Unusual Allylpalladium Carboxylate Complexes: Identification of the Resting State of Catalytic Enantioselective Decarboxylative Ketone Allylic Alkylation Reactions

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Materials and Methods:

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon atmosphere using dry, deoxygenated solvents. Solvents were purchased from Fisher Scientific, dried by passage through an activated alumina column under ultra high purity (UHP) argon, and either stored under UHP argon or stored over 4Å molecular sieves in a nitrogen glove-box after drying. Solvents stored over molecular sieves were filtered immediately before use to remove sieve dust. Petroleum ether was obtained from Fisher Scientific and is defined here as petroleum fractions that boil from 36–60 °C. All filtrations performed in a glove box or otherwise associated directly or indirectly with inorganic or organometallic complexes were performed exclusively with scintillated glass Buchner funnels or using 2.4 mm GF/A Whatman glass microfibre filter paper. Unless otherwise stated, all starting materials were purchased from Sigma-Aldrich or Alfa Aesar, and used as received. Tetrabutylammonium difluorotriphenylsilicate (TBAT) was purchased from Sigma-Aldrich and azeotropically dried five times from acetonitrile, backfilled with argon and then stored in a nitrogen glove box until immediately prior to use. Tris(dibenzylideneacetone)dipalladium(0) [$Pd_2(dba)_3$] and $PdCl_2$ were purchased from Strem and stored in either a desiccator or a nitrogen glove box until immediately before use. 1-Methyl-2-oxo-cyclohexanecarboxylic acid allyl ester (β-ketoester **2**),[1] trimethyl(2-methylcyclohex-1-enyloxy)silane (**SI 1**),[2] allyl 2-methylcyclohex-1-enyl carbonate (**SI 2**),[2] and (*S*)-*t*-BuPHOX ligand (**3**),[2,3] were prepared by known methods. 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). SiliCycle® SiliaFlash® P60 Academic Silica Gel (particle size 40-63 μm; pore diameter 60 Å), was used for flash chromatography. ^1H, ^{13}C, ^{31}P, and ^{19}F NMR spectra were recorded on a Varian Inova 600 (at 600 MHz and 150 MHz for ^1H and ^{13}C respectively), a Varian Inova 500 (at 500 MHz and 125 MHz for ^1H and ^{13}C respectively), or a Varian Mercury 300 (at 300 MH, 75 MHz, 121.4 MHz, and 282 MHz for ^1H, ^{13}C, ^{31}P and ^{19}F respectively). ^1H NMR spectra are reported relative to residual $CHCl_3$ (δ 7.26) or to the downfield proton in residual $THF_{d\text{-}7}$ (δ 3.58). Data for ^1H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity,[a] coupling constant (Hz),[b] integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, comp. m = complex multiplet, app. = apparent, br. = broad. ^{13}C NMR spectra are reported relative to $CDCl_3$ (δ 77.16) or to the downfield carbon in $THF_{d\text{-}8}$ (δ 67.57). ^{31}P NMR spectra are reported relative to H_3PO_4 (δ 0.00) as an external standard consisting of 85% neat phosphoric acid or to free (*S*)-*t*-

[a] In many cases hyperfine coupling could be observed but was not resolved enough to be calculable. In such cases the larger coupling is calculated and the relevant multiplicities are indicated but terminated with m (multiplet) to signify the unresolved hyperfine coupling. For example (tm, J = 7.2 Hz, 1H) indicates a triplet of 7.2 Hz, with irresolvable hyperfine coupling. This is done in place of reporting the entire resonance as a multiplet for the purpose of reproducibility on lower field strength NMR spectrometers where only the larger calculable splitting(s) will be observed.

[b] When a lower case subscript is shown with the coupling constant, it indicates what type of splitting the constant is associated with in splitting patterns that consist of different multiplicities of coupling. For example (td, J_t = 5.0 Hz, J_d = 3.3 Hz, 1H) indicates that the triplet splitting has a 5.0 Hz coupling constant and the doublet has a 3.3 Hz coupling constant.

BuPHOX ligand (δ –5.95) as either an internal or external standard in $THF_{d\text{-}8}$. ^{19}F NMR spectra are reported relative to $CFCl_3$ (δ 0.00) as an external standard. Analytical achiral gas chromatography (GC) was performed with an Agilent 6850 GC utilizing a DB-WAX (30 m x 0.25 mm) column (1.0 mL/min carrier gas flow). 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. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in frequency of absorption (cm^{-1}). High-resolution mass spectra were obtained from the Caltech Mass Spectral Facility or on an Agilent 6200 Series Time-of-Flight LC/MS/TOF system. Melting points were determined on a Thomas-Hoover melting point apparatus and are uncorrected. Boiling points are measured directly during distillation and are uncorrected. Crystallographic analyses were performed at the California Institute of Technology Beckman Institute X-Ray Crystallography Laboratory. Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained upon request, free of charge, by quoting the publication citation and the deposition numbers provided with the structures below.

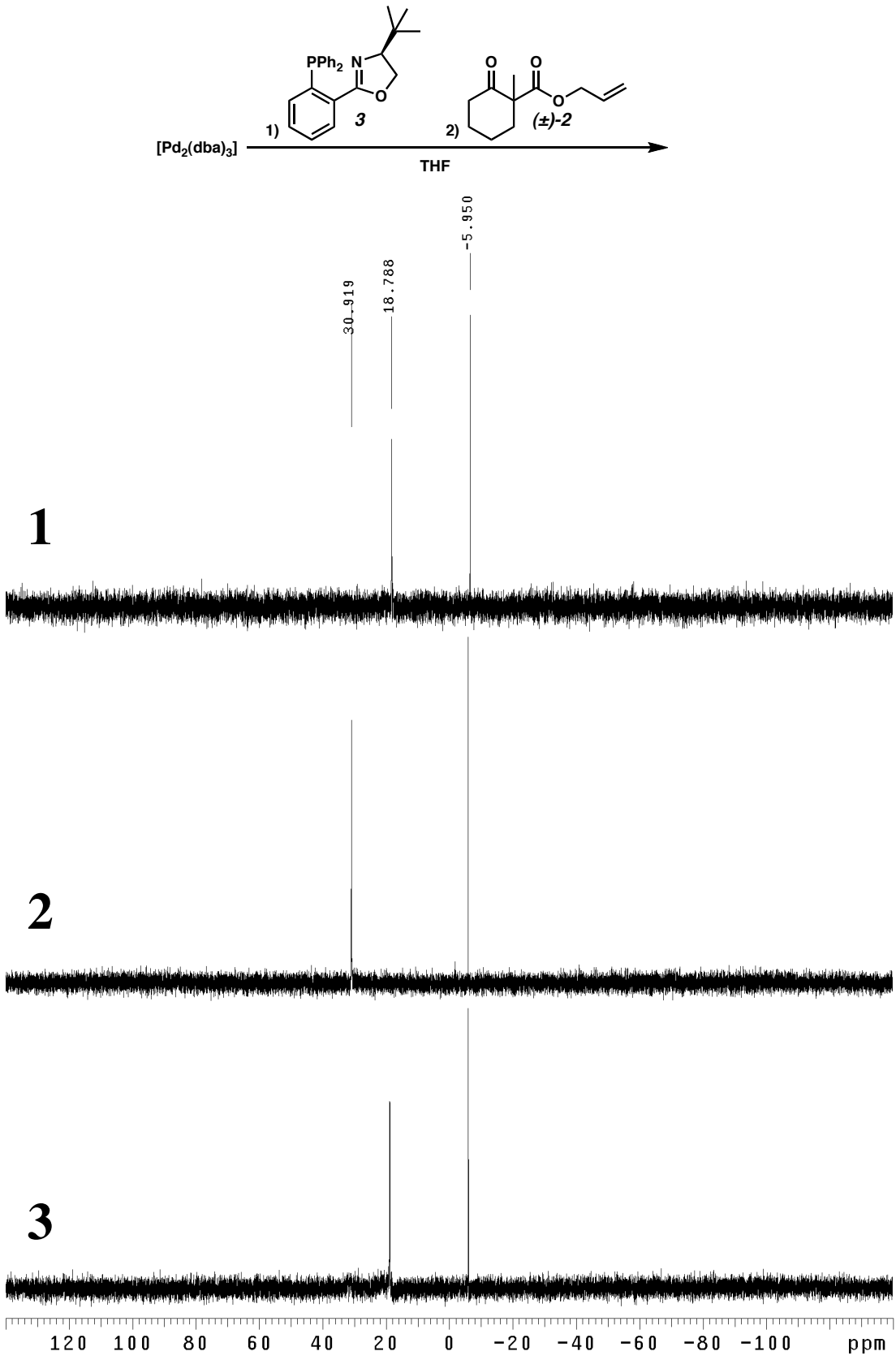
^{31}P NMR Studies:

General Notes and Procedures:

For NMR studies of the various allylic alkylation procedures, the reaction was followed by TLC. Due to air sensitivity, TLCs were taken either by cycling the NMR tube into a nitrogen glove box and taking an aliquot, or by connecting the NMR tube through its septum to an argon line with a needle while sampling the solution with a second needle and TLC spotter under slight argon overpressure. The most common product of air exposure was the phosphine oxide of (*S*)-*t*-BuPHOX ligand (page 34 of this supporting information contains characterization data for (*S*)-*t*-BuPHOX oxide for reference.)

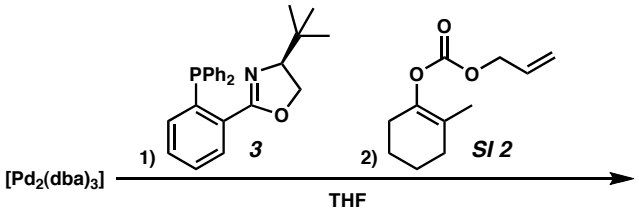
The Decarboxylative Allylic Alkylation of β-ketoester 2 Monitored by ^{31}P NMR:

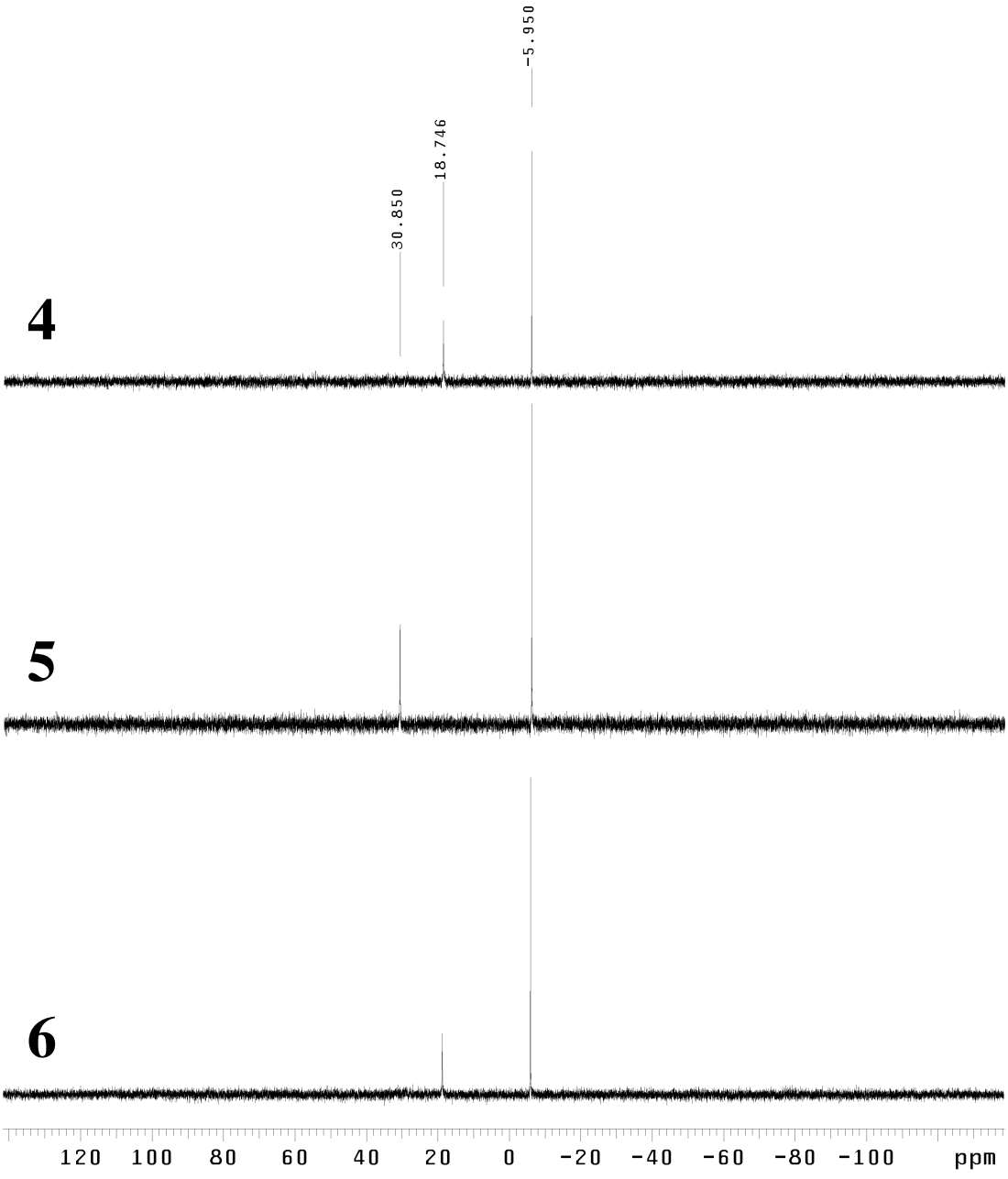
In a nitrogen atmosphere glove box [$Pd_2(dba)_3$] (3.0 mg, 3.3 μmol, 1 equiv) was placed in a 1-dram vial. (*S*)-*t*-Bu-PHOX ligand (**3**) (3.3 mg, 8.5 μmol, 2.6 equiv) was weighed in a second 1-dram vial. THF (1 mL) was filtered through a pipette with glass filter paper directly into the vial containing the (*S*)-*t*-Bu-PHOX ligand (**3**). The solution was mixed manually by pipette until all the material had dissolved forming a clear colorless solution. The solution was then moved by pipette to the vial containing [$Pd_2(dba)_3$]. This solution was mixed manually by pipette for 1 min during which time a dark red-purple solution formed that then lightened to a dark but richly orange color. This solution was then filtered through a pipette filter with glass filter paper directly into an NMR tube, separating a bright, richly orange filtrate from a black amorphous precipitate presumed to be colloidal Pd(0) particles. The NMR tube was then sealed with a septum and removed from the glove box. NMR spectrum # 1 was taken at this time. Neat 1-methyl-2-oxo-cyclohexanecarboxylic acid allyl ester (β-ketoester **2**) (12.3 mg, 62.8 μmol, 19.1 equiv) was added to the NMR tube via a 25 μL Hamilton syringe in a single portion. The NMR tube was shaken vigorously for 30 s, and the solution quickly changed color from a rich orange to a lighter yellow-green. NMR spectrum # 2 was taken at this time. The NMR tube was then placed in an oil bath regulated at 24 °C and warmed for 3 h, which was 20 min longer than it took for the solution's color to change from a light yellow-green to a rich orange. NMR spectrum # 3 was taken at this time.


PPh2
N
O
3
1)
2)
O
O
O
(±)-2
[Pd2(dba)3]
THF
30.919
18.788
-5.950
1
2
3
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
ppm

The Decarboxylative Allylic Alkylation of Allyl 2-methylcyclohex-1-enyl carbonate (SI 2) Monitored by ^{31}P NMR:

In a nitrogen glove box (*S*)-*t*-BuPHOX ligand (3.3 mg, 8.5 μmol, 1.3 equiv) was weighed into a half-dram vial. [$Pd_2(dba)_3$] (2.9 mg, 3.2 μmol, 0.5 equiv) was weighed into a second half-dram vial. Anhydrous THF (1 mL) was filtered through a pipette filter with glass filter paper into the half-dram vial containing the PHOX ligand. The solution was mixed manually via pipette for a little less then 1 min until all material had dissolved. The resulting solution was transferred via pipette and added as a single portion to the half-dram vial containing the [$Pd_2(dba)_3$]. The resulting solution was mixed manually via pipette for 2 min during which time it turned a dark purple-brown. The solution was left to stand and mix via diffusion for 30 min during which time it turned an orange color. The solution was filtered though a pipette with glass filter paper to separate a bright orange solution from a small amount of black precipitate presumed to be aggregated palladium(0) metal. The NMR tube was sealed with a septum and removed from the glove box. NMR spectrum # 4 was taken at this time. Allyl 2-methylcyclohex-1-enyl carbonate (**SI 2**) (12.9 mg, 65.7 μmol, 10.3 equiv) was added in a single portion via a syringe. The tube was fully inverted and righted causing an abrupt color change from a rich orange color to a light yellow-green solution. NMR spectrum # 5 was taken at this time. The NMR tube was left to stand for 3 h at 24 °C during which time the solution turned orange. NMR spectrum # 6 was taken at this time. The solution was concentrated under a jet of nitrogen to a small amount of yellow solution. Chromatography was preformed in a pipette column on silica eluting with 5→10% Et_2O in petroleum ether affording 2-allyl-2-methylcyclohexanone (87.4% ee [assay: GC, G-TA column {100 °C isothermal for 30 min}, major enantiomer (*S*) Ret. Time = 14.897 min, minor enantiomer (*R*) Ret. Time = 17.313 min], clear colorless oil).


PPh2
N
O
3
1)
2)
O
O
O
SI 2
[Pd2(dba)3]
THF

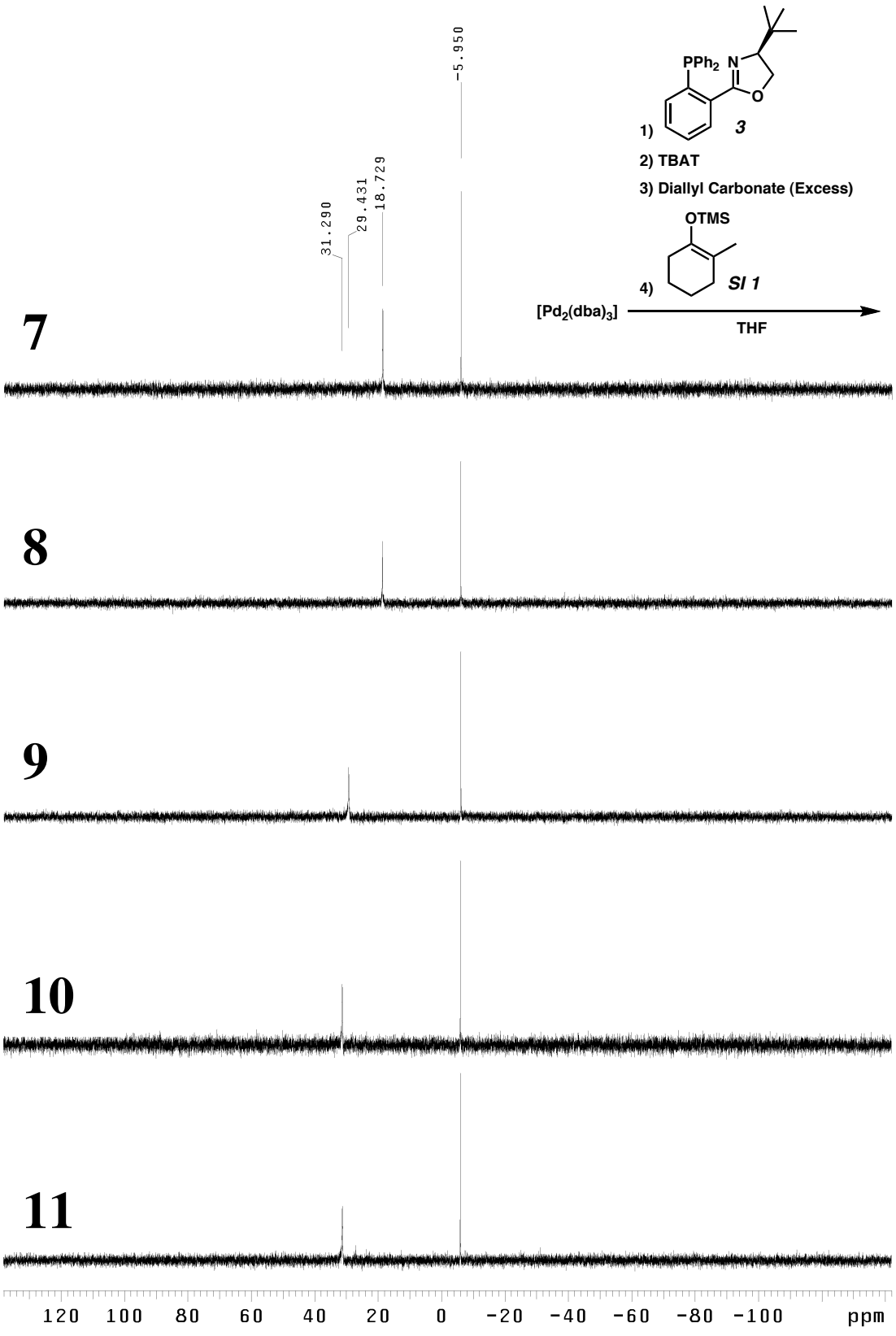

-5.950
18.746
30.850
4
5
6
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
ppm

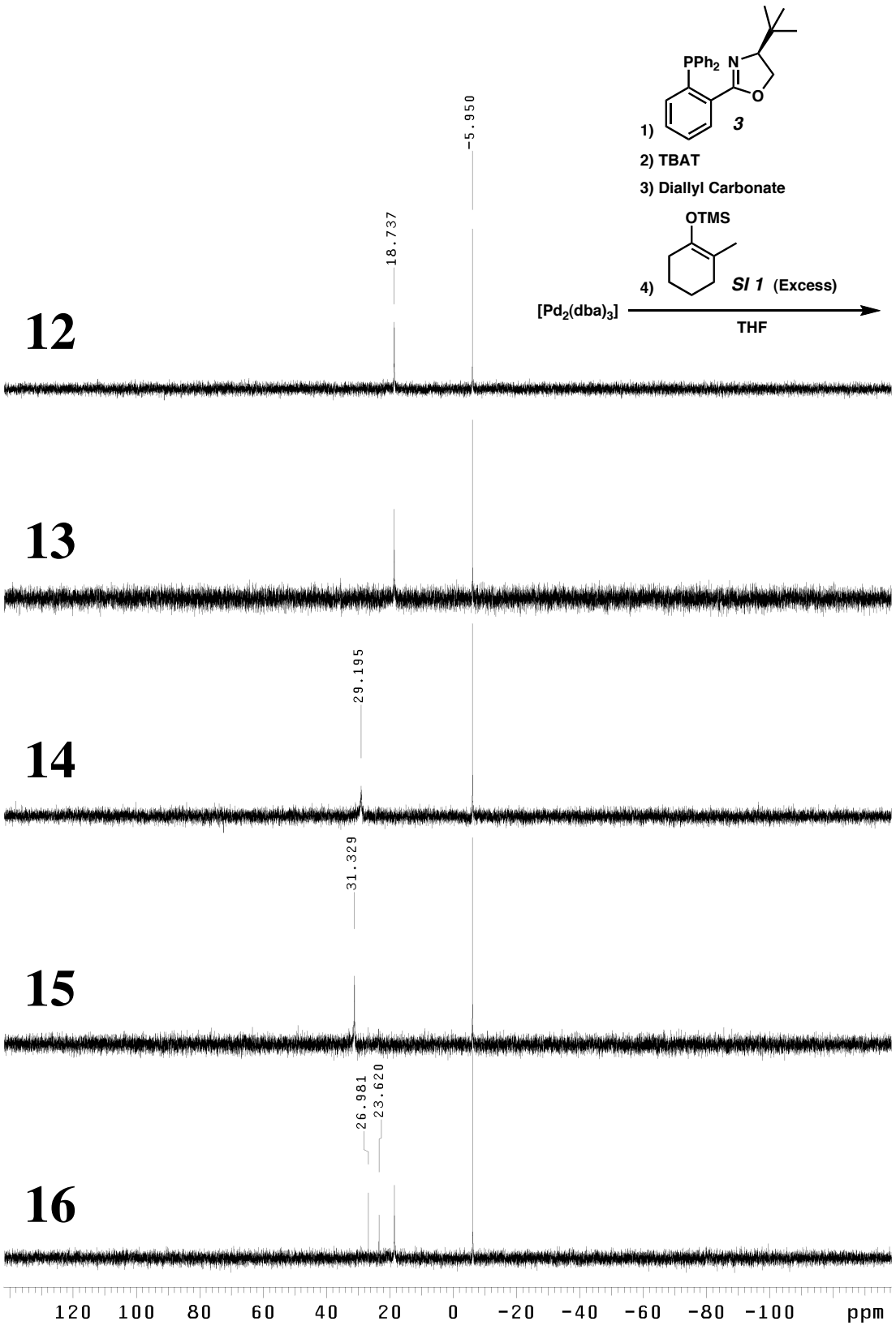
The Decarboxylative Allylic Alkylation of Trimethyl(2-methylcyclohex-1-enyloxy)silane (SI 1) Monitored by ^{31}P NMR (standard alkylation procedure):

In a nitrogen glove box (*S*)-*t*-BuPHOX ligand (3.5 mg, 9.0 μmol, 1.4 equiv) was weighed into a half-dram vial. [$Pd_2(dba)_3$] (3.0 mg, 3.3 μmol, 0.5 equiv) was weighed into a second half-dram vial. Anhydrous THF (1 mL) was added into the half-dram vial containing the PHOX ligand. The solution was mixed manually via pipette for 1 min until all of the solids had dissolved. The resulting solution was added to the half-dram vial containing the [$Pd_2(dba)_3$] via pipette in a single portion. The resulting solution was mixed manually via pipette for 2 min during which time it turned a dark purple-brown. The solution was left to stand and mix via diffusion for 30 min during which time it turned an orange color. The solution was filtered though a pipette with glass filter paper to separate a bright orange solution from a small amount of black precipitate presumed to be aggregated palladium(0) metal. The NMR tube was sealed with a septum and removed from the glove box. NMR spectrum # 7 was taken at this time. The NMR tube was the cycled back into the glove box. TBAT (3.6 mg, 6.7 μmol, 1 equiv) was weighed into a half-dram vial in the glove box. The contents of the NMR tube were emptied into the half-dram vial. The solution was mixed manually by pipette for 1 min until all the material had dissolved. The resulting solution was returned to the NMR tube, which was resealed with a septum and removed from the glove box. NMR spectrum # 8 was taken at this time. Diallyl carbonate (10 μL, 9.9 mg, 69.7 μmol, 10.6 equiv) was added via a syringe in one portion. The NMR tube was inverted once resulting in a rapid color change from a rich orange to a light yellow-green. NMR spectrum # 9 was taken at this time. Trimethyl(2-methylcyclohex-1-enyloxy)silane (**SI 1**) (10.6 mg, 67.8 μmol, 10.3 equiv) was added via a syringe in one portion. NMR spectrum # 10 was taken at this time. The NMR tube was left to stand for 10 h at 24 °C during which time the solution turned orange. NMR spectrum # 11 was taken at this time. The solution was then concentrated under a jet of nitrogen to a small amount of yellow oil. Chromatography was preformed on a pipette column on silica eluting with 5→10% Et_2O in petroleum ether affording 2-allyl-2-methylcyclohexanone (84.5% ee [assay: GC, G-TA column {100 °C isothermal for 30 min}, major enantiomer (*S*) Ret. Time = 14.897 min, minor enantiomer (*R*) Ret. Time = 17.313 min], clear colorless oil).

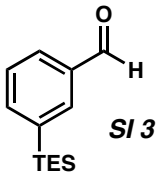
The Decarboxylative Allylic Alkylation of Trimethyl(2-methylcyclohex-1-enyloxy)silane (SI 1) Monitored by ^{31}P NMR (excess nucleophile):

The procedure above was repeated with the following changes: Diallyl carbonate (9.0 μL, 8.9 mg, 62.7 μmol, 9.8 equiv), Trimethyl(2-methylcyclohex-1-enyloxy)silane (**SI 1**) (10.5 mg, 67.2 μmol, 10.5 equiv). NMR spectra 12 to 16 were taken at the equivalent intervals to NMR spectra 7 to 11. The ee was 84.9% as measured by GC.


31.290
29.431
18.729
-5.950
PPh2
N
O
1)
3
2) TBAT
3) Diallyl Carbonate (Excess)
OTMS
4)
SI 1
[Pd2(dba)3]
THF
7
8
9
10
11
120 100 80 60 40 20 0 -20 -40 -60 -80 -100 ppm

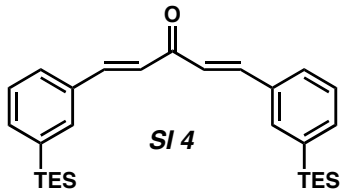

PPh2
N
O
3
1)
2) TBAT
3) Diallyl Carbonate
OTMS
4)
SI 1 (Excess)
[Pd2(dba)3]
THF
12
13
14
15
16
-5.950
18.737
29.195
31.329
26.981
23.620
120 100 80 60 40 20 0 -20 -40 -60 -80 -100 ppm

Synthesis of $[Pd_2(mtdba)_3]$:



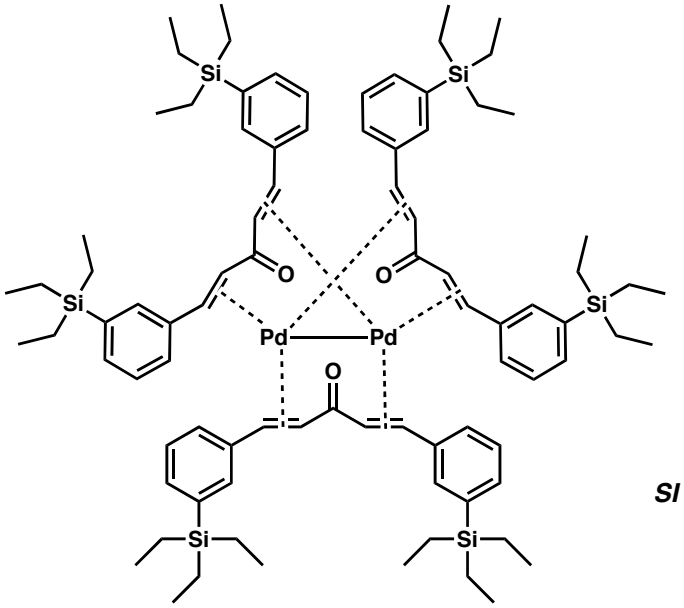
SI 3

3-(Triethylsilyl)benzaldehyde (SI 3): Anhydrous THF (160 mL) was added to a 250 mL 14/20 round-bottom flask with a stir bar. To this solution was added 3-bromobenzaldehyde diethylacetal (8.0 mL, 10 g, 39 mmol) via syringe. The solution was cooled to –78 °C and *n*-BuLi (2.5 M solution in hexanes, 36 mL, 90 mmol, 2.3 equiv) was added dropwise to the cooled stirring solution via syringe over 45 min. The solution was left to stir at –78 °C for 2 h. Triethylsilylchloride (7.6 mL, 6.8 g, 45 mmol, 1.2 equiv) was added via syringe over 15 min. The solution was stirred for 3 h at –78 °C, and allowed to warm to and maintain room temperature over 8 h. The solution was quenched with aq HCl (2 N, 90 mL) and diluted with diethyl ether (45 mL). The phases were spererated. The aq phase was extracted with diethyl ether (2 x 25 mL). The organic phases were merged, washed with aq saturated sodium chloride (1 x 100 mL), dried over magnesium sulfate, filtered with dichloromethane, and concentrated in vacuo. The resulting liquid was diluted with THF (6 mL), acetic acid (15 mL), and water (4 mL), and stirred for 3 h. The solution was slowly and carefully quenched with saturated aq sodium bicarbonate (100 mL) causing the rapid evolution of gas. The solution was diluted with diethyl ether (30 mL), and the phases were separated. The aq phase was extracted with diethyl ether (2 x 25 mL). The organic phases were washed with saturated aq sodium chloride (1 x 50 mL), dried over sodium sulfate, filtered with ethyl acetate, and concentrated in vacuo. The resulting yellow oil was bulb-to-bulb distilled on a kugelrohr at 0.3 torr and 130–180 °C using a 25 mL bulb before the final collection bulb to help fractionate the distillate. Volatile impurities were removed from the distillate in a kugelrohr distillation at 0.2 torr and 15–85 °C affording 3-(triethylsilyl)benzaldehyde (**SI 3**) (4.86 g, 56.5% yield, faintly colored clear oil). TLC (R_f 0.65, 5% diethyl ether in petroleum ether, observed by UV). ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.98 (s, 1H), 7.85 (ddd, J = 7.6, 1.5, 1.5 Hz, 1H), 7.75 (ddd, J = 7.3, 1.2, 1.2 Hz, 1H), 7.52 (dd, J = 7.6, 7.3 Hz, 1H), 0.97 (t, J = 7.8 Hz, 9H), 0.85 (qm, J = 7.8 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.1, 140.4, 139.1, 135.73, 135.70, 130.2, 128.5, 7.5 (br. s), 3.3; IR (neat film, NaCl) 2955, 2910, 2876, 2808, 2716, 1700, 1586, 1572, 1458, 1415, 1370, 1263, 1238, 1205, 1170, 1123, 1106, 1010, 891, 864, 790, 734, 720, 696 cm^{-1}; HRMS (LC/MS TOF, Multi Mode: APCI/ESI) *m/z* calc'd for $C_{13}H_{21}OSi$ $[M + H]^+$: 221.1356, found: 221.1361.



1,5-Bis-[3-(triethylsilyl)phenyl]penta-1,4-dien-3-one, (mtdba) (SI 4): To a 250 mL Erlenmeyer flask with a stir bar were added sodium hydroxide (1.92 g, 48.0 mmol, 5.4 equiv) and water (20 mL). Stirring was started, and once all the sodium hydroxide had dissolved, ethanol (200 proof, 34 mL) was added. The solution was cooled to 0 °C, and 3-(triethylsilyl)benzaldehyde (**SI 3**) (4.08 g, 18.5 mmol, 2.04 equiv) was added dropwise over 5 min. Acetone (650 μL, 514 mg, 8.85 mmol) was added dropwise to the cooled stirring solution over 2 min. The solution was stirred for 5 min at 0 °C, and the cold bath was removed and the solution was stirred at room temperature for 9 h. The solution was diluted with water (25 mL) and hexanes (50 mL). The aq phase was extracted with hexanes (2 x 25 mL) and 1:1 hexanes : diethyl ether (2 x 25 mL). The organic phases were washed with water (2 x 25 mL) and saturated aq sodium chloride (50 mL). The organic phases were then dried with magnesium sulfate, filtered with dichloromethane, and concentrated in vacuo. Chromatography was performed with 0.5%→5% Et_2O in petroleum ether on silica gel to afford 1,5-bis-[3-(triethylsilyl)phenyl]penta-1,4-dien-3-one (**SI 4**) (54.4% yield, bright yellow-green waxy solid). TLC (R_f 0.41, 5% ether in petroleum ether, observed by UV and stained with anisaldehyde [orange]); mp 72.5–74.5 °C;[c] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (d, J = 16.0 Hz, 2H), 7.70 (s, 2H), 7.65 (d, J = 7.7 Hz, 2H), 7.53 (d, J = 7.3 Hz, 2H), 7.41 (dd, J = 7.7, 7.3 Hz, 2H), 7.10 (d, J = 16.0 Hz, 2H), 0.98 (t, J = 7.8 Hz, 18H), 0.83 (qm, J = 7.9 Hz, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.2, 144.0, 138.8, 136.6, 134.9, 134.1, 128.39, 128.35, 125.4, 7.6, 3.4; IR (neat film, NaCl) 3047, 2954, 2909, 2874, 1652, 1619, 1456, 1415, 1394, 1323, 1237, 1187, 1096, 1010, 875, 793, 769, 735, 720 cm^{-1}; HRMS (LC/MS TOF, Multi Mode: APCI/ESI) *m/z* calc'd for $C_{29}H_{43}OSi_2$ $[M + H]^+$: 463.28524, found: 463.28502.

[c] The material becomes soft and relaxes noticeably above 68 °C but does not actually change states until the given range.



SI 5

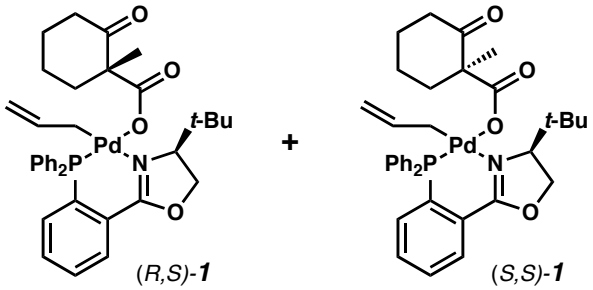
Tris{1,5-bis-[3-(triethylsilyl)phenyl]penta-1,4-dien-3-one}dipalladium(0), [Pd_2(mtdba)$_3$] (SI 5):[4] 1,5-Bis-[3-(triethylsilyl)phenyl]penta-1,4-dien-3-one (**SI 4**) (1.70 g, 3.67 mmol, 3.4 equiv) and sodium acetate (1.48 g, 18.0 mmol, 16.7 equiv) were added neat to a flame dried 100 mL round-bottom flask with a stirbar. The flask was sparged with argon. Dry methanol (44 mL) was added via syringe. Stirring was started, and the solution was heated to 58 °C in an oil bath. Palladium(II) dichloride (382.6 mg, 2.158 mmol, 2 equiv) was added to the heated stirring solution in one portion. The solution was left to stir for about 5 min until it turned a dark purple-brown color. The temperature was reduced to 40 °C, and the solution was left to stir for 2 h. The solution was filtered on a 60 mL frit, and the solid was rinsed with methanol (2 x 15 mL) and then water (2 x 25 mL). The dark purple powder was collected, dissolved in hexanes (15 mL) and was filtered on a frit rinsing with hexanes (25 mL). The filtrate was diluted with ethanol (100 mL, 200 proof), methanol (100 mL), and cooled to –20 °C in a freezer for 36 h forming crystals.[d] Crystals were recovered by filtration on a 30 mL frit and were rinsed with methanol (30 mL) yielding a first crop of tris{1,5-bis-[3-(triethylsilyl)phenyl]penta-1,4-dien-3-one}dipalladium(0) [Pd_2(mtdba)$_3$] (**SI 5**) (62.9% yield, dark purple crystalline flakes). The filtrate was concentrated in vacuo, redissolved in hexanes (2 mL), diluted with ethanol (5 mL, 200 proof), then methanol (5 mL) and left to crystallize in a –20 °C freezer. After 36 h, crystals formed. The second crop of crystals were recovered by filtration on a 15 mL frit, then were washed with methanol (4 x 5 mL) and then ethanol[e] (10 x 8 mL) yielding a second crop of tris{1,5-bis-[3-(triethylsilyl)phenyl]penta-1,4-dien-3-one}dipalladium(0) [Pd_2(mtdba)$_3$] (**SI 5**) (9.7% yield, 72.6% yield total, dark-purple crystalline flakes). mp 194 °C (decomposition); ^{1}H NMR (600 MHz, $CDCl_3$, 25 °C) δ

[d] The solution of the crude complex in hexanes is immiscible with methanol and no crystallization or precipitation occurs even on the interface between the two phases. By adding ethanol first, the methanol becomes miscible and the resulting ternary solvent system becomes ideal for crystallization at lower temperatures.

[e] The second crop of crystals often formed with an amorphous white or off-white solid. This amorphous solid is weakly soluble in ethanol and is the reason for the recommended ethanol washes of the second crystal crop.

7.68–7.79 (comp. m, 3H), 7.76 (d, J = 15.8 Hz, 0.3H), 7.69 (br. s, 0.35H), 7.63 (dm, J = 7.9 Hz, 0.18H), 7.58 (d, J = 7.3 Hz, 0.2H), 7.51–7.37 (comp. m, 3.73H), 7.34–7.12 (comp. m, 4.56H), 7.11–7.00 (comp. m, 1.54H), 6.88 (br. s, 1H), 6.79–6.61 (m, 5.34H), 6.61–648 (m, 2H), 6.15 (d, J = 14.0 Hz 1H), 6.07 (br. s, 0.67H), 5.95 (d, J = 9.7 Hz, 2H), 5.67 (br. s, 1H), 5.52–5.38 (comp. m, 1.77H), 5.38–5.20 (comp. m, 2.25H), 5.09 (d, J = 12.6 Hz, 1H), 4.94 (app. t, J = 12.8 Hz, 1.42), 4.88 (br. s, 0.91 H),[f] 1.15–0.94 (m, 54H), 0.94–0.70 (m, 36H); ^{13}C NMR (150 MHz, $CDCl_3$, –10 °C) δ 188.9, 184.6, 182.6, 181.6, 180.8, 144.0, 142.0, 138.96, 138.92, 138.7, 138.6, 138.5, 138.4, 138.1, 138.0, 137.6, 137.4, 137.1, 137.0, 136.7 136.1, 135.8, 135.2, 135.0, 134.7 134.5, 134.4, 134.05, 133.95, 133.71, 133.70, 133.35, 133.34, 133.31, 133.0, 128.5, 128.3, 128.1, 112.4 (br. s), 110.8, 110.2 (br. s), 97.7 (br. s), 96.8 (br. s), 94.3 (br. s), 91.4 (br. s), 89.2 (br. s), 85.7 (br. s), 84.4 (br. s), 84.1 (br. s), 7.71, 7.68, 7.67, 7.654, 7.647, 7.5, 3.4, 3.32, 3.28, 3.26, 3.24, 3.23, 3.1; IR (neat film, NaCl) 3080, 3045, 3023, 2954, 2909, 2875, 1621, 1585, 1570, 1544, 1464, 1416, 1386, 1323, 1297, 1239, 1186, 1120, 1082, 1010, 975, 911, 877, 861, 791, 736, 720, 686, 611 cm^{-1}; IR (Fluorolube® mull, CaF_2) 3076, 3041, 3020, 2950, 2906, 2872, 1620, 1586, 1568, 1544, 1455, 1415, 1385 cm^{-1}; HRMS (high field FAB, 2-nitrophenyl octyl ether) *m/z* calc'd for $C_{87}H_{126}O_3Pd_2Si_6$ $[M]^+$: 1601.6505, found: 1601.6477.

Synthesis, Handling, and Characterization Methods for Intermediate 1:



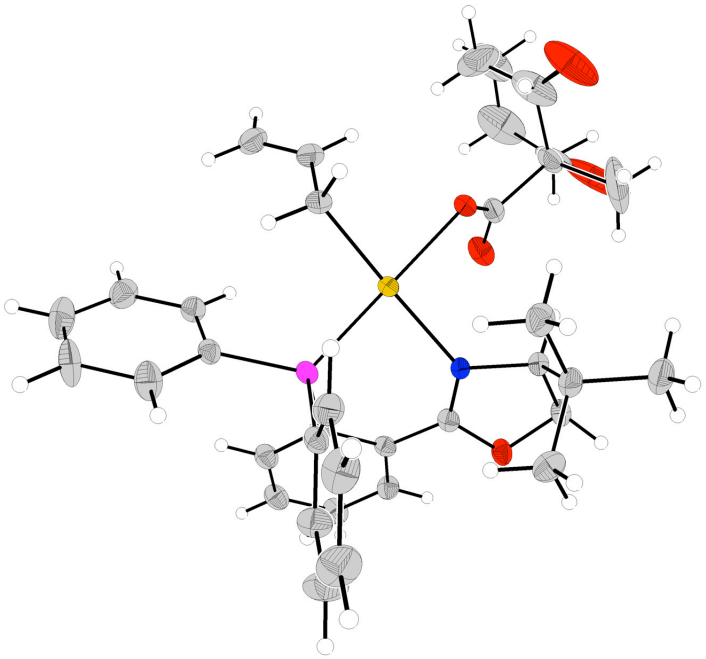
Synthesis:

Complexes (*R*,*S*)-1 and (*S*,*S*)-1: In a glove box with a nitrogen atmosphere, (*S*)-*t*-BuPHOX ligand (**3**) (148.8 mg, 384.0 mmol, 1.24 equiv) was added to a 20 mL scintillation vial. $[Pd_2(mtdba)_3]$ (**SI 5**) (248.9 mg, 155.4 mmol, 0.5 equiv) was weighed into a 1-dram vial.[g] Anhydrous THF (1 mL) was added to the 20 mL vial containing (*S*)-*t*-BuPHOX lignad (**3**). The 20 mL scintillation vial was swirled manually until all the (*S*)-*t*-BuPHOX ligand (**3**) had dissolved. Anhydrous THF (3 x 1 mL) was added into the 1-dram vial containing $[Pd_2(mtdba)_3]$ (**SI 5**), each portion was mixed manually by pipette and then added dropwise to the solution of (*S*)-*t*-BuPHOX ligand (**3**) in the 20 mL

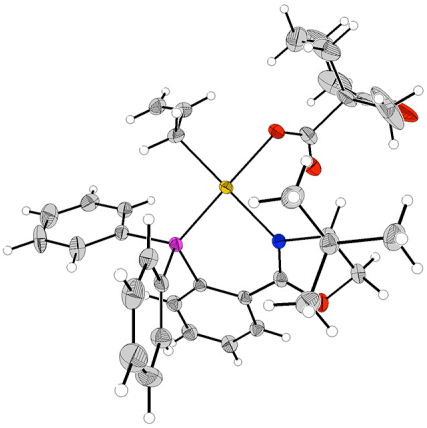
[f] This resonance overlaps significantly with the triplet immediately down field of it. The reported integrations were estimated from the combine integration of these two resonances of 2.33H.

[g] It should be noted that the use of this custom $[Pd_X(dba)_Y]$ derivative in this reaction was not arbitrarily decided upon. Numerous previously reported palladium(0) sources were employed first in this reaction including other $[Pd_X(dba)_Y]$ derivatives such as: $[Pd_2(dba)_3]$, $[Pd(dba)_2]$, $[Pd(pmdba)_2]$, and $[Pd_2(dmdba)_3]$. All other palladium(0) sources tried resulted in prohibitive purification issues.

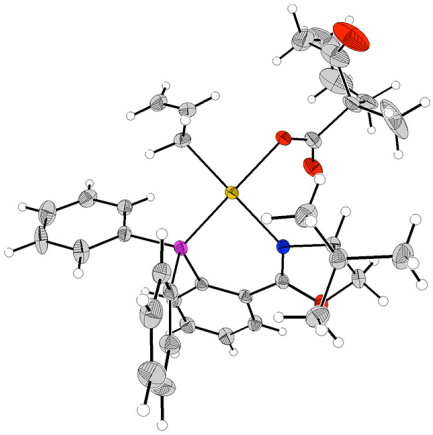
scintillation vial. The solution was swirled manually by hand for 1 min, and then left to stand and mix by diffusion for 1.5 h. The solution was cooled to –36 °C in a freezer in the glove box. Once cooled, the solution was then moved to a precooled aluminum block at –36°C in the glove box. Then, 1-methyl-2-oxo-cyclohexanecarboxylic acid allyl ester (β-ketoester **2**) (157 mg, 800 mmol, 2.57 equiv) was added via a syringe in a single portion. The solution was stirred manually for 1 min while cold, and moved to a –36 °C freezer in the glove box. The reaction was left to stand for 10 min in the freezer. The solution was then diluted with hexanes (12 mL) that had been precooled to –20 °C, and then the mixture was concentrated in vacuo in a –20 °C freezer in the glove box to roughly 10 mL. The solution was moved in 2 mL portions to another 20 mL scintillation vial in a precooled aluminum block at –36 °C where each portion was individually triturated with hexanes (5 mL) that had been precooled to –20 °C, then the supernatant was decanted via pipette. Solvent was removed from the precipitated material in vacuo at –20 °C in a freezer in the glove box to afford a mixture of complexes (*S*,*S*)-**1** and (*R*,*S*)-**1** (72.4 mg, 33.8% yield, bright yellow powder). ^{1}H NMR (600 MHz, $THF_{d\text{-}8}$, –28 °C) δ 8.19 (app. br. t, *J* = 3.5 Hz, 1H), 7.69 (app. t, *J* = 7.5 Hz, 1H), 7.62 (app. t, *J* = 7.2 Hz, 1H), 7.59–7.46 (comp. m, 8H), 7.25 (app. t. *J* = 9.0 Hz, 2H), 7.03 (app. t. *J* = 8.8 Hz, 1H), 6.23 (br. s, 1H), 5.11 (s, 1H), 4.57 (d, *J* = 9.7 Hz, 1H), 4.55–4.47 (m, 1H), 4.47 (br. s, 1H), 4.40-4.23 (comp. m, 2H), 3.06 (br. s, 0.35H), 2.94–2.85 (br. m, 1H), 2.86–2.77 (m, 0.65H), 2.48 (dd, *J* = 14.0, 13.8 Hz, 1H), 2.17 (d, *J* = 13.2 Hz, 0.35H), 2.11 (d, *J* = 12.9 Hz, 0.65H), 1.97–1.85 (m, 1H), 1.84–1.70 (m, 1H), 1.63–1.38 (m, 1H), 1.38–1.45 (m, 1H), 1.33–1.18 (m, 1.3H), 1.14 (s, 1.95H), 1.11 (s, 1.05H), 0.92–0.87 (m 0.35H), 0.69 (s, 9H); ^{13}C NMR (150 MHz, $THF_{d\text{-}8}$, –28 °C) δ 210.3, 210.2, 176.7, 176.6, 163.6, 143.8 (app. br. s), 135.8, 134.9 (d, J_{CP} = 11.0 Hz), 134.7 (d, J_{CP} = 12.2 Hz), 133.7 (d, J_{CP} = 6.6 Hz), 133.4 (d, J_{CP} = 7.7 Hz), 132.4 (d, J_{CP} = 9.4 Hz), 132.1, 131.4, 131.08, 131.02, 130.7, 130.45, 130.37, 130.04, 129.97, 129.9, 129.8, 129.3, 129.0. 106.3 (app. br. s), 70.3, 68.1, 67.9, 67.8, 59.4, 41.85, 41.81, 40.6, 40.5, 35.1, 29.2 (app. br. s), 28.9, 28.7, 25.9, 25.8, 25.7, 24.55, 24.48, 23.0, 22.9; ^{31}P NMR (121.4 MHz, $THF_{d\text{-}8}$, 24 °C) δ 30.9; ^{31}P NMR (121.4 MHz, $THF_{d\text{-}8}$, –20 °C) δ 30.8; IR (neat film, NaCl) 3065, 2956, 2930, 2858, 1708, 1662, 1623, 1613, 1571, 1483, 1465, 1437, 1372, 1346, 1313, 1243, 1166, 1142, 1117, 1099, 1062, 1029, 959, 900, 876, 848, 814, 781, 696, 675 cm^{-1}; IR (Fluorolube® mull, CaF_2) 3076, 3055, 3016, 2959, 2934, 2924, 2874, 2853, 1711, 1634, 1616, 1604, 1568, 1480, 1465, 1448, 1433, 1373 cm^{-1}; HRMS (FAB, 2-nitrophenyl octyl ether) *m/z* calc'd for $C_{28}H_{31}NOPPd$ $[M - C_8H_{11}O_3]^+$: 534.1178, found: 534.1187; X-ray quality crystals were grown by partially dissolving freshly synthesized intermediate **1** in cold (–20 °C) THF using the undissolved material to act as a nucleation site for crystals, and then the solution was layered with cold hexanes (–20 °C). Diethyl ether was added dropwise until most of the finer precipitation on the boundary between the layers had redissolved and layer diffusion was allowed to progress at –36 °C in a glove box freezer.



Superposition of diastereomers as appears in the cif file.



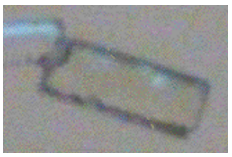
Major diastereomer

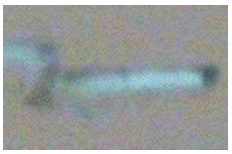


Minor diastereomer

Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 695531.

Crystal data and structure refinement for NHS20 (CCDC 695531).





Empirical formula	$C_{36}H_{42}NO_4PPd$
Formula weight	690.08
Crystallization Solvent	Ether/THF/hexanes
Crystal Habit	Blade
Crystal size	0.17 x 0.10 x 0.06 mm^3
Crystal color	Pale yellow

Data Collection

Type of diffractometer	Bruker KAPPA APEX II
Wavelength	0.71073 Å MoKα
Data Collection Temperature	100(2) K
θ range for 9986 reflections used in lattice determination	2.50 to 33.63°
Unit cell dimensions	a = 10.7719(4) Å b = 12.4117(4) Å c = 24.7631(8) Å
Volume	3310.77(19) $Å^3$
Z	4
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Density (calculated)	1.384 Mg/m^3
F(000)	1432
θ range for data collection	2.06 to 34.15°
Completeness to θ = 34.15°	94.0 %
Index ranges	$-16 \le h \le 9$, $-18 \le k \le 17$, $-39 \le l \le 35$
Data collection scan type	ω scans; 11 settings
Reflections collected	62894
Independent reflections	12522 [R_{int}= 0.0472]
Absorption coefficient	0.648 mm^{-1}
Absorption correction	None
Max. and min. transmission	0.9622 and 0.8979

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 2008)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	SHELXL-97 (Sheldrick, 2008)

Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	12522 / 0 / 402
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.778
Final R indices [I>2σ(I), 10824 reflections]	R1 = 0.0347, *w*R2 = 0.0482
R indices (all data)	R1 = 0.0454, *w*R2 = 0.0488
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.002
Average shift/error	0.000
Absolute structure parameter	-0.023(12)
Largest diff. peak and hole	1.696 and -1.113 e.Å^{-3}

Special Refinement Details

Crystals were mounted on a glass fiber using Paratone oil then placed on the diffractometer under a nitrogen stream at 100K.

The ketone oxygen (O4) is disordered over two positions, bonded to C28 (39.8%) or C32 (60.2%). The thermal ellipsoids and the difference Fourier in this area suggest there is some small rotational component to this disorder as well. The rotational component was not included in the model.

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.

Handling and Characterization Methods for Complexes (*S*,*S*)-1 and (*R*,*S*)-1:

Due to the instability of complexes (*S*,*S*)-**1** and (*R*,*S*)-**1** basic handling and the acquisition of characterization data often required special procedures to achieve good reproducible results. These procedures are outlined here.

General Handling Notes: All glassware and metalware were precooled to –36 °C in a freezer for 1 h before being allowed to come into contact with complexes (*S*,*S*)-**1** and (*R*,*S*)-**1**. If during operation, glassware or metalware warmed to the point that it was just barely perceptibly cool through triple gloves, it was resubjected to the –36 °C freezer for at least 20 min before being used again. All solvents that came in contact with complexes (*S*,*S*)-**1** and (*R*,*S*)-**1** were precooled to either –36 °C or –20 °C in a freezer as indicated. Complexes (*S*,*S*)-**1** and (*R*,*S*)-**1** were only ever exposed to argon or nitrogen atmospheres; even as a desolvated crystalline solid at subzero temperatures these complexes appear to react slowly with air and possibly moisture. Decomposition of these complexes by poor handling could be readily determined by indicative color change. Healthy samples of the complexes are a bright yellow, reminiscent of a classic highlighter pen. Air exposure leads to an orange color change while minimal thermal decomposition leads to a more subtle color change resulting in a yellow-beige hue. In cases where some decomposition had occurred, samples could be partially recovered with tolerable, but not analytical, purity by manually excising incorrectly colored regions using precooled implements. Such recovered samples are unfit for NMR or IR characterization, but give consistent results when used in reactions. Samples of complexes (*S*,*S*)-**1** and (*R*,*S*)-**1** store well as a desolvated solid at –36 °C in a glove box freezer for months, but do eventually show signs of decomposition by ^{1}H NMR.

Thin Film IR on NaCl plates: In a glove box, a few milligrams of the diastereomeric mixture of complexes (*S*,*S*)-**1** and (*R*,*S*)-**1** were added to a half dram vial in an aluminum block that had been precooled to –36 °C in a freezer. The sample was dissolved in minimal anhydrous THF that had been precooled to –36 °C in a freezer, and then the solution was carefully deposited via a pipette on a NaCl IR plate that had been precooled to –36 °C in a freezer. The IR plate was quickly moved into a small desiccator inside the glove box, and the desiccator was inserted into a –20 °C freezer in the glove box. A vacuum hose was connected to the desiccator inside the glove box in the –20 °C freezer, and a gentle vacuum was applied reducing the solution on the IR plate to a thin yellow-green film over 5 h. The thin film was then sandwiched between a second NaCl IR plate that had been precooled to –36 °C. The fine gap between the two plates was sealed over with Parafilm®, and the sealed plates were returned to the desiccator in a –20 °C freezer for 20 min. The desiccator was sealed, quickly removed from the glove box, and then partially submerged in a bucket of powdered dry ice that was carried to the spectrometer. The sealed plates were removed from the desiccator whereupon they quickly frosted over. A Kimwipe® was used to vigorously polish both exterior faces of the two-plate sandwich until they were just barely warm enough that they did not readily frost over (roughly 1 min), but that the sample in between the two plates was still cold. The two-plate sandwich was then inserted into the spectrometer just above a fresh dish full of anhydrous $CaCl_2$ and a rushing stream of nitrogen. It is recommended that new or otherwise valuable NaCl plates not be used for this procedure as they are left opaque and lightly pitted by the unavoidable quick frosting and polishing.

Fluorolube® mull IR on CaF_2 plates: In a glove box, a small amount of partially frozen Fluorolube® was spread thinly with a spatula across the center of a CaF_2 IR plate that had been precooled to –36 °C in a freezer. A few milligrams of the mixture of complexes (*S*,*S*)-**1** and (*R*,*S*)-**1** were added on top of the Fluorolube® film as a powder. The powder and Fluorolube® film were then sandwiched between a second CaF_2 IR plate that had been precooled to –36 °C in a freezer, and the materials were mulled briskly between the two cold IR plates for 1 min. The plates were sealed, moved cold to the spectrometer and spectra were taken as per the procedure for the thin film IR on NaCl plates above. Unlike NaCl plates, CaF_2 plates seem unblemished by their unavoidable exposure to frost and polishing in this procedure.

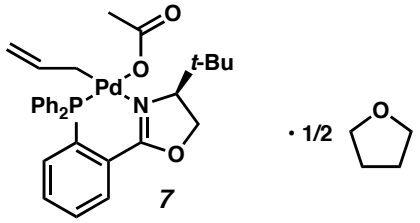
NMR Spectra (^{1}H, ^{13}C, ^{31}P): In a glove box with a nitrogen atmosphere, roughly 20 mg of the mixture of complexes (*S*,*S*)-**1** and (*R*,*S*)-**1** were added to a half dram vial in an aluminum block, both of which had been precooled to –36 °C. A fresh ampule of $THF_{d\text{-}8}$ that had been precooled to –36 °C was opened, and 0.75 mL of $THF_{d\text{-}8}$ was used portion-wise to dissolve the material and move it into an NMR tube that had been precooled to –36 °C. The tube was quickly sealed with a plastic cap and removed from the glove box where it was immediately submerged to within a few centimeters of its top in powdered dry ice in a dewar. The dewar was carried to the spectrometer, which was then cooled to the desired temperature before quickly removing the NMR tube from the dry ice and inserting it into the instrument. Phosphorus spectra obtained at reduced temperatures could not be directly referenced to phosphoric acid as outlined in Materials and Methods section due to the relatively high freezing point of the phosphoric acid standard. Instead, sub-zero ^{31}P NMR spectra were referenced to free (*S*)-*t*-BuPHOX ligand (δ –5.95) used as either an internal or external standard in $THF_{d\text{-}8}$. The reported room temperature ^{31}P NMR spectrum was recorded by generating the mixture of intermediates (*S*,*S*)-**1** and (*R*,*S*)-**1** in situ as outlined in the section on NMR experiments in this supporting information (Page 5).

Effervescent Crystals:

Synthesis: In a nitrogen glove box (*S*)-*t*-BuPHOX ligand (**3**) (96.7 mg, 250 μmol, 1.3 equiv) followed by $[Pd_2(dba)_3]$ (86.2 mg, 94.1 μmol, 0.5 equiv) were added, neat, into a 20 mL scintillation vial. Anhydrous THF (8 mL) was filtered through a pipette filter with glass filter paper directly into the 20 mL scintillation vial. The solution was mixed manually by pipette for two minutes, and then left to stand and mix by diffusion for 20 min. During this time an initially dark red-purple solution formed, which then lightened to a dark, rich, orange color. The solution was filtered through a pipette filter with glass filter paper into five separate one-dram vials evenly (1.6 mL each). This filtration separated a rich orange filtrate from a black precipitate presumed to be aggregated palladium(0) metal. The vials were sealed with plastic screw caps and removed from the box. On the bench, the vials were individually opened, and β-ketoester **2** (210 mg, 1.07 mmol, 28.5 equiv), was added by syringe to each vial after which they were resealed. The vials were then swirled manually for 5 s during which time the solution underwent a rapid color change from a rich orange to a lighter yellow green. The vials were left to stand and mix by diffusion for an additional 10 min. Each vial was then opened and inserted into a 20 mL scintillation vial containing 5 mL of hexanes for vapor diffusion. The atmosphere of each two-vial apparatus was gently displaced with a flow of argon

from a hose, and then the 20 mL vial was sealed tightly with a plastic screw cap. These self contained vapor diffusion apparati were left to slowly crystallize at –20 °C in a freezer for a week. During this time the inner vials begin to grow one of two morphisms of crystal, clear colorless fine feathery needles or clear colorless large glassy blocks. The formation of colored crystals results from impurities or improper handling. The type of morphism often varies from vial to vial, but is usually homogeneous within a given vial. Only the clear colorless large glassy blocks show visible signs of effervescence, though various characterization methods suggest that both of the crystal morphisms formed are predominantly composed of intermediate **1**, and both morphism types can be thermally decomposed to yield 2-allyl-2-methylcyclohexanone with reproducible and reasonably high enantioinduction.

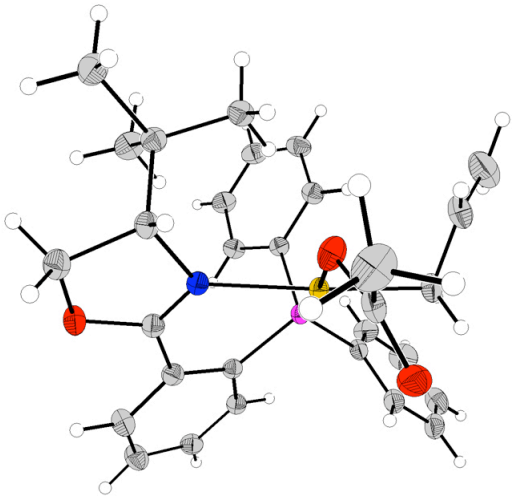
Synthesis and Characterization of Other New Molecules:



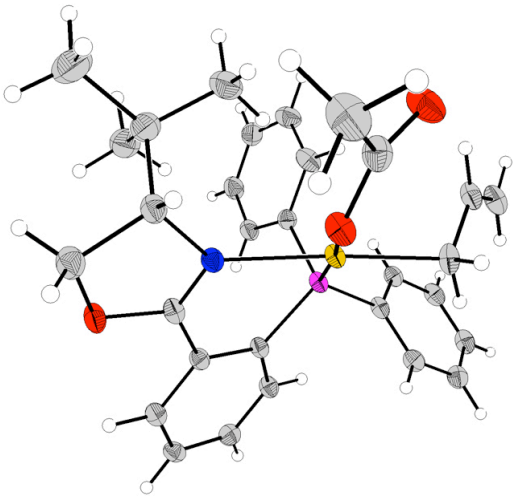
7

Allyl Acetate Complex half THF adduct 7: In a nitrogen glove box (*S*)-*t*-BuPHOX ligand (**3**) (75.6 mg, 195 μmol, 1.3 equiv) was weighed into a 20 mL scintillation vial. $[Pd_2(mtdba)_3]$ (**SI 5**) (120.2 mg, 75.06 μmol, 0.5 equiv) was weighed into a 1-dram vial. Anhydrous THF (0.5 mL) was added to the 20 mL scintillation vial, which was swirled manually for 30 s until all of the (*S*)-*t*-BuPHOX ligand (**3**) had dissolved. Anhydrous THF (3 x 0.5 mL) was added to the 1-dram vial containing $[Pd_2(mtdba)_3]$ (**SI 5**). The solution in the 1-dram vial was mixed manually by pipette resulting in the formation of a dark purple solution, which was added dropwise to the solution in the 20 mL scintillation vial containing (*S*)-*t*-BuPHOX ligand (**3**). The resulting solution in the 20 mL scintillation vial was swirled manually for 1 min, and then left to stand and mix by diffusion for 1.5 h during which time the solution turned from a dark purple to a rich orange color. Allyl acetate (146 mg, 1.46 mmol, 9.7 equiv) was added in one portion via syringe. The solution was swirled manually for 1 min then left to stand for 20 min during which time its color lightened slightly to a yellow-orange. The solution was then carefully layered with hexanes (18 mL) and allyl acetate (200 μL) and left to crystallize via layer diffusion in a –20 °C freezer in the glove box resulting in the formation of small yellow-green crystal clusters and powder. This mixture of crystals and powder was redissolved in THF (3 x 0.5 mL) and filtered through a pipette filter with glass filter paper into a 1-dram vial to separate a yellow-orange solution from a small amount of gray material. The solution was then layered with hexanes (0.5 mL) causing the solution to become cloudy with precipitate. Diethyl ether (1 mL) was added to the solution carefully, so as not to disturb the interface between the two layers, redissolving most of the finer suspended precipitate, leaving two distinct homogenous layers. The vial was then left in a –36 °C freezer to crystallize via layer diffusion. The mother liquor was decanted, the crystals were powdered, washed with hexanes (1 x 5 mL), and azeotroped

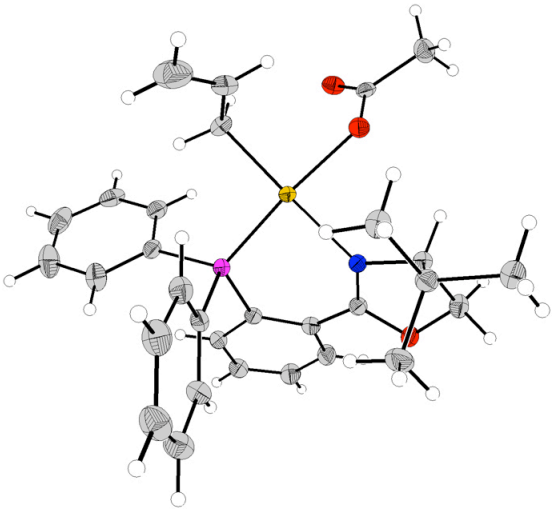
with hexanes (1 x 5 mL), before being dried in vacuo affording complex **7** as a half THF adduct (34.3 mg, 38.5% yield, yellow green powder). mp 128–131 °C (decomp); ^{1}H NMR (500 MHz, $THF_{d\text{-}8}$) δ 8.18 (ddd, J_{HP} = 4.0 Hz, J = 7.9 Hz, 1.1 Hz, 1H), 7.64 (app. tt, J = 7.7, 1.3 Hz, 1H) 7.56–7.40 (comp. m, 9H), 7.32–7.26 (m, 2H) , 7.04 (ddd, J_{HP} = 1.2 Hz, J = 10.0, 7.8, 1H), 6.19 (ddddd, J_{HP} = 1.7 Hz, J = 11.6, 11.1, 10.8, 10.2 Hz, 1H), 4.56–4.39 (comp. m, 3.7H), 4.39–4.31 (m, 1H), 3.64–3.59 (m, 2H), 2.75 (br. s, 1H), 1.99–1.84 (comp. m, 1.3 H), 1.80 (s, 3H), 1.79–1.75 (m, 2H), 0.72 (s, 9H); ^{13}C NMR (125 MHz, $THF_{d\text{-}8}$) δ 174.8, 163.5 (d, J_{CP} = 2.7 Hz), 144.1 (app. br. s), 135.9 (d, J_{CP} = 1.8 Hz), 134.96 (d, J_{CP} = 10.1 Hz), 134.86 (d, J_{CP} = 11.5 Hz), 133.22, 133.17, 133.1, 132.15, 132.16, 132.09, 132.07, 132.02, 131.73, 131.69, 131.66, 131.64, 131.4, 131.0, 130.9, 130.6, 130.1, 129.84, 129.75, 129.66, 129.58, 106.0 (app. br. s), 75.4, 70.3, 68.4, 35.1, 30.1 (app. br. s.), 26.5, 26.1, 24.9 ; ^{31}P NMR (121.4 MHz, $THF_{d\text{-}8}$) δ 31.1; IR (neat film, NaCl) 3059, 2962, 2869, 1632, 1606, 1581, 1482, 1436, 1372, 1321, 1244, 1213, 1192, 1144, 1115, 1099, 1063, 1058, 1028, 958, 928, 876, 781, 747, 730, 708; IR (Fluorolube® mull, CaF_2) 3066, 2958, 2909, 2867, 1637, 1609, 1580, 1565, 1481, 1436, 1372; HRMS (FAB, 2-nitrophenyl octyl ether) *m/z* calc'd for $C_{30}H_{35}O_3NPPd$ $[M + H]^+$: 594.1390, found: 594.1393. X-ray quality crystals were obtained by layering a concentrated THF solution of complex **7** with hexanes. Diethyl ether was added dropwise until most of the finer precipitation on the boundary between the layers had redissolved. Allyl acetate (10 μL) was added for stability, and layer diffusion was allowed to progress at – 36 °C in a freezer in a nitrogen glove box.



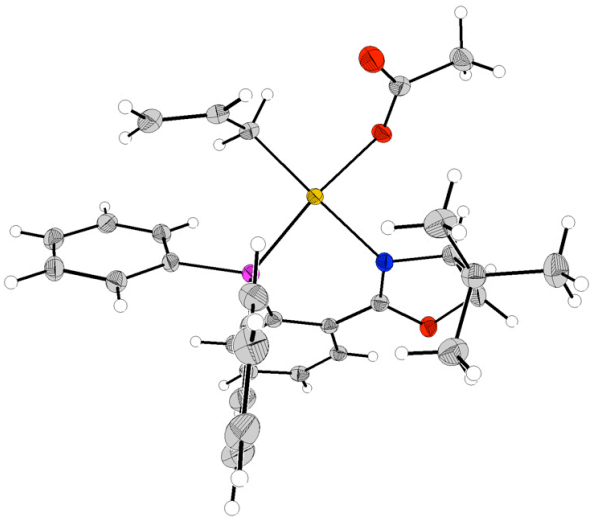
Representative anti conformation (1 of 3, side)



Syn conformation (side)



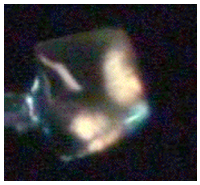
Representative anti conformation (1 of 3, top)

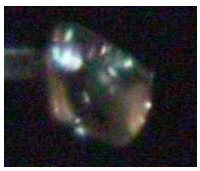


Syn conformation (top)

Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 731406.

Table 1. Crystal data and structure refinement for NHS27 (CCDC 731406).





Empirical formula	$C_{30}H_{34}NO_3PPd \bullet \_ (C_4H_8O)$
Formula weight	630.00
Crystallization Solvent	THF/ether/hexanes/ethylacetate
Crystal Habit	Fragment
Crystal size	0.23 x 0.20 x 0.19 mm^3
Crystal color	Yellow

Data Collection

Type of diffractometer	Bruker KAPPA APEX II	
Wavelength	0.71073 Å MoKα	
Data Collection Temperature	100(2) K	
θ range for 9256 reflections used in lattice determination	2.28 to 37.41°	
Unit cell dimensions	a = 10.1432(4) Å b = 34.2291(14) Å c = 17.1648(8) Å	β= 98.677(2)°
Volume	5891.3(4) $Å^3$	
Z	8	
Crystal system	Monoclinic	
Space group	$P2_1$	
Density (calculated)	1.421 Mg/m^3	

F(000)	2608
θ range for data collection	1.69 to 37.95°
Completeness to θ = 37.95°	95.1 %
Index ranges	$-17 \le h \le 14$, $-56 \le k \le 57$, $-29 \le l \le 29$
Data collection scan type	ω scans; 23 settings
Reflections collected	185638
Independent reflections	56182 [R_{int}= 0.0360]
Absorption coefficient	0.719 mm^{-1}
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7475 and 0.6888

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 2008)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	SHELXL-97 (Sheldrick, 2008)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	56182 / 11 / 1459
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.619
Final R indices [$I>2\sigma(I)$, 48665 reflections]	R1 = 0.0391, *w*R2 = 0.0579
R indices (all data)	R1 = 0.0511, *w*R2 = 0.0590
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.033
Average shift/error	0.000
Absolute structure determination	Anomalous differences
Absolute structure parameter	0.007(6)
Largest diff. peak and hole	2.788 and -1.256 e.$Å^{-3}$

Special Refinement Details

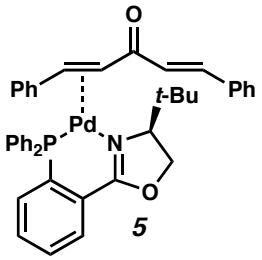
Crystals were mounted on a glass fiber using Paratone oil then placed on the diffractometer under a nitrogen stream at 100K.

There are four molecules in the asymmetric unit. Three of those four have very similar conformations with the fourth having a different orientation of the allyl and carbonyl group of the acetate ligand, see figures.

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold

expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

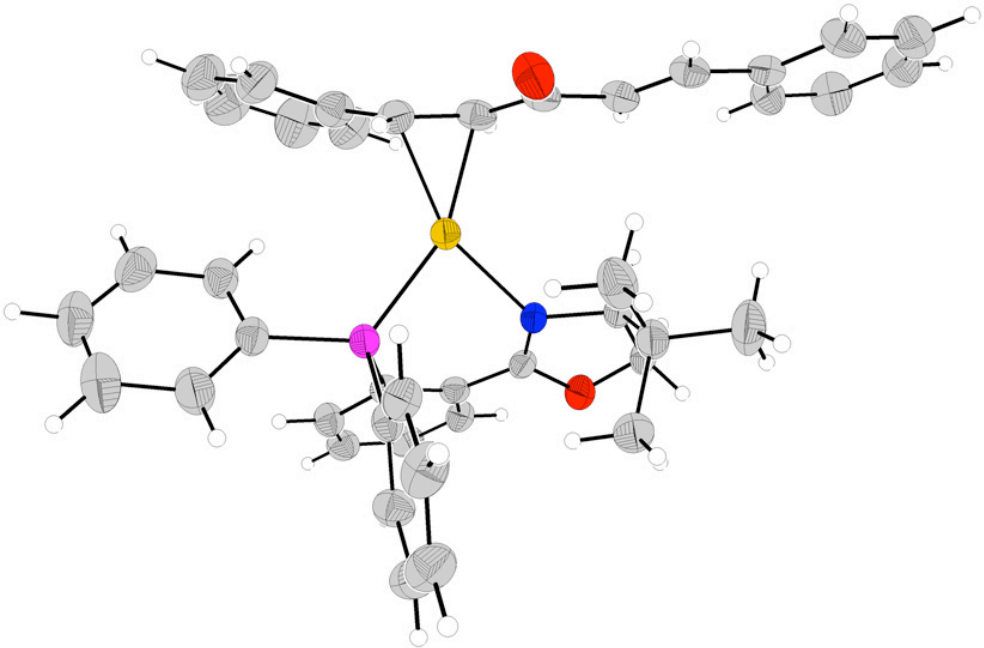
All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.



5

[(*S*)-*t*-BuPHOX]Pd(dba) precatalyst 5:[5] In a nitrogen glove box (*S*)-*t*-BuPHOX ligand (**3**) (323.4 mg, 830.4 μmol, 2.5 equiv) and [$Pd_2(dba)_3$] (302.4 mg, 330 μmol, 1 equiv) were weighed directly into a 100 mL round bottom flask with a stirbar, neat, in the order specified. Anhydrous THF (70 mL) was filtered through a pipette filter with glass filter paper and added to the flask. Stirring was started and the solution quickly became a dark red-purple color. The solution was left to stir for 8 h, turning a dark orange color with a small amount of black precipitate. The solution was filtered through a 15 mL frit separating an intensely orange-red solution from a thick silting of insoluble black powder presumed to be particulate Pd(0). The solution was concentrated in vacuo to a thin foamy red film. Minimal diethyl ether (pipette filtered, 5 x 1.2 mL) was used to dissolve the film and transfer it to a 50 mL round-bottom flask. An orange-red powder started to precipitate from the ethereal solution in the new flask. The ether solution was layered with 20 mL of hexanes, and then cooled to –36 °C in a glove box freezer. The solution was filtered on a 30 mL frit, separating a bright orange fluffy solid from a bright orange filtrate. The orange solid was rinsed with hexanes until the filtrate was almost clear (20 x 5 mL). The material was subsequently recrystallized from diethyl ether layered with hexanes, followed by a second recrystalization using toluene layered with hexanes. The solids were rinsed with 1:1 toluene/hexanes, diethyl ether, and then 1:1 Et_2O/hexanes. The material was dissolved in THF and layered with hexanes and left to precipitate at –36 °C in a glove box freezer. The resulting light yellow solution was decanted, and the solids rinsed with hexanes (2 x 3 mL). This THF/hexanes precipitation and hexanes wash was repeated four times. The material was then azeotroped in hexanes (4 x 5 mL) and dried in vacuo for 16 h to afford precatalyst **5** (300 mg, 62.2%, yellow powder). mp 144.5–147 °C; ^{1}H NMR (500 MHz, $THF_{d\text{-}8}$) δ 8.18 (br. s. 0.07H), 8.12–8.01 (m, 0.89H), 7.76–7.66 (comp. m, 0.19H), 7.61 (br. s. 0.23H), 7.53 (d, *J* = 7.3 Hz, 1.43H), 7.51–6.95 (m, 17.57H) 6.87 (br. s, 4H), 6.68 (br. s, 0.15H), 6.53 (app. t, *J* = 8.7 Hz, 1.48H), 5.04 (br. s, 0.09H), 4.89 (m, 0.73H), 4.76 (s, 0.08H), 4.63 (app. dd, *J* = 9.3, 9.0 Hz, 0.75H), 4.53 (br. s, 0.14H), 4.30 (m, 1.07H), 4.23–4.13 (m, 0.77H), 4.05 (app. dd, *J* = 9.5, 9.3 Hz, 0.75H), 4.01 (br. s, 0.2 Hz, 0.2H), 2.49 (s, 0.02H), 2.48–2.44 (comp. m, 0.04H), 2.04 (s, 0.1H), 1.37–1.26 (m, 0.24H), 0.82 (br. s, 8H), 0.42 (br. s, 1H); ^{13}C NMR (125 MHz, $THF_{d\text{-}8}$) δ 184.2, 164.6, 146.4, 143.2, 138.2, 137.4 (br. s), 136.1, 135.8, 135.6, 135.3, 135.1, 134.83, 134.75, 134.5, 134.2, 134.1, 133.4, 133.3, 132.7, 131.3, 131.2, 131.1, 130.78, 130.77, 130.6, 130.3, 129.8, 129.6, 129.5, 129.4, 129.3, 129.2, 129.1, 128.8, 128.3, 127.4 (br. s), 126.8, 125.9, 124.2, 80.2 (br. s), 79.9 (br. s), 69.5 (br. s), 68.9, 68.1, 58.3 (br. s), 35.5, 30.5; ^{31}P NMR (121.4 MHz, $THF_{d\text{-}8}$) δ 21.26 (0.1P), 18.97 (0.9P); IR (neat film, NaCl) 3055, 2958, 2867, 1638, 1622, 1581, 1568, 1496, 1472, 1435, 1359, 1332, 1310, 1280, 1239, 1202, 1141, 1108, 1095, 1068, 1054, 1028, 998, 967, 920, 862, 761, 747 cm^{-1}; IR (Fluorolube® mull, CaF_2) 3055, 3009, 2953, 2867, 1638, 1618, 1597, 1568, 1578, 1493, 1466, 1448, 1433, 1359 cm^{-1}; HRMS (FAB, 2-nitrophenyl octyl ether)

m/z calc'd for $C_{42}H_{41}PPdO_2N$ $[M + H]^+$: 728.1910, found: 728.1925. X-ray quality crystals were grown from THF via successive layer diffusion in a glove box with Et_2O at –20 °C to form seed crystals, and then hexanes at –20 °C.



Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 606912.

Table 1. Crystal data and structure refinement for NHS03 (CCDC 606912).

Empirical formula	$C_{42}H_{40}NO_2PPd \bullet C_4H_8O$
Formula weight	800.22
Crystallization Solvent	THF
Crystal Habit	Block
Crystal size	0.26 x 0.25 x 0.25 mm^3
Crystal color	Orange

Data Collection

Type of diffractometer	Bruker SMART 1000
Wavelength	0.71073 Å MoKα
Data Collection Temperature	100(2) K
θ range for 25286 reflections used in lattice determination	2.45 to 29.83°
Unit cell dimensions	a = 10.3986(4) Å b = 13.8720(5) Å c = 27.4970(10) Å
Volume	3966.4(3) $Å^3$
Z	4

Crystal system	Orthorhombic
Space group	$P2_12_12_1$
Density (calculated)	1.340 Mg/m^3
F(000)	1664
θ range for data collection	2.09 to 32.87°
Completeness to θ = 32.87°	94.5 %
Index ranges	$-15 \le h \le 15$, $-19 \le k \le 20$, $-35 \le l \le 41$
Data collection scan type	ω scans at 5 ϕ settings
Reflections collected	66411
Independent reflections	13693 [R_{int}= 0.0693]
Absorption coefficient	0.549 mm^{-1}
Absorption correction	None
Max. and min. transmission	0.8749 and 0.8704

Structure solution and Refinement

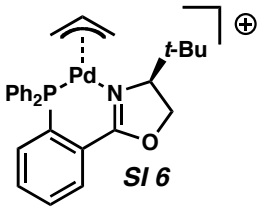
Structure solution program	Bruker XS v6.12
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions
Structure refinement program	Bruker XL v6.12
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	13693 / 39 / 468
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.482
Final R indices [I>2σ(I), 10165 reflections]	R1 = 0.0400, *w*R2 = 0.0643
R indices (all data)	R1 = 0.0642, *w*R2 = 0.0672
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.005
Average shift/error	0.000
Absolute structure parameter	-0.048(16)
Largest diff. peak and hole	0.710 and -0.467 e.$Å^{-3}$

Special Refinement Details

The crystal contains solvent of crystallization, disordered at one site in the unit cell. The solvent was modeled as THF and included in least-squares refinement with geometric restraints on all of the THF atoms. The temperature factors were allowed to refine and the values reflect the diffuse nature of the electron density in the area.

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

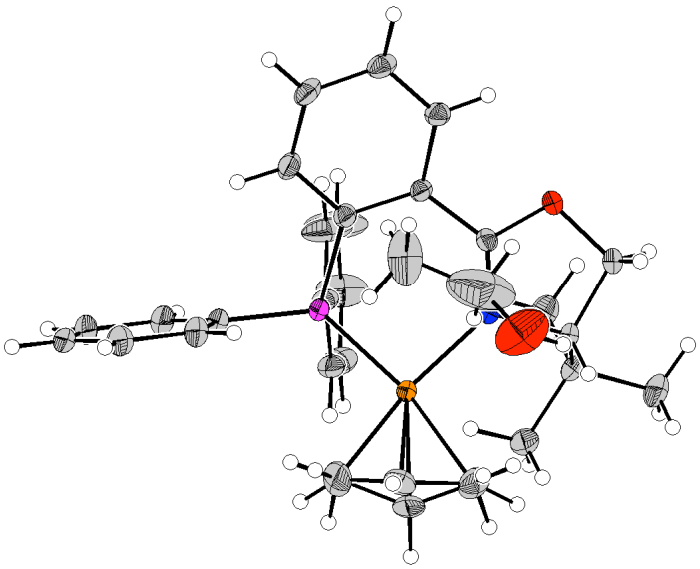
All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.



SI 6

PF_6^-

[(*S*)-*t*-BuPHOX]Pd(allyl)•PF_6 Salt (SI 6): Complex **SI 6** was prepared using Zehnder's method[6] with (*S*)-*t*-BuPHOX ligand (**3**) to afford a quantitative yield of rapidly interconverting *endo* and *exo* allyl isomers (ca. 60/40) as a light yellow powder; mp (EtOH) 152–154 °C (decomp.); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (app. ddd, J = 7.7, 4.1, 1.1 Hz, 0.6H), 8.24 (app. ddd, J = 7.7, 4.4, 1.1 Hz, 0.4H), 7.74–7.42 (comp. m, 8H), 7.39–7.11 (comp. m, 4H), 7.04–6.87 (comp. m, 1H), 5.96–5.82 (m, 0.4H), 5.82–5.67 (m, 0.6H), 4.96–4.86 (comp. m, 1H), 4.68 (app. q, J = 9.9 Hz, 1H), 4.49 (app. dt, J_d = 11.3 Hz, J_t = 3.9 Hz, 1H), 4.19 (app. dt, J_d = 11.3 Hz, J_t = 4.4 Hz, 1H), 4.03 (app. dd, J = 14.3, 9.4 Hz, 0.6H), 3.63–3.48 (comp. m, 1H), 3.32 (app. d, J = 6.6 Hz, 0.4H), 3.16 (app. d, J = 12.7 Hz, 0.4H), 2.77 (app. d, J = 12.1 Hz, 0.6H), 0.64 (s, 3.5 H), 0.56 (s, 5.5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9–164.8 (3 peaks), 134.9, 134.8, 134.0–133.3 (7 peaks), 132.9–132.6 (4 peaks), 132.2–132.1 (3 peaks), 131.8 (app. d, J = 2.3 Hz), 130.2–128.8 (13 peaks), 128.5–127.8 (5 peaks), 127.3, 122.4 (app. d, J = 6.0 Hz), 122.4, 83.3–79.4 (6 peaks), 69.8, 69.7, 58.6, 54.1, 54.0, 34.3, 25.2; ^{31}P NMR (121.4 MHz, $CDCl_3$) δ 23.2 (s, 0.6P), 22.2 (s, 0.4P), –143.4 (septet, J_{PF} = 711.0 Hz, 1P); ^{31}P NMR (121.4 MHz, $THF_{d\text{-}8}$) δ 23.5 (s, 0.67P), 22.5 (s, 0.33P), –143.8 (septet, J_{PF} = 710.4 Hz, 1P); ^{19}F NMR (242 MHz, $CDCl_3$) δ –73.7 (d, J_{FP} = 712.6 Hz); IR (Neat Film from $CDCl_3$, NaCl) 3062, 2964, 2872, 2271, 1971, 1899, 1826, 1621, 1584, 1568, 1482, 1437, 1372, 1315, 1249, 1211, 1145, 1121, 1100, 1060, 1028, 958, 913, 836, 778, 732, 697, 678 cm^{-1}; HRMS (FAB, 3-nitrobenzyl alcohol) *m*/*z* calc'd for $C_{28}H_{31}ONPPd$ $[M - PF_6]^+$: 534.1178, found 534.1182; $[\alpha]_D^{27.1}$ +256.6 (*c* 3.72, CH_2Cl_2). X-ray quality crystals were grown from EtOH.



Crystallographic data have been deposited at the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 245187.

Crystal data and structure refinement for DCB24 (CCDC 245187).

Empirical formula	$[C_{28}H_{31}NOPPd]^+ PF_6^- \bullet C_2H_5OH$
Formula weight	702.91
Crystallization Solvent	Ethanol
Crystal Habit	Fragment
Crystal size	0.35 x 0.34 x 0.23 mm^3
Crystal color	Colorless

Data Collection

Type of diffractometer	Bruker SMART 1000
Wavelength	0.71073 Å MoKα
Data Collection Temperature	100(2) K
θ range for 15322 reflections used in lattice determination	2.31 to 41.00°
Unit cell dimensions	a = 17.5183(6) Å b = 15.7792(5) Å β= 107.0990(10)° c = 11.3736(4) Å
Volume	3004.98(18) $Å^3$
Z	4
Crystal system	Monoclinic
Space group	C2
Density (calculated)	1.554 Mg/m^3
F(000)	1428
θ range for data collection	1.77 to 42.31°
Completeness to θ = 42.31°	85.0 %
Index ranges	$-32 \le h \le 32$, $-28 \le k \le 29$, $-20 \le l \le 15$
Data collection scan type	ω scans at 3 ϕ settings of 2θ=-28º and 2 at 2θ=-59º
Reflections collected	28501
Independent reflections	15572 [R_{int}= 0.0351]
Absorption coefficient	0.787 mm^{-1}
Absorption correction	SADABS
Max. and min. transmission	0.8397 and 0.7702

Structure solution and Refinement

Structure solution program	SHELXS-97 (Sheldrick, 1990)
Primary solution method	Direct methods
Secondary solution method	Difference Fourier map
Hydrogen placement	Geometric positions

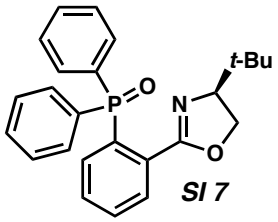
Structure refinement program	SHELXL-97 (Sheldrick, 1997)
Refinement method	Full matrix least-squares on F^2
Data / restraints / parameters	15572 / 1 / 408
Treatment of hydrogen atoms	Riding
Goodness-of-fit on F^2	1.343
Final R indices [I>2σ(I), 13582 reflections]	R1 = 0.0373, *w*R2 = 0.0725
R indices (all data)	R1 = 0.0459, *w*R2 = 0.0748
Type of weighting scheme used	Sigma
Weighting scheme used	$w=1/\sigma^2(Fo^2)$
Max shift/error	0.004
Average shift/error	0.000
Absolute structure parameter	-0.019(13)
Largest diff. peak and hole	1.422 and -0.710 e.Å^{-3}

Special Refinement Details

The allyl ligand, C26-C27-C28, is disordered in two alternate orientations, differing by "up-down" positions for C27. Additional disorder is observed in one PF_6 counterion and an included solvent molecule, modeled as ethanol hydrogen bonded to a fluorine of one counterion.

Refinement of F^2 against ALL reflections. The weighted R-factor (*w*R) and goodness of fit (S) are based on F^2, conventional R-factors (R) are based on F, with F set to zero for negative F^2. The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R-factors(gt) etc. and is not relevant to the choice of reflections for refinement. R-factors based on F^2 are statistically about twice as large as those based on F, and R-factors based on ALL data will be even larger.

All esds (except the esd in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell esds are taken into account individually in the estimation of esds in distances, angles and torsion angles; correlations between esds in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell esds is used for estimating esds involving l.s. planes.



SI 7

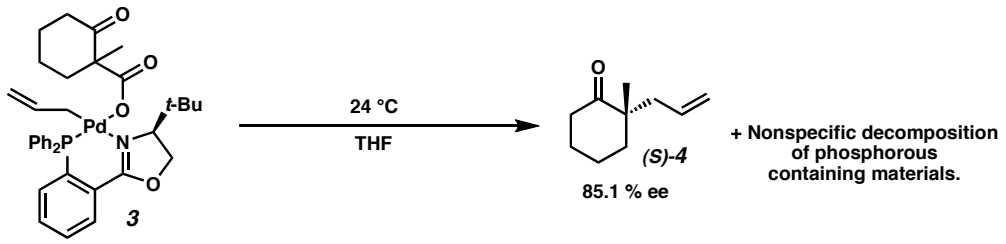
(*S*)-*t*-BuPHOX Oxide (SI 7): To a solution of (*S*)-*t*-BuPHOX ligand (**3**) (150 mg, 0.387 mmol, 1 equiv) in THF (2.5 mL) was added a 5% aqueous H_2O_2 solution (1.94 mL). After 15 min the reaction mixture was diluted with EtOAc (5 mL) and brine (5 mL), washed with 10% aqueous Na_2CO_3 (5 mL) and brine (5 mL), dried with magnesium sulfate, and filtered. Chromatography was performed with 5% methanol in dichloromethane on silica gel to afford (*S*)-*t*-BuPHOX oxide (**SI 7**) (149.3 mg, 96% yield, white foam). TLC (R_f 0.20, 3% methanol in dichloromethane); ^{1}H, NMR (300 MHz, $CDCl_3$) δ 7.95 (ddd, J = 7.5, 3.9, 1.2 Hz, 1H), 7.81–7.33 (comp. m, 7H), 7.52–7.31 (comp. m, 7H), 3.84 (dd, J = 8.1, 8.1 Hz, 1H), 3.57, (dd, J = 9.9 Hz, J = 9.9 Hz, 1H), 3.41 (dd, J = 9.9 Hz, 8.4 Hz, 1H), 0.77 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.1, 135.0 (d, J_{CP} = 10.1 Hz), 133.7 (d, J_{CP} = 107.1 Hz), 133.3 (d, J_{CP} = 11.7 Hz), 138.2 (app. dd, J_{CP} = 12.3, 1.4 Hz), 75.9, 68.8, 33.6, 25.8; ^{31}P NMR (121.4 MHz, $CDCl_3$) δ 30.3; ^{31}P NMR (121.4 MHz, $THF_{d\text{-}8}$) δ 27.2;[h] IR (Neat Film, NaCl) 3057, 2957, 2903, 2868, 2217, 1664, 1589, 1565, 1477, 1438, 1356, 1337, 1307, 1248, 1201, 1119, 1108, 1067, 1028, 963, 930, 905 cm^{-1}; HRMS (FAB) m/z calc'd for $C_{25}H_{27}O_2NP$ $[M]^+$: 404.1779, found 404.1799; $[\alpha]_D^{27.6}$ –69.3 (*c* 1.96, CH_2Cl_2).

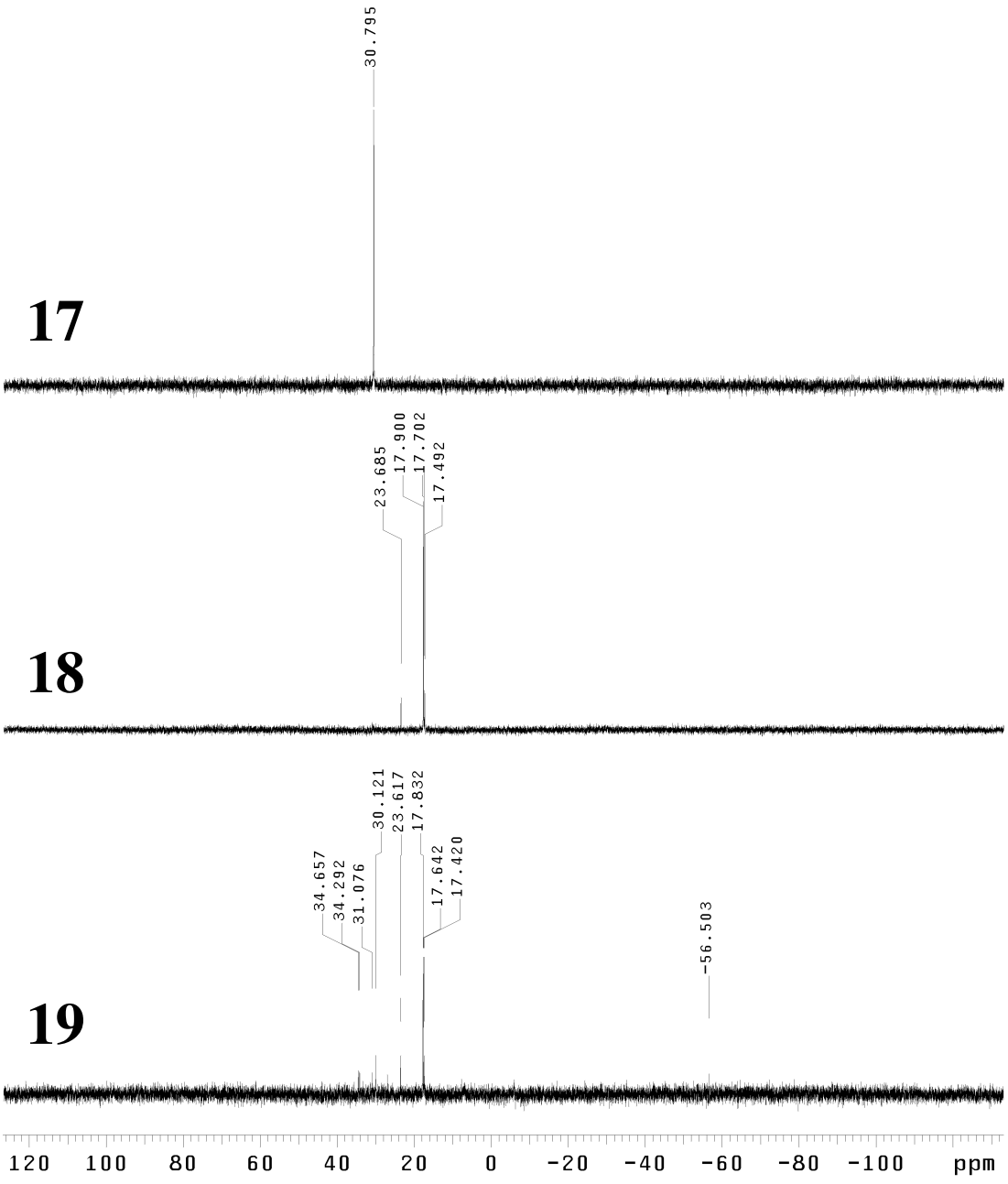
[h] Experimentally this resonance appeared to drift significantly.

Controlled thermal decomposition of Intermediate 1:

Controlled thermal decomposition of intermediate 1 in the absence of dba ligand in solution (THF):

(Until the sample left the glove box, all of the following operations were performed in a cold aluminum block with implements and containers [such as the half-dram vial and NMR tube] that had been precooled to –36°C in a glove box freezer.) In a nitrogen glove box, intermediate **1** (22.8 mg, 33.0 μmol, 1 equiv) was weighed into a half-dram vial. A 1 mL ampule of $THF_{d\text{-}8}$ that had been precooled to –36°C in a glove box freezer was opened, and its contents were used to dissolve the sample of intermediate **1** and transfer it to an NMR tube. The NMR tube was tightly sealed with a plastic cap, and was then recooled to –36 °C in a glove box freezer for 20 min. The NMR tube was then quickly removed from the glove box and immediately submerged in powdered dry ice. The NMR probe was precooled to –20 °C while the NMR tube was still submerged in dry ice. The NMR tube was removed from the dry ice, quickly inserted into the precooled spectrometer, and NMR spectrum # 17 was taken at –20 °C. The NMR tube was then allowed to sit at 24 °C outside the spectrometer for 30 minutes, during which time the solution turned from light yellow-green to a light orange color. After the 30 min spent outside the spectrometer, the NMR tube was resubmerged in dry ice until NMR spectrum # 18 was taken with the probe regulated at 24 °C, showing trace amounts of intermediate **1** left. The NMR tube was left to sit outside the spectrometer at 24 °C for 2 h during which time the solution began to turn from light orange to dark red-purple. NMR spectrum # 19 was taken at 24 °C at this time revealing complete consumption of intermediate **1**. The NMR tube was cycled into a nitrogen glove box and the solution was concentrated in vacuo to a dark purple semisolid. The semisolid was rinsed with hexanes, and this wash was saved. Attempts to separate the semisolid into its constituent compounds were unsuccessful. The hexane wash was removed from the box and concentrated in vacuo to a dark brown semisolid. Chromatography was performed with 5% ether in petroleum ether to afford (*S*)-2-allyl-2-methylcyclohexanone **4** (2.0 mg, 40% yield, 85.1% ee [assay: GC, G-TA column {100 °C isothermal for 30 min}, major enantiomer (*S*) ret. time = 14.897 min, minor enantiomer (*R*) ret. time = 17.313 min], clear colorless oil).


O
O
O
t-Bu
Pd
Ph2P
N
O
3
24 °C
THF
O
(S)-4
85.1 % ee
+ Nonspecific decomposition
of phosphorous
containing materials.


30.795
17
23.685
17.900
17.702
17.492
18
30.121
23.617
17.832
34.657
34.292
31.076
17.642
17.420
-56.503
19
120
100
80
60
40
20
0
-20
-40
-60
-80
-100
ppm

Controlled thermal decomposition of intermediate 1 in the presence of dba ligand in solution (THF) (Isolation of complex 5 only):

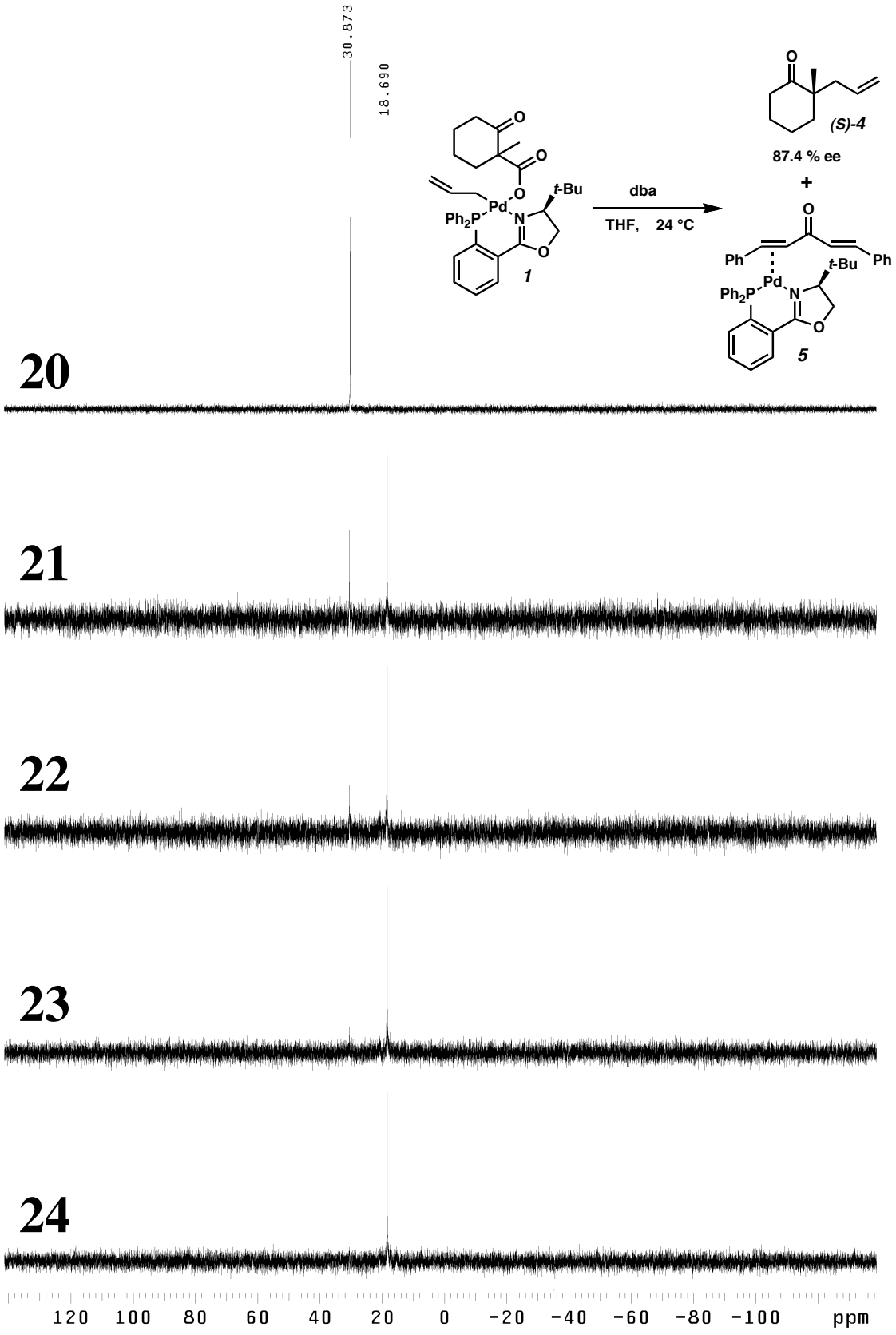
(Until the sample left the glove box, all of the following operations were performed in a cold aluminum block with implements and containers [such as the half-dram vial and NMR tube] that had been precooled to –36°C in a glove box freezer.) Intermediate **1** (11.3 mg, 16.4 μmol, 1 equiv) was weighed into a half-dram vial. Dibenzylideneacetone (9.6 mg, 46 μmol, 2.8 equiv) was added, to the half-dram vial. A 1 mL ampule of $THF_{d\text{-}8}$ that had been precooled to –36 °C in a glove box freezer was opened and the contents were added to the half dram vial. The resulting solution was mixed manually by pipette for 1 min until all the solids had dissolved forming a yellow solution. The solution was transferred to an NMR tube via pipette. The NMR tube was sealed with an appropriately sized septum, quickly removed from the glove box, and submerged in dry ice to within two inches of its cap. An initial NMR was taken at –20 °C revealing intermediate **1** as the only detectable phosphorous containing compound.[i] The tube was left to sit at 24 °C for 40 min, after which time a ^{31}P NMR spectrum indicating complete conversion to precatalyst complex **5** as the only detectable phosphorous containing compound. The NMR tube was cycled back into a nitrogen glove box, where its contents were moved to a 1-dram vial and concentrated in vacuo to roughly 50 μL of thick red-orange oil. The oil was triturated with hexanes (1 mL) and the resulting mixture was filtered in a pipette with glass filter paper. The solids were rinsed with hexanes (12 x 0.5 mL) and these washes were merged and saved. The solids were rinsed with additional hexanes (10 x 1 mL) and these washes were not saved. The saved hexane washes were left to stand for 20 min, during which time yellow-orange material began to crystallize and precipitate. These precipitated solids were then filtered in a pipette with glass filter paper. All of the samples of the precipitated red-orange material were dissolved in minimal THF, merged, and filtered through a pipette with glass filter paper into a 20 mL scintillation vial. The solution was concentrated in vacuo to a thin red film. This film was washed with diethyl ether (1 mL) and hexanes (2 x 1 mL). The remaining solids were azeotroped once from diethyl ether and twice from hexanes to afford precatlyst complex **5** (7.1 mg, 62% yield, yellow powder).

Controlled thermal decomposition of intermediate 1 in the presence of dba ligand in solution (THF) (Isolation of 2-allyl-2-methylcylcohexanone 4 only):

(Until the sample left the glove box, all of the following operations were performed in a cold aluminum block with implements and containers [such as the half-dram vial and NMR tube] that had been precooled to –36°C in a glove box freezer.) Dibenzylideneacetone (3.3 mg, 16 μmol, 1.5 equiv) was weighed into a 1-dram vial. Intermediate **1** (7.3 mg, 11 μmol, 1 equiv) was weighed into a separate half-dram vial. Anhydrous THF that had been precooled to –36 °C in the glove box freezer was added into the 1-dram vial containing the dibenzylideneacetone. The solution was mixed manually via pipette for roughly 10 s until all the material had dissolved resulting in the formation of a yellow solution. The solution was transferred via pipette to the half-dram vial containing intermediate **1** where it was mixed manually via pipette for 10 s until all the material had dissolved resulting in the formation of a yellow-green solution. The

[i] See the following procedure for representative spectra.

NMR tube was sealed with a septum, quickly removed from the glove box, and submerged in dry ice to within two inches of its top. NMR spectrum # 20 was taken at this time with the probe precooled to –20 °C. The NMR tube was then left to stand at 24 °C. After 17 min at 24 °C NMR spectrum # 21 was taken. After 22 min, NMR spectrum # 22 was taken. After 30.5 min, NMR spectrum # 23 was taken. After 40 min, NMR spectrum # 24 was taken indicating complete conversion to precatalyst **5** as the only detectable phosphorous containing compound. Tridecane (4.0 μL, 3.0 mg, 16 μmol, 1.5 equiv) was added via a 10 μL Hamilton syringe. The solution was concentrated under a jet of nitrogen to roughly 100 μL of viscous orange oil. The oil was triturated with 0.5 mL of diethyl ether and the resulting mixture was filtered through a pipette filter with a 3 cm plug of dry silica gel. The materials were eluted with diethyl ether separating a faintly pink solution from red/orange insoluble solids. The filtrate afforded 2-allyl-2-methyl-cyclohexanone (**4**) (99% GC yield [DB-WAX column {60 °C initial temp for 10 min, then ramp 5 °C/min for 36 min to 240 °C, hold at 240 °C for 12 min}, ret. time of tridecane = 13.243 min, ret. time 2-allyl-2-methylcyclohexanone = 18.399 min], 87.4% ee [assay: GC, G-TA column {100 °C isothermal for 30 min}, major enantiomer (*S*) ret. time = 14.897 min, minor enantiomer (*R*) ret. time = 17.313 min])


30.873
18.690
dba
THF, 24 °C
(S)-4
87.4 % ee
+
1
5
t-Bu
Ph
Ph2P
Pd
N
O
20
21
22
23
24
120 100 80 60 40 20 0 -20 -40 -60 -80 -100 ppm

Rate Constant and Half-Life of Complex 1 at 24 °C in THF:

Data were extracted from spectra 21 to 23 of the above reaction. Data point one at 18 min (spectrum # 21) was set to time = 0 min for the sake of the regression plot. Data from NMR spectrum # 20 were omitted as the spectrum was taken at a different temperature.

Raw Data:

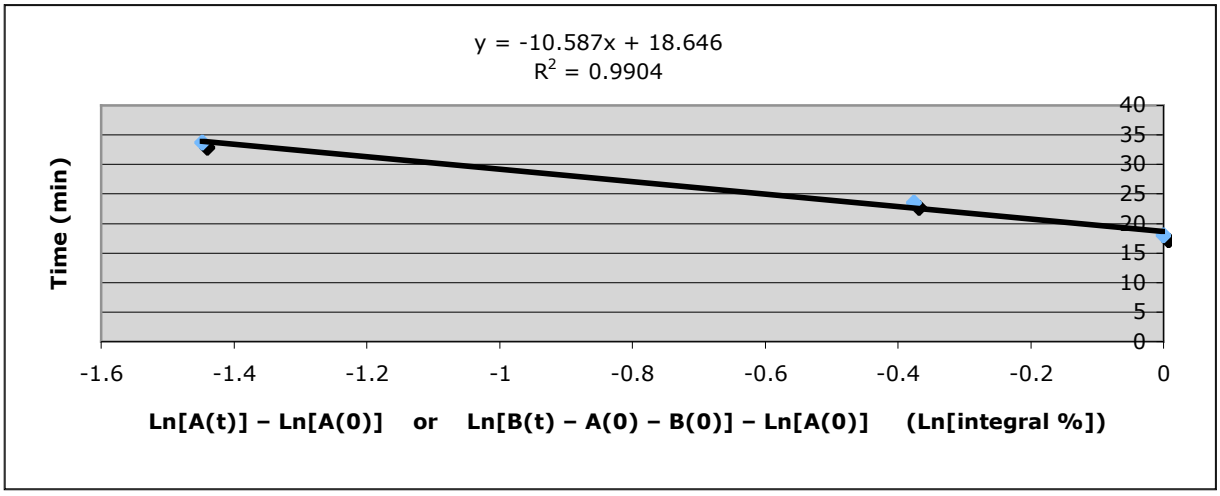
Data Point	Intermediate **1** (integral)	Catalyst **5** (integral)	Time (min)		Catalyst **5** Adjusted* (integral)
1 (spectrum 21)	0.37	1	17-19	(18)	1.1111
2 (spectrum 22)	0.23	1	22-25	(23.5)	1.1111
3 (spectrum 23)	0.07	1.01	30.5-37	(33.75)	1.1222

[*] The adjusted value of the major resonance for catalyst **5** is used instead of attempting to integrate both the major and minor resonances for catalyst **5** as the minor resonance's contribution is so small that its integration is highly affected by baseline noise giving a poor plot fit. The adjusted integral value for catalyst **5** is determined by taking the integral value of the major ^{31}P resonance for Catalyst **5**, and dividing it by its relative fraction to the total integral of 0.9. See the ^{31}P NMR characterization data for catalyst **5** on page 27 or its ^{31}P NMR spectrum reproduced on page 54 in this SI for more information on its multiple ^{31}P resonances.

Derived Data:

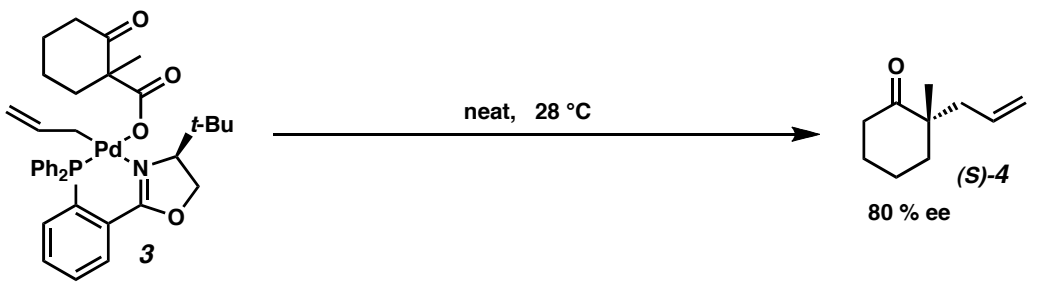
Data Point	Intermediate **1** (% ^{31}P) = A(t)	Catalyst **5** (% ^{31}P) = B(t)	Ln[A(t)] – Ln[A(0)]	Ln[B(t) – A(0) – B(0)] – Ln[A(0)]
1	0.249812	0.75019	0	0
2	0.171499	0.82850	-0.37612	-0.37612
3	0.058714	0.94129	-1.44803	-1.44803

Linear Regression plot:



=> Rate constant, k = 1/x = –9.45 x 10^{-2} min^{-1} or –1.58 x 10^{-4} s^{-1} at 24 °C

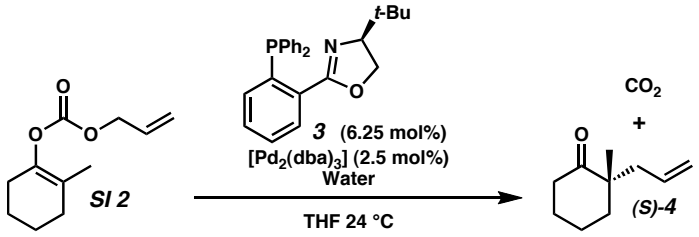
=> Half-life = [ln(0.5) / k] = 7.34 min at 24 °C



Controlled thermal decomposition of intermediate 1 in the solid state:

In a nitrogen glove box, intermediate **1** (15 mg, 22 μmol, 1 equiv) was added to a 20 mL scintillation vial. The vial was tightly sealed, and then left to stand at ambient glove box temperature (28 °C). After 36 h the decomposed material, now black in color, was moved to the bench where it was partially dissolved by pulverization under diethyl ether (5 x 1 mL) with manual grinding by a stainless steel spatula. The resulting heterogeneous mixture was filtered through a pipette filter with a 2-inch plug of silica gel that had been prewetted/packed with diethyl ether, separating a dark maroon filtrate from a black insoluble solid. The filtrate was concentrated under a jet of nitrogen to a dark maroon oil with some small darkly colored crystalline masses. Chromatography was performed on a pipette column eluting with 5% diethyl ether in petroleum ether affording 2-allyl-2-methylcyclohexanone (80% ee [assay: GC, G-TA column {100 °C isothermal for 30 minuets}, major enantiomer (*S*) ret. time = 14.897 min, minor enantiomer (*R*) ret. time = 17.313 min], clear colorless oil).

Water Tolerance Experiments:



Water (equiv)	Yield*	ee*
0	99.9%	88.5%
0.55	99.6%	86.7%
1.6	88.1%	83.8%
8.3	70.3%	60.9%
17	66.8%	48.8%
33	67.9%	40.5%

[*] Average of three runs, see table below.

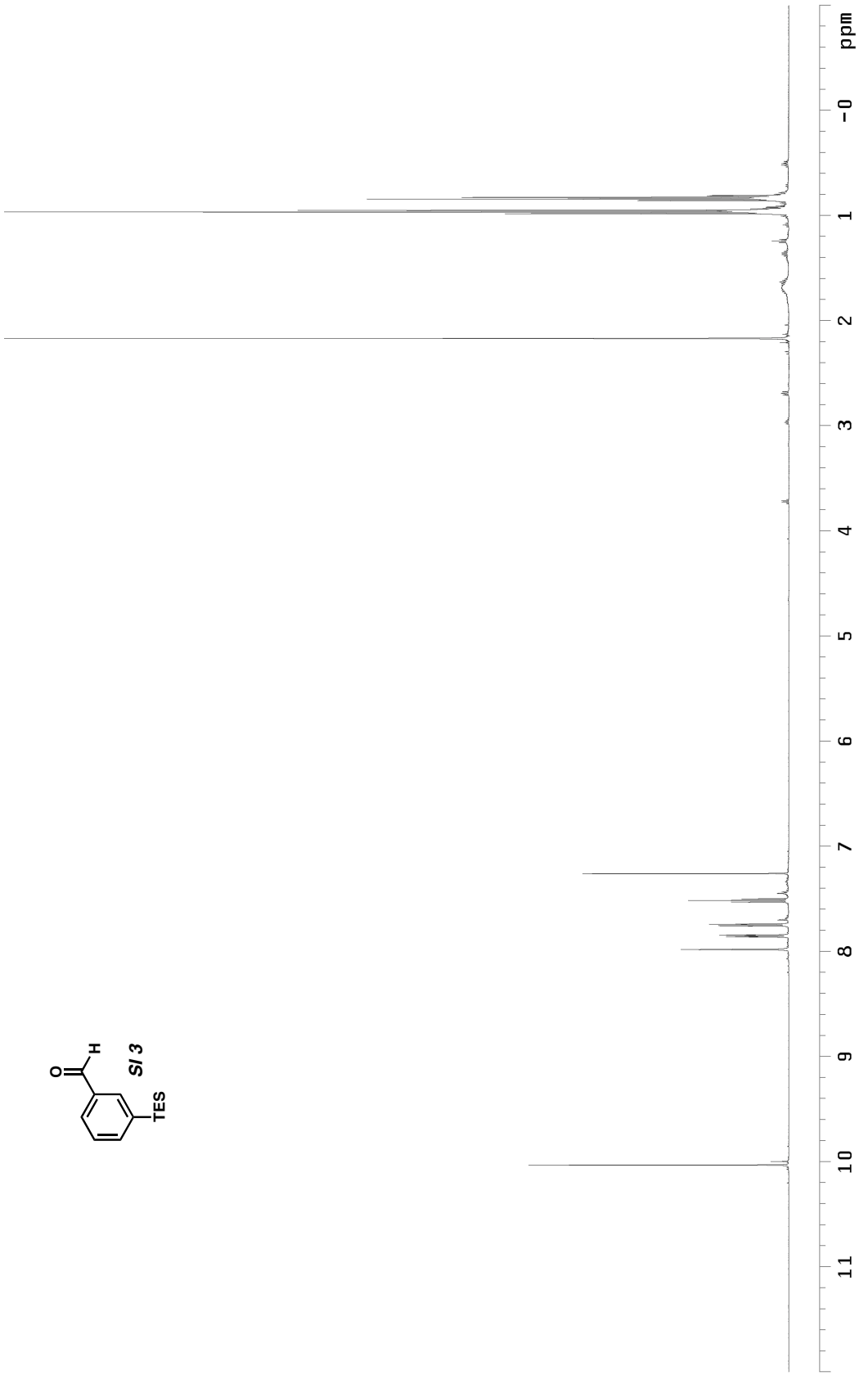
Complete Table of Runs:

Water (L, equiv)	Time (h)	GC Conversion (%)	GC Yield (%)	ee (%)

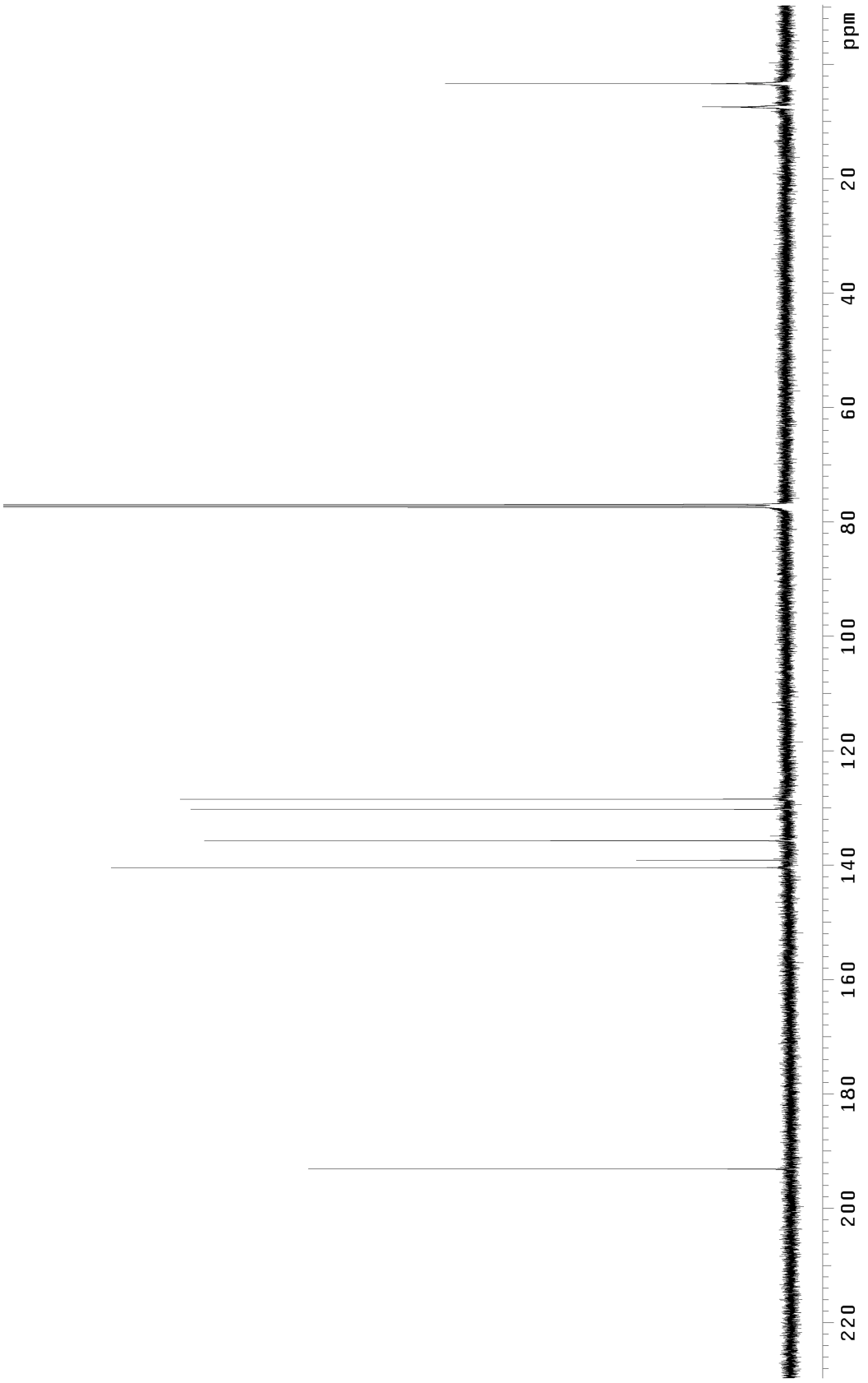
0.0 μL = 0 equiv	1.5	100 %	100.5 %	88.5 %
“”	1.0	100 %	101.6 %	88.4 %
“”	1.0	100 %	97.2 %	88.7 %
Averaged =	*1.2*	*100 %*	*99.9 %*	*88.5 %*
1.0 μL = 0.55 equiv	1.5	100 %	100.6 %	86.6 %
“”	0.5	100 %	103.0 %	87.0 %
“”	0.5	100 %	95.4 %	86.6 %
Averaged =	*0.8*	*100 %*	*99.6 %*	*86.7 %*
3.0 μL = 1.6 equiv	0.75	100 %	88.5 %	83.6 %
“”	0.5	100 %	87.4 %	83.9 %
“”	0.5	100 %	88.3 %	84.0 %
Averaged =	*0.6*	*100 %*	*88.1 %*	*83.8 %*
15 μL = 8.3 equiv	0.75	100 %	75.3 %	60.3 %
“”	0.5	100 %	70.8 %	62.4 %
“”	0.5	100 %	70.3 %	59.9 %
Averaged =	*0.6*	*100 %*	*70.3 %*	*60.9%*
30 μL = 17 equiv	0.75	100 %	67.8 %	50.4 %
“”	0.75	100 %	65.6 %	48.7 %
“”	0.75	100 %	66.9 %	47.4 %
Averaged =	*0.75*	*100 %*	*66.8 %*	*48.4 %*
60 μL = 33 equiv	1.5	100 %	64.3 %	40.4 %
“”	1.0	100 %	73.5 %	40.0 %
“”	6.0	78.2 %	(66.0 %)[*]	41.0 %
Averaged =	*2.8*	*92.7 %*	*67.9 %*	*40.5 %*

[*] Based on conversion. The uncorrected yield was 51.6%.

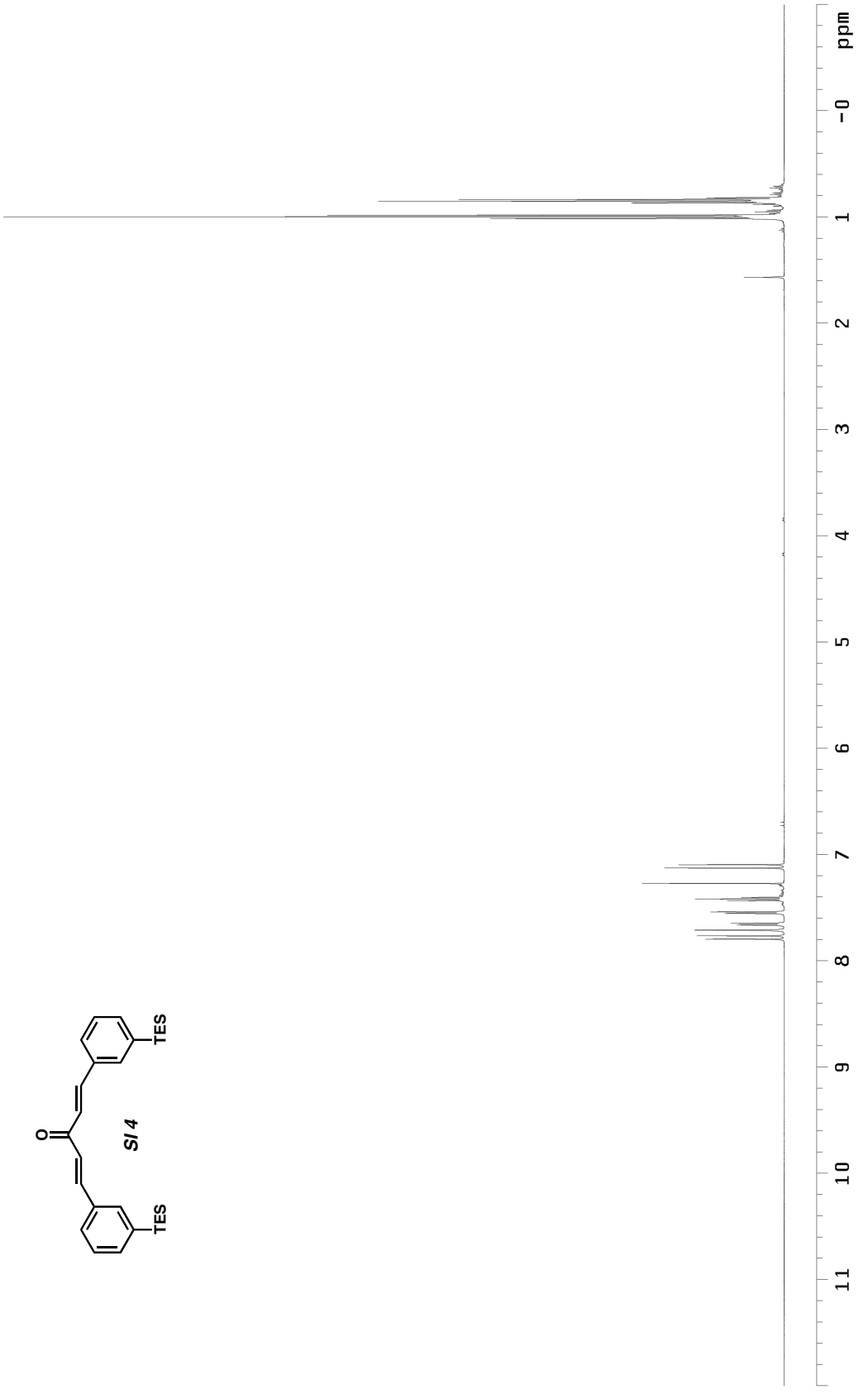
General Procedure: A 1-dram vial equipped with a magnetic stir bar was flame dried under vacuum. After cooling under dry argon, [$Pd_2(dba)_3$] (4.6 mg, 0.005 mmol, 0.05 equiv) and (*S*)-*t*-BuPHOX ligand (**3**) (0.0125 mmol, 0.125 equiv) were added. After the flask was flushed with argon, THF (3.0 mL) was added and the contents were stirred at 25 °C for 30 min. Tridecane (12.25 μL), water, and then carbonic acid allyl ester 2-methyl-cyclohex-1-enylmethyl ester (19.6 mg, 0.1 mmol, 1.0 equiv) were added by syringe in the given order. When the reaction was complete by TLC, the reaction mixture was diluted with hexanes (5 mL), filtered through a small plug of silica gel and analyzed by GC. A GC yield was determined on DB-WAX column (70 °C initial temp, 5 °C/min ramp to 180 °C), tridecane ret. time = 7.000 min, ketone **4** ret. time = 12.309 min, carbonate **SI 2** ret. Time = 17.771 min. Enantiopurity was determined by GC on a GT-A column (100°C isothermal for 30 min) major enantiomer (*S*) ret. time = 14.897 min, minor enantiomer (*R*) ret. time = 17.313 min.



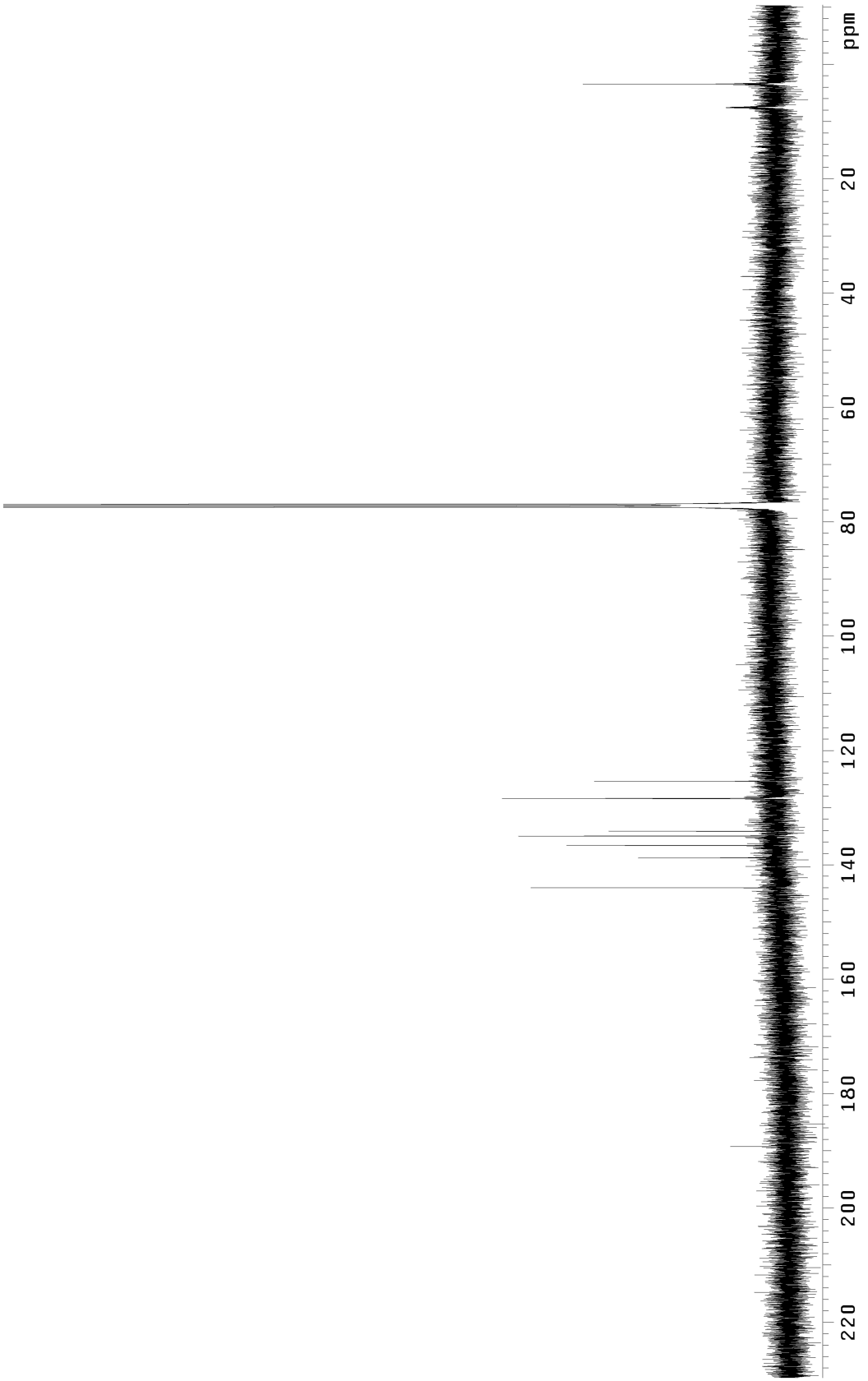
^{1}H NMR spectrum of 3-(triethylsilyl)benzaldehyde (**SI 3**) in $CDCl_3$



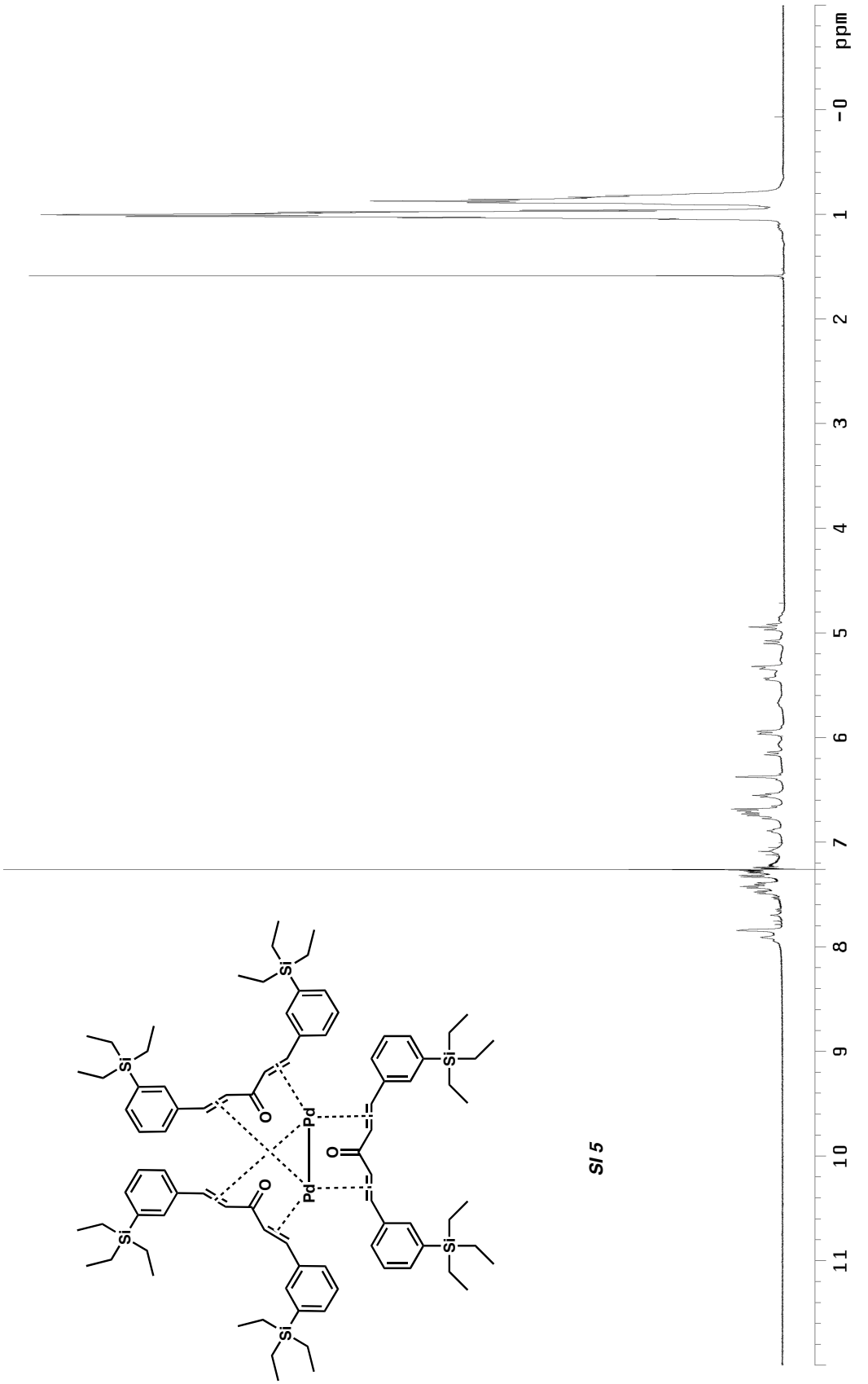
^{13}C NMR spectrum of 3-(triethylsilyl)benzaldehyde (**SI 3**) in $CDCl_3$



^{1}H NMR spectrum of 1,5-bis-[3-(triethylsilyl)phenyl]penta-1,4-dien-3-one, mtdba (**SI 4**) in $CDCl_3$

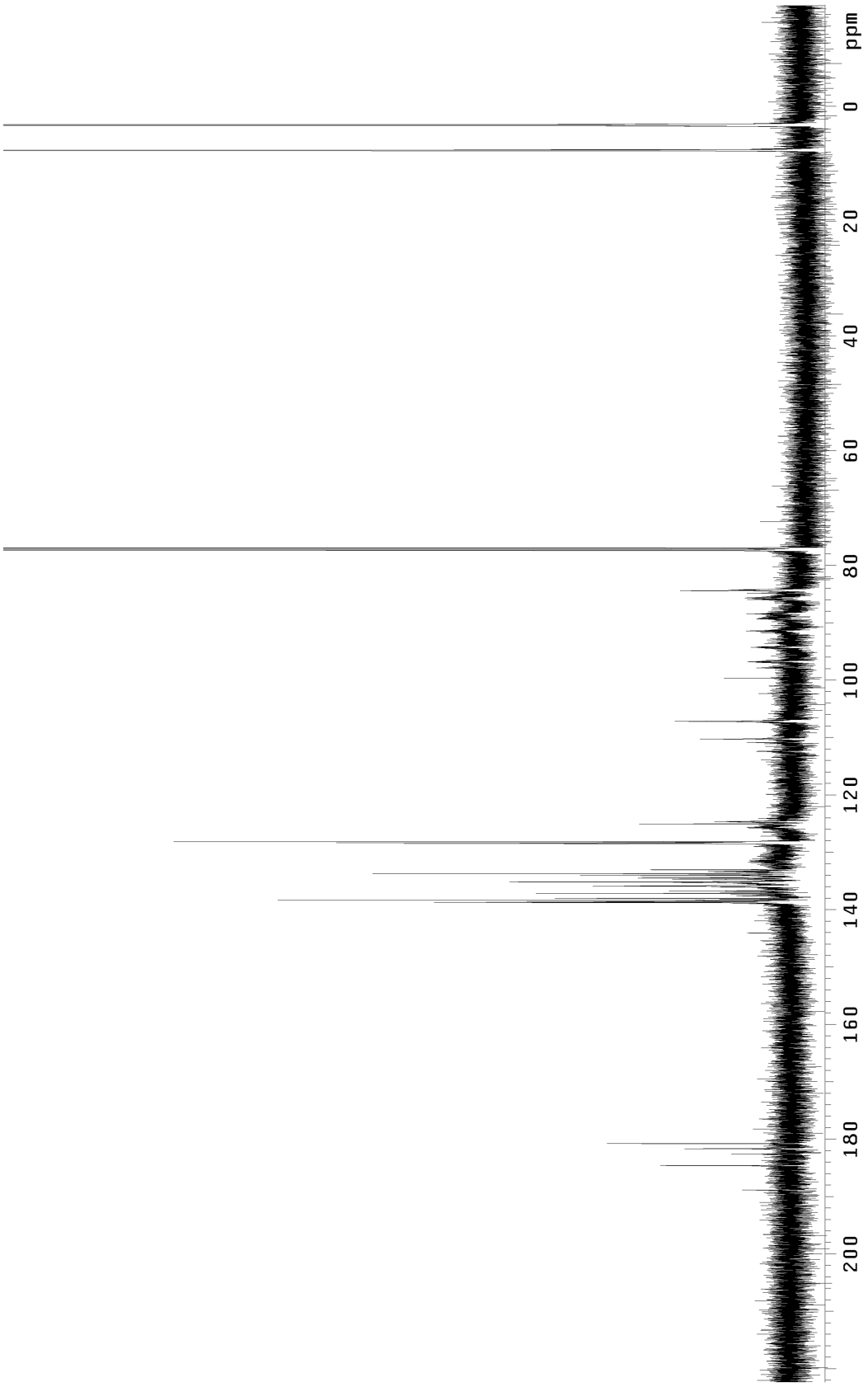


^{13}C NMR spectrum of 1,5-bis-[3-(triethylsilyl)phenyl]penta-1,4-dien-3-one, mtdba (**SI 4**) in $CDCl_3$

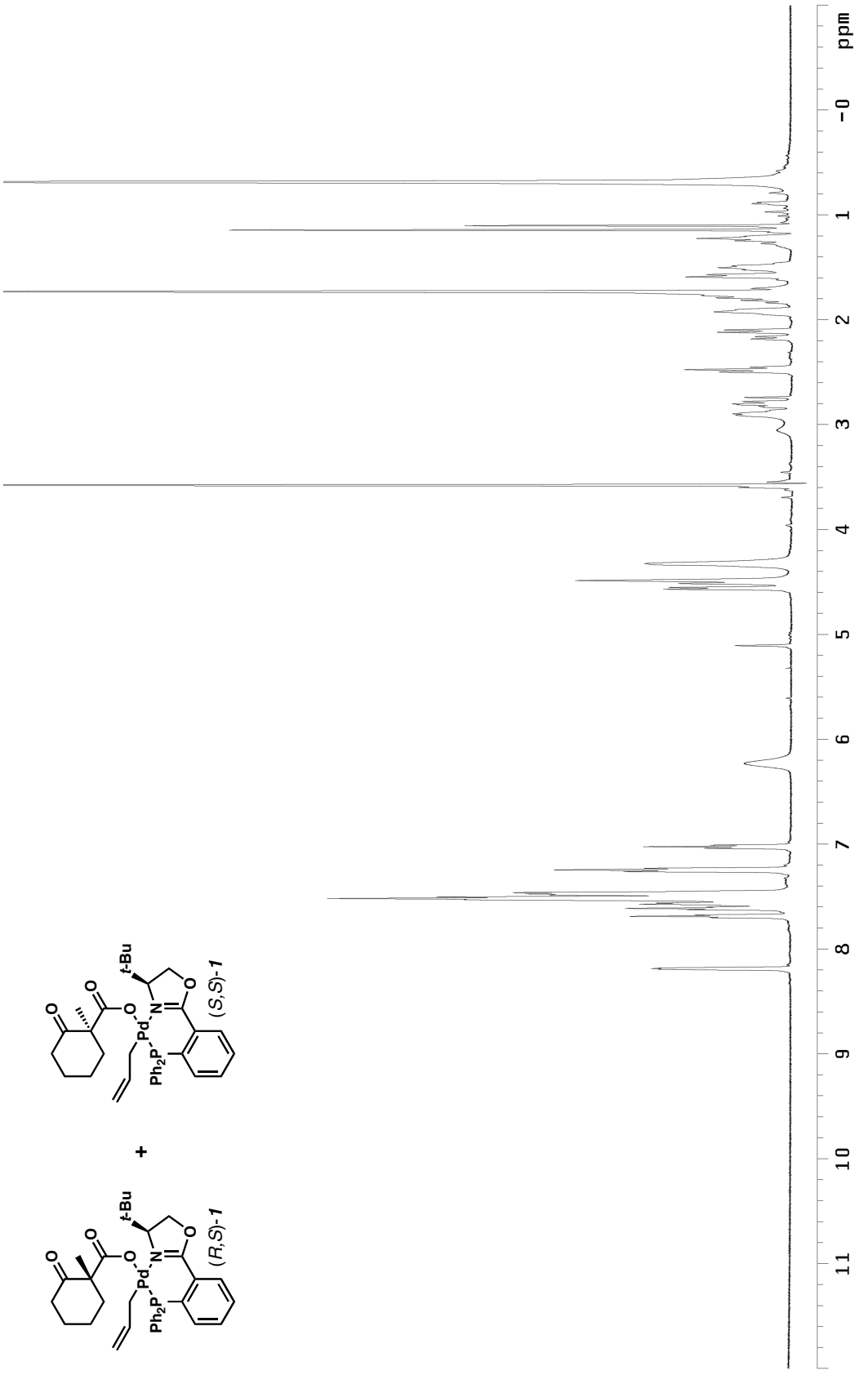


SI 5

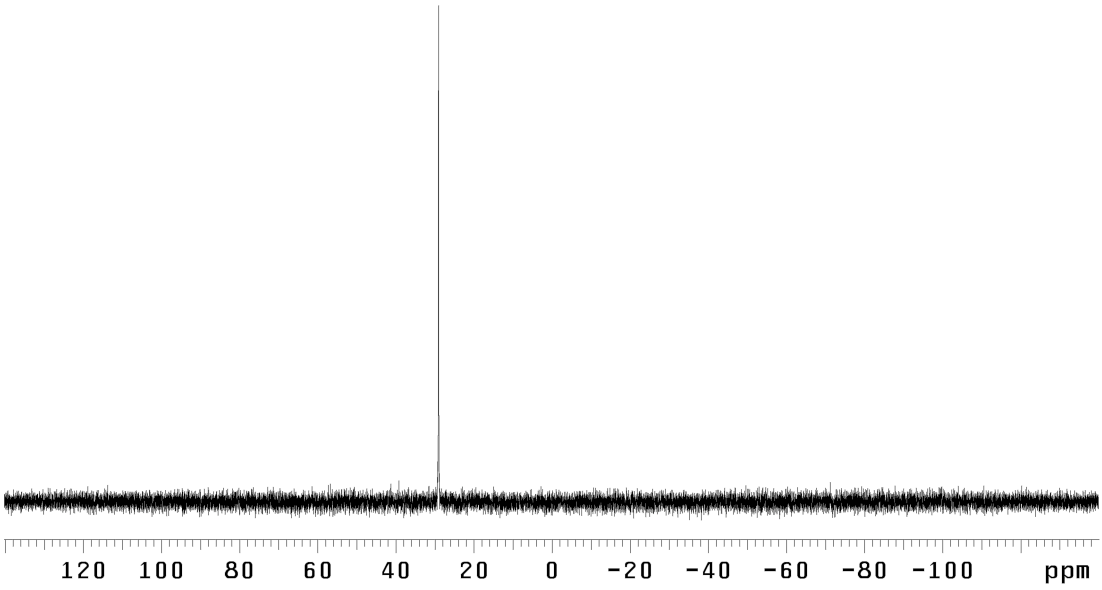
^{1}H NMR spectrum of $[Pd_2(mtdba)_3]$ (**SI 5**) in $CDCl_3$



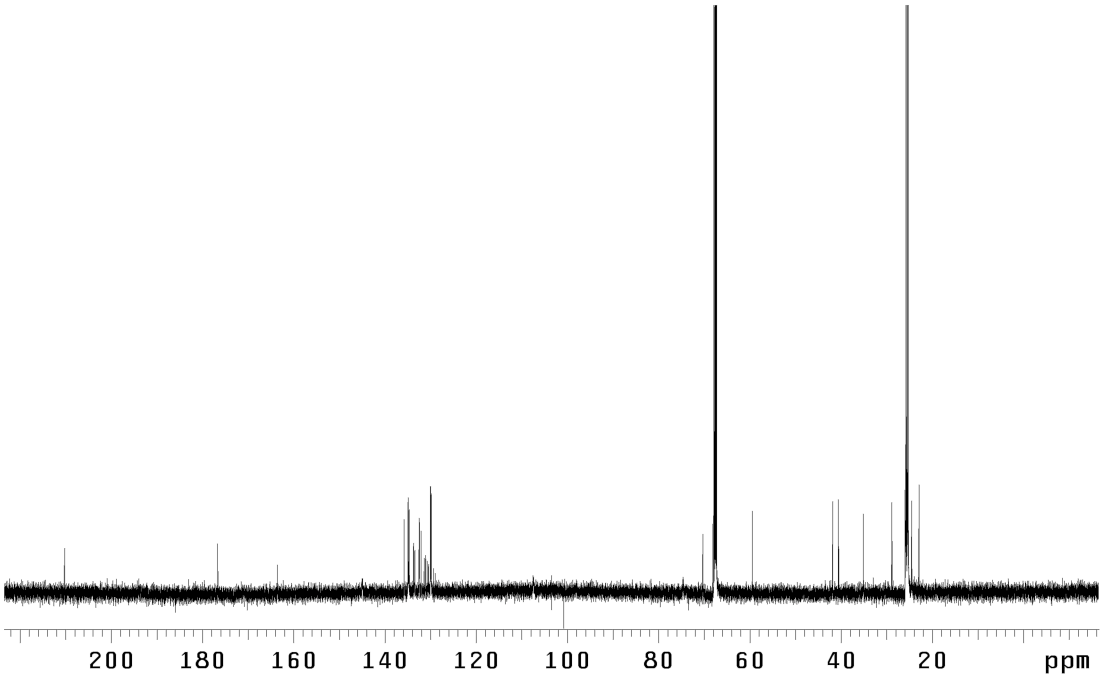
^{13}C NMR spectrum of $[Pd_2(mtdba)_3]$ (**SI 5**) in $CDCl_3$



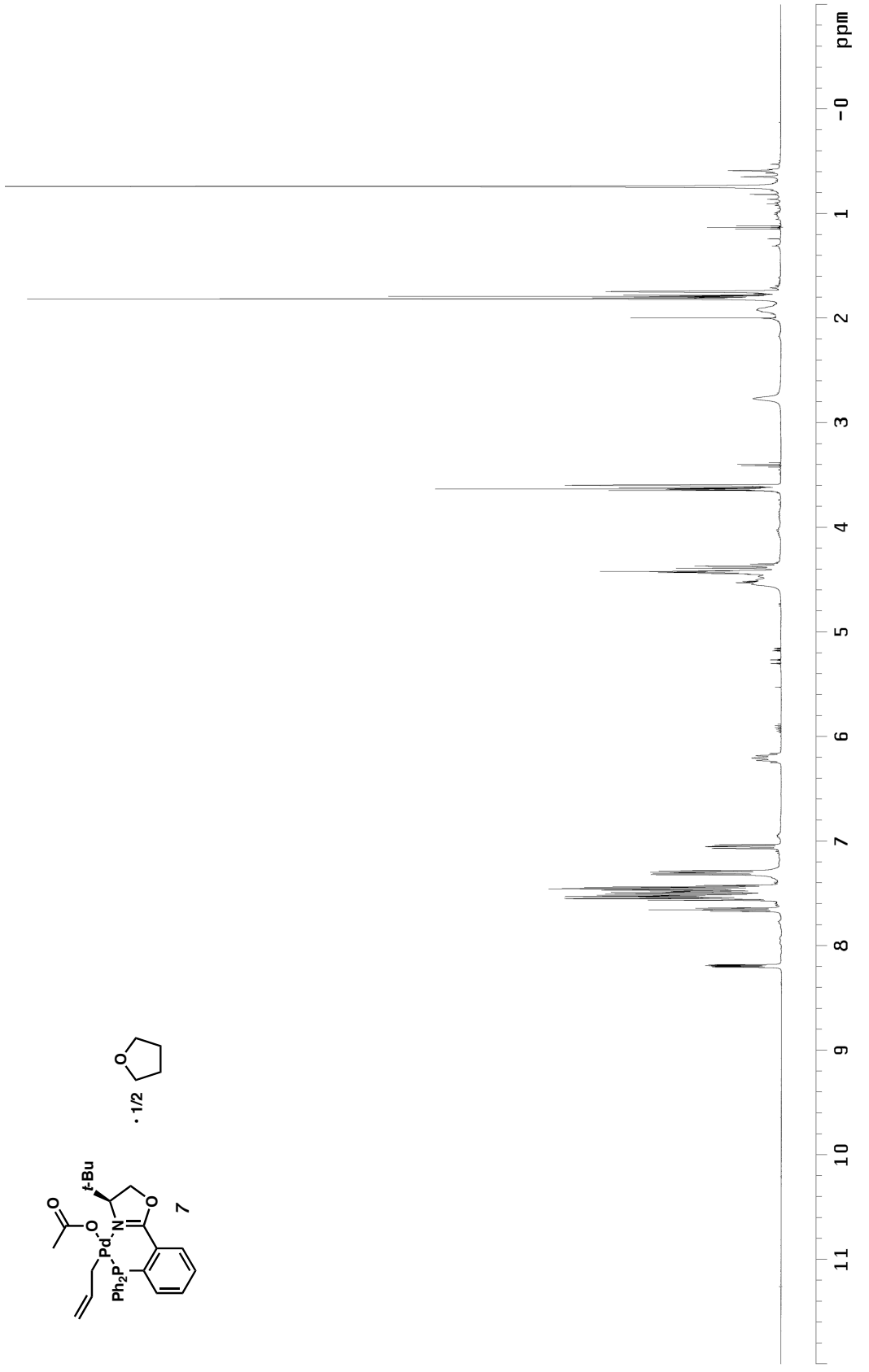
^{1}H NMR spectrum of intermediate **1** in $THF_{d\text{-}8}$ at –28 °C



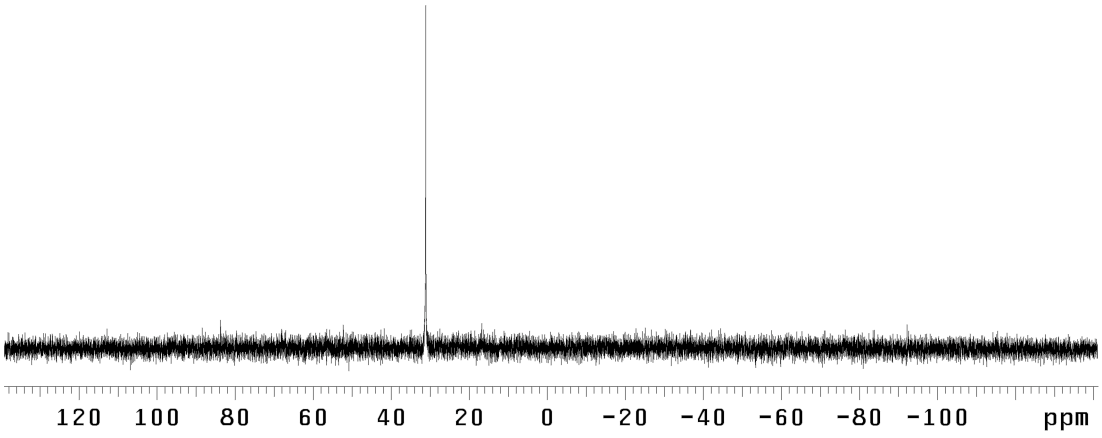
^{31}P NMR spectrum of intermediate (**1**) in $THF_{d\text{-}8}$ at –28 °C



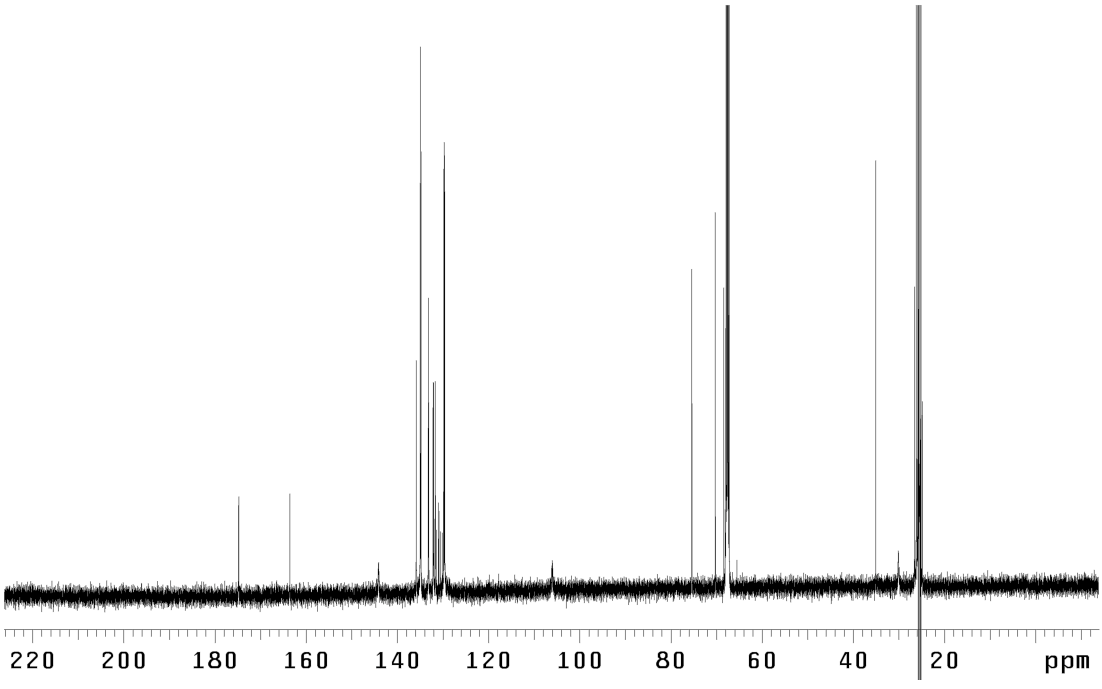
^{13}C NMR spectrum of intermediate (**1**) in $THF_{d\text{-}8}$ at –28 °C



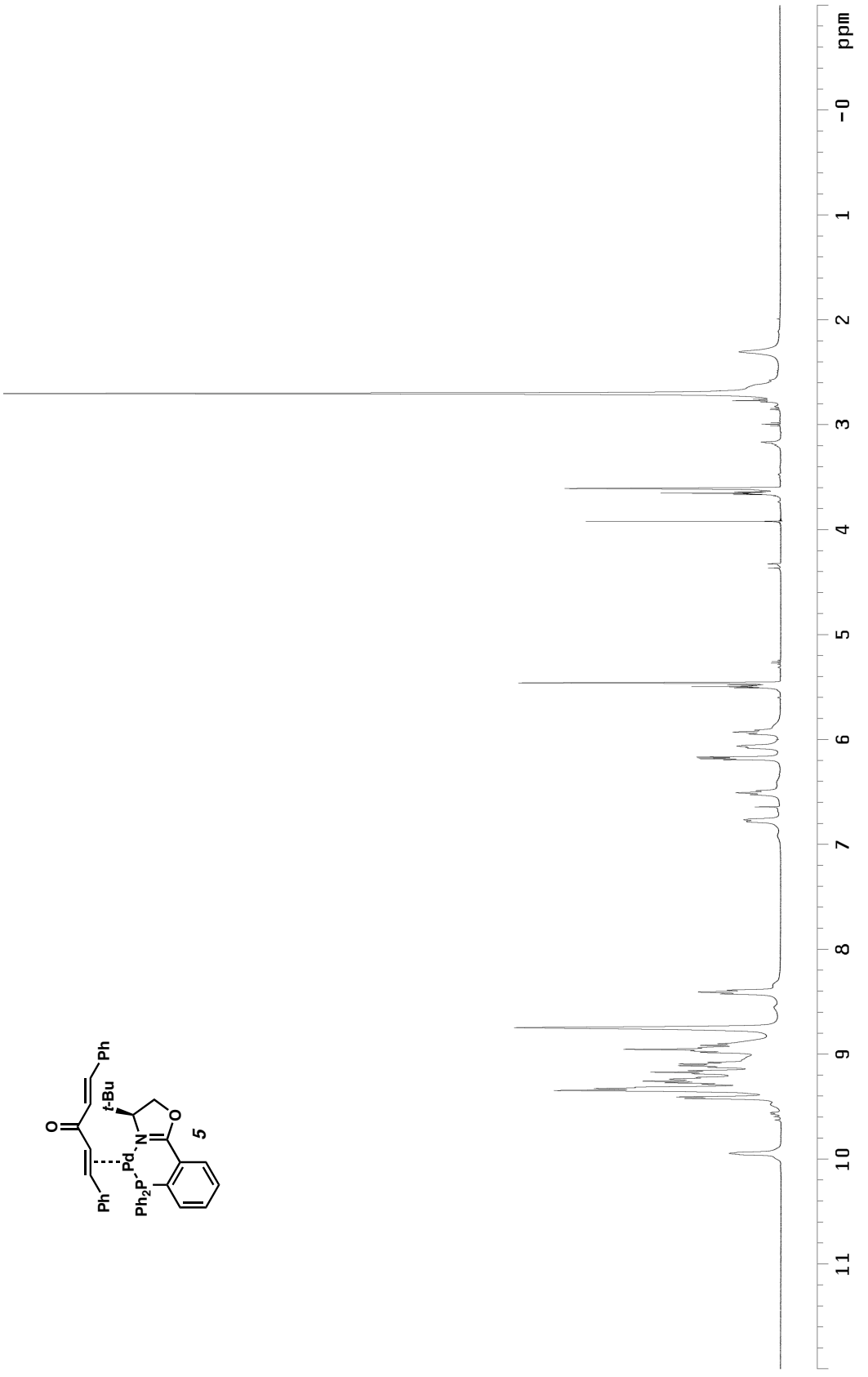
^{1}H NMR spectrum of [(*S*)-*t*-BuPHOX]Pd(allyl)(OAc)•1/2THF (**7**) in



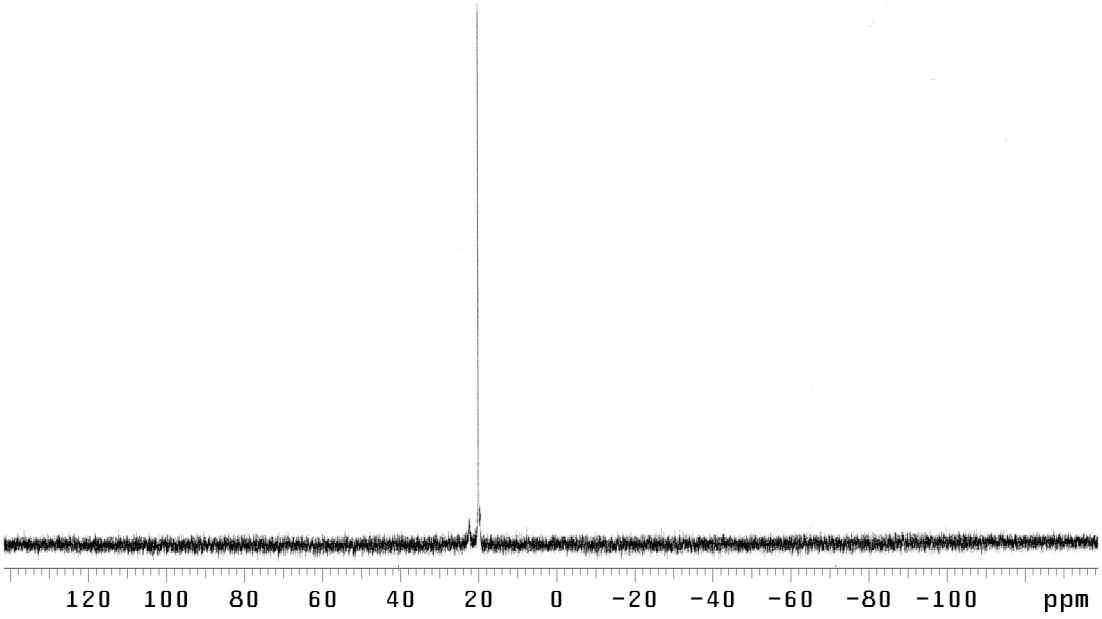
^{31}P NMR spectrum of [(*S*)-*t*-BuPHOX]Pd(allyl)(OAc)•1/2THF (**7**) in $THF_{d\text{-}8}$



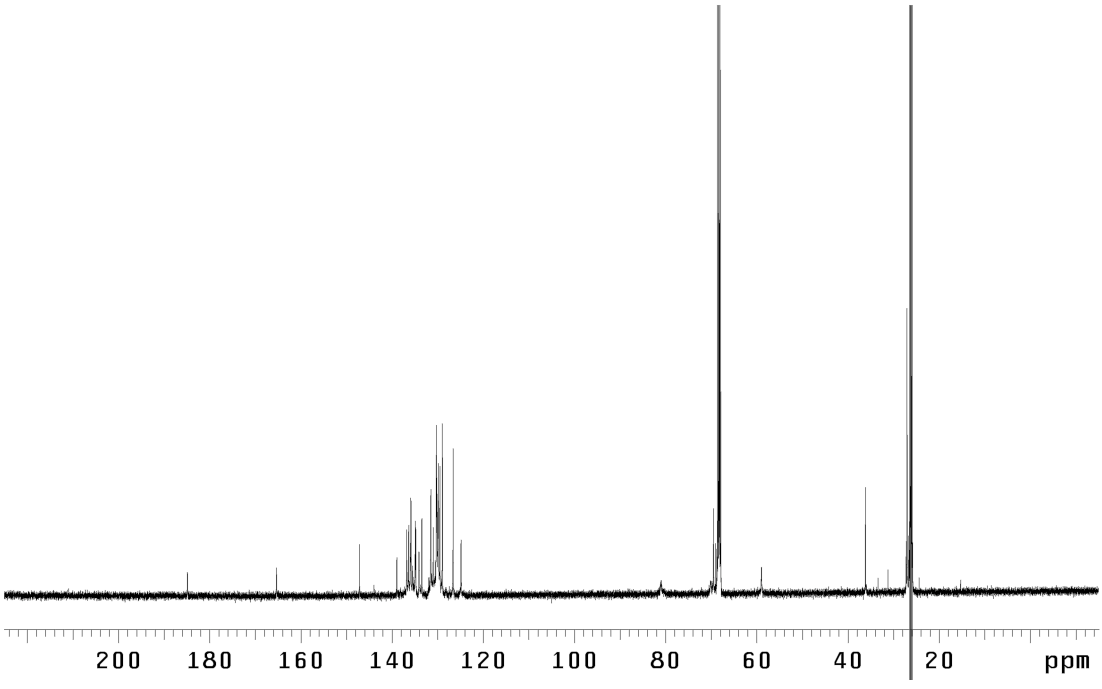
^{13}C NMR spectrum of [(*S*)-*t*-BuPHOX]Pd(allyl)(OAc)•1/2THF (**7**) in $THF_{d\text{-}8}$



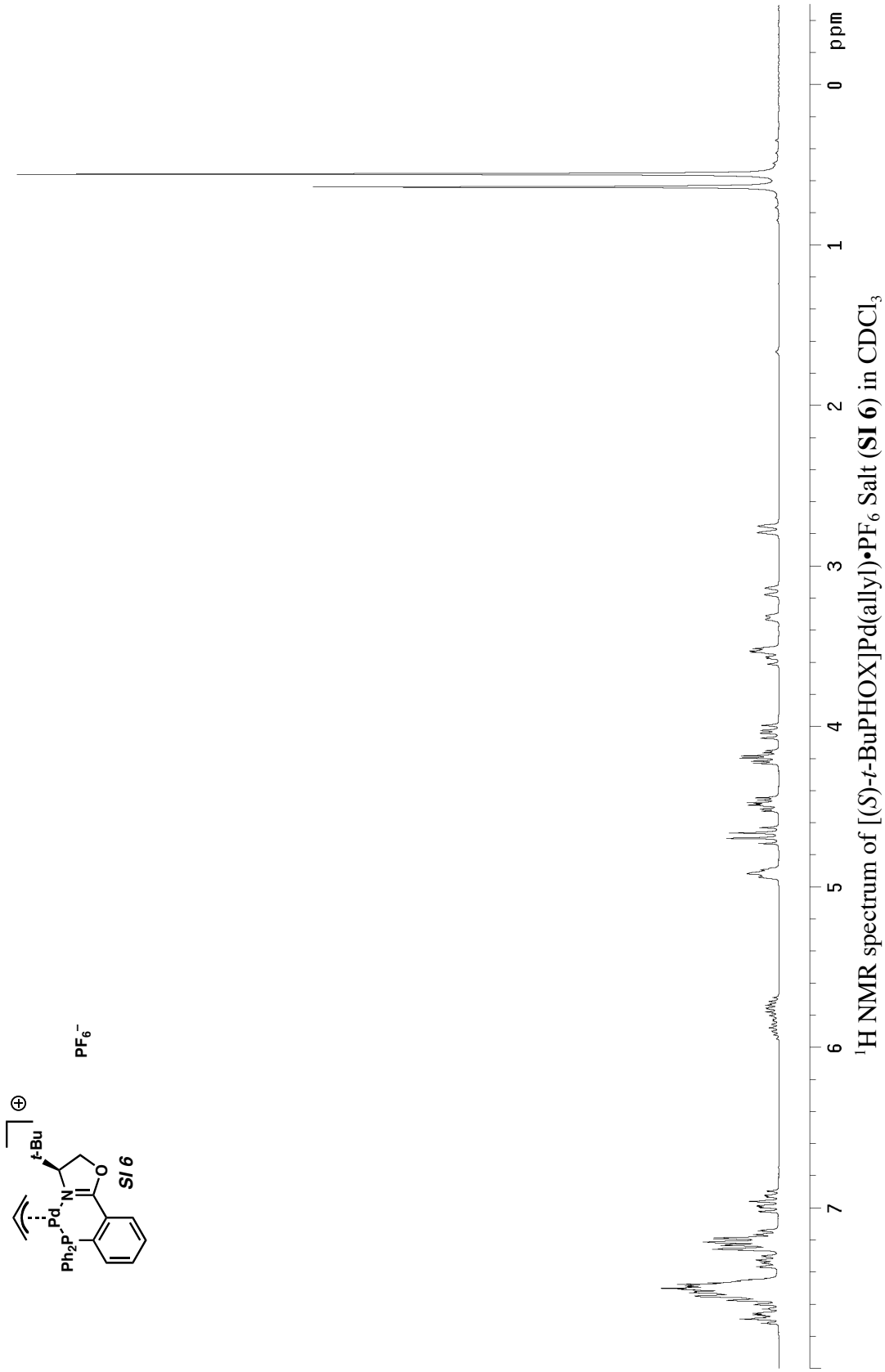
^{1}H NMR spectrum of [(*S*)-*t*-BuPHOX]Pd(dba) (**5**) in $THF_{d\text{-}8}$



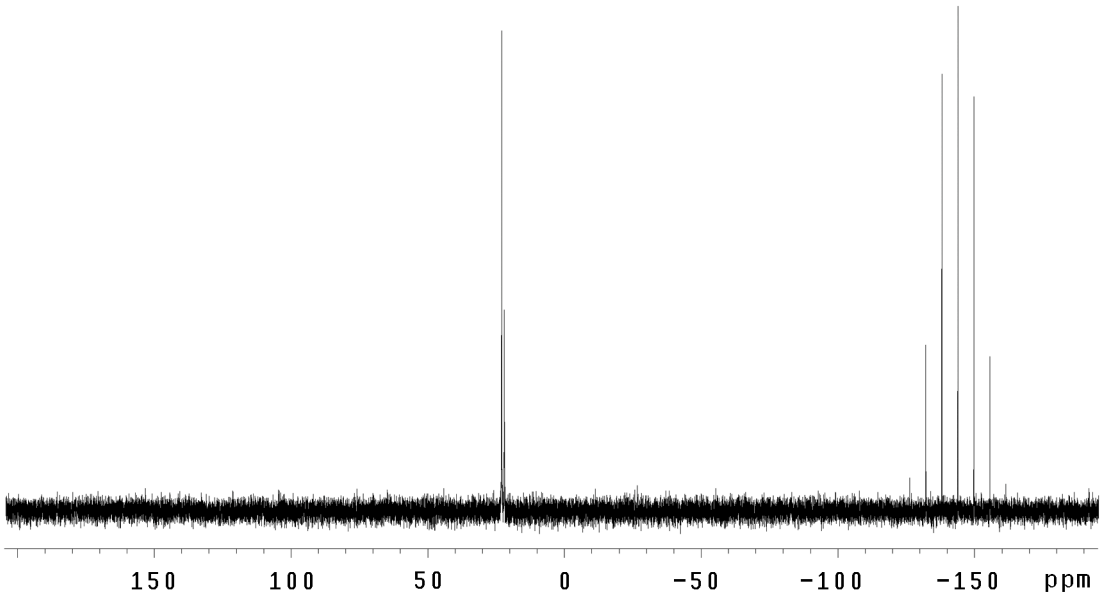
^{31}P NMR spectrum of [(*S*)-*t*-BuPHOX]Pd(dba) (**5**) in $THF_{d\text{-}8}$



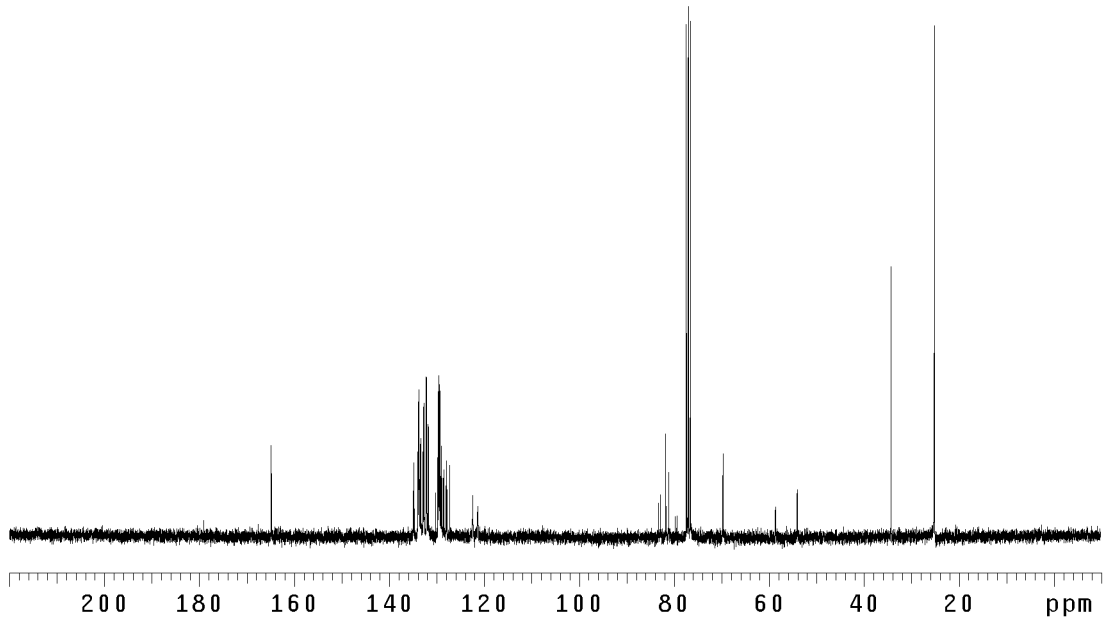
^{13}C NMR spectrum of [(*S*)-*t*-BuPHOX]Pd(dba) (**5**) in $THF_{d\text{-}8}$



^{1}H NMR spectrum of [(*S*)-*t*-BuPHOX]Pd(allyl)•PF_6 Salt (**SI 6**) in $CDCl_3$

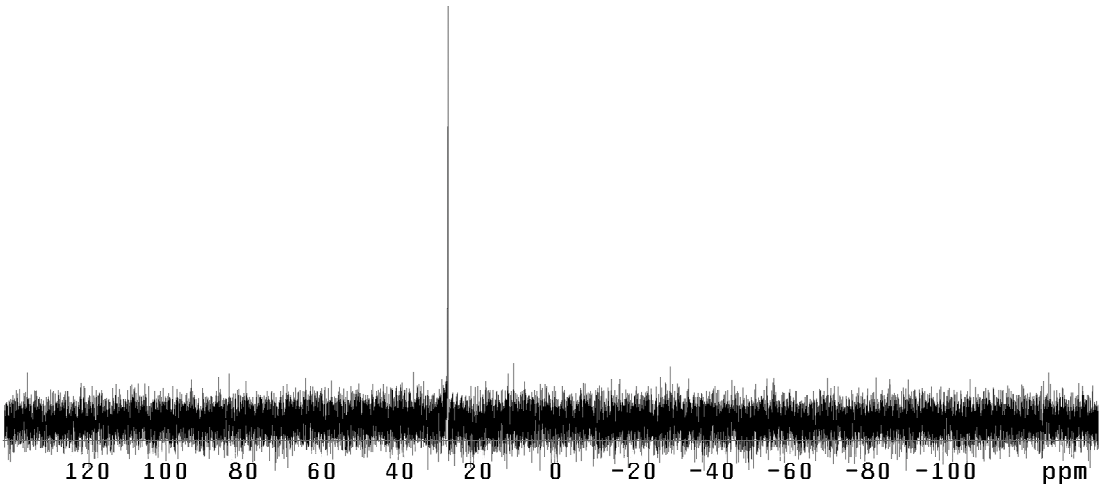


^{31}P NMR of [(*S*)-*t*-BuPHOX]Pd(allyl)•PF_6 Salt (**SI 6**) in $THF_{d\text{-}8}$

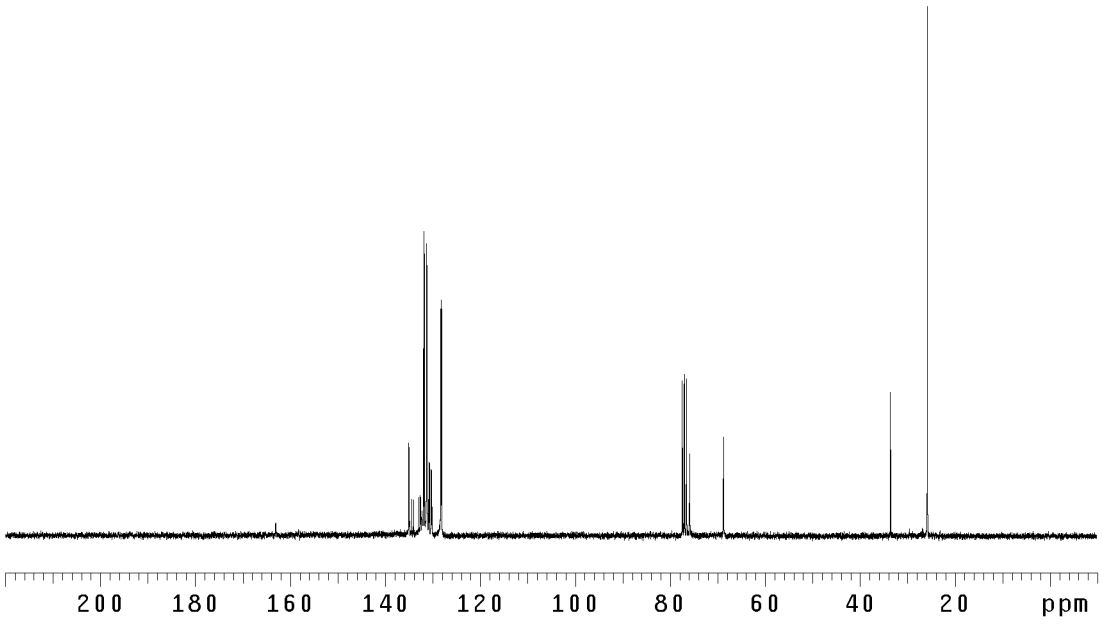


^{13}C NMR of [(*S*)-*t*-BuPHOX]Pd(allyl)•PF_6 Salt (**SI 6**) in $CDCl_3$

^{1}H NMR spectrum of (*S*)-*t*-BuPHOX oxide (**SI 7**) in $CDCl_3$



^{31}P NMR spectrum of (*S*)-*t*-BuPHOX oxide (**SI 7**) in $THF_{d\text{-}8}$



^{13}C NMR spectrum of (*S*)-*t*-BuPHOX oxide (**SI 7**) in $CDCl_3$

References:

[1] J. T. Mohr, M. R. Krout, B. M. Stoltz, *Org. Synth.* **2009**, *86*, 194–211.

[2] D. C. Behenna, B. M. Stoltz, *J. Am. Chem. Soc.* **2004**, *126*, 15044–15045.

[3] a) M. R. Krout, J. T. Mohr, B. M. Stoltz, *Org. Synth.* **2009**, *86*, 181–193; b) K. Tani, D. C. Behenna, R. M. McFadden, B. M. Stoltz, *Org. Lett.* **2007**, *9*, 2529–2531; c) M. Peer, J. C. de Jong, M. Kiefer, T. Langer, H. Rieck, H. Schell, P. Sennhenn, J. Sprinz, H. Steinhagen, B. Wiese, G. Helmchen, *Tetrahedron* **1996**, *52*, 7547–7583.

[4] $[Pd_2(mtdba)_3]$ is highly dynamic in solution giving the observed intricate NMR spectra and fractional resonance integrations. This dynamic nature has been reported for all published $[Pd_x(dba)_y]$ derivatives as of this writing. For examples see: I. J. S. Fairlamb, A. R. Kapdi, A. F. Lee, *Org. Lett.* **2004**, *6*, 4435-4438.

[5] Complex **5** exists as a mixture of dba rotomers in solution. For a study of relevant palladium dba complexes see: W. A. Herrmann, W. R. Thiel, C. Broßmer, K. Öfele, T. Priermeier, W. Scherer, *J. Organomet. Chem.* **1993**, *461*, 51-61.

[6] S. Liu, J. F. K. Müller, M. Beuburger, S. Schaffner, M. Zehnder, *J. Organomet. Chem.* **1997**, *549*, 283–293.