Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

for

Full Chirality Transfer in the Synthesis of Hindered Tertiary Boronic Esters under In Situ Lithiation–Borylation Conditions

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General Procedures

Reaction mixtures were stirred magnetically. Air- and moisture-sensitive reactions were carried out in flame-dried glassware under argon atmosphere using standard Schlenk manifold technique. All required fine chemicals were purchased from Acros Organics, Alfa Aesar, Inochem-Frontier Scientific or Sigma-Aldrich and used as received unless otherwise mentioned. *n*-Butyllithium (*n*BuLi) was received from Acros Organics as a 1.6 M solution in hexane and the molarity was verified by titration with *N*-benzylbenzamide.[1] Petrol refers to the fraction of petroleum ether boiling at 40–60 °C. Anhydrous THF, CH_2Cl_2, toluene, hexane, acetonitrile and Et_2O were dried by passing through a modified Grubbs system[2] of alumina columns, manufactured by Anhydrous Engineering, stored over 3Å molecular sieves (25% of total volume) and were transferred under argon *via* syringe. Anhydrous *tert*-butyl methyl ether (TBME), triethylamine, 2,2,6,6-tetramethylpiperidine (TMP) were distilled over CaH_2 and were transferred under argon *via* syringe. Microwave reactions were carried out in a Biotage Initiator EXP EU microwave synthesiser. ^{1}H Nuclear Magnetic Resonance (NMR) spectra were recorded in $CDCl_3$ 300, 400 or 500 MHz on a Joel Lambda 300, Joel ECP 400, a Varian 400-MR, a VNMRS500a or a Bruker Cryo 500 MHz Fourier transform spectrometer. Chemical shifts (δ_H) are quoted in parts per million (ppm) and referred to the residual protio solvent signals of $CHCl_3$ (7.26 ppm). ^{1}H NMR coupling constants are reported in hertz and refer to apparent multiplicities. Data are reported as follows: chemical shift, multiplicity (s = singlet, br. s = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, sept = septet, m = multiplet, dd = doublet of doublet, etc.), coupling constant, integration, and assignment. ^{13}C NMR spectra were recorded at 101 or 126 MHz. Chemical shifts (δ_C) are quoted in ppm referenced to $CHCl_3$ (77.0 ppm). ^{11}B NMR spectra were measured using Norell S-200-QTZ quartz NMR tubes at 96 or 128 MHz with complete proton decoupling. ^{19}F NMR spectra were recorded at 283, 376 or 470 MHz. Mass spectra were recorded by the University of Bristol, School of Chemistry departmental mass spectrometry service using electron impact ionisation (EI), chemical ionisation (CI) or electrospray ionisation (ESI) techniques for low- and high-resolution mass spectra. HRMS EI and CI were performed on a VG Analytical Autospec mass spectrometer at 70 eV. HRMS ESI was performed on either a Bruker Daltonics Apex IV, 7-Tesla FT-ICR or microTOF II. Samples were submitted in EtOAc or CH_2Cl_2. For low resolution mass spectra (m/z) only molecular ions (M^+ or $M+H^+$) and major peaks are reported with intensities quoted as percentage of the base peak. All infrared spectra were recorded on the neat compounds using a PerkinElmer Spectrum One FT-IR spectrometer, irradiating between 4000 cm^{-1} and 600 cm^{-1}. Only strong and selected absorbances (ν_{max}) are reported. Analytical TLC was performed on aluminium backed silica plates (Merck, Silica Gel 60 F_{254}, 0.25 mm). Compounds were visualised by fluorescence quenching or by staining the plates with 5% solution of phosphomolybdic acid ($H_3PMo_{12}O_{40}$) in EtOH followed by heating. Flash column chromatography was performed on silica gel (Aldrich, Silica Gel 60, 40–63 μm). All mixed solvent eluents are reported as v/v solutions. Optical rotations were obtained using a Bellingham + Stanley Ltd. ADP220 polarimeter at 589 nm (Na D-line) in a cell with a path length of 1 dm. Specific rotation values are given in (deg mL)/(g dm). Melting points were measured with a Reichert hot stage apparatus and are uncorrected. Chiral high performance liquid chromatography (HPLC) separations were performed on an Agilent 1100 Series HPLC unit equipped with UV-vis diode-array detector monitored at 210.8 nm, using Daicel Chiralpak ADH, AD-3, AS-H, IA, IB or IC columns (4.6 × 250 mm^2, 5 μm) fitted with respective guards (4 × 10 mm^2). Supercritical fluid chromatography (SFC) was performed on a Thar SFC investigator using a Daicel Chiralpak IA, IB, IC columns or a Whelk-O1(4.6 × 250 mm^2, 5 μm).

General Procedures

Preparation of enantioenriched secondary carbamates

GP1 –*Reduction of benzylic ketones*

To a solution of ketone (10.0 mmol, 1 eq.) in MeOH (7 mL) and THF (10 mL) at 0 °C was added $NaBH_4$ (567 mg, 15.0 mmol, 1.5 eq.) portionwise over 5 minutes with vigorous stirring. The reaction was then warmed to rt and stirred for 30 min at which point TLC (20% EtOAc:petrol) indicated complete loss of starting material. The reaction was quenched by addition of $NH_4Cl_{(aq)}$ (5 mL) and diluted with H_2O (10 mL) and EtOAc (100 mL). The layers were separated and the organic layer was washed sequentially with H_2O (15 mL) and brine (2 × 15 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the racemic secondary alcohol which was used without further purification.

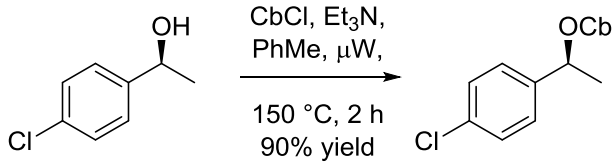
GP2 – *Enzymatic resolution of benzylic alcohols*

To a solution of benzylic alcohol (9.8 mmol, 1 eq.) in solvent (4 mL) was added acrylic resin bound lipase from *Candida Antarctica* (59 mg, 6 mg per mmol of alcohol) followed by vinyl acetate (4.3 mL, 49 mmol, 5 eq.). The suspension was then heated to 50 °C, stirred for 16 h at which point chiral HPLC indicated the alcohol had *er*>99:1. The reaction was filtered through a plug of SiO_2 with EtOAc, concentred *in vacuo* and purified by flash column chromatography (20% EtOAc:petrol) to give the enantioenriched (*S*)-alcohol and (*R*)-acetate products.

GP3 – *Carbamoylation of secondary benzylic alcohols*

To a solution of benzylic alcohol (3.47 mmol, 1.00 eq.) in PhMe (3.5 mL) in a sealable microwave vial under N_2 was added *N*,*N*-diisopropylcarbamoyl chloride (681 mg, 4.16 mmol, 1.20 eq.) followed by Et_3N (0.63 mL, 4.51 mmol, 1.30 eq.). The vial was then sealed and heated under microwave irradiation at 150 °C for 2 h. The reaction was then cooled to room temperature, filtered through a plug of SiO_2 with Et_2O, concentrated *in vacuo* and purified by either bulb-to-bulb distillation or flash chromatography under reduced pressure to give pure product.

1-(4′-chlorophenyl)eth-1-yl diisopropylcarbamate 4



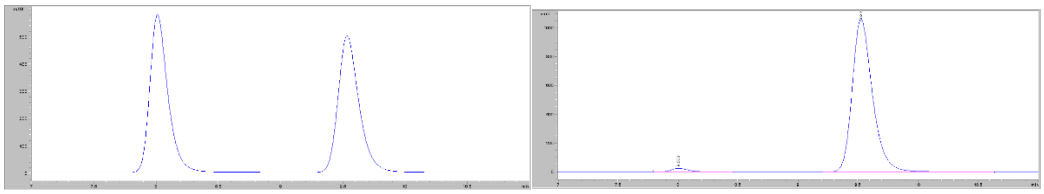
Prepared according to **GP3** using (*S*)-1-(4-chlorophenyl)ethan-1-ol (541 mg, 3.47 mmol, 98:2 *er*), CbCl (678 mg, 4.16 mmol), Et_3N (0.63 mL, 4.51 mmol) and PhMe (3.5 mL). The product carbamate **4** (0.89 g, 90%, 98:2 *er*) was obtained as a clear colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.27 (m, 4 H, HAr), 5.80 (q, J = 6.6, 1 H, CHOCb), 4.08 (br. m, 1 H, $CH(CH_3)_2$), 3.78 (br. m, 1 H, $CH(CH_3)_2$), 1.52 (d, J = 6.6, 3 H, CH_3), 1.21 (br. m, 12 H, CH_3).

^{13}C NMR (101 MHz, $CDCl_3$) δ 155.0 (NCO), 141.5 (C), 133.3 (CCl), 128.7 (CH), 127.6 (CH), 72.1 (CHOCb), 45.6 (br., $CH(CH_3)_2$), 22.8 (CH_3), 20.9 (br., CH_3).

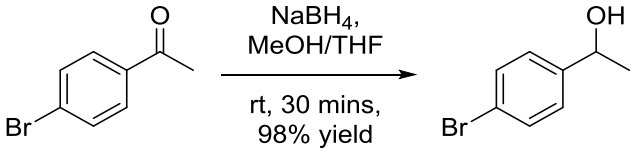
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ −18 (*c* 0.9, $CHCl_3$);

Chiral HPLC IA column with guard, 10% IPA in hexane, 1 mL/min, 216 nm, t_R= 8.0 min (minor), t_R= 9.5 min (major).



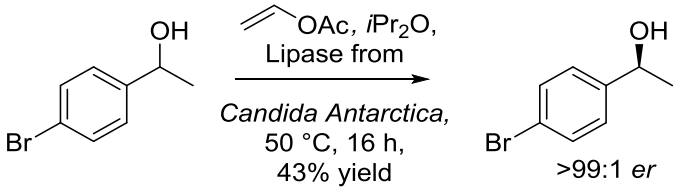
Analytical data were consistent with literature values.[3]

1-Hydroxy-1-(4′-bromophenyl)ethane *rac*-**21**



Prepared according to **GP1** using 1-(4-bromophenyl)ethan-1-one (2.00 g, 10.0 mmol), MeOH (7 mL), THF (7 mL) and $NaBH_4$ (567 mg, 15.0 mmol). The product alcohol *rac*-**21** (1.98 g, 98%) was obtained as a colourless oil. For characterisation data *vide infra.*

(1*S*)-1-Hydroxy-1-(4′-bromophenyl)ethane (*S*)-**21**



Prepared according to **GP2** using alcohol *rac*-**21** (1.96 g, 9.77 mmol), vinyl acetate (4.3 mL, 49 mmol), lipase (60 mg) and *i*Pr_2O (4 mL). The product alcohol (*S*)-**21** (842 mg, 43%, >99:1 *er*) was isolated as a colourless oil.

R_f (20% EtOAc:PE) 0.15;

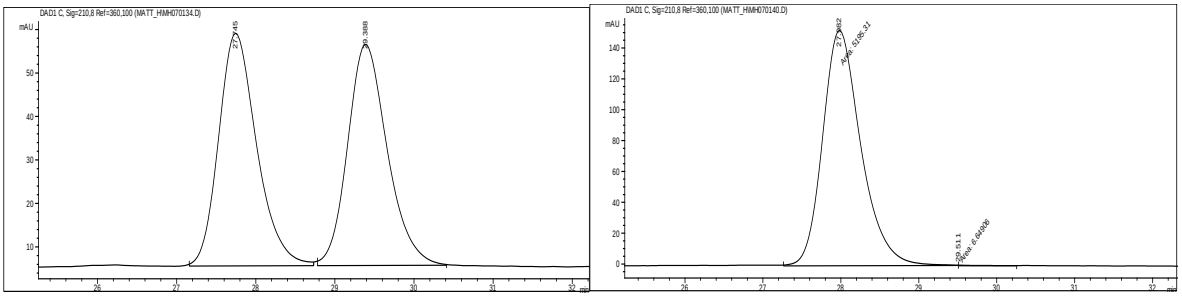
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50-7.44 (2H, m, Ar-H), 7.28-7.22 (2H, m, Ar-H), 4.87 (1H, q, J = 6.4, C*H*OH), 1.85 (1H, br. s, OH), 1.47 (3H, d, J = 6.4, CH_3).

^{13}C NMR ($CDCl_3$, 101 MHz) δ 144.9 (4° C-Ar), 131.7 (2 × C-Ar), 127.3 (2 × C-Ar), 121.3 (4° C-Ar), 69.9 (C*H*OH), 25.4 (CH_3).

IR ν_{max} (neat)/cm^{-1} : 3338 (OH), 2972 (C-H Ar), 1488, 1084, 1008, 820.

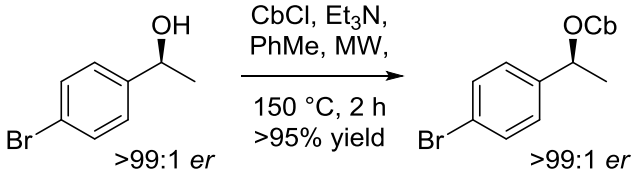
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{22}}$ −20.5 (*c* 1.17, $CHCl_3$); Lit.[4] $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{25}}$ −25.6 (*c* 3.4, $CHCl_3$)

Chiral HPLC (Chiralpak IB, rt, 0.5 mL/min, 2% IPA:hexane); t_R: 27.8 min (major), 29.5 min (minor).



Analytical data were consistent with literature values.[4]

1-(4′-bromophenyl)eth-1-yl diisopropylcarbamate 22



Prepared according to **GP3** using alcohol (*S*)-**21** (730 mg, 3.47 mmol, >99:1 *er*), CbCl (681 mg, 4.16 mmol), Et_3N (0.63 mL, 4.5 mmol) and PhMe (3.5 mL). The product carbamate **22** (1.13 g, >95%, >99:1 *er*) was obtained as a clear colourless oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.46 (2H, d, J = 8.5, Ar-H), 7.23 (2H, d, J = 8.5, Ar-H), 5.78 (1H, q, J = 6.7, OCH), 4.30-3.65 (2H, br. m, 2 × NCH), 1.52 (3H, d, J = 6.7, $OCHCH_3$), 1.27-1.12 (12H, br. m, 2 × $NCH(CH_3)_2$).

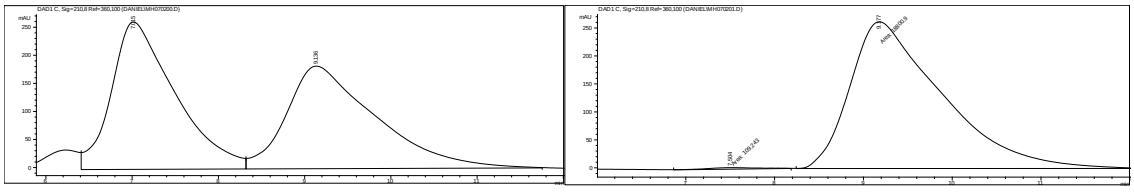
^{13}C NMR ($CDCl_3$, 101 MHz) δ 154.9 (C=O), 142.0 (4° C-Ar), 131.6 (2 × C-Ar), 127.9 (2 × C-Ar), 121.4 (C-Br), 72.1 (OCH), 45.9 (br., 2 × NCH), 22.7 ($OCH\mathit{C}H_3$), 21.2 (br., 2 × $NCH(\mathit{C}H_3)_2$).

IR ν_{max} (neat)/cm^{-1} : 2970 (C-H Ar), 1685 (C=O), 1285, 1046, 821.

HRMS (CI) calc'd for $C_{15}H_{23}NO_2Br$ $[M+H]^+$ 328.0912, found: 328.0901.

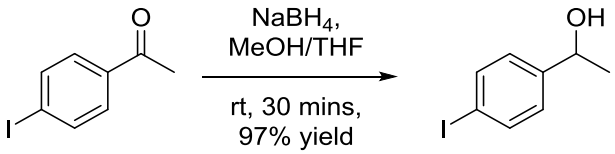
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ +4.5 (*c* 1.57, $CHCl_3$).

Chiral HPLC (AD-3, rt, 0.5 mL/min, 10% IPA:hexane); t_R: 7.8 min (major), 9.5 min (minor).



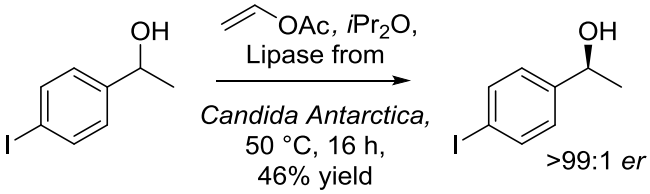
Analytical data were consistent with literature values.[3]

1-Hydroxy-1-(4′-iodophenyl)ethane *rac*-**23**



Prepared according to **GP1** using 1-(4-iodophenyl)ethan-1-one (2.46 g, 10.0 mmol), MeOH (7 mL), THF (7 mL) and $NaBH_4$ (567 mg, 15.0 mmol). The product alcohol rac-**23** (2.40 g, 97%) was obtained as a white solid. For characterisation data *vide infra.*

(1*S*)-1-Hydroxy-1-(4′-iodophenyl)ethane (*S*)-**23**



Prepared according to **GP2** using alcohol *rac*-**23** (15 g, 60.5 mmol), vinyl acetate (27.9 mL, 300 mmol), lipase (1.15 g) and CH_2Cl_2 (43 mL). The product (*S*)-alcohol (*S*)-**23** (6.8 g, 46%, >99:1 *er*) was isolated as a yellow solid.

R$_f$ (20% EtOAc:PE) 0.19

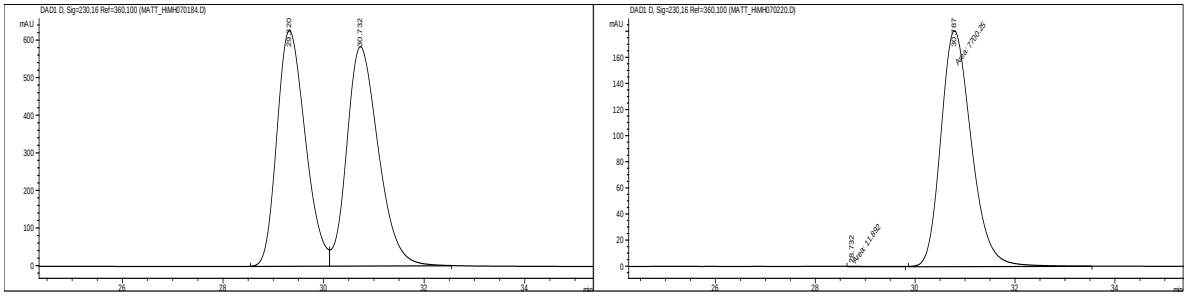
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (2H, d, J = 8.5, Ar-H), 7.10 (2H, d, J = 8.5, Ar-H), 4.82 (1H, q, J = 6.5, OCH), 2.13 (br. s, OH), 1.44 (3H, d, J = 6.5, $OCHCH_3$).

^{13}C NMR ($CDCl_3$, 101 MHz) δ 145.6 (4° C-Ar), 137.6 (2 × C-Ar), 127.5 (2 × C-Ar), 92.8 (C-I), 69.9 (OCH), 25.3 ($OCHCH_3$).

IR ν_{max} (neat)/cm^{-1} : 3369 (OH), 2973 (Ar C-H), 1241, 1004, 818.

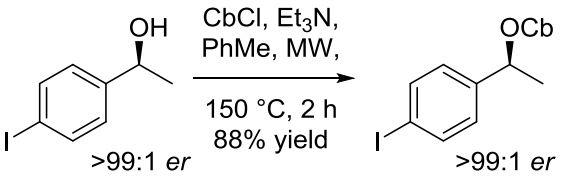
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ −29.7 (*c* 0.37, Et_2O).

Chiral HPLC (Chiralpak AS-H with guard, rt, 0.4 mL/min, 2% IPA:hexane); t_R: 28.7 min (minor), 30.8 min (major).



Analytical data were consistent with literature values.[5]

1-(4′-Iodophenyl)eth-1-yl diisopropylcarbamate 12



Prepared according to **GP3** using alcohol (*S*)-**23** (3.0 g, 12 mmol, >99:1 *er*), CbCl (2.1 g, 12.7 mmol), Et_3N (1.8 mL, 13.0 mmol) and PhMe (12.7 mL). The product carbamate **12** (7.89 g, 88%, >99:1 *er*) was obtained as a white solid.

R_f (20% EtOAc:PE) 0.49.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.67 (2H, d, J = 8.3, Ar-H), 7.10 (2H, d, J = 8.3, Ar-H), 5.76 (1H, q, J = 6.6, C*H*OCb), 4.28-3.56 (2H, br. m, 2 × NC*H*$(CH_3)_2$), 1.51 (3H, d, J = 6.6, CH_3), 1.30-1.12 (12H, br. m, 2 × NCH(C*H*$_3)_2$).

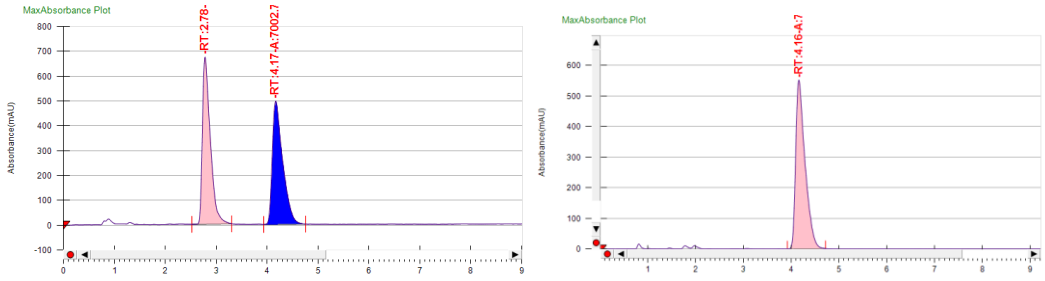
^{13}C NMR ($CDCl_3$, 101 MHz) δ 155.0 (C=O), 142.8 (4° C-Ar), 137.7 (2 × C-Ar), 128.2 (2 × C-Ar), 93.0 (CI), 72.3 (*C*HOCb), 46.0 (br., 2 × N*C*H$(CH_3)_2$), 22.8 (CH_3), 21.0 (br., 2 × NCH(*C*H$_3)_2$).

IR ν_{max} (neat)/cm^{-1} : 2970 (Ar C-H), 1689 (C=O), 1287, 1069.

HRMS (CI) calc'd for $C_{15}H_{23}NO_2I$ $[M+H]^+$ 376.0774, found: 376.0774.

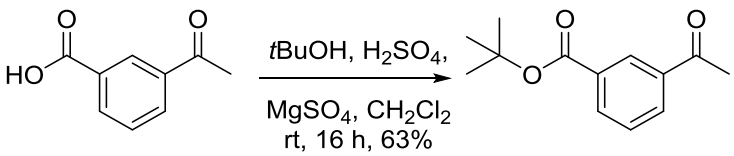
$[\alpha]_D^{21}$ +1.0 (*c* 1.0, $CHCl_3$)

Chiral SFC (IC, 4.0 mL/min, 10% co-solvent (50% IPA:hexane), 125 bar, 40 °C; t_R: 2.8 min (minor), 4.2 min (major).



Analytical data were consistent with literature values.[3]

***tert*-butyl 3-acetylbenzoate 24**



Flame dried $MgSO_4$ (1.44 g, 12 mmol) was suspended in dry DCM (15 mL) under N_2 and concentrated H_2SO_4 (0.16 mL, 3 mmol) was added dropwise and the reaction was stirred vigorously at room temperature for 20 minutes. Benzoic acid (0.5 g, 3 mmol) was added followed by the dropwise addition of *t*BuOH (1.5 mL, 15 mmol) at 0 °C. The round bottom flask was then sealed and the suspension was stirred for 16 hours. The reaction mixture was quenched through addition of saturated aqueous

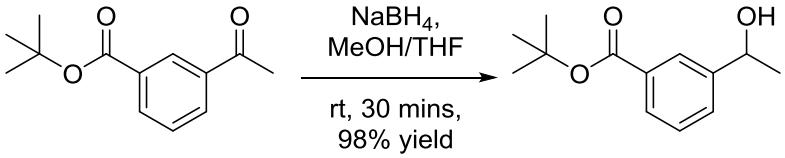
$NaHCO_3$(aq) (50 mL) and extracted with diethyl ether (3 x 50 mL), dried over $MgSO_4$, filtered, concentrated *in vacuo.* The residue was purified by column chromatography (10% EtOAc/*n*hexane) to give the ester **24** (0.42 g, 1.9 mmol, 63%).

^{1}H NMR ($CDCl_3$, 400 MHz), δ 8.53 (1H, t, *J* = 1.8, ArH), 8.18 (1H, td, *J* =7.7, 1.4, ArH), 8.12 (1H, td, *J* = 7.7, 1.5, ArH), 7.53 (1H, t, *J* = 7.8, ArH), 2.65 (3H, s, CH_3), 1.62 (9H, s, tBu CH_3).

^{13}C NMR ($CDCl_3$, 101MHz), δ 197.6 (ester C=O), 165.1 (ketone C=O), 137.3 (4° ArC), 133.9 (ArCH), 132.7 (4° ArC), 131.9 (ArCH), 129.5 (ArCH), 128.8 (ArCH), 81.9 (tBu 4°C), 28.3 (tBu CH_3), 26.9 (CH_3).

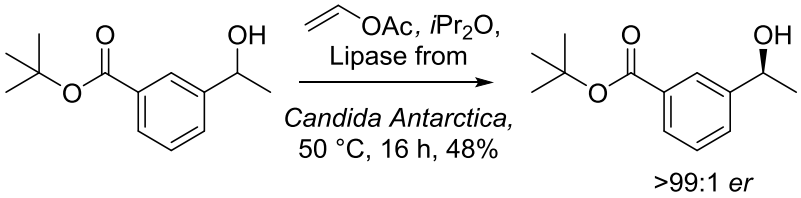
Data were consistent with literature values.[6]

***tert*-butyl 3-(1-hydroxyethyl)benzoate** rac-**25**



Prepared according to **GP1** using tert-butyl 3-acetylbenzoate **24** (1.25 g, 5.7 mmol), MeOH (4 mL), THF (4 mL) and $NaBH_4$ (316 mg, 8.5 mmol). The product alcohol rac-**25** (1.23 g, 98%) was obtained as a clear colourless oil.

***tert*-butyl (S)-3-(1-hydroxyethyl)benzoate** (*S*)-**25**



Prepared according to **GP2** using alcohol *rac*-**25** (804 mg, 3.6 mmol), diisopropyl ether (2.0 mL), vinyl acetate (2.1 mL, 22.5 mmol) and Lipase (22 mg). Purification by column chromatography (15% EtOAC:PE) gave the product *alcohol* (*S*)-**25** (385 mg, 48% yield, >99:1 *er*) as a colourless oil.

R_f (20% EtOAc:PE) 0.23.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.98 (1H, br. s, Ar-H), 7.90 (1H, dt, *J* = 7.8, 1.4, Ar-H), 7.56 (1H, br. d, *J* = 7.8, Ar-H), 7.40 (1H, dd, *J* = 7.8, 7.8, Ar-H), 4.96 (1H, q, *J* = 6.4, C*H*OH), 1.87 (1H, br. s, OH), 1.60 (9H, s, $C(CH_3)_3$), 1.52 (3H, d, *J* = 6.4, CH_3).

^{13}C NMR ($CDCl_3$, 101 MHz) δ 165.9 (C=O), 146.1 (4° C-Ar), 132.4 (4° C-Ar), 129.6 (C-Ar), 128.7 (C-Ar), 128.6 (C-Ar), 126.5 (C-Ar), 81.3 (O*C*$(CH_3)_3$), 70.3 (*C*HOH), 28.4 (O*C*(*C*$H_3)_3$), 25.4 (CH_3).

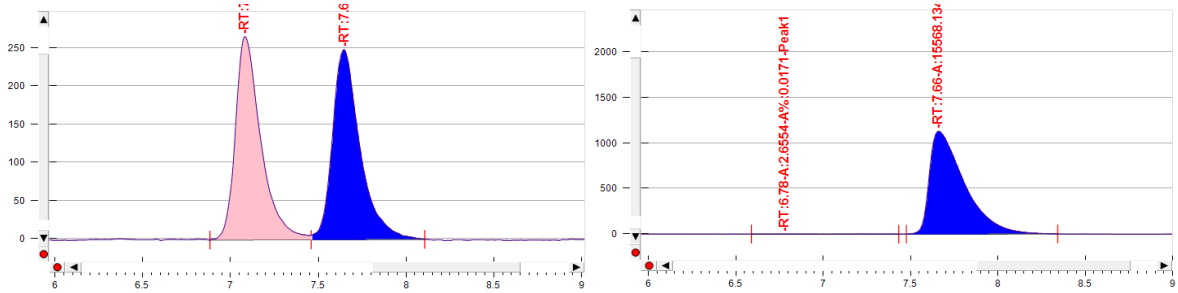
IR ν_{max} (neat)/cm^{-1} : 3418 (OH), 2975(CH_3), 2931(CH_3), 1712(C=O), 1368 (C=C), 1296(C-O), 1158, 757 (=C-H).

m/z (ESI) 245 (100, [M+Na]), 167 (80, [M+H-*t*Bu]), 149 (50, [M-O*t*Bu]).

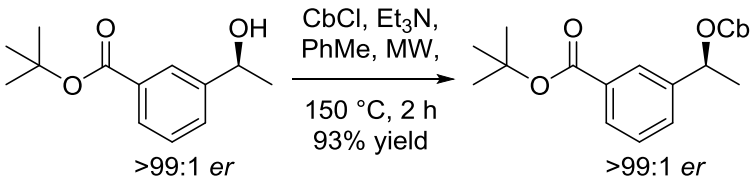
HRMS (ESI) calc'd. for $C_{13}H_{18}NaO_3$ $[M+Na]^+$ 245.1148; found: 245.1140.

$[\alpha]_D^{21}$ −31.9 (*c* 1.6, $CHCl_3$).

Chiral SFC (Chiralpak IA, 4.0 mL/min, 5% co-solvent (50% IPA:hexane), 125 bar, 40 °C); t_R: 6.8 min (minor), 7.7 min (major).



***tert*-butyl (*S*)-3-(1-((diisopropylcarbamoyl)oxy)ethyl)benzoate 26**



Prepared according to **GP3** using alcohol (*S*)-**25** (426 mg, 1.92 mmol, >99:1 *er*), CbCl (377 mg, 2.30 mmol), Et_3N (0.35 mL, 2.50 mmol) and PhMe (3 mL). The product carbamate **26** (624 mg, 93%, >99:1 *er*) was obtained as a clear colourless oil.

R_f (20% EtOAc:PE) 0.47.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.98 (1H, dd, *J* = 1.7, 1.7, Ar-H), 7.90 (1H, ddd, *J* = 7.7, 1.7, 1.7, Ar-H), 7.50 (1H, dt, *J* = 7.7, 1.7, 1.7, Ar-H), 7.39 (1H, dd, *J* = 7.7, 7.7, Ar-H), 5.87 (1H, q, *J* = 6.6, C*H*OCb), 4.29-3.57 (2H, br. m, 2 × NC*H*$(CH_3)_2$), 1.59 (9H, s, C$(CH_3)_3$), 1.55 (3H, d, *J* = 6.6, CH_3), 1.36-1.08 (12H, br. m, 2 × NCH(C*H*$_3)_2$).

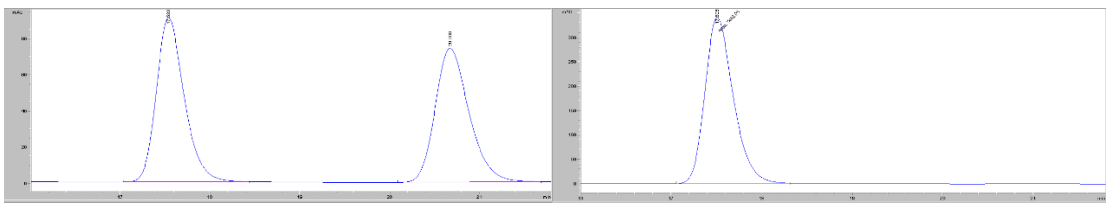
^{13}C NMR ($CDCl_3$, 101 MHz) δ 165.7 (CO_2*t*Bu C=O), 155.1 (CbO C=O), 143.3 (4° C-Ar), 132.4 (4° C-Ar), 130.2 (C-Ar), 128.7 (C-Ar), 128.5 (C-Ar), 126.9 (C-Ar), 81.1 (*C*$(CH_3)_3$), 72.5 (*C*HOCb), 46.1 (br., 2 × N*C*H$(CH_3)_2$), 28.3 (C(*C*$H_3)_3$), 23.1 (CH_3), 21.4 (br., 2 × NCH(*C*$H_3)_2$).

IR ν_{max} (neat)/cm^{-1} : 2974 (Ar C-H), 1712 (C=O), 1687 (C=O), 1289, 1157, 756.

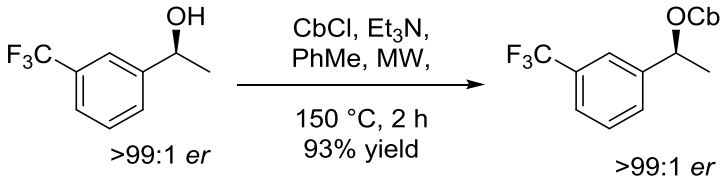
HRMS (EI) calc'd. for $C_{20}H_{32}NO_4$ $[M+H]^+$ 350.2331; found: 350.2332.

$[\alpha]_D^{20}$ −2 (*c* 1, $CHCl_3$).

Chiral HPLC (IA with guard, 1% IPA, 0.5 mL/min, 210 nm), t_R = 17.5 (major), t_R = 20.1 (minor).



(*S*)-1-(3-(trifluoromethyl)phenyl)ethyl diisopropylcarbamate 27



Prepared according to **GP3** using (*S*)-1-(3-(trifluoromethyl)phenyl)ethan-1-ol (>99:1 *er*) gave *carbamate* **27** in >99:1 *er*.

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, *J* = 0.5, 1H, ArH), 7.55 – 7.47 (m, 2H, ArH), 7.47 – 7.38 (m, 1H, ArH), 5.87 (q, *J* = 6.6, 1H, C*H*OH), 4.20 – 3.66 (m, 2 × NC*H*$(CH_3)_2$), 1.54 (d, *J* = 6.7, 3H, CH_3), 1.20 (d, J = 7.4, 12H, 2 × NCH(C*H*$_3)_2$).

^{13}C NMR (76 MHz, $CDCl_3$) δ 154.77 (C=O), 144.09 (4°ArC), 130.85 (q, *J* = 32.2 *C*CF_3), 129.43 (q, *J* = 1.2 Ar-CH), 128.97 (Ar-CH), 124.30 (q, *J* = 3.8, Ar-CH), 124.20 (CF_3, q, *J* = 272.3), 122.63 (q, *J* = 3.9, Ar-CH), 72.03 (CH), 45.89 (CH), 22.83 (CH_3), 21.04 (CH_3).

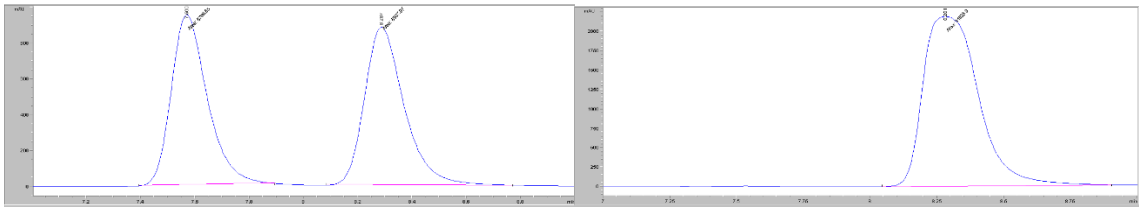
^{19}F NMR (283 MHz, $CDCl_3$) δ −62.63 (s);

HRMS (ESI) Calcd for $C_{16}H_{22}F_3NNaO_2$(M+Na): 340.1495, Found: 340.1498;

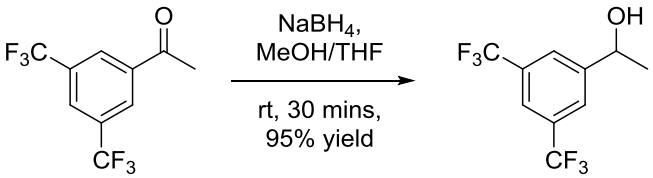
IR ν_{max} (neat)/cm^{-1}: 2935, 1689, 1477, 1436, 1370, 1326, 1285, 1203, 1162, 1069, 1046, 907, 803, 769, 702.

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{21}}$ +2 (*c* 1, $CHCl_3$)

Chiral HPLC (IA column with guard, 10% IPA in hexane), 0.5 mL/min, 210 nm, t_R= 7.5 mins (minor) t_R= 8.3 mins (major).

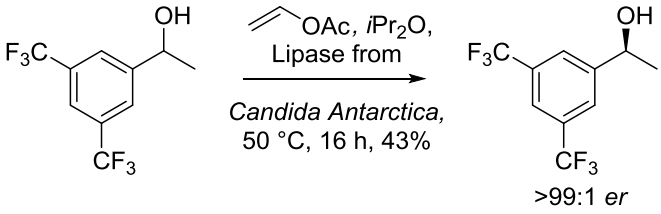


1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-ol *rac*-**28**



Prepared according to **GP1** using 3′,5′-Bis(trifluoromethyl)acetophenone (3.13 g, 12 mmol), MeOH (8.4 mL), THF (8.4 mL) and $NaBH_4$ (0.69 g, 18.3 mmol). The product alcohol *rac*-**28** (2.91 g, 95%) was obtained as a white solid. For characterisation data *vide infra.*

(*S*)-1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-ol (*S*)-**28**



Prepared according to **GP2** using alcohol *rac*-**28** (2.6 g, 10 mmol), vinyl acetate (4.3 g, 56 mmol), lipase (60 mg), *i*Pr$_2$O (4 mL) and flame dried 4Å molecular sieve powder (1 g). The product alcohol (*S*)-**28** (1.10 g, 43%, >99:1 *er*) was isolated as a white solid.

***R*$_f$** (20% EtOAc : *n*-hexane) 0.48

M.p. 74-75°C

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85 (s, 2H, ArH), 7.79 (s, 1H, ArH), 5.06 (s, 1H, CHOH), 1.93 (s, 1H, OH), 1.54 (d, J = 6.6, 3H, CH_3)

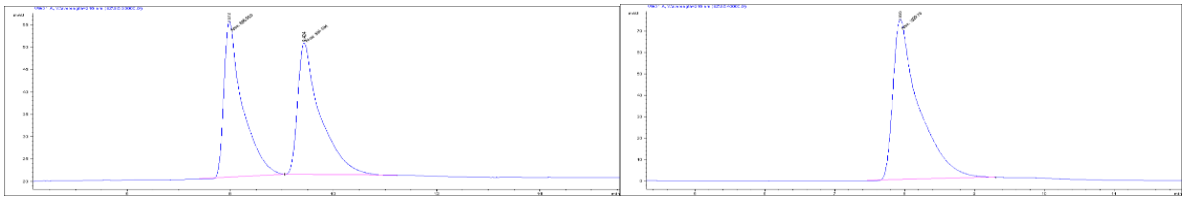
^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.4 (4° ArC) 132.1 (q, J = 33.1, CCF_3), 125.7 (Ar-CH), 121.2 (Ar-CH), 123.5 (q, J = 273, CF_3), 69.4 (COH), 25.7 (CH_3)

^{19}F NMR ($CDCl_3$, 377 MHz) δ −62.80

$[\alpha]_D^{21}$ −17 (c 0.86, CH_2Cl_2) Lit. $[\alpha]_D^{20}$ = –24.1 (c 1.0, $CHCl_3$) for *S* isomer >99.9% ee.[7]

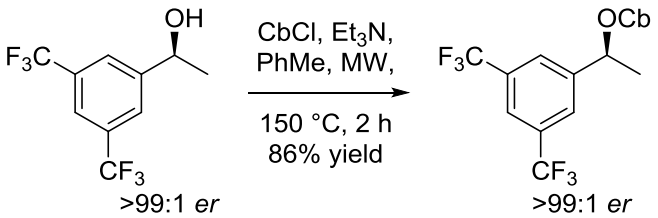
Chiral HPLC (CHIRACEL OD column without guard, 2% IPA: n-hexane), flow rate: 1.0 mL/min; t_R = 7.9 min; t_R (minor) = 9.4 mins; t_R (major)= 7.9 min)

er >99:1



Data were consistent with literature values.[8]

(*S*)-1-(3,5-bis(trifluoromethyl)phenyl)ethyl diisopropylcarbamate 29



Prepared according to **GP3** using (*S*)-1-(3,5-bis(trifluoromethyl)phenyl)ethan-1-ol (*S*)-**28** (0.85 g, 3.29 mmol, >99:1 *er*) gave *carbamate* **29** (86%, 1.10 g,>99:1 *er*).

R$_f$ = 0.69 (1:2 EtOAc : n-hexane)

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.78 (s, 3H, ArH), 5.93 (q, J = 6.7, 1H, CH), 3.95 (m, 2H, CH), 1.59 (d, J = 6.7, 3H, CH_3), 1.23 (s, 12H, CH_3)

^{13}C NMR ($CDCl_3$, 125 MHz) δ 154.5 (C=O), 145.9 (4°C), 131.8 (q, J = 33.1, CCF_3), 126.1 (ArCH), 121.5 (ArCH), 123.4 (q, J = 273, CF_3), 71.5 (C-O), 45.6 (C-N), 46.1 (Br. m, CH), 22.9 (CH_3), 21.2 (CH_3), 21.1 (Br. m, CH_3)

^{19}F NMR ($CDCl_3$, 377 MHz) δ −62.8

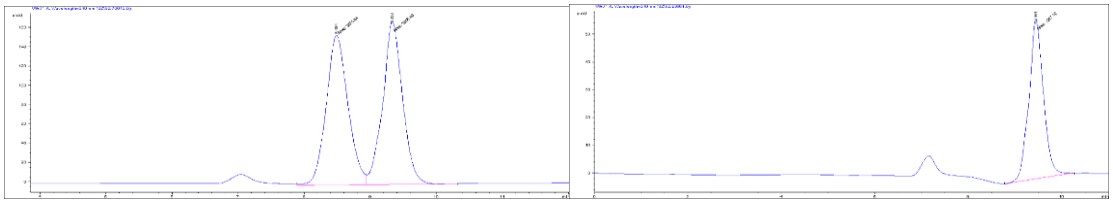
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{21}}$ +11 (c 1, $CHCl_3$)

HRMS (ESI) calc'd for $C_{17}H_{21}F_6NO_2$ [M+Na]+ 408.1369, found: 408.1376

IR(cm^{-1}) 2979 (CH_3), 1684 (C=O), 1440 (aromatic C=C), 1163 (C-N), 1113 (C-F), 897 (aromatic C-H)

Chiral HPLC (CHIRACEL IC column with guard, 1% IPA: *n*-hexane), flow rate: 0.5 mL/min; t_R (minor) = 8.4 min, t_R (major)= 9.3 min

er >99:1



Synthesis of tertiary alcohols from secondary benzylic carbamates

GP4 – *Lithiation-borylation of benzylic secondary carbamates using LTMP*

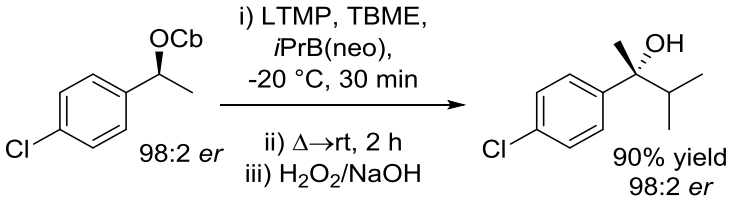
Preparation of LTMP

To a solution of 2,2,6,6-Tetramethylpiperidine (0.11 mL, 0.65 mmol) in dry TBME (0.25 mL) cooled to 0 °C was added *n*BuLi (1.53M in hexanes, 0.41 mL, 0.63 mmol) dropwise. The reaction was then warmed to rt and stirred for 30 min giving a clear colourless 1M solution of LTMP.

Note: Occasionally LTMP will precipitate out of solution, we have found that addition of the suspension does not negatively impact the lithiation-borylation reactions. However, addition of 1 mL of TBME rather than 0.25 mL is sufficient to redissolve LTMP.

To a solution of benzylic carbamate (0.5 mmol) and boronic ester (0.65 mmol) in dry TBME (1 mL) cooled to −20 °C was added a solution of LTMP (*vide supra*) dropwise. The light yellow solution was then stirred at −20 °C for 30 min before warming to room temperature and stirring for a further 2 h, at which point analysis of ^{11}B NMR data indicated no presence of an "ate" complex. A solution of 2:1 NaOH (2 M) and H_2O_2 (30% v/v) was added (1 mL/mmol) and the reaction mixture was stirred vigorously overnight. The reaction was diluted with H_2O (5 mL), the layers separated and the aqueous layer was extracted into Et_2O (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by flash column chromatography to give the product tertiary benzylic alcohol.

(*R*)-2-(4-Chlorophenyl)-3-methylbutan-2-ol 5



Prepared according to **GP4** using (S)-1-(4-chlorophenyl)ethyl diisopropylcarbamate **4** (0.13 g, 0.5 mmol, 98:2 *er*), iPrB(neo) (0.12 mL, 0.65 mmol) and LTMP (0.63 mmol) to yield tertiary alcohol **5** (0.090 g, 90%, 98:2 *er*) as a pale yellow oil.

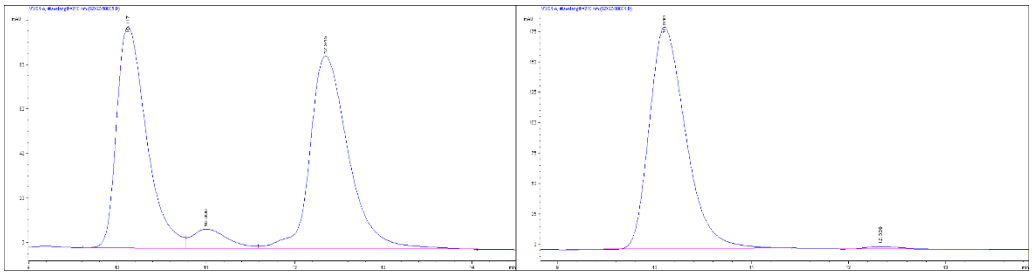
$\mathbf{R}_f$ (17.5% Et_2O:*n*hexane) 0.18.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36 (2H, d, J = 8.6, ArCH), 7.29 (2H, d, J = 8.6, ArCH), 1.98 (1H, hept, J = 6.8, CH), 1.66 (1H, s, OH), 1.50 (3H, s, CH_3), 0.89 (3H, d, J = 6.8, $CH(CH_3)_2$), 0.79 (3H, d, J = 6.8, $CH(CH_3)_2$).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.3 (4° C-Cl), 132.2 (4° ArC), 127.9 (Ar-CH), 126.8 (Ar-CH), 76.5 (C-OH), 38.6 (CH_3), 26.8 (CH), 17.4 (CH_3), 17.1 (CH_3).

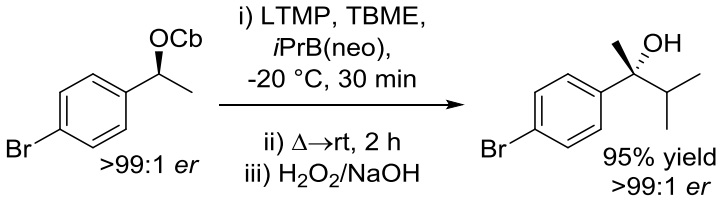
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ +16 (*c* 1.0, $CHCl_3$).

Chiral HPLC (Chiralpak IC, rt, 0.5 mL/min, 2% IPA:hexane); t_R: 10.9 min (major), 12.3 min (minor).



Data were consistent with literature values.[3]

(*R*)-2-(4-Bromophenyl)-3-methylbutan-2-ol 6



Prepared according to **GP4** using carbamate **22** (98 mg, 0.30 mmol, >99:1 *er*), *i*PrB(neo) (68 µL, 0.39 mmol) and LTMP (0.38 mmol) to yield *tertiary alcohol* **6** (69 mg, 95%, >99:1 *er*) as a colourless oil.

R_f (20% EtOAc:PE) 0.34.

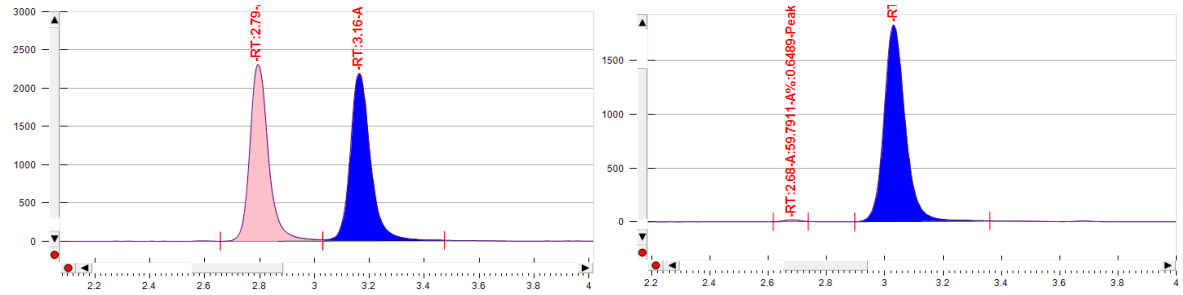
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44 (2H, br. d, J = 8.5, Ar-H), 7.29 (2H, br. d, J = 8.5, Ar-H), 1.97 (1H, hept, J = 6.8, C*H*(CH_3)$_2$), 1.60 (1H, br. s, OH), 1.50 (3H, s, CH_3), 0.89 (3H, d, J = 6.8, CH(C*H*$_3$)$_2$), 0.78 (3H, d, J = 6.8, CH(C*H*$_3$)$_2$).

^{13}C NMR ($CDCl_3$, 101 MHz) δ 146.9 (4° C-Ar), 131.0 (2 × C-Ar), 127.3 (2 × C-Ar), 120.5 (C-Br), 76.7 (COH), 38.7 (CH), 27.0 (CH_3), 17.5 (CH(*C*H$_3$)$_2$), 17.2 (CH(*C*H$_3$)$_2$).

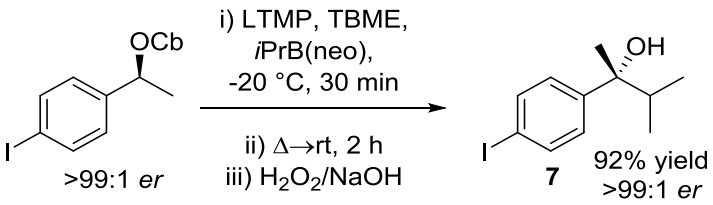
IR ν_{max} (neat)/cm^{-1} : 3447 (OH), 2969 (Ar C-H), 1486, 1077 (C-Br), 1007.

$[\alpha]_D^{20}$ +20.7 (*c* 1.50, $CHCl_3$).

Chiral SFC (Whelk O-1, 4.0 mL/min, 5% co-solvent (50% IPA:hexane), 125 bar, 40 °C; t_R: 2.7 min (minor), 3.0 min (major).



(*R*)-2-(4-Iodophenyl)-3-methylbutan-2-ol 7



Prepared according to **GP4** using carbamate **12** (187 mg, 0.50 mmol, >99:1 *er*), *i*PrB(neo) (101 mg, 0.65 mmol) and LTMP (0.65 mmol) to yield *benzylic alcohol* **7** (134 mg, 92%, >99:1 *er*) as a yellow oil.

R_f (20% Et_2O:Pentane) 0.64.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64 (2H, d, J = 8.5, Ar-H), 7.17 (2H, d, J = 8.5, Ar-H), 1.97 (1H, dt, J = 13.6, 6.8, C*H*(CH_3)$_2$), 1.66 (1H, s, OH), 1.49 (3H, s, CH_3), 0.89 (3H, d, J = 6.8, CH(C*H*$_3$)$_2$), 0.78 (3H, d, J = 6.8, CH(C*H*$_3$)$_2$).

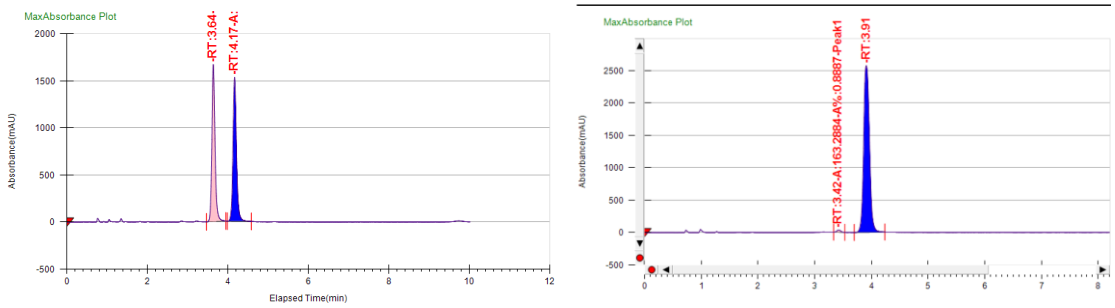
^{13}C NMR ($CDCl_3$, 101 MHz) δ 147.7 (4° C-Ar), 137.0 (2 × C-Ar), 127.6 (2 × C-Ar), 92.0 (4° C-I), 76.7 (4° C), 38.6 (CH), 26.9 (CH_3), 17.5 (CH(*C*H$_3$)$_2$), 17.1 (CH(*C*H$_3$)$_2$).

IR ν_{max} (neat)/cm^{-1} : 3455 (OH), 2969 (Ar C-H), 1483, 1003.

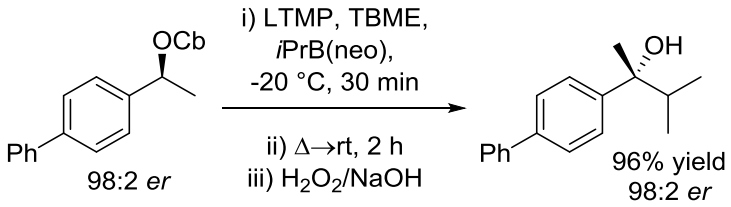
HRMS (ESI) calc'd. for $C_{11}H_{15}IONa$ $[M+Na]^+$ 313.0065; found: 313.0042.

$[\alpha]_D^{20}$ +52.0 (*c* 1.0, CH_2Cl_2).

Chiral SFC (Whelk-01, 4.0 mL/min, 5% co-solvent (50% IPA:hexane), 125 bar, 40 °C; t_R: 3.4 min (minor), 3.9 min (major).



(*R*)-2-([1,1'-biphenyl]-4-yl)-3-methylbutan-2-ol 8



Prepared according to GP4 using (*S*)-1-([1,1'-biphenyl]-4-yl)ethyl diisopropylcarbamate[9] (163 mg, 0.5 mmol, 98:2 *er*), *i*PrB(neo) (101 mg, 0.65 mmol) and LTMP (0.65 mmol) to yield *tertiary alcohol* **8** (114 mg, 96%, 98:2 *er*) as a yellow solid.

$\boldsymbol{R_f}$ = 0.46 (20% EtOAc in *n*Hexane)

M.p. = 77-79ºC, CH_2Cl_2

^{1}H NMR ($CDCl_3$, 400 MHz), δ 7.63-7.55 (4H, m, ArH), 7.52-7.41 (4H, m, ArH), 7.37-7.31 (1H, m, ArH), 2.07 (1H, hept, *J*= 6.9, CH), 1.65 (1H, s, OH), 1.57 (3H, s, CH_3), 0.94 (3H, d, *J*= 6.9, CH(CH_3)$_2$), 0.86 (3H, d, J= 6.9, CH(CH_3)$_2$).

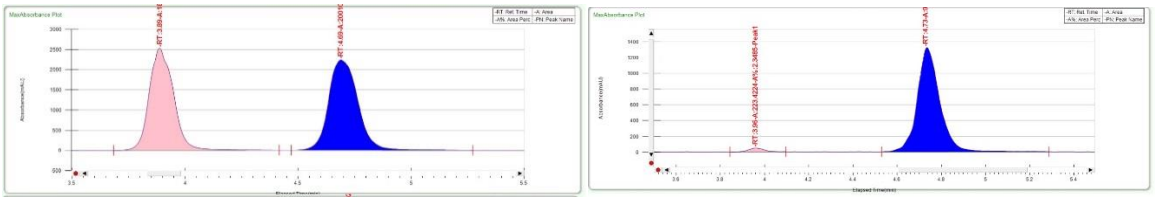
^{13}C NMR ($CDCl_3$, 101MHz), δ 147.6 (4° ArC), 141.0 (4° ArC), 139.4 (4° ArC), 127.3 (Ar-CH), 127.2 (Ar-CH), 126.7 (Ar-CH), 125.9 (Ar-CH), 76.8 (4° *C*OH), 38.7 (CH), 26.9 (CH_3), 17.6 (CH_3), 17.3 (CH_3).

IR ν_{max} (neat)/cm^{-1}: 3452 (OH), 3028 (ArCH), 2967 (CH_3), 2874 (CH_3), 2937 (CH_3), 1599 (ArCC), 1072 (C-O), 766 (ArCH), 696 (ArCH).

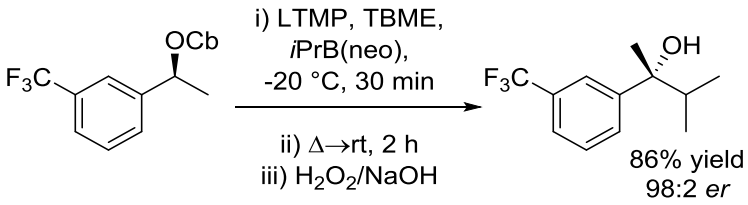
HRMS(ESI) calc'd for $C_{17}H_{20}ONa$ $[M+Na]^+$ 263.14, found: 263.1406.

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ +23 (*c* 1, $CHCl_3$).

Chiral SFC (Whelk-O1 column, iso 20%, 4 mL/min, 125 bar, co-solvent: 10% IPA/Hex) t_R 3.96 min (minor), t_R 4.73 mins (major).



(R)-3-methyl-2-(3-(trifluoromethyl)phenyl)butan-2-ol 9



Prepared according to **GP4** using (S)-1-(3-(trifluoromethyl)phenyl)ethyl diisopropylcarbamate **26** (0.16 g, 0.5 mmol, >99:1 *er*), *i*PrB(neo) (0.12 mL, 0.65 mmol) and LTMP (0.63 mmol) to yield (S)-3-methyl-2-(3-(trifluoromethyl)phenyl)butan-2-ol **9** (0.1 g, 0.43 mmol, 86%, 98:2 *er*) as a yellow oil.

R_f (17.5% Et_2O:PE) 0.25

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.71 (1H, s, ArH), 7.60 (1H, d, J = 7.6, ArH), 7.46 (2H, m, ArH), 2.02 (1H, hept, J = 6.8), 1.68 (1H, s, OH), 1.55 (3H, s, CH_3), 0.92 (3H, d, J = 6.8, CH_3), 0.79 (3H, d, J = 6.8).

^{13}C NMR ($CDCl_3$, 101 MHz) δ 148.9 (ArC), 130.2 (q, J = 31.9, **C**CF3), 128.9 (m, ArH), 128.4 (ArCH), 124.5 (q, J = 274, CF_3), 123.4 (q, J =3.8, ArCH), 122.3 (q, J = 3.9, ArCH) 76.8 (COH), 38.7 (CH), 27.2 (CH_3), 17.5 (CH_3), 17.1 (CH_3).

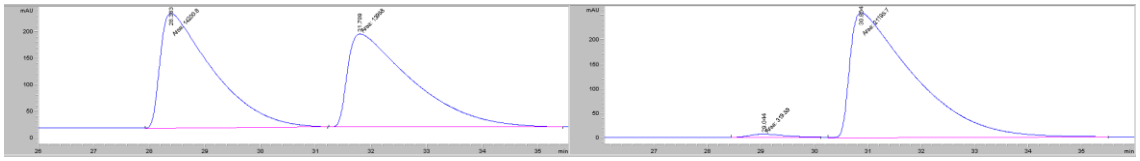
^{19}F NMR ($CDCl_3$, 377 MHz) δ −62.54 (s).

$[\alpha]_D^{20}$ +4.6 (*c* 0.86, $CHCl_3$).

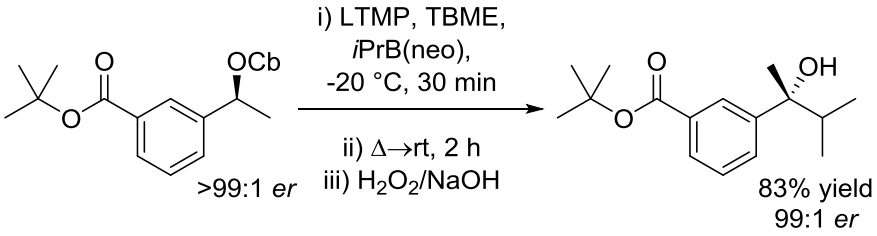
IR ν_{max} (neat)/cm^{-1} : 3500 (OH), 2972 (CH_3), 1454 (ArCC), 1374, 1220, 1163, 1122, 1074, 1003, 903, 851, 803, 778.

HRMS (ESI) Calcd for $C_{12}H_{14}F_3$(M+H-H2O): 215.1042, Found: 215.1042

Chiral HPLC IA column with guard, 100% hexane, 1 mL/min, 210 nm, t_R= 29 mins (minor), t_R= 30.8 mins (major).



tert-Butyl (R)-3-(2-hydroxy-3-methylbutan-2-yl)benzoate 11



Prepared according to **GP4** using carbamate **27** (105 mg, 0.30 mmol, >99:1 *er*), *i*PrB(neo) (68 µL, 0.39 mmol) and LTMP (0.38 mmol) to yield *benzylic alcohol* **11** (66 mg, 83%, 99:1 *er*) as a colourless oil.

$\mathbf{R}_f$ (20% EtOAc:PE) 0.43.

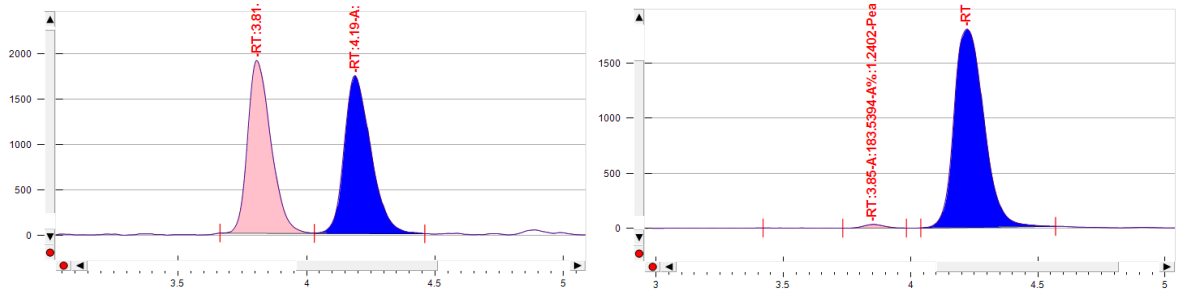
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.03 (1H, dd, J = 2.0, 1.4, ArH), 7.85 (1H, ddd, J = 7.7, 1.4, 1.2, ArH), 7.61 (1H, ddd, J = 7.7, 2.0, 1.2, ArH), 7.37 (1H, t, J = 7.7, ArH), 2.04 (1H, hept, J = 6.8, CH), 1.75 (1H, s, OH), 1.59 (9H, s, C(C*H*$_3$)), 1.54 (3H, s, CH_3), 0.90 (3H, d, J = 6.8, CH_3), 0.78 (3H, d, J = 6.8, CH_3).

^{13}C NMR ($CDCl_3$, 101 MHz) δ 166.2 (4 °C), 148.3 (4 °C), 131.8 (CH), 129.6 (CH), 127.9 (CH), 127.6 (CH), 126.3 (CH), 81.1 (4 °C), 76.8 (4 °C), 38.6 (CH), 28.3 (CH_3), 27.0 (CH_3), 17.5 (CH_3), 17.2 (CH_3).

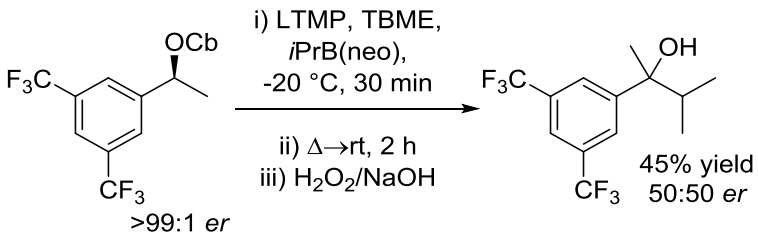
HRMS (ESI) calc'd. for $C_{16}H_{24}NaO_3$ $[M+Na]^+$ 287.1618; found: 287.1607.

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{21}}$ −31.1 (*c* 0.9, $CHCl_3$).

Chiral SFC (Whelk O-1, 4.0 mL/min, 5% co-solvent (50% IPA:hexane), 125 bar, 40 °C; t_R: 3.9 min (2*S*, minor enantiomer), 4.2 min (2*R*, major enantiomer) *er* >99:1.



(*rac*)-2-(3,5-bis(trifluoromethyl)phenyl)-3-methylbutan-2-ol 10



Prepared according to **GP4** using (*S*)-1-(3,5-bis(trifluoromethyl)phenyl)ethyl diisopropylcarbamate **29** (0.19 g, 0.5 mmol), iPrB(neo) (0.12 mL, 0.65 mmol) and LTMP (0.63 mmol) to yield *rac*-2-(3,5-bis(trifluoromethyl)phenyl)-3-methylbutan-2-ol **10** (0.07 g, 0.22 mmol, 45%, *racemic*) as a yellow oil.

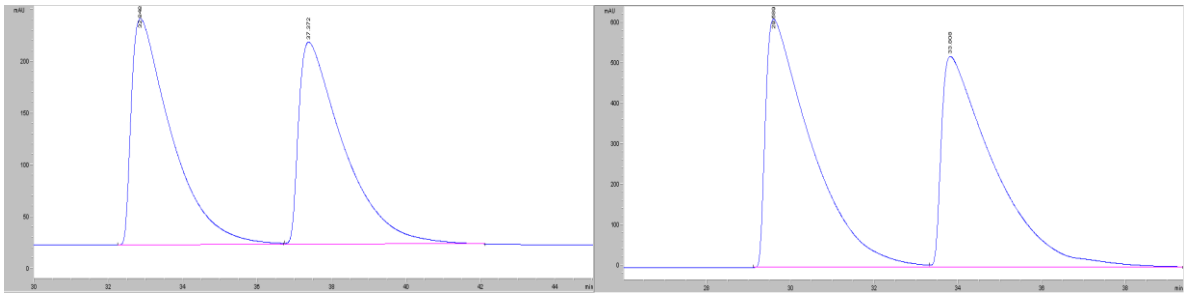
$\mathbf{R}_f$= 0.38 (1:5 Et_2O : *n*-hexane).

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.90 (s, 2H, ArH), 7.76 (s, 1H, ArH), 2.04 (m, 1H, CH), 1.58 (2, 3H, CH_3), 0.95 (d, J = 6.7, 3H, CH_3), 0.78 (d, J = 6.8, 3H, CH_3).

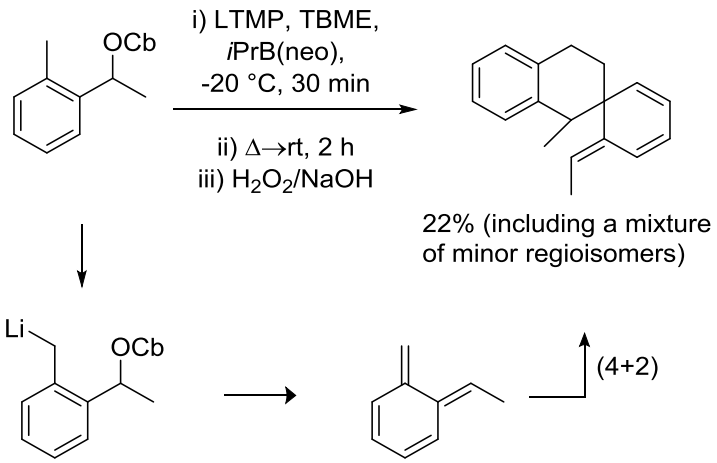
^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.6 (C), 131.3 (q, J = 33, CCF_3), 125.8 (CH), 123.6 (q, J = 271.8, CF_3), 120.6 (CH), 76.7 (C), 38.7 (CH), 27.5(CH_3), 17.4 (CH_3), 16.9 (CH_3).

^{19}F NMR ($CDCl_3$, 377 MHz) δ −62.62.

Chiral HPLC (CHIRACEL IA column with guard, 100% *n*-hexane, flow rate: 0.5 mL/min, room temperature, 210 nm; t_R = 29.6 min, t_R= 33.8 min - racemic standard is on the left.



Attempted In Situ Lithiation–Borylation of *ortho*-methyl carbamate.



Procedure conducted according to **GP4** using carbamate shown (100 mg, 0.38 mmol), *i*PrB(neo) (76.5 mg, 0.49 mmol) and LTMP (0.48 mmol) to yield a (4+2) dimer, which was isolated with a mixture of other regioisomers (20 mg, 22%).

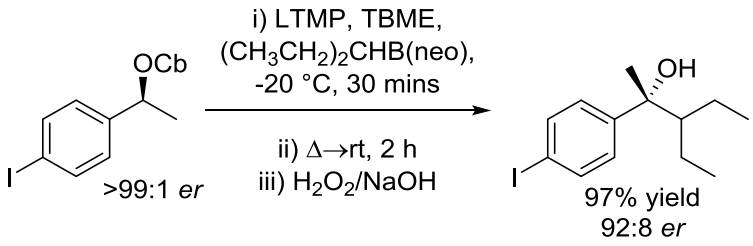
R_f (100% hexane) 0.46.

^{1}H NMR ($CDCl_3$, 400 MHz, major isomer) δ 7.15–7.09 (4H, m, Ar-H), 6.43 (2H, br. d, J = 10.1 Hz, alkenyl), 5.97–5.86 (3H, m, alkenyl), 5.19 (1H, br. q, J = 7.0, alkenyl), 2.96–2.75 (3H, m, CH_2CH_2 and CH), 1.99 (1H, ddd, J = 13.3, 9.5, 6.3 Hz, CH_2CH_2), 1.72 (3H, d, J = 7.0 Hz, CH_3), 1.72 (1H, d, CH_2CH_2), 1.09 (3H, d, J = 7.1 Hz, CH_3).[10]

^{13}C NMR ($CDCl_3$, 101 MHz) δ 141.8, 138.9, 138.5, 136.1, 128.3, 128.2, 125.9, 124.9, 122.8, 122.1, 122.0, 43.8, 43.0, 30.6, 30.5, 25.5, 18.2, 13.1.

LRMS (GC-MS, EI): 236 [M^+]

(*R*)-3-ethyl-2-(4-iodophenyl)pentan-2-ol 16



Prepared according to **GP4** using carbamate **12** (78 mg, 0.21 mmol, >99:1 *er*), $(CH_2CH_3)_2CHB(neo)$[11] (50 mg, 0.27 mmol) and LTMP (0.27 mmol) to yield *tertiary alcohol* **16** (64 mg, 97%, 92:8 *er*) as a colourless oil.

R$_f$ (20% Et_2O:pentane) 0.6.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (2H, d, J =8.4, Ar-H), 7.18 (2H, d, J =8.4, Ar-H), 1.62 (1H, br, OH), 1.60-1.52 (1H, m, CH), 1.49 (3H, s, CCH_3), 1.46-1.36 (2H, m, CH_2), 1.31-1.18 (1H, m, CH*H*), 1.18-1.06 (1H, m, C*H*H), 0.95-0.77 (6H, m, $(CH_3)_2$).

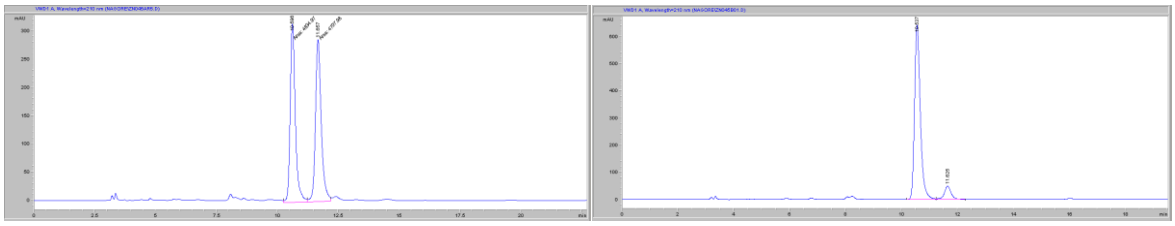
^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.4 (4^o C-Ar), 136.9 (2 × C-Ar), 127.3 (2 × C-Ar), 91.8 (4^o C-I), 77.6 (4^o C), 52.1 (CH), 27.4 (CCH_3), 22.5 (CH_2), 22.2 (CH_2), 13.5 (CH_2CH_3), 13.4 (CH_2CH_3).

IR ν_{max} (neat)/cm^{-1} : 3463 (OH), 2960 (Ar C-H), 1483 (Ar C-C), 1389, 1003, 818.

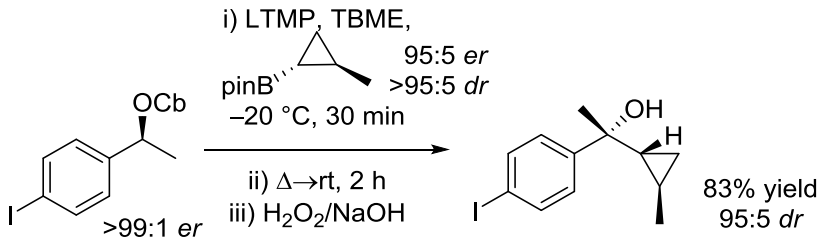
HRMS (ESI) calc'd. for $C_{13}H_{19}INaO$ $[M+Na]^+$ 341.0373; found: 341.0371.

$[\alpha]_D^{20}$ +4.0 (*c* 1, CH_2Cl_2).

Chiral HPLC (Chiralpak IA with guard, rt, 1.0 mL/min, 2% IPA:hexane); t_R: 10.5 min (2*R*, major enantiomer), 11.6 min (2*S*, minor enantiomer) *er* 92:8.



(*R*)-1-(4-iodophenyl)-1-((1*R*,2*R*)-2-methylcyclopropyl)ethan-1-ol 14



Prepared according to GP4 using carbamate **12** (79 mg, 0.21 mmol, >99:1 *er*), 2-methylcyclopropaneB(pin)[12] (50 mg, 0.27 mmol, 95:5 *er*, >95:5 *dr*) and LTMP (0.27 mmol) to yield *benzylic alcohol* **14** (44 mg, 68%) as a yellow oil. The product was obtained as a mixture of diastereomers (anti:syn 95:5 by ^{1}H NMR).

R$_f$ (20% Et$_2$O:pentane) 0.8.

Analytical data for the major anti diastereomer.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64 (2H, d, *J* = 8.5, Ar-H), 7.24 (2H, d, *J* = 8.5, Ar-H), 1.57 (1H, s, OH), 1.42 (3H, s, CCH_3), 1.01 (3H, d, *J* = 5.9, CHC*H*$_3$), 0.96-0.83 (1H, m, C*H*CH_3), 0.82-0.69 (1H, m, CCH), 0.63-0.52 (1H, m, CH*H*), 0.31-0.23 (1H, m, C*H*H).

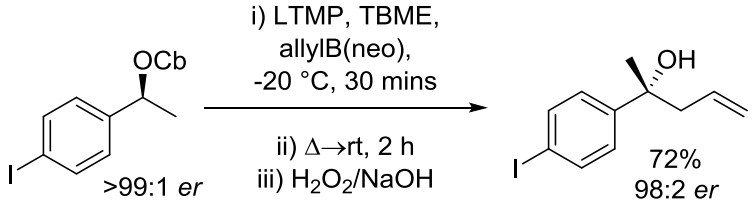
^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.1 (4^o C-Ar), 137.0 (2 × C-Ar), 127.3 (2 × C-Ar), 92.2 (4^o C-I), 73.2 (4^o C), 31.4 (*C*HCH_3), 28.7 (C*C*H$_3$), 18.6 (CH*C*H$_3$), 10.2 (CH_2), 9.0 (C*C*H).

IR ν_{max} (neat)/cm^{-1} : 3418 (OH), 2949 (Ar C-H), 1483 (Ar C-C), 1389, 1003, 816.

HRMS (ESI) calc'd. for $C_{12}H_{15}INaO$ $[M+Na]^+$ 325.0060; found: 325.0064.

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ +2.0 (*c* 1, CH_2Cl_2).

(*R*)-2-(4-iodophenyl)pent-4-en-2-ol 15



Prepared according to GP4 using carbamate **12** (131 mg, 0.35 mmol, >99:1 *er*), allylB(neo) (69 mg, 0.45 mmol) and LTMP (0.45 mmol) to yield *tertiary alcohol* **15** (72 mg, 72%, 98:2 *er*) as a light yellow oil.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.66 (2H, d, *J* = 8.5, Ar-H), 7.18 (2H, d, *J* = 8.5, Ar-H), 5.69-5.51 (1H, m, CH), 5.13 (2H, d, *J* = 12.4, CHC*H*$_2$), 2.65 (1H, dd, *J* = 13.8, 6.5, CCH*H*), 2.47 (1H, dd, *J* = 13.8, 8.3, CC*H*H), 2.07 (1H, br, OH), 1.52 (3H, s, CH_3).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.4 (4° C-Ar), 137.2 (2 × C-Ar), 133.2 (*C*HCH$_2$), 127.0 (2 × C-Ar), 119.9 (CH*C*H$_2$), 92.1 (4° C-I), 73.4 (4° C), 48.3 (C*C*H$_2$), 29.8 (CH_3).

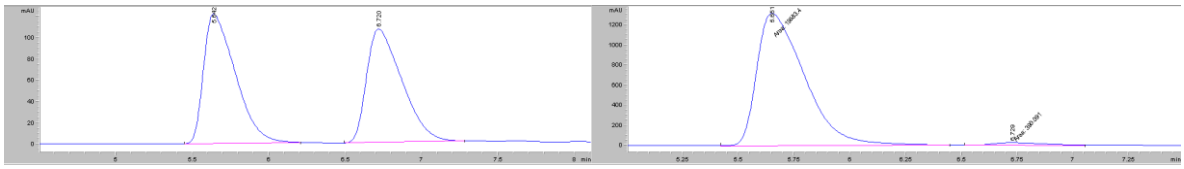
R$_f$ (20% Et$_2$O:pentane) 0.7.

IR ν_{max} (neat)/cm^{-1} : 3420 (OH), 2975 (Ar C-H), 1482 (Ar C-C), 1392, 1003, 819.

HRMS (EI) calc'd. for $C_{13}H_{13}INaO$ $[M+Na]^+$ 310.9903; found: 310.9906.

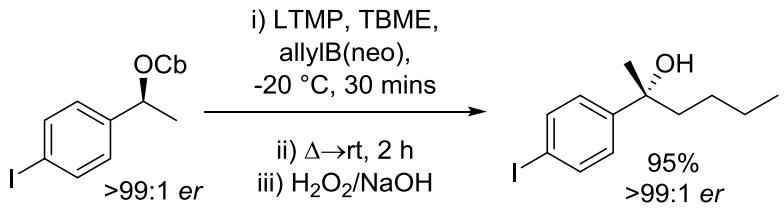
$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ +26.0 (*c* 1, CH_2Cl_2).

Chiral HPLC (Chiralpak IC with guard, rt, 1.0 mL/min, 3% IPA:hexane); t_R: 5.6 min (major), 6.7 min (minor).



Data were consistent with literature values.[13]

(*R*)-2-(4-iodophenyl)hexan-2-ol 13



Prepared according to GP4 using carbamate **12** (131 mg, 0.35 mmol, >99:1 *er*), ^{n}BuB(neo) (77 mg, 0.45 mmol) and LTMP (0.45 mmol) to yield *tertiary alcohol* **13** (101 mg, 95%, >99:1 *er*) as a colourless oil.

R$_f$ (20% Et$_2$O:pentane) 0.73.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (2H, d, *J* = 8.5, Ar-H), 7.17 (2H, d, *J* = 8.5, Ar-H), 1.82 (1H, s, OH), 1.80-1.73 (2H, m, C*H*$_2$CH$_2$CH$_2$CH$_3$), 1.52 (3H, s, CCH$_3$), 1.35-1.16 (3H, m, CH$_2$C*H*$_2$C*H*HCH$_3$), 1.16-0.99 (1H, m, CH$_2$CH$_2$CH*H*CH$_3$), 0.84 (3H, t, *J* = 7.1, CH$_3$).

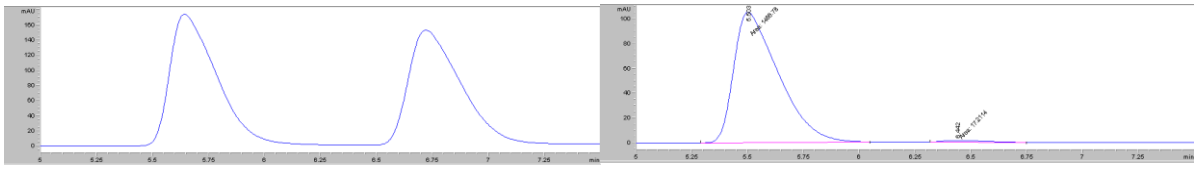
^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.8 (4° C-Ar), 137.1 (2 × C-Ar), 127.1 (2 × C-Ar), 91.9 (4° C-I), 74.6 (4° C), 43.8 (*C*H$_2$CH$_2$CH$_2$CH$_3$), 30.2 (C*C*H$_3$), 26.1 (CH$_2$*C*H$_2$CH$_2$CH$_3$), 23.0 (CH$_2$CH$_2$*C*H$_2$CH$_3$), 14.0 (CH$_2$*C*H$_3$).

IR ν_{max} (neat)/cm^{-1} : 3394 (OH), 2931 (Ar C-H),1483 (Ar C-C), 1389, 1003, 820;

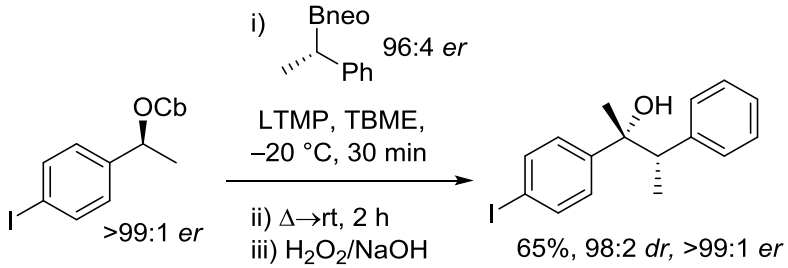
HRMS (ESI) calc'd. for $C_{12}H_{17}INaO$ $[M+Na]^+$ 327.0216; found: 327.0219;

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ +2.0 (*c* 1, CH_2Cl_2);

Chiral HPLC (Chiralpak IC with guard, rt, 1.0 mL/min, 3% IPA:hexane); t_R: 5.6 min (major), 6.4 min (minor).



(2R,3S)-2-(4-iodophenyl)-3-phenylbutan-2-ol, 18



A solution of LTMP (0.45 mmol, *vide supra*) was added dropwise to a mixture of benzylic carbamate **12** (100 mg, 0.26 mmol, >99:1 *er*) and (*S*)-1-Phenylethyl neopentyl boronic ester (80 mg, 0.34 mmol, 96:4 *er*) in dry TBME (0.8 mL) at −20 °C. The light yellow solution was then stirred at −20 °C for 30 min before warming to room temperature and stirring for a further 2 h. The reaction mixture was concentrated *in vacuo* and filtered through a plug of SiO_2 with 1% Et_2O in hexane (to remove traces of remaining **12**). The filtrate was concentrated *in vacuo* and re-dissolved in THF (1.2 mL). A solution of 2:1 NaOH (2 M) and H_2O_2 (30% v/v) was added (1 mL/mmol) at 0 °C and the reaction mixture was stirred vigorously overnight at room temperature. The reaction was diluted with Et_2O (5 mL) and H_2O (5 mL), the layers separated and the aqueous layer was extracted into Et_2O (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by flash column chromatography to give the product tertiary benzylic alcohol **18** as a colourless oil (61mg, 0.17 mmol, 65%).

R_f (anti isomer, 20% Et_2O in hexane): 0.34

^{1}H NMR ($CDCl_3$, 400 MHz), δ 7.65 (2H, d, *J*= 8.4, Ar-H), 7.33-7.21 (5H, m, Ar-H), 7.18 (2H, d, *J* = 8.5, Ar-H), 3.05 (1H, q, *J* = 7.1, CH), 1.65 (1H, s, OH), 1.32 (3H, s, CH_3), 1.08 (2H, d, *J* = 7.1, CH_3).

^{13}C NMR ($CDCl_3$, 101 MHz), 147.1 (4 °ArC), 142.5 (4 °ArC), 137.1 (ArCH), 129.3 (ArCH), 128.3 (ArCH), 127.5 (ArCH), 126.9 (ArCH), 92 (4 °ArC), 76.1 (COH), 50.5 (CH), 29.9 (CH_3), 15.8 (CH_3).

IR (neat, cm^{-1}) 3565 (OH), 3059 (ArCH), 3025 (ArCH), 2972 (CH_3), 2932 (CH_3), 1583 (ArCC), 1483 (ArCC), 1389 (CH_3), 1003 (ArCH).

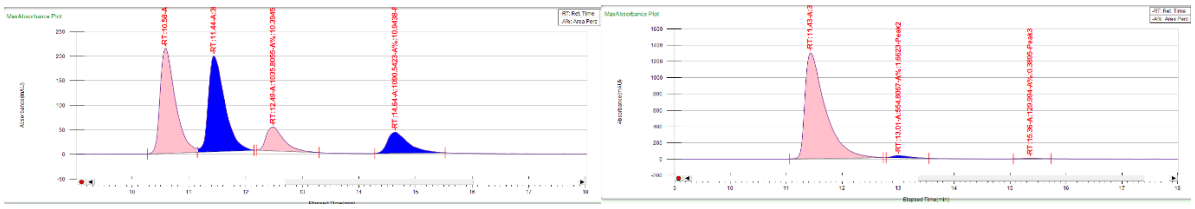
HRMS (EI+) calc'd. for $C_{16}H_{16}I$ $[M\text{-}OH]^+$ 335.0297; found: 335.0298.

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\boldsymbol{20}}$ -12 (*c* 1, $CHCl_3$)

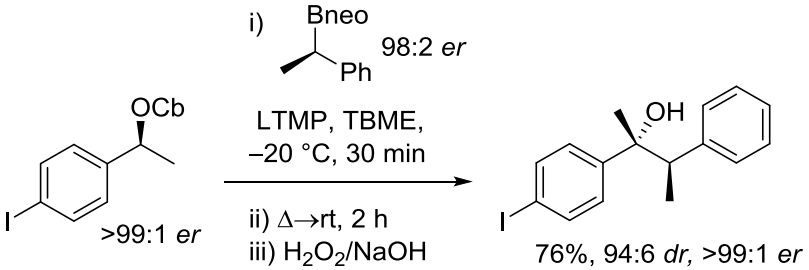
dr (crude) = 98:2 (anti:syn)

er = >99:1 (major diastereoisomer)

Chiral SFC (Whelk column, iso 10%, 3mL/min, 150 bar, co-solvent: Hexane, 40 °C) t_R = 10.6 (major diastereoisomer, minor), 11.4 min (major diastereomer, major), 13.0 min (minor diastereoisomer), 15.4 min (minor diastereoisomer).



(2R,3R)-2-(4-iodophenyl)-3-phenylbutan-2-ol, 17



A solution of LTMP (0.45 mmol, *vide supra*) was added dropwise to a mixture of benzylic carbamate **12** (100mg, 0.26mmol, >99:1 *er*) and (*R*)-1-phenylethyl neopentyl boronic ester (80 mg, 0.34 mmol, 98:2 *er*) in dry TBME (0.8 mL) at −20 °C. The light yellow solution was then stirred at −20 °C for 30 min before warming to room temperature and stirring for a further 2 h. The reaction mixture was concentrated *in vacuo* and filtered through a plug of SiO_2 with 1% Et_2O in hexane (to remove traces of remaining **12**). The filtrate was concentrated *in vacuo* and re-dissolved in THF (1.2 mL). A solution of 2:1 NaOH (2 M) and H_2O_2 (30% v/v) was added (1 mL/mmol) at 0 °C and the reaction mixture was stirred vigorously overnight at room temperature. The reaction was diluted with Et_2O (5 mL) and H_2O (5 mL), the layers separated and the aqueous layer was extracted into Et_2O (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated *in vacuo* and purified by flash column chromatography to give the product tertiary benzylic alcohol **17** as a colourless oil (71mg, 0.21 mmol, 76%)

R_f (anti isomer, 20% Et_2O in hexane): 0.24

^{1}H NMR ($CDCl_3$, 400 MHz), δ 7.62 – 7.57 (2H, m, ArH), 7.26 – 7.17 (3H, m, ArH), 7.05 (4H, m, ArH), 3.11 (1H, q, *J* = 7.2, CH), 1.78 (1H, s, OH), 1.53 (3H, s, CH_3), 1.27 (3H, d, *J* = 7.2, CH_3).

^{13}C NMR ($CDCl_3$, 101 MHz), δ 146.8 (4° ArC), 141.9 (4° ArC), 136.8 (ArCH), 129.4 (ArCH), 128.1 (ArCH), 128.0 (ArCH), 126.9 (ArCH), 92.4 (4° ArC), 76.4 (COH), 50.5 (CH), 26.1 (CH_3), 15.7 (CH_3).

IR (neat, cm^{-1}) 3452 (OH), 3059 (ArCH), 3026 (ArCH), 2971 (CH_3), 2933 (CH_3), 1583 (ArCC), 1484 (ArCC), 1391 (CH_3), 1003 (ArCH).

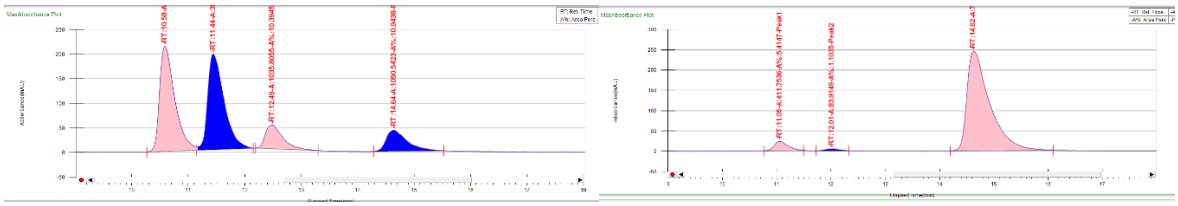
HRMS (EI+) calc'd. for $C_{16}H_{16}I$ $[M\text{-}OH]^+$ 335.0297; found: 335.0285;

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ + 83 (*c* 1, $CHCl_3$)

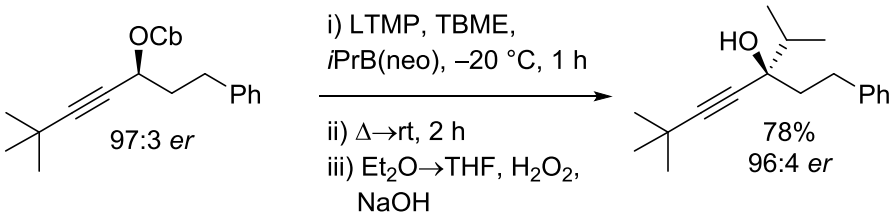
dr (crude) = 94:6 (syn:anti)

er = >99:1 (major diastereoisomer)

Chiral SFC: **(**Whelk column, iso 10%, 3mL/min, 150 bar, co-solvent: Hexane, 40 °C) t_R = 10.6 (minor diastereoisomer), 11.4 min (minor diastereomer), 13.0 min (major diastereoisomer, minor), 15.4 min (major diastereoisomer, major).



(*R*)-3-isopropyl-6,6-dimethyl-1-phenylhept-4-yn-3-ol 20



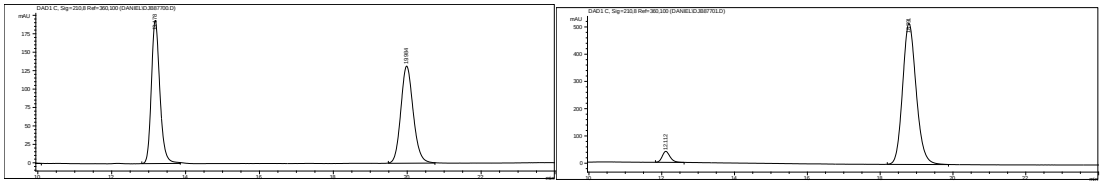
Prepared using a modified version of GP4 (1 h at −20 °C): (*S*)-6,6-dimethyl-1-phenylhept-4-yn-3-yl diisopropylcarbamate[14] **19** (171 mg, 0.50 mmol, 97:3 *er*), 2-isopropyl-5,5-dimethyl-1,3,2-dioxaborinane (101 mg, 0.65 mmol) and LTMP (0.63 mmol) to yield *benzylic alcohol* **20** (100 mg, 78% yield) as a yellow solid in 96:4 *er* by chiral HPLC.

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.34 – 7.15 (m, 5H), 2.86 (ddd, J = 9.5, 6.4, 2.5, 2H), 1.96 – 1.80 (m, 3H), 1.80 (br. s., 1H), 1.25 (s, 9H), 1.03 (d, J = 6.7, 3H), 1.00 (d, J = 6.8, 3H).

^{13}C NMR ($CDCl_3$, 100 MHz) δ 142.7 (C), 128.5 (CH), 128.4 (CH), 125.7 (CH), 94.4 (C), 79.9 (C), 74.5 (C), 41.6 (CH_2), 37.8 (CH), 31.1 (CH_3), 30.9 (CH_2), 27.4 (C), 18.1 (CH_3), 17.1 (CH_3).

$[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ +3.0 (*c* 1, CH_2Cl_2); Lit.[14] $[\boldsymbol{\alpha}]_{\boldsymbol{D}}^{\mathbf{20}}$ +5.0 (*c* 1, CH_2Cl_2);

Chiral HPLC (Chiralpak IA with guard, rt, 0.7mL/min, 1% IPA:hexane); t_R: 12.1 min (minor), 18.2 min (major) *er* 96:4;



Data were consistent with literature values.[14]

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10 This data is consistent with that reported in the following Ph.D. Thesis: James Robert Macias, Ph.D. Thesis, Iowa State University, 1987.
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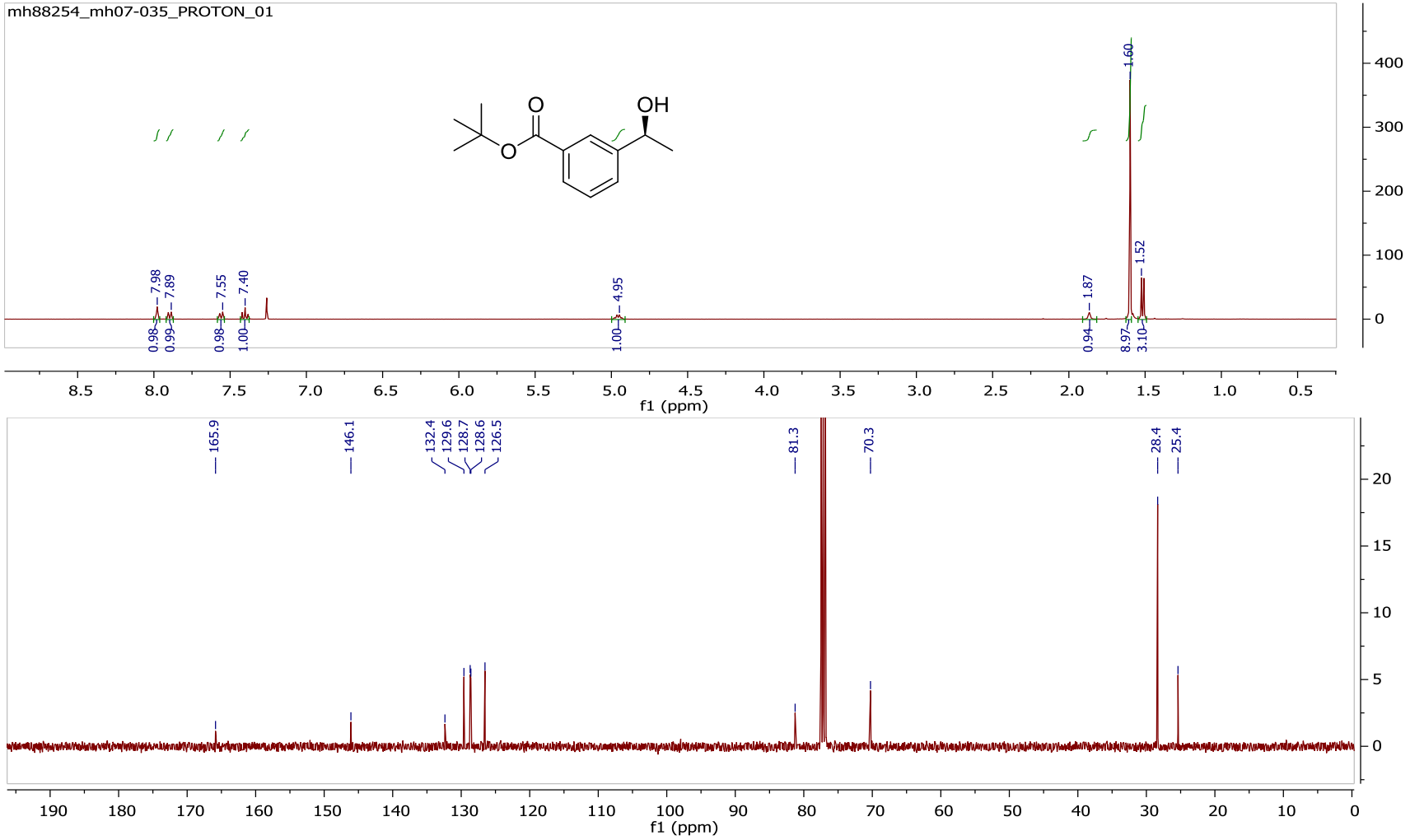
^{1}H and ^{13}C NMR Spectra of Novel Compounds

for

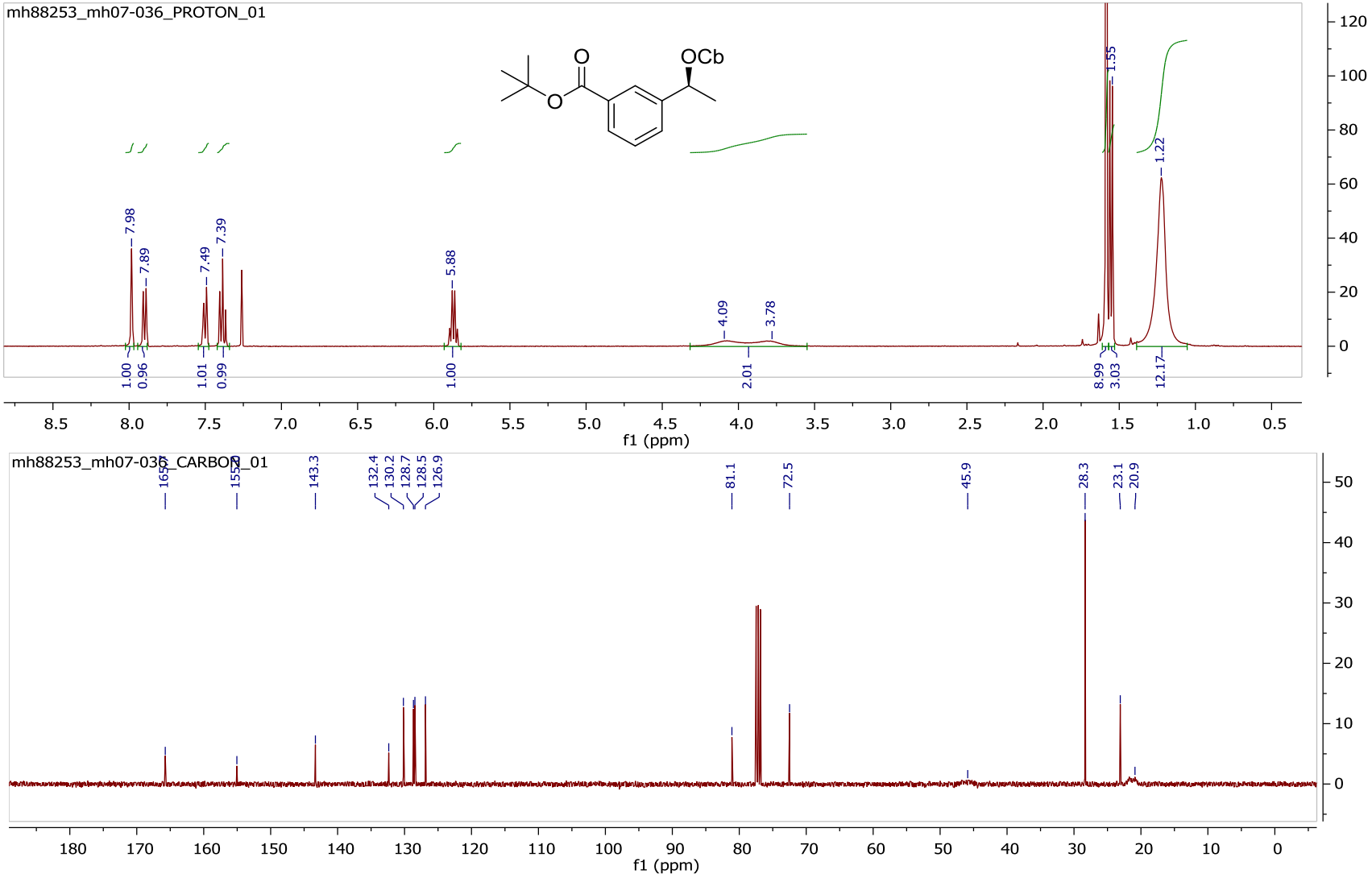
Full Chirality Transfer in the Synthesis of Hindered Tertiary Boronic Esters under In Situ Lithiation–Borylation Conditions

D. J. Blair,‡ S. Zhong,‡ M. J. Hesse, N. Zabaleta , E. L. Myers, V. K. Aggarwal*

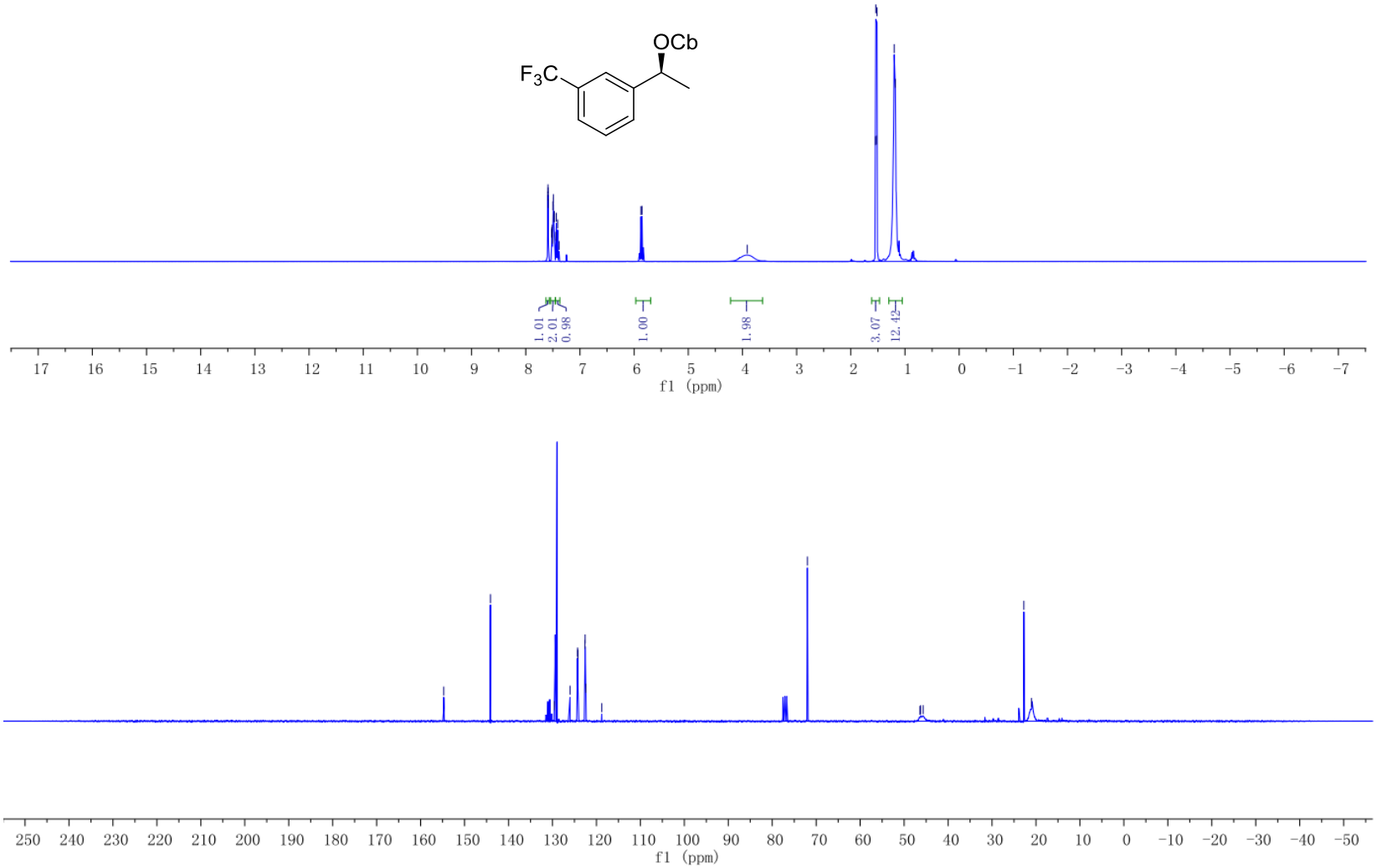
Tert-butyl 3-(1-hydroxyethyl)benzoate (*S*)**-25**



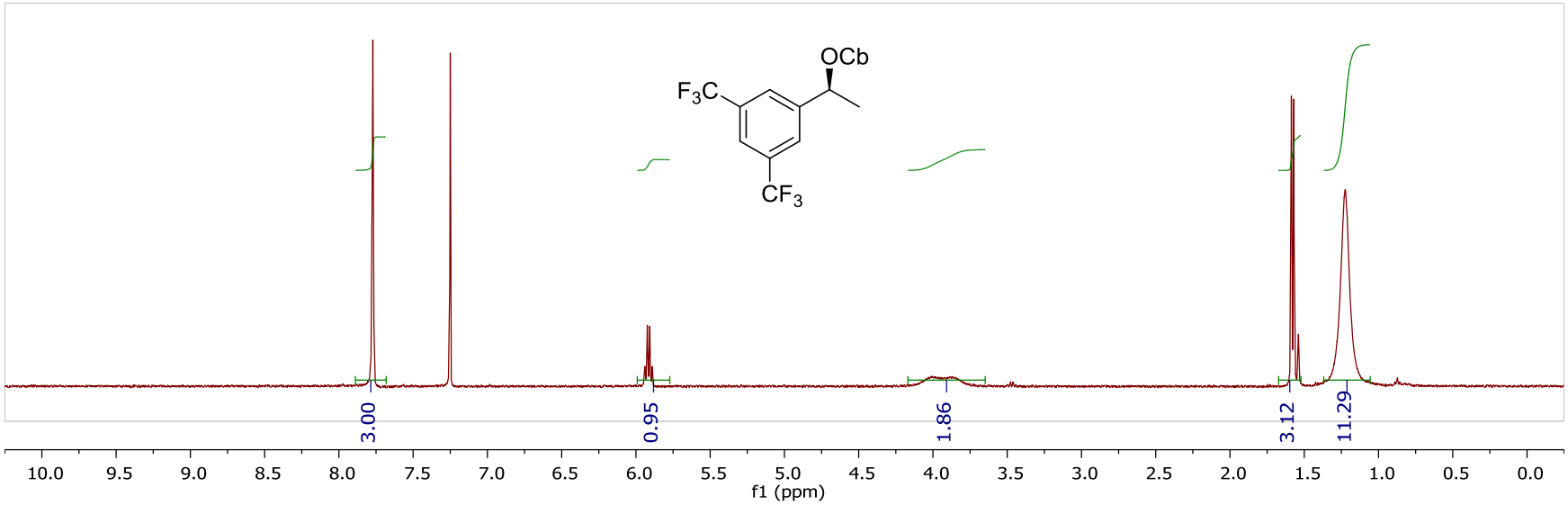
tert-butyl (_S_)-3-(1-((diisopropylcarbamoyl)oxy)ethyl)benzoate 26

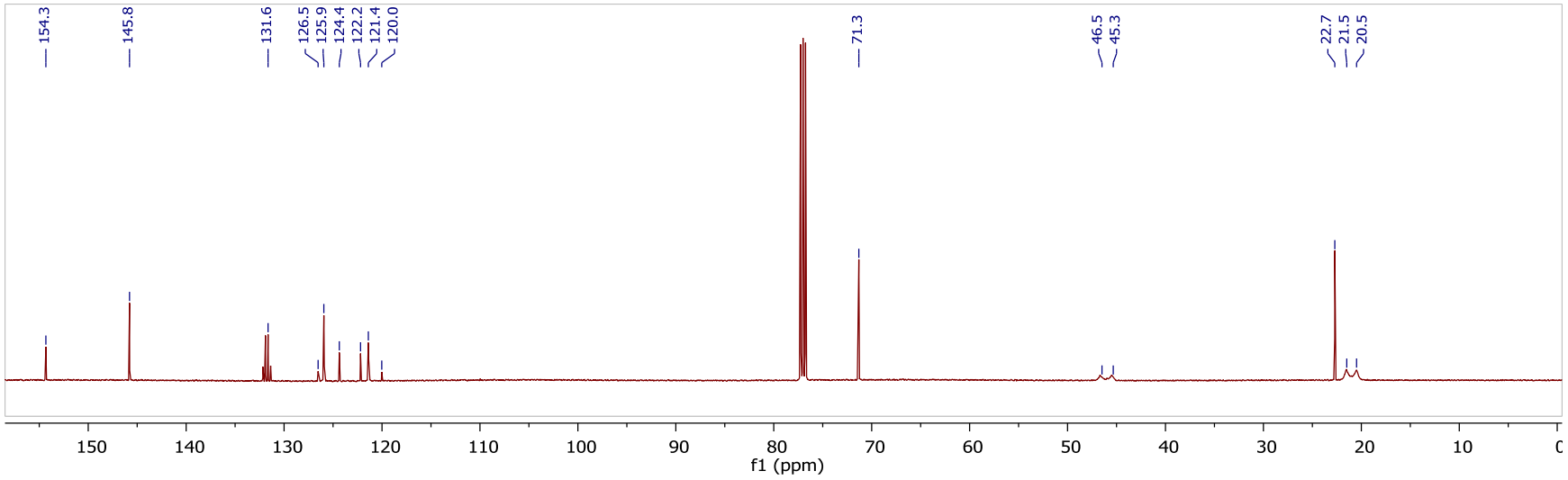


(*S*)-1-(3-(trifluoromethyl)phenyl)ethyl diisopropylcarbamate 26

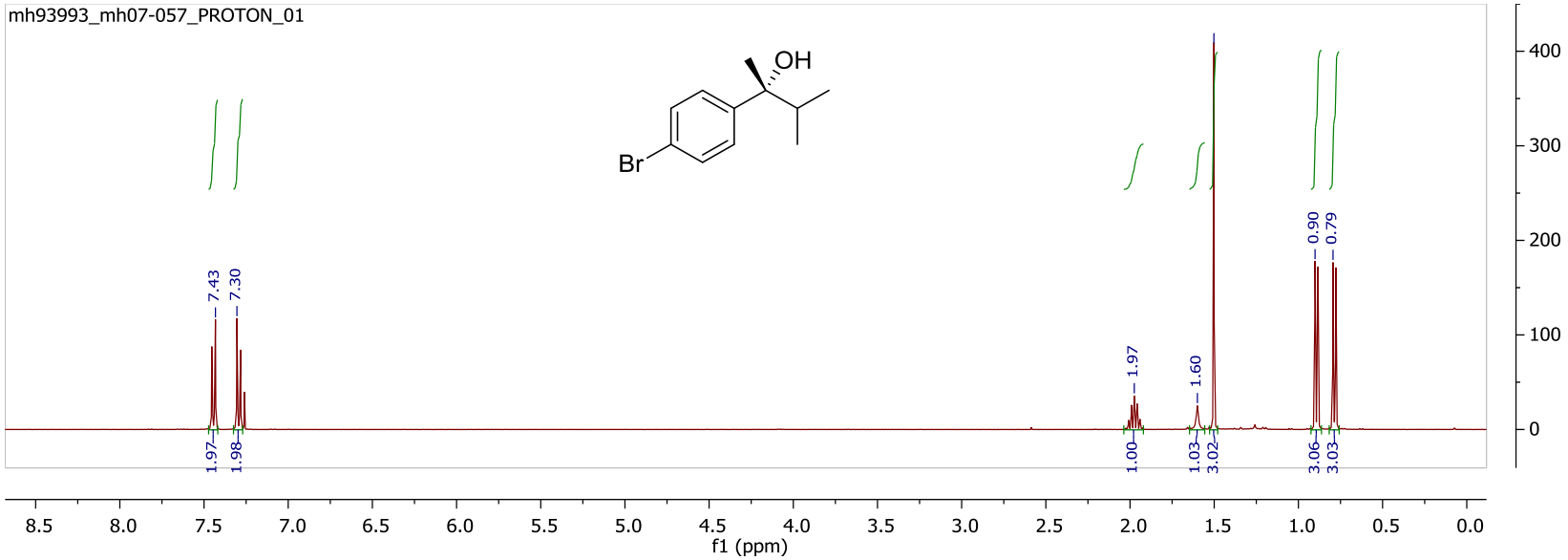


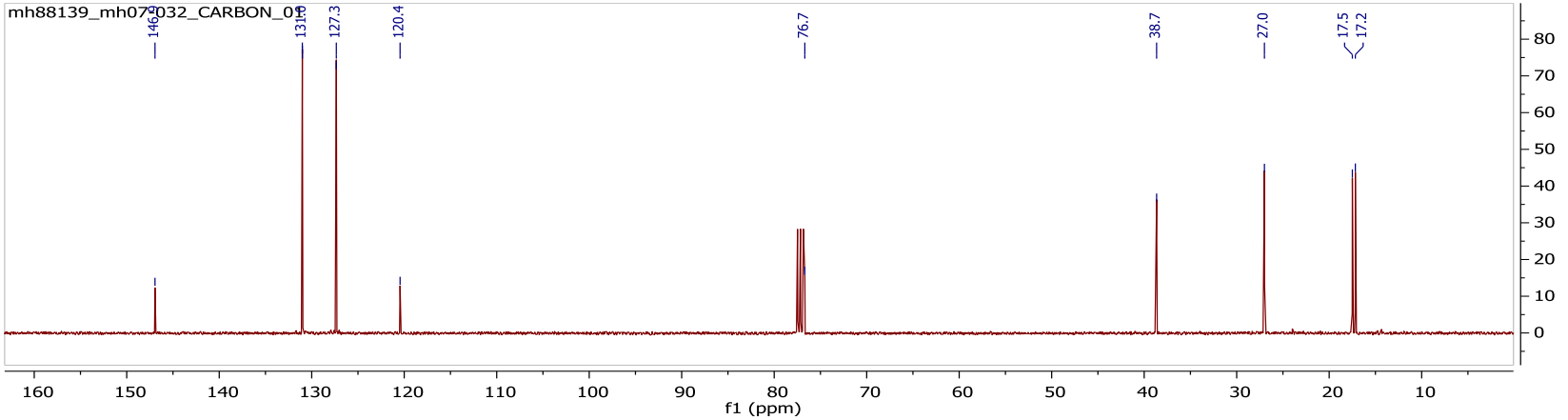
(S)-1-(3,5-bis(trifluoromethyl)phenyl)ethyl diisopropylcarbamate 29



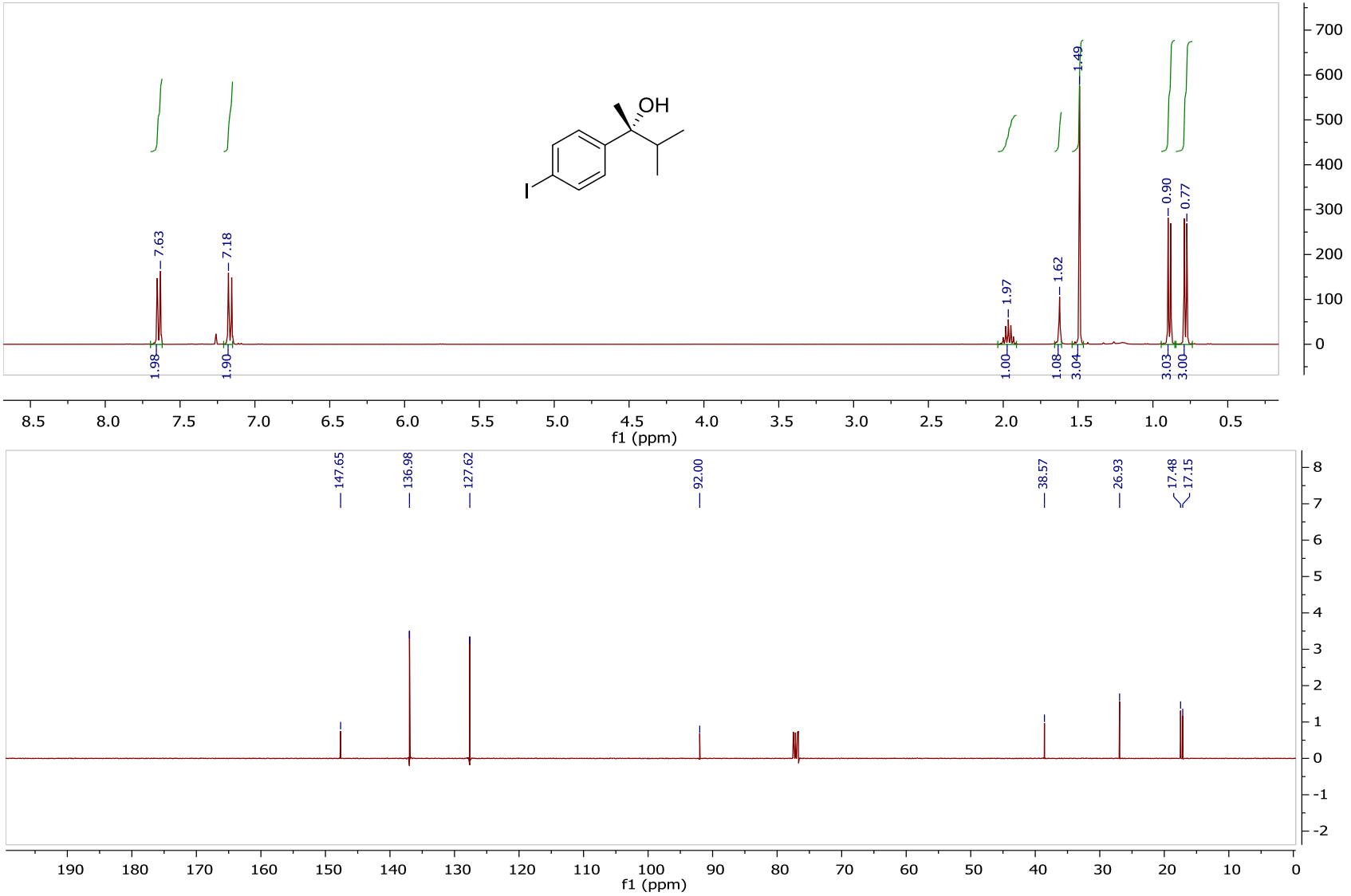


(*R*)-2-(4-bromophenyl)-3-methylbutan-2-ol 6

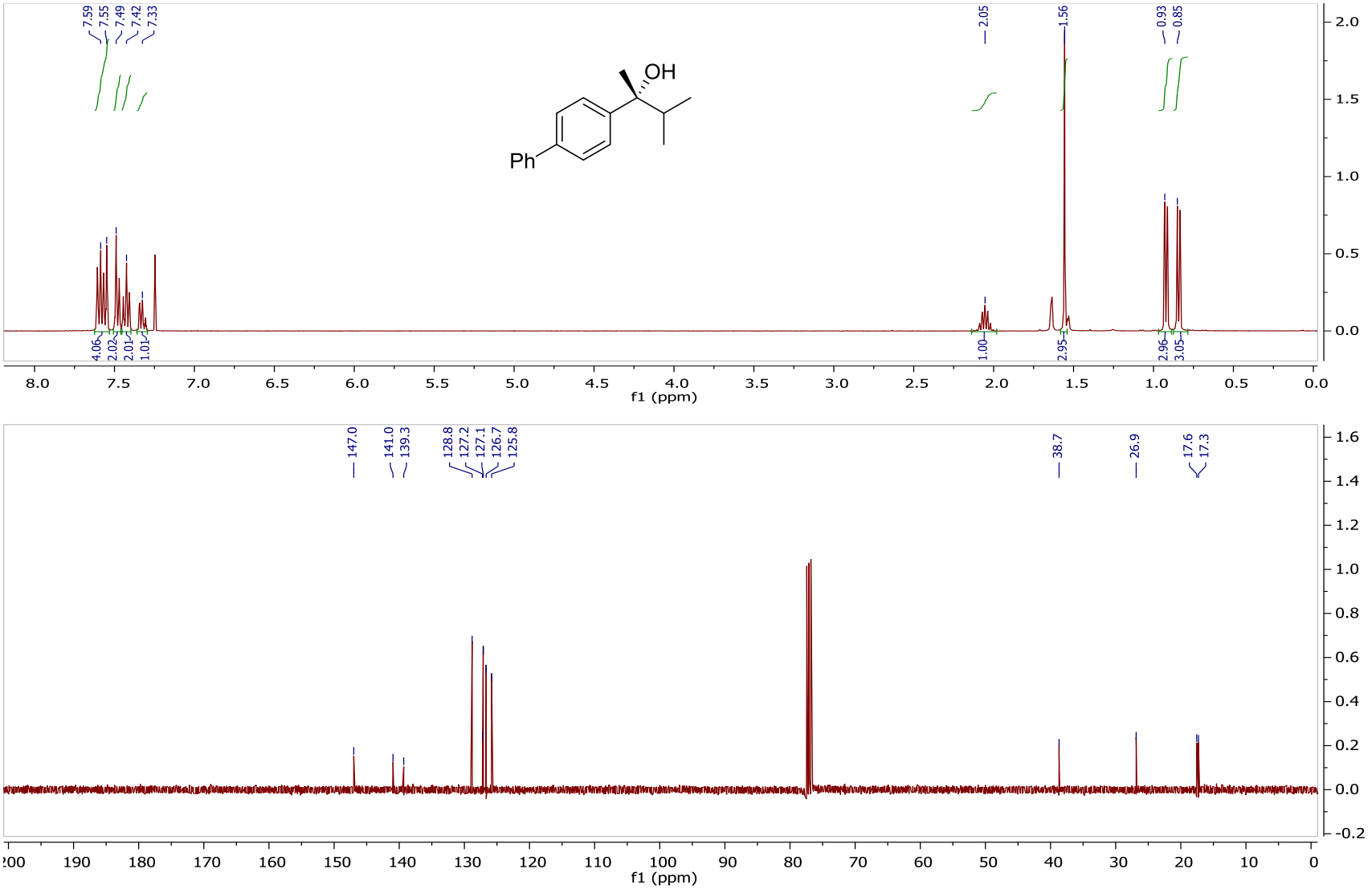




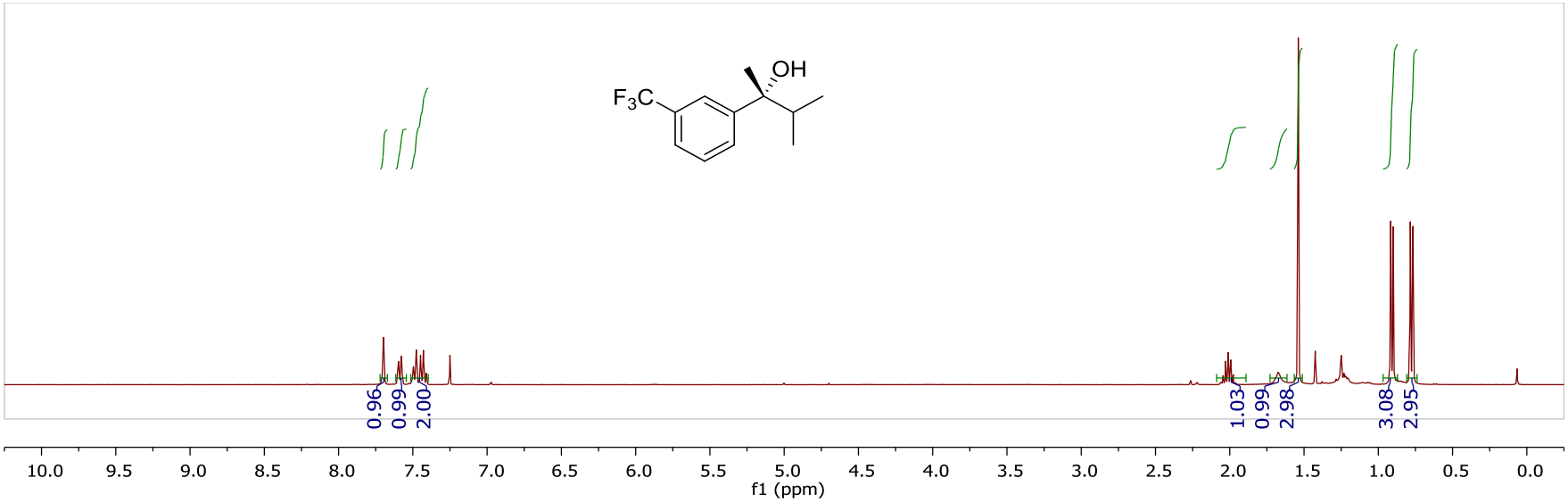
(*R*)-2-(4-Iodophenyl)-3-methylbutan-2-ol 7

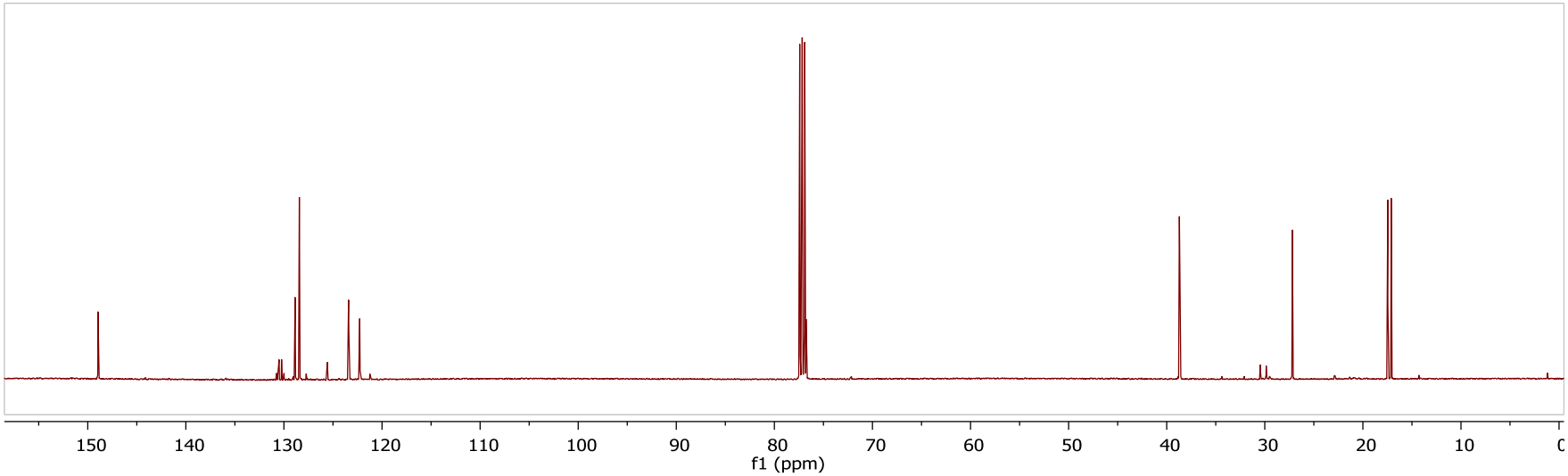


(*R*)-2-([1,1'-biphenyl]-4-yl)-3-methylbutan-2-ol 8

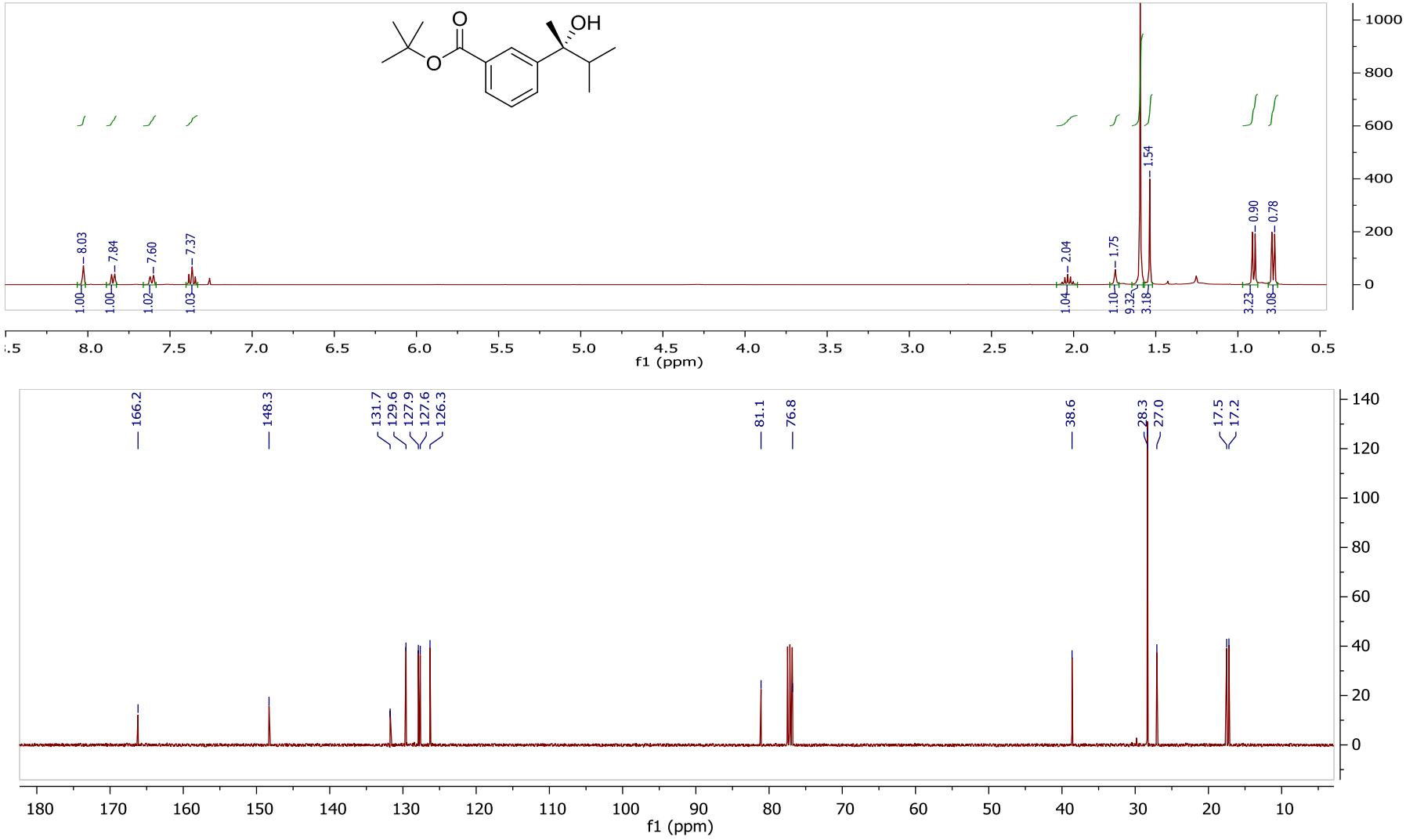


(*R*)-3-methyl-2-(3-(trifluoromethyl)phenyl)butan-2-ol 9

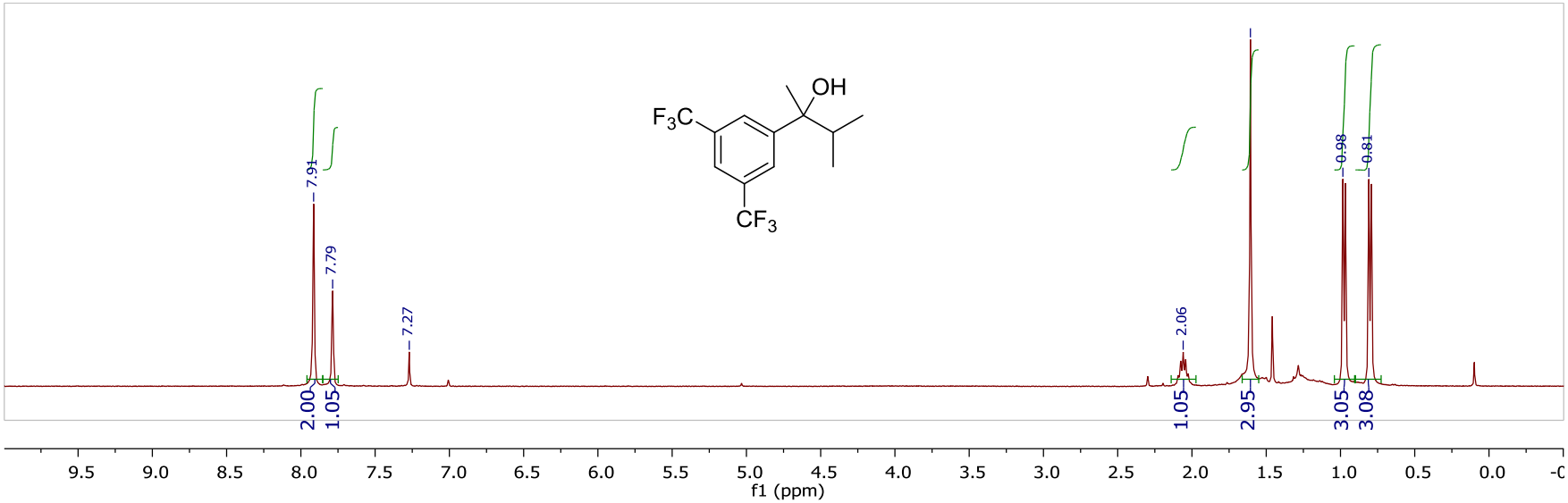


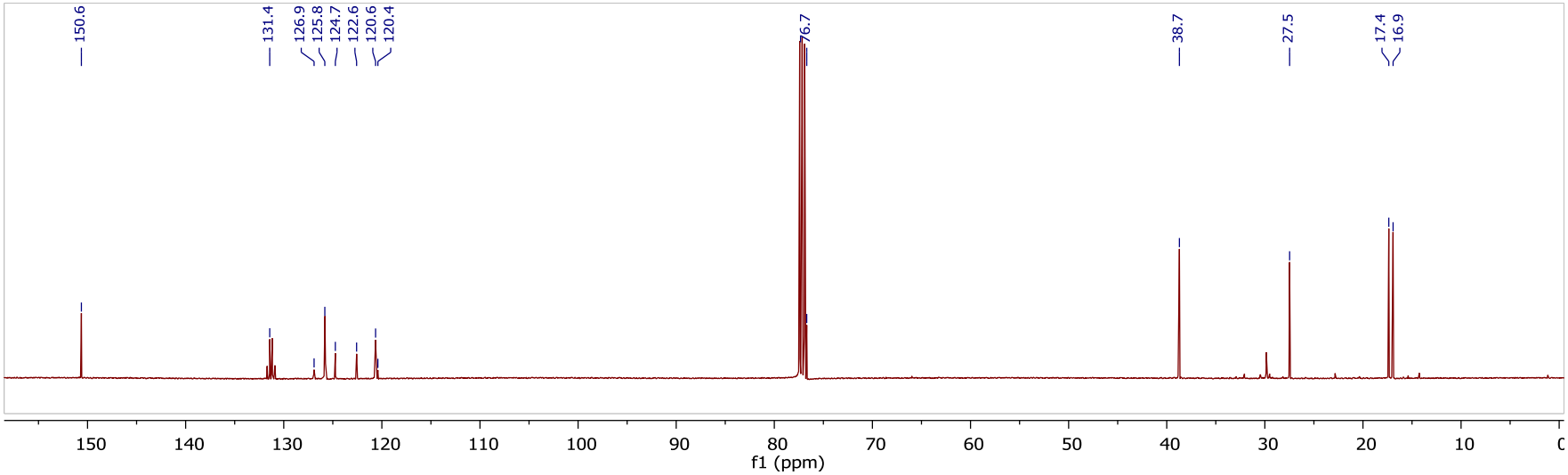


tert-butyl (*R*)-3-(2-hydroxy-3-methylbutan-2-yl)benzoate 11

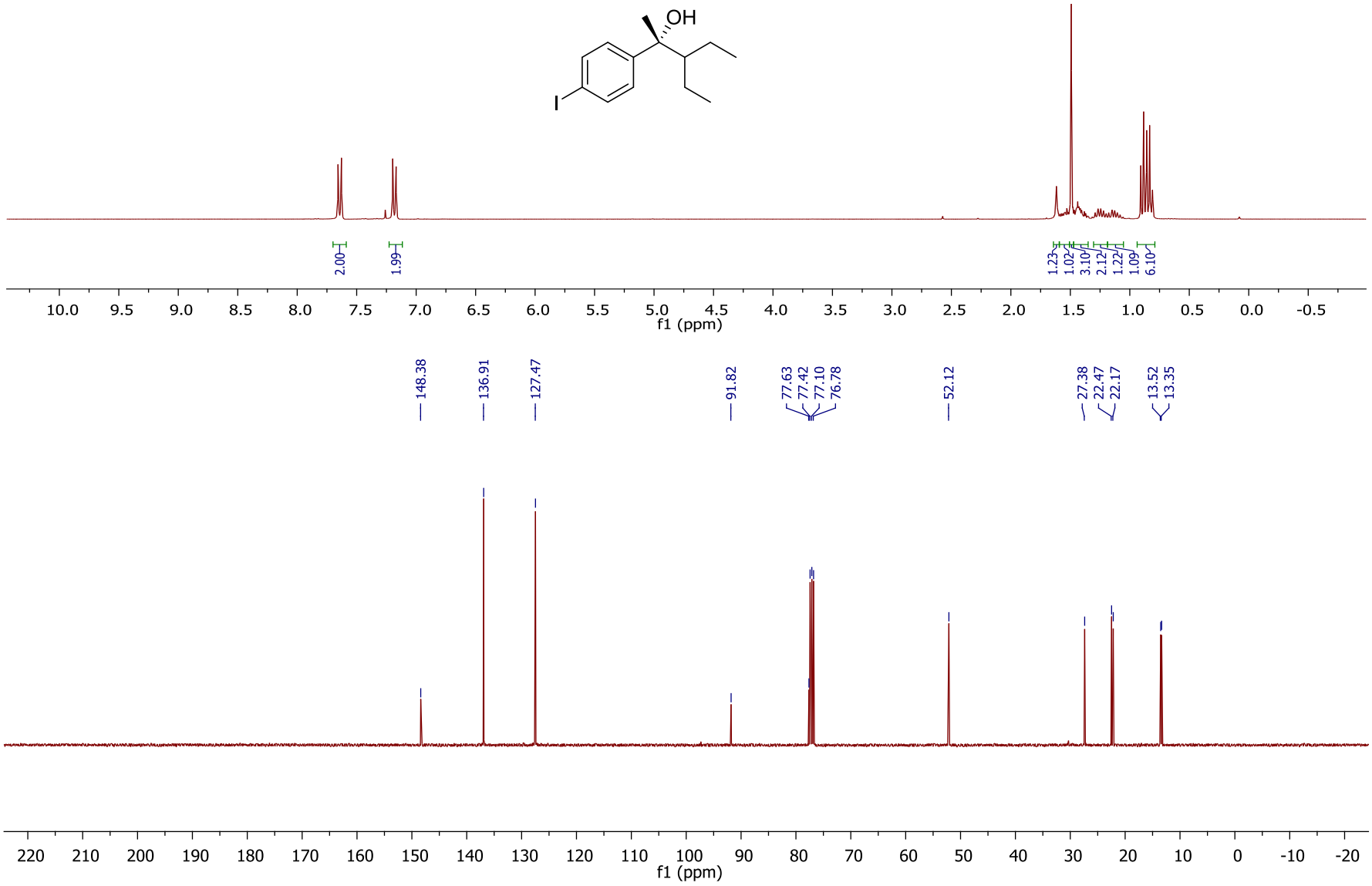


(*rac*)-2-(3,5-bis(trifluoromethyl)phenyl)-3-methylbutan-2-ol 10

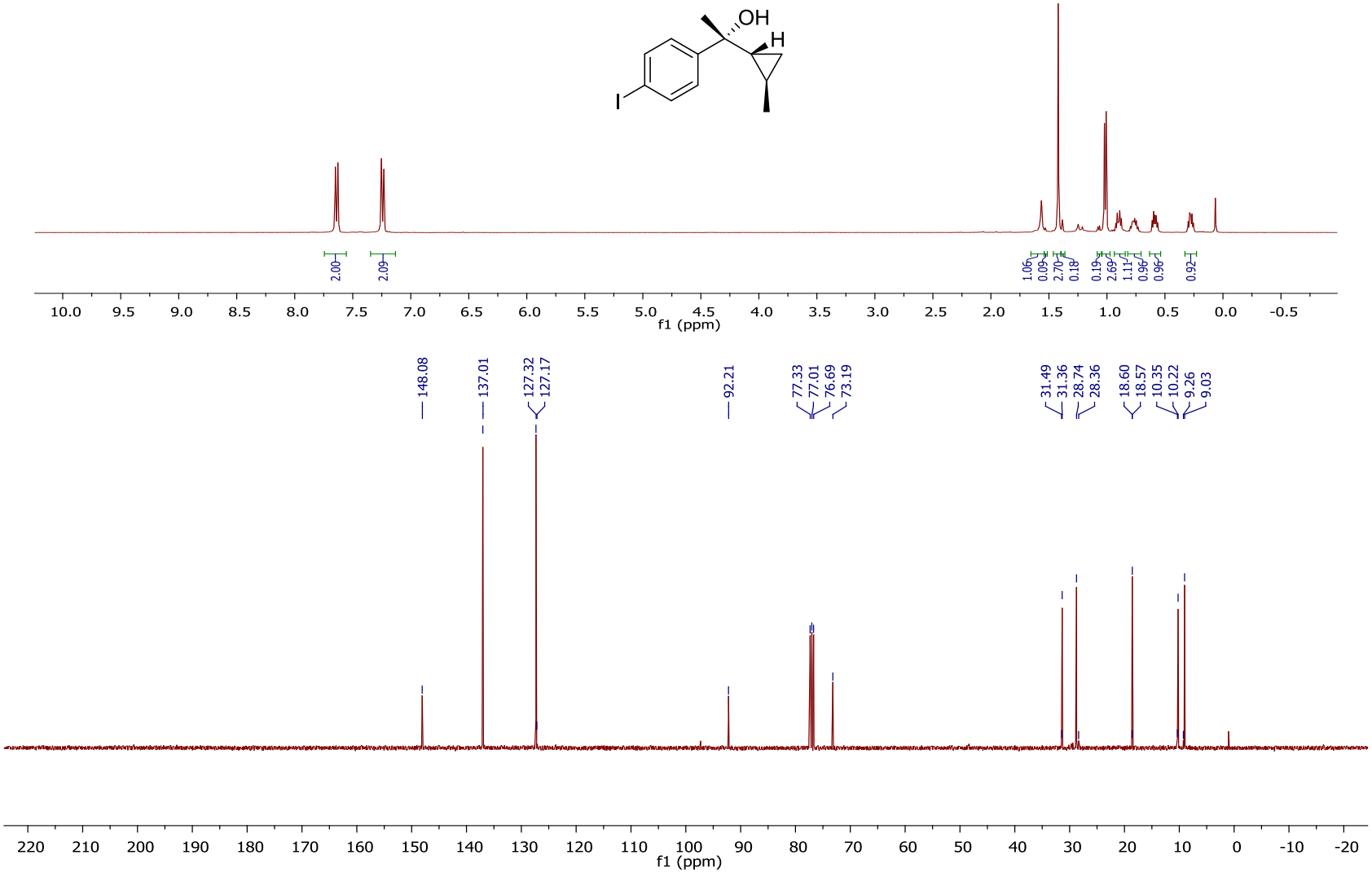




(*R*)-3-ethyl-2-(4-iodophenyl)pentan-2-ol 16



(*R*)-1-(4-iodophenyl)-1-((1*R*,2*R*)-2-methylcyclopropyl)ethan-1-ol 14



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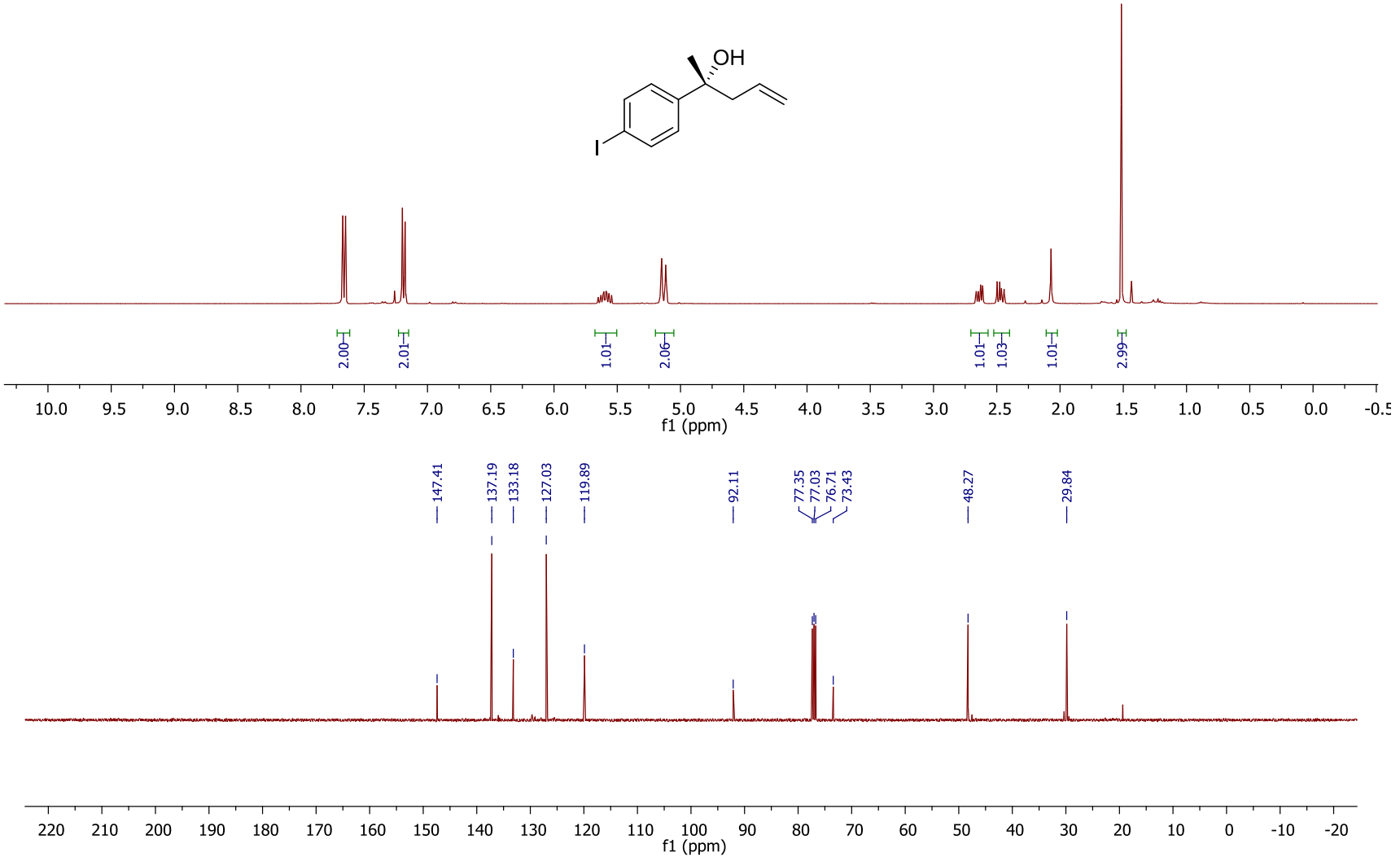
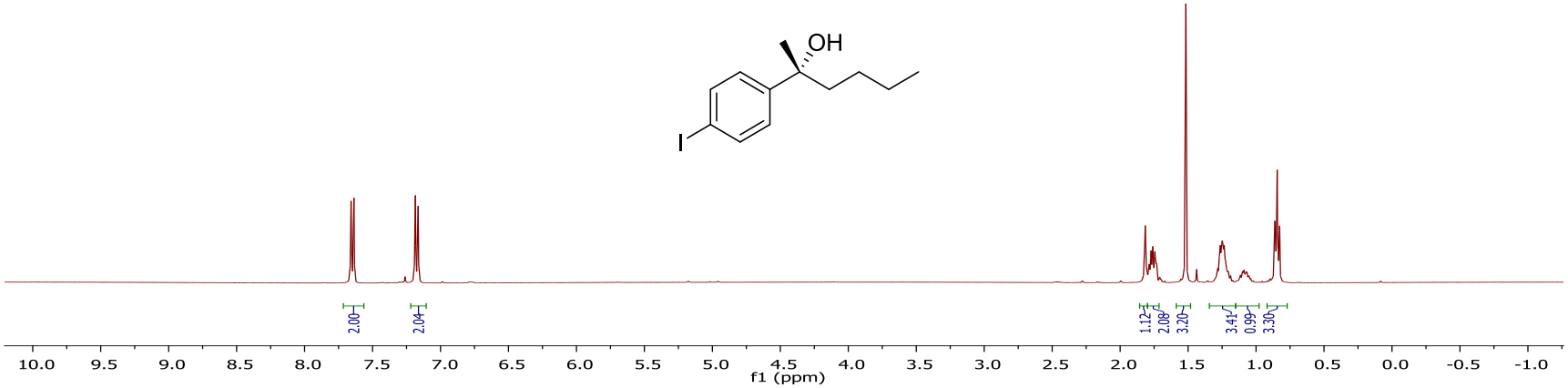
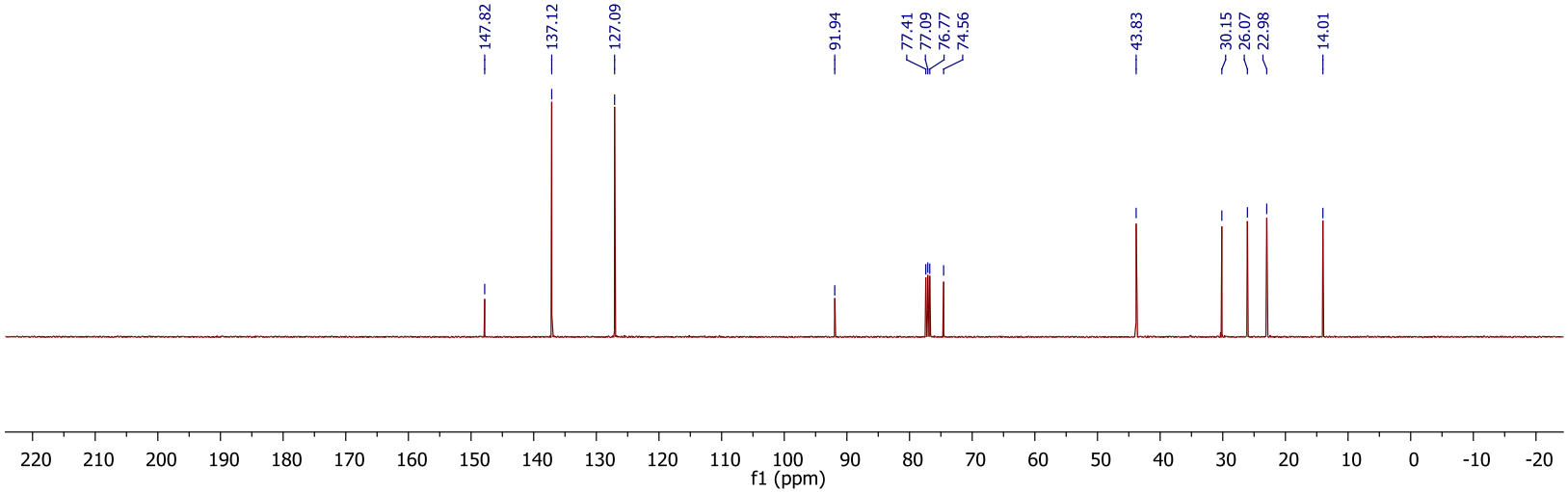
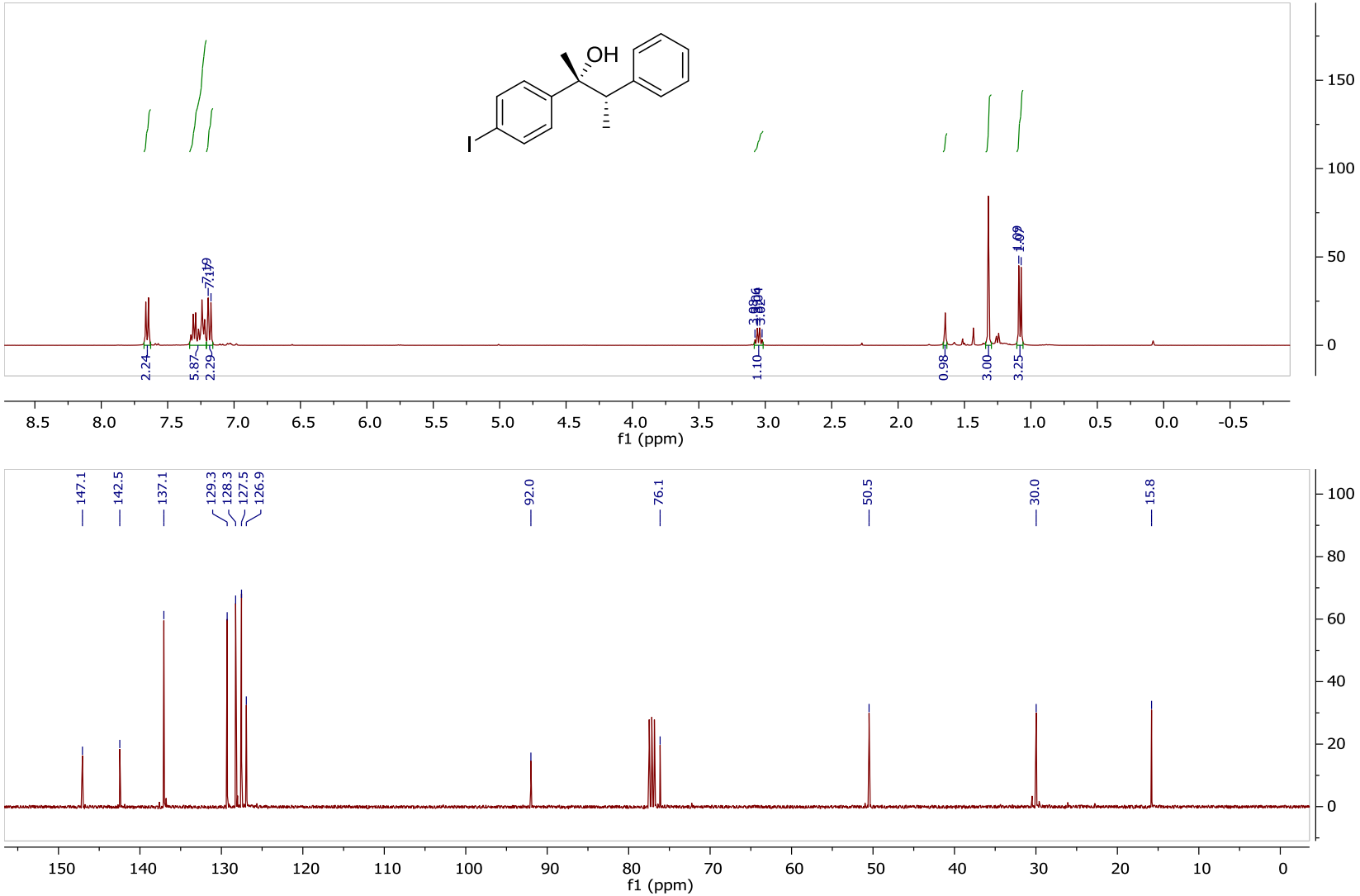


(*R*)-2-(4-iodophenyl)hexan-2-ol 13





(2R,3S)-2-(4-iodophenyl)-3-phenylbutan-2-ol, 18



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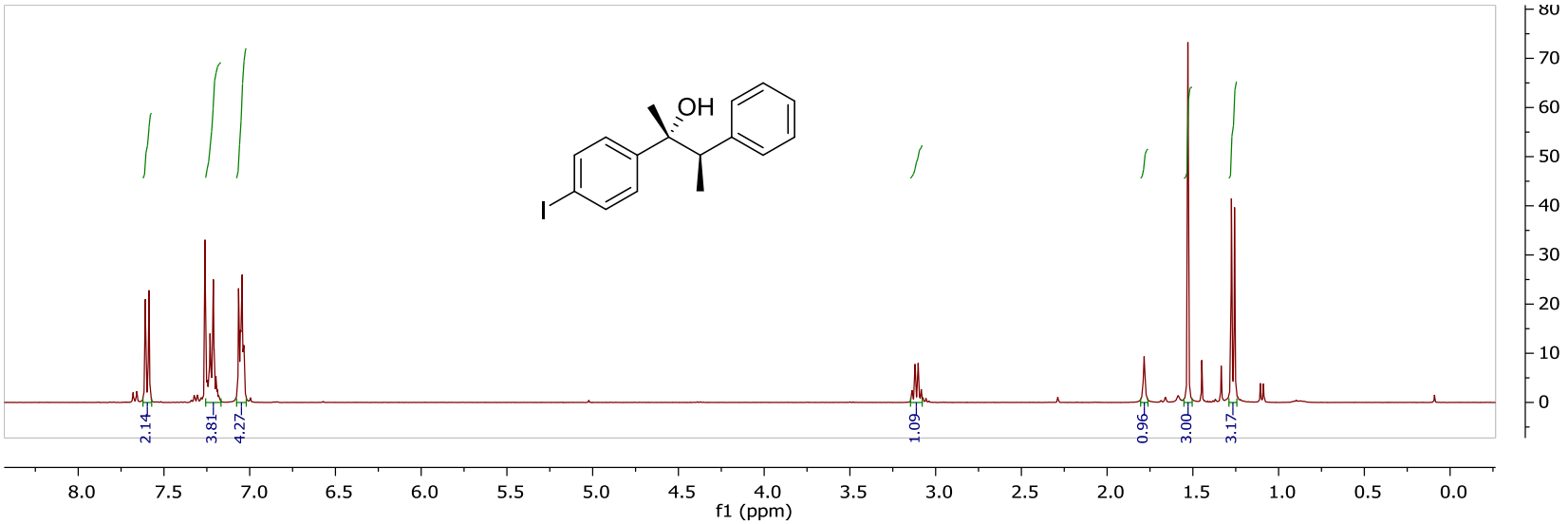

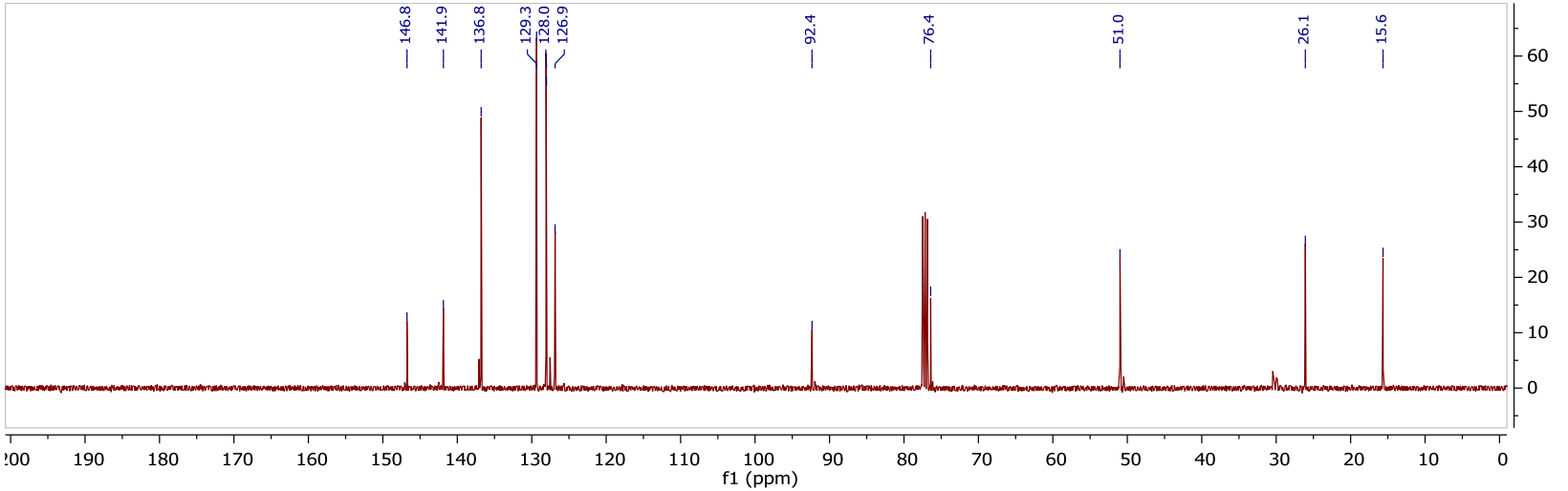

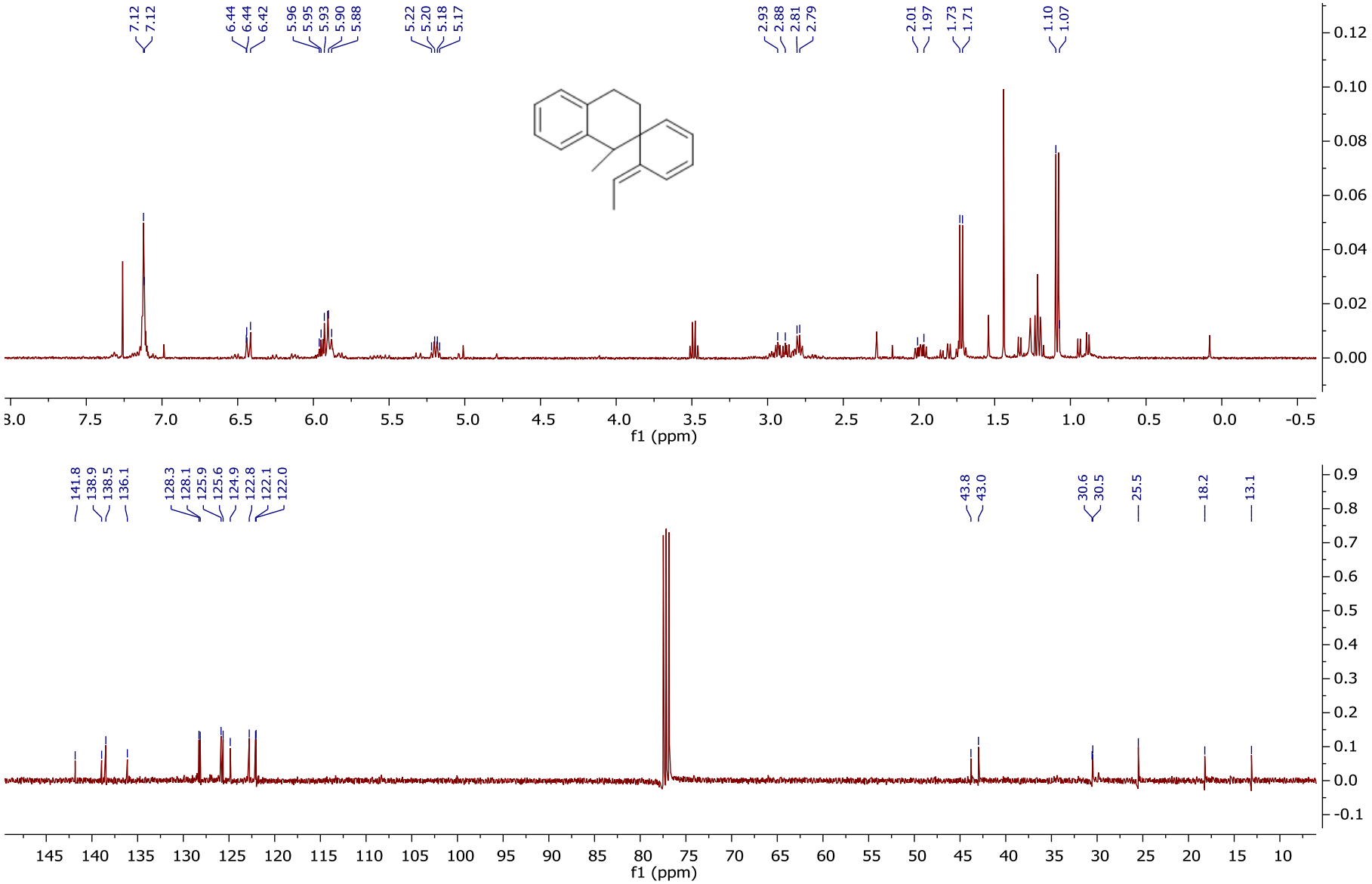
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2.79
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1.71
1.10
1.07
0.12
0.10
0.08
0.06
0.04
0.02
0.00
f1 (ppm)
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138.5
136.1
128.3
128.1
125.9
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124.9
122.8
122.1
122.0
43.8
43.0
30.6
30.5
25.5
18.2
13.1
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0.2
0.1
0.0
-0.1
f1 (ppm)