FUNCTIONAL GROUP TOLERANT NICKEL-CATALYZED CROSS-COUPLING REACTION FOR ENANTIOSELECTIVE CONSTRUCTION OF 3^0 METHYL-BEARING STEREOCENTERS

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SUPPORTING INFORMATION

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I. GENERAL PROCEDURES

All reactions were set up under an atmosphere of N_2. All glassware was either oven or flame-dried prior to use. Dichloromethane (CH_2Cl_2), tetrahydrofuran (THF) and toluene (PhMe) were degassed with argon and then passed through two 4 x 36 inch columns of anhydrous neutral A-2 alumina (8 x 14 mesh; LaRoche Chemicals; activated under a flow of argon at 350 ºC for 12 h) to remove H_2O. All other solvents were purchased "anhydrous" commercially, or purified as

described (vide infra). Flash chromatography was performed using Silica Gel 60 (170-400 mesh) from Fisher Scientific or silver-impregnated silica gel.[1] Analytical thin-layer chromatography (TLC) was performed using Silica Gel 60 F254 precoated plates (0.25 mm thickness). Visualization was accomplished by irradiation with a UV lamp and/or staining with *p*-anisaldehyde (PAA), cerium-ammonium-molybdate (CAM), or potassium permanganate ($KMnO_4$) solutions. Melting points (mp) were obtained using a Mel-Temp melting point apparatus and are uncorrected. ^{1}H NMR spectra were recorded on Bruker GN-500 (500 MHz ^{1}H, 125.7 MHz ^{13}C), CRYO-500 (500 MHz ^{1}H, 125.7 MHz ^{13}C), DRX-400 (400 MHz ^{1}H, 100 MHz ^{13}C, 376.5 MHz ^{19}F) spectrometers. Proton chemical shifts are reported in ppm (δ) relative to internal tetramethylsilane (TMS, δ 0.00). Data is reported as follows: chemical shift, multiplicity [singlet (s), broad singlet (br s), doublet (d), triplet (t), quartet (q), pentet (p), doublet of doublets (dd), broad doublet of doublets (br dd), doublet of triplets (dt), doublet of quartets (dq), doublet of pentets (dp), doublet of doublet of doublets (ddd), doublet of triplet of doublets (dtd), doublet of doublet of doublets of doublets (dddd), triplet of doublets (td), triplet of triplets (tt), quartet of doublets (qd), apparent triplet (at), apparent pentet (ap), apparent sextet (as), apparent doublet of doublets (add), apparent pentet of doublets (apd), multiplet (m)], coupling constants [Hz], integration. Carbon chemical shifts are reported in ppm (δ) relative to the respective solvent resonance as the internal standard ($CDCl_3$, δ 77.16 ppm). Unless otherwise indicated, NMR data were collected at 25 ºC. Infrared spectra were obtained on a Thermo Scientific Nicolet iS5 spectrometer with an iD5 ATR tip (neat) and are reported in terms of frequency of absorption (cm $^{-1}$). High-resolution mass spectrometry was performed by the University of California, Irvine Mass Spectrometry Center. Optical rotations were measured with a Rudolph Research Analytical Autopol III Automatic Polarimeter. SFC determinations of enantiopurity were performed on a Berger Analytical instrument using a Daicel™ Chiralpak® column (AS-H, AD-H, OD-H, or OJ-H; 100 psi, 215 nm, 50 °C).

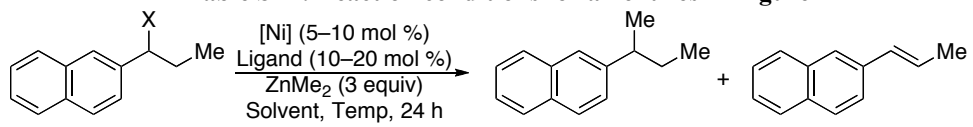
All Grignard and zinc reagents were titrated with iodine prior to use.[2] Activated manganese oxide was prepared according to a procedure reported by Attenburrow.[3] [{(*R*)-H_8-BINOLate}Ti(O*i*-Pr)$_2$]$_n$ **SI 24** (0.13 g, 0.28 mmol, 0.10 equiv) was prepared according to a procedure reported by Walsh.[4] 2-naphthyltitanium triisopropoxide **SI 25** was prepared according to a procedure reported by Gau.[5] 2-(Methylthio)acetic acid **51** was prepared according to a procedure reported by Pan.[6] 2-(Methylthio)acetic acid is also commercially available. Grignard reagent **SI 35** was prepared according to a procedure reported by Normant.[7] 4-Hydroxybutyl benzoate **SI 42** was prepared according to a procedure reported by Carotti.[8] 3-Morpholinopropyl chloride **SI 44** was prepared according to Tung.[9] 1-Tosyl-1*H*-indole-3-carboxaldehyde **SI 50** was prepared according to a procedure reported by Carreira.[10] (*S*)-(1-tritylaziridin-2-yl)diphenylmethanol **49** was prepared according to a procedure by Braga.[11] 2-(benzoylthio)acetic acid **SI 58** and 2-(benzoylthio)-2-methylpropanoic acid **SI 59** were prepared according to a procedure reported by Eisenhut.[12] Methyl 6-formyl-2-naphthoate **47** was prepared according to a procedure reported by Diaz.[13] Benzo[b]thiophen-2-yllithium **54** was prepared according to a procedure reported by Denis.[14] All other reagents were purchased commercially and used as received.

II. EXPERIMENTAL

A. A COMPLETE LIST OF CONDITIONS FOR FIGURE 2

Many experiments were performed with each activating group presented in the paper. The results in Figure 2 of the main document represent the optimal results for each directing group. Table SI 1 comprises the exact conditions for each reaction.

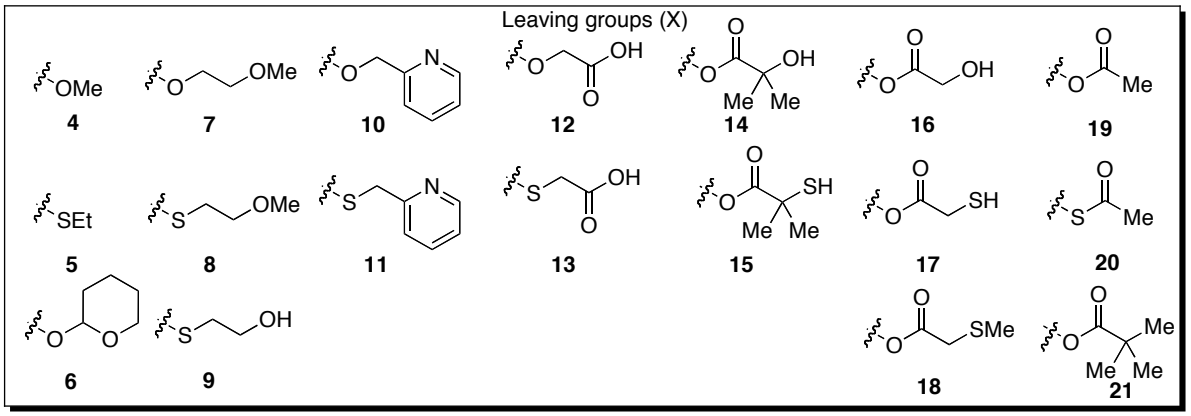
Table SI 1. Reaction conditions for all entries in Figure 2



4–21 **22** **23**

Entry	Starting Material	Yield **22** (%)[a]	es[b]	Yield **23** (%)[a]	Ni source (x equiv)	Ligand (2x)	Solvent	Temp (°C)
1[c]	**4**	0	ND	0	$Ni(cod)_2$ (0.05)	DPEphos	PhMe	100
2	**5**	13	ND	41	$Ni(cod)_2$ (0.05)	Xantphos	PhMe	50
3	**6**	0	ND	0	$Ni(cod)_2$ (0.05)	rac-BINAP	PhMe	rt
4	**7**	0	ND	0	$Ni(cod)_2$ (0.05)	DPEphos	PhMe	rt
5	**8**	6	ND	7	$Ni(cod)_2$ (0.05)	DPEphos	PhMe	50
6	**9**	58	58	38	$Ni(cod)_2$ (0.05)	DPEphos	PhMe	50
7	**10**	51	86	7	$NiCl_2$•DME (0.10)	*rac*-BINAP	PhMe	rt
8	**11**	41	27	44	$NiCl_2$•DME (0.10)	*rac*-BINAP	PhMe	rt
9	**12**	70	27	13	$NiCl_2$•DME (0.10)	*rac*-BINAP	PhMe	rt
10	**13**	60	67	21	$Ni(cod)_2$ (0.05)	DPEphos	PhMe	rt
11	**14**	59	97	18	$Ni(acac)_2$ (0.10)	DPEphos	THF	rt
12	**15**	67	98	18	$NiCl_2$•DME (0.10)	DPEphos	Et_2O	rt
13	**16**	71	79	27	$NiCl_2$•DME (0.10)	DPEphos	PhMe	rt
14	**17**	62	99	13	$NiCl_2$•DME (0.10)	DPEphos	THF	rt
15	**18**	75	99	20	$NiCl_2$•DME (0.10)	DPEphos	PhMe	rt
16	**19**	79	61	13	$NiCl_2$•DME (0.10)	DPEphos	PhMe	rt
17	**19**	62	98	28	$NiCl_2$•DME (0.10)	Xantphos	PhMe	rt
18	**20**	48	ND	8	$NiCl_2$•DME (0.10)	DPEphos	PhMe	rt
19	**21**	84	87	15	$NiCl_2$•DME (0.10)	DPEphos	PhMe	rt
20	**21**	45	99	28	$NiCl_2$•DME (0.10)	Xantphos	PhMe	rt

[a]Yields determined by ^1H NMR with PhTMS as internal standard or by GC analysis with dodecane as the internal standard; [b]enantiospecificity (es) = (ee of the product)/(ee of the starting material); [c]Reaction run with 1.0 equiv of $MgBr_2$

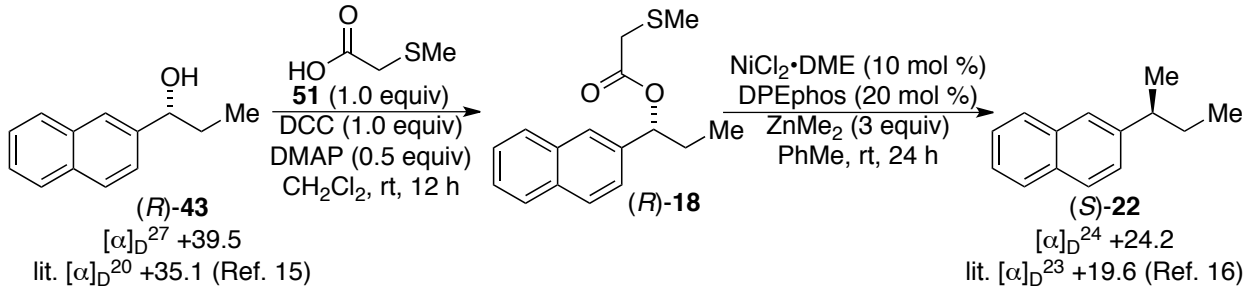


B. STEREOCHEMICAL PROOFS

The absolute configurations of the products of cross-coupling reactions were assigned for five examples. Those experiments are summarized below. In all five examples, we confirm that the cross-coupling reaction proceeds with inversion. For full experimental details of synthesis of starting materials, cross-coupling reactions, and derivatization of products, including full characterization for all of these compounds, please see subsequent sections of this document.

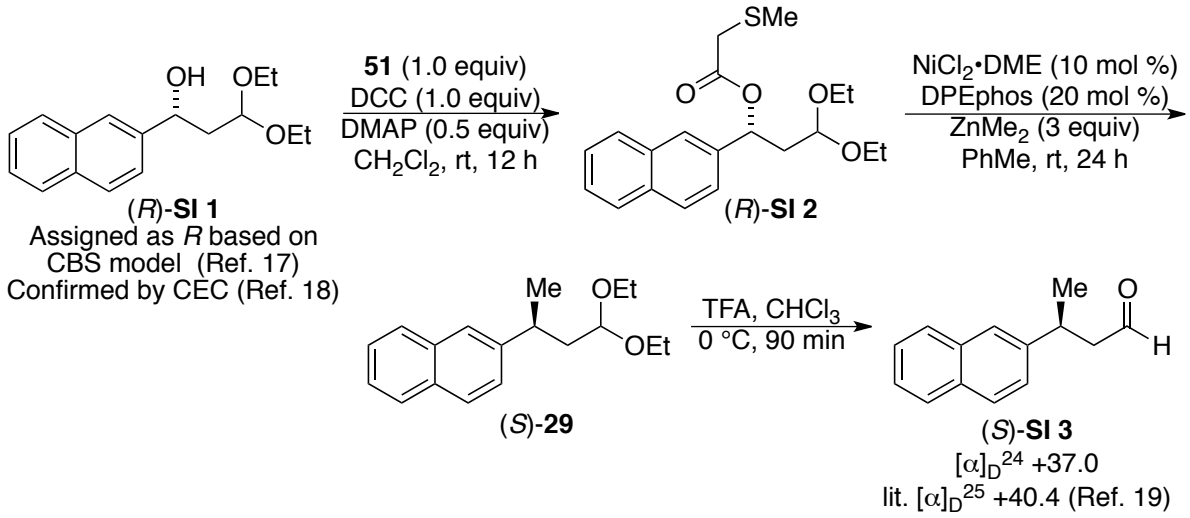
The absolute configurations of all other products were assigned based on the assumption that the cross-coupling reaction proceeds with inversion. These assignments are summarized in Table SI 2. Table SI 2 also summarizes how the absolute configuration of each alcohol was assigned; full experimental details, including characterization data, are provided in Section F.

Scheme SI 1. Stereochemical Course of the Cross-Coupling Reaction



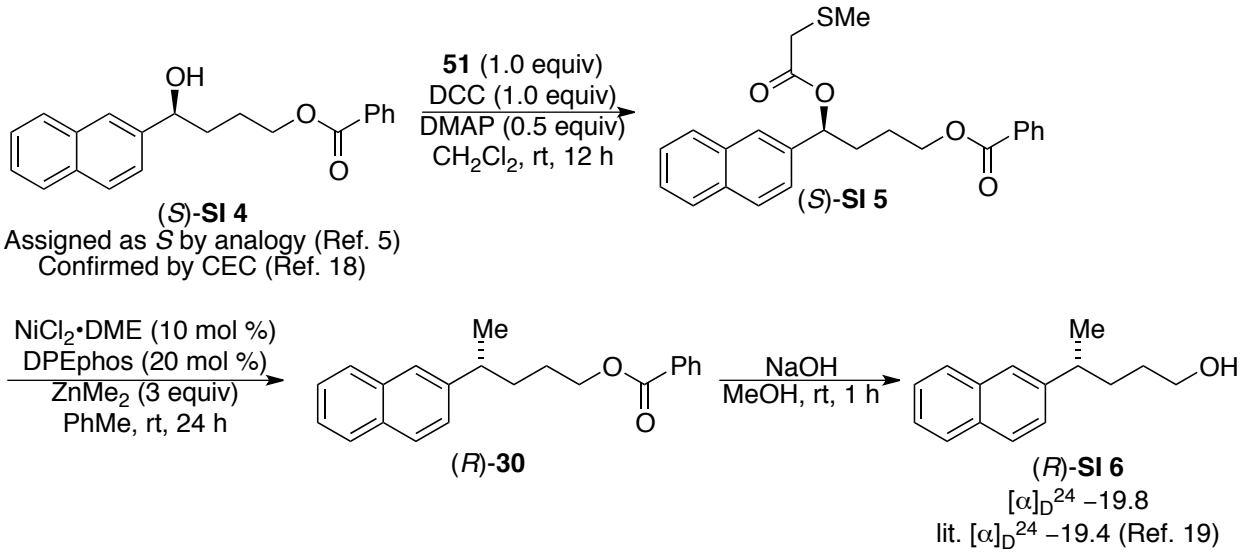
Enantioenriched alcohol (*R*)-**43** was prepared by enantioselective alkylation (vida infra) and the stereochemistry was verified by comparison of the optical rotation to the literature value.[15] Conversion to ester (*R*)-**18**, followed by stereospecific cross-coupling produced (*S*)-**22**, the stereochemistry of which was determined by comparison of the optical rotation to the literature value.[16] This product corresponds to net inversion in the cross-coupling reaction.

Scheme SI 2. Stereochemical Course of the Cross-Coupling Reaction



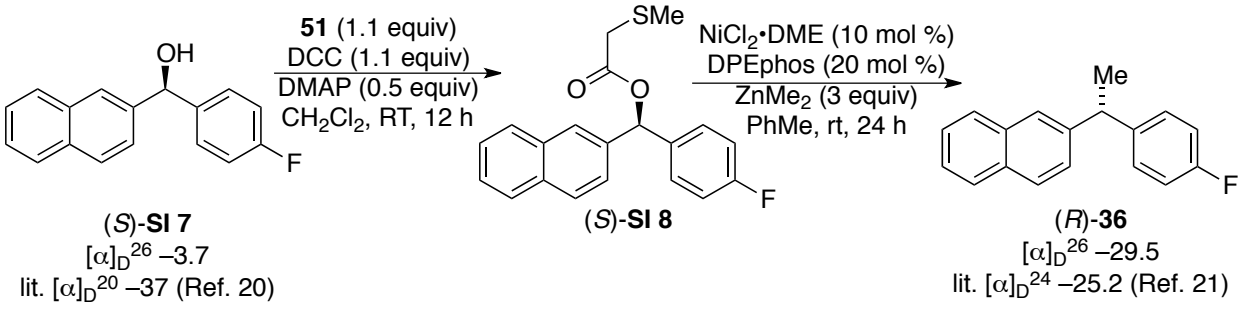
Enantioenriched alcohol (*R*)-**SI 1** was prepared by enantioselective CBS reduction (vida infra). Absolute configuration was assigned based on the accepted model for selectivity in CBS reductions[17] and confirmed by Competing Enantioselective Conversion (CEC).[18] Conversion to ester (*R*)-**SI 2**, followed by stereospecific cross-coupling produced (*S*)-**29**. The acetal was then removed to reveal aldehyde (*S*)-**SI 3**, the stereochemistry of which was determined by comparison of the optical rotation to the literature value.[19] This product corresponds to net inversion in the cross-coupling reaction.

Scheme SI 3. Stereochemical Course of the Cross-Coupling Reaction



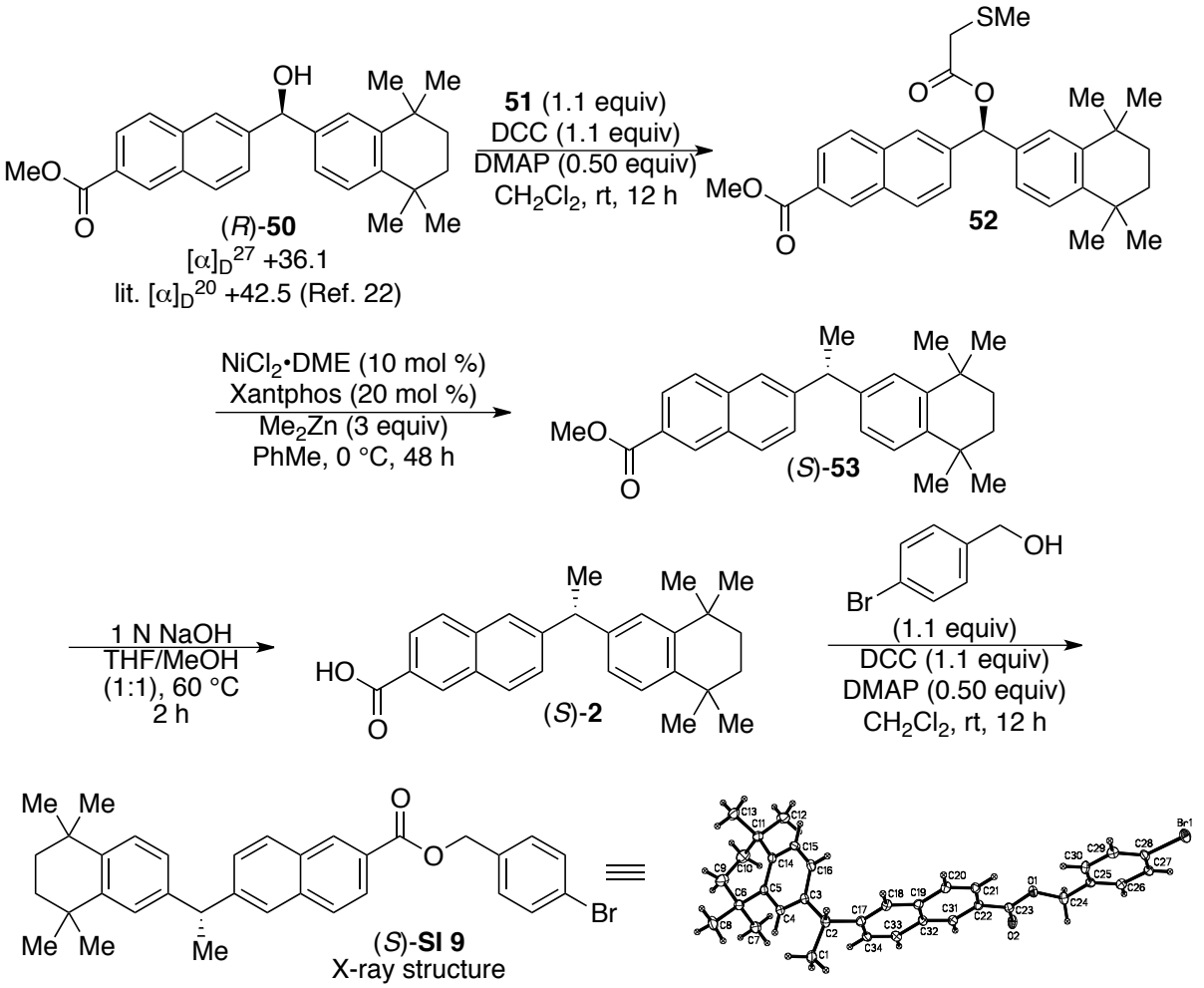
Enantioenriched alcohol (*S*)-**SI 4** was prepared by enantioselective titanium-catalyzed arylation (vida infra). Absolute configuration assigned as *S* by analogy to similar compounds synthesized by Gau[5] and confirmed by Competing Enantioselective Conversion (CEC).[18] Conversion to ester (*S*)-**SI 5**, followed by stereospecific cross-coupling produced (*R*)-**30**. The benzoyl protecting group was then removed to reveal alcohol (*S*)-**SI 6**, the stereochemistry of which was determined by comparison of the optical rotation to the literature value.[19] This product corresponds to net inversion in the cross-coupling reaction.

Scheme SI 4. Stereochemical Course of the Cross-Coupling Reaction



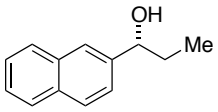
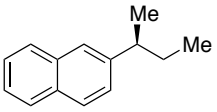
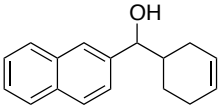
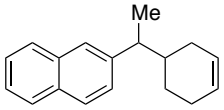
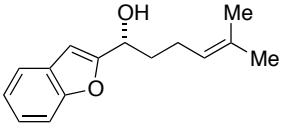
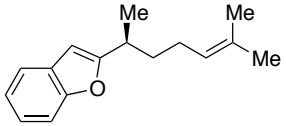
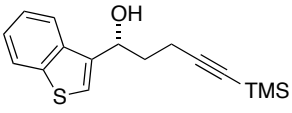
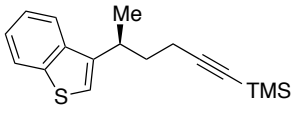
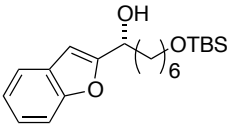
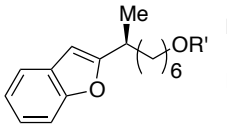
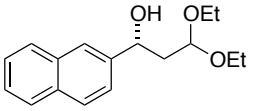
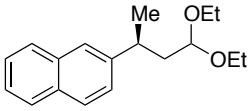
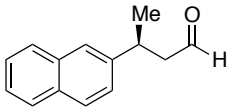
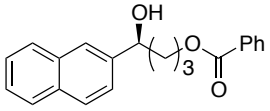
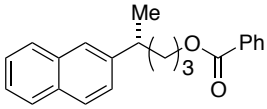
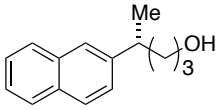
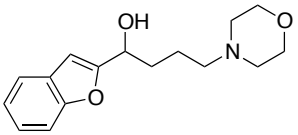
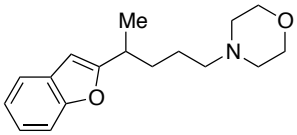
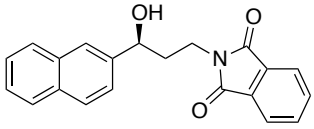
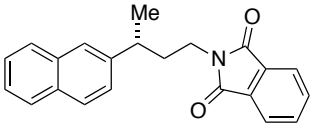
Enantioenriched alcohol (*S*)-**SI 7** was prepared by enantioselective arylation (vida infra) and the stereochemistry was verified by comparison of the optical rotation to the literature value.[20] Conversion to ester (*S*)-**SI 8**, followed by stereospecific cross-coupling produced (*R*)-**36**, the stereochemistry of which was determined by comparison of the optical rotation to the literature value.[21] This product corresponds to net inversion in the cross-coupling reaction.

Scheme SI 5. Stereochemical Course of the Cross-Coupling Reaction



Enantioenriched alcohol (*R*)-**50** was prepared by enantioselective arylation (vida infra) and the stereochemistry was verified by comparison of the optical rotation to the literature value.[22] Conversion to ester (*R*)-**52**, followed by stereospecific cross-coupling produced (*S*)-**53**. Transesterification over two steps afforded (*S*)-**SI 9**, the absolute configuration of which was determined by X-ray crystallography. See Section IV for crystallographic data. This product corresponds to net inversion in the cross-coupling reaction.

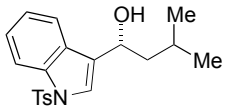
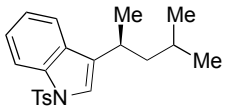
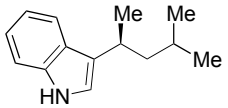
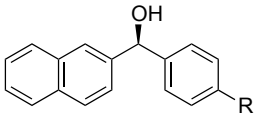
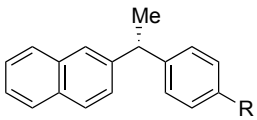
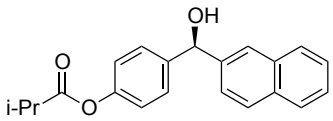
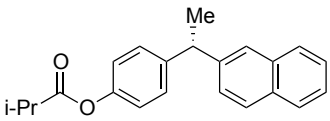
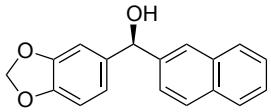
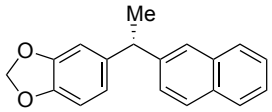
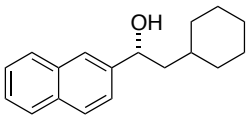
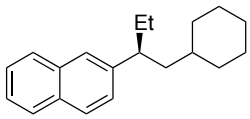
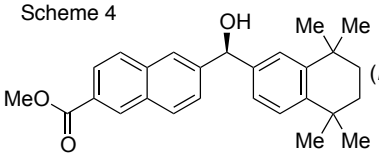
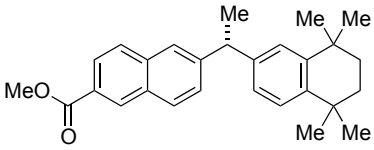
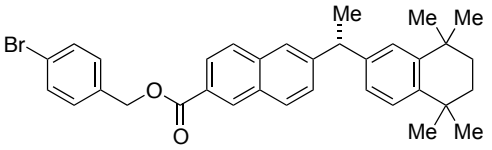
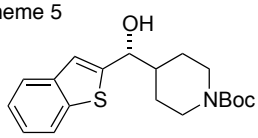
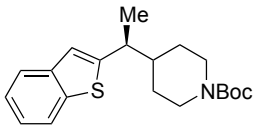
Table SI 2. Configuration of Starting Materials and Products

Alcohol		Configuration[a] Assigned by:	Product		Configuration[b] Assigned by:
Table 1					
	(*R*)-**43**	*R* (+) lit $[\alpha]_D$		(*S*)-**22**	*S* (+) lit $[\alpha]_D$
	**SI 10**	*racemic*		**24**	*racemic*
	(*R*)-**SI 11**	*R* (–) CBS model CEC confirm		**25**	*S* (+) by analogy
	(*R*)-**SI 12**	*R* (–) CBS model CEC confirm		**26**	*S* (+) by analogy
	(*R*)-**SI 13**	*R* (+) CBS model CEC confirm		R' = TBS **27** R' = H **28**	*S* (+) by analogy *S* (+) by analogy
	(*R*)-**SI 1**	*R* (+) CBS model CEC confirm		(*S*)-**29**	*S* (+) lit $[\alpha]_D$ of derivative
				(*S*)-**SI 3**	*S* (+) lit $[\alpha]_D$
	(*S*)-**SI 4**	*S* (–) analogy to Ti arylation CEC confirm		(*R*)-**30**	*R* (–) lit $[\alpha]_D$ of derivative
				(*R*)-**SI 6**	*R* (–) lit $[\alpha]_D$
	**SI 14**	*racemic*		**31**	*racemic*
	(*S*)-**SI 15**	*S* (–) analogy to Ti arylation CEC confirm		**32**	*R* (–) by analogy

[a]For optical rotation for each compound, see the characterization data. For CBS model, see Ref. 17. For Competing Enantioselective Conversion (CEC), see Ref. 18. For Ti-catalyzed arylation of alkyl aldehydes, see Ref. 5. For Zn-mediated arylation of aryl aldehydes, see Ref. 11.

[b]For optical rotation for each compound, see the characterization data. In the absence of known optical rotations, the absolute configurations of products were assigned based on the assumption that the cross-coupling reaction proceeds with inversion. This is by analogy to the compounds in the stereochemical proof section (Schemes SI 1-5).

Table SI 2 Continued

Alcohol	Configuration[a] Assigned by:	Product	Configuration[a] Assigned by:
Scheme 3			
	(*R*)-**SI 16** *R* CBS model	 **34**	*S* (+) by analogy
		 **SI 17**	*S* (–) by analogy
Table 2			
 R = H (S)-**SI 18** *S* (–) lit $[\alpha]_D$ R = F (*S*)-**SI 7** *S* (–) lit $[\alpha]_D$ R = CF_3 (*S*)-**SI 19** *S* (–) lit $[\alpha]_D$ R = OMe (*S*)-**SI 20** *S* (+) analogy to Zn arylation		 R = H **35** *R* (–) lit $[\alpha]_D$ R = F (*R*)-**36** *R* (–) lit $[\alpha]_D$ R = CF_3 **37** *R* (–) by analogy R = OMe **38** *R* (–) by analogy
	(*R*)-**SI 21** *R* (–) analogy to Zn arylation		**39** *S* (+) by analogy
	(*R*)-**SI 22** *S* (–) analogy to Zn arylation		**40** *R* (+) by analogy
Eq 1			
	(*R*)-**SI 23** *R* (+) CBS model CEC confirm		**45** *S* (+) by analogy
Scheme 4			
	(*R*)-**50** *R* (+) lit $[\alpha]_D$		(*S*)-**53** *S* (–) X-Ray of derivative
			(*S*)-**SI 9** *S* (–) X-Ray
Scheme 5			
	(*R*)-**56** *R* (–) CBS model CEC confirm		**58** *S* (+) by analogy

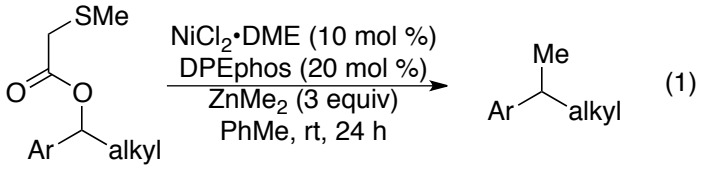
[a]For optical rotation for each compound, see the characterization data. For CBS model, see Ref. 17. For Competing Enantioselective Conversion (CEC), see Ref. 18. For Ti-catalyzed arylation of alkyl aldehydes, see Ref. 5. For Zn-mediated arylation of aryl aldehydes, see Ref. 11.

[b]For optical rotation for each compound, see the characterization data. In the absence of known optical rotations, the absolute configurations of products were assigned based on the assumption that the cross-coupling reaction proceeds with inversion. This is by analogy to the compounds in the stereochemical proof section (Schemes SI 1-5).

C. General Cross-Coupling Procedures

The general cross-coupling procedures will be used throughout the SI. Method A was used to couple singly benzylic substrates (Table 1). Method B was used to couple benzhydryl substrates (Table 2). Method C was used to couple diethylzinc (Scheme 3). In each instance the general method is used, it is specified by letter (A, B, or C) and the exact amounts of reagents used for each reaction are listed for the specific compounds synthesized.

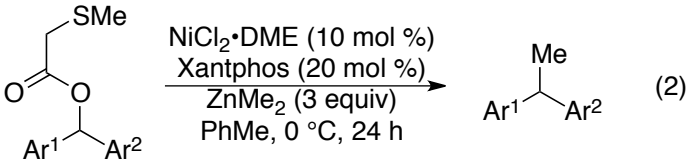
Method A: Cross-Coupling of Singly Benzylic Electrophiles (Table 1)



(1)

In a glovebox, a flame-dried 7 mL vial equipped with a stir bar was charged with $NiCl_2$•DME (0.10 equiv) and DPEphos (0.20 equiv). The reaction vial was capped with a screw-cap fitted with a septum and PhMe was added. After a 5 min pre-stir, substrate (1.0 equiv) was added and the reaction was removed from the glovebox. The reaction vial was equipped with a nitrogen line and allowed to stir for approximately 5 min. $ZnMe_2$ (3.0 equiv) was then added resulting in an immediate color change from slightly pink to dark orange. After 24 h, the reaction was quenched with isopropyl alcohol and filtered through a plug of silica gel (100% Et_2O).

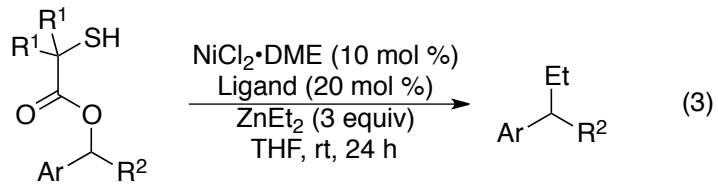
Method B: Cross-Coupling of Benzhydryl Electrophiles (Table 2)



(2)

In a glovebox, a flame-dried 7 mL vial equipped with a stir bar was charged with $NiCl_2$•DME (0.10 equiv) and Xantphos (0.20 equiv). The reaction vial was capped with a screw-cap fitted with a septum and PhMe was added. After a 5 min pre-stir, substrate (1.0 equiv) was added and the reaction was removed from the glovebox. The reaction vial was equipped with a nitrogen line and cooled to 0 °C. $ZnMe_2$ (3.0 equiv) was added resulting in an immediate color change from colorless to orange. After 48 h at 0 °C, the reaction was quenched with isopropyl alcohol, and filtered through a plug of silica gel (100% Et_2O).

METHOD C: CROSS-COUPLING WITH DIETHYLZINC (TABLE 3)

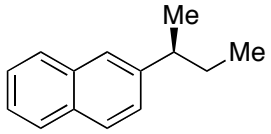


(3)

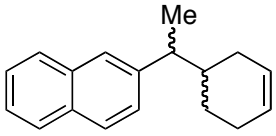
In a glovebox, a flame-dried 7 mL vial equipped with a stir bar was charged with $NiCl_2$•DME (0.10 equiv) and DPEphos (0.20 equiv). The reaction vial was capped with a screw-cap fitted with a septum and THF was added. After a 5 min pre-stir, substrate (1.0 equiv) was added and the reaction was removed from the glovebox. The reaction vial was equipped with a nitrogen line and allowed to stir for approximately 5 min. A freshly prepared solution of $ZnEt_2$ (3.0 equiv) was then added resulting in an immediate color change from purple to dark orange. After 24 h, the reaction was quenched with isopropyl alcohol and filtered through a plug of silica gel (100% Et_2O).

PREPARATION OF $ZnEt_2$ SOLUTION: In a glovebox, $ZnEt_2$ (0.60 mL, 5.9 mmol) and PhMe (2.4 mL) were combined in a flame-dried 7 mL vial equipped with a stir bar and equipped with a screw-cap fitted with a septum, resulting in a 1.6 M solution.

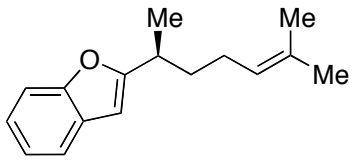
D. CHARACTERIZATION DATA FOR PRODUCTS 22–32 (TABLE 1)



(*S*)-2-(sec-butyl)naphthalene (*S*)-22 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), DPEphos (22 mg, 0.040 mmol, 0.20 equiv), substrate (*R*)-**18** (0.80 mL, 0.20 mmol, 1.0 equiv, 0.25 M in PhMe), and $ZnMe_2$ (0.33 mL, 0.60 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2.4 mL). Purification by flash chromatography with silver impregnated silica gel (100% pentane) afforded the title compound as a colorless oil (30 mg, 81%). Analytical data are consistent with literature values.[23] **TLC R_f** = 0.5 (pentane, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.82–7.42 (m, 3H), 7.60 (s, 1H), 7.42 (apd, *J* = 7.31, 1.40, 2H), 7.34 (dd, *J* = 8.5, 1.6, 1H), 2.76 (sextet, *J* = 7.0, 1H), 1.77–1.61 (m, 2H), 1.32 (d, *J* = 6.9, 3H), 0.85 (t, *J* = 7.4, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 145.3, 133.8, 132.3, 128.0, 127.71, 127.67, 126.0, 125.9, 125.3, 125.2, 42.0, 31.2, 22.0, 12.5; **$[\alpha]_D^{24}$** +24.2 (*c* 1.0, $CHCl_3$), lit.[16] $[\alpha]_D^{23}$ +19.6 (neat, 65% ee (*S*)-enantiomer); **SFC** analysis (OD-H, 1.0% hexanes, 2.5 mL/min, 215 nm) indicated 98% ee: t_R (major) = 5.9 min, t_R (minor) = 6.3 min.

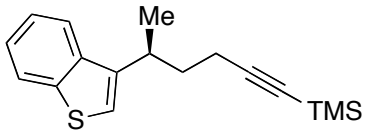


2-(1-(cyclohex-3-en-1-yl)ethyl)naphthalene 24 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), DPEphos (22 mg, 0.040 mmol, 0.20 equiv), substrate **SI 27** (0.40 mL, 0.20 mmol, 1.0 equiv, 0.5 M in PhMe), and $ZnMe_2$ (0.32 mL, 0.60 mmol, 3.0 equiv, 1.9 M in PhMe) in PhMe (2.8 mL). Purification by flash chromatography (100% pentane) afforded the title compound as 5:1 mixture with the elimination byproduct (41 mg, calculated as 34 mg, 71%, dr 1:1 by ^{1}H NMR integration). Compound **24** was re-purified by silica gel chromatography to obtain a sample of analytically pure material. **TLC R_f** = 0.9 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.81–7.76 (m, 3H), 7.59 (d, *J* = 2.4, 1H), 7.46–7.32 (m, 3H), 5.71–5.52 (m, 2H), 2.71–2.66 (m, 1H), 2.28–1.51 (m, 6H), 1.39–1.12 (m, 4H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 144.6, 144.4, 133.64, 133.62, 132.3, 127.88, 127.85, 127.71, 127.66, 127.3, 126.9, 126.8, 126.6, 126.42, 126.38, 126.1, 126.0, 125.9, 125.2, 45.8, 45.2, 40.20, 40.15, 30.7, 29.9, 27.4, 26.6, 25.8, 25.7, 19.4, 19.2; **IR** (neat, cm^{-1}) 3019, 2963, 2910, 1506, 1434, 908; **HRMS** (TOF MS EI+) *m*/*z*: $[M]^+$ calculated for $C_{18}H_{20}$ 236.1565, found 236.1555.

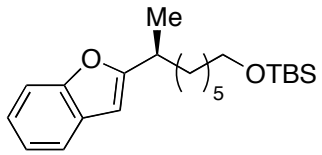


2-((*S*)-6-methyl-5-hepten-2-yl)benzofuran 25 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), DPEphos (22 mg, 0.040 mmol, 0.20 equiv), substrate (*R*)-**SI 30** (0.80 mL, 0.20 mmol, 1.0 equiv, 0.25 M in PhMe), and $ZnMe_2$ (0.33 mL, 0.60 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2.4 mL). Purification by flash chromatography (100% pentane) afforded the title compound as 12:1 mixture with the elimination byproduct (42 mg, calculated as 39 mg, 86% desired product). Compound **25** was re-purified by silica gel chromatography to obtain a sample of analytically pure material. **TLC R_f** = 0.5 (100% pentane, UV active, stain with CAM); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.48 (dd, *J* = 6.9, 1.8, 1H), 7.41 (d, *J* = 7.8, 1H), 7.18 (apd, *J* = 7.1, 1.4, 2H), 6.36 (s, 1H), 5.11 (tt, *J* = 7.1, 1.3, 1H), 2.94 (sextet, *J* = 6.9, 1H), 2.01 (q, *J* = 7.4, 2H), 1.84 (as, *J* = 7.2, 1H), 1.67 (s, 3H), 1.67–1.54 (m, 1H), 1.57 (s, 3H), 1.33 (d, *J* = 6.9, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.0, 154.7, 132.1, 129.0, 124.2,

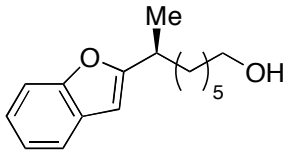
123.1, 122.4, 120.4, 110.9, 100.8, 35.6, 33.3, 25.9, 25.8, 19.2, 17.9; **IR** (neat, cm^{-1}) 2967, 2925, 1254, 1253, 795, 738; **HRMS** (TOF MS EI+) *m/z*: $[M]^+$ calculated for $C_{16}H_{20}O$ 228.1514, found 228.1508; $[\alpha]^{25}_D$ + 61.0 (*c* 0.86, $CHCl_3$); **SFC** analysis (OJ-H, 1.0% hexanes, 3.0 mL/min, 215 nm) indicated 93% ee: t_R (major) = 4.3 min, t_R (minor) = 5.0 min.



(*S*)-(5-(benzo[b]thiophen-3-yl)hex-1-yn-1-yl)trimethylsilane 26 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), DPEphos (22 mg, 0.040 mmol, 0.20 equiv), substrate (*R*)-**SI 34** (0.80 mL, 0.20 mmol, 1.0 equiv, 0.25 M in PhMe), and $ZnMe_2$ (0.33 mL, 0.60 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2.4 mL). Purification by flash chromatography (0–5% Et_2O in pentane) afforded the title compound as a colorless oil (46 mg, 81%). **TLC R_f** = 0.3 (pentane, UV active, stain with CAM); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.85 (add, *J* = 7.5, 2.3, 2H), 7.35 (apd, *J* = 7.2, 1.0, 2H), 7.09 (s, 1H), 3.37 (sextet, *J* = 6.9, 1H), 2.34–2.18 (m, 2H), 2.03 (as, *J* = 6.9, 1H), 1.80 (as, *J* = 6.9, 1H), 1.38 (d, *J* = 6.9, 3H), 0.17 (s, 9H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 141.8, 140.8, 138.8, 124.3, 123.9, 123.0, 122.1, 120.0, 107.3, 85.1, 36.1, 31.9, 20.3, 18.2, 0.3; **IR** (neat, cm^{-1}) 2959, 2173, 1427, 1248, 871, 759; **HRMS** (TOF MS EI+) *m/z*: $[M]^+$ calculated for $C_{17}H_{22}SSi$ 286.1212, found 286.1212; $[\alpha]_D^{29}$ +57.6 (*c* 1.0, $CHCl_3$); **SFC** analysis (OJ-H, 1.0% hexanes, 3.0 mL/min, 215 nm) indicated 96% ee: t_R (major) = 3.4 min, t_R (minor) = 3.9 min.

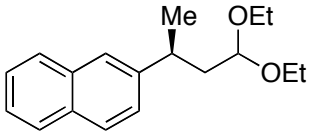


(*S*)-((7-(benzofuran-2-yl)octyl)oxy)(*tert*-butyl)dimethylsilane 27 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (2.2 mg, 0.010 mmol, 0.10 equiv), DPEphos (11 mg, 0.020 mmol, 0.20 equiv), substrate (*R*)-**SI 38** (0.40 mL, 0.10 mmol, 1.0 equiv 0.25 M in PhMe), and $ZnMe_2$ (0.17 mL, 0.30 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (1.2 mL). Purification by flash chromatography with silver impregnated silica gel (2% Et_2O in pentane) afforded the title compound as a colorless oil (27 mg, 75%). **TLC R_f** = 0.3 (2% Et_2O in pentane, UV active, stains with CAM); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.48 (dd, *J* = 7.1, 1.3, 1H), 7.41 (d, *J* = 7.8, 1H), 7.18 (apd, *J* = 7.6, 1.3, 2H), 6.35 (s, 1H), 3.58 (t, *J* = 6.6, 2H), 2.92 (sextet, *J* = 6.9, 1H), 1.83–1.73 (m, 1H), 1.62–1.53 (m, 1H), 1.53–1.44 (m, 2H), 1.38–1.26 (m, 9H), 0.88 (s, 9H), 0.04 (s, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 164.1, 154.6, 129.0, 123.1, 122.4, 120.4, 110.9, 100.7, 63.4, 35.5, 33.7, 33.0, 29.6, 27.3, 26.1, 25.9, 19.2, 18.5, −5.1; **IR** (neat, cm^{-1}) 2928, 2856, 1455, 1253, 1096, 834; **HRMS** (TOF MS ES+) *m/z*: $[M + H]^+$ calculated for $C_{22}H_{37}O_2Si$ 361.2563, found 361.2561; $[\alpha]_D^{28}$ +18.7 (*c* 1.0, $CHCl_3$); **SFC** analysis (OJ-H, 1.0% hexanes, 3.0 mL/min, 215 nm) indicated 88% ee: t_R (major) = 3.2 min, t_R (minor) = 3.6 min.

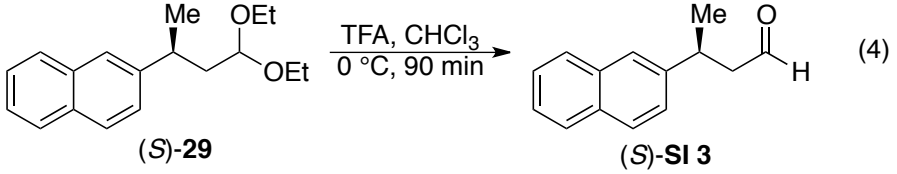


(*S*)-7-(benzofuran-2-yl)octan-1-ol 28 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (2.2 mg, 0.010 mmol, 0.10 equiv), DPEphos (11 mg, 0.020 mmol, 0.20 equiv), substrate (*R*)-**SI 39** (0.40 mL, 0.10 mmol, 1.0 equiv 0.25 M in PhMe), and $ZnMe_2$ (0.17 mL, 0.30 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (1.2 mL). Purification by flash chromatography with silver impregnated silica gel (10–40% Et_2O in pentane) afforded the title compound as a colorless oil (19 mg, 77%). **TLC R_f** = 0.5 (1:1 Et_2O/pentane, UV active, stains with CAM); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.48 (dd, *J*

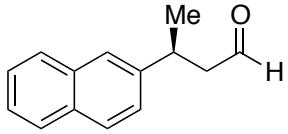
= 6.9, 1.5, 1H), 7.41 (d, *J* = 7.7, 1H), 7.18 (apd, *J* = 7.1, 1.2, 2H), 6.36 (s, 1H), 3.62 (br dd, *J* = 9.4, 6.2, 2H), 2.92 (sextet, *J* = 6.9, 1H), 1.85–1.72 (m, 1H), 1.66–1.48 (m, 3H), 1.40–1.27 (m, 9H), 1.20 (br s, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 164.0, 154.6, 129.0, 123.1, 122.4, 120.4, 110.9, 100.7, 63.1, 35.5, 33.7, 32.9, 29.5, 27.2, 25.8, 19.1; **IR** (neat, cm^{-1}) 3326, 2930, 1454, 1253, 795, 739; **HRMS** (TOF MS EI+) *m/z*: $[M]^+$ calculated for $C_{16}H_{22}O_2$ 246.1620, found 246.1616; **$[\alpha]_D^{29}$** +44.1 (*c* 0.97, $CHCl_3$); **SFC** analysis (OJ-H, 10.0% IPA, 3.0 mL/min, 215 nm) indicated 90% ee: t_R (major) = 4.7 min, t_R (minor) = 5.4 min.



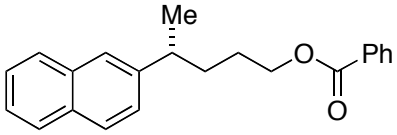
(*S*)-2-(4,4-diethoxybutan-2-yl)naphthalene (*S*)-29 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (2.2 mg, 0.010 mmol, 0.10 equiv), DPEphos (11 mg, 0.020 mmol, 0.20 equiv), substrate (*R*)-**SI 2** (1.0 mL, 0.10 mmol, 1.0 equiv 0.10 M in PhMe), and $ZnMe_2$ (0.17 mL, 0.30 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (0.60 mL). Purification by flash chromatography (2–5% Et_2O in pentane) afforded the title compound as a colorless oil (22 mg, 81%). **TLC R_f** = 0.3 (5% Et_2O in pentane, UV active, stain with CAM); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.84–7.75 (m, 3H), 7.63 (s, 1H), 7.43 (ap, *J* = 7.6, 2H), 7.37 (dd, *J* = 8.4, 1.1, 1H), 4.30 (t, *J* = 6.0, 1H), 3.64 (dq, *J* = 9.2, 7.1, 1H), 3.54 (dq, *J* = 9.3, 7.1, 1H), 3.45–3.36 (m, 2H), 3.06 (sextet, *J* = 7.2, 1H), 2.05–1.94 (m, 2H), 1.34 (d, *J* = 7.1, 3H), 1.22 (t, *J* = 7.0, 3H), 1.13 (t, *J* = 7.0, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 144.4, 133.8, 132.4, 128.2, 127.71, 127.70, 126.0, 125.8, 125.4, 125.3, 101.6, 61.5, 60.9, 41.9, 36.3, 22.8; **IR** (neat, cm^{-1}) 2971, 1372. 1124, 1055, 745; **HRMS** (TOF MS ES+) *m/z*: $[M + Na]^+$ calculated for $C_{18}H_{24}O_2Na$ 295.1674, found 295.1668; **$[\alpha]_D^{28}$** +29.6 (*c* 1.0, $CHCl_3$); **SFC** analysis (OJ-H, 1.0% IPA, 3.0 mL/min, 215 nm) indicated 89% ee: t_R (minor) = 5.7 min, t_R (major) = 6.2 min.



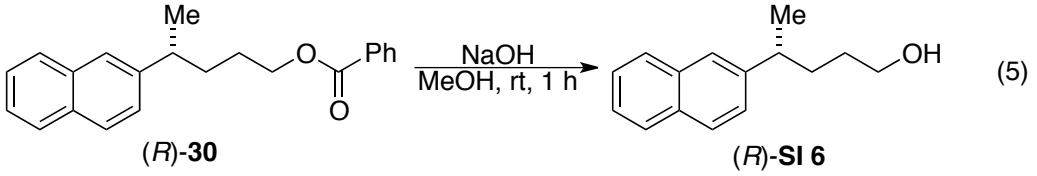
(4)



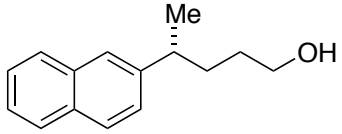
(*S*)-3-(naphthalene-2-yl)butanal (*S*)-SI 3 was prepared according to a modified Ellison.[24] Acetal (*S*)-**29** (34 mg, 0.12 mmol, 1.0 equiv) was dissolved in wet $CHCl_3$ (2 mL) and cooled to 0 °C. The reaction mixture was treated with TFA (50% aq. solution, 1 mL) and stirred at the same temperature for 90 min. The reaction was quenched with sat. $NaHCO_3$ (2 mL) and extracted with CH_2Cl_2 (3 x 1 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by flash chromatography (5–10% Et_2O in pentane) to afford the title compound as a colorless oil (17 mg, 71%). Analytical data are consistent with literature values.[19] **TLC R_f** = 0.1 (5% Et_2O in pentane, UV active, stain with $KMnO_4$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.74 (t, *J* = 1.7, 1H), 7.79 (at, *J* = 7.0, 3H), 7.65 (s, 1H), 7.45 (apd *J* = 6.8, 1.1, 2H), 7.37 (dd, *J* = 8.5, 1.2, 1H), 3.53 (sextet, *J* = 7.1, 1H), 2.86 (ddd, *J* = 16.7, 6.8, 1.4, 1H), 2.74 (ddd, *J* = 16.7, 7.7, 1.8, 1H), 2.41 (d, *J* = 6.9, 3H); **$[\alpha]_D^{24}$** +37.0 (*c* 0.9, Et_2O), lit.[19] $[\alpha]_D^{25}$ +40.4 (*c* 0.2, Et_2O, >95% ee (*S*)-enantiomer); **SFC** analysis (OJ-H, 5.0% IPA, 3.0 mL/min, 215 nm) indicated 84% ee: t_R (major) = 6.5 min, t_R (minor) = 7.2 min.



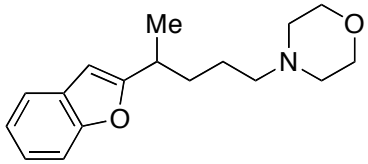
(*R*)-4-(naphthalen-2-yl)pentyl benzoate (*R*)-30 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), DPEphos (22 mg, 0.040 mmol, 0.20 equiv), substrate (*S*)-**SI 5** (82 mg, 0.20 mmol, 1.0 equiv), and $ZnMe_2$ (0.33 mL, 0.60 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (3.2 mL). Purification by flash chromatography with silver impregnated silica gel (5% Et_2O in pentane) afforded the title compound as a colorless oil (52 mg, 81%). **TLC** $\mathbf{R_f}$ = 0.3 (5% Et_2O in pentane, UV active, stain with CAM); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.01 (d, *J* = 7.3, 2H), 7.82 (m, 3H), 7.62 (s, 1H), 7.52 (t, *J* = 7.3, 1H), 7.47–7.38 (m, 4H), 7.35 (d, *J* = 8.6, 1H), 4.28 (t, *J* = 6.4, 2H), 2.92 (sextet, *J* = 6.9, 1H), 1.90–1.56 (m, 4H), 1.36 (d, *J* = 6.9, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 166.7, 144.5, 133.7, 132.9, 132.4, 130.5, 129.7, 128.4, 128.2, 127.72, 127.66, 126.0, 125.7, 125.4, 125.3, 65.1, 39.9, 34.5, 27.1, 22.6; **IR** (neat, cm^{-1}) 2957, 1714, 1270, 1110, 709; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{22}H_{22}O_2Na$ 341.1518, found 341.1515; $\mathbf{[\alpha]_D^{26}}$ –6.8 (*c* 1.0, $CHCl_3$); **SFC** analysis (AD-H, 5.0% MeOH, 3.0 mL/min, 215 nm) indicated 97% ee: t_R (minor) = 6.7 min, t_R (major) = 7.3 min.



(*R*)-**30** (*R*)-**SI 6** (5)

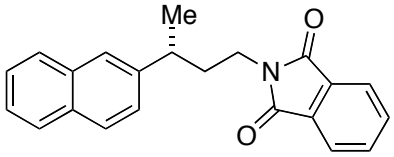


(*R*)-4-(naphthalen-2-yl)pentan-1-ol (*R*)-SI 6 was prepared according to a modified procedure by Sato.[25] Ester (*R*)-**30** (37 mg, 0.12 mmol, 1.0 equiv) was treated with a solution of NaOH in MeOH (1%, 5 ml). The reaction was stirred at rt for 1 h and then MeOH was removed in vacuo. The solid residue was taken up in H_2O (2 mL) the mixture was extracted with EtOAc (3 x 1 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by flash chromatography (40% Et_2O in pentane) to afford the title compound as a viscous colorless oil (19 mg, 72%). Analytical data are consistent with literature values.[19] **TLC** $\mathbf{R_f}$ = 0.3 (40% Et_2O in pentane, UV active, stain with $KMnO_4$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.79 (at, *J* = 7.0, 3H), 7.60 (s, 1H), 7.43 (ap, *J* = 7.2, 2H), 7.34 (d, *J* = 8.6, 1H), 3.59 (t, *J* = 6.5, 2H), 2.88 (sextet, *J* = 7.0, 1H), 1.74 (q, *J* = 7.7, 2H), 1.61–1.50 (m, 1H), 1.50–1.38 (m, 1H), 1.34 (d, *J* = 6.9, 3H), 1.21 (br s, 1H); $\mathbf{[\alpha]_D^{24}}$ –19.8 (*c* 0.9, $CHCl_3$), lit.[19] $[\alpha]_D^{24}$ –19.4 (*c* 0.3, $CHCl_3$, >95% ee, (*R*)-enantiomer); **SFC** analysis (OJ-H, 5.0% MeOH, 3.0 mL/min, 215 nm) indicated 96% ee: t_R (minor) = 13.6 min, t_R (major) = 14.5 min.

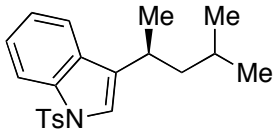


4-(4-(benzofuran-2-yl)pentyl)morpholine 31 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), DPEphos (22 mg, 0.040 mmol, 0.20 equiv), substrate **SI 46** (0.40 mL, 0.20 mmol, 1.0 equiv, 0.5 M in PhMe), and $ZnMe_2$ (0.32 mL, 0.60 mmol, 3.0 equiv, 1.9M in PhMe) in PhMe (2.8 mL). Purification by flash chromatography (100% Et_2O) afforded the title compound as 16:1 mixture with the elimination byproduct (39 mg, calculated as 37 mg, 68%). Compound **31** was re-purified by silica gel chromatography to obtain a sample of analytically pure material. **TLC** $\mathbf{R_f}$ = 0.4 (100% Et_2O, UV active); **mp** 48–49

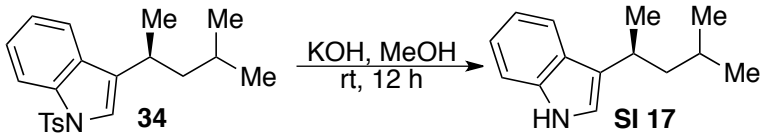
°C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.48 (d, *J* = 6.9, 1H), 7.40, (d, *J* = 7.5, 1H), 7.20–7.17 (m, 2H), 6.37 (s, 1H), 3.69 (t, *J* = 4.6, 4H), 2.99–2.91 (m, 1H), 2.40 (br s, 4H), 2.33 (t, *J* = 7.6, 2H), 1.84–1.76 (m, 1H), 1.64–1.59 (m, 3H), 1.34 (d, *J* = 7.0, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 163.5, 154.7, 128.9, 123.3, 122.5, 120.4, 110.9, 101.0, 67.1, 59.1, 53.9, 33.7, 33.4, 24.3, 19.2; **IR** (neat, cm^{-1}) 2934, 2853, 1454, 1298, 1253, 1166, 1137; **HRMS** (TOF MS ES+) *m*/*z*: $[M + H]^+$ calculated for $C_{17}H_{24}O_2N$ 274.1807, found 274.1813.



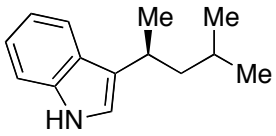
(*R*)-2-(3-(naphthalen-2-yl)butyl)isoindoline-1,3-dione 32 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (2.2 mg, 0.010 mmol, 0.13 equiv), DPEphos (11 mg, 0.020 mmol, 0.25 equiv), substrate (*S*)-**SI 48** (0.20 mL, 0.080 mmol, 1.0 equiv, 0.50 M in PhMe), and $ZnMe_2$ (0.17 mL, 0.30 mmol, 3.8 equiv, 1.8 M in PhMe) in PhMe (1.4 mL). Purification by flash chromatography (5–15% Et_2O in pentane) afforded the title compound as a white solid (21 mg, 80%). **TLC R_f** = 0.5 (4:1 hexane/EtOAc, UV active, stain with CAM); **mp** 73–76 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.76 (d, *J* = 8.2, 1H), 7.73–7.64 (m, 4H), 7.61 (s, 1H), 7.60–7.54 (m, 2H), 7.41 (t, *J* = 7.3, 1H), 7.35 (t, *J* = 7.5, 2H), 3.67 (t, *J* = 7.2, 2H), 2.96 (as, *J* = 7.0, 1H), 2.24 (dq, *J* = 13.7, 8.3, 1H), 2.00 (as, *J* = 6.5, 1H), 1.37 (d, *J* = 6.9, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 168.5, 143.6, 133.8, 133.6, 133.3, 132.0, 128.3, 127.7, 127.6, 126.0, 125.44, 125.41, 125.2, 123.0, 38.4, 37.0, 35.8, 23.1; **IR** (neat, cm^{-1}) 2960, 1705, 1396, 747, 715; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{22}H_{19}NO_2Na$ 352.1313, found 352.1314; **$[\alpha]_D^{25}$** –3.1 (*c* 0.72, $CHCl_3$); **SFC** analysis (OJ-H, 10.0% MeOH, 3.0 mL/min, 215 nm) indicated 94% ee: t_R (major) = 6.9 min, t_R (minor) = 7.6 min.



(*S*)-3-(4-methylpentan-2-yl)-1-tosyl-1H-indole 34 was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (3.3 mg, 0.015 mmol, 0.10 equiv), DPEphos (16 mg, 0.030 mmol, 0.20 equiv), substrate **33** (0.30 mL, 0.15 mmol, 1.0 equiv, 0.5 M in PhMe), and $ZnMe_2$ (0.23 mL, 0.45 mmol, 3.0 equiv, 1.9 M in PhMe) in PhMe (2.1 mL). Purification by flash chromatography (2–5% Et_2O in pentane) afforded the title compound as a colorless oil (49 mg, 91%). **TLC R_f** = 0.7 (4:1 Hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.97 (d, *J* = 8.3, 1H), 7.71 (d, *J* = 8.3, 2H), 7.51 (d, *J* = 7.9, 1H), 7.30–7.18 (m, 5H), 2.99 (sextet, *J* = 7.1, 1H), 2.32 (s, 3H), 1.65–1.50 (m, 2H), 1.44–1.37 (m, 1H), 1.27 (d *J* = 6.9, 3H), 0.88 (at, *J* = 6.8, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 144.6, 135.7, 135.4, 130.7, 129.9, 129.5, 126.8, 124.6, 123.0, 121.8, 120.0, 114.0, 46.3, 28.5, 25.8, 23.1, 22.6, 21.7, 21.1; **IR** (neat, cm^{-1}) 2956, 1446, 1365, 1279, 1172, 1120, 1090; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{21}H_{25}O_2NSNa$ 378.1504, found 378.1501; **$[\alpha]_D^{27}$** +0.94 (*c* 1.5, $CHCl_3$). Enantiomeric excess determined after deprotection, see **SI 1**.

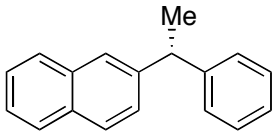


(6)

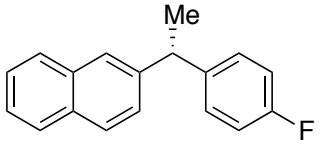


(*S*)-3-(4-methylpentan-2-yl)-1*H*-indole SI 17 was prepared according to a modified procedure by Kozikowski.[26] To a stirred solution of **34** (10 mg, 0.030 mmol, 1.0 equiv) in wet MeOH (2 mL) was added powdered KOH (0.50 g, 10 mmol, 33 equiv). The reaction was stirred at ambient temperature overnight, after which the reaction was acidified with 3N HCl until pH <7. The crude product was extracted with Et_2O (3 x 5 mL) and the combined organics were dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography (10% Et_2O in pentane) afforded the title compound as a yellow oil (5.0 mg, 88%). Analytical data are consistent with literature values.[27] **TLC R_f** = 0.7 (4:1 Hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.88 (br s, 1H), 7.66 (d, *J* = 7.8, 1H), 7.35 (d, *J* = 8.1, 1H), 7.17 (t, *J* = 7.5, 1H), 7.09 (t, *J* = 7.4, 1H), 6.95 (d, *J* = 2.2, 1H), 3.11 (sextet, *J* = 7.2, 1H), 1.75–1.58 (m, 2H), 1.48–1.41 (m, 1H), 1.32 (d, *J* = 7.0, 3H), 0.92 (d, *J* = 4.8, 3H), 0.90 (d, *J* = 5.0, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 136.6, 127.0, 123.2, 121.9, 119.9, 119.5, 119.1, 111.3, 47.3, 28.6, 25.9, 23.1, 22.8, 22.0; **$[\alpha]_D^{26}$** –1.6 (*c* 0.24, $CHCl_3$); **SFC** analysis (AD-H, 5.0% IPA, 1.0 mL/min, 215 nm) indicated 96% ee: t_R (minor) = 36.3 min, t_R (major) = 38.1 min.

E. Characterization Data for Products 35–40 (Table 2)

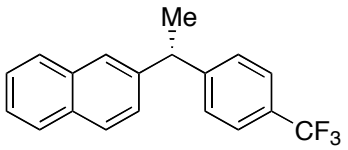


(*R*)-2-(1-phenylethyl)naphthalene 35 was prepared according to Method B. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), Xantphos (22 mg, 0.040 mmol, 0.20 equiv), substrate (*S*)-**SI 52** (0.40 mL, 0.20 mmol, 1.0 equiv, 0.50 M in PhMe), and $ZnMe_2$ (0.33 mL, 0.60 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2.8 mL). Purification by flash chromatography (10% Et_2O in pentane) afforded the title compound as a colorless oil (43 mg, 87%). Analytical data are consistent with literature values.[28] **TLC R_f** = 0.8 (4:1 Hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.80–7.69 (m, 4H), 7.43 (apd, *J* = 7.0, 1.8, 2H), 7.31–7.26 (m, 5H), 7.20–7.16 (m, 1H), 4.31 (q, *J* = 7.2, 1H), 1.71 (d, *J* = 7.2, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 146.4, 143.9, 133.7, 132.2, 128.5, 128.1, 127.89, 127.86, 127.7, 127.0, 126.2, 126.1, 125.50, 125.48, 45.0, 21.9; **$[\alpha]_D^{26}$** –42.5 (*c* 0.78, $CHCl_3$), lit.[23] $[\alpha]_D^{23}$ –46.2 (*c* 1.0, $CHCl_3$, 99% ee); **SFC** analysis (OD-H, 2.0% IPA, 2.5 mL/min, 215 nm) indicated 98% ee: t_R (minor) = 12.2 min, t_R (major) = 12.8 min.

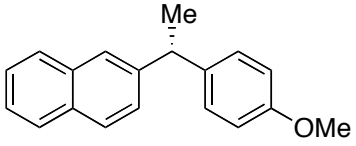


(*R*)-2-(1-(4-(fluoro)phenyl)ethyl)naphthalene (*R*)-36 was prepared according to Method B. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), Xantphos (22 mg, 0.040 mmol, 0.20 equiv), substrate (*S*)-**SI 8** (0.40 mL, 0.20 mmol, 1.0 equiv, 0.50 M in PhMe), and $ZnMe_2$ (0.33 mL, 0.60 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2.8 mL). Purification by flash chromatography (2–10% Et_2O in pentane) afforded the title compound as a white solid (45 mg, 89%). Analytical data are consistent with literature values.[21] **TLC R_f** = 0.8 (4:1 Hexane/EtOAc, UV active); **mp**

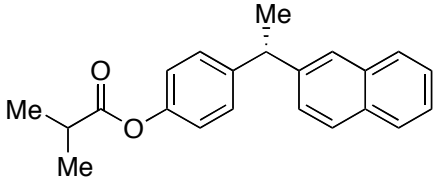
52–55 °C; lit.[21] mp 54–58 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.79–7.73 (m, 3H), 7.66 (s, 1H), 7.43 (ap, J = 7.0, 2H), 7.27–7.18 (m, 3H), 6.98–6.94 (m, 2H), 4.28 (q, J = 7.2, 1H), 1.71 (d, J = 7.2, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 161.4 (d, $J_{(C–F)}$ = 244.1 Hz), 143.7, 142.0 (d, $J_{(C–F)}$ = 3.2 Hz), 133.6, 132.2, 129.3 (d, $J_{(C–F)}$ = 7.4 Hz), 128.2, 127.8, 127.7, 126.8, 126.2, 125.6, 125.4, 115.2 (d, $J_{(C–F)}$ = 21.3 Hz), 44.2, 22.0; **$[\alpha]_D^{26}$** –29.5 (*c* 1.57, $CHCl_3$), lit.[21] $[\alpha]_D^{24}$ –25.2 (*c* 1.88, $CHCl_3$, 95% ee, (*R*)-enantiomer); **SFC** analysis (OD-H, 2.0% IPA, 2.5 mL/min, 215 nm) indicated 93% ee: t_R (minor) = 11.11 min, t_R (major) = 12.14 min.



(*R*)-2-(1-(4-(trifluoromethyl)phenyl)ethyl)naphthalene 37 was prepared according to Method B. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), Xantphos (22 mg, 0.040 mmol, 0.20 equiv), substrate (*S*)-**SI 53** (0.40 mL, 0.20 mmol, 1.0 equiv, 0.50 M in PhMe), and $ZnMe_2$ (0.33 mL, 0.60 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2.8 mL). Purification by flash chromatography (10% Et_2O in pentane) afforded the title compound as a colorless oil (47 mg, 78%). **TLC R_f** = 0.8 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.80–7.68 (m, 4H), 7.52 (d, J = 8.1, 2H), 7.44 (ap, J = 6.2, 2H), 7.34 (d, J = 7.9, 2H), 7.25 (d, J = 8.4, 1H), 4.34 (q, J = 7.1, 1H), 1.73 (d, J = 7.2, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 150.4, 142.8, 133.6, 132.3, 128.6 (q, $J_{C–F}$ = 32.4, 1C), 128.4, 128.2, 127.9, 127.8, 126.7, 126.3, 125.8, 125.6, 125.5 (q, $J_{C–F}$ = 3.7, 2C), 124.4 (q, $J_{C–F}$ = 271.8, 1C), 44.9, 21.7; **IR** (neat, cm^{-1}) 2970, 1739, 1322, 1112, 1069, 840; **HRMS** (TOF MS Cl+) *m*/*z*: $[M + Na]^+$ calculated for $C_{19}H_{15}F_3Na$ 300.1126, found 300.1123; **$[\alpha]_D^{28}$** –34.2 (*c* 0.71, $CHCl_3$); **SFC** analysis (OD-H, 2.0% IPA, 2.5 mL/min, 215 nm) indicated 91% ee: t_R (minor) = 11.2 min, t_R (major) = 12.5 min.

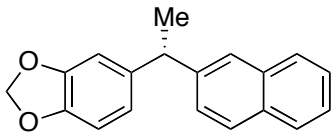


(*R*)-2-(1-(4-methoxyphenyl)ethyl)naphthalene 38 was prepared according to Method B. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), Xantphos (22 mg, 0.040 mmol, 0.20 equiv), substrate (*R*)-**SI 54** (0.40 mL, 0.20 mmol, 1.0 equiv, 0.50 M in PhMe), and $ZnMe_2$ (0.33 mL, 0.60 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2.8 mL). Purification by flash chromatography (10% Et_2O in pentane) afforded the title compound as a colorless oil (49 mg, 93%). Analytical data are consistent with literature values.[29] **TLC R_f** = 0.6 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.78–7.66 (m, 4H), 7.41 (apd, J = 7.2, 1.8, 2H), 7.28 (dd, J = 8.4, 1.6, 1H), 7.16 (d, J = 8.7, 2H), 6.82 (d, J = 8.6, 2H), 4.25 (q, J = 7.2, 1H), 3.75 (s, 3H), 1.69 (d, J = 7.1, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 158.0, 144.3, 138.5, 133.7, 132.1, 128.8, 128.1, 127.8, 127.7, 126.9, 125.5, 125.3, 113.9, 55.4, 44.1, 30.5, 22.1; **$[\alpha]_D^{28}$** –32.1 (*c* 0.83, $CHCl_3$); **SFC** analysis (OJ-H, 5.0% IPA, 3.0 mL/min, 215 nm) indicated 95% ee: t_R (major) = 20.8 min, t_R (minor) = 23.0 min.



(*S*)-4-(1-(naphthalen-2-yl)ethyl)phenyl isobutyrate 39 was prepared according to Method B. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), Xantphos (22 mg, 0.040 mmol, 0.20 equiv), substrate (*R*)-**SI 56** (0.40 mL, 0.20 mmol, 1.0 equiv, 0.50 M in PhMe), and $ZnMe_2$ (0.33 mL, 0.60 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2.8 mL). Purification by flash chromatography (30% benzene in pentane) afforded the title compound as a colorless oil (46 mg, 76%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active);

^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.78–7.68 (m, 4H), 7.43 (ap, *J* = 7.1, 2H), 7.30–7.23 (m, 3H), 6.98 (d, *J* = 8.4, 2H), 4.31 (q, *J* = 7.1, 3H), 2.77 (septet, *J* = 7.0, 1H), 1.71 (d, *J* = 7.1, 1H), 1.29 (d, *J* = 7.0, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 175.9, 149.2, 143.67, 143.65, 133.6, 132.3, 128.8, 128.1, 127.9, 127.7, 126.9, 126.1, 125.6, 125.5, 121.4, 44.4, 34.3, 22.0, 19.1; **IR** (neat, cm^{-1}) 2969, 1753, 1505, 1203, 1165, 1129, 1094; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{22}H_{22}O_2Na$ 341.1518, found 341.1526 **$[\alpha]_D^{28}$** +28.5 (*c* 0.82, $CHCl_3$); **SFC** analysis (OD-H, 3.0% IPA, 3 mL/min, 215 nm) indicated 97% ee: t_R (major) = 13.7 min, t_R (minor) = 14.7 min.

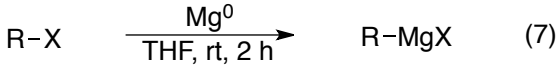


(*R*)-5-(1-(naphthalen-2-yl)ethyl)benzo[*d*][1,3]dioxole 40 was prepared according to Method B. The following amounts of reagents were used: $NiCl_2$•DME (4.4 mg, 0.020 mmol, 0.10 equiv), Xantphos (22 mg, 0.040 mmol, 0.20 equiv), substrate (*R*)-**SI 57** (0.40 mL, 0.20 mmol, 1.0 equiv, 0.50 M in PhMe), and $ZnMe_2$ (0.33 mL, 0.60 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2.8 mL). Purification by flash chromatography (10% Et_2O in pentane) afforded the title compound as a colorless oil (54 mg, 98%). **TLC R_f** = 0.6 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.80–7.67 (m, 4H), 7.43 (apd, *J* = 7.3, 1.8, 2H), 7.29 (dd, *J* = 8.5, 1.7, 1H), 6.73 (s, 1H), 6.72 (d, *J* = 7.4, 2H), 5.89 (s, 2H), 4.22 (q, *J* = 7.2, 1H), 1.68 (d, *J* = 7.2, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 147.8, 145.9, 143.9, 140.5, 133.6, 132.2, 128.1, 127.9, 127.7, 126.8, 126.1, 125.5, 125.3, 120.7, 108.5, 108.2, 101.0, 44.7, 22.1; **IR** (neat, cm^{-1}) 2966, 2892, 1598, 1484, 1223, 1034, 937; **HRMS** (TOF MS ES+) *m*/*z*: $[M]^+$ calculated for $C_{19}H_{16}O_2$ 276.1150, found 276.1152; **$[\alpha]_D^{28}$** +29.7 (*c* 0.80, $CHCl_3$); **SFC** analysis (OD-H, 3.0% IPA, 3.0 mL/min, 215 nm) indicated 90% ee: t_R (major) = 15.3 min, t_R (minor) = 16.9 min.

F. General Procedures for Starting Material Synthesis

The general procedures for starting material synthesis will be used throughout the rest of the SI. In each instance a general method is used, it is specified by letter (D, E etc.) and the exact amounts of reagents used for each reaction are listed for the specific compounds synthesized.

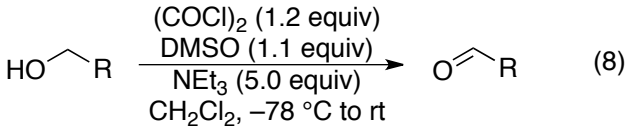
Method D: Grignard Preparation



(7)

Magnesium turnings (1.5 equiv) were added to a two-neck round-bottom flask equipped with a stir bar and condenser. The reaction apparatus was flame-dried under vacuum and cooled under N_2. THF was added to the reaction apparatus, followed by a single crystal of I_2 (ca. 2 mg). The organohalide (1.0 equiv) was added portion-wise over 1 h. The reaction was stirred at ambient temperature for an additional hour and then titrated.[2]

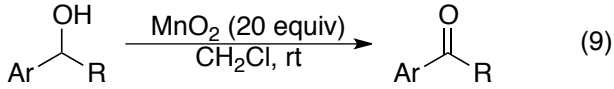
METHOD E: SWERN OXIDATION



(8)

Modified from a procedure reported by Cossy.[30] A solution of DMSO (1.1 equiv) in anhydrous CH_2Cl_2 was added drop-wise to a stirred solution of oxalyl chloride (1.2 equiv) in anhydrous CH_2Cl_2 at –78 °C, under a positive pressure of N_2. After 15 min, a solution of alcohol (1.0 equiv) in anhydrous CH_2Cl_2 was added drop-wise to the reaction mixture. The reaction was then stirred for an additional 30 min at –78 °C followed by the addition of triethylamine (5.0 equiv). After an additional 10 min of stirring at –78 °C, the reaction was allowed to warm to ambient temperature. The reaction mixture was then diluted with additional CH_2Cl_2 and washed with sat. NH_4Cl and then brine (x 2). The organic layer was then dried over $MgSO_4$, filtered, and concentrated in vacuo.

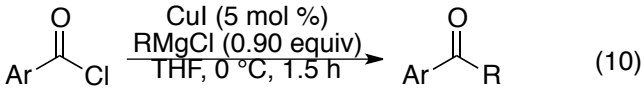
METHOD F: OXIDATION OF BENZYLIC ALCOHOLS



(9)

Modified from a procedure reported by Wipf.[31] Activated MnO_2 (20 equiv) was added to a solution of alcohol (1.0 equiv) in wet CH_2Cl_2 and the reaction was stirred vigorously at ambient temperature until complete by TLC (typically 24 h). The heterogeneous mixture was then passed through a plug of celite with additional CH_2Cl_2 and concentrated in vacuo.

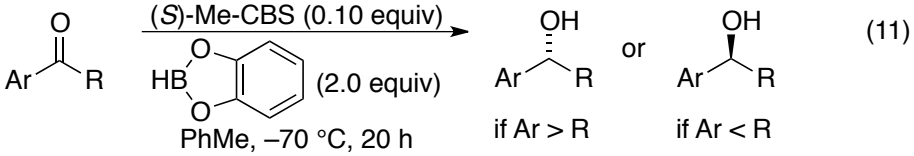
METHOD G: COPPER-CATALYZED ADDITION OF GRIGNARD REAGENTS TO ACID CHLORIDES



(10)

Modified from a procedure reported by Hultzsch.[32] In a glovebox, CuI (0.050 equiv) was added to a flame-dried round-bottom flask equipped with a stirbar. The flask was capped with a septum and removed from the glovebox. Anhydrous THF and acid chloride (0.90 equiv) were added to the flask resulting in a suspension. The reaction mixture was cooled to 0 °C and the Grignard reagent (0.90 equiv) was added drop-wise over 30 min. After an additional hour of stirring at 0 °C, the reaction mixture was concentrated in vacuo. The crude residue was dissolved in CH_2Cl_2 and washed with 1 M HCl resulting in precipitate formation. The layers were separated and the organic layer was filtered through a plug of celite to remove the copper salts. The filtrate was then washed with $NaHCO_3$, dried over Na_2SO_4, filtered, and concentrated in vacuo.

METHOD H: CBS REDUCTION WITH CATECHOLBORANE

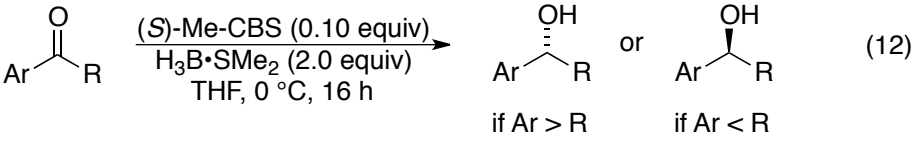


(11)

Modified from a procedure reported by Okamura.[33] In a glovebox, (*S*)-Me-CBS-oxazaborolidine (0.10 equiv) was added to a flame-dried round-bottom flask equipped with a stir bar. The flask was capped with a septum and taken out of the glovebox. Anhydrous PhMe and ketone (1.0 equiv) were added and the reaction mixture was stirred at ambient temperature until complete dissolution. The reaction was then cooled to –70 °C and catecholborane (1.5–2.0 equiv) was added drop-wise via syringe. After stirring for 20 h at –70 °C, wet methanol was added to quench the excess borane and the reaction was allowed to warm to ambient temperature. Sat. NH_4Cl was added to the reaction flask and the mixture was extracted with Et_2O (x 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo.

The above model for stereoselectivity is described by Corey.[17]

METHOD I: CBS REDUCTION WITH SMe_2•BH_3

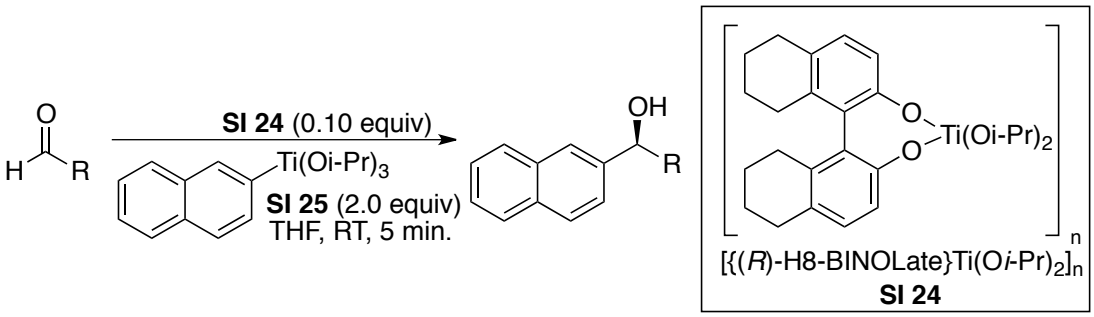


(12)

Modified from a procedure reported by Panek.[34] In the glovebox, (*S*)-Me-CBS-oxazaborolidine (0.10 equiv) was added to a flame-dried round-bottom flask equipped with a stir bar. The flask was capped with a septum and taken out of the box. Anhydrous THF was added to the flask followed by H_3B•SMe_2 (2.0 equiv). The reaction flask was cooled to −20 °C and ketone (1.0 equiv) as a solution in THF was added drop-wise over 15 min. After 16 h, methanol (0.5 mL) was slowly added to quench the excess borane. The reaction mixture was then partitioned between sat. NH_4Cl and EtOAc and the aqueous layer was extracted with EtOAc (x 2). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo.

The above model for stereoselectivity is described by Corey.[17]

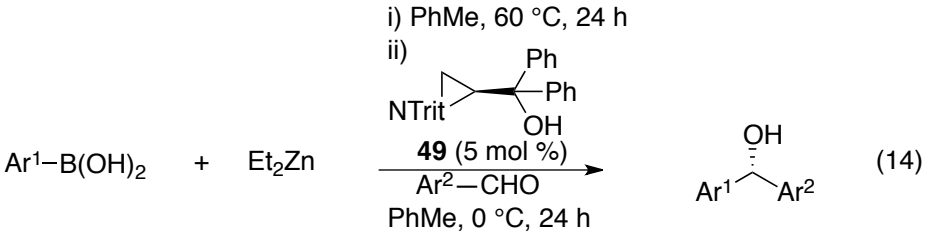
METHOD J: ENANTIOSELECTIVE ARYLATION OF ALKYL ALDEHYDES



(13)

Modified from a procedure reported by Gau.[5] In the glovebox, [{(*R*)-H_8-BINOLate}$Ti(O$*i*-$Pr)_2]_n$ **SI 24** (0.10 equiv) and 2-naphthyltitanium triisopropoxide **SI 25** (2.0 equiv) were added to a dry 50 mL round bottom flask equipped with a stir bar. The flask was capped with a septum and taken out of the glovebox. Anhydrous THF followed by alkyl aldehyde (1.0 equiv) were then added to flask. After stirring for 5 min at ambient temperature, the reaction was quenched with 2 M NaOH and extracted with ethyl acetate (x 3). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo.

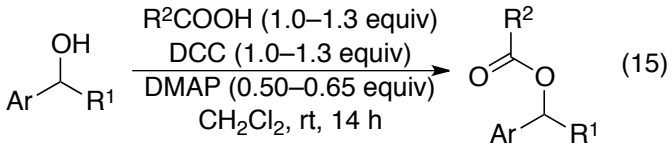
METHOD K: ENANTIOSELECTIVE ARYLATION OF ARYL ALDEHYDES



(14)

Modified from a procedure reported by Braga.[11] To a solution of boronic acid (2.4 equiv) in toluene was added diethylzinc (7.2 equiv, 1.0 M in toluene), and the solution was heated and stirred at 65 °C for 24 h. Upon cooling to 0 °C, (*S*)-(1-tritylaziridin-2-yl)diphenylmethanol **49** (0.050 equiv) was added as a solution in toluene. After stirring for 10 min, aldehyde (1.0 equiv) was added, also as a solution in toluene. The reaction was stirred at 0 °C for 20 h before quenching with 1 N hydrochloric acid. The product was extracted with EtOAc (x 3) and the combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo.

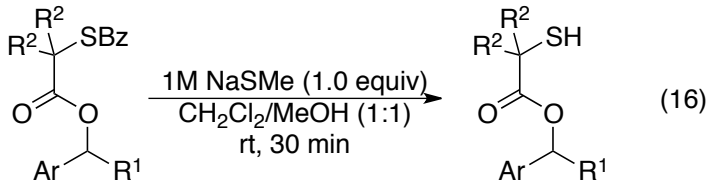
METHOD L: DCC COUPLING



(15)

Modified from a procedure reported by Meyer.[35] To a stirred solution of carboxylic acid (1.0–1.3 equiv) and alcohol (1.0 equiv) in CH_2Cl_2 were added 4-dimethylaminopyridine (0.50–0.65 equiv) and *N*,*N*'-dicyclohexylcarbodiimide (1.0–1.3 equiv). After stirring at ambient temperature for 20 h, the resulting opaque white mixture was filtered through Celite and concentrated in vacuo.

METHOD M: DEPROTECTION OF BENZOYL THIOLS

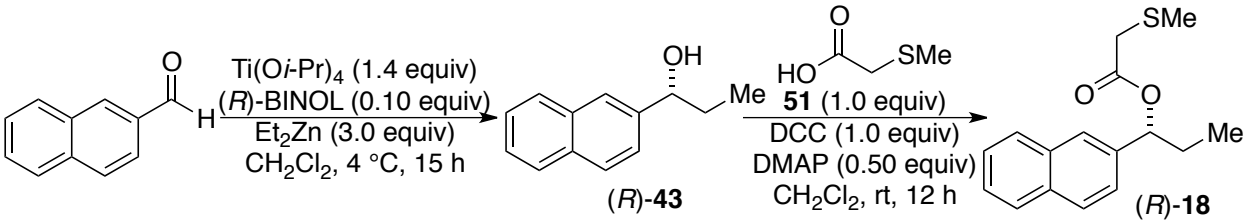


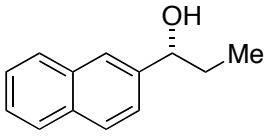
(16)

Modified from a procedure reported by Wallace and Springer.[36] NaSMe (1.0 equiv) was added to a stirred solution of ester (1.0 equiv) in a 1:1 mixture of wet MeOH and CH_2Cl_2. After 15 min, the reaction was quenched with 0.1 M HCl (2.0 equiv) and extracted with CH_2Cl_2 (x 3). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo.

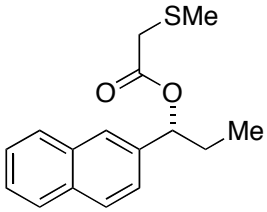
G. STARTING MATERIALS FOR TABLE 1

Scheme SI 6. Synthesis of substrate for Table 1, entry 1



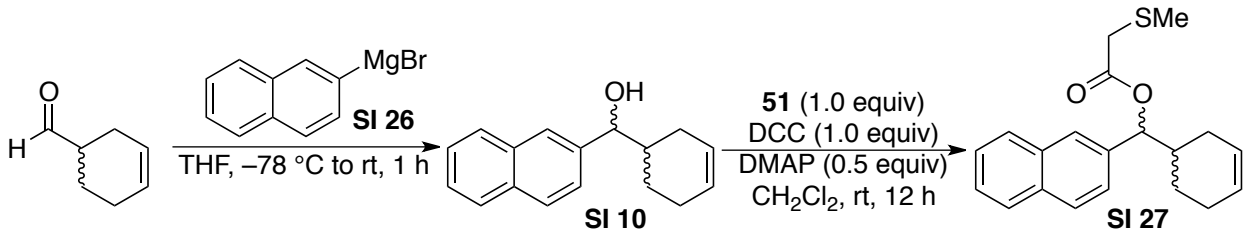


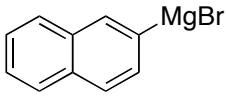
(*R*)-1-(2-naphthalenyl)-1-propanol (*R*)-43 was prepared according to a modified procedure reported by Chan.[37] To a solution of (*R*)-binapthol (0.82 g, 2.9 mmol, 0.10 equiv) in CH_2Cl_2 (220 mL) was added titanium isopropoxide (12 mL, 40 mmol, 1.4 equiv), and the solution was stirred at ambient temperature for 10 min. Diethylzinc (43 mL, 86 mmol, 3.0 equiv, 2.0 M in hexane) was added and the mixture was stirred for an additional 10 min at ambient temperature. The reaction mixture was cooled to 0 °C and a solution of 2-naphthaldehyde (4.5 g, 29 mmol, 1.0 equiv) in CH_2Cl_2 (25 mL) was added drop-wise. After stirring overnight at 4 °C, the reaction was quenched by the addition of 1 M HCl (200 mL). The reaction mixture was then extracted with CH_2Cl_2 (3 x 100 mL) and the combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resultant solid co-crystallized with (*R*)-BINOL from hexane/EtOAc and then was purified by flash chromatography (5–10% acetone in hexane) to afford the title compound as a white solid (3.50 g, 66%). Absolute configuration was assigned as *R* by comparison of optical rotation with literature values. Analytical data are consistent with literature values.[38] **TLC R_f** = 0.3 (4:1 hexane/EtOAc, UV active); **mp** 39–42 °C, lit.[23] mp 37–38 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.88–7.80 (m, 3H), 7.78 (s, 1H), 7.52–7.43 (m, 3H), 4.78 (dt, *J* = 6.5, 3.3, 1H), 1.98–1.78 (m, 2H), 1.92 (d, *J* = 3.3, 1H), 0.95 (t, *J* = 7.4, 3H); **$[\alpha]_D^{27}$** +39.5 (*c* 1.0, $CHCl_3$), lit.[15] $[\alpha]_D^{20}$ +35.1 (*c* 2.4, $CHCl_3$, 92% ee, (*R*)-enantiomer); **SFC** analysis (OD-H, 10.0% IPA, 2.5 mL/min, 215 nm) indicated 98% ee: t_R (minor) = 9.1 min, t_R (major) = 9.7 min.



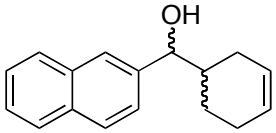
(*R*)-1-(2-naphthalenyl)propyl 2-(methylthio)acetate (*R*)-18 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (0.21 g, 2.0 mmol, 1.0 equiv), alcohol (*R*)-**43** (0.37 g, 2.0 mmol, 1.0 equiv), 4-dimethylaminopyridine (0.12 g, 1.0 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.41 g, 2.0 mmol, 1.0 equiv), and CH_2Cl_2 (11 mL). The crude residue was purified by flash chromatography (2.5–5% Et_2O in pentane) to afford to the title compound as a colorless oil (0.48 g, 87%) **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.86–7.72 (m, 4H), 7.51–7.39 (m, 3H), 5.87 (t, *J* = 6.8, 1H), 3.23 (s, 2H), 2.14 (s, 3H), 2.09–1.99 (m, 1H), 1.99–1.88 (m, 1H), 0.93 (t, *J* = 7.4, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.7, 137.6, 133.23, 133.20, 128.4, 128.1, 127.8, 126.3, 126.2, 125.9, 124.4, 78.6, 36.1, 29.3, 16.3, 10.1; **IR** (neat, cm^{-1}) 2969, 1726, 1267, 1125, 817, 747; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{16}H_{18}O_2SNa$ 297.0925, found 297.0928; **$[\alpha]^{27}_D$** + 95.1 (*c* 0.99, $CHCl_3$); **SFC** analysis (OD-H, 5.0% IPA, 3.0 mL/min, 215 nm) indicated 98% ee: t_R (major) = 5.1 min, t_R (minor) = 6.0 min.

Scheme SI 7. Synthesis of substrate for Table 1, entry 2

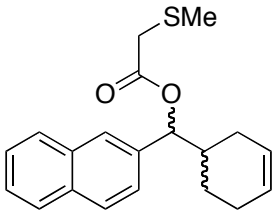




2-naphthylmagnesium bromide SI 26 was prepared according to Method D. The following amounts of reagents were used: 2-bromonaphthlene (4.1 g, 20 mmol, 1.0 equiv), magnesium (0.96 g, 40 mmol, 2.0 equiv), THF (18 mL). Grignard titrated to 0.49 M.[2]

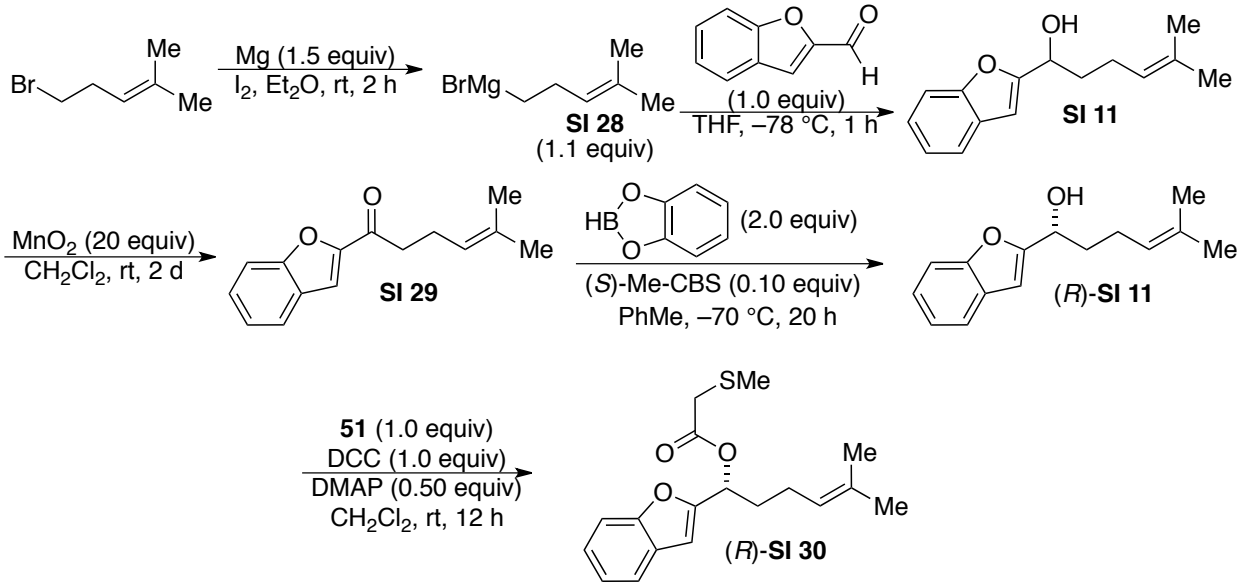


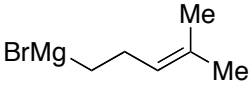
Cyclohex-3-enyl(naphthalen-2-yl)methanol SI 10. To a cooled (0 °C) solution of *rac*-cyclohex-3-enecarbaldehyde (0.23 mL, 2.0 mmol, 1.0 equiv) in THF (10 mL) was added Grignard **SI 26** (4.9 mL, 2.4 mmol, 1.2 equiv, 0.49 M in THF). The reaction was stirred and allowed to warm to ambient temperature. After 2 h, the remaining Grignard was quenched with sat. NH_4Cl, and the aqueous was extracted with EtOAc (2 x 20 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The product was purified by flash chromatography (5–20% EtOAc in hexanes) to afford the title compound as a white solid (0.35 g, 72%, dr = 52:48 by NMR integration). **TLC R_f** = 0.4 (4:1 hexane/EtOAc, UV active); **mp** 83–86 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.82 (d, *J* = 8.6, 3H), 7.45 (d, *J* = 5.5, 1H), 7.49–7.44 (m, 3H), 5.71–5.54 (m, 2H), 4.64 (d, *J* = 6.5, 0.52H), 4.57 (d, *J* = 7.8, 0.48H), 2.26–1.98 (m, 6H), 1.76–1.24 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 141.0, 140.9, 133.3, 133.2, 133.1, 128.33, 128.25, 128.05, 128.04, 127.8, 127.3, 127.0, 126.33, 126.27, 126.1, 125.98, 125.96, 125.74, 125.66, 124.7, 79.0, 78.8, 40.99, 40.94, 28.4, 27.7, 25.4, 25.2, 24.9; **IR** (neat, cm^{-1}) 3419, 3021, 2916, 2888, 2834, 1435, 1301; **HRMS** (TOF MS EI+) *m*/*z*: $[M]^+$ calculated for $C_{17}H_{18}O$ 238.1358, found 238.1396.



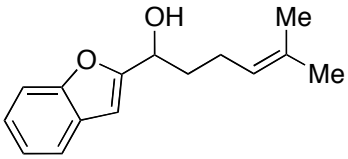
Cyclohex-3-enyl(naphthalen-2-yl)methyl 2-(methylthio)acetate SI 27 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (0.11 g, 1.0 mmol, 1.0 equiv), alcohol **SI 10** (0.24 g, 1.0 mmol, 1.0 equiv), 4-dimethylaminopyridine (61 mg, 0.50 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.21 mg, 1.0 mmol, 1.0 equiv), and CH_2Cl_2 (6 mL). The crude residue was purified by flash chromatography (10–20% EtOAc in hexanes) to afford to the title compound as a colorless oil (0.31 g, 95%, dr = 53:47 by ^{1}H NMR integration). **TLC R_f** = 0.5 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.83–7.81 (m, 4H), 7.48–7.45 (m, 3H), 5.78 (d, *J* = 7.9, 0.53H), 5.73 (d, *J* = 8.9, 0.47H), 5.69–5.53 (m, 2H), 3.23 (s, 2H), 2.27–1.97 (m, 7H), 1.73–1.71 (m, 1H), 1.59–1.22 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.8, 169.7, 136.7, 136.5, 133.24, 133.22, 122.1, 128.33, 128.31, 128.2, 127.8, 127.3, 127.1, 126.8, 126.7, 126.4, 126.26, 126.25, 125.8, 125.6, 124.78, 124.75, 81.1, 80.6, 39.2, 39.0, 36.12, 36.10, 28.1, 27.9, 25.0, 24.91, 24.89, 16.38, 16.37; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{20}H_{22}O_2SNa$ 349.1238, found 349.1244.

Scheme SI 8. Synthesis of substrate for Table 1, entry 3

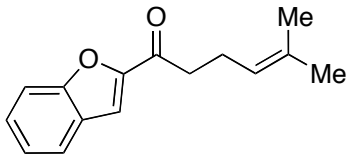




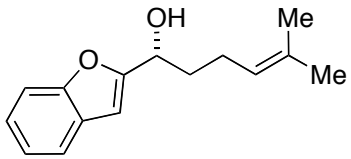
(4-methylpent-3-en-1-yl)magnesium bromide SI 28. Magnesium turnings (0.18 g, 7.5 mmol, 1.5 equiv) were added to a 2-neck round-bottom flask equipped with a stir bar, a condenser and septa tops. The reaction apparatus was flame-dried under vacuum and cooled under N_2. Et_2O (1 mL) was added to the reaction flask. 5-bromo-2-methyl-2-pentene (0.67 mL, 5.0 mmol, 1.0 equiv), as a solution in Et_2O (3 mL), was then added to the reaction flask portion-wise over 1 h. The reaction was stirred at ambient temperature for an additional hour and then titrated to 0.71 M.[2]



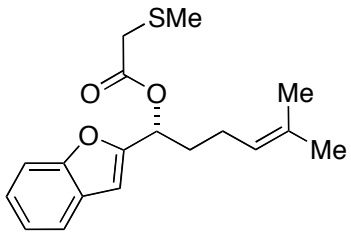
1-(2-benzofuryl)-5-methyl-4-hexen-1-ol SI 11. Benzofuran-2-carbaldehyde (0.47 g, 3.2 mmol, 1.0 equiv) and anhydrous THF (5 mL) were added to a flame-dried 50 mL round-bottom flask equipped with a stir bar and a septum. The homogeneous solution was cooled to –78 °C and Grignard **SI 28** (4.8 mL, 3.4 mmol, 1.1 equiv, 0.71 M in Et_2O) was added drop-wise over 15 min. The reaction mixture was allowed to warm to ambient temperature over 1 h. The reaction was then quenched with sat. NH_4Cl and extracted with Et_2O (3 x 10 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by flash chromatography (2–10% EtOAc in hexanes) to afford the title compound as a colorless oil (0.49 g, 66%). **TLC** $\mathbf{R_f}$ = 0.3 (4:1 hexane/EtOAc, UV active, stains blue with PAA); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.52 (d, *J* = 7.2, 1H), 7.44 (d, *J* = 7.9, 1H), 7.25 (td, *J* = 7.2, 1.1, 1H), 7.20 (td, *J* = 7.2, 0.9, 1H), 6.59 (s, 1H), 5.15 (tt, *J* = 7.2, 1.2, 1H), 4.81 (dd, *J* = 12.7, 5.7, 1H), 2.20 (d, *J* = 5.3, 1H), 2.14 (q, *J* = 7.3, 2H), 1.97 (m, 2H), 1.69 (s, 3H), 1.60 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 159.6, 154.9, 132.9, 128.3, 124.2, 123.5, 122.8, 121.1, 111.3, 102.6, 68.0, 35.6, 25.9, 24.1, 17.9; **IR** (neat, cm^{-1}) 3358, 2919, 1454, 1253, 740; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{15}H_{18}O_2Na$ 253.1205, found 253.1208.



1-(2-benzofuryl)-5-methyl-4-hexen-1-one SI 29 was prepared according to Method F. The following amounts of reagents were used: MnO_2 (2.3 g, 26 mmol, 20 equiv), alcohol **SI 11** (0.30 g, 1.3 mmol, 1.0 equiv), and CH_2Cl_2 (20 mL). The crude residue was purified by flash chromatography (5% Et_2O in hexanes) to afford **SI 29** as a slightly yellow solid (0.27 g, 92%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active, stains turquoise with PAA); **mp** 48–49 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.70 (d, *J* = 7.9, 1H), 7.58 (d, *J* = 8.4, 1H), 7.49 (s, 1H), 7.47 (t, *J* = 7.9, 1H), 7.31 (t, *J* = 7.6, 1H), 5.18 (tt, *J* = 7.2, 1.2, 1H), 2.99 (t, *J* = 7.5, 2H), 2.46 (q, *J* = 7.4, 2H), 1.69 (s, 3H), 1.65 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 191.3, 155.7, 152.8, 133.3, 128.3, 127.2, 124.0, 123.4, 122.6, 112.7, 112.6, 39.3, 25.8, 23.0, 17.8; **IR** (neat, cm^{-1}) 2907, 1681, 1560, 1153, 841, 751; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{15}H_{16}O_2Na$ 251.1048, found 251.1057.

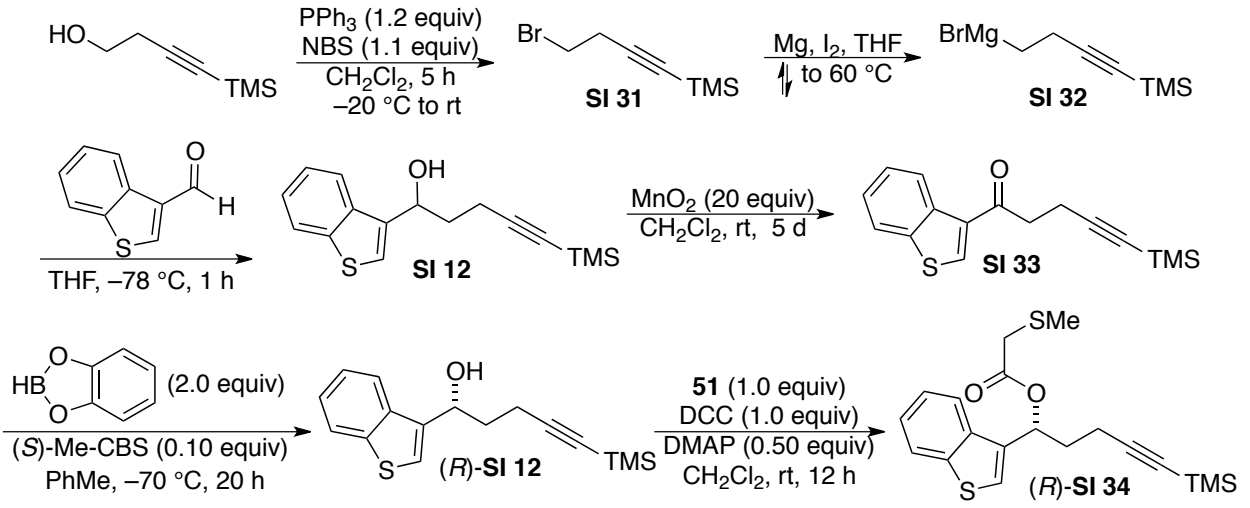


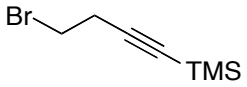
(*R*)-1-(2-benzofuryl)-5-methyl-4-hexen-1-ol (*R*)-SI 11 was prepared according to Method H. The following amounts of reagents were used: (*S*)-Me-CBS-oxazaborolidine (21 mg, 0.076 mmol, 0.10 equiv), ketone **SI 29** (0.17 g, 0.76 mmol, 1.0 equiv), catecholborane (0.12 mL, 1.1 mmol, 1.5 equiv), and PhMe (7 mL). The crude residue was purified by flash chromatography (2–10% EtOAc in hexane) to afford the title compound as a colorless oil (0.15 g, 68%). Absolute configuration assigned as *R* based on the accepted model for selectivity in CBS reductions[17] and confirmed by Competing Enantioselective Conversion (CEC).[18] For analytical data see *rac*-alcohol **SI 11**. **$[\alpha]_D^{26}$** –19.1 (*c* 1.0, $CHCl_3$); **SFC** analysis (OJ-H, 10.0% MeOH, 3.0 mL/min, 215 nm) indicated 93% ee: t_R (major) = 3.8 min, t_R (minor) = 4.4 min.



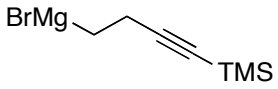
(*R*)-1-(2-benzofuryl)-5-methyl-4-hexen-2-(methylthio)acetate (*R*)-SI 30 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (61 mg, 0.58 mmol, 1.0 equiv), alcohol (*R*)-**SI 11** (0.13 g, 0.58 mmol, 1.0 equiv), 4-dimethylaminopyridine (35 mg, 0.29 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.12 g, 0.58 mmol, 1.0 equiv), and CH_2Cl_2 (4 mL). The crude residue was purified by flash chromatography (5% Et_2O in pentane) to afford to the title compound as a colorless oil (0.48 g, 87%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.54 (d, *J* = 7.6, 1H), 7.46 (d, *J* = 8.2, 1H), 7.28 (td, *J* = 7.7, 1.2, 1H), 7.21 (td, *J* = 7.3, 0.8, 1H), 6.72 (s, 1H), 5.99 (at, *J* = 6.5, 1H), 5.11 (br s, 1H), 3.24 (d, *J* = 14.6, 1H), 3.20 (d, *J* = 15.3, 1H), 2.18 (s, 3H), 2.15–2.03 (m, 4H), 1.67 (s, 3H), 1.60 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.6, 154.9, 154.8, 133.1, 127.9, 124.7, 123.0, 122.7, 121.4, 111.5, 105.4, 69.8, 35.9, 32.7, 25.8, 23.9, 17.8, 16.4; **IR** (neat, cm^{-1}) 2920, 1732, 1454, 1252, 1126, 958; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{18}H_{22}O_3SNa$ 341.1187, found 341.1178; **$[\alpha]_D^{26}$** +150.9 (*c* 0.69, $CHCl_3$); **SFC** analysis (OJ-H, 10.0% MeOH, 3.0 mL/min, 215 nm) indicated 93% ee: t_R (minor) = 2.1 min, t_R (major) = 2.4 min.

Scheme SI 9. Synthesis of substrate for Table 1, entry 4

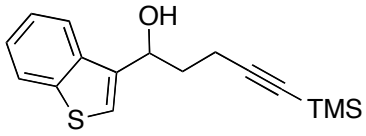




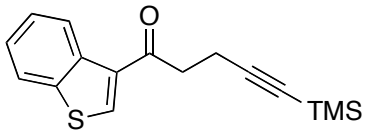
(4-bromobut-1-yn-1-yl)trimethylsilane SI 31 was prepared according to a modified procedure by Steliou.[39] A flame-dried 250 mL round-bottom flask equipped with a stir bar and a septum was charged with 4-trimethylsilyl-3-butyn-1-ol (3.0 g, 21 mmol, 1.0 equiv). The flask was placed under reduced pressure and back-filled with nitrogen (x 3). CH_2Cl_2 (35 mL) was then added and the flask cooled to –20 °C. Triphenylphospine (6.6 g, 25 mmol, 1.2 equiv) was added followed by recrystallized NBS (4.1 g, 23 mmol, 1.1 equiv). The reaction mixture was allowed to warm to ambient temperature and the progress of the reaction was followed by TLC. Once complete (5 h), Et_2O (150 mL) was added and the organics were successively washed with sat. $NaHCO_3$ (30 mL x 2) and brine (30 mL). The organics were then dried over $MgSO_4$, filtered and concentrated in vacuo. The resultant solid was then suspended in hexanes (300 mL) and stirred vigorously for 15 min. The suspension was then filtered through a plug of celite and the filtrate was concentrated in vacuo. The crude was purified by flash chromatography (100% petroleum ether) to afford the title compound as a colorless oil (3.2 g, 75%). Analytical data are consistent with literature values.[40] **TLC R_f** = 0.5 (100 % petroleum ether, stain with $KMnO_4$); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 3.43 (t, *J* = 7.5, 2H), 2.77 (t, *J* = 7.5, 2H), 0.16 (s, 9H).



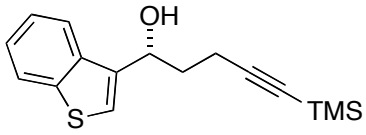
4-trimethylsilyl-3-butynyl-1-magnesium bromide SI 32 was prepared according to a modified procedure reported by Waldman.[41] A 100 mL 3-neck round-bottom flask, equipped with a reflux condenser, an addition funnel, and a stir bar was charged with magnesium turnings (0.57 g, 24 mmol, 1.5 equiv), flame-dried under reduced pressure and cooled under nitrogen. Anhydrous THF (3 mL) was added to the reaction flask followed by iodine to activate the magnesium. Substrate **SI 31** (3.2 g, 16 mmol, 1.0 equiv), as a solution in THF (19 mL), was transferred to the addition funnel. The solution of alkyl bromide **SI 31** was added drop-wise to the activated magnesium turnings. Gentle heating with a heat gun was necessary to initiate the reaction after which the reaction continued at a reflux for the remainder of the addition. Upon completion, the addition funnel was rinsed with an additional 1 mL of anhydrous THF and the reaction was stirred at 60 °C for an additional 30 min. The resultant Grignard reagent was cooled to ambient temperature and titrated to 0.44 M.[2]



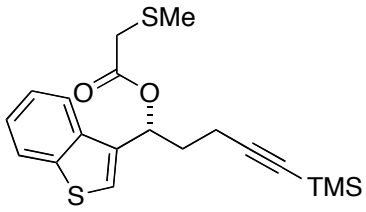
1-(3-benzothiophenyl)-5-(trimethylsilyl)-4-pentyn-1-ol SI 12. Benzothiophene-3-carbaldehyde (0.60 g, 3.7 mmol, 1.0 equiv) was added to a flame-dried 50 mL round-bottom flask equipped with a stir bar and a septum. The flask was then evacuated and back-filled with nitrogen three times. Anhydrous THF (4 mL) was added to the flask and the homogeneous solution was cooled to –78 °C. Grignard **SI 32** (10 mL, 4.5 mmol, 1.2 equiv, 0.44 M in THF) was added via syringe and the reaction mixture was allowed to stir at –78 °C until complete by TLC (1 h). The reaction was then quenched with sat. NH_4Cl (10 mL) and extracted with Et_2O (3 x 10 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography (2–10% EtOAc in hexanes) to afford the title compound as a yellow oil (1.1 g, 95%). **TLC R_f** = 0.5 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.92–7.83 (m, 2H), 7.40 (s, 1H), 7.40–7.33 (m, 2H), 5.30 (dt, *J* = 8.1, 3.8, 1H) 2.49 (ddd, *J* = 17.1, 7.8, 7.0, 1H), 2.38 (dt, *J* = 17.1, 6.4, 1H), 2.27 (d, *J* = 3.7, 1H), 2.19–2.02 (m, 2H), 0.18 (s, 9H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 141.1, 139.4, 137.2, 124.6, 124.2, 123.1, 122.3, 122.2, 106.8, 85.9, 69.1, 36.1, 16.9, 0.3; **IR** (neat, cm^{-1}) 3385, 1739, 1248, 837, 758; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{16}H_{20}OSSiNa$ 311.0902, found 311.0904.



1-(3-benzothiophenyl)-5-(trimethylsilyl)-4-pentyn-1-one SI 33 was prepared according to Method F. The following amounts of reagents were used: MnO_2 (5.0 g, 58 mmol, 16 equiv), alcohol **SI 12** (0.75 g, 2.6 mmol, 1.0 equiv), and CH_2Cl_2 (30 mL). The crude residue was recrystallized from hexanes/EtOAc to afford SI 4 as a white crystalline solid (0.51 g, 68%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active); **mp** 96–99 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.75 (d, *J* = 8.2, 1H), 8.31 (s, 1H), 7.86 (d, *J* = 8.2, 1H) 7.49 (t, *J* = 7.7, 1H), 7.41 (t, *J* = 7.6, 1H), 3.24 (t, *J* = 7.6, 2H), 2.70 (t, *J* = 7.5, 2H), 0.14 (s, 9H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 193.2, 139.9, 137.1, 136.6, 134.9, 126.0, 125.7, 125.6, 122.4, 105.9, 85.5, 39.2, 15.1, 0.2; **IR** (neat, cm^{-1}) 3087, 2180, 1667, 842, 762; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{16}H_{18}OSSiNa$ 309.0745, found 309.0742.

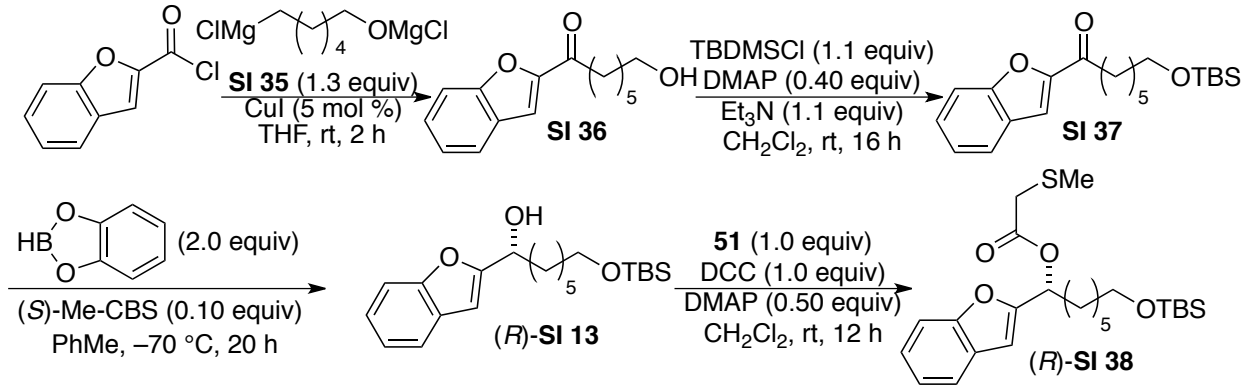


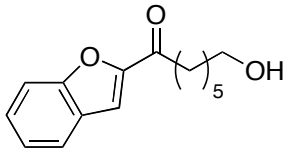
(*R*)-1-(3-benzothiophenyl)-5-(trimethylsilyl)-4-pentyn-1-ol (*R*)-SI 12 was prepared according to Method H. The following amounts of reagents were used: (*S*)-Me-CBS-oxazaborolidine (18 mg, 0.066 mmol, 0.10 equiv), ketone **SI 33** (0.19 g, 0.66 mmol, 1.0 equiv), catecholborane (0.11 mL, 1.0 mmol, 1.5 equiv), and PhMe (7 mL). The crude residue was purified by flash chromatography (2–10% EtOAc in hexanes) to afford the title compound as a colorless oil (0.15 g, 80%). Absolute configuration assigned as *R* based on the accepted model for selectivity in CBS reductions[17] and confirmed by Competing Enantioselective Conversion (CEC).[18] For analytical data see *rac*-alcohol **SI 12**. **$[\alpha]_D^{28}$** –16.3 (*c* 1.2, $CHCl_3$); **SFC** analysis (AD-H, 3.0% MeOH, 3.0 mL/min, 215 nm) indicated 96% ee: t_R (minor) = 6.7 min, t_R (major) = 8.1 min.



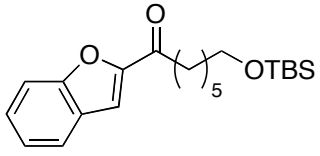
(*R*)-1-(benzo[b]thiophen-3-yl)-5-(trimethylsilyl)pent-4-yn-1-yl 2-(methylthio)acetate (*R*)-SI 34 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (54 mg, 0.51 mmol, 1.0 equiv), alcohol (*R*)-**SI 12** (0.15 g, 0.51 mmol, 1.0 equiv), 4-dimethylaminopyridine (31 mg, 0.29 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.11 g, 0.51 mmol, 1.0 equiv), and CH_2Cl_2 (4 mL). The crude residue was purified by flash chromatography (2–5% Et_2O in pentane) to afford to the title compound as a colorless oil (0.18 g, 89%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.93 (dd, *J* = 7.1, 1.1, 1H), 7.85 (dd, *J* = 7.3, 1.1, 1H), 7.45 (s, 1H), 7.37 (apd, *J* = 7.5, 1.2, 2H), 6.36 (dd, *J* = 7.1, 5.5, 1H), 3.22 (s, 2H), 2.45–2.17 (m, 4H), 2.14 (s, 3H), 0.17 (s, 9H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.3, 140.8, 137.0, 134.7, 124.7, 124.4, 123.8, 123.1, 122.3, 105.6, 86.0, 71.2, 35.9, 34.0, 16.6, 16.3, 0.2; **IR** (neat, cm^{-1}) 2958, 2174, 1731, 1249, 1128, 839; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{19}H_{24}O_2S_2SiNa$ 399.0885, found 399.0879; **$[\alpha]_D^{26}$** +9.7 (*c* 1.0, $CHCl_3$); **SFC** analysis (AD-H, 15.0% IPA, 1.0 mL/min, 215 nm) indicated 97% ee: t_R (major) = 6.8 min, t_R (minor) = 7.8 min.

Scheme SI 10. Synthesis of substrate for Table 1, entry 5



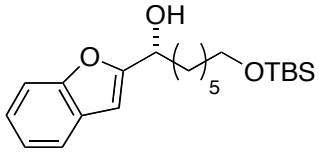


1-(benzofuran-2-yl)-3-hydroxypropan-1-one SI 36 was prepared according to Method G. The following amounts of reagents were used: CuI (32 mg, 0.17 mmol, 0.050 equiv), benzofuran-2-carbonyl chloride (0.60 g, 3.3 mmol, 1.0 equiv) Grignard reagent **SI 35** (5.0 mL, 3.2 mmol, 0.95 equiv, 0.63 M in THF), and THF (3.5 mL). The crude material was carried to the next step without purification (0.42 g).

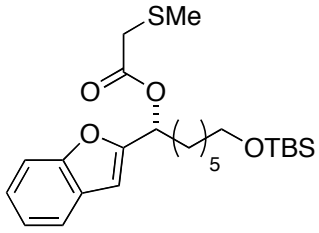


1-(2-benzofuryl)-7-[(*tert*-butyldimethylsilyl)oxy]-1-heptanone SI 37 was prepared according to a modified procedure reported by Hernandez.[42] *tert*-Butyldimethylsilyl chloride (0.28 g, 1.9 mmol, 1.1 equiv) was added to a stirred solution of crude alcohol **SI 36** (0.42 g, 1.7 mmol, 1.0 equiv), dimethylaminopyridine (84 mg, 0.69 mmol, 0.40 equiv), and triethylamine (0.26 mL, 1.9 mmol, 1.1 equiv) in anhydrous CH_2Cl_2 (17 mL) under N_2. The reaction was allowed to stir overnight (14 h) and subsequently quenched with sat. NH_4Cl and extracted with CH_2Cl_2 (3 x 10 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography

(2–10% Et_2O in pentane) to afford the title compound as a slightly yellow oil (0.22 g, 53%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.70 (d, *J* = 7.9, 1H), 7.58 (d, *J* = 8.4, 1H), 7.49 (s, 1H), 7.47 (t, *J* = 8.1, 1H), 7.30 (t, *J* = 7.5, 1H), 3.61 (t, *J* = 6.5, 2H), 2.95 (t, *J* = 7.5, 2H), 1.79 (p, 7.3, 2H), 1.54 (p, *J* = 6.7, 2H), 1.48–1.34 (m, 4H), 0.89 (s, 9H), 0.05 (s, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 191.7, 155.7, 152.8, 128.2, 127.2, 124.0, 123.4, 112.7, 112.6, 63.3, 39.0, 32.8, 29.2, 26.1, 25.7, 24.4, 18.5, –5.2; **IR** (neat, cm^{-1}) 2928, 2856, 1683, 1558, 1096, 833; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{21}H_{32}O_3SNa$ 383.2018, found 383.2015.

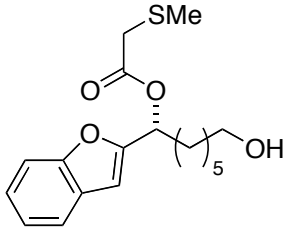


(*R*)-1-(2-benzofuryl)-7-[(*tert*-butyldimethylsilyl)oxy]-1-heptanol (*R*)-SI 13 was prepared according to Method H. The following amounts of reagents were used: (*S*)-Me-CBS-oxazaborolidine (21 mg, 0.077 mmol, 0.10 equiv), ketone **SI 37** (0.28 g, 0.77 mmol, 1.0 equiv), catecholborane (0.12 mL, 1.2 mmol, 1.5 equiv), and PhMe (7 mL). The crude residue was purified by flash chromatography (2–10% EtOAc in hexanes) to afford the title compound as a colorless oil (0.28 g, 91%). Absolute configuration assigned as *R* based on the accepted model for selectivity in CBS reductions[17] and confirmed by Competing Enantioselective Conversion (CEC).[18] **TLC R_f** = 0.4 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.52 (d, *J* = 7.4, 1H), 7.44 (d, *J* = 7.9, 1H), 7.25 (td, *J* = 7.7, 1.3, 1H), 7.20 (t, *J* = 7.3, 1H), 6.59 (s, 1H), 4.79 (dd, *J* = 10.2, 6.3, 1H), 3.58 (t, *J* = 6.6, 2H), 2.20 (d, *J* = 4.4, 1H) 2.01–1.84 (m, 2H), 1.56–1.42 (m, 3H), 1.42–1.26 (m, 5H), 0.89 (s, 9H), 0.04 (s, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 159.6, 154.9, 128.3, 124.2, 122.9, 121.1, 111.3, 102.6, 68.4, 63.4, 35.7, 32.9, 29.3, 26.1, 25.8, 25.5, 18.5, −5.1; **IR** (neat, cm^{-1}) 3362, 2929, 2856, 1253, 1097, 881; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{21}H_{34}O_3SiNa$ 385.2175, found 385.2177; **$[\alpha]_D^{27}$** +3.8 (*c* 0.99, $CHCl_3$); **SFC** analysis (OD-H, 5.0% MeOH, 3.0 mL/min, 215 nm) indicated 88% ee: t_R (major) = 11.1 min, t_R (minor) = 12.1 min.



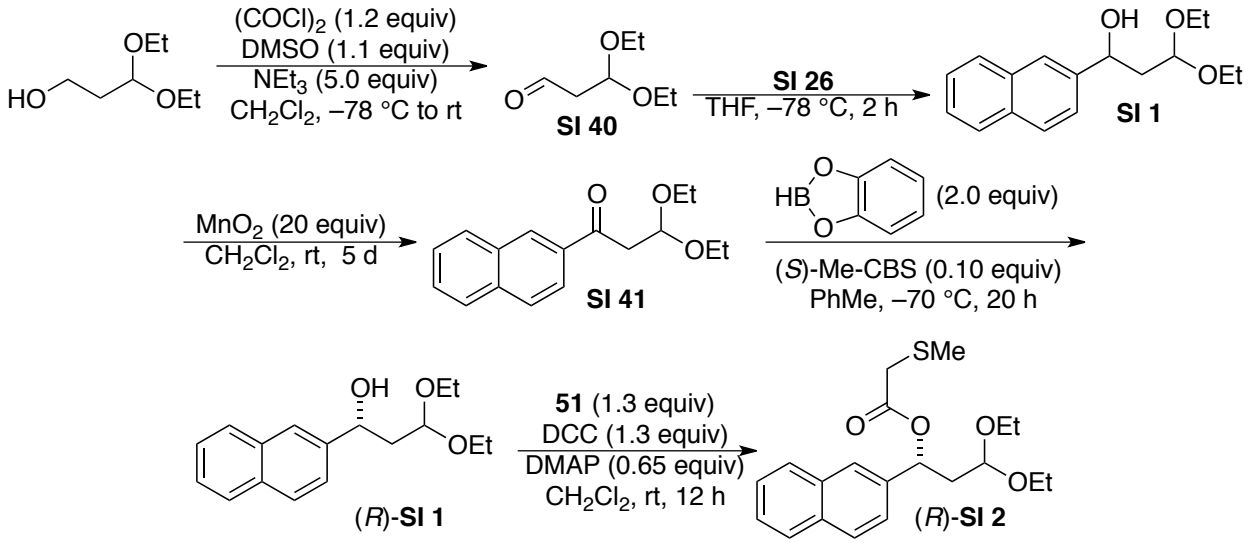
(*R*)-1-(benzofuran-2-yl)-7-((*tert*-butyldimethylsilyl)oxy)heptyl 2-(methylthio)acetate (*R*)-SI 38 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (59 mg, 0.65 mmol, 1.0 equiv), alcohol (*R*)-**SI 13** (0.24 g, 0.65 mmol, 1.0 equiv), 4-dimethylaminopyridine (40 mg, 0.32 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.13 g, 0.65 mmol, 1.0 equiv), and CH_2Cl_2 (5 mL). The crude residue was purified by flash chromatography (2–5% Et_2O in pentane) to afford to the title compound as a colorless oil (0.27 g, 92%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.55 (d, *J* = 7.5, 1H), 7.47 (d, *J* = 8.2, 1H), 7.28 (td, *J* = 7.7, 1.2, 1H), 7.22 (t, *J* = 7.4, 1H), 6.72 (s, 1H), 5.99 (t, *J* = 7.1, 1H), 3.60 (t, *J* = 6.5, 2H), 3.24 (d, *J* = 14.9, 1H), 3.20 (d, *J* = 15.0, 1H), 2.18 (s, 3H), 2.06 (q, *J* = 7.0, 2H), 1.49 (p, *J* = 6.7, 2H), 1.45–1.24 (m, 6H), 0.88 (s, 9H), 0.03 (s, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.7, 154.93, 154.91, 127.9, 124.7, 123.0, 121.4, 111.5, 105.3, 70.2, 63.3, 35.9, 32.8, 32.6, 29.1, 26.1, 25.7, 25.3, 18.5, 16.4, –5.1; **IR** (neat, cm^{-1}) 2928, 1733, 1252, 1096, 836; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{24}H_{38}O_4SSiNa$ 473.2158, found 473.2154; **$[\alpha]_D^{26}$** –26.8 (*c* 1.2, $CHCl_3$); **SFC** analysis (AD-H, 15.0% IPA, 1.0 mL/min, 215 nm) indicated 90% ee: t_R (minor) = 7.0 min, t_R (major) = 7.4 min.

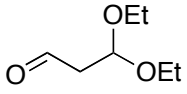
(17)



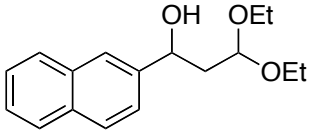
(*R*)-1-(benzofuran-2-yl)-7-hydroxyheptyl 2-(methylthio)acetate (*R*)-SI 39 was prepared according to a modified procedure reported by Corey.[43] Tetrabutylammonium fluoride (0.44 mL, 0.44 mmol, 2.0 equiv, 1.0 M in THF) was added to a stirred solution of substrate (*R*)-**SI 38** (0.10 g, 0.22 mmol, 1.0 equiv) in anhydrous THF (1.0 mL) at 5 °C. After 5 min, the reaction was warmed to ambient temperature and stirred for an additional 50 min before quenching with sat. NH_4Cl. The reaction mixture was then extracted with Et_2O (3x 3mL). The combined organics were washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography (20–40% EtOAc in hexanes to afford the title compound as a colorless oil (49 mg, 66%). **TLC** $\mathbf{R_f}$ = 0.5 (1:1 hexane/EtOAc, UV active, stain with CAM); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.55 (d, *J* = 7.6, 1H), 7.50 (d, *J* = 8.2, 1H), 7.29 (td, *J* = 7.7, 1.2, 1H), 7.22 (td, *J* = 7.5, 0.6, 1H), 6.72 (s, 1H), 5.99 (t, *J* = 7.1, 1H), 3.62 (t *J* = 6.2, 2H), 3.24 (d, *J* = 15.2, 1H), 3.20 (d, *J* = 14.8, 1H), 2.18 (s, 3H), 2.07 (q, *J* = 7.2, 2H), 1.60–1.50 (m, 2H), 1.49–1.28 (m, 6H), 1.22 (br s, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.7, 154.9, 154.8, 127.9, 124.7, 123.0, 121.4, 111.5, 105.3, 70.2, 63.0, 35.9, 32.7, 32.5, 29.1, 25.7, 25.3, 16.4; **IR** (neat, cm^{-1}) 3335, 2927, 1730, 1253, 1127, 751; **HRMS** (TOF MS ES+) *m/z*: $[M + Na]^+$ calculated for $C_{18}H_{24}O_4SNa$ 359.1293, found 359.1306; $\mathbf{[\alpha]_D^{27}}$ +95.5 (*c* 0.53, $CHCl_3$); **SFC** analysis (OJ-H, 10.0% IPA, 3.0 mL/min, 215 nm) indicated 92% ee: t_R (minor) = 6.5 min, t_R (major) = 11.4 min.

Scheme SI 11. Synthesis of substrate for Table 1, entry 7

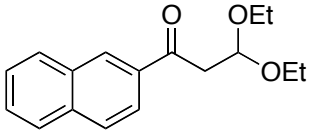




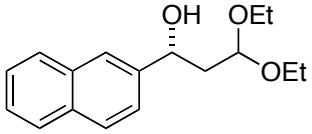
3,3-diethoxy-1-propanal SI 40 was prepared according Method E. The following amounts of reagents were used: DMSO (0.78 mL, 11 mmol, 1.1 equiv) in CH_2Cl_2 (17 mL), oxalyl chloride (1.0 mL, 12 mmol, 1.2 equiv) in CH_2Cl_2 (15 mL) 3,3-diethoxy propanol (1.5 g, 10 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL), and triethylamine (7.7 mL, 50 mmol, 5.0 equiv). The crude yellow oil was used without further purification. Analytical data was consistent with literature values.[44] **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.76 (t, *J* = 1.9, 1H), 4.96 (t, *J* = 5.5, 1H), 3.69 (dq, *J* = 9.1, 7.2, 2H), 3.56 (dq, *J* = 9.1, 7.2, 2H), 2.73 (dd, *J* = 5.4, 2.0, 2H), 1.22 (t, *J* = 7.0, 6H)



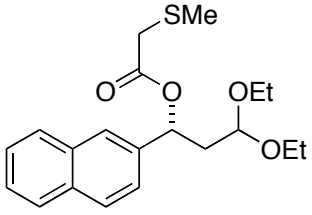
3,3-diethoxy-1-(2-naphthalenyl)-1-propanol SI 1. Grignard **SI 26** (9.0 mL, 4.4 mmol, 1.1 equiv, 0.5 M in THF) was added to a solution of aldehyde **SI 40** (0.59 g, 4.0 mmol, 1.0 equiv) in anhydrous THF (10 mL) at –78 °C. The reaction was stirred for 2 h at –78 °C. Subsequently, the reaction was quenched with sat. NH_4Cl and warmed to ambient temperature. The crude reaction mixture was extracted with Et_2O (3 x 20 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude residue was purified by flash chromatography (5–20% EtOAc in hexane with 1% TEA) to afford the title compound as a slightly yellow oil (0.27 g, 25%). **TLC R_f** = 0.2 (4:1 hexane/EtOAc, stain with CAM); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.88–7.75 (m, 4H), 7.50–7.38 (m, 3H), 5.05 (dd, *J* = 9.0, 2.6, 1H), 4.69 (t, *J* = 5.4, 1H), 3.77 (br s, 1H), 3.72 (dq, *J* = 9.3, 7.1, 1H) 3.65 (dq, *J* = 9.3, 7.1, 1H), 3.56–3.47 (m, 2H), 2.15 (ddd, *J* = 14.3, 8.9, 5.9, 1H), 2.07 (ddd, *J* = 14.3, 4.9, 3.3, 1H), 1.23 (t, *J* = 7.2, 3H), 1.21 (t, *J* = 7.0, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 141.7, 133.4, 132.9, 128.2, 128.0, 127.7, 126.1, 125.8, 124.3, 124.1, 102.0, 71.0, 62.4, 61.7, 42.5, 15.5, 15.4; **IR** (neat, cm^{-1}) 3446, 2972, 1739, 1123, 1050, 818; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{17}H_{22}O_3Na$ 297.1467, found 297.1476.



3,3-diethoxy-1-(2-naphthalenyl)-1-propanone SI 41 was prepared according to Method F. The following amounts of reagents were used: alcohol **SI 1** (0.44 g, 1.6 mmol, 1.0 equiv), manganese oxide (4.8 g, 55 mmol, 34 equiv) in CH_2Cl_2 (20 mL). The crude residue was purified by flash chromatography (5–10% EtOAc in hexanes) to afford the title compound as a yellow oil (0.38 g, 88%). **TLC R_f** = 0.4 (4:1 hexane/EtOAc, stains orange with CAM); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.49 (s, 1H), 8.03 (dd, *J* = 8.6, 1.7, 1H), 7.96 (d, *J* = 8.3, 1H), 7.88 (t, *J* = 8.7, 2H) 7.60 (td, *J* = 7.5, 1.2, 1H), 7.55 (td, *J* = 7.5, 1.1, 1H), 5.17 (t, *J* = 5.6, 1H), 3.76 (dq, *J* = 9.3, 7.1, 2H), 3.62 (dq, *J* = 9.2, 7.1, 2H), 3.43 (d, *J* = 5.5, 2H), 1.2 (t, *J* = 7.1, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 197.3, 135.7, 134.7, 132.6, 130.4, 129.8, 128.6, 128.5, 127.9, 126.9, 124.0, 100.1, 62.9, 43.9, 15.4. **IR** (neat, cm^{-1}) 2972, 1739, 1680, 1376, 1112, 1055, 745; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{17}H_{20}O_3Na$ 295.1310, found 295.1308.

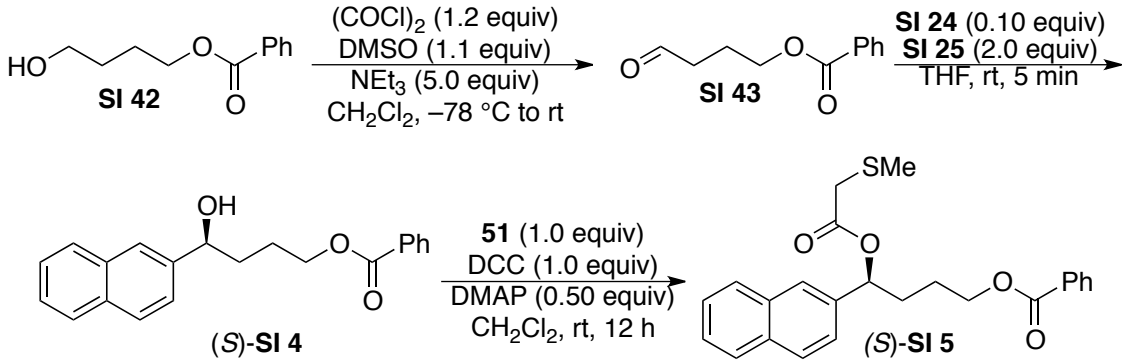


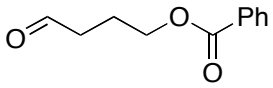
(*R*)-3,3-diethoxy-1-(2-naphthalenyl)-1-propanol (*R*)-SI 1 was prepared according to Method H. The following amounts of reagents were used: (*S*)-Me-CBS-oxazaborolidine (20 mg, 0.073 mmol, 0.10 equiv), ketone **SI 41** (0.20 g, 0.73 mmol, 1.0 equiv), catecholborane (0.12 mL, 1.1 mmol, 1.5 equiv), and PhMe (7 mL). The crude compound was carried to the next step without purification (70 mg). Optical rotation and absolute configuration assignment was performed on a sample obtained using Method I which resulted in clean material but with lower ee. **$[\alpha]_D^{27}$** +16.8 (*c* 0.99, $CHCl_3$, 86% ee). Absolute configuration assigned as *R* based on the accepted model for selectivity in CBS reductions[17] and confirmed by Competing Enantioselective Conversion (CEC).[18] For analytical data see *rac*-alcohol **SI 1**.



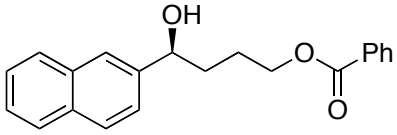
(*R*)-3,3-diethoxy-1-(2-naphthalenyl)propyl-2-(methylthio)acetate (*R*)-SI 2 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (34 mg, 0.32 mmol, 1.3 equiv), alcohol (*R*)-**SI 1** (70 mg, 0.29 mmol, 1.0 equiv), 4-dimethylaminopyridine (20 mg, 0.16 mmol, 0.65 equiv), *N*,*N*'-dicyclohexylcarbodiimide (66 mg, 0.32 mmol, 1.3 equiv), and CH_2Cl_2 (2 mL). The crude residue was purified by flash chromatography (5–15% Et_2O in pentane) to afford to the title compound as a colorless oil (48 mg, 52%). **TLC R_f** = 0.5 (4:1 hexane/EtOAc, UV active, stains with CAM); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.90–7.78 (m, 4H), 7.53–7.44 (m, 3H), 6.06 (dd, *J* = 8.6, 5.7, 1H), 4.54 (t, *J* = 5.8, 1H), 3.66 (ap, *J* = 7.6, 2H), 3.49 (dq, *J* = 9.2, 7.1, 2H), 3.20 (t, *J* = 14.7, 2H), 2.41 (ddd, *J* = 14.1, 8.7, 5.2, 1H), 2.18 (dt, *J* = 14.2, 6.1, 1H), 2.12 (s, 3H), 1.22 (t, *J* = 7.1, 3H), 1.20 (t, *J* = 7.0, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.3, 137.3, 133.24, 133.23, 128.6, 128.2, 127.8, 126.4, 126.3, 126.0, 124.3, 99.9, 74.2, 62.1, 61.1, 40.5, 36.0, 16.3, 15.5, 15.4; **IR** (neat, cm^{-1}) 2974, 1731, 1269, 1122 1057; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{20}H_{26}O_4SNa$ 385.1450, found 385.1448; **$[\alpha]_D^{28}$** +58.6 (*c* 0.99, $CHCl_3$); **SFC** analysis (OJ-H, 5.0% MeOH, 3.0 mL/min, 215 nm) indicated 89% ee: t_R (major) = 3.2 min, t_R (minor) = 3.6 min.

Scheme SI 12. Synthesis of substrate for Table 1, entry 8

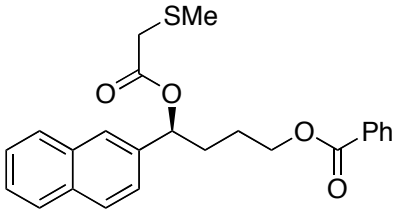




3-formylpropyl benzoate SI 43 was prepared according to Method E. The following amounts of reagents were used: DMSO (0.78 mL, 11 mmol, 1.1 equiv) in CH_2Cl_2 (17 mL), oxalyl chloride (1.0 mL, 12 mmol, 1.2 equiv) in CH_2Cl_2 (15 mL), alcohol **SI 42** (1.9 g, 10 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL), and triethylamine (7.7 mL, 50 mmol, 5.0 equiv). The crude yellow oil was used without purification. Analytical data are consistent with literature values.[45] **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.82 (s, 1H), 8.02 (d, *J* = 7.3, 2H), 7.56 (t, *J* = 7.4, 1H), 7.44 (t, *J* = 7.6, 2H), 4.36 (t, *J* = 6.3, 2H), 2.64 (t, *J* = 7.1, 2H), 2.12 (p, *J* = 6.7, 2H).

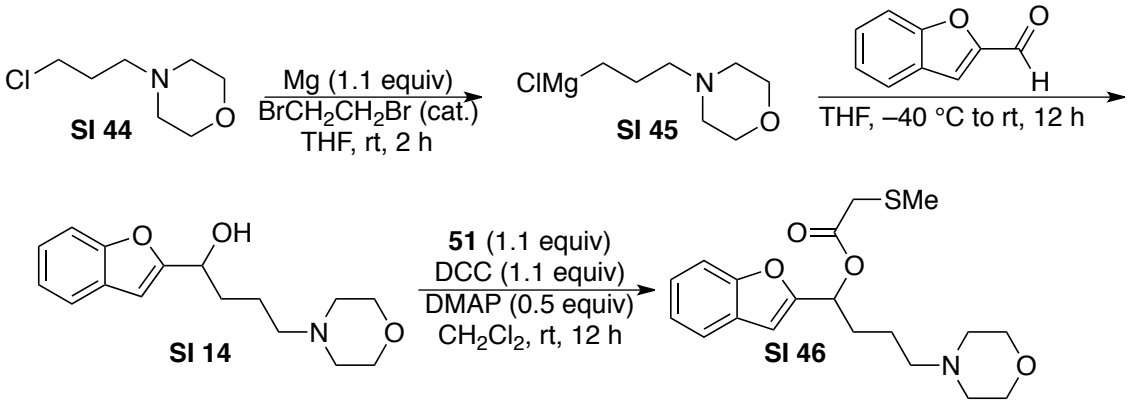


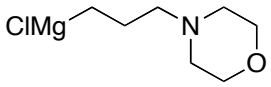
(*S*)-4-hydroxy-4-(naphthalen-2-yl)butyl benzoate (*S*)-SI 4 was prepared according to Method J. The following amounts of reagents were used: catalyst **SI 24** (0.13 g, 0.28 mmol, 0.10 equiv), organotitanium reagent **SI 25** (2.0 g, 5.7 mmol, 2.0 equiv), in THF (16 mL), and aldehyde **SI 43** (0.55 g, 2.8 mmol, 1.0 equiv) in THF (6 mL). The crude residue was purified by flash chromatography (5–20% EtOAc in hexane) to afford the title compound as a slightly yellow solid (0.78 g, 86%, 62% ee). The solid was then successively recrystallized to improve the ee: first from hexane/EtOAc to afford a white solid (82% ee), then from hexane/CH_2Cl_2 (92% ee), and once again from hexane/CH_2Cl_2 (97% ee). Absolute configuration assigned as *S* by analogy to similar compounds synthesized by Gau[5] and confirmed by Competing Enantioselective Conversion (CEC).[18] **TLC R_f** = 0.3 (4:1 hexane/EtOAc, UV active); **mp** 51–54 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.01 (d, *J* = 7.2, 2H), 7.87–7.78 (m, 4H), 7.54 (t, *J* = 7.3, 1H), 7.52–7.45 (m, 3H), 7.42 (t, *J* = 7.7, 2H), 4.96–4.89 (m, 1H), 4.35 (at, *J* = 7.7, 2H), 2.07 (d, *J* = 3.2, 1H), 2.06–1.89 (m, 3H), 1.88–1.75 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 166.8, 141.8, 133.4, 133.2, 133.0, 130.4, 129.7, 128.6, 128.5, 128.1, 127.8, 126.4, 126.1, 124.8, 124.1, 74.4, 64.9, 35.4, 25.3; **IR** (neat, cm^{-1}) 3272, 1716, 1270, 1094, 707; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{21}H_{20}O_3Na$ 343.1310, found 343.1310; **$[\alpha]_D^{28}$** –25.7 (*c* 1.0, $CHCl_3$); **SFC** analysis (AD-H, 20.0% IPA, 3.0 mL/min, 215 nm) indicated 97% ee: t_R (major) = 7.2 min, t_R (minor) = 8.4 min.



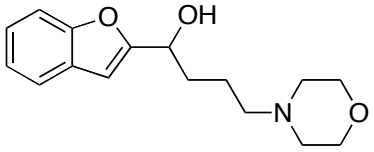
(*S*)-4-(2-(methylthio)acetoxy)-4-(naphthalen-2-yl)butyl benzoate (*S*)-SI 5 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (68 mg, 0.49 mmol, 1.0 equiv), alcohol (*S*)-**SI 4** (0.21 g, 0.64 mmol, 1.0 equiv), 4-dimethylaminopyridine (39 mg, 0.32 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.13 g, 0.64 mmol, 1.0 equiv), and CH_2Cl_2 (4 mL). The crude residue was purified by flash chromatography (5% Et_2O in pentane) to afford to the title compound as a white solid (0.23 g, 87%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active); **mp** 61–62 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.01 (d, *J* = 7.6, 2H), 7.87–7.80 (m, 4H), 7.55 (t, *J* = 7.4, 1H), 7.51–7.45 (m, 3H), 7.42 (t, *J* = 7.6, 2H), 6.01 (t, *J* = 6.9, 1H), 4.39–4.30 (m, 2H), 3.23 (s, 2H), 2.25–2.15 (m, 1H), 2.15–2.04 (m, 1H), 2.13 (s, 3H), 1.95–1.84 (m, 1H), 1.84–1.73 (m, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.6, 166.6, 137.3, 133.3, 133.2, 133.1, 130.3, 129.7, 128.6, 128.5, 128.2, 127.8, 126.5, 126.4, 125.9, 124.1, 76.7, 64.5, 36.0, 32.9, 25.1, 16.4; **IR** (neat, cm^{-1}) 2916, 1711, 1275, 1136, 705; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{24}H_{24}O_4SNa$ 431.1293, found 431.1274; **$[\alpha]_D^{28}$** –67.2 (*c* 1.0, $CHCl_3$); **SFC** analysis (AD-H, 20.0% MeOH, 3.0 mL/min, 215 nm) indicated 97% ee: t_R (minor) = 3.9 min, t_R (minor) = 4.4 min.

Scheme SI 13. Synthesis of substrate for Table 1, entry 9



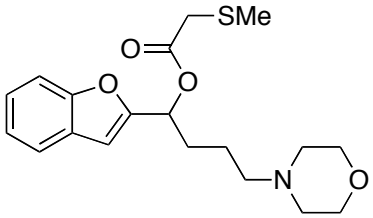


(3-morpholinopropyl)magnesium chloride SI 45 was prepared according to Method D with the following exception: dibromoethane (0.01 mL) was added dropwise with the first portion of the alkyl chloride to promote Grignard initiation and the reaction was heated to reflux for 4 h. The following amounts of reagents were used: 3-morpholinopropyl chloride **SI 44** (0.82 g, 5.0 mmol, 1.0 equiv), magnesium (0.14 g, 5.5 mmol, 1.1 equiv), THF (5 mL). Grignard was titrated to 0.65 M.[2]



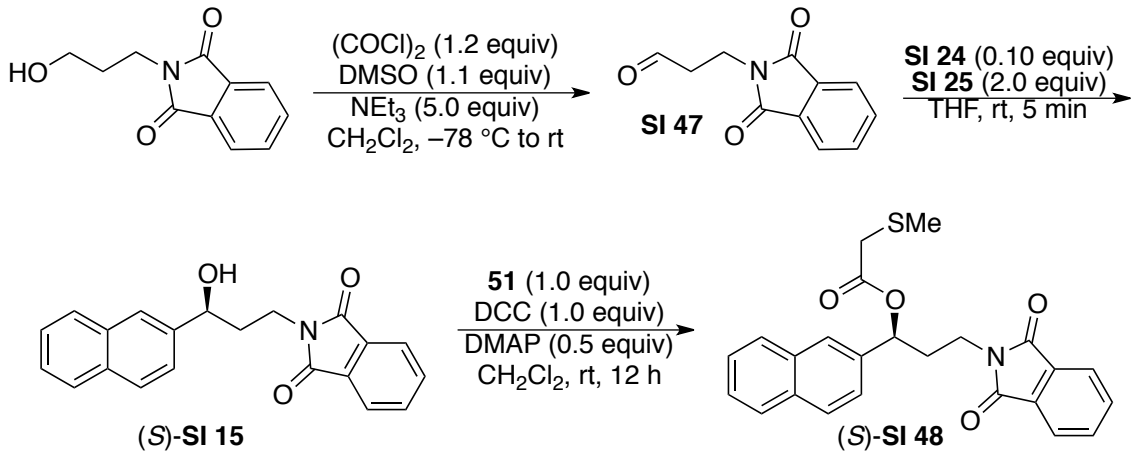
1-(benzofuran-2-yl)-4-morpholinobutan-1-ol SI 14. To a cooled (–40 °C) solution of benzofuran-2-carboxaldehyde (0.11 mL, 0.87 mmol, 1.0 equiv) in THF (9 mL) was added Grignard **SI 45** (2.0 mL, 0.65 M, 1.3 mmol, 1.5 equiv). The reaction was stirred and allowed to warm to ambient temperature overnight. The remaining Grignard was quenched with sat. NH_4Cl, and the aqueous layer was extracted with Et_2O (2 x 10 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The product was purified by flash chromatography (50–

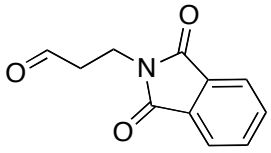
100% EtOAc in hexanes with 1% NEt_3) to afford the title compound as white solid (0.15 g, 62%). **TLC R_f** = 0.1 (100% EtOAc, UV active); **mp** 67–70 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.52 (dd, *J* = 7.1, 1.3, 1H), 7.43 (d, *J* = 7.8, 1H), 7.24–7.17 (m, 2H), 6.62 (s, 1H), 4.84 (t, *J* = 4.7, 1H), 3.82–3.76 (m, 4H), 2.53 (br s, 4H), 2.44 (t, *J* = 5.6, 2H), 2.15–2.10 (m, 2H), 1.74–1.68 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 161.1, 154.9, 125.6, 123.7, 122.6, 120.8, 111.2, 102.0, 68.1, 66.5, 59.3, 53.5, 36.3, 22.9; **IR** (neat, cm^{-1}) 3088, 2817, 1252, 1113, 1066, 1044; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{16}H_{21}NO_3Na$ 298.1419, found 298.1422.



1-(benzofuran-2-yl)-4-morpholinobutyl 2-(methylthio)acetate SI 46 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (0.10 g, 0.93 mmol, 1.1 equiv), alcohol **SI 14** (0.23 g, 0.85 mmol, 1.0 equiv), 4-dimethylaminopyridine (52 mg, 0.42 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.19 mg, 0.93 mmol, 1.1 equiv), and CH_2Cl_2 (4 mL). The crude residue was purified by flash chromatography (50–100% Et_2O in pentane) to afford to the title compound as a colorless oil (0.17 g, 54%). **TLC R_f** = 0.2 (100% EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.54 (d, *J* = 7.1, 1H), 7.46 (d, *J* = 8.0, 1H), 7.29 (td, *J* = 8.5, 1.2, 1H), 7.22 (td, *J* = 7.6, 0.9, 1H), 6.73 (s, 1H), 6.02 (t, *J* = 7.0, 1H), 3.69 (t, *J* = 4.6, 4H), 3.22 (s, 2H), 2.39 (m, 6H), 2.18 (s, 3H), 2.15–2.08 (m, 2H), 1.61–1.52 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.6, 154.9, 154.6, 127.9, 124.8, 133.1, 121.4, 111.5, 105.4, 70.0, 67.1, 58.4, 53.8, 35.9, 30.5, 22.4, 16.4; **IR** (neat, cm^{-1}) 2953, 2853, 2808, 1731, 1453, 1252, 1116; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{19}H_{25}NO_4SNa$ 386.1402, found 386.1409.

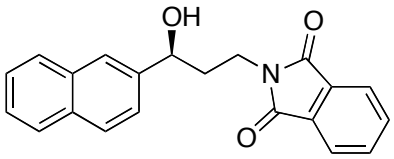
Scheme SI 14. Synthesis of substrate for Table 1, entry 10



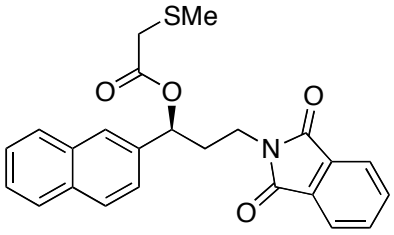


3-Phthalimidopropanal SI 47 was prepared according to a modified procedure reported by Timmerman.[46] Oxalyl chloride (1.07 mL, 1.59 g, 12.5 mmol, 1.25 equiv) was combined with anhydrous CH_2Cl_2 (20 mL) in a flame-dried 100 mL round-bottom flask equipped with a stir bar and an N_2 line. The reaction flask was cooled to –78 °C and a solution of DMSO (1.88 mL, 2.07 g, 26.5 mmol, 2.65 equiv) in 5 mL anhydrous CH_2Cl_2 was added drop-wise. After completion of the addition, the reaction was allowed to stir for 15 min. Subsequently, a solution

of 3-phthalimidopropanol (2.05 g, 10.0 mmol, 1.00 equiv) in 10 mL anhydrous CH_2Cl_2 was added drop-wise to the reaction mixture. The reaction was stirred for an additional 30 min at –78 °C followed by the addition of triethylamine (7.67 mL, 5.57 g, 55.0 mmol, 5.5 equiv). The reaction was allowed to warm to ambient temperature before the addition of water (25 mL). After stirring for 30 min, the organic and aqueous layers were separated and the organic layer was washed with H_2O (3 x 15 mL). The combined organic layers were dried with Na_2SO_4, filtered, and concentrated in vacuo to yield crude **SI 47** (1.49 g, 72%). The resultant white solid was used without further purification. Analytical data was consistent with literature values.[47] **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 9.83 (t, *J* = 1.3, 1H), 7.85 (add, *J* = 5.3, 3.2, 2H), 7.23 (add, *J* = 5.5, 3.0, 2H), 4.04 (t, *J* = 7.0, 2H), 2.88 (td, *J* = 7.0, 1.3, 2H).



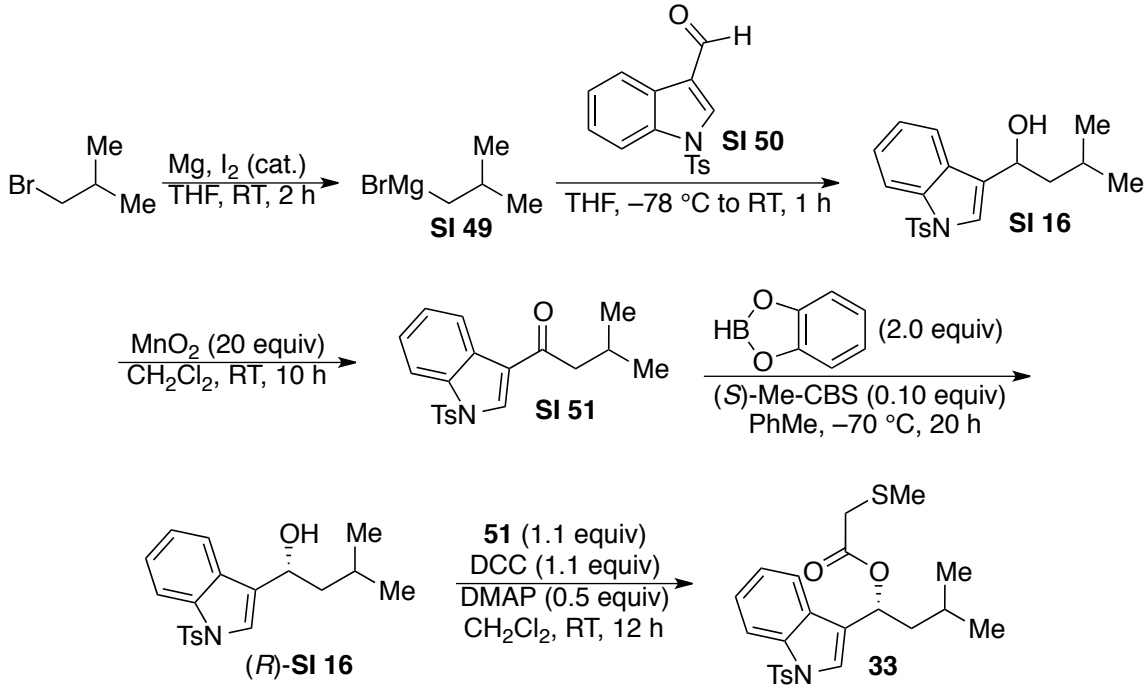
(*S*)-3-phthlimido-1-(2-naphthalenyl)-1-propanol (*S*)-SI 15 was prepared according to Method J. The following amounts of reagents were used: catalyst **SI 24** (0.13 g, 0.28 mmol, 0.10 equiv), organotitanium reagent **SI 25** (2.0 g, 5.7 mmol, 2.0 equiv) in THF (16 mL), and aldehyde **SI 47** (0.58 g, 2.8 mmol, 1.0 equiv) in THF (6 mL). The crude residue was purified by flash chromatography (10–40% EtOAc in hexanes with 1% TEA) to afford the title compound as a slightly yellow solid (0.55 g, 59%, 63% ee). The solid was then recrystallized first from hexane/CH_2Cl_2 to afford a white crystalline solid (63% ee) and subsequently twice from Et_2O/CH_2Cl_2 (96% ee). Absolute configuration assigned as *S* by analogy to similar compounds synthesized by Gau[5] and confirmed by Competing Enantioselective Conversion (CEC).[18] **TLC R_f** = 0.2 (4:1 hexane/EtOAc, UV active); **mp** 124–127 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.80–7.71 (m, 6H), 7.63 (add, *J* = 5.3, 3.1, 2H), 7.46–7.37 (m, 3H), 4.85 (br s, 1H), 3.91 (t, *J* = 6.5, 2H), 3.08 (s, 1H), 2.24–2.11 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 168.7, 141.0, 134.0, 133.3, 132.9, 132.0, 128.4, 128.0, 127.7, 126.2, 125.9, 124.5, 123.9, 123.3, 71.5, 37.4, 34.9; **IR** (neat, cm^{-1}) 3482, 1697, 1396, 1372, 1346, 1072, 720; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{21}H_{17}NO_3Na$ 354.1106, found 354.1105; **$[\alpha]_D^{27}$** –16.1 (*c* 1.0, $CHCl_3$); **SFC** analysis (AD-H, 30.0% IPA, 3.0 mL/min, 215 nm) indicated 95% ee: t_R (major) = 17.7 min, t_R (minor) = 20.9 min.

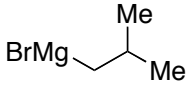


(S)-3-(1,3-dioxoisoindolin-2-yl)-1-(naphthalen-2-yl)propyl 2-(methylthio)acetate (*S*)-SI 48 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (52 mg, 0.49 mmol, 1.0 equiv), alcohol (*S*)-**SI 15** (0.16 g, 0.49 mmol, 1.0 equiv), 4-dimethylaminopyridine (30 mg, 0.25 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.10 g, 0.49 mmol, 1.0 equiv), and CH_2Cl_2 (3 mL). The crude residue was purified by flash chromatography (5–30% EtOAc in hexanes) to afford to the title compound as a colorless, thick oil which was then triturated with pentane to a sticky solid (0.11 g, 52%). **TLC R_f** = 0.8 (1:1 hexane/EtOAc, UV active, stain with $KMnO_4$); **mp** 62–65 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.84–7.70 (m, 6H), 7.66–7.59 (m, 2H), 7.48–7.38 (m, 3H), 5.96 (t , *J* = 6.8, 1H), 3.93–3.75 (m, 2H), 3.24 (s, 2H), 2.48–2.33 (m, 2H), 2.13 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.5, 168.3, 136.7, 134.0, 133.13, 133.10, 131.9, 128.6, 128.1, 127.7, 126.4, 126.3, 125.9, 123.9, 123.2, 74.7, 35.9, 34.7, 34.4, 16.3; **IR** (neat, cm^{-1}) 2923, 1705, 1395, 1262, 1123, 717; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{24}H_{21}NO_4SNa$ 442.1089, found

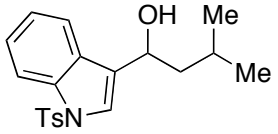
442.1074; $[\alpha]_D^{28}$ –41.8 (*c* 0.80, $CHCl_3$); **SFC** analysis (OJ-H, 30.0% MeOH, 3.0 mL/min, 215 nm) indicated 94% ee: t_R (minor) = 3.8 min, t_R (major) = 5.1 min.

Scheme SI 15. Synthesis of substrate for Table 1, entry 11

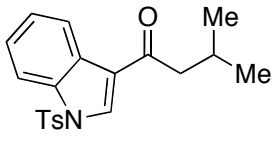




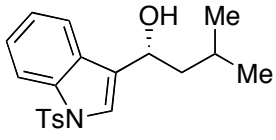
***iso*-butylmagnesium bromide SI 49** was prepared according to Method D, with the following exception: dibromoethane (0.01 mL) was added dropwise with the first portion of the alkyl bromide to promote Grignard initiation. The following amounts of reagents were used: 1-bromo-2-methylpropane (1.1 mL, 10.0 mmol, 1.0 equiv), magnesium (0.36 g, 15 mmol, 1.5 equiv), THF (8 mL). Grignard titrated to 0.87 M.[2]



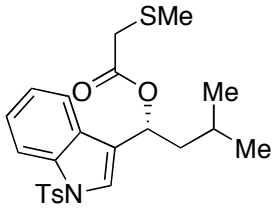
3-methyl-1-(1-tosyl-1*H*-indol-3-yl)butan-1-ol SI 16. To a cooled (–78 °C) solution of aldehyde **SI 50** (1.5 g, 5.0 mmol, 1.0 equiv) in THF (25 mL) was added Grignard reagent **SI 49** (6.3 mL, 5.5 mmol, 1.1 equiv, 0.87 M in THF). The reaction was let stir and warm to ambient temperature. After 2 h, the remaining Grignard was quenched with sat. NH_4Cl, and the aqueous layer was extracted with EtOAc (2 x 10 mL). The combined organics were washed with brine, dried with $MgSO_4$, filtered, and concentrated in vacuo. The product was purified by flash chromatography (10% EtOAc in hexanes) to afford the title compound as gummy oil (1.5 g, 82%). **TLC** $\mathbf{R_f}$ = 0.3 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.98 (d, *J* = 8.3, 1H), 7.76 (d, *J* = 8.3, 2H), 7.65 (d, *J* = 7.8, 1H), 7.50 (s, 1H), 7.32 (t, *J* = 8.3, 1H), 7.25 – 7.19 (m, 3H), 5.00 (dt, *J* = 8.4, 4.3, 1H), 2.34 (s, 3H), 1.86–1.66 (m, 4H), 0.96 (d, *J* = 6.1, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 145.1, 135.7, 135.4, 130.0, 129.1, 127.0, 126.5, 125.0, 123.3, 122.7, 120.6, 113.9, 66.3, 46.3, 25.0, 23.3, 22.3, 21.7; **IR** (neat, cm^{-1}) 2954, 1596, 1364, 1170, 118, 1093; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{20}H_{23}NO_3SNa$ 380.1296, found 380.1300.



3-methyl-1-(1-tosyl-1H-indol-3-yl)butan-1-one SI 51 was prepared according to Method F. The following amounts of reagents were used: MnO_2 (5.8 g, 67 mmol, 20 equiv), alcohol **SI 16** (1.2 g, 3.4 mmol, 1.0 equiv), and CH_2Cl_2 (40 mL). The product was purified by flash chromatography (10% EtOAc in hexanes) to afford the title compound a white solid (1.1 g, 90%). **TLC R_f** = 0.5 (4:1 hexane/EtOAc, UV active); **mp** 98–99 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.35 (d, *J* = 7.2, 1H), 8.20 (s, 1H), 7.92 (d, *J* = 7.2, 1H), 7.83 (d, *J* = 8.4, 2H), 7.35 (apd, *J* = 7.4, 1.6, 2H), 7.28 (d, *J* = 8.2, 2H), 2.75 (d, *J* = 7.0, 2H), 2.37 (s, 3H), 2.32 (septet, *J* = 6.7, 1H), 1.02 (d, *J* = 6.7, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 196.3, 146.0, 135.0, 134.7, 131.8, 130.4, 127.8, 127.3, 125.8, 124.9, 123.4, 121.9, 113.2, 49.2, 25.7, 22.9, 21.8; **IR** (neat, cm^{-1}) 3140, 2953, 1672, 1597, 1365, 1167, 1145, 1087, 1105; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{20}H_{21}NO_3SNa$ 378.1140, found 378.1127.



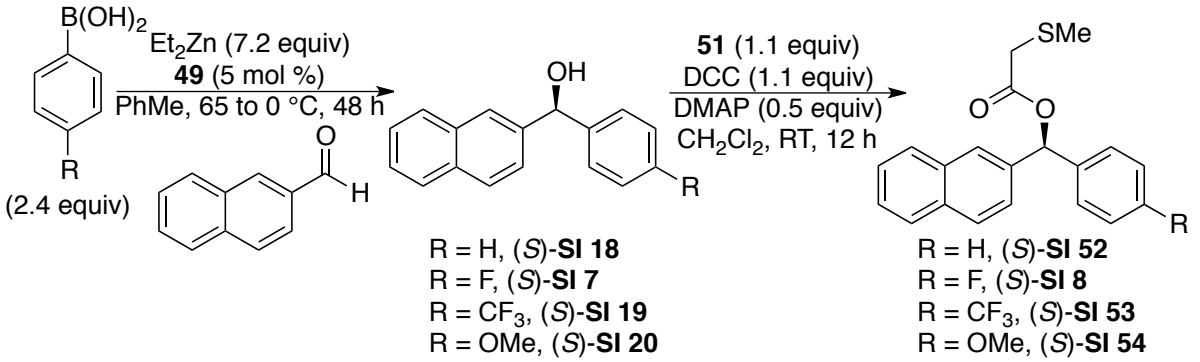
(*R*)-3-methyl-1-(1-tosyl-1H-indol-3-yl)butan-1-ol (*R*)-SI 16 was prepared according to Method H. The following amounts of reagents were used: (*S*)-Me-CBS-oxazaborolidine (55 mg, 0.20 mmol, 0.10 equiv), ketone **SI 51** (0.71 g, 2.0 mmol, 1.0 equiv), catecholborane (0.26 mL, 2.4 mmol, 1.2 equiv), and PhMe (20 mL). The crude residue was used without purification. See *rac*-alcohol **SI 16** for analytical data. Absolute configuration assigned as *R* based on the accepted model for selectivity in CBS reductions.[17]

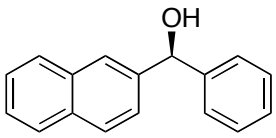


(*R*)-3-methyl-1-(1-tosyl-1H-indol-3-yl)butyl 2-(methylthio)acetate 33 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (0.25 g, 2.4 mmol, 1.2 equiv), crude alcohol (*R*)-**SI 16** (0.72 g, 2.0 mmol, 1.0 equiv), 4-dimethylaminopyridine (0.12 g, 1.0 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.49 mg, 2.4 mmol, 1.2 equiv), and CH_2Cl_2 (8 mL). The crude residue was purified by flash chromatography (5–10% Et_2O in pentane with 0.5% Et_3N) to afford to the title compound as a yellow oil (84 mg, 9% over 2 steps). **TLC R_f** = 0.5 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.96 (d, *J* = 8.2, 1H), 7.74 (d, *J* = 8.3, 2H), 7.64 (d, *J* = 7.7, 1H), 7.59 (s, 1H), 7.33–7.21 (m, 4H), 6.17 (dd, *J* = 8.5, 5.6, 1H), 3.16 (s, 2H), 2.33 (s, 3H), 2.06 (s, 3H), 2.00 (ddd, *J* = 13.7, 8.6, 6.3, 1H), 1.79 (ddd, *J* = 14.0, 7.6, 5.7, 1H), 1.61 (septet, *J* = 6.7, 1H), 0.96 (d, *J* = 4.3, 3H), 0.94 (d, *J* = 4.3, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.7, 145.2, 135.4, 135.2, 130.0, 128.9, 127.0, 125.1, 124.2, 123.4, 122.0, 120.5, 113.9, 68.8, 43.5, 36.0, 24.9, 22.9, 22.4, 21.7, 16.3; **IR** (neat, cm^{-1}) 2956, 1727, 1446, 1328, 1173, 1120; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{23}H_{27}NO_4S_2Na$ 468.1279, found 468.1266; **$[\alpha]_D^{30}$** +41.1 (*c* 0.97, $CHCl_3$); **SFC** analysis (AD-H, 5.0 % IPA, 3.0 mL/min, 215 nm) indicated 95% ee: t_R (major) = 12.0 min, t_R (minor) = 15.7 min.

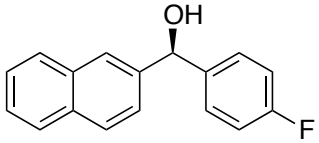
H. STARTING MATERIALS FOR TABLE 2

Scheme SI 16. Synthesis of substrates for Table 2, entry 1–3

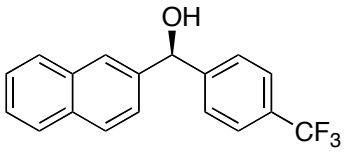




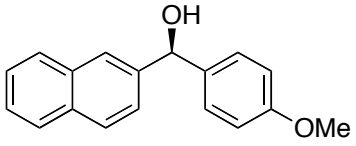
(*S*)-naphthalen-2-yl(phenyl)methanol (*S*)-SI 18 was prepared according to Method K. The following amounts of reagents were used: phenylboronic acid (0.73 g, 6.0 mmol, 2.4 equiv), diethylzinc (18 mL, 18 mmol, 7.2 equiv, 1.0 M in PhMe), aminoalcohol **49** (59 mg, 0.13 mmol, 0.050 equiv), 2-naphthaldehyde (0.39 g, 2.5 mmol, 1.0 equiv), and PhMe (38 mL). Purification by flash chromatography (25% EtOAc in hexane) to afforded the title compound as a white solid (0.55 g, 94%). The product was recrystallized (100% hexane) to yield higher enantiopurity (99% ee). Absolute configuration was assigned as *S* by comparison of optical rotation with literature values. Analytical data are consistent with literature values.[48] **TLC** $\mathbf{R_f}$ = 0.3 (4:1 hexane/EtOAc, UV active); **mp** 79–80 °C, lit.[48] mp 82–83 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.86–7.75 (m, 4H), 7.47–7.22 (m, 8H), 5.96 (s, 1H), 2.36 (s, 1H); **$[\alpha]_D^{26}$** –4.1 (*c* 1.2, benzene), lit.[48] $[\alpha]_D$ +7.4 (c 0.77, benzene, 98% ee, (*R*)-enantiomer); **SFC** analysis (OD-H, 20% IPA, 3.0 mL/min, 215 nm) indicated 99% ee: t_R (major) = 6.8 minutes, t_R (minor) = 7.9 minutes.



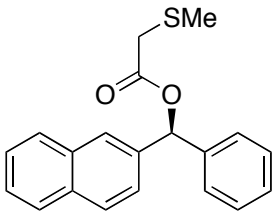
(*S*)-naphthalen-2-yl(4-(fluoro)phenyl)methanol (*S*)-SI 7 was prepared according to the Method K. The following amounts of reagents were used: 4-fluorophenylboronic acid (0.84 g, 6.0 mmol, 2.4 equiv), diethylzinc (18 mL, 18 mmol, 7.2 equiv, 1.0 M in PhMe), aminoalcohol **49** (75 mg, 0.15 mmol, 0.060 equiv), 2-naphthaldehyde (0.39 g, 2.5 mmol, 1.0 equiv), and PhMe (38 mL). Purification by flash chromatography (25% EtOAc/hexane) afforded the title compound as a white solid (0.62 g, 98%). Absolute configuration was assigned as *S* by comparison of optical rotation with literature values. Analytical data are consistent with literature values.[49] **TLC** $\mathbf{R_f}$ = 0.3 (4:1 hexane/EtOAc, UV active); **mp** 61–63 °C; **^{1}H NMR** (400 MHz, CDCl3) δ 7.86–7.78 (m, 4H), 7.50–7.45 (m, 2H), 7.30–7.35 (m, 3H), 7.04–76.98 (m, 2H), 5.98 (s, 1H), 2.36 (s, 1H); **$[\alpha]_D^{26}$** –3.7 (*c* 3.06, EtOH); lit.[20] $[\alpha]_D^{20}$ –37 (*c* 30.9, EtOH, 98% ee, (*S*)-enantiomer); **SFC** analysis (OD-H, 15% IPA, 3 mL/min, 215 nm) indicated 95% ee: t_R (major) = 7.97 minutes, t_R (minor) = 9.34 minutes.



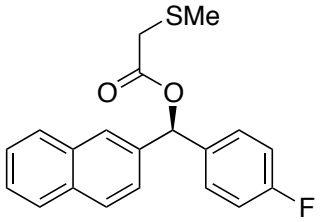
(*S*)-naphthalen-2-yl(4-(trifluoromethyl)phenyl)methanol (*S*)-SI 19 was prepared according to the Method K. The following amounts of reagents were used: 4-(trifluoromethyl)phenylboronic acid (1.1 g, 6.0 mmol, 2.4 equiv), diethylzinc (18 mL, 18 mmol, 7.2 equiv, 1.0 M in PhMe), aminoalcohol **49** (59 mg, 0.13 mmol, 0.050 equiv), 2-naphthaldehyde (0.39 g, 2.5 mmol, 1.0 equiv), and PhMe (38 mL). The product was purified by flash chromatography (25% EtOAc in hexane) to afford the title compound as a white solid (0.64 g, 85%). The product was then recrystallized from hexanes to yield higher enantiopurity (96% ee). Absolute configuration was assigned as *S* by comparison of optical rotation with literature values. Analytical data are consistent with literature values.[50] **TLC R_f** = 0.2 (4:1 hexane/EtOAc, UV active); **mp** 101–103 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.87–7.80 (m, 4H), 7.58 (q, *J* = 8.4, 4H), 7.49 (at, *J* = 3.8, 2H), 7.40 (dd, *J* = 8.5, 1.7, 1H), 6.05 (s, 1H), 2.39 (s, 1H); **$[\alpha]_D^{26}$** –44.4 (*c* 1.0, $CHCl_3$), lit.[50] $[\alpha]_D$ –45.3 (*c* 2.2, $CHCl_3$, 90% ee, (*S*)-enantiomer); **SFC** analysis (OD-H, 20.0% IPA, 3.0 mL/min, 215 nm) indicated 96% ee: t_R (major) = 4.7 min, t_R (minor) = 5.1 min.



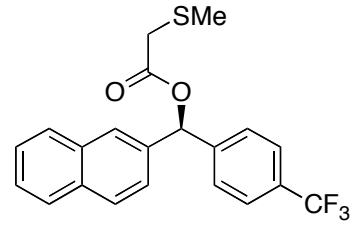
(*S*)-(4-methoxyphenyl)(naphthalen-2-yl)methanol (*S*)-SI 20 was prepared according to Method K. The following amounts of reagents were used: 4-methoxyphenylboronic acid (0.91 g, 6.0 mmol, 2.4 equiv), diethylzinc (18 mL, 18 mmol, 7.2 equiv, 1.0 M in PhMe), aminoalcohol **49** (59 mg, 0.13 mmol, 0.050 equiv), 2-naphthaldehyde (0.39 g, 2.5 mmol, 1.0 equiv), and PhMe (38 mL). The product was purified by flash chromatography (25% EtOAc in hexane) to afford the title compound as a white solid (0.63 g, 96%). The product was then recrystallized from hexanes/EtOAc to yield higher enantiopurity (99% ee). Absolute configuration assigned as *S* by analogy to **(*S*)-SI 18** made by the same method. Analytical data are consistent with literature values.[51] **TLC R_f** = 0.2 (4:1 hexane/EtOAc, UV active); **mp** 88–90 °C, lit.[51] mp 84 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.90 (s, 1H), 7.85–7.78 (m, 3H), 7.49–7.44 (m, 2H), 7.41 (dd, *J* = 8.8, 1.7, 1H), 7.33 (dt, *J* = 8.7, 2.5, 2H), 6.87 (dt, *J* = 8.7, 2.5, 2H), 5.98 (d, *J* = 3.2, 1H), 3.79 (s, 3H), 2.24 (d, *J* = 3.4, 1H); **$[\alpha]_D^{29}$** +22.6 (*c* 0.56, THF), lit.[51] $[\alpha]_D^{20}$ –31.4 (*c* 0.26, THF, 91% ee); **SFC** analysis (OD-H, 20.0% IPA, 3.0 mL/min, 215 nm) indicated 95% ee: t_R (major) = 8.3 min, t_R (minor) = 9.5 min.



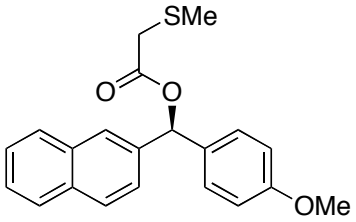
(*S*)-naphthalen-2-yl(phenyl)methyl 2-(methylthio)acetate (*S*)-SI 52. Prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (0.15 g, 1.4 mmol, 1.1 equiv), alcohol **(*S*)-SI 18** (0.30 g, 1.3 mmol, 1.0 equiv), 4-dimethylaminopyridine (78 mg, 0.64 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.29 g, 1.4 mmol, 1.1 equiv), and dichloromethane (7 mL). The crude residue was purified by flash chromatography (10% Et_2O in pentane) to afford the title compound as a slightly yellow oil (0.27 g, 84%). **TLC R_f** = 0.6 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.87 (s, 1H), 7.84–7.80 (m, 3H), 7.50–7.40 (m, 5H), 7.36–7.28 (m, 3H), 7.07 (s, 1H), 3.32 (s, 2H), 2.15 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.4, 139.9, 137.3, 133.2, 133.1, 128.7, 128.6, 128.28, 128.25, 127.8, 127.4, 126.49, 126.46, 126.2, 125.0, 77.9, 36.1, 16.4; **IR** (neat, cm^{-1}) 3028, 2918, 1729, 1258, 1120; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{20}H_{18}O_2SNa$ 345.0925, found 345.0937; **$[\alpha]_D^{26}$** –26.8 (*c* 1.2, $CHCl_3$); **SFC** analysis (AD-H, 10.0% IPA, 3.0 mL/min, 215 nm) indicated >99% ee: t_R (minor) = 11.6 min, t_R (major) = 12.7 min.



(*S*)-(4-fluorophenyl)(naphthalen-2-yl)methyl 2-(methylthio)acetate (*S*)-SI 8 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (63 mg, 0.60 mmol, 1.2 equiv), alcohol **(*S*)-SI 7** (0.13 g, 0.50 mmol, 1.0 equiv), 4-dimethylaminopyridine (31 mg, 0.25 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.14 g, 0.6 mmol, 1.2 equiv), and dichloromethane (3 mL). The crude residue was purified by silica gel chromatography (25% Et_2O in pentane) to afford the title compound as a colorless oil (0.15 g, 90%). **TLC R_f** = 0.5 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.85–7.80 (m, 4H), 7.50–7.48 (m, 2H), 7.40–7.36 (m, 3H), 7.05–7.01 (m, 3H), 3.31 (s, 2H), 2.14 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.3, 162.6 (d, $J_{(C–F)}$ = 246.9 Hz), 137.5, 135.7 (d, $J_{(C–F)}$ = 3.2 Hz), 133.2, 133.1, 129.3 (d, $J_{(C–F)}$ = 8.3 Hz), 128.7, 128.3, 128.3, 127.8, 126.59, 126.56, 126.1, 124.8, 115.6 (d, $J_{(C–F)}$ = 21.3 Hz), 77.2, 36.0, 16.4; **IR** (film, cm^{-1}) 3056, 2919, 1729, 1603, 1508, 1258; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{20}H_{17}FO_2SNa$ 363.0831, found 363.0834; **$[\alpha]_D^{26}$** –11.9 (*c* 1.08, $CHCl_3$); **SFC** analysis (OD-H, 5.0% IPA, 2.5 mL/min, 215 nm) indicated 96% ee: t_R (minor) = 14.02 min, t_R (major) = 15.09 min.



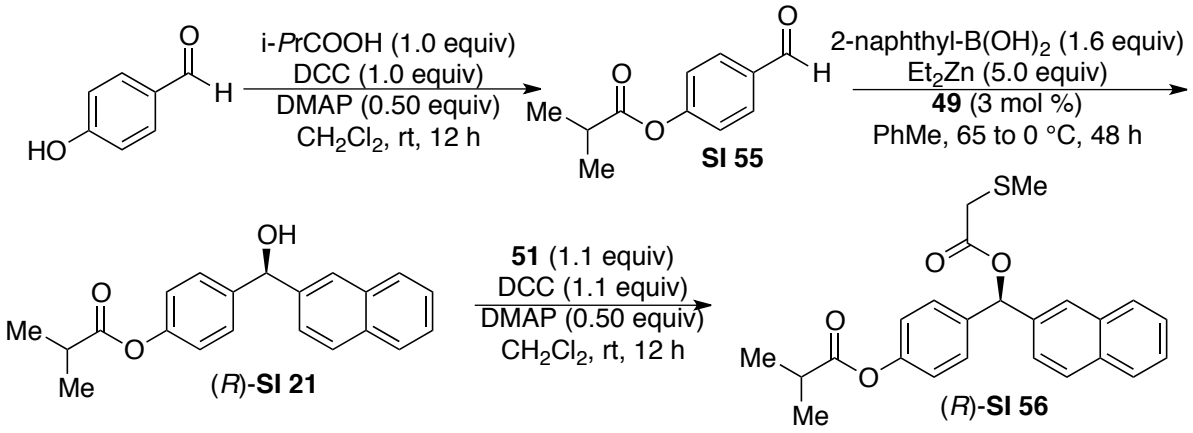
(*S*)-naphthalen-2-yl(4-(trifluoromethyl)phenyl)methyl 2-(methylthio)acetate (*S*)-SI 53 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (74.0 mg, 0.703 mmol, 1.10 equiv), alcohol (*S*)-**SI 19** (193 mg, 0.640 mmol, 1.00 equiv), 4-dimethylaminopyridine (39 mg, 0.32 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (144 mg, 0.703 mmol, 1.10 equiv), and dichloromethane (2 mL). The crude residue was purified by flash chromatography (25% Et_2O in pentane) to afford the title compound as a colorless oil (0.24 g, 94%). **TLC R_f** = 0.5 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.87 (s, 1H), 7.85–7.80 (m, 3H), 7.62 (d, *J* = 8.5, 2H), 7.55 (d, *J* = 8.2, 2H), 7.51–7.49 (m, 2H), 7.40 (dd, *J* = 8.7, 1.8, 1H), 7.09 (s, 1H), 3.32 (s, 2H), 2.16 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.2, 143.8, 136.4, 133.21, 133.16, 130.3 (q, $J_{C–F}$ = 32.8, 1C), 128.9, 128.3, 127.8, 127.4, 126.72, 126.68, 126.6, 125.7 (q, $J_{C–F}$ = 3.7, 2C), 124.7, 124.1 (q, $J_{C–F}$ = 271.8, 1C), 77.2, 36.0, 16.4; **IR** (neat, cm^{-1}) 2920, 1734, 1323, 1163, 1118, 1065; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{21}H_{17}F_3O_2S$ 413.0799, found 413.0811; **$[\alpha]_D^{26}$** –46.3 (*c* 1.1, $CHCl_3$); **SFC** analysis (OD-H, 5.0% IPA, 2.5 mL/min, 215 nm) indicated 97% ee: t_R (minor) = 11.4 min, t_R (major) = 12.2 min.

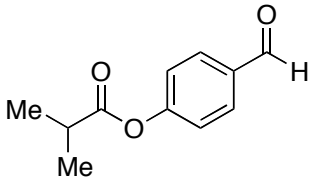


(*S*)-(4-methoxyphenyl)(naphthalen-2-yl)methyl 2-(methylthio)acetate (*S*)-SI 54 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (35 mg, 0.33 mmol, 1.10 equiv), alcohol (*S*)-**SI 20** (78 mg, 0.30 mmol, 1.00 equiv), 4-dimethylaminopyridine (18 mg, 0.15 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (68 mg, 0.33 mmol, 1.10 equiv), and dichloromethane (2 mL). The crude residue was purified by flash chromatography (25% Et_2O in pentane) to afford the title compound as a colorless oil (0.10 g, 96%). **TLC R_f** = 0.3 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.87 (s, 1H), 7.84–7.80 (m, 3H), 7.50–7.45 (m, 2H), 7.41 (dd, *J* = 8.8, 1.7, 1H), 7.32 (dt, *J* = 8.8, 2.5, 2H), 7.03 (s, 1H), 6.87 (dt, *J* = 8.8, 2.5, 2H), 3.79 (s, 3H), 3.31 (s, 2H), 2.15 (s,

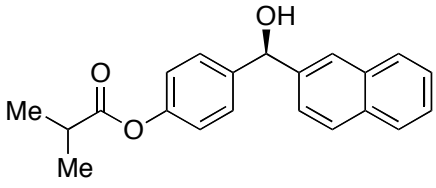
3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.4, 159.6, 137.5, 133.2, 133.0, 132.0, 129.0, 128.5, 128.3, 127.8, 126.5, 126.4, 125.8, 124.9, 114.1, 77.6, 55.4, 36.1, 16.4; **IR** (neat, cm^{-1}) 2918, 1728, 1512, 1246, 1157; **HRMS** (TOF MS ES+) *m/z*: $[M + Na]^+$ calculated for $C_{21}H_{20}O_3SNa$ 375.1031, found 375.1023; **$[\alpha]_D^{26}$** +22.2 (*c* 0.85, $CHCl_3$); **SFC** analysis (OD-H, 5.0% IPA, 3.0 mL/min, 215 nm) indicated 95% ee: t_R (minor) = 20.6 min, t_R (major) = 22.2 min.

Scheme SI 17. Synthesis of substrate for Table 2, entry 4



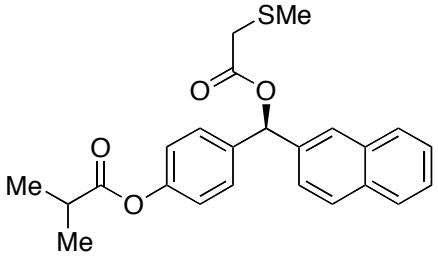


4-formylphenyl isobutyrate SI 55 was prepared according to Method L. The following amounts of reagents were used: isobutyric acid (0.91 mL, 10 mmol, 1.0 equiv), 4-hydroxybenzaldehyde (1.2 g, 10 mmol, 1.0 equiv), 4-dimethylaminopyridine (0.61 g, 5.0 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (2.1 g, 10 mmol, 1.0 equiv), and dichloromethane (50 mL). The crude residue was purified by flash chromatography (10% EtOAc in hexane) to afford the title compound as a colorless semi-solid (1.5 g, 79%). Analytical data are consistent with literature values.[52] **TLC R_f** = 0.3 (4:1 hexane/EtOAc, UV active) **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 10.0 (s, 1H), 7.92 (d, *J* = 8.5, 2H), 7.27 (d, *J* = 8.5, 2H), 2.84 (septet, *J* = 7.0, 1H), 1.34 (d, *J* = 6.9, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 191.1, 175.0, 155.8, 134.0, 131.3, 122.4, 116.0, 34.3, 19.1.



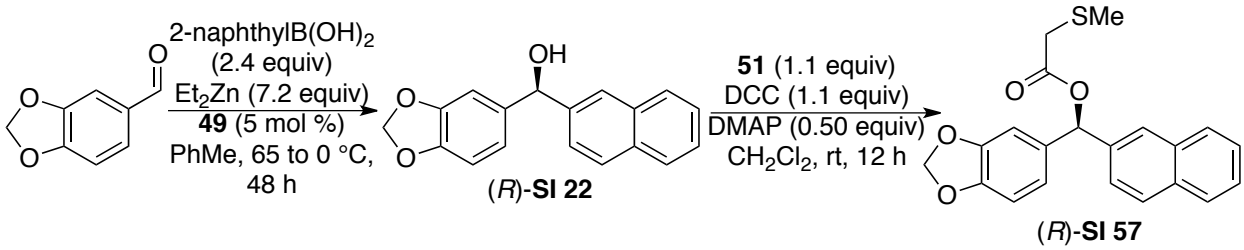
(*R*)-4-(hydroxy(naphthalen-2-yl)methyl)phenyl isobutyrate (*R*)-SI 21 was prepared according to Method K. The following amounts of reagents were used: 2-naphthylboronic acid (1.0 g, 6.0 mmol, 1.7 equiv), diethylzinc (18 mL, 18 mmol, 5.0 equiv, 1.0 M in PhMe), aminoalcohol **49** (59 mg, 0.13 mmol, 0.030 equiv), aldehyde **SI 55** (0.70 g, 3.6 mmol, 1.0 equiv), and PhMe (36 mL). Purification by flash chromatography (25% EtOAc in hexane) afforded the title compound as a white solid (0.70 g, 61%). The product was recrystallized from EtOAc/hexanes to yield higher enantiopurity (97% ee). Absolute configuration assigned as *R* based on predictive model described by Braga.[11] **TLC R_f** = 0.2 (4:1 hexane/EtOAc, UV active); **mp** 124–128 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.88 (s, 1H), 7.84–7.78 (m, 3H), 7.50–7.45 (m, 2H), 7.45–7.40 (m, 3H), 7.05 (d, *J* = 8.4, 2H), 6.01 (s, 1H), 2.78 (septet, *J* = 7.0, 1H), 2.34 (s, 1H), 1.30 (d, *J* = 7.0, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 175.7, 150.4, 141.1, 141.0, 133.3, 133.0, 128.5, 128.2, 127.9, 127.8, 126.4, 126.2, 125.2, 124.9, 121.7, 76.0, 34.3, 19.1; **IR** (neat,

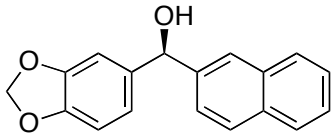
cm^{-1}) 3277, 2970, 1746, 1164, 754; **HRMS** (TOF MS ES+) *m*/*z*: [M + Na]$^+$ calculated for $C_{21}H_{20}O_3Na$ 343.1310, found 343.1304; **[α]$_D^{29}$** –10.8 (*c* 0.19, $CHCl_3$); **SFC** analysis (OJ-H, 15% IPA, 3.0 mL/min, 215 nm) indicated 97% ee: t_R (minor) = 12.8 min, t_R (major) = 13.8 min.



(*R*)-4-((2-(methylthio)acetoxy)(naphthalen-2-yl)methyl) phenyl isobutyrate (*R*)-SI 56 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (93 mg, 0.88 mmol, 1.1 equiv), alcohol (*R*)-**SI 21** (0.26 g, 0.80 mmol, 1.0 equiv), 4-dimethylaminopyridine (49 mg, 0.40 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.18 g, 0.88 mmol, 1.1 equiv), and dichloromethane (4 mL). The crude residue was purified by flash chromatography (25% Et_2O in pentane) to afford the title compound as a slightly yellow oil (0.27 g, 81%). **TLC R$_f$** = 0.4 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.87 (s, 1H), 7.84–7.80 (m, 3H), 7.51–7.48 (m, 2H), 7.41 (d, *J* = 8.5, 3H), 7.07 (s, 1H), 7.06 (d, *J* = 8.5, 2H), 3.31 (s, 2H), 2.79 (septet, *J* = 7.04, 1H), 2.15 (s, 3H), 1.30 (d, *J* = 7.04, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 175.6, 169.3, 150.7, 137.2, 137.0, 133.2, 133.1, 128.64, 128.60, 128.3, 127.8, 126.54, 126.51, 126.2, 125.0, 121.8, 77.3, 36.1, 34.3, 19.0, 16.4; **IR** (neat, cm^{-1}) 2974, 1753, 1731, 1506, 1203, 1165; **HRMS** (TOF MS ES+) *m*/*z*: [M + Na]$^+$ calculated for $C_{24}H_{24}O_4SNa$ 431.1293, found 431.1276; **[α]$_D^{26}$** +8.6 (*c* 1.1, $CHCl_3$); **SFC** analysis (OJ-H, 10% IPA, 3.0 mL/min, 215 nm) indicated 98% ee: t_R (major) = 8.6 min, t_R (minor) = 11.0 min.

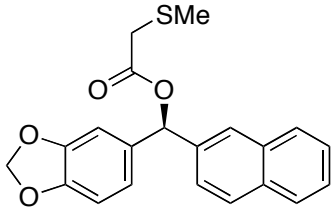
Scheme SI 18. Synthesis of substrate for Table 2, entry 5





(*S*)-benzo[*d*][1,3]dioxol-5-yl(naphthalen-2-yl)methanol (*R*)-SI 22 was prepared according to Method K. The following amounts of reagents were used: 2-naphthylboronic acid (1.0 g, 6.0 mmol, 2.4 equiv), diethylzinc (18 mL, 18 mmol, 7.2 equiv, 1.0 M in PhMe), aminoalcohol **49** (59 mg, 0.13 mmol, 0.050 equiv), piperonyl aldehyde (0.38 g, 2.5 mmol, 1.0 equiv), and PhMe (38 mL). Purification by flash chromatography (5–25% EtOAc in hexane) afforded the title compound as a white solid (0.62 g, 89%). The product was recrystallized from DCM/pentane to yield higher enantiopurity (93% ee). Absolute configuration assigned as *S* based on predictive model described by Braga.[11] **TLC R$_f$** = 0.3 (4:1 hexane/EtOAc, UV active); **mp** 64–66 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.86 (s, 1H), 7.83–7.76 (m, 3H), 7.48–7.43 (m, 2H), 7.40 (dd, *J* = 8.5, 1.6, 1H), 6.86 (d, *J* = 6.4, 2H), 6.75 (d, *J* = 8.5, 1H), 5.90–5.88 (m, 3H), 2.35 (br s, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 148.0, 147.2, 141.2, 137.9, 133.3, 133.0, 128.4, 128.2, 127.8, 126.3, 126.1, 124.8, 124.7, 120.4, 108.2, 107.5, 101.2, 76.2; **IR** (neat, cm^{-1}) 3363, 2889, 1500, 1485, 1444, 1239, 1035; **HRMS** (TOF MS ES+) *m*/*z*: [M]$^+$ calculated for $C_{18}H_{14}O_3$

278.0943, found 278.0938; **[α]$_D^{29}$** –12.0 (*c* 0.86, $CHCl_3$); **SFC** analysis (OD-H, 15.0% IPA, 3.0 mL/min, 215 nm) indicated 93% ee: t_R (minor) = 14.0 min, t_R (major) = 15.8 min.

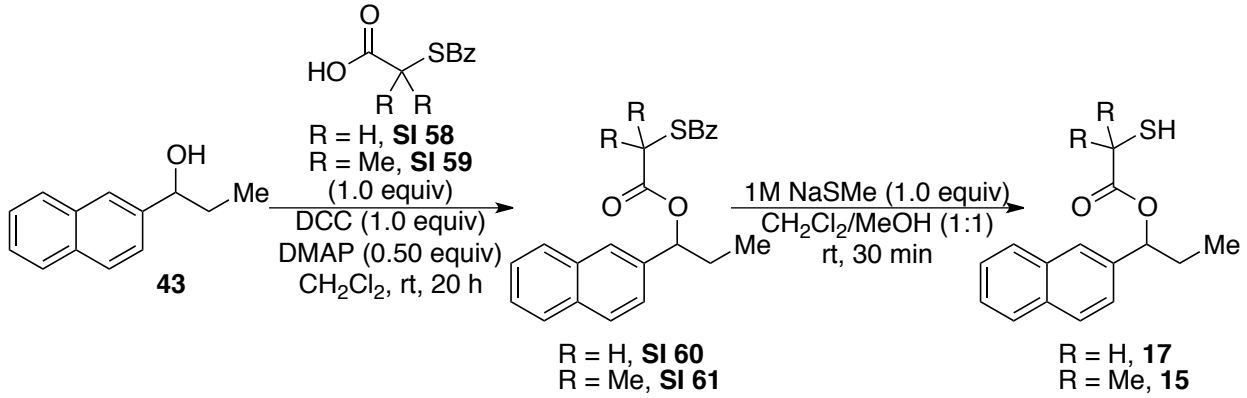


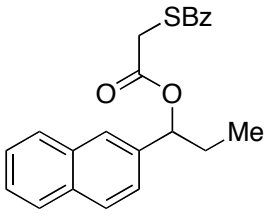
(*S*)-benzo[*d*][1,3]dioxol-5-yl(naphthalen-2-yl)methyl 2-(methylthio)acetate (*R*)-SI 57 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (93 mg, 0.88 mmol, 1.1 equiv), alcohol (*R*)-**SI 22** (0.22 g, 0.80 mmol, 1.0 equiv), 4-dimethylaminopyridine (49 mg, 0.40 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.18 g, 0.88 mmol, 1.1 equiv), and dichloromethane (4 mL). Purification by flash chromatography (10% Et_2O in pentane) afforded the title compound as an off-white oil (0.24 g, 82%). **TLC R_f** = 0.3 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.87–7.78 (m, 4H), 7.51–7.45 (m, 2H), 7.41 (dd, *J* = 8.5, 1.6, 1H), 6.98 (s, 1H), 6.88 (td, *J* = 8.0, 1.7, 2H), 6.77 (d, *J* = 8.0, 1H), 5.93 (d, *J* = 1.7, 2H), 3.31 (s, 2H), 2.16 (s, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.3, 148.0, 147.6, 137.3, 133.8, 133.2, 133.1, 128.6, 128.3, 127.8, 126.5, 126.4, 125.8, 124.8, 121.3, 108.3, 108.0, 101.3, 77.7, 36.1, 16.4; **IR** (neat, cm^{-1}) 2918, 1727, 1487, 1236, 1121; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{21}H_{18}O_4SNa$ 389.0823, found 389.0826; **[α]$_D^{30}$** –5.7 (*c* 0.87, $CHCl_3$); **SFC** analysis (OJ-H, 10.0% IPA, 3.0 mL/min, 215 nm) indicated 95% ee: t_R (major) = 13.3 min, t_R (minor) = 15.7 min.

I. Cross-Coupling of Diethylzinc (Table 3)

1) Starting Material Synthesis

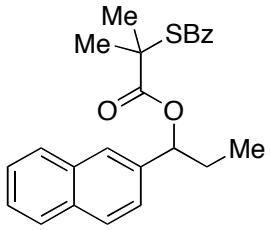
Scheme SI 19. Synthetic sequence for starting material synthesis



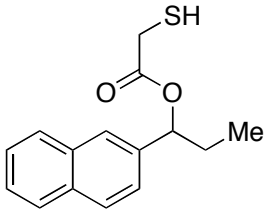


1-(naphthalen-2-yl)propyl 2-(benzoylthio)acetate SI 60 was prepared according Method L. The following amounts of reagents were used: carboxylic acid **SI 58** (0.53 g, 2.7 mmol, 1.0 equiv), alcohol **43** (0.50 g, 2.7 mmol, 1.0 equiv), 4-dimethylaminopyridine (0.16 g, 1.3 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.55 g, 2.7 mmol, 1.0 equiv), and CH_2Cl_2 (14 mL). The crude residue was purified by flash chromatography (5–10% EtOAc in hexanes) to afford the title compound as a viscous colorless oil (0.92 g, 93%). **TLC R_f** = 0.5 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.95 (d, *J* = 7.4, 2H), 7.83–7.45 (m, 4H), 7.55 (t, *J* = 7.4, 1H), 7.48–7.38 (m, 5H), 5.89 (t, *J* = 7.8, 1H), 3.97 (d, *J*

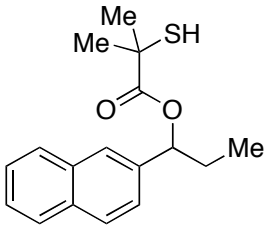
= 16.0, 1H), 3.89 (d, *J* = 16.0, 1H), 2.11–1.87 (m, 2H), 0.92 (t, *J* = 7.4, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 190.0, 168.2, 137.3, 136.3, 133.8, 133.2 (2C), 128.8, 128.4, 128.1, 127.7, 127.5, 126.3, 126.2, 125.9, 124.3, 79.2, 31.7, 29.2, 10.0; **IR** (neat, cm^{-1}) 1736, 1666, 1152, 909, 686; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{22}H_{20}O_3SNa$ 387.1031, found 387.1030.



1-(naphthalen-2-yl)propyl 2-(benzoylthio)-2-methylpropanoate SI 61 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **SI 59** (0.36 g, 1.6 mmol, 1.0 equiv), alcohol **43** (0.30 g, 1.6 mmol, 1.0 equiv), 4-dimethylaminopyridine (98 mg, 0.81 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.33 g, 1.6 mmol, 1.0 equiv), and CH_2Cl_2 (9 mL). The crude residue was purified by flash chromatography (5–10% EtOAc in hexanes) to afford the title compound as a viscous yellow oil which solidified upon standing for several days to a white crystalline solid (0.32 g, 58%). **TLC R_f** = 0.6 (4:1 hexane/EtOAc, UV active); **mp** 56–60 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.86–7.68 (m, 6H), 7.54 (t, *J* = 7.4, 1H), 7.48–7.34 (m, 5H), 5.89 (t, *J* = 6.8, 1H), 2.08–1.83 (m, 2H), 1.70 (s, 3H), 1.68 (s, 3H), 0.88 (t, *J* = 7.4, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 190.9, 173.2, 137.8, 136.8, 133.5, 133.2, 133.1, 128.7, 128.22, 128.18, 127.7, 127.3, 126.1, 126.0. 125.8, 124.4, 78.8, 51.4, 29.3, 26.2, 26.1, 10.0; **IR** (neat, cm^{-1}) 2970, 1732, 1661, 1157, 904, 689; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{24}H_{24}O_3SNa$ 415.1344, found 415.1337.



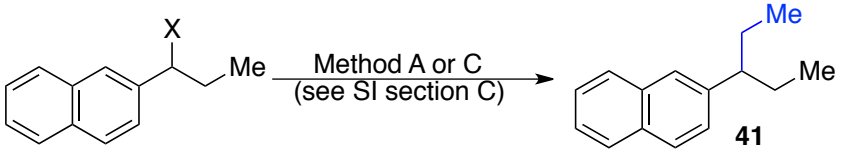
1-(naphthalen-2-yl)propyl 2-mercaptoacetate 17 was prepared according to Method M. The following amounts of reagents were used: NaSMe (1.6 mL, 1.6 mmol, 1.0 equiv, 1.0 M in MeOH), substrate **SI 60** (0.59 g, 1.6 mmol, 1.0 equiv), wet MeOH (8 mL) and CH_2Cl_2 (8 mL). The crude residue was purified by flash chromatography (2% Et_2O in pentane) and then heated to 40 °C under reduced pressure overnight to remove volatile byproducts which coeluted with the product. The title compound was isolated as a colorless oil (0.33 g, 78%). **TLC R_f** = 0.5 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.89–7.73 (m, 4H), 7.52–7.39 (m, 3H), 5.85 (t, *J* = 6.9, 1H), 3.31 (dd, *J* = 14.9, 8.4, 2H), 3.26 (dd, *J* = 15.0, 8.2, 1H), 2.12–1.86 (m, 2H), 0.93 (t, *J* = 7.4, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 170.3, 137.3, 133.21, 133.18, 128.5, 128.1, 127.8, 126.4, 126.3, 126.0, 124.3, 79.0, 29.2, 26.9, 10.1; **IR** (neat, cm^{-1}) 2968, 1731, 1143, 817, 746; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{15}H_{16}O_2SNa$ 283.0769, found 283.0767.



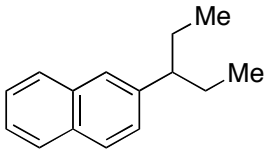
1-(naphthalen-2-yl)propyl 2-mercapto-2-methylpropanoate 15 was prepared according to Method M. The following amounts of reagents were used: NaSMe (0.76 mL, 0.76 mmol, 1.0 equiv, 1.0M in MeOH), substrate **SI 61** (0.30 g, 0.76 mmol, 1.0 equiv) in a mixture of MeOH (4 mL) and CH_2Cl_2 (4 mL), 30 min. The crude residue was purified by flash chromatography (5% Et_2O in pentane) and then heated to 40 °C under reduced pressure to remove volatile byproducts that coeluted with the product. The title compound was isolated as a colorless oil (68 mg, 31%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.87–7.81 (m, 3H), 7.80 (s, 1H), 7.51–7.43 (m, 3H), 5.82 (t, *J* = 6.8, 1.7, 1H), 2.43 (s, 1H), 2.06 (apparent septet, *J* = 7.3, 1H), 1.94 (apparent septet *J* = 7.0, 1H), 1.62 (s, 3H), 1.61 (s, 3H), 0.96 (t, *J* = 7.4, 3H); **^{13}C NMR**

($CDCl_3$, 125 MHz) δ 174.3, 137.7, 133.3, 133.2, 128.4, 128.2, 127.8, 126.3, 126.2, 125.7, 124.2, 78.6, 45.2, 29.5, 29.2, 29.1, 10.1; **IR** (neat, cm^{-1}) 2970, 1727, 1462, 1262, 1154, 1125; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{17}H_{20}O_2SNa$ 311.1082, found 311.1087.

2) OPTIMIZATION



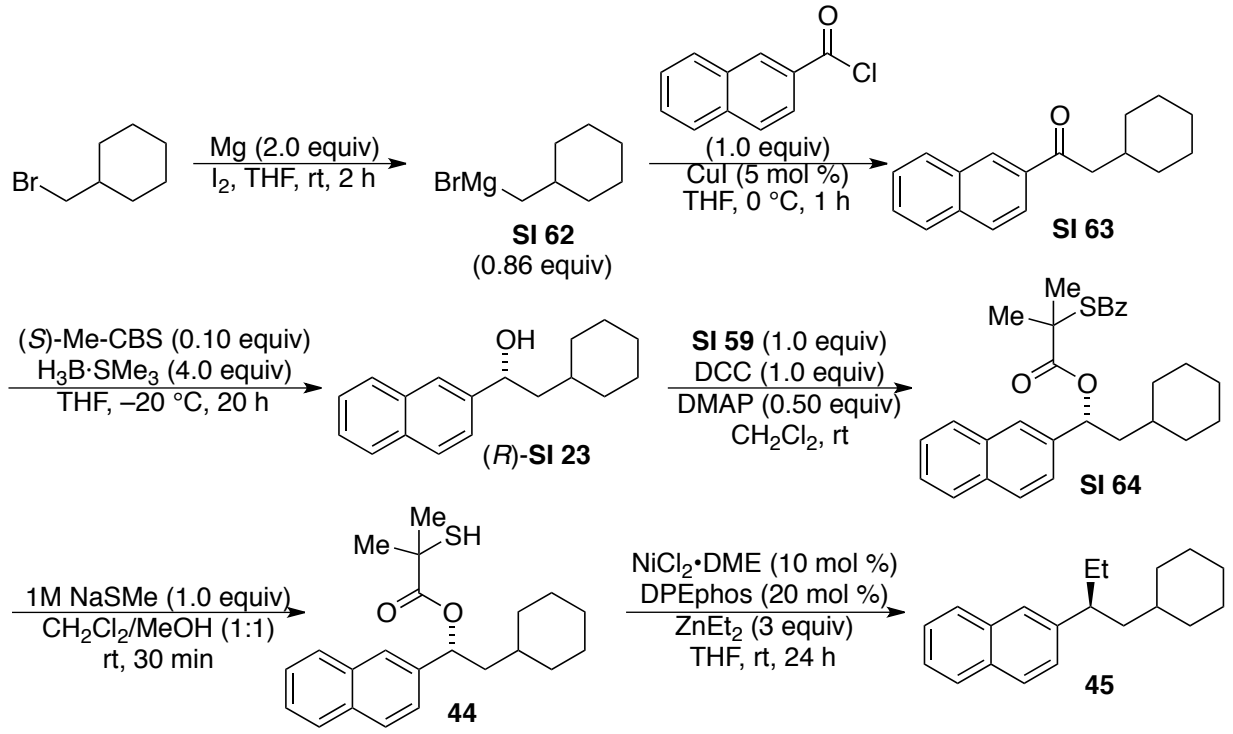
(18)

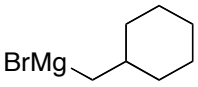


2-(pentan-3-yl)naphthalene 41 was prepared according to either Method A or C depending on the leaving group. Analytical data was consistent with literature values.[53] **TLC R_f** = 0.5 (100% pentane, UV active); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.83–7.75 (m, 3H), 7.56 (s, 1H), 7.42 (apd, *J* = 7.6, 1.5, 2H), 7.31 (dd, *J* = 8.5, 1.6, 1H), 2.48 (apparent septet, *J* = 4.8, 1H), 1.83–1.71 (m, 2H), 1.71–1.58 (m, 2H), 0.79 (t, *J* = 7.4, 6H).

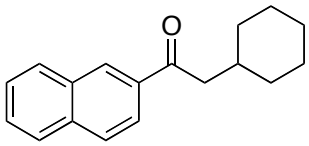
3) DETERMINATION OF ENANTIOSPECIFICITY (EQ 1)

Scheme SI 20. Synthesis of 43 from Equation 1

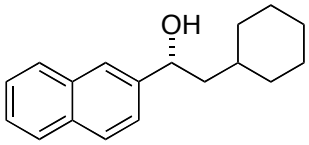




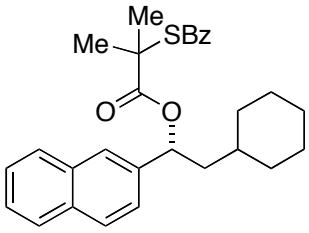
(cyclohexylmethyl)magnesium bromide SI 62 was prepared according to Method D. The following amounts of reagents were used: magnesium turnings (1.9 g, 80 mmol, 2.0 equiv), I_2 (ca. 2 mg), (bromomethyl)cyclohexane (5.5 mL, 40 mmol, 1.0 equiv), and anhydrous THF (40 mL). The Grignard titrated to 0.56 M.[2]



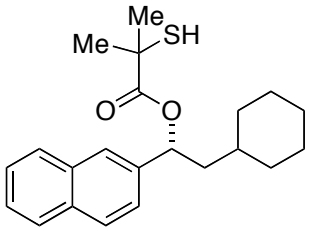
2-cyclohexyl-1-(naphthalen-2-yl)ethan-1-one SI 63 was prepared according to Method G. The following amounts of reagents were used: CuI (0.25 g, 1.3 mmol, 0.050 equiv), 2-naphthoyl chloride (5.1 g, 27 mmol, 1.0 equiv), Grignard reagent **SI 62** (37 mL, 21 mmol, 0.86 equiv, 0.56 M in THF), and THF (60 mL). The crude residue was recrystallized to afford the title compound as a white crystalline solid (1.6 g, 31%). **TLC R_f** = 0.4 (5% EtOAc in hexanes, UV active); **mp** 74–76 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.45 (s, 1H), 8.03 (dd, *J* = 8.7, 1.7 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.91–7.85 (m, 2H), 7.59 (td, *J* = 7.5, 1.3, 1H), 7.54 (td, *J* = 7.4, 1.5, 1H), 2.95 (d, *J* = 6.9 Hz, 2H), 2.10–1.98 (m, 1H), 1.81 (d, *J* = 12.3, 2H), 1.76–1.62 (m, 3H), 1.38–1.24 (m, 2H), 1.24–1.14 (m, 1H), 1.14–0.99 (qd, *J* = 12.1, 2.8, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 200.4, 135.7, 135.0, 132.7, 129.9, 129.7, 128.51, 128.46, 127.9, 126.8, 124.2, 46.4, 34.9, 33.7, 26.4, 26.3; **IR** (neat, cm^{-1}) 2918, 2849, 1684, 815, 744; **HRMS** (TOF MS ES+) *m/z*: $[M + Na]^+$ calculated for $C_{18}H_{20}ONa$ 275.1412, found 275.1413.



(*R*)-2-cyclohexyl-1-(naphthalen-2-yl)ethan-1-ol (*R*)-SI 23 was prepared according to Method I. The following amounts of reagents were used: (*S*)-Me-CBS-oxazaborolidine (0.75 g, 3.0 mmol, 0.10 equiv) and $H_3B{\bullet}SMe_2$ (0.64 mL, 6.0 mmol, 2.0 equiv) in THF (15 mL), and ketone **SI 63** (0.75 g, 3.0 mmol, 1.0 equiv) in THF (15 mL). The crude residue was purified by flash chromatography (5–20% EtOAc in hexanes)[§] to afford the title compound as a white solid (0.42 g, 55%). Absolute configuration assigned as *R* based on the accepted model for selectivity in CBS reductions[17] and confirmed by Competing Enantioselective Conversion (CEC).[18] **TLC R_f** = 0.3 (9:1 hexane/EtOAc, UV active); **mp** 99–100 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 7.84–7.82 (m, 3H), 7.78 (s, 1H), 7.49–7.45 (m, 3H), 4.96 (m, 1H), 1.85–1.77 (m, 4H), 1.71–1.60 (m, 4H), 1.51–1.40 (m, 1H), 1.29–1.13 (m, 3H), 1.04–0.92 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 142.8, 133.5, 133.1, 128.4, 128.1, 127.8, 126.3, 125.9, 124.6, 124.3, 72.4, 47.1, 34.4, 34.1, 33.1, 26.7, 26.4, 26.3; **IR** (neat cm^{-1}) 3594, 2926, 2852, 1448; **HRMS** (TOF MS ES+) *m/z*: $[M + Na]^+$ calculated for $C_{18}H_{22}ONa$ 277.1568, found 277.1567; **$[\alpha]_D^{28}$** +23.8 (*c* 1.0, $CHCl_3$); **SFC** analysis (AS-H, 3.0% IPA, 3.0 mL/min, 215 nm) indicated 87% ee: t_R (minor) = 12.9 min, t_R (major) = 13.5 min.



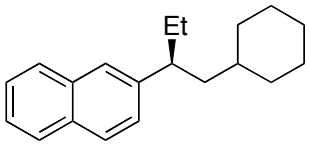
(*R*)-2-cyclohexyl-1-(naphthalen-2-yl)ethyl 2-(benzoylthio)-2-methylpropanoate (*R*)-SI 64 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **SI 59** (0.27 g, 1.2 mmol, 1.0 equiv), alcohol (*R*)-**SI 23** (0.30 g, 1.2 mmol, 1.0 equiv) 4-dimethylaminopyridine (45 mg, 0.55 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (0.24 g, 1.2 mmol, 1.0 equiv), and dichloromethane (6 mL). The crude residue was purified by flash chromatography (5% Et_2O in pentane) to afford the title compound as a white solid (0.30 g, 58%). **TLC R_f** = 0.6 (4:1 hexane/EtOAc, UV active); **mp** 101–104 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.86–7.67 (m, 6H), 7.54 (t, *J* = 7.4, 1H), 7.48–7.35 (m, 5H), 6.03 (dd, *J* = 9.2, 5.3, 1H), 1.95 (ddd, *J* = 14.1, 9.3, 5.6, 1H), 1.82 (d, *J* = 13.5, 1H), 1.72–1.50 (m, 5H), 1.68 (s, 3H), 1.64 (s, 3H), 1.37–1.24 (m, 1H) 1.16–0.83 (m, 5H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 190.7, 173.2, 138.6, 136.7, 133.6, 133.3, 133.1, 128.6, 128.3, 128.2, 127.7, 127.3, 126.1, 126.0, 125.7, 124.4, 75.4, 51.2, 44.2, 34.0, 33.8, 32.8, 26.6, 26.2, 26.11, 26.07, 26.0; **IR** (neat, cm^{-1}) 2921, 1739, 1654, 1156, 910, 691; **HRMS** (TOF MS ES+) *m/z*: $[M + Na]^+$ calculated for $C_{29}H_{32}O_3SNa$ 483.1970, found 483.1950; **$[\alpha]_D^{27}$** +18.6 (*c* 1.0, $CHCl_3$); **SFC** analysis (OD-H, 15.0% IPA, 3.0 mL/min, 215 nm) indicated 92% ee: t_R (major) = 5.9 min, t_R (minor) = 6.5 min.



(*R*)-2-cyclohexyl-1-(naphthalen-2-yl)ethyl 2-mercapto-2-methylpropanoate 44 was prepared according to Method M. The following amounts of reagents were used: NaSMe (0.54 mL, 0.54 mmol, 1.0 equiv, 1.0 M in MeOH), (*R*)-**SI 64** (0.25 g, 0.54 mmol, 1.0 equiv) in MeOH (5.4 mL), 5 min. The crude residue was purified by flash chromatography (2% Et_2O in pentane) and then heated to 40 °C under reduced pressure overnight to remove volatile byproducts that coeluted with the desired product. The title compound was isolated as a white solid (96 mg, 50%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active); **mp** 82–86 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.86–7.78 (m, 4H), 7.50–7.43 (m, 3H), 5.89 (dd, *J* = 8.8, 5.7, 1H), 2.40 (s, 1H), 1.98

[§] The material must be dry-loaded to avoid isolating the borane adduct.

(ddd, J = 14.1, 8.9, 6.2, 1H), 1.83–1.56 (m, 6H), 1.59 (s, 6H), 1.42–1.31 (m, 1H), 1.28–1.11 (m, 3H), 1.07–0.90 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 174.3, 138.4, 133.3, 133.2, 128.5, 128.2, 127.8, 126.3, 126.2, 125.6, 124.2, 75.3, 45.1, 44.1, 34.3, 33.7, 33.0, 29.2, 29.1, 26.6, 26.3, 26.2; **IR** (neat, cm^{-1}) 2922, 2851, 1720, 1259, 1153, 743; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calculated for $[C_{22}H_{28}O_2SNa$ 379.1708, found 379.1707; **$[\alpha]_D^{28}$** +52.3 (c 1.0, $CHCl_3$); **SFC** analysis (OJ-H, 3.0% IPA, 3.0 mL/min, 215 nm) indicated 92% ee: t_R (minor) = 8.8 min, t_R (major) = 9.5 min.

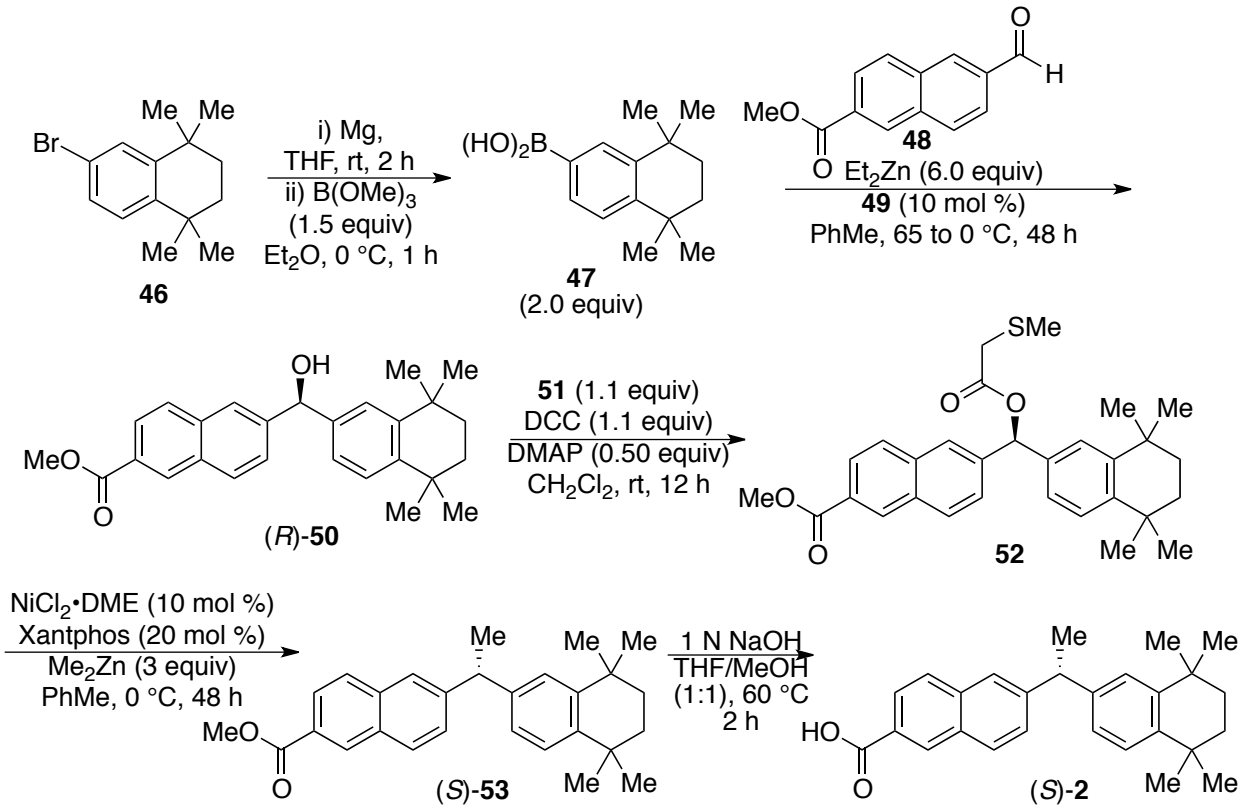


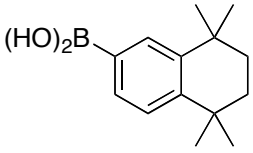
(*S*)-2-(1-cyclohexylbutan-2-yl)naphthalene 45 was prepared according to Method C. The following amounts of reagents were used: $NiCl_2$•DME (2.2 mg, 0.010 mmol, 0.10 equiv), DPEphos (11 mg, 0.020 mmol, 0.20 equiv), substrate **44** (0.20 mL, 0.10 mmol, 1.0 equiv, 0.50 M in PhMe), $ZnEt_2$ (0.20 mL, 0.30 mmol, 3.0 equiv, 1.6 M in PhMe) and THF (1.4 mL). The crude residue was purified by flash chromatography with silver impregnated silica gel (100% pentane) to afford the title compound as a 91:1 mixture with the reduction byproduct (16 mg, calculated as 14 mg, 52%). Compound **45** was re-purified by silica gel chromatography to obtain a sample of analytically pure material. **TLC R_f** = 0.5 (100% pentane, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.85–7.73 (m, 3H), 7.56 (s, 1H), 7.43 (apd, J = 7.5, 1.3, 2H), 7.31 (dd, J = 8.5, 1.6, 1H), 2.70 (apparent septet, J = 4.9, 1H), 1.83 (d, J = 12.9, 1H), 1.75–1.46 (m, 8H), 1.15–0.99 (m, 4H), 0.95–0.79 (m, 2H), 0.76 (t, J = 7.3, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 143.8, 133.7, 132.2, 127.9, 127.73, 127.67, 126.5, 126.2, 125.8, 125.1, 44.8, 44.6, 35.0, 34.4, 33.0, 30.4, 26.8, 26.4, 26.3, 12.4; **IR** (neat, cm^{-1}) 2991, 2950, 1447, 815, 743; **HRMS** (TOF MS EI+) m/z: $[M]^+$ calculated for $C_{20}H_{26}$ 266.2035, found 266.2046; **$[\alpha]_D^{25}$** +8.8 (c 0.72, $CHCl_3$); **SFC** analysis (OJ-H, 1.0% IPA, 2.5 mL/min, 215 nm) indicated 90% ee: t_R (major) = 9.3 min, t_R (minor) = 10.6 min.

J. Synthesis of Retinoic Acid Receptor Ligand 2 (Scheme 4)

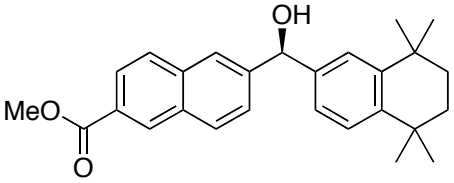
1) Enantioselective Synthesis of **2**

Scheme SI 21. Synthetic sequence for preparation of RAR ligand 2



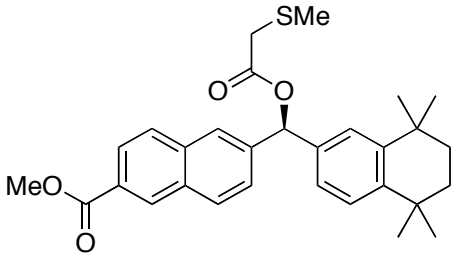


5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-ylboronic acid 47 was prepared according to a modified procedure by Frohn.[54] Under a nitrogen atmosphere, a flame-dried round-bottom flask was charged with magnesium turnings (0.11 g, 4.7 mmol, 2.5 equiv) and THF (2 mL). 6-bromo-1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene **46** (0.52 g, 2.0 mmol, 1.0 equiv) was added and the mixture was stirred for 2 h at ambient temperature before being cooled to 0 °C. Meanwhile, trimethyl borate (0.28 g, 2.7 mmol, 1.5 equiv) was dissolved in Et_2O (1 mL) and cooled to 0 °C. Pre-cooled Grignard solution was added to trimethyl borate solution and the reaction was allowed to stir. After for 1 h at 0 °C, the reaction was quenched with 1 M HCl. The organics were extracted with Et_2O (3 x 5 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. The off-white solid obtained was used without further purification. **^{1}H NMR** ($CDCl_3$, 400 MHz,) δ 7.46 (d, J = 7.8, 1H), 7.29 (dd, J = 3.4, 5.9, 1H), 7.11 (dd, J = 3.5, 6.1, 1H), 1.74 (s, 2H), 1.68 (s, 2H), 1.40 (s, 6H), 1.34 (s, 6H), 0.87 (br s, 2H).

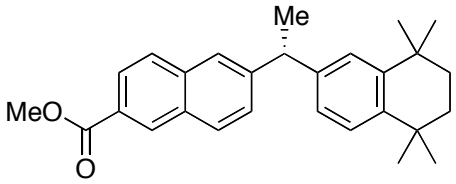


(*R*)-methyl 6-(hydroxy(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)methyl)-2-naphthoate (*R*)-50 was prepared according to Method K. The following amounts of reagents were used: boronic acid **47** (0.16 g, 0.70 mmol, 2.0 equiv), diethylzinc (2.1 mL, 2.1 mmol, 6.0

equiv, 1.0 M in toluene), aminoalcohol **49** (24 g, 0.035 mmol, 0.10 equiv), methyl 6-formyl-2-naphthoate **48** (75 mg, 0.35 mmol, 1.0 equiv), PhMe (6 mL). The product was purified by flash chromatography (10% EtOAc in hexane) to afford the title compound as a white solid (0.13 g, 94%). Absolute configuration was assigned as *R* by comparison of optical rotation with literature values. Analytical data are consistent with literature values.[51] **TLC** $\mathbf{R_f}$ = 0.4 (4:1 hexane/EtOAc, UV active); **mp** 159–161 °C, lit.[51] mp 154 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.57 (s, 1H), 8.01 (dd, *J* = 8.5, 1.6, 1H), 7.97 (s, 1H), 7.89 (t, *J* = 7.6, 2H), 7.52 (dd, *J* = 8.7, 1.9, 1H), 7.38 (d, *J* = 2.0, 1H), 7.27–7.25 (m, 1H), 7.09 (dd, *J* = 8.0, 2.0, 1H), 5.97 (d, *J* = 3.3, 1H), 3.98 (s, 3H), 2.26 (d, *J* = 3.5, 1H), 1.67 (s, 4H), 1.27–1.24 (m, 12H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 167.4, 145.4, 144.8, 144.0, 140.5, 135.6, 132.0, 130.9, 129.7, 128.5, 127.5, 127.1, 125.8, 125.7, 125.1, 124.7, 124.1, 76.5, 52.4, 35.2, 35.1, 34.5, 34.3, 32.01, 32.00, 31.96, 31.95; **IR** (neat, cm^{-1}) 3525, 2956, 1697, 1430, 1297, 1123, 757; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{27}H_{30}O_3Na$ 425.2093, found 425.2093; $\mathbf{[\alpha]_D^{29}}$ +36.1 (*c* 0.58, THF), lit.[22] $[\alpha]_D^{20}$ +45.2 (c 0.31, THF, >99.8% ee, (*R*)-enantiomer); **SFC** analysis (OD-H, 15.0% IPA, 3.0 mL/min, 215 nm) indicated 94% ee: t_R (major) = 9.8 min, t_R (minor) = 12.6 min.

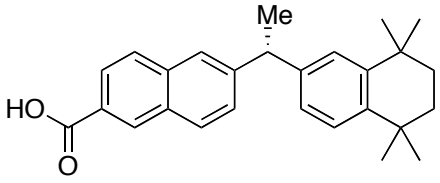


(*R*)-methyl 6-((2-(methylthio)acetoxy)(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)methyl)-2-naphthoate 52 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (32 mg, 0.30 mmol, 1.2 equiv), alcohol (*R*)-**50** (0.10 g, 0.25 mmol, 1.0 equiv), 4-dimethylaminopyridine (15 mg, 0.13 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (62 mg, 0.30 mmol, 1.2 equiv), and CH_2Cl_2 (1 mL). Purification by flash chromatography (10% Et_2O in pentane) afforded the title compound as a white foam (0.11 g, 90%). **TLC** $\mathbf{R_f}$ = 0.5 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.58 (s, 1H), 8.07 (dd, *J* = 8.4, 1.7, 1H), 7.93–7.87 (m, 3H), 7.52 (dd, *J* = 8.7, 1.7, 1H), 7.36 (d, *J* = 2.0, 1H), 7.25 (s, 1H), 7.08 (dd, *J* = 8.0, 2.2, 1H), 7.03 (s, 1H), 3.98 (s, 3H), 3.32 (s, 2H), 2.16 (s, 3H), 1.67 (s, 4H), 1.25 (s, 12H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 169.4, 167.3, 145.3, 145.1, 140.1, 136.2, 135.4, 132.1, 130.9, 129.8, 128.5, 127.8, 127.0, 125.84, 125.80, 127.7, 125.6, 124.6, 77.8, 52.4, 36.1, 35.10, 35.05, 34.5, 34.3, 32.0, 31.9, 16.4; **IR** (neat, cm^{-1}) 2956, 2922, 1719, 1278, 1195; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{30}H_{34}O_4SNa$ 513.2076, found 513.2061; $\mathbf{[\alpha]_D^{29}}$ +3.2 (*c* 0.92, $CHCl_3$); **SFC** analysis (OD-H, 10.0% IPA, 3.0 mL/min, 215 nm) indicated 93% ee: t_R (major) = 10.3 min, t_R (minor) = 12.3 min.

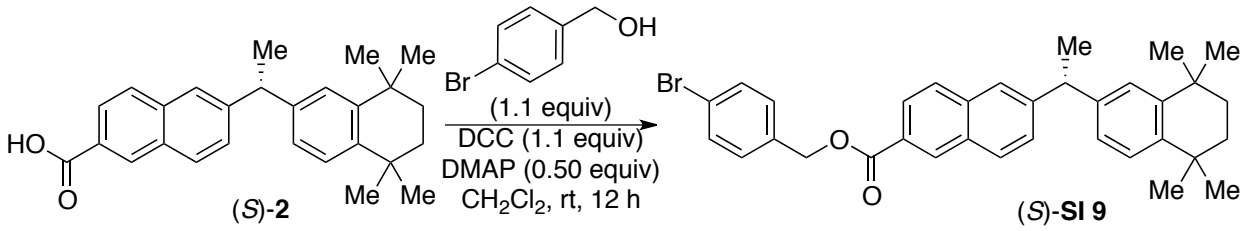


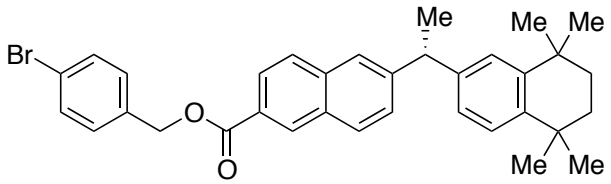
(*S*)-methyl 6-(1-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)ethyl)-2-naphthoate (*S*)-53 was prepared according to Method B. The following amounts of reagents were used: $NiCl_2$•DME (3.3 mg, 0.015 mmol, 0.10 equiv), Xantphos (17 mg, 0.03 mmol, 0.20 equiv), substrate (*R*)-**52** (0.30 mL, 0.15 mmol, 1.0 equiv, 0.50 M in PhMe), and $ZnMe_2$ (0.25 mL, 0.45 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2.1 mL). Purification by flash chromatography (2–5% Et_2O in pentane) afforded the title compound as a white solid (55 mg, 92%). **TLC** $\mathbf{R_f}$ = 0.6 (4:1 hexane/EtOAc, UV active); **mp** 117–120 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz) δ 8.55 (s, 1H), 8.03 (dd, *J* = 8.7, 1.7, 1H), 7.83 (t, *J* = 7.7, 2H), 7.72 (s, 1H), 7.40 (dd, *J* =

8.8, 1.8, 1H), 7.21 (d, J = 2.9, 1H), 7.19 (d, J = 3.3, 1H), 6.97 (dd, J = 8.1, 1.8, 1H), 4.26 (q, J = 7.1, 1H), 3.97 (s, 3H), 1.71 (d, J = 7.2, 3H), 1.66 (s, 4H), 1.25–1.23 (m, 12H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 167.5, 147.1, 144.9, 142.8, 142.4, 135.9, 131.2, 130.9, 129.4, 128.1, 127.9, 126.9, 126.7, 125.8, 125.42, 125.39, 125.0, 52.3, 45.0, 35.3, 35.2, 34.4, 34.1, 32.1, 32.0 (3C), 21.9; **IR** (neat, cm^{-1}) 2955, 1715, 1457, 1434, 1289, 1233, 1186; **HRMS** (TOF MS ES+) m/z: $[M + Na]^+$ calculated for $C_{28}H_{32}O_2Na$ 423.2300, found 423.2303; **$[\alpha]_D^{27}$** –23.0 (c 0.94, $CHCl_3$); **SFC** analysis (OD-H, 3.0% IPA, 3.0 mL/min, 215 nm) indicated 90% ee: t_R (minor) = 21.7 min, t_R (major) = 24.2 min.



(*S*)-6-(1-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)ethyl)-2-naphthoic acid (*S*)-2 was prepared according to a modified procedure by Yu.[22] To a stirred solution of ester (*S*)-**53** (42 mg, 0.12 mmol, 1.0 equiv) in THF (1 mL) and methanol (1 mL) was added 1 N NaOH (2 mL, 2.0 mmol, 20 equiv). The reaction was heated and let stir at 60 °C for 2 hours before acidification with cold 1 N HCl (3 mL). The aqueous layer was extracted with EtOAc (3 x 5 mL), washed with brine (2 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo to afford the title compound as a white solid (38 mg, 92%). Analytical data are consistent with literature values.[22] **mp** 193–195 °C; **^{1}H NMR** (DMSO, 400 MHz) 8.55 (s, 1H), 8.03–7.96 (m, 4H), 7.53 (dd, J = 8.6, 1.4, 1H), 7.32 (d, J = 1.5, 1H), 7.23 (d, J = 8.1, 1H), 7.05 (dd, J = 8.0, 1.5, 1H), 4.31 (q, J = 7.2, 1H), 1.70 (d, J = 7.3, 3H), 1.63 (s, 4H), 1.24 (s, 6H), 1.22 (s, 3H), 1.21 (s, 3H); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.65 (s, 1H), 8.08 (dd, J = 8.7, 1.6, 1H), 7.88 (d, J = 6.1, 1H), 7.86 (d, J = 6.3, 1H), 7.75 (s, 1H), 7.42 (dd, J = 8.6, 1.6, 1H), 7.21 (d, J = 3.9, 1H), 7.20 (d, J = 2.2, 1H), 6.97 (dd, J = 8.3, 1.8, 1H), 4.28 (q, J = 7.3, 1H), 1.73 (d, J = 7.4, 3H), 1.66 (s, 4H), 1.25–1.24 (m, 12H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 171.8, 147.6, 144.9, 142.9, 142.4, 136.3, 131.9, 131.2, 129.6, 128.3, 128.0, 126.7, 126.0, 125.8, 125.6, 125.5, 125.0, 45.0, 35.3, 35.2, 34.4, 34.1, 32.1, 32.0 (3C), 21.9; **IR** (neat, cm^{-1}) 2954, 1677, 1628, 1428, 1286; **$[\alpha]_D^{29}$** –23.2 (c 0.73, $CHCl_3$).

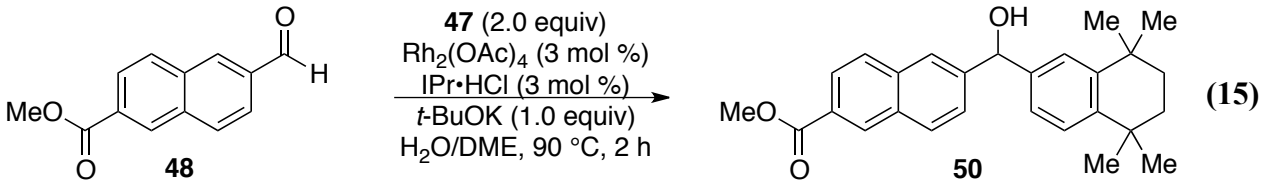




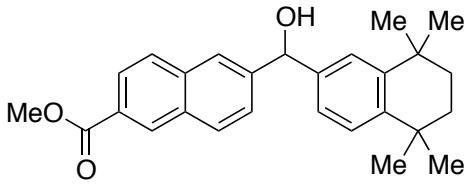
4-bromobenzyl (*S*)-6-(1-(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)ethyl)-2-naphthoate (*S*)-SI 9 was prepared according to Method L. The following amounts of reagents were used: carboxylic acid (*S*)-**2** (19 mg, 0.050 mmol, 1.0 equiv), (4-bromophenyl)methanol (10 mg, 0.055 mmol, 1.1 equiv), 4-dimethylaminopyridine (3.1 mg, 0.025 mmol, 0.50 equiv), *N*,*N*'-dicyclohexylcarbodiimide (11 mg, 0.055 mmol, 1.1 equiv), and dichloromethane (1 mL). The crude residue was purified by silica gel chromatography (10% Et_2O in pentane), to afford the title compound as a white solid (0.024 g, 86%). A single crystal

suitable for X-ray crystallographic analysis was grown by slow evaporation from ether-pentanes. For X-ray crystallographic data, see Section IV. **TLC** $\mathbf{R_f}$ = 0.6 (4:1 hexane/EtOAc, UV active); **m.p.** 122–123 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.56 (s, 1H), 8.03 (dd, *J* = 8.8, 1.6, 1H), 7.84 (d, *J* = 4.6, 1H), 7.82 (d, *J* = 4.5, 1H), 7.72 (s, 1H), 7.54–7.51 (m, 2H), 7.41–7.34 (m, 3H), 7.20–7.19 (m, 2H), 6.96 (dd, *J* = 8.3, 2.3, 1H), 5.36 (s, 2H), 4.26 (q, *J* = 7.3, 1H), 1.71 (d, *J* = 7.1, 3H), 1.65 (s, 4H), 1.24 (d, *J* = 1.7, 6H), 1.23 (d, *J* = 2.6, 6H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ166.6, 147.3, 144.9, 142.8, 142.4, 136.0, 135.3, 131.9, 131.2, 131.1, 130.0, 129.4, 128.2, 128.0, 126.7, 126.6, 125.8, 125.4, 125.0, 122.4, 66.1, 45.0, 35.3, 35.2, 34.4, 34.1, 32.1, 32.0 (3C) ; **IR** (neat, cm^{-1}) 2922, 1726, 1285, 1239, 1197, 1008; **HRMS** (TOF MS ES+) *m/z*: $[M + Na]^+$ calculated for $C_{34}H_{35}O_2BrNa$ 577.1718, found 577.1720; $\mathbf{[\alpha]_D^{26}}$ –8.4 (*c* 0.235, $CHCl_3$).

2) PREPARATION OF RACEMIC ALCOHOL STANDARD



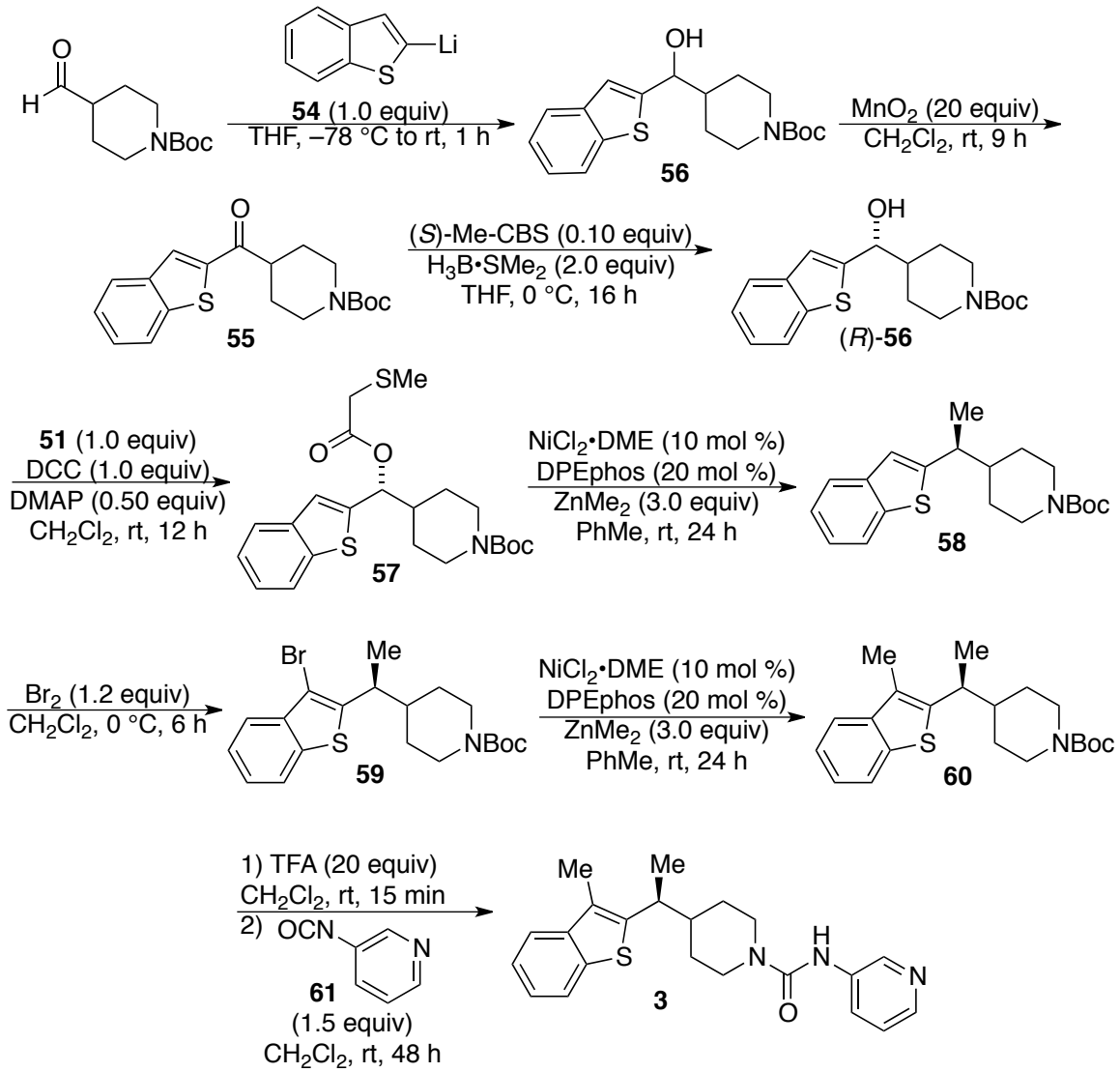
(15)

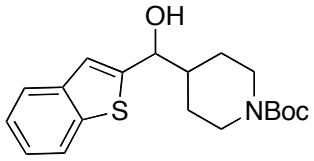


Methyl 6-(hydroxy(5,5,8,8-tetramethyl-5,6,7,8-tetrahydronaphthalen-2-yl)methyl)-2-naphthoate 50. Grignard addition to prepare **50** was unreliable, thus a Rh-catalyzed arylation was used instead, according to a modified procedure by Gois.[55] A flame-dried 10 mL pear-shaped flask equipped with a stir bar was charged with rhodium(II) acetate (1.6 mg, 0.0036 mmol, 0.030 equiv) and dimethoxyethane (0.3 mL). The resulting turquoise solution was let stir 5 min before the addition of boronic acid **47** (55 mg, 0.24 mmol, 2.0 equiv), 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride (1.5 mg, 0.0036 mmol, 0.030 equiv), KO*t*-Bu (14 mg, 0.12 mmol, 1.0 equiv), and aldehyde **48** (26 mg, 0.12 mmol, 1.0 equiv). To this brown solution was added H_2O (60 μL) and the reaction vessel was fitted with a reflux condenser before heating to 90 °C. After 2 h, the reaction was cooled to ambient temperature and partitioned between sat. aqueous $NaHCO_3$ (1 mL) and EtOAc (1 mL). The aqueous layer was extracted with EtOAc (2 x 2 mL). The combined organics were washed with brine (2 mL), dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification of the crude residue by flash chromatography (10% EtOAc in hexanes) afforded the title compound as a pale yellow solid (0.032 g, 66%). For analytic data see (*R*)-**50**.

K. Synthesis of Fatty Acid Amide Hydrolase Inhibitor 3 (Scheme 5)

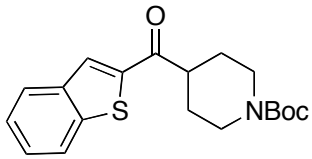
Scheme SI 22. Synthetic sequence for preparation of FAAH inhibitor 3



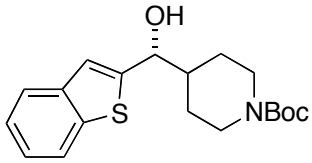


***tert*-butyl 4-(benzo[b]thiophen-2-yl(hydroxy)methyl)piperidine-1-carboxylate 56.** Lithiate **54** (8.0 mL, 5.0 mmol, 1.0 equiv, 0.63 M in Et_2O/Hexanes) was added to a stirring solution of 1-Boc-piperidine-4-carboxaldehyde (1.1 g, 5.0 mmol, 1.0 equiv) in THF (4 mL) at −78 °C. The reaction was allowed to warm to ambient temperature over 1 h and subsequently quenched with sat. NH_4Cl and extracted with EtOAc (3 x 10 mL). The combined organics were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. The crude residue was purified by flash chromatography (20–30% EtOAc in hexanes with 1% TEA) to afford the title compound as a white crystalline solid (1.3 g, 75%) **TLC R_f** = 0.2 (4:1 hexane/EtOAc, UV active); **mp** 129–132 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz, 323 K) δ 7.76 (d, J = 8.1, 1H), 7.67 (d, J = 7.7, 1H), 7.30 (td, J = 7.4, 1.2, 1H), 7.26 (td, J = 7.6, 1.4, 1H),

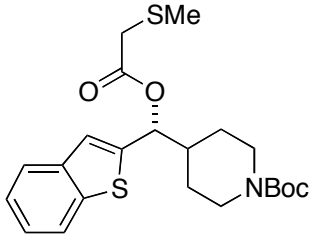
7.11 (s, 1H), 4.66 (dd, J = 7.2, 2.6, 1H), 4.11 (d, J = 12.8, 1H), 4.03 (d, J = 12.8, 1H), 2.71–2.54 (m, 3H), 1.95 (dp, J = 13.2, 2.7, 1H), 1.81 (dddd, J = 14.9, 11.4, 7.4, 3.6, 1H), 1.42 (s, 9H), 1.28 (qd, J = 12.4, 4.3, 1H), 1.20 (qd, J = 12.4, 4.5, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz, 323 K) δ 155.0, 148.0, 139.6, 124.4, 124.3, 123.5, 122.6, 121.1, 79.5, 74.8, 43.9, 43.8 (br s, 2C), 28.59, 28.57, 28.2; **IR** (neat, cm^{-1}) 3433, 2938, 1653, 1428, 1168, 744; **HRMS** (TOF MS ES+) *m*/*z*: [M + Na]$^+$ calculated for $C_{19}H_{25}NO_3SNa$ 370.1453, found 370.1464.



***tert*-butyl 4-(benzo[b]thiophene-2-carbonyl)piperidine-1-carboxylate 55** was prepared according to Method F. The following amounts of reagents were used: MnO_2 (2.6 g, 30 mmol, 20 equiv), alcohol **56** (0.53 g, 1.5 mmol, 1.0 equiv), wet CH_2Cl_2 (20 mL), 9 h. The crude residue was purified by flash chromatography (20–40% EtOAc in hexanes) to afford the title compound as a white powder (0.38 g, 72%). **TLC R_f** = 0.3 (4:1 hexane/EtOAc, UV active, stains with CAM); **mp** 130–132 °C; **^{1}H NMR** ($CDCl_3$, 500 MHz, 323 K) δ 7.96 (s, 1H), 7.87 (d, J = 7.9, 1H), 7.85 (dd, J = 8.1, 0.7, 1H), 7.45 (td, J = 7.6, 1.2, 1H), 7.39 (td, J = 7.5, 1.1, 1H), 4.18 (d, J = 13.1, 2H), 3.36 (tt, J = 11.0, 3.9, 1H), 2.93 (td, J = 12.7, 2.6, 2H), 1.91 (dd, J = 13.3, 2.4, 2H), 1.79 (dtd, J = 13.6, 11.5, 4.3, 2H), 1.47 (s, 9H); **^{13}C NMR** ($CDCl_3$, 125 MHz, 323 K) δ 196.3, 154.8, 142.9, 142.7, 139.3, 128.8, 127.6, 126.0, 125.2, 123.1, 79.8, 45.4, 43.4 (br s), 28.8, 28.6; **IR** (neat, cm^{-1}) 2928, 1688, 1651, 1161, 753; **HRMS** (TOF MS ES+) *m*/*z*: [M + Na]$^+$ calculated for $C_{19}H_{23}NO_3SNa$ 368.1296, found 368.1290.

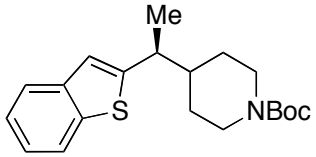


***tert*-butyl (*R*)-4-(benzo[b]thiophen-2-yl(hydroxy)methyl) piperidine-1-carboxylate (*R*)-56** was prepared according to Method I with the following exception: The reaction was set up at 0 °C and then transferred to a cold room where it was allowed to stir at 4 °C. The following amounts of reagents were used: (*S*)-Me-CBS-oxazaborolidine (15 mg, 0.053 mmol, 0.10 equiv) and $H_3B{\bullet}SMe_2$ (0.11 mL, 1.1 mmol, 2.0 equiv) in THF (3 mL), and ketone **55** (0.18 g, 0.53 mmol, 1.0 equiv), as a solution in THF (3 mL). The crude residue was purified by flash chromatography (20–30% EtOAc in hexanes with 1% TEA) to afford the title compound as a white crystalline solid (0.18 g, 99%, 68% ee). Recrystallization from CH_2Cl_2/hexanes afforded white crystals of reduced ee, therefore, the mother liquor from three successive recrystallizations was pooled together to afford the title compound in 95% ee. Absolute configuration assigned as *R* based on the accepted model for selectivity in CBS reductions[17] and confirmed by Competing Enantioselective Conversion (CEC).[18] See *rac*-alcohol **52** for analytical data. **mp** 138–140 °C; **$[\alpha]_D^{29}$** –24.2 (*c* 1.0, $CHCl_3$); **SFC** analysis (OJ-H, 15.0% MeOH, 3.0 mL/min, 215 nm) indicated 93% ee: t_R (minor) = 3.9 min, t_R (major) = 4.9 min.

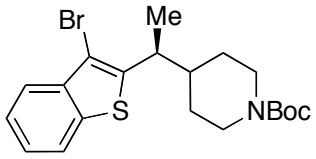


***tert*-butyl (*R*)-4-(benzo[b]thiophen-2-yl(2-(methylthio)acetoxy) methyl)piperidine-1-carboxylate 57** was prepared according to Method L. The following amounts of reagents were used: carboxylic acid **51** (24 mg, 0.23 mmol, 1.1 equiv), alcohol (*R*)-**56** (72 mg, 0.21 mmol, 1.0 equiv), 4-dimethylaminopyridine (14 mg, 0.11 mmol, 0.55 equiv), *N*,*N*'-dicyclohexylcarbodiimide (47 mg, 0.23 mmol, 1.1 equiv), CH_2Cl_2 (2 mL). The crude residue was purified by flash chromatography (20–30% Et_2O in pentane) to afford the title compound as a viscous oil (75 mg,

83%). **TLC R_f** = 0.3 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 500 MHz, 323K) δ 7.76 (d, *J* = 7.8, 1H), 7.71 (dd, *J* = 7.0, 1.6, 1H), 7.31 (apd, *J* = 7.2, 1.5, 2H), 7.25 (s, 1H), 5.91 (d, *J* = 7.2, 1H), 4.15 (d, *J* = 12.8, 1H), 4.08 (d, *J* = 13.0, 1H), 3.22 (d, *J* = 14.3, 1H), 3.18 (d, *J* = 14.4, 1H), 2.71 (td, *J* = 12.7, 1.9, 1H), 2.66 (td, *J* = 12.6, 1.9, 1H), 2.15 (s, 3H), 2.11–2.01 (m, 1H), 1.92 (dp, *J* = 13.1, 2.7, 1H), 1.52 (dp, *J* = 13.0, 2.8, 1H), 1.44 (s, 9H), 1.33 (qd, *J* = 12.5, 4.4, 1H), 1.24 (qd, *J* = 12.7, 5.5, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz, 323 K) δ 169.3, 154.8, 142.0, 139.7, 139.2, 124.8, 124.6, 123.9, 123.5, 122.5, 79.6, 76.3, 43.6 (br s, 2C), 42.0, 36.0, 28.6, 28.4, 28.3, 16.4; **IR** (neat, cm^{-1}) 2921, 1733, 1686, 1422, 1129; **HRMS** (TOF MS ES+) *m/z*: $[M + Na]^+$ calculated for $C_{22}H_{29}NO_4S_2Na$ 458.1436, found 458.1422; **$[\alpha]_D^{26}$** +24.3 (*c* 1.0, $CHCl_3$); **SFC** analysis (OJ-H, 15.0% MeOH, 3 mL/min, 215 nm) indicated 94% ee: t_R (minor) = 3.6 min, t_R (major) = 4.0 min.



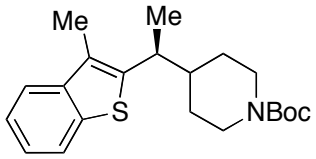
***tert*-butyl (*S*)-4-(1-(benzo[b]thiophen-2-yl)ethyl)piperidine-1-carboxylate 58** was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (3.1 mg, 0.014 mmol, 0.10 equiv), DPEphos (15 mg, 0.028 mmol, 0.20 equiv), substrate **57** (0.56 mL, 0.14 mmol, 1.0 equiv, 0.25 M in PhMe), and $ZnMe_2$ (0.23 mL, 0.42 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (1.7 mL). Purification by flash chromatography (15% Et_2O in pentane) afforded the title compound as a 94:6 mixture of desired product and β-H elimination byproduct (44 mg, calculated as 42 mg, 87%). Compound **58** was re-purified by silica gel chromatography to obtain a sample of analytically pure material. **TLC R_f** = 0.6 (4:1 hexane/EtOAc, UV active, stain with CAM); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.77 (d, *J* = 7.9, 1H), 7.67 (d, *J* = 7.7, 1H), 7.31 (td, *J* = 7.5, 0.9, 1H), 7.25 (td, *J* = 7.5, 1.1, 1H), 6.99 (s, 1H), 4.14 (br s, 1H), 4.06 (br s, 1H), 2.89 (p, *J* = 7.1, 1H), 2.64 (t, *J* = 12.3, 1H), 2.61 (t, *J* = 12.3, 1H), 1.81 (d, *J* = 13.2, 1H), 1.68–1.51 (m, 2H), 1.44 (s, 9H), 1.37 (d, *J* = 7.0, 3H), 1.29–1.08 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz, 323 K) δ 154.9, 150.9, 140.0, 139.1, 124.2, 123.7, 122.7, 122.3, 120.3, 79.4, 44.3 (br s, 2C), 43.4, 41.6, 30.6, 29.6, 28.6, 19.4; **IR** (neat, cm^{-1}) 2975, 1680, 1424, 1169, 748; **HRMS** (TOF MS ES+) *m/z*: $[M + Na]^+$ calculated for $C_{20}H_{27}NO_2SNa$ 338.1660, found 368.1666; **$[\alpha]_D^{25}$** +58.3 (*c* 0.93, $CHCl_3$); **SFC** analysis (OJ-H, 10.0% MeOH, 3.0 mL/min, 215 nm) indicated 93% ee: t_R (major) = 4.4 min, t_R (minor) = 5.0 min.



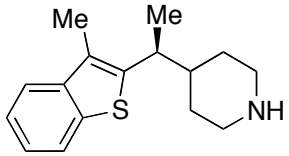
***tert*-butyl-(*S*)-4-(1-(3-bromobenzo[b]thiophen-2-yl)ethyl) piperidine-1-carboxylate 59** was prepared according to a modified procedure reported by Kose.[56] Bromine (33 μL, 0.63 mmol, 1.3 equiv) was added to a stirring solution of **58**[**] (77% ee, 0.17 g, 0.49 mmol, 1.0 equiv) in anhydrous THF (3.5 mL) at 0 °C. The reaction was then transferred to a cold room and stirred at 4 °C. After 6 h, the reaction was quenched by the successive addition of aq. $Na_2S_2O_3$ (5 mL, 10% by wt.) and $NaHCO_3$ (5 mL, 10% by wt.) The reaction mixture was extracted with EtOAc (3 x 5 mL) and the combined organics were washed with brine, dried over Na_2SO_4, filtered and concentrated in vacuo. The crude residue was purified by flash chromatography (100% CH_2Cl_2) to afford the title compound as a colorless oil (50 mg, 24%). **TLC R_f** = 0.7 (4:1 hexane/EtOAc, UV active, stain with CAM); **^{1}H NMR** ($CDCl_3$, 500 MHz, 323 K) δ 7.76 (d, *J* = 8.0, 1H), 7.73 (d, *J* = 8.1, 1H), 7.40 (td, *J* = 7.5, 1.0, 1H), 7.32 (td, *J* = 7.6, 1.2, 1H), 4.15 (d, *J* = 12.8, 1H), 4.03 (d, *J* = 12.8, 1H), 3.27 (dq, *J* = 8.6, 7.0, 1H), 2.69 (td, *J* = 12.9, 2.6, 1H), 2.60 (td, *J* = 12.8, 2.6, 1H), 1.95–1.87 (m, 1H), 1.73–1.65

[**] Starting material for this reaction was pooled from several experiments. The combined ee = 77%

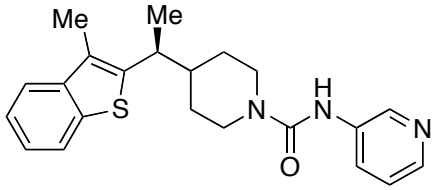
(m, 1H), 1.55–1.47 (m, 1H), 1.44 (s, 9H), 1.34 (d, *J* = 7.0, 3H), 1.30–1.18 (m, 2H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 155.0, 145.6, 138.3, 137.1, 125.12, 125.08, 123.1, 122.5, 106.0, 79.5, 44.2, 44.1, 43.3, 40.7, 30.5, 30.0, 28.7, 19.3; **IR** (neat, cm^{-1}) 2974, 1687, 1422, 1166, 727; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{20}H_{26}BrNO_2SNa$ 446.0765, found 446.0750; **$[\alpha]_D^{28}$** +36.6 (*c* 1.2, $CHCl_3$); **SFC** analysis (OJ-H, 4.0% MeOH, 2.5 mL/min, 215 nm) indicated 76% ee: t_R (major) = 9.3 min, t_R (minor) = 10.3 min.



***tert*-butyl-(*S*)-4-[1-(3-methylbenzo[b]thiophen-2-yl)ethyl] piperidine-1-carboxylate 60** was prepared according to Method A. The following amounts of reagents were used: $NiCl_2$•DME (2.6 mg, 0.012 mmol, 0.10 equiv), DPEphos (13 mg, 0.024 mmol, 0.20 equiv), substrate **59** (50 mg, 0.12 mmol, 1.0 equiv), and $ZnMe_2$ (0.20 mL, 0.36 mmol, 3.0 equiv, 1.8 M in PhMe) in PhMe (2 mL). The crude residue was purified by flash chromatography (15% Et_2O in pentane) to afford the title compound as a colorless oil (32 mg, 75%). **TLC R_f** = 0.6 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 500 MHz, 323 K) δ 7.74 (d, *J* = 8.0, 1H), 7.60 (d, *J* = 8.1, 1H), 7.33 (td, *J* = 7.6, 1.1, 1H), 7.25 (td, *J* = 7.6, 1.1, 1H), 4.15 (d, *J* = 12.8, 1H), 4.00, (d, *J* = 12.6, 1H), 3.00 (dq, *J* = 8.8, 6.9, 1H), 2.68 (td, *J* = 12.8, 2.5, 1H), 2.57 (td, *J* = 12.8, 2.4, 1H), 2.30 (s, 3H), 1.93 (dp, *J* = 12.7, 2.6, 1H), 1.65–1.54 (m, 1H), 1.54–1.47 (m, 1H), 1.44 (s, 9H), 1.33 (d, *J* = 7.0, 3H), 1.21 (qd, *J* = 12.3, 4.4, 1H), 1.09 (qd, *J* = 12.4, 4.4, 1H); **^{13}C NMR** ($CDCl_3$, 125 MHz, 323 K) δ 155.0, 145.0, 141.0, 138.4, 126.6, 124.0, 123.8, 122.4, 121.5, 79.4, 44.3 (br s, 2C), 43.9, 39.2, 30.9, 30.4, 28.7, 20.1, 12.1; **IR** (neat, cm^{-1}) 2973, 1688, 1422, 1170,728; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{21}H_{29}NO_2SNa$ 382.1817, found 382.1812; **$[\alpha]_D^{25}$** +59.1 (*c* 0.82, $CHCl_3$); **SFC** analysis (OD-H, 5.0% MeOH, 3.0 mL/min, 215 nm) indicated 72% ee: t_R (major) = 4.4 min, t_R (minor) = 4.9 min.



(*S*)-4-(1-(3-methylbenzo[b]thiophen-2-yl)ethyl)piperidine SI 65 was prepared according to a modified procedure by Davis.[57] TFA (0.12 mL, 1.6 mmol, 20 equiv) was added to a stirred solution of **60** (28 mg, 0.078 mmol, 1.0 equiv) in anhydrous CH_2Cl_2 (2 mL) at 0 °C under an atmosphere of nitrogen. The reaction was then warmed to ambient temperature and stirred until complete by TLC (30 min) and then quenched with sat. $NaHCO_3$ (5 mL). The reaction mixture was extracted with CH_2Cl_2 (3 x 3 mL) and the combined organics were washed with brine, dried with Na_2SO_4, filtered, and concentrated in vacuo. The resultant yellow oil was carried on without further purification (20 mg, 99%). **TLC R_f** = 0 (4:1 hexane/EtOAc, UV active); **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 7.76 (d, *J* = 7.8, 1H), 7.61 (d, *J* = 7.9, 1H), 7.34 (td, *J* = 7.6, 1.0, 1H), 7.26, (td, *J* = 7.5, 1.1, 1H), 3.16 (d, *J* = 12.0, 1H), 3.06–2.96 (m, 2H), 2.91 (td, *J* = 12.2, 2.2, 1H), 2.49 (td, *J* = 12.2, 2.1, 1H), 2.45 (br s, 1H), 2.32 (s, 3H), 1.98 (d, *J* = 12.8, 1H), 1.62–1.46 (m, 2H), 1.39–1.18 (m, 1H), 1.32 (d, *J* = 6.9, 3H), 1.12 (qd, *J* = 12.2, 3.4, 1H).



(*S*)-4-(1-(3-methylbenzo[b]thiophen-2-yl)ethyl)-N-(pyridin-3-yl)piperidine-1-carboxamide 3 was prepared according to a modified procedure reported by Carruthers.[58] Crude amine **SI 65** (20 mg, 0.078 mmol, 1.0 equiv), pyridine-3-isocyanate **61** (14 mg, 0.12 mmol, 1.5 equiv), anhydrous CH_2Cl_2 (1 mL) and anhydrous DMF (1 mL) were combined in a 7 mL vial equipped with a stir bar and an N_2 line. After 48 h of stirring at ambient temperature, the reaction was quenched with sat. $NaHCO_3$ and extracted with CH_2Cl_2. The crude residue was purified by flash chromatography (2–5% MeOH in CH_2Cl_2 with 1% TEA) to afford the title compound as a white solid (20 mg, 68% over 2 steps). **TLC** $\mathbf{R_f}$ = 0.5 (10% MeOH and 1% TEA in CH_2Cl_2); **mp** 145–148 °C; **^{1}H NMR** ($CDCl_3$, 400 MHz) δ 8.40 (d, *J* = 2.0, 1H), 8.23 (d, *J* = 4.5, 1H), 7.96 (dq *J* = 8.4, 1.2, 1H), 7.78 (d, *J* = 8.0, 1H), 7.62 (d, *J* = 7.9, 1H), 7.36 (t, *J* = 7.4, 1H), 7.28 (d, *J* = 7.4, 1H), 7.20 (dd, *J* = 8.4, 4.8, 1H), 6.62 (s, 1H), 4.19 (d, *J* = 13.3, 1H), 3.98 (d, *J* = 13.4, 1H), 3.03 (dq, *J* = 8.5, 7.0, 1H), 2.88 (td, *J* = 12.9, 2.5, 1H), 2.78 (td, *J* = 12.9, 2.3, 1H), 2.31 (s, 3H), 2.05 (d, *J* = 13.2, 1H), 1.78–1.56 (m, 2H), 1.42–1.13 (m, 2H), 1.36 (d, *J* = 6.9, 3H); **^{13}C NMR** ($CDCl_3$, 125 MHz) δ 154.6, 144.4, 144.1, 141.2, 140.8, 138.1, 136.3, 127.3, 126.8, 124.0, 123.9, 123.7, 122.4, 121.6, 44.9, 44.7, 43.7, 39.0, 30.6, 30.3, 20.2, 12.2; **IR** (neat, cm^{-1}) 3307, 2921, 1641, 1524, 1266, 754; **HRMS** (TOF MS ES+) *m*/*z*: $[M + Na]^+$ calculated for $C_{22}H_{25}N_3OSNa$ 402.1616, found 402.1614; $\mathbf{[\alpha]_D^{26}}$ +85.2 (*c* 0.75, $CHCl_3$).

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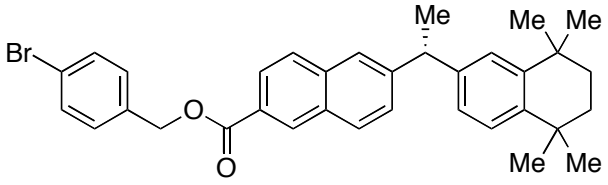
IV. CRYSTALLOGRAPHIC DATA



(*S*)-**SI 9**
Scheme SI 6.

X-ray Data Collection, Structure Solution and Refinement for (*S*)-**SI 9**. CCDC 940966 contains the supplementary crystallographic data for this structure. These data can be obtained via www.ccdc.cam.ac.uk/conts/retrieving.html. The crystal was obtained by slow evaporation from ether over pentane.

A colorless crystal of approximate dimensions 0.321 x 0.153 x 0.050 mm was mounted on a glass fiber and transferred to a Bruker SMART APEX II diffractometer. The APEX2[1] program package was used to determine the unit-cell parameters and for data collection (30 sec/frame scan time for a sphere of diffraction data). The raw frame data was processed using SAINT[2] and SADABS[3] to yield the reflection data file. Subsequent calculations were carried out using the SHELXTL[4] program. The diffraction symmetry was 2/*m* and the systematic absences were consistent with the monoclinic space groups $P2_1$ and $P2_1/m$. It was later determined that space group $P2_1$ was correct.

The structure was solved by direct methods and refined on F^2 by full-matrix least-squares techniques.[5] The analytical scattering factors[6] for neutral atoms were used throughout the analysis. Hydrogen atoms were included using a riding model.

At convergence, wR2 = 0.0902 and Goof = 1.071 for 339 variables refined against 6467 data (0.74 Å), R1 = 0.0401 for those 5869 data with $I > 2.0\sigma(I)$. The absolute structure was assigned by refinement of the Flack[7] parameter.

References.

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Definitions:

$wR2 = [\Sigma[w(F_o^2-F_c^2)^2] / \Sigma[w(F_o^2)^2]]^{1/2}$

$R1 = \Sigma||F_o|-|F_c|| / \Sigma|F_o|$

$Goof = S = [\Sigma[w(F_o^2-F_c^2)^2] / (n-p)]^{1/2}$ where n is the number of reflections and p is the total number of parameters refined.

The thermal ellipsoid plot is shown at the 50% probability level.

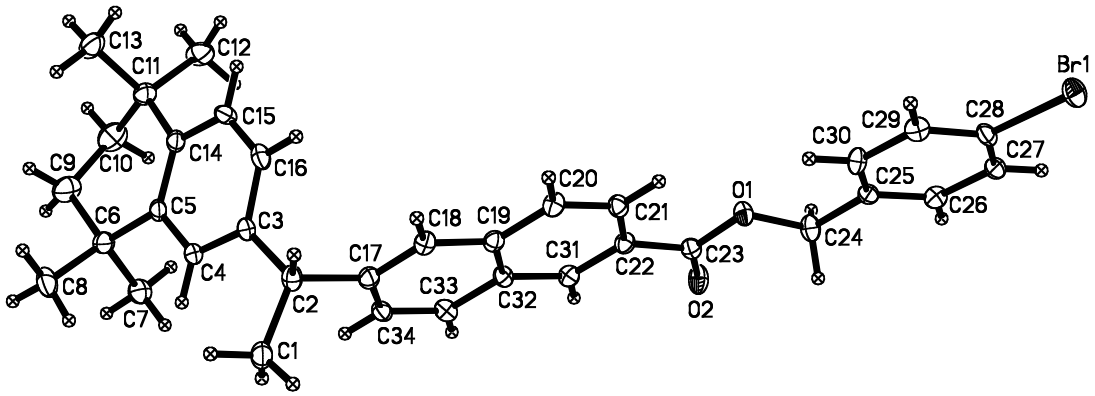


Table 1. Crystal data and structure refinement for erj13.

Identification code	erj13 (Elizabeth Swift)	
Empirical formula	$C_{34}\ H_{35}\ Br\ O_2$	
Formula weight	555.53	
Temperature	88(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 8.3009(7) Å	α= 90°.
	b = 5.7479(5) Å	β= 90.5440(11)°.
	c = 28.630(2) Å	γ = 90°.
Volume	1366.0(2) Å^3	
Z	2	
Density (calculated)	1.351 Mg/m^3	
Absorption coefficient	1.534 mm^{-1}	
F(000)	580	
Crystal color	colorless	
Crystal size	0.321 x 0.153 x 0.050 mm^3	
Theta range for data collection	2.134 to 28.782°	
Index ranges	$-11 \le h \le 11$, $-7 \le k \le 7$, $-38 \le l \le 38$	
Reflections collected	14421	
Independent reflections	6467 [R(int) = 0.0303]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7458 and 0.6256	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6467 / 1 / 339
Goodness-of-fit on F^2	1.071
Final R indices [I>2sigma(I) = 5869 data]	R1 = 0.0401, wR2 = 0.0885
R indices (all data, 0.74 Å)	R1 = 0.0458, wR2 = 0.0902
Absolute structure parameter	0.042(5)
Largest diff. peak and hole	1.076 and -0.752 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for erj13. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	-58(1)	7413(1)	-2215(1)	22(1)
O(1)	2582(3)	2752(6)	-143(1)	18(1)
O(2)	4190(4)	31(5)	185(1)	23(1)
C(1)	5682(5)	8589(8)	2902(1)	23(1)
C(2)	3986(5)	8002(7)	2725(1)	18(1)
C(3)	2923(5)	6761(7)	3081(1)	17(1)
C(4)	3503(5)	5754(8)	3490(1)	18(1)
C(5)	2506(5)	4511(7)	3798(1)	16(1)
C(6)	3285(5)	3493(8)	4241(1)	21(1)
C(7)	4503(5)	1602(8)	4098(1)	23(1)
C(8)	4181(6)	5418(9)	4519(1)	28(1)
C(9)	2013(5)	2468(14)	4566(1)	31(1)
C(10)	730(6)	1189(9)	4311(2)	33(1)
C(11)	-273(5)	2812(9)	3980(1)	23(1)
C(12)	-1292(5)	1213(8)	3668(2)	28(1)
C(13)	-1369(6)	4397(9)	4256(2)	32(1)
C(14)	883(5)	4257(7)	3685(1)	17(1)
C(15)	295(5)	5360(8)	3282(1)	20(1)
C(16)	1281(5)	6598(7)	2987(1)	19(1)
C(17)	4016(5)	6541(7)	2278(1)	18(1)
C(18)	3215(4)	7247(10)	1885(1)	17(1)
C(19)	3192(5)	5904(7)	1471(1)	16(1)
C(20)	2359(5)	6627(7)	1061(1)	17(1)
C(21)	2399(5)	5328(7)	663(1)	17(1)
C(22)	3267(5)	3201(7)	652(1)	16(1)
C(23)	3417(5)	1807(6)	218(1)	16(1)
C(24)	2929(5)	1714(7)	-591(1)	19(1)
C(25)	2129(4)	3143(7)	-972(1)	16(1)
C(26)	2202(4)	2281(11)	-1425(1)	18(1)
C(27)	1537(5)	3550(7)	-1797(1)	18(1)
C(28)	812(5)	5661(7)	-1707(1)	17(1)

C(29)	699(5)	6552(8)	-1257(1)	20(1)
C(30)	1385(5)	5261(7)	-887(1)	19(1)
C(31)	4060(4)	2416(10)	1047(1)	16(1)
C(32)	4042(5)	3756(7)	1464(1)	16(1)
C(33)	4871(5)	3016(6)	1879(1)	17(1)
C(34)	4844(5)	4381(8)	2272(1)	18(1)

Table 3. Bond lengths [Å] and angles [°] for erj13.

Br(1)-C(28)	1.906(4)
O(1)-C(23)	1.352(4)
O(1)-C(24)	1.446(4)
O(2)-C(23)	1.210(5)
C(1)-C(2)	1.529(6)
C(2)-C(3)	1.531(5)
C(2)-C(17)	1.532(5)
C(3)-C(4)	1.386(5)
C(3)-C(16)	1.390(6)
C(4)-C(5)	1.410(6)
C(5)-C(14)	1.390(6)
C(5)-C(6)	1.534(5)
C(6)-C(9)	1.533(6)
C(6)-C(7)	1.542(6)
C(6)-C(8)	1.549(6)
C(9)-C(10)	1.482(7)
C(10)-C(11)	1.564(7)
C(11)-C(13)	1.516(6)
C(11)-C(14)	1.529(6)
C(11)-C(12)	1.530(6)
C(14)-C(15)	1.399(6)
C(15)-C(16)	1.379(6)
C(17)-C(18)	1.362(5)
C(17)-C(34)	1.420(6)
C(18)-C(19)	1.414(5)
C(19)-C(20)	1.420(5)
C(19)-C(32)	1.422(6)
C(20)-C(21)	1.362(5)
C(21)-C(22)	1.420(6)
C(22)-C(31)	1.379(5)
C(22)-C(23)	1.486(5)
C(24)-C(25)	1.512(5)
C(25)-C(30)	1.387(6)
C(25)-C(26)	1.391(5)

C(26)-C(27)	1.400(6)
C(27)-C(28)	1.380(6)
C(28)-C(29)	1.390(5)
C(29)-C(30)	1.409(6)
C(31)-C(32)	1.421(5)
C(32)-C(33)	1.430(5)
C(33)-C(34)	1.372(5)

C(23)-O(1)-C(24)	114.0(3)
C(1)-C(2)-C(3)	114.6(3)
C(1)-C(2)-C(17)	112.0(3)
C(3)-C(2)-C(17)	108.4(3)
C(4)-C(3)-C(16)	117.8(4)
C(4)-C(3)-C(2)	124.0(3)
C(16)-C(3)-C(2)	118.2(3)
C(3)-C(4)-C(5)	122.6(4)
C(14)-C(5)-C(4)	118.7(4)
C(14)-C(5)-C(6)	123.5(4)
C(4)-C(5)-C(6)	117.8(3)
C(9)-C(6)-C(5)	111.2(3)
C(9)-C(6)-C(7)	110.3(4)
C(5)-C(6)-C(7)	108.8(3)
C(9)-C(6)-C(8)	107.0(4)
C(5)-C(6)-C(8)	110.4(4)
C(7)-C(6)-C(8)	109.1(3)
C(10)-C(9)-C(6)	112.8(3)
C(9)-C(10)-C(11)	112.3(5)
C(13)-C(11)-C(14)	110.2(4)
C(13)-C(11)-C(12)	109.5(3)
C(14)-C(11)-C(12)	110.6(3)
C(13)-C(11)-C(10)	111.1(4)
C(14)-C(11)-C(10)	109.0(3)
C(12)-C(11)-C(10)	106.4(4)
C(5)-C(14)-C(15)	118.3(4)
C(5)-C(14)-C(11)	122.7(4)
C(15)-C(14)-C(11)	119.0(4)

C(16)-C(15)-C(14)	122.2(4)
C(15)-C(16)-C(3)	120.2(4)
C(18)-C(17)-C(34)	118.9(4)
C(18)-C(17)-C(2)	121.0(4)
C(34)-C(17)-C(2)	120.1(3)
C(17)-C(18)-C(19)	122.1(5)
C(18)-C(19)-C(20)	122.4(4)
C(18)-C(19)-C(32)	118.8(4)
C(20)-C(19)-C(32)	118.7(3)
C(21)-C(20)-C(19)	121.1(4)
C(20)-C(21)-C(22)	120.4(4)
C(31)-C(22)-C(21)	120.2(4)
C(31)-C(22)-C(23)	117.8(4)
C(21)-C(22)-C(23)	121.9(3)
O(2)-C(23)-O(1)	123.1(3)
O(2)-C(23)-C(22)	124.7(3)
O(1)-C(23)-C(22)	112.1(3)
O(1)-C(24)-C(25)	109.0(3)
C(30)-C(25)-C(26)	119.9(4)
C(30)-C(25)-C(24)	123.0(3)
C(26)-C(25)-C(24)	117.1(4)
C(25)-C(26)-C(27)	120.3(5)
C(28)-C(27)-C(26)	119.0(4)
C(27)-C(28)-C(29)	122.0(4)
C(27)-C(28)-Br(1)	119.0(3)
C(29)-C(28)-Br(1)	119.0(3)
C(28)-C(29)-C(30)	118.2(4)
C(25)-C(30)-C(29)	120.6(4)
C(22)-C(31)-C(32)	120.2(5)
C(31)-C(32)-C(19)	119.4(4)
C(31)-C(32)-C(33)	121.8(4)
C(19)-C(32)-C(33)	118.8(3)
C(34)-C(33)-C(32)	119.9(4)
C(33)-C(34)-C(17)	121.4(4)

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for erj13. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	28(1)	19(1)	20(1)	3(1)	-5(1)	-1(1)
O(1)	22(1)	18(2)	14(1)	-2(1)	-2(1)	2(1)
O(2)	36(2)	18(2)	16(1)	0(1)	1(1)	6(1)
C(1)	26(2)	27(2)	17(2)	-4(2)	2(2)	-5(2)
C(2)	25(2)	16(2)	14(2)	-1(1)	1(1)	-4(2)
C(3)	18(2)	18(2)	13(2)	-4(1)	-1(1)	-1(1)
C(4)	16(2)	23(2)	14(2)	-5(2)	0(1)	-2(2)
C(5)	18(2)	18(2)	12(2)	-3(2)	-1(1)	1(2)
C(6)	19(2)	29(2)	16(2)	4(2)	1(2)	1(2)
C(7)	25(2)	22(2)	22(2)	2(2)	-1(2)	1(2)
C(8)	35(3)	32(3)	17(2)	-3(2)	-8(2)	6(2)
C(9)	28(2)	42(2)	24(2)	14(3)	5(2)	2(3)
C(10)	35(3)	31(3)	34(3)	7(2)	9(2)	-5(2)
C(11)	19(2)	28(3)	22(2)	-3(2)	4(1)	-6(2)
C(12)	22(2)	24(2)	38(2)	-7(2)	4(2)	-8(2)
C(13)	25(2)	39(3)	33(2)	-15(2)	11(2)	-10(2)
C(14)	19(2)	18(2)	14(2)	-2(2)	0(2)	2(2)
C(15)	14(2)	25(2)	21(2)	-5(2)	-4(2)	1(2)
C(16)	24(2)	20(2)	13(2)	-1(1)	-4(2)	2(2)
C(17)	18(2)	20(2)	15(2)	1(2)	2(1)	-5(2)
C(18)	20(2)	14(2)	16(2)	0(2)	3(1)	-2(2)
C(19)	17(2)	16(2)	16(2)	-1(2)	2(1)	-3(2)
C(20)	21(2)	13(2)	16(2)	1(1)	3(2)	3(2)
C(21)	18(2)	17(2)	14(2)	3(2)	-1(1)	-1(2)
C(22)	17(2)	15(2)	15(2)	0(1)	2(1)	2(1)
C(23)	17(2)	15(2)	16(2)	0(1)	-1(1)	-2(1)
C(24)	28(2)	14(2)	15(2)	-2(1)	-2(2)	0(2)
C(25)	15(2)	17(2)	16(2)	-2(1)	-1(1)	-4(1)
C(26)	19(2)	15(2)	20(2)	0(2)	2(1)	1(2)
C(27)	17(2)	21(2)	16(2)	-3(2)	-2(2)	-4(2)
C(28)	17(2)	19(2)	15(2)	5(2)	-5(1)	-3(2)

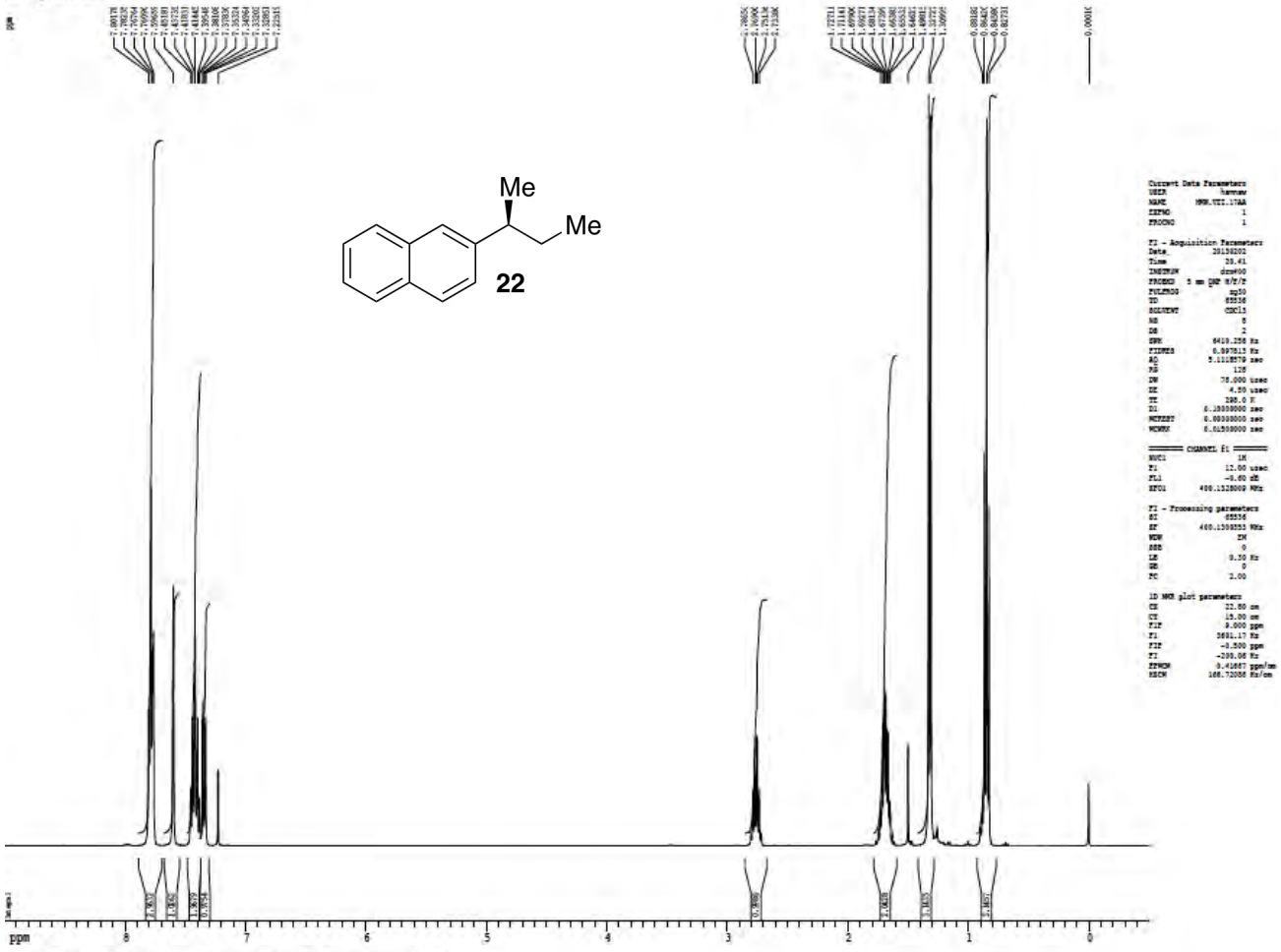
C(29)	20(2)	17(2)	22(2)	1(2)	1(2)	-1(2)
C(30)	26(2)	17(2)	12(2)	-2(2)	2(2)	0(2)
C(31)	18(2)	13(2)	18(2)	-1(2)	1(1)	1(2)
C(32)	17(2)	15(2)	14(2)	3(2)	-2(1)	-1(2)
C(33)	19(2)	13(2)	20(2)	2(1)	-3(1)	-1(1)
C(34)	16(2)	25(2)	14(2)	3(2)	-2(2)	-4(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for erj13.

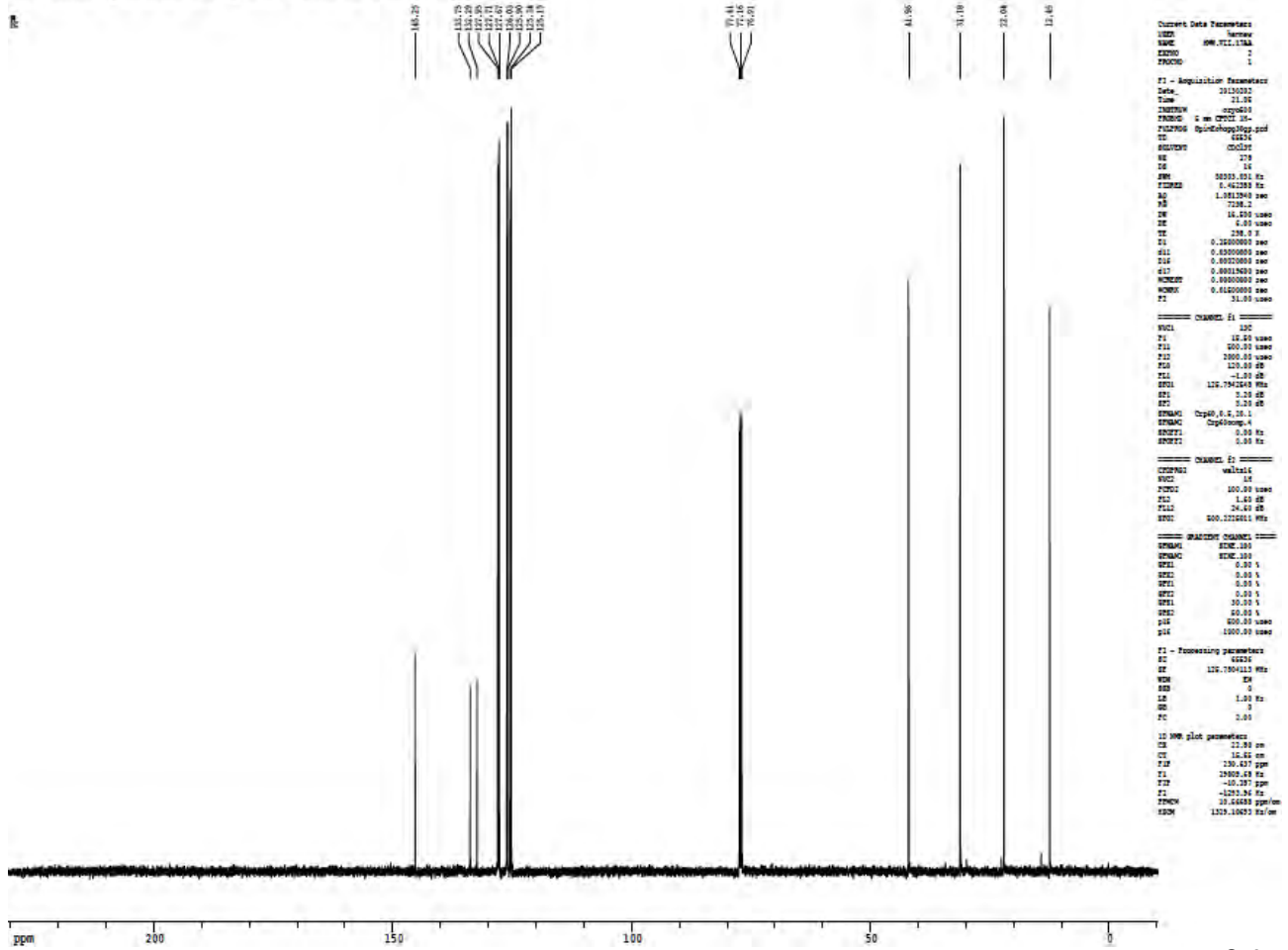
	x	y	z	U(eq)
H(1A)	5610	9522	3187	35
H(1B)	6253	9474	2662	35
H(1C)	6269	7146	2969	35
H(2A)	3445	9507	2645	22
H(4A)	4615	5908	3564	21
H(7A)	3930	320	3944	35
H(7B)	5063	1015	4377	35
H(7C)	5289	2268	3883	35
H(8A)	3420	6651	4601	42
H(8B)	5041	6070	4327	42
H(8C)	4649	4750	4805	42
H(9A)	2545	1398	4790	38
H(9B)	1517	3744	4748	38
H(10A)	-1	454	4539	40
H(10B)	1225	-65	4123	40
H(12A)	-2016	2155	3473	42
H(12B)	-1931	170	3864	42
H(12C)	-584	290	3469	42
H(13A)	-2096	5224	4042	48
H(13B)	-716	5526	4432	48
H(13C)	-2003	3465	4475	48
H(15A)	-821	5252	3210	24
H(16A)	837	7341	2719	23
H(18A)	2654	8687	1889	20
H(20A)	1765	8040	1064	20
H(21A)	1842	5849	391	20
H(24A)	2518	98	-601	23
H(24B)	4108	1672	-640	23
H(26A)	2706	826	-1482	22
H(27A)	1584	2965	-2107	22

H(29A)	174	7992	-1201	24
H(30A)	1338	5846	-577	22
H(31A)	4621	976	1041	19
H(33A)	5439	1582	1882	21
H(34A)	5392	3869	2546	22

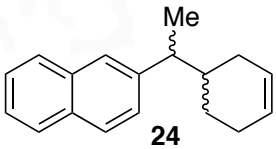
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling



1H spectrum



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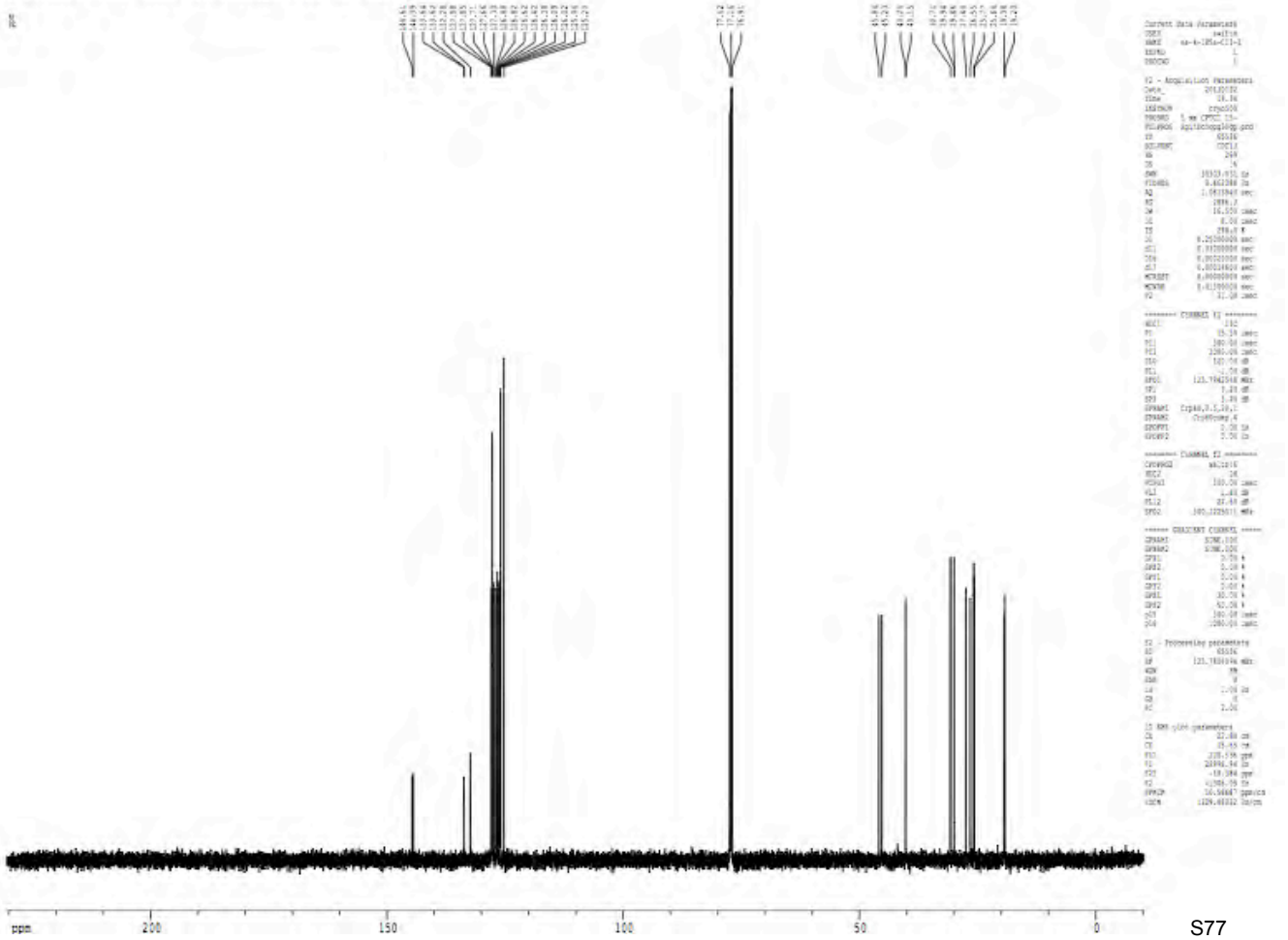
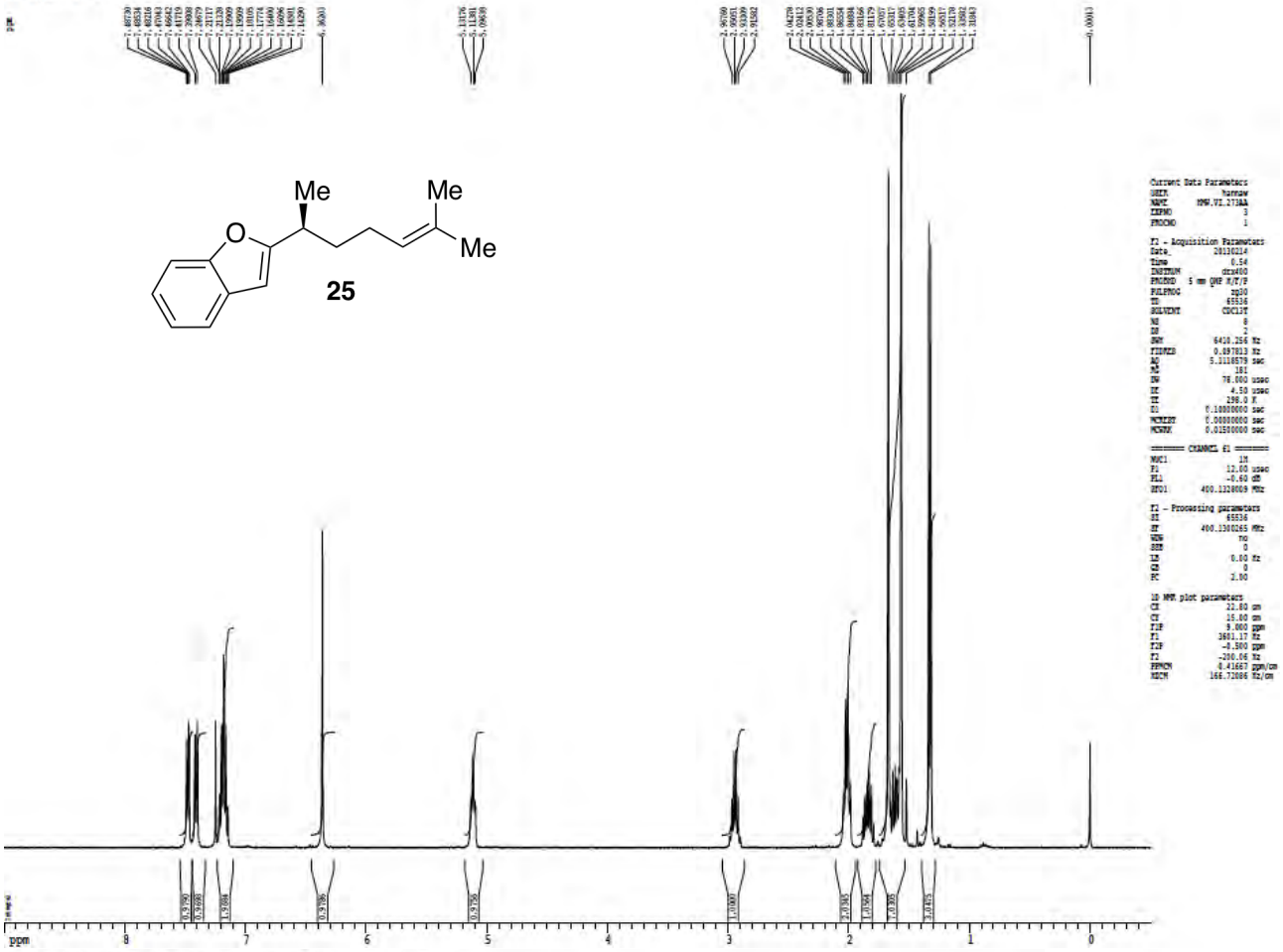
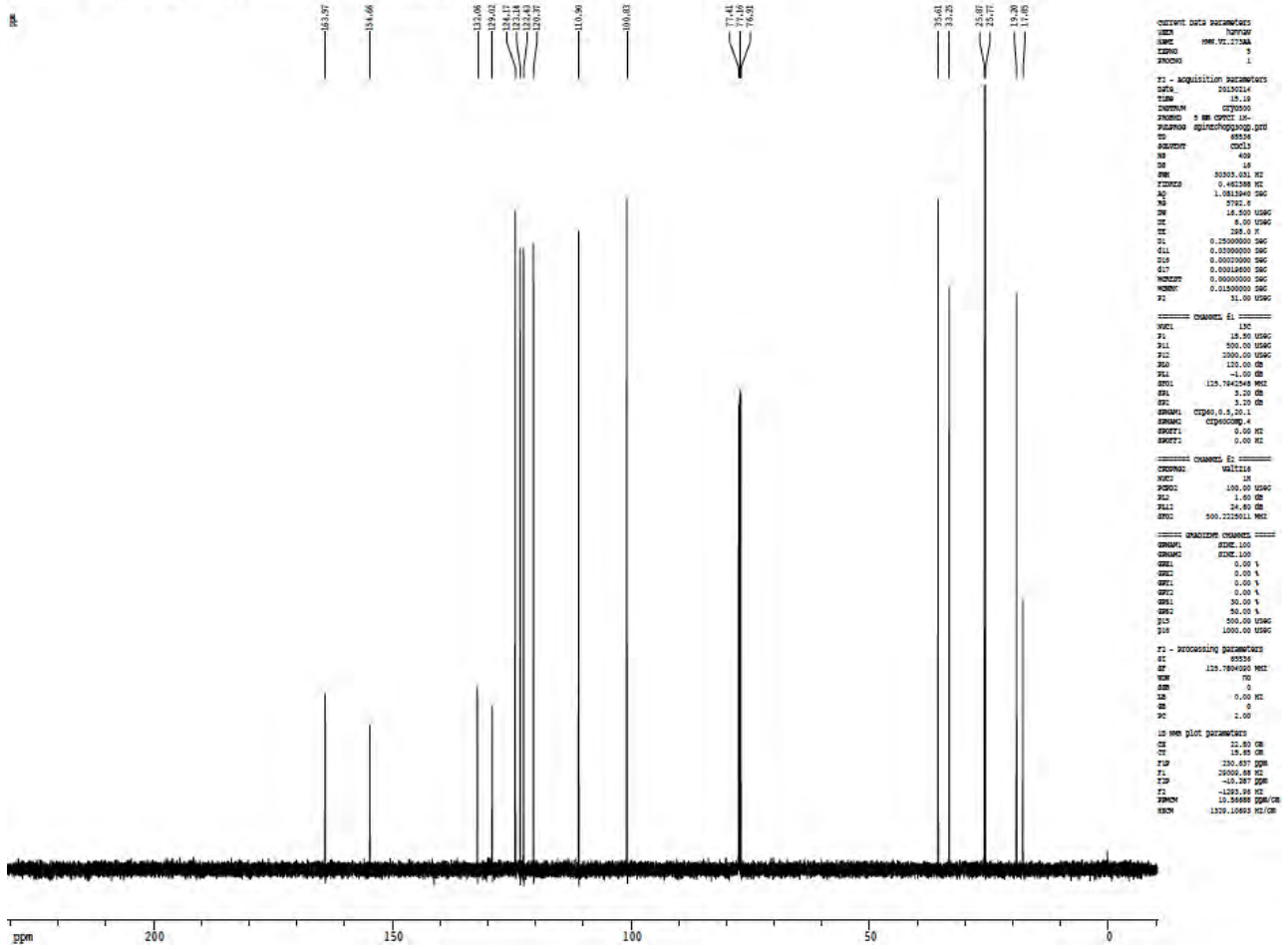
Z-restored spin-echo 13C spectrum with 1H decoupling

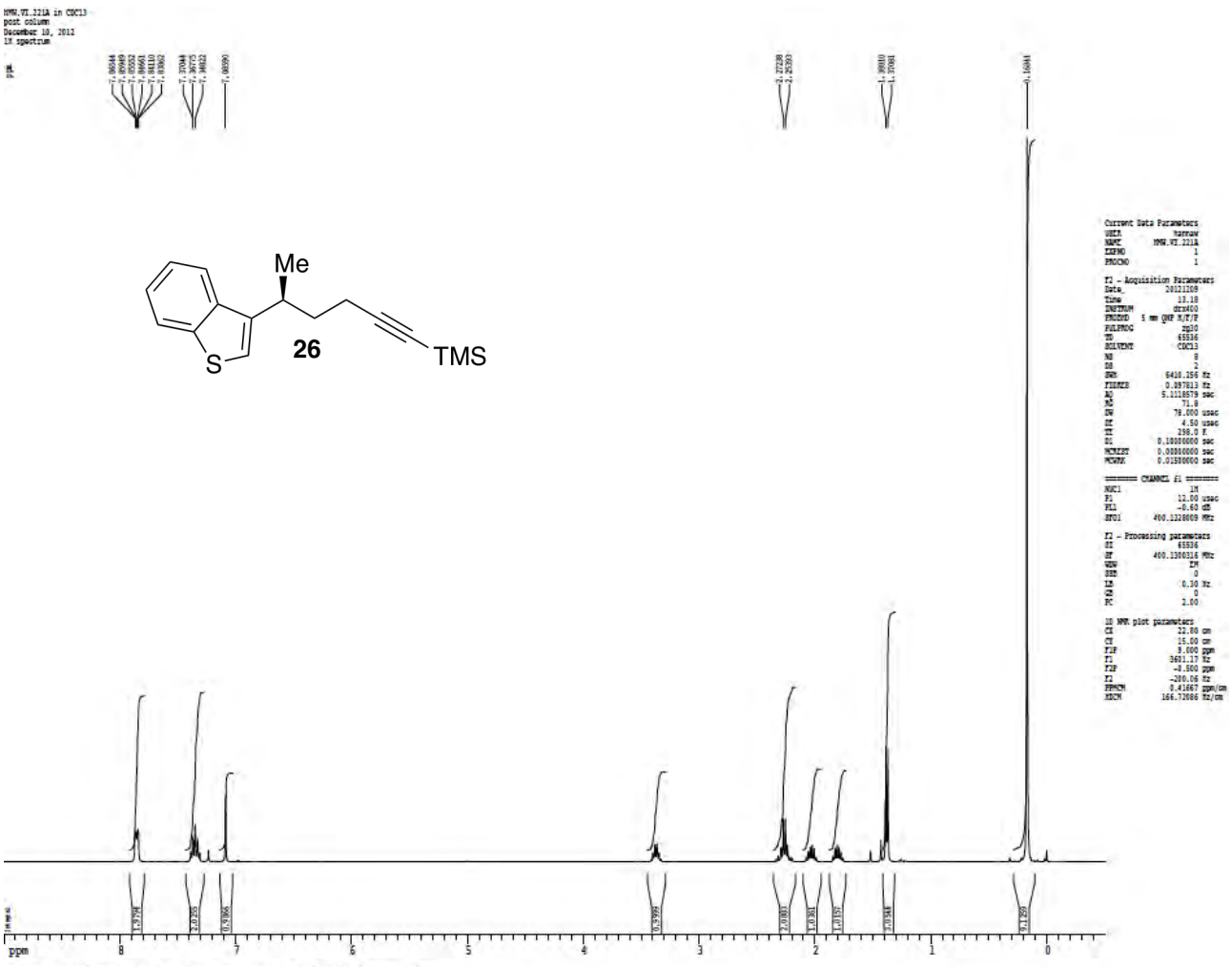


1H spectrum

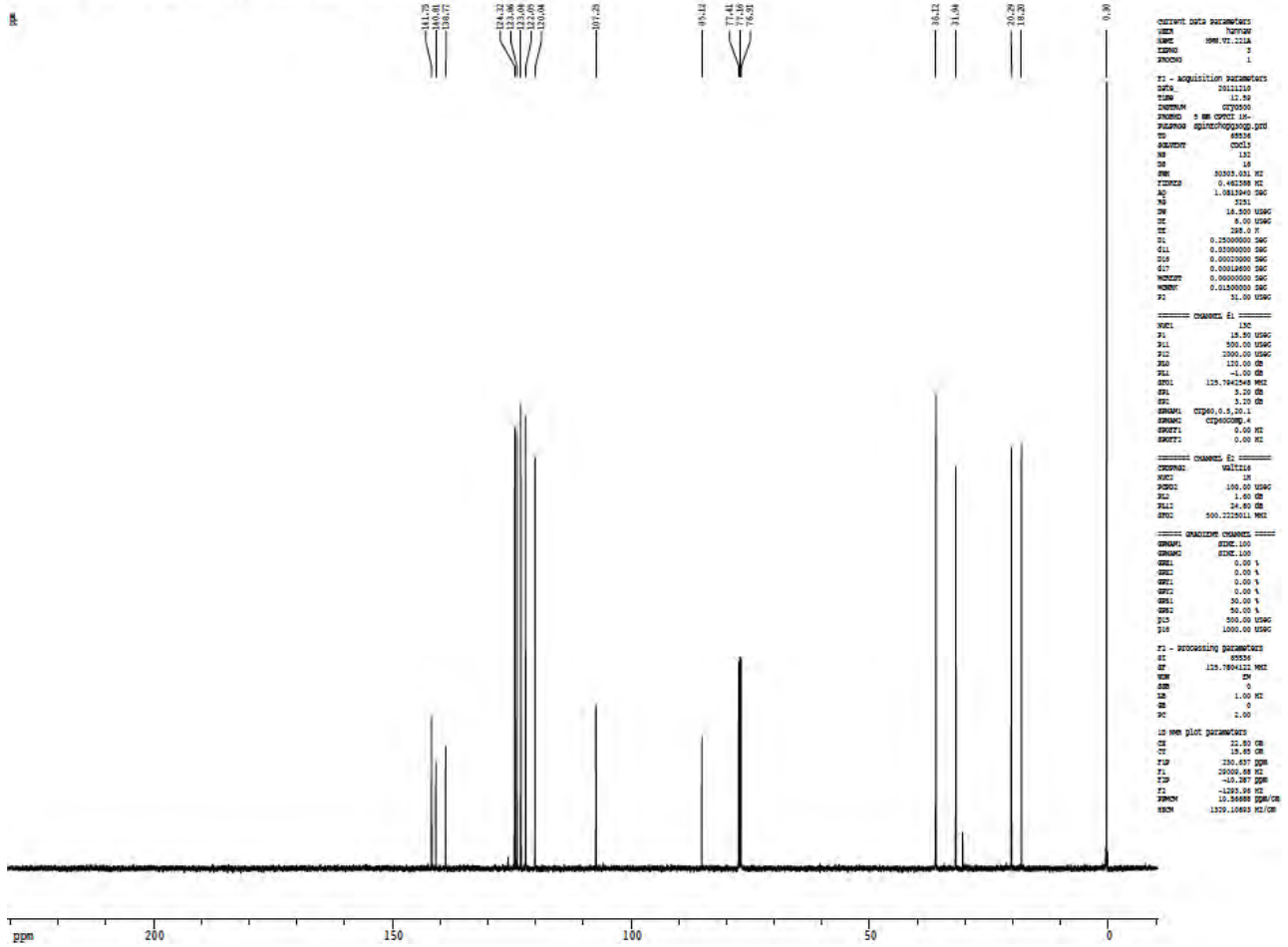


Z-restored spin-echo 13C spectrum with 1H decoupling

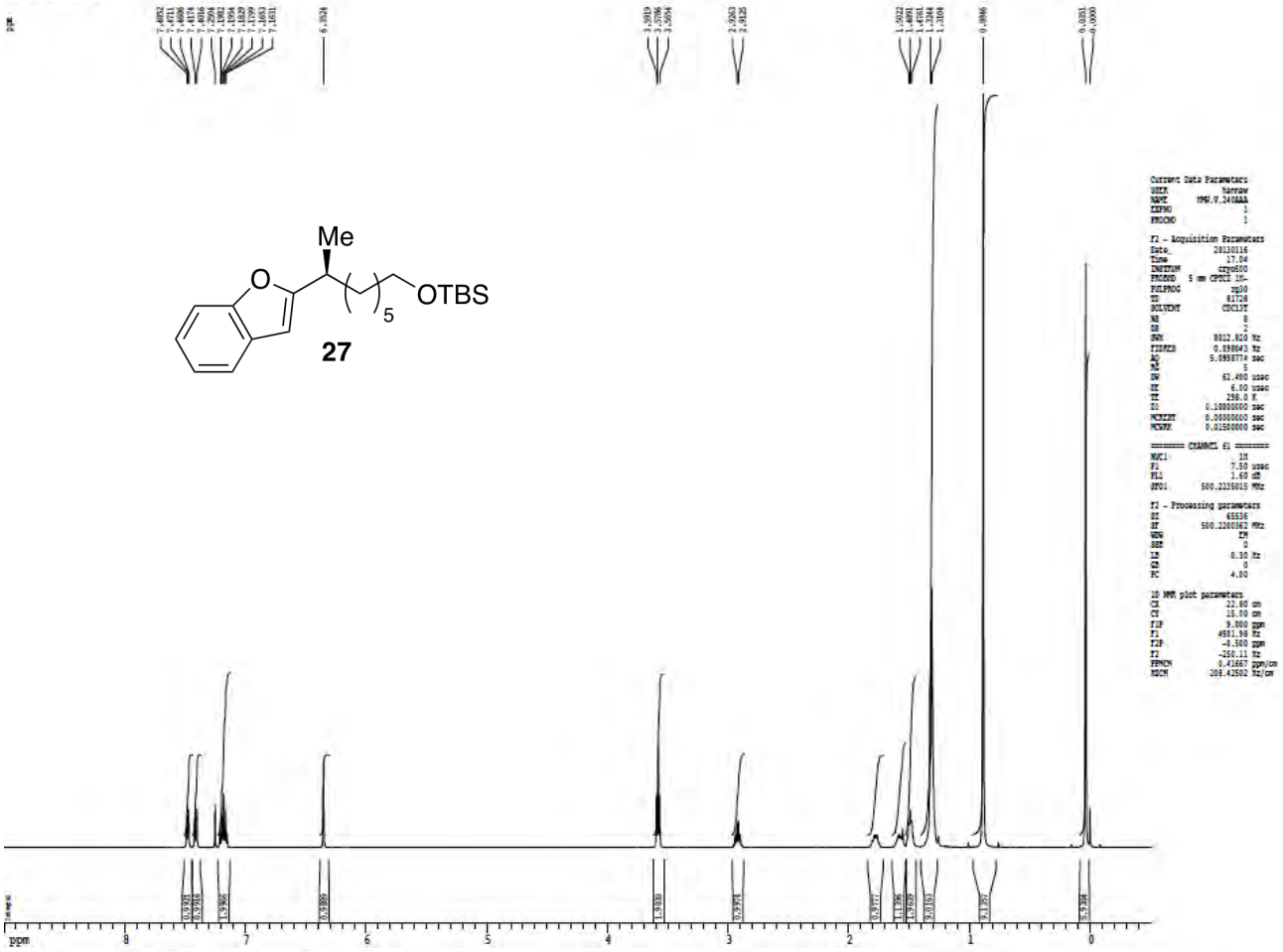




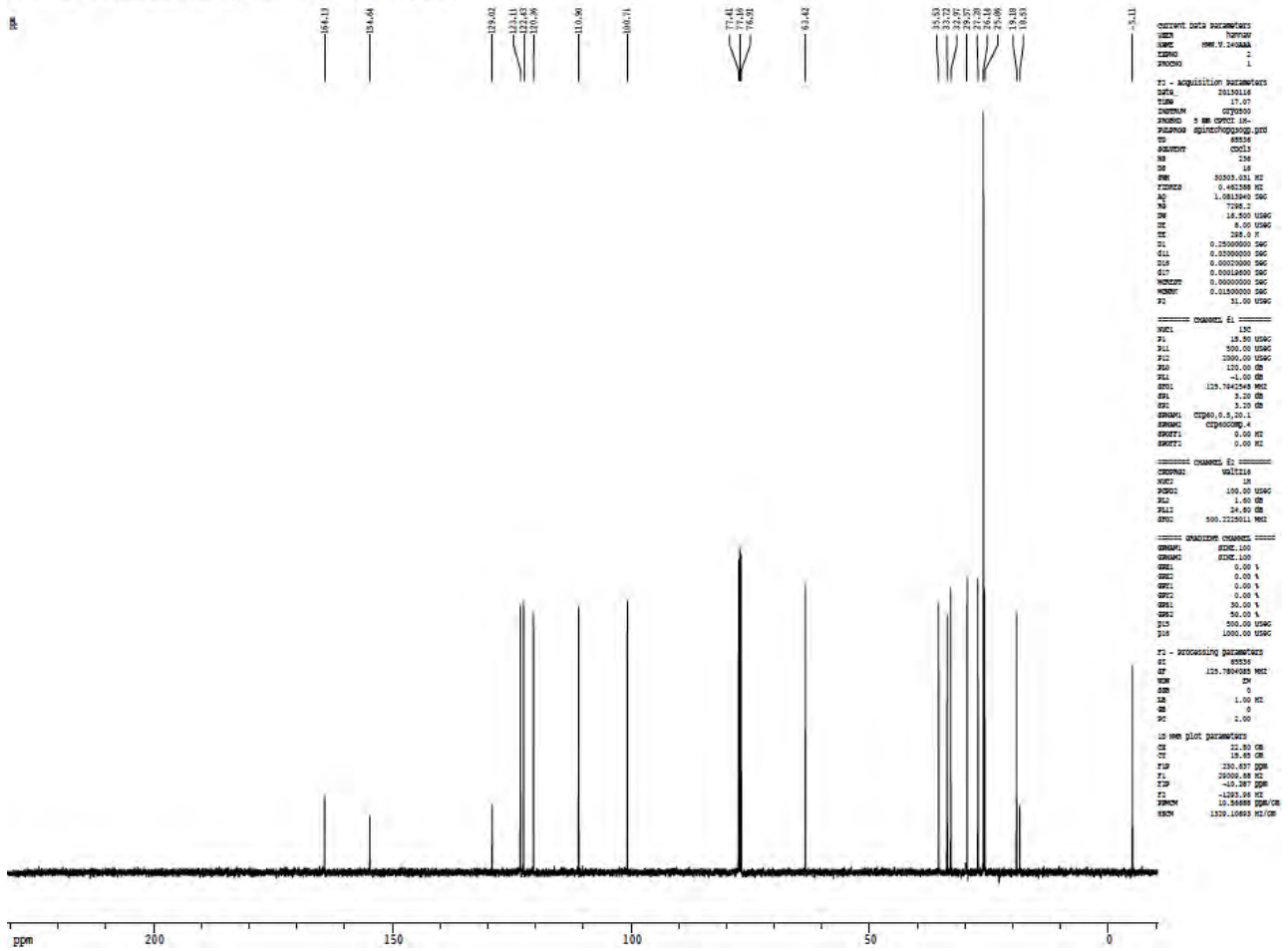
Z-restored spin-echo 13C spectrum with 1H decoupling



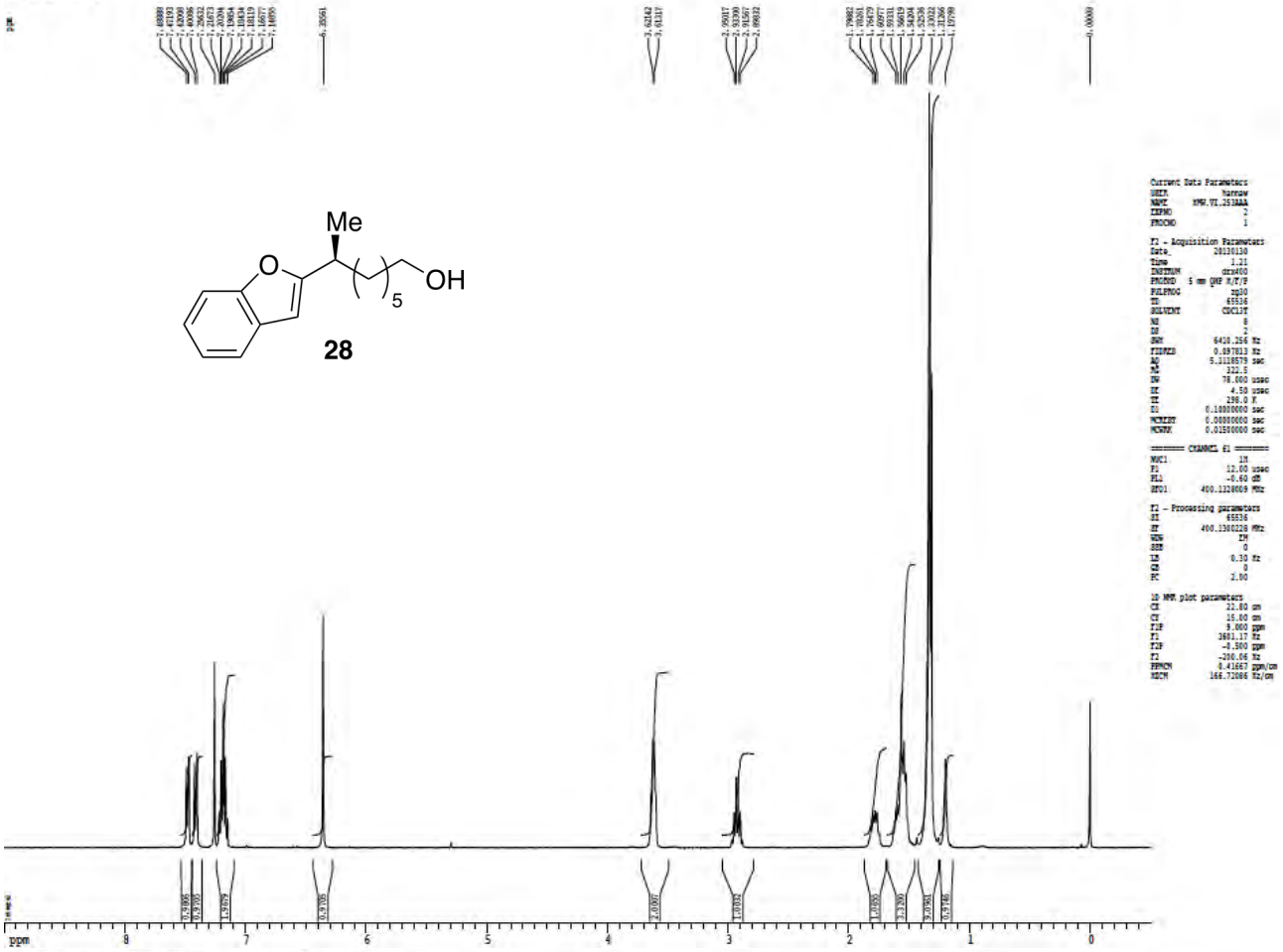
1H spectrum



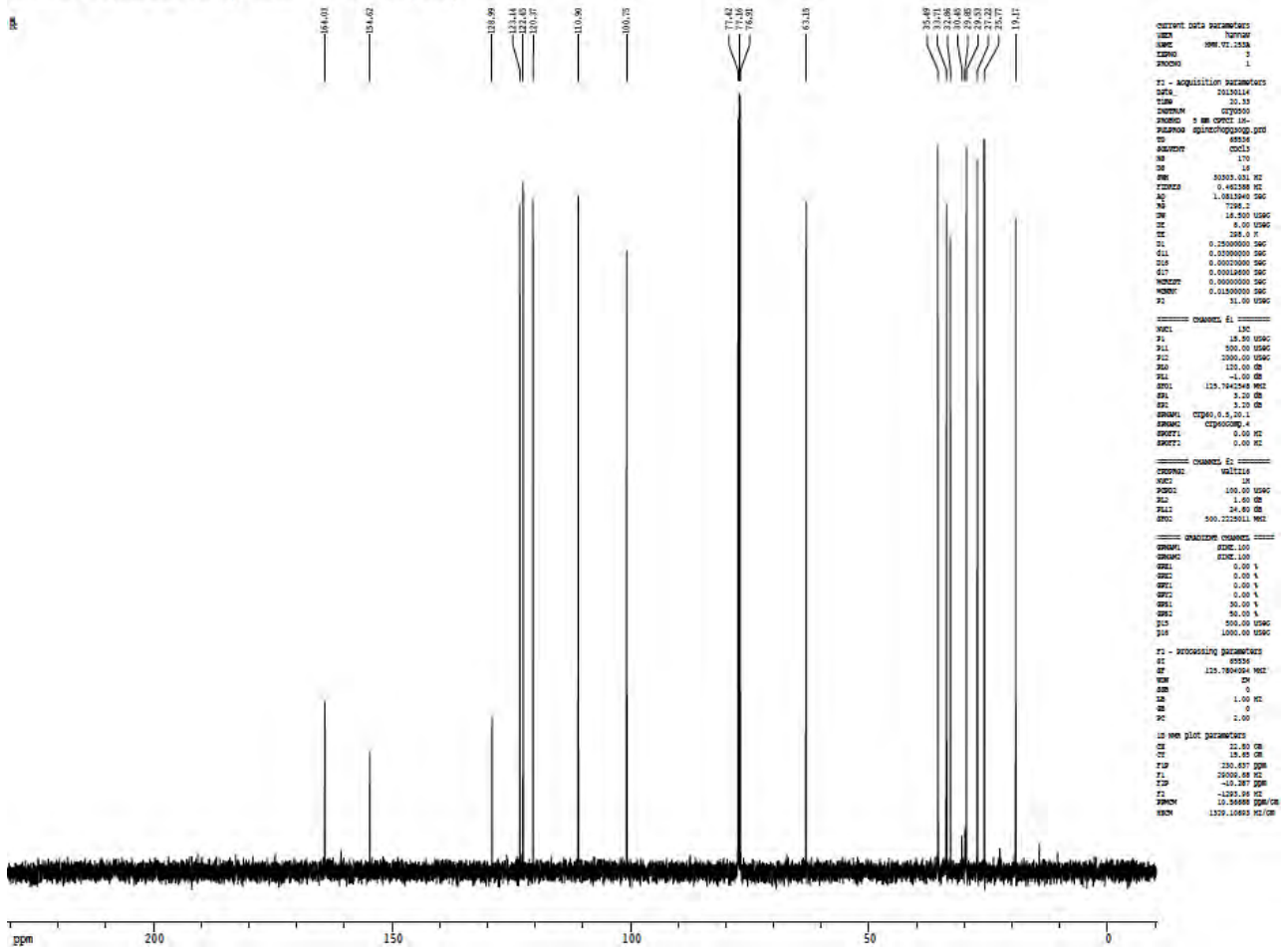
Z-restored spin-echo 13C spectrum with 1H decoupling



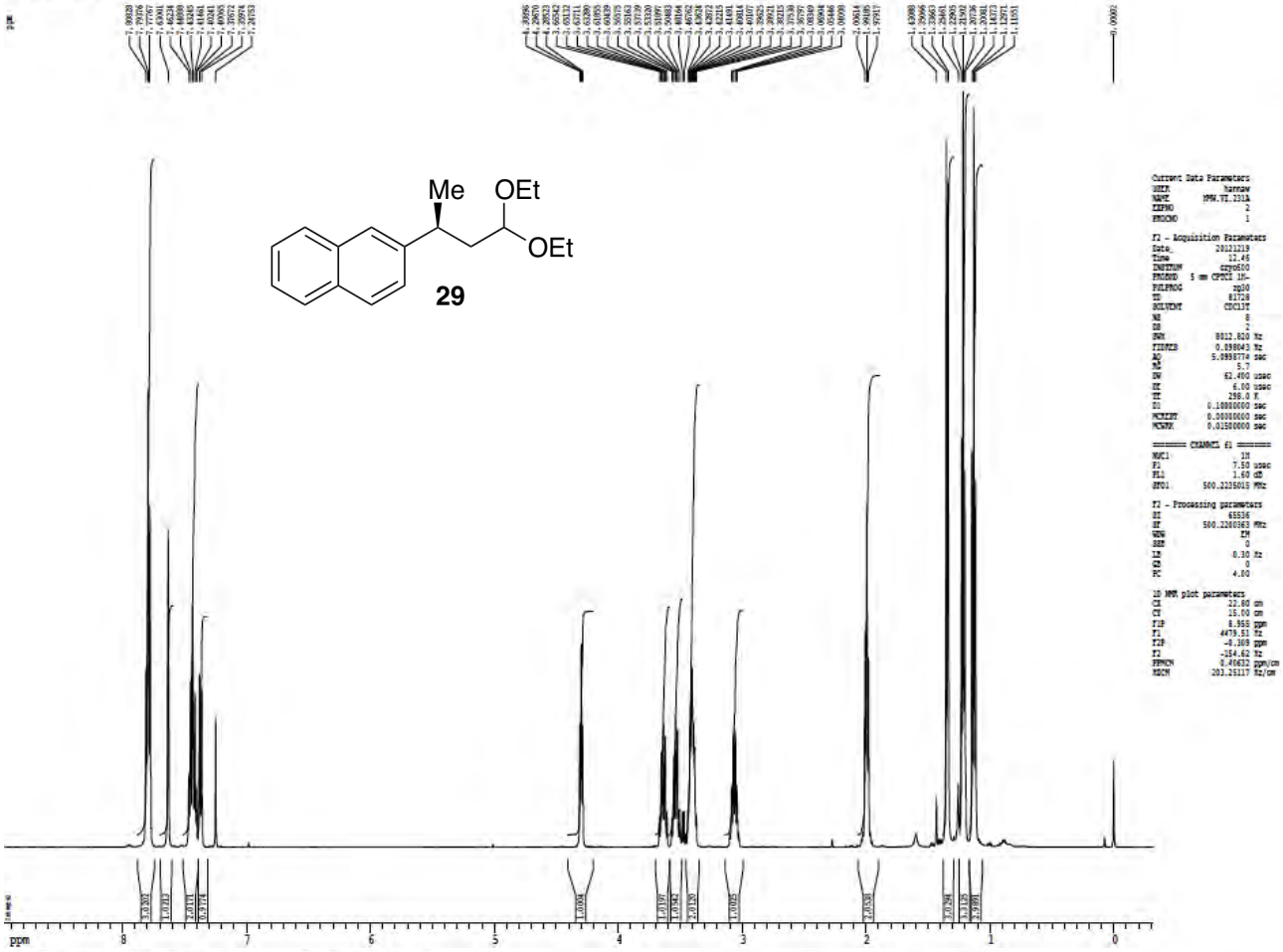
1H spectrum



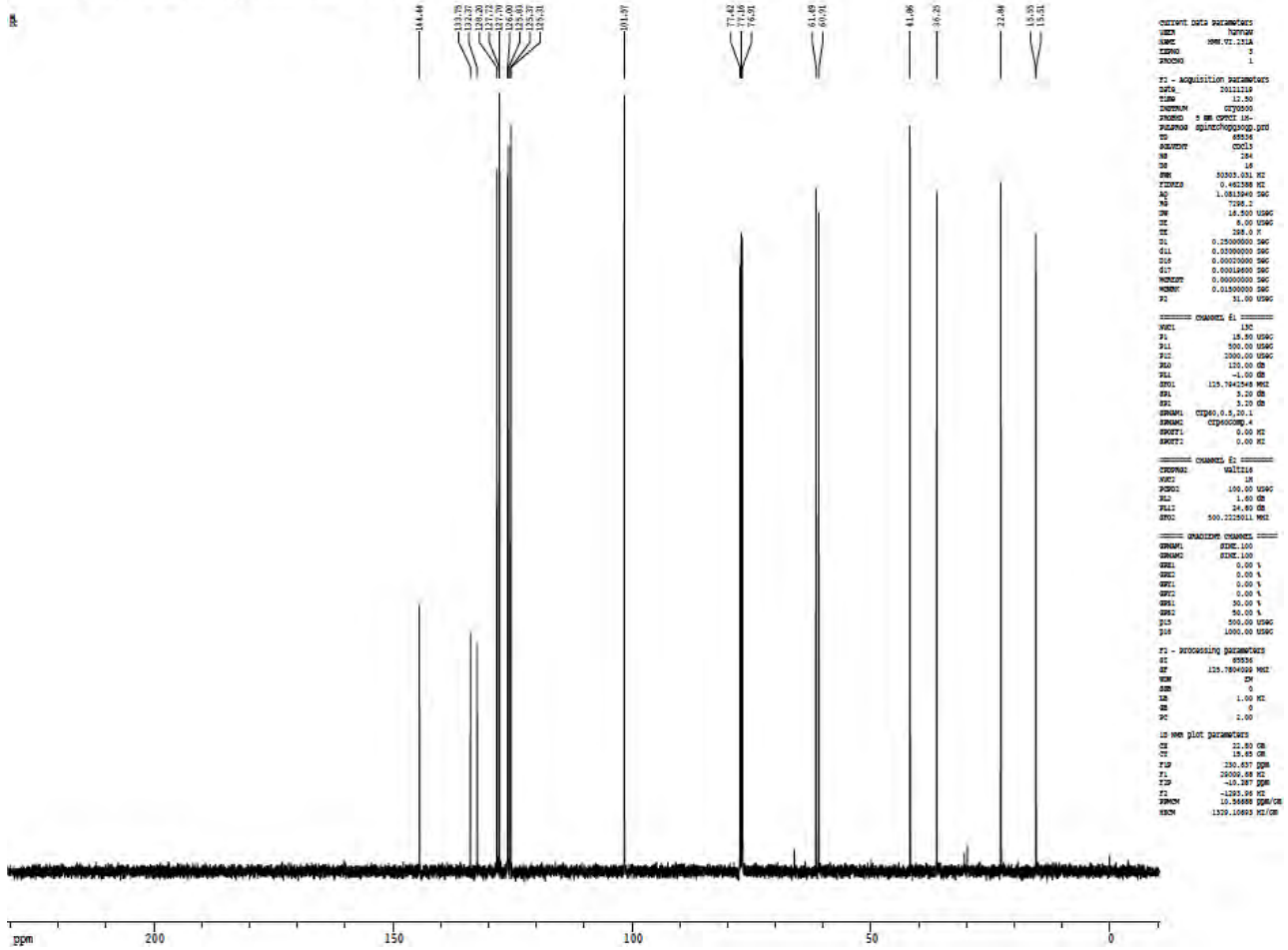
Z-restored spin-echo 13C spectrum with 1H decoupling



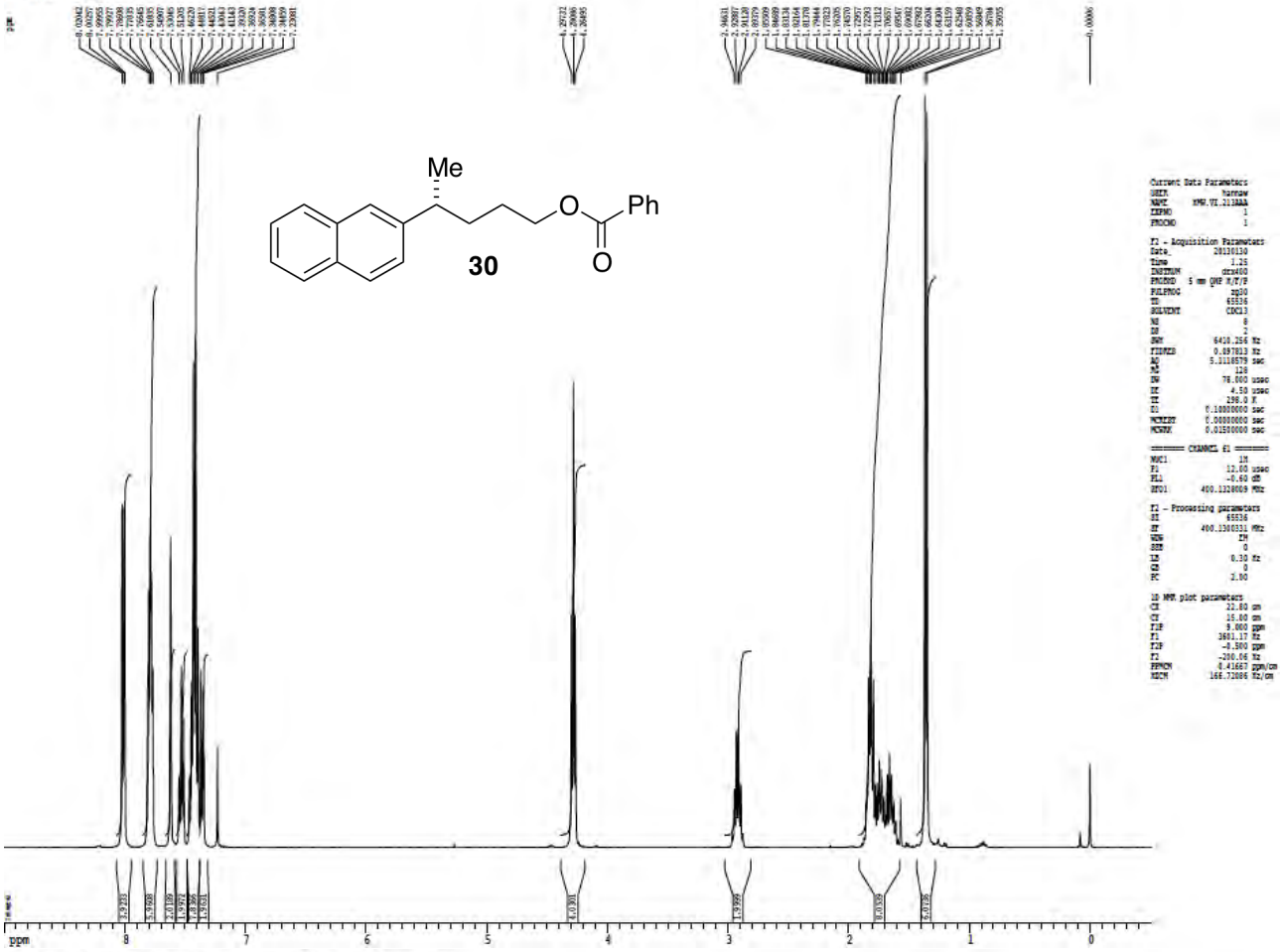
1H spectrum



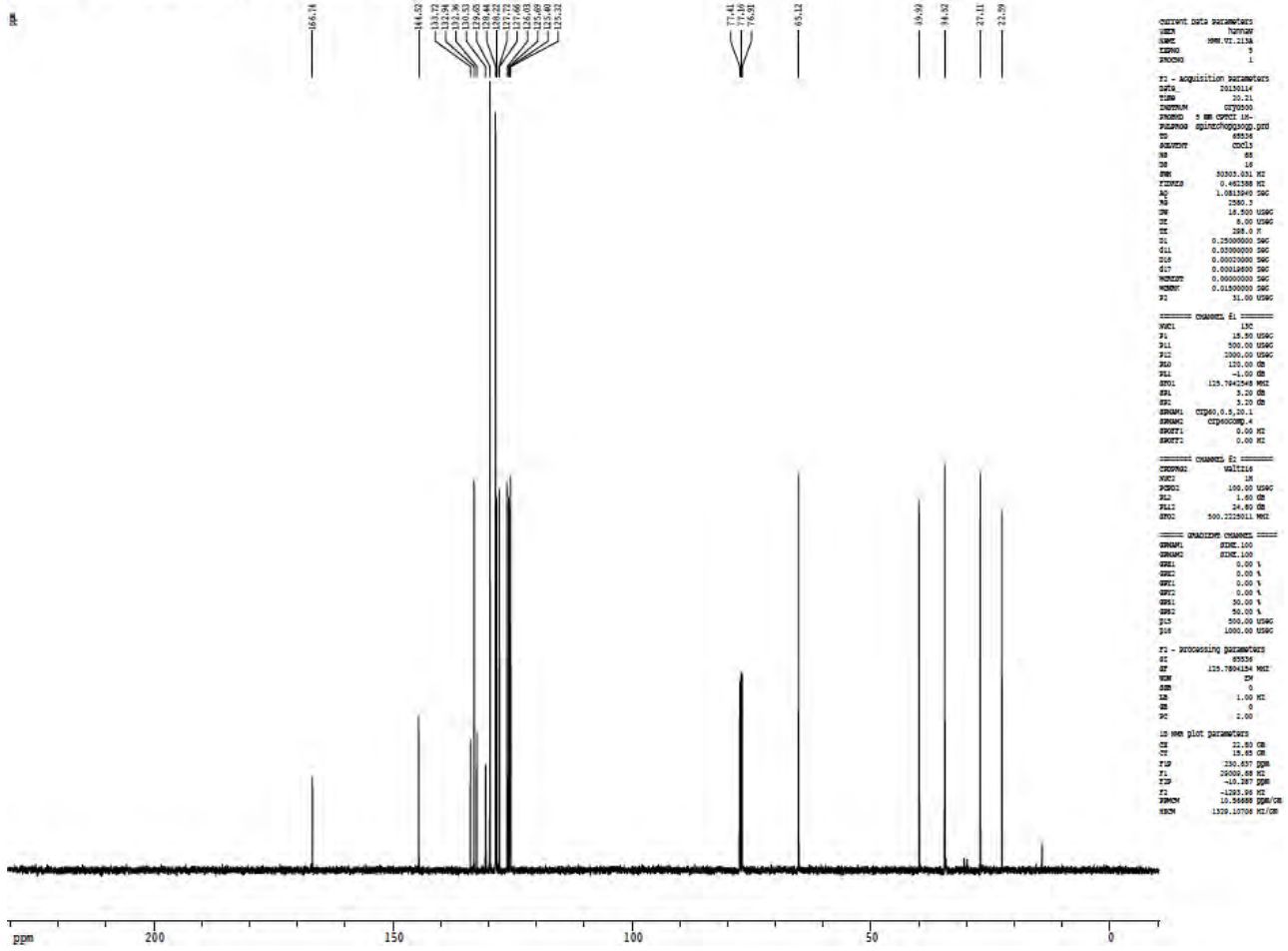
Z-restored spin-echo 13C spectrum with 1H decoupling



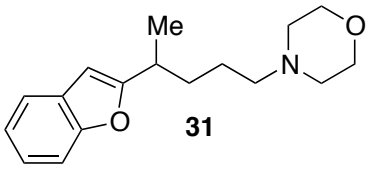
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling



1H spectrum



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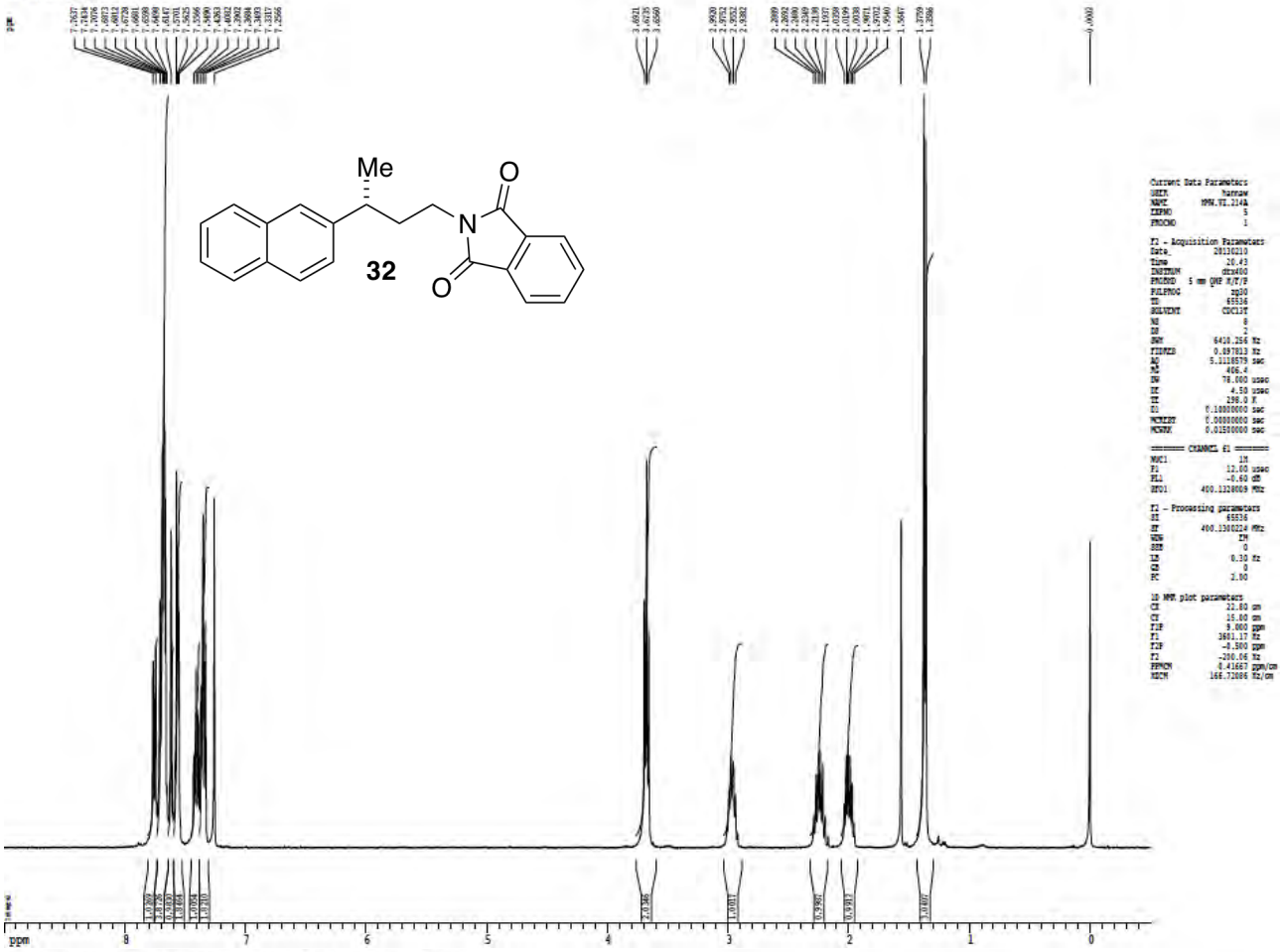
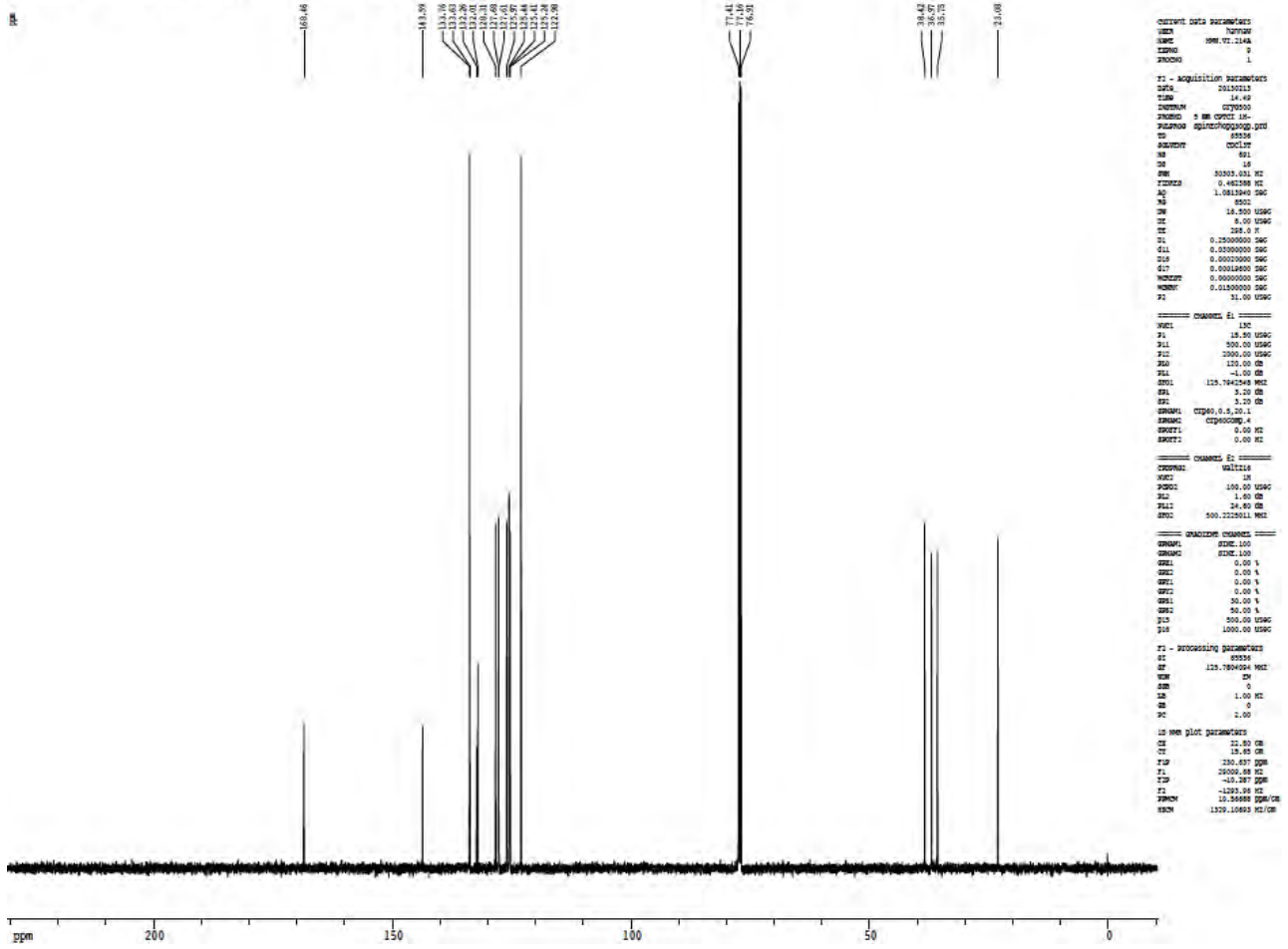
Z-restored spin-echo 13C spectrum with 1H decoupling

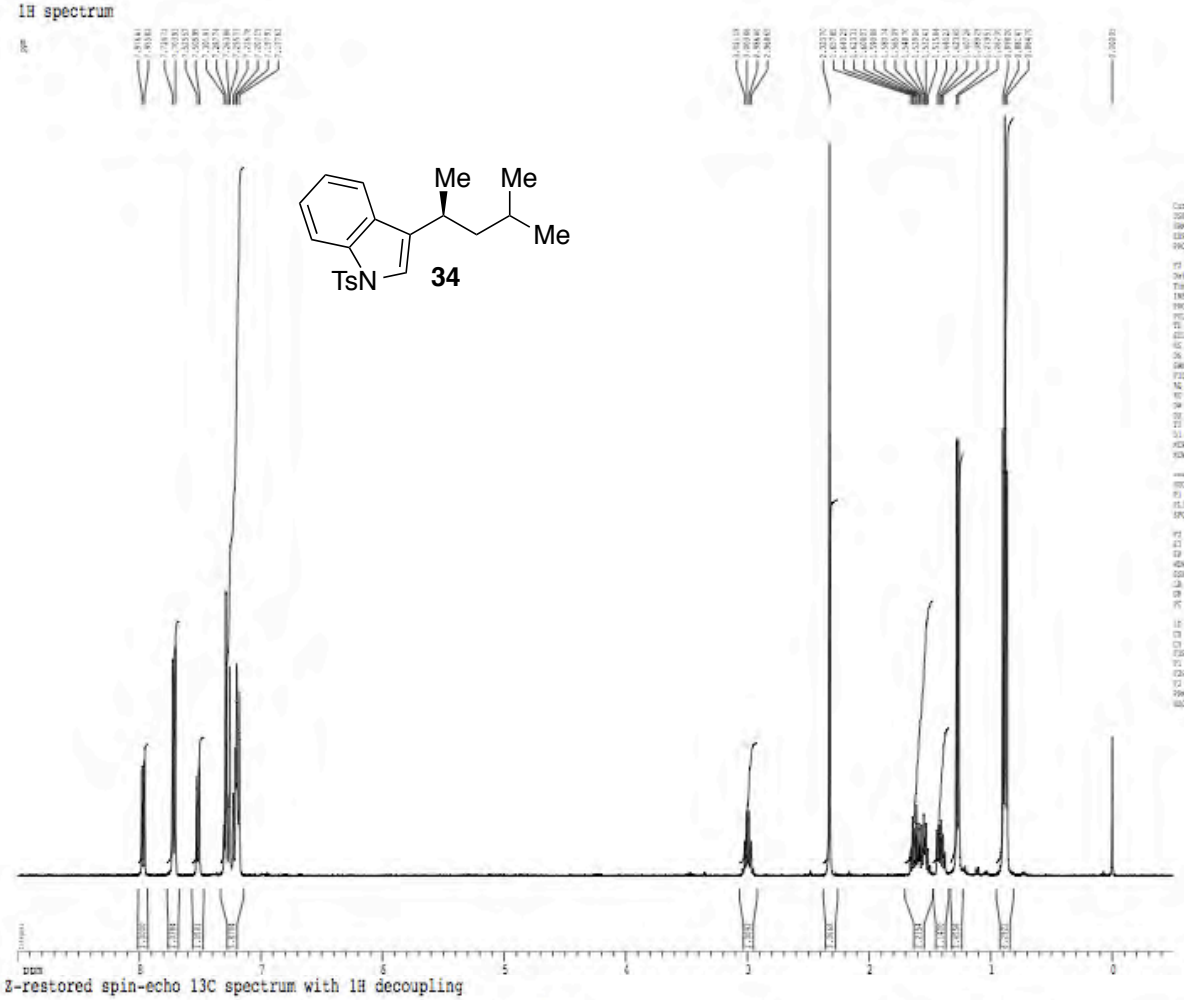
1H spectrum



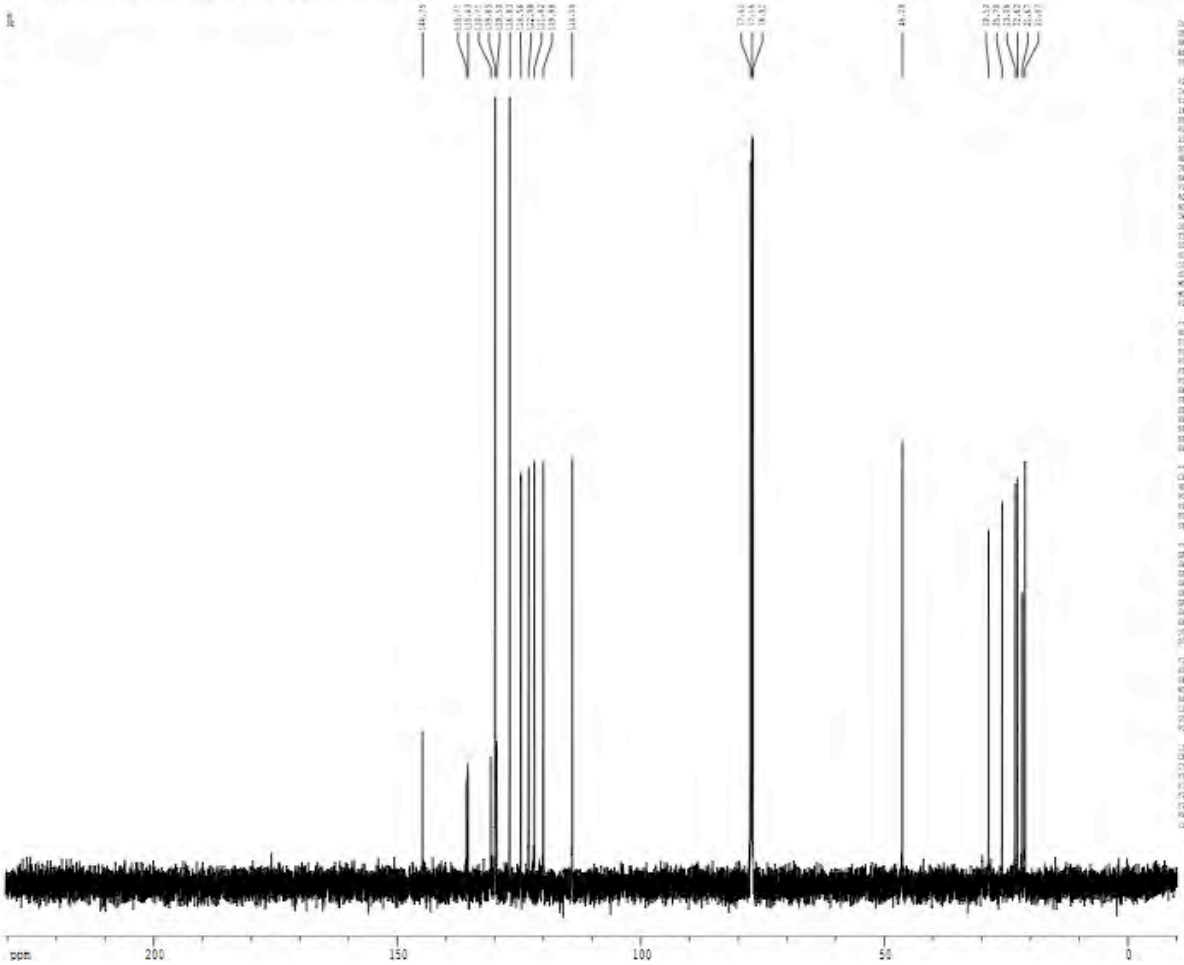
Z-restored spin-echo 13C spectrum with 1H decoupling



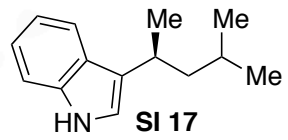
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling



1H spectrum



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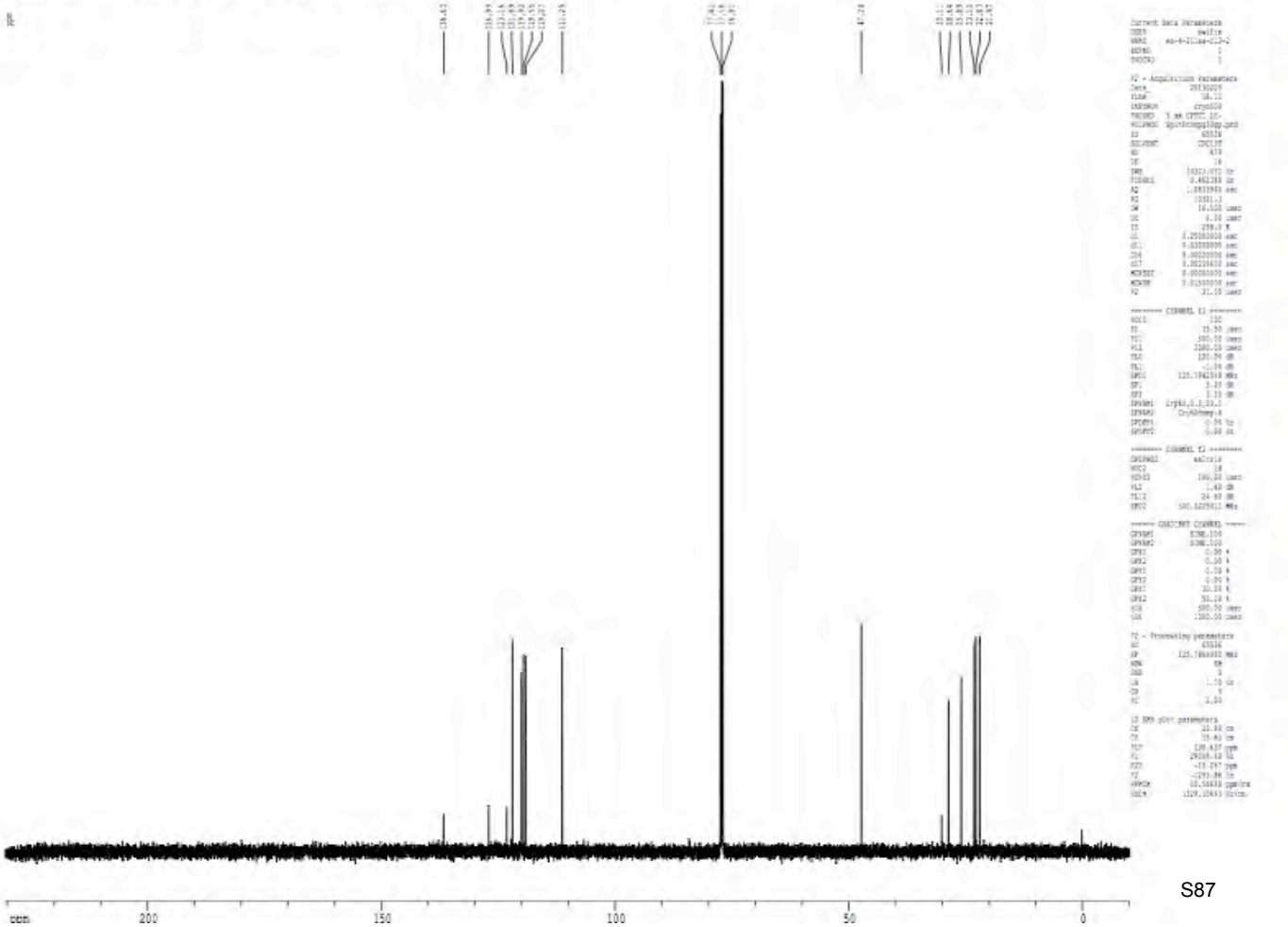
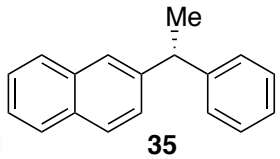
Z-restored spin-echo 13C spectrum with 1H decoupling



1H spectrum



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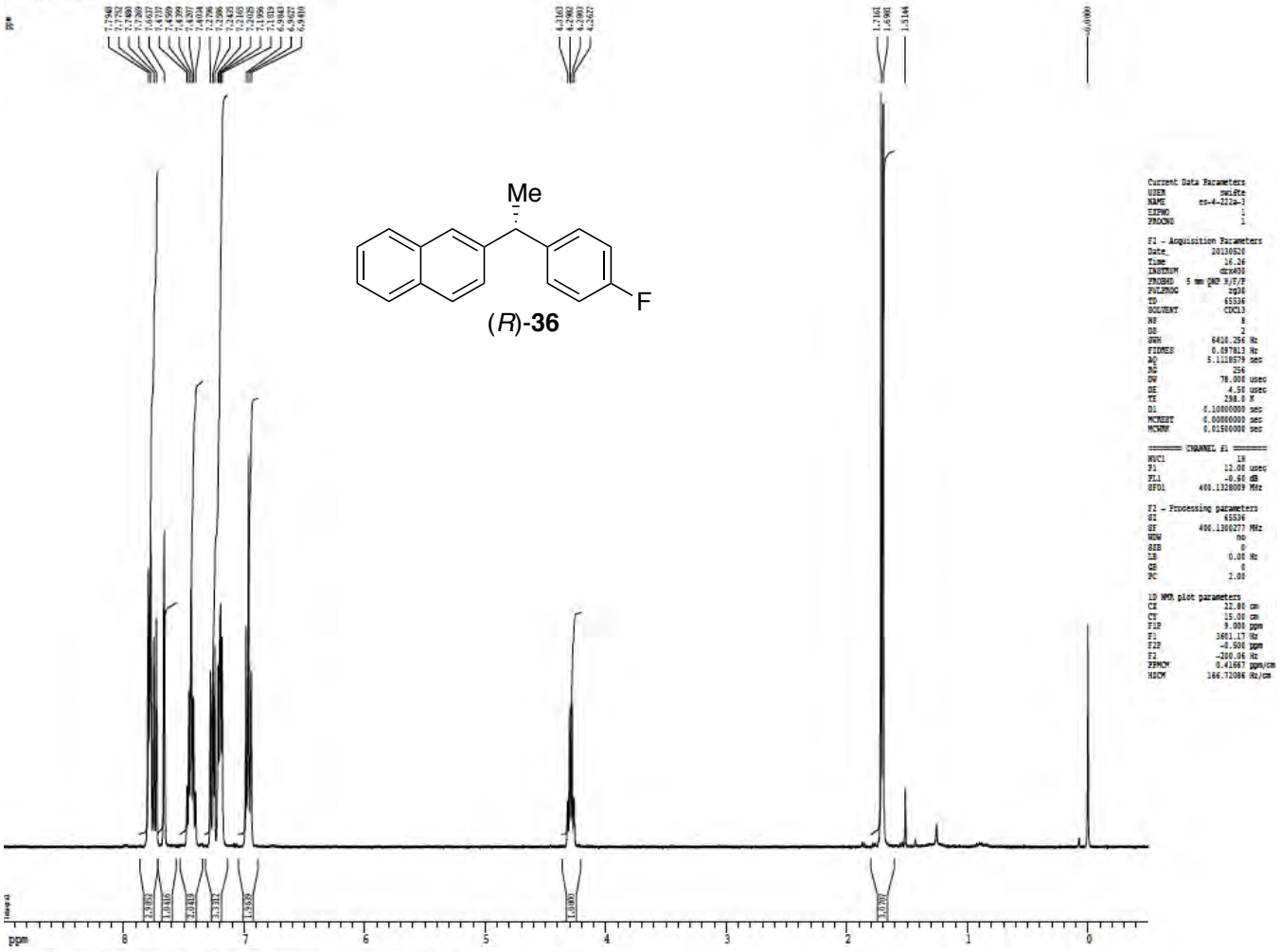
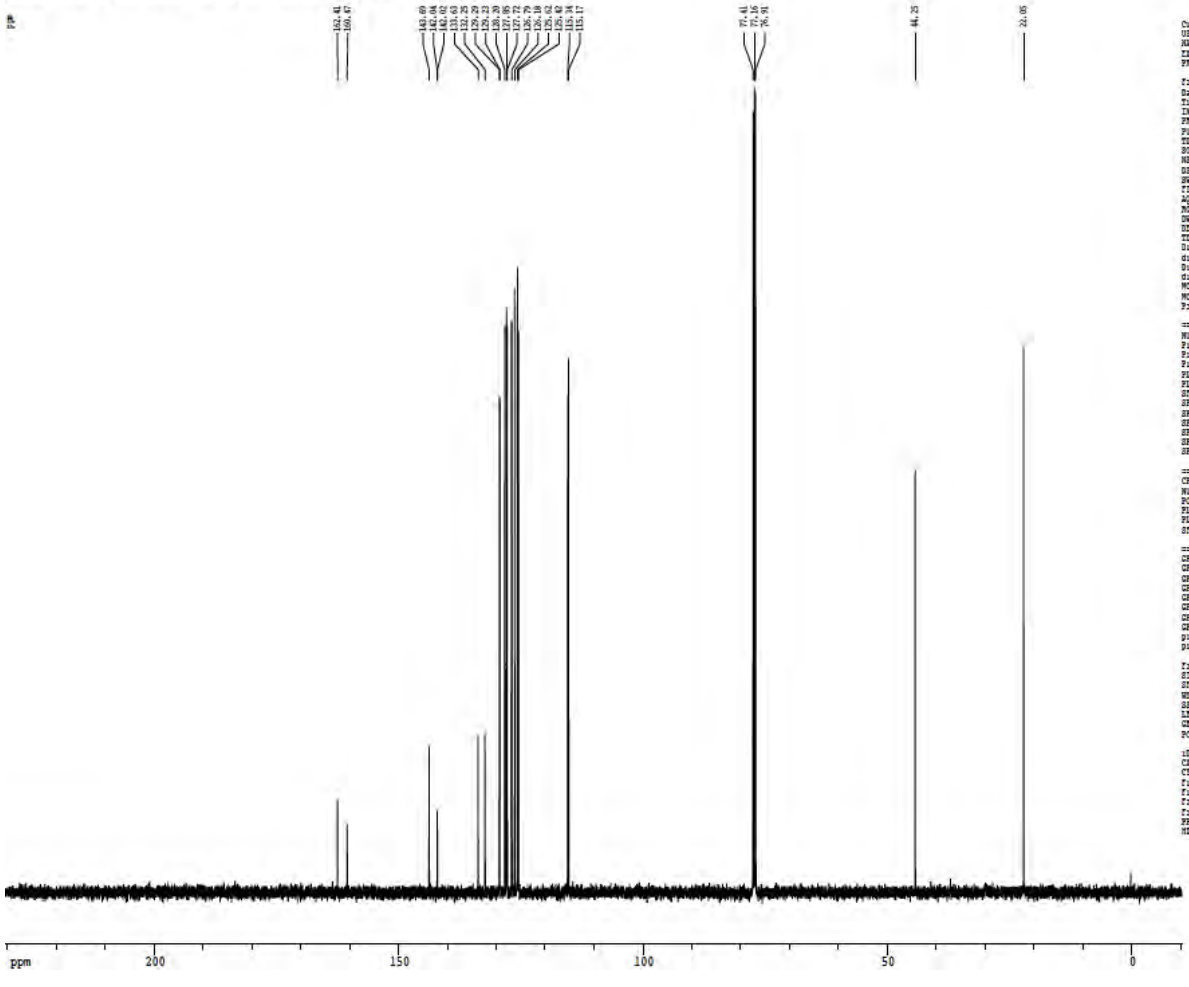
Z-restored spin-echo 13C spectrum with 1H decoupling

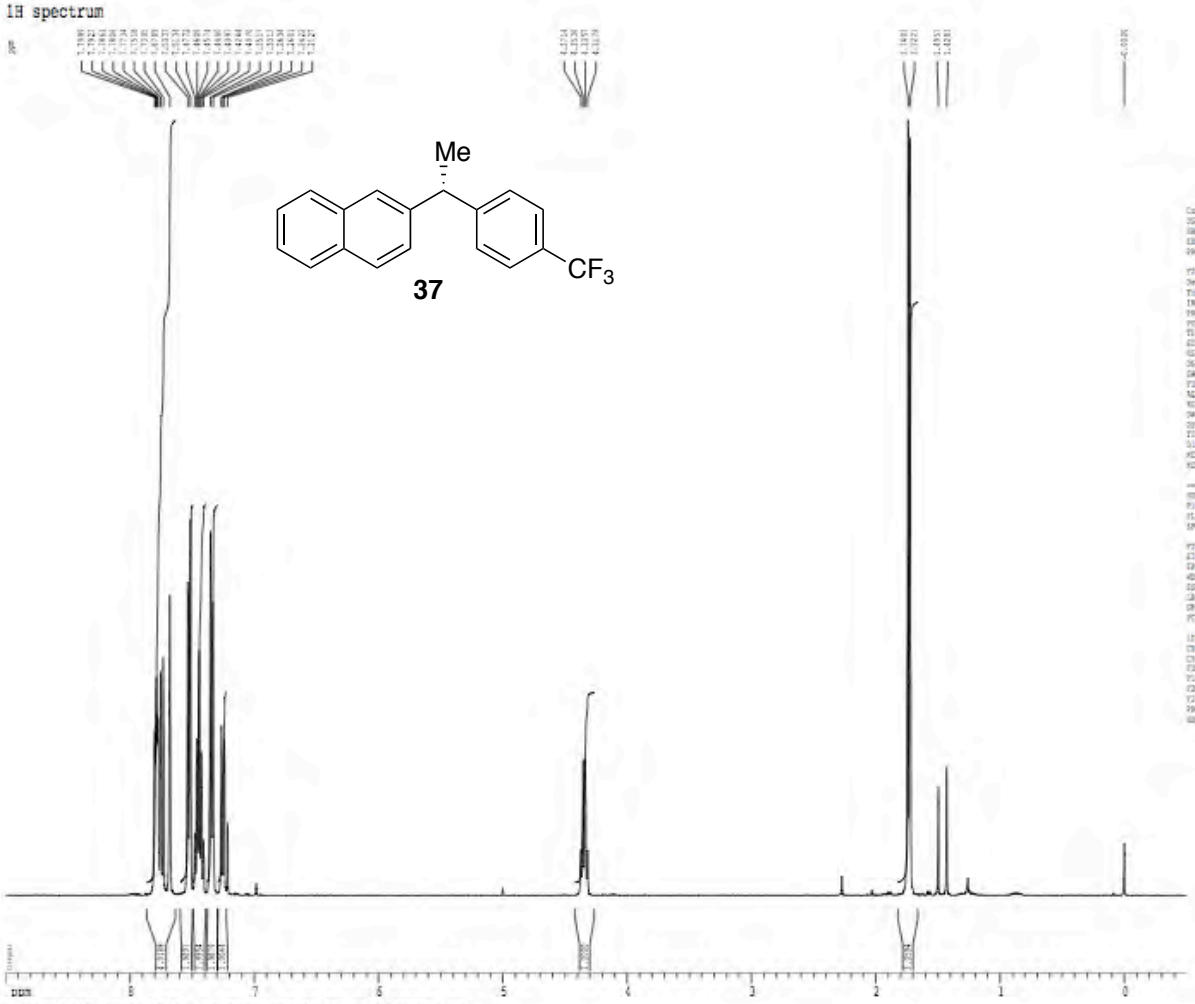
1H spectrum



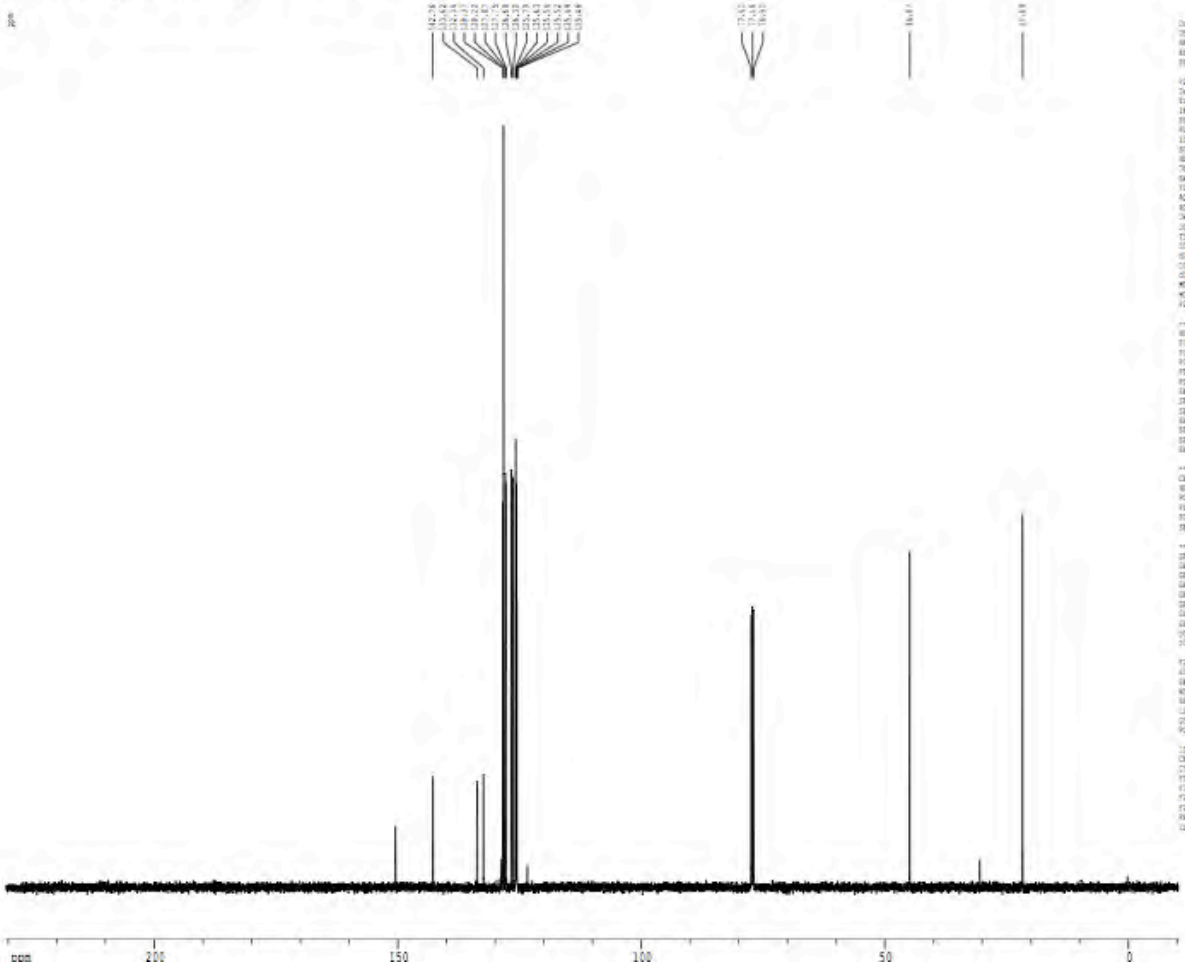
Z-restored spin-echo 13C spectrum with 1H decoupling



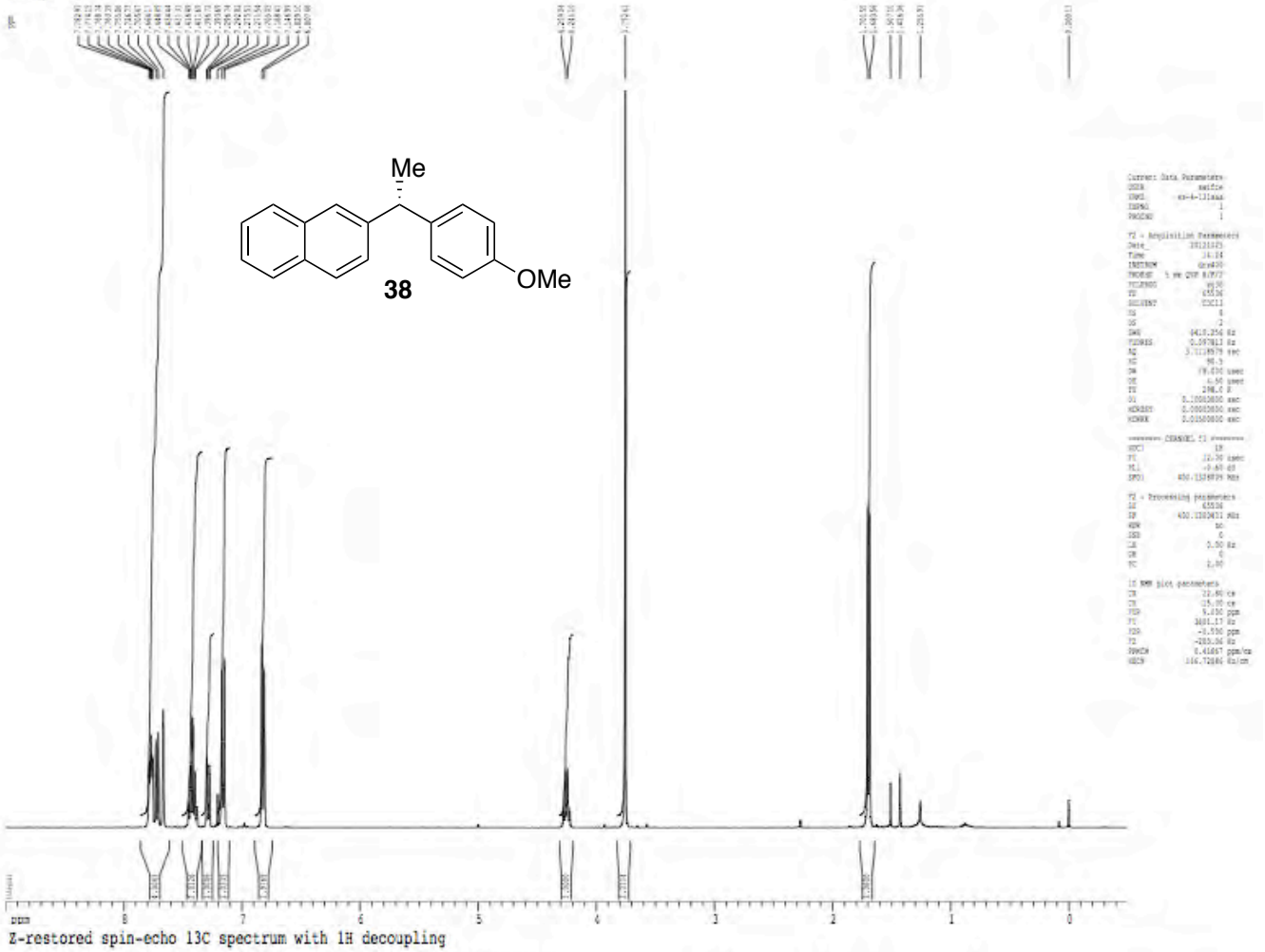
1H spectrum



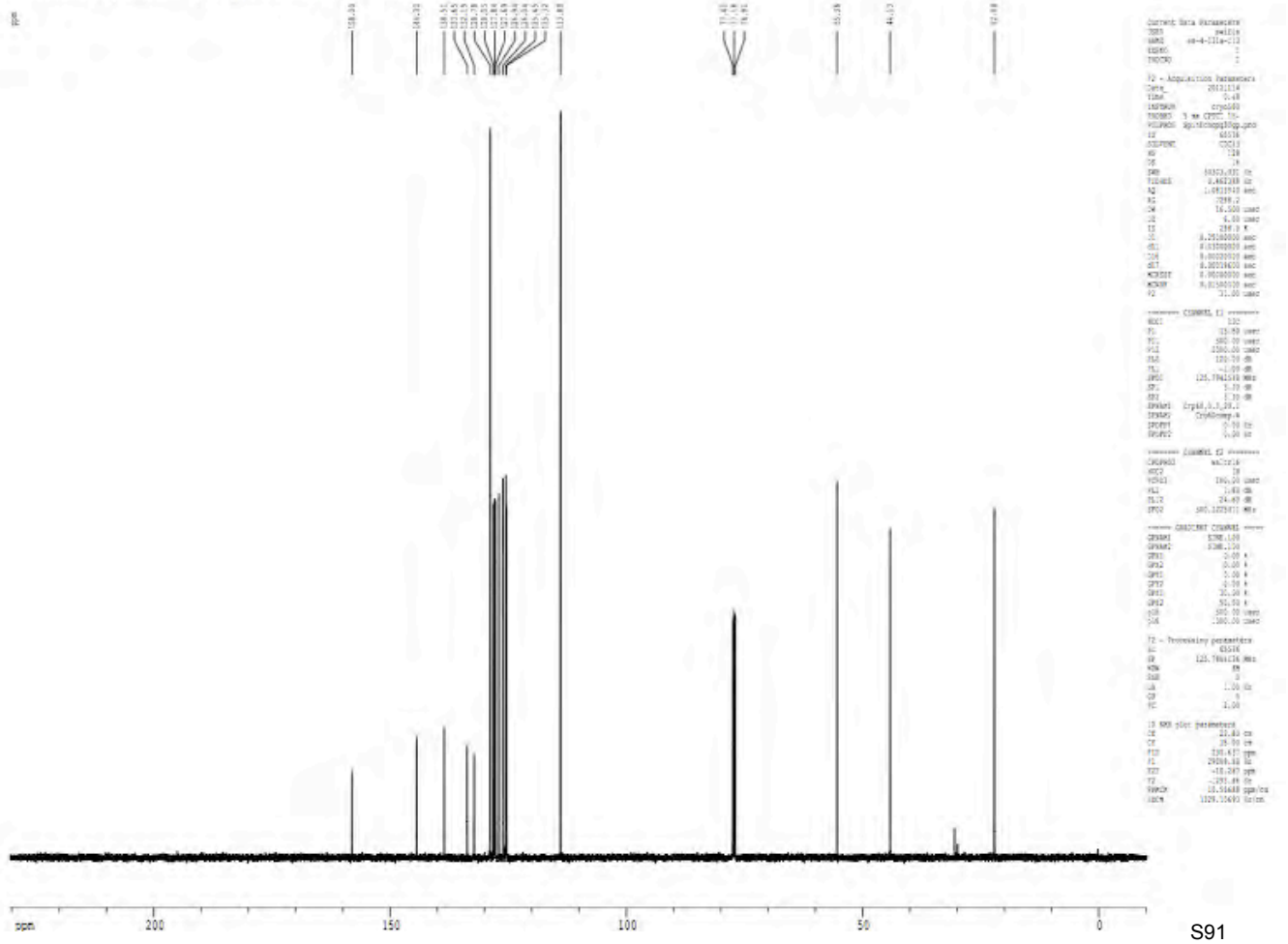
Z-restored spin-echo 13C spectrum with 1H decoupling



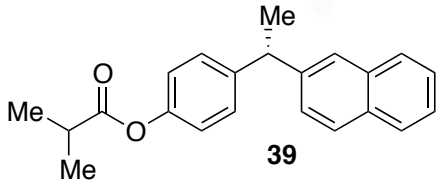
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling



1H spectrum



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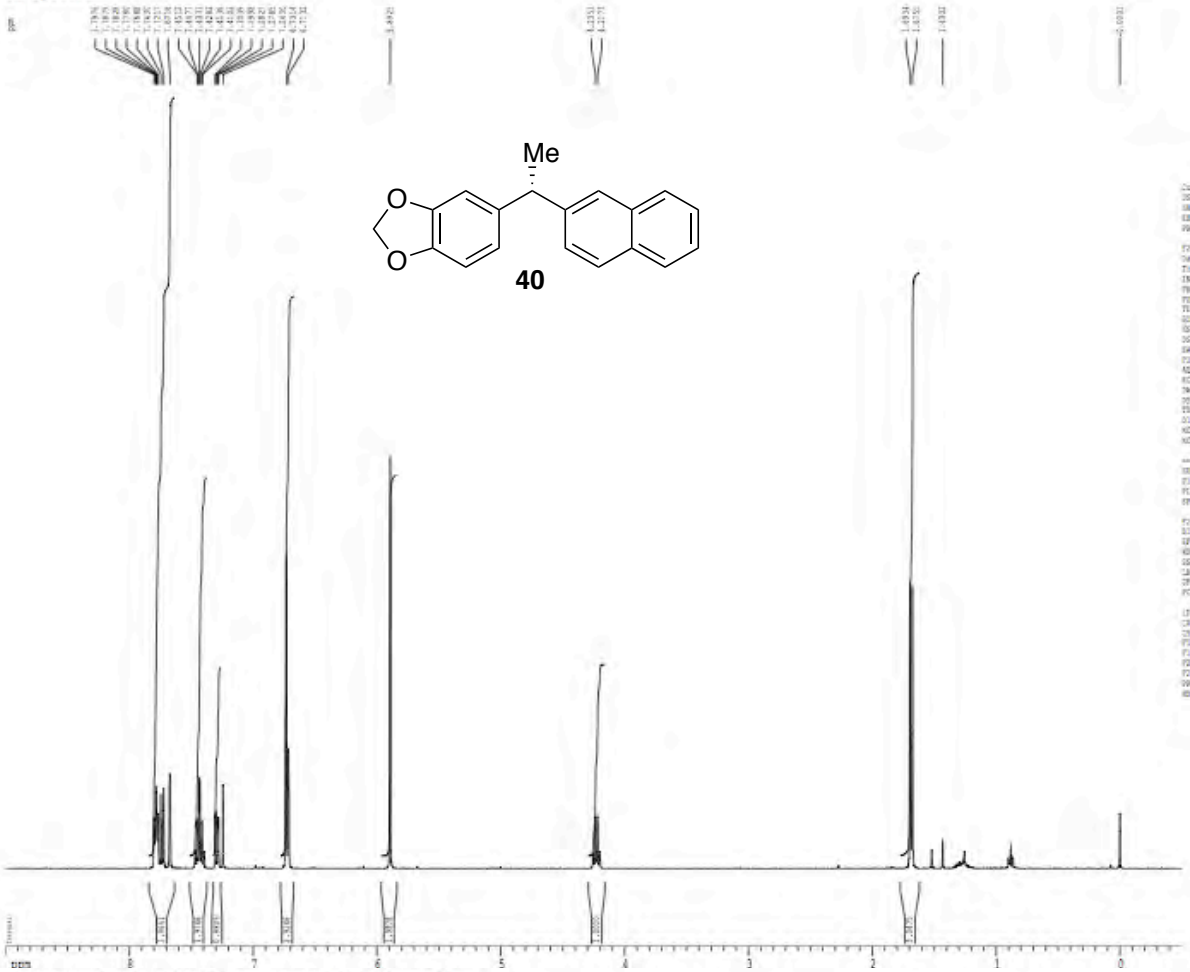
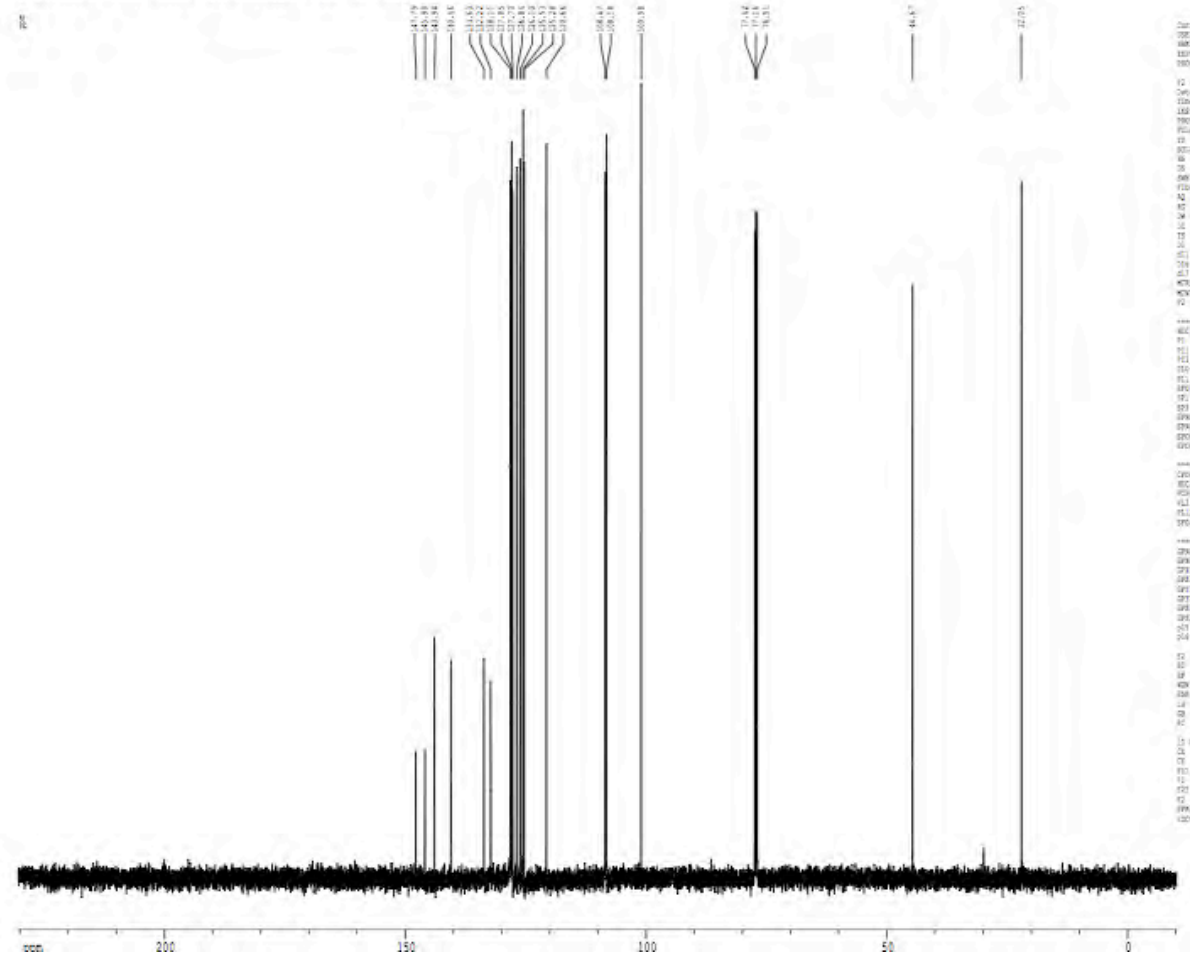
Z-restored spin-echo 13C spectrum with 1H decoupling

1H spectrum

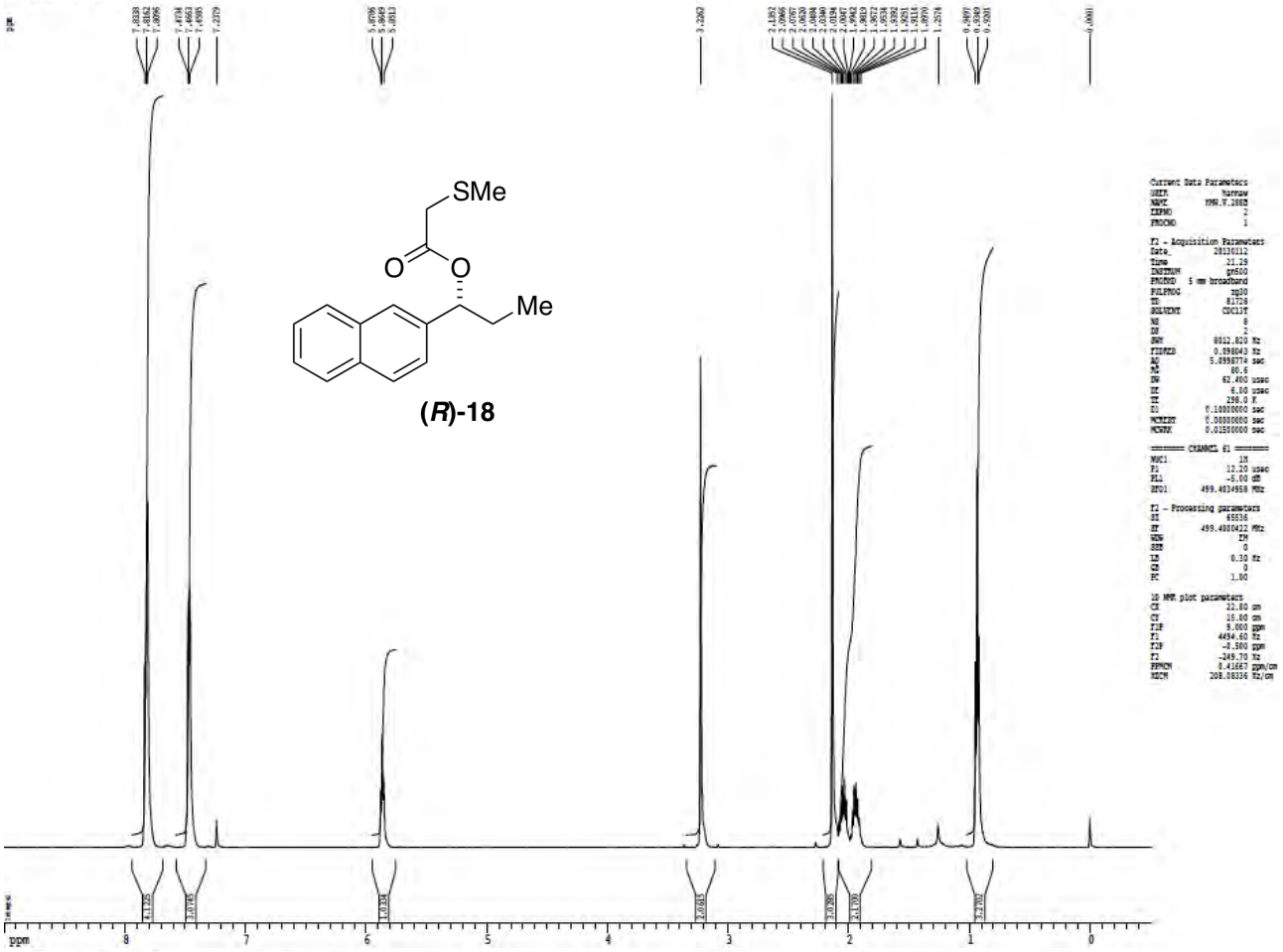


40

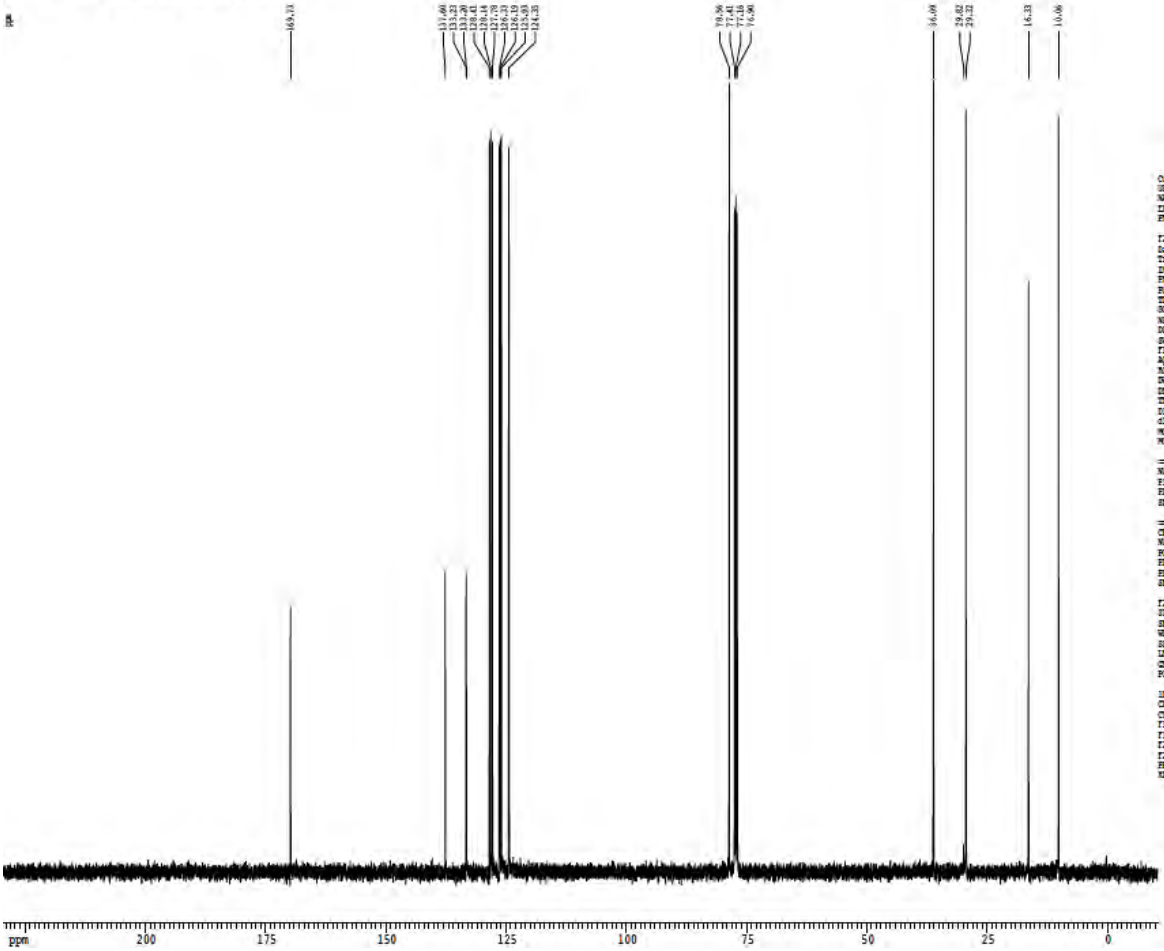
Z-restored spin-echo 13C spectrum with 1H decoupling



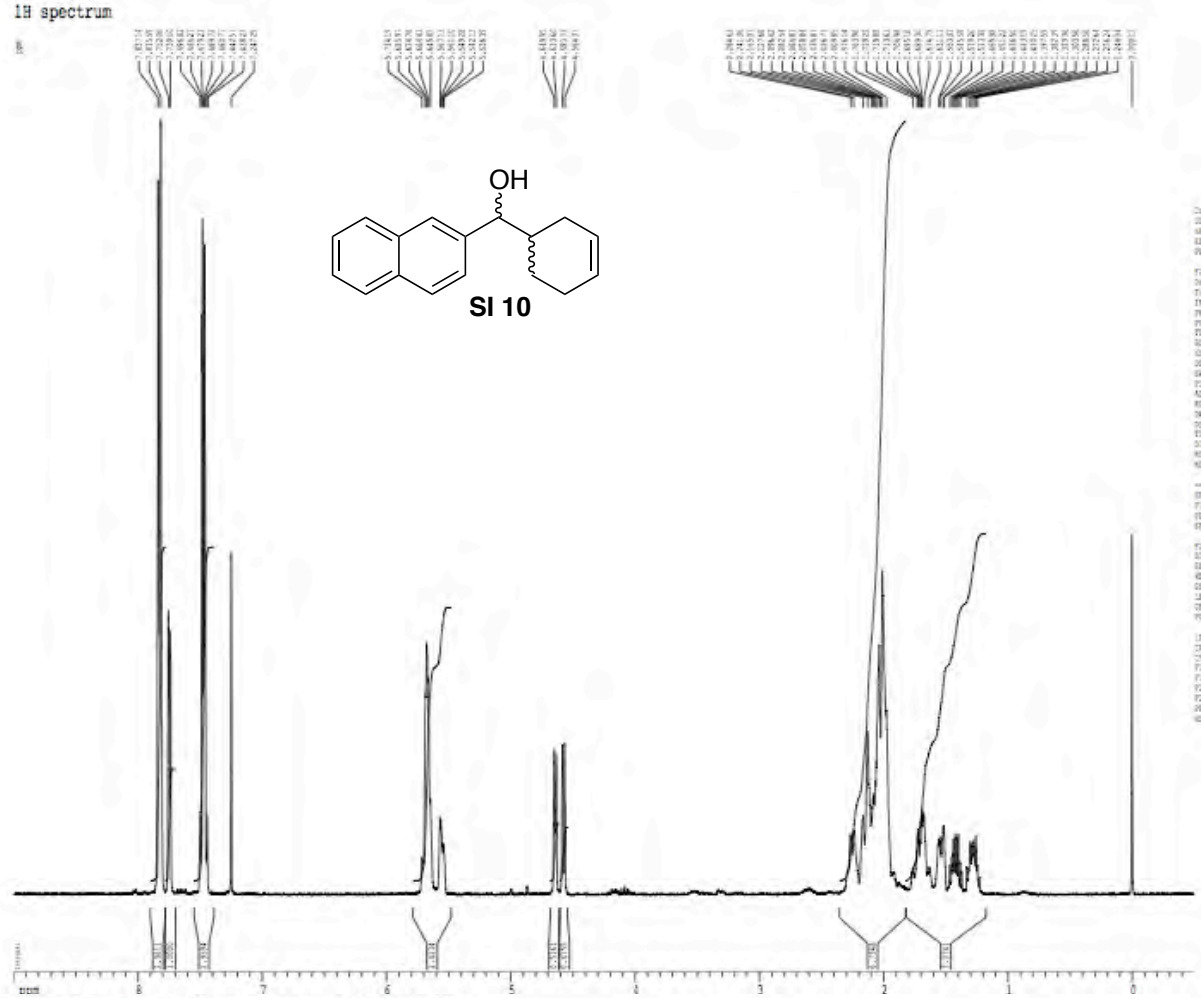
1H spectrum



13C spectrum with 1H decoupling



1H spectrum



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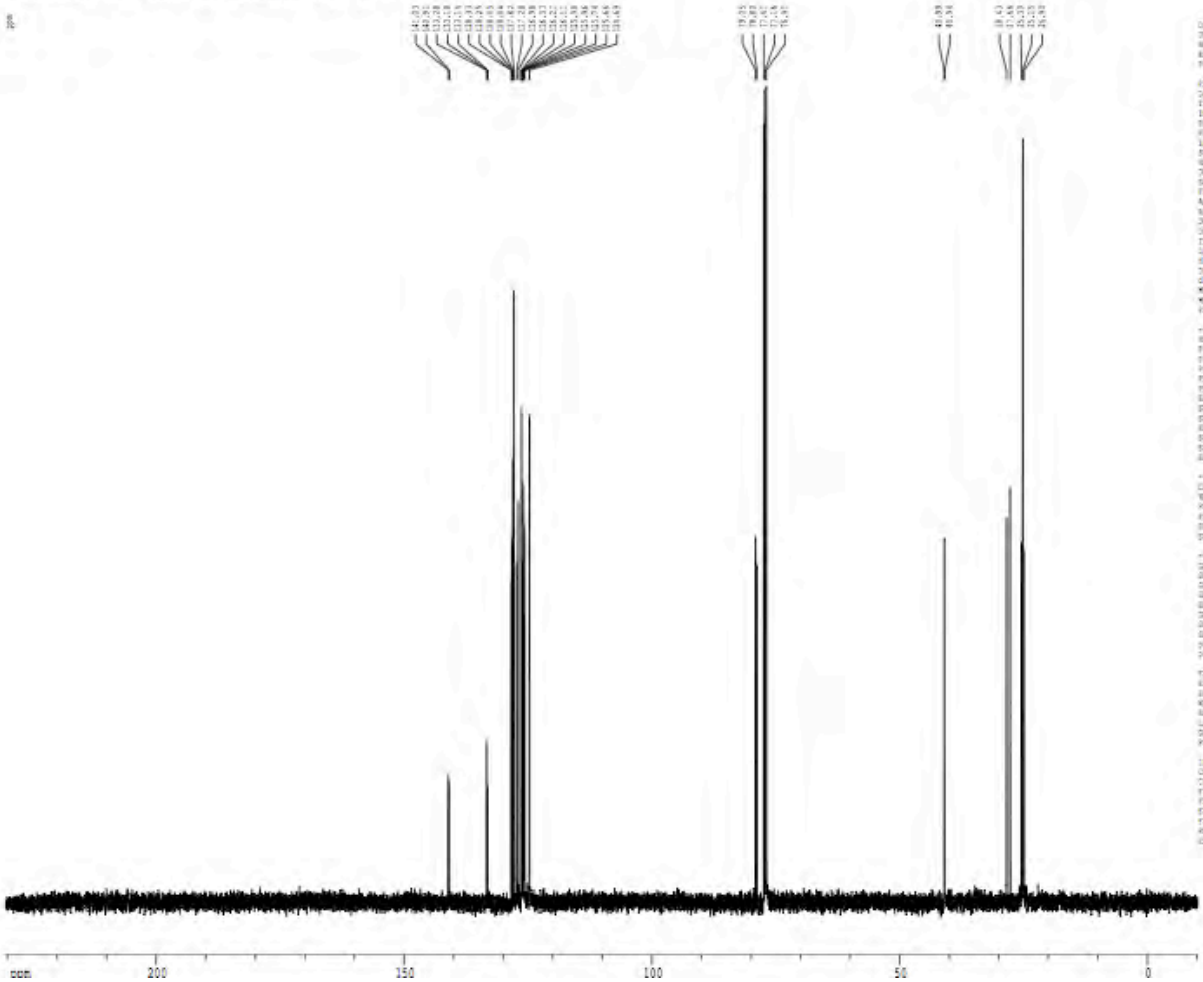
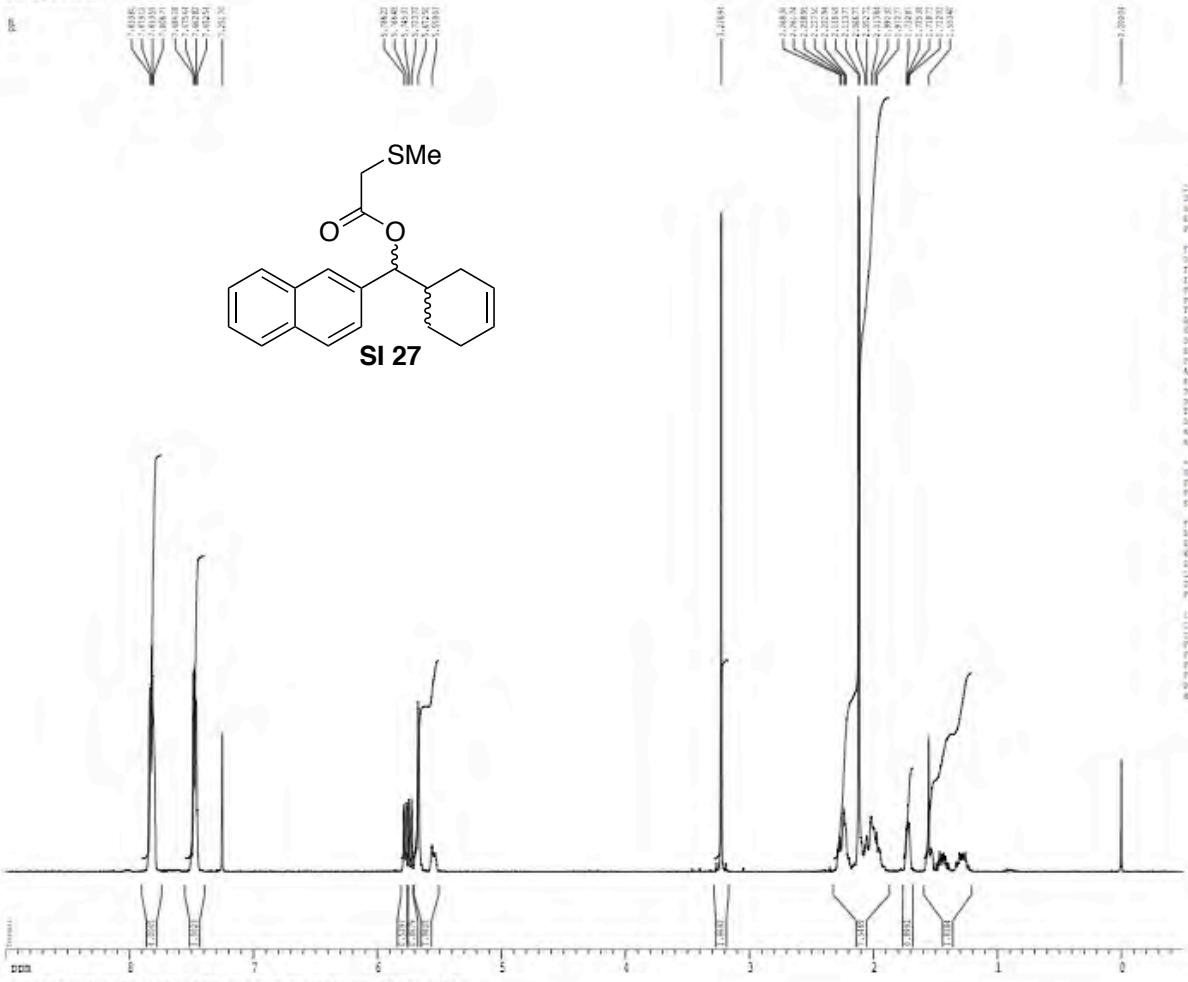
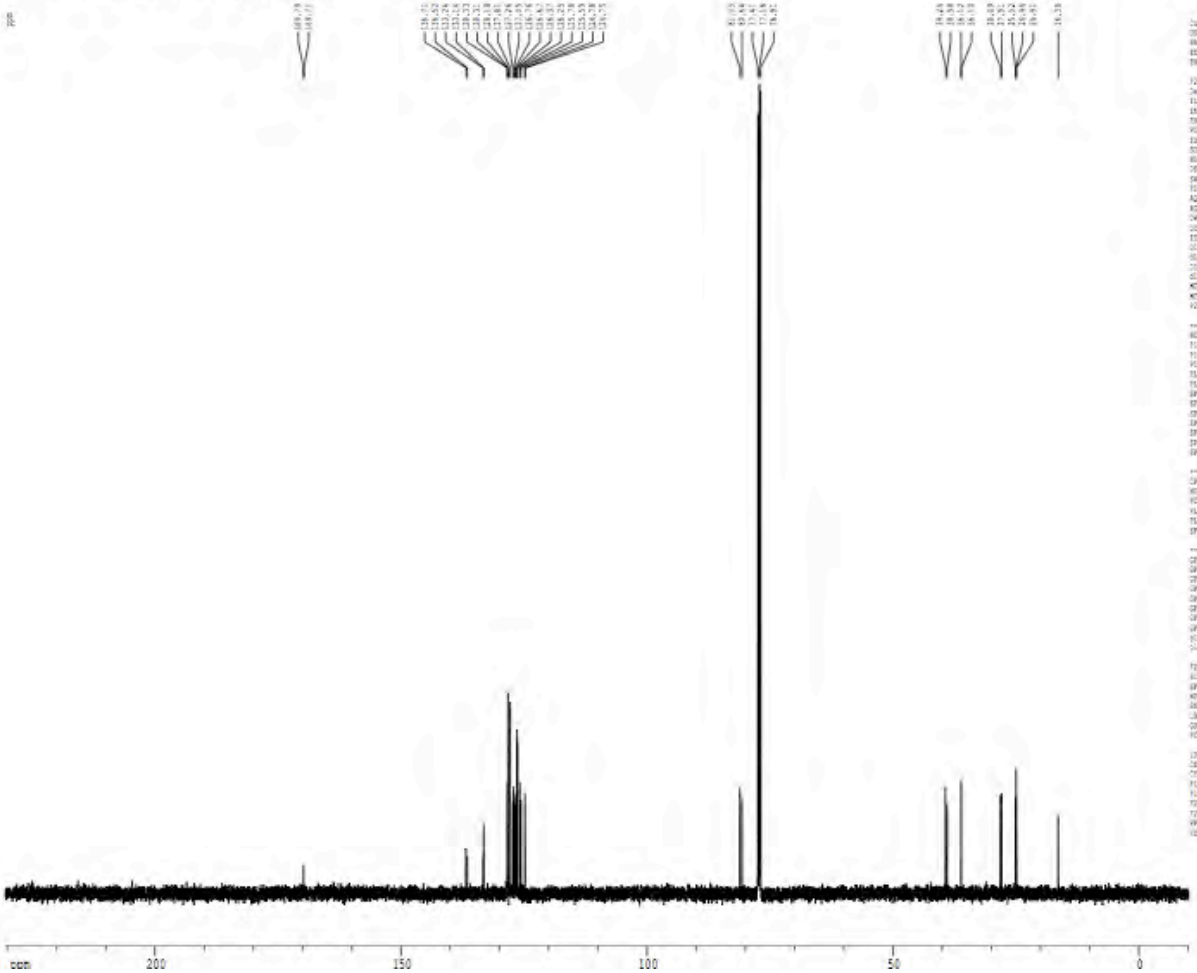
Z-restored spin-echo 13C spectrum with 1H decoupling



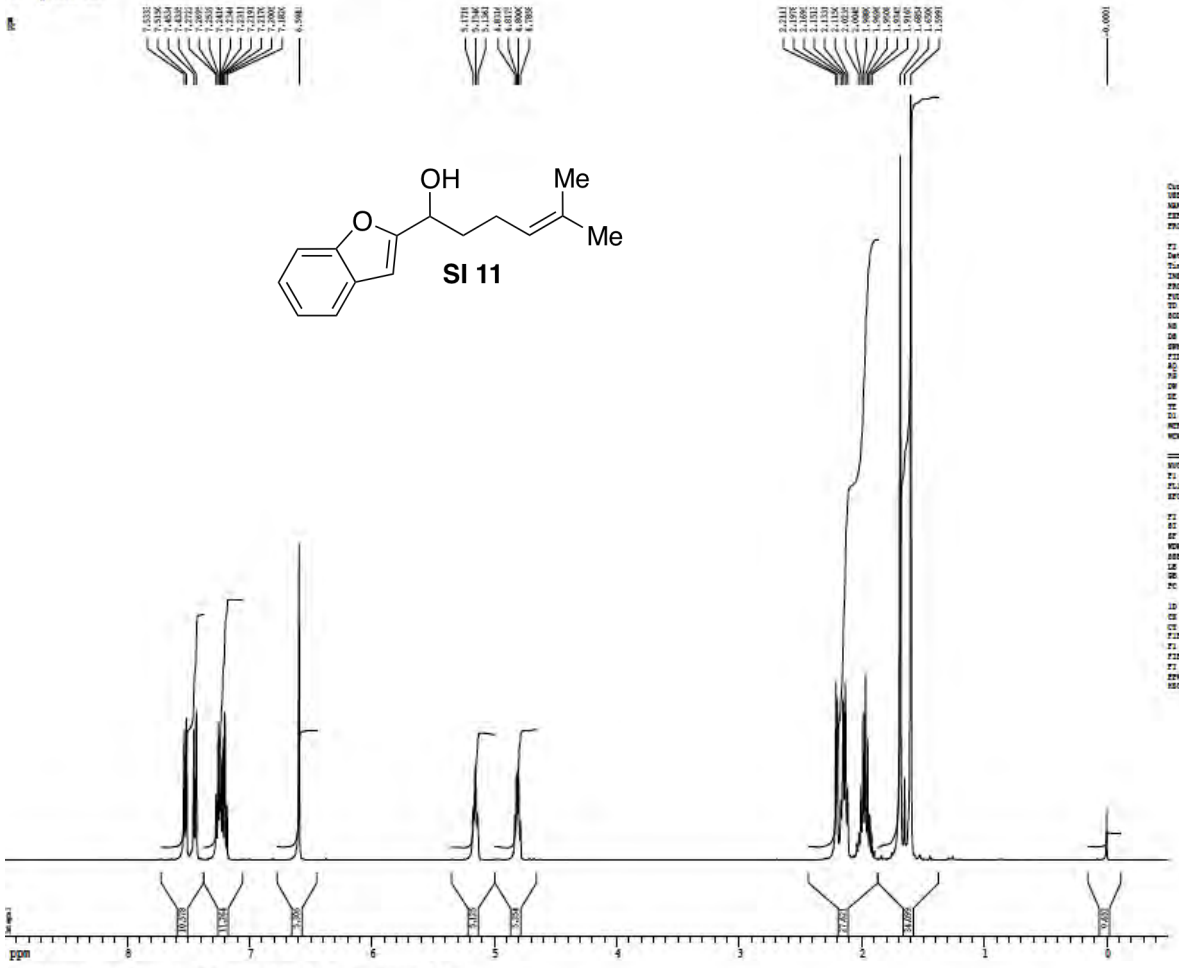
1H spectrum



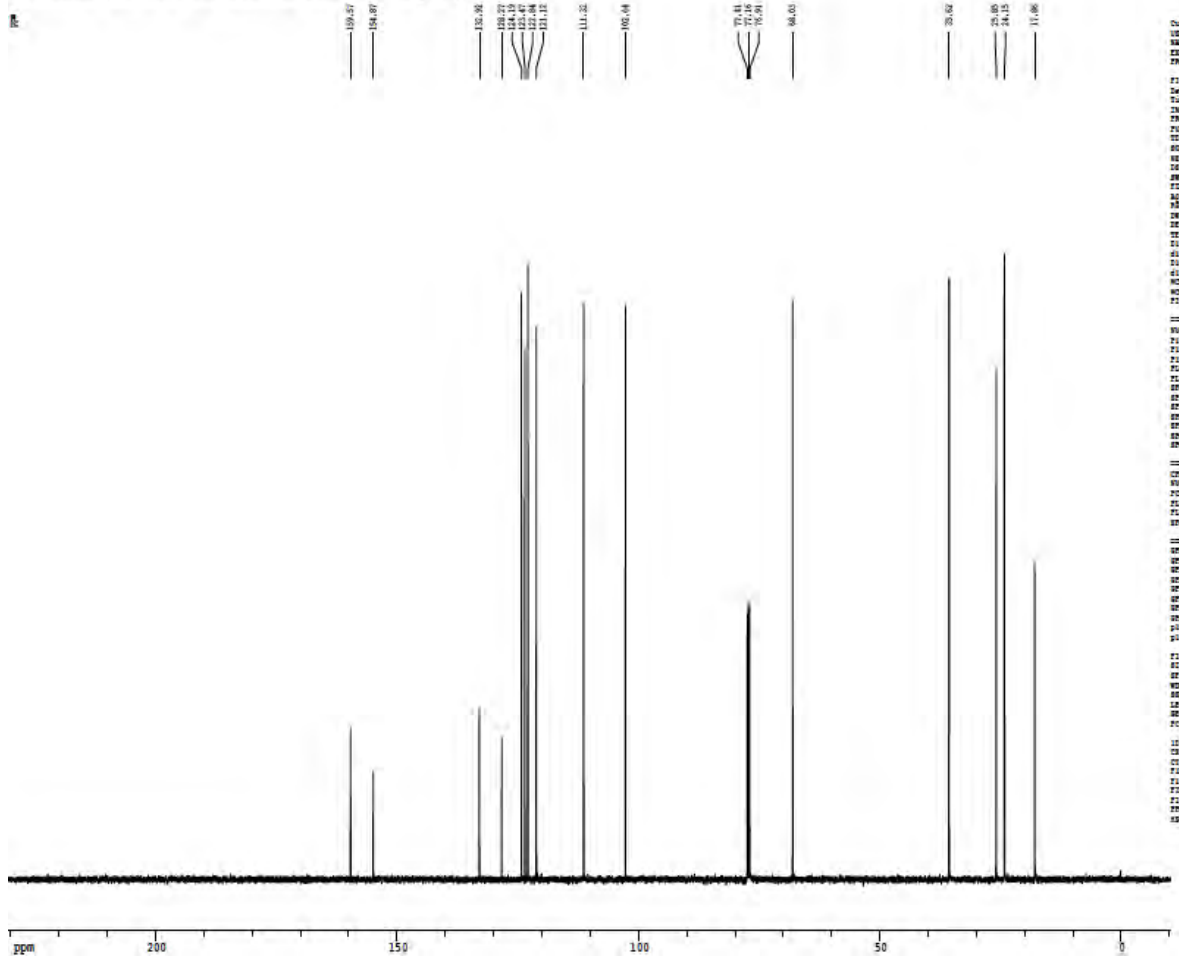
Z-restored spin-echo 13C spectrum with 1H decoupling



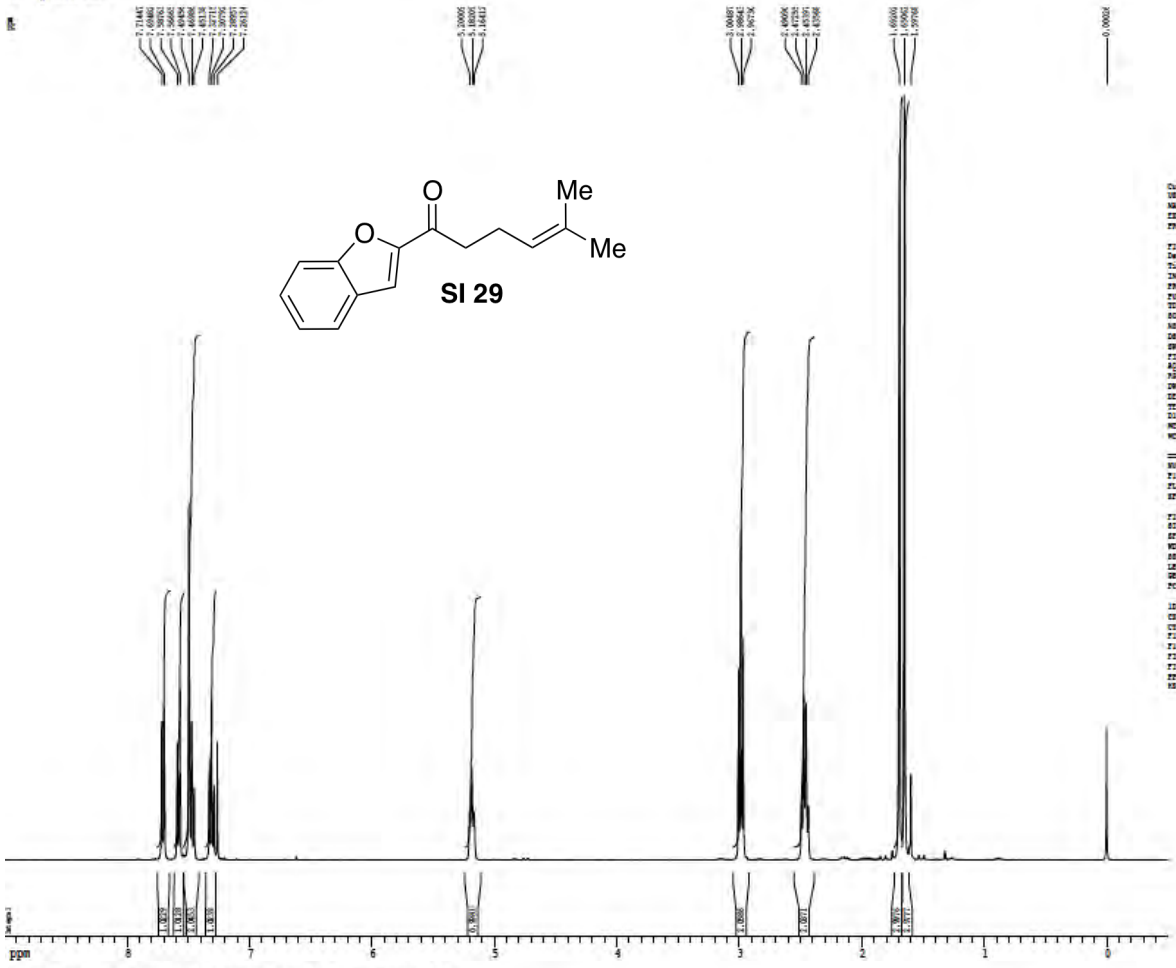
1H spectrum



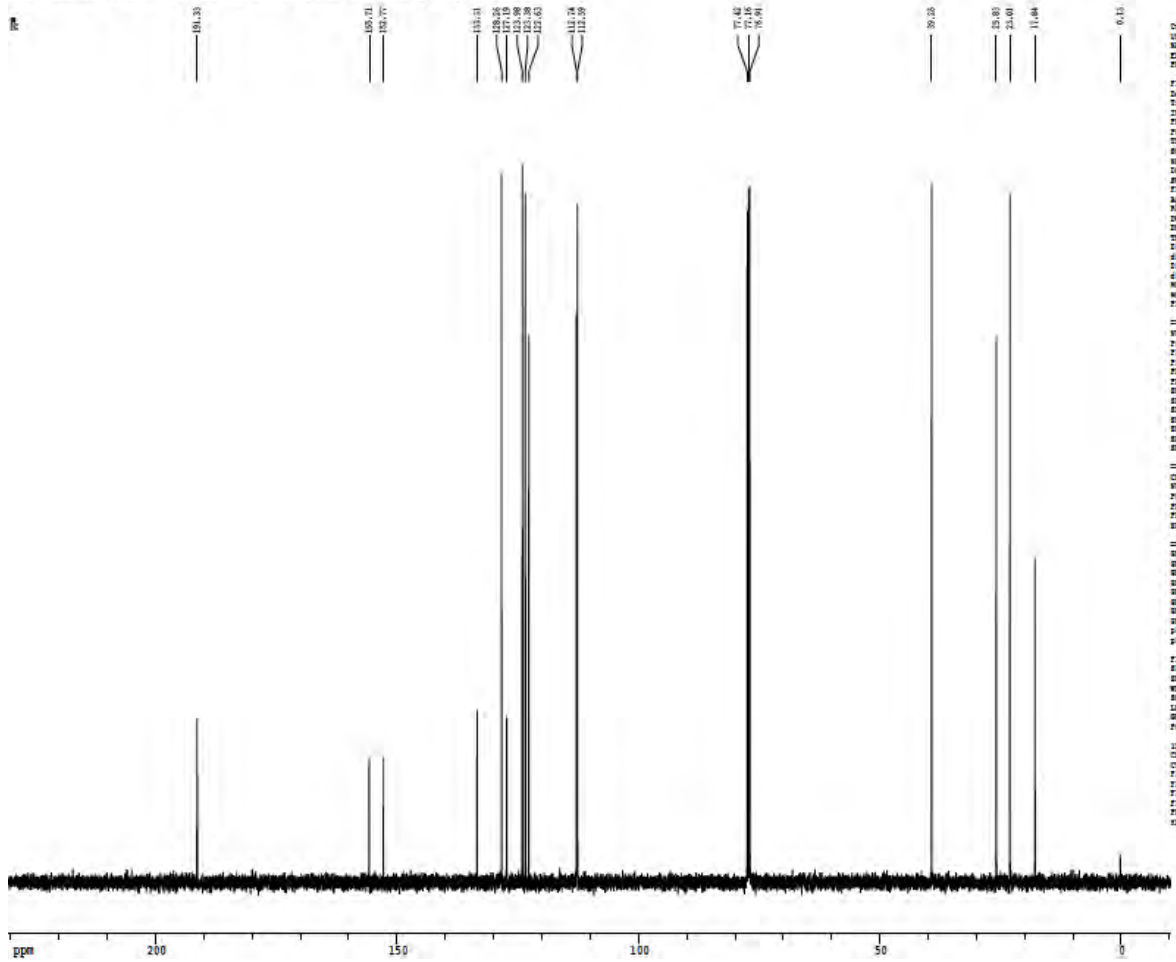
Z-restored spin-echo 13C spectrum with 1H decoupling



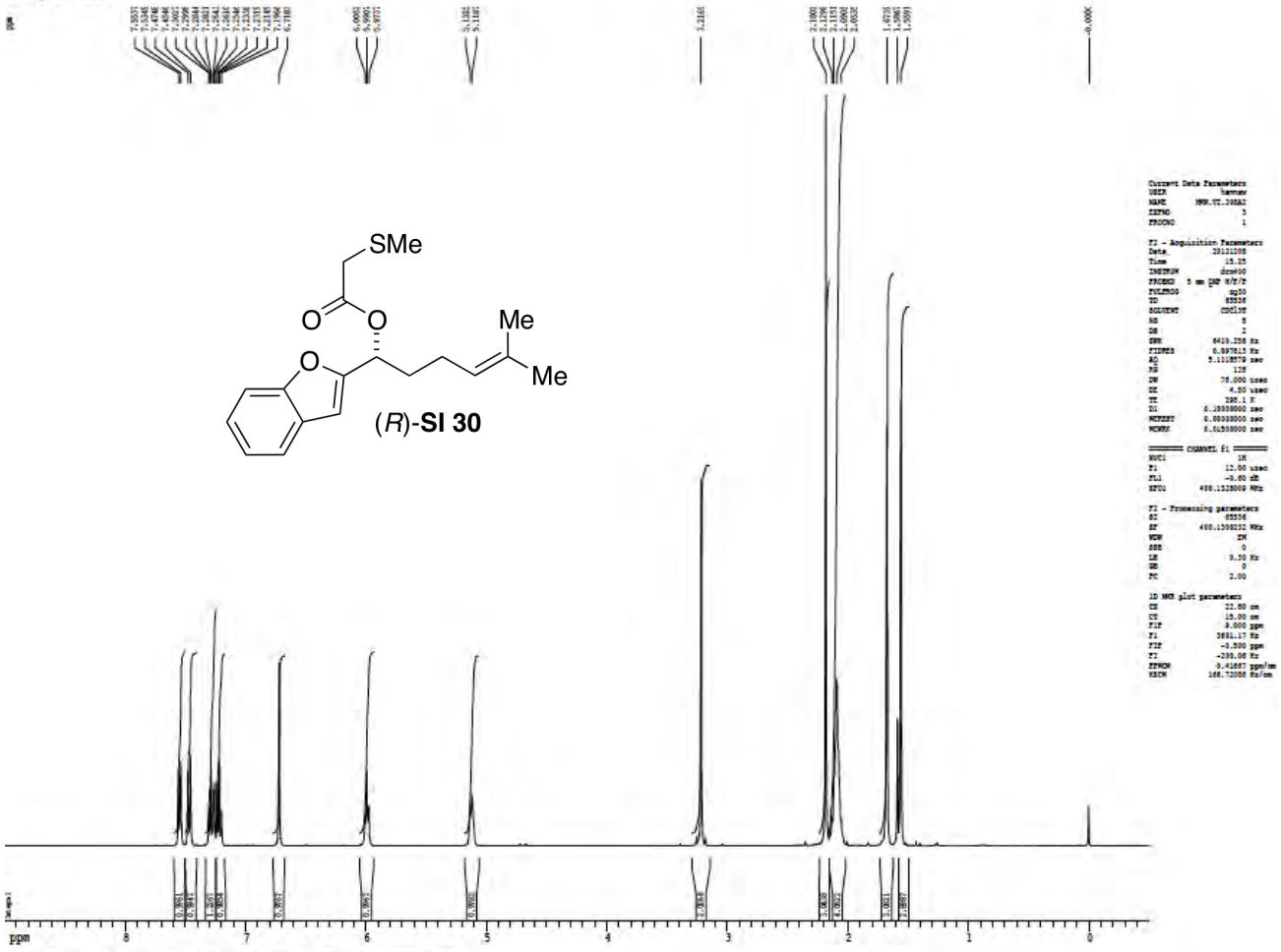
1H spectrum



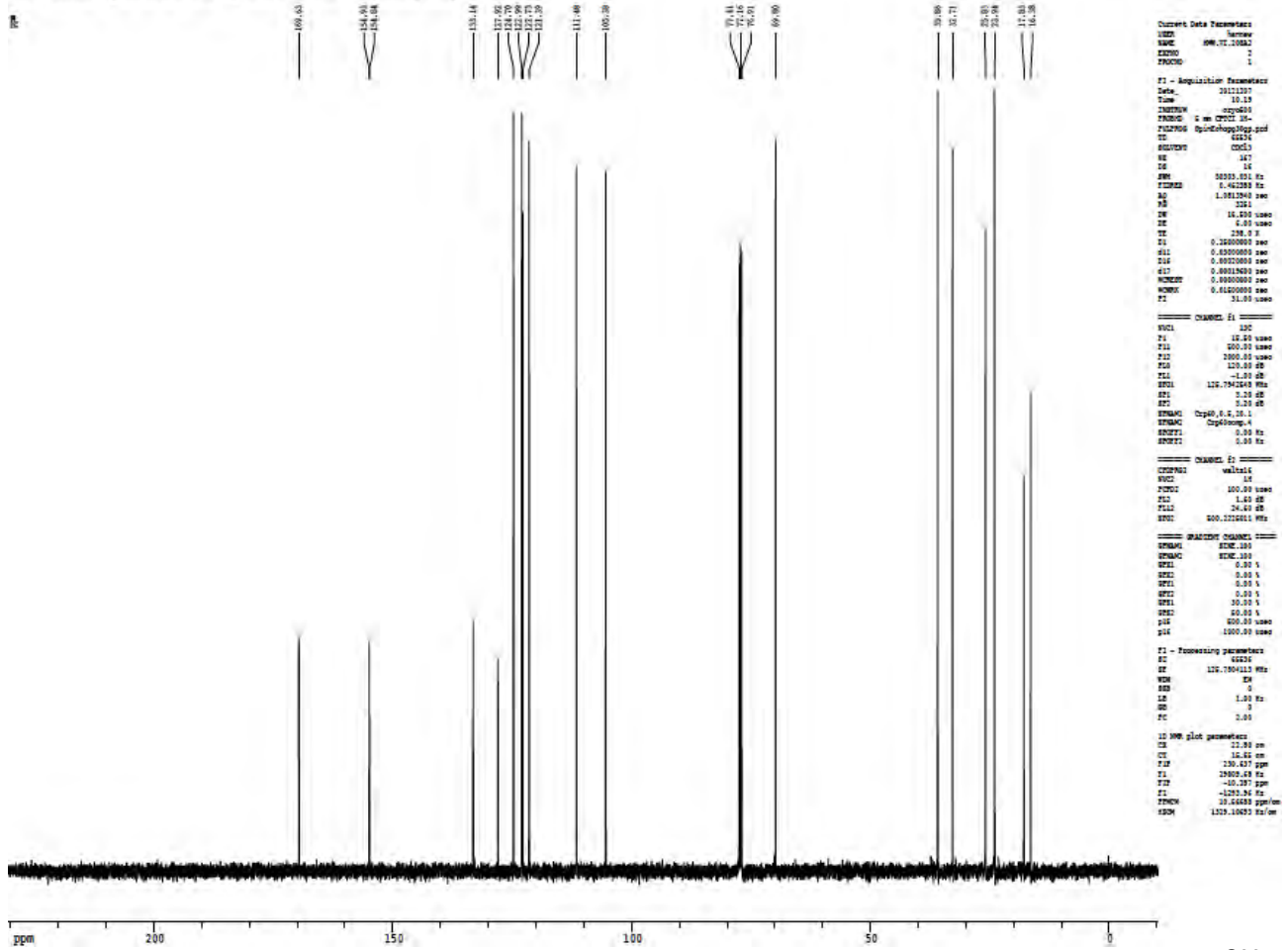
Z-restored spin-echo 13C spectrum with 1H decoupling



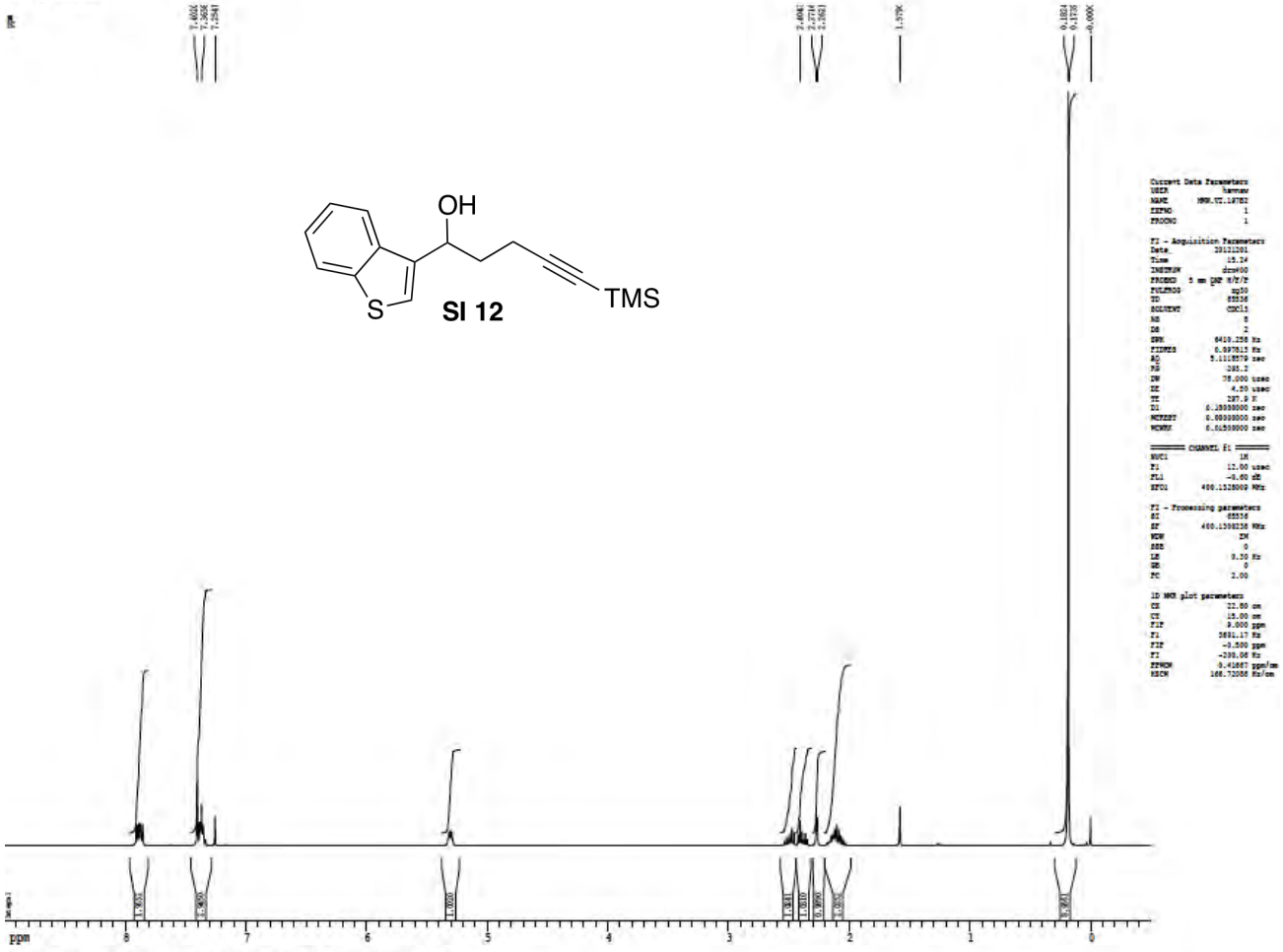
1H spectrum



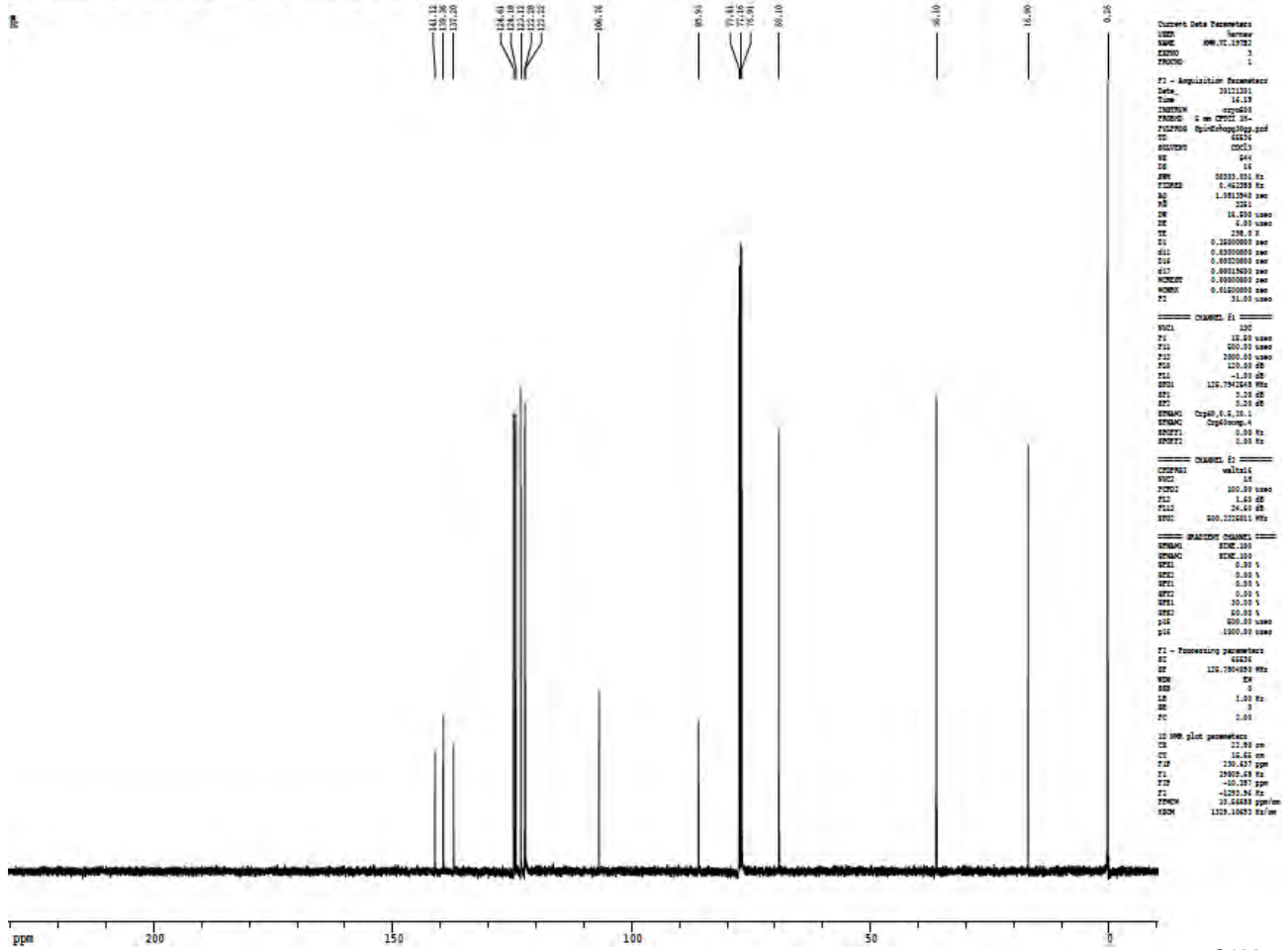
Z-restored spin-echo 13C spectrum with 1H decoupling



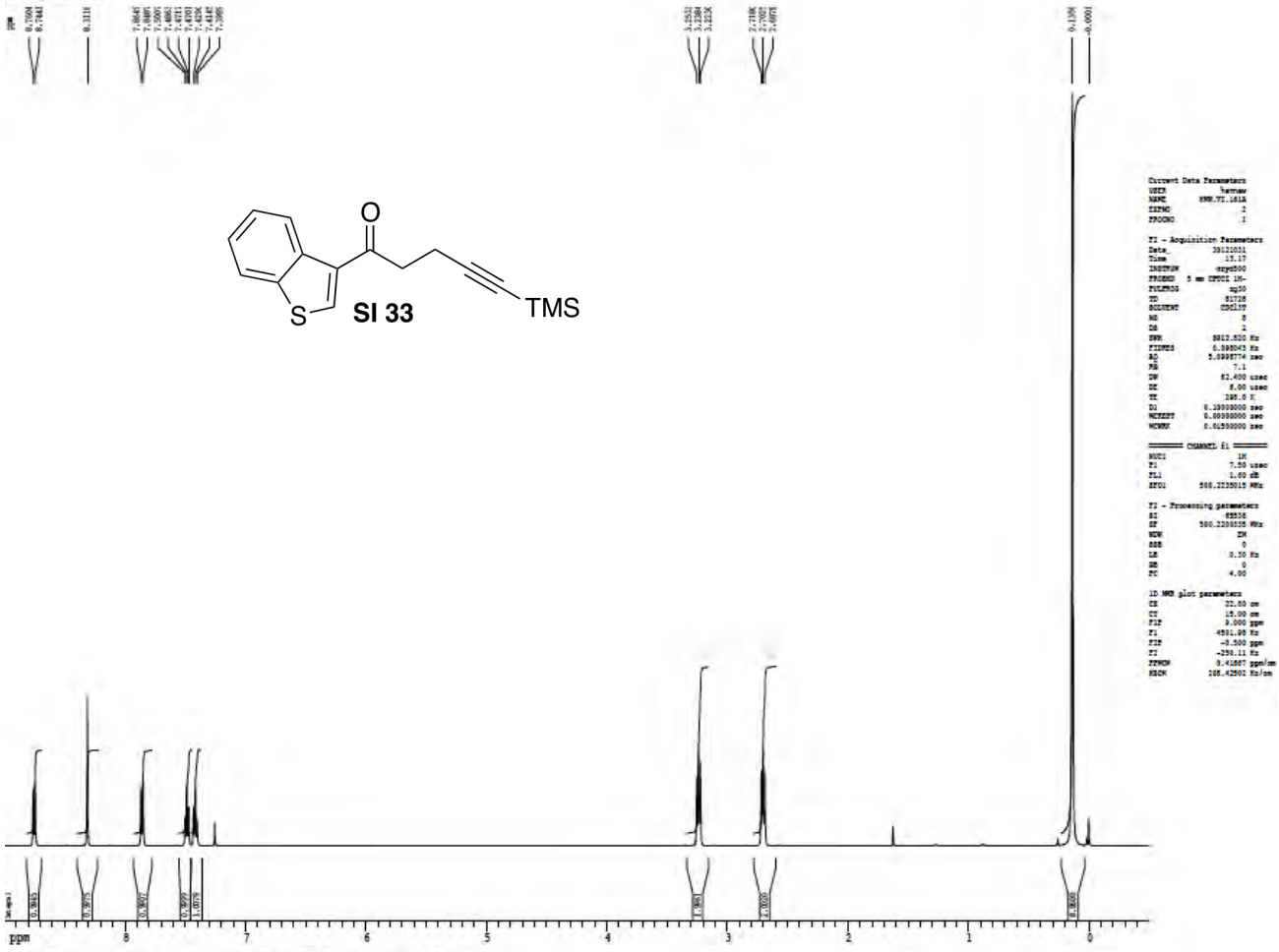
1H spectrum



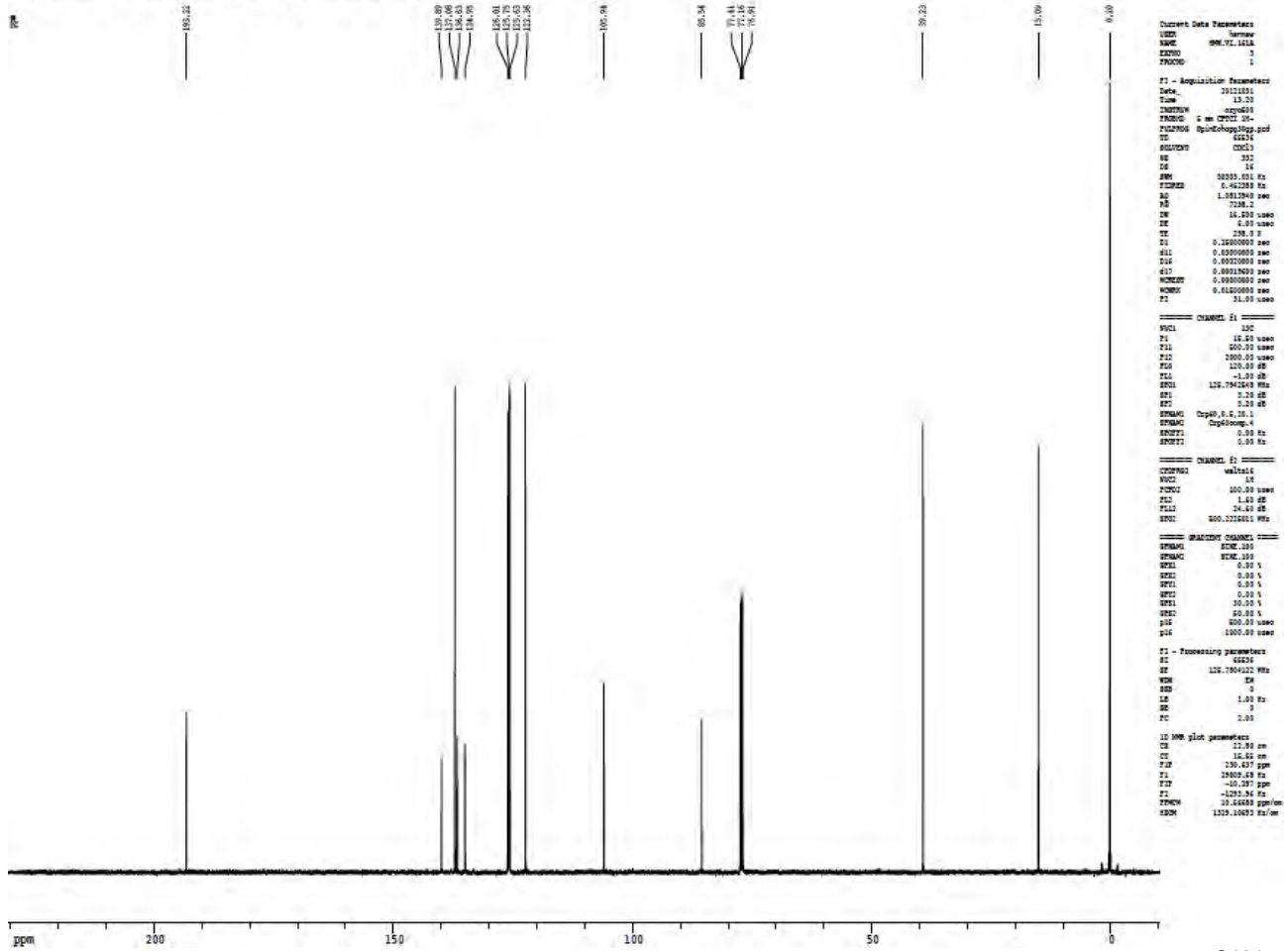
Z-restored spin-echo 13C spectrum with 1H decoupling



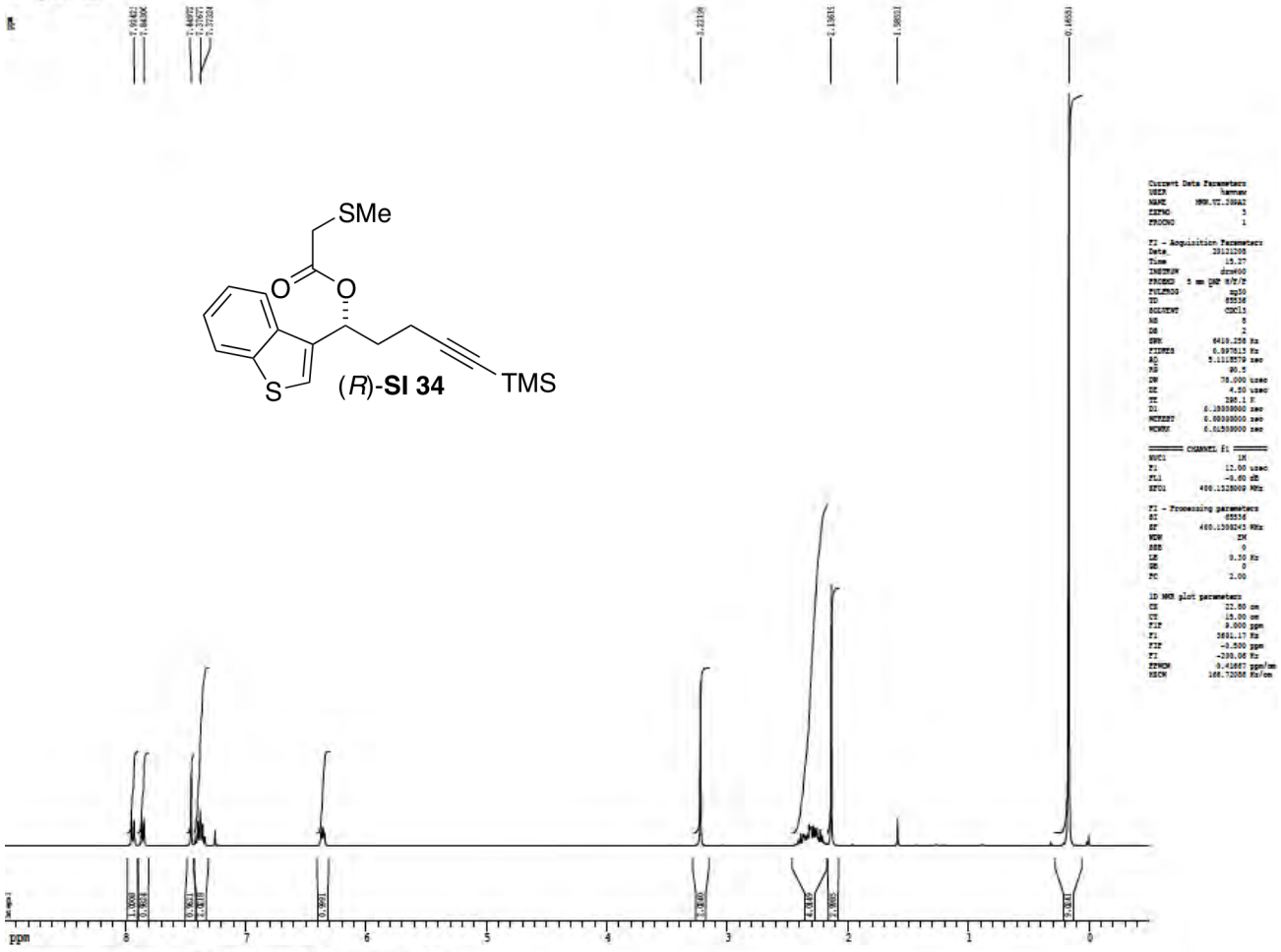
1H spectrum



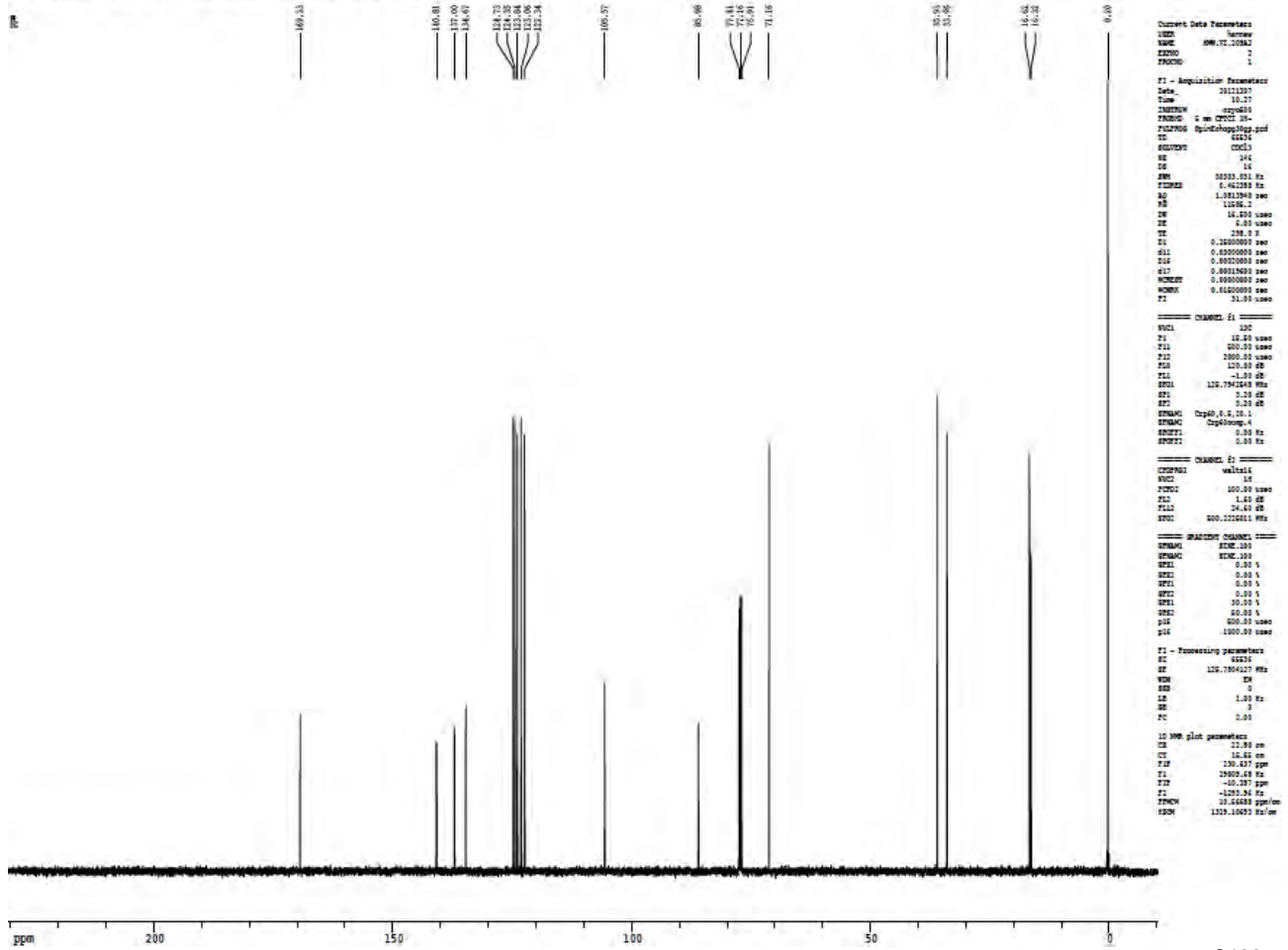
Z-restored spin-echo 13C spectrum with 1H decoupling



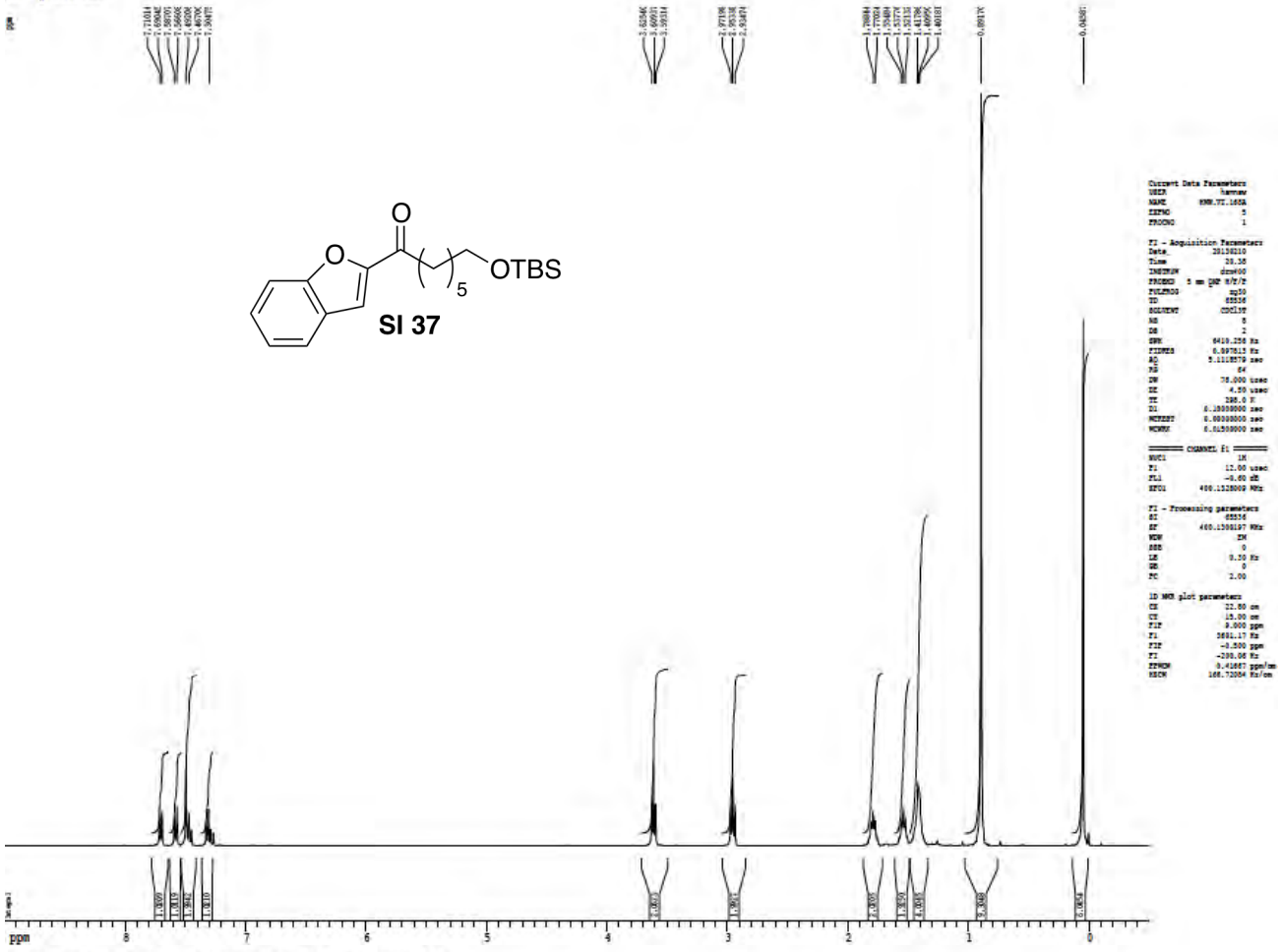
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling



1H spectrum



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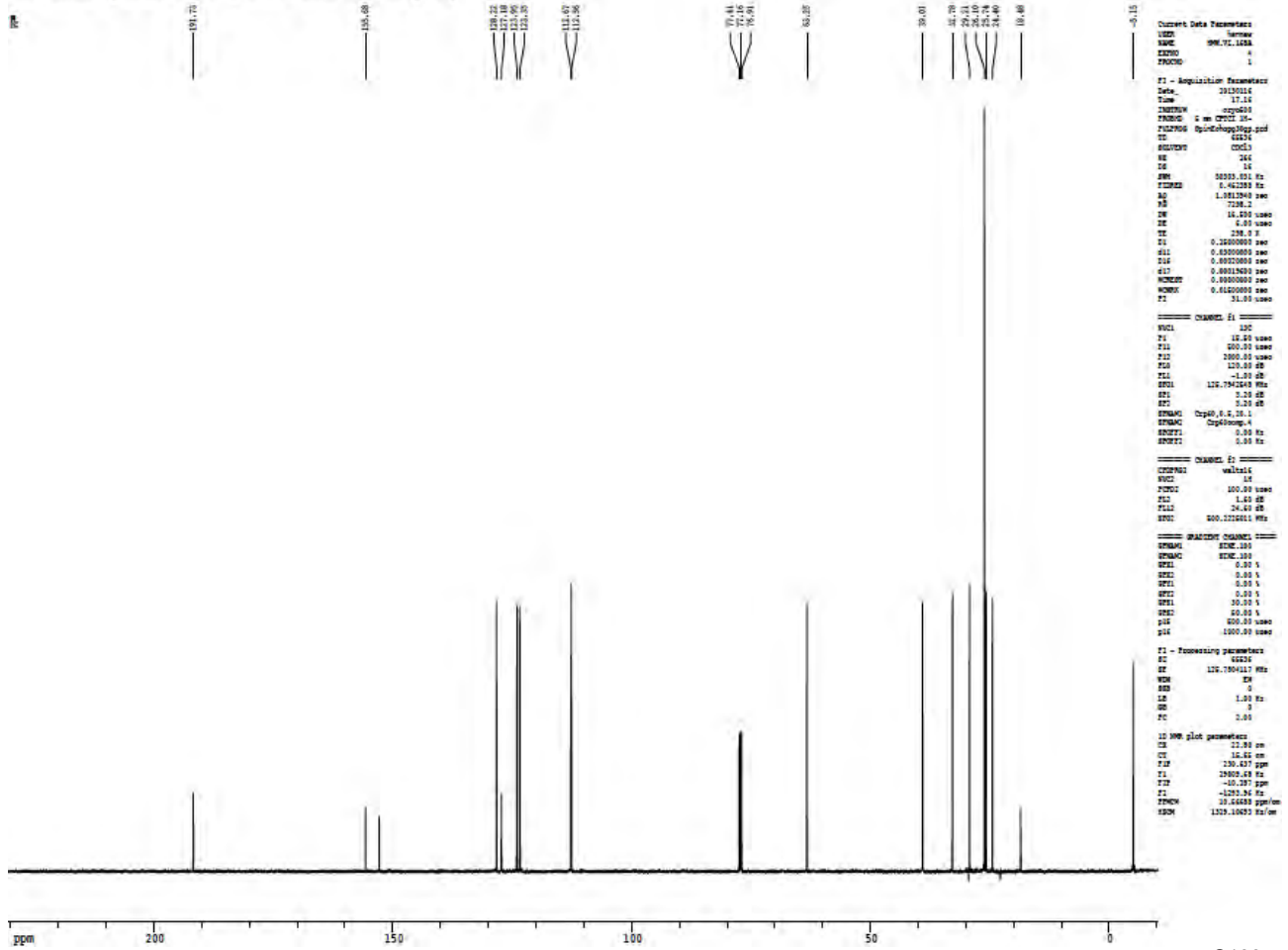
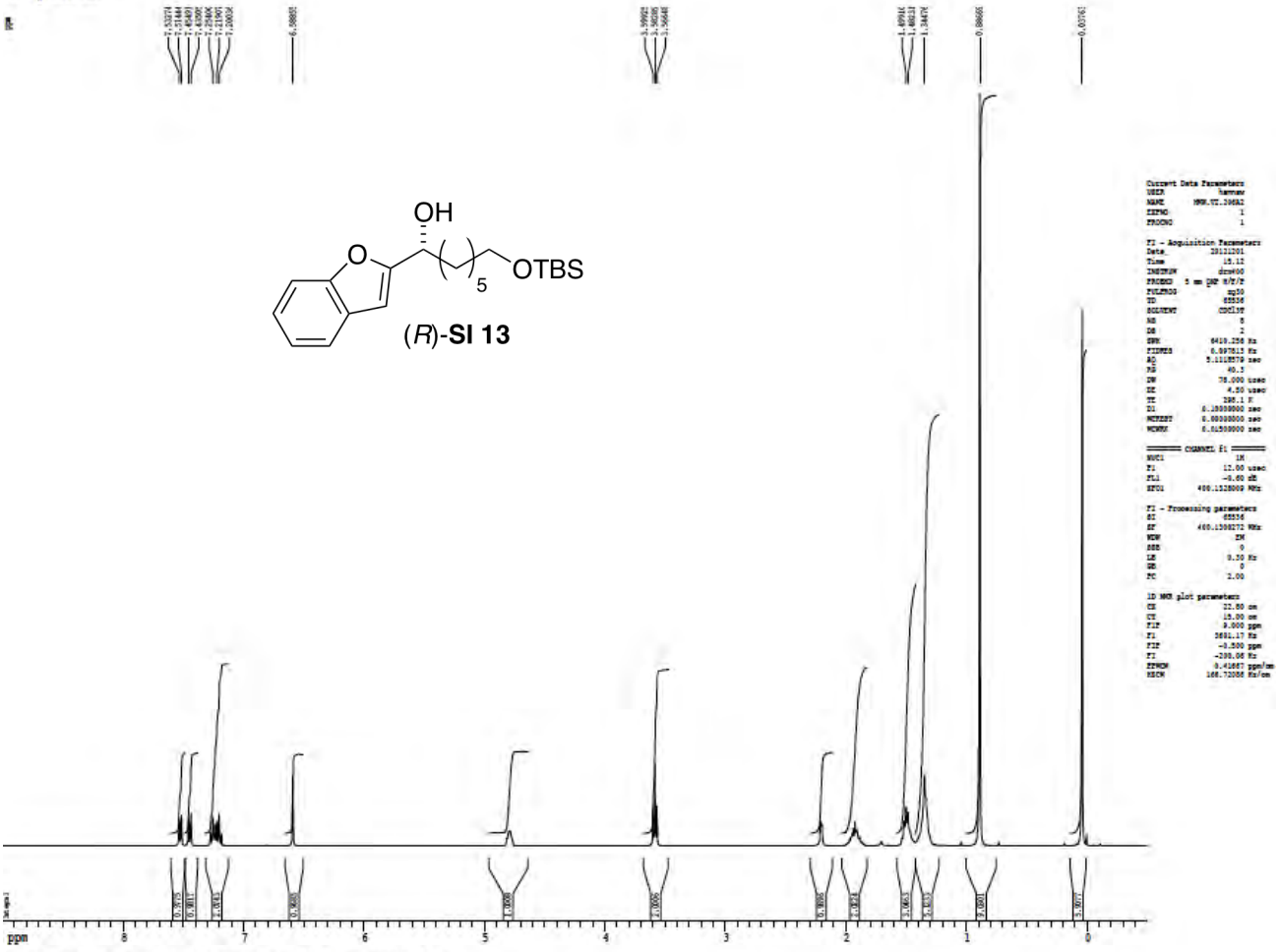
Z-restored spin-echo 13C spectrum with 1H decoupling

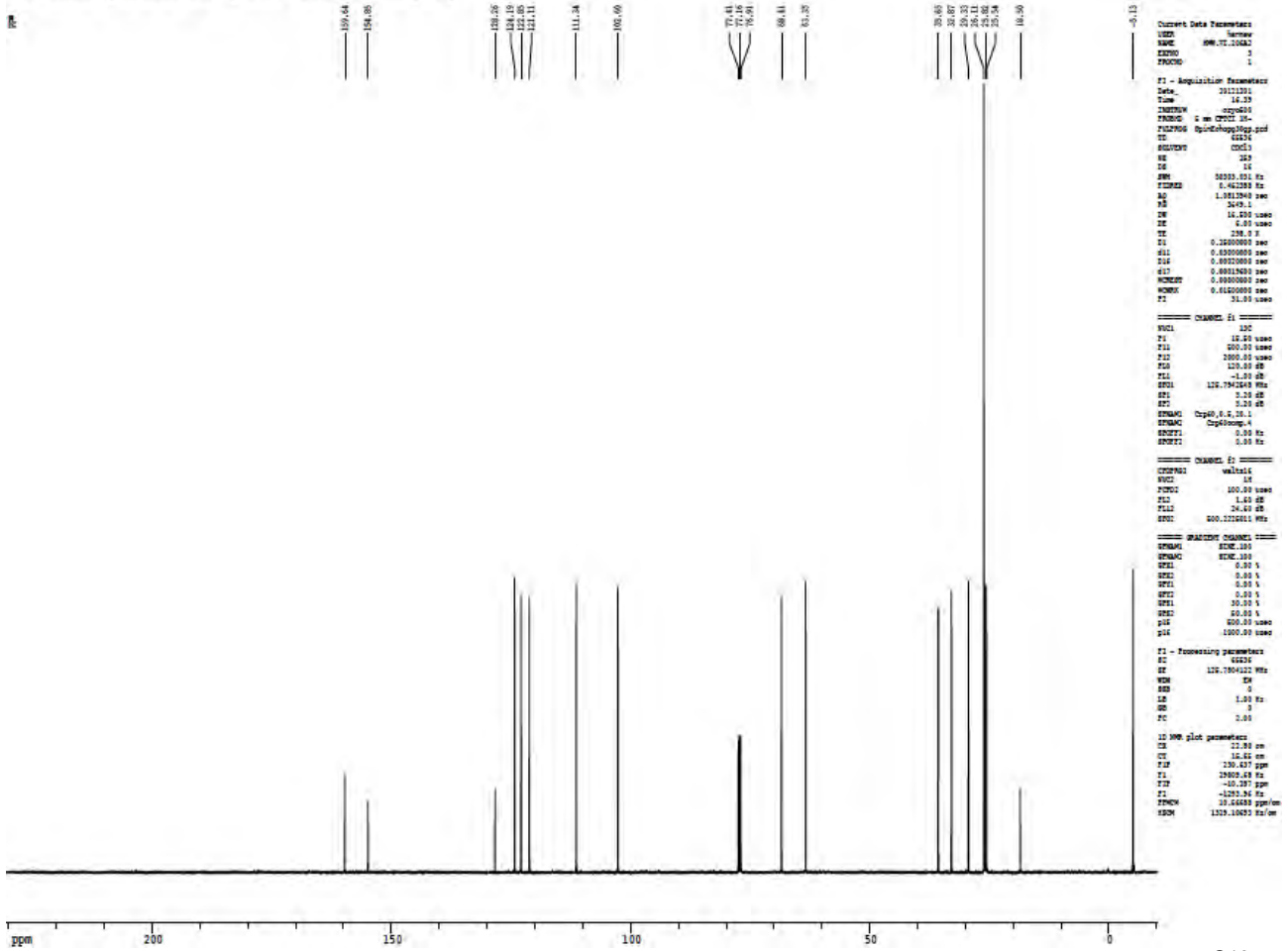


1H spectrum

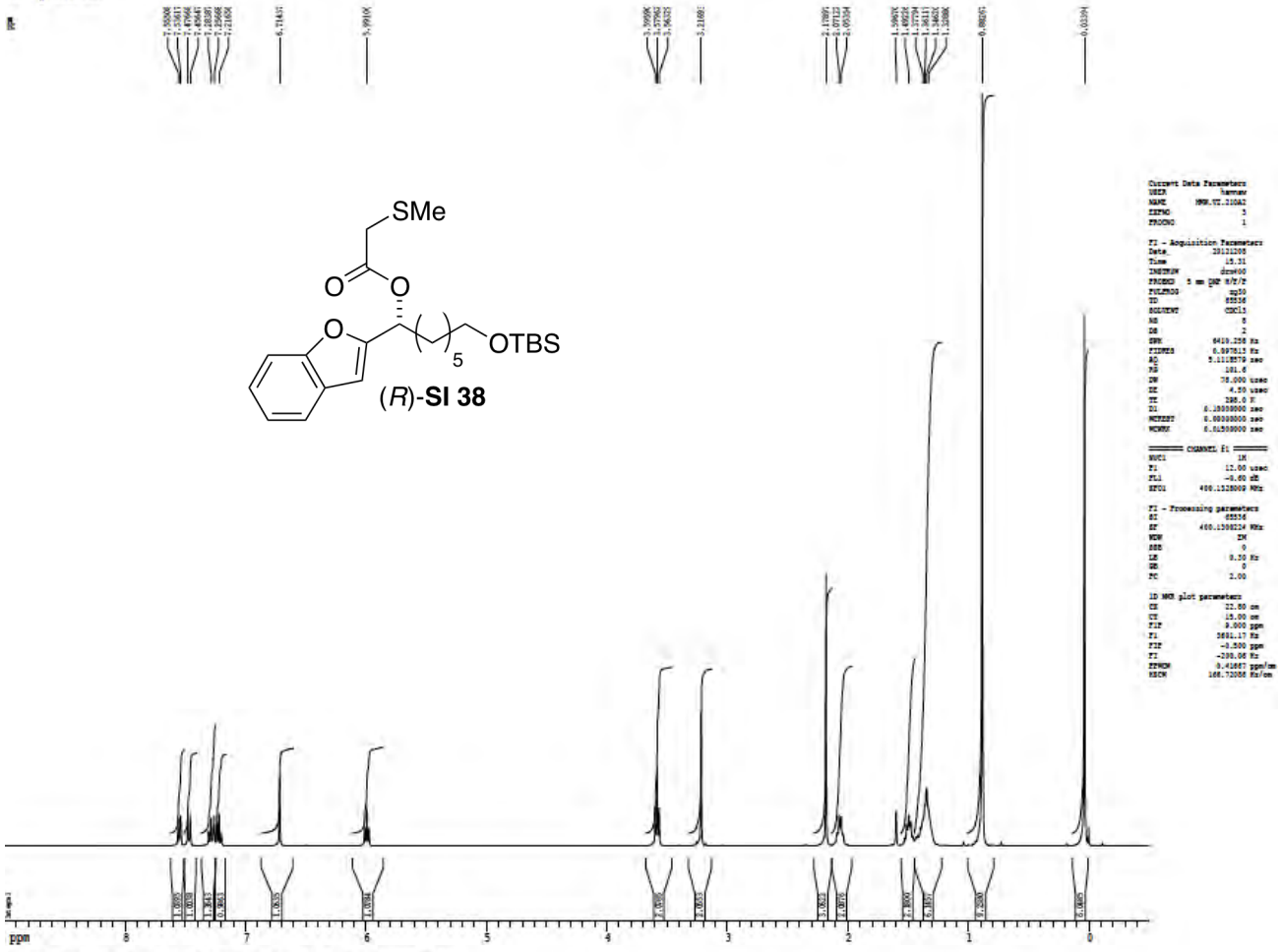


(*R*)-**SI 13**

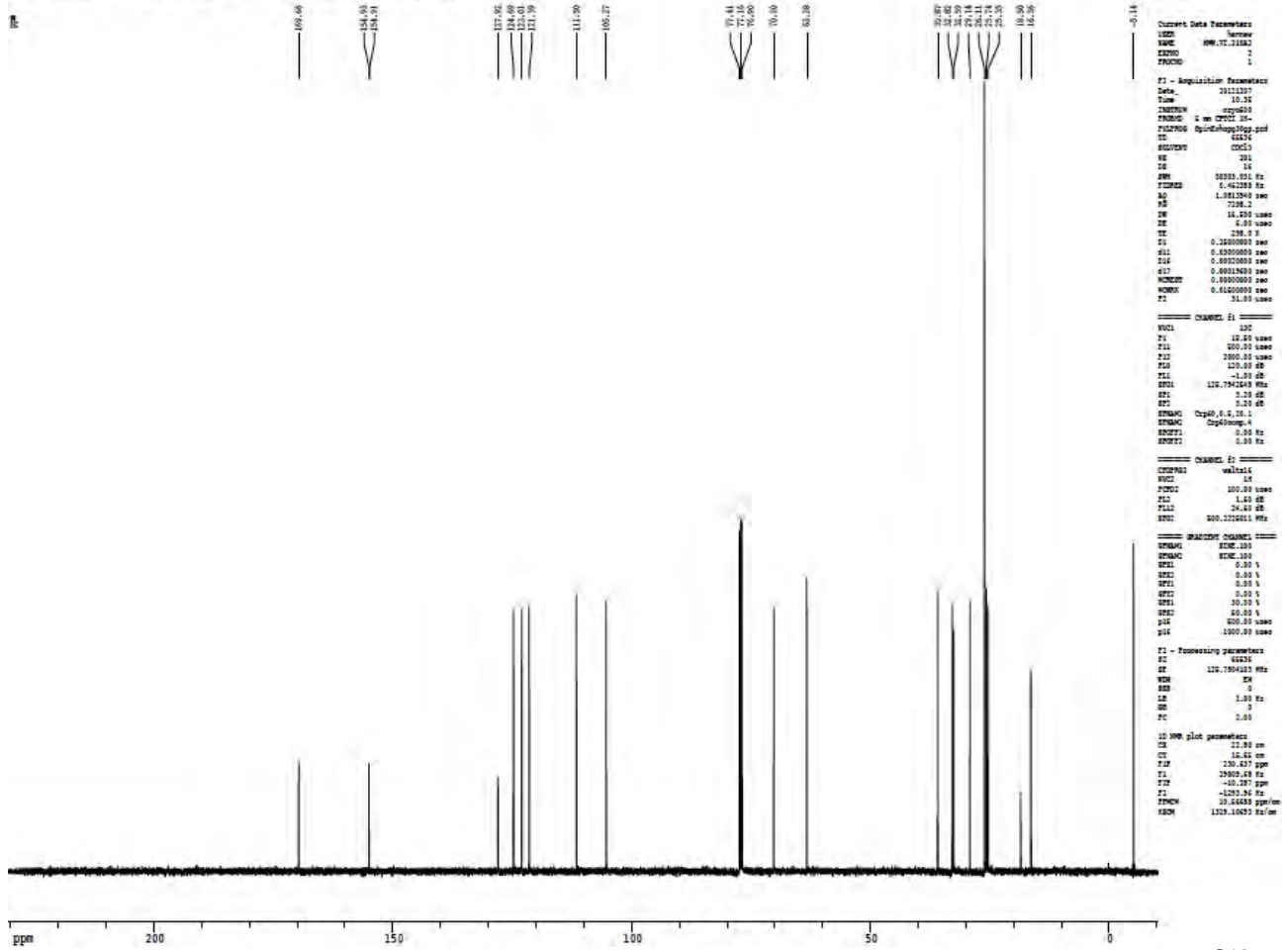
Z-restored spin-echo 13C spectrum with 1H decoupling



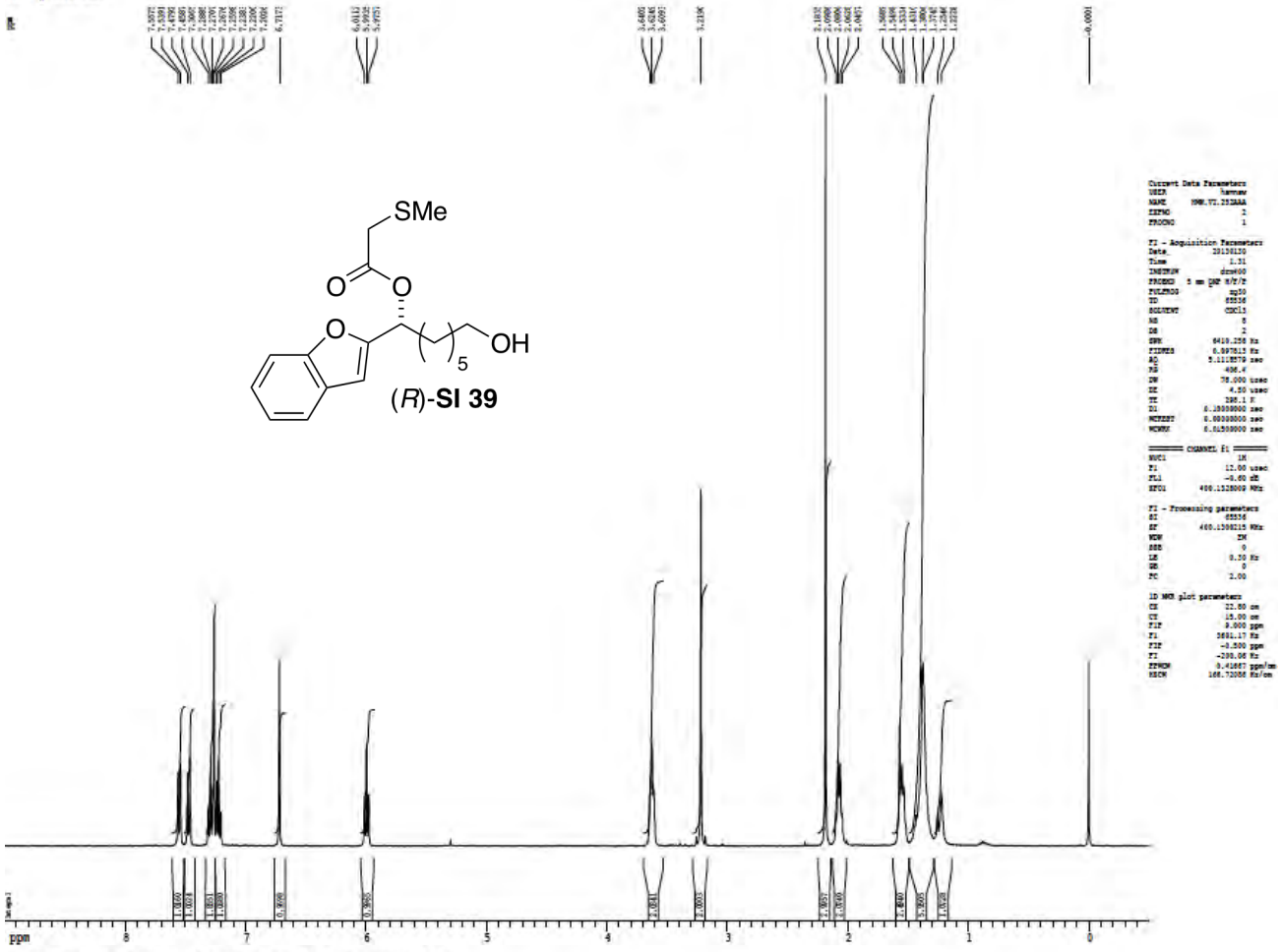
1H spectrum



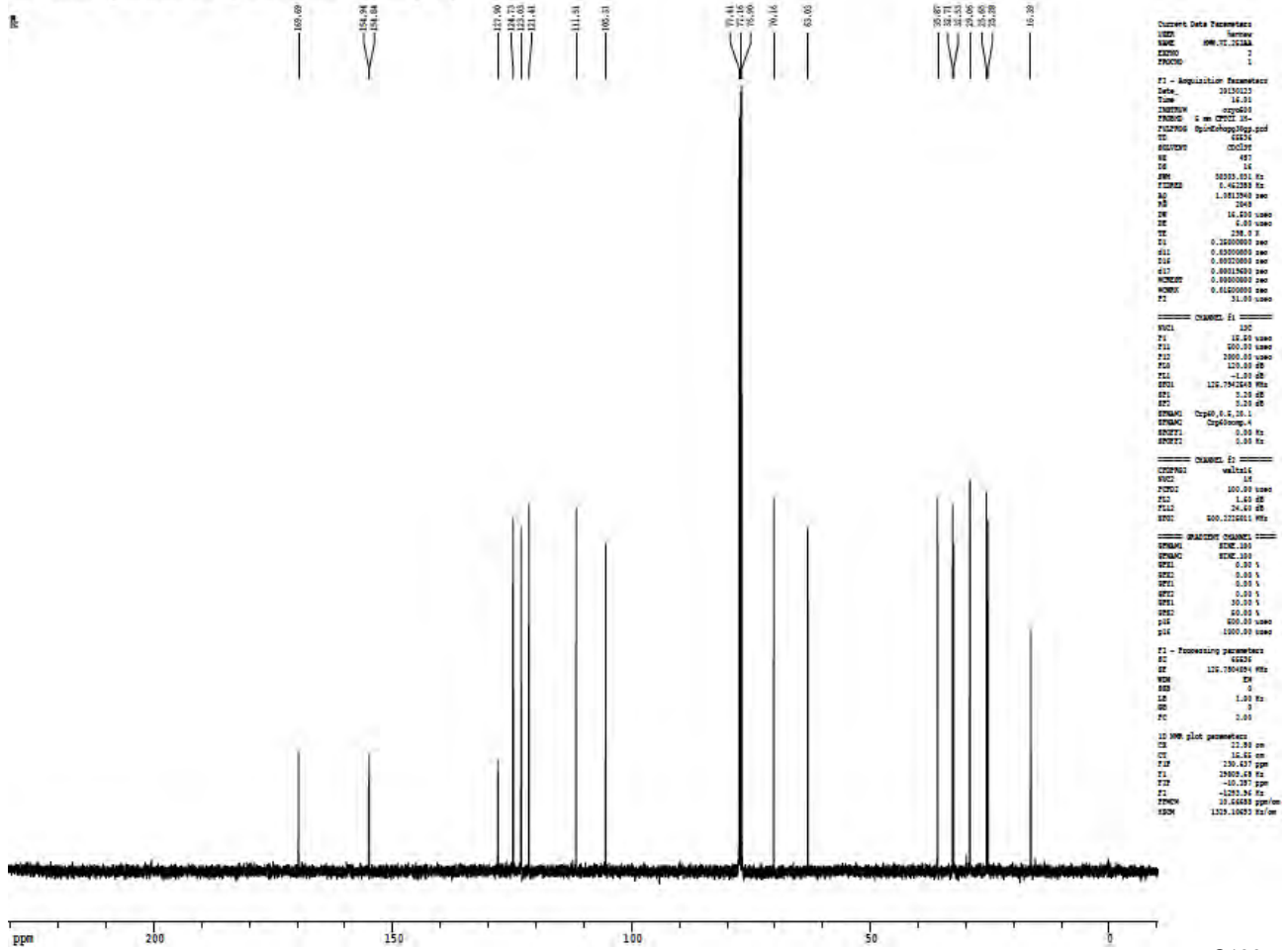
Z-restored spin-echo 13C spectrum with 1H decoupling



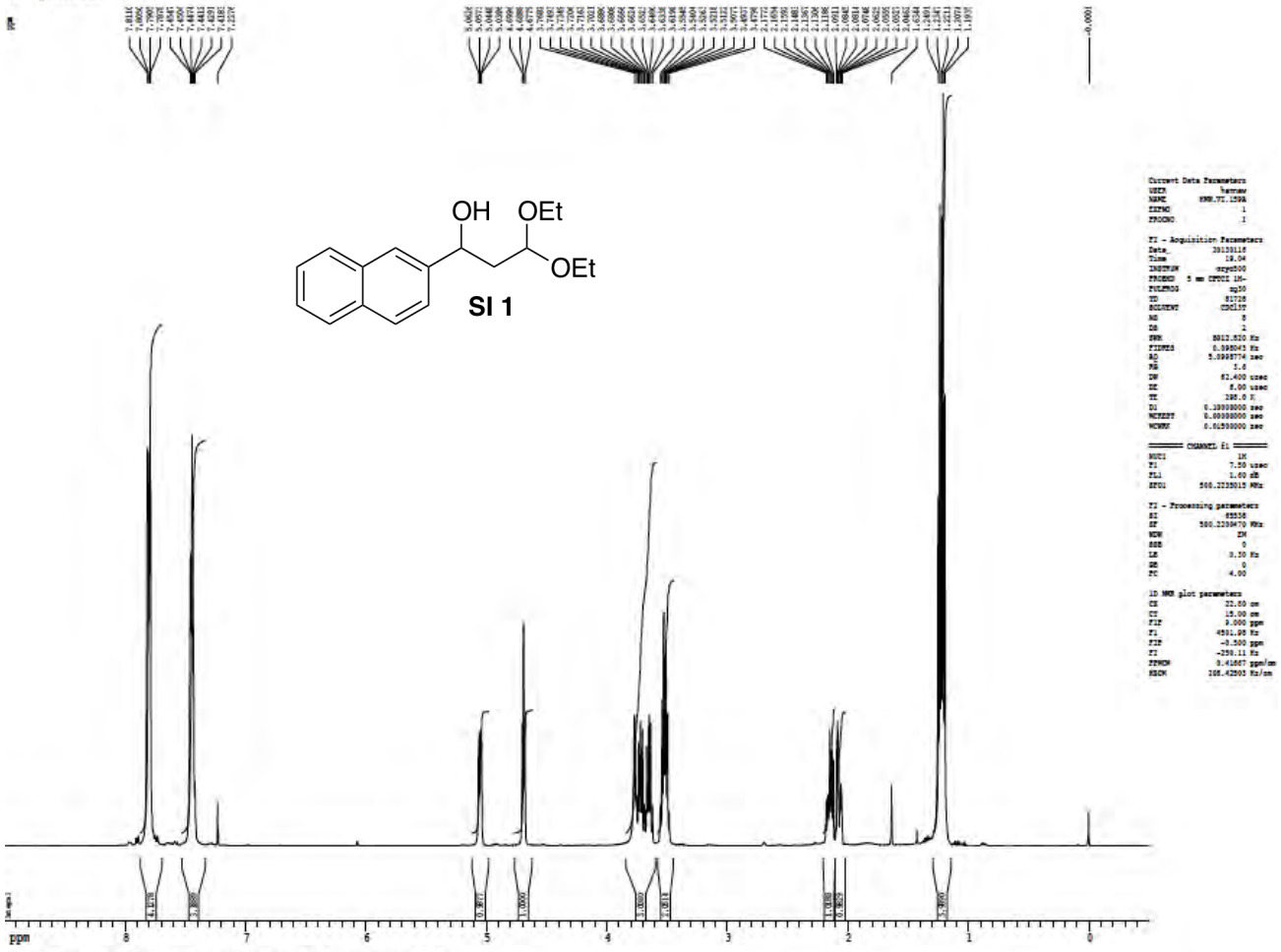
1H spectrum



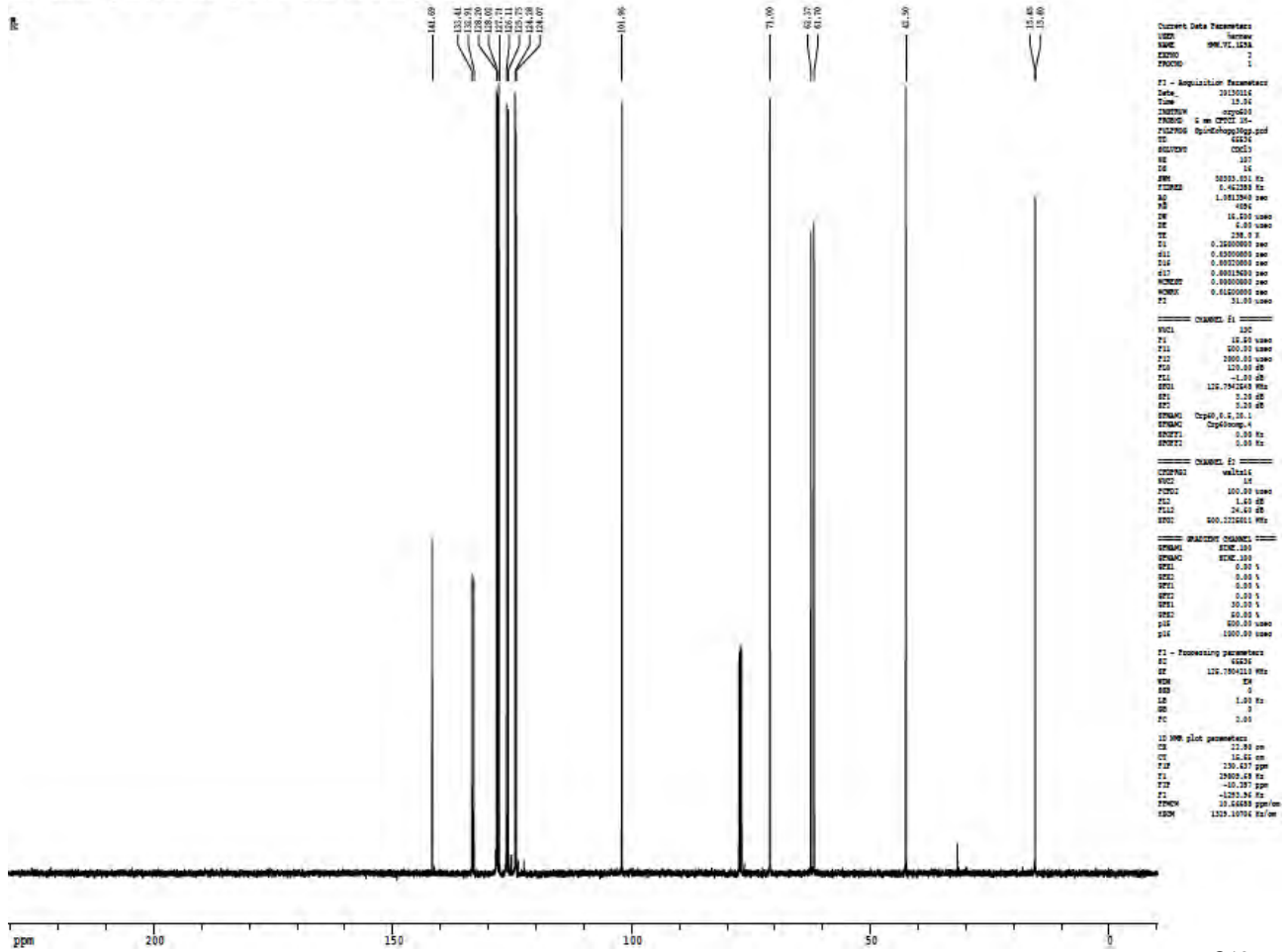
Z-restored spin-echo 13C spectrum with 1H decoupling



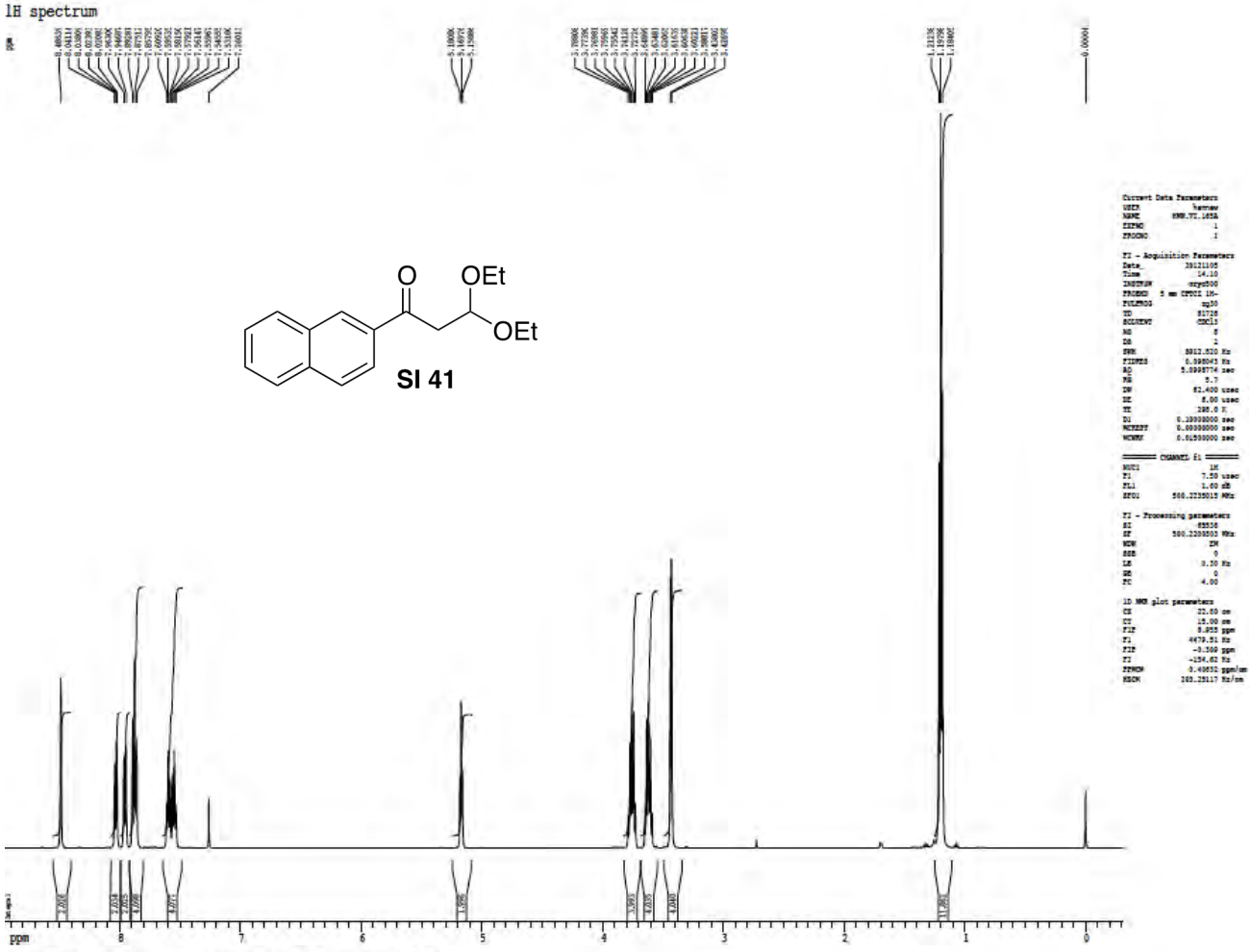
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling

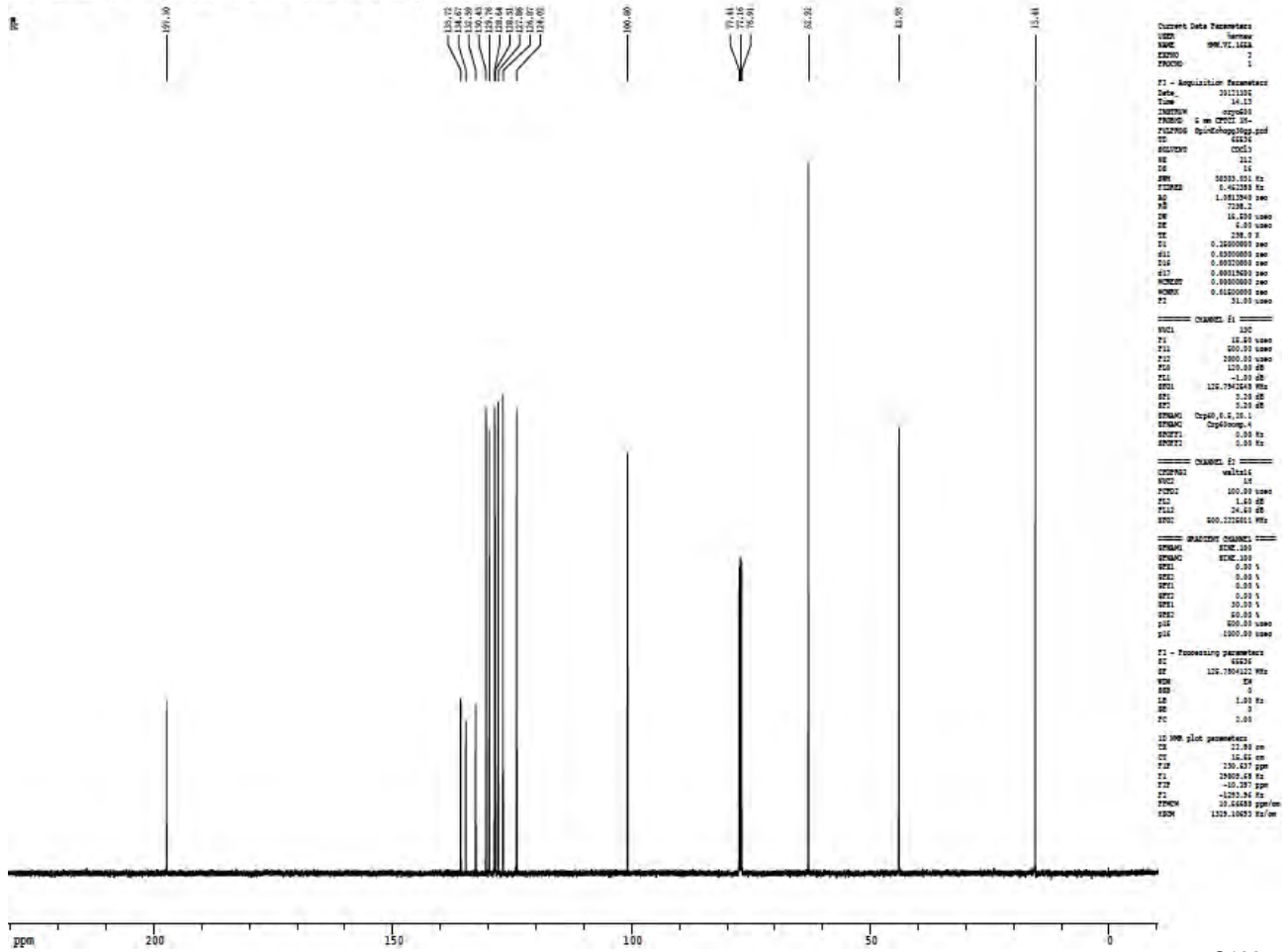


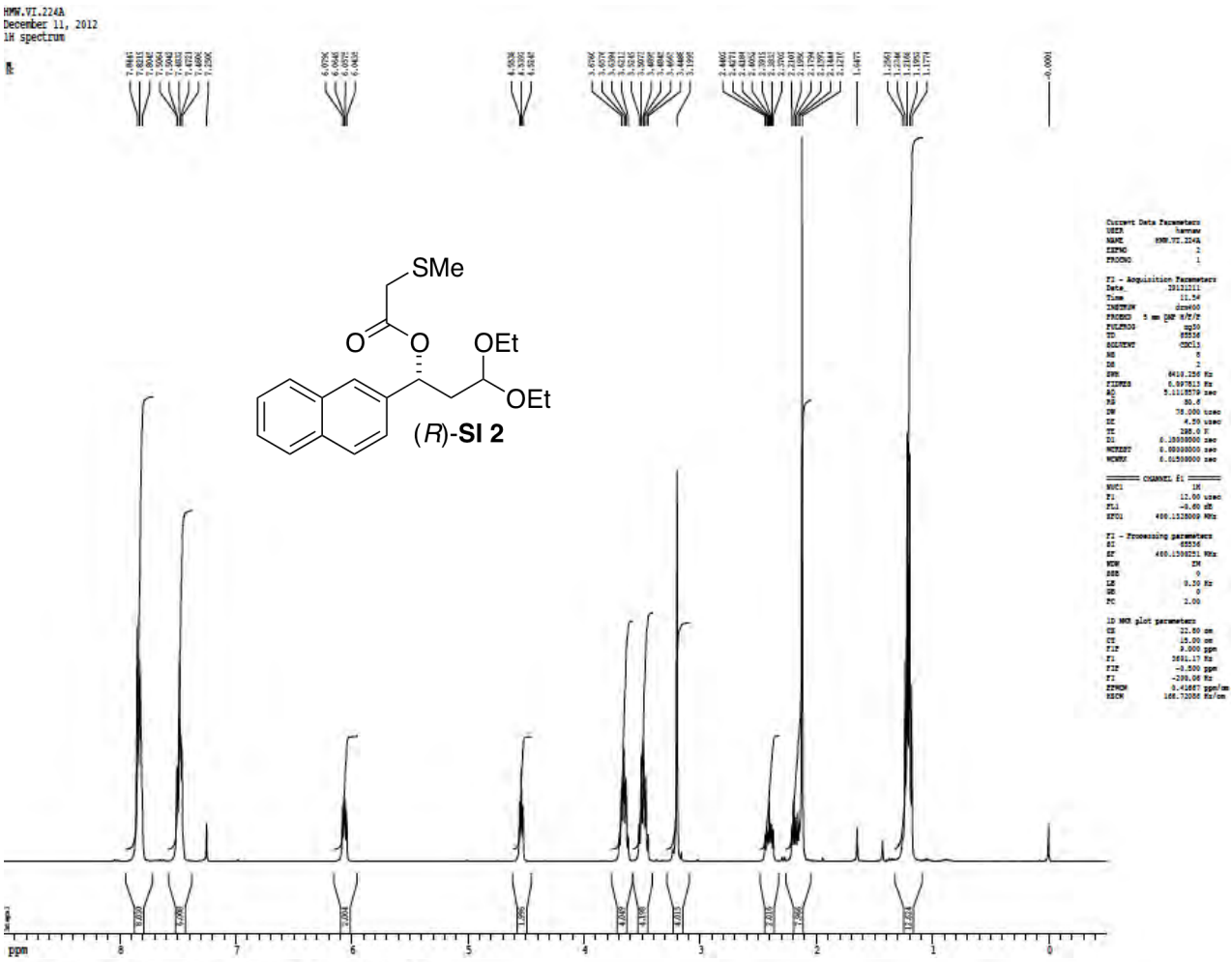
1H spectrum



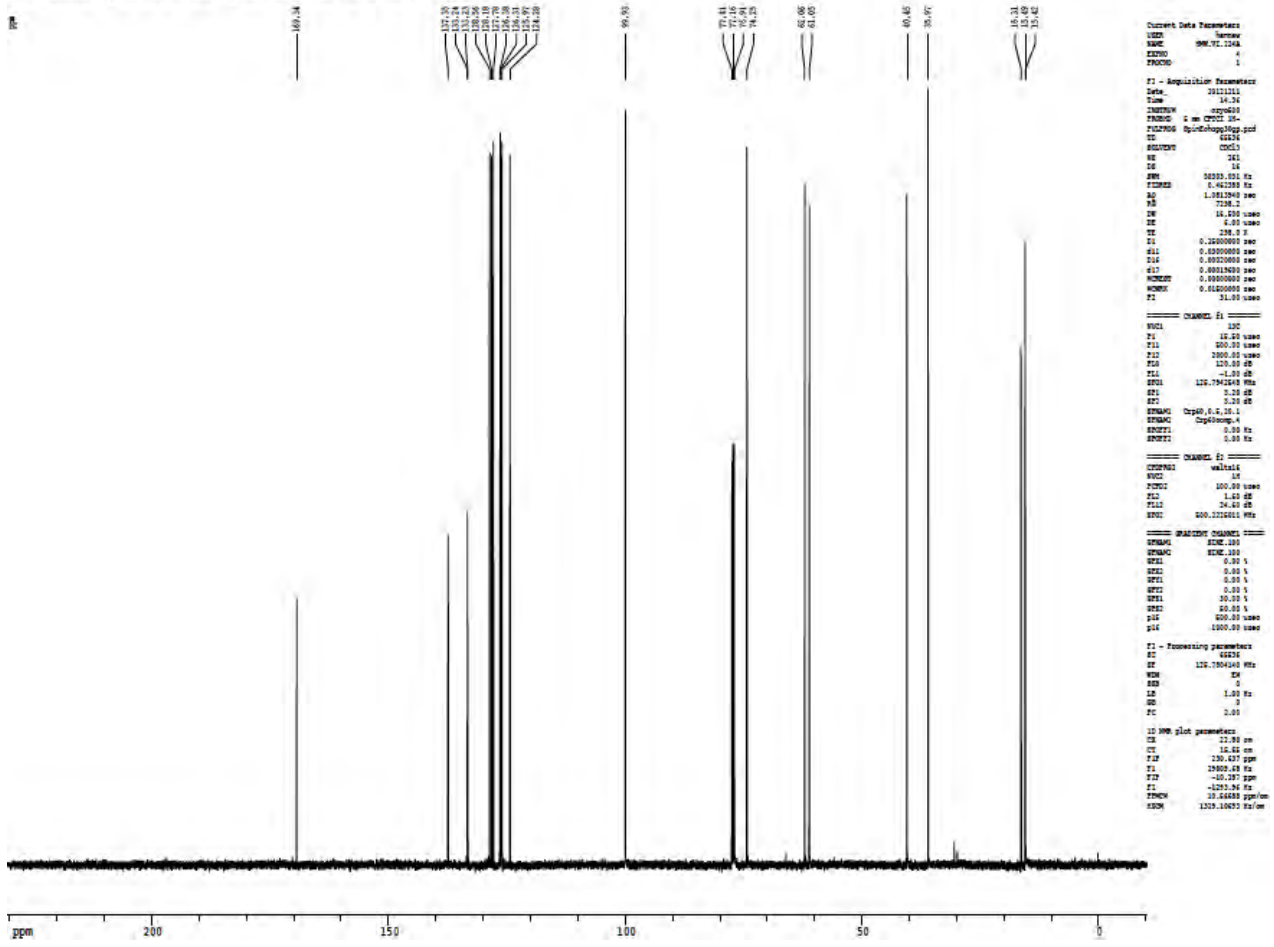
SI 41

Z-restored spin-echo 13C spectrum with 1H decoupling

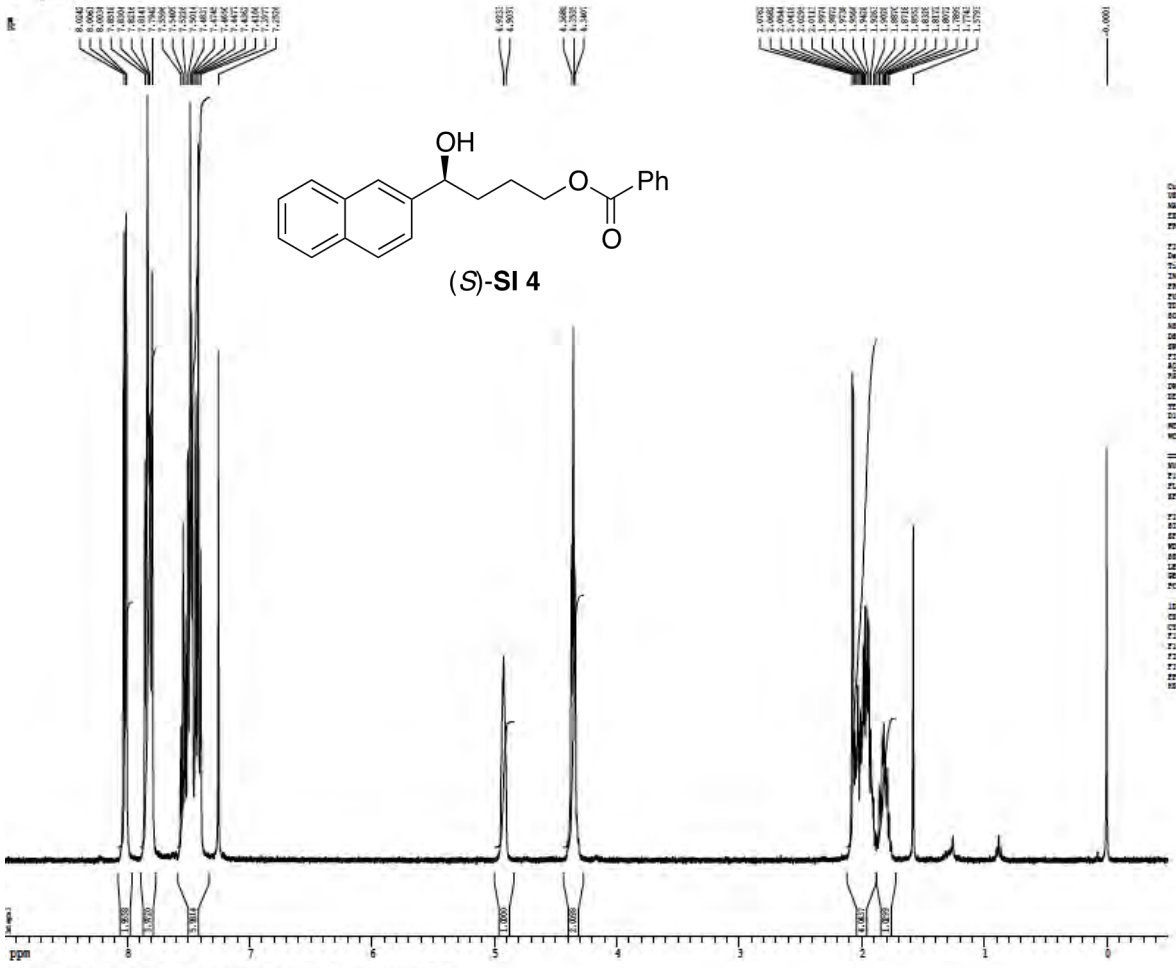




Z-restored spin-echo 13C spectrum with 1H decoupling

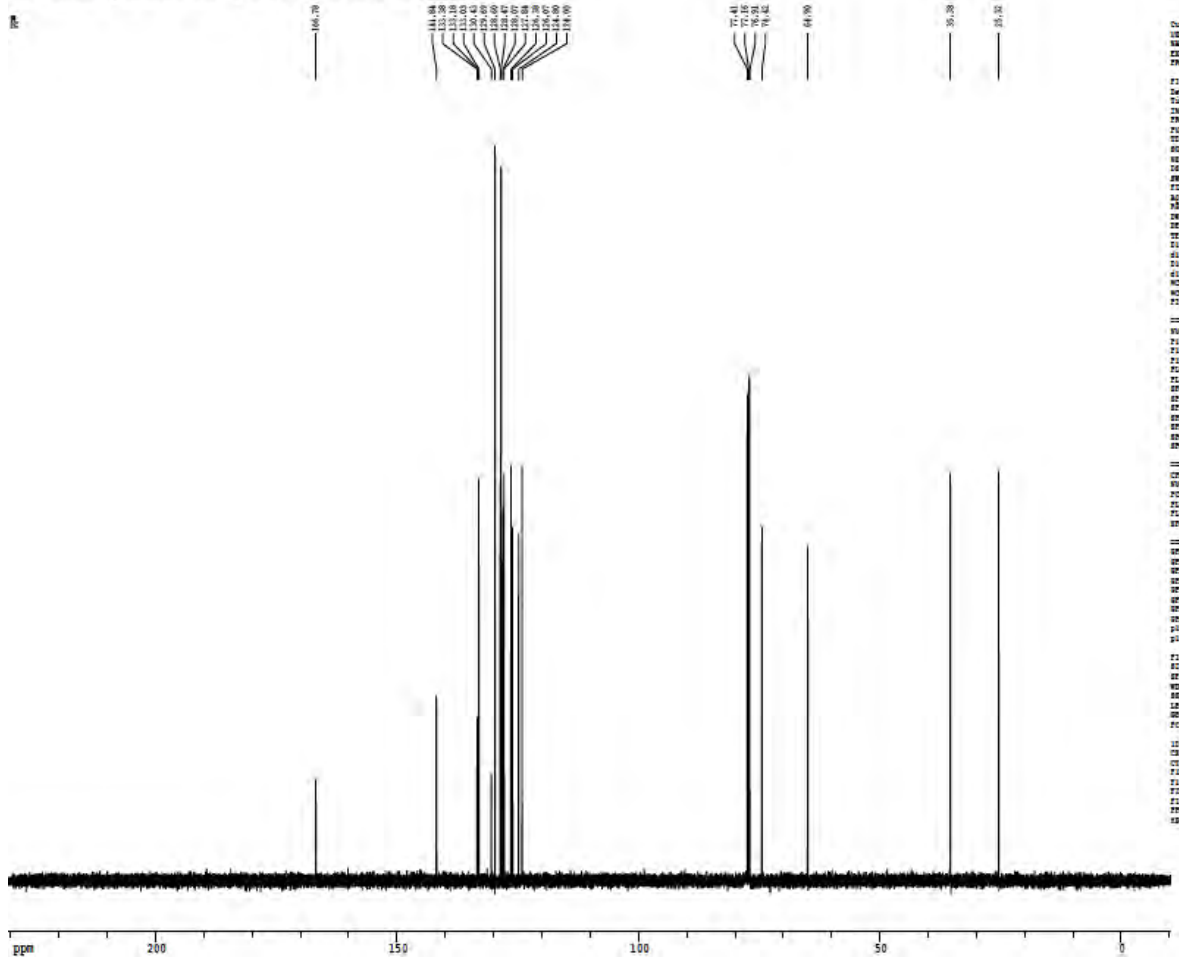


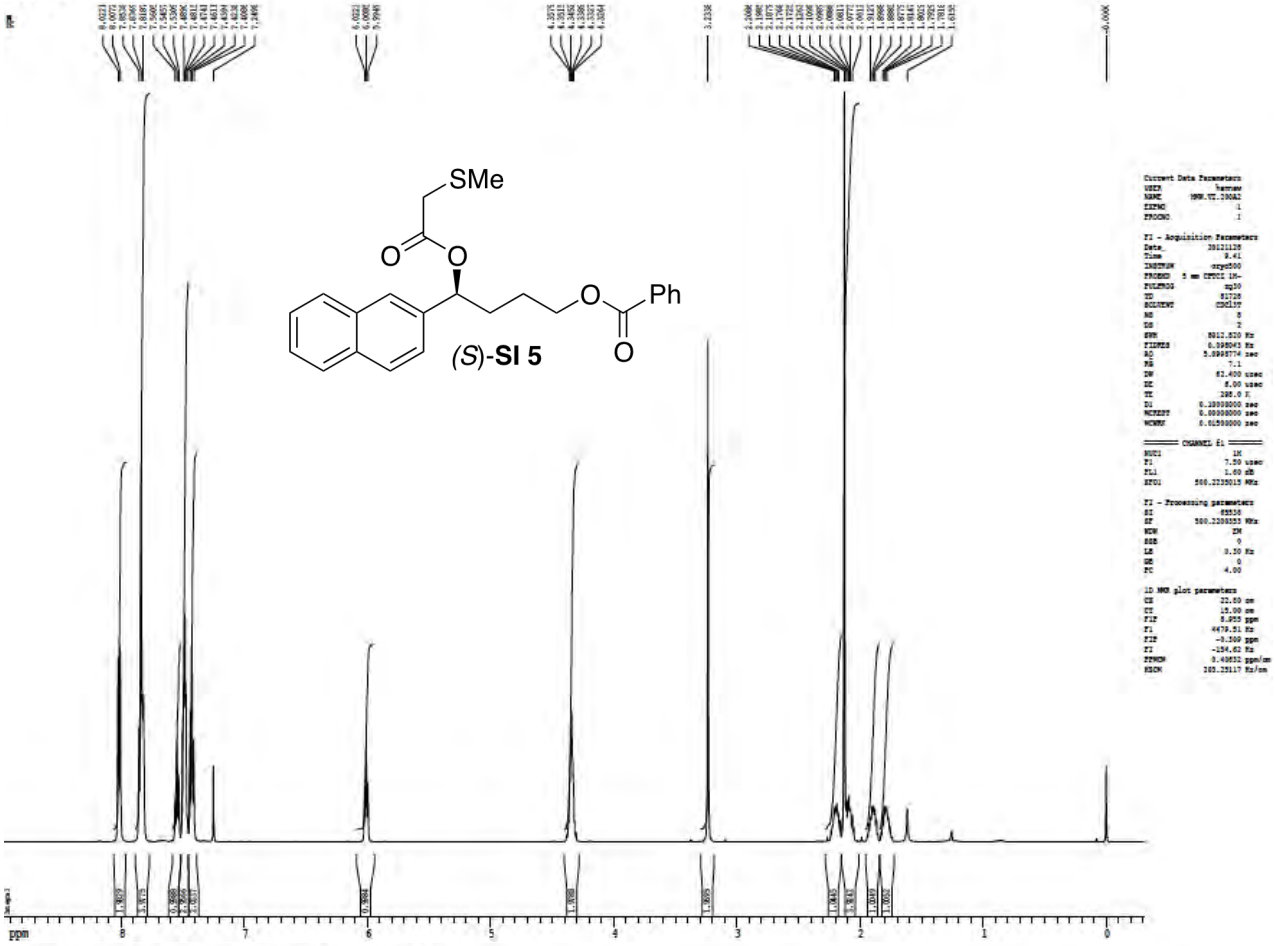
1H spectrum



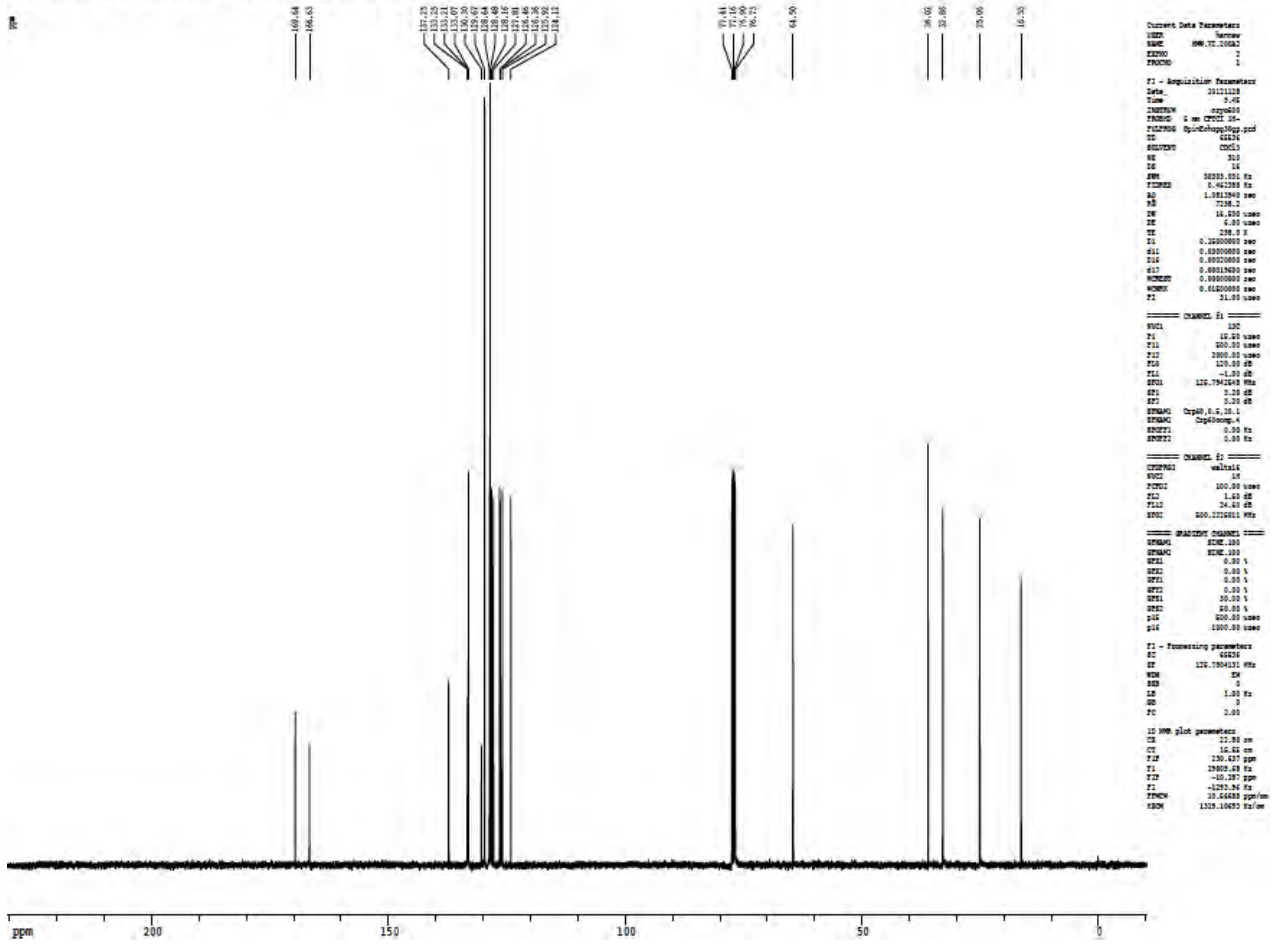
(*S*)-**SI 4**

Z-restored spin-echo 13C spectrum with 1H decoupling

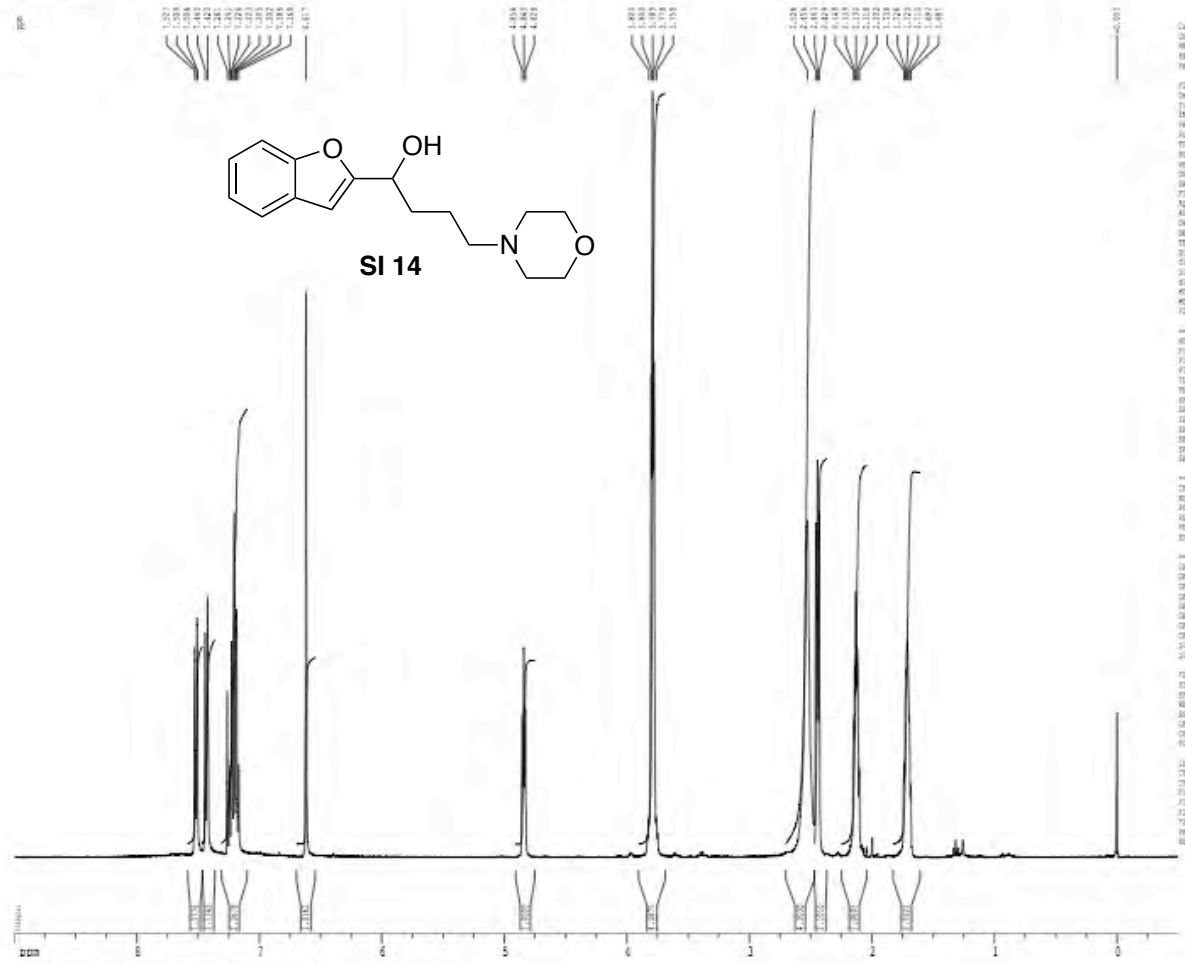




Z-restored spin-echo 13C spectrum with 1H decoupling

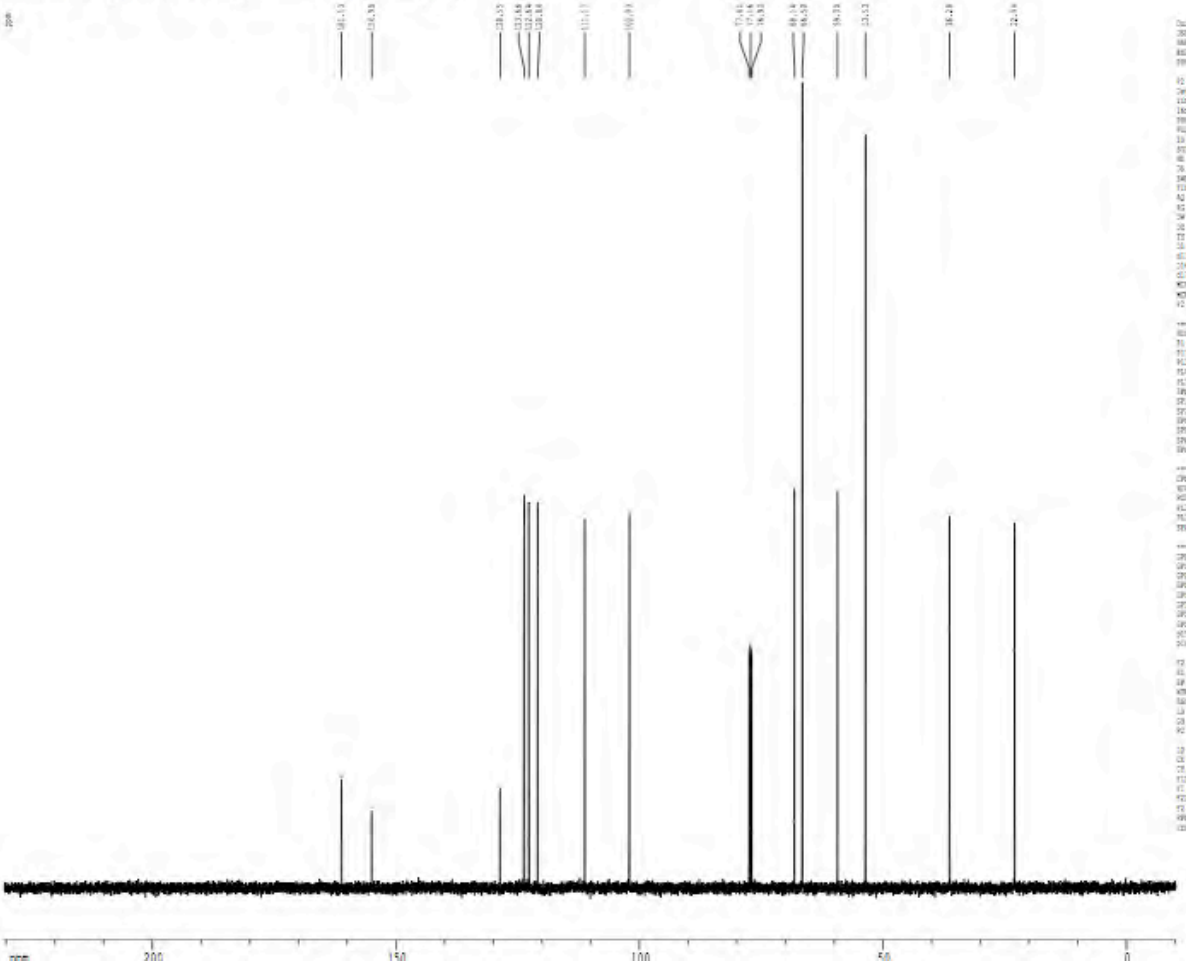


1H Spectrum

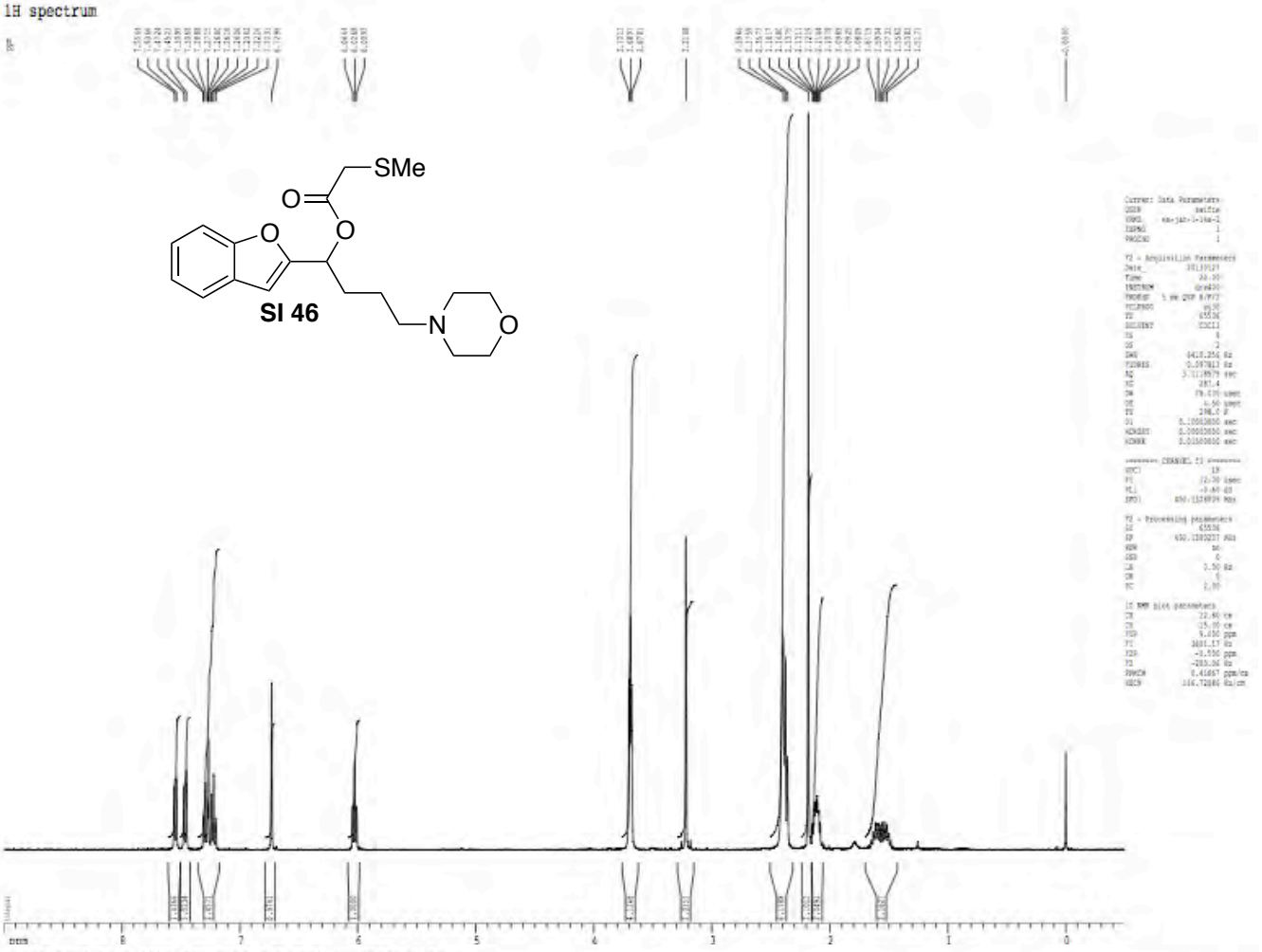


SI 14

Z-restored spin-echo 13C spectrum with 1H decoupling

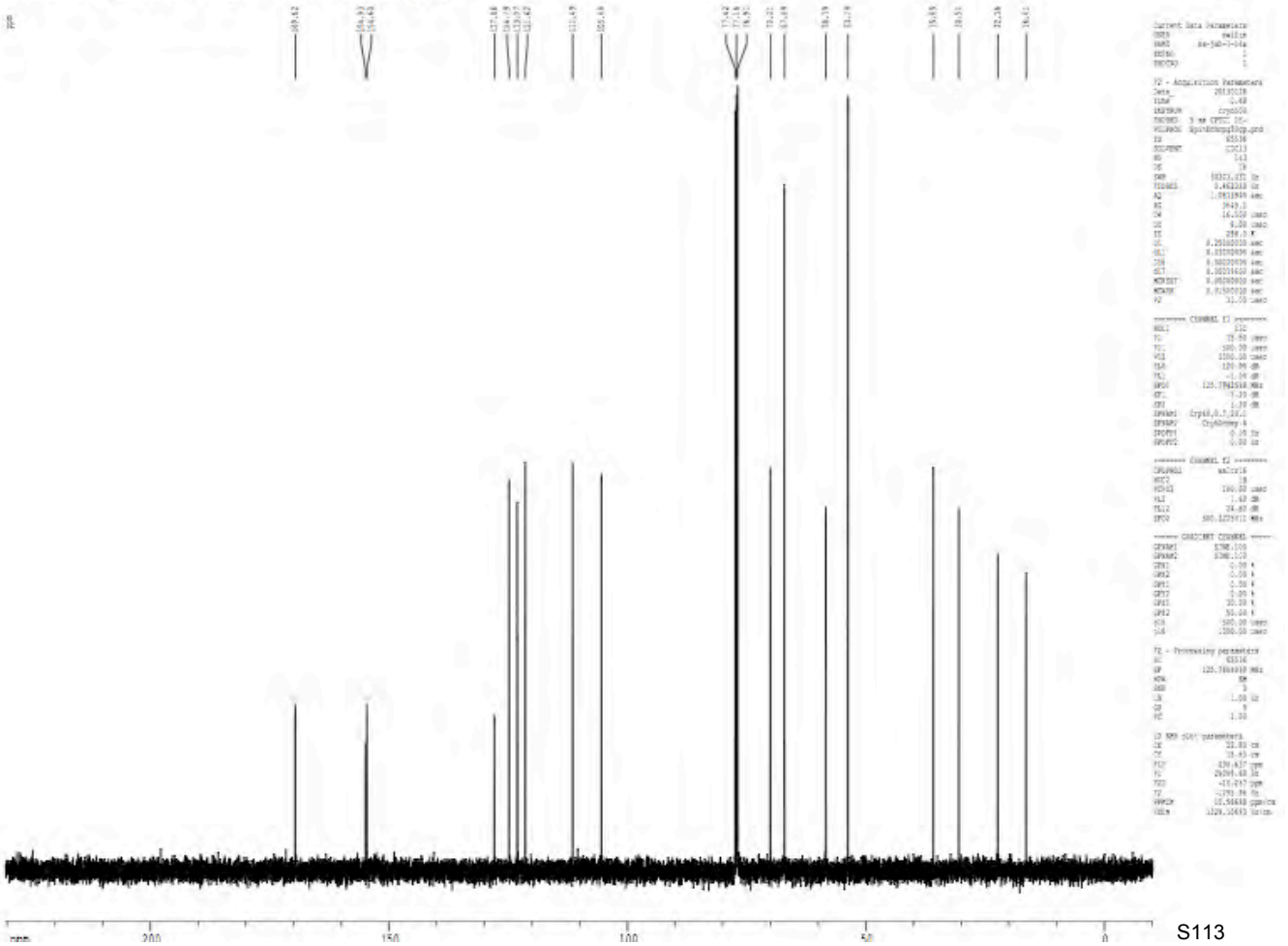


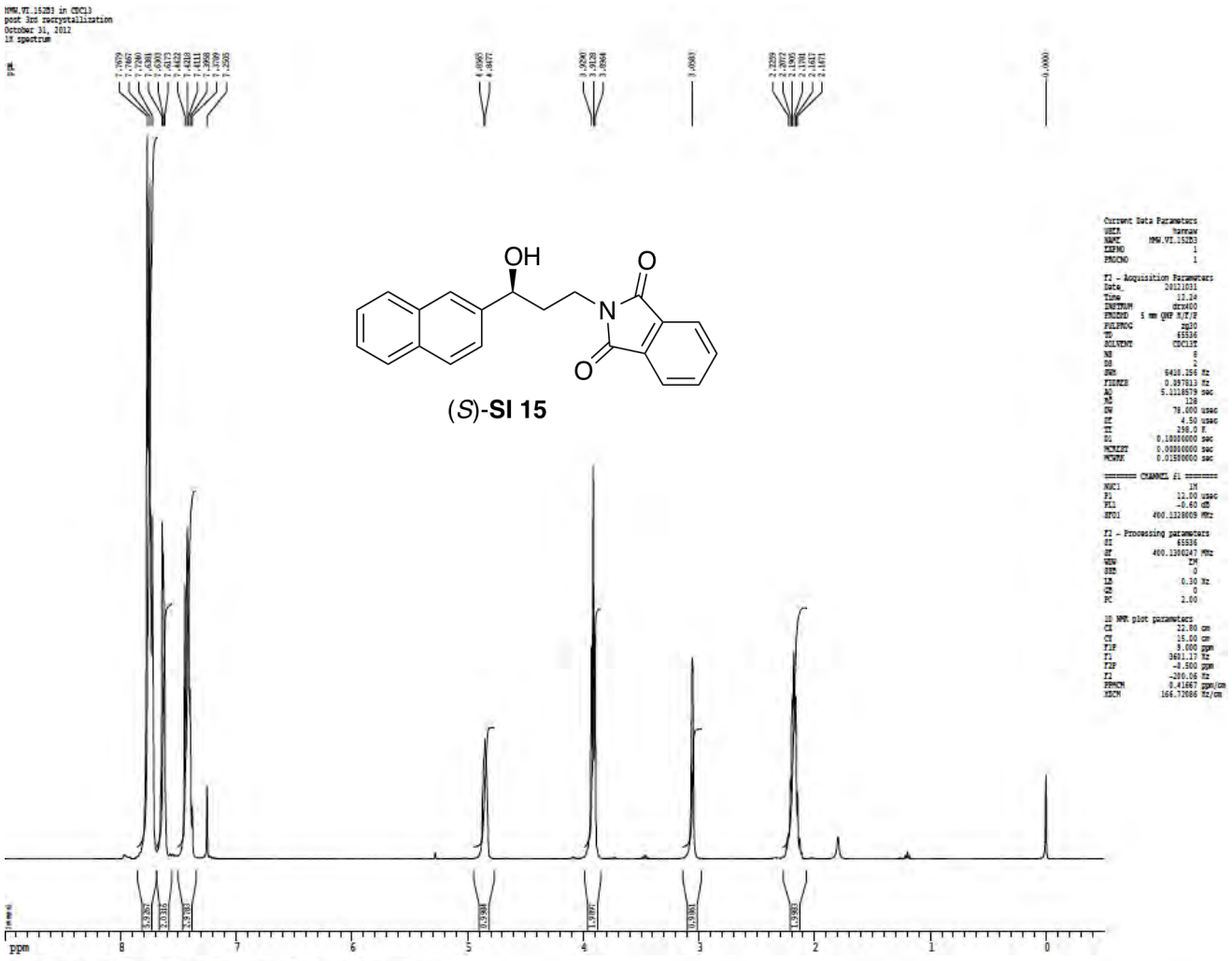
1H spectrum



SI 46

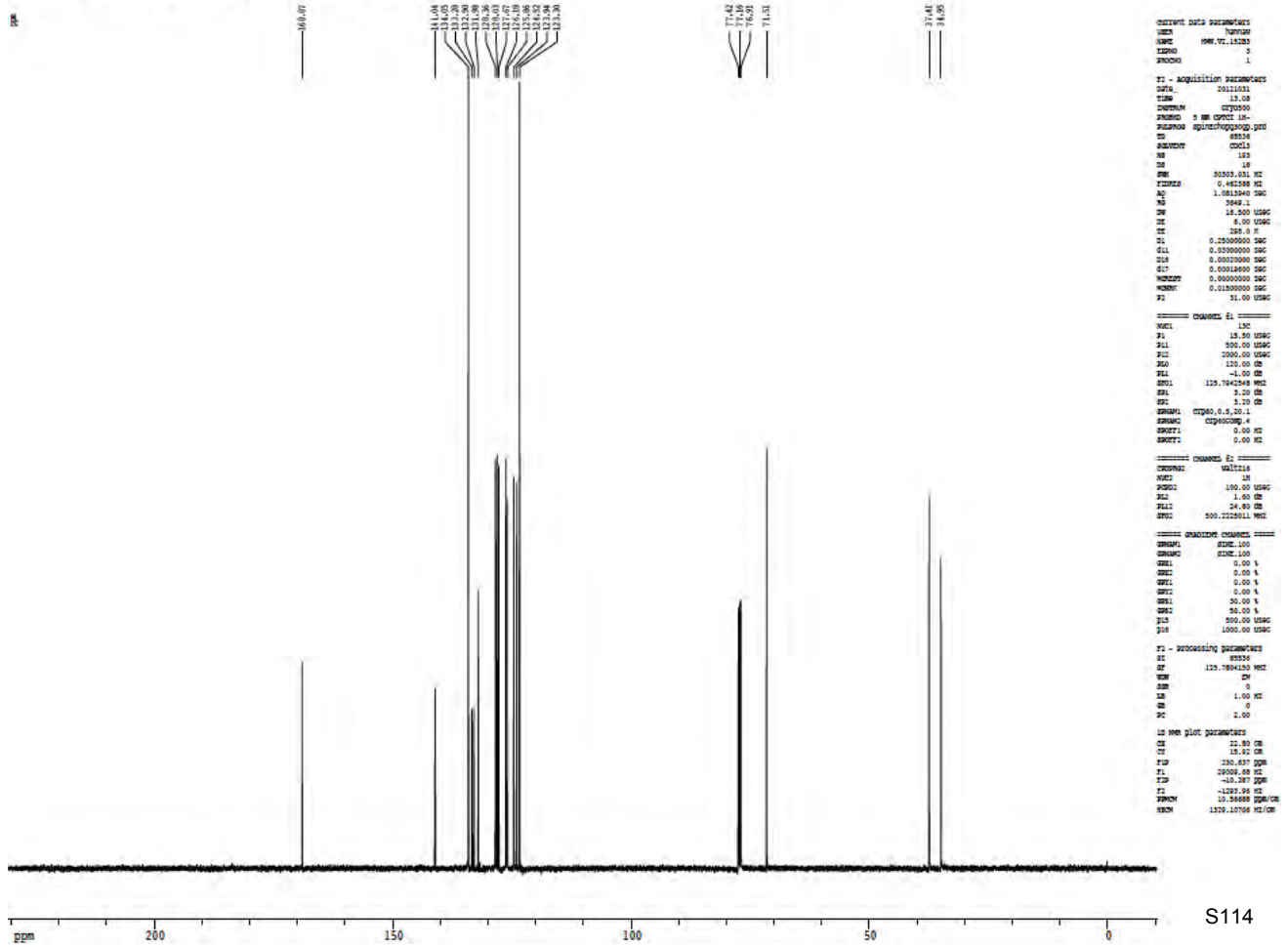
Z-restored spin-echo 13C spectrum with 1H decoupling



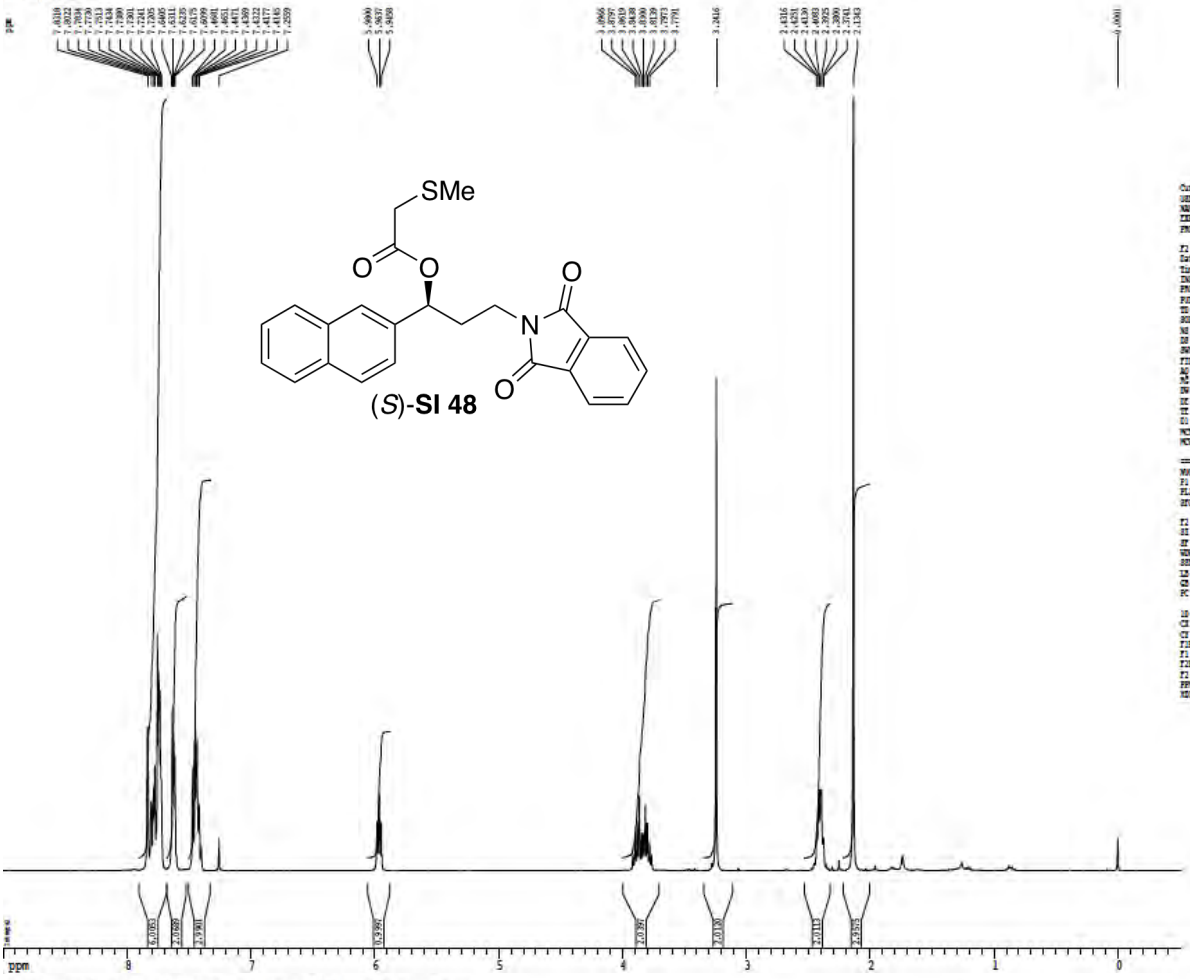


(*S*)-**SI 15**

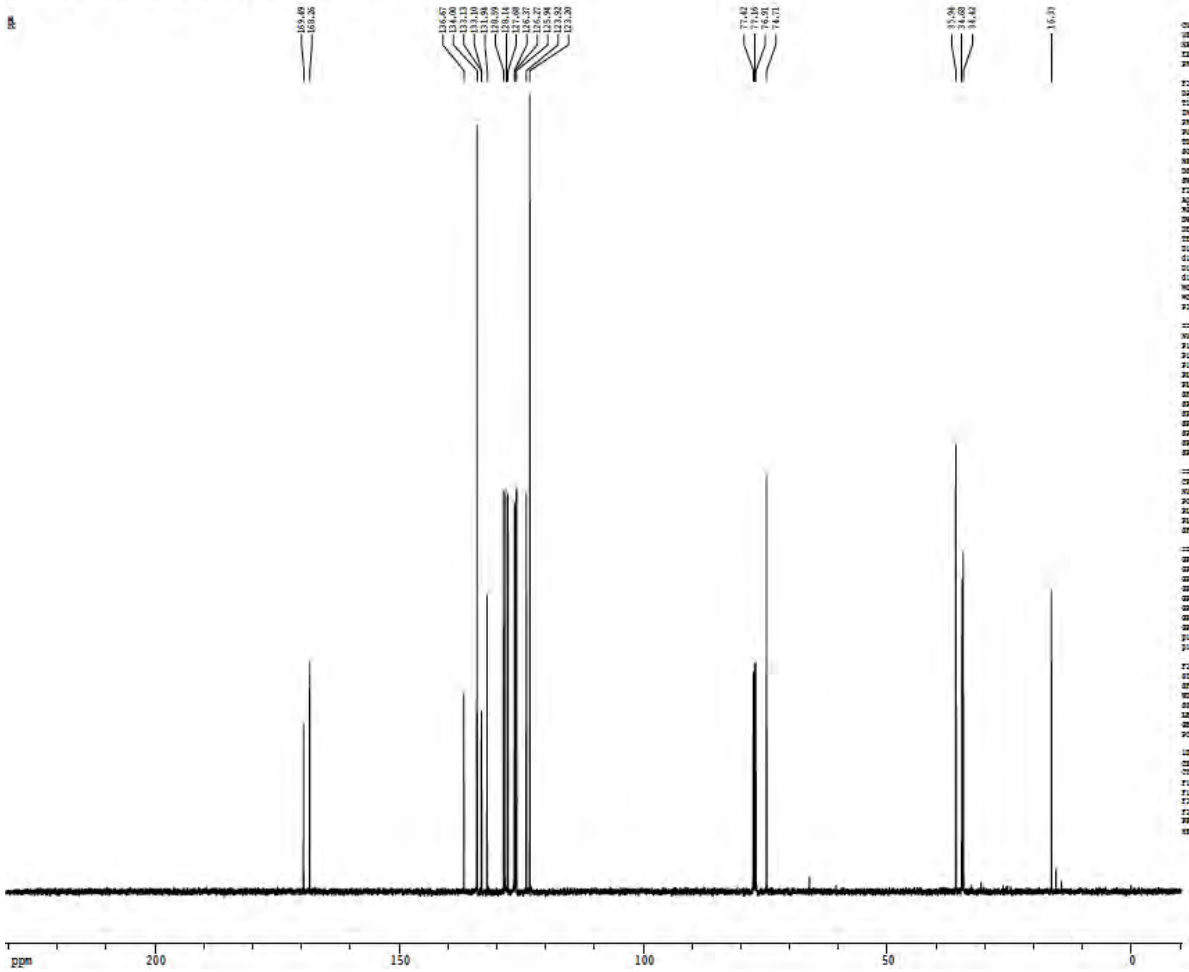
Z-restored spin-echo 13C spectrum with 1H decoupling



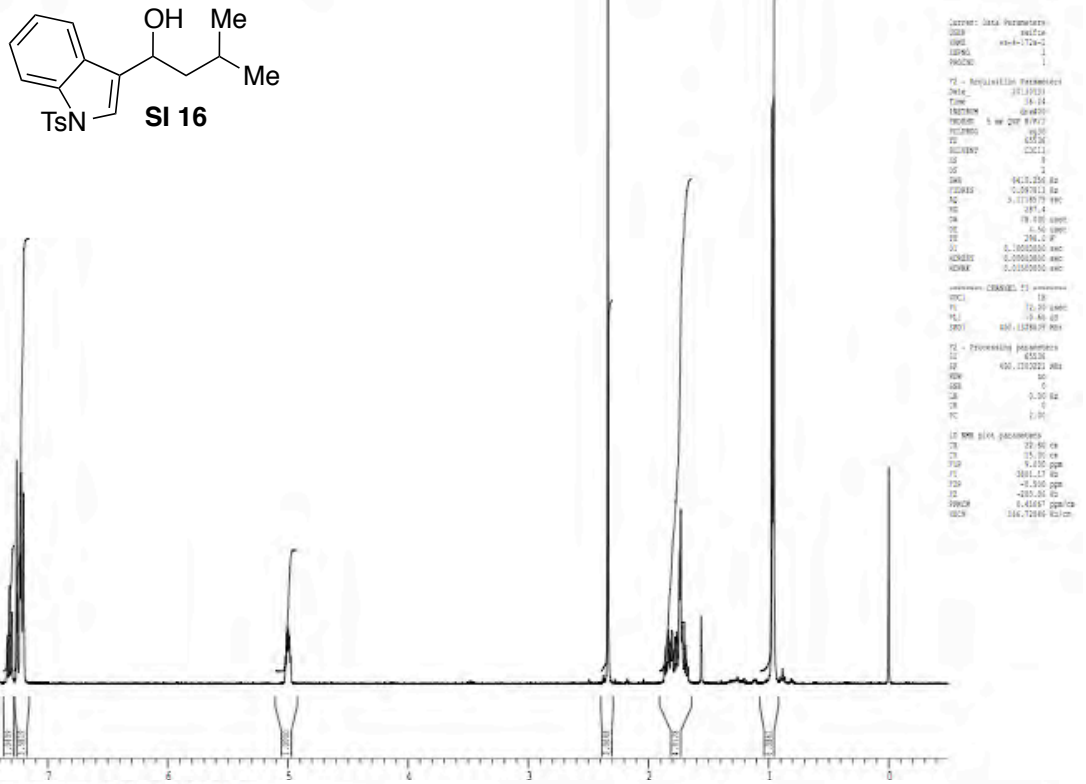
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling

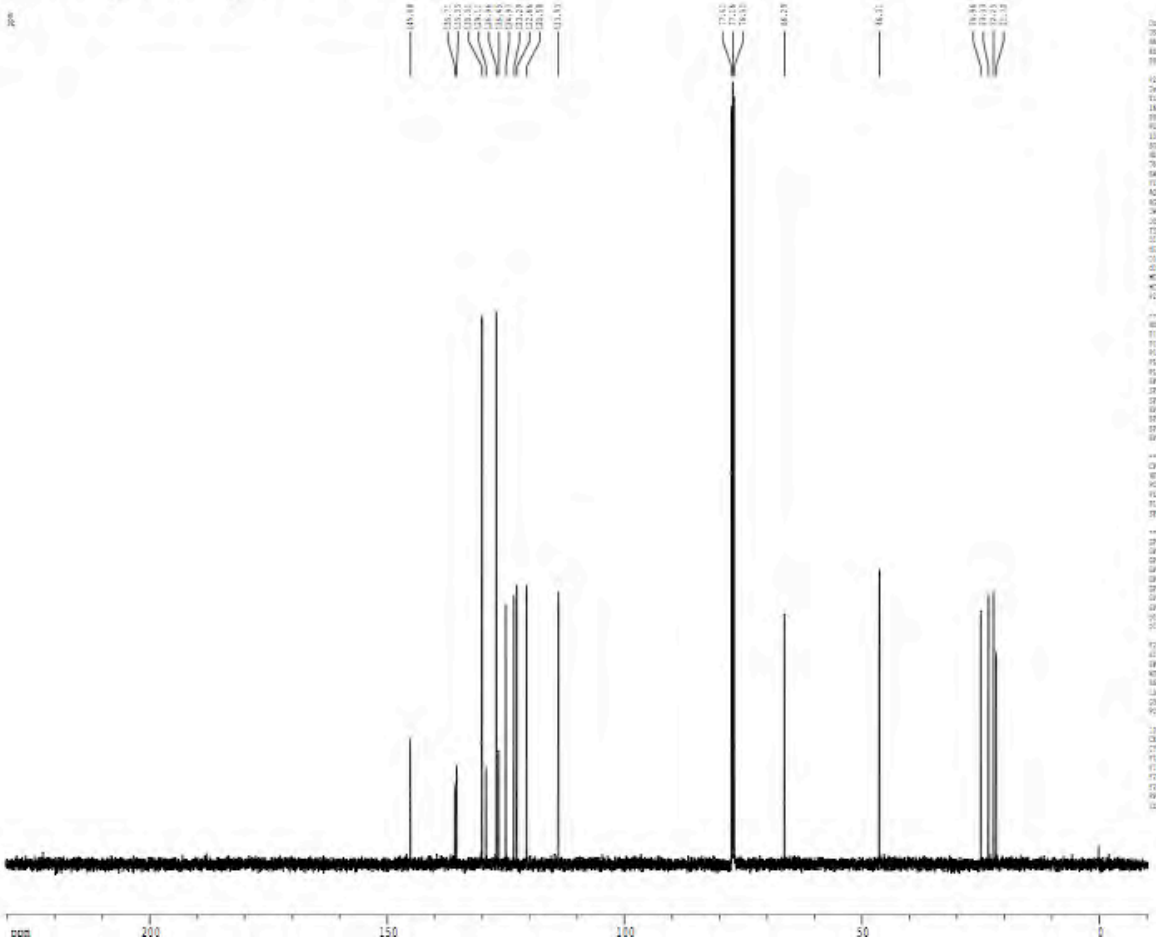


1H spectrum

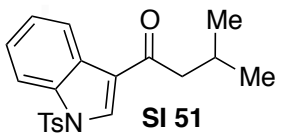


SI 16

Z-restored spin-echo 13C spectrum with 1H decoupling



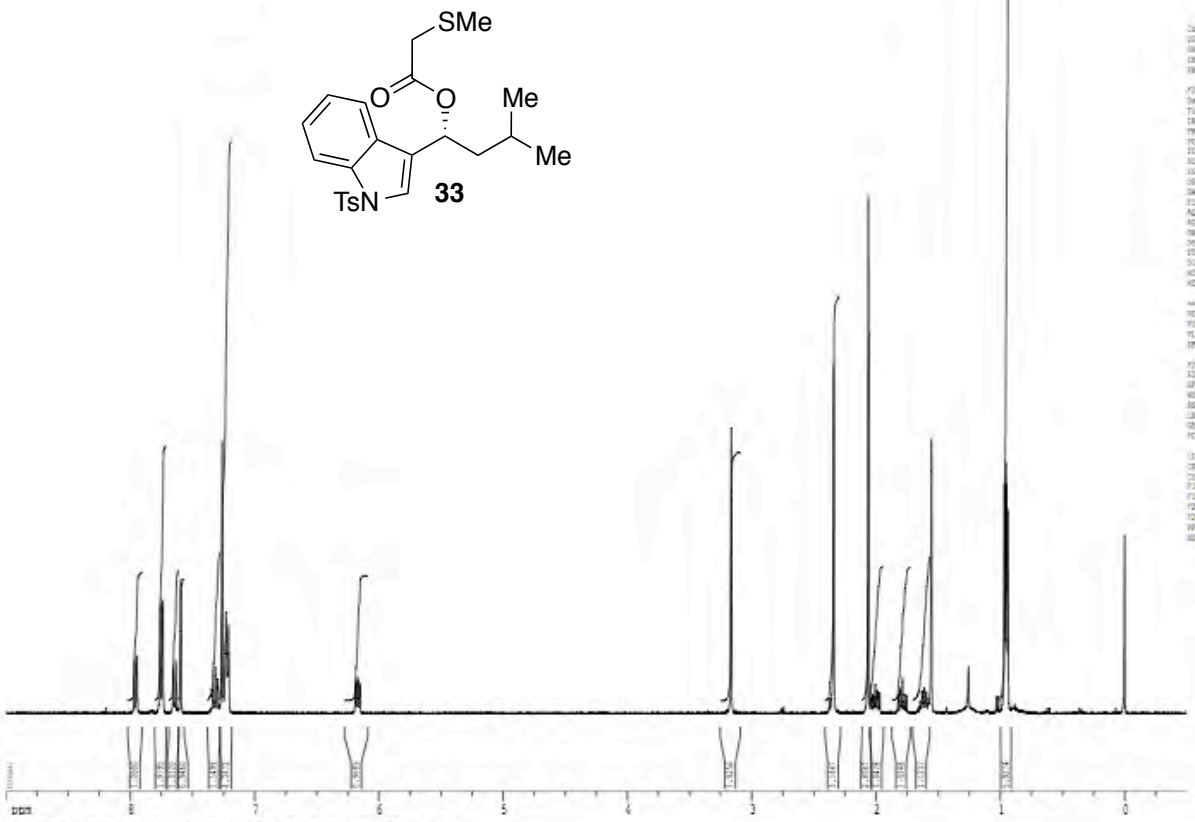
1H spectrum



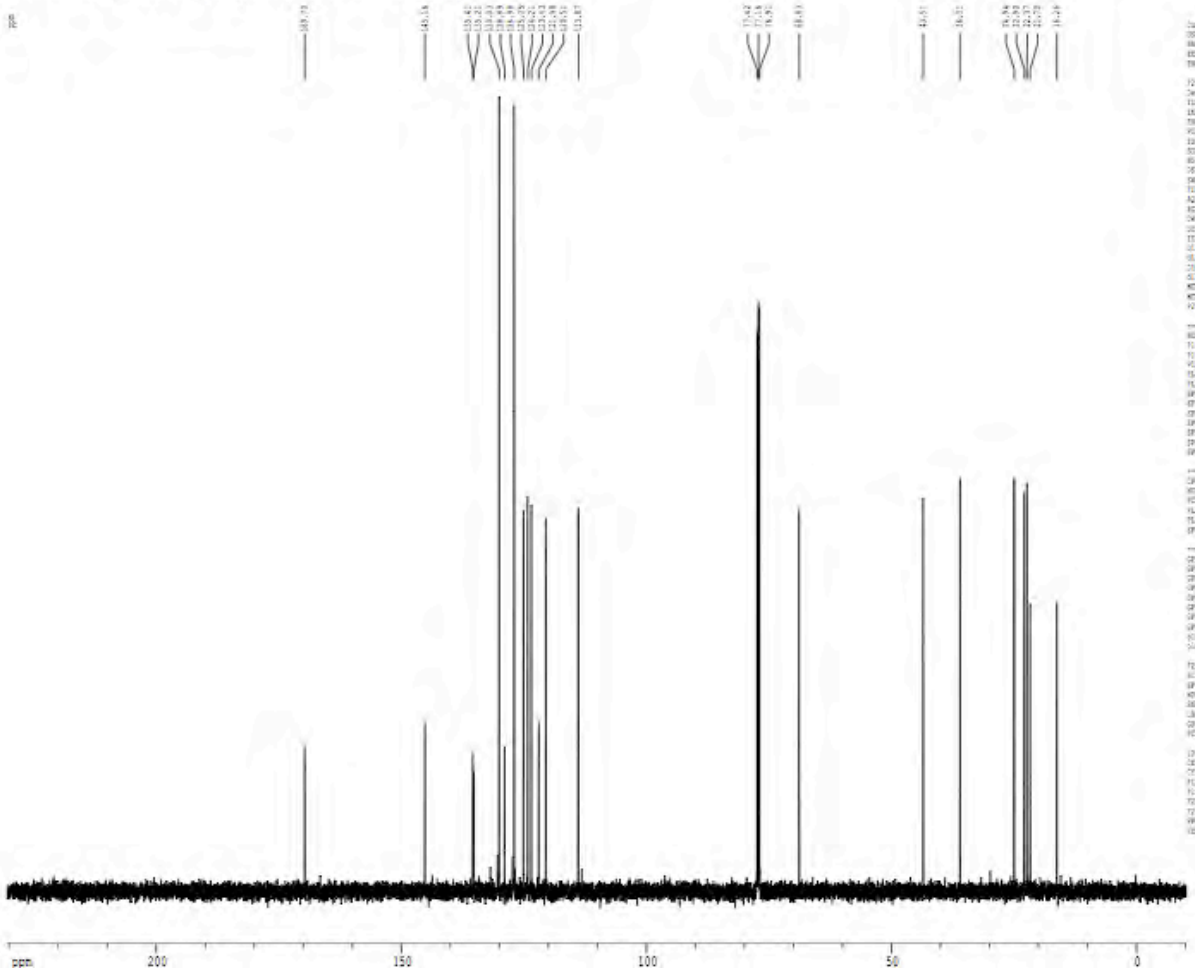
SI 51

Z-restored spin-echo 13C spectrum with 1H decoupling

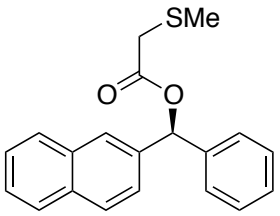
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling



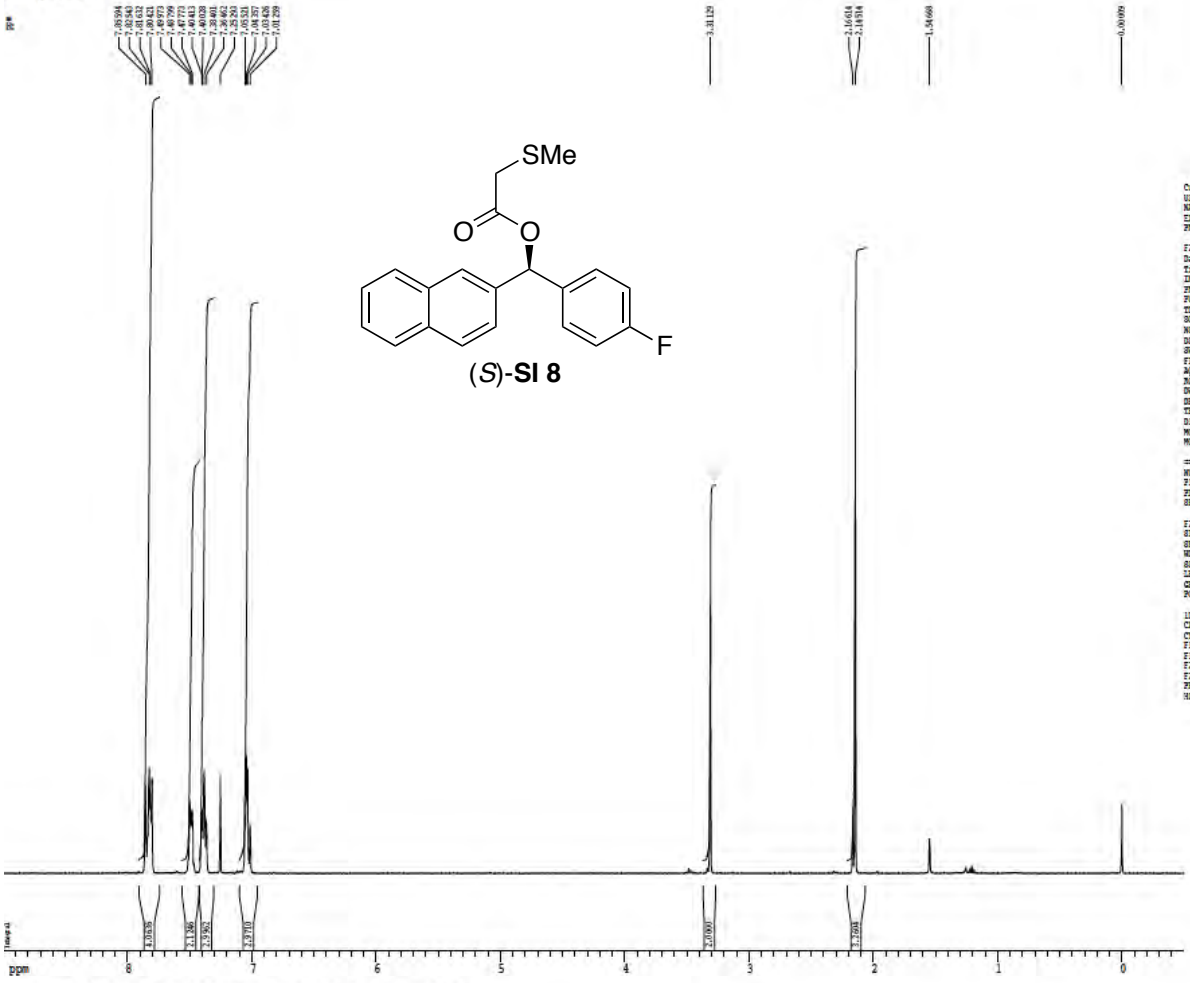
1H spectrum



(*S*)-**SI 52**

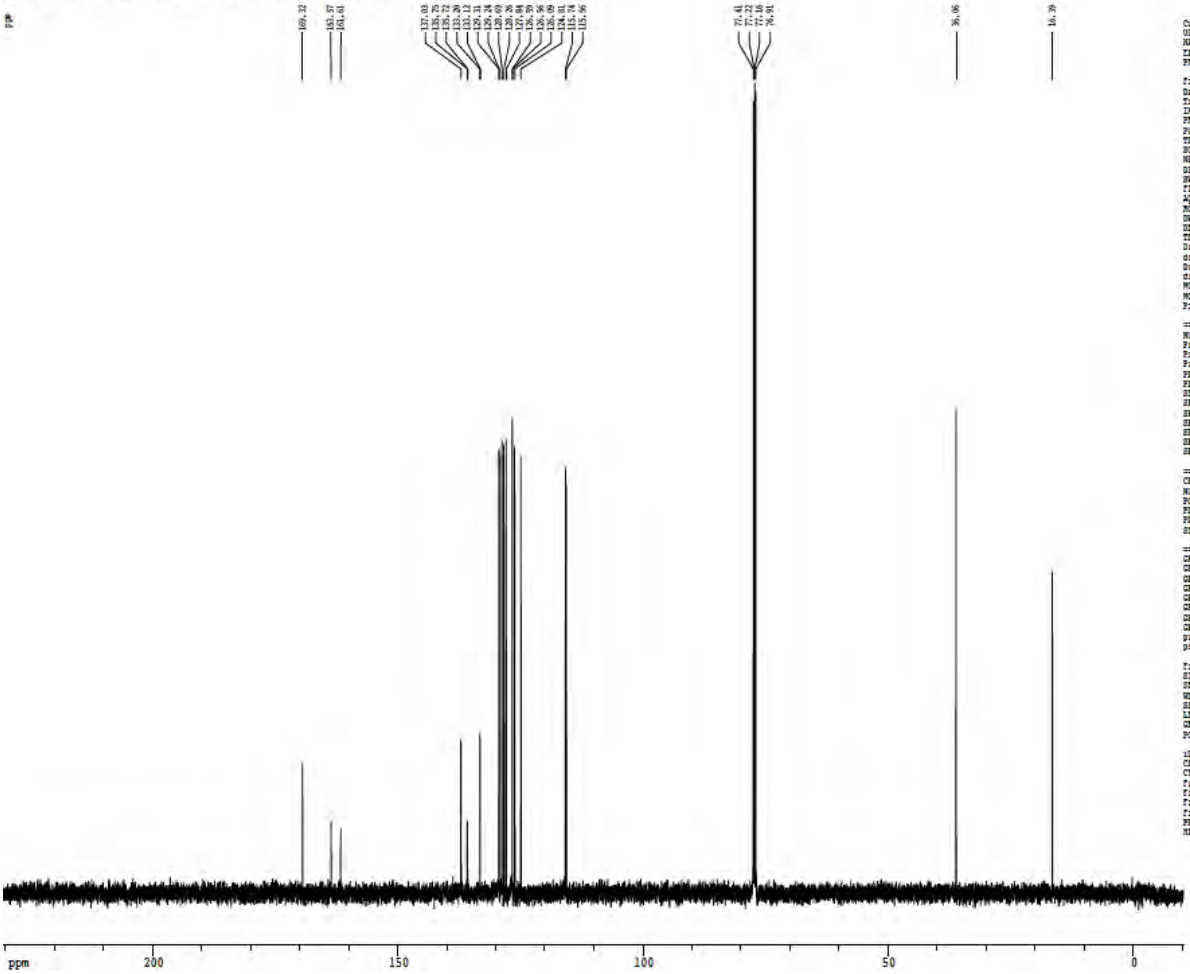
Z-restored spin-echo 13C spectrum with 1H decoupling

1H spectrum

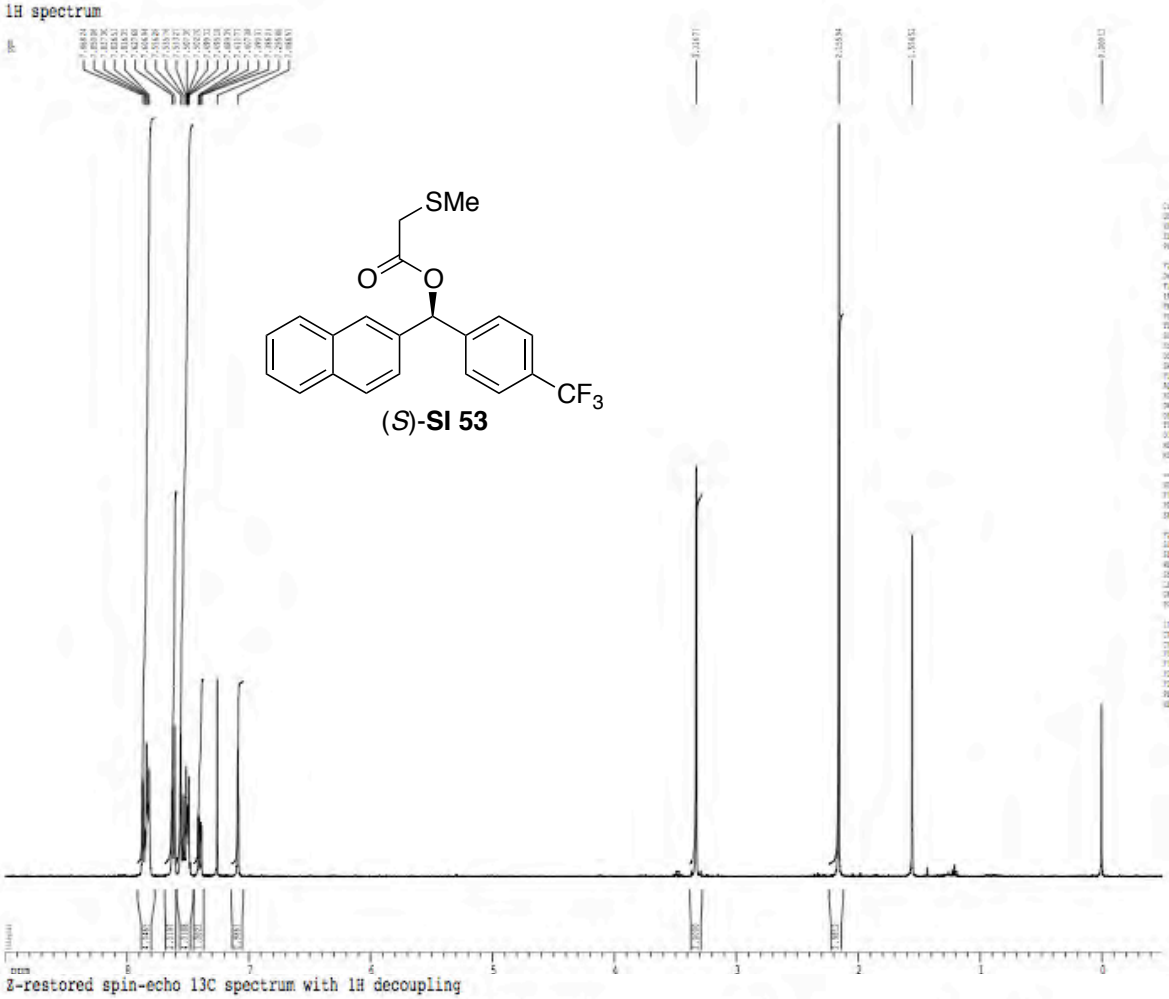


(*S*)-**SI 8**

Z-restored spin-echo 13C spectrum with 1H decoupling

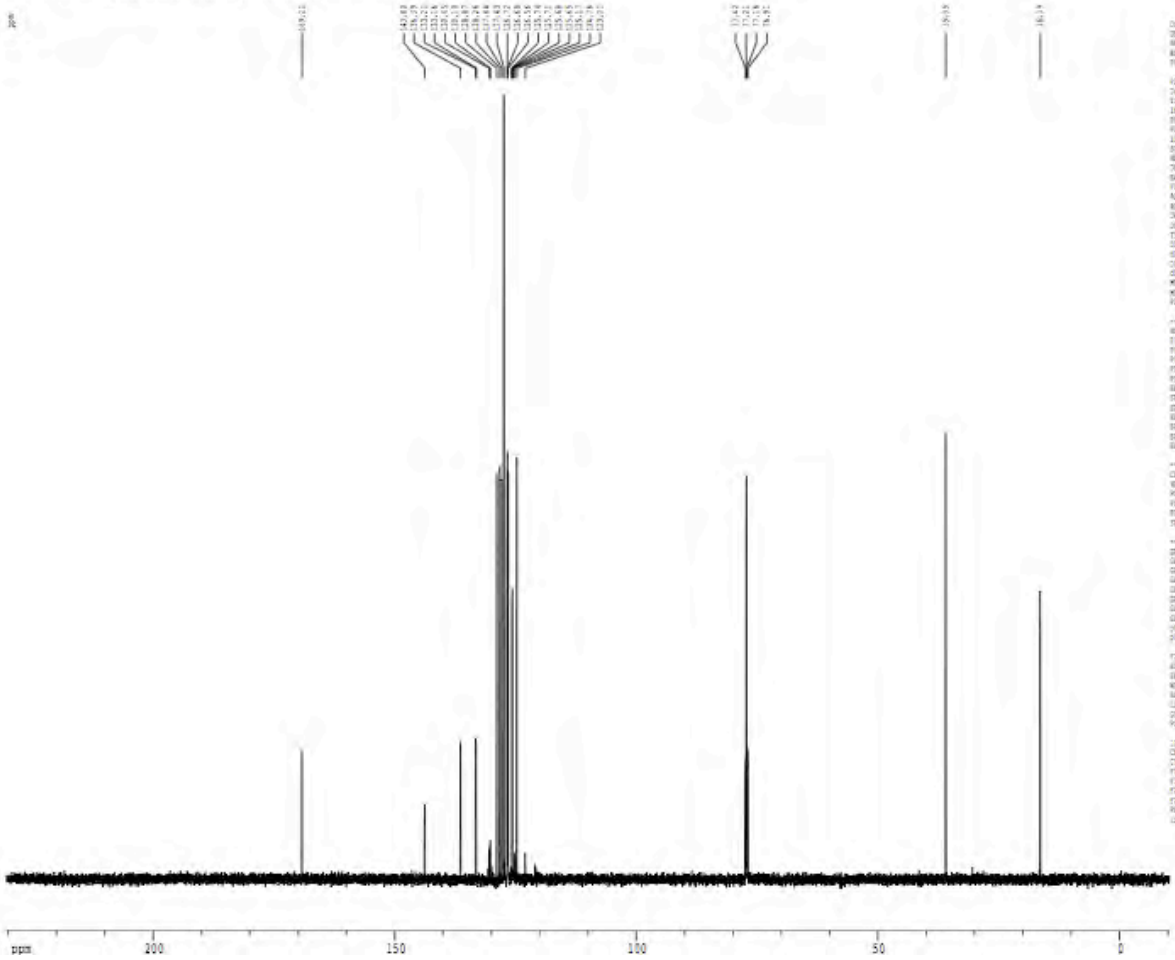


1H spectrum

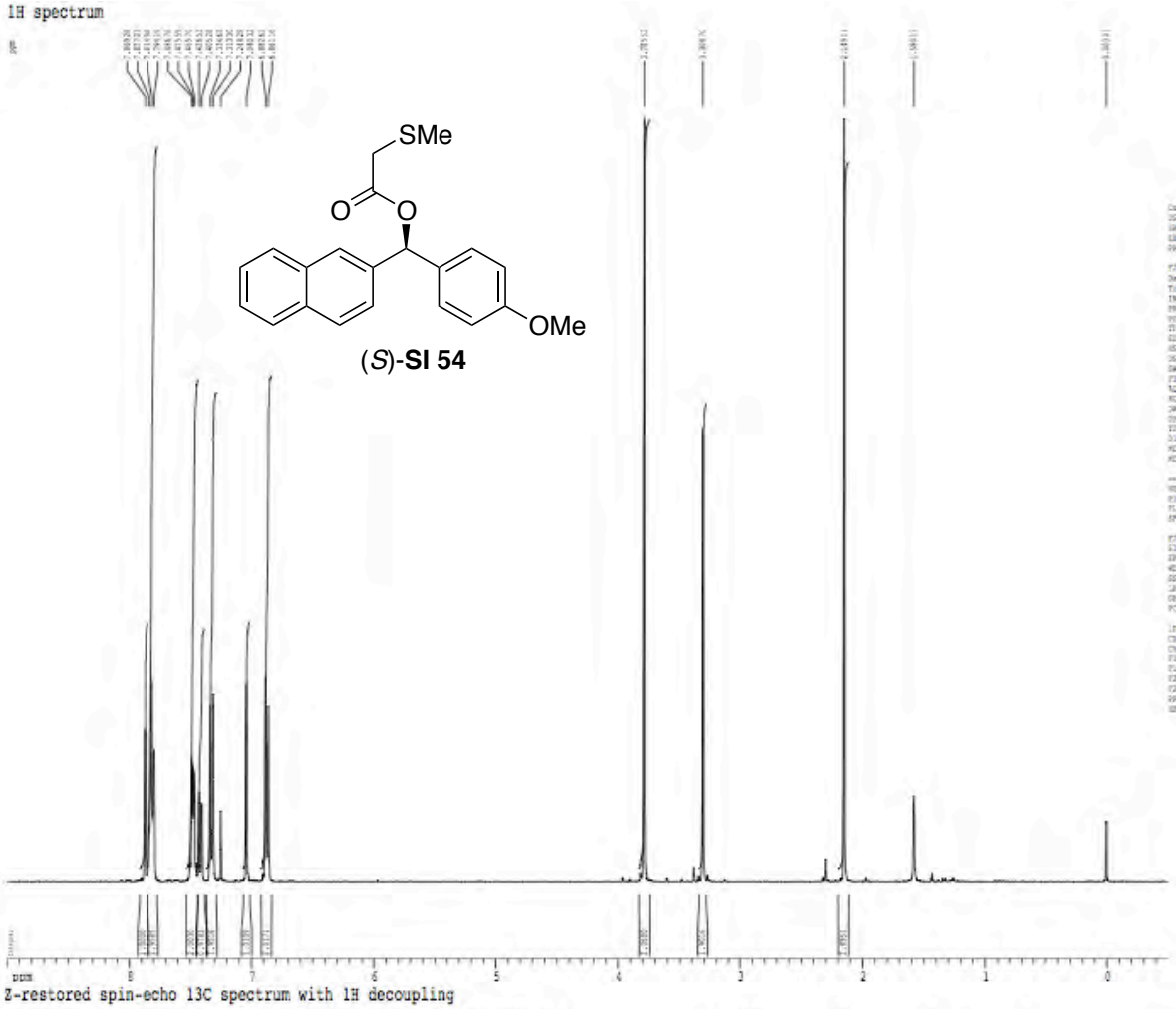


(*S*)-**SI 53**

Z-restored spin-echo 13C spectrum with 1H decoupling

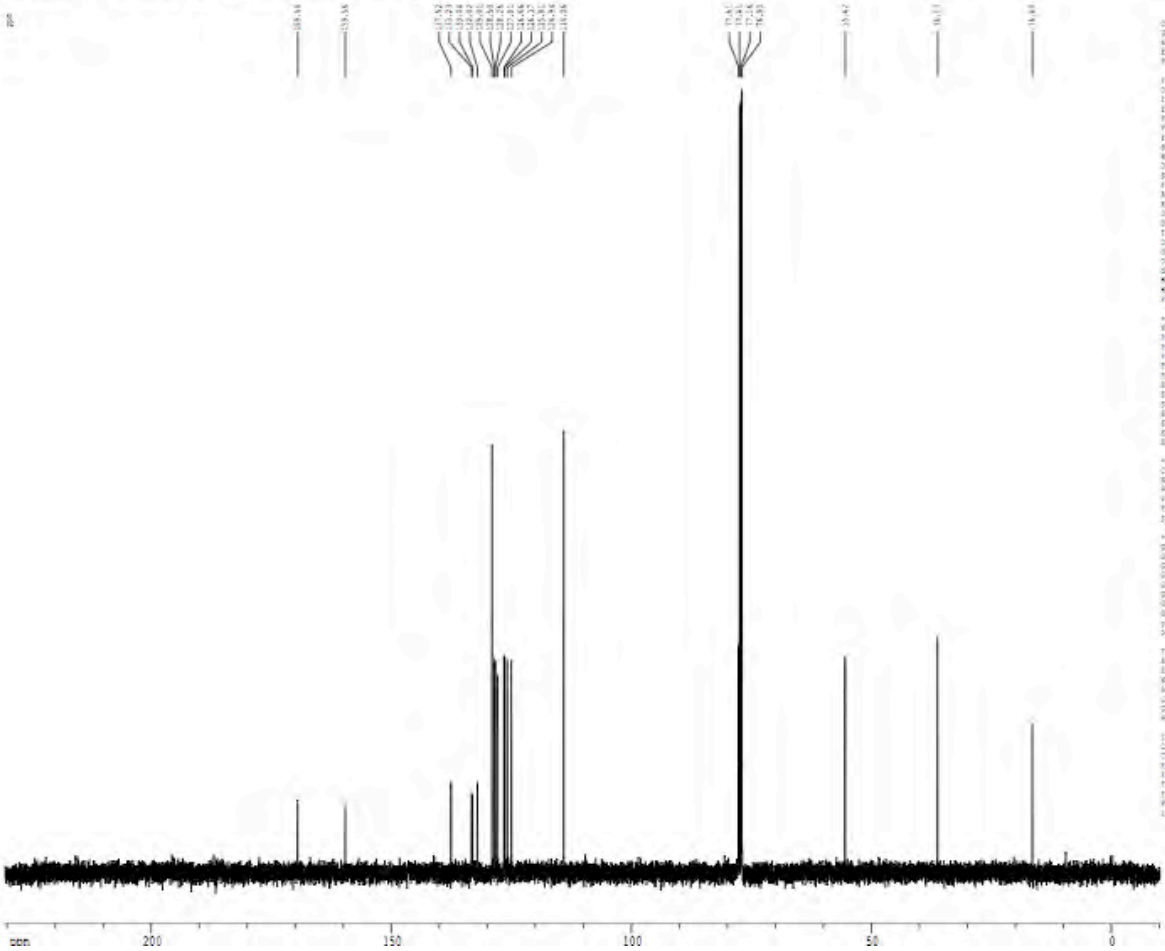


1H spectrum

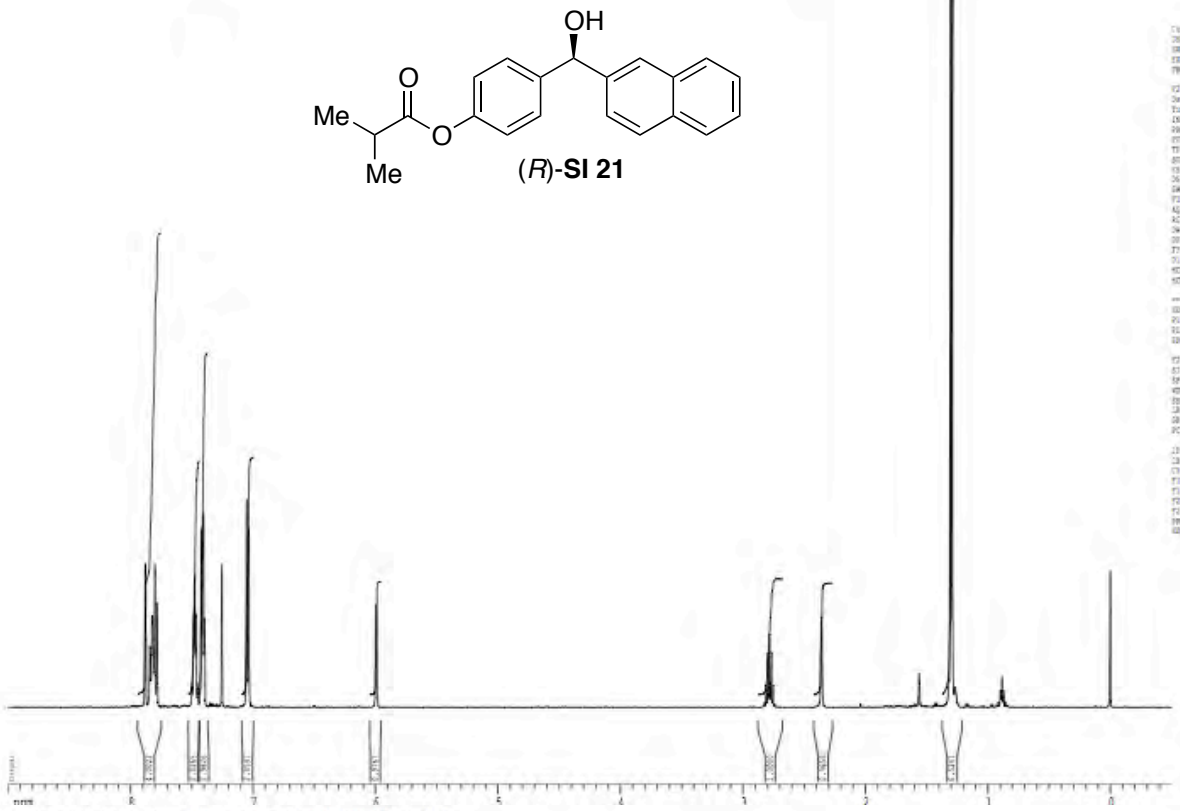


(*S*)-**SI 54**

Z-restored spin-echo 13C spectrum with 1H decoupling

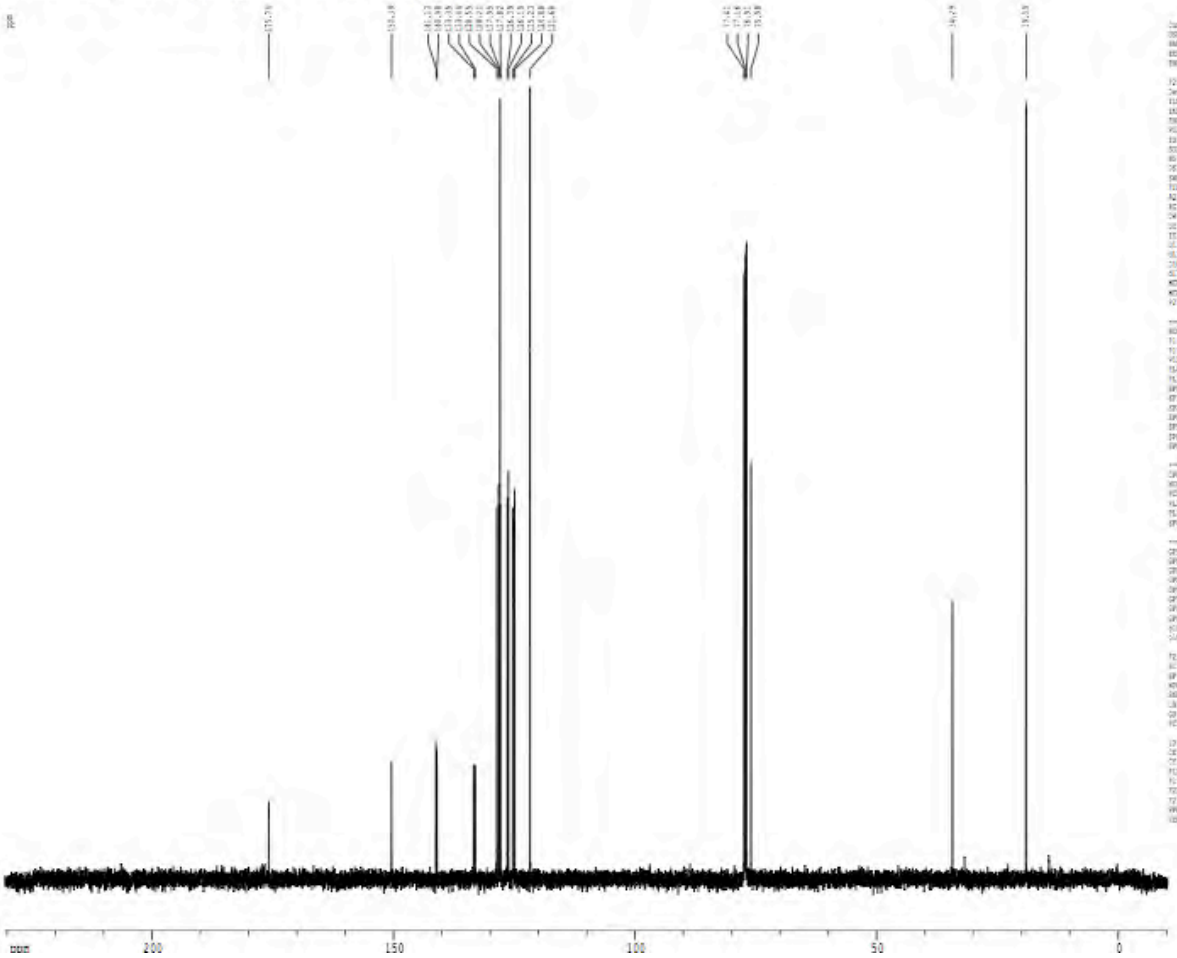


1H spectrum

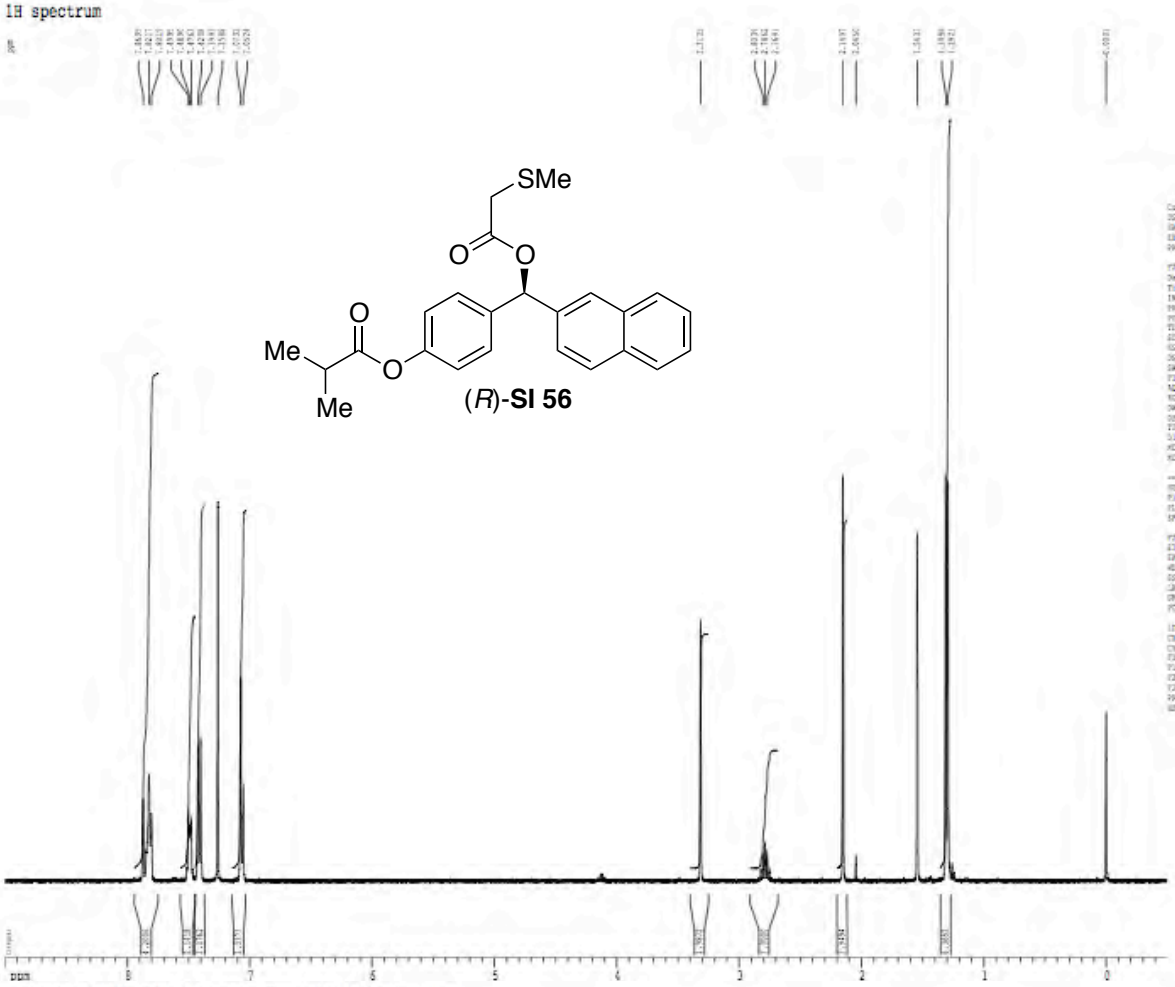


(*R*)-**SI 21**

Z-restored spin-echo 13C spectrum with 1H decoupling

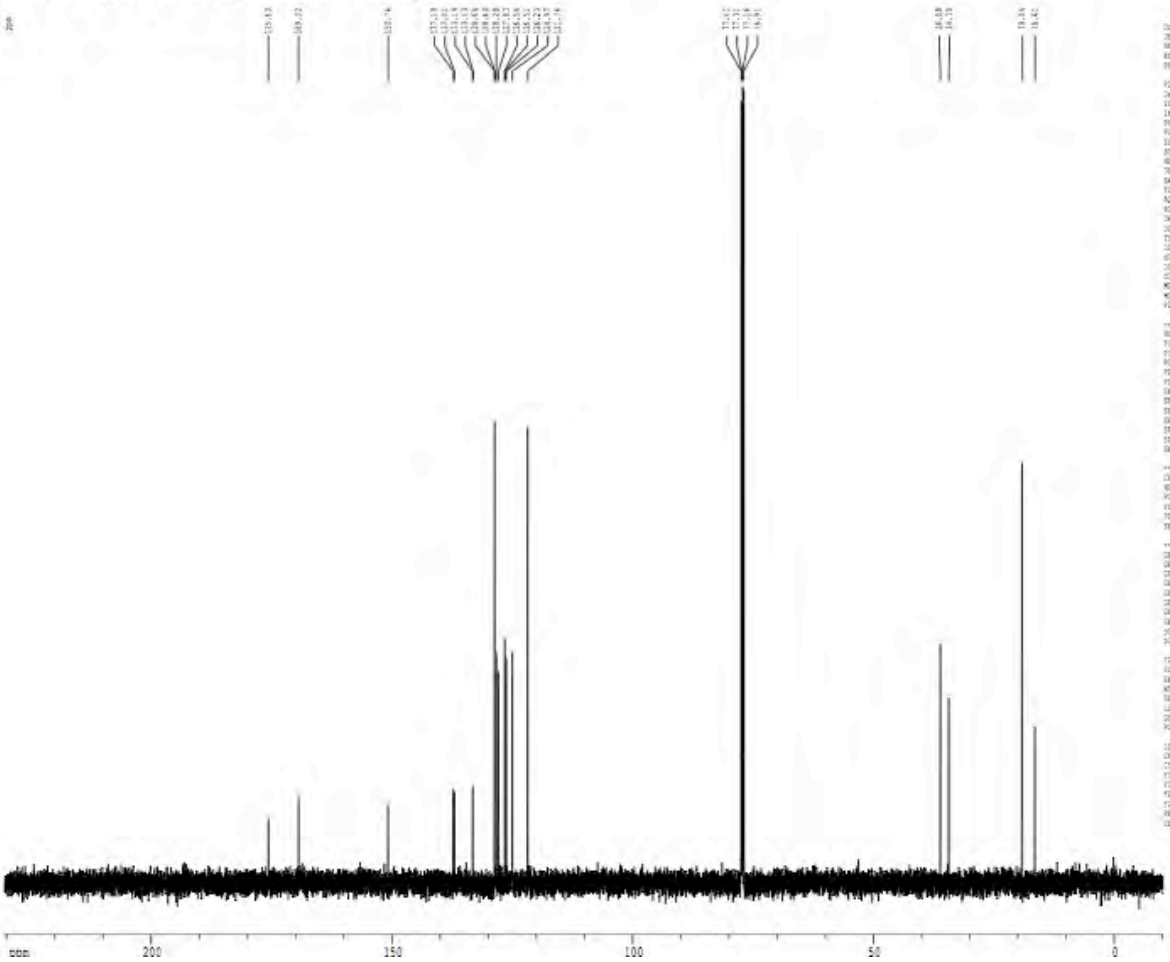


1H spectrum

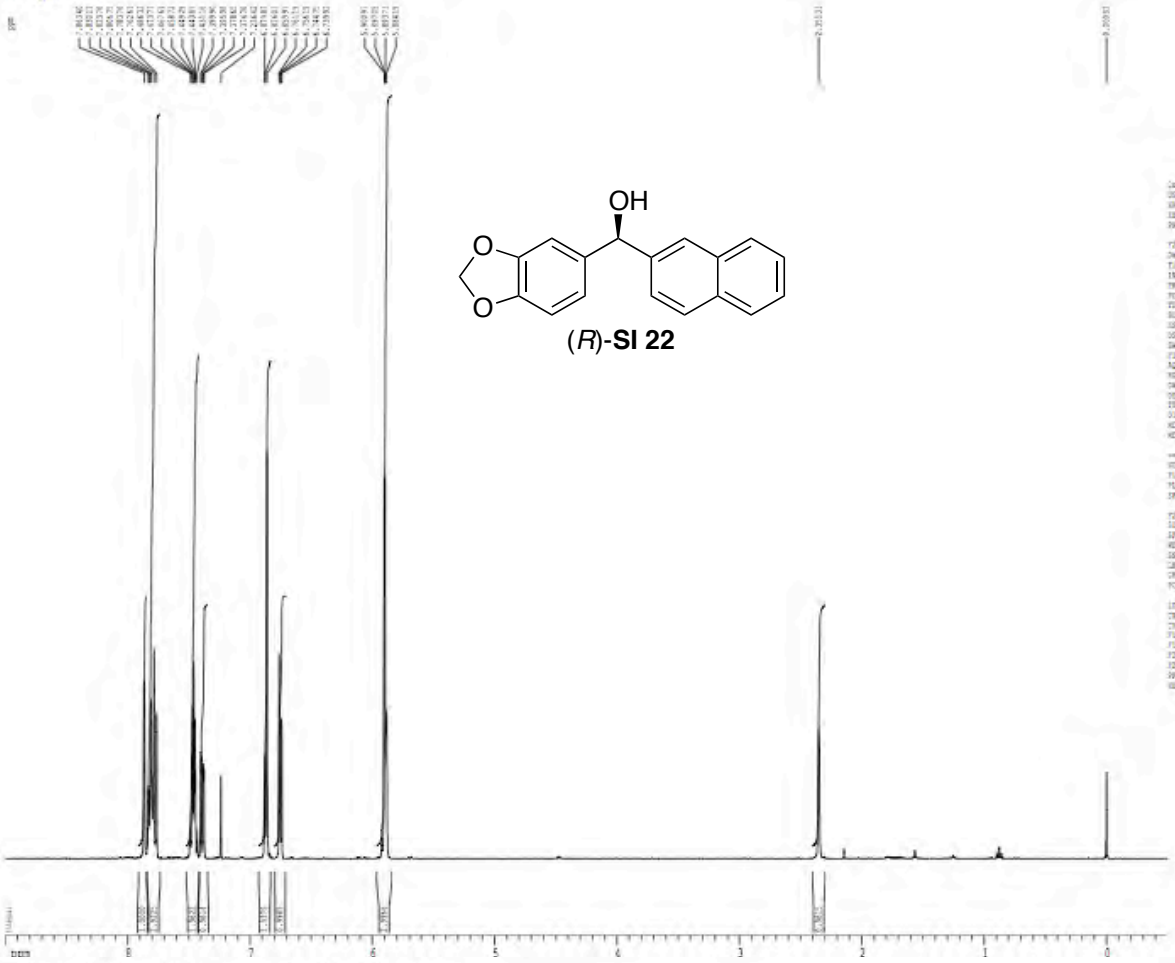


(*R*)-**SI 56**

Z-restored spin-echo 13C spectrum with 1H decoupling

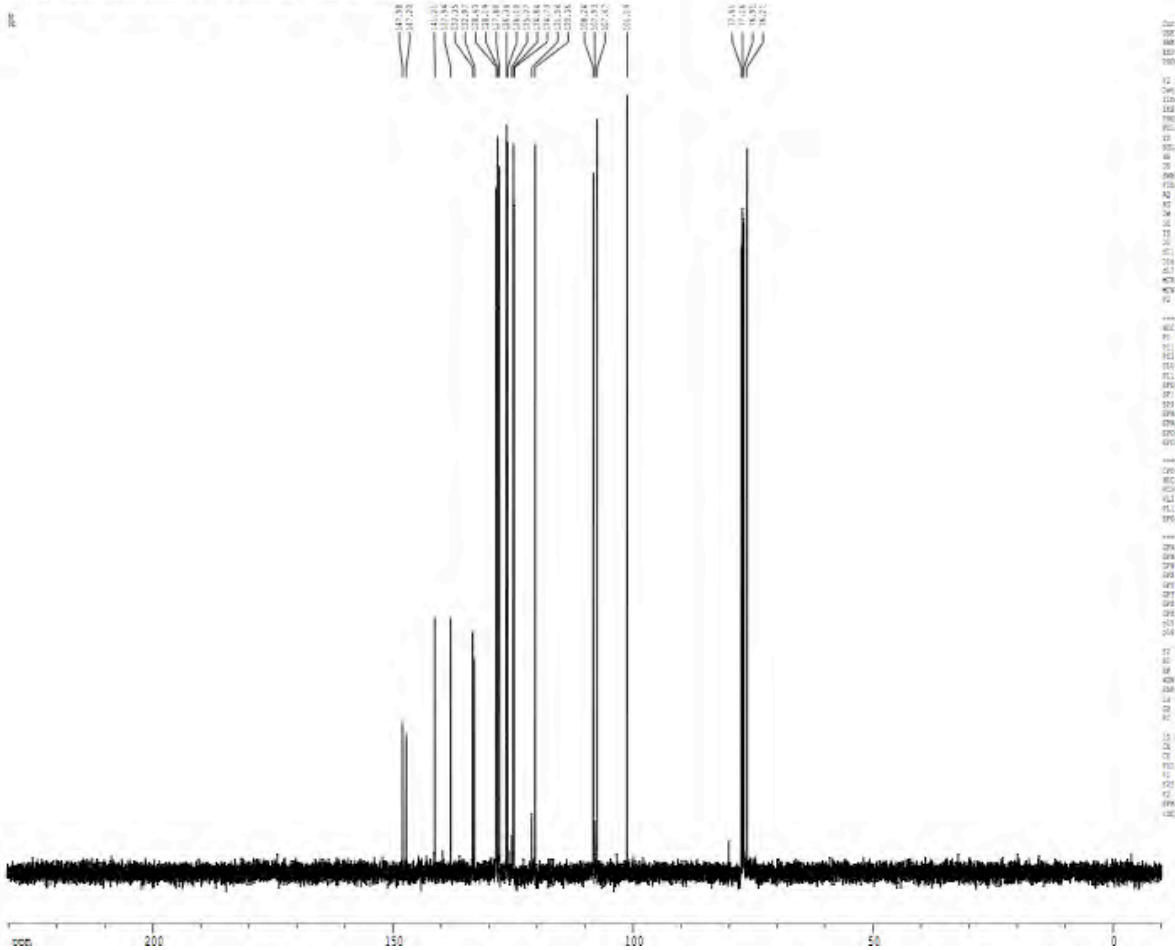


1H spectrum

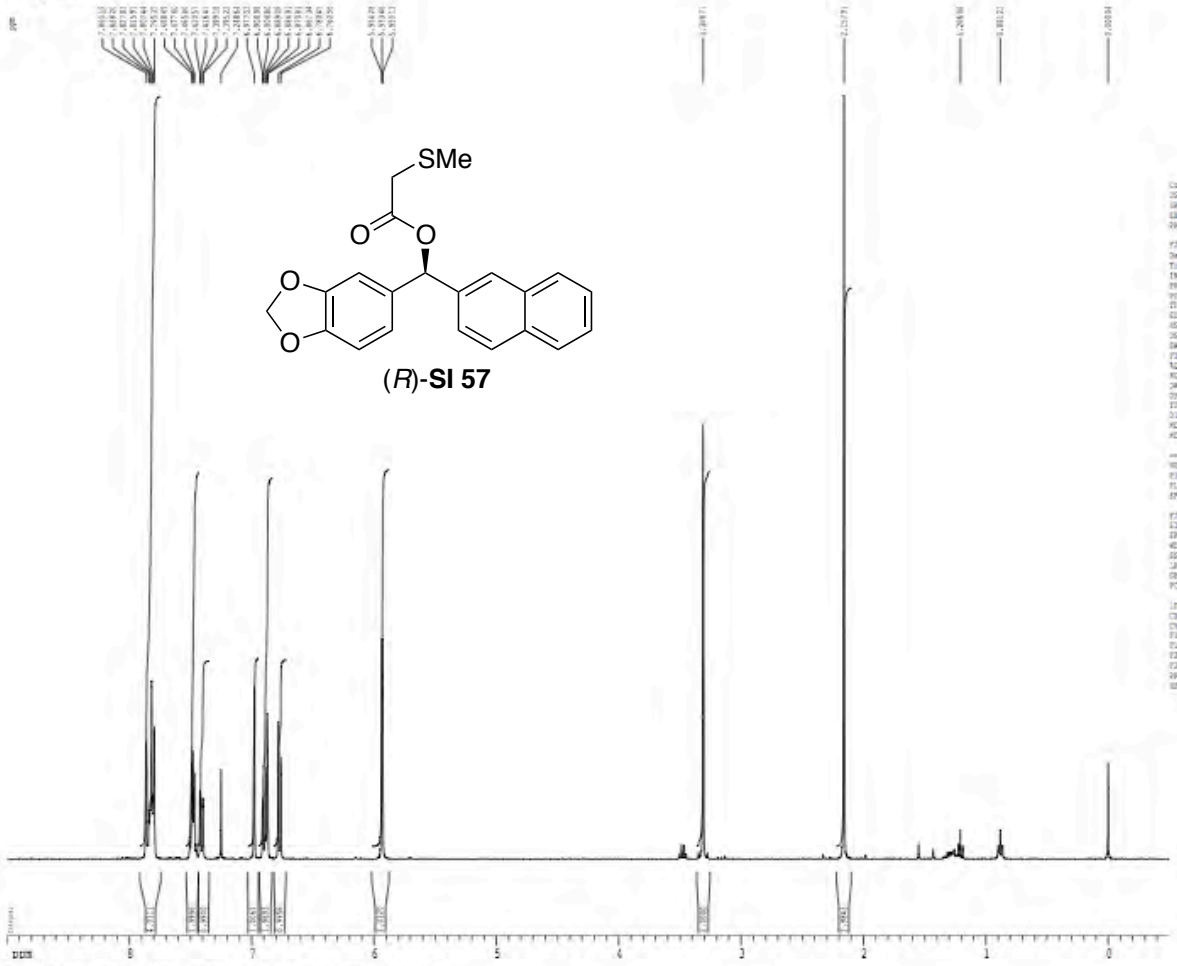


(*R*)-**SI 22**

Z-restored spin-echo 13C spectrum with 1H decoupling

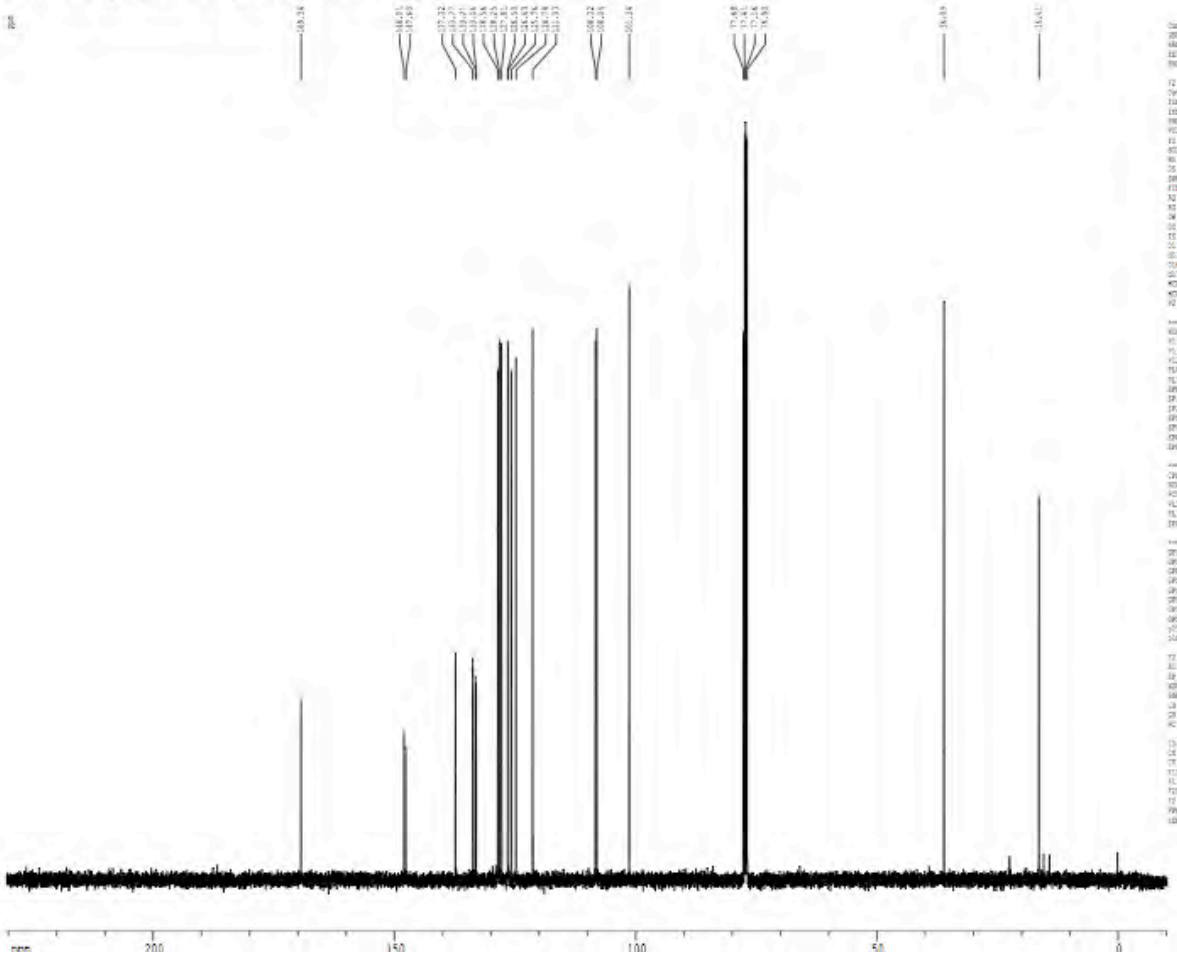


1H spectrum

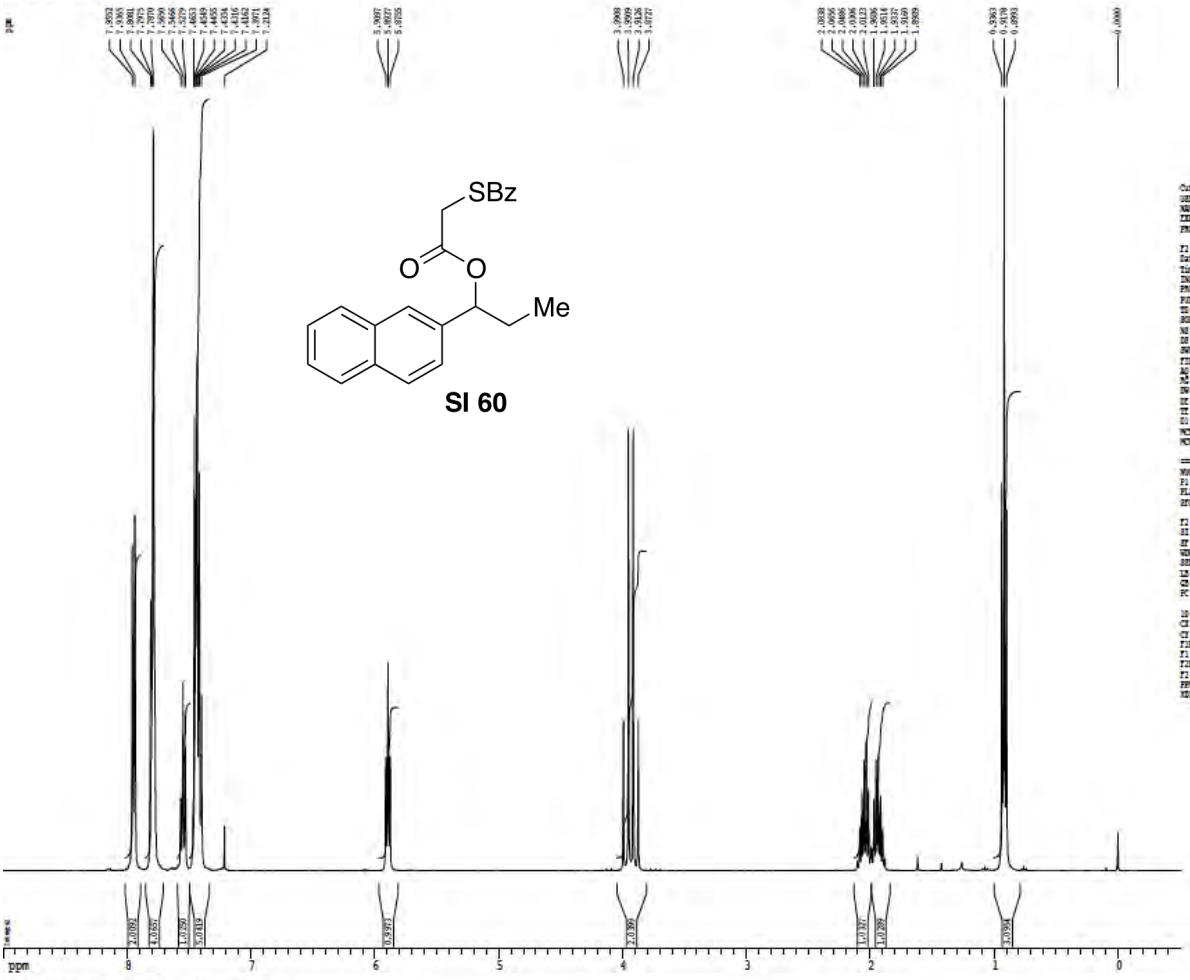


(*R*)-**SI 57**

Z-restored spin-echo 13C spectrum with 1H decoupling

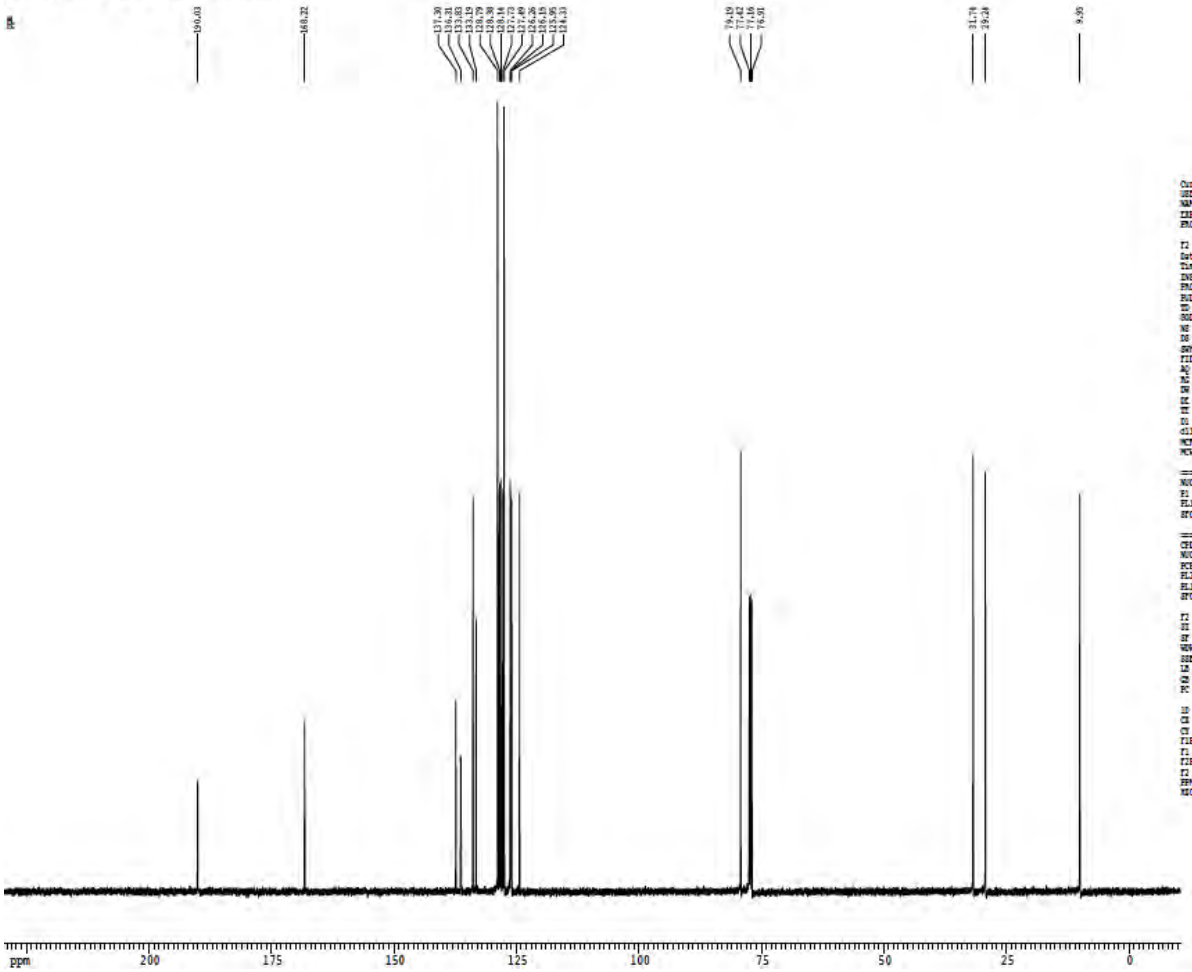


1H spectrum

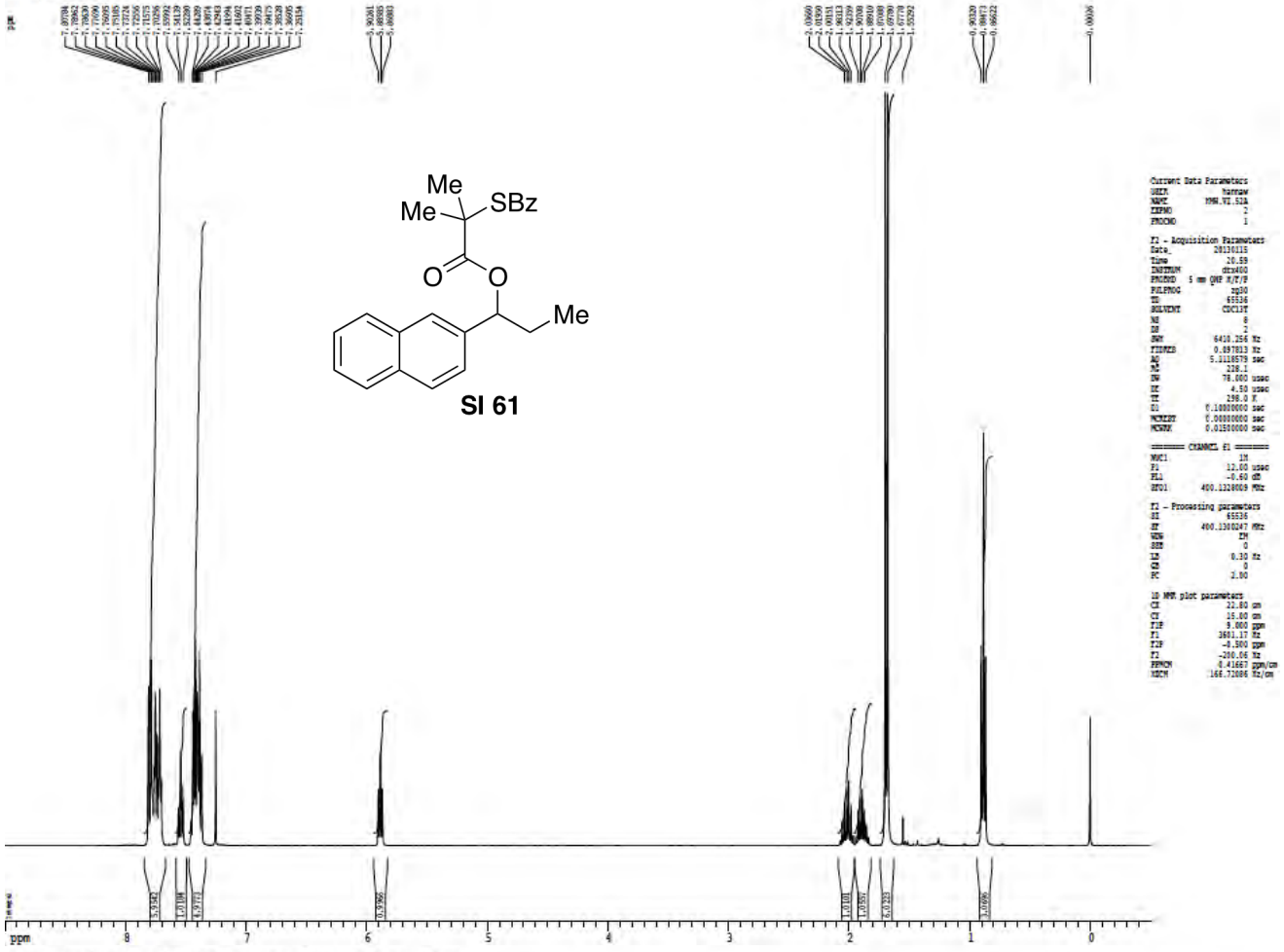


SI 60

13C spectrum with 1H decoupling

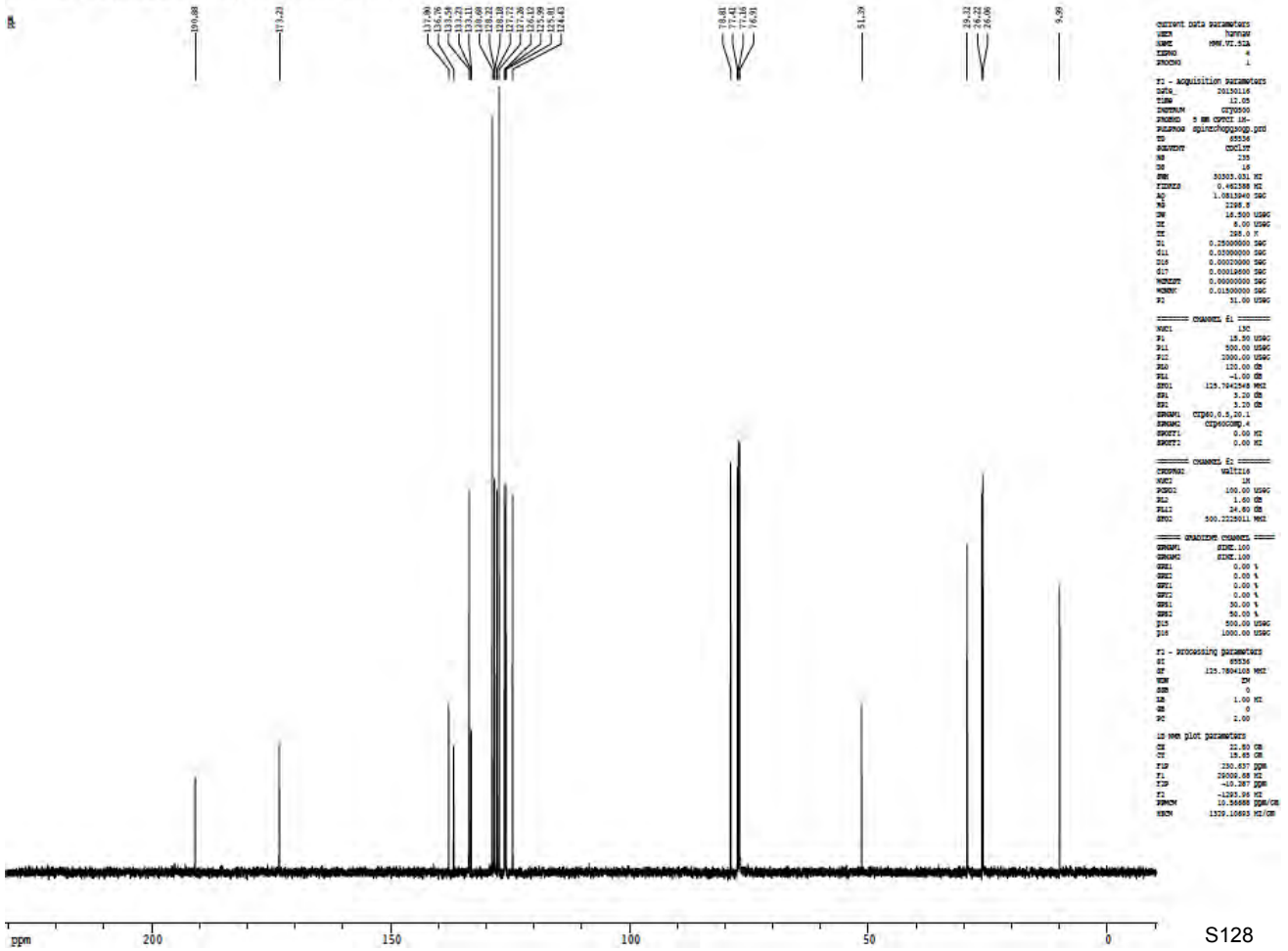


1H spectrum

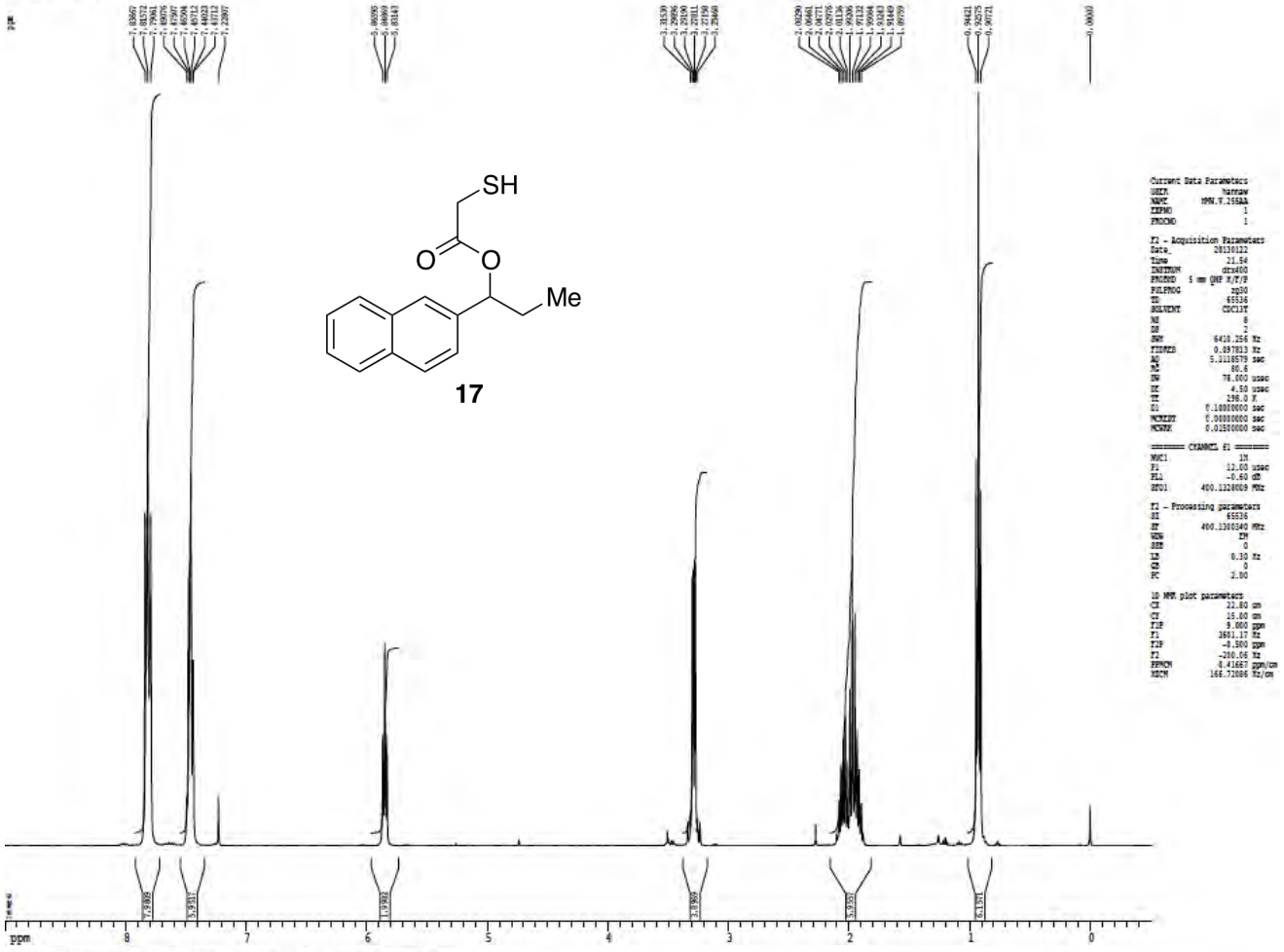


SI 61

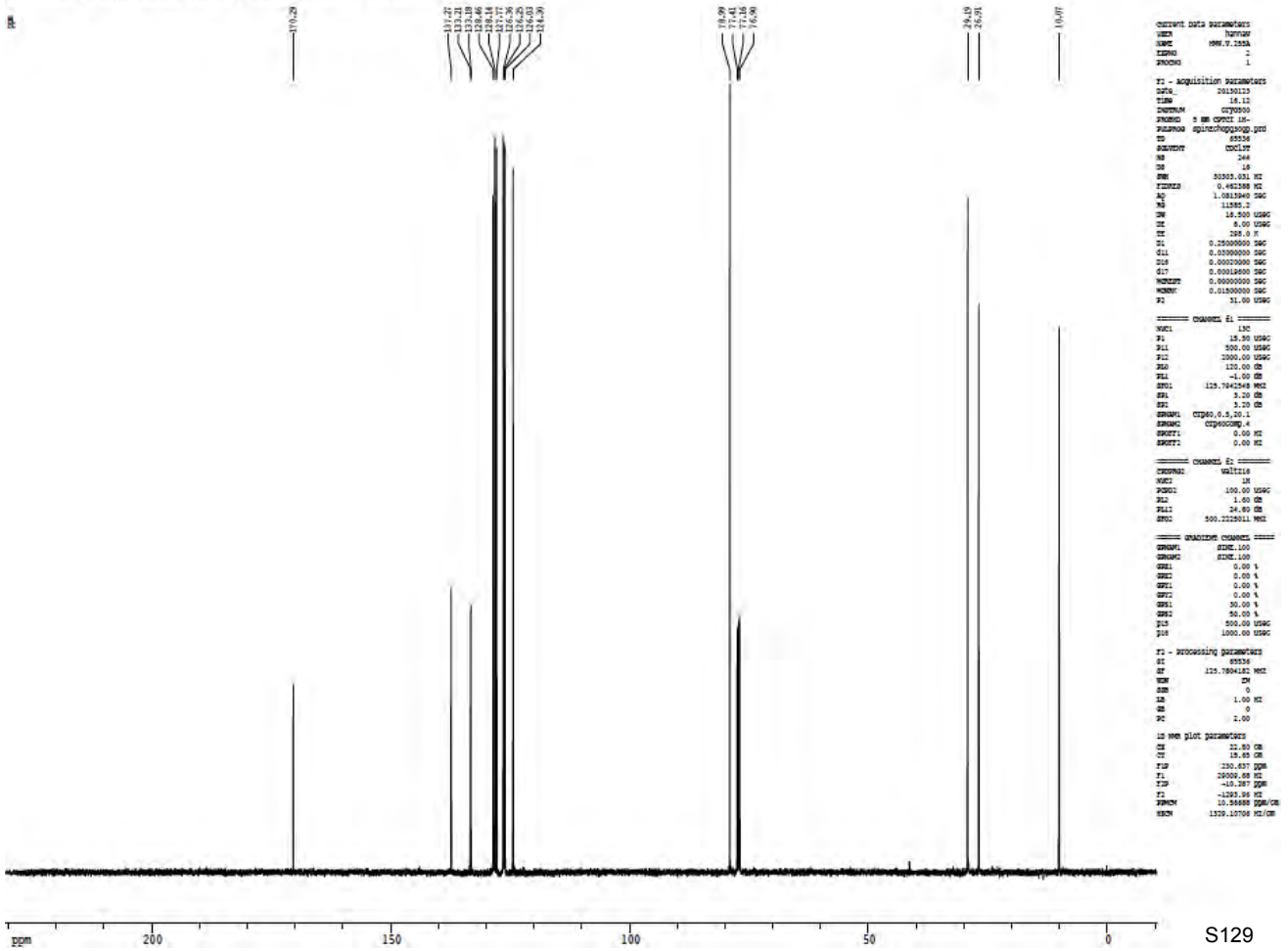
Z-restored spin-echo 13C spectrum with 1H decoupling



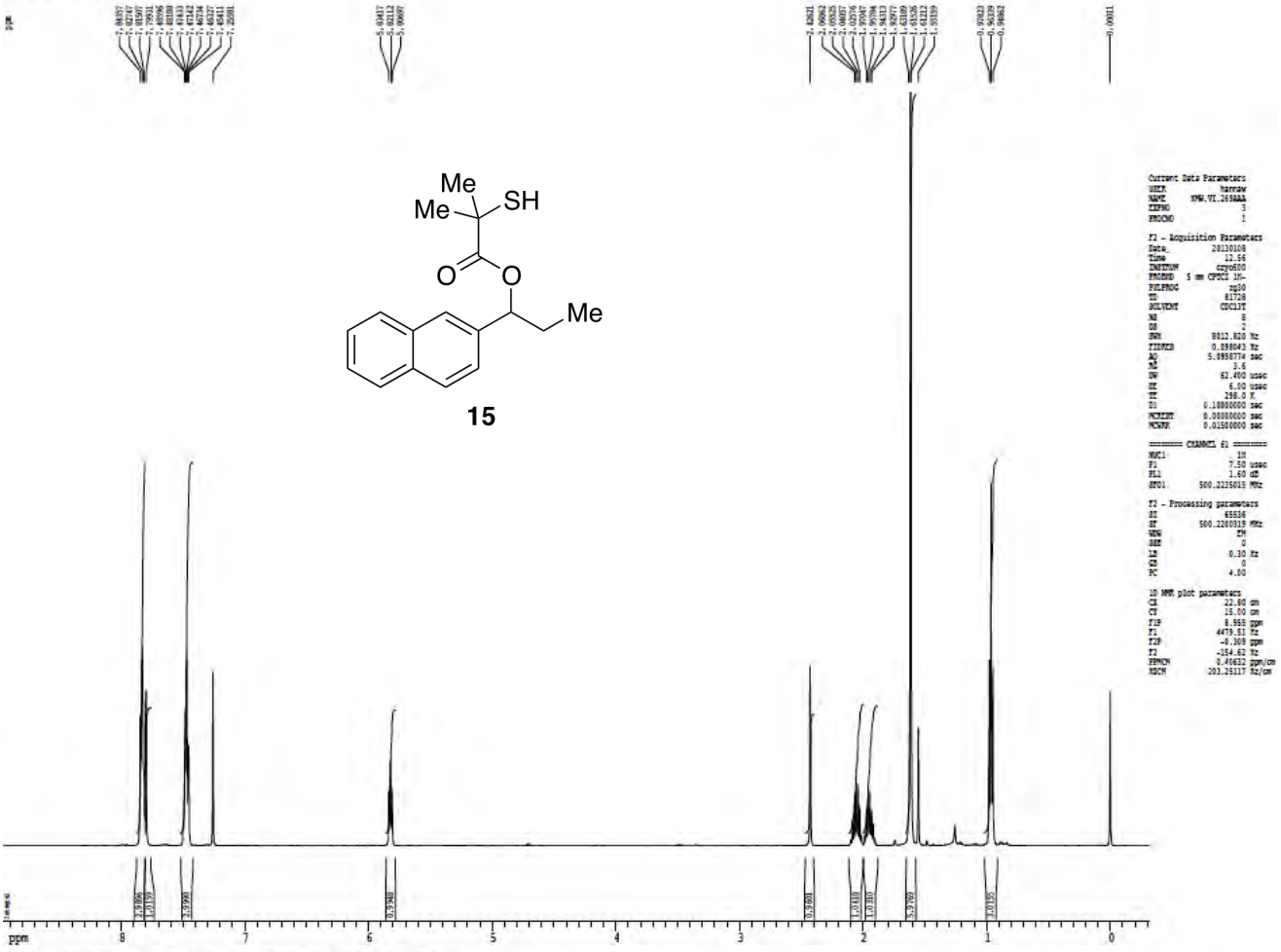
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling

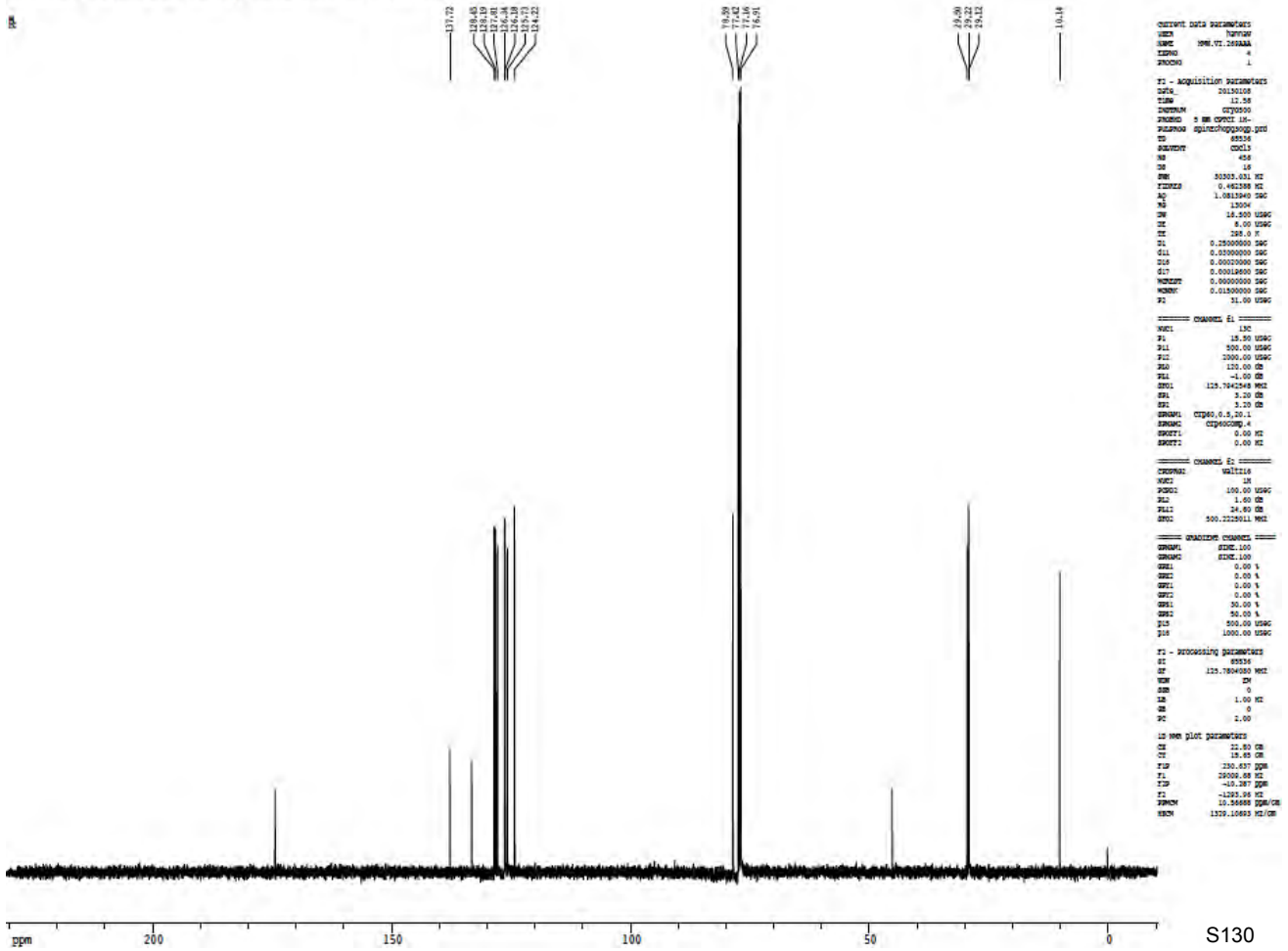


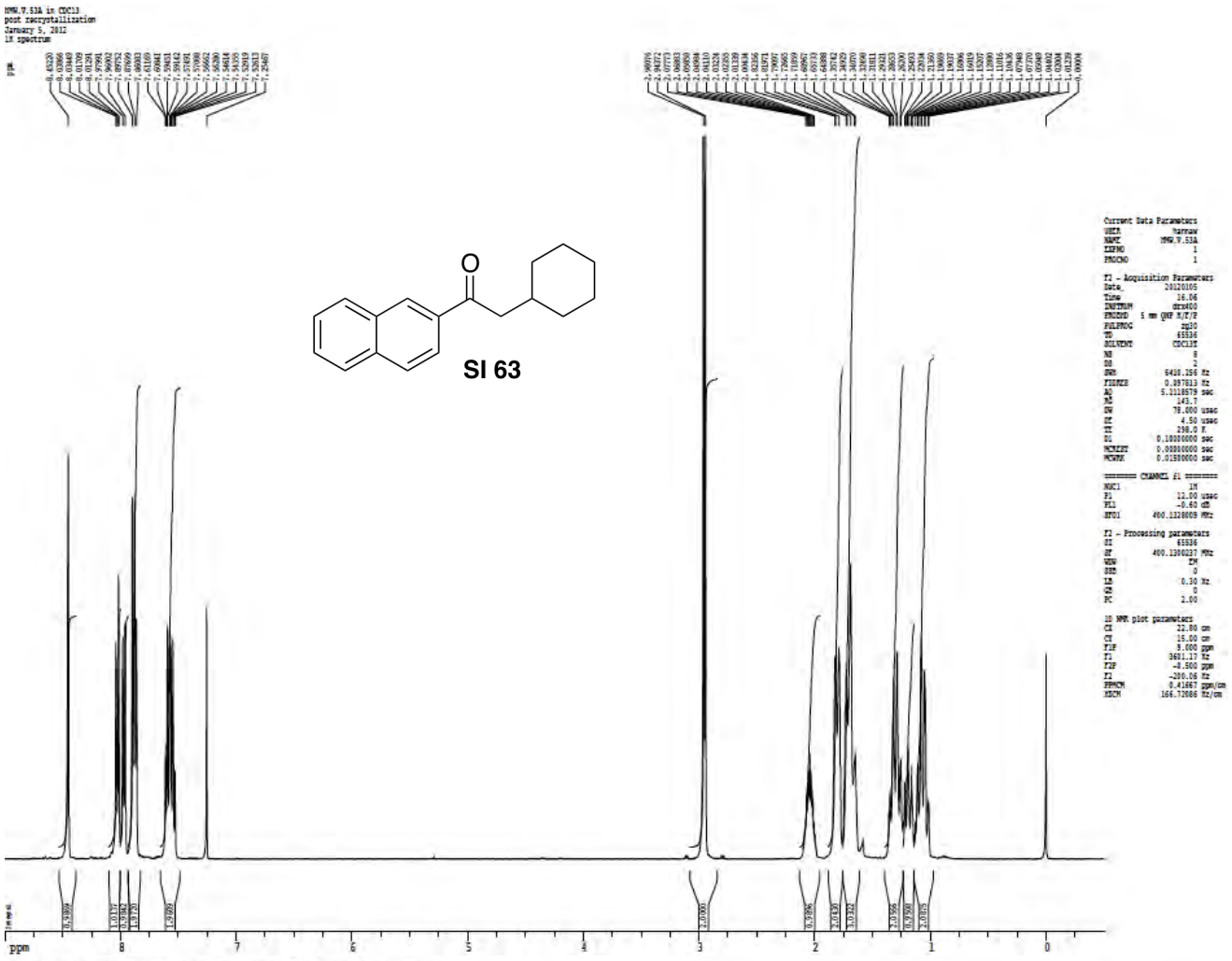
1H spectrum



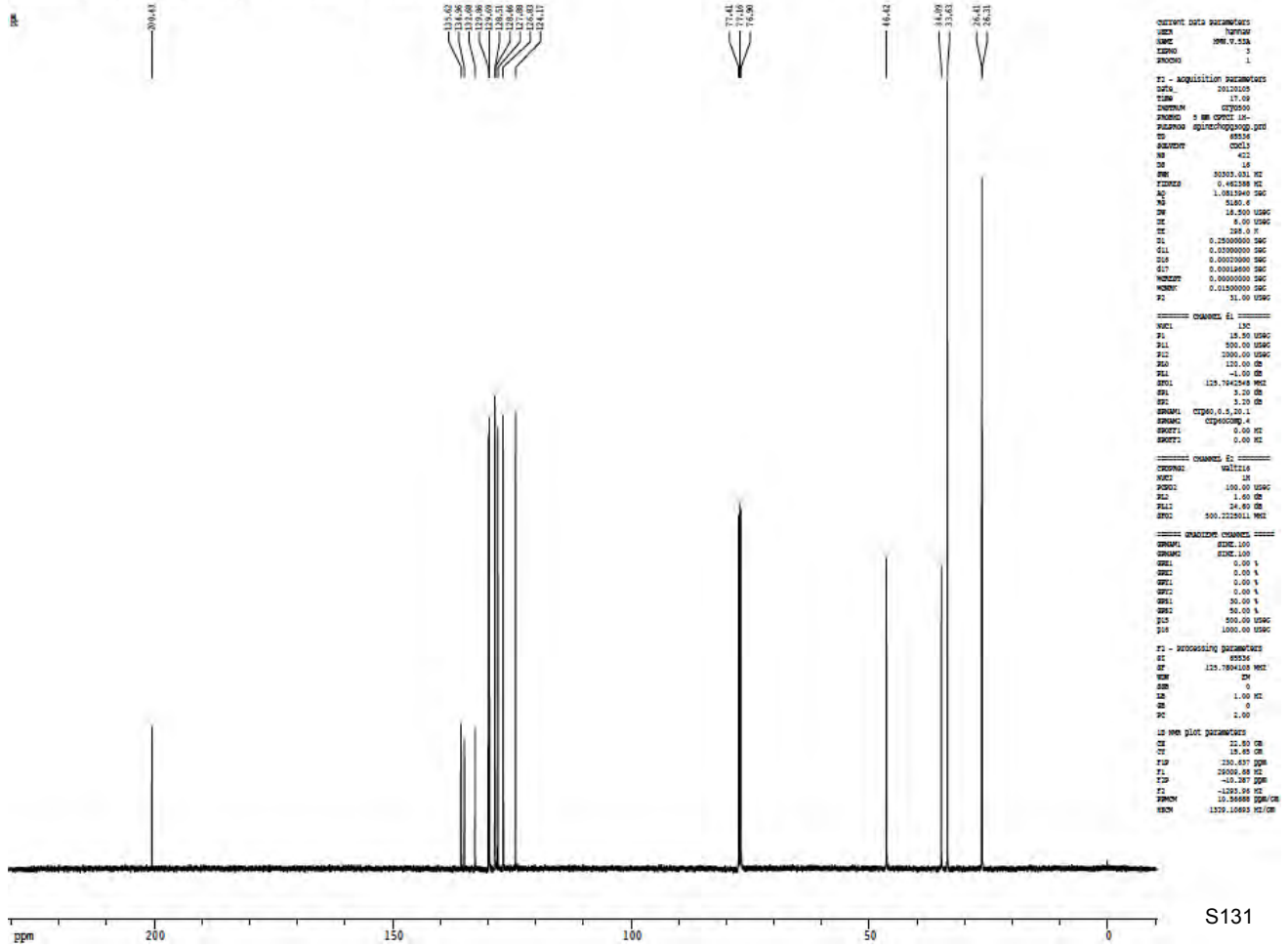
15

Z-restored spin-echo 13C spectrum with 1H decoupling

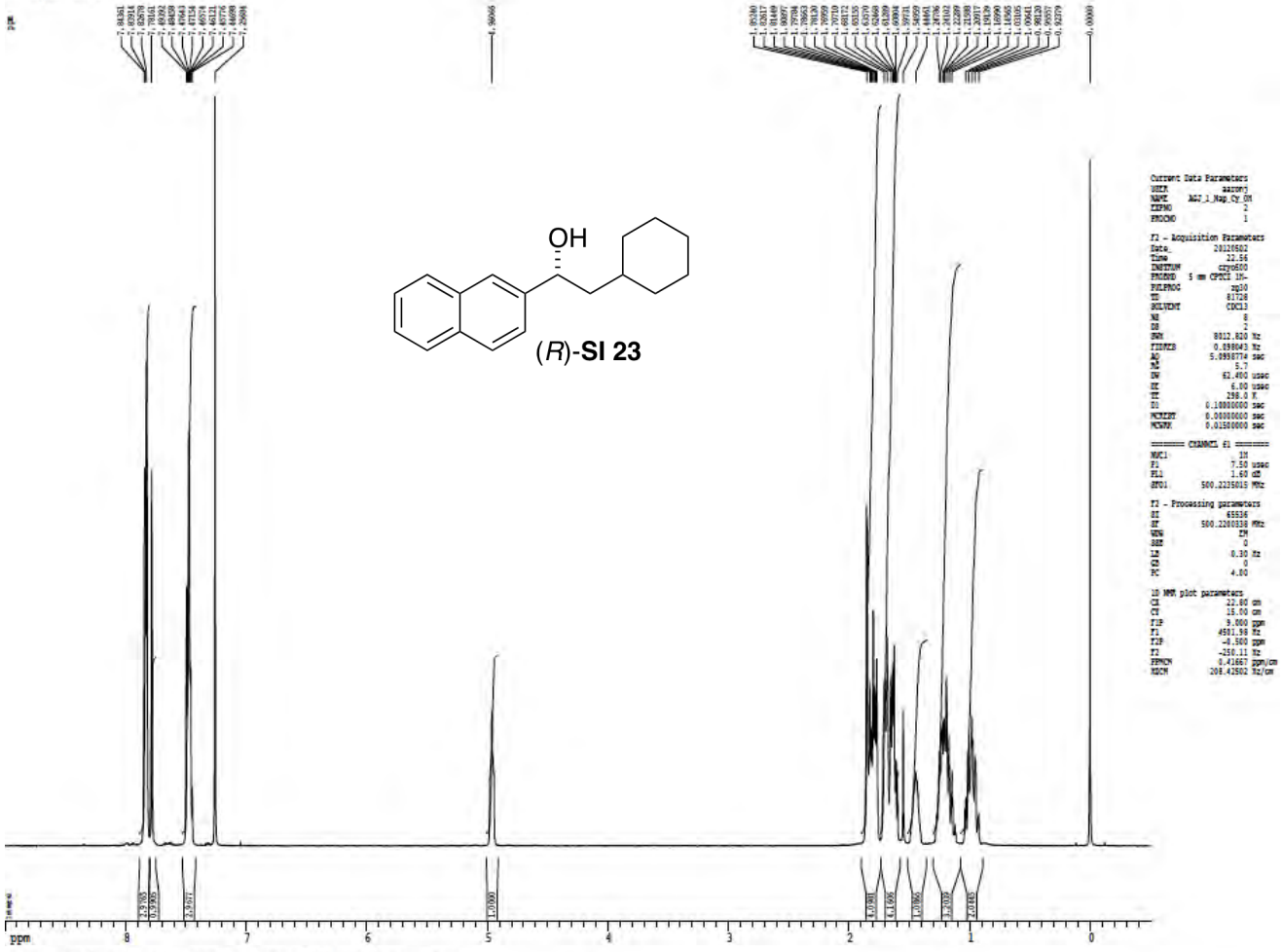




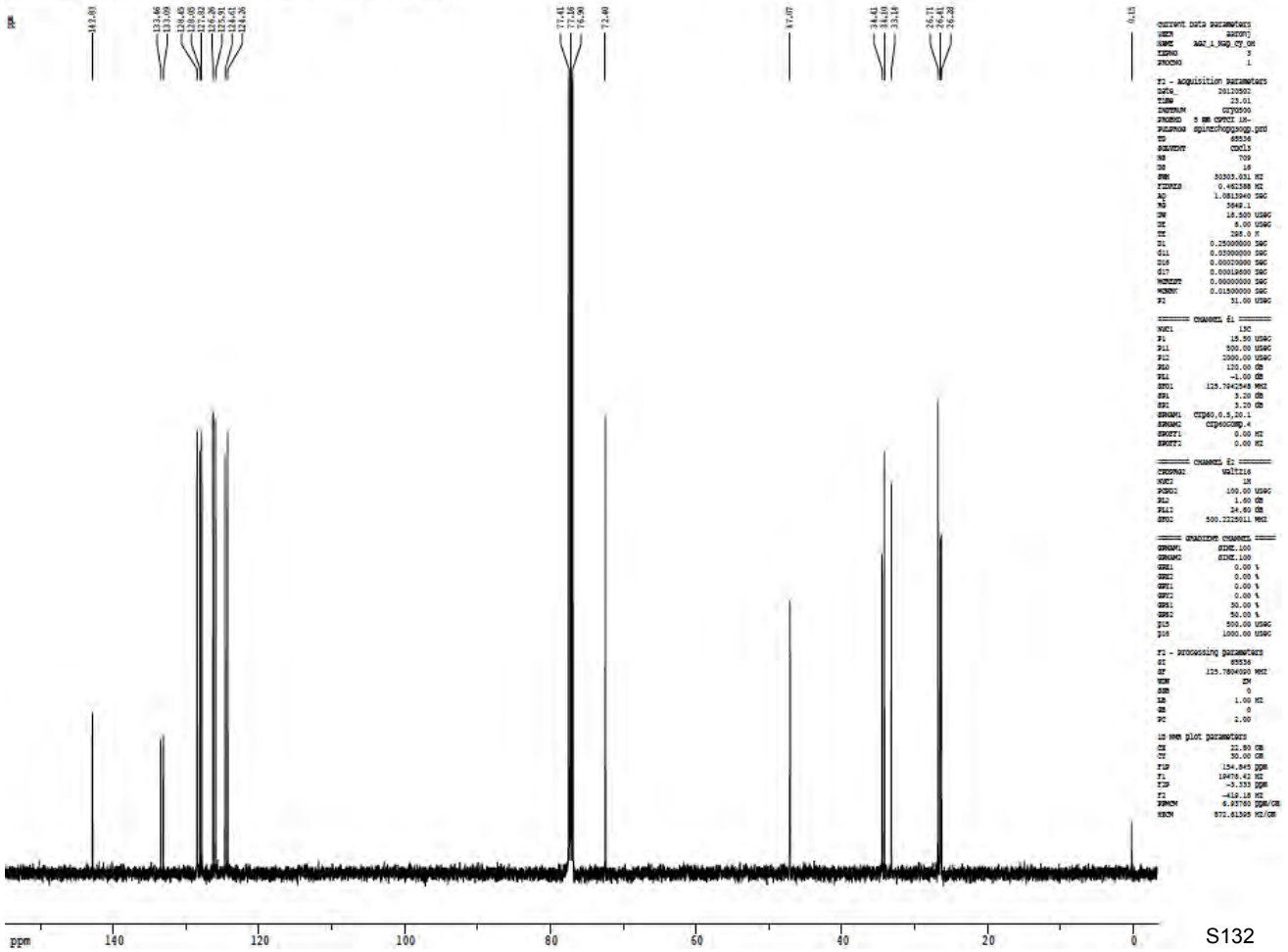
Z-restored spin-echo 13C spectrum with 1H decoupling



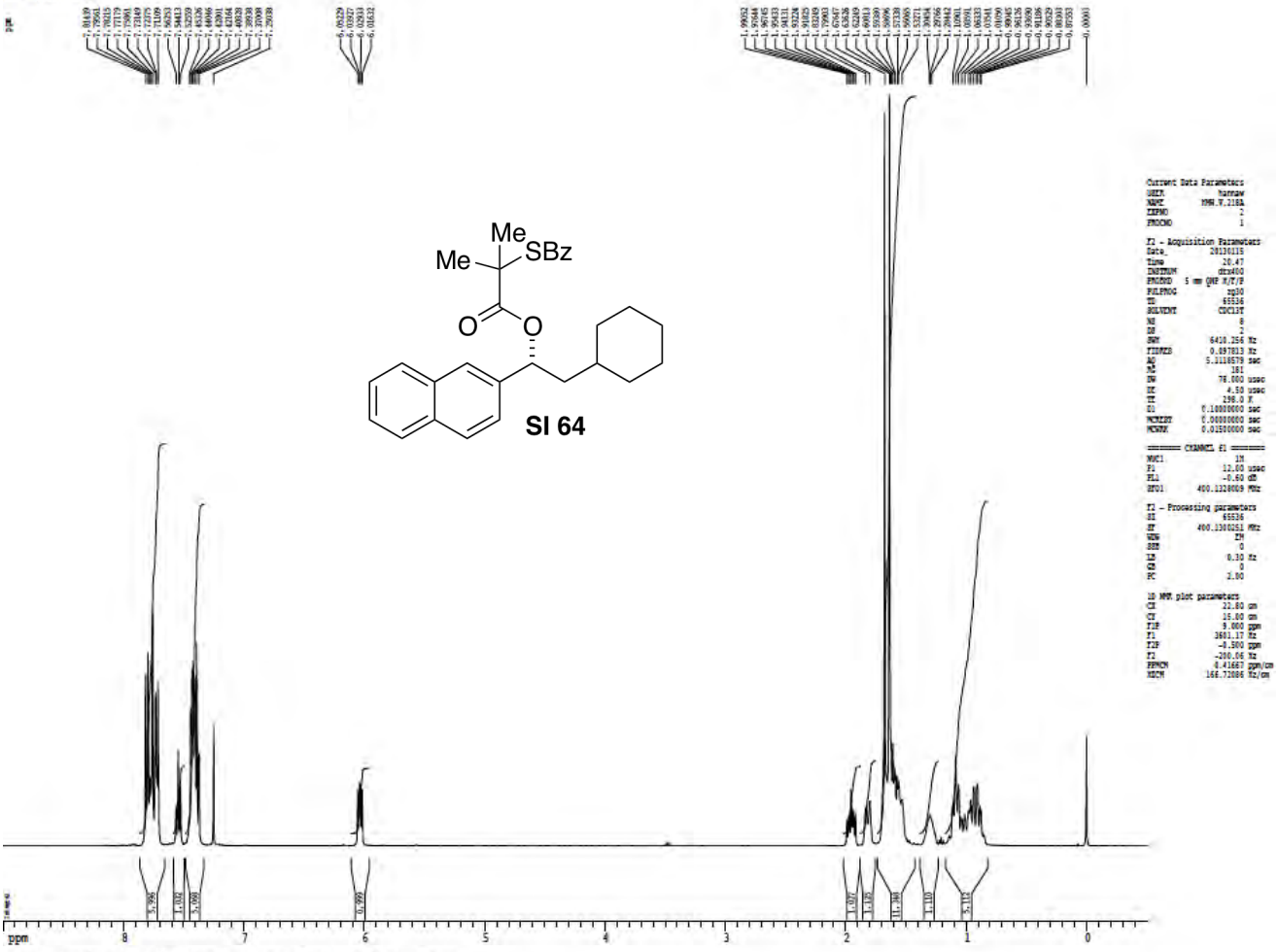
1H spectrum



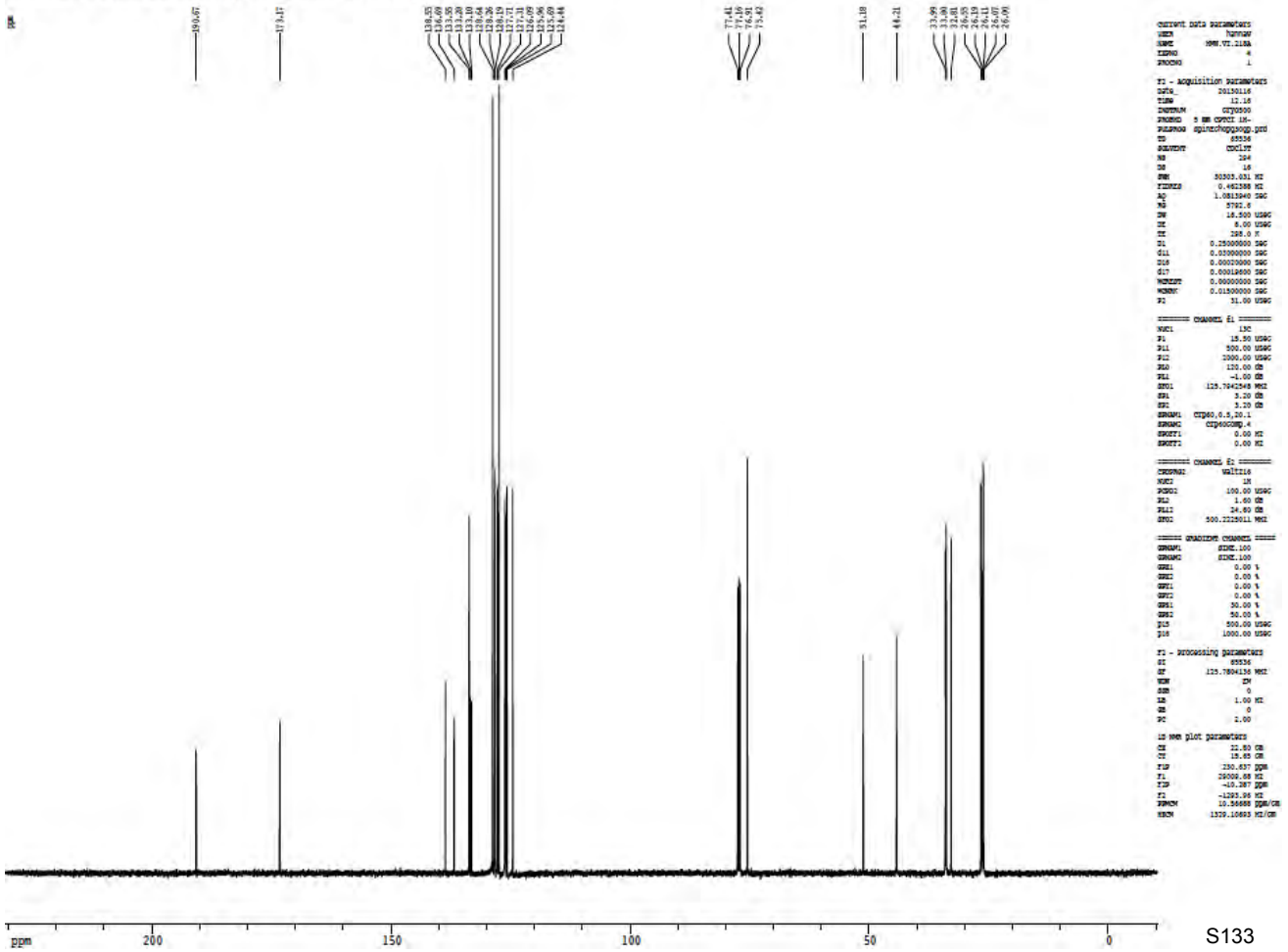
Z-restored spin-echo 13C spectrum with 1H decoupling



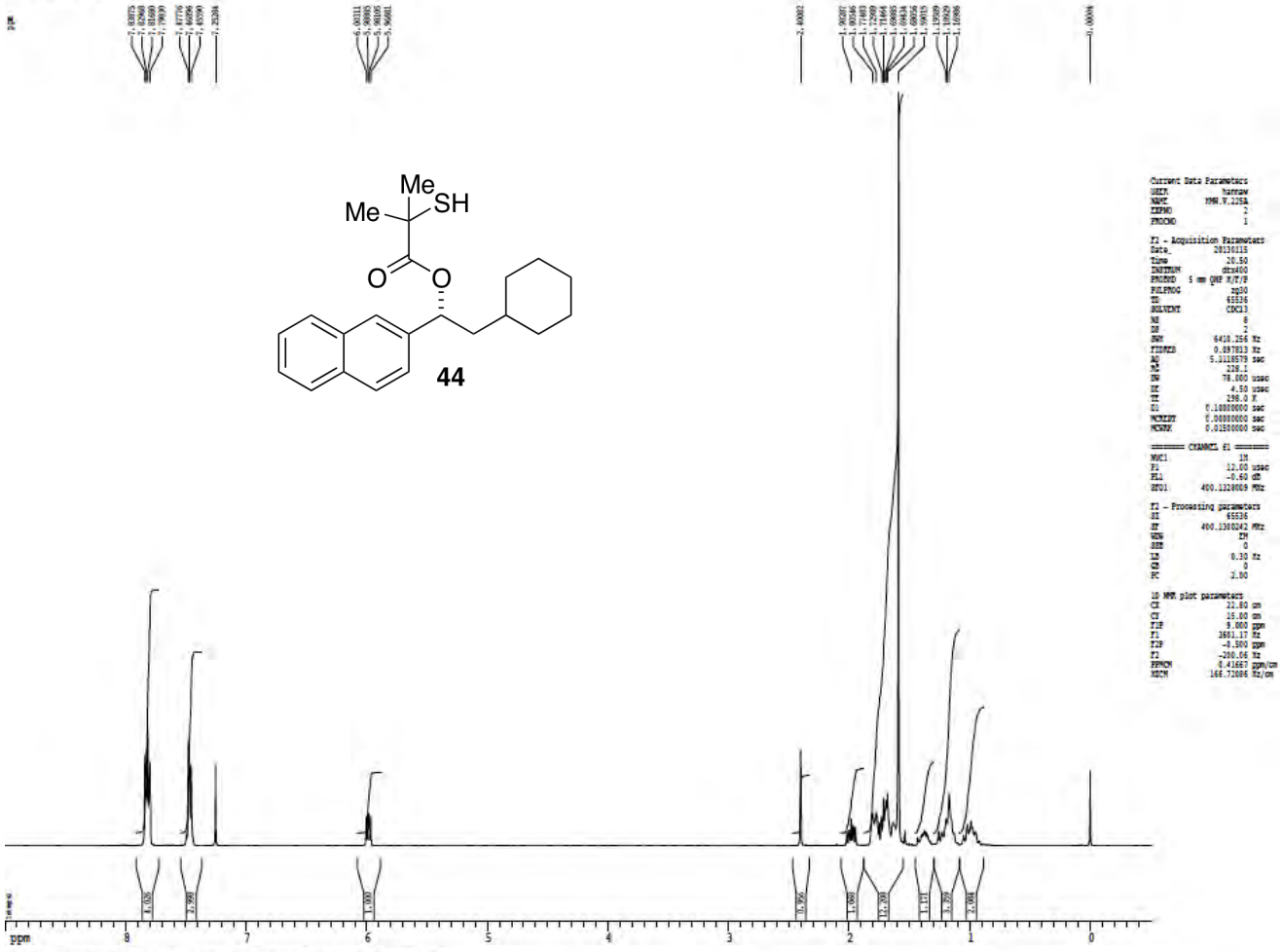
1H spectrum



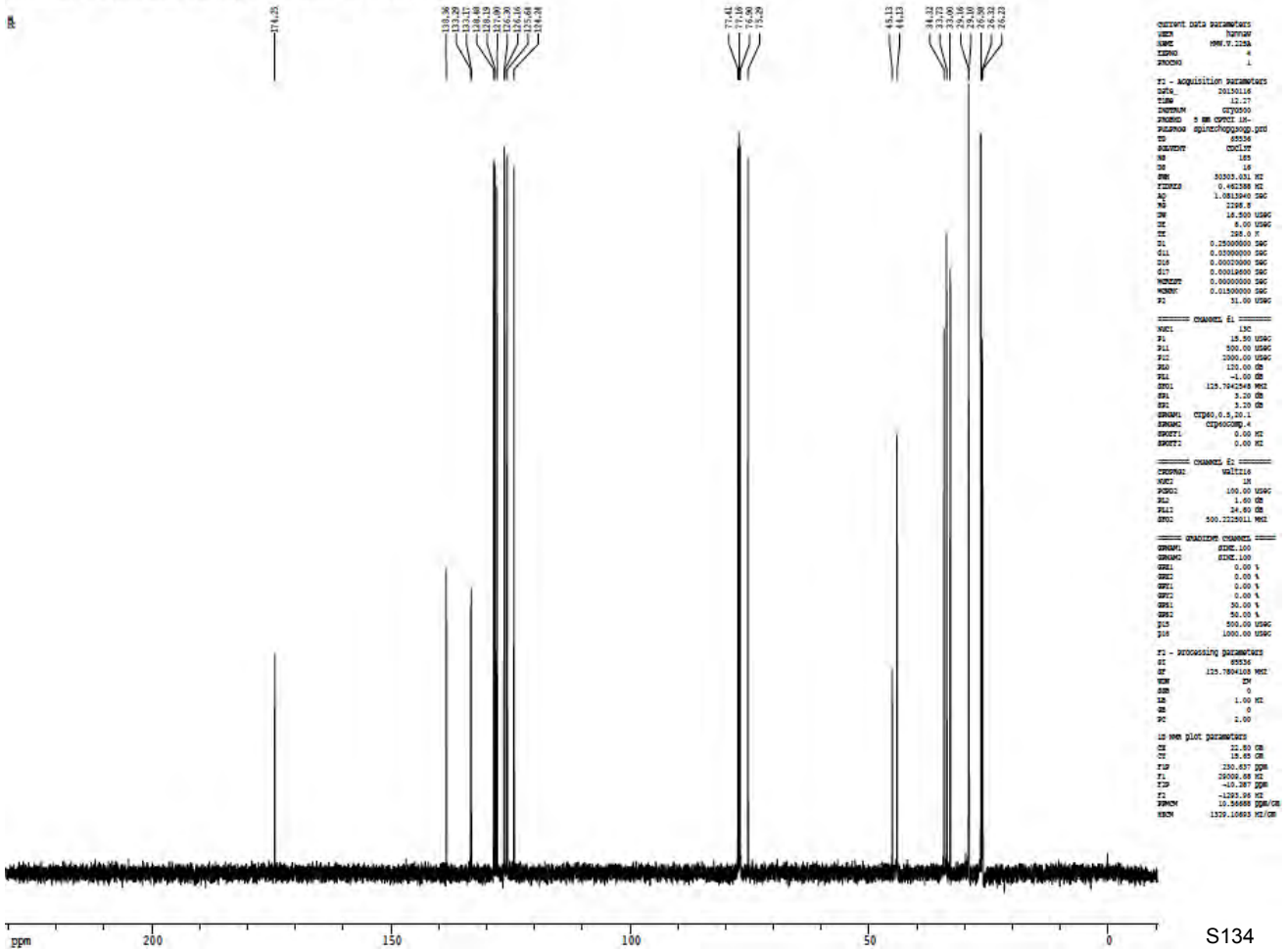
Z-restored spin-echo 13C spectrum with 1H decoupling



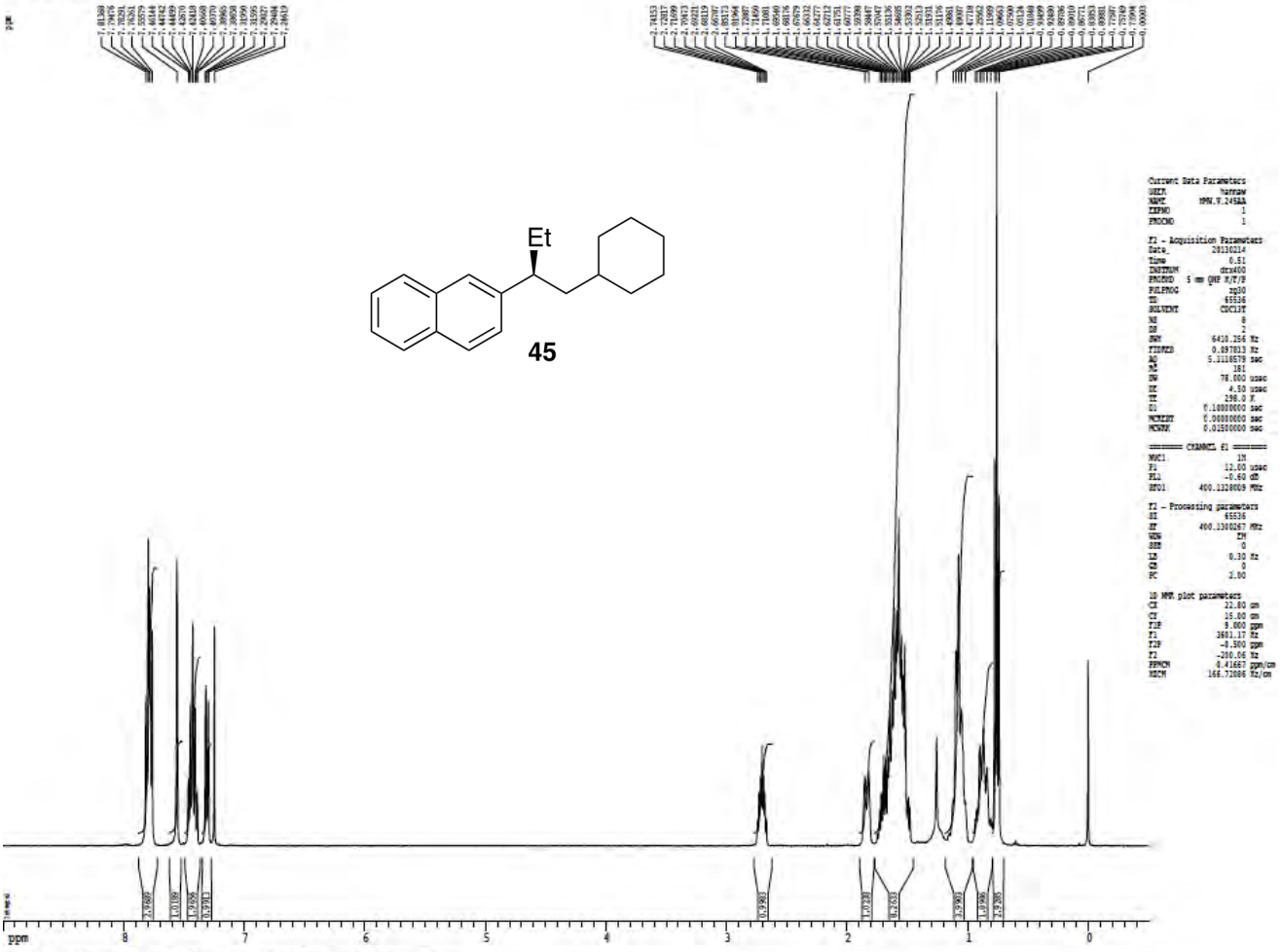
1H spectrum



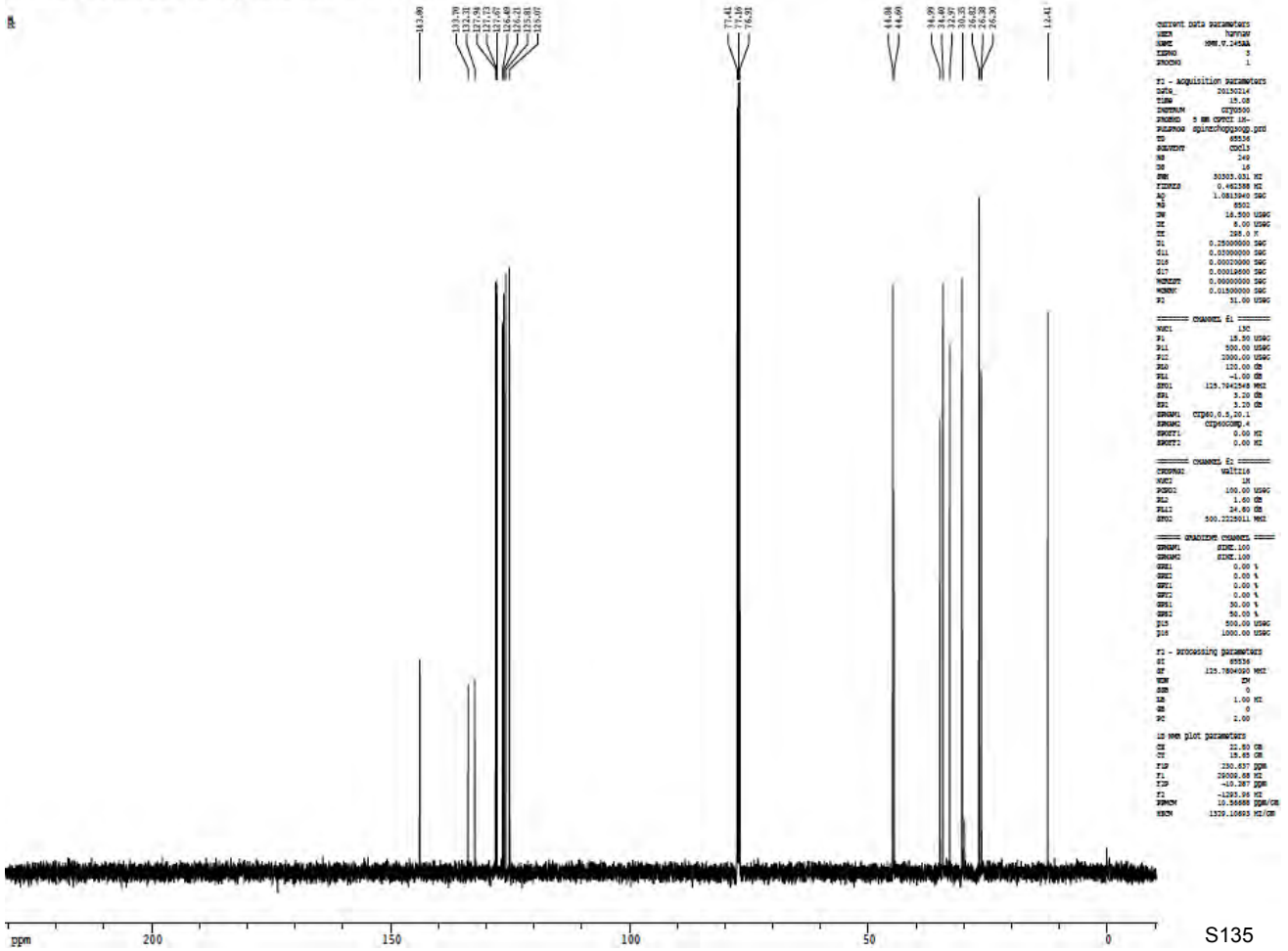
Z-restored spin-echo 13C spectrum with 1H decoupling



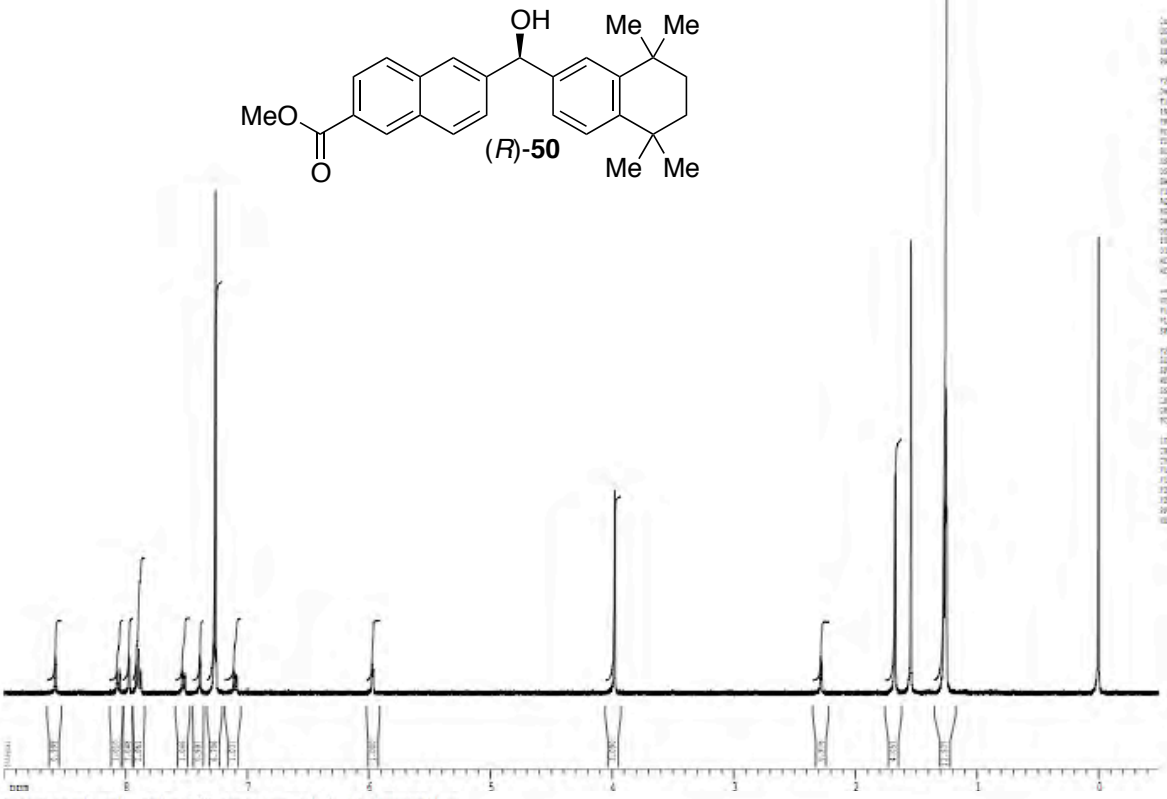
1H spectrum



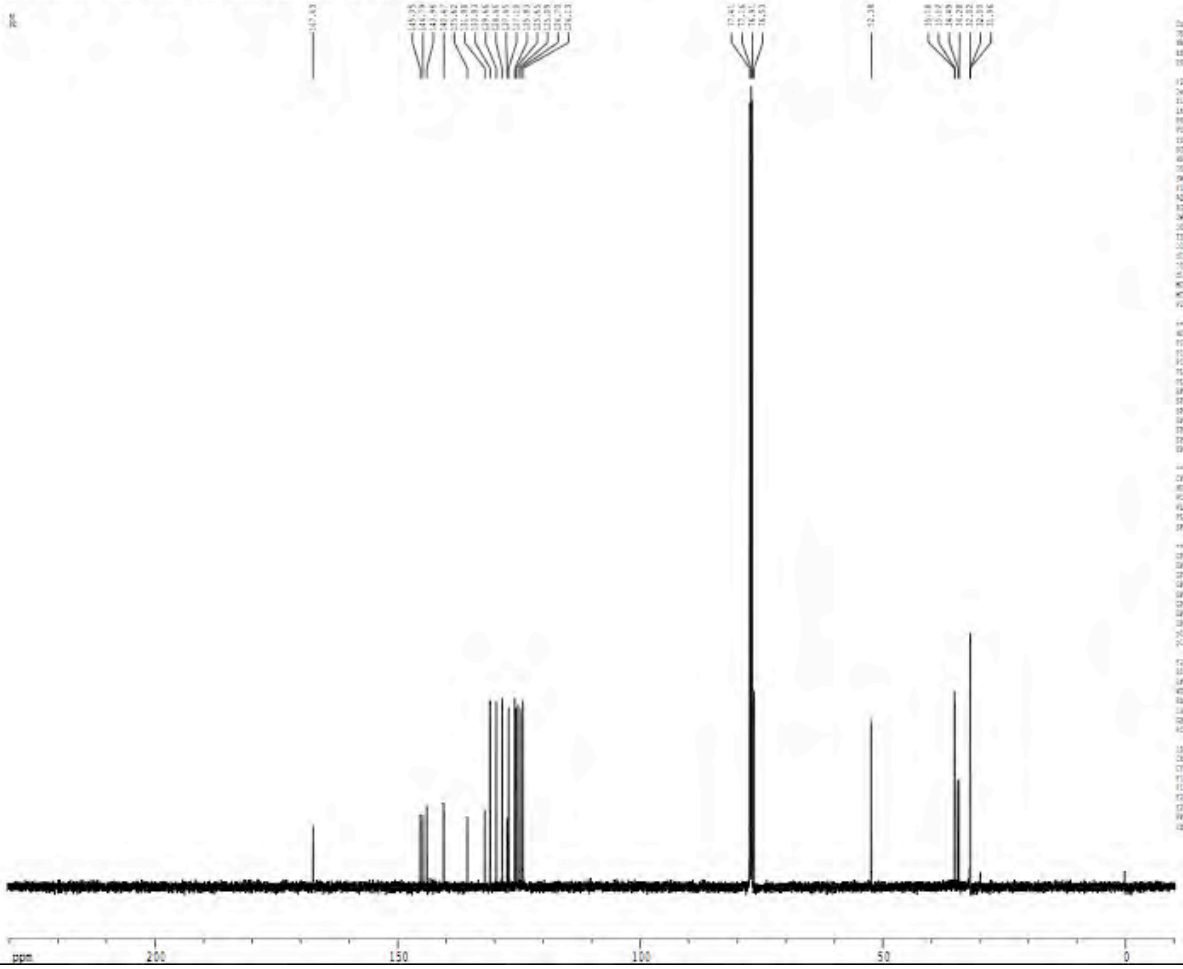
Z-restored spin-echo 13C spectrum with 1H decoupling



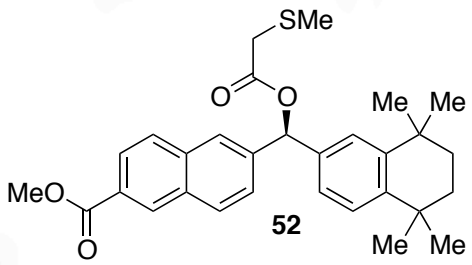
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling

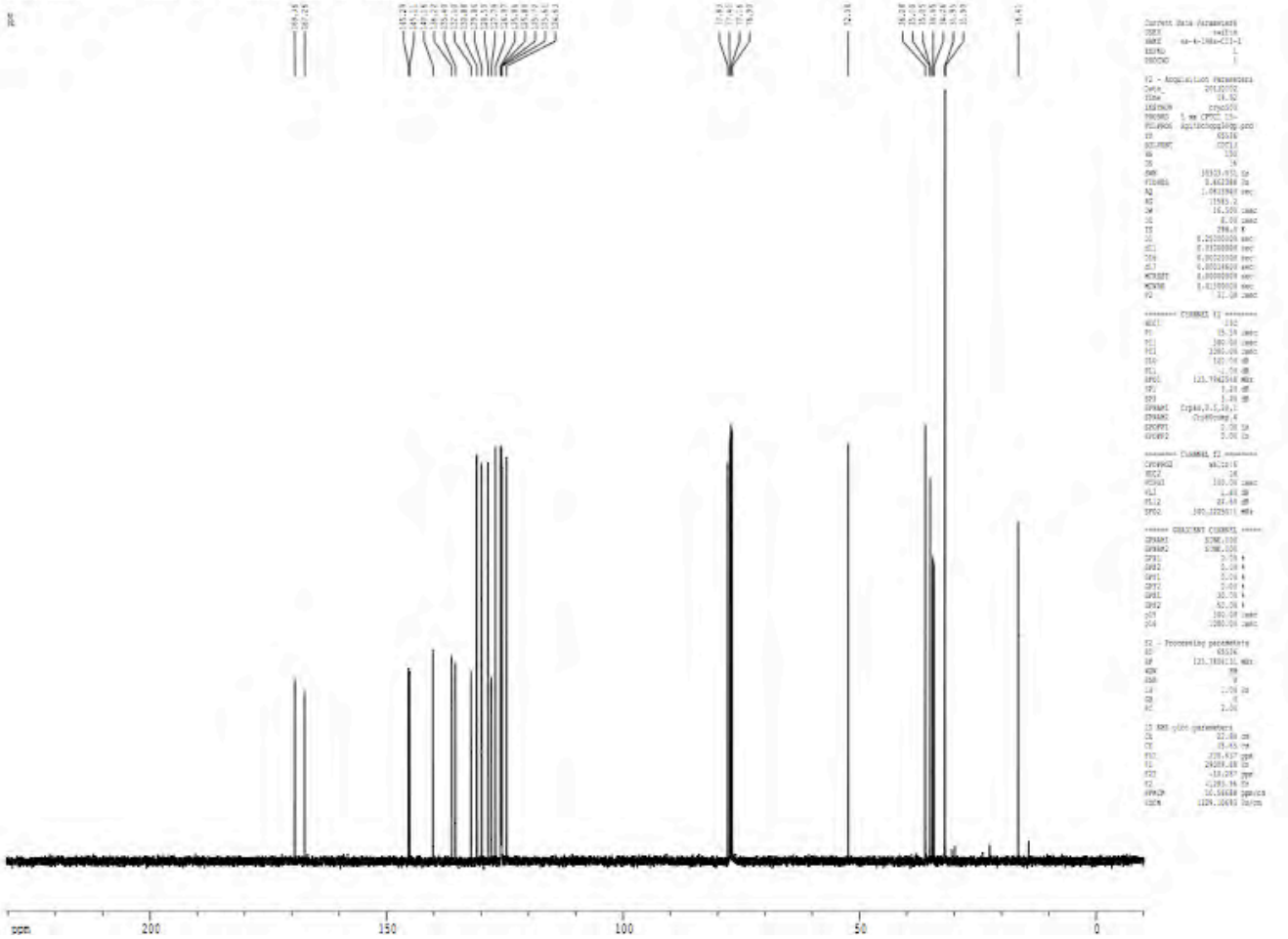


1H spectrum

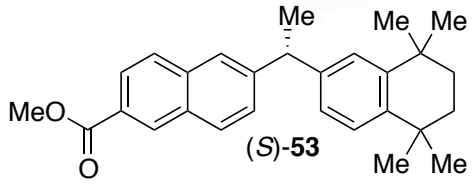


52

Z-restored spin-echo 13C spectrum with 1H decoupling



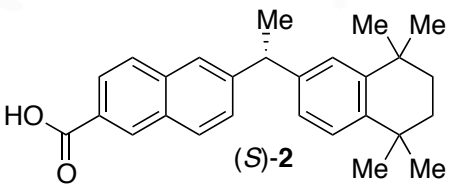
1H spectrum



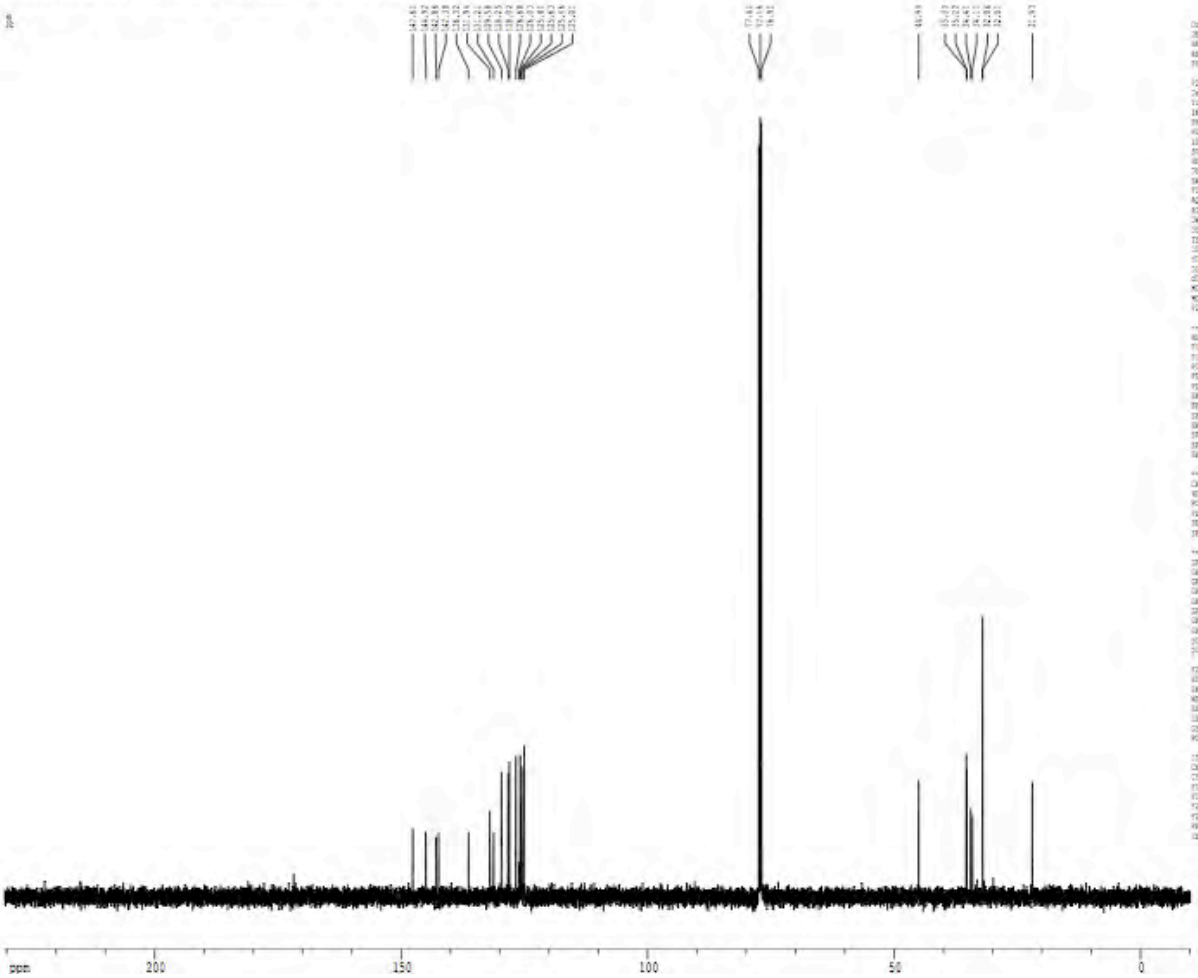
(*S*)-**53**

Z-restored spin-echo 13C spectrum with 1H decoupling

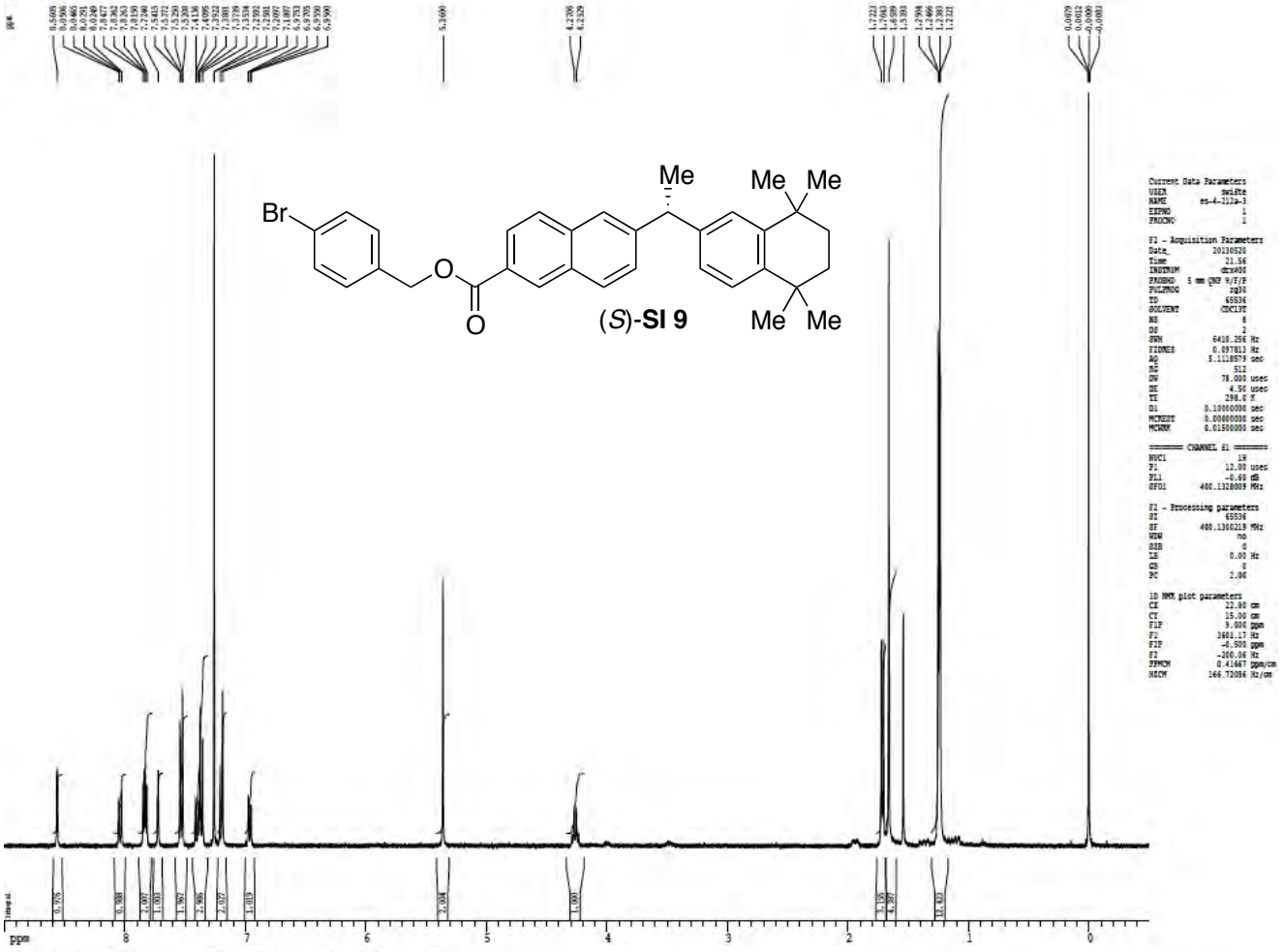
1H spectrum



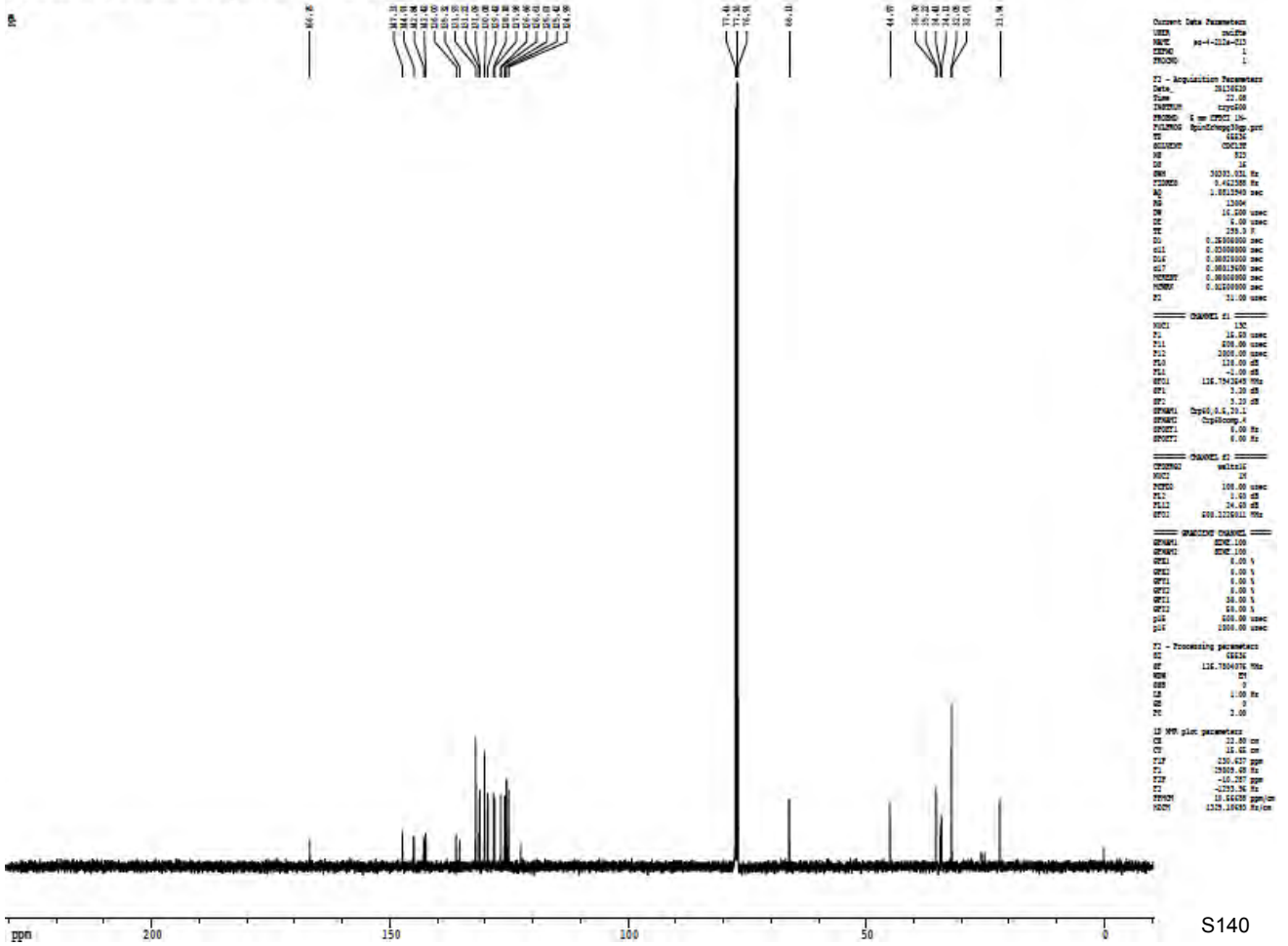
Z-restored spin-echo 13C spectrum with 1H decoupling



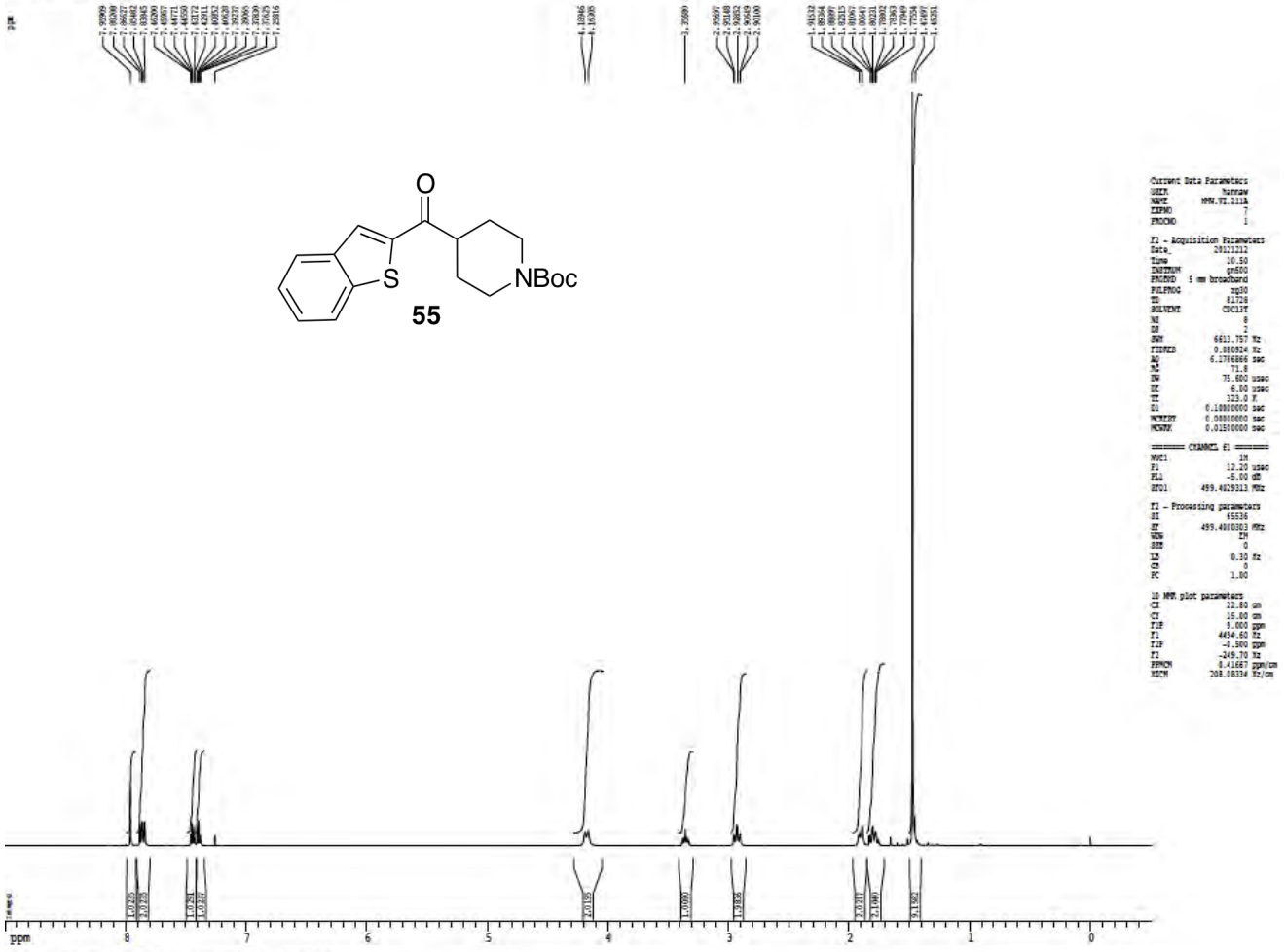
1H spectrum



Z-restored spin-echo 13C spectrum with 1H decoupling

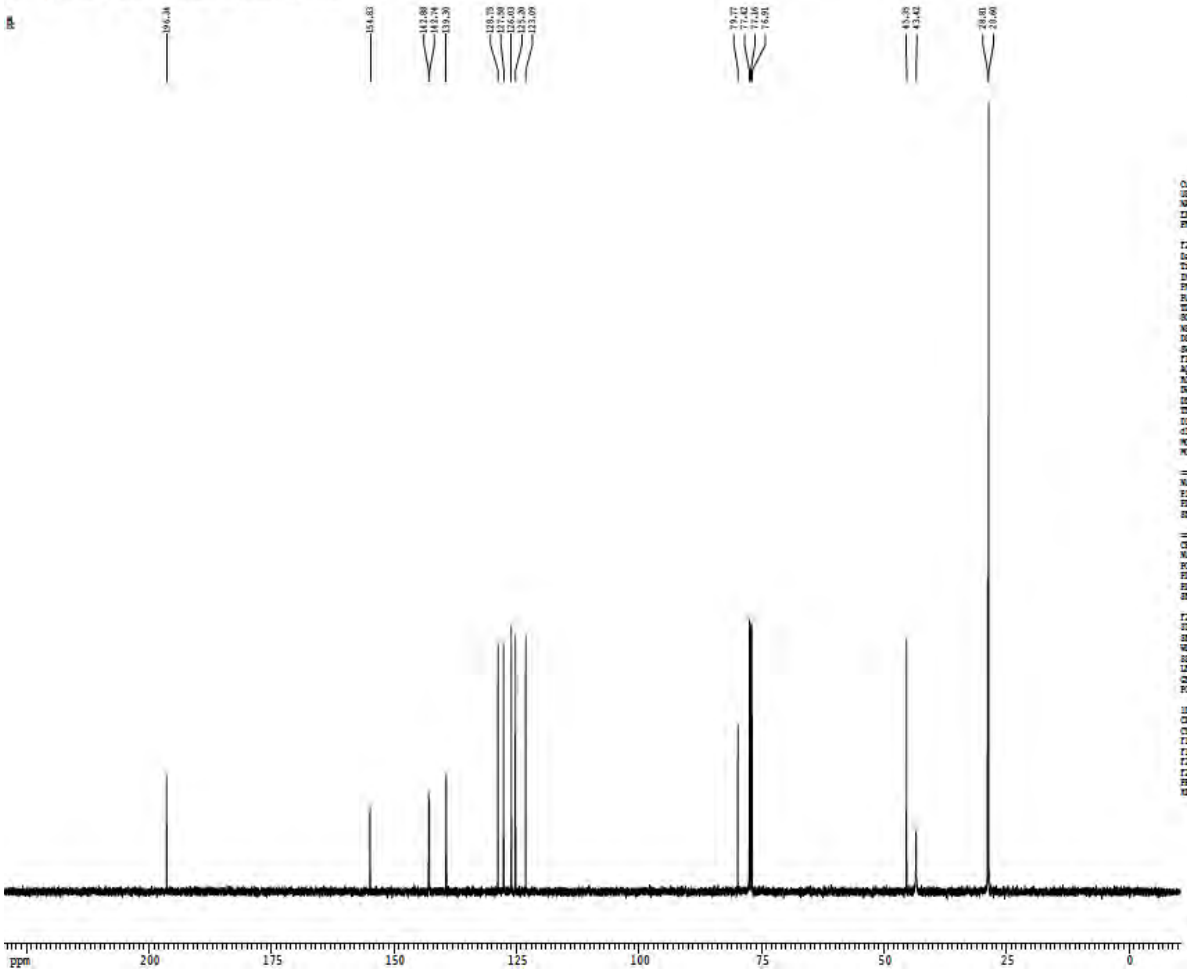


1H spectrum @ 323K

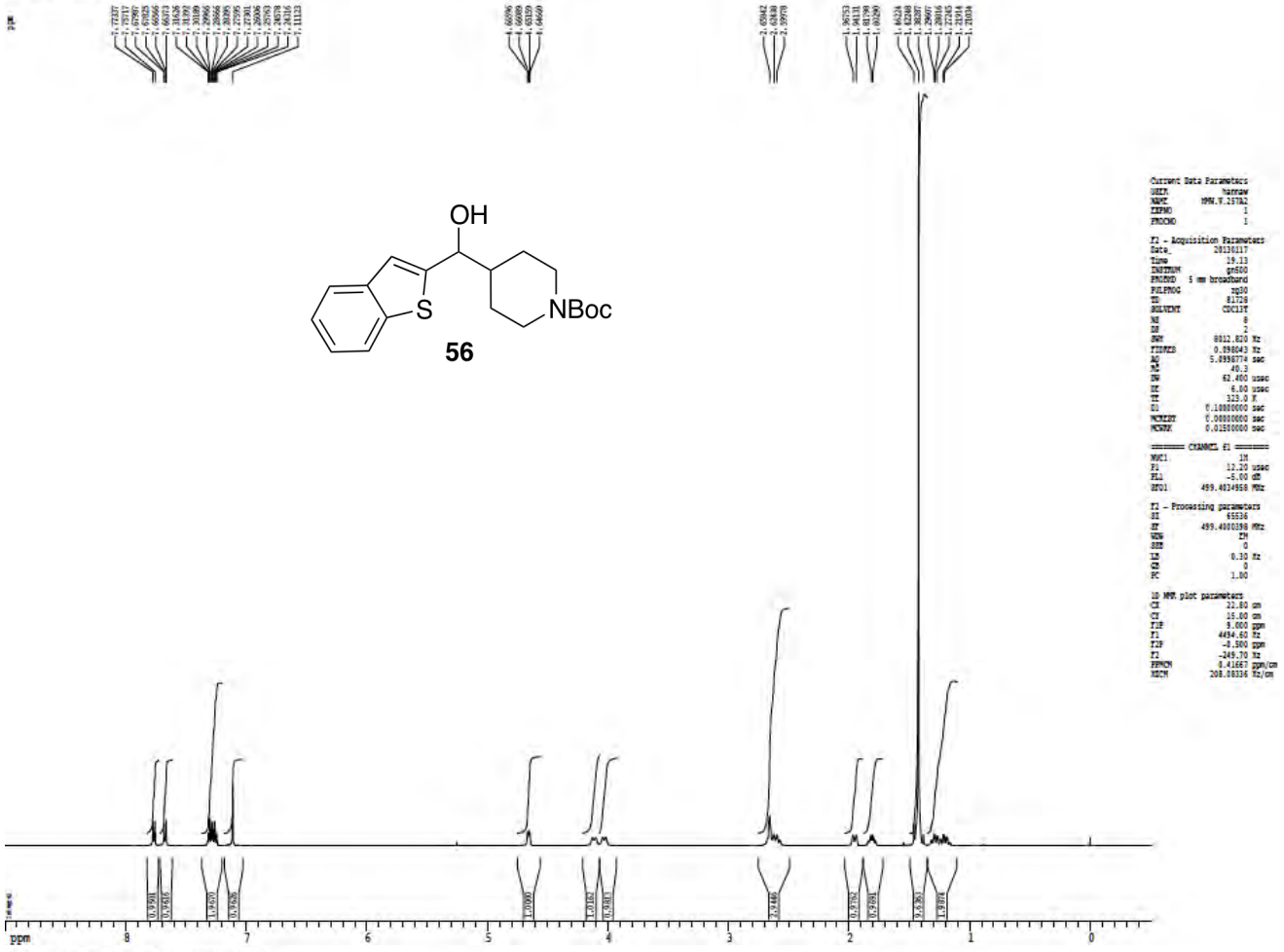


55

13C spectrum with 1H decoupling @ 323K

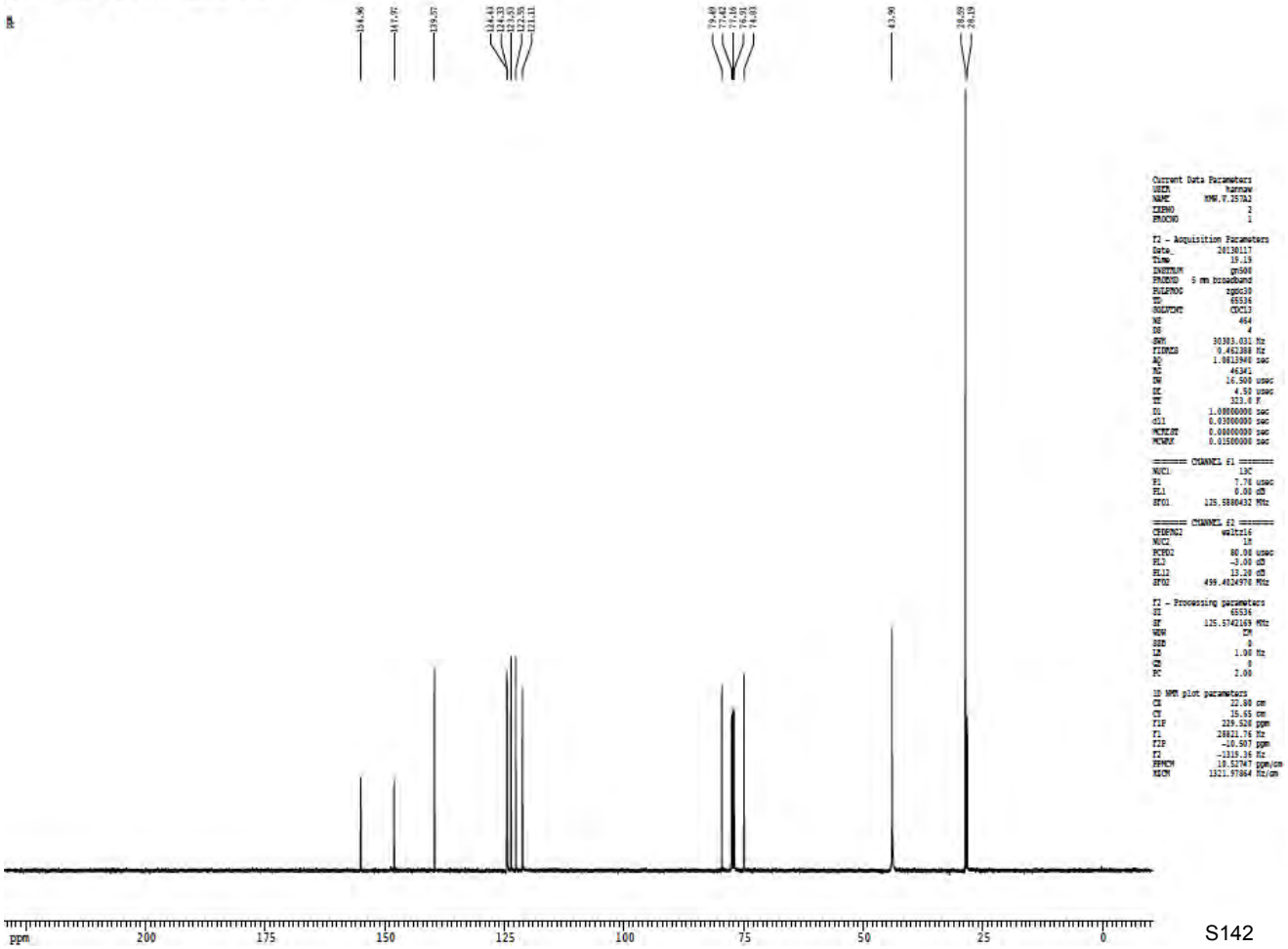


1H spectrum

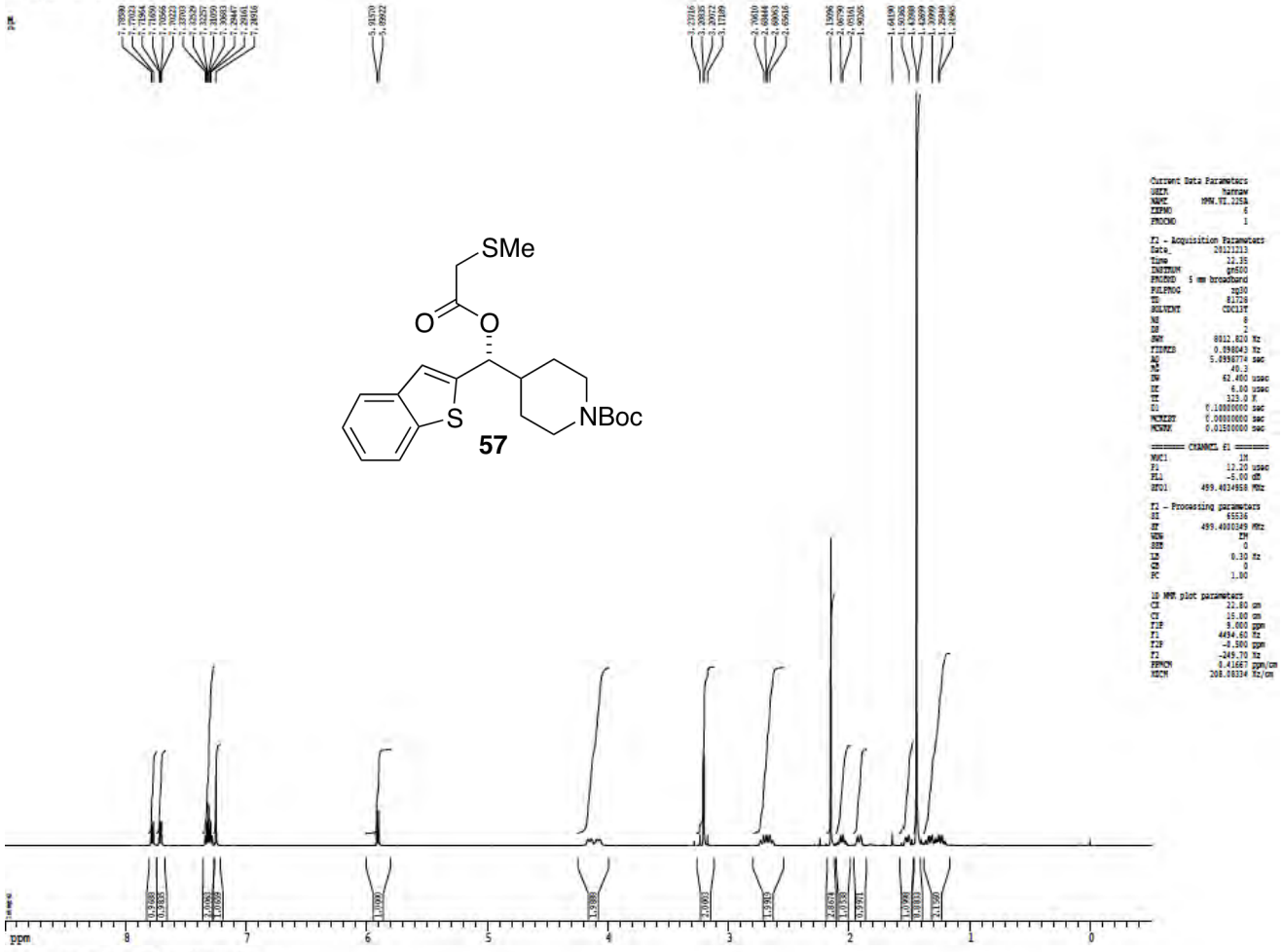


56

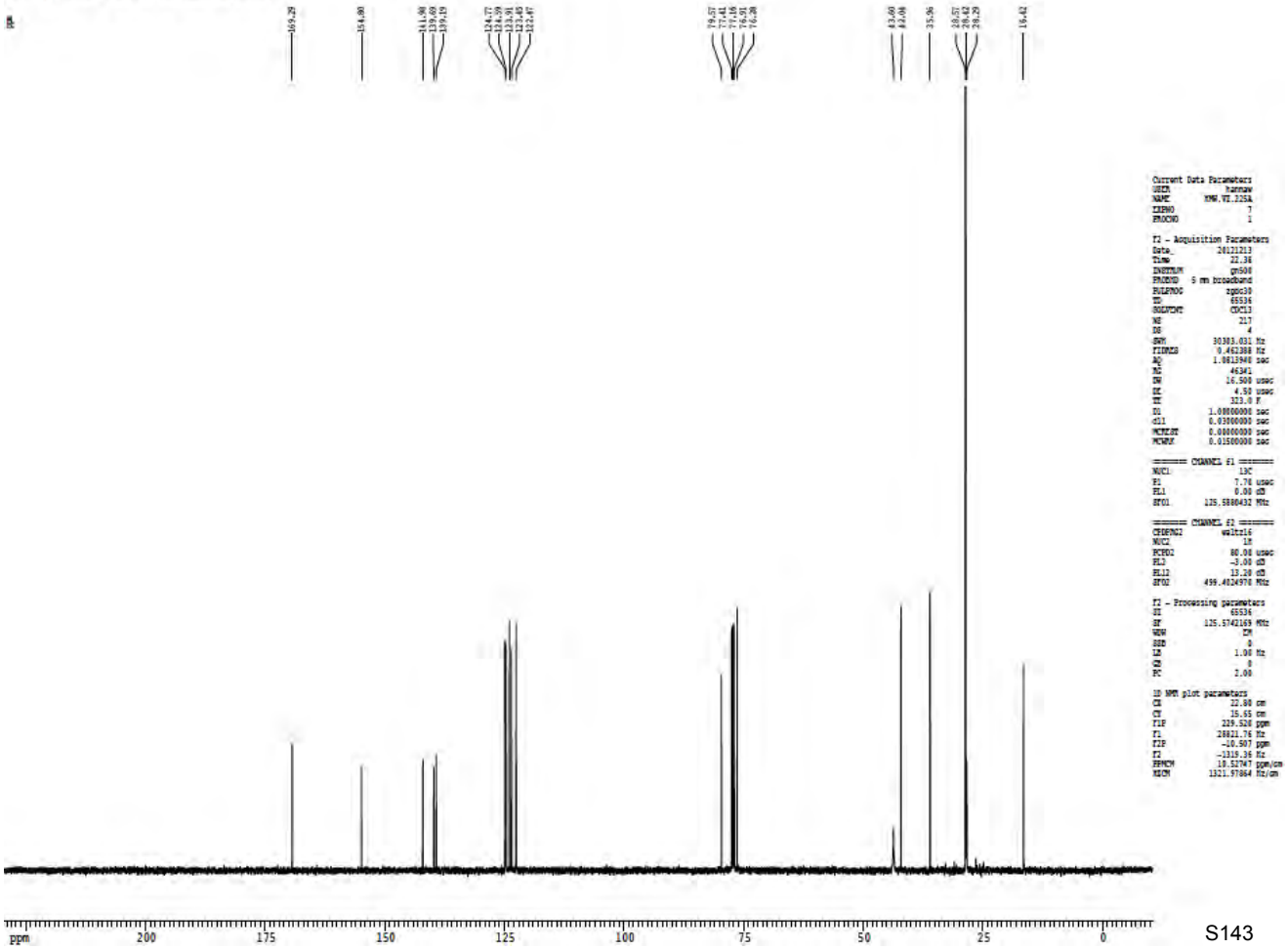
13C spectrum with 1H decoupling

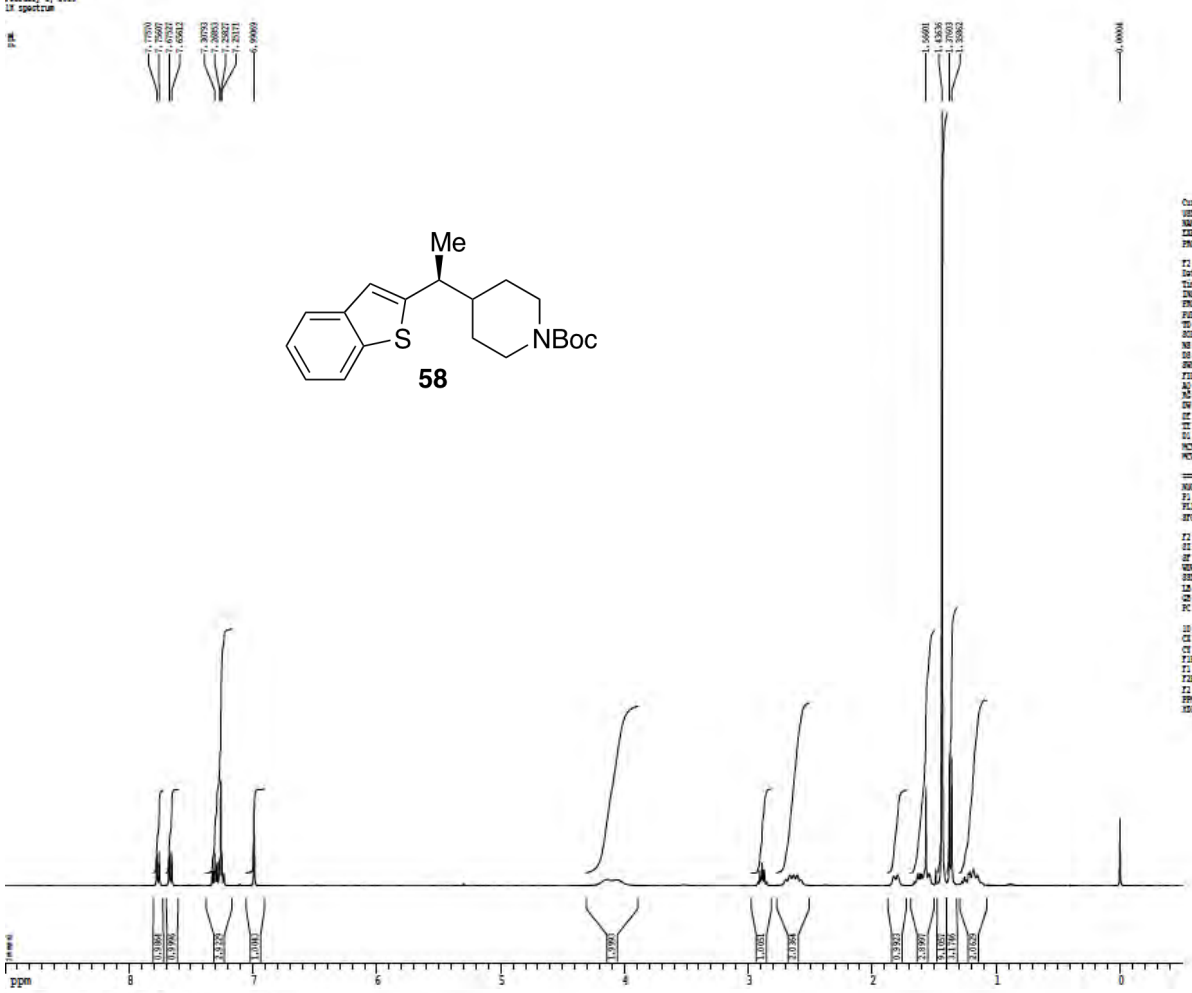


1H spectrum



13C spectrum with 1H decoupling





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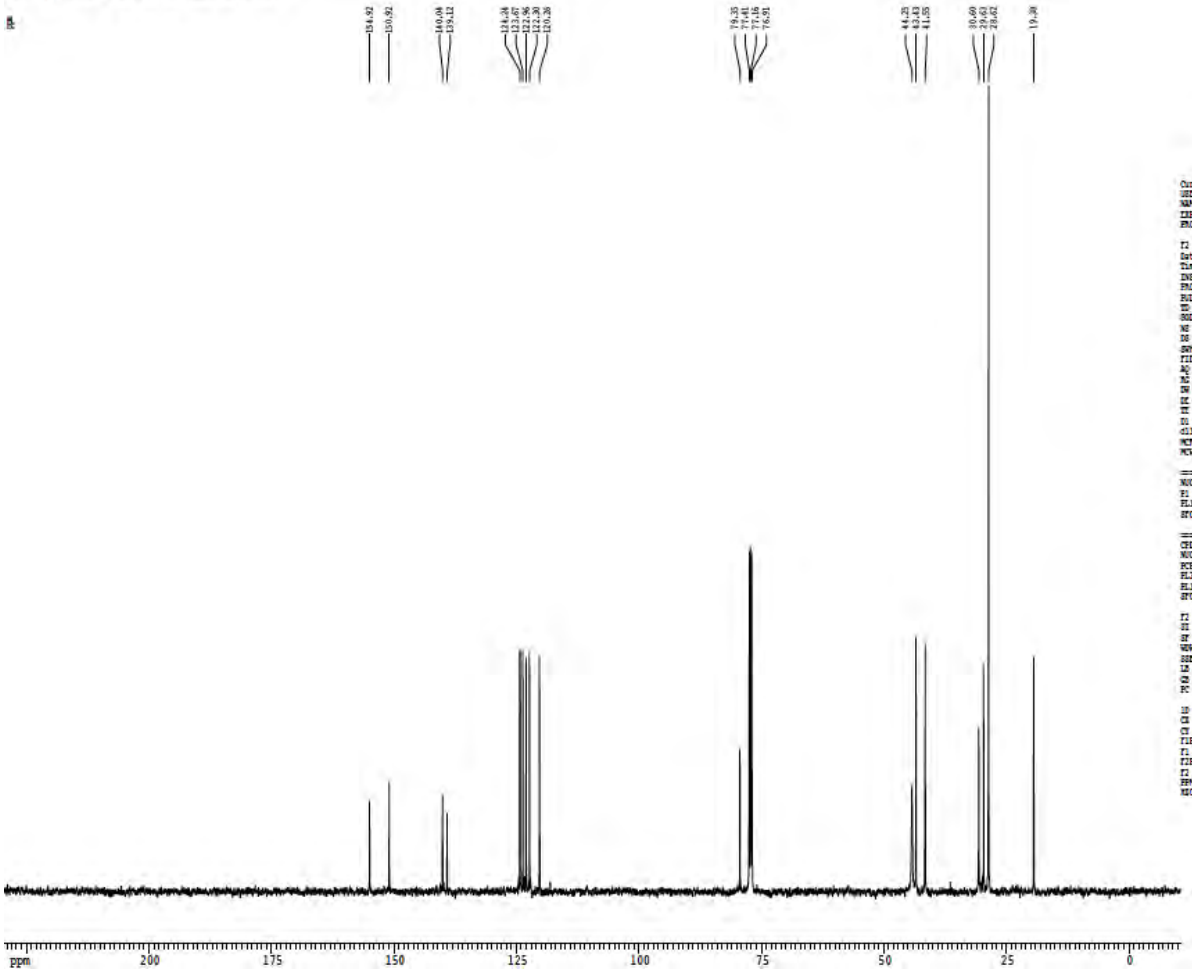
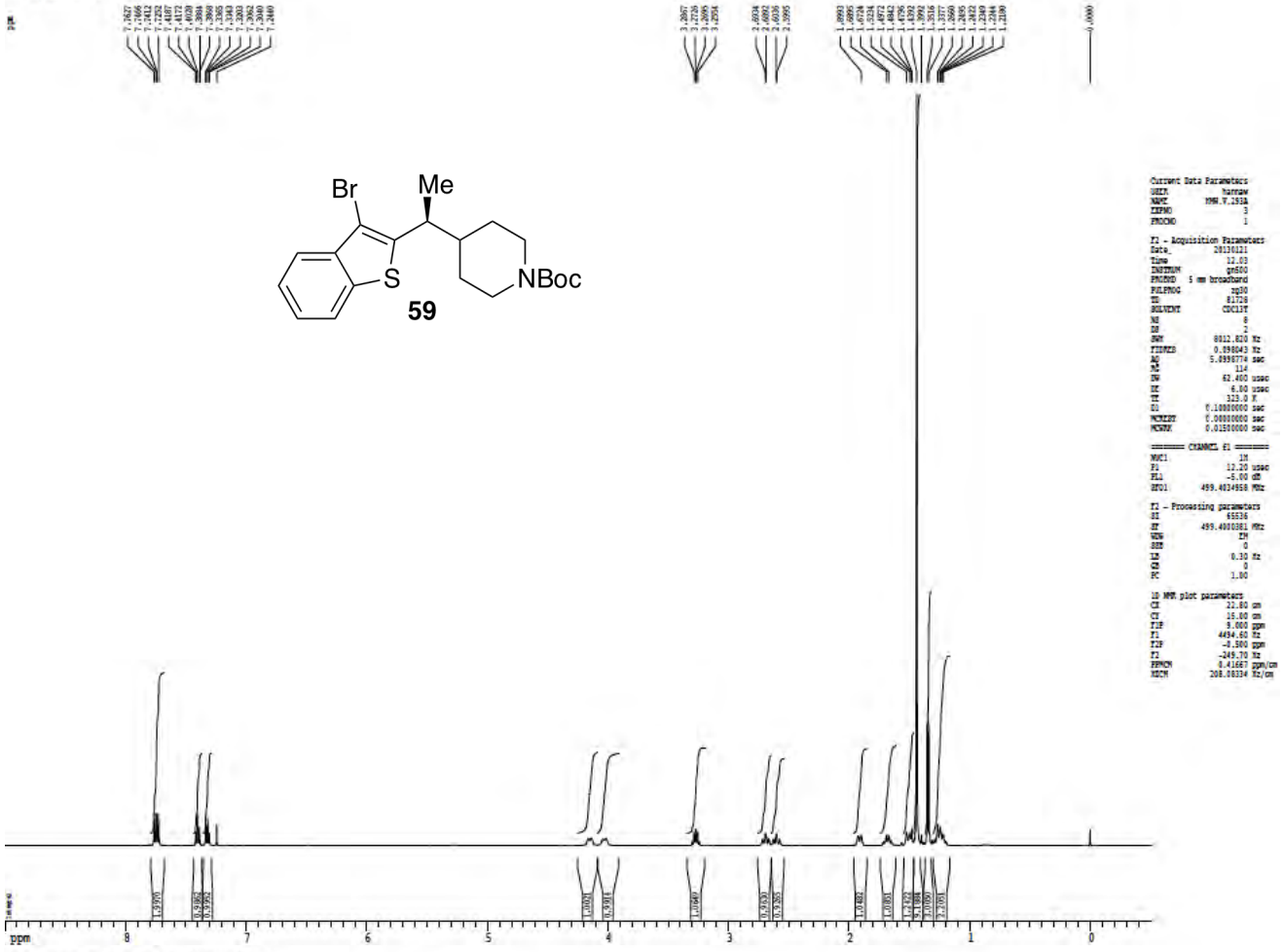
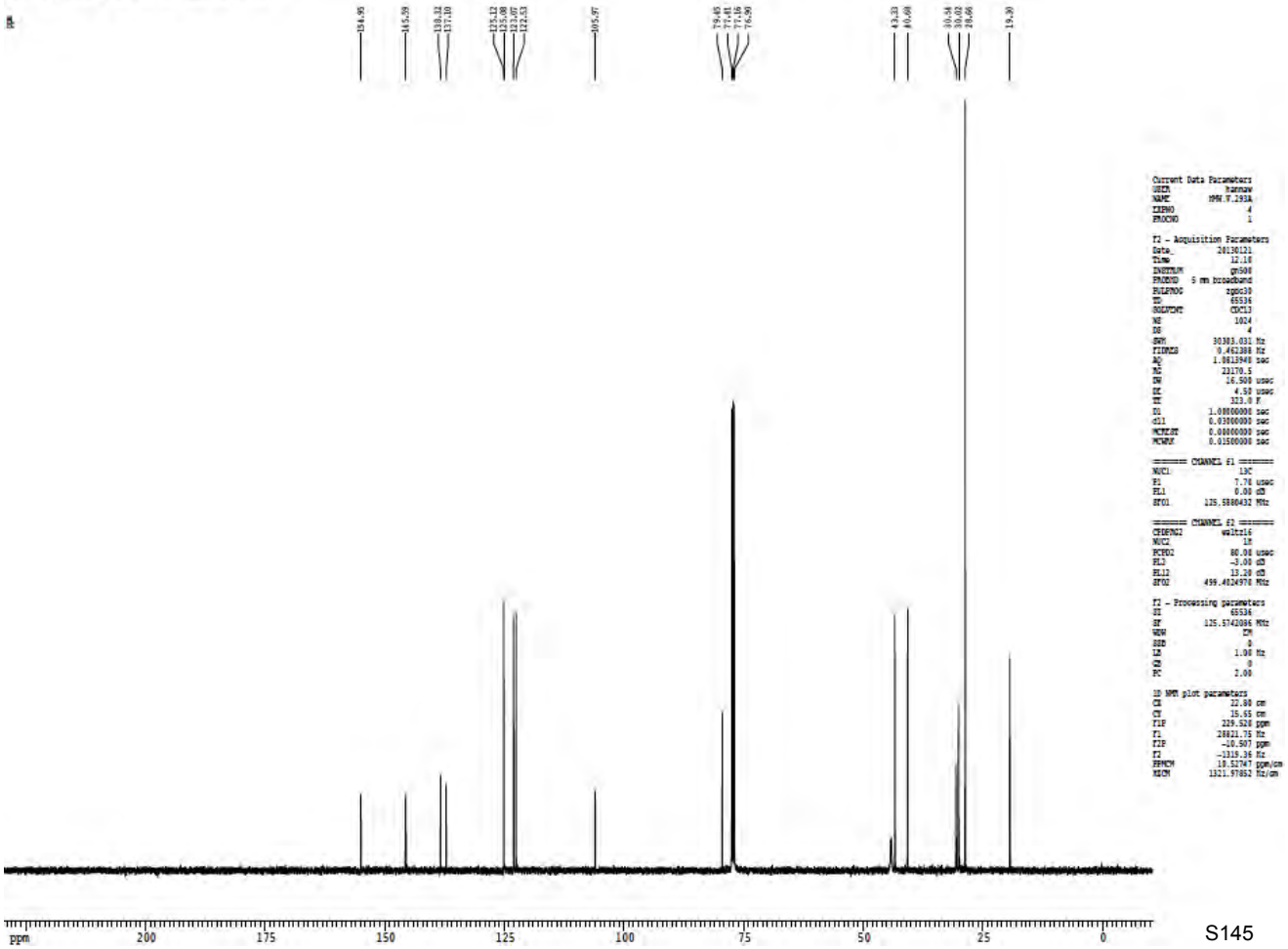
13C spectrum with 1H decoupling



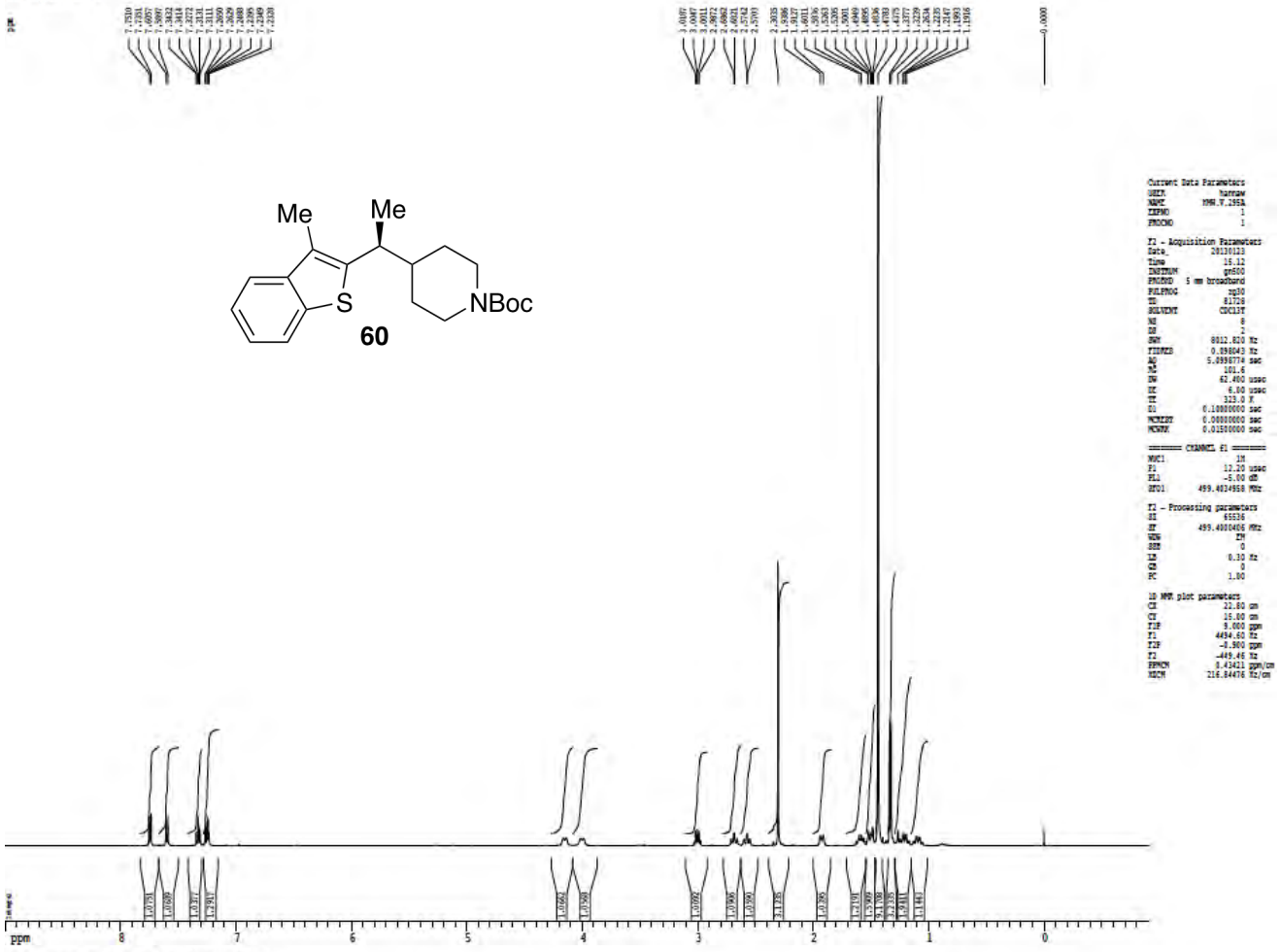
1H spectrum



13C spectrum with 1H decoupling

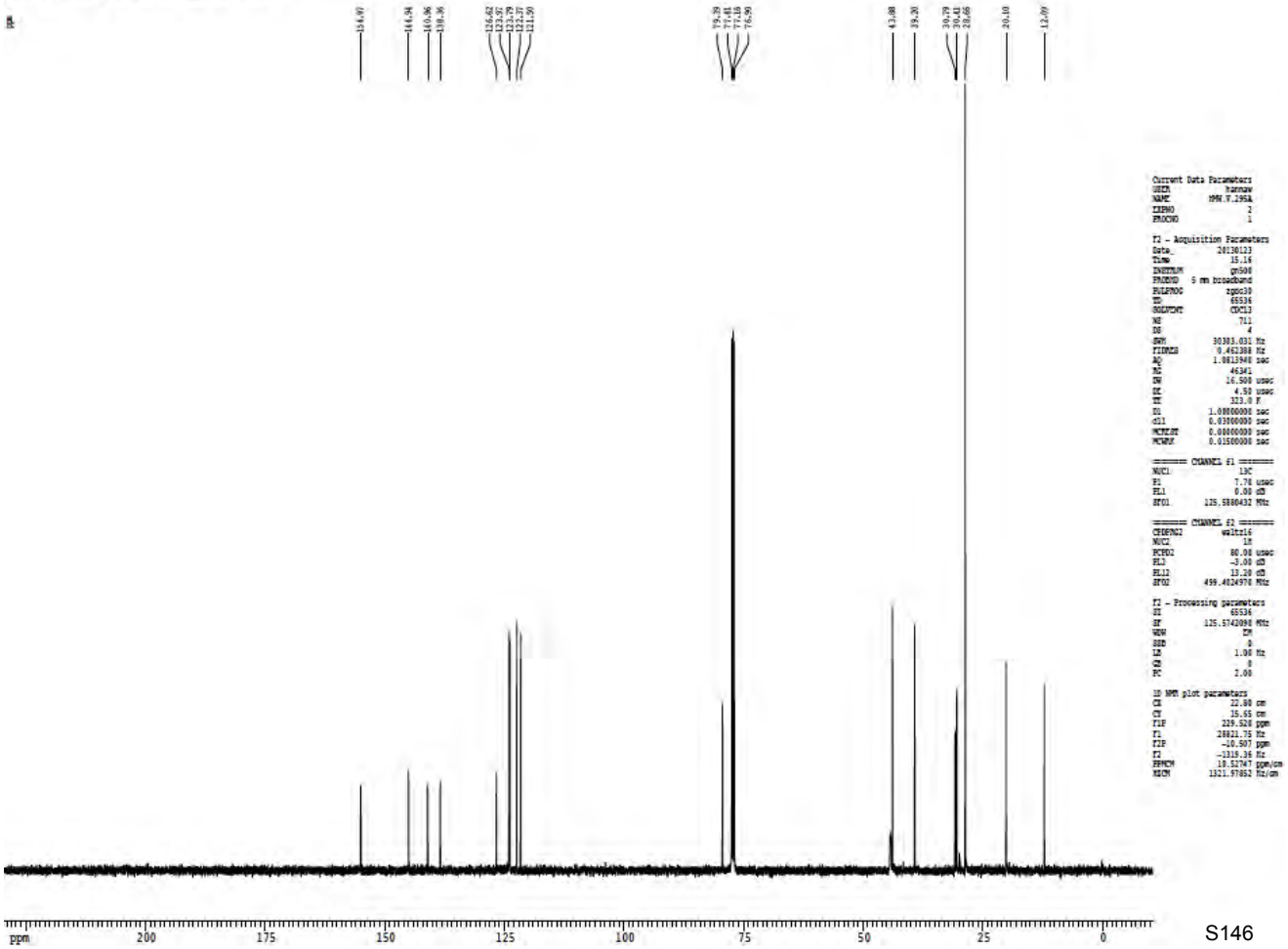


1H spectrum

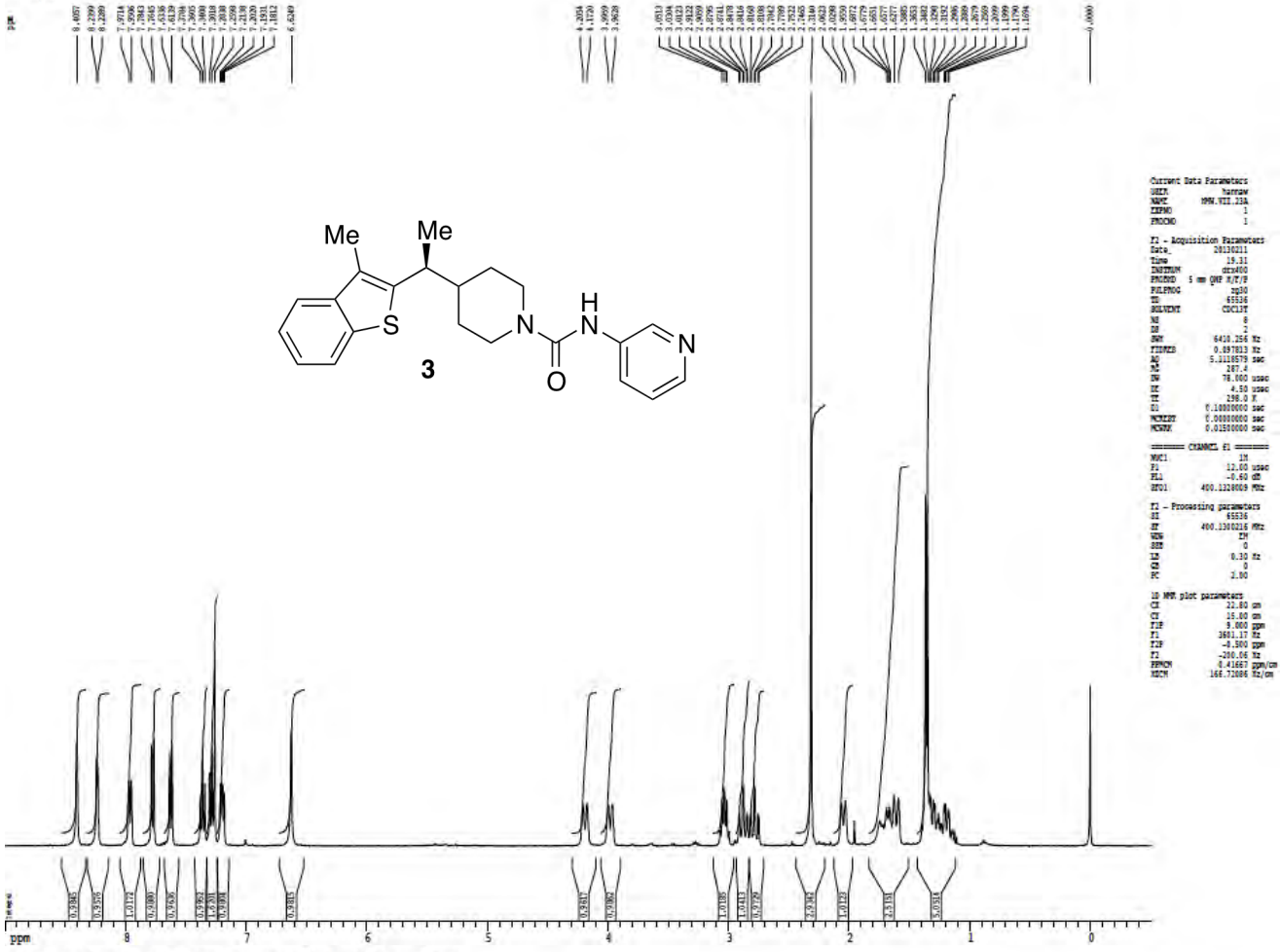


60

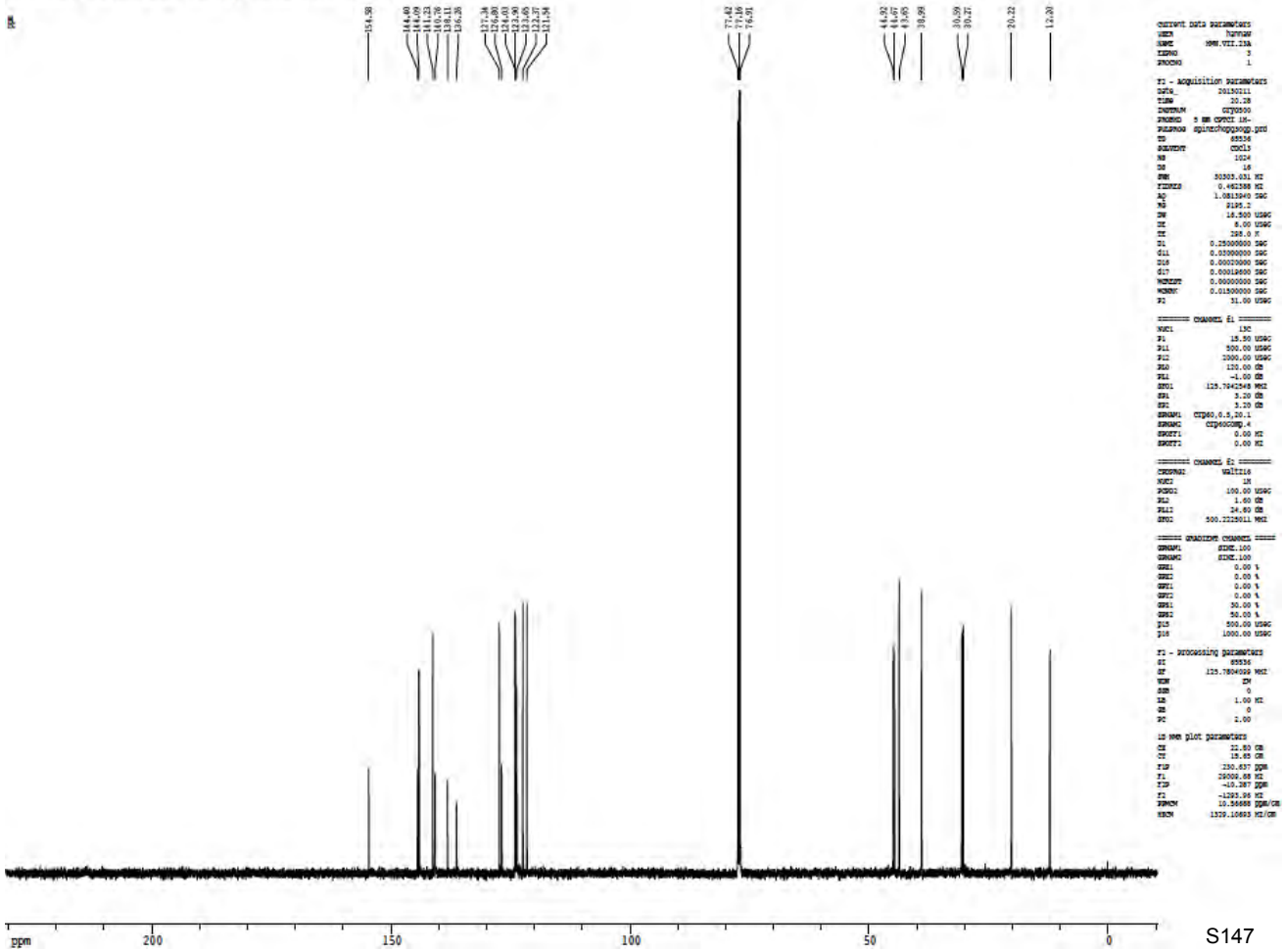
13C spectrum with 1H decoupling

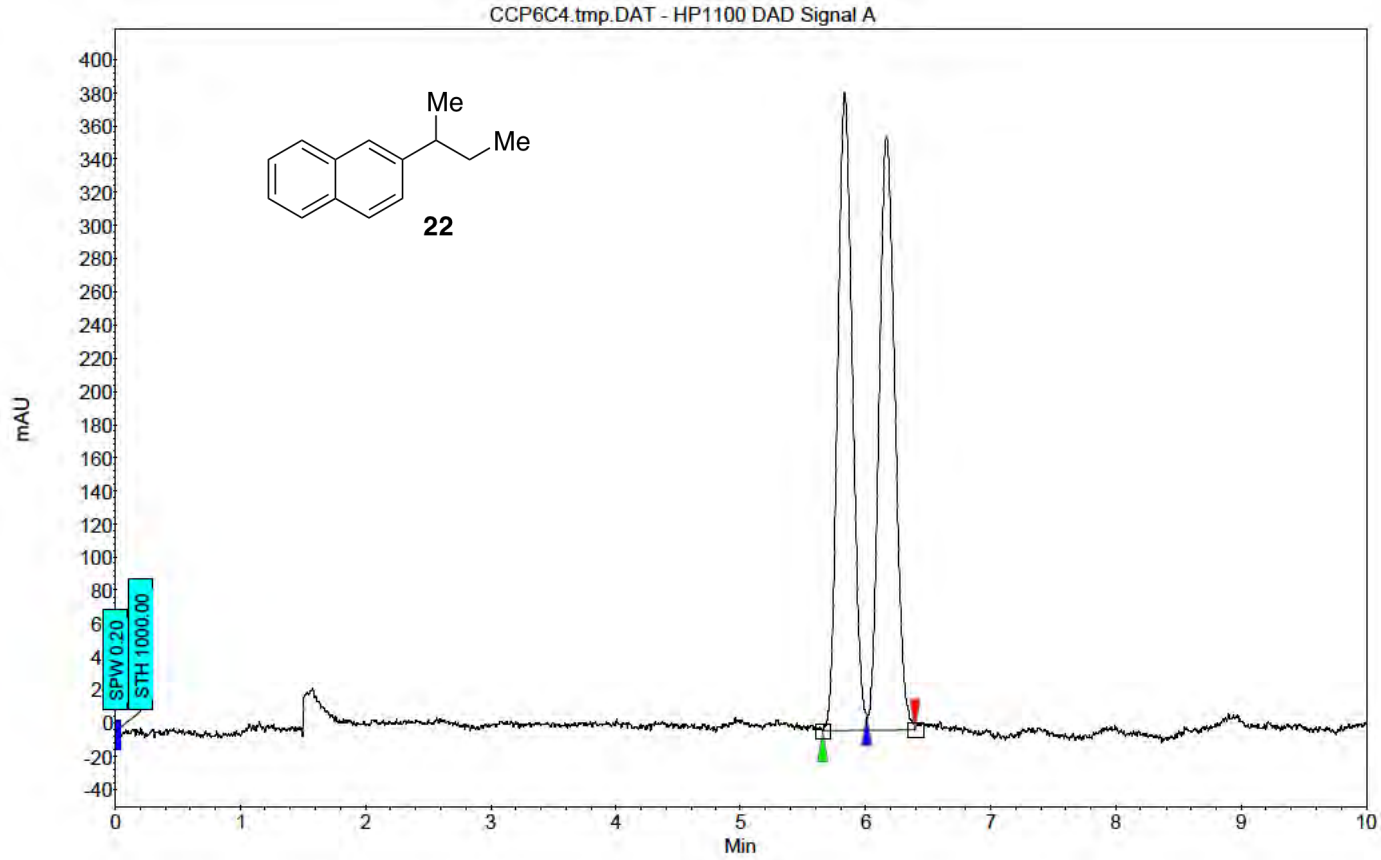


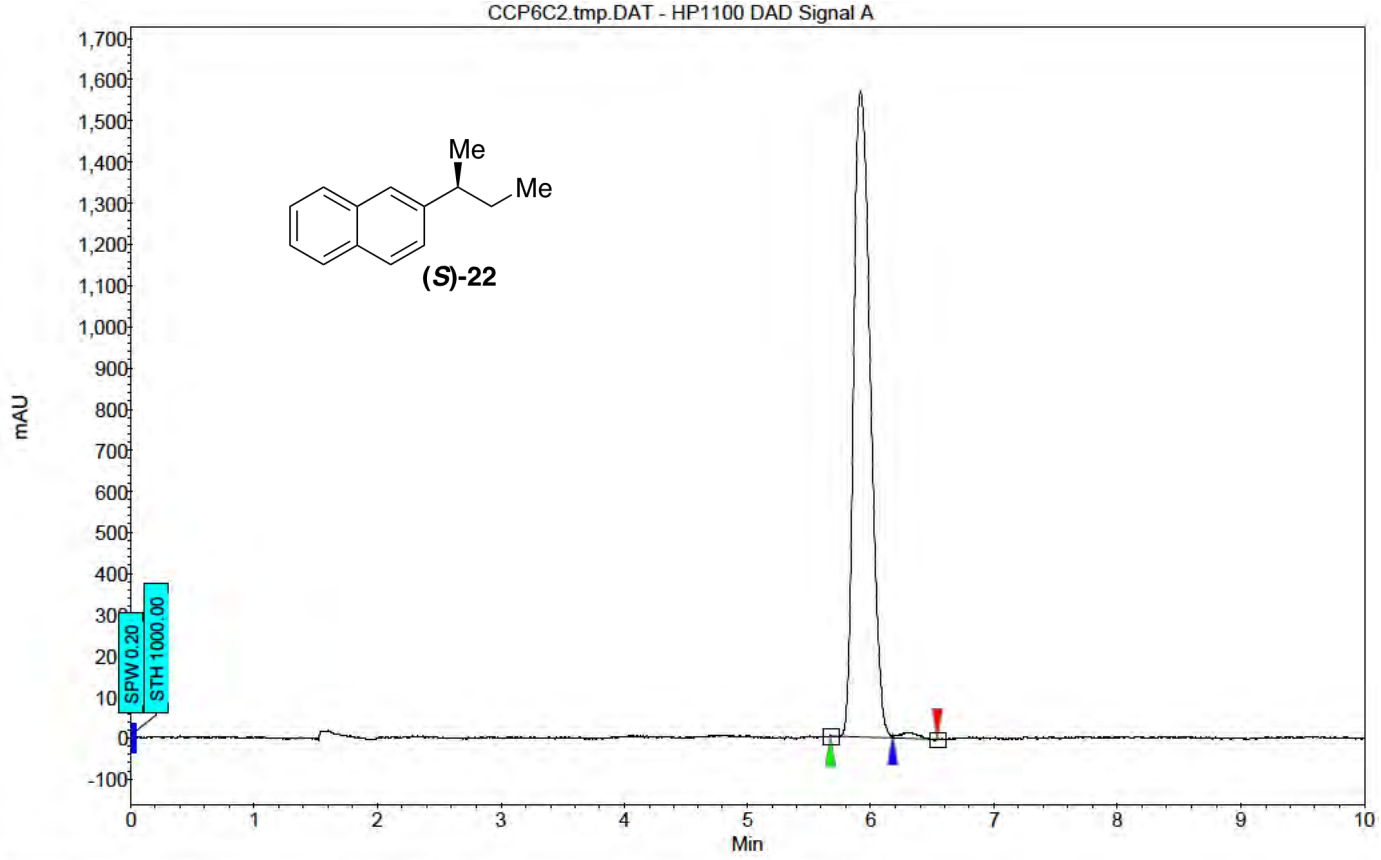
1H spectrum



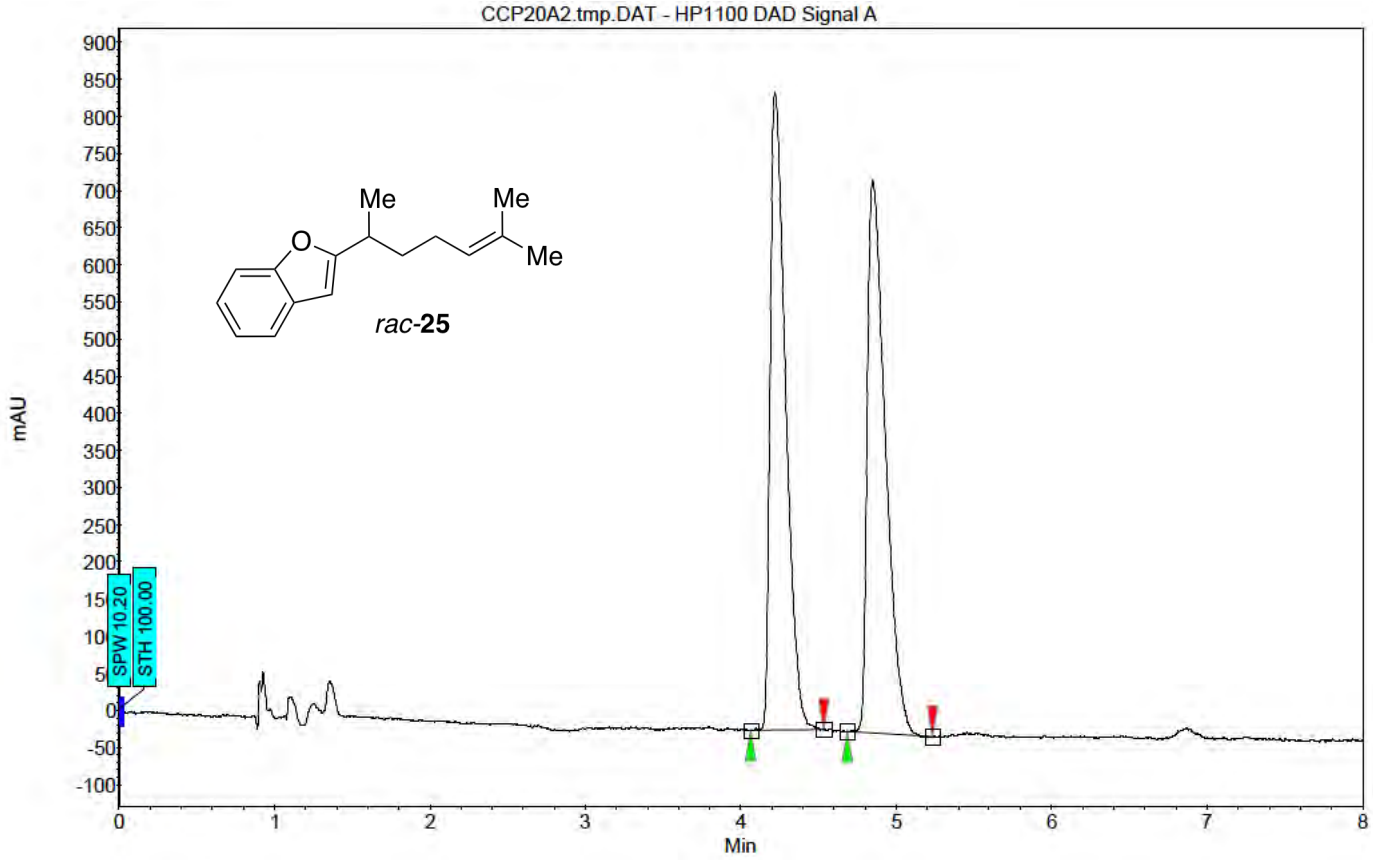
Z-restored spin-echo 13C spectrum with 1H decoupling

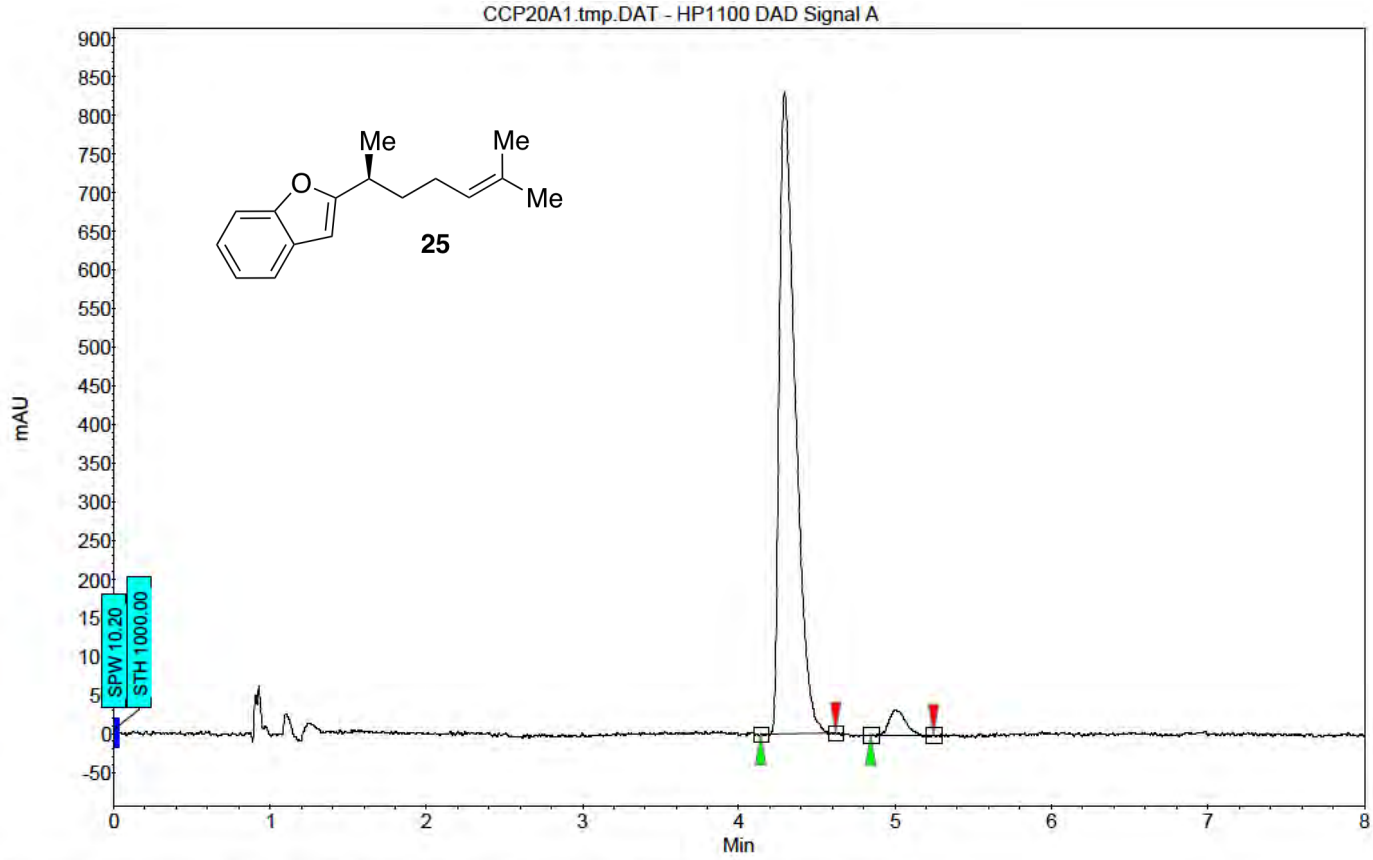




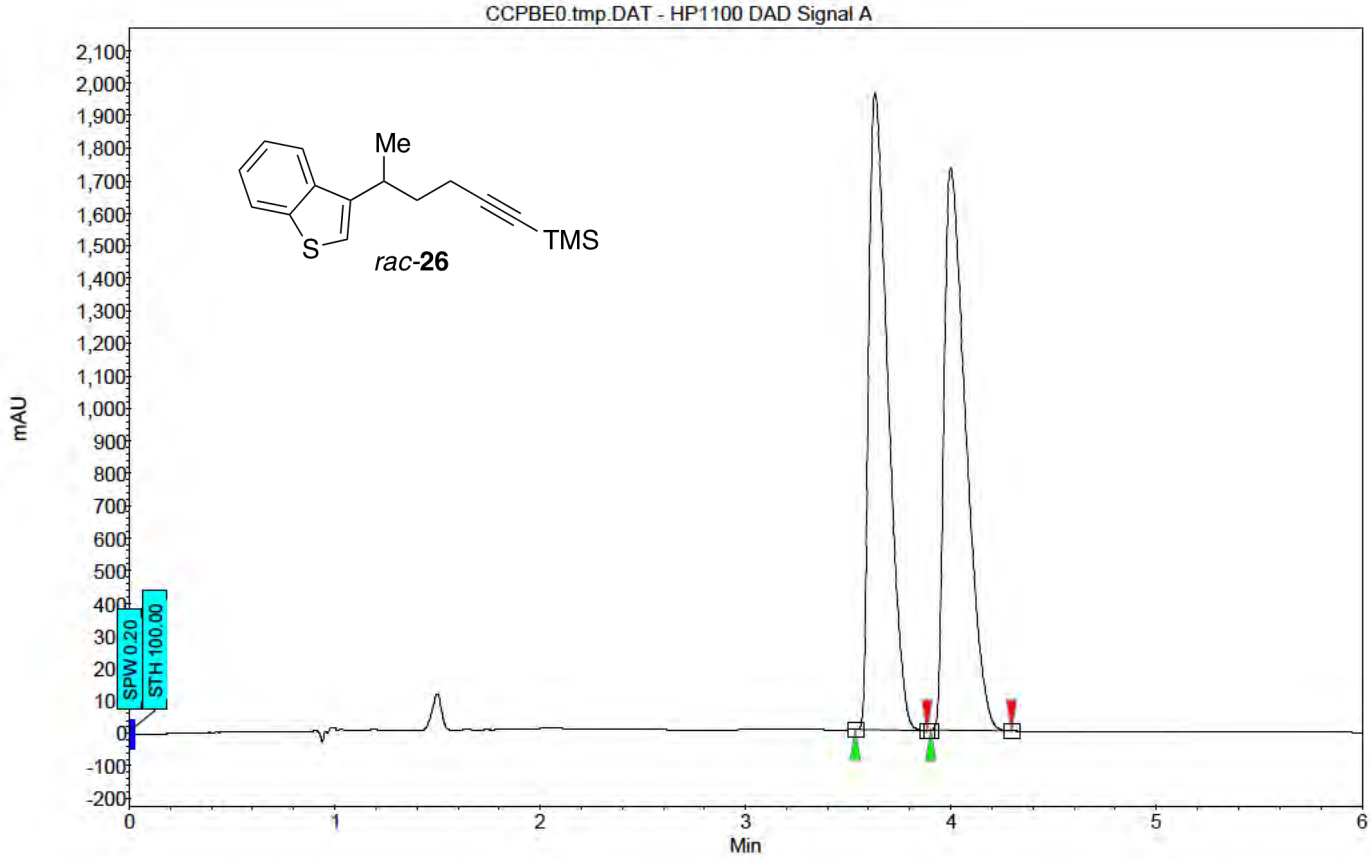


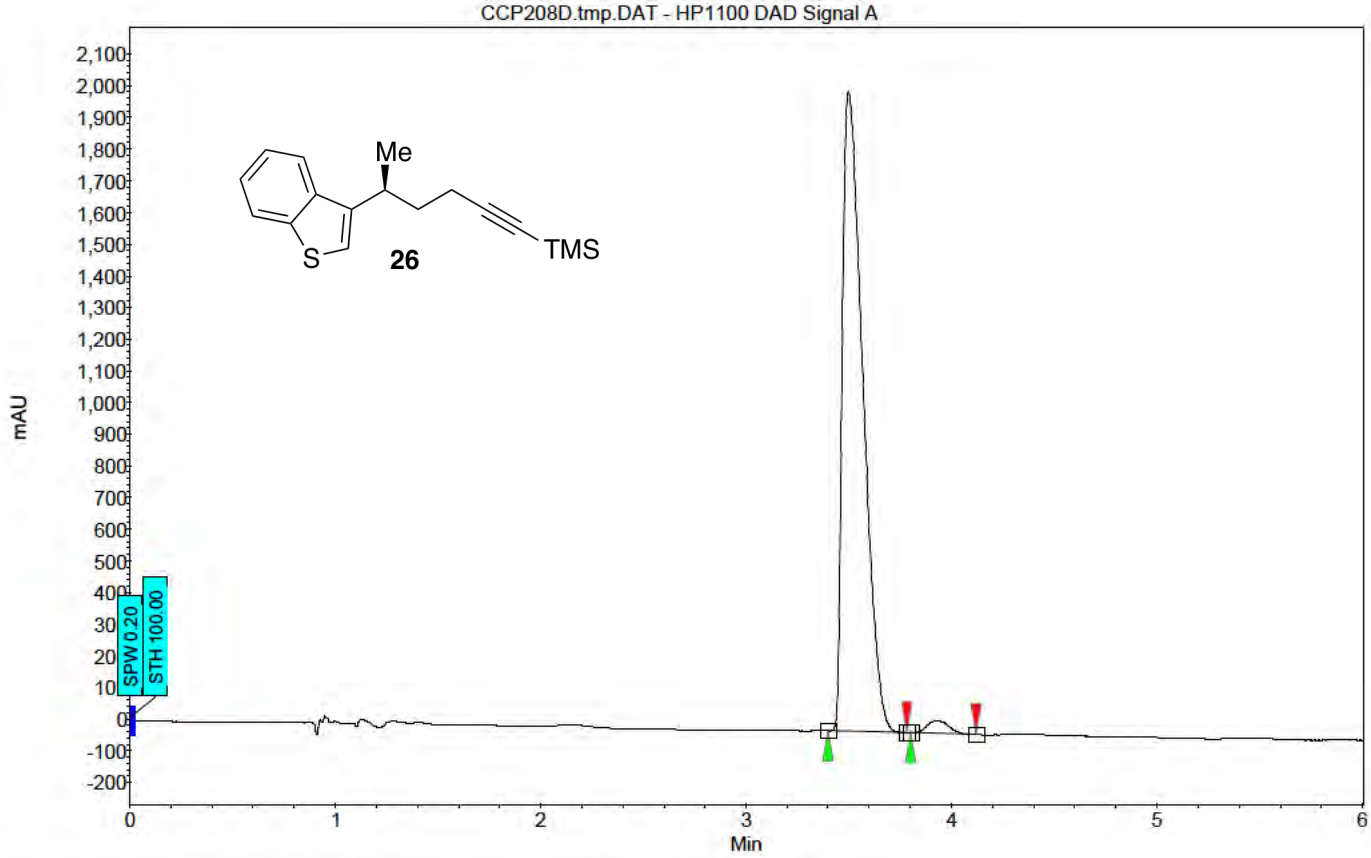
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.68	5.92	6.18	0.00	98.96	1568.2	246.5	98.964
2	UNKNOWN	6.18	6.29	6.54	0.00	1.04	15.7	2.6	1.036
Total						100.00	1583.9	249.1	100.000



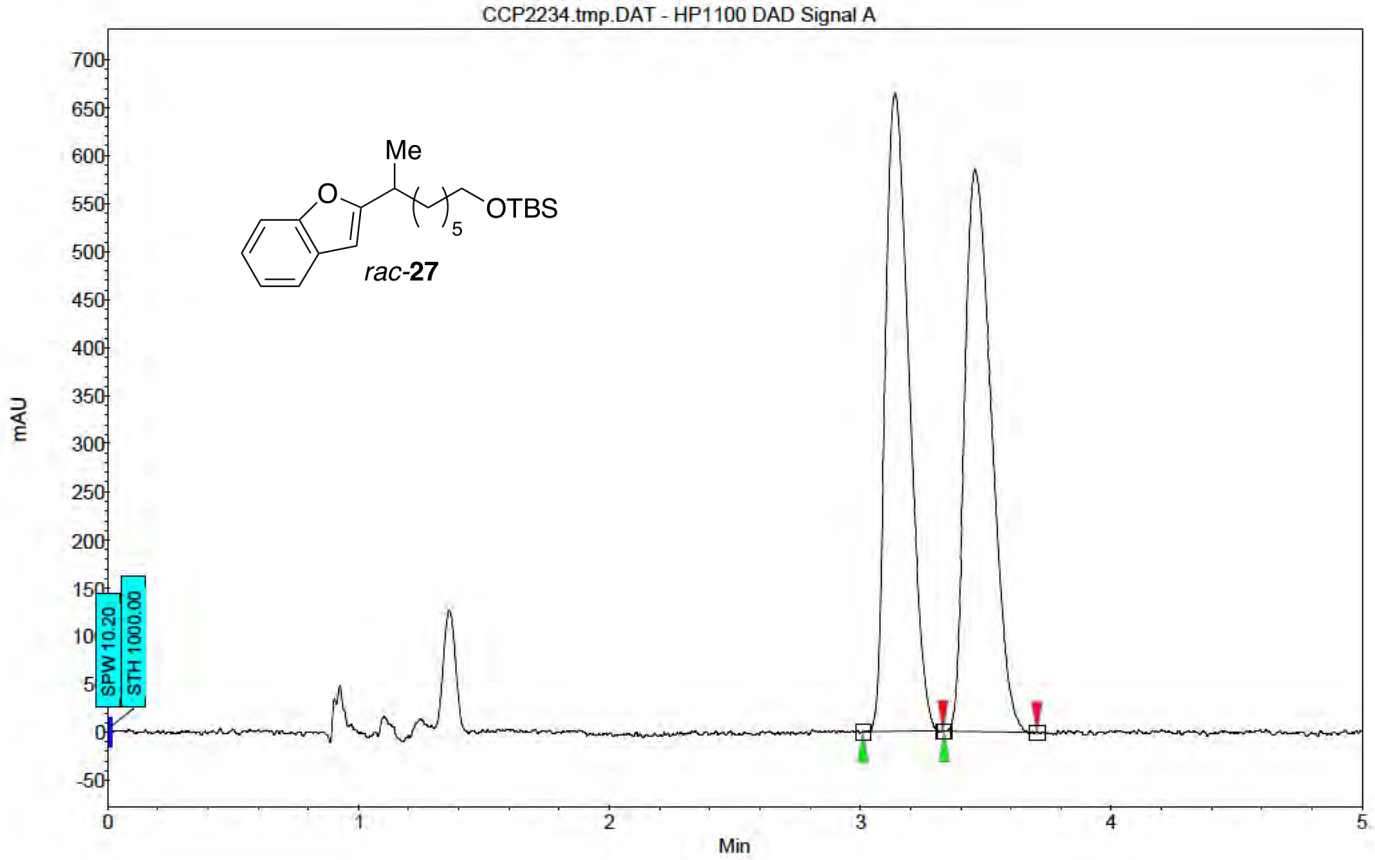


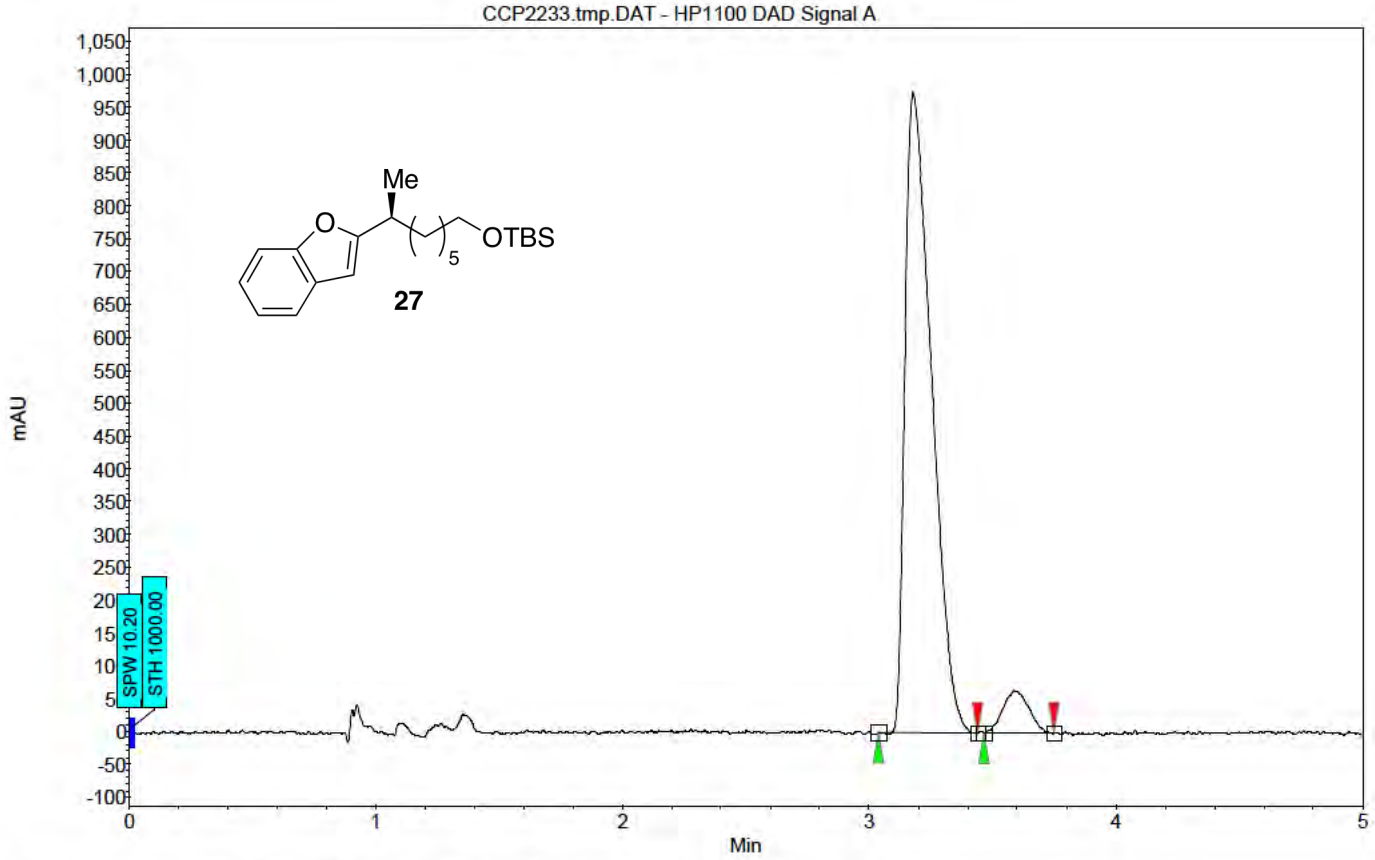
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.14	4.29	4.62	0.00	96.37	828.7	97.5	96.371
2	UNKNOWN	4.84	5.00	5.25	0.00	3.63	31.8	3.7	3.629
Total						100.00	860.5	101.2	100.000



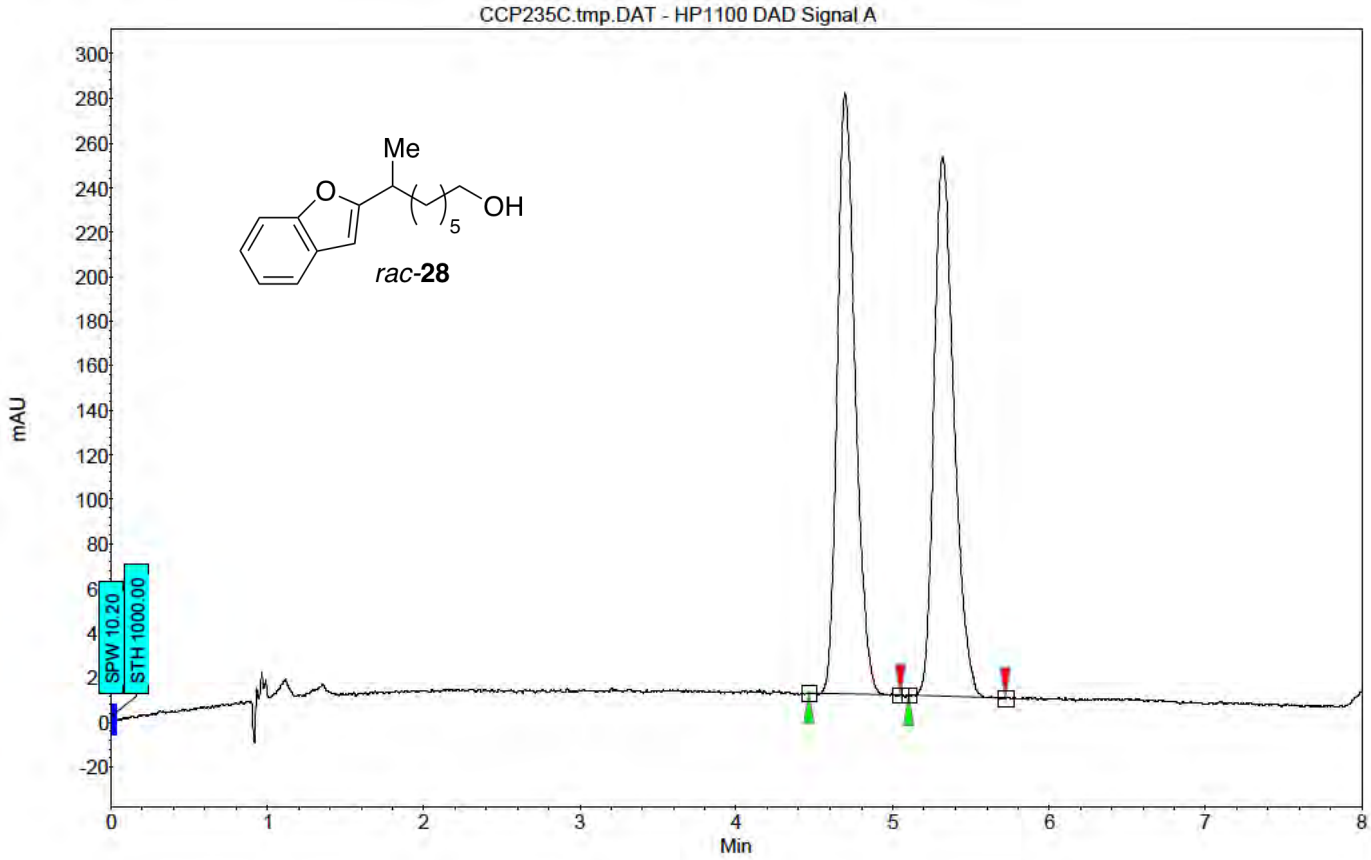


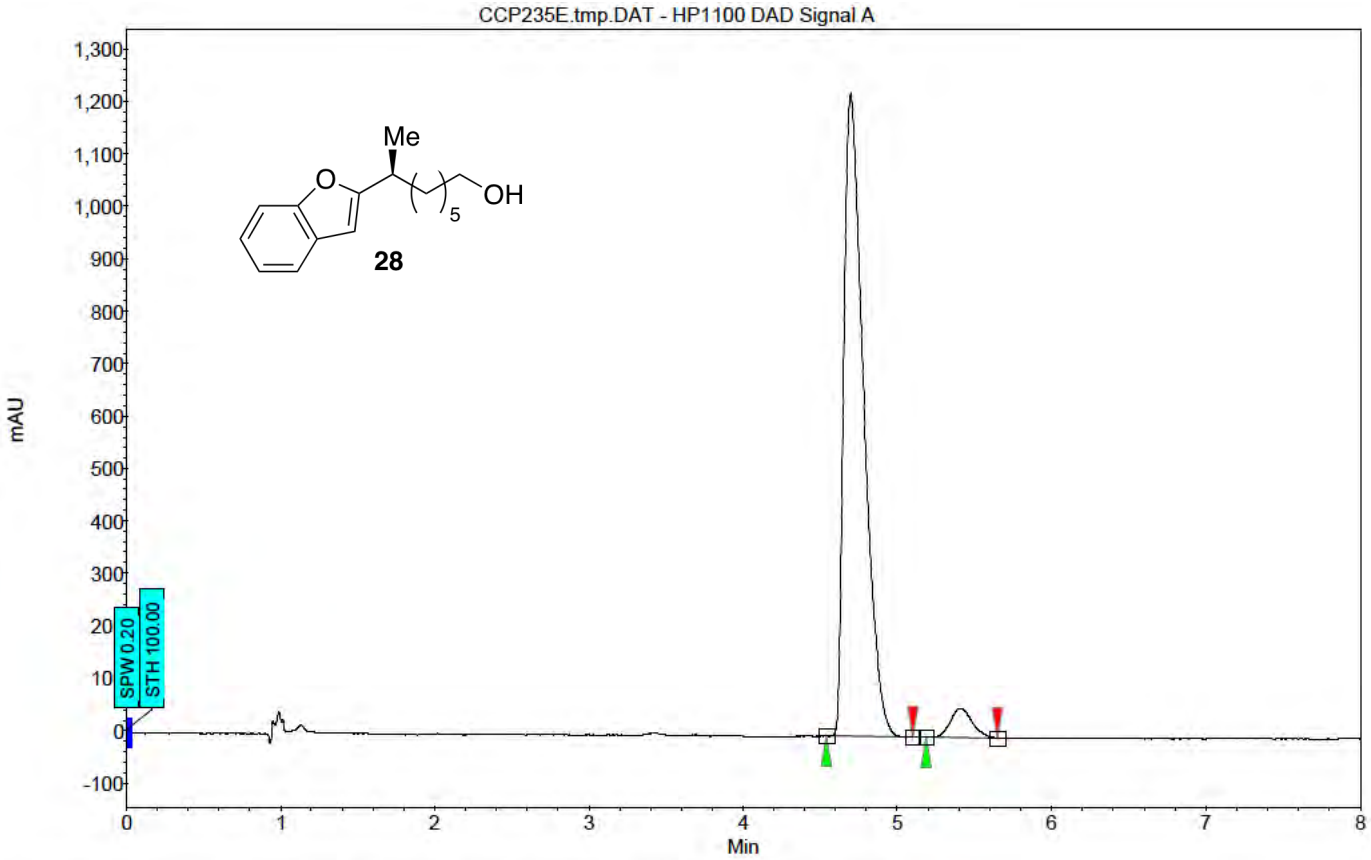
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.40	3.50	3.78	0.00	97.95	2017.3	232.3	97.946
2	UNKNOWN	3.80	3.93	4.12	0.00	2.05	41.7	4.9	2.054
Total						100.00	2059.1	237.2	100.000



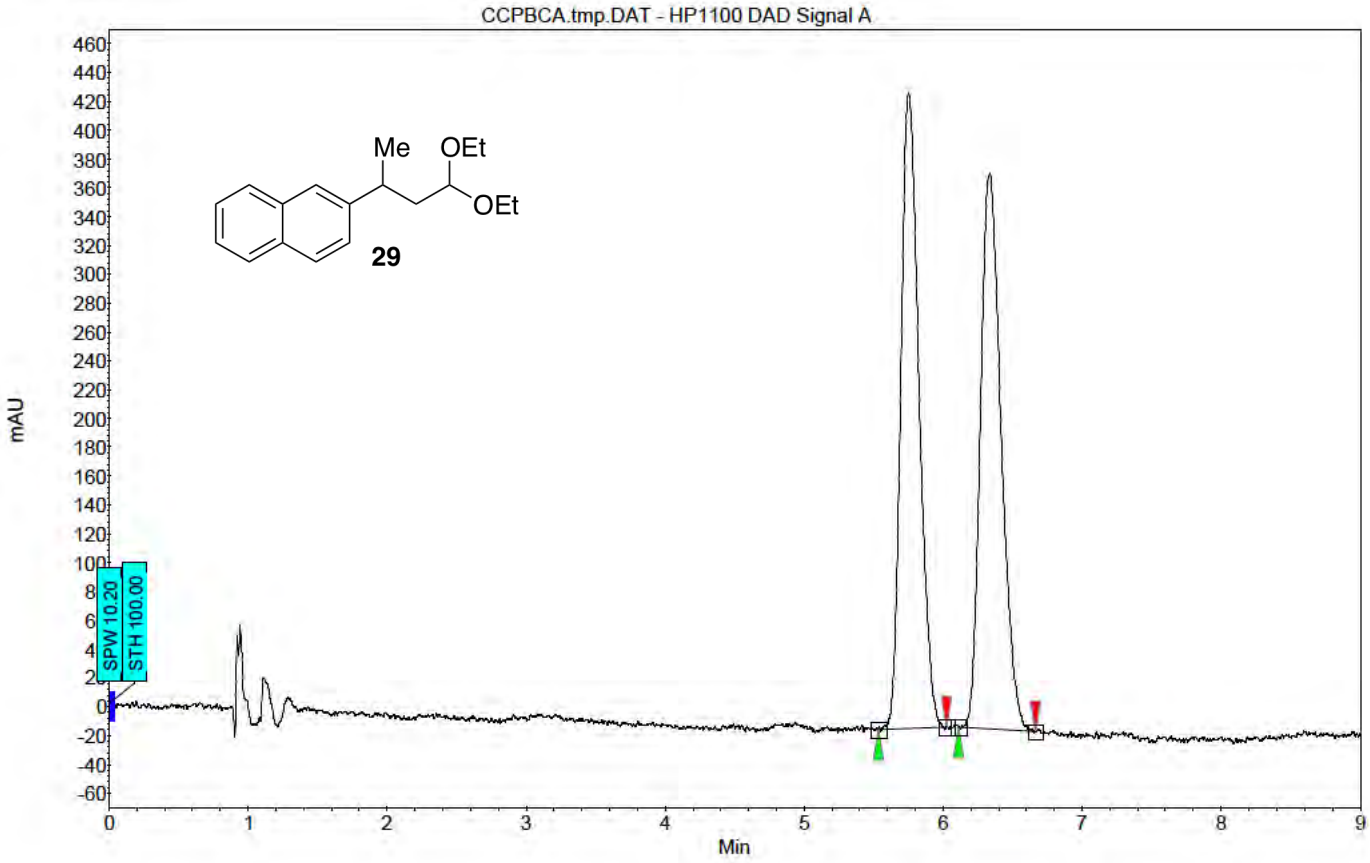


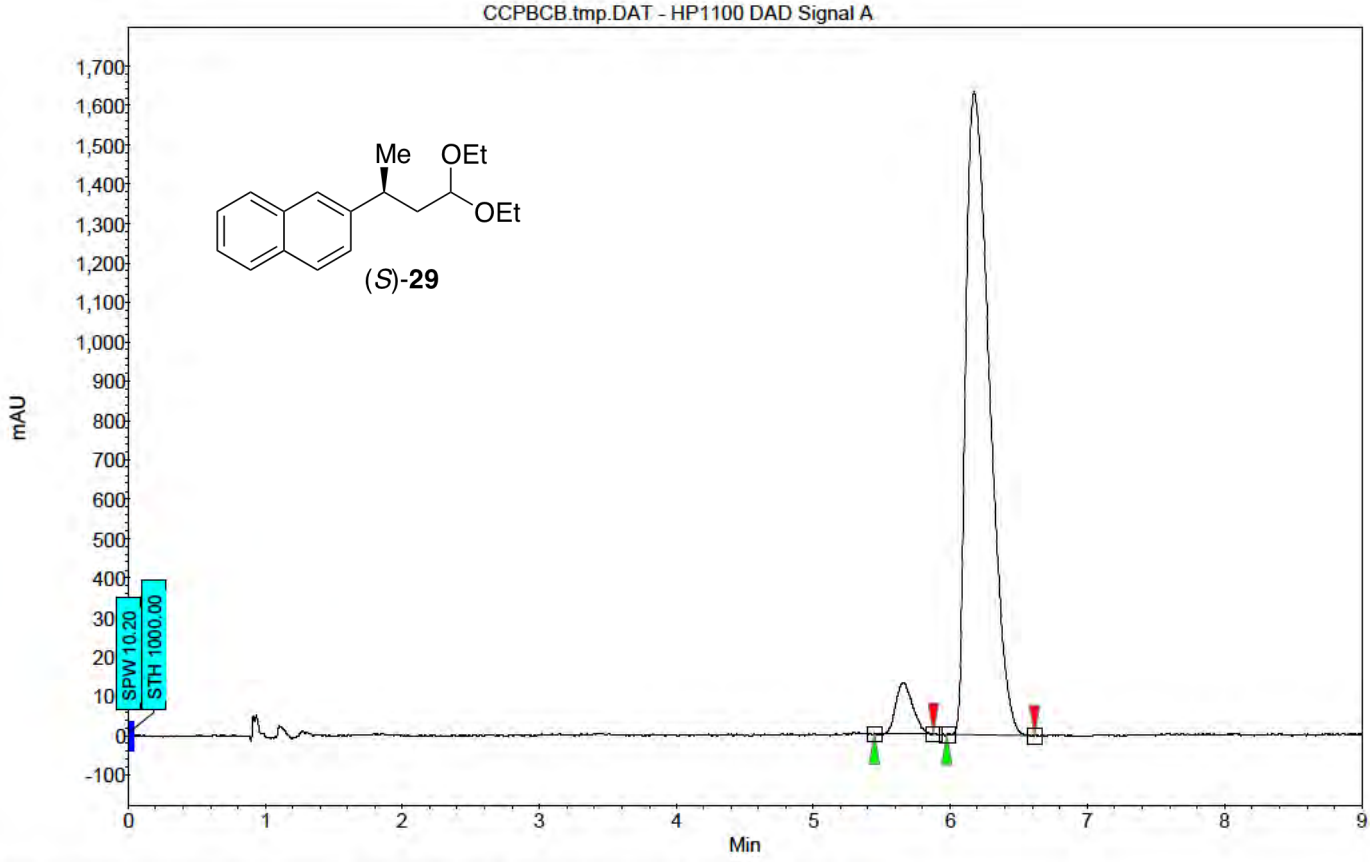
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.04	3.18	3.44	0.00	93.91	973.9	121.5	93.911
2	UNKNOWN	3.47	3.59	3.75	0.00	6.09	64.4	7.9	6.089
Total						100.00	1038.3	129.3	100.000



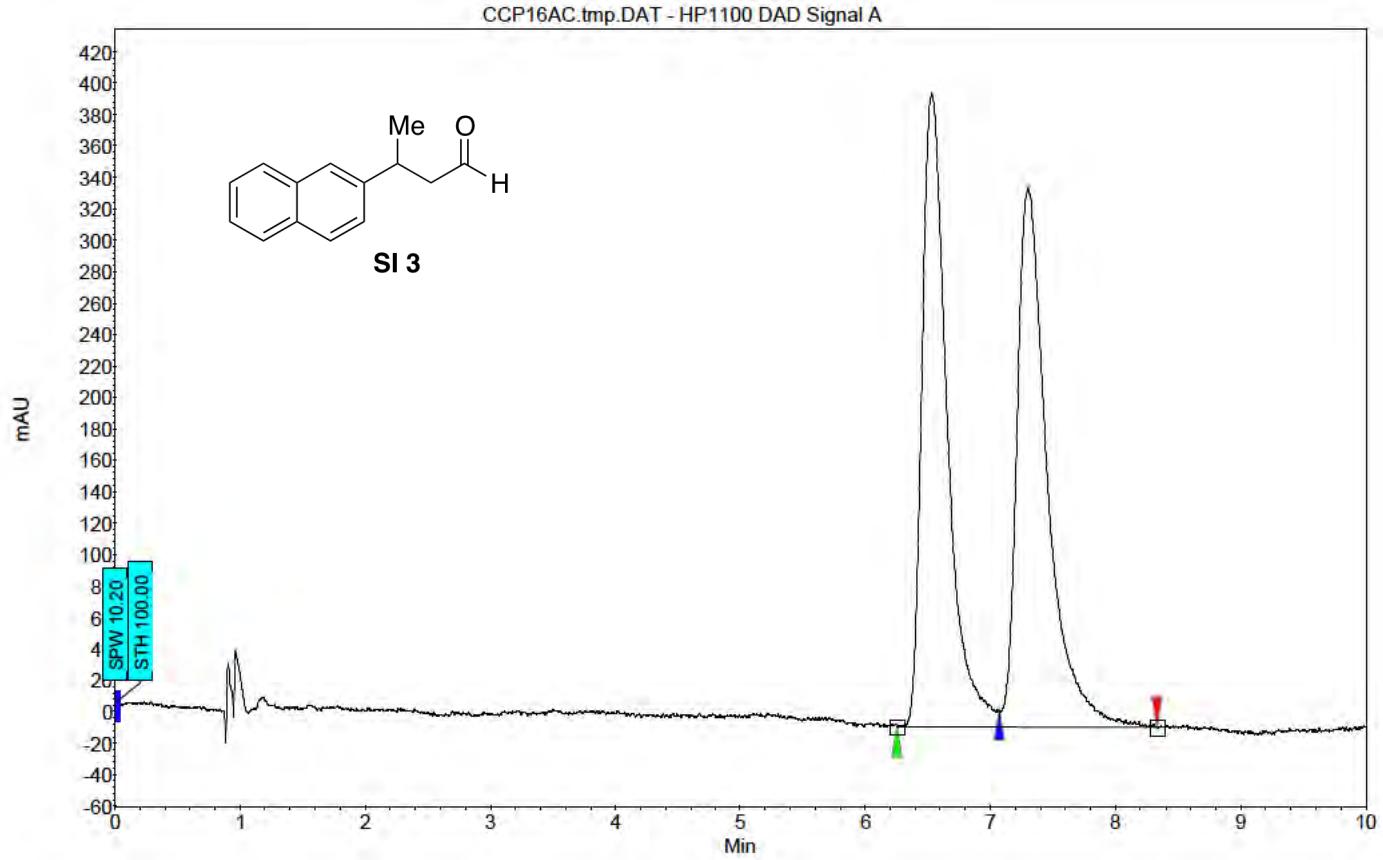


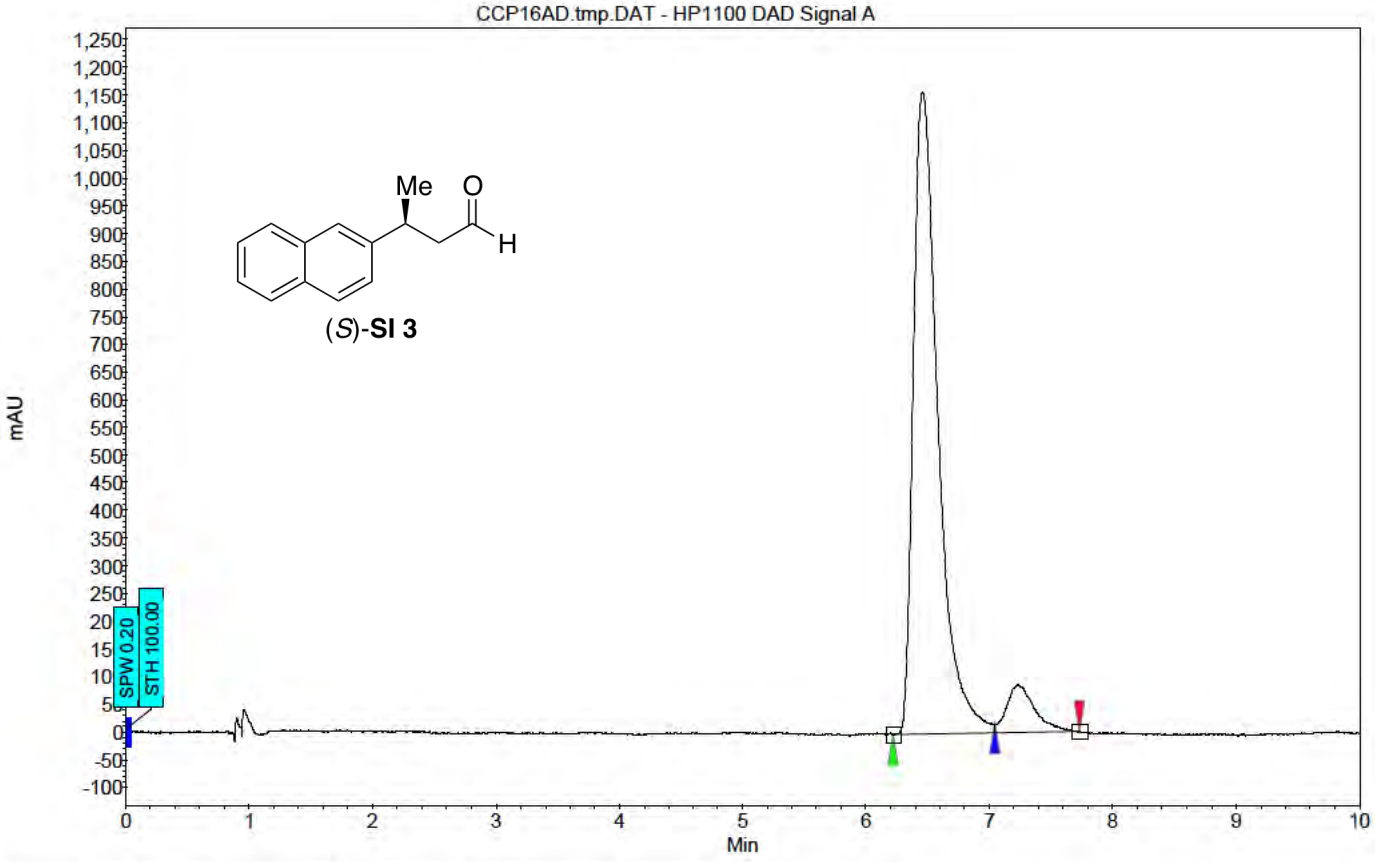
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.54	4.70	5.10	0.00	95.24	1224.0	181.6	95.242
2	UNKNOWN	5.19	5.41	5.65	0.00	4.76	56.0	9.1	4.758
Total						100.00	1280.0	190.7	100.000



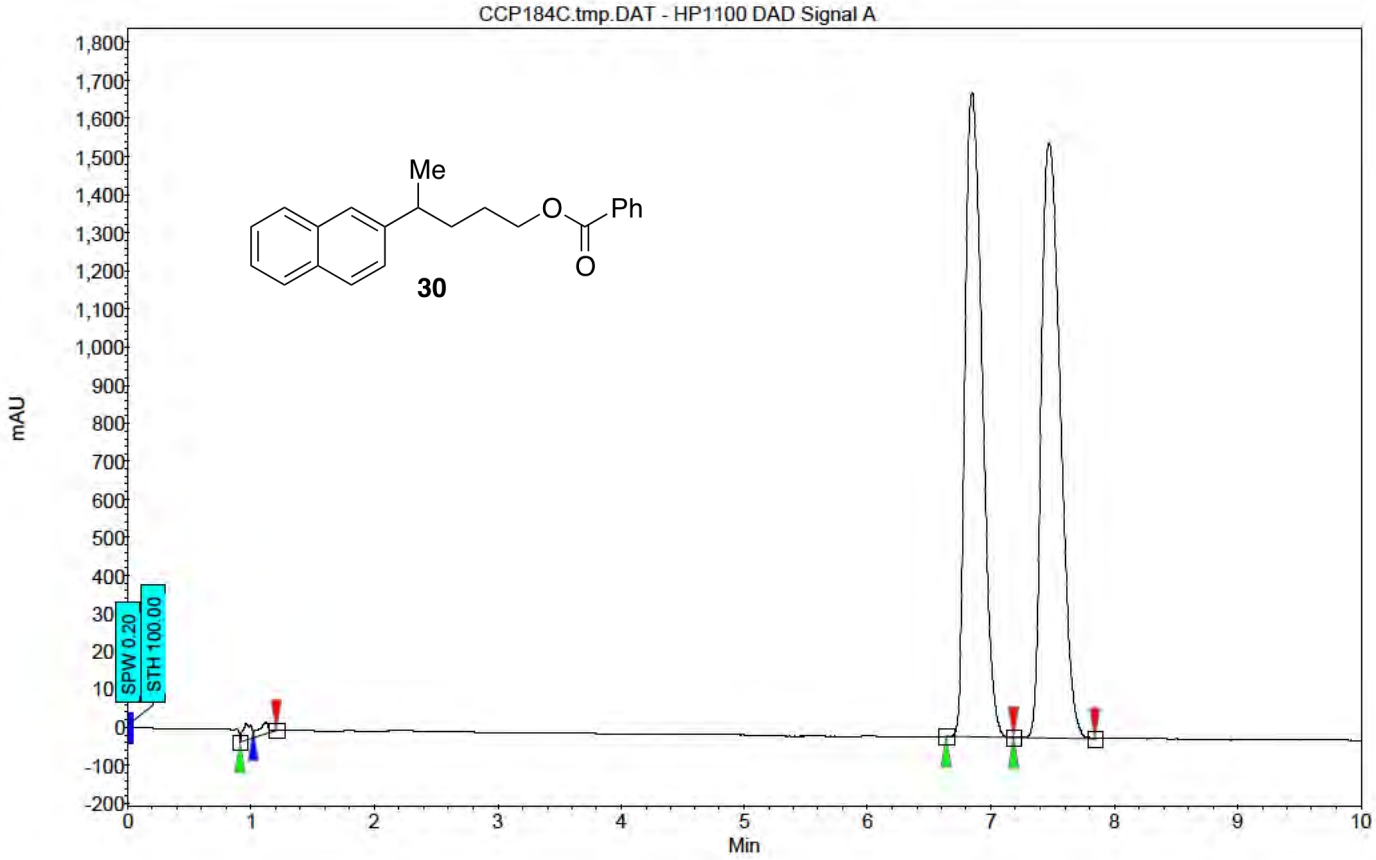


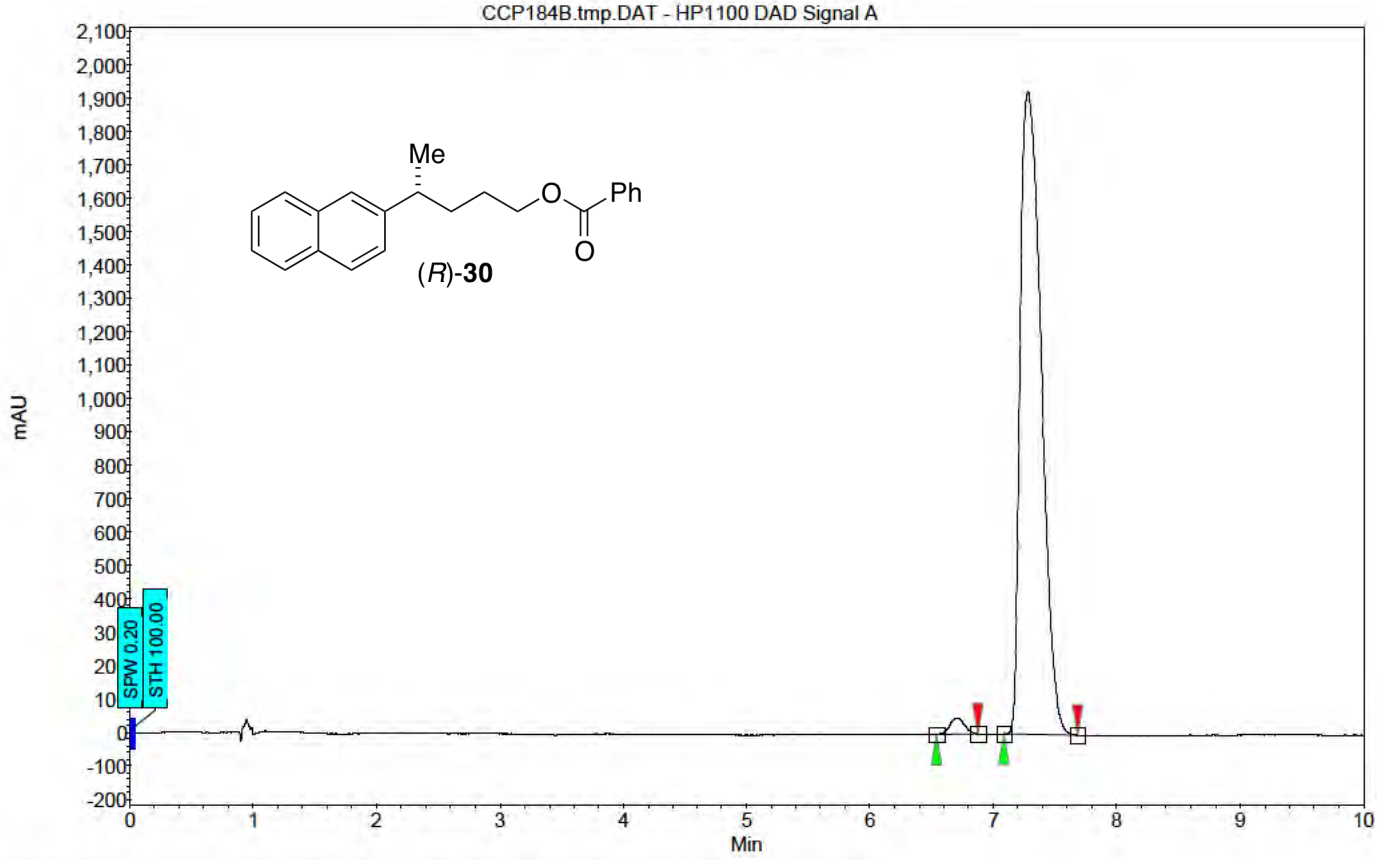
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.45	5.66	5.88	0.00	5.34	128.7	18.3	5.342
2	UNKNOWN	5.98	6.17	6.62	0.00	94.66	1630.9	324.9	94.658
Total						100.00	1759.7	343.3	100.000



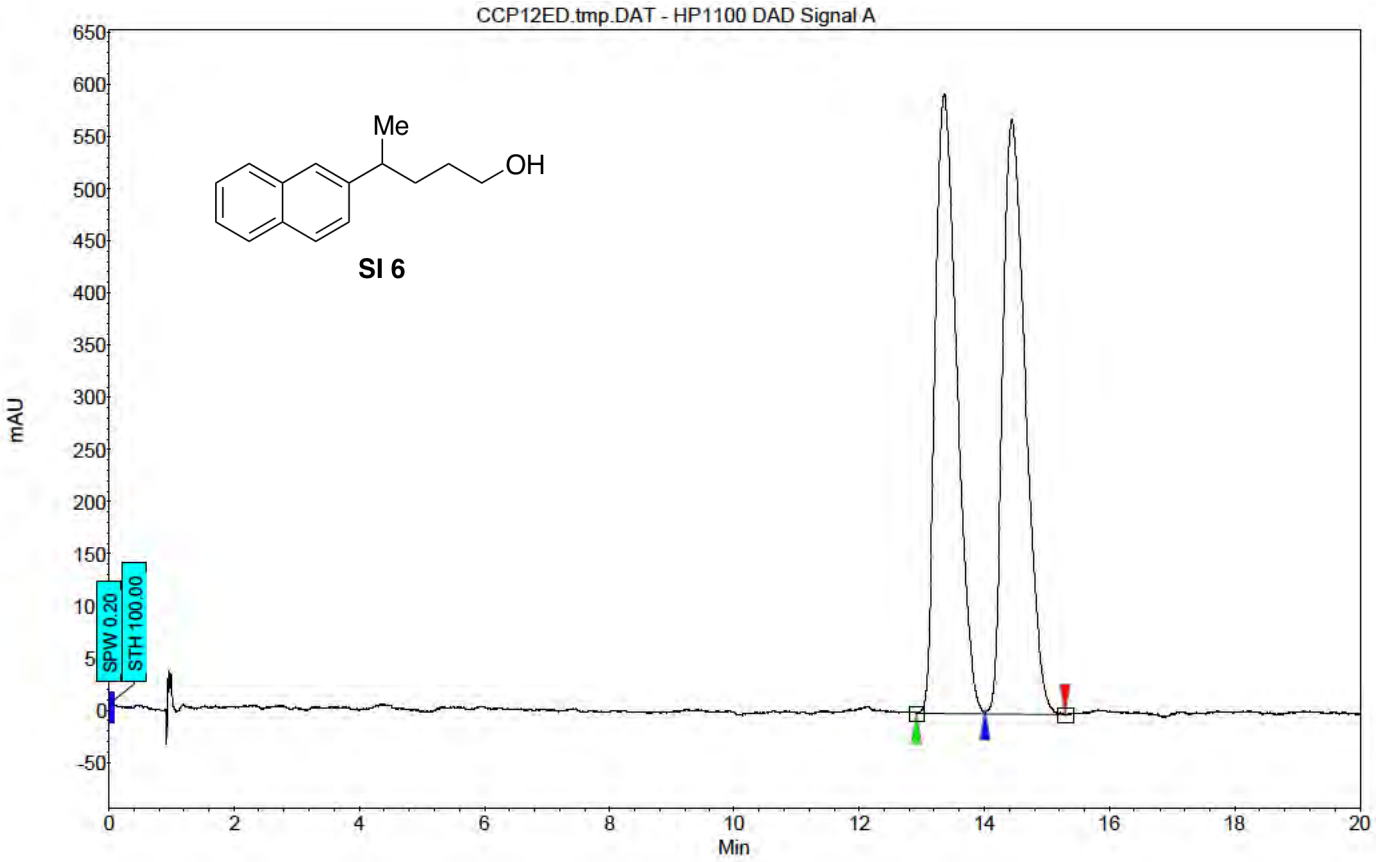


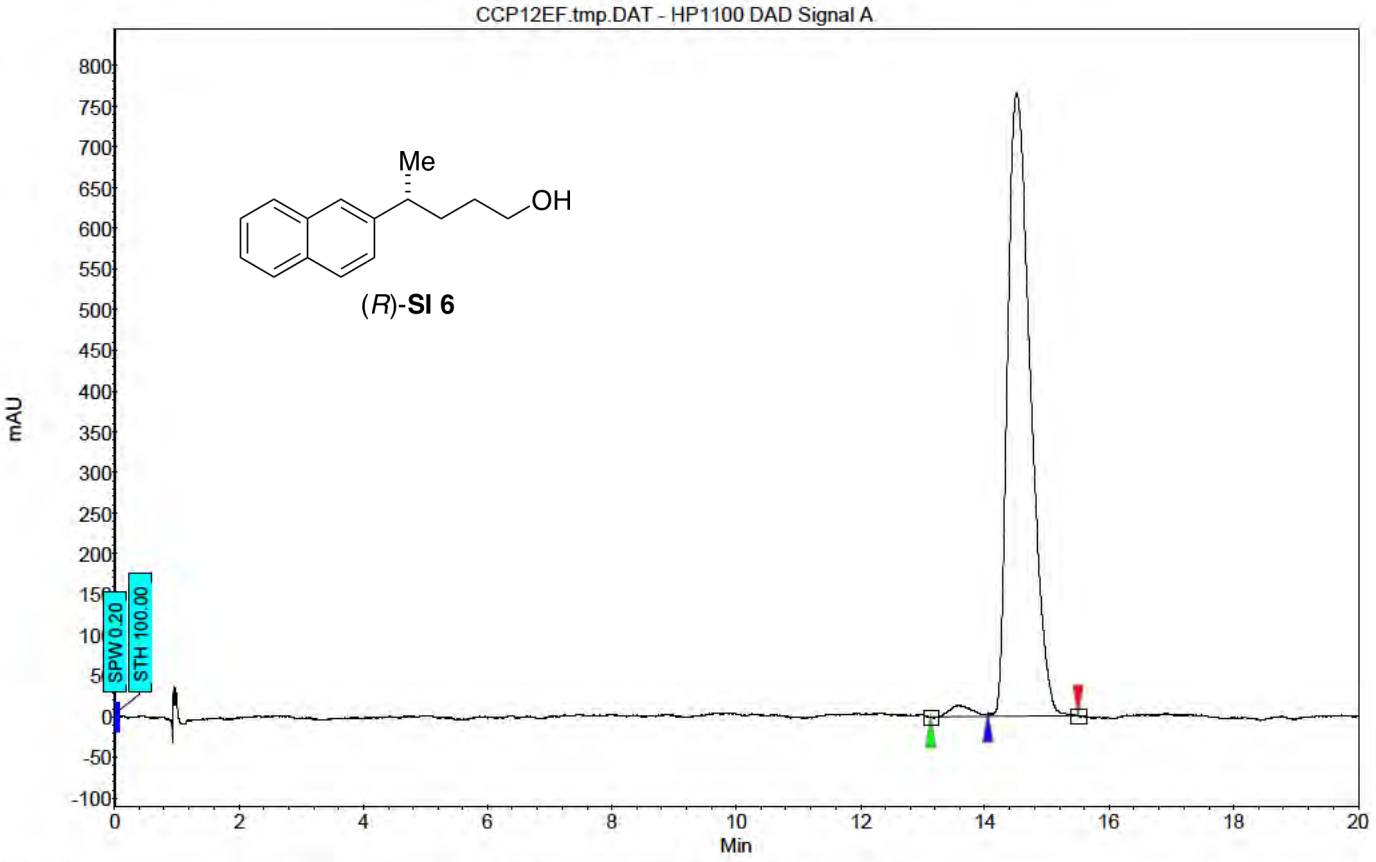
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.22	6.46	7.04	0.00	92.20	1157.6	267.9	92.202
2	UNKNOWN	7.04	7.23	7.73	0.00	7.80	86.2	22.7	7.798
Total						100.00	1243.7	290.5	100.000



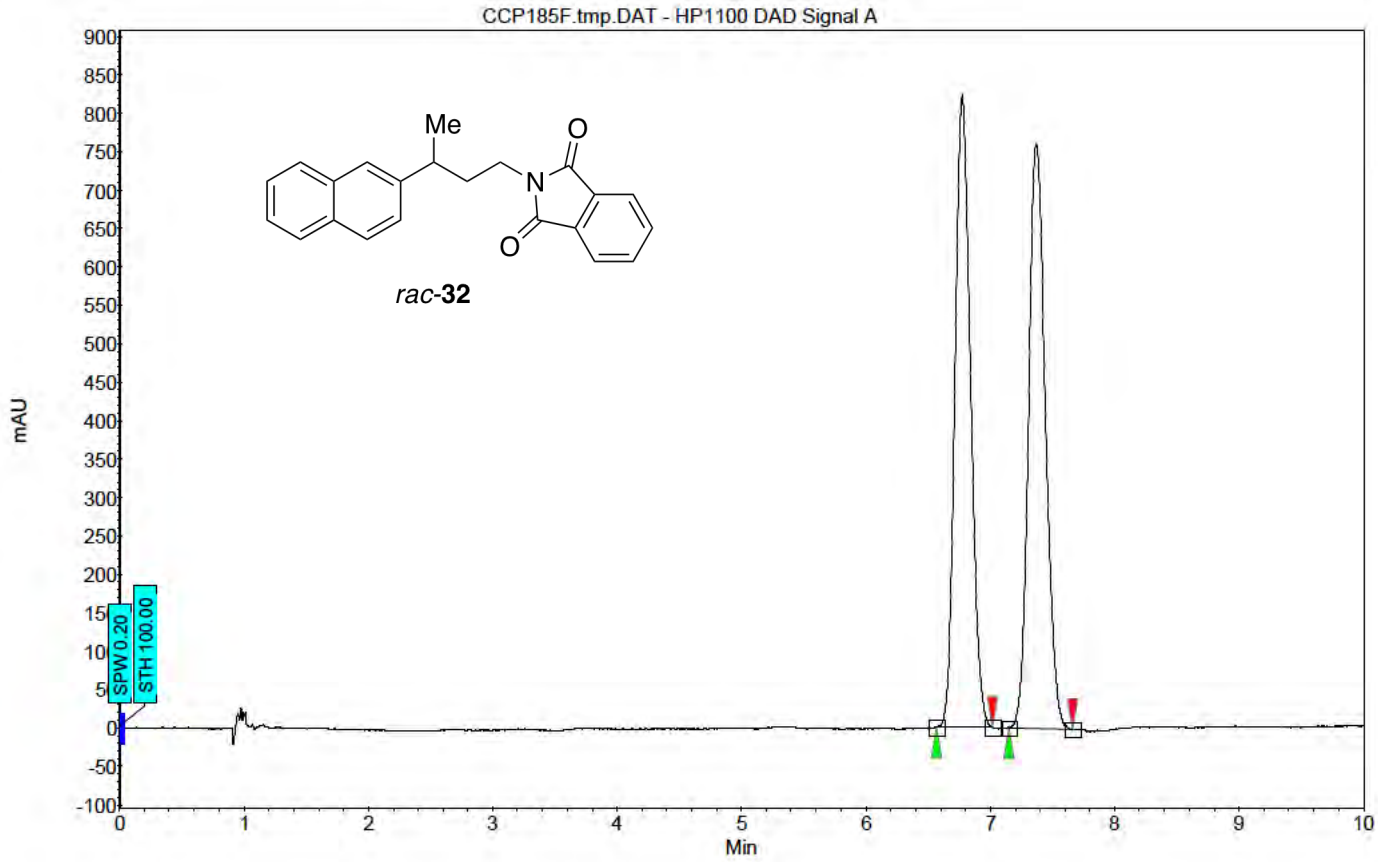


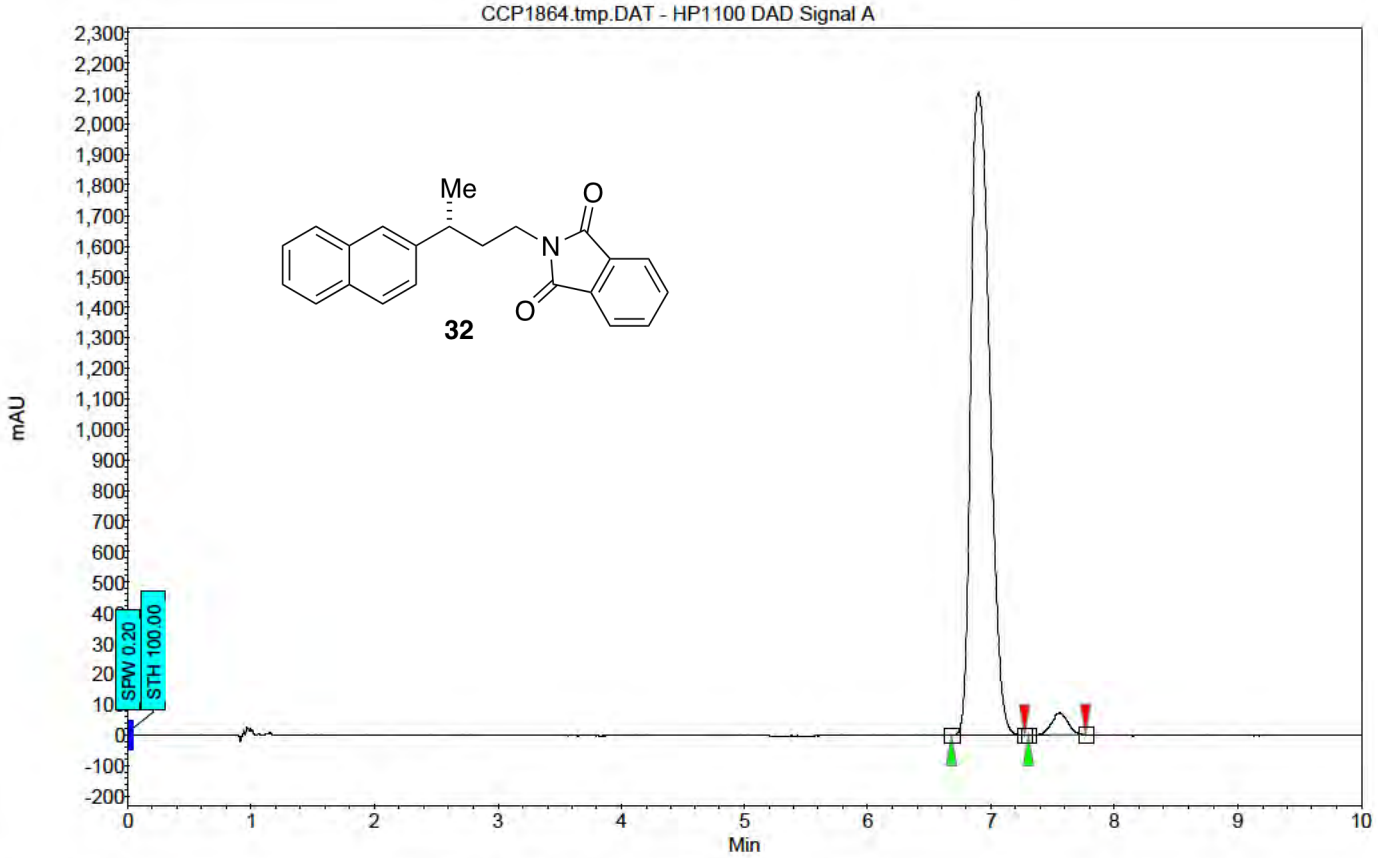
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	6.54	6.71	6.88	0.00	1.67	48.6	6.5	1.671
1	UNKNOWN	7.09	7.28	7.69	0.00	98.33	1924.0	380.3	98.329
Total						100.00	1972.6	386.7	100.000



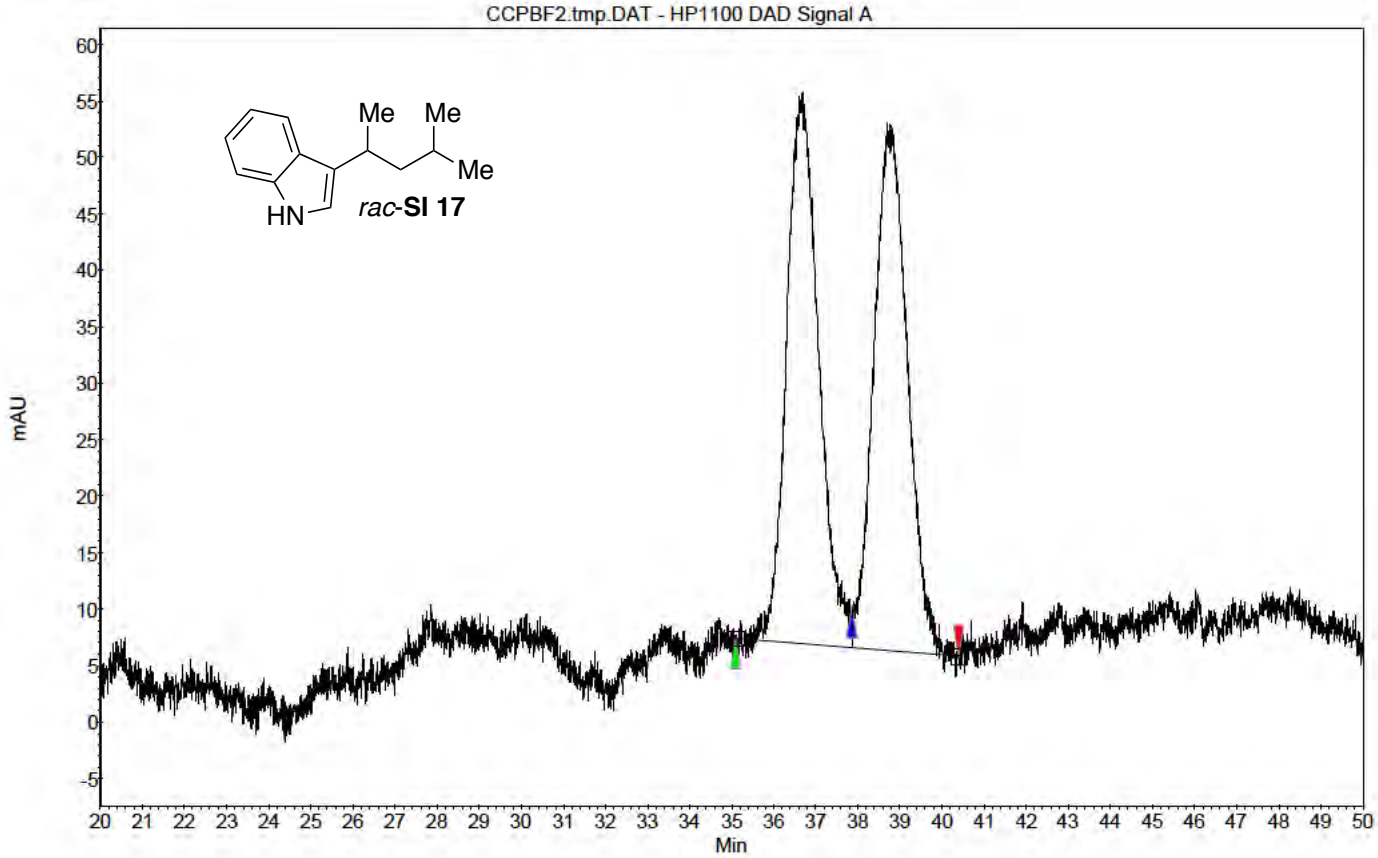


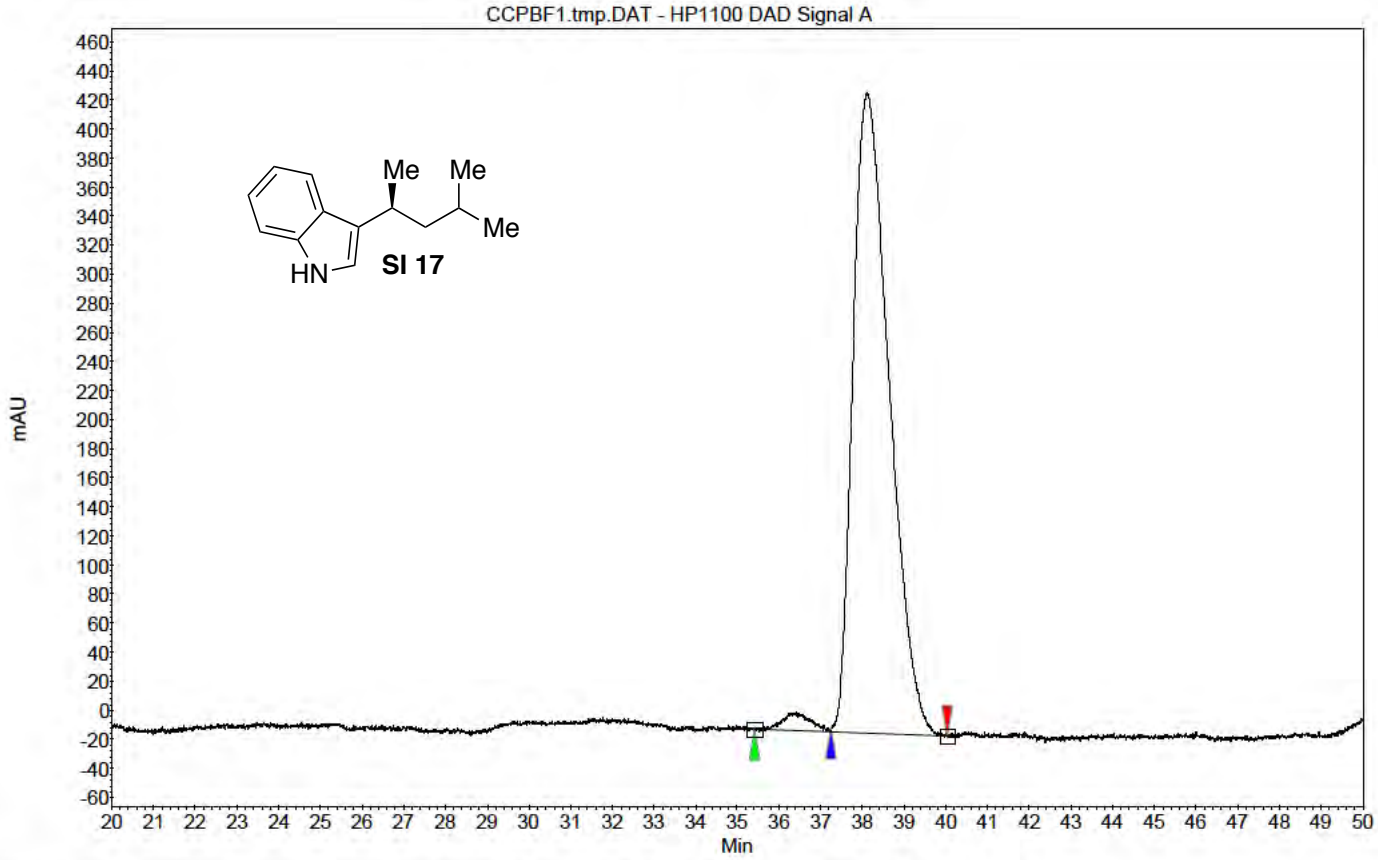
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	13.13	13.58	14.04	0.00	1.79	14.7	5.9	1.789
2	UNKNOWN	14.04	14.51	15.49	0.00	98.21	764.3	323.8	98.211
Total						100.00	778.9	329.7	100.000



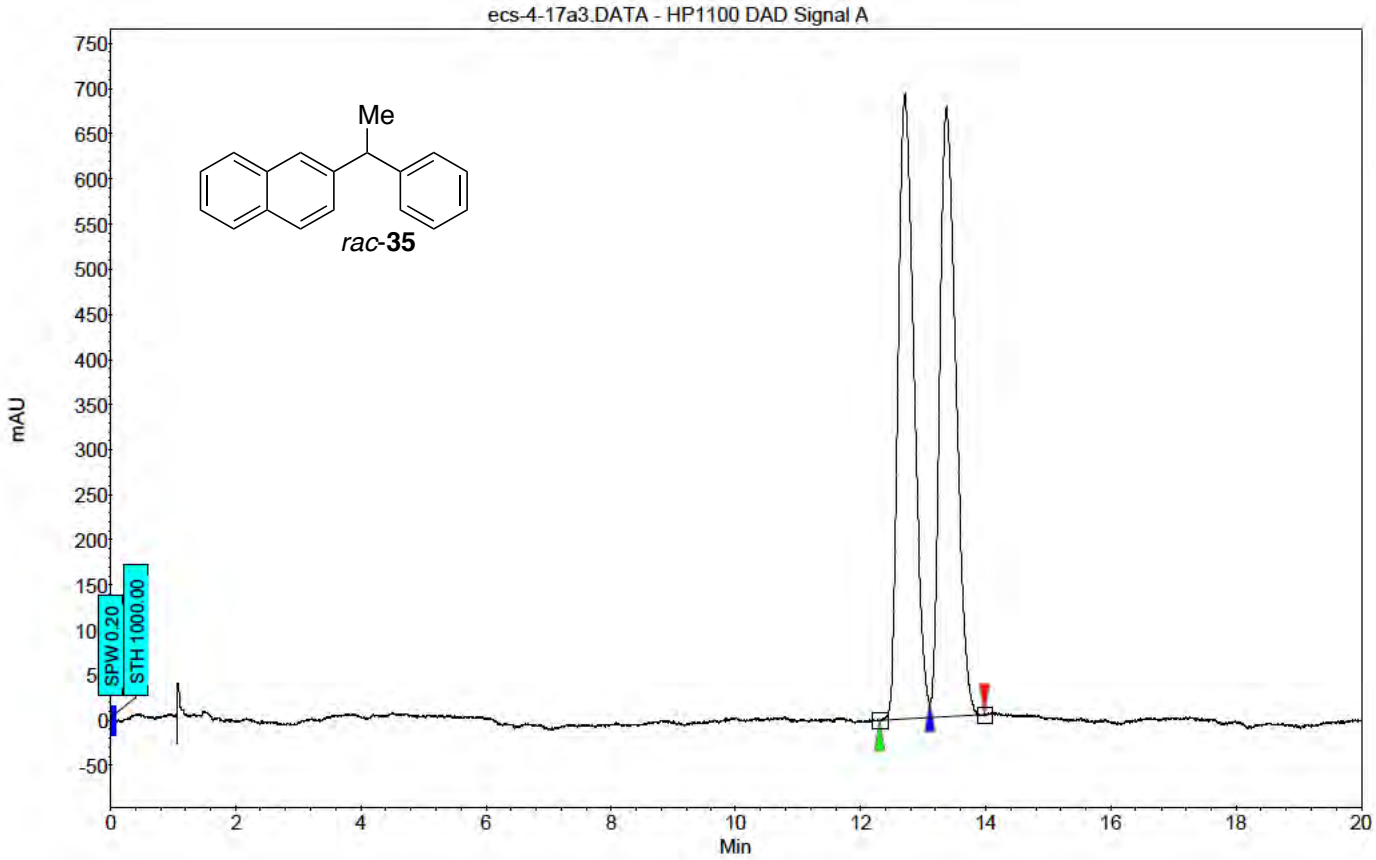


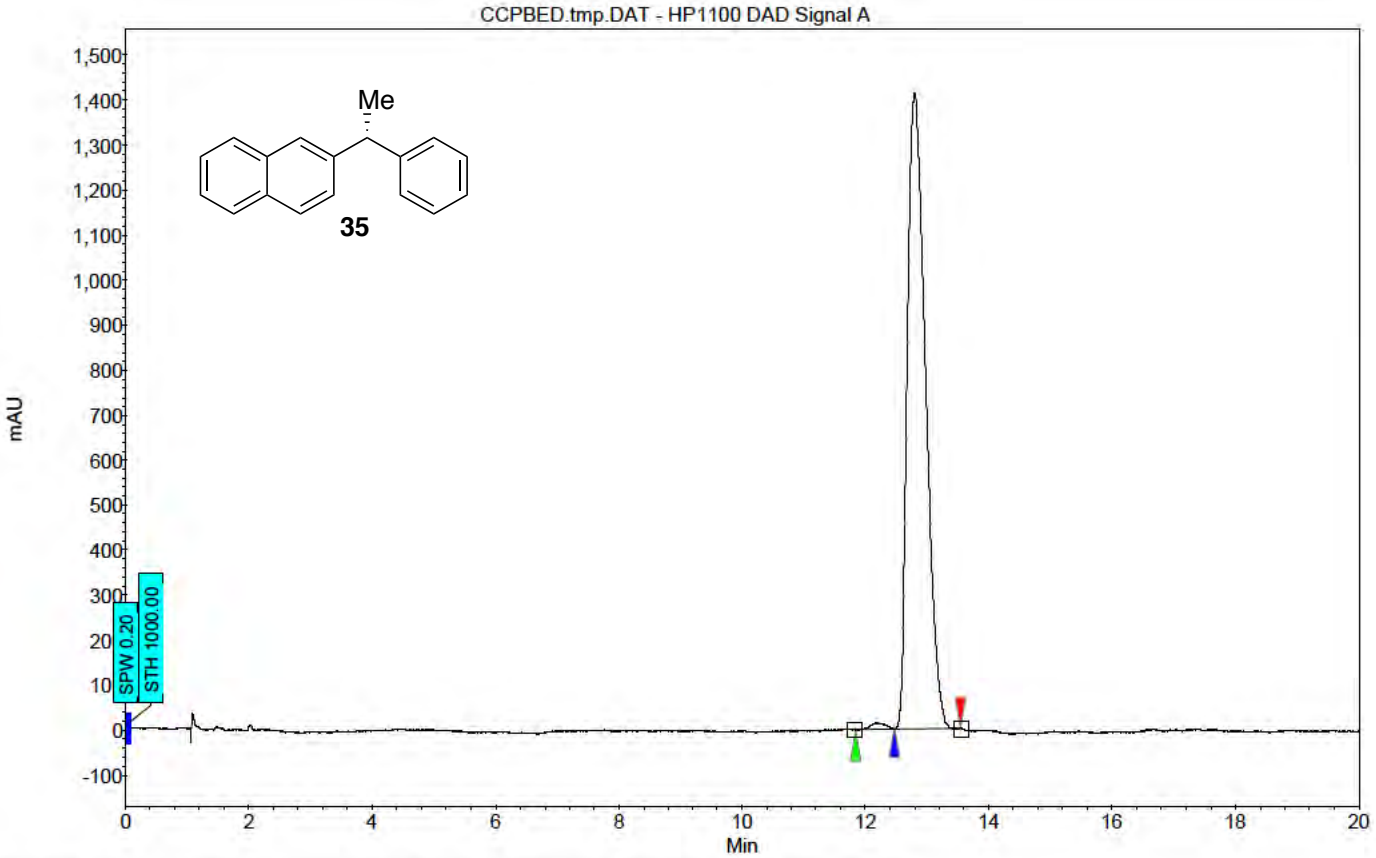
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.68	6.90	7.27	0.00	97.13	2101.8	371.3	97.129
2	UNKNOWN	7.30	7.56	7.77	0.00	2.87	70.3	11.0	2.871
Total						100.00	2172.1	382.3	100.000



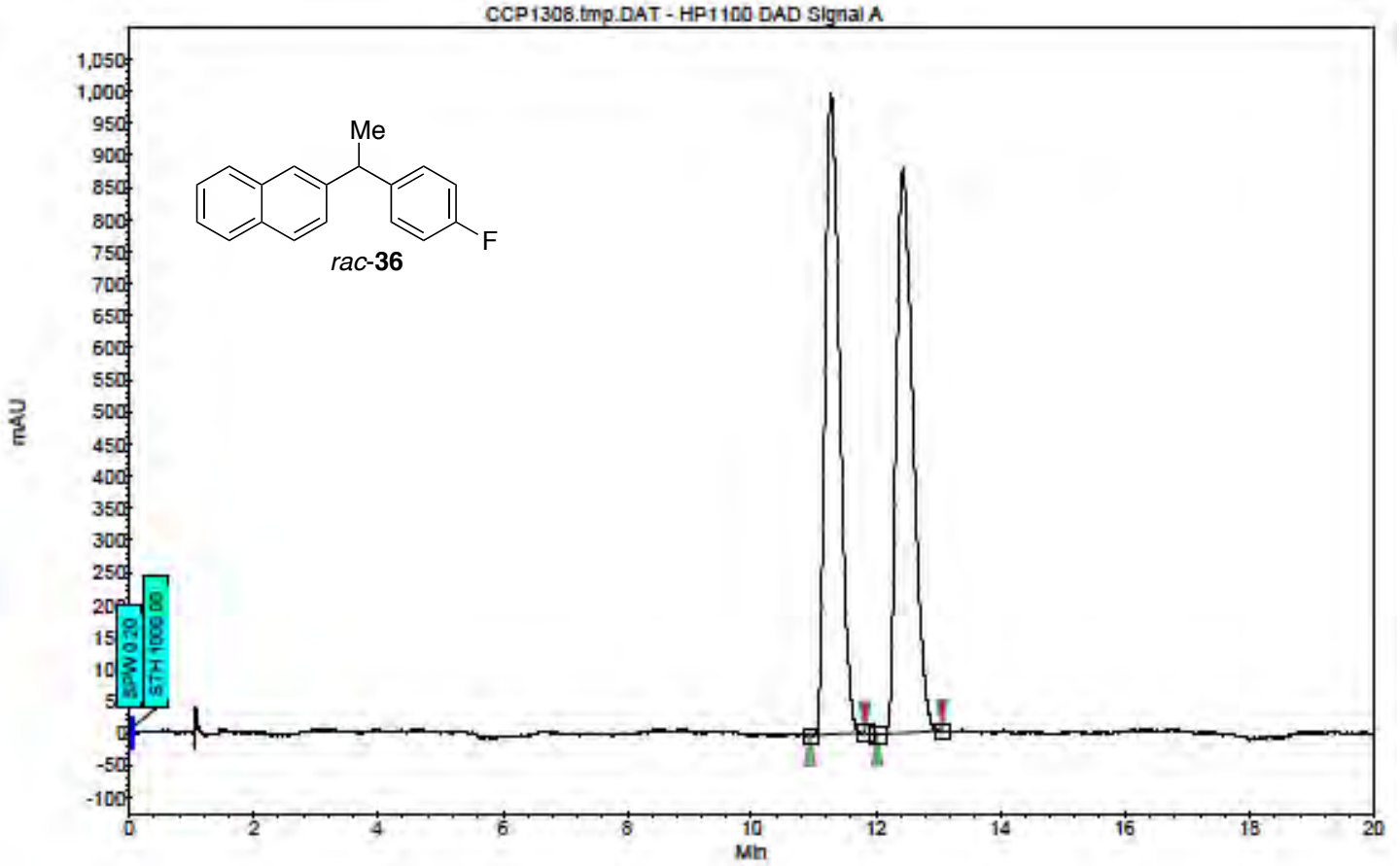


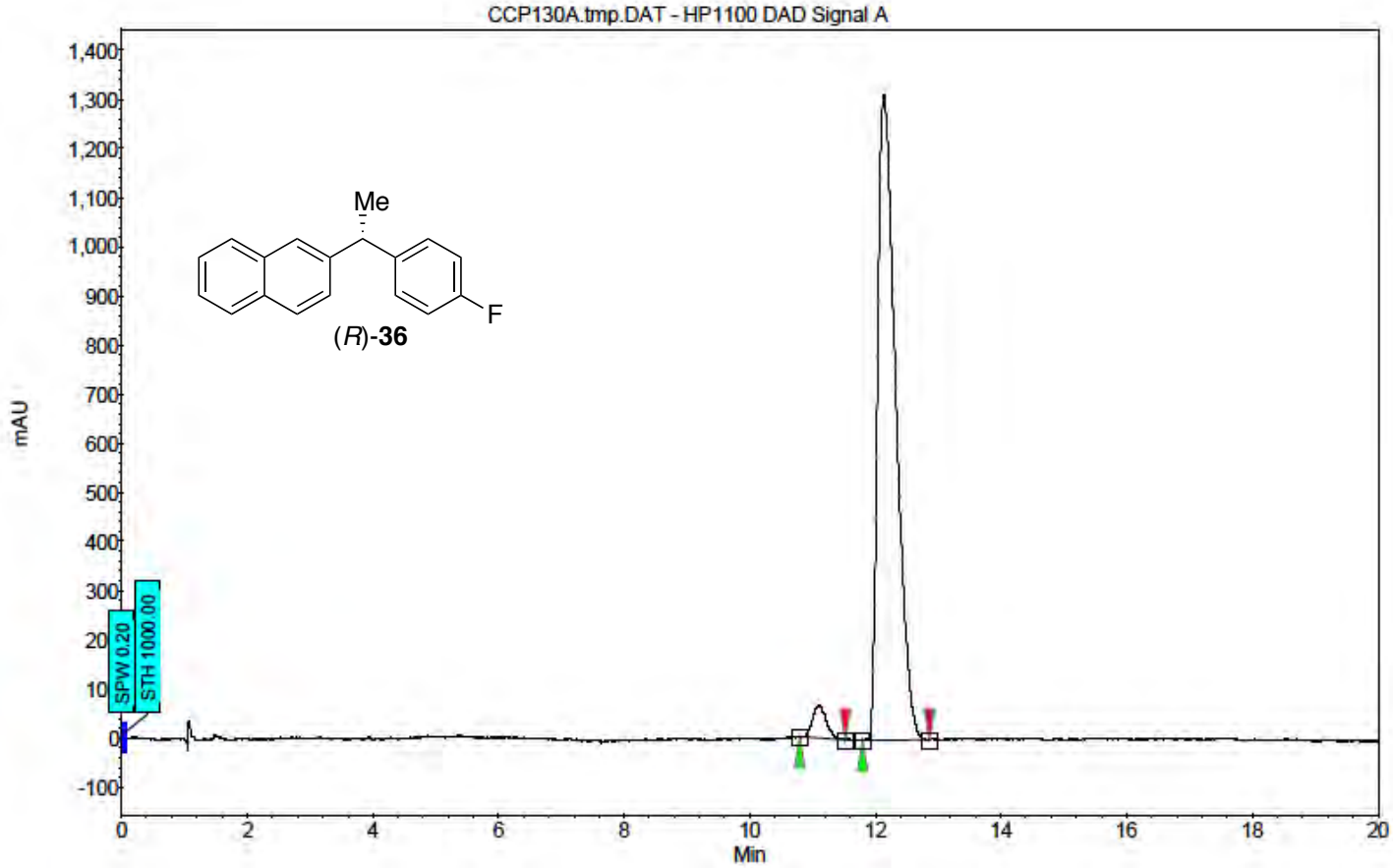
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	35.43	36.34	37.24	0.00	2.03	12.0	9.2	2.032
2	UNKNOWN	37.24	38.10	40.03	0.00	97.97	440.0	443.4	97.968
Total						100.00	452.0	452.5	100.000



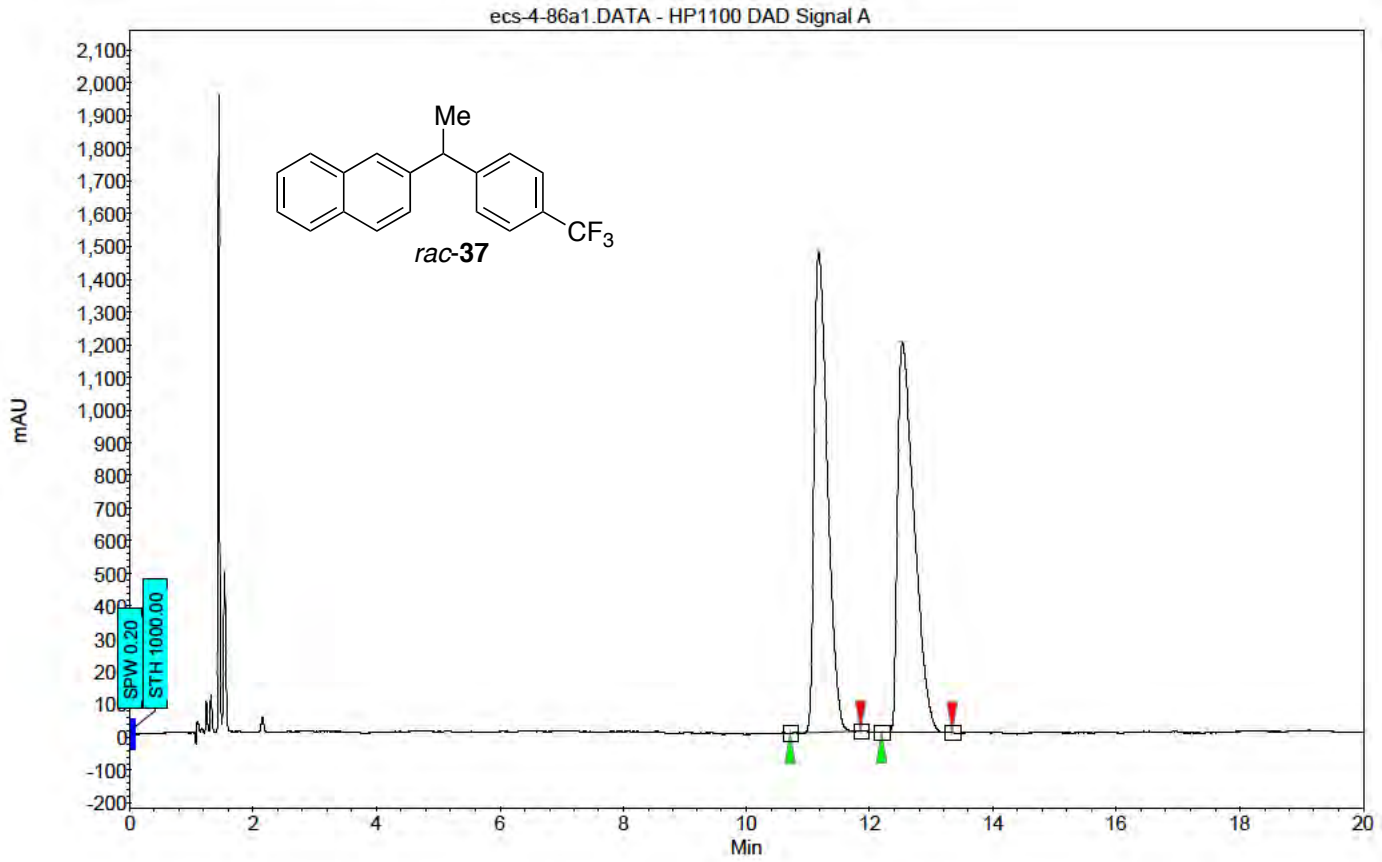


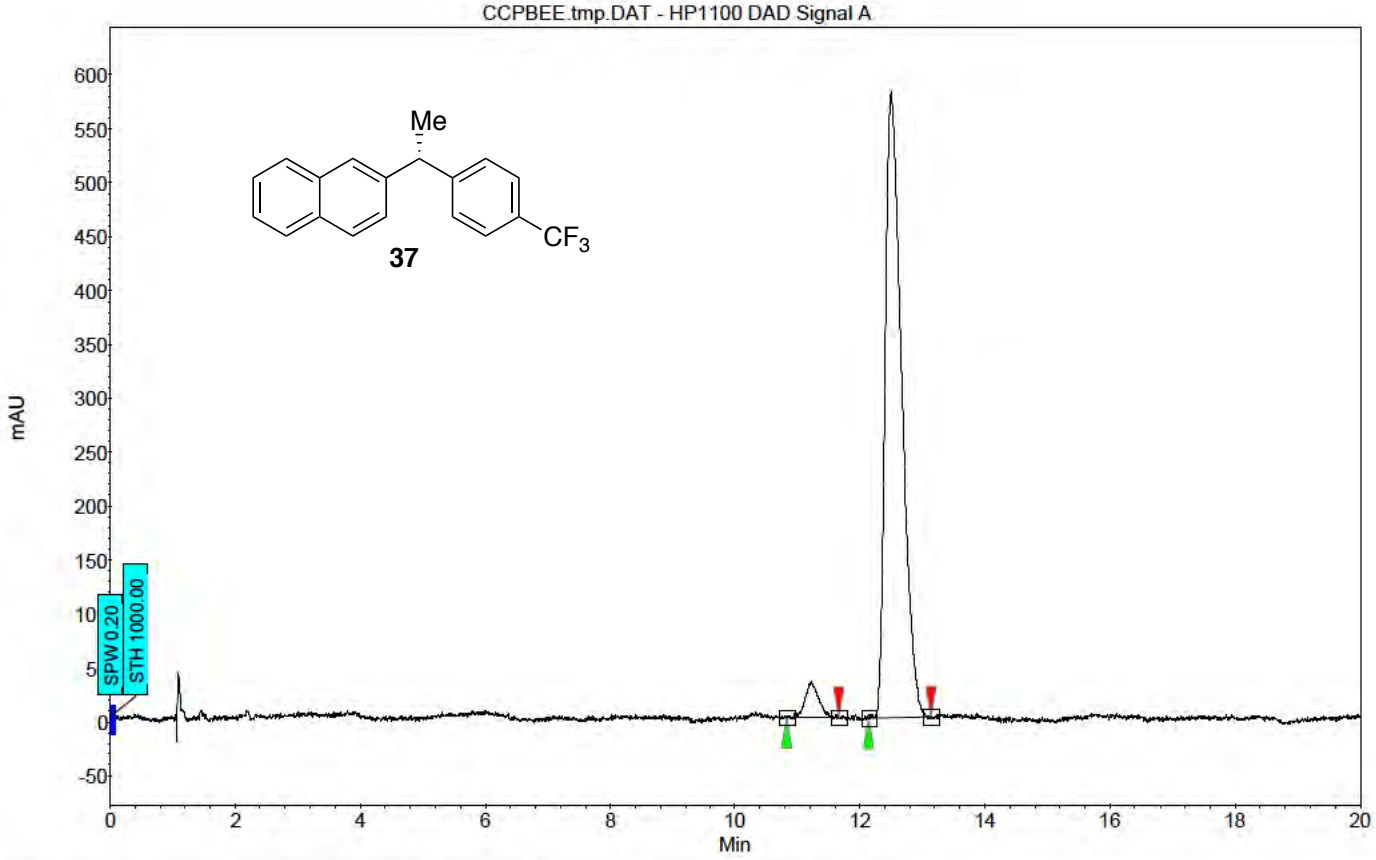
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	11.84	12.20	12.47	0.00	0.82	15.6	4.0	0.824
1	UNKNOWN	12.47	12.80	13.55	0.00	99.18	1411.1	481.4	99.176
Total						100.00	1426.7	485.4	100.000



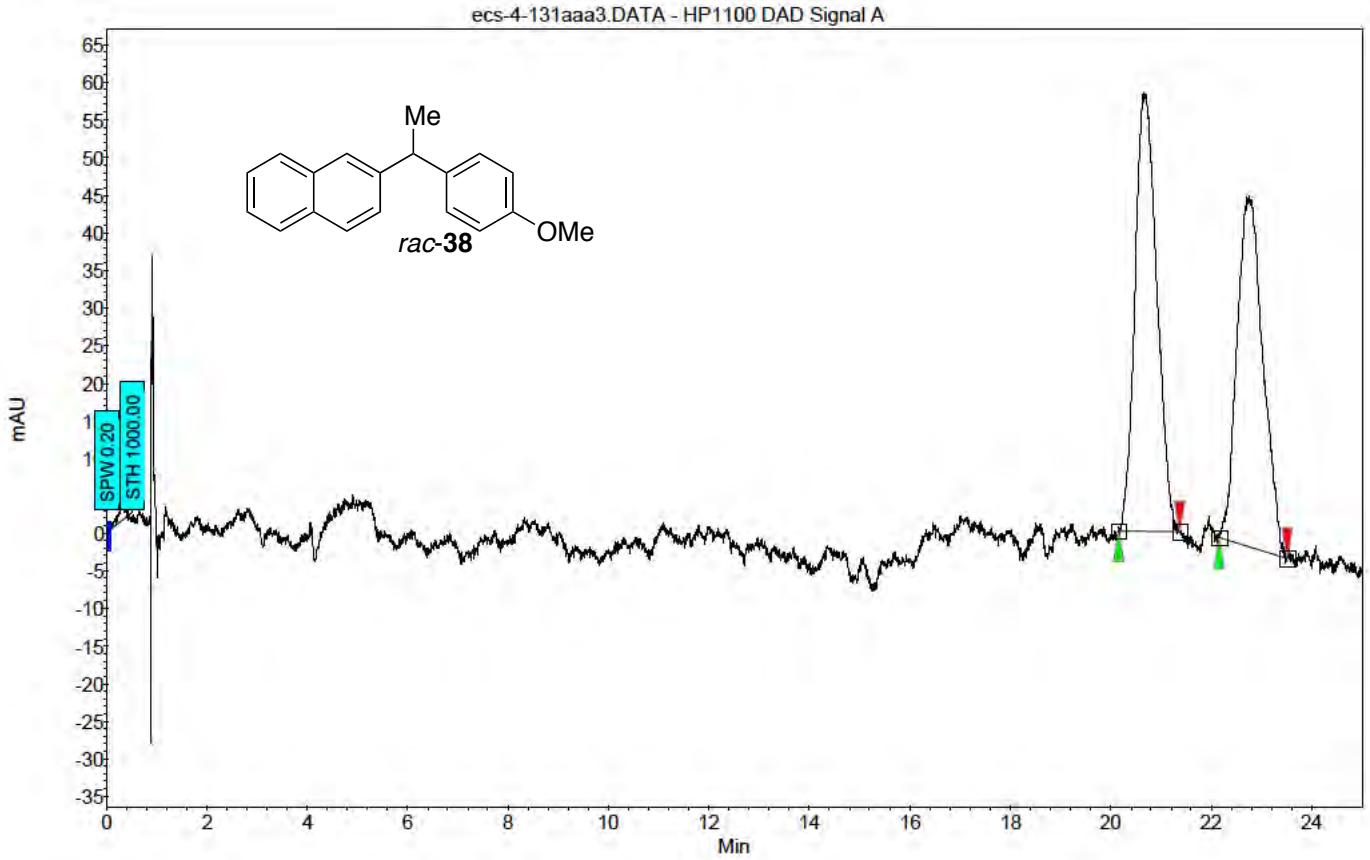


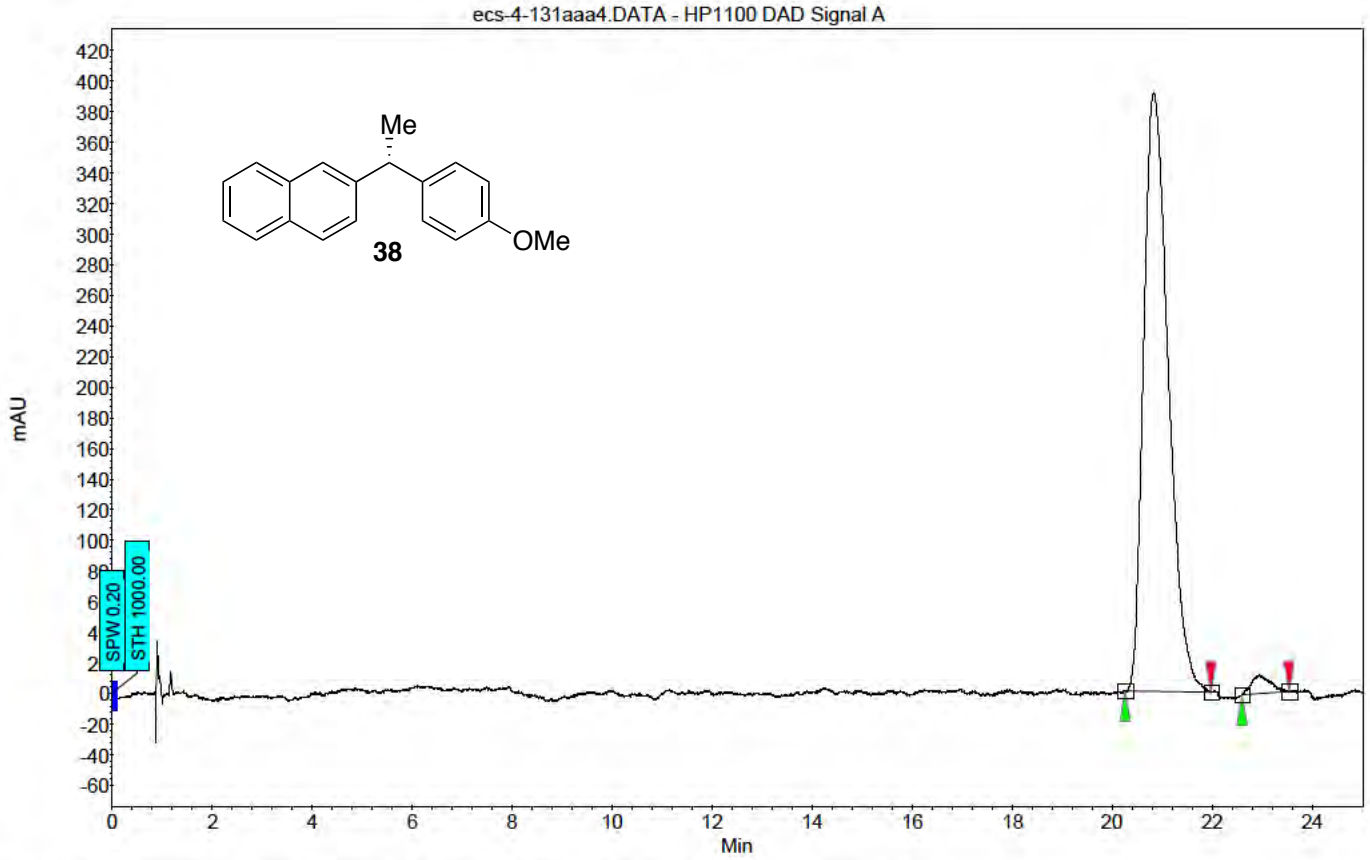
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	10.80	11.11	11.52	0.00	3.69	67.1	16.7	3.687
2	UNKNOWN	11.80	12.14	12.86	0.00	96.31	1313.8	436.0	96.313
Total						100.00	1380.8	452.7	100.000



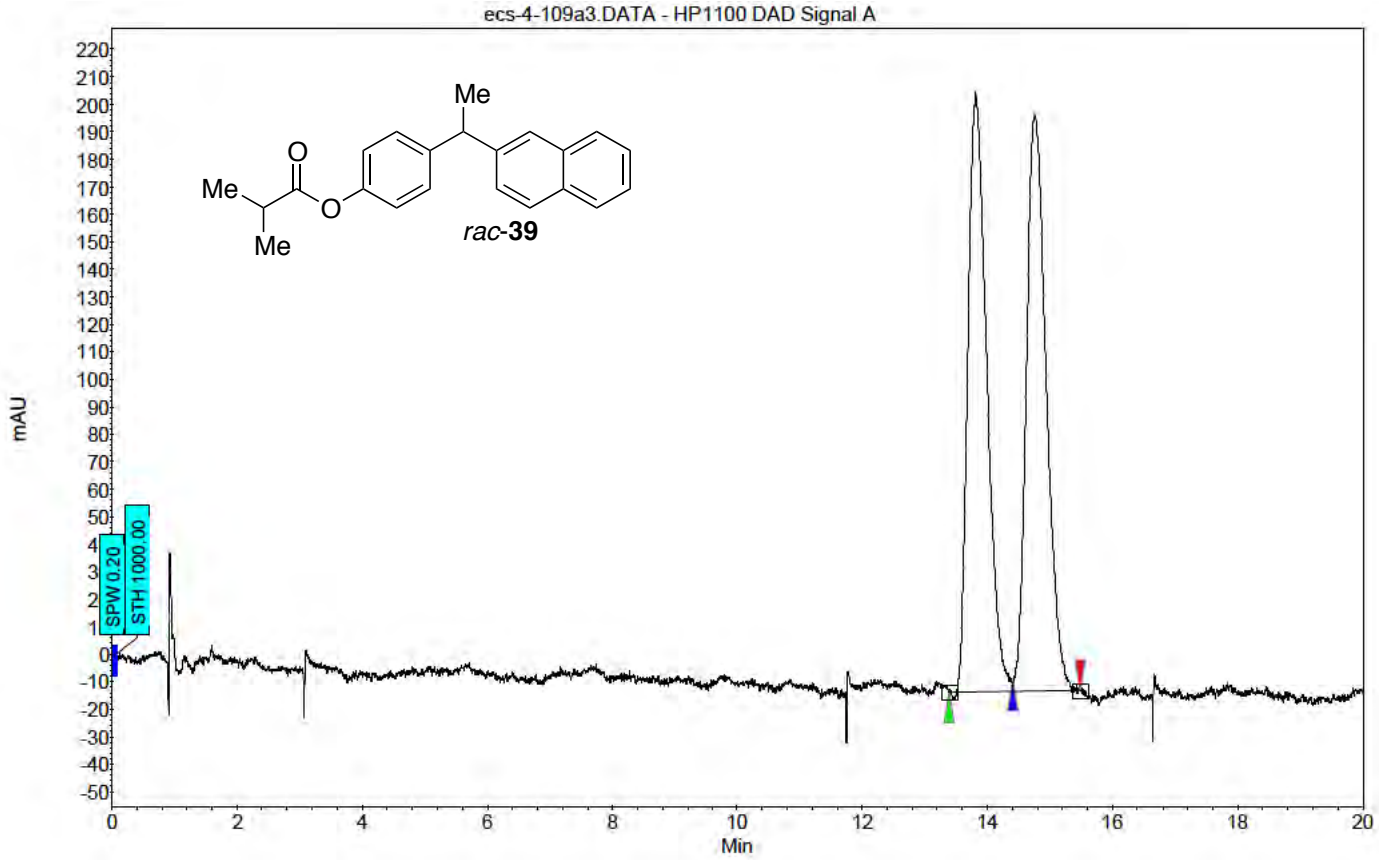


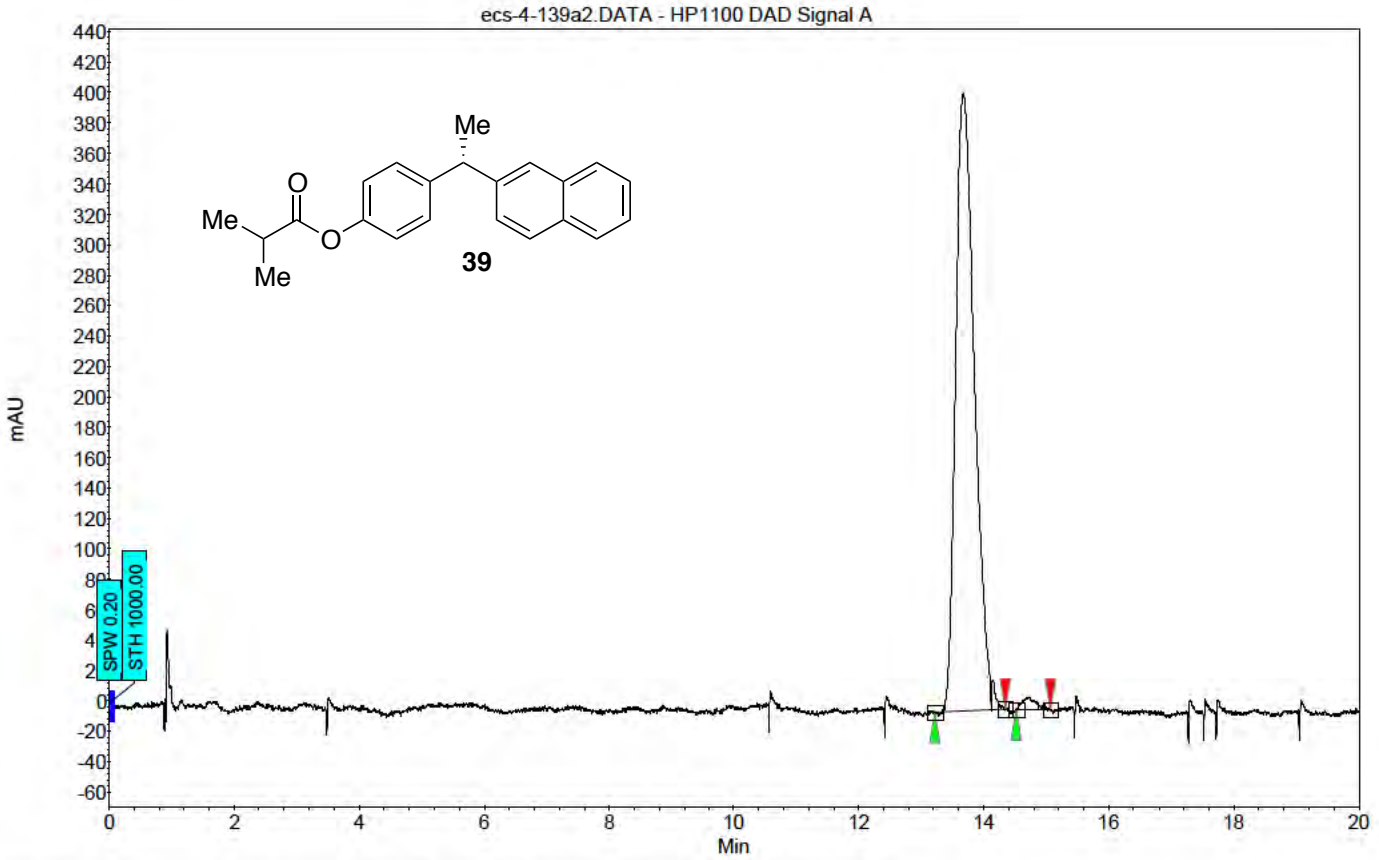
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	10.82	11.23	11.66	0.00	4.51	33.2	8.4	4.510
1	UNKNOWN	12.13	12.50	13.14	0.00	95.49	580.5	176.9	95.490
Total						100.00	613.7	185.3	100.000



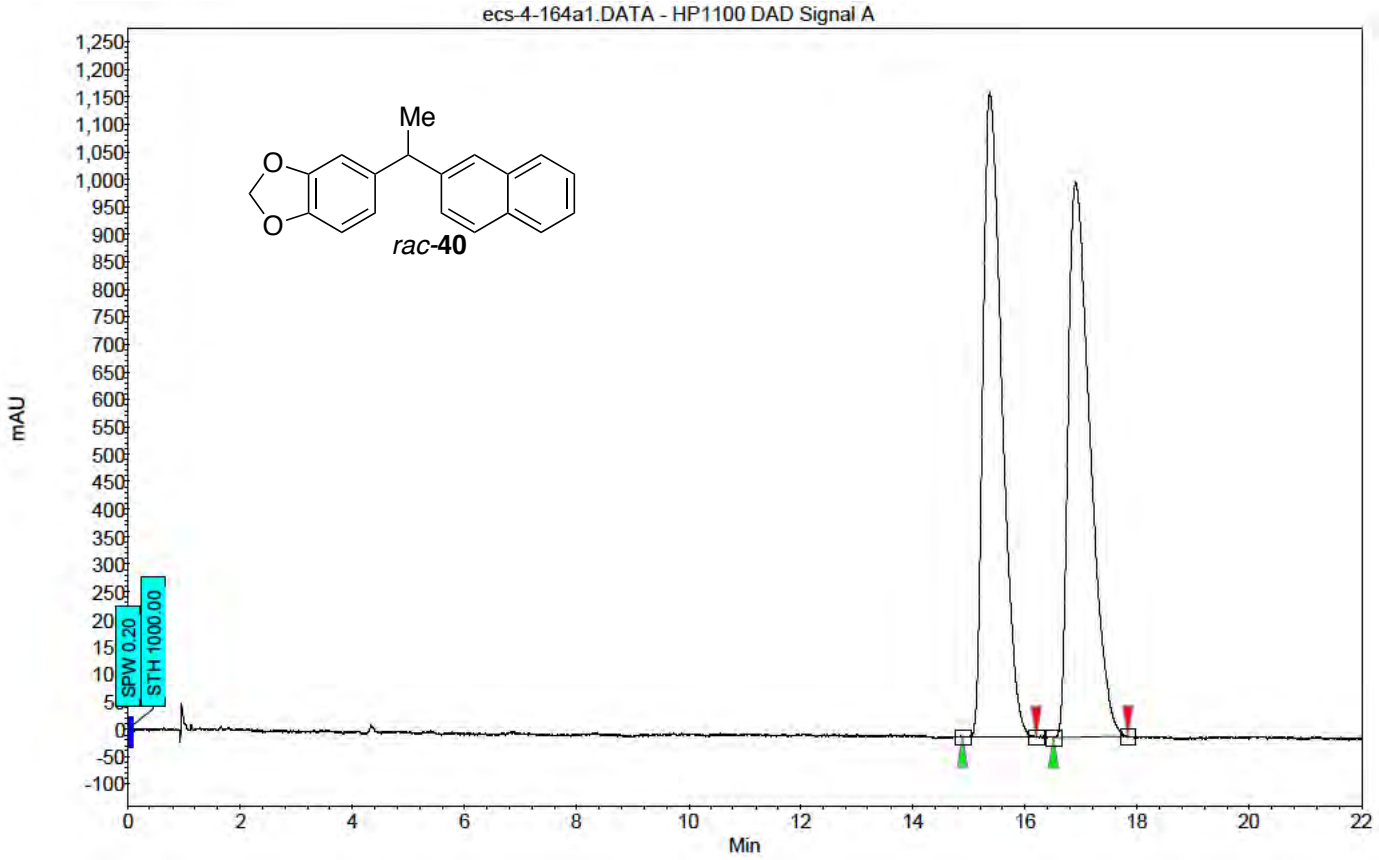


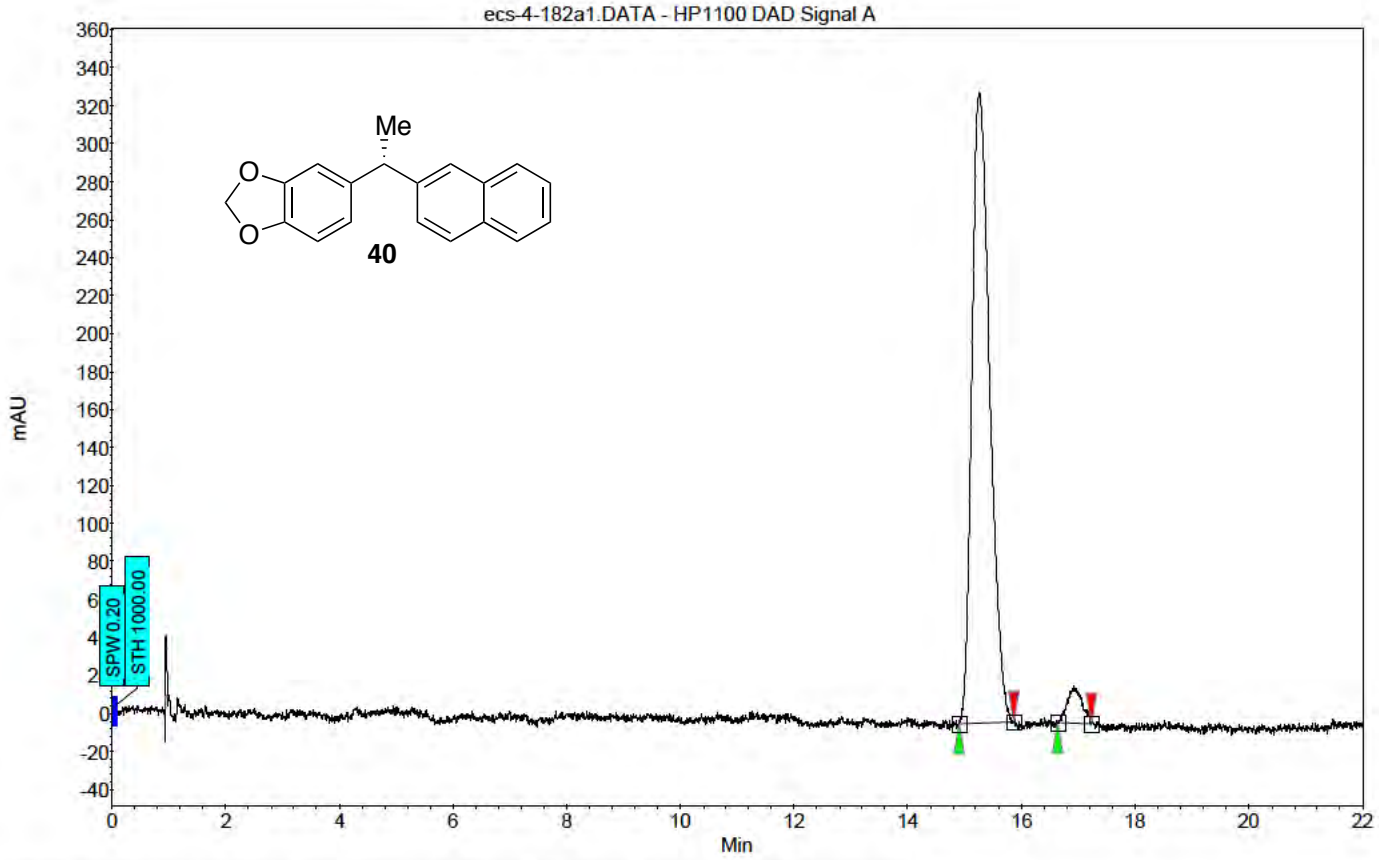
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	20.25	20.82	21.97	0.00	97.67	390.5	223.6	97.672
2	UNKNOWN	22.59	22.95	23.53	0.00	2.33	12.5	5.3	2.328
Total						100.00	403.0	228.9	100.000



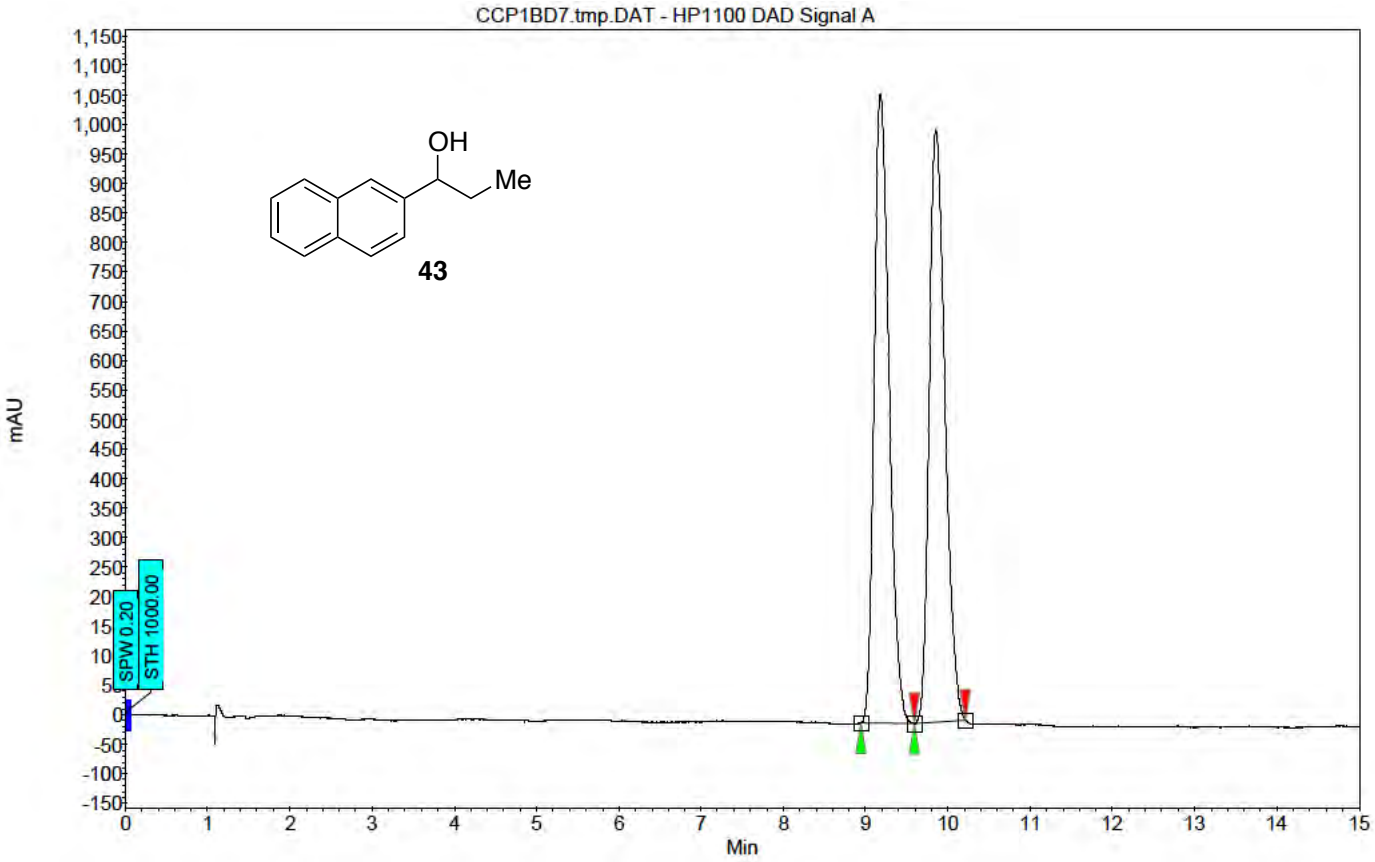


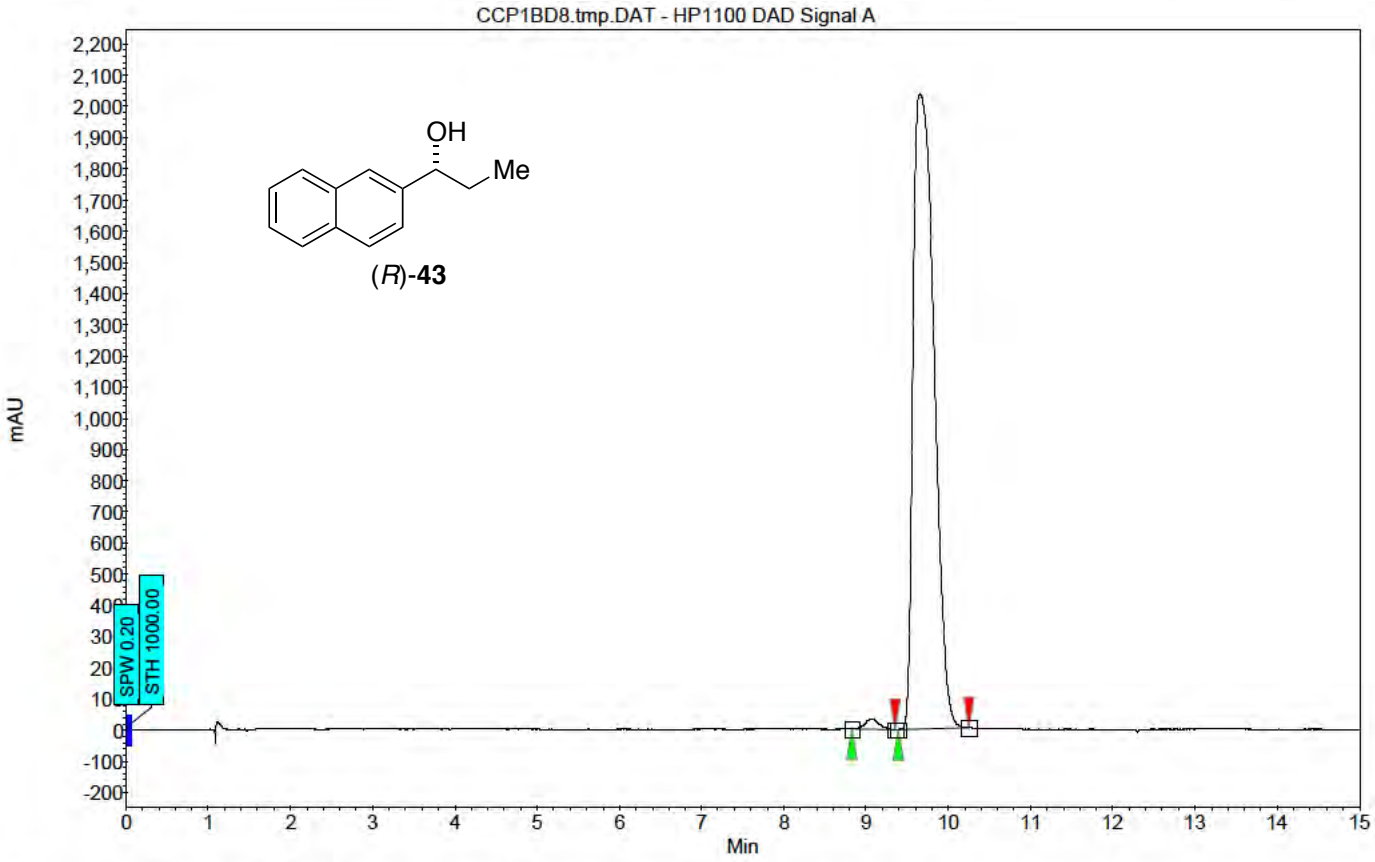
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	13.22	13.67	14.34	0.00	98.50	405.8	142.5	98.498
2	UNKNOWN	14.52	14.71	15.06	0.00	1.50	8.1	2.2	1.502
Total						100.00	414.0	144.7	100.000



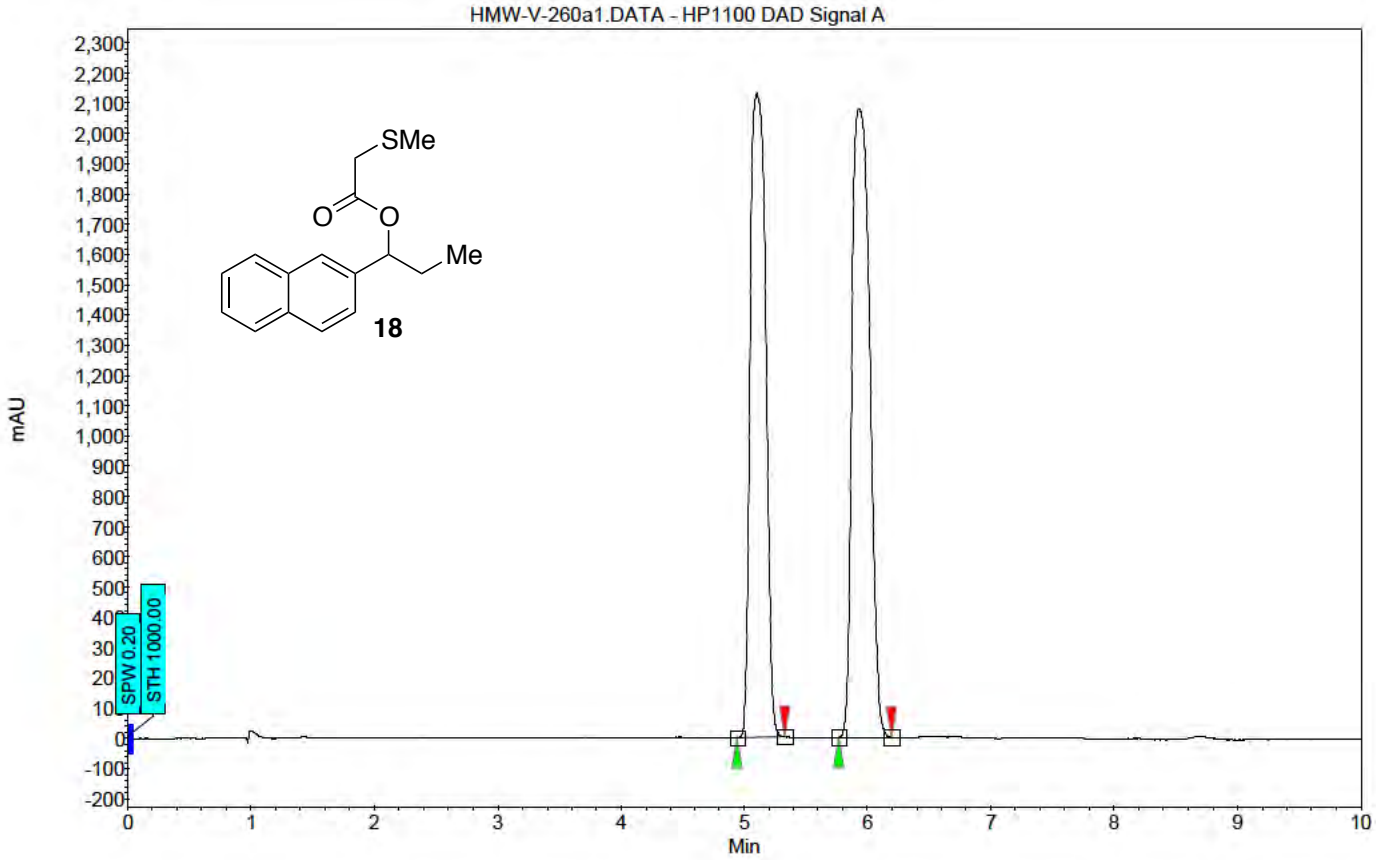


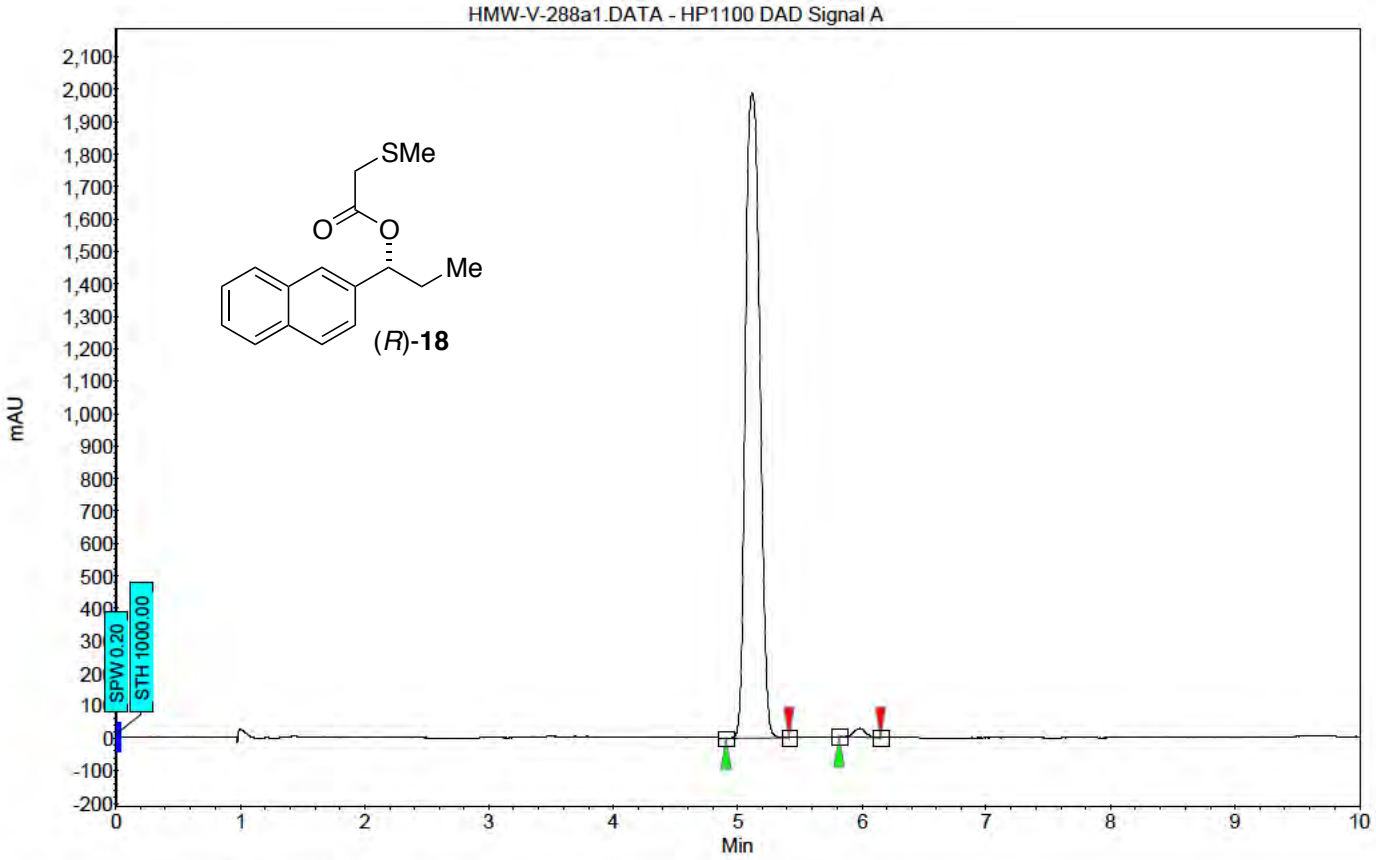
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	14.90	15.26	15.86	0.00	95.54	331.5	120.8	95.543
2	UNKNOWN	16.64	16.93	17.23	0.00	4.46	19.3	5.6	4.457
Total						100.00	350.9	126.4	100.000





Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.83	9.07	9.35	0.00	1.05	33.5	6.4	1.048
2	UNKNOWN	9.39	9.66	10.25	0.00	98.95	2034.5	600.3	98.952
Total						100.00	2067.9	606.6	100.000





Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
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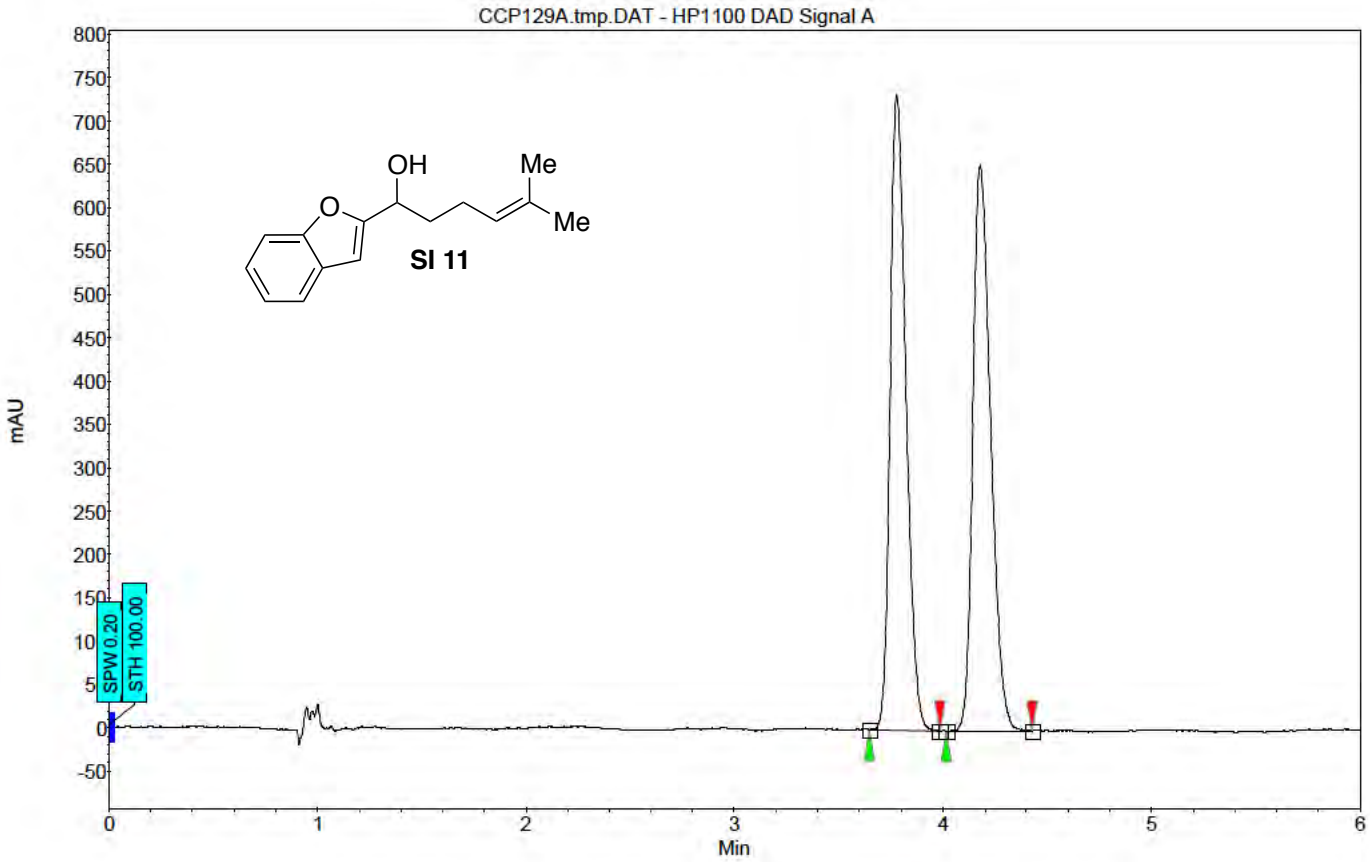
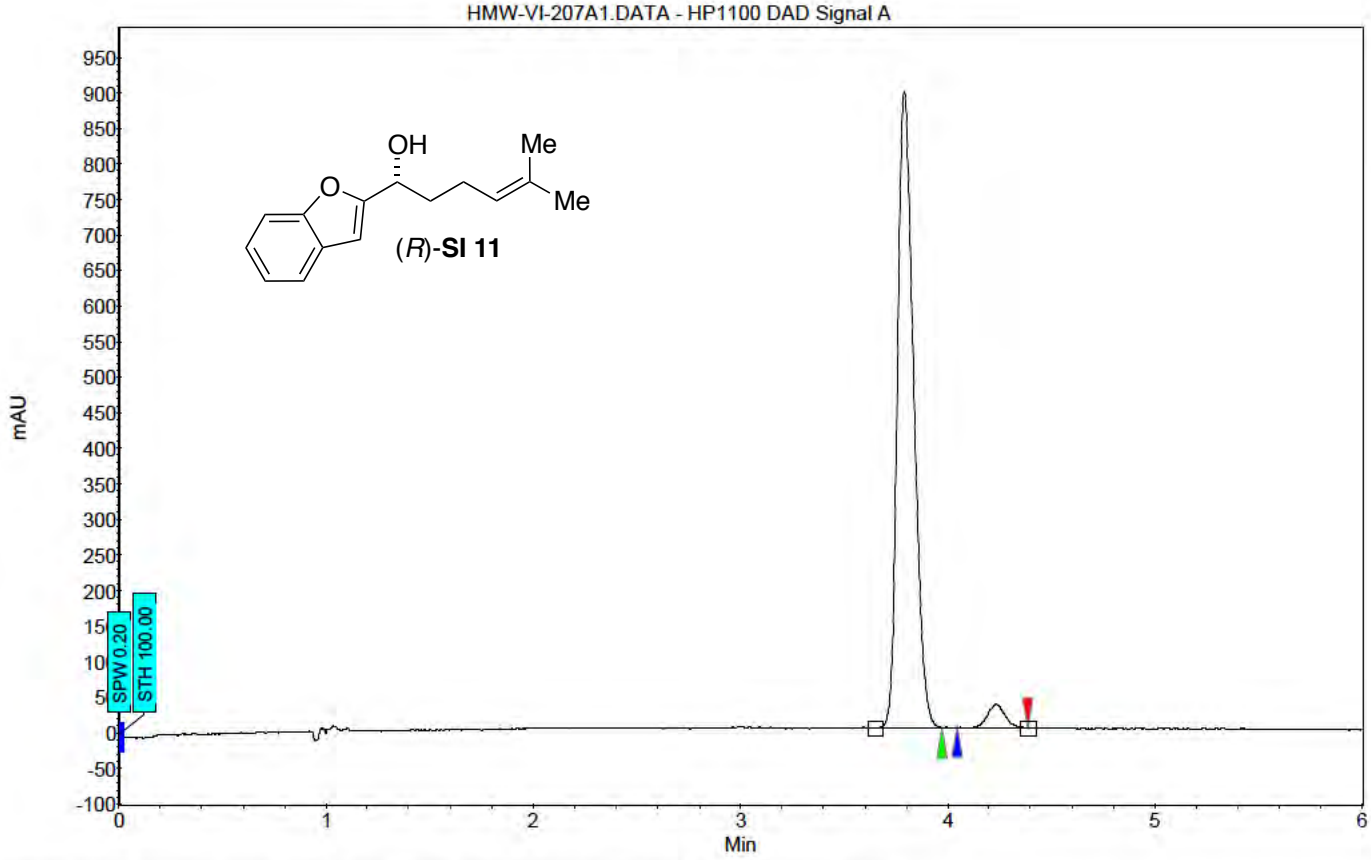
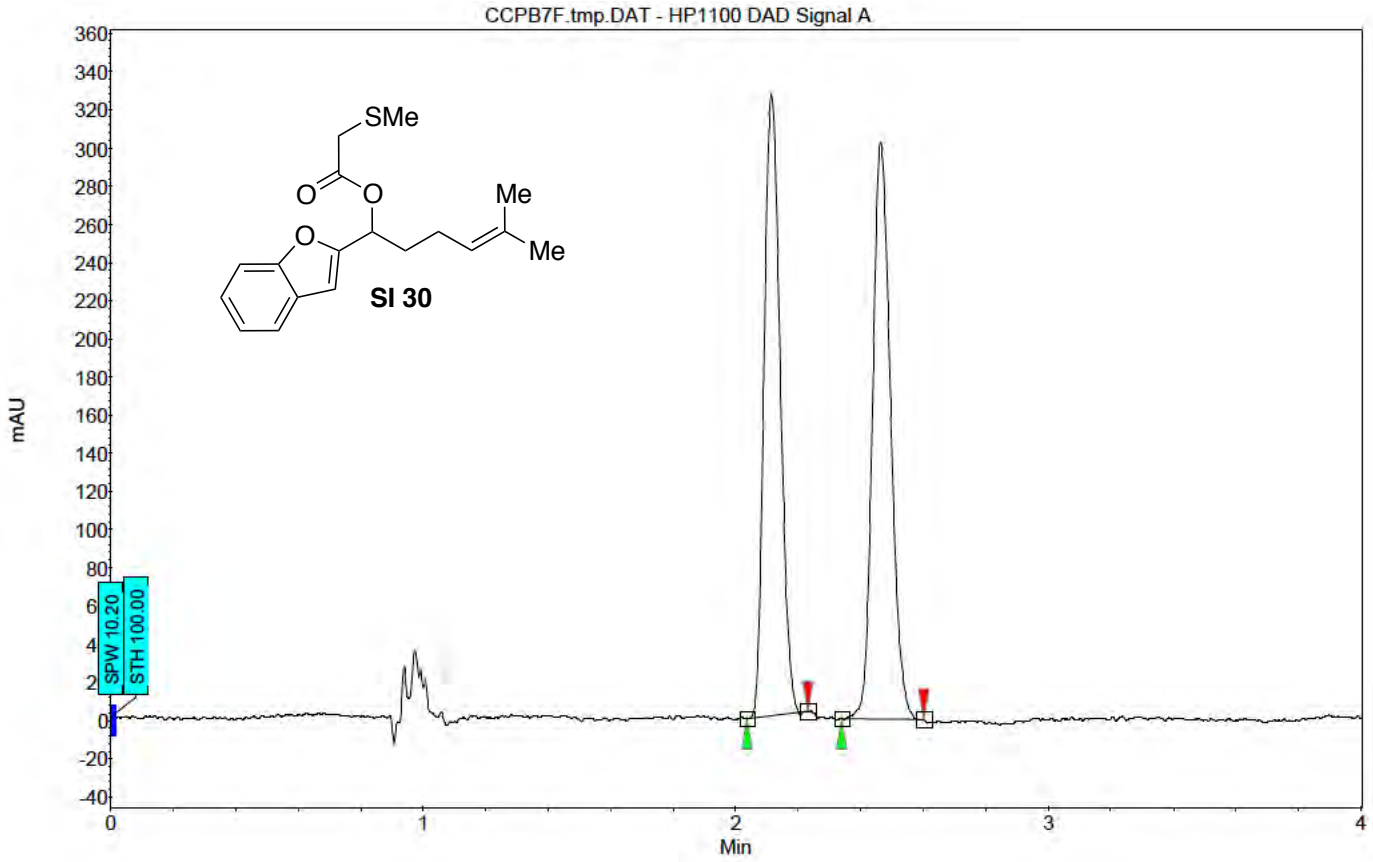
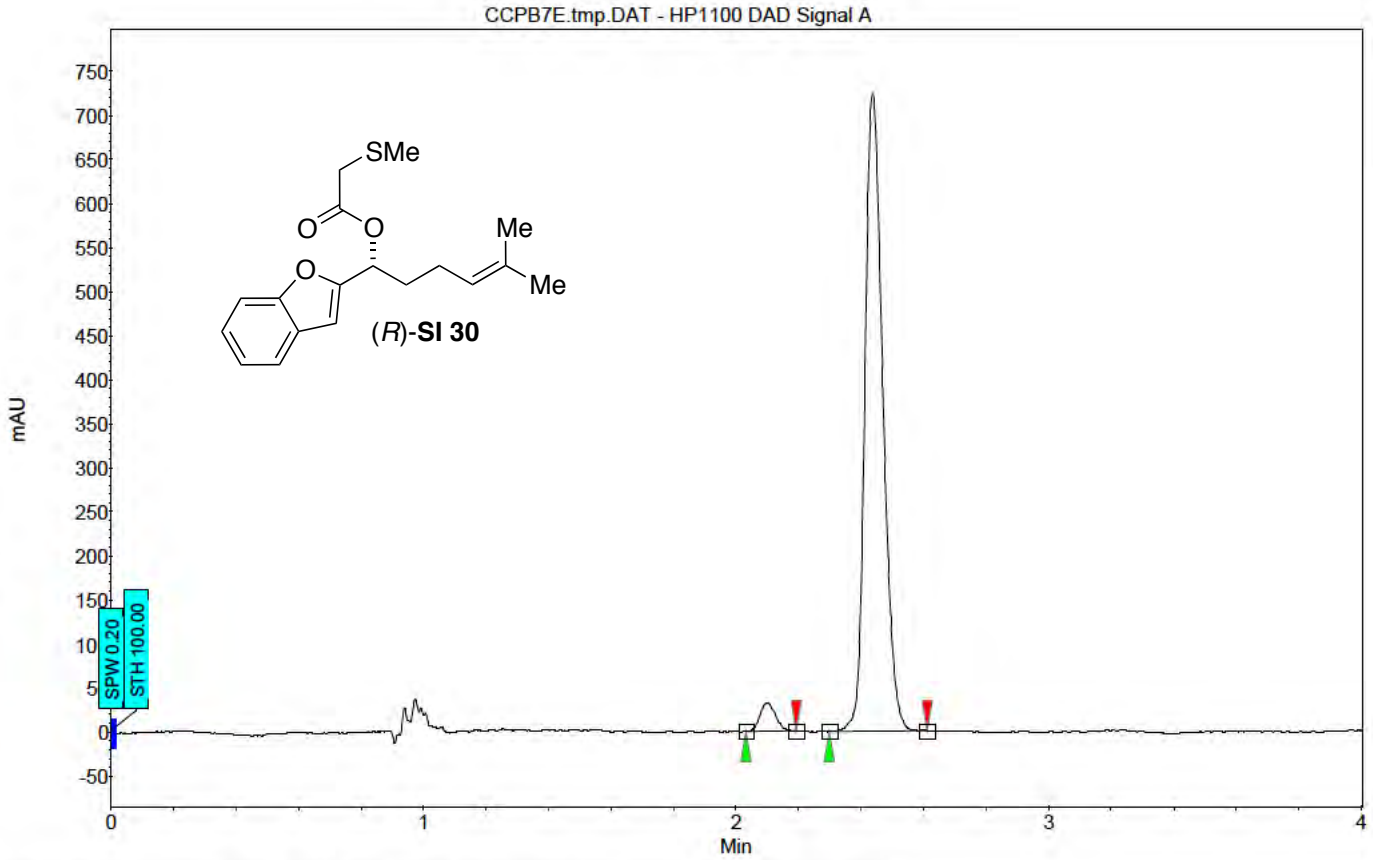
1	UNKNOWN	4.91	5.12	5.41	0.00	98.84	1986.9	264.7	98.838
2	UNKNOWN	5.82	5.98	6.15	0.00	1.16	26.8	3.1	1.162
Total						100.00	2013.7	267.8	100.000



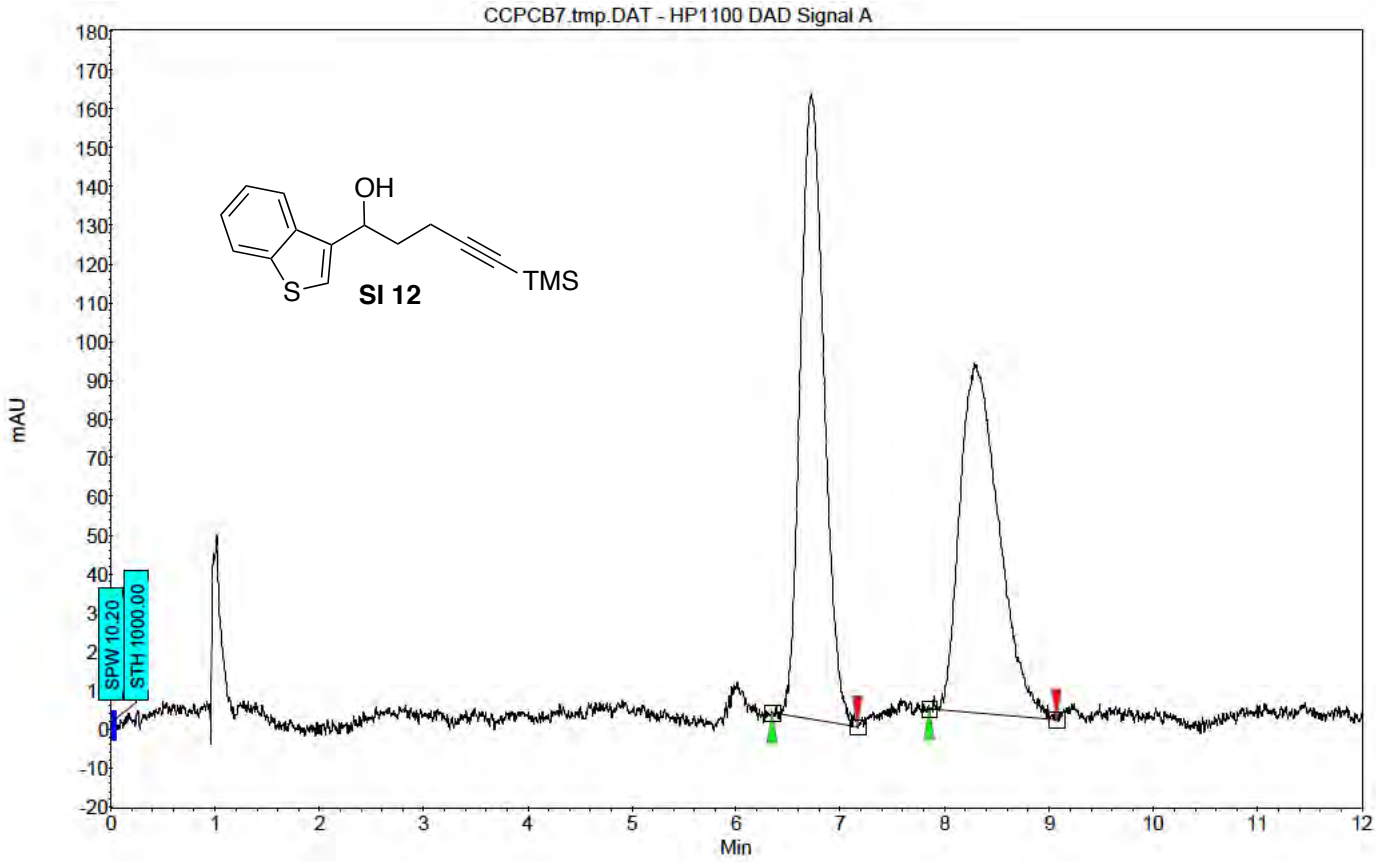


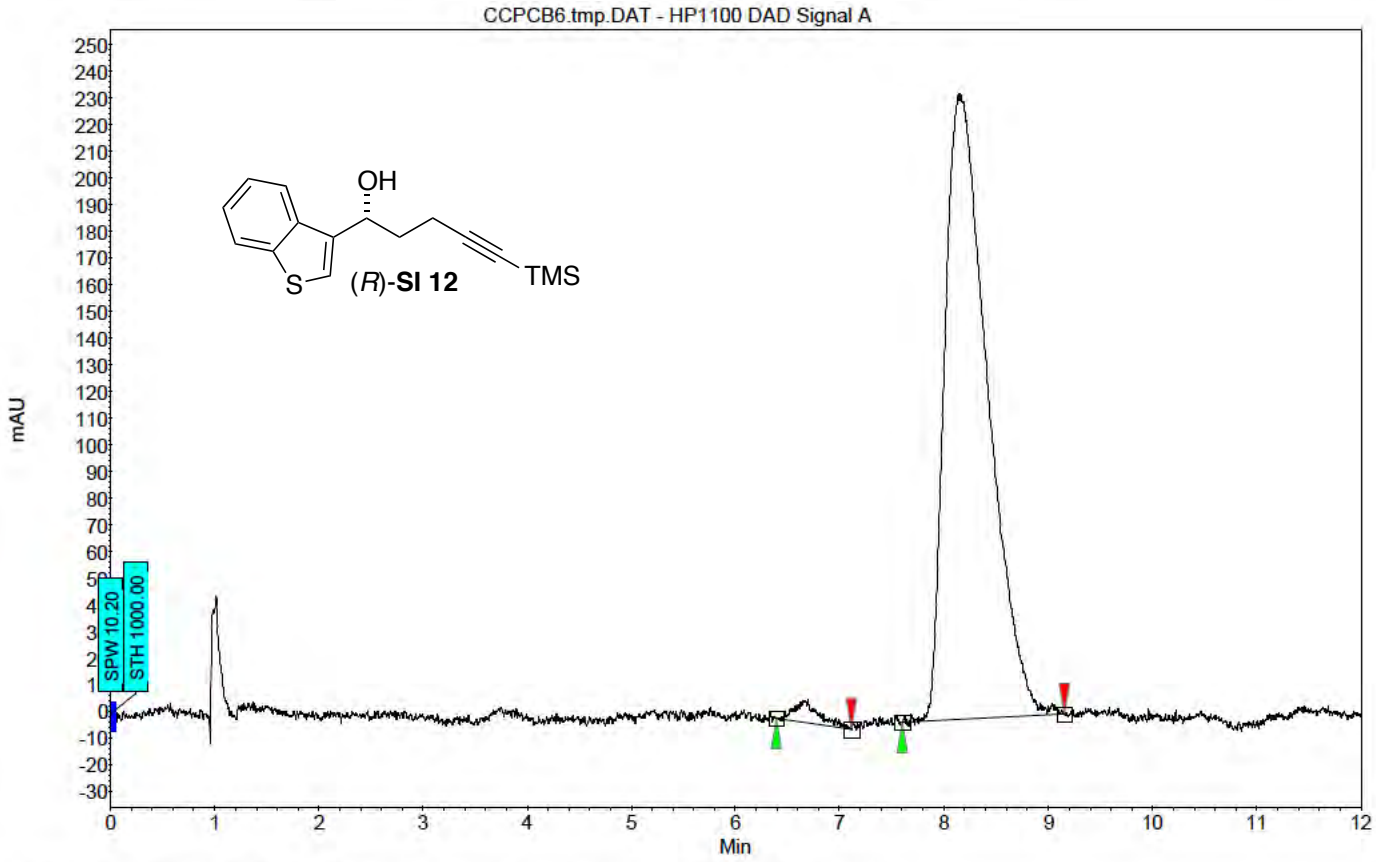
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.97	3.99	4.04	0.00	1.68	1.4	0.1	1.679
2	UNKNOWN	4.04	4.23	4.39	0.00	98.32	34.2	3.5	98.321
Total						100.00	35.7	3.6	100.000



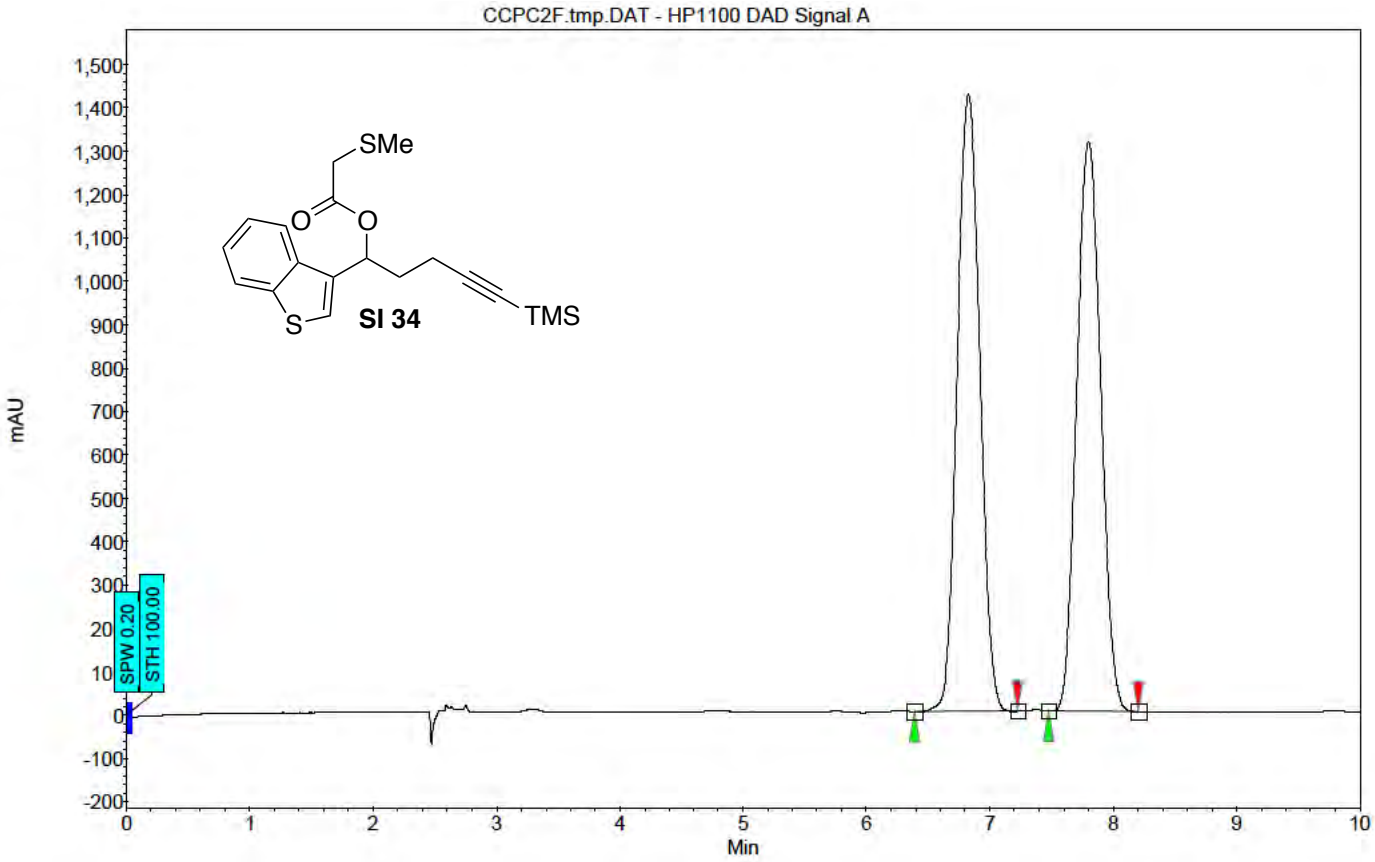


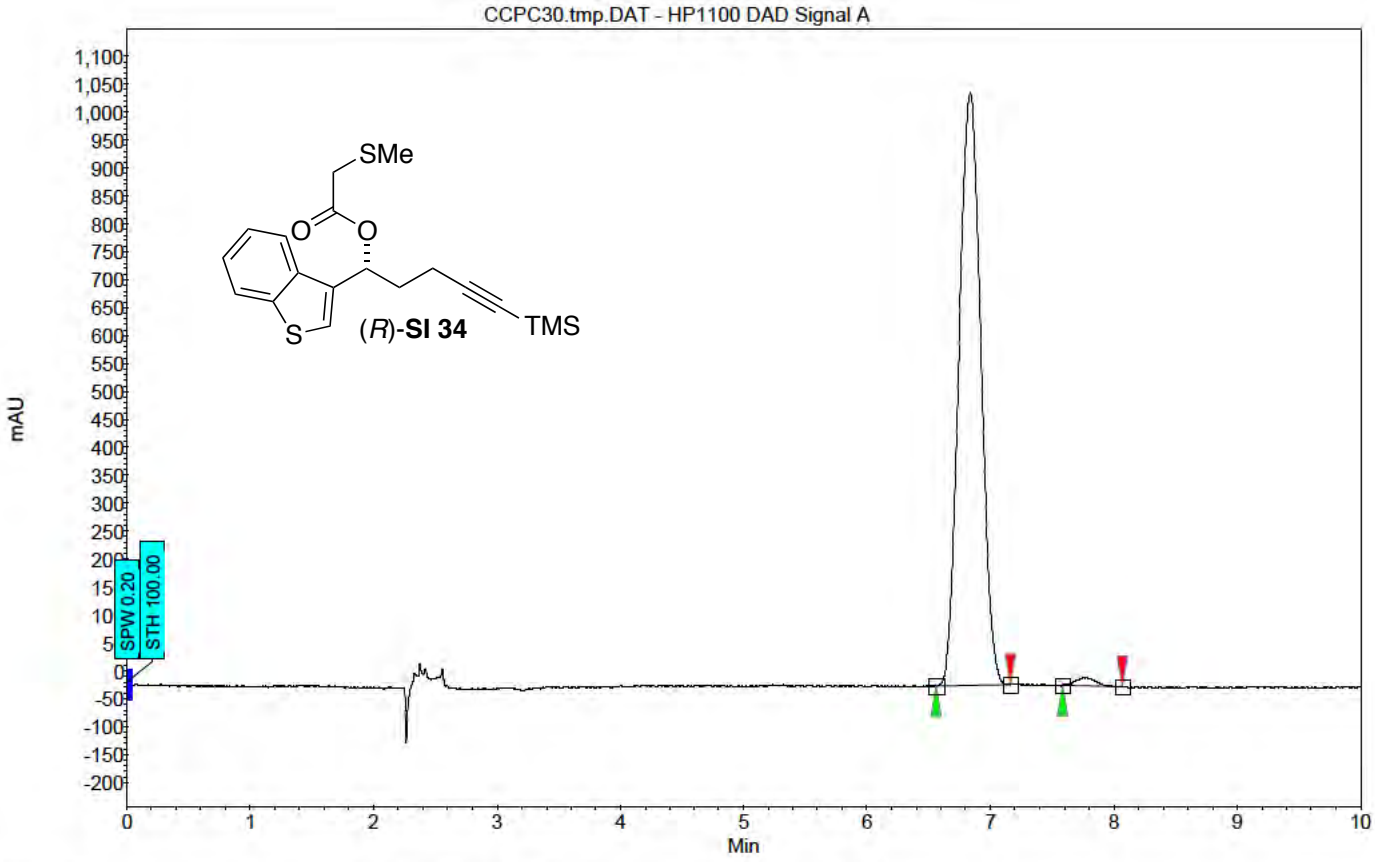
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	2.03	2.10	2.19	0.00	3.73	32.4	1.9	3.732
2	UNKNOWN	2.30	2.44	2.61	0.00	96.27	722.7	47.8	96.268
Total						100.00	755.1	49.7	100.000



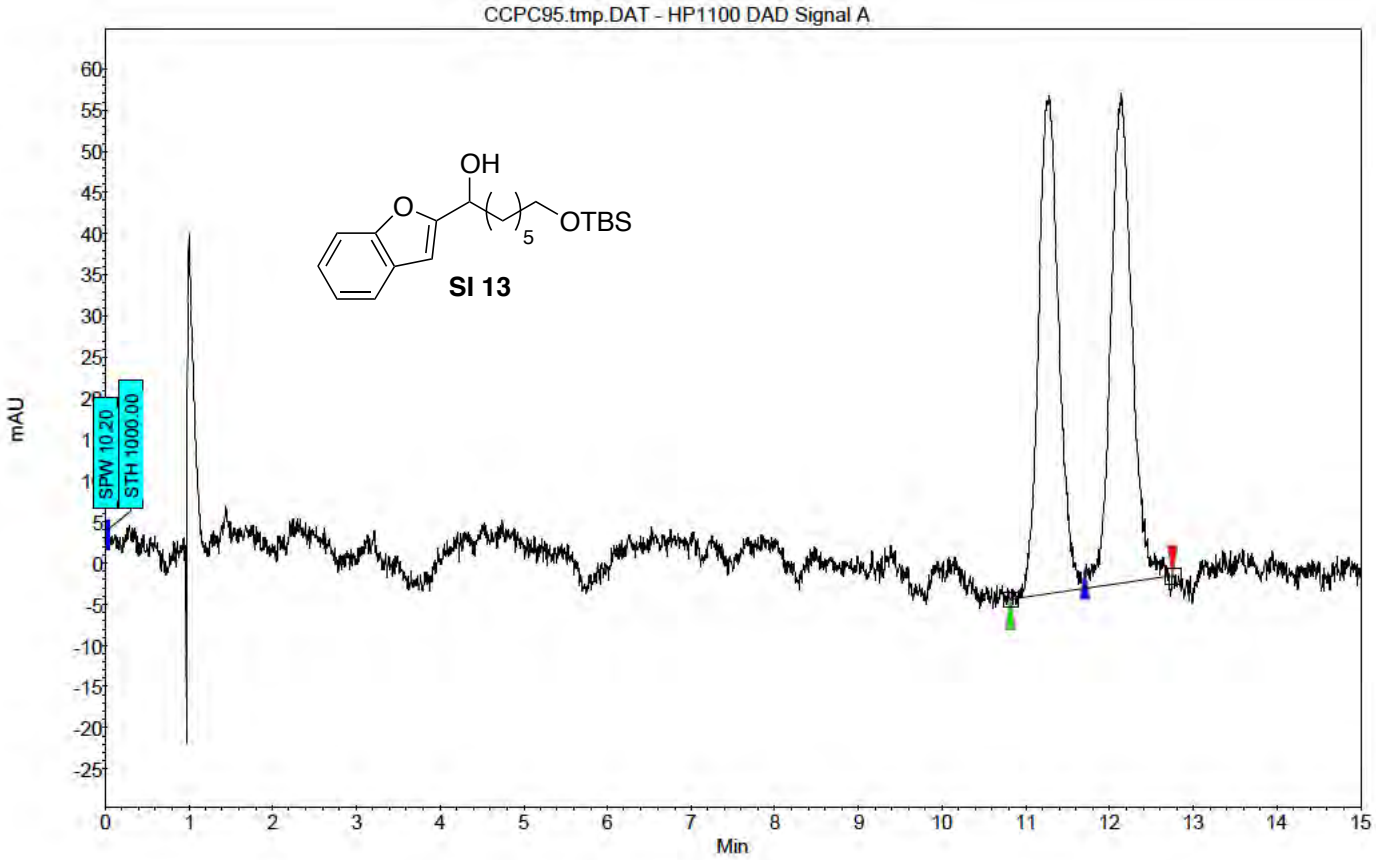


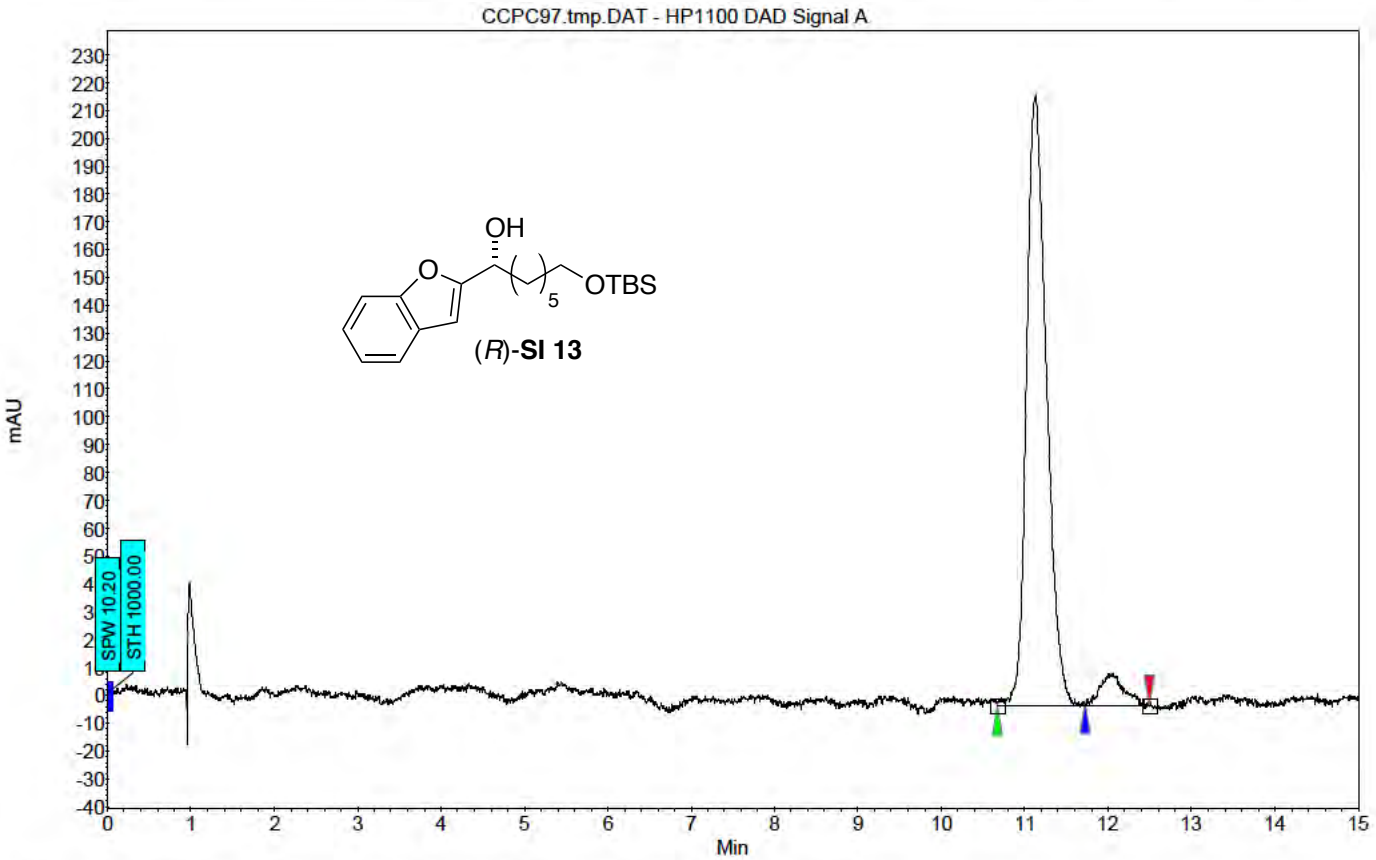
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.39	6.69	7.11	0.00	1.93	8.5	2.2	1.925
2	UNKNOWN	7.60	8.14	9.16	0.00	98.07	234.3	111.6	98.075
Total						100.00	242.9	113.8	100.000



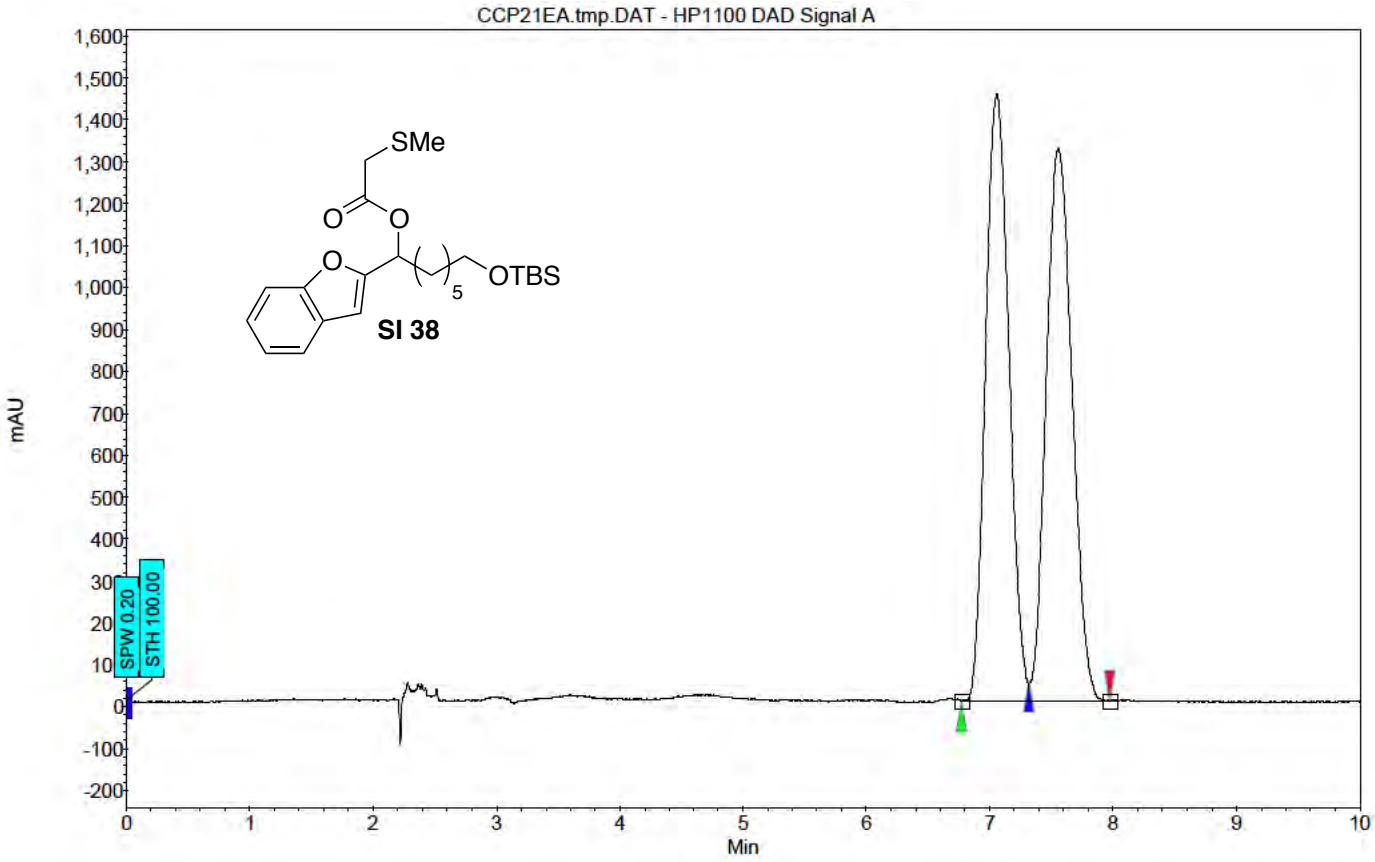


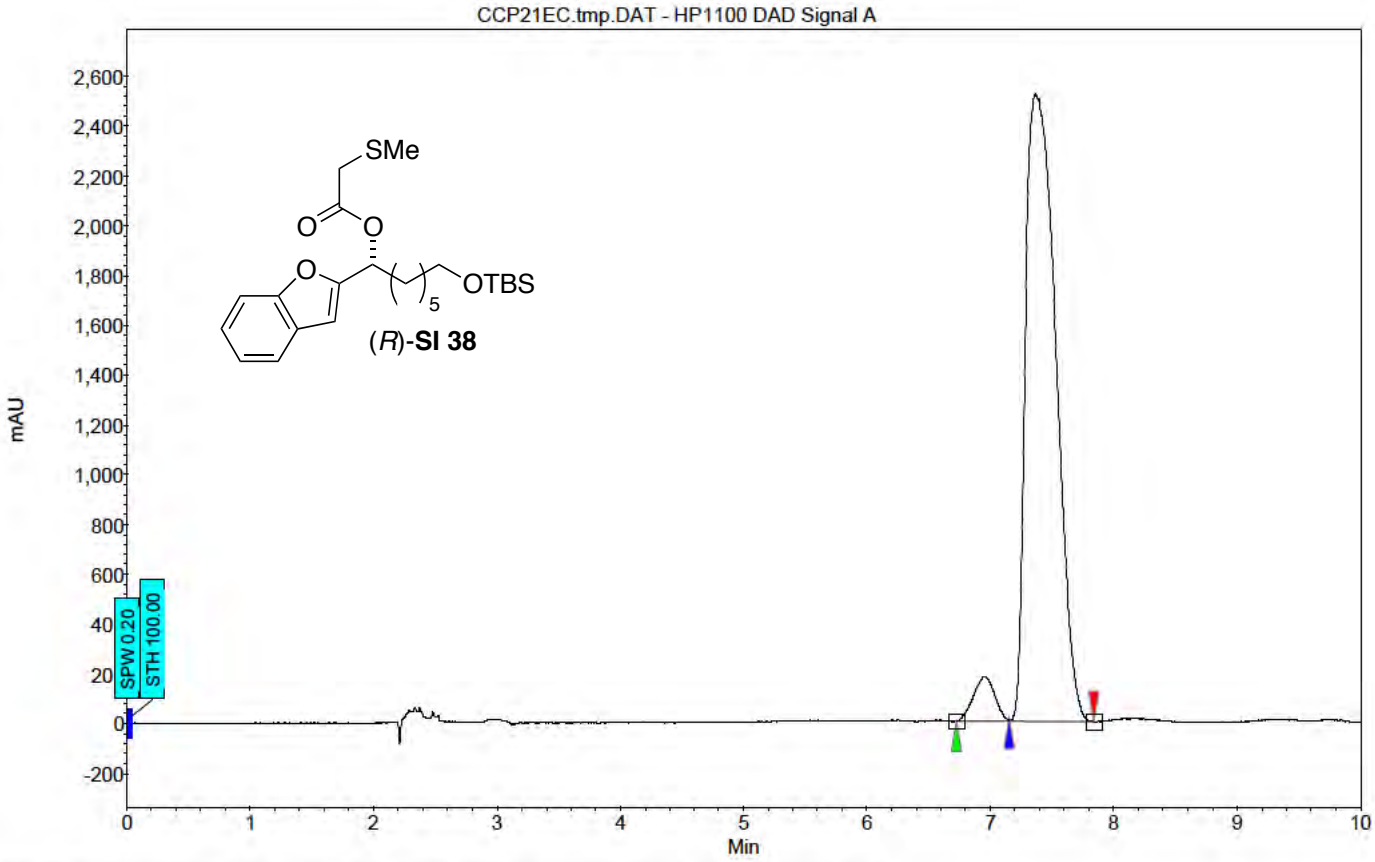
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.56	6.84	7.16	0.00	98.76	1058.4	217.6	98.756
2	UNKNOWN	7.58	7.79	8.07	0.00	1.24	15.2	2.7	1.244
Total						100.00	1073.6	220.4	100.000



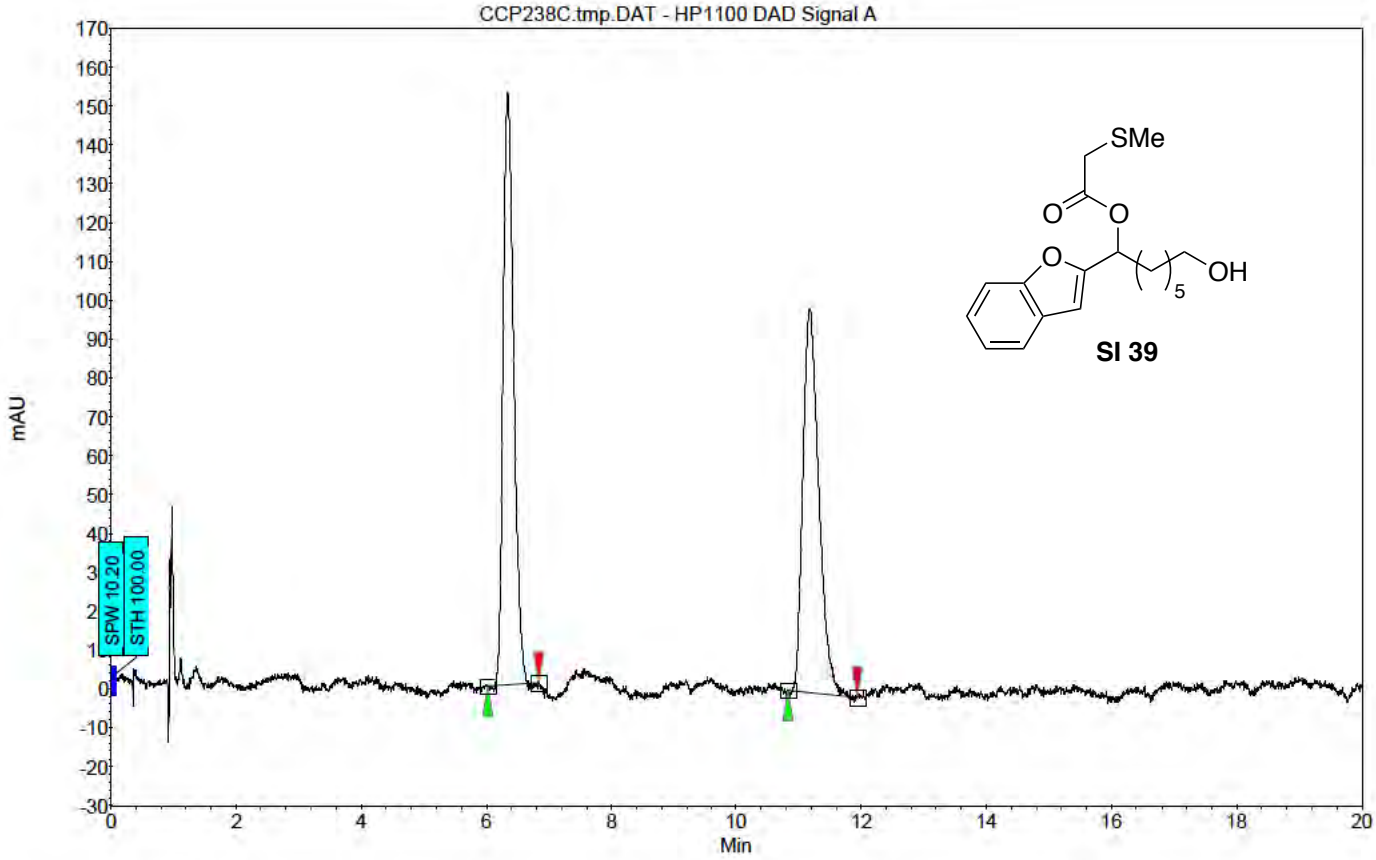


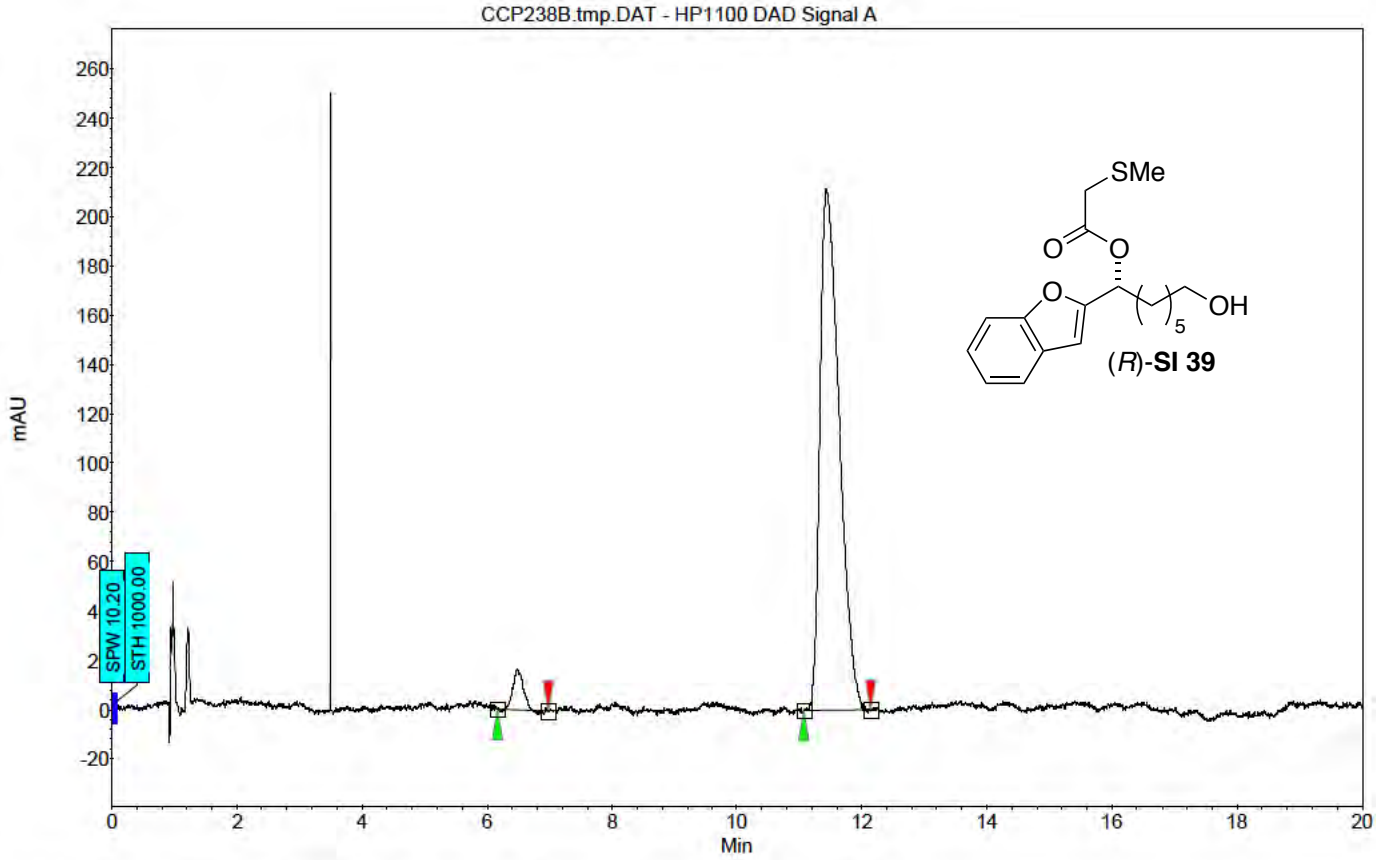
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	10.68	11.13	11.73	0.00	94.13	219.0	60.5	94.127
2	UNKNOWN	11.73	12.06	12.50	0.00	5.87	11.7	3.8	5.873
Total						100.00	230.7	64.3	100.000



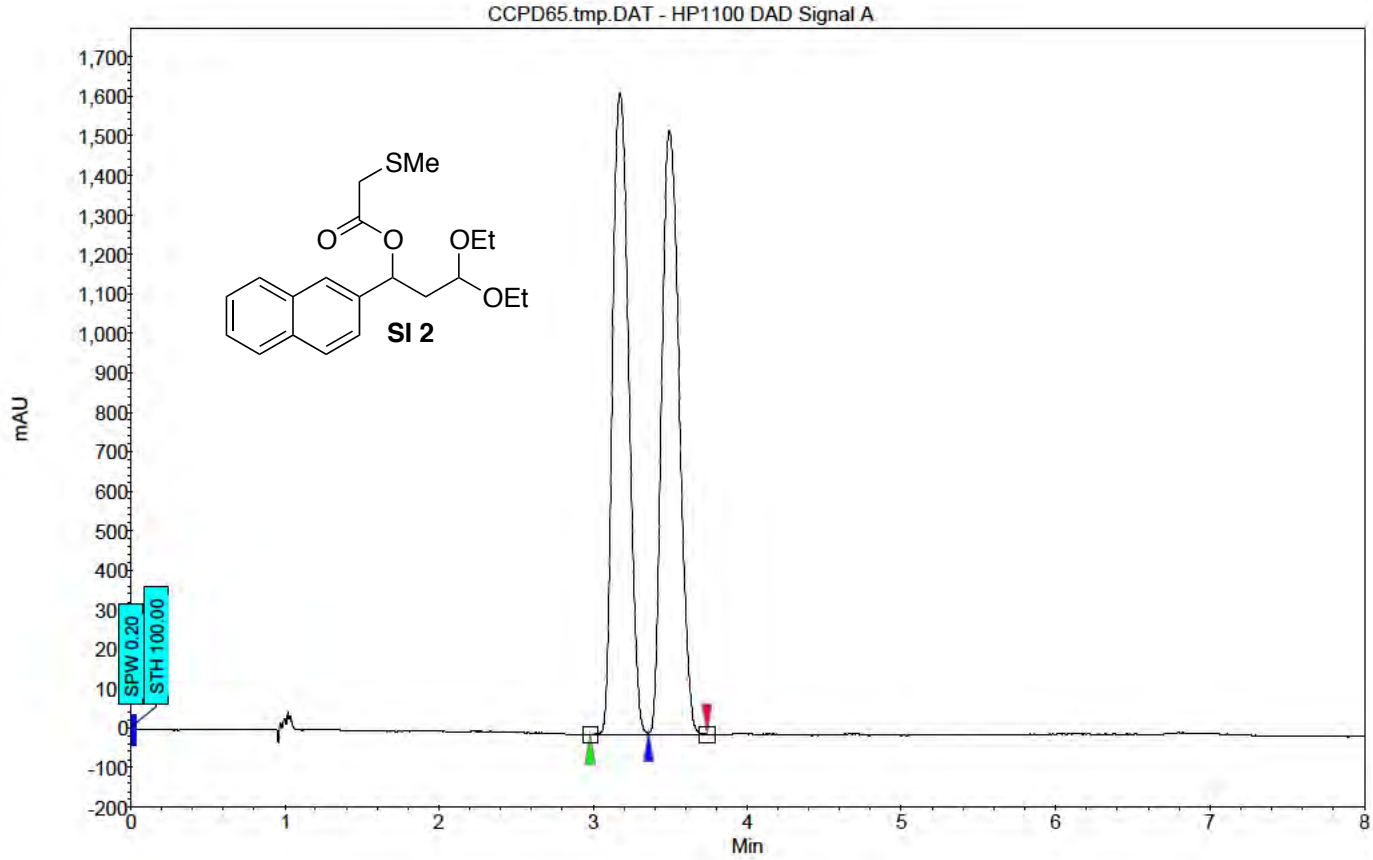


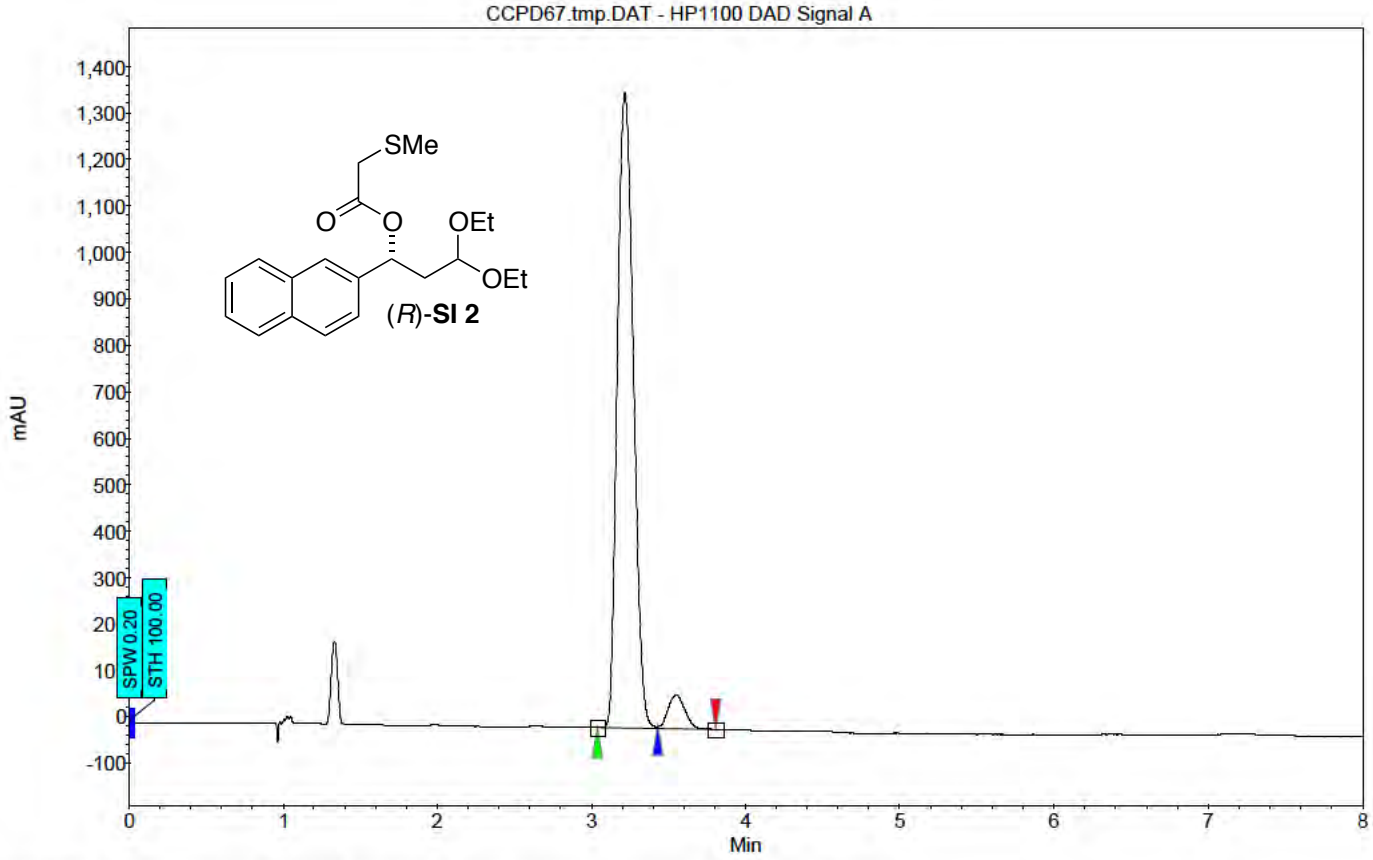
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.72	6.97	7.16	0.00	4.79	178.1	35.9	4.790
2	UNKNOWN	7.16	7.36	7.84	0.00	95.21	2518.9	714.2	95.210
Total						100.00	2697.0	750.1	100.000



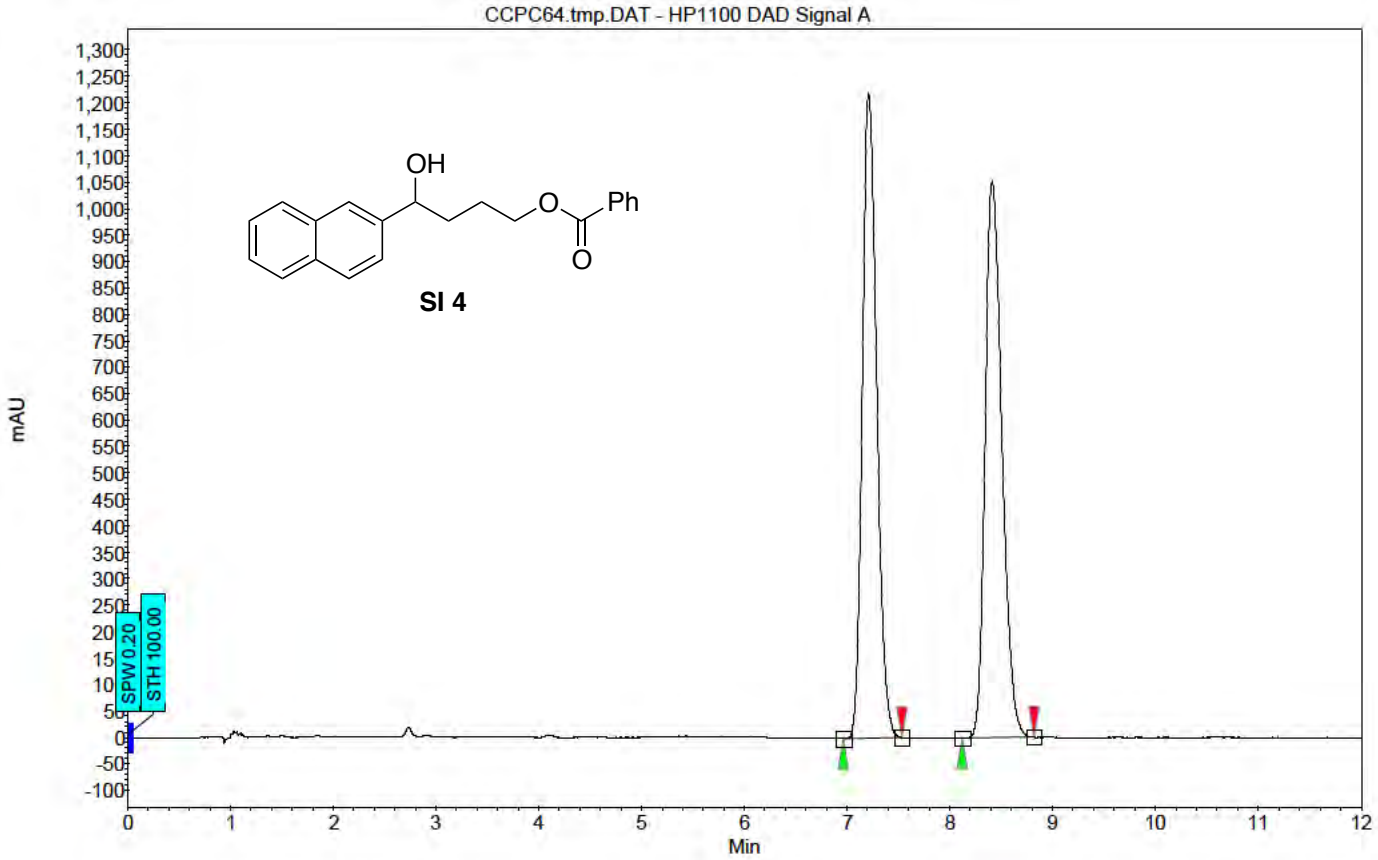


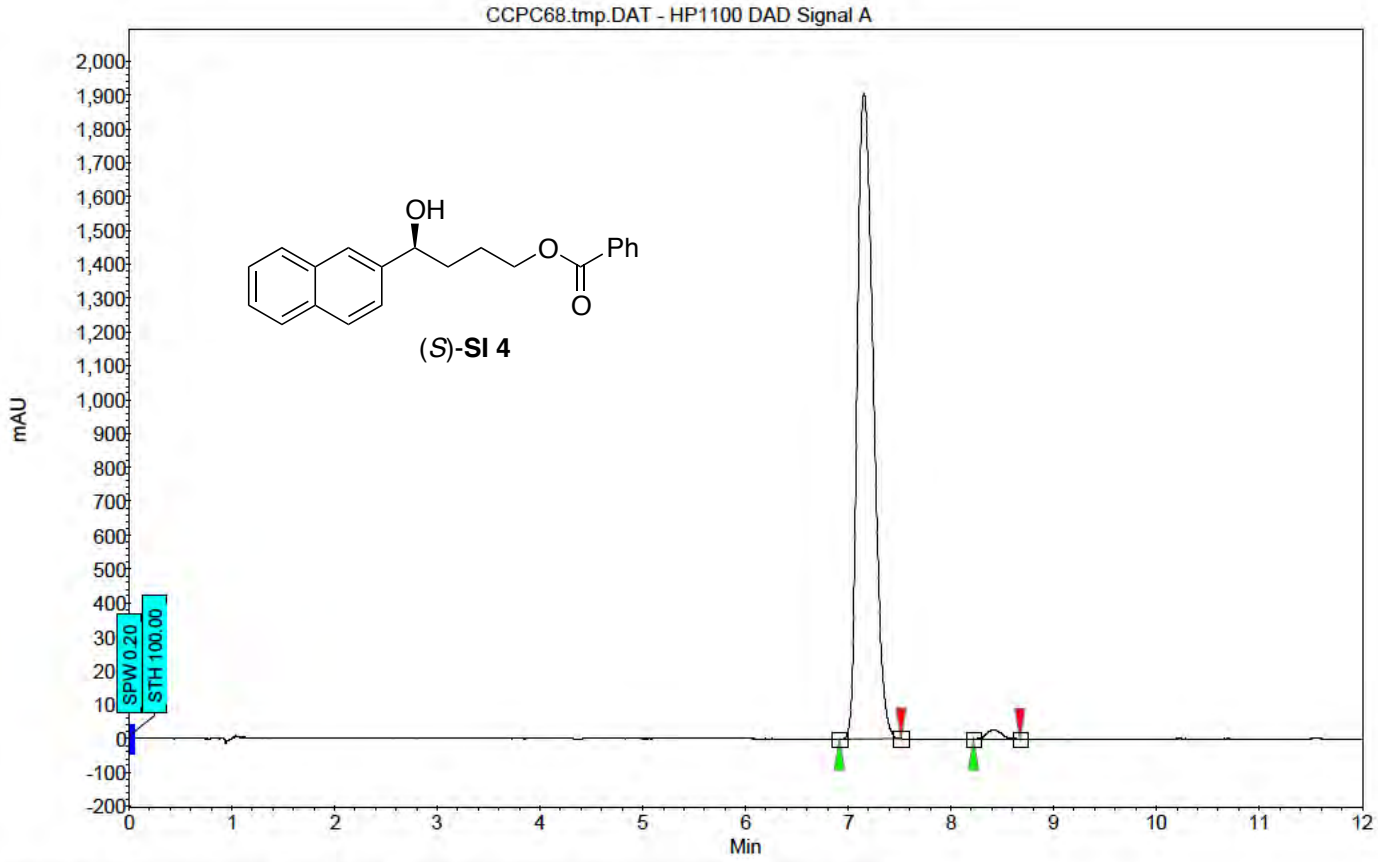
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.17	6.48	6.97	0.00	3.79	16.1	3.0	3.789
2	UNKNOWN	11.07	11.44	12.13	0.00	96.21	211.6	75.4	96.211
Total						100.00	227.7	78.3	100.000



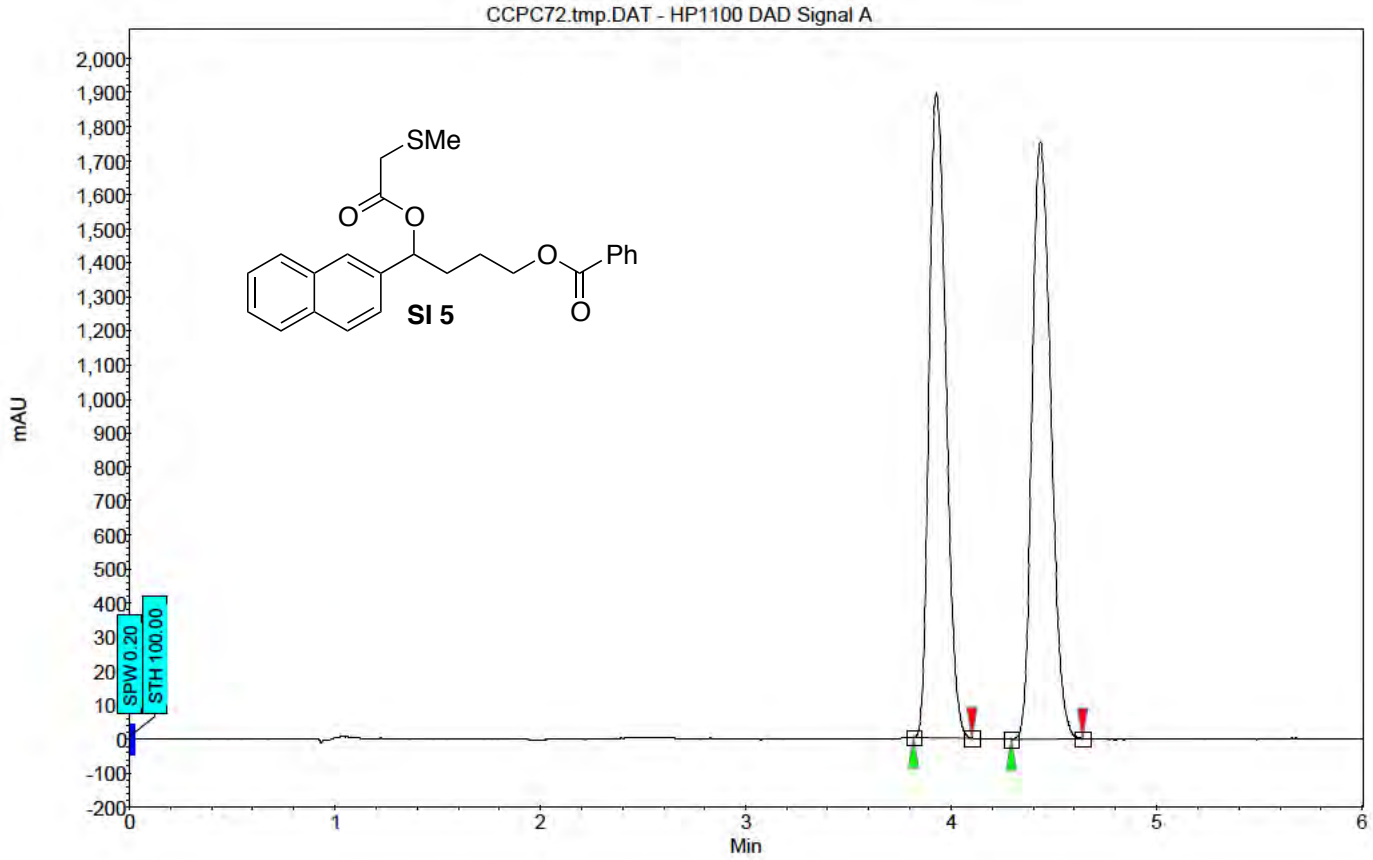


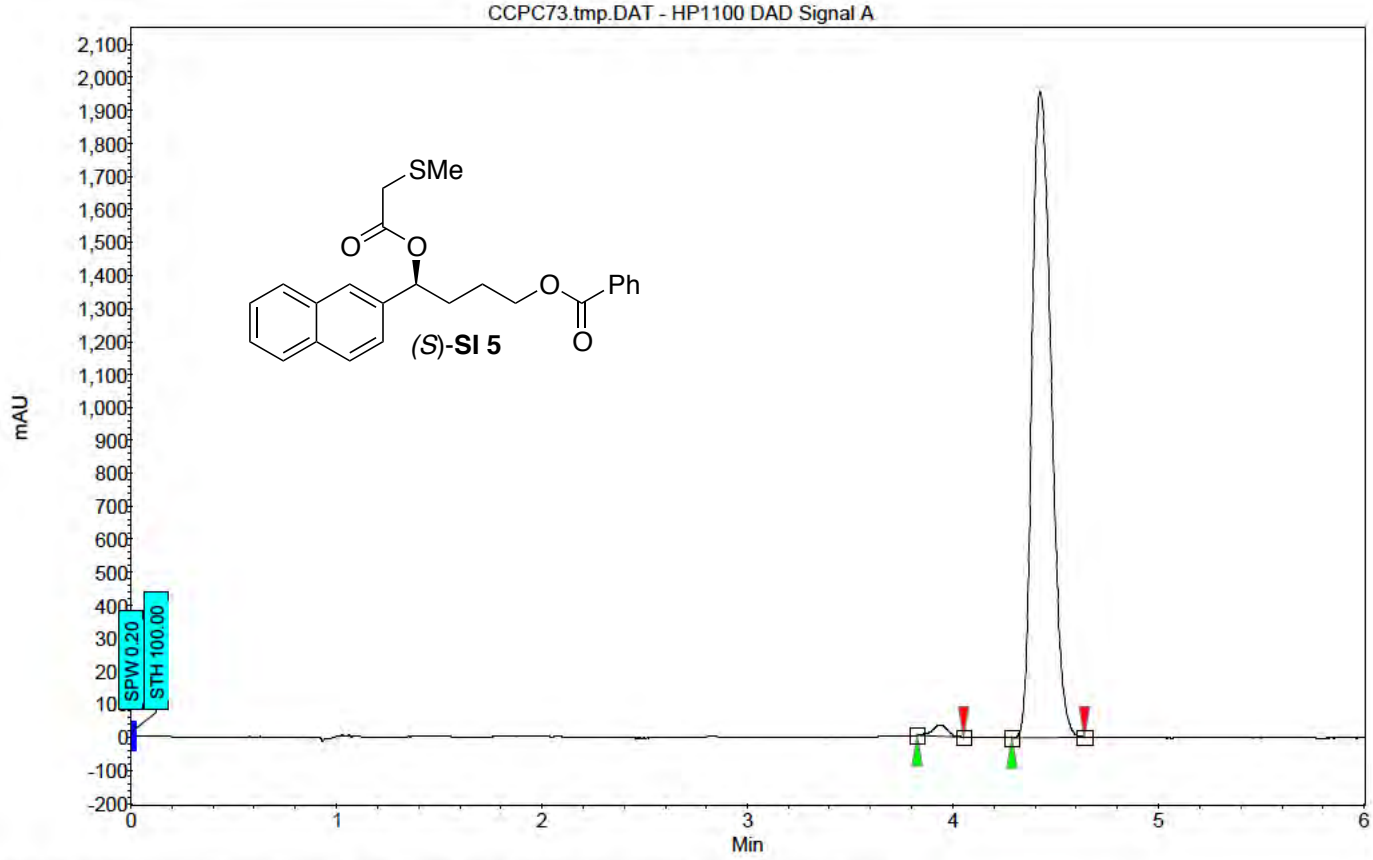
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.04	3.22	3.43	0.00	94.75	1367.1	164.9	94.747
2	UNKNOWN	3.43	3.55	3.81	0.00	5.25	73.6	9.1	5.253
Total						100.00	1440.7	174.0	100.000



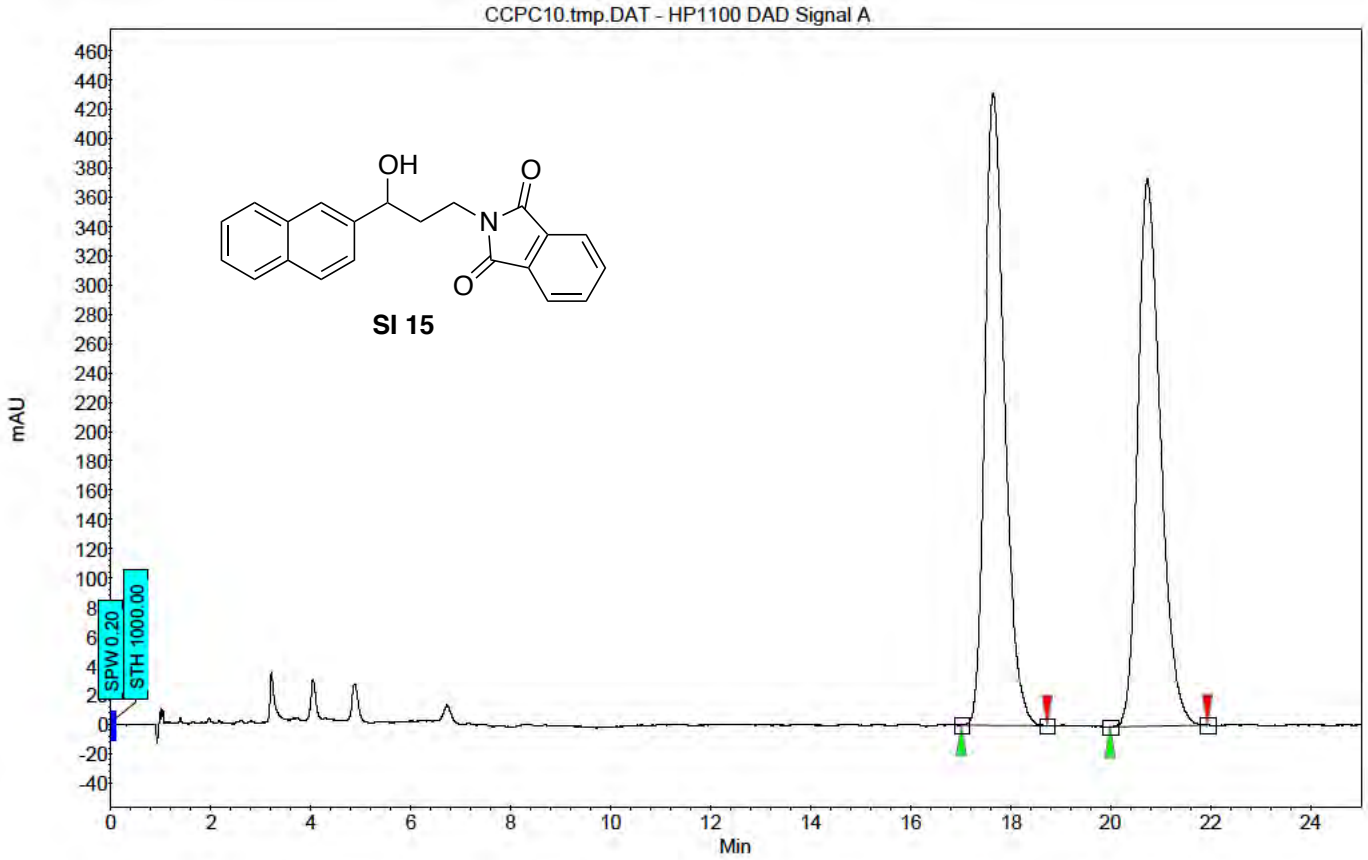


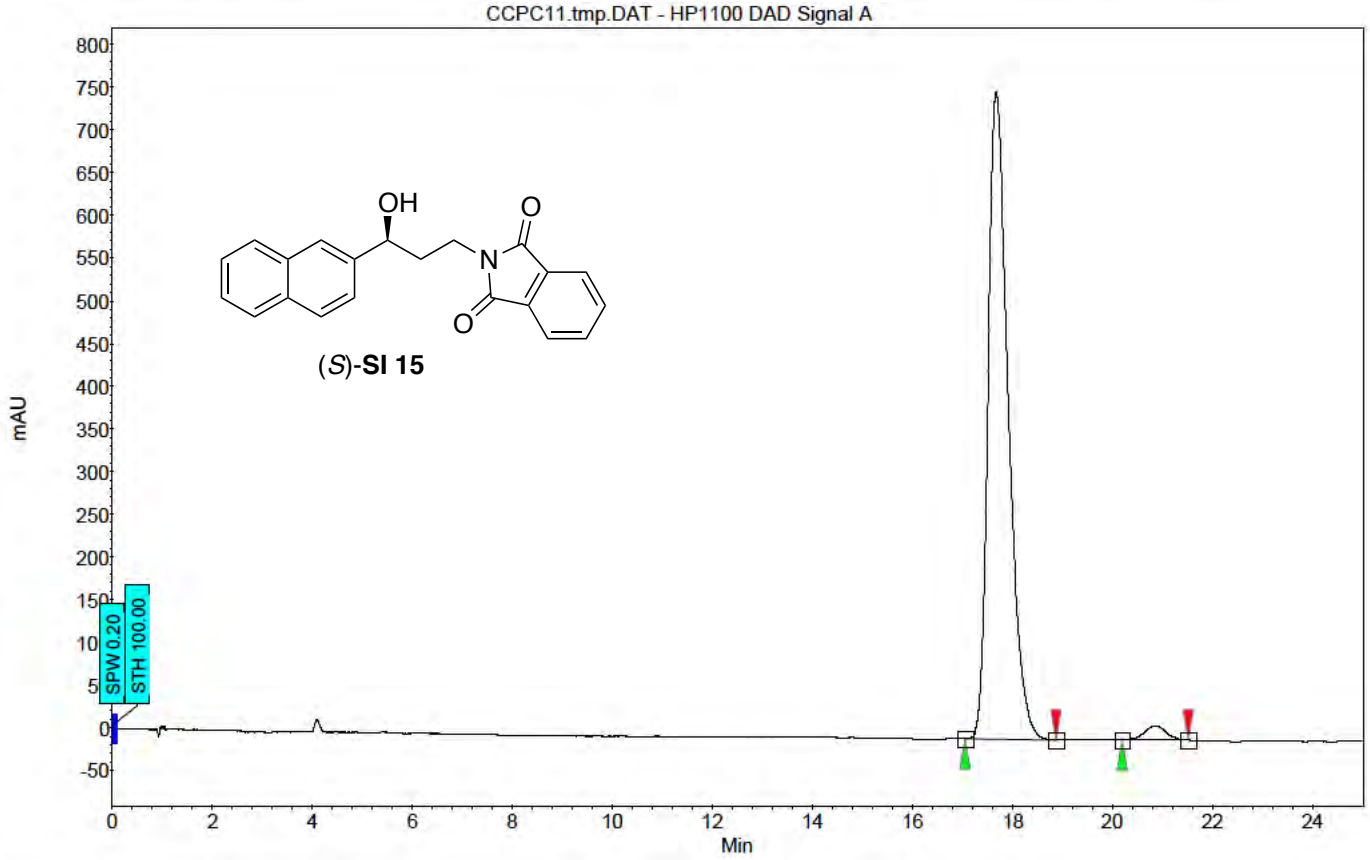
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.91	7.15	7.52	0.00	98.61	1904.2	344.0	98.608
2	UNKNOWN	8.22	8.42	8.67	0.00	1.39	27.4	4.9	1.392
Total						100.00	1931.7	348.9	100.000



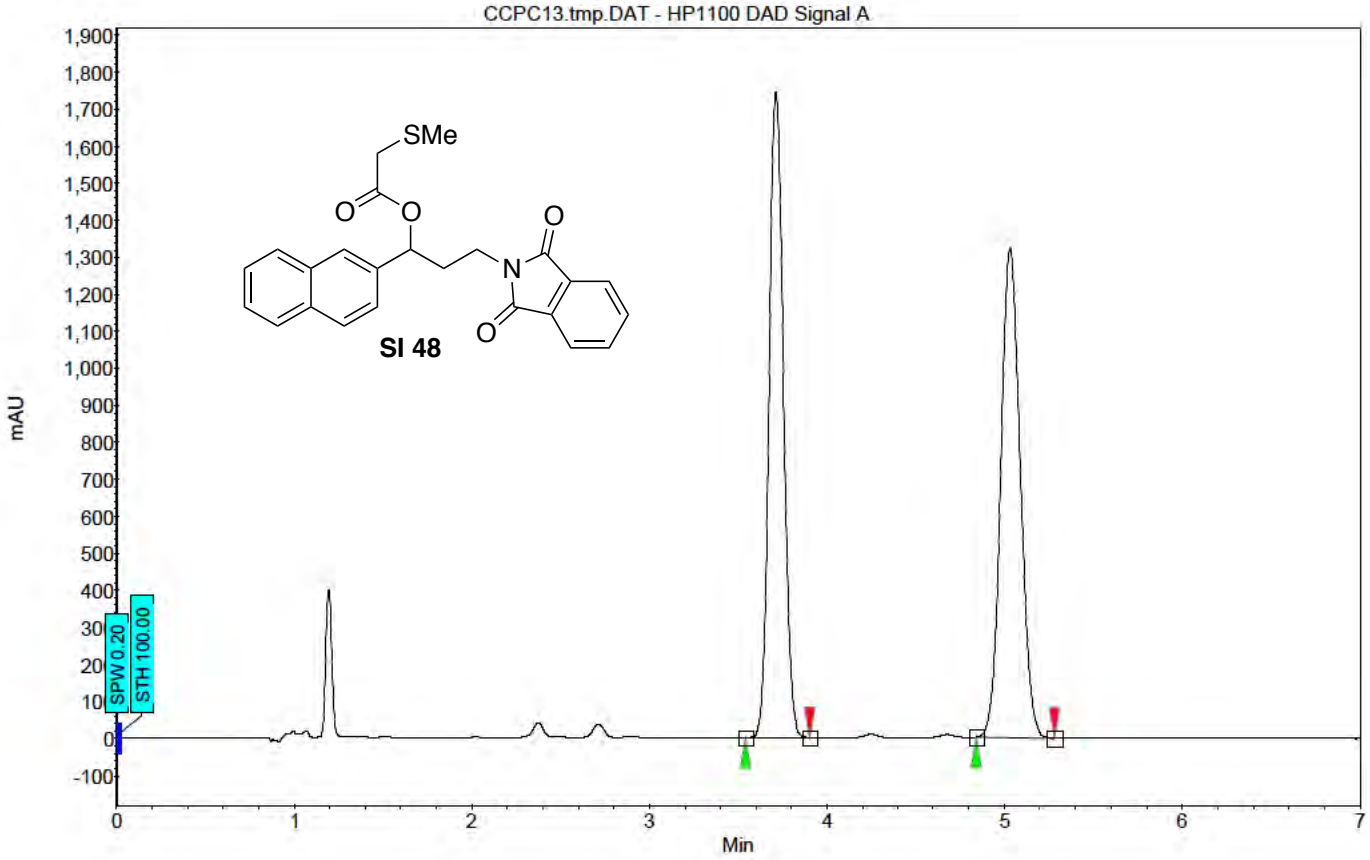


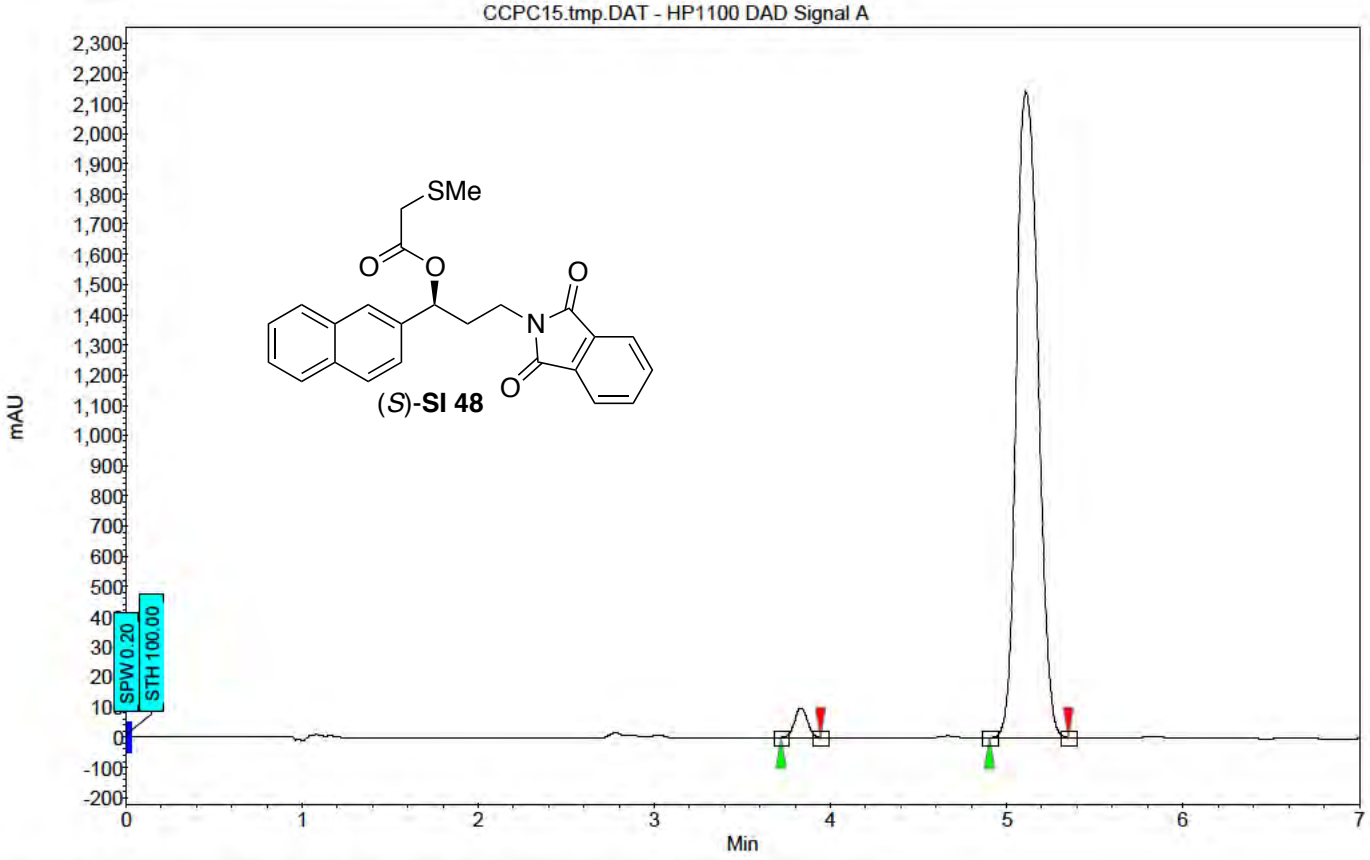
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	3.83	3.94	4.05	0.00	1.36	33.6	2.9	1.356
1	UNKNOWN	4.29	4.42	4.64	0.00	98.64	1956.1	210.4	98.644
Total						100.00	1989.7	213.3	100.000



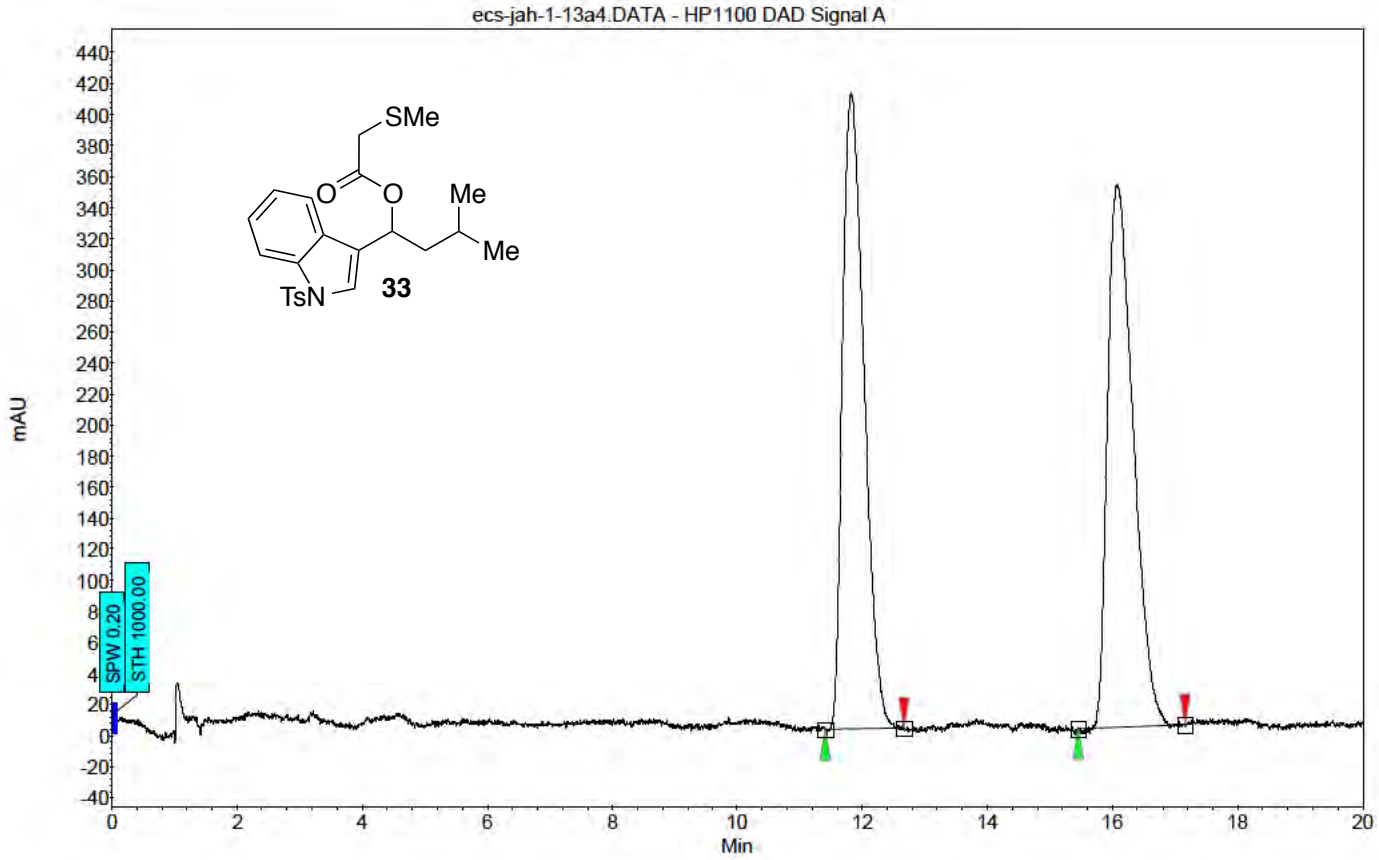


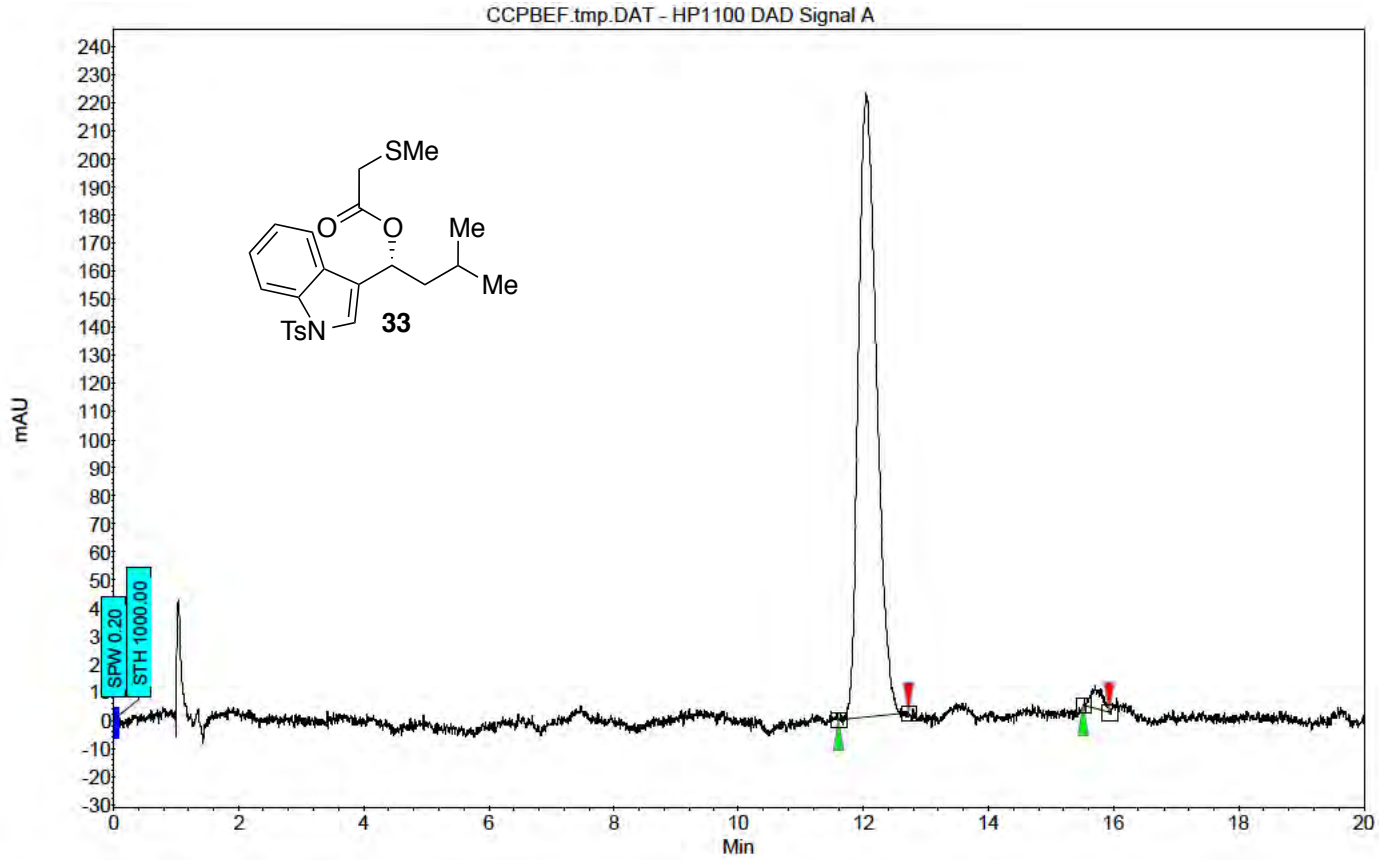
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	17.05	17.67	18.86	0.00	97.63	756.9	352.6	97.629
2	UNKNOWN	20.19	20.86	21.51	0.00	2.37	16.6	8.6	2.371
Total						100.00	773.5	361.2	100.000



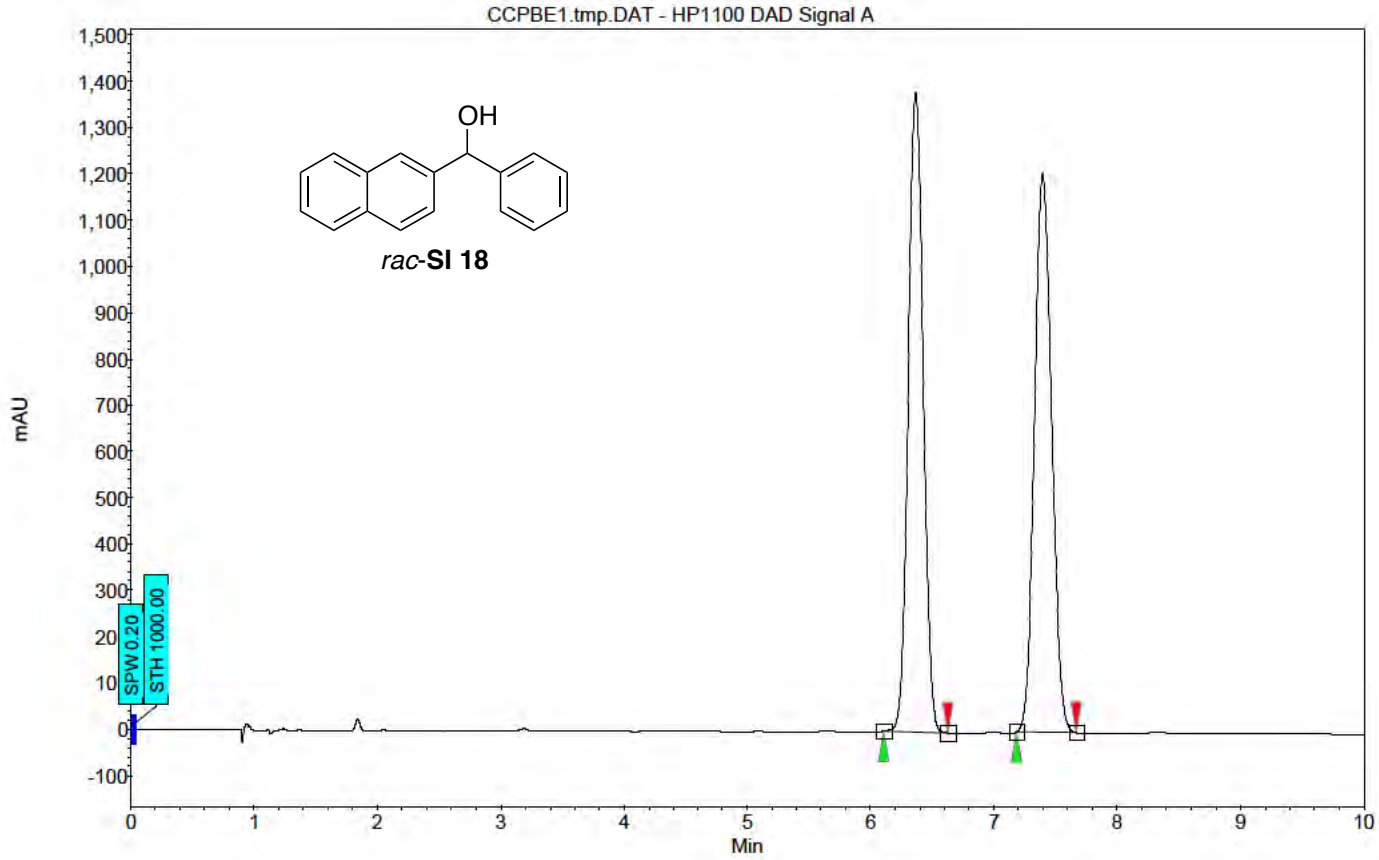


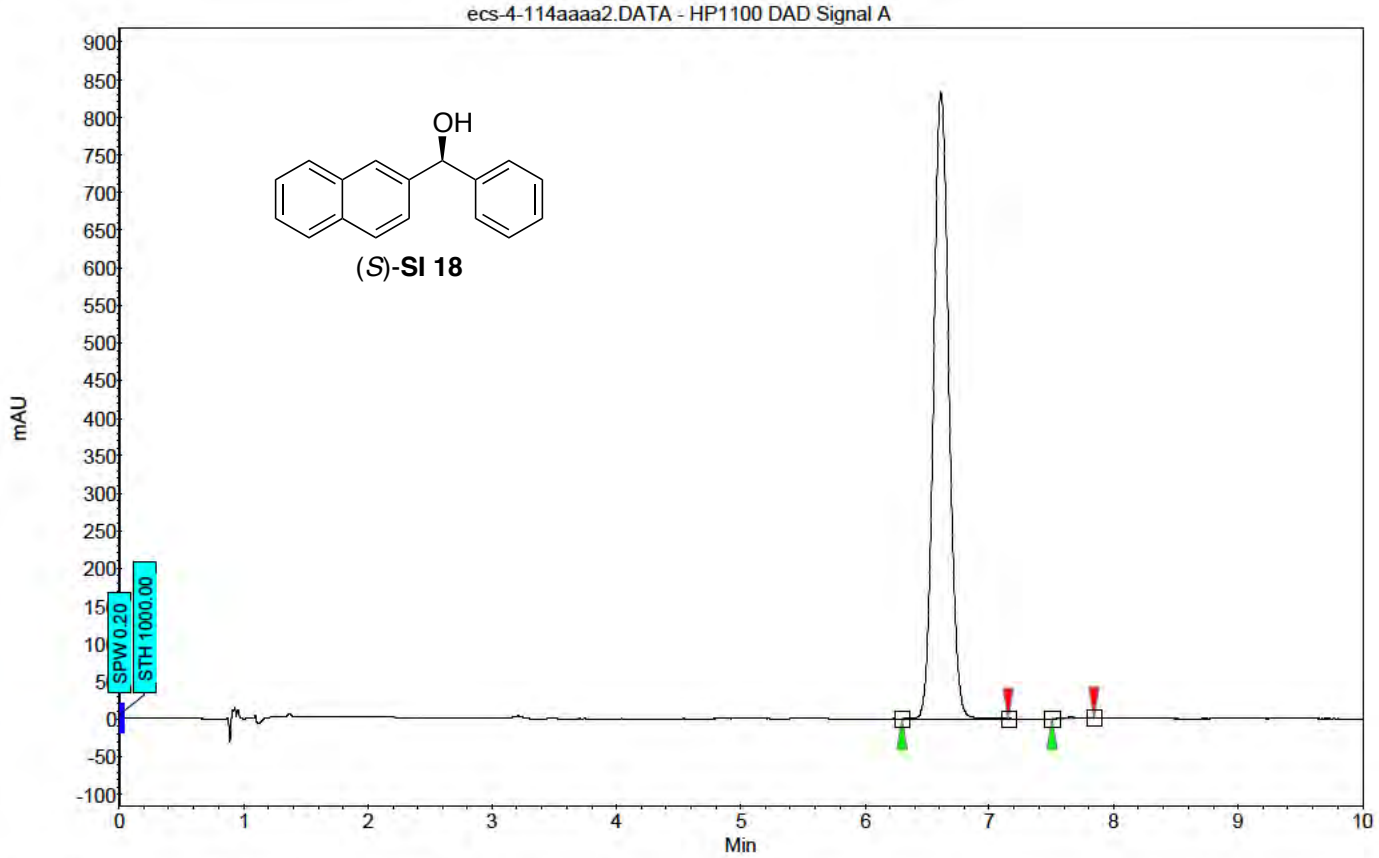
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.72	3.83	3.95	0.00	2.70	99.2	8.5	2.695
2	UNKNOWN	4.90	5.11	5.35	0.00	97.30	2139.2	306.8	97.305
Total						100.00	2238.4	315.3	100.000



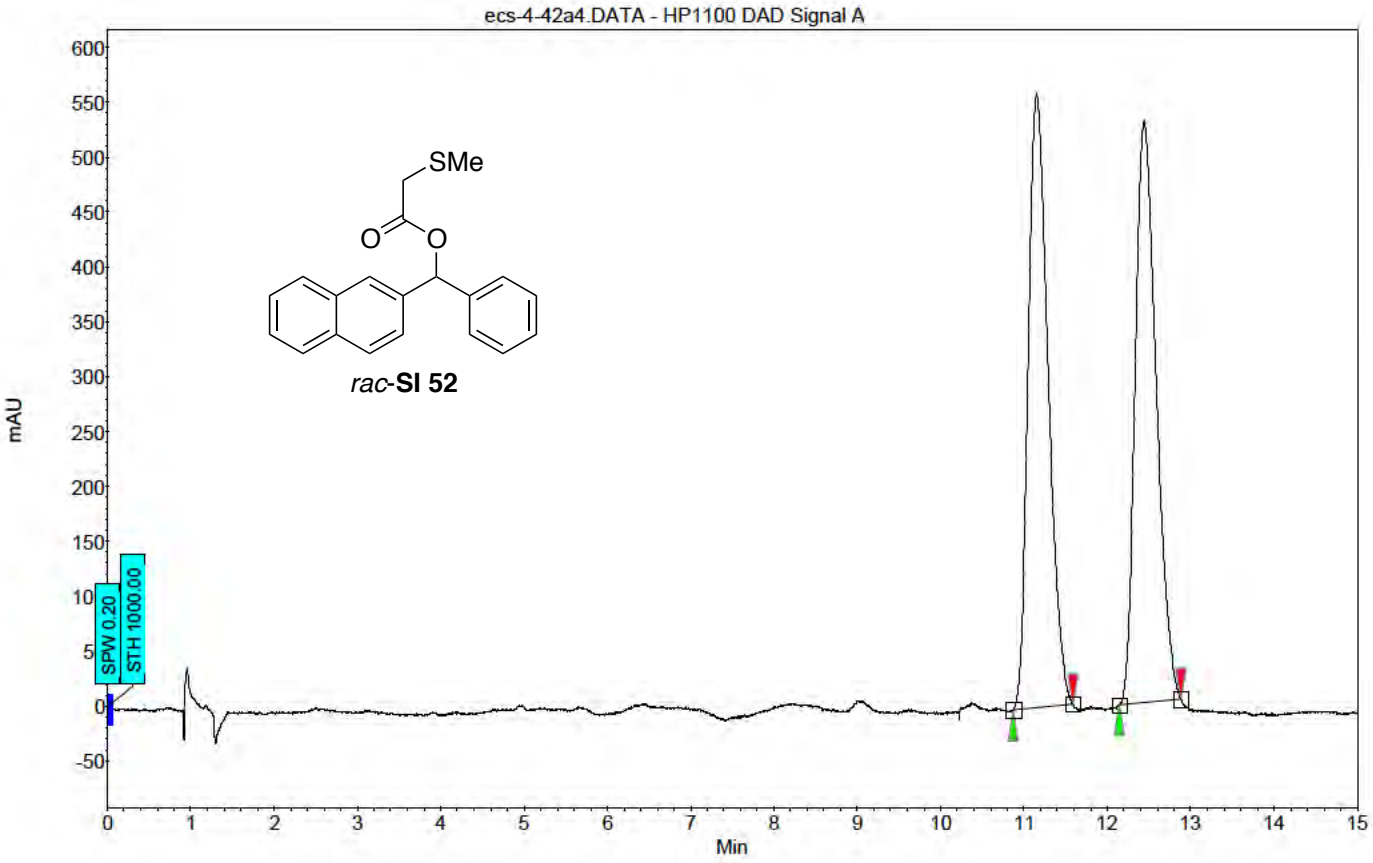


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.60	12.04	12.72	0.00	97.94	221.7	74.6	97.936
2	UNKNOWN	15.51	15.70	15.93	0.00	2.06	8.2	1.6	2.064
Total						100.00	229.9	76.2	100.000

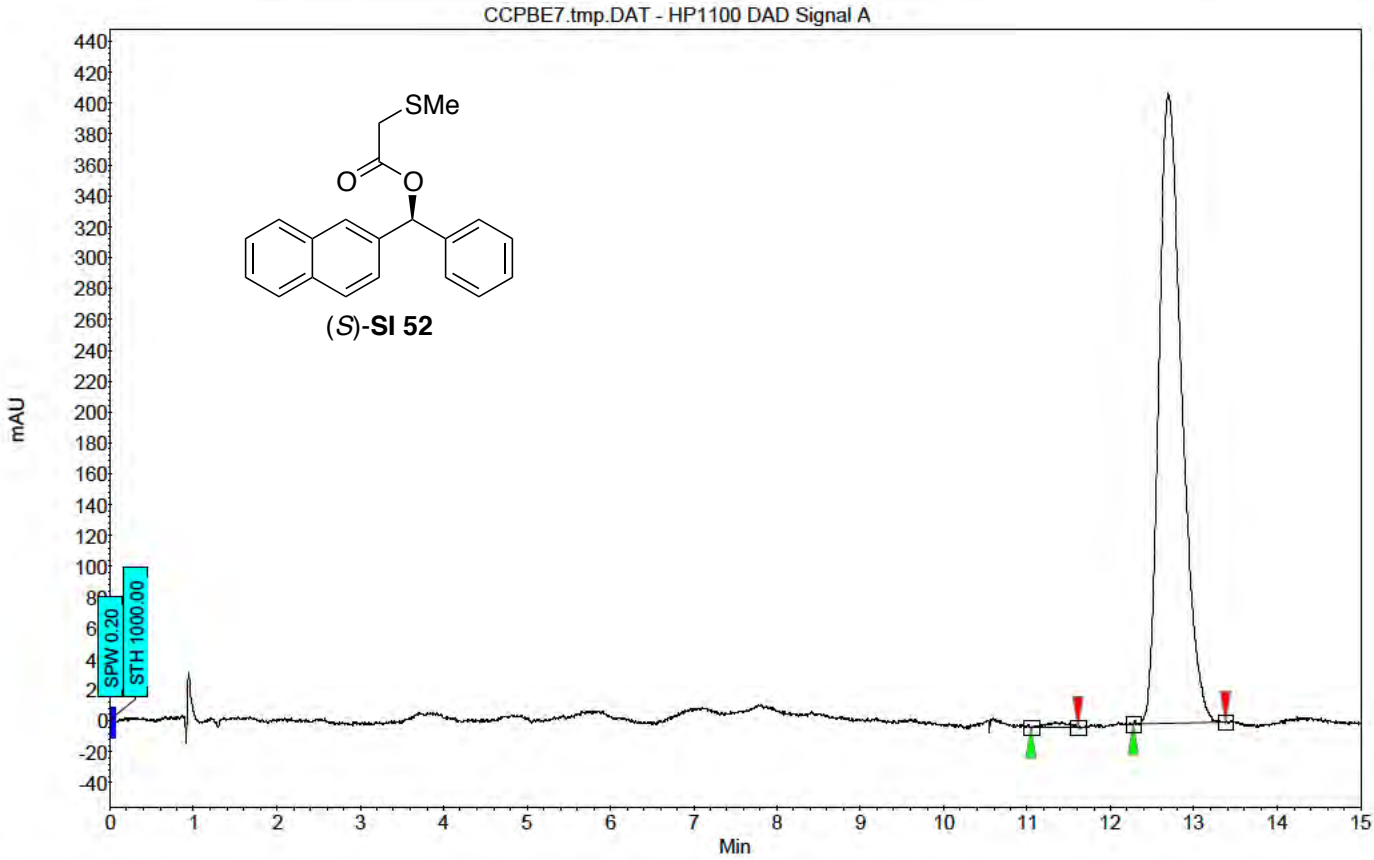




Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.30	6.61	7.15	0.00	99.80	832.1	118.7	99.800
2	UNKNOWN	7.50	7.65	7.84	0.00	0.20	1.6	0.2	0.200
Total						100.00	833.8	119.0	100.000

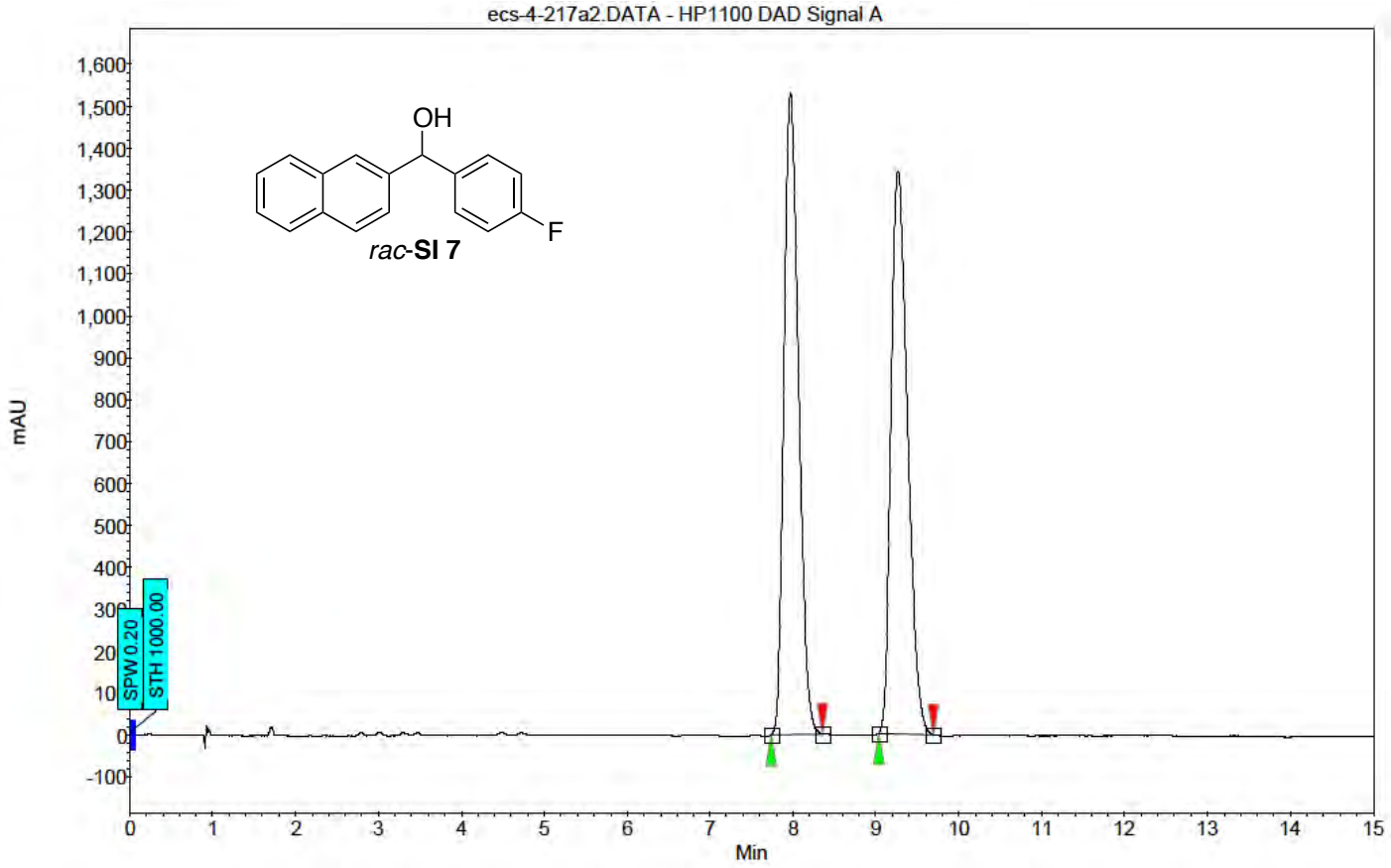


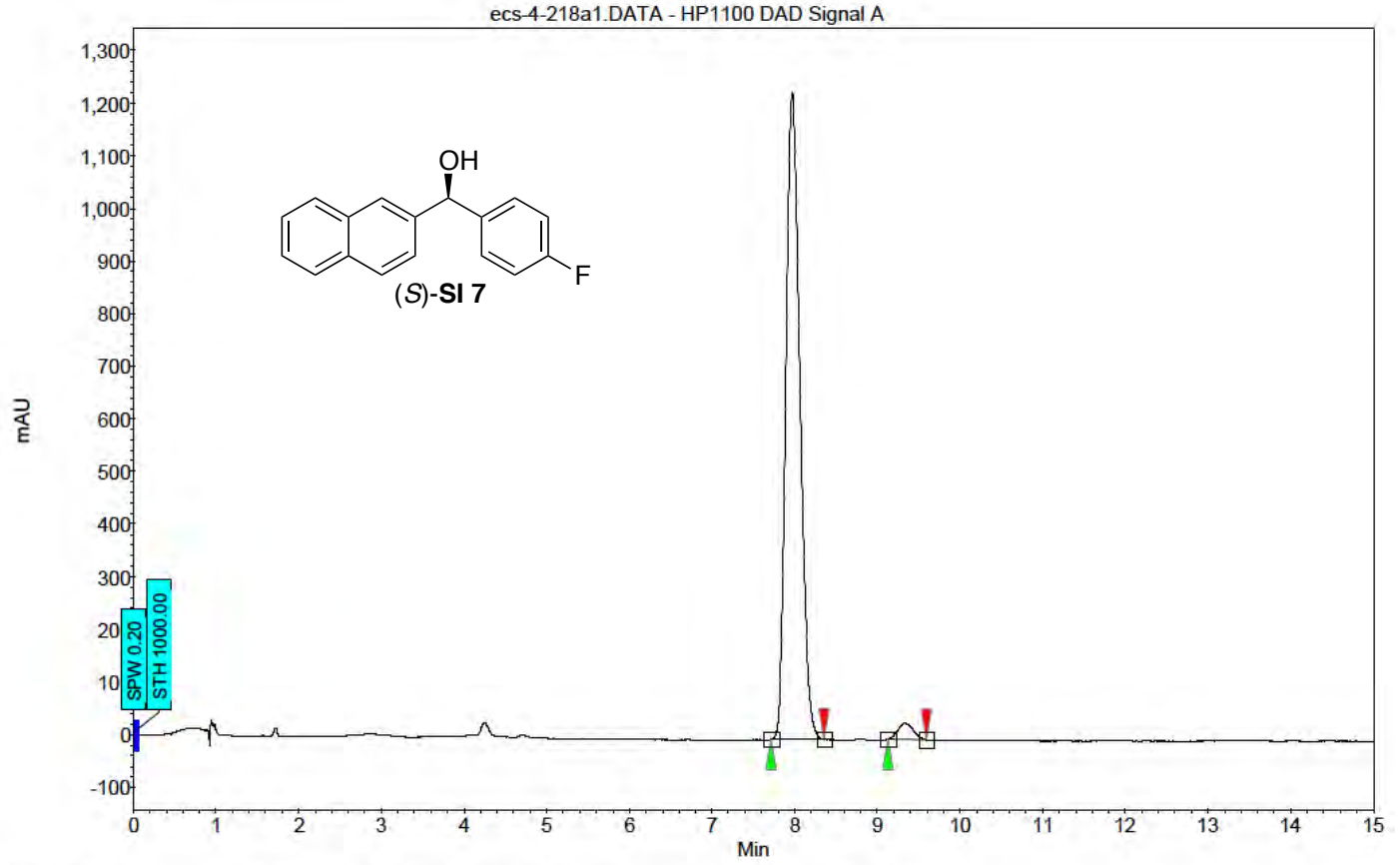
rac-**SI 52**



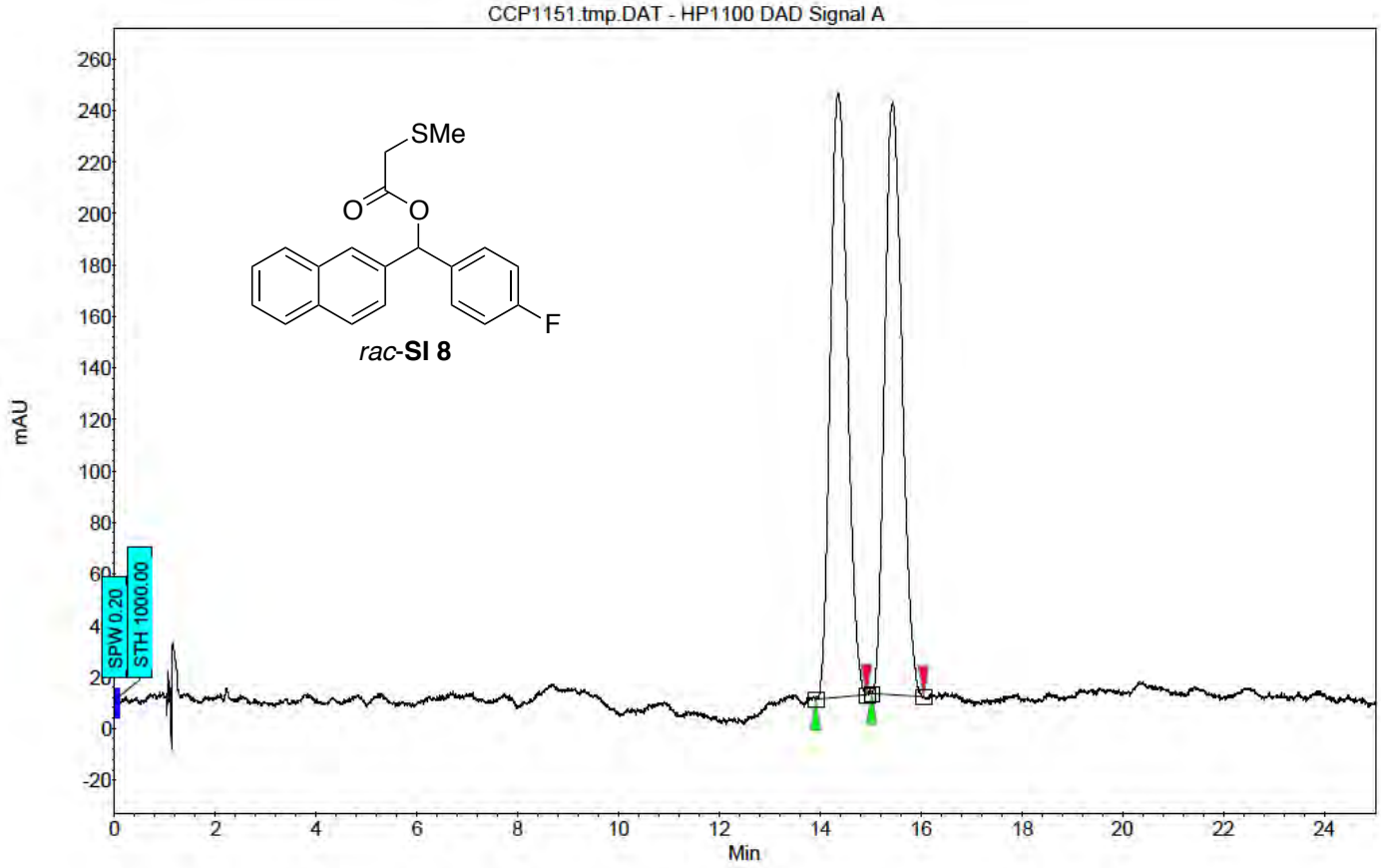
(*S*)-**SI 52**

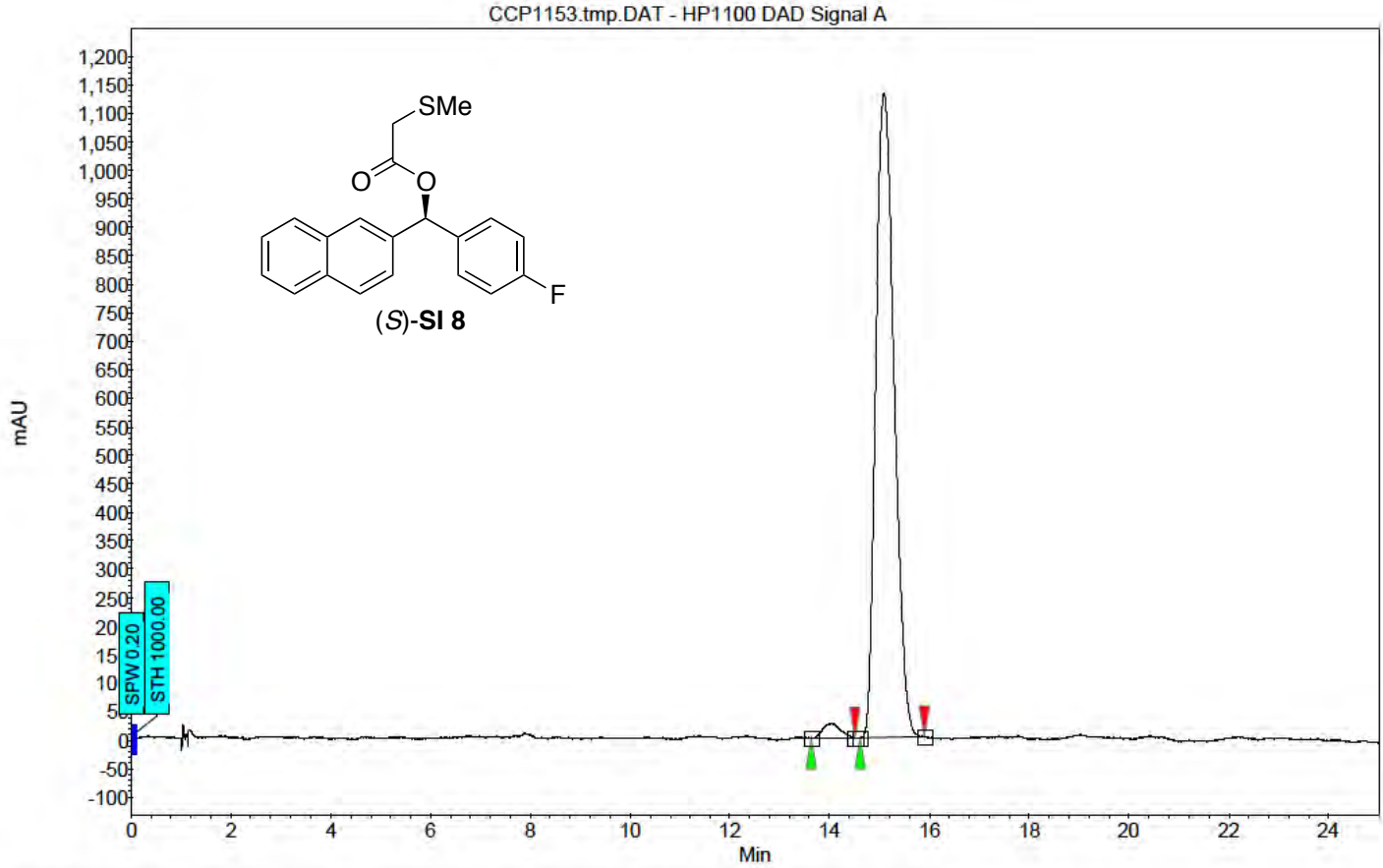
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	11.05	11.42	11.61	0.00	0.65	3.8	0.9	0.651
1	UNKNOWN	12.27	12.70	13.38	0.00	99.35	407.2	129.8	99.349
Total						100.00	411.0	130.6	100.000



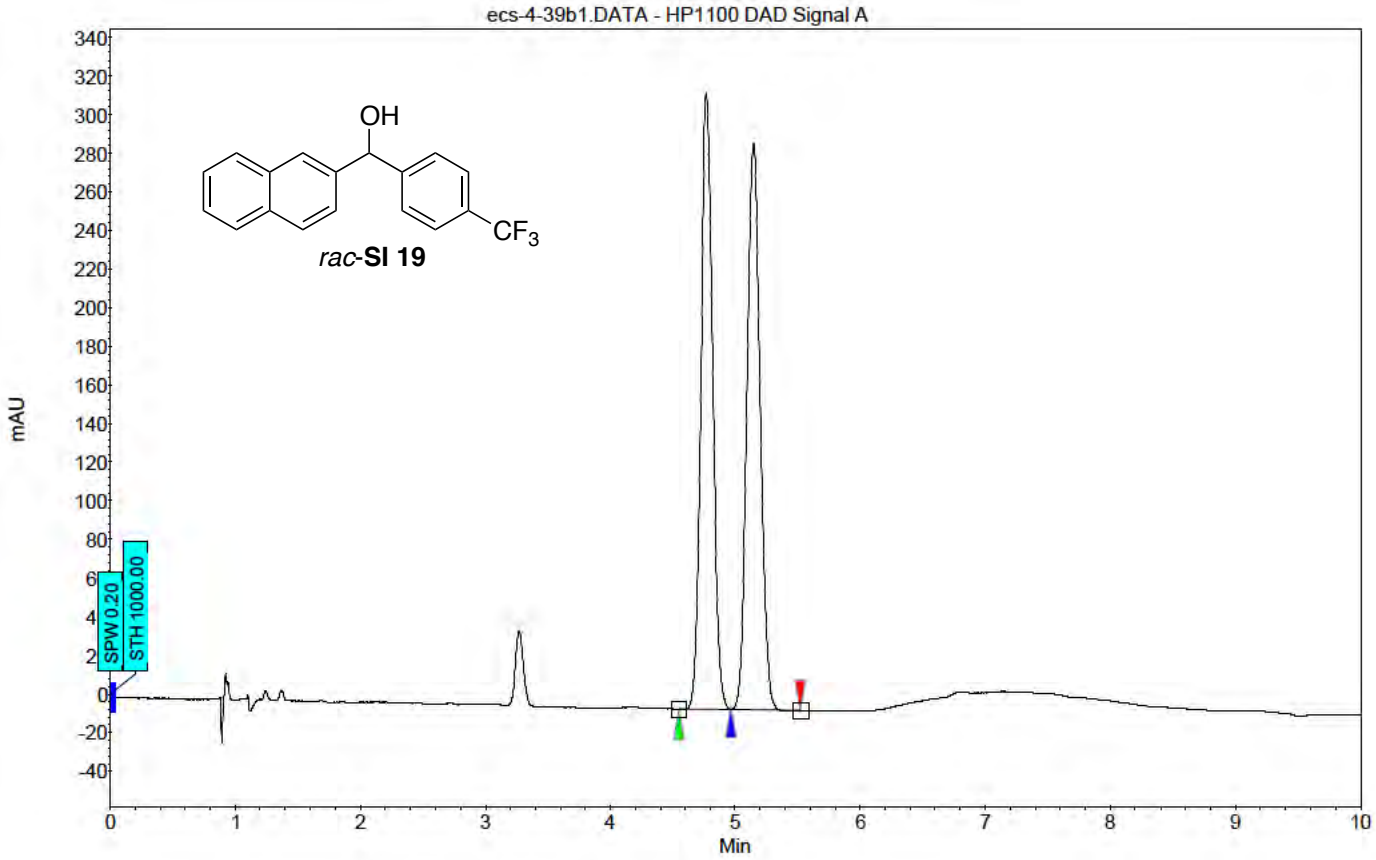


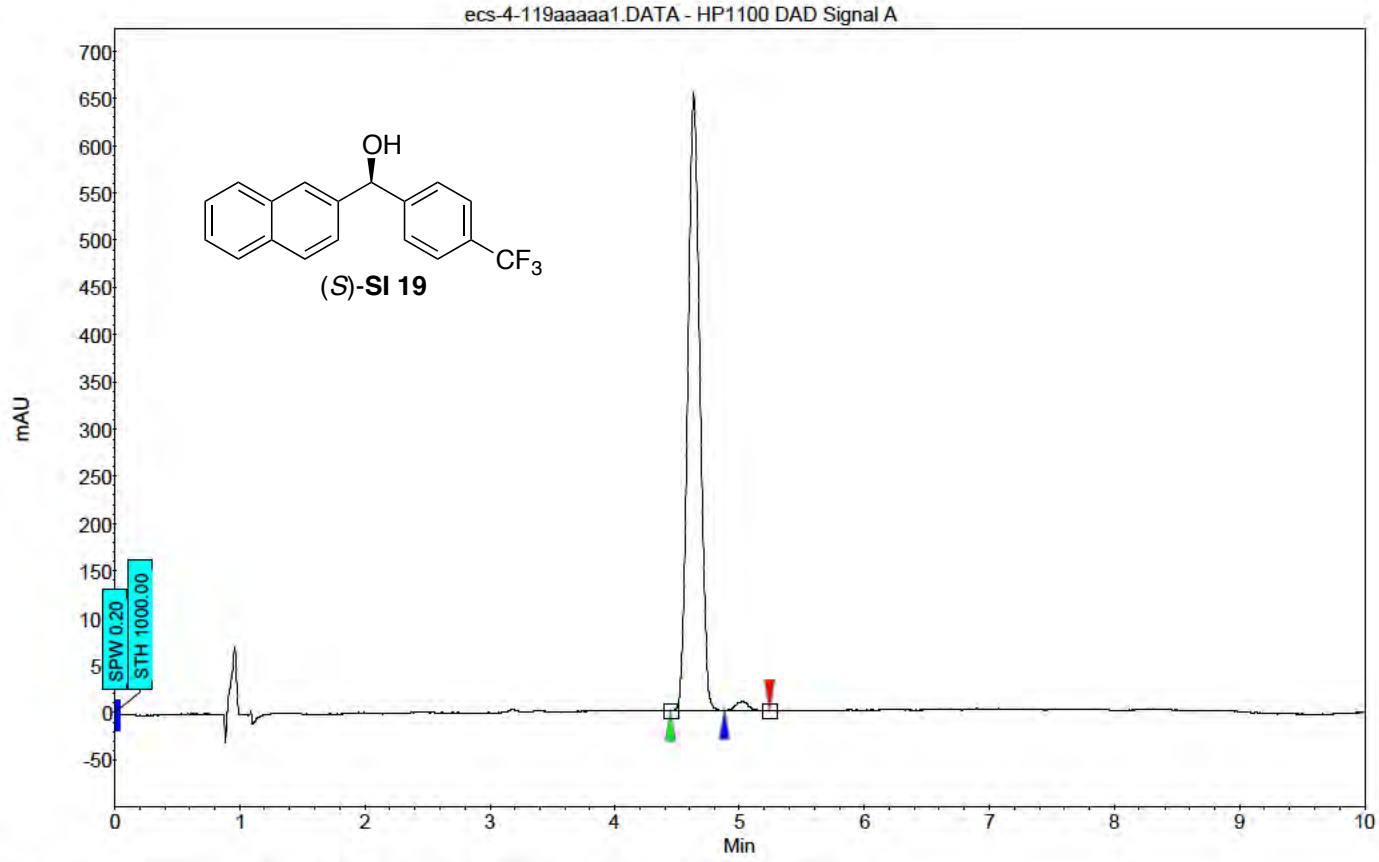
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	7.72	7.97	8.36	0.00	97.39	1227.3	241.3	97.394
2	UNKNOWN	9.13	9.34	9.59	0.00	2.61	30.4	6.5	2.606
Total						100.00	1257.7	247.8	100.000



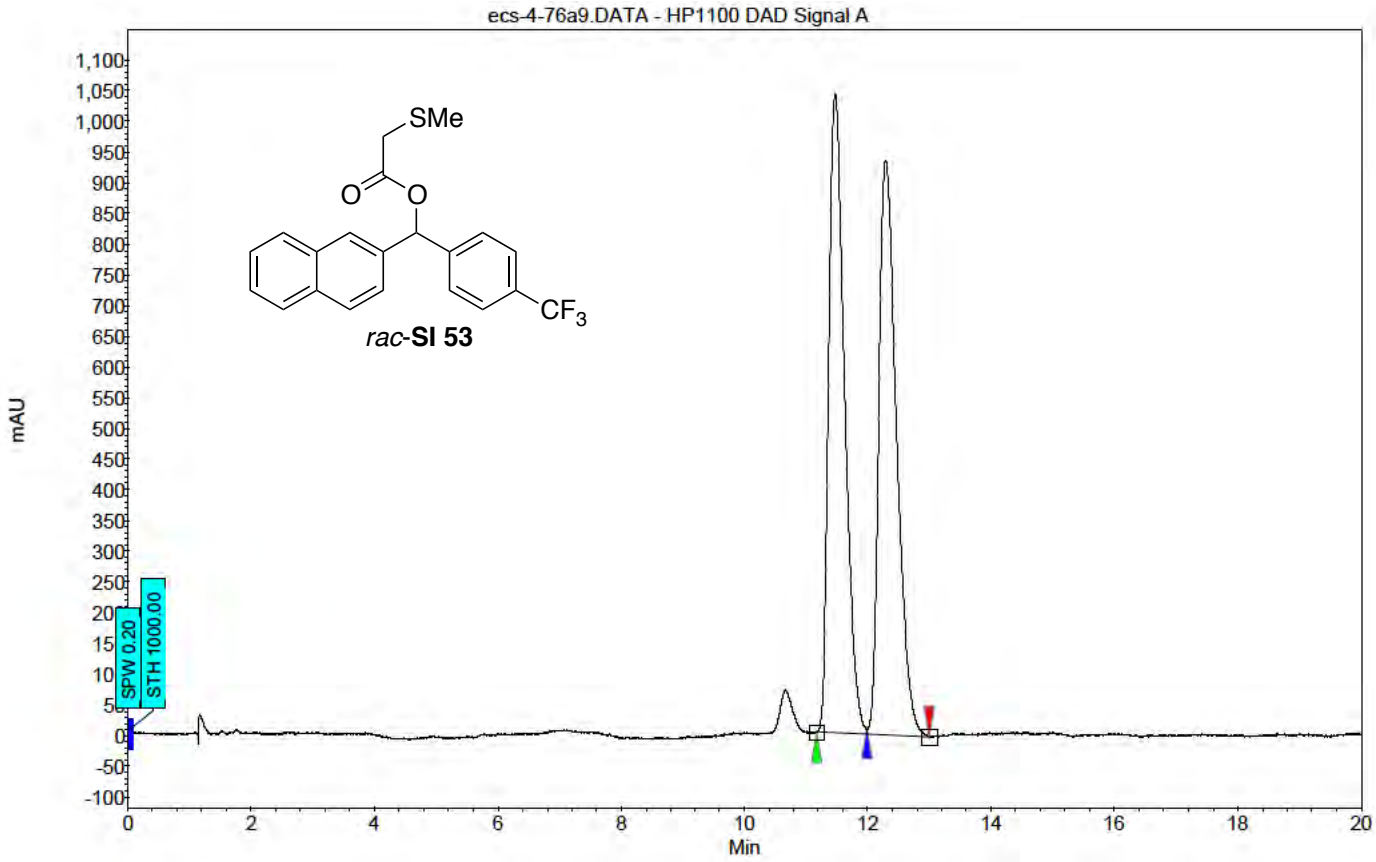


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	13.63	14.02	14.51	0.00	2.02	26.1	10.0	2.024
2	UNKNOWN	14.61	15.09	15.90	0.00	97.98	1129.2	483.6	97.976
Total						100.00	1155.3	493.5	100.000

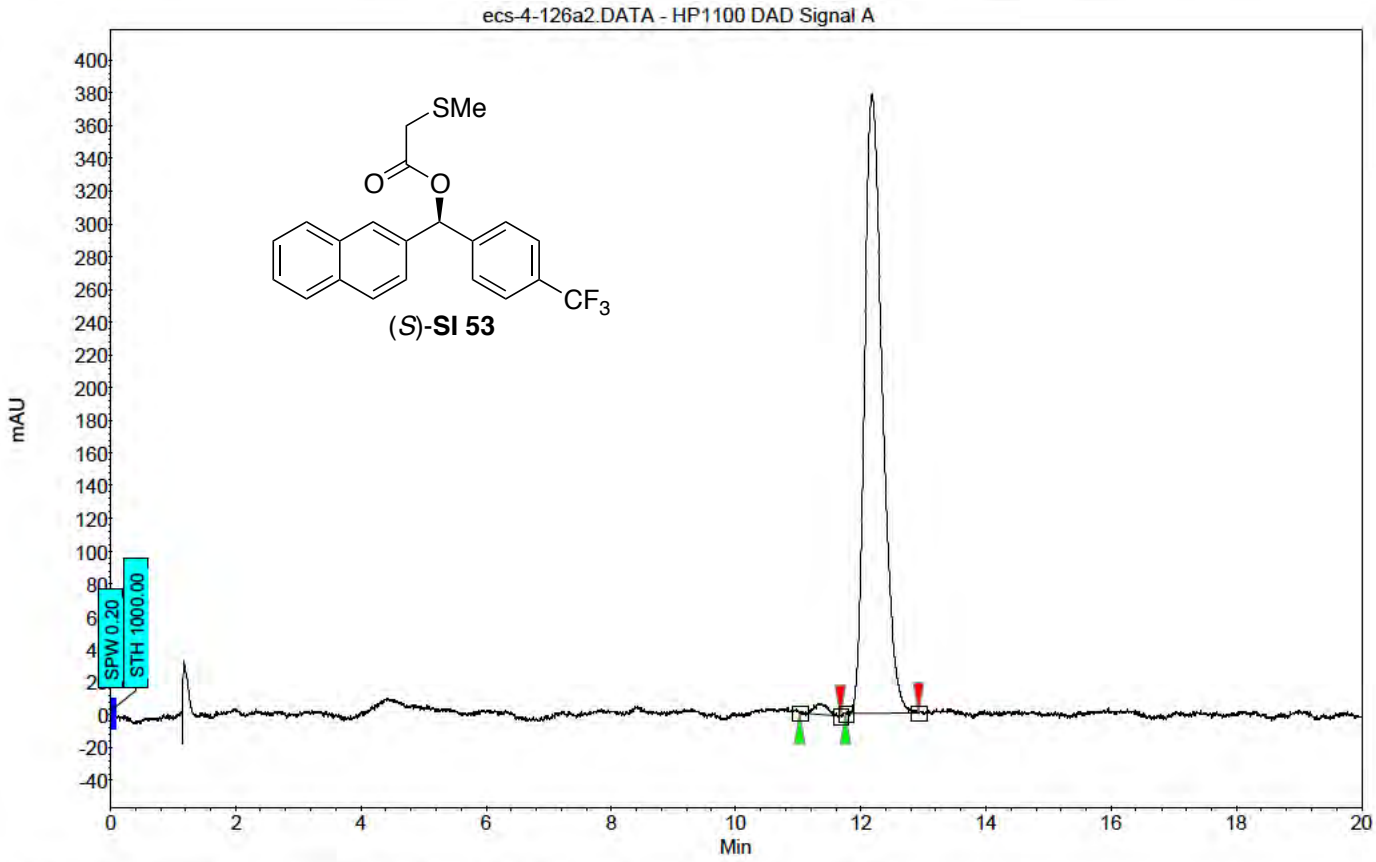




Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.44	4.63	4.88	0.00	98.24	653.3	73.3	98.243
2	UNKNOWN	4.88	5.02	5.24	0.00	1.76	9.8	1.3	1.757
Total						100.00	663.1	74.6	100.000

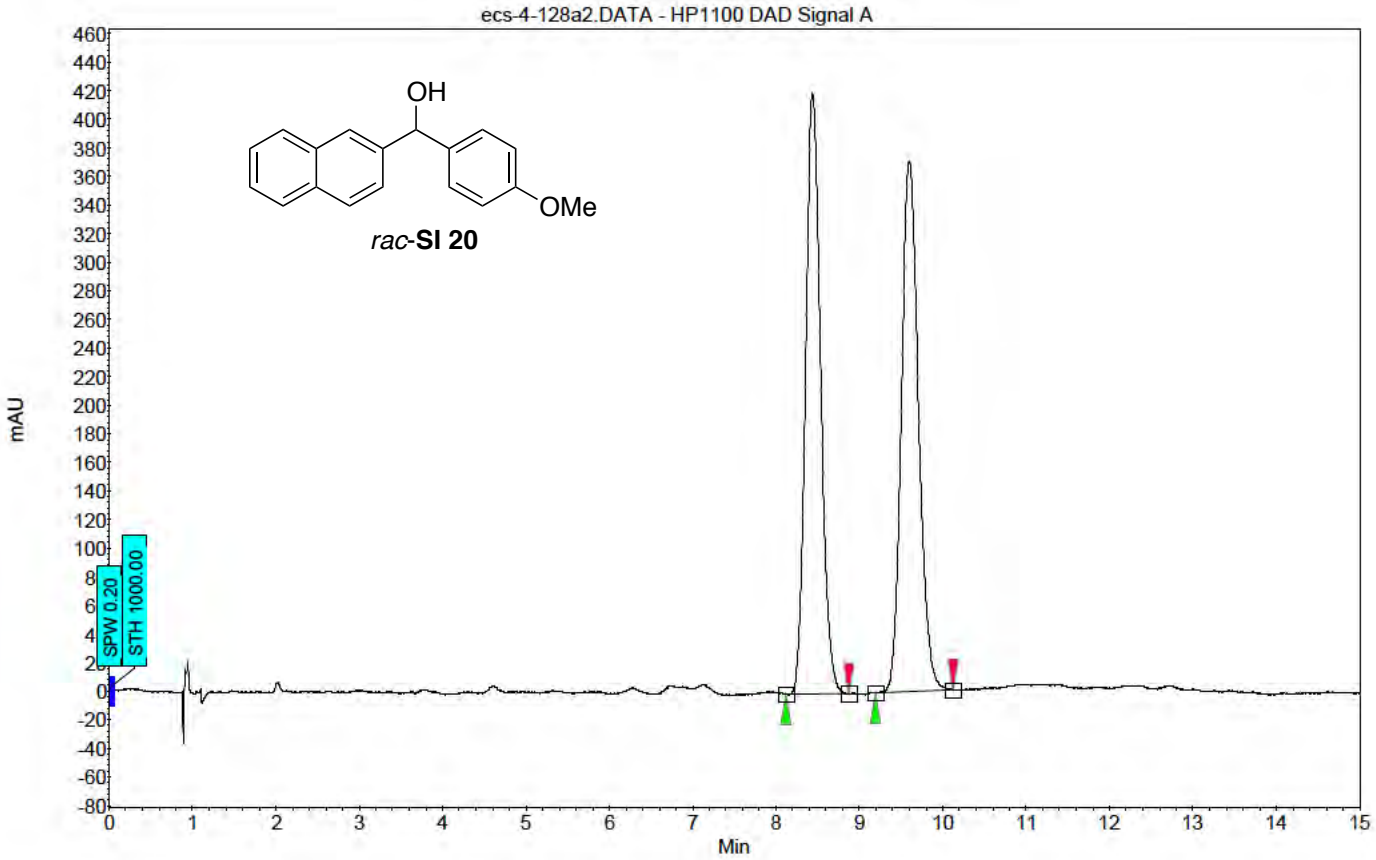


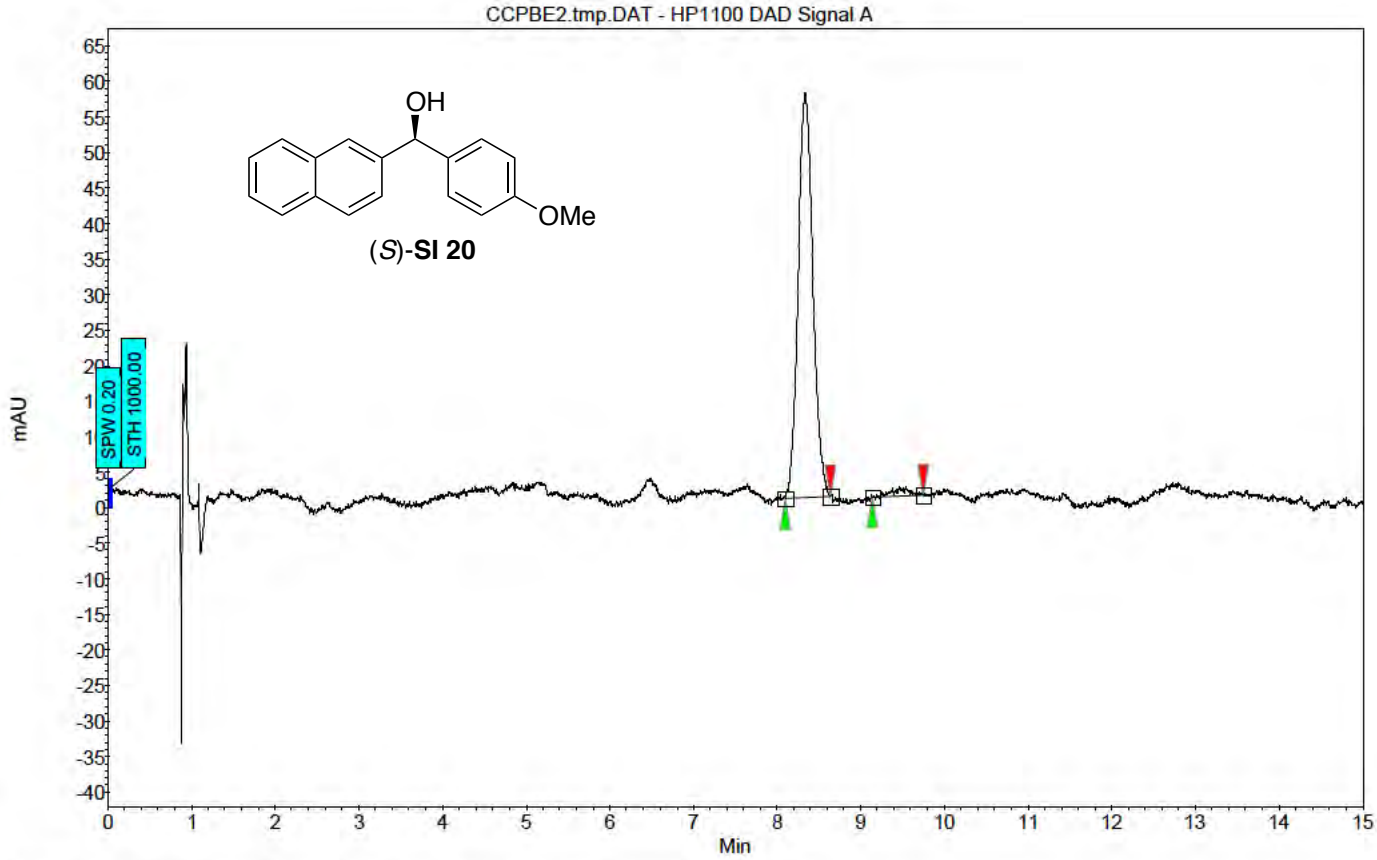
rac-**SI 53**



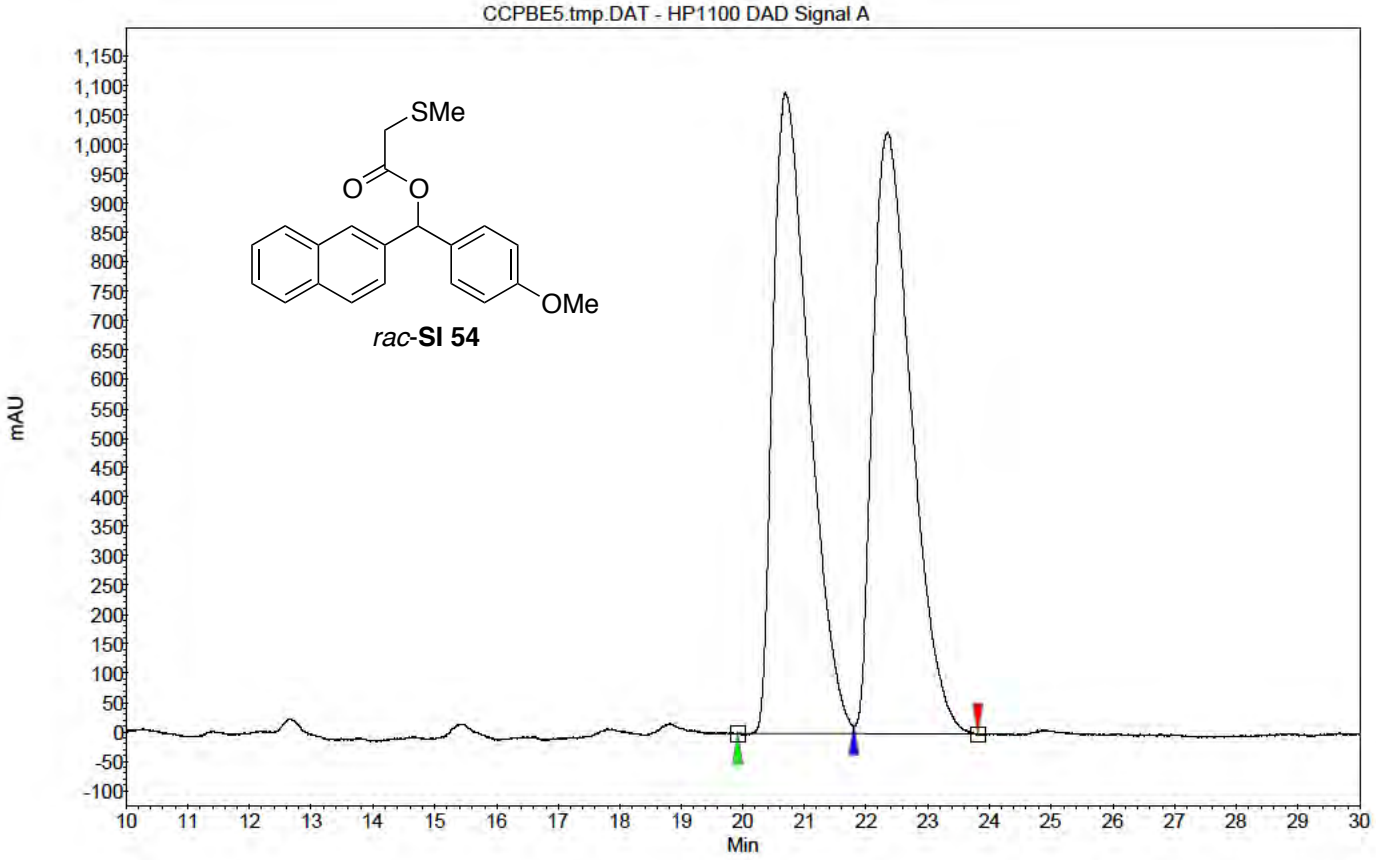
(*S*)-**SI 53**

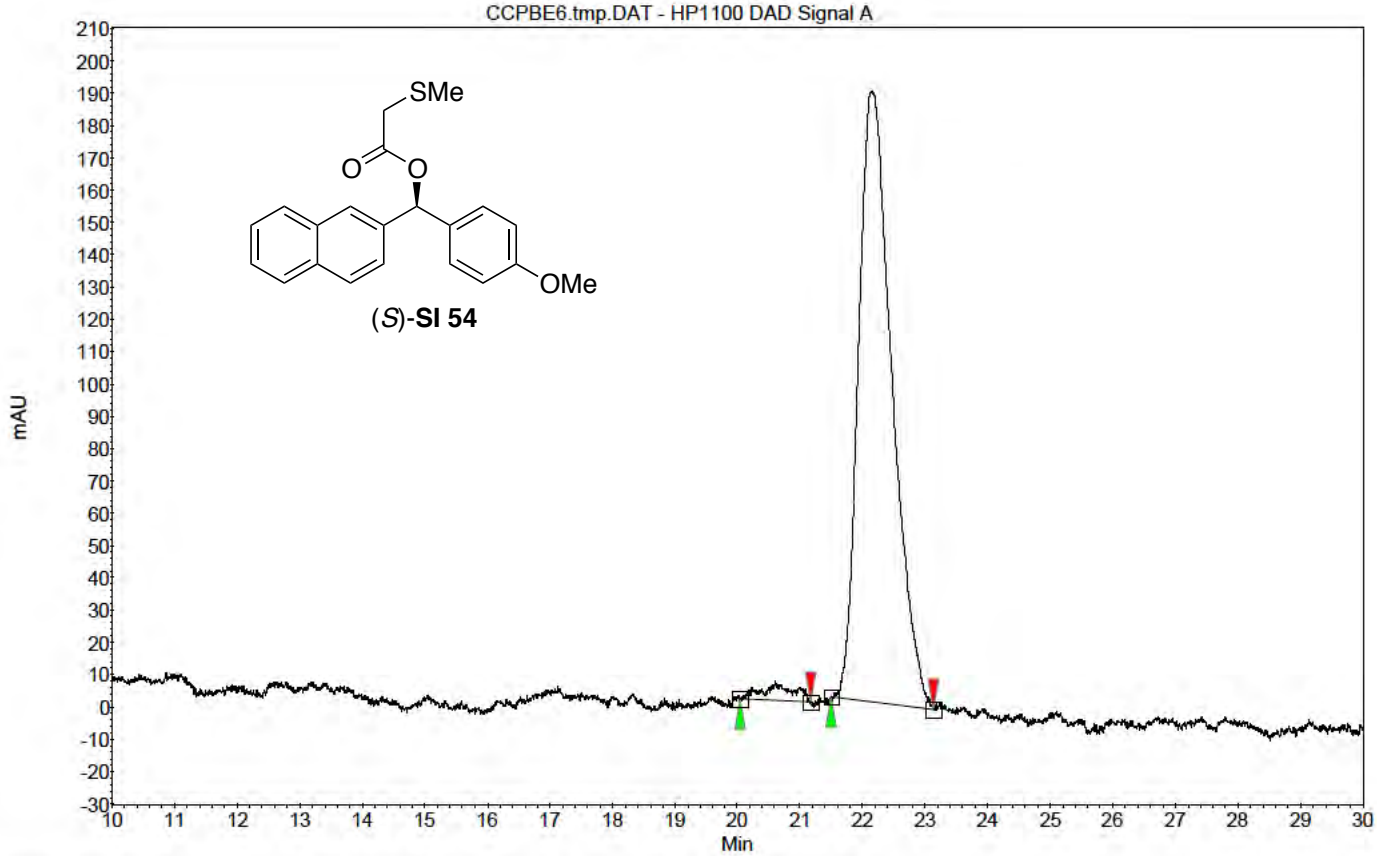
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.02	11.38	11.67	0.00	1.28	6.8	1.6	1.283
2	UNKNOWN	11.75	12.18	12.92	0.00	98.72	377.9	125.0	98.717
Total						100.00	384.7	126.6	100.000



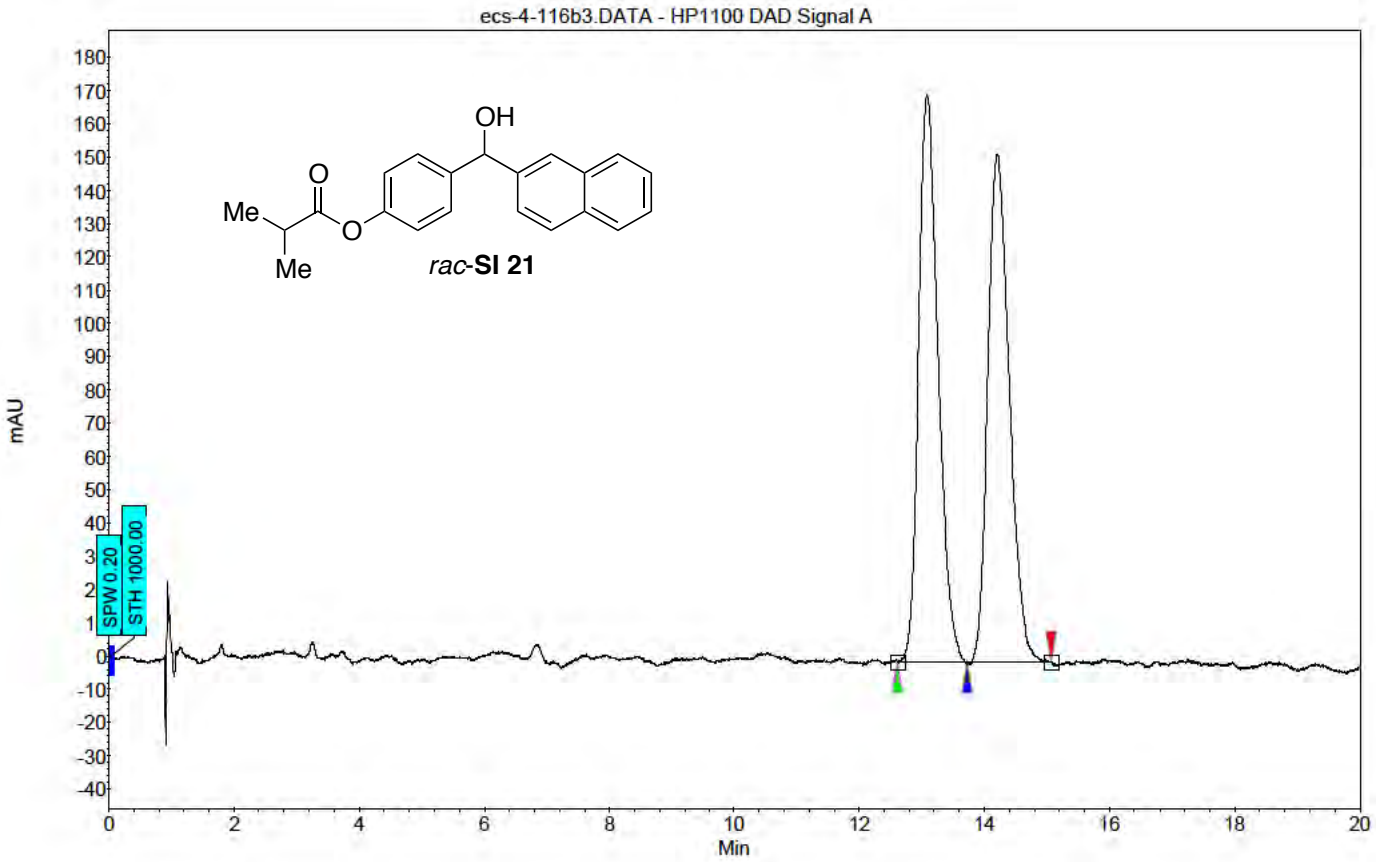


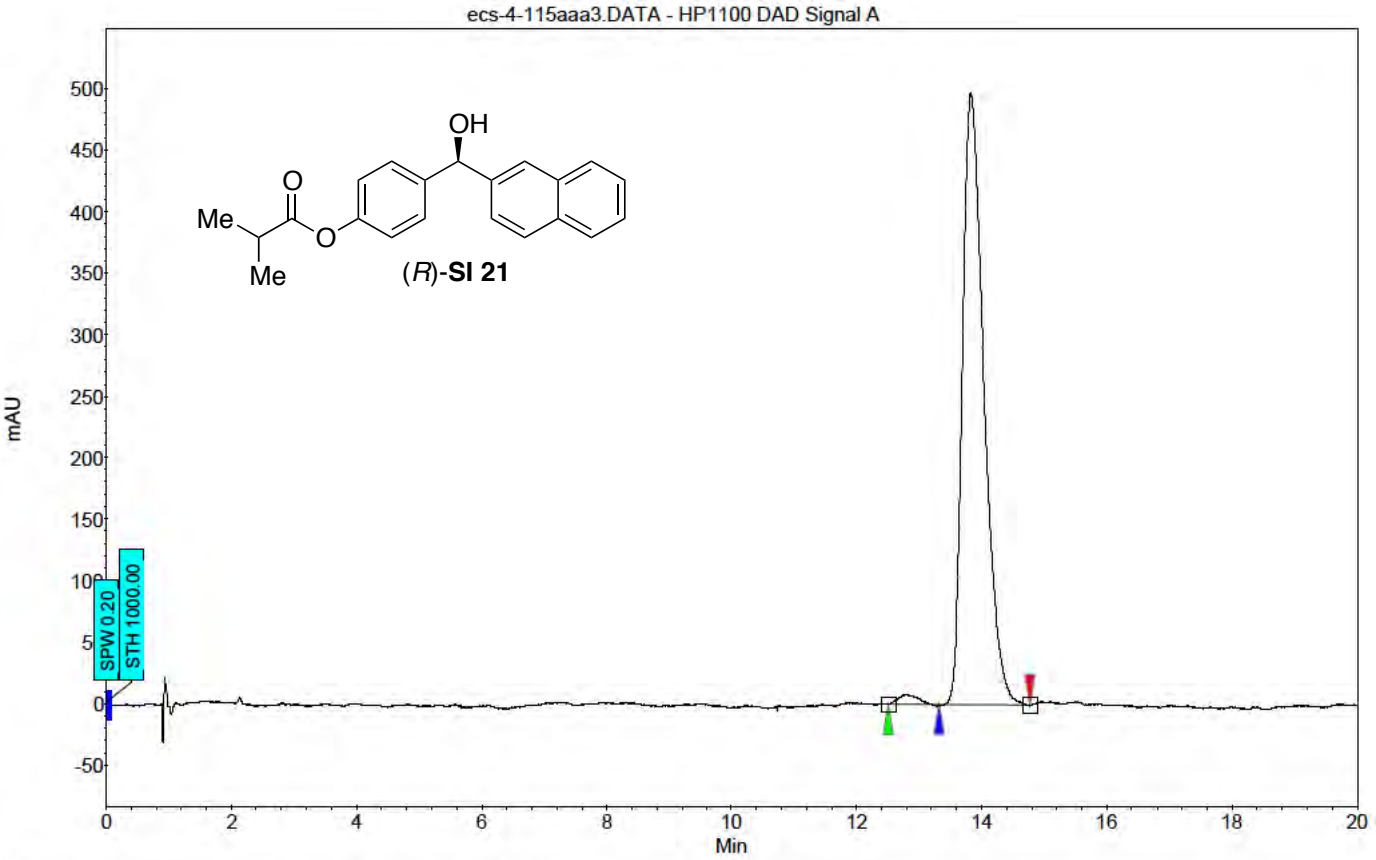
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.10	8.34	8.64	0.00	97.59	56.9	11.6	97.586
2	UNKNOWN	9.14	9.54	9.75	0.00	2.41	1.3	0.3	2.414
Total						100.00	58.2	11.9	100.000



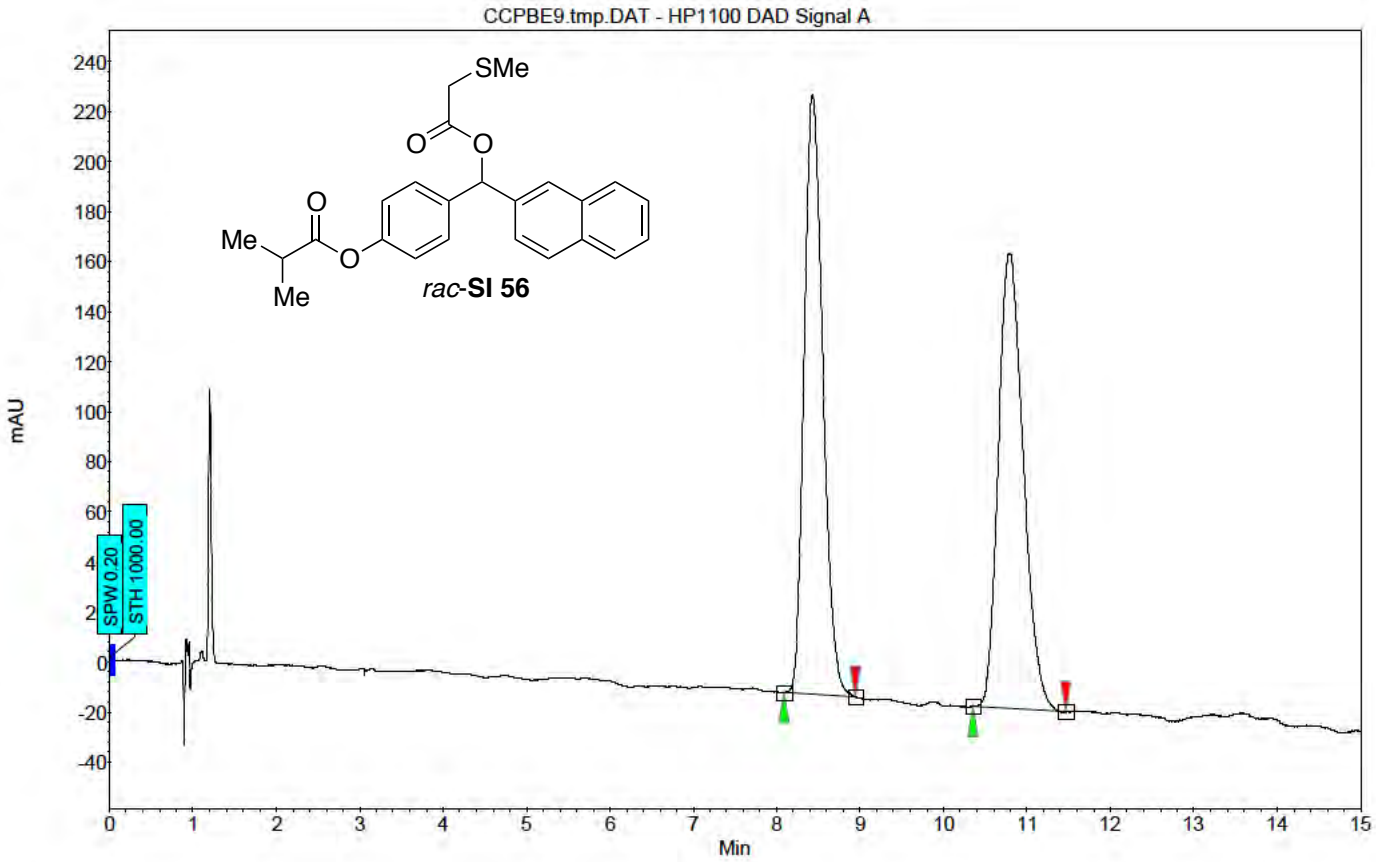


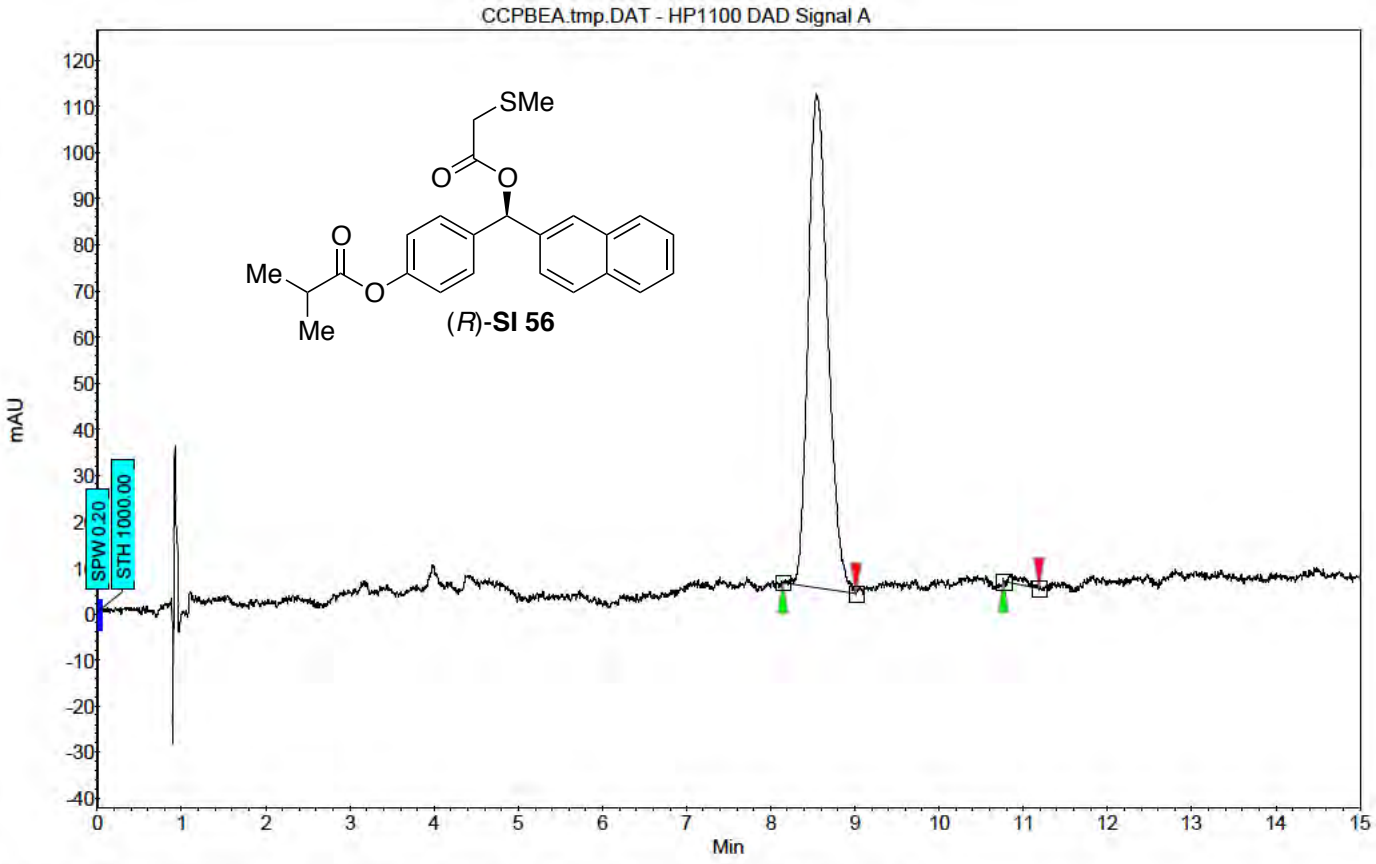
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	20.04	20.61	21.17	0.00	2.55	6.2	3.1	2.555
1	UNKNOWN	21.50	22.16	23.13	0.00	97.45	188.8	117.3	97.445
Total						100.00	195.0	120.4	100.000



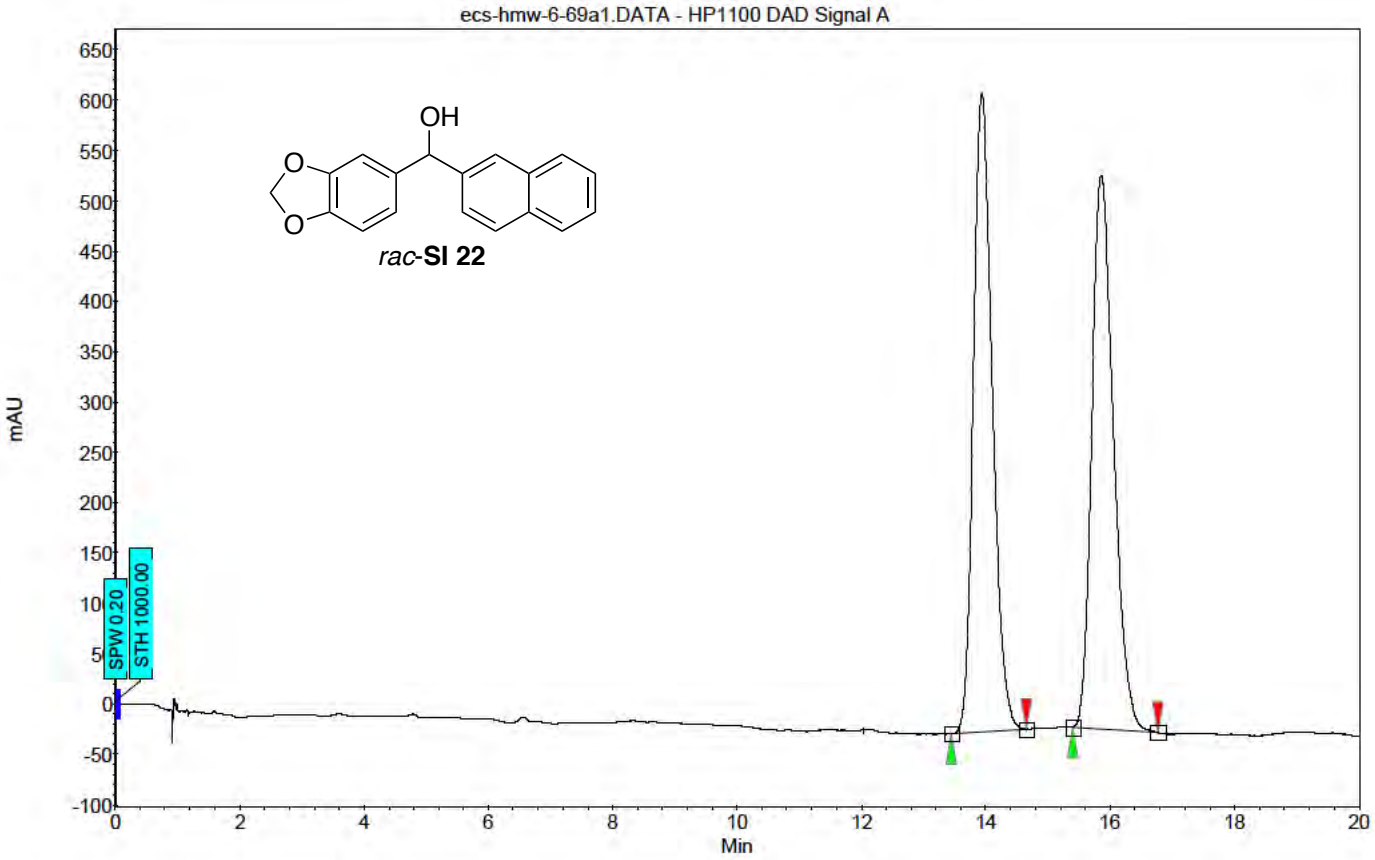


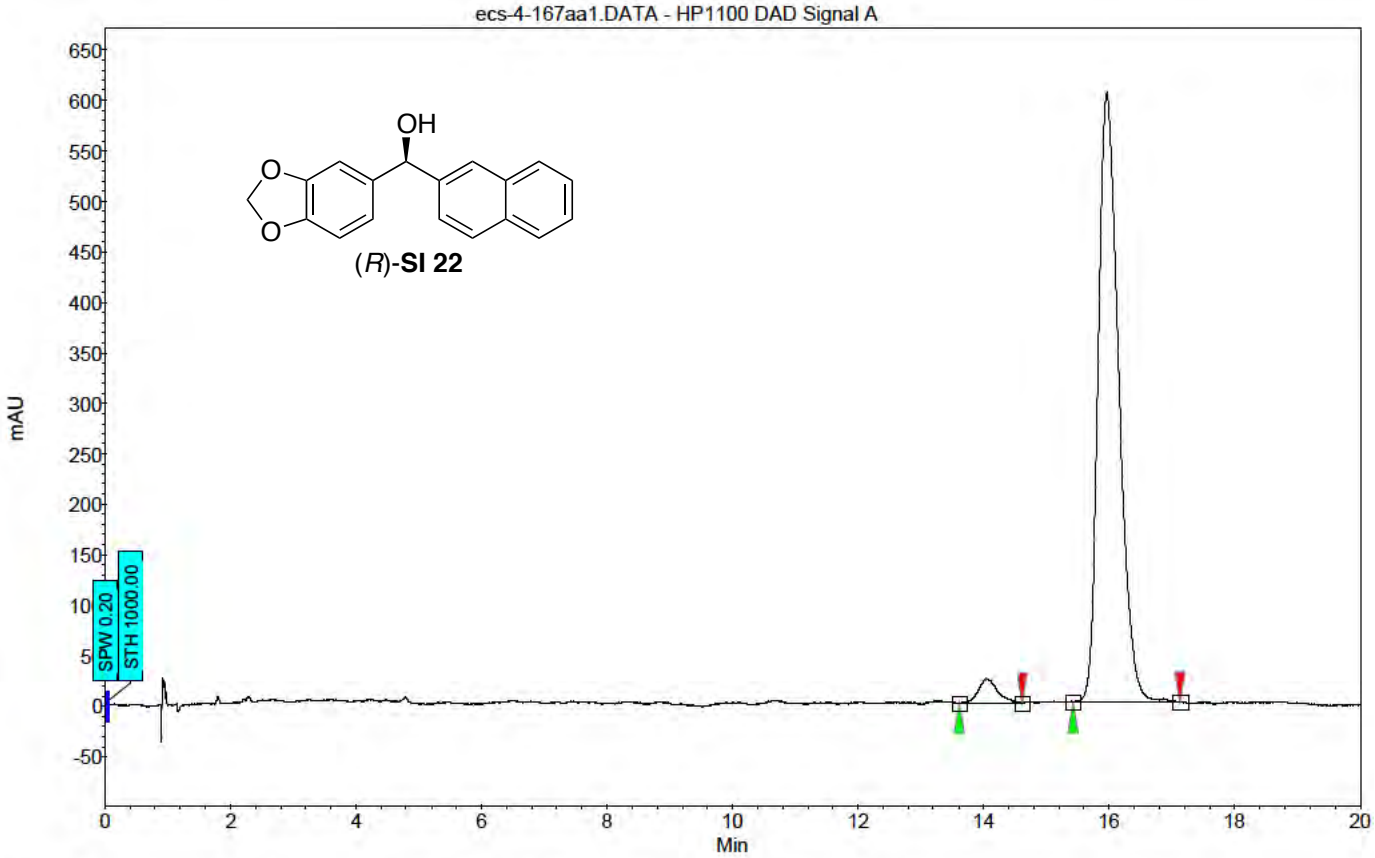
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	12.50	12.81	13.32	0.00	1.46	8.5	2.9	1.459
2	UNKNOWN	13.32	13.83	14.77	0.00	98.54	496.8	197.4	98.541
Total						100.00	505.3	200.3	100.000



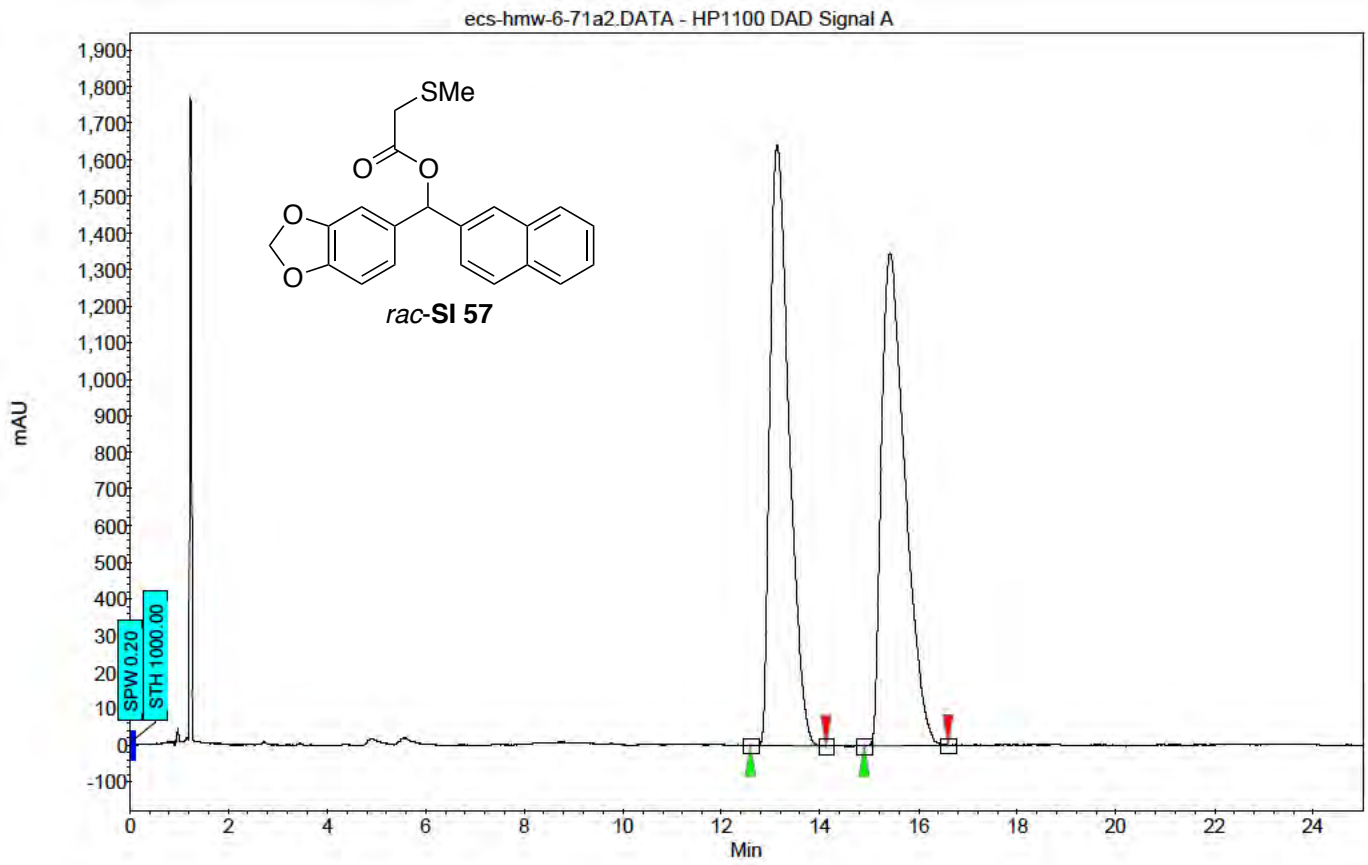


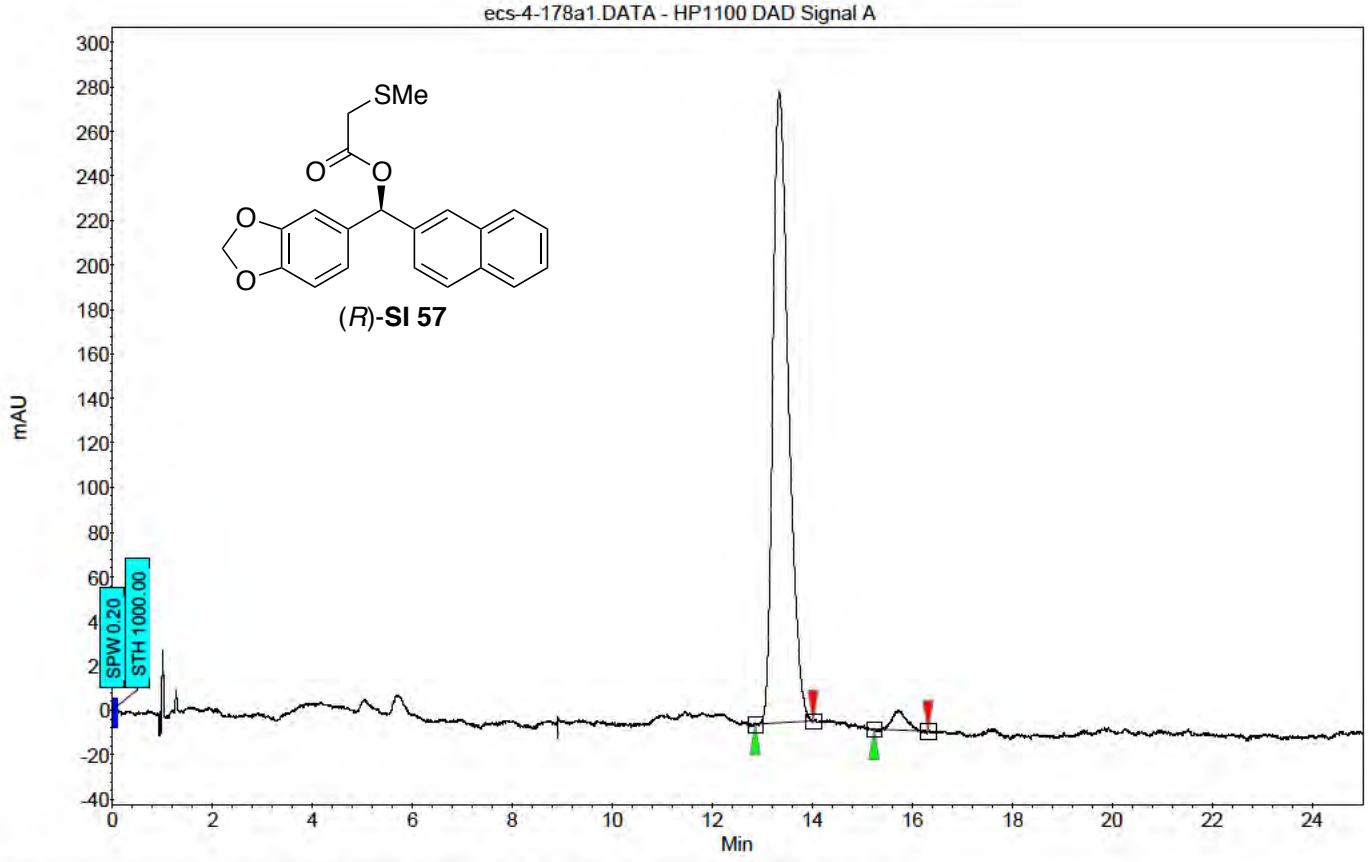
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.15	8.55	9.01	0.00	98.85	106.9	28.9	98.854
2	UNKNOWN	10.77	11.01	11.19	0.00	1.15	1.8	0.3	1.146
Total						100.00	108.7	29.3	100.000



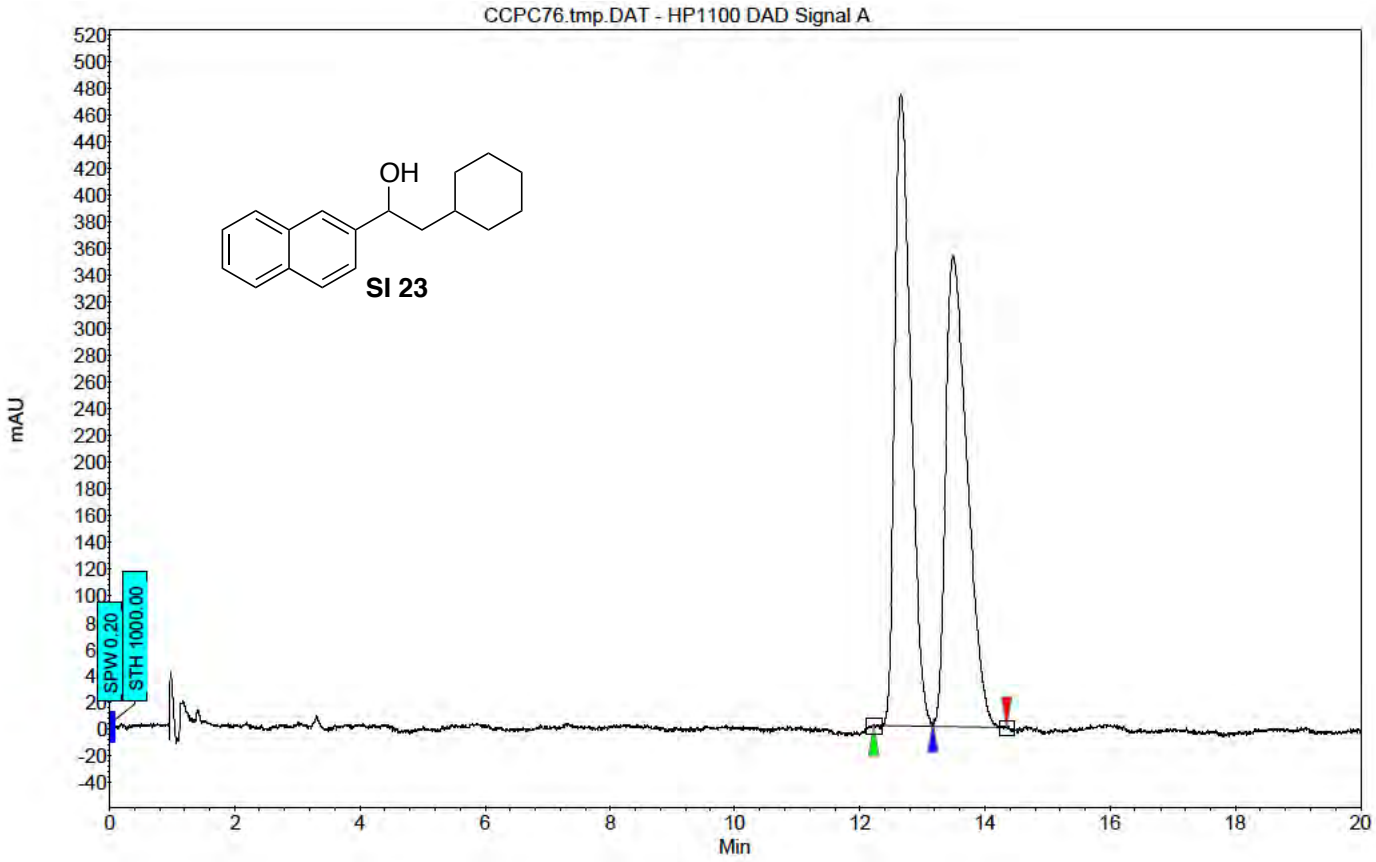


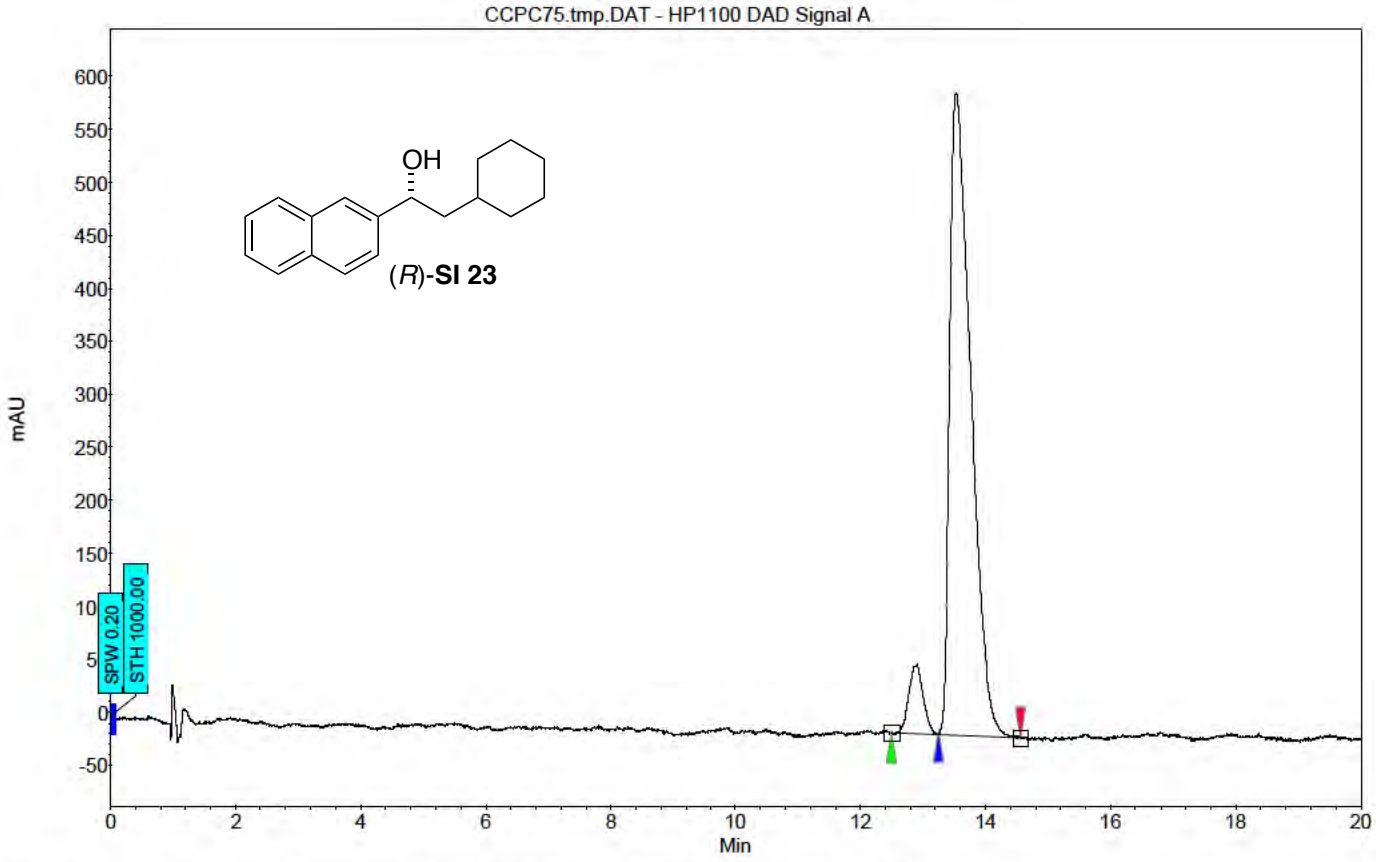
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	13.61	14.05	14.62	0.00	3.52	24.4	8.4	3.524
2	UNKNOWN	15.43	15.97	17.13	0.00	96.48	603.3	228.9	96.476
Total						100.00	627.8	237.2	100.000



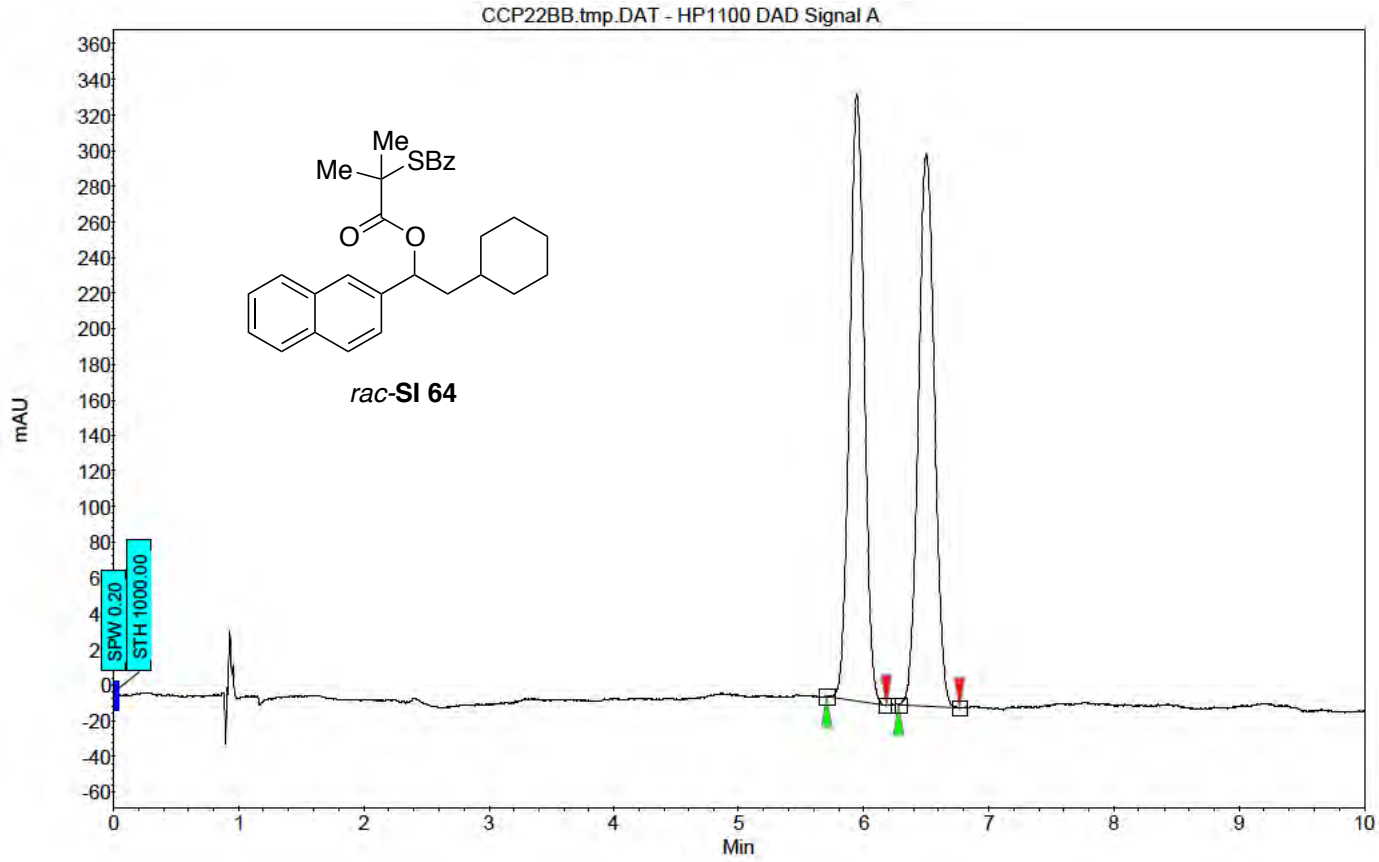


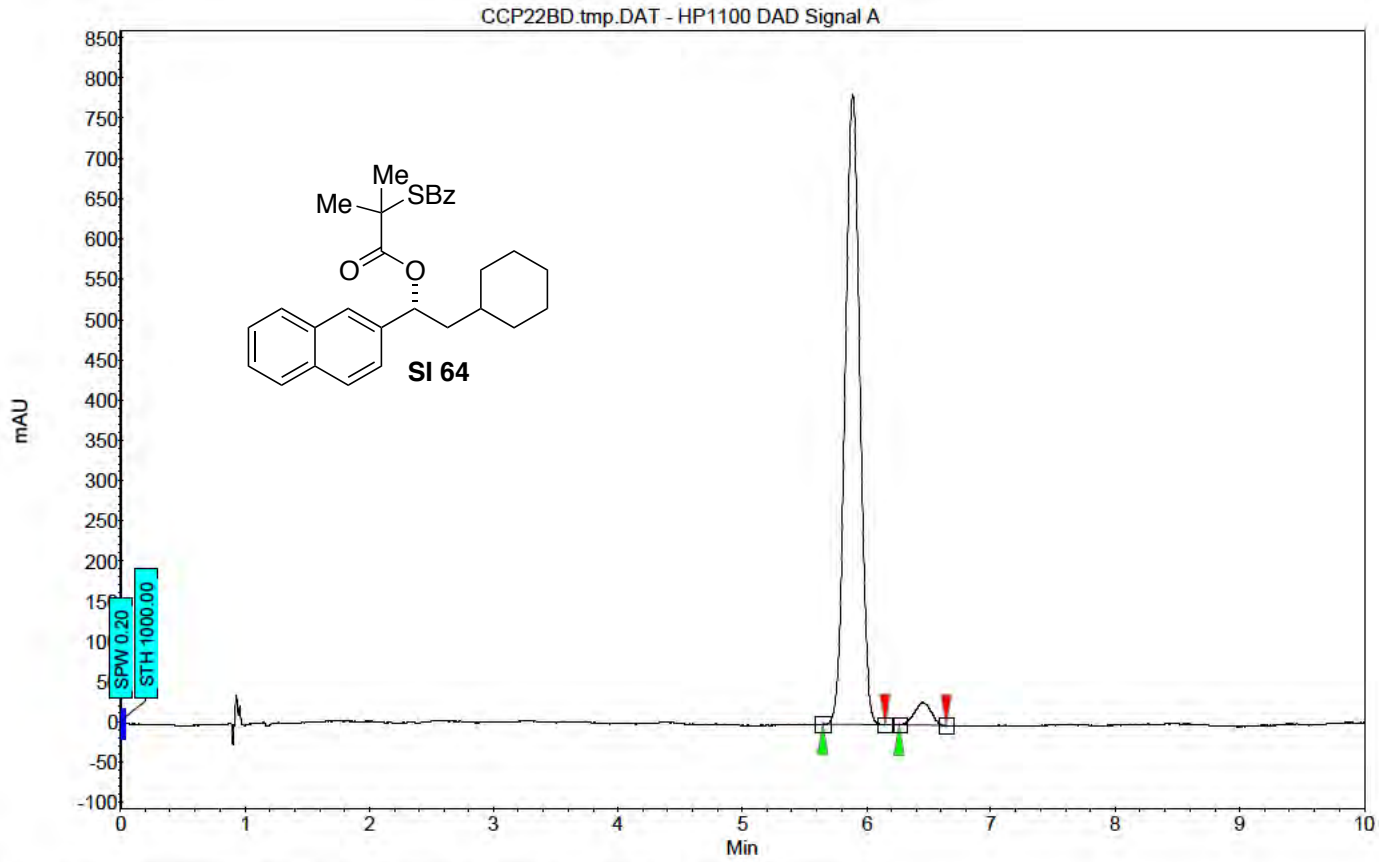
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	12.87	13.34	14.02	0.00	97.33	283.3	102.5	97.330
2	UNKNOWN	15.24	15.73	16.32	0.00	2.67	9.0	2.8	2.670
Total						100.00	292.2	105.3	100.000



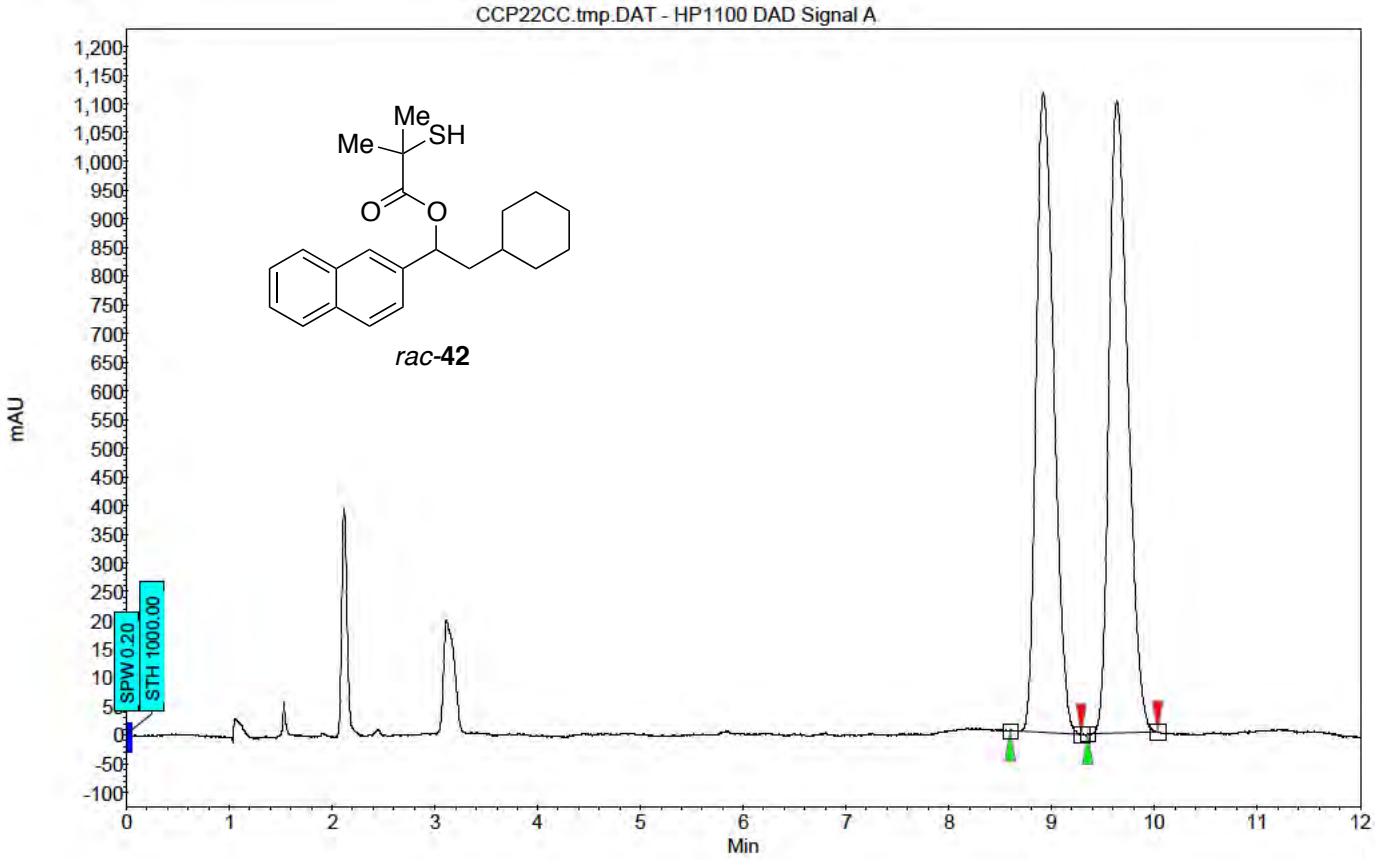


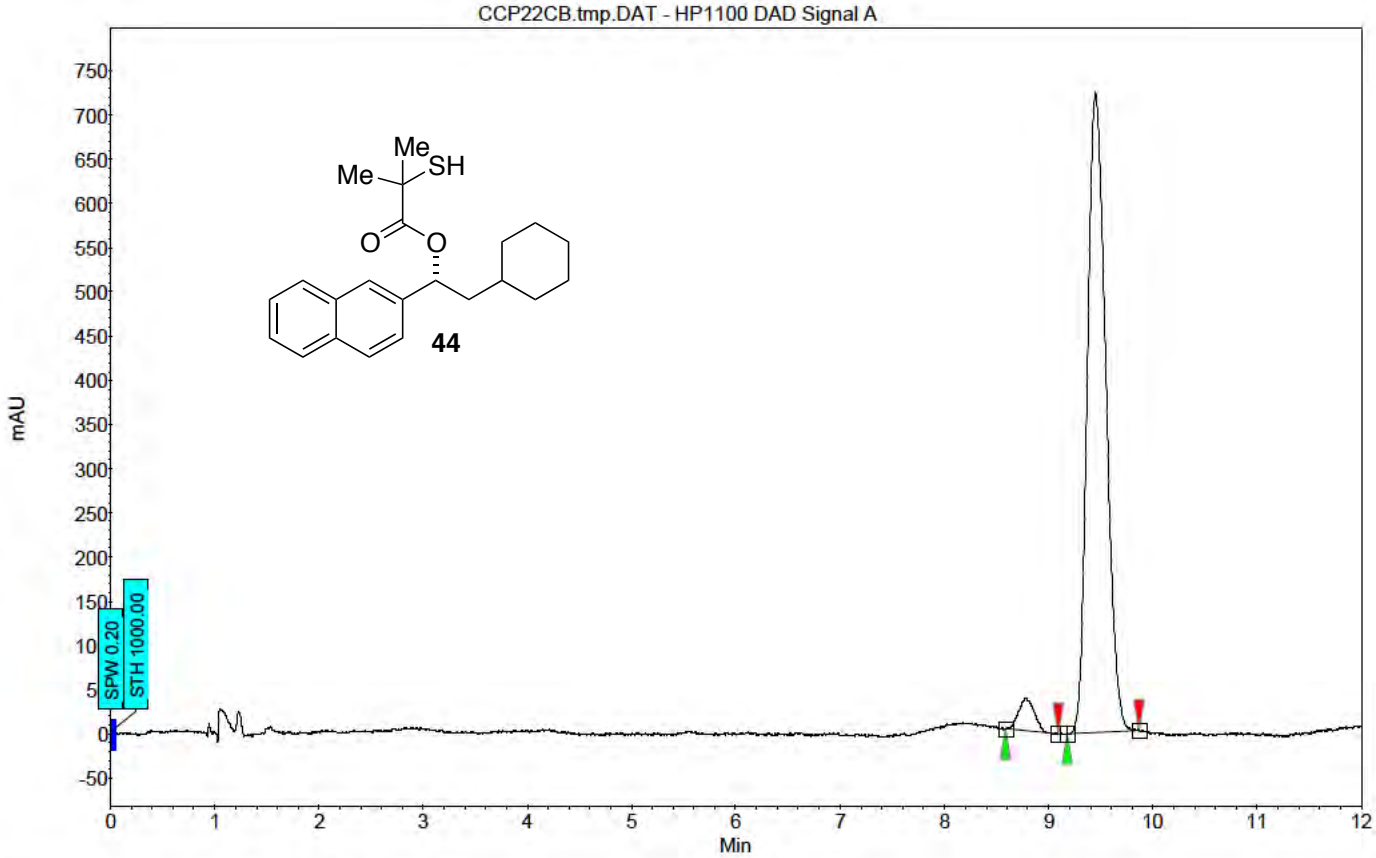
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	12.50	12.90	13.25	0.00	6.85	65.5	17.4	6.852
2	UNKNOWN	13.25	13.53	14.56	0.00	93.15	605.4	236.4	93.148
Total						100.00	670.9	253.7	100.000



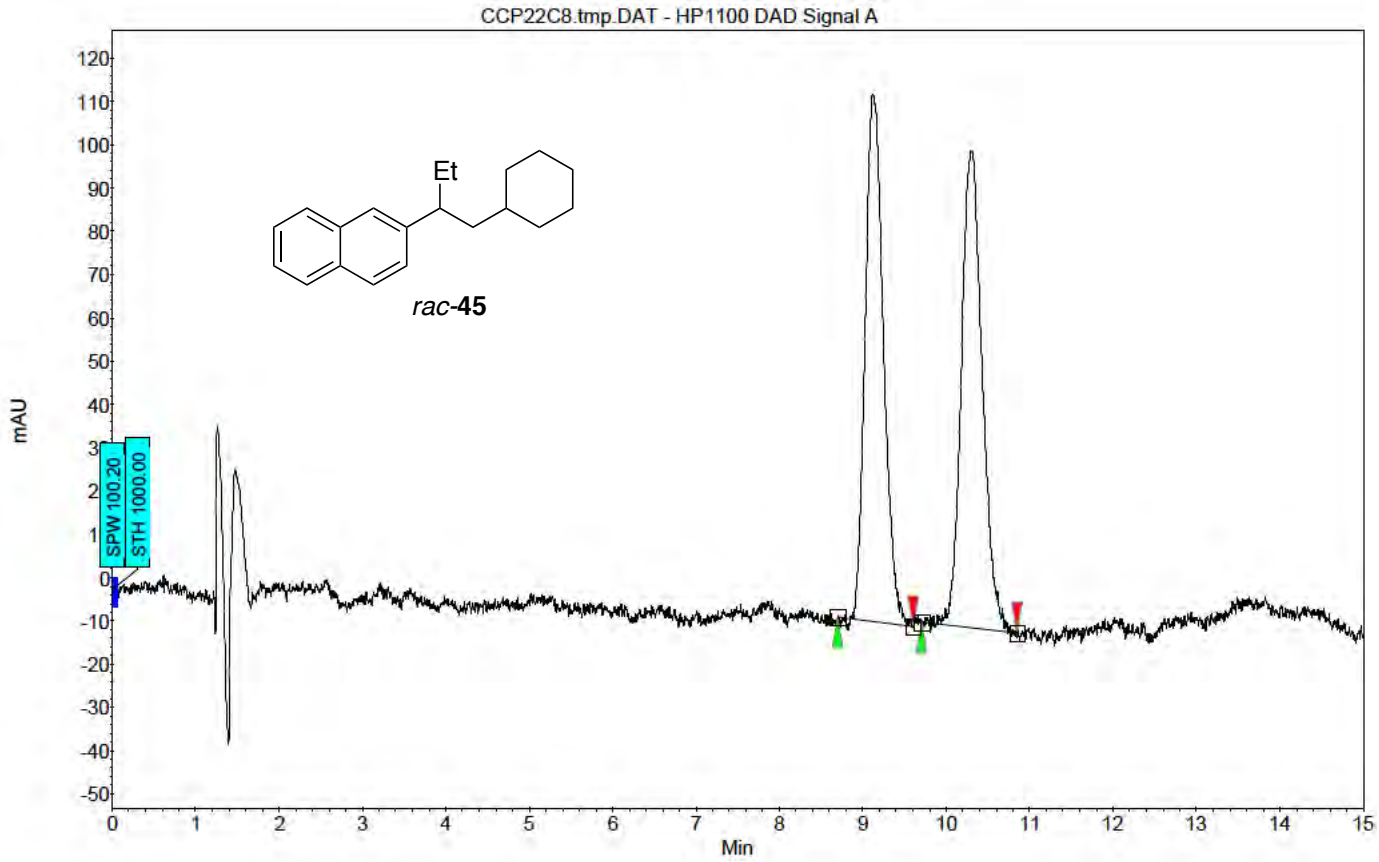


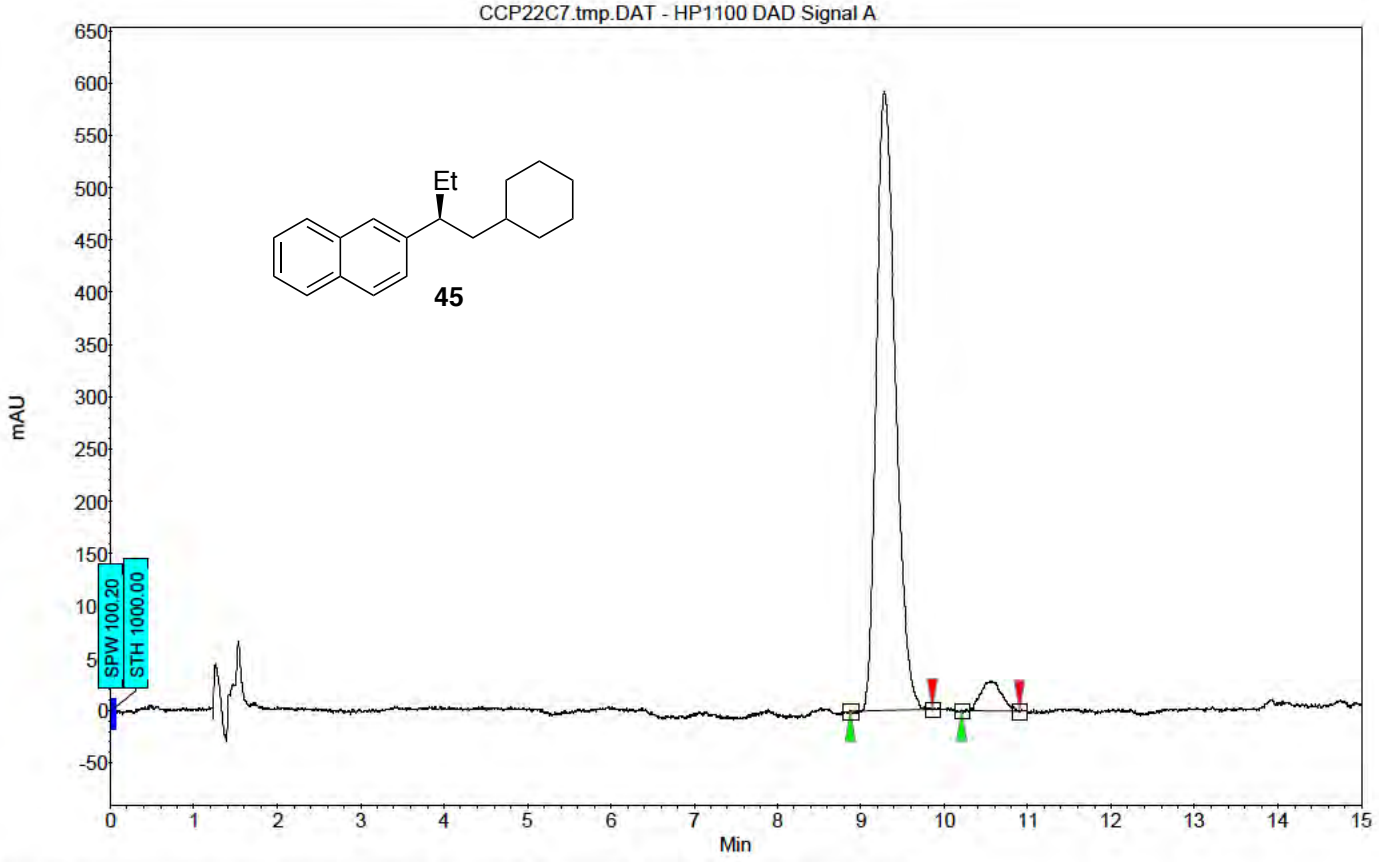
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.65	5.89	6.15	0.00	96.13	781.2	107.2	96.132
2	UNKNOWN	6.26	6.45	6.64	0.00	3.87	27.7	4.3	3.868
Total						100.00	808.9	111.5	100.000



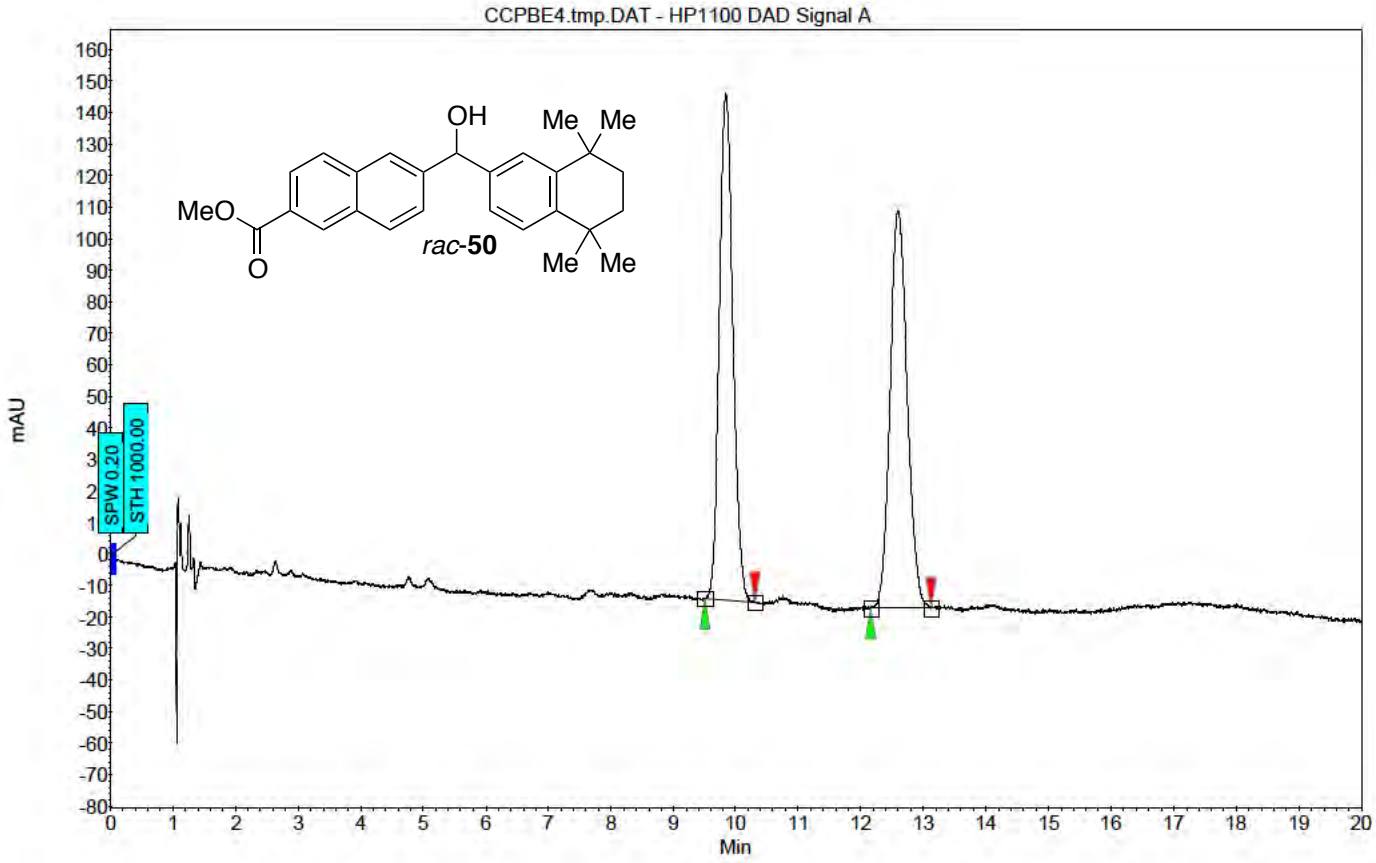


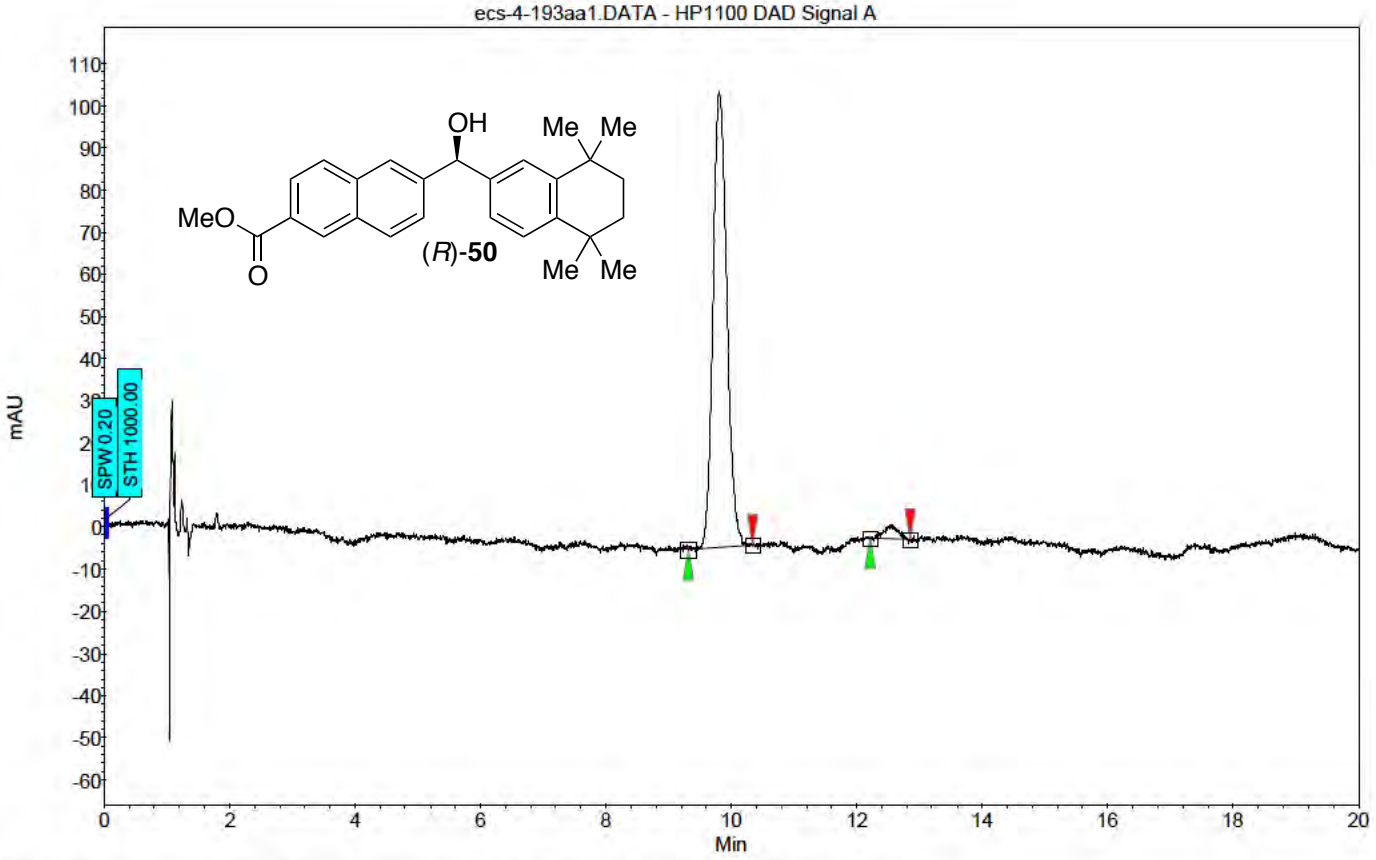
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.59	8.78	9.09	0.00	4.16	37.1	6.5	4.161
2	UNKNOWN	9.18	9.45	9.87	0.00	95.84	723.5	148.6	95.839
Total						100.00	760.6	155.0	100.000



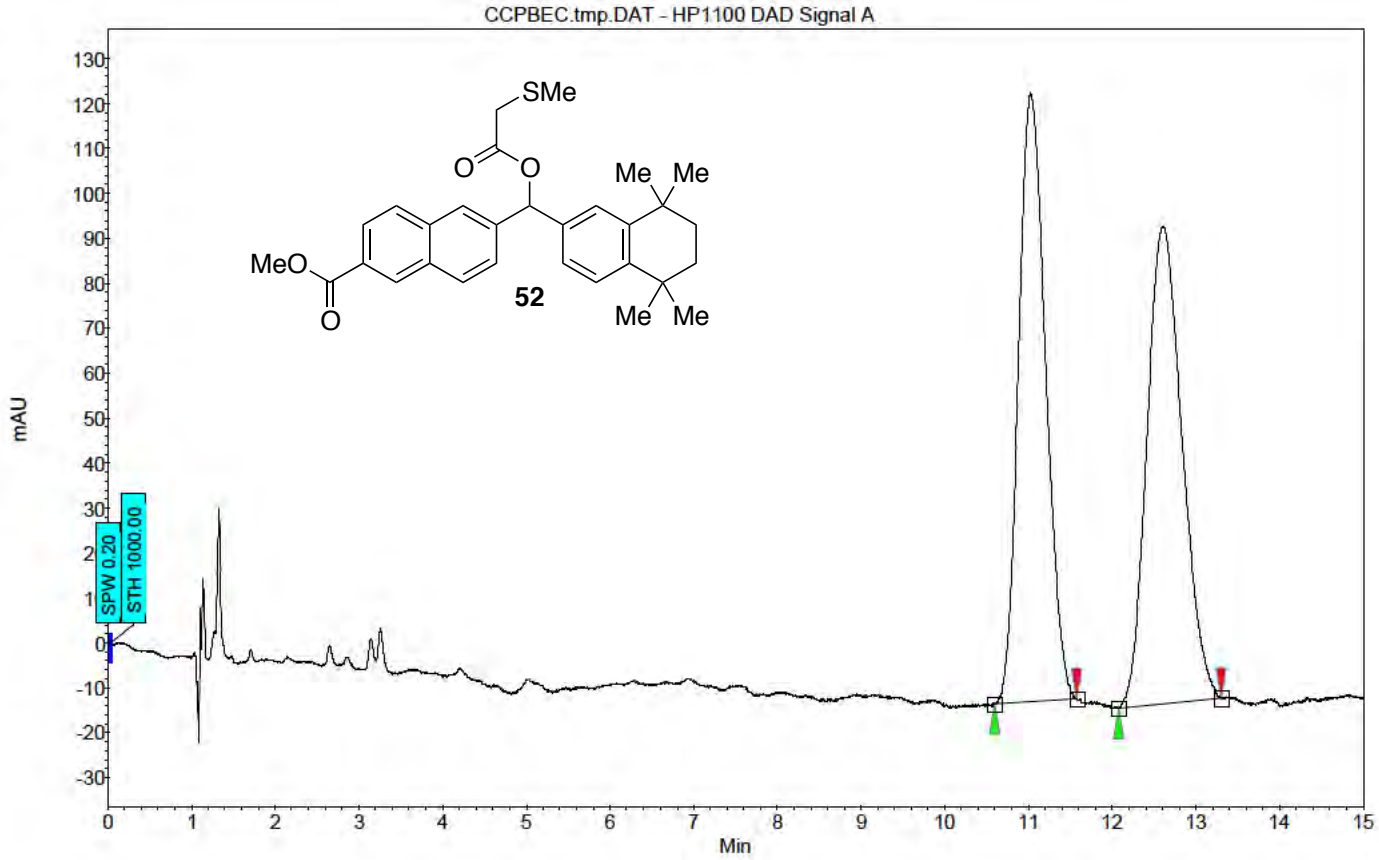


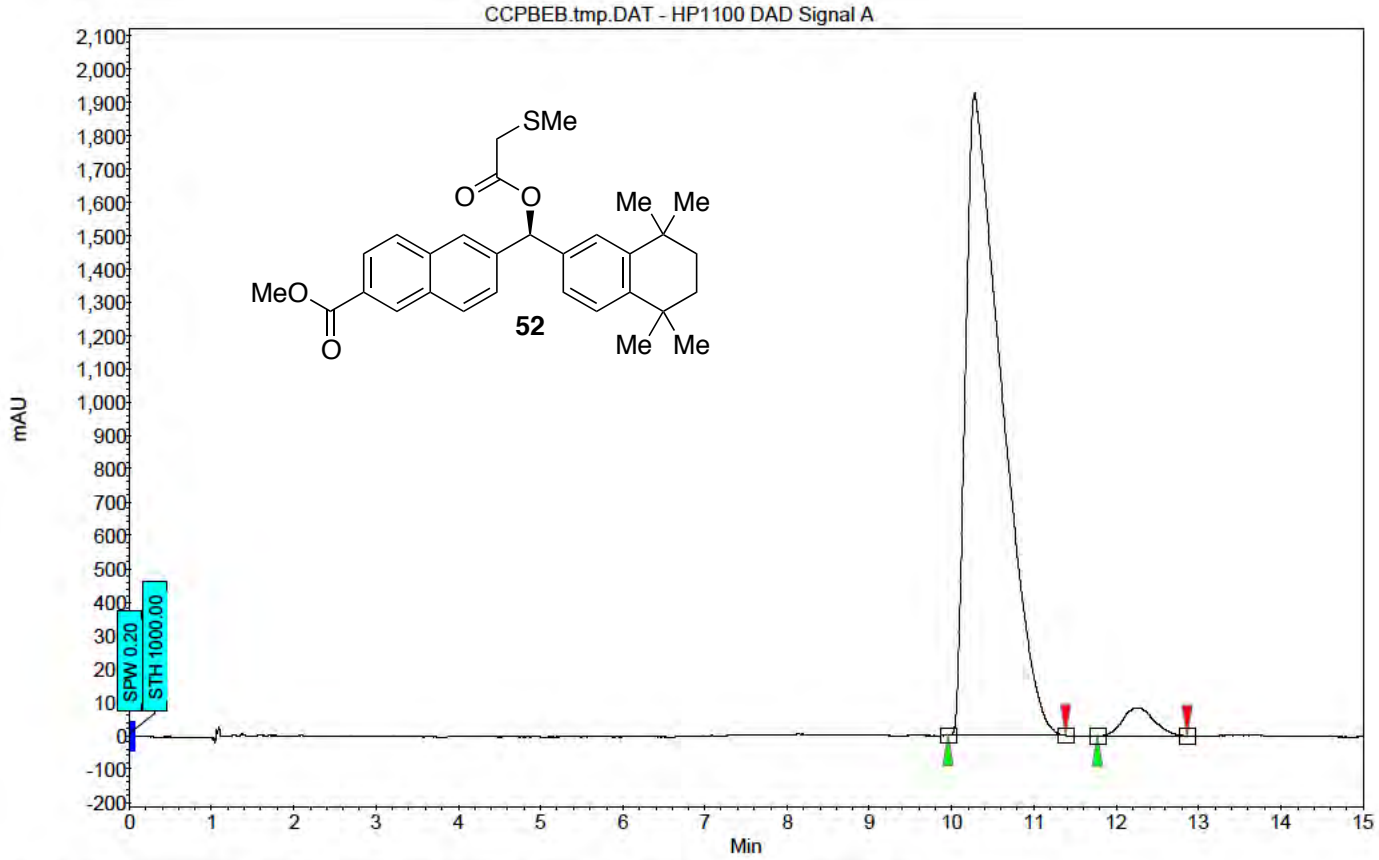
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.87	9.29	9.85	0.00	95.01	591.2	156.5	95.007
2	UNKNOWN	10.21	10.56	10.90	0.00	4.99	28.8	8.2	4.993
Total						100.00	619.9	164.8	100.000



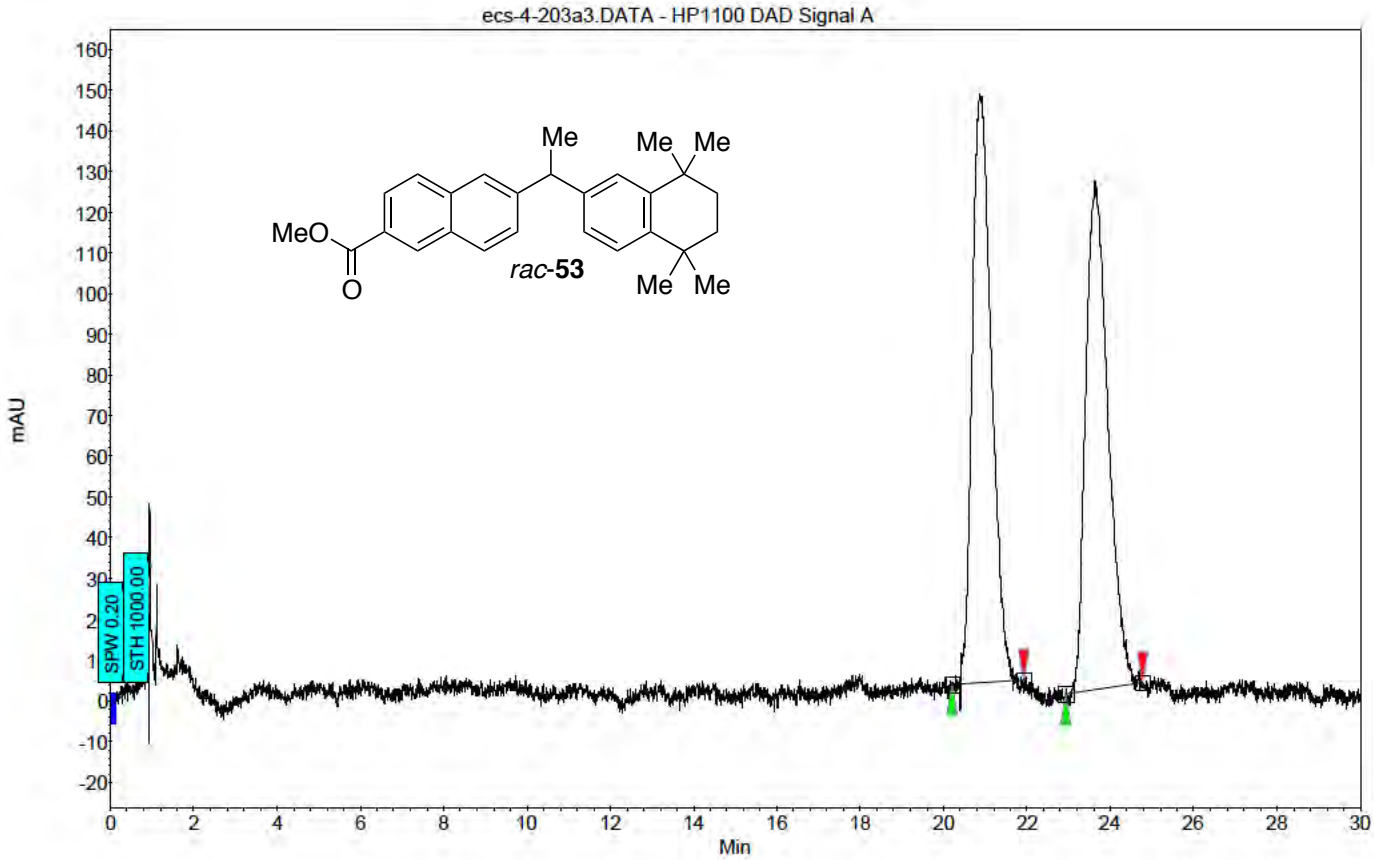


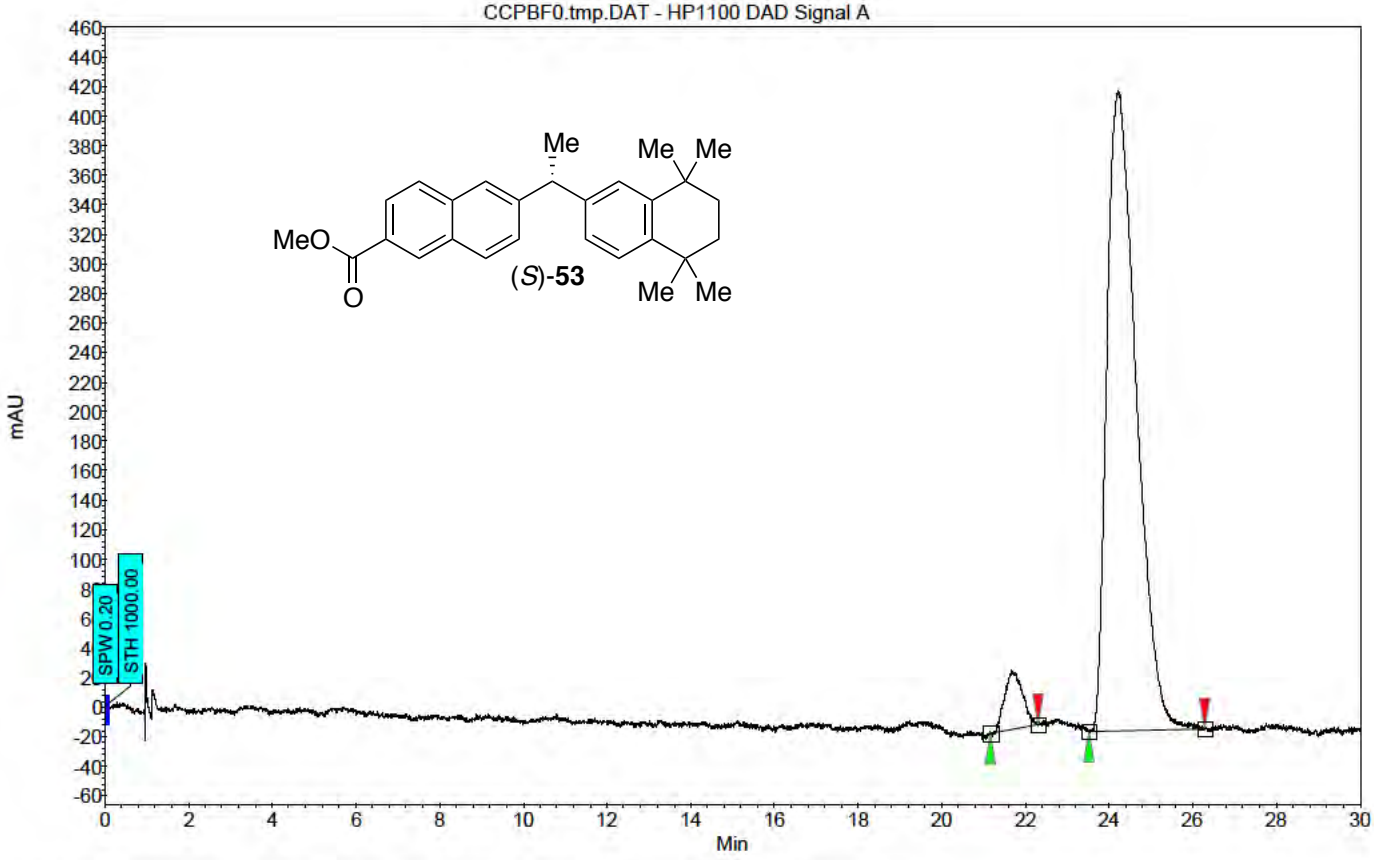
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	9.32	9.82	10.35	0.00	97.11	108.1	27.5	97.114
2	UNKNOWN	12.22	12.55	12.86	0.00	2.89	3.2	0.8	2.886
Total						100.00	111.4	28.3	100.000



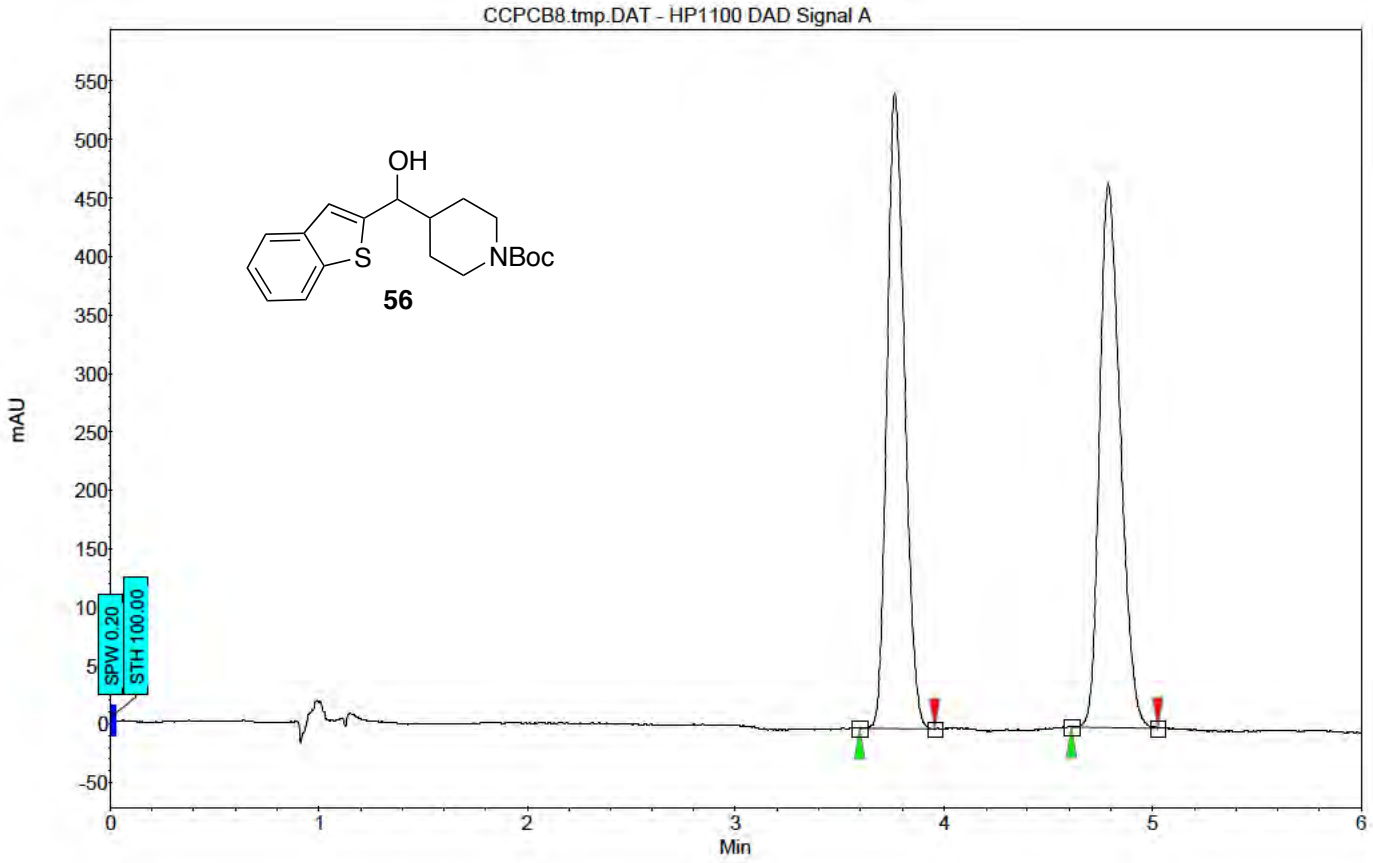


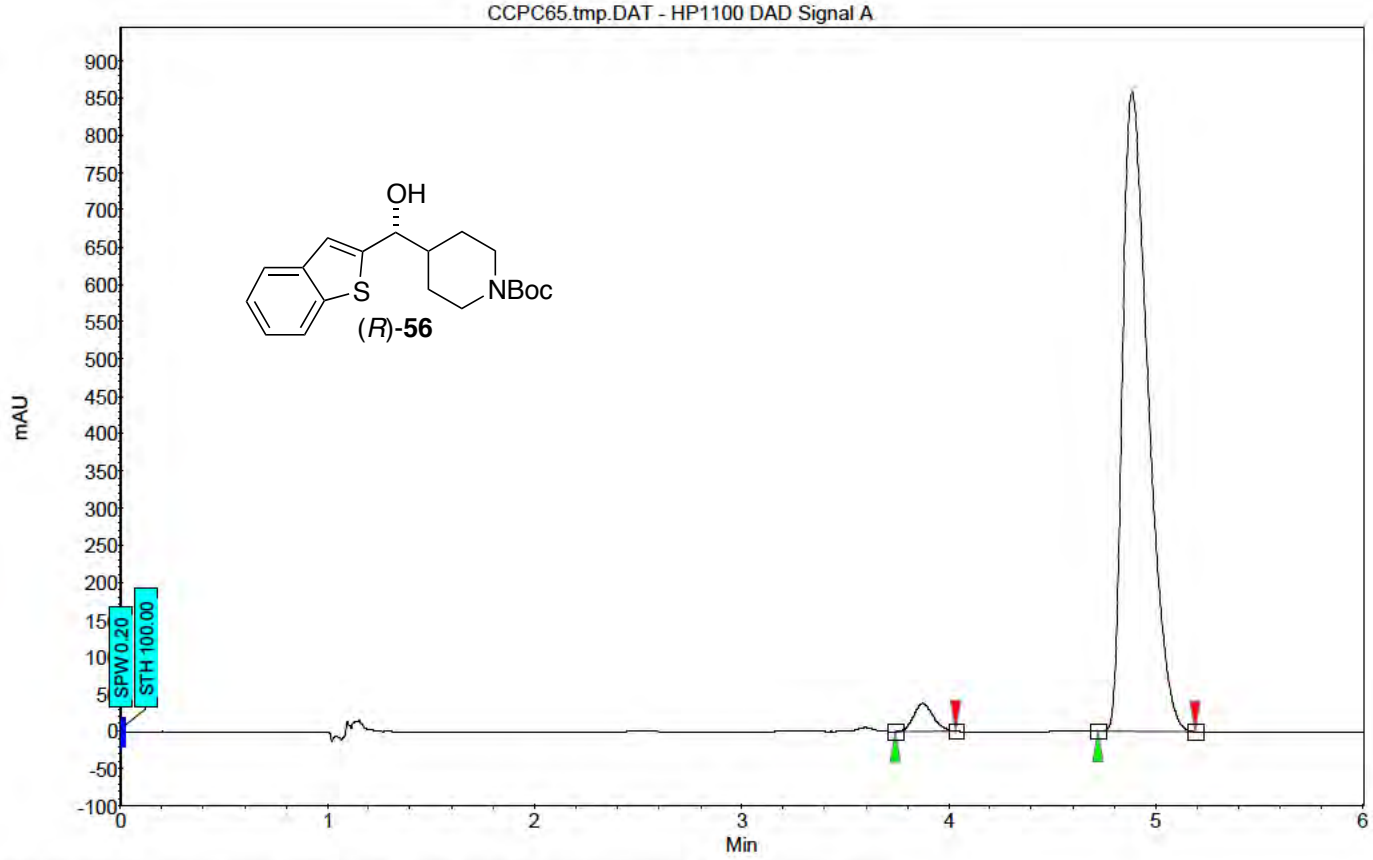
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	9.96	10.28	11.38	0.00	96.39	1926.3	975.5	96.386
2	UNKNOWN	11.77	12.26	12.86	0.00	3.61	84.5	36.6	3.614
Total						100.00	2010.7	1012.1	100.000



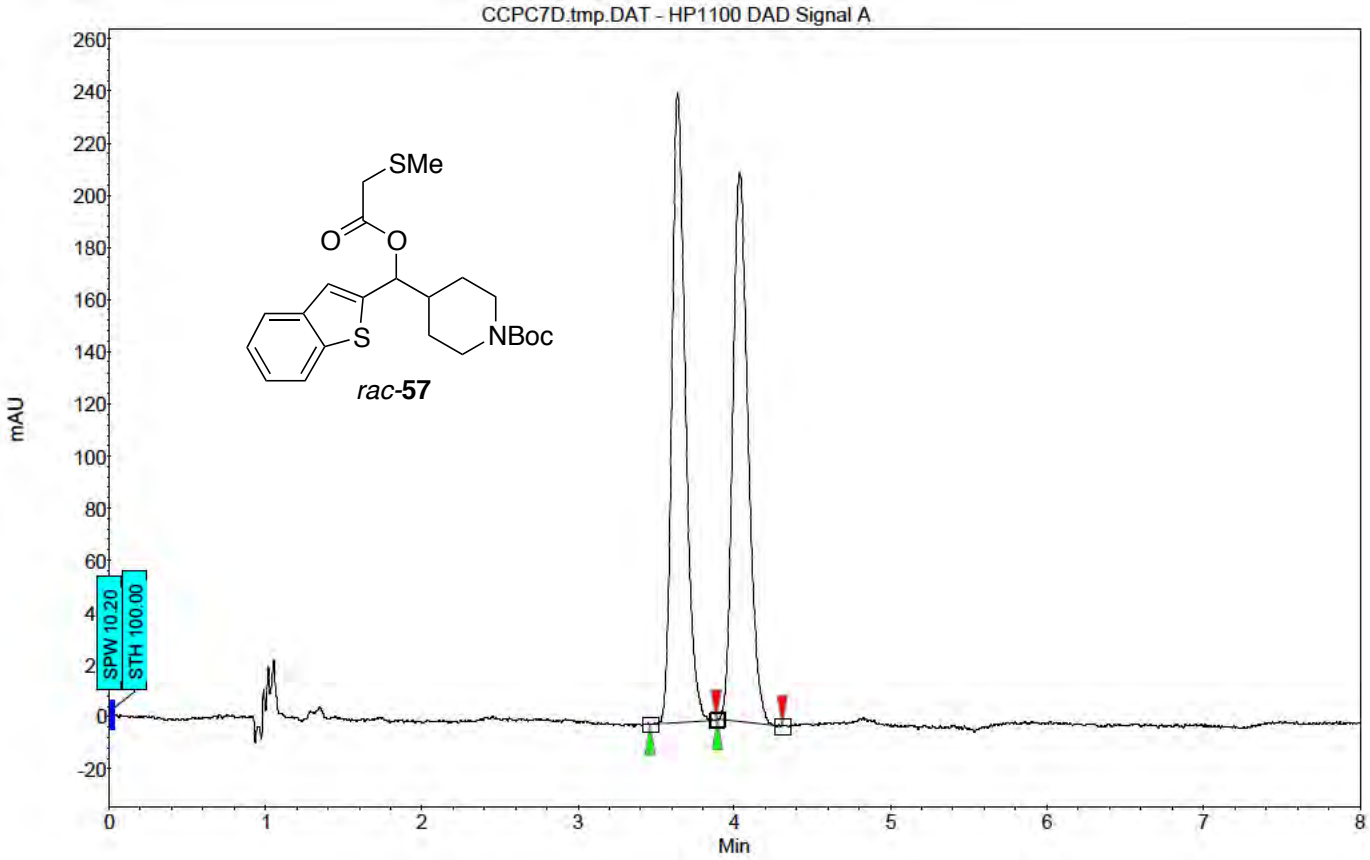


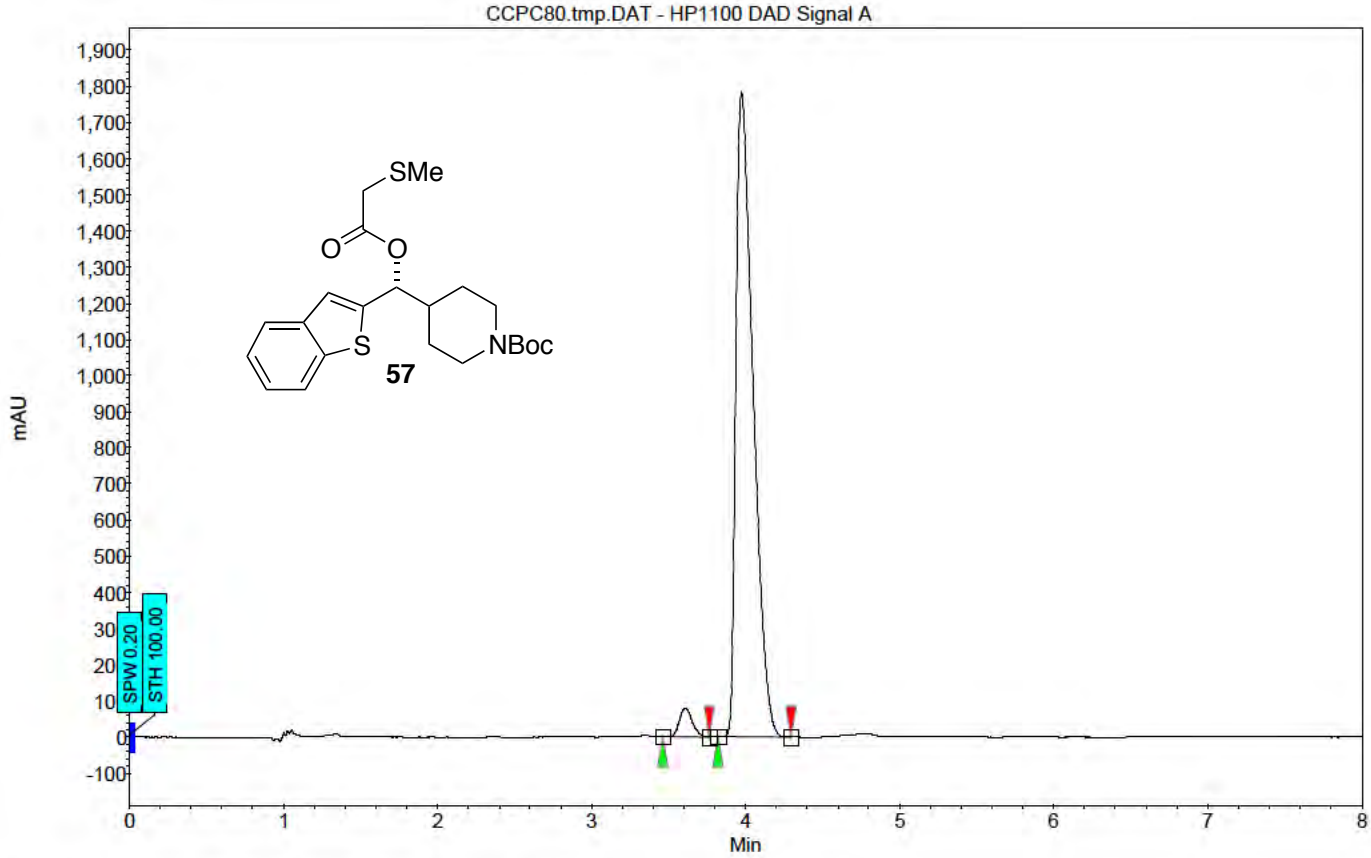
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	21.17	21.66	22.30	0.00	5.24	39.9	19.4	5.236
1	UNKNOWN	23.52	24.20	26.28	0.00	94.76	432.6	351.6	94.764
Total						100.00	472.5	371.0	100.000



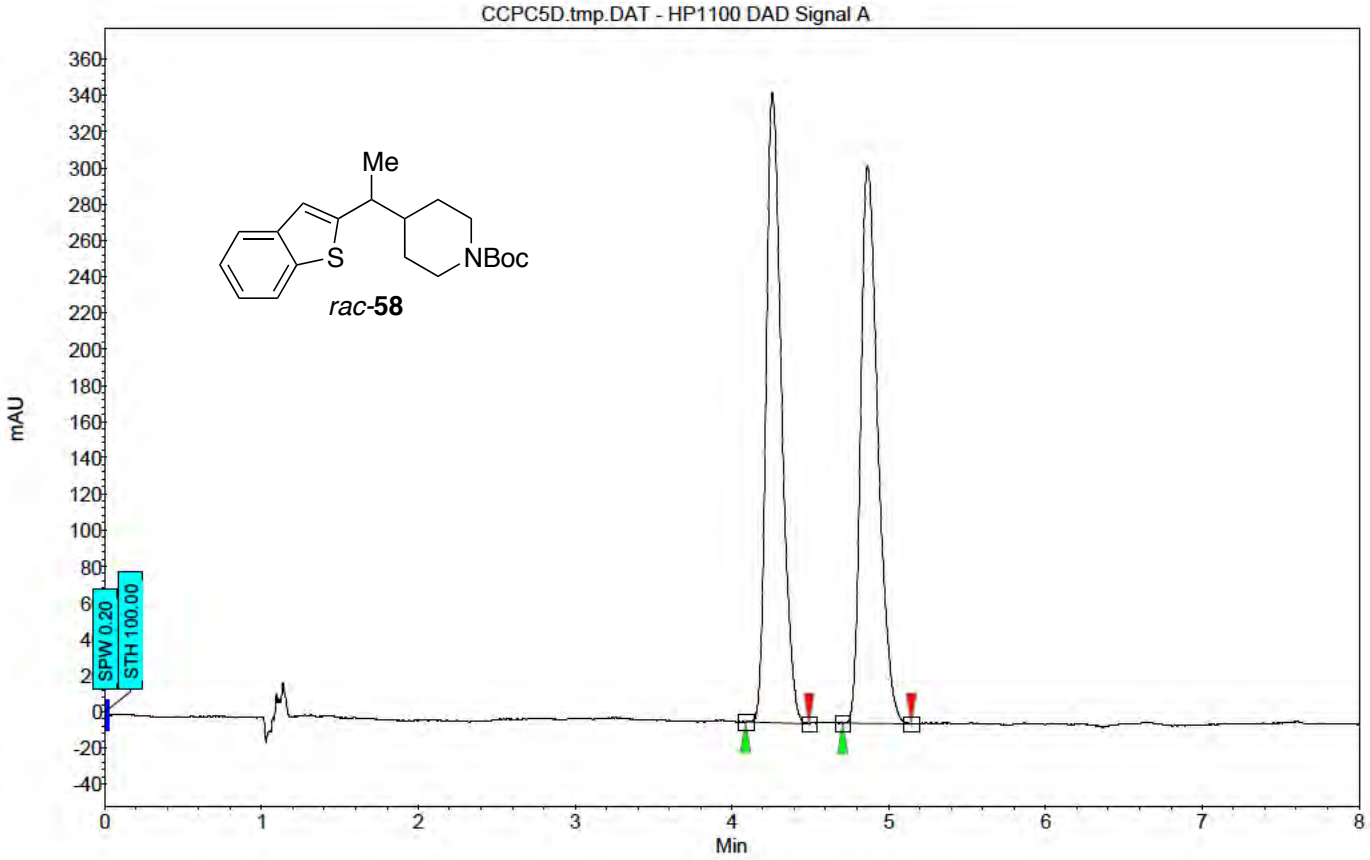


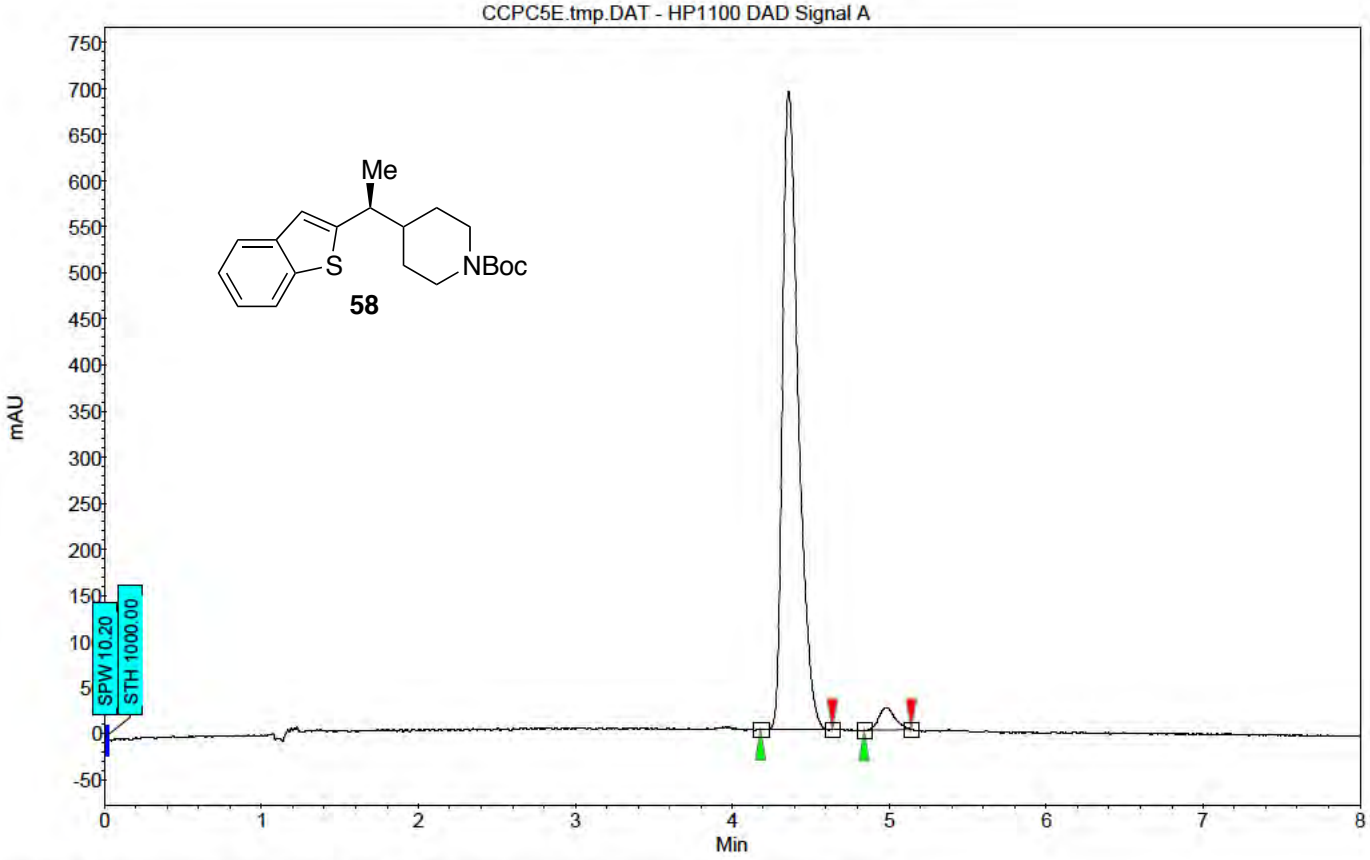
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.74	3.88	4.03	0.00	3.25	37.6	4.1	3.254
2	UNKNOWN	4.72	4.89	5.19	0.00	96.75	857.8	122.8	96.746
Total						100.00	895.5	126.9	100.000



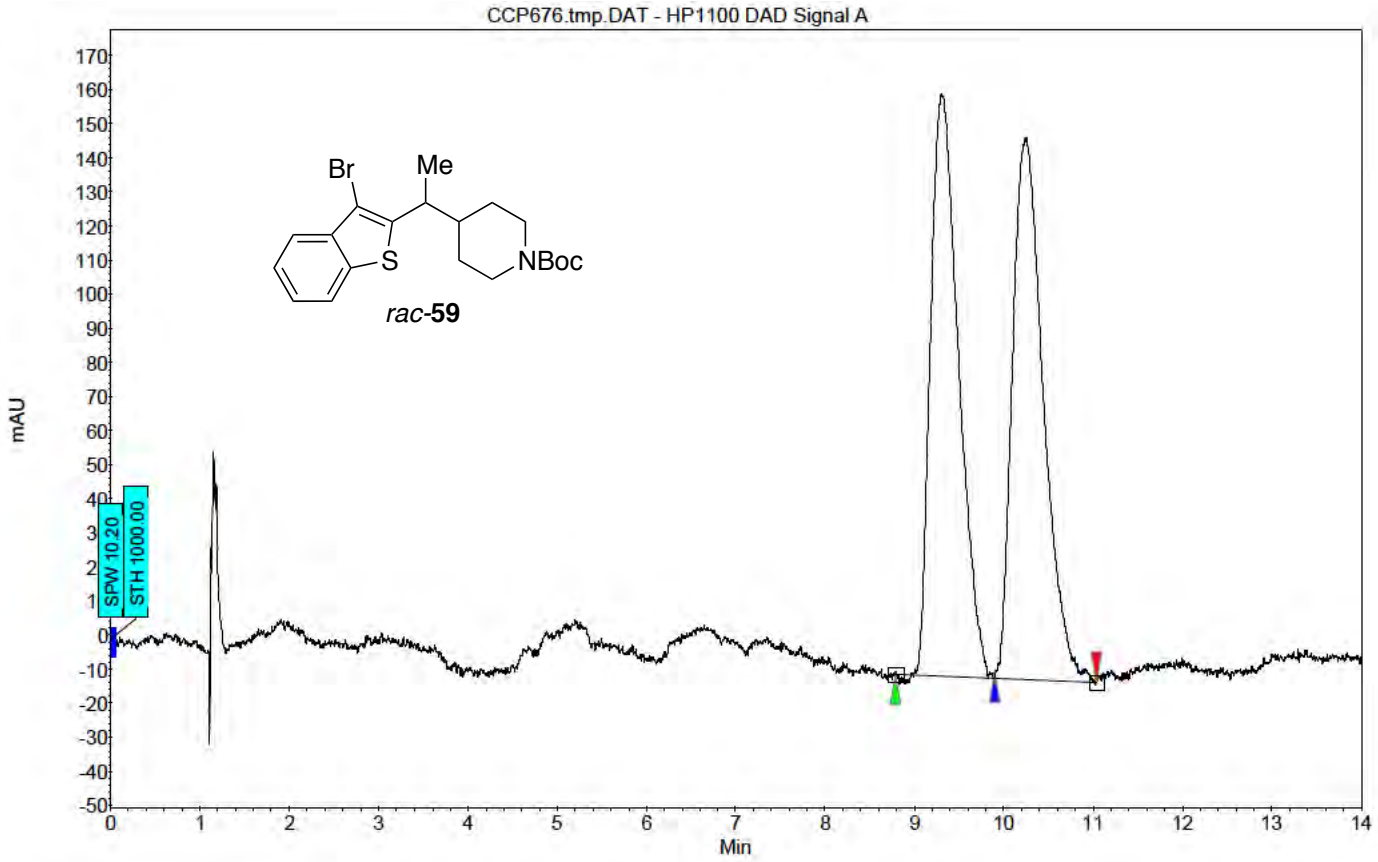


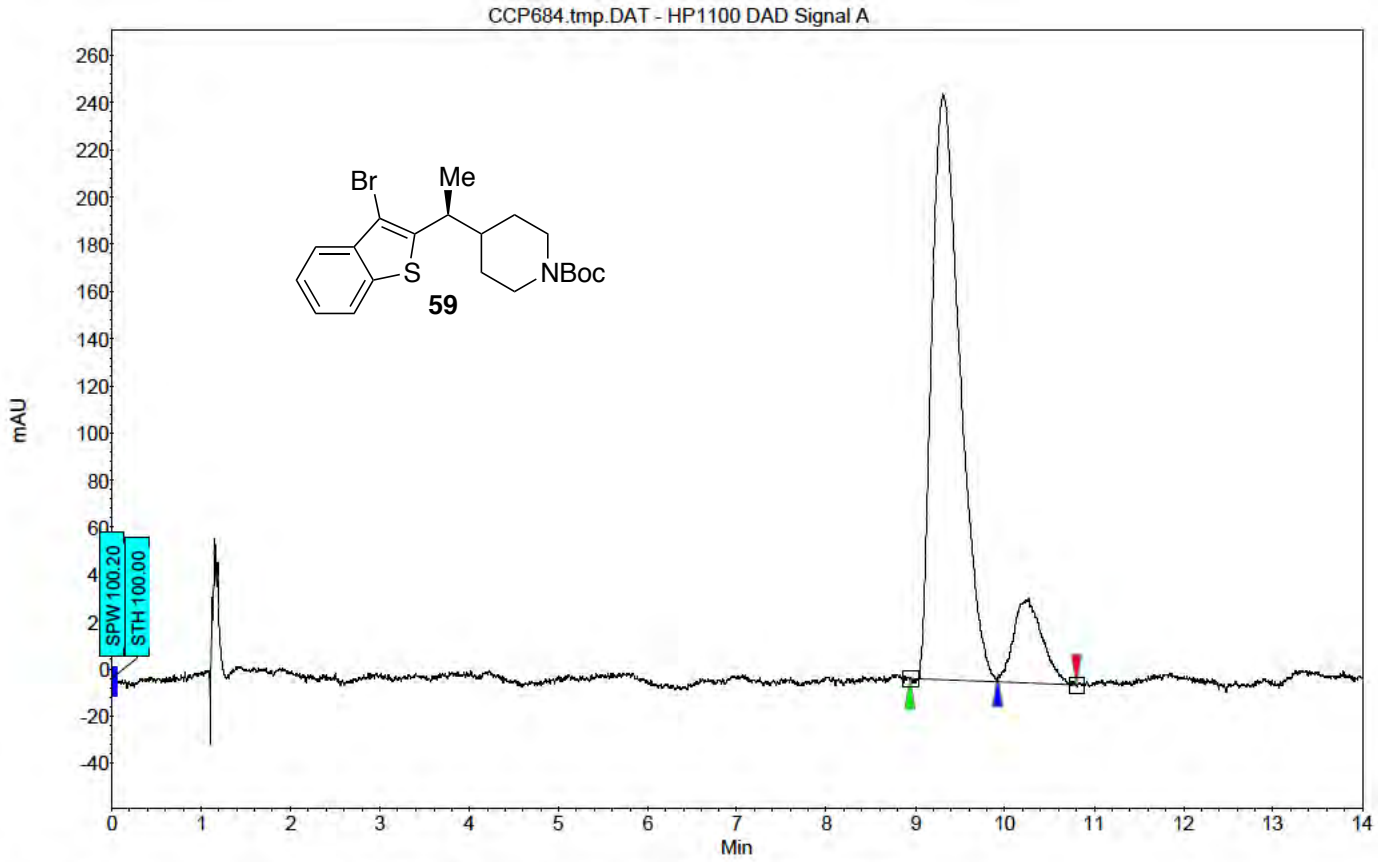
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	3.46	3.61	3.77	0.00	3.22	80.0	7.7	3.224
2	UNKNOWN	3.82	3.98	4.30	0.00	96.78	1781.1	230.5	96.776
Total						100.00	1861.1	238.2	100.000



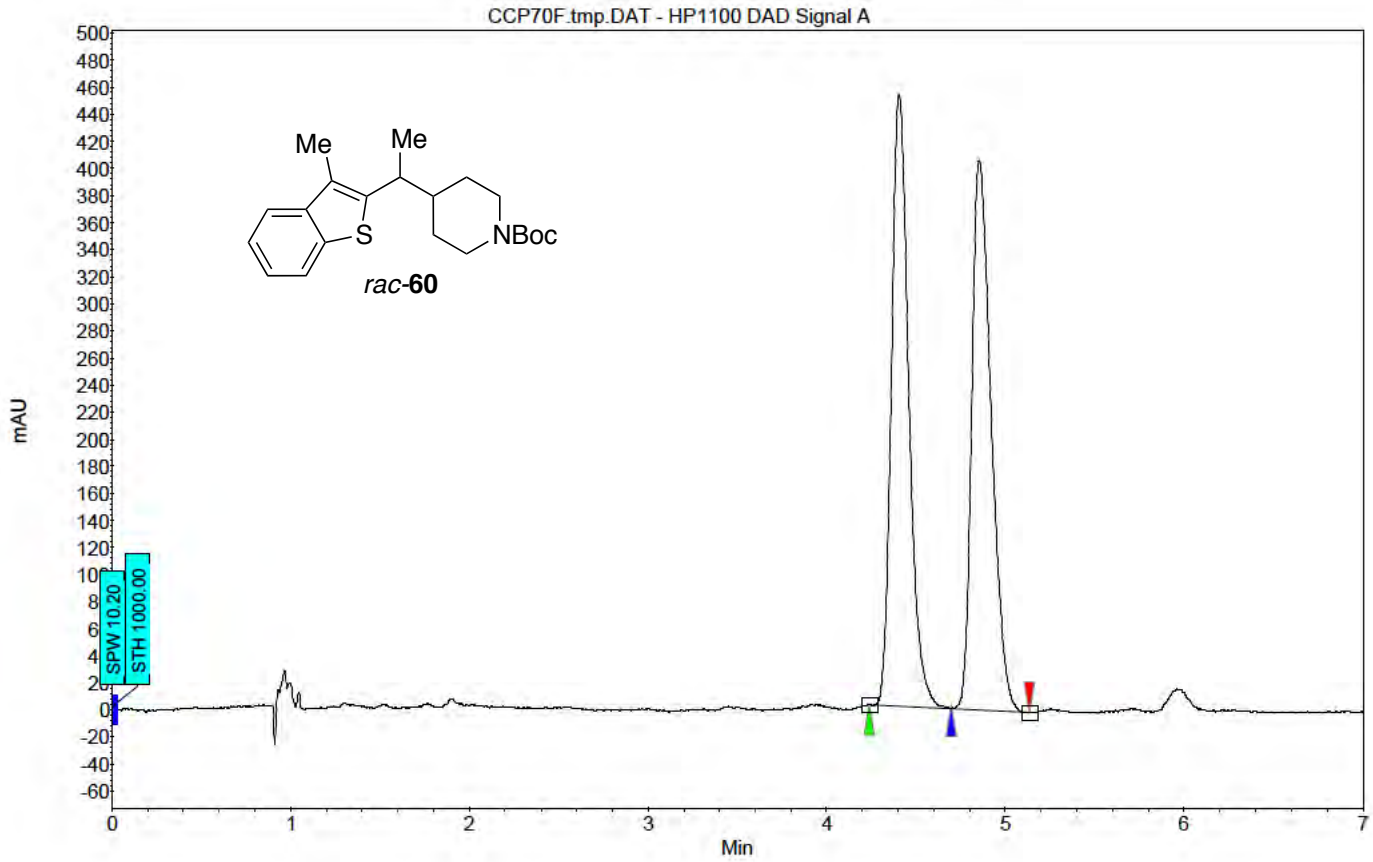


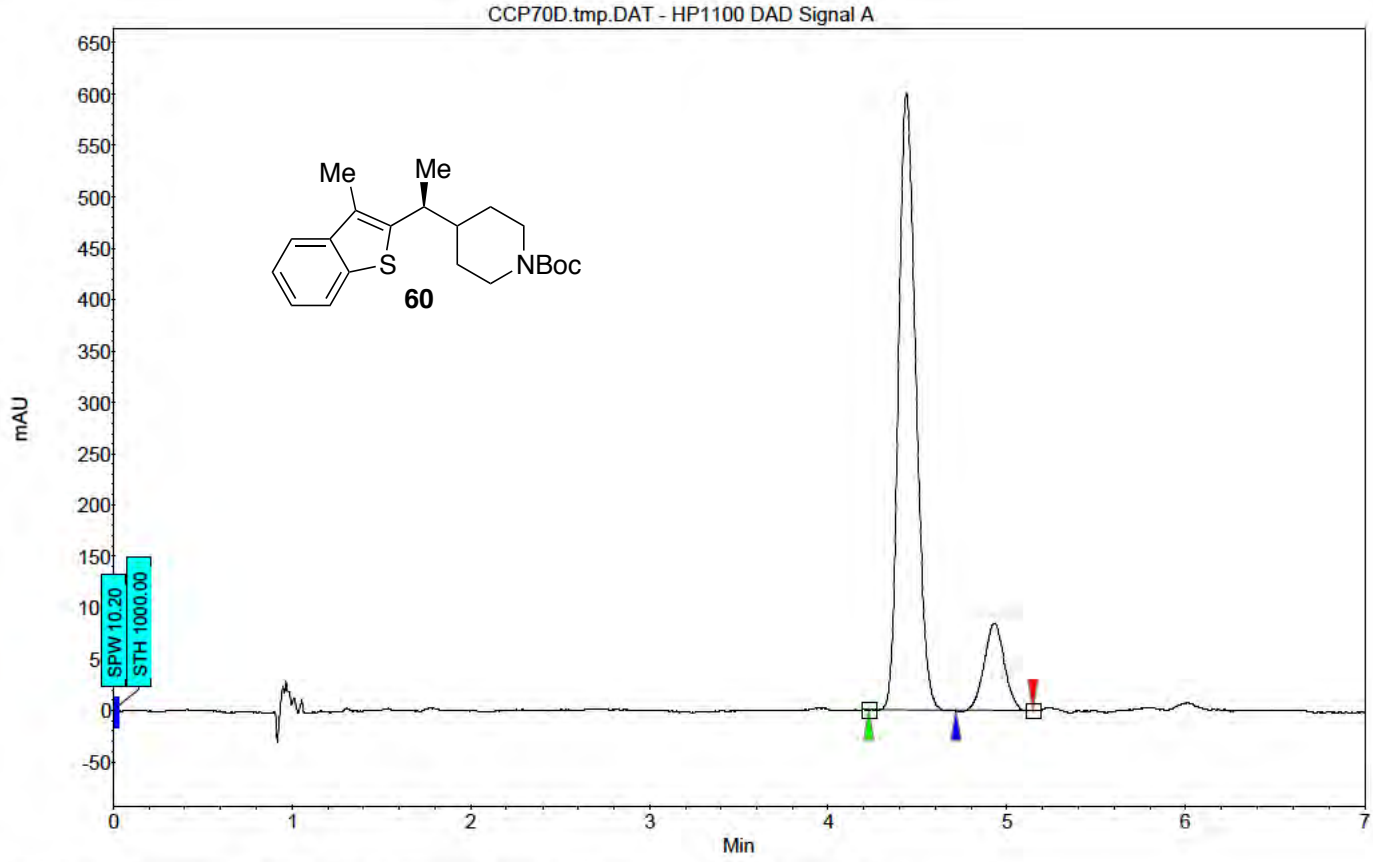
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.18	4.36	4.64	0.00	96.44	692.0	80.8	96.437
2	UNKNOWN	4.84	4.98	5.14	0.00	3.56	24.5	3.0	3.563
Total						100.00	716.5	83.8	100.000





Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.94	9.32	9.92	0.00	87.30	247.9	90.4	87.299
2	UNKNOWN	9.92	10.27	10.80	0.00	12.70	35.5	13.2	12.701
Total						100.00	283.3	103.6	100.000





Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.23	4.44	4.72	0.00	85.91	600.3	67.3	85.908
2	UNKNOWN	4.72	4.93	5.15	0.00	14.09	85.0	11.0	14.092
Total						100.00	685.3	78.3	100.000