Electronic Supplementary Information (ESI)

"Optically pure γ-butyrolactones and epoxy esters *via* two stereocentered HKR of 3-substitued epoxy esters: a formal synthesis of (-)-paroxetine, Ro 67-8867 and (+)-eldanolide"

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1. General Information

Solvents were purified and dried by standard procedures before use. Optical rotations were measured using sodium D line on a JASCO-181 digital polarimeter. IR spectra were recorded on a Perkin-Elmer model 683 B and absorption is expressed in cm^{-1}. ^{1}H NMR

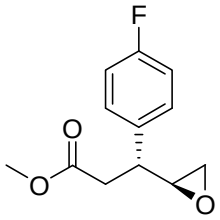
and ^{13}C NMR spectra were recorded on Brucker AC-200 spectrometer unless mentioned otherwise. Elemental analysis was carried out on a Carlo Erba CHNS-O analyzer. Purification was done using column chromatography (60-120 mesh). Enantiomeric excesses were determined on Agilent HPLC instrument equipped with a chiral column. HRMS data were recorded on a Thermo Scientific Q-Exactive, Accela 1250 pump.

2. Experimental Section

2.1 A general experimental procedure for Hydrolytic Kinetic Resolution (HKR) of 3-substituted epoxy esters (7a-h & 10 a-d):

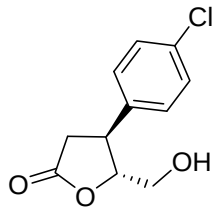
To a solution of (*R*,*R*)- or (*S*,*S*)-(salen)Co(II)complex (0.024 mmol, 0.5 mol %) in toluene (1 mL), acetic acid (0.014 g, 0.24 mmol) was added. It was allowed to stir at 25 °C in open air for 30 min. during which time the color changed from orange-red to a dark brown and it was then concentrated under reduced pressure to get the Co(III)-salen complex-**6** as brown colored solid. To this racemic 3-substituted epoxy esters **7/10** (4.85 mmol) and H_2O (0.043 g, 2.42 mmol) was added at 0 °C. The reaction was allowed to warm to 25 °C and stirred for 12 h. After completion of reaction (monitored by TLC). The crude product was purified by column chromatography over silica gel to give chiral epoxy esters **9a-g** and **12a-d** [solvent system; petroleum ether: ethyl acetate (9:1)] and chiral γ-butyrolactones **8a-g** and **11a-d** [solvent system; petroleum ether: ethyl acetate (1:1)] in pure form.

(*R*)-methyl 3-(4-fluorophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9b)



Yield: 49%, colorless thick liquid; $[\alpha]_D^{25}$ = -7.47 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1736; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.56 (dd, *J* = 2.8, 4.8 Hz, 1H), 2.68-2.75 (m, 2H), 2.86 (dd, *J* = 5.5, 15.6 Hz, 1H), 3.01 (m, 2H), 3.60 (s, 3H), 7.01 (m, 2H), 7.21 (m, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 37.20, 43.97, 46.74, 51.66, 55.11, 115.81 (d, *J* = 21.2 Hz), 129.27 (d, *J* = 8.1 Hz), 135.51 (d, *J* = 3.3 Hz), 162.00 (d, *J* = 245.9 Hz), 171.74; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{12}H_{14}FO_3$: 225.0921 found: 225.0921; **Optical purity**: 99% ee determined by HPLC analysis (Chiral OJ-H column, *n*-hexane/ 2-propanol (90:10), 0.5 mL/min, 254 nm) Retention time: t_{major} = 23.61 and t_{minor} = 29.29 min.

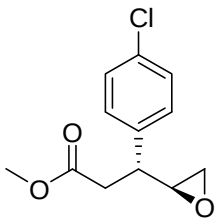
(4*S*, 5*R*)-4-(4-chlorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8c)



Yield: 45%, colorless thick liquid; $[\alpha]_D^{25}$ = -26.6 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1777, 3438; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.35 (br s, 1H), 2.72 (dd, *J* = 9.6, 17.7 Hz, 1H), 3.03 (dd, *J* = 9.1, 17.7 Hz, 1H), 3.60-3.78 (m, 2H), 3.92-4.00 (m, 1H), 4.48 (m, 1H), 7.21 (d, *J* = 8.5 Hz, 2H), 7.35 (d, *J* = 8.6 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 37.17, 41.37, 61.63, 86.94, 128.59, 129.37, 133.70, 137.85, 175.88; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{11}H_{12}ClO_3$: 227.0469 found: 227.0470; **Optical purity**: 98% ee determined

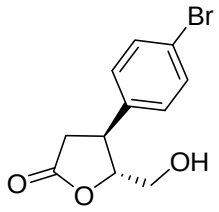
by HPLC analysis (Chiral OJ-H column, *n*-hexane/ 2-propanol (50:50), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 11.21 and t_{major} = 11.64 min.

(*R*)-methyl 3-(4-chlorophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9c)



Yield: 48%, colorless thick liquid; $[\alpha]_D^{25}$ = -11.8 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1736; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.56 (dd, *J* = 2.4, 4.7 Hz, 1H), 2.65-3.09 (m, 5H), 3.60 (s, 3H), 7.16 (m, 2H), 7.30 (m, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 36.93, 44.03, 46.65, 51.64, 54.89, 128.85, 129.01, 133.14, 138.29, 171.59; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{12}H_{14}ClO_3$: 241.0626 found: 241.0626; **Optical purity**: 98% ee determined by HPLC analysis (OD-H column, *n*-hexane/ 2-propanol (90:10), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 12.79 and t_{major} = 13.53 min.

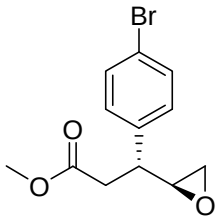
(4*S*, 5*R*)-4-(4-bromophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8d)



Yield: 46%, colorless thick liquid; $[\alpha]_D^{25}$ = -21.2 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1775, 3440; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.30 (br s, 1H), 2.72 (dd, *J* = 9.6, 17.8 Hz, 1H), 3.03 (dd, *J* = 9.1, 17.7 Hz, 1H), 3.59-3.77 (m, 2H), 3.93-3.99 (m, 1H), 4.48 (m, 1H), 7.15 (d, *J* = 8.5 Hz, 2H), 7.50 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 37.04,

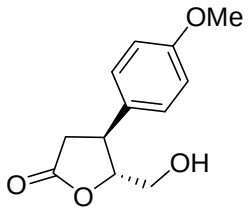
41.35, 61.48, 86.94, 121.55, 128.93, 132.19, 138.31, 176.16; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{11}H_{12}BrO_3$: 270.9964 found: 270.9965; **Optical purity**: 96% ee determined by HPLC analysis (Chiral OJ-H column, *n*-hexane/ 2-propanol (50:50), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 11.91 and t_{major} = 12.47 min.

(*R*)-methyl 3-(4-bromophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9d)



Yield: 48%, colorless thick liquid; $[\alpha]_D^{25}$ = -8.8 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1734; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.55 (dd, *J* = 2.3, 4.7 Hz, 1H), 2.65-3.09 (m, 5H), 3.60 (s, 3H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.3 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 36.76, 43.99, 46.52, 51.54, 54.71, 121.12, 129.33, 131.70, 138.79, 171.45; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{12}H_{14}BrO_3$: 285.0121 found: 285.0121; **Optical purity**: 96% ee determined by HPLC analysis (OD-H column, *n*-hexane/ 2-propanol (95:5), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 13.54 and t_{major} = 14.33 min.

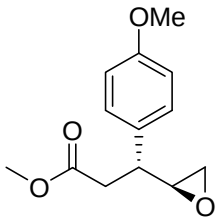
(4*S*, 5*R*)-5-(hydroxymethyl)-4-(4-methoxyphenyl)dihydro- furan-2(3*H*)-one (8e)



Yield: 48%, colorless solid m.p.: 93 °C; $[\alpha]_D^{25}$ = -26.6 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1764, 3449; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.17-2.32 (m, 1H), 2.73 (dd, *J* = 10.2, 17.8

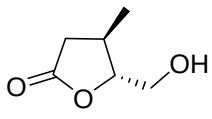
Hz, 1H), 2.98 (dd, *J* = 8.9, 17.7 Hz, 1H), 3.58-3.71 (m, 2H), 3.80 (s, 3H), 3.89-3.97 (m, 1H), 4.47 (m, 1H), 6.88 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 37.33, 41.25, 55.19, 61.67, 87.33, 114.51, 128.23, 131.06, 159.05, 176.15; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{12}H_{15}O_4$: 223.0965 found: 223.0964; **Optical purity**: 97% ee determined by HPLC analysis (Chiral OJ-H column, *n*-hexane/ 2-propanol (50:50), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 13.27 and t_{major} = 14.03 min.

(*R*)-methyl 3-(4-methoxyphenyl)-3-((*S*)-oxiran-2-yl)propano- ate (9e)



Yield: 47%, colorless liquid; **$[\alpha]_D^{25}$** = -25.0 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1735; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.56 (dd, *J* = 2.5, 4.8 Hz, 1H), 2.70-3.08 (m, 5H), 3.6 (s, 3H), 3.79 (s, 3H), 6.84 (d, *J* = 8.6 Hz, 2H), 7.15 (d, *J* = 8.7 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 37.41, 44.04, 46.82, 51.48, 55.00, 55.30, 114.03, 128.54, 131.70, 158.68, 171.86; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{13}H_{17}O_4$: 237.1121 found: 237.1119; **Optical purity**: 96% ee determined by HPLC analysis (OD-H column, *n*-hexane/ 2-propanol (90:10), 0.5 mL/min, 254 nm) Retention time: t_{minor}= 14.90 and t_{major} = 15.54 min.

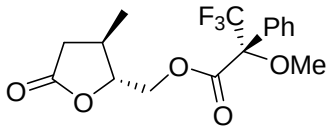
(4*R*, 5*R*)-5-(hydroxymethyl)-4-methyldihydrofuran-2(3*H*)-one (8f)



Yield: 46%, colorless liquid; **$[\alpha]_D^{25}$** = -51.0 (*c* 1, $CHCl_3$) {lit.[1] $[\alpha]_D$ +49.4 for its antipode }; **IR**: ($CHCl_3$, cm^{-1}) 1770, 3419; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 1.17 (d, *J* = 6.6 Hz, 3H), 2.16 (br s, 1H), 2.21 (dd, *J* = 8.6, 16.8 Hz, 1H), 2.43-2.65 (m, 1H), 2.76 (dd, *J* = 8.5, 16.8 Hz, 1H), 3.61-3.72 (m, 1H), 3.87-3.97 (m, 1H), 4.13 (m, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 17.67, 30.88, 36.80, 62.10, 87.46, 177.07; **Anal.** Calcd for $C_6H_{10}O_3$ requires C, 55.37; H, 7.74; found C, 55.39; H, 7.80%. **Optical purity**: 97% determine from Mosher's ester.

Synthesis of Mosher's Ester

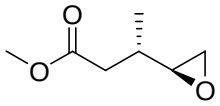
(2*R*)-((2*R*,3*R*)-tetrahydro-3-methyl-5-oxofuran-2-yl)methyl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate:



To a stirred solution of **8f** (50 mg, 0.38 mmol), DCC (95 mg, 0.46 mmol) and catalytic N,N-diaminopyridine (5 mg, 10 mol%), Mosher's acid [(R)-(+)-α-Methoxy-α-trifluoro-methylphenyl acetic acid] (108 mg, 0.46mmol) in CH_2Cl_2 (2 mL) was added at 0 ^oC and allowed to stir for 2 h at same tempreture. After the completion of reaction (monitored by TLC), it was quenched with water and extracted with CH_2Cl_2 (2 x 3 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product corresponding Mosher's ester. Column chromatographic purification with silica gel using petroleum ether: ethyl acetate (7:3) as eluent gave to give pure corresponding Mosher's ester.

Yield: 68%, colorless liquid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.17 (d, *J* = 6.8 Hz, 3H), 2.16 (dd, *J* = 8.3, 17.3 Hz, 1H), 2.34 (m, 1H), 2.64 (dd, *J* = 8.5, 17.6 Hz, 1H), 3.53 (s, 3H), 4.25 (m, 1H), 4.39 (dd, *J* = 5.3, 12.3 Hz, 1H), 4.57 (dd, *J* = 2.8, 12.1 Hz, 1H), 7.41 (m, 3H), 7.51 (m, 2H); **^{19} F NMR** (400 MHz, $CDCl_3$+CF_3COOH) δ -72.17 (minor diasteromer, integral = 1%), -72.27 (major diastereomer, integral = 58.46%) [Ratio of diasteromer major : minor, 98.32 : 1.68]

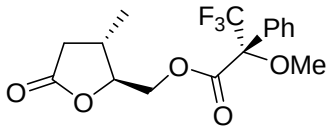
(*S*)-methyl 3-((*S*)-oxiran-2-yl)butanoate (9f)



Yield: 48%, colorless liquid; **$[\alpha]_D^{25}$** = +3.5 (*c* 1, $CHCl_3$) {lit.[2] $[\alpha]_D^{25}$ +3.8 (*c* 2, $CHCl_3$)}; **IR**: ($CHCl_3$, cm^{-1}) 1737; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 1.03 (d, *J* = 6.9 Hz, 3H), 1.86 (m, 1H), 2.27 (dd, *J* = 8.2, 15.2 Hz, 1H), 2.50-2.60 (m, 2H), 2.73-2.84 (m, 2H), 3.69 (s, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 15.66, 33.24, 38.05, 46.11, 51.33, 55.43, 172.35; **Anal**. Calcd for $C_7H_{12}O_3$ requires C, 58.32; H, 8.39; found C, 58.28; H, 8.42%.

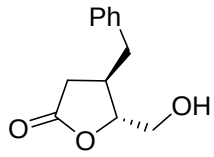
Optical purity: 96% determine from Mosher's ester (Note: epoxide **9f** was opened with water using non-chiral way then corresponning lactone is used for the preparation of corresponding Mosher's ester).

(2*R*)-((2*S*,3*S*)-tetrahydro-3-methyl-5-oxofuran-2-yl)methyl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate:



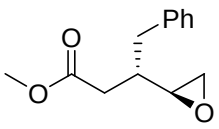
Yield: 56%, colorless liquid,**^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.16 (d, *J* = 6.8 Hz, 3H), 2.13 (dd, *J* = 7.8, 17.6 Hz, 1H), 2.30 (m, 1H), 2.57 (dd, *J* = 8.5, 17.3 Hz, 1H), 3.54 (s, 3H), 4.27 (m, 1H), 4.34 (dd, *J* = 4.3, 12.3 Hz, 1H), 4.61 (dd, *J* = 2.5, 12.1 Hz, 1H), 7.41 (m, 3H), 7.50 (m, 2H); **^{19} F NMR** (400 MHz, $CDCl_3$+CF_3COOH) δ -72.26 (major diastereomer, integral = 51.56%), -72.36 (minor diasteromer, integral = 1%) [Ratio of diasteromer major : minor , 98.10 : 1.90].

(4*R*, 5*R*)-4-benzyl-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8g)



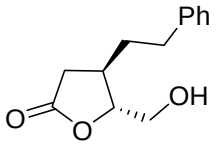
Yield: 47%, colorless thick liquid; **$[\alpha]_D^{25}$** = -38.0 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1773, 3421; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.12 (t, *J* = 6.6 Hz, 1H), 2.26-2.42 (m, 1H), 2.64-2.86 (m, 4H), 3.40-3.52 (m, 1H), 3.72-3.83 (m, 1H), 4.28 (m, 1H), 7.13-7.18 (m, 2H), 7.23-7.36 (m, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 34.90, 37.50, 39.19, 62.83, 85.33, 126.70, 128.68, 138.10, 176.80; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{12}H_{15}O_3$: 207.1016 found: 207.1014; **Optical purity**: 99% ee determined by HPLC analysis (Chiral OD-H column, *n*-hexane/ 2-propanol (50:50), 0.5 mL/min, 254 nm) Retention time: t_{major} = 9.94 and t_{minor} = 11.41 min.

(*S*)-methyl 3-((*S*)-oxiran-2-yl)-4-phenylbutanoate (9g)



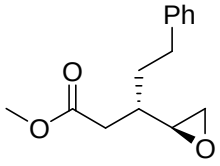
Yield: 48%, colorless liquid; $[\alpha]_D^{25}$ = -3.0 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1737; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.01 (m, 1H), 2.26 (dd, *J* = 2.7, 4.8 Hz, 1H), 2.32-2.56 (m, 2H), 2.60-2.89 (m, 4H), 3.67 (s, 3H), 7.14-7.31 (m, 5H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 35.89, 37.55, 40.47, 47.01, 51.42, 54.20, 126.28, 128.31, 129.01, 138.89, 172.37; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{13}H_{17}O_3$: 221.1172 found: 221.1172; **Optical purity**: 97% ee determined by HPLC analysis (OD-H column, *n*-hexane/ 2-propanol (90:10), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 13.08 and t_{major} = 13.56 min.

(4*R*, 5*R*)-5-(hydroxymethyl)-4-phenethyldihydrofuran-2(3*H*)-one (8h)



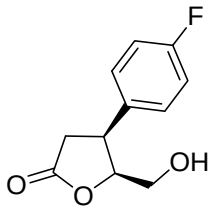
Yield: 48%, colorless thick liquid; $[\alpha]_D^{25}$ = -54.8 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1772, 3440; **^{1}H NMR** (200 MHz, $CDCl_3$) 1.69-2.00 (m, 2H), 2.19-2.31 (m, 2H), 2.36-2.54 (m, 1H), 2.62-2.81 (m, 3H), 3.57-3.68 (m, 1H), 3.86-3.93 (m, 1H), 4.23 (m, 1H), 7.12-7.33 (m, 5H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 33.71, 35.14, 35.21, 35.85, 62.89, 85.93, 126.26, 128.19, 128.57, 140.68, 176.77; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{13}H_{17}O_3$: 221.1172 found: 221.1169; **Optical purity**: 96% ee determined by HPLC analysis (Chiral OD-H column, *n*-hexane/ 2-propanol (50:50), 0.5 mL/min, 254 nm) Retention time: t_{major} = 13.45 and t_{minor} = 14.48 min.

(*S*)-methyl 3-((*S*)-oxiran-2-yl)-5-phenylpentanoate (9h)



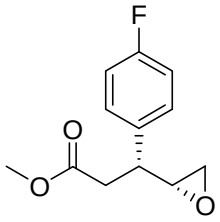
Yield: 48%, colorless liquid; $[\alpha]_D^{25}$ = -5.9 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1743; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 1.77 (m, 3H), 2.34-2.87 (m, 7H), 3.68 (s, 3H), 7.14-7.30 (m, 5H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 33.01, 33.25, 36.48, 38.18, 47.18, 51.42, 54.52, 125.91, 128.11, 128.33, 141.42, 172.43; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{14}H_{19}O_3$: 235.1329 found: 235.1329; **Optical purity**: 96% ee determined by HPLC analysis (OD-H column, *n*-hexane/ 2-propanol (90:10), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 14.79 and t_{major} = 15.35 min.

(4*S*, 5*S*)-4-(4-fluorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (11b)



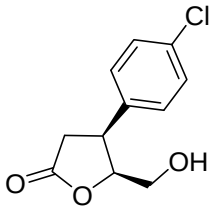
Yield: 46%, colorless solid m.p.: 113 °C; $[\alpha]_D^{25}$ = -156.12 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1774, 3415; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.15 (br s, 1H), 2.84 (dd, *J* = 9.1, 17.3 Hz, 1H), 3.01 (dd, *J* = 8.7, 17.3 Hz, 1H), 3.33-3.44 (m, 1H), 3.51-3.62 (m, 1H), 3.88 (q, *J* = 8.6 Hz, 1H), 4.74 (m, 1H), 7.01-7.09 (m, 2H), 7.21-7.28 (m, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 34.81, 42.82, 61.94, 83.12, 115.81 (d, *J* = 21.6 Hz), 129.38 (d, *J* = 7.7 Hz), 132.16 (d, *J* = 3.1 Hz), 162.26 (d, *J* = 247.4 Hz), 176.34; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{11}H_{12}FO_3$: 211.0765 found: 211.0766; **Optical purity**: 98% ee determined by HPLC (OJ-H column, *n*-hexane/ 2-propanol (50:50), 0.5 mL/min, 254 nm) Retention time: t_{major} = 10.83 and t_{minor} = 18.58 min.

(*R*)-methyl 3-(4-fluorophenyl)-3-((*R*)-oxiran-2-yl)propanoate (12b)



Yield: 48%, colorless liquid; $[\alpha]_D^{25}$ = +10.4 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1736; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.43 (dd, *J* = 2.5, 4.8 Hz, 1H), 2.56-2.82 (m, 3H), 3.09-3.15 (m, 1H), 3.24-3.34 (m, 1H), 3.63 (s, 3H), 6.95-7.04 (m, 2H), 7.16-7.26 (m, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 36.71, 42.22, 45.69, 51.63, 54.36, 115.60 (d, *J* = 21.2 Hz), 129.51 (d, *J* = 8.1 Hz), 135.04 (d, *J* = 3.3 Hz), 162.00 (d, *J* = 245.9 Hz), 171.62; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{12}H_{14}FO_3$: 225.0921 found: 225.0921; **Optical purity**: 98% ee determined by HPLC analysis (OD-H column, *n*-hexane/ 2-propanol (90:10), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 12.77 and t_{major} = 13.11 min.

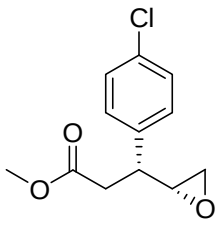
(4*S*, 5*S*)-4-(4-chlorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (11c)



Yield: 47%, colorless solid m.p.: 108 °C; $[\alpha]_D^{25}$ = -110.11 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1775, 3436; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.29 (t, *J* = 6.3 Hz, 1H), 2.86 (dd, *J* = 9.1, 17.3 Hz, 1H), 3.00 (dd, *J* = 8.7, 17.3 Hz, 1H), 3.36 (m, 1H), 3.57 (m, 1H), 3.87 (q, *J* = 8.6 Hz, 1H), 4.75 (m, 1H), 7.19 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.6 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 34.53, 42.74, 61.66, 83.28, 128.95, 129.15, 133.55, 134.92, 176.87; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{11}H_{12}ClO_3$: 227.0469 found: 227.0470; **Optical**

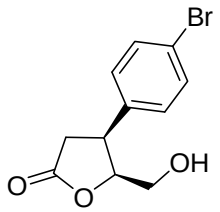
purity: 99% ee determined by (OJ-H column, *n*-hexane/ 2-propanol (50:50), 0.5 mL/min, 254 nm) Retention time: t_{major} = 10.99 and t_{minor} = 12.08 min.

(*R*)-methyl 3-(4-chlorophenyl)-3-((*R*)-oxiran-2-yl)propanoate (12c)



Yield: 46%, colorless liquid; $[\alpha]_D^{25}$ = + 9.4 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1736; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.44 (dd, *J* = 2.6, 4.8 Hz, 1H), 2.57-2.83 (m, 3H), 3.10-3.16 (m, 1H), 3.23-3.33 (m, 1H), 3.63 (s, 3H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.6 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 36.56, 42.40, 45.76, 51.71, 54.25, 128.71, 129.30, 133.11, 137.79, 171.58; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{12}H_{14}ClO_3$: 241.0626 found: 241.0626; **Optical purity**: 97% ee determined by HPLC analysis (OD-H column, *n*-hexane/ 2-propanol (90:10), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 13.15 and t_{major} = 13.54 min.

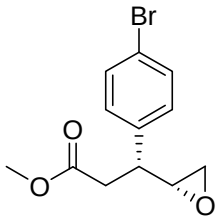
(4*S*, 5*S*)-4-(4-bromophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (11d)



Yield: 46%, colorless thick liquid; $[\alpha]_D^{25}$ = -108.8 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1773, 3440; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.13 (br s, 1H), 2.83 (dd, *J* = 9.0, 17.2 Hz, 1H), 3.01 (dd, *J* = 8.7, 17.3 Hz, 1H), 3.40 (m, 1H), 3.57 (m, 1H), 3.86 (q, *J* = 8.6 Hz, 1H), 4.74

(m, 1H), 7.15 (d, *J* = 8.5 Hz, 2H), 7.49 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 34.54, 43.03, 61.85, 82.92, 121.88, 129.54, 132.08, 135.48, 176.27; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{11}H_{12}BrO_3$: 270.9964 found: 270.9965; **Optical purity**: 98% ee determined by HPLC analysis (OJ-H column, *n*-hexane/ 2-propanol (50:50), 0.5 mL/min, 254 nm) Retention time: t_{major} = 12.33 and t_{minor} = 13.41 min.

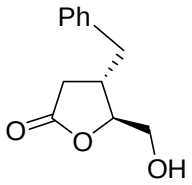
(*R*)-methyl 3-(4-bromophenyl)-3-((*R*)-oxiran-2-yl)propanoate (12d)



Yield: 48%, colorless liquid; **$[\alpha]_D^{25}$** = +8.8 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1735; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.44 (dd, *J* = 2.6, 4.9 Hz, 1H), 2.56-2.82 (m, 3H), 3.10-3.16 (m, 1H), 3.21-3.31 (m, 1H), 3.63 (s, 3H), 7.11 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 36.50, 42.47, 45.74, 51.69, 54.17, 121.24, 129.68, 131.67, 138.34, 171.52; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{12}H_{14}BrO_3$: 285.0121 found: 285.0121; **Optical purity**: 97% ee determined by HPLC analysis (OD-H column, *n*-hexane/ 2-propanol (90:10), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 14.36 and t_{major} = 15.09 min.

(4*S*, 5*S*)-4-benzyl-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8i)

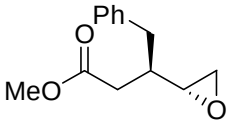
(Synthesized using (*R*,*R*)-Co(III)-salen complex)



Yield: 48%, colorless thick liquid; $[\alpha]_D^{25}$ = +38.2 (*c* 1, $CHCl_3$); **Optical purity**: 99% ee determined by HPLC analysis (Chiral OD-H column, *n*-hexane/ 2-propanol (50:50), 0.5 mL/min, 254 nm) Retention time: t_{minor} = 9.82 and t_{major} = 11.34 min.

(*R*)-methyl 3-((*R*)-oxiran-2-yl)-4-phenylbutanoate (9i)

(Synthesized using (*R*,*R*)-Co(III)-salen complex)

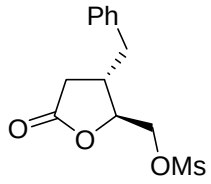


Yield: 45%, colorless liquid; $[\alpha]_D^{25}$ = +3.1 (*c* 1, $CHCl_3$); **Optical purity**: 98% ee determined by (OD-H column, *n*-hexane/ 2-propanol (90:10), 0.5 mL/min, 254 nm) Retention time: t_{major} = 13.01 and t_{minor} = 13.50 min.

2.2 ((2*R*, 3*S*)-3-(4-fluorophenyl)-5-oxotetrahydrofuran-2-yl)methyl methanesulfonate (17)

To a solution of lactone **8b**/**8i** (4.76 mmol) in CH_2Cl_2 (15 mL), triethyl amine (0.86 mL, 6.19 mmol) and Mesyl chloride (0.44 mL, 5.71 mmol) was added at 0 ^oC under nitrogen atmosphere. The resulting solution was stirred at same temperature for 1 h. After the completion of the reaction (monitored by TLC), it was quenched with water and extracted with CH_2Cl_2 (3 x 10 mL). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product **17**/**17a**. Column chromatographic purification with silica gel using petroleum ether: ethyl acetate (7:3) as eluent gave **17**/**17a** in pure form.

((2*S*, 3*S*)-3-benzyl-5-oxotetrahydrofuran-2-yl)methyl methanesulfonate (17a)

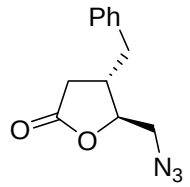


Yield: 93%, colorless solid m.p.: 78 °C; $[\alpha]_D^{25}$ = +26.0 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1782; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.27-2.42 (m, 1H), 2.63-2.85 (m, 4H), 2.99 (s, 3H), 4.05 (dd, *J* = 4.7, 11.7 Hz, 1H), 4.23 (dd, *J* = 2.7, 11.7 Hz, 1H), 4.43 (m, 1H), 7.14-7.35 (m, 5H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 34.29, 37.45, 38.02, 38.95, 69.01, 81.05, 127.05, 128.67, 128.91, 137.48, 174.82; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{13}H_{17}O_5S$: 285.0791 found: 285.0790.

2.3 (4*S*, 5*R*)-5-(azidomethyl)-4-(4-fluorophenyl)dihydrofuran-2(3*H*)-one (18)

To a stirred mixture of crude **17/17a** (3.47 mmol) in DMF (10 mL), sodium azide (0.27 g, 4.16 mmol) was added. Reaction mixture was stirred for 8 h at 80 ^{o}C. After the completion of the reaction (monitored by TLC), it was extracted with EtOAc (3 x 10 mL), washed with water, brine and dried over anhydrous Na_2SO_4. The combined organic layer was concentrated under reduced pressure to give the crude azido lactone **18/18a**, which was purified by column chromatography with silica gel using petroleum ether: ethyl acetate (8:2) as eluent gave pure **18/18a** as colorless oil.

(4*S*, 5*S*)-5-(azidomethyl)-4-benzyldihydrofuran-2(3*H*)-one (18a)



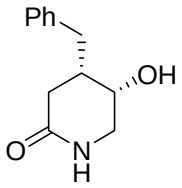
Yield: 95%, colorless liquid; $[\alpha]_D^{25}$ = +78.5 (*c* 1, $CHCl_3$); **IR**: ($CHCl_3$, cm^{-1}) 1781, 2104; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.26-2.42 (m, 1H), 2.66-2.86 (m, 4H), 3.16 (dd, *J* = 4.6, 13.4 Hz, 1H), 3.45 (dd, *J* = 3.4, 13.3 Hz, 1H), 4.33 (m, 1H), 7.13-7.17(m, 2H), 7.25-7.37 (m, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 34.52, 38.91, 39.11, 53.06, 82.40, 126.99, 128.59, 128.85, 137.66, 174.83; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{12}H_{14}N_3O_2$: 232.1081 found: 232.1080.

2.4 (4*S*, 5*R*)-4-(4-fluorophenyl)-5-hydroxypiperidin-2-one (19)

To a solution of **18/18a** (4.25 mmol) in dry methanol $Pd(OH)_2$ (0.05 g) was added and the reaction mixture was stirred under an atmosphere of H_2 (1 atm) for 24 h at 25 ^{o}C. After the completion of the reaction (monitored by TLC), the reaction mixture was filtered over

celite and the filtrate was concentrated under reduced pressure to provide the **19/19a**, which was purified by column chromatography using ethyl acetate: methanol (9:1) to obtain pure **19/19a**.

(4*S*, 5*S*)-4-benzyl-5-hydroxypiperidin-2-one (19a)



Yield: 92%, colorless solid m.p.: 213 °C; $[\alpha]_D^{25}$ = +7.3 (*c* 1, MeOH); **IR**: ($CHCl_3$, cm^{-1}) 1642, 3440; **^{1}H NMR** (200 MHz, MeOH-d_4 + $CDCl_3$) δ 2.03-2.24 (m, 3H), 2.51 (dd, *J* = 6.8, 13.1 Hz, 1H), 2.71 (dd, *J* = 7.0 13.0 Hz, 1H), 3.21 (m, 2H), 3.75 (s, 1H), 7.08-7.20 (m, 5H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 33.54, 38.92, 40.36, 49.99, 64.66, 127.38, 129.61, 130.30, 141.08, 174.68; **HRMS (*m/z*)**: calculated $[M+H]^+$ for $C_{12}H_{16}NO_2$: 206.1176 found: 206.1177.

2.5 (3*R*, 4*S*)-1-benzyl-4-(4-fluorophenyl)piperidin-3-ol (20)

To a solution of lactum **19** (0.5 g, 2.39 mmol) in dry THF (10 mL), $BH_3{\cdot}SMe_2$ (0.45 mL, 4.78 mmol) was added dropwise at 0 ^oC under nitrogen atmosphere and the mixture was then refluxed for 6 h. After the completion of the reaction (monitored by TLC), the solvent (THF) was removed under reduced pressure. Without purification, the crude amino alcohol was then dissolved in CH_2Cl_2/H_2O (1:1, 10 mL) and Na_2CO_3 (0.75 g, 7.71 mmol) was added, followed by dropwise addition of benyl bromide (0.34 mL, 2.87 mmol). The reaction mixture was refluxed for 8 h. After the completion of the reaction (monitored by TLC), it was extracted with CH_2Cl_2 (3 x 5 mL), washed with water, brine and dried over

anhydrous Na_2SO_4. The combined organic layer was concentrated under reduced pressure to give the crude **20**, which was purified by column chromatographic purification with silica gel using petroleum ether: ethyl acetate (7:3) as eluent gave **20** in pure form.

(3*S*, 4*S*)-4-benzylpiperidin-3-ol (4)

To a solution of lactum **19a** (0.49 g, 2.39 mmol) in dry THF (10 mL), $BH_3{\cdot}SMe_2$ (0.45 mL, 4.78 mmol) was added dropwise at 0 ^oC under nitrogen atmosphere and the mixture was then refluxed for 6 h. After the completion of the reaction (monitored by TLC), the solvent (THF) was removed under reduced pressure to give the crude product **4**, which was purified by column chromatography with silica gel using petroleum ether: ethyl acetate (6:4) as eluent gave pure **4** as colorless solid.

2.6 (*S*)-1-benzyl-4-(4-fluorophenyl)piperidin-3-one (21)

To a stirred solution of oxalyl chloride (0.15 mL, 1.75 mmol) in dry CH_2Cl_2 (3 mL), DMSO (0.2 mL, 2.63 mmol) was added at -78 ^oC under nitrogen atmosphere. The reaction mixture was stirred for 20 min. followed by the addition of a solution of alcohol **20** (0.25 g, 0.88 mmol) in CH_2Cl_2 (1 mL). After stirring for 1 h at -78 ^oC, triethyl amine (0.5 mL, 3.5 mmol) was added and reaction mixture was stirred at room temperature for additional 15 min, after which it was quenched with H_2O (5 mL). The organic phase was separated and the aqueous phase extracted with CH_2Cl_2 (3 x 3 mL), the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the corresponding crude aldehyde **21**, which was used for next reaction without purification.

2.7 (*S*)-1-benzyl-4-(4-fluorophenyl)-3-(methoxymethylene)piperidine (22)

To a stirred solution of methoxymethyltriphenylphoshonium chloride (0.48 g, 1.41 mmol) in dry THF (3 mL), *n*-butyl lithium (1.6 M in hexane, 0.5 mL, 0.84 mmol) was added dropwise at 0 ^{o}C under nitrogen atmosphere. The resulting red solution was stirred at this temperature for 1 h, after which solution of **21** (0.2 g, 0.7 mmol) in THF (1.5 mL) was added dropwise and the reaction mixture was allowed to stirred for another 48 h at 0 ^{o}C After the completion of the reaction (monitored by TLC), it was extracted with CH_2Cl_2 (3 x 5 mL), washed with water, brine and dried over anhydrous Na_2SO_4. The combined organic layer was concentrated under reduced pressure to give the crude **22**, which upon column chromatographic purification with silica gel using petroleum ether: ethyl acetate (8:2) as eluent gave pure **22** as colorless oil

(Spectral data is in good agreement with reported values, ref. 3)

2.8 ((3*S*, 4*R*)-1-benzyl-4-(4-fluorophenyl)piperidin-3-yl)methanol (2)

To a solution of enol ether **22** (0.06 g, 0.19 mmol) in THF (3 mL), 0.1 M aqueous H_2SO_4 (2.8 mL, 0.28 mmol) was added. The solution was refluxed for 12 h, after which it was allowed to cool to room temperature and a saturated solution of $NaHCO_3$ (10 mL) was added. The resulting mixture was extracted with diethyl ether (3 x 5 mL), washed with water, brine and dried over anhydrous Na_2SO_4. The combined organic layer was concentrated under reduced pressure to give the corresponding crude aldehyde, which was used for next reaction without further purification.

To the solution of this crude aldehyde in methanol (2 mL), $NaBH_4$ (0.007 g, 0.21 mmol) was added at 0 ^oC and the stirred reaction mixture stirred for 1 h at 25 ^oC. After the completion of the reaction (monitored by TLC), it was treated with 2 N aq. Sodium hydroxide (5 mL) and extracted with CH_2Cl_2 (3 x 5 mL), washed with water, brine and dried over anhydrous Na_2SO_4. The combined organic layer was concentrated under reduced pressure to give the crude **2**, which was purified by column chromatography with silica gel using petroleum ether: ethyl acetate (8:2) as eluent gave pure **2** as colorless oil.

(Spectral data and optical rotation are in good agreement with reported values, ref. 3, 4)

2.9 (+)-Eldanolide (1)

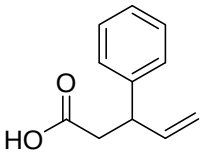
To a stirred solution of $CuBr.SMe_2$ (0.128 g, 0.62 mmol, 30 mol %) in THF (5 mL), 2-methyl-1-propenylmagnesium bromide (0.5 M in THF, 10 mL, 5.2 mmol) was added at -20 ^oC under nitrogen atmosphere and stirring was continued for 30 min. The solution of epoxide **9f** (0.39 g, 2.08 mmol) in THF (5 mL) was added dropwise and the stirring continued for 3 h at -20 ^oC to 0 ^oC. Then the mixture was quenched with saturated aq. ammonium chloride solution (5 mL) and the product extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine, dried over anhyd. Na_2SO_4 and concentrated under reduced pressure to give crude product **1** which upon column chromatographic purification with silica gel using petroleum ether: ethyl acetate (9:1) as eluent gave pure **1** as colorless oil.

(Spectral data and optical rotation are in good agreement with reported values, ref. 5)

2.10 General procedure for the synthesis of acyclic olefinic acid (14)

A mixture of allylic alcohol **13** (37.31 mmol), triethyl orthoacetate (37.31 mmol) and hexanoic acid (0.23 mL, 1.85 mmol) was placed in a round-bottomed flask equipped with thermometer, Claisen head and condenser. The solution was heated with distillation of ethanol (upto 70-150 ^{o}C). After 3 h distillation of ethanol slows and another 0.1-mL portion of hexanoic acid was added. Additional portions (0.1 mL) of hexanoic acid were added again after at 3rd and 4th h followed by continued heating for next the next 6 h. After which it was allowed to cool and aq. solution of potassium hydroxide (2.9 g, 52.2 mmol, 20 ml), methanol (60 mL) was added. The resulting mixture was refluxed for 4 h and then allowed to cool to room temperature. After that the resulting solution washed with diethyl ether and acidified with dil HCl. The acidic solution was extracted with diethyl ether and the organic layer dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product **14.** The crude material was used as such for next reaction without any further purification.

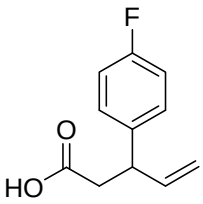
3-phenylpent-4-enoic acid (14a)



Yield: 90%, colorless solid m.p.: 48 ^{o}C; **IR**: ($CHCl_3$, cm^{-1}) 1638, 1708, 3028; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.69 (dd, *J* = 7.5, 15.7 Hz, 1H), 2.82 (dd, *J* = 7.9, 15.7 Hz, 1H), 3.83 (q, *J* = 7.3 Hz, 1H), 5.04 (d, *J* = 5.5 Hz, 1H), 5.11 (s, 1H), 5.89-6.06 (m, 1H), 7.18-7.33 (m, 5H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 40.00, 45.13, 115.03, 126.80, 127.51, 128.63,

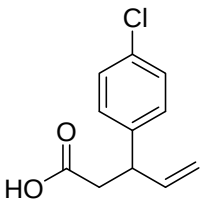
139.93, 142.07, 178.37; **Anal**. Calcd for $C_{11}H_{12}O_2$ requires C, 74.98; H, 6.86; found C, 74.70; H, 6.80%.

3-(4-fluorophenyl)pent-4-enoic acid (14b)



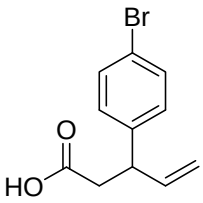
Yield: 88%, colorless solid m.p.: 82 °C; **IR**: ($CHCl_3$, cm^{-1}) 1509, 1710, 2912, 2987, 3035, 3076; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.66 (dd, *J* = 7.7, 15.7 Hz, 1H), 2.81 (dd, *J* = 7.7, 15.7 Hz, 1H), 3.83 (q, *J* = 7.4 Hz, 1H), 5.01-5.12 (m, 2H), 5.86-6.03 (m, 1H), 6.94-7.02 (m, 2H), 7.13-7.20 (m, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 40.06, 44.34, 115.18 (d, *J* = 4.7 Hz) , 129.13 (d, *J* = 7.7 Hz), 137.72 (d, *J* = 3.3 Hz), 139.81, 164.16 (d, *J* = 245.0 Hz), 178.23; **Anal**. Calcd for $C_{11}H_{11}O_2F$ requires C, 68.03; H, 5.71; found C, 68.11; H, 5.75%.

3-(4-chlorophenyl)pent-4-enoic acid (14c)



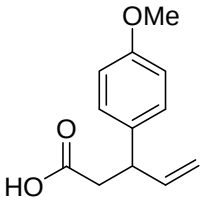
Yield: 85%, colorless solid m.p.: 100 °C; **IR**: ($CHCl_3$, cm^{-1}) 1496, 1707, 2610, 2905; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.70 (dd, *J* = 7.7, 15.8 Hz, 1H), 2.81 (dd, *J* = 7.6, 14.4 Hz, 1H), 3.83 (q, *J* = 7.3 Hz, 1H), 5.02-5.13 (m, 2H), 5.85-6.02 (m, 1H), 7.13 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 39.83, 44.46, 115.45, 128.83, 128.95, 139.50, 140.48, 178.07; **Anal**. Calcd for $C_{11}H_{11}O_2Cl$ requires C, 62.72; H, 5.26; found C, 62.65; H, 5.18%.

3-(4-bromophenyl)pent-4-enoic acid (14d)



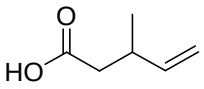
Yield: 84%, colorless solid m.p.: 108 °C; **IR**: ($CHCl_3$, cm^{-1}) 1706, 3044; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.70 (dd, *J* = 7.7, 15.8 Hz, 1H), 2.81 (dd, *J* = 7.6, 15.8 Hz, 1H), 3.79 (q, *J* = 7.6 Hz, 1H), 5.02-5.13 (m, 2H), 5.84- 6.01 (m, 1H), 7.08 (d, *J* = 8.3 Hz, 2H), 7.42 (d, *J* = 8.3 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 39.75, 44.51, 115.52, 120.78, 129.34, 131.78, 139.41, 140.99, 178.03; **Anal**. Calcd for $C_{11}H_{11}O_2Br$ requires C, 51.79; H, 4.35; found C, 51.68; H, 4.32%.

3-(4-methoxyphenyl)pent-4-enoic acid (14e)



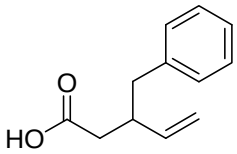
Yield: 88%, colorless solid m.p.: 78 °C; **IR**: ($CHCl_3$, cm^{-1}) 1512, 1610, 1708, 2836, 2956; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.69 (dd, *J* = 7.5, 15.5 Hz, 1H), 2.75 (dd, *J* = 7.7, 15.4 Hz, 1H), 3.78 (s, 3H), 3.81 (m, 1H), 5.00-5.09 (m, 2H), 5.86-6.03 (m, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 7.11 (d, *J* = 8.6 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 40.13, 44.31, 55.13, 114.02, 114.68, 128.49, 134.10, 140.29, 158.38, 178.37; **Anal**. Calcd for $C_{12}H_{14}O_3$ requires C, 69.88; H, 6.84; found C, 69.74; H, 6.94%.

3-methylpent-4-enoic acid (14f)



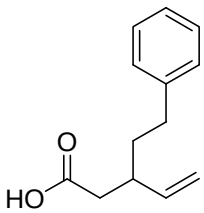
Yield: 78%, colorless liquid; **IR**: ($CHCl_3$, cm^{-1}) 1711, 2967, 3083; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 1.10 (d, *J* = 6.7 Hz, 3H), 2.31 (dd, *J* = 7.6, 15.0 Hz, 1H), 2.39 (dd, *J* = 6.8, 15.2 Hz, 1H), 2.62-2.76 (m, 1H), 4.95-5.09 (m, 2H), 5.70-5.87 (m, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 19.68, 34.09, 41.11, 113.66, 142.08, 179.24; **Anal**. Calcd for $C_6H_{10}O_2$ requires C, 63.14; H, 8.83; found C, 63.20; H, 8.75%.

3-benzylpent-4-enoic acid (14g)



Yield: 92%, colorless liquid; **IR**: ($CHCl_3$, cm^{-1}) 1495, 1641, 1693, 2675, 3071; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.33 (dd, *J* = 8.2, 15.5 Hz, 1H), 2.41 (dd, *J* = 5.7, 15.4 Hz, 1H), 2.67-2.95 (m, 3H), 4.96-5.05 (m, 2H), 5.64-5.82 (m, 1H), 7.12-7.31 (m, 5H) ; **^{13}C NMR** (50 MHz, $CDCl_3$): δ 38.56, 40.87, 41.32, 115.42, 126.27, 128.30, 129.28, 139.16, 139.93, 179.19; **Anal**. Calcd for $C_{12}H_{14}O_2$ requires C, 75.76; H, 7.42; found C, 75.72; H, 7.50%.

3-phenethylpent-4-enoic acid (14h)

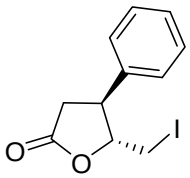


Yield: 85%, colorless liquid; **IR**: ($CHCl_3$, cm^{-1}) 1603, 1641, 1708, 3025; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 1.64-1.80 (m, 2H), 2.34-2.43 (m, 2H), 2.51-2.68 (m, 3H), 5.07 (s, 1H), 5.15 (d, *J* = 3.9 Hz, 1H), 5.60-5.74 (m, 1H), 7.13-7.30 (m, 5H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 33.31, 36.15, 39.84, 39.91, 116.05, 125.84, 128.35, 140.25, 141.88, 178.96; **Anal**. Calcd for $C_{13}H_{16}O_2$ requires C, 76.44; H, 7.90; found C, 76.45; H, 7.95%.

2.11 General procedure for the synthesis of *trans*-iodolatone product (15)

To a solution of olefinic acid **14** (5.68 mmol) in acetonitrile (20 mL), solid I_2 (4.6 g, 18.17 mmol) was added at 0 ^oC under nitrogen atmosphere, the reaction mixture was protected from light and stirred for 24 h. After the completion of the reaction (monitored by TLC), it was quenched by addition of saturated solution of aq. $NaHCO_3$ followed by extraction with diethyl ether. Organic layer was separated and washed with 20% aq. $Na_2S_2O_3$ until colorless, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product **15**. Column chromatographic purification with silica gel using petroleum ether: ethyl acetate (8:2) as eluent gave **15** in pure form.

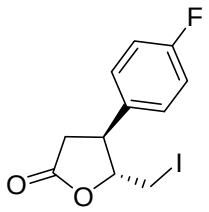
5-(iodomethyl)-4-phenyldihydrofuran-2(3*H*)-one (15a)



Yield: 89%, colorless thick liquid; **IR**: ($CHCl_3$, cm^{-1}) 1780; **^{1}H NMR** (200 MHz, $CDCl_3$) 2. 82 (dd, *J* = 9.6, 17.9 Hz, 1H), 3.07 (dd, *J* = 9.01, 17.8 Hz, 1H), 3.34 (dd, *J* = 4.4, 11.2 Hz, 1H), 3.45-3.59 (m, 2H), 4.31 (m, 1H), 7.24-7.42 (m, 5H); **^{13}C NMR** (50 MHz,

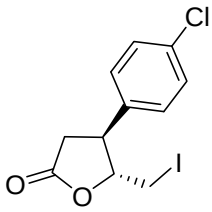
$CDCl_3$): δ 6.33, 36.86, 47.19, 83.99, 127.13, 128.01, 129.25, 138.36, 174.08; **Anal**. Calcd for $C_{11}H_{11}O_2I$ requires C, 43.73; H, 3.67; found C, 43.72; H, 3.70%.

4-(4-fluorophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (15b)



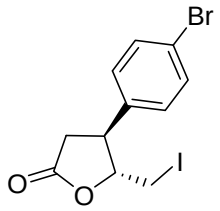
Yield: 82%, colorless thick liquid; **IR**: ($CHCl_3$, cm^{-1}) 1781; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.76 (dd, *J* = 9.2, 17.81 Hz, 1H), 3.07 (dd, *J* = 9.1, 17.9 Hz, 1H), 3.29-3.60 (m, 3H), 4.27 (m, 1H), 7.03-7.12 (m, 2H), 7.21-7.28 (m, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 1.14, 37.10, 43.36, 82.62, 116.17 (d, *J* = 21.6 Hz), 129.78 (d, *J* = 8.1 Hz), 132.28 (d, *J* = 3.3 Hz), 162.0 (d, *J* = 248.1 Hz), 175.19; **Anal**. Calcd for $C_{11}H_{10}O_2FI$ requires C, 41.27; H, 3.15; found C, 41.30; H, 3.12%.

4-(4-chlorophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (15c)



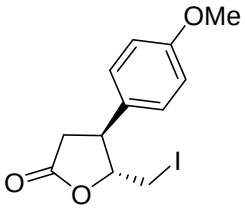
Yield: 80%, colorless thick liquid; **IR**: ($CHCl_3$, cm^{-1}) 1789; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.75 (dd, *J* = 9.1, 17.8 Hz, 1H), 3.07 (dd, *J* = 9.2, 17.9 Hz, 1H), 3.29-3.59 (m, 3H), 4.28 (m, 1H), 7.20 (d, *J* = 8.5 Hz, 2H), 7.36 (d, *J* = 8.6 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 5.99, 36.82, 46.62, 83.84, 128.52, 129.53, 134.05, 137.11, 173.73; **Anal**. Calcd for $C_{11}H_{10}ClO_2I$ requires C, 39.26; H, 2.99; found C, 39.28; H, 3.02%.

4-(4-bromophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (15d)



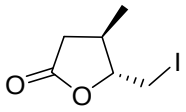
Yield: 82%, colorless thick liquid; IR: ($CHCl_3$, cm^{-1}) 1782; **^{1}H NMR** (200 MHz, $CDCl_3$ δ 2.75 (dd, *J* = 9.1, 17.8 Hz, 1H), 3.07 (dd, *J* = 9.1, 17.8 Hz, 1H), 3.29-3.58 (m, 3H), 4.28 (m, 1H), 7.15 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 6.20, 36.65, 46.52, 83.60, 121.69, 128.86, 132.15, 137.29, 173.75; **Anal**. Calcd for $C_{11}H_{10}BrO_2I$ requires C, 34.68; H, 2.65; found C, 34.70; H, 2.68%.

5-(iodomethyl)-4-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (15e)



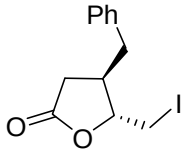
Yield: 85%, colorless thick liquid; **IR**: ($CHCl_3$, cm^{-1}) 1783; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.64-2.84 (m, 1H), 2.97-3.10 (m, 1H), 3.28-3.54 (m, 3H), 3.81 (s, 3H), 4.24 (m, 1H), 6.89 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 6.25, 36.93, 46.55, 55.16, 84.13, 114.55, 128.16, 130.00, 159.21, 174.07; **Anal**. Calcd for $C_{12}H_{13}O_3I$ requires C, 43.39; H, 3.95; found C, 43.45; H, 3.88%.

5-(iodomethyl)-4-methyldihydrofuran-2(3*H*)-one (15f)



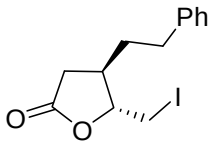
Yield: 80%, colorless liquid; **IR**: ($CHCl_3$, cm^{-1}) 1778; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 1.24 (d, *J* = 6.6 Hz, 3H), 2.24 (dd, *J* = 7.8, 17.2 Hz, 1H), 2.34-2.55 (m, 1H), 2.81 (dd, *J* = 8.3, 17.1 Hz, 1H), 3.37 (m, 2H), 4.04 (q, *J* = 5.5 Hz, 1H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 6.00, 18.19, 35.75, 36.55, 84.45, 174.70; **Anal**. Calcd for $C_6H_9O_2I$ requires C, 30.02; H, 3.78; found C, 30.10; H, 3.82%.

4-benzyl-5-(iodomethyl)dihydrofuran-2(3*H*)-one (15g)



Yield: 85%, colorless solid m.p.: 62 °C; **IR**: ($CHCl_3$, cm^{-1}) 1782; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.31-2.44 (m, 1H), 2.64-2.89 (m, 4H), 3.08 (dd, *J* = 4.4, 10.9 Hz, 1H), 3.27 (dd, *J* = 5.4, 10.9 Hz, 1H), 4.17 (q, *J* = 5.2 Hz, 1H), 7.15-7.38 (m, 5H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 7.26, 34.48, 39.25, 42.16, 82.24, 126.89, 128.61, 128.75, 137.58, 174.50; **Anal**. Calcd for $C_{12}H_{13}O_2I$ requires C, 45.59; H, 4.14; found C, 45.62; H, 4.20%.

5-(iodomethyl)-4-phenethyldihydrofuran-2(3*H*)-one (15h)



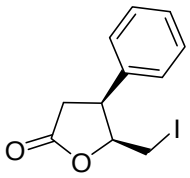
Yield: 82%, colorless thick liquid; **IR**: ($CHCl_3$, cm^{-1}) 1778; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 1.64-2.07 (m, 2H), 2.23-2.41 (m, 2H), 2.55-2.88 (m, 3H), 3.26-3.42 (m, 2H), 4.15 (q, *J*

= 5.3 Hz, 1H), 7.13-7.33 (m, 5H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 7.26, 34.48, 39.25, 42.16, 82.24, 126.89, 128.61, 128.75, 137.58, 174.50; **Anal**. Calcd for $C_{13}H_{15}O_2I$ requires C, 47.29; H, 4.58; found C, 47.22; H, 4.50%.

2.12 General procedure for the synthesis of *cis*-iodolatone product (16)

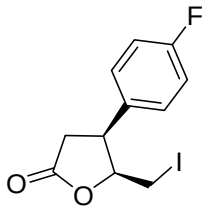
To a solution of olefinic acid **14** (5.68 mmol) in chloroform (20 mL), aq. $NaHCO_3$ (0.95 g, 11.36 mmol) in 20 mL of water, solid I_2 (2.88 g, 11.36 mmol) was added at 0 ^{o}C under nitrogen atmosphere, the reaction mixture protected from light and stirred for 6 h. After the completion of the reaction (monitored by TLC), organic layer was separated and washed with 20% aq. $Na_2S_2O_3$ until colorless, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the crude product **16**. Column chromatographic purification with silica gel using petroleum ether: ethyl acetate (9:1) as eluent gave **16** in pure form.

5-(iodomethyl)-4-phenyldihydrofuran-2(3*H*)-one (16a)



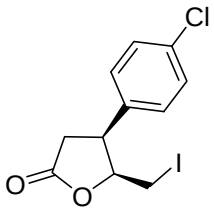
Yield: 80%, colorless solid m.p.: 104 °C; **IR**: ($CHCl_3$, cm^{-1}) 1782; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.65-2.87 (m, 2H), 3.01-3.16 (m, 2H), 3.83-3.92 (m, 1H), 4.94 (m, 1H), 7.19-7.24 (m, 2H), 7.33-7.38 (m, 3H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 1.51, 36.82, 44.05, 82.83, 128.02, 128.10, 128.96, 136.45, 175.37; **Anal**. Calcd for $C_{11}H_{11}O_2I$ requires C, 43.73; H, 3.67; found C, 43.82; H, 3.75%.

4-(4-fluorophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (16b)



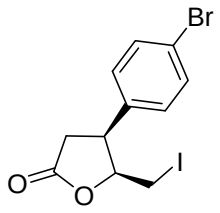
Yield: 76%, colorless solid m.p.: 99 °C; **IR**: ($CHCl_3$, cm^{-1}) 1785; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.60-2.81 (m, 2H), 3.02-3.20 (m, 2H), 3.88 (m, 1H), 4.92 (m, 1H), 7.00-7.10 (m, 2H), 7.17-7.26 (m, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 1.13, 37.08, 43.36, 86.62, 115.75 (d, J = 21.6 Hz), 129.78 (d, J = 8.1 Hz), 132.23 (d, J = 3.3 Hz), 162.33 (d, J = 248.1 Hz), 175.17; **Anal**. Calcd for $C_{11}H_{10}O_2FI$ requires C, 41.27; H, 3.15; found C, 41.18; H, 3.27%.

4-(4-chlorophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (16c)



Yield: 75%, colorless thick liquid; **IR**: ($CHCl_3$, cm^{-1}) 1780; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.60-2.81 (m, 2H), 3.02-3.21 (m, 2H), 3.86 (m, 1H), 4.92 (m, 1H), 7.17 (d, J = 8.5 Hz, 2H), 7.34 (d, J = 8.6 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 1.06, 36.95, 43.50, 82.47, 129.17, 129.41, 134.12, 134.96, 175.07; **Anal**. Calcd for $C_{11}H_{10}ClO_2I$ requires C, 39.26; H, 2.99; found C, 3.28; H, 2.84%.

4-(4-bromophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (16d)



Yield: 71%, colorless thick liquid; **IR**: ($CHCl_3$, cm^{-1}) 1782; **^{1}H NMR** (200 MHz, $CDCl_3$) δ 2.60-2.81 (m, 2H), 3.02-3.21 (m, 2H), 3.85 (m, 1H), 4.92 (m, 1H), 7.11 (d, *J* = 8.5 Hz, 2H), 7.48 (d, *J* = 8.5 Hz, 2H); **^{13}C NMR** (50 MHz, $CDCl_3$): δ 1.19, 36.79, 43.51, 82.34, 122.12, 129.68, 132.05, 135.43, 175.07; **Anal**. Calcd for $C_{11}H_{10}BrO_2I$ requires C, 34.68; H, 2.65; found C, 3.58; H, 2.74%.

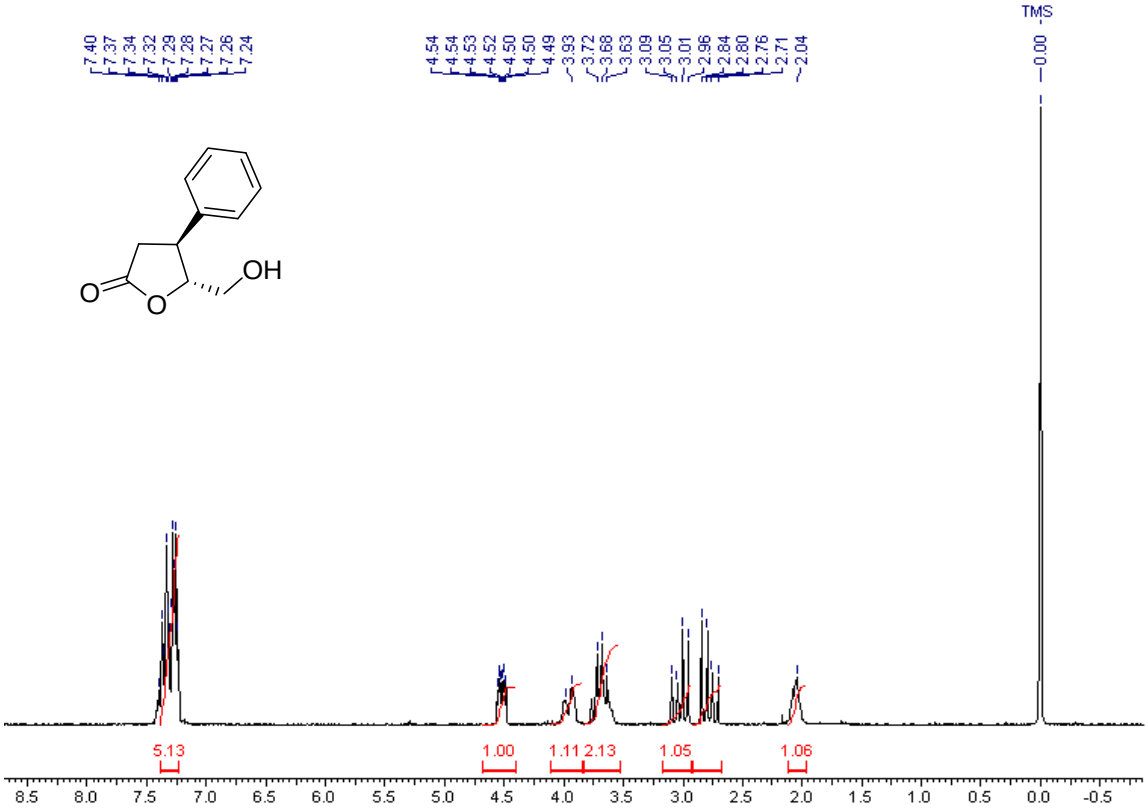
2.13 General procedure for the synthesis of *anti* and *syn* epoxy esters (7a-h & 10 a-d)

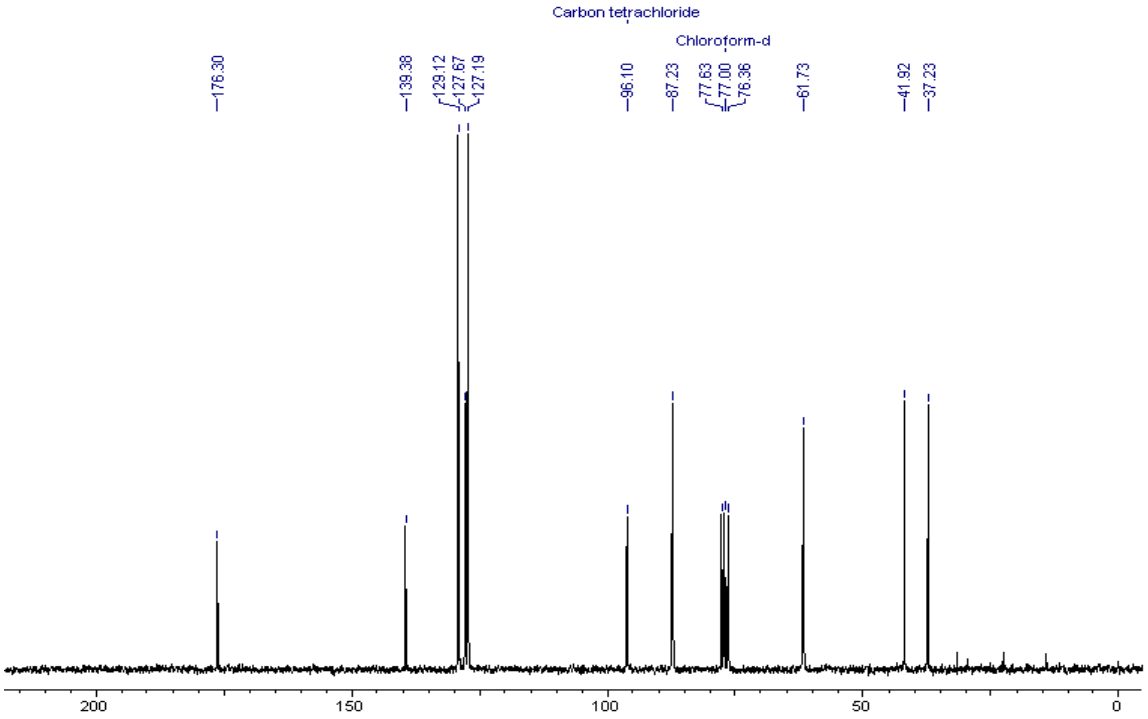
To a solution of iodolactone **15** or **16** (3.3 mmol) in methanol (15 mL) finely powdered anhydrous Na_2CO_3 (0.38 g, 3.63 mmol) was added and the reaction mixture refluxed for 8 h under nitrogen atmosphere. After the completion of the reaction (monitored by TLC), the resulting reaction mixture was concentrated under reduced pressure and partitioned between 50 mL water and 50 mL diethyl ether. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give the corresponding crude product **7** or **10**. Column chromatographic purification with silica gel using petroleum ether: ethyl acetate (9:1) as eluent gave **7** or **10** pure in form.

3. Referances releveant to supporting information:

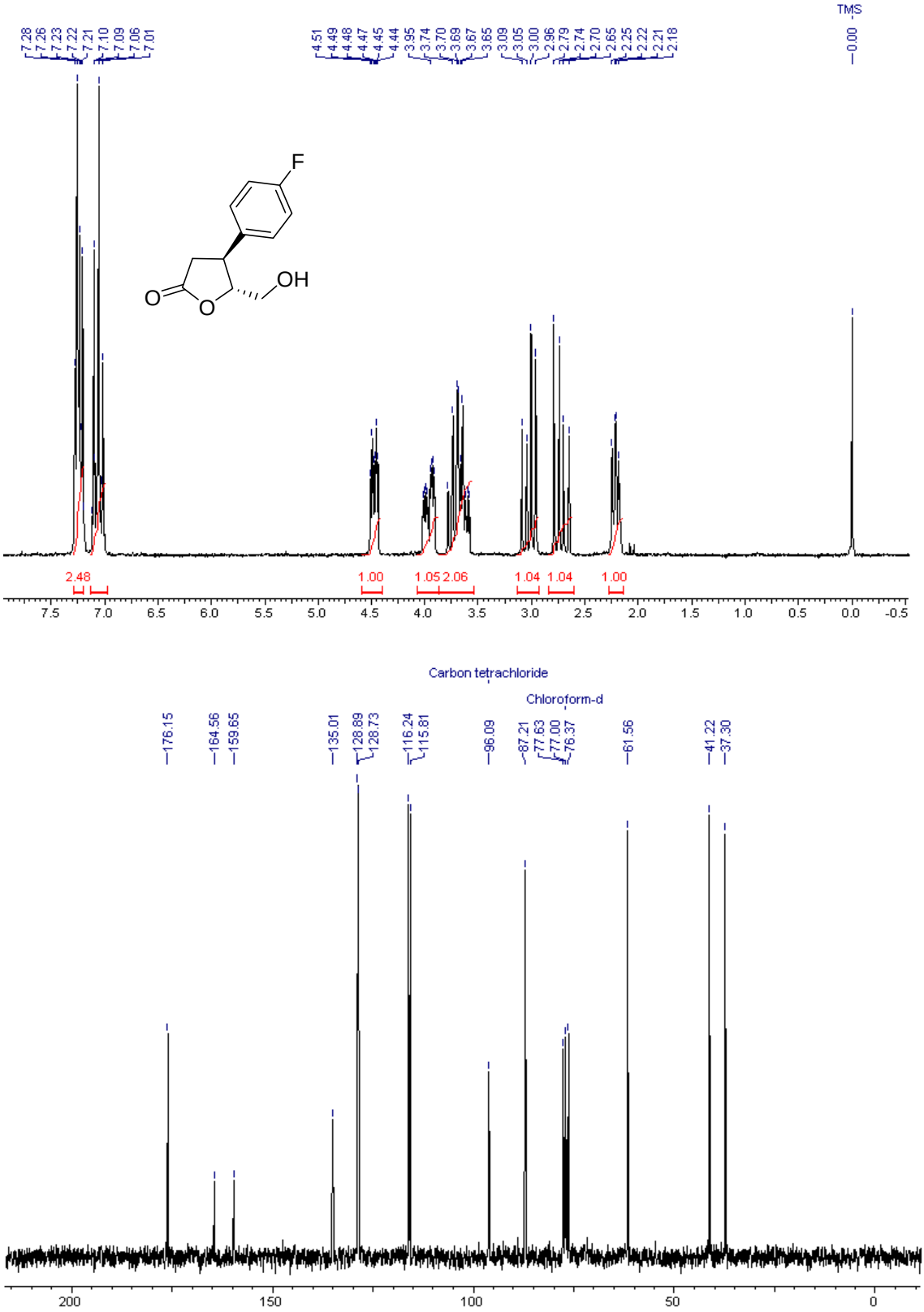
1. H.-J. Ha, K.-N. Yoon, S.-Y. Lee, Y.-S. Park, M.-S. Lim and Y.-G. Yim, *J. Org. Chem*., 1998, **63**, 8062.
2. J. S. Yadav and P. S. R. Reddy, *Synthesis*, 2007, 1070.
3. Koech, P. K.; Krische, M. J. *Tetrahedron*, **2006**, *62*, 10594.
4. Bower, J. F.; Riis-Johannessen, T.; Szeto, P.; Whitehead, A. J.; Gallagher, T. *Chem. Commun.*, **2007**, 728.
5. Kong, L.; Zhuang, Z.; Chen, Q.; Deng, H.; Tang, Z.; Jia, X.; Li, Y.; Zhai, H. *Tetrahedron: Asymmetry*, **2007**, *18*, 451.

4. Spectra

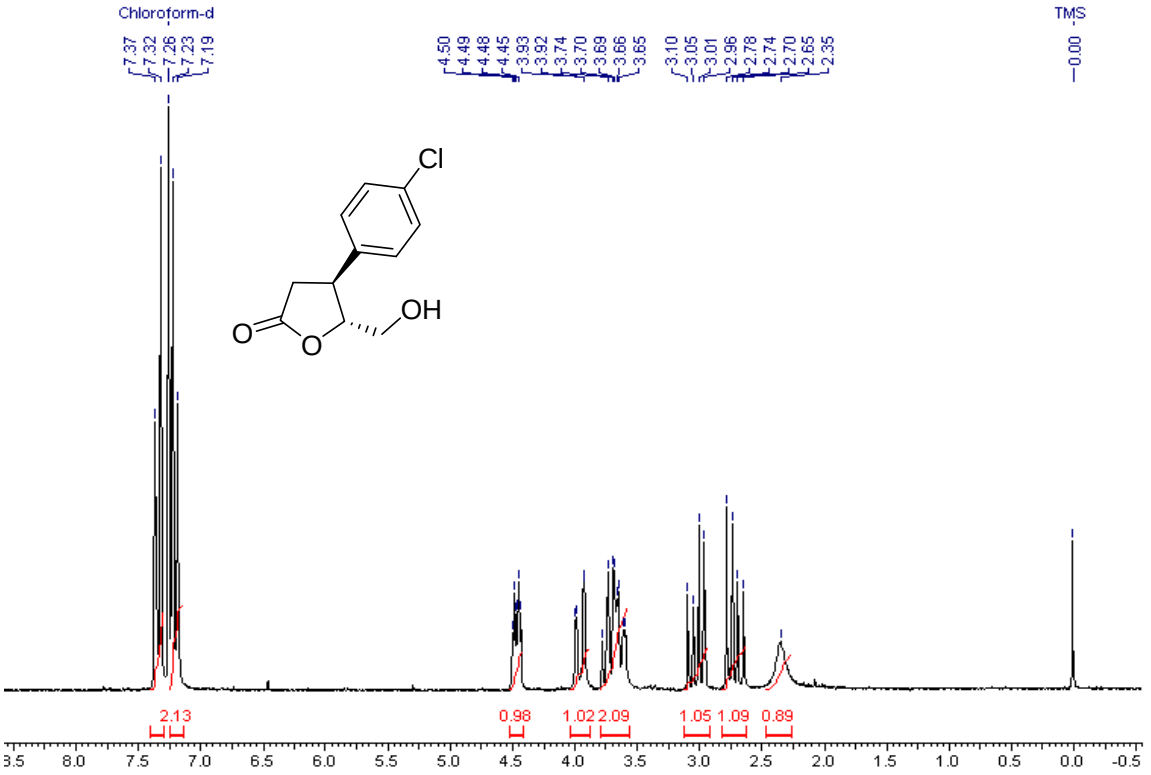


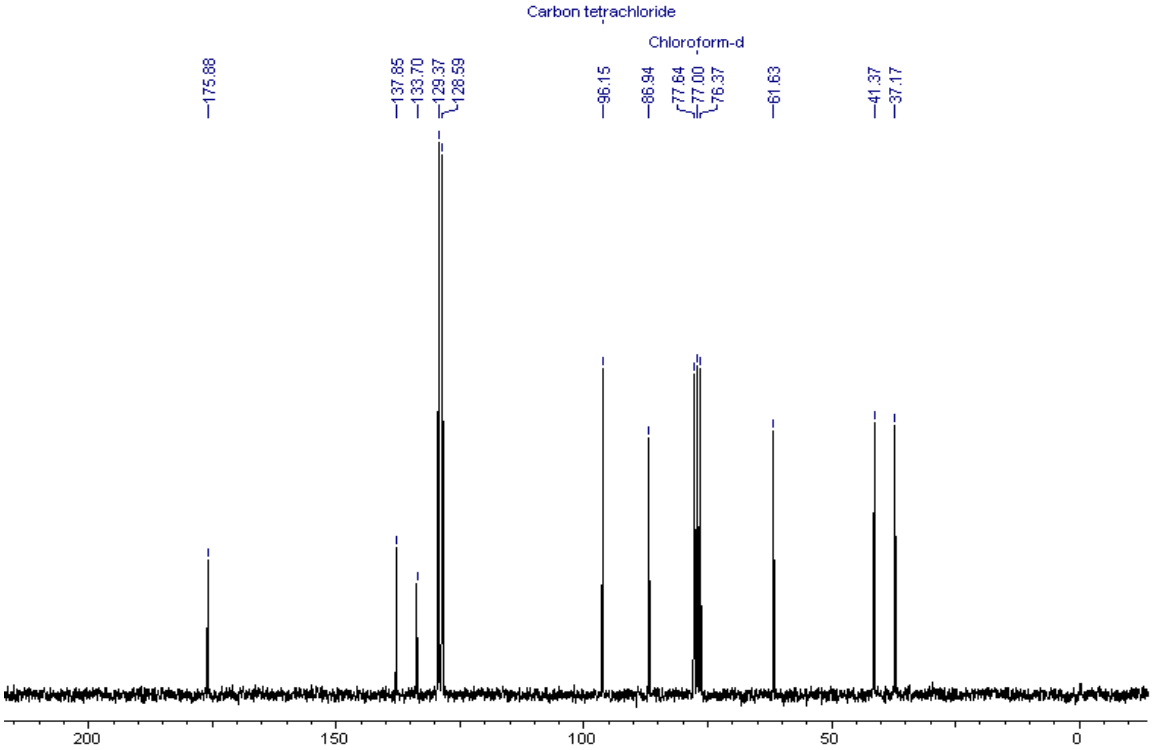


(4*S*,5*R*)-5-(hydroxymethyl)-4-phenyldihydrofuran-2(3*H*)-one (8a)

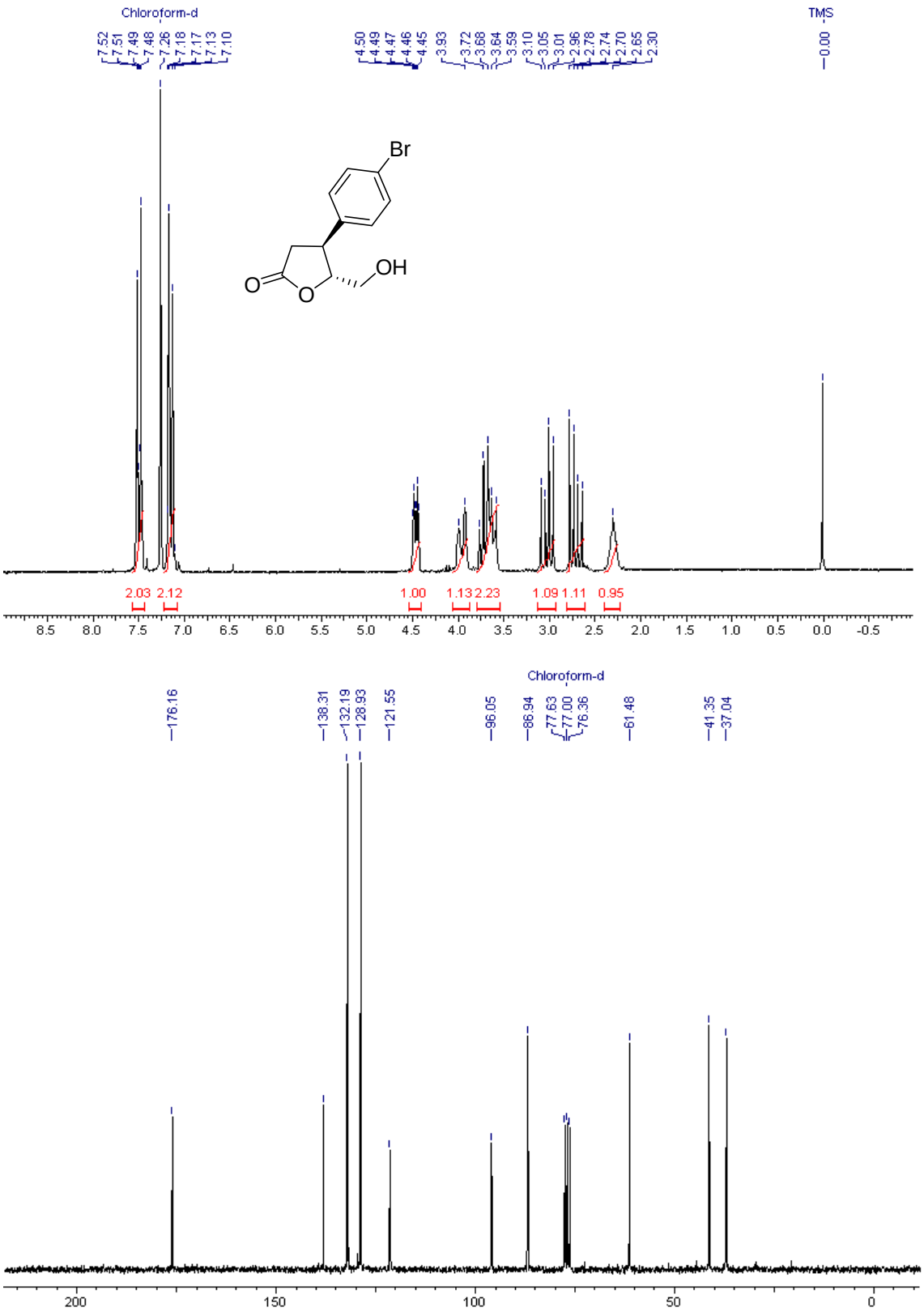


(4*S*,5*R*)-4-(4-fluorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8b)

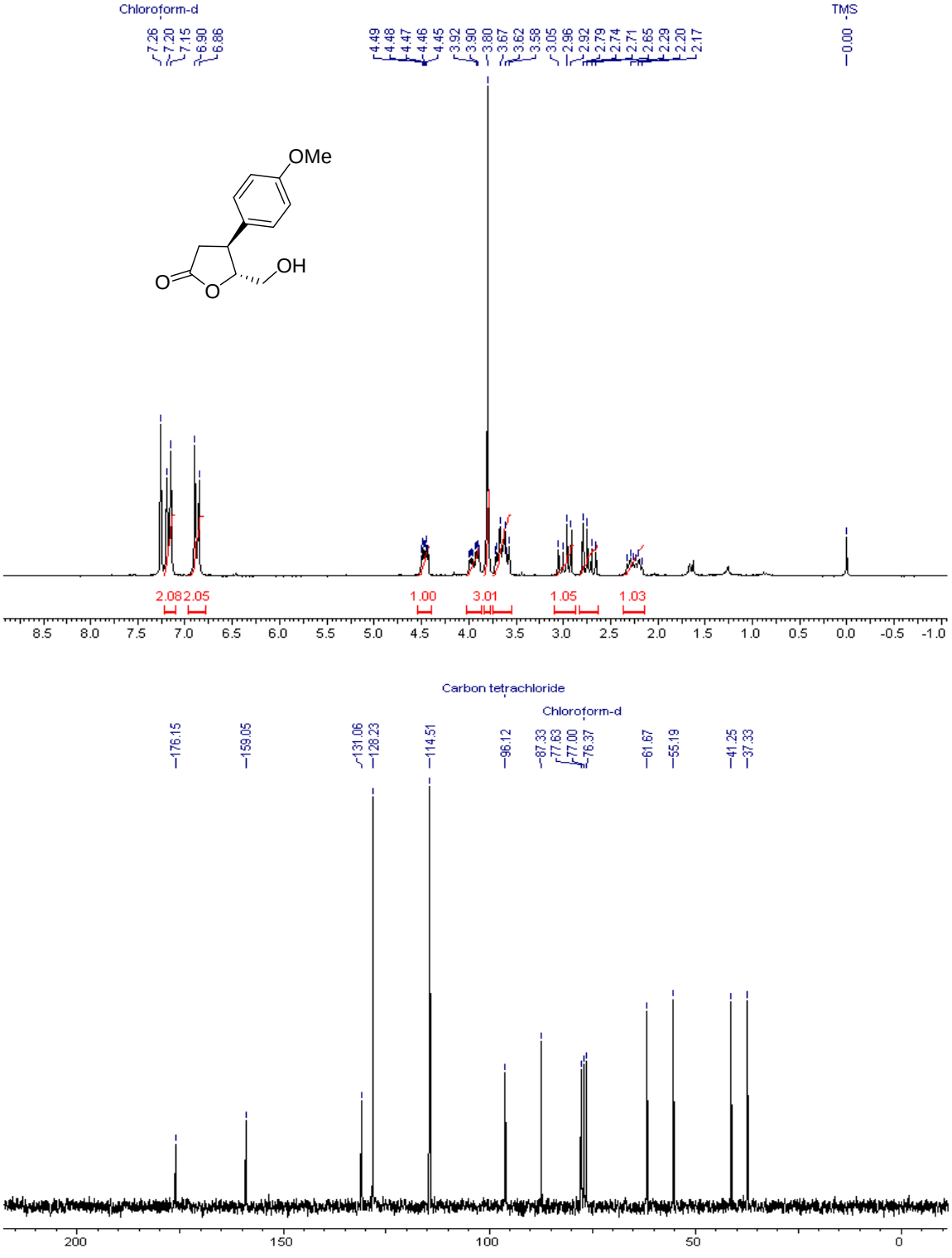




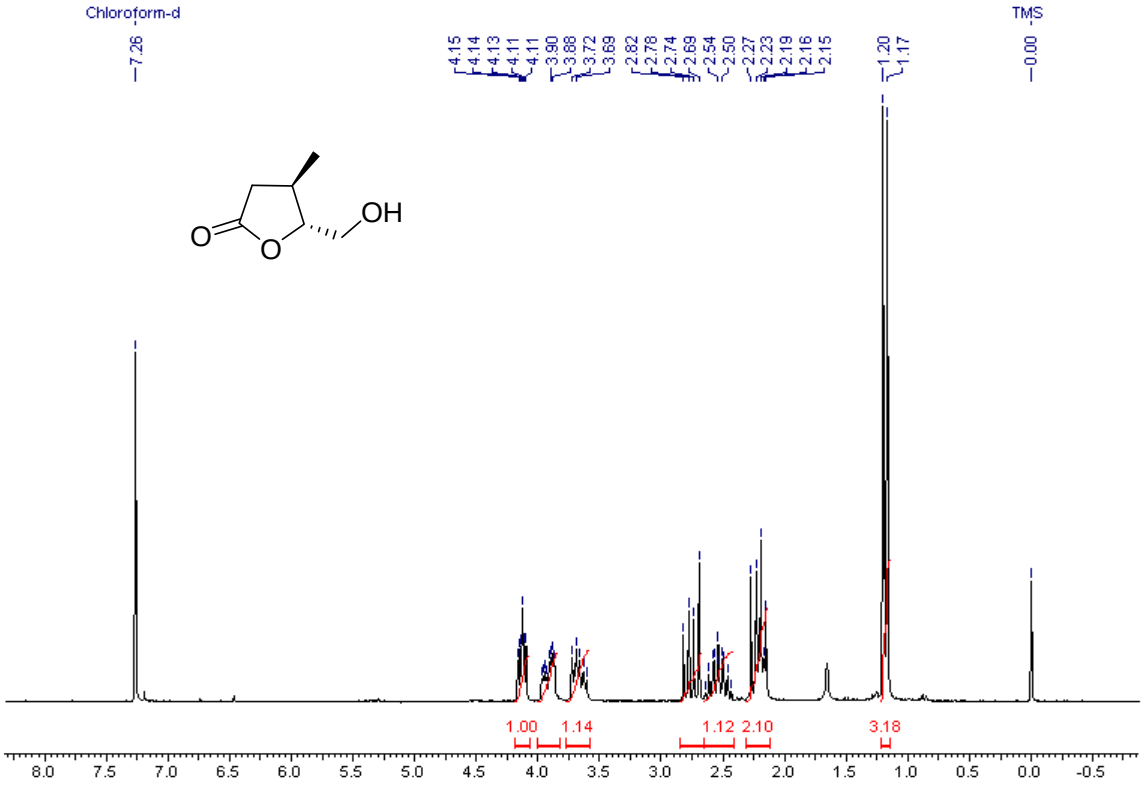
(4*S*,5*R*)-4-(4-chlorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8c)

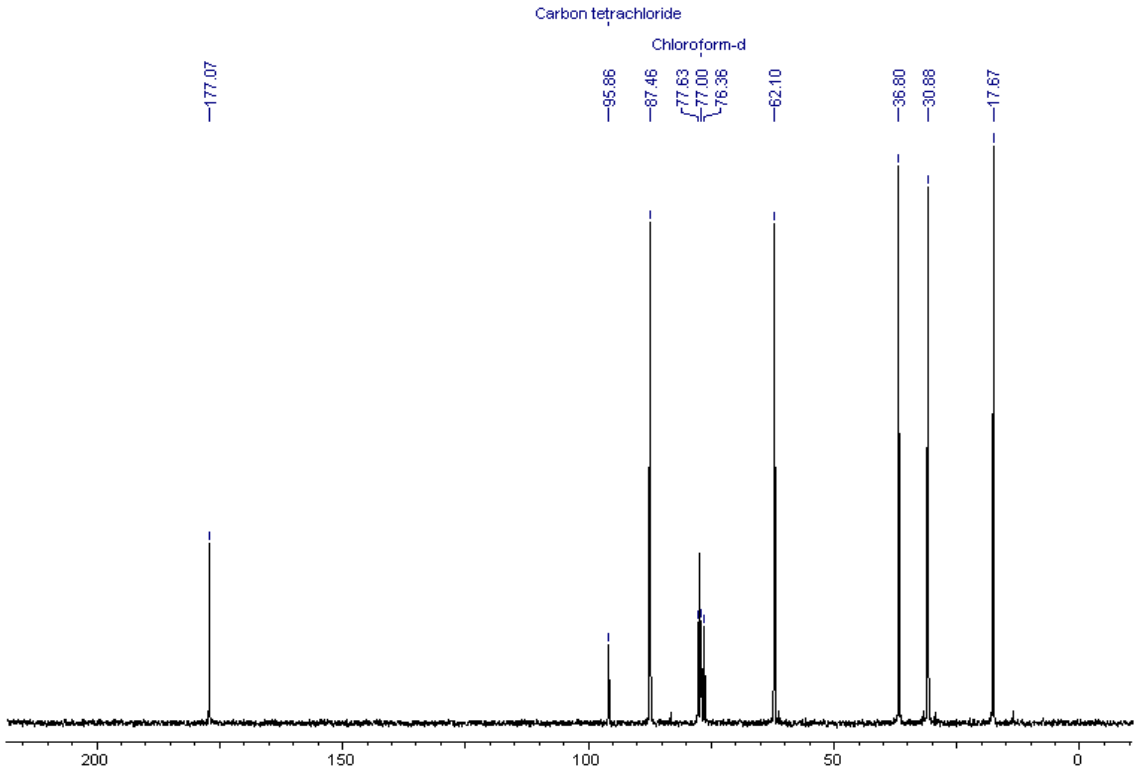


(4*S*,5*R*)-4-(4-bromophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8d)

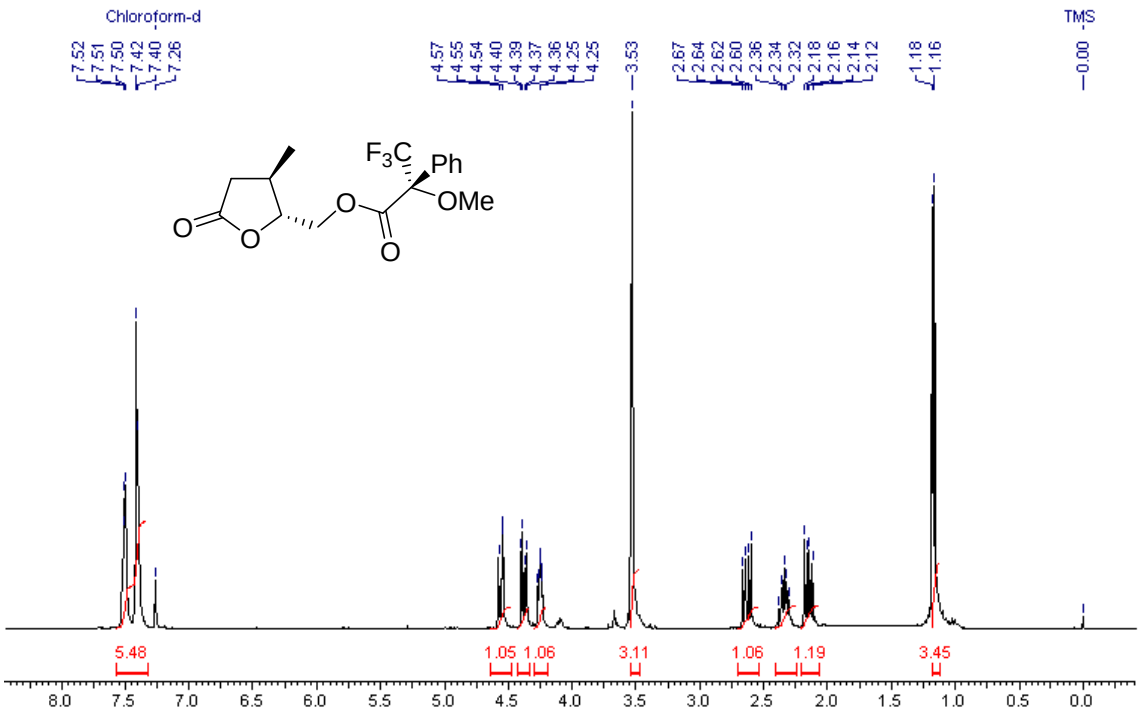


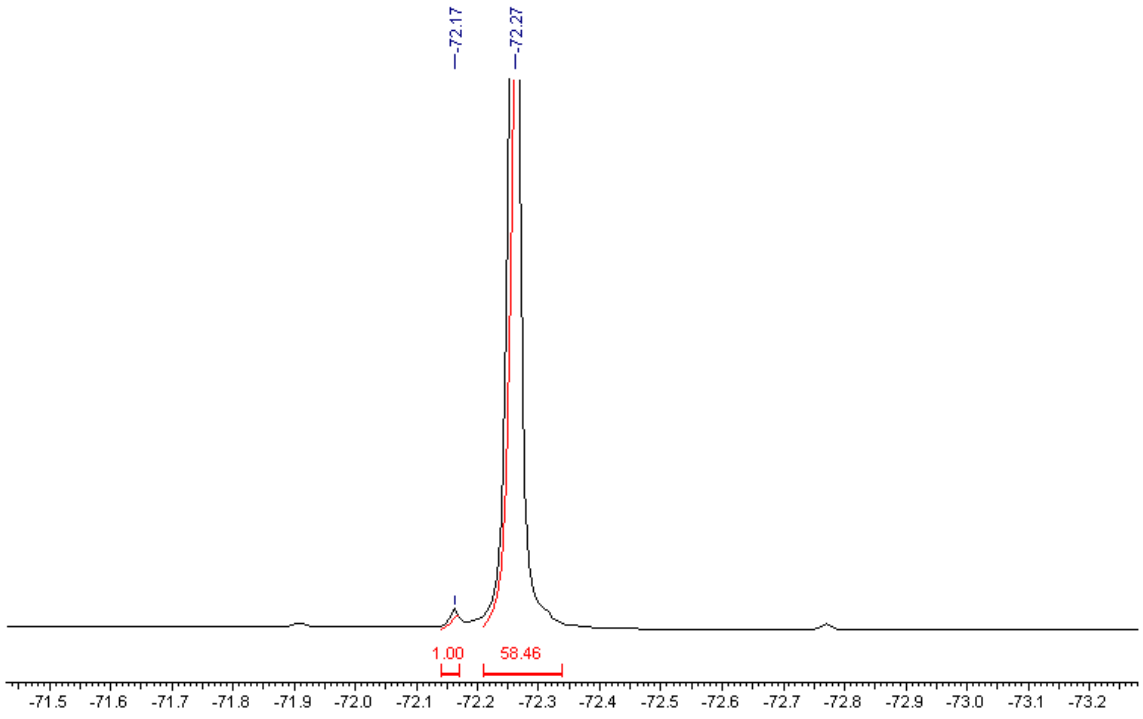
(4*S*,5*R*)-5-(hydroxymethyl)-4-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (8e)



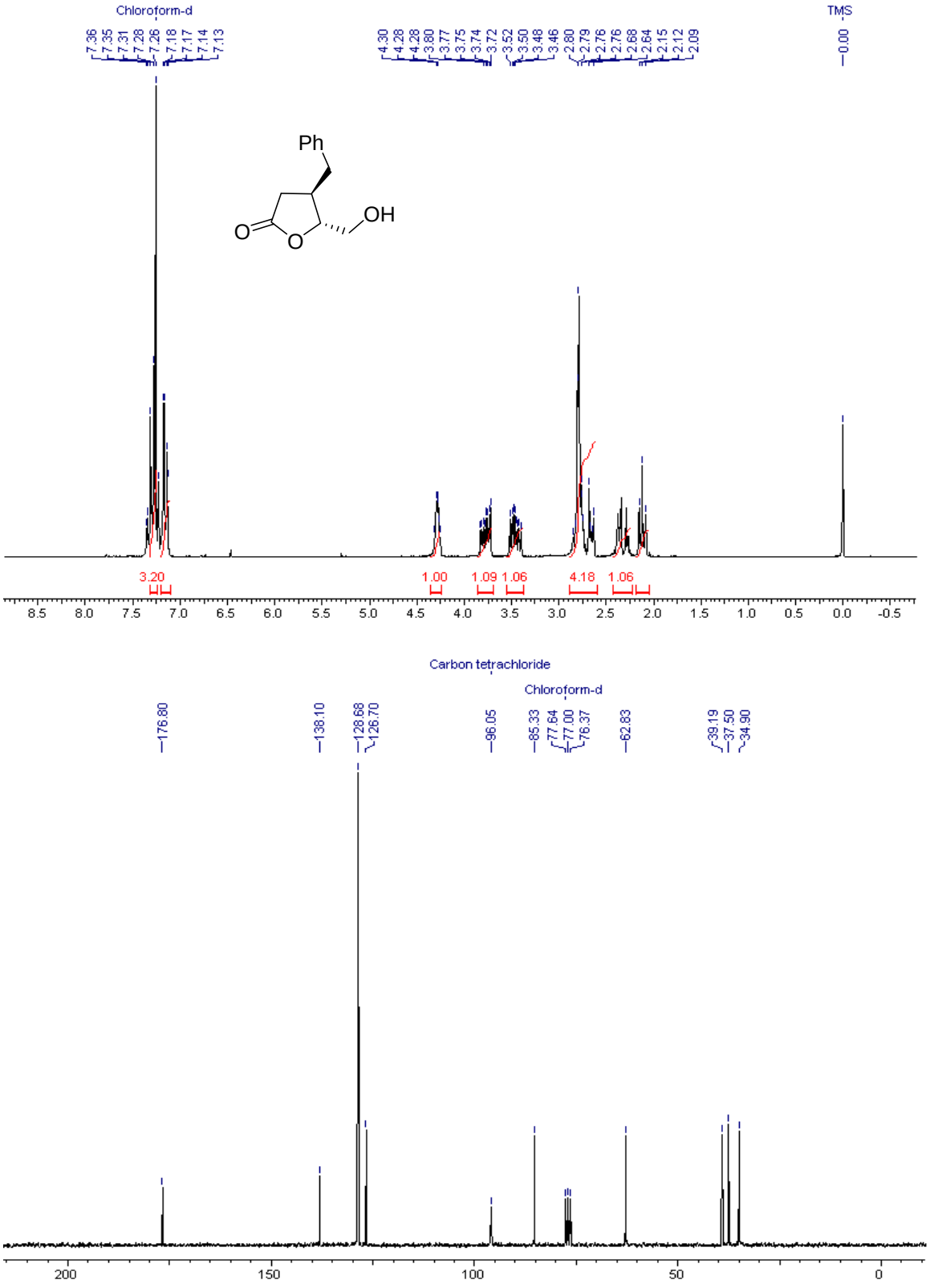


(4*R*,5*R*)-5-(hydroxymethyl)-4-methyldihydrofuran-2(3*H*)-one (8f)

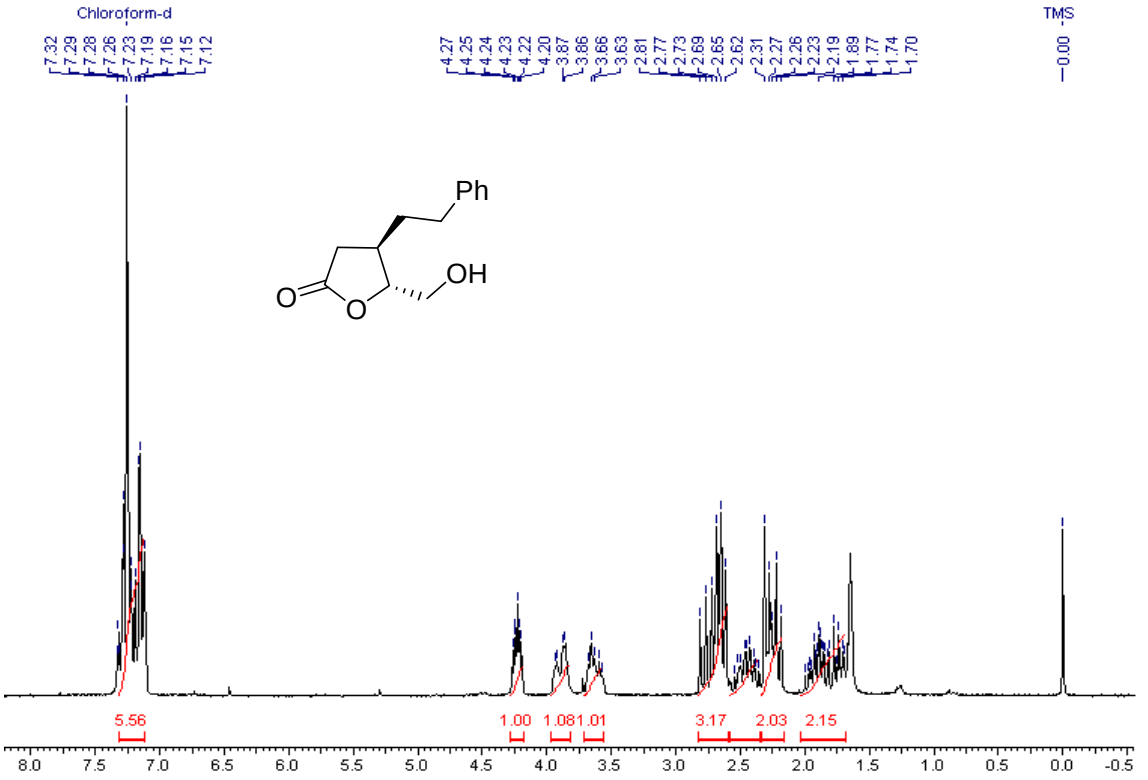


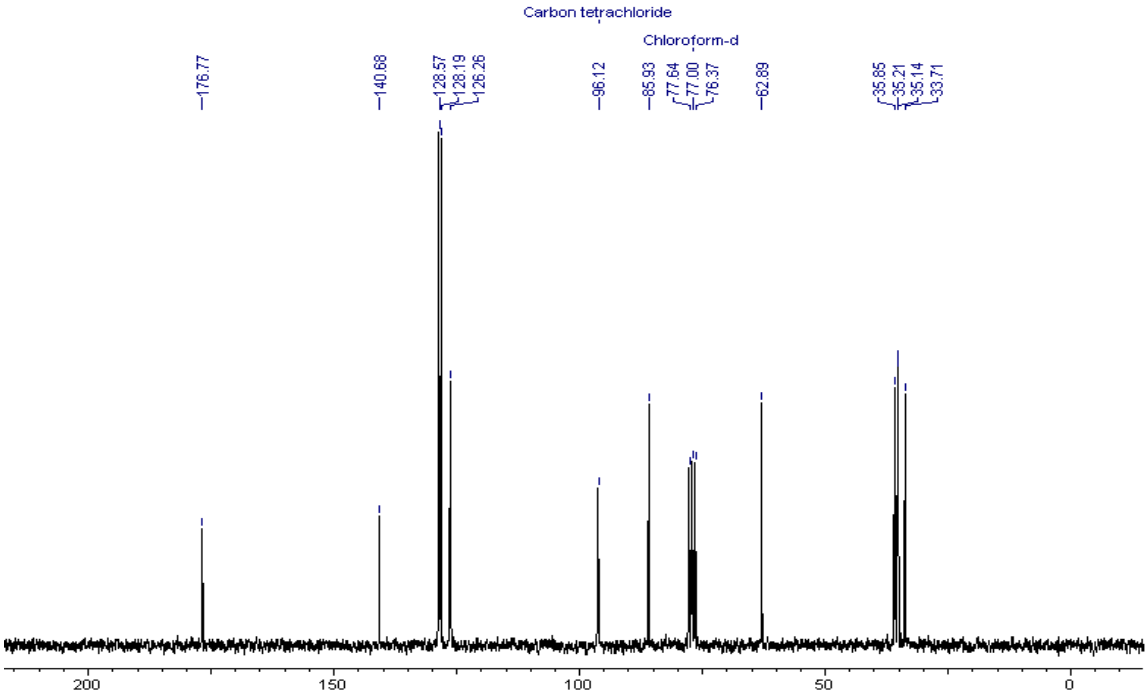


(2*R*)-((2*S*,3*S*)-tetrahydro-3-methyl-5-oxofuran-2-yl)methyl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate

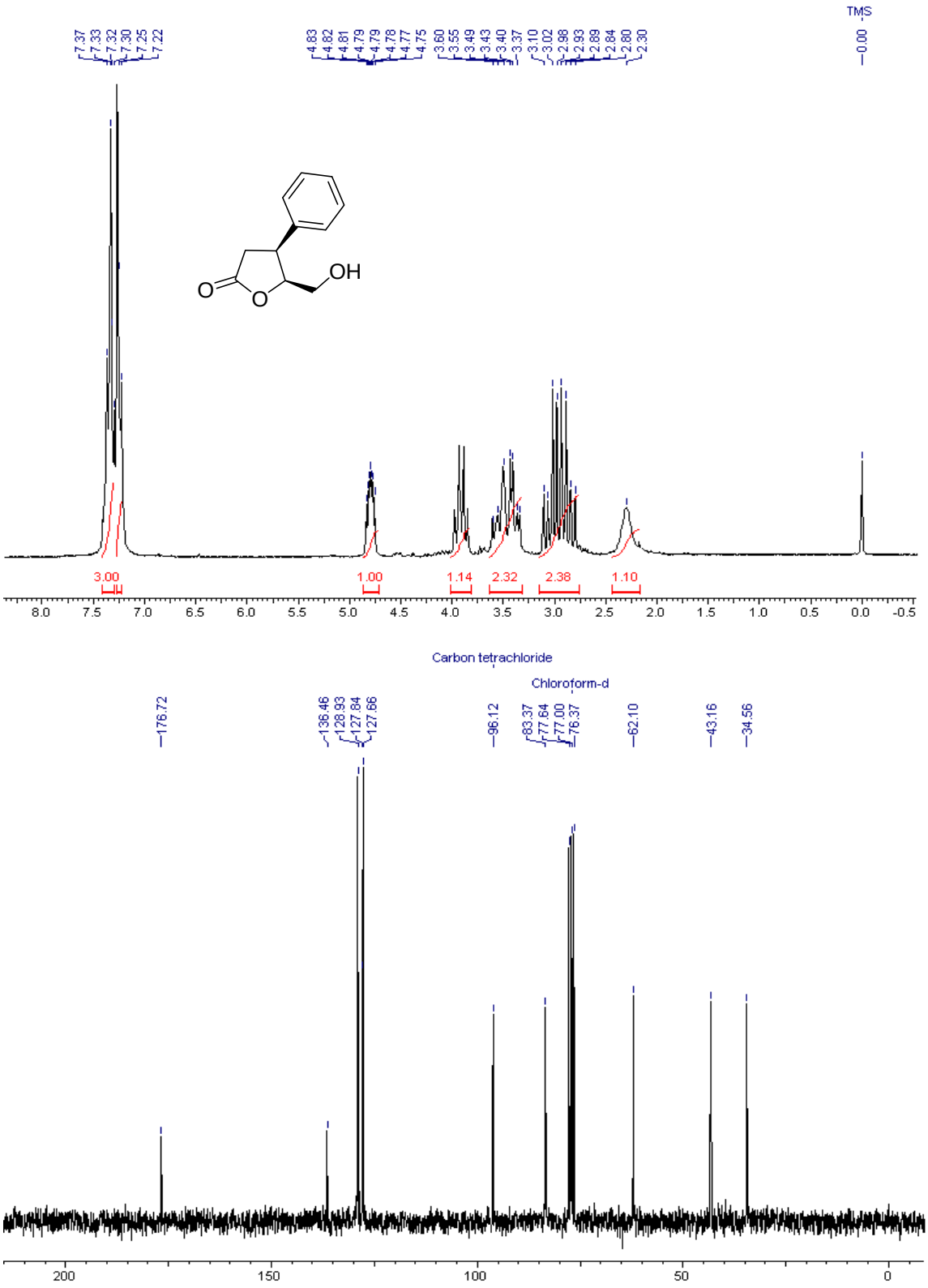


(4*R*,5*R*)-4-benzyl-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8g)

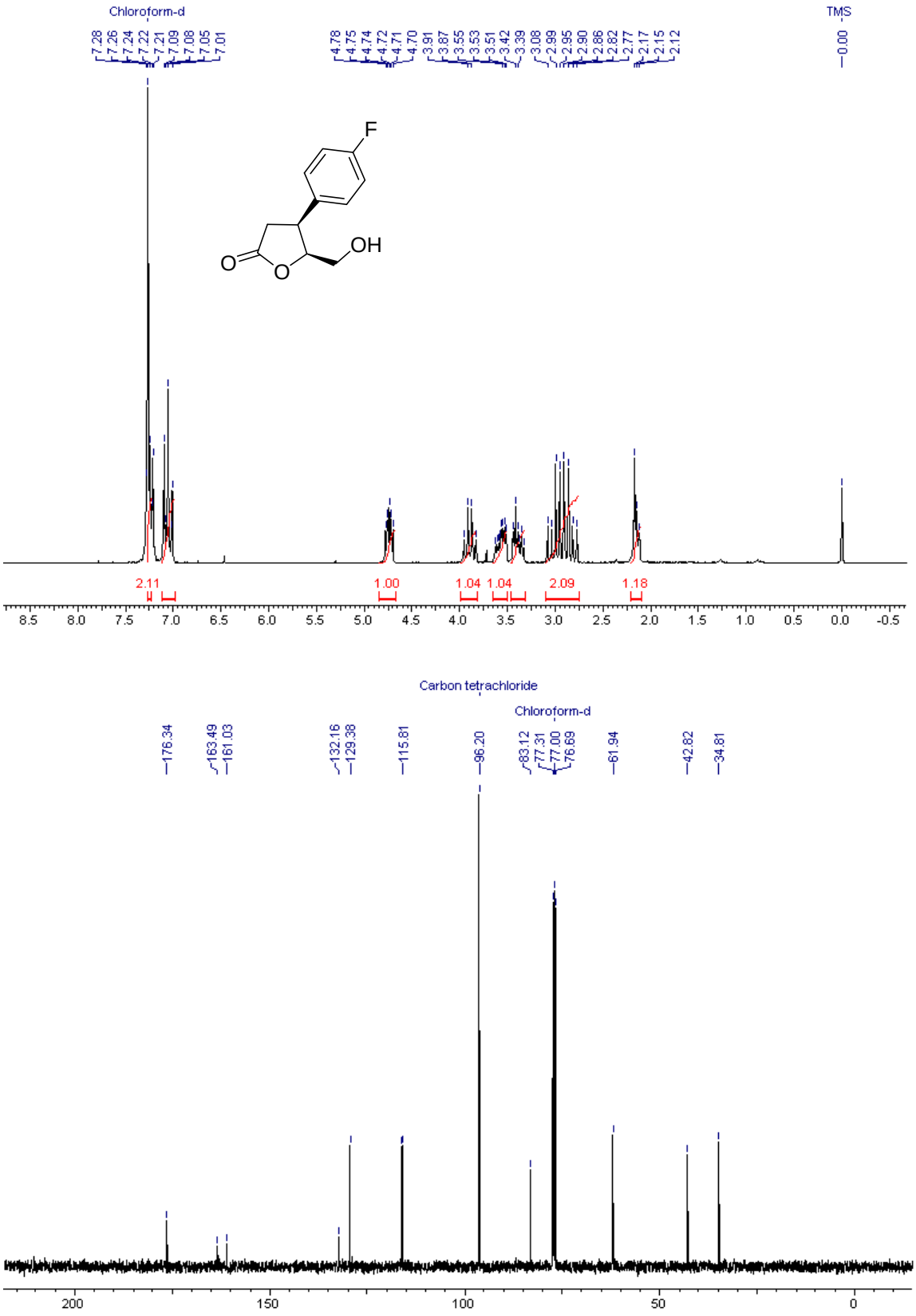




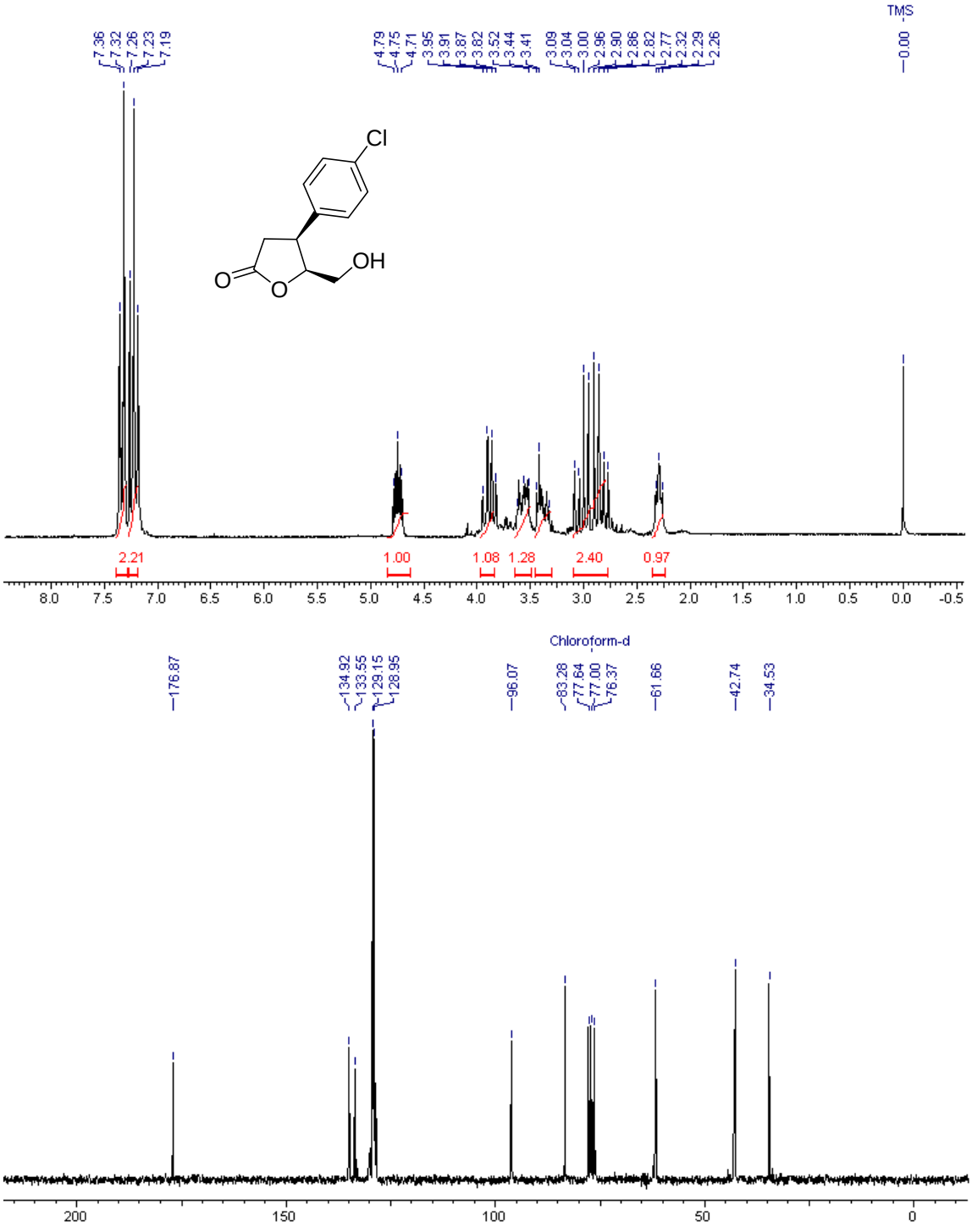
(4*R*,5*R*)-5-(hydroxymethyl)-4-phenethyldihydrofuran-2(3*H*)-one (8h)



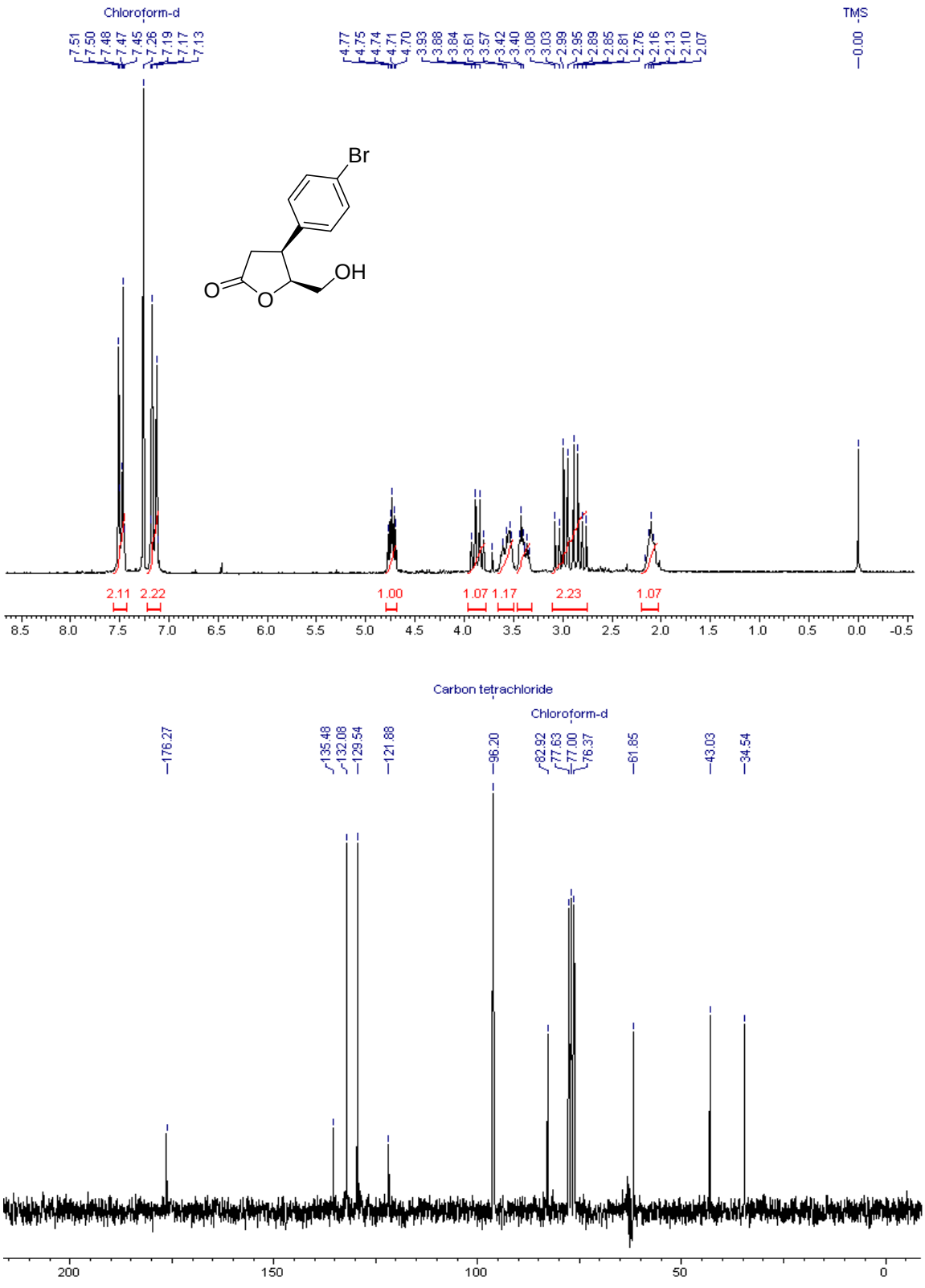
(4*S*,5*S*)-5-(hydroxymethyl)-4-phenyldihydrofuran-2(3*H*)-one (11a)



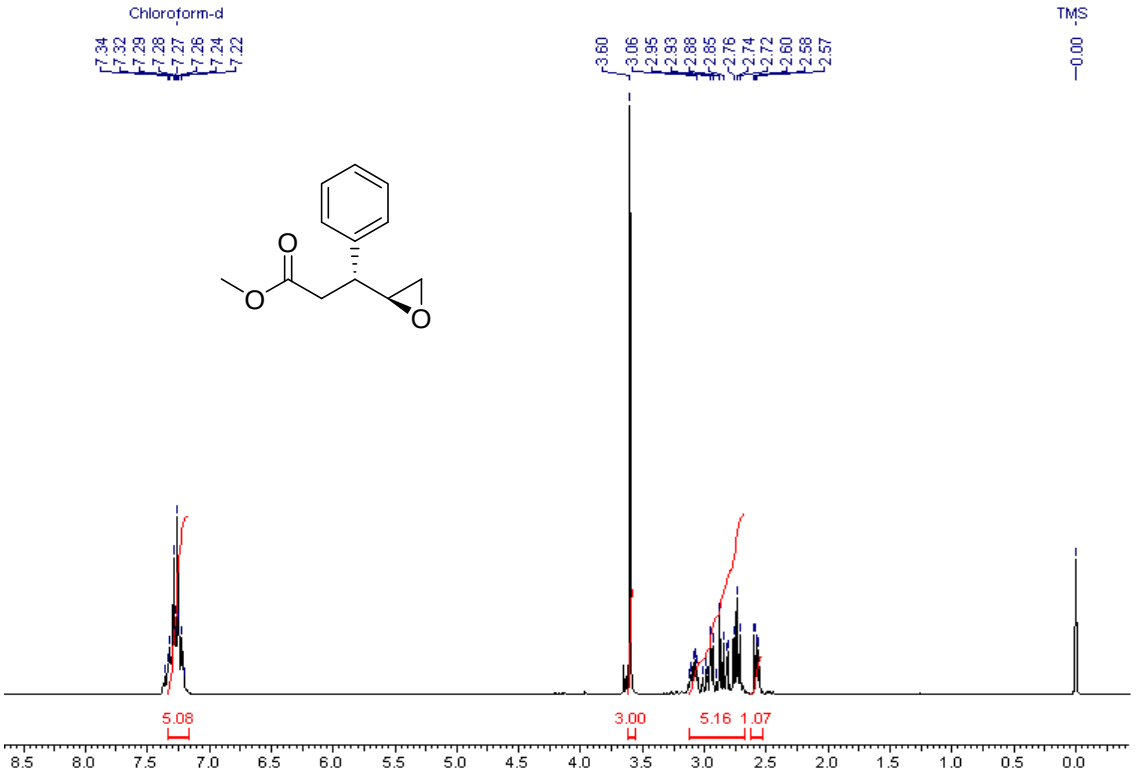
(4*S*,5*S*)-4-(4-fluorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (11b)

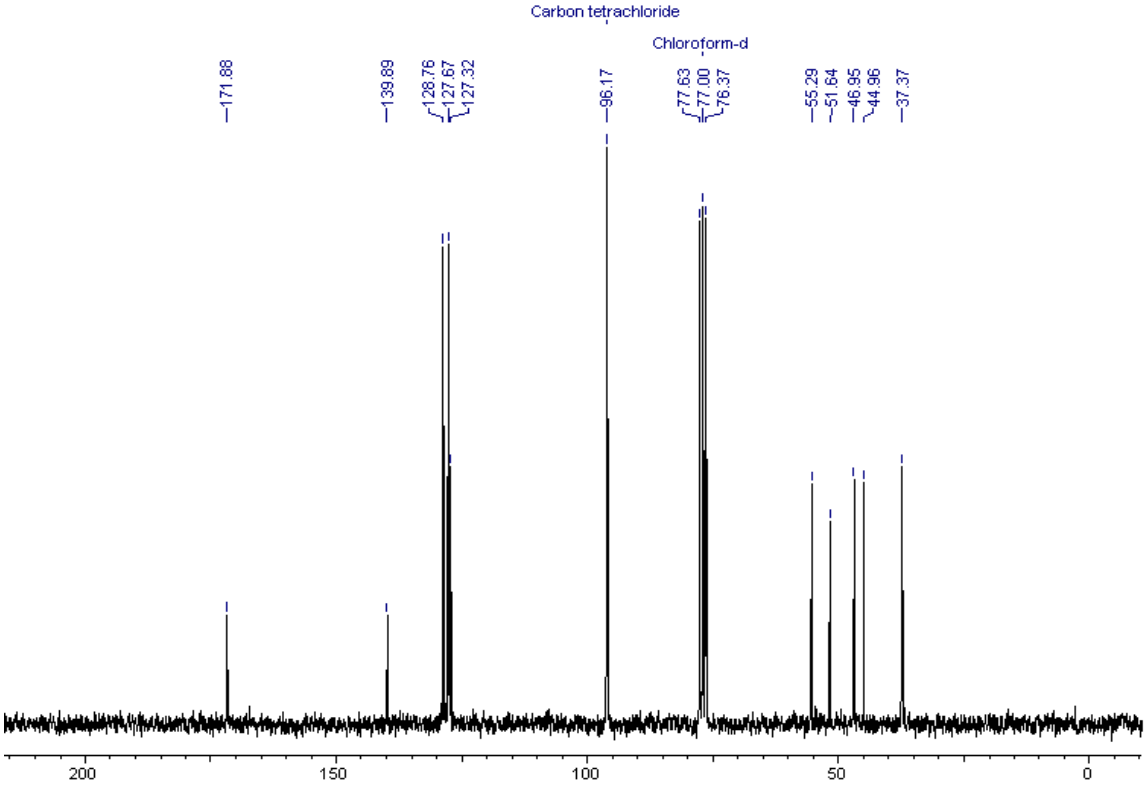


(4*S*,5*S*)-4-(4-chlorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (11c)

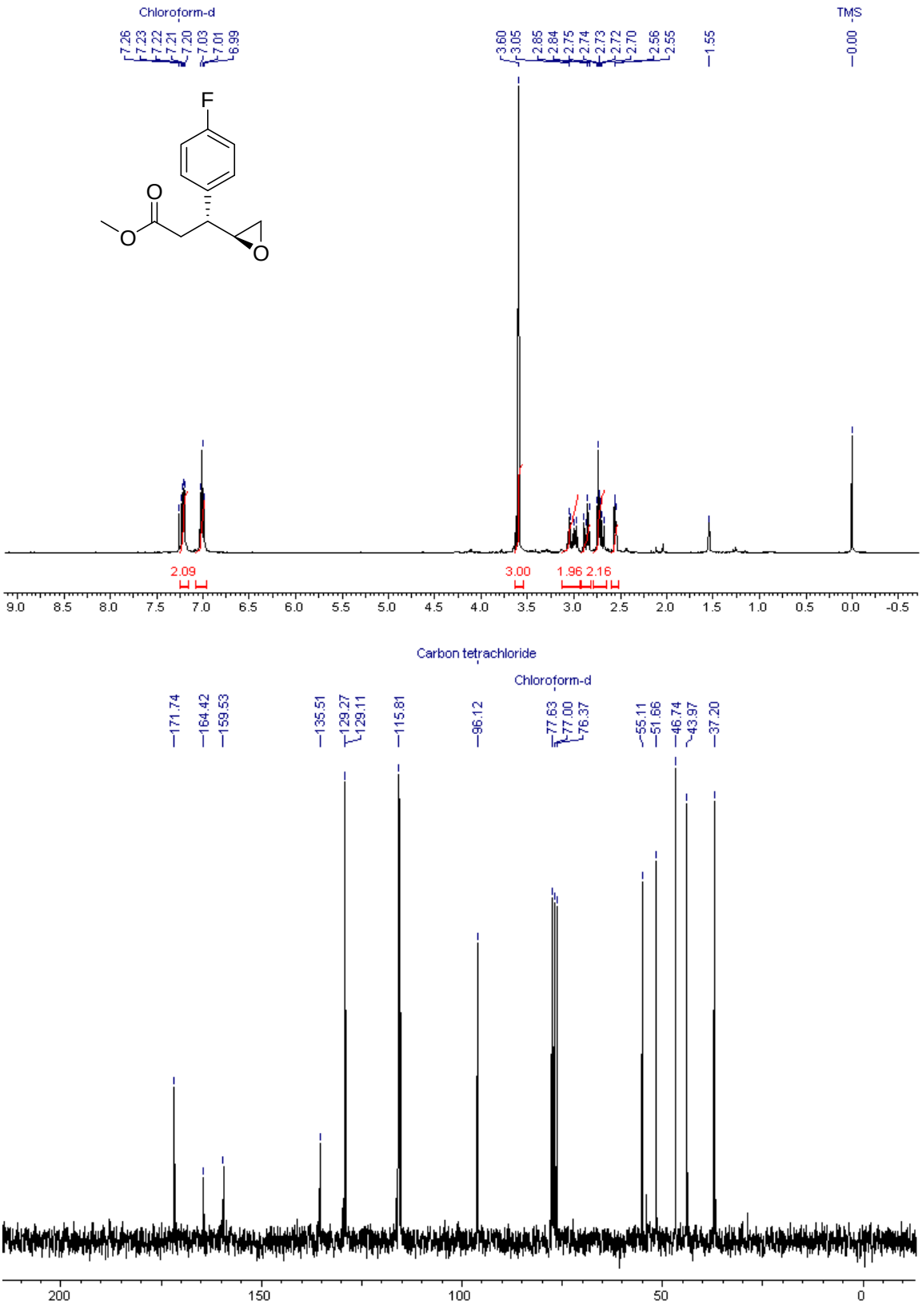


(4*S*,5*S*)-4-(4-bromophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (11d)

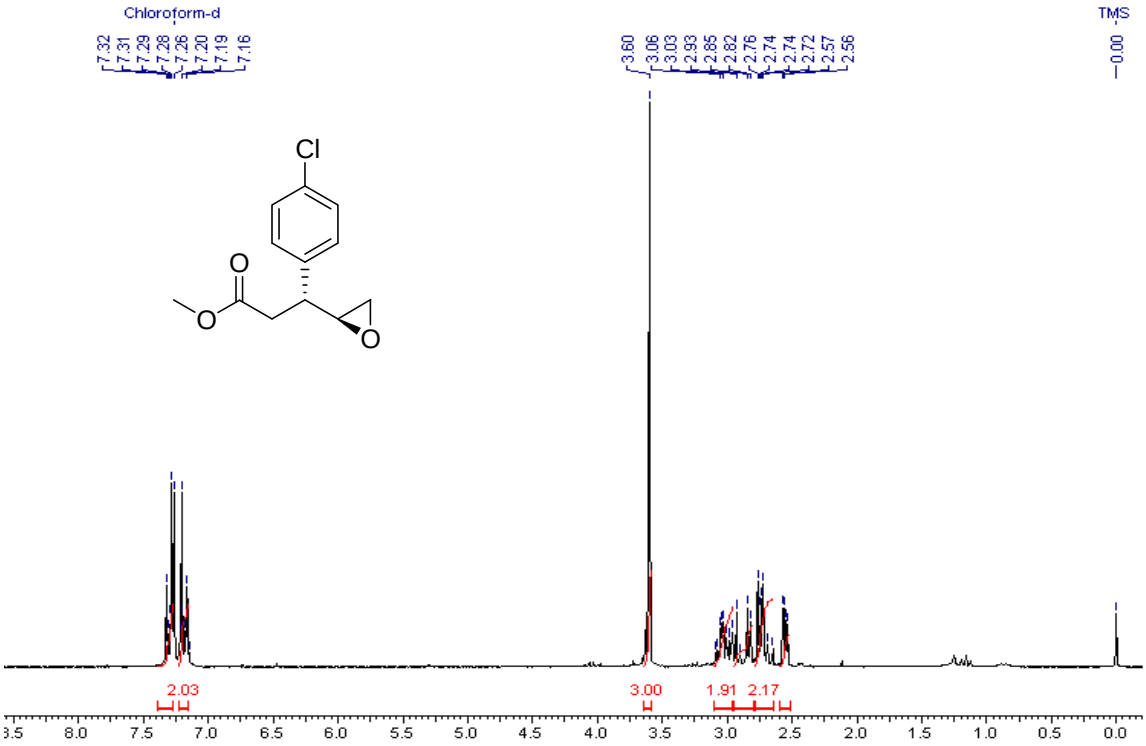


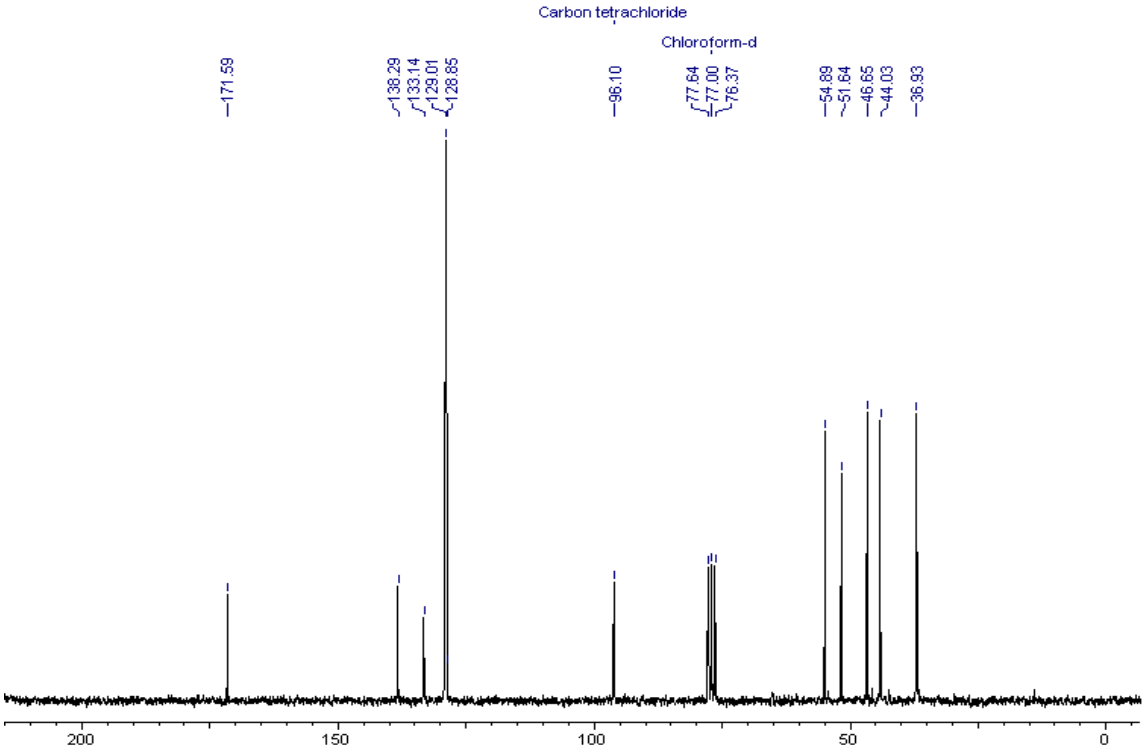


(*R*)-methyl 3-((*S*)-oxiran-2-yl)-3-phenylpropanoate (9a)

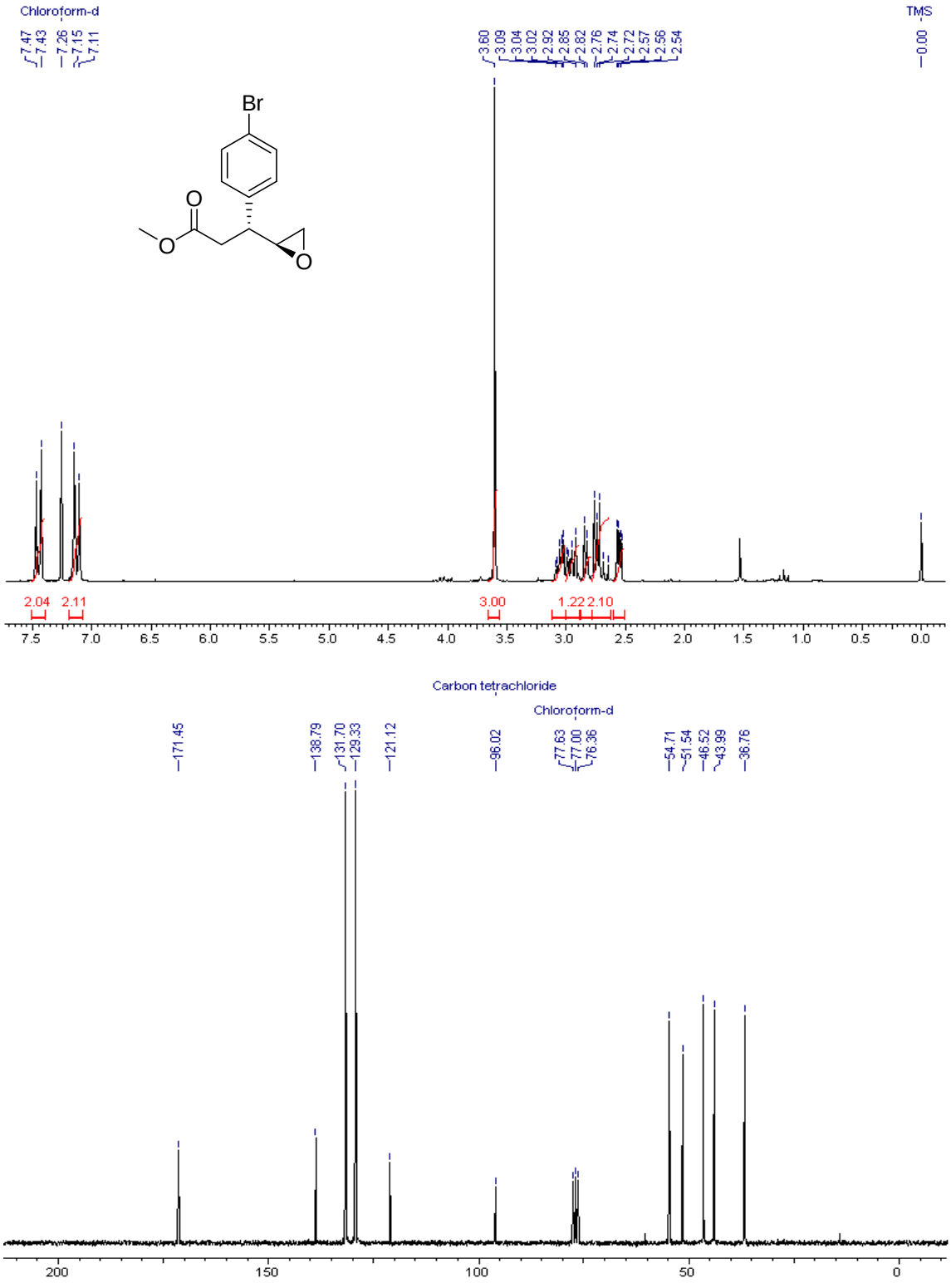


(*R*)-methyl 3-(4-fluorophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9b)

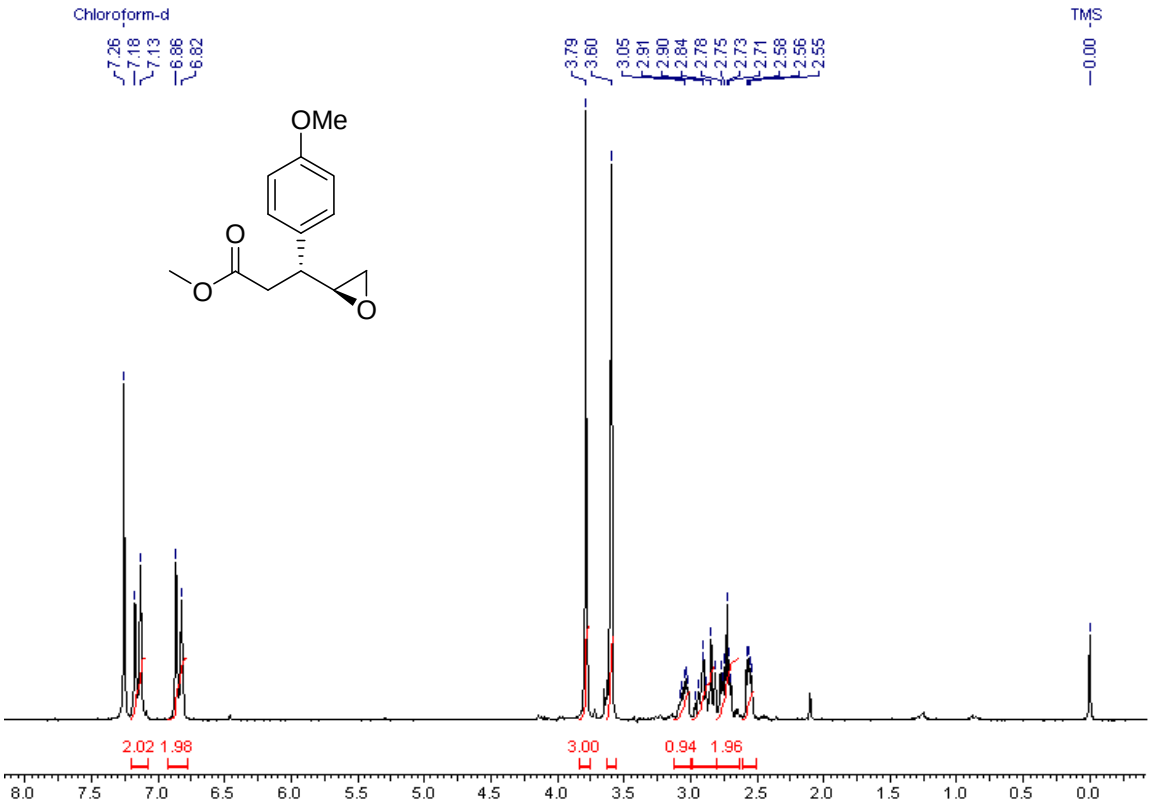


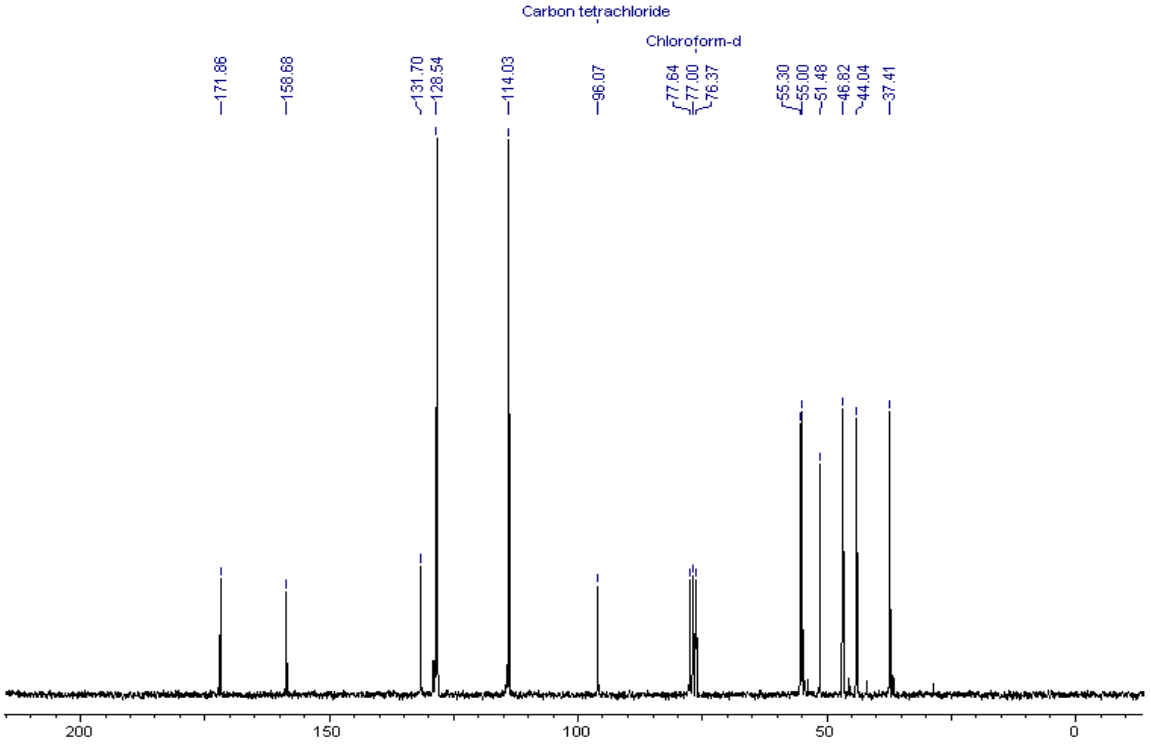


(*R*)-methyl 3-(4-chlorophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9c)

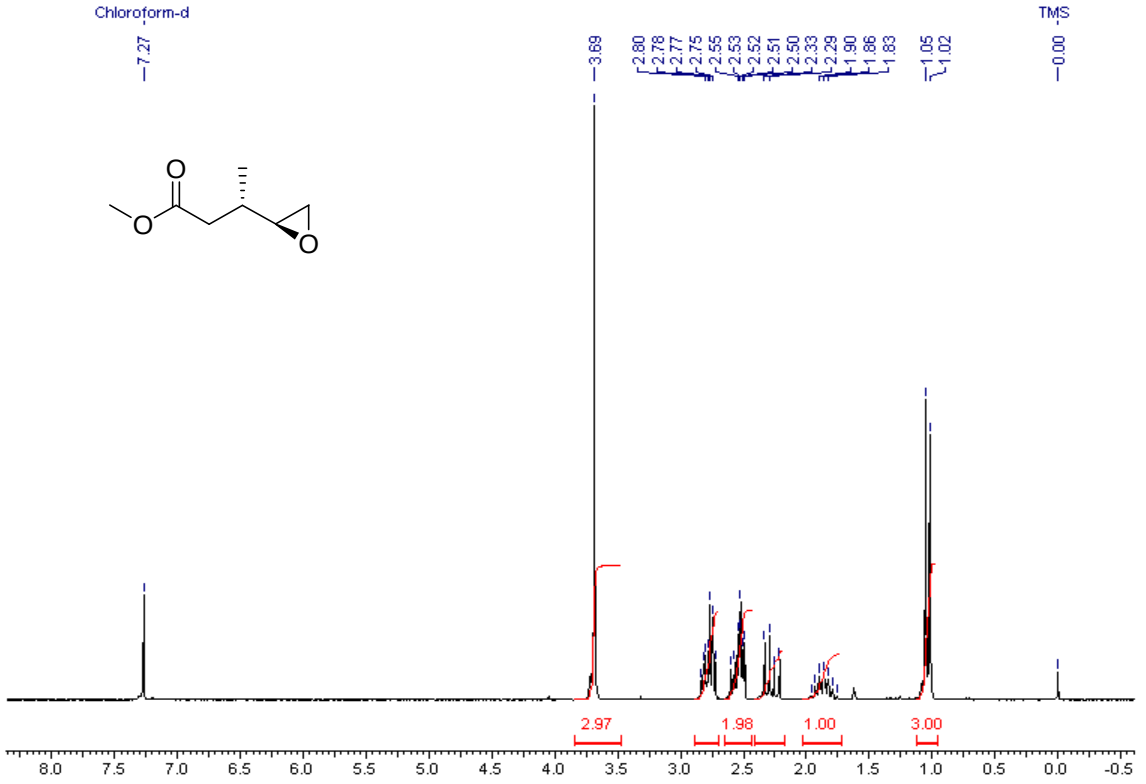


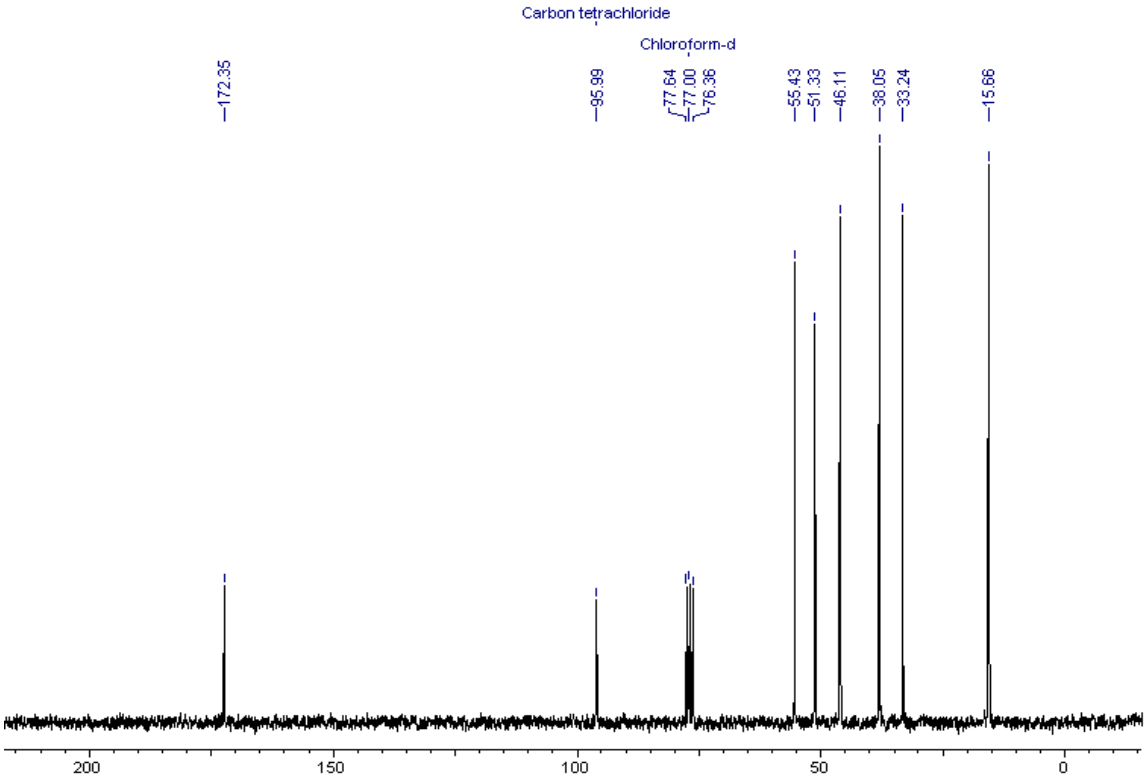
(*R*)-methyl 3-(4-bromophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9d)



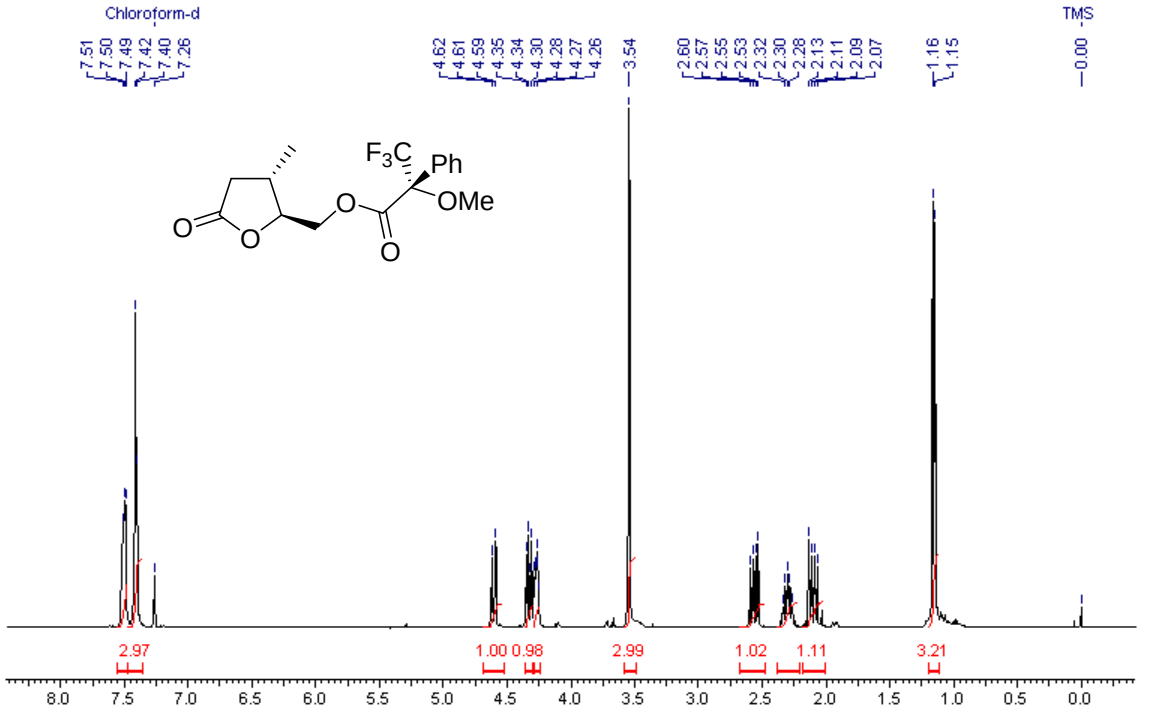


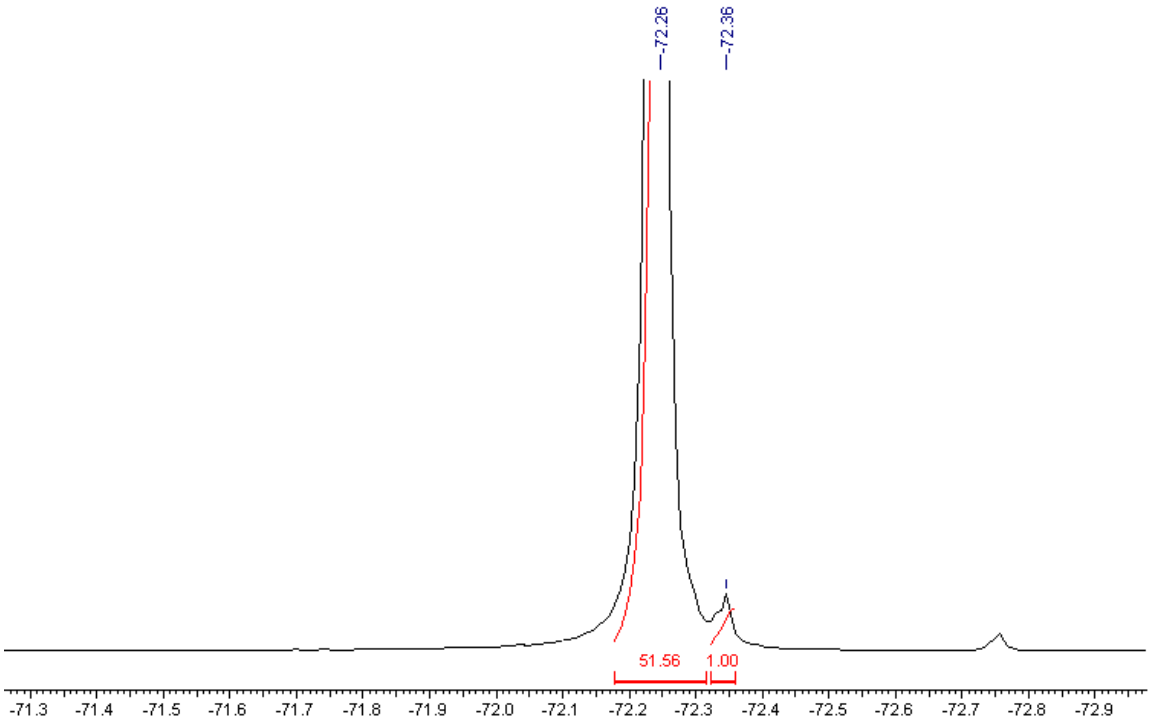
(*R*)-methyl 3-(4-methoxyphenyl)-3-((*S*)-oxiran-2-yl)propanoate (9e)



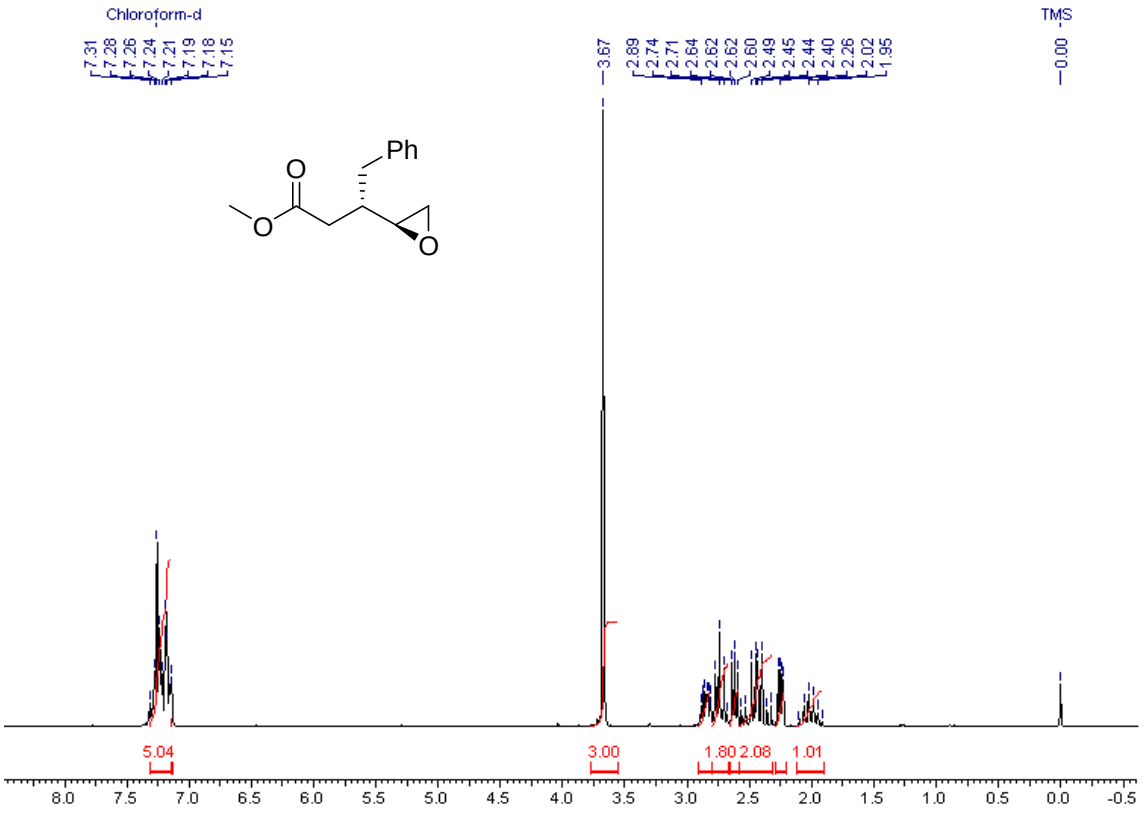


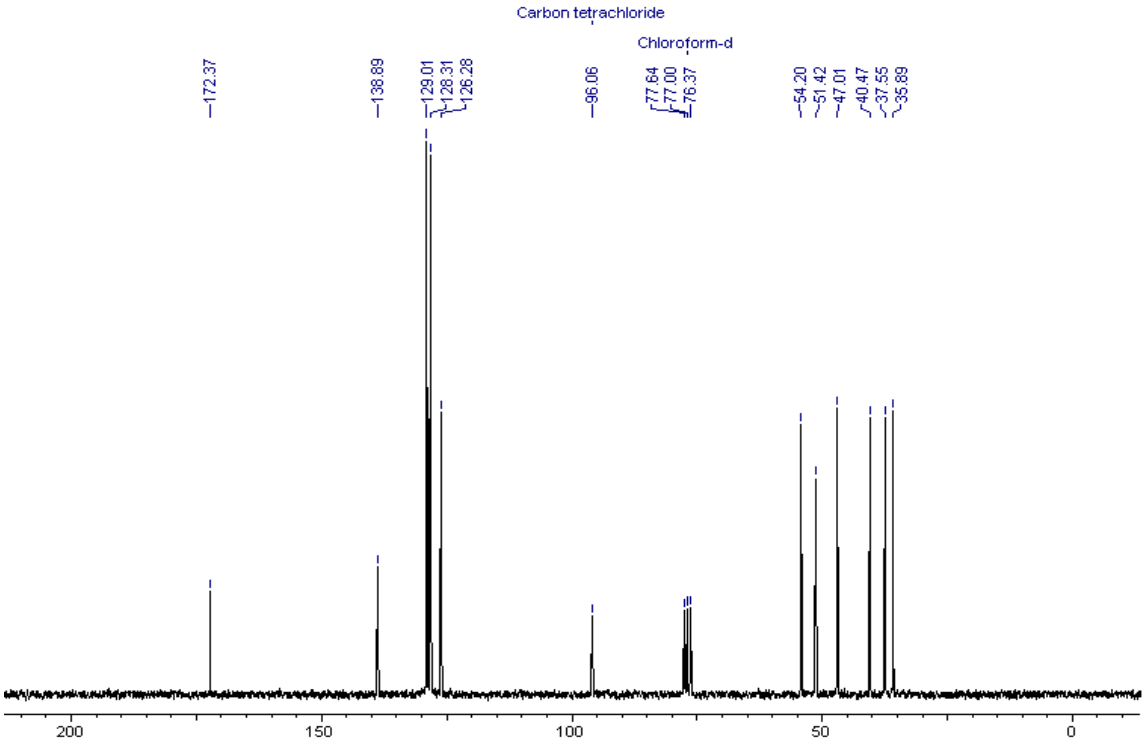
(*S*)-methyl 3-((*S*)-oxiran-2-yl)butanoate (9f)



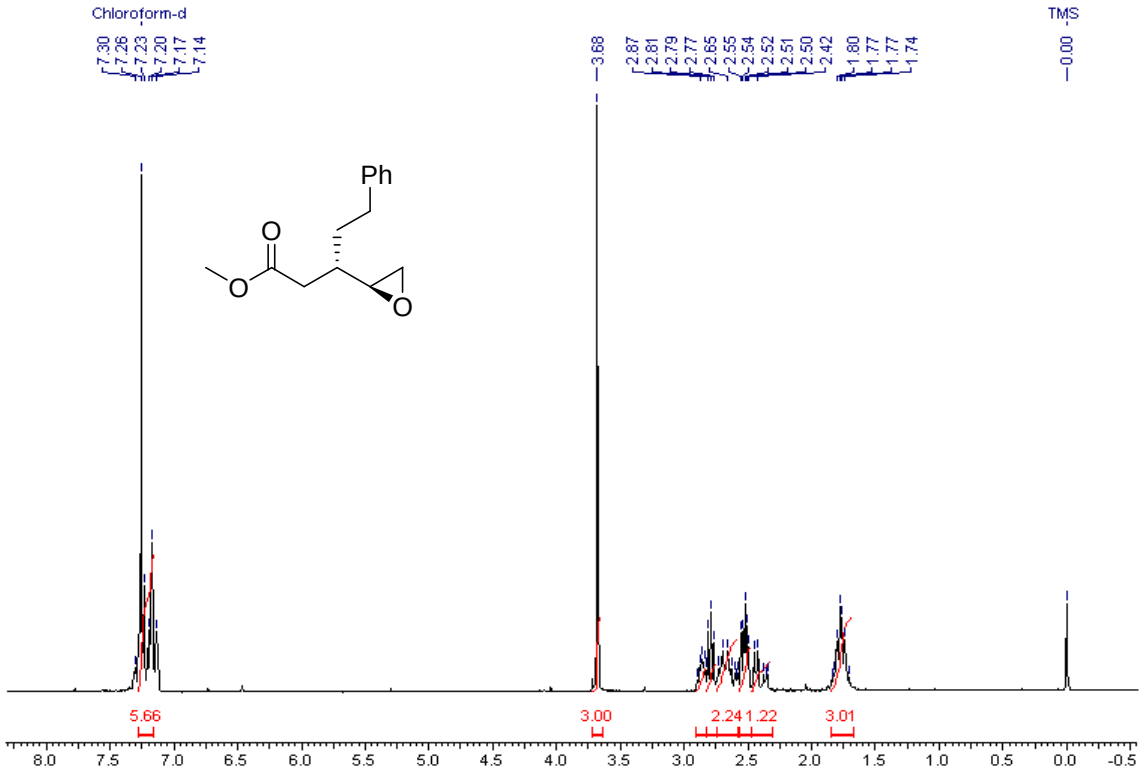


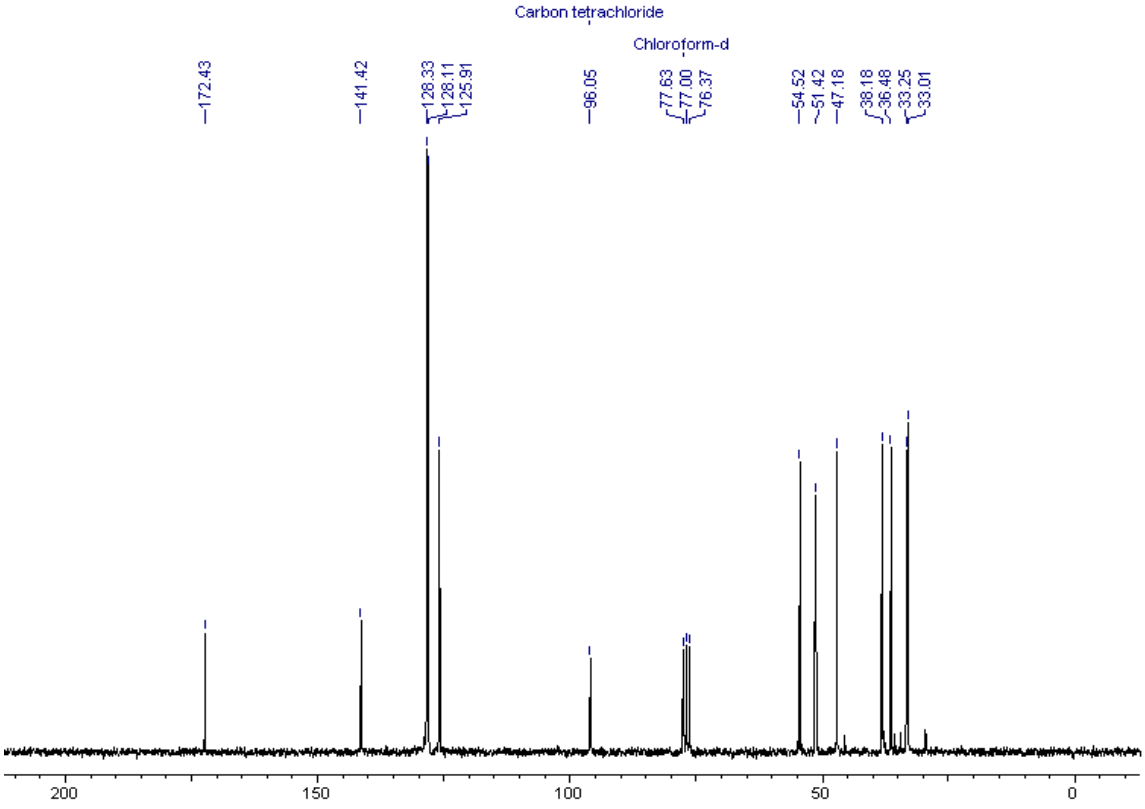
(2*R*)-((2*S*,3*S*)-tetrahydro-3-methyl-5-oxofuran-2-yl)methyl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate



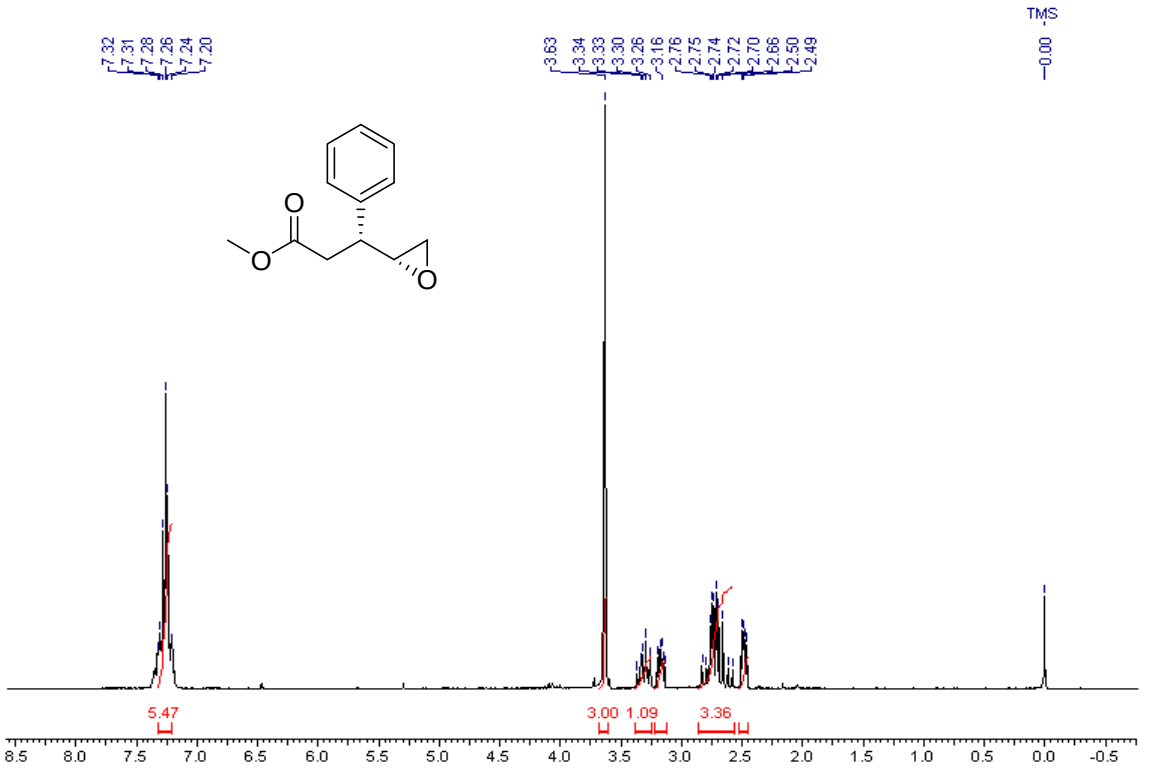


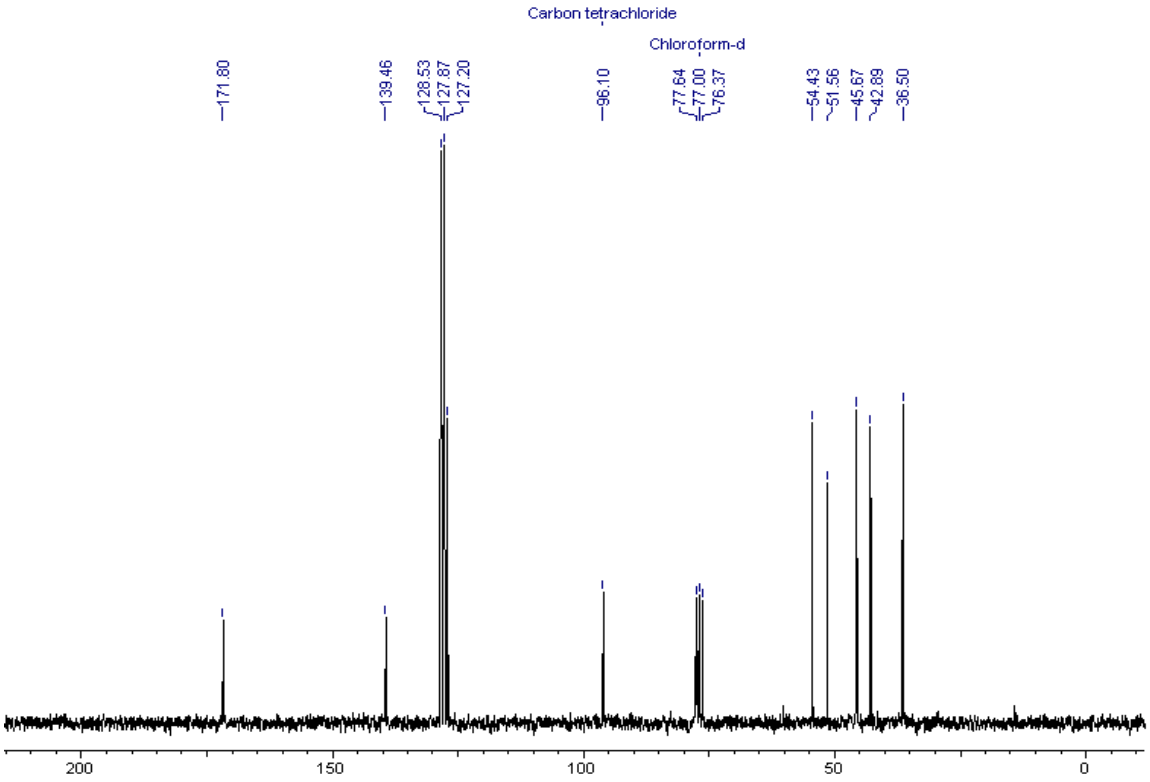
(*S*)-methyl 3-((*S*)-oxiran-2-yl)-4-phenylbutanoate (9g)



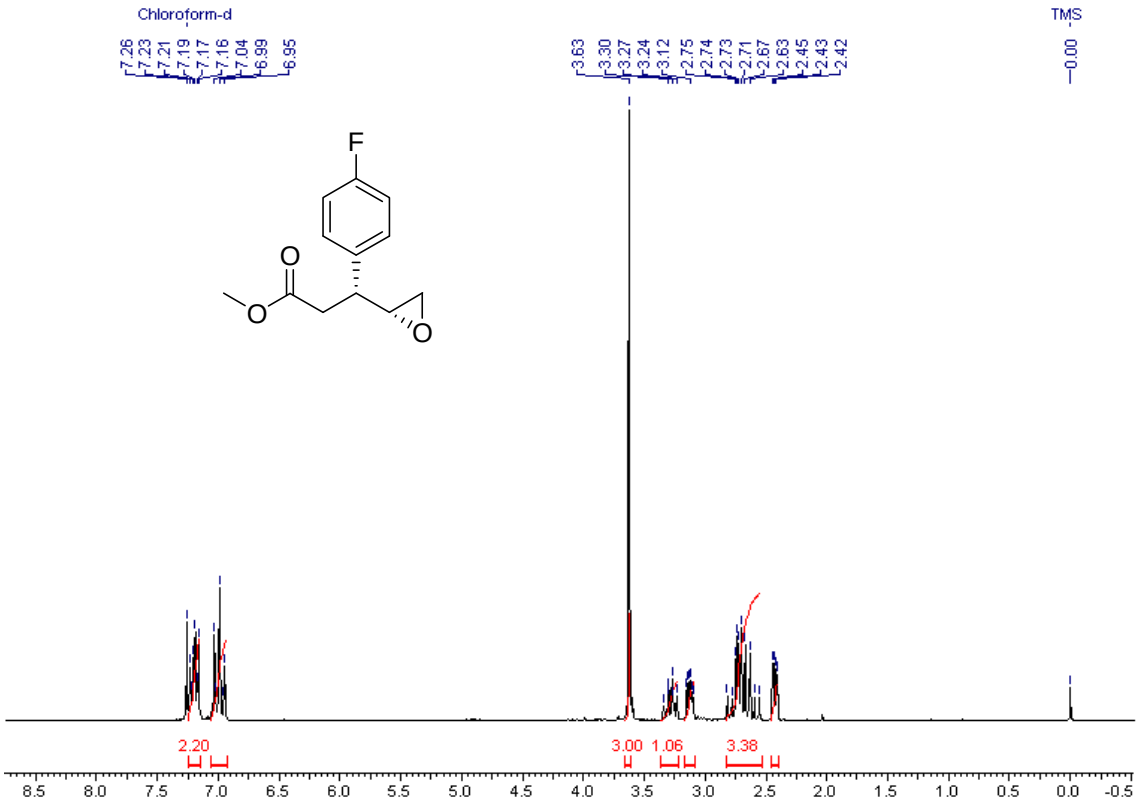


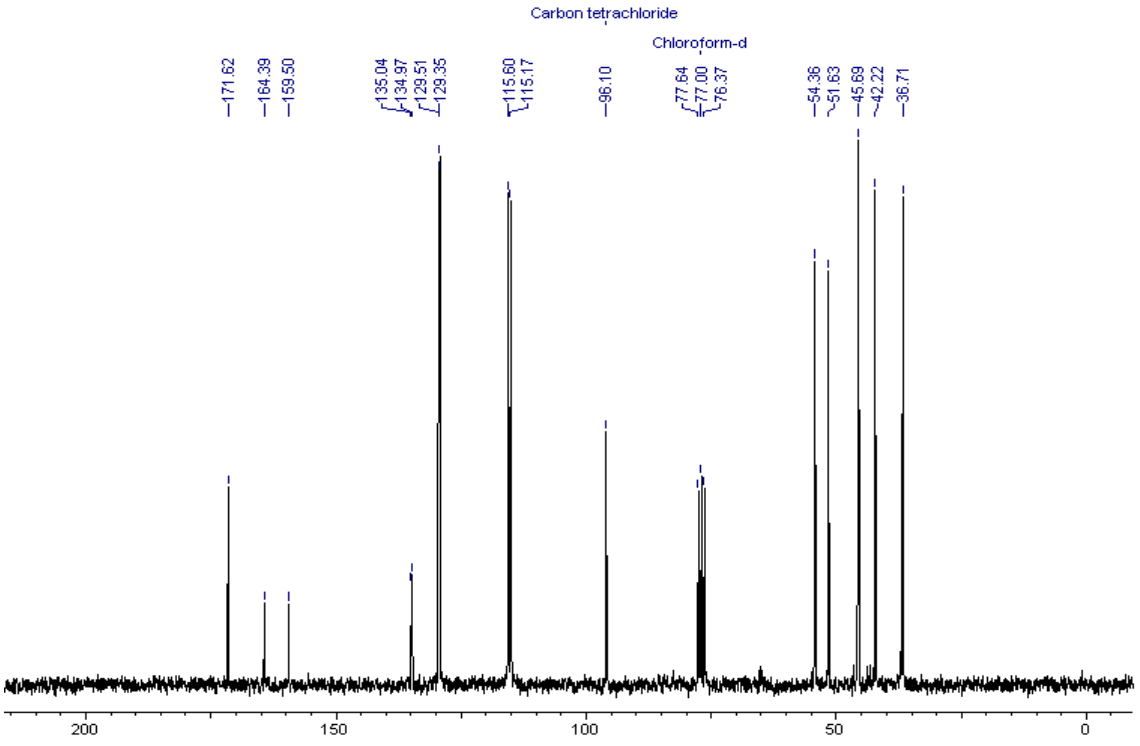
(*S*)-methyl 3-((*S*)-oxiran-2-yl)-5-phenylpentanoate (9h)



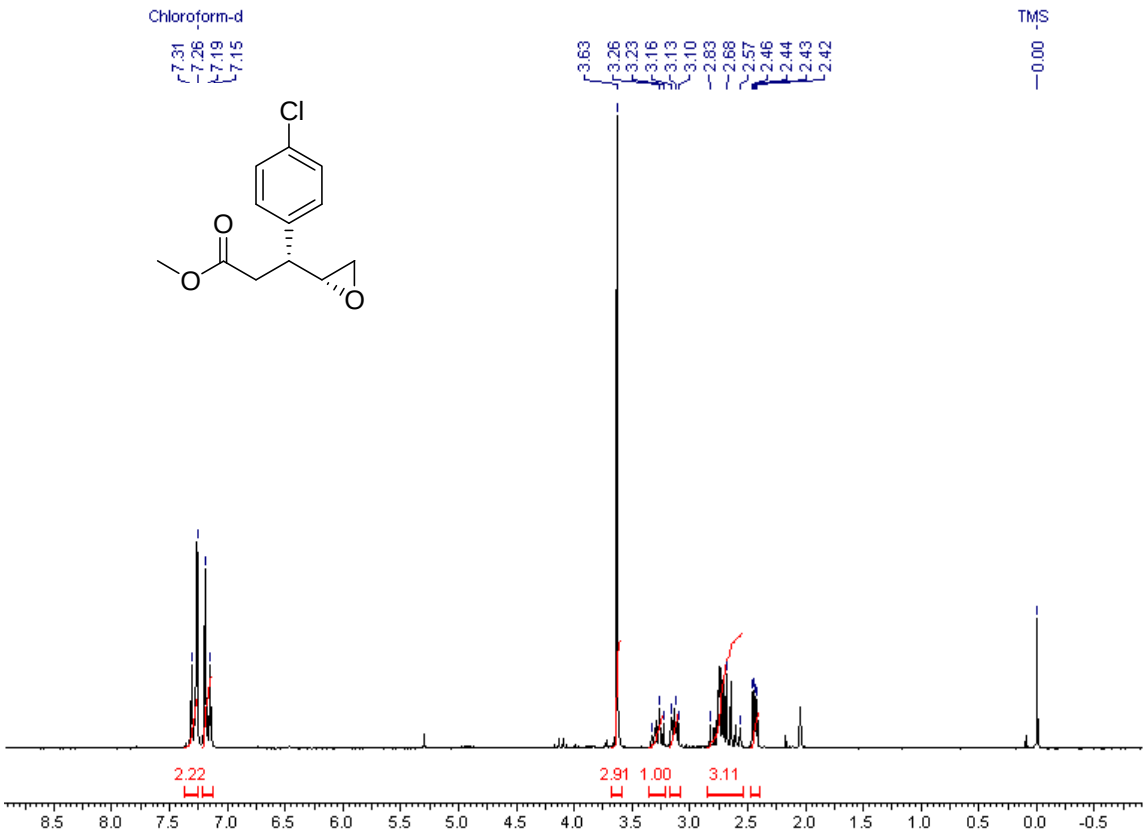


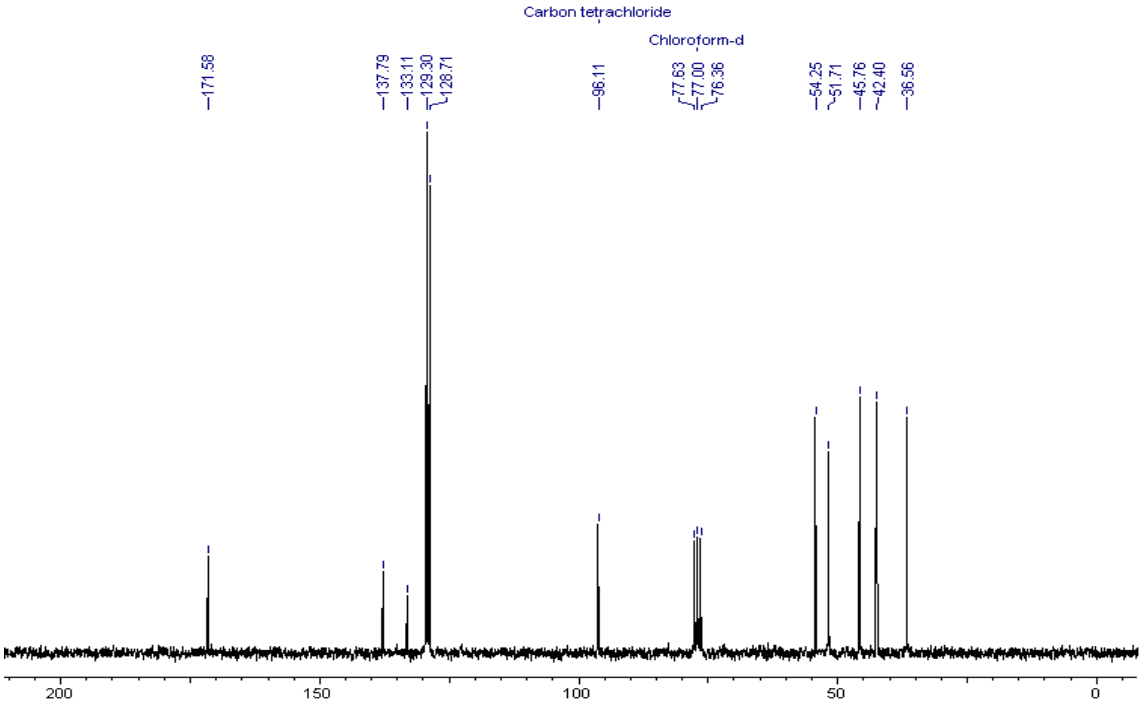
(*R*)-methyl 3-((*R*)-oxiran-2-yl)-3-phenylpropanoate (12a)



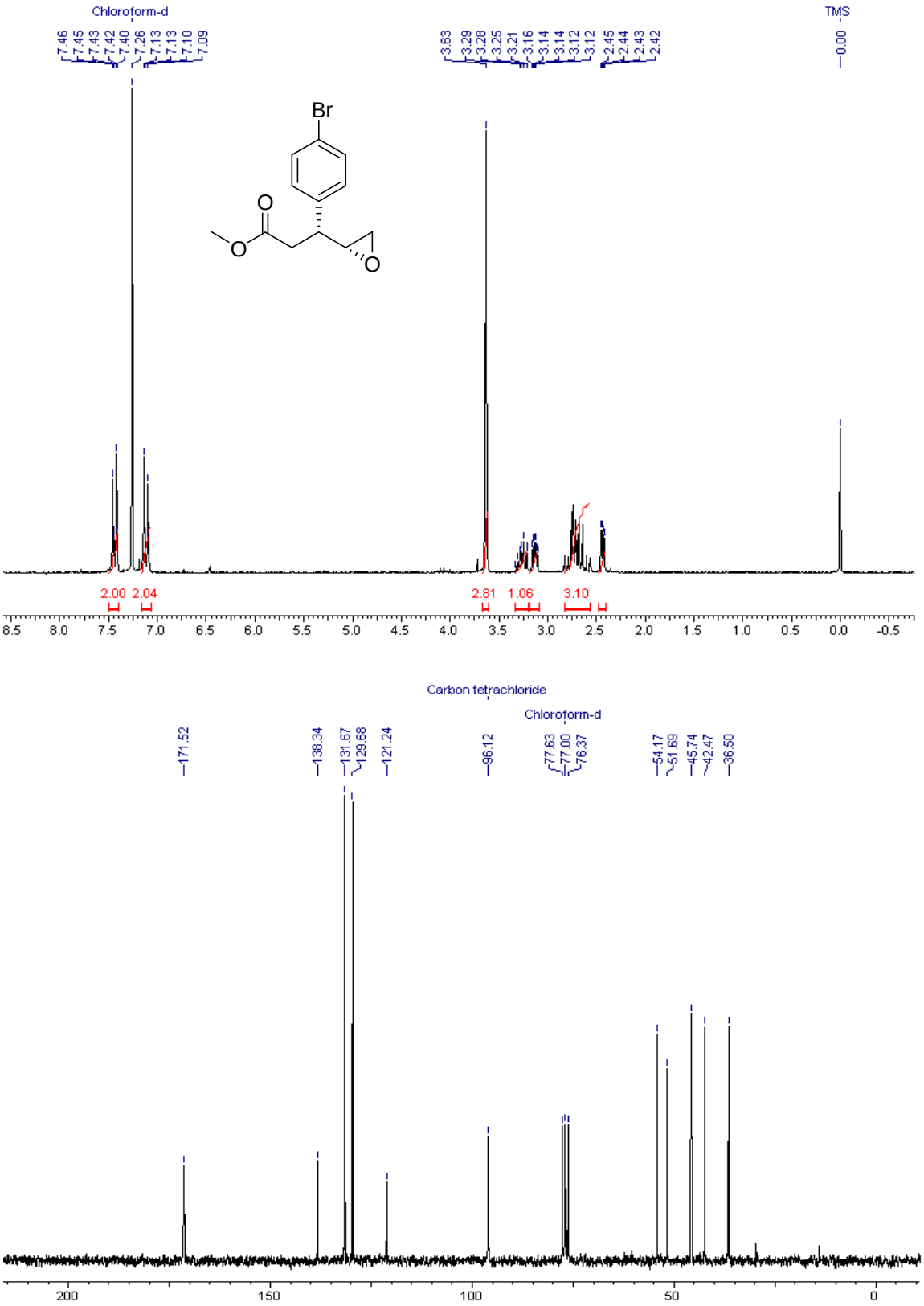


(*R*)-methyl 3-(4-fluorophenyl)-3-((*R*)-oxiran-2-yl)propanoate (12b)

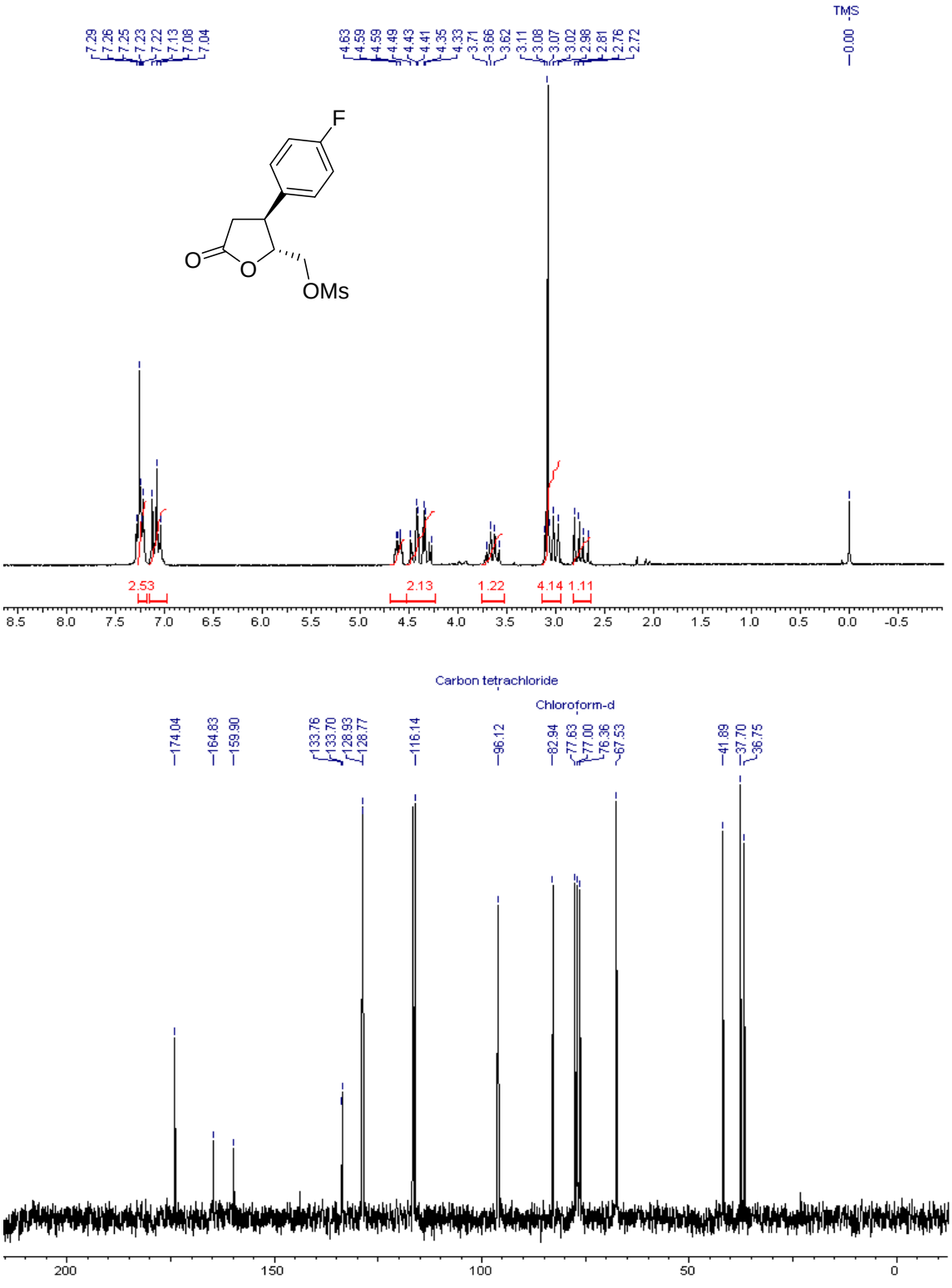




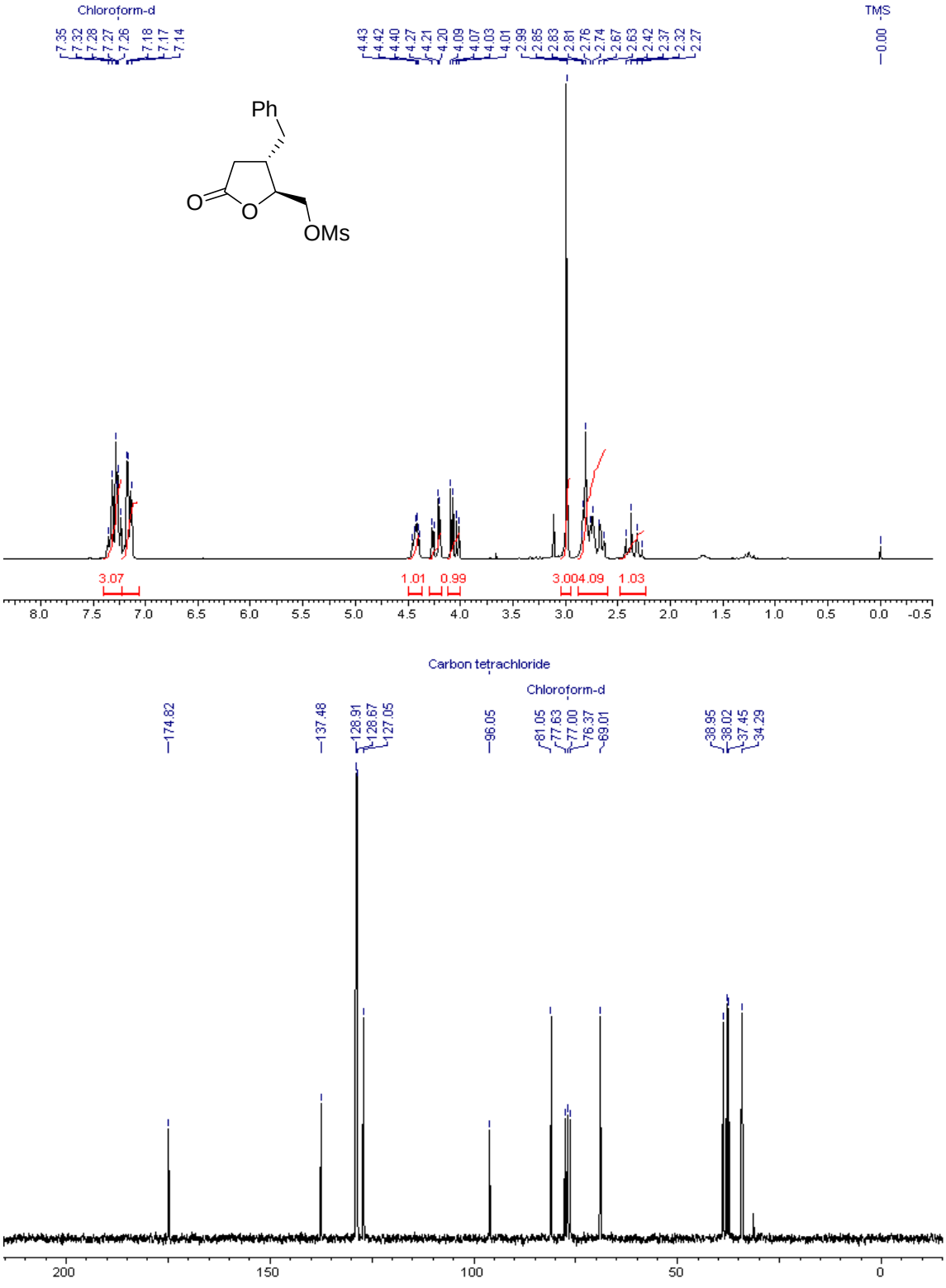
(*R*)-methyl 3-(4-chlorophenyl)-3-((*R*)-oxiran-2-yl)propanoate (12c)



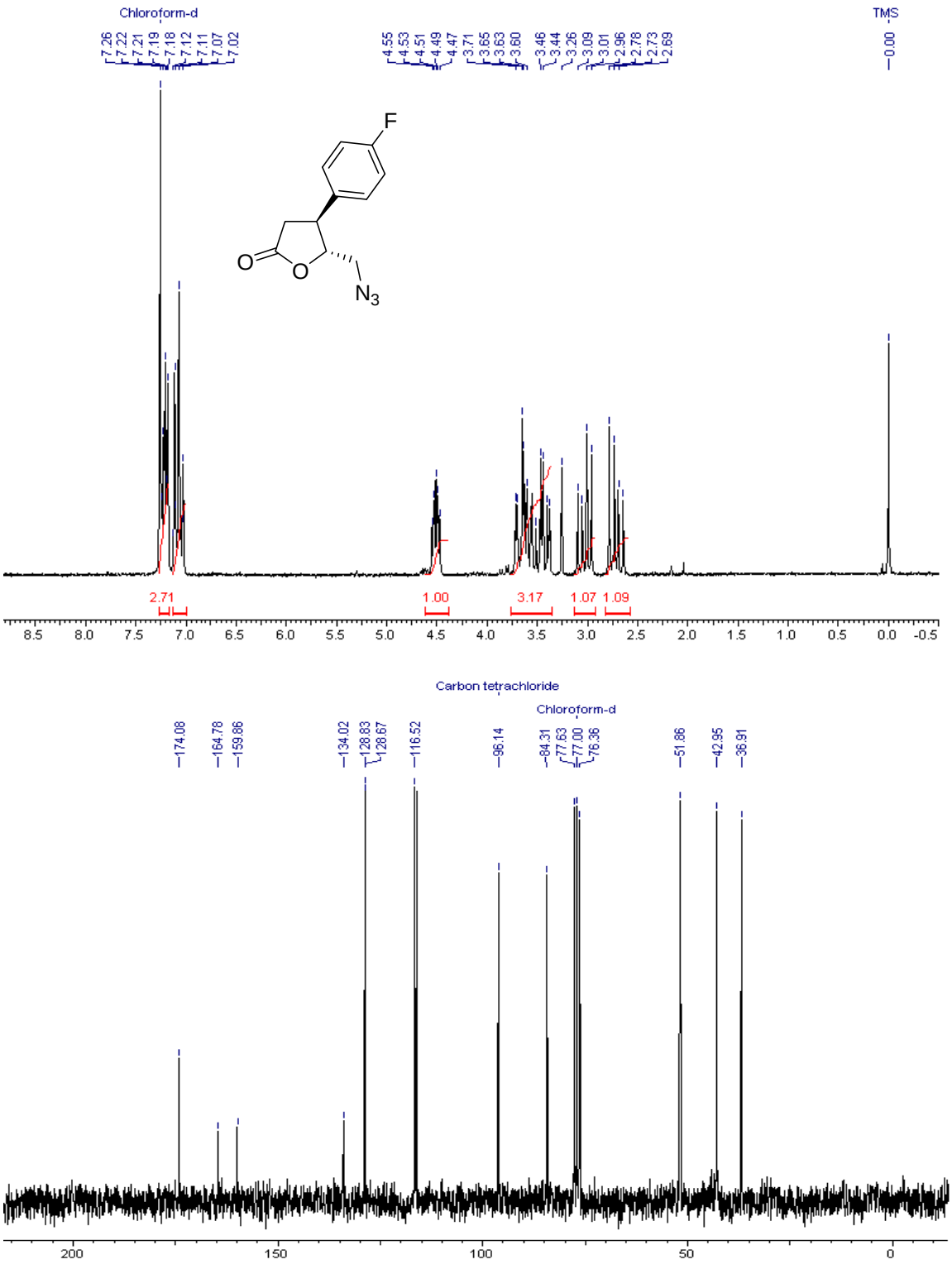
(*R*)-methyl 3-(4-bromophenyl)-3-((*R*)-oxiran-2-yl)propanoate (12d)



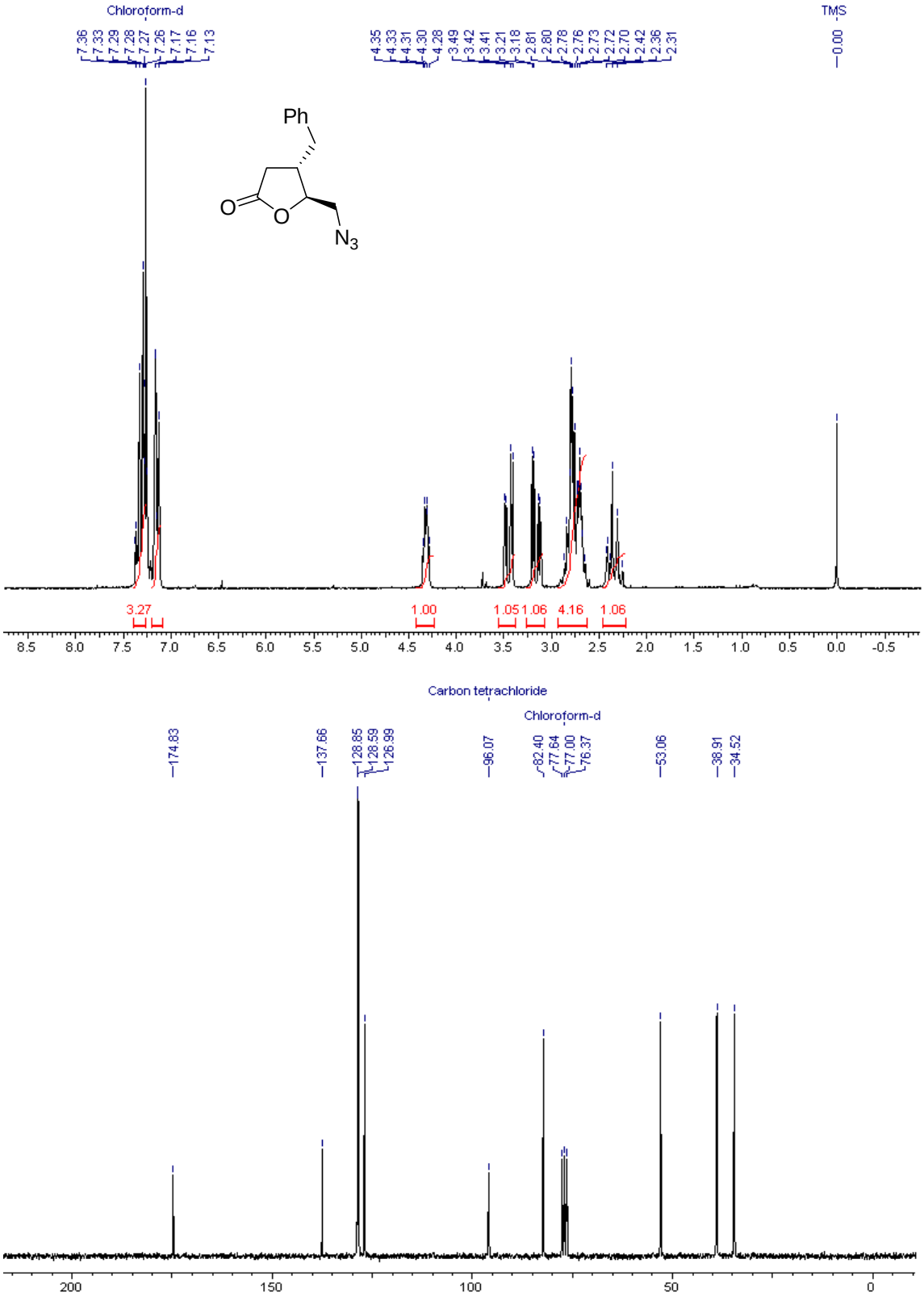
((2*R*,3*S*)-3-(4-fluorophenyl)-5-oxotetrahydrofuran-2-yl)methyl methanesulfonate (17)



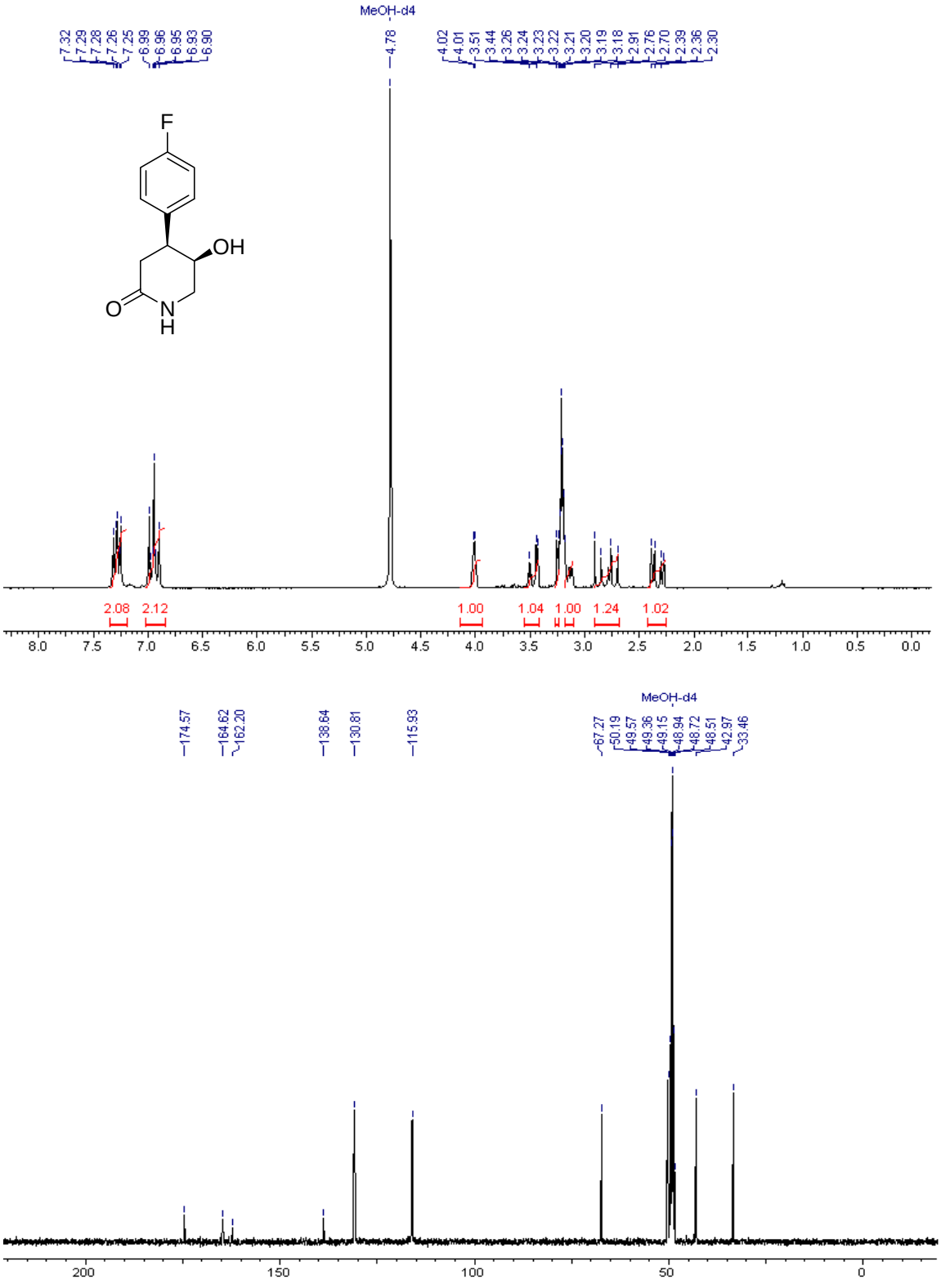
((2*S*,3*S*)-3-benzyl-5-oxotetrahydrofuran-2-yl)methyl methanesulfonate (17a)



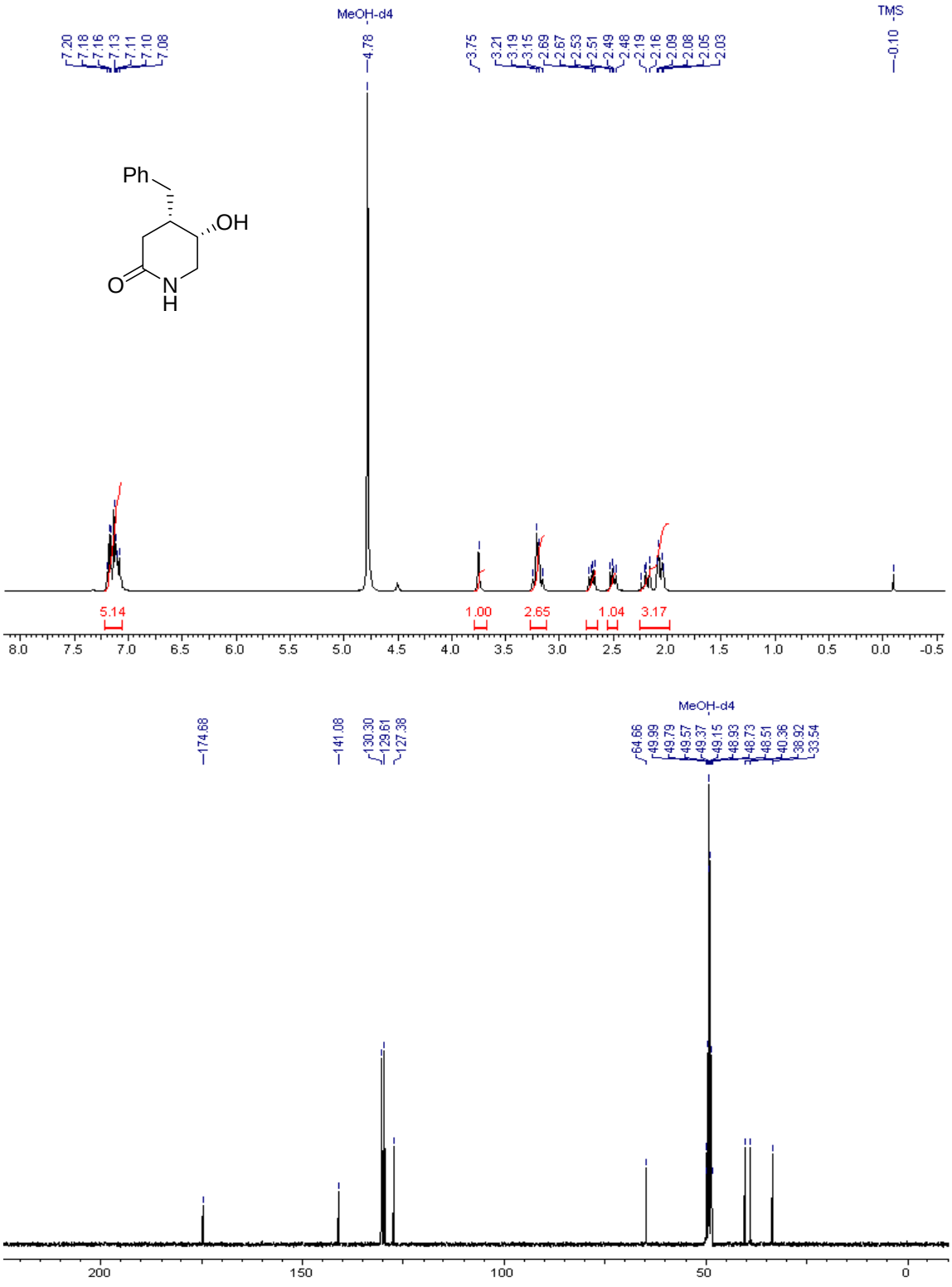
(4*S*,5*R*)-5-(azidomethyl)-4-(4-fluorophenyl)dihydrofuran-2(3*H*)-one (18)



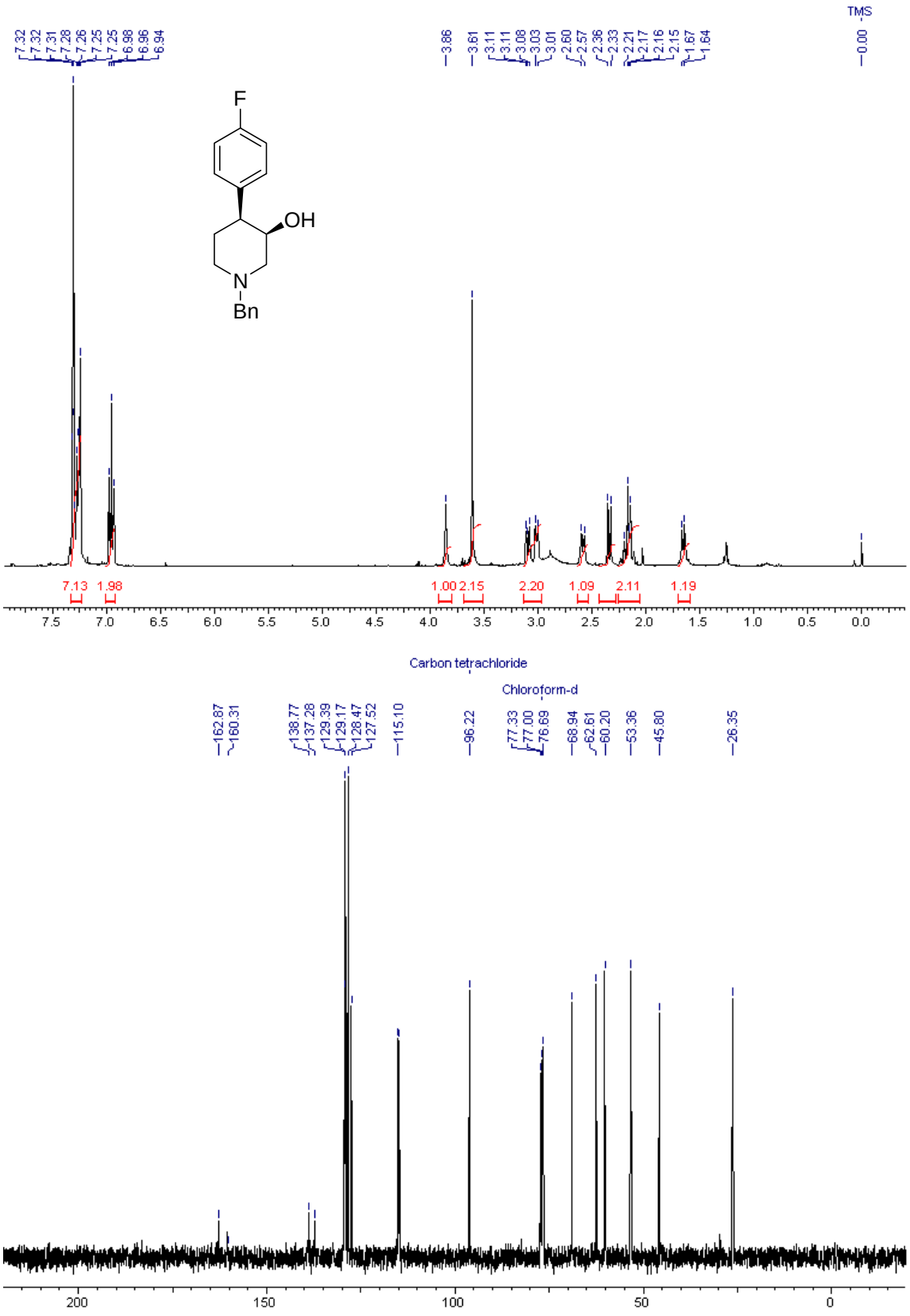
(4*S*,5*S*)-5-(azidomethyl)-4-benzyldihydrofuran-2(3*H*)-one (18a)



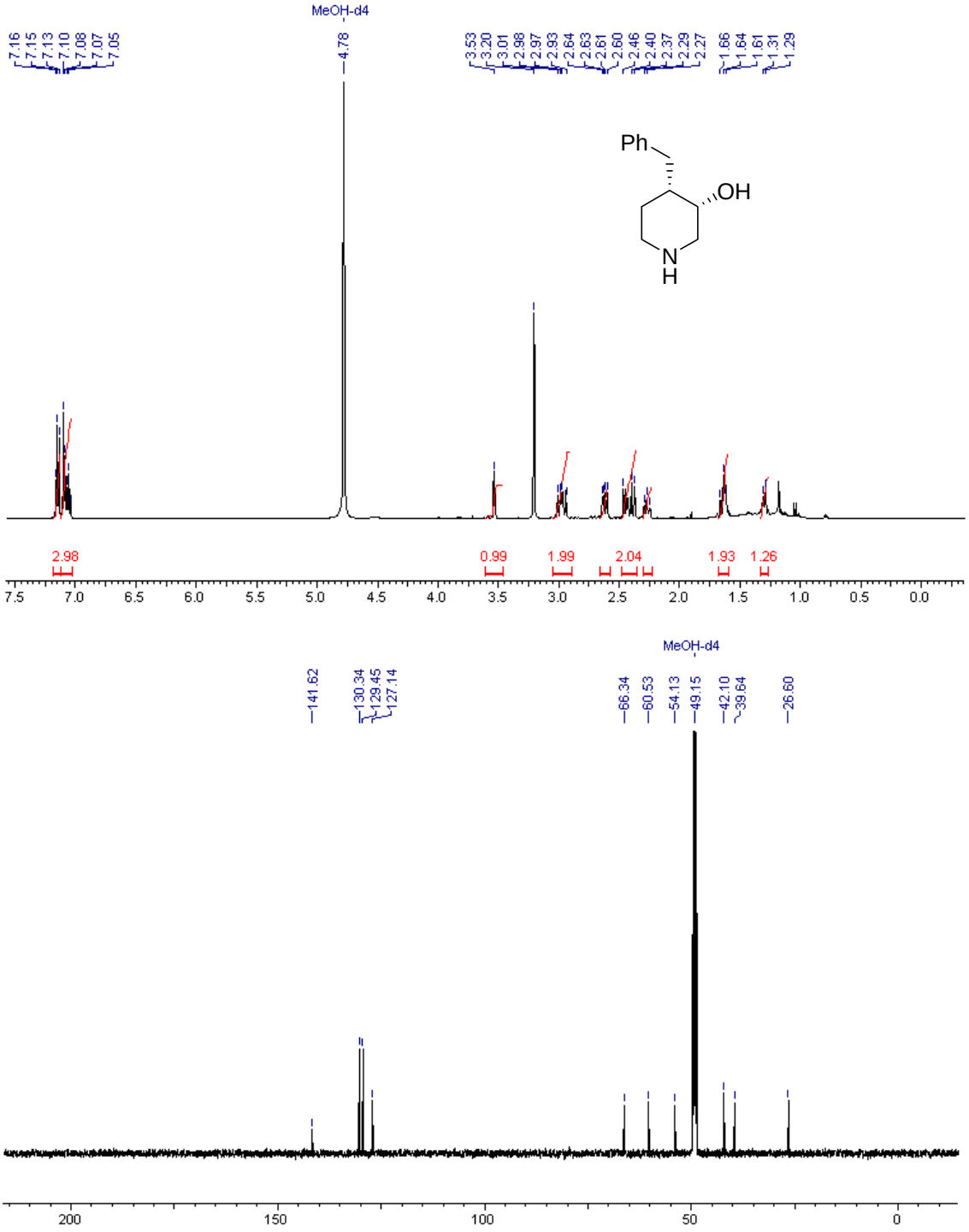
(4*S*,5*R*)-4-(4-fluorophenyl)-5-hydroxypiperidin-2-one (19)



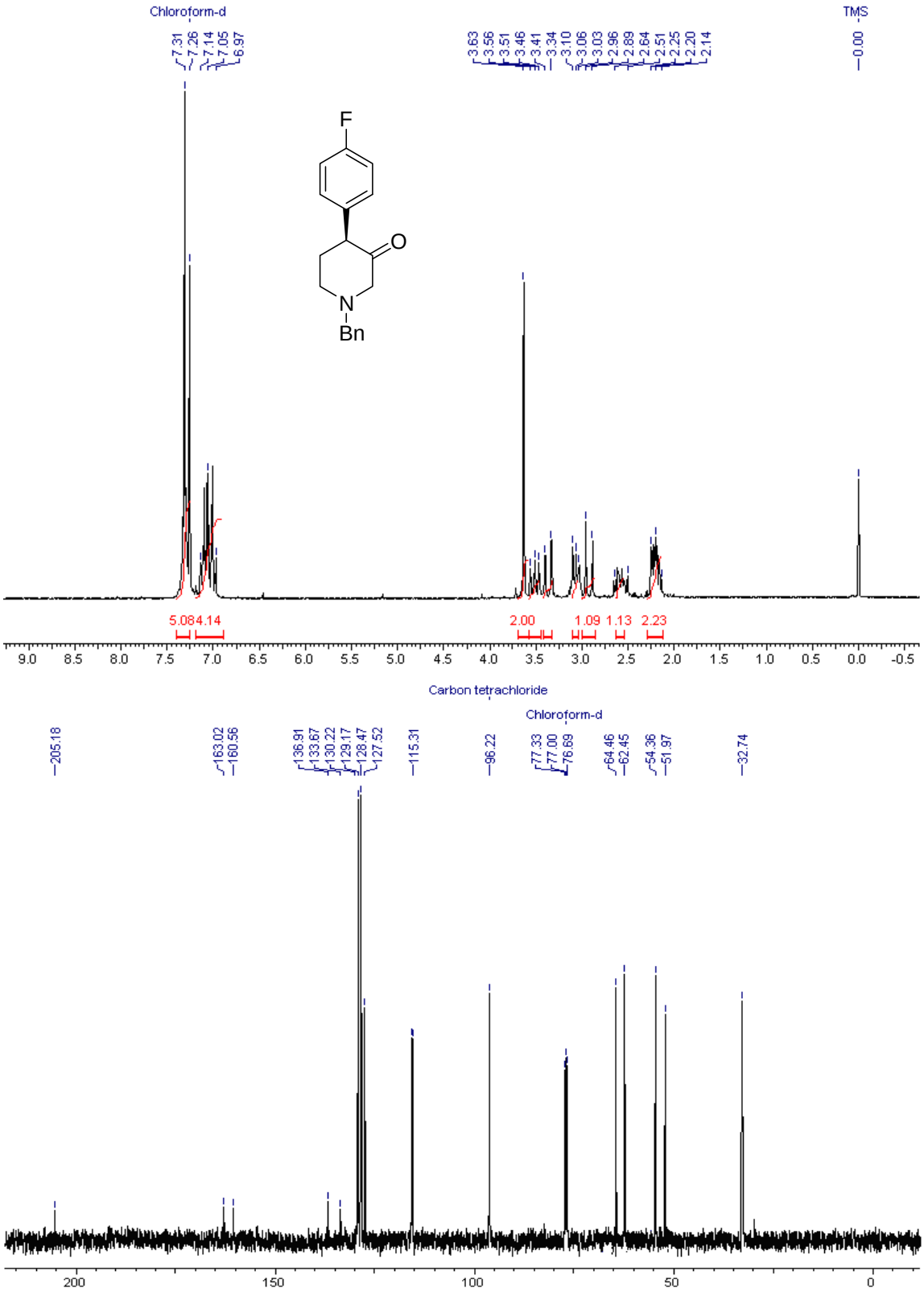
(4*S*,5*S*)-4-benzyl-5-hydroxypiperidin-2-one (19a)



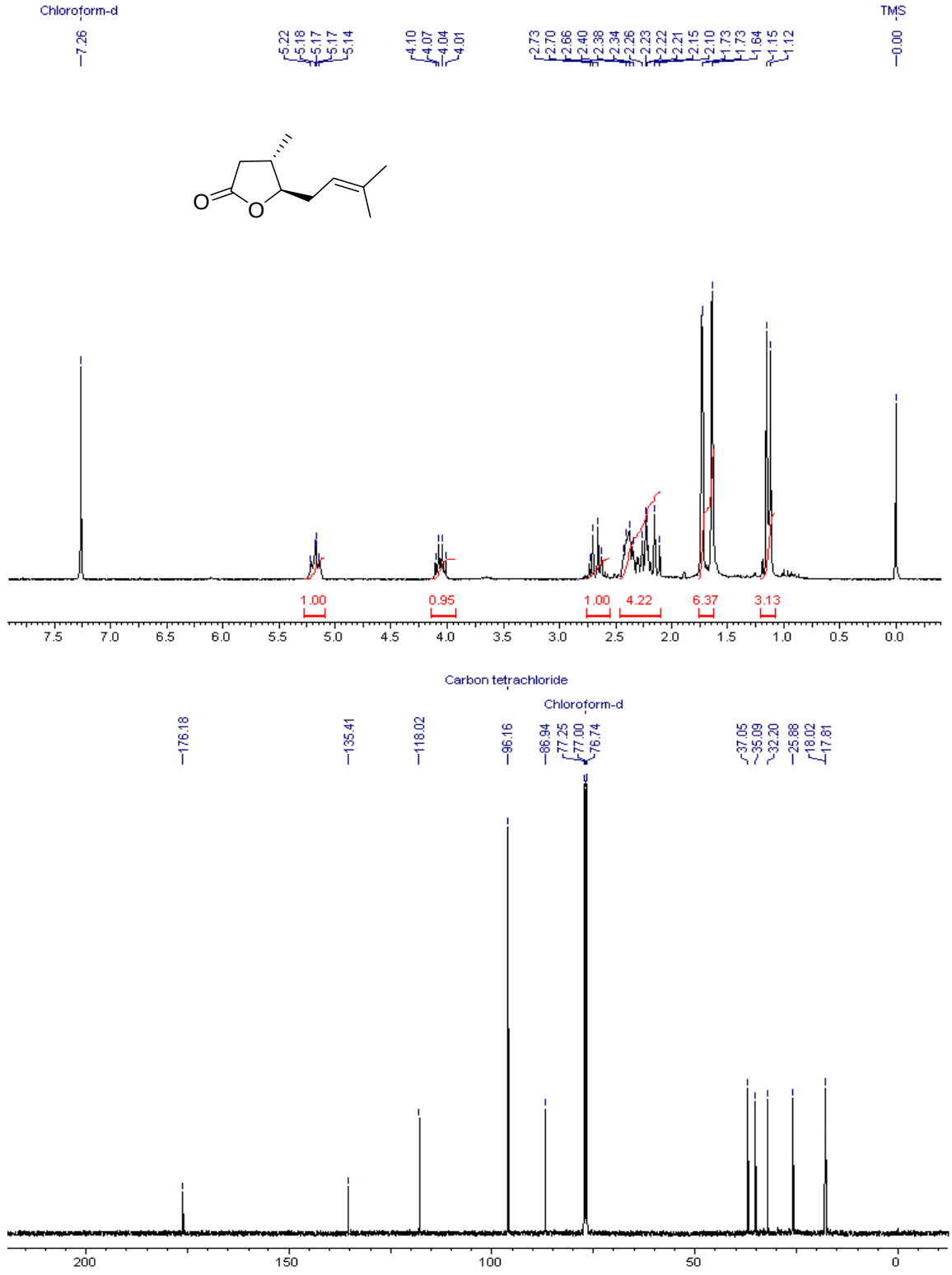
2.6 (3*R*,4*S*)-1-benzyl-4-(4-fluorophenyl)piperidin-3-ol (20)



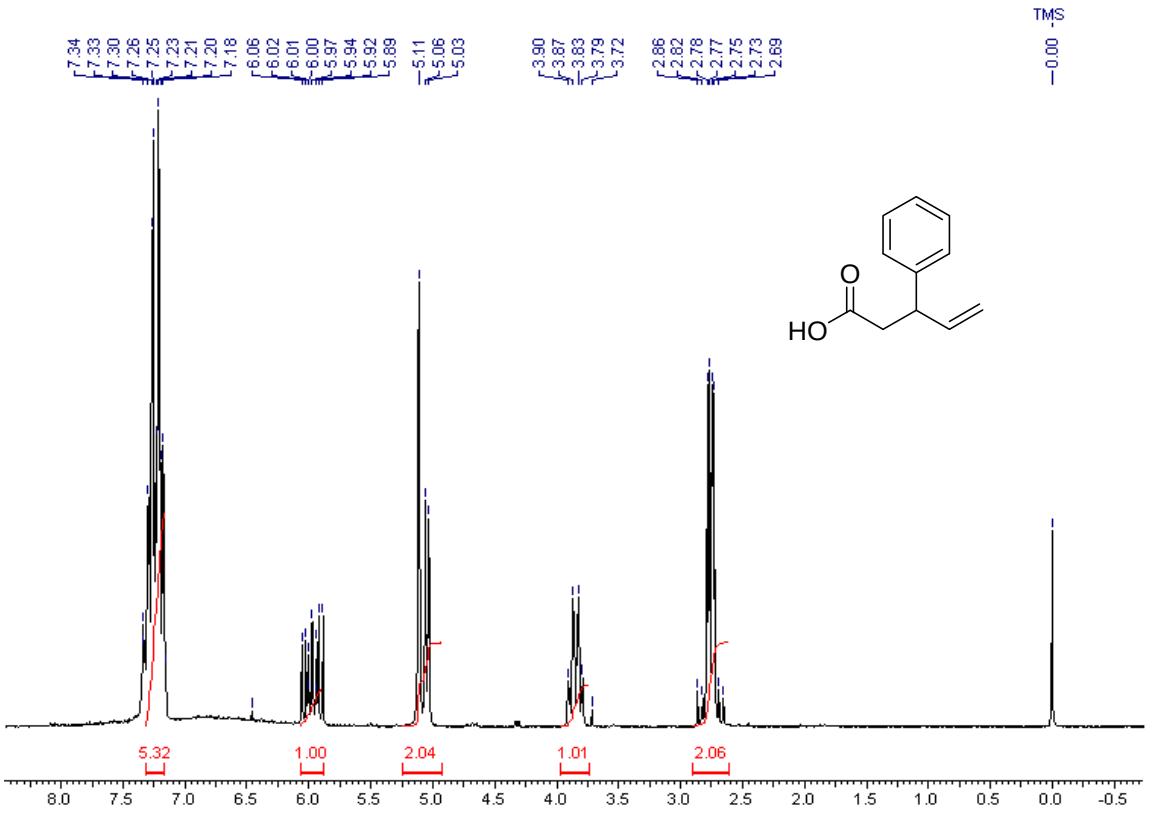
(3*S*,4*S*)-4-benzylpiperidin-3-ol (4)

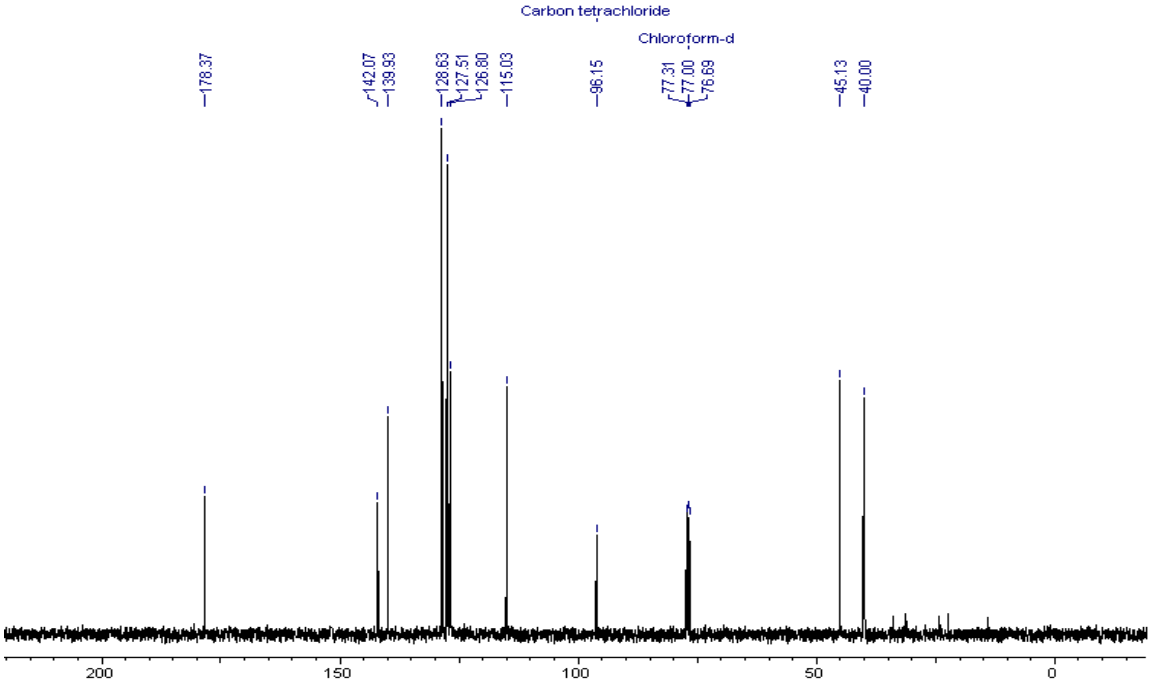


(*S*)-1-benzyl-4-(4-fluorophenyl)piperidin-3-one (21)

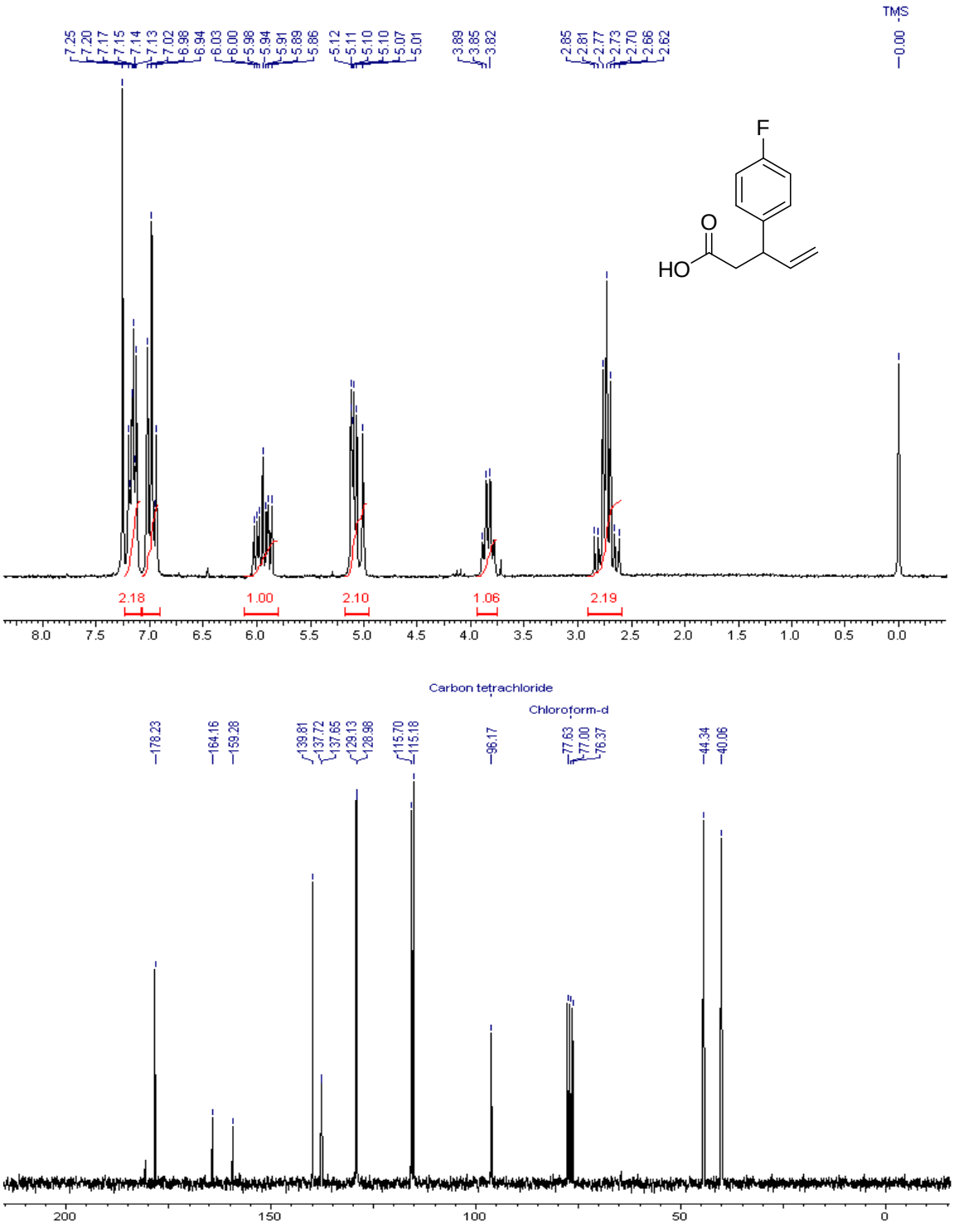


(+)-Eldanolide (1)

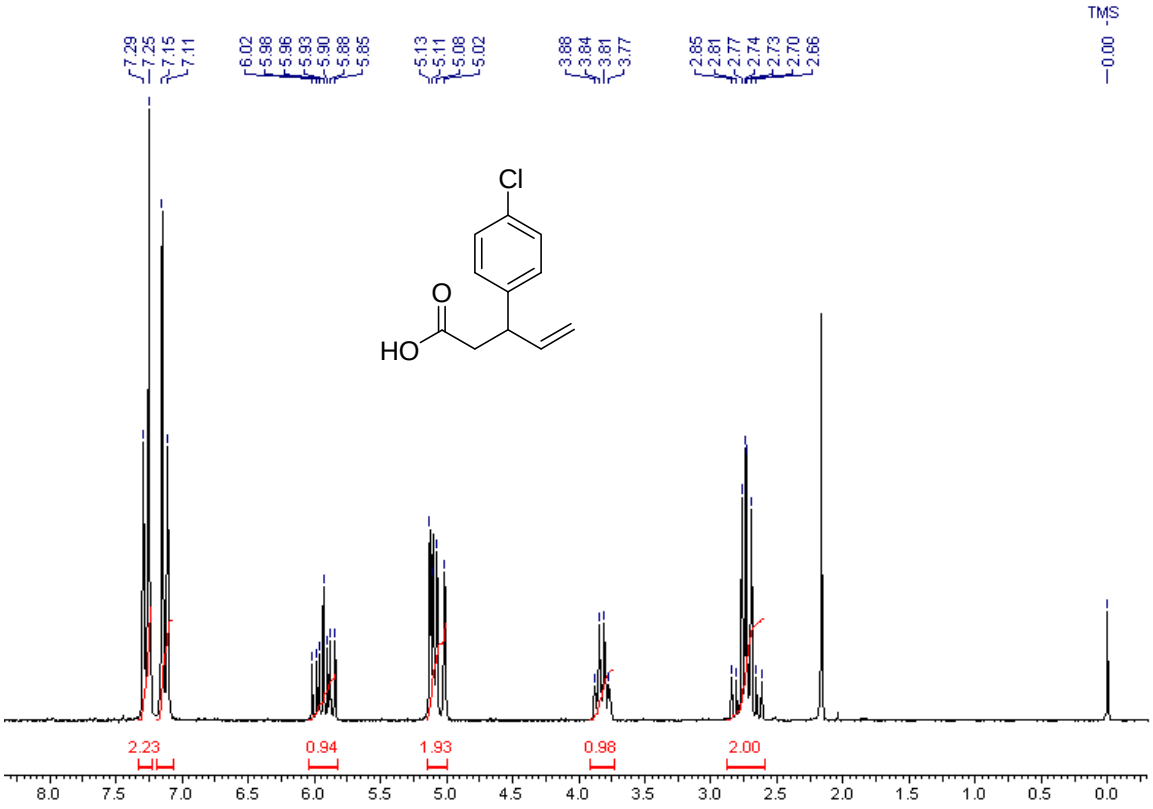


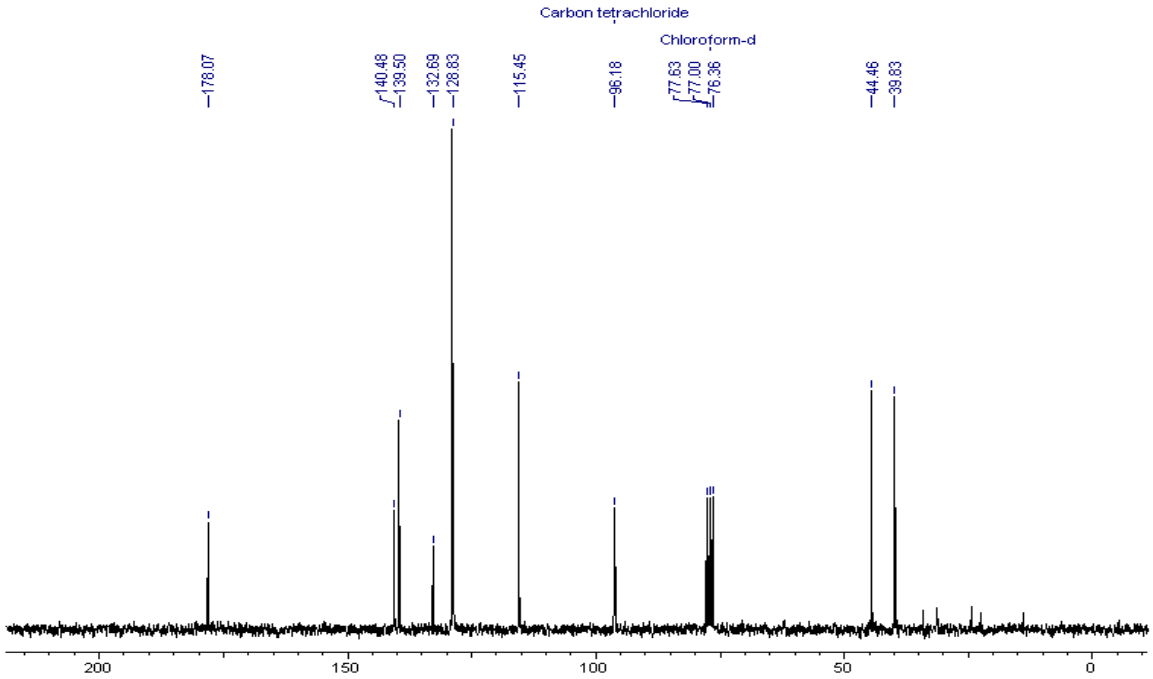


3-phenylpent-4-enoic acid (14a)

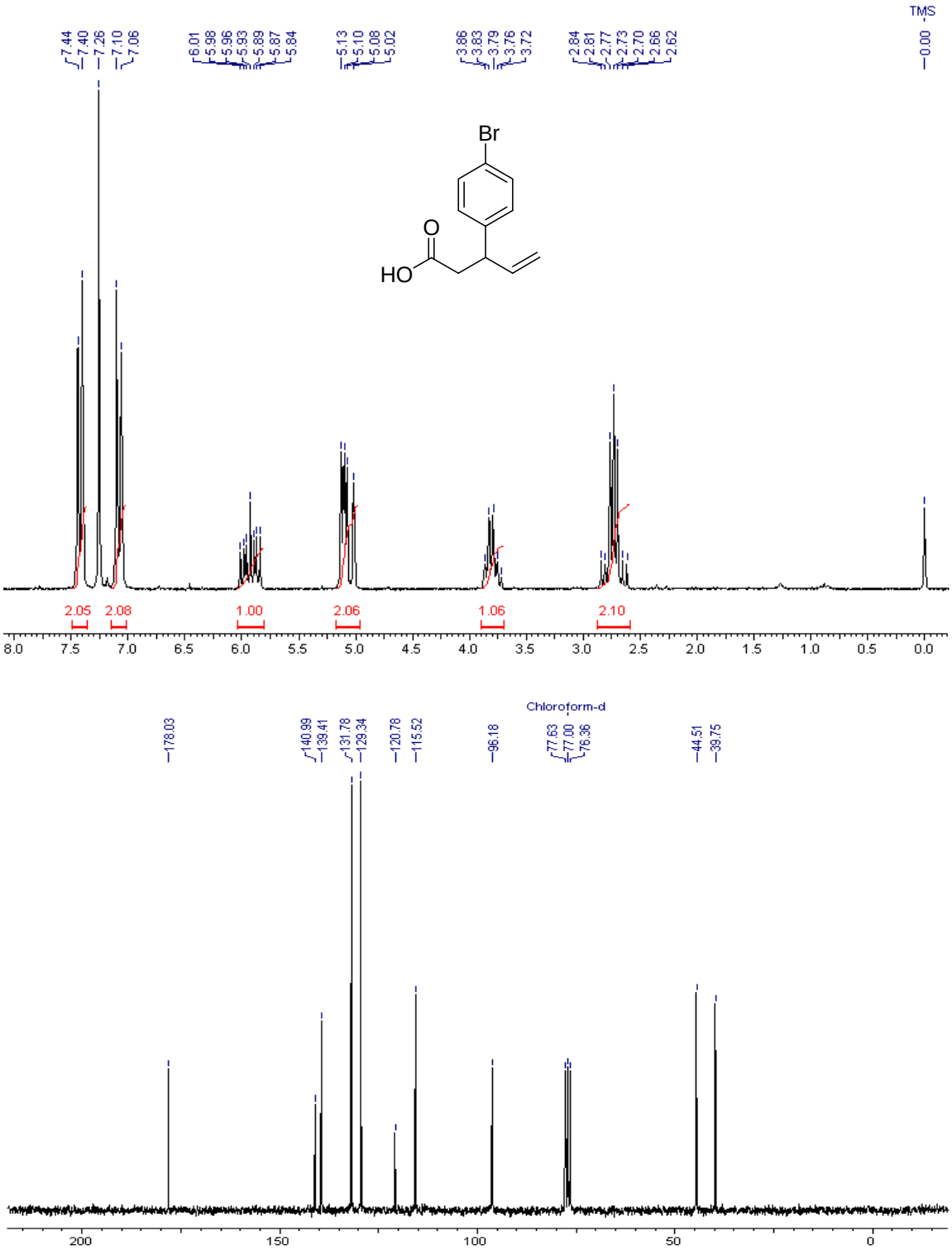


3-(4-fluorophenyl)pent-4-enoic acid (14b)

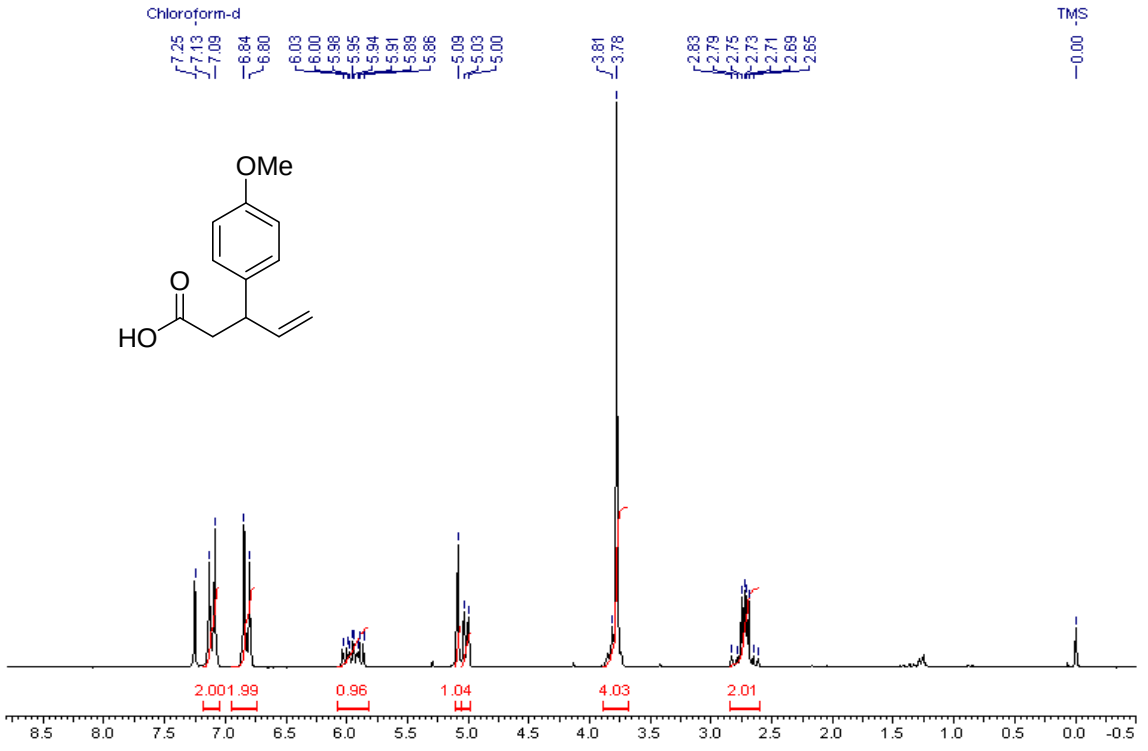


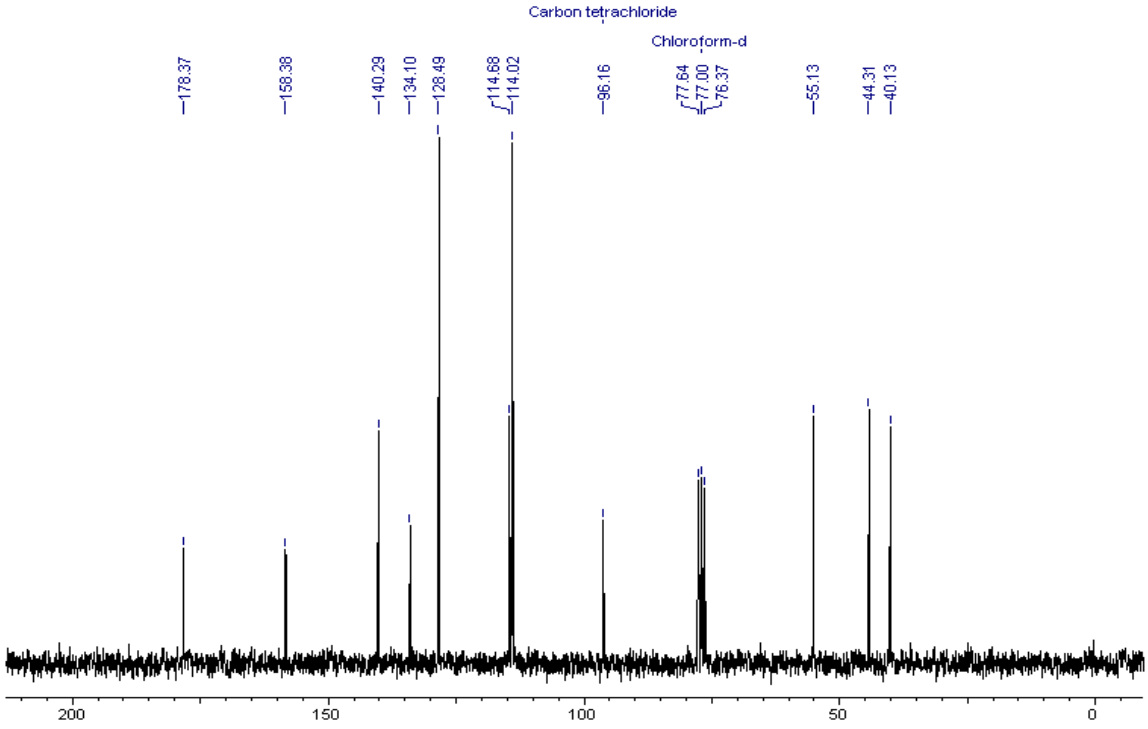


3-(4-chlorophenyl)pent-4-enoic acid (14c)

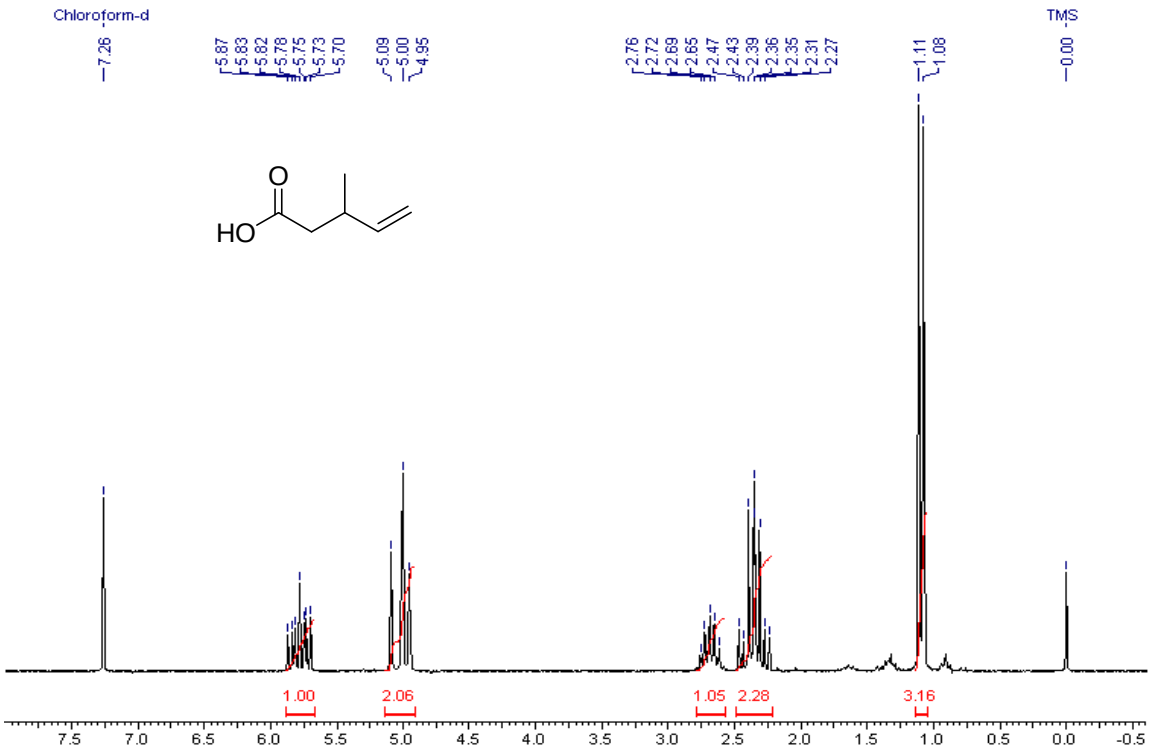


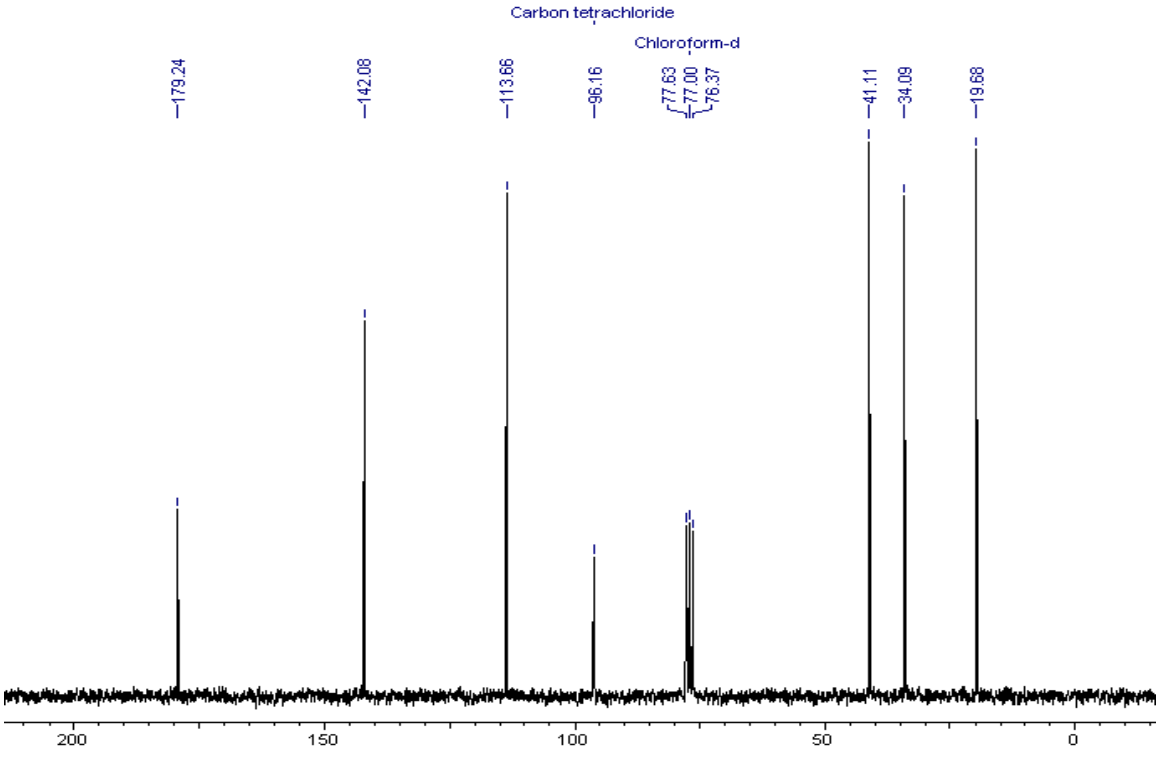
3-(4-bromophenyl)pent-4-enoic acid (14d)



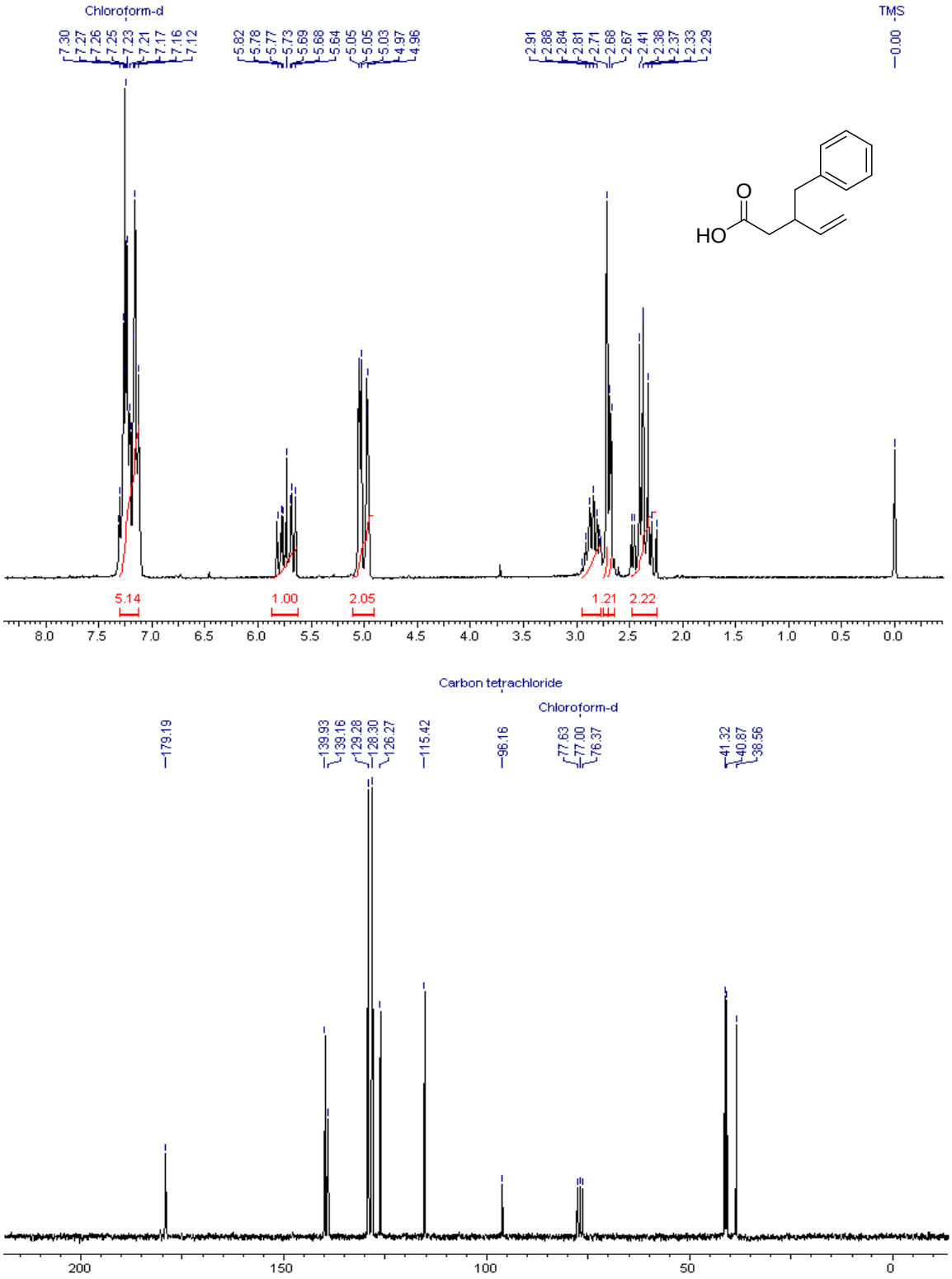


3-(4-methoxyphenyl)pent-4-enoic acid (14e)

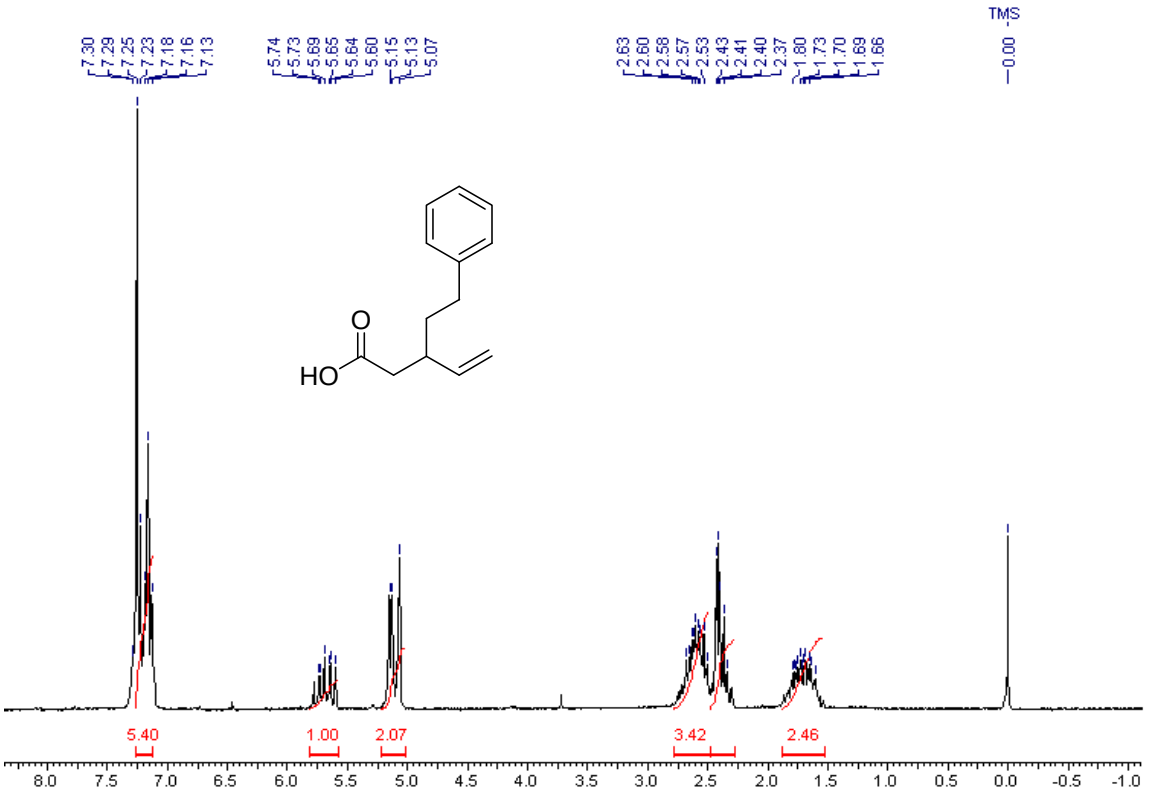


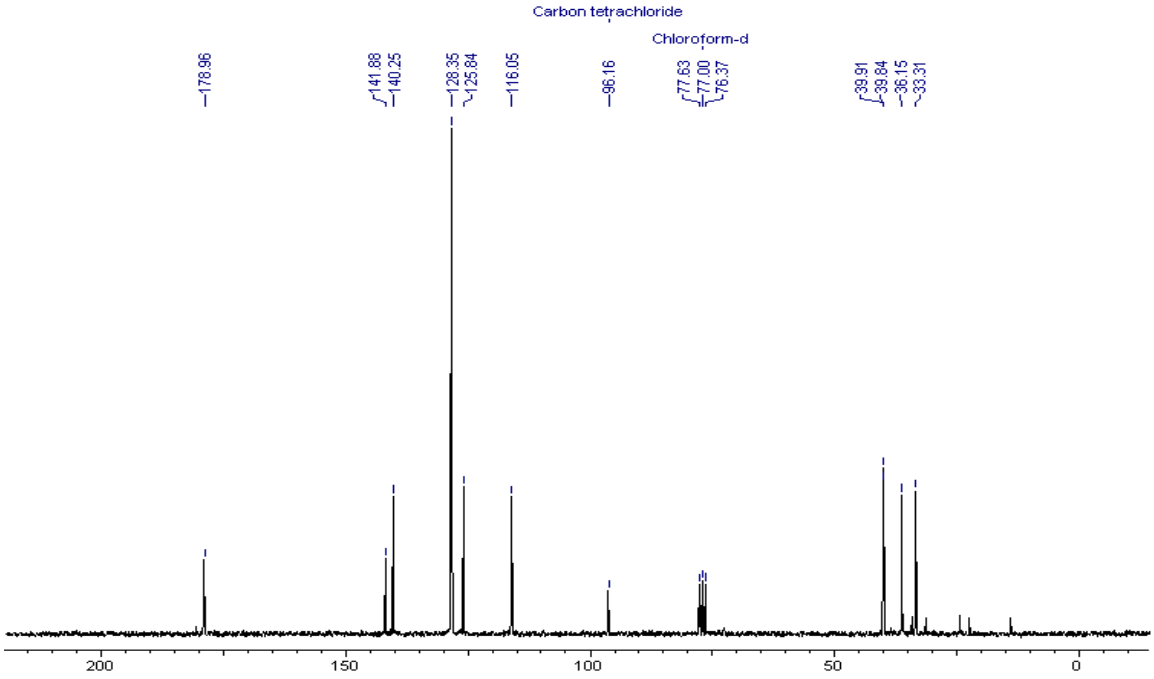


3-methylpent-4-enoic acid (14f)

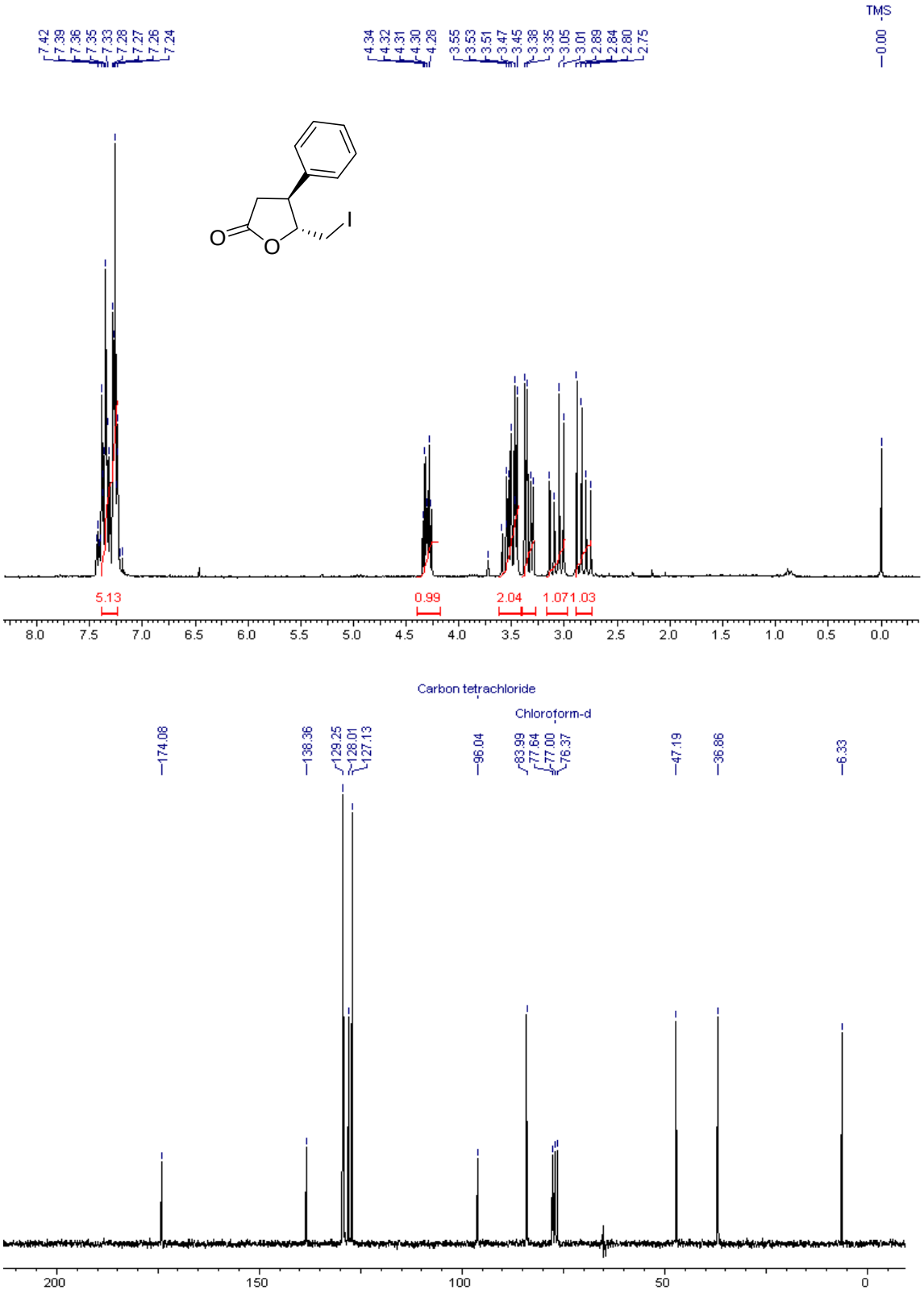


3-benzylpent-4-enoic acid (14g)

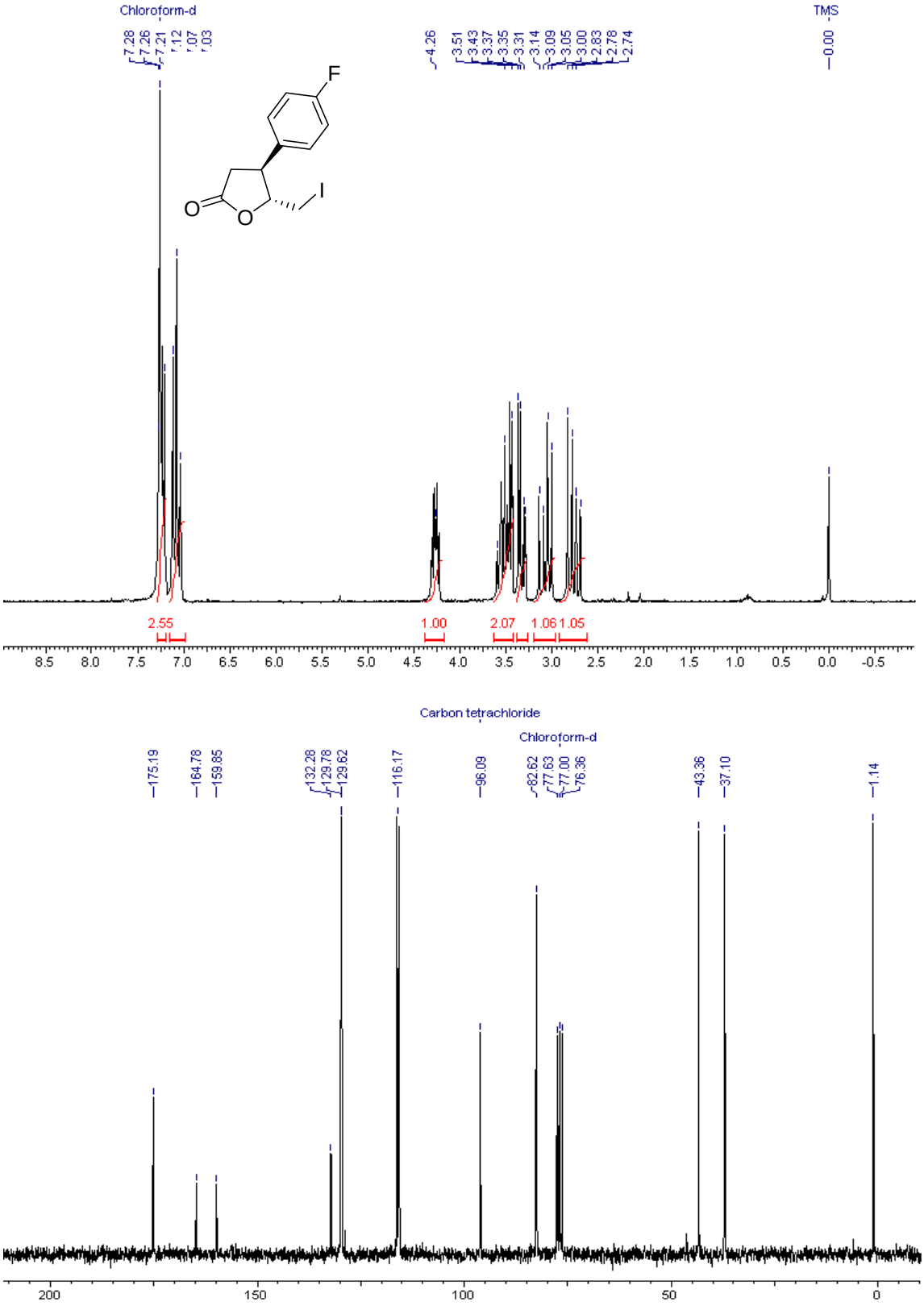




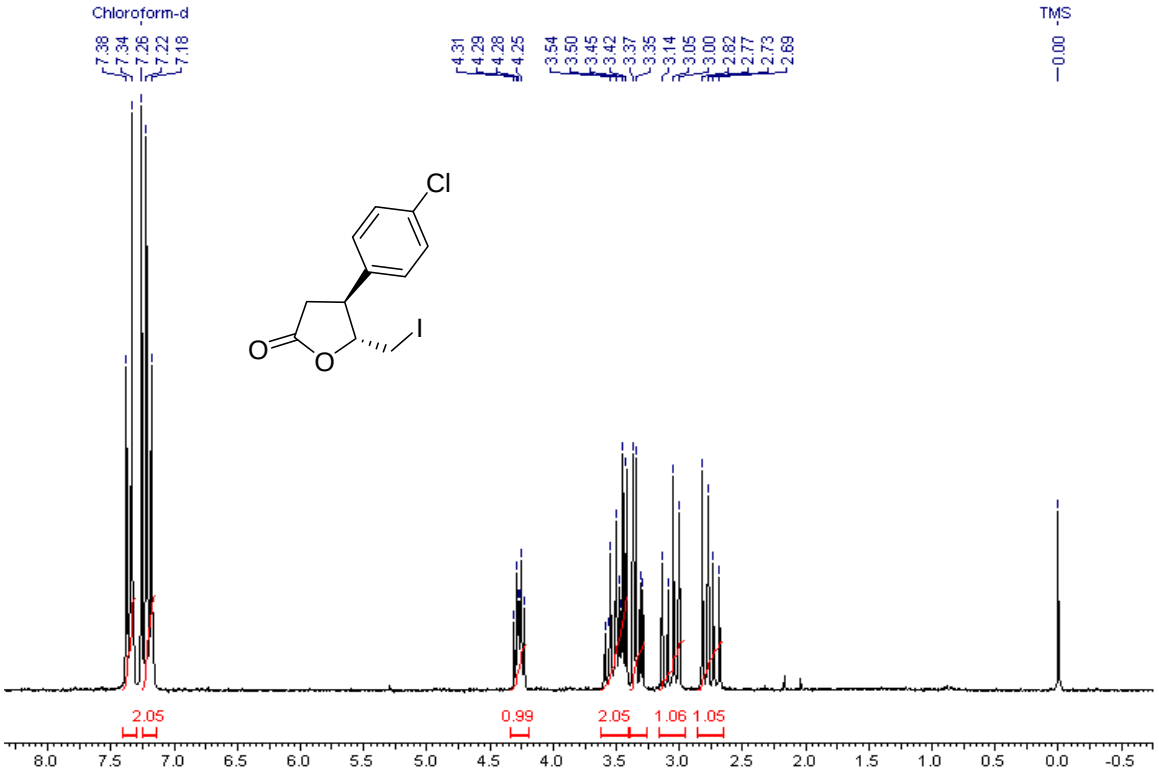
3-phenethylpent-4-enoic acid (14h)

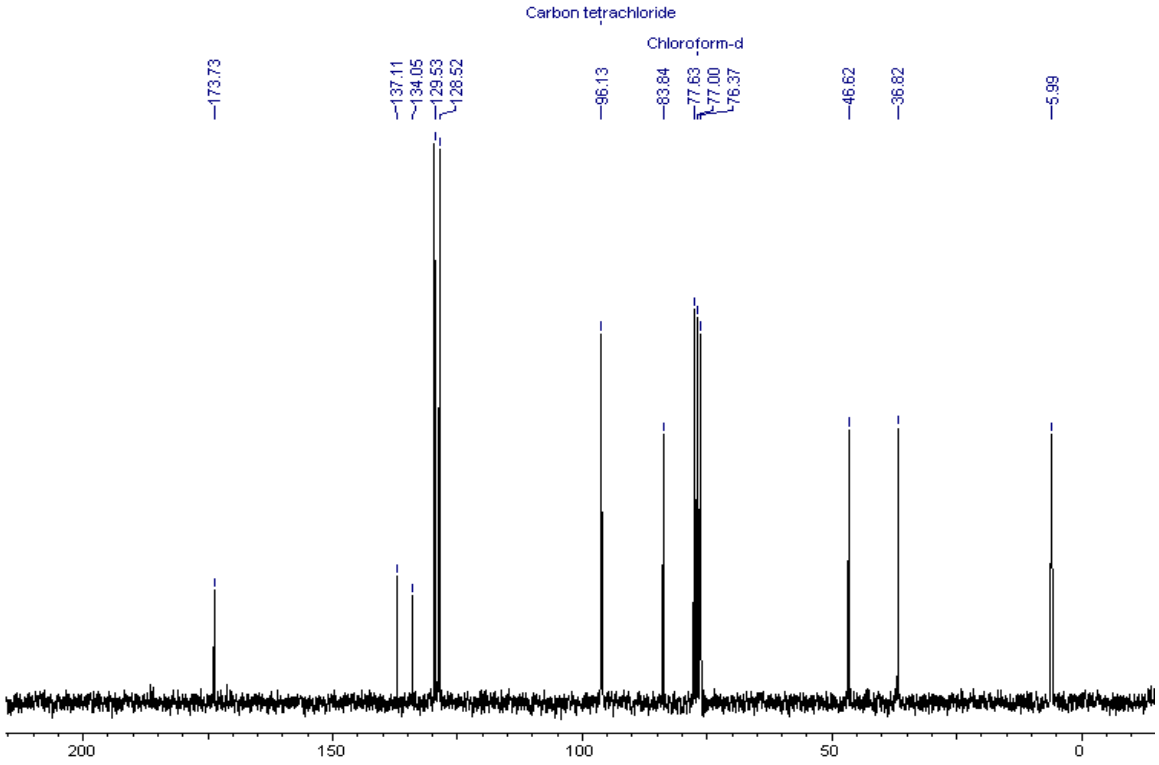


5-(iodomethyl)-4-phenyldihydrofuran-2(3*H*)-one (15a)

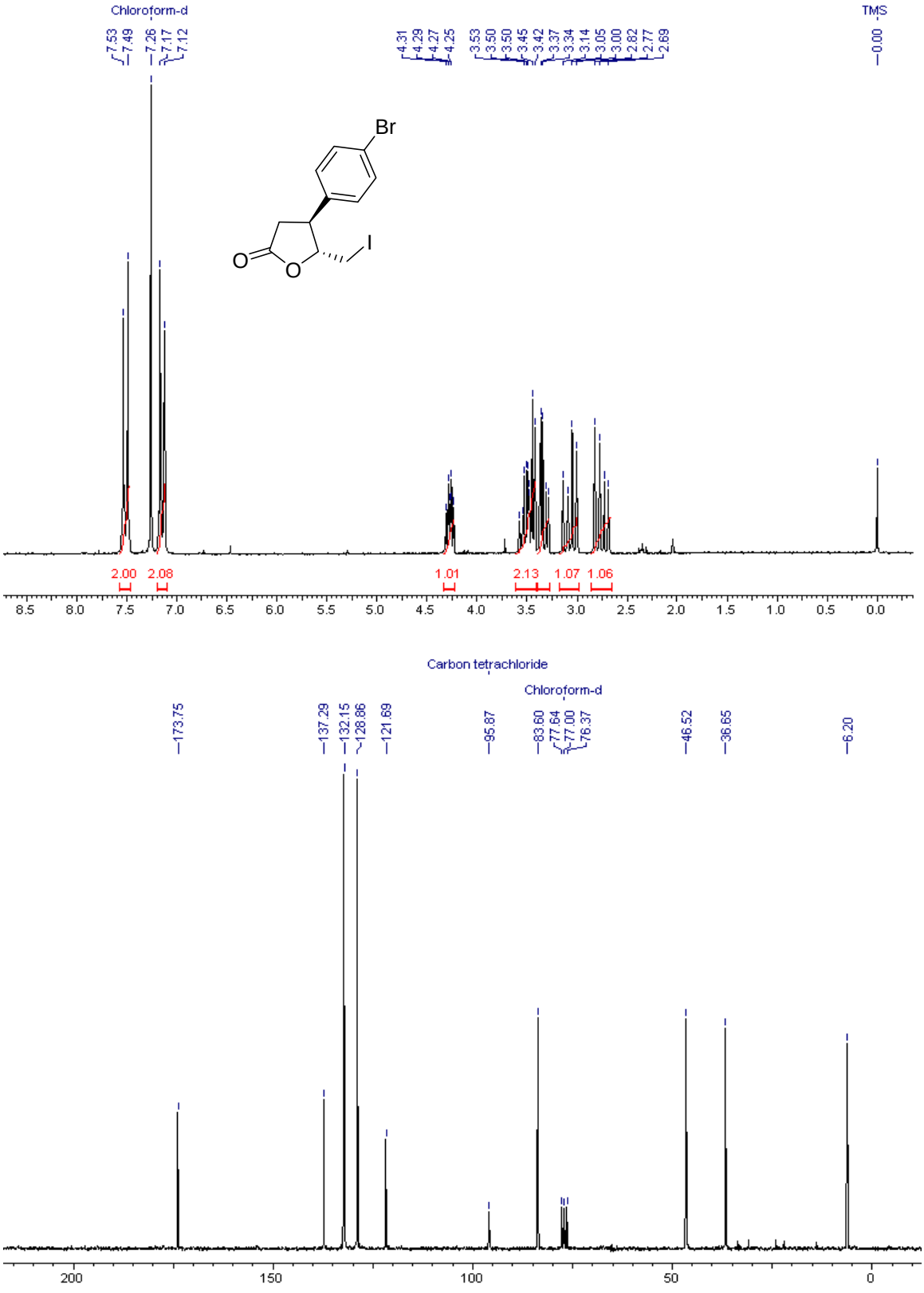


4-(4-fluorophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (15b)

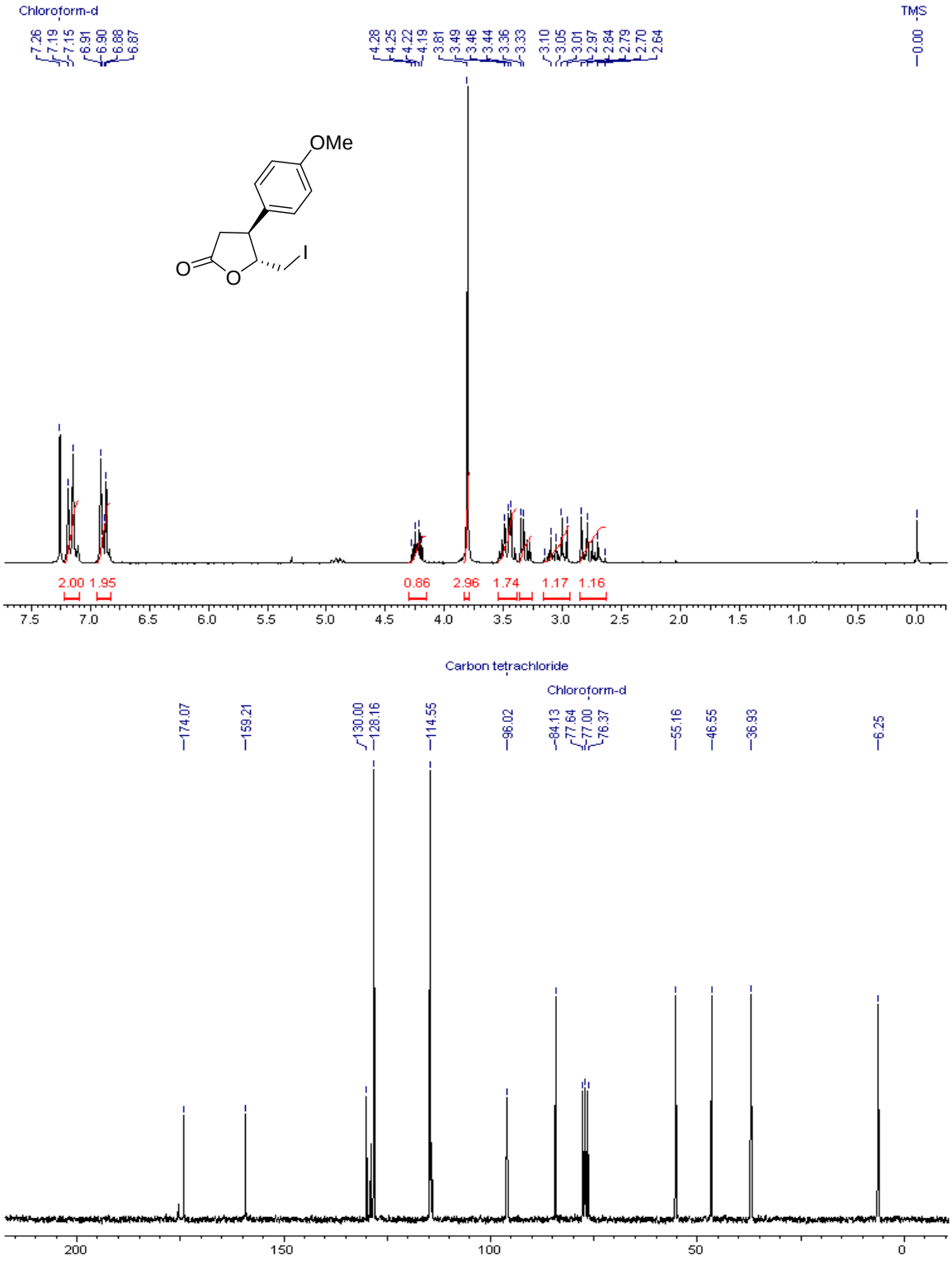




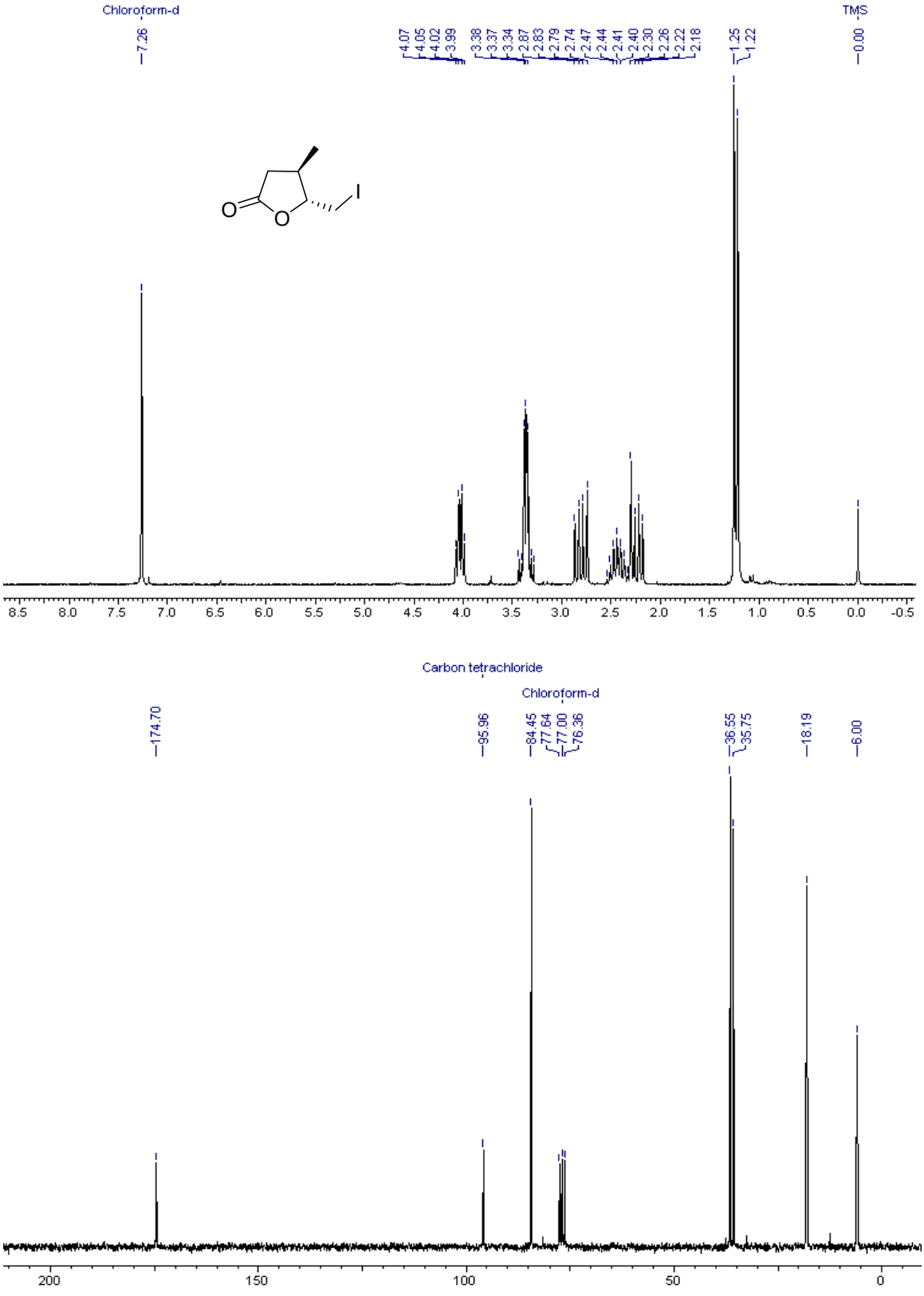
4-(4-chlorophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (15c)



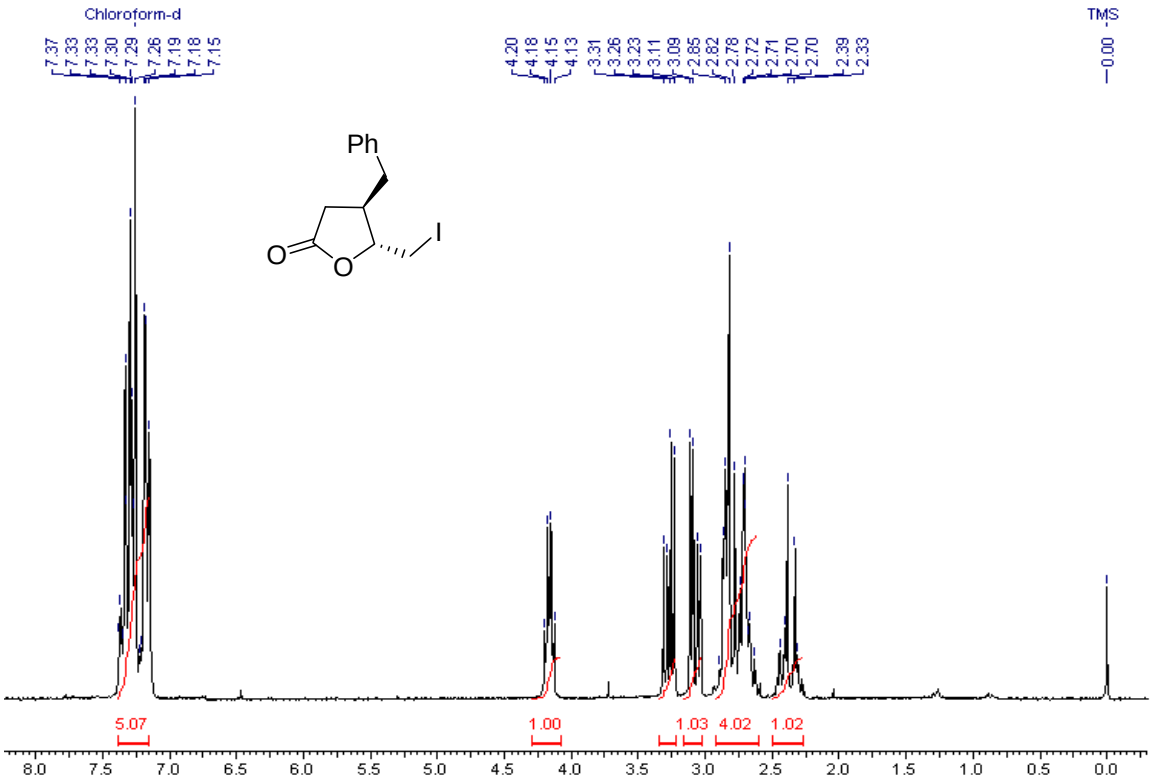
4-(4-bromophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (15d)

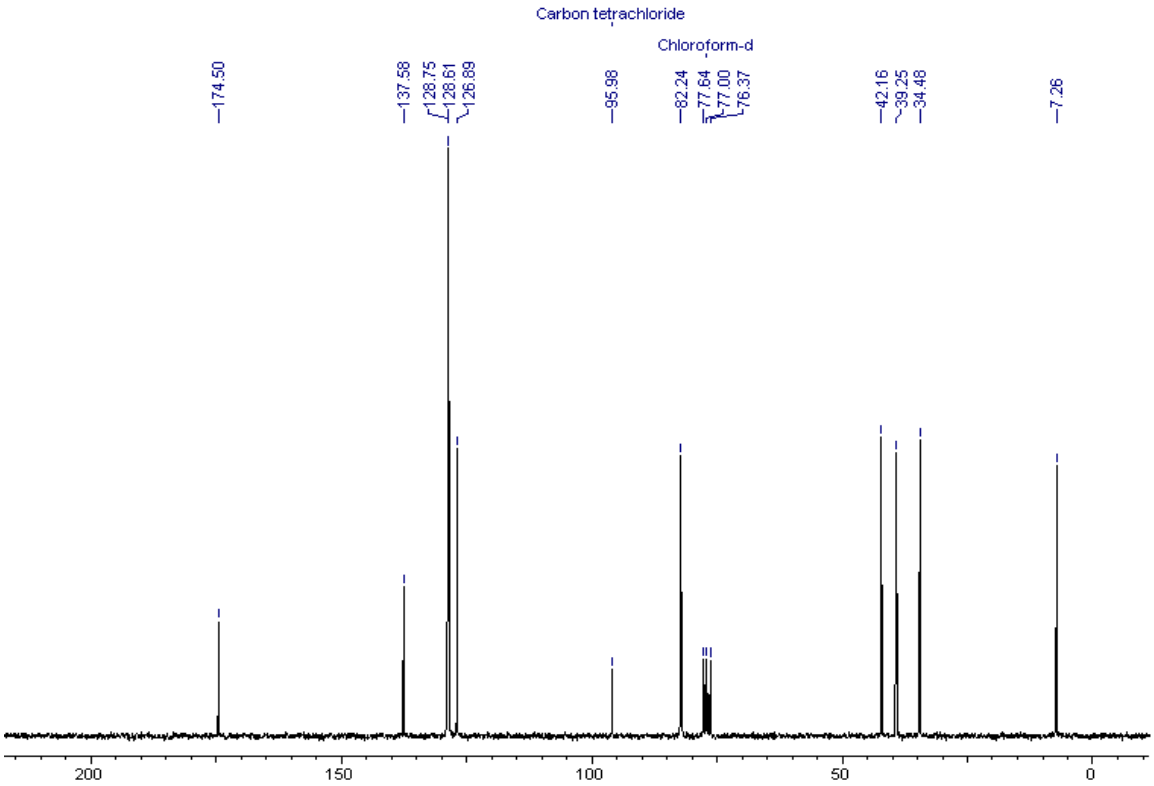


5-(iodomethyl)-4-(4-methoxyphenyl)dihydrofuran-2(3*H*)-one (15e)

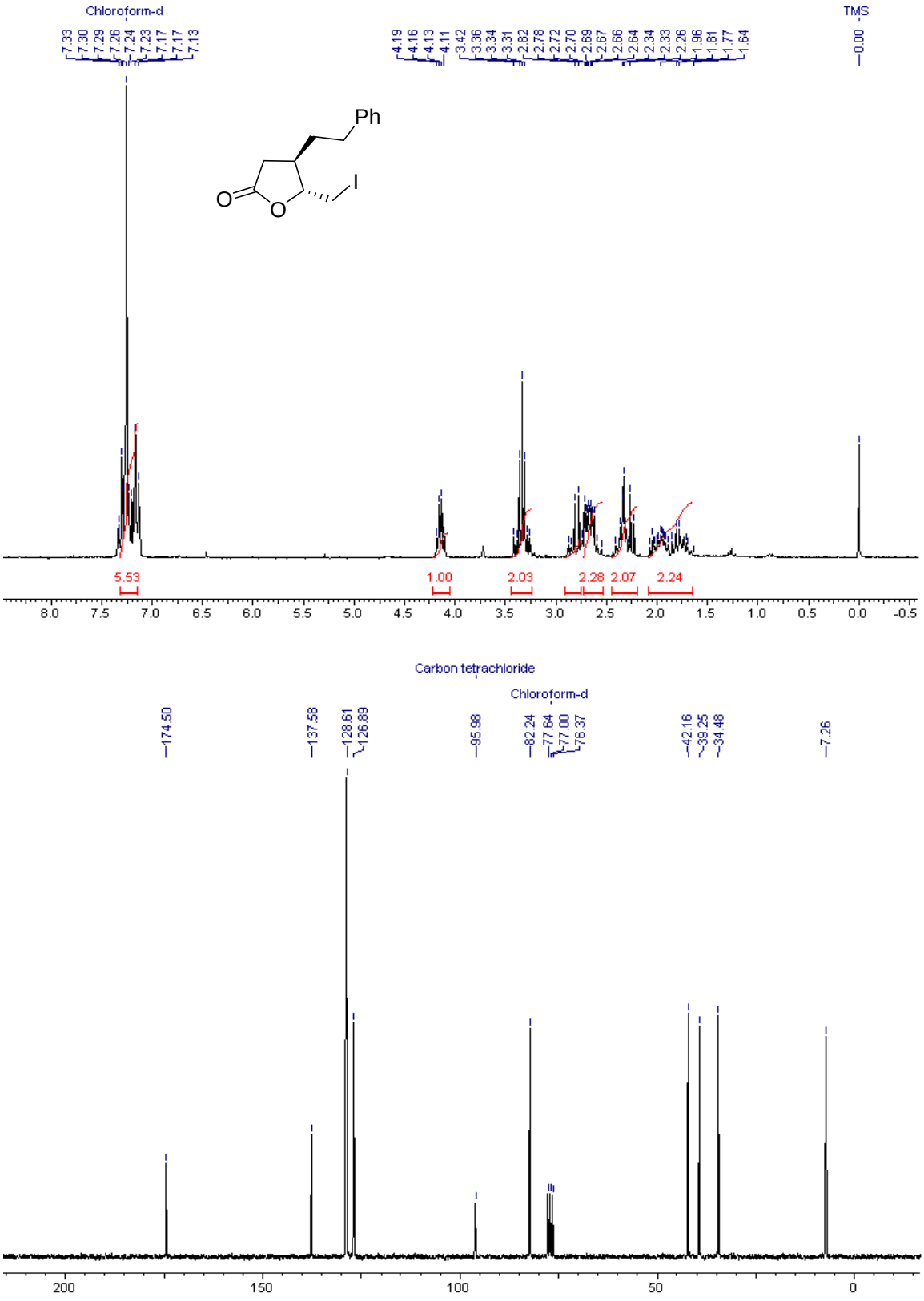


5-(iodomethyl)-4-methyldihydrofuran-2(3*H*)-one (15f)

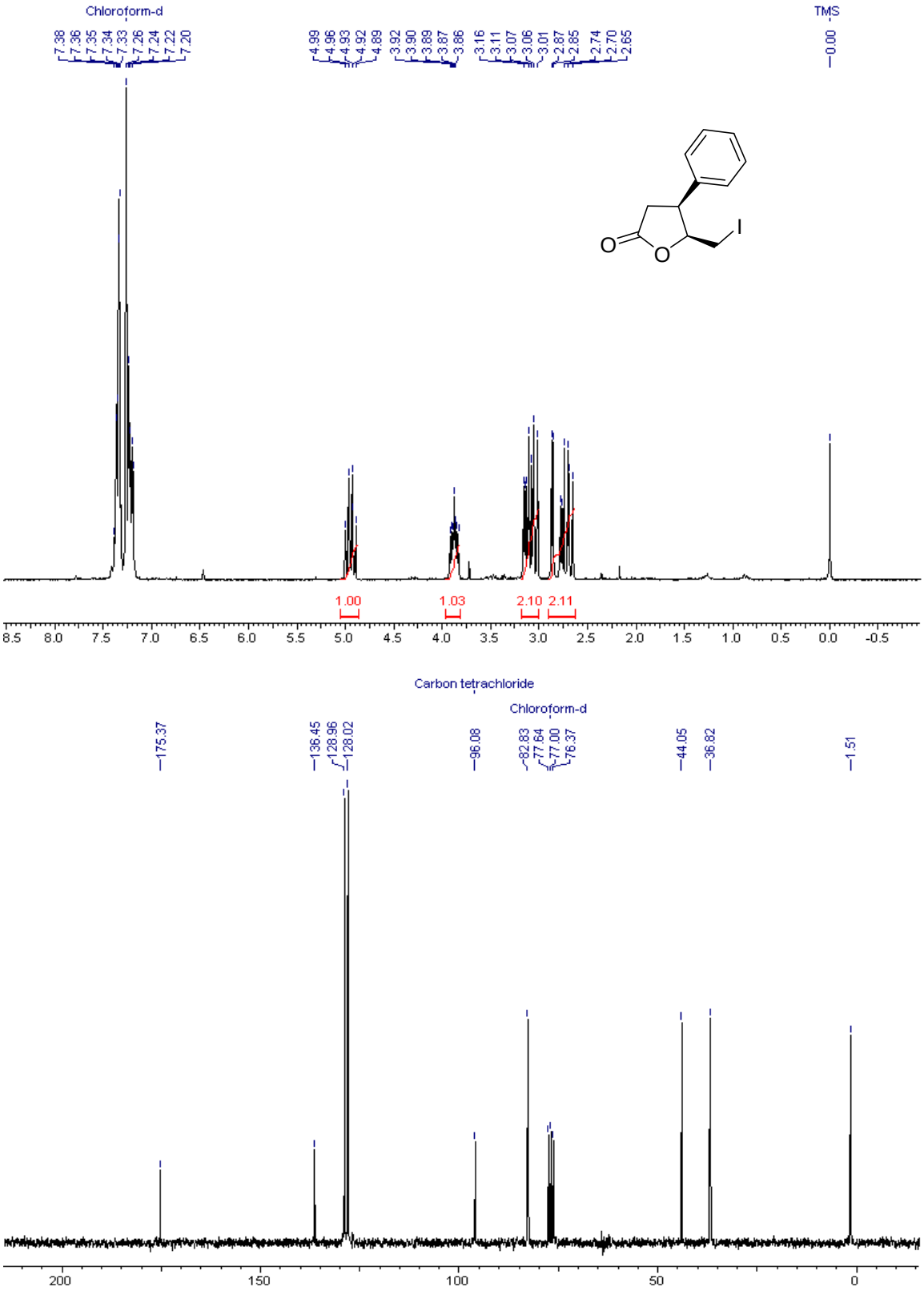




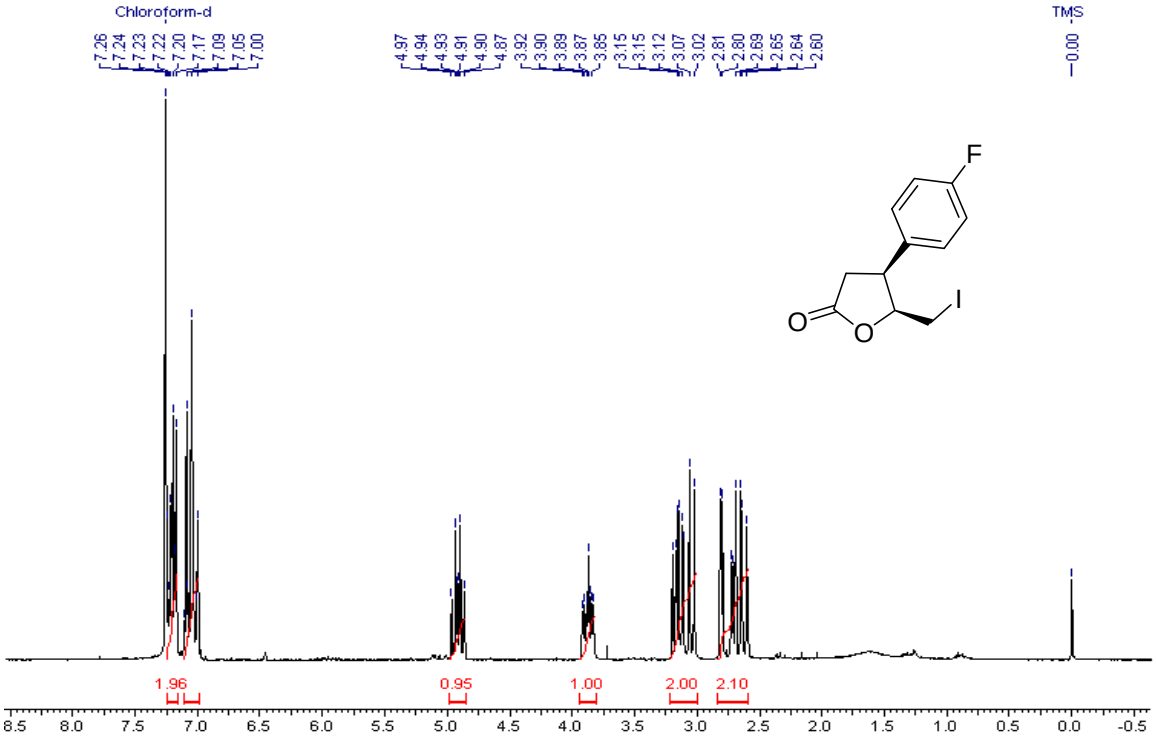
4-benzyl-5-(iodomethyl)dihydrofuran-2(3*H*)-one (15g)

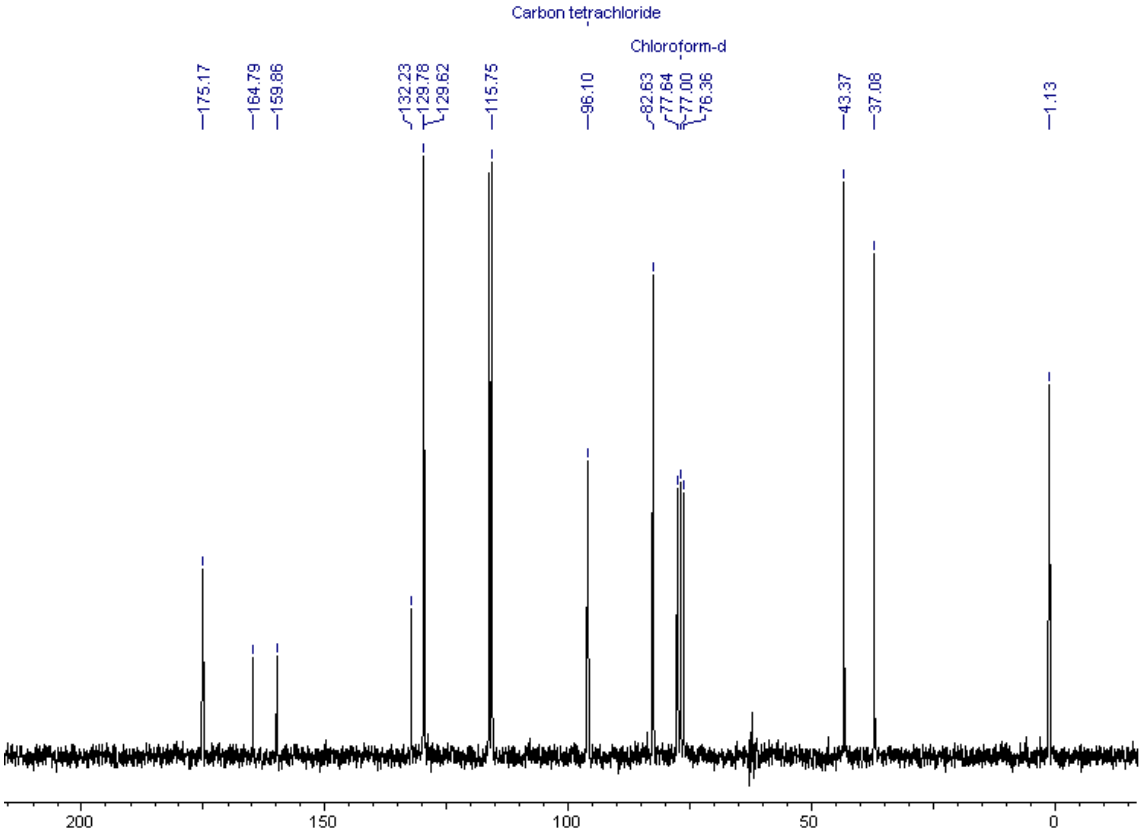


5-(iodomethyl)-4-phenethyldihydrofuran-2(3*H*)-one (15h)

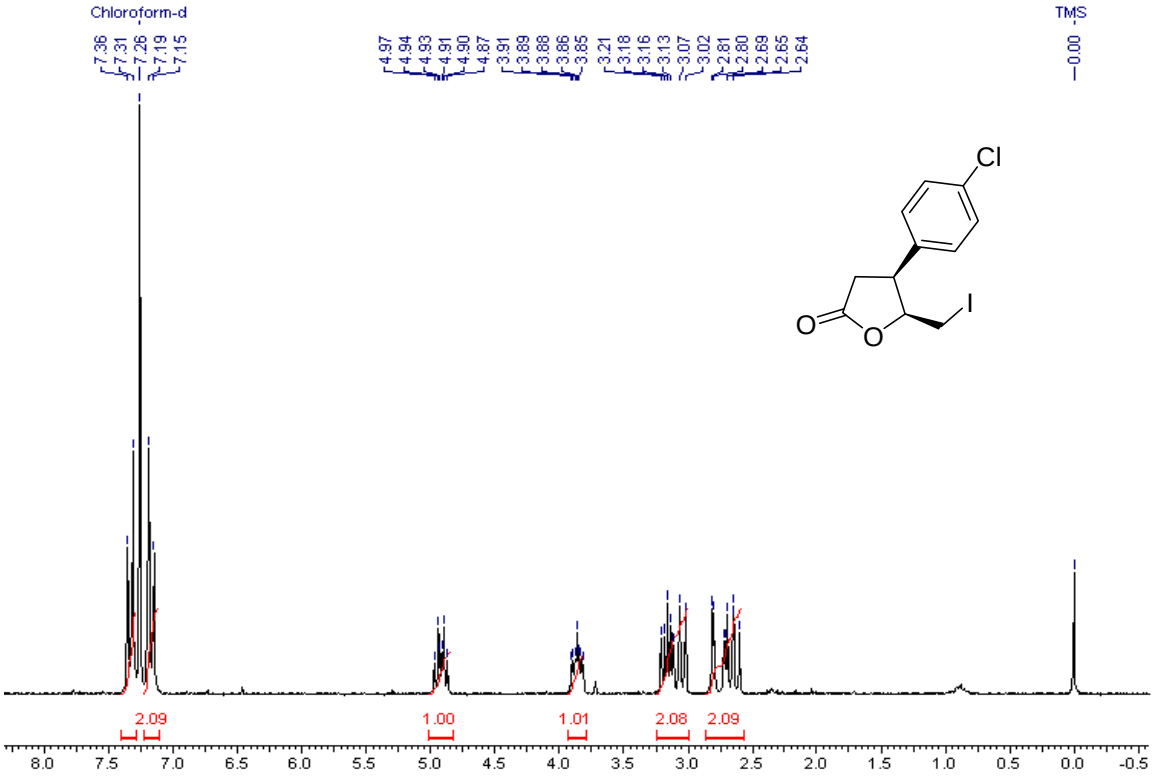


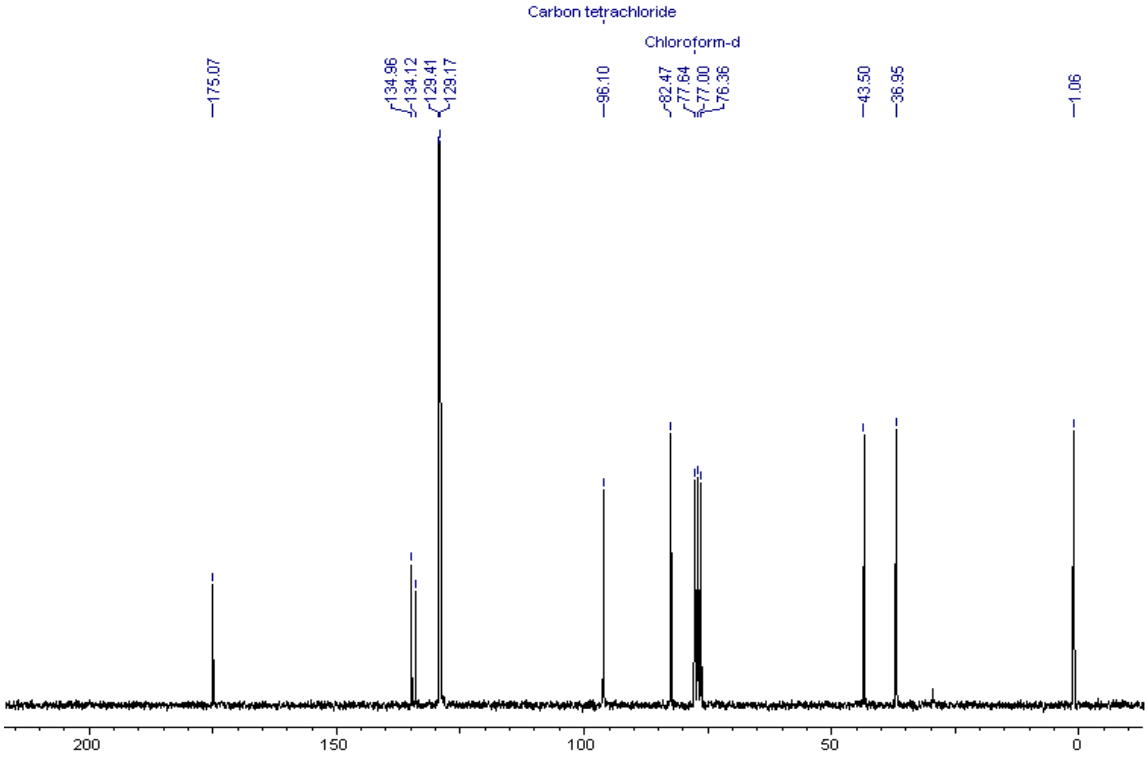
5-(iodomethyl)-4-phenyldihydrofuran-2(3*H*)-one (16a)



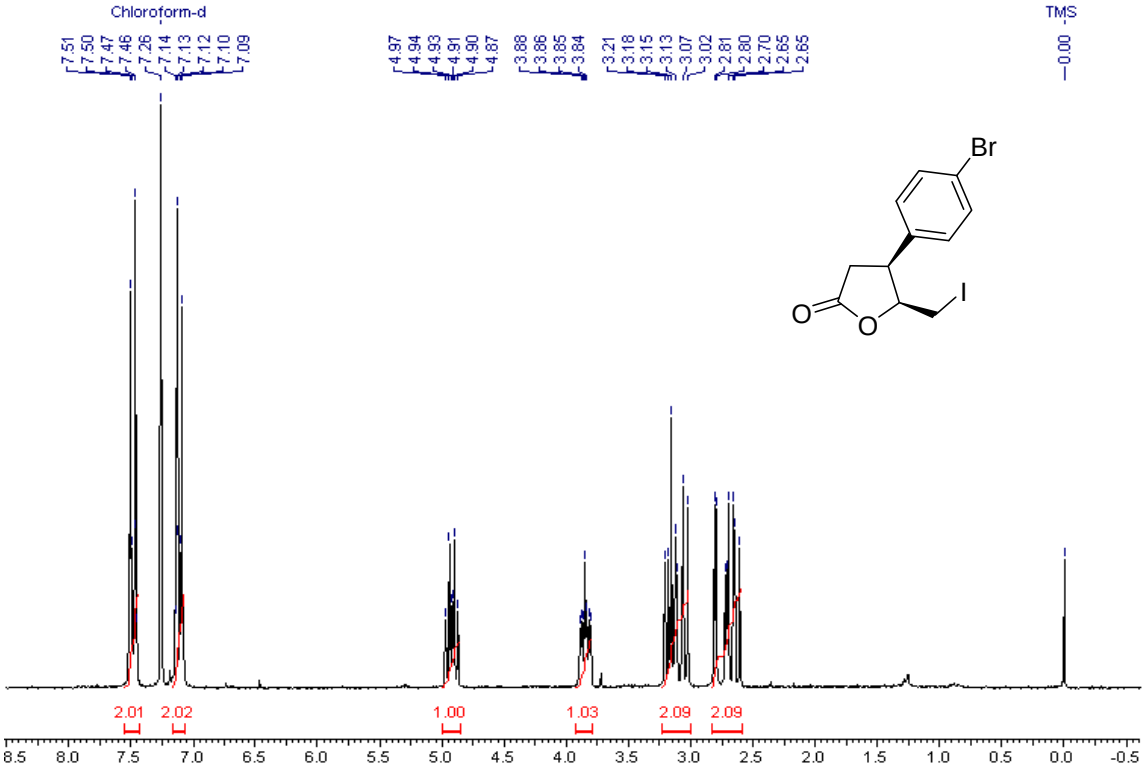


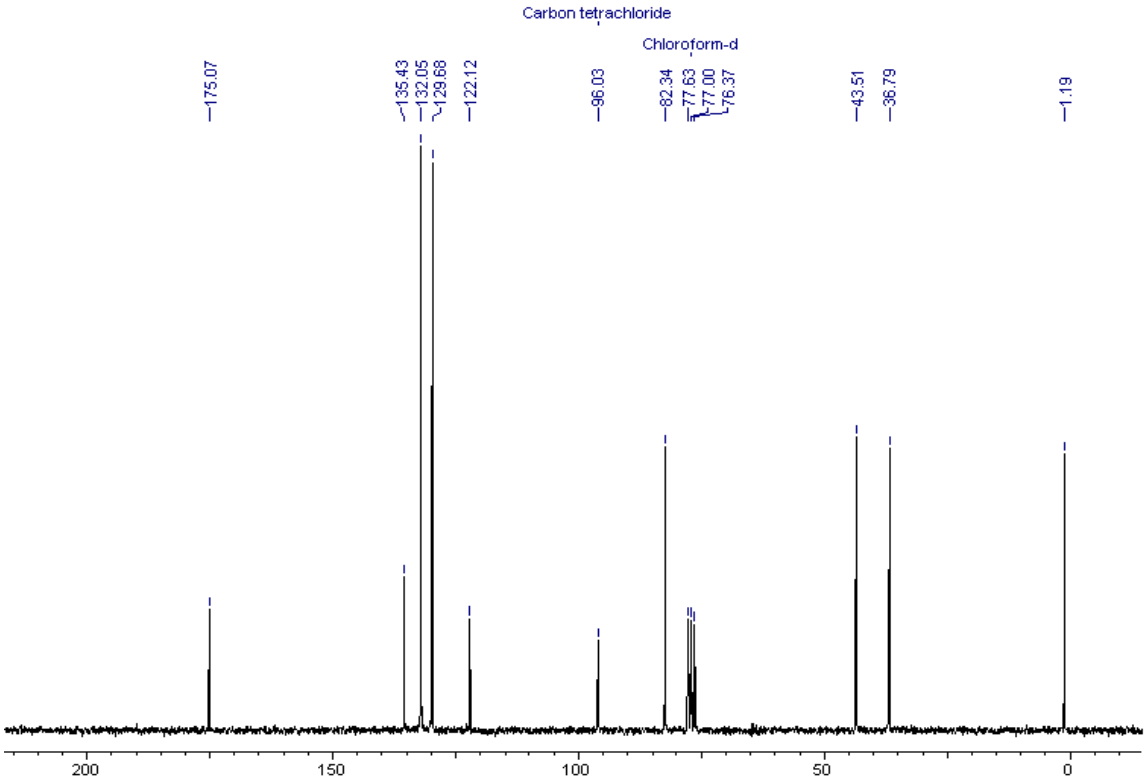
4-(4-fluorophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (16b)





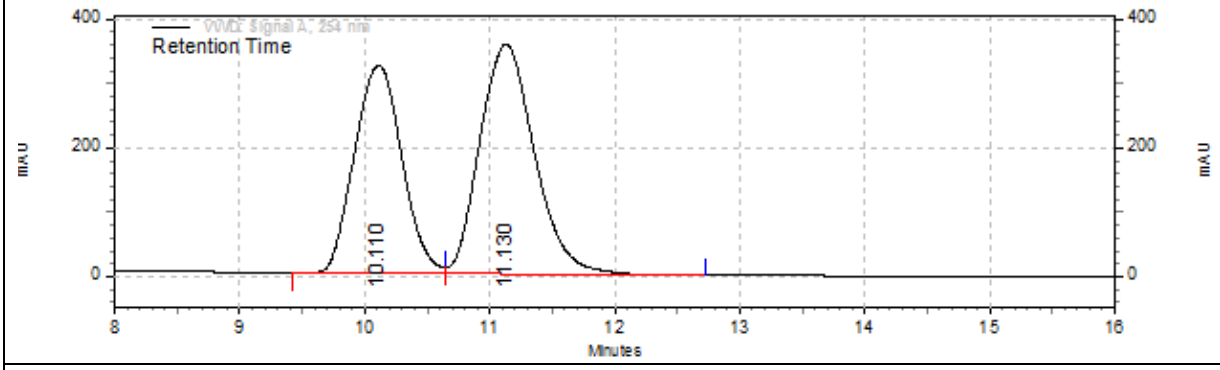
(4*S*,5*S*)-4-(4-chlorophenyl)-dihydro-5-(iodomethyl)furan-2(3*H*)-one (16c)

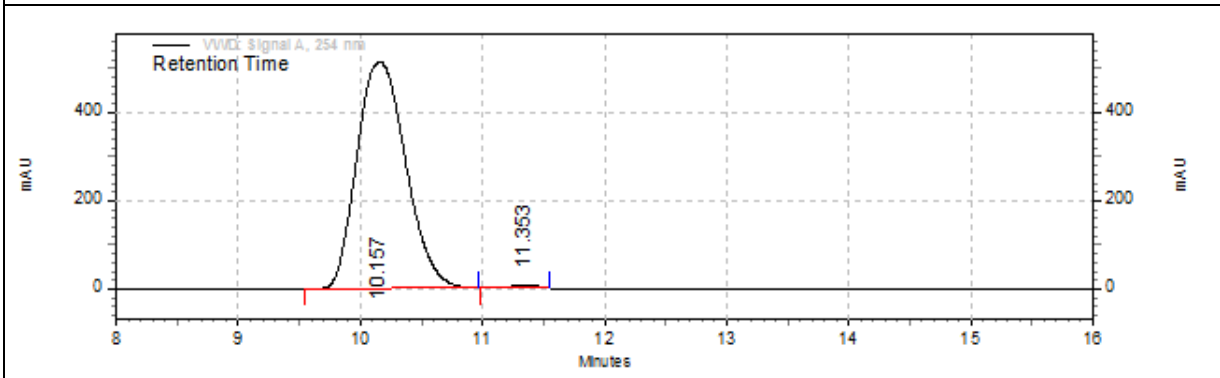




4-(4-bromophenyl)-5-(iodomethyl)dihydrofuran-2(3*H*)-one (16d)

HPCL Chromatogram



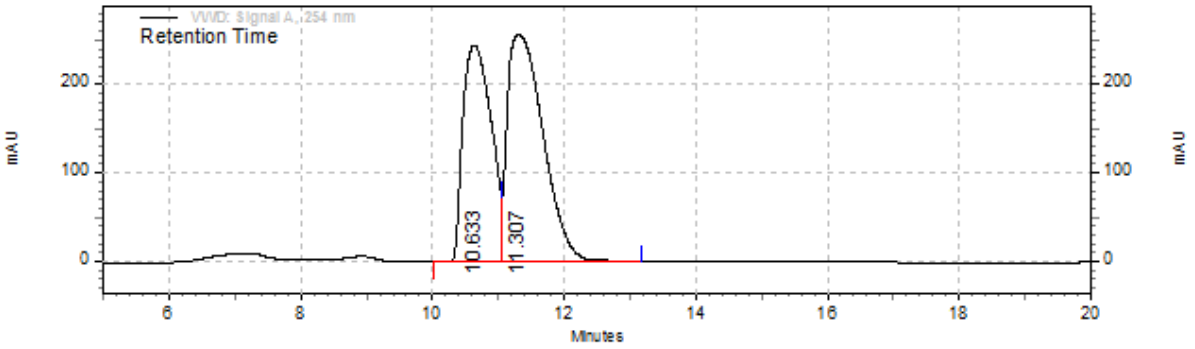


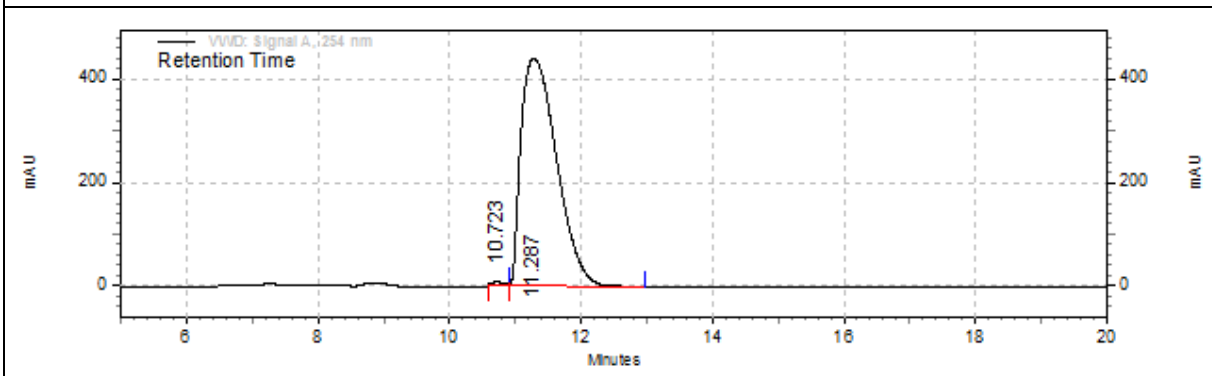
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
10.157	239861276	99.56	8617320	99.39
11.353	1070458	0.44	52774	0.61
Totals	240931734	100.00	8670094	100.00

Column :Chiracel OD-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*S*, 5*R*)-5-(hydroxymethyl)-4-phenyldihydrofuran-2(3*H*)-one (8a)



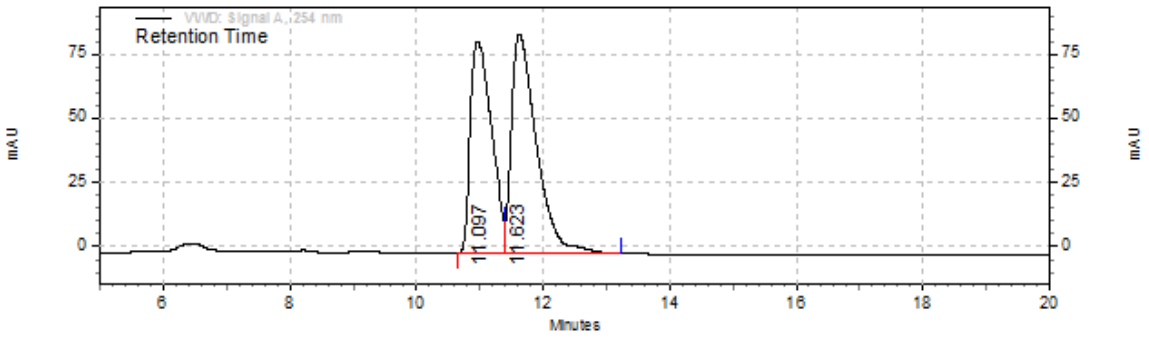


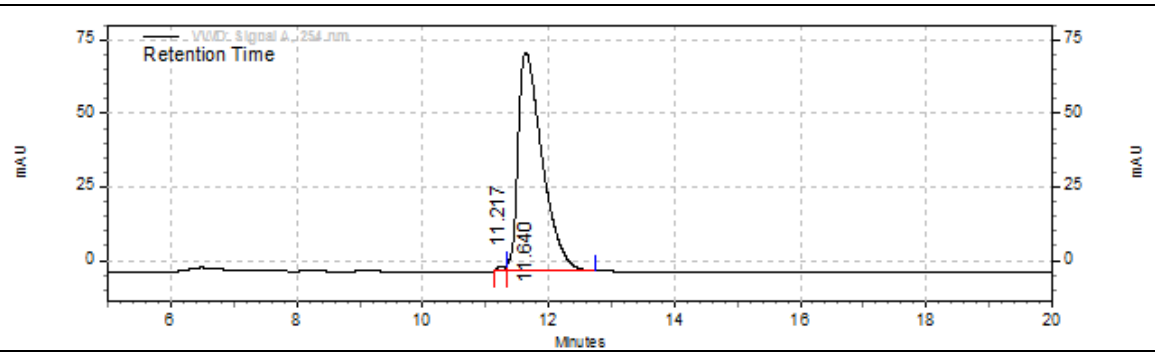
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
10.723	1145220	0.41	84440	1.14
11.287	276138259	99.59	7342750	98.86
Totals	277283479	100.00	7427190	100.00

Column :Chiracel OJ-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*S*, 5*R*)-4-(4-fluorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8b)



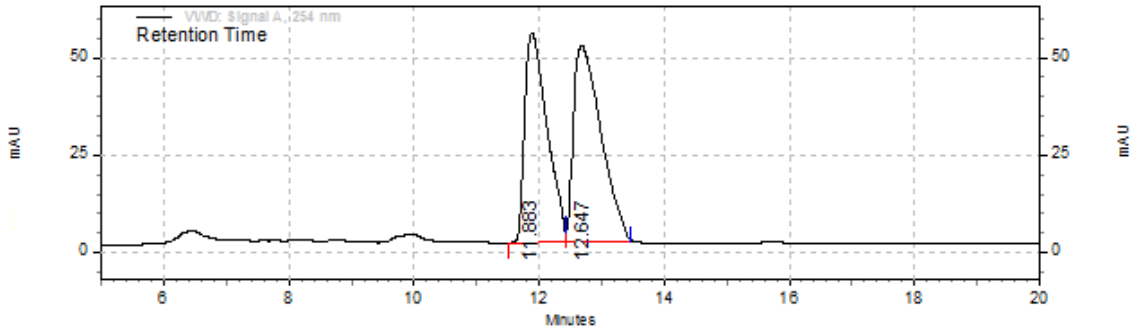


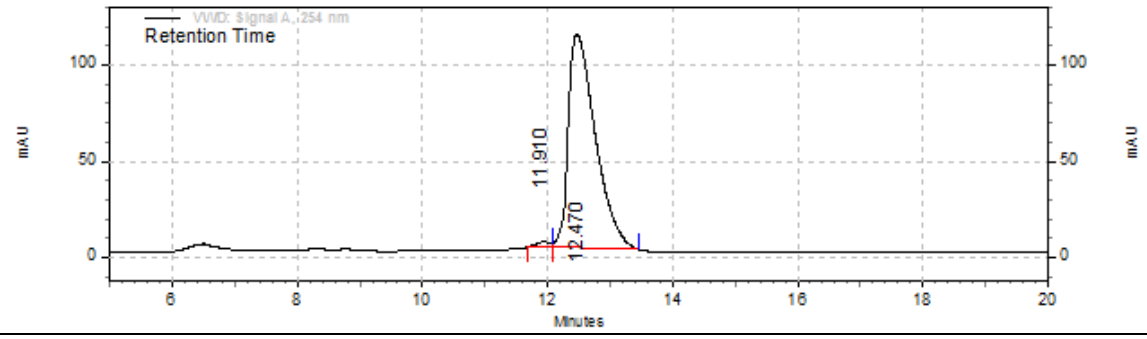
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
11.217	385194	1.15	39712	3.09
11.640	33195399	98.85	1245458	96.91
Totals	33580593	100.00	1285170	100.00

Column :Chiracel OJ-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*S*, 5*R*)-4-(4-chlorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8c)



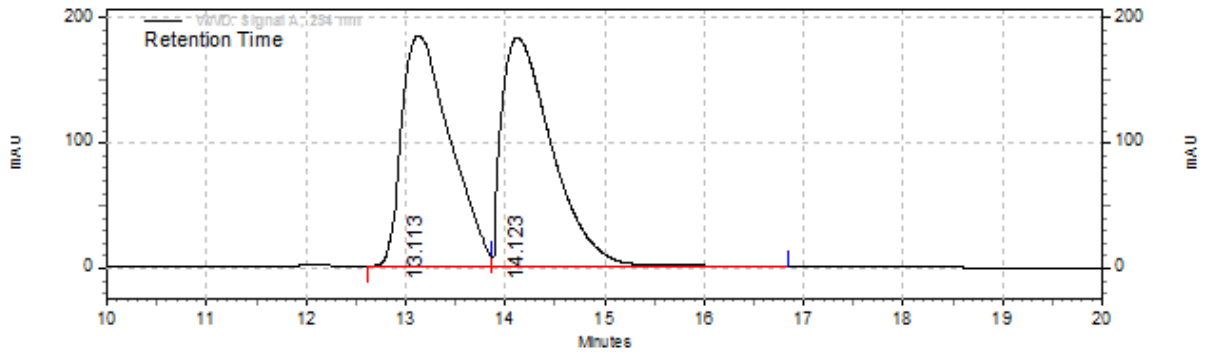


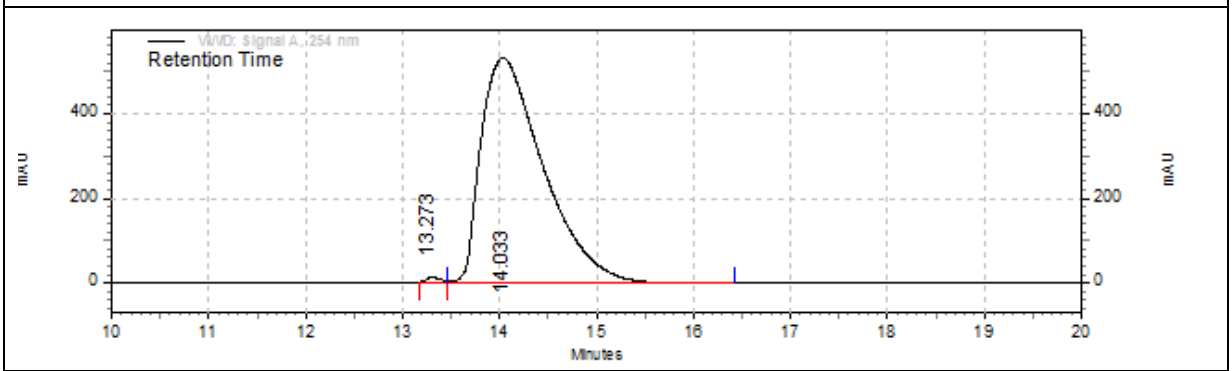
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
11.910	1174002	1.89	63064	2.84
12.470	60942491	98.11	2157502	97.16
Totals	62116493	100.00	2220566	100.00

Column :Chiracel OJ-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*S*, 5*R*)-4-(4-bromophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8d)



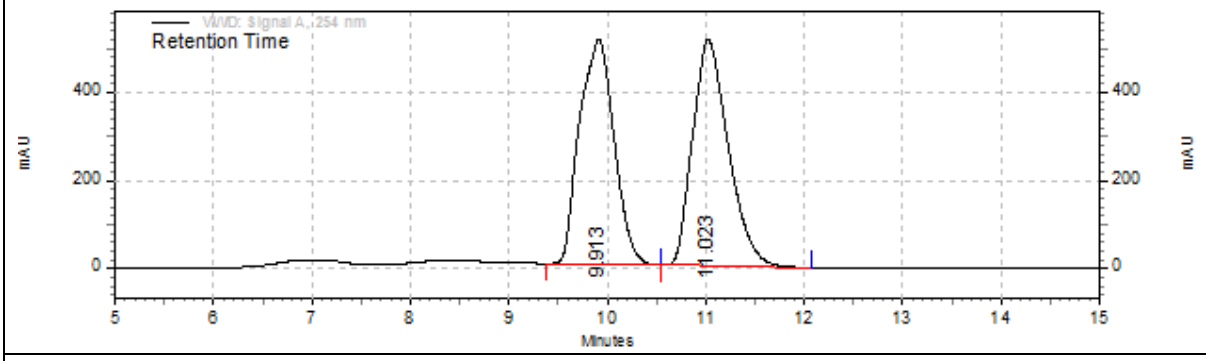


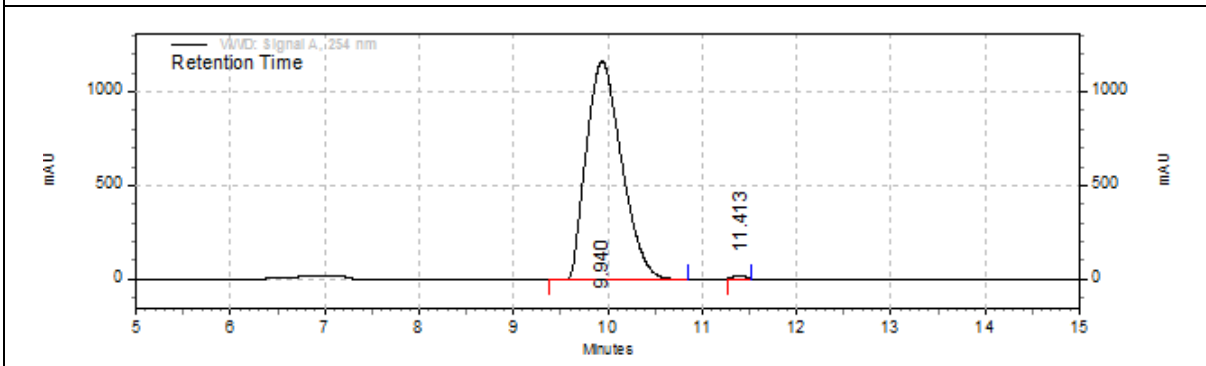
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
13.273	6404390	1.58	342368	3.70
14.033	398481392	98.42	8914216	96.30
Totals	404885782	100.00	9256584	100.00

Column :Chiracel OJ-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*S*, 5*R*)-5-(hydroxymethyl)-4-(4-methoxyphenyl)dihydro- furan-2(3*H*)-one (8e)



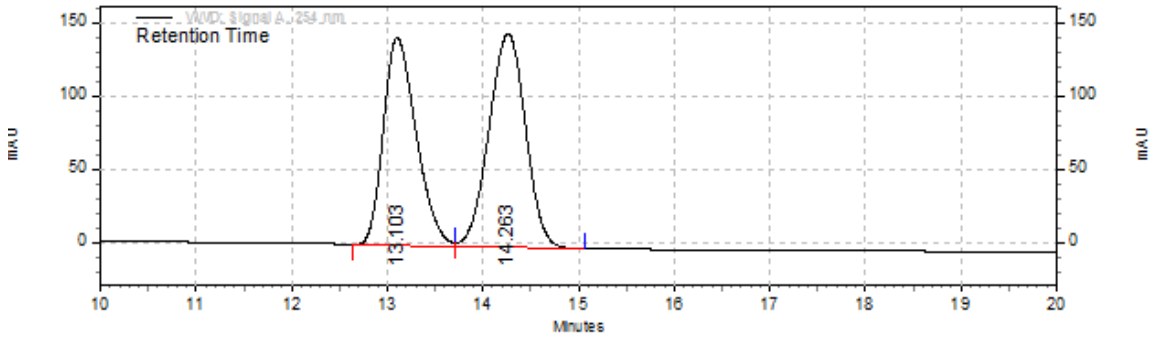


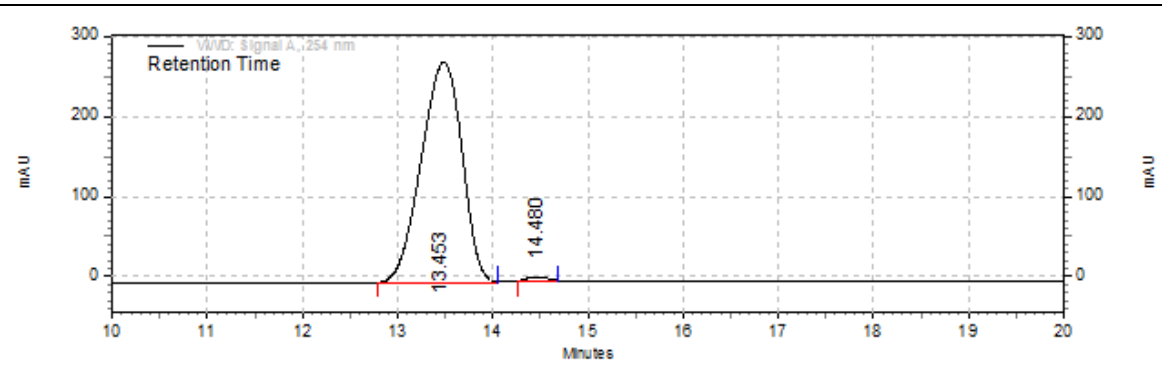
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
9.940	514230213	99.44	19588723	97.40
11.413	2897113	0.56	522812	2.60
Totals	517127326	100.00	20111535	100.00

Column :Chiracel OD-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*R*, 5*R*)-4-benzyl-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8g)





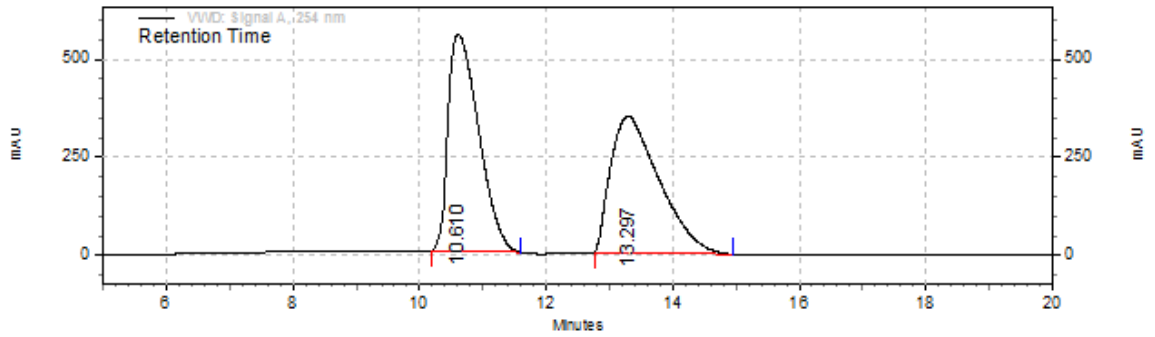
VWD: Signal A, 254 nm

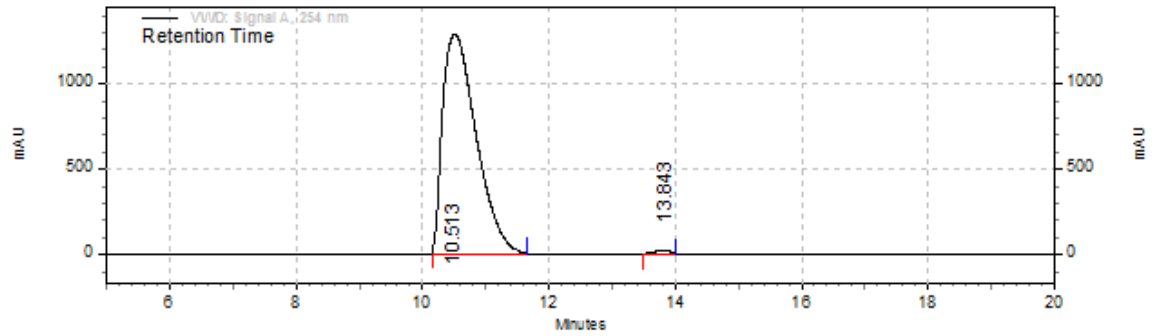
Results

Retention Time	Area	Area %	Height	Height %
13.453	141439488	98.10	4730300	97.33
14.480	2739399	1.90	129764	2.67
Totals	144178887	100.00	4860064	100.00

Column :Chiracel OD-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*R*, 5*R*)-5-(hydroxymethyl)-4-phenethyldihydrofuran-2(3*H*)-one (8h)



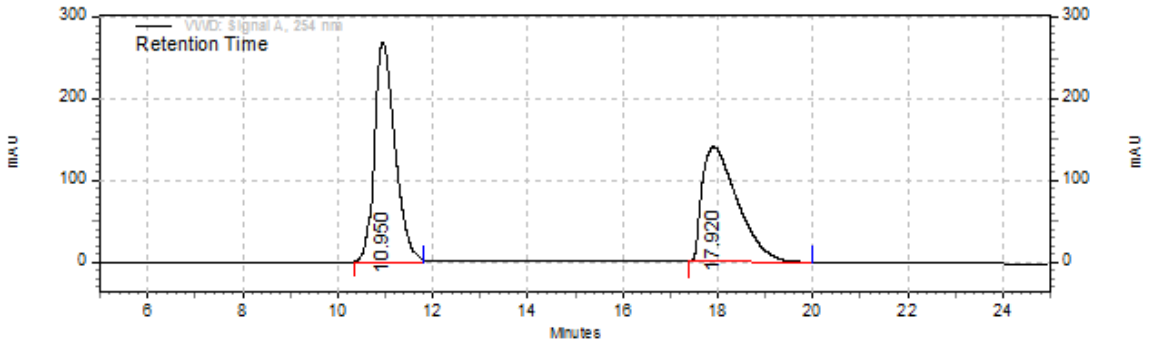


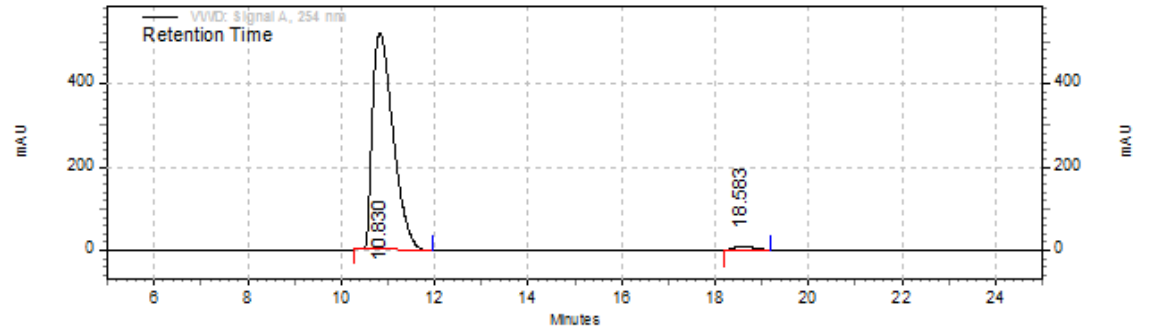
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
10.513	770861957	98.87	21199435	97.24
13.843	8810296	1.13	601712	2.76
Totals	779672253	100.00	21801147	100.00

Column :Chiracel OJ-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*S*, 5*S*)-5-(hydroxymethyl)-4-phenyldihydrofuran-2(3*H*)-one (11a)



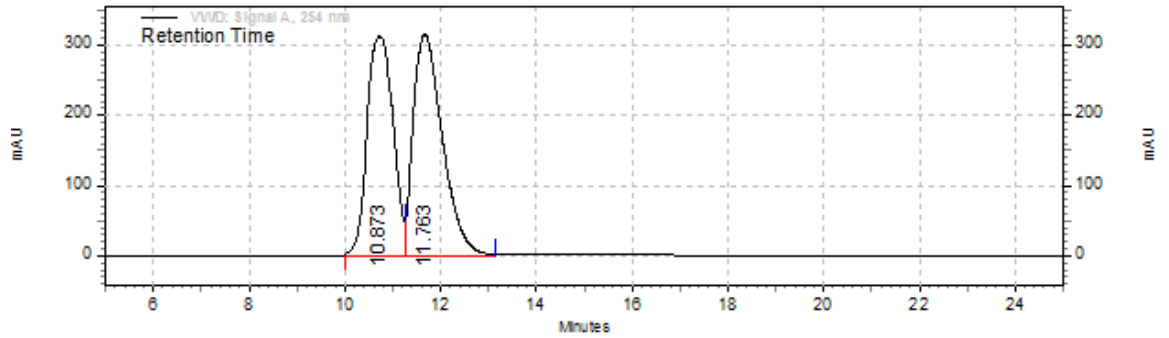


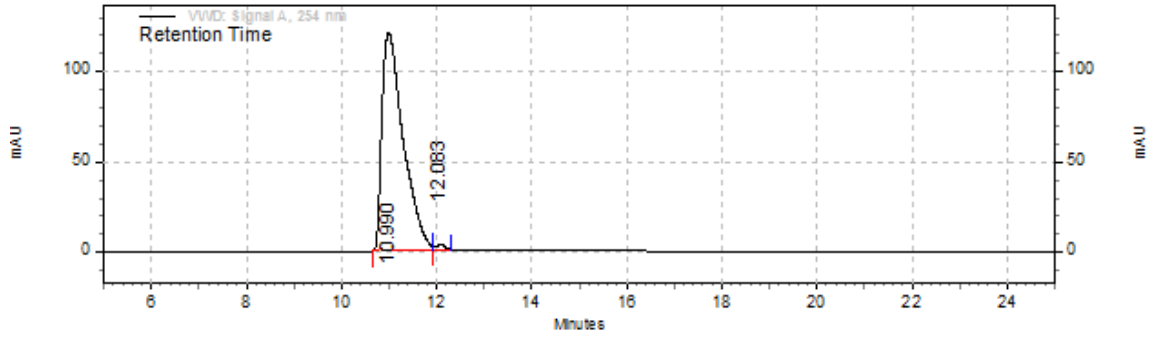
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
10.830	268706835	99.18	8661347	97.96
18.583	2221613	0.82	180255	2.04
Totals	270928448	100.00	8841602	100.00

Column :Chiracel OJ-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*S*, 5*S*)-4-(4-fluorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (11b)



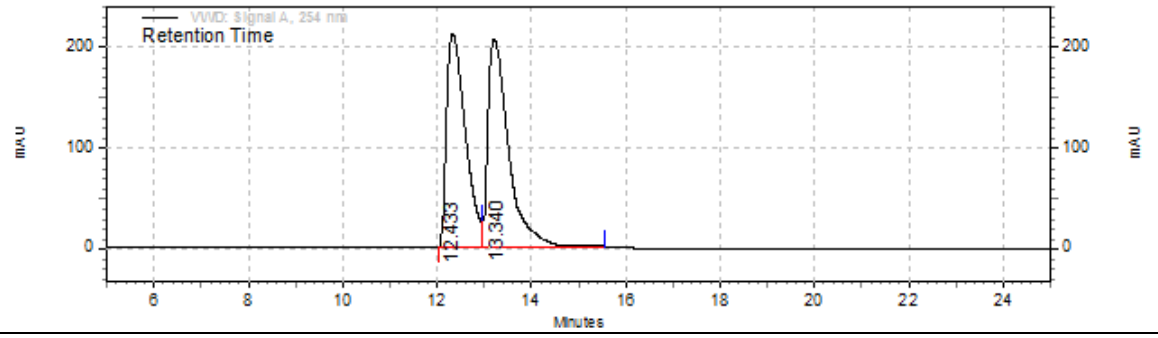


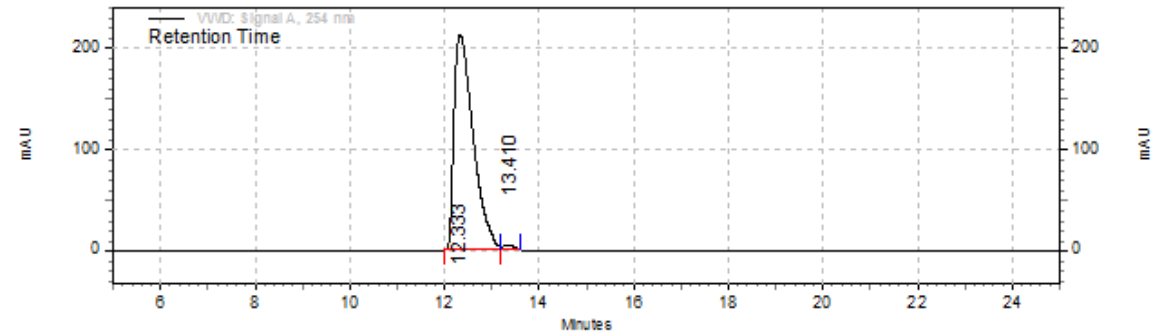
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
10.990	59650033	99.29	1996754	98.39
12.083	428803	0.71	32736	1.61
Totals	60078836	100.00	2029490	100.00

Column :Chiracel OJ-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*S*, 5*S*)-4-(4-chlorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (11c)



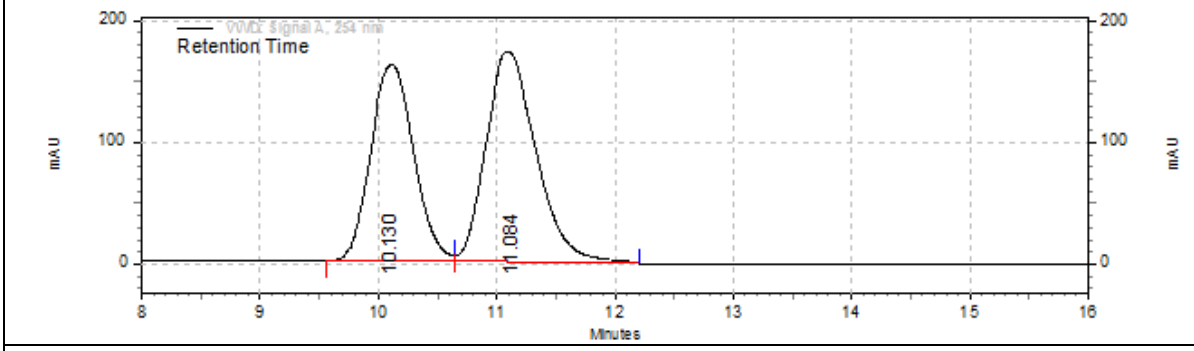


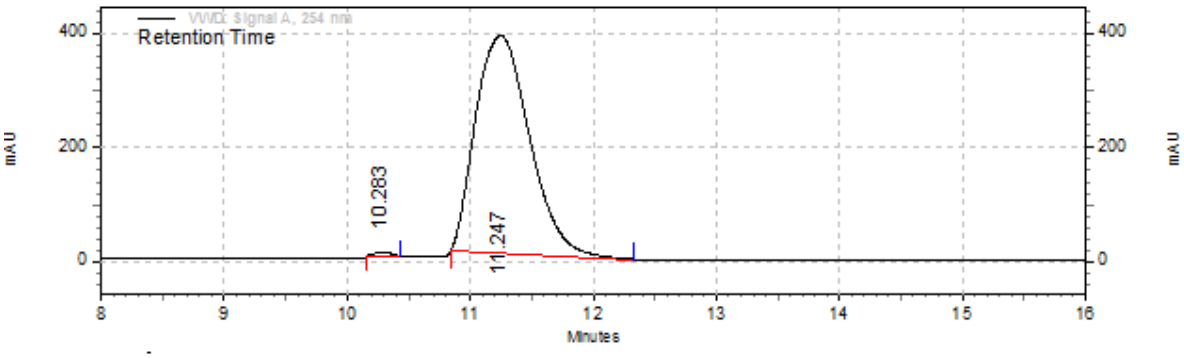
VWD: Signal A, 254 nm Results

Retention Time	Area	Area %	Height	Height %
12.333	116895600	98.83	4258259	97.94
13.410	1383868	1.17	89565	2.06
Totals	118279468	100.00	4347824	100.00

Column :Chiracel OJ-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(50:50)
Wavelength :254 nm
Flow rate :0.5ml/min

(4*S*, 5*S*)-4-(4-bromophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (11d)



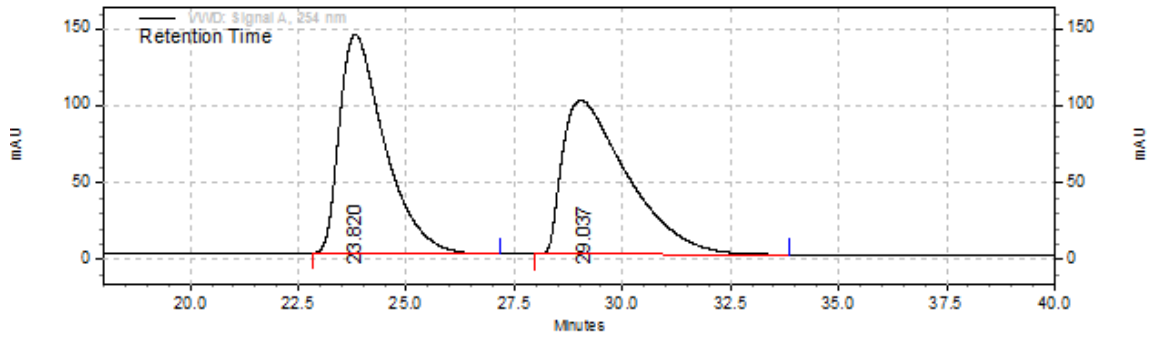


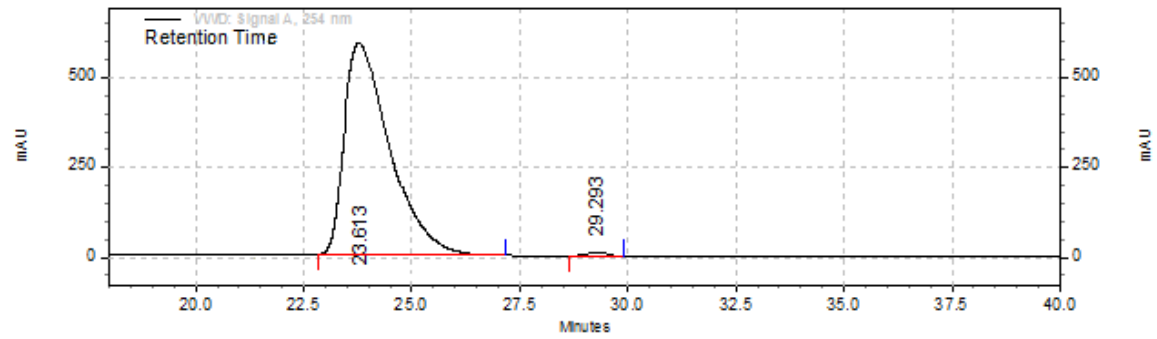
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
10.283	2605821	1.31	150721	2.29
11.247	195852243	98.69	6430035	97.71
Totals	198458064	100.00	6580756	100.00

Column :Chiracel OD-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(10:90)
Wavelength :254 nm
Flow rate :0.5ml/min

(*R*)-methyl 3-((*S*)-oxiran-2-yl)-3-phenylpropanoate (9a)



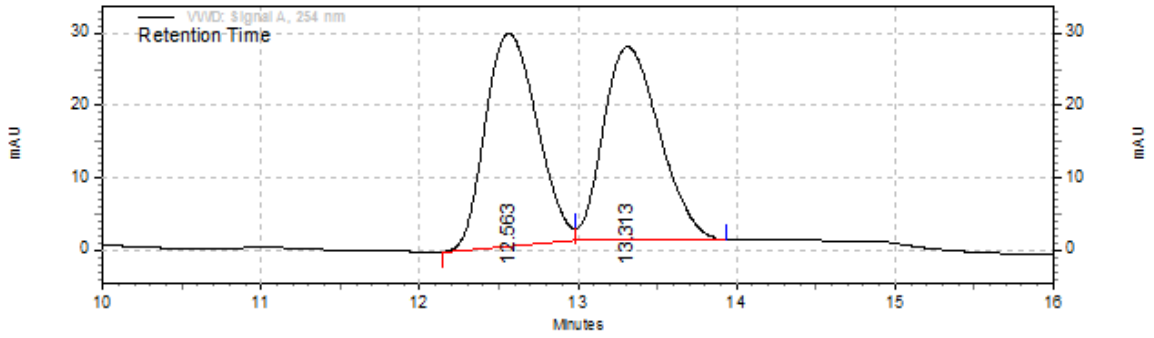


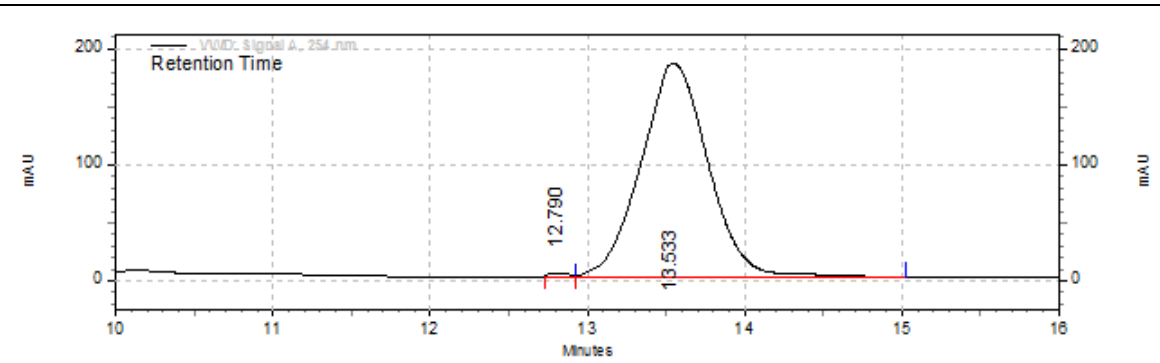
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
23.613	744775659	99.35	10081948	99.10
29.293	4872714	0.65	91561	0.90
Totals	749648373	100.00	10173509	100.00

Column :Chiracel OJ-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(10:90)
Wavelength :254 nm
Flow rate :0.5ml/min

(*R*)-methyl 3-(4-fluorophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9b)



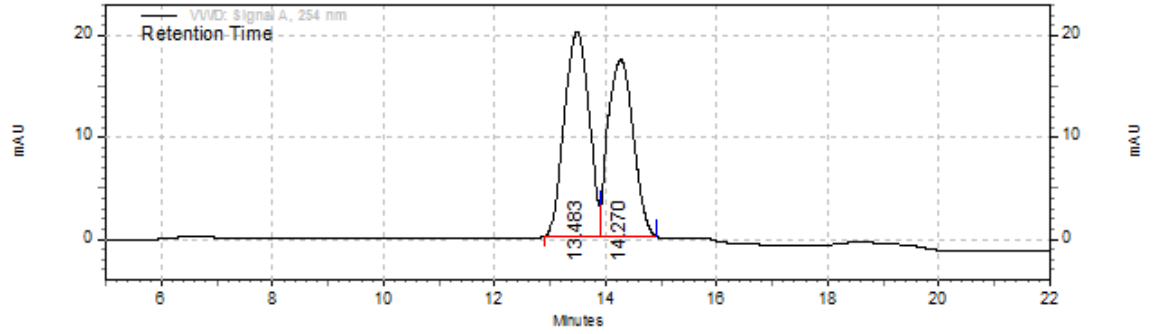


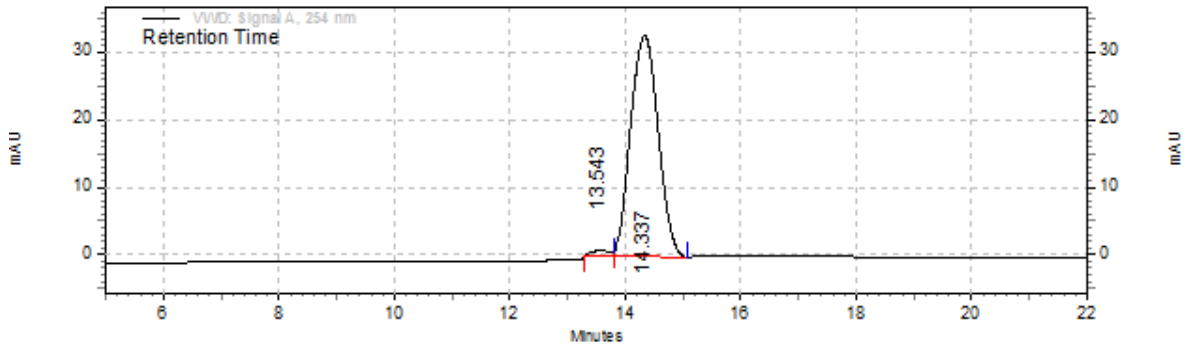
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
12.790	1271922	1.00	23145	0.70
13.533	127169261	99.00	3283293	99.30
Totals	128441183	100.00	3306438	100.00

Column :Chiracel OD-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(10:90)
Wavelength :254 nm
Flow rate :0.5ml/min

(*R*)-methyl 3-(4-chlorophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9c)



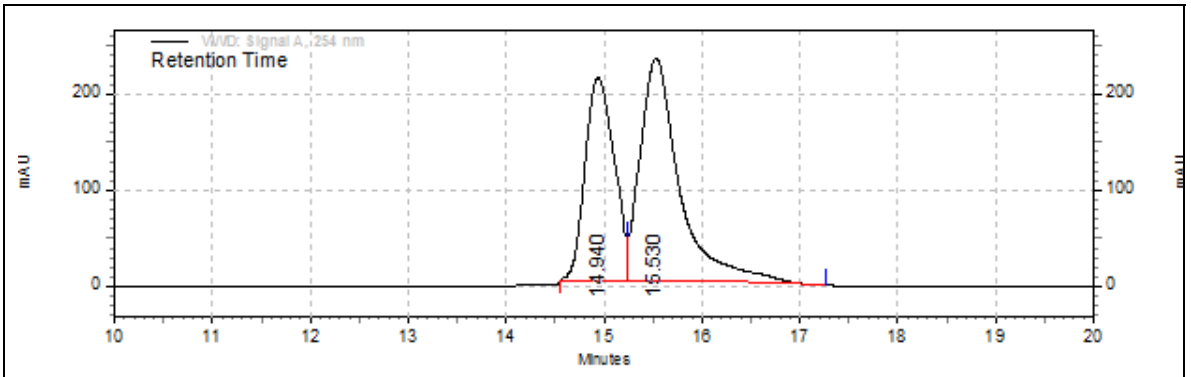


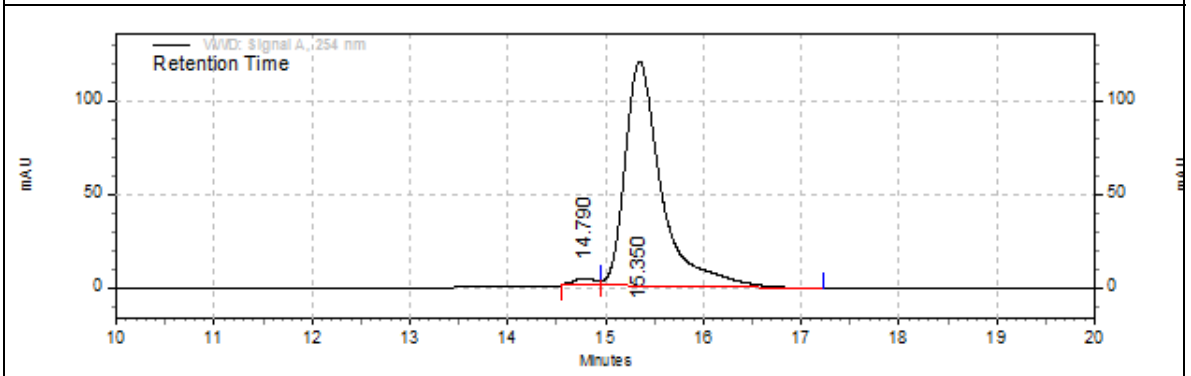
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
13.543	360799	1.81	13201	2.15
14.337	19572852	98.19	600822	97.85
Totals	19933651	100.00	614023	100.00

Column :Chiracel OD-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(5:95)
Wavelength :254 nm
Flow rate :0.5ml/min

(*R*)-methyl 3-(4-bromophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9d)



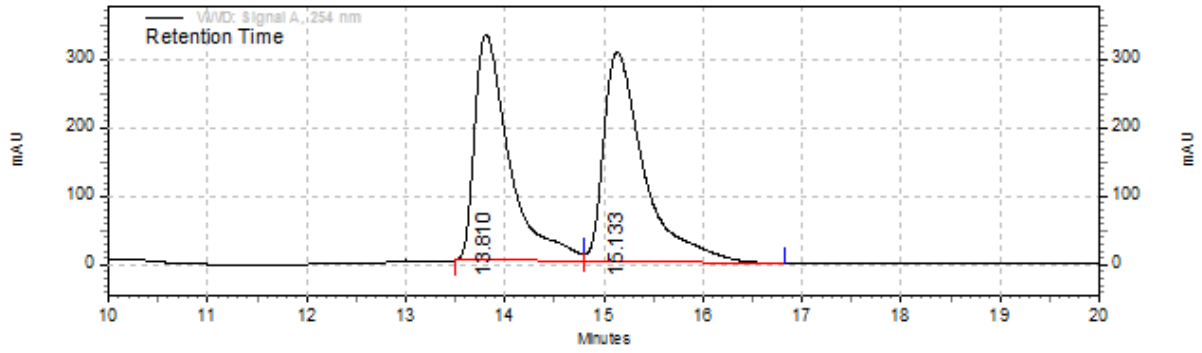


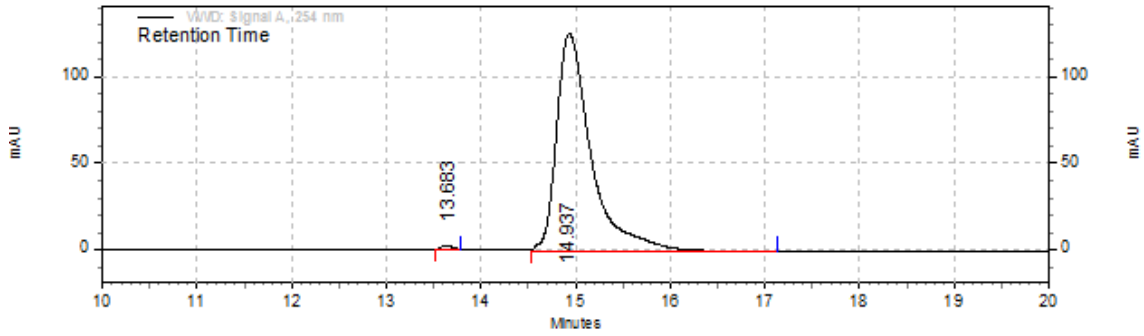
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
14.790	1095969	2.09	54486	2.64
15.350	51342728	97.91	2012792	97.36
Totals	52438697	100.00	2067278	100.00

Column :Chiracel OD-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(10:90)
Wavelength :254 nm
Flow rate :0.5ml/min

(*S*)-methyl 3-((*S*)-oxiran-2-yl)-5-phenylpentanoate (9h)



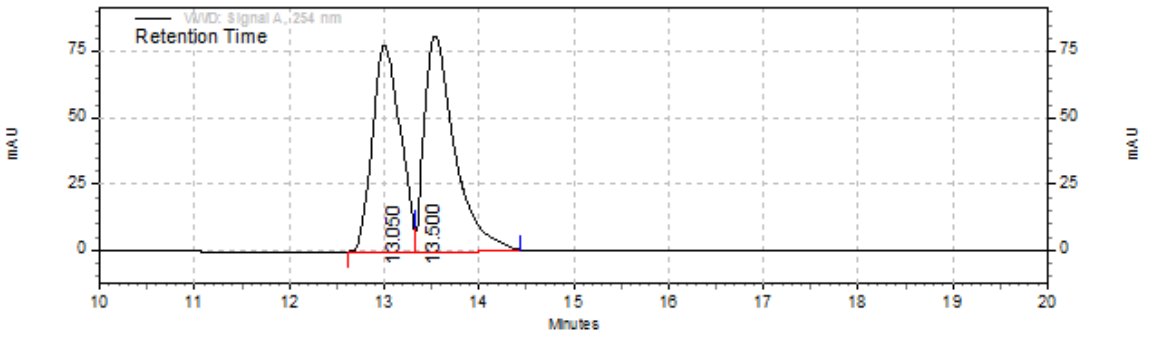


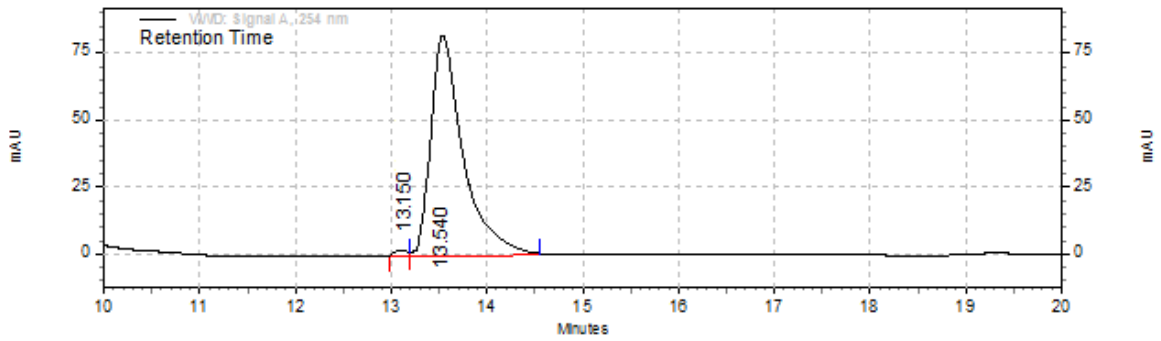
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
13.683	1085101	1.28	86506	2.47
14.937	83688409	98.72	3415774	97.53
Totals	84773510	100.00	3502280	100.00

Column :Chiracel OD-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(10:90)
Wavelength :254 nm
Flow rate :0.5ml/min

(*R*)-methyl 3-((*R*)-oxiran-2-yl)-3-phenylpropanoate (12a)



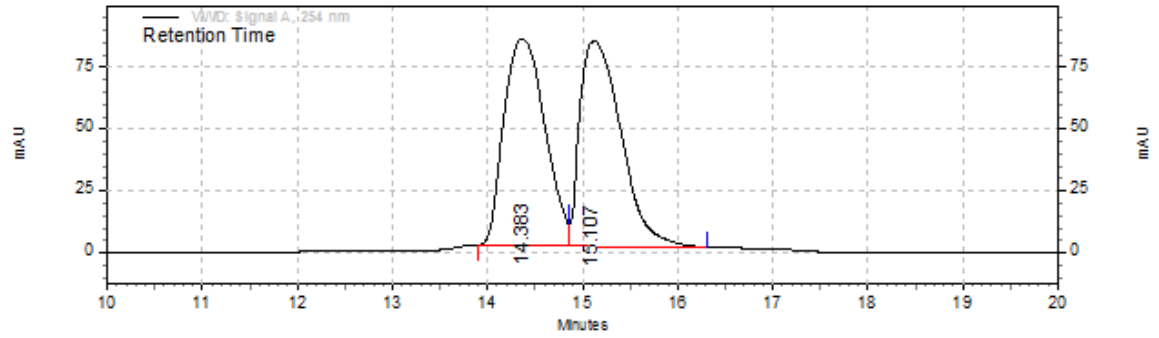


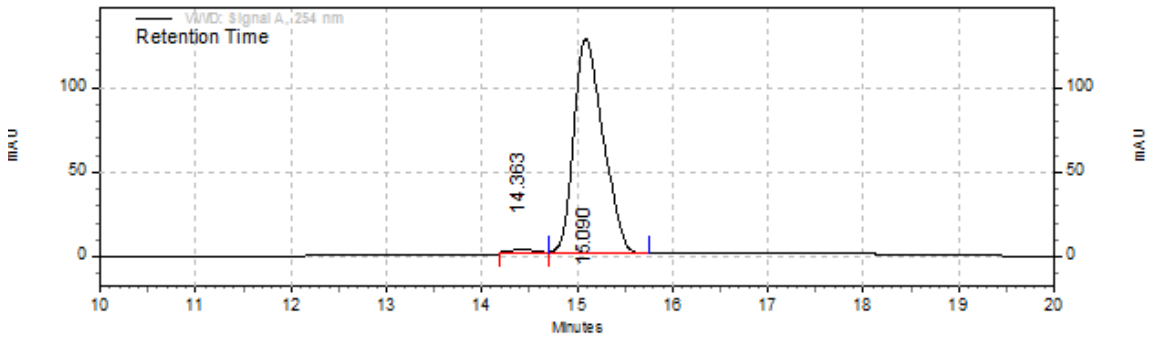
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
13.150	703311	1.59	51813	2.94
13.540	43530094	98.41	1710546	97.06
Totals	44233405	100.00	1762359	100.00

Column :Chiracel OD-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(10:90)
Wavelength :254 nm
Flow rate :0.5ml/min

(*R*)-methyl 3-(4-chlorophenyl)-3-((*R*)-oxiran-2-yl)propanoate (12c)





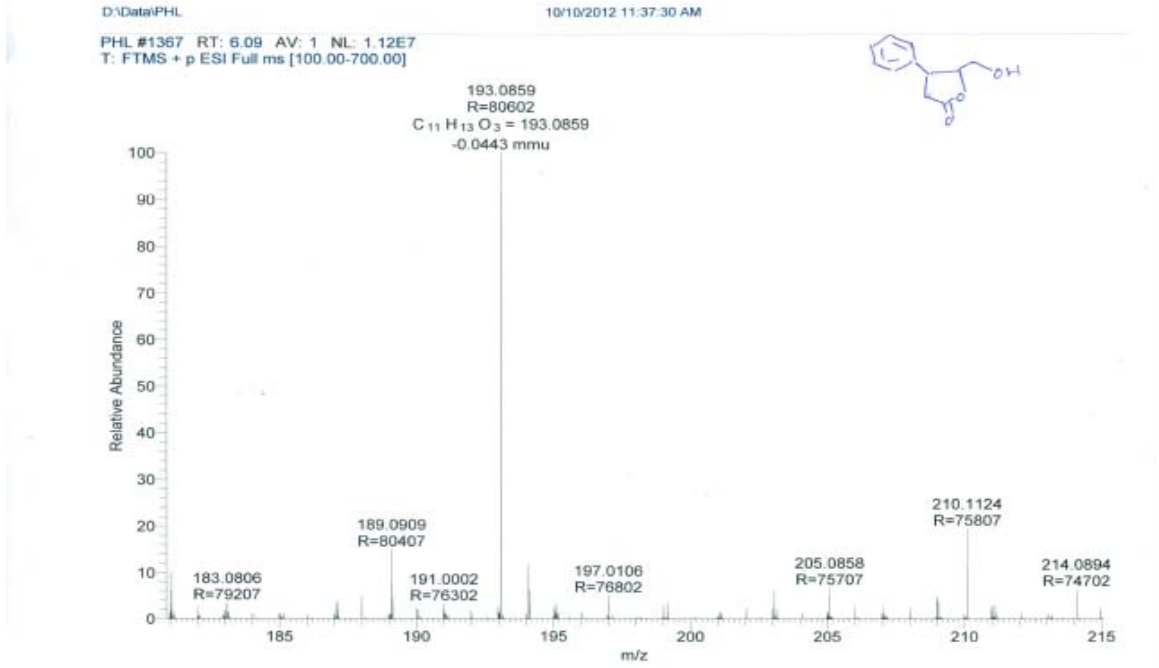
VWD: Signal A, 254 nm
Results

Retention Time	Area	Area %	Height	Height %
14.363	889081	1.70	42135	1.83
15.090	51409808	98.30	2260328	98.17
Totals	52298889	100.00	2302463	100.00

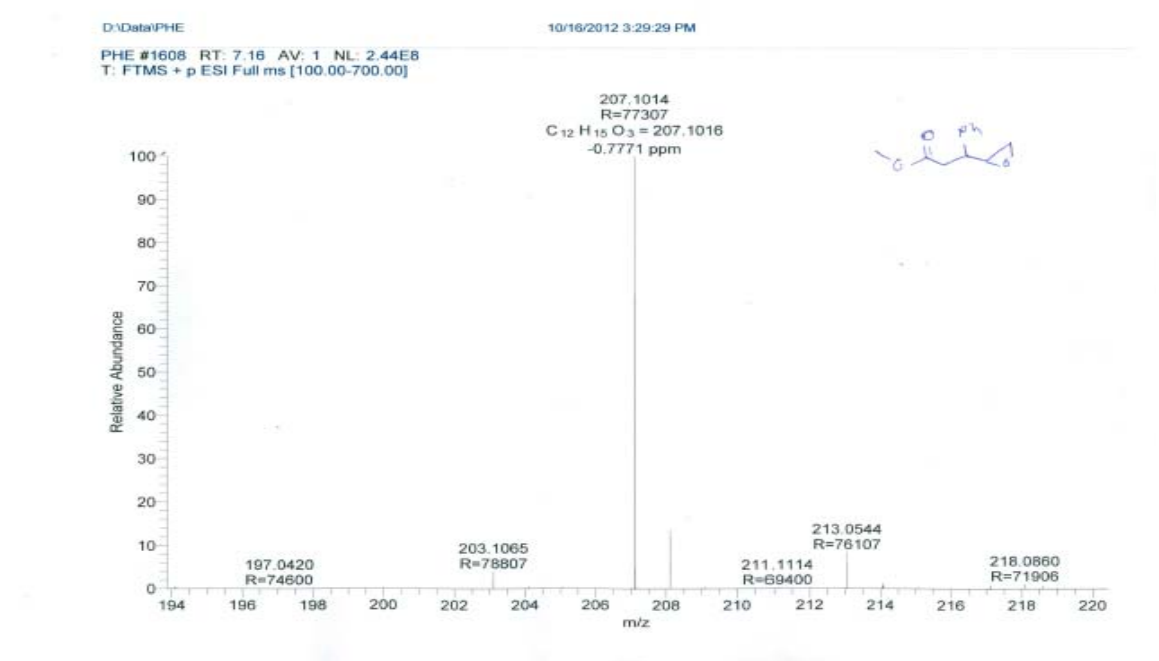
Column :Chiracel OD-H (4.6X250 nm)
Mobile Phase :IPA:n-Hexane(10:90)
Wavelength :254 nm
Flow rate :0.5ml/min

(*R*)-methyl 3-(4-bromophenyl)-3-((*R*)-oxiran-2-yl)propanoate (12d)

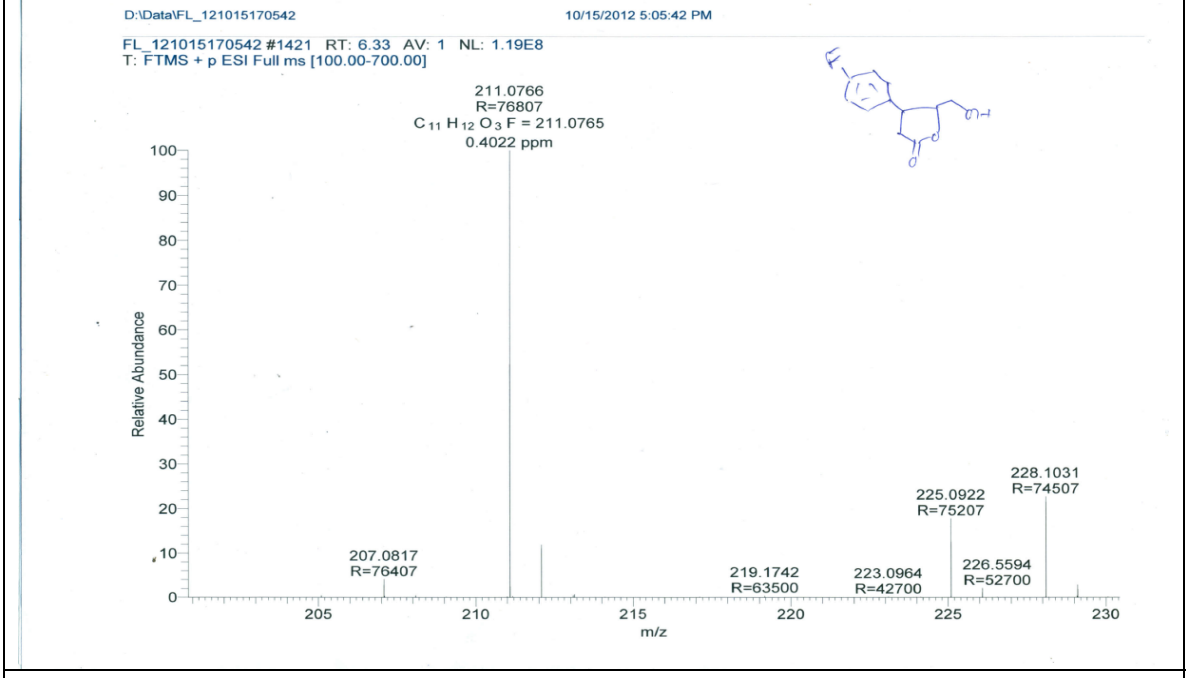
HRMS



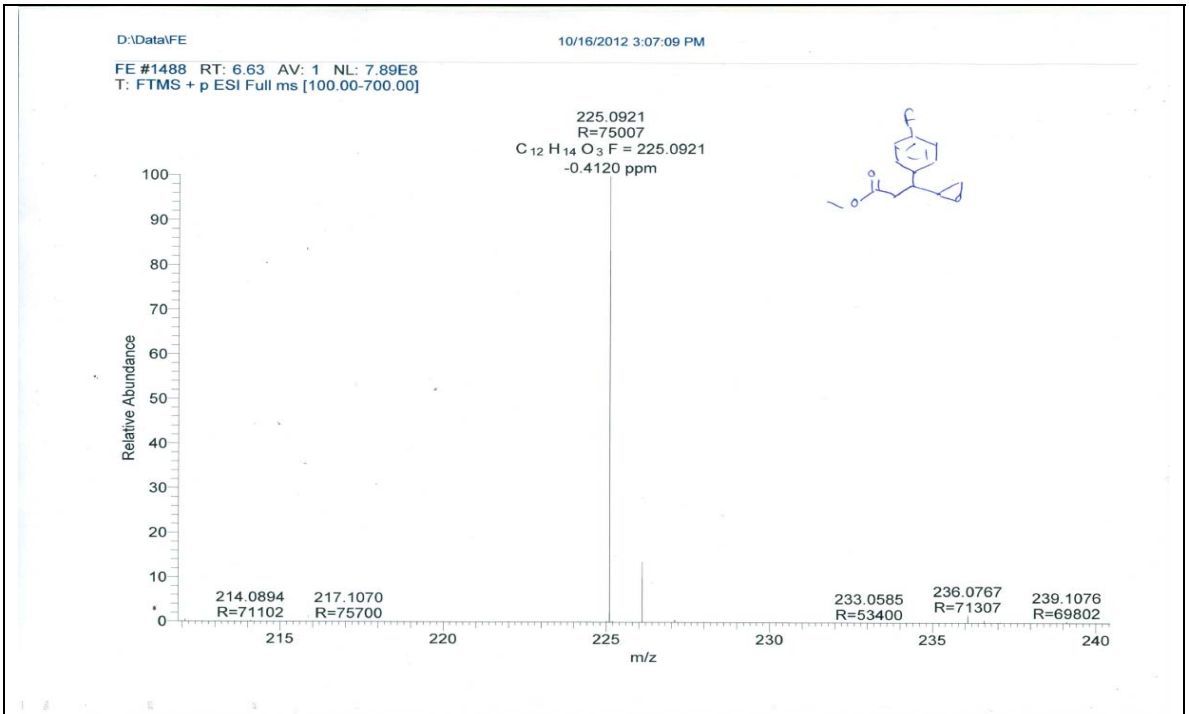
(4*S*, 5*R*)-5-(hydroxymethyl)-4-phenyldihydrofuran-2(3*H*)-one (8a)



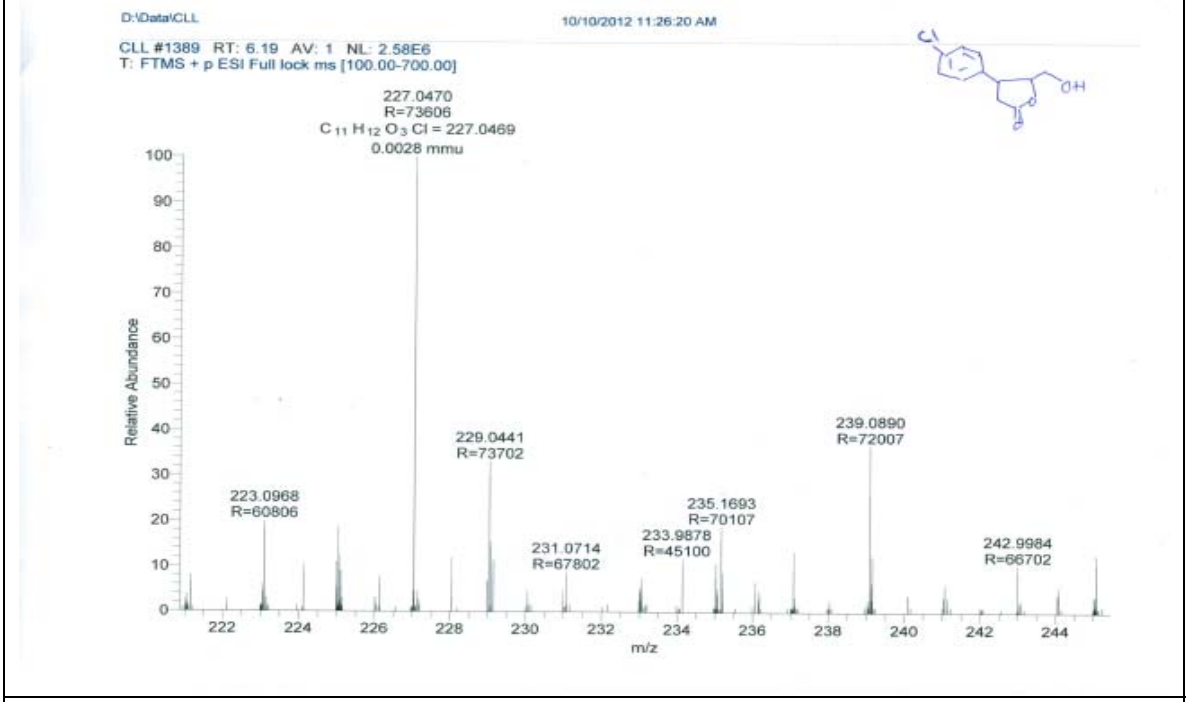
(*R*)-methyl 3-((*S*)-oxiran-2-yl)-3-phenylpropanoate (9a)



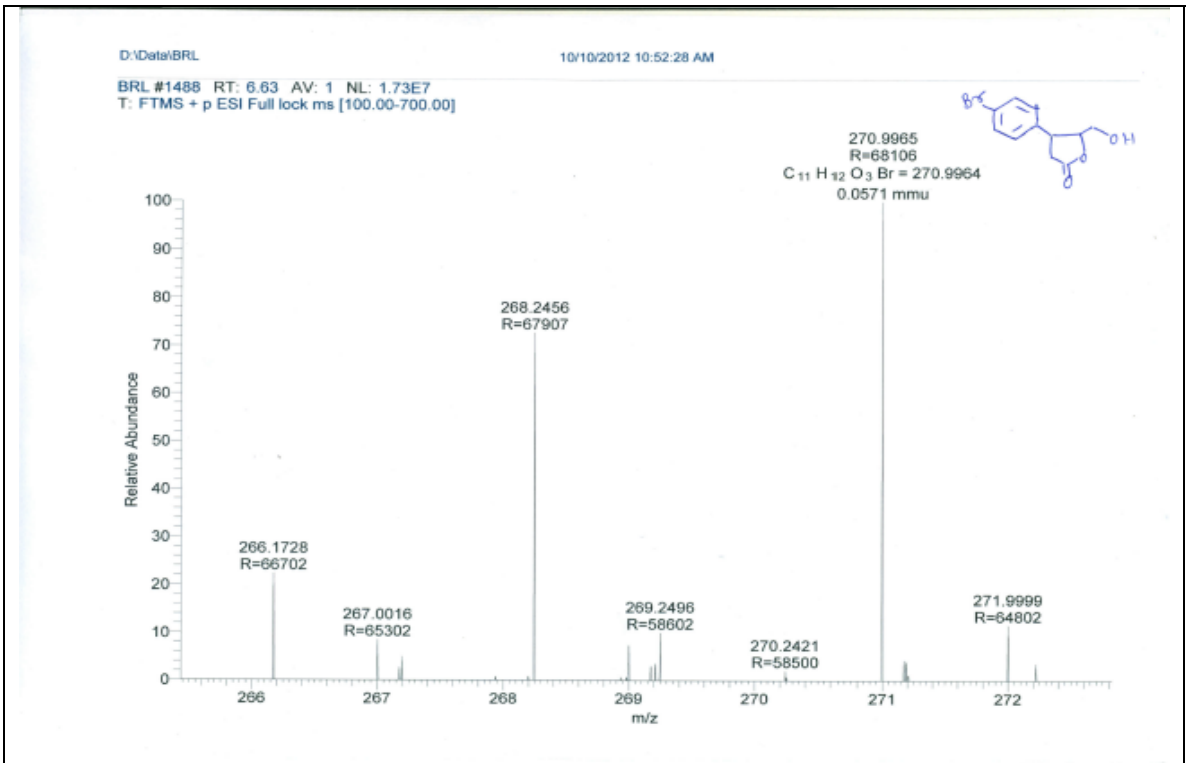
(4*S*, 5*R*)-4-(4-fluorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8b)



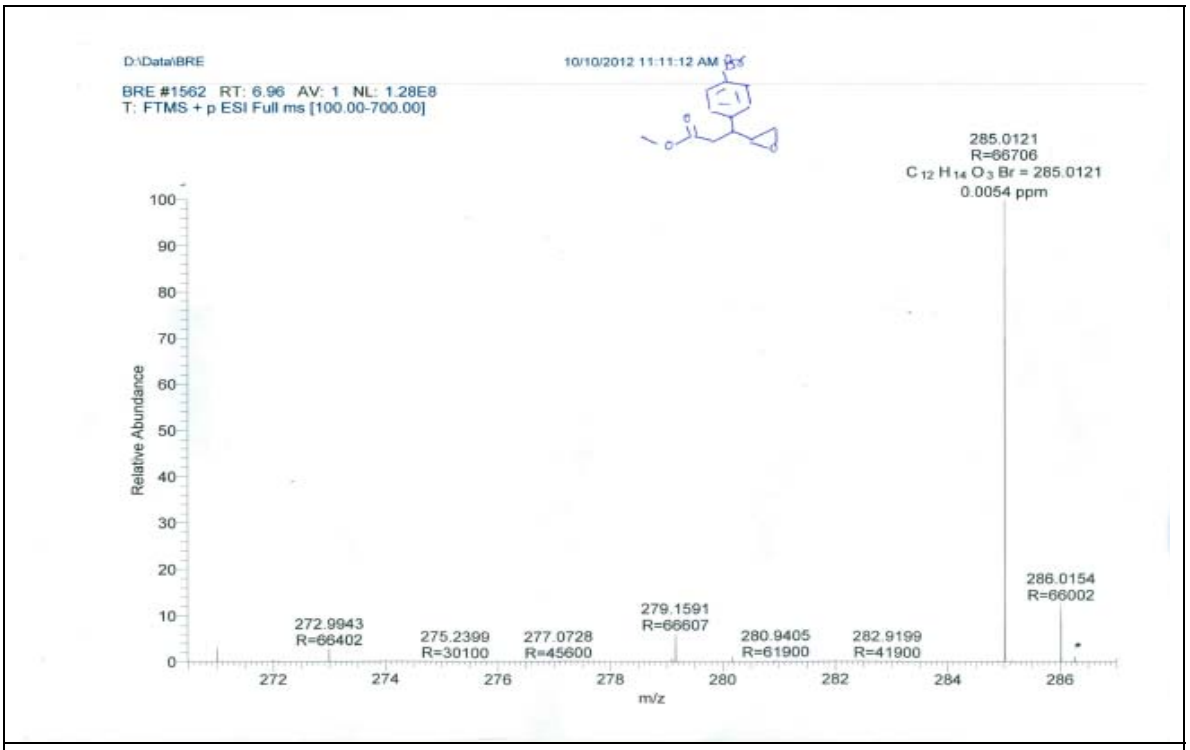
(*R*)-methyl 3-(4-fluorophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9b)



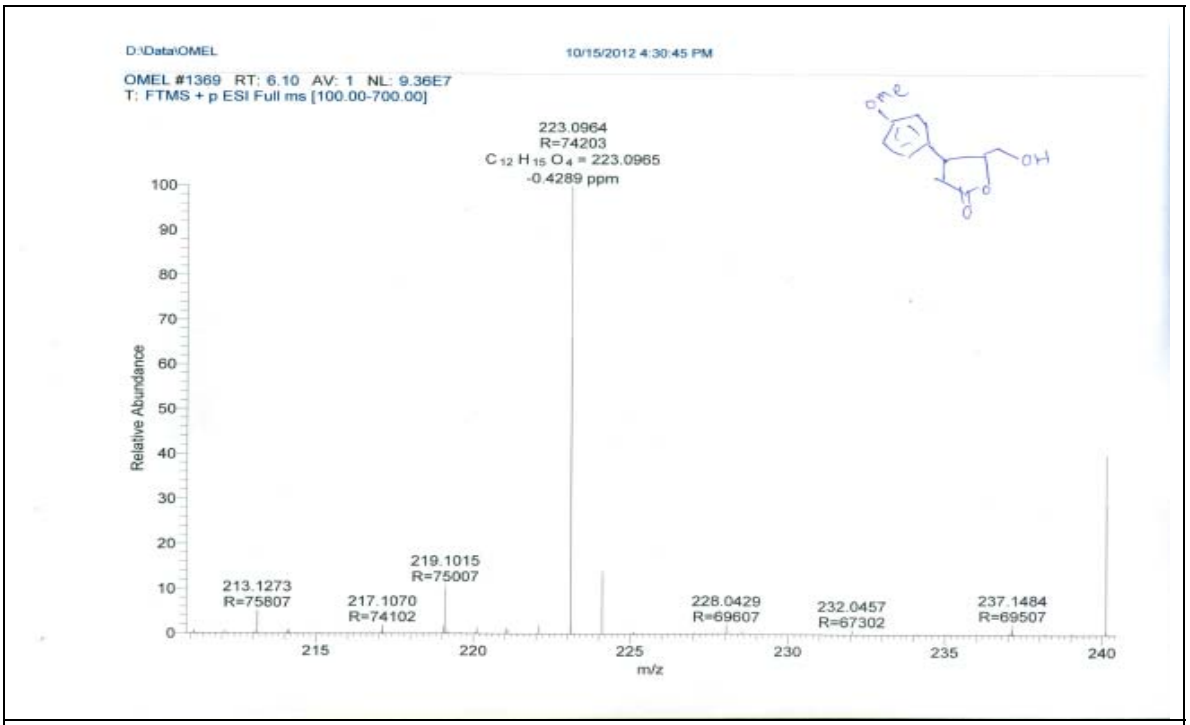
(4*S*, 5*R*)-4-(4-chlorophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8c)



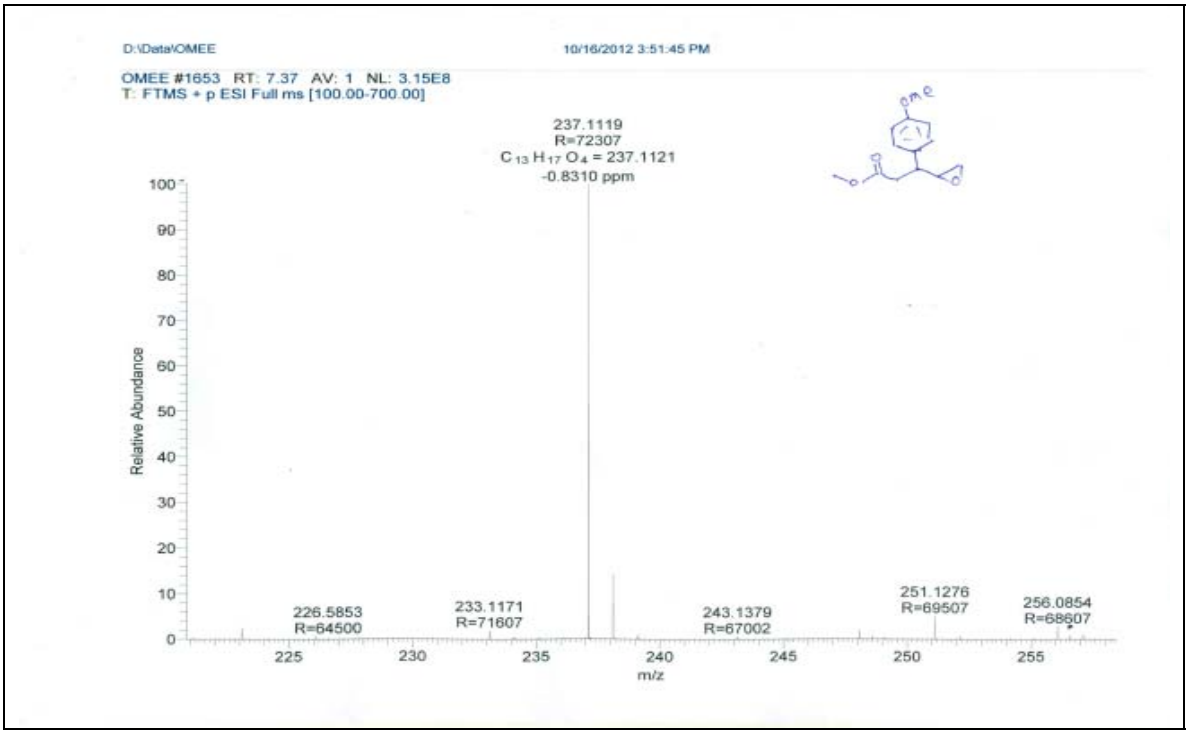
(4*S*, 5*R*)-4-(4-bromophenyl)-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8d)



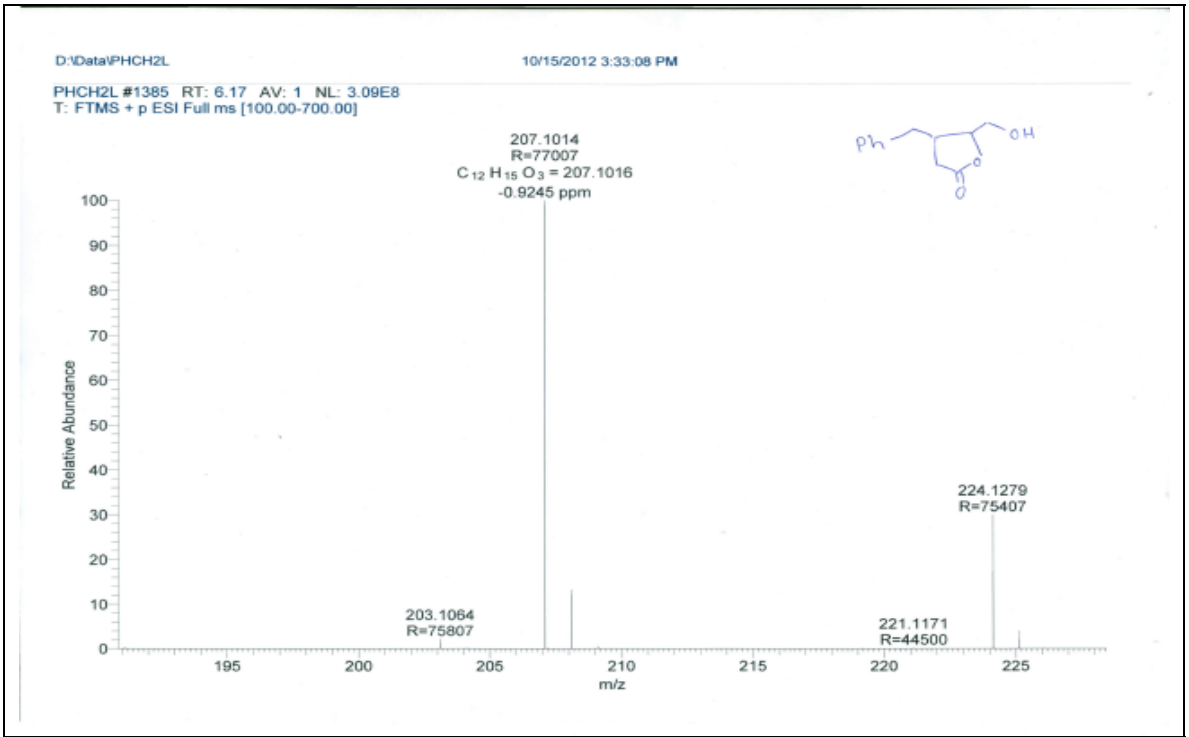
(*R*)-methyl 3-(4-bromophenyl)-3-((*S*)-oxiran-2-yl)propanoate (9d)



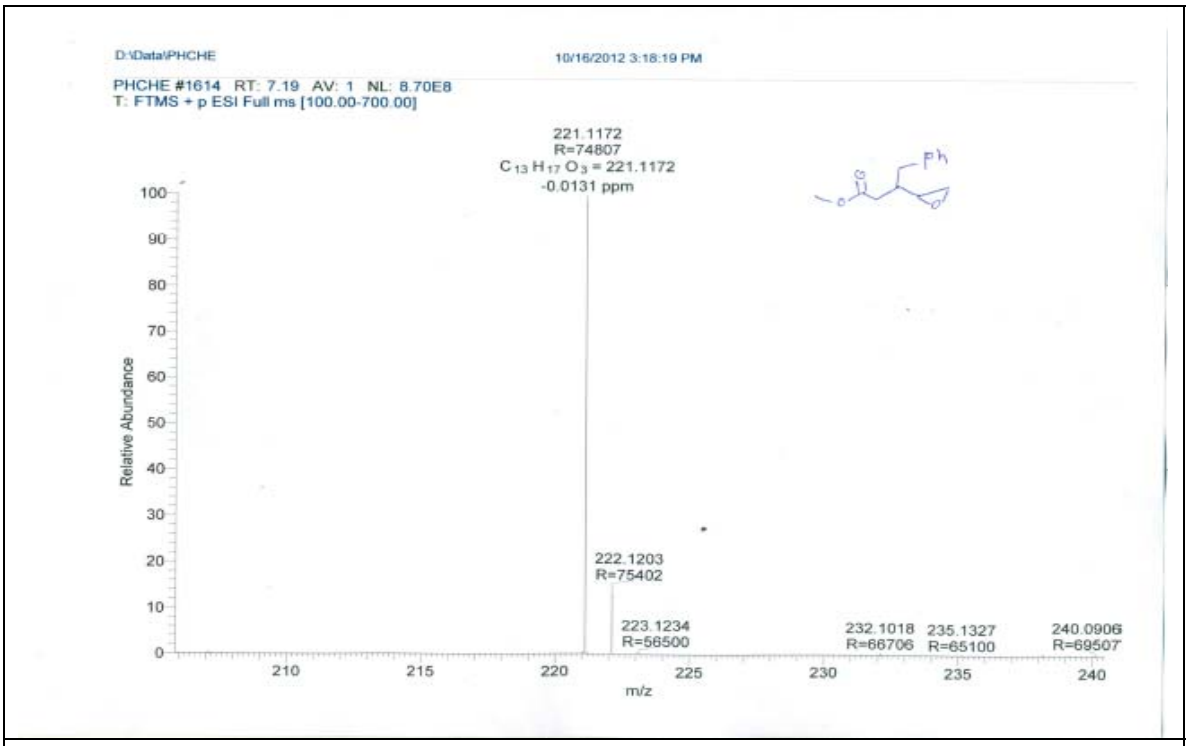
(4*S*, 5*R*)-5-(hydroxymethyl)-4-(4-methoxyphenyl)dihydro- furan-2(3*H*)-one (8e)



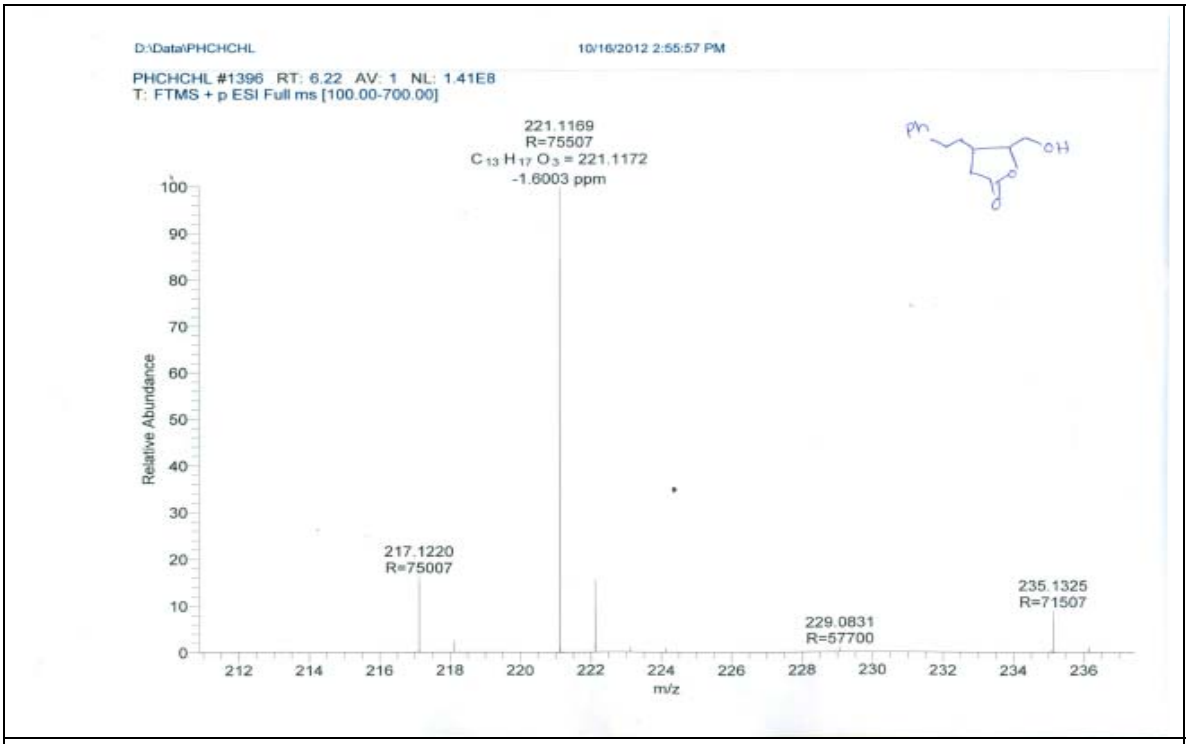
(*R*)-methyl 3-(4-methoxyphenyl)-3-((*S*)-oxiran-2-yl)propano- ate (9e)



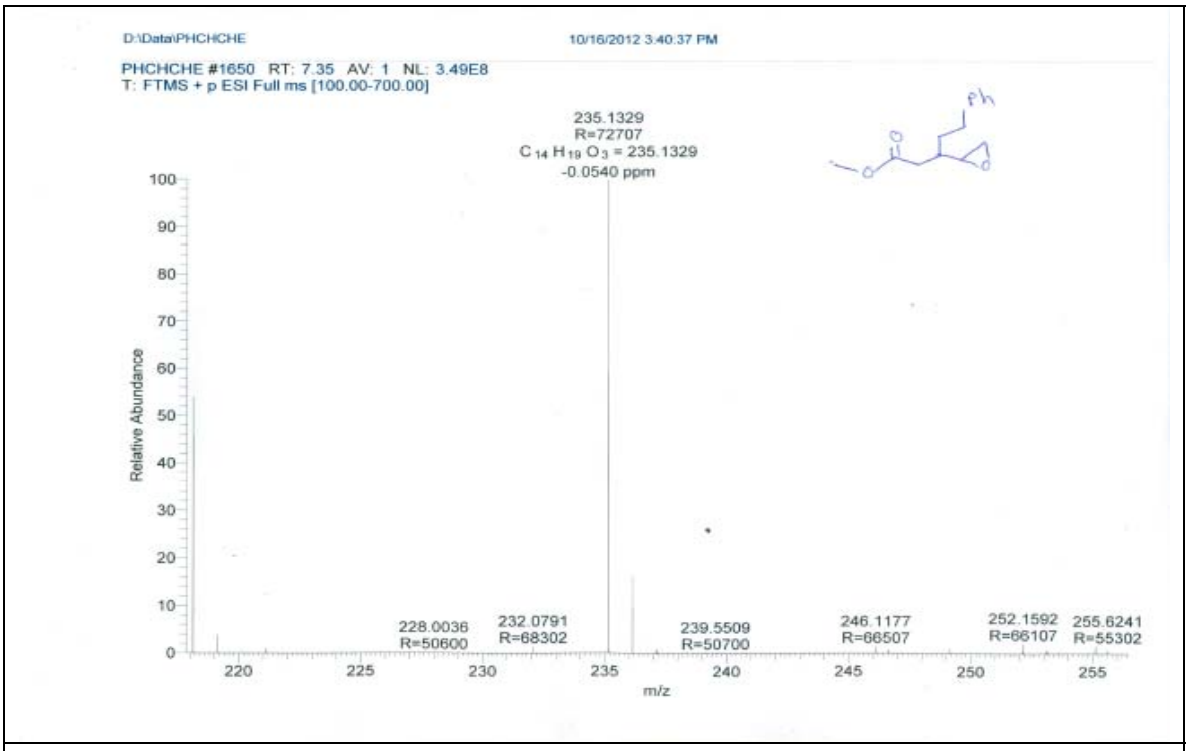
(4*R*, 5*R*)-4-benzyl-5-(hydroxymethyl)dihydrofuran-2(3*H*)-one (8g)



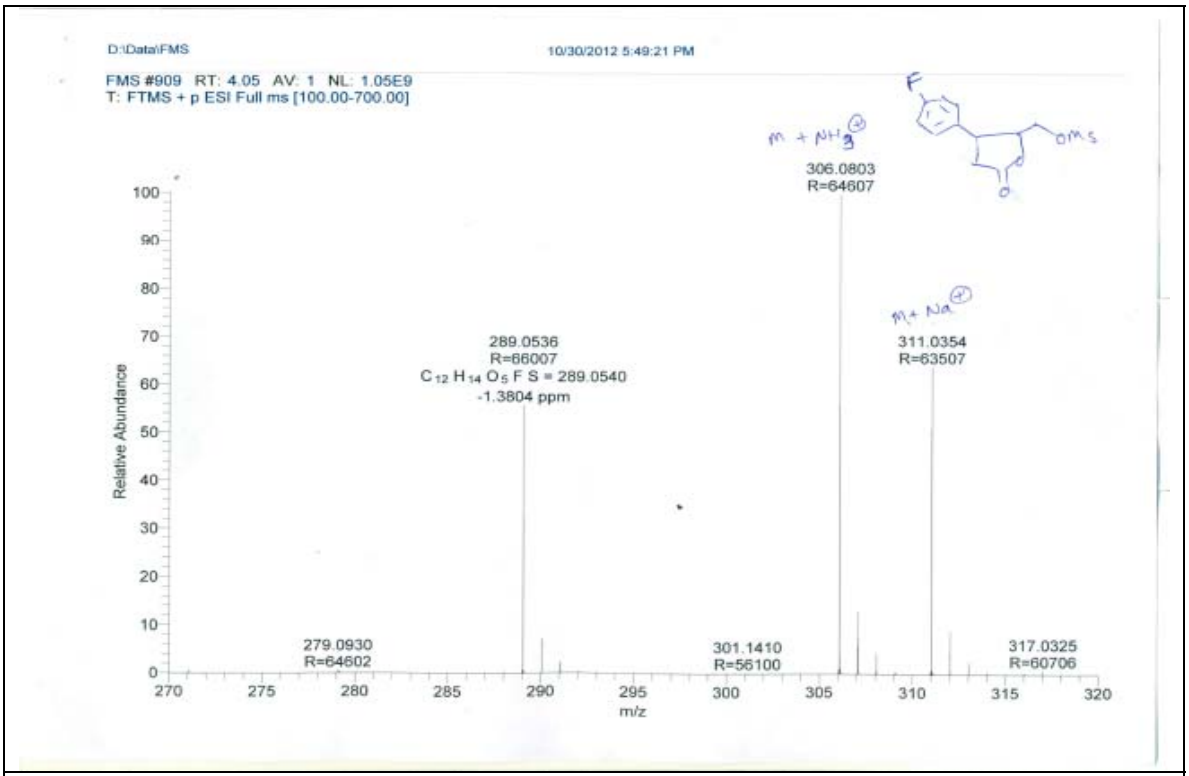
(*S*)-methyl 3-((*S*)-oxiran-2-yl)-4-phenylbutanoate (9g)



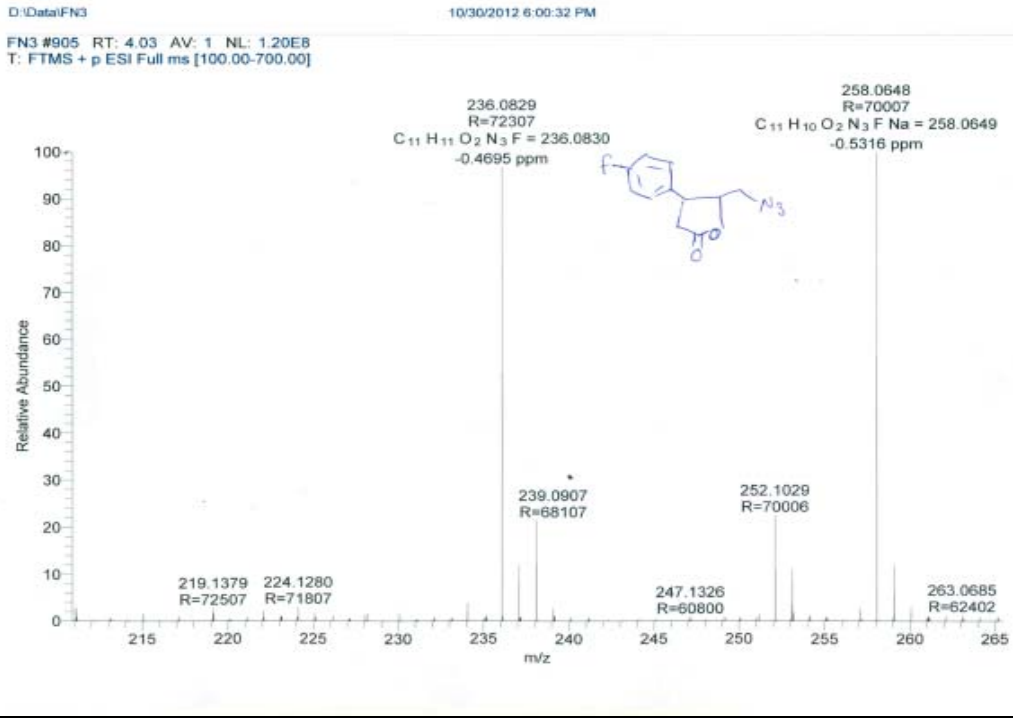
(4*R*, 5*R*)-5-(hydroxymethyl)-4-phenethyldihydrofuran-2(3*H*)-one (8h)



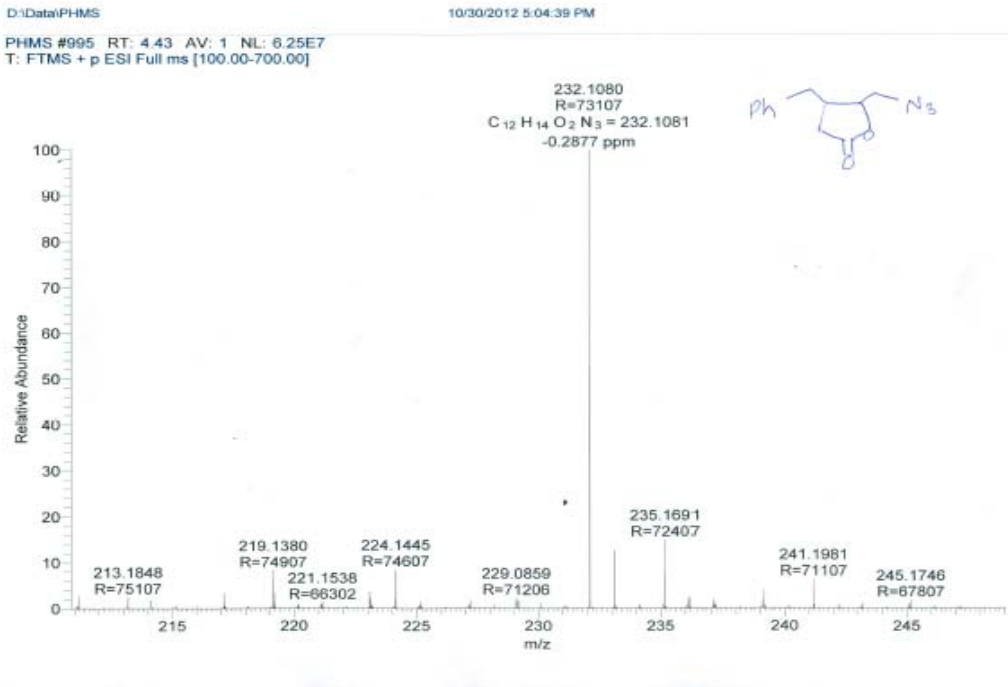
(*S*)-methyl 3-((*S*)-oxiran-2-yl)-5-phenylpentanoate (9h)



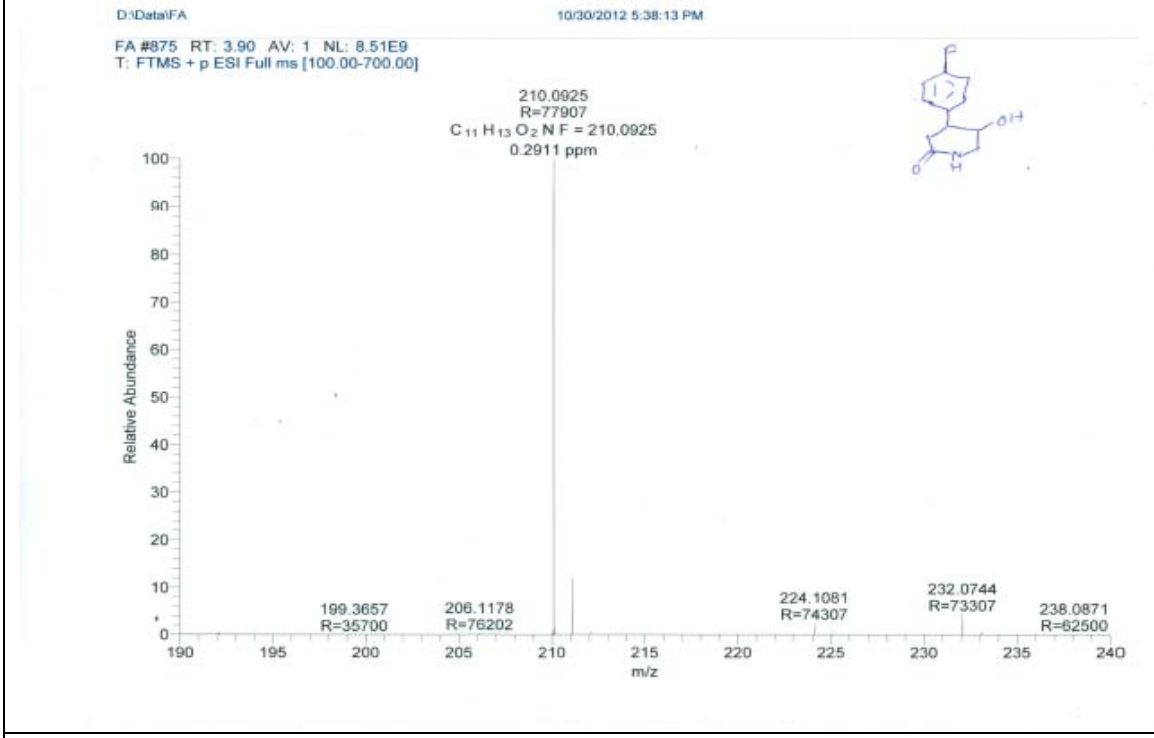
((2*R*, 3*S*)-3-(4-fluorophenyl)-5-oxotetrahydrofuran-2-yl)methyl methanesulfonate (17)



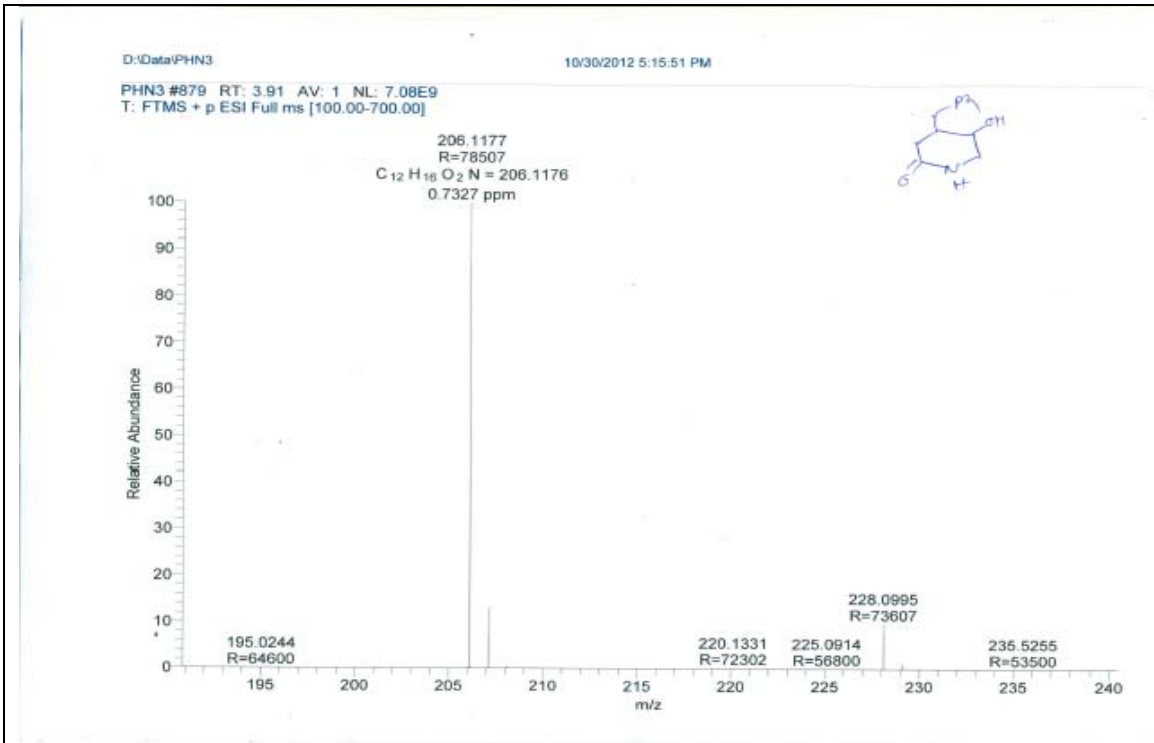
(4*S*, 5*R*)-5-(azidomethyl)-4-(4-fluorophenyl)dihydrofuran-2(3*H*)-one (18)



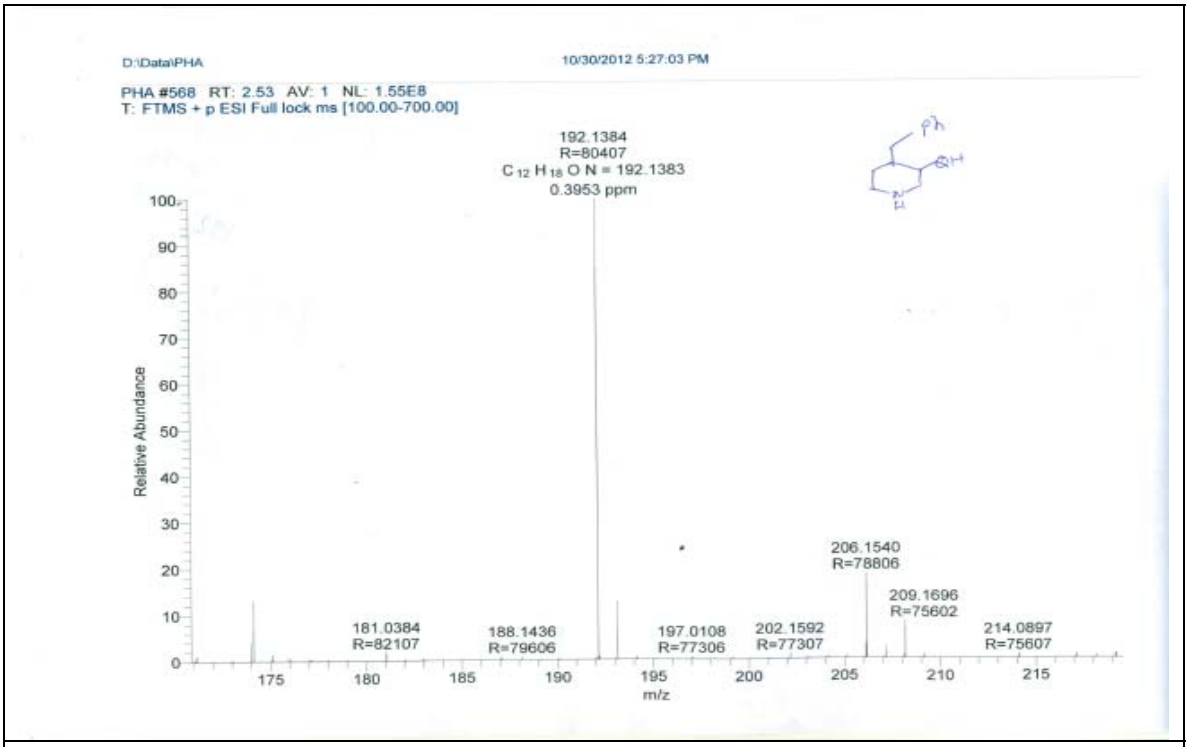
(4*S*, 5*S*)-5-(azidomethyl)-4-benzyldihydrofuran-2(3*H*)-one (18a)



(4*S*, 5*R*)-4-(4-fluorophenyl)-5-hydroxypiperidin-2-one (19)



(4*S*, 5*S*)-4-benzyl-5-hydroxypiperidin-2-one (19a)



(3*S*, 4*S*)-4-benzylpiperidin-3-ol (4)