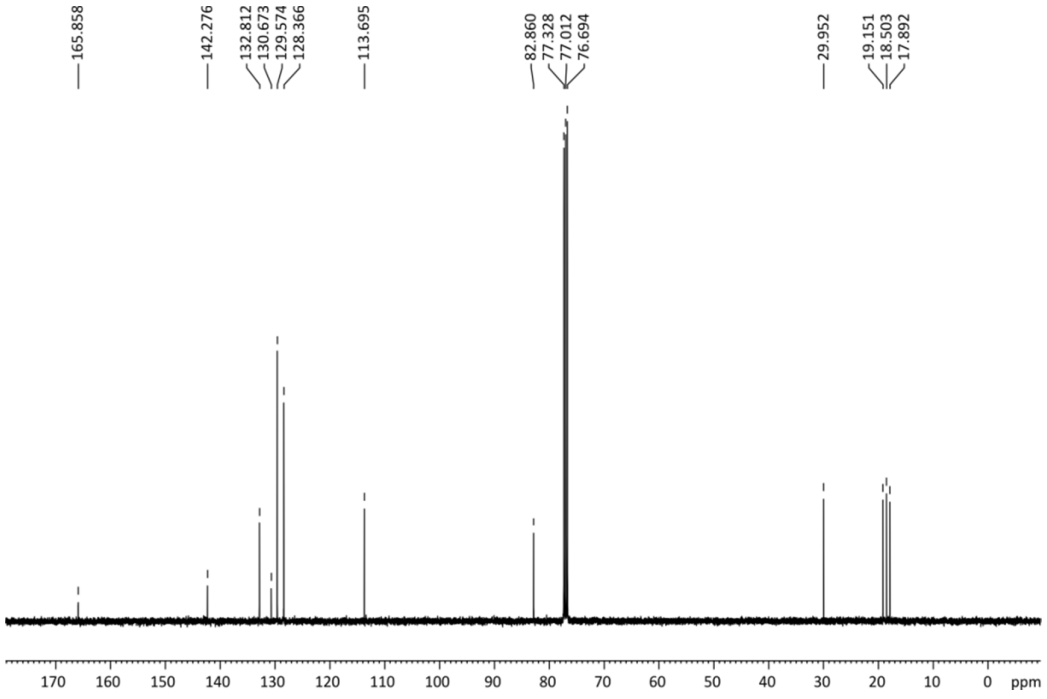


Figure SI29. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of *rac*-**4d**

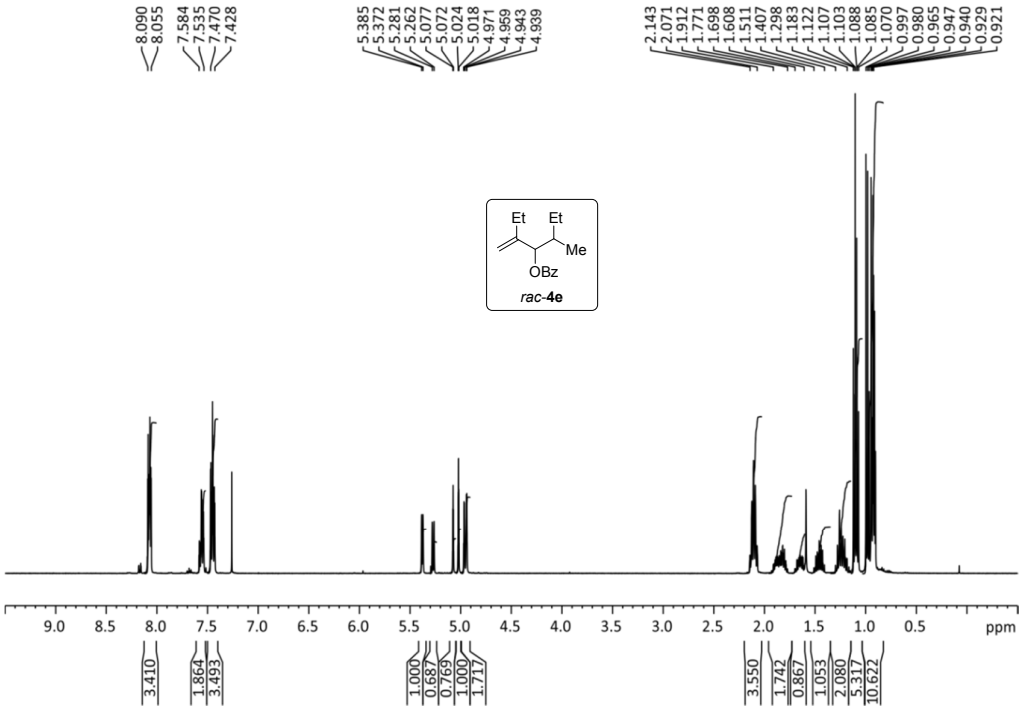


Figure SI30. ^{1}H NMR (400 MHz, $CDCl_3$) of *rac*-**4e**

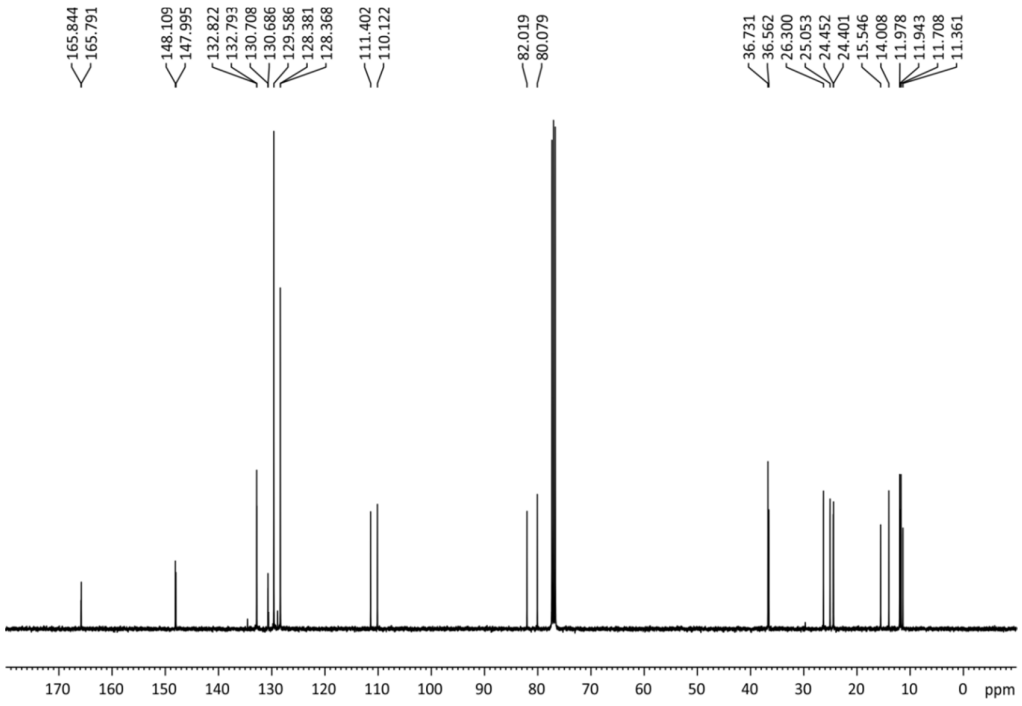


Figure SI31. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) of *rac*-**4e**

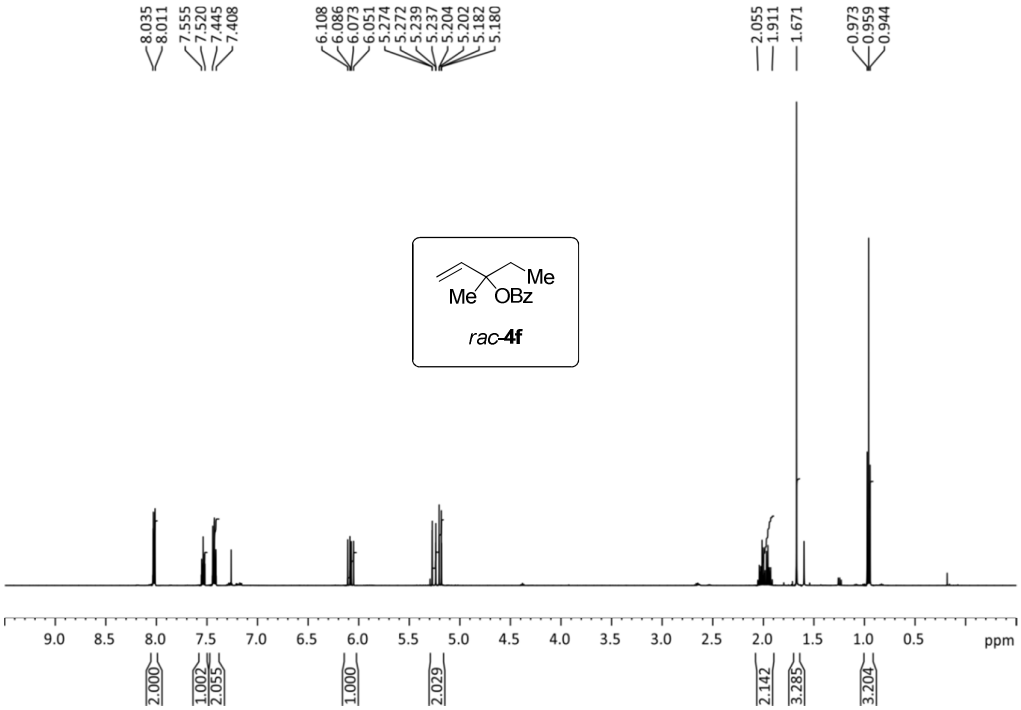


Figure SI32. ^{1}H NMR (500 MHz, $CDCl_3$) of *rac*-**4f**

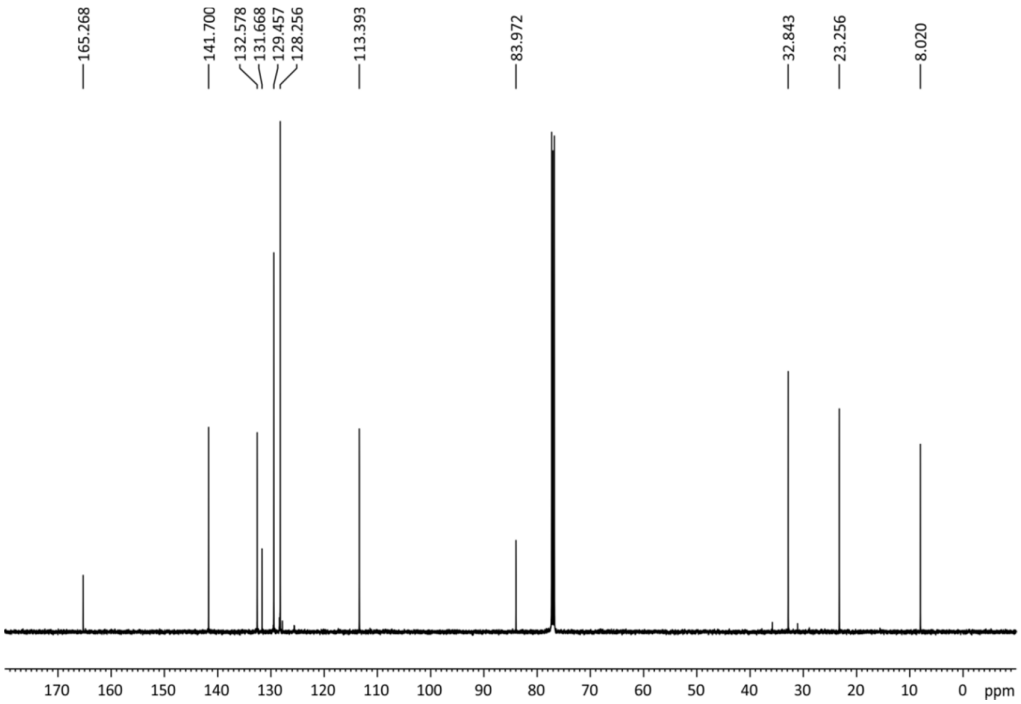


Figure SI33. $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) of *rac*-**4f**

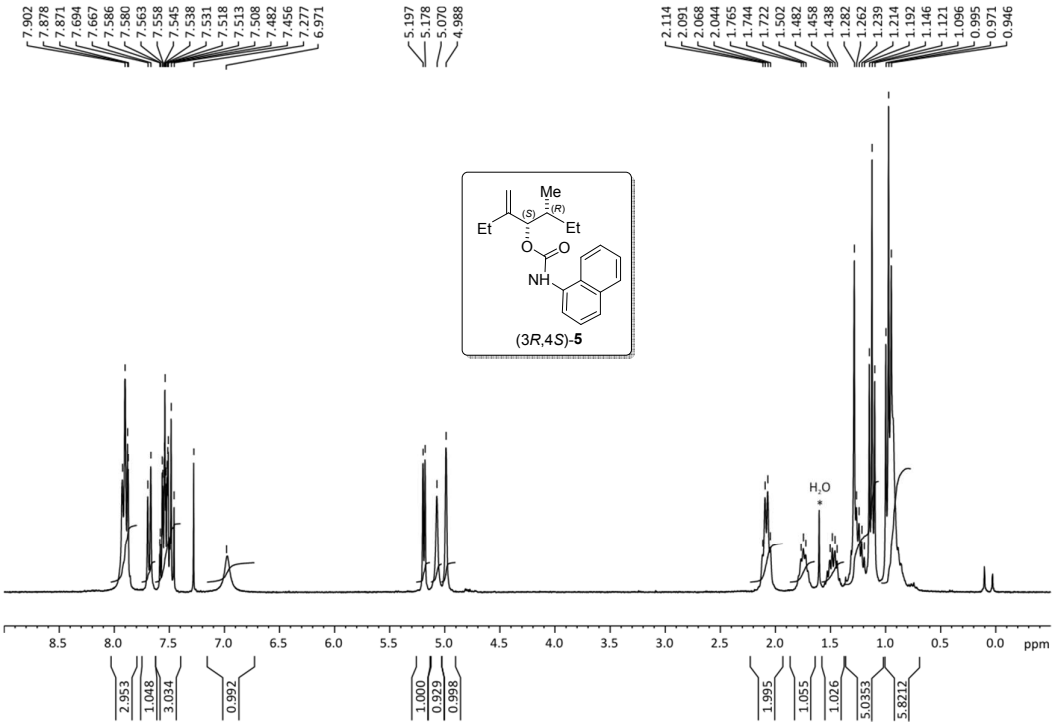


Figure SI34. ^{1}H NMR (300 MHz, $CDCl_3$) of (3*R*,4*S*)-**5**

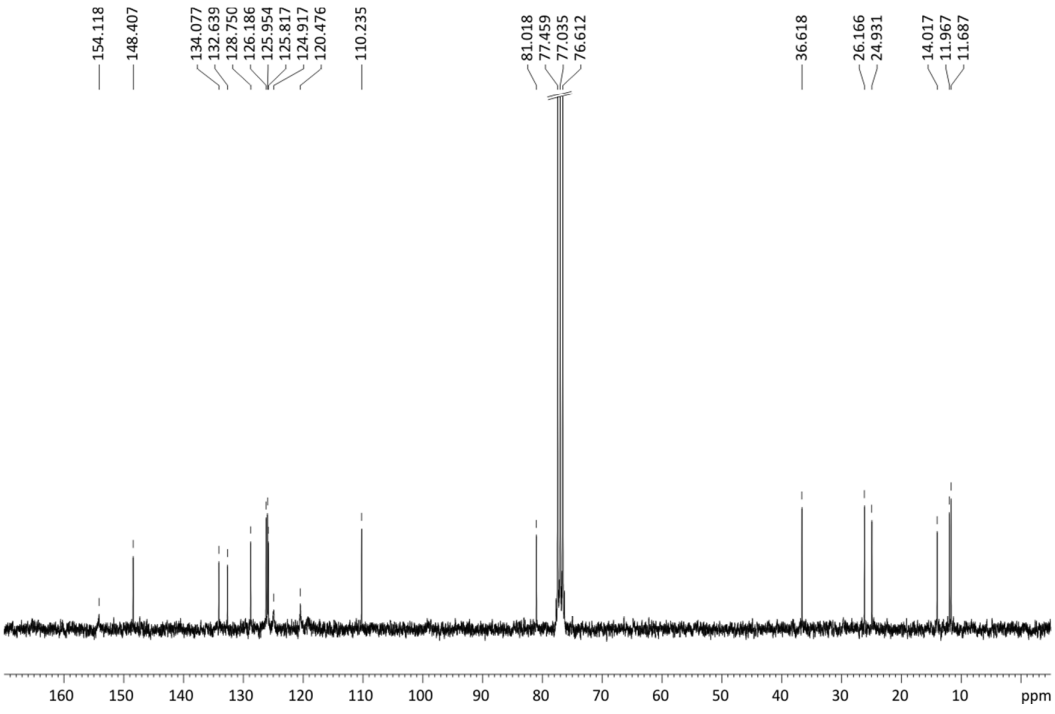
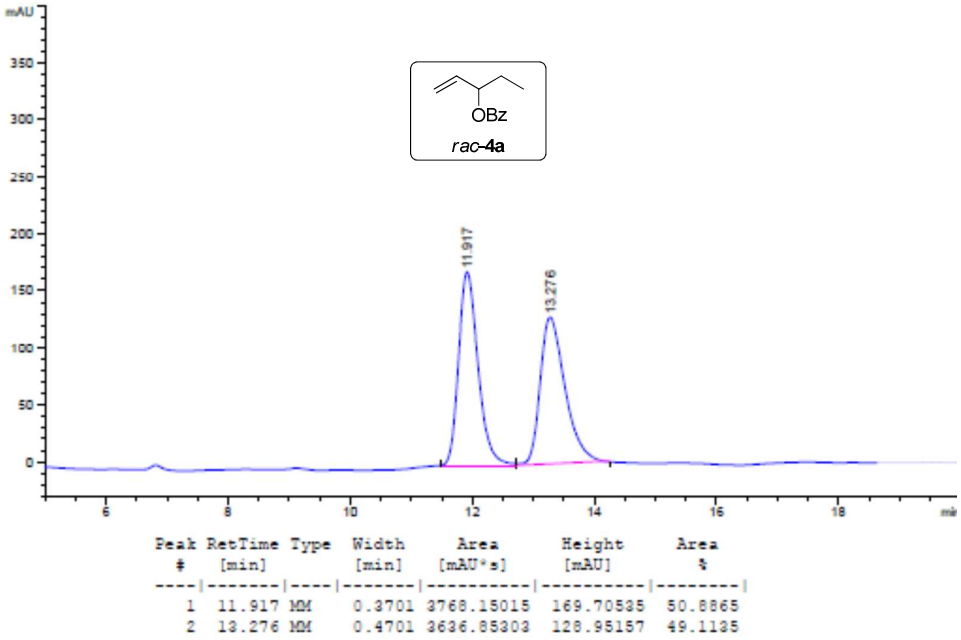


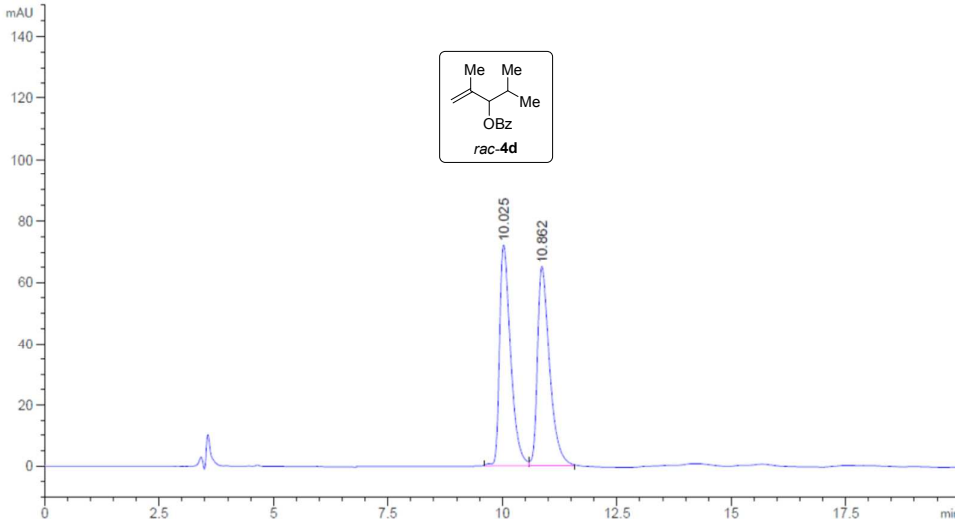
Figure SI35. $^{13}C\{^{1}H\}$ NMR (75 MHz, $CDCl_3$) of (3*R*,4*S*)-**5**

(J) HPLC chromatograms of racemic compounds *rac*-4a and *rac*-4d–f



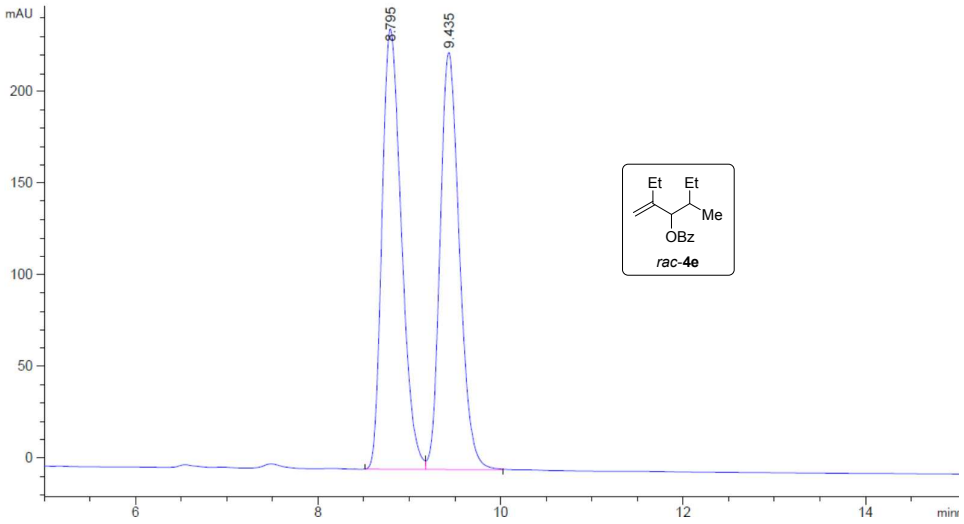
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.917	MM	0.3701	3768.15015	169.70535	50.8865
2	13.276	MM	0.4701	3636.85303	128.95157	49.1135

Figure SI36. Chiral HPLC trace for *rac*-**4a**



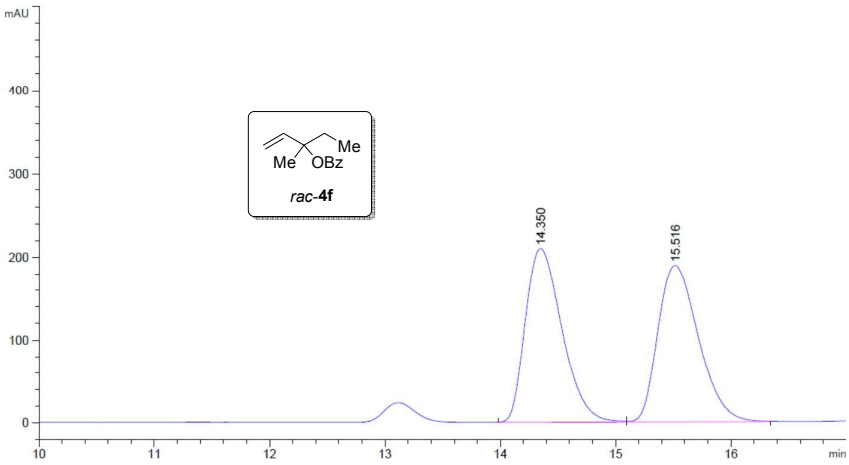
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.025	BV	0.2530	1208.76453	72.30396	50.1591
2	10.862	VB	0.2793	1201.09509	65.08539	49.8409

Figure SI37. Chiral HPLC trace for *rac*-**4d**



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.795	BV	0.2303	3548.33374	240.21742	51.4648
2	9.435	VB	0.2294	3346.34399	227.82498	48.5352

Figure SI38. Chiral HPLC trace for *rac*-**4e**[*]

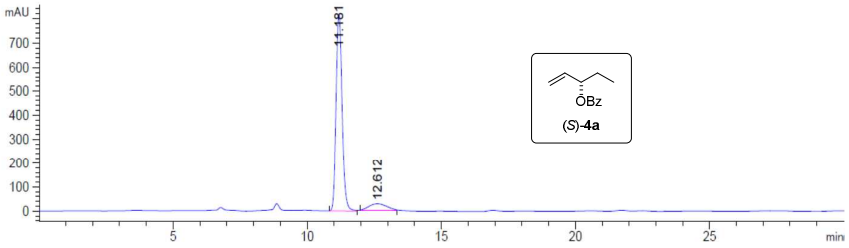


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.350	BV	0.3449	4617.93945	209.69554	50.0042
2	15.516	VB	0.3825	4617.15918	189.37022	49.9958

Figure SI39. Chiral HPLC trace for *rac*-**4f**

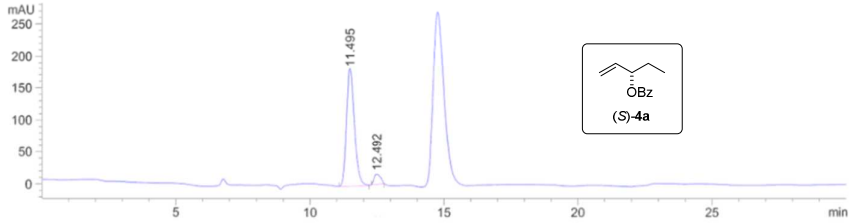
(*) The corresponding enantiomers of the *syn*- and *anti*-diastereisomers coelute at the same time.

(K) Selected HPLC data from catalytic experiments



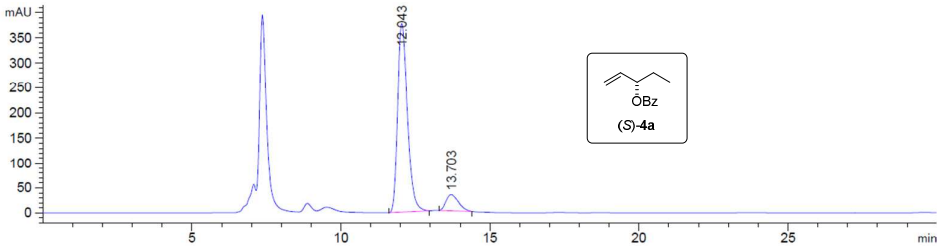
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.181	BB	0.2469	1.27657e4	814.22974	91.8225
2	12.612	MM	0.7285	1136.88062	26.01112	8.1775

Figure SI40. Chiral HPLC trace for the desymmetrization of **1a**, product (*S*)-**4a** (Table 3, entry 1)



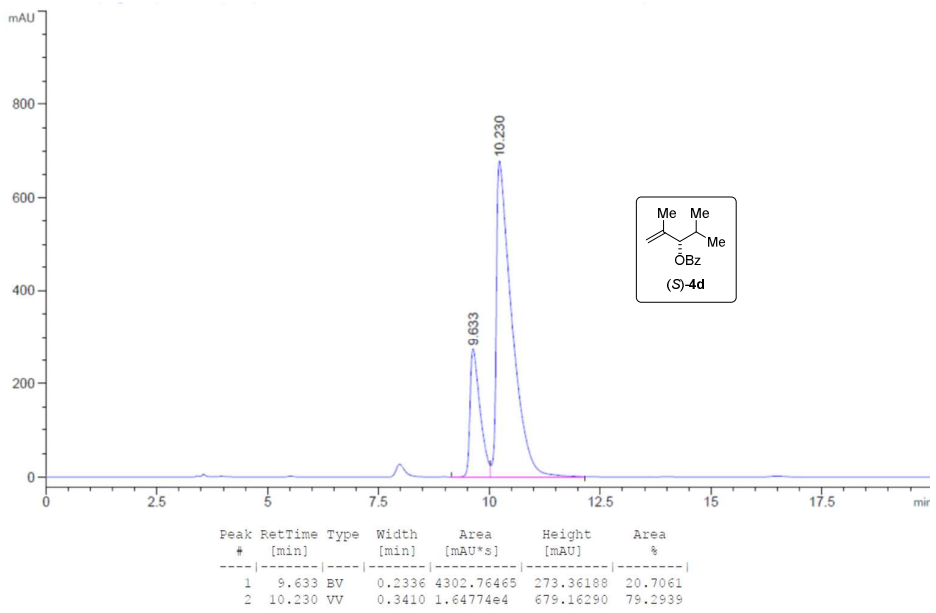
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.495	MM	0.3430	3766.34741	182.99191	93.7435
2	12.492	MM	0.2424	251.36679	17.28370	6.2565

Figure SI41. Chiral HPLC trace for the desymmetrization of **1b**, product (*S*)-**4a** (Table 3, entry 2)



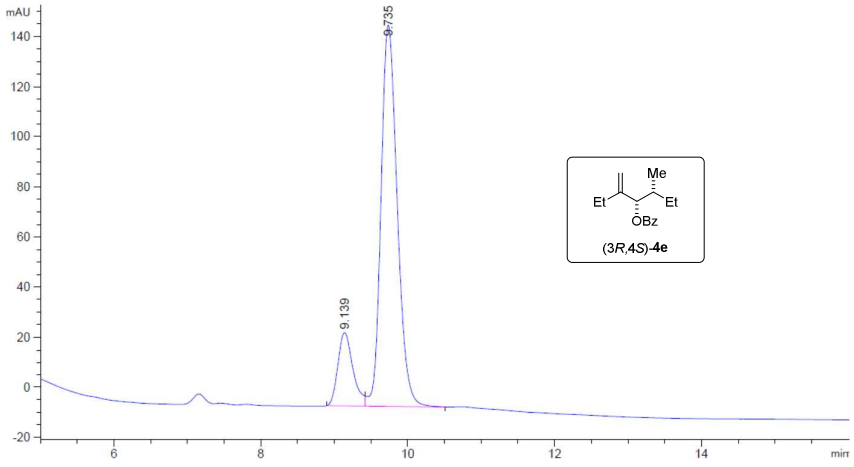
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.043	MM	0.3811	8625.76563	377.21033	90.1547
2	13.703	MM	0.4810	941.96759	32.63612	9.8453

Figure SI42. Chiral HPLC trace for the desymmetrization of **1c**, product (*S*)-**4a** (Table 3, entry 3)



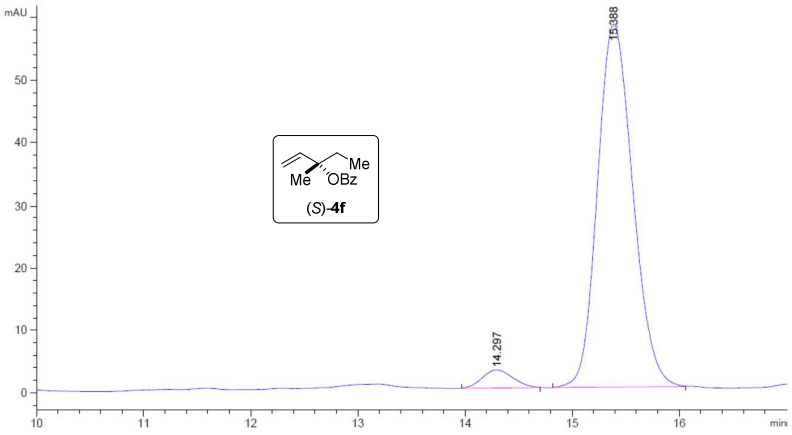
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.633	BV	0.2336	4302.76465	273.36188	20.7061
2	10.230	VV	0.3410	1.64774e4	679.16290	79.2939

Figure SI43. Chiral HPLC trace for the desymmetrization of **1d**, product (*S*)-**4d** (Table 3, entry 4)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.139	MF	0.2376	420.01080	29.46686	15.2261
2	9.735	FM	0.2562	2338.48926	152.15088	84.7739

Figure SI44. Chiral HPLC trace for the desymmetrization of **1e**, product (3*R*,4*S*)-**4e** (Table 3, entry 5)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.297	MM	0.3314	56.95283	2.86452	4.1137
2	15.388	MM	0.3821	1327.50537	57.90999	95.8863

Figure SI45. Chiral HPLC trace for the desymmetrization of **1f**, product (*S*)-**4f** (Table 3, entry 6)

(L) References

(1) Boccara, N.; Maitte, P. *Bull. Soc. Chim. Fr.* **1972**, 1448-1462.

(2) Breit, B.; Breuninger, D. *J. Am. Chem. Soc.* **2004**, *126*, 10244-10245.

(3) Shing, T. K. M.; Zhu, X. Y.; Yeung, Y. Y. *Chem. - Eur. J.* **2003**, *9*, 5489-5500.

(4) Nguyen, B.; Brown, J. M. *Adv. Synth. Catal.* **2009**, *351*, 1333-1343.

(5) Bassetti, M.; D'Annibale, A.; Fanfoni, A.; Minissi, F. *Org. Lett.* **2005**, *7*, 1805-1808.

(6) 2-Butenyl-magnesium bromide was prepared following the procedure reported in ref. 2

(7) Geurts, K.; Fletcher, S. P.; Feringa, B. L. *J. Am. Chem. Soc.* **2006**, *128*, 15572-15573.

(8) Data collection with APEX II version v2013.4-1. Bruker (2007). Bruker AXS Inc., Madison, Wisconsin, USA.

(9) Data reduction with Bruker SAINT version V8.30c. Bruker (2007). Bruker AXS Inc., Madison, Wisconsin, USA.

(10) SADABS: V2012/1 Bruker (2001). Bruker AXS Inc., Madison, Wisconsin, USA. Blessing, R. H. *Acta Crystallogr., Sect. A: Found. Crystallogr.* **1995**, *A51*, 33-38.

(11) SHELXT: Sheldrick, G. M. *Acta Crystallogr., Sect. A: Found. Crystallogr.* **2015**, *71*, 3-8.

(12) SHELXle: Huebschle, C. B.; Sheldrick, G. M.; Dittrich, B. *J. Appl. Crystallogr.* **2011**, *44*, 1281-1284.

(13) SHELXL: Sheldrick, G. M. *Acta Crystallogr., Sect. C: Struct. Chem.* **2015**, *71*, 3-8.