Supporting Information for:

Homogeneous Pd-Catalyzed Enantioselective Decarboxylative Protonation

Smaranda C. Marinescu, Toyoki Nishimata, Justin T. Mohr, and Brian M. Stoltz*

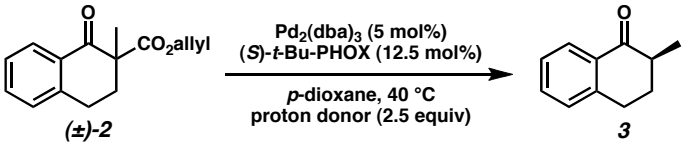
The Arnold and Mabel Beckman Laboratories of Chemical Synthesis, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125, USA

Table of Contents:

Materials and Methods. Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. *p*-Dioxane and C_6D_6 were distilled over sodium prior to use unless specifically noted. Other solvents were dried by passage through an activated alumina column under argon. Brine solutions are saturated aqueous sodium chloride solutions. Tris(dibenzylideneacetone)dipalladium(0) ($Pd_2(dba)_3$) was purchased from Strem and stored in a dessicator under argon atmosphere prior to use. Phosphinooxazoline ligands[1] and β-ketoesters substrates[2] were prepared by the method reported in our previous work. All the starting materials were purchased from Aldrich or Alfa Aersar and used as received, unless otherwise stated. Sodium hydride (NaH) was purchased as a 60% dispersion in mineral oil from Acros and used as received. Meldrum's acid was recrystallized from ethyl acetate prior to use. Reaction temperatures were controlled by an IKAmag temperature modulator. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, anisaldehyde, $KMnO_4$, or CAM staining. ICN Silica gel (particle size 0.032-0.063 mm) was used for flash chromatography. Analytical chiral HPLC was performed with an Agilent 1100 Series HPLC utilizing a Chiracel OD-H or Chiralpak AD column (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. with visualization at 254 nm, unless otherwise stated. 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). Optical rotations were measured with a Jasco P-1010 polarimeter at 589 nm. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 spectrometer (at 300 MHz and 75 MHz, respectively), and are reported relative to Me_4Si (δ 0.0 ppm). Temperature controlled ^{1}H NMR kinetic experiments were performed on a Varian Inova 500 MHz. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Data for ^{13}C are reported in terms of chemical shift. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). Melting points were determined using a Thomas capillary melting point apparatus and the values reported are uncorrected. High resolution mass spectra were obtained from the Caltech Mass Spectral Facility.

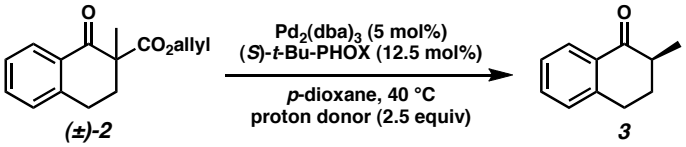
Screening of Achiral Proton Donors (Table 1)

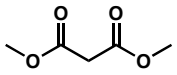
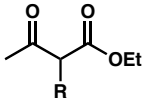
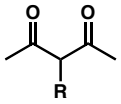
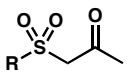
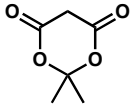
The reactions were carried out using the following sample procedure.



Sample Procedure for Screening of the Achiral Proton Donors:
A 10 mL Schlenk tube equipped with a magnetic stir bar, and a teflon stopcock was flame dried under vacuum (3x, backfill with dry argon). After cooling to ambient temperature under dry argon, $Pd_2(dba)_3$ (4.5 mg, 0.005 mmol, 0.05 equiv, 5 mol%), (*S*)-*t*-Bu-PHOX (4.6 mg, 0.0125 mmol, 0.125 equiv, 12.5 mol%), and freshly distilled *p*-dioxane (1 mL) were added, and the resulting mixture was stirred vigorously at 40 ºC for 30 min. A *p*-dioxane solution (2 mL) of allyl β-ketoester **2** (24.4 mg, 0.1 mmol, 1.0 equiv) and achiral proton donor (0.25 mmol, 2.5 equiv) was added to the reaction mixture at 40 °C. When the reaction was complete by TLC, the reaction mixture was filtered through a pad of SiO_2 and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography on SiO_2 using 5% Et_2O in petroleum ether as the eluent. The ee of the product **3** was determined by chiral HPLC using a Chiracel OD-H column with 1% 2-propanol in hexanes as the eluent.

Table 1. Screening of Achiral Proton Donors[a]



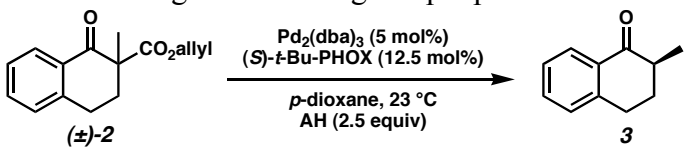
Entry	Proton Donor		Time (h)	Conversion (%)[b]	ee (%)[c]
1			24	85	62
2		R = H	24	50	80
3		R = F	24	55	89
4		R = H	24	95	50
5		R = Ac	2	100	74
6		R = Ms	3	100	88
7		R = Me	24	42	89
8		R = Ph	24	63	90
9		R = *p*-Tol	5	100	84
10			0.2	100	85
11[d]			0.5	100	90
12[e]			24	50	95
13[f]			1.5	100	43

[a] Reactions performed with 0.1 mmol of (±)-**2** at 0.033 M in *p*-dioxane. [b] Measured by ^{1}H NMR spectroscopy. [c] Measured by chiral HLPC. [d] Reaction performed at 23 °C. [e] Reaction performed at 0 °C in THF solvent. [f] Reaction performed with 90 mg of 4 Å MS.

3-(Methylsulfonyl)pentane-2,4-dione (Table 1, Entry 6) was prepared according to the literature method.[3]

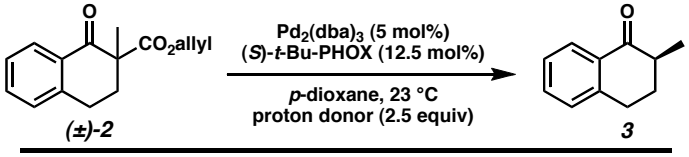
Screening of Meldrum's Acid Derivatives (Table 2)

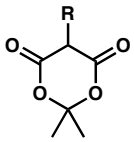
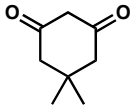
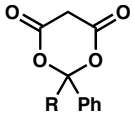
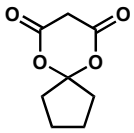
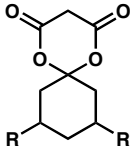
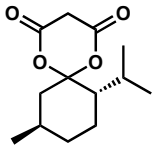
The reactions were carried out using the following sample procedure.



Sample Procedure for Screening of Meldrum's Acid Derivatives:
A 1 dram glass vial equipped with a magnetic stir bar, a screw cap, and a septum was flame dried under vacuum (3x, backfill with dry argon). After cooling to ambient temperature under dry argon, $Pd_2(dba)_3$ (4.5 mg, 0.005 mmol, 0.05 equiv, 5 mol%), (*S*)-*t*-Bu-PHOX (4.6 mg, 0.0125 mmol, 0.125 equiv, 12.5 mol%), and freshly distilled *p*-dioxane (1 mL) were added, and the resulting mixture was stirred vigorously at 40 ºC for 30 min. A *p*-dioxane solution (2 mL) of allyl β-ketoester **2** (24.4 mg, 0.1 mmol, 1.0 equiv) and Meldrum's acid derivative (AH) (0.25 mmol, 2.5 equiv) was added to the reaction mixture at 23 °C. When the reaction was complete by TLC, the reaction mixture was filtered through a pad of SiO_2 and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography on SiO_2 using 5% Et_2O in petroleum ether as the eluent. The ee of the product **3** was determined by chiral HPLC using a Chiracel OD-H column with 1% 2-propanol in hexanes as the eluent.

Table 2. Screening of Meldrum's Acid Derivatives[a]



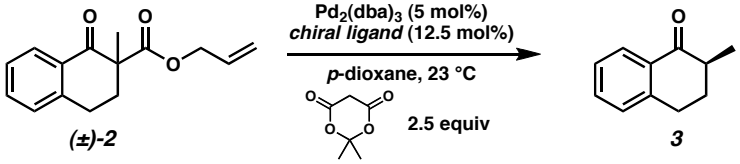
Entry	Proton Donor		Time (h)	Conversion (%)[b]	ee (%)[c]
1		R = H	0.5	100	90
2		R = Me	0.2	100	90
3		R = Ph	24	86	68
4		R = Allyl	1	100	67
5		R = Ac	24	1	51
6			24	8	43
7		R = H	5	100	85
8		R = Me	4	100	84
9			24	25	93
10		R = H	24	86	91
11		R = Me	24	100	76
12			24	100	90
13[d]			24	100	–90

[a] Reactions performed with 0.1 mmol of (±)-**2** at 0.033 M in *p*-dioxane. [b] Measured by ^{1}H NMR spectroscopy. [c] Measured by chiral HLPC. [d] Reaction performed with (*R*)-*t*-Bu-PHOX (12.5 mol%).

Meldrum's acid derivatives in entries 4[4], 8[5], 12, and 13[6] (Table 2) were prepared by literature methods.

Screening of Chiral Ligands (Table SI1)

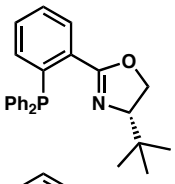
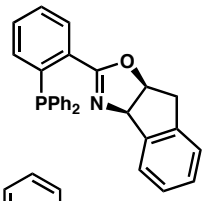
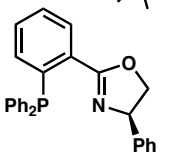
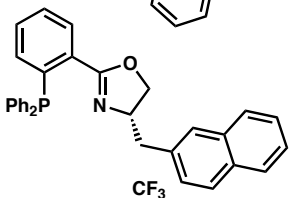
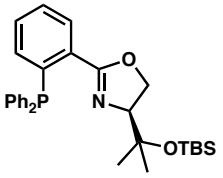
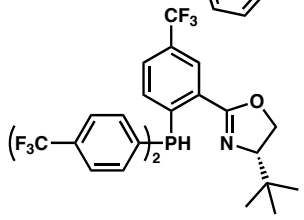
Optimization reactions were carried out using the following sample procedure.



Sample Procedure for Optimization Reactions:

A 1 dram glass vial equipped with a magnetic stir bar, a screw cap, and a septum was flame dried under vacuum (3x, backfill with dry argon). After cooling to ambient temperature under dry argon, $Pd_2(dba)_3$ (4.5 mg, 0.005 mmol, 0.05 equiv, 5 mol%), chiral ligand (0.0125 mmol, 0.125 equiv, 12.5 mol%), and freshly distilled *p*-dioxane (1 mL) were added, and the resulting mixture was stirred vigorously at 40 ºC for 30 min. A *p*-dioxane solution (2 mL) of β-ketoester **2** (24.4 mg, 0.1 mmol, 1.0 equiv) and Meldrum's acid (36 mg, 0.25 mmol, 2.5 equiv) was added to the reaction mixture at 23 °C. When the reaction was complete by TLC, the reaction mixture was filtered through a pad of SiO_2 and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography on SiO_2 using 5% Et_2O in petroleum ether as the eluent. The ee of the product was determined by chiral HPLC using a Chiracel OD-H column with 1% 2-propanol in hexanes as the eluent.

Table SI 1. Optimization of Chiral Ligand[a]

Entry	Chiral Ligand	ee (%)[b] of 3	Entry	Chiral Ligand	ee (%)[b] of 3
1		90	4		–82
2		–77	5		67
3		–79	6		80

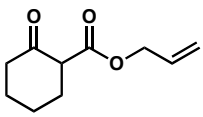
[a]Reactions performed with 0.1 mmol of (±)-**2** at 0.033 M in solvent. [b]Measured by chiral HPLC.

Chiral ligands shown in Table SI 1, entries 1–6 were prepared in our previous work.[1]

Enantioconvergent Decarboxylative Protonations (Table 3)

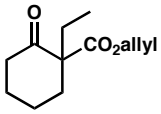
Substrates shown in Table 3, entries 1, 3, 5, 6, 7, 8, and 9 were prepared in our previous work.[2]

Data for substrate compounds:



SI1

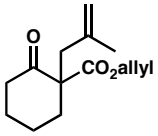
SI1 was prepared using the Dieckmann Cyclization method from our previous work.[2]



SI2

Table 3, Entry 2

Prepared from **SI1** by general alkylation method (EtI, K_2CO_3, acetone, reflux).[2] Purified by flash chromatography (SiO_2, 2.5 → 5% Et_2O in hexane). 36% yield. R_f = 0.24 (10% Et_2O in hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88 (dddd, *J* = 17.4, 10.8, 6.0, 6.0 Hz, 1H), 5.31 (dddd, *J* = 17.4, 3.0, 1.8, 1.8 Hz, 1H), 5.23 (dddd, *J* = 10.2, 2.4, 0.9, 0.9 Hz, 1H), 4.62 (app. ddd, *J* = 6.0, 1.5, 1.5 Hz, 1H), 4.62 (app. ddd, *J* = 6.0, 1.5, 1.5 Hz, 1H), 2.55-2.37 (comp. m, 3H), 1.96 (app. q, *J* = 7.5 Hz, 1H), 1.92 (app. q, *J* = 7.8 Hz, 1H), 1.80-1.54 (comp. m, 4H), 1.48-1.36 (m, 1H), 0.84 (app. t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.9, 171.6, 131.5, 118.9, 65.6, 61.2, 41.1, 35.5, 27.6, 22.5, 8.7; IR (Neat Film NaCl) 3087, 2943, 2867, 1714, 1649, 1452, 1439, 1234, 1203, 1153, 1100, 992, 974, 934 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{12}H_{18}O_3$ $[M]^+$: 210.1256, found 210.1258.

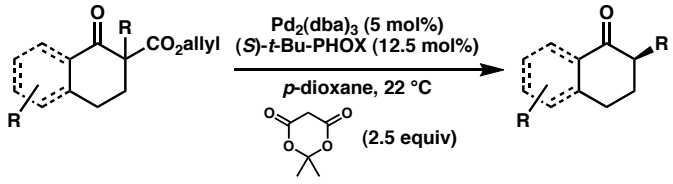


SI3

Table 3, Entry 4

Prepared from **SI1** by general alkylation method (3-chloro-2-methyl propene, K_2CO_3, acetone, reflux).[2] Purified by flash chromatography (SiO_2, 5 → 10% Et_2O in pentane). 67% yield. R_f = 0.25 (10% Et_2O in pentane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89 (dddd, *J* = 17.1, 10.2, 5.7, 5.7 Hz, 1H), 5.32 (dddd, *J* = 17.1, 3.0, 1.5, 1.5 Hz, 1H), 5.25 (dddd, *J* = 10.5, 2.7, 1.2, 1.2 Hz, 1H), 4.82 (app. dd, *J* = 1.8, 1.2 Hz, 1H), 4.66 (app. t, *J* = 0.8 Hz, 1H), 4.64-4.51 (comp. m, 2H), 2.75 (d, *J* = 14.0 Hz, 1H), 2.36 (d, *J* = 14.0 Hz, 1H), 2.62-2.29 (comp. m, 4H), 2.09-1.95 (m, 1H), 1.84-1.72 (m, 2H), 1.66 (s, 3H), 1.52-1.39 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.3, 171.4, 141.4, 131.6, 119.3, 115.6, 66.0, 61.0, 42.4, 41.3, 36.2, 27.8, 24.0, 22.7; IR (Neat Film NaCl) 2946, 1716, 1646, 1452, 1377, 1186, 1086, 989, 898 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{14}H_{20}O_3$ $[M]^+$: 236.1412, found 236.1401.

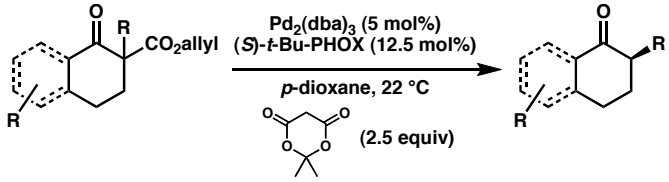
General Procedure for the Enantioconvergent Protonation

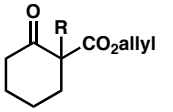
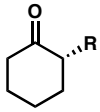
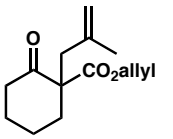
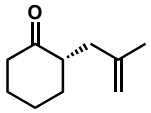
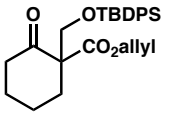
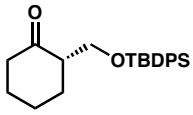
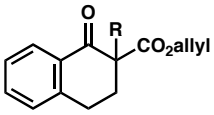
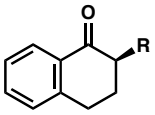
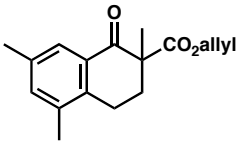
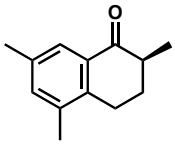
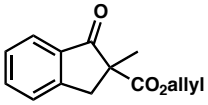
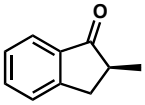


A 25 mL round bottom flask equipped with a magnetic stir bar, and a septum was flame dried under vacuum (3x, backfill with dry argon). After cooling to ambient temperature under dry argon, $Pd_2(dba)_3$ (13.7 mg, 0.015 mmol, 0.05 equiv, 5 mol%), (*S*)-*t*-Bu-PHOX (14.5 mg, 0.0375 mmol, 0.125 equiv, 12.5 mol%), and freshly distilled *p*-dioxane (4.5 mL) were added, and the

resulting mixture was stirred vigorously at 40 ºC for 30 min. A *p*-dioxane solution (4.5 mL) of β-ketoester (0.30 mmol, 1.0 equiv) and Meldrum's acid (108.1 mg, 0.75 mmol, 2.5 equiv) was added to the reaction mixture at 22 °C. When the reaction was complete by TLC, the reaction mixture was filtered through a pad of SiO_2 and the filtrate was concentrated under reduced pressure.

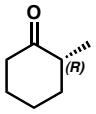
Table 3. Enantioconvergent Decarboxylative Protonations.



Entry	Substrate	Product		ee A (%)	Time (h)	Yield (%)	ee B (%)
1			R = Me	88	0.5	99[b]	86 (*R*)
2			R = Et	92	0.5	99[b]	89 (*R*)
3			R = Bn	83	0.5	90	78 (*S*)
4				91	5	87	89
5				85	0.5	97	80
6			R = Me	90	0.5	86	77 (*S*)
7			R = Allyl	82	0.5	83	77 (*R*)
8				–	0.5	77	77
9				–	0.5	79	61 (*S*)

[a] Reactions were performed on two different scales, A: 0.1 mmol of substrate, and B: 0.3 mmol of substrate, each at 0.033 M in *p*-dioxane. Column ee A reflects results for conditions A; time, isolated yield, and ee B are reported for conditions B. The major enantiomer was the same under either set of conditions. [b] GC yield using tridecane as internal standard.

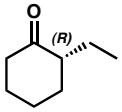
Data for product compounds:
Products were prepared using the above procedure, unless specifically stated otherwise.



SI4

(*R*)-(–)-2-Methylcyclohexanone (Table 3, Entry 1):[7]
Yield determined by GC using tridecane (30.0 μL) as an internal standard. 99% GC yield. Purified by flash chromatography (SiO_2, 5% Et_2O in petroleum ether). 86% ee. $[\alpha]_D^{20.8}$ –9.0 (*c* 0.50, MeOH, 86% ee).

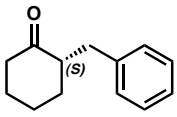
The absolute configuration was established by comparison of the optical rotation to the literature value for (*S*)-(+)-2-methylcyclohexanone: $[\alpha]_D$ +12.2 (*c* 4, MeOH, 87% ee).[8]



SI5

(*R*)-(–)-2-Ethylcyclohexanone (Table 3, Entry 2):[7]
Yield determined by GC using tridecane (30.0 μL) as an internal standard. 99% GC yield. Purified by flash chromatography (SiO_2, 5% Et_2O in petroleum ether). 89% ee. $[\alpha]_D^{23.7}$ –22.4 (*c* 0.30, MeOH, 88% ee).

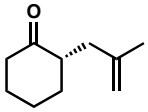
The absolute configuration was established by comparison of the optical rotation to the literature value for (*R*)-(–)-2-ethylcyclohexanone: $[\alpha]_D^{25}$ –23.6 (*c* 4.31, MeOH).[8]



SI6

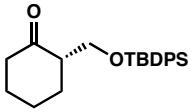
(*S*)-(–)-2-Benzylcyclohexanone (Table 3, Entry 3):[7]
Purified by flash chromatography (SiO_2, 5% Et_2O in petroleum ether). 90% yield, 78% ee. $[\alpha]_D^{23.6}$ –37.6 (*c* 1.36, MeOH, 78% ee).

The absolute configuration was established by comparison of the optical rotation to the literature value for (*R*)-(+)-2-benzylcyclohexanone: $[\alpha]_D$ +41.4 (*c* 5, MeOH, 88% ee),[8] and has been correlated to (1*S,2S)*-(+)-2-benzylcyclohexanol to confirm assignment.[9]



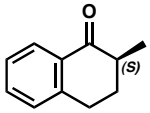
SI7

(–)-2-(2-Methylallyl)cyclohexanone (Table 3, Entry 4):[10]
Purified by flash chromatography (SiO_2, 5% Et_2O in petroleum ether). 87% yield, 89% ee. $[\alpha]_D^{21.2}$ –31.1 (*c* 0.25, CH_2Cl_2, 82% ee).



SI8

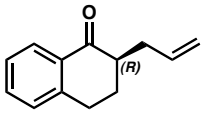
(–)-2-((*tert*-butyldiphenylsilyloxy)methyl)cyclohexanone (Table 3, Entry 5):[11]
Purified by flash chromatography (SiO_2, 5% Et_2O in petroleum ether). 97% yield, 80% ee. m p 67-69 °C. R_f = 0.23 (10% Et_2O in petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71-7.63 (comp. m, 4H), 7.46-7.34 (comp. m, 6H), 4.01 (dd, J = 10.4, 4.8 Hz, 1H), 3.67 (dd, J = 10.4, 7.8 Hz, 1H), 2.62-2.48 (m, 1H), 2.43-2.21 (comp. m, 3H), 2.12-1.97 (m, 1H), 1.96-1.82 (m, 1H), 1.75-1.61 (m, 2H), 1.53-1.40 (m, 1H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.2, 135.8 (2C), 133.9, 133.8, 129.8, 127.8, 63.2, 53.0, 42.3, 31.1, 27.8, 27.1, 24.8, 19.5; IR (Neat Film NaCl) 2932, 2858, 1709, 1472, 1428, 1390, 1113, 1054, 823, 740, 702 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{23}H_{30}SiO_2$ $[M]^+$: 366.2015, found 366.2001. $[\alpha]_D^{23.8}$ –15.2 (*c* 1.05, CH_2Cl_2, 80% ee).



3

(*S*)-(–)-2-Methyl-1-tetralone (Table 3, Entry 6):[7]
Purified by flash chromatography (SiO_2, 5% Et_2O in petroleum ether). 86% yield, 77% ee. $[\alpha]_D^{23.6}$ –38.4 (*c* 0.54, *p*-dioxane, 77% ee).

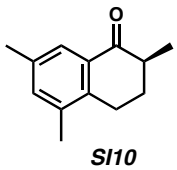
The absolute configuration was determined by comparison of the observed optical rotation to a literature value for (*S*)-2-methyl-1-tetralone: $[\alpha]_D^{22}$ –51.2 (*c* 2.5, *p*-dioxane).[12]



SI9

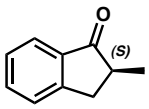
(*R*)-(–)-2-Allyl-1-tetralone (Table 3, Entry 7):[13]
Purified by flash chromatography (SiO_2, 5% Et_2O in petroleum ether). 83% yield, 77% ee. $[\alpha]_D^{23.6}$ –24.1 (*c* 1.02, MeOH, 77% ee).

The absolute configuration was established by comparison of the optical rotation to the literature value for (*R*)-(–)-2-allyl-1-tetralone: $[\alpha]_D^{23}$ –29.7 (*c* 1.21, MeOH, 97% ee).[13]



SI10

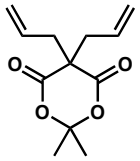
(–)-2,5,7-Trimethyl-1-tetralone (Table 3, Entry 8):[14]
Purified by flash chromatography (SiO_2, 5% Et_2O in petroleum ether). 77% yield, 77% ee. $[\alpha]_D^{23.7}$ –23.2 (*c* 1.05, CH_2Cl_2, 77% ee).



SI11

(*S*)-(+)-2-Methyl-1-indanone (Table 3, Entry 9):[7]
Purified by flash chromatography (SiO_2, 5% Et_2O in petroleum ether). 79% yield, 61% ee. $[\alpha]_D^{23.6}$ +21.2 (*c* 0.23, *p*-dioxane, 61% ee).

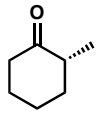
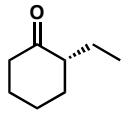
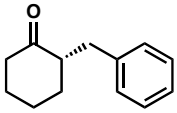
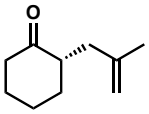
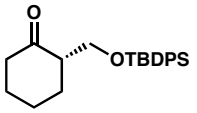
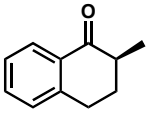
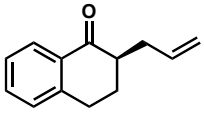
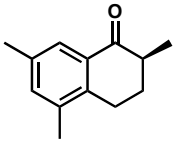
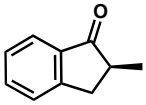
The absolute configuration was established by comparison of the optical rotation to the literature value for (*R*)-2-methyl-1-indanone: $[\alpha]_D^{22}$ –42 (*c* 1.72, *p*-dioxane).[12]



4

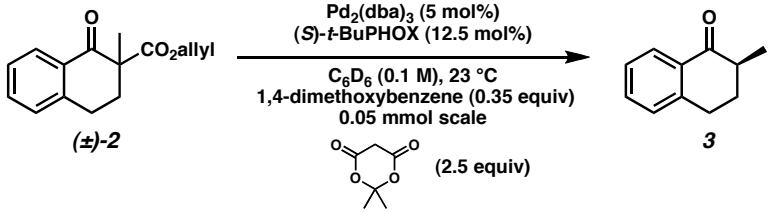
5,5-Diallyl-2,2-dimethyl-1,3-dioxane-4,6-dione[4] **(Figure 1)**
Purified by flash chromatography (SiO_2, 5% Et_2O in petroleum ether).

Table SI 2. Methods for the determination of enantiomeric excess.

Entry	Product	Assay Conditions	retention time of major isomer (min)	retention time of minor isomer (min)	% ee
1	 ***SI4***	GC G-TA 70 ° isotherm	19.406	18.306	86
2	 ***SI5***	GC G-TA 70 ° isotherm	36.643	34.987	89
3	 ***SI6***	HPLC Chiralpak AD 1% EtOH in hexane isocratic, 1.0 mL/min	11.637	9.885	78
4	 ***SI7***	GC G-TA 100 ° isotherm	17.133	18.672	89
5	 ***SI8***	HPLC Chiralpak AD 1% i-PrOH in hexane isocratic, 1.0 mL/min	5.553	6.217	80
6	 ***3***	HPLC Chiracel OD-H 1% i-PrOH in hexane isocratic, 1.0 mL/min	8.723	8.075	77
7	 ***SI9***	HPLC Chiracel OD-H 0.1% i-PrOH in heptane isocratic, 1.0 mL/min	24.007	20.561	77
8	 ***SI10***	HPLC Chiracel OD-H 1% i-PrOH in hexane isocratic, 1.0 mL/min	7.283	7.787	77
9	 ***SI11***	HPLC Chiracel OD-H 1% i-PrOH in hexane isocratic, 1.0 mL/min	10.239	9.446	61

Kinetic Studies for the Enantioconvergent Protonation

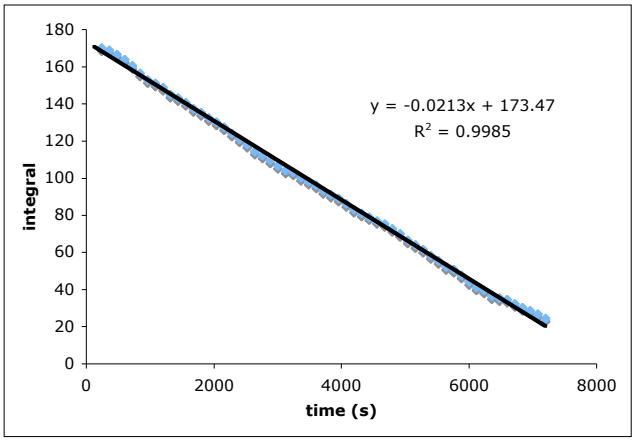
Determination of Substrate Order

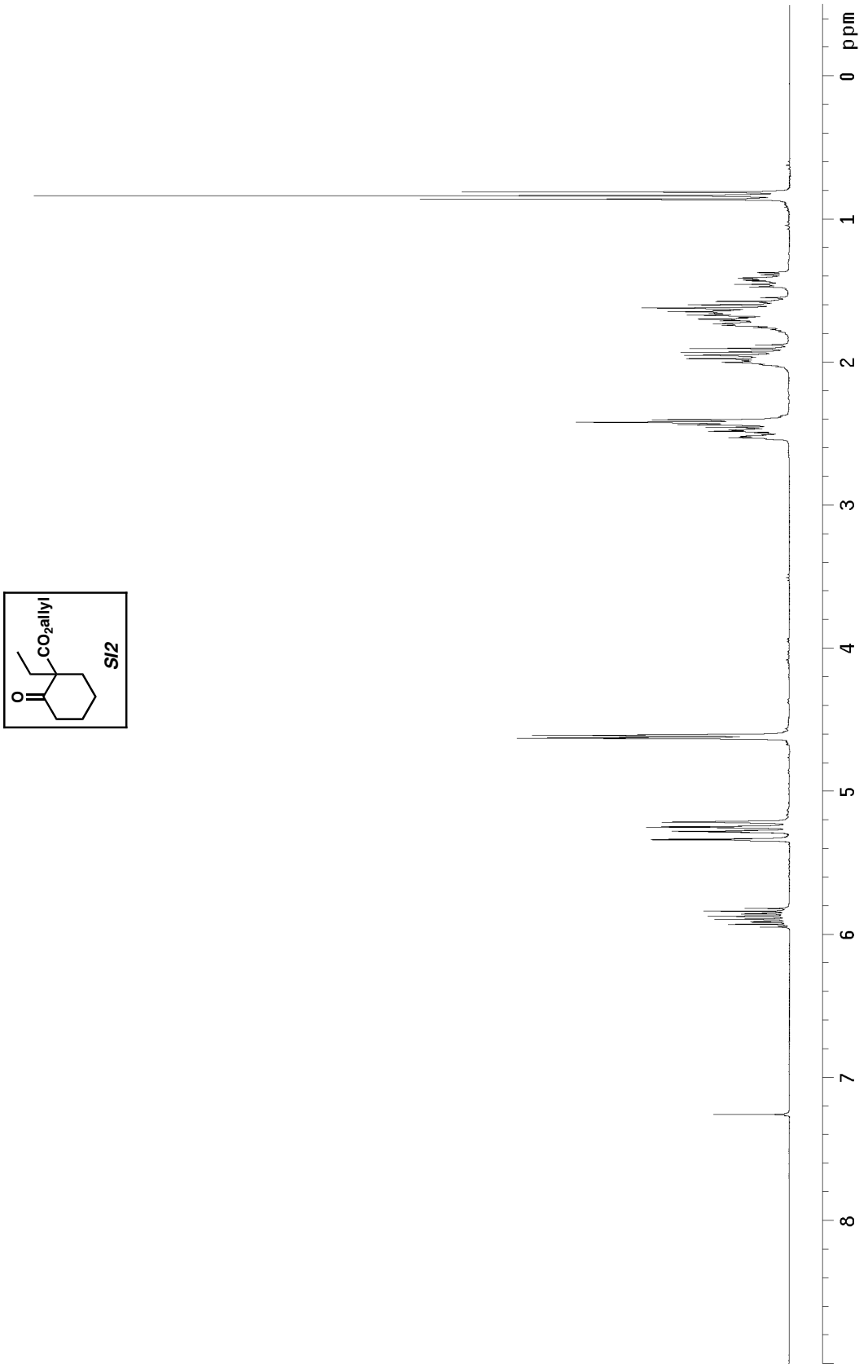


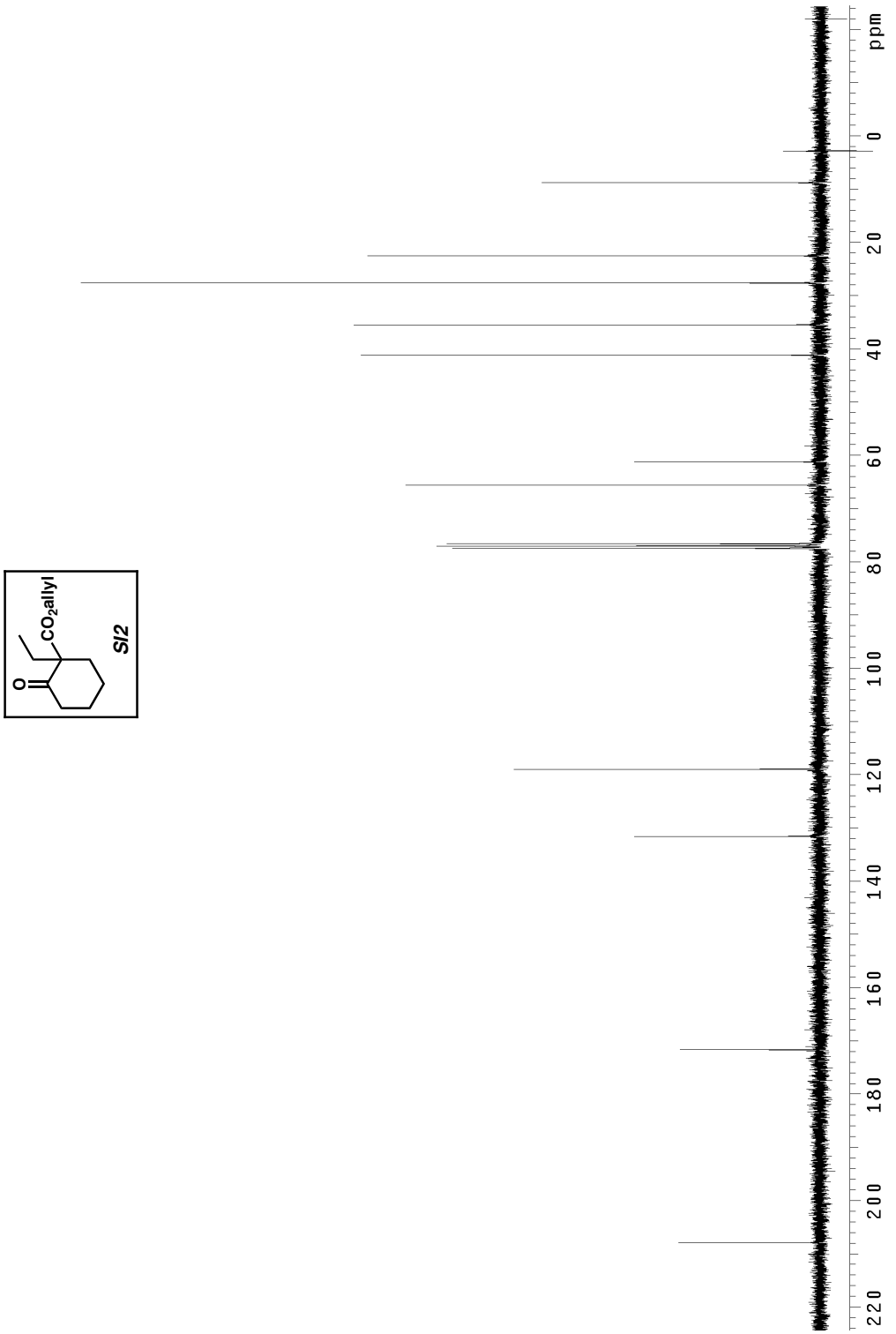
Solid $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol, 0.05 equiv, 5 mol%) and (*S*)-*t*-Bu-PHOX (2.4 mg, 0.00625 mmol, 0.125 equiv, 12.5 mol%) were placed in a NMR tube equipped with a screw cap and a Teflon septum. The NMR tube was then placed under vacuum and backfilled with argon (3x). C_6D_6 (0.2 mL, dried over sodium benzophenone ketyl) was added to the NMR tube via syringe under a positive pressure of argon. The mixture was heated at 40 °C for 30 min. A C_6D_6 solution (0.3 mL total) of allyl β-ketoester **2** (0.05 mmol, 1.0 equiv), 1,4-dimethoxybenzene (2.4 mg, 0.0175 mmol, 0.35 equiv), and Meldrum's acid (18 mg, 0.125 mmol, 2.5 equiv) was added to the reaction mixture at 23 °C under argon. Reaction progress was monitored by ^{1}H NMR spectroscopy at 23 ºC, where integral areas of the allylic protons of **2** (δ 4.30 ppm, m, 2H) relative to the phenyl protons of the 1,4-dimethoxybenzene internal standard (δ 3.34 ppm, s, 6H) were obtained at 2 minute intervals. The experiment was concluded upon complete conversion of **2**, which was determined by the disappearance of the allylic protons of **2**.

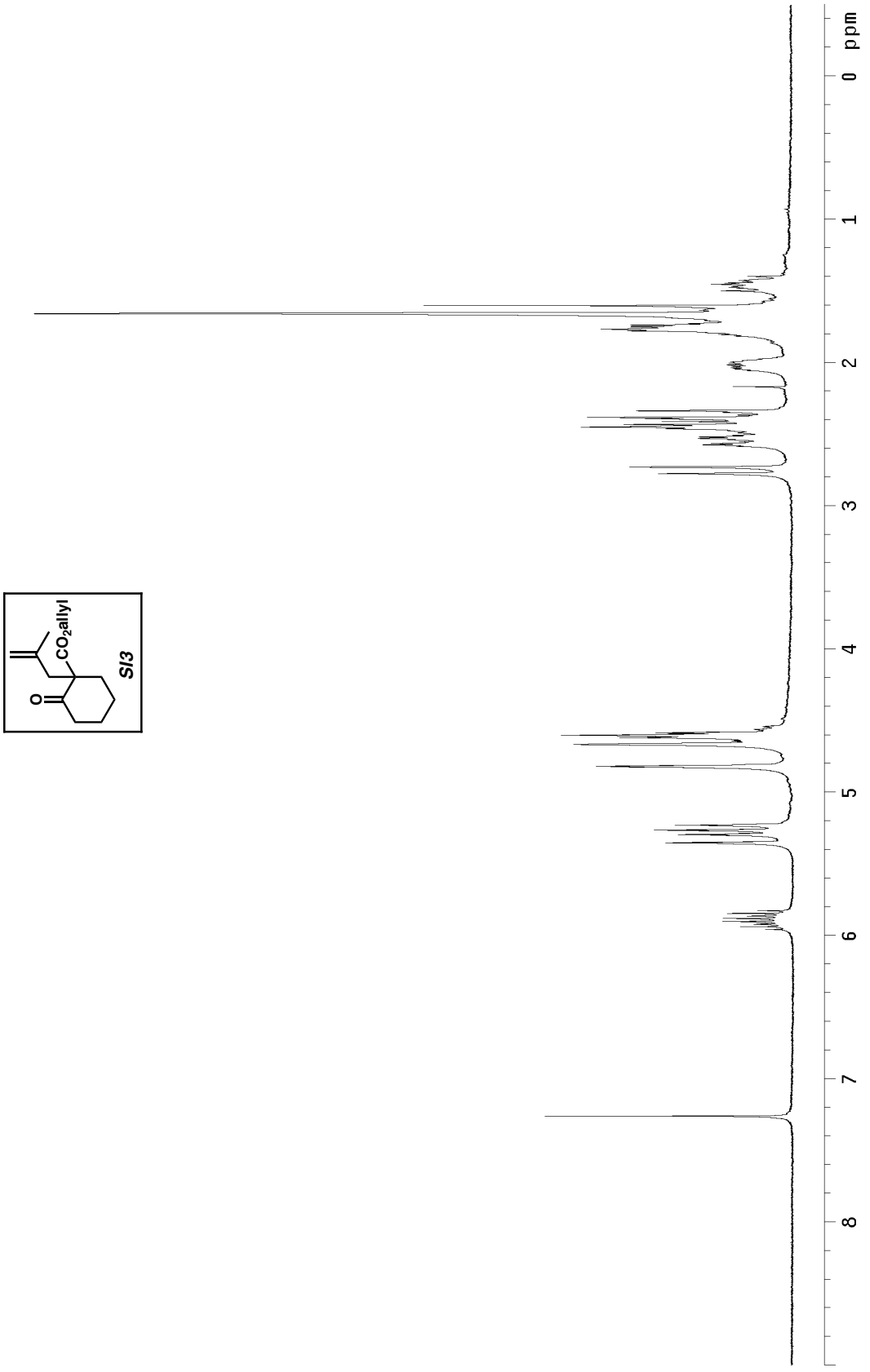
Analysis of consumption of **2** over time is consistent with a zero-order dependence in allyl β-ketoester (Figure SI1).

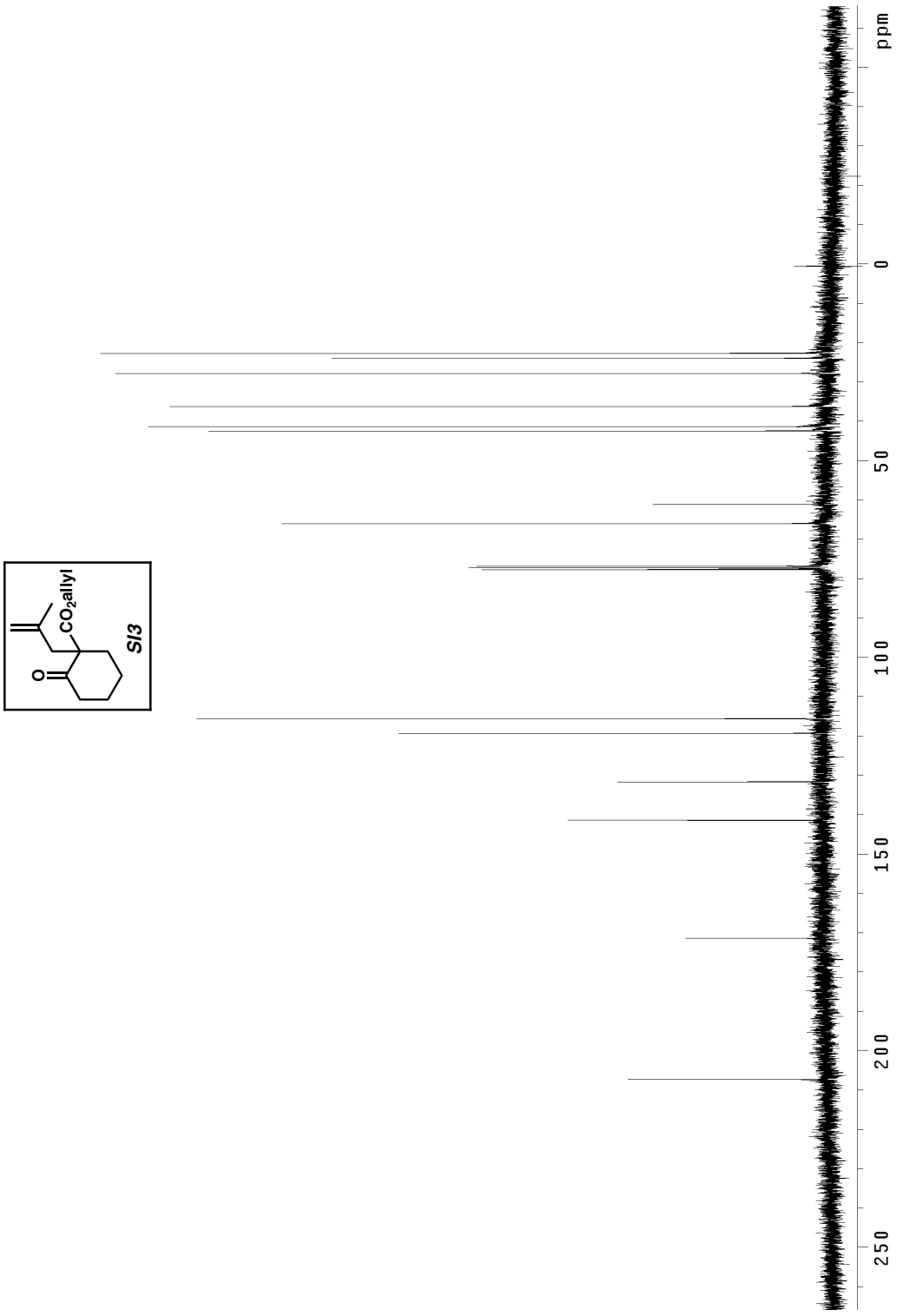
Figure SI1. Plot of Consumption of Allyl β-ketoester **2** versus Time as Observed by ^{1}H NMR Spectroscopy

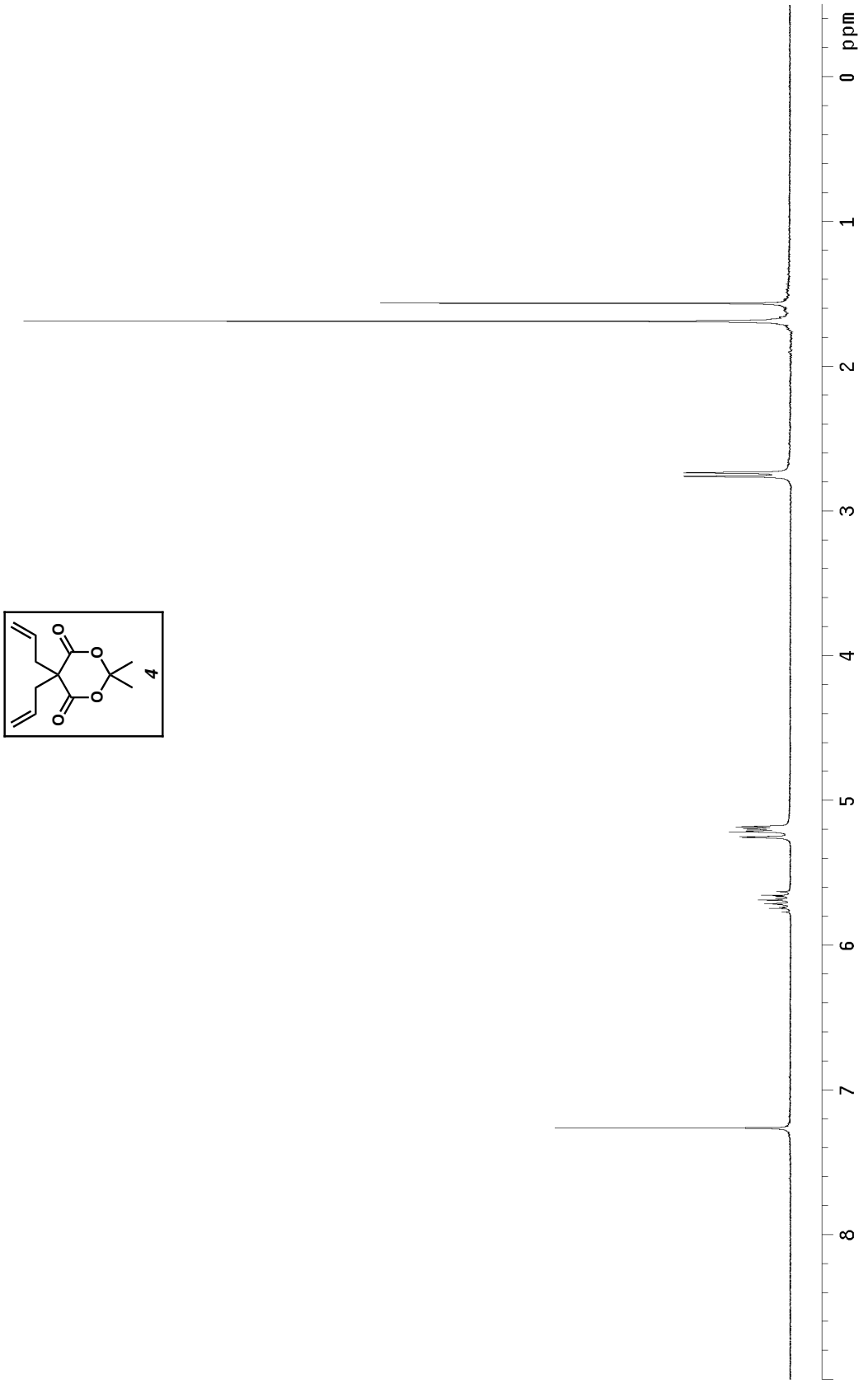


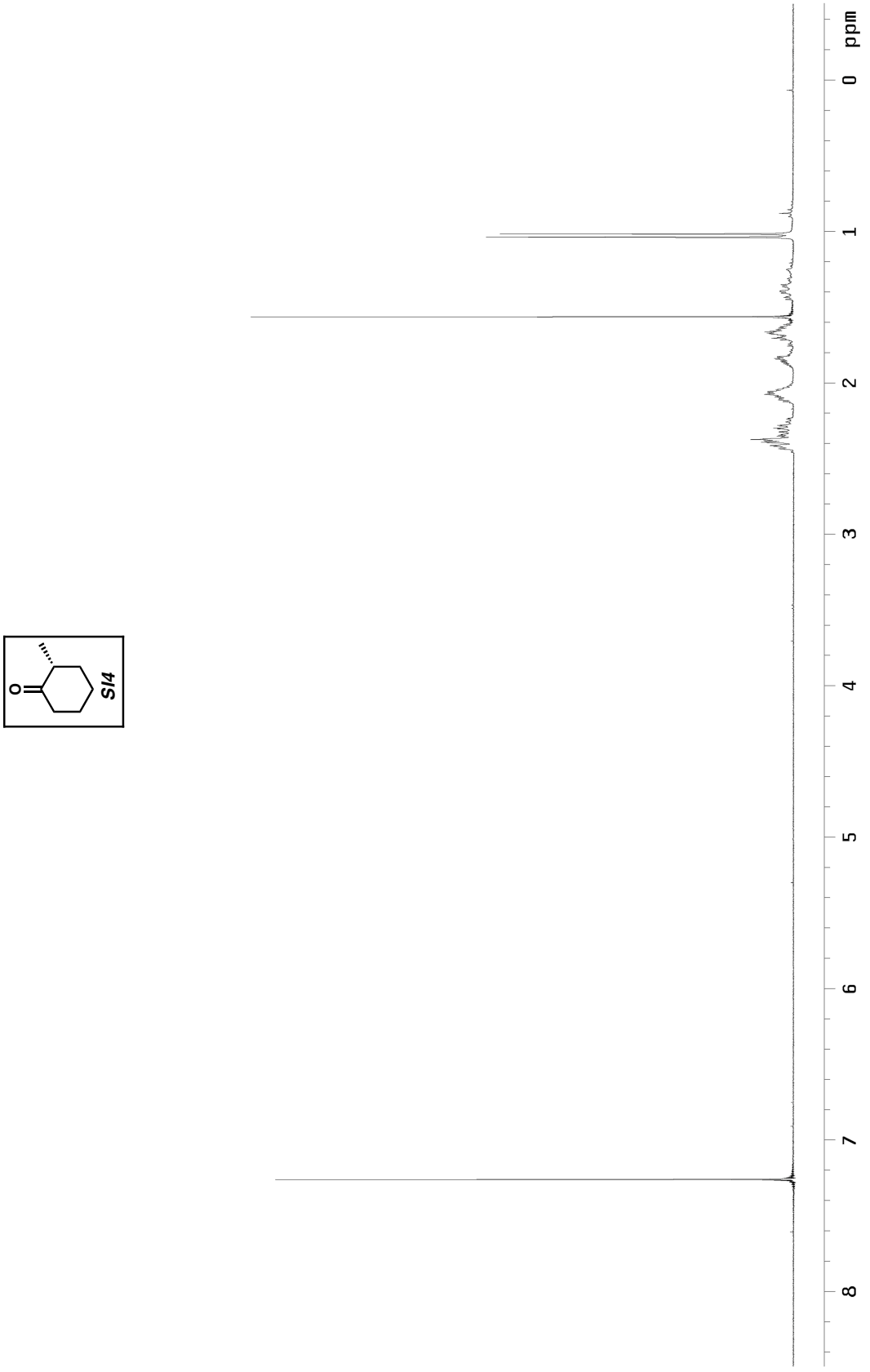

O
CO2allyl
SI2
ppm
0
1
2
3
4
5
6
7
8

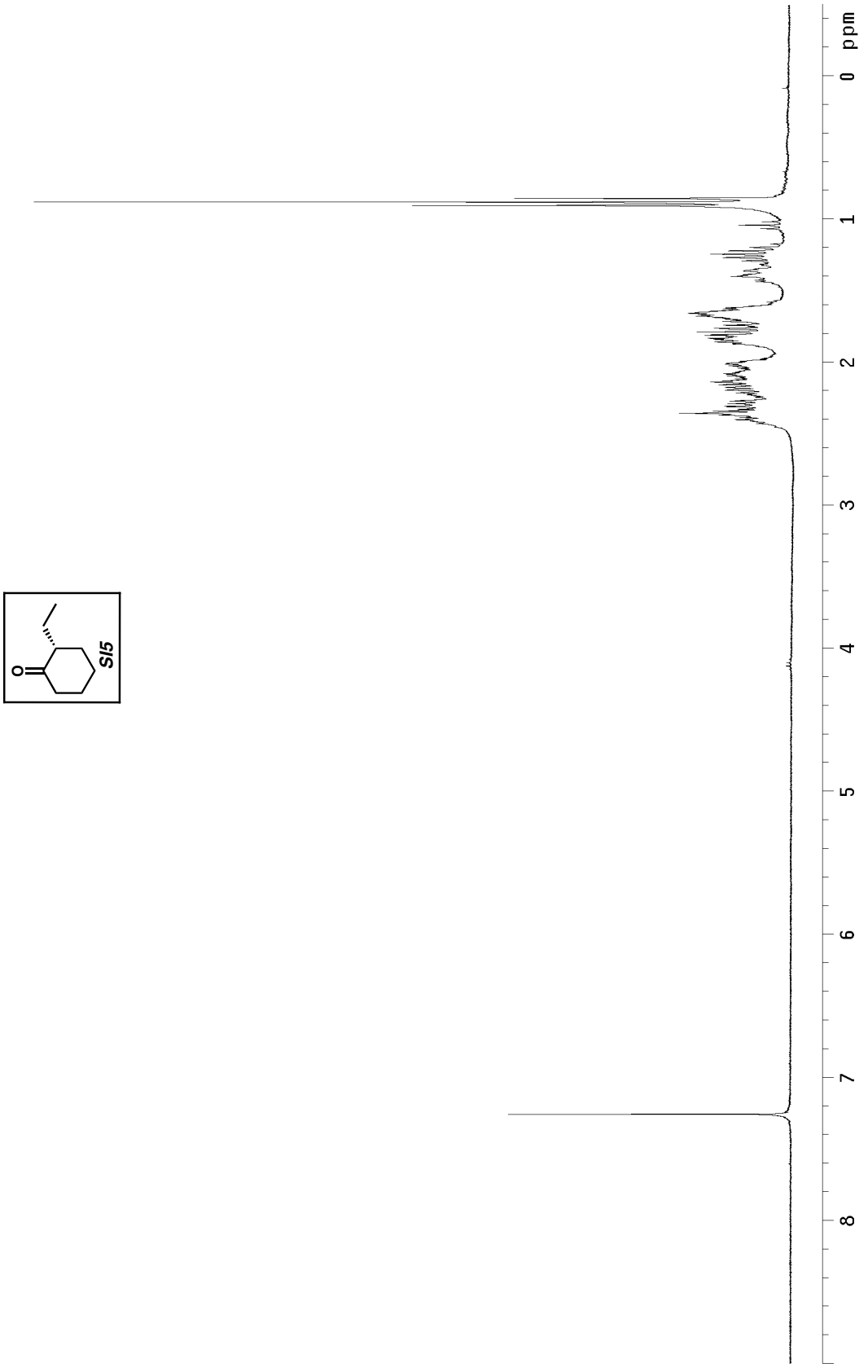

O
CO2allyl
SI2
ppm
0
20
40
60
80
100
120
140
160
180
200
220

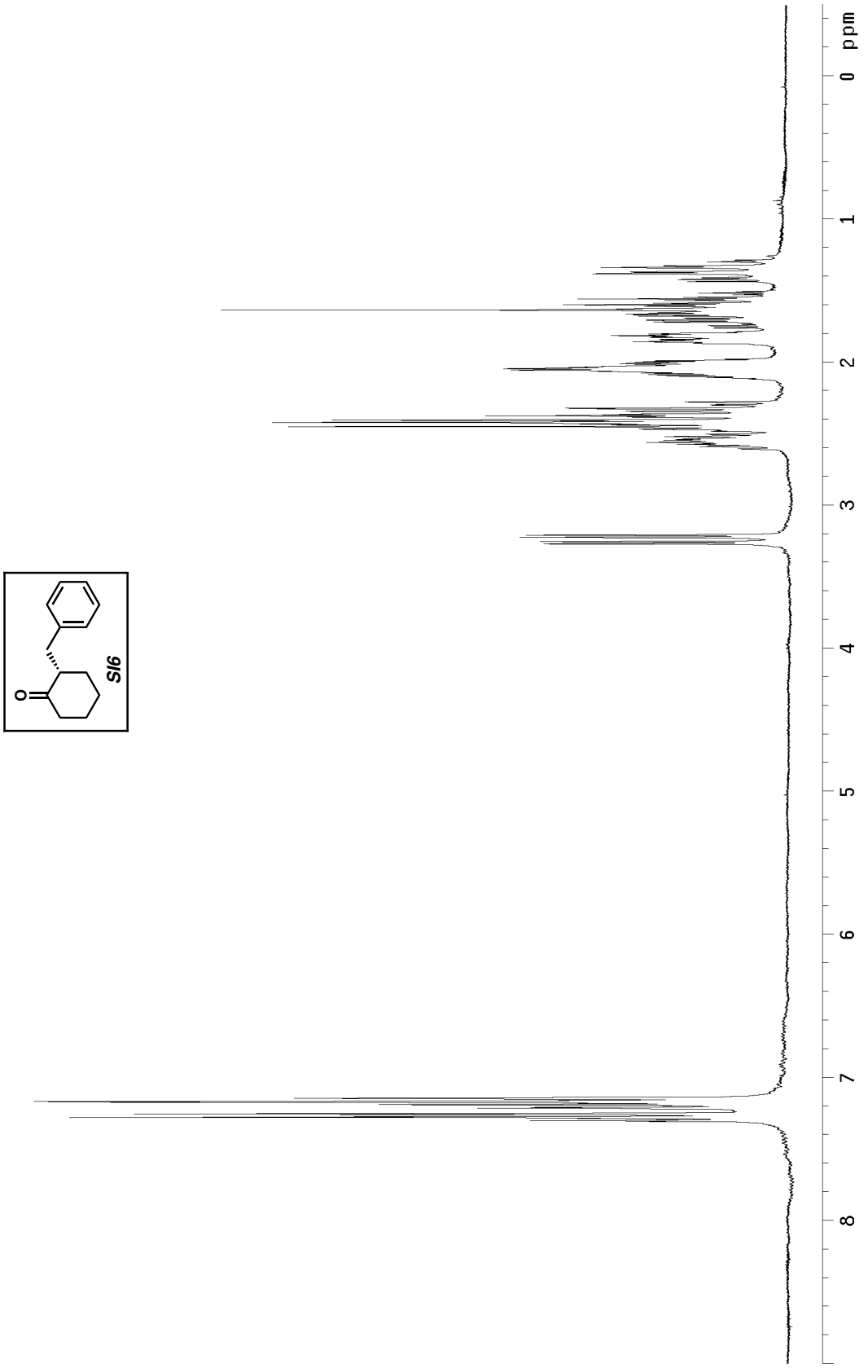

CO2allyl
O
SI3
ppm
0
1
2
3
4
5
6
7
8

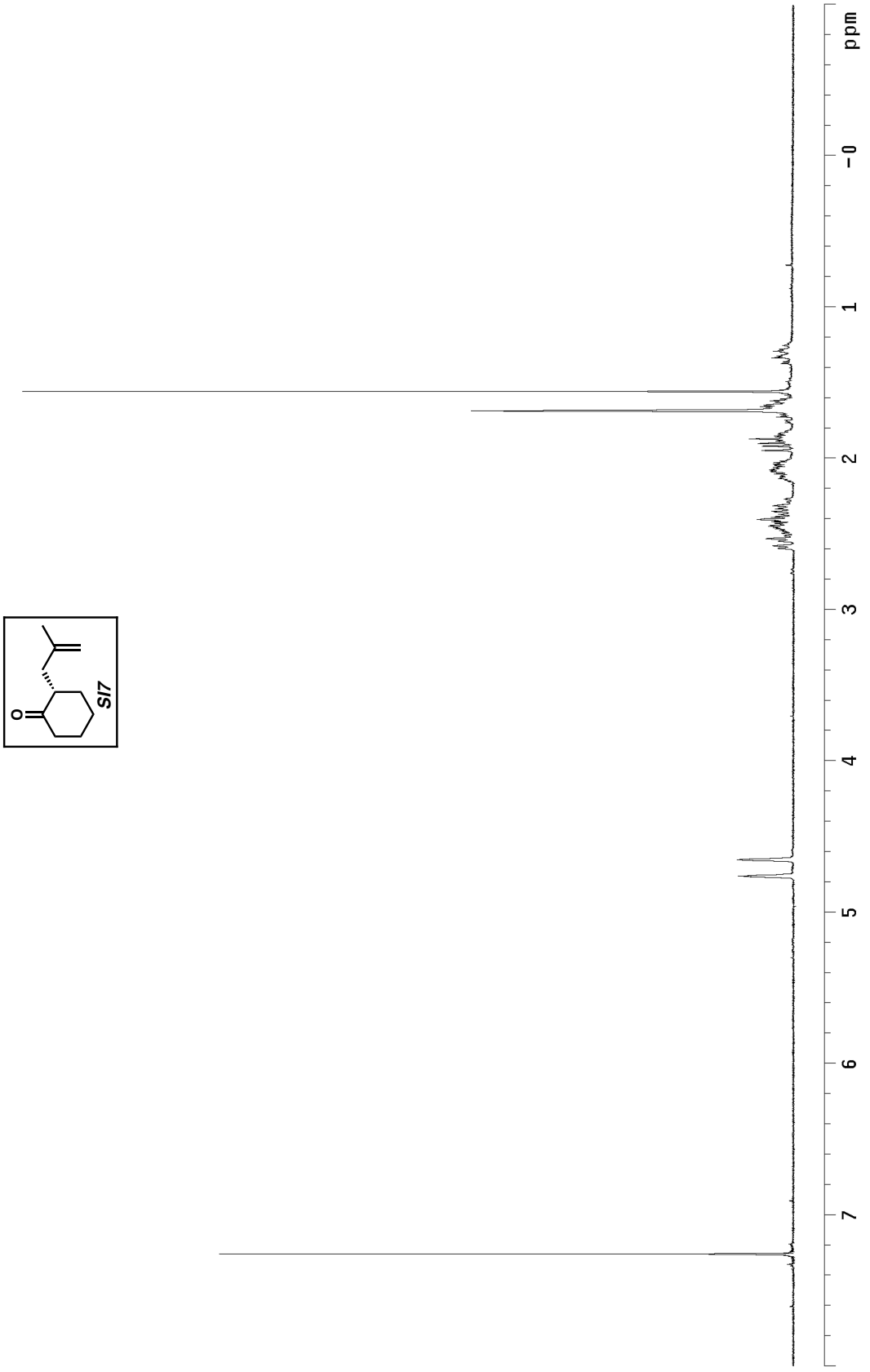

CO2allyl
O
SI3
ppm
0
50
100
150
200
250

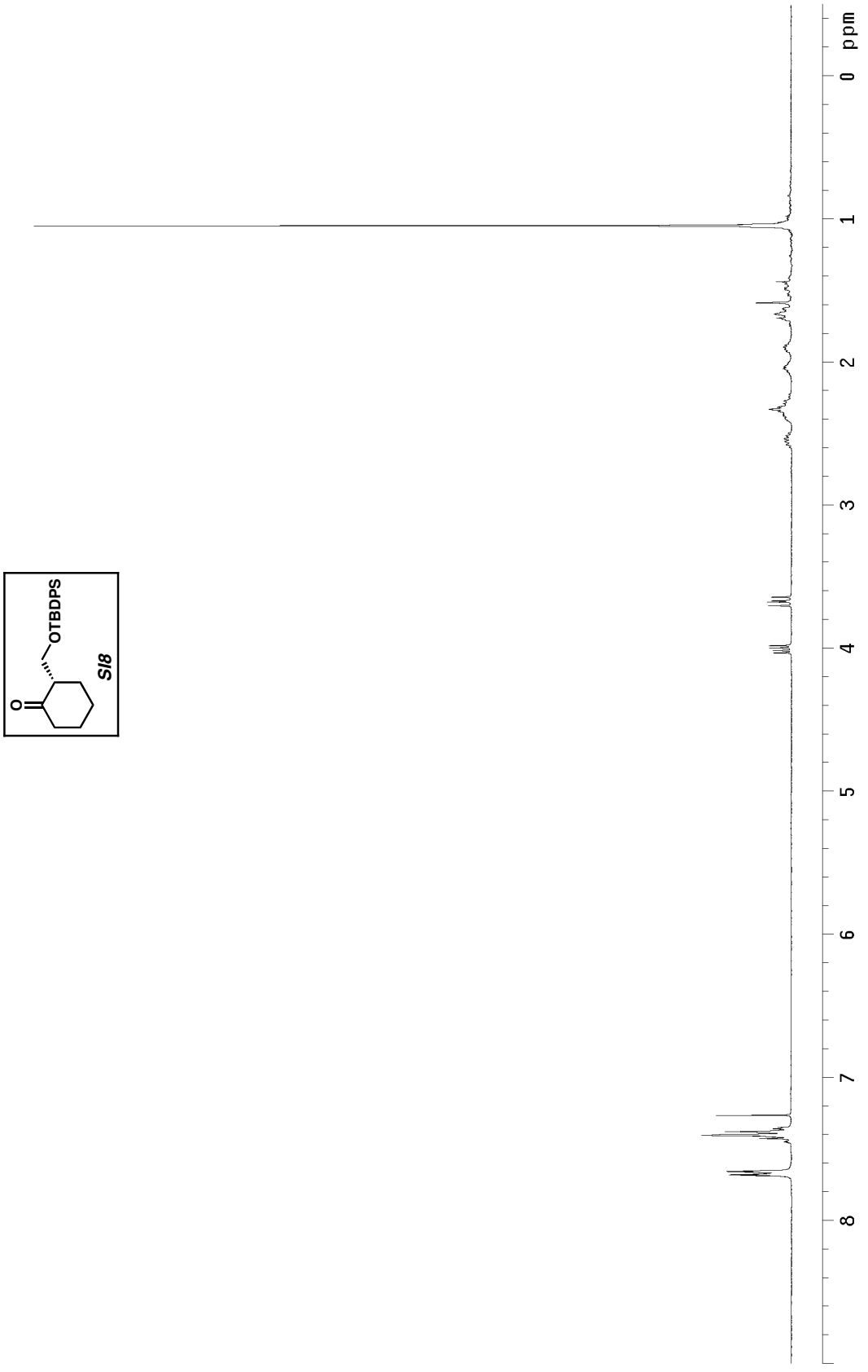

4
ppm
0
1
2
3
4
5
6
7
8

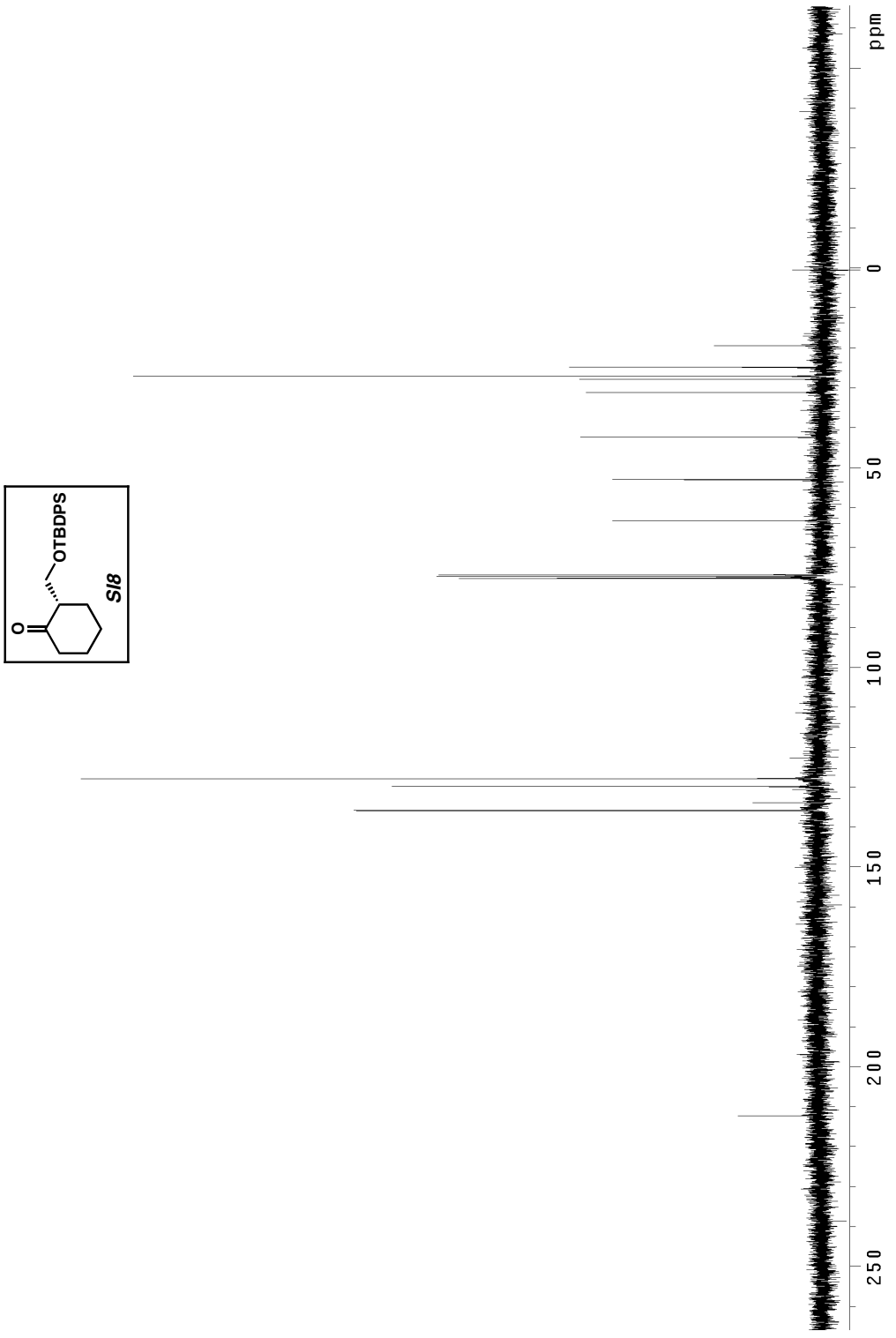

SI4
ppm
0
1
2
3
4
5
6
7
8

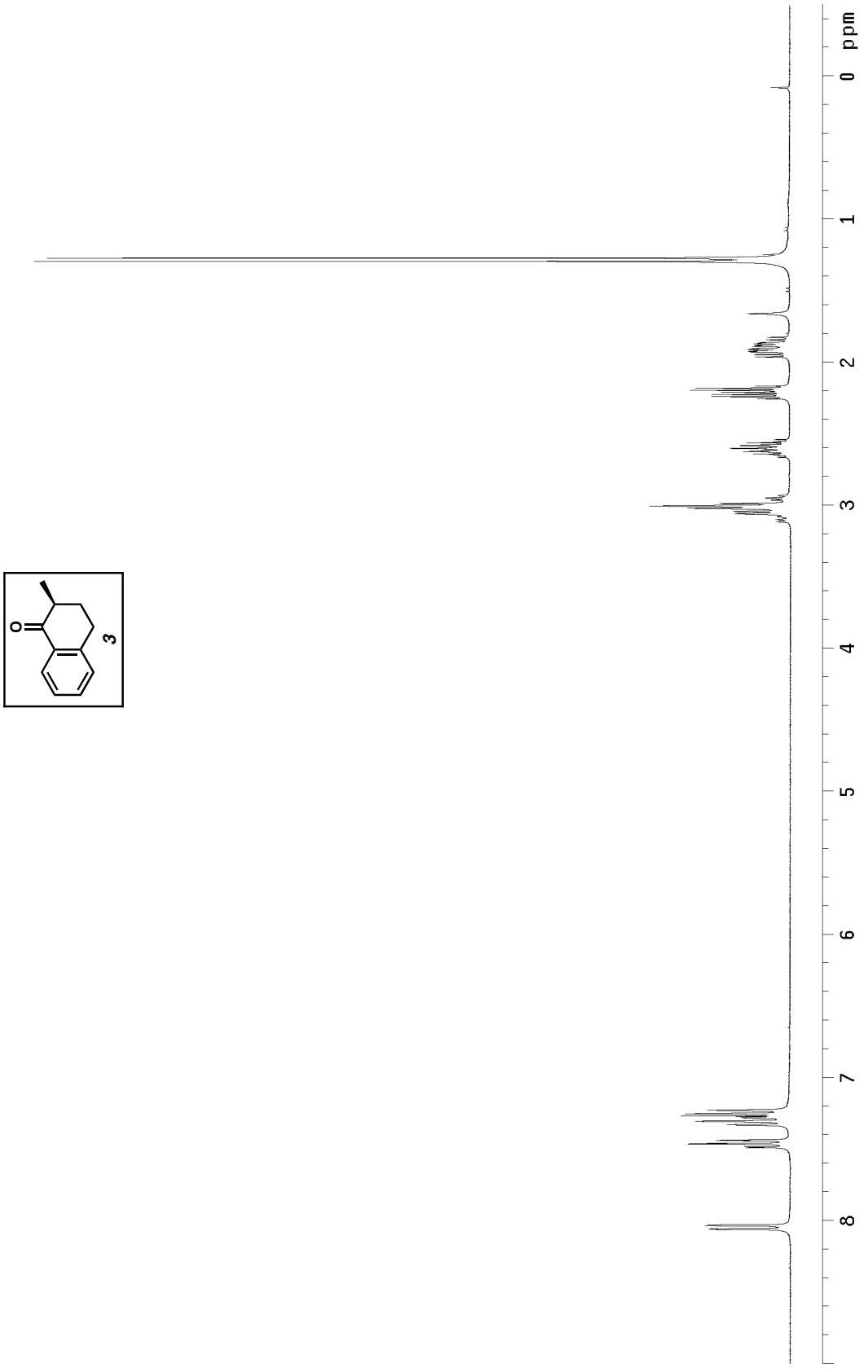

SI5
O
ppm
0
1
2
3
4
5
6
7
8

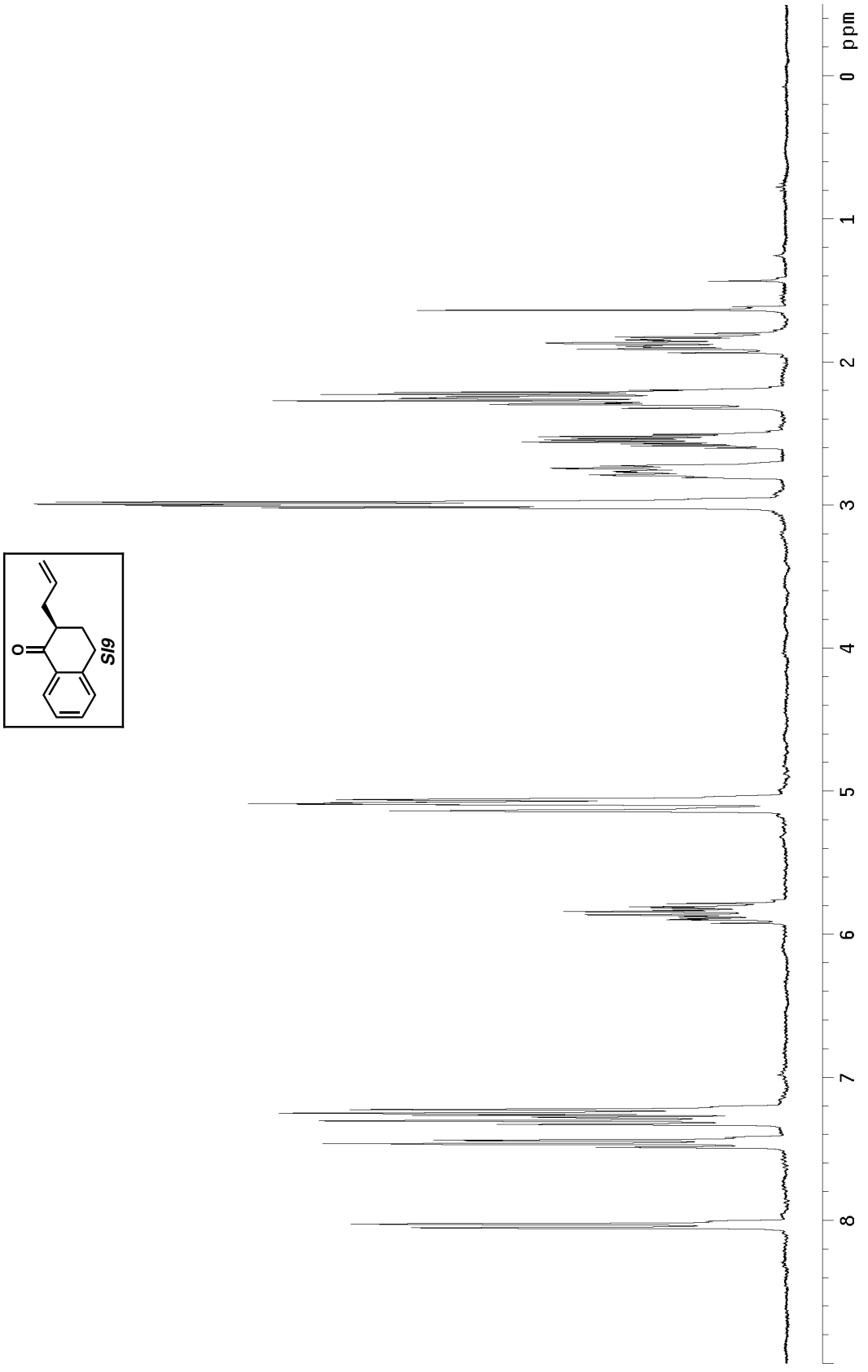

SI6
O
ppm
0
1
2
3
4
5
6
7
8

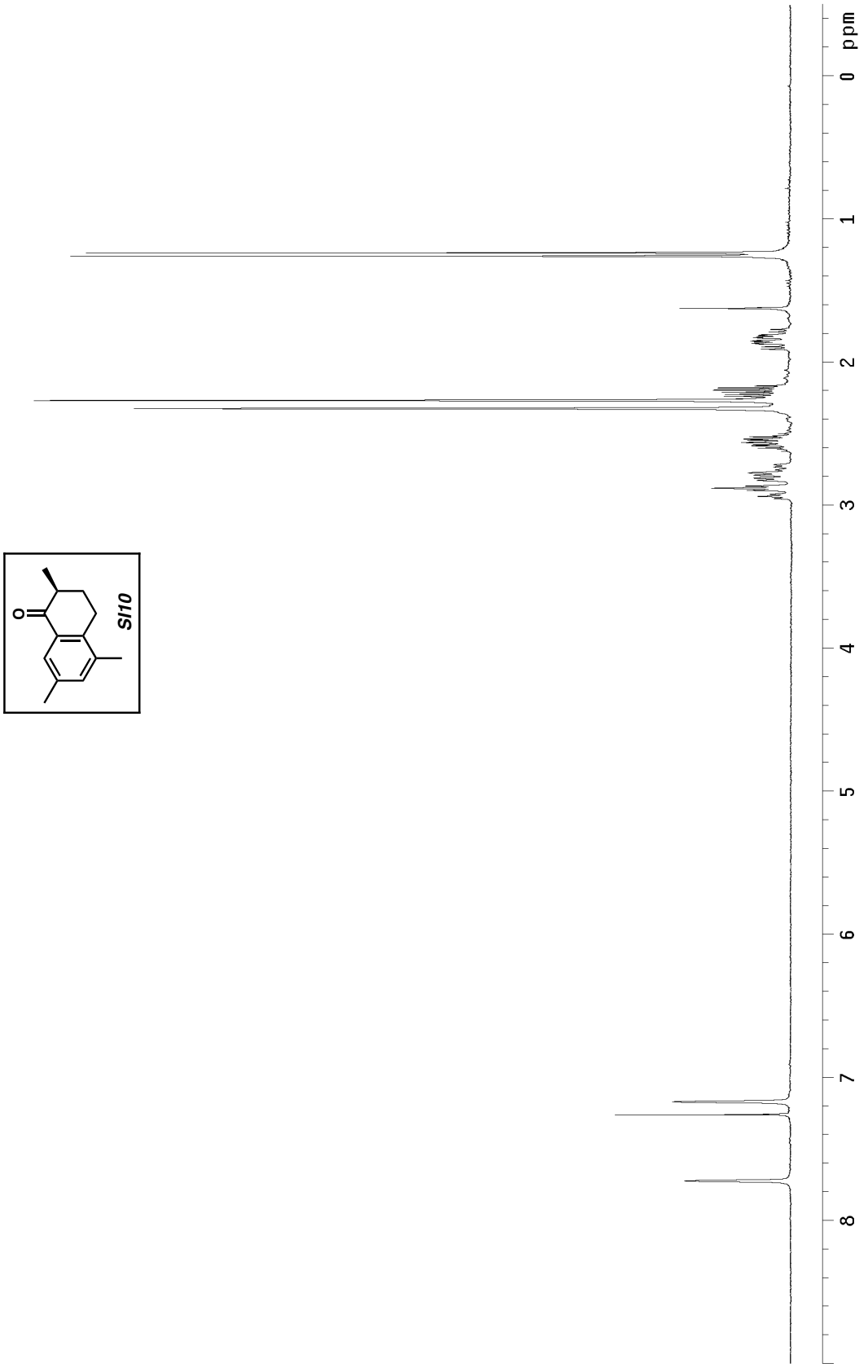

SI7
O
ppm
-0
1
2
3
4
5
6
7

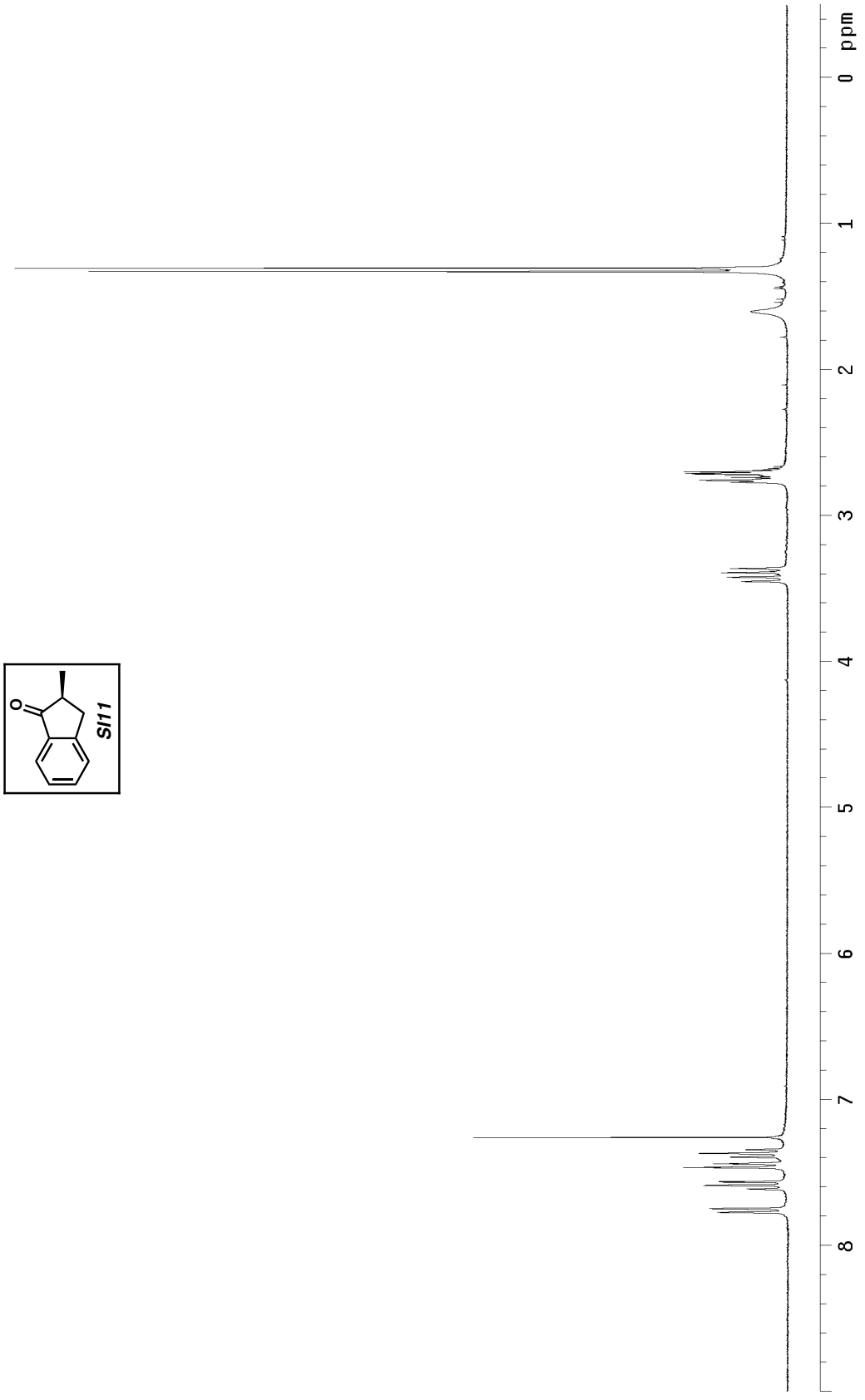

OTBDPS
O
SI8
ppm
0
1
2
3
4
5
6
7
8


OTBDPS
O
SI8
ppm
0
50
100
150
200
250


O
3
ppm
0
1
2
3
4
5
6
7
8


O
SI9
8
7
6
5
4
3
2
1
0
ppm


O
SI10
ppm
0
1
2
3
4
5
6
7
8


O
SI11
0
1
2
3
4
5
6
7
8
ppm

References:

[1] (a) Behenna, D. C.; Stoltz, B. M. *J. Am. Chem. Soc.* **2004**, *126*, 15044–15045. (b) Tani, K.; Behenna, D. C.; McFadden, R. M.; Stoltz, B. M. *Org. Lett.* **2007**, *9*, 2529–2531.

[2] (a) Mohr, J. T.; Behenna, D. C.; Harned, A. M.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 6924–6927. (b) Mohr, J. T.; Nishimata, T.; Behenna, D. C.; Stoltz, B. M. *J. Am. Chem. Soc.* **2006**, *128*, 11348–11349.

[3] Schwarzenbach, G.; Felder, E. *Helv. Chim. Acta*, **1944**, 27, 1044–1060.

[4] (a) Bouillon, G.; Schank, K.; *Chem. Ber.* **1980**, *113*, 2630–2635. (b) Kayaki, Y.; Koda, T.; Ikariya, T. *J. Org. Chem*. **2004**, *69*, 2595–2597.

[5] Henning, H. G.; Stemplinger, G.; Rothe, K. *Liebigs Ann. Chem.* **1992**, *8*, 813–816.

[6] (a) Ramachary, D. B.; Barbas, C. F., III *Chem.–Eur. J.* **2004**, *10*, 5323–5331. (b) Sato, M.; Hisamichi, H.; Kaneko, C.; Suzaki, N.; Furuya, T.; Inukai, N. *Tetrahedron Lett*. **1989**, *30*, 5281–5284. (c) Sato, M.; Ban, H.; Kaneko, C. *Tetrahedron Lett*. **1997**, *38*, 6689–6692.

[7] Racemic material is commercially available.

[8] (a) Meyers, A. I.; Williams, D. R.; Druelinger, M. *J. Am. Chem. Soc.* **1976**, *98*, 3032–3033. (b) Meyers, A. I.; Williams, D. R.; Erickson, G. W.; White, S.; Druelinger, M. *J. Am. Chem. Soc.* **1981**, *103*, 3081–3087.

[9] (a) Mohr, J. T.; Nishimata, T.; Behenna, D. C.; Stoltz, B. M. *J. Am. Chem. Soc.* **2006**, *128*, 11348–11349. (b) Fogliato, G.; Fronza, G.; Fuganti, C.; Lanati, S.; Rallo, R.; Rigoni, R.; Servi, S. *Tetrahedron* **1995**, *51*, 10231–10240.

[10] Hirao, T.; Fujii, T.; Ohshiro, Y. *Tetrahedron* **1994**, *50*, 10207–10214.

[11] Buisson, D.; Azerad, R. *Tetrahedron: Asymmetry* **1996**, *7*, 9–12.

[12] Jaouen, G.; Meyer, A. *J. Am. Chem. Soc.* **1975**, *97*, 4667–4672.

[13] Trost, B. M.; Xu, J. *J. Am. Chem. Soc.* **2005**, *127*, 2846–2847.

[14] (a) Nagasampagi, B. A.; Dev, S.; Rai, C.; Murthy, K. L. *Tetrahedron* **1966**, *22*, 1949–1976. (b) Heimgartner, H.; Zsindely, J.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1973**, *56*, 2924–2945.