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I. General Experimental:

Enzymatic Screening: Alcohol oxidase [EC 1.1.3.13; from *Hansenula* sp. lyophilized powder, 20-40 nominal units/mg protein (Bradford)], peroxidase (EC 1.11.1.7; from horseradish, Type VI, lyophilized powder, 250-330 nominal units/mg solid) and 2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS) were purchased from Sigma. Enzyme assays and cuvette-ISES assays were performed on either a Shimadzu UV-2101PC or a Shimadzu UV-2401PC spectrophotometer. The former instrument is equipped with a CPS-260 six cell positioner with thermoelectric temperature control, while the latter features a twelve cell changer and water-jacketing temperature control (set at 25 °C for all experiments reported). Quartz cuvettes (Hellma) of 1 cm path length and a nominal volume of 1 mL were used. For comparison of ISES reporting rates (mAbs min^{-1} by UV/vis spectrophotometry) in the aqueous layer with actual conversions to halo-carbocyclization product in the organic layer, GC was employed, using a Varian model CP-3380 with flame ionization detection.

Synthesis: Air sensitive reactions were conducted under inert atmosphere (N_2 or Ar) using oven-dried glassware. Methylene chloride was distilled from CaH_2. THF, Et_2O and benzene were distilled from sodium benzophenone ketyl. 1,1,2-Trichloroethane was distilled from P_2O_5. Other reagents were obtained from commercial sources and used without further purification. Reaction progress was monitored by TLC or GC-MS (HP model 5890 GC with model 5972 MS). Flash chromatography was performed using Merck silica gel 60 (230-400 mesh). ^1H NMR spectra were recorded on Bruker-DRX-Avance-600, 500, 400, or 300 MHz instruments with chemical shifts reported relative to residual $CHCl_3$ (7.25 ppm). Proton-decoupled ^{13}C NMR spectra were acquired on Bruker-DRX-Avance-600, 500, 400, or 300 MHz instruments with chemical shifts reported relative to $CDCl_3$ (77.0 ppm). High resolution mass spectra were acquired at the Nebraska Center for Mass Spectrometry (University of Nebraska).

II. Enzyme Standardization:

A. Stock Solutions. The following solutions were made for the standardization of enzymes:

- 2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)diammonium salt (**ABTS**; 2 mM in 100 mM potassium phosphate buffer, pH 7.5)
- Alcohol oxidase (**A0**; from *Hansenula* sp. in100 mM potassium phosphate buffer, pH 7.5; determined to be 0.62 mU/μL, after standardization – *vide infra*)
- Peroxidase [Type VI from horseradish (**HRP**) in 100 mM potassium phosphate buffer, pH 7.5; determined to be 1.46 mU/μL, after standardization – *vide infra*]
- MeOH (aq; 1 mM) and
- H_2O_2 [aq; 0.3% (w/w)]

Enzyme units were calculated by measuring the rate of formation of the ABTS radical cation at 405 nm (*vide infra*), using an extinction coefficient of 36.8 mM^{-1} cm^{-1}.[1] For AO, one S.I. unit is taken as the amount of enzyme catalyzing the oxidation of 1 μmol of methanol per min, with concomitant formation of 1 μmol of H_2O_2 per min. This

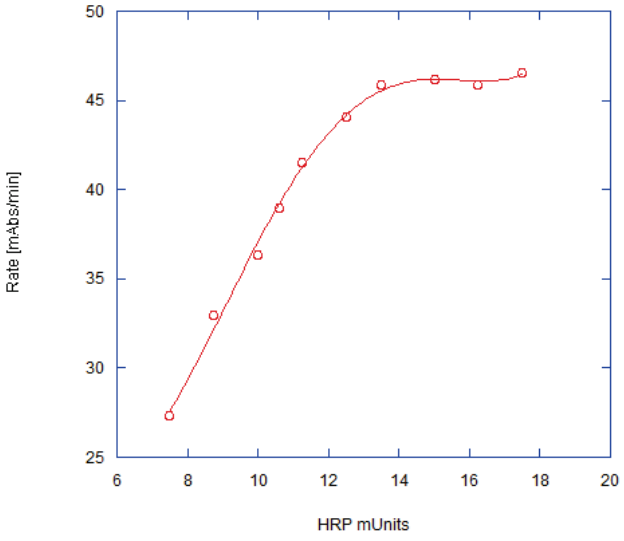
leads to the oxidation of 2 μmol of ABTS to the corresponding radical cation, in a coupled assay with HRP. For HRP, one S.I. unit is taken as the amount of enzyme that will catalyze the reduction of 1.0 μmol of H_2O_2 per min, again resulting in the formation of 2 μmol of the ABTS radical cation per min.

B. Standardization of HRP. The assay cuvette contained ABTS (2 mM; 950 μL of stock sol'n), and HRP (17 μL of stock sol'n). The reaction was initiated by the addition of H_2O_2 [33.3 μL of the 0.3 % (w/w) stock sol'n], which typically gave a rate of 1.83 Abs/min at 25 °C @ 405 nm. This corresponds to 1.46 mU of HRP per μL of stock solution.

C. Standardization of AO. The assay cuvette contained the following components: 2 mM ABTS (950 μL stock), HRP stock solution (20 μL; 29.2 mU), and AO stock solution (20 μL). The reaction was initiated by the addition of 10 μL of 1 mM methanol stock solution, which typically gave a rate of 0.92 Abs/min at 25 °C, 405 nm. This corresponds to 0.62 mU of AO per μL of stock solution.

D. Examination of the Two Enzyme Couple for ISES -Titration of HRP. Since the AO assay is a two enzyme coupled assay, it was important to establish standard conditions for ISES, under which the second enzyme, HRP, is not partially rate limiting. Toward this end, the amount of HRP was titrated up against a fixed amount of AO reporting enzyme, until such point as the overall observed rate leveled off. The assay cuvette contained the following components: ABTS (2 mM, 834-872 μL stock), AO (6.25 mU; 69.7 μL @ 0.09 mU/μL), and MeOH (50 μM; 50 μL of 1 mM stock methanol solution). The reaction was initiated by the addition of HRP (HRP units added varied from 1 – 19 mU - as displayed on the x-axis).

Figure S1: Titration of HRP for the Coupled Assay

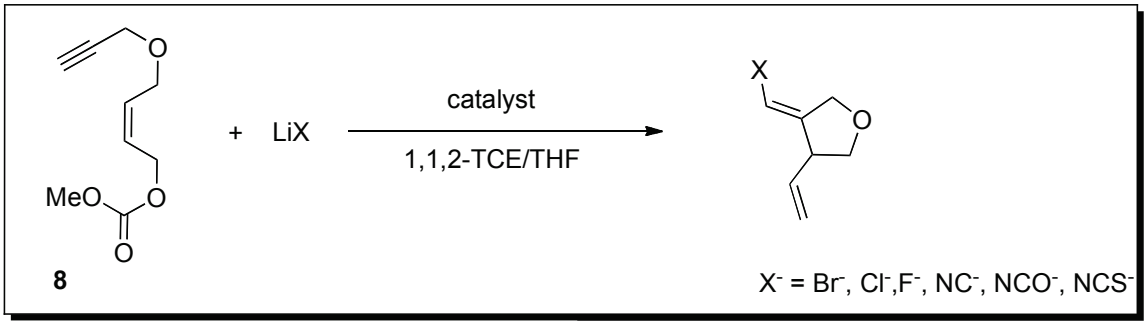


The data are displayed in Figure S1. One can see from the titration curve that for 6.25 mU of AO, 10 mU to 15 mU of HRP defines the cusp, after which the second enzyme is no longer partially rate limiting. This corresponds to an HRP:AO ratio of 1.6-2.4. Therefore, to insure that ISES experiments were run under conditions above this threshold, a twofold excess of HRP units to AO units was employed for all such coupled assays.

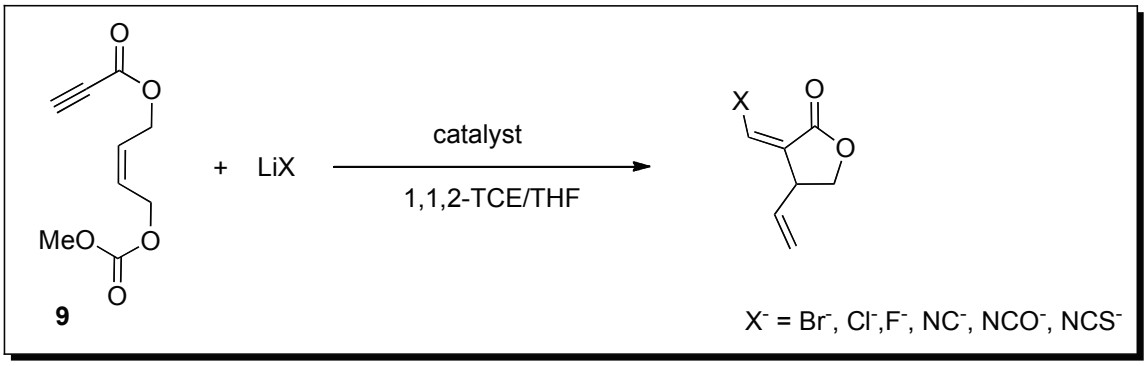
III. Colorimetric-ISES of Metal-(Pseudo)halide Combinations:

Colorimetric ISES was carried out across a set of three model halometalation/carbocyclization test substrates, as depicted in Schemes S1a-1c. A library of 64 metal complex catalyst candidates was assembled, in four distinct arrays of 16 complexes, as delineated in Section IIIA, below.

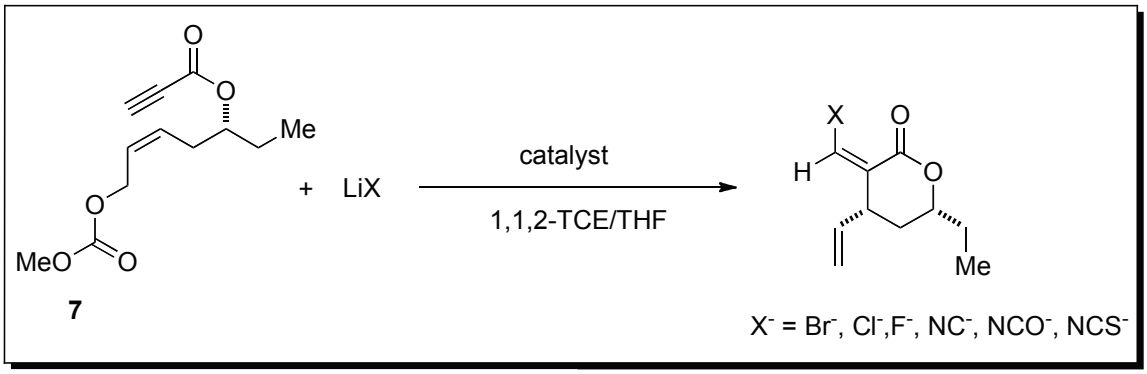
Scheme S1a: Model *5-exo-trig* Ether Cyclization



Scheme S1b: Model *5-exo-trig* Ester Cyclization

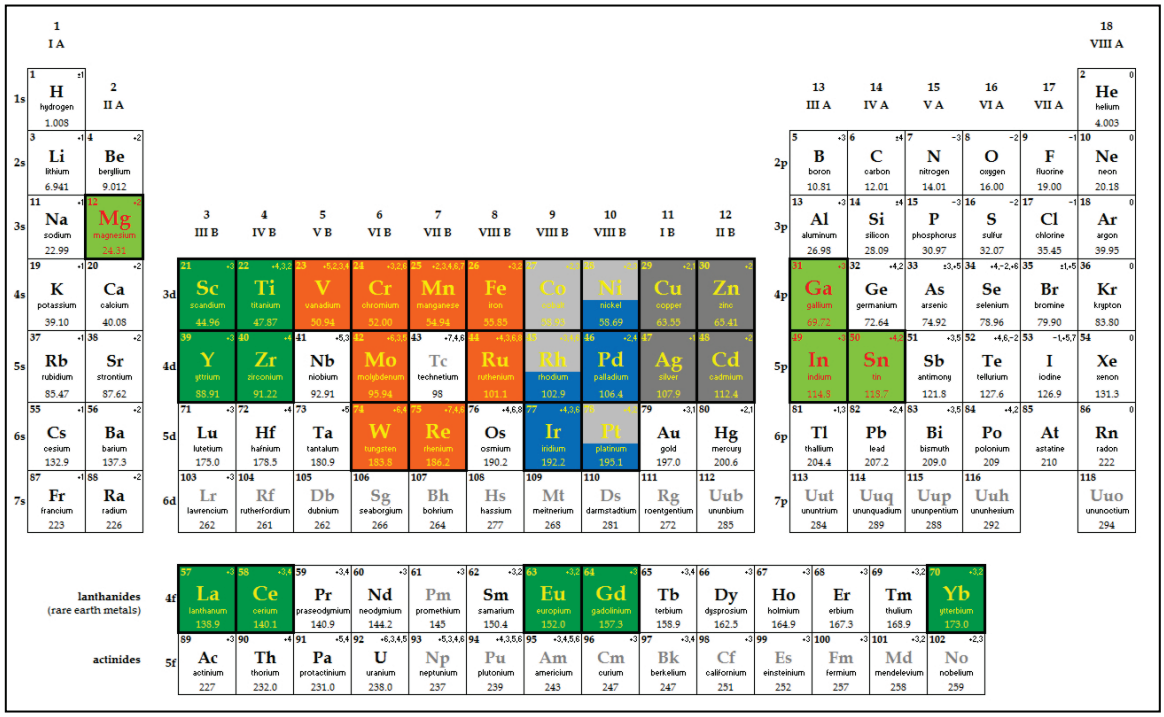


Scheme S1c: Model *6-exo-trig* Ester Cyclization



A. Assembly of Catalyst Candidate Array

Figure S2: Periodic Table Coverage



Color coding (all arrays contain 16 metal complex catalyst candidates):

(1) main group/d3-d4/lanthanide array - ***green***
(2) d5-d8 array - ***orange***
(3) d9-d10 array - ***blue***
(4) d9-s2d10 (groups 9-12) array - ***grey***

(1) main group/d3-d4/lanthanide array

Magnesium bromide	$[MgBr_2]$
Gallium (III) acetylacetonate	$[Ga(acac)_3]$
Indium (II) chloride	$[InCl_2]$
Indium (III) acetylacetonate	$[In(acac)_3]$
Indium (III) trifluoromethanesulfonate	$[In(OTf)_3]$
Indium (III) chloride	$[InCl_3]$
Tin (IV) acetate	$[Sn(OAc)_4]$
Zirconium (IV) chloride	$[ZrCl_4]$
Scandium trifluoromethanesulfonate	$[Sc(OTf)_3]$
Yttrium trifluoromethanesulfonate	$[Y(OTf)_3]$
Lanthanum trifluoromethanesulfonate	$[La(OTf)_3]$
bis(Cyclopentadienyl)titanium dichloride	$[Ti(Cp)_2Cl_2]$
Cerium (III) chloride	$[CeCl_3]$
Europium chloride	$[EuCl_3]$
Gadolinium (III) trifluoromethanesulfonate	$[Gd(OTf)_3]$
Ytterbium (III) trifluoromethanesulfonate	$[Yb(OTf)_3]$

(2) d5-d8 array

Vanadyl acetylacetonate	$[VO(acac)_2]$
Chromium (III) acetate	$[Cr(OAc)_3]$
cis-Tetracarbonylbis(piperidine)molybdenum	$[Mo(pip)_2(CO)_4]$
Tricarbonyltris(propionitrile)molybdenum	$[Mo(NCEt)_3(CO)_3]$
Cycloheptatriene molybdenum tricarbonyl	$[Mo(CO)_3(C_7H_8)]$
Molybdenum hexacarbonyl	$[Mo(CO)_6]$
Molybdenum (II) acetate dimer	$[Mo(OAc)_2]_2$
Molybdenum (III) bromide	$[MoBr_3]$
Mesitylene tungsten tricarbonyl	$[W(CO)_3(Mes)]$
Manganese (III) acetate	$[Mn(OAc)_3]$
i-Propylcyclopentadienyl rhenium tricarbonyl	$[i\text{Pr-CpRe}(CO)_3]$
Iron (II) acetate	$[Fe(OAc)_2]$
Chlorodicarbonyl[1-(*i*-propylamino)-2,3,4,5-tetraphenylcyclopentadienyl]ruthenium (II)	$[RuCl(CO)_2(C_{32}H_{28}N)]$
Norbornadiene molybdenum tetracarbonyl	$[Mo(CO)_4(nbd)]$
(1R,2R)-(-)-1,2-cyclohexanediamine N,N'-bis(3,5-di-t-butylsalicylidene) manganese (III) chloride	[Mn (III) (salen)Cl]
Ruthenium (III) acetylacetonate	$[Ru(acac)_3]$

(3) d9-d10 array

(Cyclooctadiene)iridium (I) chloride dimer	$[Ir(cod)Cl]_2$
(Cyclooctadiene)rhodium (I) chloride dimer	$[Rh(cod)Cl]_2$
Rhodium (I) norbornadiene chloride dimer	$[RhCl(nbd)]_2$
1,3-Dimesityl-4,5-dihydroimidazol-2-ylidene rhodium(cyclooctadiene) chloride	$[Rh(SIMes)(cod)Cl]$
Tris(triphenylphosphine) rhodium (I) chloride	$[Rh(PPh)_3Cl]$
Rhodium (III) acetylacetonate	$[Rh(acac)_3]$
Pentamethylcyclopentadienyl rhodium (III) chloride dimer	$[Rh(Cp^*)Cl_2]_2$
Rhodium (II) bis(acetate) dimer	$[Rh(OAc)_2]_2$
Rhodium (II) bis(trifluoroacetate) dimer	$[Rh(O_2CCF_3)_2]_2$
Rhodium (II) bis(heptafluorobutyrate) dimer	$[Rh(O_2CC_3F_7)_2]_2$
Nickel (II) acetate	$[Ni(OAc)_2]$
Nickel (II) acetylacetonate	$[Ni(acac)_2]$
Platinum (IV) chloride	$[PtCl_4]$
cis-bis(Benzonitrile)dichloroplatinum (II)	$[Cl_2Pt(NCPh)_2]$
Dichloropalladium (II) bis(benzonitrile)	$[Cl_2Pd(NCPh)_2]$
Palladium (II) acetylacetonate	$[Pd(acac)_2]$

(4) d9-s2d10 (groups 9-12) array

Chlorotris(triphenylphosphine) cobalt(I)	$[Co(PPh_3)_3Cl]$
Cobalt (II) chloride	$[CoCl_2]$
(1*R*,2*R*)-(-)-1,2-cyclohexanediamine N,N'-bis(3,5-di-*t*-butylsalicylidene) cobalt (II)	
Chlorodicarbonyl rhodium (I) dimer	$[RhCl(CO)_2]_2$
(Acetylacetonate)(1,5-cyclooctadiene) rhodium (I)	[Rh(acac)(cod)]
Bis(cyclooctadiene)nickel	$[Ni(cod)_2]$
Dichloro [1,1'-bis(diphenylphosphino)ferrocene]nickel	$[NiCl_2(dppf)]$
Dichloro bis(trimethylphosphite)nickel (II)	$[NiCl_2[P(OMe)_3]_2]$
Dichloro bis(triphenylphosphine)nickel (II)	$[NiCl_2(PPh_3)_2]$
Dichloro bis(triphenylphospine)platinum (II)	$[PtCl_2(PPh_3)_2]$
Platinum (II) chloride	$[PtCl_2]$
Cis-bis(acetonitrile)dichloro platinum (II)	$[Cl_2Pt(NCCH_3)_2]$
Copper(II) acetylacetonate	$[Cu(acac)_2]$
Silver acetylacetonate	[Ag(acac)]
Zinc acetate	$[Zn(OAc)_2]$
Cadmium chloride	$[CdCl_2]$

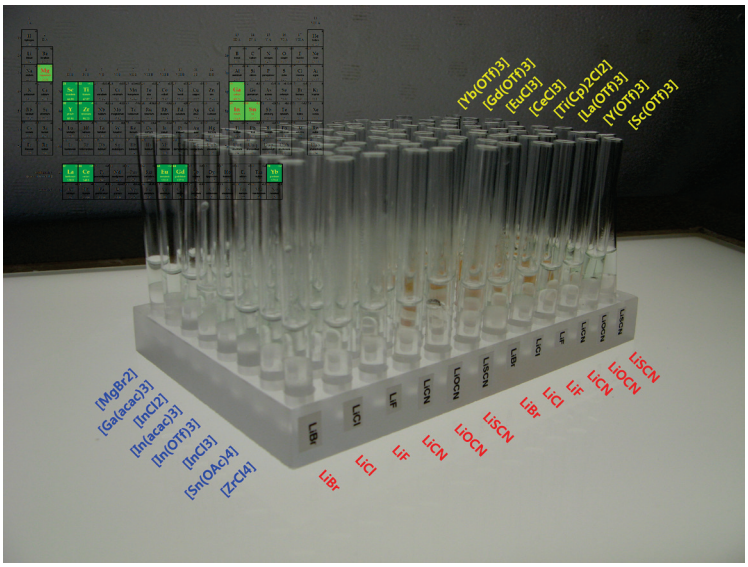
B. Experimental Procedure for Visual Colorimetric-ISES

For ease of visualization, each 96 well plate was outfitted with Fisher disposable culture tubes (6 x 50 mm). Each test reaction was run in a total of only 300 μL (200 μL lower organic layer, 100 μL upper aqueous layer). The aqueous layer consisted of ABTS (2 mM, 96 μL of 2 mM stock), AO (2 μL, 0.62 mU/μL), and HRP (2 μL, 1.5 mU/μL). The organic layer included substrate (33 μL of 300 mM stock in 1,1,2-trichloroethane (TCE), 50 mM final conc.), catalyst (157 μL of 6.4 mM stock in TCE, 5 mM final conc.) and nucleophile [10 μL of 2.0 M stock in THF, 100 mM final conc.]. The organic layer was loaded by the sequential addition of (pseudo)halide, substrate, and catalyst. *Note*: The LiCl and LiOCN nucleophiles were not fully soluble, so these (pseudo)halides were loaded as slurries. LiSCN was added as a solid. This was followed immediately by the addition of the aqueous reporting layer, using a 12 channel Apogent Equalizer multichannel pipetter. Each of the 96 reactions was then monitored colorimetrically for the formation of the green ABTS radical cation indicator, in the aqueous reporting layer. Using this method, for a given substrate, sixteen different metal catalyst candidates were screened, in parallel, against six different nucleophiles, giving a total of ninety six combinations per plate. A total of four such plates was required to screen the entire catalyst candidate library, for a given substrate. This same protocol was followed for the other two substrates, with all assays covering a total of 12 plates (12 x 96 = 1152 combinations) screened.

C. Results

The colorimetric ISES results are organized according to metal array below. Namely, for each array of 16 metal complexes, a photograph of the *5-exo-trig* ether plate is shown, followed by a schematic diagram of each of the three screening plates, for the *5-exo-trig* ether, *5-exo-trig* ester and *6-exo-trig* ester, respectively. These are scored by the naked eye at t = 10 min, as (+) - Abs_{405} ~ 0.1-0.3; (++) - Abs_{405} ~ 0.3-0.5; (+++) - Abs_{405} > 0.5. (Note: Absorbance ranges were estimated by comparing experimenter (JAF and/or SB) scores on test samples with actual spectrophotometer readings @ 405 nm for the same samples).

a. Main group/d3-d4/lanthanide array



***5-exo-trig*-ether**

$[MgBr_2]$	+	-	-	-	-	-	+	-	-	-	+	-	$[Yb(OTf)_3]$
$[Ga(acac)_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Gd(OTf)_3]$
$[InCl_2]$	+	+	+	-	-	-	-	-	-	-	-	-	$[EuCl_3]$
$[In(acac)_3]$	-	-	-	-	-	-	+	-	-	-	+	-	$[CeCl_3]$
$[In(OTf)_3]$	-	-	+	+	-	-	-	-	-	-	-	-	$[Ti(Cp)_2Cl_2]$
$[InCl_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[La(OTf)_3]$
$[Sn(OAc)_4]$	-	-	+	+	-	-	-	-	-	-	-	-	$[Y(OTf)_3]$
$[ZrCl_4]$	-	-	-	-	-	-	+	-	-	-	-	-	$[Sc(OTf)_3]$
	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	

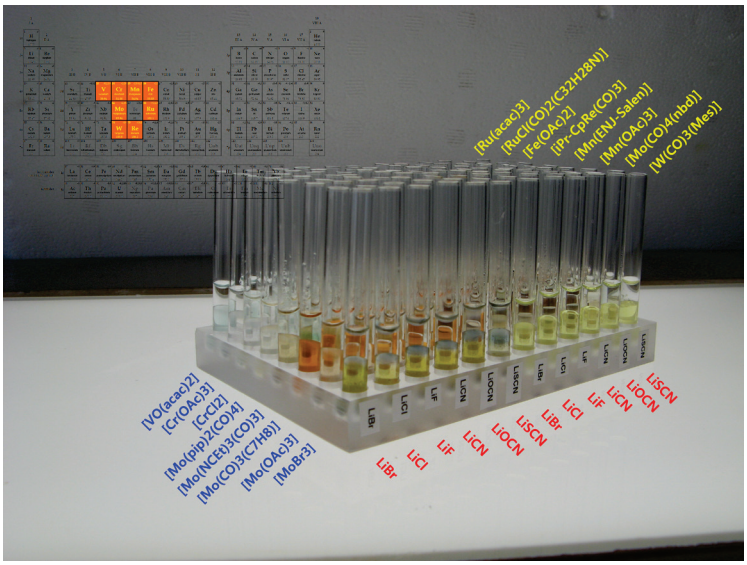
***5-exo-trig* ester**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[MgBr_2]$	+	+	-	-	-	-	-	-	-	-	+	-	$[Yb(OTf)_3]$
$[Ga(acac)_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Gd(OTf)_3]$
$[InCl_2]$	+	+	-	-	-	-	-	-	-	-	-	-	$[EuCl_3]$
$[In(acac)_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[CeCl_3]$
$[In(OTf)_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Ti(Cp)_2Cl_2]$
$[InCl_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[La(OTf)_3]$
$[Sn(OAc)_4]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Y(OTf)_3]$
$[ZrCl_4]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Sc(OTf)_3]$

***6-exo-trig* ester**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[MgBr_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Yb(OTf)_3]$
$[Ga(acac)_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Gd(OTf)_3]$
$[InCl_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[EuCl_3]$
$[In(acac)_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[CeCl_3]$
$[In(OTf)_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Ti(Cp)_2Cl_2]$
$[InCl_3]$	-	-	-	-	-	-	-	-	-	-	+	-	$[La(OTf)_3]$
$[Sn(OAc)_4]$	-	-	-	-	-	-	-	-	-	-	+	-	$[Y(OTf)_3]$
$[ZrCl_4]$	-	-	-	-	-	-	-	-	-	-	+	-	$[Sc(OTf)_3]$

b. d5-d8 array



***5-exo-trig*-ether**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[VO(acac)_2]$	-	-	-	-	-	-	+	+	+	+	+	+	$[Ru(acac)_3]$
$[Cr(OAc)_3]$	+	+	+	+	-	-	+	+	+	+	+	+	$[RuCl(CO)_2(C_{32}H_{28}N)]$
$[CrCl_2]$	+	-	-	+	+	-	+	+	+	+	+	-	$[Fe(OAc)_2]$
$[Mo(pip)_2(CO)_4]$	+	-	-	-	+	-	+	+	-	+	+	-	[*i*Pr-CpRe$(CO)_3$]
$[Mo(NCEt)_3(CO)_3]$	+	-	-	-	-	+	+	-	-	-	-	-	[Mn(III)-salen-Cl]
$[Mo(CO)_3(C_7H_8)]$	+	+	+	+	+	-	+	-	-	-	-	-	$[Mn(OAc)_3]$
$[Mo(OAc)_2]_2$	+	+	-	+	+	-	-	-	-	-	-	-	$[Mo(CO)_4(nbd)]$
$[MoBr_3]$	+	+	+	+	+	+	+	+	+	+	+	+	$[W(CO)_3(Mes)]$

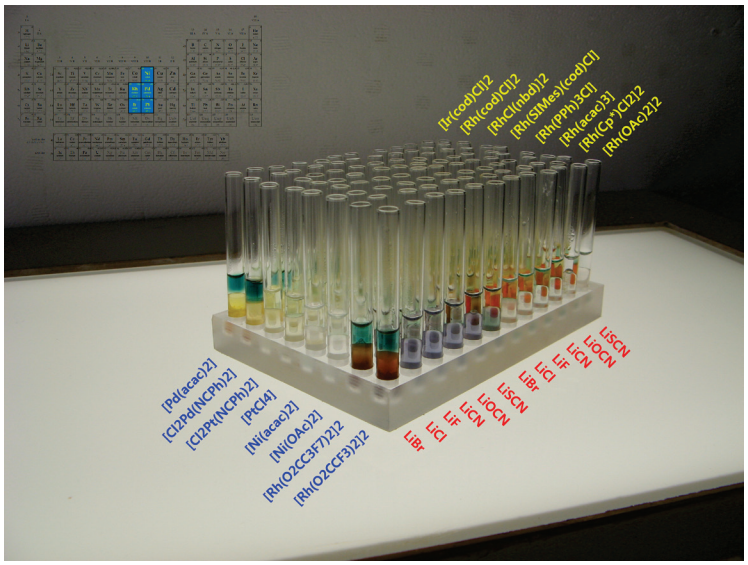
***5-exo-trig* ester**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[VO(acac)_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Ru(acac)_3]$
$[Cr(OAc)_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[RuCl(CO)_2(C_{32}H_{28}N)]$
$[CrCl_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Fe(OAc)_2]$
$[Mo(pip)_2(CO)_4]$	-	-	-	-	-	-	-	-	-	-	-	-	[*i*Pr-CpRe$(CO)_3$]
$[Mo(NCEt)_3(CO)_3]$	+	-	-	-	-	-	-	-	-	-	-	-	[Mn(III)-salen-Cl]
$[Mo(CO)_3(C_7H_8)]$	+	-	-	-	-	-	-	-	-	-	-	-	$[Mn(OAc)_3]$
$[Mo(OAc)_2]_2$	-	-	-	-	-	-	+	-	-	-	-	-	$[Mo(CO)_3(nbd)]$
$[MoBr_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[W(CO)_3(Mes)]$

***6-exo-trig* ester**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[VO(acac)_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Ru(acac)_3]$
$[Cr(OAc)_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[RuCl(CO)_2(C_{32}H_{28}N)]$
$[CrCl_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Fe(OAc)_2]$
$[Mo(pip)_2(CO)_4]$	-	-	-	-	-	-	-	-	-	-	-	-	[*i*Pr-CpRe$(CO)_3$]
$[Mo(NCEt)_3(CO)_3]$	-	-	-	-	-	-	-	-	-	-	-	-	[Mn(III)-salen-Cl]
$[Mo(CO)_3(C_7H_8)]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Mn(OAc)_3]$
$[Mo(OAc)_2]_2$	-	-	-	-	-	-	-	-	-	-	-	-	$[Mo(CO)_3(nbd)]$
$[MoBr_3]$	-	-	-	-	-	-	-	-	-	-	-	-	$[W(CO)_3(Mes)]$

c. d9-d10 array



***5-exo-trig*-ether**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[Pd(acac)_2]$	+++	+	-	+	-	-	+	+	+	+	+	+	$[Ir(cod)Cl]_2$
$[Cl_2Pd(NCPh)_2]$	+++	++	-	++	-	++	-	-	-	-	-	+	$[Rh(cod)Cl]_2$
$[Cl_2Pt(NCPh)_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[RhCl(nbd)]_2$
$[PtCl_4]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Rh(SIMes)(cod)Cl]$
$[Ni(acac)_2]$	-	-	-	-	-	-	+	+	+	+	+	+	$[Rh(PPh)_3Cl]$
$[Ni(OAc)_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Rh(acac)_3]$
$[Rh(O_2CC_3F_7)_2]_2$	+++	-	-	+	-	-	-	-	-	-	-	+	$[Rh(Cp^*)Cl_2]_2$
$[Rh(O_2CCF_3)_2]_2$	+++	-	-	-	+	-	-	-	-	-	-	-	$[Rh(OAc)_2]_2$

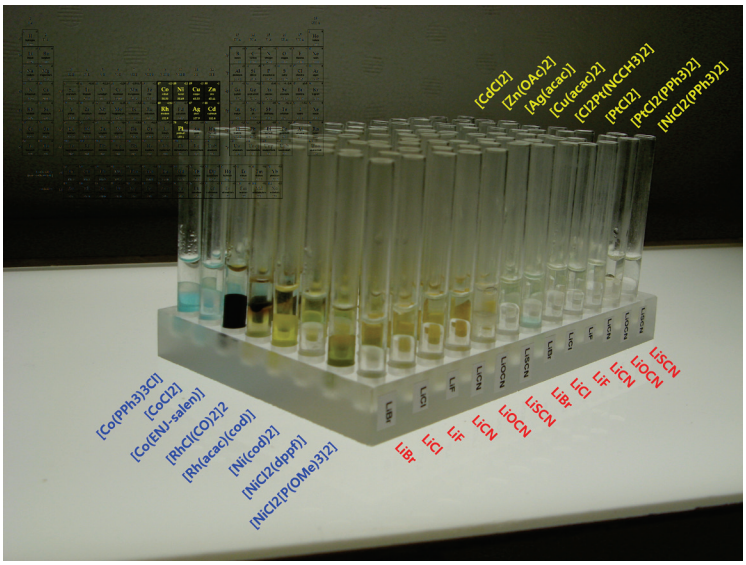
***5-exo-trig* ester**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[Pd(acac)_2]$	++	+	-	-	-	-	+	+	+	+	+	+	$[Ir(cod)Cl]_2$
$[Cl_2Pd(NCPh)_2]$	++	+	-	-	-	-	-	-	-	-	-	-	$[Rh(cod)Cl]_2$
$[Cl_2Pt(NCPh)_2]$	-	-	-	-	-	-	+	-	-	+	-	-	$[RhCl(nbd)]_2$
$[PtCl_4]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Rh(SIMes)(cod)Cl]$
$[Ni(acac)_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Rh(PPh)_3Cl]$
$[Ni(OAc)_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Rh(acac)_3]$
$[Rh(O_2CC_3F_7)_2]_2$	+++	-	-	+	-	-	-	-	-	-	-	+	$[Rh(Cp^*)Cl_2]_2$
$[Rh(O_2CCF_3)_2]_2$	+++	-	-	-	+	-	-	-	-	-	-	-	$[Rh(OAc)_2]_2$

***6-exo-trig* ester**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[Pd(acac)_2]$	+	-	-	-	-	-	-	-	-	-	-	-	$[Ir(cod)Cl]_2$
$[Cl_2Pd(NCPh)_2]$	++	+	+	++	-	+	-	-	-	-	-	-	$[Rh(cod)Cl]_2$
$[Cl_2Pt(NCPh)_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[RhCl(nbd)]_2$
$[PtCl_4]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Rh(SIMes)(cod)Cl]$
$[Ni(acac)_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Rh(PPh)_3Cl]$
$[Ni(OAc)_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Rh(acac)_3]$
$[Rh(O_2CC_3F_7)_2]_2$	++	-	-	-	+	-	-	-	-	-	-	-	$[Rh(Cp^*)Cl_2]_2$
$[Rh(O_2CCF_3)_2]_2$	++	-	-	-	-	-	-	-	-	-	-	-	$[Rh(OAc)_2]_2$

d. d9-s2d10 (groups 9-12) array



***5-exo-trig*-ether**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[Co(PPh_3)_3Cl]$	-	-	-	-	-	-	-	-	-	-	-	-	$[CdCl_2]$
$[CoCl_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Zn(OAc)_2]$
[Co(II)-salen]	-	-	-	-	-	-	-	-	-	-	-	-	[Ag(acac)]
$[RhCl(CO)_2]_2$	-	-	-	-	-	-	-	-	-	-	-	-	$[Cu(acac)_2]$
[Rh(acac)(cod)]	-	-	-	-	-	-	-	-	-	-	-	-	$[Cl_2Pt(NCCH_3)_2]$
$[Ni(cod)_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[PtCl_2]$
$[NiCl_2(dppf)]$	-	-	-	-	-	-	-	-	-	-	-	-	$[PtCl_2(PPh_3)_2]$
$[NiCl_2[P(OMe)_3]_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[NiCl_2(PPh_3)_2]$

***5-exo-trig* ester**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[Co(PPh_3)_3Cl]$	-	-	-	-	+	-	-	-	-	-	-	-	$[CdCl_2]$
$[CoCl_2]$	-	+	+	+	-	+	-	-	-	-	-	-	$[Zn(OAc)_2]$
[Co(II)-salen]	-	-	-	-	-	-	-	-	-	-	-	-	[Ag(acac)]
$[RhCl(CO)_2]_2$	-	-	-	-	-	-	-	-	-	-	-	-	$[Cu(acac)_2]$
[Rh(acac)(cod)]	-	-	-	-	-	-	-	-	-	-	-	-	$[Cl_2Pt(NCCH_3)_2]$
$[Ni(cod)_2]$	+	+	+	+	-	+	-	-	-	-	-	-	$[PtCl_2]$
$[NiCl_2(dppf)]$	-	-	-	-	-	-	+	+	+	+	-	+	$[PtCl_2(PPh_3)_2]$
$[NiCl_2[P(OMe)_3]_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[NiCl_2(PPh_3)_2]$

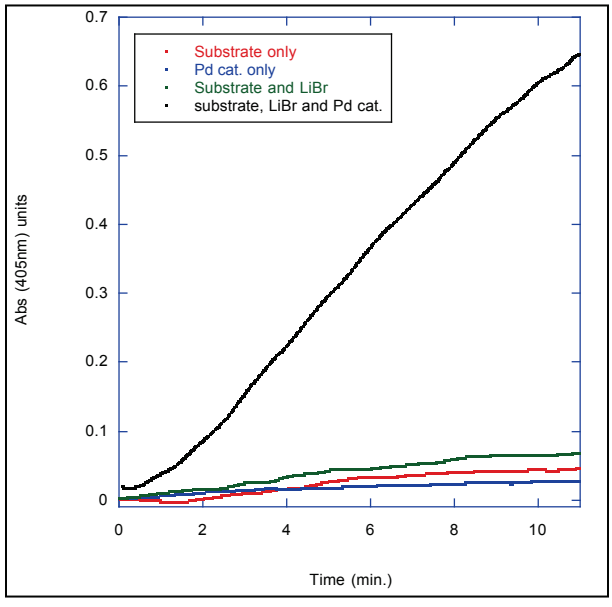
***6-exo-trig* ester**

	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	LiBr	LiCl	LiF	LiCN	LiOCN	LiSCN	
$[Co(PPh_3)_3Cl]$	-	-	-	-	-	-	-	-	-	-	-	-	$[CdCl_2]$
$[CoCl_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[Zn(OAc)_2]$
[Co(II)-salen]	-	-	-	-	-	-	-	-	-	-	-	-	[Ag(acac)]
$[RhCl(CO)_2]_2$	-	-	-	-	-	-	-	-	-	-	-	-	$[Cu(acac)_2]$
[Rh(acac)(cod)]	-	-	-	-	-	-	-	-	-	-	-	-	$[Cl_2Pt(NCCH_3)_2]$
$[Ni(cod)_2]$	+	+	+	-	-	+	-	-	-	-	+	-	$[PtCl_2]$
$[NiCl_2(dppf)]$	-	-	-	-	-	-	+	+	+	+	-	-	$[PtCl_2(PPh_3)_2]$
$[NiCl_2[P(OMe)_3]_2]$	-	-	-	-	-	-	-	-	-	-	-	-	$[NiCl_2(PPh_3)_2]$

IV. Control Experiments for ISES

Prior to seeking to quantitate relative rates for 'hits" of interest from colorimetric ISES, control experiments were run to establish the fidelity of the assay. Negative controls were run to probe for any spurious colorimetric changes due to interaction with the reporting enzymes or cofactor with transition metal, halide salt and/or substrate. All such control cuvettes were outfitted with the complete upper enzymatic (AO/HRP) reporting layer, plus the reduced ABTS peroxidase co-substrate. The results are displayed in Figure S3, and demonstrate negligible rates for all negative control cuvettes, in comparison with the rate exhibited by the positive control cuvette.

Figure S3: Control Experiments-Background Rates



Specifically, the following conditions were employed. In each control cuvette, the upper aqueous layer contained ABTS (2 mM; 480 μL of 2 mM stock), AO (10 μL; 0.62 mU/μL), and HRP (10 μL; 1.5 mU/μL). The organic layer consisted of 1,1,2-trichloroethane containing 5% THF (v/v -300 μL total volume).

- In the first (positive) control cuvette, the organic layer contained 15 μmol of *5-exo-trig* ester substrate, 30 μmol of LiBr, and 1.5 μmol of dichloro(bisbenzonitrile)-palladium(II).
- The second control cuvette lacked catalyst, containing only 15 μmol of substrate and 30 μmol of LiBr.
- The third control cuvette lacked both catalyst and halide salt, with the organic layer containing only 15 μmol of substrate.
- Finally, the fourth control cuvette contained catalyst [1.5 μmol of the dichloro(bisbenzonitrile)palladium(II)], but lacked substrate and halide salt.

In all control experiments, the organic layers were loaded first, followed immediately by careful loading of the aqueous layers thereupon. Control rates were followed by parallel observation of ABTS radical cation formation (405 nm) with a Shimadzu UV/Vis 2101 PC spectrophometer, with automated six-cell changer.

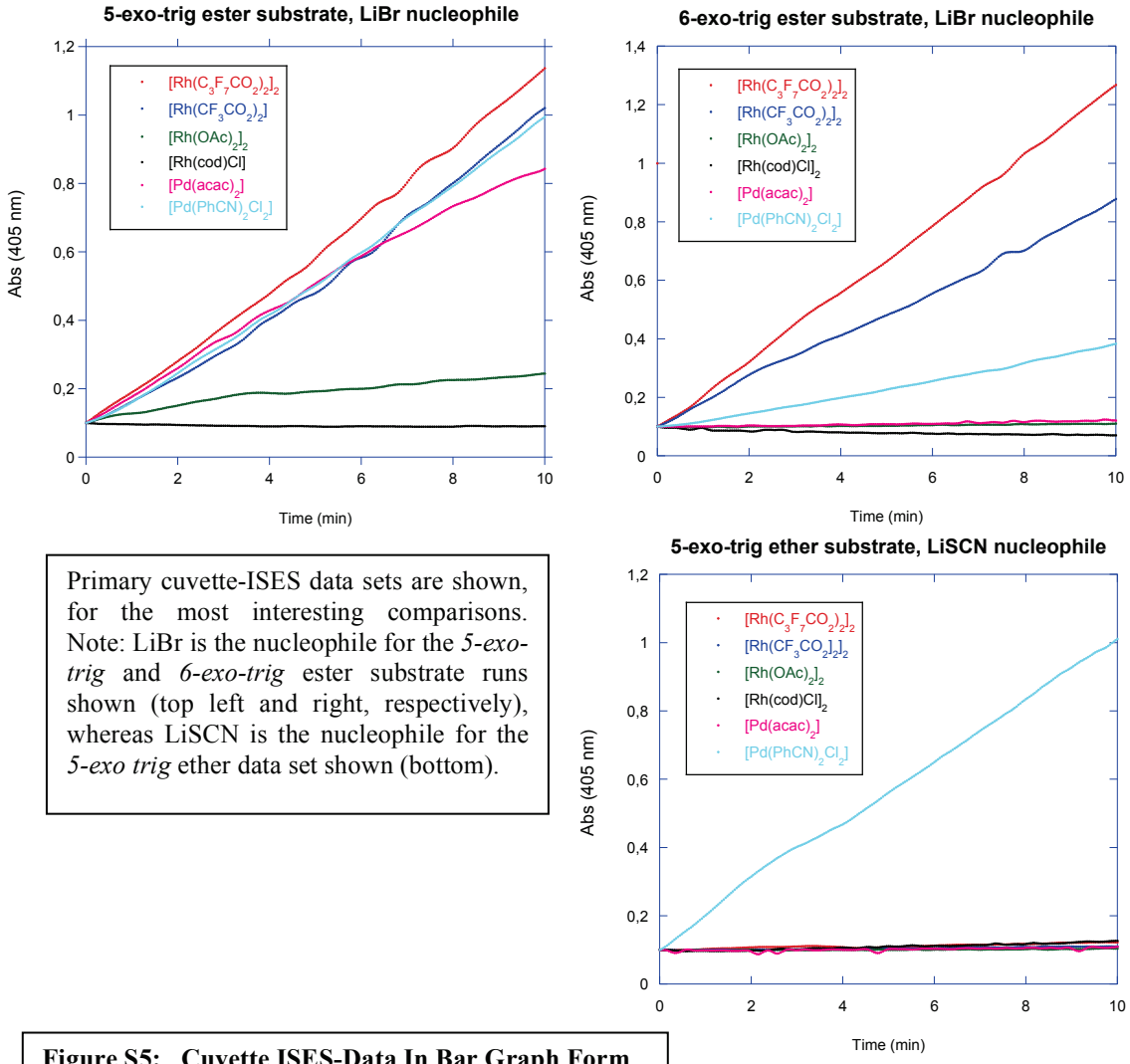
V. Cuvette-ISES

Next, cuvette-ISES was used to obtain a more quantitative readout on relative rates, for catalyst combinations of interest, arising from the first pass, colorimetric-ISES overview. These generally correspond to those catalytic combinations scoring (++) or greater in the colorimetric screen, or to important negative controls (e.g. Rh(I), Rh(III) and $[Rh(II)(OAc)_2]_2$, in light of the positive results seen for the Rh(II) perfluorocarboxylate catalysts).

For each catalyst screen, the upper aqueous layer contained ABTS (2 mM, 480 μL of 2 mM stock), AO (10 μL, 0.62 mU/μL), and HRP (10 μL, 1.5 mU/μL). The organic layer contained substrate (43 μL of 350 mM stock in TCE, 50 mM final conc.), catalyst (242 μL of 6.2 mM stock in TCE, 5 mM final conc.), and (pseudo)halide salt (15 μL, 2.0 M in THF, 100 mM final conc.). Immediately following preparation of the organic layers, the upper aqueous layers were loaded thereupon. All six cuvettes were then followed by the parallel observation at 405 nm, spectrophotometrically, with the multi-cell positioner held at 25 °C, as before.

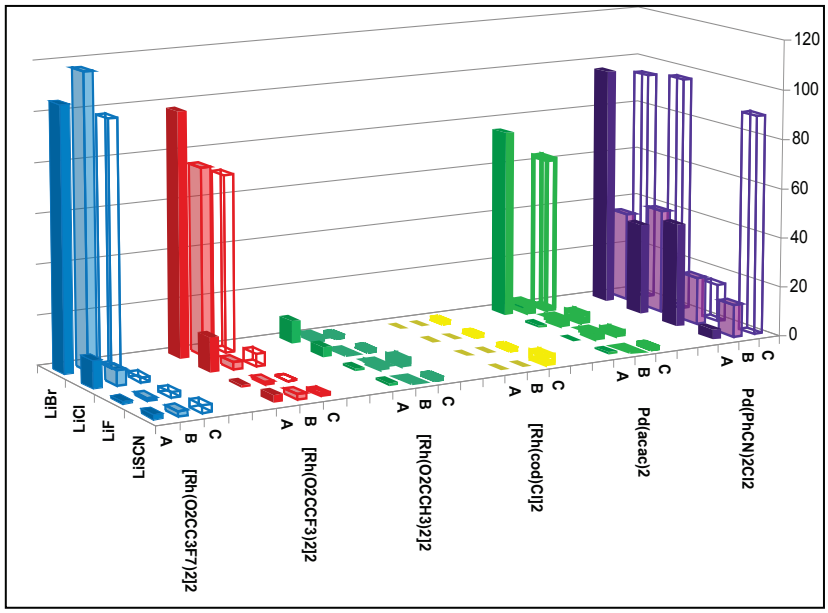
Figure S4 includes primary cuvette-ISES data for parallel runs involving the most interesting active catalytic combinations (primarily Rh(II)-perfluorocarboxylates, $Pd(II)(acac)_2$ and $(PhCN)_2PdCl_2$ with LiBr and the latter catalyst also with LiSCN) and key control catalysts (i.e. other Rh(II) and Rh(I) complexes, for example). A more complete set of cuvette-ISES data is plotted, in four dimensional bar graph form, in Figure S5.

Figure S4 – Typical Cuvette-ISES Data Across All Three Model Substrates



Primary cuvette-ISES data sets are shown, for the most interesting comparisons. Note: LiBr is the nucleophile for the *5-exo-trig* and *6-exo-trig* ester substrate runs shown (top left and right, respectively), whereas LiSCN is the nucleophile for the *5-exo trig* ether data set shown (bottom).

Figure S5: Cuvette ISES-Data In Bar Graph Form

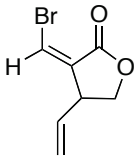
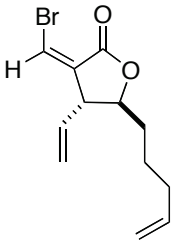
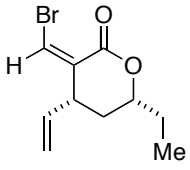
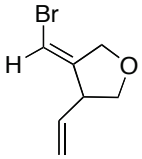
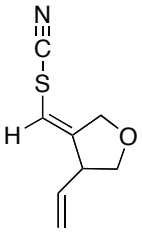


Four dimensional bar graph, depicting the information-rich, semi-quantitative readout from cuvette-ISES. Along the x-axis and y-axis are displayed, respectively, candidate metal complex and (pseudo)halide salts, screened. The z-axis delineates the observed rate (in $mAbs_{405}$/min). The x-axis is further subdivided to provide substrate specificity information: (i) filled bars = *5-exo-trig* ester; (ii) lightly shaded bars = *6-exo-trig* ester; (iii) hollow bars = *5-exo trig* ether (left to right).

VI. Comparison with Standard RB-Flask Conditions

Catalytic combinations identified as "hits" by colorimetric and cuvette-ISES were next examined under standard synthetic organic reaction conditions. The first goal here was to isolate, identify and characterize the major reaction product under such conditions, to firmly establish the viability of the desired halometalation-carbocyclization manifold. A secondary, and equally important, goal here was to examine whether relative rate rankings generated by cuvette-ISES, under biphasic conditions, correlate well with observed conversions/isolated yields under standard, essentially anhydrous organic reaction conditions. From a comparison of the conversions in Table S1, and the bar heights in Figure S5, a good correlation is seen between isolated yields under standard conditions, and relative rates estimated by biphasic-ISES. In fact, as is the case for the bromomethylene THF-ether product, ISES is very useful for screening reactions producing volatile products. In such cases, ISES estimates may provide a more accurate measure of catalyst efficiency than would be obtained with typical isolation procedures, owing to product volatility.

Table S1: Conversions for Halo-Carbocyclizations Under Standard Organic Reaction Conditions

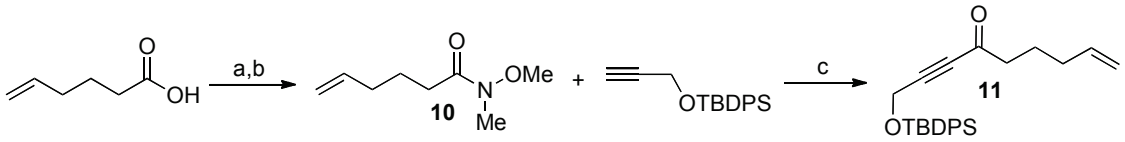
	Halometalation-Carbocyclization Product				
Catalyst					
$[Rh(C_3F_7CO_2)_2]_2$	90%	85% (11:1 dr)*	64% (> 20:1 dr)*	66%** (37%)	< 1%
$[Rh(CF_3CO_2)_2]_2$	90%	80% (10:1 dr)*	58% (>20:1 dr)*	62%** (42%)	-
$[Pd(acac)_2]$	94%	89% (19:1 dr)	< 15%*	73%**	-
$[Pd(PhCN)_2Cl_2]$	95%	92% (20:1 dr)	30% (>20:1 dr)*	85%** (48%)	89%*

*Reactions carried out at 60 °C for 6 h. **Yields determined by GC using a calibration curve generated with known quantities of authentic isolated product. Note that isolated yields (in parentheses) are lower than conversions established by GC, due to the volatility of the substituted tetrahydrofuran reaction product, in this case.

VII. Synthesis of Cyclization Substrates

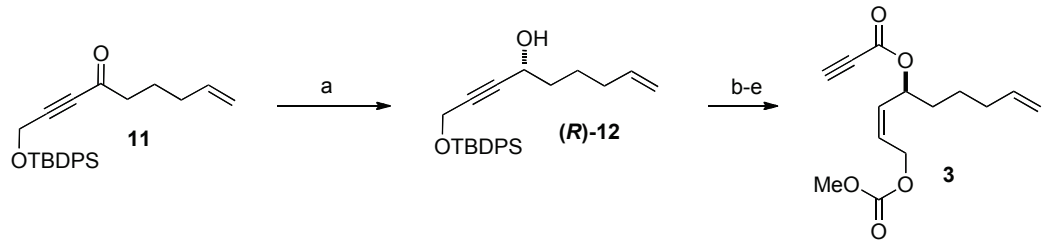
A. Xanthanolide core-leading 5-*exo-trig* ester and model ester

Scheme S1: Preparation of Key Ynone Intermediate



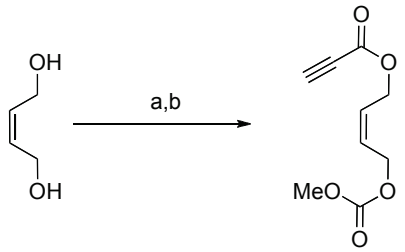
Reagents and Conditions: (a) CDI (1.3 eq), THF 93%, (b) N,O-dimethylhydroxylamine hydrochloride (1.3 eq.), NaH(cat), THF 92%, (c) nBuLi, THF -78 ^{o}C, 84 %.

Scheme S2: Synthesis of the Xanthanolide Core-leading 5-*exo-trig* Ester



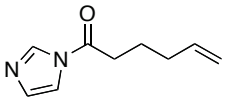
Reagents and Conditions: (a) *(R)*-Alpine-Borane (2.0 eq.) 75%, 91% ee, (b) Lindlar's catalyst (10% w/w), MeOH w/3% pyridine, H_2 (balloon pressure) 90% (c) TBAF (2.0 eq.), THF 98% (d) methylchloroformate (2 eq), pyridine, 0 ^{o}C, 68% (e) propiolic acid (2.0 eq), PPh_3 (2.0 eq.), DIAD (2.0 eq.), THF, 0 ^{o}C 84%.

Scheme S3: Synthesis of the Unsubstituted Model 5-*exo-trig* Ester



Reagents and conditions: (a) methyl chloroformate (0.5 eq), pyridine, 0^{o} C, 70%, (b) DIAD (2 eq), PPh_3 (2 eq.), propiolic acid (2.0 eq.), THF, 0^{o} C, 85%

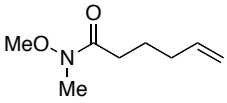
5-Hexenoyl Imidazolide



To solution of 5-hexenoic acid (8.9 mL, 75 mmol) in THF (100 mL) was added carbonyl di-imidazole (12.2 g, 75 mmol). The resulting mixture was stirred at room temperature overnight. The THF was then removed under reduced pressure and the resulting residue was dissolved in diethyl ether (100 mL) and washed with 3 portions of saturated NH_4Cl (aq), $NaHCO_3$ (aq) and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the title imidazolide (11.2 g, 91%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.89 (apt. p, J = 7.2 Hz, 1H), 2.16 ppm (apt. q, J = 7.1 Hz, 2H), 2.83 (t, J = 7.4 Hz, 2H), 5.03 (m, 1H), 5.76 (ddt, J = 16.9, 10.3, 6.7 Hz, 1H), 7.06 (s, 1H), 7.44 (s, 1H), 8.12 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 22.9, 32.6, 34.1, 115.9, 116.1, 130.9, 136.0, 136.9, 169.3.

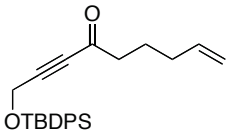
N-Methoxy-N-Methylhex-5-enamide (10)



To a mixture of 5-hexenoyl imidazolide (5.0 g, 30.4 mmol), and N,O- dimethylhydroxylamine hydrochloride (4.46 g, 45.7 mmol) in THF (80 mL) was added NaH (cat.). The resulting mixture was stirred at rt overnight. The THF was then removed under reduced pressure and the resulting residue was dissolved in 100 mL of diethyl ether and washed with 3 x sat'd NH_4Cl (aq), $NaHCO_3$ (aq.), and brine. The organic layer was then dried over Na_2SO_4, filtered, and concentrated in vacuo to give **10** (4.44 g, 93%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ 1.71 (app q, J = 7 Hz, 2H), 2.10 (app q, J = 7 Hz, 2H), 2.40 (t, J = 7.5 Hz, 2H), 3.15 (s, 3H), 3.65 (s, 3H), 4.98 (m, 1H), 5.78 (ddt, J = 16.9, 10.3, 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 23.7, 31.1, 32.2, 33.2, 61.1, 115.0, 138.1, 174.4.

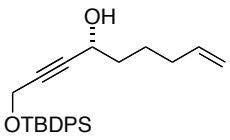
1-(*tert*-Butyldiphenylsilyloxy)non-8-en-2-yn-4-one (11)



To a solution of *tert*-butyldiphenylsilyl propargyl ether (7.57 g, 25.7 mmol) in THF (50 mL) was added *n*-BuLi (16.1 mL, 25.7 mmol) at 0 °C. The resulting mixture was then allowed to stir for 30 min at which point the reaction mixture was cooled to -78 °C and a solution of **10** (3.0 g, 19.1 mmol) in THF (50 mL) was added via syringe. The reaction mixture was then stirred with slow warming to rt. After 5 h the reaction was quenched by the addition of saturated NH_4Cl (aq.), then extracted with ethyl acetate. The organic layer was then dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was then purified by silica gel column chromatography using first hexanes then a mixture of hexanes and ethyl acetate (20:1 = v:v) to give **11** (6.34 g, 84%) as a pale yellow oil.

^{1}H NMR (300 MHz, $CDCl_3$), δ 1.01 (s, 9H), 1.71 (app q, J = 7 Hz, 2H), 2.06 (app q, J = 7 Hz, 2H), 2.47 (t, J = 7 Hz, 2H), 4.46 (s, 2H), 5.02 (m, 2H), 5.78 (ddt, J = 16.9, 10.3, 6.7 Hz, 1H), 7.42 (m, 6H), 7.69 (d, J = 7.9 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 19.1, 22.9, 26.7, 32.8, 44.4, 52.4, 84.1, 90.0, 115.5, 127.8, 130.0, 132.5, 135.6, 137.5, 187.4. HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_{25}H_{30}O_2SiLi$ $(M+Li)^+$ 397.2175, obsd. 397.2181

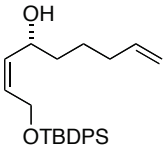
(*4R*)-1-O-(*tert*-Butyldiphenylsilyl)-non-8-en-2-yn-1,4-diol [(*R*)-12]



To **11** (4.7 g, 12 mmol) was added a solution of *(R)*-Alpine-Borane (48 mL, 0.5 M in THF) at 0 °C. The reaction mixture was stirred with gradual warming to room temperature. After 48 h, the THF was removed under reduced pressure and the resulting residue was dissolved in 50 mL of diethyl ether. The resulting mixture was cooled to 0 °C and ethanolamine (1.46 mL, 24 mmol) was added via syringe. This was allowed to stir at 0 °C for 1h. The reaction mixture was then filtered over a bed of Celite™ and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography, using first 75 ml of hexanes, then dichloromethane to give **(*R*)-12** (3.5 g, 75%) in 95.5:4.5 er (chiral HPLC: Pirkle-(*S,S*)-Whelk-O column, 1 mL/min, Hex:iPrOH 99:1, see HPLC trace below), as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$), δ 1.05 (s, 9H), 1.49 (app q, J = 7 Hz, 2H), 1.6 (m, 2H), 2.05 (app q, J = 7 Hz, 2H), 4.3 (app q, J = 6 Hz, 1H), 4.36 (d, J = 0.9 Hz, 2H), 4.99 (dd, J = 17, 10 Hz, 2H), 5.78 (ddt, J = 17, 10, 7 Hz, 1H), 7.41 (m, 6H), 7.71 (d, J = 7 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$), δ 19.1, 24.3, 26.7, 33.3, 36.9, 52.9, 62.3, 83.3, 86.2, 114.8, 127.7, 129.8, 133.2, 133.2, 135.7, 138.4; $[\alpha]^{24}_D$ = +5.4 (*c* 0.45, $CHCl_3$); HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_{25}H_{32}O_2SiLi$ $(M+Li)^+$ 399.2332, obsd. 399.2330

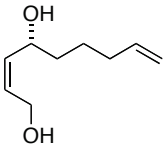
(*4R,2Z*)-1-(tert-Butyldiphenylsilyloxy)nona-2,8-dien-4-ol (19)



A solution of **(*R*)-11** (2.0 g, 5.1 mmol), Lindlar catalyst (200 mg, 10% w/w) in MeOH (10 mL), poisoned with pyridine (0.3 mL), was placed under H_2 (balloon pressure). The reaction mixture was stirred for 1 h, then filtered through a bed of Celite™. The solvent was evaporated under reduced pressure. The resulting residue was dissolved in diethyl ether and extracted with $CuSO_4$ (sat'd, aq). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure giving **19** (1.81 g, 90%), as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$), δ 1.04 (s, 9H), 1.38 (m, 4H), 1.99 (app q, J = 6.8 Hz, 2H), 4.23 (m, 3H), 4.90 (dq, J = 9.0, 1.0 Hz, 1H), 4.95 (dq, J = 17.1, 1.7 Hz, 1H), 5.42 (dd, J = 11.0, 8.6 Hz, 1H), 5.72 (m, 2H), 7.41 (m, 6H), δ 7.68 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 24.5, 26.8, 33.6, 36.4, 60.3, 67.6, 114.6, 127.7, 127.9, 129.7, 129.9, 130.4, 133.4, 133.5, 134.0, 135.6, 135.7, 138.6; HRMS (CI, isobutane) *m/z* Calcd for $C_{25}H_{33}OSI$ $(M+H\ (-H_2O))^+$ 377.2301, obsd. 377.2298; $[\alpha]^{24}_D$ = +20.2 (*c* 0.98, $CHCl_3$).

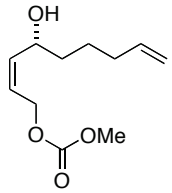
(4*R*,2*Z*)-Nona-2,8-diene-1,4-diol (20)



To **19** (1.26 g, 3.2 mmol) was added TBAF (6.0 mL, 1.0 M in THF) and the resulting reaction mixture was stirred for 2 h at room temperature. The reaction was quenched by the addition of saturated NH_4Cl (aq.) and extracted (6 x) with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was further purified by flash chromatography using a gradient of 40-50% ethyl acetate/hexanes, giving **20** (490 mg, 98%) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$), δ 1.3-1.65 (m, 4H), 2.06 (app q, *J* = 6.7 Hz, 2H), 4.10 (ddd, *J* = 12.8, 5.6, 1.2 Hz, 1H), 4.29 (ddd, *J* = 12.8, 7.6, 1.2 Hz, 1H) 4.42 (app q, *J* = 6.8 Hz, 1H), 4.93 (m, 1H), 5.00 (dq, *J* = 17.2, 1.7 Hz, 1H), 5.52 (ddt, *J* = 11.2, 8.4, 1.2 Hz, 1H), 5.75 (m, 2H), ^{13}C NMR (100 MHz, $CDCl_3$), δ 24.6, 33.6, 36.7, 58.5, 67.6, 114.8, 130.2, 135.3, 138.5; HRMS (CI, isobutane) *m/z* Calcd for C_9H_{13} (M+H (-2H_2O))$^+$ 121.1016, obsd. 121.0999; $[\alpha]^{24}_D$ = +23.3 (*c* 0.75, $CHCl_3$).

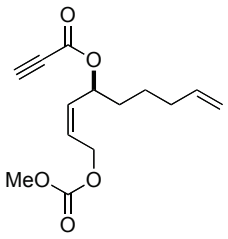
(2*Z*,4*R*)- 1-Methoxycarbonyloxy-2,8-nonadien-4-ol (21)



To a solution of **20** (470 mg, 3.0 mmol) in pyridine (4.5 mL) at 0 °C was added methyl chloroformate (0.49 mL, 6.0 mmol) via syringe. The resulting mixture was stirred for 2 h, and quenched by the addition of saturated $CuSO_4$ (aq) and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was then purified by silica gel column chromatography using a mixture of hexanes and ethyl acetate (5:1, v:v) giving **21** (440 mg, 68% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 (m, 4H), 2.06 (app q, *J* = 6.9 Hz, 2H), 2.23 (br s, 1H), 3.76 (s, 3H), 4.48 (app q, *J* = 6.9 Hz, 1H), 4.58 (ddd, *J* = 12.6, 6.0, 1.0 Hz, 1H), 4.87 (ddd, *J* = 12.6, 8.0, 0.9 Hz, 1H), 4.93 (m, 1H), 4.99 (dq, *J* = 17.2, 1.6 Hz, 1H), 5.62 (m, 2H), 5.78 (ddt, *J* = 16.9, 10.2, 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 33.5, 36.3, 54.9, 63.5, 67.3, 114.7, 124.1, 138.2, 138.5, 155.9; $[\alpha]^{24}_D$ = +18.2 (*c* 0.53, $CHCl_3$); HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_{11}H_{18}O_4Li$ (M+Li)$^+$ 221.1365, obsd. 221.1369.

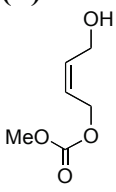
(*4S,2Z*)-1-Methoxycarbonyloxy-2,8-nonadien-4-yl Propiolate (3)



To a mixture of **21** (420 mg, 2.0 mmol), propiolic acid (0.27 g, 4.0 mmol) and PPh_3 (1.1 g, 4.0 mmol) in THF (75 mL) was added diisopropyl azodicarboxylate (0.4 g, 4.0 mmol) at 0 °C. After stirring for 30 min at 0 °C, the reaction mixture was concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography using hexanes/ethyl acetate (6:1) to give **3** (440 mg, 84%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.37 (m, 2H), 1.60 (m, 1H), 1.72 (m, 1H), 2.06 (app q, *J* = 7.1 Hz, 2H), 2.86 (s, 1H), 3.78 (s, 3H), 4.74 (dd, *J* = 13, 6.3 Hz, 1H), 4.82 (dd, *J* = 13, 6.6 Hz, 1H), 4.96 (br d, *J* = 9.9 Hz, 1H), 5.0 (dq, *J* = 17.4, 1.6 Hz, 1H), 5.54 (m, 2H), 5.76 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.0, 33.2, 33.5, 54.9, 63.5, 72.3, 74.65, 74.69, 115.1, 127.7, 131.3, 137.9, 151.9, 155.5; $[\alpha]^{24}_D$ = -66.6 (*c* 1.02, $CHCl_3$); HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_{14}H_{18}O_5Li$ (M+Li)$^+$ 273.1314, obsd. 273.1316.

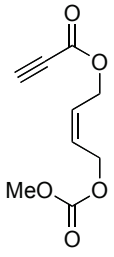
(*Z*)-1-Methoxycarbonyloxybut-2-en-4-ol (22)



To a solution of (2*Z*)-buten-1,4-diol (4.1 mL, 50 mmol) in pyridine (50 mL) at 0 °C was added methyl chloroformate (2.0 mL, 25 mmol) via syringe. The resulting mixture was then stirred for 2 h, and quenched by the addition of saturated $CuSO_4$ (aq) and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced

pressure. The resulting residue was then purified by silica gel column chromatography using a mixture of hexanes and ethyl acetate (3:2, v:v) giving **22** (2.4 g, 70%) as a colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.24 (br, 1H), 3.76 (s, 3H), 4.24 (d, J = 6.58 Hz, 2H), 4.71 (d, J = 7.09 Hz, 2H), 5.64 (m, 1H), 5.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.9, 58.3, 63.2, 124.9, 134.1, 155.8; HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_6H_{10}O_4Li$ $(M+Li)^+$ 153.0739, obsd. 153.0746.

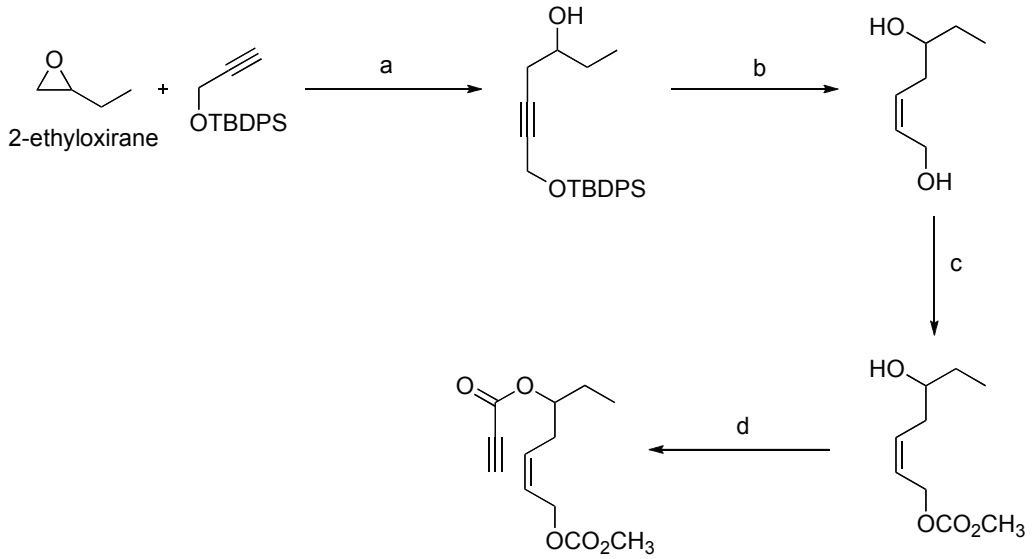
(*Z*)-4-(Methoxycarbonyloxy)but-2-enyl propiolate (9)



To a mixture of **22** (2.0 g, 13.7 mmol), propiolic acid (1.69 mL, 27.4 mmol) and PPh_3 (6.47 g, 24.7 mmol) in THF (100 mL) was added diisopropyl azodicarboxylate (5.39 mL, 27.4 mmol) at 0 °C. After stirring for 1.5 h at 0 °C, the reaction was quenched by addition of brine and extracted with diethyl ether. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography using a mixture of hexanes and ethyl acetate (6:1 = v:v) to give **9** (2.40, 89%) as a colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 2.90 (s, 1H), 3.78 (s, 3H), 4.73 (d, J = 5.7 Hz, 2H), 4.80 (d, J = 5.7 Hz, 2H), 5.74-5.85 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.9, 61.4, 63.1, 74.3, 75.2, 127.2, 128.5, 152.3, 155.5. HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_9H_{10}O_5$ $(M+Li)^+$ 205.0688, obsd. 205.0682.

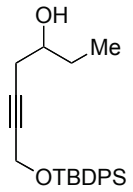
B. Model 6-*exo-trig* ester

Scheme S4: Synthesis of Model 6-*exo-trig* Ester.



(a) i. nBuLi, 0°C 30 min, ii. $BF_3.Et_2O$, -78°C to -50°C, 78% (b) i. Lindlar, H_2, MeOH, pyridine, ii. TBAF, THF 0°C to r. t., 85% over 2 steps, (c) pyridine, methyl chloroformate 0°C, 67%, (d) DIAD, PPh_3, Propiolic acid, THF, 0°C, 1.5 h, 88%.

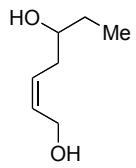
7-(*tert*-Butyldiphenylsilyloxy)hept-5-yn-3-ol (23):



To a solution of *tert*-butyldiphenyl(prop-2-ynyloxy)silane (5.0 g, 17.0 mmol) in THF (60 mL) was added BuLi (12.75 mL of a 1.6 M solution, 20.4 mmol) at 0°C. After 30 minutes, the reaction mixture was cooled down to -78°C and neat 2-ethyloxirane (1.76 mL, 20.4 mmol) was added dropwise, followed by BF_3-Et_2O (3.23 mL, 25.5 mmol). The reaction mixture was allowed to warm slowly to -50°C and quenched by addition of $NaHCO_3$ (sat'd, aq.) and Et_2O. The organic phase was dried over Na_2SO_4 and evaporated. The residue was purified by silica gel column chromatography (10% AcOEt in hexanes) to give **23** (4.87 g, 78%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.6 Hz, 3H), 1.05 (s, 9H), 1.49 (app t, *J* = 7.6 Hz, 2H), 1.74 (br s, 1H), 3.56 (app q, *J* = 6.8 Hz, 1H), 2.26 (ddt, *J* = 16.8, 7.2, 2.4 Hz, 1H), 2.38 (ddt, *J* = 16.4, 4.4, 2.0 Hz, 1H), 4.33 (app t, *J* = 2.0 Hz, 2H), 7.36-7.45 (m, 6H), 7.70-7.72 (dd, *J* = 7.6, 1.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.9, 19.1, 26.7, 27.2, 29.0, 52.8, 71.3, 81.0, 81.9, 127.7, 129.8, 133.2, 133.2, 135.6; HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_{23}H_{30}O_2SiLi$ $(M+Li)^+$ 373.2175, obsd. 373.2169.

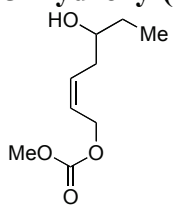
(2*Z*)-Hepten-1,5-diol (24):



To a solution of 7-(*tert*-butyldiphenylsilyloxy)hept-5-yn-3-ol **23** (6.6 g, 18.0 mmol) in MeOH (150 mL) and pyridine (20 mL) under a balloon pressure of dihydrogen was added Lindlar catalyst (660 mg). After 4 h, the reaction mixture as filtered through Celite™, washed with MeOH and evaporated. The resulting residue was dissolved in THF (90 mL) and cooled to 0°C. TBAF (36 mL of a 1M solution in THF, 36.0 mmol) was added and the solution allowed to warm to rt. After 4 h, $NaHCO_3$ (50 mL, sat'd) was added and the aqueous layer was extracted with Et_2O (4x). The organic phase was dried over Na_2SO_4 and evaporated. The residue was purified by silica gel column chromatography (30%-40% AcOEt in hexanes) to give **24** (2.00 g, 85% for 2 steps).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, *J* = 7.4 Hz, 3H), 1.44-1.59 (m, 2H), 1.95 (br s, 1H), 2.16 (br s, 1H), 2.23-2.29 (m, 2H), 3.57 (app t, *J* = 5.8 Hz, 1H), 4.08-4.11 (m, 1H), 4.17-4.22 (m, 1H), 5.65 (app q, *J* = 7.6 Hz, 1H), 5.85-5.87 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.0, 29.9, 34.5, 57.5, 72.0, 129.6, 131.3; HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_7H_{15}O_2$ $(M+H)^+$ 131.1067, obsd. 131.1078.

5-Hydroxy-(2*Z*)-hept-2-enyl Methyl Carbonate (25):

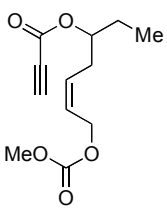


To a solution of (2*Z*)-hepten-1,5-diol **24** (2.0 g, 15.4 mmol) in pyridine (20 mL) at 0°C was added methyl chloroformate (1.77 mL, 23.1 mmol). After 30 min at 0°C, the reaction was stopped by addition of $CuSO_4$ (sat'd aq.) and Et_2O, and the organic layer was dried over Na_2SO_4 and evaporated. The curde product was purified by silica gel column chromatography (20-25% AcOEt in hexanes) to give **25** (1.95 g, 67%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, *J* = 7.2 Hz, 3H), 1.44-1.56 (m, 2H), 1.88 (br. d, *J* = 4.4 Hz, 1H), 2.29 (app t, *J* = 6.6 Hz, 2H), 3.56 (app sextet, *J* = 5.6 Hz, 1H), 3.75 (s, 3H),

4.65 (dd, *J* = 12.8, 6.4 Hz, 1H), 4.72 (dd, *J* = 12.8, 6.8 Hz, 1H), 5.65-5.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.9, 29.7, 35.0, 54.7, 63.6, 72.3, 125.4, 131.8, 155.8; HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_9H_{17}O_4$ $(M+H)^+$ 189.1127, obsd. 189.1123.

(5*Z*)-7-(Methoxycarbonyloxy)hept-5-en-3-yl Propiolate (7):

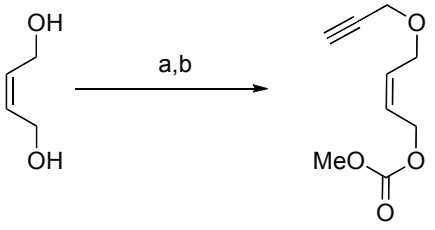


To a solution of 5-hydroxy-(2*Z*)-hept-2-enyl methyl carbonate **25** (1.95 g, 10.4 mmol) and triphenylphosphine (4.87g, 18.6 mmol) in THF (100 mL) at 0°C was added propiolic acid (1.29 mL, 20.8 mmol) and DIAD (4.1 mL, 20.8 mmol). After 1.5 hour, brine and Et_2O were added and the organic layer was dried over Na_2SO_4 and evaporated. Purification by silica gel flash chromatography (2 to 10% AcOEt in hexanes) gave **7** (2.2 g, 88%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.5 Hz, 3H), 1.64 (apt. p, *J* = 7.5 Hz, 2H), 2.38-2.50 (m, 2H), 2.87 (s, 1H), 3.77 (s, 3H), 4.65 (dd, *J* = 12.5, 6.0 Hz, 1H), 4.71 (dd, *J* = 12.5, 7.0 Hz, 1H), 4.94 (apt. p, *J* = 6.3 Hz), 5.62-5.73 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.5, 26.5, 31.7, 54.7, 63.3, 74.7, 77.0, 126.1, 129.5, 152.4, 155.6; HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_{12}H_{17}O_5$ $(M+H)^+$ 241.1071, obsd. 241.1083.

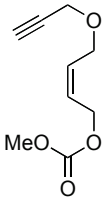
C. 5-*exo-trig* Ether.

Scheme S5: Synthesis of 5-*exo-trig* Ether.



Reagents and conditions: (a) Propargyl bromide (1.0 eq), NaH (2.0 eq), THF 70%, (b) methyl chloroformate (0.5 eq), pyridine, 0º C 85%.

Methyl 4-(Prop-2'-ynyloxy)-2*Z*-butenyl Carbonate (8)



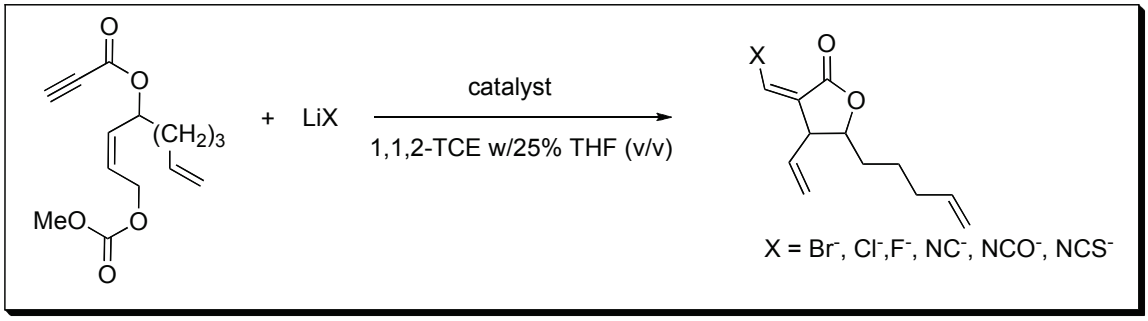
To a solution of 4-(prop-2'-ynyloxy)-2Z-buten-1-ol[7] (1.6 g, 12.7 mmol) in pyridine (20 mL) at 0 °C was added methyl chloroformate (1.5 mL, 19.1 mmol) via syringe. The resulting mixture was stirred for 2 h, and quenched by the addition of saturated $CuSO_4$ (aq) and extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The resulting residue was then purified by silica gel flash chromatography [hexanes/ethyl acetate (5:1)] giving **8** (2.0 g, 85%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (t, *J* = 2.4 Hz, 1H), 3.77 (s, 3H), 4.13 (d, *J* = 2.4 Hz, 2H), 4.17 (br. d, *J* = 5.6, 2H), 4.72 (br. d, *J* = 5.6 Hz, 2H), 5.70-5.81 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.8, 57.3, 63.5, 64.9, 74.7, 79.3, 126.9, 130.4, 155.6; HRMS (CI, NaOAc [$MeOH/H_2O$ (3:1)]) *m/z* Calcd for $C_9H_{12}O_4Na$ $(M+Na)^+$ 207.0634, obsd. 207.0643.

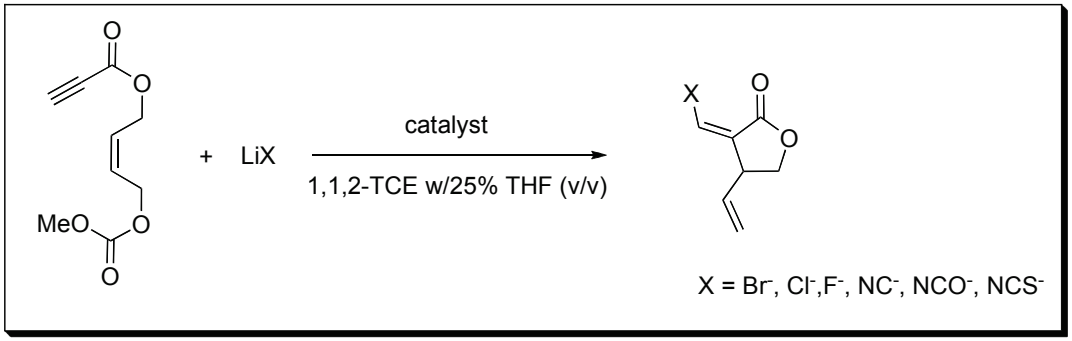
VIII. Cyclization Procedures

A. Xanthanolide Core-Leading 5-*exo-trig* Ester and Model Ester.

Scheme S6a: Xanthatin Core-Leading 5-*exo-trig* Halometalation/Carbocyclization

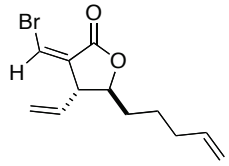


Scheme S6b: Model Ester 5-*exo-trig* Halometalation/Carbocyclization



Halometalation/Cyclization General Procedure. A flame dried flask was charged with **3** (typically 0.1 mmol), LiBr (1.0 mmol), rhodium(II) heptafluorobutyrate (0.01 mmol), 3 ml of distilled 1,1,2-trichloroethane, and 1 mL THF. The reaction mixture was either **(A)** stirred at rt, **(B**) heated to 60°C with stirring until TLC indicated complete consumption of starting material. The reaction mixture was filtered through Celite™ and concentrated under reduced pressure. Purification via silica gel flash chromatography with hexanes/ethyl acetate (~9:1) to give pure cyclization product (i.e. **13** in this case)

(4*R*,5*S*,3*Z*)-3-(Bromomethylene)-5-(pent-4'-enyl)-4-vinyltetrahydrofuran-2-one (13)

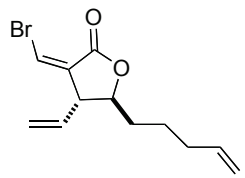


From **3** (26 mg, 0.1 mmol), LiBr (25 mg, 0.3 mmol) and $Pd(acac)_2$ (3.0 mg, 0.01 mmol) following General Procedure **A** with stirring for 4 h (crude NMR shows 19:1 trans:cis), was obtained, following chromatography, **13** (23 mg, 88%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.62 (m, 4H), 2.09 (app q, J = 7.1, 2H), 3.24 (app dt, J = 8.0, 2.8 Hz, 1H), 4.12 (app dt, J = 8.0, 4.0 Hz, 1H), 4.93 (m, 2H), 5.27 (dt, J = 17, 1 Hz, 1H), 5.33 (dd, J = 10.0, 1.0 Hz, 1H), 5.64 (ddd,

J = 17.0, 10.0, 8.0 Hz, 1H), 5.76 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1H), 6.73 (d, *J* = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 33.2, 33.4, 53.9, 81.3, 115.2, 116.4, 121.0, 133.2, 133.6, 137.8, 166.6; $[\alpha]^{24}_D$ = -90.7 (*c* 0.65, $CHCl_3$); HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_{12}H_{15}O_2BrLi$ $(M+Li)^+$ 277.0415, obsd. 277.0410.

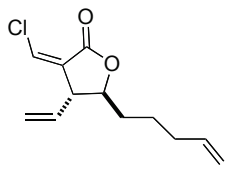
(4*R*,5*S*,3*Z*)-3-(Bromomethylene)-5-(pent-4'-enyl)-4-vinyltetrahydrofuran-2-one (13)



From **4** (731 mg, 2.7 mmol), LiBr (1.4 g, 16.2 mmol), and $[Rh(CO_2C_3F_7)_2]_2$ (28 mg, 0.027 mmol) following General Procedure **B** with stirring for 17 h (crude NMR shows 11:1 trans:cis), was obtained, following chromatography, **13** (583 mg, 78%) as a colorless oil.

On a smaller scale (0.1 mmol), **13** (23 mg) was obtained I 85% yield, after column chromatography,

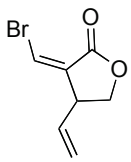
(4*R*,5*S*,3*Z*)-3-(Chloromethylene)-5-(pent-4'-enyl)-4-vinyltetrahydrofuran-2-one (26)



From **3** (27 mg, 0.1 mmol), LiCl (26 mg, 0.6 mmol), and $[Pd(PhCN)_2Cl_2]$ (3.8 mg, 0.01 mmol) following General Procedure **A** with stirring for 18 h, (crude NMR shows >20:1 trans:cis), was obtained, following chromatography, **2** (16.2 mg, 72%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.63 (m, 4H), 2.08 (m, 2H), 3.31 (ddd, *J* = 8.12, 8.11, 2.75 Hz, 1H), 4.13 (td, *J* = 7.66, 4.42 Hz, 1H), 4.98 (m, 2H), 5.27 (d, *J* = 17.1 Hz, 1H), 5.32 (dd, *J* = 10.0, 1.13 Hz, 1H), 5.65 (ddd, *J* = 16.9, 10.1, 8.49 Hz, 1H), 5.76 (ddt, *J* = 17.1, 10.2, 6.77 Hz, 1H), 6.48 (d, *J* = 2.82 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.5, 33.2, 33.5, 52.4, 81.7, 115.2, 120.9, 128.2, 130.6, 133.8, 137.8, 166.1; HRMS (FAB, 3-NBA) *m/z* Calcd for $C_{12}H_{16}O_2Cl$ $(M+H)^+$ 227.0839, obsd. 227.0841.

3*Z*-(Bromomethylene)-4-vinyltetrahydrofuran-2-one (27)



From **9** (20 mg, 0.1 mmol), LiBr (85 mg, 1.0 mmol), and $[Rh(CO_2C_3F_7)_2]_2$ (10.5 mg, 0.01 mmol) following General Procedure **A** with stirring for 6 h, was obtained, following chromatography, **27** (18 mg, 90%) as a colorless oil.

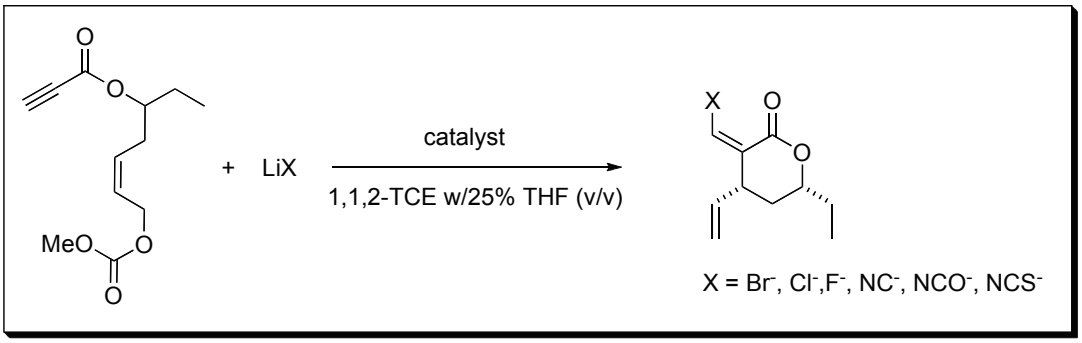
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 (app dq, *J* = 2.5, 8.2 Hz, 1H), 3.98 (apt. t, *J* = 8.0 Hz, 1H), 4.46 (t, *J* = 8.8 Hz, 1H), 5.27 (d, *J* = 16.8 Hz, 1H), 5.31 (d, *J* = 8.8 Hz, 1H), 5.69 (ddd, *J* = 17.1, 10.0, 8.2 Hz, 1H), 5.92 (d, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 47.2, 69.1, 117.1, 120.3, 131.8, 133.9, 167.0; HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_7H_8BrO_2$ $(M+H)^+$ 202.9708, obsd. 202.9703.

From **9** (20 mg, 0.1 mmol), LiBr (85 mg, 1.0 mmol), and $[Pd(acac)_2]$ (10.5 mg, 0.01 mmol) following General Procedure **A** with stirring for 6 h, was obtained, following chromatography, **27** (19 mg, 94% yield) as a colorless oil.

From **9** (20 mg, 0.1 mmol), LiBr (85 mg, 1.0 mmol), and $[Pd(PhCN)_2Cl_2]$ (10.5 mg, 0.01 mmol) following General Procedure **A** with stirring for 6 h, was obtained, following chromatography, **27** (19.3 mg, 95% yield) as a colorless oil.

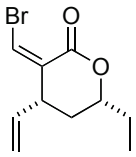
B. Homoallylic Propiolate 6-*exo-trig* Ester.

Scheme S7: 6-*exo-trig* Halometalation/Carbocylization



Halometalation/Cyclization General Procedure. A flame dried flask was charged with **7** (typically 0.1 mmol), LiBr (1.0 mmol), rhodium(II) heptafluourobutyrate (0.01 mmol), 3 ml of distilled 1,1,2-trichloroethane, and 1 mL THF. The reaction mixture was heated to 60°C with stirring. The reaction mixture was filtered through Celite™ and concentrated under reduced pressure. Purification by SiO_2 flash chromatography using a mixture of hexanes and ethyl acetate (9:1 v/v) gave homogeneous **28**.

(±)-(4*R*,6*R*)-3*Z*-(Bromomethylene)-6-ethyl-4-vinyltetrahydro-2H-pyran-2-one (28)



From **7** (24 mg, 0.1 mmol), LiBr (85 mg, 1.0 mmol), and $[Rh(CO_2C_3F_7)_2]_2$ (10.5 mg, 0.01 mmol) following the General Procedure with stirring for 6 h (crude NMR shows >20:1 cis:trans), was obtained **28** (16 mg), following chromatography, in 64% yield, as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (t. q, J = 7.6 Hz, 3H), 1.55-1.80 (m, 3H), 2.07 (ddd, J = 14.0, 6.4, 2.0 Hz, 1H), 3.33 (m, 1H), 4.16 (m, 1H), 5.13 (d, J = 10.8 Hz, 1H), 5.14 (d, J = 16.4 Hz, 1H), 5.67 (ddd, J = 17.6, 10.0, 8.0 Hz, 1H), 6.86 (d, J = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.3, 28.2, 34.7, 44.3, 79.4, 117.1, 119.2, 132.9, 138.1, 163.6. HRMS (CI, methane) *m/z* Calcd for $C_{10}H_{14}O_2Br$ $(M+H)^+$ 245.0177, obsd. 245.0175

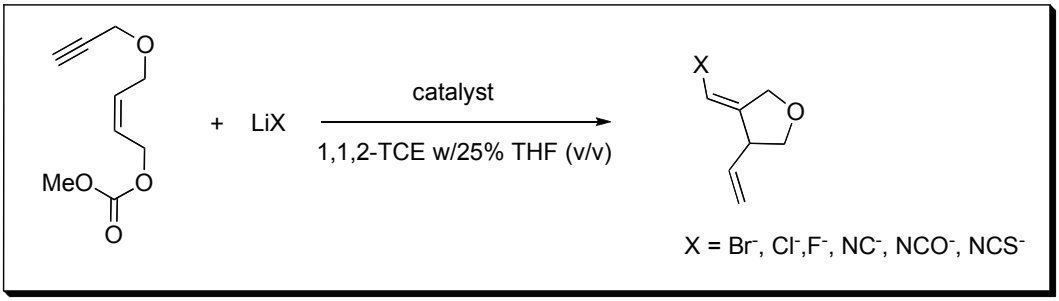
From **7** (20 mg, 0.1 mmol), LiBr (85 mg, 1.0 mmol), and $[Rh(CF_3CO_2)_2]_2$ (10.5 mg, 0.01 mmol) following the General Procedure with stirring for 6 h (crude NMR shows >20:1 cis:trans), was obtained, following chromatography, **28** (14 mg, 58% yield) as a colorless oil.

From **7** (24 mg, 0.1 mmol), LiBr (85 mg, 1.0 mmol), and $[Pd(acac)_2]$ (10.5 mg, 0.01 mmol) following the General Procedure with stirring for 6 h, crude NMR indicated <15% conversion.

From **7** (24 mg, 0.1 mmol), LiBr (85 mg, 1.0 mmol), and $[Pd(PhCN)_2Cl_2]$ (10.5 mg, 0.01 mmol) following the General Procedure with stirring for 6 h (crude NMR shows >20:1 cis:trans), was obtained, following chromatography, **28** (7 mg, 30% yield) as a colorless oil.

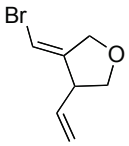
C. 5-*exo-trig* Ether.

Scheme S8: 5-*exo-trig* Ether Halometalation/Carbocyclization.



Halometalation/Cyclization General Procedure. A flame dried flask was charged with **8** (typically 0.1 mmol), LiBr (1.0 mmol), rhodium(II) heptafluourobutyrate (0.01 mmol), 3 ml of distilled 1,1,2-trichloroethane, and 1 mL THF. The reaction mixture was then either **(A)** stirred at rt, **(B**) heated to 60°C with stirring. The reaction mixture was filtered through Celite™ and concentrated under reduced pressure. Purification was by silica gel flash chromatography with hexanes/ethyl acetate (9:1 v/v) to give **29**.

3*Z*-(Bromomethylene)-4-vinyltetrahydrofuran (29)



From **8** (18 mg, 0.10 mmol), LiBr (85 mg, 1.0 mmol) and $Cl_2Pd(PhCN)_2$ (4 mg, 0.01 mmol) following General Procedure **A** with stirring for 10 h, was obtained, following chromatography, **29** (9 mg, 48% yield) as a volatile colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.34 (apt. q, *J* = 8.8 Hz, 1H), 3.61 (t, *J* = 8.8 Hz, 1H), 4.16 (apt. t, *J* = 8.0 Hz, 1H), 4.32 (apt. dt, J = 14.8, 2.8 Hz, 1H), 4.30 (ddd, *J* = 14.8, 2.4, 0.8 Hz, 1H), 5.17 (d, *J* = 17.0 Hz, 1H), 5.18 (dd, *J* = 10.4, 1.2 Hz, 1H), 5.63 (ddd, *J* = 17.0, 10.4, 8.4 Hz, 1H), 5.92 (apt. q, *J* = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.3, 72.4, 74.3, 98.3, 118.4, 134.8, 147.7. HRMS (CI, methane) *m/z* Calcd for $C_7H_{10}OBr$ $(M+H)^+$ 188.9915, obsd. 188.9965.

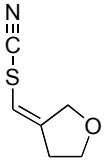
- *Note:* The low isolated here is due to product volatility (see next example).

From **8** (18 mg, 0.10 mmol), LiBr (85 mg, 1.0 mmol) and $Pd(acac)_2$ (3 mg, 0.01 mmol) following General Procedure **A** with stirring for 10 h, was obtained, **29** (73% yield by GC) as a volatile colorless oil.

From **8** (18 mg, 0.10 mmol), LiBr (85 mg, 1.0 mmol) and $[Rh(C_3F_7CO_2)_2]_2$ (4 mg, 0.01 mmol) following General Procedure **A** with stirring for 10 h, was obtained, following chromatography, **29** (7 mg, 37% yield) as a volatile colorless oil – *Note:* The low isolated here is due to product volatility (*vide supra*).

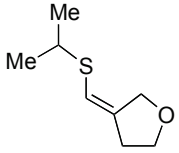
From **8** (18 mg, 0.10 mmol), LiBr (85 mg, 1.0 mmol) and $[Rh(CF_3CO_2)_2]_2$ (4 mg, 0.01 mmol) following General Procedure **A** with stirring for 10 h, was obtained, following chromatography, **29** (8 mg, 42% yield) as a volatile colorless oil - *Note:* The low isolated here is due to product volatility (*vide supra*).

3*Z*-(Thiocyanato)methylene-4-vinyltetrahydrofuran (30)



From **8** (1.84 g, 10 mmol), LiSCN (4.5 g, 70.0 mmol) and $Cl_2Pd(PhCN)_2$ (383 mg, 0.01 mmol) following General Procedure **B** with sirring for 20 h, was obtained, following chromatography, **30** (1.4 g, 84% yield) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.45 (apt. q, *J* = 8.2 Hz, 1H), 3.58 (t, *J* = 8.7 Hz, 1H), 4.16 (apt. t, *J* = 8.1 Hz, 1H), 4.42 (dt, J = 15.1, 2.4 Hz, 1H), 4.54 (dd, *J* = 15.1, 2.2 Hz, 1H), 5.23 (dd, *J* = 16.9, 10.2 Hz, 1H), 5.6 (ddd, *J* = 16.9, 10.2, 8.4 Hz, 1H), 5.83 (q, *J* = 2.47 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 50.7, 70.1, 73.4, 102.3, 119.5, 108.8, 133.8, 156.9; HRMS (FAB, glycerol) *m/z* Calcd for C_8H_9NOSLi $(M-H)^+$ 166.0327, obsd. 166.0324.

3*Z*-(Isopropylthio)methylene-4-vinyltetrahydrofuran (31)



To a solution of **30** (50 mg, 0.30 mmol) in THF (3 mL) was added isopropyl magnesium chloride (1.5 mmol, 1.0 M in THF) at 0°C. The resulting mixture was then stirred for 0.5 h. The reaction was quenched by the addition of saturated NH_4Cl(aq), followed by extraction with ether. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by SiO2 flash chromatography with hexanes/ethyl acetate (8:2, v:v) gave **31** (45 mg, 80% yield) as a colorless oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (d, *J* = 2.4 Hz, 3H), 1.28 (d, *J* = 2.4 Hz, 3H), 3.05 (heptet, *J* = 6.8 Hz, 1H), 3.32 (dq, *J* = 7.6, 1.0 Hz, 1H), 3.49 (app t, *J* = 8.4 Hz, 1H), 4.07 (apt. t, *J* = 8.0 Hz, 1H), 4.27 (dt, *J* = 14.0, 2.4 Hz, 1H), 4.35 (dt, *J* = 14.4, 2.0 Hz, 1H), 5.12 (d, *J* = 17.2 Hz, 1H), 5.14 (d, *J* = 10.4 Hz, 1H), 5.59 (ddd, *J* = 16.8, 10.0, 8.4 Hz, 1H), 5.80 (app q, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.4, 23.5, 49.8, 70.4, 73.4, 114.1, 117.5, 136.1, 142.1; HRMS (FAB, glycerol) *m/z* Calcd for $C_{10}H_{16}OSLi$ $(M-H)^+$ 183.0844, obsd. 183.0846.

IX. Control Experiments for Halometalation/Carbocyclization

A. Acid & Base negative and positive controls

TFA - Negative Control

To a solution of **9** (simplified 5-*exo*-*trig* ester) (20 mg, 0.1 mmol) in a 3:1 mixture of 1,1,2-trichoroethane/THF (4 mL) was added LiBr (87 mg, 1 mmol) and TFA (3 μL, 0.04 mmol). The resulting mixture was heated during 6 h at 55°C. No product formation was detected by TLC or in the crude ^{1}H NMR spectrum.

Base - Positive Controls

To a solution of **9** (simplified 5-*exo-trig* ester) (10 mg, 0.05 mmol) in a 3:1 mixture of 1,1,2-trichoroethane/THF (2 mL) was added LiBr (26 mg, 0.3 mmol), $[Rh^{II}(O_2CC_3F_7)_2]_2$ (5.3 mg, 0.005 mmol) and 2,6-di*tert*butyl-4-methyl pyridine (4.1 mg, 0.02 mmol) or 1,5,7-triazabicyclo[4.4.0]dec-5-ene (bound to polystyrene, 2.6 mmol base/g resin, 7.7. mg, 0.02 mmol) or no added base. The 3 resulting mixtures were heated during 6 h at 55°C. Complete conversion to product **27** (as the only product) was detected by TLC and in the crude ^{1}H NMR spectra in all 3 cases.

B. Rh(II)-Perfluorocarboxylate Catalyst Loading

5 mol% catalyst:

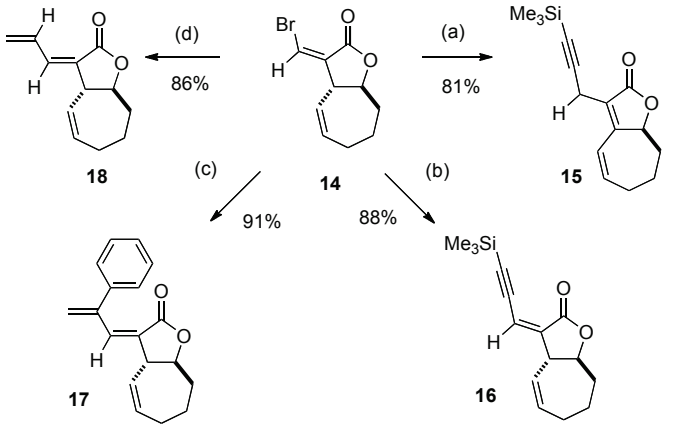
To a solution of **9** (simplified 5-*exo-trig* ester) (40 mg, 0.2 mmol) in a 3:1 mixture of 1,1,2-trichoroethane/THF (8 mL) was added LiBr (104 mg, 1.2 mmol) and $[Rh^{II}(O_2CC_3F_7)_2]_2$ (10.5 mg, 0.01 mmol). The resulting mixture was heated during 6 h at 55°C. The solvents were evaporated, the residue resuspended in dichloromethane and filtered over a plug of Celite™. Analysis of the ^{1}H NMR spectrum showed complete conversion of starting material to product. Purification by silica gel column chromatography (10% EtOAc in hexanes) yielded product **27** (35 mg, 86% yield).

2.5 mol% catalyst:

To a solution of **9** (simplified 5-*exo-trig* ester) (40 mg, 0.2 mmol) in a 3:1 mixture of 1,1,2-trichoroethane/THF (8 mL) was added LiBr (104 mg, 1.2 mmol) and $[Rh^{II}(O_2CC_3F_7)_2]_2$ (5.3 mg, 0.005 mmol). The resulting mixture was heated at 55°C. An aliquot taken after 6 h showed 94% conversion (^{1}H NMR).

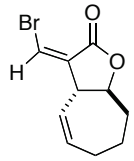
X. Xanthanolide Core Tailoring Chemistry

Scheme S9: Synthetic Elaboration of Xanthanolide Core.



(a) trimethylsilylacetylene (1.1 eq.), CuI (5 mol%), $Cl_2Pd(PPh_3)_2$ (2 mol%), Et_2NH, rt, 1 h, (b) tri-n-butyl(trimethylsilylethynyl)tin (1.1 eq.), Pd_2dba_3 (2 mol %), tris-(2-furyl)phosphine (20 mol%), THF, 50 °C, 2 h. (c) 1-phenylvinylzinc bromide (3 eq.),$Pd(PPh_3)_4$ (5 mol %), THF, 50 °C, 1 h. (d) tributylvinyl tin (1.1 eq.), Pd_2dba_3 (2 mol %), tris-(2-furyl)phosphine (20 mol %), THF, 50 °C, 4.5 h.

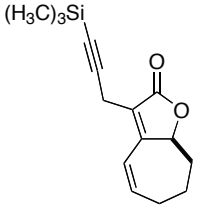
(3a*R*,4*Z*,8a*S*)-3*Z*-(Bromomethylene)-3,3a,6,7,8,8a-hexahydro-2*H*-cyclohepta[b]-furan-2-one (14)



A clean dry flask was charged with **13** (573 mg, 2.1 mmol), and Grubbs I catalyst (86.4 mg, 0.1 mmol) in CH_2Cl_2. The resulting solution was then stirred at reflux for 1 h. The reaction mixture was then concentrated and the resulting residue subjected to SiO2 chromatography with hexanes/ethyl actetate (9:1, v/v) to provide homogeneous **14** (513 mg, 97%) as white solid.

mp 143-144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (q, *J* = 12.1 Hz, 1H), 1.81 (m, 2H), 2.12 (m, 1H), 2.26 (m, 1H), 2.51 (m, 1H), 3.87 (m, 1H), 3.57 (m, 1H), 5.74 (dt, *J* = 10.2, 2.7 Hz, 1H), 6.11 (m, 1H), 6.82 (d, *J* = 3.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.3, 27.7, 35.6, 49.7, 79.7, 112.8, 126.4, 133.4, 136.7, 167.0; HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_{10}H_{11}O_2BrLi$ $(M+Li)^+$ 249.0102, obsd. 249.0115.

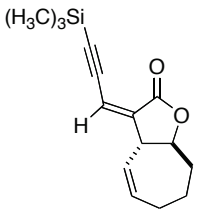
(3a*S*,4*Z*)-3-(3'-(Trimethylsilyl)prop-2-ynyl)-6,7,8,8a-tetrahydro-2*H*-cyclohepta[b]furan-2-one (15)



To a mixture of **14** (73 mg, 300 μmol), CuI (3.2 mg, 16.5 μmol), and $Cl_2Pd(PPh_3)_2$ (4.2 mg, 6 μmol) in diethylamine (4 mL) was added trimethylsilylacetylene (32 mg, 330 μmol). After stirring for 1 h at room temperature, the reaction mixture was filtered through Celite™ and concentrated under reduced pressure. Purification was carried out via flash chromatography with hexanes/ethyl acetate (5:1 = v:v) to give **15** (63 mg, 81%) as pale brown oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.13 (s, 9H), 1.58 (m, 1H), 1.77 (m, 1H), 1.89 (m, 1H), 2.27 (m, 2H), 2.49 (m, 1H), 3.22 (d, *J* = 18.9 Hz, 1H), 3.31 (d, *J* = 18.9 Hz, 1H), 4.85 (dd, *J* = 11.5, 4.6 Hz, 1H), 6.26 (ddd, *J* = 11.9, 6.5, 4.6 Hz, 1H), 6.75 (d, *J* = 11.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.11, 15.1, 23.2, 29.4, 31.8, 82.0, 86.4, 101.1, 120.1, 120.6, 140.7, 159.8, 173.0; HRMS (FAB, 3-NBA) *m/z* Calcd for $C_{15}H_{21}O_2Si$ $(M+H)^+$ 261.1311, obsd. 261.1301.

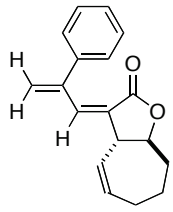
(3a*R*,4*Z*,8a*S*)-3*Z*-(3'-(Trimethylsilyl)prop-2'-ynylidene)-3,3a,6,7,8,8a-hexahydro-2*H*-cyclo-hepta[b]-furan-2-one (16).



To a mixture of Pd_2dba_3 (5.5 mg, 6 μmol), and tris-(2-furyl)phosphine (14 mg, 60 μmol) in THF (3 mL) was added **14** (73 mg, 300 μmol). After 10 min stirring at rt, a solution of tri-n-*butyl*(trimethylsilylethynyl)tin (128 mg, 330 μmol) in THF (2 mL) was added. The resulting mixture was stirred at 50 °C for 2 h. The reaction mixture was filtered through a Celite™, and concentrated under reduced pressure. The resulting residue was purified by silica gel column chromatography using a mixture of hexanes and ethyl acetate (15:1 = v:v) to give **16** (69 mg, 88%) as white solid.

mp140-142 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.227 (s, 9H), 1.40 (m, 1H), 1.82 (m, 2H), 2.11 (m, 1H), 2.29 (m, 1H), 2.49 (m, 1H), 3.63 (m, 1H), 3.81 (ddd, *J* = 11.2, 9.5, 3.5 Hz, 1H), 5.57 (ddd, *J* = 10.2, 3.8, 2.6 Hz, 1H), 6.02 (d, *J* = 3.4 Hz, 1H), 6.09 (dddd, *J* = 10.4, 7.8, 5.1, 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -0.39, 23.4, 27.7, 35.8, 48.0, 80.0, 99.3, 108.6, 114.1, 126.9, 136.4, 140.2, 167.2; HRMS (FAB, 3-NBA) *m/z* Calcd for $C_{15}H_{21}O_2Si$ $(M+H)^+$ 261.1311, obsd. 261.1302.

(3a*R*,4*Z*,8a*S*)-3*Z*-[(2'-Phenyl)allylidene]-3,3a,6,7,8,8a-hexahydro-2*H*-cyclo-hepta[b]-furan-2-one (17)

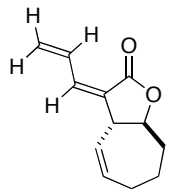


To a mixture of **14** (97 mg, 400 μmol), and $Pd(PPh_3)_4$ (23 mg, 20 μmol) in THF (8 mL) was added α-styrenylzinc bromide (2.4 mL of 0.5 M solution in THF, 1.2 mmol). The reaction mixture was then stirred at 50 °C for 1 h. The reaction was then quenched by the addition of a saturated aqueous ammonium chloride solution, followed by extraction with diethyl ether. The organic layer was dried over anhydrous $MgSO_4$, filtered, and then concentrated under reduced pressure. Purification by SiO_2 chromatography with hexanes/ethyl acetate (10:1 = v:v) gave **17** (97 mg, 91%) as a pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.36 (m, 1H), 1.80 (m, 2H), 2.00 (m, 1H), 2.09 (m, 1H), 2.50 (m, 1H), 3.71 (br, 1H), 3.87 (ddd, *J* = 11.1, 9.2, 3.4 Hz, 1H), 5.45 (d, *J* = 0.8 Hz, 1H), 5.52 (ddd, *J* = 10.2, 4.7, 2.3 Hz, 1H), 5.67 (dddd, *J* = 10.3, 7.8, 5.3, 2.5 Hz, 1H), 5.79 (s, 1H), 7.32 (m, 5H), 7.40 (dd, *J* = 3.7, 1.01 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.8, 26.8, 36.1, 46.5, 81.0, 121.3, 126.8, 128.2, 128.5, 130.9, 133.3, 136.3, 138.6, 142.8, 171.6; HRMS (FAB, 3-NBA+Li) *m/z* Calcd for $C_{18}H_{18}O_2Li$ $(M+Li)^+$ 273.1467, obsd. 273.1457.

(3a*R*,4*Z*,8a*S*)-3*Z*-Allylidene-3,3a,6,7,8,8a-hexahydro-2*H*-cyclo-hepta[b]-furan-2-one (18)

To a mixture of Pd_2dba_3 (5.5 mg, 6 μmol), and tris-(2-furyl)phosphine (14 mg, 60 μmol) in THF (3 mL) was added **16** (73 mg, 300 μmol). After 10 min stirring at rt, a solution of tributylvinyltin (105 mg, 330 μmol) in THF (2 mL) was added to the reaction mixture. The resulting mixture was then stirred at 50 °C for 4.5 h. The reaction mixture was then filtered through a Celite™ pad and concentrated, in vacuo. Final purification via flash chromatography with hexanes/ethyl acetate (15:1 = v:v) provided **18** (49 mg, 86%) as a white solid.

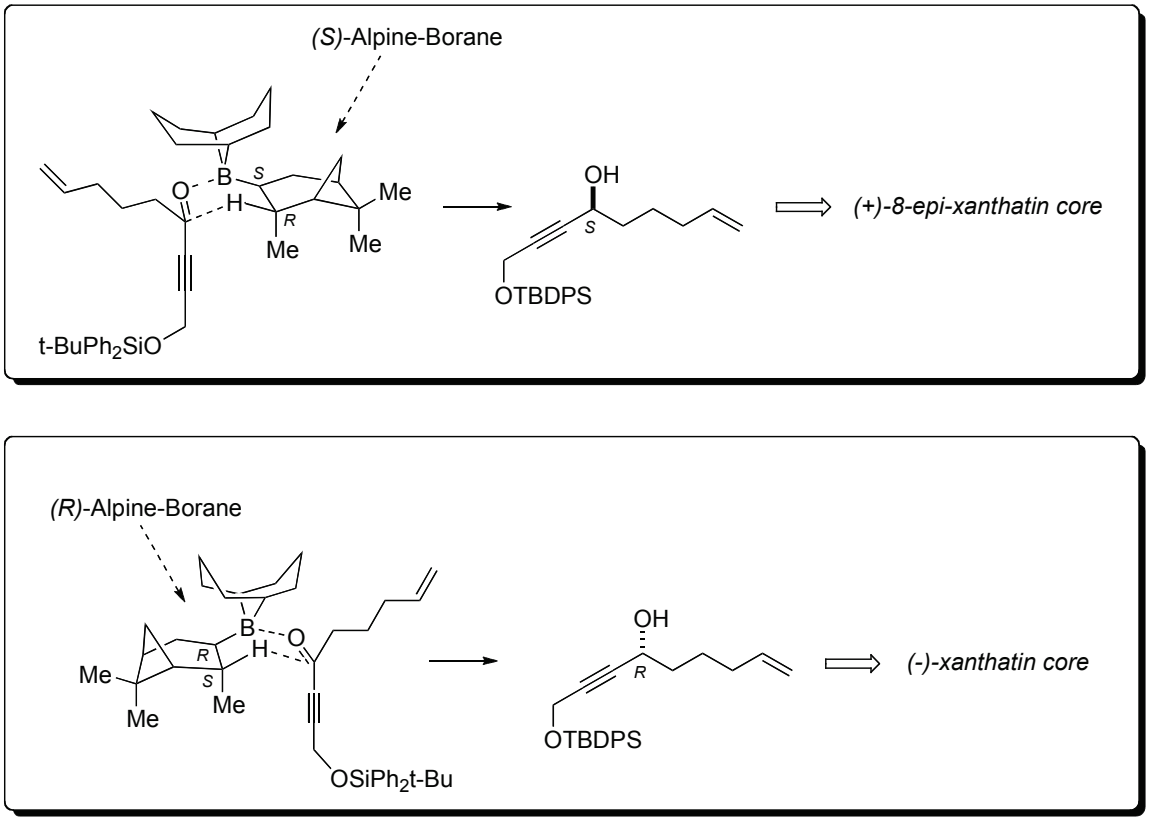


mp 76-77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (m, 1H), 1.84 (m, 2H), 2.14 (m, 1H), 2.29 (m, 1H), 2.48 (m, 1H), 3.64 (brd, *J* = 8.5 Hz, 1H), 3.86 (ddd, *J* = 11.1, 9.7, 3.5 Hz, 1H), 5.49 (m, 2H), 5.80 (ddd, *J* = 10.3, 3.9, 2.5 Hz, 1H), 6.08 (dddd, *J* = 10.3, 8.0, 5.1, 2.5 Hz, 1H), 6.51 (dd, *J* = 11.2, 3.1 Hz, 1H), 7.69 (dddd, *J* = 17.0, 11.2, 11.0, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.4, 27.8, 35.8, 47.6, 80.5, 124.9, 127.6, 128.3, 131.5, 135.8, 136.7, 169.4; HRMS (FAB) *m/z* Calcd for $C_{12}H_{15}O_2$ $(M+H)^+$ 191.1072, obsd. 191.1076.

XI. Determination of Absolute Stereochemistry

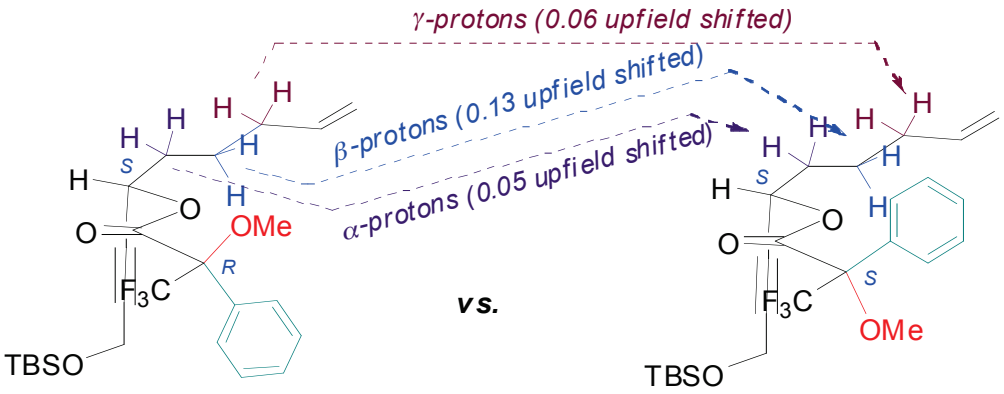
A. Predicted Stereochemistry Using the Midland Model.

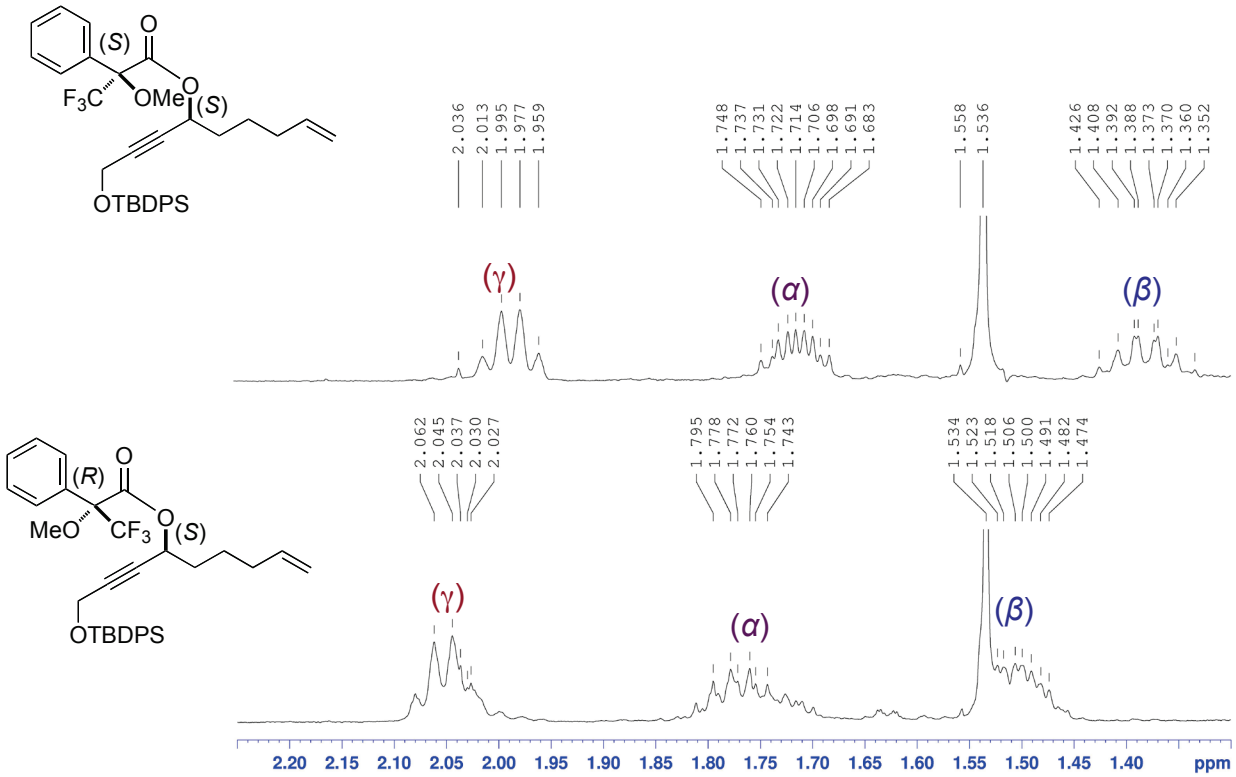
Figure S10: Predicted Stereochemistry of the Alpine-Borane™-Ynone Reductions



B. Absolute Stereochemical Assignment by the Kakisawa Method (Mosher Ester Shifts)

Figure S11: Observed Stereochemistry as Assigned by Mosher Ester Chemical Shift Perturbation:





C. Confirmation of Absolute Stereochemistry by Chemical Correlation.
To a solution of alkene **XX** (**cis-double bond, *R*-alcohol from AlpineBorane reduction**, 300 mg, 0.76 mmol) in dichloromethane (30 mL) was added 1st generation Grubbs catalyst (63 mg, 0.076 mmol). The resulting mixture was refluxed for 40 min. After cooling to rt and evaporation, SiO_2 chromatography (10-15% EtOAc/hexanes) gave (*R*)-(+)-2-cyclohexen-1-ol (38 mg, 51% yield), $[\alpha]^{20}_D$ +103.3° (c 1.05, $CHCl_3$) for 92% ee, lit.[2] (*S*)-(-)-2-cyclohexen-1-ol, $[\alpha]^{23}_D$ -104.5° (c 1.0, $CHCl_3$) for 93% ee.

XII. References:

(1) (a) Szutowicz, A.; Kobes, R. D.; Orsulak, P. J. *Anal. Biochem.* **1984,** *138*, 86-94; (b) Scott, S. L., Espenson, J. H. *J. Phys. Chem.* **1993**, 97, 6710-6714

(2) Brown, H. C.; Jadhav, P.; Bhat, K. *J. Am. Chem. Soc.* **1985**, *107*, 2564-2565.

(3) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092-4096.

(4) Rieser, M. J.; Hui, Y. H.; Rupprecht, J. K.; Kozlowski, J. F.; Wood, K. V.; McLaughlin, J. L.; Hanson, P. R.; Zhuang, Z.; Hoye, T. R. *J. Am. Chem. Soc.* **1992**, *114*, 10203-10213.

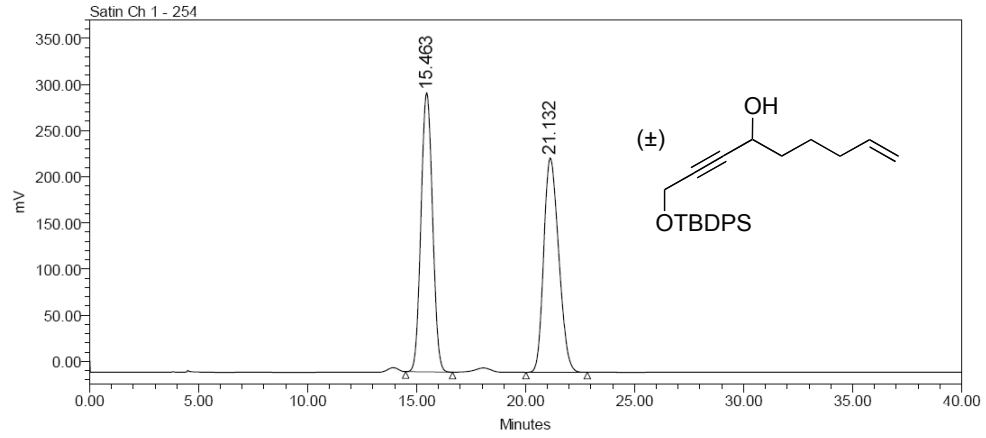
(5) Midland, M. M, McDowell, D. C., Hatch, R. L., Tramontano, A., *J. Am. Chem. Soc.* **1980**, *102*, 867-869.

(6) Kraus, T. C. "Metal cyanates from alkyl carbamates." **1985**, US 4496529 A 19850129.

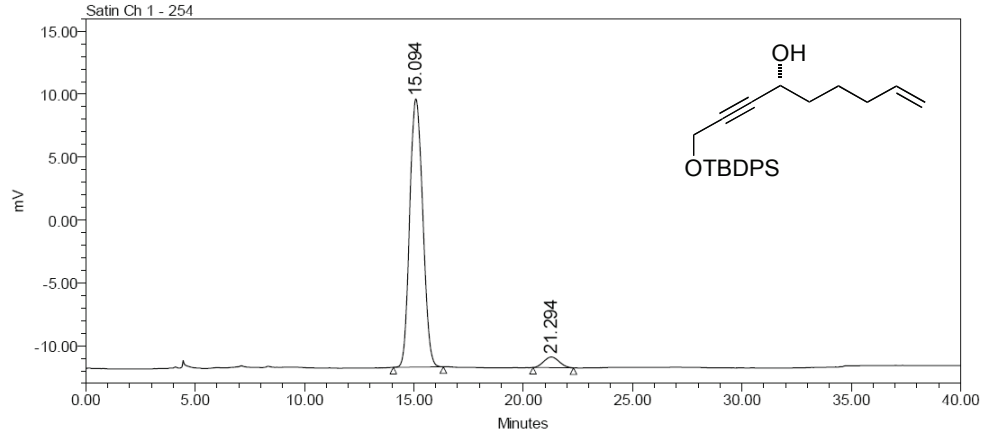
(7) Zhao, L.; Lu, X.; *J. Org. Chem.* **2005**, 70, 4059-4063

XIII. Characterization

a. HPLC Traces



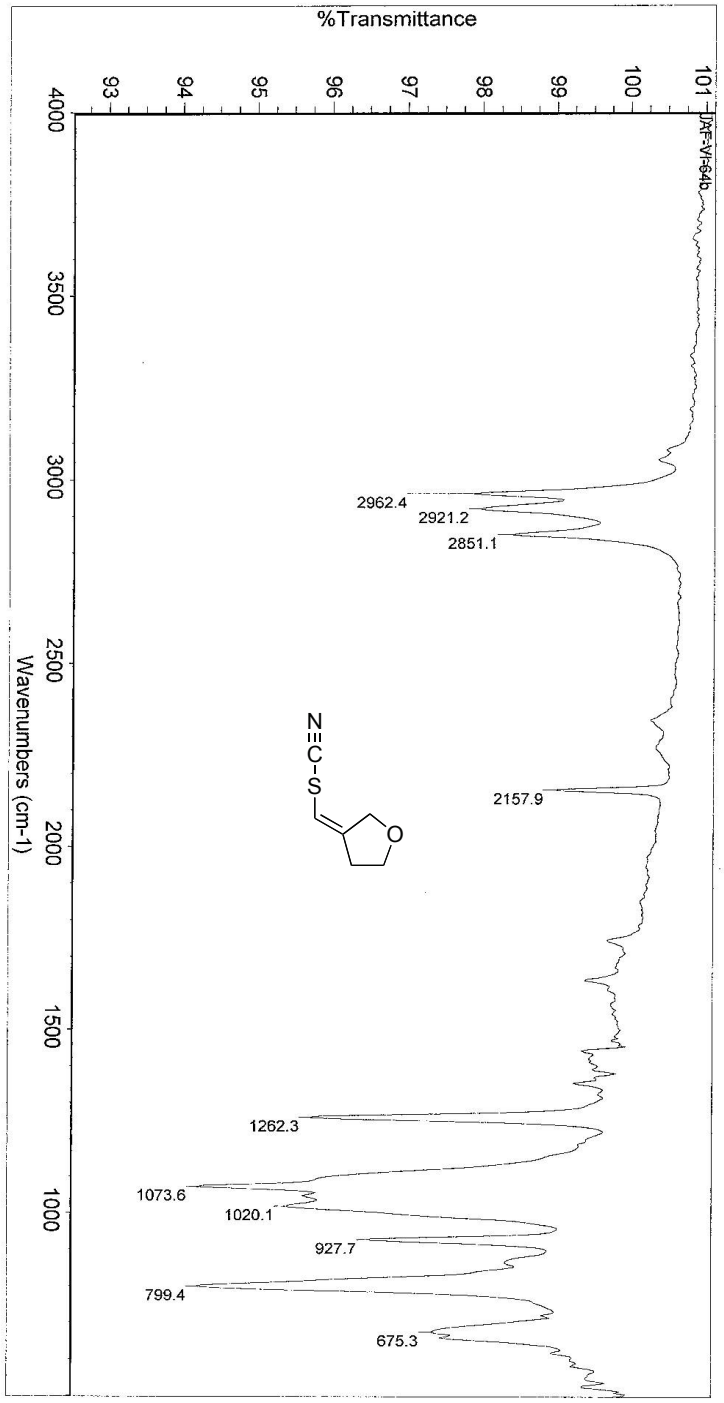
	Peak Name	RT	Area	% Area	Height
1	Peak1	15.463	11144692	50.08	302328
2	Peak2	21.132	11110048	49.92	231890



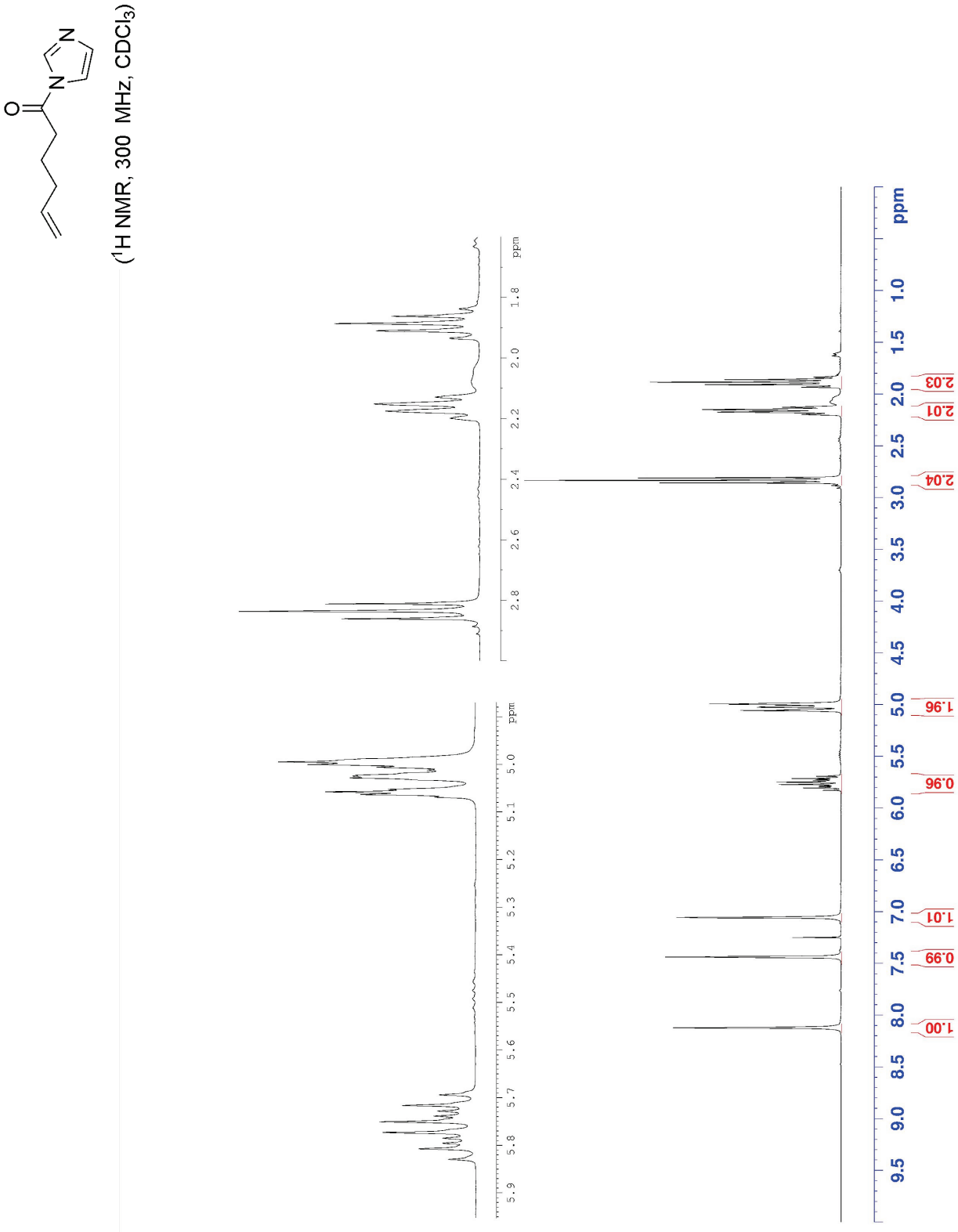
	Peak Name	RT	Area	% Area	Height
1	Peak1	15.094	884536	95.49	21318
2	Peak2	21.294	41807	4.51	849

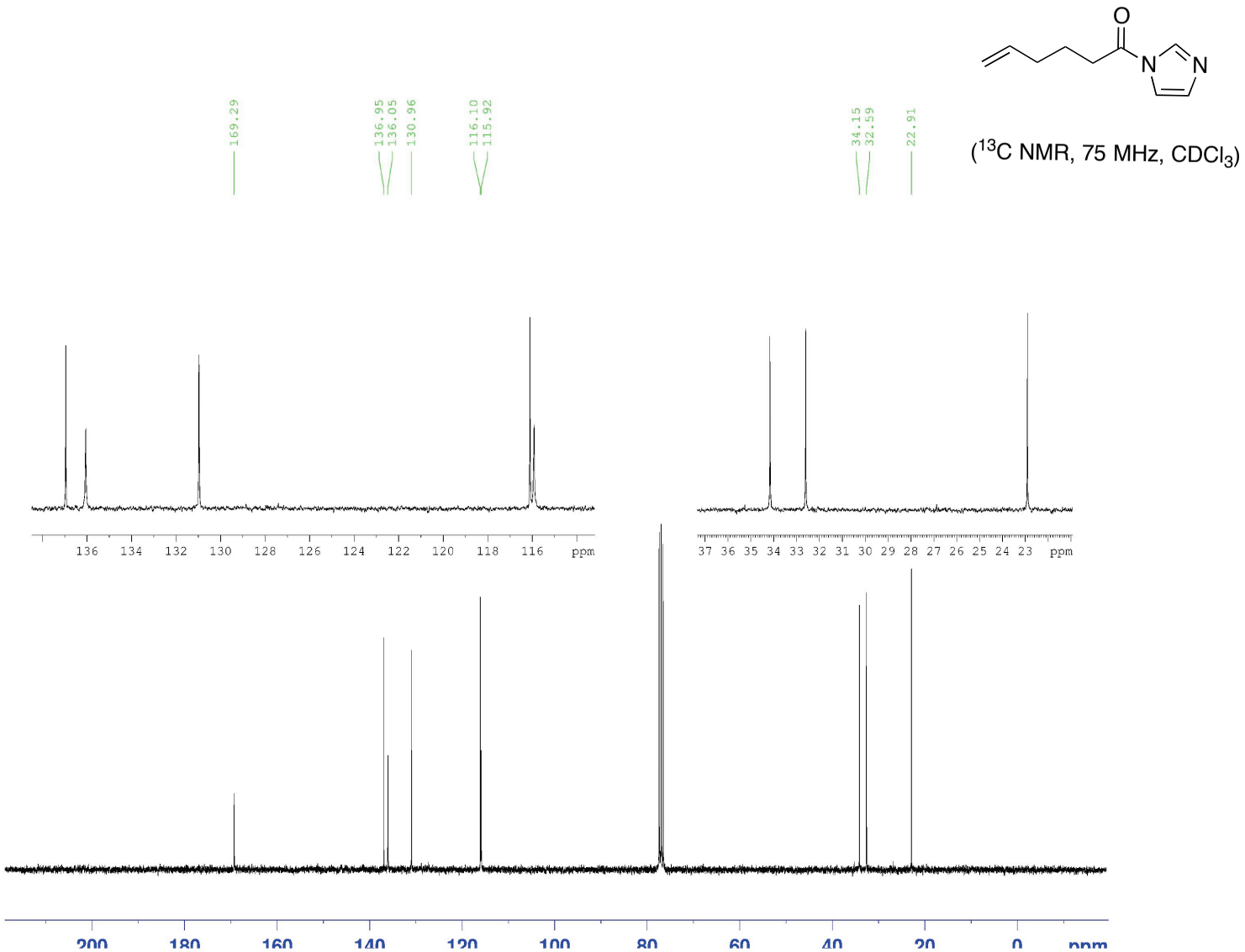
Column: Pirkle - (*S,S*)-Whelk-O
Eluent: Hexane/i-PrOH (99:1)
Flow Rate: 1 mL/min

B. IR of Thiocyanate Cyclization Product

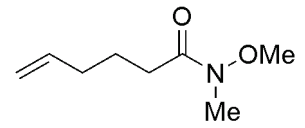


C. Copies of ^{1}H and ^{13}C NMR Spectra

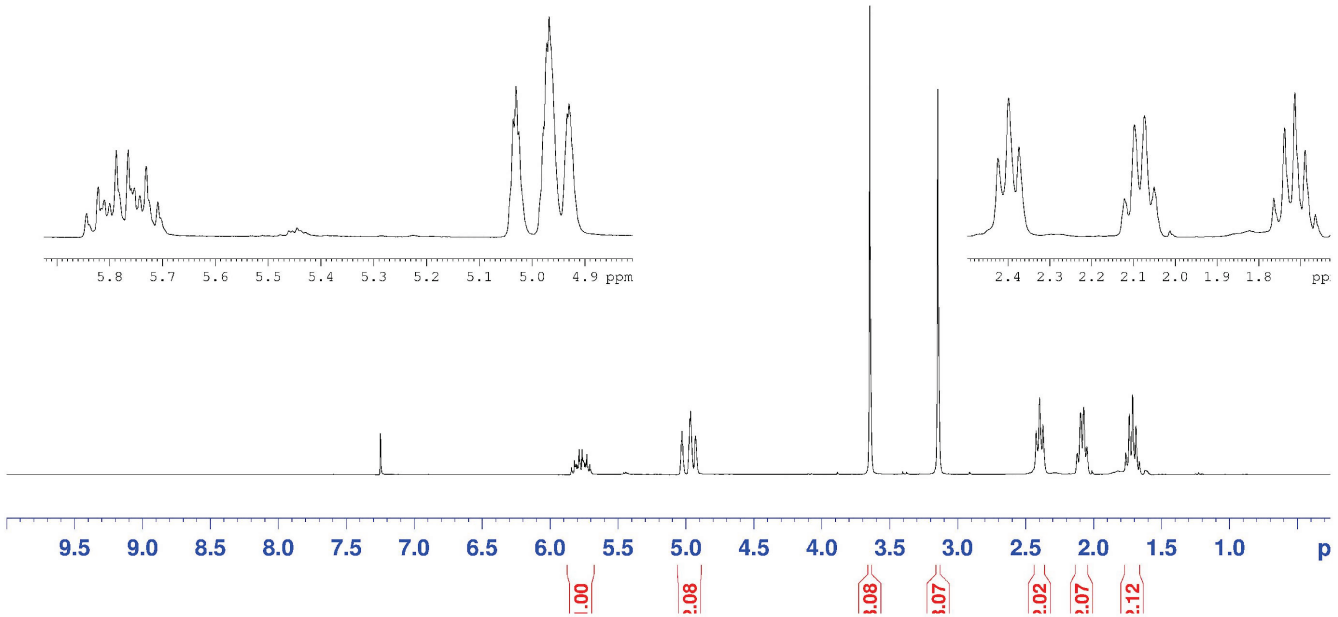


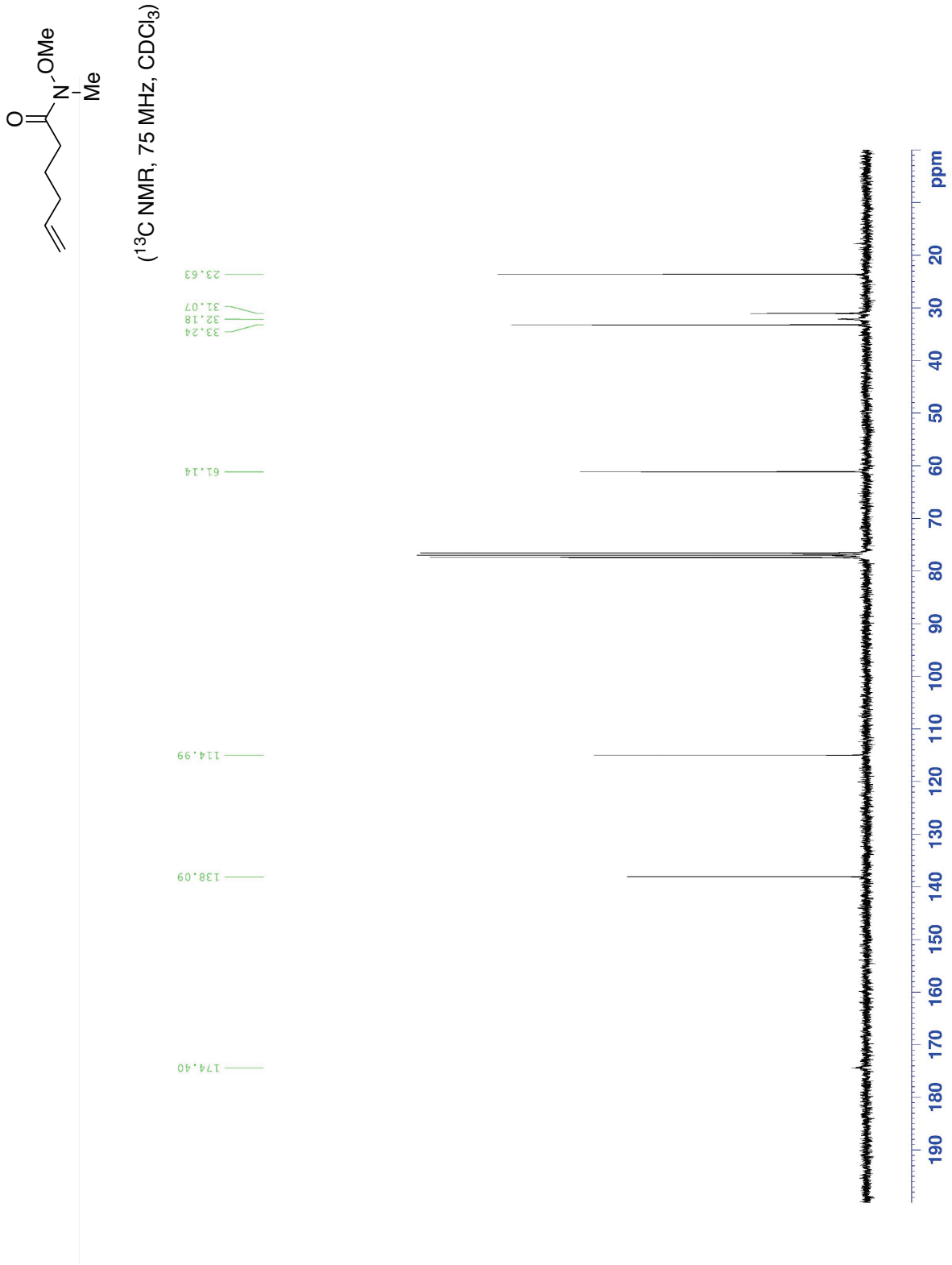


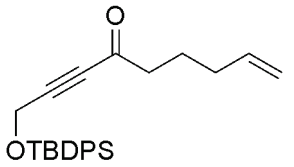
(^{13}C NMR, 75 MHz, $CDCl_3$)



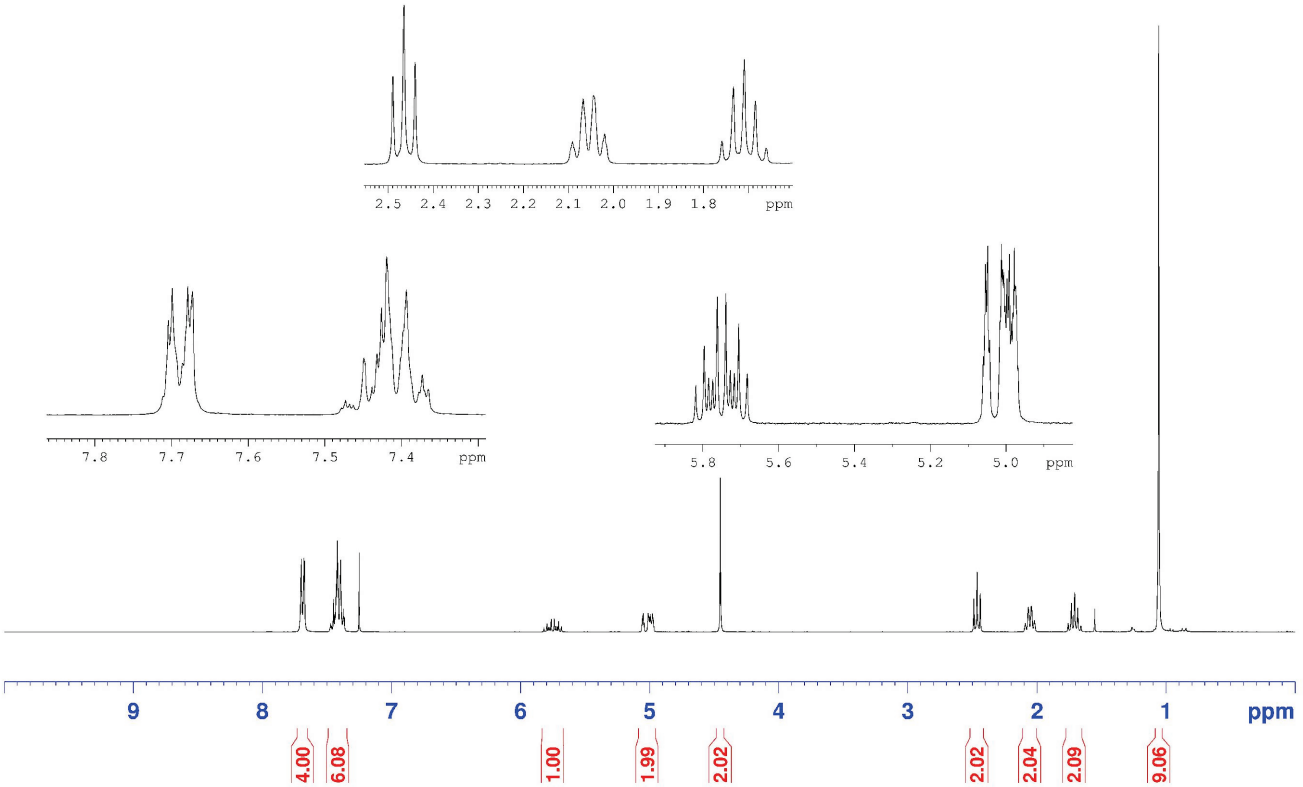
(^{1}H NMR, 300 MHz, $CDCl_3$)

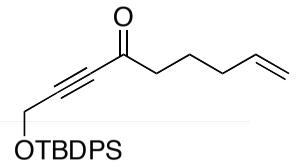



O
OMe
N
Me
(^{13}C NMR, 75 MHz, CDCl$_3$)
23.63
31.07
32.18
33.24
61.14
114.99
138.09
174.40
ppm

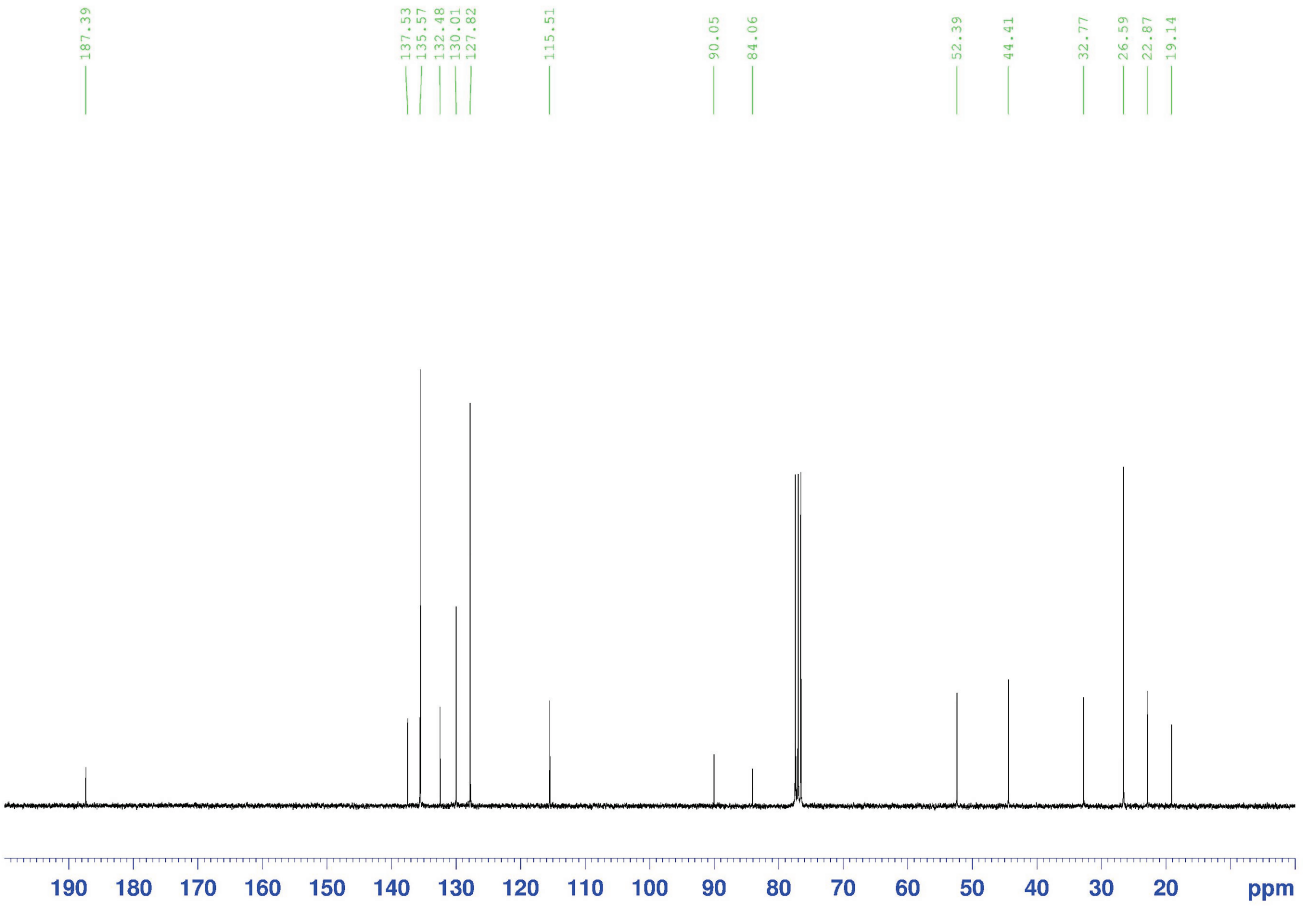


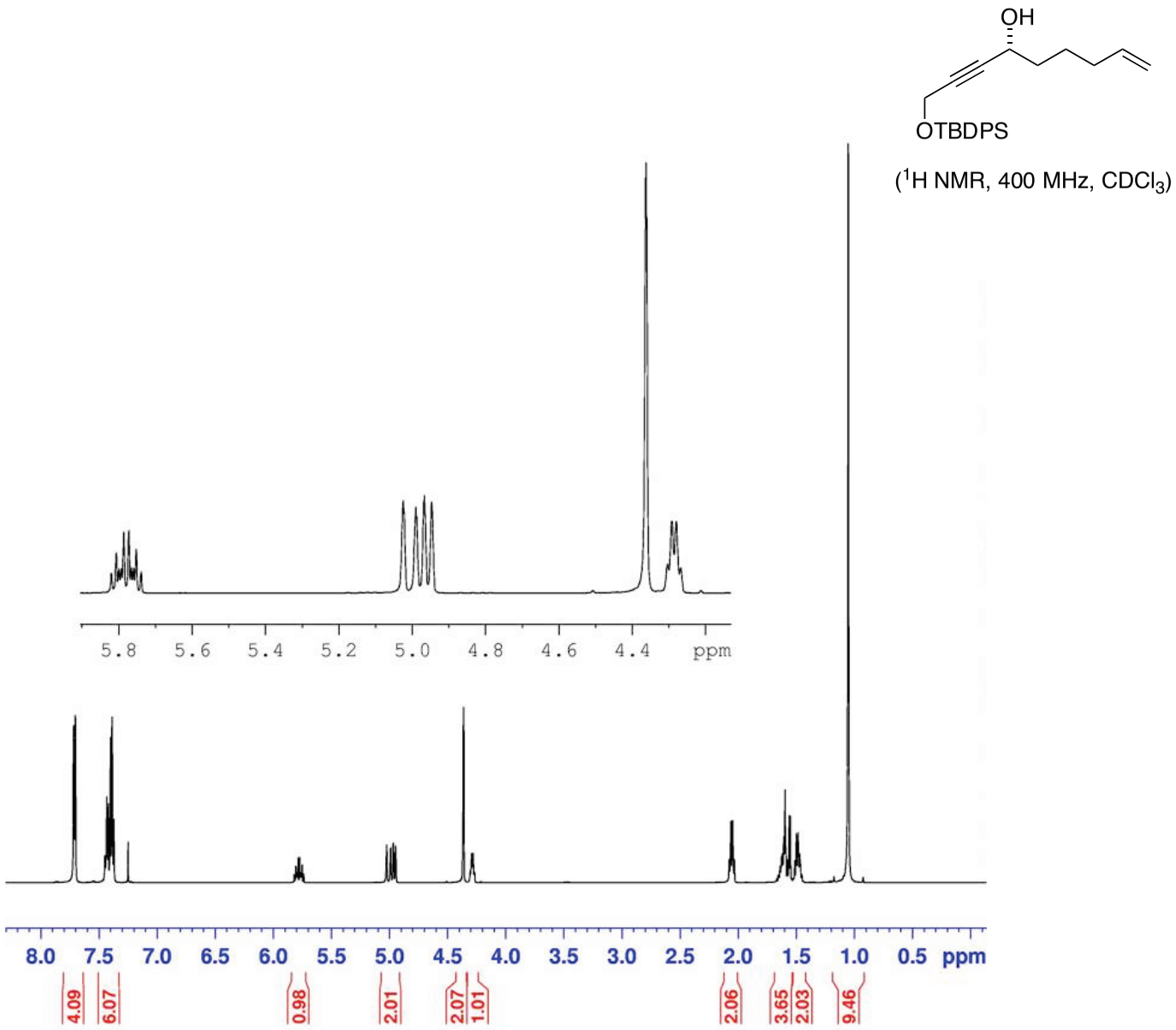
(^{1}H NMR, 300 MHz, $CDCl_3$)

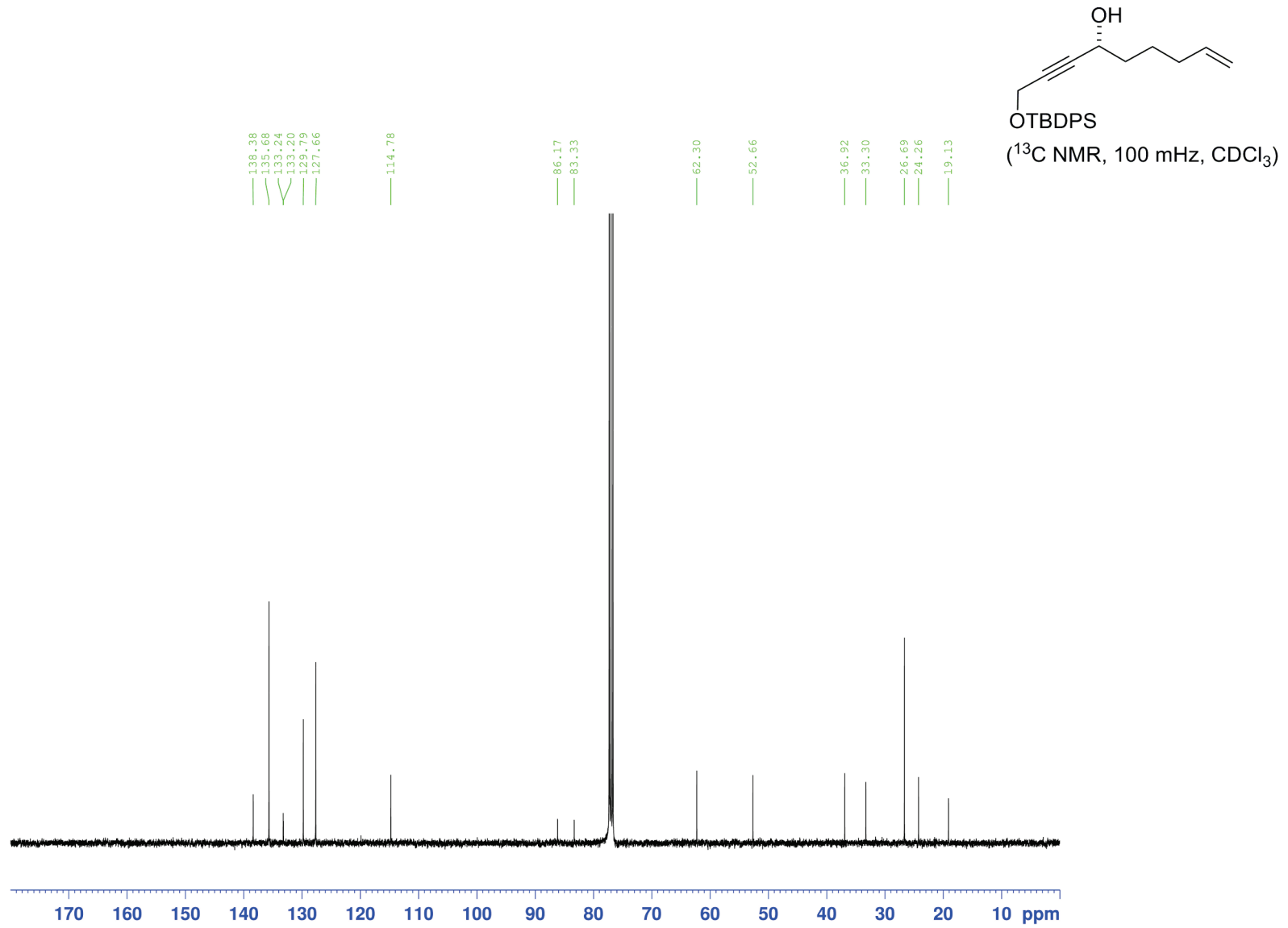


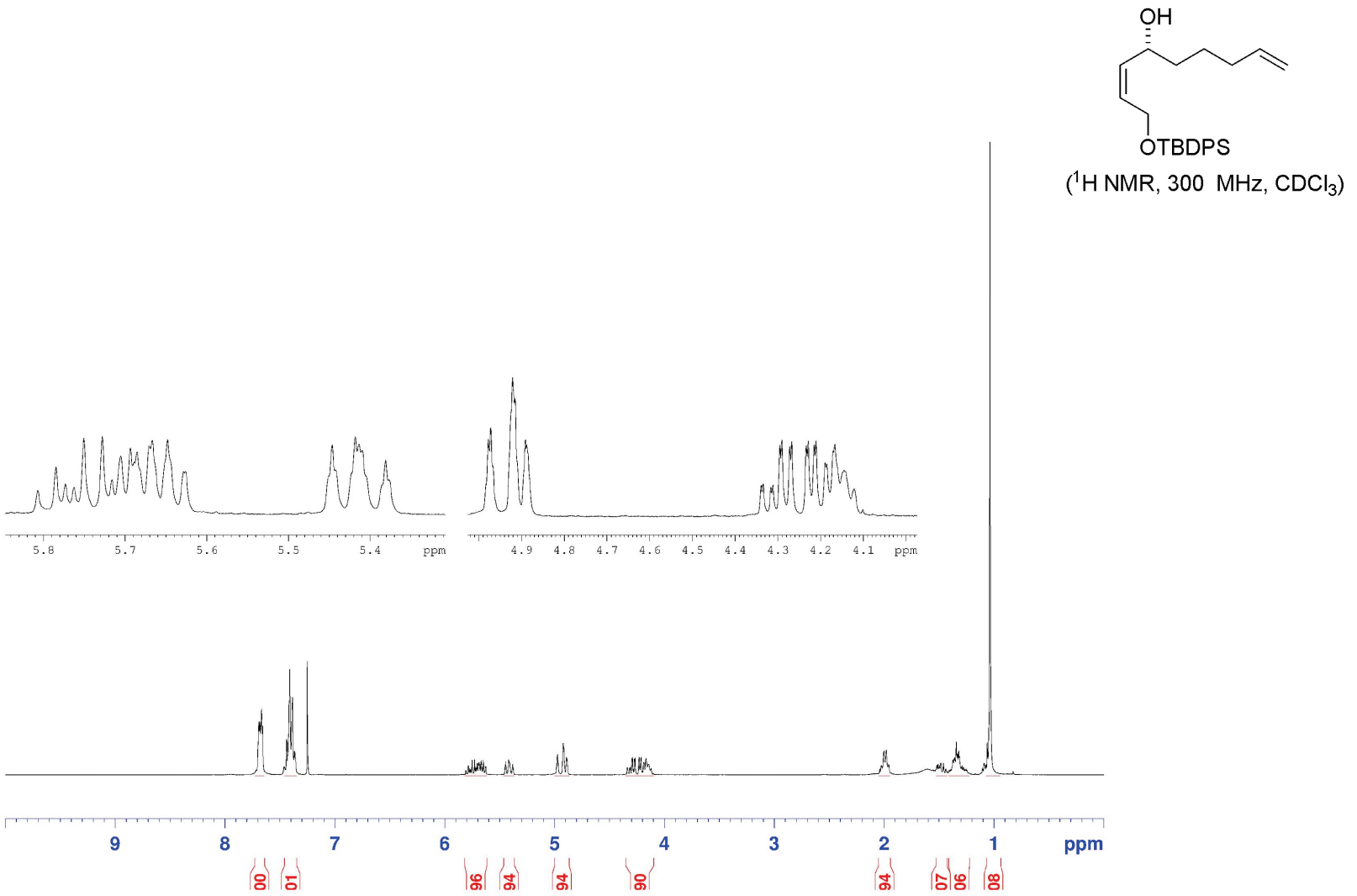


(^{13}C NMR, 75 MHz, $CDCl_3$)




OH
OTBDPS
(1H NMR, 400 MHz, CDCl3)
5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 ppm
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
4.09
6.07
0.98
2.01
2.07
1.01
2.06
3.65
2.03
9.46


OH
OTBDPS
(^{13}C NMR, 100 mHz, $CDCl_3$)
138.38
135.68
133.24
133.20
129.79
127.66
114.78
86.17
83.33
62.30
52.66
36.92
33.30
26.69
24.26
19.13
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


OH
OTBDPS
(1H NMR, 300 MHz, CDCl3)
5.8
5.7
5.6
5.5
5.4
ppm
4.9
4.8
4.7
4.6
4.5
4.4
4.3
4.2
4.1
ppm
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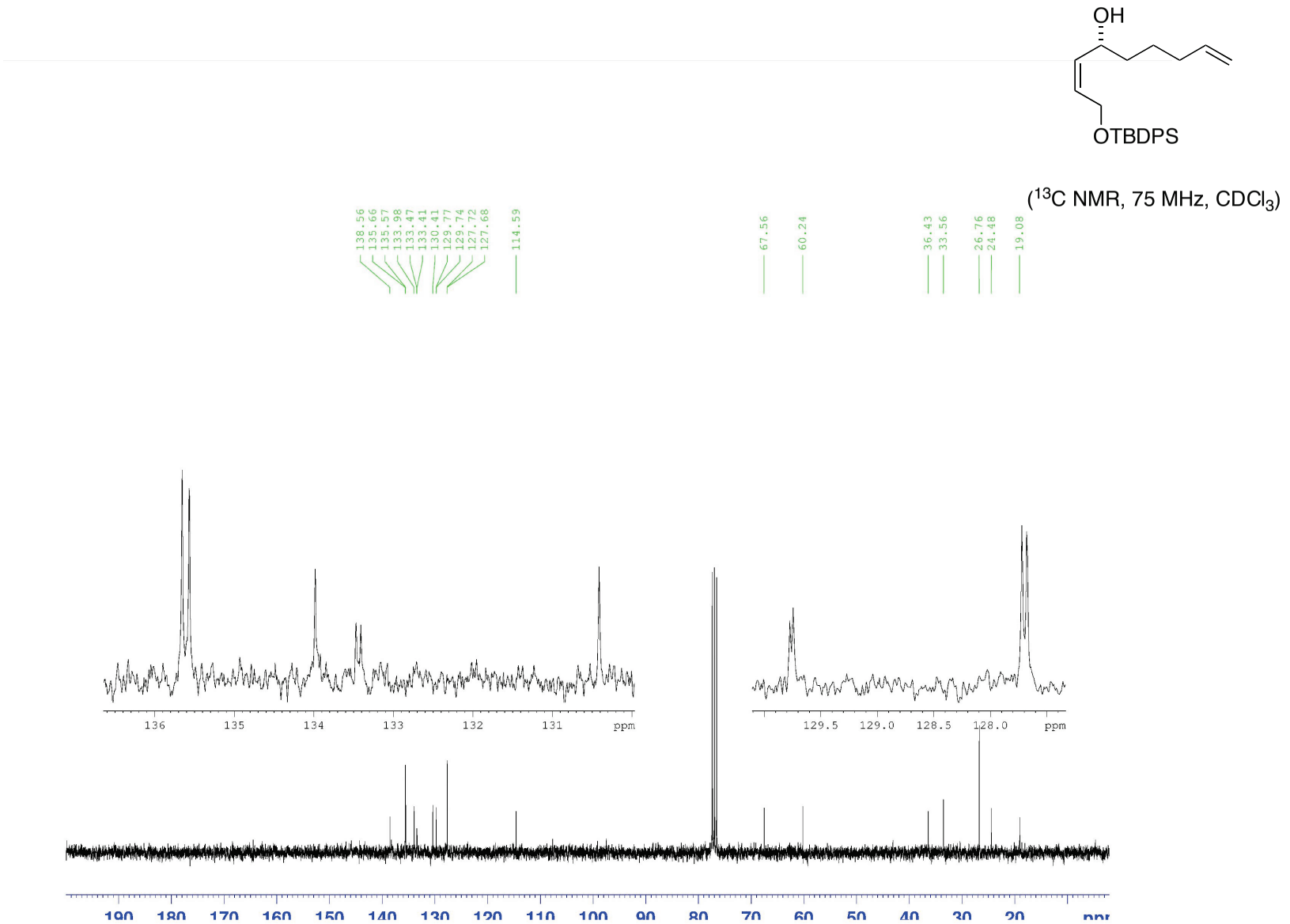
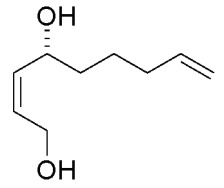
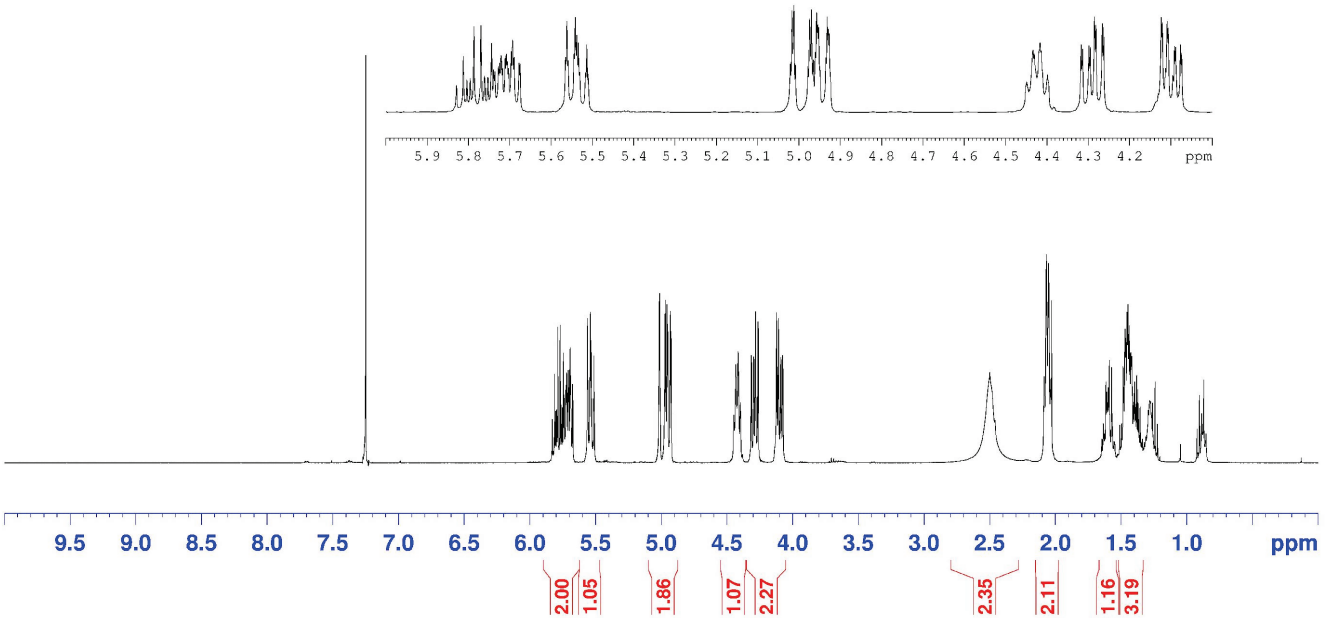
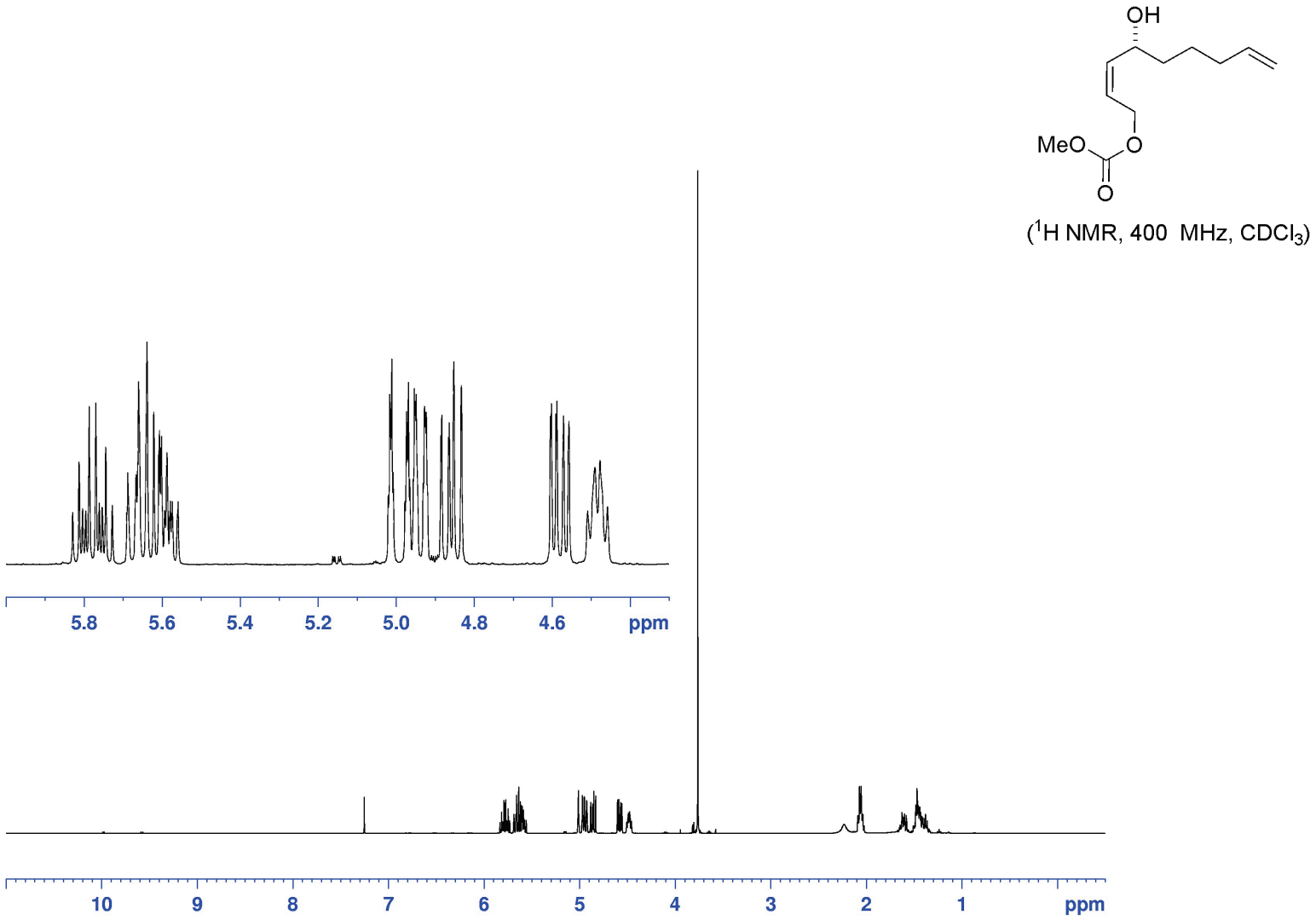
ppm
00
01
96
94
94
90
94
07
06
08

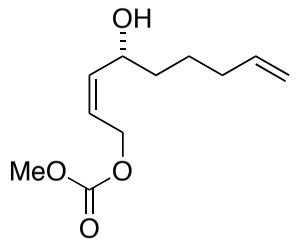

OH
OTBDPS
(^{13}C NMR, 75 MHz, $CDCl_3$)
138.56
135.66
135.57
133.98
133.47
133.41
130.41
129.77
129.74
127.72
127.68
114.59
67.56
60.24
36.43
33.56
26.76
24.48
19.08
136
135
134
133
132
131
ppm
129.5
129.0
128.5
128.0
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm



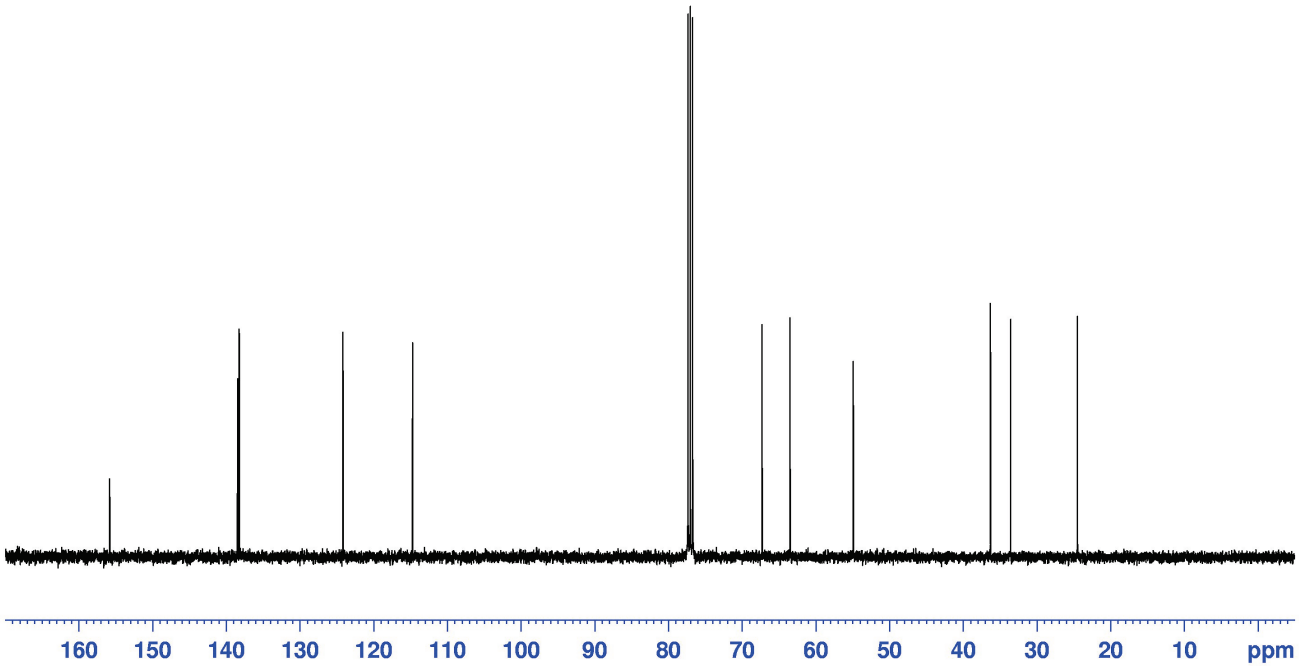
(^{1}H NMR, 400 MHz, $CDCl_3$)

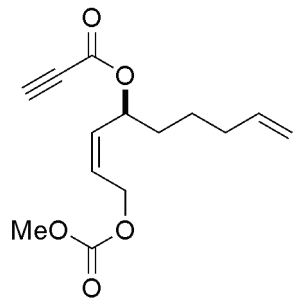



OH
MeO
O
O
(1H NMR, 400 MHz, CDCl3)
5.8
5.6
5.4
5.2
5.0
4.8
4.6
ppm
10
9
8
7
6
5
4
3
2
1
ppm

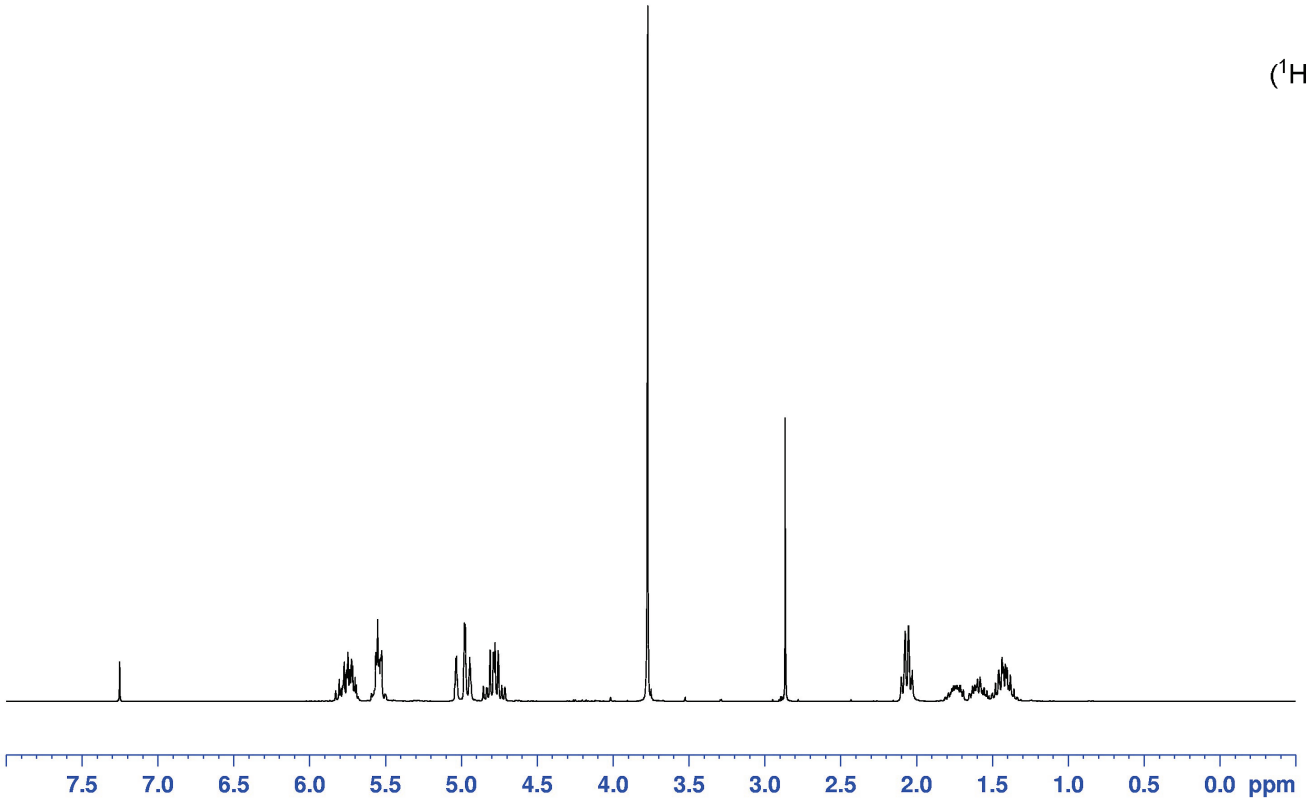


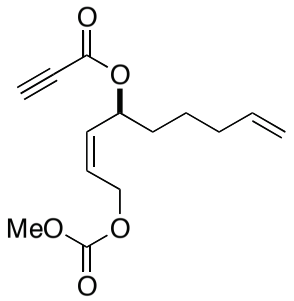
(^{13}C NMR, 100 MHz, $CDCl_3$)



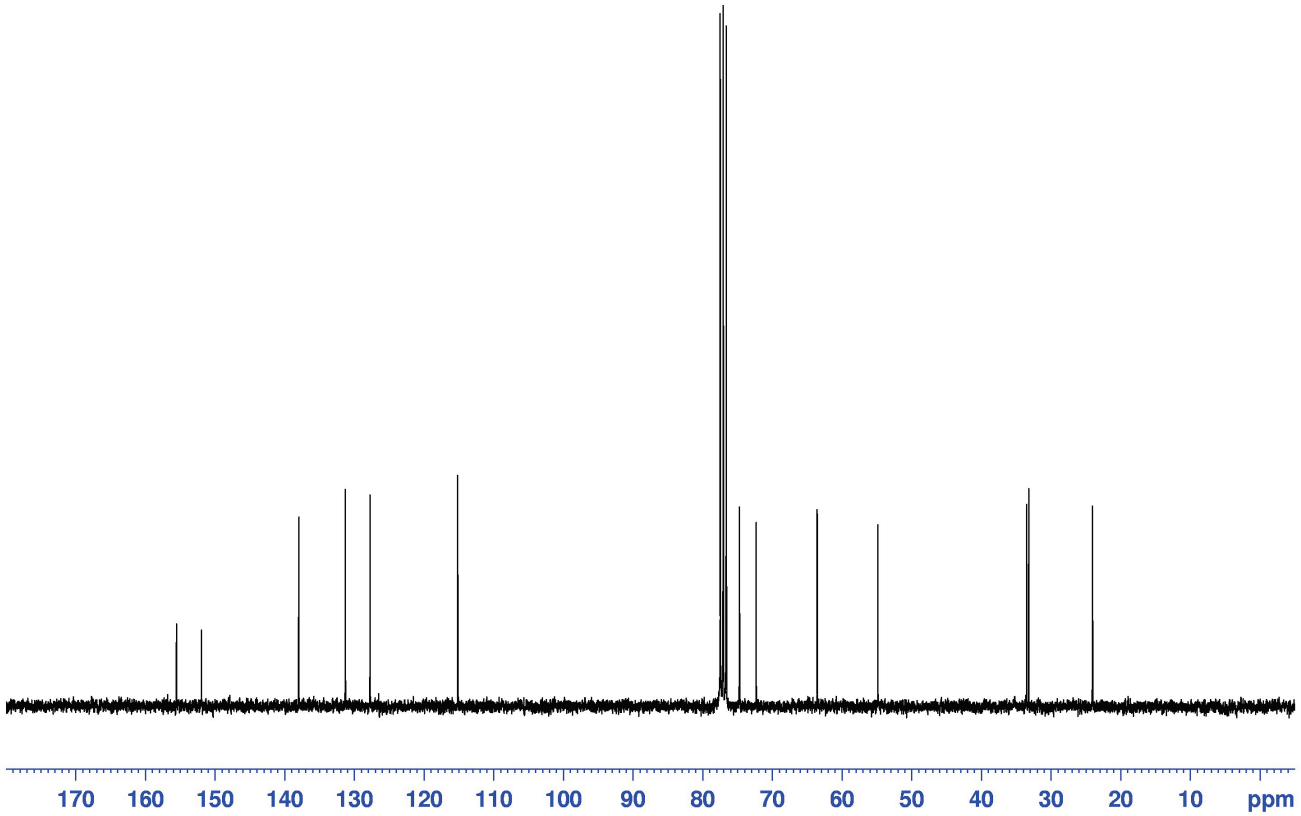


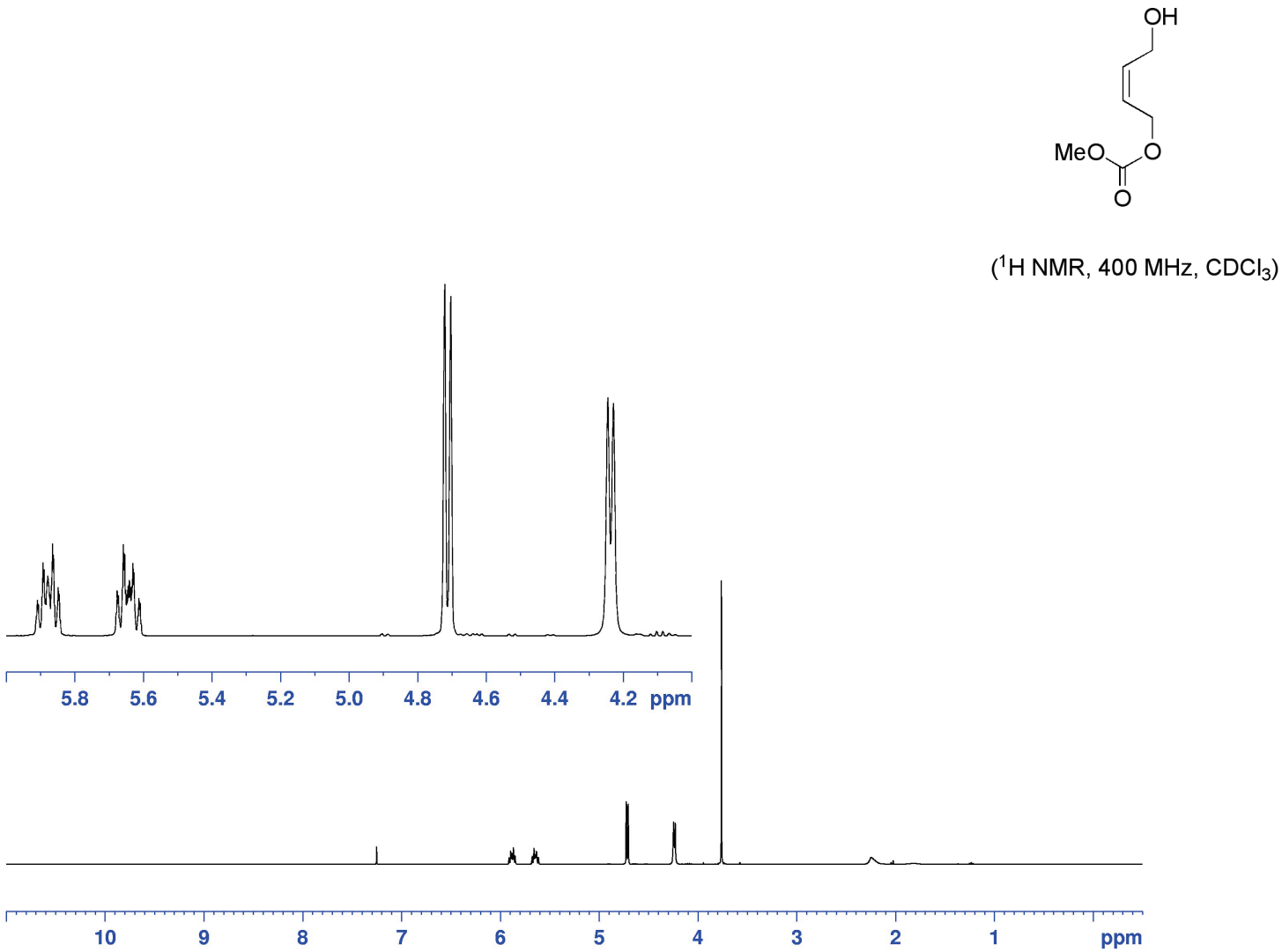
(^{1}H NMR, 300 MHz, $CDCl_3$)

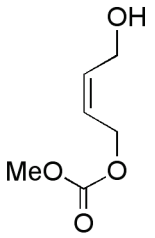




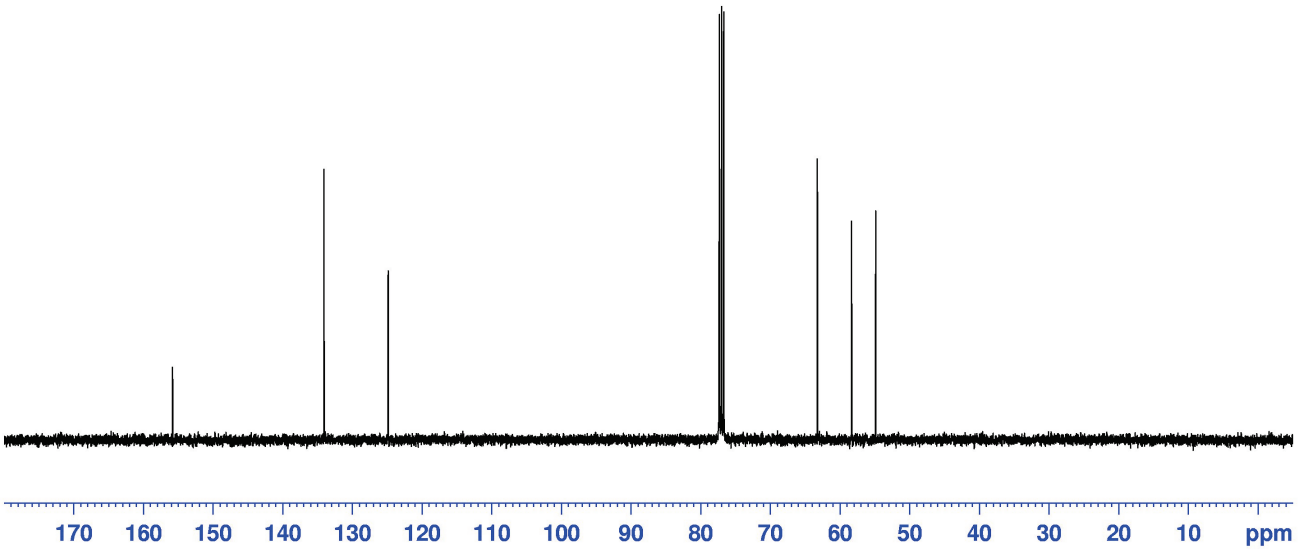
(^{13}C NMR, 75 MHz, $CDCl_3$)

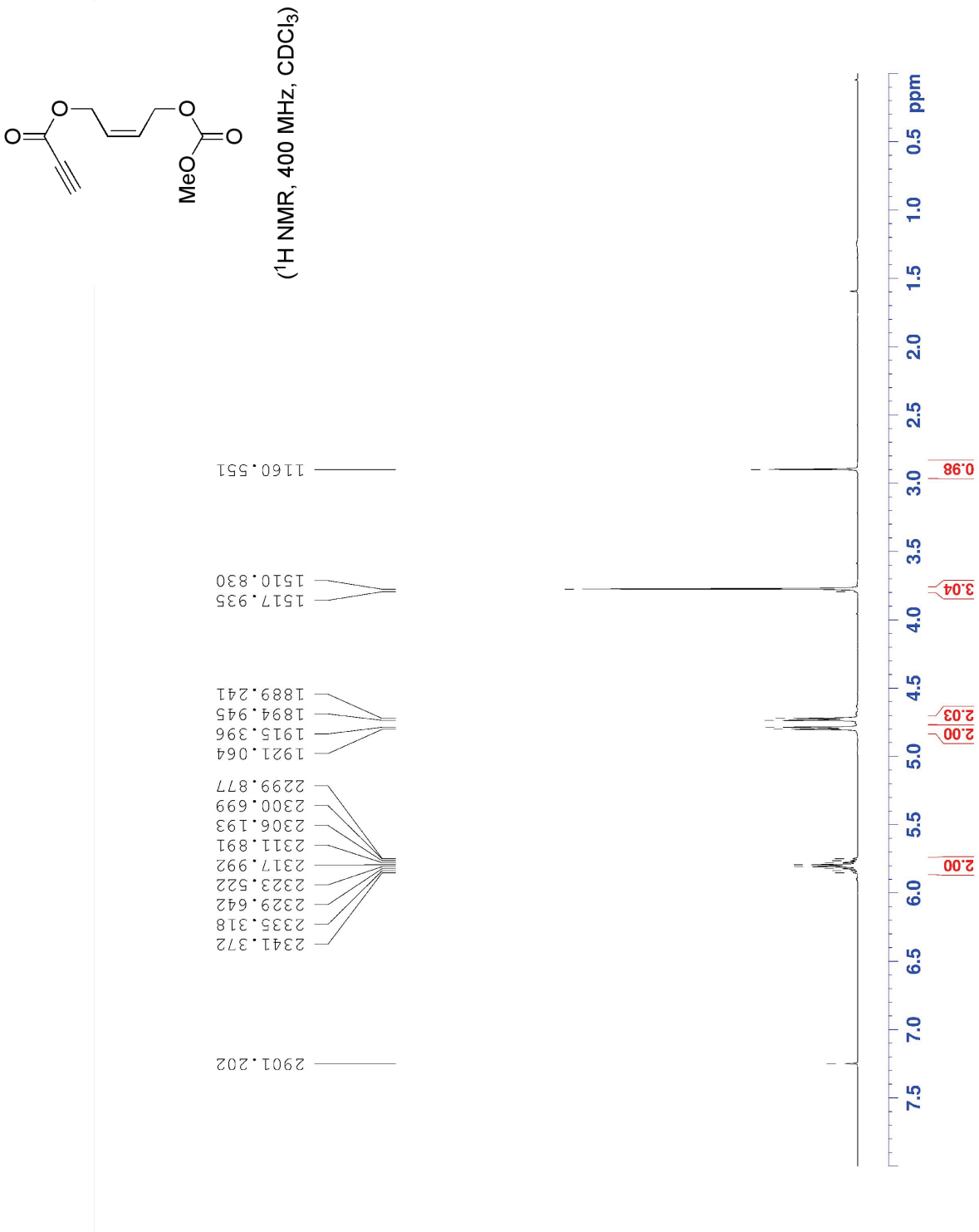


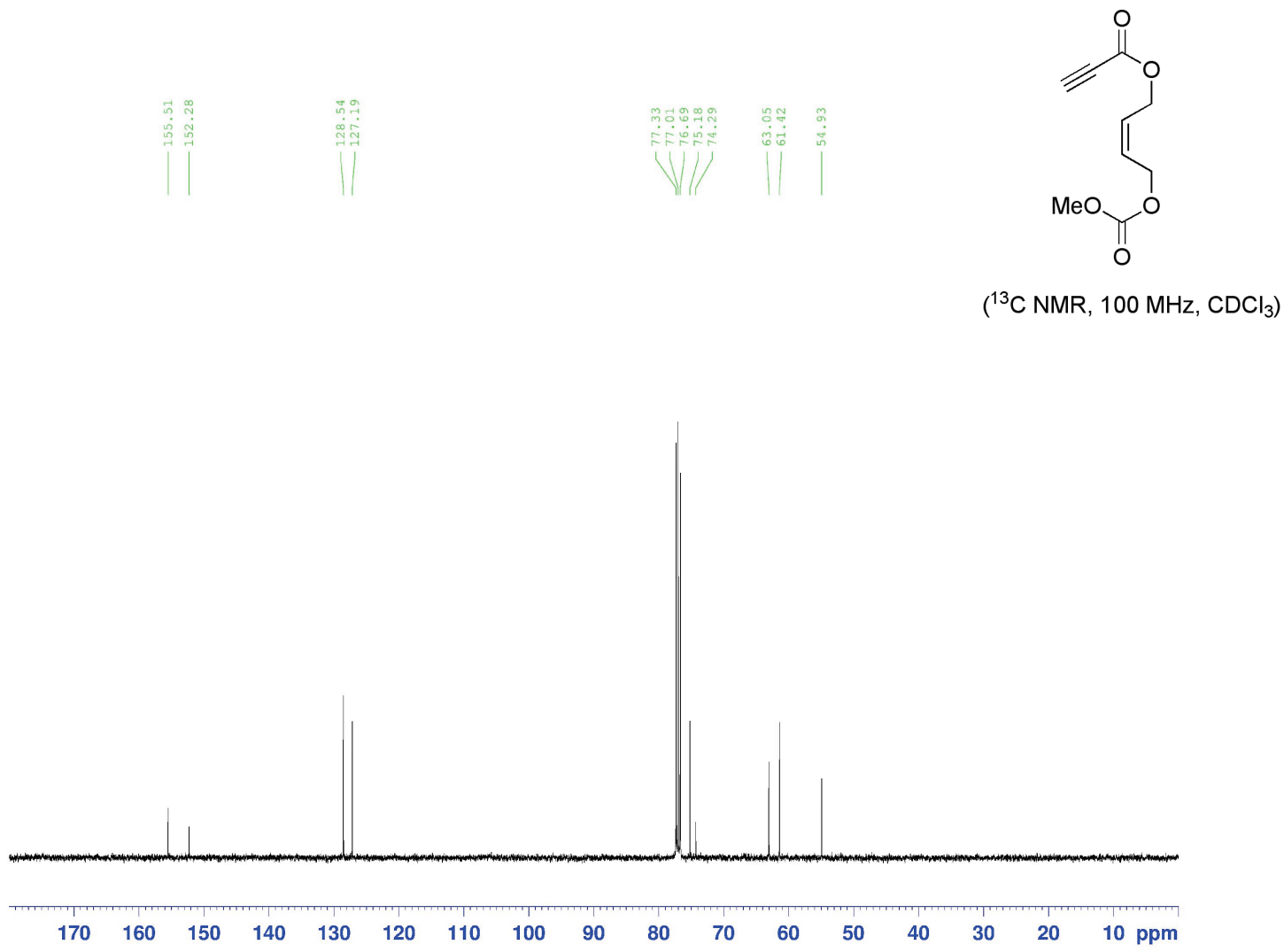

OH
MeO
O
O
(1H NMR, 400 MHz, CDCl3)
5.8
5.6
5.4
5.2
5.0
4.8
4.6
4.4
4.2
ppm
10
9
8
7
6
5
4
3
2
1
ppm



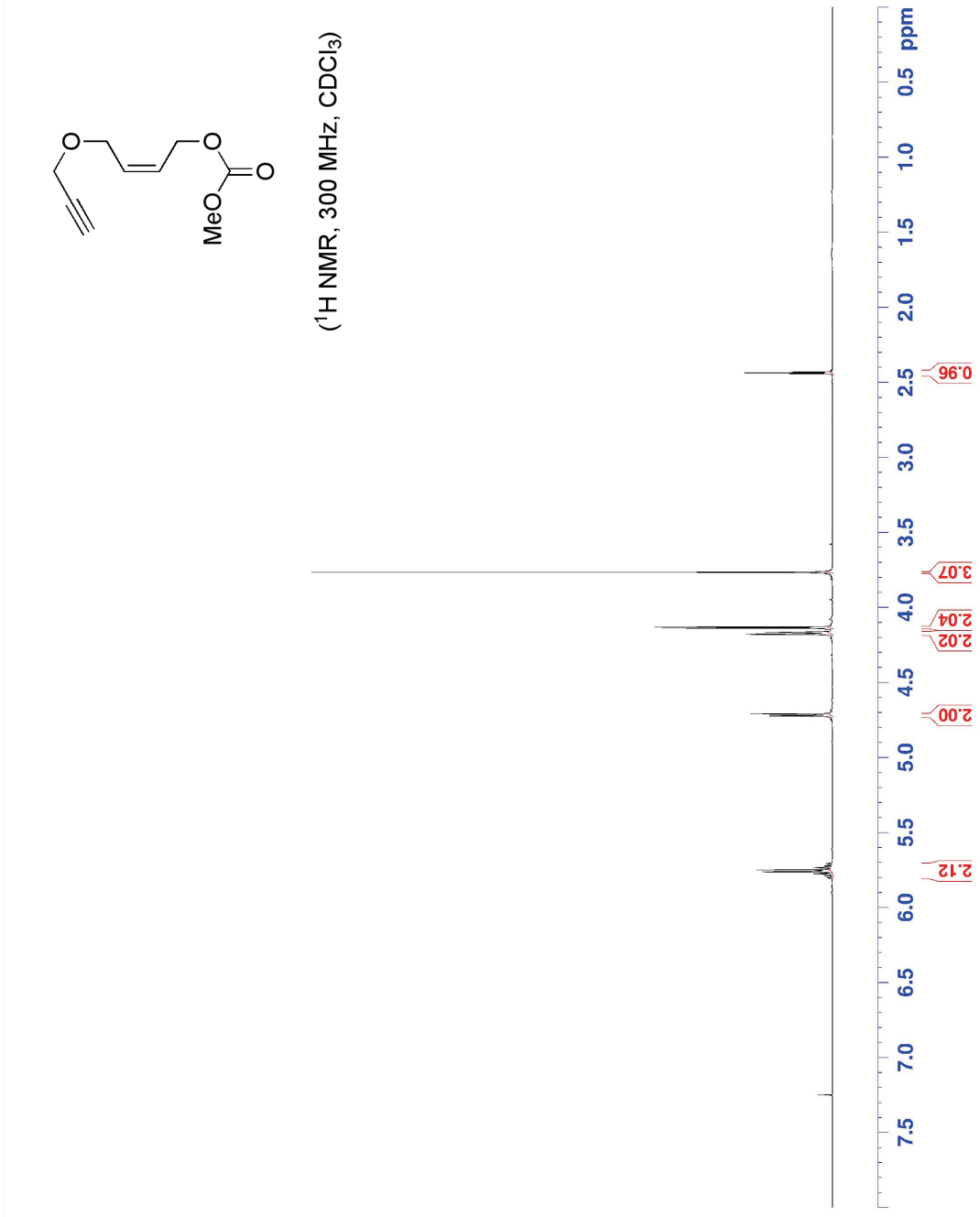
(^{13}C NMR, 100 MHz, $CDCl_3$)

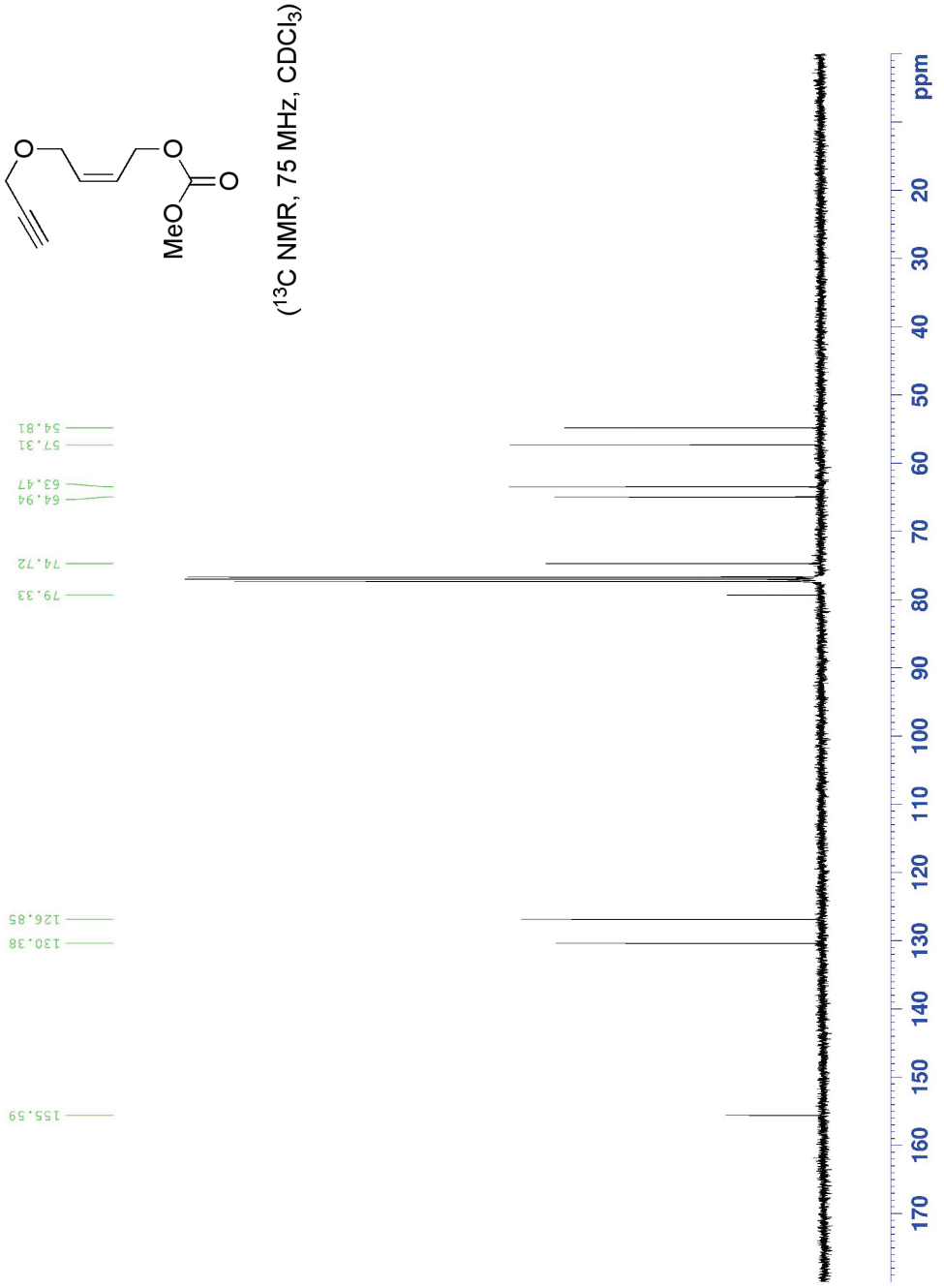


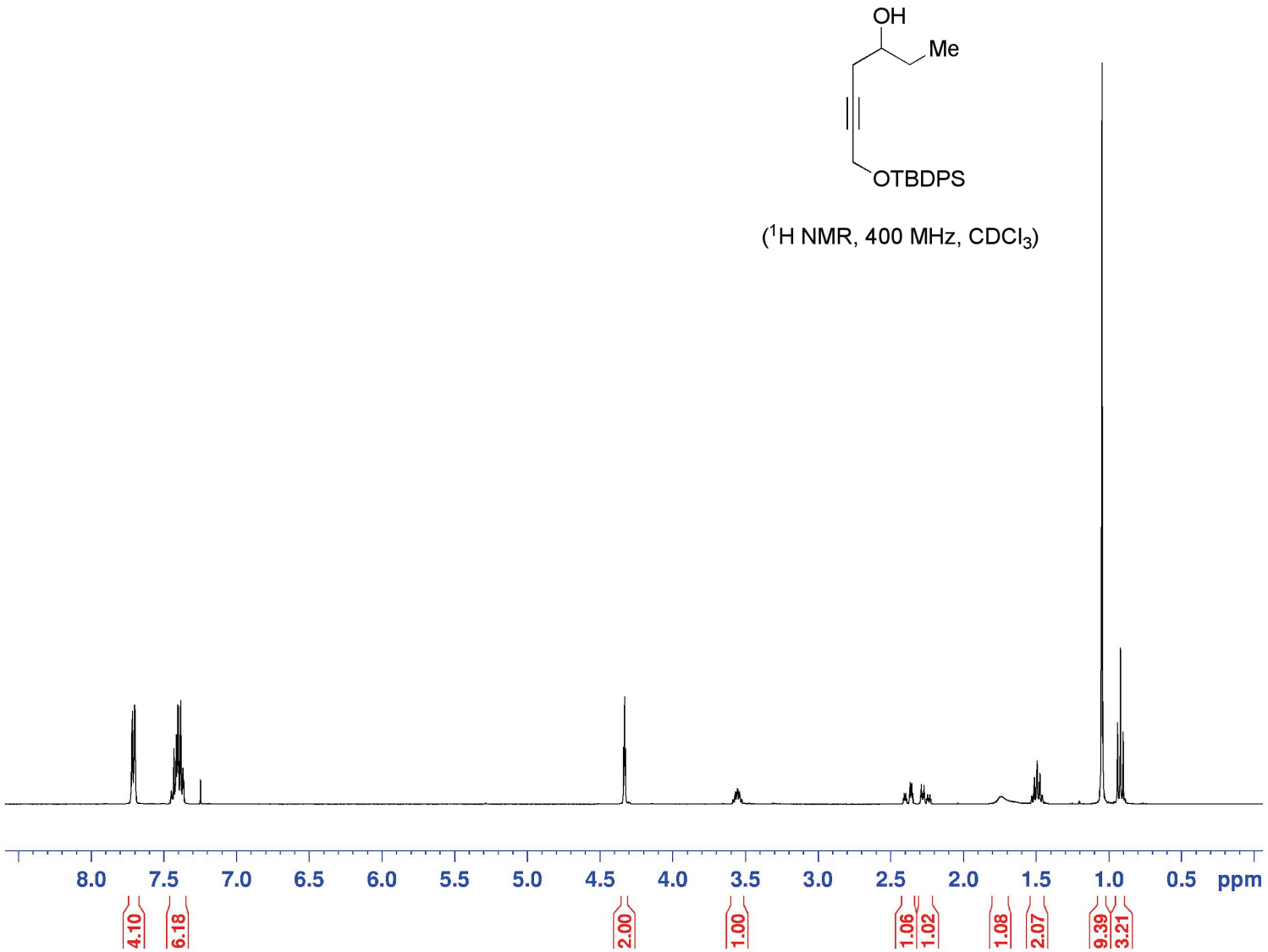

MeO
(1H NMR, 400 MHz, CDCl3)
11 60.551
1510.830
1517.935
1889.241
1894.945
1915.396
1921.064
2299.877
2300.699
2306.193
2311.891
2317.992
2323.522
2329.642
2335.318
2341.372
2901.202
0.98
3.04
2.03
2.00
2.00
ppm

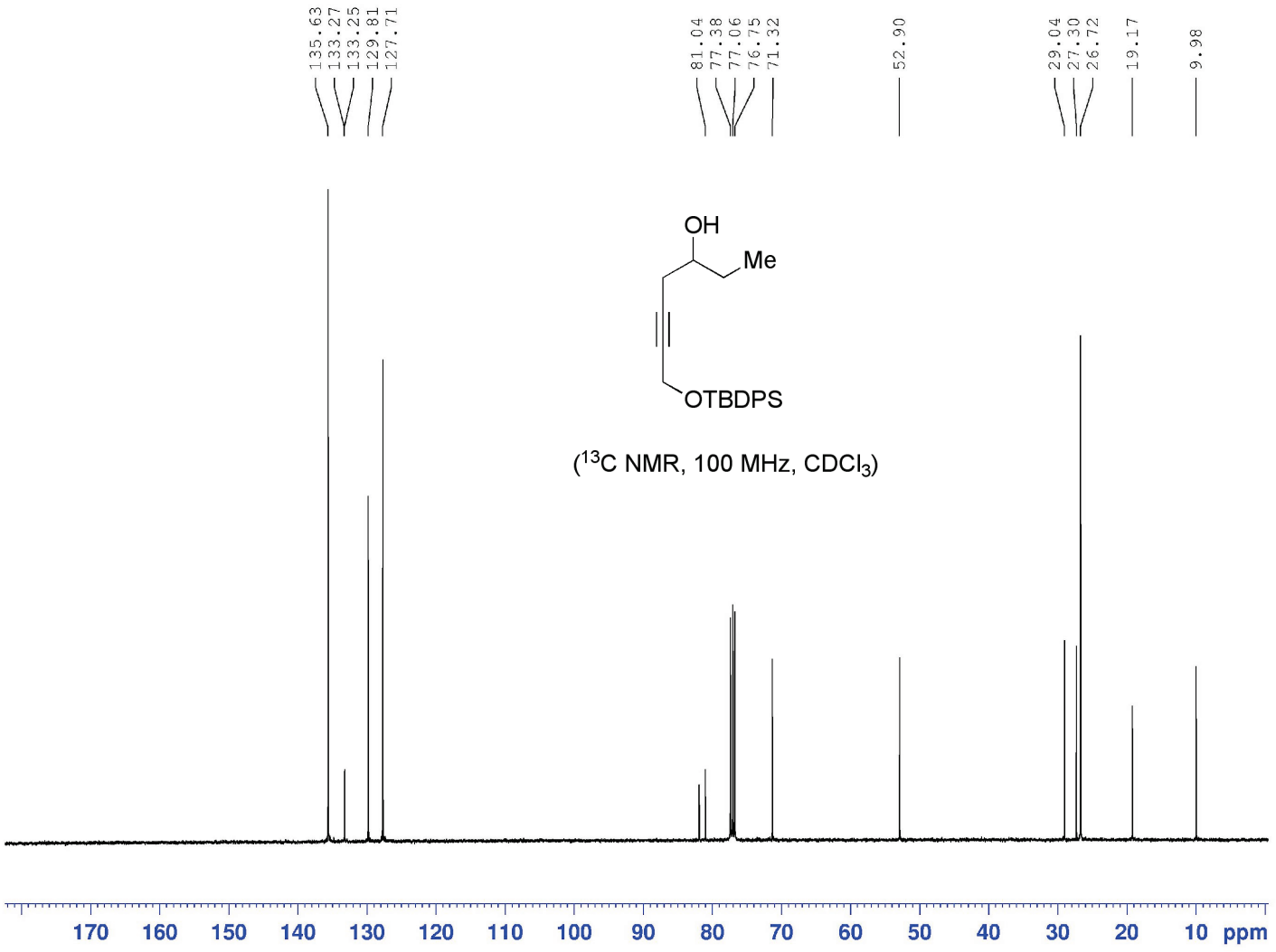


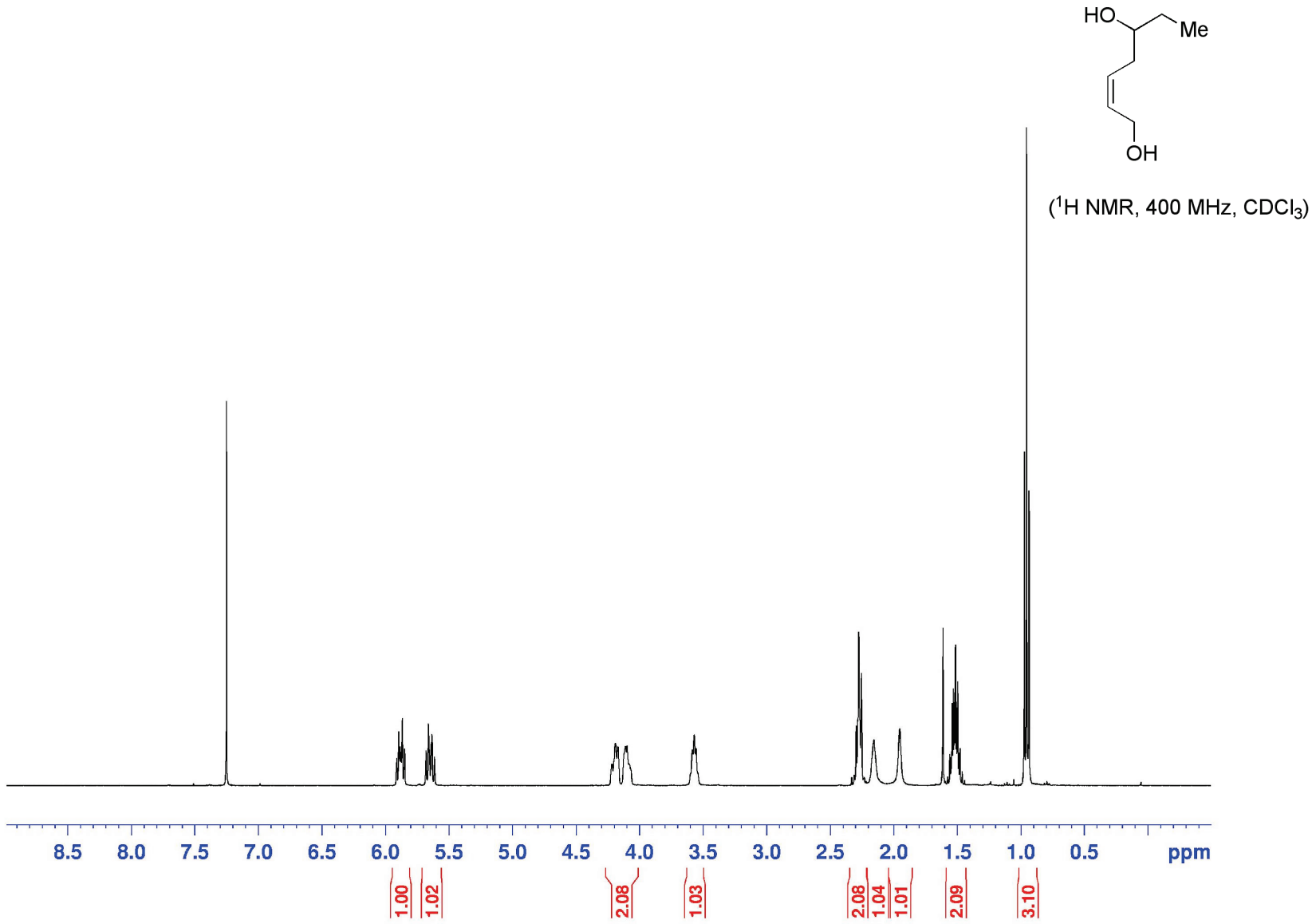
(^{13}C NMR, 100 MHz, $CDCl_3$)

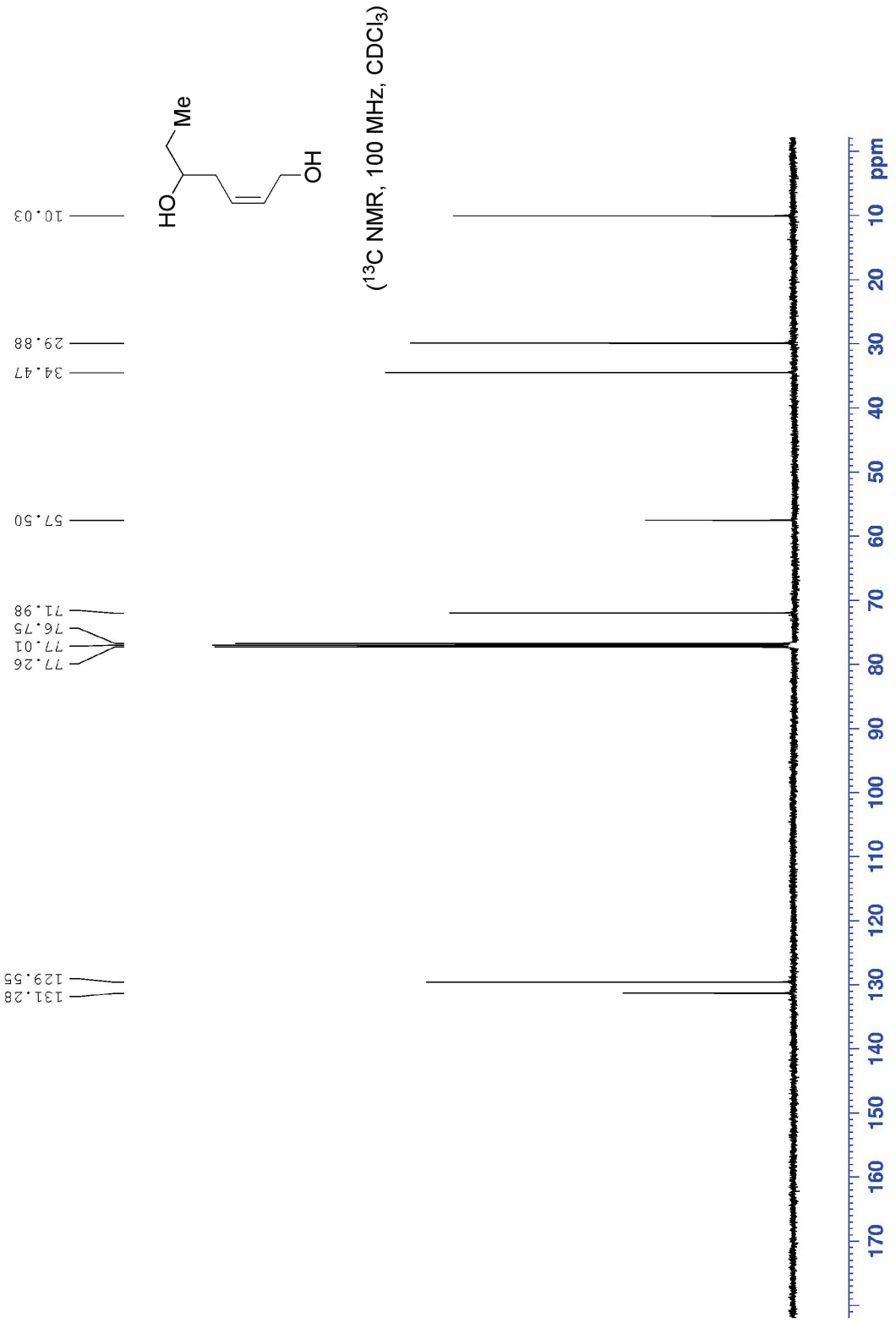

MeO
O
O
O
O
(^{1}H NMR, 300 MHz, CDCl$_3$)
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
0.96
3.07
2.04
2.02
2.00
2.12

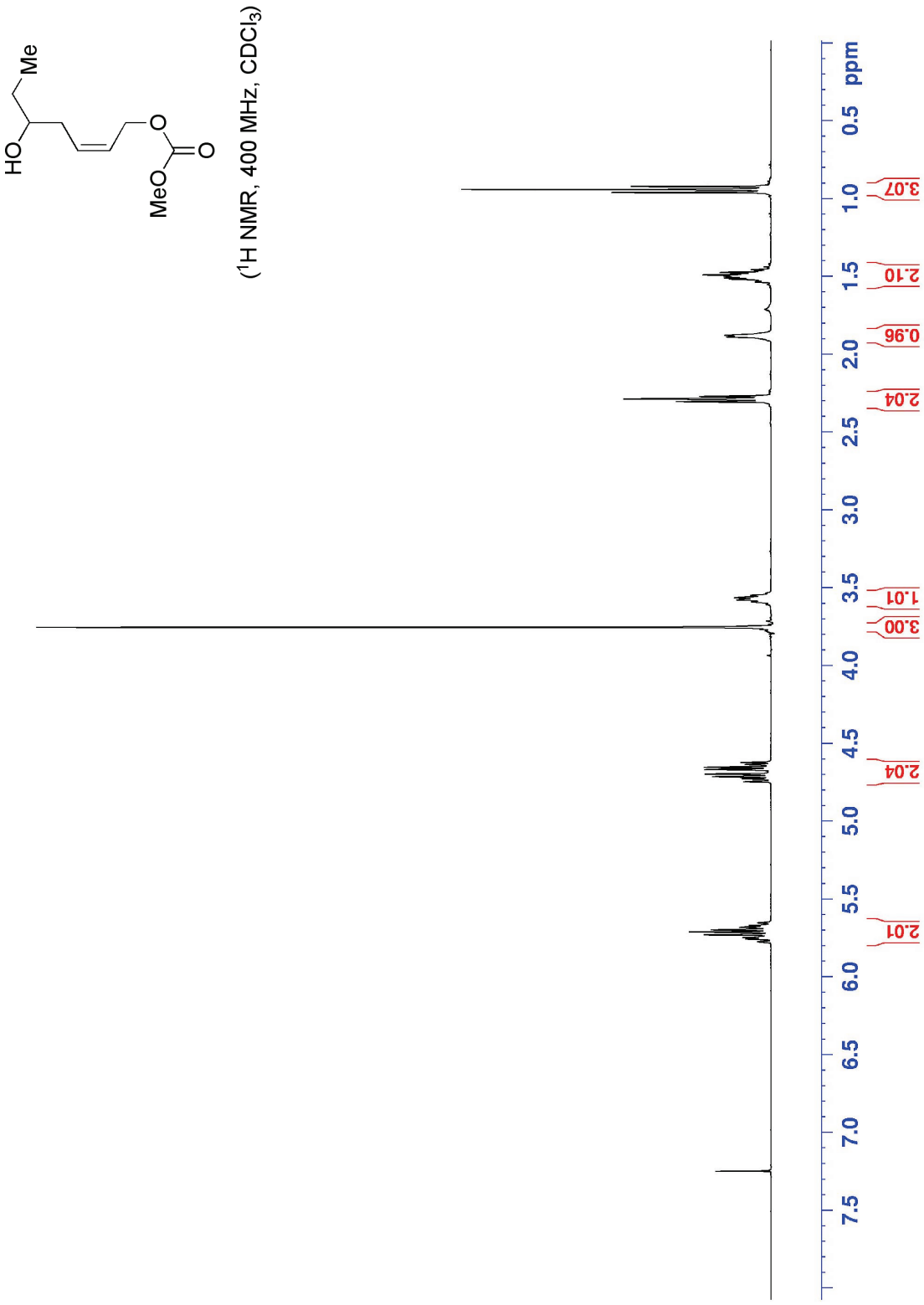

(^{13}C NMR, 75 MHz, $CDCl_3$)
MeO
O
O
O
54.81
57.31
63.47
64.94
74.72
79.33
126.85
130.38
155.59
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170

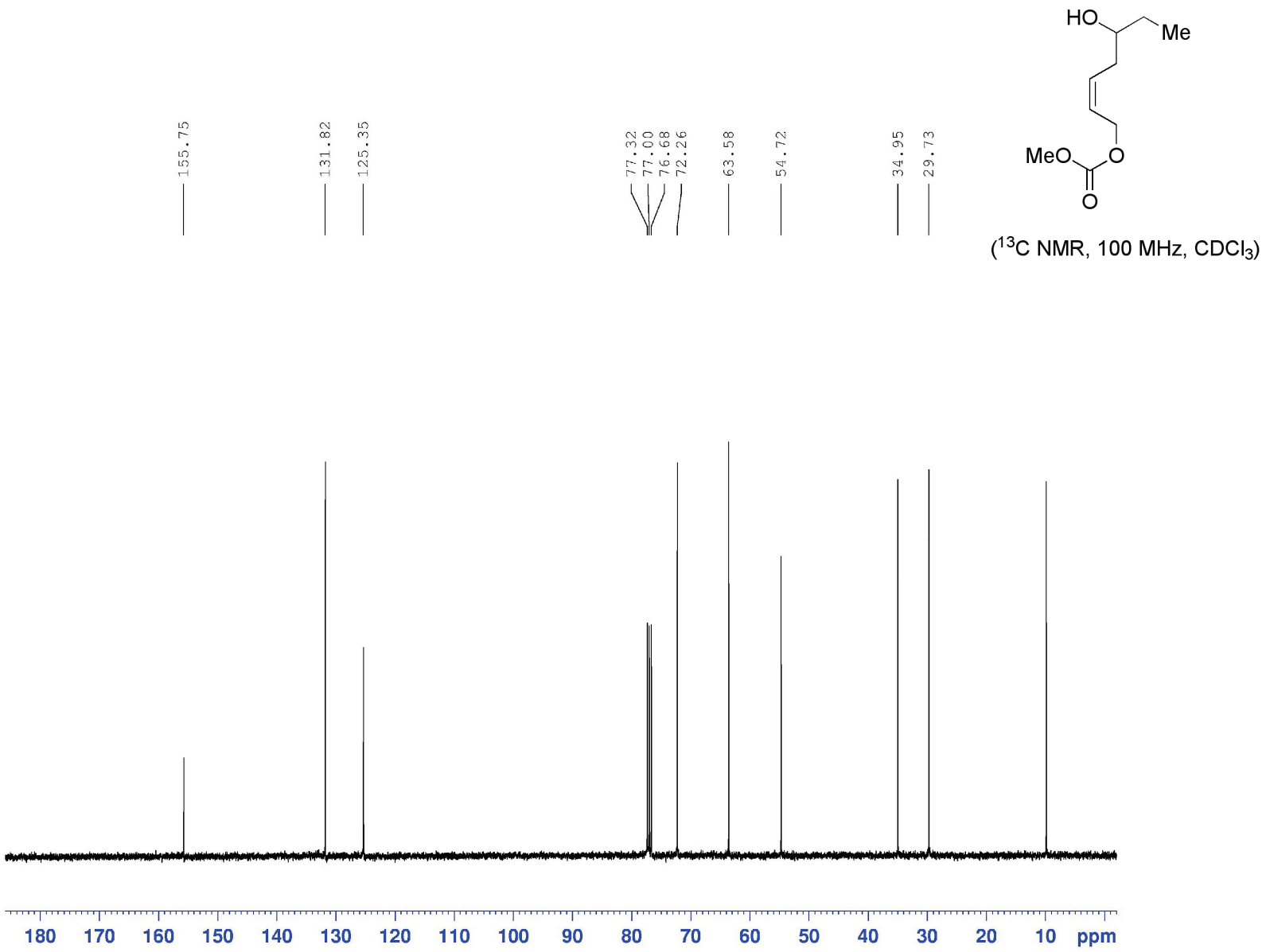

OH
Me
OTBDPS
(1H NMR, 400 MHz, CDCl3)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.10
6.18
2.00
1.00
1.06
1.02
1.08
2.07
9.39
3.21


135.63
133.27
133.25
129.81
127.71
81.04
77.38
77.06
76.75
71.32
52.90
29.04
27.30
26.72
19.17
9.98
OH
Me
OTBDPS
(13C NMR, 100 MHz, CDCl3)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

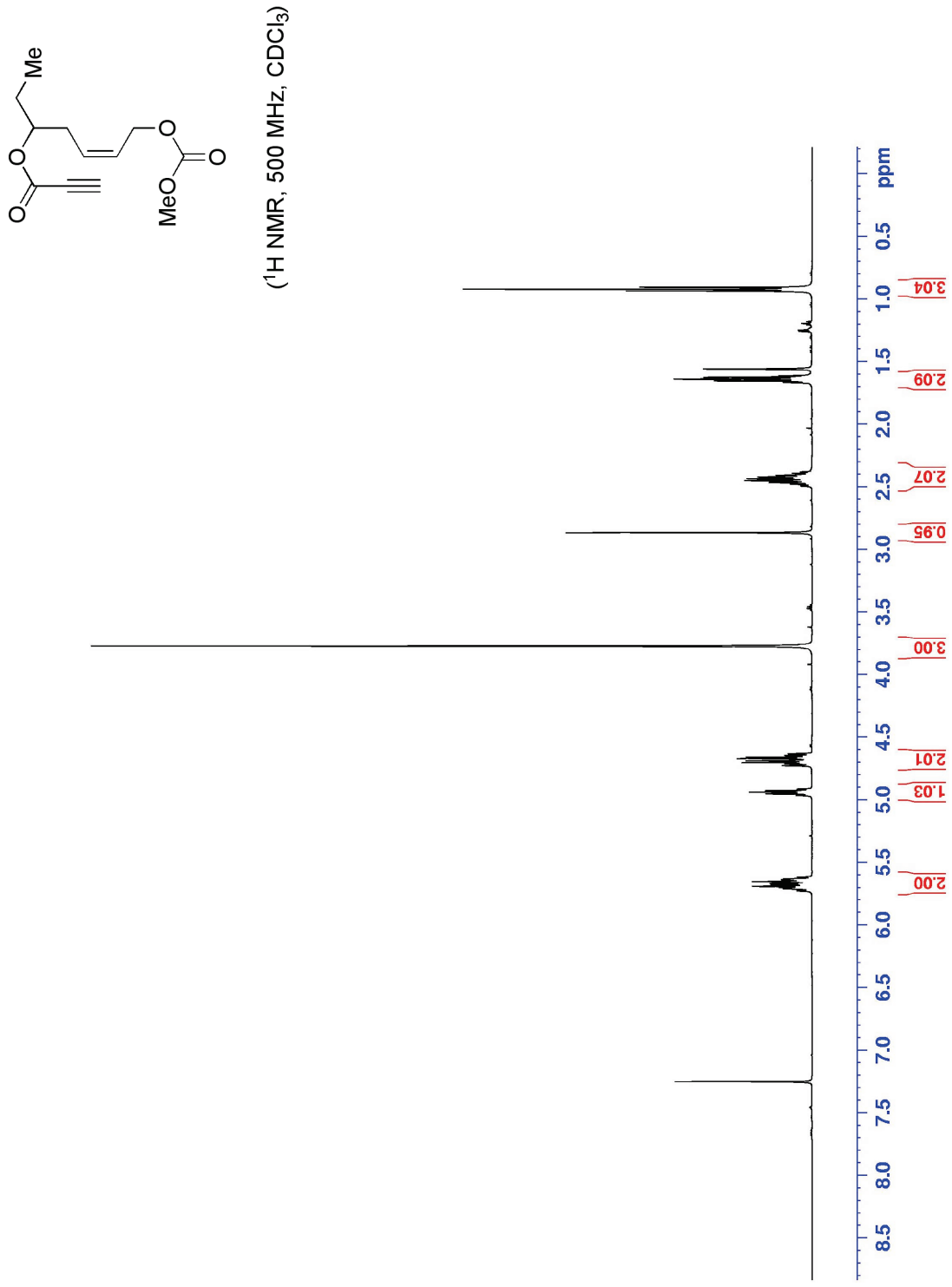

HO
Me
OH
(1H NMR, 400 MHz, CDCl3)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.02
2.08
1.03
2.08
1.04
1.01
2.09
3.10

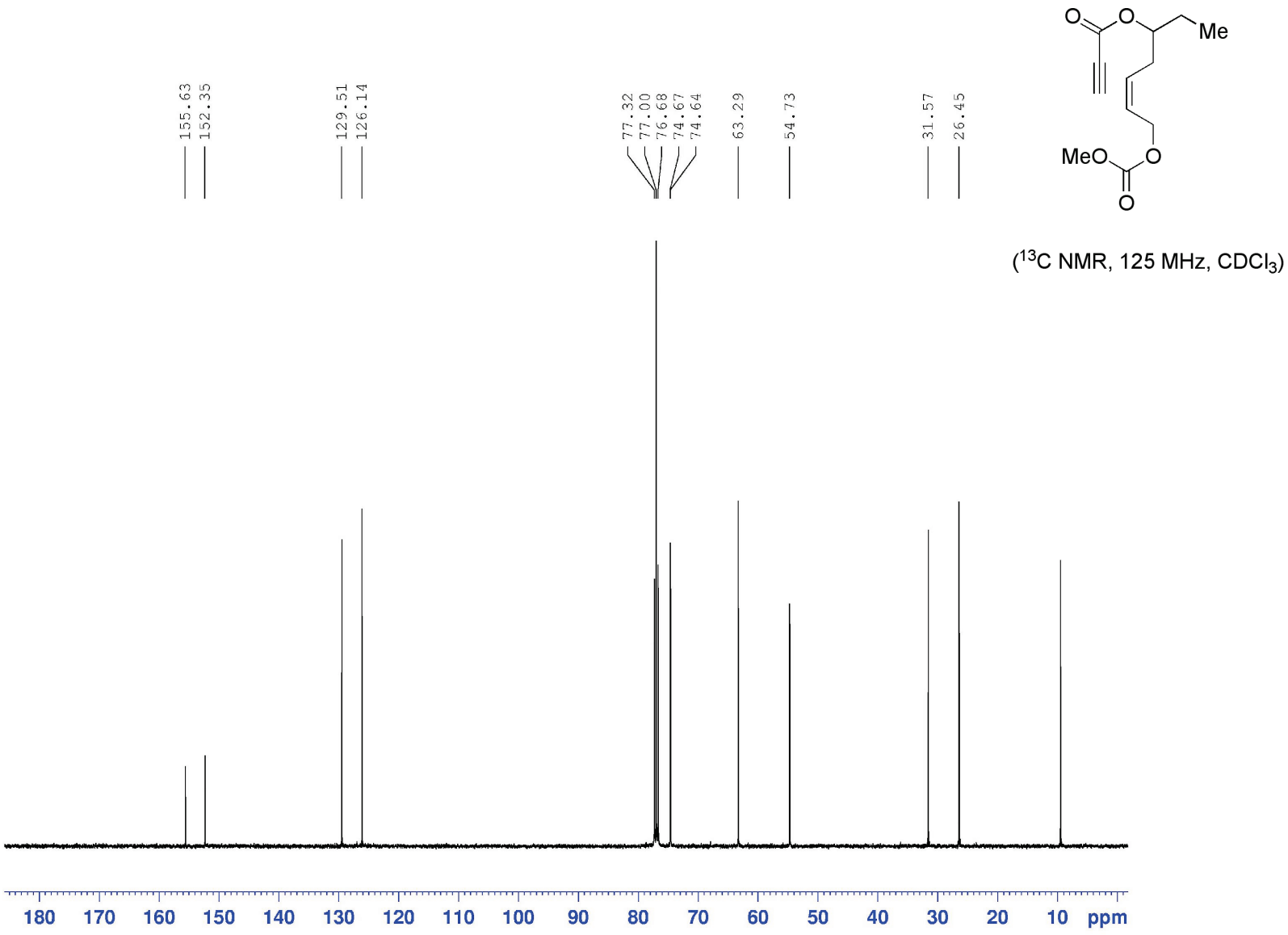

(13C NMR, 100 MHz, CDCl3)
Me
HO
OH
10.03
29.88
34.47
57.50
71.98
76.75
77.01
77.26
129.55
131.28
ppm


Me
HO
O
O
MeO
O
(1H NMR, 400 MHz, CDCl3)
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
3.07
2.10
0.96
2.04
1.01
3.00
2.04
2.01

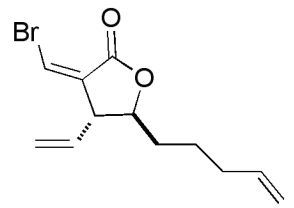


(^{13}C NMR, 100 MHz, $CDCl_3$)

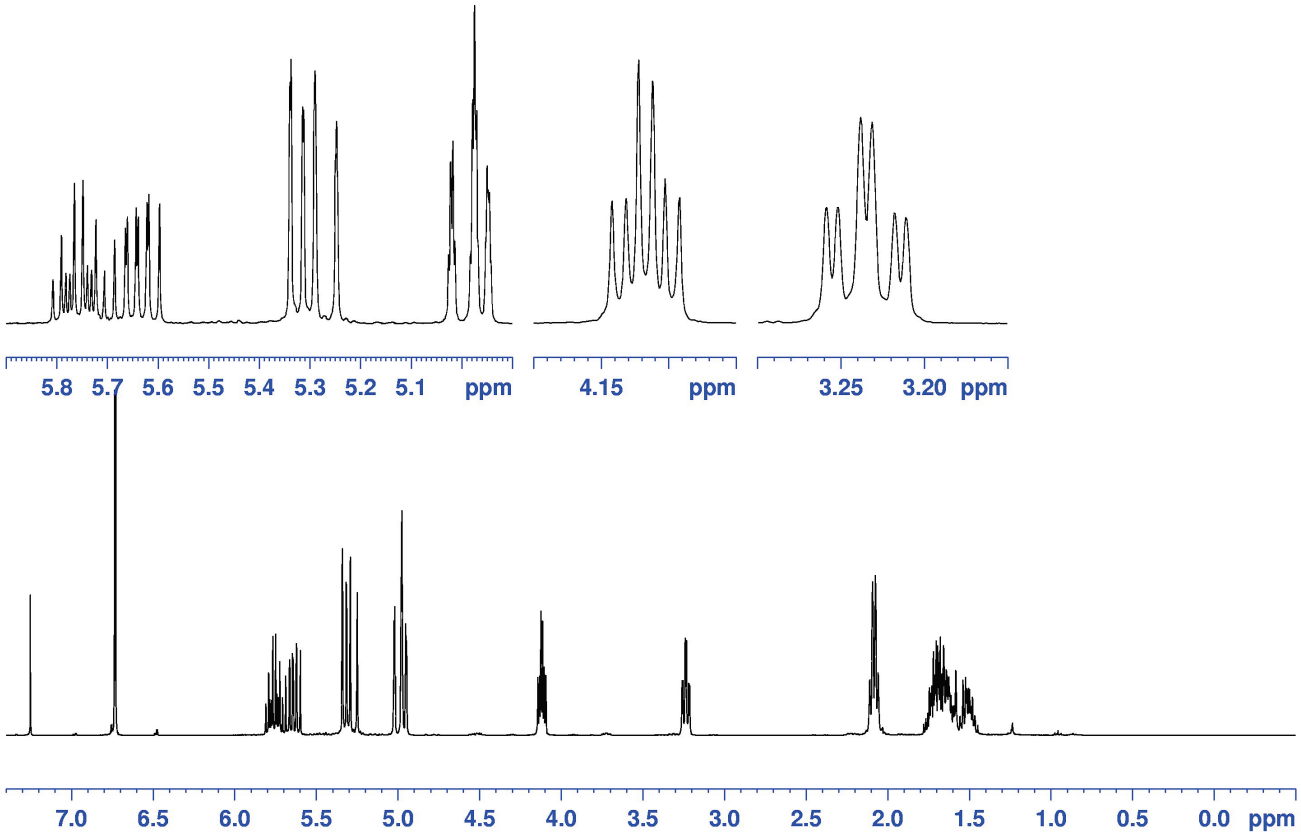

Me
O
O
O
O
MeO
O
(1H NMR, 500 MHz, CDCl3)
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
3.04
2.09
2.07
0.95
3.00
2.01
1.03
2.00

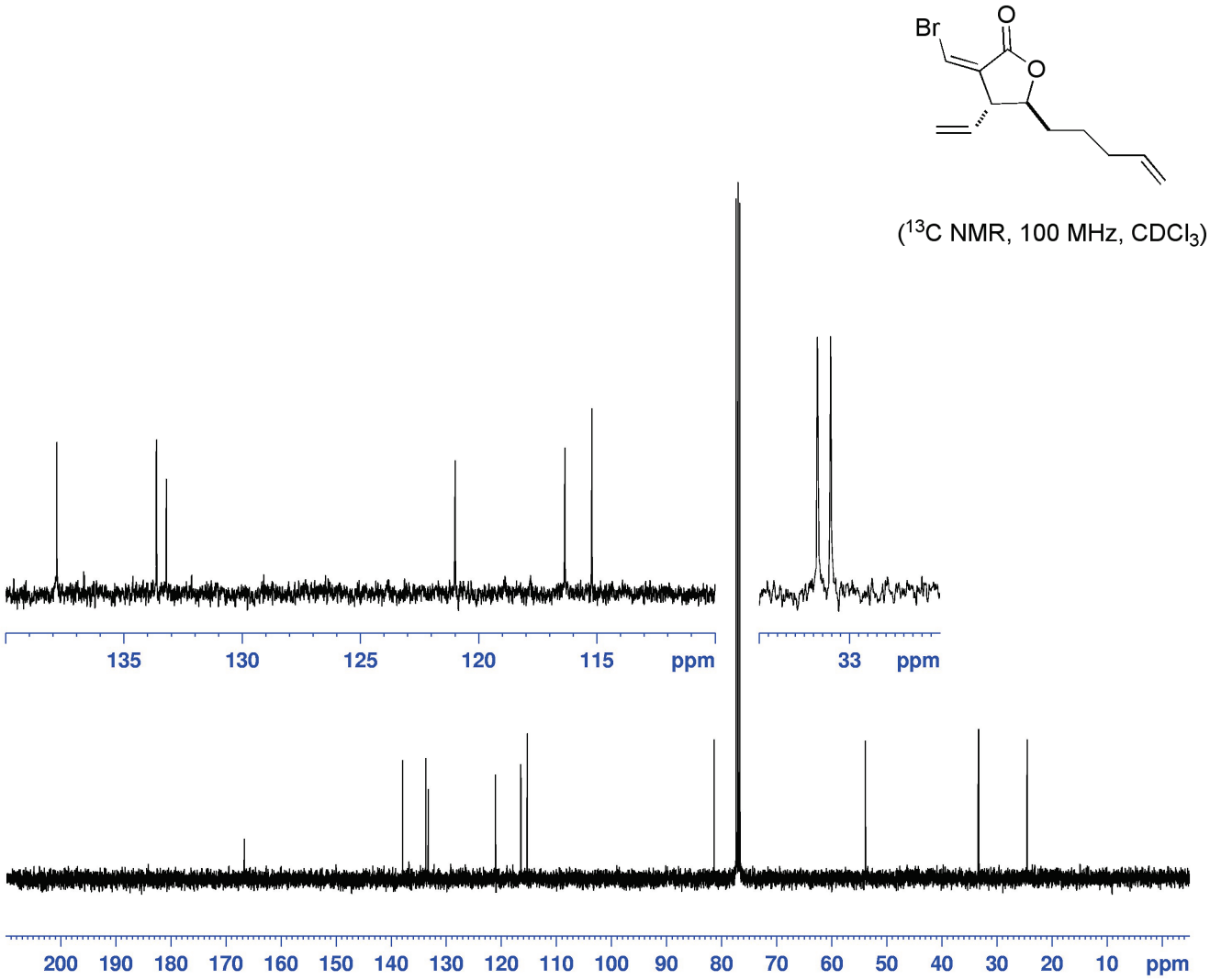


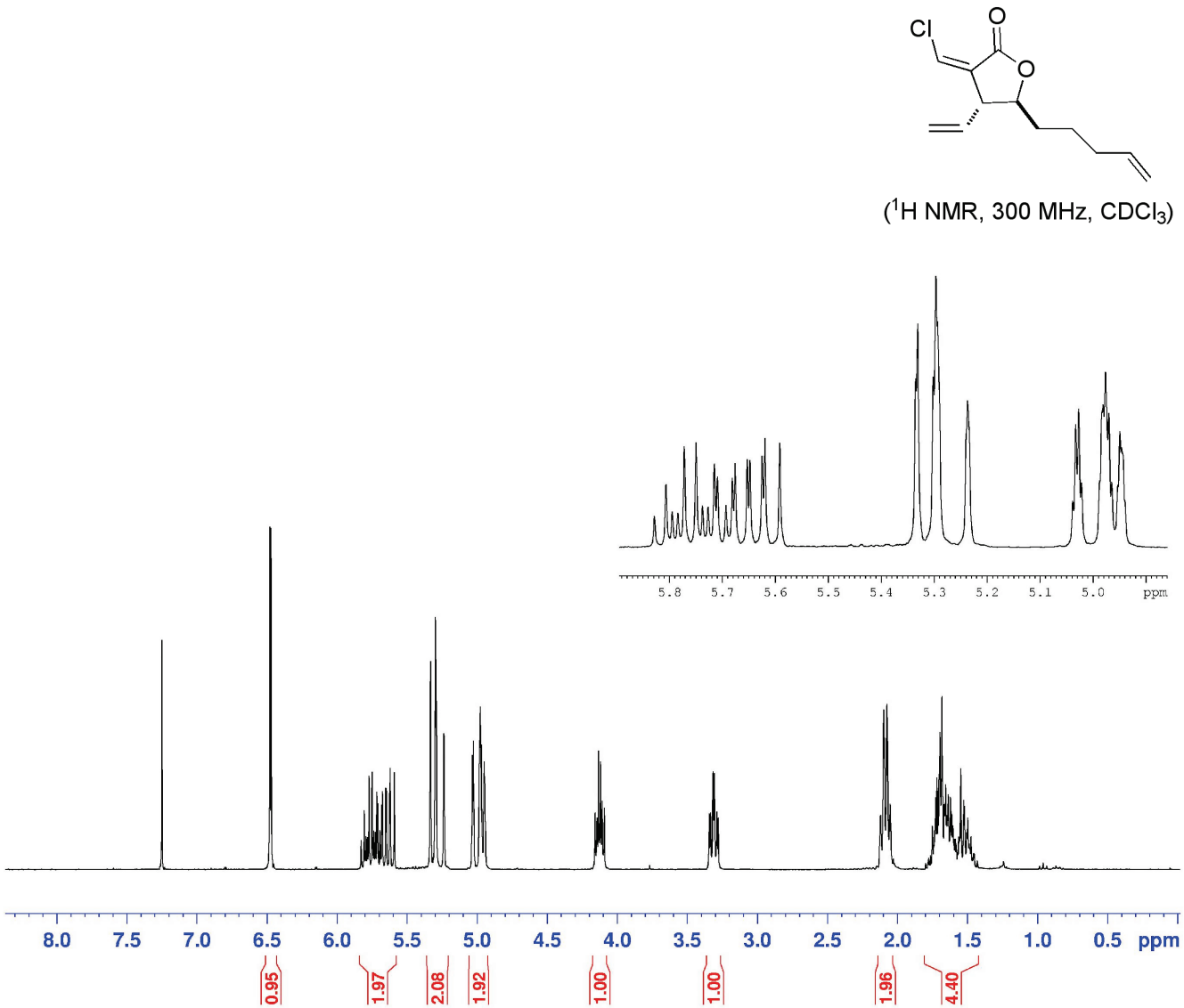
(^{13}C NMR, 125 MHz, $CDCl_3$)

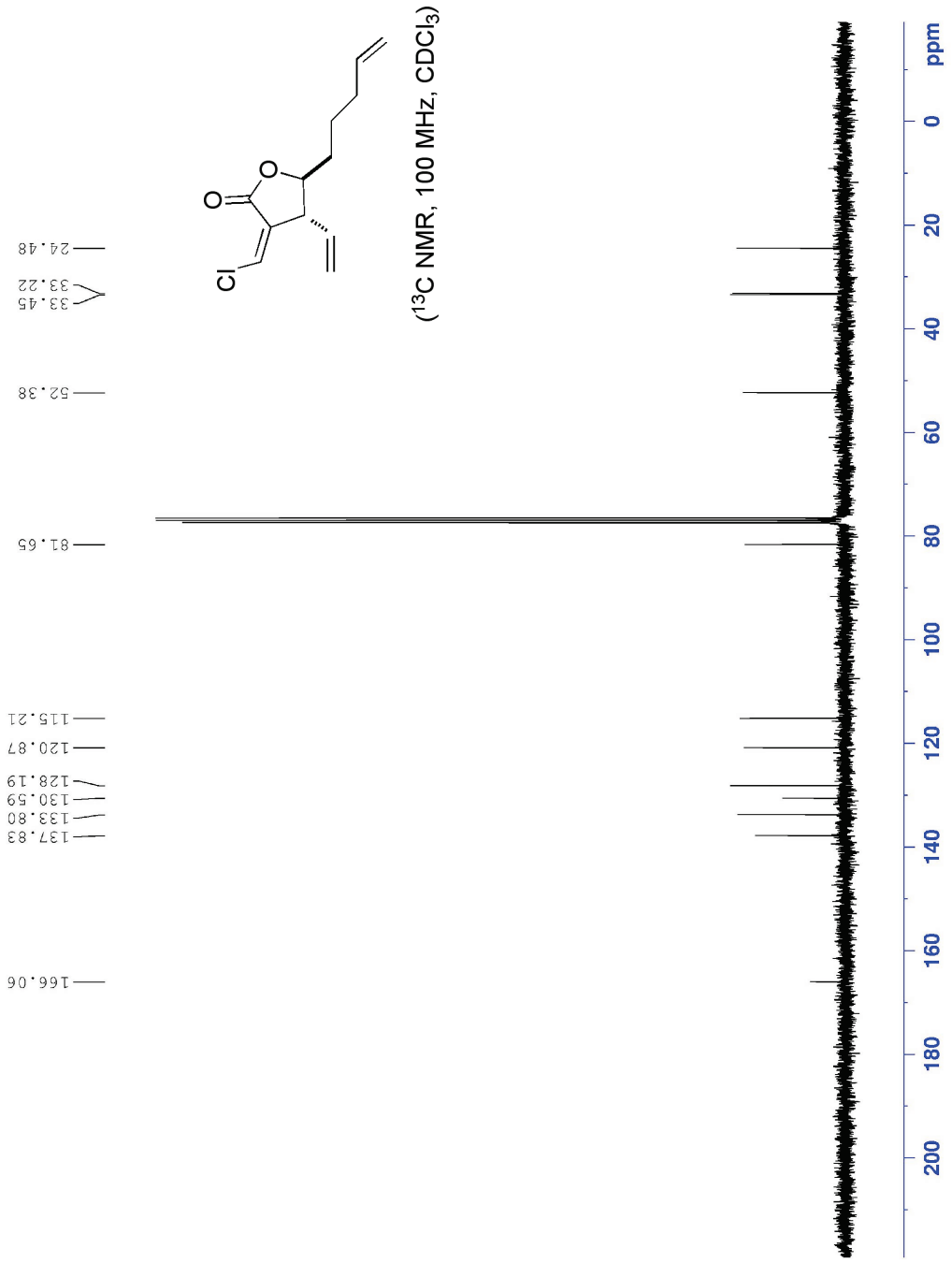


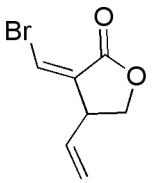
(^{1}H NMR, 400 MHz, $CDCl_3$)



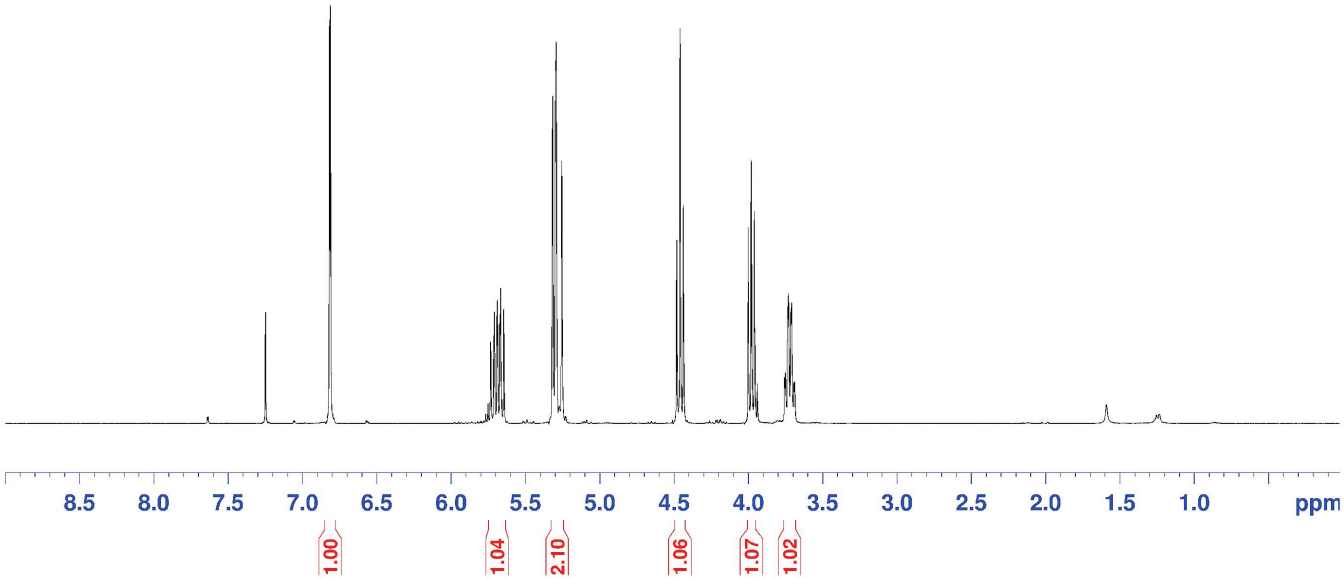

Br
O
O
(13C NMR, 100 MHz, CDCl3)
135
130
125
120
115
ppm
33
ppm
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

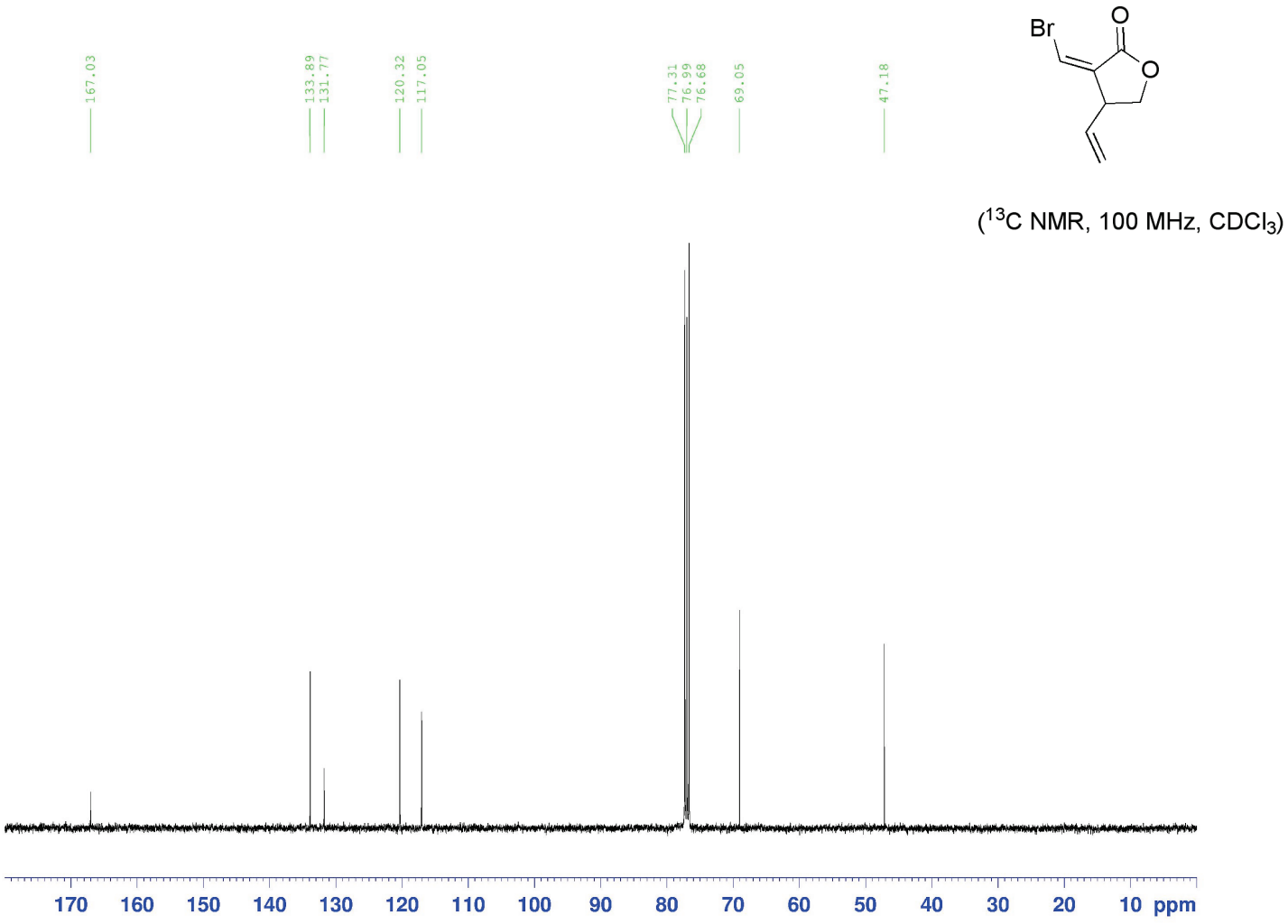

Cl
O
O
(1H NMR, 300 MHz, CDCl3)
5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 ppm
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.95
1.97
2.08
1.92
1.00
1.00
1.96
4.40


(^{13}C NMR, 100 MHz, $CDCl_3$)
Cl
O
O
24.48
33.22
33.45
52.38
81.65
115.21
120.87
128.19
130.59
133.80
137.83
166.06
ppm
0
20
40
60
80
100
120
140
160
180
200

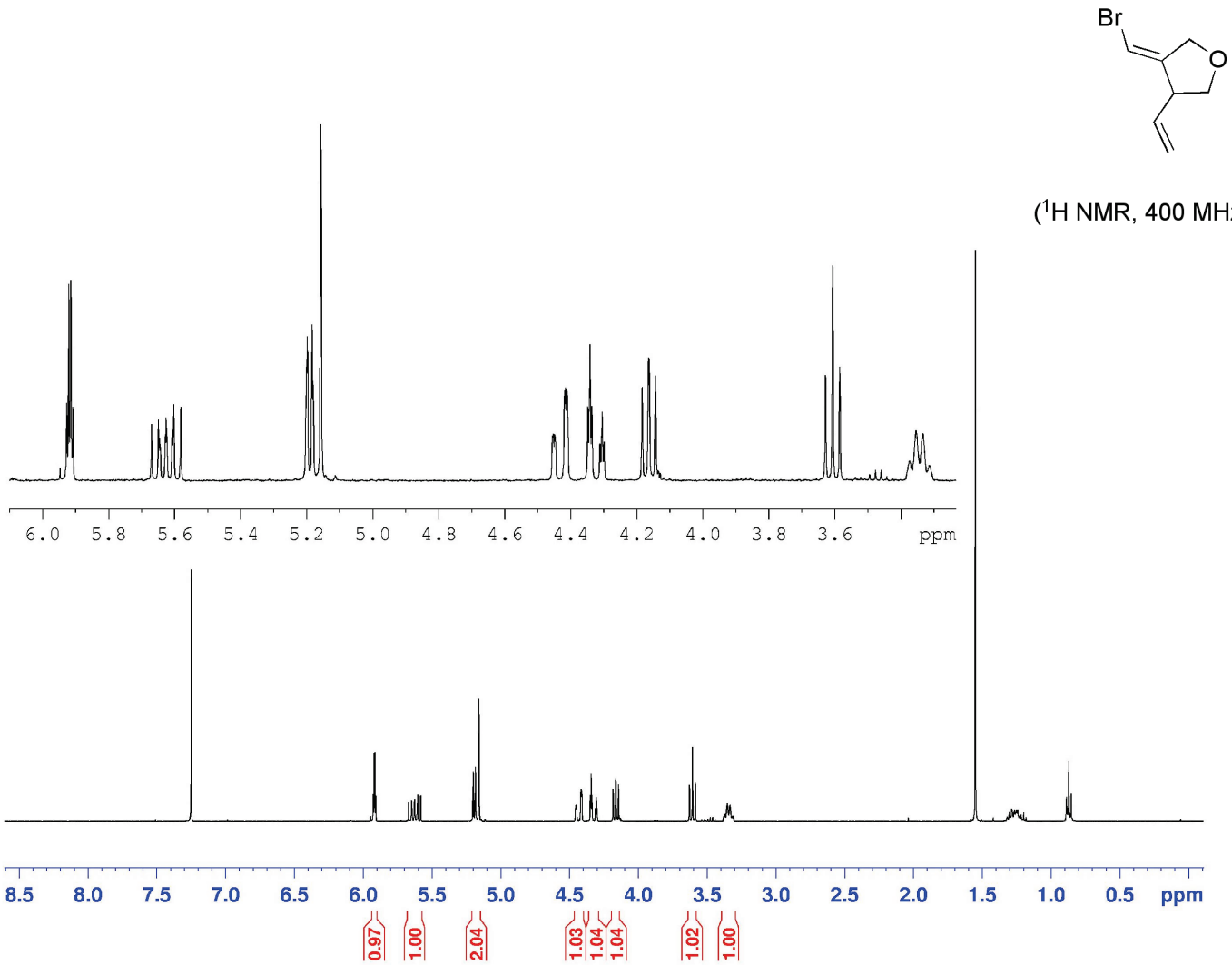


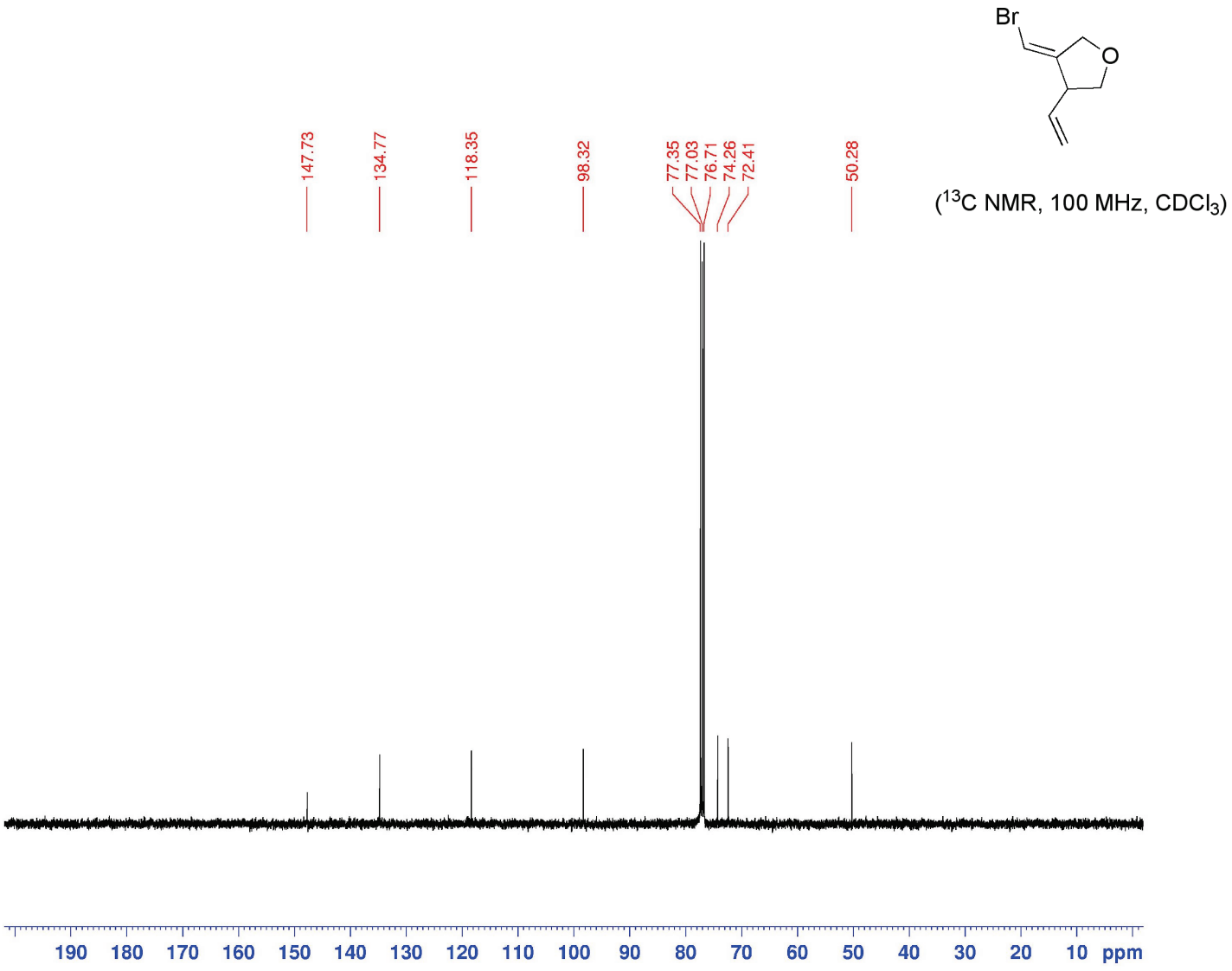
(^{1}H NMR, 400 MHz, $CDCl_3$)

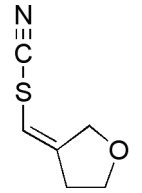




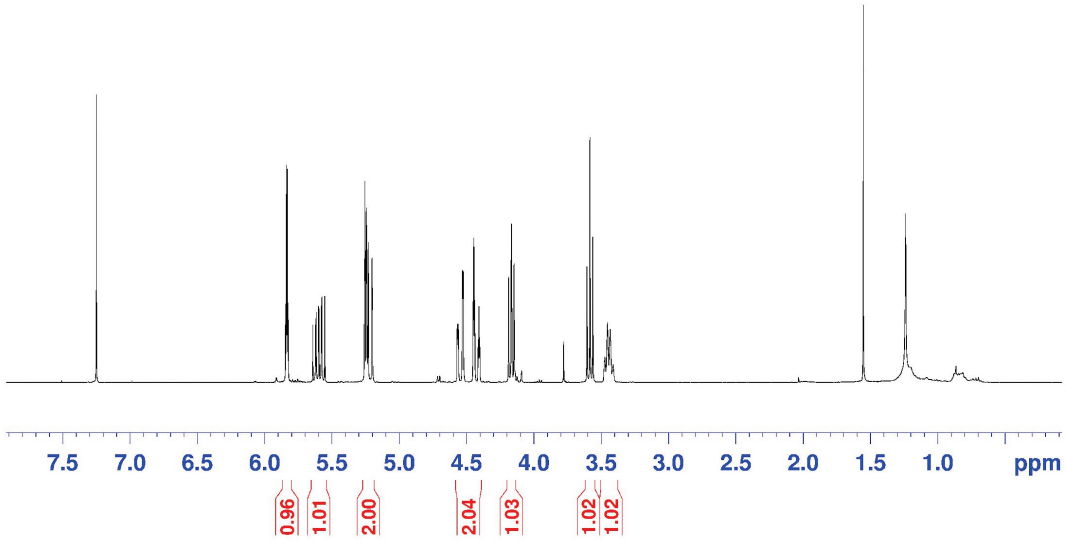
(^{13}C NMR, 100 MHz, $CDCl_3$)

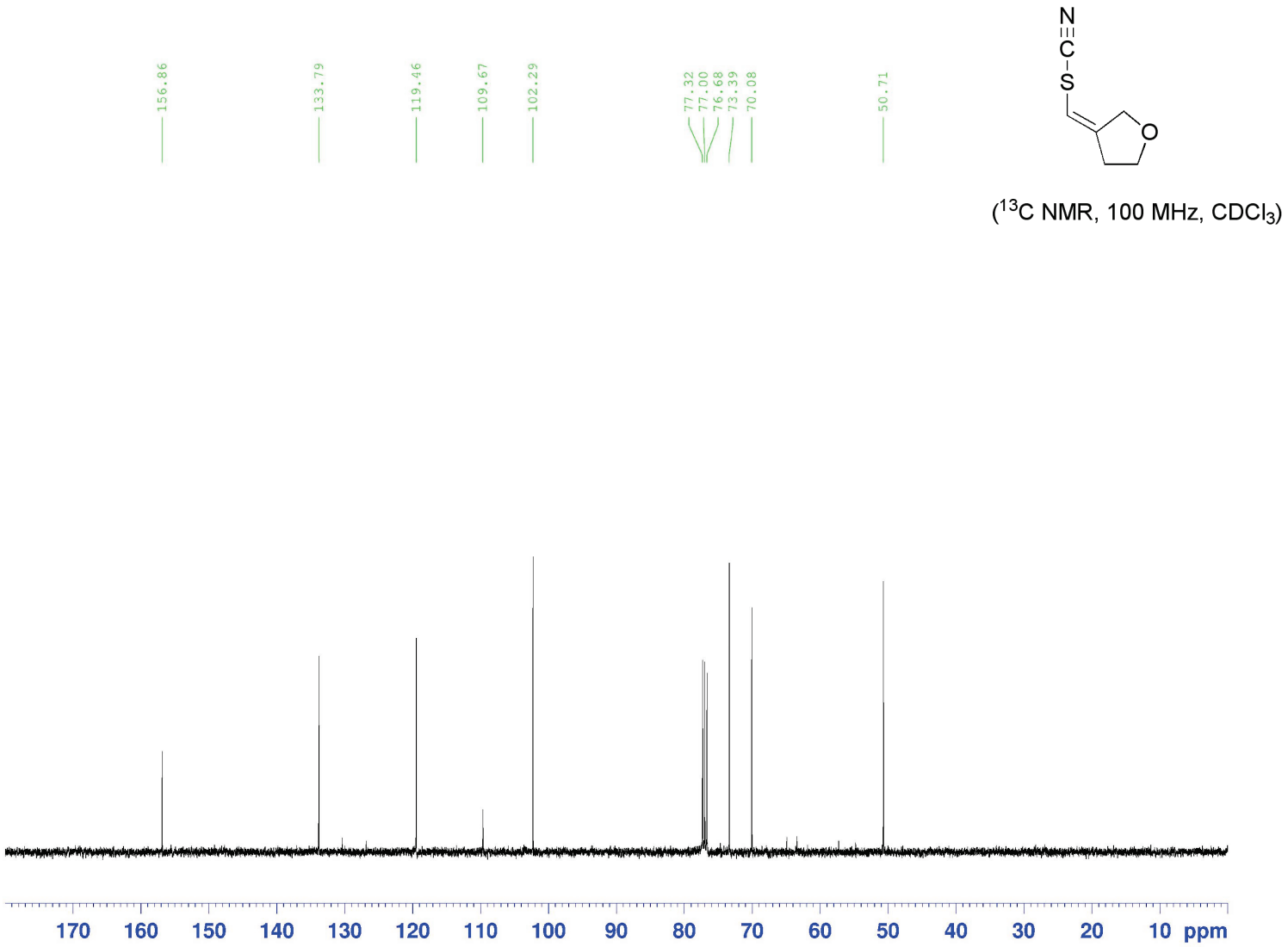

Br
O
(1H NMR, 400 MHz, CDCl3)
6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 ppm
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
0.97
1.00
2.04
1.03
1.04
1.04
1.02
1.00


Br
O
147.73
134.77
118.35
98.32
77.35
77.03
76.71
74.26
72.41
50.28
(^{13}C NMR, 100 MHz, $CDCl_3$)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

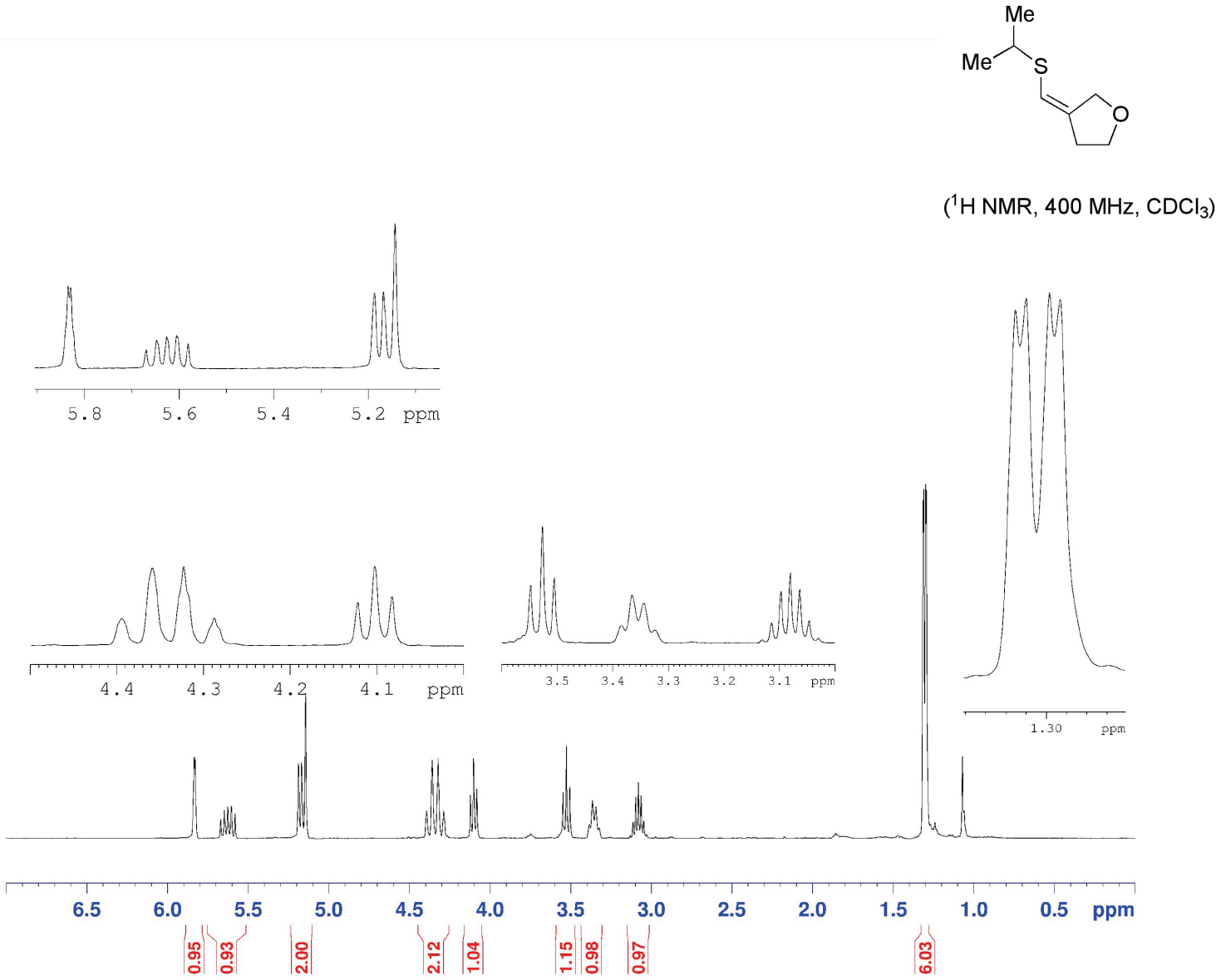


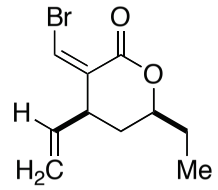
(^{1}H NMR, 400 MHz, $CDCl_3$)



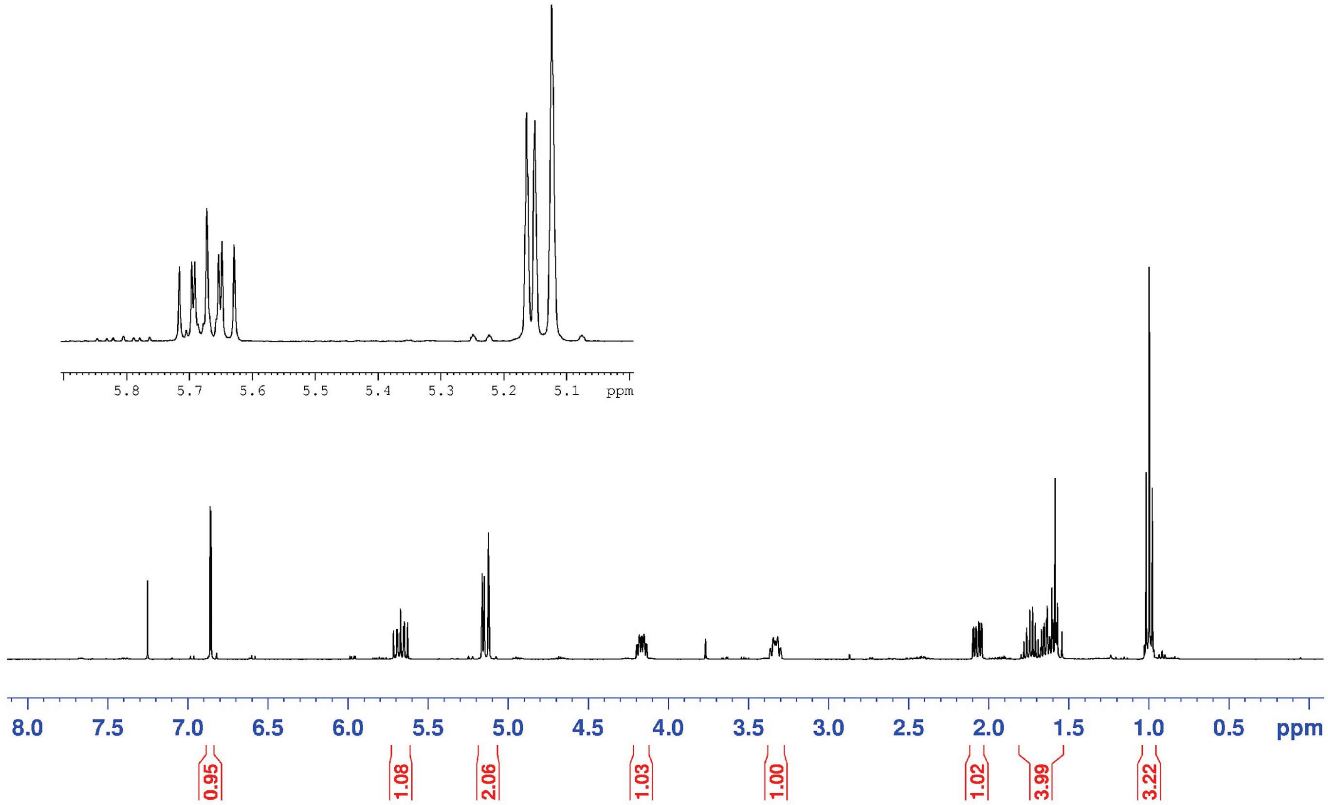


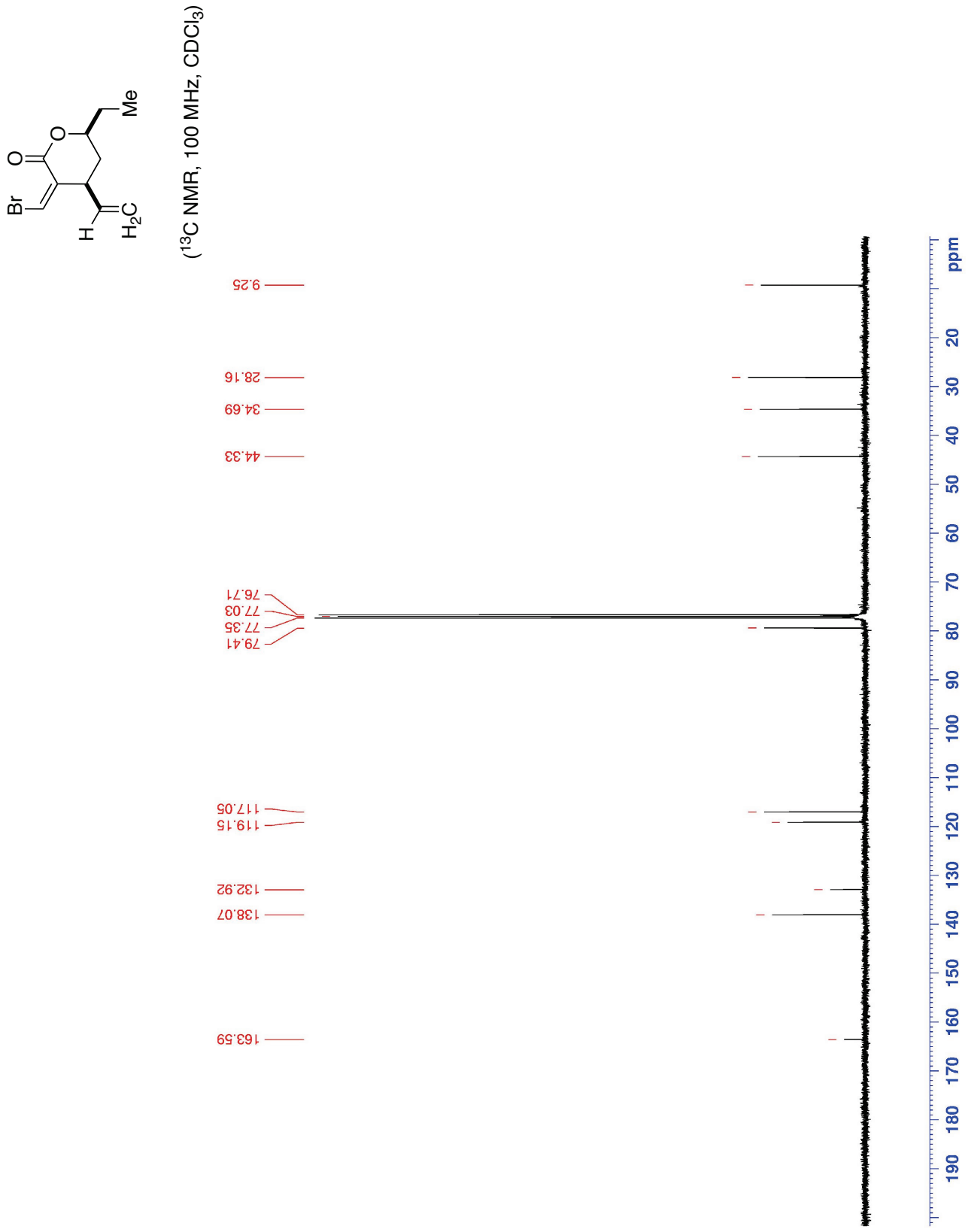
(^{13}C NMR, 100 MHz, $CDCl_3$)

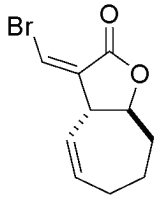

Me
Me
S
O
(1H NMR, 400 MHz, CDCl3)
5.8
5.6
5.4
5.2 ppm
4.4
4.3
4.2
4.1 ppm
3.5
3.4
3.3
3.2
3.1 ppm
1.30 ppm
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5 ppm
0.95
0.93
2.00
2.12
1.04
1.15
0.98
0.97
6.03



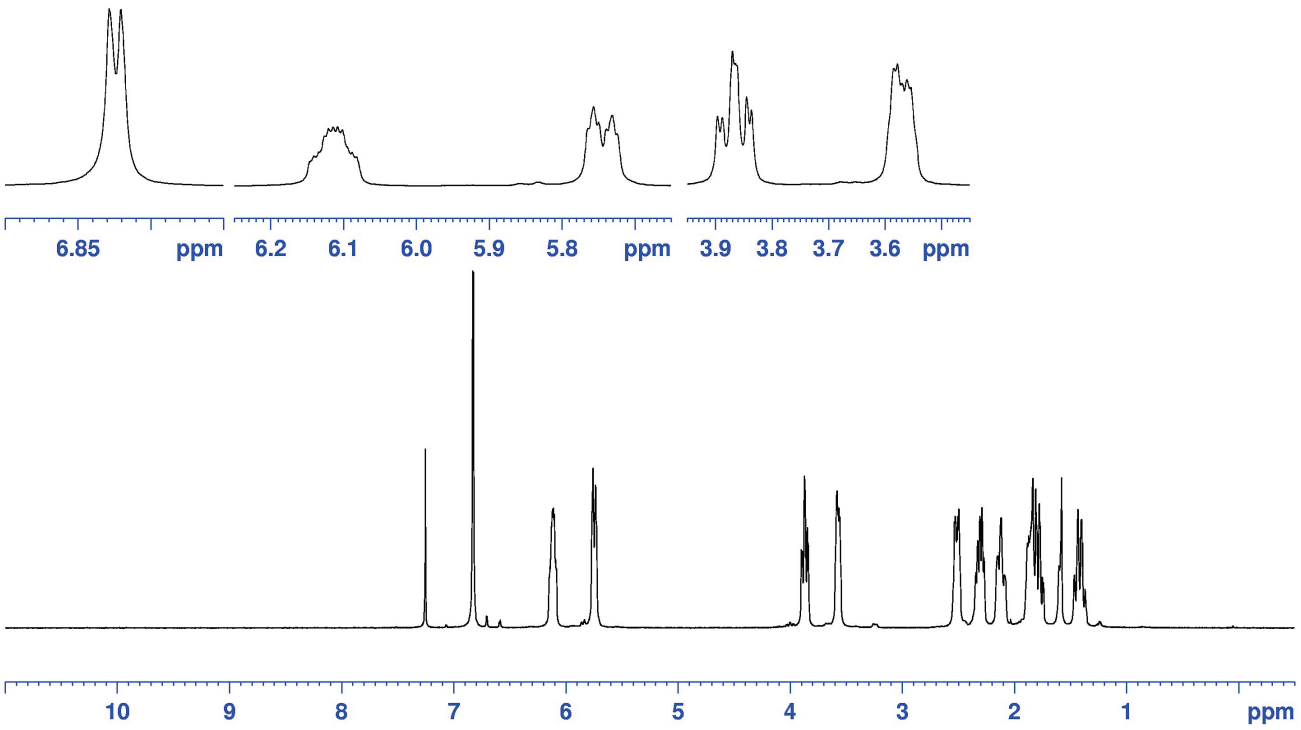
(^{1}H NMR, 400 MHz, $CDCl_3$)

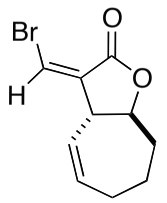



Br
O
O
Me
H
H2C
(13C NMR, 100 MHz, CDCl3)
9.25
28.16
34.69
44.33
76.71
77.03
77.35
79.41
117.05
119.15
132.92
138.07
163.59
ppm
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190

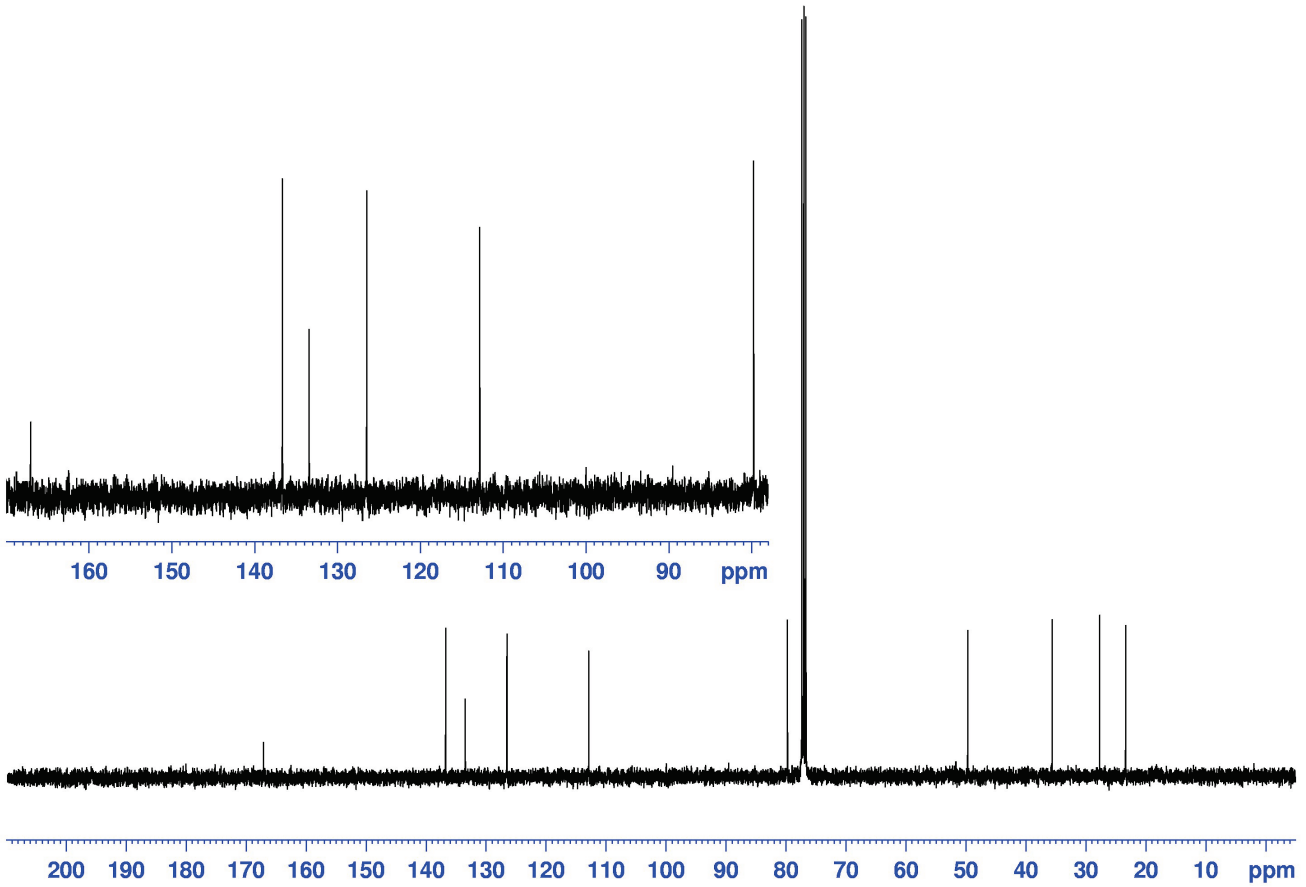


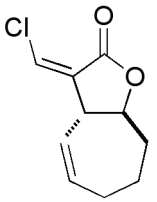
(^{1}H NMR, 400 MHz, $CDCl_3$)



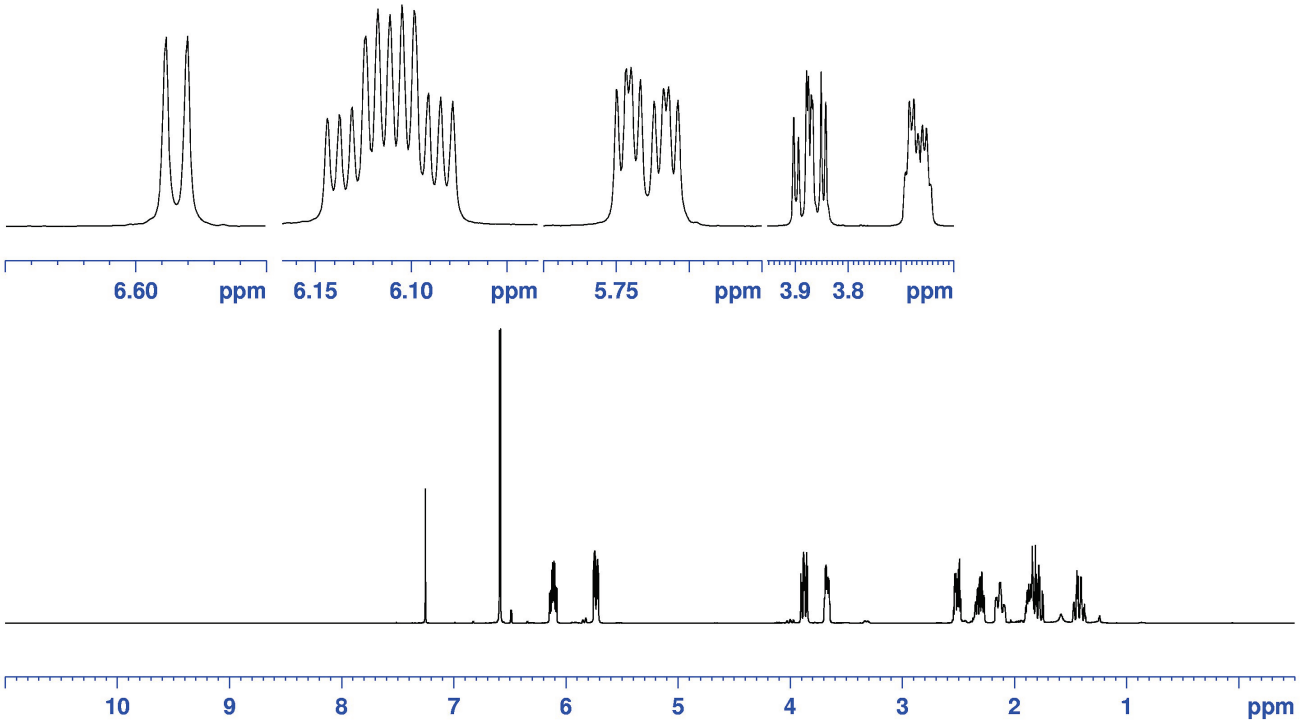


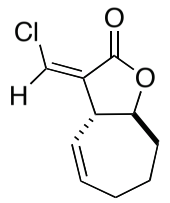
(^{13}C NMR, 100 MHz, $CDCl_3$)



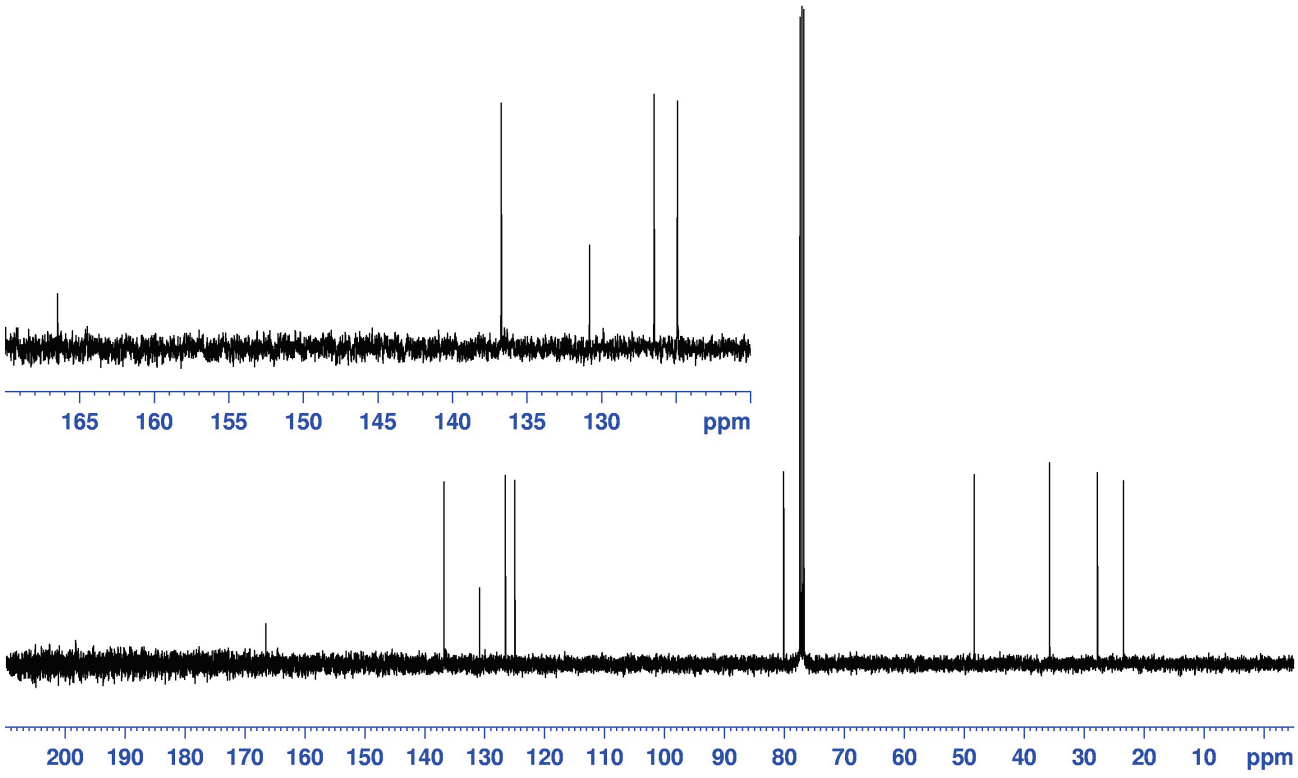


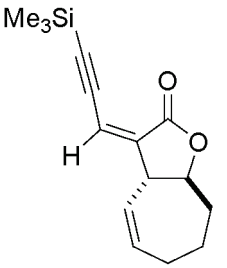
(^{1}H NMR, 400 MHz, $CDCl_3$)



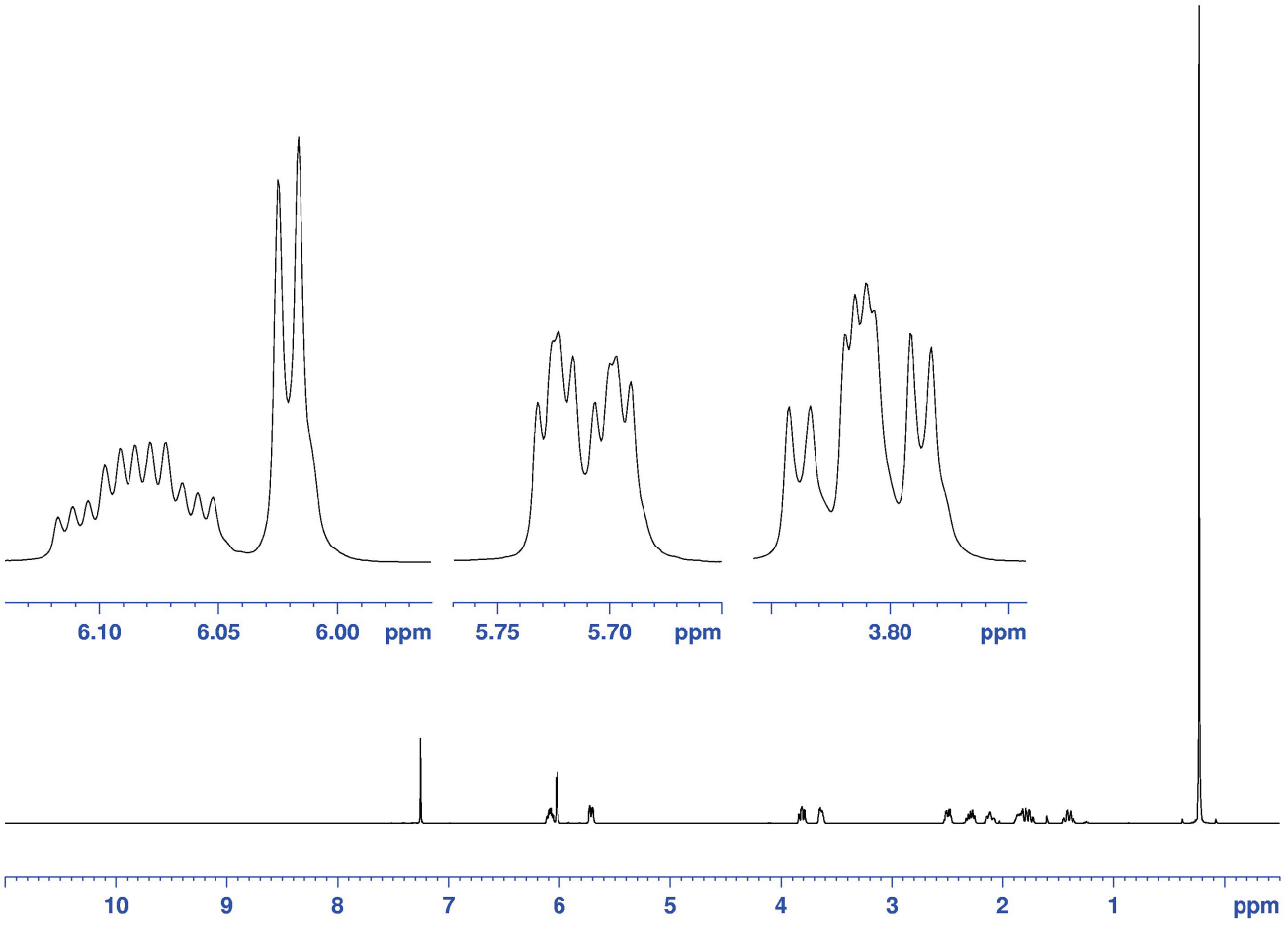


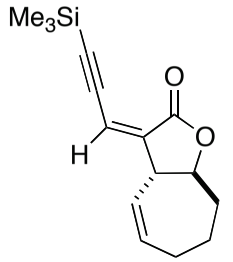
(^{13}C NMR, 100 MHz, $CDCl_3$)



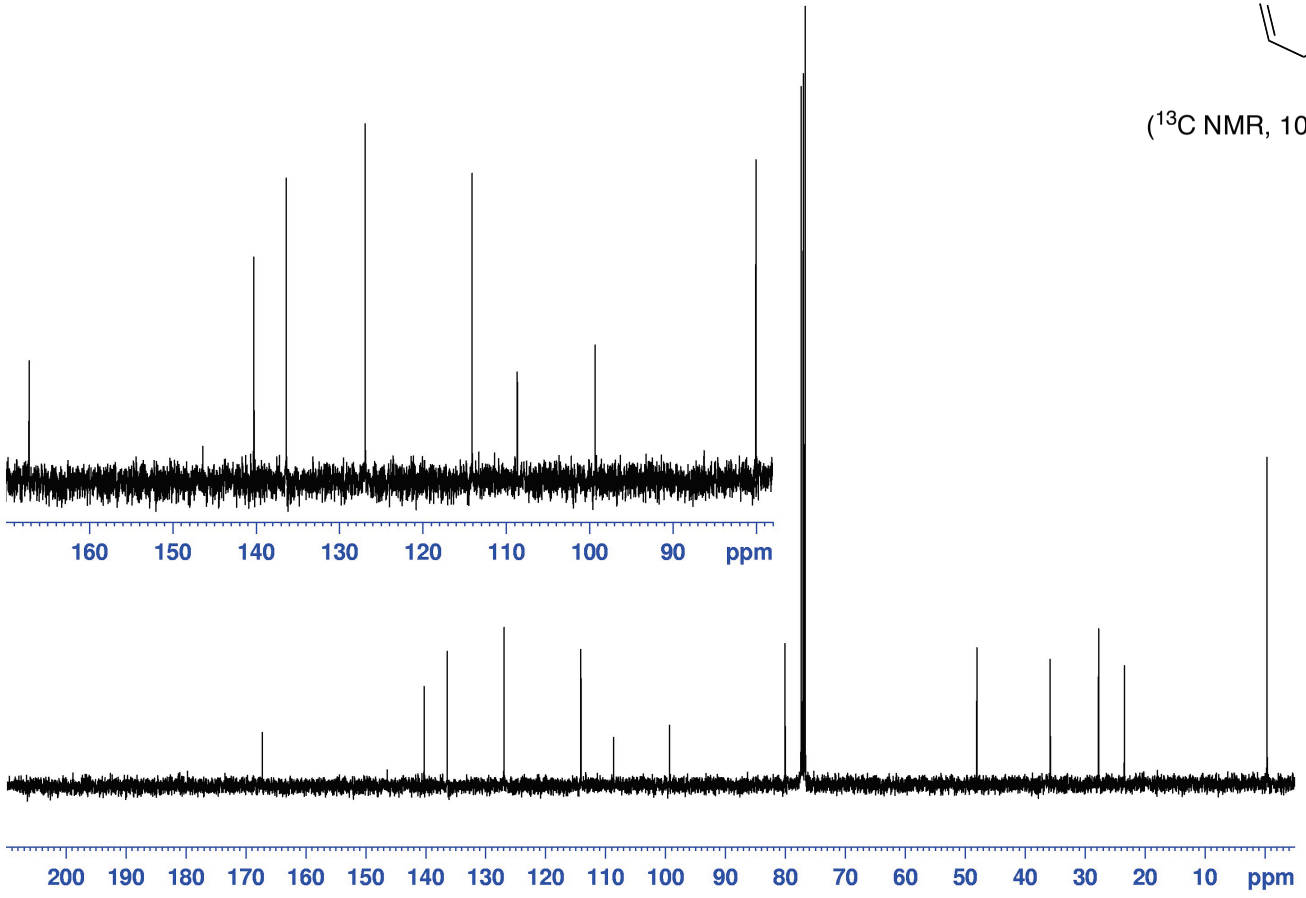


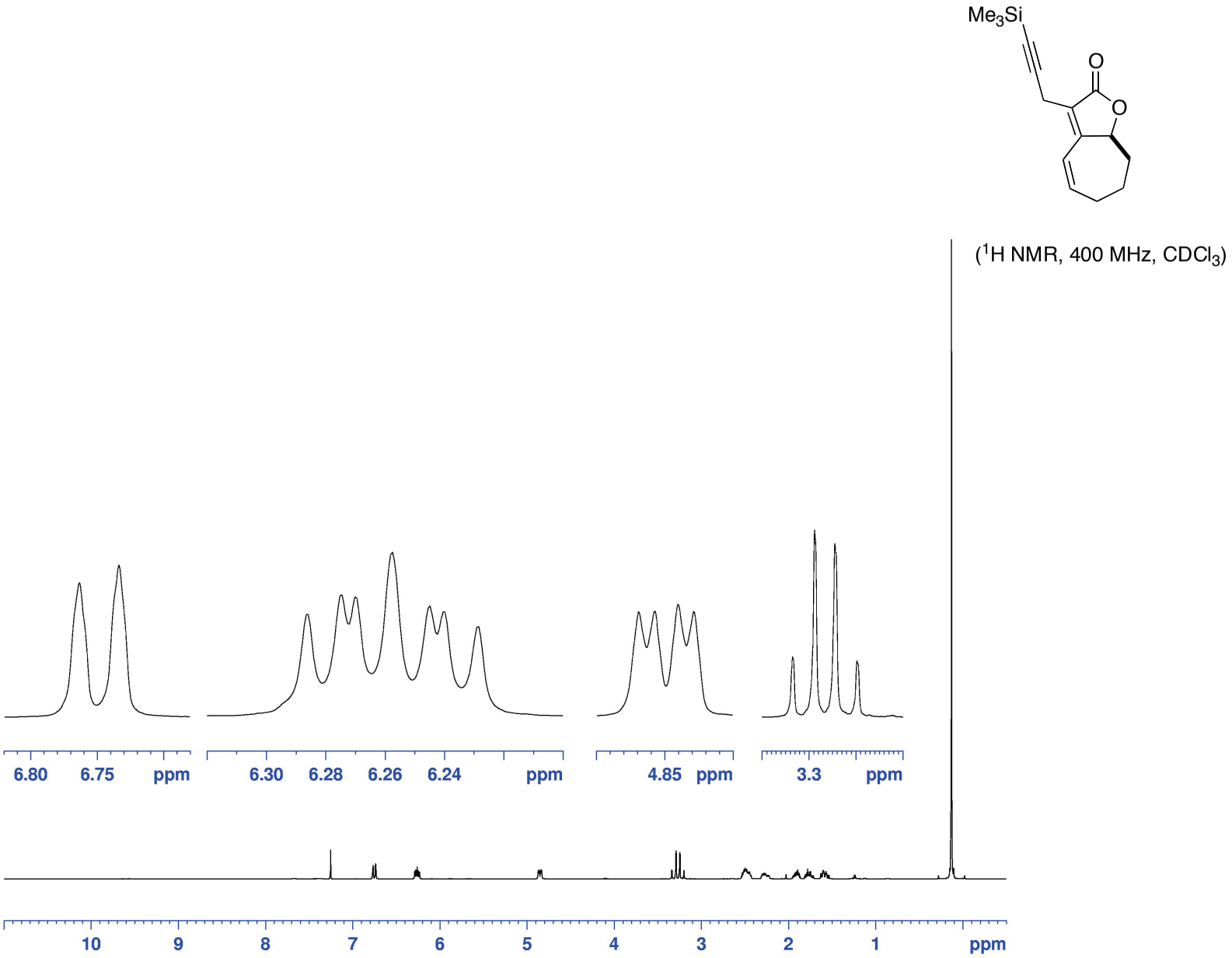
(^{1}H NMR, 400 MHz, $CDCl_3$)

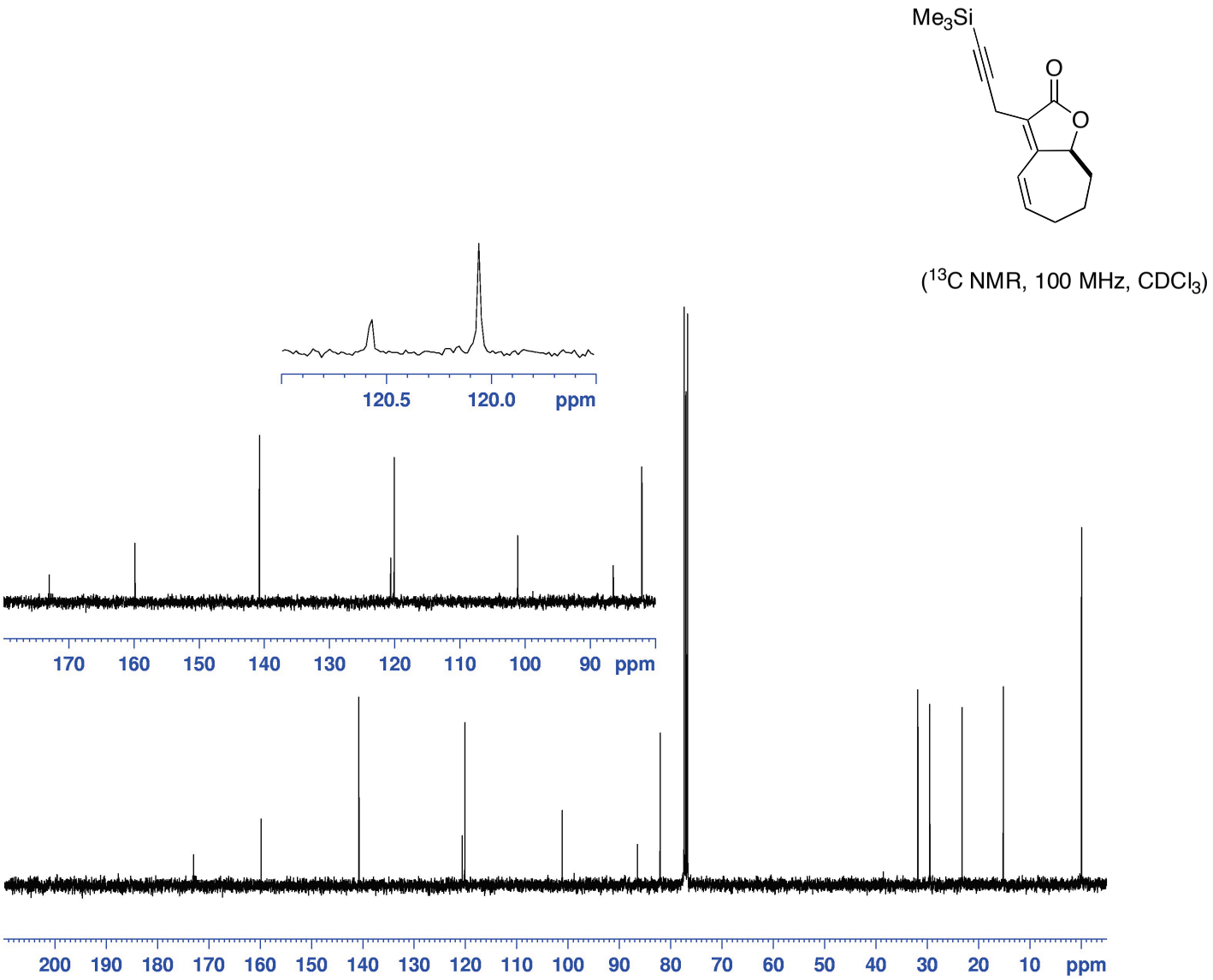


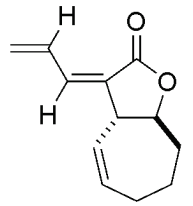


(^{13}C NMR, 100 MHz, $CDCl_3$)

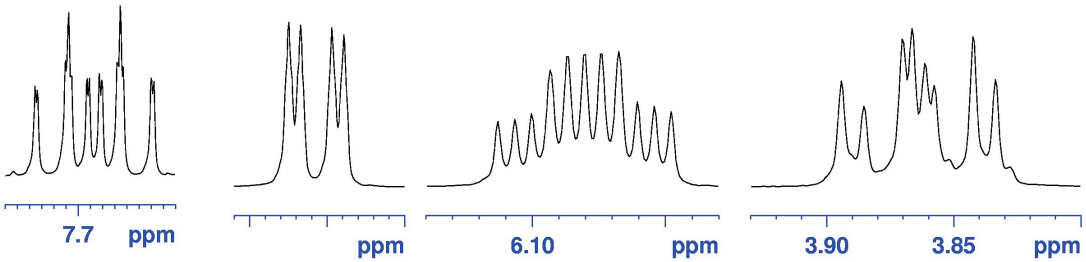


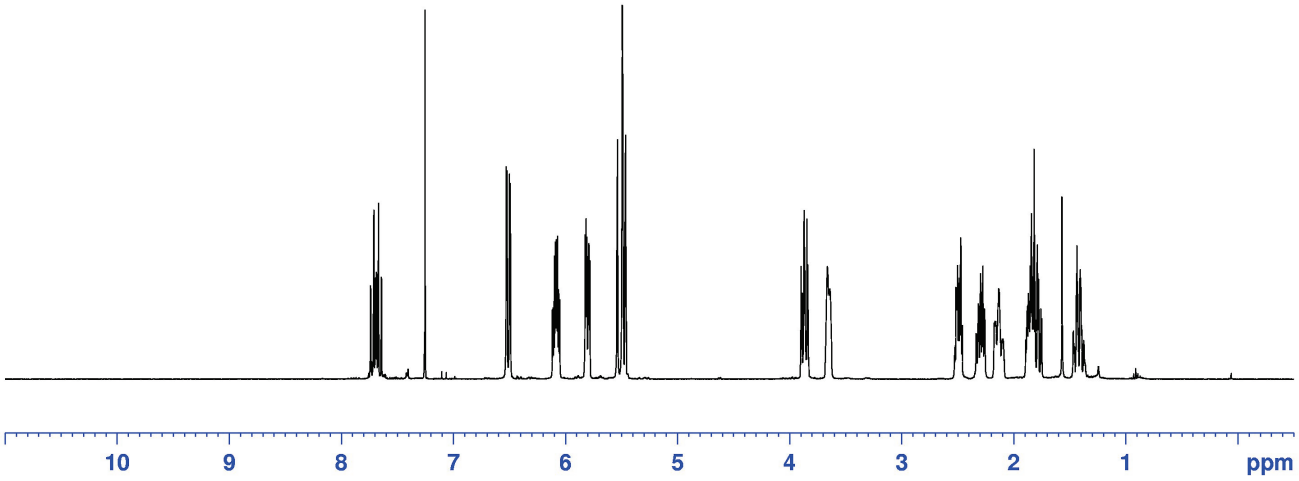

Me3Si
O
O
(1H NMR, 400 MHz, CDCl3)
6.80
6.75
ppm
6.30
6.28
6.26
6.24
ppm
4.85
ppm
3.3
ppm
10
9
8
7
6
5
4
3
2
1
ppm

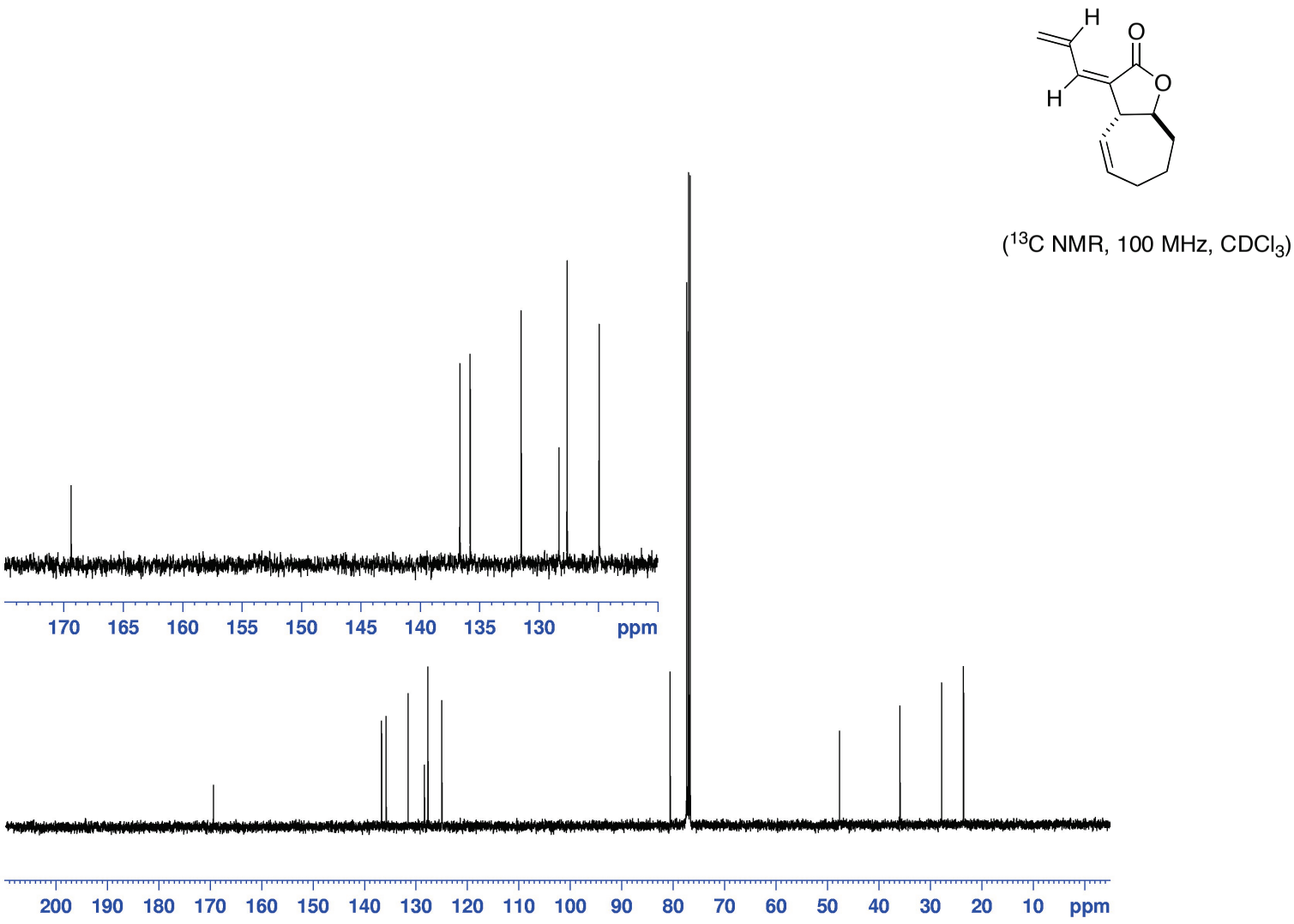

Me3Si
O
O
(13C NMR, 100 MHz, CDCl3)
120.5
120.0
ppm
170
160
150
140
130
120
110
100
90
ppm
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

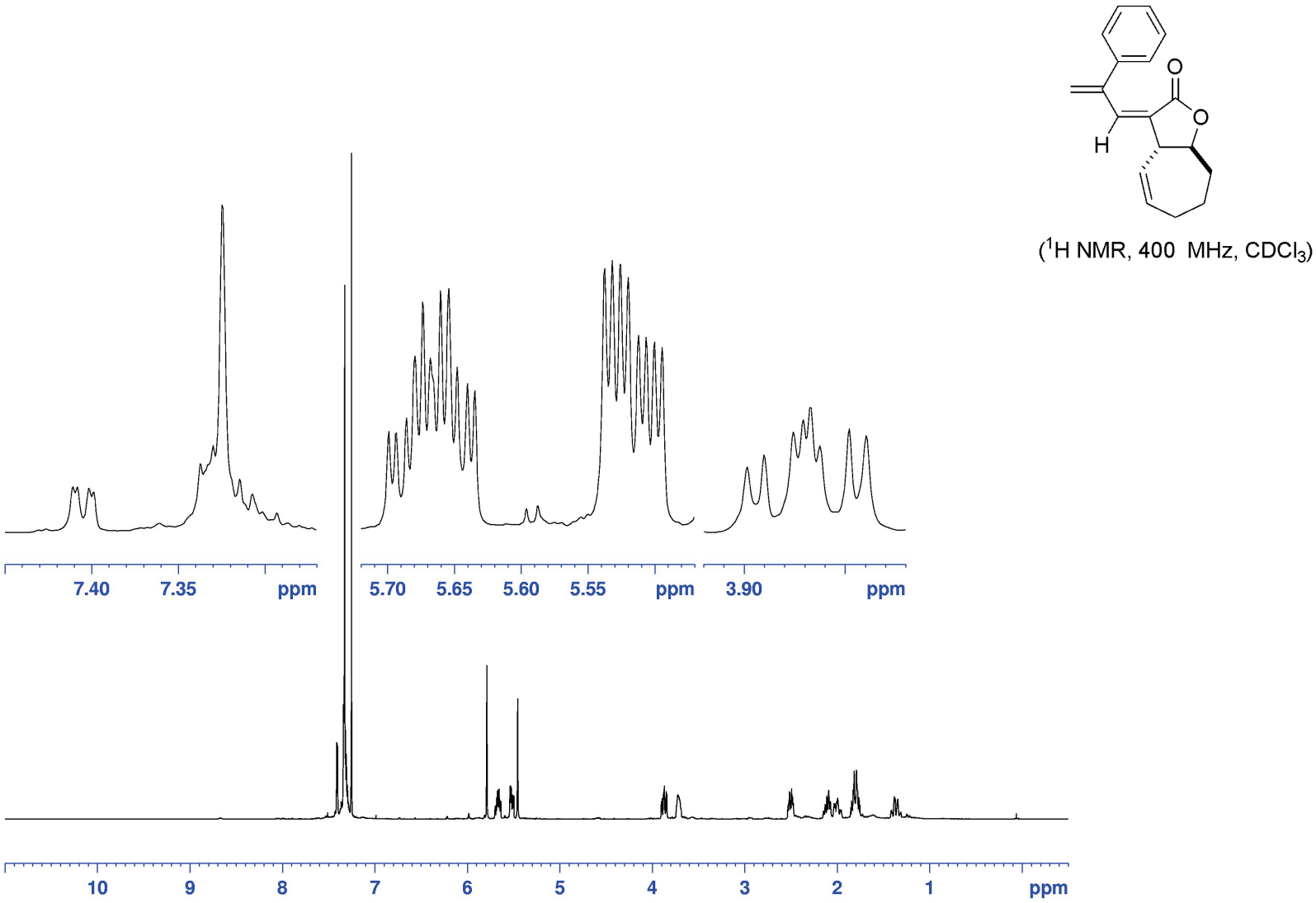


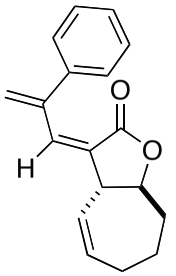
(^{1}H NMR, 400 MHz, $CDCl_3$)



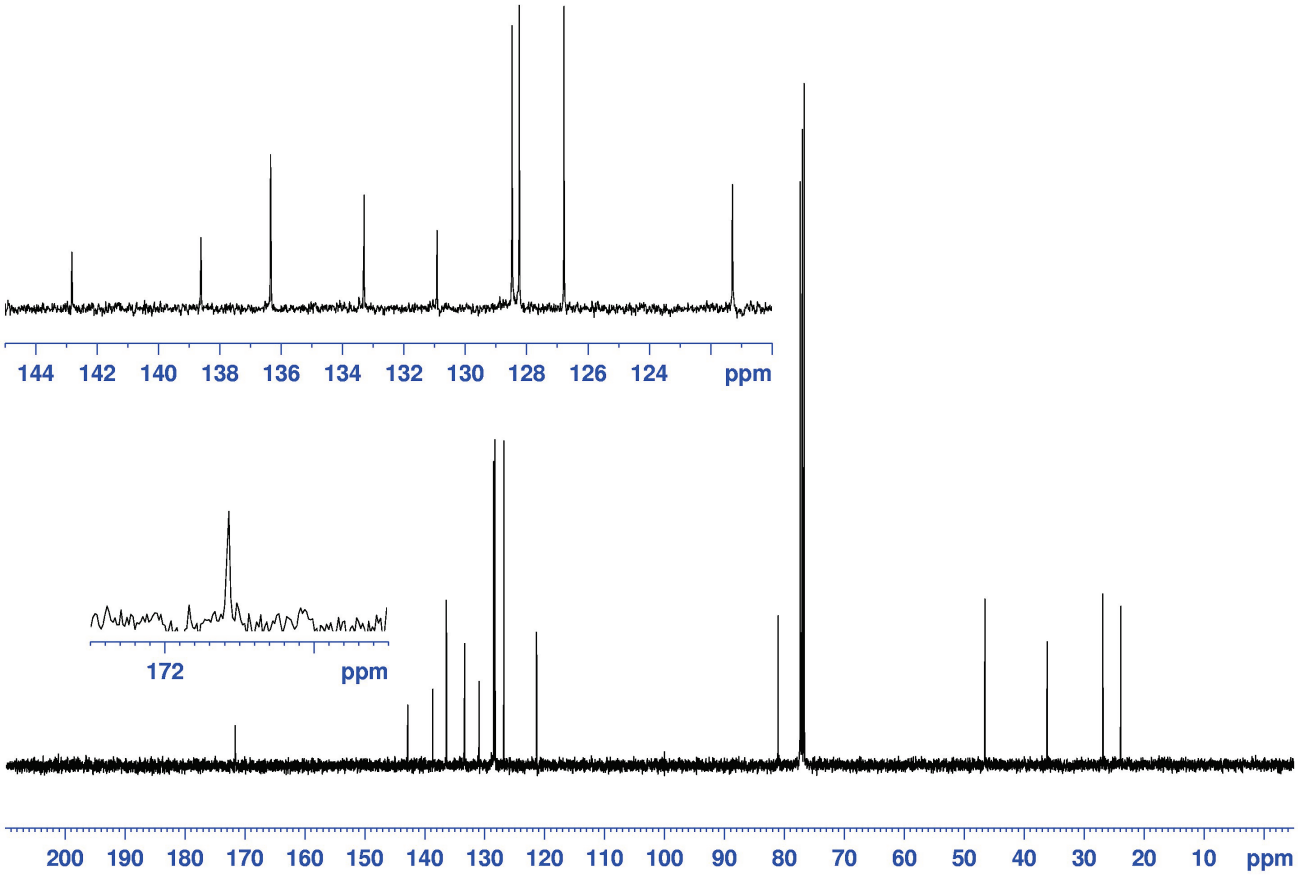


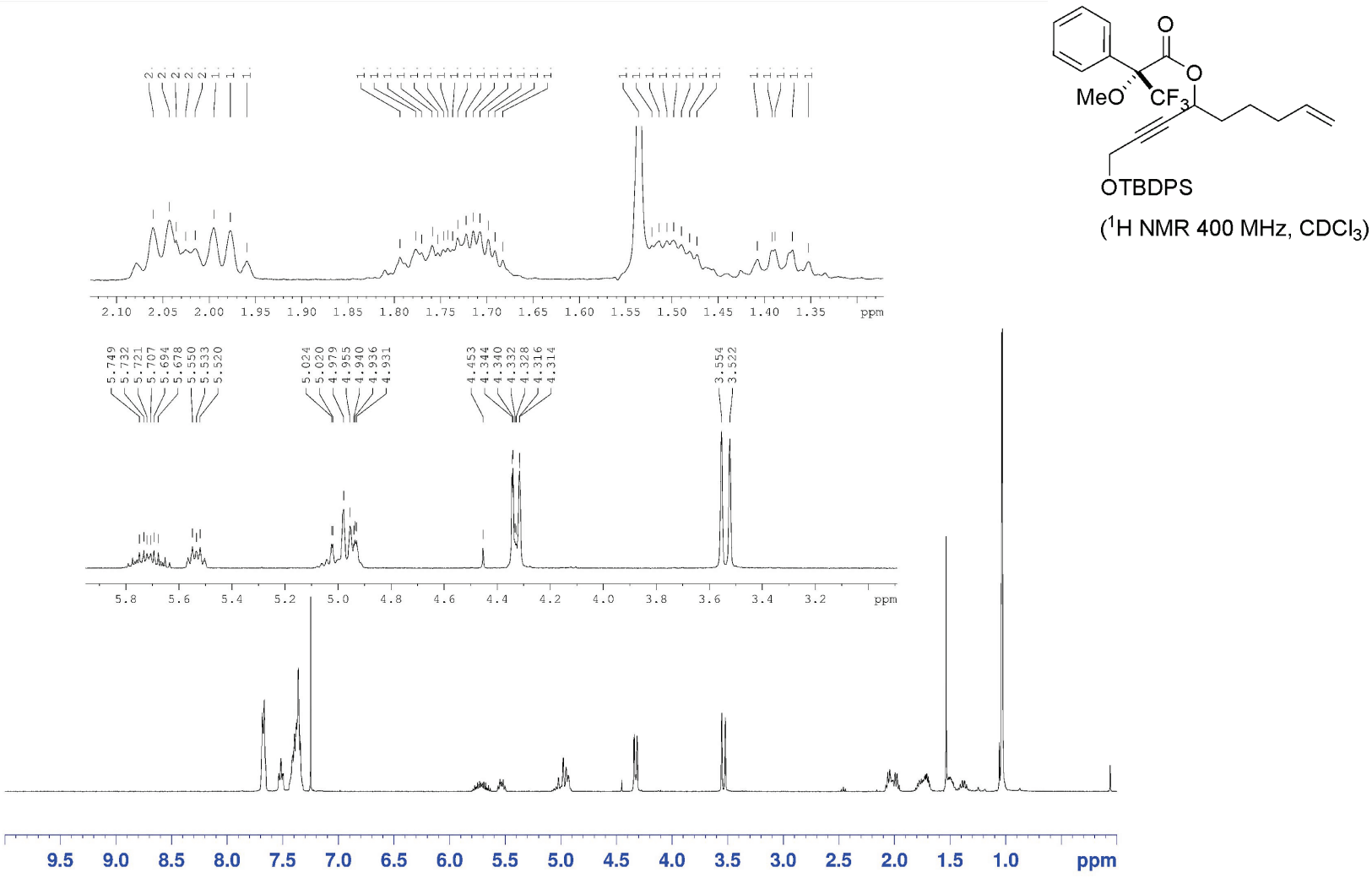

H
O
H
O
(^{13}C NMR, 100 MHz, $CDCl_3$)
170 165 160 155 150 145 140 135 130 ppm
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

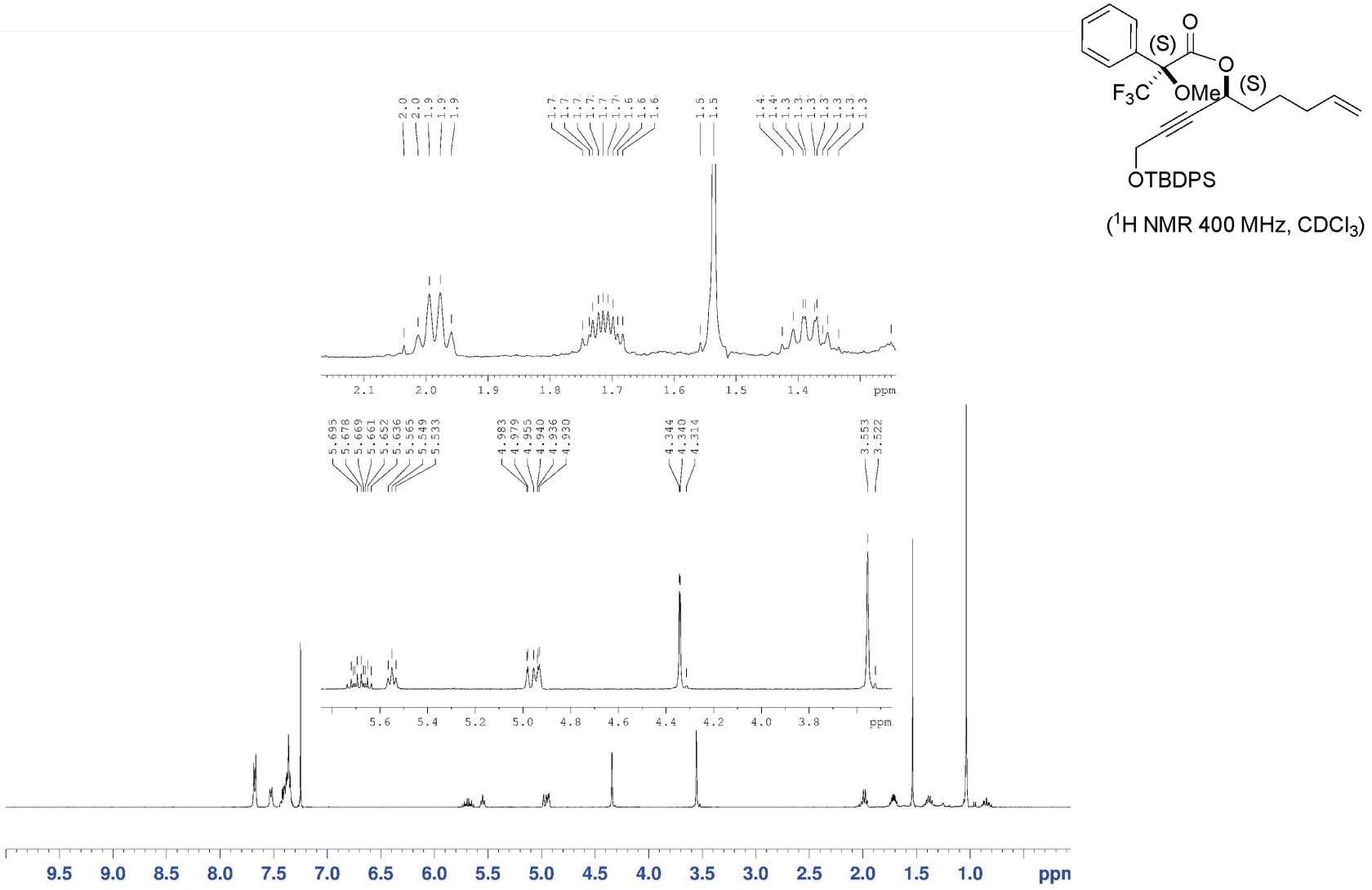

O
O
H
(1H NMR, 400 MHz, CDCl3)
7.40
7.35
ppm
5.70
5.65
5.60
5.55
ppm
3.90
ppm
10
9
8
7
6
5
4
3
2
1
ppm



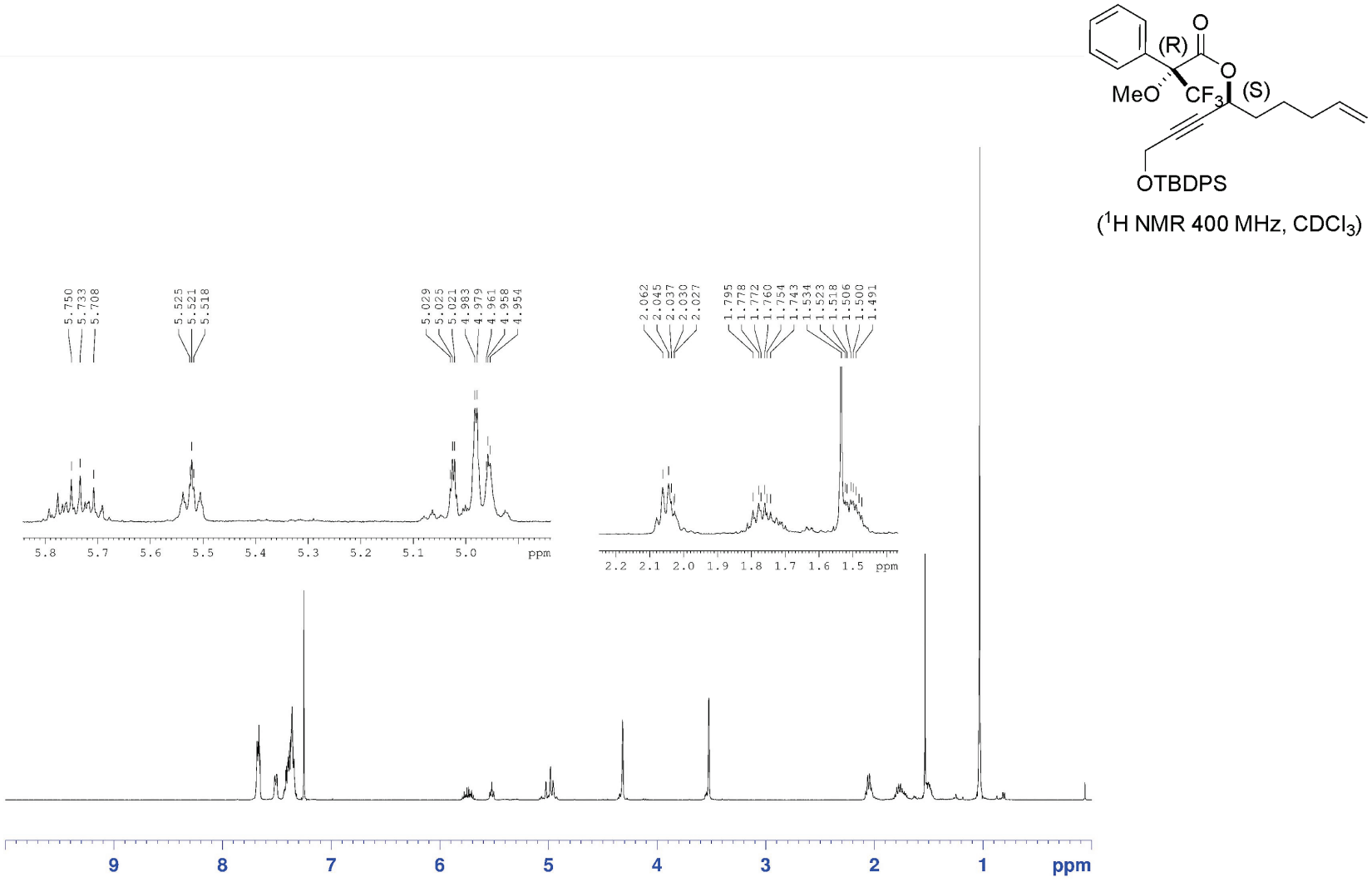
(^{13}C NMR, 100 MHz, $CDCl_3$)

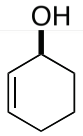



MeO
CF3
O
O
OTBDPS
(1H NMR 400 MHz, CDCl3)
ppm



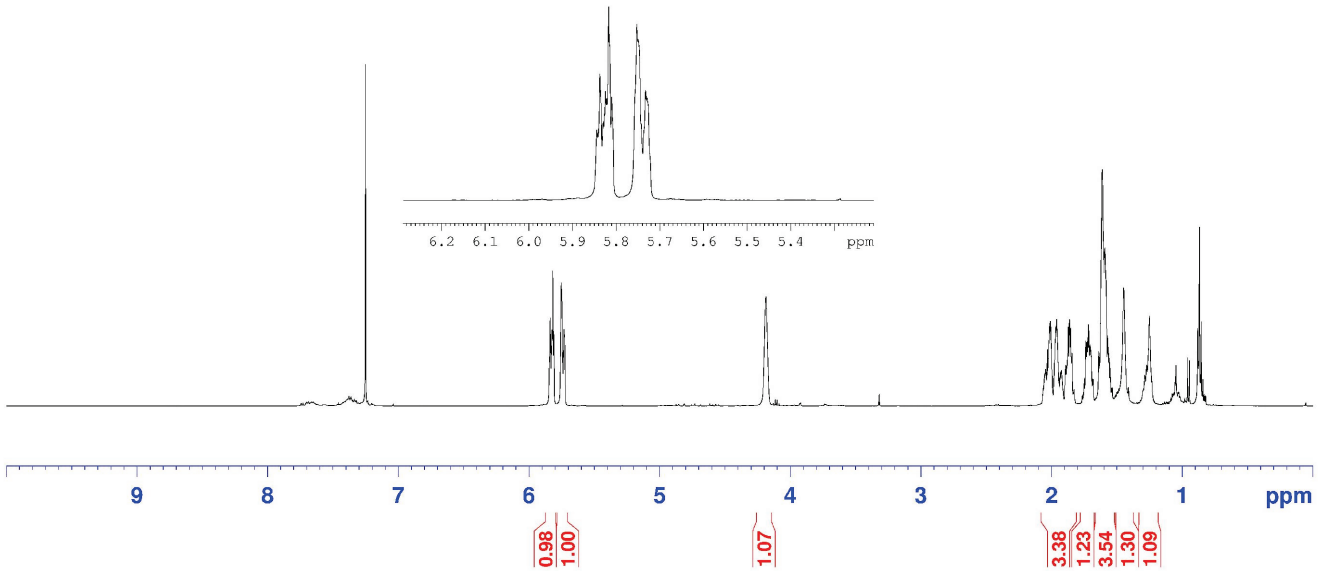
(^{1}H NMR 400 MHz, $CDCl_3$)


O
(R)
O
MeO
CF3
(S)
OTBDPS
(1H NMR 400 MHz, CDCl3)
5.750
5.733
5.708
5.525
5.521
5.518
5.029
5.025
5.021
4.983
4.979
4.961
4.958
4.954
2.062
2.045
2.037
2.030
2.027
1.795
1.778
1.772
1.760
1.754
1.743
1.534
1.523
1.518
1.506
1.500
1.491
5.8 5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 ppm
2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 ppm
9 8 7 6 5 4 3 2 1 ppm

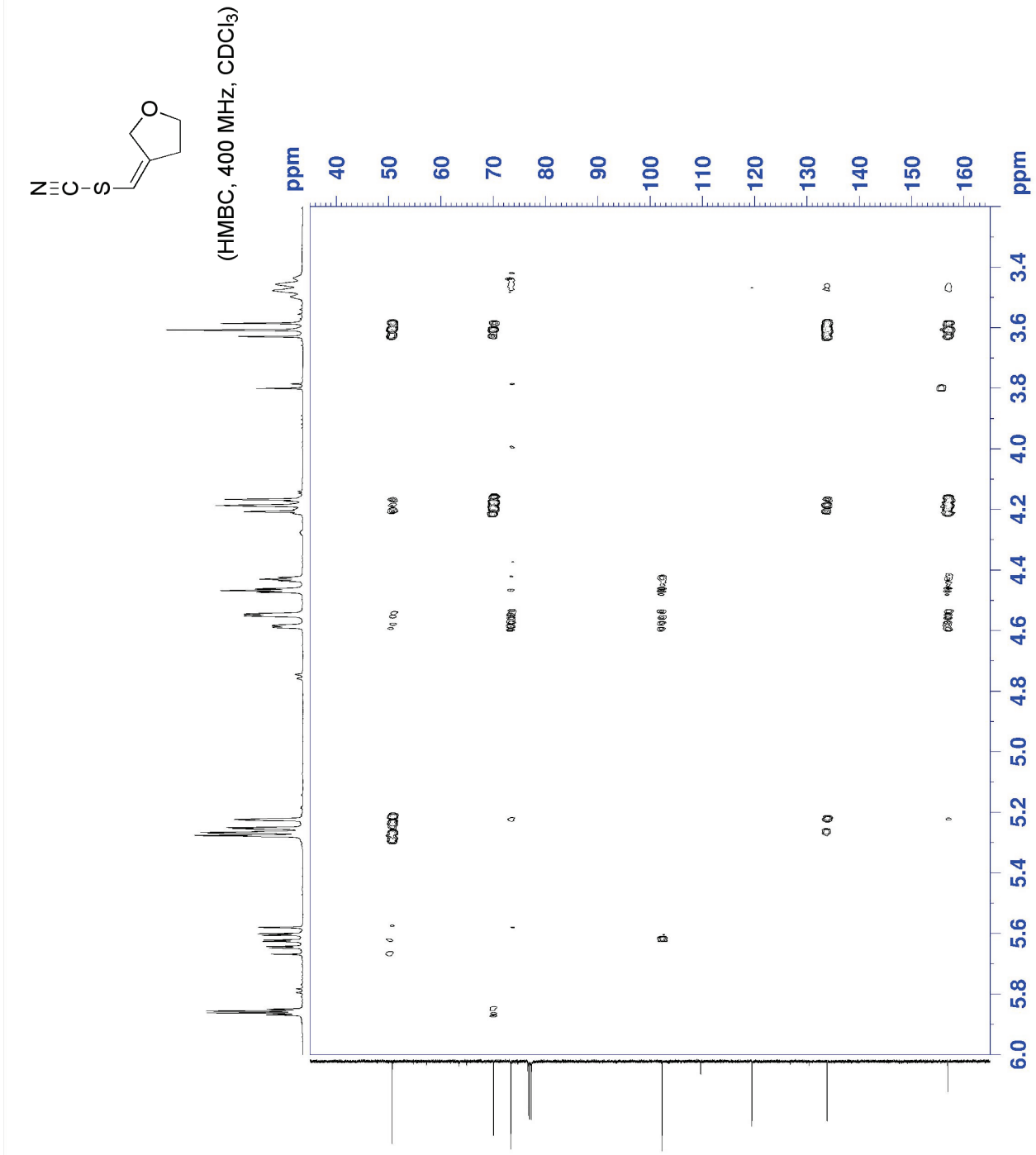


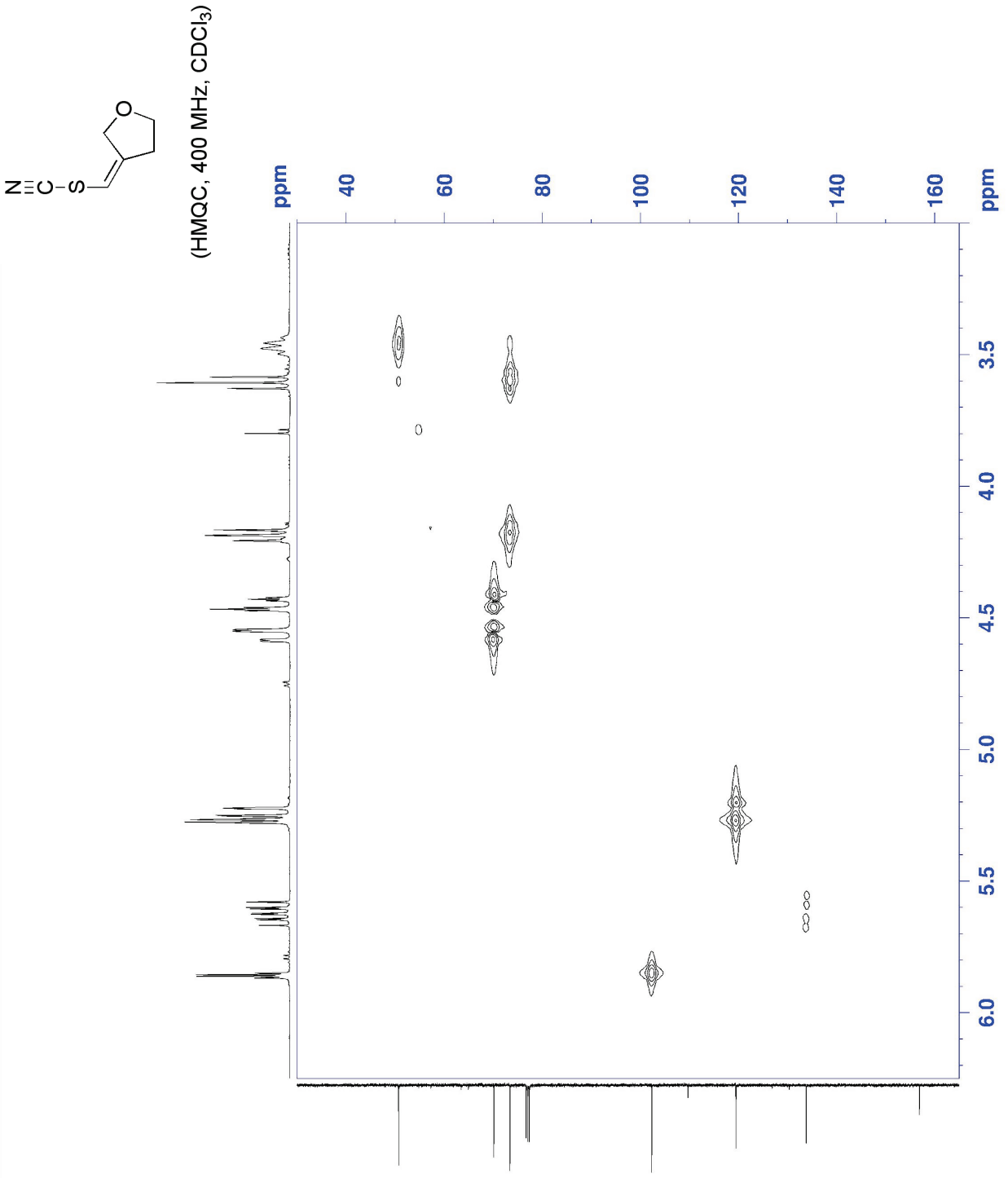
(^{1}H NMR, 500 MHz, $CDCl_3$)

(RCM product for proof of absolute stereochemistry)



Copies of HMQC and HMBC Spectra




(HMQC, 400 MHz, CDCl3)
ppm
40
60
80
100
120
140
160
3.5
4.0
4.5
5.0
5.5
6.0
ppm