Palladium-Catalyzed Asymmetric Alkylation in the Synthesis of Cyclopentanoid and Cycloheptanoid Core Structures Bearing All-Carbon Quaternary Stereocenters

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Supporting Information (Experimental Procedures)

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Materials and Methods. Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Reaction progress was monitored by thin-layer chromatography (TLC). THF was distilled over sodium/fluorenone or dried by passage through an activated alumina column under argon prior to use. *p*-Dioxane was distilled over sodium or dried by passage through an activated alumina column under argon prior to use. Methanol was distilled over $Mg(OMe)_2$ prior to use. Other solvents were dried by passage through an activated alumina column under argon. Diisopropylamine and triethylamine was distilled over CaH_2 prior to use. Iodomethane, iodoethane, acrylonitrile, methyl vinyl ketone, and acrolein were distilled prior to use. Purified water was obtained using a Barnstead NANOpure Infinity UV/UF system. Brine solutions are saturated aqueous solutions of sodium chloride. $MePh_3PBr$ from Sigma-Aldrich was stored in a glove box prior to use. NaH (60% wt. dispersion in mineral oil) from Sigma-Aldrich was purified by trituration with hexanes under a N_2 atmosphere and removal of residual solvent under vacuum. $LiOCH_2CF_3$ was prepared according to the method of Shreeve.[1] Allyl cyanoformate was prepared according to the method of Mander or Rattigan.[2] Gramine methiodide was prepared according to the method of Armen.[3] The procedure of Maruyama and Naruta was used to prepare 1-chloro-2,4-pentadiene (92:8 *E*:*Z)*.[4] Grignard and organolithium reagents were purchased from Sigma-Aldrich or prepared according to previously reported procedures.[5] Phosphinooxazoline (PHOX) ligands **L1** ((*S*)-*t*-Bu-PHOX)[6] and **L2** ((*S*)-*p*-$(CF_3)_3$-*t*-Bu-PHOX)[7] were prepared by methods described in our previous work. Tris(4,4'-methoxydibenzylideneacetone)dipalladium(0) ($Pd_2(pmdba)_3$) was prepared according to the method of Ibers[8a] or Fairlamb.[8b] Herrmann–Beller's catalyst was prepared according to a literature procedure.[9] All other reagents were purchased from Sigma-Aldrich, Acros Organics, Strem, or Alfa Aesar and used as received unless otherwise stated. Reaction temperatures were controlled by an IKAmag temperature modulator. Microwave-assisted reactions were performed in a Biotage Initiator 2.5 microwave reactor. Glove box manipulations were performed under a N_2 atmosphere. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching, *p*-anisaldehyde, or $KMnO_4$ staining. Silia*Flash* P60 Academic Silica gel (particle size 0.040–0.063 mm) or ICN silica gel (particle size 0.032–0.0653 mm) was used for flash column chromatography. Automated flash column chromatography was performed on a Teledyne Isco CombiFlash R_f system. ^{1}H NMR spectra were recorded on a Varian Mercury 300 MHz, a Varian 400 MR 400 MHz, or a Varian Inova 500 MHz spectrometer and are reported relative to residual $CHCl_3$ (δ 7.26 ppm). ^{13}C NMR spectra were recorded on a Varian Mercury 300 MHz, a Varian 400 MR 400 MHz, or a Varian Inova 500 MHz spectrometer (at 75 MHz, 100 MHz, and 125 MHz respectively) and are reported relative to $CDCl_3$ (δ 77.16 ppm). ^{19}F spectra were recorded on a Varian Mercury 300 MHz or a Varian Inova 500 MHz spectrometer (at 282 MHz and 470 MHz respectively) and are reported without the use of a reference peak. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration. Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d = broad doublet, app = apparent. Data for ^{13}C and ^{19}F NMR are reported in terms of chemical shifts (δ ppm). IR spectra were obtained using a Perkin Elmer Paragon 1000 or Perkin Elmer Spectrum BXII spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-1010 or Jasco P-2000 polarimeter operating on the sodium D-line (589 nm) using a 100 mm path-length cell and are reported as: $[\alpha]_D^T$ (concentration in g/100 mL, solvent, ee). Melting points were measured using a Thomas-Hoover capillary melting point apparatus and the reported

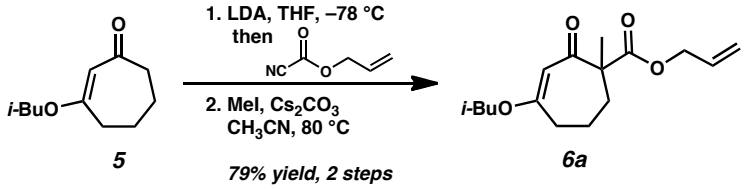
values are uncorrected. Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing a Chiralcel AD or OD-H column (4.6 mm x 25 cm) obtained from Daicel Chemical Industries Ltd. with visualization at 254 nm. Analytical chiral SFC was performed with a Mettler Toledo SFC supercritical CO_2 analytical chromatography system with a Chiralcel AD-H column (4.6 mm x 25 cm) with visualization at 254 nm/210 nm. Analytical chiral GC was performed with an Agilent 6850 GC utilizing a G-TA (30 m x 0.25 mm) column (1.0 mL/min carrier gas flow). High-resolution mass spectra (HRMS) were obtained from the Caltech Mass Spectral Facility (EI+ or FAB+) or on an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+).

List of Abbreviations. The following abbreviations are used in experimental procedures:

CDI = 1,1'-carbonyldiimidazole
DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene
DDQ = 2,3-dichloro-5,6-dicyano-*p*-benzoquinone
DMA = *N,N'*-dimethylacetamide
DMAD = dimethyl acetylenedicarboxylate
DMAP = 4-(dimethylamino)pyridine
DMF = *N,N'*-dimethylformamide
DMSO = dimethylsulfoxide
DIBAL = diisobutylaluminum hydride
HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol
i-Bu = isobutyl
IPA = isopropanol
LDA = lithium diisopropylamide
MsCl = methanesulfonyl chloride
$Pd_2(pmdba)_3$ = tris(4,4'-methoxydibenzylideneacetone)dipalladium(0)
PHOX = phosphinooxazoline ligand
PPTS = pyridinium *p*-toluenesulfonate
TBAA = tetrabutylammonium acetate
TBAF = tetrabutylammonium fluoride
TBAI = tetrabutylammonium iodide
TBDPS = *tert*-butyldiphenylsilyl
TBDPSCl = *tert*-butyl(chloro)diphenylsilane
TBSOTf = *tert*-butyldimethylsilyl trifluoromethanesulfonate
TBME = *tert*-butyl methyl ether
TFE = 2,2,2-trifluoroethanol
TMG = 1,1,3,3-tetramethylguanidine.
TMS = trimethylsilyl
TMSCl = chlorotrimethylsilane
Selectfluor = 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate)
μwaves = microwave irradiation

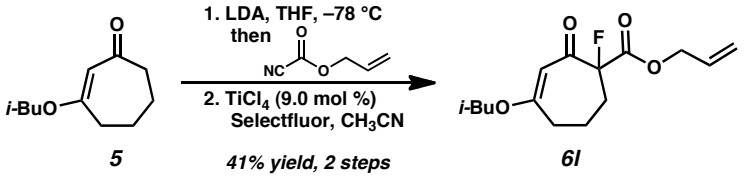
Procedures for the Preparation of β-Ketoesters 6

Vinylogous ester **5** and β-ketoesters **6a–k**, **6m** were prepared according to previously reported procedures.[10,11]



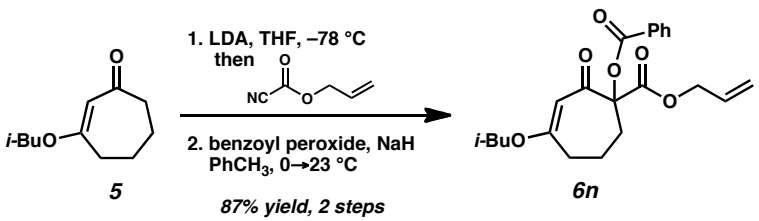
β-Ketoester 6a. To a solution of diisopropylamine (6.46 mL, 46.1 mmol, 1.20 equiv) in THF (180 mL) in a 500 mL round-bottom flask at 0 °C was added *n*-BuLi (17.2 mL, 44.2 mmol, 2.57 M in hexanes, 1.15 equiv) dropwise over 15 min using a syringe pump. After 15 min of stirring at 0 °C, the mixture was cooled to –78 °C using an acetone/CO_2(s) bath. A solution of vinylogous ester **5** (7.01 g, 38.4 mmol, 1.00 equiv) in THF (20 mL) was added dropwise over 20 min using a syringe pump. After an additional 1 h of stirring at –78 °C, allyl cyanoformate (4.60 mL, 42.2 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at –78 °C for 2.5 h, quenched by addition of sat. aqueous NH_4Cl and H_2O (30 mL each), and allowed to warm to ambient temperature. The reaction was diluted with Et_2O (100 mL) and the phases were separated. The aqueous phase was extracted with Et_2O (2 x 100 mL). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford a pale orange oil.

The crude oil was dissolved in CH_3CN (130 mL) in a 500 mL round-bottom flask and treated with MeI (7.2 mL, 115 mmol, 3.00 equiv) and Cs_2CO_3 (16.76 g, 49.9 mmol, 1.30 equiv). The flask was fitted with a condenser, immersed in an oil bath, and heated to 80 °C with vigorous stirring. After 12 h of stirring at 80 °C, the reaction was allowed to cool to ambient temperature, diluted with EtOAc (100 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford an orange oil. The crude product was purified by flash column chromatography (SiO_2, 5 x 15 cm, 19:1→9:1 Hexanes:EtOAc, dry-loaded using Celite) to afford β-ketoester **6a** (8.51 g, 30.4 mmol, 79% yield over 2 steps) as a pale yellow oil; R_f = 0.43 (4:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (dddd, *J* = 17.1, 10.7, 5.6, 5.6 Hz, 1H), 5.39 (s, 1H), 5.29 (app dq, *J* = 17.1, 1.5 Hz, 1H), 5.20 (app dq, *J* = 10.5, 1.4 Hz, 1H), 4.62 (dddd, *J* = 13.3, 5.6, 1.2, 1.2 Hz, 1H), 4.56 (dddd, *J* = 13.4, 5.6, 1.2, 1.2 Hz, 1H), 3.54–3.42 (m, 2H), 2.59 (ddd, *J* = 17.8, 9.8, 3.9 Hz, 1H), 2.45–2.38 (m, 2H), 2.02–1.94 (m, 2H), 1.84–1.75 (m, 1H), 1.70 (ddd, *J* = 14.4, 7.3, 4.4 Hz, 1H), 1.43 (s, 3H), 0.94 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.1, 174.0, 173.5, 132.0, 118.4, 105.2, 74.8, 65.8, 59.1, 34.3, 33.9, 27.9, 24.2, 21.4, 19.3; IR (Neat Film NaCl) 2959, 2936, 2875, 1734, 1650, 1613, 1456, 1384, 1233, 1170, 1115, 994 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{16}H_{24}O_4$ $[M]^{+\bullet}$: 280.1675; found 280.1686.



***β*-Ketoester 6l.** To a solution of diisopropylamine (0.92 mL, 6.58 mmol, 1.20 equiv) in THF (27 mL) in a 100 mL round-bottomed flask at 0 °C in an ice/water bath was added *n*-BuLi (2.56 mL, 2.46 M in hexanes, 6.30 mmol, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 °C, the mixture was cooled to –78 °C using an acetone/CO_2(s) bath. A solution of vinylogous ester **5** (1.00 g, 5.48 mmol, 1.00 equiv) in THF (2 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at –78 °C, allyl cyanoformate (0.67 mL, 6.02 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at –78 °C for 2.5 h, quenched by addition of 50% sat. aqueous NH_4Cl (8 mL), and then allowed to warm to ambient temperature. The reaction mixture was diluted with Et_2O (25 mL) and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 25 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a pale orange oil.

The crude oil was dissolved in CH_3CN (55 mL) in a 100 mL round-bottomed flask under N_2 and $TiCl_4$ (53.7 μL, 0.49 mmol, 9.0 mol %) was added dropwise, giving a dark purple-brown mixture. After 10 min, Selectfluor (2.33 g, 6.58 mmol, 1.20 equiv) was added in one portion. After 3.5 h, the reaction mixture was an orange suspension. The reaction was concentrated under reduced pressure and the orange residue was partitioned between water (25 mL) and Et_2O (25 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 25 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by automated flash column chromatography using Teledyne Isco CombiFlash R_f (SiO_2, 25 g loading cartridge, 120 g column, 10% EtOAc in Hexanes) to afford *β*-ketoester **6l** (639 mg, 2.25 mmol, 41% yield over 2 steps) as a pale yellow oil; R_f = 0.44 (4:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (dddd, *J* = 17.1, 10.7, 5.6, 5.6 Hz, 1H), 5.39 (s, 1H), 5.29 (ddd, *J* = 17.1, 2.9, 1.5 Hz, 1H), 5.20 (app d, *J* = 10.5 Hz, 1H), 4.59 (dddd, *J* = 19.0, 13.2, 5.6, 1.2 Hz, 2H), 3.50 (dd, *J* = 9.3, 6.8 Hz, 1H), 3.47 (dd, *J* = 9.3, 6.6 Hz, 1H), 2.59 (ddd, *J* = 17.8, 9.8, 3.9 Hz, 1H), 2.45–2.38 (m, 2H), 2.02–1.94 (m, 1H), 1.84–1.75 (m, 1H), 1.70 (ddd, *J* = 14.4, 7.3, 4.4 Hz, 1H), 1.43 (s, 3H), 0.94 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.1 (d, J_{CF} = 24.1 Hz), 178.0, 167.6 (d, J_{CF} = 25.4 Hz), 131.3, 119.0, 102.0 (d, J_{CF} = 1.1 Hz), 99.3 (d, J_{CF} = 193.5 Hz), 75.3, 66.6, 34.0 (d, J_{CF} = 2.1 Hz), 31.9 (d, J_{CF} = 22.5 Hz), 27.8, 20.7 (d, J_{CF} = 1.7 Hz), 19.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ –148.54 (dd, *J* = 35.4, 20.7 Hz); IR (Neat Film NaCl) 3086, 2960, 2938, 2876, 1752, 1654, 1649, 1603, 1471, 1453, 1422, 1403, 1385, 1369, 1282, 1249, 1229, 1204, 1176, 1137, 1095, 1045, 991, 953, 927, 874, 862, 843, 829, 795, 758 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{15}H_{21}O_4F$ $[M]^{+\bullet}$: 284.1425; found 284.1424.

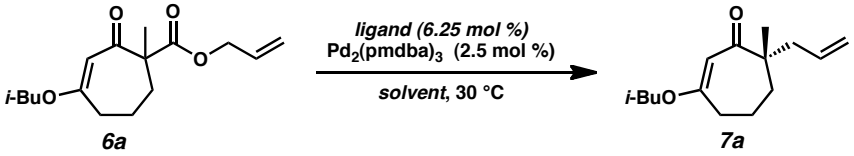


***β*-Ketoester 6n.** To a solution of diisopropylamine (1.84 mL, 13.15 mmol, 1.20 equiv) in THF (54 mL) in a 250 mL round-bottomed flask at 0 °C in an ice/water bath was added *n*-BuLi (5.12 mL, 2.51 M in hexanes, 12.60 mmol, 1.15 equiv) dropwise over 10 min. After 15 min of stirring at 0 °C, the mixture was cooled to –78 °C using an acetone/CO_2(s) bath. A solution of vinylogous ester **5** (2.00 g, 10.96 mmol, 1.00 equiv) in THF (4 mL) was added dropwise using positive pressure cannulation. After an additional 1 h of stirring at –78 °C, allyl cyanoformate (1.34 mL, 12.06 mmol, 1.10 equiv) was added dropwise over 10 min. The mixture was stirred at –78 °C for 2.5 h, quenched by addition of 50% sat. aqueous NH_4Cl (16 mL), and then allowed to warm to ambient temperature. The reaction mixture was diluted with Et_2O (20 mL) and the layers were separated. The aqueous phase was extracted with Et_2O (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a pale orange oil (2.92 g).

Half of the crude oil (1.46 g) was dissolved in toluene (30 mL) in a 100 mL round-bottomed flask, cooled to 0 °C, and stirred vigorously as hexane-washed NaH (197 mg, 8.22 mmol, 1.50 equiv) was added in one portion. Evolution of gas was observed and the reaction mixture was stirred at 0 °C for 30 min. Benzoyl peroxide (1.99 g, 8.22 mmol, 1.50 equiv) was added slowly portionwise, giving a thick, pasty suspension. The reaction was warmed to ambient temperature and diluted with toluene (20 mL) to give a more freely stirring turbid yellow mixture. After 30 min, the reaction was diluted with toluene (50 mL) and washed with H_2O (2 x 5 mL) and brine (2 x 5 mL). The aqueous layers were combined and extracted with EtOAc (2 x 25 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2, 5 x 13 cm, 10:1 Hexanes:EtOAc) to afford *β*-ketoester **6n** (1.85 g, 4.79 mmol, 87% yield over 2 steps) as a pale yellow oil; R_f = 0.46 (4:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09–7.99 (m, 2H), 7.64–7.53 (m, 1H), 7.50–7.38 (m, 2H), 5.89 (dddd, *J* = 17.2, 10.5, 5.7, 5.7 Hz, 1H), 5.42 (s, 1H), 5.31 (app dq, *J* = 17.2, 1.5 Hz, 1H), 5.20 (app dq, *J* = 10.4, 1.3 Hz, 1H), 4.80–4.62 (m, 2H), 3.57 (d, *J* = 6.5 Hz, 2H), 2.87–2.46 (m, 4H), 2.12–1.85 (m, 3H), 0.96 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 192.1, 175.9, 168.0, 165.1, 133.6, 131.7, 130.0, 129.6, 128.6, 118.7, 102.2, 88.8, 75.2, 66.6, 33.8, 31.2, 27.9, 21.2, 19.2, 19.2; IR (Neat Film NaCl) 3070, 2960, 2937, 2875, 1753, 1727, 1661, 1605, 1471, 1452, 1423, 1384, 1369, 1315, 1280, 1222, 1206, 1175, 1107, 1097, 1070, 1044, 1026, 1002, 933, 849, 792 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{22}H_{26}O_6$ $[M]^{+\bullet}$: 386.1733; found 386.1729.

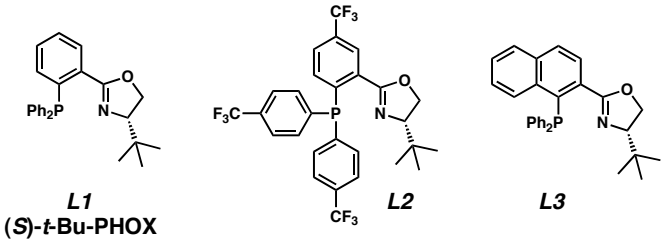
Enantioselective Pd-Catalyzed Decarboxylative Alkylation Screening Protocol

Table SI-1. Solvent Screen for the Enantioselective Alkylation of 6a[a]



entry	ligand	solvent	yield (%)[b]	ee (%)[c]
1	*L1*	THF[e]	94	84
2	*L1*	1,4-dioxane	86	84
3	*L1*	2-methyl THF	75	85
4	*L1*	TBME[e]	88	85
5	*L1*	Et_2O	93	86
6	*L1*	PhH	84	86
7	*L1*	$PhCH_3$	91	88
8[d]	*L2*	$PhCH_3$	57	90
9	*L3*	$PhCH_3$	77	72

[a] *Conditions*: *β*-ketoester **6a** (1.0 equiv), $Pd_2(pmdba)_3$ (2.5 mol %), ligand (6.25 mol %) in solvent (0.1 M) at 30 °C; pmdba = 4,4'-methoxydibenzylideneacetone. [b] Isolated yield. [c] Determined by chiral HPLC or SFC. [d] Increased catalyst loadings were required to achieve full conversion: $Pd_2(pmdba)_3$ (5 mol %), **L2** (12.5 mol %). [e] THF = tetrahydrofuran, TBME = *tert*-butyl methyl ether, 2-methyl THF = 2-methyl tetrahydrofuran.

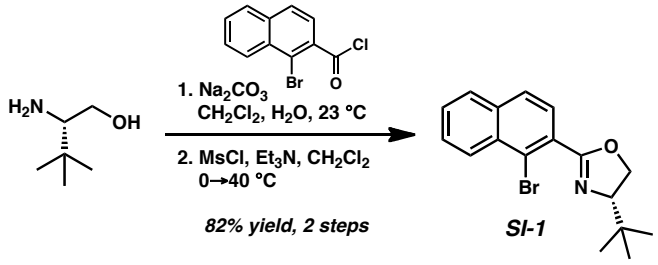


L1 (*S*)-*t*-Bu-PHOX *L2* *L3*

Enantioselective Allylation Screen to Produce Vinylogous Ester 7a *(0.20 mmol scale)*. To a 25 mL flask was added $Pd_2(pmdba)_3$ (5.00 μmol, 2.5 mol %) and ligand **L** (12.5 μmol, 6.25 mol %). The flask was evacuated/backfilled with N_2 (3 cycles, 5 min evacuation per cycle). Solvent (most of total volume, 0.1 M final concentration) was added and the black suspension was stirred for 30 min at 30 °C using an oil bath. A solution of *β*-ketoester **6a** (0.20 mmol, 1.00 equiv) in solvent (remainder of total volume) was transferred to the catalyst solution using positive pressure cannulation. When judged complete by TLC analysis, the reaction was filtered through a small plug of SiO_2, eluted with Et_2O, and concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, 1.5 x 15 cm, 9:1→6:1 Hexanes:EtOAc) or preparative TLC (SiO_2, 2:1 Hexanes:EtOAc) provided vinylogous ester **7a** for analysis. HPLC conditions: 1% IPA in Hexanes, 1.0 mL/min, OD-H column, t_R (min): major = 6.30, minor = 7.26. (For characterization data, see p. 11).

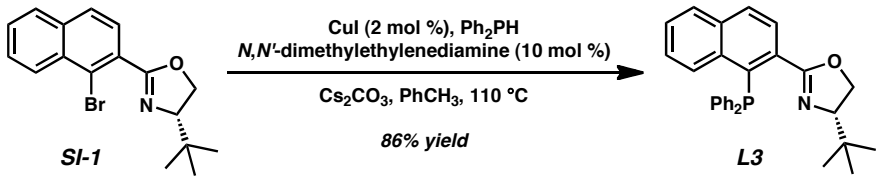
Procedures for the Synthesis of Ligands L3 and L4

Ligands **L1**[6] and **L2**[7] were prepared according to previously reported procedures.

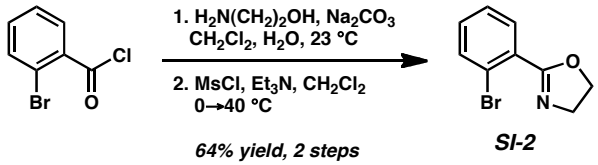


Dihydrooxazole SI-1. (*S*)-*tert*-Leucinol (1.02 g, 8.66 mmol, 1.00 equiv) was placed in a 250-mL round-bottom flask and dissolved in CH_2Cl_2 (14 mL). Na_2CO_3 (2.75 g, 26.0 mmol, 3.00 equiv) in H_2O (27.0 mL) was added dropwise via syringe to the vigorously stirred biphasic system. To the biphasic mixture was added a solution of 1-bromonaphthalene-2-carbonyl chloride (2.68 g, 9.96 mmol, 1.15 equiv) in CH_2Cl_2 (15 mL). The reaction was stirred vigorously at 23 °C for 9.5 h. The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (4 x 50 mL). The combined organics were stirred with KOH (10 mL, 10 mmol, 1.0 N in MeOH) for 30 min then transferred to a separatory funnel. H_2O (10 mL) was added and the mixture was neutralized with HCl (6.0 M in H_2O). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (4 x 50 mL). The combined organics were dried over $MgSO_4$ and concentrated under reduced pressure to afford the intermediate amide (3.03 g) as a pale yellow solid.

The intermediate amide (3.03 g) was dissolved in CH_2Cl_2 (43.3 mL) in a 100-mL 3-neck round-bottom flask fitted with a reflux condenser. The solution was cooled to 0 °C by use of an ice/water bath and Et_3N (2.90 mL, 20.8 mmol, 2.40 equiv) was added. Methanesulfonyl chloride (0.77 mL, 9.96 mmol, 1.15 equiv) was added dropwise. The reaction mixture was stirred at 0 °C for 30 min and heated to 40 °C in a water bath. After 21 h of stirring, the mixture was allowed to cool to ambient temperature and saturated aqueous $NaHCO_3$ was added. The biphasic system was stirred vigorously for 5 min and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (2 x 50 mL). The combined organics were washed with brine (50 mL), dried over $MgSO_4$, and concentrated under reduced pressure to afford a pale yellow oil. The crude oil was purified by flash chromatography (SiO_2, 3 x 15 cm, 9:1 Hexanes:EtOAc) to afford **SI-1** (2.36 g, 7.12 mmol, 82% yield over two steps) as a pale yellow oil that solidifies when placed in a –20 °C freezer; R_f = 0.73 (9:1 $CHCl_3$:MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (dd, *J* = 7.7, 0.5 Hz, 1H), 7.85–7.81 (m, 2H), 7.64 (d, *J* = 8.5 Hz, 1H), 7.60 (app dt, *J* = 8.2, 1.3 Hz, 1H), 7.56 (app dt, *J* = 6.9, 1.3 Hz, 1H), 4.46 (dd, *J* = 10.4, 8.5 Hz, 1H), 4.33 (dd, *J* = 8.5, 8.0 Hz, 1H), 4.17 (dd, *J* = 10.4, 8.2 Hz, 1H), 1.05 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.8, 134.9, 132.3, 128.8, 128.3, 128.3, 128.0, 127.8, 127.7, 126.9, 123.2, 76.9, 69.2, 34.1, 26.1; IR (Neat Film NaCl) 3065, 2956, 2899, 2863, 1667, 1620, 1594, 1556, 1499, 1476, 1463, 1393, 1372, 1362, 1339, 1321, 1300, 1238, 1264, 1210, 1161, 1104, 1024, 977, 956, 920, 817, 752 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{17}H_{18}ONBr$ $[M]^{+\bullet}$: 331.0572; found 331.0583; $[\alpha]_D^{20.0}$ –64.0 (*c* 0.92, $CHCl_3$); mp = 66–68 °C.



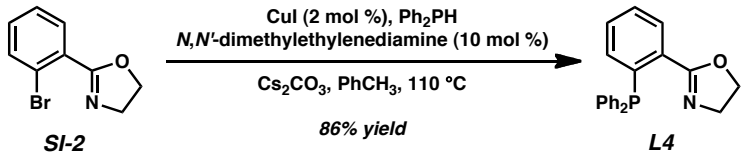
Phosphine Ligand L3. Prepared by the typical method as described for **L4** below by employing **SI-1** (830.6 mg, 2.50 mmol). After 24 h of stirring, the reaction mixture was filtered through a plug of Celite, eluted with CH_2Cl_2 (2 x 25 mL), and concentrated under reduced pressure. The crude oil was passed through a short plug of silica (SiO_2, 2.5 x 8 cm, Hexanes→9:1 CH_2Cl_2:Et_2O) to afford a bright yellow oil. The crude oil was purified by flash chromatography (SiO_2, 2.5 x 25 cm, 19:1 Hexanes:Acetone and then 2.5 x 21 cm, 9:1→6:1 Hexanes:EtOAc) to afford **L3** (950.8 mg, 2.17 mmol, 87% yield) as a bright yellow foam; R_f = 0.21 (9:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.1 Hz, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.72 (dd, *J* = 8.3, 2.9 Hz, 1H), 7.45 (app dt, *J* = 7.8, 1.7 Hz, 2H), 7.41–7.38 (m, 3H), 7.29–7.22 (m, 6H), 7.16 (ddd, *J* = 8.3, 6.9, 1.0 Hz, 1H), 4.17–4.15 (m, 2H), 3.91 (dd, *J* = 9.8, 8.8 Hz, 1H), 0.97 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6 (d, J_{CP} = 5.1 Hz), 137.5 (d, J_{CP} = 33.1 Hz), 136.8, (d, J_{CP} = 14.7 Hz), 136.5 (d, J_{CP} = 14.7), 134.9, 134.7 (d, J_{CP} = 33.6 Hz), 133.1 (d, J_{CP} = 26.7 Hz), 132.2 (d, J_{CP} = 17.5 Hz), 132.1 (d, J_{CP} = 17.5 Hz), 131.5 (d, J_{CP} = 0.9 Hz), 129.1 (d, J_{CP} = 7.4 Hz), 129.0, 128.4 (d, J_{CP} = 6.0 Hz), 127.8 (d, J_{CP} = 8.3 Hz), 126.6 (d, J_{CP} = 8.7 Hz), 126.4 (d, J_{CP} = 40.5 Hz), 76.8, 69.0, 34.1, 26.3; ^{31}P NMR (121 MHz, $CDCl_3$) δ –9.33 (s); IR (Neat Film NaCl) 3054, 2954, 2867, 1665, 1584, 1478, 1434, 1364, 1244, 1094, 1026, 986, 962, 922, 824 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{29}H_{28}NOP$ $[M]^{+\bullet}$: 437.1908; found 437.1908; $[\alpha]_D^{26.1}$ –38.2 (*c* 1.59, *n*-Hexane).



2-(2-Bromo-phenyl)-4,5-dihydrooxazole SI-2. To a solution of ethanolamine (1.32 mL, 21.9 mmol, 1.20 equiv) in CH_2Cl_2 (60 mL) in a 250-mL round-bottom flask was added a solution of Na_2CO_3 (5.80 g, 54.7 mmol, 3.00 equiv) in H_2O (45 mL). Neat 2-bromobenzoyl chloride (4.00 g, 2.38 mL, 18.2 mmol, 1.00 equiv) was added dropwise via syringe to the vigorously stirred biphasic system. The reaction flask was capped with a yellow plastic stopper and stirred for 7.5 h at 23 °C. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (2 x 25 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a white solid. The crude product was dissolved in CH_2Cl_2 (50 mL) and hexanes (10 mL) was added. The solution was concentrated to ~25 mL under reduced pressure resulting in precipitation of the intermediate amide (4.02 g, 16.4 mmol, 90% yield) as a white solid.

The intermediate amide (2.0 g, 8.2 mmol, 1.00 equiv) was dissolved in CH_2Cl_2 (62 mL) in a 100-mL round-bottom flask equipped with a reflux condenser. Et_3N (3.43 mL, 24.5 mmol, 3.00 equiv) was added and the solution was cooled to 0 °C by use of an ice/water bath. Methanesulfonyl chloride (952 μL, 12.3 mmol, 1.50 equiv) was added dropwise. The reaction mixture was stirred at 0 °C for 30 min and heated to 40 °C in an oil bath. After 5 h of stirring, the resulting yellow solution was allowed to cool to ambient temperature, diluted with CH_2Cl_2 (25

mL), and washed with H_2O (2 x 25 mL) and brine (25 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to afford a thick, pale yellow oil. The crude oil was purified by flash chromatography (SiO_2, 5 x 10 cm, 6:2:2 Hexanes:EtOAc:Toluene) to afford 2-(2-bromo-phenyl)-4,5-dihydrooxazole **SI-2** (1.31 g, 5.79 mmol, 71% yield); R_f = 0.45 (9:1 $CHCl_3$:MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.8, 2.0 Hz, 1H), 7.65 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.35 (app dt, *J* = 7.6, 1.2 Hz, 1H), 7.29 (app dt, *J* = 7.6, 1.7 Hz, 1H), 4.46 (t, *J* = 9.6 Hz, 2H), 4.12 (t, *J* = 9.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.0, 134.1, 131.8, 131.5, 129.8, 127.2, 122.0, 67.8, 55.5; IR (Neat Film NaCl) 3390, 3070, 2966, 2904, 2868, 1729, 1646, 1589, 1432, 1362, 1328, 1272, 1243, 1093, 1026, 938 cm^{-1}; HRMS (EI+) *m/z* calc'd for C_9H_8BrNO $[M]^{+\bullet}$: 224.9789; found 224.9779.



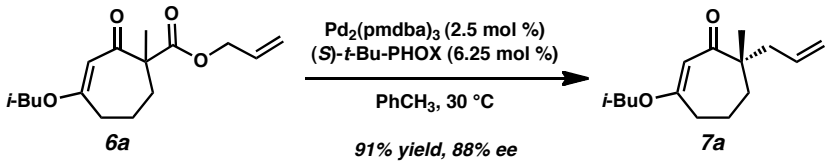
2-(2-Diphenylphosphanyl-phenyl)-4,5-dihydrooxazole L4. A 250-mL Schlenk flask was charged with CuI (66.7 mg, 0.35 mmol, 2 mol %), Ph_2PH (3.85 mL, 22.1 mmol, 1.25 equiv), *N,N'*-dimethylethylenediamine (191 mL, 1.77 mmol, 10 mol %), and toluene (18 mL). The solution was stirred at 23 °C for 20 min. 2-(2-Bromo-phenyl)-4,5-dihydrooxazole **SI-2** (4.0 g, 17.7 mmol, 1.00 equiv) was azeotroped with toluene (2 x 5 mL) under reduced pressure, dissolved in toluene (18 mL), and transferred quantitatively to the Schlenk flask by use of positive pressure cannulation. Cs_2CO_3 (8.65 g, 26.5 mmol, 1.50 equiv) was added in one portion and the flask was evacuated/backfilled with Ar (three cycles). The teflon valve was sealed and the yellow heterogeneous reaction mixture was stirred vigorously, immersed in an oil bath, and heated to 110 °C. After 20 h of stirring at 110 °C, the mixture was allowed to cool to ambient temperature and filtered through a pad of Celite using CH_2Cl_2 (2 x 50 mL). The filtrate was concentrated under reduced pressure to afford a clear orange oil. The crude oil was flushed through a plug of silica gel (SiO_2, 5 x 10 cm, Hexanes→9:1 CH_2Cl_2:Et_2O) to afford 2-(2-diphenylphosphanyl-phenyl)-4,5-dihydrooxazole **L4** (5.03 g, 15.2 mmol, 86% yield) as a colorless viscous oil that crystallized upon standing; R_f = 0.50 (7:3 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.6, 3.4 Hz, 1H), 7.37–7.26 (comp. m, 12H), 6.89 (dd, *J* = 4.1, 7.6 Hz, 1H), 4.08 (t, *J* = 9.5 Hz, 2H), 3.78 (t, *J* = 9.5 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.5 (d, J_{CP} = 2.8 Hz), 139.1 (d, J_{CP} = 24.9 Hz), 138.0 (d, J_{CP} = 11.5 Hz), 134.1 (d, J_{CP} = 20.7 Hz), 133.7 (d, J_{CP} = 1.8 Hz), 131.9 (d, J_{CP} = 18.9 Hz), 130.5, 129.9 (d, J_{CP} = 2.8 Hz), 128.7, 128.5 (d, J_{CP} = 7.4 Hz), 128.1, 67.2, 55.0; ^{31}P NMR (121 MHz, $CDCl_3$) δ –3.99 (s); IR (Neat Film NaCl) 3053, 3000, 2971, 2901, 2876, 1650, 1585, 1562, 1478, 1434, 1354, 1326, 1248, 1133, 1089, 1070, 1041, 974, 942, 898, 743 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{21}H_{19}NOP$ $[M+H]^+$: 332.1204; found 332.1218; mp = 99–101 °C.

Procedures for Synthesis of Enantioenriched Vinylogous Esters 7 using Enantioselective Decarboxylative Alkylation Reactions

Chiral vinylogous esters **7a–k**, **7m**, **7o–q** were prepared according to previously reported procedures.[10] Racemic reactions were performed using $Pd(PPh_3)_4$ (5 mol %) or achiral PHOX

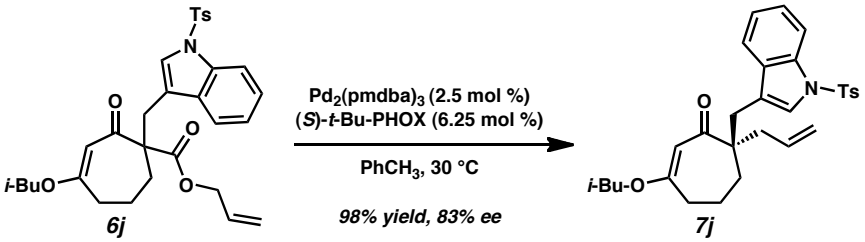
ligand **L4** (6.25 mol %) and $Pd_2(pmdba)_3$ (2.5 mol %) in toluene at 30 °C. For the synthesis of ligand **L4**, see p. 10.

General Method SI-A: Schlenk Manifold Method



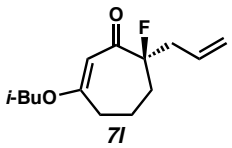
Vinylogous Ester 7a ***(Table 2, entry 1).*** $Pd_2(pmdba)_3$ (5.0 mg, 4.5 μmol, 2.5 mol %) and (*S*)-*t*-Bu-PHOX (4.4 mg, 11 μmol, 6.25 mol %) were placed in a 1 dram vial. The flask was evacuated/backfilled with N_2 (3 cycles, 10 min evacuation per cycle). Toluene (1.3 mL, sparged with N_2 for 1 h immediately before use) was added and the black suspension was immersed in an oil bath preheated to 30 °C. After 30 min of stirring, β-ketoester **6a** (50.7 mg, 0.181 mmol, 1.00 equiv) was added as a solution in toluene (0.5 mL, sparged with N_2 immediately before use) using positive pressure cannulation. The dark orange catalyst solution turned olive green immediately upon addition of β-ketoester **6a**. The reaction was stirred at 30 °C for 21 h, allowed to cool to ambient temperature, filtered through a silica gel plug (2 x 2 cm, Et_2O), and concentrated under reduced pressure. The crude oil was purified by preparative TLC (SiO_2, 4:1 Hexanes:EtOAc) to afford vinylogous ester **7a** (38.8 mg, 0.164 mmol, 91% yield, 88% ee) as a pale yellow oil; R_f = 0.31 (3:1 Hexanes:Et_2O); ^1H NMR (500 MHz, $CDCl_3$) δ 5.72 (dddd, *J* = 16.6, 10.5, 7.3, 7.3 Hz, 1H), 5.31 (s, 1H), 5.05–5.00 (m, 2H), 3.50 (dd, *J* = 9.3, 6.6 Hz, 1H), 3.47 (dd, *J* = 9.3, 6.6 Hz, 1H), 2.53–2.42 (m, 2H), 2.38 (dd, *J* = 13.7, 7.1 Hz, 1H), 2.20 (dd, *J* = 13.7, 7.8 Hz, 1H), 1.98 (app sept, *J* = 6.6 Hz, 1H), 1.86–1.70 (m, 3H), 1.62–1.56 (m, 1H), 1.14 (s, 3H), 0.95 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.7, 171.3, 134.6, 117.9, 105.0, 74.5, 51.5, 45.4, 36.1, 35.2, 28.0, 25.2, 19.9, 19.3, 19.3; IR (Neat Film NaCl) 2960, 2933, 2873, 1614, 1470, 1387, 1192, 1171, 998, 912 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{15}H_{24}O_2$ $[M]^{+\bullet}$: 236.1776; found 236.1767; $[\alpha]_D^{25.6}$ –69.04 (*c* 1.08, $CHCl_3$, 88.0% ee); HPLC conditions: 1% IPA in Hexanes, 1.0 mL/min, OD-H column, t_R (min): major = 6.30, minor = 7.26.

General Method SI-B: Glove Box Method



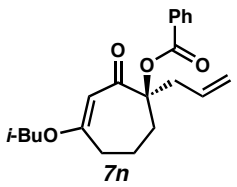
Vinylogous Ester 7j ***(Table 2, entry 10).*** A 20 mL scintillation vial was loaded with β-ketoester **6j** (447 mg, 0.81 mmol, 1.00 equiv). A separate 20 mL scintillation vial was loaded with $Pd_2(pmdba)_3$ (19.7 mg, 0.051 mmol, 6.25 mol %), (*S*)-*t*-Bu-PHOX (22.3 mg, 0.020 mmol, 2.5 mol %), and magnetic stir bar. The two vials and a teflon-lined hard cap were

evacuated/backfilled with N_2 in a glove box antechamber (3 cycles, 5 min evacuation per cycle) before being transferred into the glove box. Toluene (5 mL) was added to the vial containing $Pd_2(pmdba)_3$ and (*S*)-*t*-BuPHOX. The vial was capped and heated to 30 °C for 30 min. During this time, the mixture developed a dark orange color. *β*-Ketoester **6j** was dissolved in toluene (3 mL) and added to the catalyst solution dropwise, causing the solution to turn olive green. The solution was stirred at 30 °C in a heating block. The capped vial was removed from the glove box after 29 h of stirring. The crude product was concentrated under reduced pressure and purified by flash column chromatography (SiO_2, 5 x 25 cm, 15:1→10:1→8:1→6:1 Hexanes:EtOAc) to afford vinylogous ester **7j** (403 mg, 0.796 mmol, 98% yield, 82.9% ee) as a thick, white semi-solid. R_f = 0.49 (4:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (dm, *J* = 8.4 Hz, 1H), 7.70 (dm, *J* = 8.4 Hz, 2H), 7.48 (dm, *J* = 7.9 Hz, 1H), 7.31–7.13 (m, 5H), 5.86–5.68 (m, 1H), 5.32 (s, 1H), 5.13–5.00 (m, 2H), 3.42 (dd, *J* = 17.0, 7.7 Hz, 1H), 3.38 (dd, *J* = 17.0, 7.6 Hz, 1H), 3.20 (dd, *J* = 14.2, 0.7 Hz, 1H), 2.73 (d, *J* = 14.1 Hz, 1H), 2.51 (dddd, *J* = 13.7, 6.9, 1.3, 1.3 Hz, 1H), 2.44–2.15 (m, 6H), 1.92 (app sept, *J* = 6.7 Hz, 1H), 1.76–1.46 (m, 4H), 0.92 (d, *J* = 6.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.2, 171.7, 144.8, 135.4, 135.0, 134.1, 132.4, 129.8, 126.9, 125.4, 124.5, 123.2, 120.1, 119.6, 118.6, 113.8, 106.4, 74.6, 55.9, 44.1, 36.3, 33.0, 31.9, 27.9, 21.7, 19.5, 19.3; IR (Neat Film NaCl) 3584, 3401, 2068, 2958, 2930, 2873, 1609, 1494, 1470, 1448, 1422, 1402, 1368, 1306, 1279, 1215, 1188, 1174, 1120, 1097, 1020, 975, 916, 876, 813, 782, 747 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{30}H_{36}O_4NS$ $[M+H]^+$: 506.2365; found 506.2358; $[\alpha]_D^{25.0}$ +9.10 (*c* 1.00, $CHCl_3$, 82.9% ee); HPLC conditions: 5.0% EtOH in Hexanes, 1.0 mL/min, AD column, t_R (min): major = 11.11, minor = 16.64.



7l

Vinylogous Ester 7l ***(Table 2, entry* 12).** Prepared using General Method SI-A. 172.5 mg, 0.552 mmol, 98% yield. Flash column chromatography (SiO_2, 3 x 24 cm, 20:1→15:1→10:1 Hexanes:EtOAc); R_f = 0.59 (4:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89–5.72 (m, 1H), 5.28 (s, 1H), 5.18–5.08 (m, 2H), 3.53 (dd, *J* = 10.6, 6.5 Hz, 1H), 3.50 (dd, *J* = 10.6, 6.6 Hz, 1H), 2.80–2.46 (m, 3H), 2.46–2.33 (m, 1H), 2.22–1.67 (m, 5H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.2 (d, J_{CF} = 24.9 Hz), 176.9 (d, J_{CF} = 1.8 Hz), 131.9 (d, J_{CF} = 4.4 Hz), 119.3, 101.7, 101.2 (d, J_{CF} = 180.6 Hz), 75.0, 42.1 (d, J_{CF} = 23.2 Hz), 34.4 (d, J_{CF} = 23.2 Hz), 34.1 (d, J_{CF} = 2.4 Hz), 27.9, 21.7 (d, J_{CF} = 2.1 Hz), 19.3, 19.2; ^{19}F NMR (282 MHz, $CDCl_3$) δ –145.81 (m); IR (Neat Film NaCl) 3086, 2960, 1752, 1654, 1649, 1603, 1471, 1453, 1422, 1403, 1385, 1369, 1282, 1249, 1229, 1204, 1176, 1137, 1095, 1066, 145, 991, 927, 873, 843, 795, 758 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{14}H_{21}O_2F$ $[M]^{+\bullet}$: 240.1526; found 240.1524; $[\alpha]_D^{25.0}$ +0.61 (*c* 1.02, $CHCl_3$, 91.2% ee); HPLC conditions: 1.0% IPA in Hexanes, 1.0 mL/min, OD-H column, t_R (min): minor = 8.05, major = 8.80.

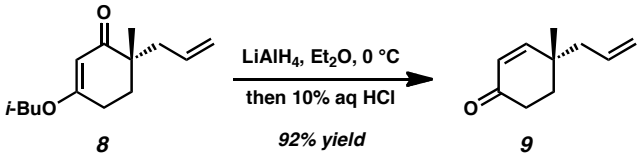


7n

Vinylogous Ester 7n ***(Table 2, entry 14).*** Prepared using General Method SI-A. 589.8 mg, 1.72 mmol, 75% yield. Flash column chromatography (SiO_2, 5 x 13 cm, 20:1→15:1→10:1→6:1 Hexanes:EtOAc); R_f = 0.57 (4:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03–7.96 (m, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 5.96–5.78 (m, 1H), 5.27 (s, 1H), 5.19–5.08 (m, 2H), 3.42 (dd, *J* = 9.4, 6.6 Hz, 1H), 3.39 (dd, *J* = 9.4, 6.5 Hz, 1H), 3.06 (dddd, *J* = 14.8, 6.7, 1.4, 1.4 Hz, 1H), 2.83–2.67 (m, 2H), 2.55–2.34 (m, 2H), 2.10–1.74 (m, 4H), 0.80 (dd, *J* = 6.6, 4.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.1, 174.3, 165.5, 133.1, 132.5, 130.6, 129.7, 128.5, 119.2, 102.1, 88.6, 74.9, 40.8, 34.0, 27.7, 21.9, 19.1, 19.0; IR (Neat Film NaCl) 3073, 2959, 2934, 2873, 1718, 1672, 1649, 1613, 1479, 1451, 1421, 1382, 1368, 1315, 1291, 1258, 1231, 1199, 1174, 1108, 1070, 1026, 1004, 919, 866, 820, 801, 762, 715 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{21}H_{26}O_4$ $[M]^{+\bullet}$: 342.1815; found 342.1831; $[\alpha]_D^{25.0}$ +79.72 (*c* 1.02, $CHCl_3$, 57.1% ee); HPLC conditions: 1.0% IPA in Hexanes, 1.0 mL/min, OD-H column, t_R (min): major = 18.28, minor = 22.01.

Synthetic Studies on Vinylogous Esters 8/7a and 12/5

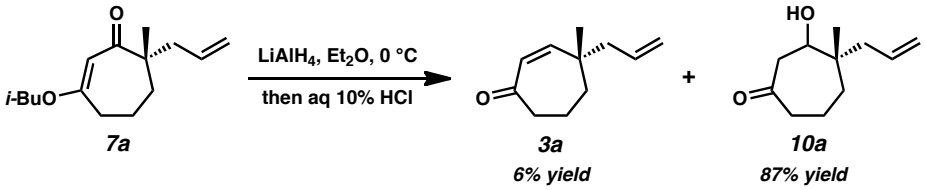
Vinylogous esters **5** and **8** were prepared according to previously reported procedures.[10]



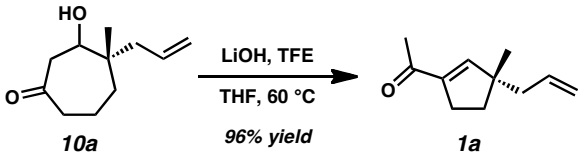
8 *9*

Cyclohexenone 9. A 50 mL round-bottom flask was charged with Et_2O (11.1 mL) and cooled to 0 °C in an ice/water bath. $LiAlH_4$ (13.6 mg, 0.36 mmol, 0.55 equiv) was added in one portion. After 10 min, a solution of vinylogous ester **8** (146 mg, 0.66 mmol, 1.00 equiv) in Et_2O (2.0 mL) was added dropwise using positive pressure cannulation. After 30 min of stirring at 0 °C, an additional portion of $LiAlH_4$ (2.5 mg, 0.066 mmol, 0.10 equiv) was added. After 60 min of stirring, the reaction was quenched by slow addition of aqueous HCl (1.0 mL, 10% w/w). The resulting biphasic system was allowed to warm to ambient temperature and stirred vigorously for 8.5 h. The phases were separated and the aqueous phase was extracted with Et_2O (3 x 15 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified using flash column chromatography (SiO_2, 2 x 25 cm, 10:1→4:1→1:1→1:2 Hexanes:Et_2O) to afford cyclohexenone **9** (90.5 mg, 0.60 mmol, 92% yield) as a yellow oil; R_f = 0.51 (4:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.67 (d, *J* = 10.2 Hz, 1H), 5.88 (d, *J* = 10.2 Hz, 1H), 5.79 (dddd, *J* = 16.8, 10.3, 7.4, 7.4 Hz, 1H), 5.20–5.01 (m, 2H), 2.54–2.36 (m, 2H), 2.29–2.10 (m, 2H), 2.05–1.89 (m, 1H), 1.85–1.69 (m, 1H), 1.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 199.4, 158.4, 133.4, 127.6, 118.6, 45.2, 35.7, 34.1, 33.6, 24.7; IR (Neat Film NaCl) 3077, 3005, 2960, 2917, 2868, 2849, 1682, 1639, 1616, 1459, 1419,

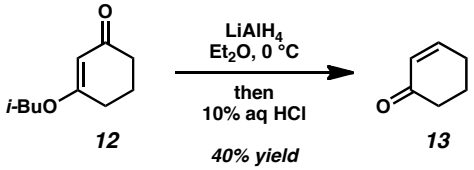
1390, 1373, 1332, 1250, 1223, 1193, 1115, 996, 961, 918, 871, 803, 757 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{10}H_{14}O$ $[M]^{+\bullet}$: 150.1045; found 150.1056; $[\alpha]_D^{25.0}$ +26.72 (*c* 1.02, $CHCl_3$, 86.3% ee).



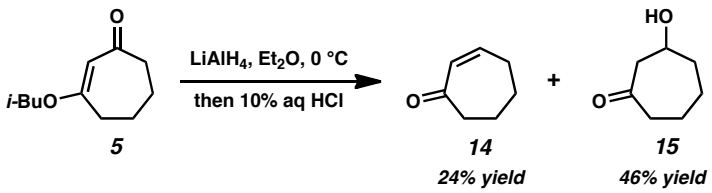
Cycloheptenone 3a and ***β*-Hydroxyketone 10a.** For procedure and characterization data, see General Method A, p. 18–19.



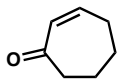
Acylcyclopentene 1a. For procedure and characterization data, see General Method E, p. 21.



Cyclohexenone 13. A 25 mL round-bottom flask with magnetic stir bar and $LiAlH_4$ (22.8 mg, 0.60 mmol, 0.60 equiv) was charged with Et_2O (4 mL) and cooled to 0 °C in an ice/water bath. After 10 min, a solution of vinylogous ester **12** (168.23 mg, 1.00 mmol, 1.00 equiv) in Et_2O (1 mL) was added dropwise using positive pressure cannulation. After 30 min of stirring at 0 °C, the reaction was quenched by slow addition of aqueous HCl (2.60 mL, 10% w/w). The resulting biphasic system was allowed to warm to ambient temperature. The phases were separated and the aqueous phase was extracted with Et_2O (3 x 10 mL). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated carefully under reduced pressure in an ice-water bath. The crude product purified using flash column chromatography (SiO_2, 2 x 25 cm, 5:1→4:1 Hexanes:EtOAc) to afford cyclohexenone **13** (39.4 mg, 0.41 mmol, 40% yield) as a volatile pale yellow oil. Spectra for the compound match data for commercially available material.

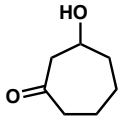


Cycloheptenone 14 and β-Hydroxyketone 15. A 50 mL round-bottom flask with magnetic stir bar and $LiAlH_4$ (806 mg, 21.2 mmol, 0.60 equiv) was charged with Et_2O (8 mL) and cooled to 0 °C in an ice/water bath. After 10 min, a solution of vinylogous ester **5** (328.2 mg, 1.80 mmol, 1.00 equiv) in Et_2O (2 mL) was added dropwise using positive pressure cannulation. After 30 min of stirring at 0 °C, the reaction was quenched by slow addition of aqueous HCl (4.73 mL, 10% w/w). The resulting biphasic system was allowed to warm to ambient temperature. The phases were separated and the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated carefully under reduced pressure in an ice-water bath. The crude product purified using flash column chromatography (SiO_2, 2 x 25 cm, 6:1→4:1→2:1→1:1→1:2→1:4 Hexanes:EtOAc) to afford β-hydroxyketone **15** (107.1 mg, 0.84 mmol, 46% yield) as a pale yellow oil and cycloheptenone **14** (47.9 mg, 0.44 mmol, 24% yield) as a colorless oil.



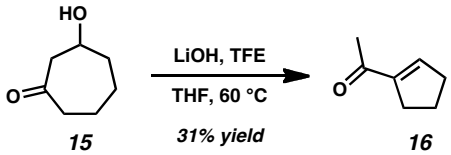
14

Cycloheptenone 14. Spectra for the compound match data for commercially available material.



15

β-Hydroxyketone 15. R_f = 0.26 (1:1 Hexanes:EtOAc); ^1H NMR (500 MHz, $CDCl_3$) δ 4.18–3.97 (m, 1H), 2.89–2.67 (m, 2H), 2.55–2.35 (m, 2H), 2.10 (br s, 1H), 1.95–1.69 (m, 5H), 1.65–1.49 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 212.6, 67.5, 51.8, 44.4, 38.8, 24.4, 23.8; IR (Neat Film NaCl) 3420, 2930, 2861, 1696, 1449, 1410, 1349, 1263, 1196, 1157, 1109, 1043, 1016, 929, 878, 829, 752, 710 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_7H_{12}O_2$ $[M]^{+\bullet}$: 128.0837; found 128.0828.

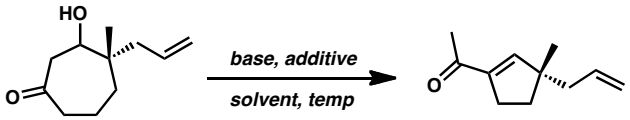


Acylcyclopentene 16. Alcohol **15** (101.3 mg, 0.79 mmol, 1.00 equiv) was dissolved in THF (7.9 mL) in a 20 mL scintillation vial with magnetic stir bar. The solution was treated with 2,2,2-trifluoroethanol (86.4 μL, 1.19 mmol, 1.50 equiv) and anhydrous LiOH (28.4 mg, 1.19 mmol, 1.50 equiv). The headspace of the vial was purged with N_2 and the vial was capped with a teflon-

lined hard cap and stirred at 60 °C in a heating block. After 16 h of stirring, the suspension was allowed to cool to ambient temperature, diluted with Et_2O (150 mL), dried over Na_2SO_4 (30 min of stirring), filtered, and concentrated carefully under reduced pressure in an ice-water bath. The crude product was purified using flash column chromatography (SiO_2, 2 x 20 cm, 15:1→10:1 Hexanes:Et_2O) to afford acylcyclopentene **16** (27 mg, 0.25 mmol, 31% yield) as a colorless fragrant oil. Spectra for the compound match data for commercially available material.

Ring Contraction Screening Protocol

Table SI-2. Ring Contraction Screen of β-Hydroxyketone 10a[a]



10a *1a*

entry	base	additive	solvent	T (°C)	conversion (%)	time (h)	yield (%)[b]
1	LiO*t*-Bu	—	*t*-BuOH	40	100	9	71
2	LiO*t*-Bu	—	THF	40	100	8	60
3	NaO*t*-Bu	—	THF	40	100	5	81
4	KO*t*-Bu	—	THF	40	100	5	85
5	NaOH	—	THF	60	100	4	89
6	KOH	—	THF	60	100	4	87
7	LiOH	—	THF	60	78	24	19[d]
8	LiOH	*t*-BuOH	THF	60	98	24	78
9	LiOH	HFIP[c]	THF	60	99	12.5	87
10	LiOH	TFE[c]	THF	60	99	12.5	96
11	$LiOCH_2CF_3$	—	THF	60	—	10	90[e]
12	$CsOH·H_2O$	—	THF	60	100	4	48
13	Cs_2CO_3	—	THF	60	67	24	61
14	Cs_2CO_3	TFE[c]	THF	60	100	12.5	86
15	Cs_2CO_3	TFE[c]	CH_3CN	60	100	12.5	100
16	NaO*t*-Bu	*t*-BuOH	THF	40	100	8	52
17	KO*t*-Bu	*t*-BuOH	THF	40	100	8	57
18	LiOH	*t*-BuOH	THF	40	87	24	77
19	LiOH	TFE[c]	THF	40	73	24	73
20	LiOH	HFIP[c]	THF	40	84	24	81
21	CsF	—	CH_3CN	60	86	24	10

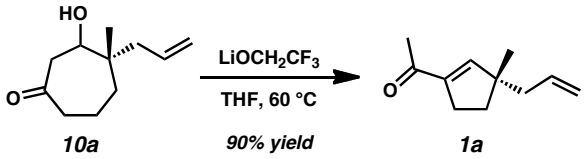
[a] *Conditions*: β-hydroxyketone **10a** (1.0 equiv), additive (1.5 equiv), base (1.5 equiv), solvent (0.1 M) at indicated temperature for 9–24 h. [b] GC yield using an internal standard at ≥ 98% conversion unless otherwise stated. [c] HFIP = 1,1,1,3,3,3-hexafluoro-2-propanol; TFE = 2,2,2-trifluoroethanol. [d] Several reaction intermediates observed by TLC and GC analysis; proceeded to 78% conversion. [e] Isolated yield.

Ring Contraction Screen to Produce Acylcyclopentene 1a *(0.10 mmol scale, Table 1, entries 1–4 and Table SI-2, entries 1–10)*. A benzene solution of β-hydroxyketone **10a** was transferred to a dry 1 dram vial and concentrated under reduced pressure to obtain a starting mass. To this vial was added a magnetic stir bar and 1,4-diisopropylbenzene (internal standard). The contents were solvated in either *t*-BuOH or THF (0.1 M). After complete solvation, an appropriate additive (*t*-BuOH, TFE, or HFIP; 1.50 equiv) was added, followed by base (1.50 equiv). The head space of the vial was purged with N_2 and the vial was capped with a teflon-lined hard cap

and stirred at the appropriate temperature (40 or 60 °C) in a heating block. Reaction progress was initially followed by TLC analysis and when necessary, aliquots were removed and flushed through a small SiO_2 plug with EtOAc for GC analysis. GC conditions: 90 °C isothermal for 5 min, then ramp 10 °C/min to 250 °C, DB-WAX column, t_R (min): 1,4-diisopropylbenzene = 5.3, acylcyclopentene **1a** = 9.3, *β*-hydroxyketone **10a** = 17.1 and 17.2 (two diastereomers). (For characterization data, see p. 19, 21).

Additional Conditions. Additional reaction conditions are listed in Table SI-2, entries 16–21.

Unsuccessful Conditions. No reaction was observed using the following bases, with or without TFE additive: DBU, TMG, Na_2CO_3, K_2CO_3, $BaCO_3$, CaH_2. DBU = 1,8-diazabicyclo [5.4.0]undec-7-ene, TMG = 1,1,3,3-tetramethylguanidine.

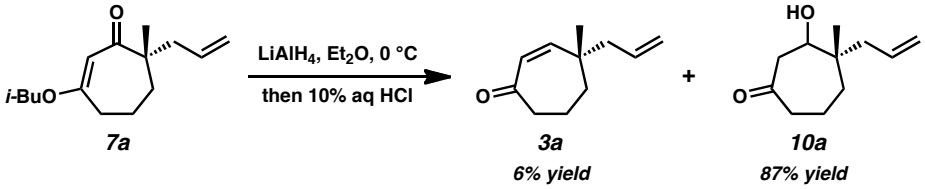


Ring Contraction using $LiOCH_2CF_3$ *(Table SI-2, entry 11).* *β*-Hydroxyketone **10a** (30.0 mg, 0.16 mmol, 1.00 equiv) was measured into a 1 dram vial with magnetic stir bar with a septum-fitted screw cap. $LiOCH_2CF_3$[1] (26.0 mg, 0.25 mmol, 1.50 equiv) was measured into a separate 1 dram vial, capped with a septum, evacuated/backfilled with N_2 (3 cycles, 5 min evacuation per cycle), and dissolved in THF (0.5 mL). The solution was cannulated into the vial containing *β*-hydroxyketone along with additional THF rinses (2 x 0.5 mL). The yellow solution was stirred at 60 °C in a heating block. After 10 h, the reaction was cooled to ambient temperature. The turbid brown solution was diluted with Et_2O and stirred with Na_2SO_4 for 30 min. The reaction was filtered and concentrated in vacuo at 0 °C in an ice/water bath. The residue was purified by flash column chromatography (SiO_2, 1 x 20 cm, 15:1 Hexanes:Et_2O) to afford acylcyclopentene **1a** (24.4 mg, 0.149 mmol, 90% yield) as a clear, colorless oil. (For characterization data, see p. 21).

Procedures for the Synthesis of Acylcyclopentenes 1 by Ring Contraction

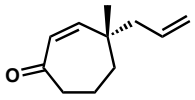
β-Hydroxyketones **10a–j**, **10m, 10o–r**, cycloheptenones **3a**, **3r**, and acylcyclopentenes **1a–j**, **1m, 1o–r** were prepared according to previously reported procedures.[10] For *β*-hydroxyketone intermediate **10n**, R_f, IR, and HRMS data are reported and ^{1}H NMR and IR spectra are provided for reference. Representative procedures for General Methods A–E are described below.

General Method A: Lithium Aluminum Hydride Reduction / 10% Aq HCl Hydrolysis



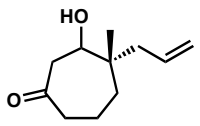
7a → *3a* (6% yield) + *10a* (87% yield)

Cycloheptenone 3a and ***β*-Hydroxyketone 10a.** A 500 mL round-bottom flask with magnetic stir bar was charged with Et_2O (150 mL) and cooled to 0 °C in an ice/water bath. $LiAlH_4$ (806 mg, 21.2 mmol, 0.55 equiv) was added in one portion. After 10 min, a solution of vinylogous ester **7a** (9.13 g, 38.6 mmol, 1.00 equiv) in Et_2O (43 mL) was added dropwise using positive pressure cannulation. The grey suspension was stirred for 40 min and additional $LiAlH_4$ (148 mg, 3.9 mmol, 0.10 equiv) was added in one portion. After an additional 30 min of stirring at 0 °C, the reaction was quenched by slow addition of aqueous HCl (110 mL, 10% w/w). The resulting biphasic system was allowed to warm to ambient temperature and stirred vigorously for 8.5 h. The phases were separated and the aqueous phase was extracted with Et_2O (3 x 100 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was azeotroped with toluene (3 x 20 mL) and purified using flash column chromatography (SiO_2, 5 x 15 cm, 9:1→3:1 Hexanes:EtOAc, dry-loaded using Celite) to afford *β*-hydroxyketone **10a** (6.09 g, 33.41 mmol, 87% yield, 1.3:1 dr) as a colorless semi-solid and cycloheptenone **3a** (387 mg, 6% yield) as a colorless oil.



3a

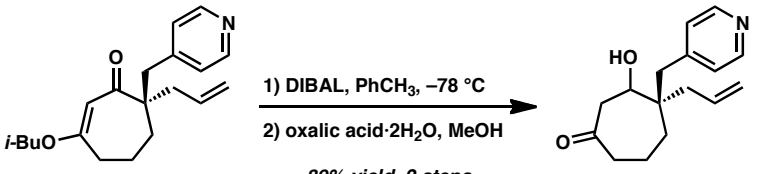
Cycloheptenone 3a. R_f = 0.54 (7:3 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.04 (dd, *J* = 12.9, 0.7 Hz, 1H), 5.82 (d, *J* = 12.9 Hz, 1H), 5.75 (dddd, *J* = 17.1, 10.3, 7.8, 7.1 Hz, 1H), 5.10 (dddd, *J* = 10.3, 1.2, 1.2, 1.2 Hz, 1H), 5.08–5.03 (m, 1H), 2.65–2.52 (m, 2H), 2.19 (app dd, *J* = 13.7, 6.8 Hz, 1H), 2.11 (app dd, *J* = 13.7, 8.1 Hz, 1H), 1.84–1.76 (m, 3H), 1.68–1.63 (m, 1H), 1.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.7, 152.5, 133.8, 128.6. 118.6, 47.2, 45.1, 42.7, 38.2, 27.1, 18.4; IR (Neat Film NaCl) 3076, 3011, 2962, 2934, 2870, 1659, 1454, 1402, 1373, 1349, 1335, 1278, 1208, 1172, 997, 916, 874, 822, 772 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{11}H_{16}O$ $[M]^{+\bullet}$: 164.1201; found 164.1209; $[\alpha]_D^{21.0}$ –9.55 (*c* 1.07, $CHCl_3$, 88.0% ee).



10a

***β*-Hydroxyketone 10a *(Table 4, entry 1)*.** R_f = 0.23 (7:3 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ **major epimer**: 5.88 (dddd, *J* = 15.1, 9.0, 7.6, 7.6 Hz, 1H), 5.12–5.08 (m, 2H), 3.70 (dd, *J* = 4.9, 3.9 Hz, 1H), 2.86 (dd, *J* = 15.6, 1.7 Hz, 1H), 2.65 (dd, *J* = 15.6, 7.3 Hz, 1H), 2.54–2.43 (m, 2H), 2.24 (dd, *J* = 13.7, 7.8 Hz, 1H), 2.07 (dd, *J* = 13.4, 7.3 Hz, 1H), 1.99 (dd, *J* = 15.9, 4.4 Hz, 1H), 1.82–1.69 (m, 2H), 1.45–1.41 (m, 1H), 0.96 (s, 3H); **minor epimer:** 5.83 (dddd, *J* = 14.9, 10.3, 7.6, 7.6 Hz, 1H), 5.12–5.06 (m, 2H), 3.68 (dd, *J* = 4.1, 2.4 Hz, 1H) 2.80 (dd, *J* = 15.4, 2.4 Hz, 1H), 2.74 (dd, *J* = 15.4, 8.1 Hz 1H), 2.46–2.38 (m, 2H), 2.18 (dd, *J* = 13.9, 7.3 Hz, 1H), 2.09 (dd, *J* = 12.9, 7.8 Hz, 1H), 1.82–1.65 (m, 3H) 1.50–1.47 (m, 1H), 1.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ **major epimer**: 213.2, 135.0, 118.1, 72.9, 46.7, 44.9, 44.2, 41.0, 36.3, 21.9, 18.9; **minor epimer**: 212.6, 134.2, 118.3, 73.3, 47.2, 42.8, 41.0, 35.9, 22.6, 18.7; IR (Neat Film NaCl) 3436, 3074, 2932, 1692, 1638, 1443, 1403, 1380, 1352, 1318, 1246, 1168, 1106, 1069, 999, 913, 840 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{11}H_{18}O_2$ $[M]^{+\bullet}$: 182.1313; found 182.1307; $[\alpha]_D^{22.8}$ –57.10 (*c* 2.56, $CHCl_3$, 88.0% ee).

General Method B: DIBAL Reduction / Oxalic Acid Hydrolysis



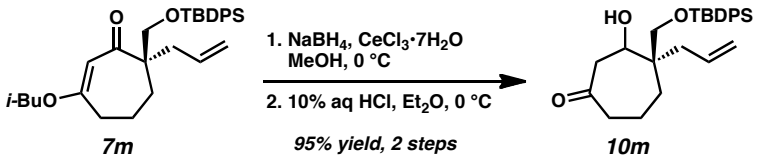
7i ***10i***

***β*-Hydroxyketone 10i.** A 25 mL pear shaped flask was charged with vinylogous ester **7i** (29.4 mg, 0.094 mmol, 1.00 equiv) and toluene (3.0 mL). The solution was cooled to –78 °C using an acetone/CO_2(s) bath. A 1.0 M solution of DIBAL in toluene (112.6 μL, 0.113 mmol, 1.00 equiv) was added dropwise and the solution was stirred for 10 min. MeOH (180 μL), $Na_2SO_4 \cdot 10H_2O$ (1.08 g), and Celite (360 mg) were added. The reaction was stirred vigorously and allowed to warm slowly to ambient temperature. The mixture was filtered through a Celite plug (3 x 3 cm, EtOAc), and concentrated in vacuo. R_f = 0.28, broad (1:2 Hexanes:EtOAc).

The crude hydroxy isobutyl enol ether was added to a 25 mL round-bottom flask and dissolved in MeOH (4.0 mL). Oxalic acid dihydrate (354.9 mg, 2.82 mmol, 30.0 equiv) was added in one portion. After 1 h of stirring, the reaction was neutralized to pH 7 with 1 M aqueous pH 7 NaH_2PO_4/Na_2HPO_4 buffer (6 mL). The biphasic mixture was stirred vigorously for 10 min and the phases were separated. The aqueous layer was extracted with Et_2O (4 x 15 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified using flash column chromatography (SiO_2, 1.5 x 25 cm, 4:1→2:1→1:2 Hexanes:Acetone) to afford *β*-hydroxyketone **10i** as a mixture of diastereomers (21.6 mg, 0.083 mmol, 89% yield over 2 steps, 2.8:1 dr) as a clear, colorless residue which solidified upon standing. R_f = 0.10 (2:1 Hexanes:Acetone); ^{1}H NMR (300 MHz, $CDCl_3$) mixture of two diastereomers, see **Figure SI-43** in the Supporting Information of ref. 10; IR (Neat Film NaCl) 3391, 3201, 3073, 2929, 2865, 1699, 1636, 1603, 1557, 1497, 1456, 1418,

1352, 1332, 1297, 1258, 1222, 1187, 1161, 1113, 1069, 1005, 995, 972, 915, 886, 851, 802, 735 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_{22}O_2N$ $[M+H]^+$: 260.1650; found 260.1649.

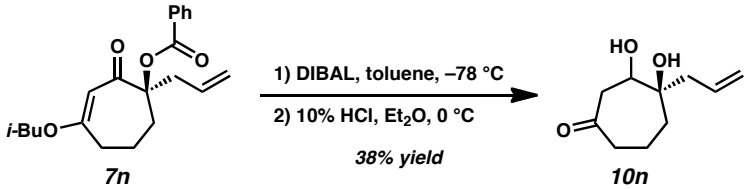
General Method C: Luche Reduction / 10% Aq HCl Hydrolysis



***β*-Hydroxyketone 10m.** A 100 mL round-bottom flask with magnetic stir bar was charged with vinylogous ester **7m** (65.6 mg, 0.134 mmol, 1.00 equiv) and anhydrous MeOH (8.3 mL). The solution was cooled to 0 °C in an ice/water bath. $CeCl_3 \cdot 7H_2O$ (78.2 mg, 0.21 mmol, 1.56 equiv) was added in one portion and the mixture was stirred for 5 min. Addition of $NaBH_4$ (23.8 mg, 0.63 mmol, 4.70 equiv) led to the evolution of gas and a turbid solution that became clear after several minutes. The reaction was stirred at 0 °C. After 15 min, the reaction was diluted with CH_2Cl_2 (20 mL) until turbid, filtered through a Celite plug (3 x 3 cm, CH_2Cl_2), and concentrated in vacuo. The residue was taken up in CH_2Cl_2, filtered through a Celite plug (3 x 5 cm, CH_2Cl_2), and concentrated in vacuo a second time. R_f = 0.33 (10:1 Hexanes:EtOAc).

The crude hydroxy isobutyl enol ether was added to a 25 mL round-bottom flask with a magnetic stir bar and dissolved in Et_2O (3.8 mL). The vigorously stirred solution was cooled to 0 °C and aqueous HCl (384 μL, 10% w/w) was added dropwise via syringe. After 30 min, the reaction was allowed to warm to ambient temperature and extracted with Et_2O (3 x 5 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified using flash column chromatography (SiO_2, 1.5 x 25 cm, 6:1→4:1 Hexanes:EtOAc) to afford *β*-hydroxyketone **10m** as a mixture of diastereomers (55.6 mg, 0.13 mmol, 95% yield over 2 steps, 3.5:1 dr) as a colorless oil; R_f = 0.22, 0.28 (two diastereomers) (4:1 Hexanes:EtOAc); ^1H NMR (300 MHz, $CDCl_3$) mixture of two diastereomers, see **Figure SI-45** in the Supporting Information of ref. 10; IR (Neat Film NaCl) 3468, 3072, 3050, 2999, 3013, 2931, 2895, 2858, 2248, 1960, 1891, 1823, 1772, 1698, 1638, 1590, 1472, 1462, 1446, 1428, 1391, 1361, 1337, 1260, 1222, 1186, 1172, 1158, 1113, 1088, 1030, 1006, 999, 976, 914, 841, 823, 810, 740 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{27}H_{37}O_3Si$ $[M+H]^+$: 437.2512; found 437.2517.

General Method D: DIBAL Reduction / 10% Aq HCl Hydrolysis

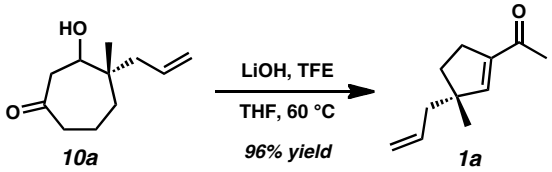


***β*-Hydroxyketone 10n.** A 50 mL pear shaped flask was charged with vinylogous ester **7n** (100 mg, 0.292 mmol, 1.00 equiv) and toluene (9.5 mL). The solution was cooled to –78 °C using an acetone/CO_2(s) bath. A 1.0 M solution of DIBAL in toluene (963 μL, 0.963 mmol, 1.00 equiv)

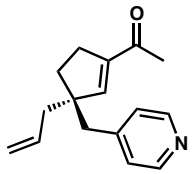
was added dropwise and the mixture was stirred for 15 min. MeOH (1.0 mL), $Na_2SO_4 \cdot 10\ H_2O$ (6.0 g), and Celite (1.2 g) were added and the mixture was stirred vigorously and allowed to warm slowly to ambient temperature. The mixture was filtered through a Celite plug (3 x 3 cm, EtOAc), and concentrated in vacuo. $R_f = 0.30$ (2:1 Hexanes:EtOAc).

The crude hydroxy isobutyl enol ether was added to a 50 mL pear shaped flask, dissolved in Et_2O (10 mL), and cooled to 0 °C in an ice/water bath. Aqueous HCl (0.835 mL, 10% w/w) was added dropwise and the biphasic mixture was stirred vigorously at 0 °C. After 40 min or stirring, additional aqueous HCl (0.835 mL, 10% w/w) was added. After 1.5 h, the layers were separated and the aqueous layer was extracted with Et_2O (5 x 15 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified using flash column chromatography (SiO_2, 1.5 x 25 cm, 10:1→6:1→4:1→2:1→1:1→1:2 Hexanes:EtOAc) to afford β-hydroxyketone **10n** as a mixture of diastereomers (20.3 mg, 0.110 mmol, 38% yield over 2 steps) as a clear, colorless oil; R_f = 0.19 (1:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) mixture of two diastereomers, see **Figure SI-10**; IR (Neat Film NaCl) 3369, 3077, 3011, 2947, 2924, 1688, 1641, 1469, 1439, 1343, 1268, 1216, 1193, 1128, 1108, 1079, 1052, 1032, 1019, 999, 966, 909, 889, 808, 731 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{10}H_{15}O_2$ $[M–OH]^+$: 167.1067; found 167.1066.

General Method E: β-Hydroxyketone Ring Contraction

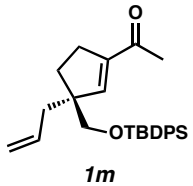


Acylcyclopentene 1a. Alcohol **10a** (6.09 g, 33.4 mmol, 1.00 equiv) was dissolved in THF (334 mL) in a 500 mL round-bottom flask. The solution was treated with 2,2,2-trifluoroethanol (3.67 mL, 50.1 mmol, 1.50 equiv) and anhydrous LiOH (1.20 g, 50.1 mmol, 1.50 equiv). The flask was fitted with a condenser, purged with N_2, and heated to 60 °C using an oil bath. After 18 h of stirring, the suspension was allowed to cool to ambient temperature, diluted with Et_2O (150 mL), dried over Na_2SO_4 (30 min of stirring), filtered, and concentrated carefully under reduced pressure, allowing for a film of ice to form on the outside of the flask. The crude product was purified using flash column chromatography (SiO_2, 5 x 15 cm, 15:1 Hexanes:Et_2O) to afford acylcyclopentene **1a** (5.29 g, 32.2 mmol, 96% yield) as a colorless fragrant oil; R_f = 0.67 (8:2 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.45 (app t, J = 1.7 Hz, 1H), 5.76 (dddd, J = 16.4, 10.7, 7.3, 7.3 Hz, 1H), 5.07–5.03 (m, 2H), 2.59–2.48 (m, 2H), 2.30 (s, 3H), 2.21–2.14 (m, 2H), 1.85 (ddd, J = 12.9, 8.3, 6.3 Hz, 1H), 1.64 (ddd, J = 12.9, 8.5, 6.1 Hz, 1H), 1.11 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 151.9, 143.8, 134.9, 117.8, 50.0, 45.3, 36.0, 29.7, 26.8, 25.6; IR (Neat Film NaCl) 3077, 2956, 2863, 1668, 1635, 1616, 1454, 1435, 1372, 1366, 1309, 1265, 1213, 1177, 993, 914, 862 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{11}H_{17}O$ $[M+H]^{+\bullet}$: 165.1279; found 165.1281; $[\alpha]_D^{21.4}$ +17.30 (*c* 0.955, $CHCl_3$, 88.0% ee); GC conditions: 80 °C isothermal, GTA column, t_R (min): major = 54.7, minor = 60.2.



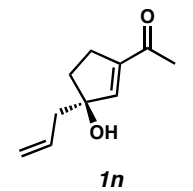
1i

Acylcyclopentene 1i ***(Table 4, entry 9).*** Prepared using General Method E. 15.7 mg, 0.065 mmol, 90% yield. Flash column chromatography (SiO_2, 1.5 x 16 cm, 2:1→1:1 Hexanes:Acetone); R_f = 0.47 (2:1 Hexanes:Acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.49 (br d, *J* = 3.8 Hz, 2H), 7.04 (d, *J* = 5.7 Hz, 2H), 6.40 (dd, *J* = 1.7, 1.7 Hz, 1H), 5.75 (dddd, *J* = 17.3, 10.3, 7.3, 7.3 Hz, 1H), 5.16–5.04 (m, 2H), 2.77 (d, *J* = 13.0 Hz, 1H), 2.71 (d, *J* = 13.0 Hz, 1H), 2.52–2.39 (m, 1H), 2.33–2.35 (m, 1H), 2.28 (s, 3H), 2.24–2.20 (m, 2H), 1.85–1.80 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) 196.8, 149.6, 148.6, 147.3, 145.4, 134.0, 125.7, 118.8, 54.2, 44.4, 43.3, 33.3, 30.0, 27.0; IR (Neat Film NaCl) 3401, 3071, 3025, 2922, 2856, 1668, 1640, 1618, 1600, 1557, 1495, 1441, 1415, 1373, 1318, 1277, 1265, 1220, 1194, 1071, 994, 917, 874, 844, 810, 763 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{16}H_{19}ON$ $[M]^{+\bullet}$: 176.1467; found 176.1458; $[\alpha]_D^{25.0}$ –8.58 (*c* 0.77, $CHCl_3$, 84.6% ee).



1m

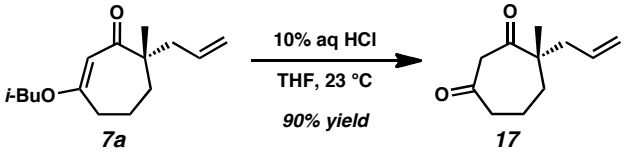
Acylcyclopentene 1m ***(Table 4, entry 11).*** Prepared using General Method E. 32.6 mg, 0.078 mmol, 96% yield. Flash column chromatography (SiO_2, 1 x 20 cm, 15:1 Hexanes:Et_2O); R_f = 0.60 (4:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67–7.60 (m, 4H), 7.47–7.34 (m, 6H), 6.50 (dd, *J* = 1.8, 1.8 Hz, 1H), 5.71 (dddd, *J* = 17.0, 10.1, 7.8, 6.9 Hz, 1H), 5.12–5.08 (m, 1H), 5.06–5.02 (m, 1H), 3.57 (d, *J* = 9.8 Hz, 1H), 3.53 (d, *J* = 9.8 Hz, 1H), 2.54–2.48 (m, 2H), 2.38 (ddd, *J* = 13.8, 6.9, 1.1 Hz, 1H), 2.31–2.25 (m, 1H), 2.29 (s, 3H), 1.81–1.72 (m, 2H), 1.07 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.2, 148.5, 145.7, 135.8, 135.7, 134.5, 133.6, 133.6, 129.9, 129.9, 127.8, 118.0, 69.1, 56.5, 40.4, 30.7, 30.0, 27.0, 26.8, 19.5; IR (Neat Film NaCl) 3072, 3050, 2999, 2956, 2931, 2896, 2857, 1671, 1639, 1618, 1472, 1463, 1427, 1367, 1320, 1266, 1232, 1188, 1112, 998, 936, 915, 864, 824, 740 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{27}H_{34}O_2Si$ $[M]^{+\bullet}$: 433.1712; found 433.1694; $[\alpha]_D^{25.0}$ –17.58 (*c* 0.94, $CHCl_3$, 51.4% ee).



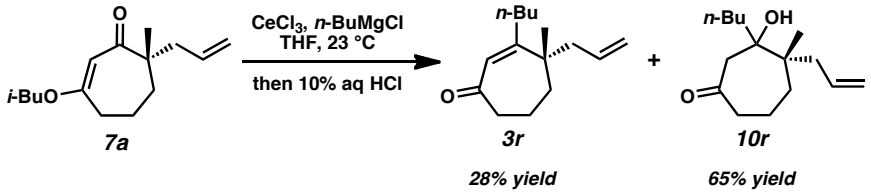
1n

Acylcyclopentene 1n ***(Table 4, entry 15).*** Prepared using General Method E. 12.2 mg, 0.073 mmol, 67% yield. Flash column chromatography (SiO_2, 1.5 x 25 cm, 10:1→4:1→2:1→1:1

Hexanes:EtOAc); R_f = 0.44 (1:1 Hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.48 (app t, *J* = 1.9 Hz, 1H), 5.91–5.77 (dddd, *J* = 16.5, 10.7, 7.4, 7.4 Hz, 1H), 5.23–5.15 (m, 2H), 2.67 (dddd, *J* = 17.0, 8.9, 4.1, 1.7 Hz, 1H), 2.50–2.40 (m, 3H), 2.33 (s, 3H), 2.14 (ddd, *J* = 13.7, 8.5, 4.1 Hz, 1H), 2.03 (br s, 1H), 1.91 (ddd, *J* = 13.7, 9.0, 5.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) 197.5, 145.9, 145.5, 132.9, 119.8, 85.2, 44.9, 37.4, 29.1, 27.0; IR (Neat Film NaCl) 3400, 3077, 3004, 2961, 2929, 2856, 1841, 1668, 1622, 1428, 1372, 1295, 1267, 1228, 1205, 1173, 1070, 1057, 1016, 998, 966, 935, 917, 862, 831, 776 cm^{-1}; HRMS (MM: ESI-APCI+) *m/z* calc'd for $C_{10}H_{13}O$ $[M–OH]^+$: 149.0961; found 149.0967; $[\alpha]_D^{25.0}$ –22.45 (*c* 1.22, $CHCl_3$, 57.1% ee).

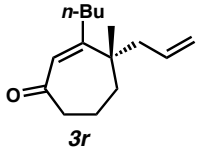


Cyclic Dione 17. A 20 mL scintillation vial equipped with a stir bar was charged with vinylogous ester **7a** (144.6 mg, 0.61 mmol, 1.00 equiv), THF (1 mL), and aqueous HCl (1 mL, 10% w/w, 2.87 mmol, 4.69 equiv). After 4.5 h of vigorous stirring, the solution was diluted with H_2O (5 mL) and transferred to a separatory funnel where the aqueous phase was extracted four times with Et_2O. The combined organics (70 mL) were dried over $MgSO_4$, filtered, and concentrated. The crude oil was purified by flash chromatography (SiO_2, 27.5 x 2 cm, 100% Hexanes→10% EtOAc in Hexanes) to afford cyclic dione **17** (99.4 mg, 0.55 mmol, 90% yield) as a pale yellow oil; R_f = 0.48 (30% EtOAc in Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.69 (d, J = 14.0 Hz, 1H), 5.12–5.04 (m, 2H), 3.72 (d, J = 14.0 Hz, 1H), 3.53 (d, J = 14.0 Hz, 1H), 2.48 (t, J = 6.6 Hz, 2H), 2.40 (dddd, J = 13.9, 7.1, 1.2, 1.2 Hz, 1H), 2.22 (dddd, J = 13.9, 7.7, 1.1, 1.1 Hz, 1H), 2.02–1.75 (m, 4H), 1.15 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.4, 203.7, 133.1, 119.1, 57.6, 50.9, 43.5, 42.9, 36.7, 21.9, 19.8; IR (Neat Film NaCl) 3076, 2972, 2935, 2871, 1719, 1695, 1639, 1463, 1417, 1378, 1337, 1210, 1160, 1112, 1059, 1026, 921 cm^{-1}; HRMS (EI+) calc'd for $C_{11}H_{16}O_2$ $[M]^{+\bullet}$: 180.1150; found 180.1165; $[\alpha]_D^{25.0}$ –19.38 (*c* 1.00, $CHCl_3$, 88.0% ee).



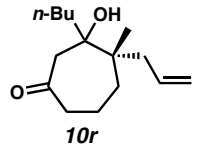
Cycloheptenone 3r and ***β*-Hydroxyketone 10r.** $CeCl_3 \cdot 7H_2O$ (419 mg, 1.13 mmol, 2.55 equiv) in a 100 mL round-bottom flask was immersed in a preheated oil bath at 150 °C and placed under vacuum for 4 h while stirring. The flask was cooled to ambient temperature, backfilled with N_2, and charged with THF (4 mL). After 15 h of stirring, additional THF (4 mL) and *n*-butylmagnesium chloride solution (1.2 mL, 1.86 M in THF, 2.23 mmol, 5.02 equiv) were added to the flask. The resulting slurry was stirred for 4.25 h before vinylogous ester **7a** (105 mg, 0.444 mmol, 1.00 equiv) dissolved in THF (1 mL) was added using positive pressure cannulation followed by two THF rinses (2 x 0.5 mL). After 45 min of stirring, the reaction was quenched by addition of aqueous HCl (10 mL). The phases were separated and the aqueous layer was

extracted with EtOAc (3 x 15 mL). The combined organic phases were washed with brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography using a Teledyne Isco CombiFlash R_f system (SiO_2, 25 g loading cartridge, 12 g column, multi-step gradient, hold 0% [1 min]→ramp to 10% [5 min]→hold 10% [31 min]→100% EtOAc in Hexanes [10 min]) to afford cycloheptenone **3r** (28 mg, 0.13 mmol, 28% yield) and *β*-hydroxyketone **10r** (69 mg, 0.29 mmol, 65% yield) as pale yellow oils.



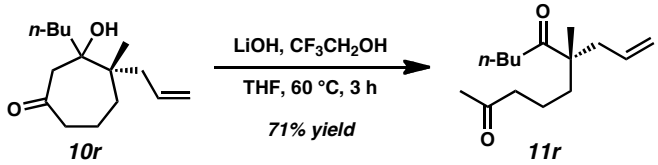
3r

Cycloheptenone 3r. R_f = 0.68 (30% EtOAc in Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 (s, 1H), 5.63 (dddd, *J* = 16.9, 10.3, 7.9, 6.7 Hz, 1H), 5.10–4.98 (m, 2H), 2.61–2.54 (m, 2H), 2.37 (dddd, *J* = 14.1, 6.7, 1.3, 1.3 Hz, 1H), 2.18–2.03 (m, 3H), 1.85–1.72 (m, 3H), 1.66–1.56 (m, 1H), 1.53–1.43 (m, 2H), 1.37 (app. septuplet, *J* = 7.3 Hz, 2H), 1.15 (s, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.4, 163.0, 134.2, 128.7, 118.1, 45.7, 45.3, 44.4, 38.8, 34.0, 32.4, 25.7, 23.0, 17.6, 14.1; IR (Neat Film NaCl) 3076, 2957, 2933, 2872, 1652, 1611, 1467, 1414, 1379, 1342, 1263, 1218, 1178, 1109, 1072, 996, 962, 914, 841, 780, 713 cm^{-1}; HRMS (MM: ESI–APCI+) calc'd for $C_{15}H_{25}O$ $[M+H]^+$: 221.1900; found 221.1905; $[\alpha]_D^{25.0}$ –33.17 (*c* 1.17, $CHCl_3$, 88.0% ee).



10r

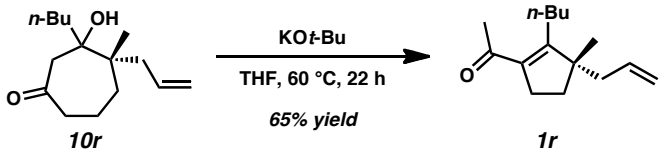
***β*-Hydroxyketone 10r.** R_f = 0.48 (30% EtOAc in Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) mixture of two diastereomers, see **Figure SI-66** in the Supporting Information of ref. 10; IR (Neat Film NaCl) 3502, 3073, 2956, 2871, 1695, 1638, 1468, 1404, 1380, 1341, 1286, 1181, 1125, 1052, 1028, 998, 913, 868, 796, 732 cm^{-1}; HRMS (MM: ESI–APCI+) calc'd for $C_{15}H_{27}O_2$ $[M+H]^+$: 239.2006; found 239.2013.



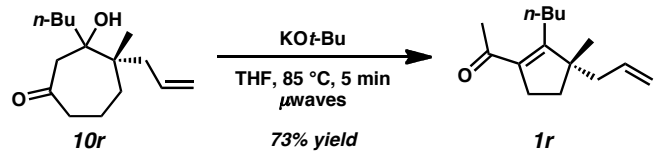
10r *11r*

Linear Dione 11r. A 50 mL round-bottom flask equipped with a magnetic stir and fitted with a water condenser was charged with *β*-hydroxyketone **10r** (56.9 mg, 0.24 mmol, 1.00 equiv), THF (3 mL), TFE (60 μL, 0.83 mmol, 3.50 equiv), and LiOH (17.3 mg, 0.72 mmol, 3.03 equiv). The flask was backfilled with argon and lowered into a preheated oil bath (60 °C). After 3 h, the reaction was removed from the bath, allowed to cool to room temperature, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 3 x 21 cm, 10%→20%→30% EtOAc in Hexanes) to afford linear dione **11r** (40.1 mg, 0.17 mmol, 71% yield) as a pale yellow oil; R_f = 0.57 (30% EtOAc in Hexanes);

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68–5.57 (m, 1H), 5.06–4.98 (m, 2H), 2.43 (t, J = 7.3 Hz, 2H), 2.39 (t, J = 6.4 Hz, 2H), 2.31 (dddd, J = 14.0, 7.3, 1.2, 1.2 Hz, 1H), 2.18 (dddd, J = 14.0, 7.7, 1.2, 1.2 Hz, 1H), 2.11 (s, 3H), 1.63–1.34 (m, 6H), 1.33–1.24 (m, 2H), 1.10 (s, 3H), 0.89 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.9, 208.6, 133.9, 118.1, 50.9, 44.0, 42.6, 37.4, 37.4, 30.1, 25.9, 22.6, 21.1, 18.7, 14.1; IR (Neat Film NaCl) 3076, 2958, 2933, 2873, 1718, 1701, 1639, 1465, 1409, 1378, 1360, 1256, 1230, 1174, 1142, 1120, 1029, 994, 916, 766, 728 cm^{-1}; HRMS (MM: ESI–APCI+) calc'd for $C_{15}H_{27}O_2$ $[M+H]^+$: 239.2006; found 239.2005; $[\alpha]_D^{25.0}$ 5.57 (*c* 1.17, $CHCl_3$, 88.0% ee).



Acylcyclopentene 1r. A 25 mL round-bottom flask equipped with a stir bar and fitted with a water condenser was charged with *β*-hydroxyketone **10r** (91.5 mg, 0.38 mmol, 1.00 equiv), THF (4 mL), and KO*t*-Bu (66.5 mg, 0.59 mmol, 1.55 equiv). The flask was lowered into a preheated oil bath (60 °C) and stirred overnight. Additional THF (4 mL) was added after 19 h of heating. After an additional 3 h, the reaction was removed from the bath, allowed to cool to room temperature, dried over Na_2SO_4, filtered through a silica gel plug, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 3 x 27 cm, 100% pentane→2%→5%→10% Et_2O in pentane) to afford acylcyclopentene **1r** (55.1 mg, 0.25 mmol, 65% yield) as a pale yellow oil; R_f = 0.81 (30% EtOAc in Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77–5.65 (m, 1H), 5.08–5.00 (m, 2H), 2.60–2.49 (m, 2H), 2.45–2.37 (m, 1H), 2.24–2.17 (m, 4H), 2.15–2.10 (m, 2H), 1.85 (ddd, *J* = 12.8, 7.7, 6.2 Hz, 1H), 1.60–1.51 (m, 1H), 1.47–1.34 (m, 4H), 1.06 (s, 3H), 0.93 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.8, 164.2, 135.0, 134.7, 117.6, 52.6, 43.8, 35.0, 32.1, 31.5, 30.4, 27.6, 24.7, 23.8, 14.0; IR (Neat film NaCl) 3075, 3002, 2957, 2930, 2870, 2859, 1677, 1653, 1639, 1602, 1456, 1432, 1373, 1355, 1311, 1275, 1258, 1188, 1141, 1089, 995, 959, 913, 848, 801, 726 cm^{-1}; HRMS (MM: ESI–APCI+) calc'd for $C_{15}H_{25}O$ $[M+H]^+$: 221.1900; found 221.1900; $[\alpha]_D^{25.0}$ –1.44 (*c* 1.35, $CHCl_3$, 88.0% ee).

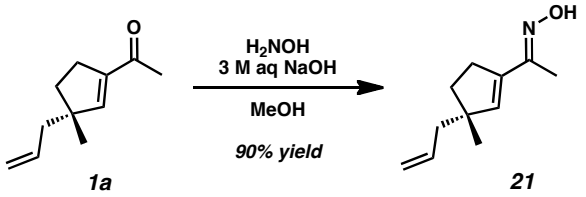


Acylcyclopentene 1r. KO*t*-Bu (32 mg, 0.283 mmol, 1.62 equiv), THF (1.75 mL), and *β*-hydroxyketone **10r** (175 *μ*L, 1.0 M in benzene, 0.175 mmol, 1.00 equiv) were added to a 0.5–2.0 mL microwave vial with a magnetic spin vane. The pale yellow solution was subjected to microwave irradiation in a Biotage Initiator microwave reactor (temperature: 85 °C, sensitivity: normal). After 5 min of irradiation, the crimp cap was removed and Na_2SO_4 was added to the vial. The contents were filtered through a silica gel plug with Et_2O, concentrated under reduced

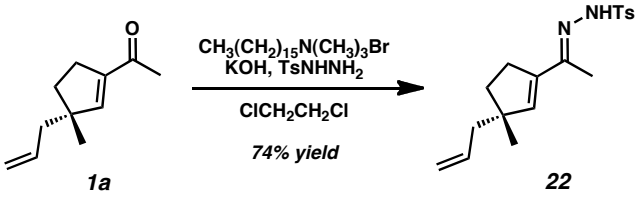
pressure, and purified by flash column chromatography (5% Et_2O in Pentane) to yield acylcyclopentene **1r** (31 mg, 0.14 mmol, 73% yield) as a pale yellow oil.

Procedures for the Synthesis of Acylcyclopentene Derivatives 21–24, 28, 42

Acylcyclopentene derivatives **18–20**, **25–27**, **29–32**, **35–39**, **41** were prepared according to previously reported procedures.[10]

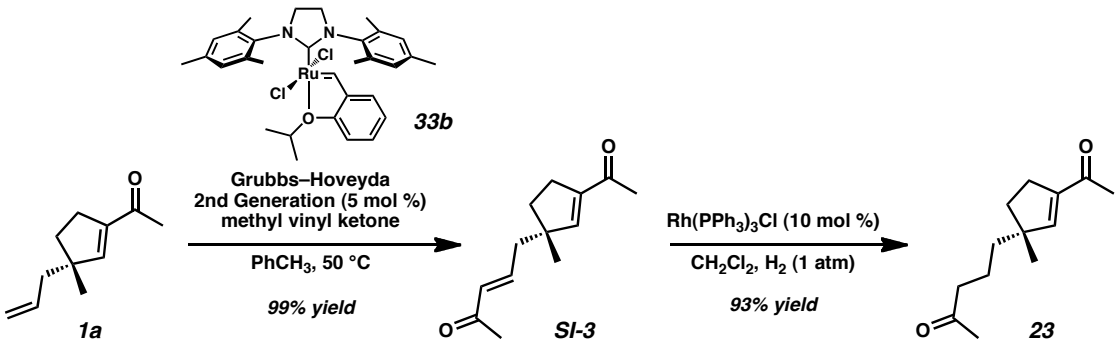


Oxime 21. A 1 dram vial with magnetic stir bar was charged with acylcyclopentene **1a** (40.0 mg, 0.24 mmol, 1.00 equiv), MeOH (0.24 mL), 50% wt aqueous hydroxylamine (47 μL, 0.76 mmol, 3.13 equiv), and 3 M aqueous NaOH (125 μL, 0.376 mmol, 0.51 equiv). After 9 d, the reaction was diluted with Et_2O (10 mL) and H_2O (2 mL) and stirred vigorously for several minutes. The layers were separated and the aqueous layer was extracted with Et_2O (5 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was taken up in CH_2Cl_2, filtered through a cotton plug, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 1.5 x 20 cm, 20:1→15:1 Hexanes:EtOAc) to afford oxime **21** (39.3 mg, 0.21 mmol, 90% yield) as a clear oil; R_f = 0.52 (4:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.73 (br s, 1H), 5.90 (br t, J = 1.5 Hz, 1H), 5.85–5.66 (m, 1H), 5.02 (m, 2H), 2.70–2.45 (m, 2H), 2.14 (m, 2H), 2.05 (s, 3H), 1.85 (ddd, J = 12.9, 8.1, 6.6 Hz, 1H), 1.65 (ddd, J = 12.8, 8.3, 6.3 Hz, 1H), 1.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 141.8, 139.1, 135.6, 117.2, 48.9, 45.9, 36.3, 30.6, 26.2, 11.3; IR (Neat Film NaCl) 3272, 3233, 3075, 3003, 2952, 2925, 2864, 1639, 1455, 1437, 1414, 1379, 1322, 1280, 1103, 1010, 995, 913, 850, 828, 756, 715 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_8H_{12}NO$ [M–C_3H_5]$^+$: 138.0919; found 138.0960; $[\alpha]_D^{25.0}$ +21.34 (*c* 1.57, $CHCl_3$, 88.0% ee).



Tosylhydrazone 22. A 25 mL flask with magnetic stir bar was charged with acylcyclopentene **1a** (40.0 mg, 0.24 mmol, 1.00 equiv), 1,2-dichloroethane (2.7 mL), cetyltrimethylammonium bromide (26.6 mg, 0.073 mmol, 0.30 equiv), KOH (136.7 mg, 2.44 mmol, 10.0 equiv), and $TsHNNH_2$ (271.9 mg, 1.46 mmol, 6.00 equiv), forming a thick white suspension. After 43 h, the reaction was quenched by the addition of sat. aqueous NH_4Cl (5 mL). The mixture was extracted with CH_2Cl_2 (5 x 10 mL) and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography

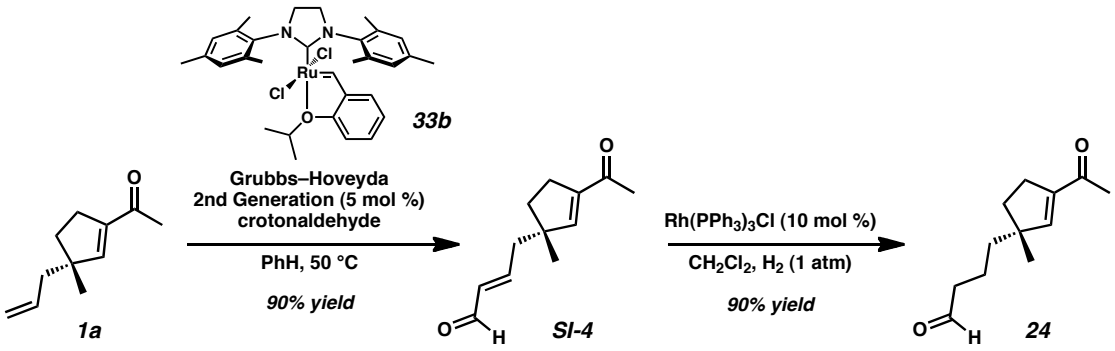
using a Teledyne Isco CombiFlash R_f system (SiO_2, 3 x 25 cm, 4:1→3:1 Hexanes:EtOAc) to afford tosylhydrazone **22** (196.7 mg, 0.94 mmol, 74% yield) as a clear oil; R_f = 0.41 (2:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.3 Hz, 2H), 7.54 (br s, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.85 (app t, *J* = 1.6 Hz, 1H), 5.81–5.62 (m, 1H), 5.06–4.92 (m, 2H), 2.58–2.48 (m, 2H), 2.43 (s, 3H), 2.19–2.00 (m, 2H), 1.89 (s, 3H), 1.85–1.71 (m, 1H), 1.71–1.50 (m, 1H), 1.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.5, 144.1, 142.4, 141.6, 135.5, 135.4, 129.5, 128.3, 117.2, 49.3, 45.8, 36.2, 30.7, 26.1, 21.7, 12.9; IR (Neat Film NaCl) 3217, 3072, 2953, 2924, 2864, 1706, 1639, 1618, 1598, 1495, 1454, 1401, 1337, 1307, 1292, 1212, 1185, 1168, 1094, 1059, 1029, 996, 914, 870, 850, 830, 813, 706 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{15}H_{19}O_2N_2S$ $[M–C_3H_5]^+$: 291.1167; found 291.1181; $[\alpha]_D^{25.0}$ +34.25 (*c* 1.05, $CHCl_3$, 88.0% ee).



Bis-enone SI-3. To an oven-dried reaction tube with magnetic stir bar was added acylcyclopentene **1a** (50 mg, 0.304 mmol, 1.00 equiv). The headspace was purged with N_2 and dry degassed toluene (2.0 mL, sparged with N_2 for 1 h immediately before use) was added, followed by methyl vinyl ketone (124 μL, 1.53 mmol, 5.03 equiv). Grubbs–Hoveyda 2nd Generation catalyst (9.5 mg, 15.2 μmol, 5 mol %) was quickly added to the reaction, giving the solution an olive green color. A reflux condenser was attached and the reaction was inserted into a 50 °C heating block. The solution quickly developed a dark brown color. After 2 h, the reaction was cooled to ambient temperature. The solution was filtered through a short silica gel plug (2 x 4 cm, Et_2O). The filtrate was concentrated under reduced pressure and the brown residue was purified by flash column chromatography (SiO_2, 2 x 25 cm, 10:1→4:1→2:1→1:1 Hexanes:EtOAc) to afford bis-enone **SI-3** (62.3 mg, 0.30 mmol, 99% yield) as a brown liquid; R_f = 0.31 (2:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.71 (ddd, *J* = 15.5, 7.6, 7.6 Hz, 1H), 6.42 (s, 1H), 6.10 (d, *J* = 15.8 Hz, 1H), 2.68–2.40 (m, 2H), 2.33 (dd, *J* = 7.6, 0.9 Hz, 2H), 2.28 (s, 3H), 2.22 (s, 3H), 1.84 (ddd, *J* = 14.7, 8.2, 6.6 Hz, 1H), 1.70 (ddd, *J* = 13.1, 8.4, 6.1 Hz, 1H), 1.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.1, 197.1, 150.2, 144.3, 143.8, 133.8, 50.1, 43.7, 36.2, 29.8, 27.3, 26.8, 25.7; IR (Neat Film NaCl) 3584, 3318, 2956, 2866, 1697, 1669, 1626, 1454, 1429, 1365, 1308, 1254, 1182, 1098, 1021, 982, 937, 867 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{13}H_{18}O_2$ $[M]^{+\bullet}$: 206.1307; found 206.1303; $[\alpha]_D^{25.0}$ +47.61 (c 1.02, $CHCl_3$, 88.0% ee).

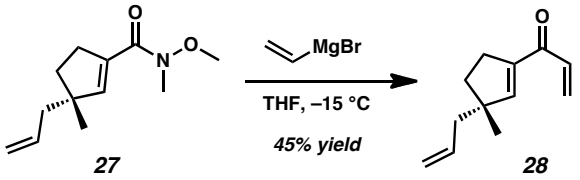
Mono-enone 23. An oven-dried 2-neck flask fitted with a magnetic stir bar, rubber septum, and glass T-joint with 14/20 adapter was charged with bis-enone **SI-3** (50.0 mg, 0.24 mmol, 1.00 equiv) and evacuated/backfilled with N_2 in a glove box antechamber (3 cycles, 5 min evacuation per cycle) before being transferred into the glove box. CH_2Cl_2 (2.5 mL) and $Rh(PPh_3)_3Cl$ (22.4

mg, 0.024 mmol, 10 mol %) were added to the flask, giving a red solution. The flask was sealed with a septum on one neck and T-joint (set to the closed position) on the other neck and carefully brought out of the glove box. A H_2 balloon was attached to the T-joint and the flask was gently evacuated/backfilled with H_2 (3 cycles, 2 min evacuation per cycle). After 10 h of stirring, the brown reaction mixture was filtered through a short silica gel plug (2 x 4 cm, Et_2O) and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 2 x 25 cm, 10:1→4:1→2:1 Hexanes:Et_2O) to afford enone **23** (46.8 mg, 0.23 mmol, 93% yield) as an orange liquid; R_f = 0.40 (2:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.43 (app t, *J* = 1.7 Hz, 1H), 2.65–2.46 (m, 2H), 2.40 (t, *J* = 7.1 Hz, 2H), 2.27 (s, 3H), 2.11 (s, 3H), 1.88–1.72 (m, 1H), 1.71–1.46 (m, 3H), 1.46–1.29 (m, 2H), 1.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.8, 197.5, 152.0, 143.6, 50.0, 44.2, 40.4, 36.1, 30.1, 29.7, 26.8, 25.6, 19.4; IR (Neat Film NaCl) 2998, 2953, 2866, 1716, 1667, 1616, 1456, 1427, 1367, 1308, 1270, 1225, 1190, 1170, 1103, 1058, 1021, 841, 871, 726 cm^{-1}; HRMS (EI+) m/z calc'd for $C_{13}H_{20}O_2$ $[M]^{+\bullet}$: 208.1463; found 208.1460; $[\alpha]_D^{25.0}$ +25.55 (c 1.46, $CHCl_3$, 88.0% ee).



Bis-enone SI-4. To a 2-neck round-bottomed flask with magnetic stir bar and attached reflux condenser was added acylcyclopentene **24** (100 mg, 0.608 mmol, 1.00 equiv). The flask was evacuated/backfilled with N_2 (3 cycles, 30 s evacuation per cycle). Dry degassed benzene (8.0 mL, sparged with N_2 for 1 h immediately before use) was added, followed by crotonaldehyde (251 μL, 3.06 mmol, 5.03 equiv). Grubbs–Hoveyda 2nd Generation catalyst (19.0 mg, 30.4 μmol, 5 mol %) was quickly added to the reaction, giving the solution an olive green color. The flask was immersed in a 50 °C oil bath. The solution quickly developed a dark brown color. After 2 h, the reaction was cooled to ambient temperature. Several drops of ethyl vinyl ether were added and the reaction mixture was stirred for 5 min. The mixture was concentrated under reduced pressure and the brown residue was purified by flash column chromatography (SiO_2, 2 x 25 cm, 10:1→4:1→2:1 Hexanes:EtOAc) to afford bis-enone **SI-4** (105.4 mg, 0.55 mmol, 90% yield) as a brown oil; R_f = 0.38 (2:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 (d, *J* = 7.8 Hz, 1H), 6.76 (app dt, *J* = 15.4, 7.6 Hz, 1H), 6.42 (app t, *J* = 1.8 Hz, 1H), 6.13 (app ddt, *J* = 15.5, 7.8, 1.3 Hz, 1H), 2.68–2.50 (m, 2H), 2.45 (dd, *J* = 7.6, 1.3 Hz, 2H), 2.28 (s, 3H), 1.85 (ddd, *J* = 13.1, 8.4, 6.5 Hz, 1H), 1.72 (ddd, *J* = 13.1, 8.5, 6.0 Hz, 1H), 1.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 197.0, 193.5, 154.0, 149.7, 144.5, 135.6, 50.1, 43.9, 36.1, 29.8, 26.8, 25.8; IR (Neat Film NaCl) 3359, 3317, 3041, 2957, 2928, 2867, 2820, 2743, 2708, 1691, 1668, 1636, 1618, 1456, 1431, 1378, 1369, 1341, 1308, 1269, 1203, 1162, 1149, 1109, 1093, 1036, 1013, 978, 936, 893, 868 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{12}H_{17}O_2$ $[M+H]^+$: 193.1229; found 193.1224; $[\alpha]_D^{25.0}$ +46.07 (c 1.13, $CHCl_3$, 88.0% ee).

Mono-enone 24. An oven-dried 2-neck flask fitted with a magnetic stir bar, rubber septum, and a glass T-joint with 14/20 adapter was charged with and bis-enone **SI-4** (42.8 mg, 0.22 mmol, 1.00 equiv) and evacuated/backfilled with N_2 in a glove box antechamber (3 cycles, 5 min evacuation per cycle) before being transferred into the glove box. CH_2Cl_2 (2.5 mL) and $Rh(PPh_3)_3Cl$ (10.3 mg, 0.011 mmol, 5 mol %) were added to the flask, giving a red solution. The flask was sealed with a septum on one neck and T-joint (set to the closed position) on the other neck and carefully brought out of the glove box. A H_2 balloon was attached to the T-joint and the flask was gently evacuated/backfilled with H_2 (five cycles, 2 min evacuation per cycle). After 20 h of stirring, an additional portion of $Rh(PPh_3)_3Cl$ (10.3 mg, 0.011 mmol, 5 mol %) in CH_2Cl_2 (0.5 mL) was added to the reaction using positive pressure cannulation. After 1.5 h of stirring, the reaction was diluted with Et_2O, filtered through a short silica gel plug (2 x 4 cm, Et_2O), and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 2 x 25 cm, 10:1→4:1 Hexanes:Et_2O) to afford enone **24** (39.2 mg, 0.20 mmol, 90% yield) as an pale colorless oil; R_f = 0.48 (2:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.75 (t, *J* = 1.5 Hz, 1H), 6.44 (app t, *J* = 1.7 Hz, 1H), 2.59–2.48 (m, 2H), 2.43 (td, *J* = 7.1, 1.4 Hz, 2H), 2.28 (s, 3H), 1.88–1.73 (m, 1H), 1.73–1.51 (m, 3H), 1.51–1.33 (m, 2H), 1.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.3, 197.5, 151.7, 143.8, 50.0, 44.5, 40.4, 36.1, 29.8, 26.8, 25.6, 17.8; IR (Neat Film NaCl) 3427, 3314, 3042, 2951, 2865, 2721, 1723, 1665, 1616, 1457, 1411, 1378, 1367, 1340, 1308, 1269, 1193, 1156, 1105, 1060, 1034, 1020, 970, 942, 867, 801 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{12}H_{18}O_2$ $[M]^{+\bullet}$: 194.1307; found 194.1321; $[\alpha]_D^{25.0}$ +32.50 (c 0.69, $CHCl_3$, 88.0% ee).

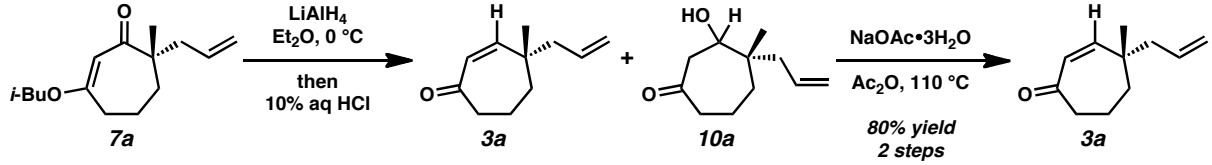


Divinylketone 28. A 25 mL round-bottomed flask with magnetic stir bar was charged with amide **27**[10] (97.0 mg, 0.46 mmol, 1.00 equiv), evacuated/backfilled with N_2 (3 cycles, 5 min evacuation per cycle), dissolved in THF (3.0 mL), and cooled to –15 °C using an ethylene glycol/CO_2(s) bath. The yellow solution became cloudy. Vinylmagnesium bromide solution (1.38 mL, 1.0 M in THF, 1.38 mmol, 3.00 equiv) was added dropwise. The solution was maintained at –15 °C for 20 min before the flask was allowed to warm to ambient temperature. The reaction was quenched by addition into sat. aqueous NH_4Cl (2.0 mL) using positive pressure cannulation. The mixture was extracted with Et_2O (3 x 10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2, 2 x 25 cm, 0%→1%→2%→3% Et_2O in Hexanes) to afford divinylketone **28** (36.2 mg, 0.21 mmol, 45% yield) as a pale yellow liquid; R_f = 0.68 (4:1 Hexanes:EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88 (dd, *J* = 17.1, 10.5 Hz, 1H), 6.53 (app t, *J* = 1.7 Hz, 1H), 6.28 (dd, *J* = 17.1, 1.9 Hz, 1H), 5.85–5.65 (m, 1H), 5.69 (dd, *J* = 10.5, 1.9 Hz, 1H), 5.11–4.99 (m, 2H), 2.76–2.50 (m, 2H), 2.29–2.09 (m, 2H), 1.87 (ddd, *J* = 12.9, 8.2, 6.8 Hz, 1H), 1.67 (ddd, *J* = 12.9, 8.3, 6.3 Hz, 1H), 1.13 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.9, 152.1, 143.7, 134.8, 132.6, 127.7, 117.8, 50.3, 45.3, 35.8, 30.1, 25.5; IR (Neat Film NaCl) 3584, 3400, 3078, 2955, 2927, 2866, 1622, 1606, 1453, 1440, 1408, 1374, 1348, 1308, 1255, 1204, 1169, 1059, 981, 956, 915, 783

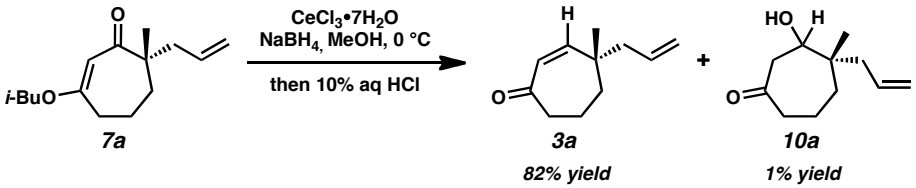
cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_9H_{11}O$ $[M–C_3H_5]^+$: 135.0846; found 135.0810; $[\alpha]_D^{25.0}$ +0.84 (c 0.81, $CHCl_3$, 88.0% ee).

Procedures for Carbonyl Transposition to γ-Quaternary Cycloheptenones 3

Grignard and organolithium reagents were purchased from Sigma-Aldrich or prepared according to previously reported procedures.[5] Cycloheptenones **3a**, **3r–ab** were prepared according to previously reported procedures.[5,10] Representative procedures for General Methods F–H are described below.

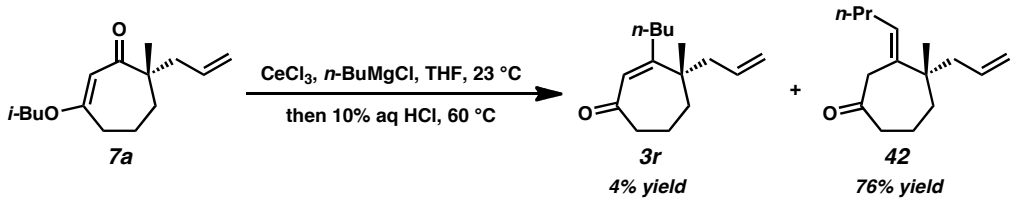


Cycloheptenone 3a. A round-bottom flask charged with vinylogous ester **7a** (367.0 mg, 1.55 mmol, 1.00 equiv) and THF (5 mL, 0.3 M) was cooled in a 0 °C bath (water/ice) and $LiAlH_4$ (34.0 mg, 0.90 mmol, 0.58 equiv) was added. After 25 min of stirring, the reaction was quenched at 0 °C with the addition of aqueous HCl (10 mL, 10% w/w) and transferred to a separatory funnel where the aqueous phase was extracted with EtOAc (3 x 10 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. To the resulting crude oil was added Ac_2O (3.8 mL) and $NaOAc•3H_2O$ (1.28 g, 9.43 mmol, 6.08 equiv) and the mixture was lowered into a preheated oil bath (110 °C). After 15 h of heating, the reaction was allowed to cool to ambient temperature and quenched with K_2CO_3 (5.59 g, 40.5 mmol) and water (10 mL). After an addition 30 min of stirring, the solution was transferred to a separatory funnel where the aqueous phase was extracted with EtOAc (4 x 10 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 2 x 16 cm, 20:1 Hexanes:EtOAc) to afford cycloheptenone **3a** (203.9 mg, 1.24 mmol, 80% yield) as a pale yellow oil. (For characterization data, see p. 18–19).

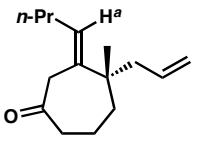


Cycloheptenone 3a and β-Hydroxyketone 10a. A 100 mL round-bottom flask with magnetic stir bar was charged with vinylogous ester **7a** (186.8 mg, 0.79 mmol, 1.00 equiv) and anhydrous MeOH (14 mL). The solution was cooled to 0 °C (water/ice bath). $CeCl_3•7H_2O$ (294.5 mg, 0.79 mmol, 1.56 equiv) was added in one portion and the mixture was stirred for 5 min. Portionwise addition of $NaBH_4$ (89.7 mg, 2.37 mmol, 3.00 equiv) at 0 °C led to the evolution of gas and a turbid solution that became clearer after several minutes. TLC analysis indicated that no starting material remained after 2 min. Consequently, the reaction was quenched by dropwise addition of

aqueous HCl (2 mL, 10% w/w) at 0 °C. After an additional 10 min of stirring, the reaction was diluted with CH_2Cl_2 (60 mL) and H_2O (2 mL). The layers were separated. The aqueous layer was extracted with CH_2Cl_2 (6 x 5 mL). The combined organic layers were washed with sat. aqueous $NaHCO_3$ (2 x 5 mL) and brine (2 x 5 mL), dried over Na_2SO_4, filtered, and evaporated to give a pale yellow oil. The crude mixture was purified using flash chromatography (SiO_2, 2 x 25 cm, 20:1→15:1→3:1 Hexanes:EtOAc) to afford volatile enone **3a** (106.9 mg, 0.645 mmol, 82% yield) as a pale yellow oil and β-hydroxyketone **10a** as a mixture of diastereomers (1.4 mg, 0.0077 mmol, 1% yield, 3.5:1 dr) as a colorless oil. (For characterization data of **3a** and **10a**, see p. 18–19).

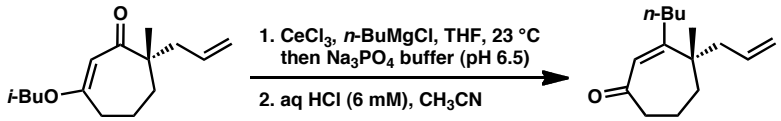


Cycloheptenone 3r and Cycloheptenone Isomer 42. An oven dried 15 mL round-bottom flask equipped with a magnetic stir bar was cycled into a glove box. The flask was loaded with anhydrous cerium chloride (130.4 mg, 0.53 mmol, 2.49 equiv), fitted with a septum, removed from the glove box, and connected to an argon-filled Schlenk manifold. A portion of THF (5.5 mL) was added, rinsing the cerium chloride to the bottom of the flask. As the resulting thick white slurry was stirred, a solution of *n*-butylmagnesium chloride (340 μL, 1.89 M in THF, 0.64 mmol, 3.03 equiv) was added and the mixture turned pale yellow. After 45 min of stirring, neat vinylogous ester **7a** (50.2 mg, 0.21 mmol, 1.00 equiv) was added to the flask. The slurry maintained the yellow color with the addition. TLC analysis indicated that no starting material remained after 5 min. After an additional 10 min of stirring, the reaction was quenched with aqueous HCl (1 mL, 10% w/w) and lowered into a preheated oil bath (60 °C). After 17 h, the yellow suspension was removed from the bath, cooled to ambient temperature, and transferred to a separatory funnel where the aqueous phase was extracted four times with Et_2O. The combined organics (75 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 1 x 27 cm, 100% Hexanes→2%→10% EtOAc in Hexanes) to afford moderately contaminated cycloheptenone **3r** and pure alkene isomer **42** (35.4 mg, 0.16 mmol, 76% yield) as an orange oil. Additional purification by flash chromatography (SiO_2, 1 x 27 cm, 100% Hexanes→2%→5% EtOAc in Hexanes) furnished cycloheptenone **3r** (1.7 mg at 95% purity, 0.0076 mmol, 4% yield) as a yellow oil. (For characterization data of **3r**, see p. 24).



10a

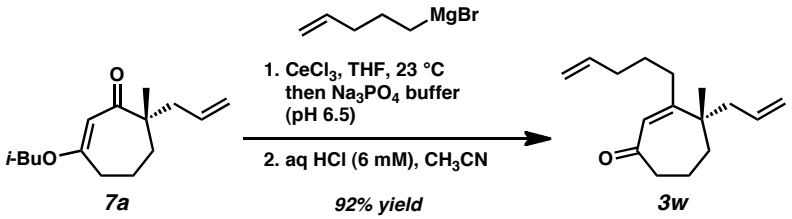
Cycloheptenone Isomer 10a. R_f = 0.76 (30% EtOAc in Hexanes); The relative alkene stereochemistry was assigned based on NOE interactions of H^a proton; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.66 (dddd, J = 16.9, 10.6, 7.9, 6.6 Hz, 1H), 5.43 (t, J = 7.1 Hz, 1H), 5.03–4.97 (m, 2H), 3.20 (d, J = 14.6 Hz, 1H), 3.13 (d, J = 14.6 Hz, 1H), 2.47–2.38 (m, 1H), 2.36–2.26 (m, 2H), 2.15–1.95 (m, 3H), 1.82–1.69 (m, 2H), 1.66–1.58 (m, 1H), 1.58–1.50 (m, 1H), 1.40–1.32 (m, 2H), 1.07 (s, 3H), 0.88 (t, J = 7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 210.0, 136.2, 135.1, 130.0, 117.2, 44.8, 43.3, 43.3, 41.8, 41.1, 30.2, 25.0, 22.9, 19.6, 13.9; IR (Neat Film NaCl) 3074, 3042, 2959, 2929, 2871, 1706, 1638, 1457, 1436, 1378, 1351, 1302, 1262, 1231, 1163, 1098, 1069, 996, 953, 912, 805, 776, 729 cm^{-1}; HRMS (EI+) calc'd for $C_{15}H_{24}O_2$ $[M]^{+\bullet}$: 220.1827; found 220.1780; $[\alpha]_D^{25.0}$ –10.92 (*c* 0.76, $CHCl_3$, 88.0% ee).



7a ***84% yield*** ***3r***

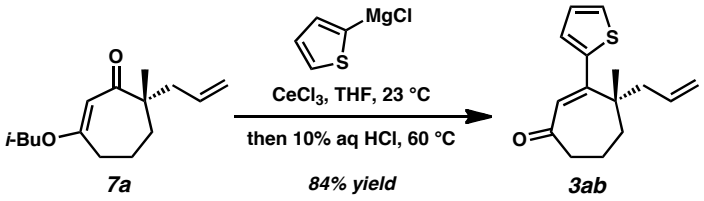
Cycloheptenone 3r. A 50 mL round-bottom flask equipped with a magnetic stir bar was cycled into a glove box. The flask was loaded with anhydrous cerium chloride (260.8 mg, 1.06 mmol, 2.50 equiv), fitted with a septum, removed from the glove box, and connected to an argon-filled Schlenk manifold. A portion of THF (8.5 mL) was added, rinsing the cerium chloride to the bottom of the flask. As the resulting thick white slurry was stirred, a solution of *n*-butylmagnesium bromide (680 μL, 1.87 M in THF, 1.27 mmol, 3.00 equiv) was added and the mixture turned grey. After 30 min of stirring, vinylogous ester **7a** (100.0 mg, 0.42 mmol, 1.00 equiv) was added neat from a Hamilton syringe and the needle was rinsed with a small portion of THF (2 mL; total THF added = 10.5 mL, 0.04 M). The color of the slurry initially transitioned to yellow with the vinylogous ester addition before turning back to grey. TLC analysis indicated that no starting material remained after 15 min. After an additional 10 min of stirring, the reaction was quenched with pH 6.5 Na_3PO_4 buffer (8 mL). A thick grey emulsion formed. The mixture was transferred to a separatory funnel where the aqueous phase was extracted four times with Et_2O. The combined organics (125 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was transferred to a 20 mL scintillation vial and concentrated under reduced pressure. A stir bar, CH_3CN (1.0 mL), and 6 mM aqueous HCl (1.0 mL) were added to the vial. The resulting cloudy solution was stirred vigorously for 5 min before being transferred to a separatory funnel where the aqueous phase was extracted four times with Et_2O. The combined organics (100 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 3 x 30 cm, 100% Hexanes→2%→5% EtOAc in Hexanes) to afford cycloheptenone **3r** (82.4 mg, 0.35 mmol, 84% yield) as a pale yellow oil. (For characterization data of **3r**, see p. 24).

General Method F: Organometallic Addition / Na_3PO_4 Buffer Quench / Dilute HCl Workup



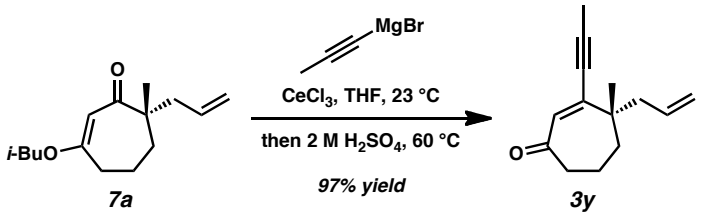
Cycloheptenone 3w. A 100 mL round-bottom flask equipped with a magnetic stir bar was cycled into a glove box. The flask was loaded with anhydrous cerium chloride (616.2 mg, 2.50 mmol, 2.50 equiv), fitted with a septum, removed from the glove box, and connected to an argon-filled Schlenk manifold. A portion of THF (13 mL) was added, rinsing the cerium chloride to the bottom of the flask. As the resulting thick white slurry was stirred, a solution of pent-4-enylmagnesium bromide (8.6 mL, 0.35 M in THF, 3.01 mmol, 3.01 equiv) was added and the mixture turned grey. After 30 min of stirring, vinylogous ester **7a** (236.3 mg, 1.00 mmol, 1.00 equiv) was cannula-transferred to the slurry from a flame-dried 10 mL conical flask using several THF rinses (3 x 4 mL; total THF added = 25 mL, 0.04 M). TLC analysis indicated that no starting material remained after 5 min. After an additional 10 min of stirring, the reaction was quenched with pH 6.5 Na_3PO_4 buffer (20 mL). A thick grey emulsion formed. The mixture was transferred to a separatory funnel where the aqueous phase was extracted four times with Et_2O. The combined organic (150 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was transferred to a 20 mL scintillation vial and concentrated under reduced pressure. A stir bar, CH_3CN (2.0 mL), and aqueous HCl (2.0 mL, 6 mM) were added to the vial. The resulting cloudy solution was stirred vigorously for 30 min before being transferred to a separatory funnel where the aqueous phase was extracted four times with Et_2O. The combined organics (75 mL) were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 3 x 30 cm, 100% Hexanes→1%→2%→5% EtOAc in Hexanes) to afford cycloheptenone **3w** (214.2 mg, 0.92 mmol, 92% yield) as a clear colorless oil; R_f = 0.65 (30% EtOAc in Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.88 (s, 1H), 5.79 (dddd, J = 16.9, 10.2, 6.7, 6.7 Hz, 1H), 5.67–5.57 (m, 1H), 5.07–4.96 (m, 4H), 2.60–2.53 (m, 2H), 2.35 (dddd, J = 14.1, 6.7, 2.5, 1.2 Hz, 1H), 2.20–2.04 (m, 5H), 1.83–1.73 (m, 3H), 1.66–1.53 (m, 3H), 1.14 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.3, 162.6, 138.2, 134.1, 128.8, 118.2, 115.3, 45.7, 45.2, 44.3, 38.7, 33.8, 33.5, 29.3, 25.7, 17.6; IR (Neat Film NaCl) 3076, 2975, 2937, 2870, 1652, 1611, 1456, 1415, 1380, 1343, 1257, 1218, 1179, 1110, 1071, 994, 913 cm^{-1}; HRMS (MM: ESI–APCI+) calc'd for $C_{16}H_{25}O$ $[M+H]^+$: 233.1900; found 233.1900; $[\alpha]_D^{25.0}$ –34.96 (*c* 1.46, $CHCl_3$, 88.0% ee).

General Method G: Organometallic Addition / Aq HCl Quench



Cycloheptenone 3ab. A 100 mL round-bottom flask equipped with a magnetic stir bar was cycled into a glove box. The flask was loaded with anhydrous cerium chloride (616.2 mg, 2.50 mmol, 2.50 equiv), fitted with a septum, removed from the glove box, and connected to an argon-filled Schlenk manifold. A portion of THF (13 mL) was added, rinsing the cerium chloride to the bottom of the flask. As the resulting thick white slurry was stirred, a solution of thiophen-2-ylmagnesium chloride (6.8 mL, 0.44 M in THF, 2.99 mmol, 2.99 equiv) was added and the mixture turned dark grey. After 30 min of stirring, vinylogous ester **7a** (236.4 mg, 1.00 mmol, 1.00 equiv) was cannula-transferred to the slurry from a flame-dried 10 mL conical flask using several THF rinses (3 x 4 mL; total THF added = 25 mL, 0.04 M). TLC analysis indicated that no starting material remained after 25 min. After an additional 5 min of stirring, the reaction was quenched with aqueous HCl (5 mL, 10% w/w) and lowered into a preheated oil bath (60 °C). After 20 h, additional aqueous HCl (5 mL, 10% w/w) was added. After 26 h, the yellow solution was removed from the bath, cooled to ambient temperature, treated with sat. aqueous $NaHCO_3$ solution (25 mL), and transferred to a separatory funnel where the aqueous phase was extracted four times with Et_2O. The combined organics (150 mL) were rinsed once with sat. aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 3 x 30 cm, 100% Hexanes→2%→5% EtOAc in Hexanes) to afford cycloheptenone **3ab** (206.1 mg, 0.84 mmol, 84% yield) as a yellow/orange oil; R_f = 0.70 (30% EtOAc in Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.27 (dd, *J* = 5.0, 1.5 Hz, 1H), 7.00–6.95 (m, 2H), 6.17 (s, 1H), 5.69 (dddd, *J* = 16.7, 10.2, 8.1, 6.4 Hz, 1H), 5.06 (dddd, *J* = 10.2, 2.0, 1.0, 1.0 Hz, 1H), 5.01 (ddd, *J* = 16.9, 3.4, 1.5 Hz, 1H), 2.74–2.59 (m, 2H), 2.50 (dddd, *J* = 14.1, 6.4, 1.4, 1.4 Hz, 1H), 2.12 (dddd, *J* = 14.1, 8.1, 1.1, 1.1 Hz, 1H), 1.96–1.84 (m, 3H), 1.77–1.68 (m, 1H), 1.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.2, 154.6, 143.8, 134.0, 133.7, 127.0, 126.7, 125.5, 118.5, 45.6, 45.1, 44.2, 38.8, 26.4, 17.7; IR (Neat Film NaCl) 3103, 3075, 2964, 2938, 2871, 1671, 1655, 1590, 1519, 1454, 1438, 1415, 1378, 1341, 1251, 1234, 1218, 1178, 1134, 1107, 1077, 1045, 996, 917, 849, 836, 761, 708 cm^{-1}; HRMS (MM: ESI–APCI+) calc'd for $C_{15}H_{19}OS$ $[M+H]^+$: 247.1151; found 247.1152; $[\alpha]_D^{25.0}$ –3.65 (*c* 1.31, $CHCl_3$, 88.0% ee).

General Method H: Organometallic Addition / Aq H_2SO_4 Quench

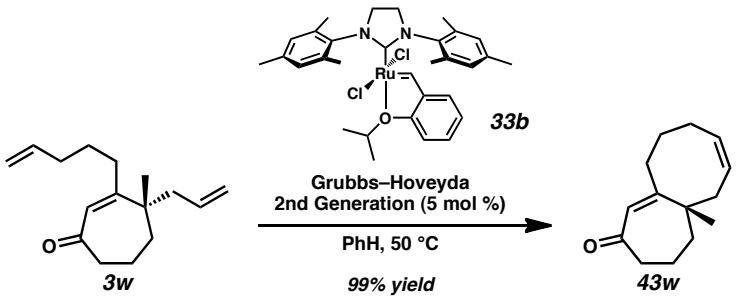


Cycloheptenone 3y. A 100 mL round-bottom flask equipped with a magnetic stir bar was cycled into a glove box. The flask was loaded with anhydrous cerium chloride (616.2 mg, 2.50 mmol, 2.50 equiv), fitted with a septum, removed from the glove box, and connected to an argon-filled Schlenk manifold. A portion of THF (13 mL) was added, rinsing the cerium chloride to the bottom of the flask. As the resulting thick white slurry was stirred, a solution of prop-1-ynylmagnesium bromide (12 mL, 0.25 M in THF, 3.00 mmol, 3.00 equiv) was added and the mixture turned yellow. After 30 min of stirring, vinylogous ester **7a** (236.4 mg, 1.00 mmol, 1.00 equiv) was cannula-transferred to the slurry from a flame-dried 10 mL conical flask using several THF rinses (3 x 4 mL; total THF added = 25 mL, 0.04 M). The slurry maintained the yellow color with the addition. TLC analysis indicated that no starting material remained after 5 min. After an additional 10 min of stirring, the reaction was quenched with 2 M H_2SO_4 (5 mL) and lowered into a preheated oil bath (60 °C). A white precipitate formed within several minutes. After 12 h, the yellow suspension was removed from the bath, cooled to ambient temperature, treated with sat. aqueous $NaHCO_3$ solution (50 mL), and transferred to a separatory funnel where the aqueous phase was extracted four times with Et_2O. The combined organics (175 mL) were rinsed once with sat. aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude oil was purified by flash chromatography (SiO_2, 3 x 30 cm, 100% Hexanes→2%→5% EtOAc in Hexanes) to afford cycloheptenone **3y** (195.4 mg, 0.97 mmol, 97% yield) as a yellow oil; R_f = 0.65 (30% EtoAc in Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.20 (s, 1H), 5.70 (dddd, J = 16.8, 10.5, 8.2, 6.6 Hz, 1H), 5.10–5.01 (m, 2H), 2.65–2.49 (m, 3H), 2.16 (dddd, J = 13.8, 8.2, 1.0, 1.0 Hz, 1H), 2.01 (s, 3H), 1.83–1.75 (m, 3H), 1.66–1.59 (m, 1H), 1.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.5, 145.6, 135.0, 134.3, 118.3, 92.9, 80.7, 46.5, 45.4, 44.6, 37.3, 27.0, 17.6, 4.7; IR (Neat Film NaCl) 3076, 2969, 2937, 2219, 1652, 1580, 1455, 1415, 1377, 1346, 1255, 1225, 1184, 1110, 998, 916, 893, 866, 813, 784, 716 cm^{-1}; HRMS (MM: ESI–APCI+) calc'd for $C_{14}H_{19}O$ $[M+H]^+$: 203.1430; found 203.1428; $[\alpha]_D^{25.0}$ –49.25 (*c* 1.21, $CHCl_3$, 88.0% ee).

Procedures for Synthesis of Cycloheptenone Derivatives 43–47

Cycloheptenone derivatives **43–47** were prepared according to previously reported procedures.[5] A representative procedure for General Method I is described below.

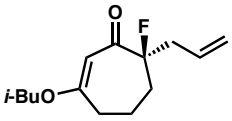
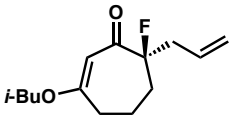
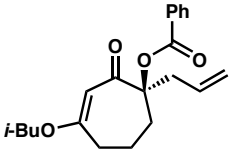
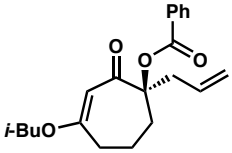
General Method I: Ring Closing Metathesis



Enone 43w. A 100 mL round-bottom flask equipped with a magnetic stir bar, fitted with a water condenser, and connected to a Schlenk manifold (through the condenser) was flame-dried three times, backfilling with argon after each drying cycle. Once cool, the flask was loaded with neat cycloheptenone **3w** (50.0 mg, 0.22 mmol, 1.00 equiv) and backfilled with argon twice. Benzene (1 h argon sparge before use, 43 mL, 0.005 M) was added to the flask, followed by Grubbs–Hoveyda 2nd Generation catalyst (6.7 mg, 0.011 mmol, 5 mol %). The solution color turned pale green with addition of catalyst. The flask was lowered into a preheated oil bath (50 °C). The reaction was removed from the oil bath after 30 min, cooled to room temperature (23 °C), and quenched with ethyl vinyl ether (1 mL). The reaction was filtered through a short silica gel plug rinsing with Et_2O and concentrated under reduced pressure. The crude oil was purified twice by flash chromatography (SiO_2, both columns 2 x 28 cm, 100% Hexanes→2%→5% EtOAc in Hexanes) to afford cycloheptenone **43w** (43.5 mg, 0.21 mmol, 99% yield) as a yellow oil; R_f = 0.56 (30% EtOAc in Hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77–5.70 (m, 1H), 5.65 (tdt, J = 10.4, 6.4, 1.3 Hz, 1H), 2.68–2.55 (m, 2H), 2.54–2.44 (m, 1H), 2.30–2.24 (m, 2H), 2.24–2.15 (m, 1H), 2.13–2.04 (m, 1H), 1.94–1.69 (m, 7H), 1.52–1.41 (m, 1H), 1.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.2, 165.6, 132.2, 131.9, 128.5, 49.0, 44.2, 39.8, 39.5, 35.5, 31.1, 27.0, 26.5, 17.8; IR (Neat Film NaCl) 3018, 2928, 2859, 1645, 1608, 1468, 1448, 1411, 1380, 1343, 1327, 1279, 1253, 1214, 1178, 1131, 1102, 1088, 1051, 1015, 987, 965, 937, 920, 899, 880, 845, 796, 777, 747 cm^{-1}; HRMS (MM: ESI–APCI+) calc'd for $C_{14}H_{21}O$ $[M+H]^+$: 205.1587; found 205.1587; $[\alpha]_D^{25.0}$ –141.99 (*c* 1.01, $CHCl_3$, 88% ee).

Methods for Determination of Enantiomeric Excess

Table SI-3. Methods for the Determination of Enantiomeric Excess (Chiral HPLC and SFC).

entry	product	compound assayed	assay conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% ee
1	 ***6l***	 ***7l***	HPLC Chiralcel OD-H 1% IPA in hexane isocratic, 1.0 mL/min	8.80	8.05	91
2	 ***6n***	 ***7n***	HPLC Chiralcel OD-H 1% IPA in hexane isocratic, 1.0 mL/min	18.28	22.01	57

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Ring Contraction Strategy for the Practical, Scalable, Catalytic Asymmetric Synthesis of Versatile γ-Quaternary Acylcyclopentenes

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Andrew M. Harned, Brian M. Stoltz*

Supporting Information (^{1}H NMR, ^{13}C NMR, IR, HPLC)

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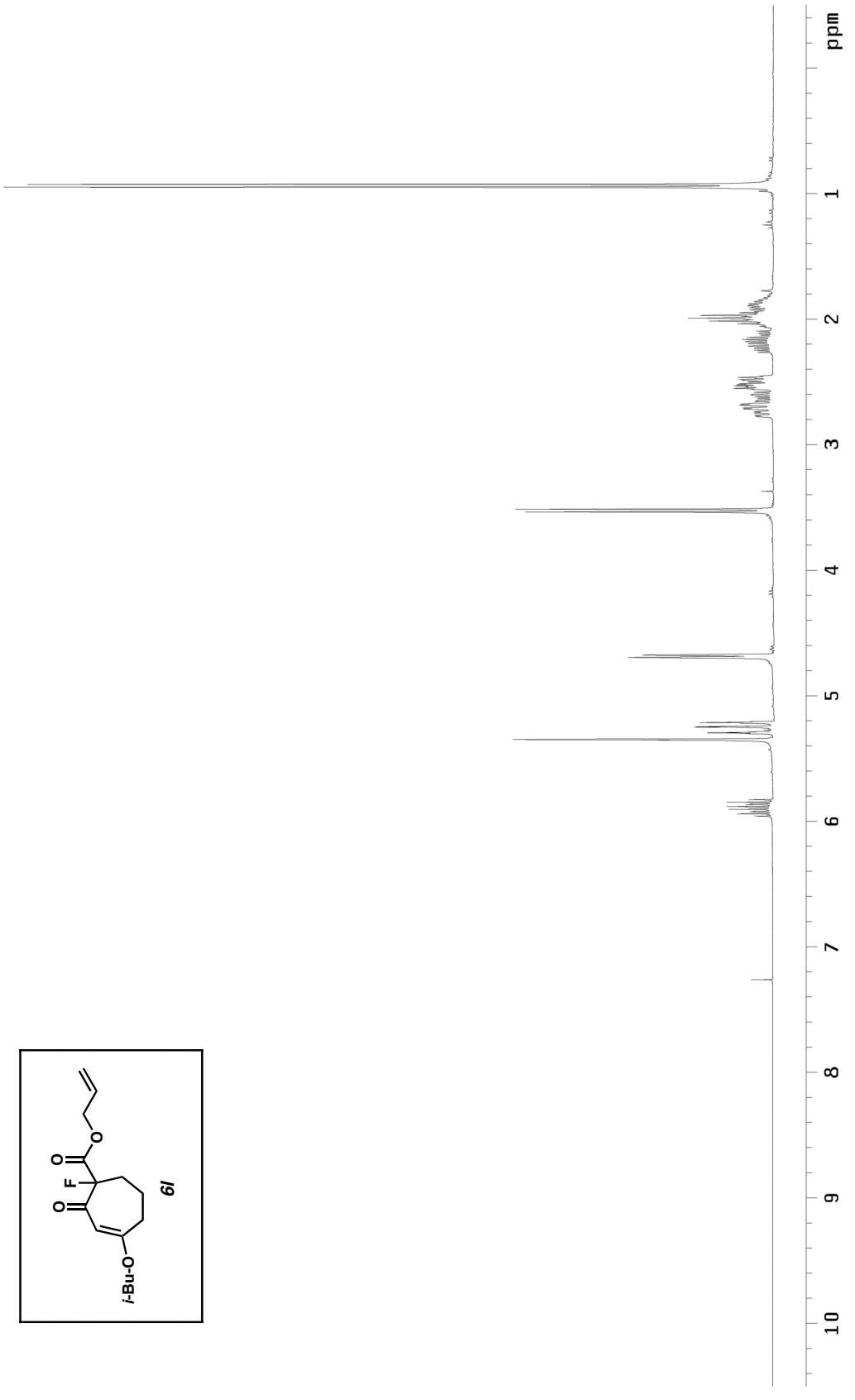

Figure SI-1A. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **6l**.

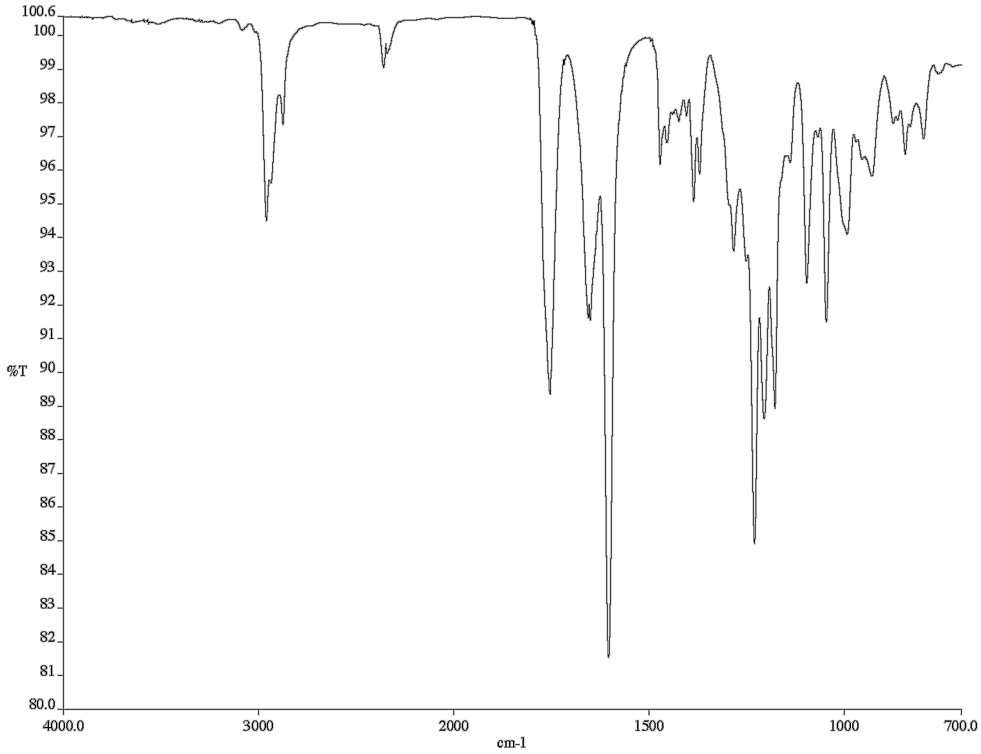

Figure SI-1B. Infrared spectrum (thin film/NaCl) of compound **6l**.

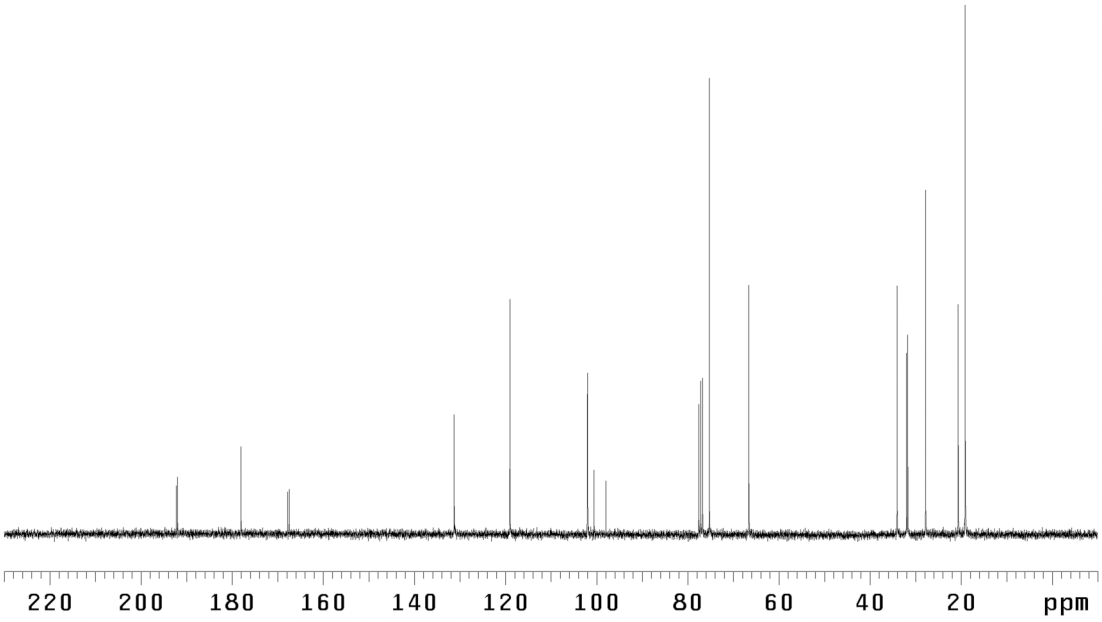

Figure SI-1C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **6l**.

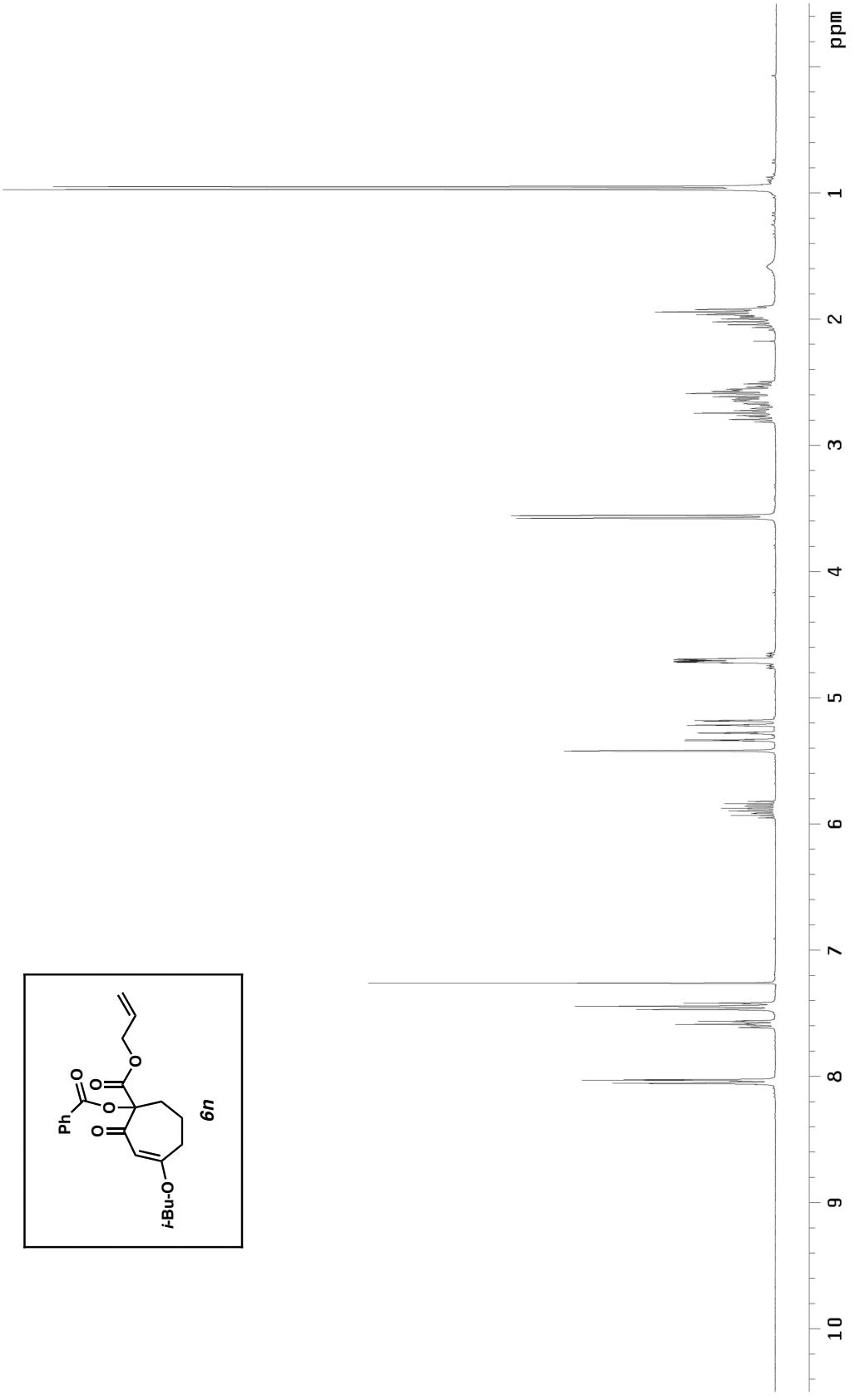

Figure SI-2A. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **6n**.

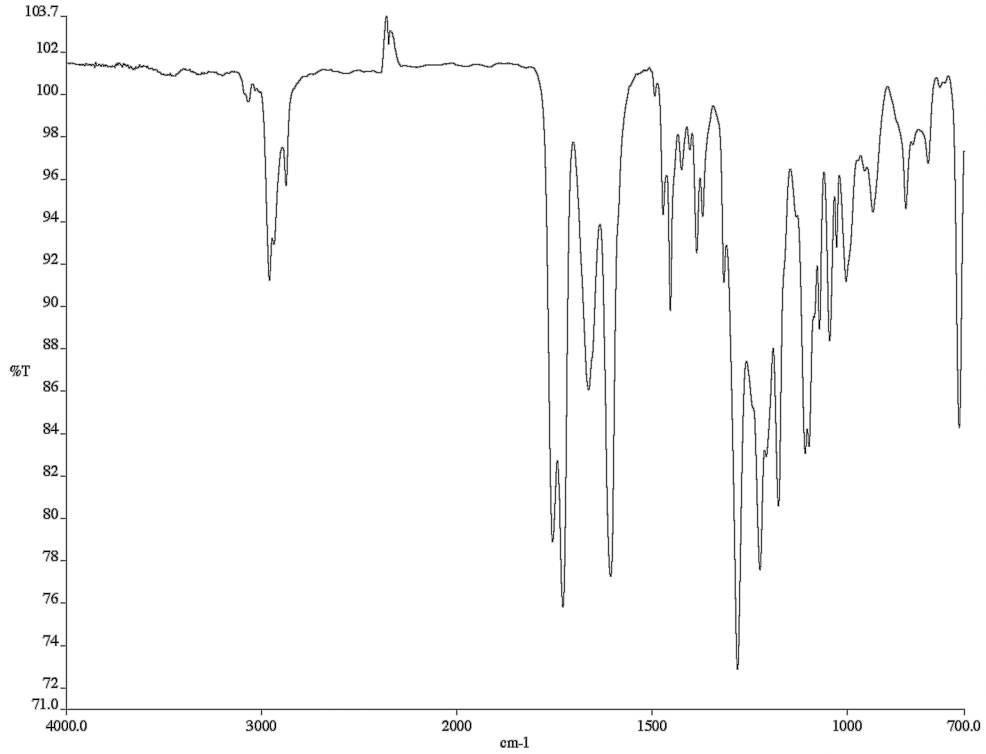

Figure SI-2B. Infrared spectrum (thin film/NaCl) of compound **6n**.

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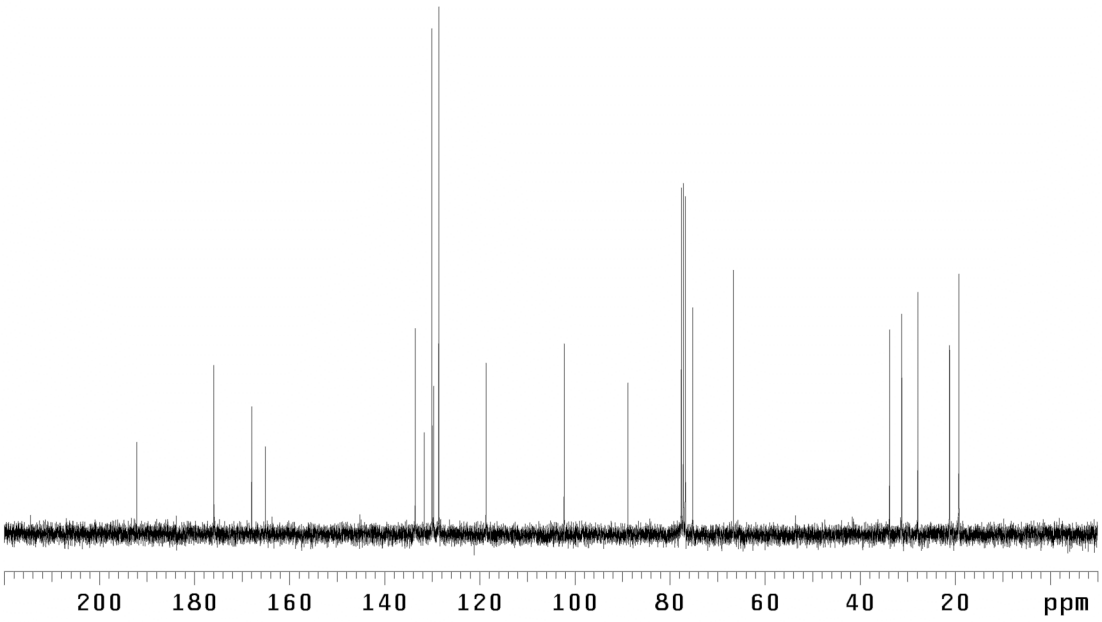


Figure SI-2C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **6n**.

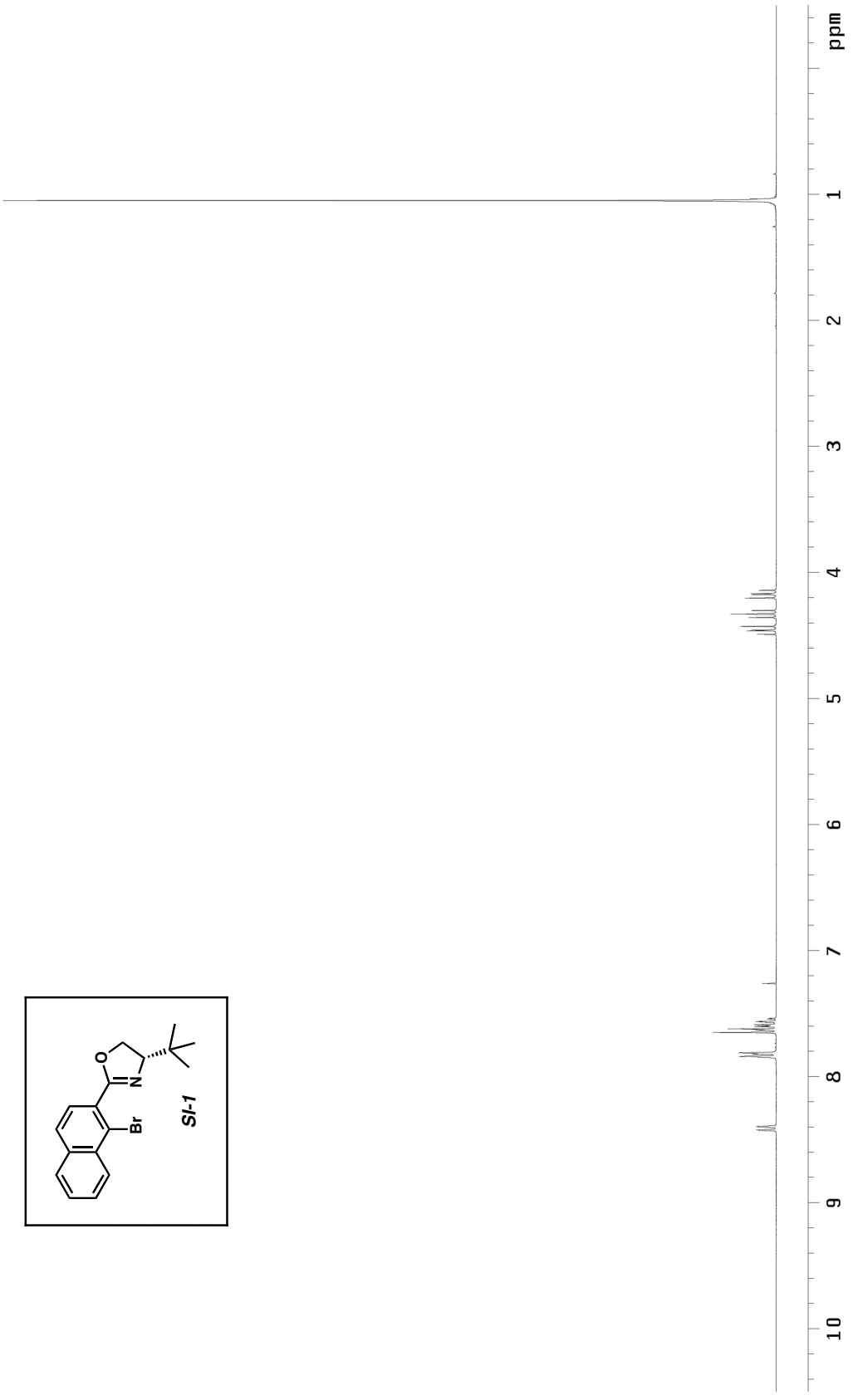


Figure SI-3A. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **SI-1**.

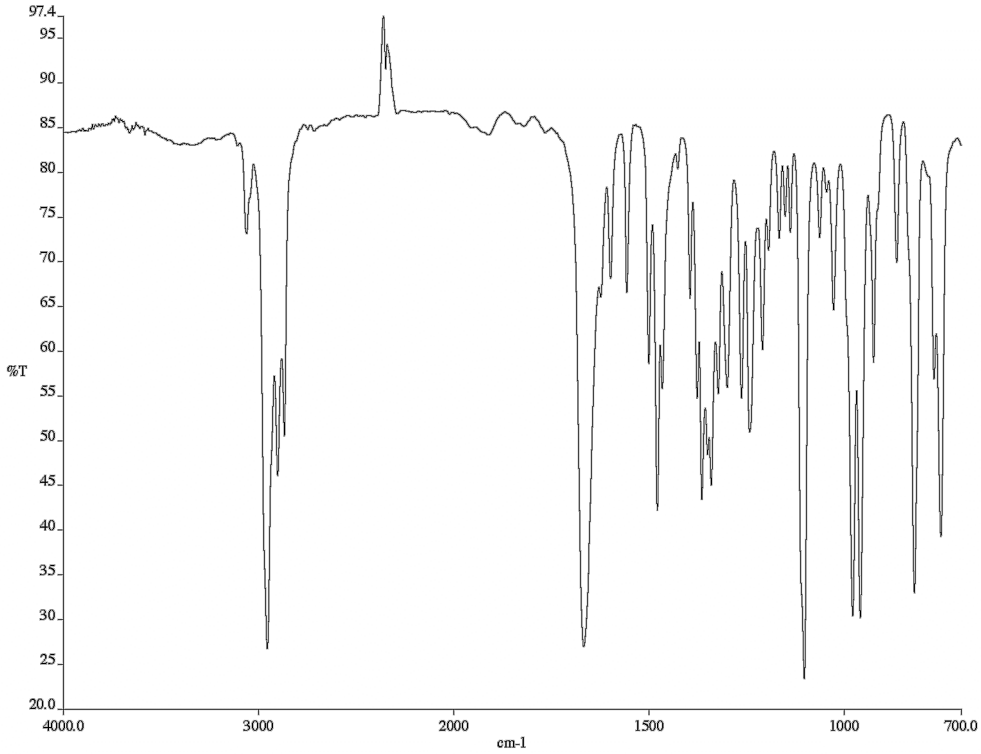


Figure SI-3B. Infrared spectrum (thin film/NaCl) of compound **SI-1**.

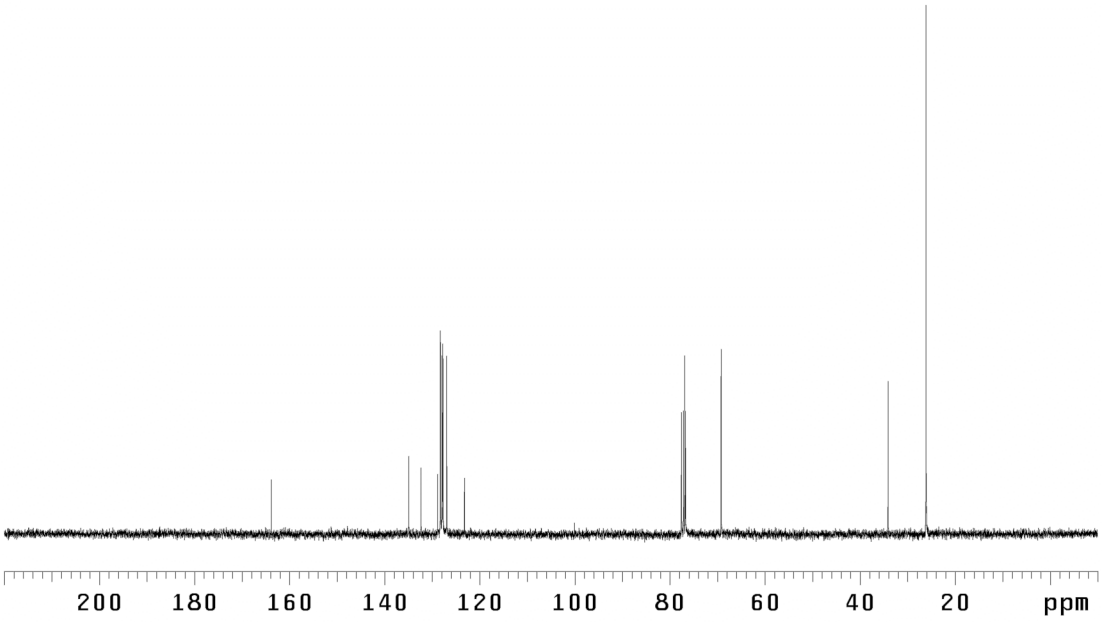


Figure SI-3C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-1**.

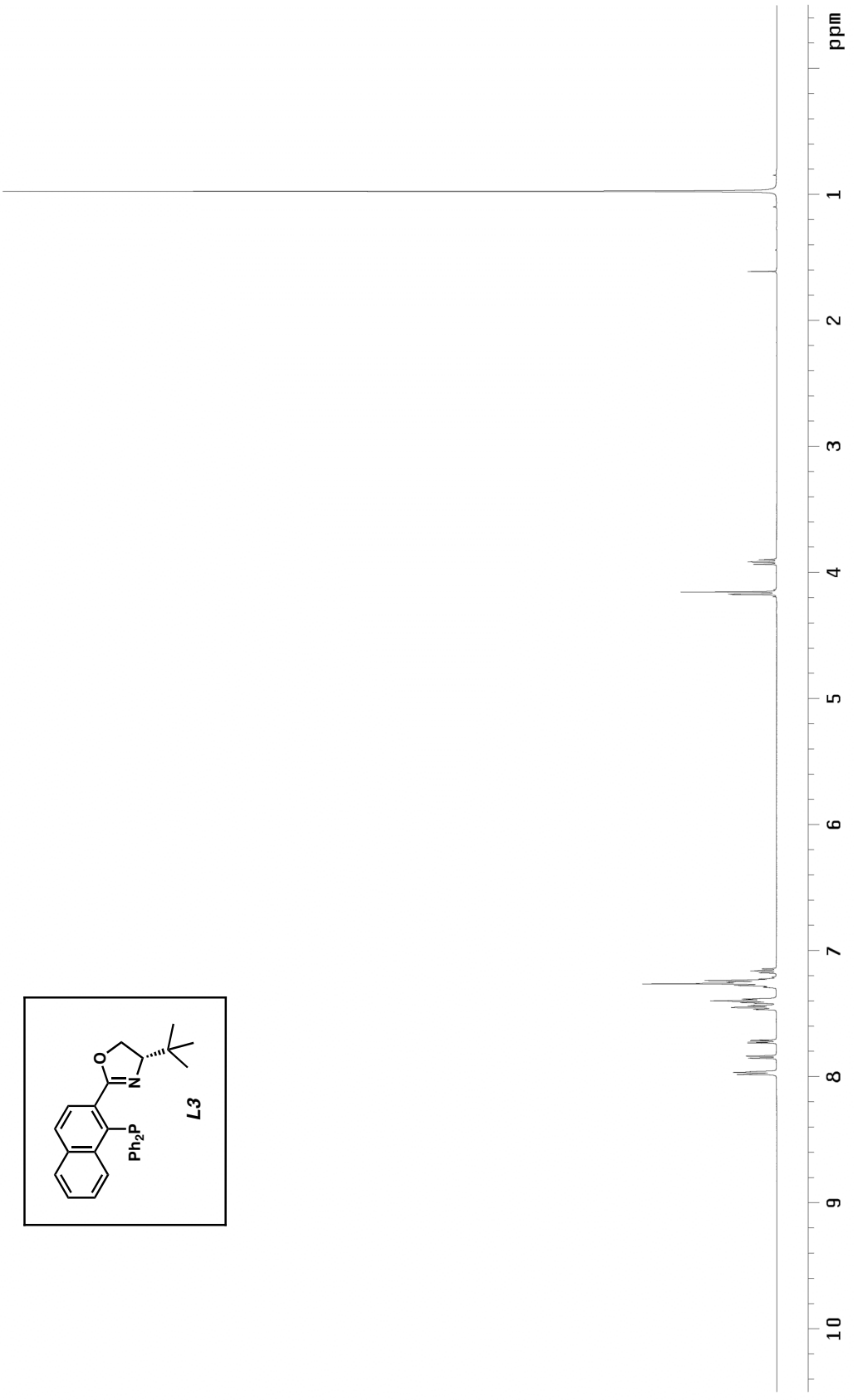


Figure SI-4A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **L3**.

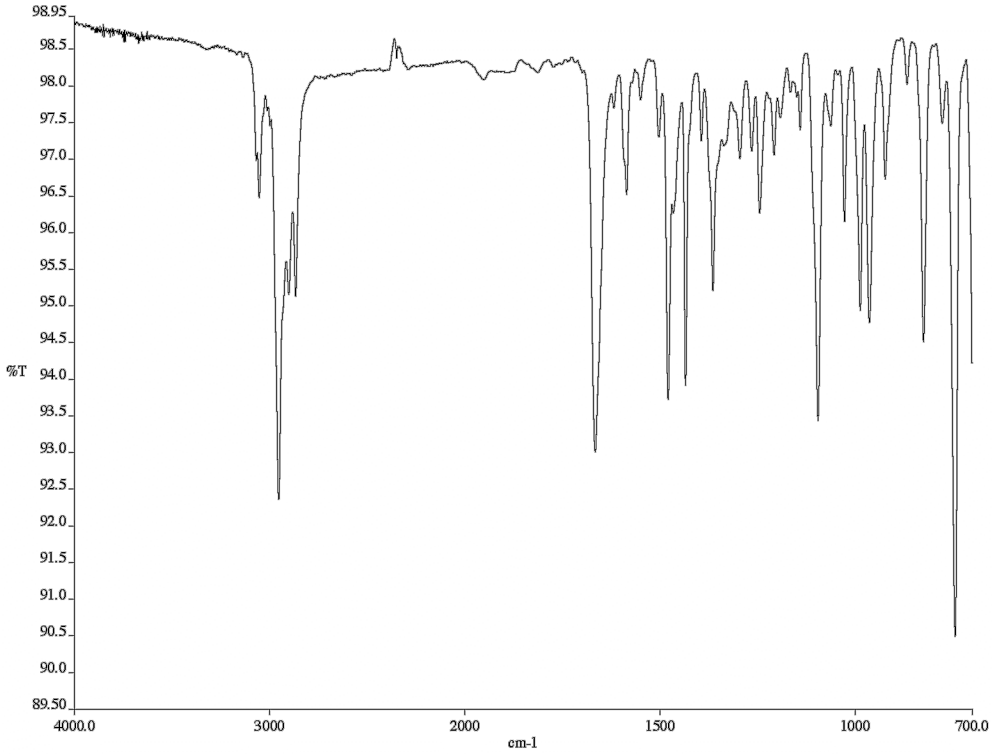


Figure SI-4B. Infrared spectrum (thin film/NaCl) of compound **L3**.

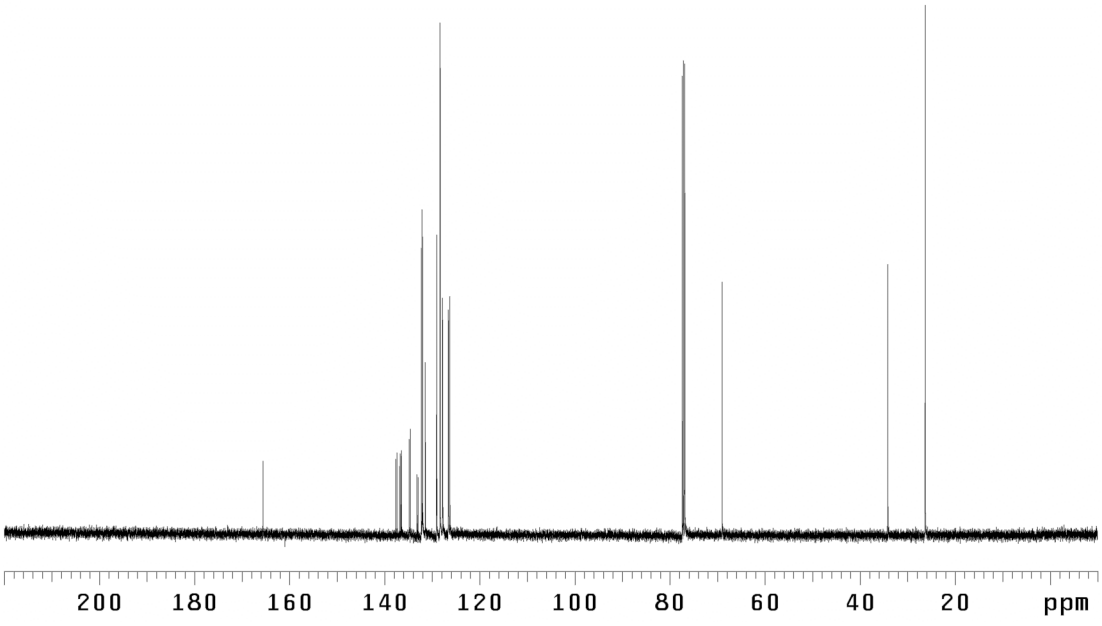
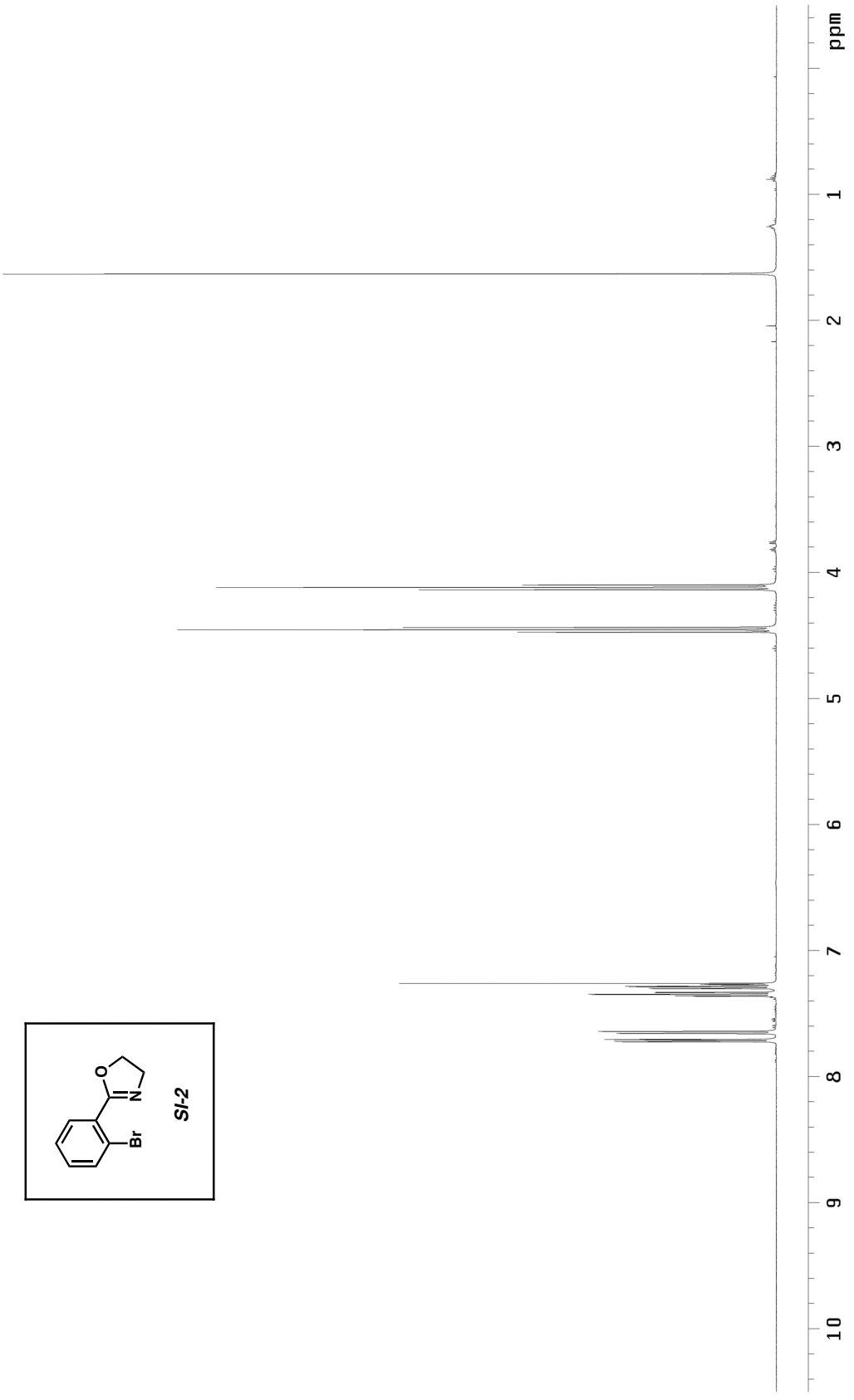


Figure SI-4C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **L3**.



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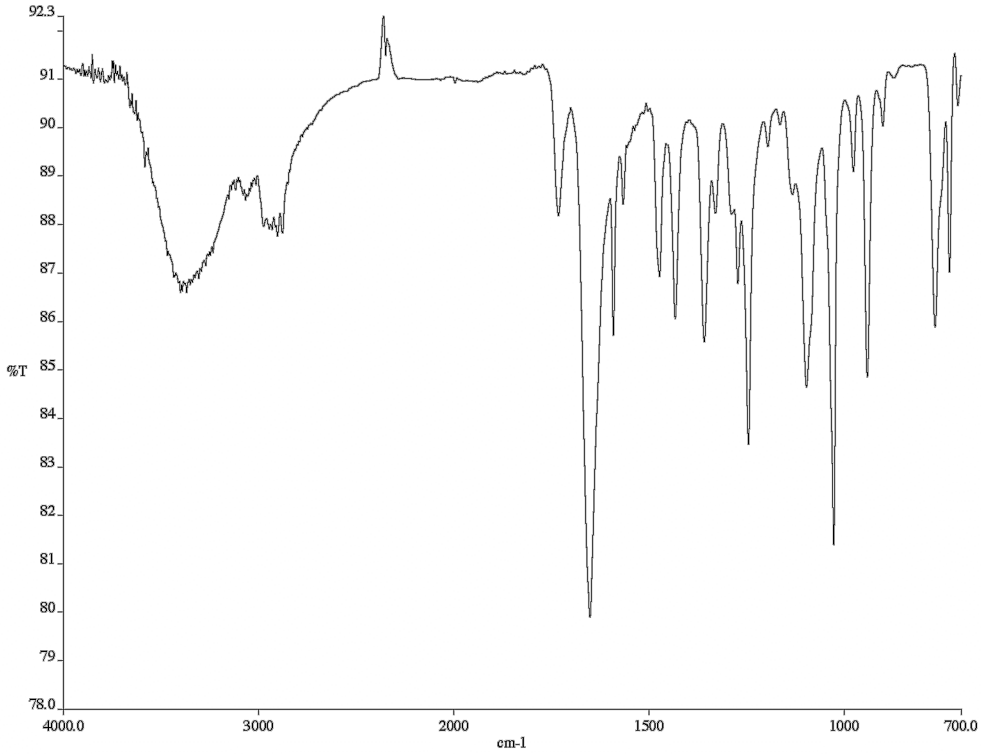


Figure SI-5B. Infrared spectrum (thin film/NaCl) of compound **SI-2**.

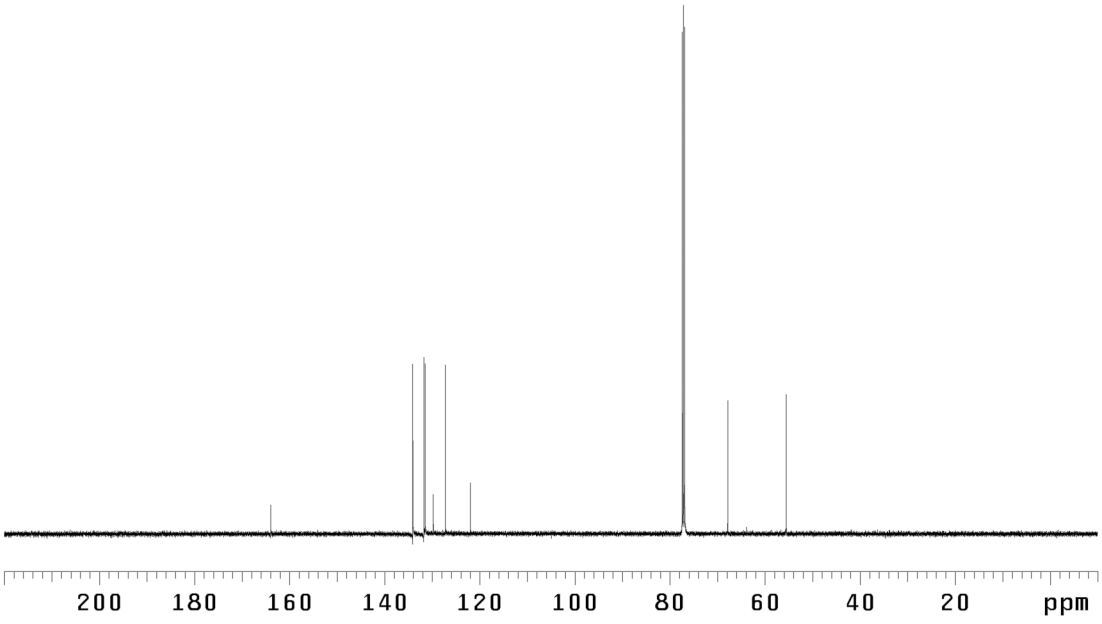


Figure SI-5C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **SI-2**.

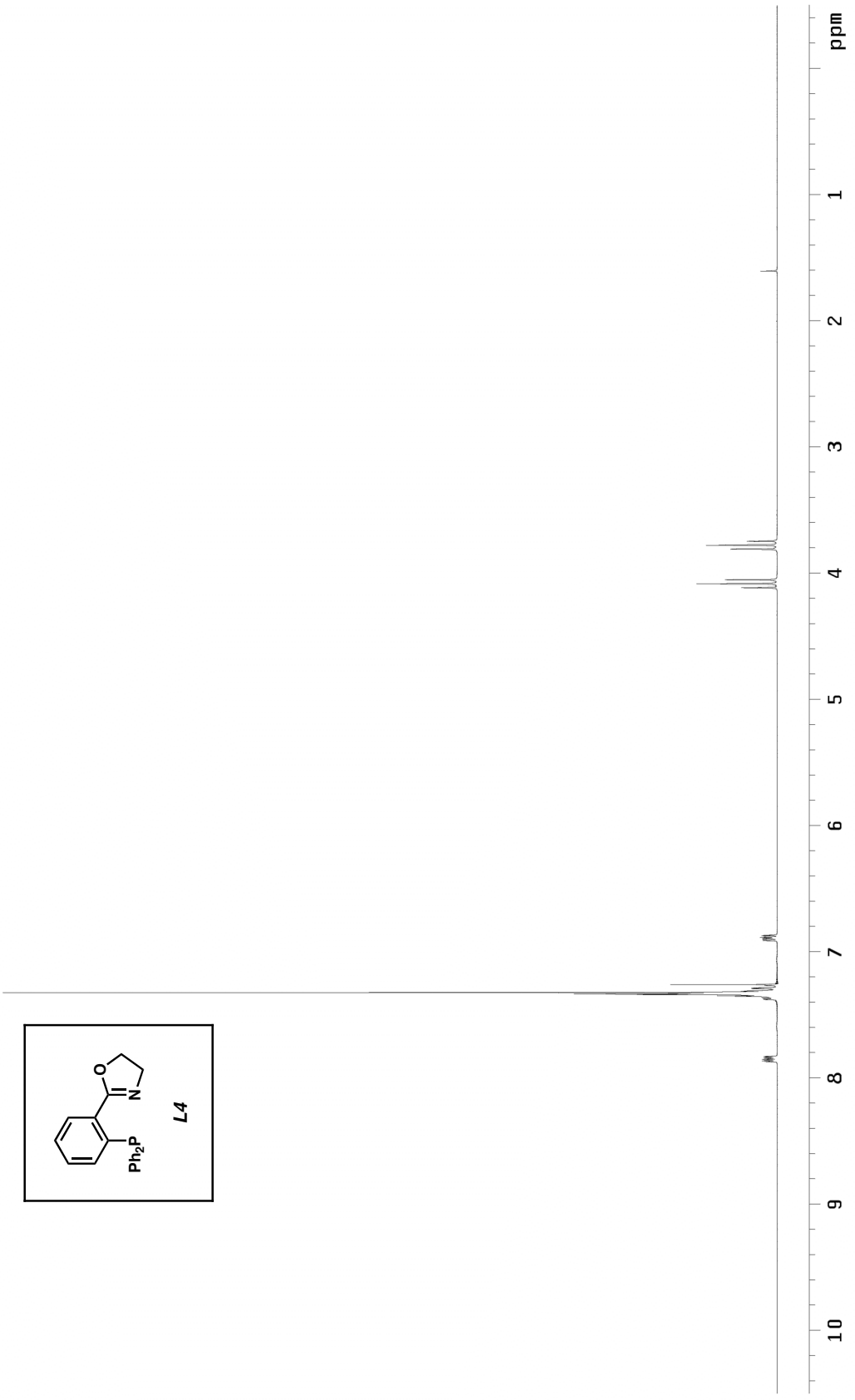


Figure SI-6A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **L4**.

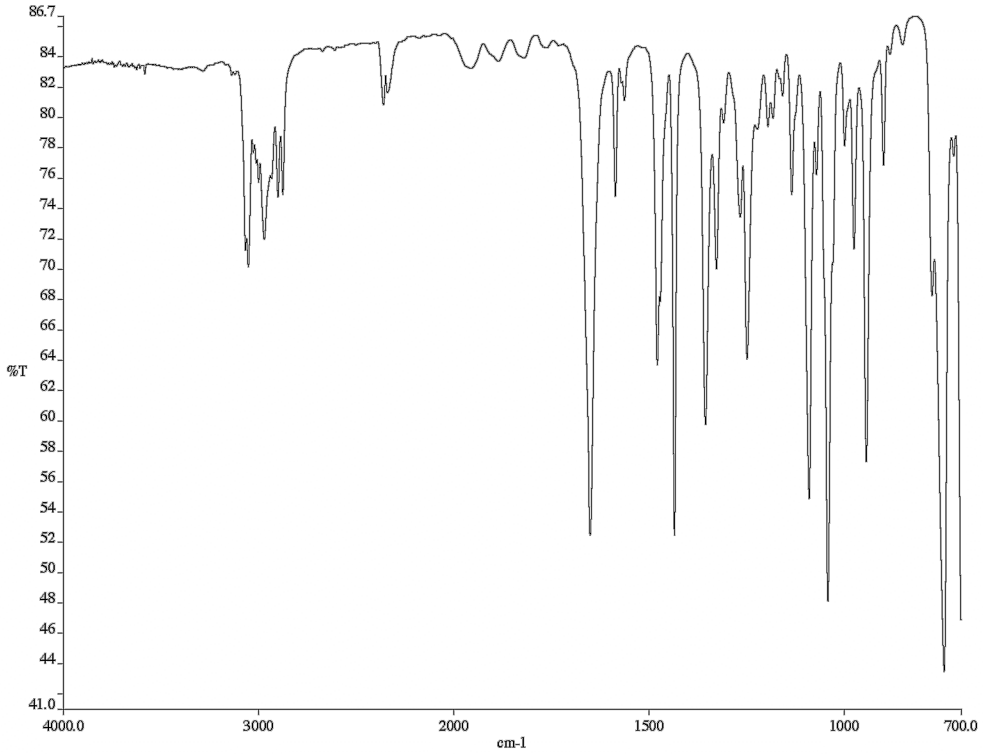


Figure SI-6B. Infrared spectrum (thin film/NaCl) of compound **L4**.

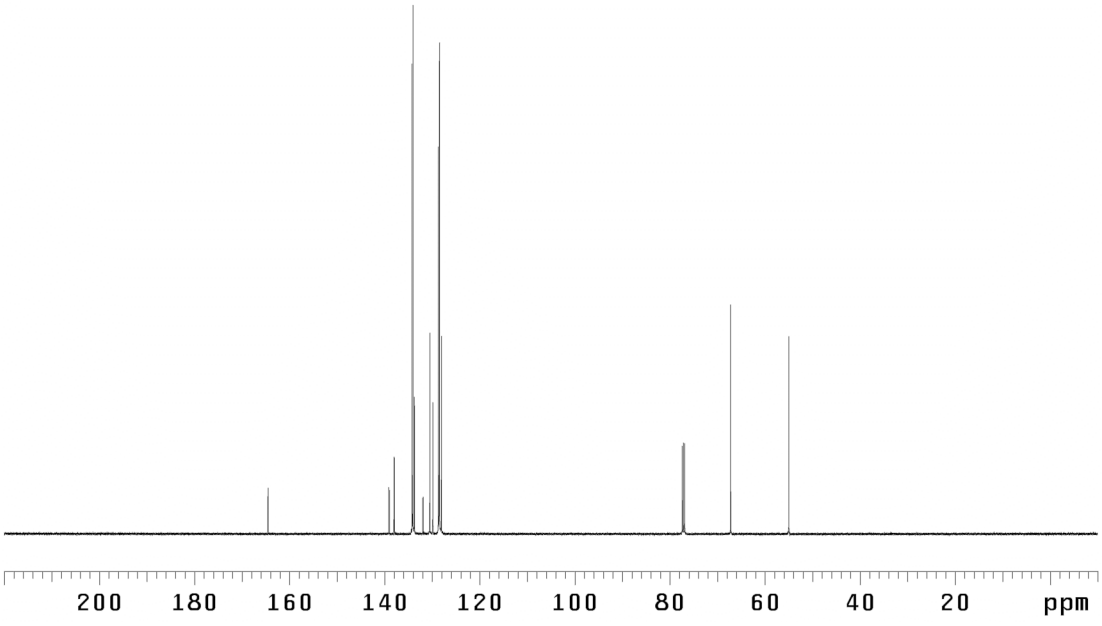
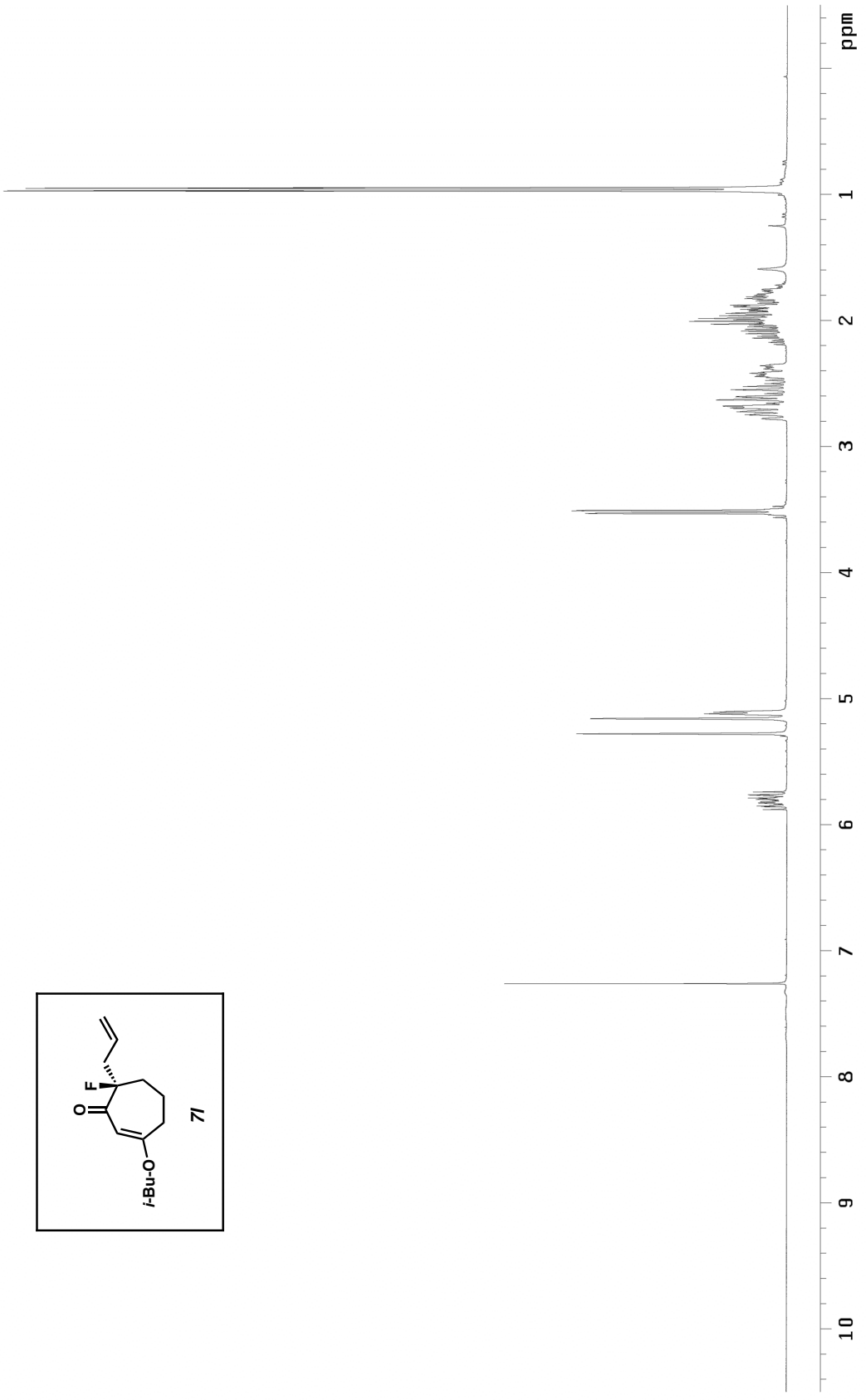


Figure SI-6C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **L4**.



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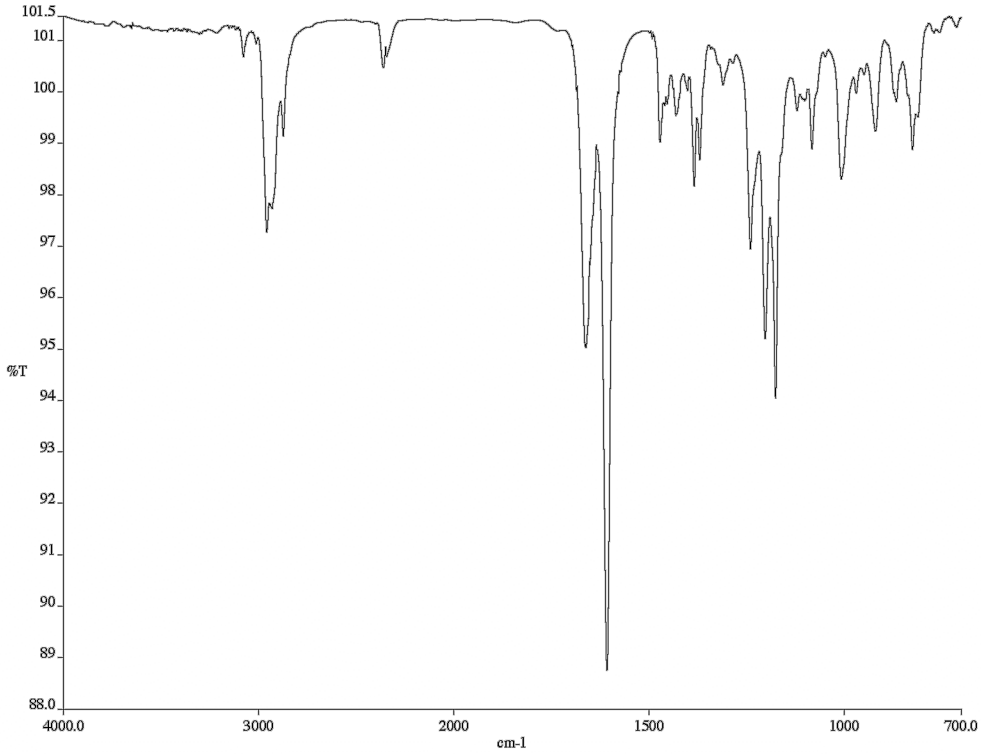


Figure SI-7B. Infrared spectrum (thin film/NaCl) of compound **7l**.

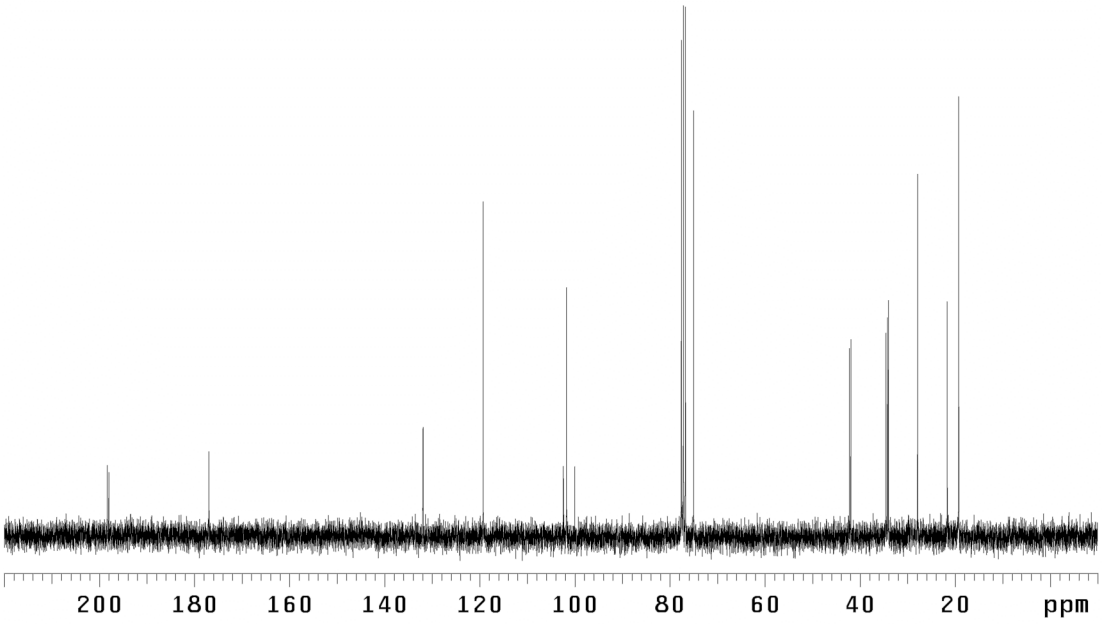
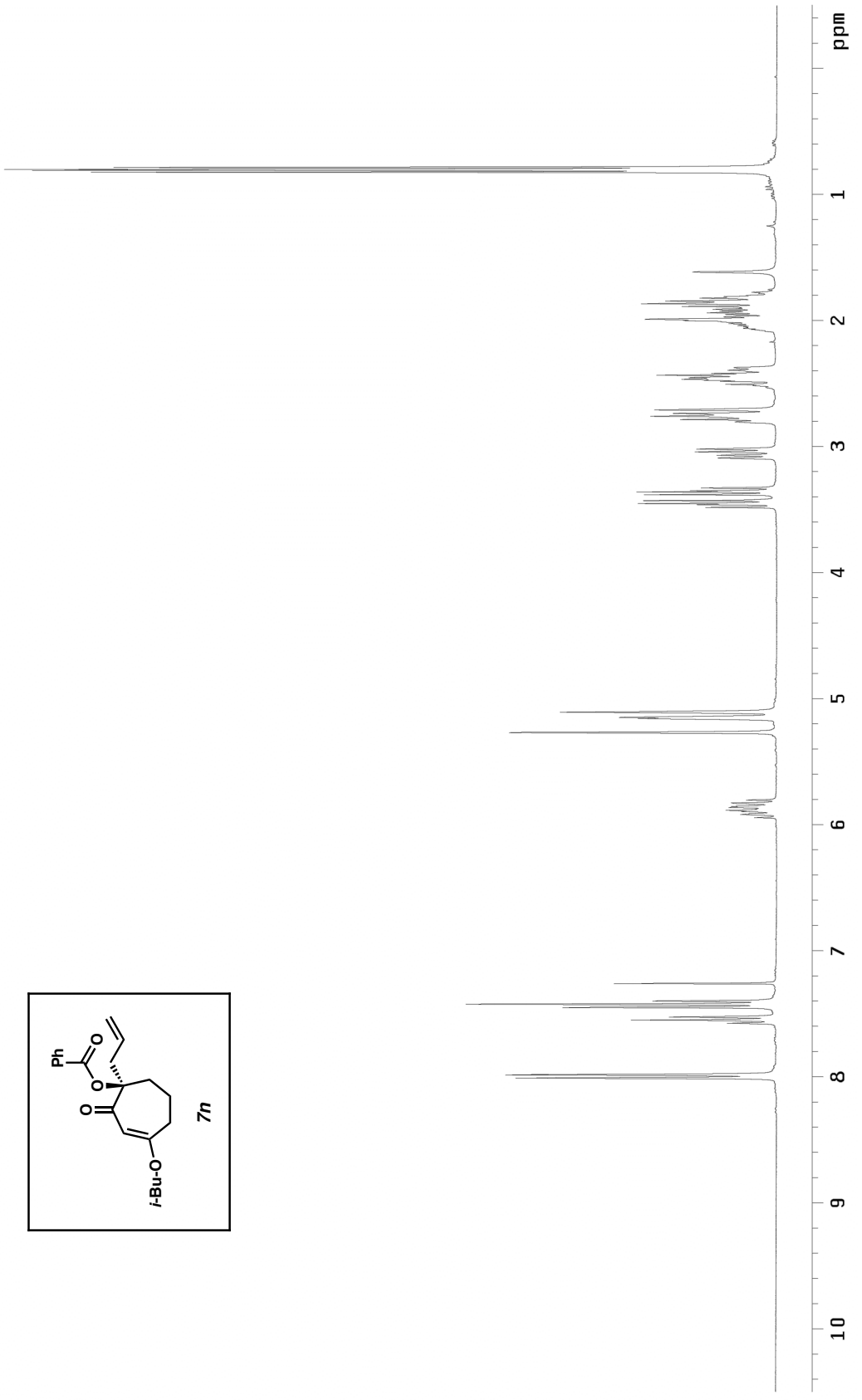


Figure SI-7C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **7l**.



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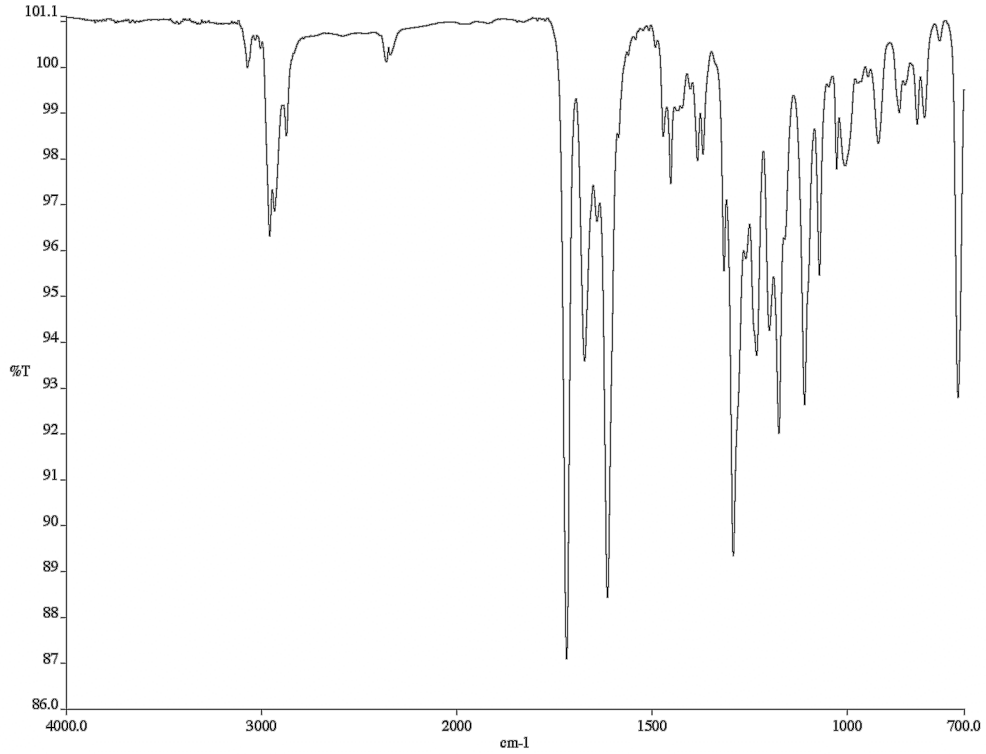


Figure SI-8B. Infrared spectrum (thin film/NaCl) of compound **7n**.

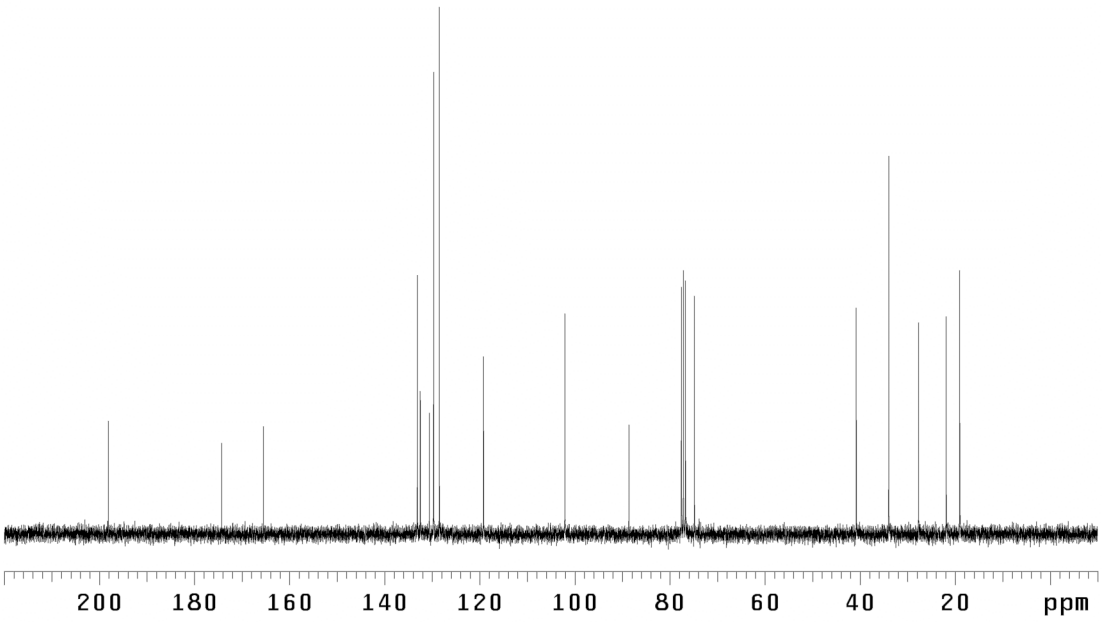


Figure SI-8C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **7n**.

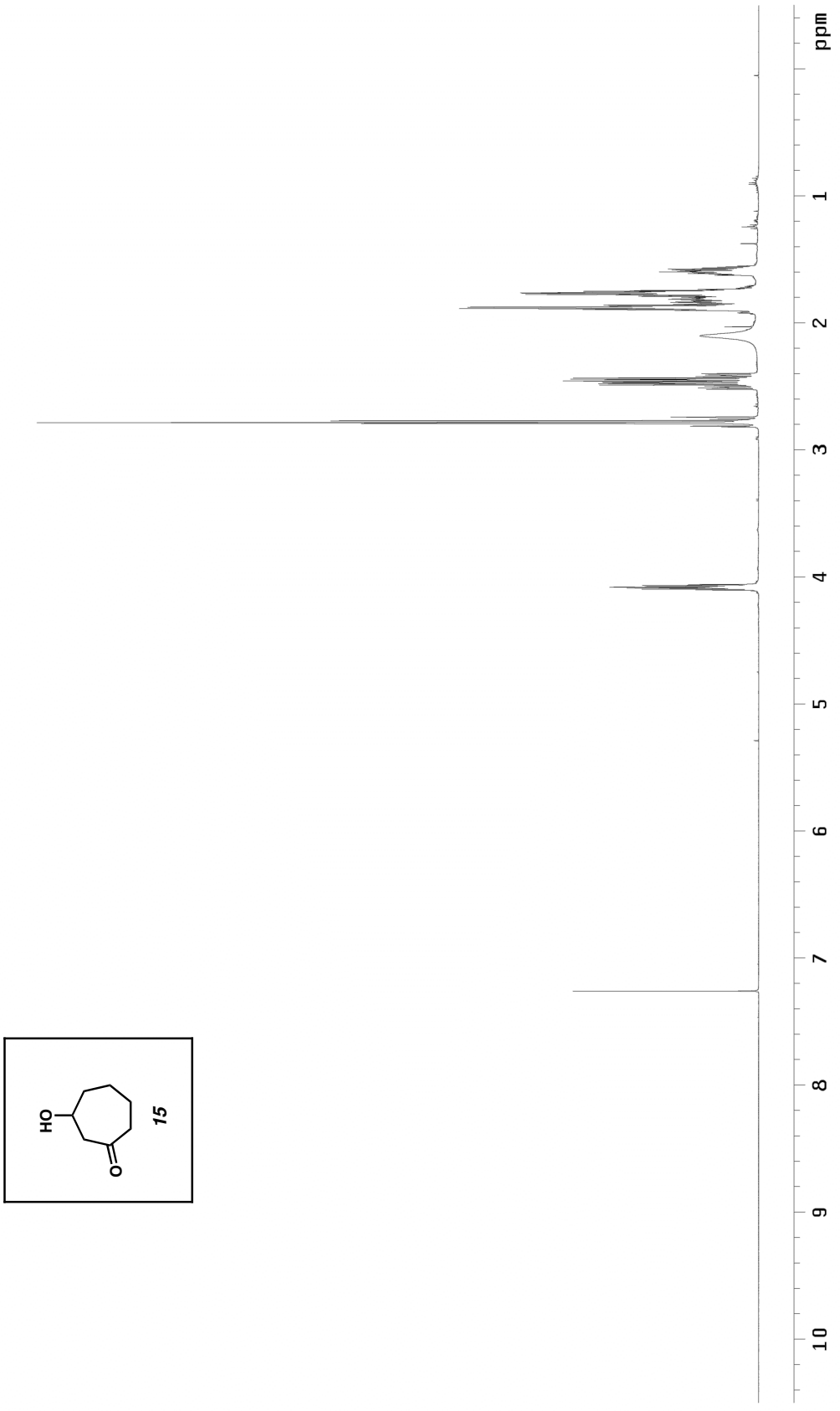


Figure SI-9A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **15**.

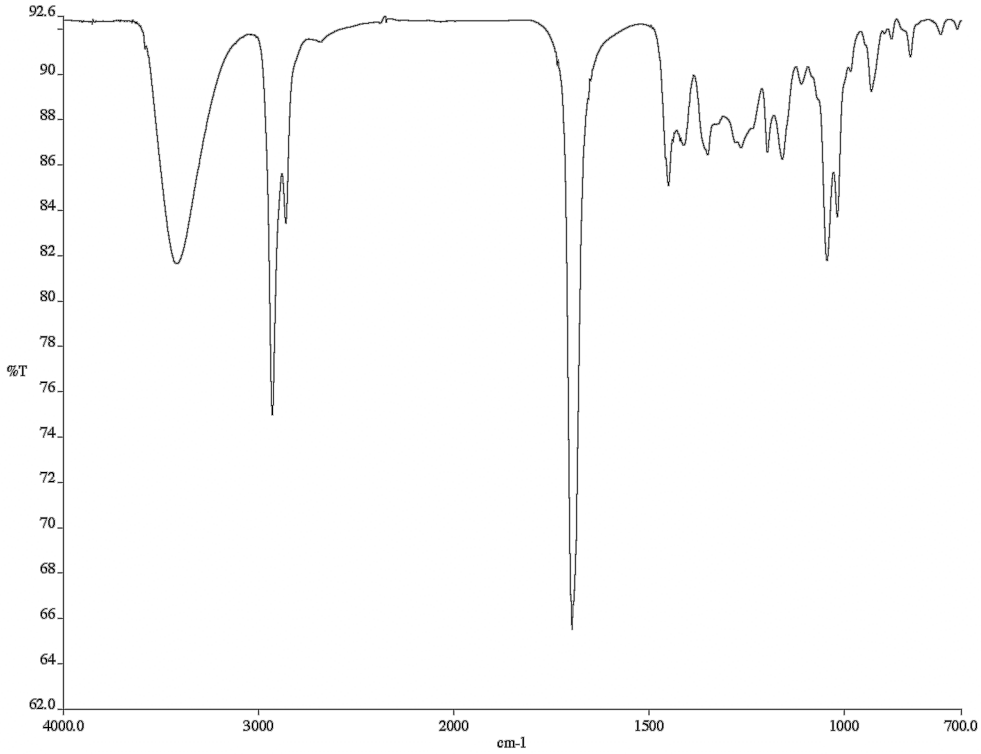


Figure SI-9B. Infrared spectrum (thin film/NaCl) of compound **15**.

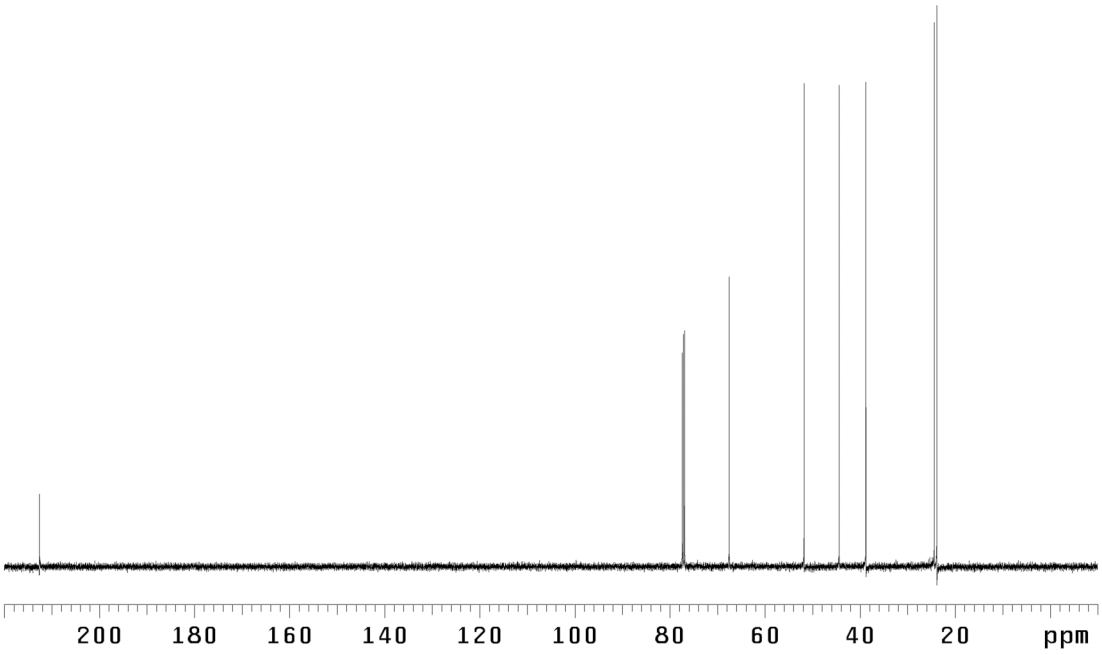
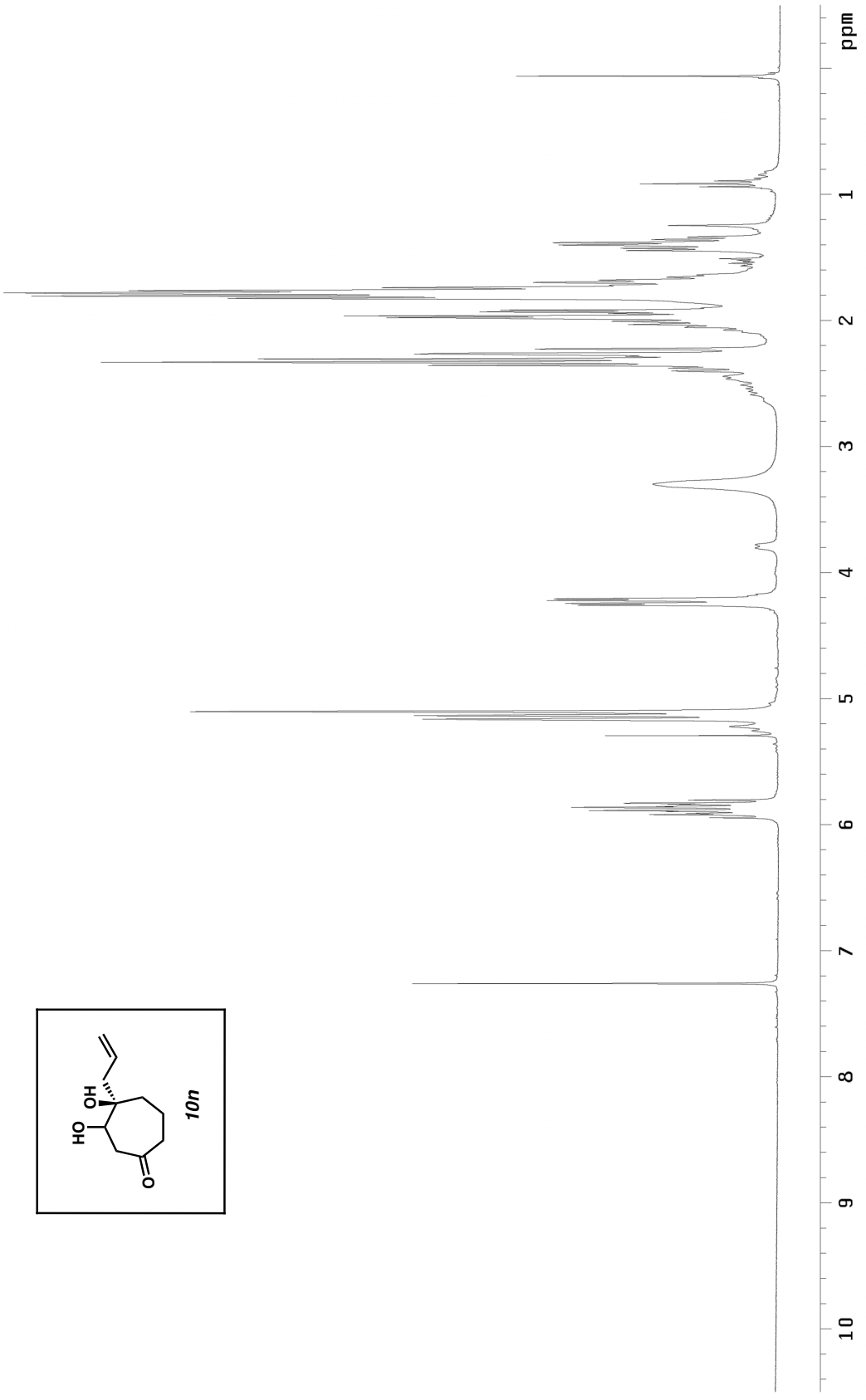


Figure SI-9C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **15**.



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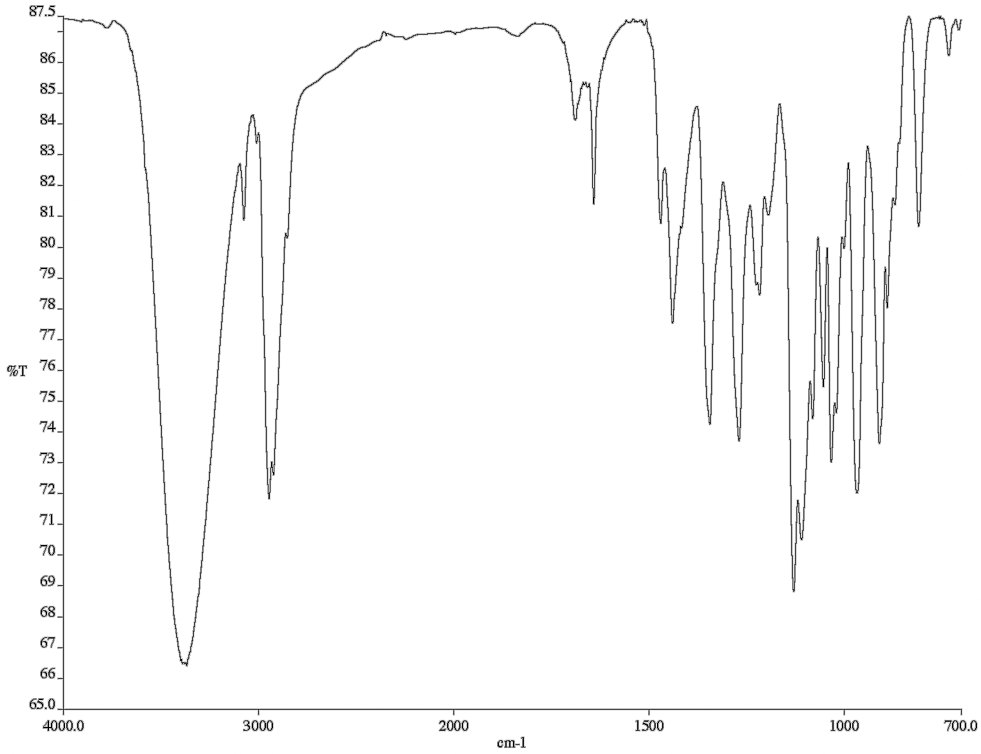


Figure SI-10B. Infrared spectrum (thin film/NaCl) of compound **10n**.

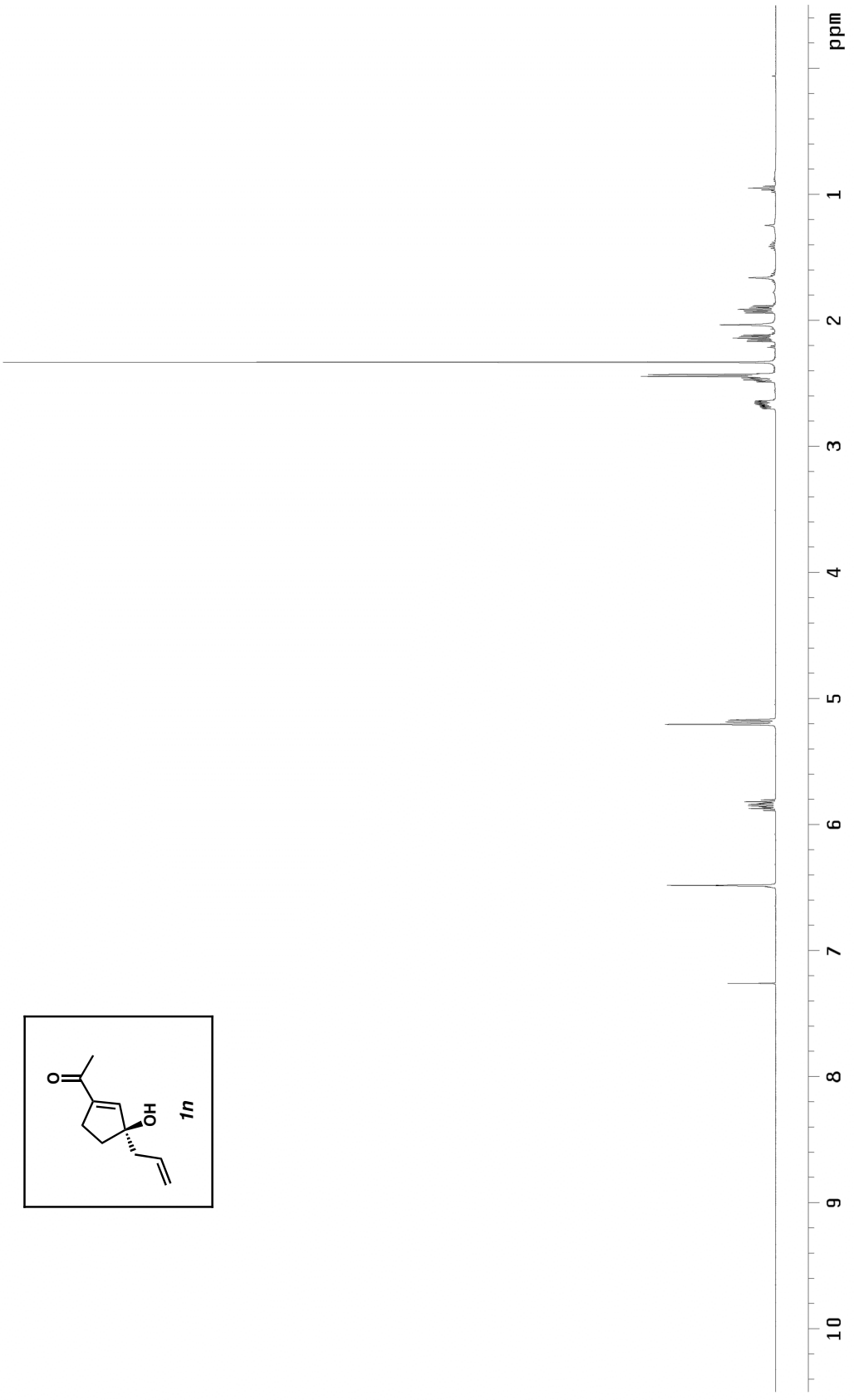


Figure SI-11A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **1n**.

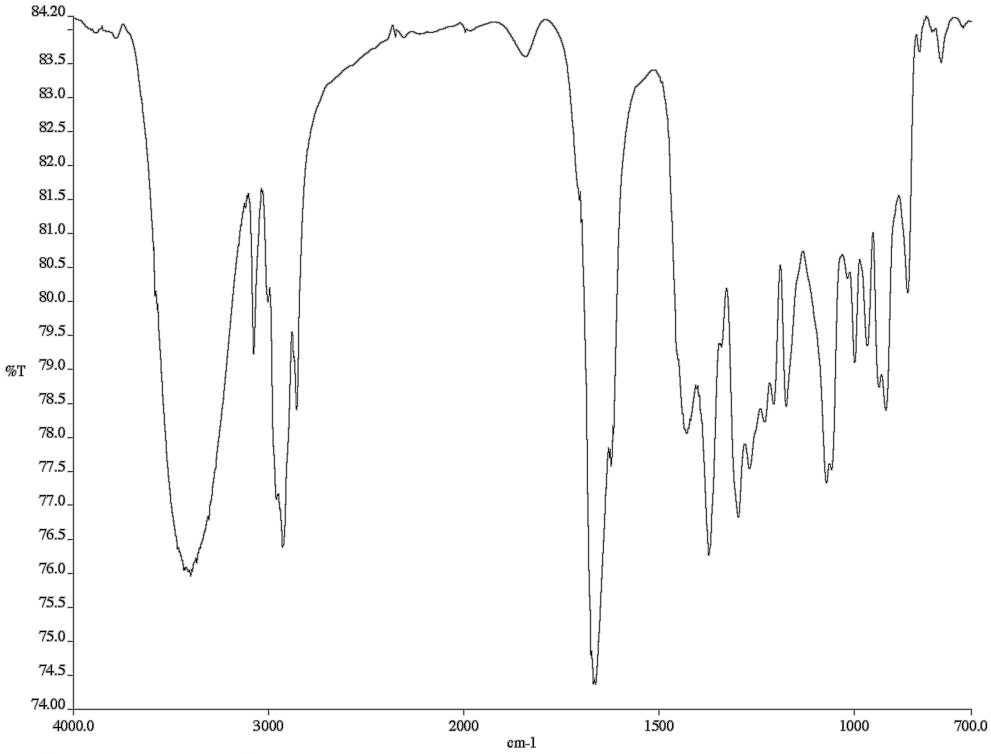


Figure SI-11B. Infrared spectrum (thin film/NaCl) of compound **1n**.

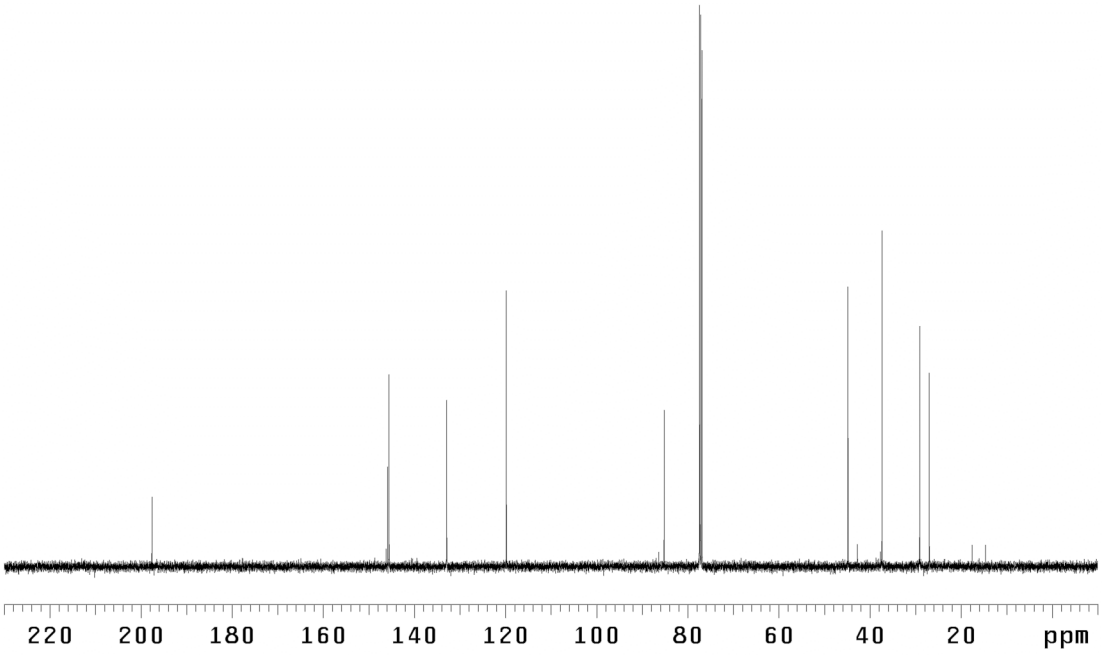
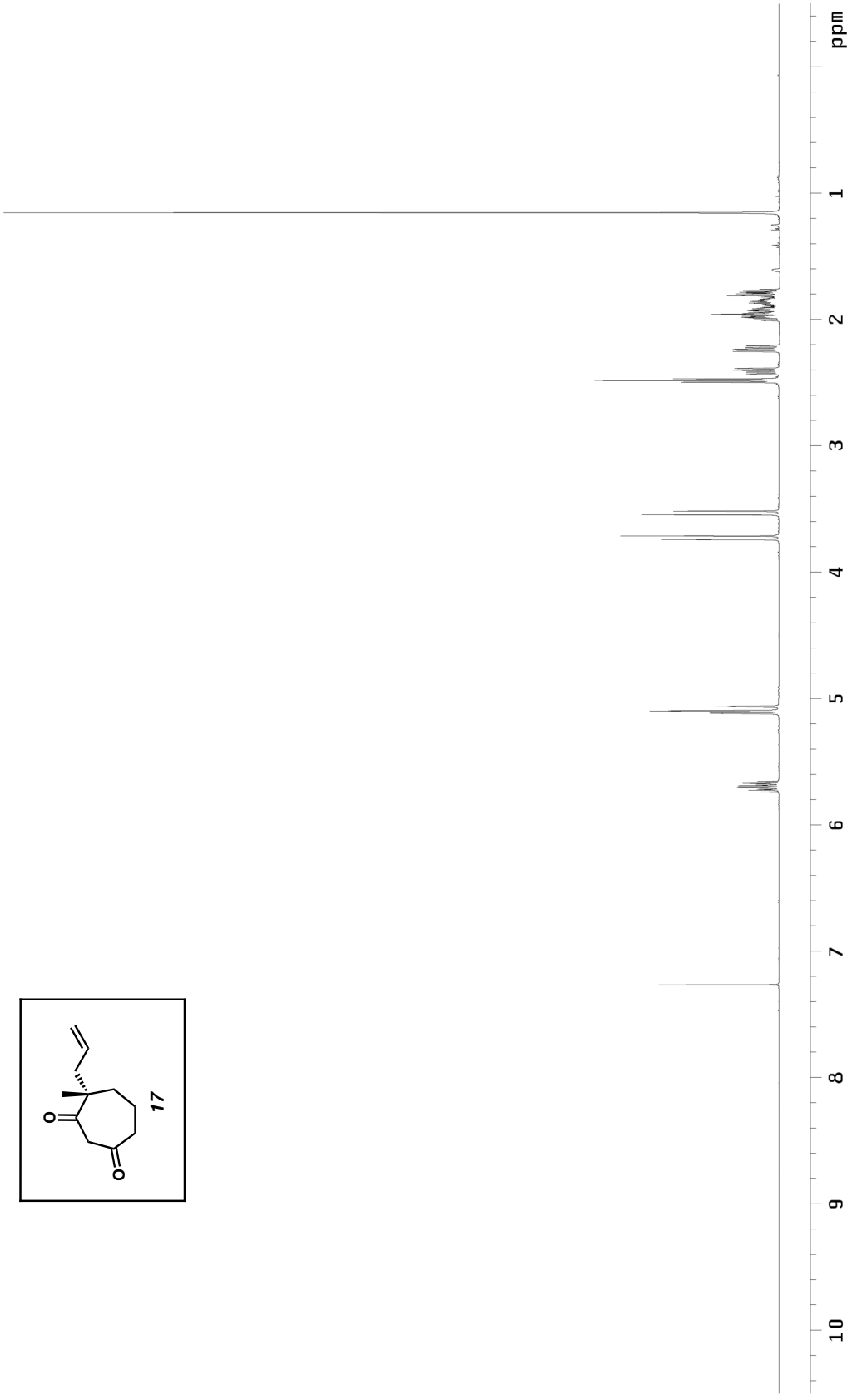


Figure SI-11C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **1n**.



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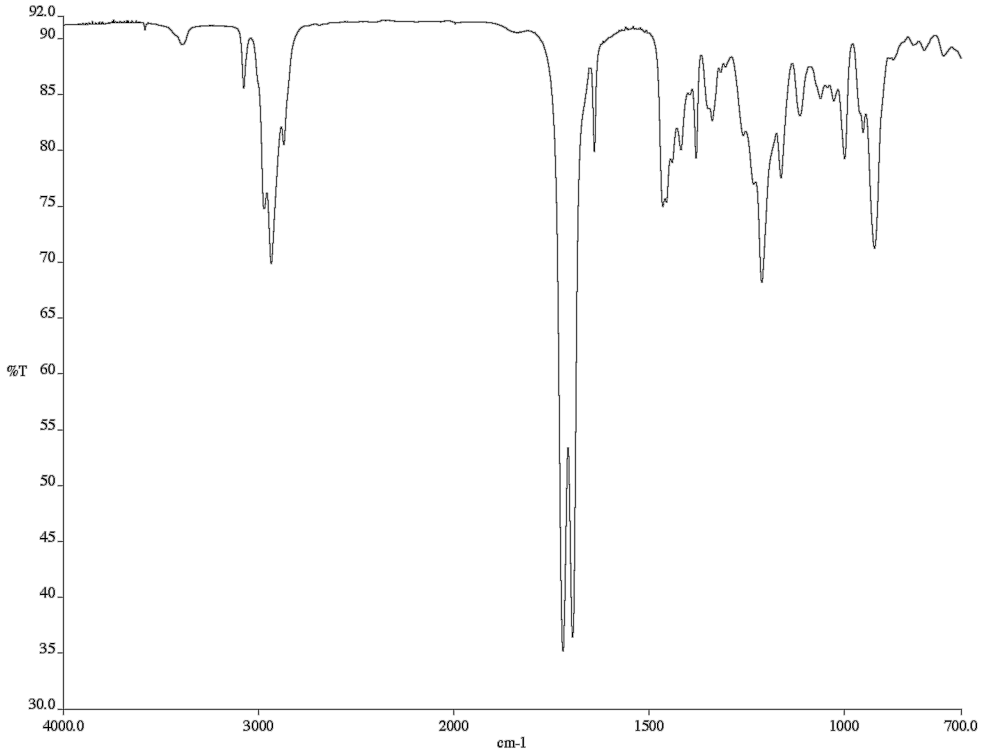


Figure SI-12B. Infrared spectrum (thin film/NaCl) of compound **17**.

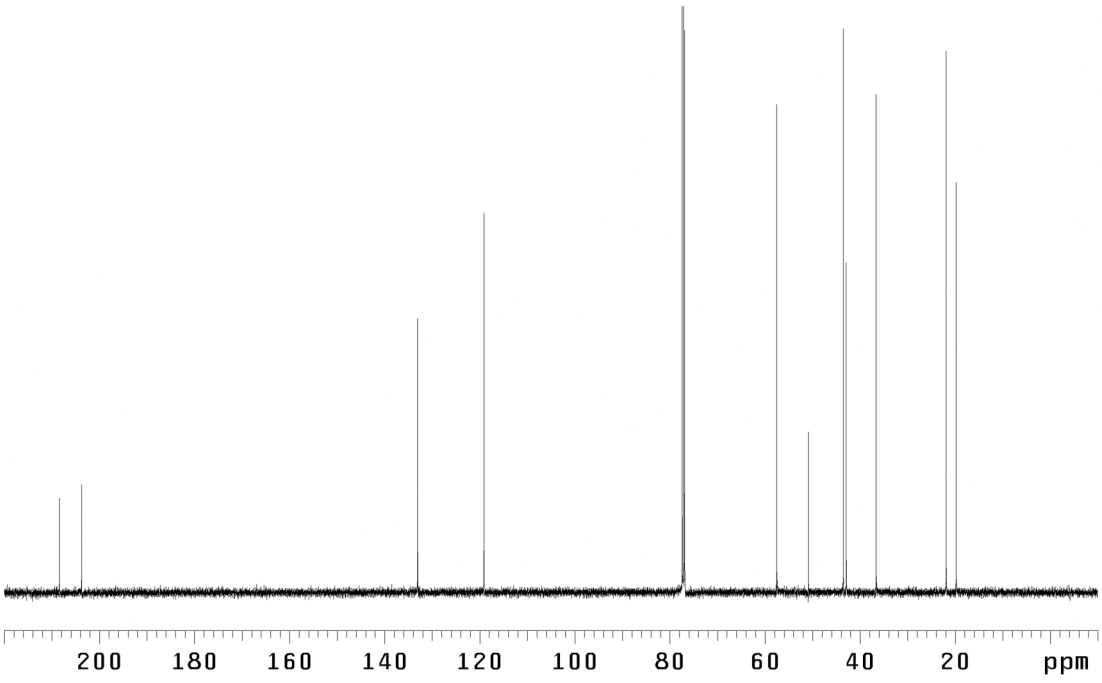


Figure SI-12C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **17**.

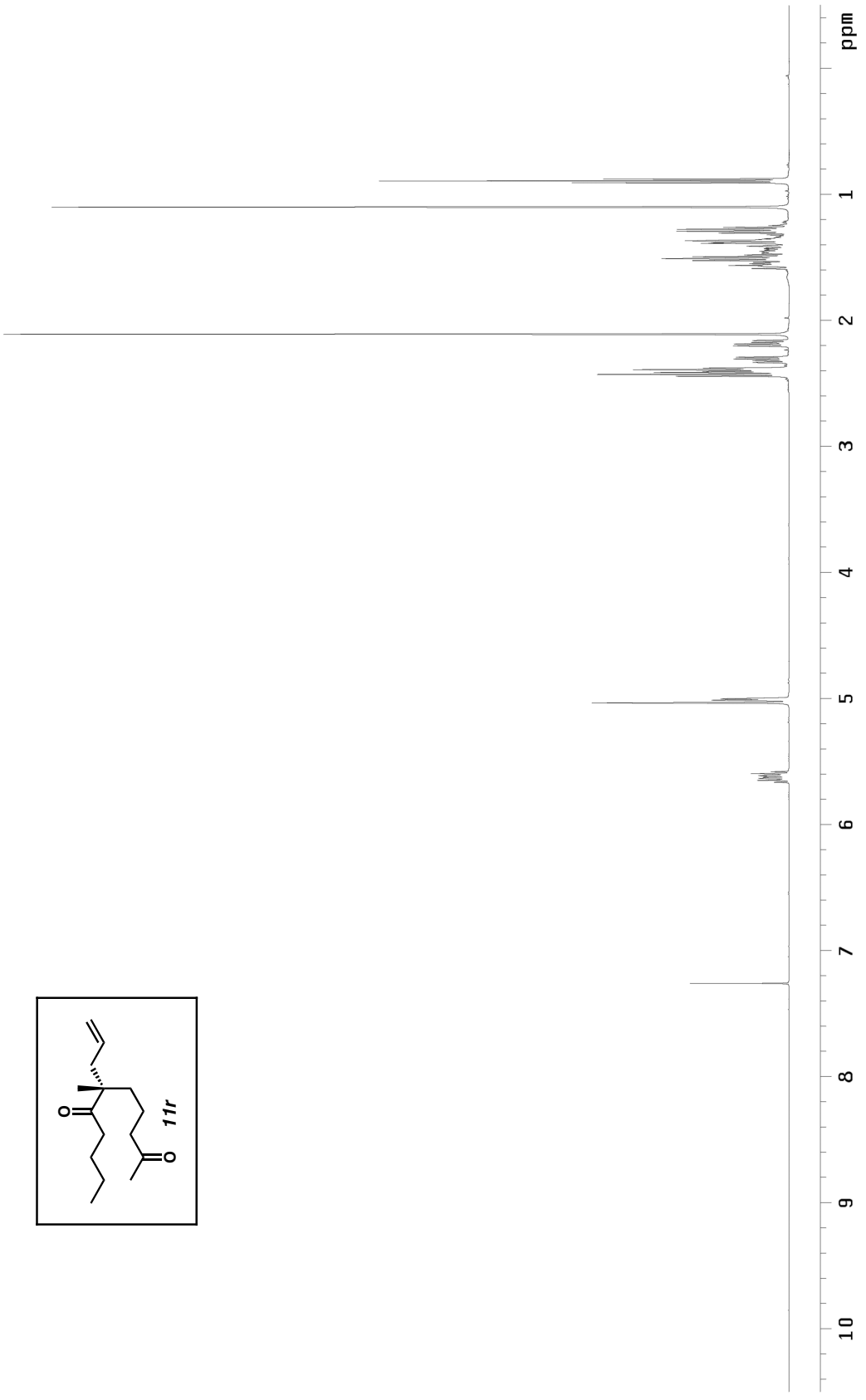


Figure SI-13A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **11r**.

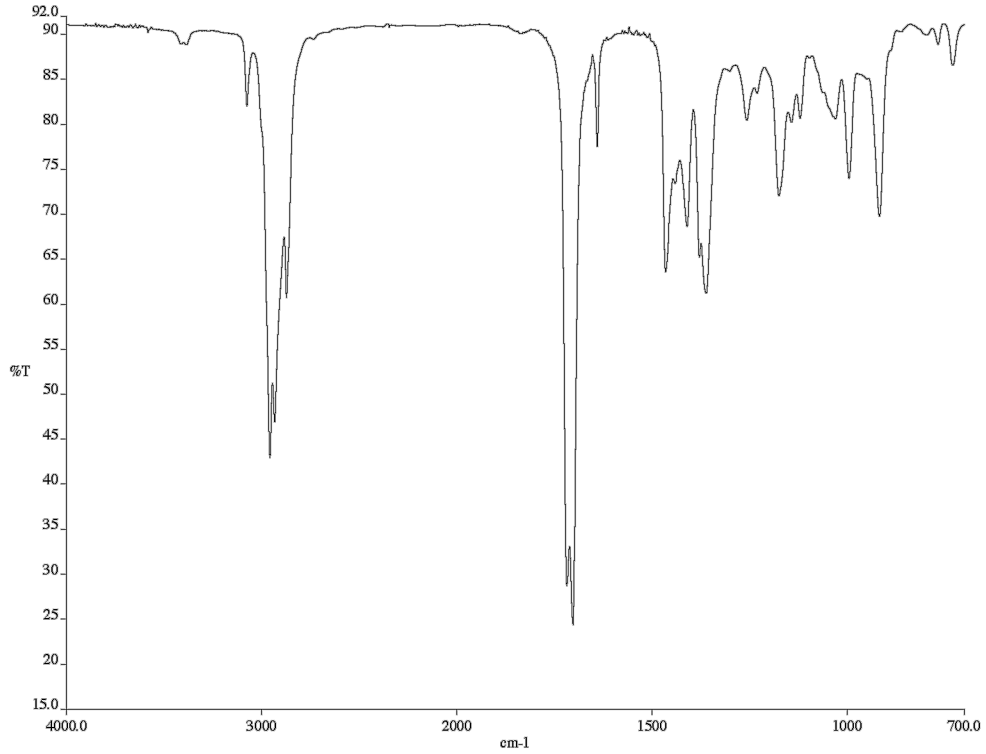


Figure SI-13B. Infrared spectrum (thin film/NaCl) of compound **11r**.

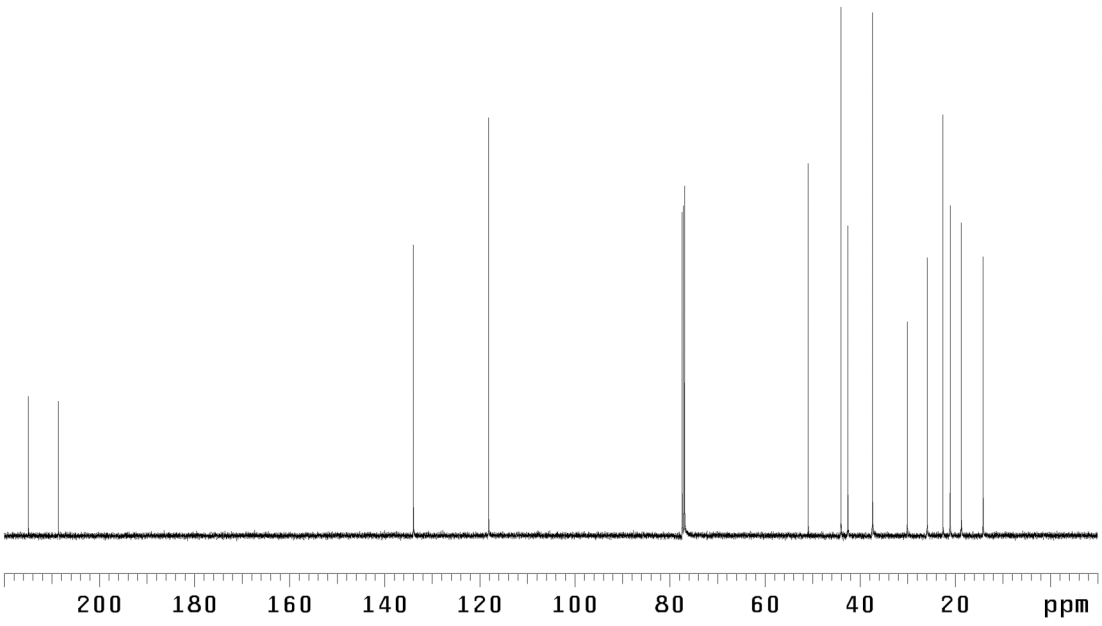
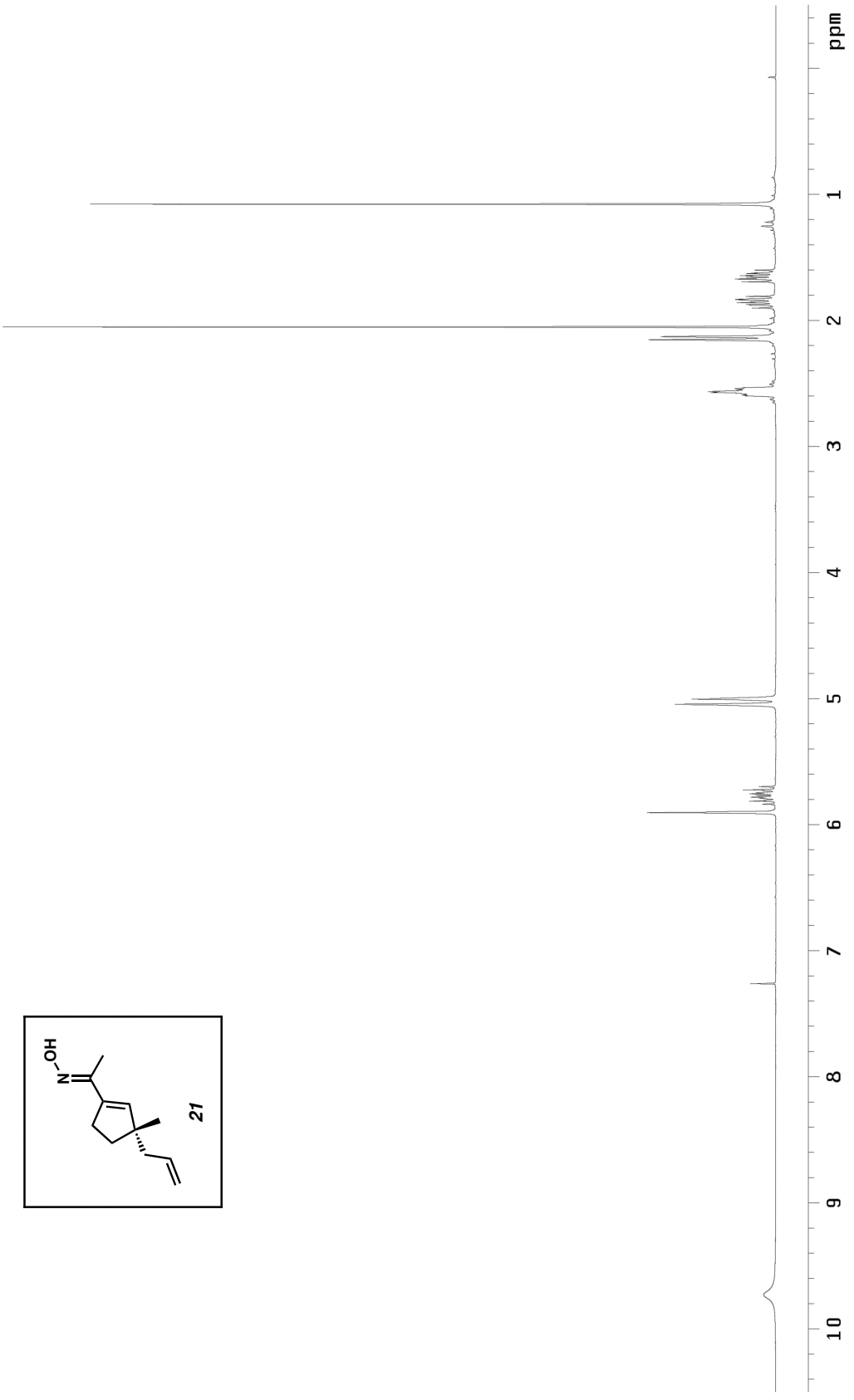


Figure SI-13C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **11r**.



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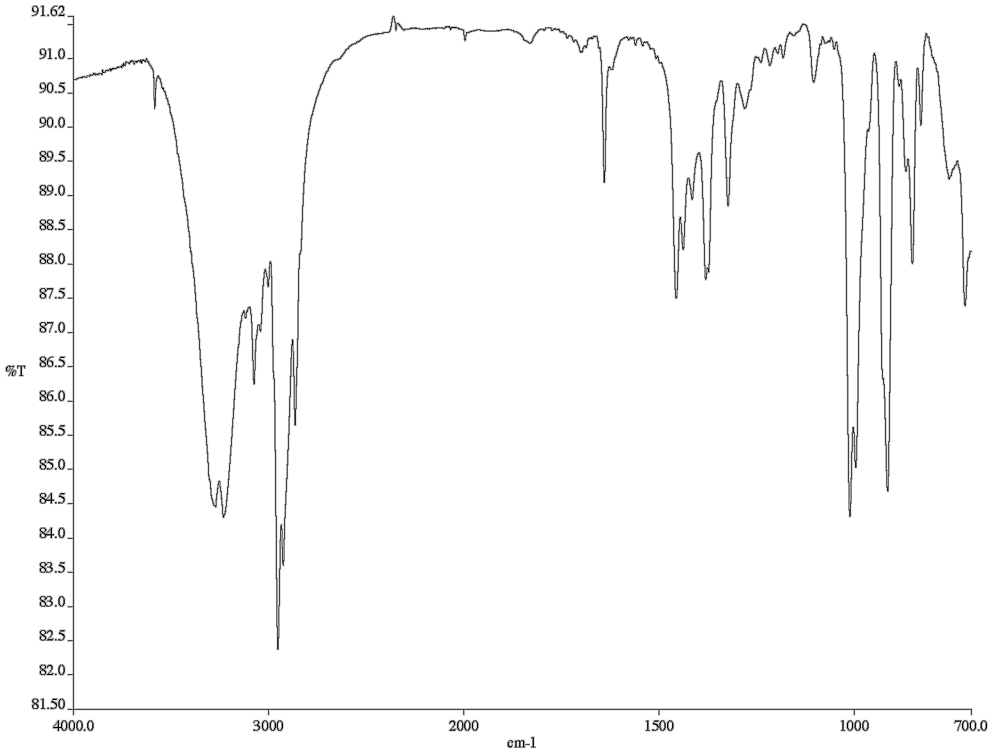

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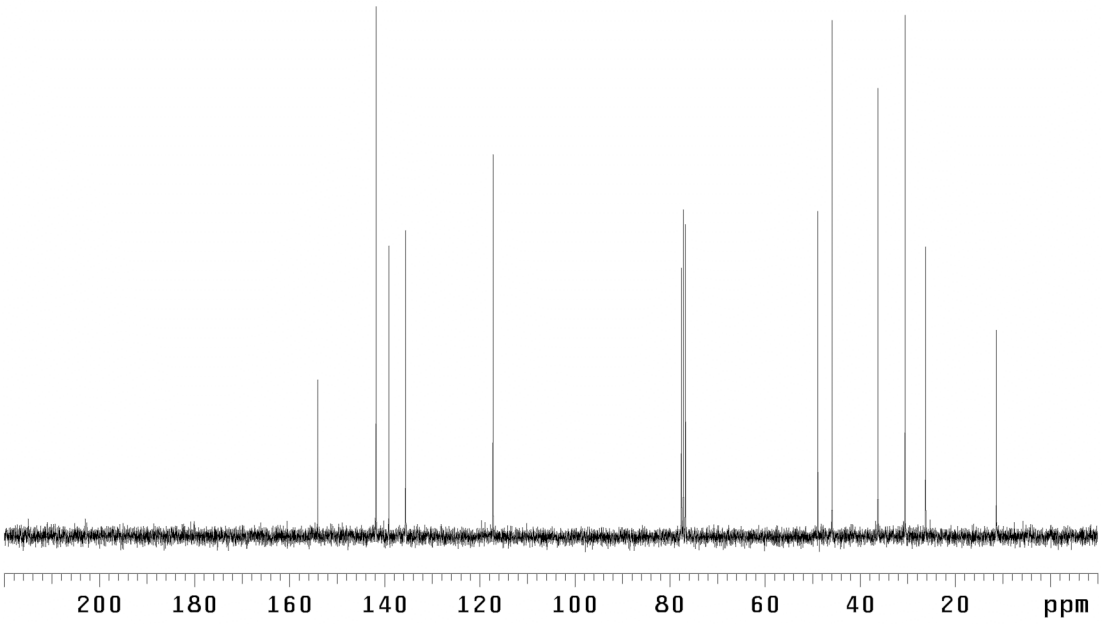

Figure SI-14C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **21**.

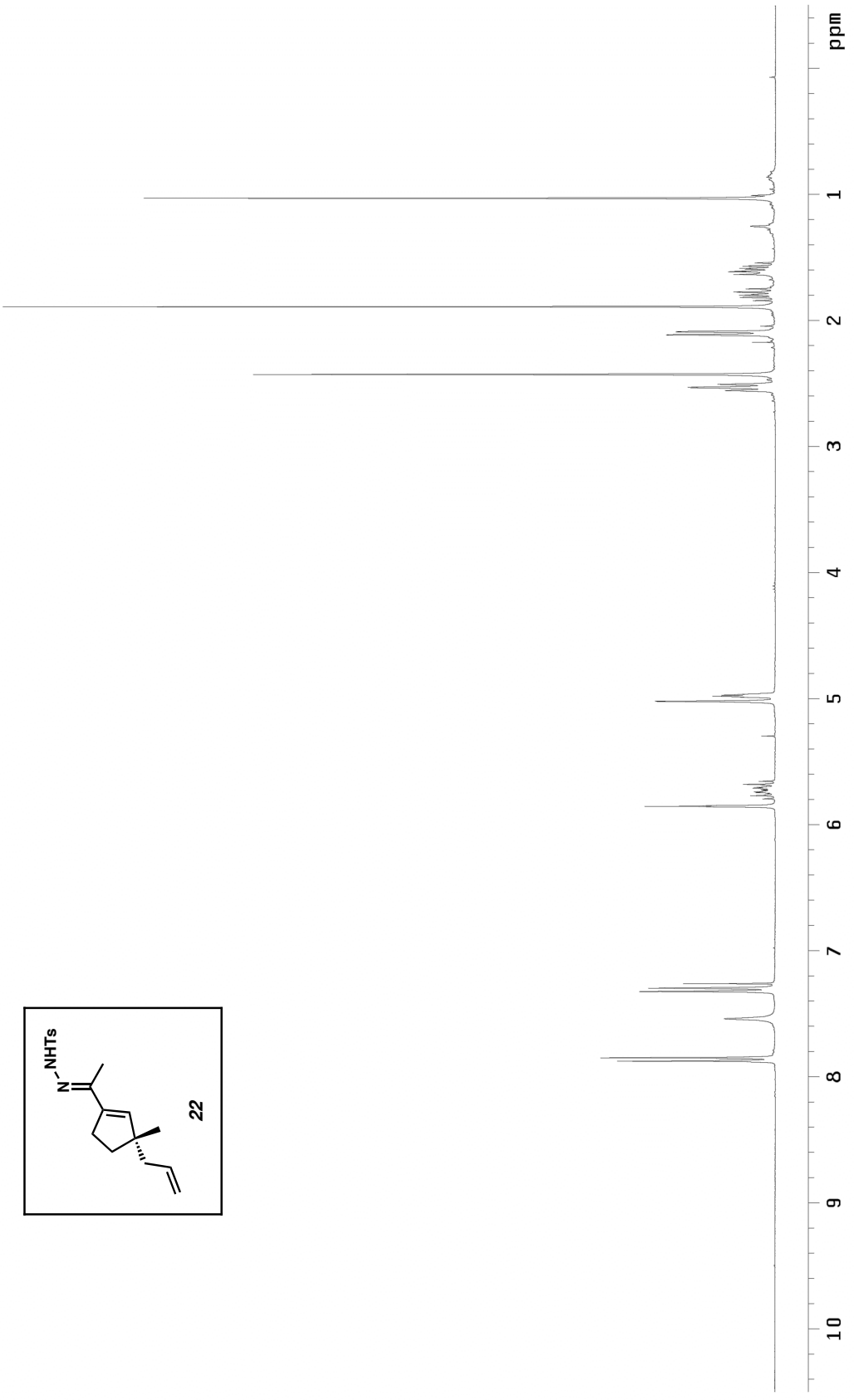

Figure SI-15A. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **22**.

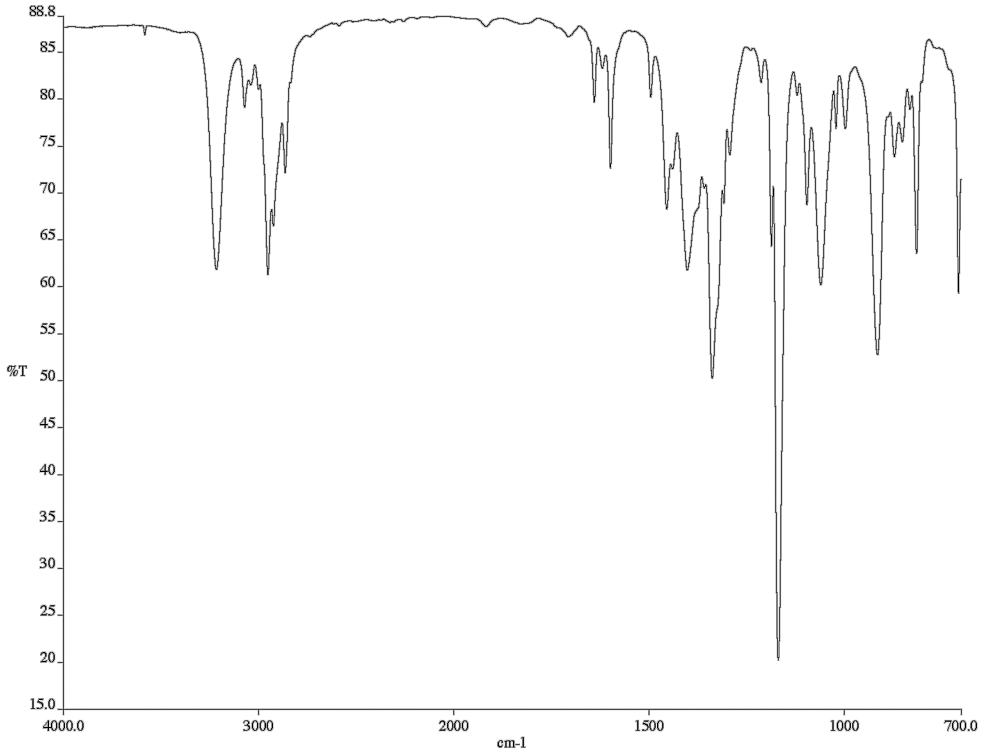

Figure SI-15B. Infrared spectrum (thin film/NaCl) of compound **22**.

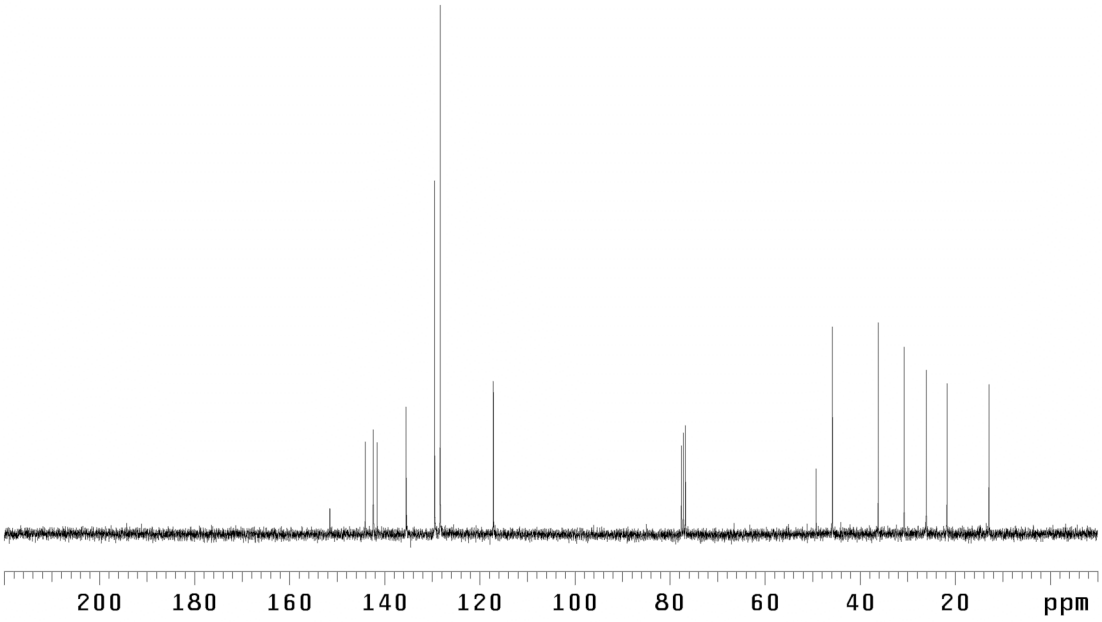

Figure SI-15C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **22**.

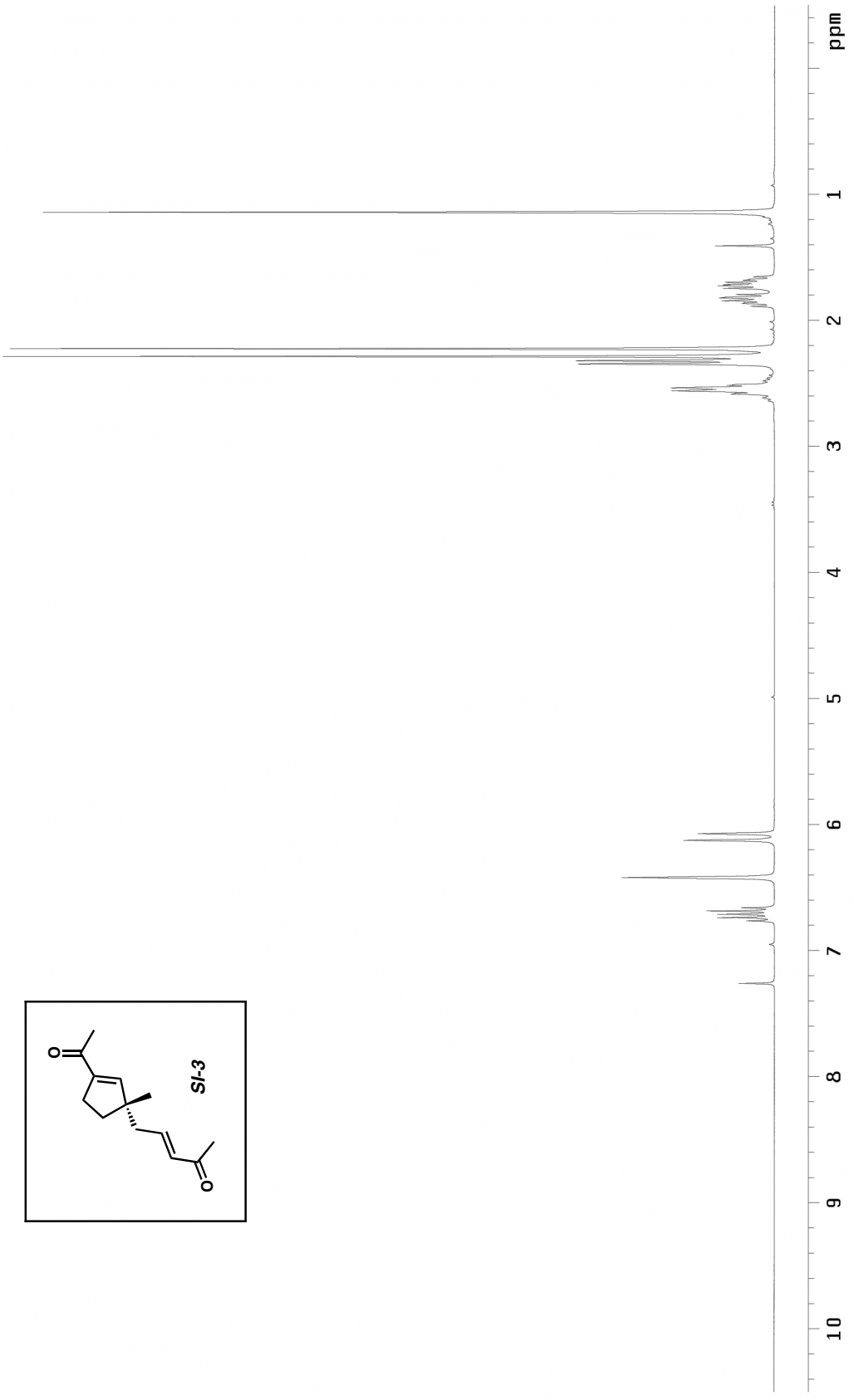

Figure SI-16A. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **SI-3**.

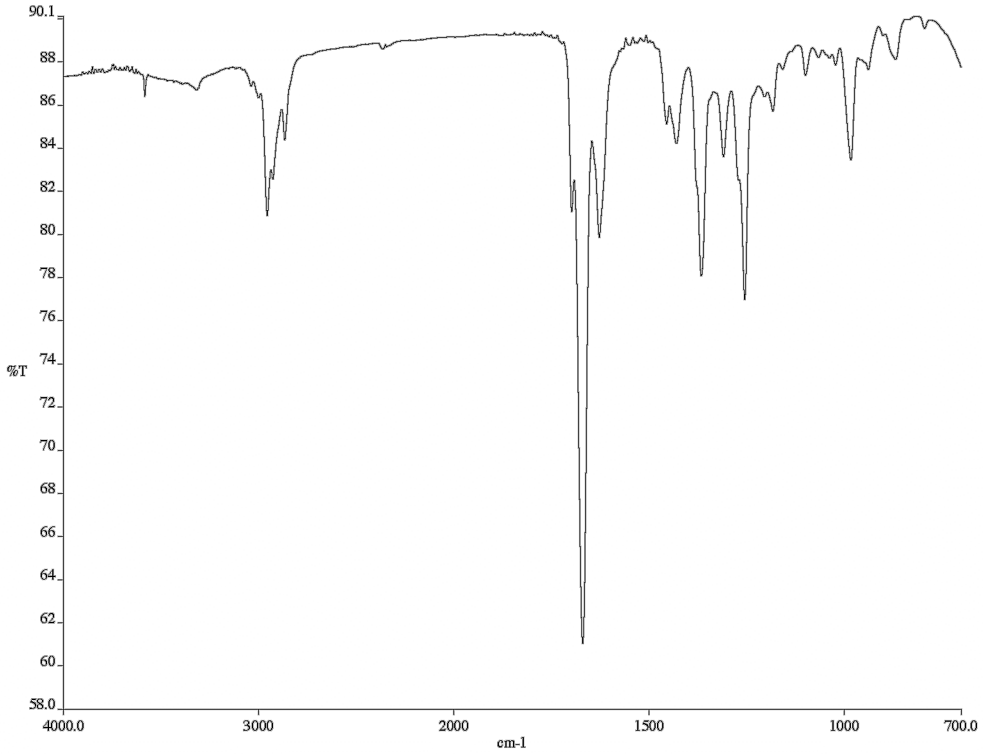

Figure SI-16B. Infrared spectrum (thin film/NaCl) of compound **SI-3**.

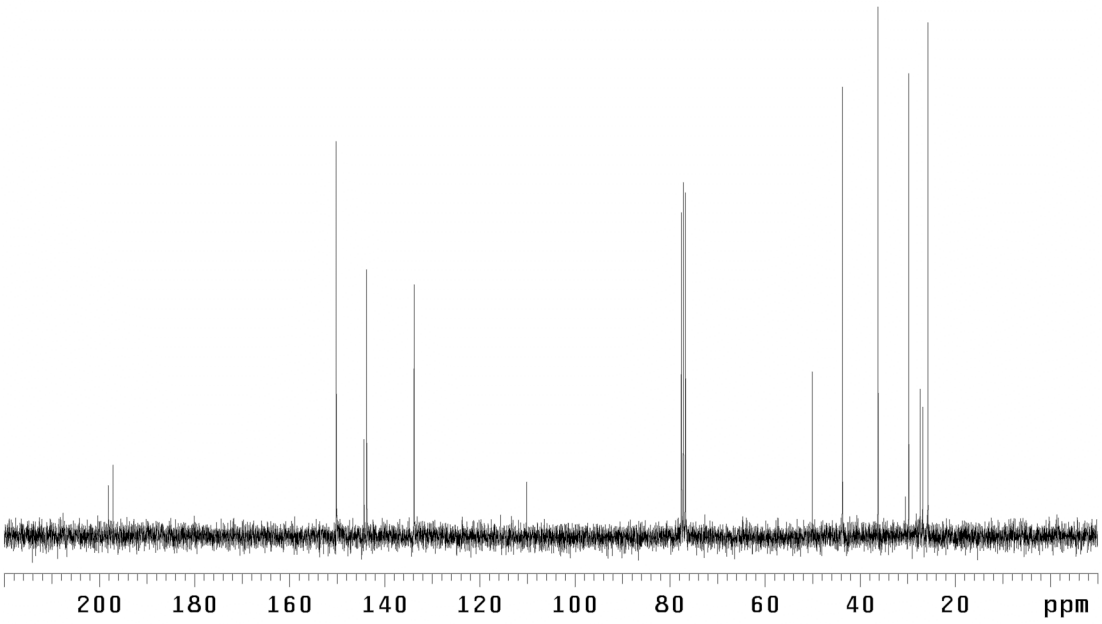

Figure SI-16C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **SI-3**.

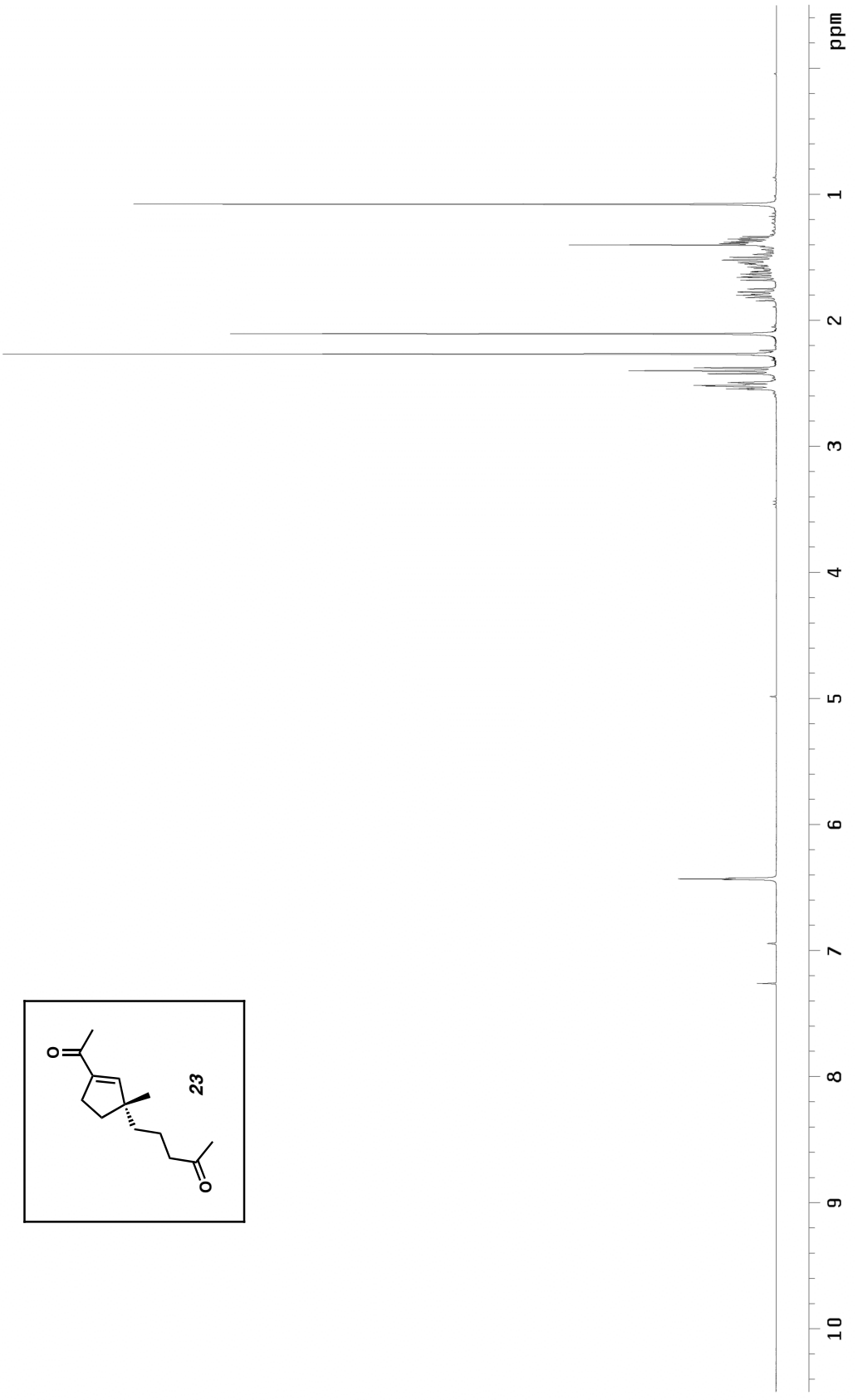

Figure SI-17A. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **23**.

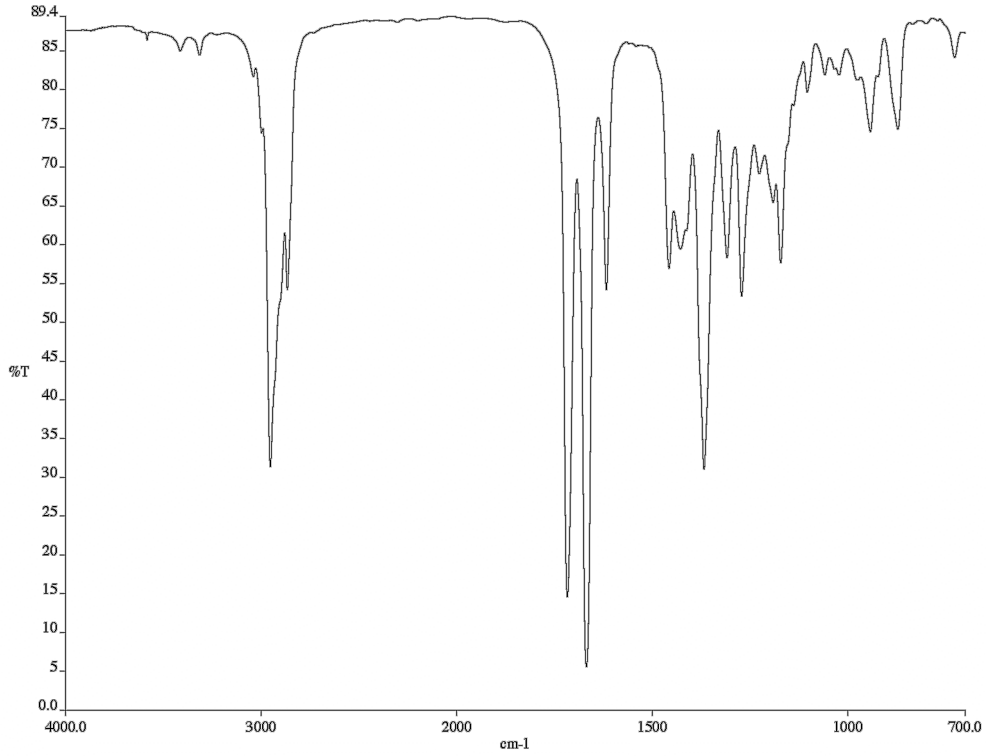

Figure SI-17B. Infrared spectrum (thin film/NaCl) of compound **23**.

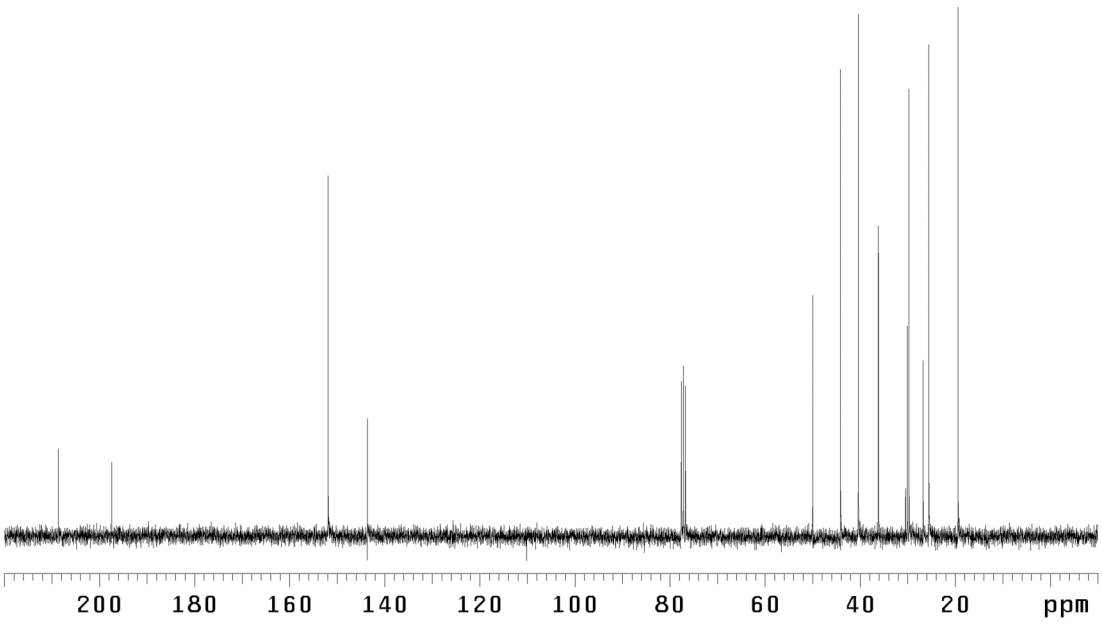

Figure SI-17C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **23**.

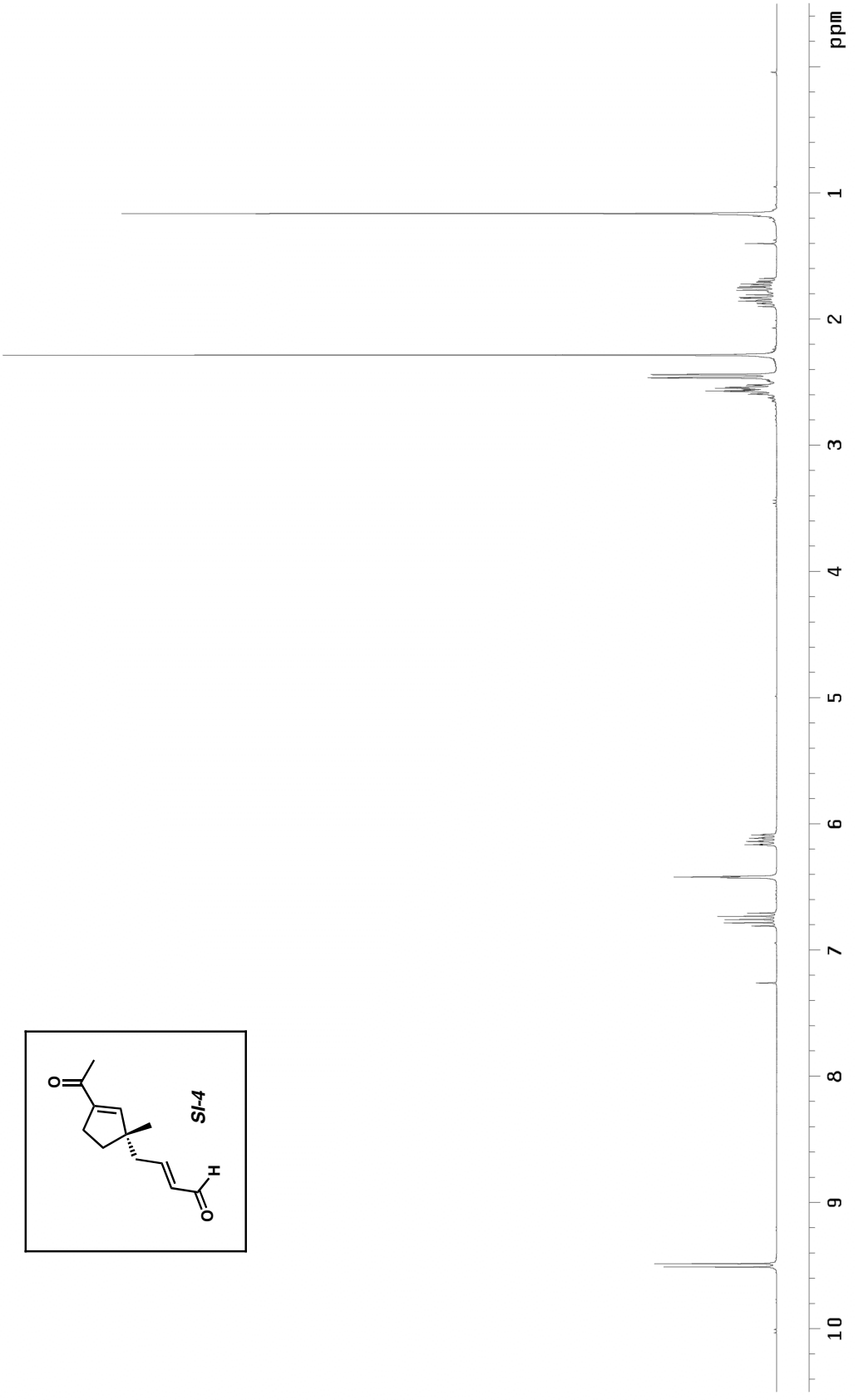

Figure SI-184. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **SI-4**.

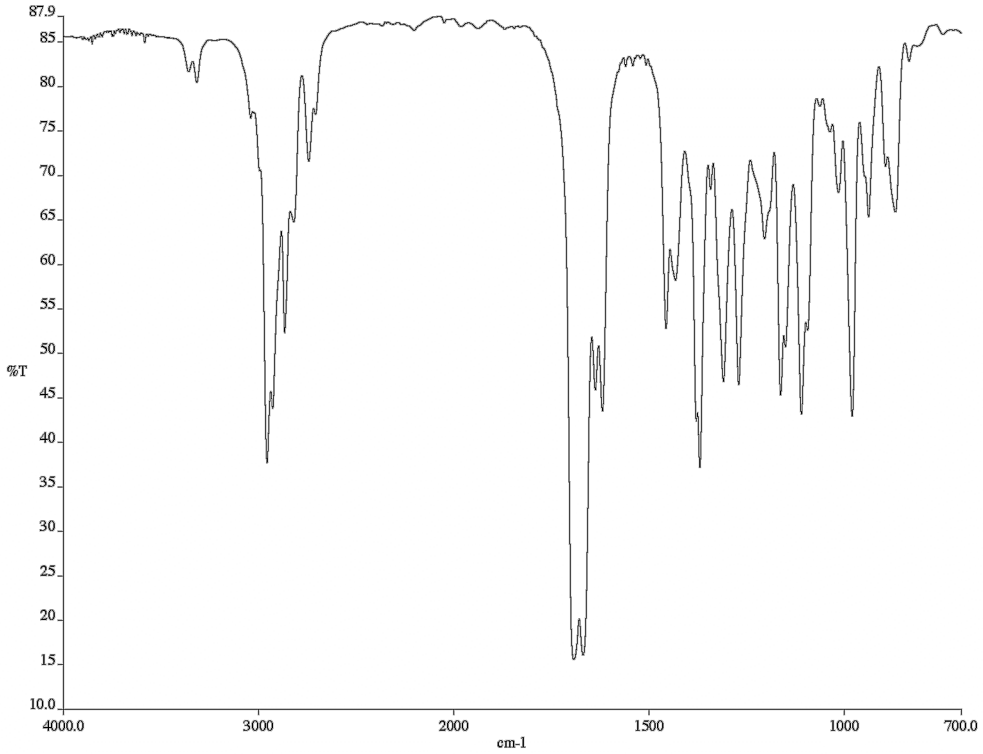

Figure SI-18B. Infrared spectrum (thin film/NaCl) of compound **SI-4**.

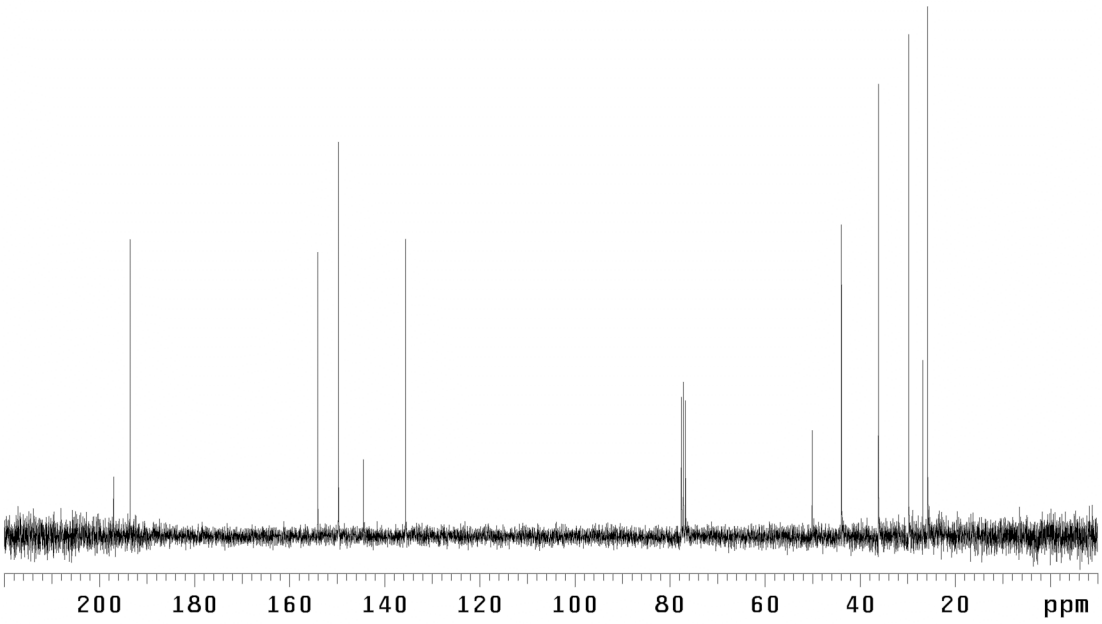

Figure SI-18C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **SI-4**.

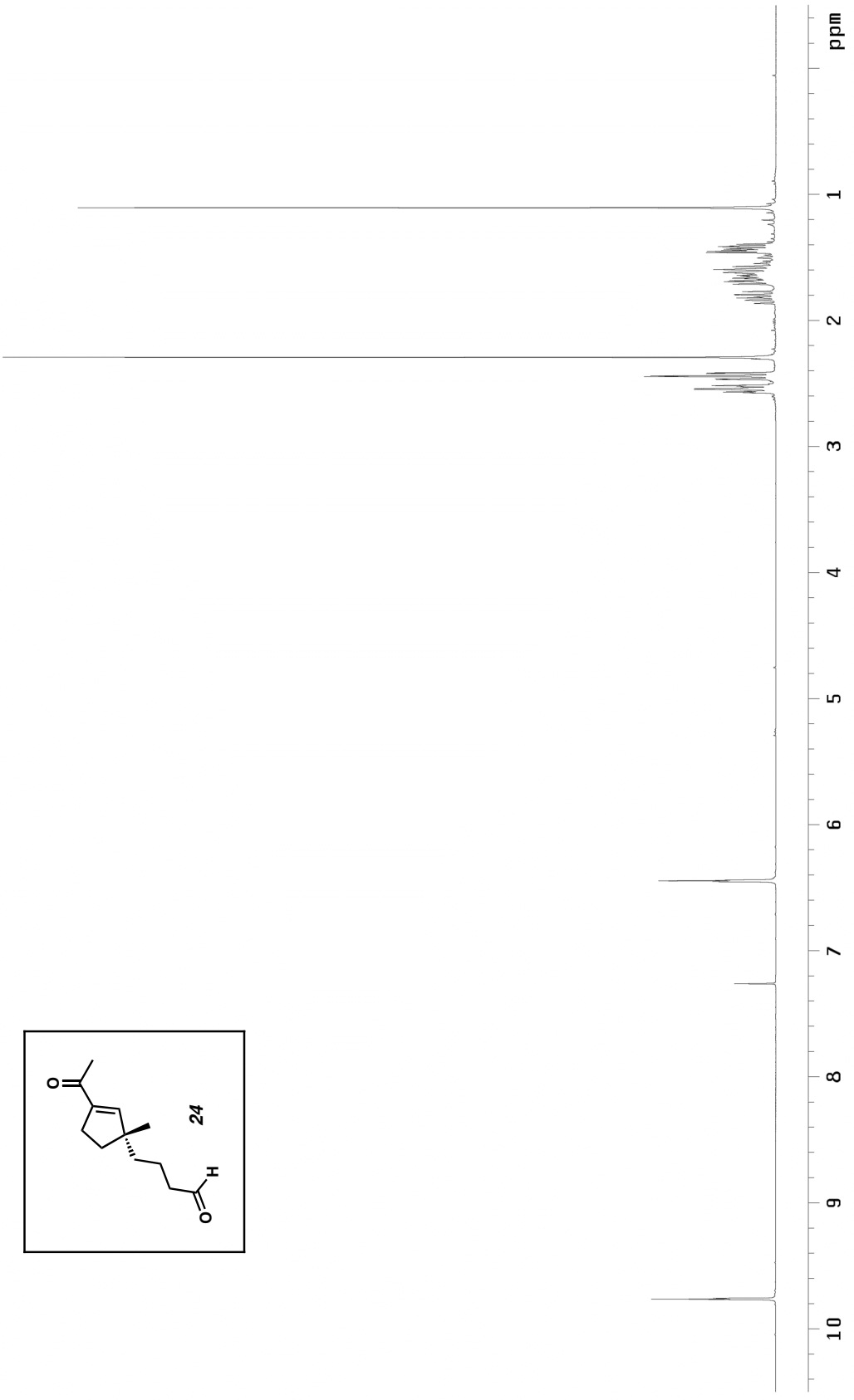

Figure SI-19A. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **24**.

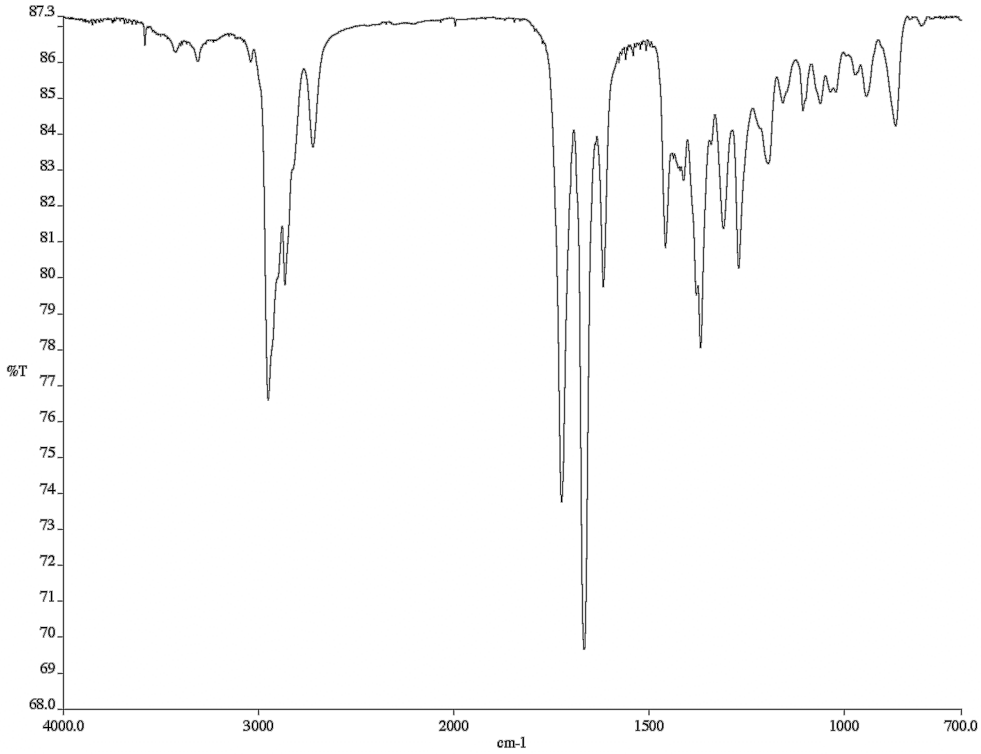

Figure SI-19B. Infrared spectrum (thin film/NaCl) of compound **24**.

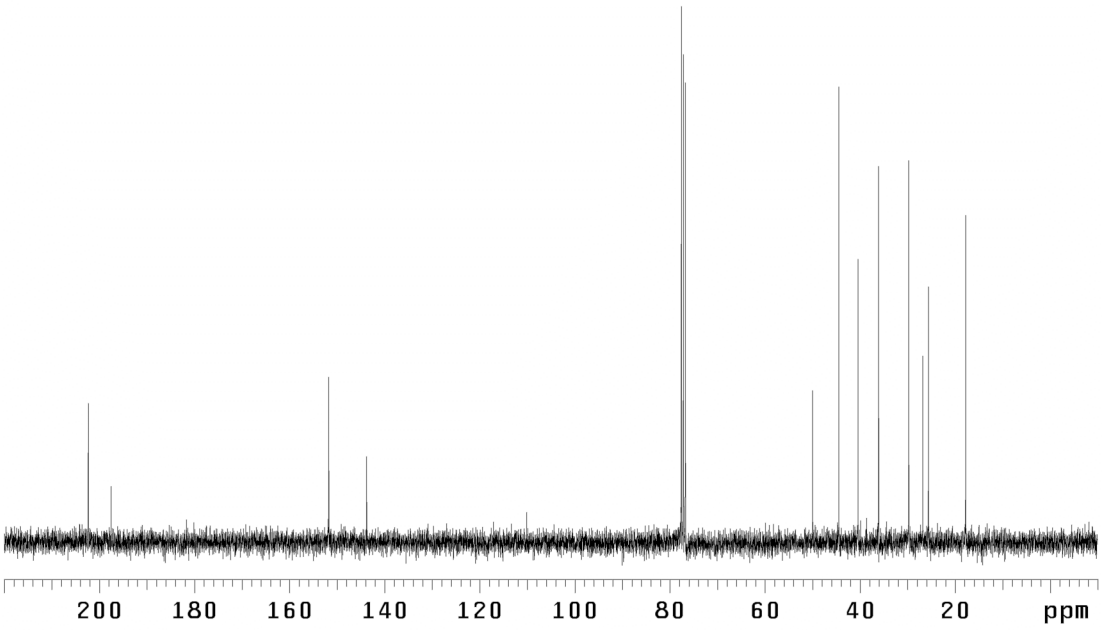

Figure SI-19C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **24**.

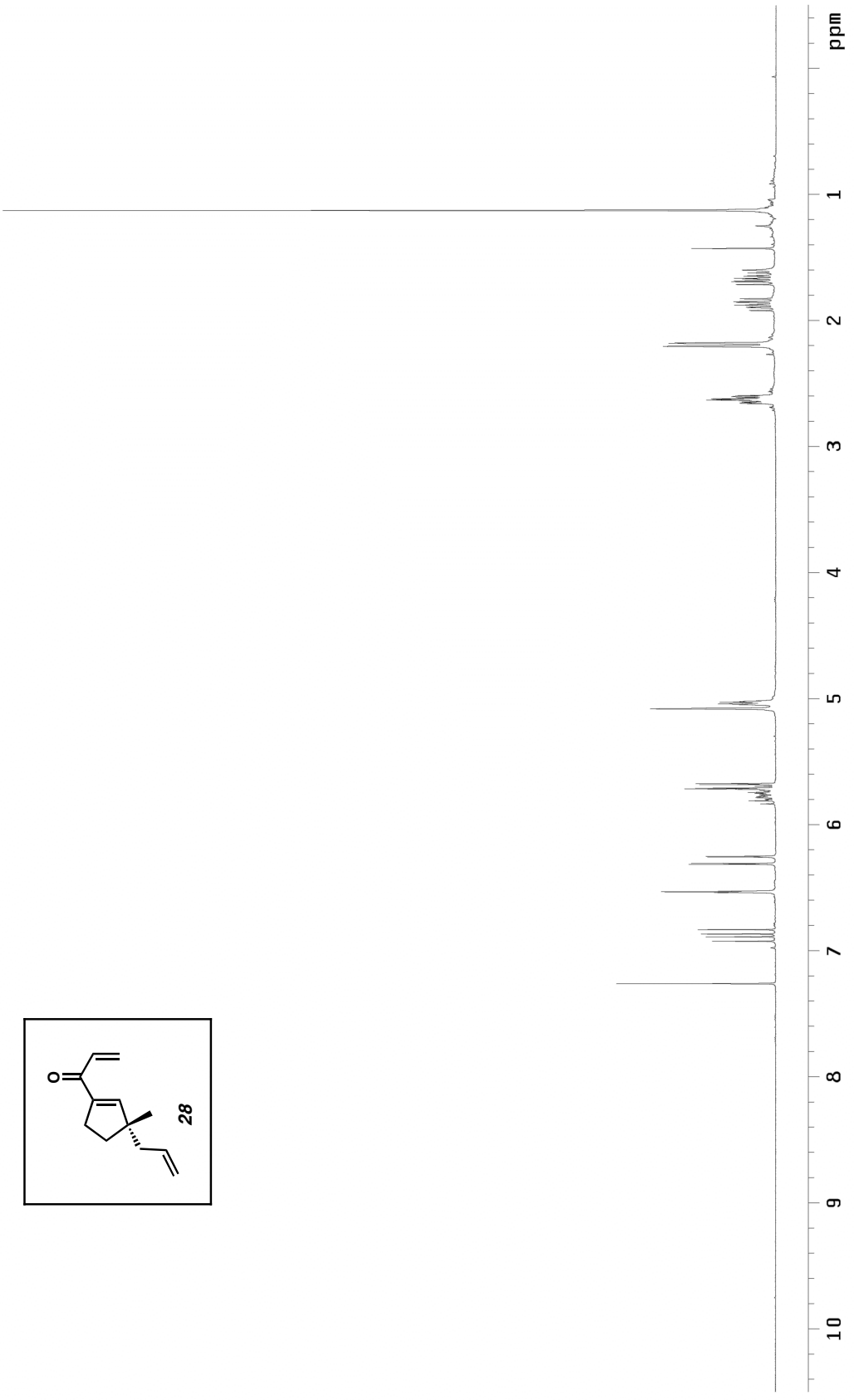

Figure SI-20A. ^{1}H NMR (300 MHz, $CDCl_3$) of compound **28**.

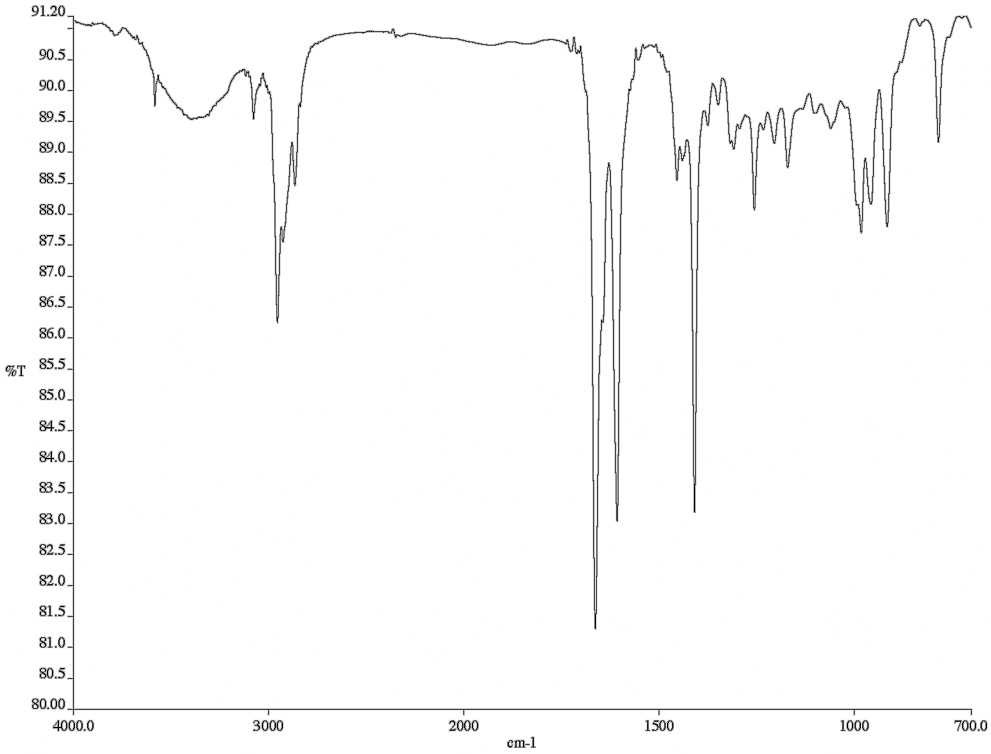

Figure SI-20B. Infrared spectrum (thin film/NaCl) of compound **28**.

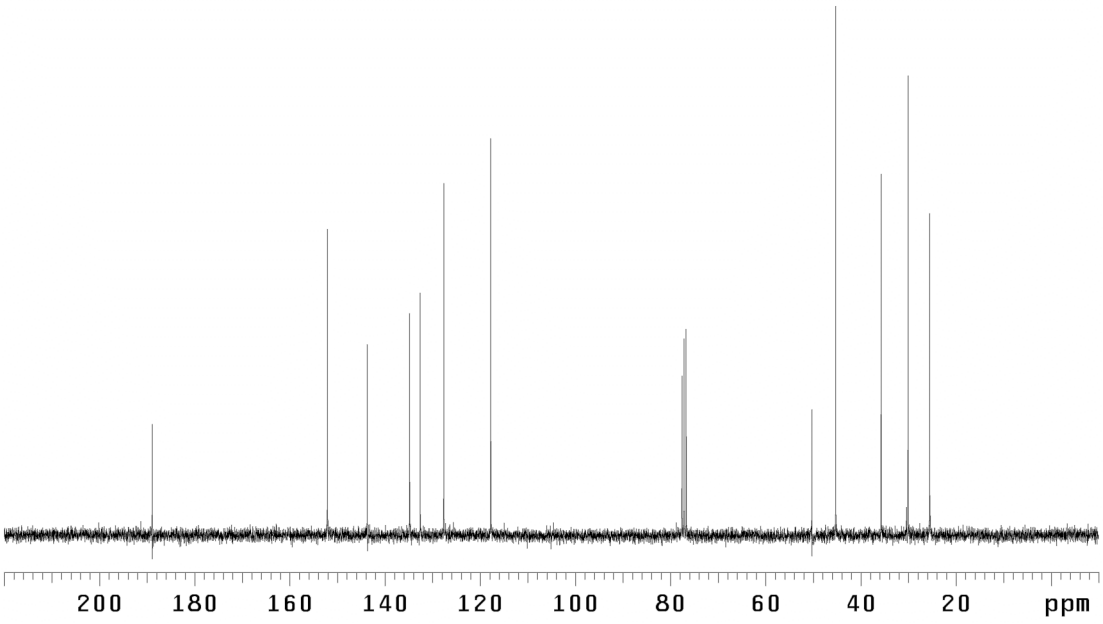

Figure SI-20C. ^{13}C NMR (75 MHz, $CDCl_3$) of compound **28**.

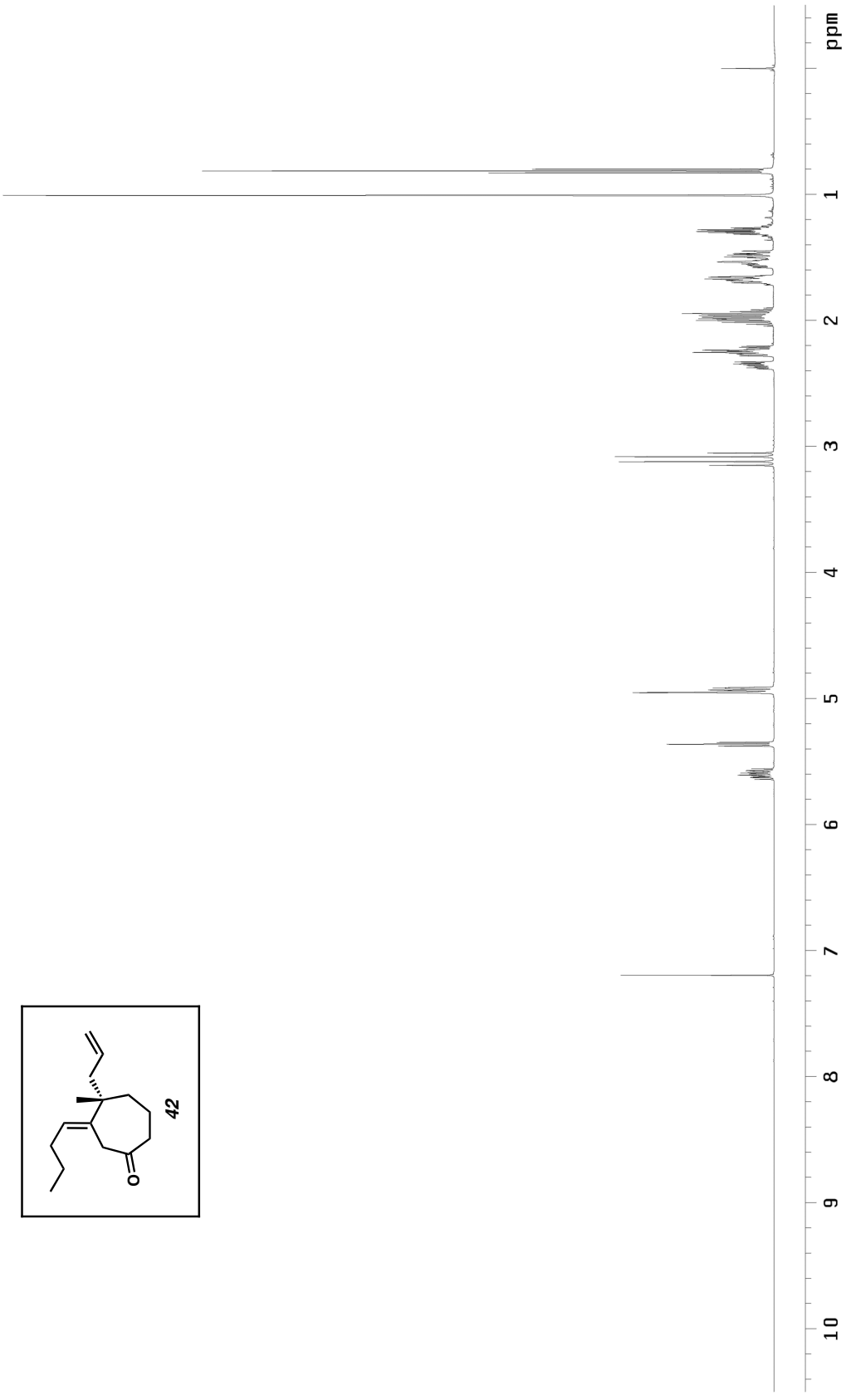

Figure SI-21A. ^{1}H NMR (500 MHz, $CDCl_3$) of compound **42**.

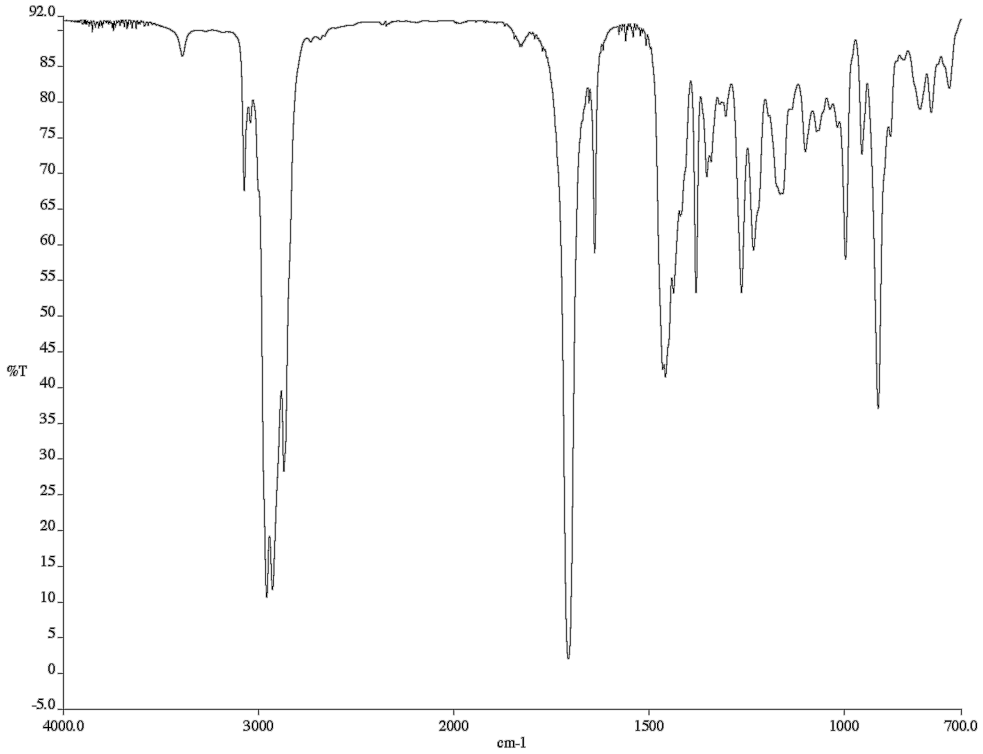

Figure SI-21B. Infrared spectrum (thin film/NaCl) of compound **42**.

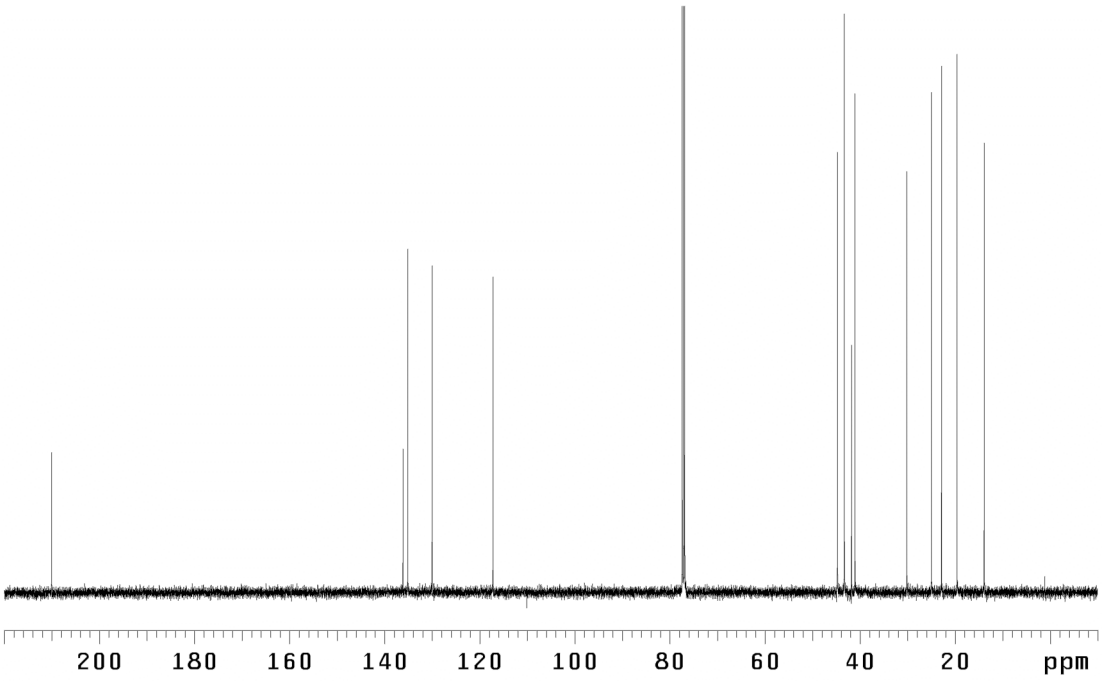

Figure SI-21C. ^{13}C NMR (125 MHz, $CDCl_3$) of compound **42**.

Data File C:\NEW HPLC FILES\6-43C.D
Sample Name: AYH-VI-43C

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Acq. Operator    : AYH                          Seq. Line :   5
Acq. Instrument : Instrument 3                   Location : Vial 93
Injection Date   : 10/9/2009 10:10:09 AM              Inj :   1
                                                Inj Volume : 5.000 µl
Acq. Method      : C:\HPCHEM\3\METHODS\D20-30.M
Last changed     : 10/9/2009 12:14:29 AM by RN
Analysis Method : C:\CHEM32\2\METHODS\POS2.M
Last changed     : 7/26/2011 10:24:10 AM by JK
                   (modified after loading)
Method Info      : POSITION #2 METHOD : Valve to Position # 2 (Column # 1).

Sample Info      : 20% D Bottle, D=5% IPA/Hex, 254 nm, 1 mL/min, 30 min, O
                   D-H
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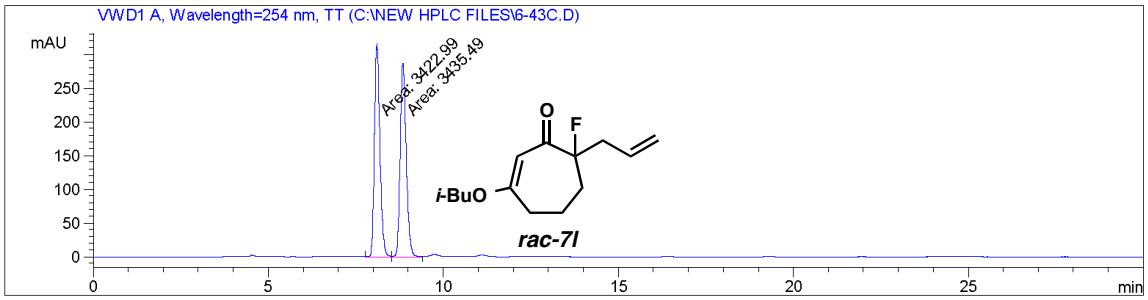


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======================================================================
                        Area Percent Report
======================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1   8.104 MF    0.1808 3422.98999  315.56567  49.9088
   2   8.849 FM    0.1995 3435.49341  287.07703  50.0912

Totals :                  6858.48340  602.64270


======================================================================
                        *** End of Report ***
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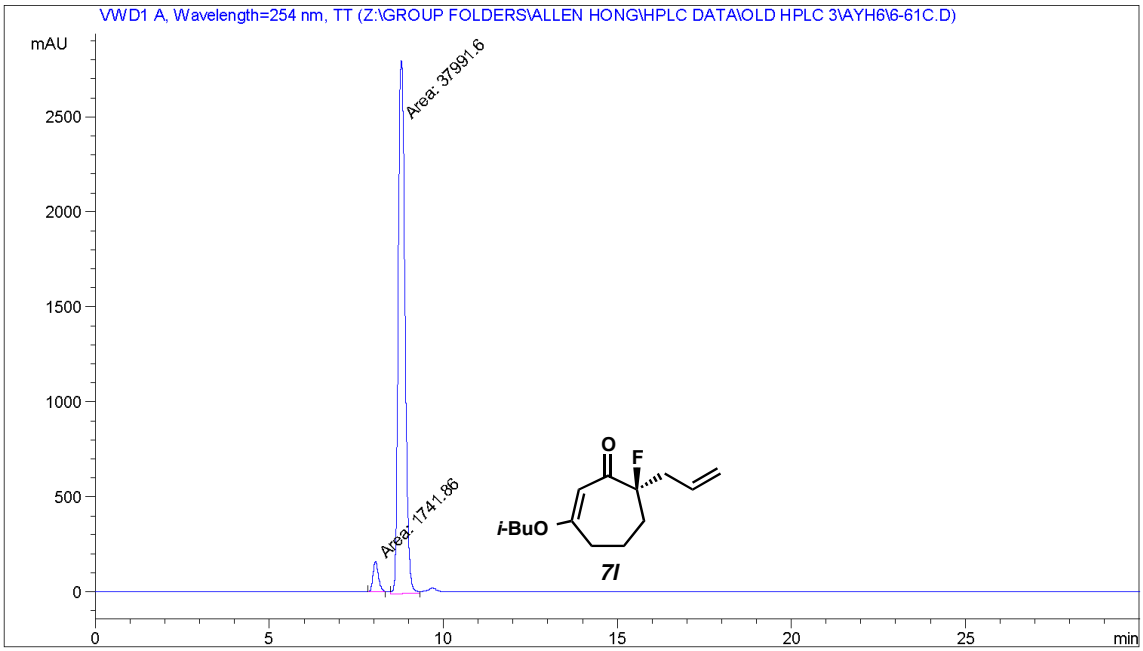
```
Data File Z:\GROUP FOLDERS\ALLEN HONG\HPLC DATA\OLD HPLC 3\AYH6\6-61C.D
Sample Name: AYH-VI-61C

    ======================================================================
    Acq. Operator   : AYH                          Seq. Line :   6
    Acq. Instrument : Instrument 3                  Location : Vial 83
    Injection Date  : 10/9/2009 10:41:07 AM              Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\HPCHEM\3\METHODS\D20-30.M
    Last changed    : 10/9/2009 12:14:29 AM by RN
    Analysis Method : C:\CHEM32\2\METHODS\POS2.M
    Last changed    : 11/3/2010 10:03:07 PM by JJD
                      (modified after loading)
    Method Info     : POSITION #2 METHOD : Valve to Position # 2 (Column # 1).

    Sample Info     : 20% D Bottle, D=5% IPA/Hex, 254 nm, 1 mL/min, 30 min, O
                      D-H
```

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    ======================================================================
                            Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=254 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1   8.053 MM    0.1810 1741.85535  160.39209   4.3839
       2   8.797 MM    0.2255 3.79916e4  2807.74292  95.6161
```

Data File C:\NEW HPLC FILES\6-227C.D
Sample Name: AYH-VI-227C

```
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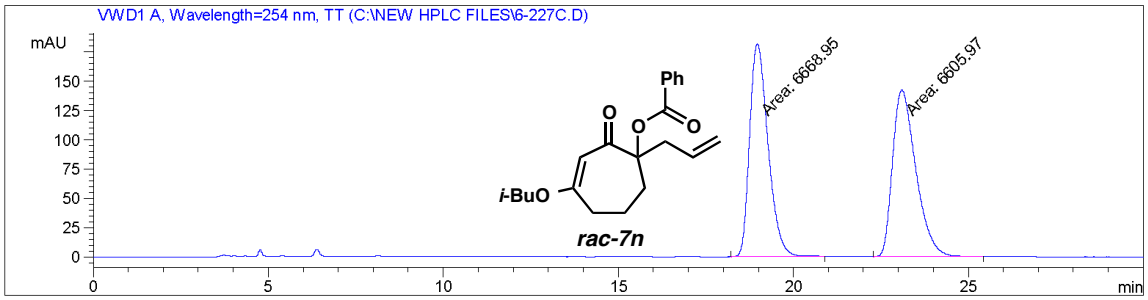
Acq. Operator    : AYH                          Seq. Line :   3
Acq. Instrument : Instrument 3                   Location : Vial 91
Injection Date   : 10/29/2009 5:35:13 PM              Inj :   1
                                                Inj Volume : 5.000 µl
Acq. Method      : C:\HPCHEM\3\METHODS\D20-30.M
Last changed     : 10/9/2009 12:14:29 AM by RN
Analysis Method : C:\CHEM32\2\METHODS\POS2.M
Last changed     : 7/26/2011 10:24:10 AM by JK
                   (modified after loading)
Method Info      : POSITION #2 METHOD : Valve to Position # 2 (Column # 1).

Sample Info      : 20% D Bottle, D=5% IPA/Hex, 210 nm, 1 mL/min, 30 min, O
                   D-H
```

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==========================================================================
                          Area Percent Report
==========================================================================

Sorted By             :      Signal
Multiplier:                   :      1.0000
Dilution:                     :      1.0000
Use Multiplier & Dilution Factor with ISTDs


Signal 1: VWD1 A, Wavelength=254 nm, TT

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]  mAU   *s    [mAU   ]      %
----|-------|----|-------|----------|----------|--------|
   1  18.972 MM    0.6100 6668.95264  182.20268  50.2372
   2  23.100 MM    0.7713 6605.96533  142.74507  49.7628

Totals :                  1.32749e4   324.94775

==========================================================================
                          *** End of Report ***
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```
Data File Z:\GROUP FOLDERS\ALLEN HONG\HPLC DATA\OLD HPLC 3\AYH6\6-229C.D
Sample Name: AYH-VI-229C

    ======================================================================
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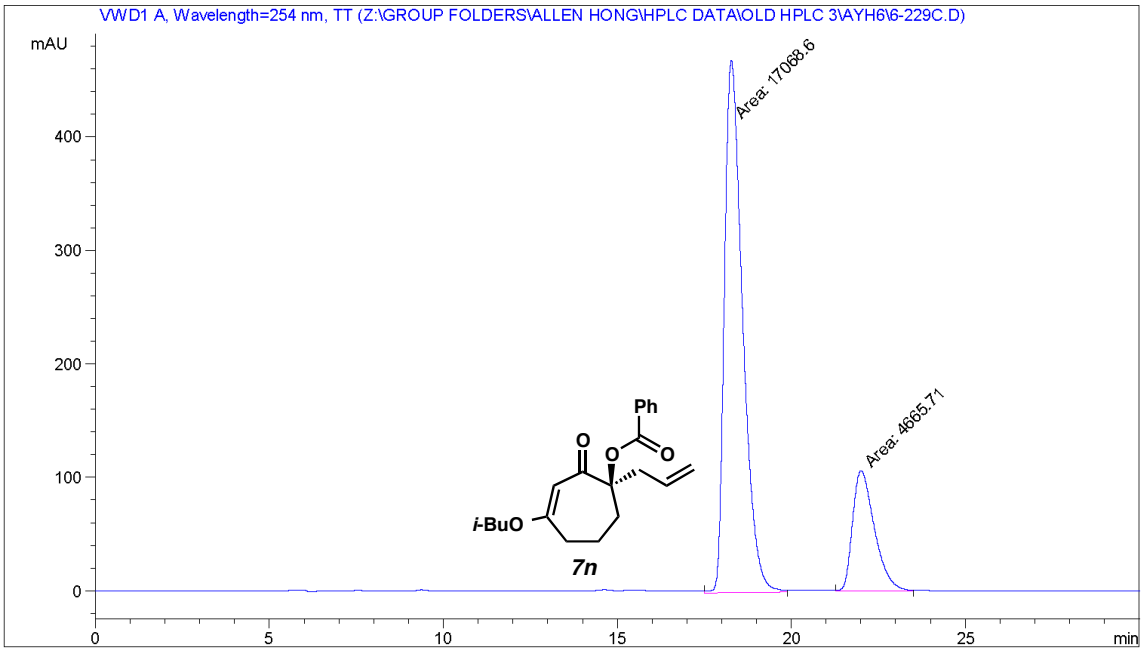
    Acq. Instrument : Instrument 3                  Location : Vial 92
    Injection Date  : 10/29/2009 9:02:09 PM              Inj :   1
                                                  Inj Volume : 5.000 µl
    Acq. Method     : C:\HPCHEM\3\METHODS\D20-30.M
    Last changed    : 10/9/2009 12:14:29 AM by RN
    Analysis Method : C:\CHEM32\2\METHODS\POS2.M
    Last changed    : 11/3/2010 10:03:07 PM by JJD
                      (modified after loading)
    Method Info     : POSITION #2 METHOD : Valve to Position # 2 (Column # 1).

    Sample Info     : 20% D Bottle, D=5% IPA/Hex, 210 nm, 1 mL/min, 30 min, O
                      D-H
```

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    ======================================================================
                              Area Percent Report
    ======================================================================

    Sorted By             :      Signal
    Multiplier:                   :      1.0000
    Dilution:                     :      1.0000
    Use Multiplier & Dilution Factor with ISTDs


    Signal 1: VWD1 A, Wavelength=254 nm, TT

    Peak RetTime Type  Width     Area      Height     Area
      #   [min]        [min]  mAU   *s    [mAU   ]      %
    ----|-------|----|-------|----------|----------|--------|
       1  18.277 MM    0.6064 1.70686e4   469.12473  78.5330
       2  22.005 MF    0.7315 4665.71143  106.30950  21.4670
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