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Supporting Information

Chemo-enzymatic synthesis of chiral 3-substituted tetrahydroquinolines by sequential biocatalytic cascade and Buchwald-Hartwig cyclization

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S1. Experimental Procedures

S1.1 Materials

3-methyl-1,2,3,4-tetrahydroquinoline was purchased from Shanghai Yuanye Bio-Technology Co., Ltd. Terrific Broth was purchased from Sangon Biotech (Shanghai) Co., Ltd. Ampicilin and kanamycin were purchased from Beijing Probe Bioscience Co., Ltd. Isopropyl β-D-1-thiogalactopyranoside (IPTG) was purchased from AMRESCO Inc. Other commercial chemicals were purchased from Shanghai Acmec Biochemical Co., Ltd and Bide Pharmatech Co., Ltd. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance III 400 MHz NMR spectrometer. The samples were analyzed by an Agilent 1200 Series HPLC System equipped with a DAD detector. Chiral HPLC columns were Daicel CHIRALPAK OD-H column (250 mm x 4.6 mm, 5 μm) , IC column (250 mm x 4.6 mm, 5 μm) , OJ-H column (250 mm × 4.6 mm, 5 μm) and AS-H column (250 mm × 4.6 mm, 5 μm). GC analysis was performed on an Agilent 7890A Series GC System with Agilent DB-5 column (300 mm x 0.25 mm x 0.25 mm). The specific rotation of the chiral products were determined by Anton Paar MCP 500. High-resolution mass spectrometry (HRMS) was carried out with Bruker Metabolic Profiler (Agilent 1200 - Sprak Prospekt2 - Bruker AVANCE III 600MHz / Bruker micrOTOF-Q II).

S1.2 Expression of recombinant Ene reductases (EREDs) and imine reductases (IREDs)

The genes of the EREDs (**Table S1)** were all synthesized by General Biosystems (General Biosystems (Anhui) Co. Ltd.) and further cloned into the *Nde*I/*Xho*I sites of pET21a, and the resulting plasmids were transformed into *E. coli* BL21 (DE3) for overexpression. The genes of the IREDs (**Table S2**) were cloned into the *Nde*I/*EcoR*I sites of pET28a, and the resulting plasmids pET28a-IR2-48 were transformed into *E. coli* BL21 (DE3) for overexpression of *N*-terminal 6×His-tagged fusion proteins. The recombinant cells were cultivated in TB medium containing 100 μg/ml ampicilin or 50 μg/ml kanamycin at 37°C with shaking at 220 rpm until $OD_{600\ nm}$ reached 0.6–0.8, and then the gene expression was induced by 0.1 mM isopropyl β-D-1-thiogalactopyranoside (IPTG) at 25°C for 20 h. The cells were harvested by centrifugation (6000 *g*, 10 min, 4°C), washed once by sodium phosphate buffer (100 mM, pH 7.5) and stored at -20°C for further use.

S1.3 Screening of EREDs towards 2a with cell-free extracts of enzymes

The reaction mixture contained 40 mM **2a**, 10% v/v DMSO, 80 mM D-glucose, 3 U/mL GDH, 0.6 mM $NADP^+$, cell-free extracts of EREDs (50 mg wet weight) in 1.0 mL sodium phosphate buffer (100 mM, pH 7.5). The reaction mixtures were incubated at 25°C with shaking at 200 rpm for 2 h, and then extracted with 1.0 mL petroleum ether / ethyl acetate (90/10). The organic extracts were dried over anhydrous sodium sulphate and analyzed by GC to measure conversion (Agilent DB-5 column, GC condition: DB-5 column (300 mm x 0.25 mm x 0.25 mm), 100°C for 0 min, 2°C/min rise to 200 °C). The product **3a** was then reduced by sodium borohydride to get alcohol **3a'**, which was then tested for *ee* values by HPLC on chiral stationary phase. The racemate of **3a'** was obtained using N8-2 from *Pseudomonas putida* with low stereoselectivity (16%).

S1.4 Preparative scale reduction of 2a and absolute configuration confirmation

The reaction mixture contained 20 mM **2a**, 10% v/v DMSO, 40 mM D-glucose, 3 U/mL GDH, 0.6 mM $NADP^+$, 0.5 mg/mL purified OYE1 in 50 mL sodium phosphate buffer (100 mM, pH 7.5). The reaction mixtures were incubated at 25°C with shaking at 200 rpm. During the reaction, 1 mL portions of the reaction mixture were taken at some timeintervals to determine conversion and *ee* values (**Figure S1**).

After 18 h, Sodium borohydride (2 eq.) was added in the reaction mixture, which was then extracted with petroleum ether / ethyl acetate (90/10). The organic phase was concentrated via evaporation under reduced pressure and then purified by column chromatography. The absolute configuration of **3a'** was assigned by comparison with the sign of specific rotation of (*S*)-2-methyl-3-phenylpropanal obtained using OYE2 (99.75% identity with OYE1) in literature.[1] The specific rotation of (*S*)-**3a'** (93%*ee*) obtained using OYE1 and (*S*)-2-methyl-3-phenylpropanal (96%*ee*) in ref.[1] were -3.850 and -11.3 (c=1.0, $CHCl_3$, 589 nm, 20°C), respectively.

S1.5 Screening of IREDs towards 3a with cell-free extracts of enzymes

First, the reaction mixture contained 20 mM **2a**, 10% v/v DMSO, 40 mM glucose , 3 U/mL GDH, 0.6 mM $NADP^+$ in 0.5 mL sodium phosphate buffer (100 mM, pH7.5) and was shaken at 25°C, 200 rpm for 18 h to achieve >99% conversion without formation of **3a'**. Then the pH of reaction mixtures were adjusted from 6.4 to 7.5 with saturated sodium carbonate solution and 0.5 mL buffer containing allylamine (80 mM), glucoce (80 mM), GDH (6 U/mL), $NADP^+$ (1.2 mM) and cell-free extracts (100 mg wet cells weight per mL) of IREDs was added, and the reaction proceeded at 25°C, 200 rpm for 18 h. The reaction was quenched by the addition of saturated sodium carbonate solution and extracted with 1.0 mL petroleum

ether / ethyl acetate (90/10). The organic extracts were dried over anhydrous sodium sulphate and analyzed by HPLC on chiral stationary phase to measure *ee* values of the products (**Table S3**).
The racemization of (*S*)-**3a** from the reduction of **2a** with OYE1 was studied under different reaction conditions. The pH of the reaction mixture of **2a** with OYE1 was adjusted to pH7.5 at the end of the reaction. The pH of the reaction mixture of **2a** with OYE1 was adjusted to pH 7.5 and 2eq. allylamine was added. The resulting mixtures and the reaction mixture (pH6.4) of **2a** with OYE1 were shaken at 25°C, 200 rpm for 5 h. The product **3a** was then reduced by sodium borohydride to get alcohol **3a'**, which was then tested for *ee* values by HPLC on chiral stationary phase.

S1.6 Purification and activity assay of the selected IREDs and EREDs

Recombinant *E. coli* cells expressing IR43, IR97 and OYE1 were harvested by centrifugation and the pellets were resuspended in sodium phosphate buffer (100 mM, pH 7.5). The cells were lysed by ultrasonication and then the cell debris was removed by centrifugation (10000 *g*, 20 min, 4°C). The resulting clarified lysate was loaded onto a 5 or 40 mL column charged with 0.1 M nickel sulfate and protein was eluted using an increasing gradient of imidazole from 20 to 500 mM at a flow rate of 3 mL/min. After being analyzed by SDS-PAGE（**Figure S2**）, the pure protein was collected and dialyzed by desalting column, then concentrated by ultrafiltration and stored at -80°C with 10% glycerol for further use.
The activities of IREDs and EREDs were determined using purified enzyme on a SpectraMax M5 microplate reader (Molecular Devices) by monitoring the decrease of NADPH at 340 nm (ε= 6220 L $M^{-1}cm^{-1}$) at 30°C. The reaction volume (200 μL) of OYE1 contained a certain amount of purified enzyme, 0.3 mM NADPH, 1 mM **2a-2j,** 10%DMSO and sodium phosphate buffer (100 mM, pH 7.5). The reaction volume (200 μL) of IR43 and IR97 contained a certain amount of purified enzyme, 0.3 mM NADPH, 10 mM **3a-3j** obtained by OYE1 catalyzed reduction of **2a-2j** without separated, 20 mM allylamine**,** 10%v/v DMSO and sodium phosphate buffer (100 mM, pH 7.5). The reaction was initiated by adding the enzyme to the mixture. One unit of enzyme is defined as the amount of protein that oxidizes 1 μmol NADPH per minute.

S1.7 Synthesis of α, β-unsaturated aldehyde 2a-2j

2a-2j were synthesized according to the methods reported in the literature.[2] They were prepared from 2-bromobenzaldehyde (**1a**), 2-chlorobenzaldehyde (**1b**), 2-bromo-3-fluorobenzaldehyde (**1c**), 2-bromo-4-fluorobenzaldehyde (**1d**), 2-bromo-5-fluorobenzaldehyde (**1e**), 2-bromo-6-fluorobenzaldehyde (**1f**), 2-bromo-3-methylbenzaldehyde (**1g**), 2-bromo-4-methylbenzaldehyde (**1h**), 3-bromothiophene-2-carbaldehyde (**1i**) and 3-bromofuran-2-carbaldehyde (**1j**) (**Figure S3**). As described in the literature, a mixture of **1a-1j** (5-50 mmol), sodium hydroxide (0.2-2 mL, 10% aq.) in MeOH was cooled to 0°C, to which propionaldehyde (1.5 eq.) was added dropwise and the resulting mixture was stirred at room temperature for 24 h. The reaction mixture was quenched with conc. aqueous HCl, followed by extractive workup with *tert*-butyl methyl ether. The extracts were dried, concentrated, and the crude products were purified by flash column chromatography on silica gel (petroleum ether / ethyl acetate=100:1) to afford the aldehyde **2a-2j.**

S1.8 One-pot biocatalytic cascade reduction and reductive amination

The biotransformation was performed starting from 20 mM α, β-unsaturated aldehyde (**2a-2j**), 40 mM allylamine, 60 mM D-glucose, 1.2 mM $NADP^+$, 5 U/mL GDH and 0.5 mg/mL purified OYE1 and 1-10 mg/mL IR43 in sodium phosphate buffer (1 mL, 100 mM, pH 7.5) containing 10% DMSO (v/v). The reactions were shaken at 25 °C with 200 rpm within 14 h. Then, the reaction was quenched by adding saturated sodium carbonate solution (100 μL) and extracted with ethyl acetate (1 mL). Conversions were determined by GC-FID analysis (Agilent DB-5 column, GC condition: DB-5 column (300 mm x 0.25 mm x 0.25 mm), 50°C for 0 min, 10 °C/min rise to 200 °C, 5 min.).
For the preparative scale one-pot biocatalytic cascade reaction, the reaction mixture containing 20 mM α, β-unsaturated aldehyde (**2a-2j**), 40 mM allylamine, 60 mM D-glucose, 1.2 mM $NADP^+$, 5 U/mL GDH and 0.5 mg/mL purified OYE1 and 1-8 mg/mL IR43 in sodium phosphate buffer (100 mM, pH 7.5) with 10% DMSO (v/v) was incubated at 25 °C. The volume of **2a-2j** was 50 mL, and a 500 mL reaction of **2a** was carried out under the same conditions (time course shown in **Figure S4**). The reaction was stopped by adding saturated sodium carbonate solution. The reaction mixtures were extracted with a co-solvent of petroleum ether / ethyl acetate (90/10). The organic phase was concentrated via evaporation under reduced pressure and then purified by column chromatography (silica gel, DCM/MeOH=98:2) to afford products **4a-4j**. The products were confirmed using NMR analysis.

S1.9 Synthesis of racemate of 4a-4j

In order to determine the *ee* value of the product **4a-4j**, we synthesized the corresponding racemates. As shown in **Figure S5**, **3a-3j** were obtained from **2a-2j** by enzyme reduction firstly. Then, a mixture of **3a-3j**, allylamine (2 eq.), anhydrous sodium sulfate and sodium carbonate in MeOH/DCM was at room temperature for 12 h, to which $NaBH_4$ (2 eq.) was added and stirred for 0.5 h. The reaction mixture was quenched with water, followed by extracted with ethyl acetate. The

extracts were dried and concentrated, and the crude products were purified by flash column chromatography on silica gel, or added 4.0 M hydrogen chloride solution in dioxane (1.5 eq.) and then isolated by filtration. They were confirmed using NMR analysis.

S1.10 Synthesis of 6a-6j

A mixture of **4a-4j**, $Pd(OAc)_2$ (0.1 eq.), 2-di-*tert*-butylphosphino-2',4',6'-triisopropylbiph (*t*-butylXPhos, 0.2 eq.) and sodium tert-butoxide (3 eq.) in 1,4-dioxane was stirred at 110°C for 6 h, and then concentrated via evaporation under reduced pressure. Next, 5% Pd/C was used to remove the allyl group at 80°C for 6 h. The mixture was filtered and concentrated by rotary evaporator. The crude product was dissolved in water with pH 1.0 and extracted with *tert*-butyl methyl ether to remove the impurity. And then, the aqueous solution was adjusted to pH 9.0 and extracted with *tert*-butyl methyl ether again to get the products. They were purified by adding 4.0 M hydrogen chloride solution in dioxane (1.5 eq.) and then isolated by filtration.

S1.11 Analytical methods

The *ee* value of product **3a'** was measured via HPLC with Daicel CHIRALPAK OH-H column. The absolute configurations of (*S*)-**4b** were determined by X-ray crystallographic analysis. The absolute configurations of other products **4a** and **4c-4i** were assigned by comparison the optical rotation with **4b**. The *ee* values of products **4a-4b** were measured via HPLC with Daicel CHIRALPAK IC and AS-H column after derivatization. The *ee* values of products **6a-6i** were measured via HPLC with Daicel CHIRALPAK OJ-H column. The detailed HPLC analytical conditions are shown in **Table S6**.

S2. Results and Discussion

S2.1 Supplementary tables

Table S1. Ene reductases used in this study.

ERED	Protein identifier	*Organism*	Ref.
BfER	WP_123917522.1	*Bacillus sp. FJAT-42376*	[3]
BpER	WP_033496060.1	*Bifidobacterium psychraerophilum*	[3]
BzER	WP_078061662.1	*Bacillus zhangzhouensis*	[3]
NdER	XP_003668369.1	*Naumovozyma dairenensis CBS 421*	[3]
N8-2	AHC69715.1	*Pseudomonas putida*	[3]
NtDBR	Q9SLN8.1	*Nicotiana tabacum*	[3]
OYE1	CAA37666.1	*Saccharomyces pastorianus*	[3]
OYE2.6	4DF2_A	*Scheffersomyces stipitis CBS 6054*	[3]
PkER	WP_119883250.1	*Paenisporosarcina sp. K2R23-3*	[3]
ReER	XP_013324131.1	*Rasamsonia emersonii CBS 393.64*	[3]
SeER	XP_018218866.1	*Saccharomyces eubayanus]*	[3]
TvER	KUL85056.1	*Talaromyces verruculosus*	[3]
Yl-4ER	XP_499654.1	*Yarrowia lipolytica CLIB122*	[3]
YlER	XP_500567.2	*Yarrowia lipolytica CLIB122*	[3]
YqjM	BAA12619.1	*Bacillus subtilis*	[3]

Table S2. Imine reductases used in this study.

IRED	Protein identifier	*Organism*	*Ref.*
IR19	WP_023587323.1	*Streptomyces thermolilacinus*	[4]
IR20	WP_027931121.1	*Amycolatopsis thermoflava*	[4]
IR21	WP_073459042.1	*Pseudonocardia thermophila*	[4]
IR22	WP_091804541.1	*Prauserella marina*	[4]
IR23	SHE96216.1	*Streptoalloteichus hindustanus*	[4]
IR24	WP_020388085.1	*Kribbella catacumbae*	[4]
IR25	WP_088993565.1	*Micromonospora echinaurantiaca*	[4]
IR26	WP_017622916.1	*Nocardiopsis chromatogenes*	[4]
IR27	WP_095494073.1	*Mesorhizobium temperatum*	[4]
IR28	OXS04712.1	*Aspergillus thermomutatus*	[4]
IR29	WP_057221059.1	*Ensifer*	[4]
IR30	WP_020496004.1	*Sciscionella marina*	[4]
IR31	WP_044567941.1	*Streptomyces iranensis*	[4]
IR32	WP_020635634.1	*Amycolatopsis alba*	[4]
IR33	WP_018011194.1	*Sinorhizobium medicae*	[4]
IR34	WP_023720294.1	*Mesorhizobium sp. LSHC420B00*	[4]
IR35	WP_015347361.1	*Myxococcus stipitatus*	[4]
IR36	WP_054311034.1	*Mesorhizobium sp. 1M-11*	[4]
IR37	WP_055997555.1	*Devosia sp. Root413D1*	[4]
IR38	WP_063893400.1	*Sinorhizobium sp. Sb3*	[4]
IR39	WP_069881969.1	*Bosea sp. BIWAKO-01*	[4]
IR40	WP_075097693.1	*Sandaracinus amylolyticus*	[4]
IR41	WP_081250846.1	*Rhizobium leguminosarum*	[4]
IR42	WP_081734918.1	*Mesorhizobium sp. L2C084A000*	[4]
IR43	WP_082312585.1	*Chelatococcus sp. CO-6*	[4]
IR44	WP_083347639.1	*Rhizobium sp. LCM 4573*	[4]
IR45	WP_083948736.1	*Aminobacter aminovorans*	[4]
IR46	WP_086088856.1	*Pseudorhodoplanes sinuspersici*	[4]
IR47	WP_086800502.1	*Streptomyces scabiei*	[4]
IR48	WP_088133675.1	*Vibrio gazogenes*	[4]
IR49	WP_091185118.1	*Paenibacillus catalpae]*	[4]
IR50	WP_097622187.1	*Rhizobium sp. L43*	[4]
IR51	WP_074958336.1	*Myxococcus fulvus*	[3]
IR52	WP_028649287.1	*Nocardiopsis sp. CNT312*	[3]
IR53	WP_024271000.1	*Shinella sp. DD12*	[3]
IR54	WP_077961001.1	*Ensifer adhaerens*	[3]
IR55	WP_119269405.1	*Phyllobacteriaceae bacterium SYSU D60010*	[3]
IR56	WP_095484516.1	*Mesorhizobium mediterraneum*	[3]
IR57	WP_112810862.1	*Rhizobiales bacterium*	[3]
IR58	WP_036254014.1	*Mesorhizobium*	[3]
IR59	WP_105371846.1	*Neorhizobium huautlense*	[3]
IR60	WP_014652774.1	*Paenibacillus mucilaginosus*	[3]
IR61	WP_053204479.1	*Jiangella muralis*	[3]
IR62	WP_073934314.1	*Streptomyces sp. CB02400*	[3]

IRED	Protein identifier	*Organism*	*Ref.*
IR63	WP_101830390.1	*Frankia canadensis*	[3]
IR64	WP_106402132.1	*Actinocorallia populi*	[3]
IR65	WP_107269705.1	*Plantactinospora sp. BC1*	[3]
IR66	WP_054288132.1	*Kibdelosporangium phytohabitans*	[3]
IR67	WP_107099103.1	*Streptomyces kanamyceticus*	[3]
IR68	WP_014910993.1	*Nocardiopsis alba*	[3]
IR69	WP_015610874.1	*Streptomyces sp. GF3587*	[3]
IR70	AKU97888.1	*Labilithrix luteola*	[3]
IR71	WP_030568324.1	*Streptomyces cyaneofuscatus*	[3]
IR72	WP_034851031.1	*Inquilinus limosus*	[3]
IR73	WP_042336938.1	*Paraburkholderia ferrariae*	[3]
IR74	WP_067485233.1	*Actinomadura hibisca*	[3]
IR75	WP_099935863.1	*Streptomyces sp. 1121.2*	[3]
IR76	WP_104983023.1	*Sorangium cellulosum*	[3]
IR77	WP_138891787.1	*Mycobacterium sp. KBS0706*	[3]
IR78	WP_140797783.1	*Myxococcus xanthus*	[3]
IR79	WP_116949466.1	*Jiangella sp. KE2-3*	[3]
IR80	WP_069109858.1	*Jiangella alba*	[3]
IR81	WP_051581142.1	*Pseudonocardia acaciae*	[3]
IR82	WP_129662656.1	*Phytoactinopolyspora endophytica*	[3]
IR83	WP_043636194.1	*Nonomuraea candida*	[3]
IR84	WP_030269222.1	*Micromonospora globosa*	[3]
IR85	WP_088833824.1	*Paenibacillus elgii*	[3]
IR86	WP_007130043.1	*Paenibacillus lactis*	[3]
IR87	WP_000739166.1	*Bacillus cereus*	[3]
IR88		Metagenome (pIR23)	[5]
IR89		Metagenome (pIR106)	[5]
IR90		Metagenome (pIR117)	[5]
IR91		Metagenome (pIR124)	[5]
IR92		Metagenome (pIR125)	[5]
IR93		Metagenome (pIR258)	[5]
IR94		Metagenome (pIR271)	[5]
IR95		Metagenome (pIR325)	[5]
IR96		Metagenome (pIR338)	[5]
IR97		Metagenome (pIR355)	[5]
IR98		Metagenome (pIR357)	[5]
IR99		Metagenome (pIR358)	[5]
IR100		Metagenome (pIR361)	[5]
IR101	WP_016642458.1	*Streptomyces aurantiacus*	this work
IR102	WP_018958930.1	*Streptomyces sp. CNB091*	this work
IR103	WP_055528718.1	*Streptomyces alboniger*	this work
IR104	WP_078965966.1	*Streptomyces aureocirculatus*	this work
IR105	WP_079183168.1	*Streptomyces sp. TSRI0281*	this work
IR106	WP_138049834.1	*Streptomyces sp. NEAU-C151*	this work
IR107	WP_141327527.1	*Myxococcus sp. AB025B*	[6]

IRED	Protein identifier	*Organism*	*Ref.*
IR108	PAQ05110.1	*Mesorhizobium temperatum*	this work
IR109	WP_163868876.1	*Myxococcus sp. AB053B]*	this work
IR110	WP_120641842.1	*Corallococcus llansteffanensis*	[6]
IR111	WP_164011897.1	*Pyxidicoccus sp. AB060A*	[6]
IR112	WP_040456307.1	*Hoeflea sp. 108*	this work
IR113	WP_095520326.1	*Mesorhizobium wenxiniae*	this work
IR114	WP_098285697.1	*Bacillus thuringiensis*	this work
IR115	WP_099476364.1	*Paenibacillus ihbetae*	this work
IR116	WP_103964206.1	*Nonomuraea solani*	this work
IR117	WP_078076200.1	*Streptomyces niveus*	this work
IR118	WP_125753405.1	*Streptomyces sp. WAC01280*	this work
IR119	WP_093151256.1	*Saccharopolyspora antimicrobica*	this work
IR120	WP_073866103.1	*Streptomyces sp. CB00072*	this work
IR121	WP_067986728.1	*Nocardia caishijiensis*	this work
IR122	WP_145871342.1	*Streptomyces capillispiralis*	this work
IR123	WP_091052229.1	*Nocardioides sp. YR527*	this work
IR124	WP_146646629.1	*Labilithrix luteola*	this work
IR125	WP_120779582.1	*Micromonospora costi*	this work
IR126	WP_132118896.1	*Actinocrispum wychmicini*	this work
IR127	WP_149853273.1	*Goodfellowiella sp. AN110305*	this work
IR128	WP_072027084.1	*Amycolatopsis keratiniphila*	this work
IR129	WP_091804538.1	*Prauserella marina*	this work
IR130	WP_143226941.1	*Actinomadura mexicana*	this work
IR131	WP_206806895.1	*Amycolatopsis sp. 195334CR*	[6]
IR132	WP_033436765.1	*Saccharothrix sp. NRRL B-16314*	[6]
IR133	WP_187341554.1	*Olivibacter sp. SDN3*	[6]
IR134	WP_084429349.1	*Kibdelosporangium aridum*	this work
IR135	WP_020660865.1	*Amycolatopsis benzoatilytica*	this work
IR136	WP_200314139.1	*Prauserella sp. ASG 168*	this work
IR137	WP_132480478.1	*Saccharopolyspora sp. 7K502*	this work
IR138	WP_189027275.1	*Nocardia rhizosphaerihabitans*	this work
IR139	WP_196417197.1	*Actinoplanes sp. NEAU-A11*	this work
IR140	WP_204075250.1	*Planotetrasporaphitsanulokensis*	this work
IR141	WP_132237834.1	*Promicromonospora sp. CF082*	this work
IR142	WP_132403551.1	*Kribbella albertanoniae*	this work
IR143	WP_062650298.1	*Streptomyces sp. NBRC 110468*	this work
IR144	WP_183655192.1	*Nonomuraea dietziae*	this work
IR145	WP_067828057.1	*Actinomadura kijaniata*	this work
IR146	WP_055602427.1	*Streptomyces aureus*	this work
IR147	WP_205083603.1	*Streptomyces sp. RHZ10*	this work
IR148	WP_187063382.1	*Streptomyces buecherae*	this work
IR149	WP_063051984.1	*Nocardia arthritidis*	this work
IR150	WP_153033184.1	*Amycolatopsis sp. YIM 10*	this work
IR151	WP_189213896.1	*Actinokineospora fastidiosa*	this work
IR152	WP_156520327.1	*Rhodococcus sp. EPR-157*	this work

IRED	Protein identifier	*Organism*	*Ref.*
IR153	WP_100750305.1	*Streptomyces*	this work
IR154	WP_107462275.1	*Streptomyces sp. MA5143a*	this work
IR155	WP_145827875.1	*Streptomyces sp. T12*	this work
IR156	WP_164735421.1	*Pseudoflavitalearhizosphaerae*	[6]
IR157	WP_038700284.1	*Sphingobacterium sp. ML3W*	this work
IR158	WP_057939766.1	*Algoriphagus resistens*	this work
IR159	WP_187342350.1	*Olivibacter sp. SDN3*	this work
IR160	WP_034685409.1	*Chryseobacterium piperi*	this work
IR161	RYY25307.1	*hitinophagaceae bacterium*	this work
IR162	WP_112745115.1	*Chryseolinea flava*	this work
IR163	WP_205686912.1	*Chitinophaga rhizosphaerae*	this work
IR164	WP_120257001.1	*Sphingobacterium detergens*	this work
IR165	WP_201667602.1	*Sphingobacterium multivorum*	this work
IR166	WP_028071301.1	*Sphingobacteriumthalpophilum*	this work
IR167	MBA3677520.1	*Sphingosinicella sp.*	this work
IR168	WP_174782375.1	*Cupriavidus gilardii*	[6]
IR169	WP_161024548.1	*Massiliaguangdongensis*	[6]
IR170	MBA2675896.1	*Ramlibacter sp.*	this work
IR171	WP_069377993.1	*Pedobactersteynii*	this work
IR172	WP_113619086.1	*Chitinophagaflava*	this work
IR173	WP_187965108.1	*Sinomicrobium sp. FJxs*	this work
IR174	WP_205760981.1	*Luteolibacter luteus*	[6]
IR175	WP_126748102.1	*Variovorax sp. DXTD-1*	this work

Table S3. *ee* values of the product **4a** obtained by IREDs**.**

IRED	*ee*%	IRED	*ee*%	IRED	*ee*%	IRED	*ee*%
IR43	99^{S}	IR32	88^{S}	IR86	75^{S}	IR55	63^{S}
IR46	99^{S}	IR99	88^{S}	IR121	75^{S}	IR171	62^{S}
IR47	99^{S}	IR110	88^{S}	IR61	74^{S}	IR37	60^{S}
IR49	99^{S}	IR24	87^{S}	IR133	74^{S}	IR88	60^{S}
IR64	99^{S}	IR174	87^{S}	IR107	73^{S}	IR103	60^{S}
IR65	99^{S}	IR31	86^{S}	IR68	72^{S}	IR169	58^{S}
IR84	99^{S}	IR109	84^{S}	IR100	72^{S}	IR168	56^{S}
IR85	99^{S}	IR35	82^{S}	IR167	72^{S}	IR156	54^{S}
IR97	99^{S}	IR51	82^{S}	IR25	70^{S}	IR71	52^{S}
IR98	99^{S}	IR70	82^{S}	IR89	70^{S}	IR36	50^{S}
IR115	99^{S}	IR92	82^{S}	IR96	70^{S}	IR39	47^{S}
IR117	99^{S}	IR131	82^{S}	IR132	70^{S}	IR94	46^{S}
IR122	99^{S}	IR23	81^{S}	IR170	70^{S}	IR162	45^{S}
IR124	99^{S}	IR67	81^{S}	IR57	7^{S}	IR79	40^{S}
IR134	99^{S}	IR161	81^{S}	IR21	68^{S}	IR45	34^{S}
IR149	99^{S}	IR40	80^{S}	IR38	68^{S}	IR166	32^{S}
IR155	99^{S}	IR93	80^{S}	IR44	68^{S}	IR30	30^{S}
IR62	98^{S}	IR159	80^{S}	IR58	68^{S}	IR54	30^{S}
IR77	98^{S}	IR130	79^{S}	IR76	68^{S}	IR74	28^{S}
IR160	97^{S}	IR56	78^{S}	IR66	66^{S}	IR102	13^{S}
IR50	95^{S}	IR111	78^{S}	IR78	66^{S}	IR19	1
IR69	95^{S}	IR104	77^{S}	IR90	66^{S}	IR63	51^{R}
IR118	95^{S}	IR33	76^{S}	IR172	66^{S}	IR95	4^{R}
IR128	95^{S}	IR20	75^{S}	IR175	65^{S}	IR105	43^{R}
IR26	92^{S}	IR60	75^{S}	IR27	64^{S}		

Table S4. 1mL one-pot biocatalytic cascade reduction and reductive amination.

Substrate	OYE1	IR43	Peak area percentage (%)			
			2a-2j	3a-4j	Imine	4a-4j
2a	0.5	1	<1	<1	14	86
2b	0.5	1	<1	7	23	69
2c	0.5	1	<1	3	<1	97
	0.5	1	<1	21	37	43
2d	0.5	4	<1	4	4	92
	0.5	6	<1	2	<1	98
	0.5	2	8	27	38	27
2e	0.5	4	<1	4	2	94
	0.5	6	<1	2	<1	98
	0.5	2	<1	23	13	64
2f	0.5	8	<1	9	11	80
	0.5	10	<1	2	2	96
	0.5	2	<1	38	56	6
2g	0.5	8	5	24	15	56
	0.5	10	5	19	12	64
	0.5	2	<1	19	22	59
2h	0.5	8	6	4	2	88
	0.5	10	7	2	2	89
2i	0.5	1	9	7	<1	84
2j	0.5	1	7	3	<1	90

Table S5. HPLC columns and conditions used for analysis of reaction samples.

Product	Column	Wavelength (nm)	Flow (mL/min)	*n*-hexane: isopropanol	Retention time(min)	
					T1	T2
3a'	OD-H	210	1	99.5:0.5	37.5^{S}	53.0^{R}
4a[a]	IC	254	0.5	97:3	34.1^{R}	35.5^{S}
4b[b]	AS-H	254	1	90:10	21.4^{R}	30.6^{S}
6a	OJ-H	254	1	85:15	9.7^{R}	11.7^{S}
6c	OJ-H	210	0.5	90:10	16.2^{R}	17.7^{S}
6d	OJ-H	210	0.5	90:10	28.2^{R}	37.5^{S}
6e	OJ-H	210	0.5	90:10	22.6^{R}	23.7^{S}
6f	OJ-H	210	0.5	98:2	44.8^{R}	46.8^{S}
6g	OJ-H	210	0.5	90:10	18.8^{S}	20.3^{R}
6h	OJ-H	210	1	85:15	16.5^{R}	22.7^{S}
6i	OJ-H	210	0.5	90:10	25.7^{A}	30.7^{B}

[a] Derivatized with Fmoc *N*-hydroxysuccinimide.

[b]Derivatized with 4-nitrobenzene sulfonyl chloride.

[c] Assignment of enantiomers (A)- and (B-) determined by order of elution.

S2.2 Supplementary figures

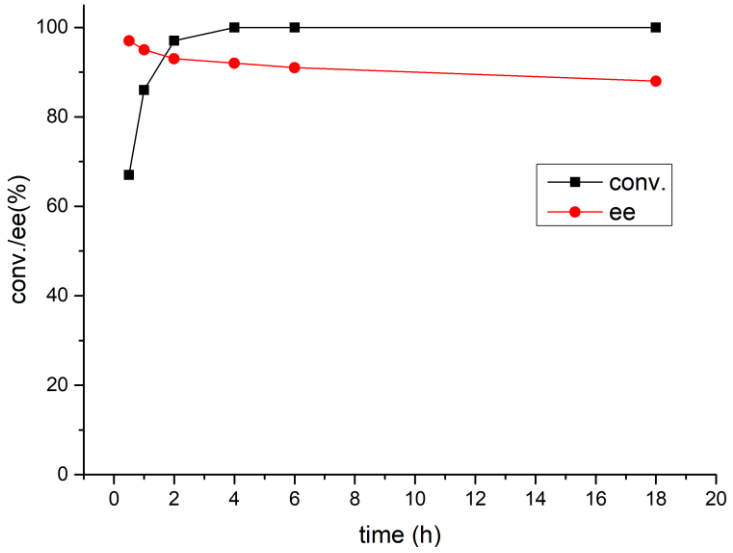

Figure S1. Conversion and stereoselectivity at different time in the reduction of **2a** using purified OYE1

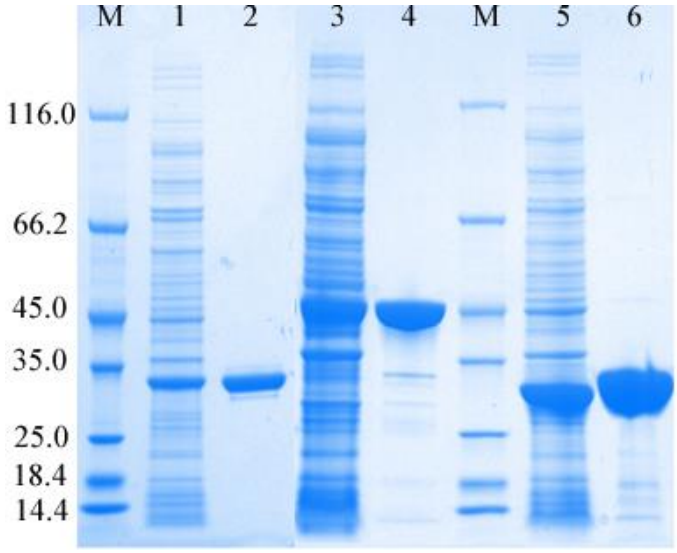

Figure S2. SDS-PAGE analysis of the purified IREDs. Lane M: protein maker; Lane 1,3,5: the supernatant of lysate of IR97, OYE1, IR43; Lane 2,4,6: purified enzyme of IR97, OYE1, IR43.

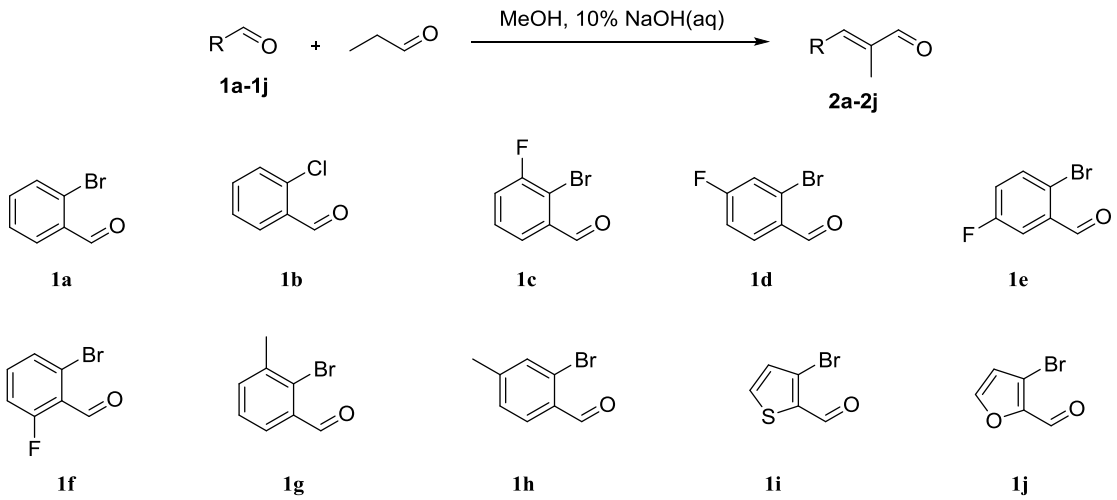

Figure S3. Synthetic routes of α,β-unsaturated aldehyde **2a-2j** used in this study.

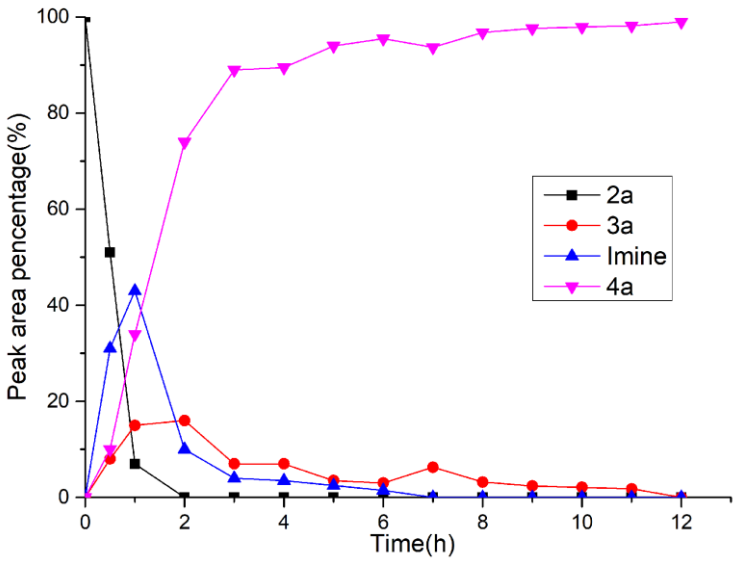

Figure S4. Time course of the preparative scale reaction in 500 mL of **2a** (The imine was confirmed by GC-MS).

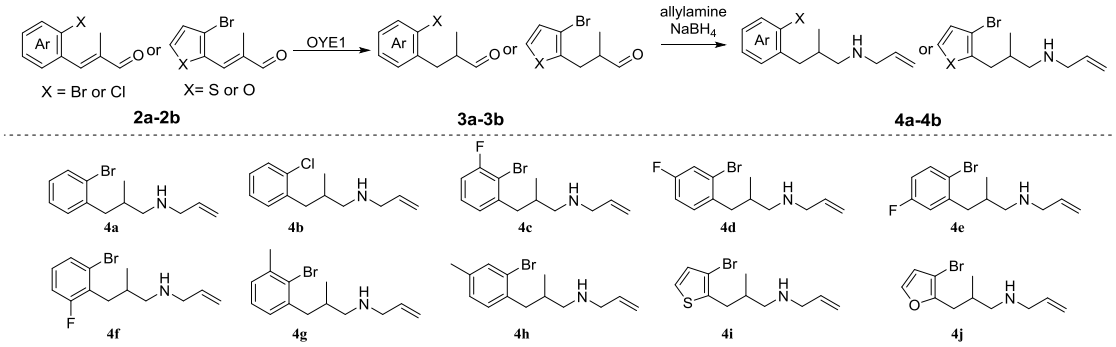

Figure S5. Synthetic routes of racemate of **4a-4j**.

S2.3 Sequence information

>OYE1

Protein sequence:

MSFVKDFKPQALGDTNLFKPIKIGNNELLHRAVIPPLTRMRALHPGNIPNRDWAVEYYTQRAQRPGTMIITEGAFISPQAGGYDNAPGVW
SEEQMVEWTKIFNAIHEKKSFVWVQLWVLGWAAFPDNLARDGLRYDSASDNVFMDAEQEAKAKKANNPQHSLTKDEIKQYIKEYVQAA
KNSIAAGADGVEIHSANGYLLNQFLDPHSNTRTDEYGGSIENRARFTLEVVDALVEAIGHEKVGLRLSPYGVFNSMSGGAETGIVAQYAYVA
GELEKRAKAGKRLAFVHLVEPRVTNPFLTEGEGEYEGGSNDFVYSIWKGPVIRAGNFALHPEVVREEVKDKRTLIGYGRFFISNPDLVDRLEK
GLPLNKYDRDTFYQMSAHGYIDYPTYEEALKLGWDKK*

Gene sequence (with codon optimization):

catATGAGTTTCGTTAAGGATTTCAAGCCGCAGGCACTGGGTGACACCAATCTGTTTAAACCGATTAAGATTGGTAACAATGAGCTGCTG
CATCGCGCCGTGATTCCGCCGCTGACCCGCATGCGCGCCCTGCACCCTGGTAATATTCCGAATCGCGATTGGGCCGTGGAATATTATACC
CAGCGTGCACAGCGCCCGGGCACCATGATTATTACCGAAGGCGCCTTTATTAGTCCGCAGGCAGGTGGTTATGATAATGCCCCGGGCGT
GTGGAGCGAAGAACAGATGGTGGAATGGACCAAAATTTTTAATGCCATTCATGAAAAGAAGAGCTTTGTGTGGGTGCAGCTGTGGGT
GCTGGGTTGGGCCGCATTTCCGGATAATCTGGCCCGTGATGGCCTGCGTTATGATAGCGCAAGTGATAATGTTTTTATGGATGCCGAACA
GGAAGCCAAAGCAAAAAAGGCCAATAATCCGCAGCATAGTCTGACCAAAGATGAAATTAAGCAGTATATTAAGGAGTACGTTCAGGCC
GCAAAAAATAGCATTGCAGCCGGTGCAGATGGTGTGGAAATTCATAGTGCCAATGGTTATCTGCTGAATCAGTTTCTGGATCCGCATAG
CAATACCCGCACCGATGAATATGGCGGCAGTATTGAAAATCGCGCCCGTTTTACCCTGGAAGTGGTTGATGCACTGGTGGAAGCAATTG
GCCATGAAAAAGTTGGTCTGCGCCTGAGTCCGTATGGTGTGTTTAATAGCATGAGTGGTGGCGCAGAAACCGGTATTGTGGCCCAGTAT
GCATACGTTGCAGGTGAACTGGAAAAACGCGCCAAAGCCGGTAAACGCCTGGCCTTTGTTCATCTGGTGGAACCGCGCGTTACCAATC
CGTTTCTGACCGAAGGTGAAGGTGAATATGAAGGTGGTAGTAATGATTTTGTTTACAGCATTTGGAAGGGCCCGGTTATTCGCGCAGG
CAATTTTGCCCTGCATCCGGAAGTGGTTCGTGAAGAAGTGAAAGATAAACGCACCCTGATTGGTTATGGTCGTTTCTTTATTAGCAATCC
GGATCTGGTTGATCGCCTGGAAAAAGGCCTGCCGCTGAATAAGTATGATCGTGATACCTTTTATCAGATGAGTGCACATGGTTATATTGA
TTATCCGACCTATGAAGAAGCCCTGAAACTGGGTTGGGATAAAAAACACCACCACCACCACCACTGA

>IR43

Protein sequence:

MTKTCVVGAGRMGSALARALLAEGIETRVWNRSPEKVAPLVAAGAHTAESLAEAVAASDVVIVNVIDYAAADALLRMPAVERALAGKVVV
QLTSGSPRQAREAGRWAAERGIAYLDGAIMATPNFIGGAETTILYSGMRQAFERHRDVLRVFGGNGVFVGEDAGHASALDTGLLTQMWG
KLFGTLQALAVVRAEGIGLEAYARYMRDFQPVVDAATDDLIARVGEGRWRGDAATLATIEAHYSAFHHLLAVGDEHGLDRVLPAALDGLFK
AALAAGHAADDFAALMRFIERGGVRHAA*

Gene sequence (with codon optimization）:

ATGACCAAAACCTGCGTTGTTGGTGCAGGTCGTATGGGTAGCGCACTGGCACGCGCACTGCTGGCAGAAGGTATTGAAACCCGCGTTT
GGAATCGCAGTCCGGAAAAAGTGGCACCGCTGGTGGCCGCCGGCGCACACACCGCAGAAAGCCTGGCAGAAGCCGTGGCCGCCAG
CGATGTGGTTATTGTGAATGTGATTGATTATGCCGCCGCAGATGCACTGCTGCGTATGCCGGCCGTGGAACGCGCCCTGGCTGGTAAAG
TTGTTGTTCAGCTGACCAGCGGTAGTCCGCGCCAGGCACGCGAAGCAGGCCGTTGGGCTGCAGAACGCGGCATTGCCTATCTGGATG
GCGCAATTATGGCAACCCCGAATTTTATTGGTGGCGCCGAAACCACCATTCTGTATAGTGGCATGCGTCAGGCATTTGAACGCCATCGTG
ATGTTCTGCGTGTGTTTGGTGGTAATGGCGTGTTTGTGGGTGAAGATGCCGGCCATGCCAGCGCCCTGGATACCGGTCTGCTGACCCA
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CGTGATTTTCAGCCGGTGGTTGATGCCGCAACCGATGATCTGATTGCACGTGTGGGTGAAGGTCGCTGGCGCGGTGACGCCGCAACCT
TAGCCACCATTGAAGCACATTATAGTGCATTTCATCATCTGCTGGCAGTGGGCGATGAACATGGCCTGGATCGCGTTCTGCCGGCAGCC
CTGGATGGTCTGTTTAAAGCCGCCCTGGCCGCAGGTCATGCCGCAGATGATTTTGCAGCACTGATGCGCTTTATTGAACGTGGCGGTGT

TCGTCATGCCGCCTAA

S2.4 Crystallographic information

To assign the absolute configuration of chiral products, the crystal of (*S*)-**4b**-HCl, (*S*)-**4c**-HCl, (*S*)-**4d**-HCl, (*S*)-**4e**-HCl, (*S*)-**4f**-HCl, (*S*)-**4g**-HCl and (*S*)-**4h**-HCl catalyzed by IR43 was obtained in ethanol/ n-butyl acetate. Crystal data for it has been deposited in the Cambridge Crystallographic Data Centre (CCDC) with number 2224137, 2241445, 2241442, 2242724, 2241443, 2241444 and 2241441, respectively.

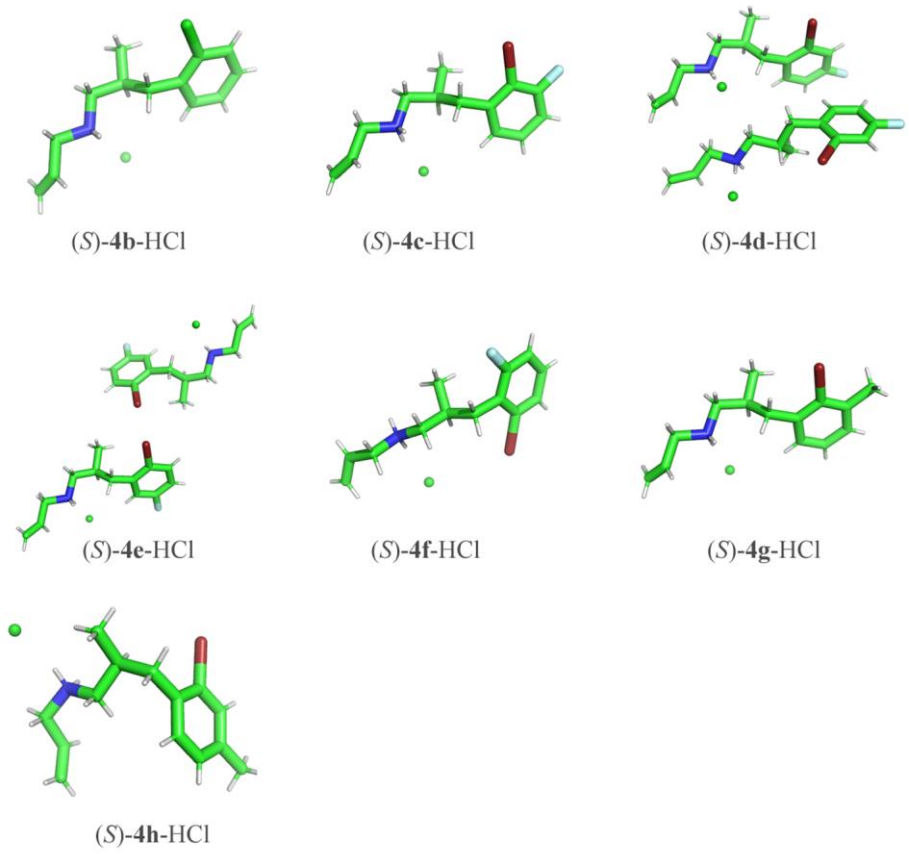


Figure S6. X-ray structure of (*S*)-**4b**-HCl (*S*)-**4c**-HCl, (*S*)-**4d**-HCl, (*S*)-**4e**-HCl, (*S*)-**4f**-HCl, (*S*)-**4g**-HCl and (*S*)-**4h**-HCl prepared by IR43.

Table S6. Crystal data and structure refinement for 2224137 **(4b)**

Identification code	2224137
Empirical formula	$C_{13}H_{19}Cl_2N$
Formula weight	260.19
Temperature/K	294.15
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	4.95940(10)
b/Å	10.73110(10)
c/Å	27.2017(3)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1447.67(4)
Z	4
ρ_{calc}g/cm^3	1.194
μ/mm^{-1}	3.822
F(000)	552
Crystal size/mm^3	0.23 × 0.2 × 0.16
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.858 to 158.51
Index ranges	-6 ≤ h ≤ 4, -13 ≤ k ≤ 13, -34 ≤ l ≤ 34
Reflections collected	18528
Independent reflections	3066 [R_{int} = 0.0323, R_{sigma} = 0.0178]
Data/restraints/parameters	3066/0/147
Goodness-of-fit on F^2	1.032
Final R indexes [I>=2σ (I)]	R_1 = 0.0297, wR_2 = 0.0858
Final R indexes [all data]	R_1 = 0.0306, wR_2 = 0.0867
Largest diff. peak/hole / e Å^{-3}	0.20/-0.19
Flack parameter	0.005(5)

Table S7. Crystal data and structure refinement for 2241445(4c)

Identification code	2241445
Empirical formula	$C_{13}H_{18}BrClFN$
Formula weight	322.64
Temperature/K	113.15
Crystal system	monoclinic
Space group	$P2_1$
a/Å	4.8988(2)
b/Å	10.7881(3)
c/Å	13.7759(4)
α/°	90
β/°	98.020(3)
γ/°	90
Volume/Å^3	720.92(4)
Z	2
ρ_{calc}g/cm^3	1.486
μ/mm^{-1}	3.027
F(000)	328.0
Crystal size/mm^3	0.26 × 0.2 × 0.16
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.814 to 52.736
Index ranges	-6 ≤ h ≤ 6, -13 ≤ k ≤ 13, -17 ≤ l ≤ 10
Reflections collected	5945
Independent reflections	2820 [R_{int} = 0.0385, R_{sigma} = 0.0484]
Data/restraints/parameters	2820/1/155
Goodness-of-fit on F^2	1.122
Final R indexes [I>=2σ (I)]	R_1 = 0.0589, wR_2 = 0.1500
Final R indexes [all data]	R_1 = 0.0615, wR_2 = 0.1517
Largest diff. peak/hole / e Å^{-3}	2.97/-0.66
Flack parameter	0.091(11)

Table S8. Crystal data and structure refinement for 2241442 (4d)

Identification code	2241442
Empirical formula	C13H18BrClFN
Formula weight	322.64
Temperature/K	113.15
Crystal system	orthorhombic
Space group	P212121
a/Å	7.6197(2)
b/Å	14.1232(3)
c/Å	27.1001(7)
α/°	90
β/°	90
γ/°	90
Volume/Å3	2916.37(12)
Z	8
ρcalcg/cm3	1.470
μ/mm-1	2.993
F(000)	1312.0
Crystal size/mm3	0.26 × 0.23 × 0.17
Radiation	Mo Kα (λ = 0.71073)
2Θ range for data collection/°	5.354 to 56.564
Index ranges	-10 ≤ h ≤ 10, -18 ≤ k ≤ 18, -35 ≤ l ≤ 36
Reflections collected	16201
Independent reflections	7206 [Rint = 0.0399, Rsigma = 0.0545]
Data/restraints/parameters	7206/0/309
Goodness-of-fit on F2	0.997
Final R indexes [I>=2σ (I)]	R1 = 0.0427, wR2 = 0.0909
Final R indexes [all data]	R1 = 0.0529, wR2 = 0.0959
Largest diff. peak/hole / e Å-3	0.76/-0.40
Flack parameter	0.011(6)

Table S9. Crystal data and structure refinement for 2242724 (4e)

Identification code	R20230217e_twin1_hklf5
Empirical formula	C13H18BrClFN
Formula weight	322.64
Temperature/K	113.15
Crystal system	monoclinic
Space group	P21
a/Å	4.83350(10)
b/Å	26.0950(6)
c/Å	11.3444(3)
α/°	90
β/°	90.954(2)
γ/°	90
Volume/Å3	1430.67(6)
Z	4
ρcalcg/cm3	1.498
μ/mm-1	3.050
F(000)	656.0
Crystal size/mm3	0.38 × 0.22 × 0.16
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.122 to 57.394
Index ranges	-6 ≤ h ≤ 5, -35 ≤ k ≤ 35, -15 ≤ l ≤ 15
Reflections collected	11088
Independent reflections	11088 [Rint = ?, Rsigma = 0.0167]
Data/restraints/parameters	11088/1/311
Goodness-of-fit on F2	1.018
Final R indexes [I>=2σ (I)]	R1 = 0.0491, wR2 = 0.1436
Final R indexes [all data]	R1 = 0.0531, wR2 = 0.1472
Largest diff. peak/hole / e Å-3	0.87/-0.80
Flack parameter	0.004(8)

Table S10. Crystal data and structure refinement for 2241443 (4f)

Identification code	2241443
Empirical formula	C13H18BrClFN
Formula weight	322.64
Temperature/K	113.15
Crystal system	orthorhombic
Space group	P212121
a/Å	4.7559(2)
b/Å	10.6799(4)
c/Å	28.6366(9)
α/°	90
β/°	90
γ/°	90
Volume/Å3	1454.53(9)
Z	4
ρcalcg/cm3	1.473
μ/mm-1	3.000
F(000)	656.0
Crystal size/mm3	0.27 × 0.23 × 0.18
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.07 to 56.554
Index ranges	-6 ≤ h ≤ 6, -11 ≤ k ≤ 14, -38 ≤ l ≤ 37
Reflections collected	8772
Independent reflections	3566 [Rint = 0.0358, Rsigma = 0.0463]
Data/restraints/parameters	3566/0/155
Goodness-of-fit on F2	1.060
Final R indexes [I>=2σ (I)]	R1 = 0.0394, wR2 = 0.0842
Final R indexes [all data]	R1 = 0.0467, wR2 = 0.0879
Largest diff. peak/hole / e Å-3	0.69/-0.29
Flack parameter	0.006(8)

Table S11. Crystal data and structure refinement for 2241444 (4g)

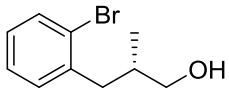
Identification code	2241444
Empirical formula	C14H21BrClN
Formula weight	318.68
Temperature/K	113.15
Crystal system	orthorhombic
Space group	P212121
a/Å	4.9604(2)
b/Å	10.8195(4)
c/Å	29.3754(10)
α/°	90
β/°	90
γ/°	90
Volume/Å3	1576.55(10)
Z	4
ρcalcg/cm3	1.343
μ/mm-1	2.758
F(000)	656.0
Crystal size/mm3	0.28 × 0.23 × 0.17
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.012 to 52.744
Index ranges	-6 ≤ h ≤ 4, -13 ≤ k ≤ 13, -36 ≤ l ≤ 30
Reflections collected	7454
Independent reflections	3206 [Rint = 0.0333, Rsigma = 0.0409]
Data/restraints/parameters	3206/0/156
Goodness-of-fit on F2	1.088
Final R indexes [I>=2σ (I)]	R1 = 0.0350, wR2 = 0.0842
Final R indexes [all data]	R1 = 0.0375, wR2 = 0.0855
Largest diff. peak/hole / e Å-3	0.86/-0.28
Flack parameter	0.010(8)

Table S12. Crystal data and structure refinement for 2241441 (4h)

Identification code	2241441
Empirical formula	C14H21BrClN
Formula weight	318.68
Temperature/K	113.15
Crystal system	monoclinic
Space group	P21
a/Å	9.5543(2)
b/Å	6.5919(2)
c/Å	12.4634(3)
α/°	90
β/°	98.424(2)
γ/°	90
Volume/Å3	776.49(3)
Z	2
ρcalcg/cm3	1.363
μ/mm-1	2.800
F(000)	328.0
Crystal size/mm3	0.24 × 0.2 × 0.15
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.31 to 69.308
Index ranges	-15 ≤ h ≤ 14, -10 ≤ k ≤ 6, -19 ≤ l ≤ 18
Reflections collected	11301
Independent reflections	5531 [Rint = 0.0287, Rsigma = 0.0424]
Data/restraints/parameters	5531/1/156
Goodness-of-fit on F2	1.029
Final R indexes [I>=2σ (I)]	R1 = 0.0380, wR2 = 0.0820
Final R indexes [all data]	R1 = 0.0495, wR2 = 0.0866
Largest diff. peak/hole / e Å-3	0.48/-0.49
Flack parameter	0.009(6)

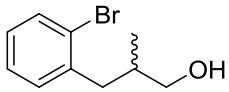
S2.5 NMR data, mass spectrum data and optical rotation of the products

(*S*)-3-(2-chlorophenyl)-2-methylpropan-1-ol((*S*)-**3a'**)



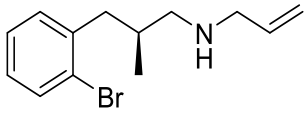
Reduction of 2 mmol **2a** catalyzed by purified OYE1 and subsequent chemical reduction gave 235 mg (*S*)-**3a'** as a light yellow oil with 51% isolated yield and 93% *ee* values. ^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.53 (d, J=8.1 Hz, 1 H), 7.18 - 7.25 (m, 2 H), 7.01 - 7.13 (m, 1 H), 3.54 (dd, J=13.4, 5.6 Hz, 2 H), 2.91 (dd, J=13.4, 6.4 Hz, 1 H), 2.54 (dd, J=13.4, 8.1 Hz, 1 H), 2.06 (dd, J=13.3, 6.7 Hz, 1 H), 0.96 ppm (d, J=6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 140.16, 132.92, 131.44, 127.72, 127.23, 124.85, 67.51, 39.60, 36.40, 16.47. HRMS calcd. for $C_{10}H_{13}BrNaO^{+}$ 251.0047 and 253.0027 $[M+Na]^{+}$, found 251.0053 and 253.0027. $[\alpha]_D^{20}$ = -3.850 (c = 1.0, $CHCl_3$).

3-(2-chlorophenyl)-2-methylpropan-1-ol(Rac-**3a'**)



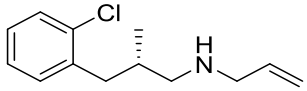
Reduction of 1 mmol **2a** catalyzed by cell-free extracts of N8-2 and subsequent chemical reduction gave 120 mg Rac-**3a'** as a light yellow oil with 52% isolated yield. ^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.49 - 7.60 (m, 1 H), 7.17 - 7.29 (m, 2 H), 7.06 (br. s., 1 H), 3.44 - 3.65 (m, 2 H), 2.91 (dd, J=13.4, 6.4 Hz, 1 H), 2.54 (dd, J=13.3, 7.9 Hz, 1 H), 2.06 (d, J=6.6 Hz, 1 H), 0.96 ppm (d, J=6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 140.16, 132.92, 131.44, 127.72, 127.23, 124.85, 67.51, 39.60, 36.40, 16.47. HRMS calcd. for $C_{10}H_{13}BrNaO^{+}$ 251.0047 and 253.0027 $[M+Na]^{+}$, found 251.0064 and 253.0034.

(*S*)-*N*-(3-(2-bromophenyl)-2-methylpropyl) prop-2-en-1-amine ((*S*)-**4a**)



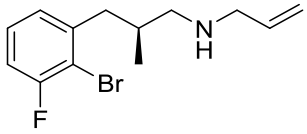
One-pot biocatalytic cascade reduction and reductive amination of 10 mmol **2a** catalyzed by purified OYE1 and IR43 gave 1.945 g (*S*)-**4a** as a light yellow oil with 74% isolated yield and >99% *ee* values.^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.58 (d, *J* = 7.8 Hz, 1 H), 7.30 - 7.20 (m, 2 H), 7.14 - 7.06 (m, 1 H), 5.96 (tdd, *J* = 6.0, 10.5, 16.9 Hz, 1 H), 5.22 (dd, *J* = 1.5, 17.1 Hz, 1 H), 5.14 (d, *J* = 10.3 Hz, 1 H), 3.31 (d, *J* = 6.1 Hz, 2 H), 2.94 (dd, *J* = 6.0, 13.3 Hz, 1 H), 2.71 - 2.63 (m, 1 H), 2.60 - 2.50 (m, 2 H), 2.18 - 2.06 (m, 1 H), 0.98 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 140.38, 136.82, 132.87, 131.44, 127.60, 127.11, 124.88, 115.96, 55.34, 52.50, 41.46, 33.80, 17.91. HRMS calcd. for $C_{13}H_{19}BrN^{+}$ 268.0695 and 270.0728 $[M+H]^{+}$, found 268.0714 and 270.0694. $[\alpha]_D^{20}$ = +15.999 (c = 1.0, MeOH).

(*S*)-*N*-(3-(2-chlorophenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4b**)



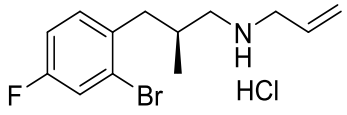
One-pot biocatalytic cascade reduction and reductive amination of 1 mmol **2b** catalyzed by purified OYE1 and IR43 gave 170 mg (*S*)-**4b** as a light yellow oil with 76% isolated yield and >99% *ee* values. ^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.33 (d, J = 7.3 Hz, 1 H), 7.22 - 7.06 (m, 3 H), 6.02 - 5.83 (m, 1 H), 5.23 - 5.00 (m, 2 H), 3.34 - 3.12 (m, 2 H), 2.88 (dd, J = 5.9, 13.4 Hz, 1 H), 2.66 - 2.56 (m, 1 H), 2.54 - 2.44 (m, 2 H), 2.11 - 1.98 (m, 1 H), 0.95 - 0.88 (m, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ =138.72, 136.92, 134.27, 131.42, 129.52, 127.32, 126.47, 115,87, 55.46, 52.55, 38.97, 33.85, 17.97. HRMS calcd. for $C_{13}H_{19}ClN^{+}$ 224.1200 $[M+H]^{+}$, found 224.1184. $[\alpha]_D^{20}$ = +15.269 (c = 1.0, MeOH).

(*S*)-*N*-(3-(2-bromo-3-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4c**)



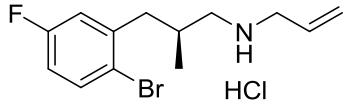
One-pot biocatalytic cascade reduction and reductive amination of 1 mmol **2c** catalyzed by purified OYE1 and IR43 gave 190 mg (*S*)-**4c** as a light yellow oil with 66% isolated yield and 97% *ee* values.^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.18 (dt, *J* = 5.7, 7.8 Hz, 1 H), 7.01 - 6.92 (m, 2 H), 5.90 (tdd, *J* = 6.0, 10.6, 16.9 Hz, 1 H), 5.24 - 5.03 (m, 2 H), 3.25 (d, *J* = 6.1 Hz, 2 H), 2.94 (dd, *J* = 6.0, 13.3 Hz, 1 H), 2.68 - 2.44 (m, 3 H), 2.13 - 1.96 (m, 1 H), 0.92 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 159.28 (d, *J* = 245 Hz), 143.05, 136.91, 127.79 (d, *J* = 8 Hz), 126.49 (d, *J* = 4 Hz), 115.91, 113.80 (d, *J* = 17 Hz), 111.71 (d, *J* = 20 Hz), 55.34, 52.57, 41.09, 33.87, 17.88. HRMS calcd. for $C_{13}H_{18}BrFN^{+}$ 286.0601 and 288.0581 $[M+H]^{+}$, found 286.0613 and 288.0595. $[\alpha]_D^{20}$ = +11.419 (c = 1.0, MeOH).

(*S*)-*N*-(3-(2-bromo-4-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine hydrochloride ((*S*)-**4d**)



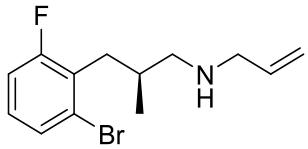
One-pot biocatalytic cascade reduction and reductive amination of 1 mmol **2d** catalyzed by purified OYE1 and IR43 gave 175 mg (*S*)-**4d**-HCl as a white soild with 61% isolated yield and >99% *ee* values. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.41 (dd, *J* = 2.6, 8.4 Hz, 1 H), 7.35 (dd, *J* = 6.1, 8.6 Hz, 1 H), 7.11 (dt, *J* = 2.6, 8.4 Hz, 1 H), 5.95 (tdd, *J* = 7.0, 10.2, 17.1 Hz, 1 H), 5.61 - 5.45 (m, 2 H), 3.68 (d, *J* = 6.8 Hz, 2 H), 3.05 - 2.85 (m, 3 H), 2.67 (dd, *J* = 8.6, 13.7 Hz, 1 H), 2.37 - 2.22 (m, 1 H), 1.04 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 161.28 (d, *J* = 247 Hz), 134.50 (d, *J* = 3 Hz), 132.39 (d, *J* = 8 Hz), 127.66, 124.14 (d, *J* = 9 Hz), 123.26, 119.58 (d, *J* = 24 Hz), 114.37 (d, *J* = 22 Hz), 52.10, 50.08, 39.25, 31.45, 15.87. HRMS calcd. for $C_{13}H_{18}BrFN^+$ 286.0601 and 288.0581 $[M+H]^+$, found 286.0612 and 288.0601. $[\alpha]_D^{20}$ = +12.039 (c = 1.0, MeOH).

(*S*)-*N*-(3-(2-bromo-5-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine hydrochloride ((*S*)-**4e**)



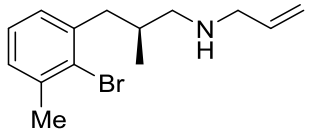
One-pot biocatalytic cascade reduction and reductive amination of 1 mmol **2e** catalyzed by purified OYE1 and IR43 gave 175 mg (*S*)-**4e** as a white soild with 61% isolated yield and 98% *ee* values. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.60 (dd, *J* = 5.4, 8.8 Hz, 1 H), 7.14 (dd, *J* = 2.9, 9.3 Hz, 1 H), 6.96 (dt, *J* = 2.9, 8.4 Hz, 1 H), 5.95 (tdd, *J* = 6.9, 10.2, 17.1 Hz, 1 H), 5.60 - 5.46 (m, 2 H), 3.73 - 3.63 (m, 2 H), 3.06 - 2.84 (m, 3 H), 2.75 - 2.62 (m, 1 H), 2.43 - 2.23 (m, 1 H), 1.05 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 161.98 (d, *J* = 245 Hz), 140.74 (d, *J* = 7 Hz), 134.16 (d, *J* = 8 Hz), 127.66, 123.27, 118.50 (d, *J* = 3 Hz), 118.02 (d, *J* = 22 Hz), 115.27 (d, *J* = 22 Hz), 52.07, 50.08, 40.05, 31.32, 15.88. HRMS calcd. for $C_{13}H_{18}BrFN^+$ 286.0601 and 288.0581 $[M+H]^+$, found 286.0619 and 288.0607. $[\alpha]_D^{20}$ = +10.129 (c = 1.0, MeOH).

(*S*)-*N*-(3-(2-bromo-6-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4f**)



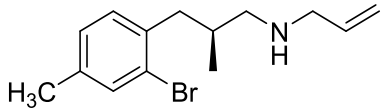
One-pot biocatalytic cascade reduction and reductive amination of 1 mmol **2f** catalyzed by purified OYE1 and IR43 gave 188 mg (*S*)-**4f** as a light yellow oil with 66% isolated yield and 98% *ee* values. ^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.34 (d, *J* = 7.8 Hz, 1 H), 7.10 - 6.93 (m, 2 H), 5.99 - 5.81 (m, 1 H), 5.23 - 5.02 (m, 2 H), 3.25 (d, *J* = 6.1 Hz, 2 H), 2.91 - 2.81 (m, 1 H), 2.71 - 2.48 (m, 3 H), 2.15 - 1.96 (m, 1 H), 0.94 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 161.38 (d, *J* = 247 Hz), 136.99, 128.83 (d, *J* = 18 Hz), 128.53 (d, *J* = 3 Hz), 128.12 (d, *J* = 9 Hz), 125.73 (d, *J* = 4 Hz), 115.79, 114.49 (d, *J* = 24 Hz), 55.47, 52.53, 34.17, 33.45, 17.88. HRMS calcd. for $C_{13}H_{18}BrFN^+$ 286.0601 and 288.0581 $[M+H]^+$, found 286.0617 and 288.0605. $[\alpha]_D^{20}$ = +13.719 (c = 1.0, MeOH).

(*S*)-*N*-(3-(2-bromo-3-methylphenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4g**)



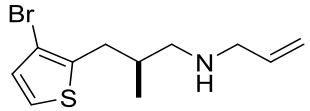
One-pot biocatalytic cascade reduction and reductive amination of 1 mmol **2g** catalyzed by purified OYE1 and IR43 gave 150 mg (*S*)-**4g** as a light yellow oil with 53% isolated yield and 98% *ee* values. ^{1}H NMR (600MHz, CHLOROFORM-d) δ = 7.13 - 7.05 (m, 2 H), 7.01 (dd, *J* = 1.7, 6.8 Hz, 1 H), 5.95 - 5.84 (m, 1 H), 5.16 (dd, *J* = 1.5, 17.2 Hz, 1 H), 5.07 (d, *J* = 10.3 Hz, 1 H), 3.24 (d, *J* = 5.9 Hz, 2 H), 2.91 (dd, *J* = 6.1, 13.4 Hz, 1 H), 2.65 - 2.60 (m, 1 H), 2.56 - 2.48 (m, 2 H), 2.41 (s, 3 H), 2.13 - 2.04 (m, 1 H), 0.92 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 140.76, 138.62, 137.04, 128.85, 128.51, 127.54, 126.42, 115.73, 55.55, 52.59, 42.28, 33.64, 24.18, 18.00. HRMS calcd. for $C_{14}H_{21}BrN^+$ 282.0852 and 284.0832 $[M+H]^+$, found 282.0861 and 284.0843. $[\alpha]_D^{20}$ = +17.199 (c = 1.0, MeOH).

(*S*)-*N*-(3-(2-bromo-4-methylphenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4h**)



One-pot biocatalytic cascade reduction and reductive amination of 1 mmol **2h** catalyzed by purified OYE1 and IR43 gave 185 mg (*S*)-**4h** as a light yellow oil with 66% isolated yield and >99% *ee* values. ^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.36 (s, 1 H), 7.10 - 6.97 (m, 2 H), 5.98 - 5.81 (m, 1 H), 5.22 - 5.03 (m, 2 H), 3.24 (d, *J* = 5.9 Hz, 2 H), 2.84 (dd, *J* = 6.1, 13.4 Hz, 1 H), 2.65 - 2.56 (m, 1 H), 2.54 - 2.41 (m, 2 H), 2.29 (s, 3 H), 2.09 - 1.94 (m, 1 H), 0.91 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 137.52, 137.20, 137.03, 133.25, 131.11, 127.94, 124.60, 115.78, 55.48, 52.60, 41.01, 33.96, 20.59, 17.92. HRMS calcd. for $C_{14}H_{21}BrN^+$ 282.0852 and 284.0832 $[M+H]^+$, found 282.0875 and 284.0848. $[\alpha]_D^{20}$ = +15.309 (c = 1.0, MeOH).

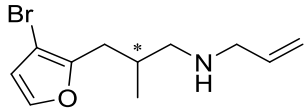
(*B*)-*N*-(3-(3-bromothiophen-2-yl)-2-methylpropyl)prop-2-en-1-amine ((*B*)-**4i**)



One-pot biocatalytic cascade reduction and reductive amination of 1 mmol **2i** catalyzed by purified OYE1 and IR43 gave 245 mg (*B*)-**4i** as a light yellow oil with 89% isolated yield and 88% *ee* values.^{1}H NMR (400MHz, CHLOROFORM-d) d = 7.27 (d, *J* = 2.0 Hz, 1 H), 6.35 (d, *J* = 1.7 Hz, 1 H), 5.90 (tdd, *J* = 6.0, 10.6, 16.9 Hz, 1 H), 5.25 - 5.03 (m, 2 H), 3.24 (d, *J* = 6.1 Hz, 2 H), 2.73 (dd, *J* = 6.1, 14.7 Hz, 1 H), 2.59 - 2.41 (m, 3 H), 2.07 (sxtd, *J* = 6.7, 13.6 Hz, 1 H), 0.94 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR

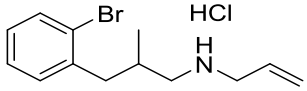
(100MHz, CHLOROFORM-d) δ = 152.21, 141.37, 137.01, 116.04, 113.67, 97.23, 55.10, 52.66, 33.29, 31.31, 18.22. HRMS calcd. for $C_{11}H_{17}BrNS^+$ 274.0230 and 276.0239 [M+H]$^+$, found 274.0279 and 276.0256. $[\alpha]_D^{20}$ = +5.200 (c = 1.0, MeOH).

N-(3-(3-bromofuran-2-yl)-2-methylpropyl)prop-2-en-1-amine (**4j**) obtained from enzymes



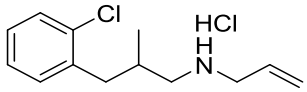
One-pot biocatalytic cascade reduction and reductive amination of 1 mmol **2j** catalyzed by purified OYE1 and IR43 gave 235 mg **4j** as a light yellow oil with 91% isolated yield. ^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.13 (d, *J* = 5.4 Hz, 1 H), 6.94 - 6.86 (m, 1 H), 5.91 (tdd, *J* = 6.0, 10.5, 16.9 Hz, 1 H), 5.22 - 5.04 (m, 2 H), 3.25 (d, *J* = 6.1 Hz, 2 H), 2.91 (dd, *J* = 5.9, 14.7 Hz, 1 H), 2.68 - 2.56 (m, 2 H), 2.54 - 2.46 (m, 1 H), 2.09 - 1.92 (m, 1 H), 0.97 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 138.01, 136.91, 129.82, 123.41, 115.92, 109.52, 54.97, 52.57, 35.36, 34.24, 18.02. HRMS calcd. for $C_{11}H_{17}BrNO^+$ 258.0488 and 260.0468 [M+H]$^+$, found 258.0495 and 260.0508. $[\alpha]_D^{20}$ = -0.710 (c = 1.0, MeOH).

N-(3-(2-bromophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4a**)



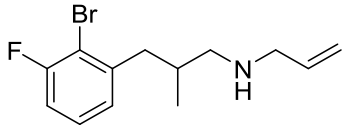
Reduction of 0.5 mmol **2a** catalyzed by purified OYE1 and subsequent chemical reductive amination gave 116 mg Rac-**4a**-HCl as a white soild with 76% isolated yield. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.57 (d, *J* = 7.8 Hz, 1 H), 7.36 - 7.27 (m, 2 H), 7.15 (ddd, *J* = 3.7, 5.1, 8.1 Hz, 1 H), 5.96 (tdd, *J* = 6.9, 10.1, 17.1 Hz, 1 H), 5.58 - 5.43 (m, 2 H), 3.67 (d, *J* = 6.8 Hz, 2 H), 3.07 - 2.86 (m, 3 H), 2.68 (dd, *J* = 8.6, 13.4 Hz, 1 H), 2.42 - 2.24 (m, 1 H), 1.04 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 138.58, 132.76, 131.50, 128.28, 127.71, 127.46, 124.28, 123.31, 52.13, 50.07, 40.12, 31.41, 16.06. HRMS calcd. for $C_{13}H_{19}BrN^+$ 268.0695 and 270.0728 [M+H]$^+$, found 268.0716 and 270.0692.

N-(3-(2-chlorophenyl)-2-methylpropyl)prop-2-en-1-amine ((Rac-**4b**)



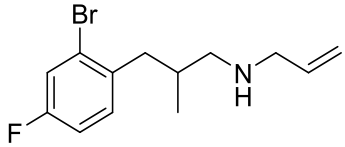
Reduction of 2 mmol **2b** catalyzed by purified OYE1 and subsequent chemical reductive amination gave 239 mg Rac-**4b**-HCl as a white soild with 46% isolated yield. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.39 (d, J = 7.3 Hz, 1 H), 7.35 - 7.20 (m, 3 H), 5.94 (tdd, J = 6.9, 10.2, 17.1 Hz, 1 H), 5.61 - 5.41 (m, 2 H), 3.72 - 3.56 (m, 2 H), 3.09 - 2.81 (m, 3 H), 2.67 (dd, J = 8.4, 13.6 Hz, 1 H), 2.38 - 2.23 (m, 1 H), 1.03 (d, J = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ=136.58, 133.82, 131.45, 129.36, 128.05, 127.66, 126.83, 123.27, 52.22, 50.05, 37.64, 31.37, 16.03. HRMS calcd. for $C_{13}H_{19}ClN^+$ 224.1200[M+H]$^+$, found 224.1196.

N-(3-(2-bromo-3-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4c**)



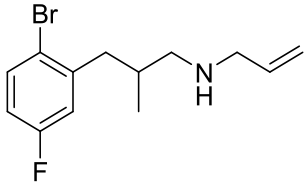
Reduction of 1 mmol **2c** catalyzed by purified OYE1 and subsequent chemical reductive amination gave 205 mg Rac-**4c** as a light yellow oil with 72% isolated yield.^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.23 - 7.14 (m, 1 H), 7.04 - 6.91 (m, 2 H), 5.99 - 5.81 (m, 1 H), 5.23 - 5.04 (m, 2 H), 3.25 (d, *J* = 5.9 Hz, 2 H), 2.94 (dd, *J* = 5.9, 13.4 Hz, 1 H), 2.68 - 2.45 (m, 3 H), 2.12 - 1.98 (m, 1 H), 0.92 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 159.26 (d, *J* = 245 Hz), 143.06, 136.95, 127.78 (d, *J* = 8 Hz), 126.48 (d, *J* = 3 Hz), 115.85, 113.82 (d, *J* = 23 Hz), 111.71 (d, *J* = 19 Hz), 55.35, 52.57, 41.09, 33.88, 17.87. HRMS calcd. for $C_{13}H_{18}BrFN^+$ 286.0601 and 288.0581 [M+H]$^+$, found 286.0608 and 288.0596.

N-(3-(2-bromo-4-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4d**)



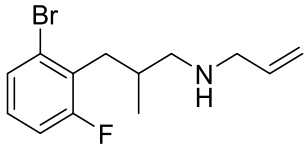
Reduction of 1 mmol **2d** catalyzed by purified OYE1 and subsequent chemical reductive amination gave 133 mg Rac-**4d** as a light yellow oil with 47% isolated yield. ^{1}H NMR (400MHz ,CHLOROFORM-d) δ = 7.28 (dd, *J* = 2.0, 8.1 Hz, 1 H), 7.19 - 7.11 (m, 1 H), 6.99 - 6.90 (m, 1 H), 5.97 - 5.84 (m, 1 H), 5.23 - 5.13 (m, 1 H), 5.08 (d, *J* = 10.0 Hz, 1 H), 3.25 (d, *J* = 5.9 Hz, 2 H), 2.86 (dd, *J* = 6.0, 13.6 Hz, 1 H), 2.59 (dd, *J* = 5.7, 11.6 Hz, 1 H), 2.54 - 2.42 (m, 2 H), 2.06 - 1.93 (m, 1 H), 0.91 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 160.78 (d, *J* = 247 Hz), 136.88, 136.24 (d, *J* = 3 Hz), 131.92 (d, *J* = 9 Hz), 124.49 (d, *J* = 10 Hz), 119.88 (d, *J* = 23 Hz), 115.91, 114.20 (d, *J* = 245 Hz), 55.25, 52.57, 40.57, 33.95, 17.81. HRMS calcd. for $C_{13}H_{18}BrFN^+$ 286.0601 and 288.0581 [M+H]$^+$, found 286.0614 and 288.0596.

N-(3-(2-bromo-5-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4e**)



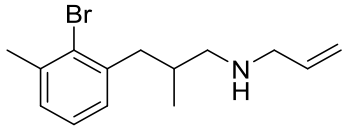
Reduction of 1 mmol **2e** catalyzed by purified OYE1 and subsequent chemical reductive amination gave 150 mg Rac-**4e** as a light yellow oil with 52% isolated yield. ^{1}H NMR (400MHz ,CHLOROFORM-d) δ = 7.47 (dd, *J* = 5.4, 8.8 Hz, 1 H), 6.93 (dd, *J* = 3.1, 9.4 Hz, 1 H), 6.79 (dt, *J* = 3.2, 8.3 Hz, 1 H), 5.97 - 5.84 (m, 1 H), 5.21 - 5.13 (m, 1 H), 5.09 (dd, *J* = 1.1, 10.1 Hz, 1 H), 3.25 (d, *J* = 5.9 Hz, 2 H), 2.88 (dd, *J* = 6.1, 13.4 Hz, 1 H), 2.63 - 2.56 (m, 1 H), 2.55 - 2.42 (m, 2 H), 2.11 - 1.95 (m, 1 H), 0.93 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 161.74 (d, *J* = 245 Hz), 142.64 (d, *J* = 7 Hz), 136.92, 133.86 (d, *J* = 8 Hz), 118.88 (d, *J* = 3 Hz), 118.11 (d, *J* = 22 Hz), 115.89, 114.73 (d, *J* = 22 Hz), 55.23, 52.57, 41.48, 33.83, 17.84. HRMS calcd. for $C_{13}H_{18}BrFN^{+}$ 286.0601 and 288.0581 $[M+H]^{+}$, found 286.0611 and 288.0588.

N-(3-(2-bromo-6-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4f**)



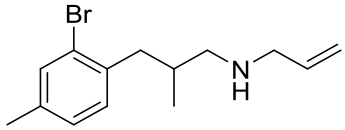
Reduction of 1.25 mmol **2f** catalyzed by purified OYE1 and subsequent chemical reductive amination gave 220 mg Rac-**4f** as a light yellow oil with 62% isolated yield. ^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.34 (d, *J* = 7.8 Hz, 1 H), 7.09 - 6.94 (m, 2 H), 5.98 - 5.84 (m, 1 H), 5.21 - 5.13 (m, 1 H), 5.08 (d, *J* = 10.3 Hz, 1 H), 3.26 (d, *J* = 5.9 Hz, 2 H), 2.86 (ddd, *J* = 2.1, 6.0, 13.2 Hz, 1 H), 2.68 - 2.52 (m, 3 H), 2.13 - 2.02 (m, 1 H), 0.95 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 161.39 (d, *J* = 247 Hz), 136.78, 128.78 (d, *J* = 19 Hz), 128.53 (d, *J* = 3 Hz), 128.14 (d, *J* = 9 Hz), 125.72 (d, *J* = 5 Hz), 115.99, 114.40 (d, *J* = 23 Hz), 55.37, 52.47, 34.16, 33.38, 17.82. HRMS calcd. for $C_{13}H_{18}BrFN^{+}$ 286.0601 and 288.0581 $[M+H]^{+}$, found 286.0611 and 288.0589.

N-(3-(2-bromo-3-methylphenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4g**)



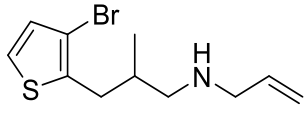
Reduction of 1.25 mmol **2g** catalyzed by purified OYE1 and subsequent chemical reductive amination gave 125 mg Rac-**4g** as a light yellow oil with 35% isolated yield. ^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.14 - 7.05 (m, 2 H), 7.03 - 6.97 (m, 1 H), 5.99 - 5.82 (m, 1 H), 5.16 (dd, *J* = 1.1, 17.2 Hz, 1 H), 5.08 (d, *J* = 10.0 Hz, 1 H), 3.25 (d, *J* = 5.9 Hz, 2 H), 2.91 (dd, *J* = 6.0, 13.3 Hz, 1 H), 2.66 - 2.58 (m, 1 H), 2.56 - 2.47 (m, 2 H), 2.41 (s, 3 H), 2.08 (sxtd, *J* = 6.7, 13.6 Hz, 1 H), 0.93 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 140.75, 138.63, 136.95, 128.86, 128.54, 127.56, 126.45, 115.85, 55.52, 52.57, 42.29, 33.62, 24.20, 18.02. HRMS calcd. for $C_{14}H_{21}BrN^{+}$ 282.0852 and 284.0832 $[M+H]^{+}$, found 282.0811 and 284.0845.

N-(3-(2-bromo-4-methylphenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4h**)



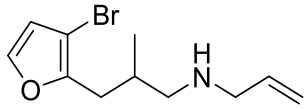
Reduction of 1.5 mmol **2h** catalyzed by purified OYE1 and subsequent chemical reductive amination gave 140 mg Rac-**4h** as a light yellow oil with 33% isolated yield. ^{1}H NMR (400MHz ,CHLOROFORM-d) δ = 7.40 (s, 1 H), 7.13 - 7.02 (m, 2 H), 6.04 - 5.87 (m, 1 H), 5.24 - 5.16 (m, 1 H), 5.12 (d, *J* = 9.3 Hz, 1 H), 3.29 (d, *J* = 6.1 Hz, 2 H), 2.88 (dd, *J* = 5.9, 13.4 Hz, 1 H), 2.65 (dd, *J* = 5.9, 11.7 Hz, 1 H), 2.58 - 2.45 (m, 2 H), 2.33 (s, 3 H), 2.13 - 1.99 (m, 1 H), 0.96 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 137.52, 137.16, 136.87, 133.26, 131.11, 127.60, 124.60, 115.94, 55.40, 52.55, 40.99, 33.91, 20.59, 17.92. HRMS calcd. for $C_{14}H_{21}BrN^{+}$ 282.0852 and 284.0832 $[M+H]^{+}$, found 282.0866 and 284.0847.

N-(3-(3-bromothiophen-2-yl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4i**)



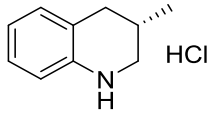
Reduction of 1.5 mmol **2i** catalyzed by purified OYE1 and subsequent chemical reductive amination gave 220 mg Rac-**4i** as a light yellow oil with 54% isolated yield. ^{1}H NMR (400MHz ,CHLOROFORM-d) δ = 7.13 (d, *J* = 5.4 Hz, 1 H), 6.90 (d, *J* = 5.4 Hz, 1 H), 5.91 (tdd, *J* = 5.9, 10.7, 16.9 Hz, 1 H), 5.17 (d, *J* = 17.1 Hz, 1 H), 5.08 (d, *J* = 10.0 Hz, 1 H), 3.25 (d, *J* = 5.9 Hz, 2 H), 2.91 (dd, *J* = 6.0, 14.5 Hz, 1 H), 2.68 - 2.55 (m, 2 H), 2.54 - 2.45 (m, 1 H), 2.07 - 1.95 (m, 1 H), 0.97 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 137.99, 136.86, 129.81, 123.41, 115.95, 109.52, 54.94, 52.55, 35.34, 34.24, 18.01. HRMS calcd. for $C_{11}H_{17}BrNS^{+}$ 274.0230 and 276.0239 $[M+H]^{+}$, found 274.0272 and 276.0259.

N-(3-(3-bromofuran-2-yl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4j**)



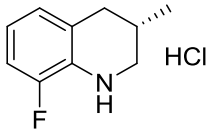
Reduction of 1.5 mmol **2j** catalyzed by purified OYE1 and subsequent chemical reductive amination gave 167 mg Rac-**4j** as a light yellow oil with 43% isolated yield. ^{1}H NMR (400MHz, CHLOROFORM-d) δ = 7.27 (d, *J* = 1.7 Hz, 1 H), 6.35 (d, *J* = 1.2 Hz, 1 H), 5.97 - 5.82 (m, 1 H), 5.17 (d, *J* = 17.1 Hz, 1 H), 5.08 (d, *J* = 10.3 Hz, 1 H), 3.24 (d, *J* = 5.6 Hz, 2 H), 2.73 (dd, *J* = 6.1, 14.7 Hz, 1 H), 2.59 - 2.42 (m, 3 H), 2.07 (sxtd, *J* = 6.7, 13.5 Hz, 1 H), 0.94 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, CHLOROFORM-d) δ = 152.08, 141.24, 136.91, 115.87, 113.54, 97.09, 54.98, 52.54, 33.17, 31.19, 18.08. HRMS calcd. for $C_{11}H_{17}BrNO^+$ 258.0488 and 260.0468 $[M+H]^+$, found 258.0495 and 260.0513.

(*S*)-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6a**)



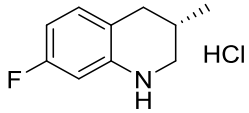
Buchwald-Hartwig amination and deallylation of 0.60 mmol (*S*)-**4a** gave 63 mg (*S*)-**6a**-HCl as a white soild with 57% isolated yield. Buchwald-Hartwig amination and deallylation from 1.0 mmol (*S*)-**4b** gave 105 mg (*S*)-**6a**-HCl as a white soild with 56% isolated yield and >99% *ee* values. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.45 - 7.27 (m, 4 H), 3.61 - 3.52 (m, 1 H), 3.14 - 2.97 (m, 2 H), 2.61 (dd, *J* = 10.6, 17.0 Hz, 1 H), 2.39 - 2.20 (m, 1 H), 1.19 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 131.28, 130.71, 129.42, 129.09, 127.44, 122.52, 47.76, 32.98, 25.91, 17.05. HRMS calcd. for $C_{10}H_{14}N^+$ 148.1121 $[M+H]^+$, found 148.1122. $[\alpha]_D^{20}$ = +60.836 (c = 0.5, MeOH).

(*S*)-8-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6c**)



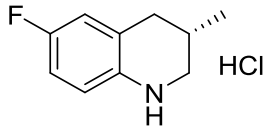
Buchwald-Hartwig amination and deallylation of 1.18 mmol (*S*)-**4c** gave 120 mg (*S*)-**6c**-HCl as a white soild with 51% isolated yield and 98% *ee* values. ^{1}H NMR (400MHz, METHANOL-d_4) d = 7.42 - 7.28 (m, 1 H), 7.21 - 7.06 (m, 2 H), 3.55 (d, *J* = 11.5 Hz, 1 H), 3.09 - 2.92 (m, 2 H), 2.55 (dd, *J* = 10.8, 17.1 Hz, 1 H), 2.19 (d, *J* = 2.7 Hz, 1 H), 1.12 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 155.60 (d, *J* = 247 Hz), 134.06, 129.85 (d, *J* = 8 Hz), 125.97 (d, *J* = 3 Hz), 117.95 (d, *J* = 14 Hz), 113.53 (d, *J* = 18 Hz), 47.52, 32.68, 25.59, 16.86. HRMS calcd. for $C_{10}H_{13}FN^+$ 166.1025 $[M+H]^+$, found 166.1025. $[\alpha]_D^{20}$ = +51.337 (c = 1.0, MeOH).

(*S*)-7-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6d**)



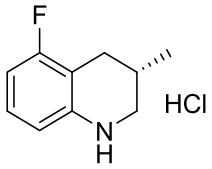
Buchwald-Hartwig amination and deallylation of 0.54 mmol (*S*)-**4d** gave 46 mg (*S*)-**6d**-HCl as a white soild with 42% isolated yield and >99% *ee* values. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.43 (dd, *J* = 6.1, 8.6 Hz, 1 H), 7.24 (dt, *J* = 2.6, 8.5 Hz, 1 H), 7.17 (dd, *J* = 2.4, 8.6 Hz, 1 H), 3.65 - 3.57 (m, 1 H), 3.13 (t, *J* = 11.6 Hz, 1 H), 3.05 (dd, *J* = 4.9, 16.9 Hz, 1 H), 2.60 (dd, *J* = 10.6, 16.7 Hz, 1 H), 2.38 - 2.23 (m, 1 H), 1.22 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 161.04 (d, *J* = 245 Hz), 132.32 (m), 130.43 (m), 127.26 (d, *J* = 4 Hz), 116.16 (d, *J* = 21 Hz), 109.66 (d, *J* = 25 Hz), 47.85, 32.43, 25.85, 16.96. HRMS calcd. for $C_{10}H_{13}FN^+$ 166.1025 $[M+H]^+$, found 166.1024. $[\alpha]_D^{20}$ = +86.955 (c = 1.0, MeOH).

(*S*)-6-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6e**)



Buchwald-Hartwig amination and deallylation of 0.45 mmol (*S*)-**4e** gave 63 mg (*S*)-**6e**-HCl as a white soild with 36% isolated yield and 98% *ee* values. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.42 - 7.30 (m, 1 H), 7.14 (br. s., 2 H), 3.58 (d, *J* = 12.0 Hz, 1 H), 3.15 - 2.98 (m, 2 H), 2.70 - 2.54 (m, 1 H), 2.28 (br. s., 1 H), 1.25 - 1.12 (m, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 162.30 (d, *J* = 247 Hz), 134.23 (d, *J* = 8 Hz), 125.49, 124.72 (d, *J* = 9 Hz), 116.82 (d, *J* = 23 Hz), 114.59 (d, *J* = 24 Hz), 47.80, 33.08, 25.57, 16.86. HRMS calcd. for $C_{10}H_{13}FN^+$ 166.1025 $[M+H]^+$, found 166.1025. $[\alpha]_D^{20}$ = +51.476 (c = 0.25, MeOH).

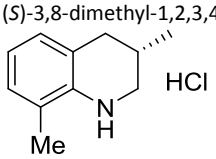
(*S*)-5-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6f**)



Buchwald-Hartwig amination and deallylation of 0.26 mmol (*S*)-**4f** gave 22 mg (*S*)-**6f**-HCl as a white soild with 42% isolated yield and 97% *ee* values. ^{1}H NMR (400MHz, METHANOL-d_4) d = 7.36 - 7.23 (m, 1 H), 7.16 - 7.02 (m, 2 H), 3.47 (d, *J* = 11.5 Hz, 1 H), 3.04 - 2.88 (m, 2 H), 2.38 - 2.26 (m, 1 H), 2.20 (d, *J* = 3.9 Hz, 1 H), 1.09 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 160.84 (d, *J* = 245 Hz), 131.12 (d, *J* = 7 Hz), 128.28 (d, *J* = 9 Hz), 119.79 (d, *J* = 22 Hz), 118.50 (d, *J* = 4

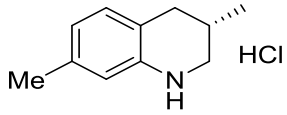
Hz), 115.22 (d, *J* = 21 Hz), 47.89, 26.36 (d, *J* = 3 Hz), 25.05, 17.09. HRMS calcd. for $C_{10}H_{13}FN^+$ 166.1025 $[M+H]^+$, found 166.1024. $[\alpha]_D^{20}$ = +74.156 (c = 0.5, MeOH).

(*S*)-3,8-dimethyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6g)**



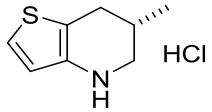
Buchwald-Hartwig amination and deallylation of 0.42 mmol (*S*)-**4g** gave 17 mg (*S*)-**6g-**HCl as a white soild with 20% isolated yield and 98% *ee* values. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.32 - 7.26 (m, 1 H), 7.24 - 7.13 (m, 2 H), 3.60 (d, *J* = 12.0 Hz, 1 H), 3.09 (t, *J* = 11.9 Hz, 1 H), 2.99 (dd, *J* = 3.7, 16.9 Hz, 1 H), 2.60 (dd, *J* = 10.9, 16.7 Hz, 1 H), 2.42 (s, 3 H), 2.22 (td, *J* = 3.7, 6.8 Hz, 1 H), 1.19 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 131.74, 131.40, 129.25, 128.70, 128.39, 128.02, 48.41, 33.60, 25.61, 16.96, 14.76. HRMS calcd. for $C_{11}H_{16}N^+$ 162.1277 $[M+H]^+$, found 162.1272. $[\alpha]_D^{20}$ = +64.856 (c = 0.5, MeOH).

(*S*)-3,7-dimethyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6h)**



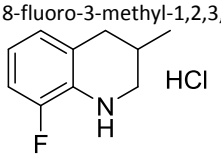
Buchwald-Hartwig amination and deallylation of 0.32 mmol (*S*)-**4h** gave 30 mg (*S*)-**6h-**HCl as a white soild with 47% isolated yield and >99% *ee* values. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.27 - 7.19 (m, 2 H), 7.12 (s, 1 H), 3.60 - 3.48 (m, 1 H), 3.05 (t, *J* = 11.7 Hz, 1 H), 2.98 (dd, *J* = 4.6, 16.9 Hz, 1 H), 2.54 (dd, *J* = 10.8, 16.9 Hz, 1 H), 2.36 (s, 3 H), 2.31 - 2.19 (m, 1 H), 1.17 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 137.90, 130.47, 129.93, 129.14, 128.05, 122.64, 47.77, 32.64, 26.00, 19.48, 17.07. HRMS calcd. for $C_{11}H_{16}N^+$ 162.1277 $[M+H]^+$, found 162.1276. $[\alpha]_D^{20}$ = +64.856 (c = 1.0, MeOH).

(*B*)-6-methyl-4,5,6,7-tetrahydrothieno[3,2-b]pyridine hydrochloride ((*B*)-**6i**)



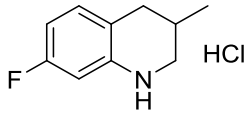
Buchwald-Hartwig amination and deallylation of 1.68 mmol (*B*)-**4i** gave 160 mg (*B*)-**6i-**HCl as a white soild with 50% isolated yield and 88% *ee* values. ^{1}H NMR (400MHz, METHANOL-d_4) d = 7.50 - 7.40 (m, 1 H), 7.05 - 6.97 (m, 1 H), 3.62 - 3.51 (m, 1 H), 3.19 - 2.97 (m, 2 H), 2.63 - 2.49 (m, 1 H), 2.37 (br. s., 1 H), 1.21 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 133.00, 125.70, 124.92, 120.50, 48.17, 29.08, 26.81, 16.65. HRMS calcd. for $C_8H_{13}NS^+$ 154.0685 $[M+H]^+$, found 154.0703. $[\alpha]_D^{20}$ = +53.537 (c = 1.0, MeOH).

8-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6c**)



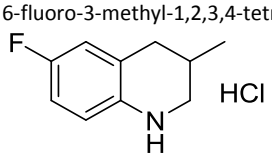
Buchwald-Hartwig amination and deallylation of 0.36 mmol Rac-**4c** gave 30 mg Rac-**6c-**HCl as a white soild with 41% isolated yield. ^{1}H NMR (400MHz, METHANOL-d_4) d = 7.48 - 7.35 (m, 1 H), 7.27 - 7.13 (m, 2 H), 3.62 (d, *J* = 12.2 Hz, 1 H), 3.15 - 3.00 (m, 2 H), 2.62 (dd, *J* = 10.6, 17.0 Hz, 1 H), 2.35 - 2.15 (m, 1 H), 1.19 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 155.58 (d, *J* = 247 Hz), 134.01, 129.75 (d, *J* = 8 Hz), 125.96 (d, *J* = 3 Hz), 118.04 (d, *J* = 13 Hz), 113.52 (d, *J* = 18 Hz), 47.51, 32.67, 25.58, 16.89. HRMS calcd. for $C_{10}H_{13}FN^+$ 166.1025 $[M+H]^+$, found 166.1034.

7-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6d**)



Buchwald-Hartwig amination and deallylation of 0.48 mmol Rac-**4d** gave 43 mg Rac-**6d-**HCl as a white soild with 44% isolated yield. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.38 (dd, *J* = 6.1, 8.3 Hz, 1 H), 7.18 (dt, *J* = 2.4, 8.4 Hz, 1 H), 7.12 (dd, *J* = 2.4, 8.8 Hz, 1 H), 3.57 (dd, *J* = 1.5, 12.0 Hz, 1 H), 3.08 (t, *J* = 11.6 Hz, 1 H), 3.01 (dd, *J* = 4.6, 16.9 Hz, 1 H), 2.56 (dd, *J* = 10.9, 16.7 Hz, 1 H), 2.35 - 2.19 (m, 1 H), 1.18 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 161.06 (d, *J* = 245 Hz), 132.32 (d, *J* = 8 Hz), 130.72 (d, *J* = 9 Hz), 127.08 (d, *J* = 3 Hz), 115.91 (d, *J* = 22 Hz), 109.50 (d, *J* = 25 Hz), 48.07, 32.48, 25.85, 17.00. HRMS calcd. for $C_{10}H_{13}FN^+$ 166.1025 $[M+H]^+$, found 166.1023.

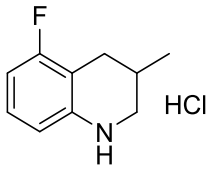
6-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6e**)



Buchwald-Hartwig amination and deallylation of 0.64 mmol Rac-**4e** gave 30 mg Rac-**6e-**HCl as a white soild with 23% isolated yield. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.35 (dd, *J* = 4.9, 9.5 Hz, 1 H), 7.16 - 7.05 (m, 2 H), 3.56 (dd, *J* = 1.3, 12.1 Hz, 1 H), 3.12 - 2.96 (m, 2 H), 2.59 (dd, *J* = 10.8, 17.1 Hz, 1 H), 2.35 - 2.17 (m, 1 H), 1.15 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR

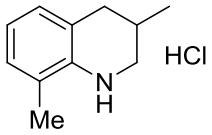
(100MHz, METHANOL-d_4) δ = 162.30 (d, *J* = 247 Hz), 134.23 (d, *J* = 8 Hz), 125.49, 124.72 (d, *J* = 9 Hz), 116.82 (d, *J* = 23 Hz), 114.59 (d, *J* = 24 Hz), 47.80, 33.08, 25.57, 16.86. HRMS calcd. for $C_{10}H_{13}FN^+$ 166.1025 $[M+H]^+$, found 166.1039.

5-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6f**)



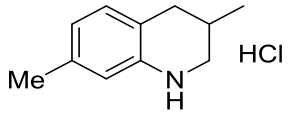
Buchwald-Hartwig amination and deallylation of 0.46 mmol Rac-**4f** gave 30 mg Rac-**6f-**HCl as a white soild with 32% isolated yield. ^{1}H NMR (400MHz, METHANOL-d_4) d = 7.39 - 7.29 (m, 1 H), 7.19 - 7.08 (m, 2 H), 3.51 (d, *J* = 11.0 Hz, 1 H), 3.08 - 2.95 (m, 2 H), 2.37 (dd, *J* = 10.6, 17.2 Hz, 1 H), 2.29 - 2.14 (m, 1 H), 1.15 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 160.86 (d, *J* = 245 Hz), 131.26 (d, *J* = 7 Hz), 128.38 (d, *J* = 10 Hz), 119.65 (d, *J* = 22 Hz), 118.32 (d, *J* = 3 Hz), 115.12 (d, *J* = 21 Hz), 47.85, 26.36 (d, *J* = 3 Hz), 25.08, 17.05. HRMS calcd. for $C_{10}H_{13}FN^+$ 166.1025 $[M+H]^+$, found 166.1032.

3,8-dimethyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6g)**



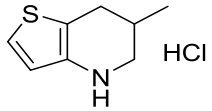
Buchwald-Hartwig amination and deallylation of 0.70 mmol Rac-**4g** gave 19 mg Rac-**6g-**HCl as a white soild with 14% isolated yield. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.32 - 7.25 (m, 1 H), 7.23 - 7.18 (m, 1 H), 7.16 (d, *J* = 7.6 Hz, 1 H), 3.64 - 3.55 (m, 1 H), 3.08 (t, *J* = 11.9 Hz, 1 H), 2.98 (dd, *J* = 2.9, 16.9 Hz, 1 H), 2.59 (dd, *J* = 10.9, 16.7 Hz, 1 H), 2.43 (s, 3 H), 2.32 - 2.13 (m, 1 H), 1.18 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 131.85, 131.46, 129.25, 128.71, 128.37, 127.97, 48.29, 33.60, 25.57, 16.99, 15.87. HRMS calcd. for $C_{11}H_{16}N^+$ 162.1277 $[M+H]^+$, found 162.1280.

3,7-dimethyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6h)**



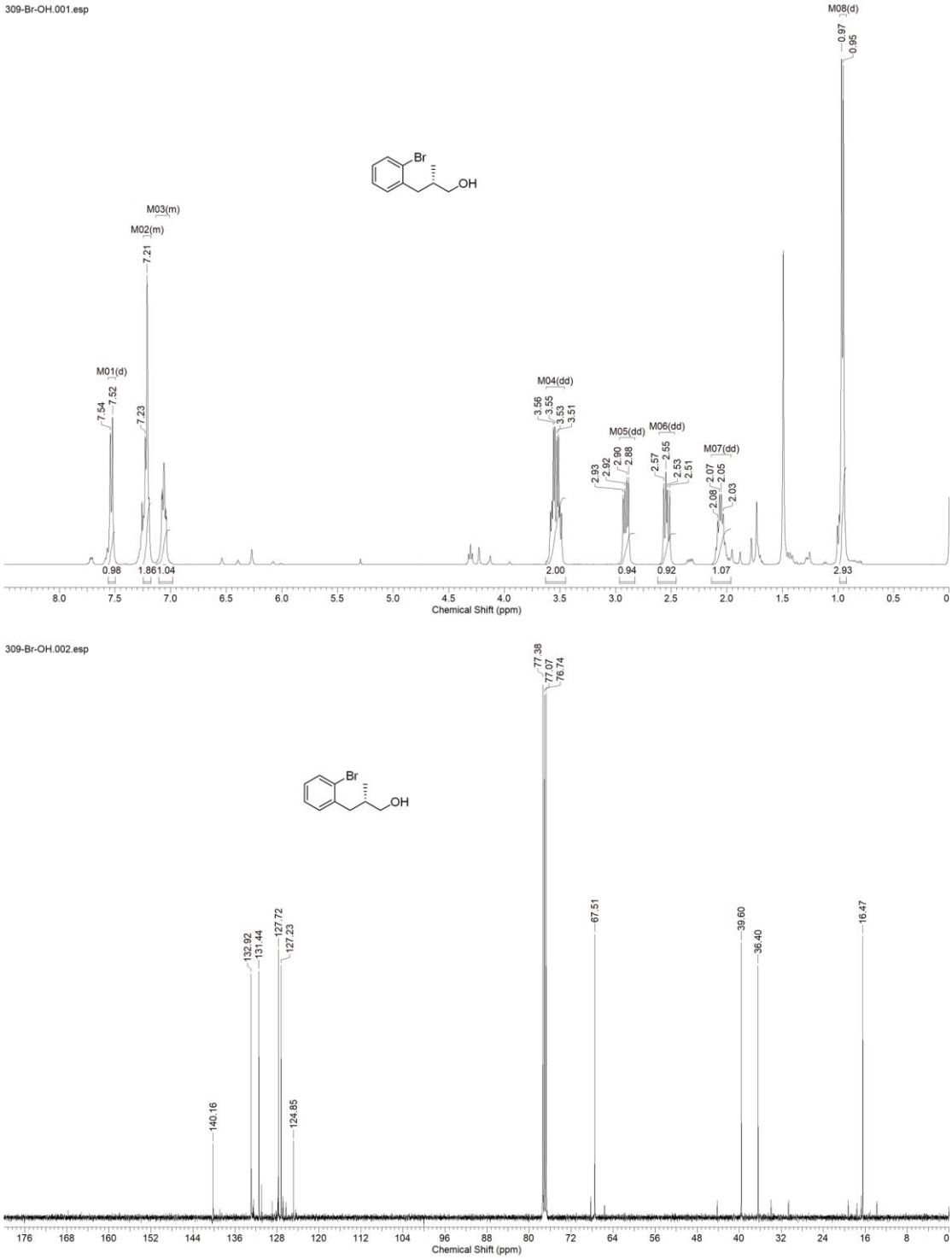
Buchwald-Hartwig amination and deallylation of 0.49 mmol Rac-**4h** gave 14 mg Rac-**6c-**HCl as a white soild with 18% isolated yield. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.27 - 7.19 (m, 2 H), 7.11 (s, 1 H), 3.55 (d, *J* = 12.0 Hz, 1 H), 3.05 (t, *J* = 11.6 Hz, 1 H), 2.98 (dd, *J* = 4.6, 16.9 Hz, 1 H), 2.54 (dd, *J* = 10.8, 16.9 Hz, 1 H), 2.36 (s, 3 H), 2.31 - 2.18 (m, 1 H), 1.17 (d, *J* = 6.8 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 137.90, 130.47, 129.92, 129.51, 128.04, 122.63, 47.77, 32.64, 26.00, 19.48, 17.07. HRMS calcd. for $C_{11}H_{16}N^+$ 162.1277 $[M+H]^+$, found 162.1290.

6-methyl-4,5,6,7-tetrahydrothieno[3,2-b]pyridine hydrochloride (Rac-**6i)**

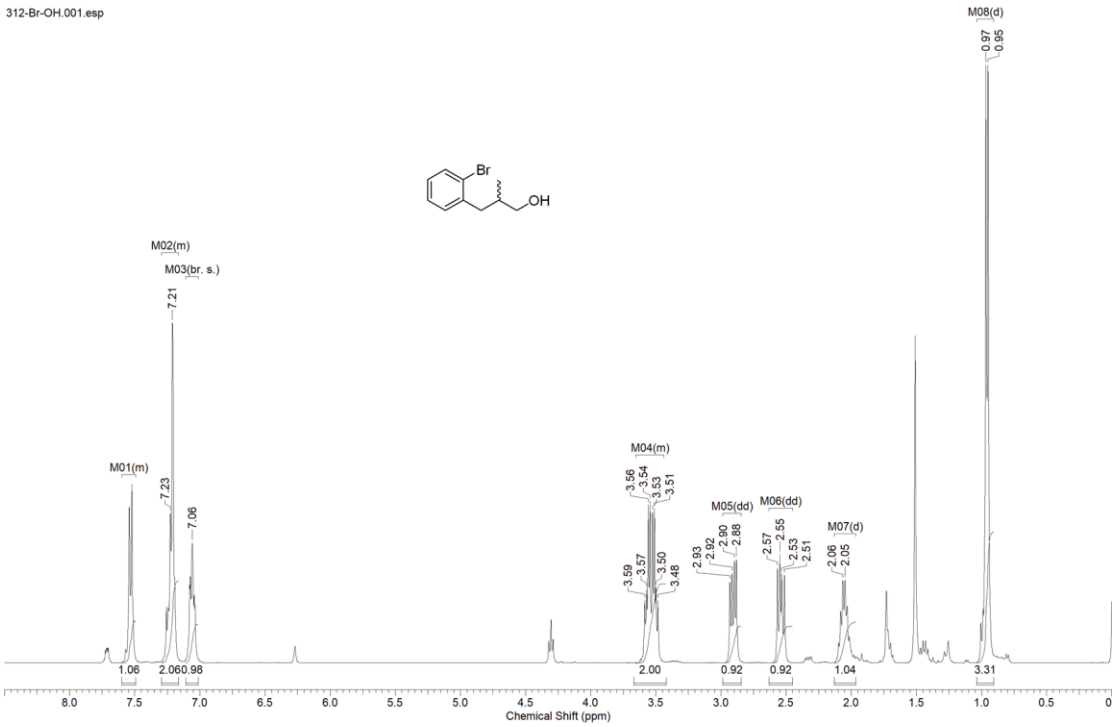


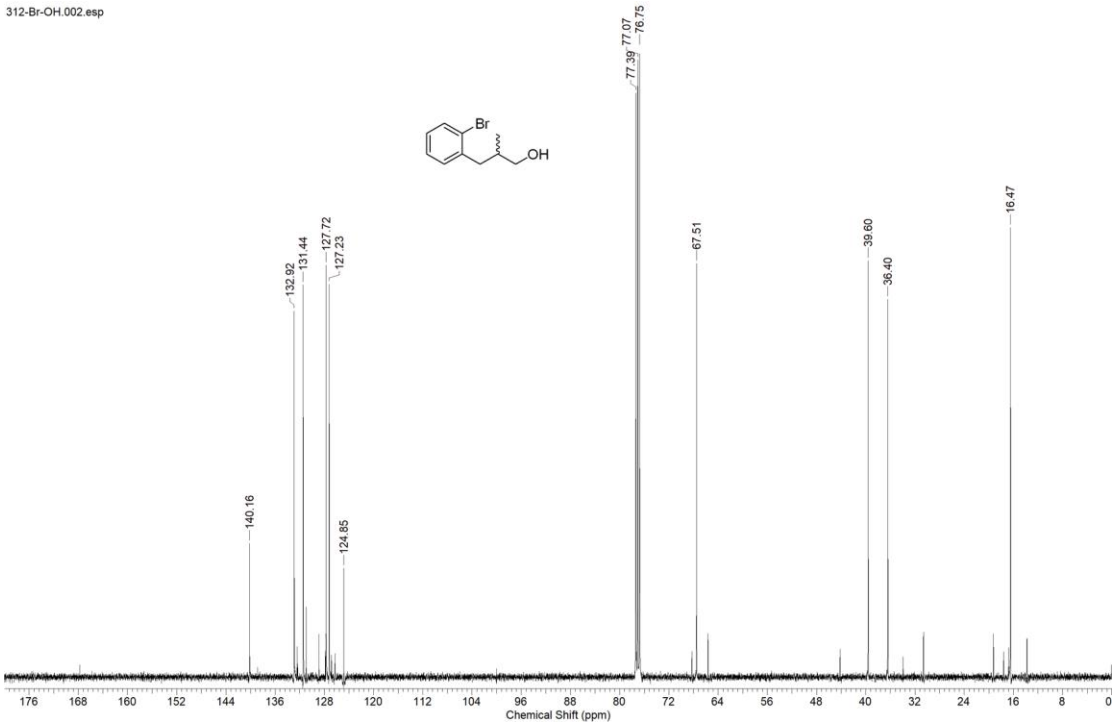
Buchwald-Hartwig amination and deallylation of 0.80 mmol Rac-**4i** gave 45 mg Rac-**6i-**HCl as a white soild with 37% isolated yield. ^{1}H NMR (400MHz, METHANOL-d_4) δ = 7.46 (d, *J* = 5.4 Hz, 1 H), 7.02 (d, *J* = 5.4 Hz, 1 H), 3.57 (dd, *J* = 2.2, 12.2 Hz, 1 H), 3.17 - 3.01 (m, 2 H), 2.56 (dd, *J* = 10.0, 16.6 Hz, 1 H), 2.44 - 2.28 (m, 1 H), 1.20 (d, *J* = 6.6 Hz, 3 H). ^{13}C NMR (100MHz, METHANOL-d_4) δ = 132.99, 125.71, 124.91, 120.50, 48.15, 29.07, 26.81, 16.64. HRMS calcd. for $C_8H_{13}NS^+$ 154.0685 $[M+H]^+$, found 154.0609.

S2.6 NMR spectra of products

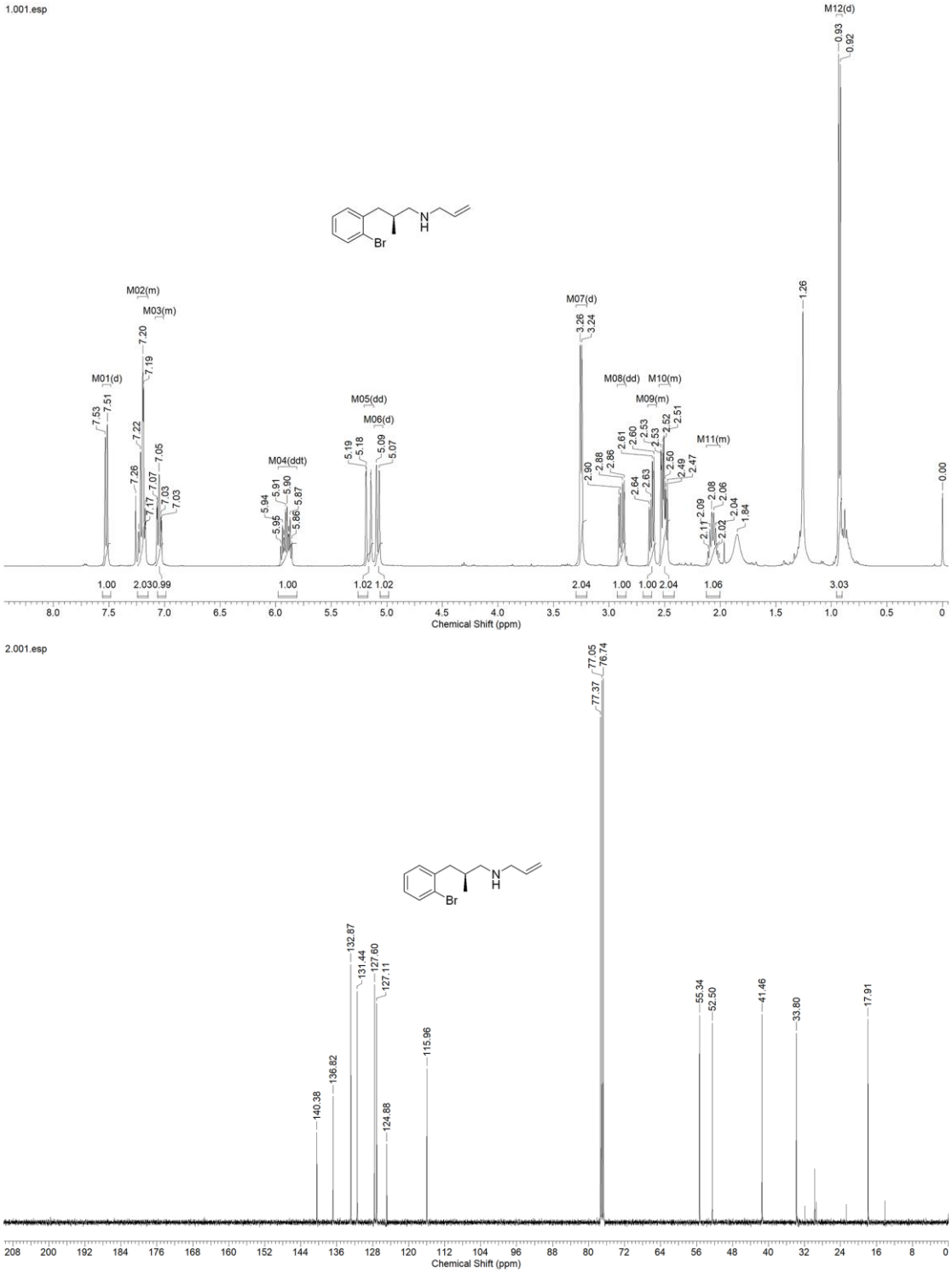


^{1}H-NMR spectra and ^{13}C-NMR spectra of (*S*)-3-(2-chlorophenyl)-2-methylpropan-1-ol((*S*)-**3a'**)



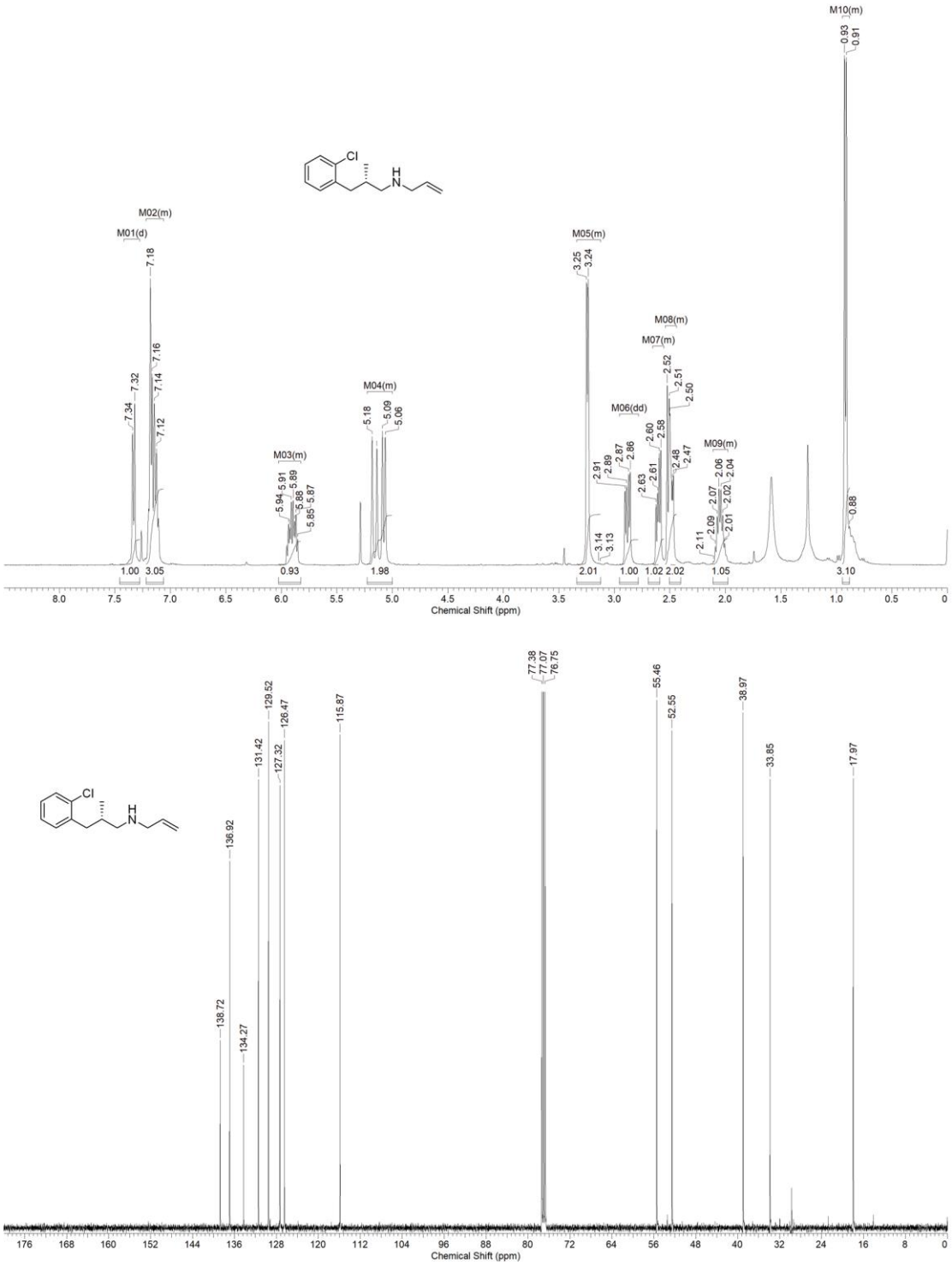


^{1}H-NMR spectra and ^{13}C-NMR spectra of 3-(2-chlorophenyl)-2-methylpropan-1-ol(Rac-**3a'**)



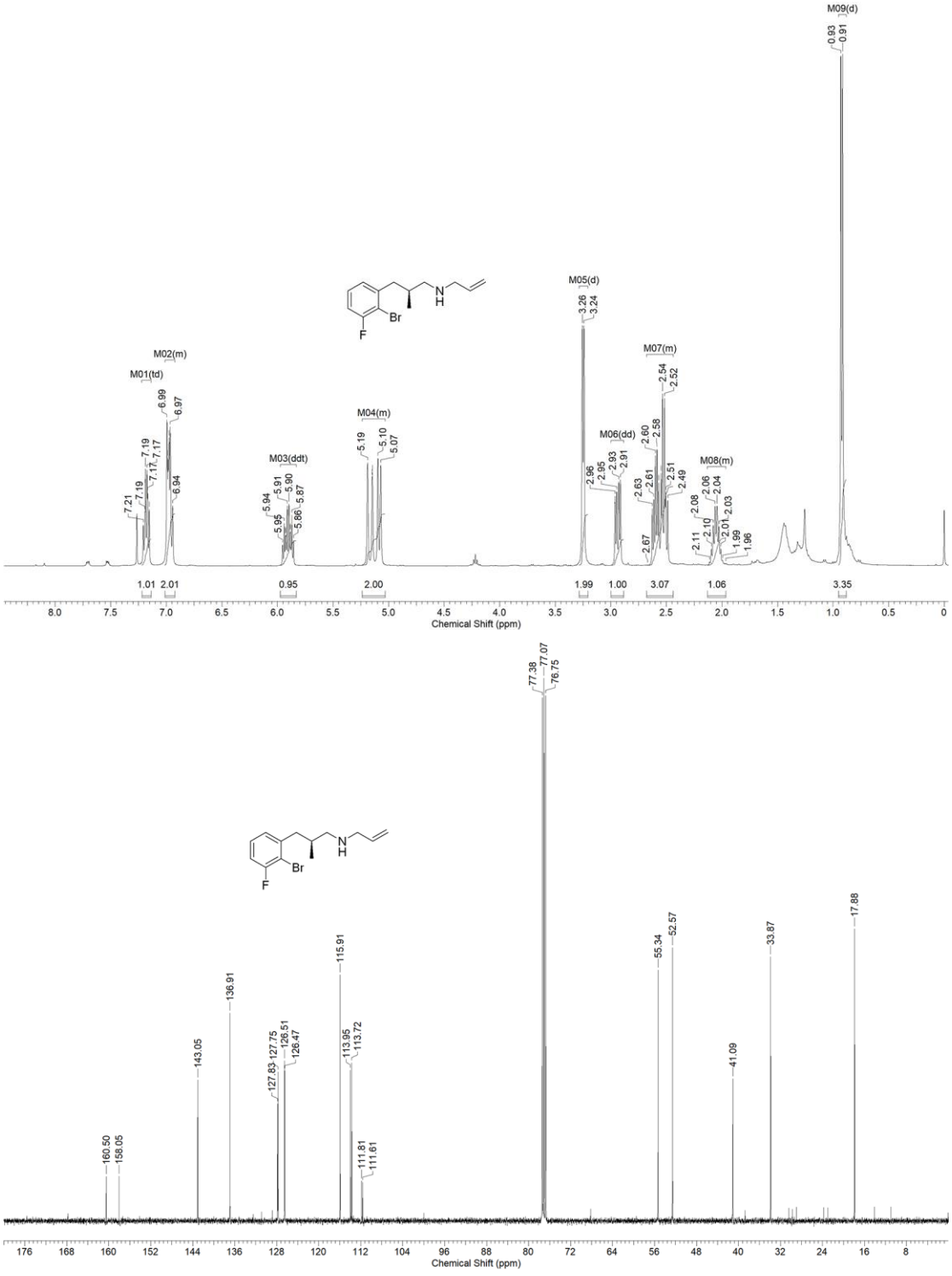
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-*N*-(3-(2-bromophenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4a**)



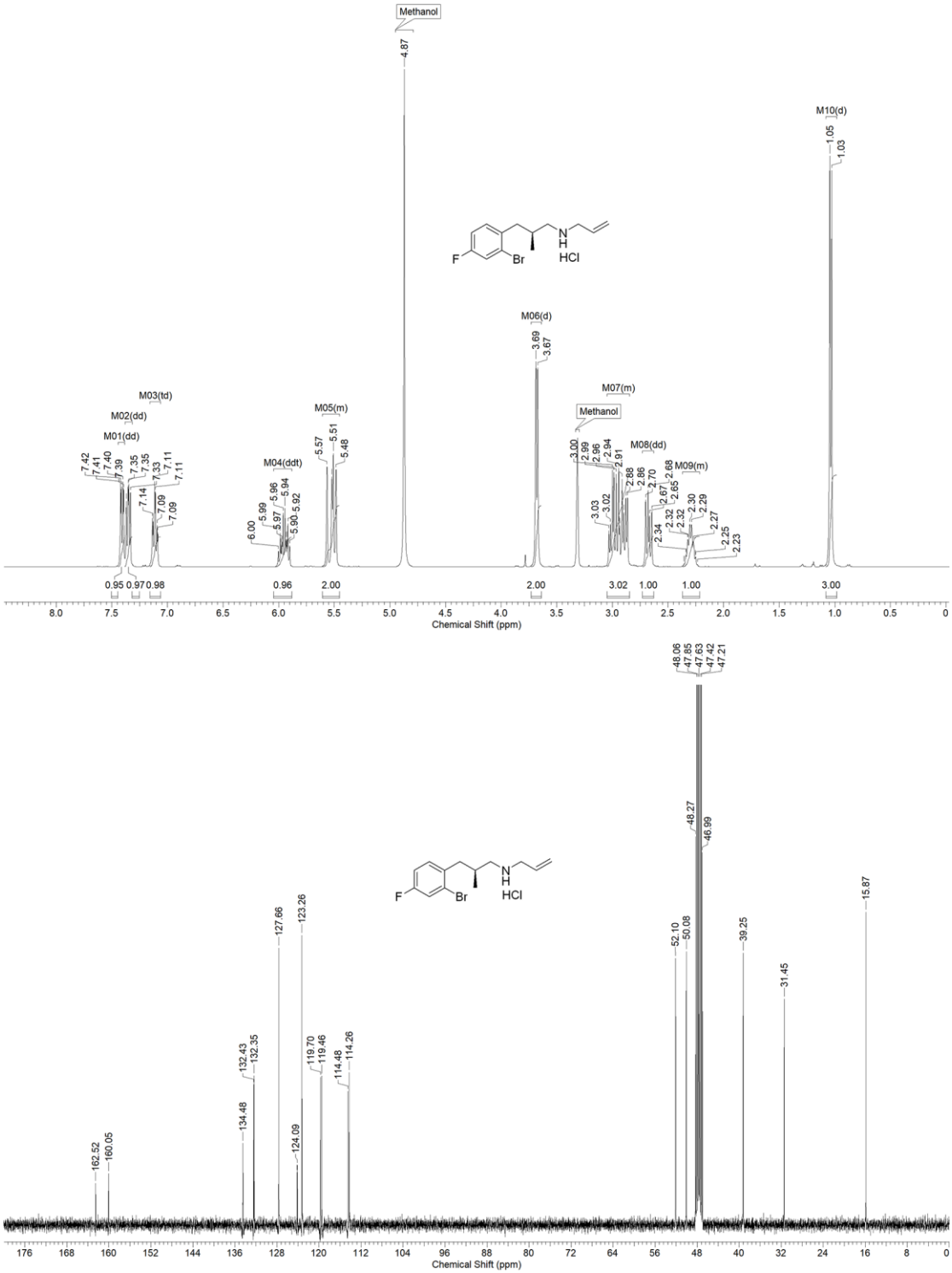
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-*N*-(3-(2-chlorophenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4b**)

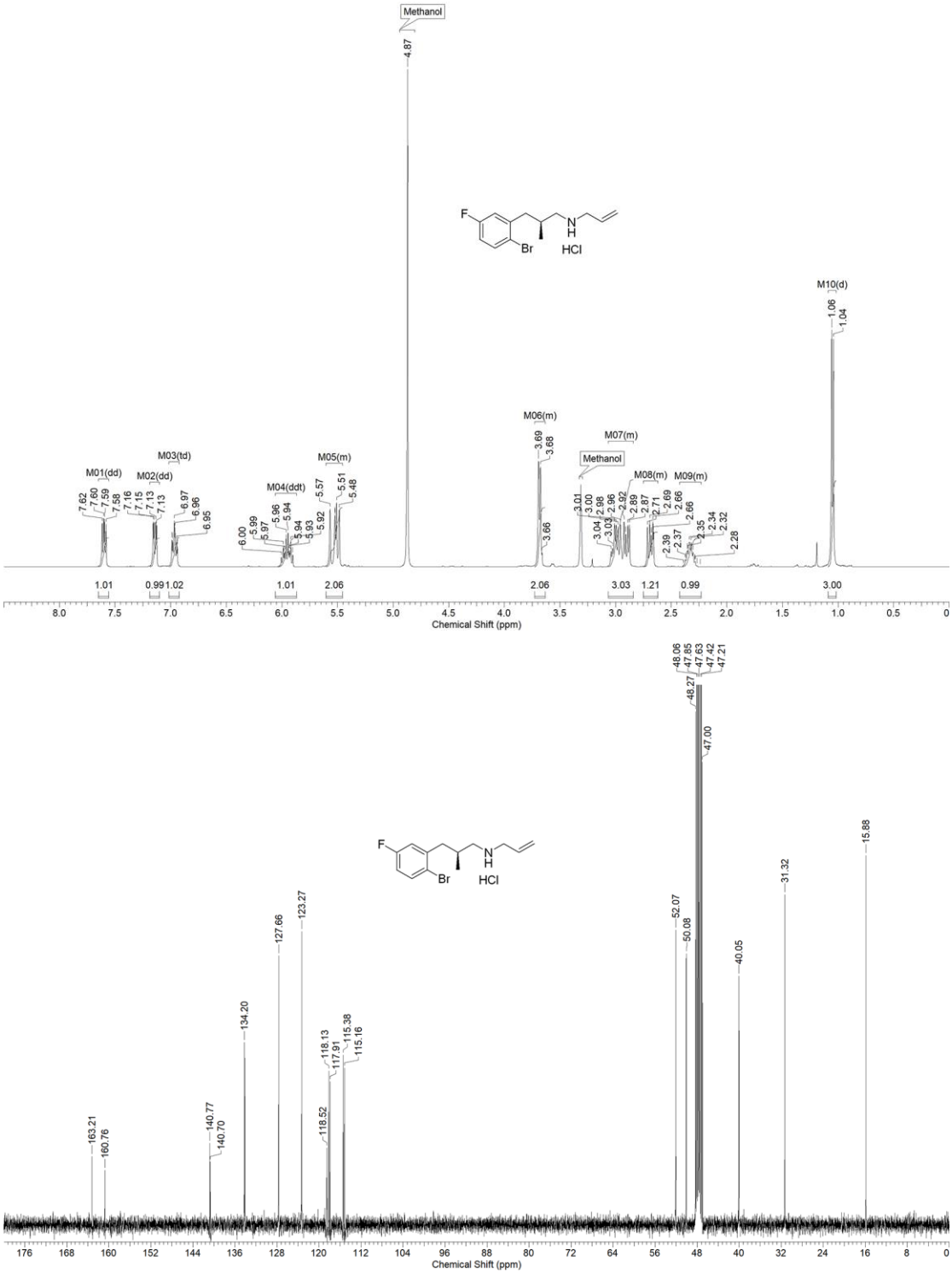


^{1}H-NMR spectra and ^{13}C-NMR spectra of

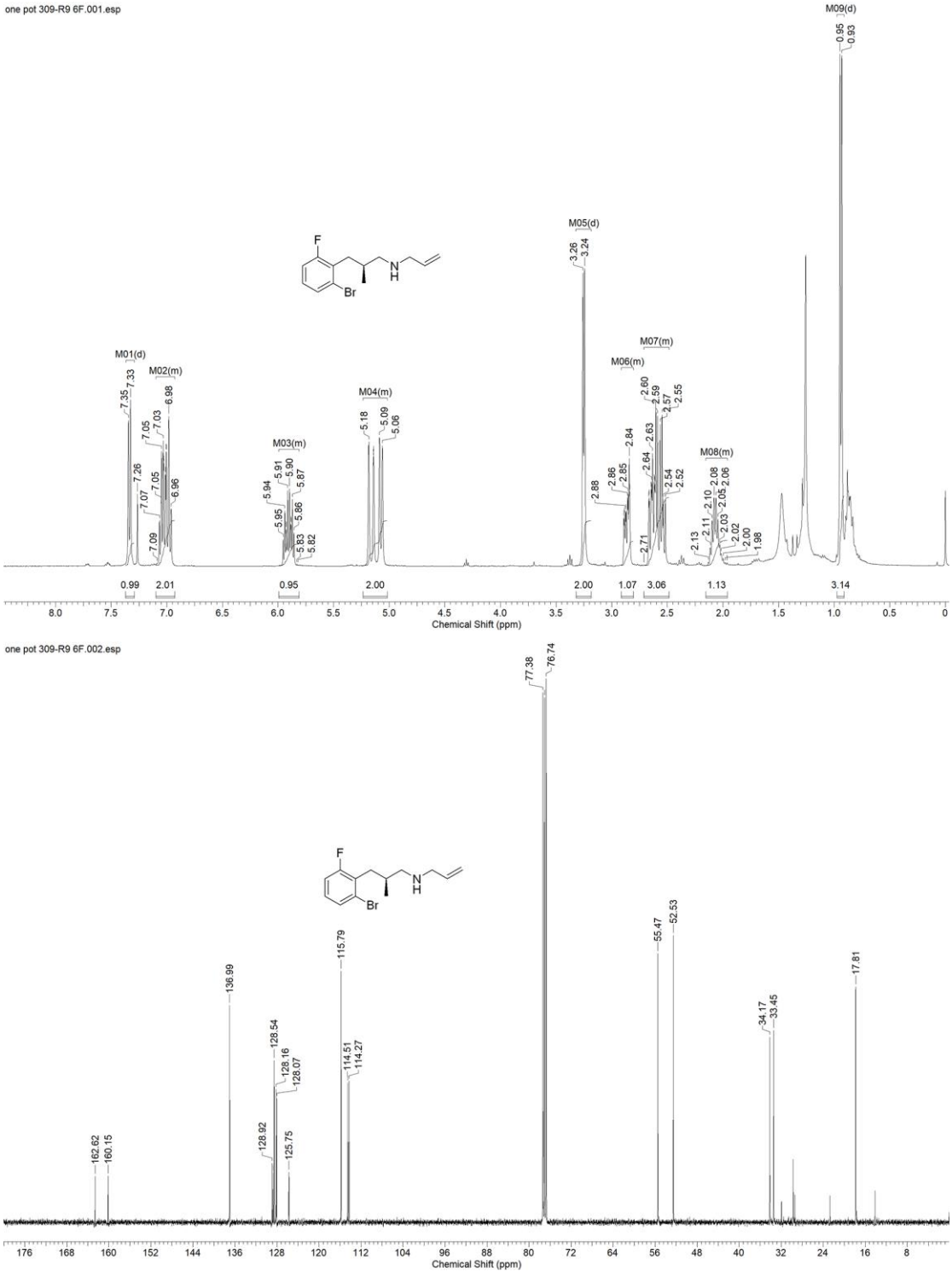
(*S*)-*N*-(3-(2-bromo-3-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4c**)



^{1}H-NMR spectra and ^{13}C-NMR spectra of (*S*)-*N*-(3-(2-bromo-4-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine hydrochloride ((*S*)-**4d**)

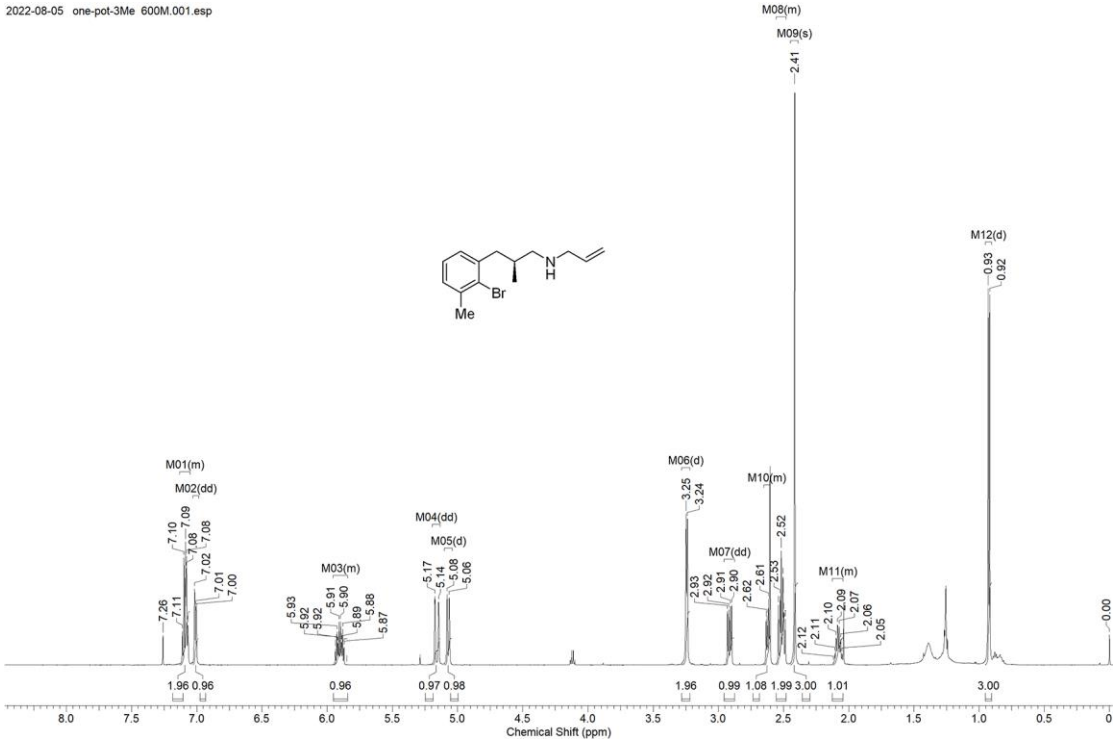


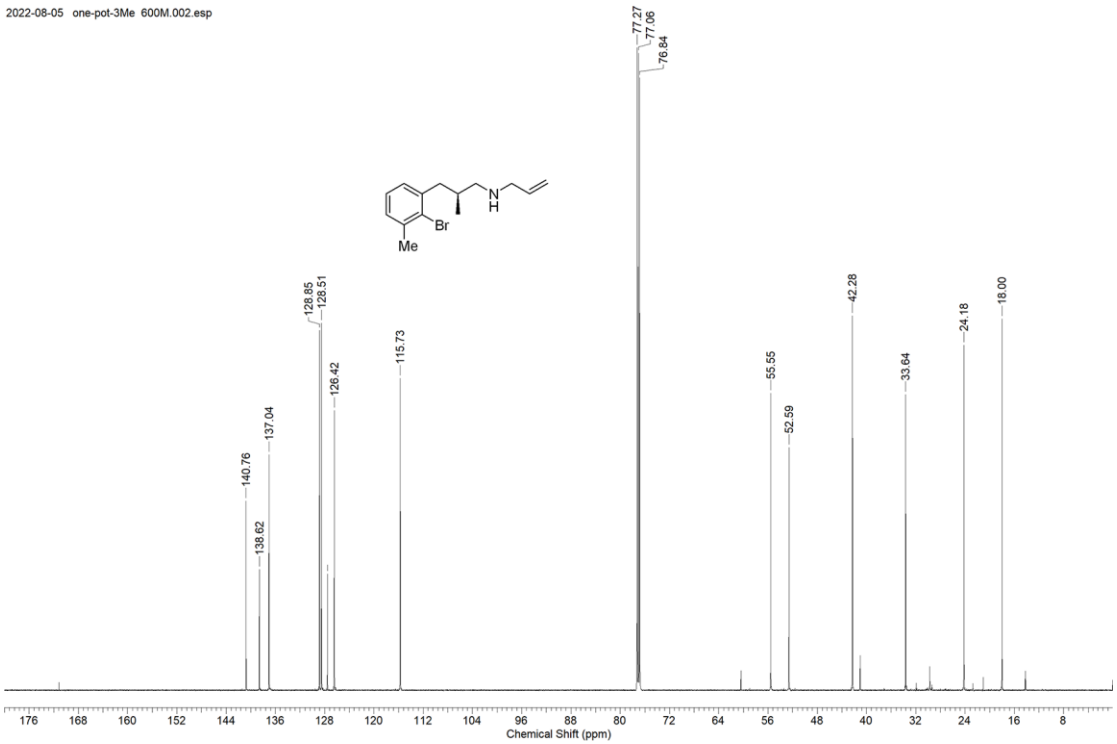
^{1}H-NMR spectra and ^{13}C-NMR spectra of (*S*)-*N*-(3-(2-bromo-5-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine hydrochloride ((*S*)-**4e**)



^{1}H-NMR spectra and ^{13}C-NMR spectra of

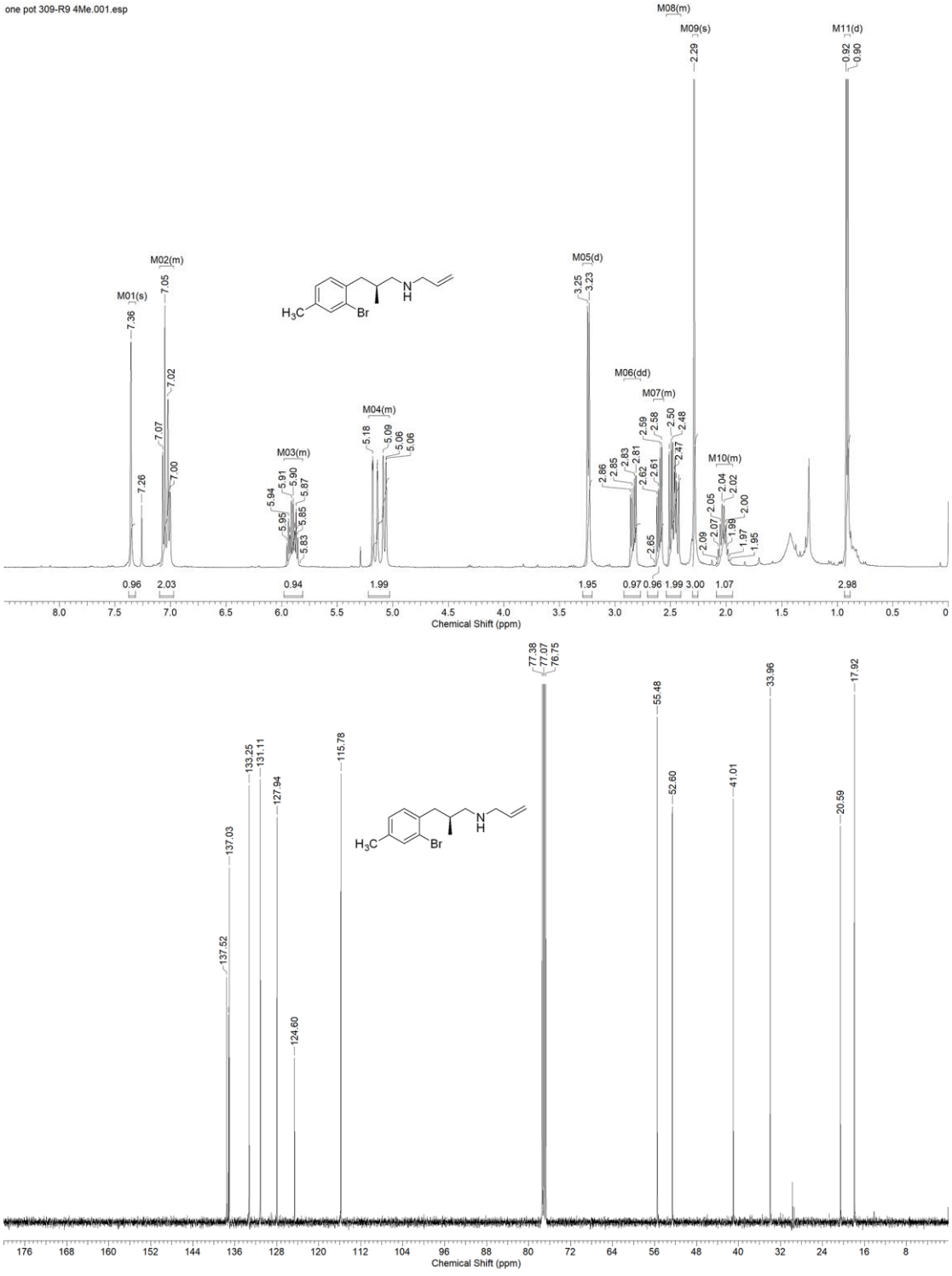
(*S*)-*N*-(3-(2-bromo-6-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4f**)





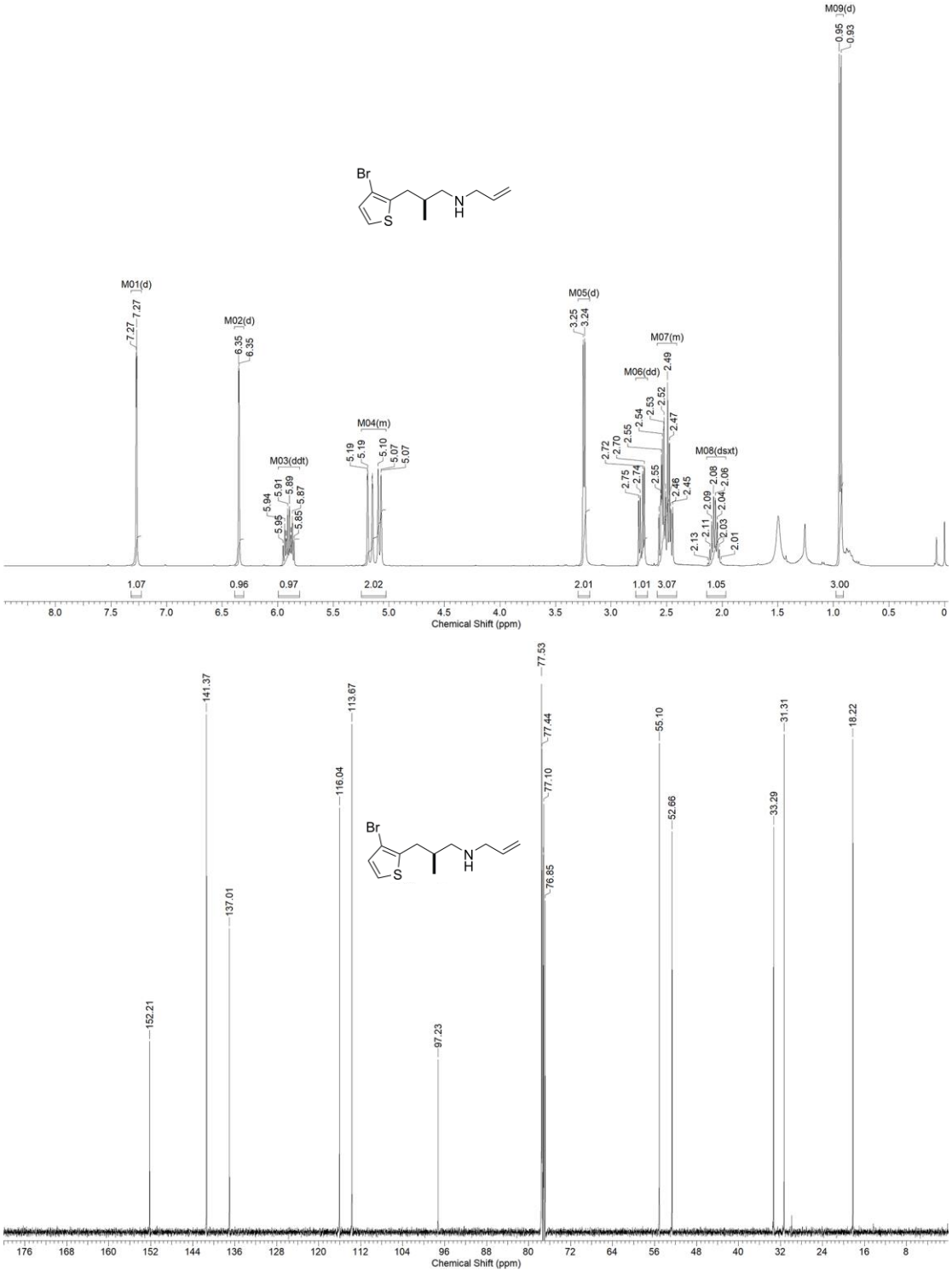
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-*N*-(3-(2-bromo-3-methylphenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4g**)



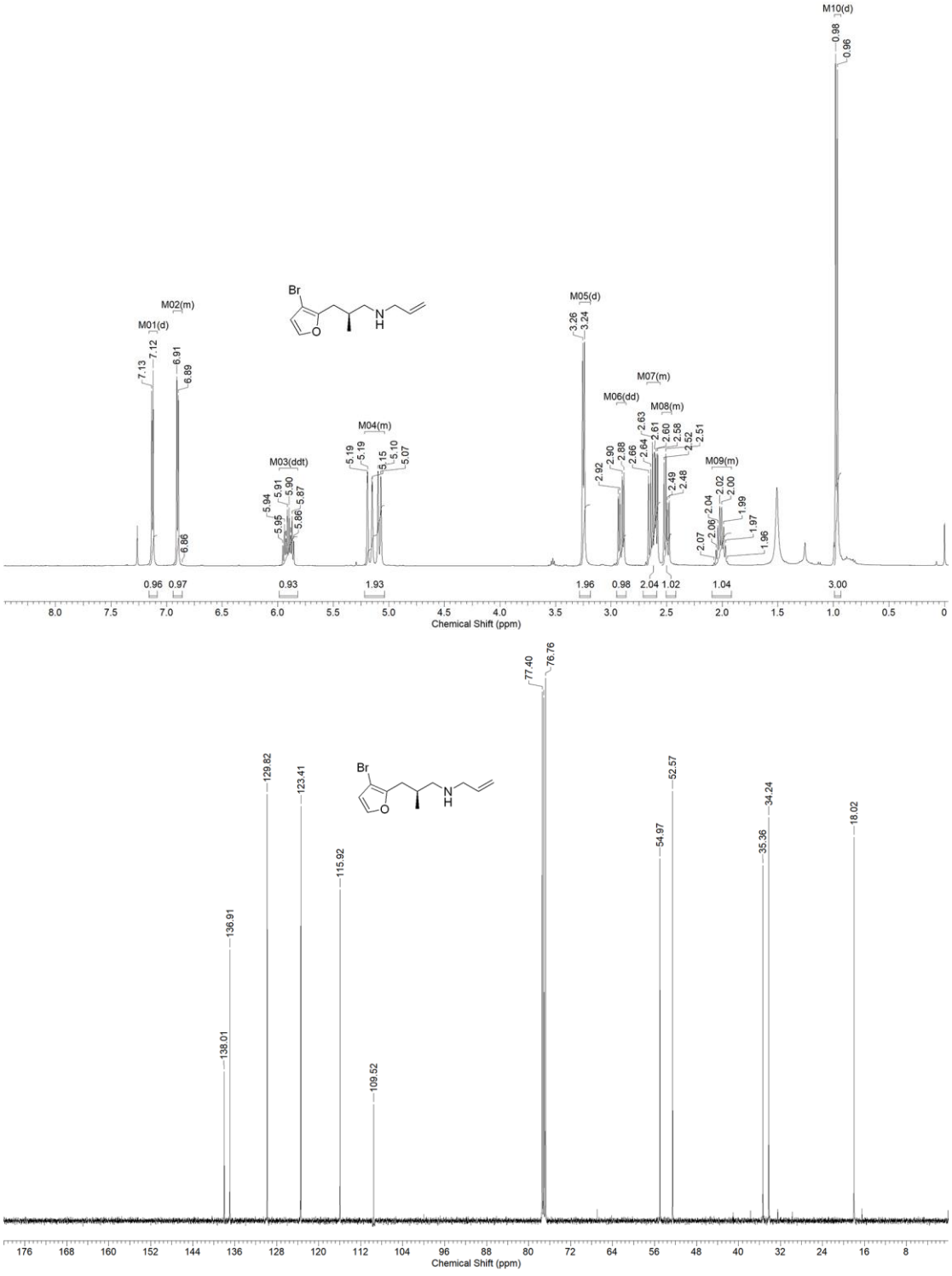
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-*N*-(3-(2-bromo-4-methylphenyl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4h**)



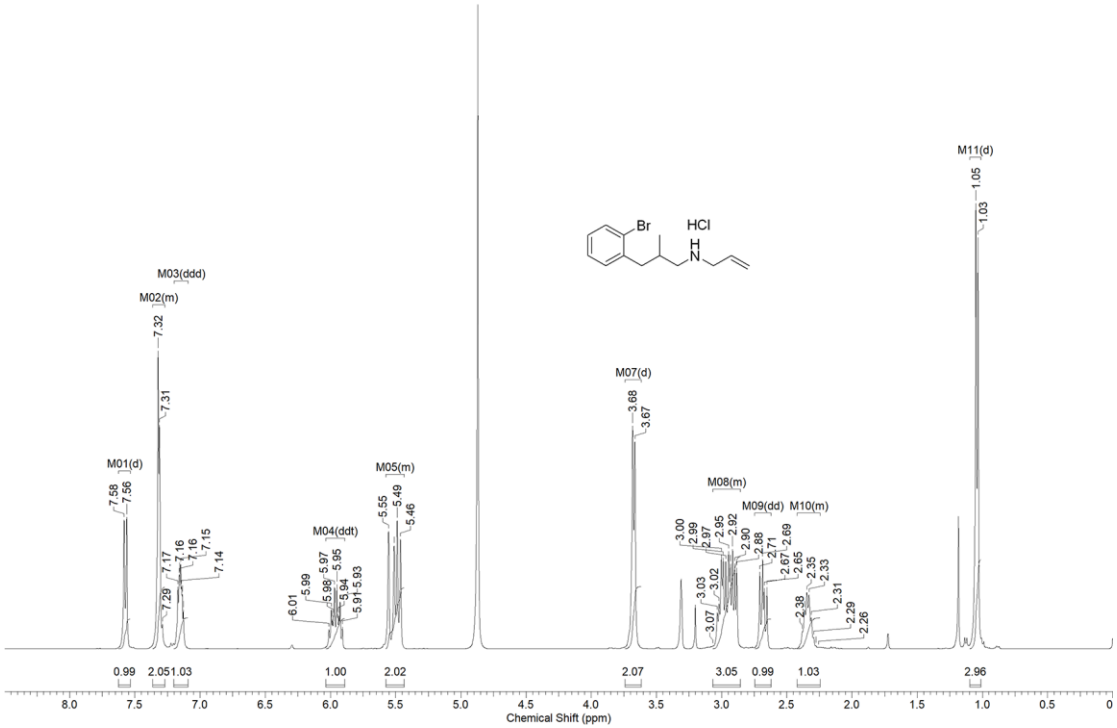
^{1}H-NMR spectra and ^{13}C-NMR spectra of

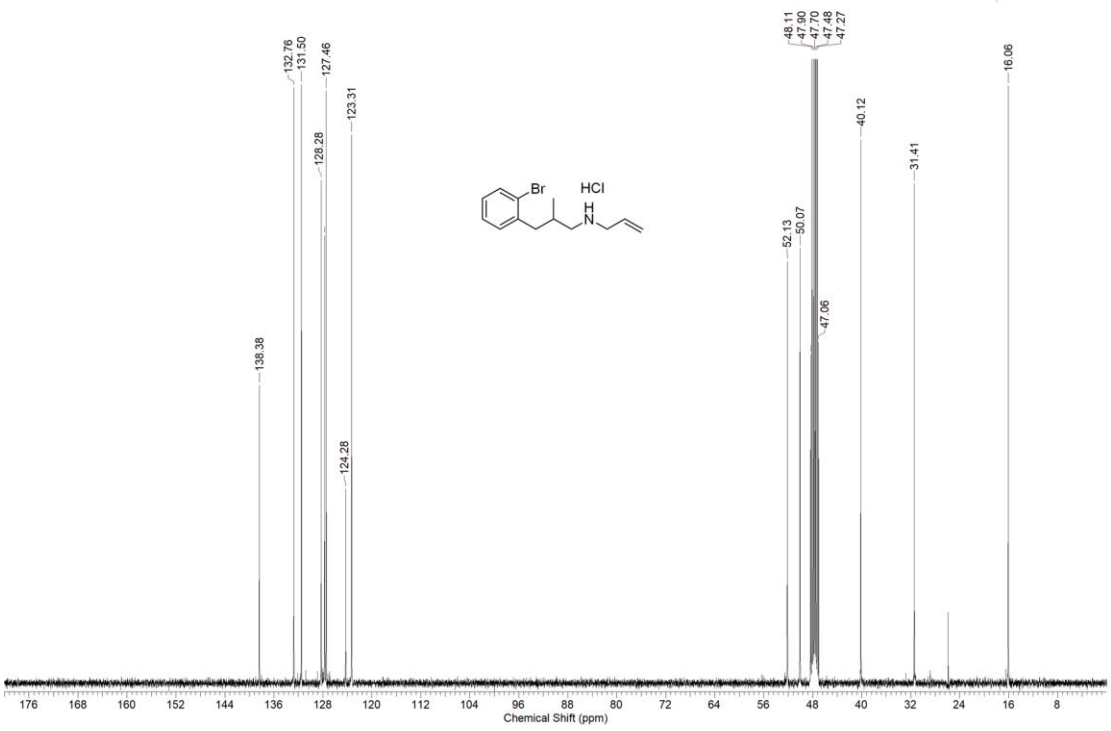
(*S*)-*N*-(3-(3-bromothiophen-2-yl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4i**)



^{1}H-NMR spectra and ^{13}C-NMR spectra of

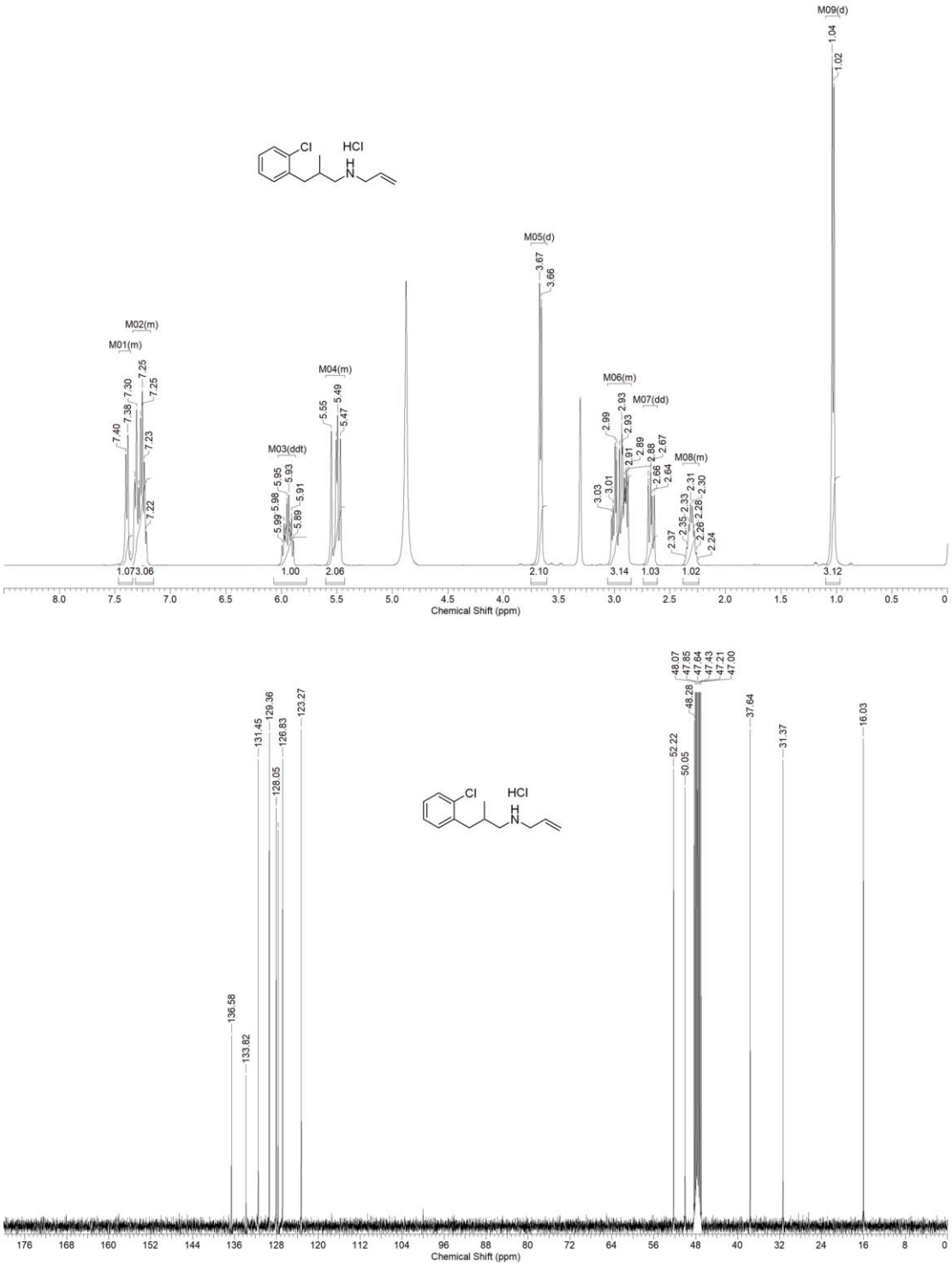
(*S*)-*N*-(3-(3-bromofuran-2-yl)-2-methylpropyl)prop-2-en-1-amine ((*S*)-**4j**)





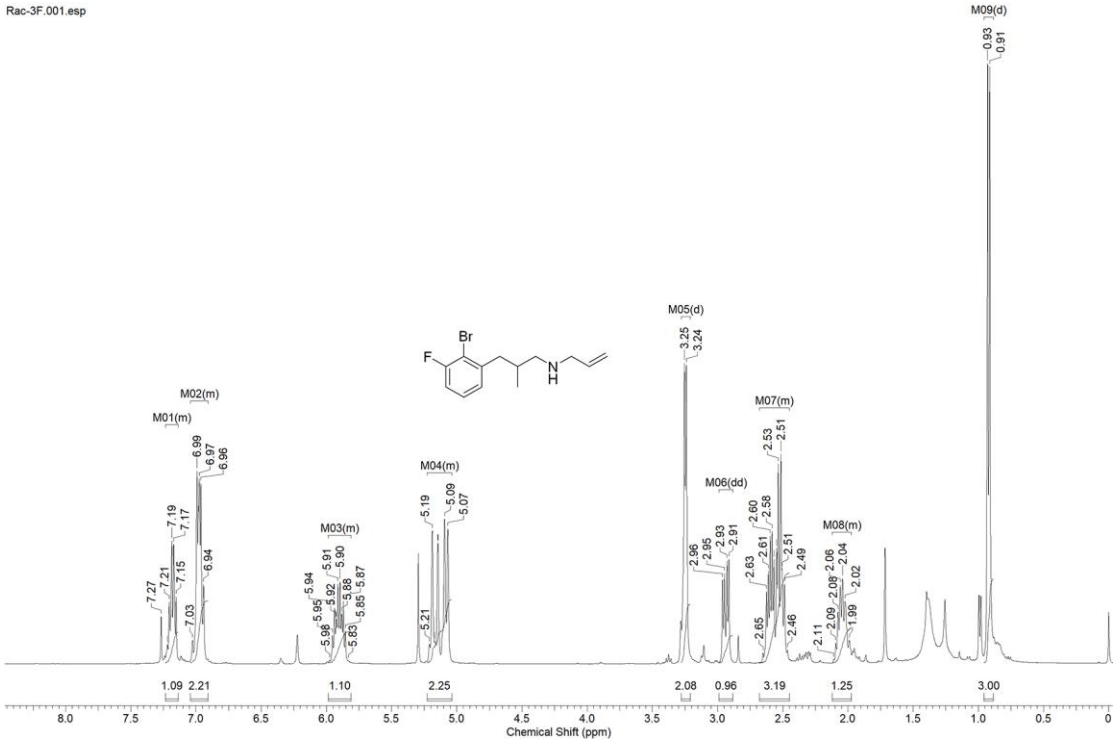
^{1}H-NMR spectra and ^{13}C-NMR spectra of

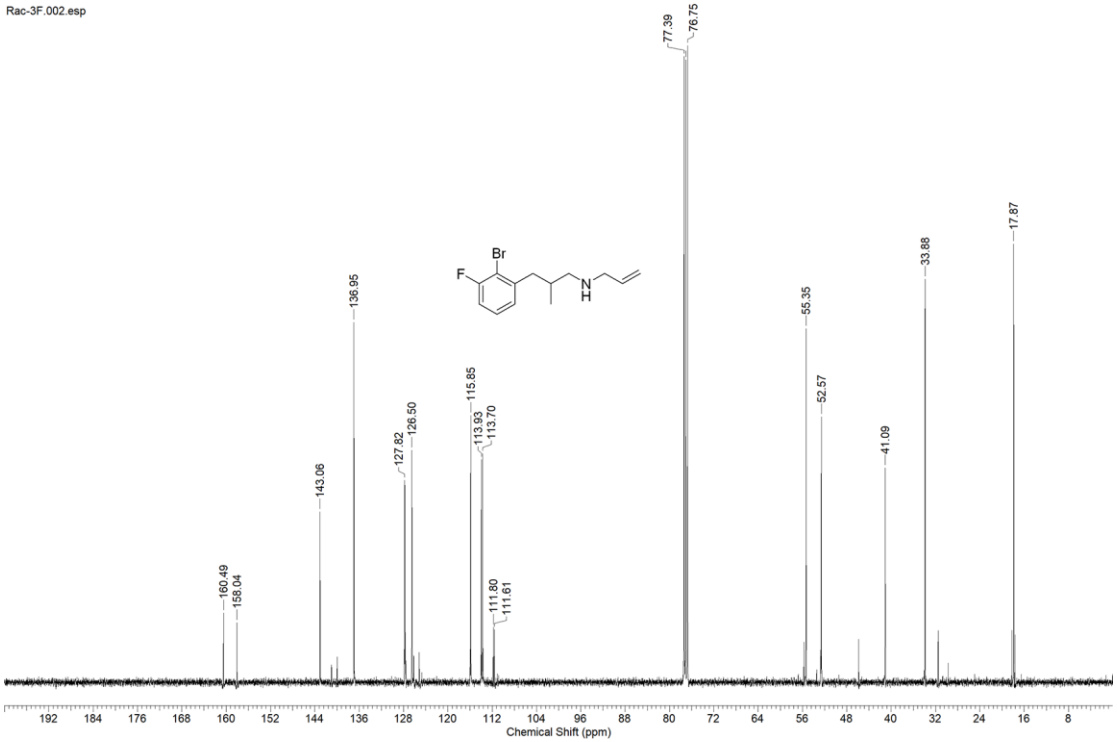
N-(3-(2-bromophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4a**)



^{1}H-NMR spectra and ^{13}C-NMR spectra of

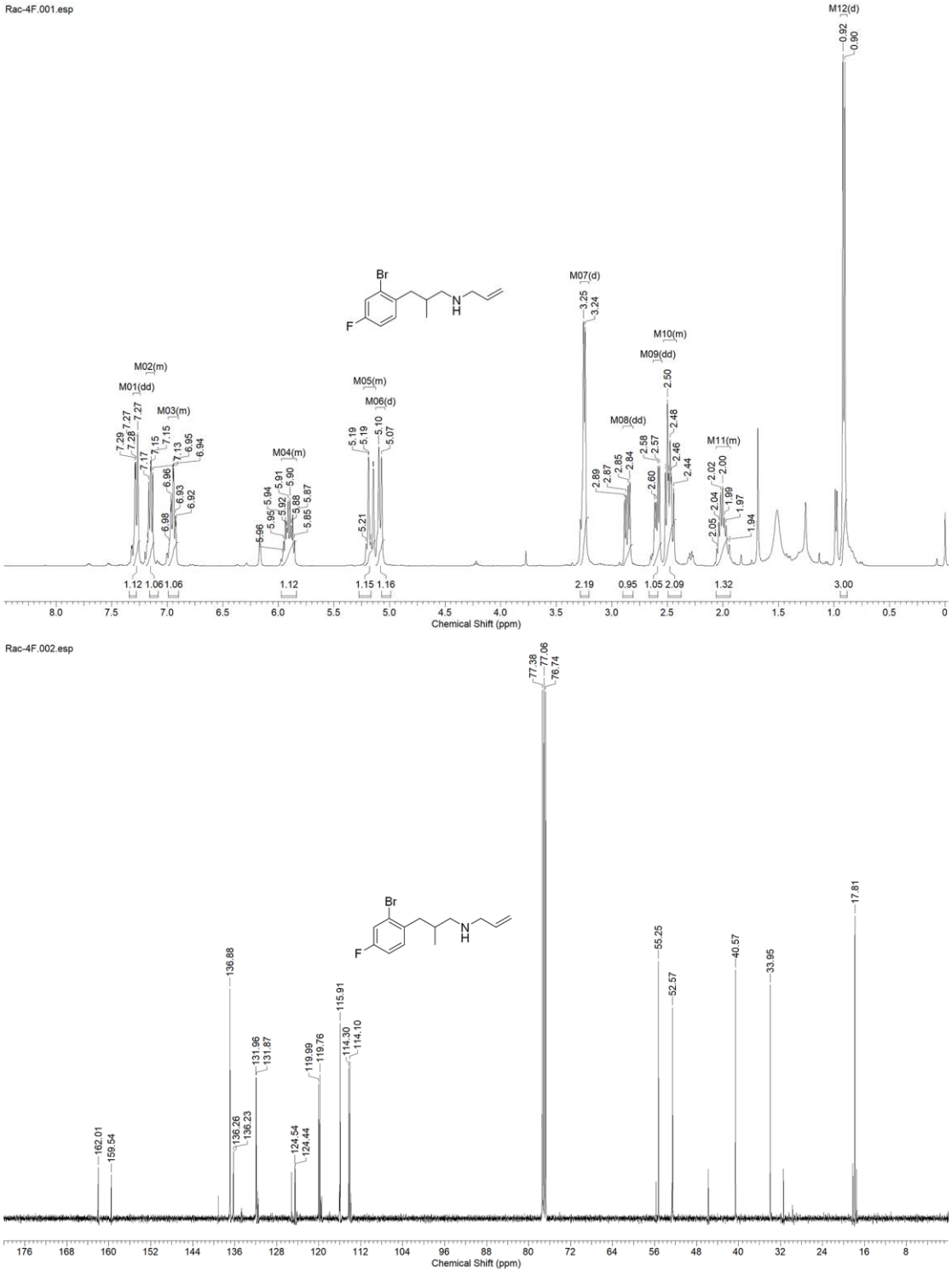
N-(3-(2-chlorophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4b**)





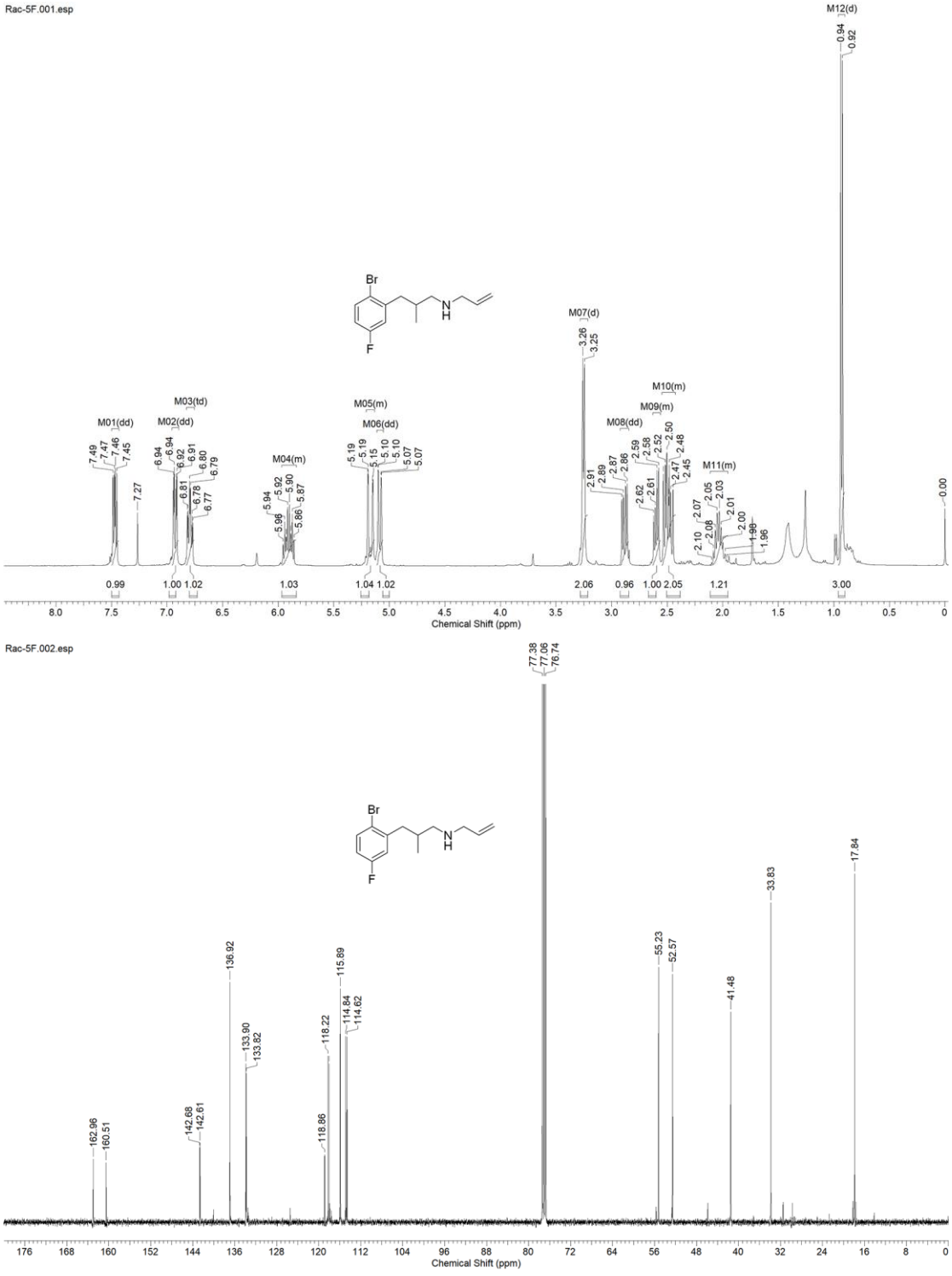
^{1}H-NMR spectra and ^{13}C-NMR spectra of

N-(3-(2-bromo-3-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4c**)



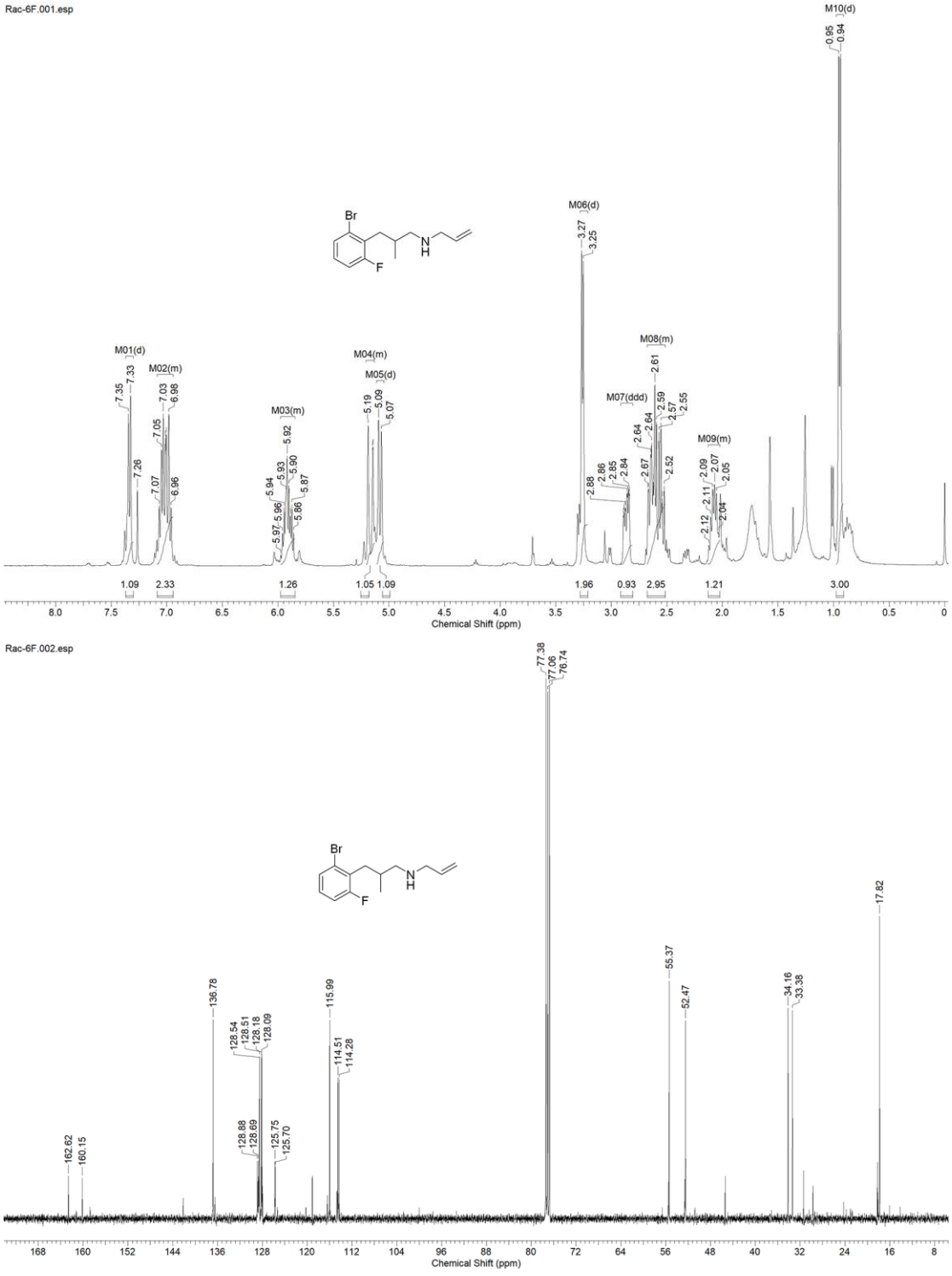
^{1}H-NMR spectra and ^{13}C-NMR spectra of

N-(3-(2-bromo-4-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4d**)



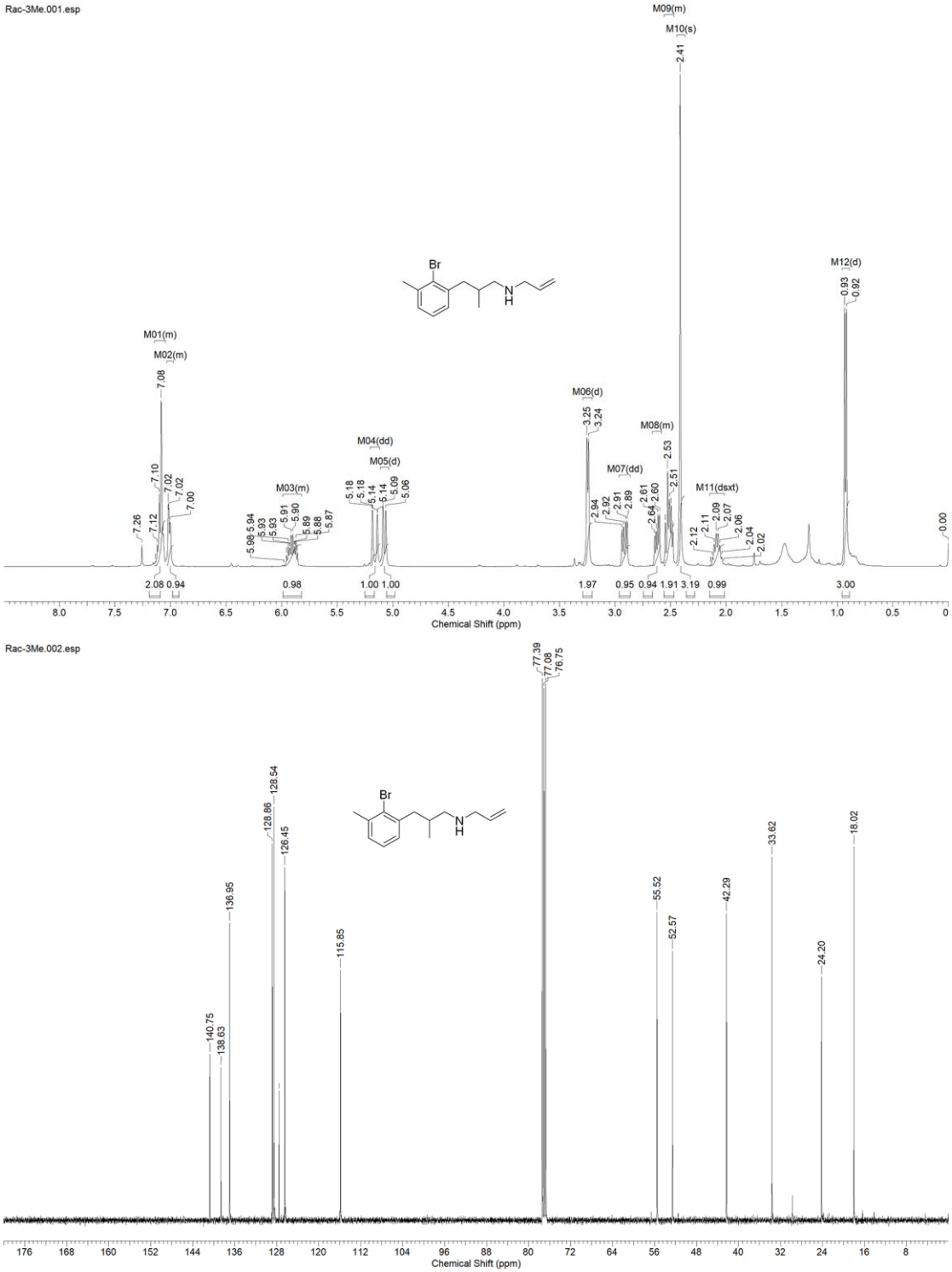
^{1}H-NMR spectra and ^{13}C-NMR spectra of

N-(3-(2-bromo-5-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4e**)



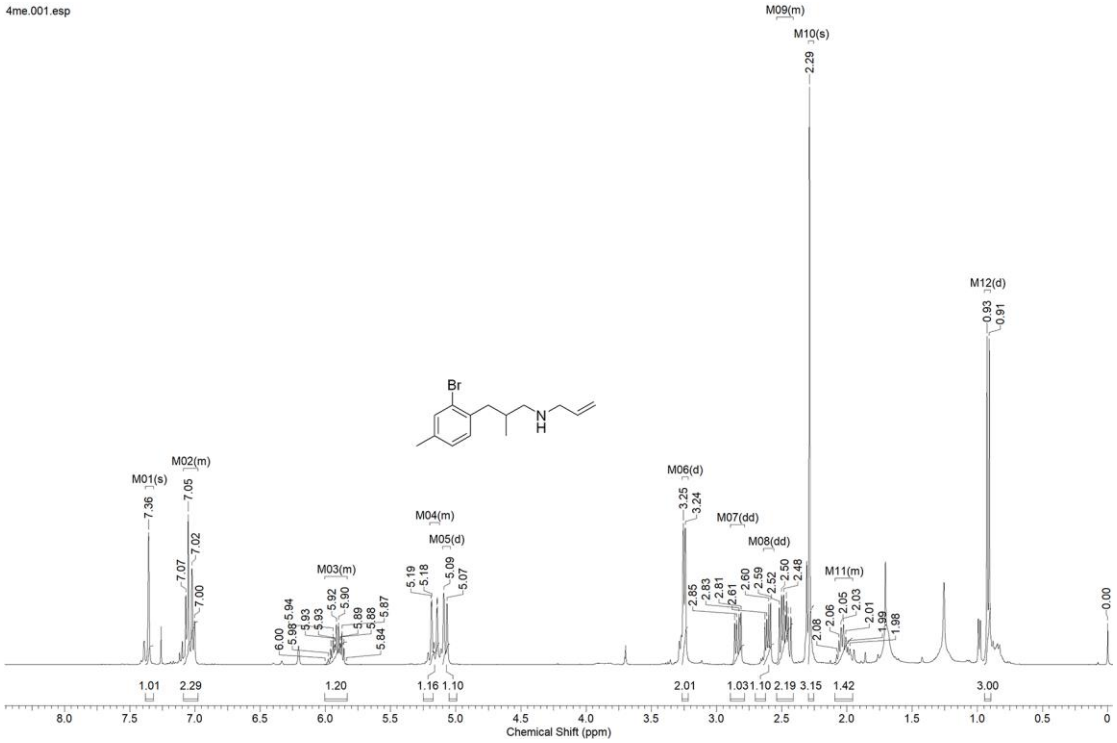
^{1}H-NMR spectra and ^{13}C-NMR spectra of

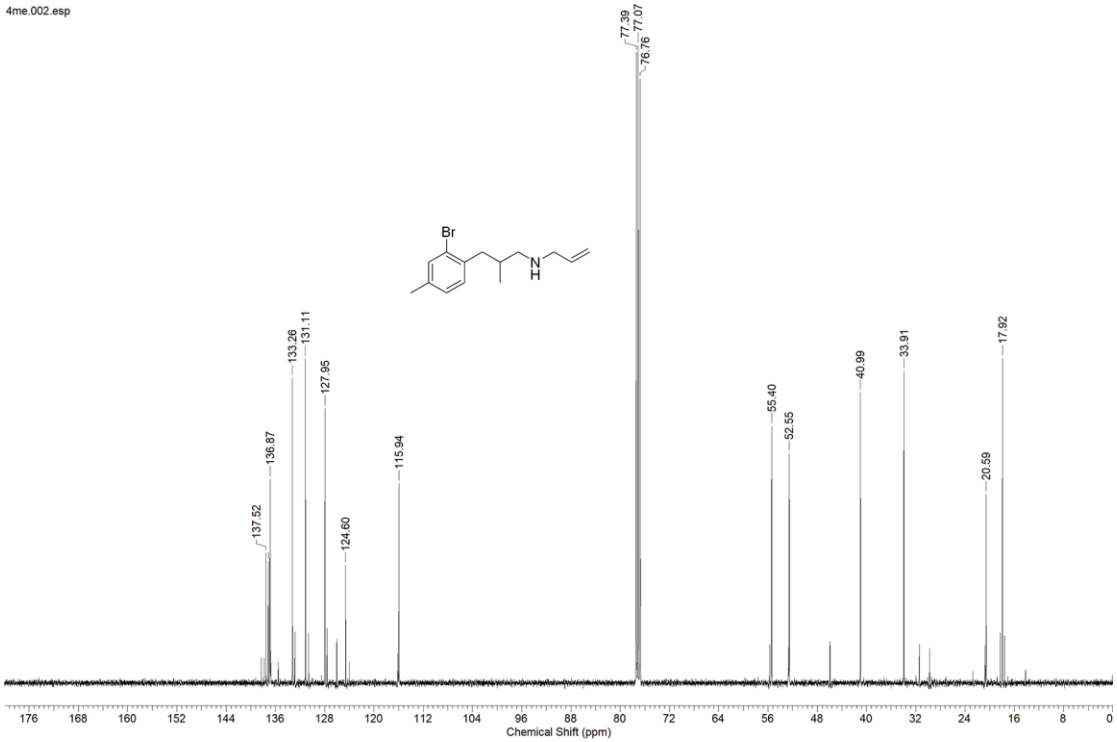
N-(3-(2-bromo-6-fluorophenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4f**)



^{1}H-NMR spectra and ^{13}C-NMR spectra of

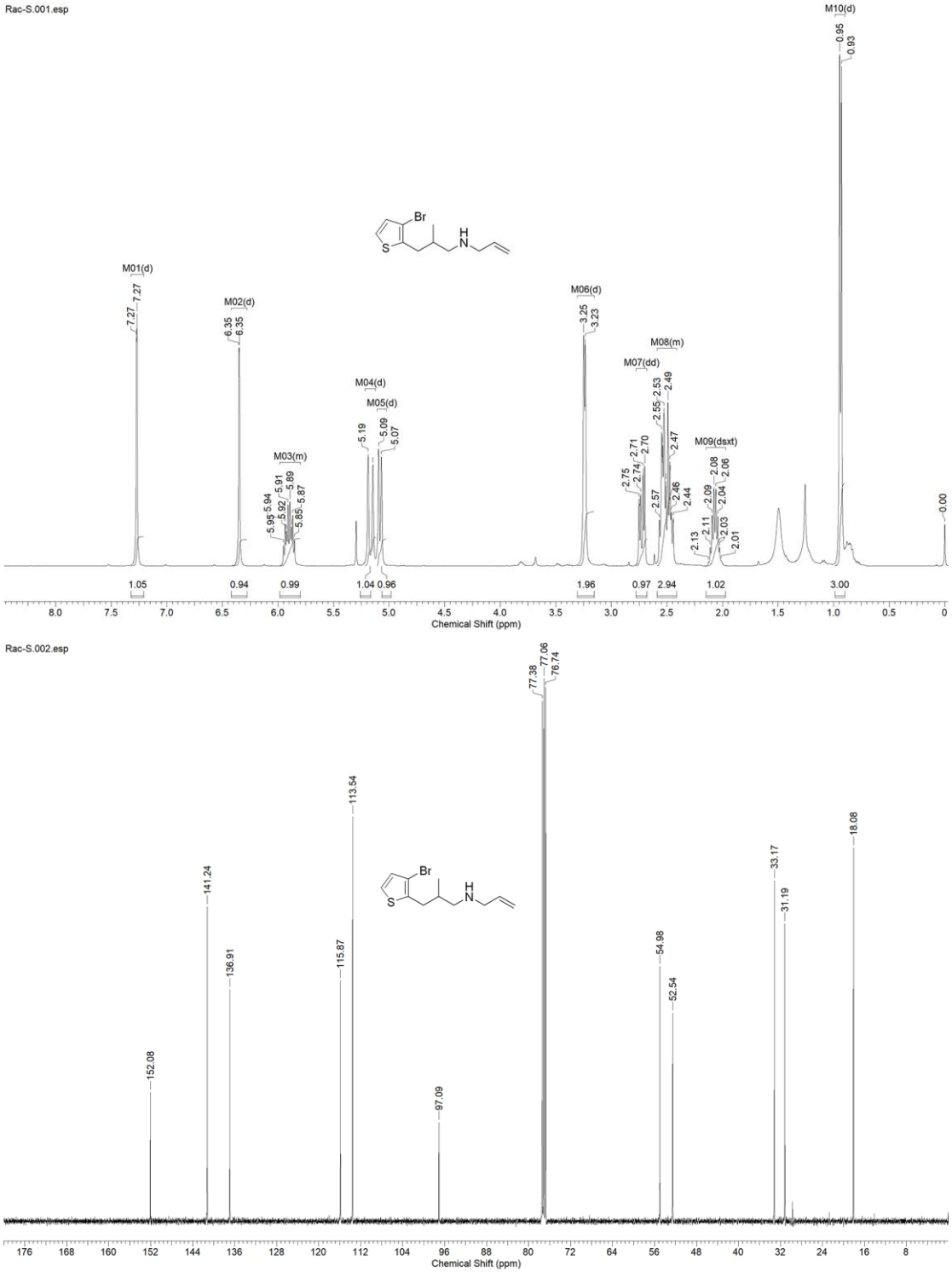
N-(3-(2-bromo-3-methylphenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4g**)





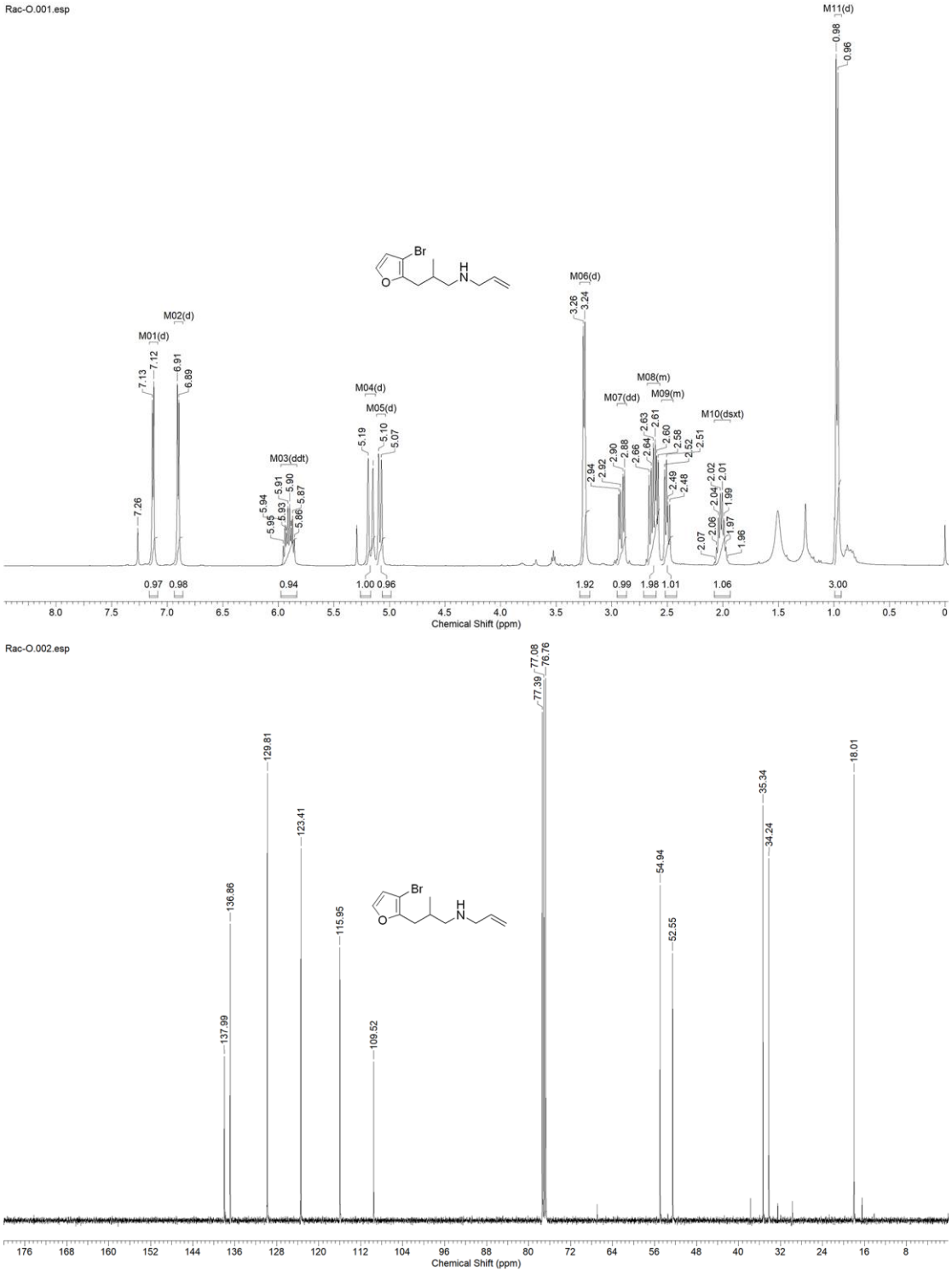
^{1}H-NMR spectra and ^{13}C-NMR spectra of

N-(3-(2-bromo-4-methylphenyl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4h**)



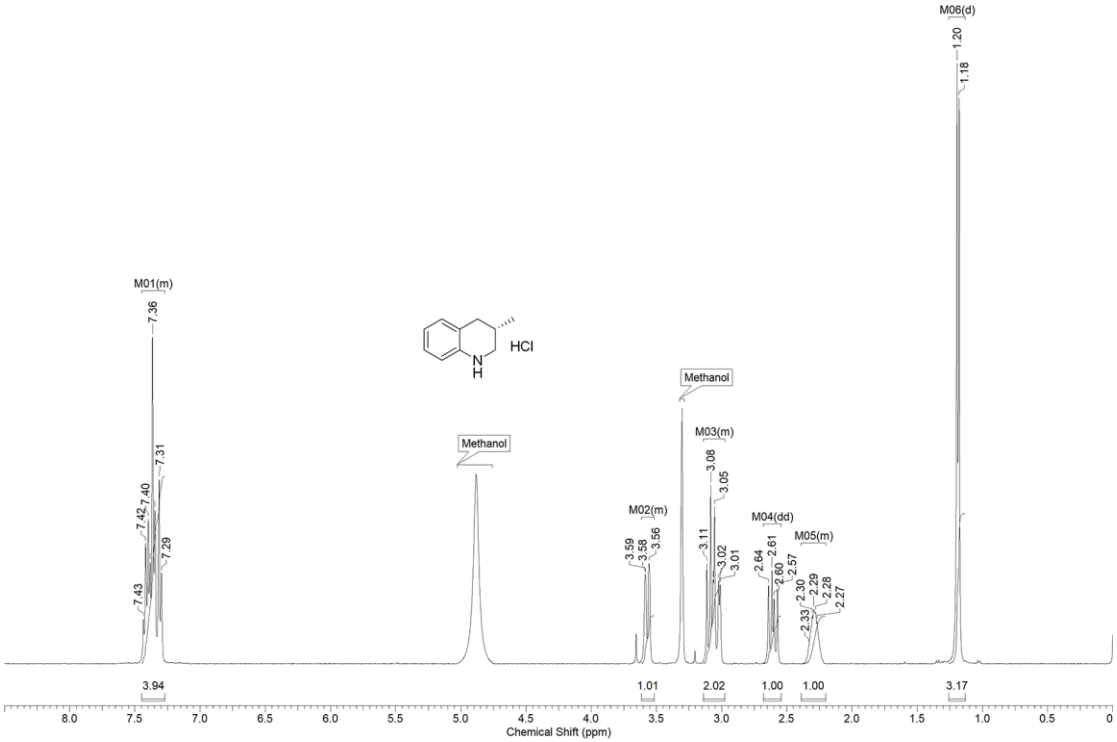
^{1}H-NMR spectra and ^{13}C-NMR spectra of

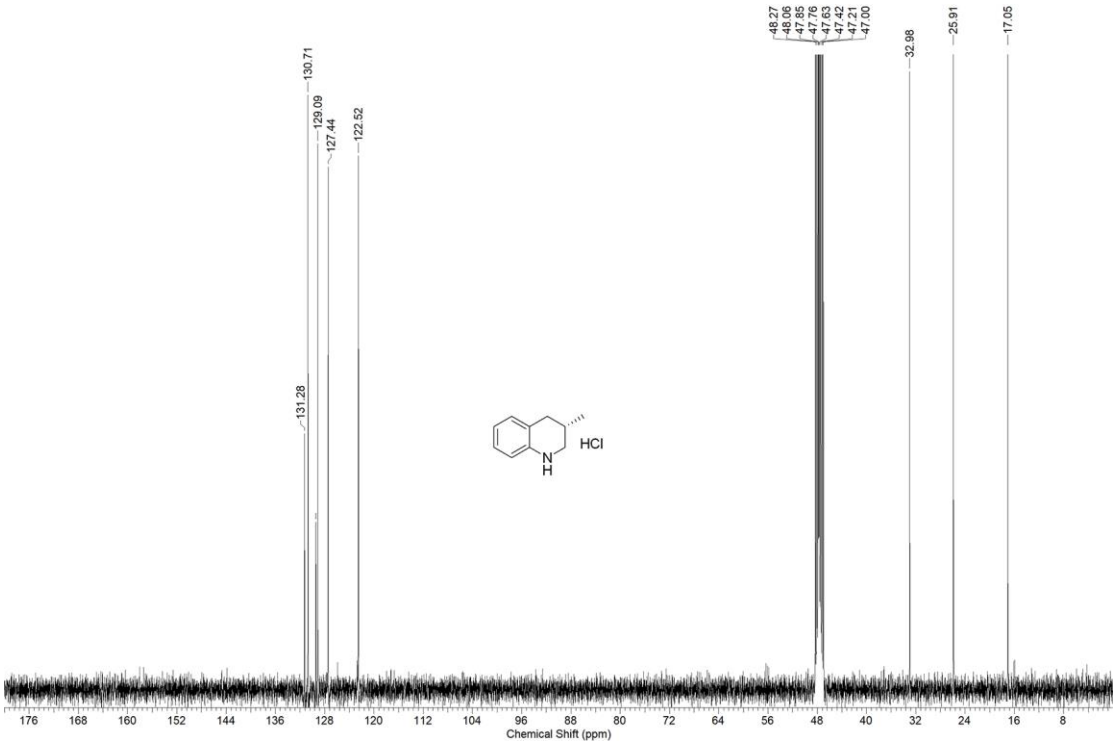
N-(3-(3-bromothiophen-2-yl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4i**)



^{1}H-NMR spectra and ^{13}C-NMR spectra of

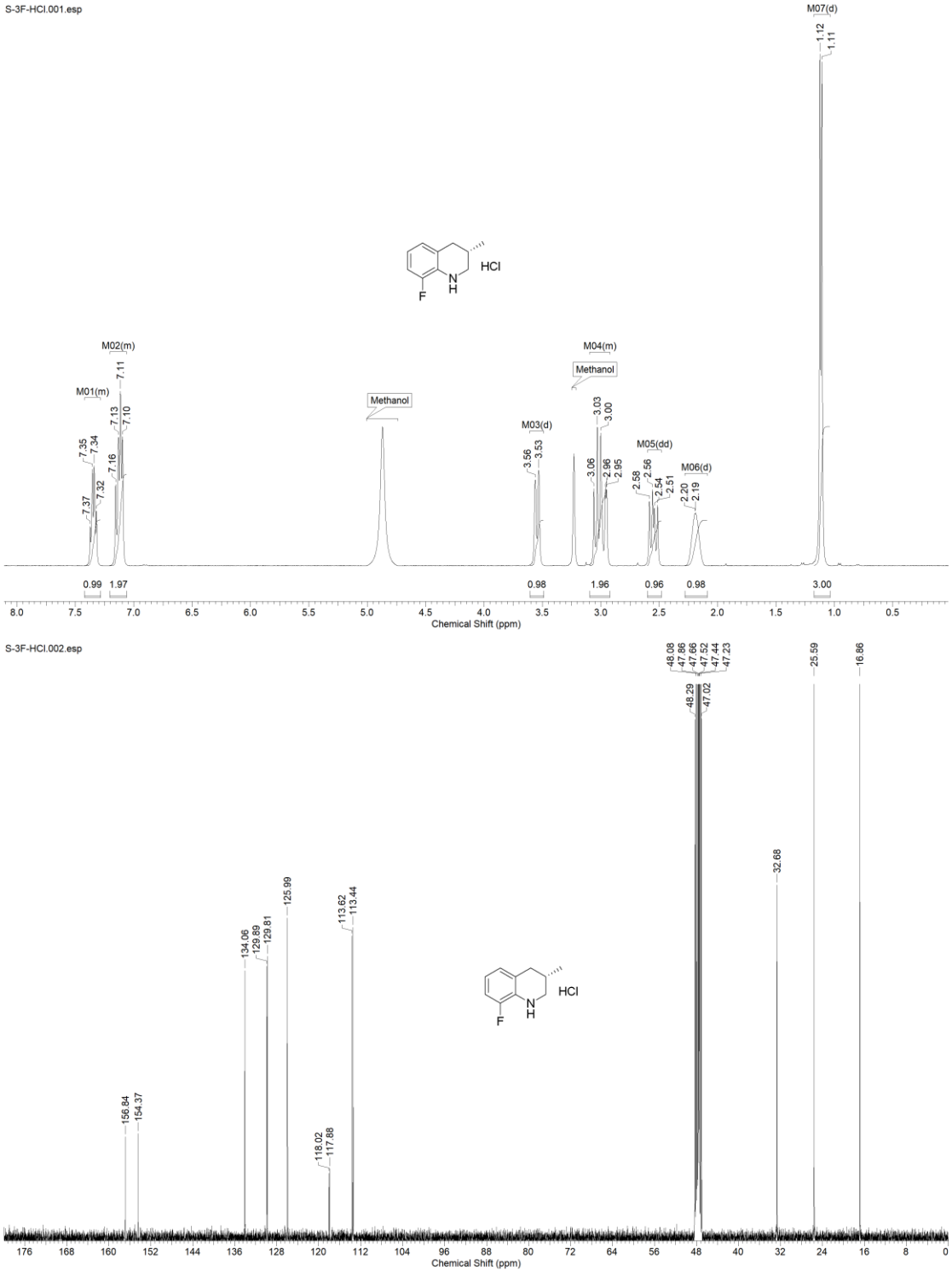
N-(3-(3-bromofuran-2-yl)-2-methylpropyl)prop-2-en-1-amine (Rac-**4j**)





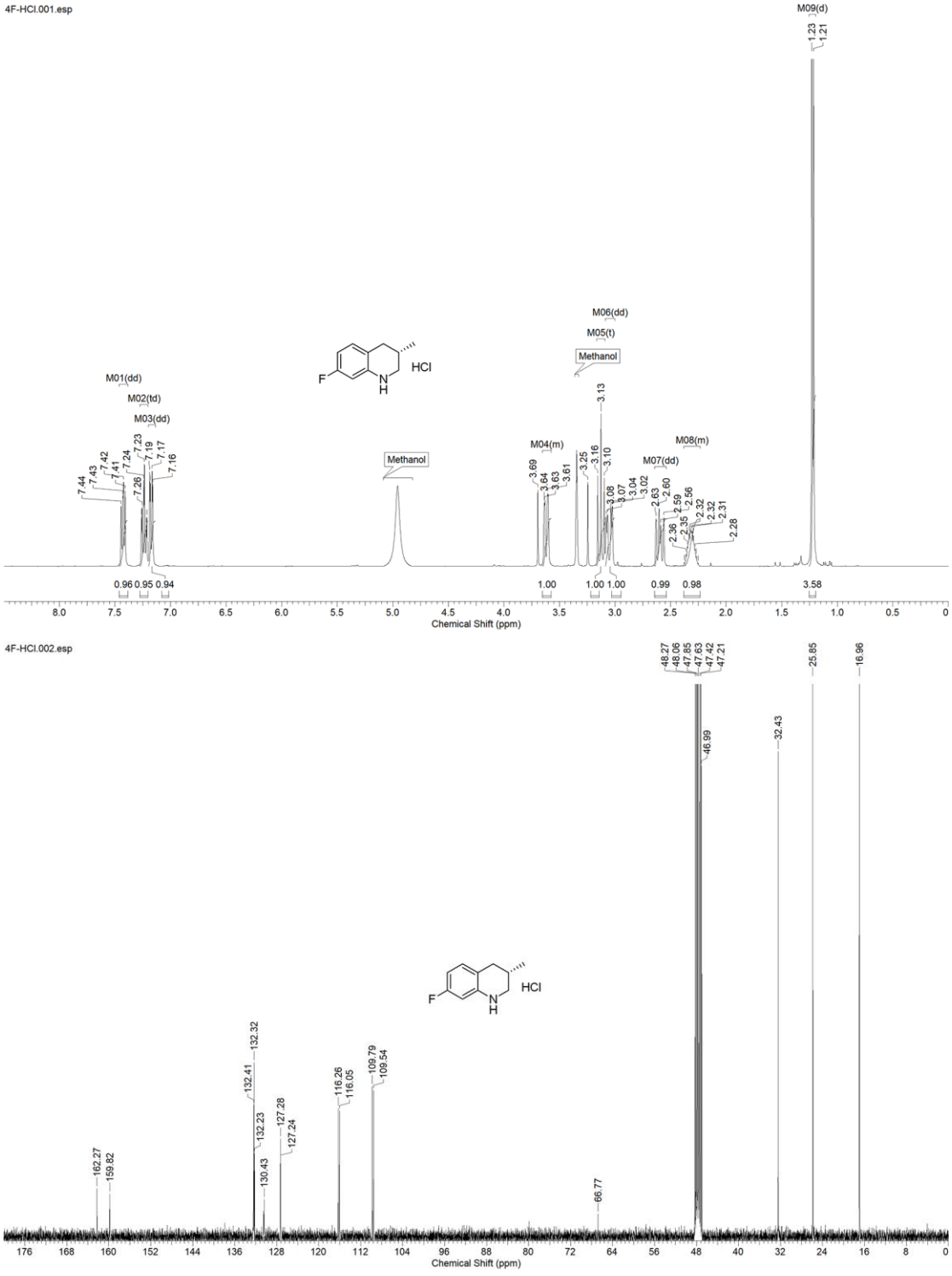
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6a**)



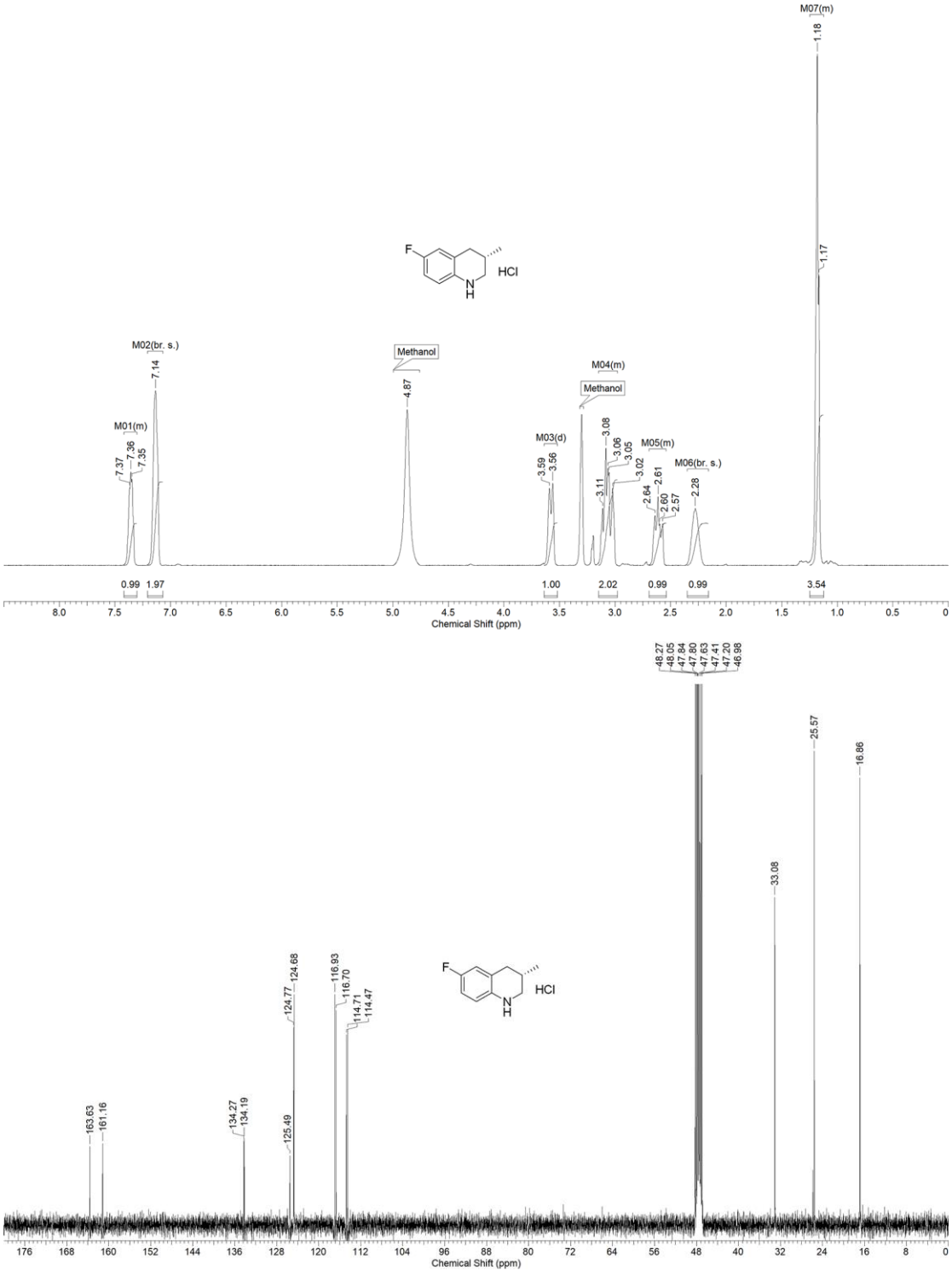
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-8-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6c**)



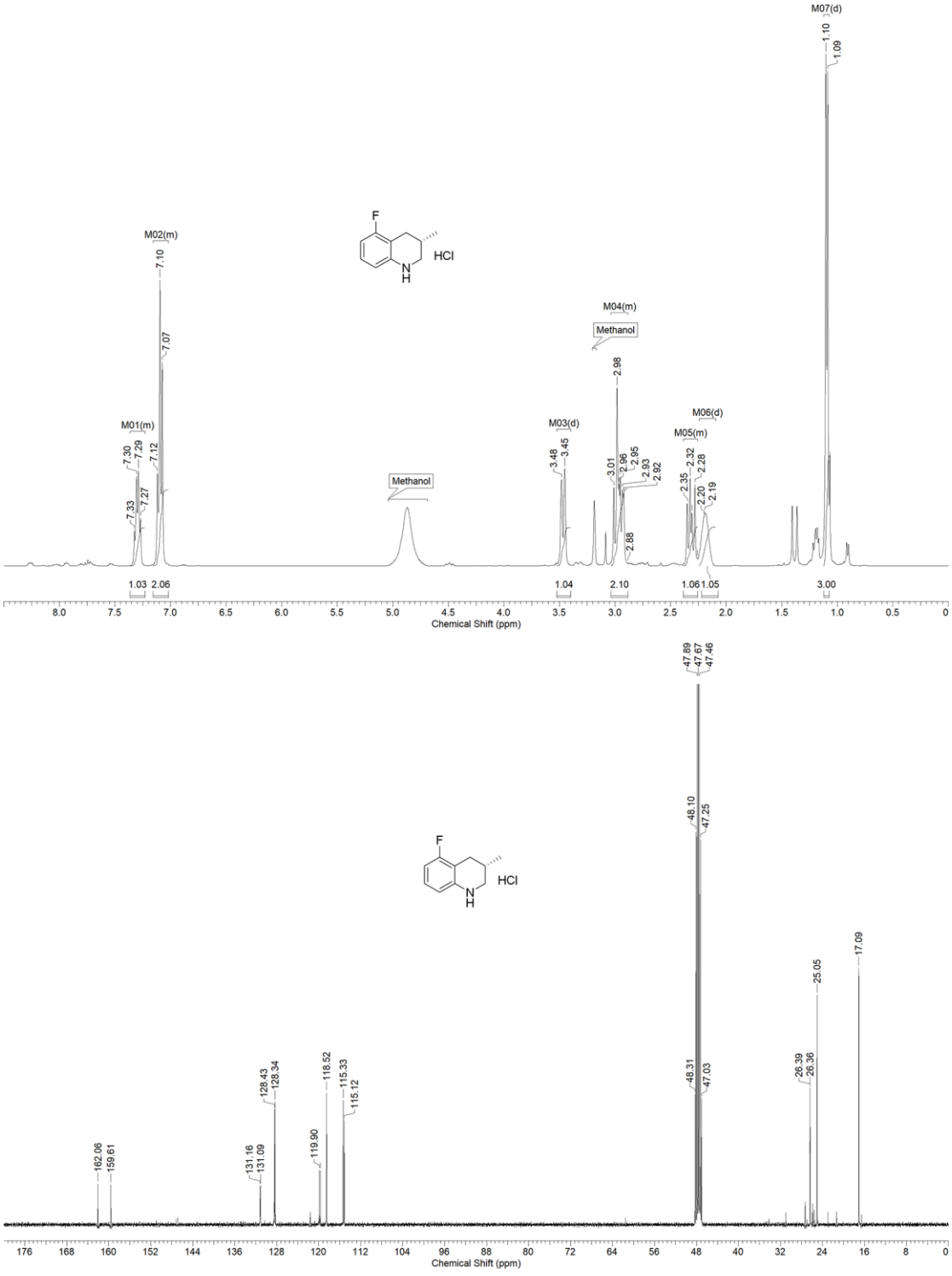
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-7-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6d**)



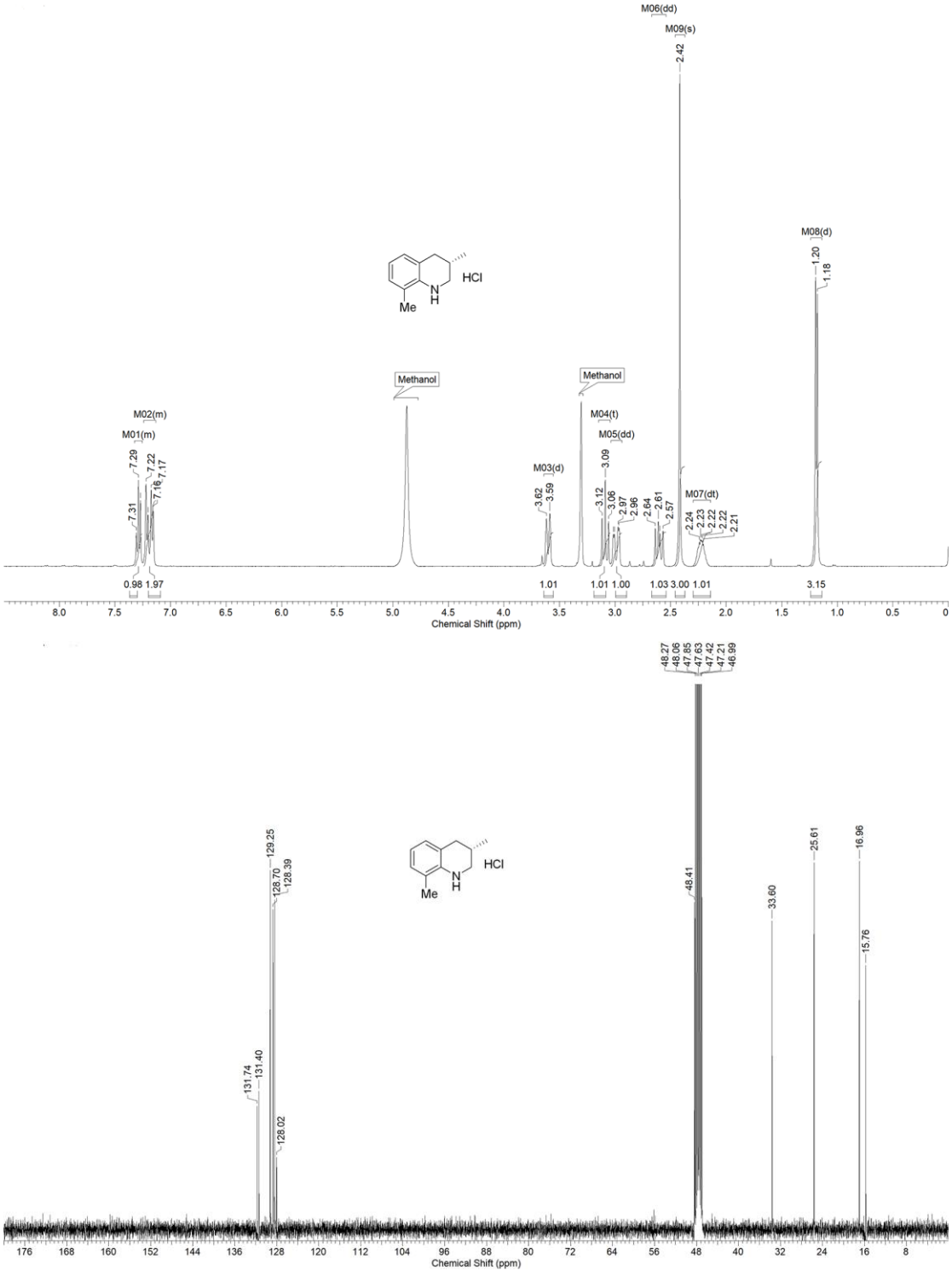
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-6-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6e**)



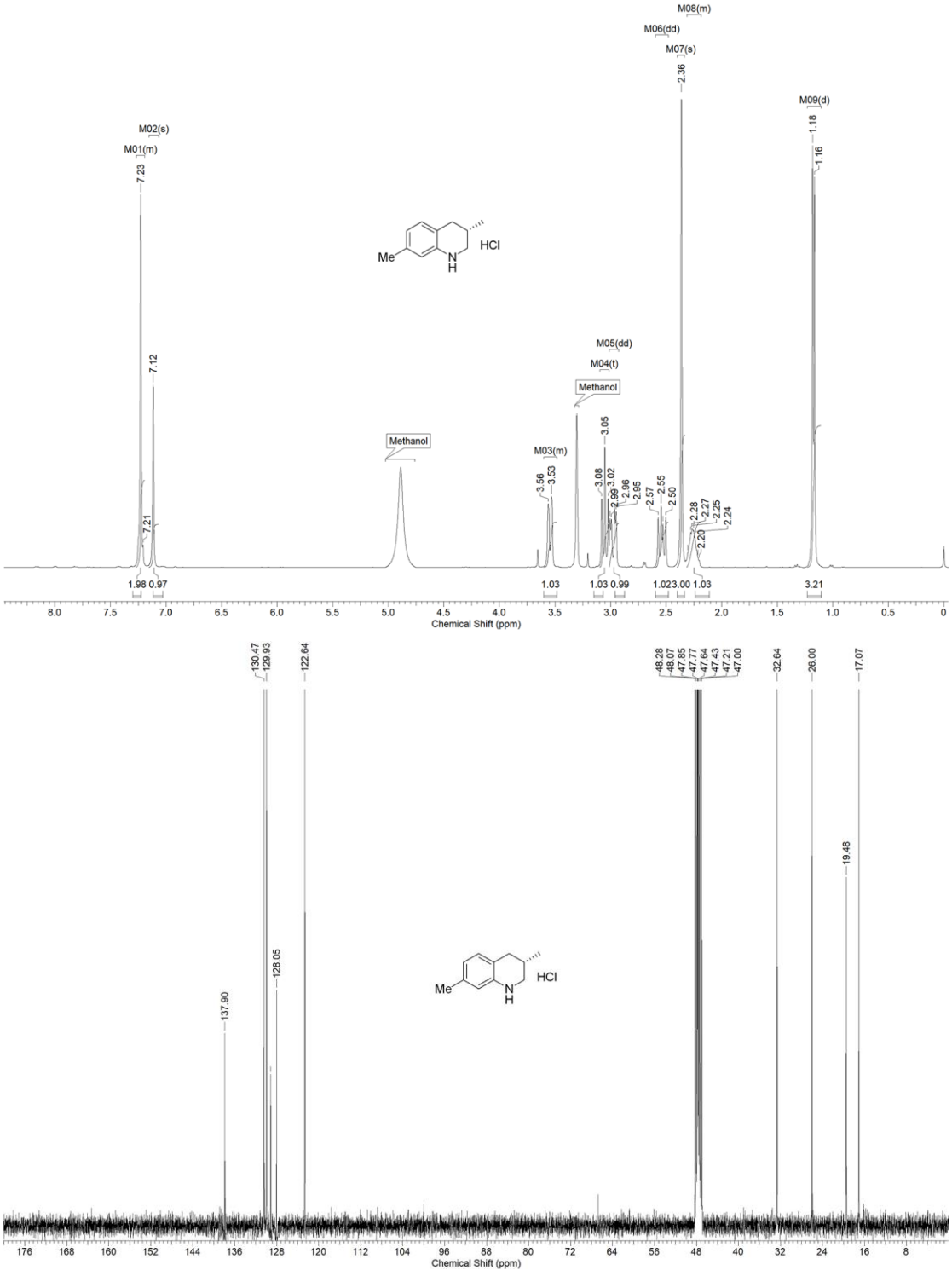
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-5-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6f**)



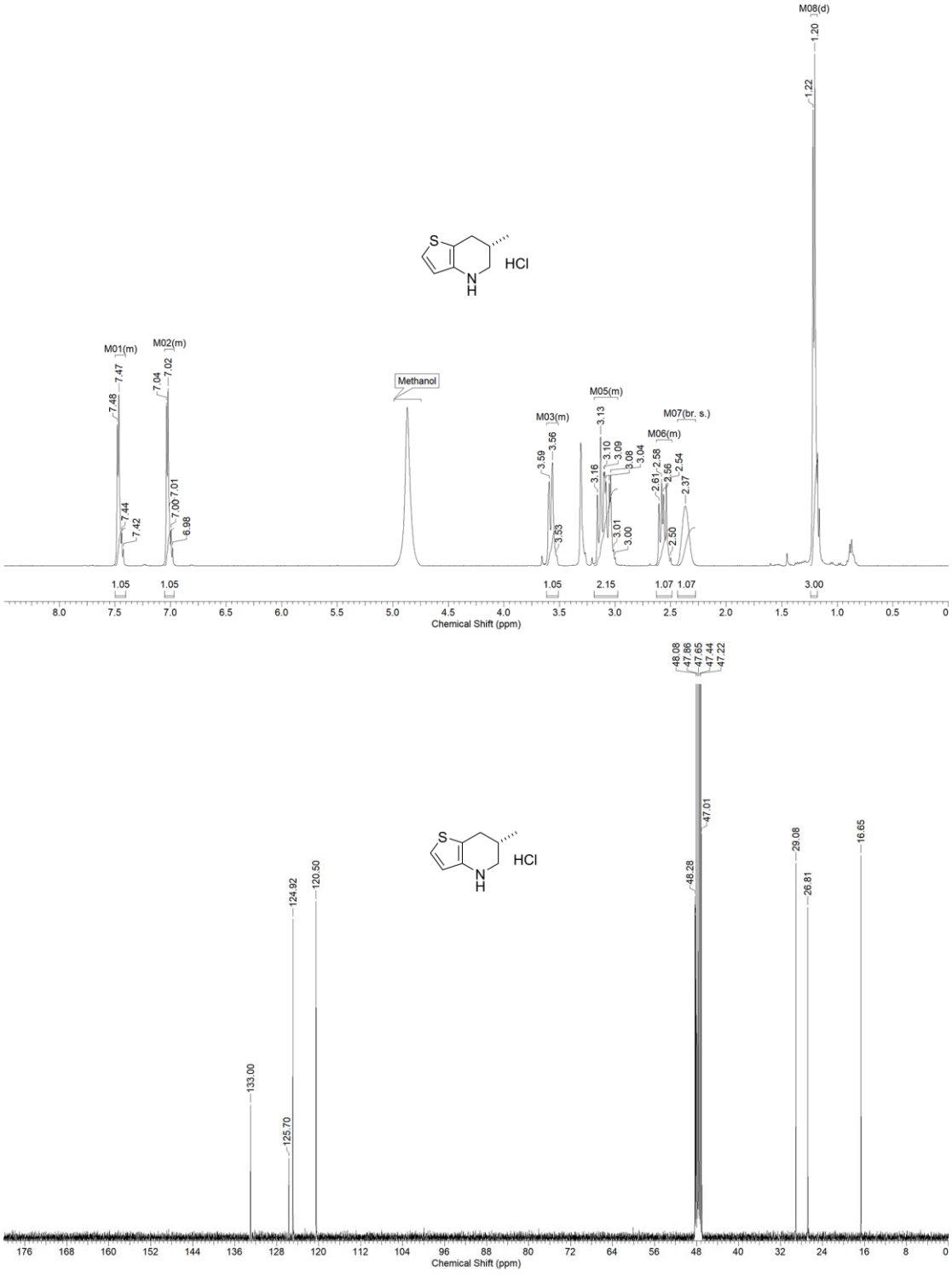
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)- 3,8-dimethyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6g**)



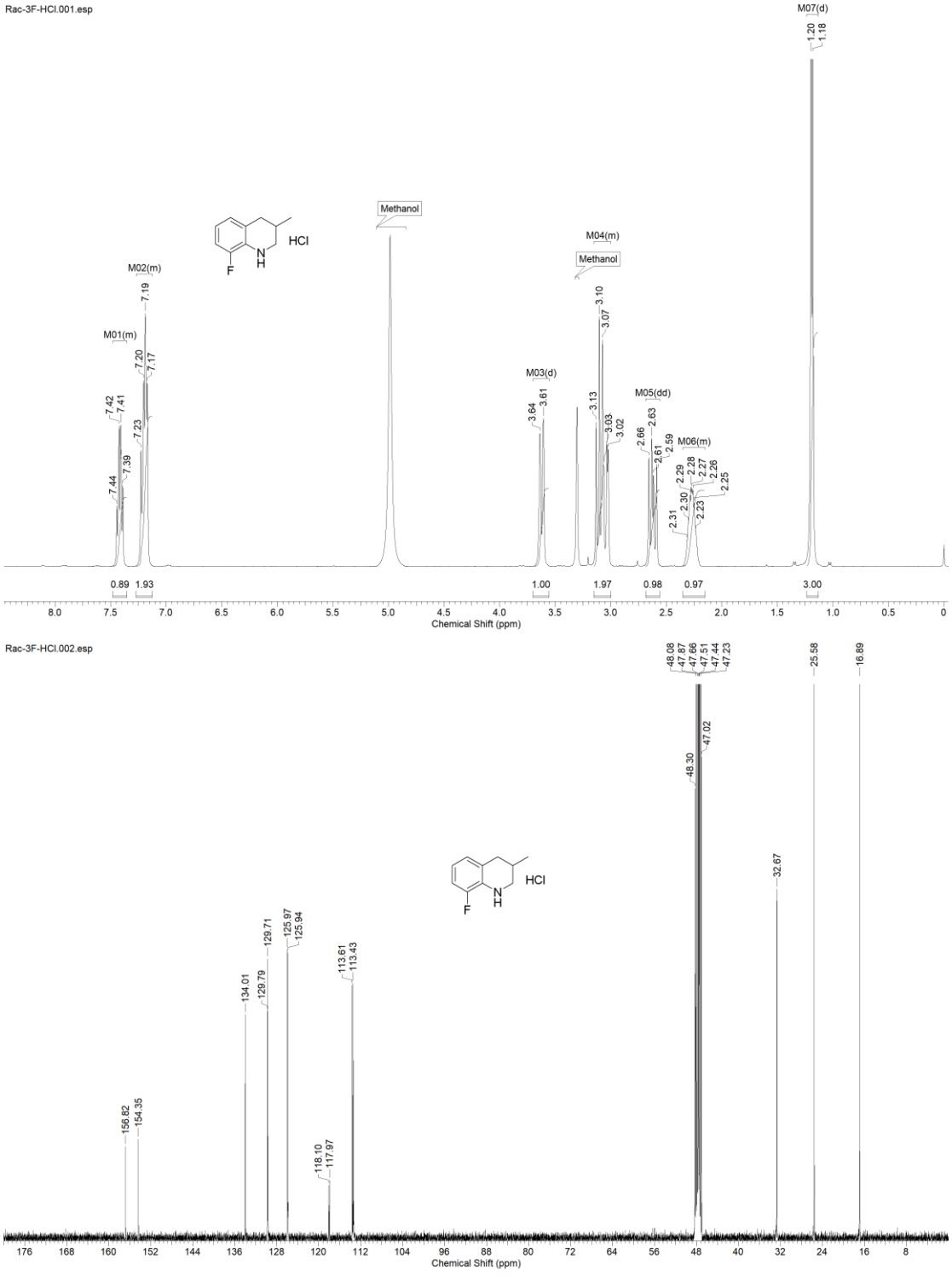
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-3,7-dimethyl-1,2,3,4-tetrahydroquinoline hydrochloride ((*S*)-**6h**)



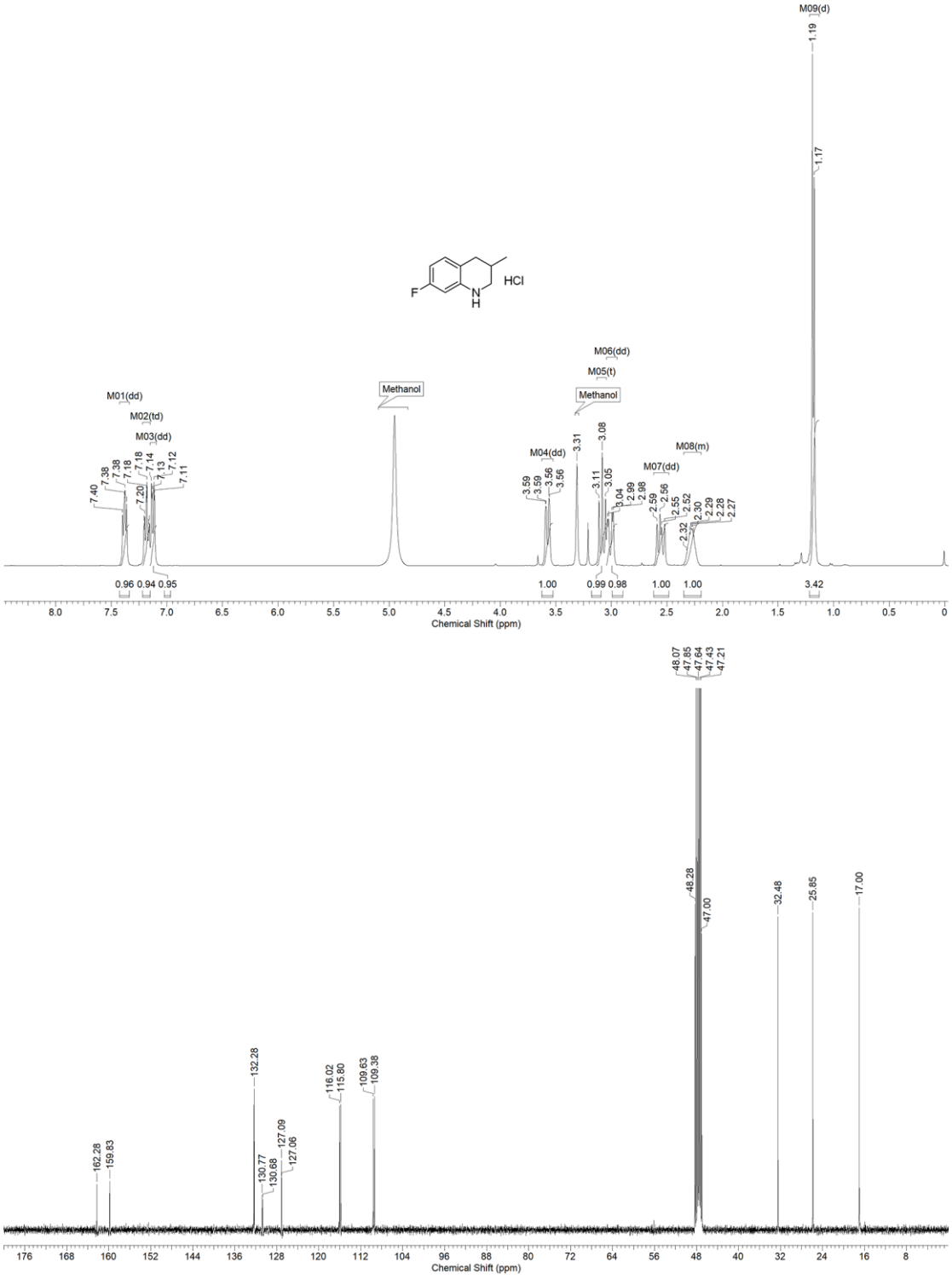
^{1}H-NMR spectra and ^{13}C-NMR spectra of

(*S*)-6-methyl-4,5,6,7-tetrahydrothieno[3,2-b]pyridine hydrochloride ((*S*)-**6i**)



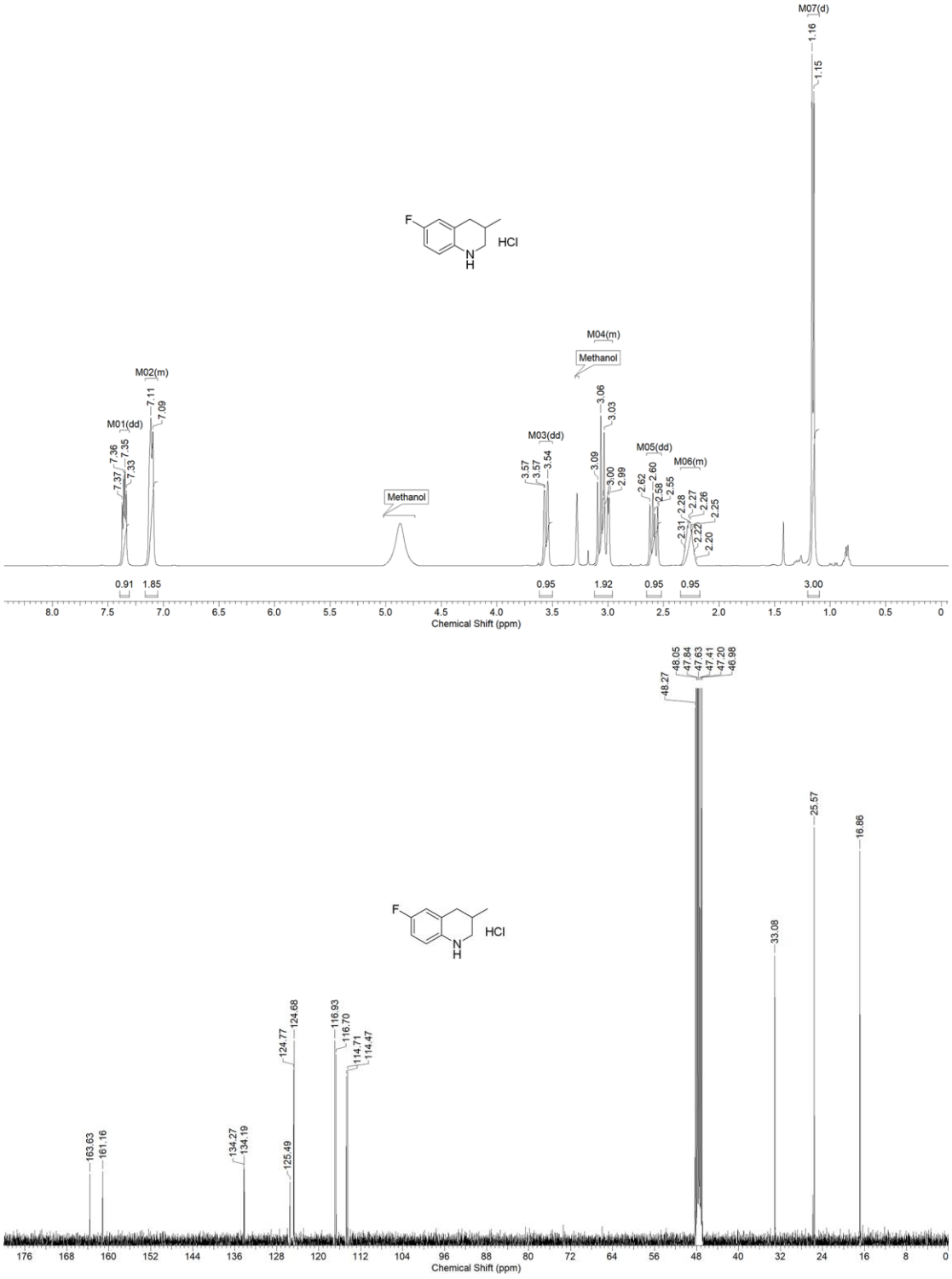
^{1}H-NMR spectra and ^{13}C-NMR spectra of

8-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6c**)



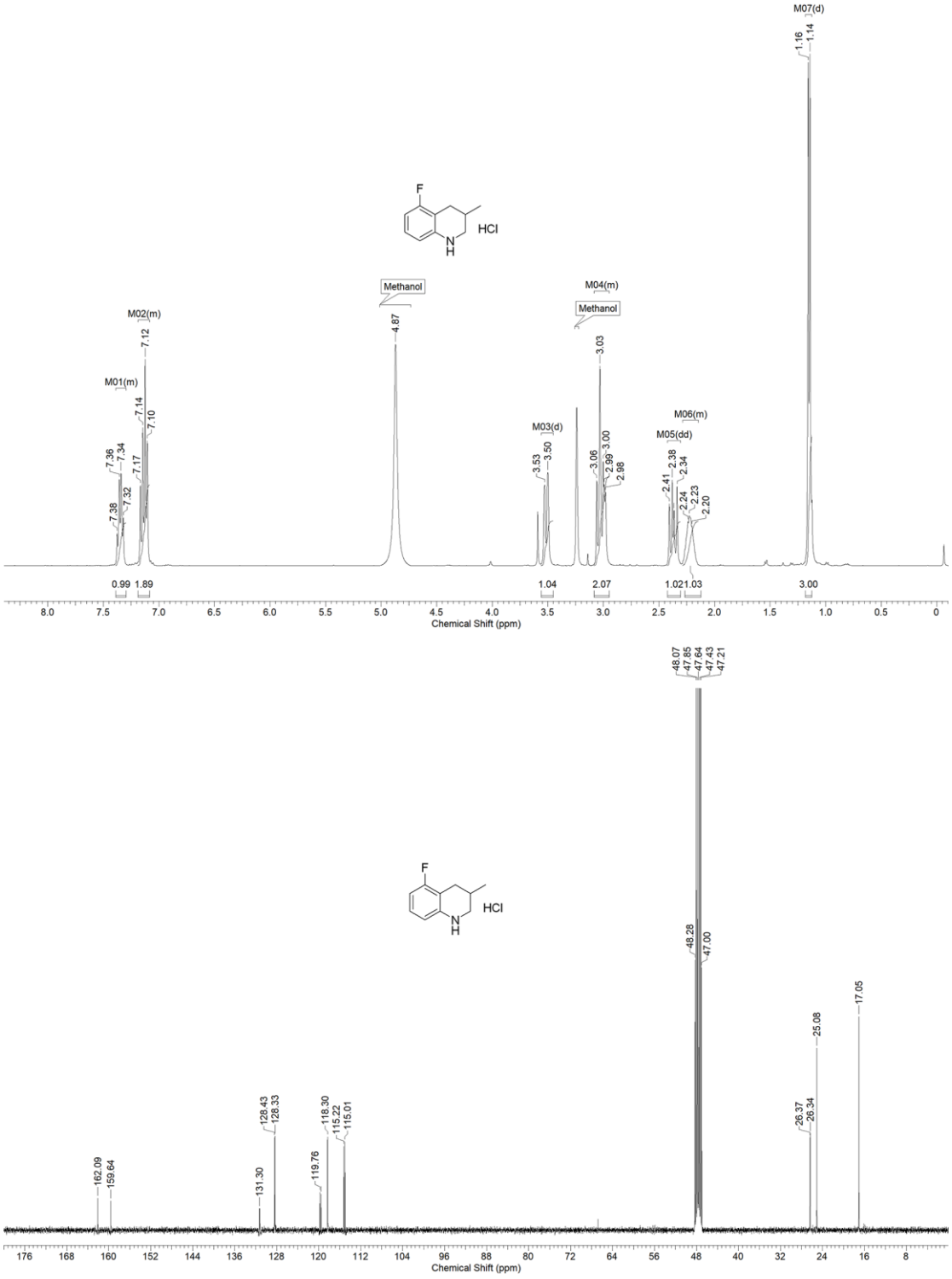
^{1}H-NMR spectra and ^{13}C-NMR spectra of

7-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6d**)



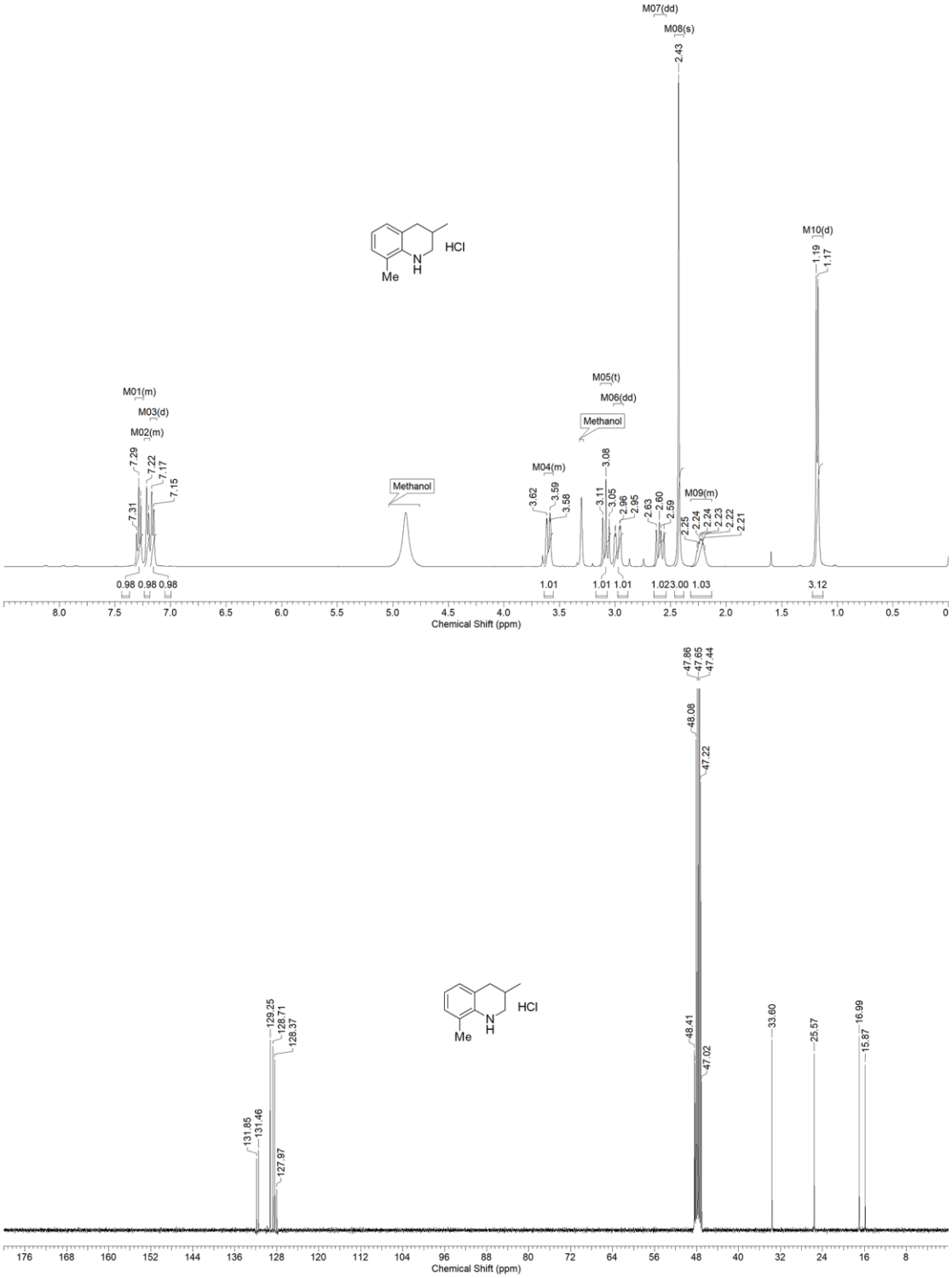
^{1}H-NMR spectra and ^{13}C-NMR spectra of

6-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6e**)



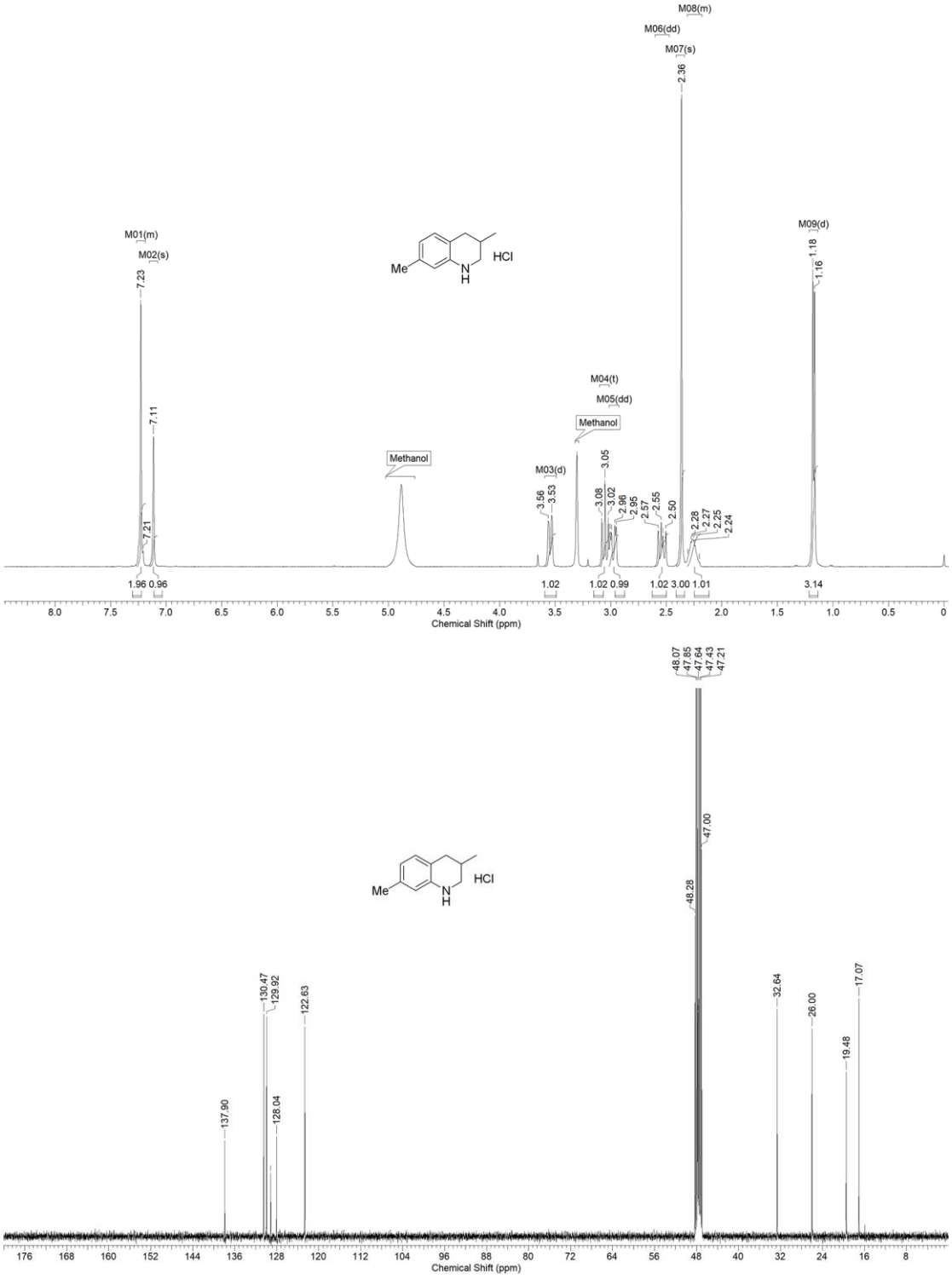
^{1}H-NMR spectra and ^{13}C-NMR spectra of

5-fluoro-3-methyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6f**)



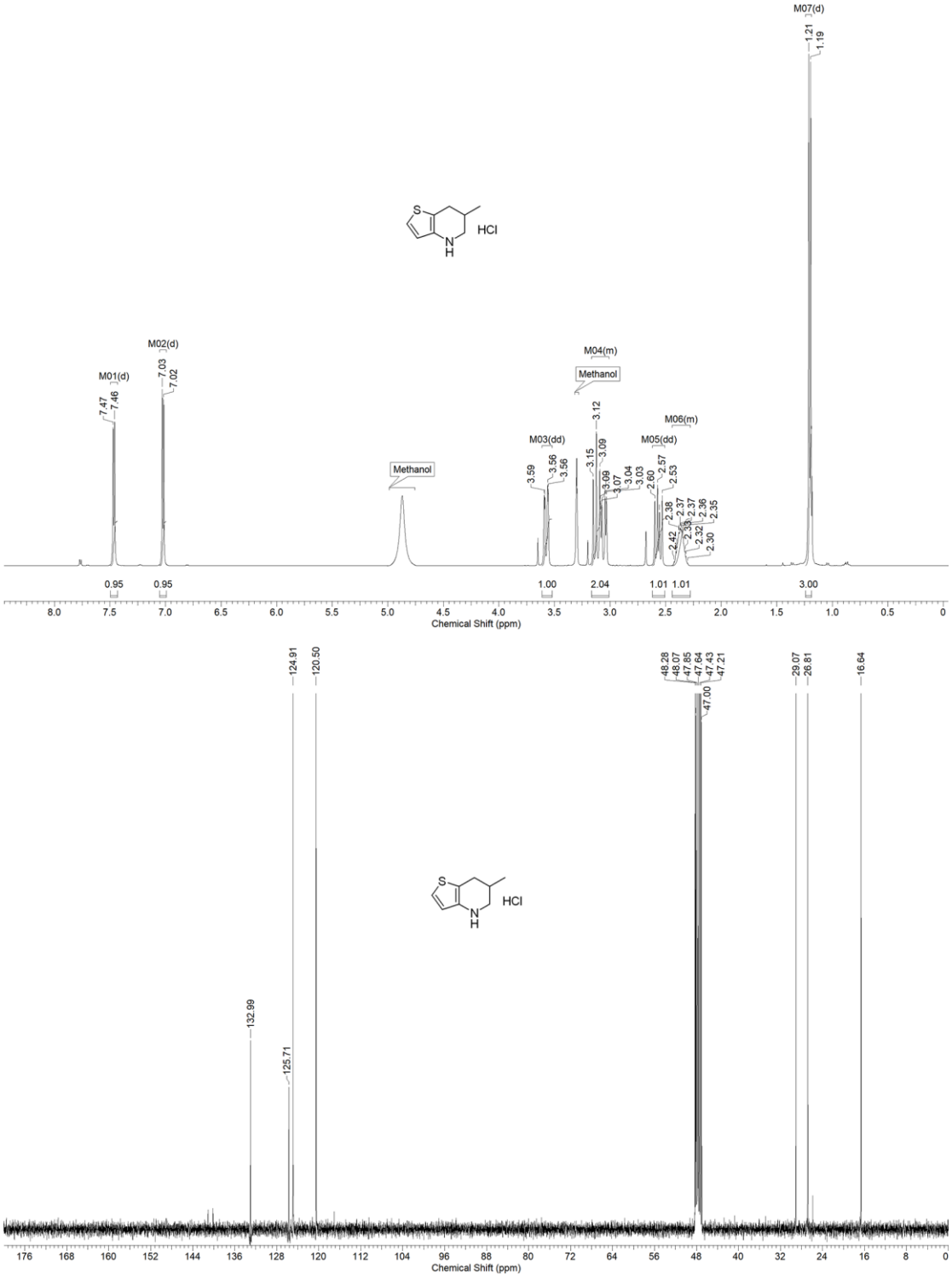
1H-NMR spectra and 13C-NMR spectra of

3,8-dimethyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6g**)



^{1}H-NMR spectra and ^{13}C-NMR spectra of

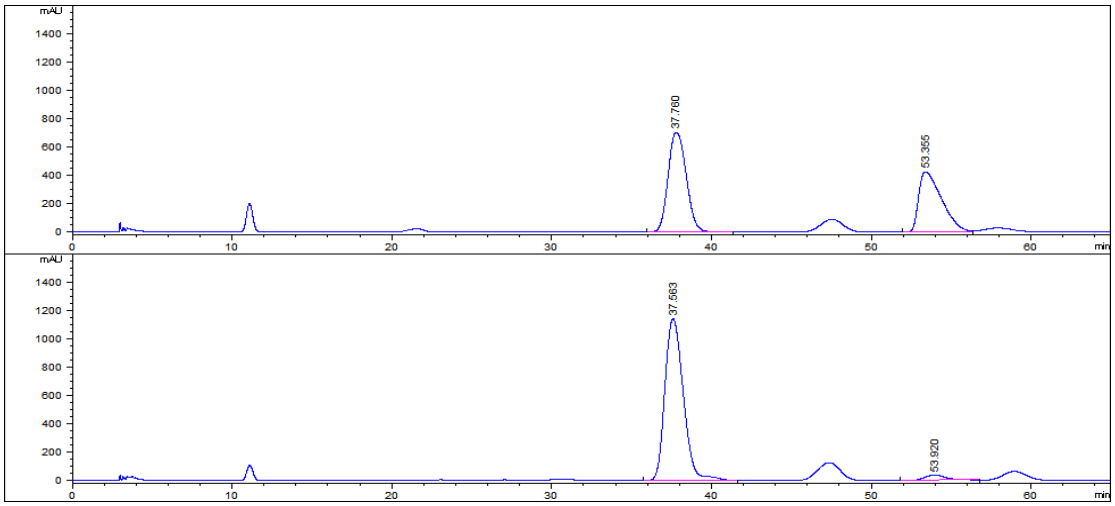
3,7-dimethyl-1,2,3,4-tetrahydroquinoline hydrochloride (Rac-**6h**)



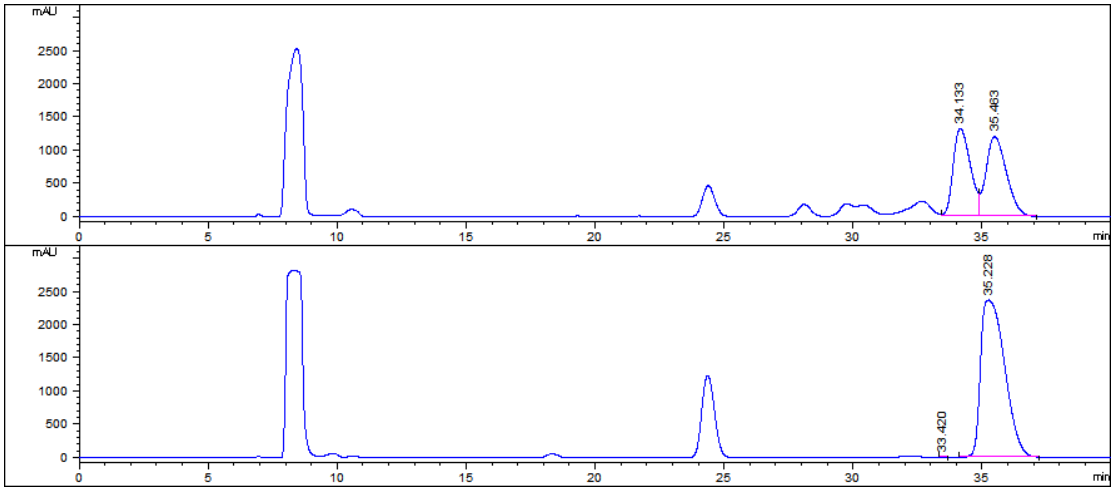
^{1}H-NMR spectra and ^{13}C-NMR spectra of

6-methyl-4,5,6,7-tetrahydrothieno[3,2-b]pyridine (Rac-**6i**)

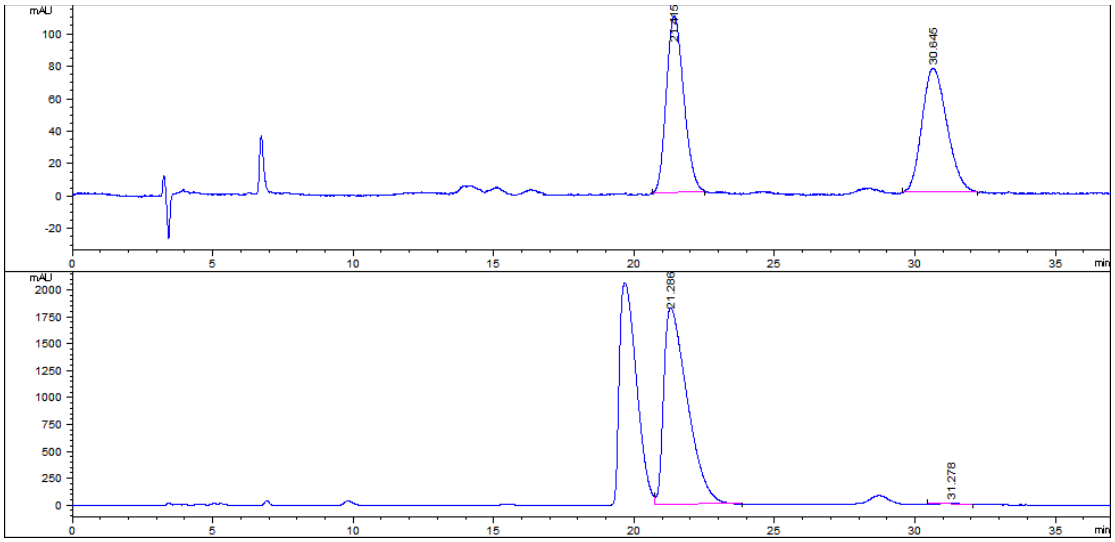
S2.7 HPLC spectra



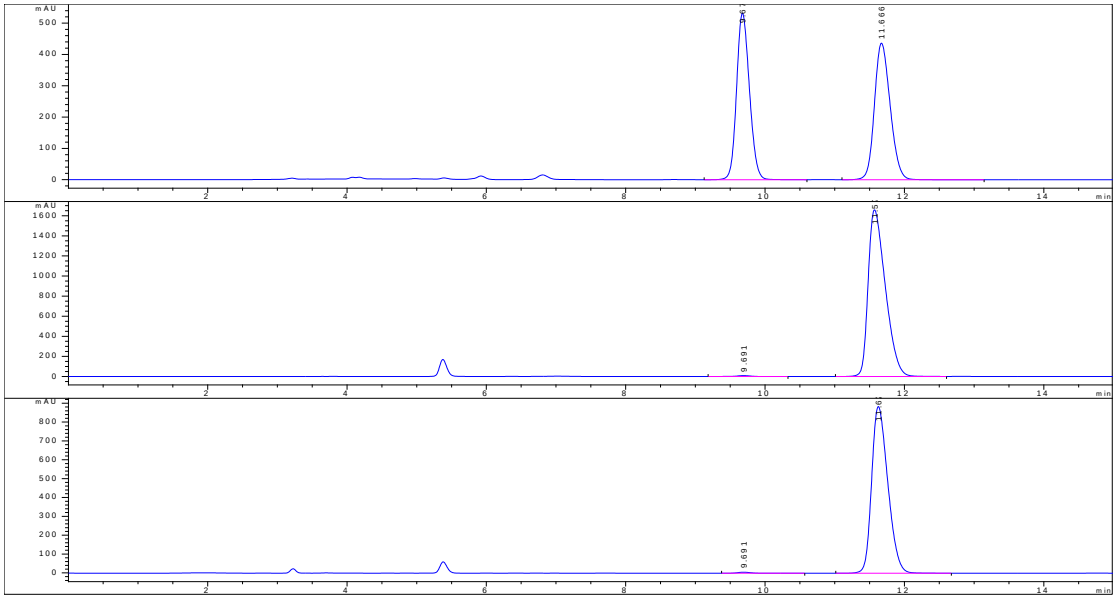
HPLC spectra of racemic **3a'** and enzymatic (*S*)-**3a'**



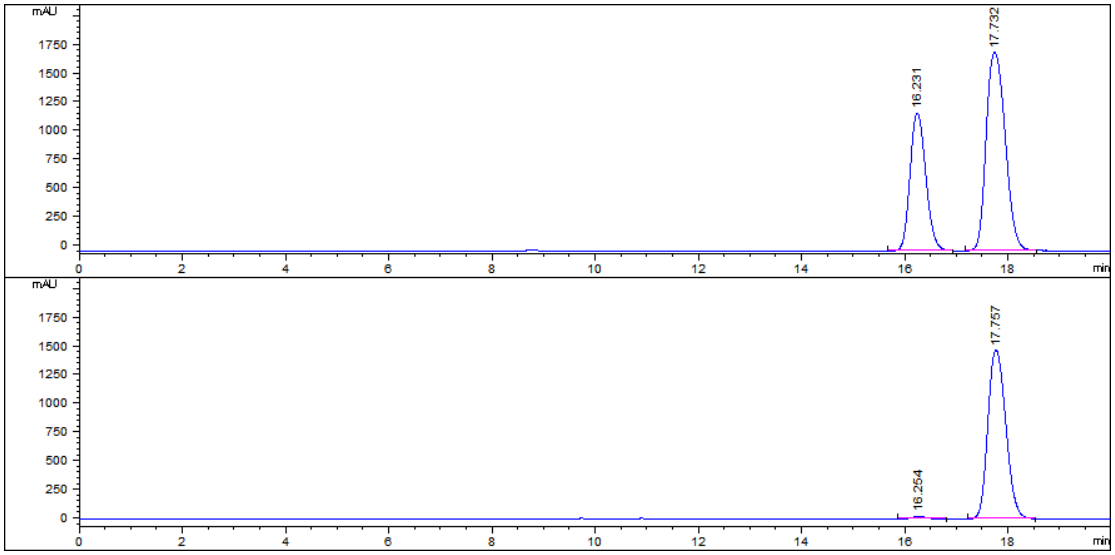
HPLC spectra of racemic **4a** and enzymatic (*S*)-**4a** derivatized with Fmoc N-hydroxysuccinimide.



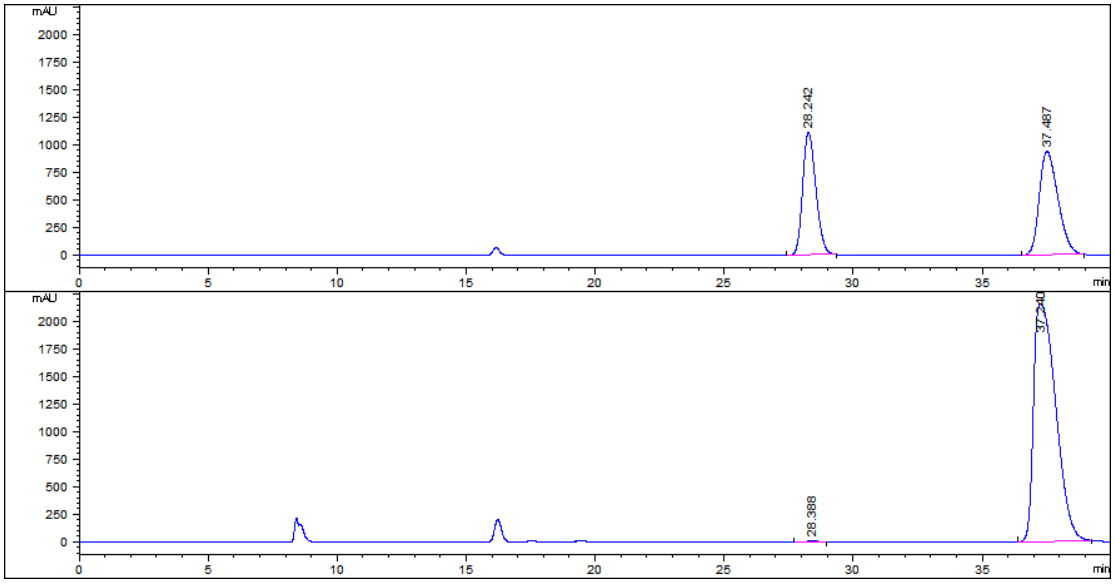
HPLC spectra of racemic **4b** and enzymatic (*S*)-**4b** derivatized with 4-nitrobenzene sulfonyl chloride.



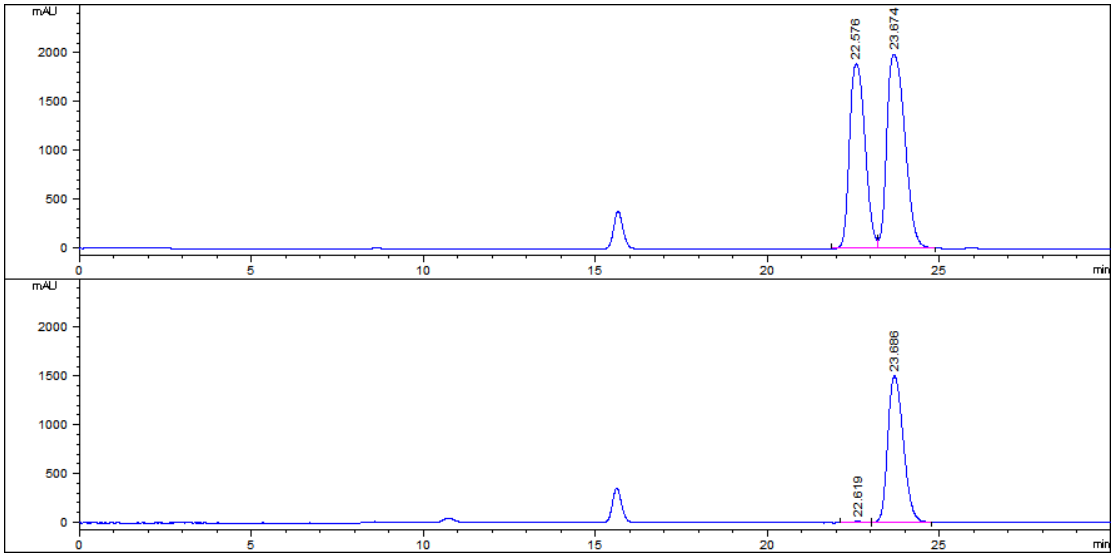
HPLC spectra of racemic **6a**, enzymatic (*S*)-**6a** from **4a** and enzymatic (*S*)-**6a** from **4b**



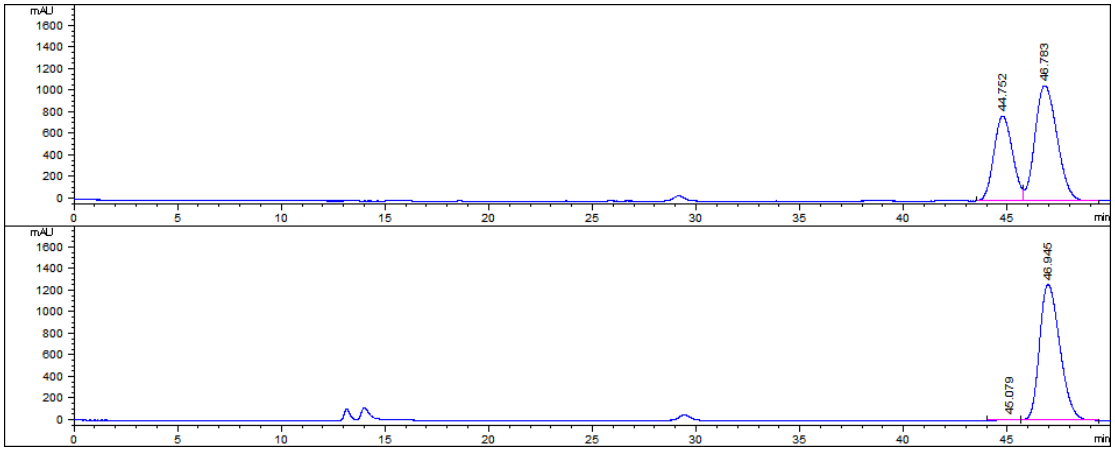
HPLC spectra of racemic **6c** and enzymatic (*S*)-**6c**



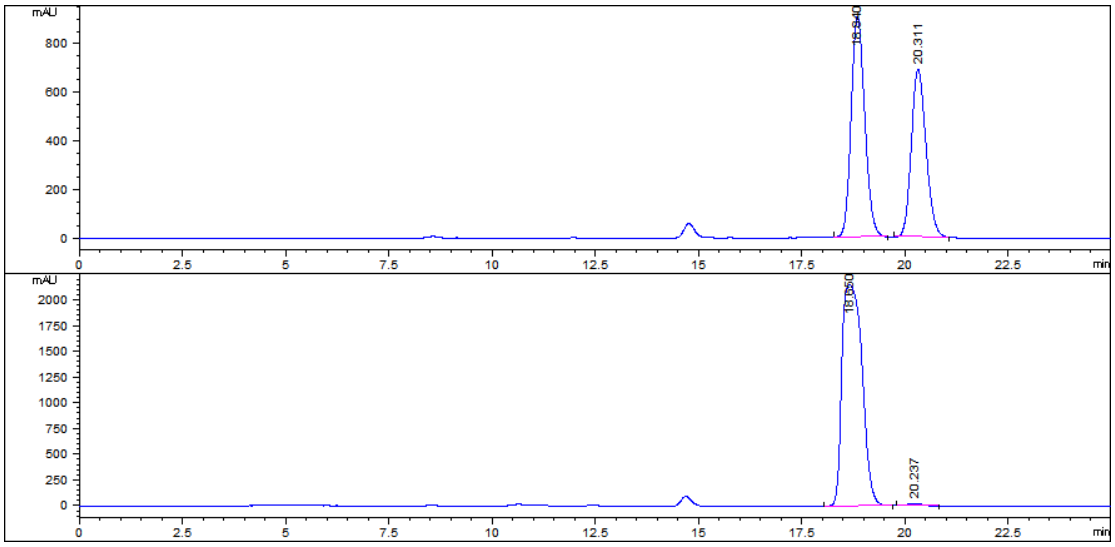
HPLC spectra of racemic **6d** and enzymatic (*S*)-**6d**



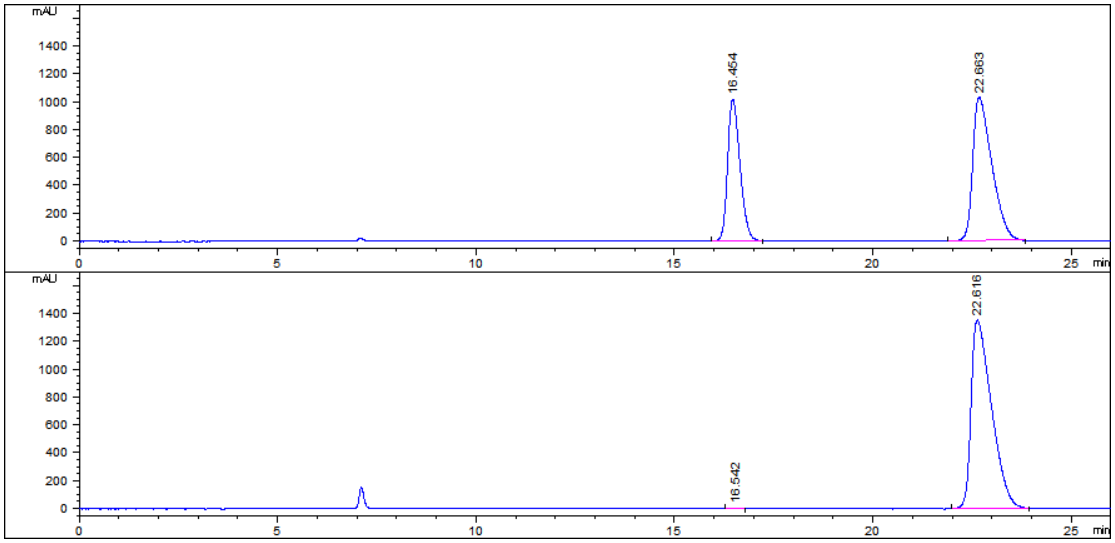
HPLC spectra of racemic **6e** and enzymatic (*S*)-**6e**



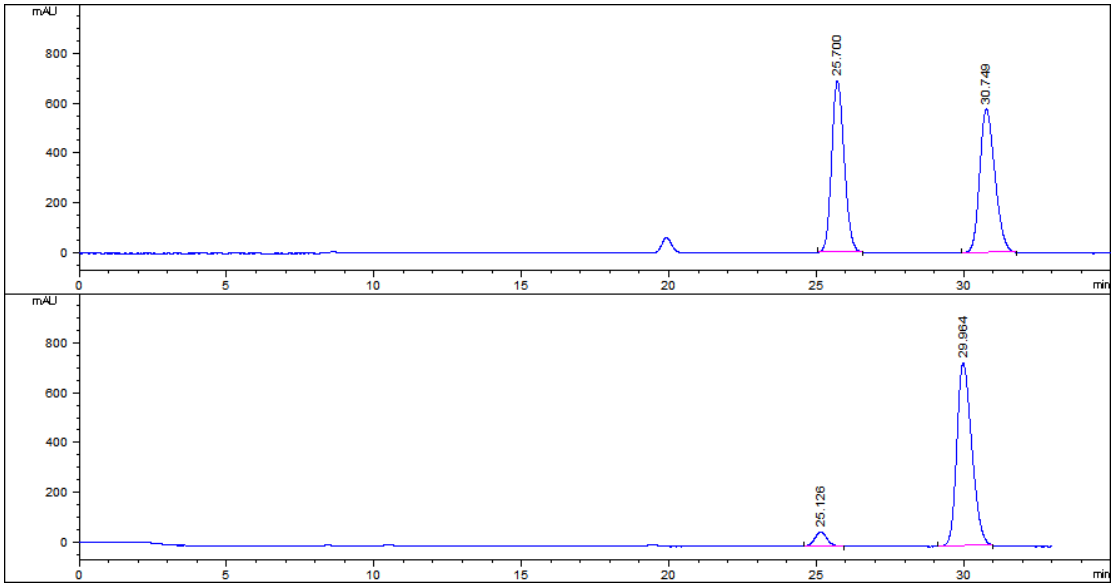
HPLC spectra of racemic **6f** and enzymatic (*S*)-**6f**



HPLC spectra of racemic **6g** and enzymatic (*S*)-**6g**

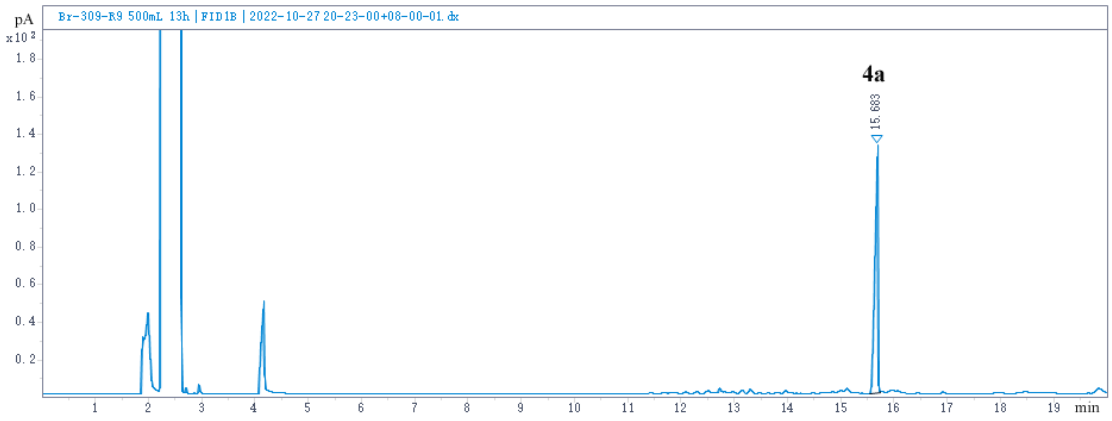


HPLC spectra of racemic **6h** and enzymatic (*S*)-**6h**

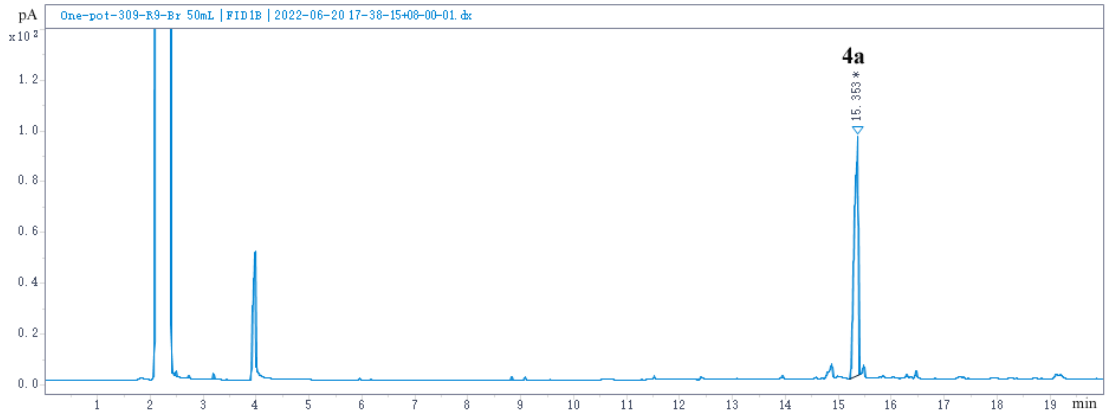


HPLC spectra of racemic **6i** and enzymatic (*S*)-**6i**

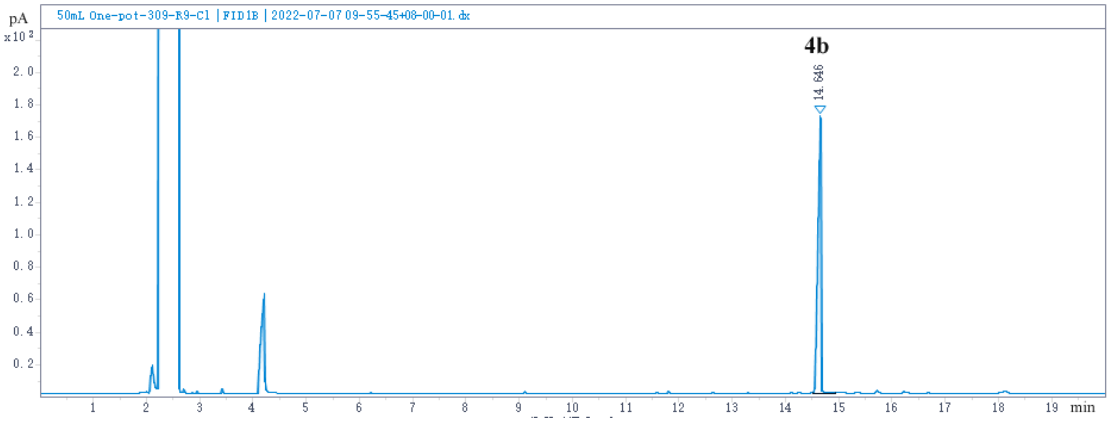
S2.8 GC spectra



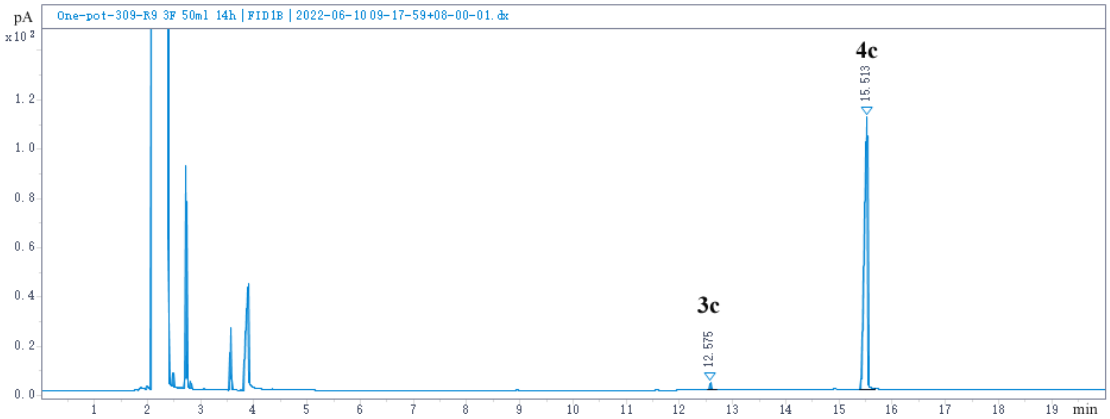
GC chromatograms of the preparative scale reaction (500 mL) crude product of **2a**.



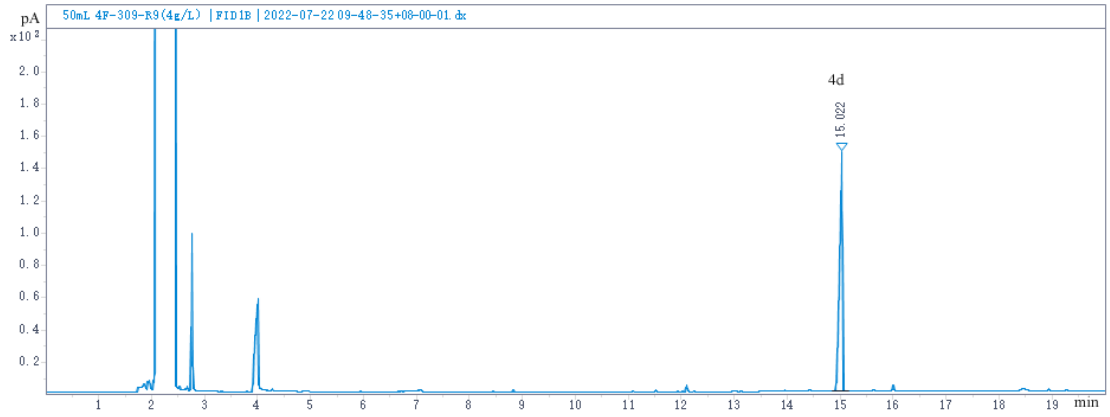
GC chromatograms of the preparative scale reaction (50 mL) crude product of **2a**.



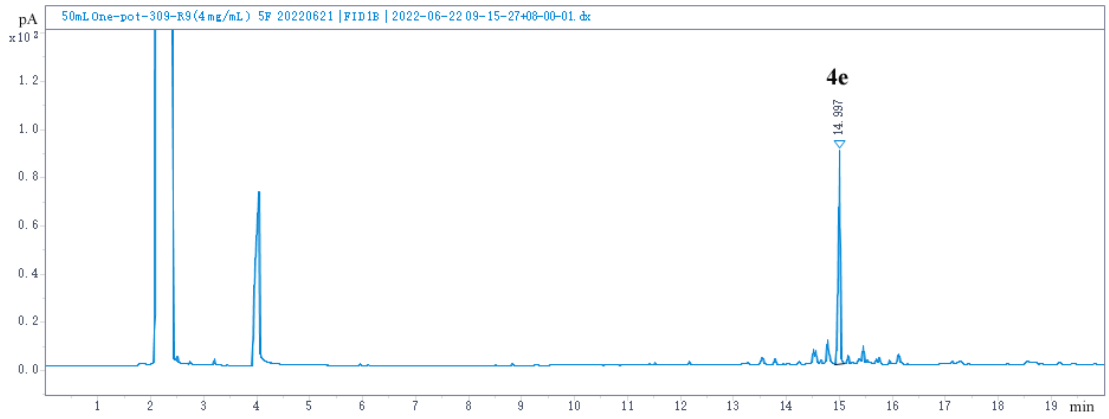
GC chromatograms of the preparative scale reaction (50 mL) crude product of **2b**.



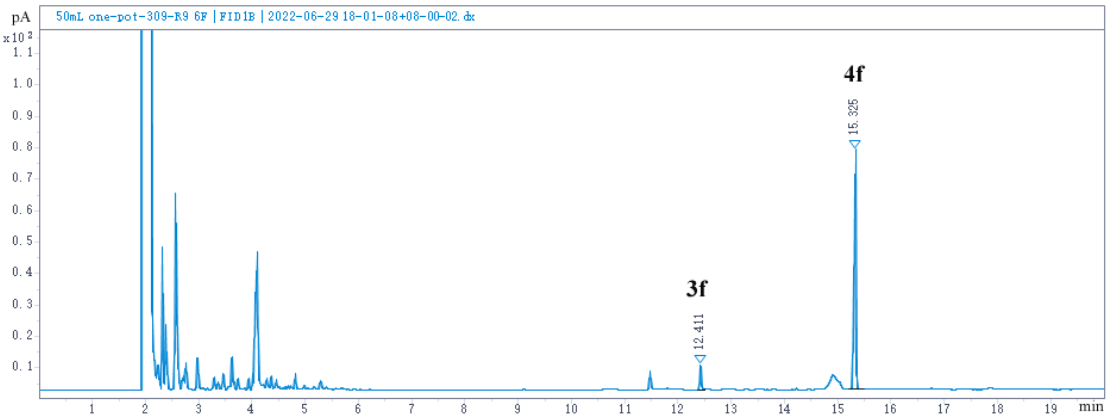
GC chromatograms of the preparative scale reaction (50 mL) crude product of **2c**.



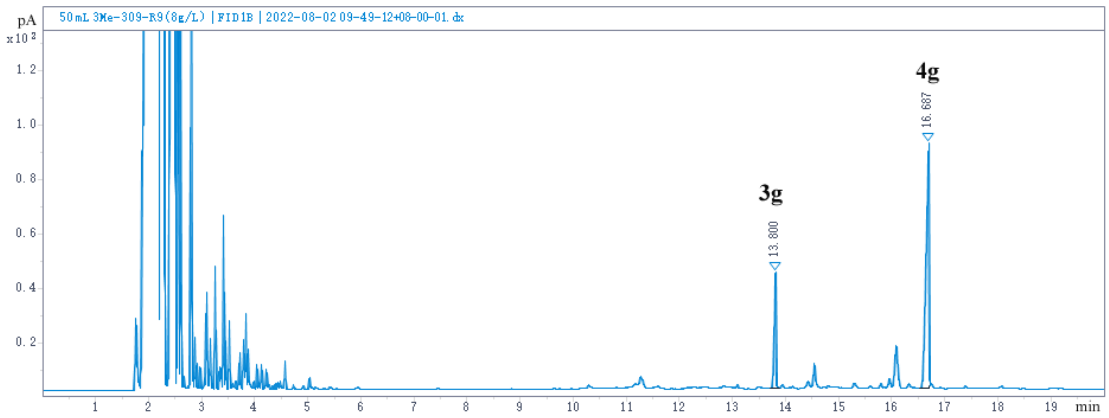
GC chromatograms of the preparative scale reaction (50 mL) crude product of **2d**.



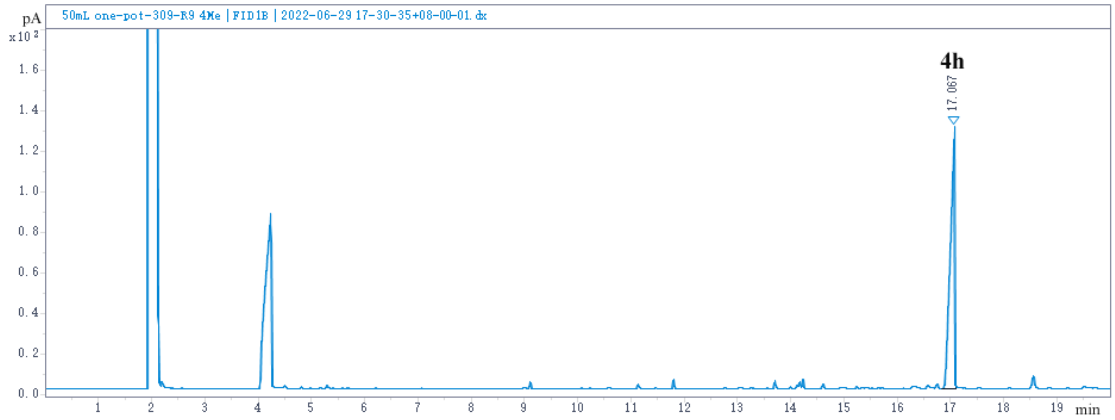
GC chromatograms of the preparative scale reaction (50 mL) crude product of **2e**.



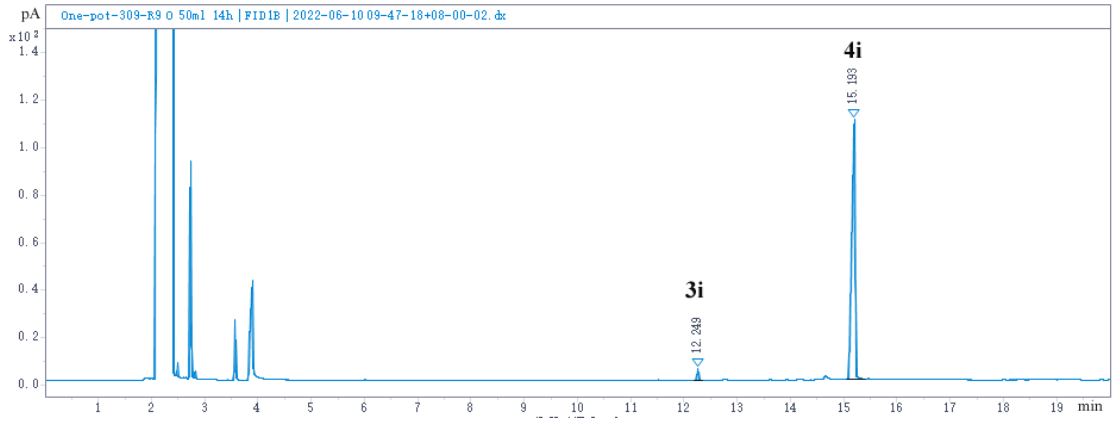
GC chromatograms of the preparative scale reaction (50 mL) crude product of **2f**.



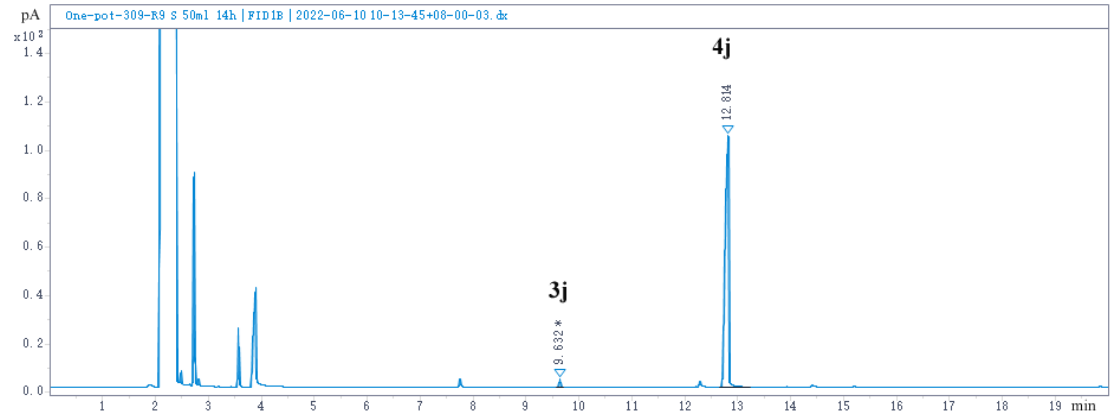
GC chromatograms of the preparative scale reaction (50 mL) crude product of **2g**.



GC chromatograms of the preparative scale reaction (50 mL) crude product of **2h**.



GC chromatograms of the preparative scale reaction (50 mL) crude product of **2i**.



GC chromatograms of the preparative scale reaction (50 mL) crude product of **2j**.

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2 W. Li, W. Duo, C. Zhuang, *Org. Lett.* 2011, **13**, 3538-3541.

3 M. Li, Y. Cui, Z. Xu, X. Chen, J. Feng, M. Wang, P. Yao, Q. Wu, D. Zhu, *Adv. Synth. Catal.* 2022, **364**, 372-379.

4 Z. Xu, P. Yao, X. Sheng, J. Li, J. Li, S. Yu, J. Feng, Q. Wu, D. Zhu, *ACS Catal*. 2020, **10**, 8780-8787.

5 (a) P. Yao, P. Cong, R. Gong, J. Li, G. G. Li, J. Ren, J. Feng, J. Lin, P. C. K. Lau, Q. Wu, D. Zhu, *ACS Catal.* 2018, **8**, 1648-1652; (b) J. R. Marshall, P. Yao, S. L. Montgomery, J. D. Finnigan, T. W. Thorpe, R. B. Palmer, J. Mangas-Sanchez, R. A. M. Duncan, R. S. Heath, K. M. Graham, D. J. Cook, S. J. Charnock, N. J. Turner, *Nat. Chem.* 2021, **13**, 140-148.

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