

Electronic Supplementary Information (ESI)

“Two Stereocentered HKR of *anti*- β,β' -diphenylpropanoxirane and *anti*-3-phenylethyloxiranes Catalysed by Co(III)(salen)-OAc Complex : An Enantioselective Synthesis of (+)-Sertraline and (+)-Naproxen”

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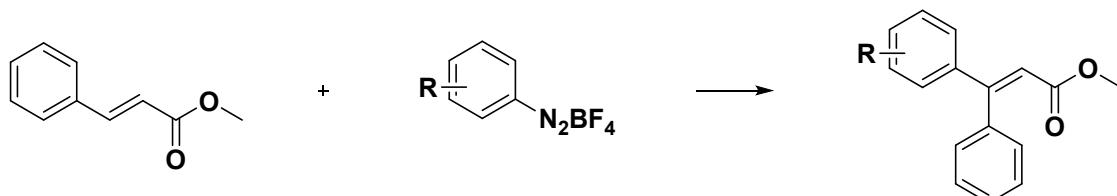
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1. General information:

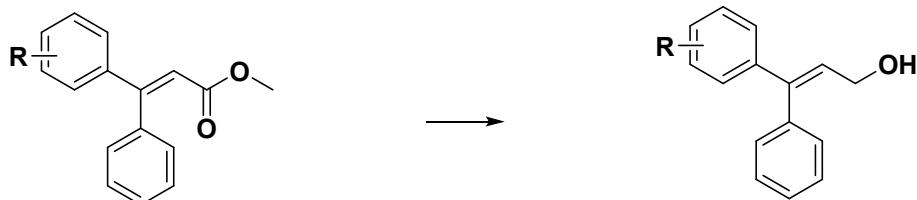
Solvents were purified and dried by standard procedures before use. Optical rotations were measured using sodium D line on a JASCO-181 digital polarimeter. IR spectra were recorded on a Perkin-Elmer model 683 B and absorption is expressed in cm^{-1} . ^1H NMR and ^{13}C NMR spectra were recorded on Brucker AC-200 spectrometer unless mentioned otherwise. The peak at δ 96.16 corresponds to the Carbon Tetrachloride in Chloroform-D. 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. Diphenyl cinnamates (10a-e)¹ and allylic alcohols (11a-e)² were prepared from known methods.

2. Synthesis of substituted methyl-3,3'-diphenylacrylate¹:



To a solution of methyl cinnamate (10 mmol) in methanol (60 mL), $\text{Pd}(\text{OAc})_2$ (10 mol%) and substitutedbenzenediazonium tetrafluoroborate (12 mmol) was added. The reaction mixture was stirred to reflux for 4 h. After completion of reaction (monitored by TLC), it was filtered through a pad of Celite and washed with methanol (3 x 15 mL). The combined filtrates were concentrated to give crude product, which upon column chromatographic purification with flash silica gel using petroleum ether: ethyl acetate (3:7) as eluent gave pure substituted methyl-3,3'-diphenylacrylate.

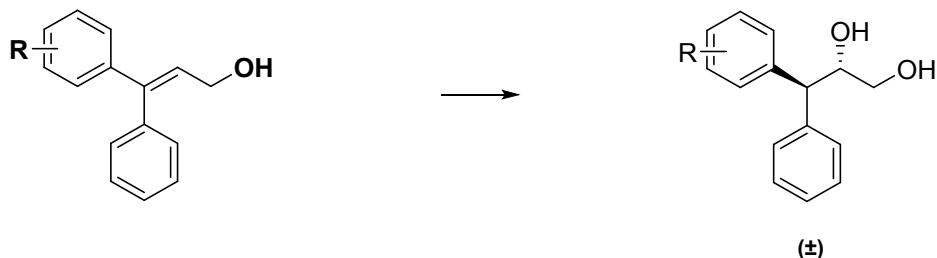
3. Synthesis of substituted 3,3'-diphenylprop-2-en-1-ol²;



To a stirred solution of the ester (3.26 mmol), in dry CH_2Cl_2 (25 mL), a solution of diisobutylaluminium hydride (1 M solution in toluene, 7.18 mmol) was added dropwise at 0 °C and the reaction mixture was stirred at this

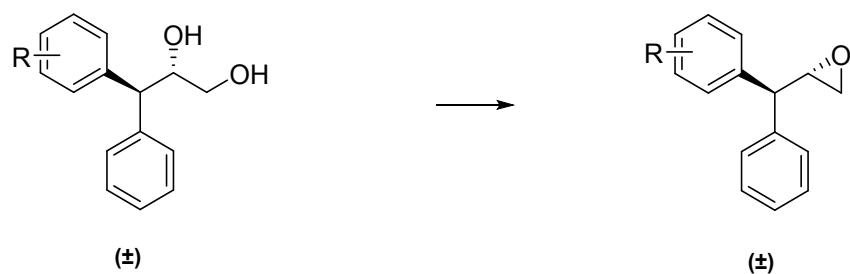
temperature for 2 h. After completion of reaction (monitored by TLC), it was diluted with a saturated solution of Rochelle salt and stirred for further 3 h. The organic phase was separated and the aqueous phase extracted twice with CH_2Cl_2 . The combined organic layers were washed with brine, dried over anhyd. Na_2SO_4 and concentrated under reduced pressure to give crude product, which upon column chromatographic purification with silica gel using petroleum ether: ethyl acetate (8:2) as eluent gave pure as colorless oil.

4. General Procedure for hydroboration of allylic alcohol :



To a stirred solution of homoallyl alcohol (9.4 mmol) in THF (5 mL) at 0 °C, BH_3SMe_2 (4.5 mmol) was added and the reaction mixture was stirred at 25 °C for 4 h. After dilution with THF/MeOH (1:1) followed by the addition of 3 M solution of NaOH (4 mL) and an aq. solution 30% H_2O_2 (4 mL), the reaction was stirred for 4 h and quenched with a saturated solution of Na_2SO_3 (20 mL). The reaction mixture was then cooled to 0 °C, diluted with sat. NaHCO_3 (35 mL) and Et_2O (35 mL). The organic layer was separated and the aqueous layer extracted with Et_2O (2 x 30 mL). The combined organic extracts were washed with brine and dried over anhyd. Na_2SO_4 and concentrated under reduced pressure to give the crude product, which upon column chromatographic purification with silica gel using petroleum ether: ethyl acetate (5:5) as eluent gave pure diol.

4. General procedure for Synthesis of Racemic oxiranes :



A solution of corresponding diol (1.18 mmol) in CH_2Cl_2 (10 mL) was treated with TsCl (1.18 mmol), Bu_2SnO (30 mol%), Et_3N (30 mmol) and DMAP (cat.) at 0 °C. After being stirred for 1 h, the mixture was extracted with CH_2Cl_2 (3 x 20 mL), washed with water and the combined organic phases were dried over anhydrous Na_2SO_4

and concentrated to give the crude tosylate. To a solution of crude tosylate in MeOH (20 mL) was added K₂CO₃ (13 mmol) and the mixture was stirred at 0 °C for 30 min. After the reaction was complete (monitored by TLC), solvent was evaporated and the residue was extracted with diethyl ether (3 × 20 mL). The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated to give the crude product which was then purified by column chromatography using petroleum ether/EtOAc (8:2 v/v) to give epoxide as a colorless oil.

References relevant to supporting information:

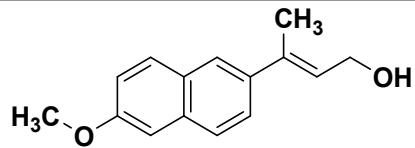
1. Pastre, Cezar J., Correia, Duarte C.R.; *Advanced Synthesis and Catalysis*, **2009**, *351* (9), 1217
2. Ebner C., Pfaltz A.; *Tetra*. **2011**, *67*, 10287-10290

Spectral Data

Methyl (E)-3-(3,4-dichlorophenyl)-3-phenylacrylate (10a)	<p>Yield: 82%, colorless oil; IR (CHCl₃, cm⁻¹): ν_{max} 699, 823, 874, 1190, 1275, 1549, 1620, 1727, 2948; ¹H NMR (200 MHz, CDCl₃): δ 3.61 (s, 3H), 6.32 (s, 1H), 7.07-7.19 (m, 3H), 7.37-7.41 (5H); ¹³C NMR (50 MHz, CDCl₃): δ 51.3, 118.1, 127.4, 128.1, 128.7, 129.0, 130.0, 130.3, 132.9, 133.7, 137.7, 140.9, 154.3, 165.7; Anal. Calcd for C₁₆H₁₂O₂Cl₂ requires C, 62.56; H, 3.94; found C, 62.50; H, 3.95%.</p>
(E)-3-(3,4-Dichlorophenyl)-3-phenylprop-2-en-1-ol (11a)	<p>Yield: 95%, colorless oil; IR (CHCl₃, cm⁻¹): ν_{max} 1055, 1130, 1430, 1520, 2847, 2956, 3430; ¹H NMR (200 MHz, CDCl₃): δ 4.22 (d, <i>J</i> = 6.8 Hz, 2H), 6.22 (t, <i>J</i> = 6.6 Hz, 1H), 7.04 (m, 3H), 7.32-73.39 (m, 5H); ¹³C NMR (50 MHz, CDCl₃): δ 60.4, 126.8, 128.0, 128.5, 129.0, 129.4, 129.6, 130.1, 132.5, 137.9, 141.8, 141.9; Anal. Calcd for C₁₅H₁₂OCl₂ requires C, 64.54; H, 4.33; found C, 64.66; H, 4.38%.</p>
Methyl-(E)-3-(4-bromophenyl)-3-phenylacrylate (10b):	<p>Yield: 84% (710 mg), Colorless thick liquid; IR: (CHCl₃, cm⁻¹) – 1738; ¹H NMR: (200 MHz, CDCl₃) δ 3.60 (d, s, 1H), 6.32 (s, 1H), 7.15 (m, 5H), 7.46 (m, 4H); ¹³C NMR (50 MHz, CDCl₃): δ 51.2, 117.1, 124.0, 128.0, 128.4, 129.8, 131.6, 138.2, 139.7, 155.7, and 165.9.</p>
(E)-3-(4-bromophenyl)-3-phenylprop-2-en-1-ol (11b):	<p>Yield: 96% (621mg), White solid, IR: (CHCl₃, cm⁻¹) – 3340; ¹H NMR: (200 MHz, CDCl₃) δ 1.55 (bs, 1H), 4.18-4.21 (d, 2H, <i>J</i>= 6Hz), 6.18-6.25 (t, 1H, <i>J</i>=6Hz), 7.08 (m, 4H), 7.34-7.42 (m, 5H); ¹³C NMR (50 MHz, CDCl₃): δ 60.6, 12.8, 127.8, 128.0, 128.4, 129.2, 129.7, 131.3, 140.8 and 147.2;</p>
Methyl-(E)-3-(4-chlorophenyl)-3-phenylacrylate (10c)	<p>Yield: 88% (652 mg), greenish gummy; ¹H NMR: (200 MHz, CDCl₃) δ 3.60 (s, 3H), 6.32 (s, 1H), 7.15-7.25 (m, 6H), 7.37-7.40 (t, 3H, <i>J</i>=4Hz); ¹³C NMR (50 MHz, CDCl₃): δ 51.2, 117.2, 128.0, 128.4, 128.6, 129.1, 129.6, 135.7, 138.3, 139.3, 155.6, 166;</p>
(E)-3-(4-chlorophenyl)-3-phenylprop-2-en-1-ol (11c)	<p>Yield: 89% (520 mg); Gummy; ¹H NMR: (200 MHz,</p>

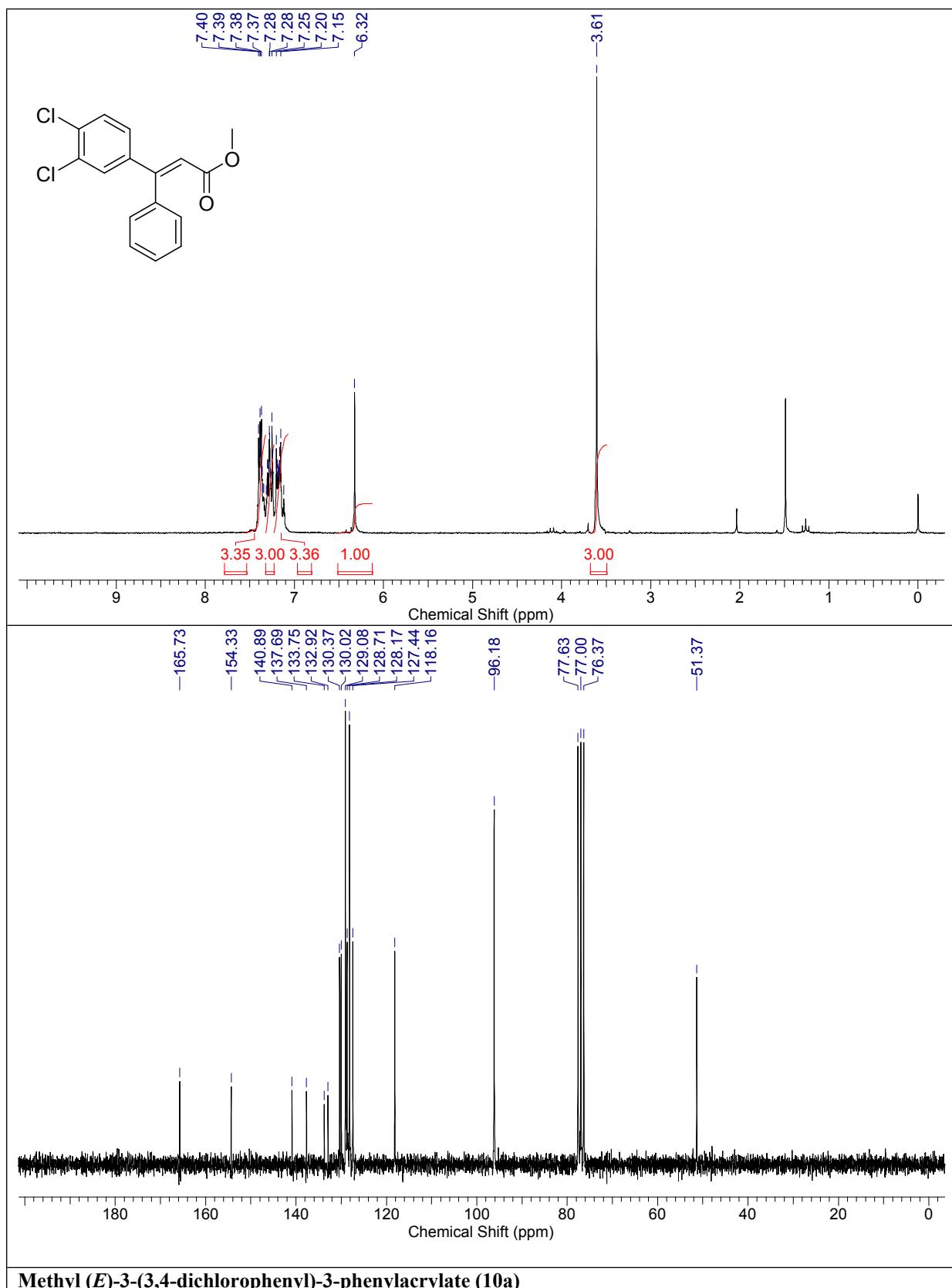
	<p>CDCl₃ δ 1.69 (bs, 1H), 4.22-4.23 (d, 2H, J=4Hz), 6.22-6.25 (t, 1H, J=8Hz), 7.15-7.21 (m, 4H), 7.28-7.25 (m, 2H), 7.35-7.41 (m, 3H); ¹³C NMR (50 MHz, CDCl₃) δ 60.6, 127.8, 127.9, 128.4, 128.9, 129.7, 133.6, 140.2, 143.1;</p>
Methyl-(E)-3-(4-fluorophenyl)-3-phenylacrylate (10d);	<p>Yield: 82% (521 mg); Gummy; ¹H NMR: (200 MHz, CDCl₃) δ 3.69 (s, 3H), 4.34 (s, 1H), 7.02-7.20 (m, 3H), 7.27-7.35 (m, 5H); ¹³C NMR (50 MHz, CDCl₃) δ 51.6, 115.3 (d, J= 21.2 Hz, CH), 116.4 (d, J= 1.6 Hz), 128.1, 128.3, 129.2, 130.5 (d, J= 8.3 Hz), 136.8 (d, J= 3.1 Hz), 138.9, 155.9, 163.3(d, J= 250.3 Hz), 166.3</p>
(E)-3-(4-fluorophenyl)-3-phenylprop-2-en-1-ol (11d):	<p>Yield: 92% (426 mg) , Colorless gummy; ¹H NMR: (200 MHz, CDCl₃) δ 1.77 (bs, 1H), 4.16-4.19 (d, 2H, J=6Hz), 6.15 (t, 1H, J=8Hz), 6.90-6.99 (t, 2H, J=8Hz), 7.10-7.25 (m, 4H), 7.30-7.39 (m, 3H); ¹³C NMR (50 MHz, CDCl₃) δ 60.6, 115.0-115.5 (d, J=21 Hz), 127.6-127.8 (d, J=7Hz), 128.3, 131.4-131.5 (d, J=8Hz), 141.7, 143.4;</p>
Methyl (E)-3-(2-fluorophenyl)-3-phenylacrylate (10e)	<p>Yield: 91% (622mg) ; Gummy; ¹H NMR: (200 MHz, CDCl₃) δ 3.6 (s, 3H), 6.32 (s, 1H), 7.05-7.11 (m, 3H), 7.19-7.24 (m, 1H), 7.30 (m, 5H); ¹³C NMR (50 MHz, CDCl₃) δ 51.2, 116.1-116.3 (d, J= 23Hz), 120.8 (d, J = 5.76 Hz), 124.0 (d, J = 4 Hz), 127.8, 128.3, 128.5, 128.7, 130.4 (d, J = 8.62 Hz), 131.4, 138.6, 150.8, 158.9, 161.4, 166.0;</p>
(E)-3-(2-fluorophenyl)-3-phenylprop-2-en-1-ol (11e)	<p>Yield: 91% (503 mg) ; White Solid; ¹H NMR(200MHz, CDCl₃) δ 1.53 (bs, 1H), 4.31-4.35 (m, 2H), 6.17(t, J=7Hz, 1H), 7.03 (ddd, J=10.8, 8.4, 1.2Hz, 1H), 7.09 (td, J=7.8 Hz, 1H), 7.16-7.21 (m, 3H), 7.23-7.27 (m, 1H), 7.30-7.36 (m, 3H); ¹³C NMR (50 MHz, CDCl₃) δ 600.4, 115.9-116.1 (d, J=23 Hz), 123.9 (d, J=2.88), 127.7, 128.2, 129.2, 131.3-131.4 (d, J=3.84), 131.7-131.8 (d, J=3.84), 138.7, 159.0, 161.5;</p>
Ethyl-(E)-3-phenylbut-2-enoate (10f)	<p>Yield: 91% (503 mg) ; colorless oil; ¹H</p>

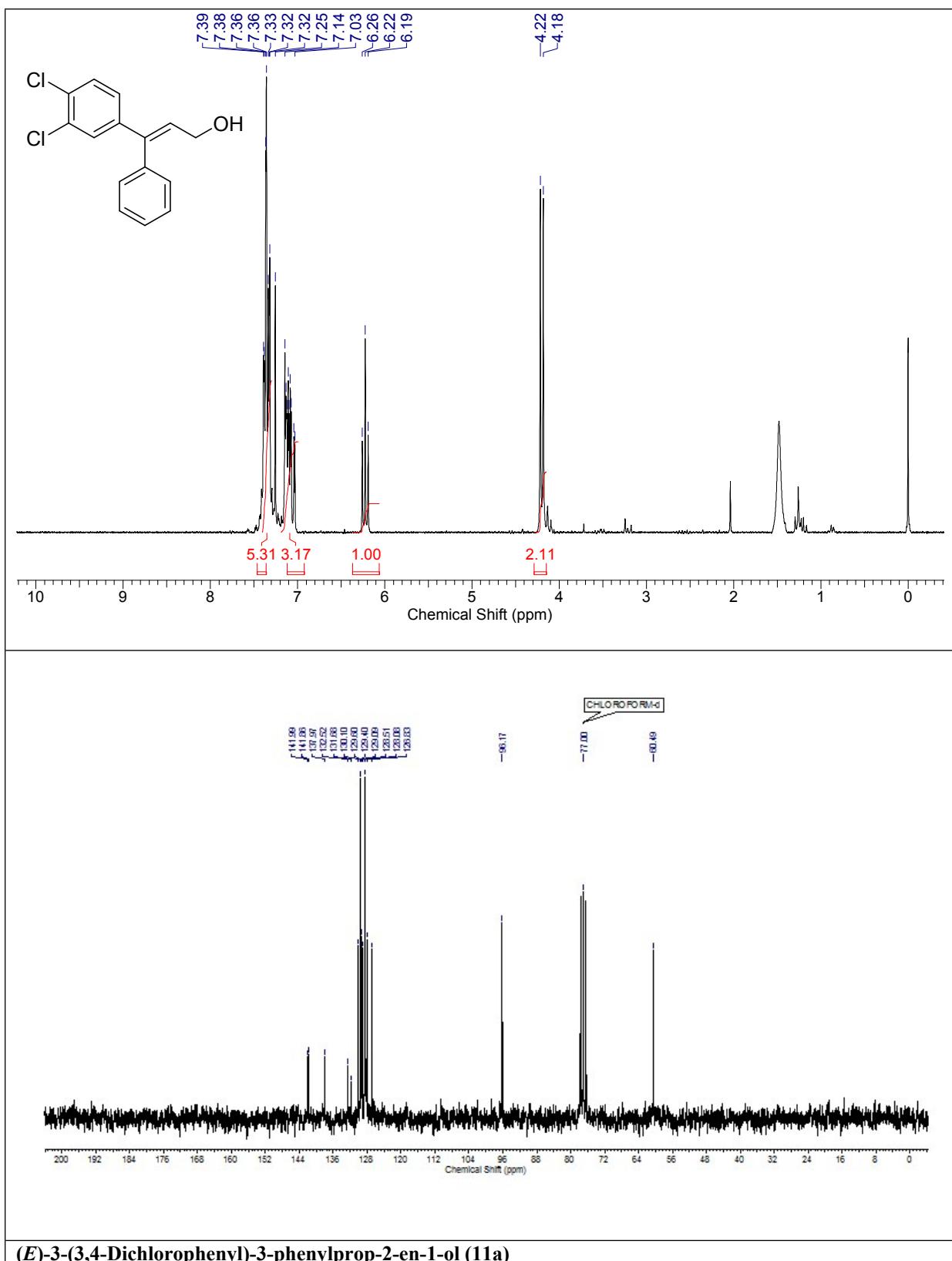
	NMR(200MHz, CDCl₃) δ 1.33 (t, 3H), 2.59 (S, 3H), 4.20-4.25 (q, 2H), 6.13-6.14 (d, 1H), 7.27-7.38 (m, 3H), 7.47-7.49 (dd, 2H); ¹³C NMR (50 MHz, CDCl ₃) δ 14.4, 17.9, 59.7, 117.2, 126.3, 128.4, 128.9, 142.3, 156.4, 166.6
(E)-3-phenylbut-2-en-1-ol (11f)	
	Yield: 96% (376 mg); ¹H NMR (200 MHz, CDCl ₃) δ 2.02 (bs, 1H), 2.05 (s, 3H), 4.29-4.33 (dd, 2H, J=6Hz), 5.89-5.98 (qt, 1H, J= 6Hz), 7.21-7.39 (m, 5H); ¹³C NMR (50 MHz, CDCl ₃) δ 16.0, 59.7, 125.7, 126.5, 127.2, 128.2, 137.6, 142.8;
Ethyl (E)-5-methyl-3-phenylhex-2-enoate (10g)	
	Yield: 90% (526 mg); Colorless Oil ¹H NMR (400 MHz, CDCl ₃) δ 0.88-0.90 (d, 6H, J= 6.87 Hz), 1.07 (t, 3H, J= 6.87 Hz), 1.52-1.62 (m, 1H), 2.31-2.33 (d, 2H, J= 7.31 Hz), 3.95-4.00 (q, 2H, J= 6.87, 7.31 Hz), 5.84 (s, 1H), 7.13-7.16 (m, 2H), 7.28-7.34 (m, 3H); ¹³C NMR (100 MHz, CDCl ₃) 14.0, 22.3, 25.8, 50.0, 59.7, 118.4, 127.2, 127.6, 127.8, 140.0, 158.6, 165.9
(E)-5-methyl-3-phenylhex-2-en-1-ol (11g)	
	Yield: 94% (404 mg); gummy; ¹H NMR (200 MHz, CDCl ₃) δ 0.83-0.86 (d, 6H, J=6.8 Hz), 1.25-1.55 (m, 3H), 2.24-2.27 (d, 2H, J=7.20 Hz), 4.01-4.04 (d, 2H, J= 7 Hz), 5.64 (t, 1H, J= 7 Hz), 7.08-7.13 (m, 2H), 7.23-7.35 (m, 3H); ¹³C NMR (100 MHz, CDCl ₃) 22.3, 26.0, 48.6, 60.1, 72.0, 128.0, 128.14, 139.9, 143.5
Ethyl-(E)-3-(6-methoxynaphthalen-2-yl)but-2-enoate (10h)	
	Yield: 91% (421 mg); Colorless Oil; ¹H NMR: (200 MHz, CDCl ₃) δ 1.30-1.37 (t, 3H, J=8Hz), 2.67-2.68 (d, 3H), 3.91 (s, 3H), 4.17-4.28 (q, 2H, J=8Hz), 6.26 (s, 1H), 7.09-7.17 (m, 2H), 7.54-7.59 (dd, 1H, J=8Hz), 7.67-7.76 (t, 2H, J=8Hz), 7.86 (s, 1H); ¹³C NMR (50 MHz, CDCl ₃) δ 14.4, 17.4, 55.2, 59.7, 105.5, 116.7, 119.3, 124.4, 125.8, 126.9, 128.6, 130.0, 134.8, 137.0, 155.2, 158.4, 166.9;
(E)-3-(6-methoxynaphthalen-2-yl) but-2-en-1-ol (11h)	
	Yield: 95% (337 mg); Colorless Oil; ¹H NMR: (200 MHz, CDCl ₃) δ 1.43 (bs, 1H), 2.17 (s, 3H), 3.91(s, 3H), 4.38-4.42 (d, 2H, J=6Hz), 6.06-6.13 (dt, 1H, J=6Hz), 7.09-7.14 (m, 2H), 7.51-7.56 (dd, 1H, J=8Hz),



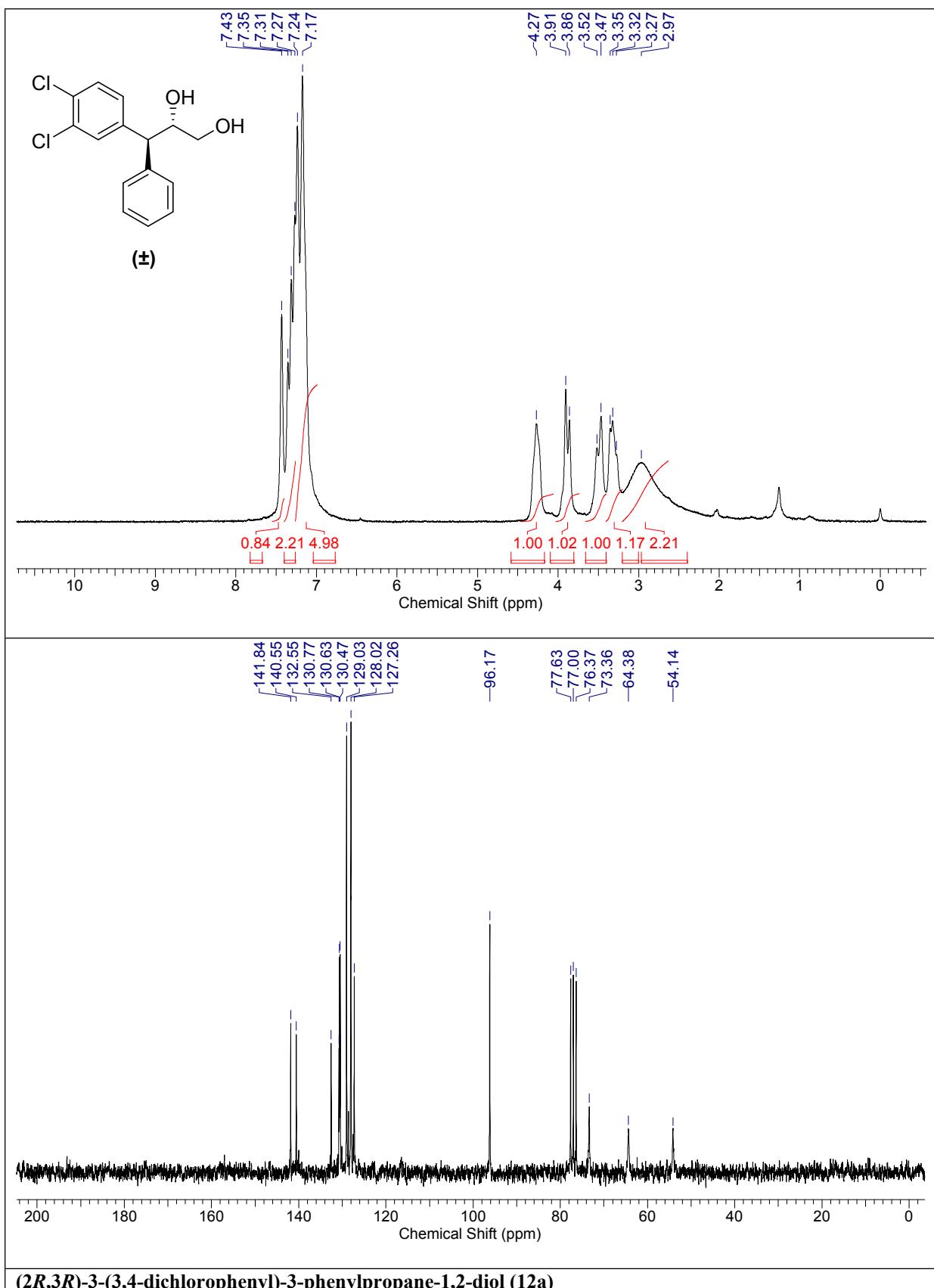
7.64-7.73 (m, 3H); ^{13}C NMR (50 MHz, CDCl_3) δ 16.0, 55.2, 60.0, 105.5, 119.0, 12.4, 124.6, 126.3, 126.7, 128.8, 129.7, 133.9, 137.7, 137.8, 157.7;

4. Spectra

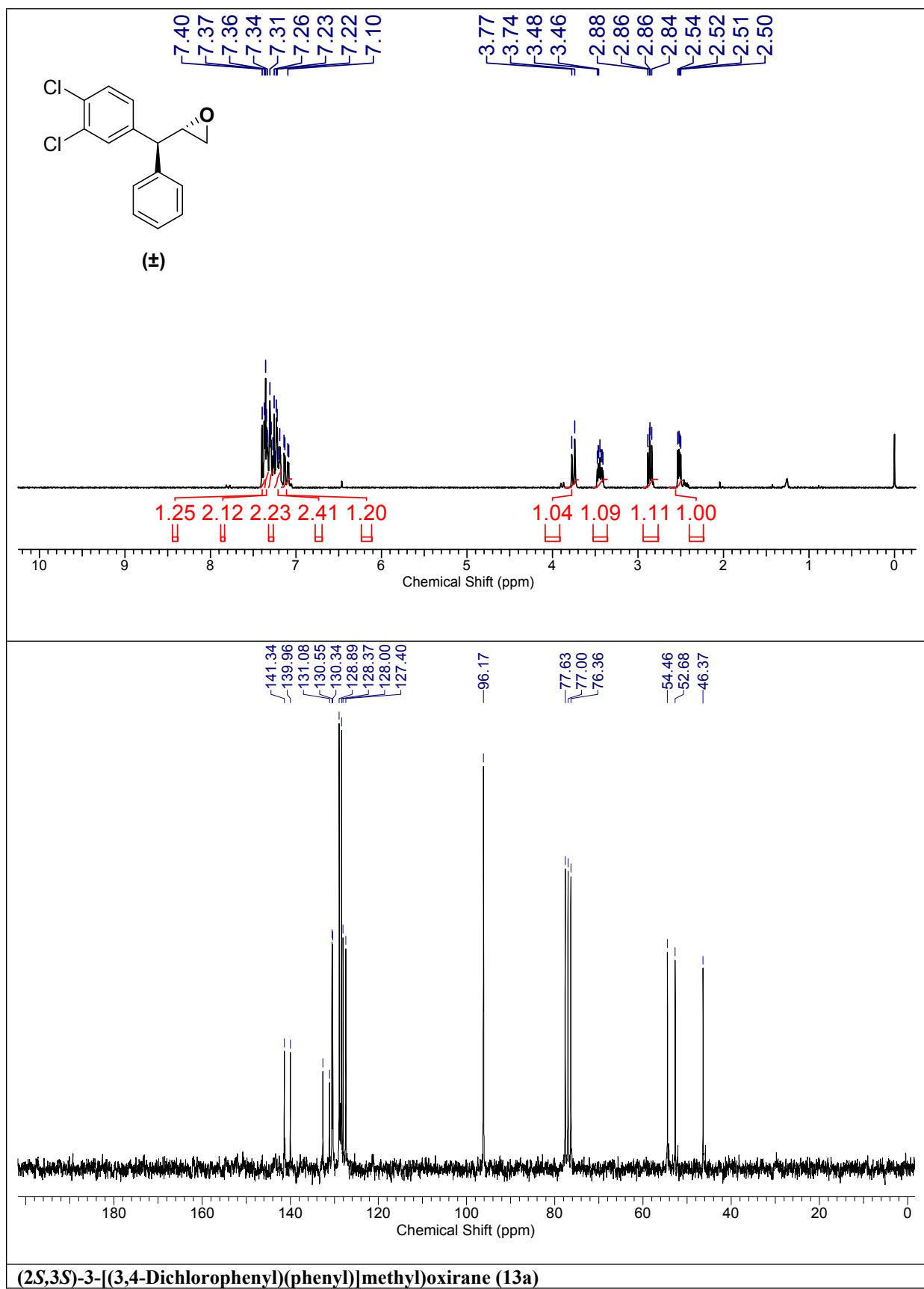


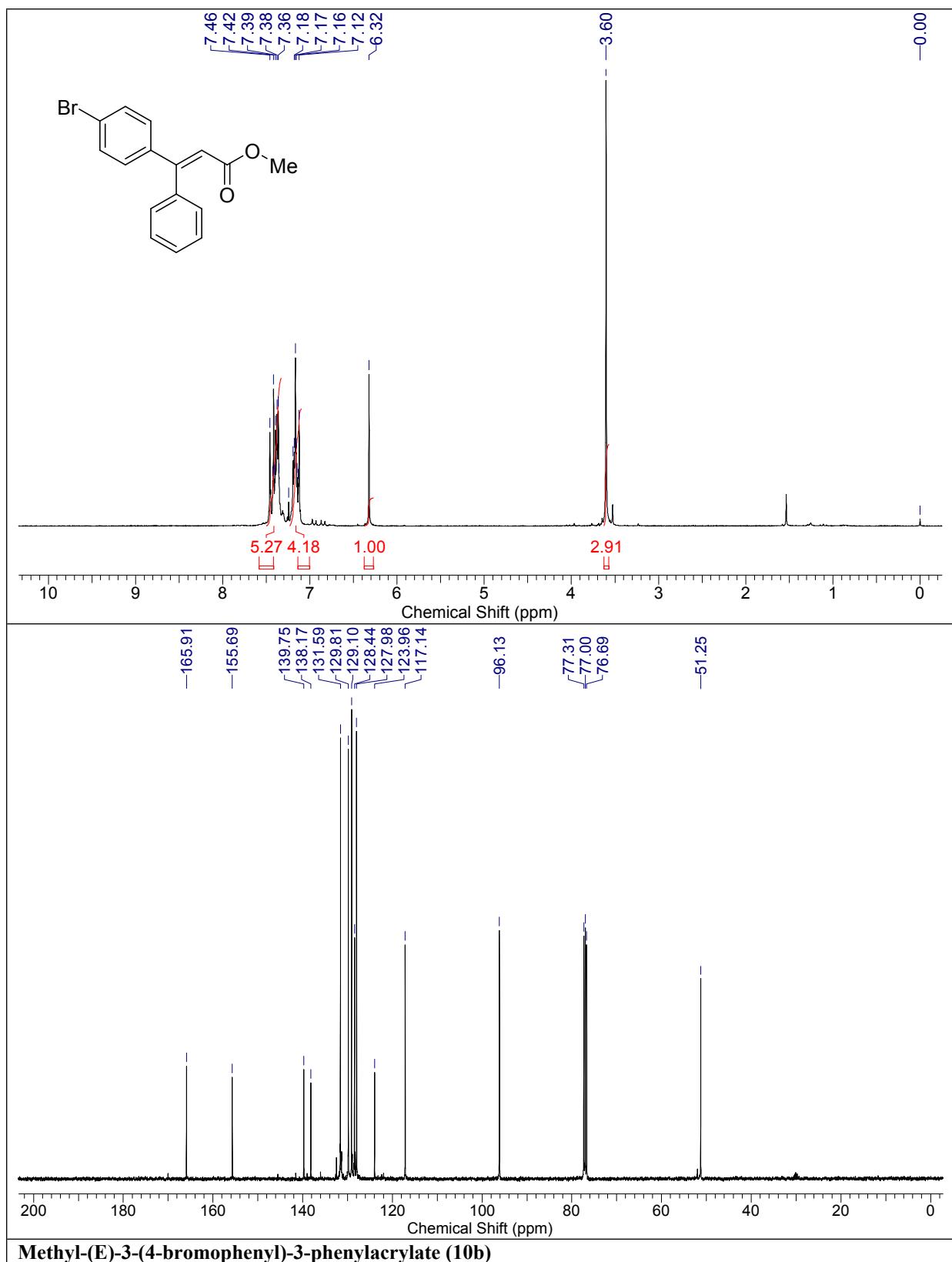


(E)-3-(3,4-Dichlorophenyl)-3-phenylprop-2-en-1-ol (11a)

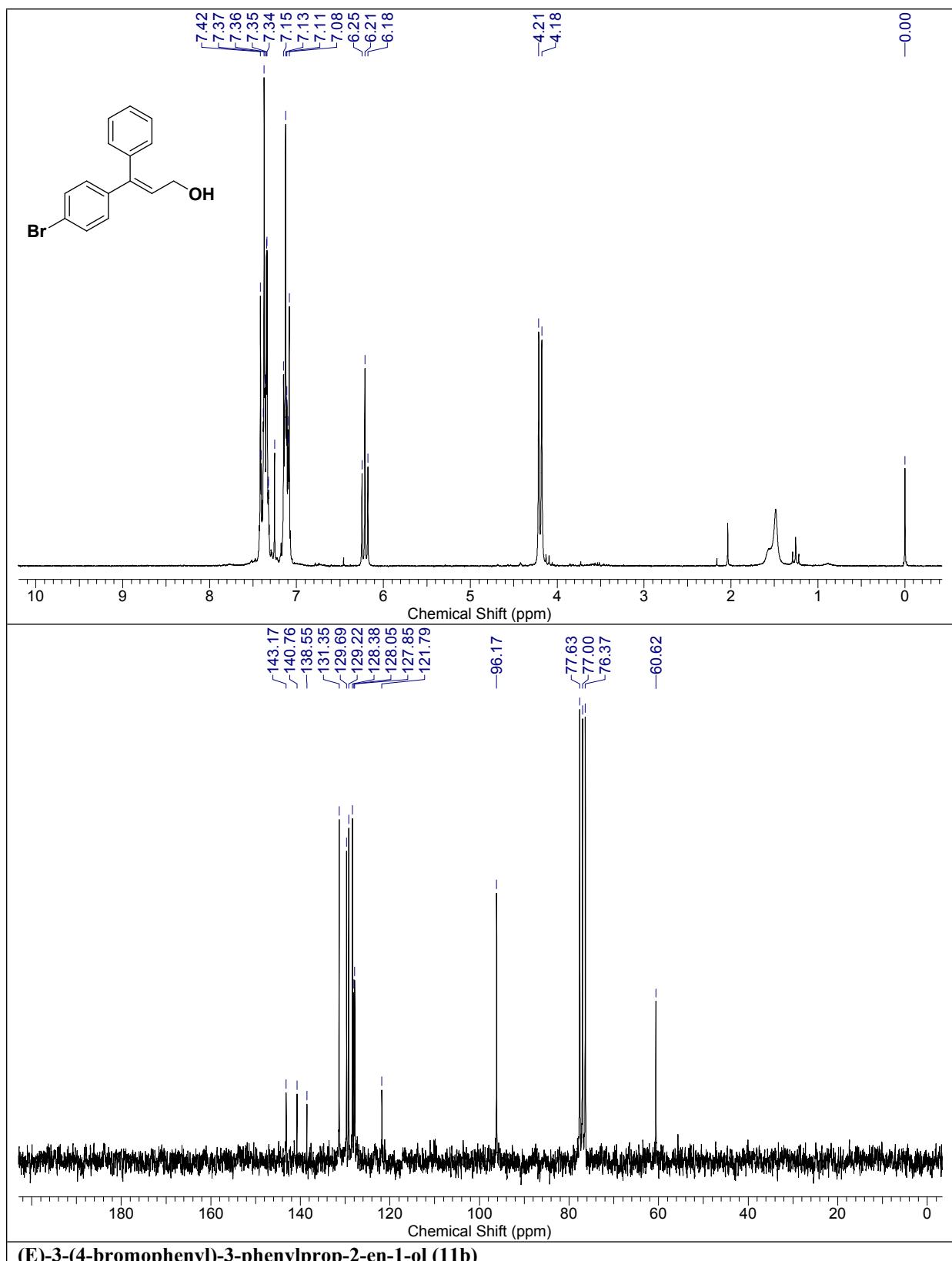


(2*R*,3*R*)-3-(3,4-dichlorophenyl)-3-phenylpropane-1,2-diol (12a)

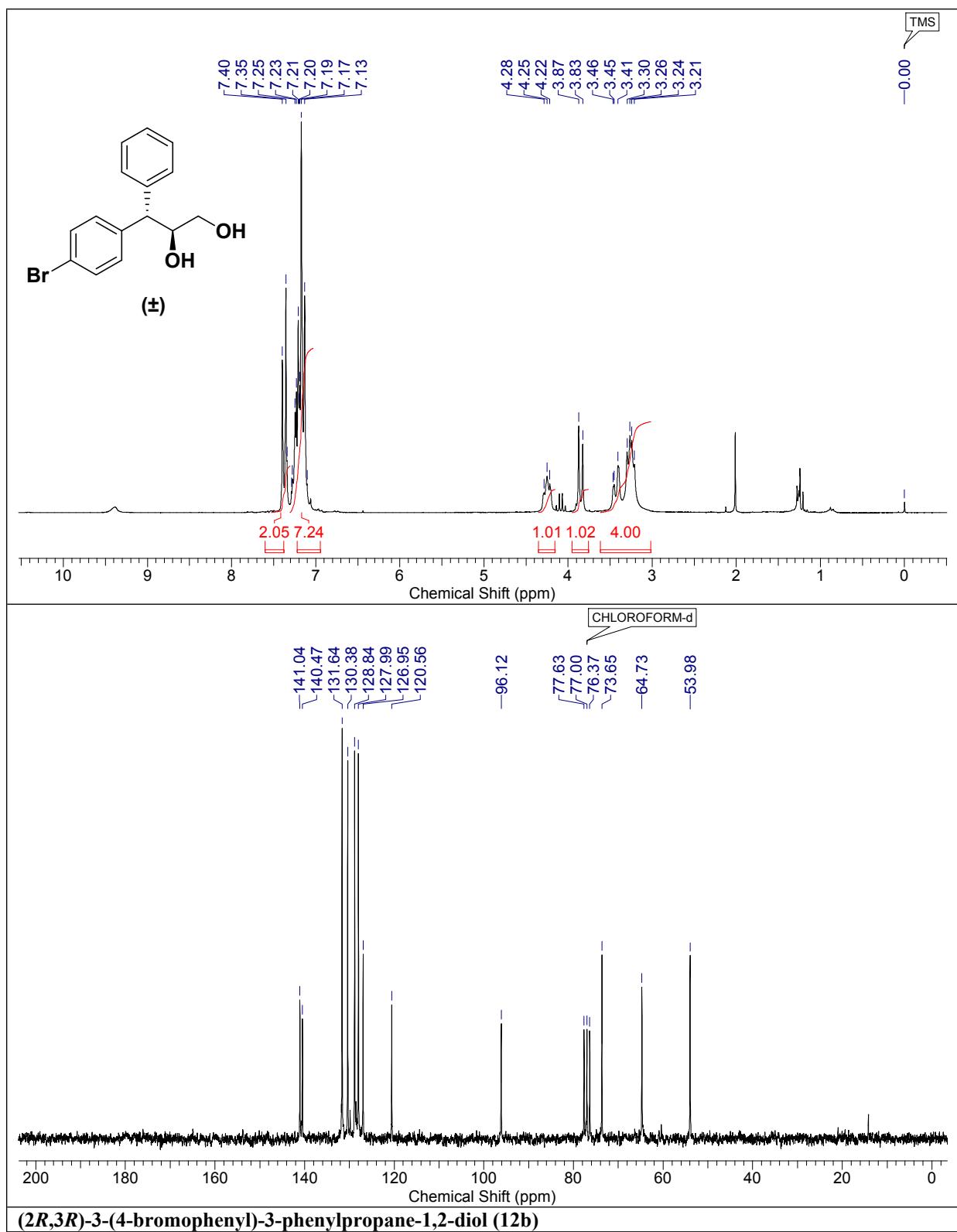


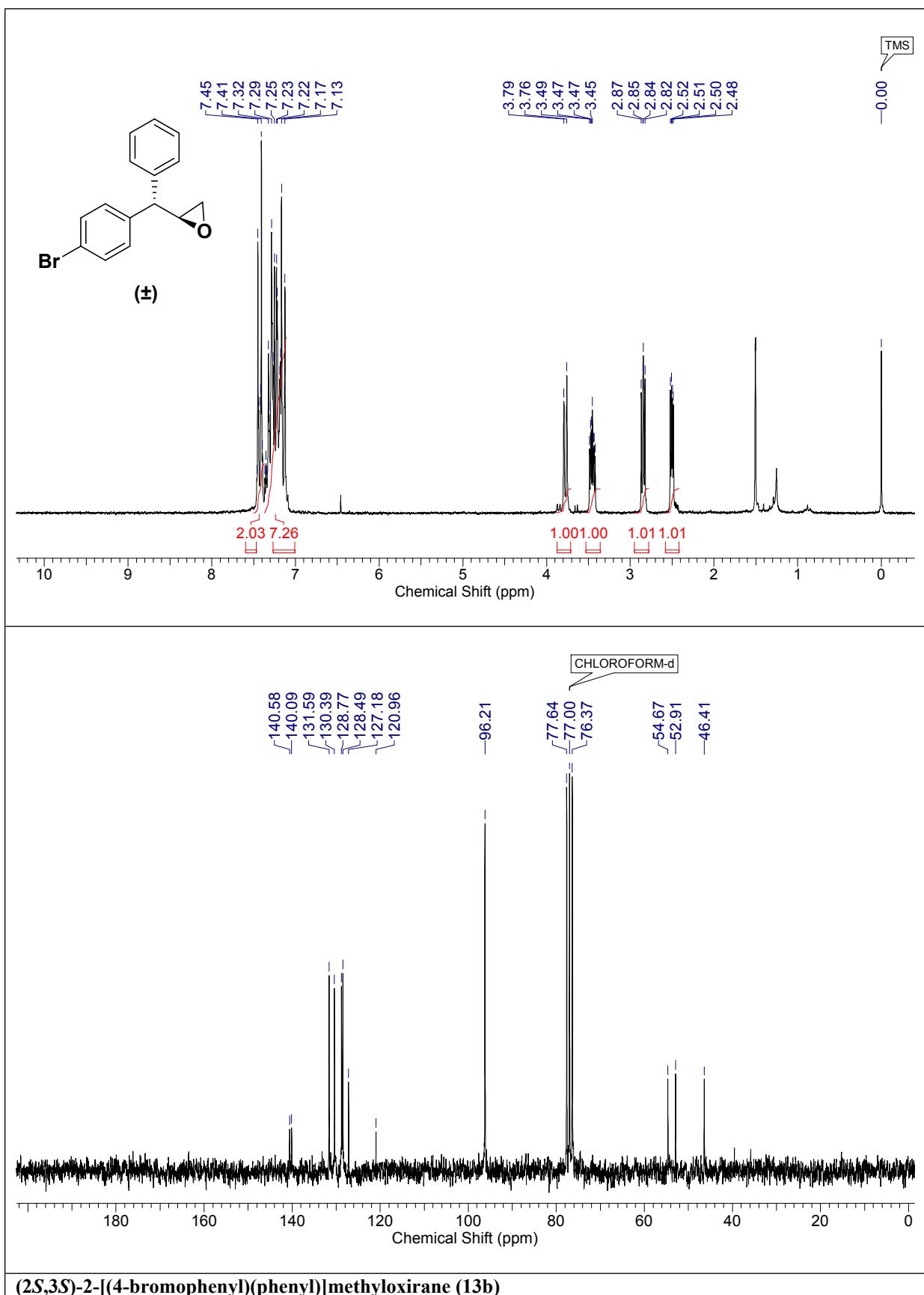


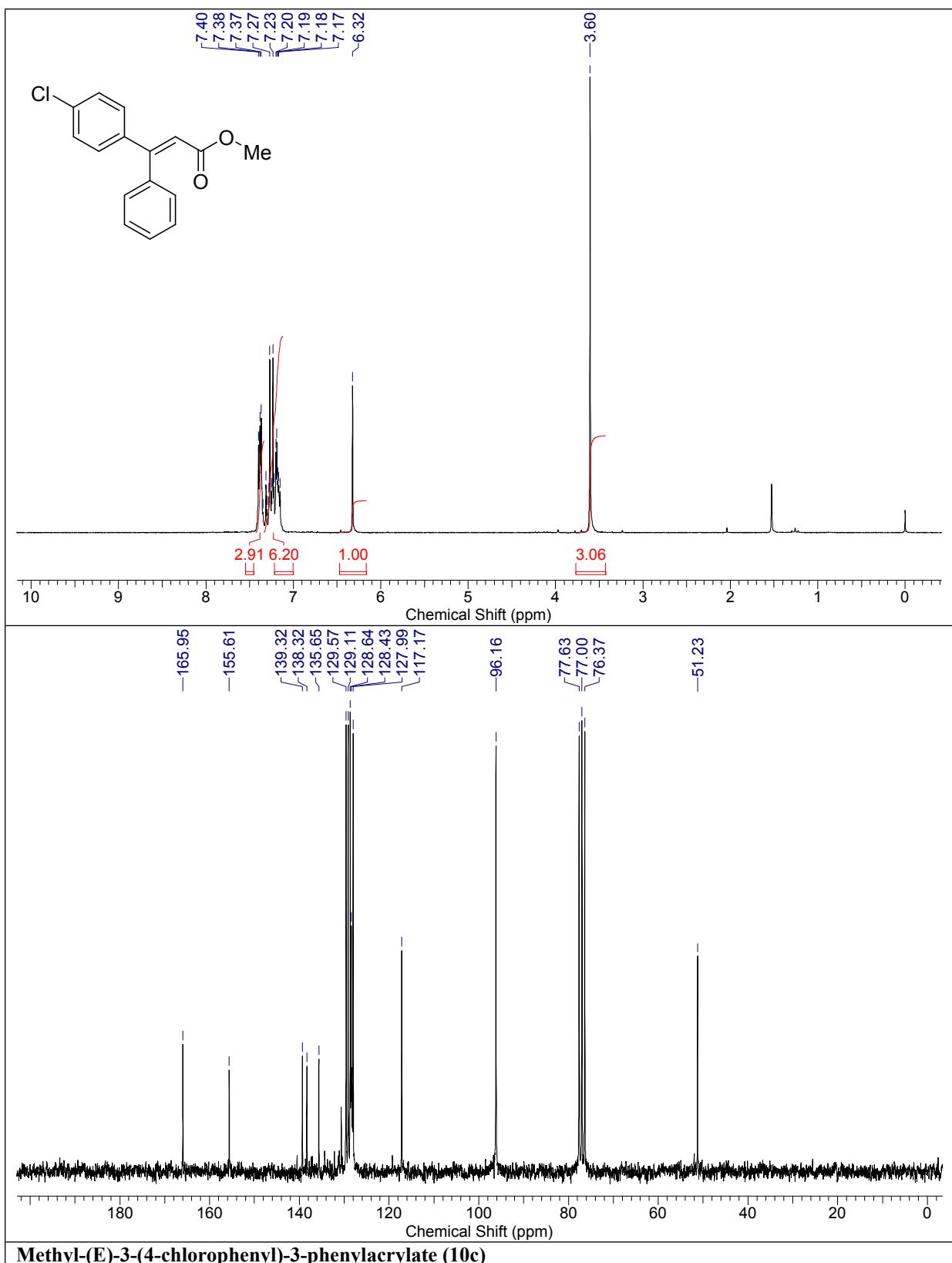
Methyl-(E)-3-(4-bromophenyl)-3-phenylacrylate (10b)

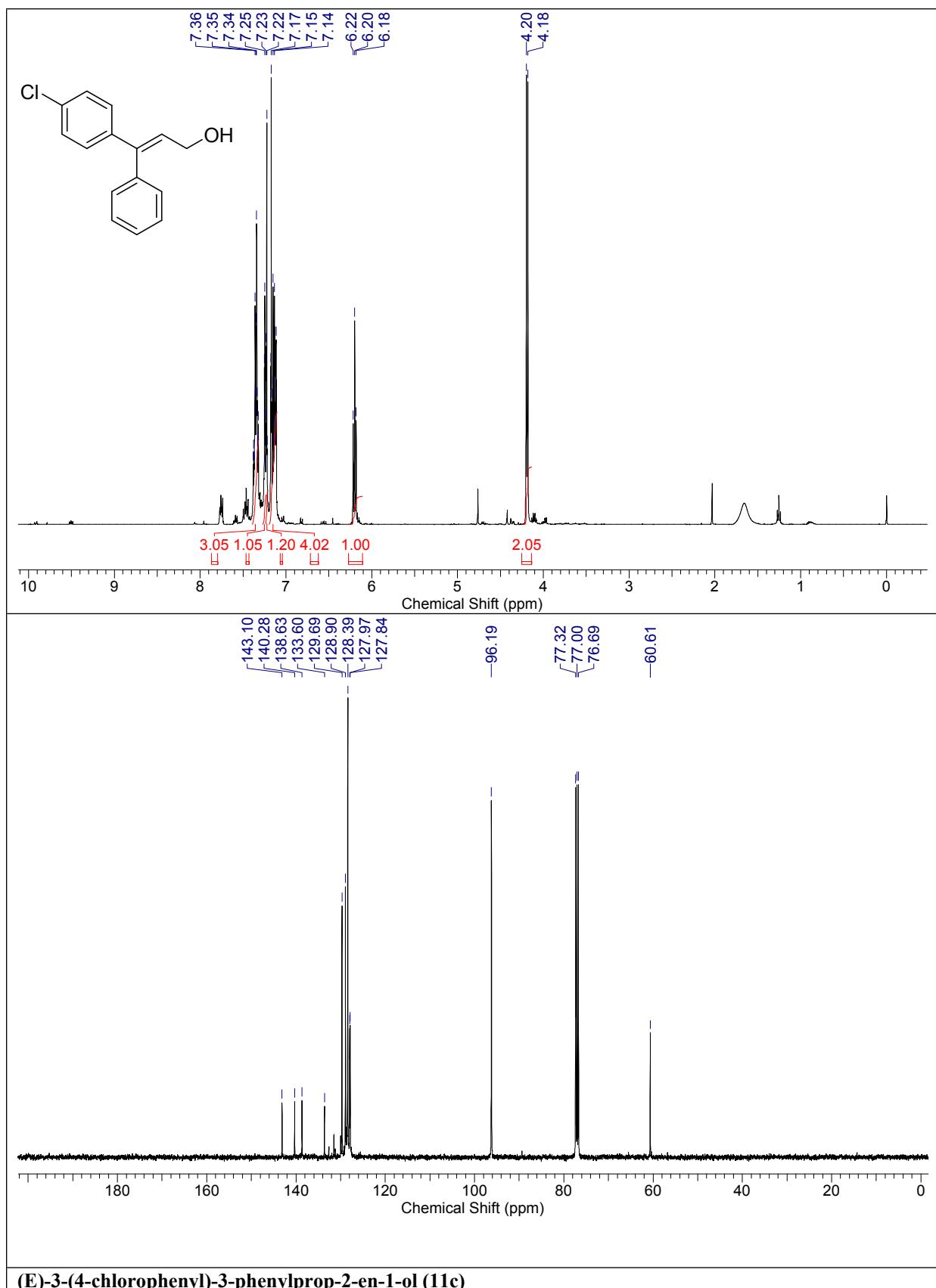


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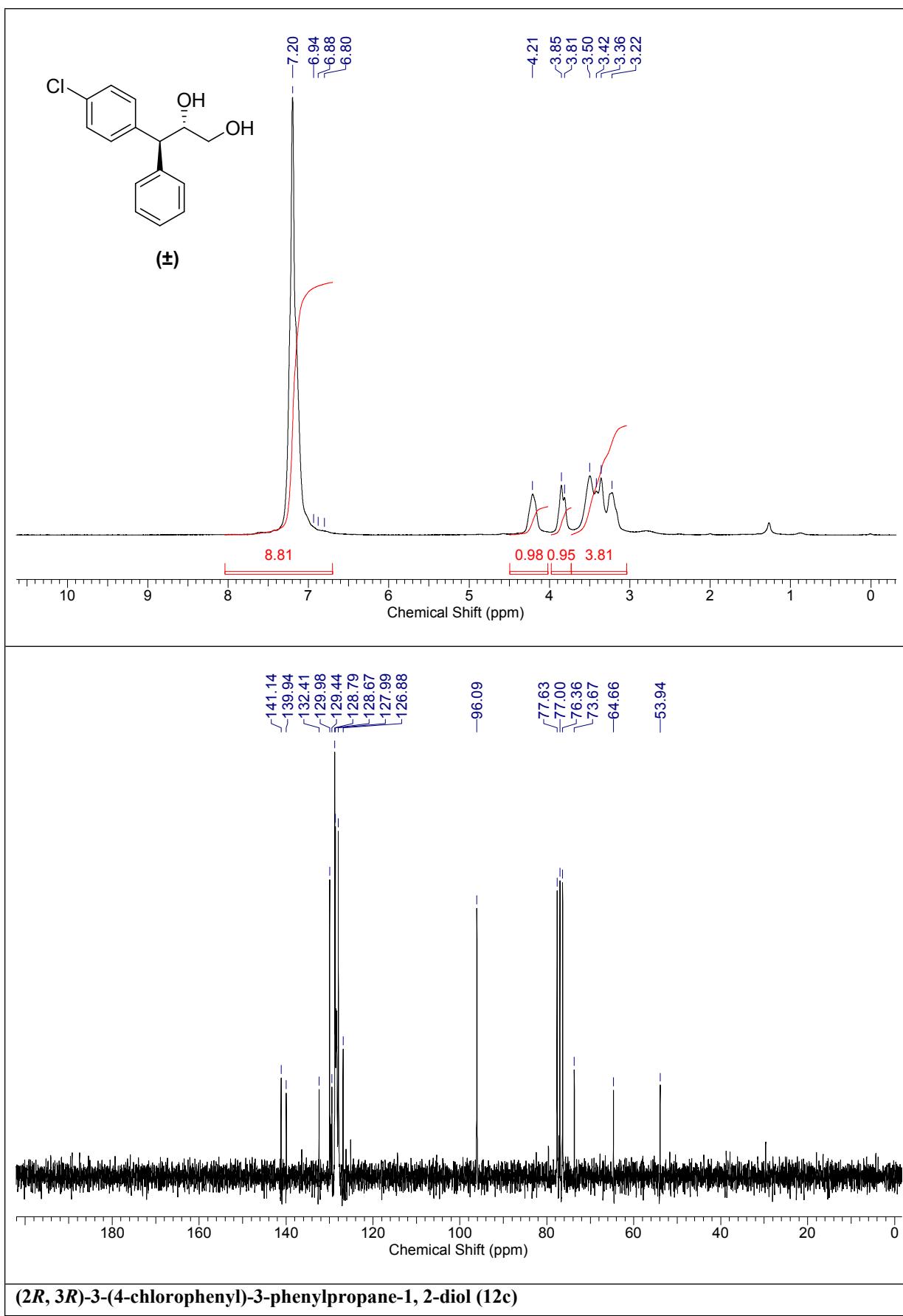


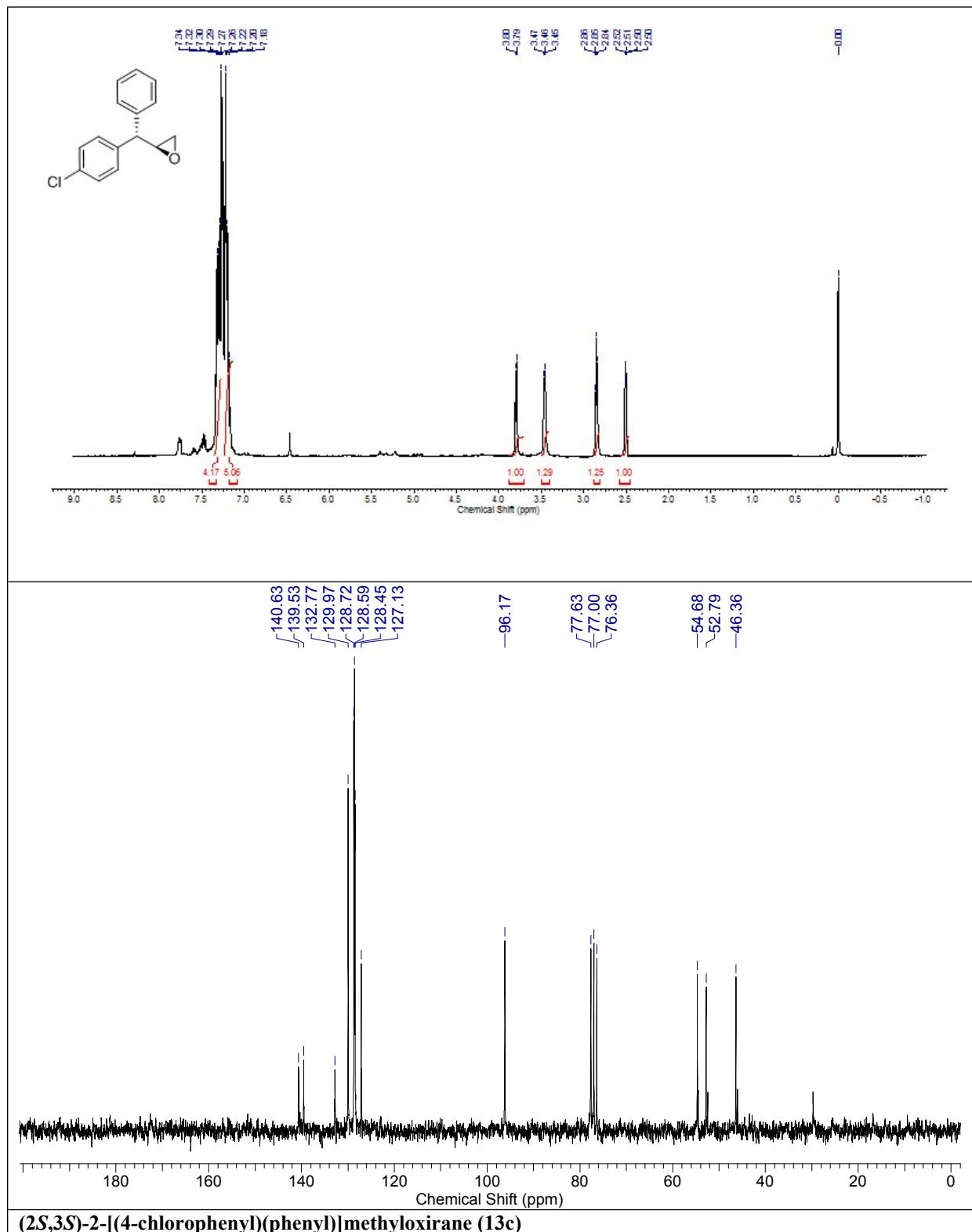


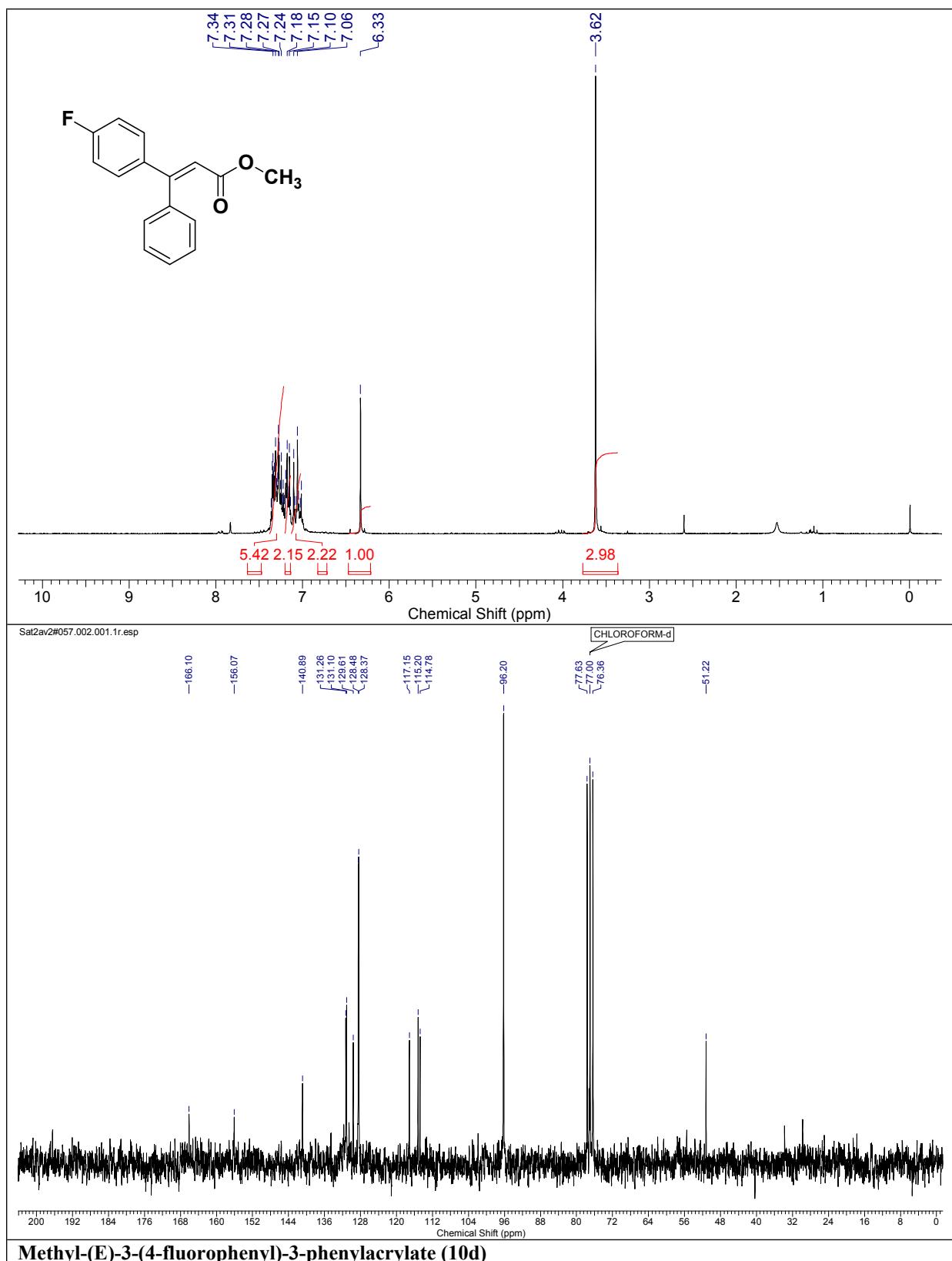


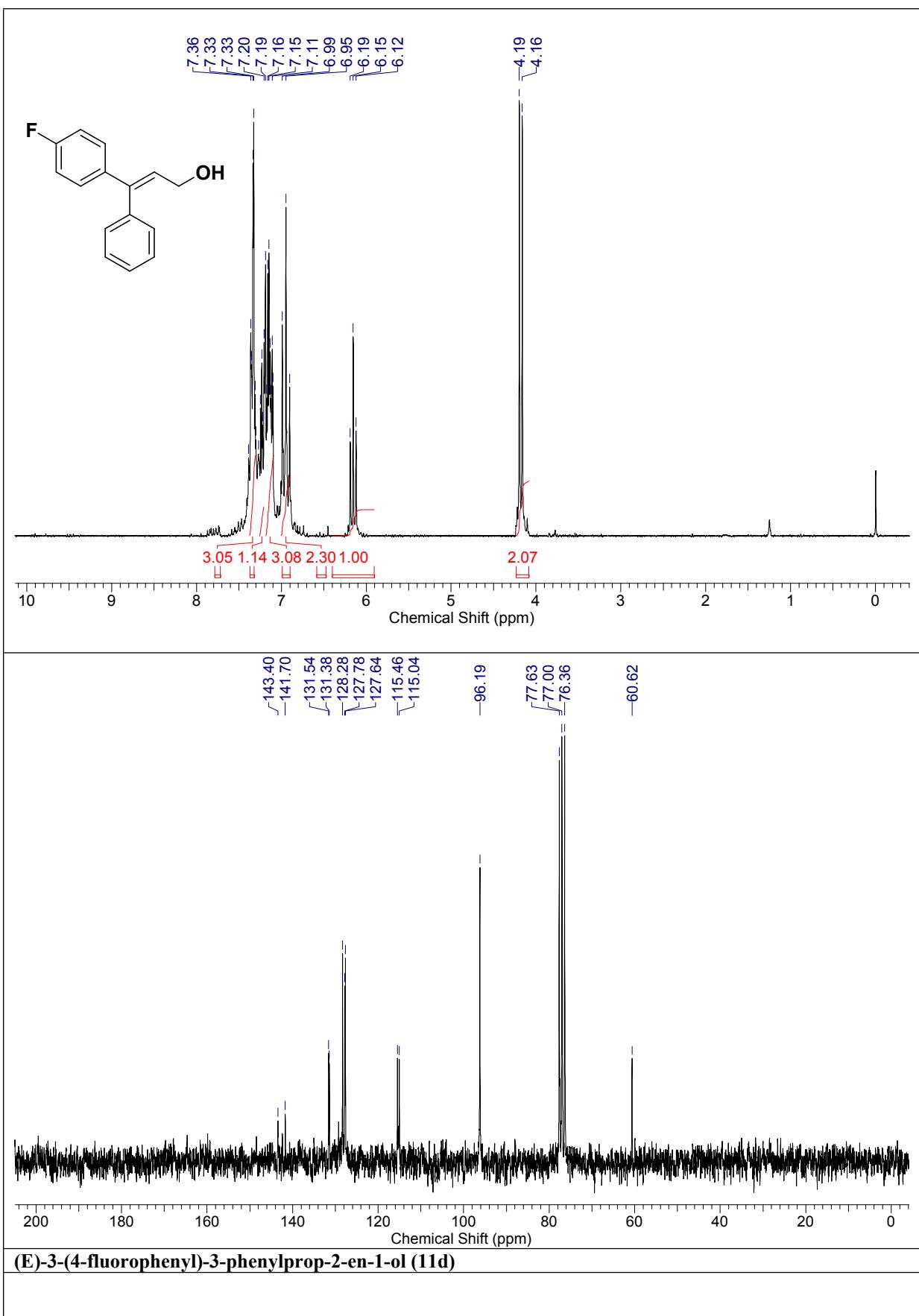


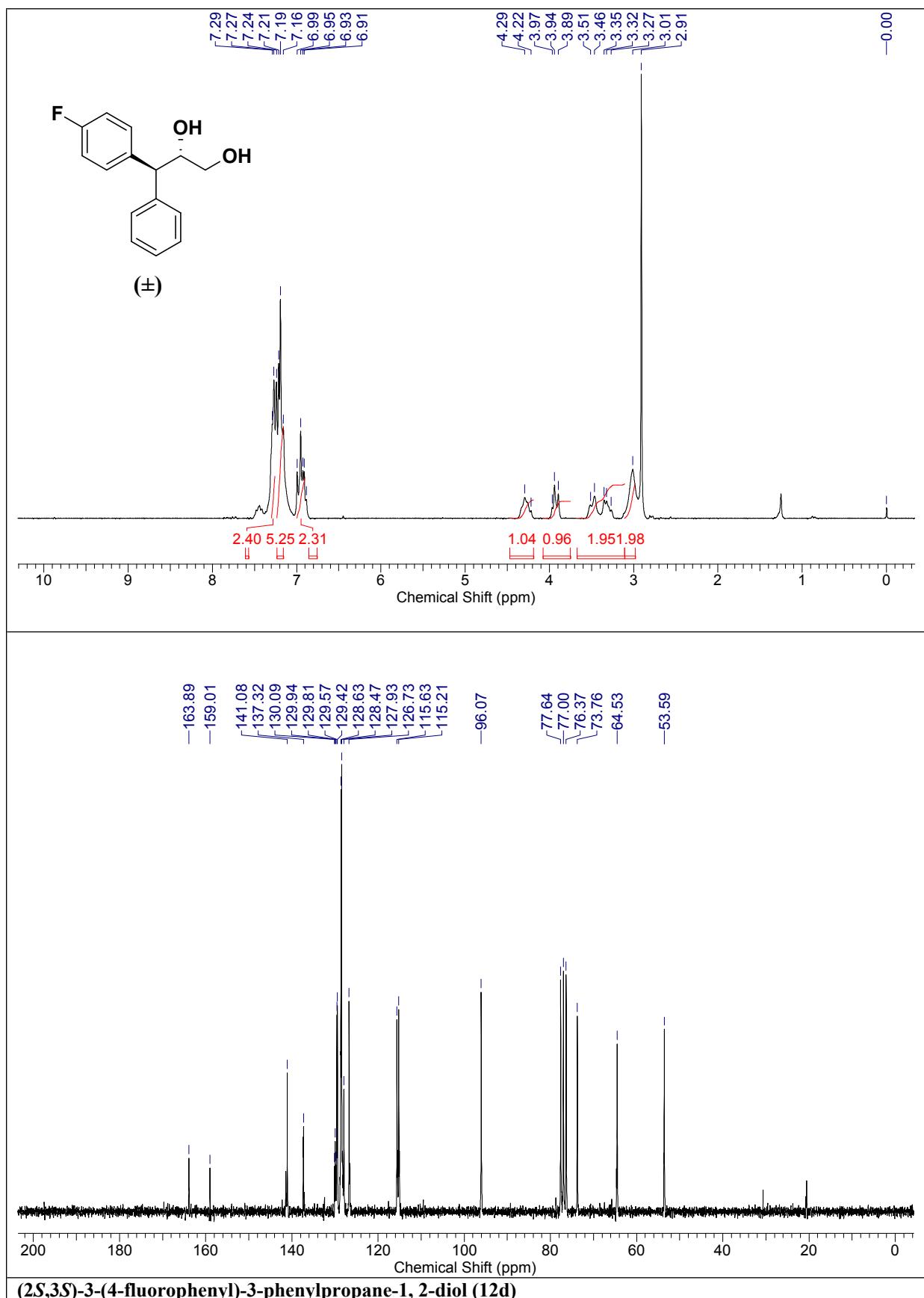
(E)-3-(4-chlorophenyl)-3-phenylprop-2-en-1-ol (11c)

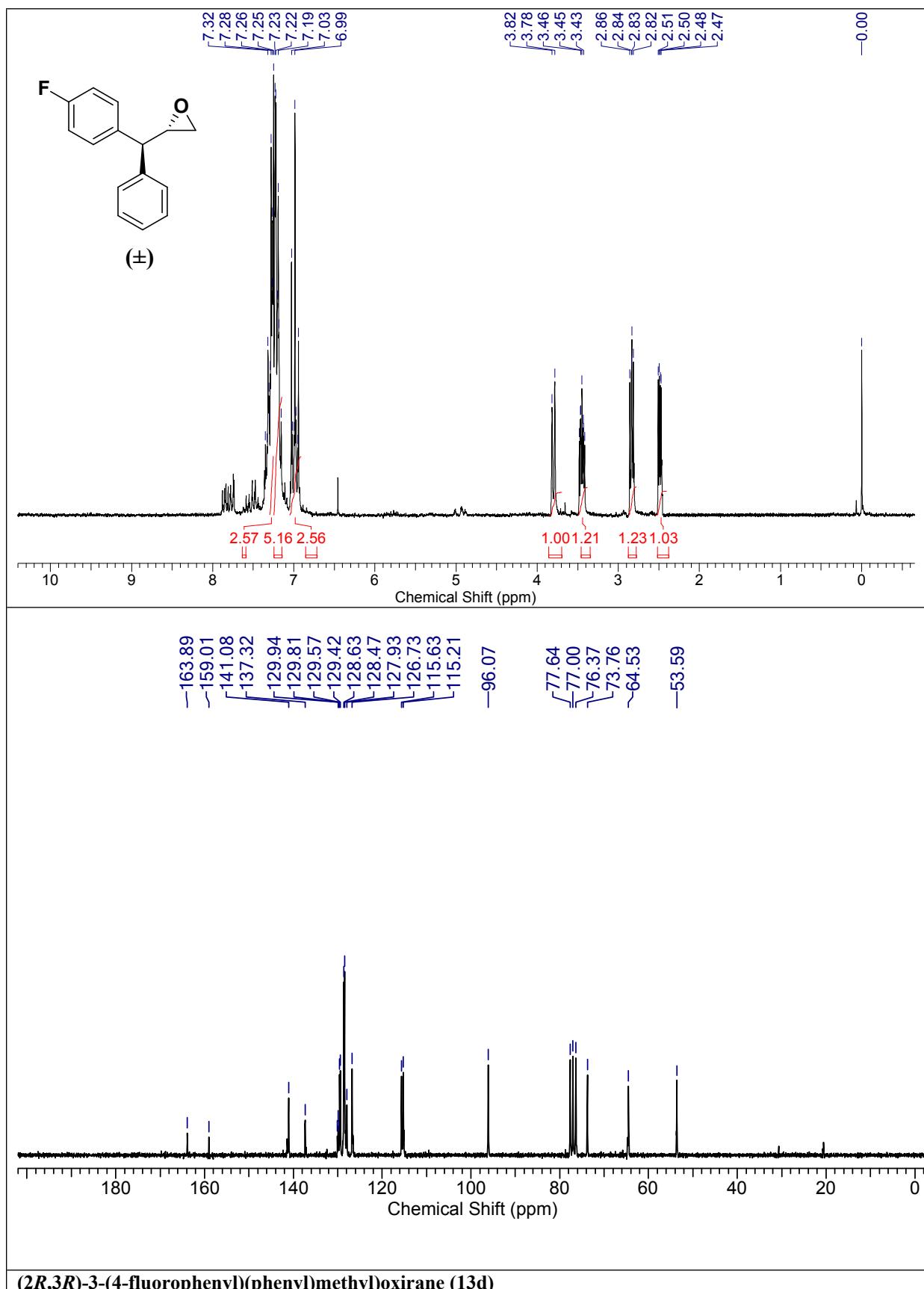


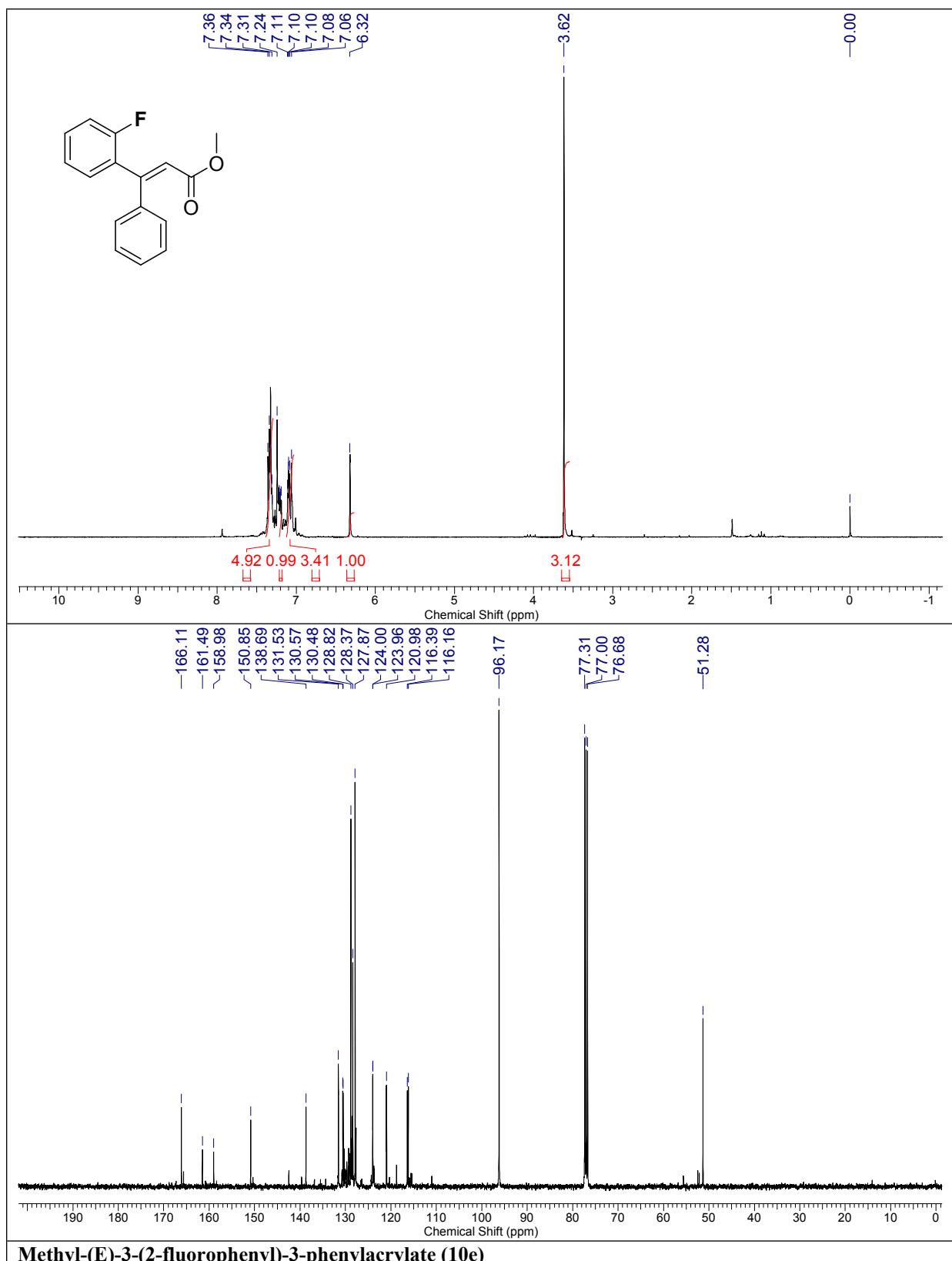


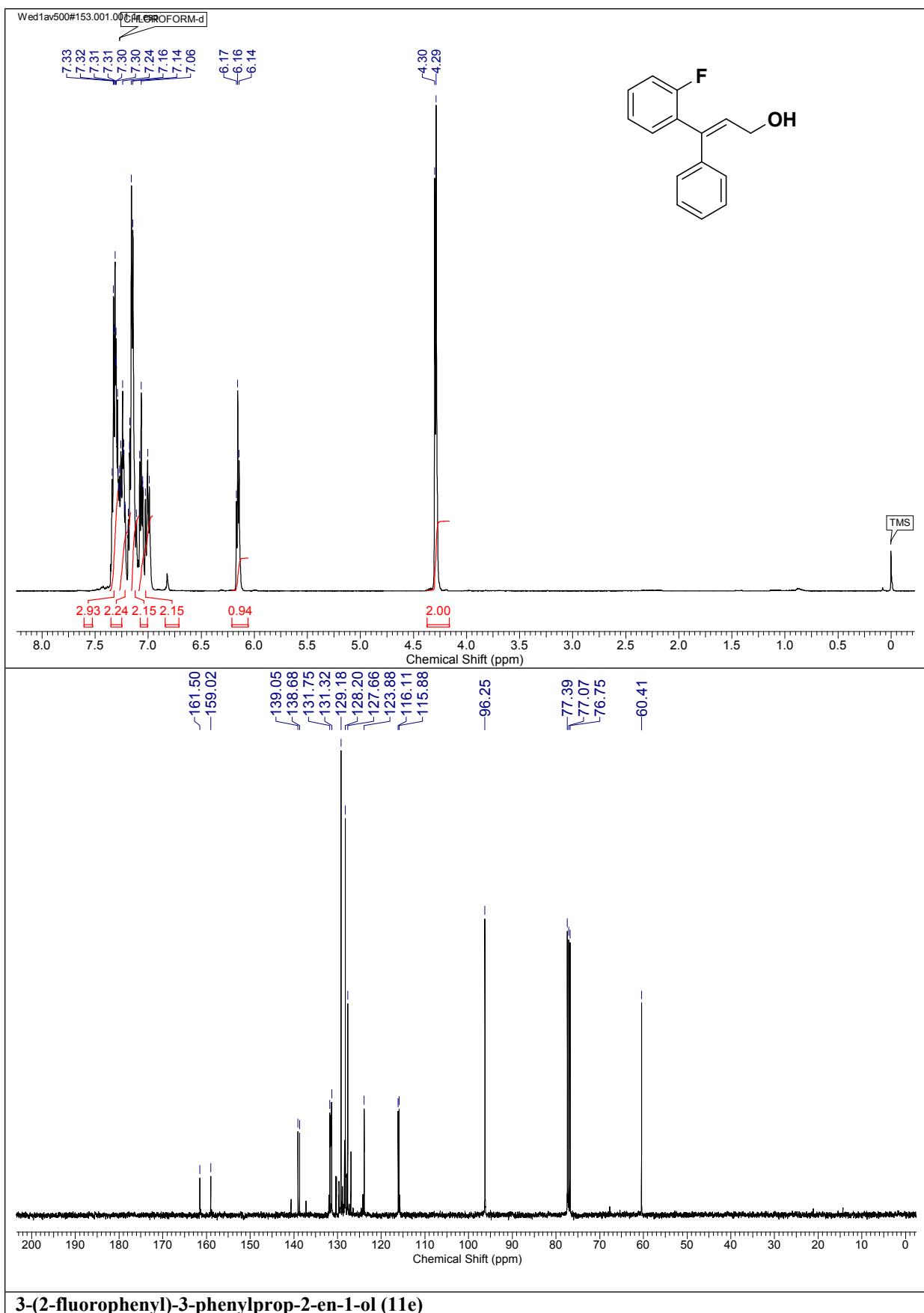


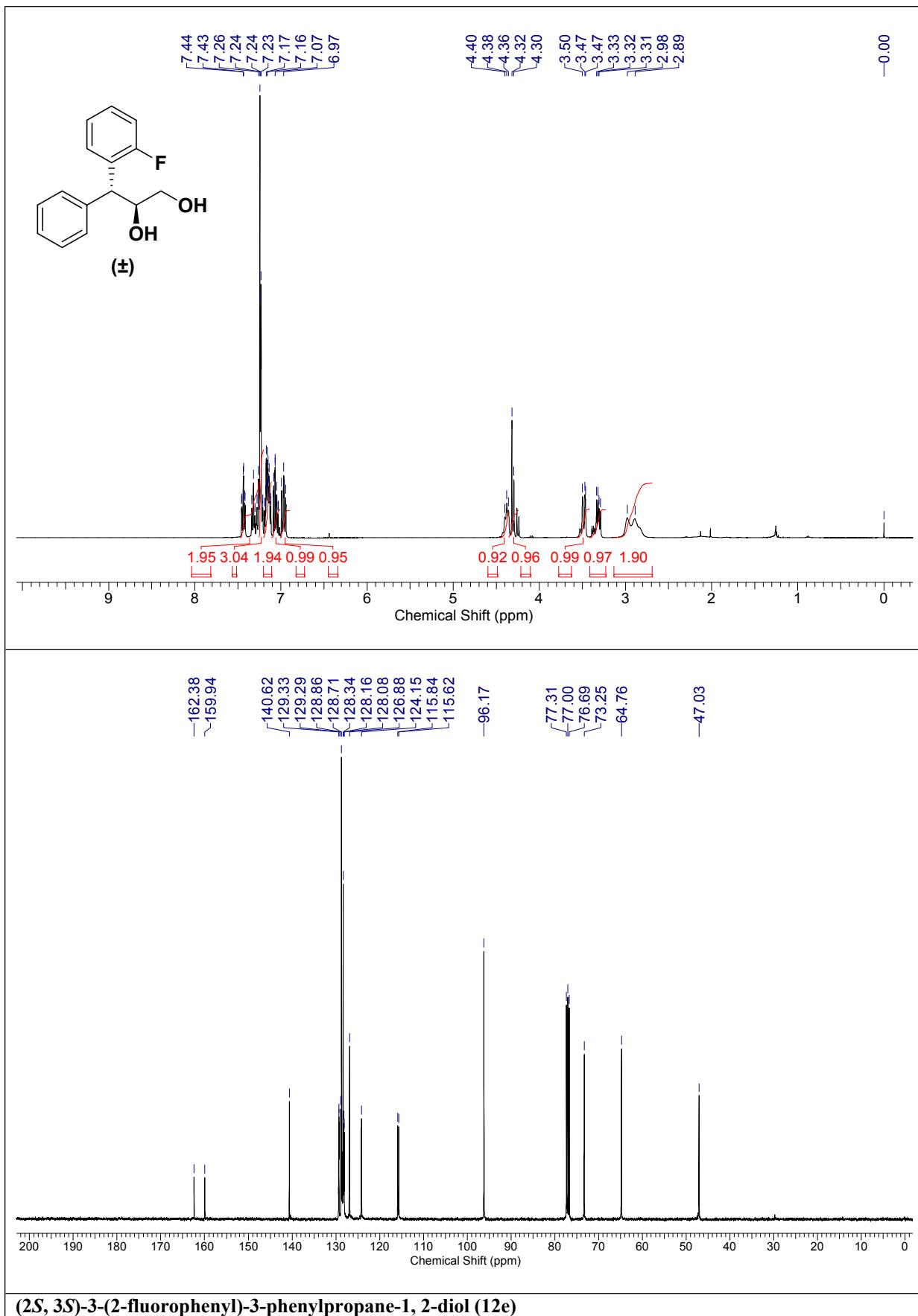




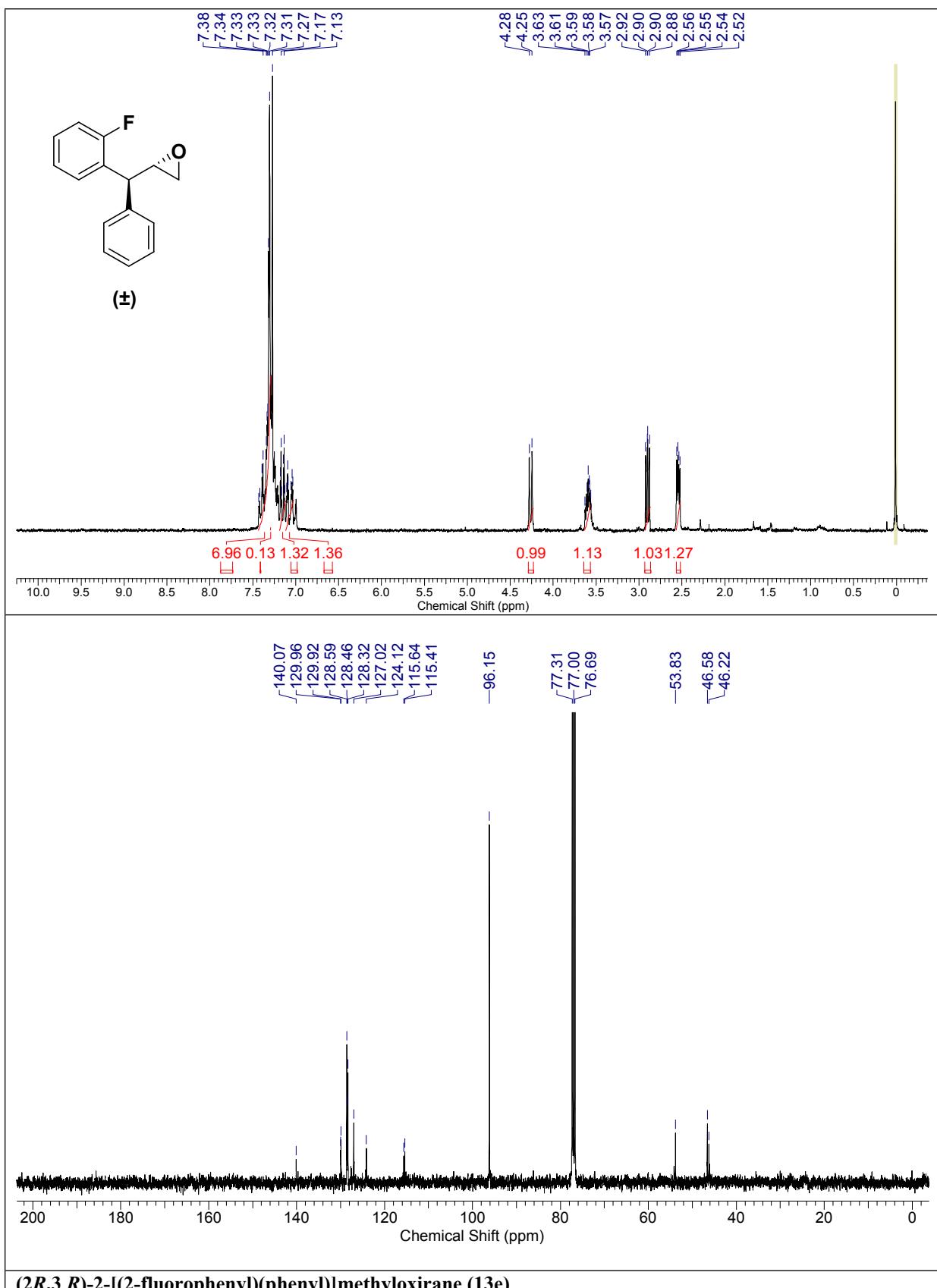


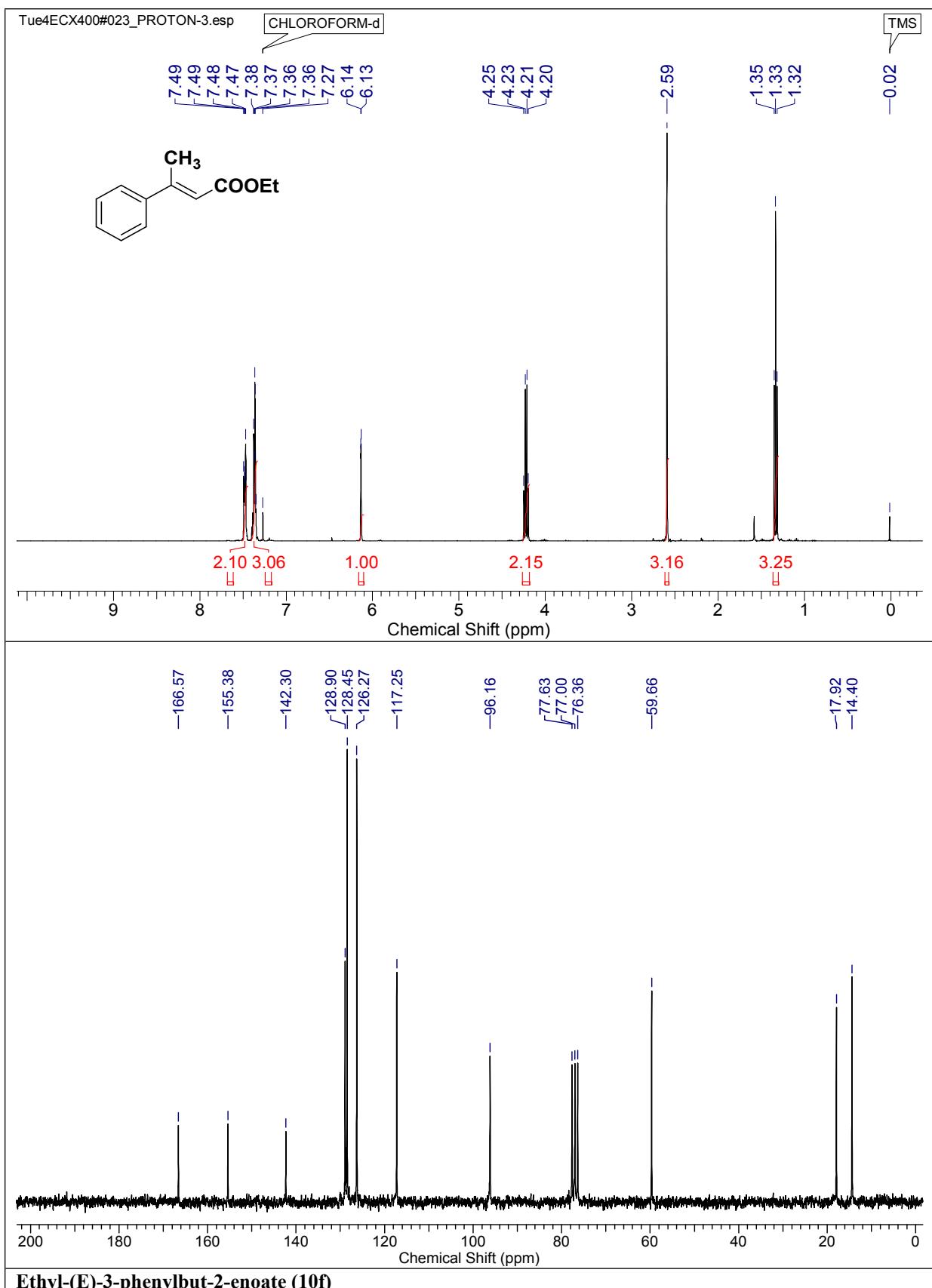


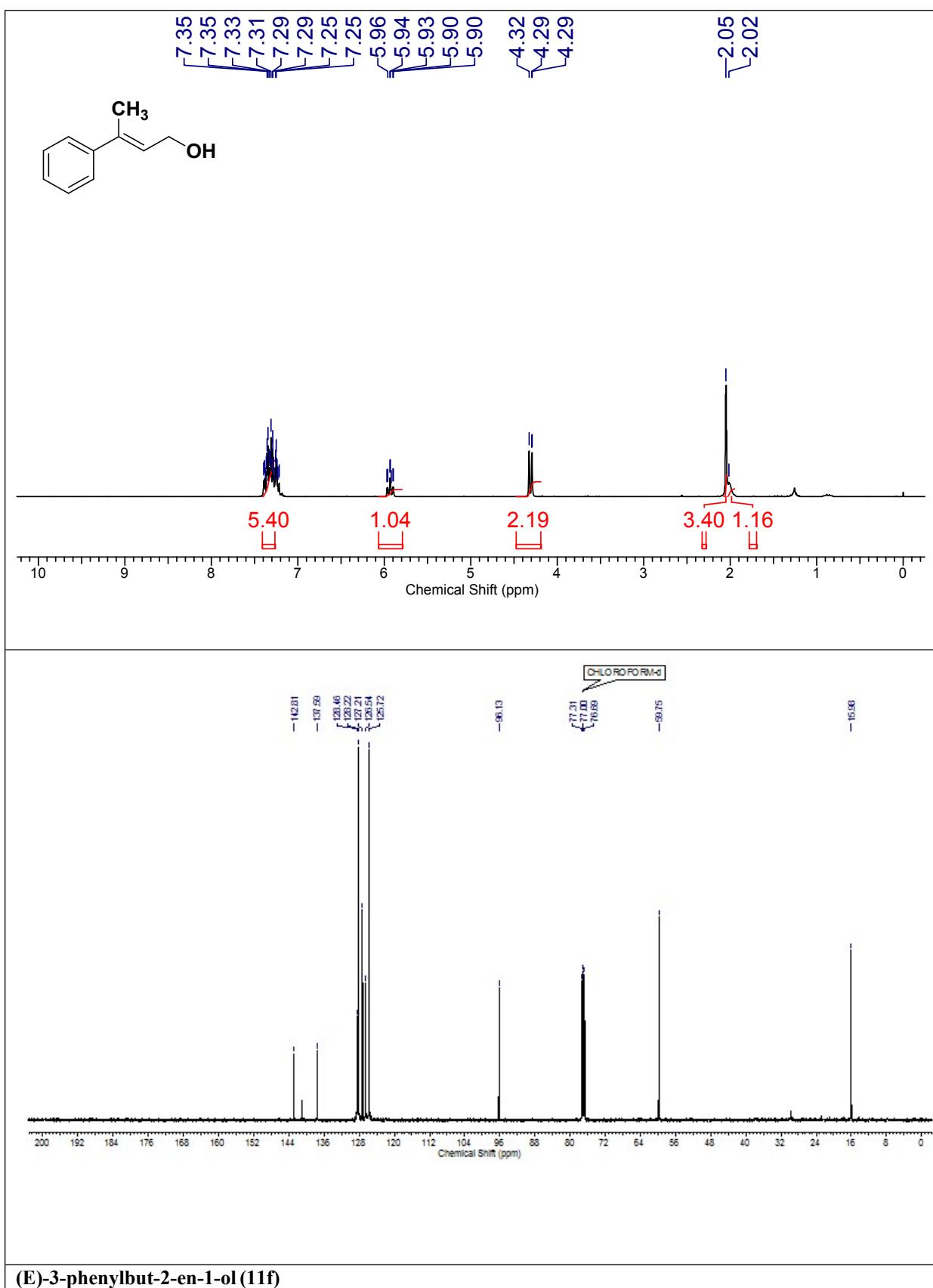




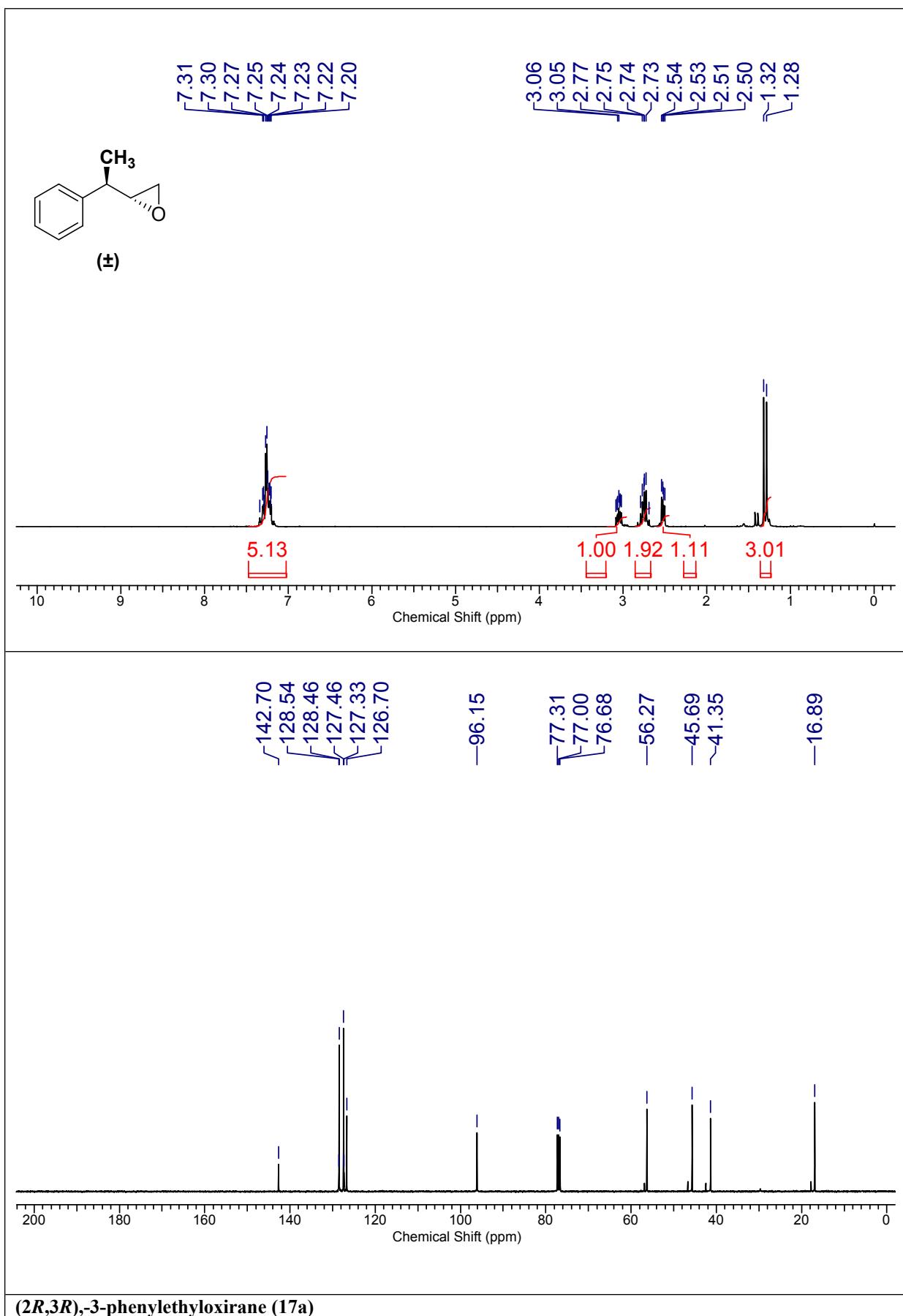
(2*S*, 3*S*)-3-(2-fluorophenyl)-3-phenylpropane-1, 2-diol (12e)

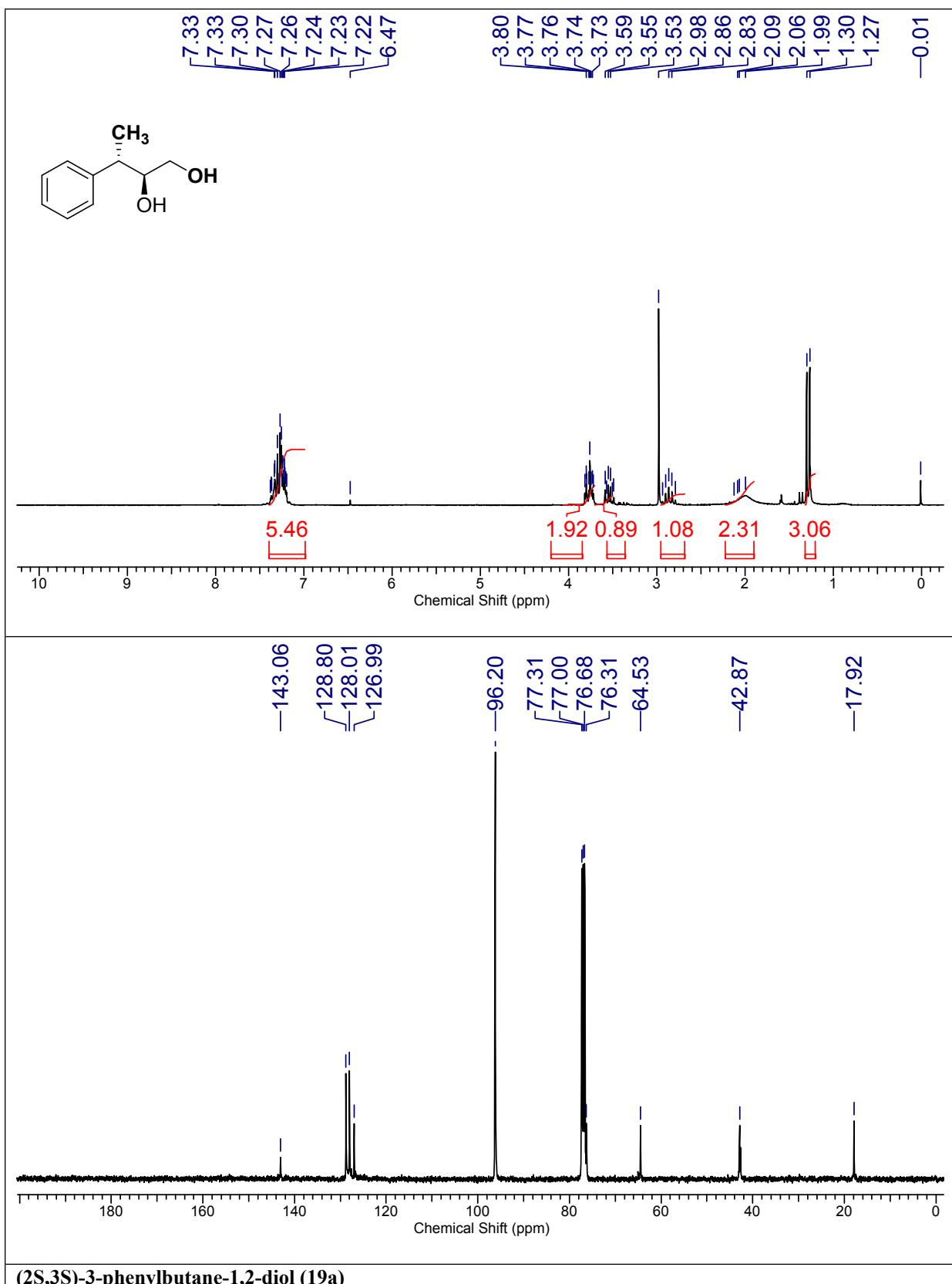


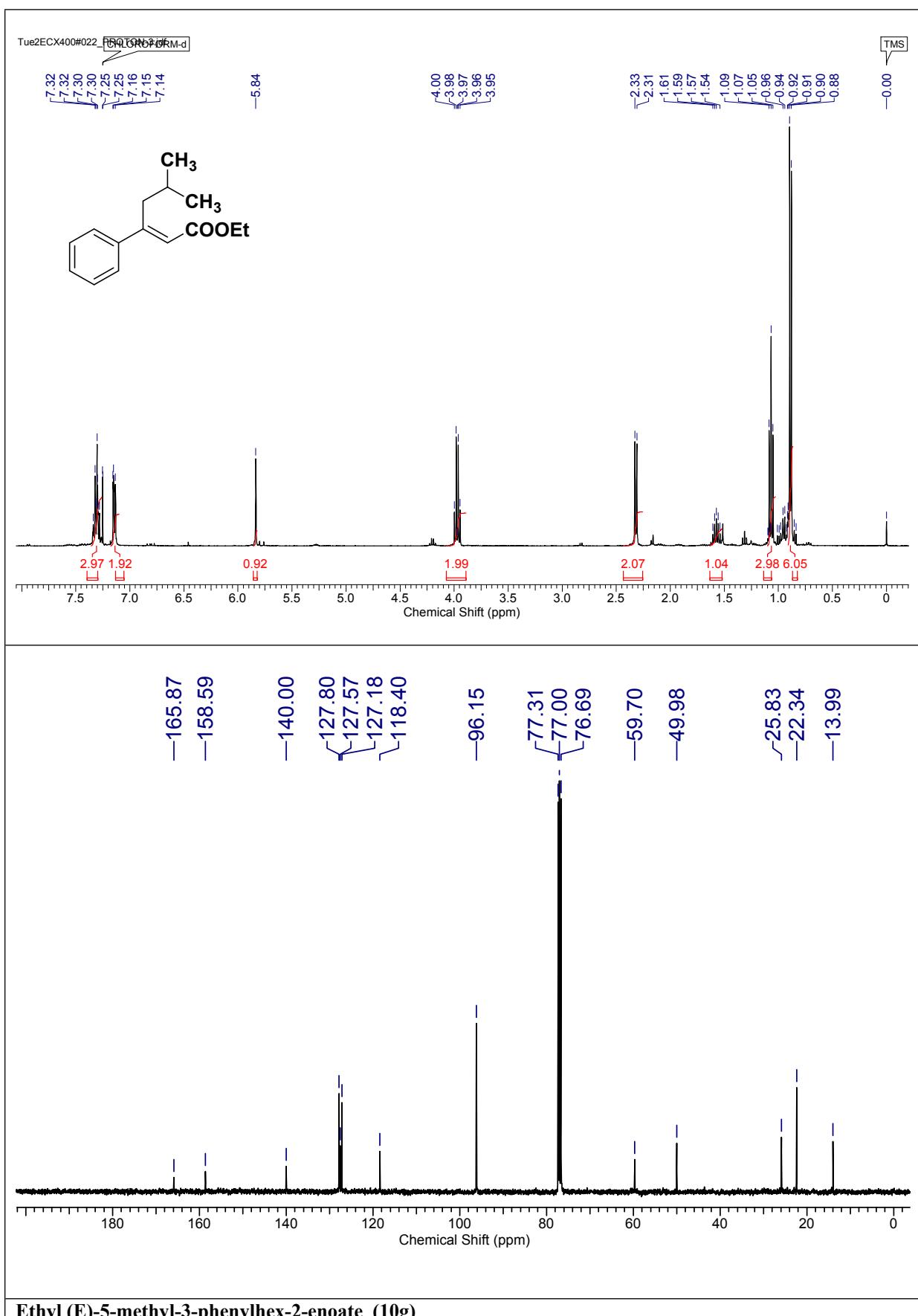


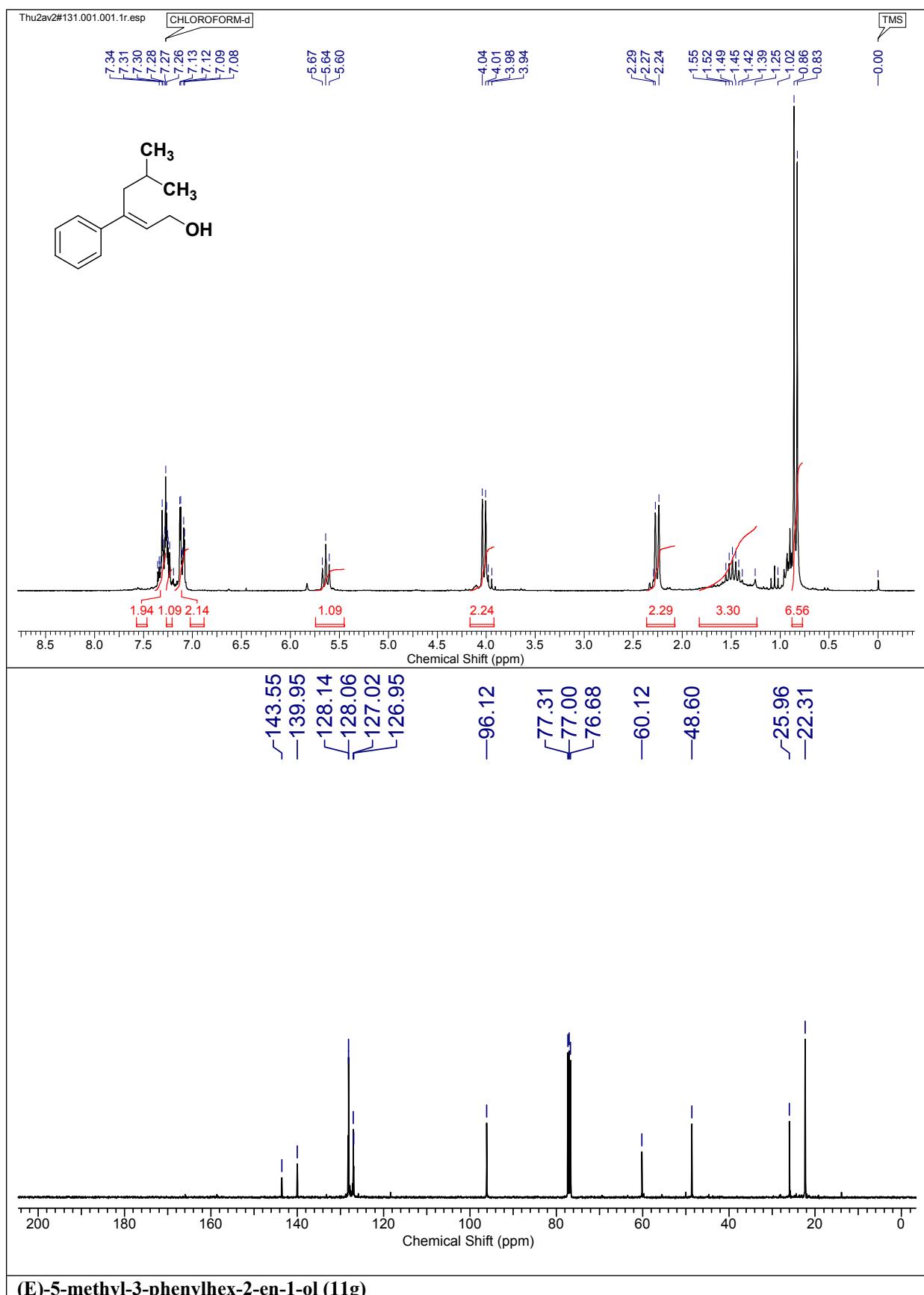


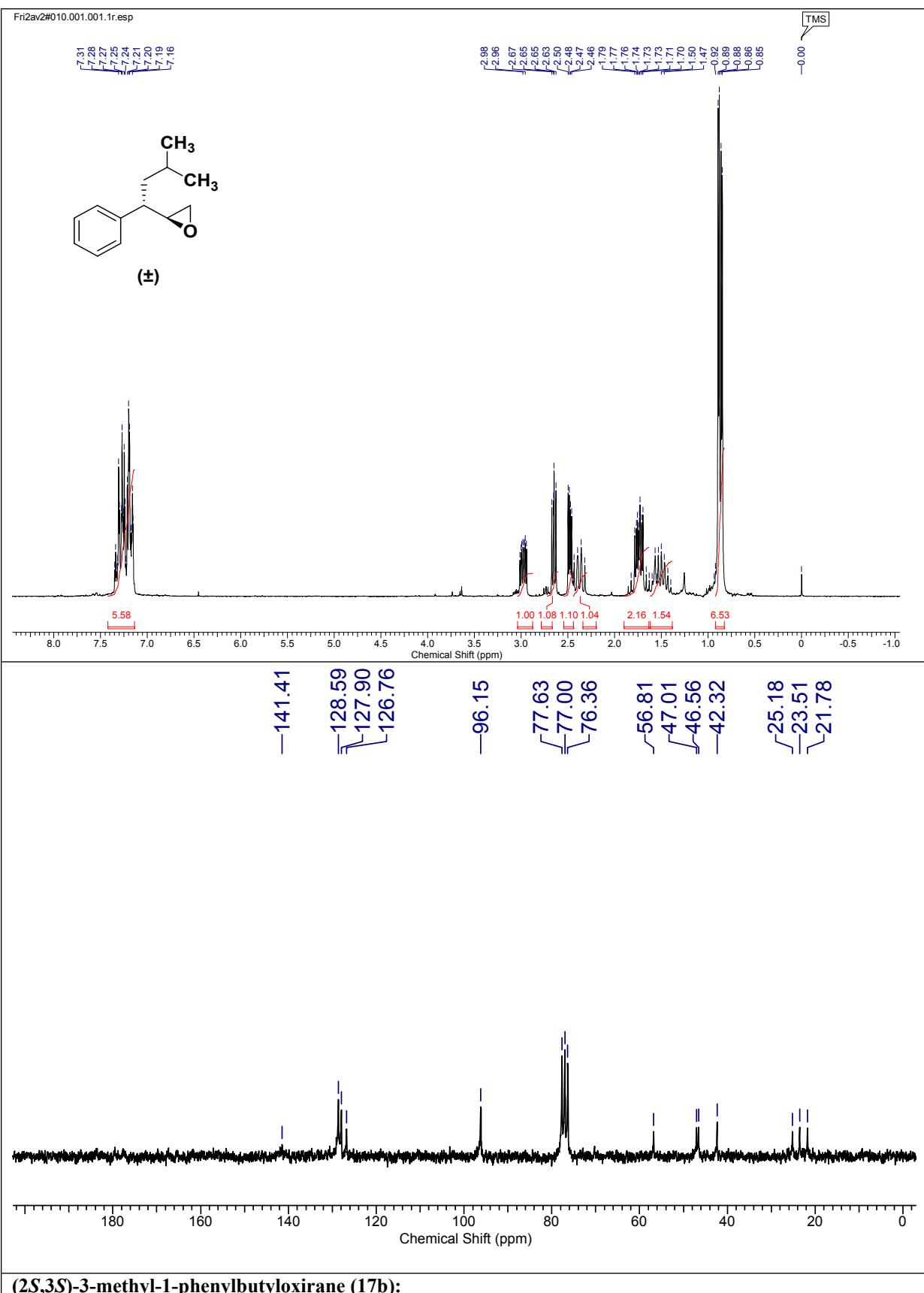
(E)-3-phenylbut-2-en-1-ol (11f)

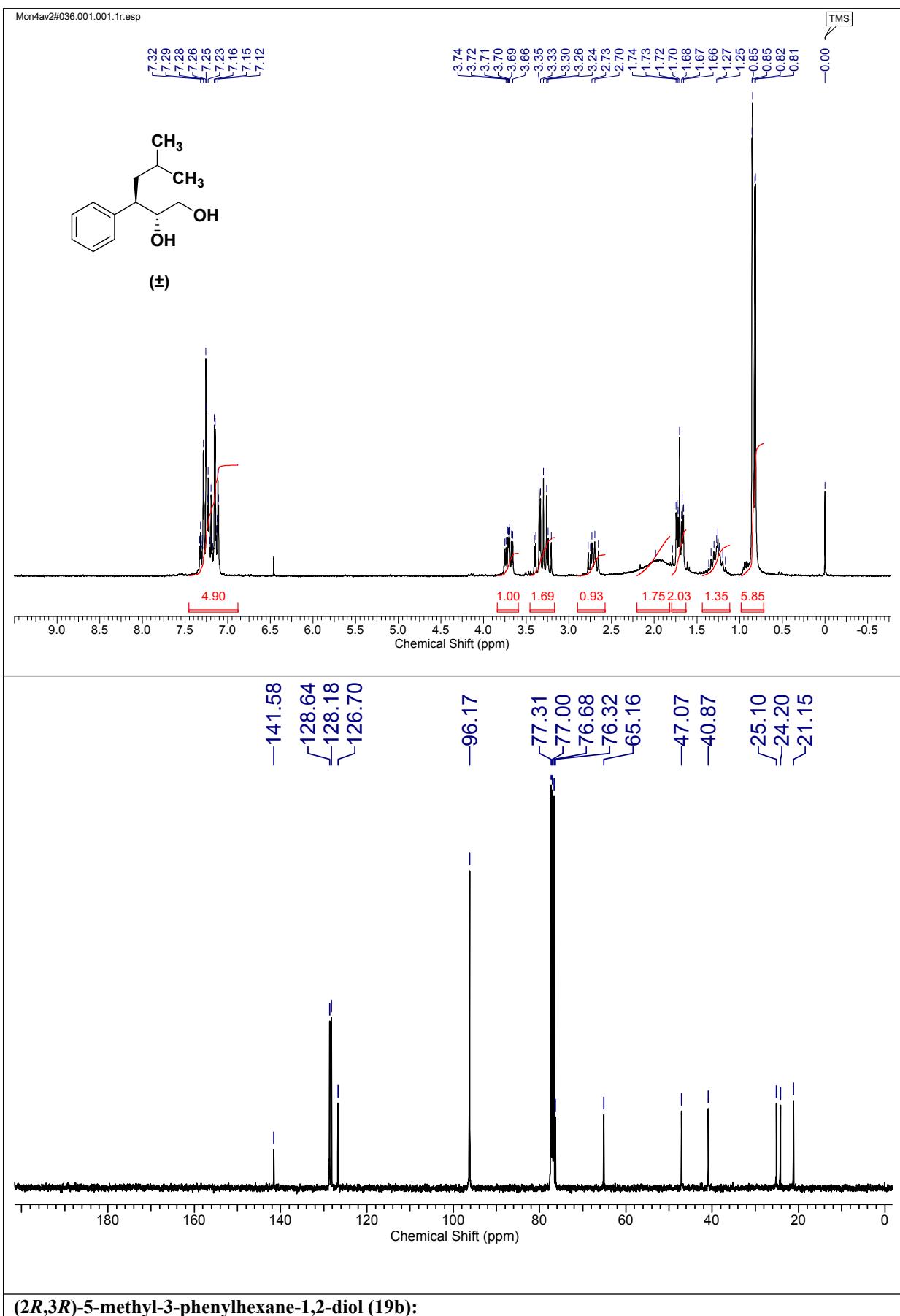


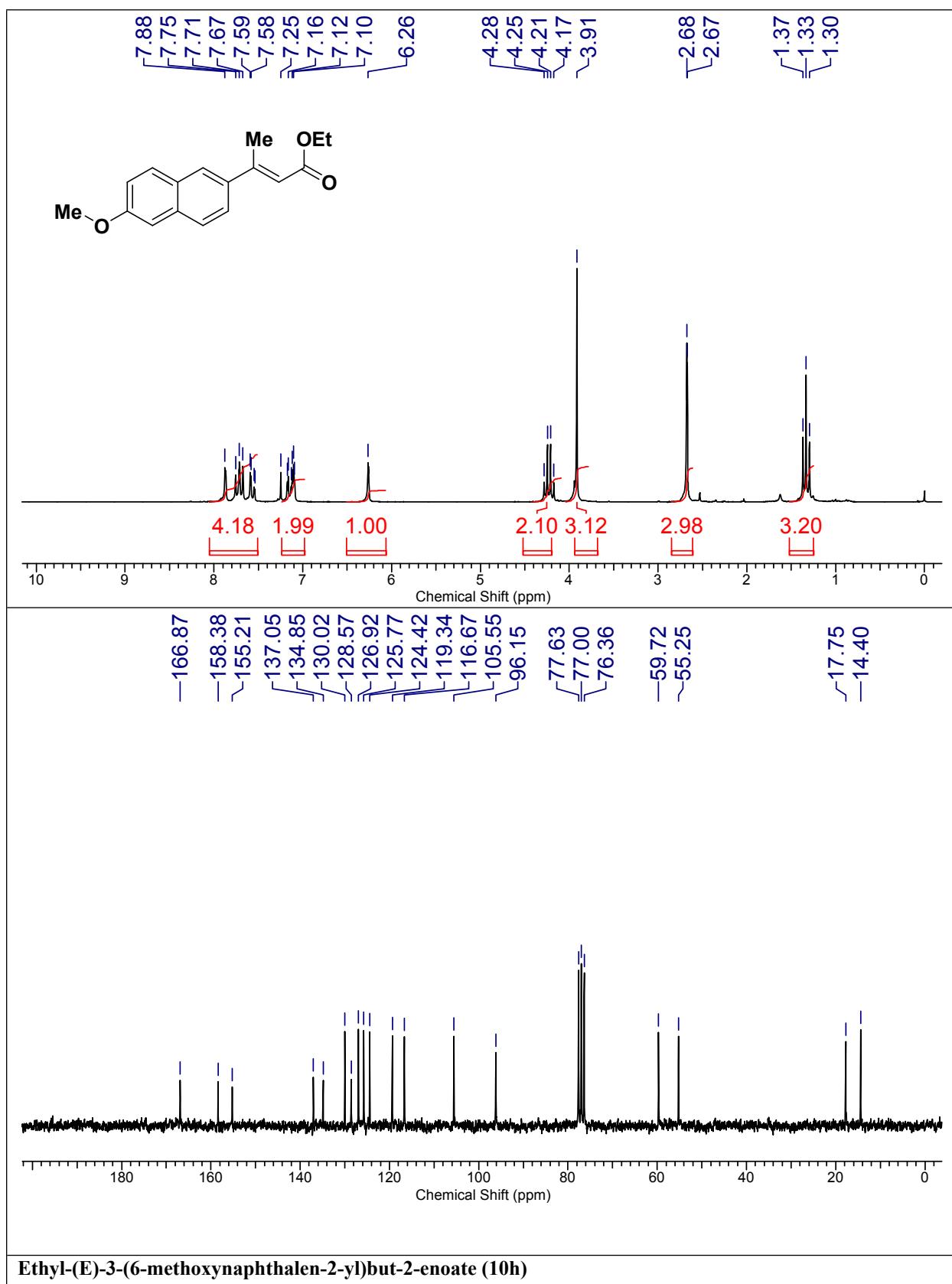


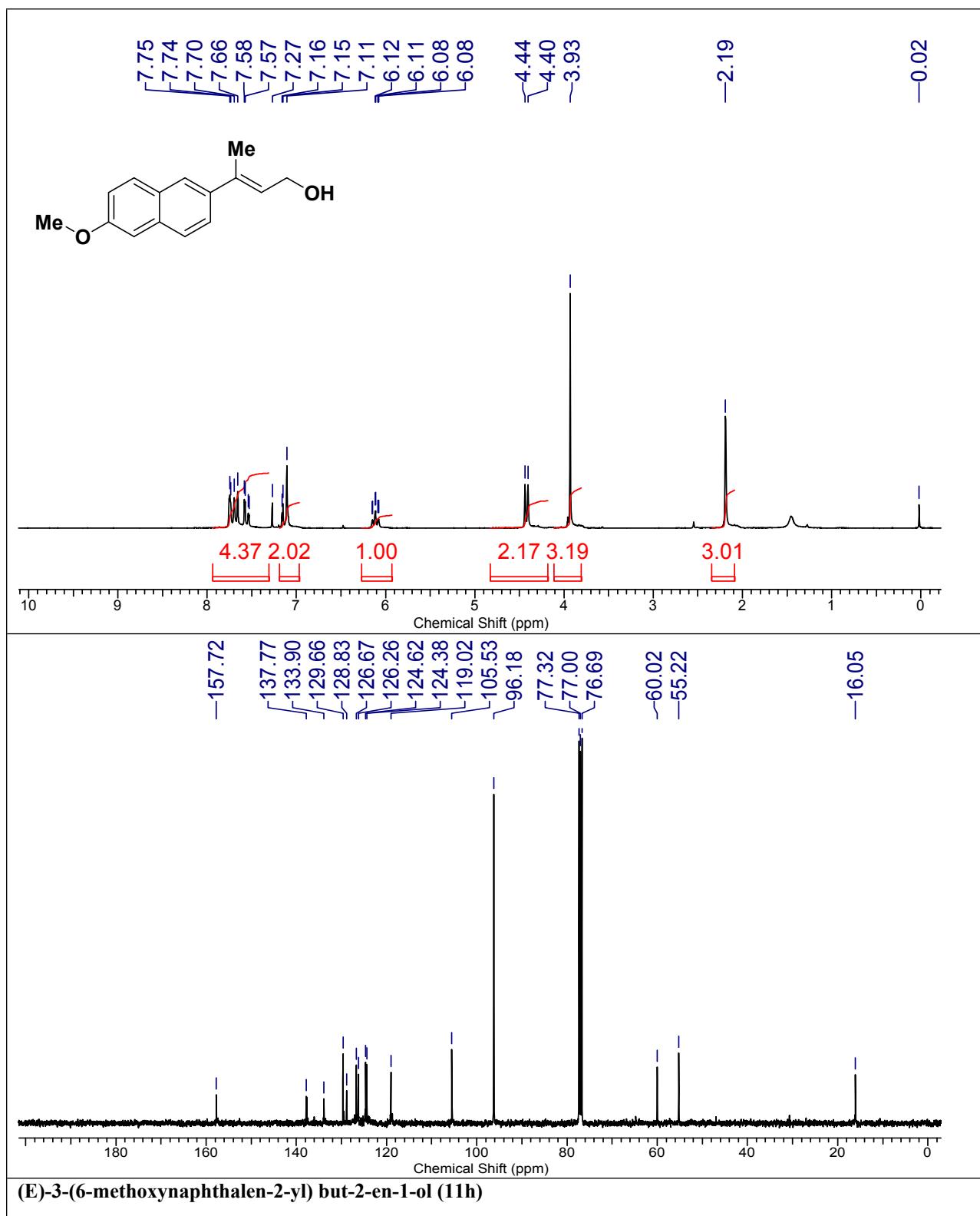


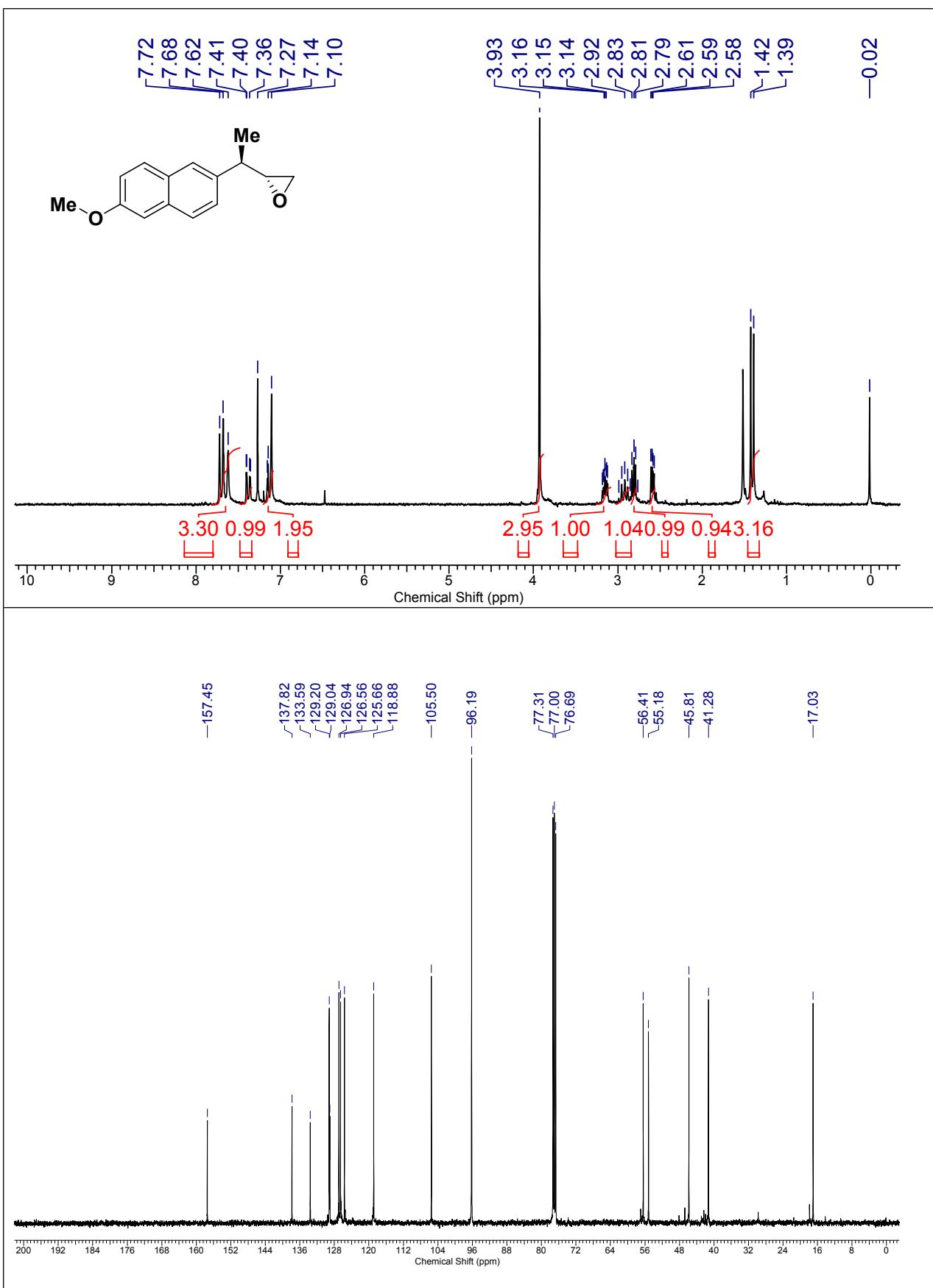




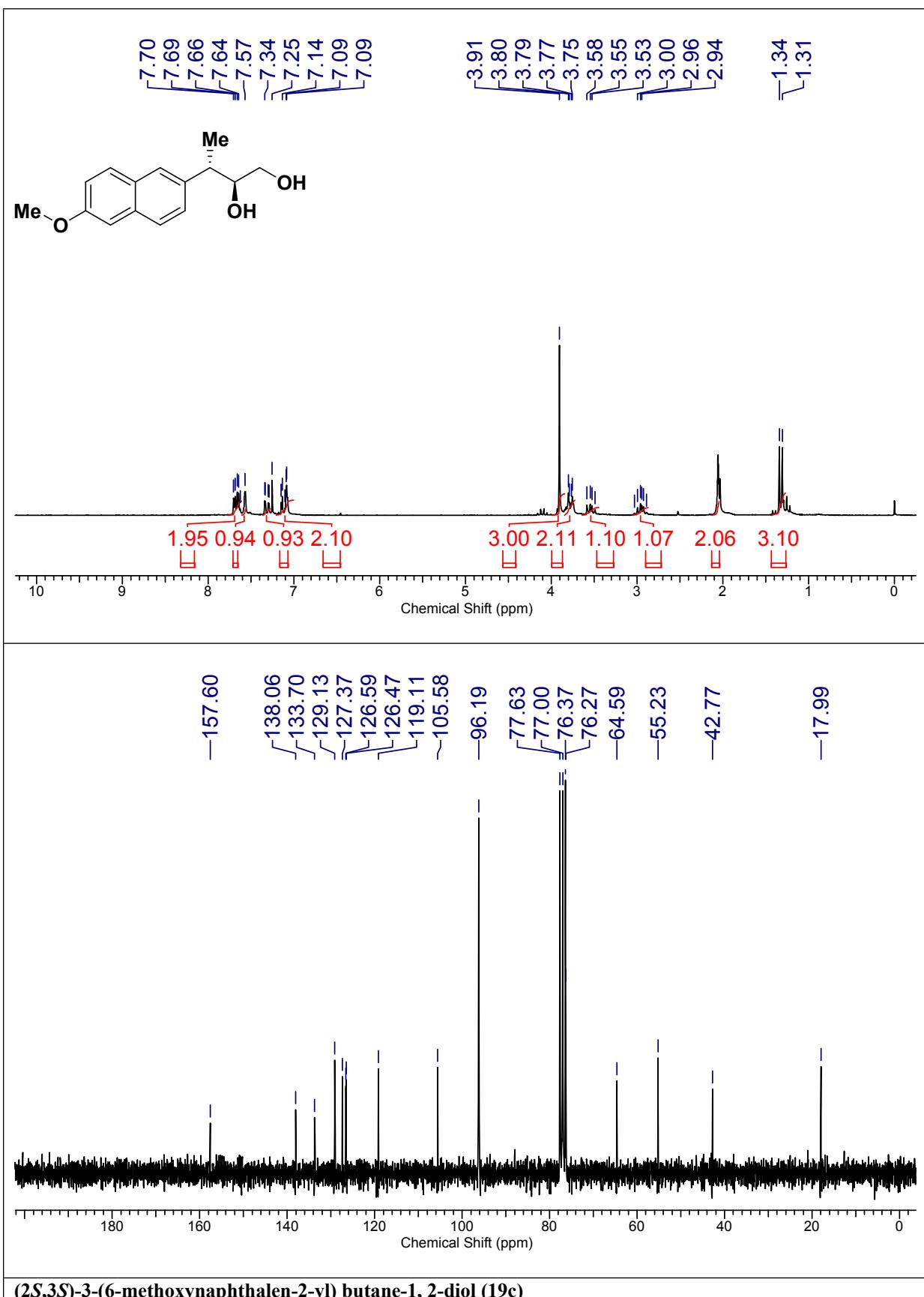




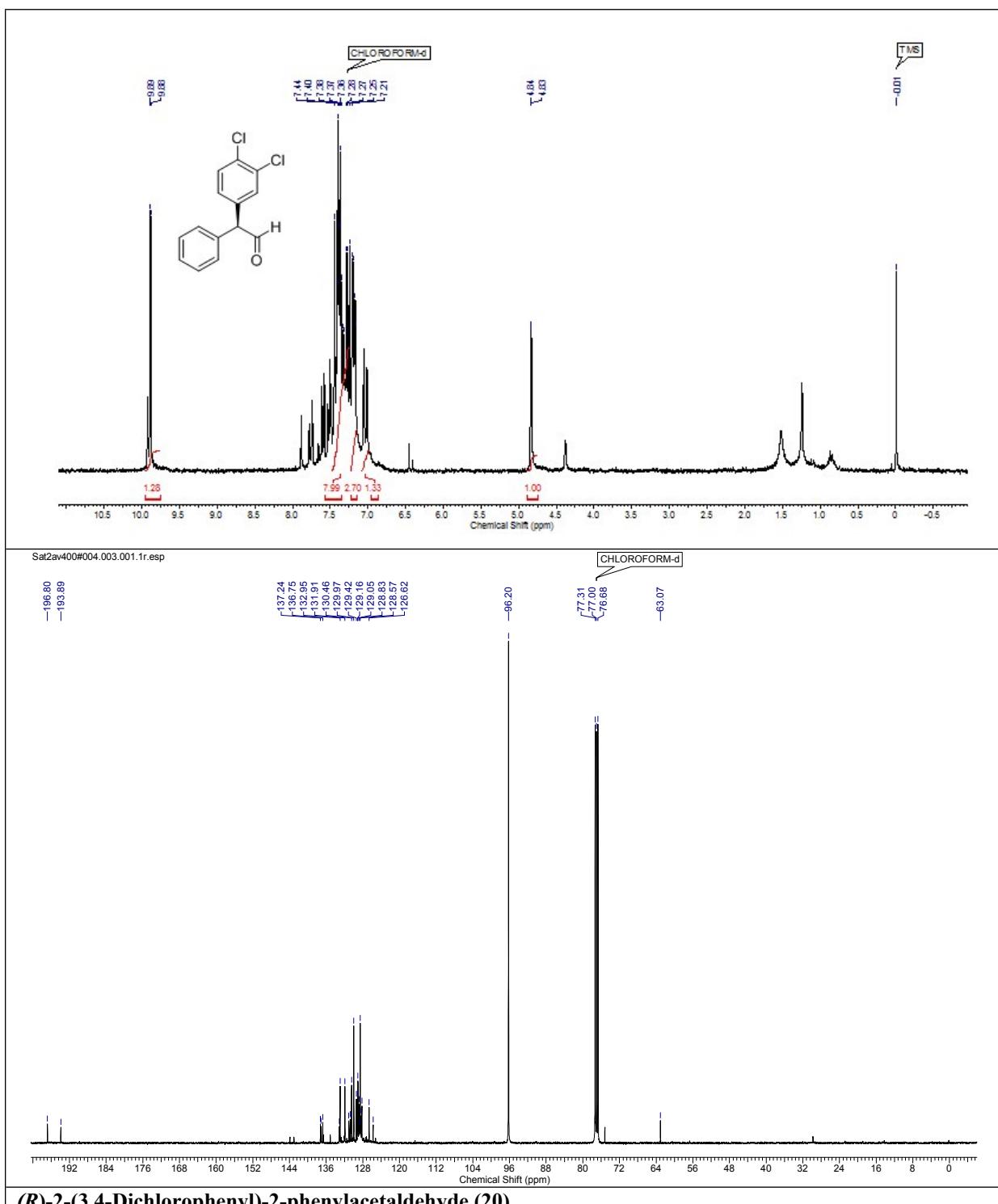


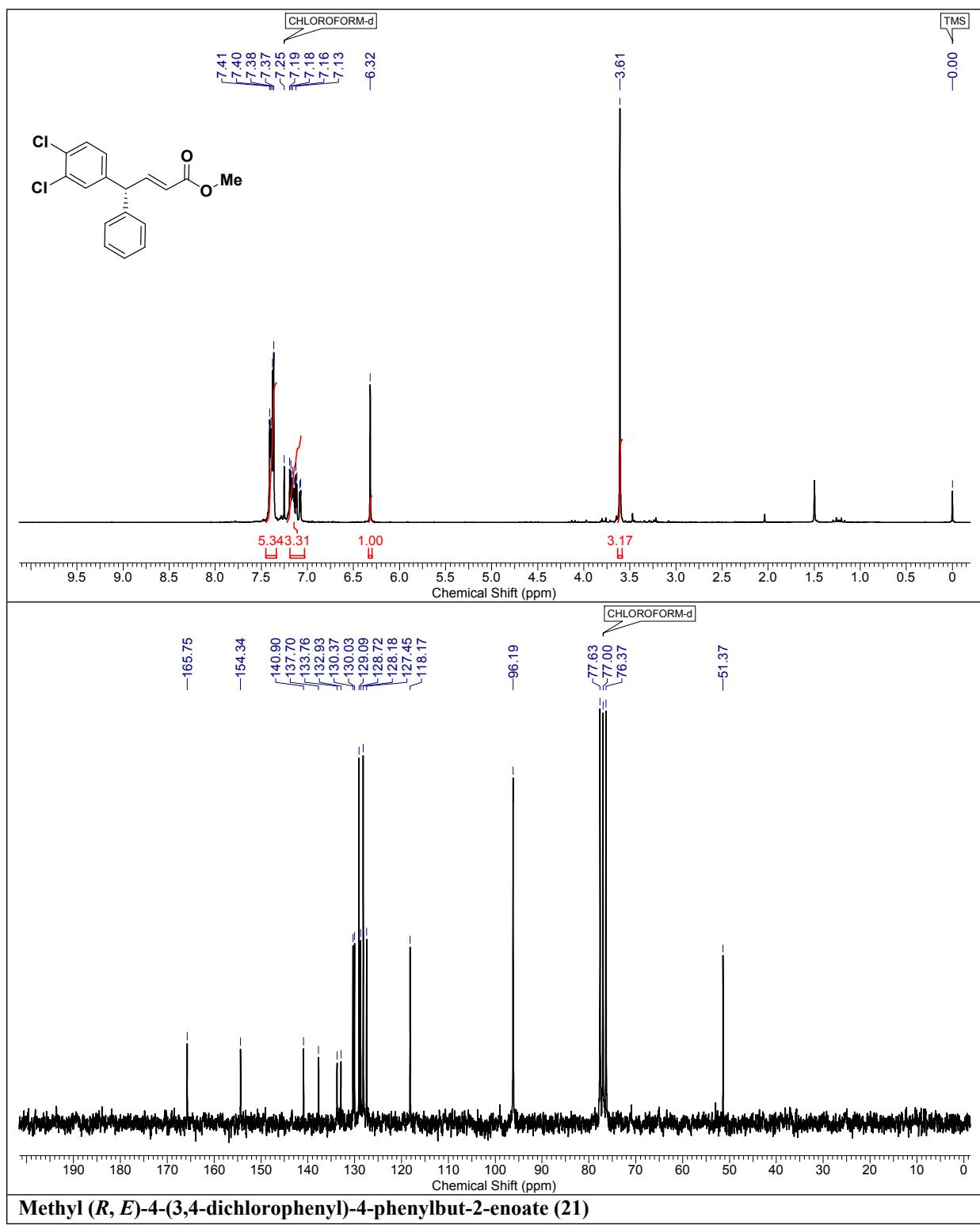


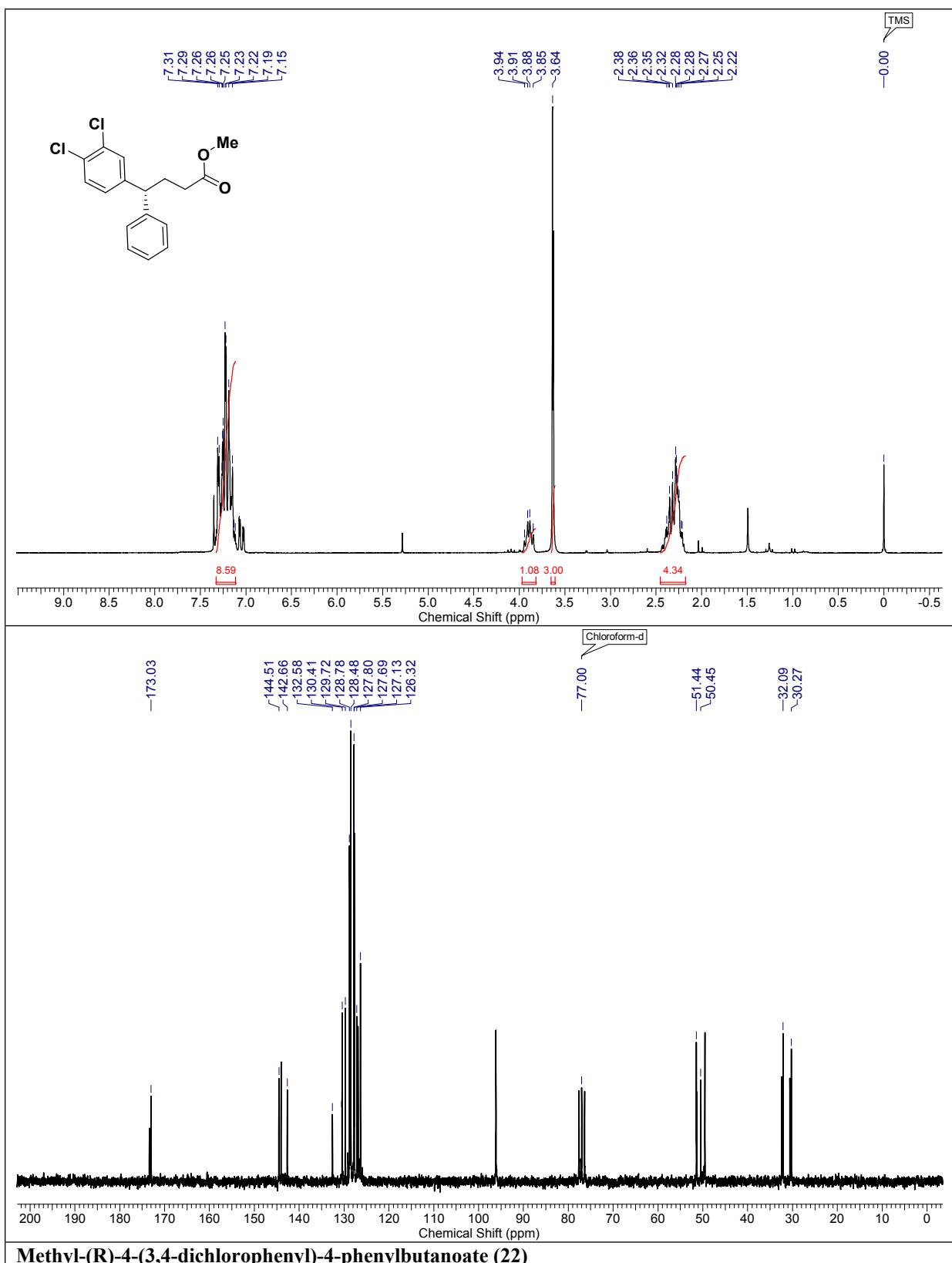
(2*R*,3*R*)-2-((*R*)-1-(6-methoxynaphthalen-2-yl) ethyl)oxirane (**17c**)

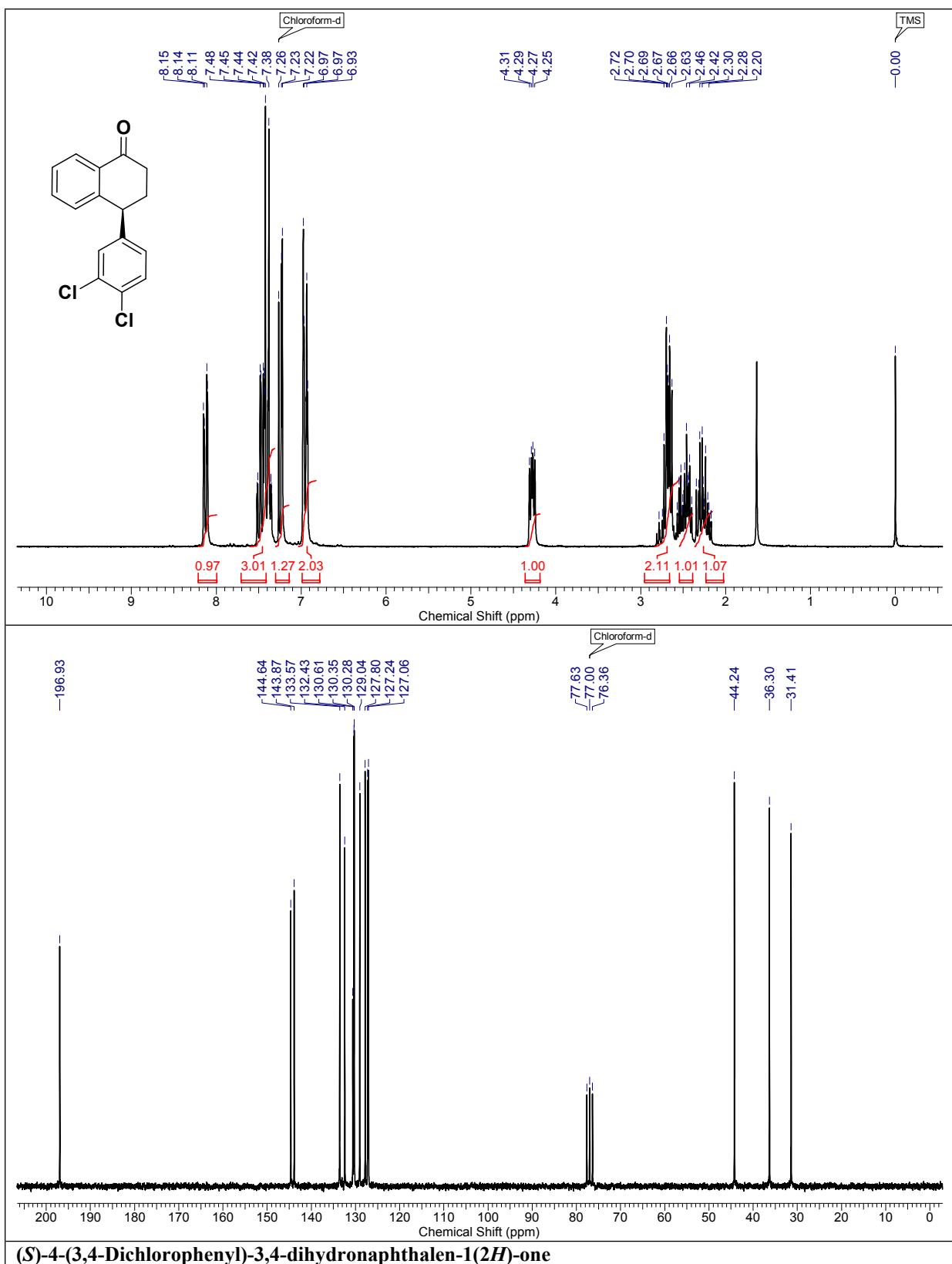


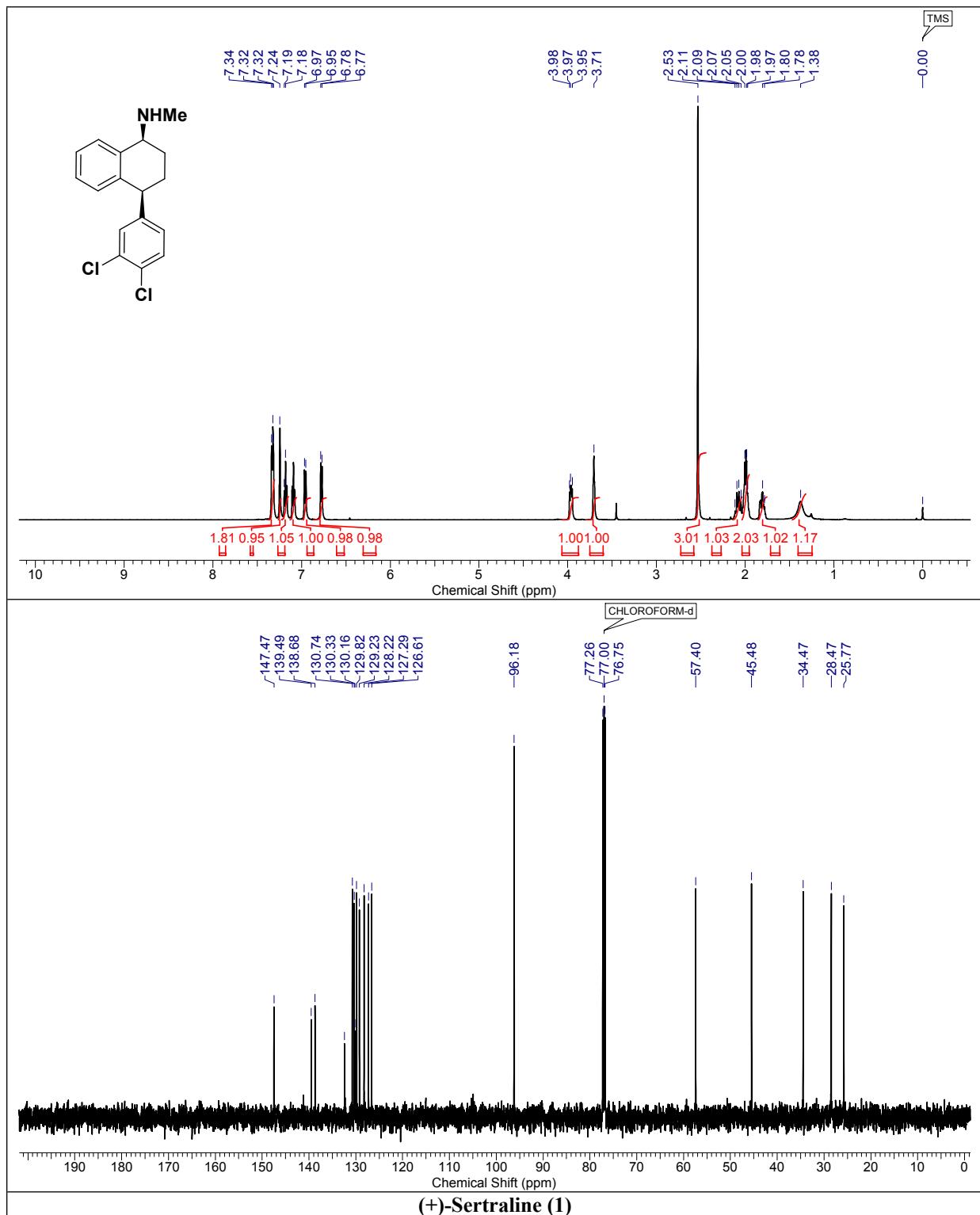
(2*S,3S*)-3-(6-methoxynaphthalen-2-yl) butane-1,2-diol (19c)

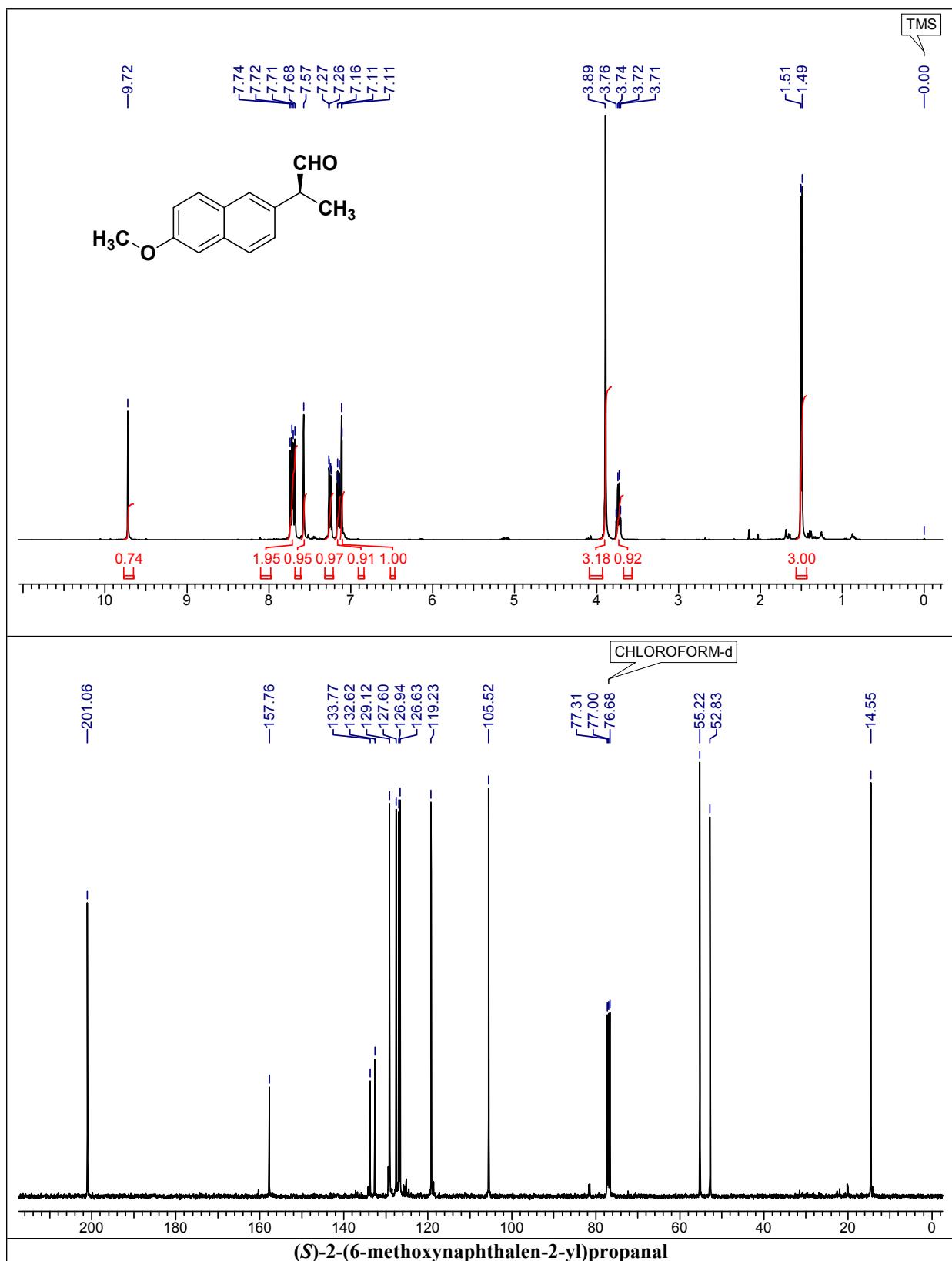


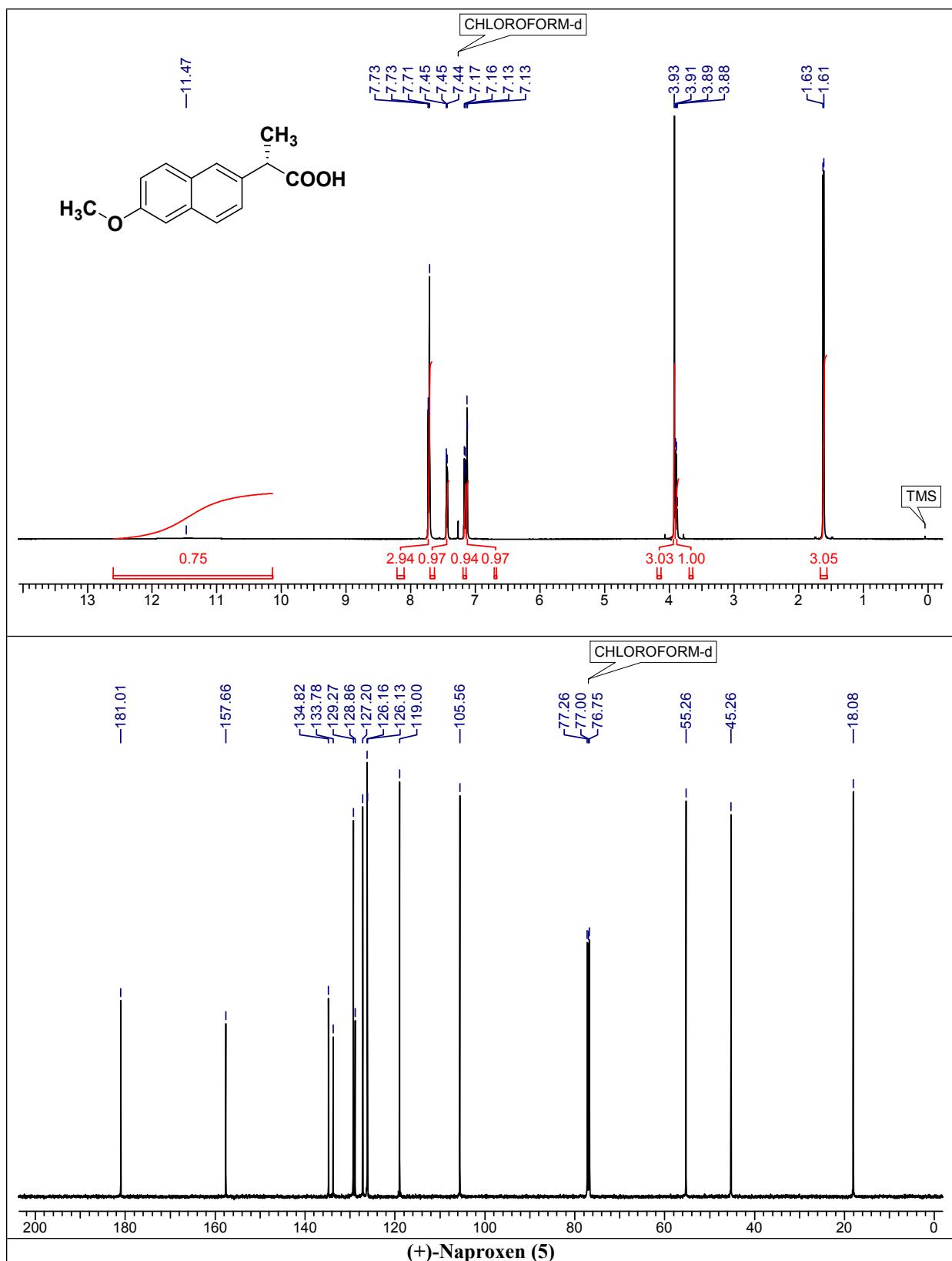


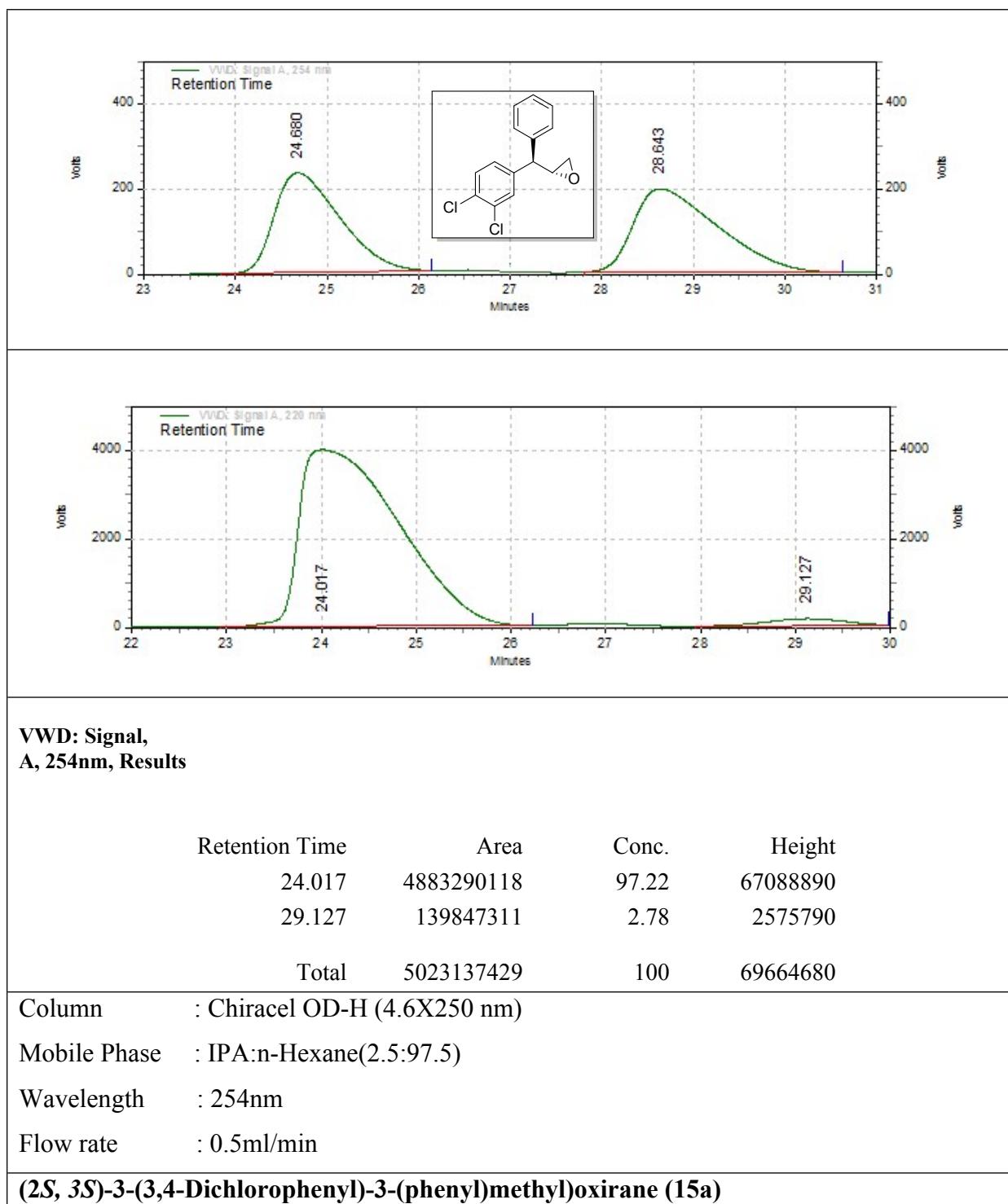


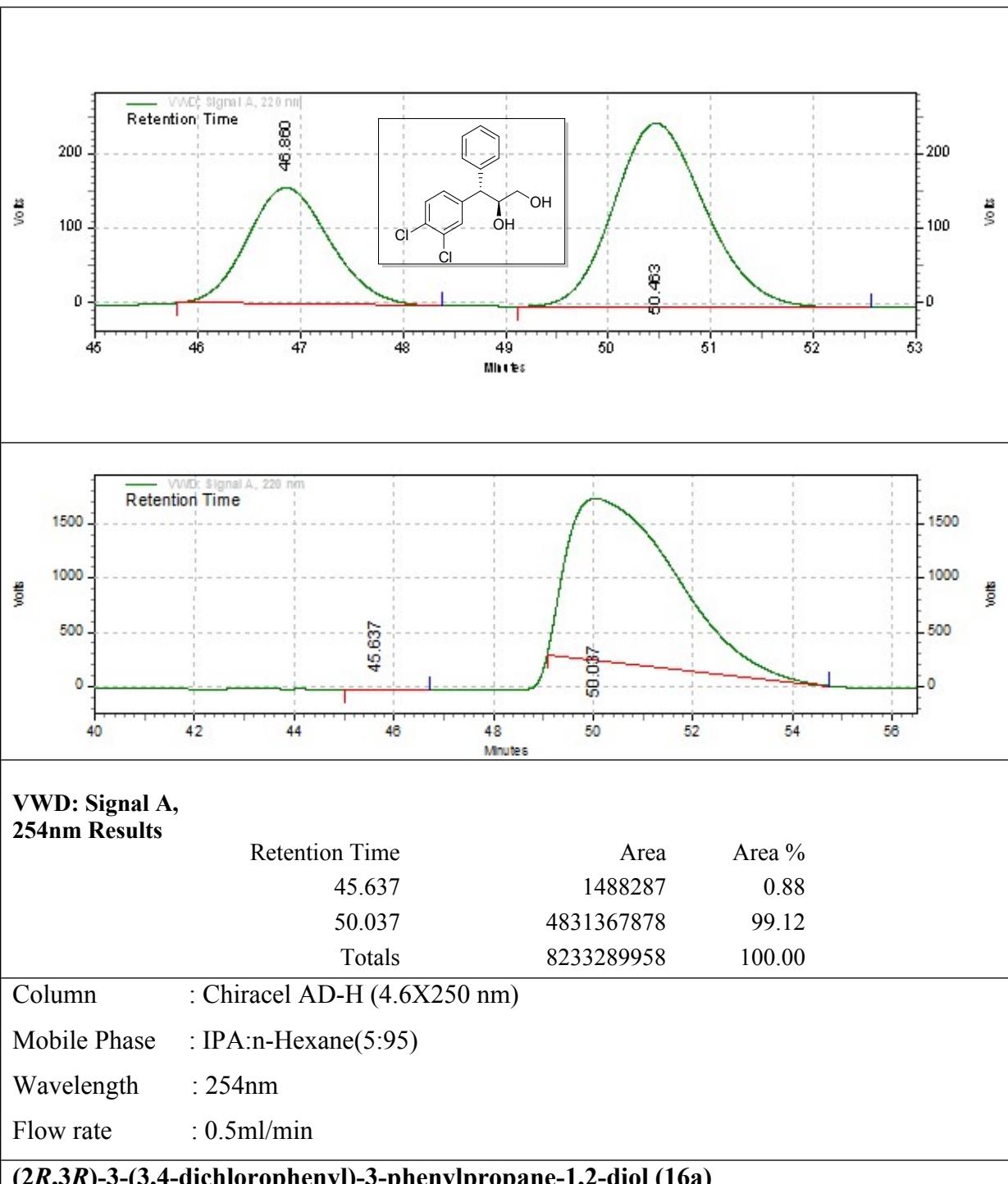


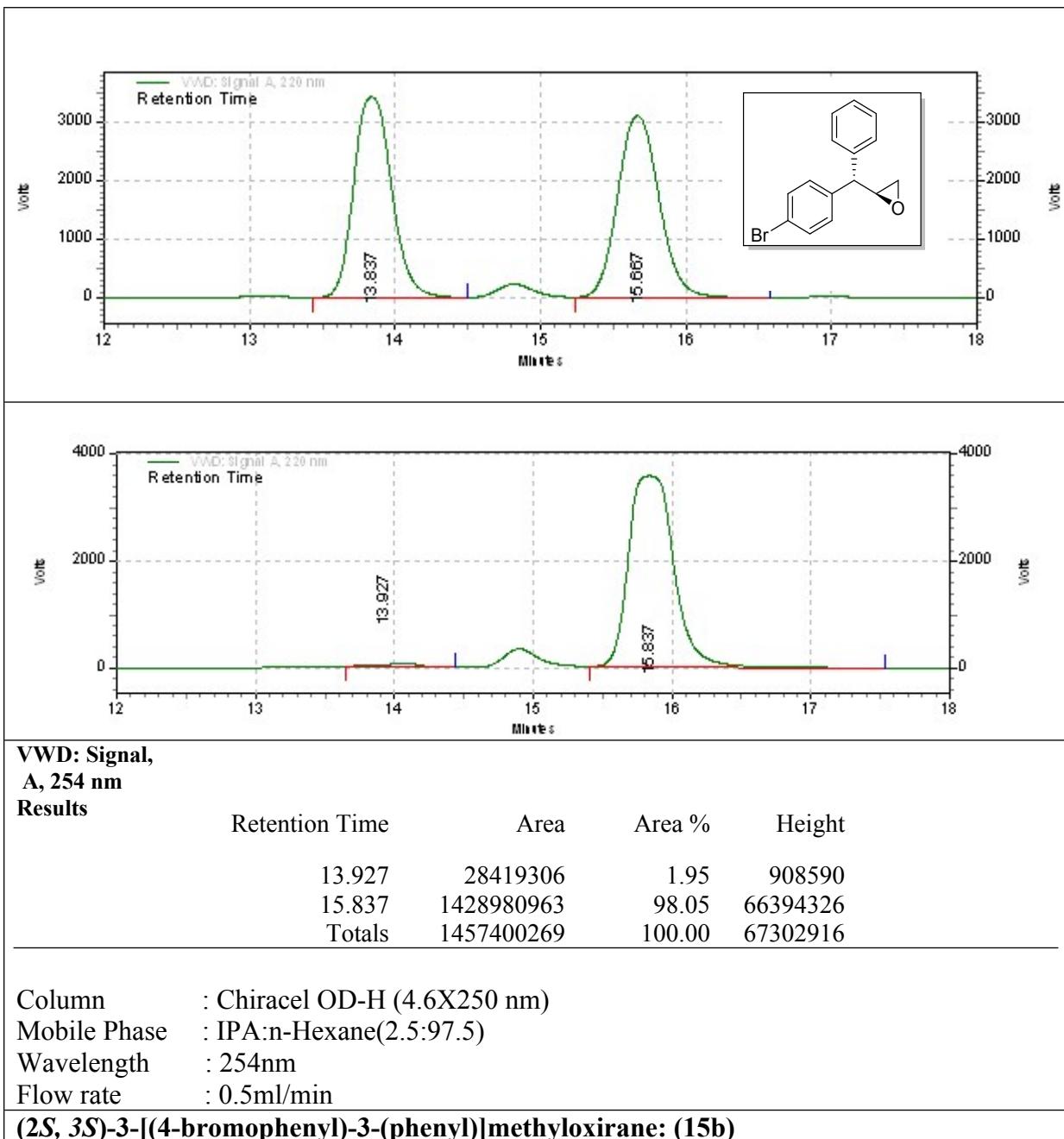


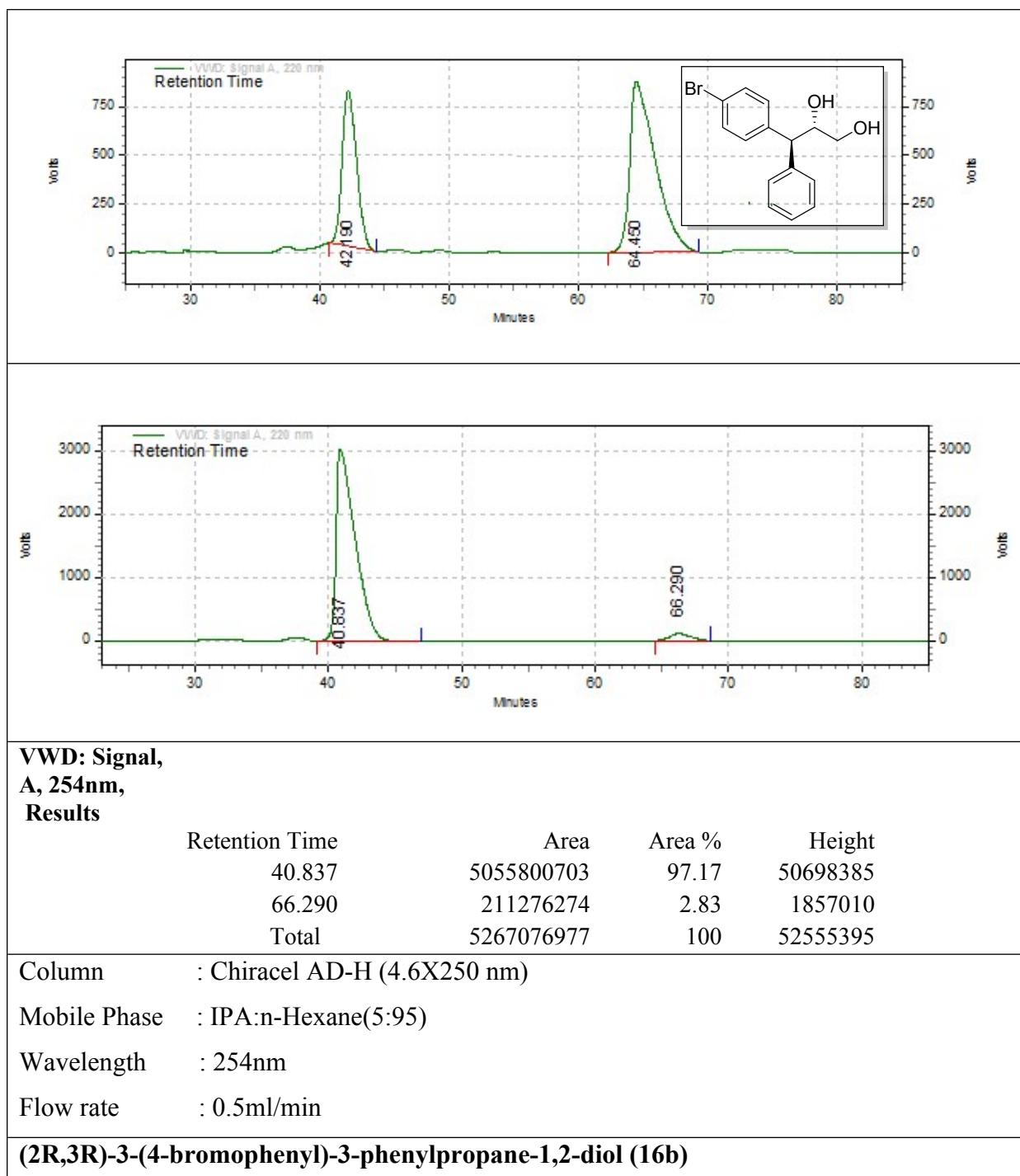


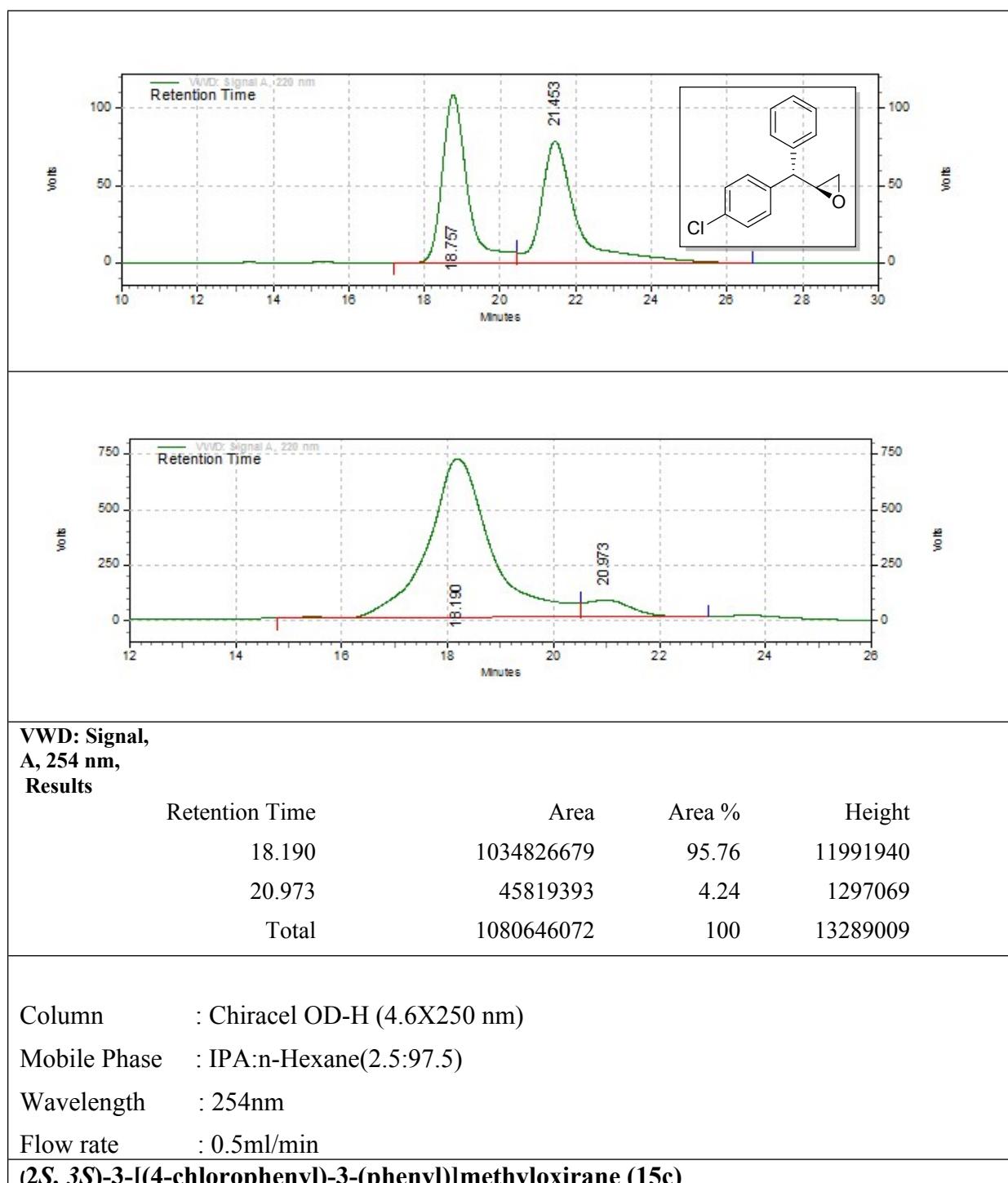


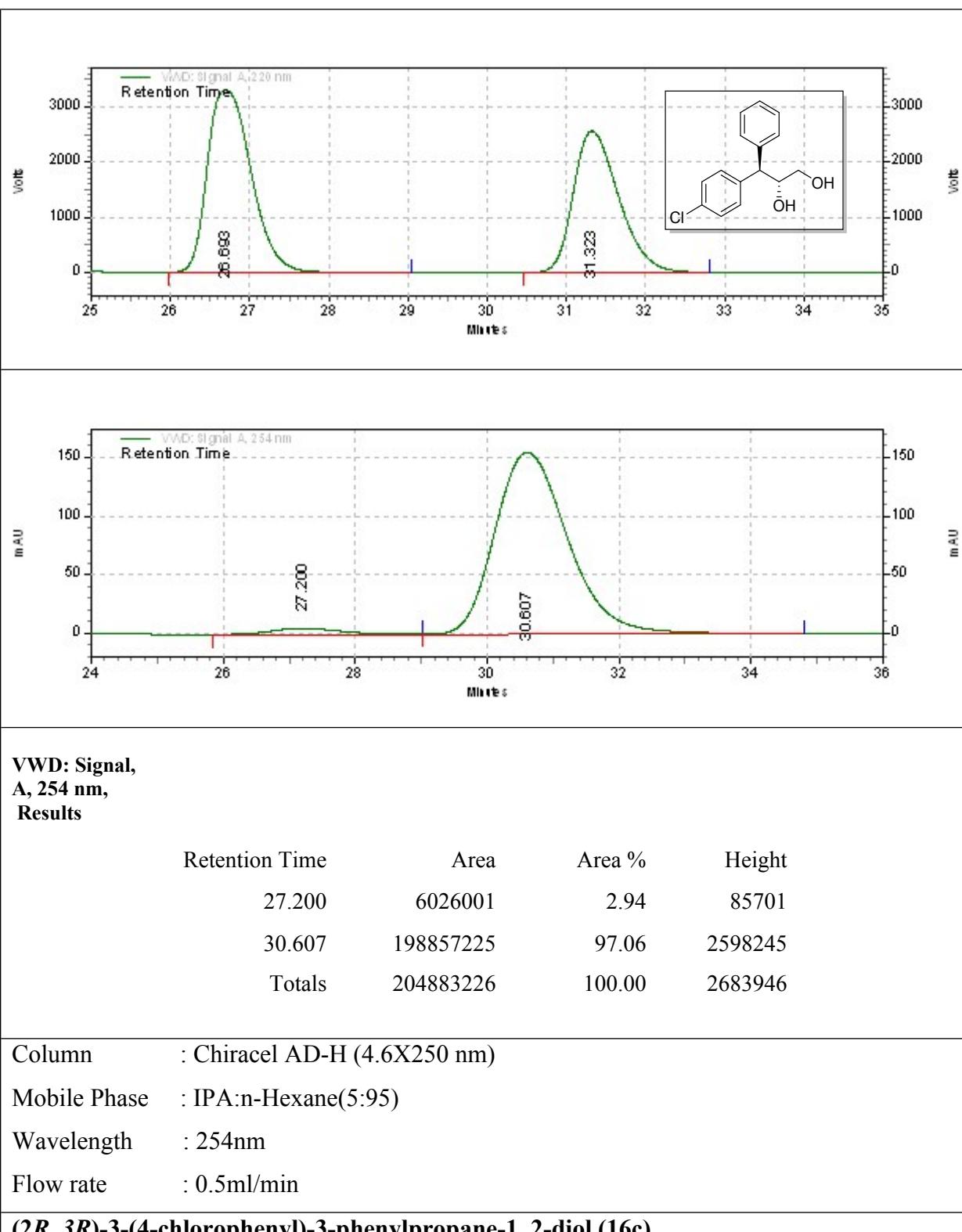


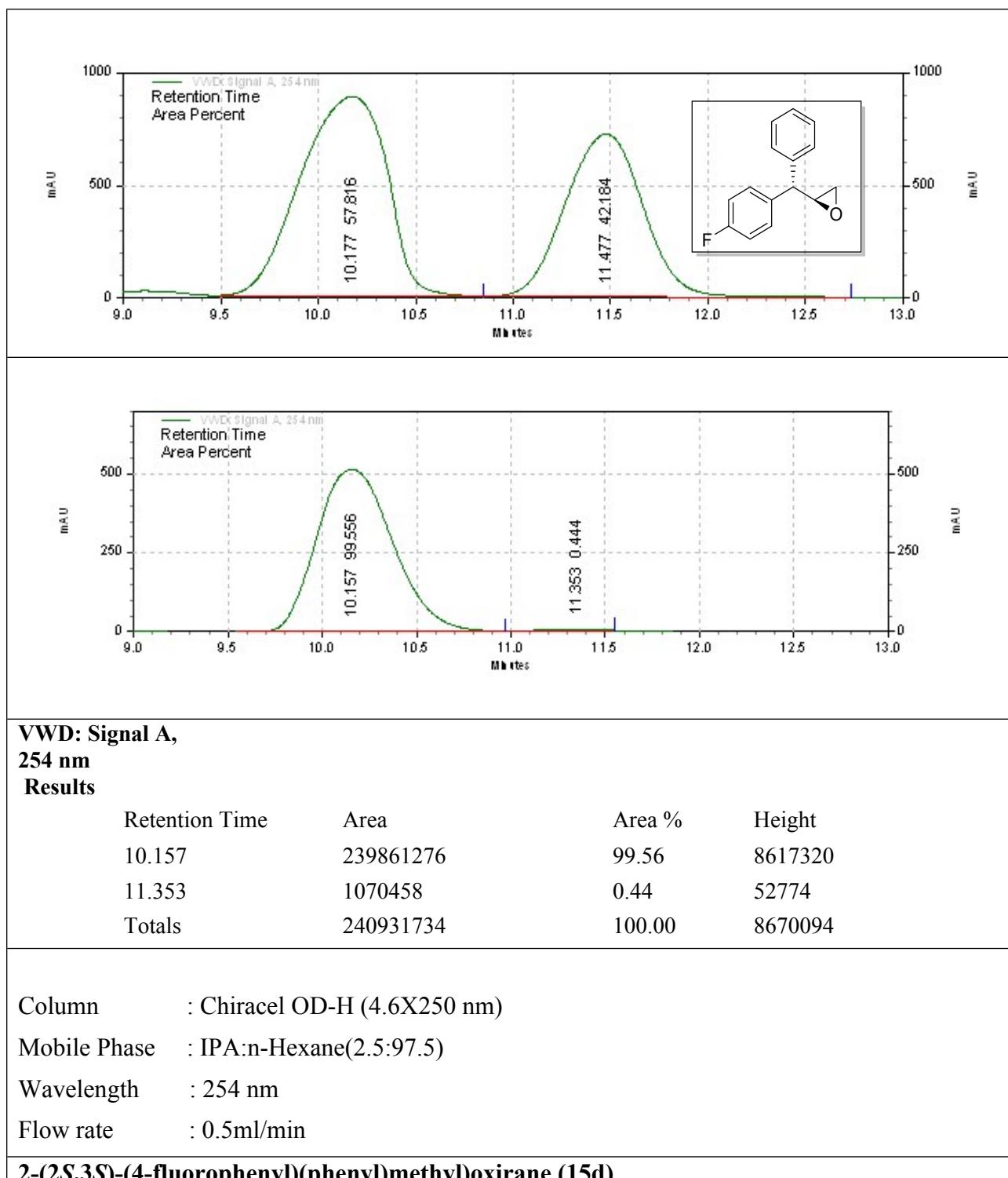


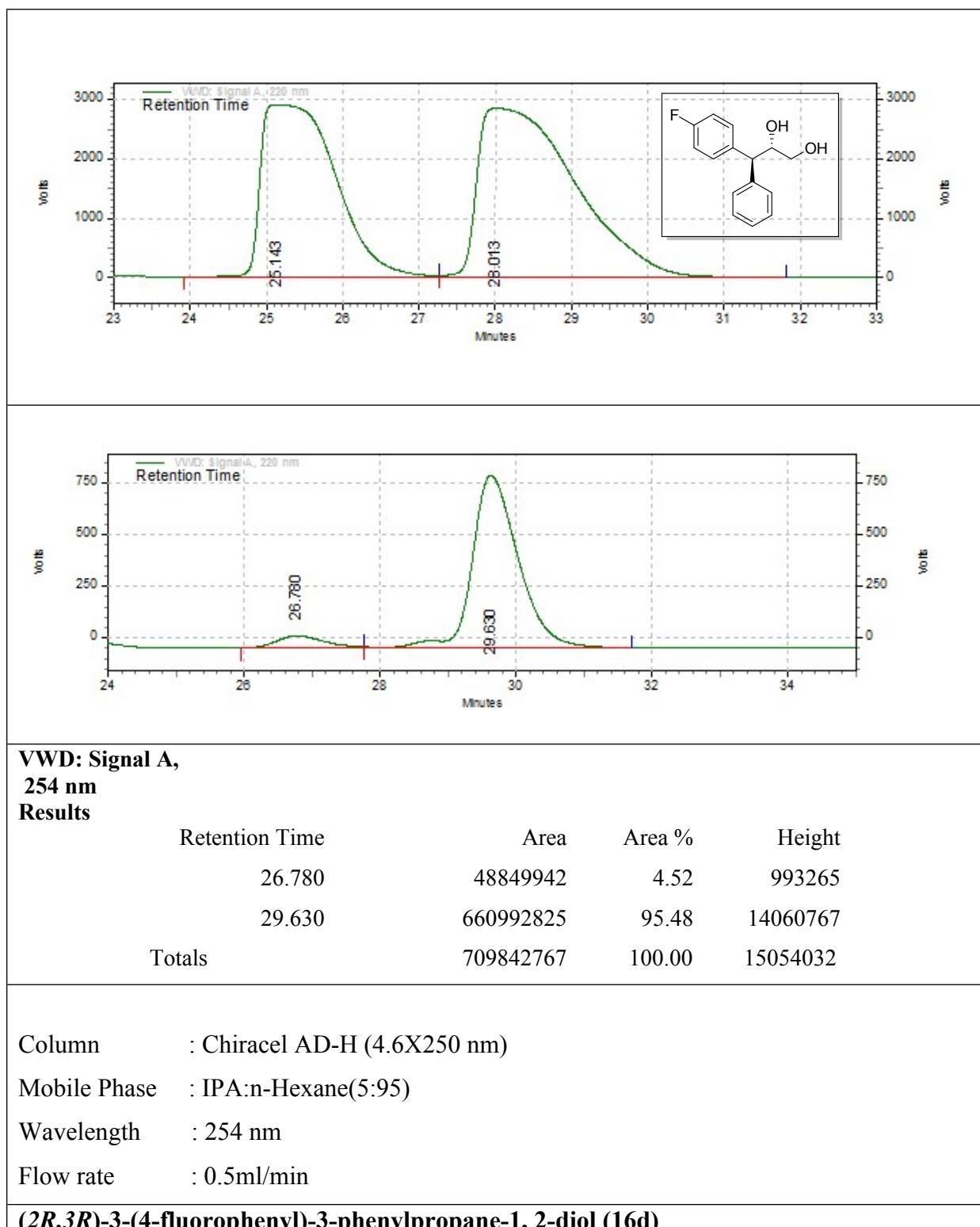


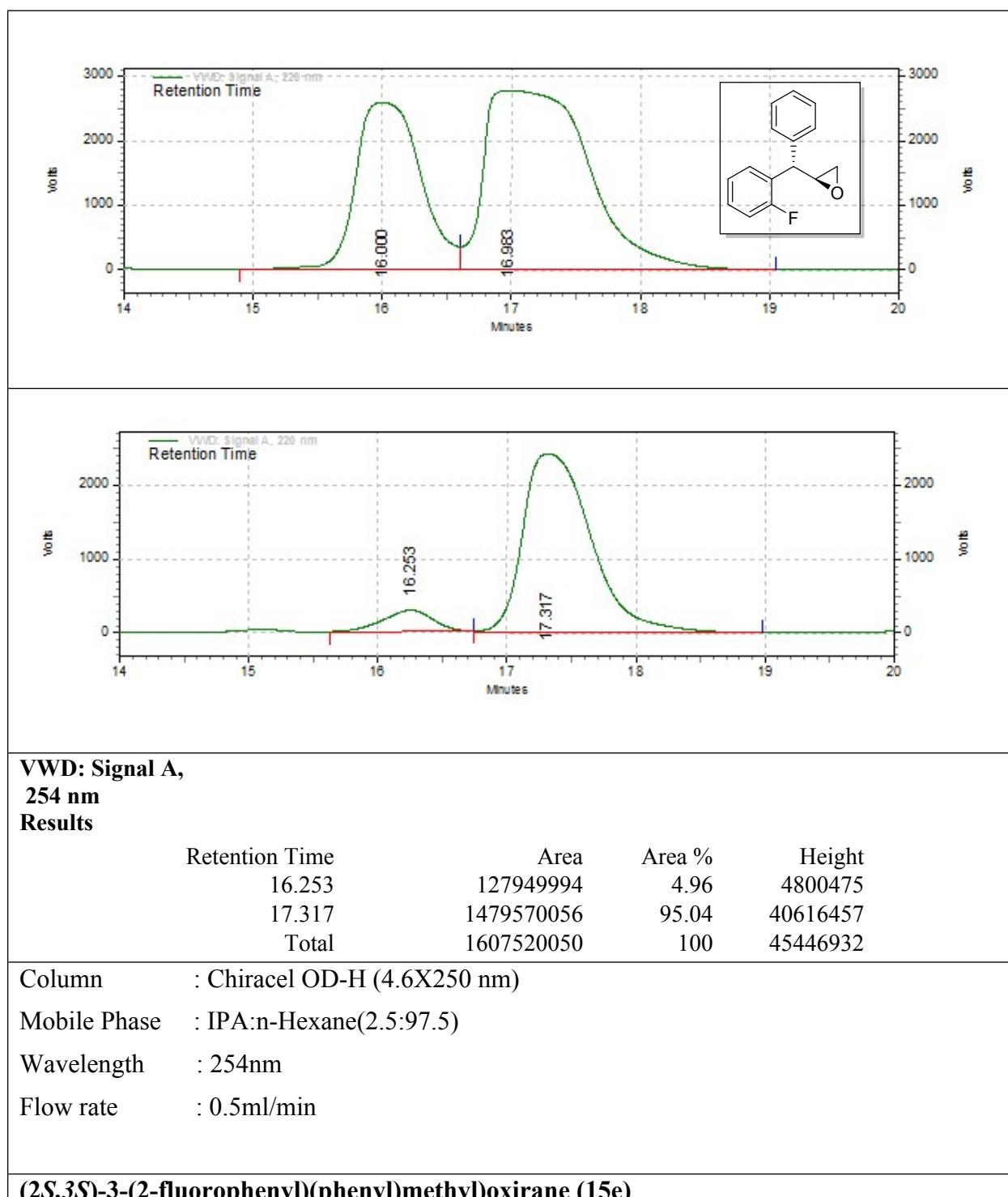


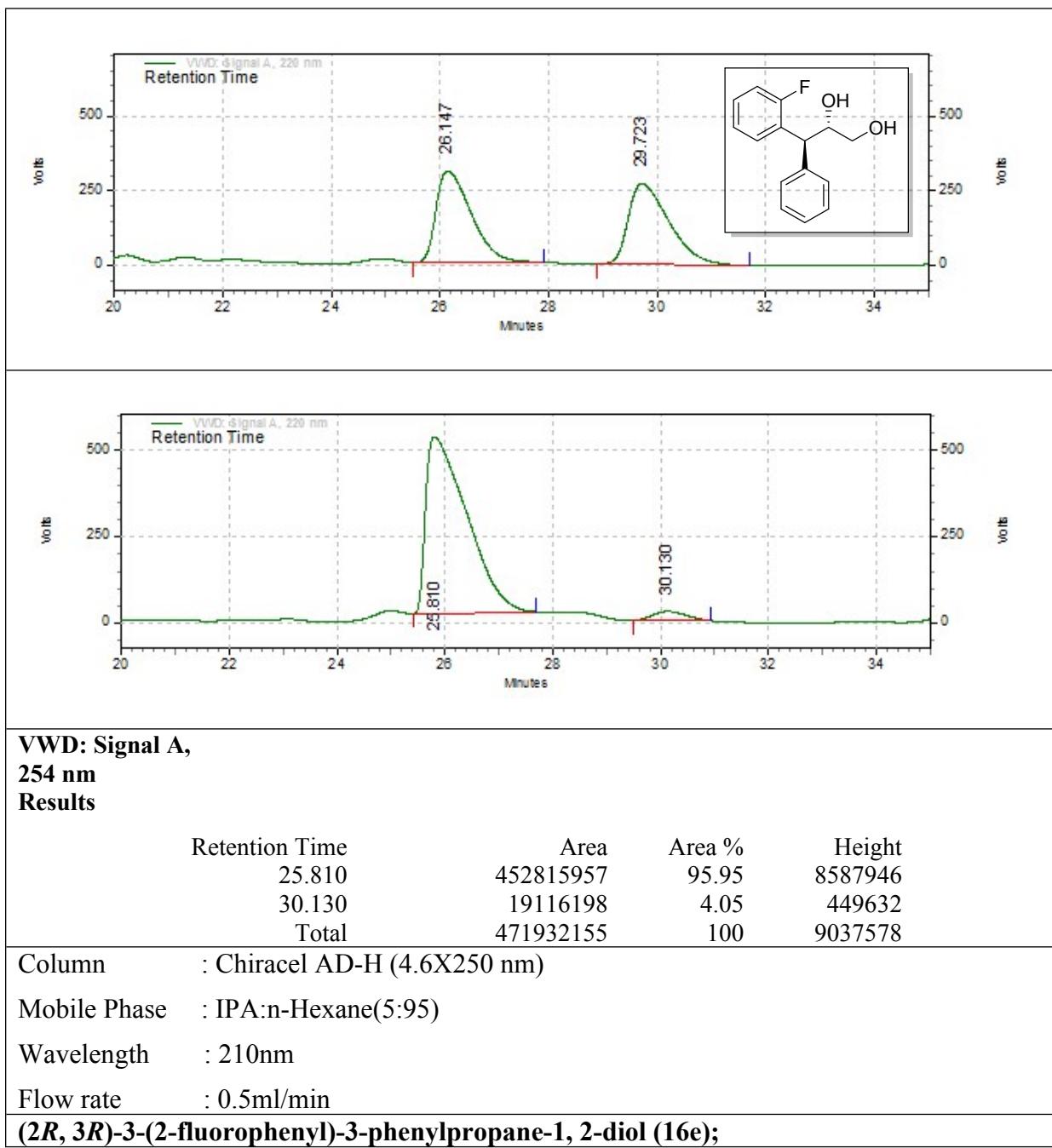


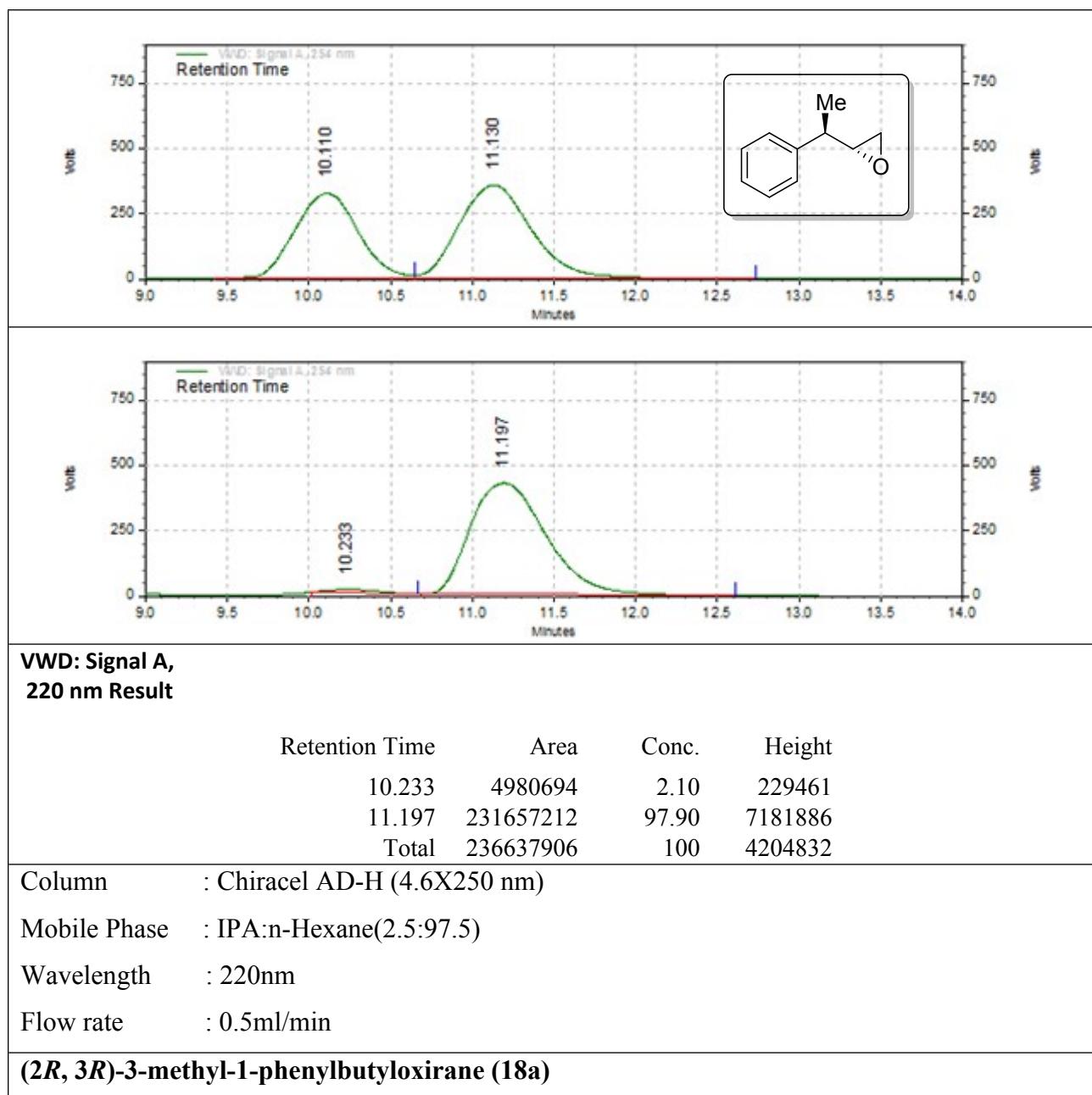


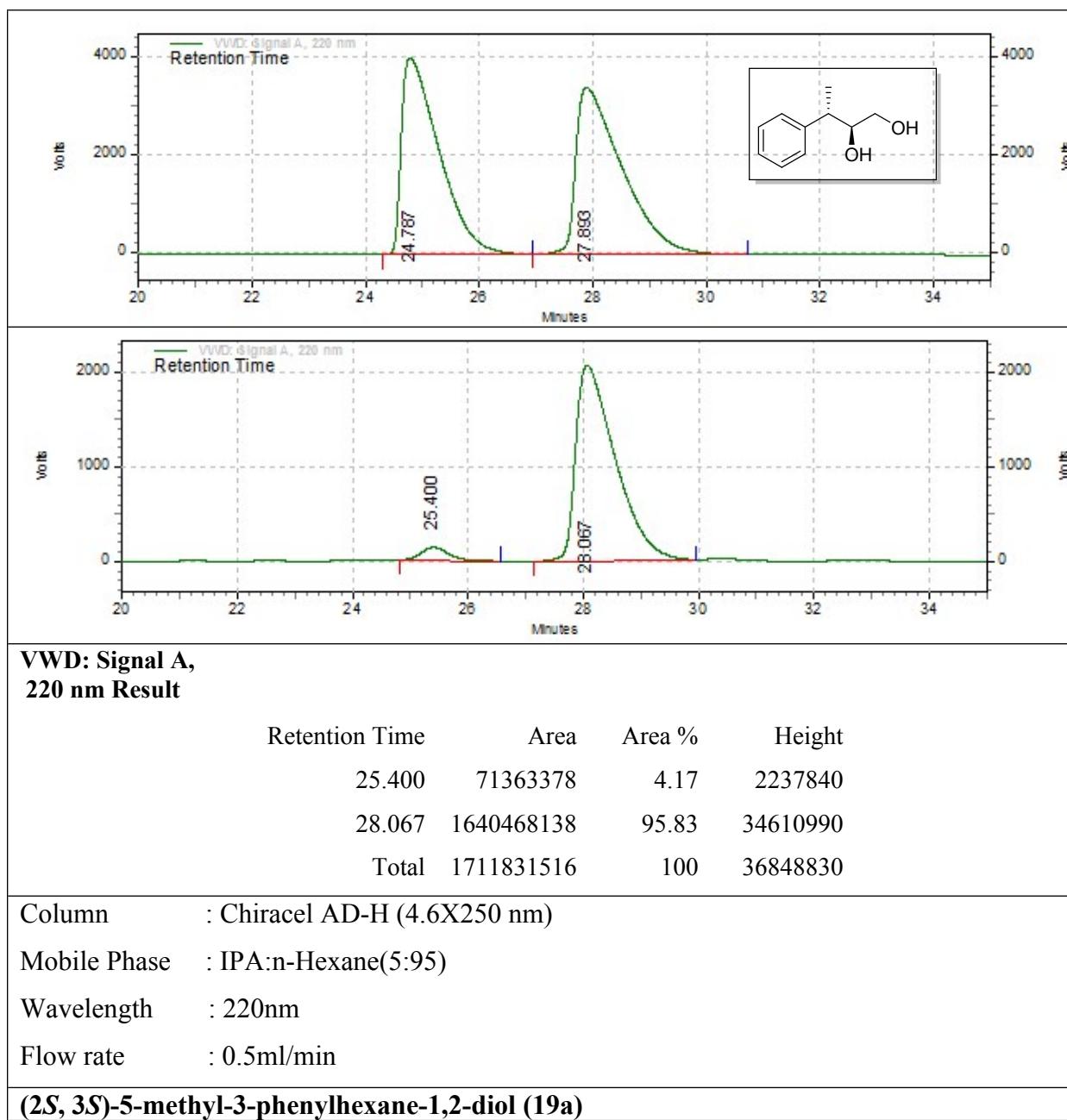


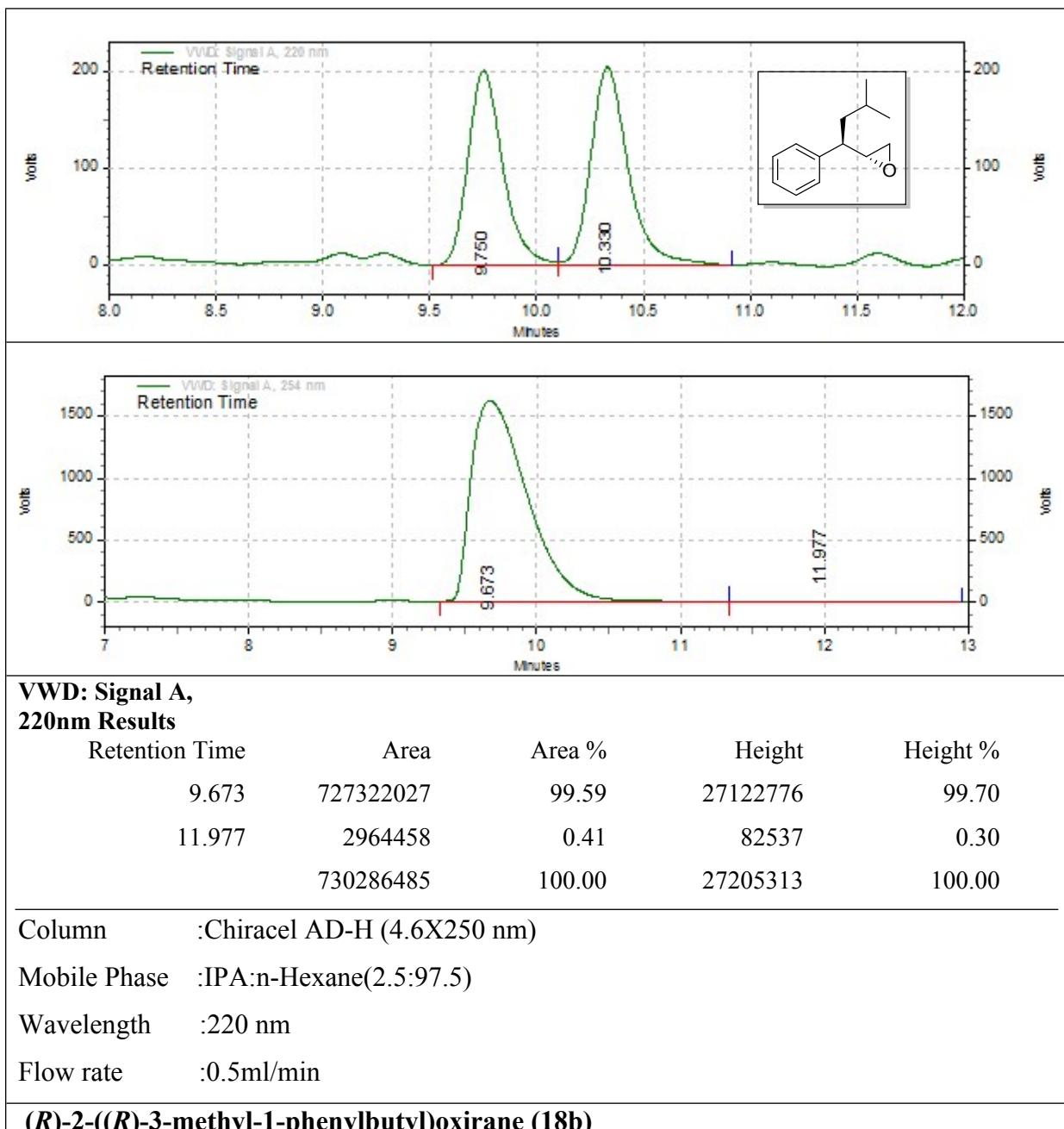


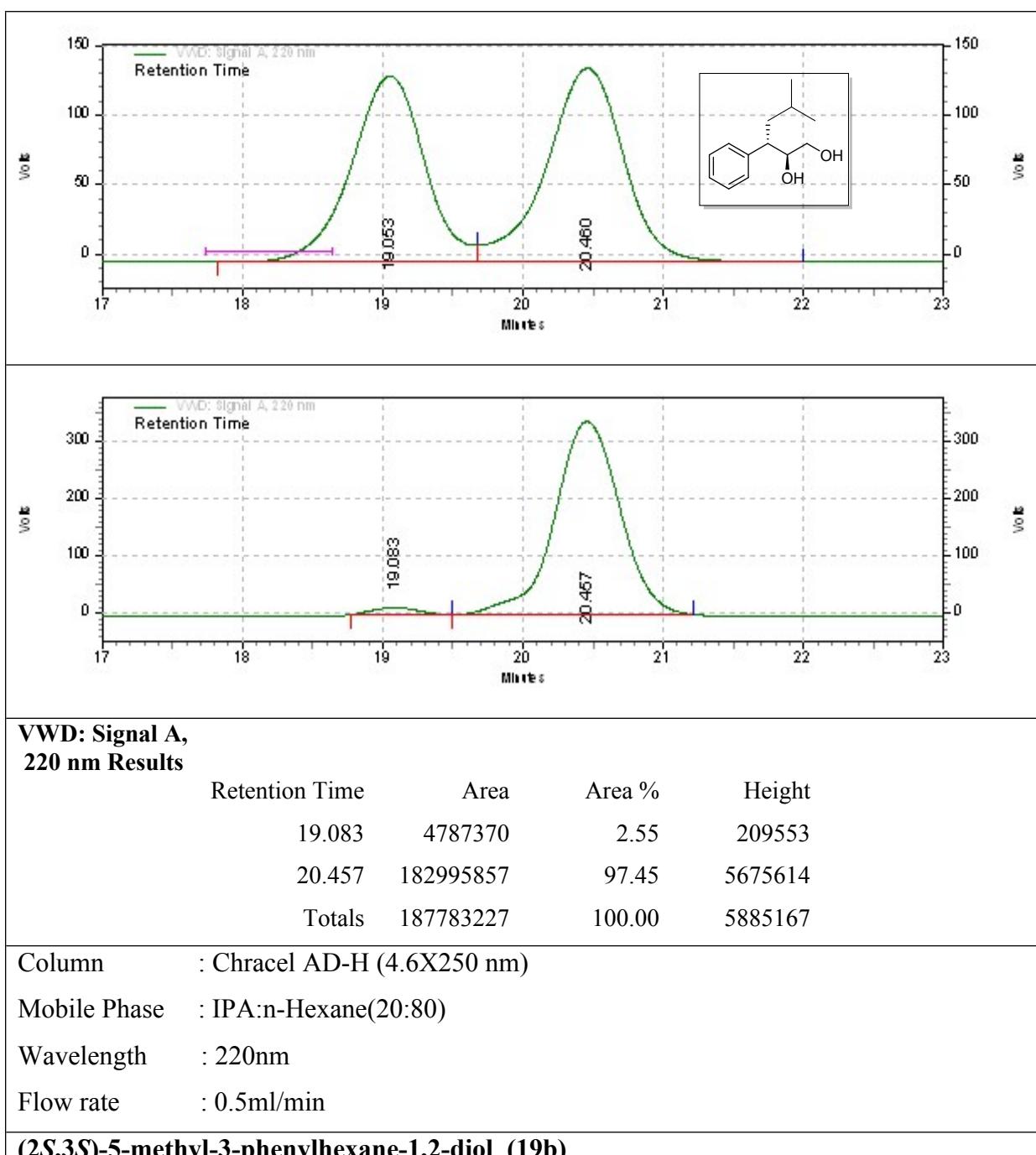


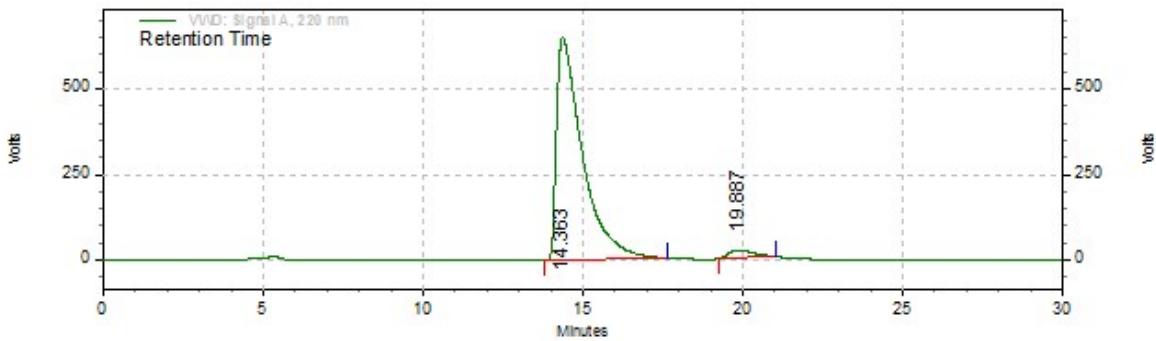
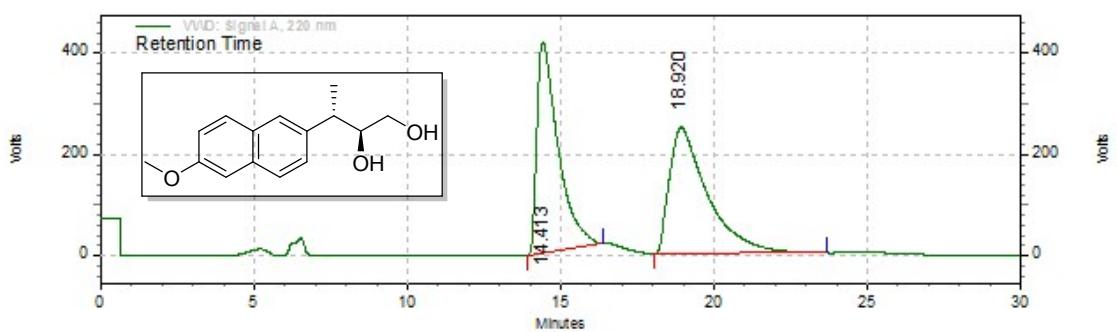












**VWD: Signal A,
220 nm Results**

Retention Time	Area	Conc.	Height
14.363	612546105	96.72	10911976
19.887	20741660	3.28	374813
Total	63287765	100	11286789

Column : Chiracel AD-H (4.6X250 nm)

Mobile Phase : IPA:n-Hexane(2.5 :97.5)

Wavelength : 220nm

Flow rate : 0.5ml/min

(2R,3R)-3-(6-methoxynaphthalen-2-yl) ethyl oxirane (18c)

