Electronic Supplementary Material (ESI) for ChemComm.

# Supporting information

## Construction of β to carbonyl stereogenic centres by asymmetric 1,4-addition of alkylzirconocenes to dienones and ynenones

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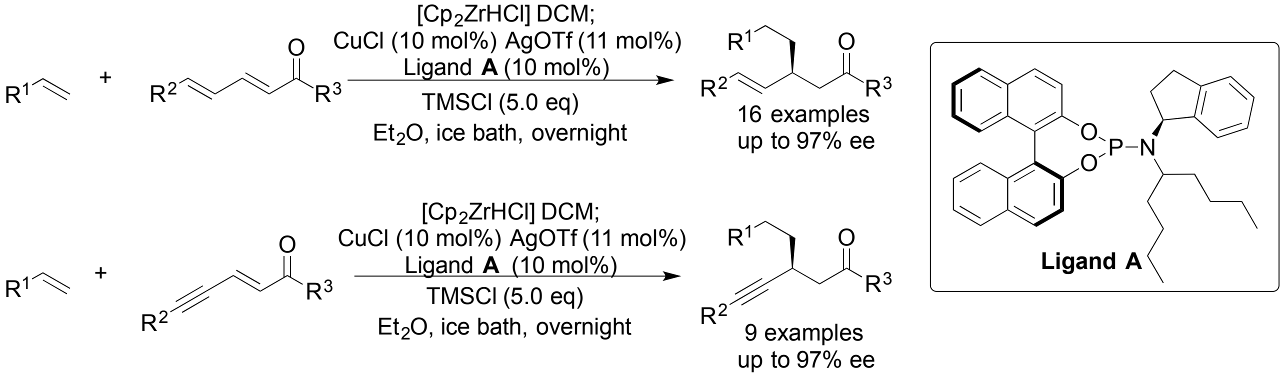

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## General information

Procedures were all carried out in flame-dried flasks with anhydrous solvents under argon protection. Analytical thin-layer chromatography was conducted on precoated glass-backed plates (Silica Gel 60 $F_{254}$, Merck). Visualization was performed by UV light (254nm), aqueous ceric ammonium molybdate (CAM), p-Anisaldehyde Stain, aqueous basic potassium permanganate stains ($KMnO_4$) and vanillin solution. Flash column chromatography was carried out using Apollo Scientific silica gel 60 (0.040 – 0.063 nm), VWR (40-63 μm) silica gel, Sigma Aldrich silica gel.

Reaction temperatures below 0 °C were obtained using a Julabo FT902 immersion cooler. 0 °C was achieved using an ice-water bath. Light sensitive reactions were processed under Aluminium foil protection.

All NMR spectra were recorded at room temperature; $^1H$ and $^{13}C$ nuclear magnetic resonance experiments were carried out using Bruker DPX-200 (200/50 MHz), AVG-400 (400/100 MHz) , AVH-400 (400/100 MHz) or AVC-500 (500/125 MHz) spectrometers. Chemical shifts are reported in ppm from the residual solvent peak. Chemical shifts ($\delta$) are given in ppm and coupling constants ($J$) are quoted in hertz (Hz). Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). Assignments were made with the assistance of COSY, DEPT-135, HSQC and NOESY NMR spectra.

Chiral HPLC separations were achieved using an Agilent 1230 Infinity series normal phase HPLC unit and HP Chemstation software. Chiralpak® columns (250 × 4.6 mm), fitted with matching Chiralpak® Guard Cartridges (10 × 4 mm), were used as specified in the text. Solvents used were of HPLC grade (Fisher Scientific, Sigma Alrich or Rathburn); all eluent systems were isocratic.

Low-resolution mass spectra were recorded using a Walters LCT premier XE. High-resolution mass spectra (EI and ESI) were recorded using a Bruker Micro TOF spectrometer by the internal service at the University of Oxford.

Infrared measurements (ATR) were carried out using a Bruker Tensor 27 FT-IR with internal calibration in the range 4000-600 $cm^{-1}$.

Optical rotations were recorded using a Perkin-Elmer 241 Polarimeter;

In those cases where silver salts were used the resulting solutions were filtered using syringe filters PTFE (0.2 μm, 13 mm diameter) from Camlab.

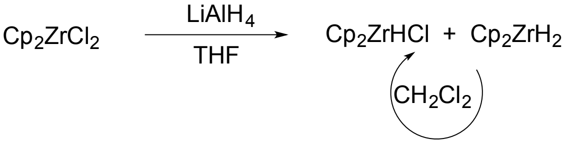
## Chemicals

Unless stated otherwise, commercially available reagents were purchased from Sigma-Aldrich, Fisher Scientific, Apollo Scientific, Acros Organics, Strem Chemicals, Alfa Aesar or TCI UK and were used without purification. Petroleum ether refers to petroleum boiling in the range 40-60°C. Deuterated solvents were purchased from Sigma-Aldrich ($CDCl_3$). Schwartz reagent was prepared according to the literature procedure from $Cp_2ZrCl_2$ provided by Alfa Aesar. CuCl which purity is 98% is purchased from Strem Chemicals, the 99.99% purity CuCl is from Sigma-Aldrich, and all of them were directly used without any further purification. All the Trimethylsilyl chloride (TMSCl) were distilled fresh and stored in Schlenk flaskes under an argon atmosphere. All phosphoramidite ligands were synthesized by the Fletcher group.

## General Methods

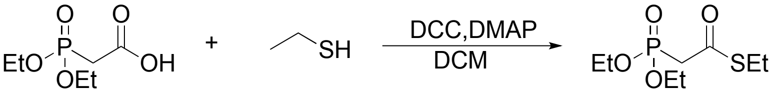
1. Preparation of Schwartz reagent[1]

$$Cp_2ZrCl_2 \xrightarrow[THF]{LiAlH_4} Cp_2ZrHCl + Cp_2ZrH_2$$



Zirconocene dichloride (30.0 g, 0.103 mol) was added to a flame-dry 250 mL Schlenk flask wrapped with aluminium foil under argon. Dry THF (120 mL) was added and the suspension was stirred at 35 °C for 30 minutes. $LiAlH_4$ in $Et_2O$ (1 M, 28.2 mmol) was added dropwise to the mixture over about 30 minutes. The resulting suspension was stirred at room temperature for 2 hours. The mixture was then Schlenk-filtered under argon and washed with tetrahydrofuran (200 mL), methylene chloride (200 mL), and diethyl ether (200 mL). The precipitate was dried under high vacuum for two hours to give a white powder (20.3 g, 75%), which is stored under argon in a small flame-dried schlenk flask while being protected from light.

2. Preparation of S-ethyl 2-(diethoxyphosphoryl) ethanethioate[2] ($(EtO)_2POCHCOSEt$)



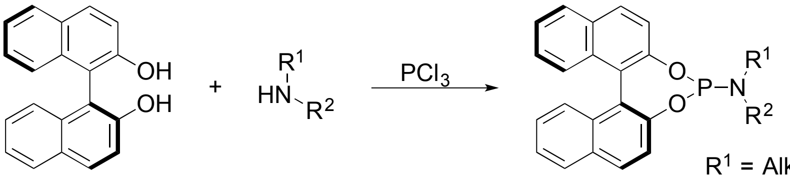
A solution of diethylphosphonoacetic acid (1.0 eq.), ethanethiol (1.0 eq.), and DMAP (0.1 eq.) in DCM was cooled to 0°C. DCC (1.0 eq.) was added in portions. The reaction mixture was left to stir overnight under argon at room temperature. The mixture was filtered through a Celite pad, and DCM was used to rinse the pad. The organic layer was washed with aqueous $NaHCO_3$, water and brine. The organic phase was dried with anhydrous $Na_2SO_4$, and the solvent was removed under reduced pressure. The product was further purified by flash chromatography (ether: pentane) to colourless oil.

## 3. Preparation of amines[3]

R, $R^1$, $R^2$ = Alkyl or H

According to a modified procedure from Davies and co-workers[3]. Ketone (2.0 eq.) was added to a stirring solution of amine in THF at room temperature. After 5 minutes, $Na(OAc)_3H$ (2.0 eq.) was tipped into the mixture. The reaction was kept under room temperature for 48 hours, and the resulting suspension was added to a 1:1 mixture of $Et_2O$ and $NaHCO_3$ (aq. sat.) and stirred for another half an hour. The mixture was partitioned between the aqueous and $Et_2O$ layers and the aqueous phase extracted with $Et_2O$ three times. The combined organic phase was concentrated in vacuo. Then HCl (aq.2 M) was added dropwise (pH = 1). The mixture was partitioned between the aqueous and organic phases, and the organic phase was extracted with HCl (aq. 2.0 M). Then DCM was added to the combined aqueous phases and NaOH (4 M) was added till the mixture became basic (pH>14). The mixture was partitioned between aqueous and organic phases. DCM was used to extract residual product from the aqueous layer (three extracts). The combined organic layers were concentrated, dried ($MgSO_4$), filtered and concentrated to give the, desired product.

## 4. Preparation of phosphoramidite ligands[4]



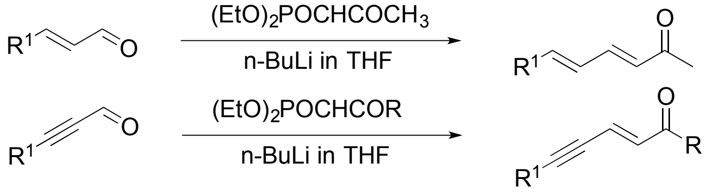
$R^1$ = Alkyl, Aryl
$R^2$ = Alkyl, Aryl

Triethylamine (5.0 eq.) was added dropwise to a stirred, ice-cooled solution of $PCl_3$ (1.0 eq.) in DCM. The ice bath was removed and the solution left to warm to room temperature before second amine (1.0 eq.) was added to the stirred solution in one portion. After 5 hours, (*S*)-binaphthol (1.0 eq.) was tipped into the suspension and the reaction mixture was left to stir for another 15 hours. The mixture was then filtered over an ~ 2cm pad of celite and silica gel, and DCM was used to rinse the pad. The filtrate was concentrated to give a yellow residue and after flash column chromatography (petroleum ether: DCM: $Et_3N$, 80:20:1; $SiO_2$) the ligand was obtained as a white crystalline solid.

## 5. Preparation of linear α, β, γ, δ-unsaturated substrates

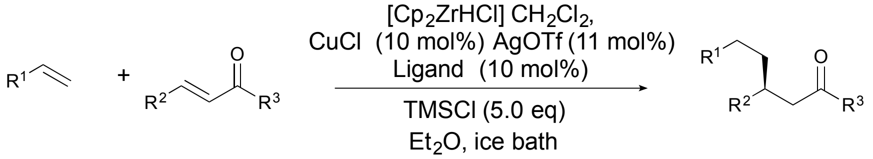
Substrate **2d**, **2e,** and **2i** were commercially available. Others were prepared according to the procedures below.

**General procedure** HWE olefination (from aldehyde)[5]



*n*-BuLi (1.5 eq. solution in hexane) was added to a stirring solution of Horner reagent (1.5 eq.) in THF at 0°C under argon. The mixture was stirred for another 20 min. A solution of aldehyde (1.0 eq.) in THF was added dropwise. The mixture was slowly warmed to room temperature and was continued overnight. The mixture was quenched with aqueous $NH_4Cl$ (sat.). The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$ three times. The combined organic materials were dried ($MgSO_4$), filtered, concentrated, and further purified by flash column chromatography (pentane: $Et_2O$; 90:10; $SiO_2$) to afford the desired product.

## 6. Copper catalysed addition on α, β,γ,δ-Unsaturated Substrates



### a. Racemic product

CuCl (0.1 eq.), and the racemic phosphoramidite ligand (0.1 eq.) were added to a flame dried round bottom flask containing 1 ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (0.11 eq.) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of alkene (2.5 eq.) in DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (2.0 eq.), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before substrate (1.0 eq.) and TMSCl (5.0 eq.) were sequentially added dropwise over about 1 min for each. Stirring at room temperature was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product.

b. Asymmetric product

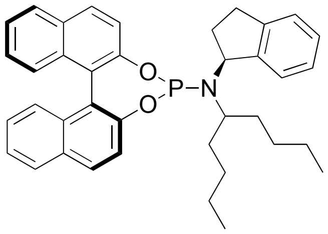
CuCl (0.1 eq.), and the phosphoramidite ligand (0.1 eq.) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (0.11 eq.) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of alkene (2.5 eq.) in DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (2.0 eq.), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before substrate (1.0 eq.) and TMSCl (5.0 eq.) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product.

## Characterization of compounds

### (+)-(11b*S*)-*N*-((*S*)-2,3-dihydro-1*H*-inden-1-yl)-*N*-(nonan-5-yl)dinaphtho[2,1-*d*:1',2'-*f*][1,3,2]dioxaphosphepin-4-amine (Ligand A)



Triethylamine (8.46 mL, 5.0 eq., 63 mmol), was added dropwise to a stirred, ice-cooled solution of $PCl_3$ (1.13 mL, 1.0 eq., 12.6 mmol) in $CH_2Cl_2$ (60 ml). The ice bath was removed and the solution left to warm to room temperature before (*S*)-N-(nonan-5-yl)-2,3-dihydro-1H-inden-1-amine (3.28g, 1.0 eq. 12.6 mmol) was added to the stirred solution in one portion. After 5 hours, (*S*)-binaphthol (3.16 g, 1.0 eq. 12.6 mmol.) was tipped into the suspension and the reaction mixture was left to stir for another 15 hours. The mixture was then filtered over an ~ 2cm pad of celite and silica gel, and $CH_2Cl_2$ (150 mL) was used to rinse the pad. The filtrate was concentrated to give a yellow residue and after flash column chromatography (petroleum ether: $CH_2Cl_2$: $Et_3N$, 80:20:1; $SiO_2$) the ligand was obtained as a white crystalline solid (2.35 g, 32%).

$^1$H NMR (500 MHz, $CDCl_3$) $\delta_H$/ppm 7.95 (d, J = 8.8 Hz, 1H, Ar-*H*), 7.90 (dd, J = 8.4 Hz, 2.2 Hz, 3H, Ar-*H*), 7.72 (d, J = 7.6 Hz, 1H, Ar-*H*), 7.61 (d, J = 8.8 Hz, 1H, Ar-*H*), 7.49 (d, J = 8.7 Hz, 1H, Ar-*H*), 7.44 – 7.37 (m, 3H, Ar-*H*), 7.34 (td, J = 7.2 Hz, 6.7 Hz, 2.0 Hz, 1H, Ar-*H*), 7.28 (tt, J = 3.9 Hz, 2.0 Hz, 2H, Ar-*H*), 7.27 – 7.19 (m, 3H, Ar-*H*), 4.76 (dt, J = 15.4 Hz, 7.8 Hz, 1H, PhC*H*NH), 3.11 – 2.86 (m, 2H, PhC$H_2$), 2.75 (dt, J = 16.1 Hz, 8.3 Hz, 1H, NHC*H*), 2.44 (d, J = 11.3 Hz, 1H, PhC$H_2$C$H_2$), 2.26 – 2.00 (m, 1H, PhC$H_2$C$H_2$), 1.78 (tt, J = 12.3 Hz, 4.4 Hz, 1H, C$H_2$), 1.72 – 1.61 (m, 1H, C$H_2$), 1.55 – 1.38 (m, 5H, C$H_2$), 1.39 – 0.97 (m, 5H, C$H_2$), 0.92 (t, J = 7.3 Hz, 3H, C$H_3$), 0.87 (t, J = 7.2 Hz, 3H, C$H_3$).

$^{13}$C NMR (126 MHz, Chloroform-d) $\delta_C$/ppm 150.2 (d, J = 8.3Hz), 149.9, 144.5, 143.3, 132.8, 131.3, 130.4, 130.2, 129.5, 128.2, 128.1, 127.4, 127.1, 127.1, 126.4, 125.9, 125.8, 125.2, 124.8, 124.60, 124.3, 124.0 (d, J = 5.4 Hz), 122.3 (d, J = 2.0 Hz)(2C), 122.3, 121.8 (d, J = 2.4 Hz), 59.7 (d, J = 21.3 Hz), 55.15 (d, J = 4.3 Hz), 36.90 (d, J = 5.4 Hz), 34.70, 31.62, 30.4, 29.3, 28.7, 23.1, 22.8, 14.23, 14.1.

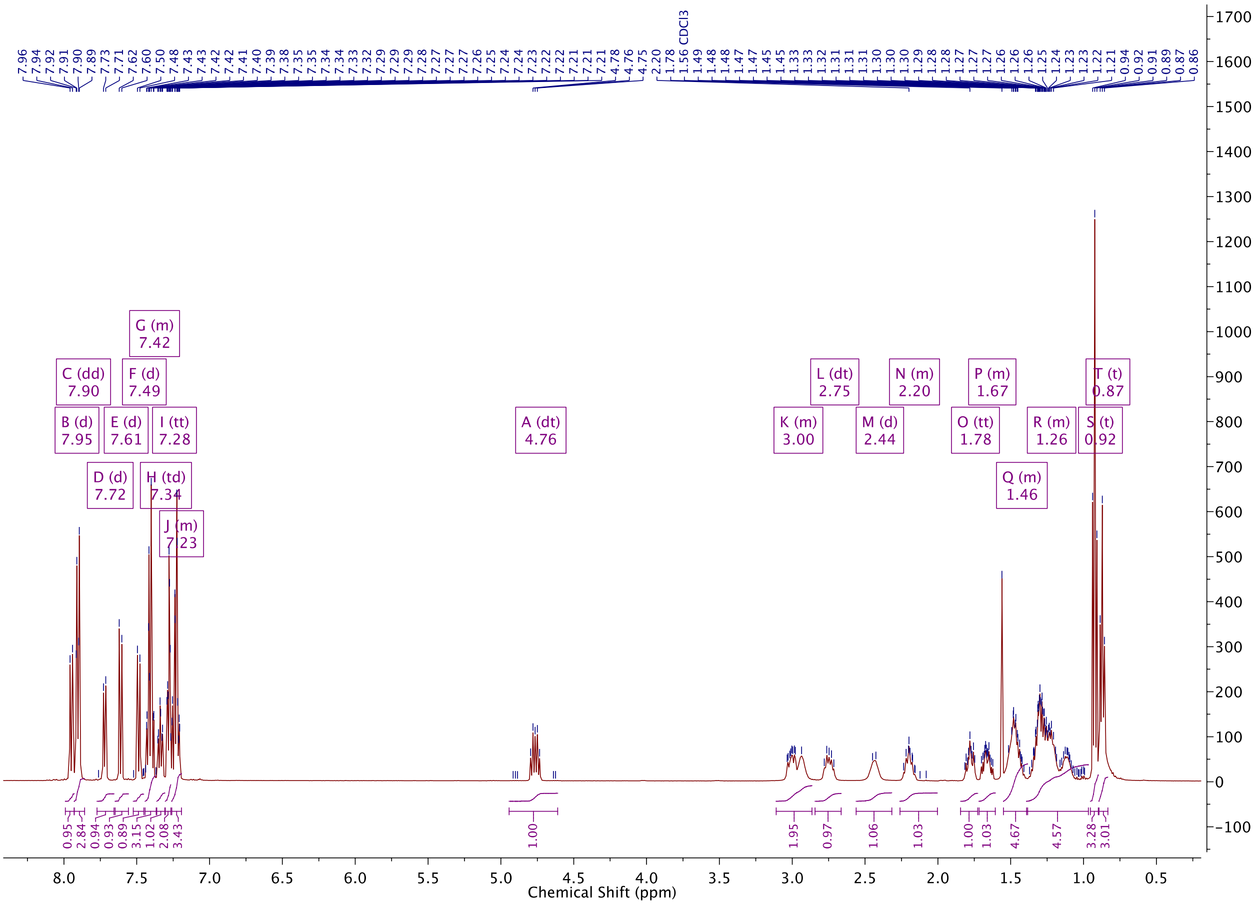
$^{31}$P NMR (162 MHz, Chloroform-d) $\delta_p$/ppm 149.9.

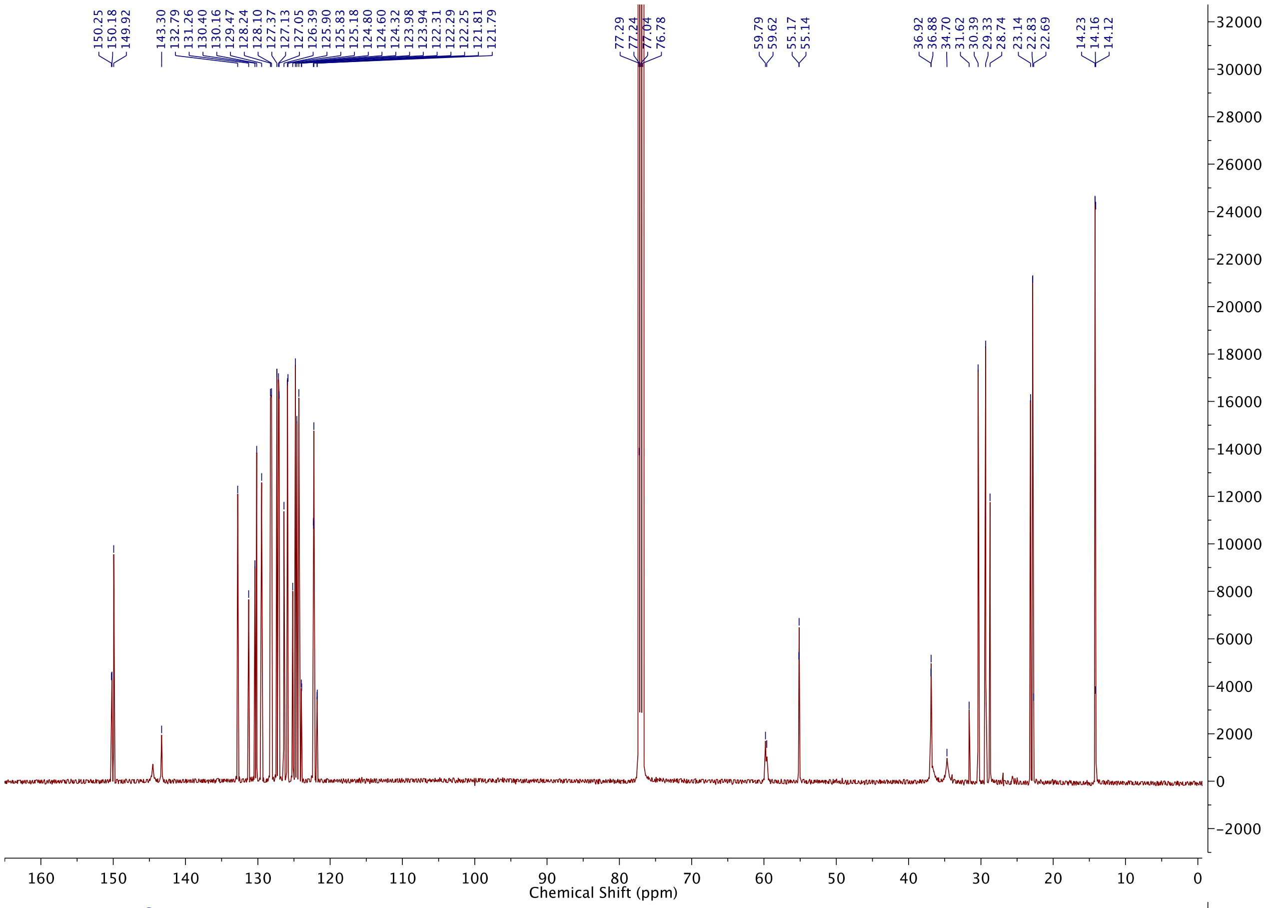
IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2955, 2857, 1590, 1462, 1024, 947, 749, 697

MS (GCMS Ammonica CI Spectrum) m/z calc. for $C_{38}H_{40}O_2NP$ $[M+H]^+$: 574.2875, found: 574.2876

$[\alpha]^{20}_{589}$ = +126.3 ° (c 1.0, $CHCl_3$)

This data was concordant with literature values[6].

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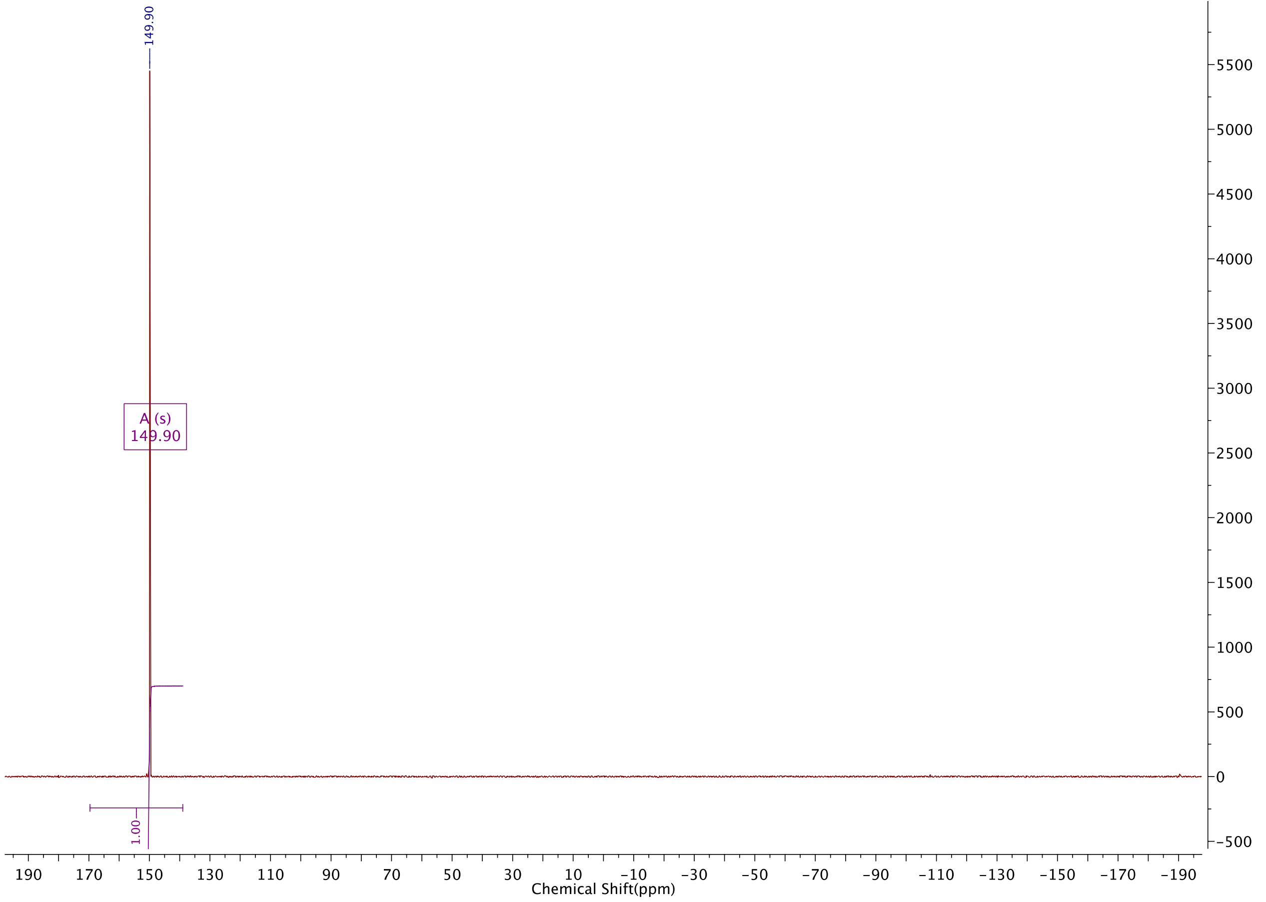
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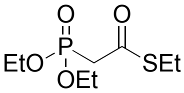
## S-ethyl 2-(diethoxyphosphoryl)ethanethioate



A solution of diethylphosphonoacetic acid (10.0 ml, 60.8 mmol, 1.0 eq.), ethanethiol (5.60ml, 60.8 mmol, 1.0 eq.), and DMAP (742mg, 6.08mmol, 0.1 eq.) in DCM was cooled to 0°C. DCC (12.6g, 60.8mg, 1.0 eq.) was added in portions. The reaction mixture was left to stir overnight under argon at room temperature. The mixture was filtered through a Celite pad, and DCM was used to rinse the pad. The organic layer was washed with aqueous $NaHCO_{3,}$ water and brine. The organic phase was dried with anhydrous $Na_2SO_4$, and the solvent was removed under reduced pressure. The product was further purified by flash chromatography (ether: pentane; 30:70) to colourless oil (10.5 g, 44mmol, 72% yield).

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 4.12 (dqd, *J* = 8.0 Hz, 7.0 Hz, 1.1 Hz, 4H, $OCH_2CH_3$), 3.16 (d, *J* = 21.3 Hz, 2H, $CH_2$COSEt), 2.88 (qd, *J* = 7.4 Hz, 0.6 Hz, 2H, $COSCH_2CH_3$), 1.29 (td, *J* = 7.1Hz, 0.6 Hz, 6H, $OCH_2CH_3$), 1.22 (t, *J* = 7.4 Hz, 3H, $COSCH_2CH_3$).

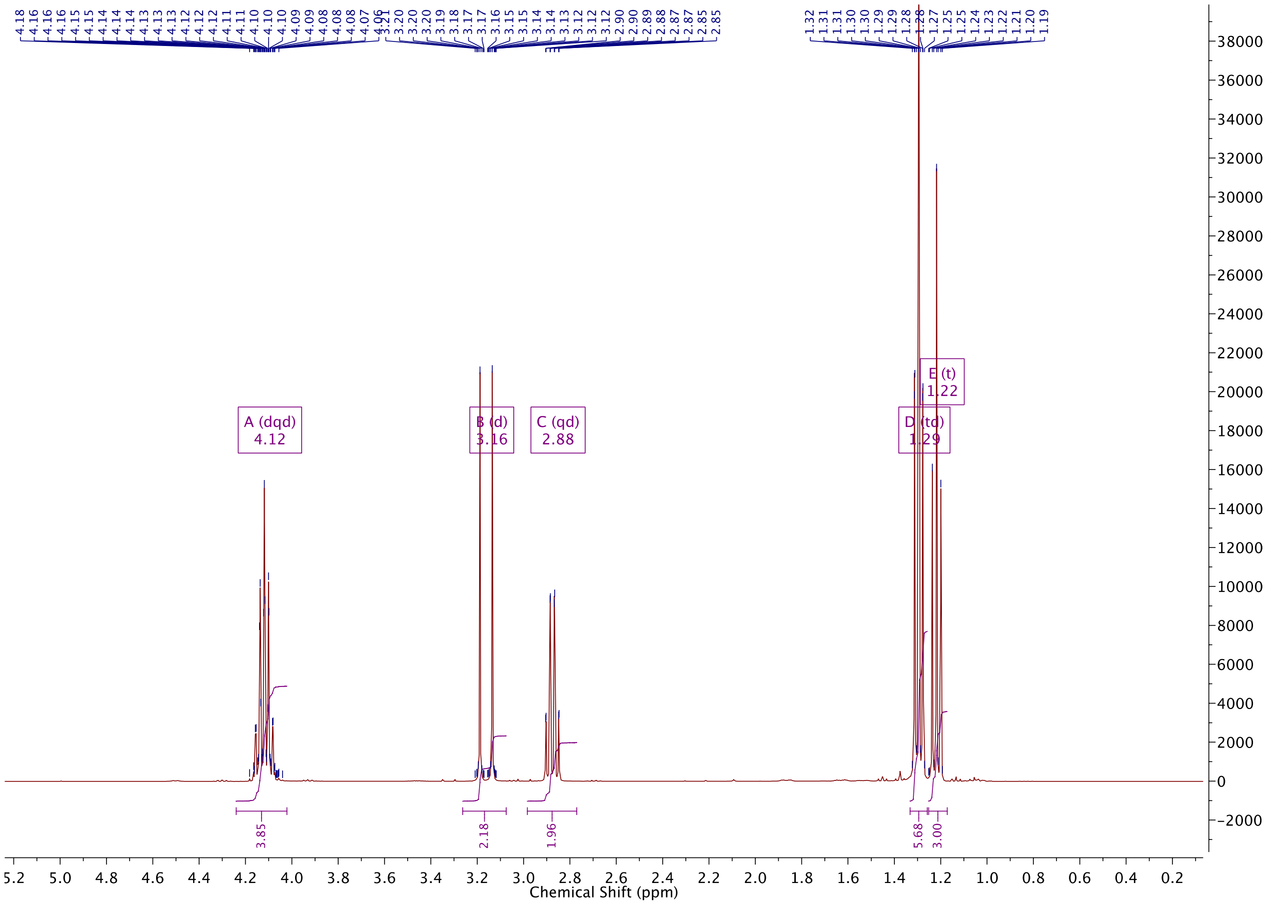
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 190.2 (d, *J* = 6.9 Hz), 62.8, 62.7, 42.8(d, J = 131.1 Hz), 24.2, 16.3, 16.2, 14.4.

$^{31}$P NMR (162 MHz, Chloroform-*d*) $\delta_P$/ppm 18.2.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 2360,1738,1680,1380,1257,1019,966

HRMS (ESI) m/z calc. for $C_8H_{18}O_4P^{32}S$, $[M+H]^+$: 241.0658, found: 241.0657

This data was concordant with literature values[2].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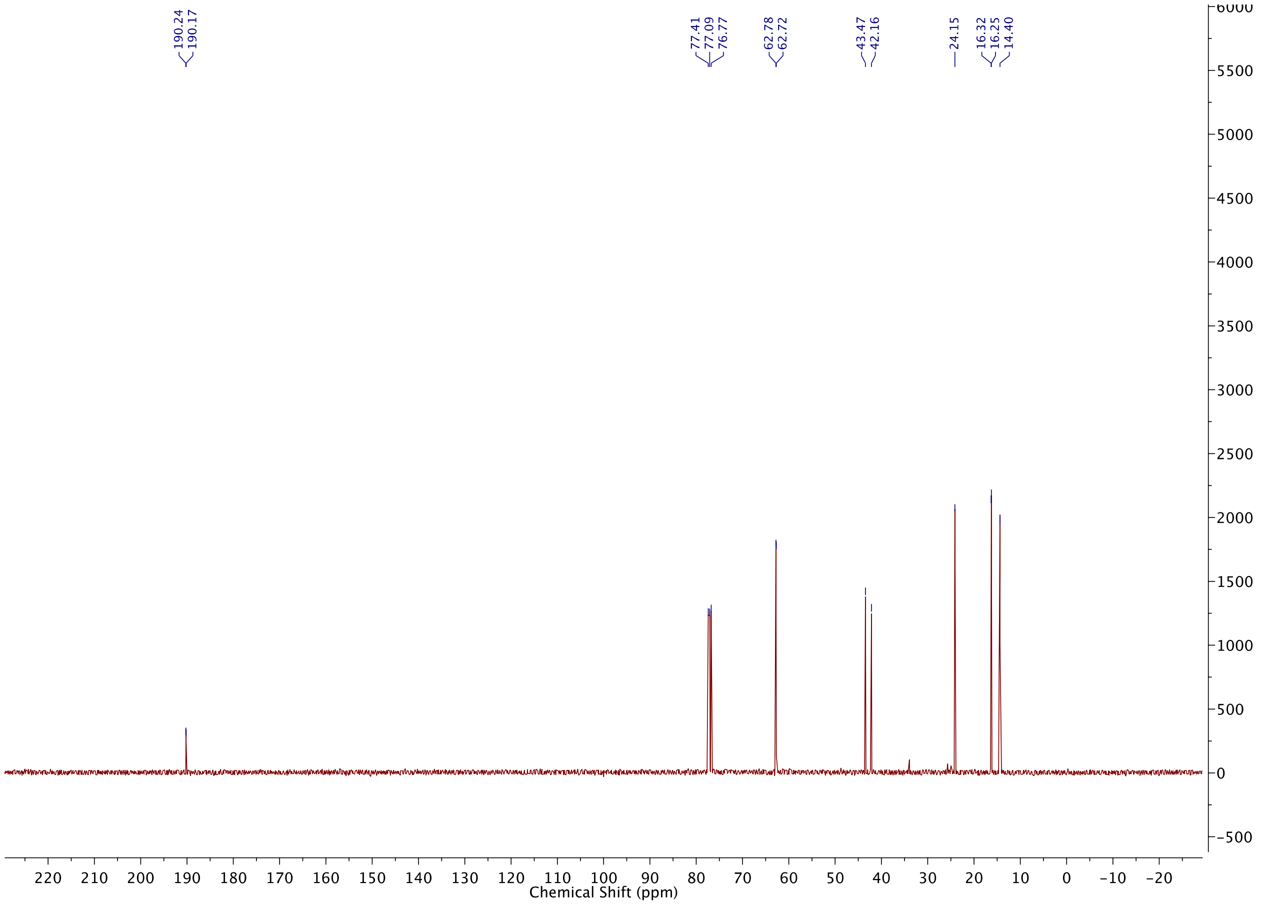
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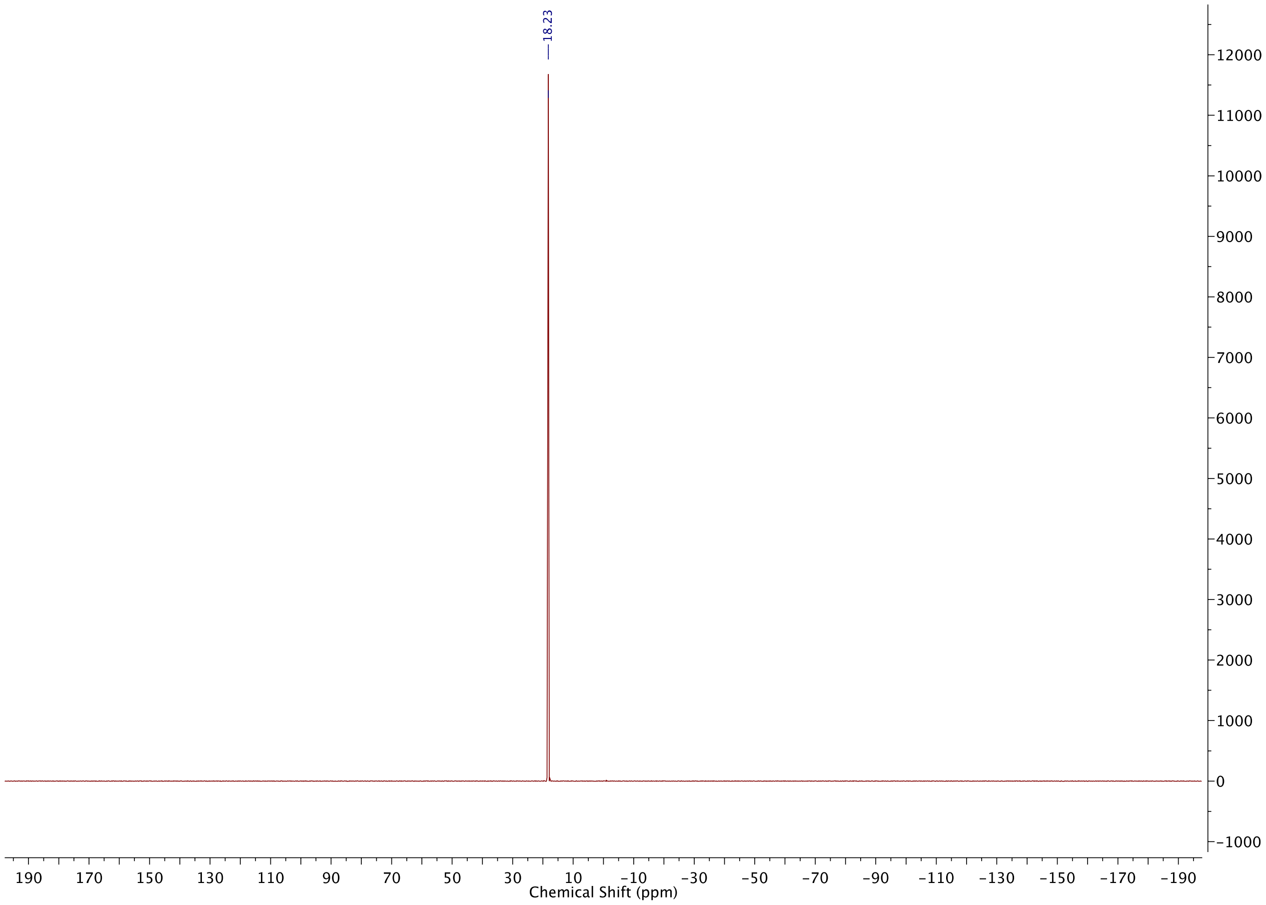
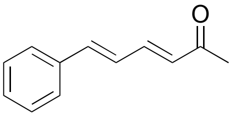


## (3E, 5E)-6-phenylhexa-3, 5-dien-2-one (2a)



*n*-BuLi (9.6 ml, 1.5 eq in hexane, 15 mmol) was added to a stirring solution of Diethyl (2-oxopropyl)phosphonate (2.92 ml, 1.5 eq, 15 mmol) in 30 ml THF at 0°C under argon. The mixture was stirred for another 20 min. A solution of cinnamaldehyde (1.25 ml, 1.0 eq., 10 mmol ) in THF was added dropwise. The mixture was slowly warmed to room temperature and was continued overnight. The mixture was quenched with aqueous $NH_4Cl$ (sat.). The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$ three times. The combined organic materials were dried ($MgSO_4$), filtered, concentrated, and further purified by flash column chromatography (pentane: $Et_2O$; 90:10; $SiO_2$) to afford the desired product (1.32 g, 7.7 mmol, 77%).

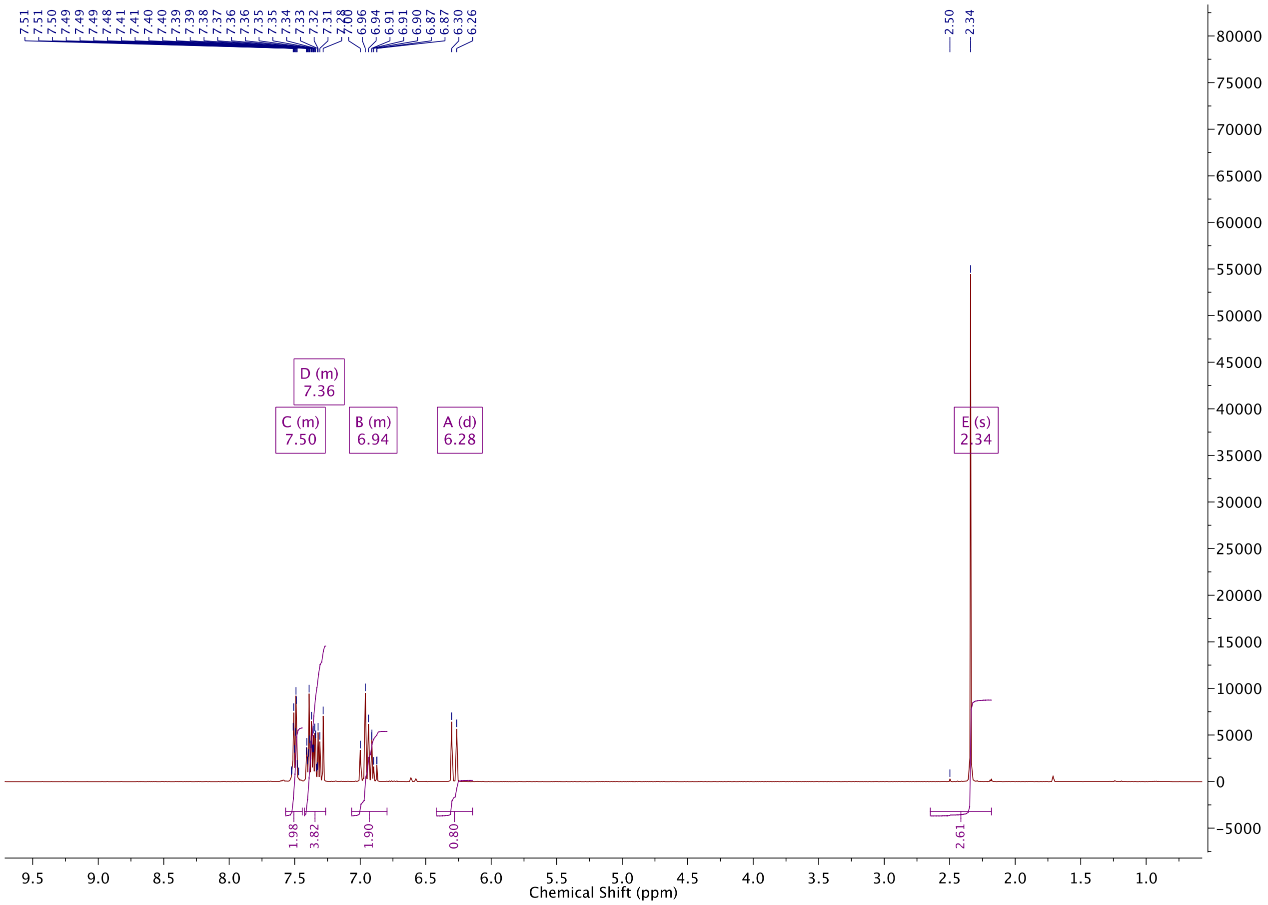
$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.57 – 7.44 (m, 2H, Ar-*H*), 7.43 – 7.26 (m, 4H, Ar-*H,* C*H*), 7.07 – 6.80 (m, 2H, C*H*), 6.28 (d, *J* = 15.5 Hz, 1H, C*H*), 2.34 (s, 3H, C$H_3$).

$^{13}C$ NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 198.4, 143.4, 141.3, 136.0, 130.5, 129.2, 128.9 (2C), 127.3 (2C), 126.7, 27.4.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1668, 1652, 1586, 1258, 990

HRMS (ESI) m/z calc. for $C_{12}H_{12}O^{35}Cl$ $[M+H]^+$: 173.0961, found: 173.0962

This data was concordant with literature values.[7]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D (m)
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C (m)
7.50
B (m)
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A (d)
6.28
E (s)
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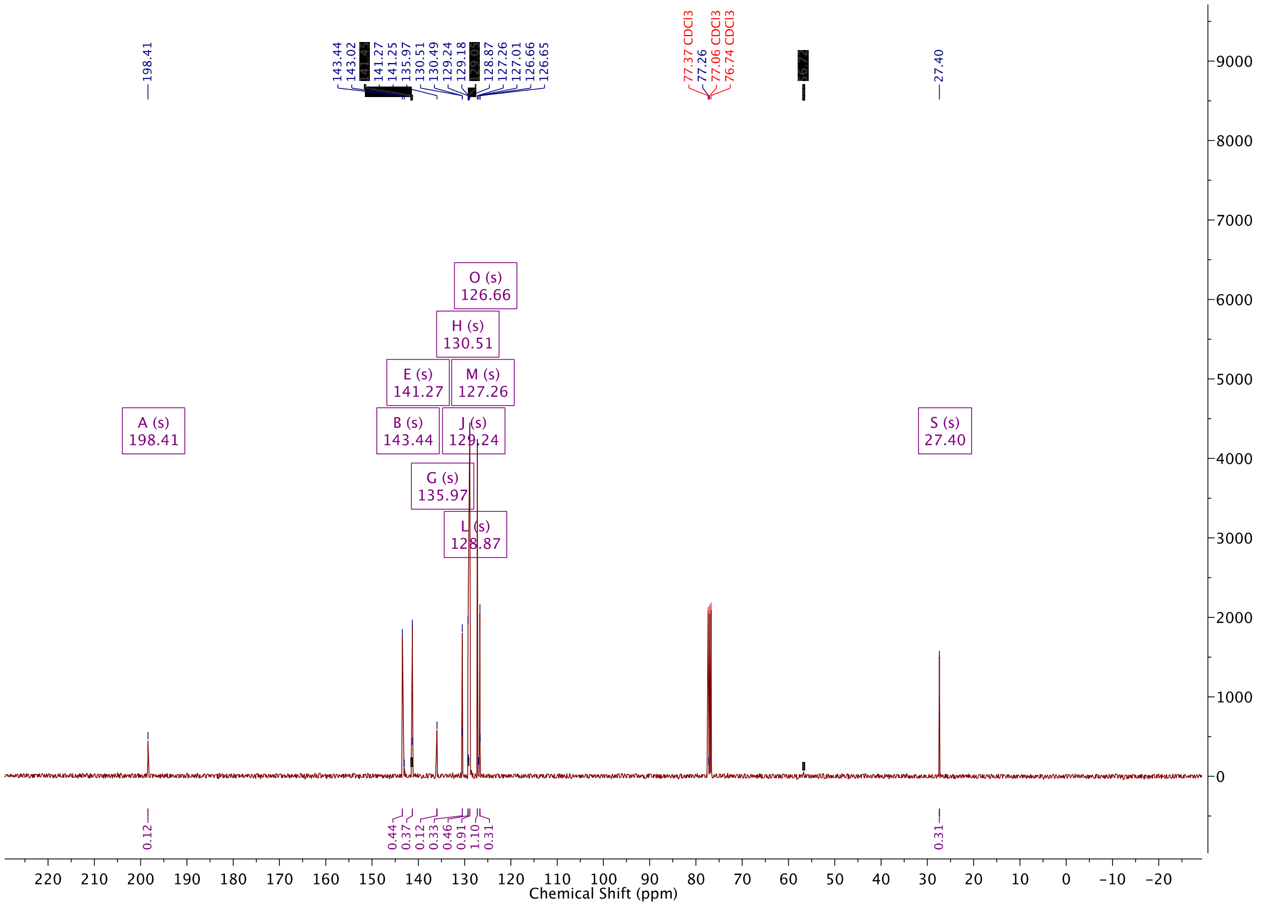
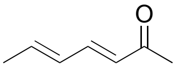
1.0
Chemical Shift (ppm)


198.41
143.44
143.02
[redacted]
141.27
141.25
135.97
130.51
130.49
129.24
129.18
[redacted]
128.87
127.26
127.01
126.66
126.65
77.37 CDCl3
77.26
77.06 CDCl3
76.74 CDCl3
[redacted]
27.40
O (s)
126.66
H (s)
130.51
E (s)
141.27
M (s)
127.26
A (s)
198.41
B (s)
143.44
J (s)
129.24
S (s)
27.40
G (s)
135.97
L (s)
128.87
0.12
0.44
0.37
0.12
0.33
0.46
0.91
1.10
0.31
0.31
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
Chemical Shift (ppm)

## (3E, 5E)-hepta-3, 5-dien-2-one (2b)



*n*-BuLi (4.8 ml, 1.5 eq in hexane, 7.5 mmol) was added to a stirring solution of Diethyl (2-oxopropyl)phosphonate (1.46 ml, 1.5 eq, 7.5 mmol) in 20 ml THF at 0°C under argon. The mixture was stirred for another 20 min. A solution of (*E*)-but-2-enal (0.53 g, 1.0 eq., 5.0 mmol ) in THF was added dropwise. The mixture was slowly warmed to room temperature and was continued overnight. The mixture was quenched with aqueous $NH_4Cl$ (sat.). The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$ three times. The combined organic materials were dried ($MgSO_4$), filtered, concentrated, and further purified by flash column chromatography (pentane: $Et_2O$; 90:10; $SiO_2$) to afford the desired product (0.35 g, 3.3 mmol, 65%).

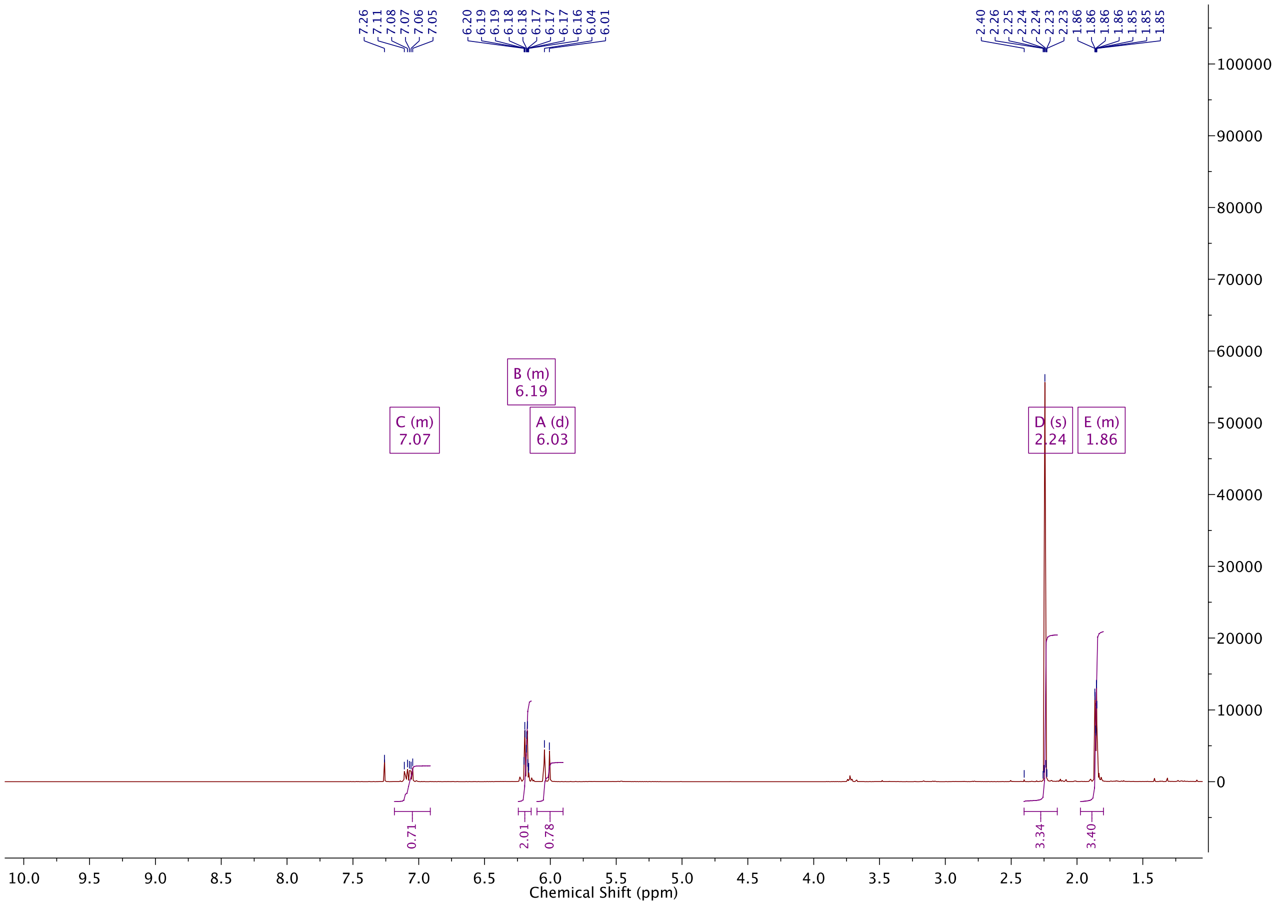
$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.18 – 6.91 (m, 1H, C*H*), 6.24 – 6.15 (m, 2H, C*H*), 6.03 (d, J = 15.1 Hz, 1H, C*H*), 2.24 (s, 3H, COC$H_3$), 1.97 – 1.80 (m, 3H, C$H_3$).

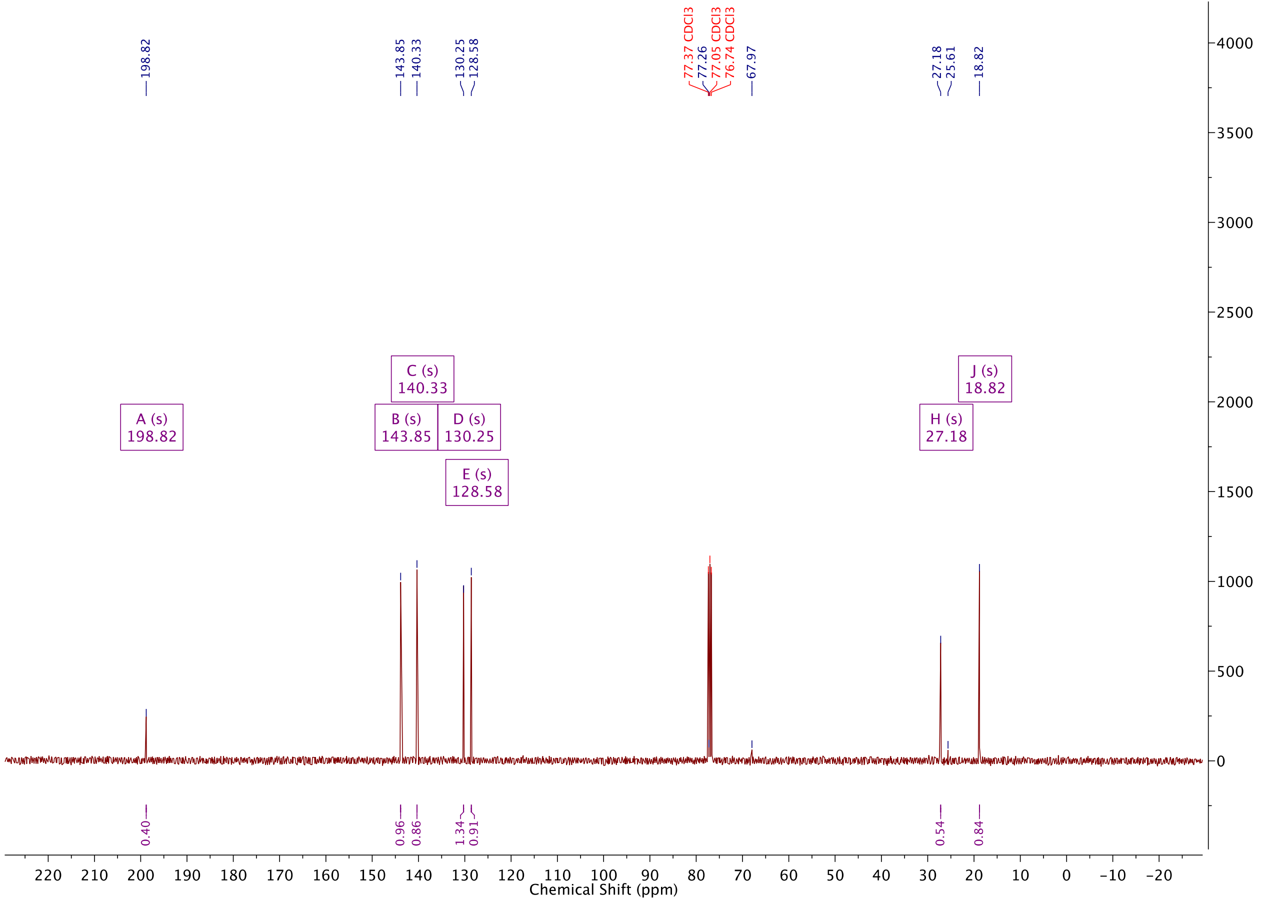
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 198.8, 143.9, 140.3, 130.3, 128.6, 27.2, 18.8.

IR ($\nu_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 2359, 1681, 1558,1362, 1256, 981

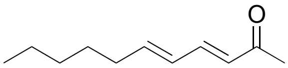
HRMS (ESI) m/z calc. for $C_7H_{11}O$ $[M+H]^+$: 111.0804, found: 111.0803

This data was concordant with literature values.[8]


7.26
7.11
7.08
7.07
7.06
7.05
6.20
6.19
6.19
6.18
6.18
6.17
6.17
6.17
6.16
6.04
6.01
2.40
2.26
2.25
2.24
2.24
2.23
2.23
1.86
1.86
1.86
1.86
1.85
1.85
1.85
B (m)
6.19
C (m)
7.07
A (d)
6.03
D (s)
2.24
E (m)
1.86
0.71
2.01
0.78
3.34
3.40
Chemical Shift (ppm)
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5
100000 90000 80000 70000 60000 50000 40000 30000 20000 10000 0


198.82
143.85
140.33
130.25
128.58
77.37 CDCl3
77.26
77.05 CDCl3
76.74 CDCl3
67.97
27.18
25.61
18.82
A (s)
198.82
C (s)
140.33
B (s)
143.85
D (s)
130.25
E (s)
128.58
J (s)
18.82
H (s)
27.18
0.40
0.96
0.86
1.34
0.91
0.54
0.84
Chemical Shift (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
4000 3500 3000 2500 2000 1500 1000 500 0

## (3E, 5E)-undeca-3, 5-dien-2-one (2c)



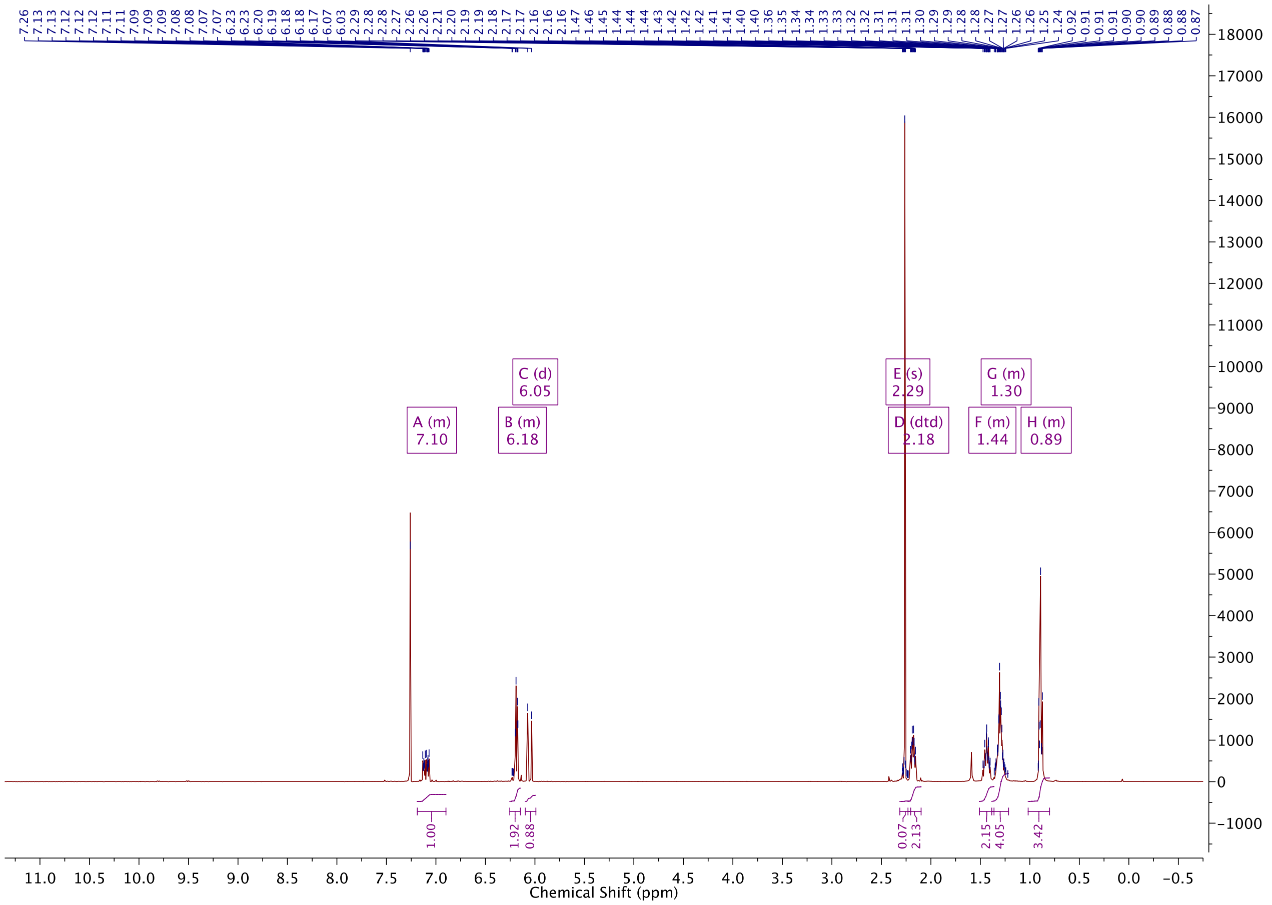
*n*-BuLi (4.8 ml, 1.5 eq in hexane, 7.5 mmol) was added to a stirring solution of Diethyl (2-oxopropyl)phosphonate (1.46 ml, 1.5 eq, 7.5 mmol) in 20 ml THF at 0°C under argon. The mixture was stirred for another 20 min. A solution of (*E*)-oct-2-enal (0.63 g, 1.0 eq., 5.0 mmol ) in 20 ml THF was added dropwise. The mixture was slowly warmed to room temperature and was continued overnight. The mixture was quenched with aqueous $NH_4Cl$ (sat.). The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$ three times. The combined organic materials were dried ($MgSO_4$), filtered, concentrated, and further purified by flash column chromatography (pentane: $Et_2O$; 90:10; $SiO_2$) to afford the desired product (0.50 g, 3.0 mmol, 60%).

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.19 – 6.90 (m, 1H, C*H*CO), 6.25 – 6.15 (m, 2H, C*H*), 6.05 (d, J = 15.6 Hz, 1H, C*H*), 2.26 (s, 3H, COC$H_3$), 2.18 (dtd, J = 7.6 Hz, 5.3 Hz, 2.6 Hz, 2H, C$H_2$CH), 1.51 – 1.36 (m, 2H, C$H_2$), 1.39 – 1.22 (m, 4H, C$H_2$), 1.02 – 0.80 (m, 3H, C$H_3$).

$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 198.8, 145.9, 144.1, 128.8 (2C), 33.1, 31.4, 28.4, 27.2, 22.5, 14.0.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2958, 2929, 1668, 1632, 1253, 997

HRMS (ESI) m/z calc. for $C_{11}H_{19}O$ $[M+H]^+$: 167.1430, found: 167.1431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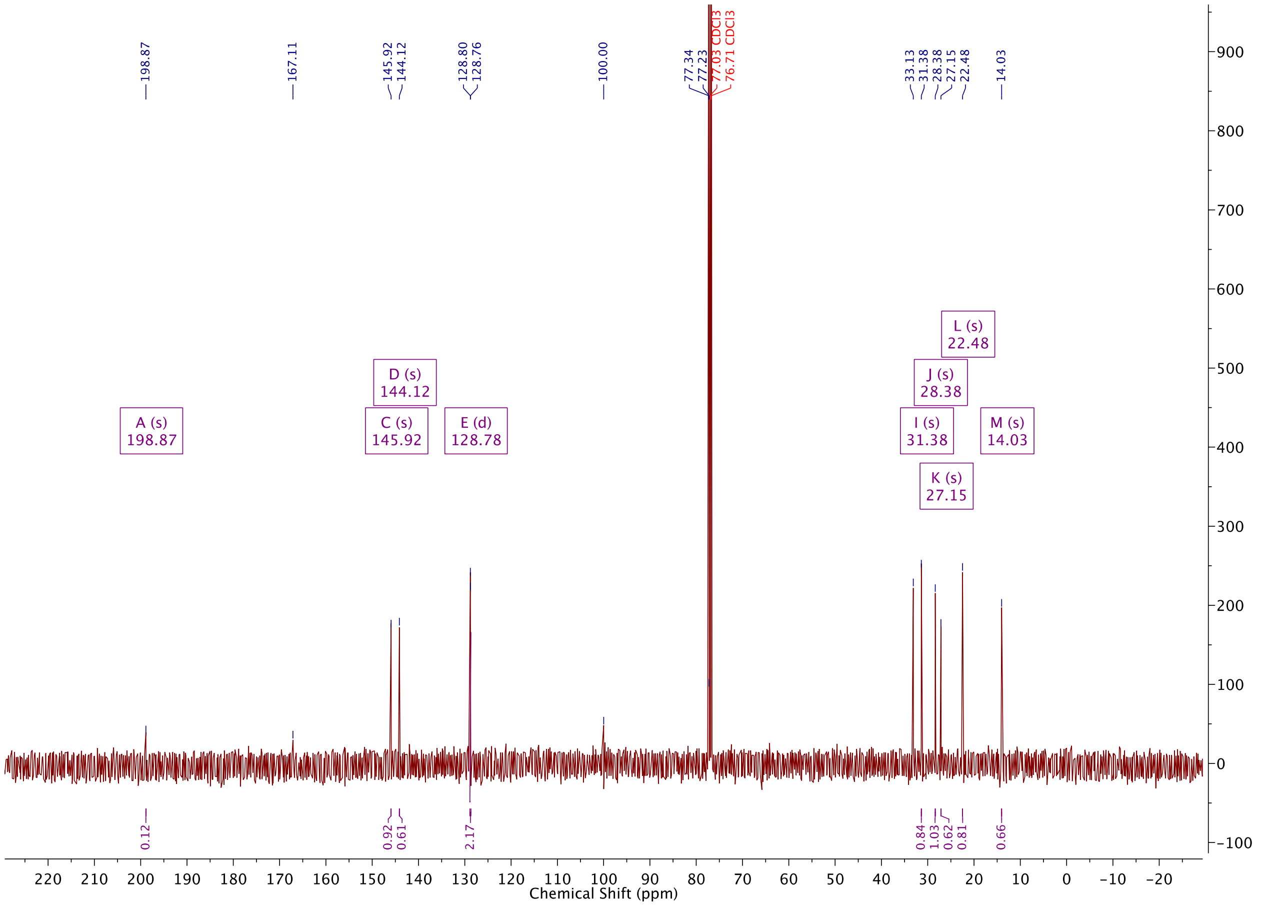
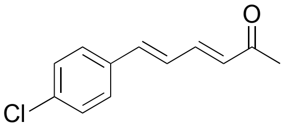
A (m)
7.10
B (m)
6.18
C (d)
6.05
E (s)
2.29
D (dtd)
2.18
G (m)
1.30
F (m)
1.44
H (m)
0.89
1.00
1.92
0.88
0.07
2.13
2.15
4.05
3.42
Chemical Shift (ppm)
11.0, 10.5, 10.0, 9.5, 9.0, 8.5, 8.0, 7.5, 7.0, 6.5, 6.0, 5.5, 5.0, 4.5, 4.0, 3.5, 3.0, 2.5, 2.0, 1.5, 1.0, 0.5, 0.0, -0.5
18000, 17000, 16000, 15000, 14000, 13000, 12000, 11000, 10000, 9000, 8000, 7000, 6000, 5000, 4000, 3000, 2000, 1000, 0, -1000


198.87
167.11
145.92
144.12
128.80
128.76
100.00
77.34
77.23
77.03 CDCl3
76.71 CDCl3
33.13
31.38
28.38
27.15
22.48
14.03
A (s)
198.87
D (s)
144.12
C (s)
145.92
E (d)
128.78
L (s)
22.48
J (s)
28.38
I (s)
31.38
M (s)
14.03
K (s)
27.15
0.12
0.92
0.61
2.17
0.84
1.03
0.62
0.81
0.66
Chemical Shift (ppm)
220, 210, 200, 190, 180, 170, 160, 150, 140, 130, 120, 110, 100, 90, 80, 70, 60, 50, 40, 30, 20, 10, 0, -10, -20
900, 800, 700, 600, 500, 400, 300, 200, 100, 0, -100

## (3E, 5E)-6-(4-chlorophenyl) hexa-3, 5-dien-2-one (2f)



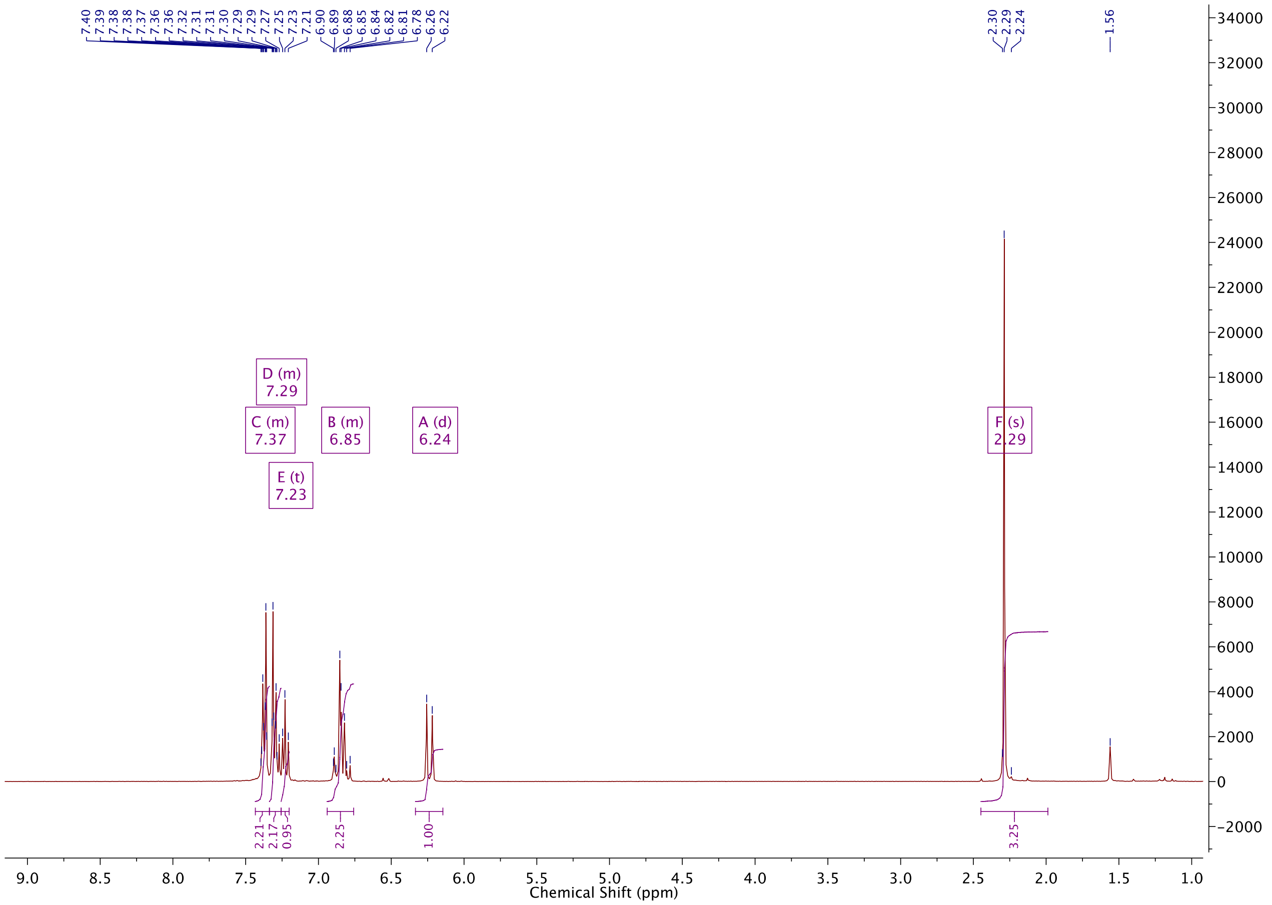
*n*-BuLi (4.8 ml, 1.5 eq in hexane, 7.5 mmol) was added to a stirring solution of Diethyl (2-oxopropyl)phosphonate (1.45 ml, 1.5 eq, 7.5 mmol) in 20 ml THF at 0°C under argon. The mixture was stirred for another 20 min. A solution of (E)-3-(4-chlorophenyl) acrylaldehyde (0.83 g, 1.0 eq., 5.0 mmol ) in THF was added dropwise. The mixture was slowly warmed to room temperature and was continued overnight. The mixture was quenched with aqueous $NH_4Cl$ (sat.). The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$ three times. The combined organic materials were dried ($MgSO_4$), filtered, concentrated, and further purified by flash column chromatography (pentane: $Et_2O$; 7:3; $SiO_2$) to afford the desired product (0.37 g, 1.8 mmol, 36%).

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.43 – 7.34 (m, 2H, Ar-*H*), 7.34 – 7.26 (m, 2H, Ar-*H*), 7.23 (t, *J* = 7.7 Hz, 1H, C*H*), 6.94 – 6.76 (m, 2H, C*H*), 6.24 (d, *J* = 15.5 Hz, 1H, C*H*), 2.29 (s, 3H, $CH_3$).

$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 198.4, 143.0, 139.7, 135.0, 134.5, 130.9, 129.1 (2C), 128.4 (2C), 127.2, 27.5.

IR ($\nu_{max}$/cm$^{-1}$, $CHCl_3$) 2980, 1650, 1616, 1588, 1360, 1251, 996

HRMS (ESI) m/z calc. for $C_{12}H_{12}O^{35}Cl$ $[M+H]^+$: 207.0571, found: 207.0572


7.40
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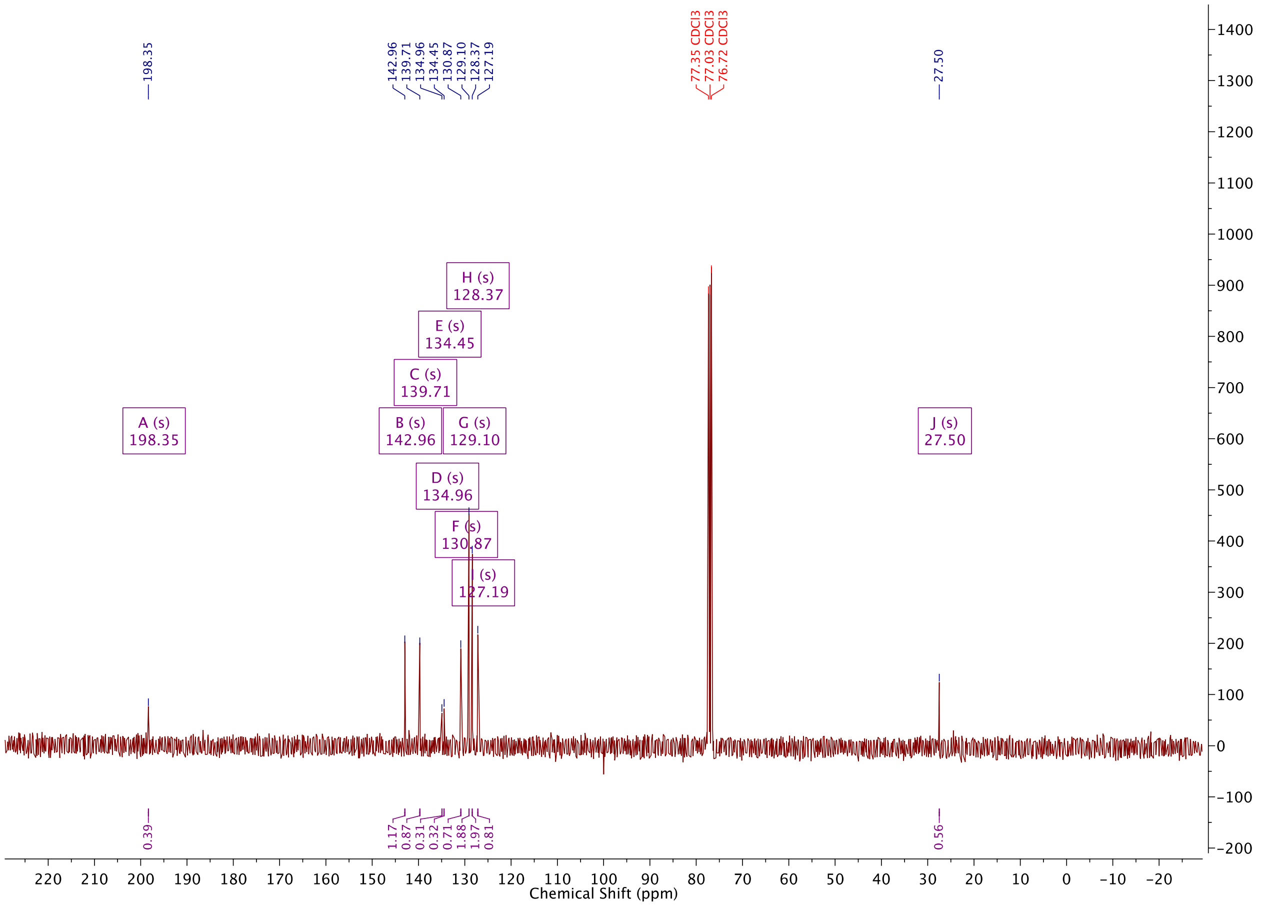
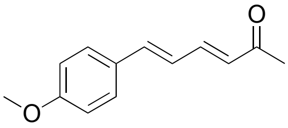
7.38
7.37
7.37
7.36
7.36
7.32
7.31
7.31
7.30
7.29
7.29
7.27
7.25
7.23
7.21
6.90
6.89
6.88
6.85
6.84
6.82
6.81
6.78
6.26
6.22
2.30
2.29
2.24
1.56
D (m)
7.29
C (m)
7.37
B (m)
6.85
A (d)
6.24
E (t)
7.23
F (s)
2.29
2.21
2.17
0.95
2.25
1.00
3.25
34000
32000
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


198.35
142.96
139.71
134.96
134.45
130.87
129.10
128.37
127.19
77.35 CDCl3
77.03 CDCl3
76.72 CDCl3
27.50
H (s)
128.37
E (s)
134.45
C (s)
139.71
A (s)
198.35
B (s)
142.96
G (s)
129.10
J (s)
27.50
D (s)
134.96
F (s)
130.87
(s)
127.19
0.39
1.17
0.87
0.31
0.32
0.71
1.88
1.97
0.81
0.56
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
-200
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
Chemical Shift (ppm)

## (3E, 5E)-6-(4-methoxyphenyl) hexa-3, 5-dien-2-one (2g)



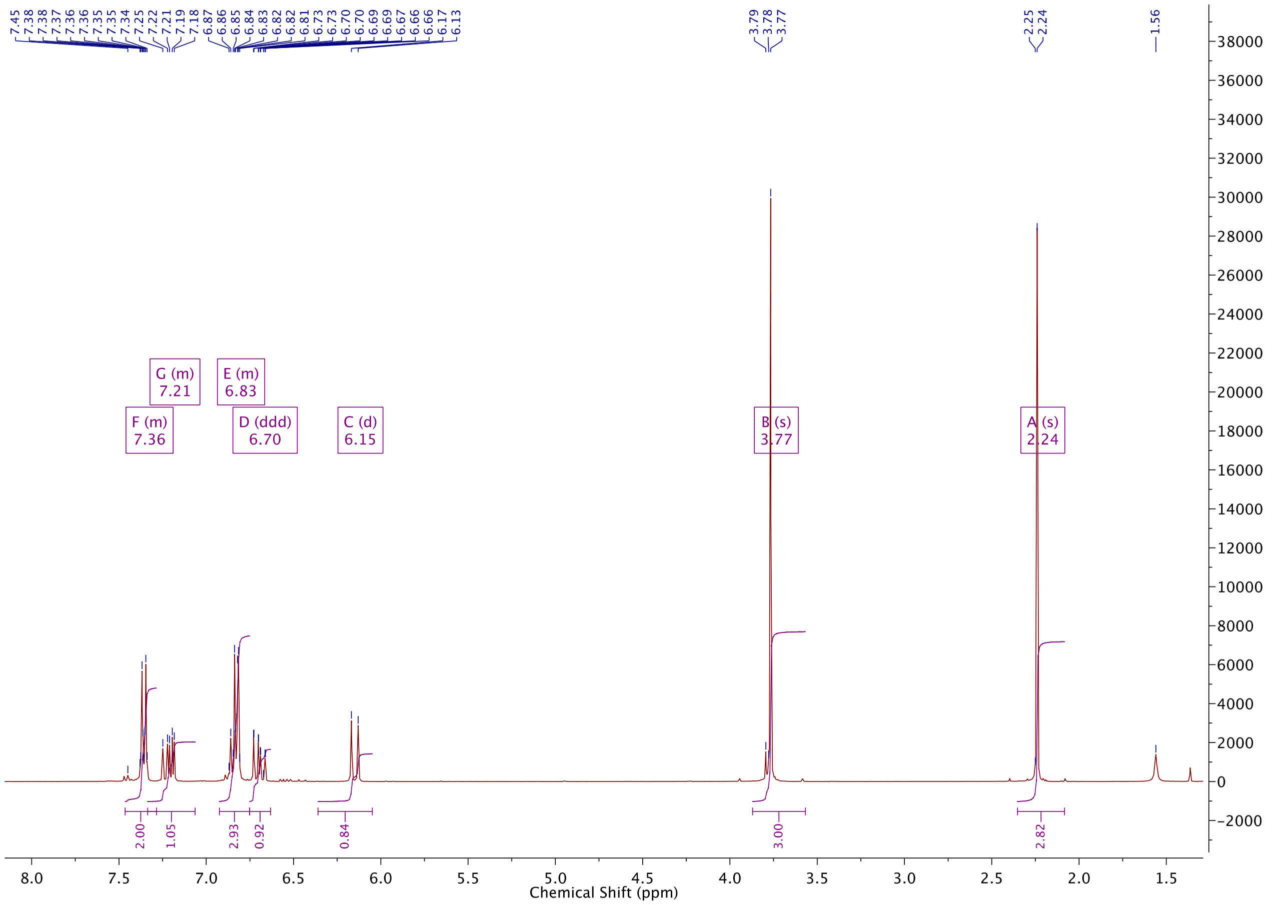
*n*-BuLi (4.8 ml, 1.5 eq in hexane, 7.5 mmol) was added to a stirring solution of Diethyl (2-oxopropyl)phosphonate (1.45 ml, 1.5 eq, 7.5 mmol) in 20 ml THF at 0°C under argon. The mixture was stirred for another 20 min. A solution of (*E*)-3-(4-methoxyphenyl) acrylaldehyde (0.81 g, 1.0 eq., 5.0 mmol ) in THF was added dropwise. The mixture was slowly warmed to room temperature and was continued overnight. The mixture was quenched with aqueous $NH_4Cl$ (sat.). The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$ three times. The combined organic materials were dried ($MgSO_4$), filtered, concentrated, and further purified by flash column chromatography (pentane: $Et_2O$; 1:1; $SiO_2$) to afford the desired product (0.32 g, 1.6 mmol, 32%).

$^1H$ NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.46 – 7.29 (m, 2H, Ar-*H*), 7.33 – 7.06 (m, 1H, C*H*), 6.92 – 6.75 (m, 3H, C*H,* Ar-*H*), 6.70 (m, 1H, C*H*), 6.15 (d, *J* = 15.5 Hz, 1H, C*H*), 3.77 (s, 3H, $OCH_3$), 2.24 (s, 3H, $CH_3$).

$^{13}C$ NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 198.5, 160.6, 144.1, 141.1, 129.4 (3C), 128.8, 124.5, 114.3 (2C), 55.4, 27.3.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1653, 1594, 1511, 1251, 990

HRMS (ESI) m/z calc. for $C_{13}H_{15}O_2$ $[M+H]^+$: 203.1067 found: 203.1066



7.45
7.38
7.38
7.37
7.36
7.36
7.35
7.35
7.34
7.25
7.22
7.21
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7.18
6.87
6.86
6.85
6.84
6.83
6.82
6.82
6.81
6.73
6.73
6.70
6.70
6.69
6.69
6.67
6.66
6.66
6.17
6.13
3.79
3.78
3.77
2.25
2.24
1.56
G (m) 7.21
E (m) 6.83
F (m) 7.36
D (ddd) 6.70
C (d) 6.15
B (s) 3.77
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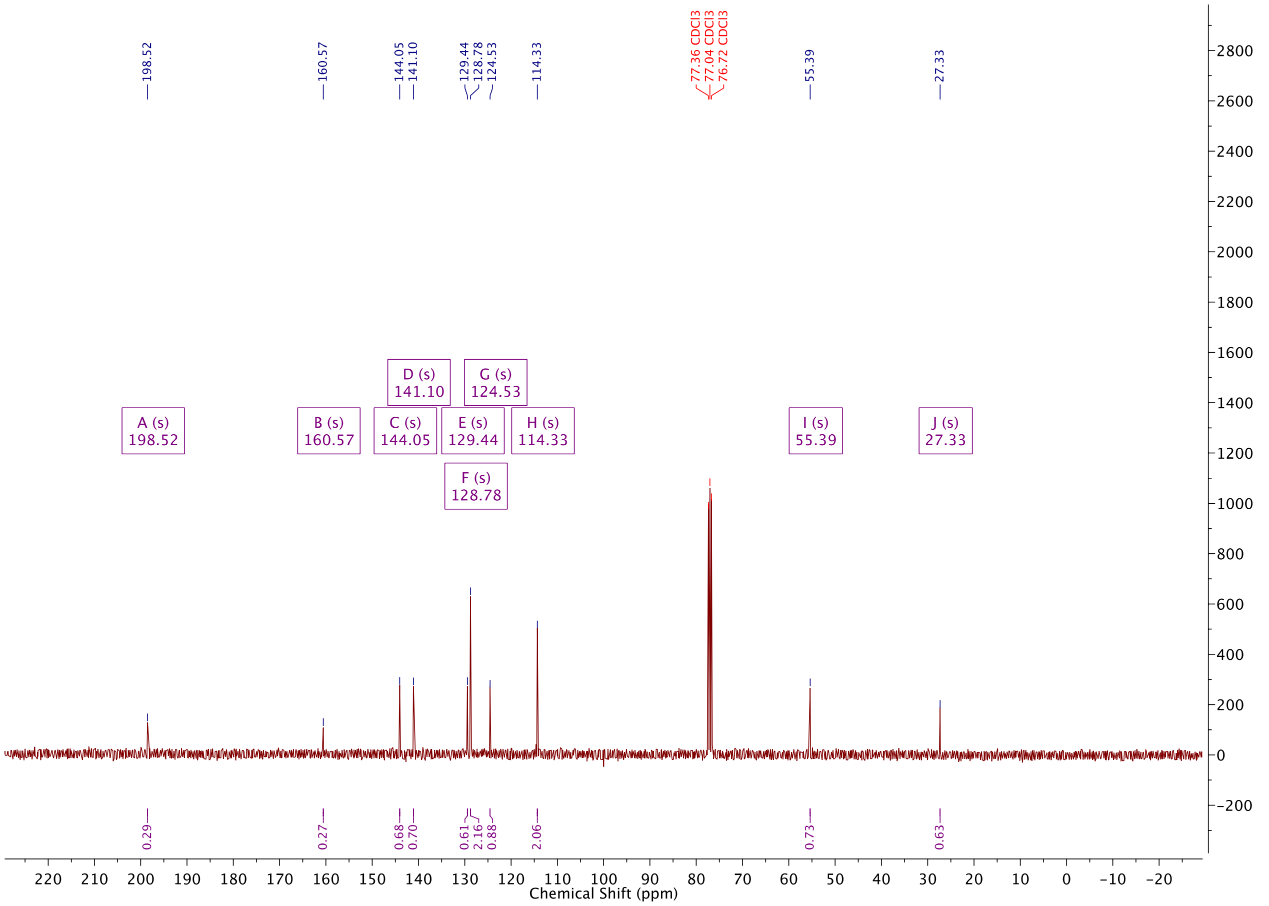
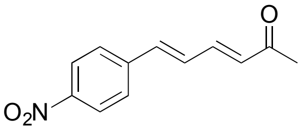
3.00
2.82
Chemical Shift (ppm)



198.52
160.57
144.05
141.10
129.44
128.78
124.53
114.33
77.36 CDCl3
77.04 CDCl3
76.72 CDCl3
55.39
27.33
D (s) 141.10
G (s) 124.53
A (s) 198.52
B (s) 160.57
C (s) 144.05
E (s) 129.44
H (s) 114.33
I (s) 55.39
J (s) 27.33
F (s) 128.78
0.29
0.27
0.68
0.70
0.61
2.16
0.88
2.06
0.73
0.63
Chemical Shift (ppm)

## (3E, 5E)-6-(4-nitrophenyl) hexa-3, 5-dien-2-one (2h)



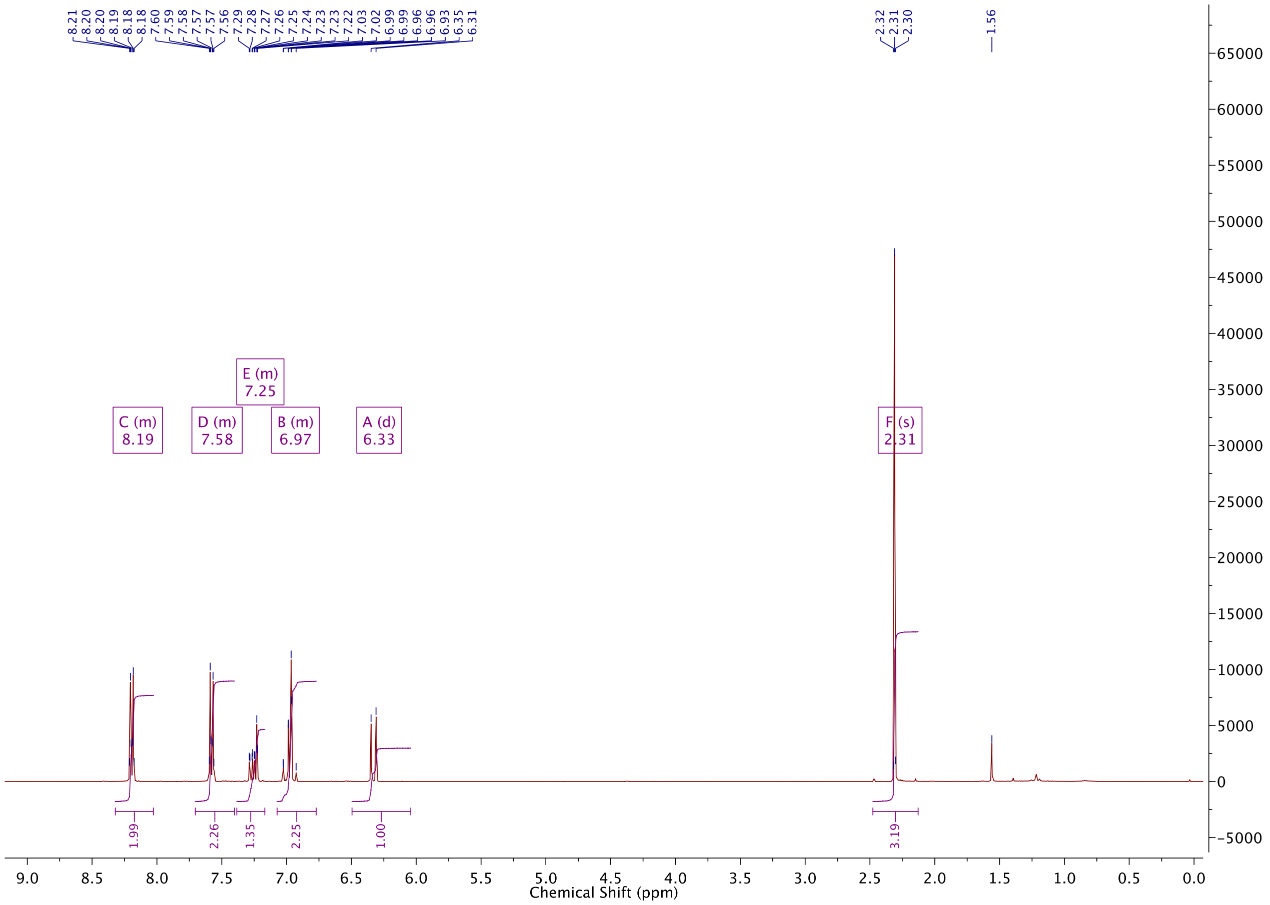
*n*-BuLi (4.8 ml, 1.5 eq in hexane, 7.5 mmol) was added to a stirring solution of Diethyl (2-oxopropyl)phosphonate (1.45 ml, 1.5 eq, 7.5 mmol) in 20 ml THF at 0°C under argon. The mixture was stirred for another 20 min. A solution of (*(E)-3-(*4-nitrophenyl) acrylaldehyde (0.89 g, 1.0 eq., 5.0 mmol ) in THF was added dropwise. The mixture was slowly warmed to room temperature and was continued overnight. The mixture was quenched with aqueous $NH_4Cl$ (sat.). The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$ three times. The combined organic materials were dried ($MgSO_4$), filtered, concentrated, and further purified by flash column chromatography (pentane: $Et_2O$; 60:40; $SiO_2$) to afford the desired product (0.31 g, 1.4 mmol, 28%).

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 8.32 – 8.03 (m, 2H, Ar-*H*), 7.70 – 7.40 (m, 2H, Ar-*H*), 7.38 – 7.17 (m, 1H, C*H*), 7.07 – 6.77 (m, 2H, C*H*), 6.33 (d, *J* = 15.5 Hz, 1H, C*H*), 2.31 (s, 3H, $CH_3$).

$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 198.1, 147.7, 142.1, 141.7, 138.0, 132.6, 130.8, 127.7 (2C), 124.2 (2C), 27.7.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1683, 1594, 1512, 1339, 997

HRMS (ESI) m/z calc. for $C_{12}H_{12}O_3N$ $[M+H]^+$: 218.0812, found: 218.0812


8.21
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7.56
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7.28
7.27
7.26
7.25
7.24
7.23
7.23
7.22
7.03
7.02
6.99
6.99
6.96
6.96
6.93
6.35
6.31
2.32
2.31
2.30
1.56
E (m)
7.25
C (m)
8.19
D (m)
7.58
B (m)
6.97
A (d)
6.33
F (s)
2.31
1.99
2.26
1.35
2.25
1.00
3.19
65000
60000
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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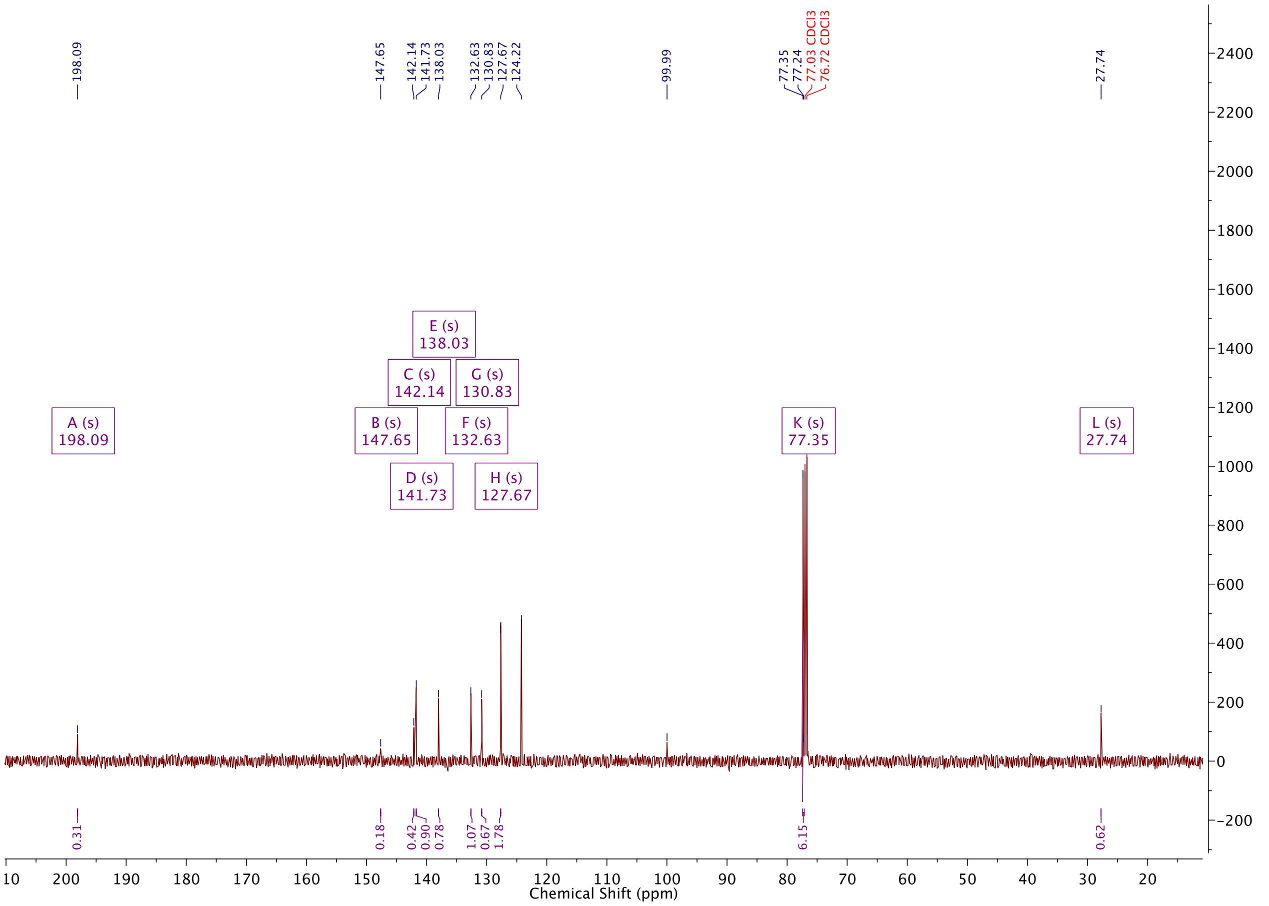
1.0
0.5
0.0
Chemical Shift (ppm)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141.73
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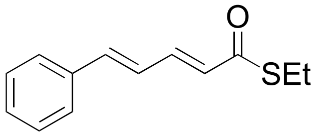
132.63
130.83
127.67
124.22
99.99
77.35
77.24
77.03 CDCl3
76.72 CDCl3
27.74
E (s)
138.03
C (s)
142.14
G (s)
130.83
A (s)
198.09
B (s)
147.65
F (s)
132.63
K (s)
77.35
L (s)
27.74
D (s)
141.73
H (s)
127.67
0.31
0.18
0.42
0.90
0.78
1.07
0.67
1.78
6.15
0.62
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
Chemical Shift (ppm)

### *S*-ethyl (2*E*,4*E*)-5-phenylpenta-2,4-dienethioate (2j)



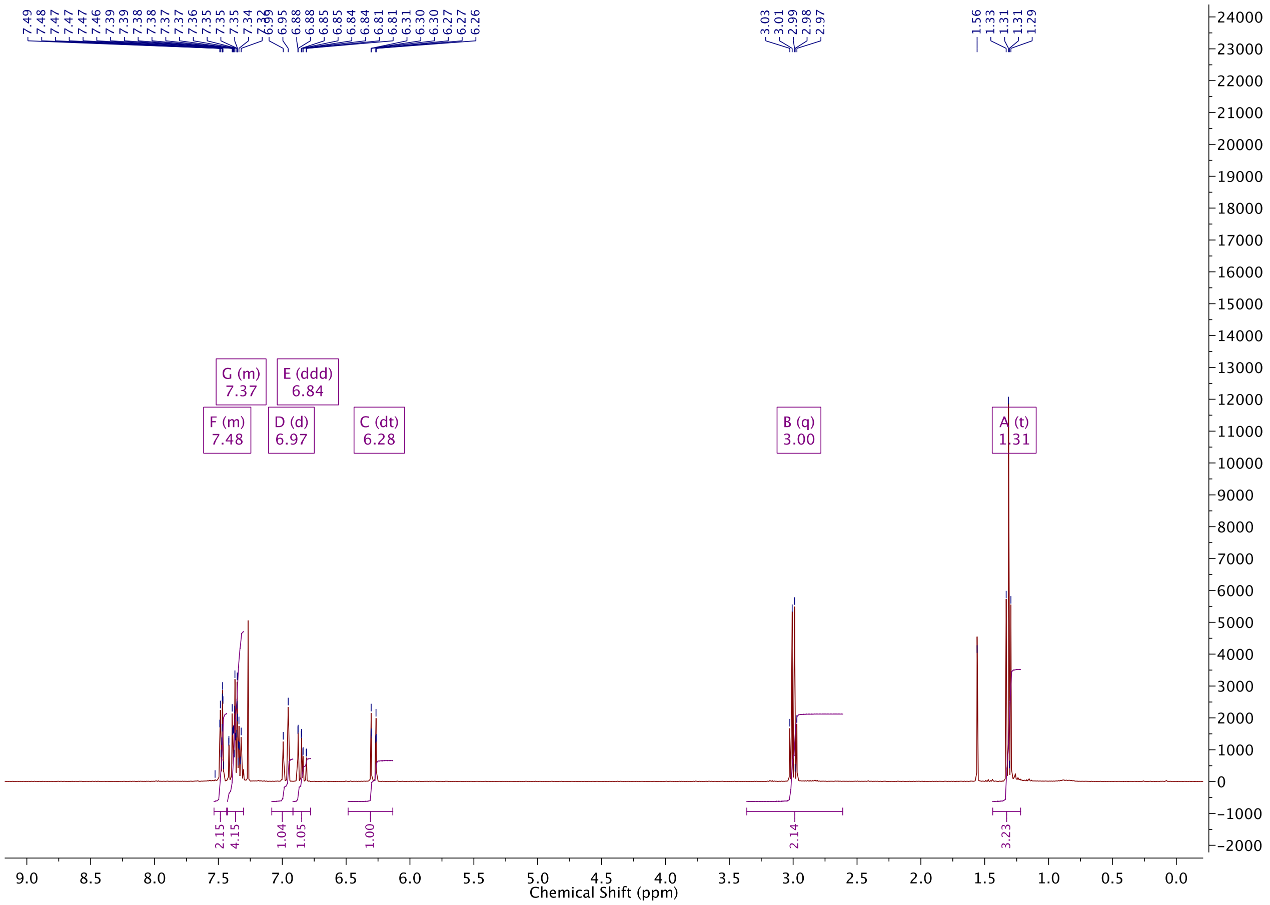
*n*-BuLi (4.8 ml, 1.0 eq in hexane, 7.5 mmol) was added to a stirring solution of S-ethyl 2-(diethoxyphosphoryl)ethanethioate (1.8 ml, 1.0 eq, 7.5 mmol) in 20 ml THF at 0°C under argon. The mixture was stirred for another 20 min. A solution of cinnamaldehyde (0.66 g, 1.0 eq., 5.0 mmol) in THF was added dropwise. The mixture was slowly warmed to room temperature and was continued overnight. The mixture was quenched with aqueous $NH_4Cl$ (sat.). The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$ three times. The combined organic materials were dried ($MgSO_4$), filtered, concentrated, and further purified by flash column chromatography (pentane: $Et_2O$; 97:3; $SiO_2$) to afford the desired product (0.67 g, 3.1 mmol, 61%).

$^1H$ NMR (400 MHz, Chloroform-d) $\delta_H$/ppm 7.53 – 7.43 (m, 2H, Ar-*H*), 7.43-7.30 (m, 4H, Ar-*H,* C*H*), 6.97 (d, J = 15.5 Hz, 1H, C*H*), 6.84 (ddd, J = 15.5 Hz, 10.8 Hz, 0.8 Hz, 1H, C*H*), 6.28 (dt, J = 15.2 Hz, 0.7 Hz, 1H, C*H*), 3.00 (q, J = 7.4 Hz, 2H, $SCH_2CH_3$), 1.31 (t, J = 7.4 Hz, 3H, $CH_3$).

$^{13}C$ NMR (101 MHz, Chloroform-d) $\delta_C$/ppm 189.9, 141.7, 140.3, 136.0, 129.2, 128.9 (2C), 128.3, 127.2 (2C), 126.1, 23.3, 14.9.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2976, 2361, 1653, 1594, 1022, 820

HRMS (ESI) m/z calc. for $C_{13}H_{15}O^{32}S$ $[M+H]^+$: 219.0838, found: 218.0840


7.49
7.48
7.47
7.47
7.46
7.39
7.39
7.38
7.38
7.37
7.37
7.36
7.35
7.35
7.34
7.32
6.99
6.95
6.88
6.88
6.85
6.85
6.84
6.84
6.81
6.81
6.31
6.30
6.27
6.27
6.26
3.03
3.01
2.99
2.98
2.97
1.56
1.33
1.31
1.31
1.29
G (m) 7.37
E (ddd) 6.84
F (m) 7.48
D (d) 6.97
C (dt) 6.28
B (q) 3.00
A (t) 1.31
2.15
4.15
1.04
1.05
1.00
2.14
3.23
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Chemical Shift (ppm)
24000
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
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11000
10000
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8000
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4000
3000
2000
1000
0
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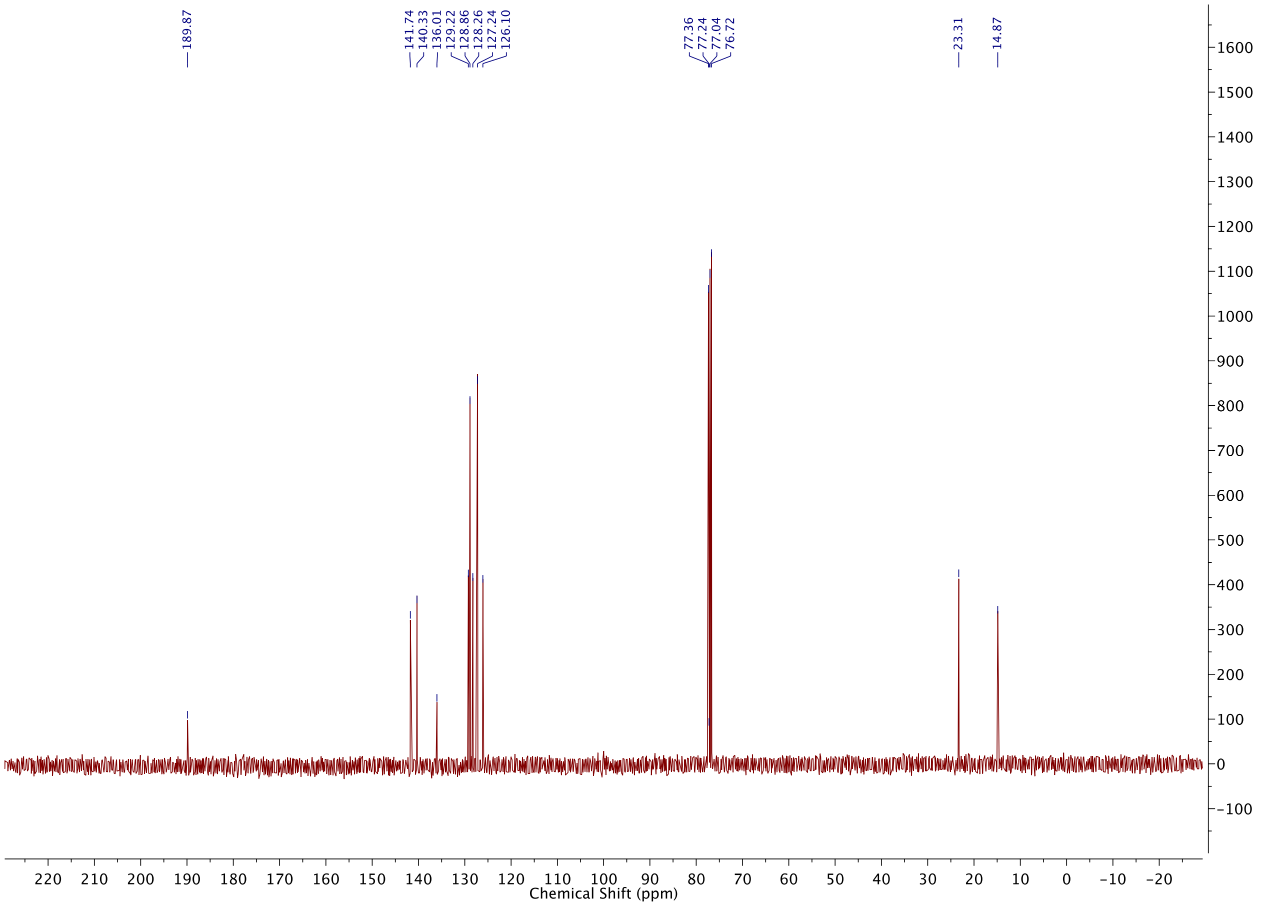
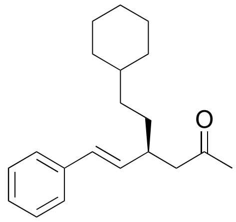
−2000


189.87
141.74
140.33
136.01
129.22
128.86
128.26
127.24
126.10
77.36
77.24
77.04
76.72
23.31
14.87
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
Chemical Shift (ppm)
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
−100

## (+)-(*S*, E)-4-(2-cyclohexylethyl)-6-phenylhex-5-en-2-one (3a)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.
To a second, flame dried, round bottom flask, containing a stirred solution of vinylcyclohexane (55 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.
The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-6-phenylhexa-3, 5-dien-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (40 mg, 14 mmol, 70%).

HPLC analysis indicated an enantiomeric excess of 90 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1.0; λ = 254 nm; major enantiomer tR = 6.90 min; minor enantiomer, tR = 7.40 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.28 – 7.17 (m, 4H, Ar-*H*), 7.16 – 7.08 (m, 1H, Ar-*H*), 6.30 (d, *J* = 15.8 Hz, 1H, C*H*), 5.92 (dd, *J* = 15.9 Hz, 8.7 Hz, 1H, C*H*), 2.68 – 2.49 (m, 1H, C*H*$CH_2COCH_3$), 2.44 (d, *J* = 6.9 Hz, 2H, $CH_2COCH_3$), 2.05 (s, 3H, $COCH_3$), 1.72 – 1.46 (m, 5H, C*H*, 2 x $CH_2$), 1.45 – 1.21 (m, 2H, $CH_2$), 1.21 – 0.98 (m, 6H, 3 x $CH_2$), 0.88 – 0.70 (m, 2H, $CH_2$).

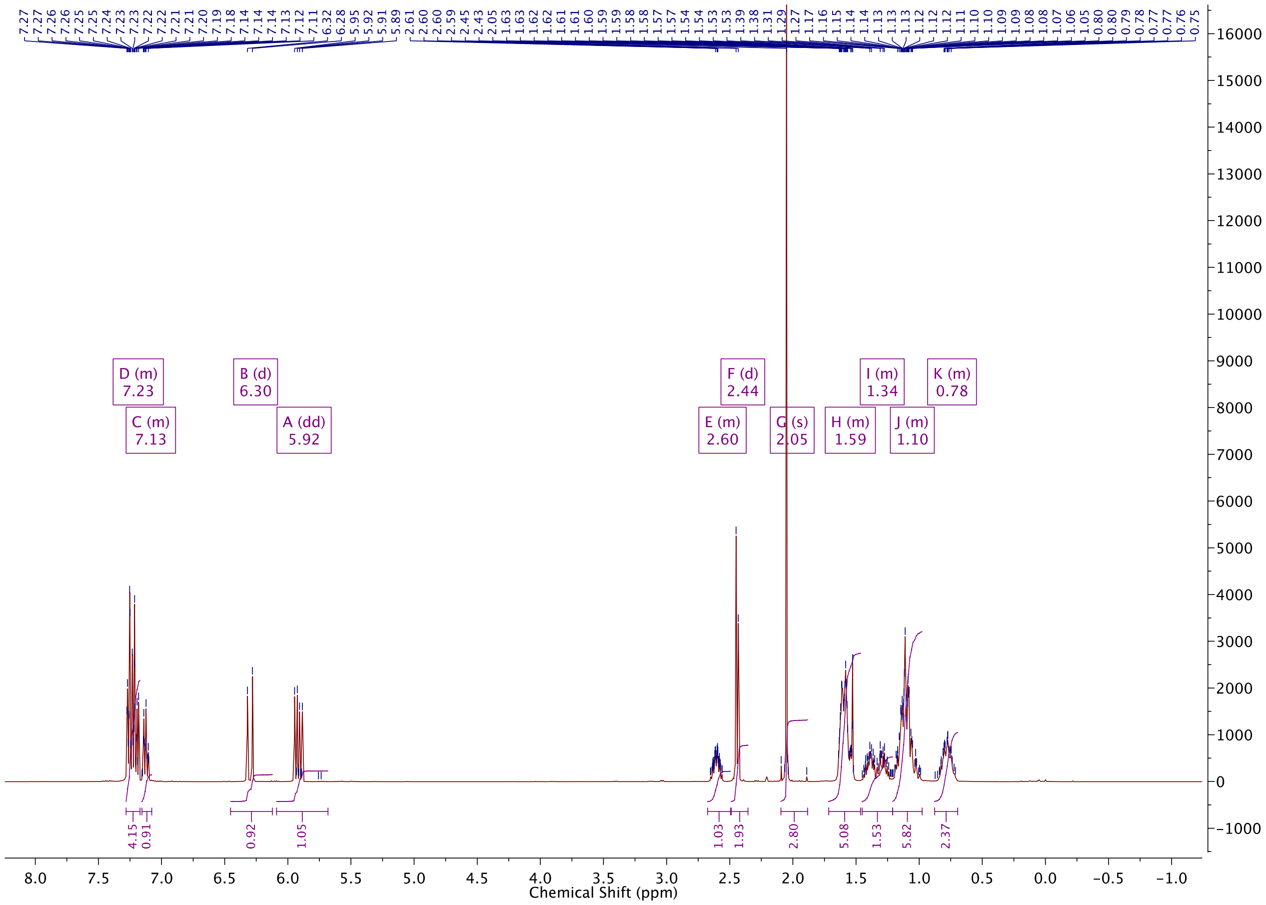
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 208.1, 137.4, 133.3, 130.2, 128.5 (2C), 127.1, 126.1 (2C), 49.6, 39.3, 37.8, 35.0, 33.5, 33.3, 32.4, 30.7, 26.7, 26.4, 26.4.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1716, 1382, 1154, 966

HRMS (ESI) m/z calc. for $C_{20}H_{29}O$ $[M+H]^+$: 285.2213 found: 285.2211

$[\alpha]^{20}_{589}$ = +10.0 ° (c 1.0, $CHCl_3$)

Absolute configuration was assigned by analogy to **3p**.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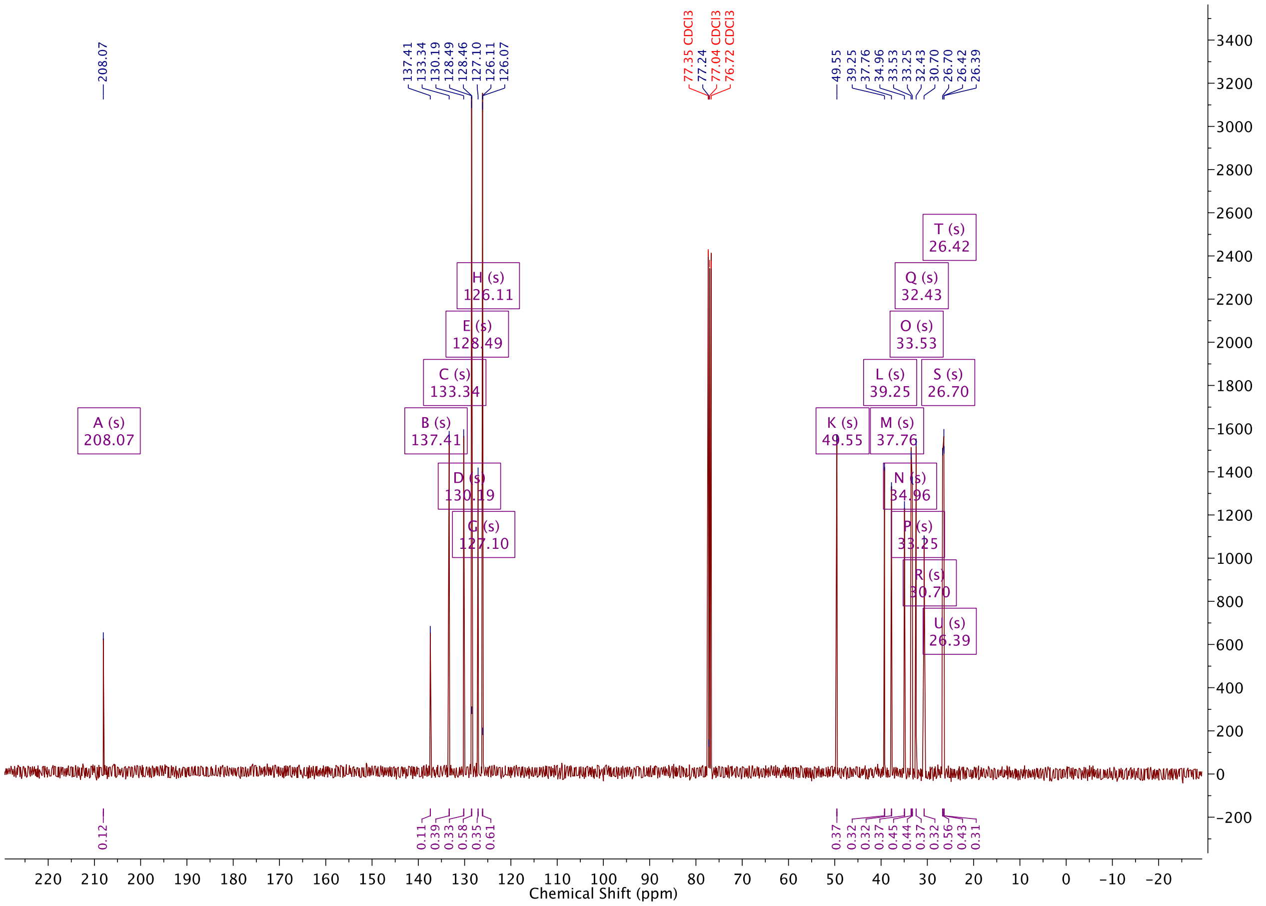
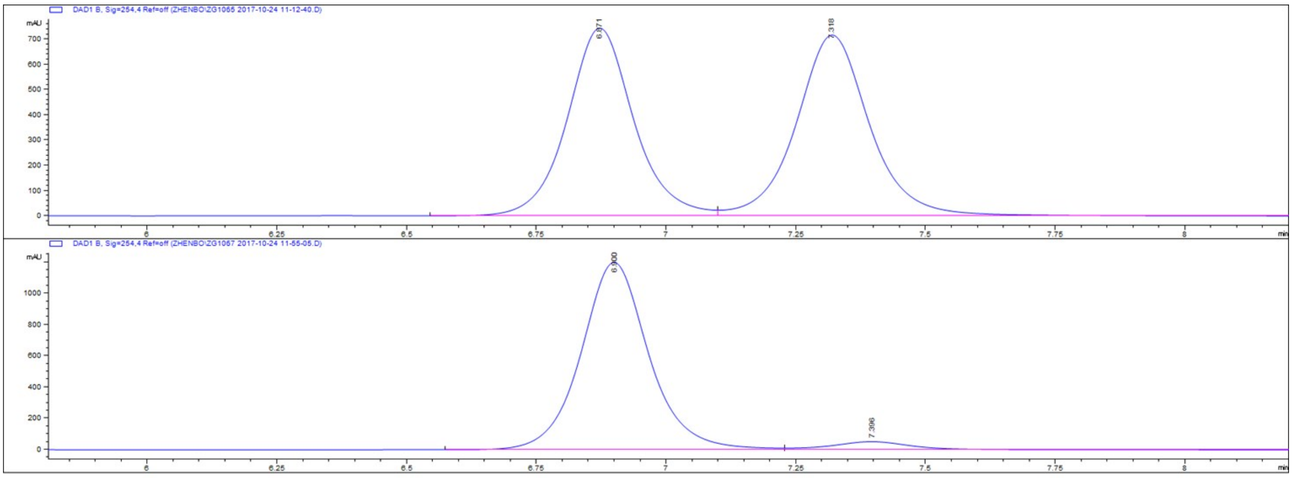
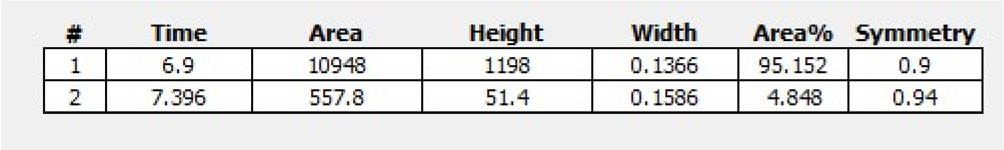
D (m)
7.23
C (m)
7.13
B (d)
6.30
A (dd)
5.92
F (d)
2.44
E (m)
2.60
G (s)
2.05
H (m)
1.59
I (m)
1.34
J (m)
1.10
K (m)
0.78
4.15
0.91
0.92
1.05
1.03
1.93
2.80
5.08
1.53
5.82
2.37
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
Chemical Shift (ppm)


208.07
137.41 133.34 130.19 128.49 128.46 127.10 126.11 126.07
77.35 CDCl3
77.24
77.04 CDCl3
76.72 CDCl3
49.55 39.25 37.76 34.96 33.53 33.25 32.43 30.70 26.70 26.42 26.39
A (s)
208.07
B (s)
137.41
C (s)
133.34
D (s)
130.19
E (s)
128.49
G (s)
127.10
H (s)
126.11
K (s)
49.55
L (s)
39.25
M (s)
37.76
N (s)
34.96
O (s)
33.53
P (s)
33.25
Q (s)
32.43
R (s)
30.70
S (s)
26.70
T (s)
26.42
U (s)
26.39
0.12
0.11 0.39 0.33 0.58 0.35 0.61
0.37 0.32 0.32 0.37 0.45 0.44 0.37 0.32 0.56 0.43 0.31
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
−200
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
Chemical Shift (ppm)

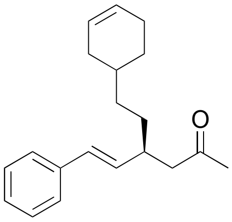
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.9 | 10948 | 1198 | 0.1366 | 95.152 | 0.9 |
| 2 | 7.396 | 557.8 | 51.4 | 0.1586 | 4.848 | 0.94 |

### (+)-(4*S*, E)-4-(2-(cyclohex-3-en-1-yl) ethyl)-6-phenylhex-5-en-2-one (3b)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 4-vinylcyclohex-1-ene (54 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-6-phenylhexa-3, 5-dien-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours,

before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (39 mg, 14 mmol, 70%).

HPLC analysis indicated an enantiomeric excess of 92 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1.0; λ = 254 nm; major enantiomer tR = 7.73 min; minor enantiomer, tR = 8.15 min].

$^1H$ NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.19 – 7.06 (m, 4H, Ar-*H*), 7.04 – 6.97 (m, 1H, Ar-*H*), 6.20 (d, *J* = 15.8 Hz, 1H, C*H*), 5.81 (dd, *J* = 15.8 Hz, 8.7 Hz, 1H, C*H*), 5.45 (d, *J* = 2.3, 2H, 2 x C*H*$CH_2$), 2.65 – 2.44 (m, 1H, C*H* $CH_2COCH_3$), 2.34 (d, *J* = 6.9 Hz, 2H, $CH_2COCH_3$), 1.94 (s, 3H, $COCH_3$), 1.90 – 1.76 (m, 2H, $CH_2$), 1.64 – 1.27 (m, 3H, C*H,* $CH_2$), 1.26 – 0.93 (m, 4H, 2 x $CH_2$).

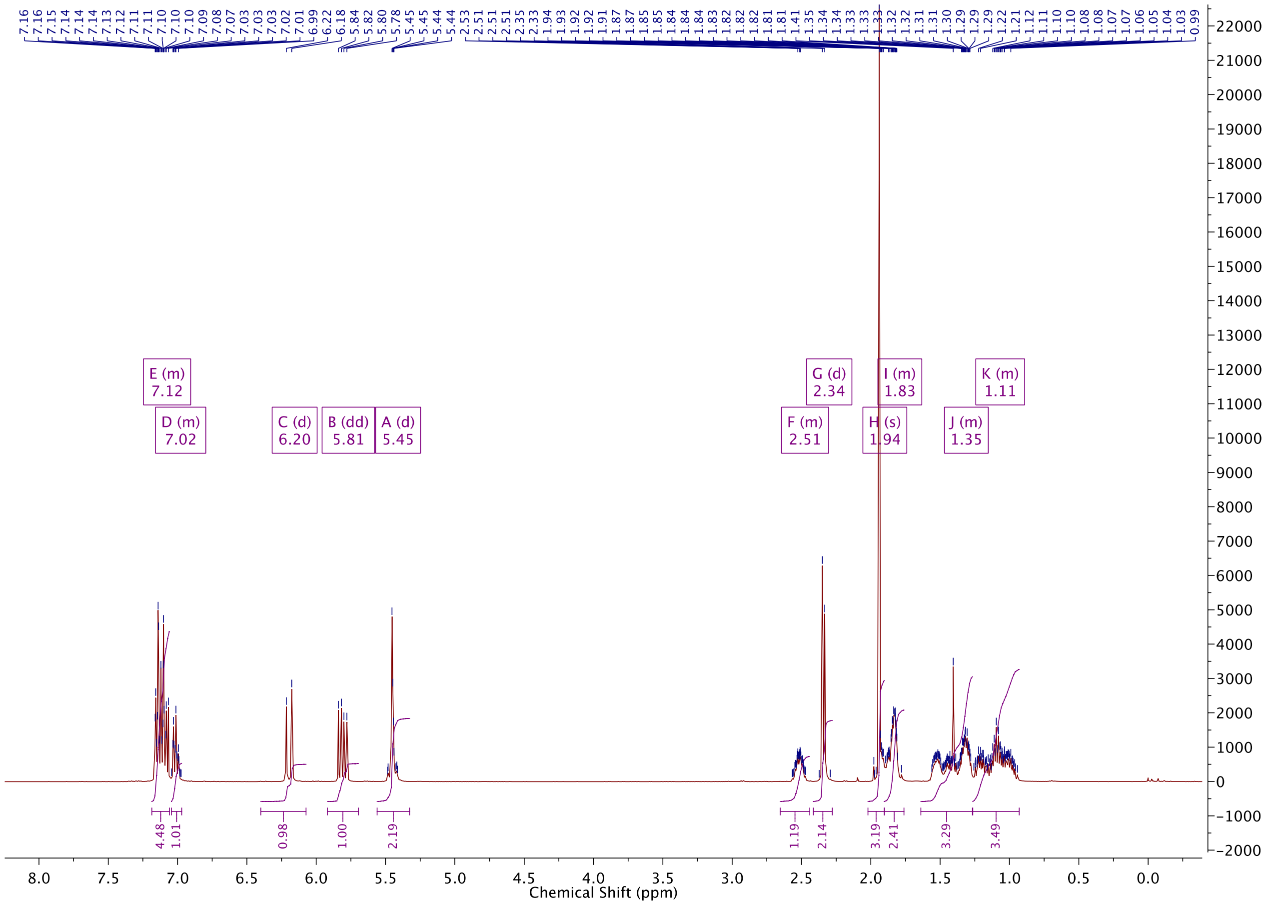
$^{13}C$ NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 208.0, 137.4, 133.2, 130.3, 128.5 (2C), 127.2, 127.1, 126.5, 126.1 (2C), 49.5, 39.2, 34.2, 33.6, 32.4, 31.9, 30.7, 28.9, 25.3.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1716, 1382, 1154, 966

HRMS (ESI) m/z calc. for $C_{20}H_{27}O$ $[M+H]^+$: 283.2056 found: 283.2057

$[\alpha]^{20}_{589}$ = +4.7 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.


7.16 7.16 7.15 7.14 7.14 7.13 7.12 7.11 7.10 7.10 7.10 7.09 7.08 7.07 7.03 7.03 7.03 7.02 7.01 6.99 6.22 6.18 5.84 5.82 5.80 5.78 5.45 5.45 5.44 5.44 2.53 2.51 2.51 2.51 2.35 2.33 1.94 1.93 1.92 1.92 1.91 1.87 1.85 1.85 1.84 1.84 1.84 1.83 1.82 1.82 1.81 1.81 1.41 1.35 1.34 1.34 1.33 1.33 1.33 1.32 1.32 1.31 1.31 1.30 1.29 1.29 1.29 1.22 1.21 1.12 1.11 1.10 1.10 1.08 1.08 1.07 1.07 1.06 1.05 1.04 1.03 1.03 0.99
E (m) 7.12
D (m) 7.02
C (d) 6.20
B (dd) 5.81
A (d) 5.45
G (d) 2.34
F (m) 2.51
I (m) 1.83
H (s) 1.94
K (m) 1.11
J (m) 1.35
4.48
1.01
0.98
1.00
2.19
1.19
2.14
3.19
2.41
3.29
3.49
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical Shift (ppm)
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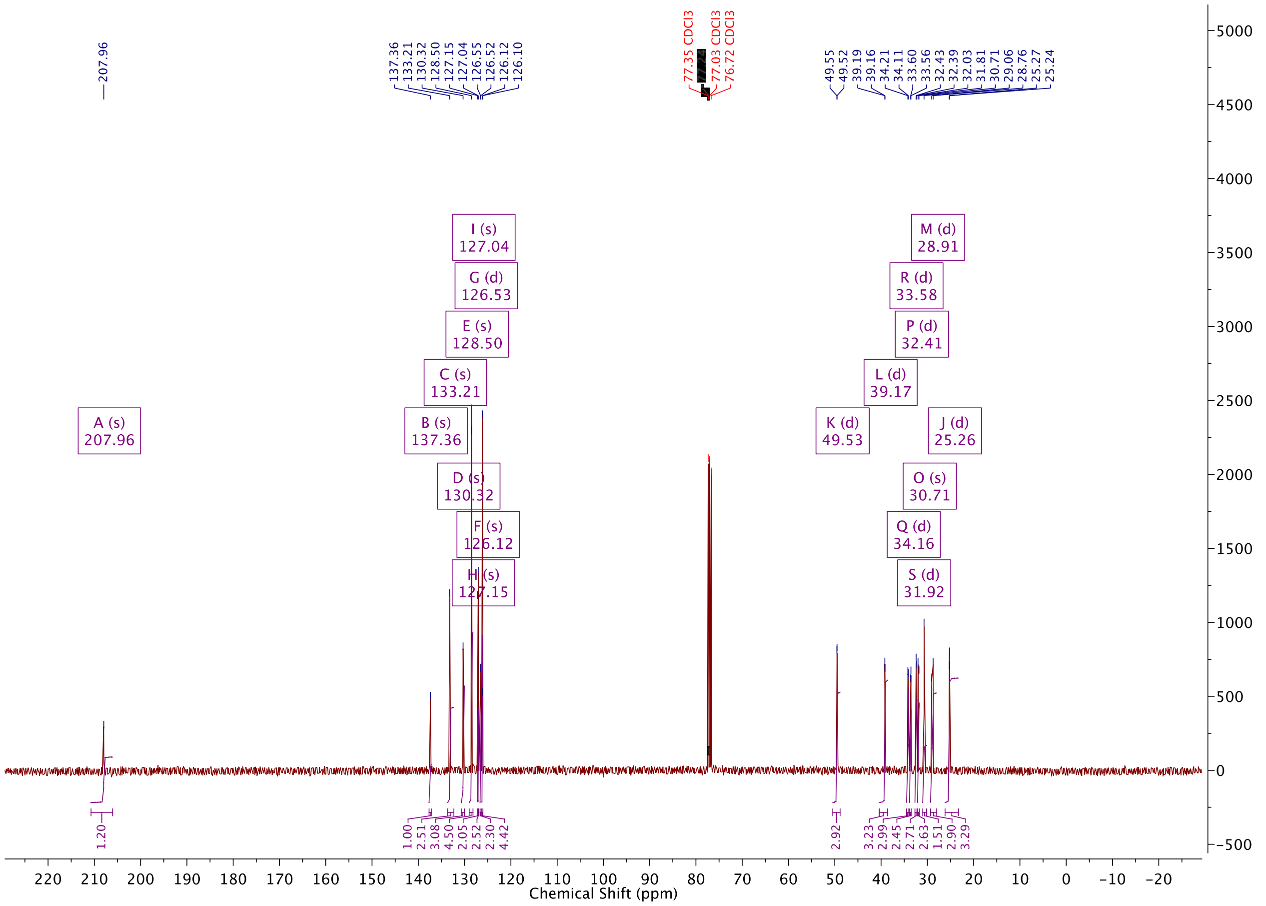
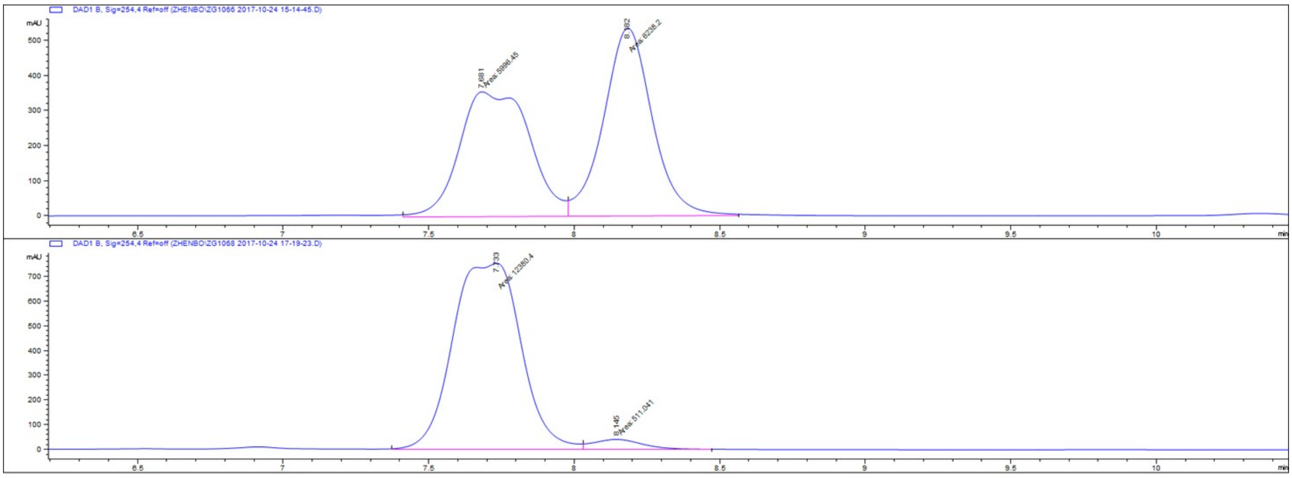
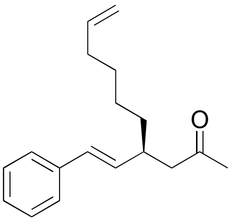

207.96
137.36 133.21 130.32 128.50 127.15 127.04 126.55 126.52 126.12 126.10
77.35 CDCl3
77.03 CDCl3
76.72 CDCl3
49.55 49.52 39.19 39.16 34.21 34.11 33.60 33.56 32.43 32.39 32.03 31.81 30.71 29.06 28.76 25.27 25.24
I (s) 127.04
G (d) 126.53
E (s) 128.50
C (s) 133.21
B (s) 137.36
A (s) 207.96
D (s) 130.32
F (s) 126.12
H (s) 127.15
M (d) 28.91
R (d) 33.58
P (d) 32.41
L (d) 39.17
K (d) 49.53
J (d) 25.26
O (s) 30.71
Q (d) 34.16
S (d) 31.92
1.20
1.00 2.51 3.08 4.50 2.05 2.52 2.30 4.42
2.92
3.23 2.99 2.45 2.71 2.63 1.51 2.90 3.29
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
Chemical Shift (ppm)
5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0 −500

HPLC trace



| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.733 | 12380.4 | 756.9 | 0.2726 | 96.036 | 1.605 |
| 2 | 8.145 | 511 | 41.8 | 0.2038 | 3.964 | 0.769 |

## (+)-(*S*, E)-4-styryldec-9-en-2-one (3c)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of hexa-1,5-diene (41 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-6-phenylhexa-3, 5-dien-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The

reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (45 mg, 16 mmol, 78%).

HPLC analysis indicated an enantiomeric excess of 63 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1; λ = 254 nm; major enantiomer tR = 7.01 min; minor enantiomer, tR = 8.10 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.39 – 7.23 (m, 4H, Ar-*H*), 7.25 – 7.17 (m, 1H, Ar-*H*), 6.39 (d, *J* = 15.8, 1H, C*H*), 6.00 (dd, *J* =15.8 Hz, 8.7 Hz, 1H, C*H*), 5.79 (ddt, *J* = 16.9 Hz, 10.2 Hz, 6.7 Hz, 1H, C*H*), 5.17 – 4.80 (m, 2H, $CH_2$), 2.73 (q, *J* = 6.9 Hz, 1H, C*H*), 2.52 (d, *J* = 6.9 Hz, 2H, $CH_2COCH_3$), 2.13 (s, 3H, $COCH_3$), 2.04 (ddt, *J* = 9.3 Hz, 7.8 Hz, 4.0 Hz, 2H, $CH_2CH{=}CH_2$), 1.53 – 1.14 (m, 6H, 3 x $CH_2$).

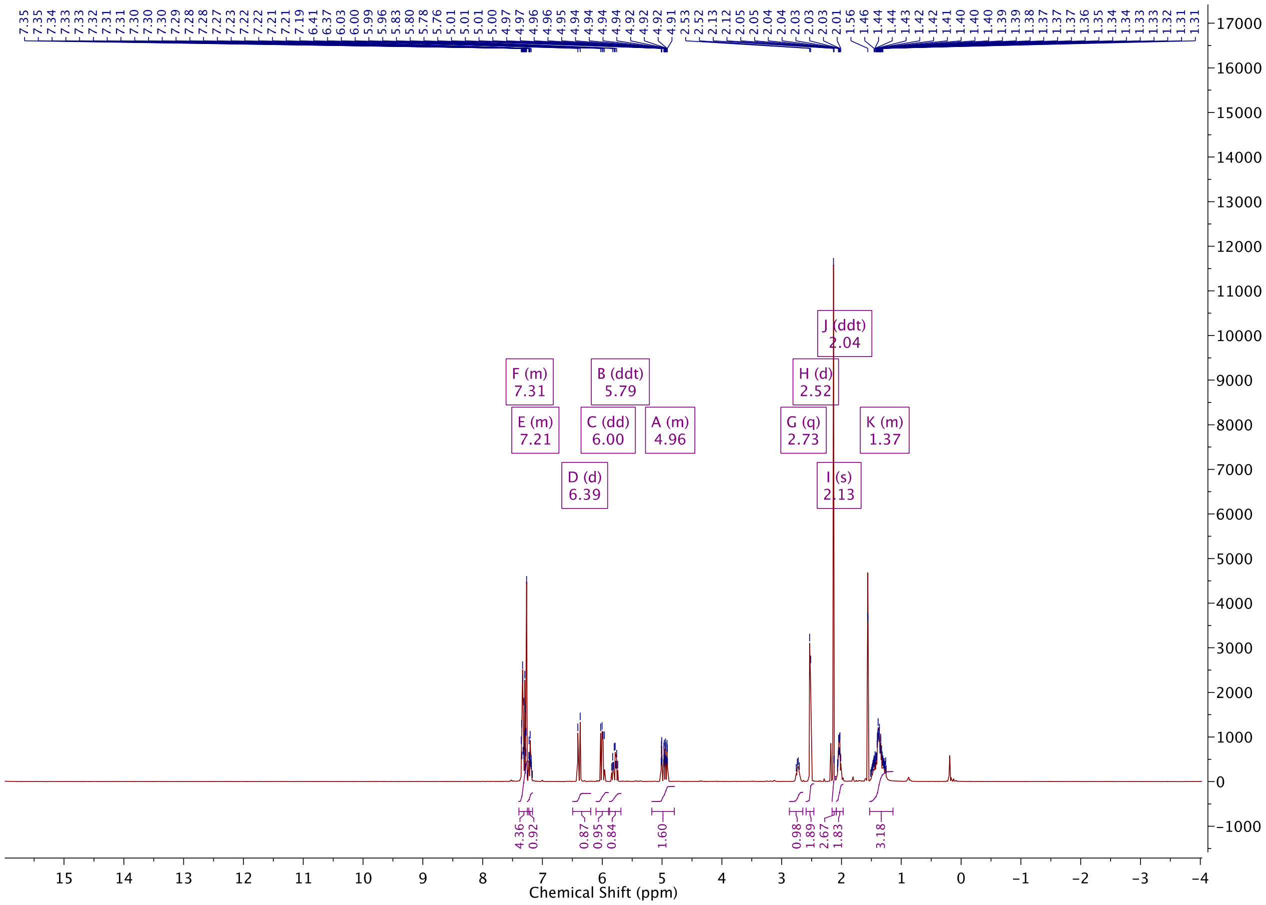
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 208.0, 138.9, 137.4, 133.1, 130.3, 128.5 (2C), 127.1, 126.1 (2C), 114.3, 49.5, 38.9, 34.9, 33.7, 30.7, 28.9, 26.7.

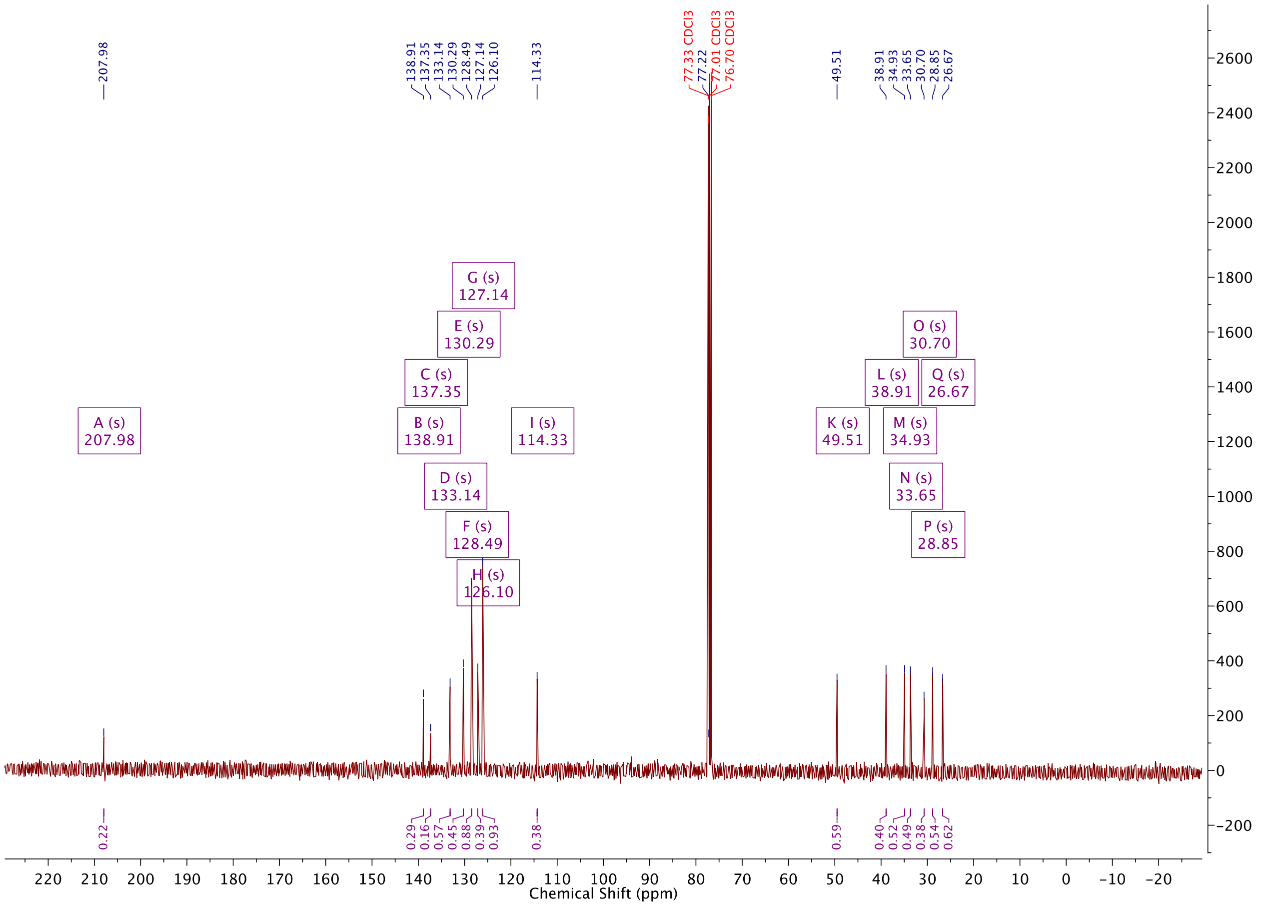
IR ($\nu_{max}$/cm$^{-1}$, $CHCl_3$) 2926, 2390, 2284, 1715, 1357, 966

HRMS (ESI) m/z calc. for $C_{18}H_{25}O$ $[M+H]^+$: 257.1900 found: 257.1900

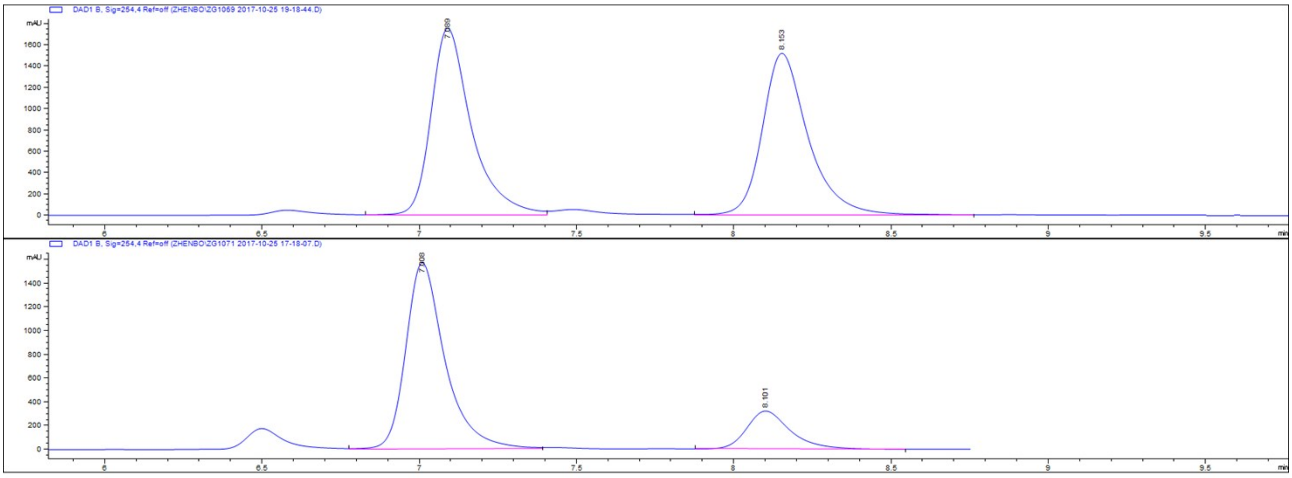
$[\alpha]^{20}_{589}$ = +6.1° (c 1.0, $CHCl_3$)

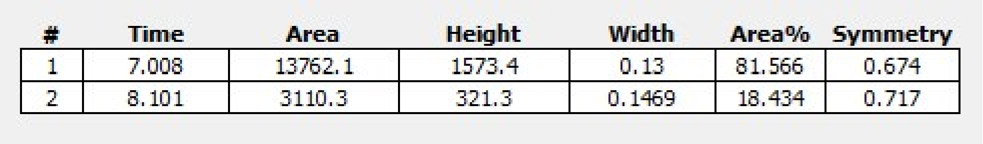
Absolute configuration assigned by analogy to **3p**.


7.35 7.35 7.34 7.33 7.33 7.32 7.31 7.31 7.30 7.30 7.30 7.29 7.28 7.28 7.27 7.23 7.22 7.22 7.21 7.21 7.19 6.41 6.37 6.03 6.00 5.99 5.96 5.83 5.80 5.78 5.76 5.01 5.01 5.01 5.00 4.97 4.97 4.96 4.96 4.95 4.94 4.94 4.94 4.94 4.92 4.92 4.92 4.91 2.53 2.52 2.13 2.12 2.05 2.04 2.04 2.03 2.03 2.03 2.01 1.56 1.46 1.44 1.44 1.43 1.42 1.42 1.41 1.40 1.40 1.39 1.39 1.38 1.38 1.37 1.37 1.37 1.36 1.35 1.35 1.34 1.34 1.33 1.33 1.33 1.32 1.31 1.31
F (m) 7.31
E (m) 7.21
B (ddt) 5.79
C (dd) 6.00
A (m) 4.96
D (d) 6.39
J (ddt) 2.04
H (d) 2.52
G (q) 2.73
I (s) 2.13
K (m) 1.37
4.36 0.92 0.87 0.95 0.84 1.60 0.98 1.89 2.67 1.83 3.18
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 −1 −2 −3 −4
Chemical Shift (ppm)
17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 −1000


207.98
138.91 137.35 133.14 130.29 128.49 127.14 126.10
114.33
77.33 CDCl3 77.22 77.01 CDCl3 76.70 CDCl3
49.51
38.91 34.93 33.65 30.70 28.85 26.67
G (s) 127.14
E (s) 130.29
C (s) 137.35
A (s) 207.98
B (s) 138.91
I (s) 114.33
D (s) 133.14
F (s) 128.49
H (s) 126.10
O (s) 30.70
L (s) 38.91
Q (s) 26.67
K (s) 49.51
M (s) 34.93
N (s) 33.65
P (s) 28.85
0.22 0.29 0.16 0.57 0.45 0.88 0.39 0.93 0.38 0.59 0.40 0.52 0.49 0.38 0.54 0.62
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
Chemical Shift (ppm)
2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 −200

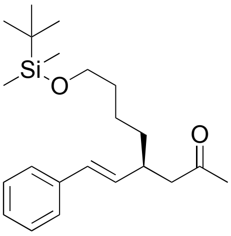
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.008 | 13762.1 | 1573.4 | 0.13 | 81.566 | 0.674 |
| 2 | 8.101 | 3110.3 | 321.3 | 0.1469 | 18.434 | 0.717 |

## (+)-(*S*, E)-8-((tert-butyldimethylsilyl) oxy)-4-styryloctan-2-one (3d)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of tert-butyldimethyl(pent-4-en-1-yloxy)silane (100 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-6-phenylhexa-3, 5-dien-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours,

before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (57 mg, 16 mmol, 79%).

HPLC analysis indicated an enantiomeric excess of 92 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1.0; λ = 254 nm; major enantiomer tR = 5.51 min; minor enantiomer, tR = 5.90 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.35 – 7.22 (m, 4H, Ar-*H*), 7.21 – 7.13 (m, 1H, Ar-*H*), 6.36 (d, *J* = 15.9 Hz, 1H, C*H*), 5.96 (dd, *J* = 15.8 Hz, 8.7 Hz, 1H, C*H*), 3.56 (t, *J* = 6.5 Hz, 2H, $CH_2O$), 2.69 (p, *J* = 7.5 Hz, 6.8 Hz, 1H, $CHCH_2COCH_3$), 2.50 (d, *J* = 6.9 Hz, 2H, $CH_2COCH_3$), 2.10 (s, 3H, $COCH_3$), 1.59 – 1.08 (m, 6H, 3 x $CH_2$), 0.84 (s, 9H 3 x $CH_3$), -0.00 (s, 6H, $SiCH_3$).

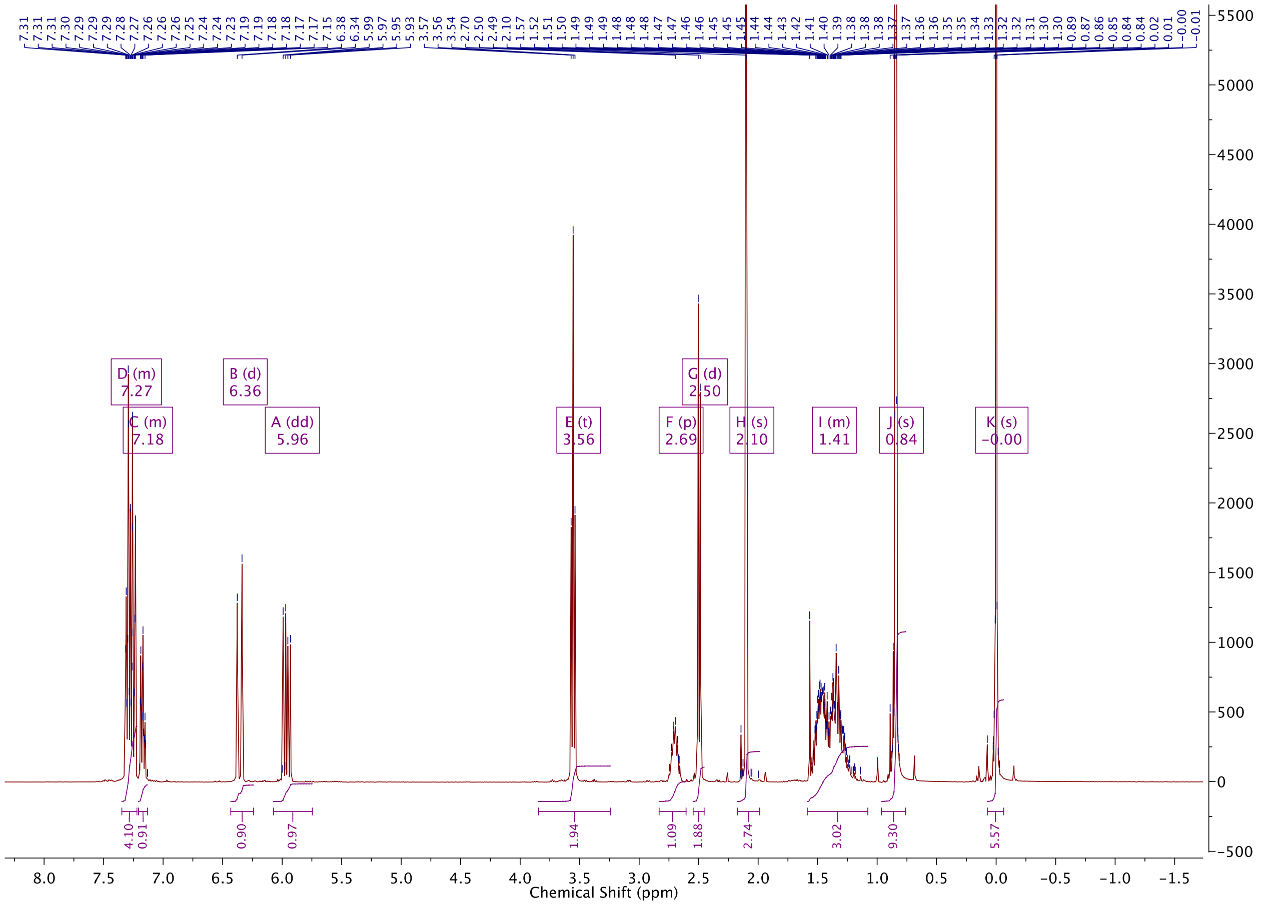
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 208.0, 137.3, 133.1, 130.4, 128.5 (2C), 127.1, 126.1 (2C), 63.1, 49.5, 39.0, 34.9, 32.8, 30.7, 26.0 (3C), 23.5, 18.4, -5.3 (2C).

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1717, 1386, 1155,966

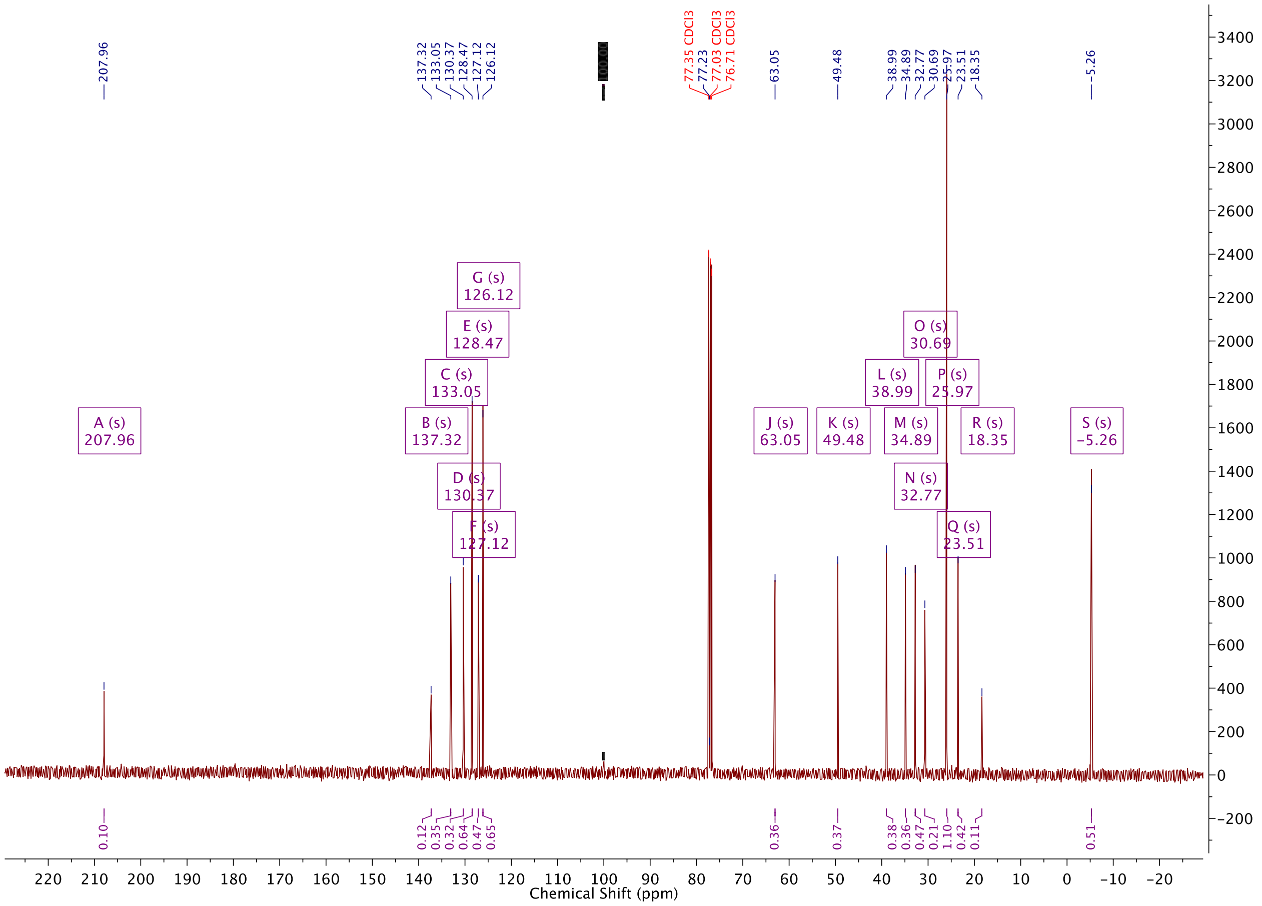
HRMS (ESI) m/z calc. for $C_{22}H_{37}O_2{}^{28}Si$ $[M+H]^+$: 361.2557, 362.2590 found: 361.2558, 362.2585

$[\alpha]^{20}_{589}$ = +4.4 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.

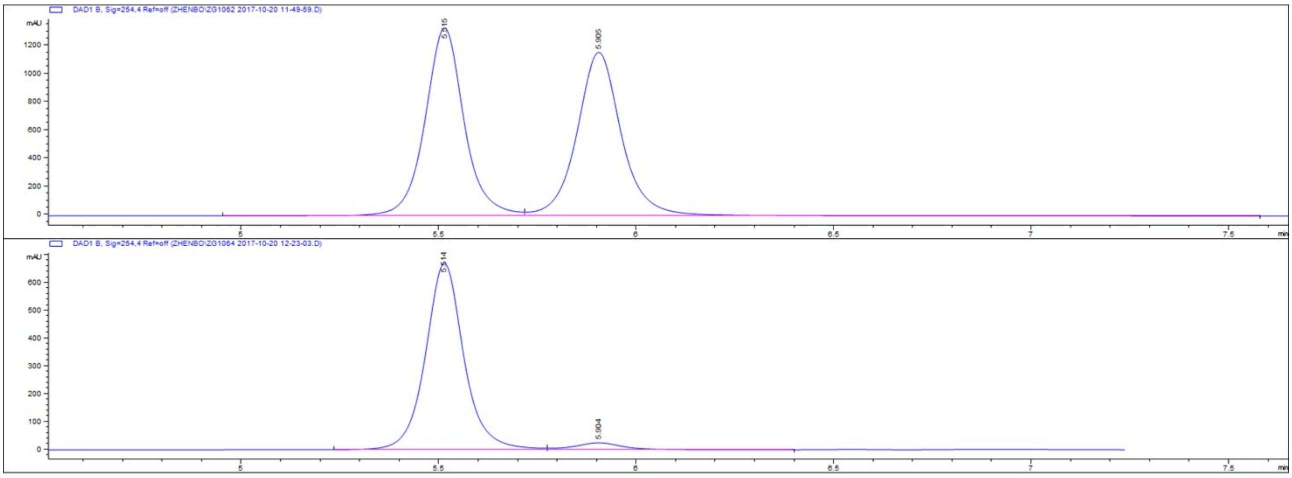


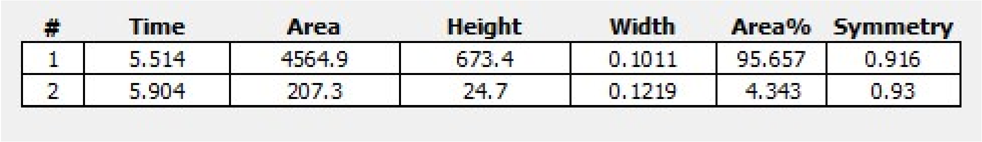
D (m)
7.27
C (m)
7.18
B (d)
6.36
A (dd)
5.96
E (t)
3.56
F (p)
2.69
G (d)
2.50
H (s)
2.10
I (m)
1.41
J (s)
0.84
K (s)
-0.00
4.10
0.91
0.90
0.97
1.94
1.09
1.88
2.74
3.02
9.30
5.57
Chemical Shift (ppm)



77.35 CDCl3
77.23
77.03 CDCl3
76.71 CDCl3
100.00
A (s)
207.96
B (s)
137.32
C (s)
133.05
D (s)
130.37
E (s)
128.47
F (s)
127.12
G (s)
126.12
J (s)
63.05
K (s)
49.48
L (s)
38.99
M (s)
34.89
N (s)
32.77
O (s)
30.69
P (s)
25.97
Q (s)
23.51
R (s)
18.35
S (s)
-5.26
Chemical Shift (ppm)

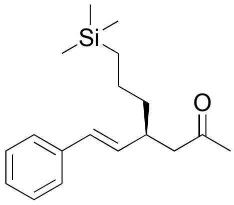
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.514 | 4564.9 | 673.4 | 0.1011 | 95.657 | 0.916 |
| 2 | 5.904 | 207.3 | 24.7 | 0.1219 | 4.343 | 0.93 |

### (+)-(*S*, E)-4-styryl-7- (trimethylsilyl) heptan-2-one (3e)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of allyltrimethylsilane (57 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-6-phenylhexa-3, 5-dien-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The

reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (45 mg, 16 mmol, 78%).

HPLC analysis indicated an enantiomeric excess of 86 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1.0; λ = 252 nm; major enantiomer tR = 6.02 min; minor enantiomer, tR = 6.86 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.41 – 7.29 (m, 4H, Ar-*H*), 7.28 – 7.21 (m, 1H, Ar-*H*), 6.42 (d, *J* = 15.8 Hz, 1H, C*H*), 6.03 (dd, *J* = 15.9 Hz, 8.7 Hz, 1H, C*H*), 2.98 – 2.64 (m, 1H, $CHCH_2COCH_3$), 2.55 (d, *J* = 6.9 Hz, 2H, $CH_2COCH_3$), 2.17 (s, 3H, $COCH_3$), 1.54 – 1.19 (m, 4H, 2 x $CH_2$), 0.75 – 0.41 (m, 2H, $CH_2Si$), -0.00 (s, 9H, $Si(CH_3)_3$).

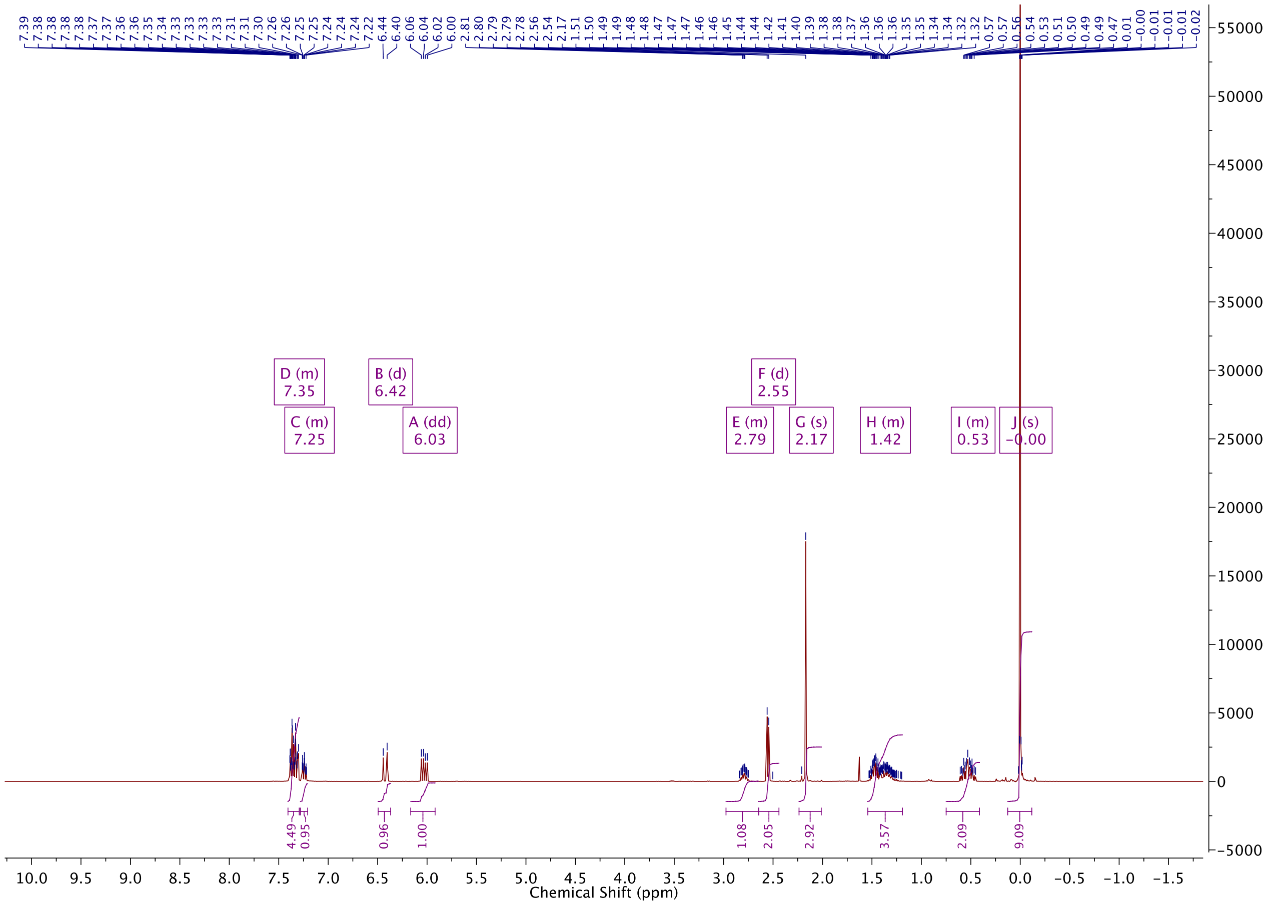
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_P$/ppm 209.7, 139.0, 134.9, 131.8, 130.1 (2C), 128.7, 127.7 (2C), 51.1, 40.6, 40.3, 32.3, 23.1, 18.2, 0.0(3C)

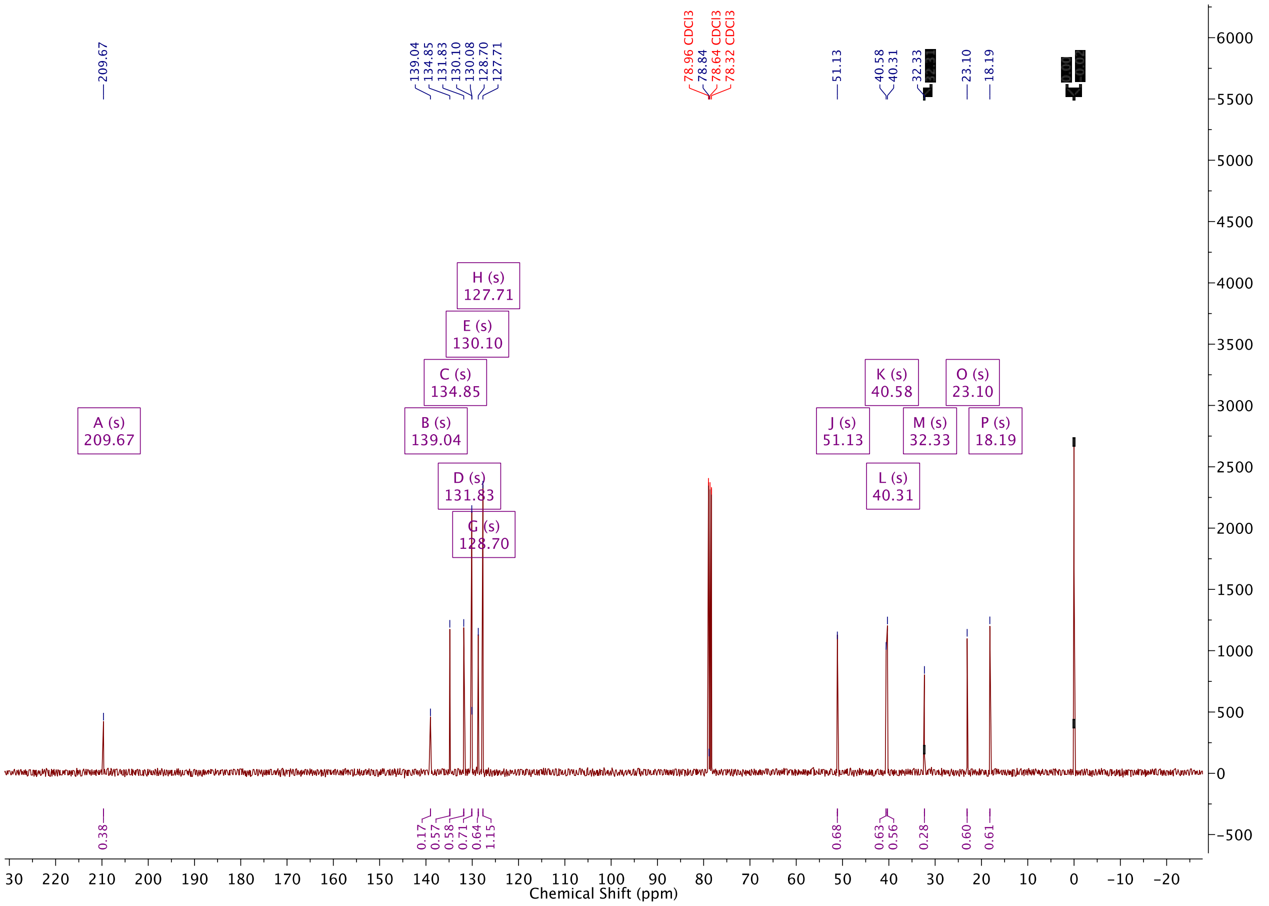
IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1716, 1382,1155, 966

HRMS (ESI) m/z calc. for $C_{18}H_{29}O^{28}Si$ $[M+H]^+$: 289.1982, found: 289.1982

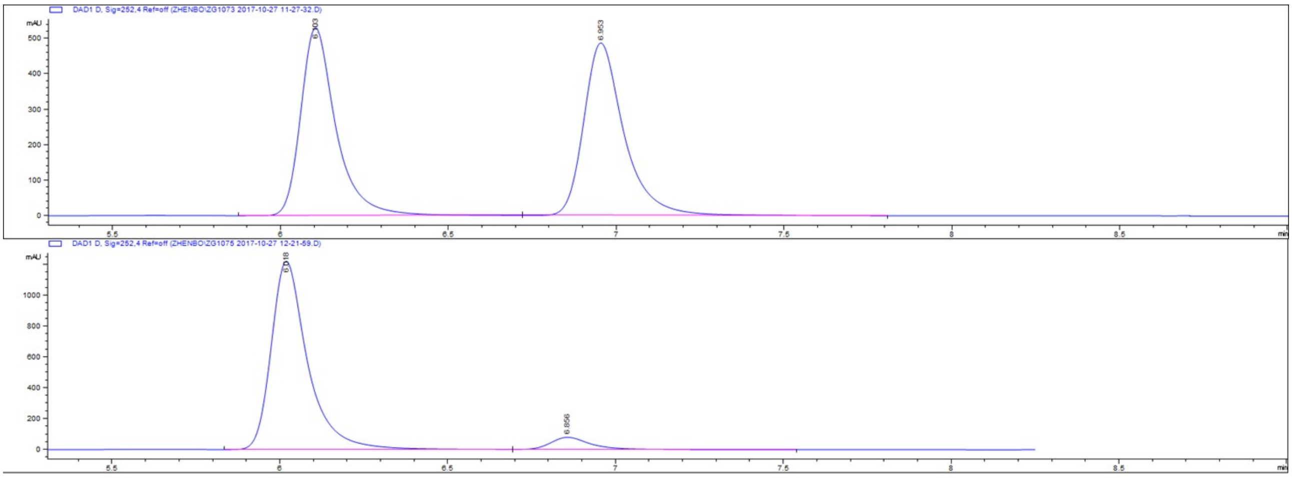
$[\alpha]^{20}_{589}$ = +0.8 ° (c 1.0, $CHCl_3$)

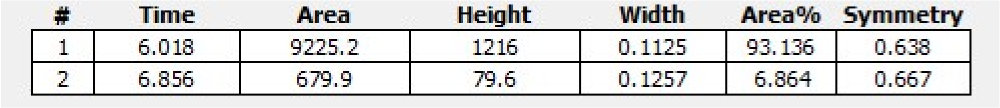
Absolute configuration assigned by analogy to **3p**.


7.39
7.38
7.38
7.38
7.37
7.36
7.36
7.35
7.34
7.33
7.33
7.33
7.33
7.31
7.30
7.26
7.25
7.25
7.24
7.24
7.24
7.22
6.44
6.40
6.06
6.04
6.02
6.00
2.81
2.80
2.79
2.79
2.78
2.56
2.54
2.17
1.51
1.50
1.49
1.49
1.48
1.47
1.47
1.46
1.46
1.45
1.44
1.42
1.41
1.40
1.39
1.38
1.38
1.37
1.36
1.36
1.35
1.35
1.34
1.32
0.57
0.57
0.56
0.54
0.53
0.51
0.50
0.49
0.49
0.47
0.01
-0.00
-0.01
-0.01
-0.01
-0.02
D (m) 7.35
C (m) 7.25
B (d) 6.42
A (dd) 6.03
F (d) 2.55
E (m) 2.79
G (s) 2.17
H (m) 1.42
I (m) 0.53
J (s) -0.00
4.49
0.95
0.96
1.00
1.08
2.05
2.92
3.57
2.09
9.09
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
Chemical Shift (ppm)


209.67
139.04
134.85
131.83
130.10
130.08
128.70
127.71
78.96 CDCl3
78.84
78.64 CDCl3
78.32 CDCl3
51.13
40.58
40.31
32.33
32.31
23.10
18.19
0.00
-0.02
H (s) 127.71
E (s) 130.10
C (s) 134.85
A (s) 209.67
B (s) 139.04
D (s) 131.83
G (s) 128.70
K (s) 40.58
O (s) 23.10
J (s) 51.13
M (s) 32.33
P (s) 18.19
L (s) 40.31
0.38
0.17
0.57
0.58
0.71
0.64
1.15
0.68
0.63
0.56
0.28
0.60
0.61
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
30
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
Chemical Shift (ppm)

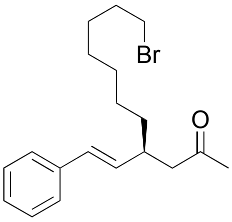
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.018 | 9225.2 | 1216 | 0.1125 | 93.136 | 0.638 |
| 2 | 6.856 | 679.9 | 79.6 | 0.1257 | 6.864 | 0.667 |

## (+)-(*S*, E)-11-bromo-4-styrylundecan-2-one (3f)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 7-bromohept-1-ene (89 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-6-phenylhexa-3, 5-dien-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The

reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (45 mg, 16 mmol, 78%).

HPLC analysis indicated an enantiomeric excess of 92 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1.0; λ = 254 nm; major enantiomer tR = 9.78 min; minor enantiomer, tR = 10.60 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.34 – 7.22 (m, 4H, Ar-*H*), 7.22 – 7.13 (m, 1H, Ar-*H*), 6.36 (d, *J* = 15.9 Hz, 1H, C*H*), 5.96 (dd, *J* = 15.8 Hz, 8.7 Hz, 1H, C*H*), 3.36 (t, *J* = 6.9 Hz, 2H, $CH_2Br$), 2.68 (m, 1H, $CHCH_2COCH_3$), 2.49 (d, *J* = 6.9 Hz, 2H, $CH_2COCH_3$), 2.10 (s, 3H, $COCH_3$), 1.92 – 1.69 (m, 2H, $CH_2$), 1.49 – 1.13 (m, 10H, 5 x $CH_2$).

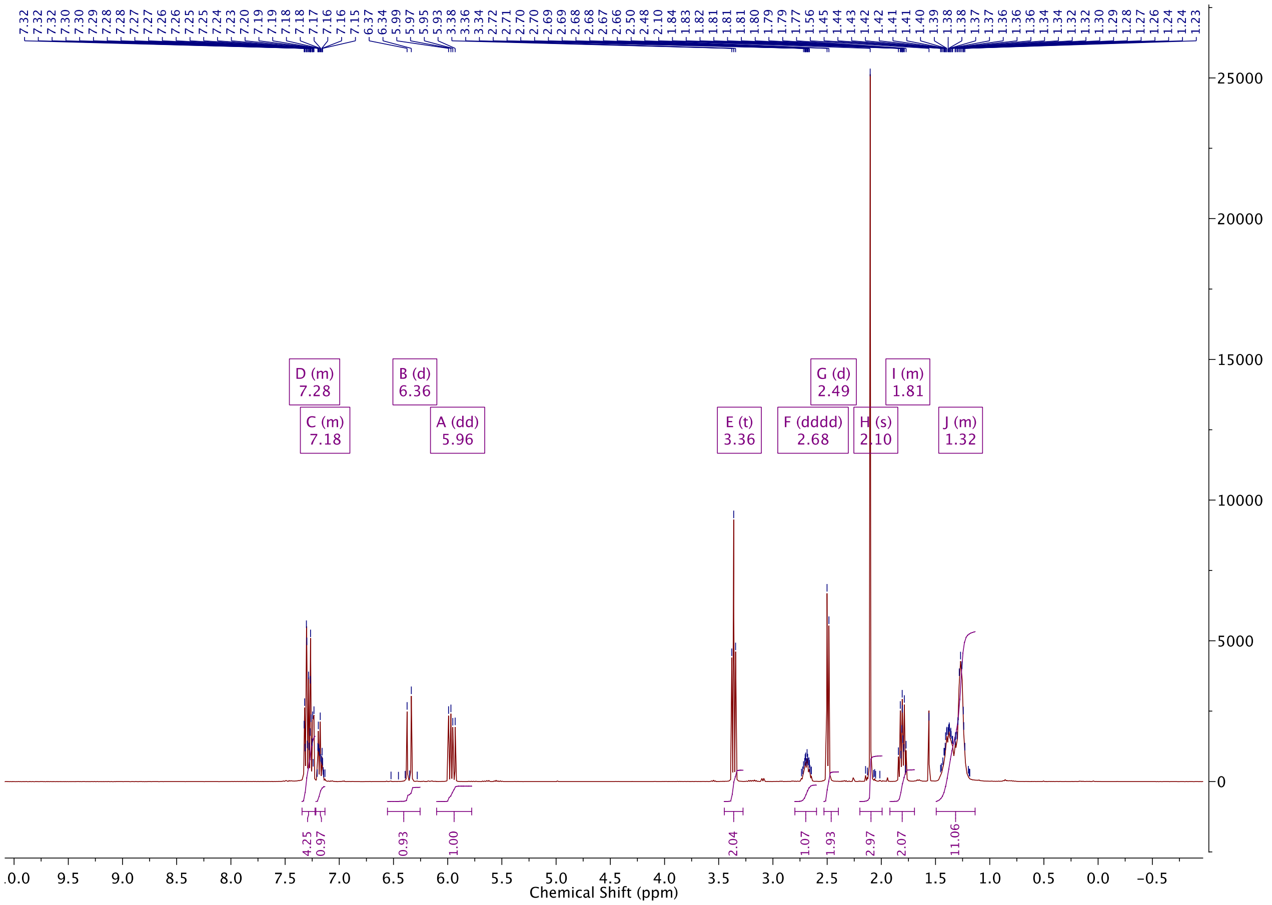
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 208.1, 137.3, 133.1, 130.3, 128.5 (2C), 127.2, 126.1 (2C), 49.5, 39.0, 35.0, 34.1, 32.8, 30.8, 29.4, 28.7, 28.1, 27.1.

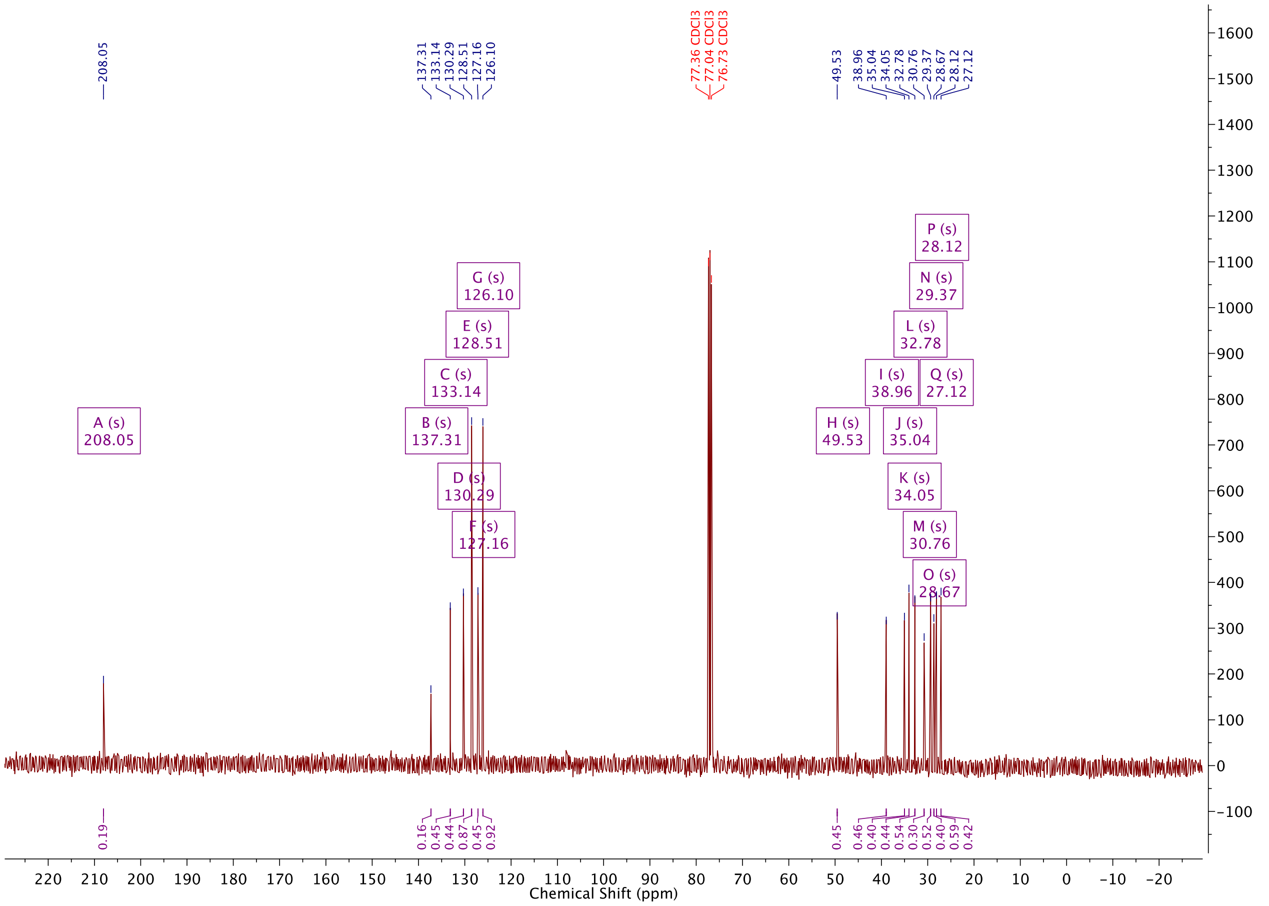
IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 2929, 1715, 1381,1157, 966

HRMS (ESI) m/z calc. for $C_{19}H_{28}O^{79}Br$ $[M+H]^+$: 351.1318, 353 .1298 found: 351.1315, 353.1294

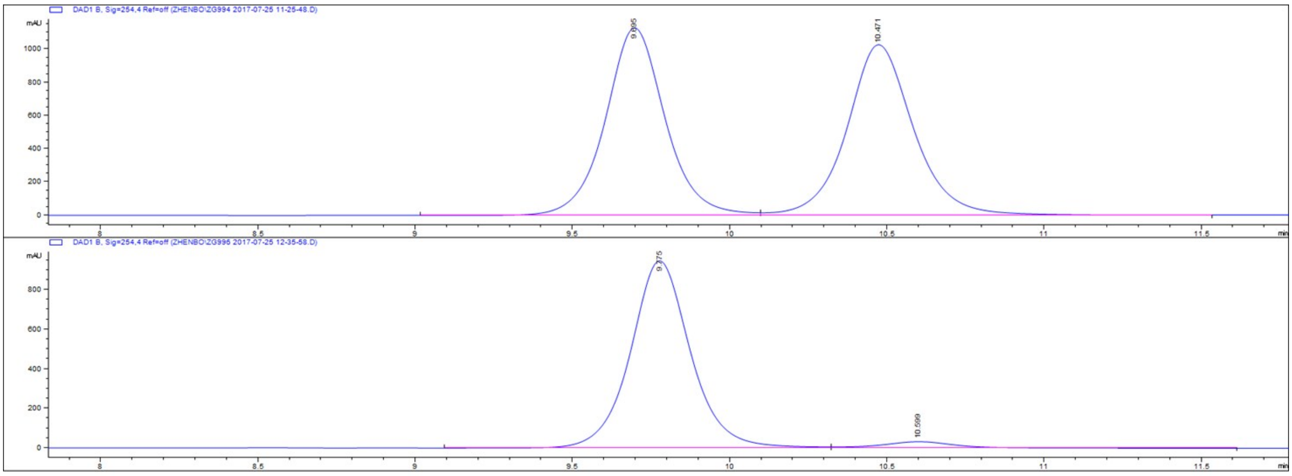
$[\alpha]^{20}_{589}$ = +6.1 ° (c 1.0, $CHCl_3$)

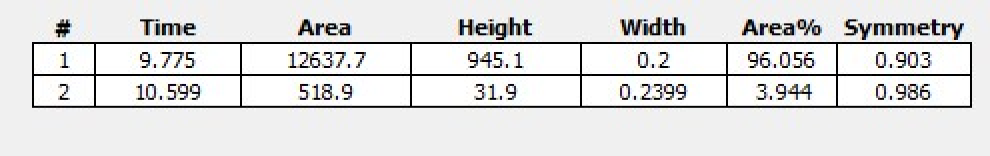
Absolute configuration assigned by analogy to **3p**.


7.32 7.32 7.32 7.30 7.30 7.29 7.28 7.28 7.27 7.27 7.26 7.26 7.25 7.25 7.24 7.23 7.20 7.19 7.19 7.18 7.18 7.17 7.16 7.16 7.15 6.37 6.34 5.99 5.97 5.95 5.93 3.38 3.36 3.34 2.72 2.71 2.70 2.69 2.69 2.68 2.68 2.67 2.66 2.50 2.48 2.10 1.84 1.83 1.82 1.81 1.81 1.81 1.80 1.79 1.77 1.56 1.45 1.44 1.43 1.42 1.42 1.41 1.41 1.40 1.39 1.38 1.38 1.37 1.37 1.36 1.36 1.36 1.34 1.34 1.32 1.32 1.30 1.29 1.28 1.27 1.26 1.24 1.24 1.23
D (m) 7.28
C (m) 7.18
B (d) 6.36
A (dd) 5.96
E (t) 3.36
F (dddd) 2.68
G (d) 2.49
H (s) 2.10
I (m) 1.81
J (m) 1.32
4.25
0.97
0.93
1.00
2.04
1.07
1.93
2.97
2.07
11.06
25000
20000
15000
10000
5000
0
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
Chemical Shift (ppm)


208.05
137.31 133.14 130.29 128.51 127.16 126.10
77.36 CDCl3 77.04 CDCl3 76.73 CDCl3
49.53 38.96 35.04 34.05 32.78 30.76 29.37 28.67 28.12 27.12
A (s) 208.05
B (s) 137.31
C (s) 133.14
D (s) 130.29
E (s) 128.51
F (s) 127.16
G (s) 126.10
H (s) 49.53
I (s) 38.96
J (s) 35.04
K (s) 34.05
L (s) 32.78
M (s) 30.76
N (s) 29.37
O (s) 28.67
P (s) 28.12
Q (s) 27.12
0.19
0.16 0.45 0.44 0.87 0.45 0.92
0.45 0.46 0.40 0.44 0.54 0.30 0.52 0.40 0.59 0.42
1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0 -100
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
Chemical Shift (ppm)

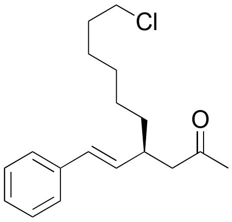
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.775 | 12637.7 | 945.1 | 0.2 | 96.056 | 0.903 |
| 2 | 10.599 | 518.9 | 31.9 | 0.2399 | 3.944 | 0.986 |

### (+)-(*S*, E)-10-chloro-4-styryldecan-2-one (3g)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 6-chlorohex-1-ene (59 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-6-phenylhexa-3,5-dien-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours,

before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (50 mg, 17 mmol, 85%).

HPLC analysis indicated an enantiomeric excess of 90 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1.0; λ = 254 nm; major enantiomer tR = 9.81 min; minor enantiomer, tR = 11.37 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.33 – 7.21 (m, 4H, Ar-*H*), 7.20 – 7.11 (m, 1H, Ar-*H*), 6.34 (d, *J* = 15.8 Hz, 1H, C*H*), 5.95 (dd, *J* = 15.8 Hz, 8.8 Hz, 1H, C*H*), 3.47 (t, *J* = 6.7 Hz, 2H, C*H*$_2$Cl), 2.77 – 2.61 (m, 1H, C*H*), 2.48 (d, *J* = 6.9 Hz, 2H, C*H*$_2$COCH$_3$), 2.09 (s, 3H, C*H*$_3$), 1.71 (dq, *J* = 8.1 Hz, 6.8 Hz, 2H, C*H*$_2$CH), 1.50 – 1.14 (m, 8H, C*H*$_2$).

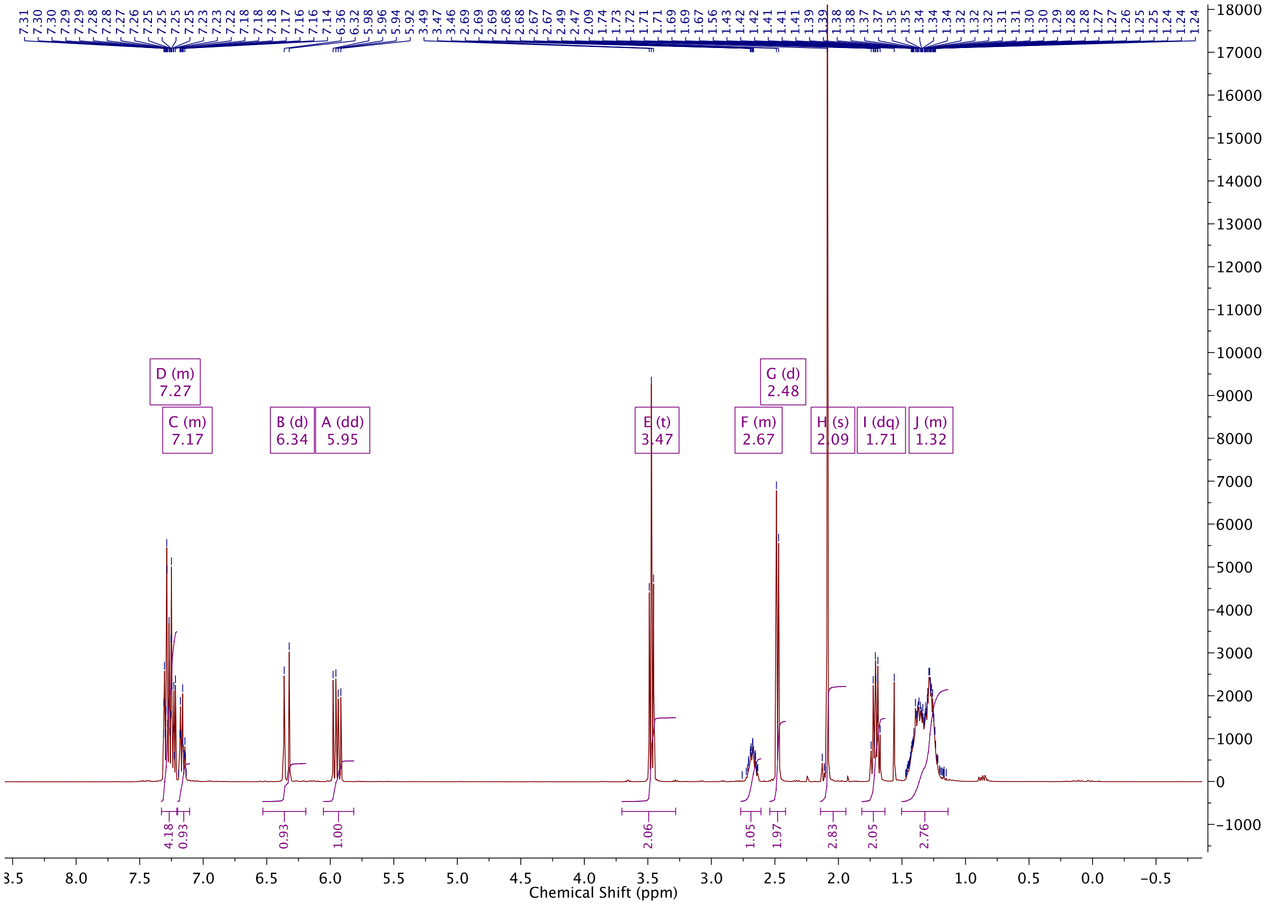
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 207.9, 137.3, 133.1, 130.4, 128.5 (2C), 127.2, 126.1 (2C), 49.5, 45.1, 38.9, 35.0, 32.6, 30.7, 28.8, 27.1, 26.8.

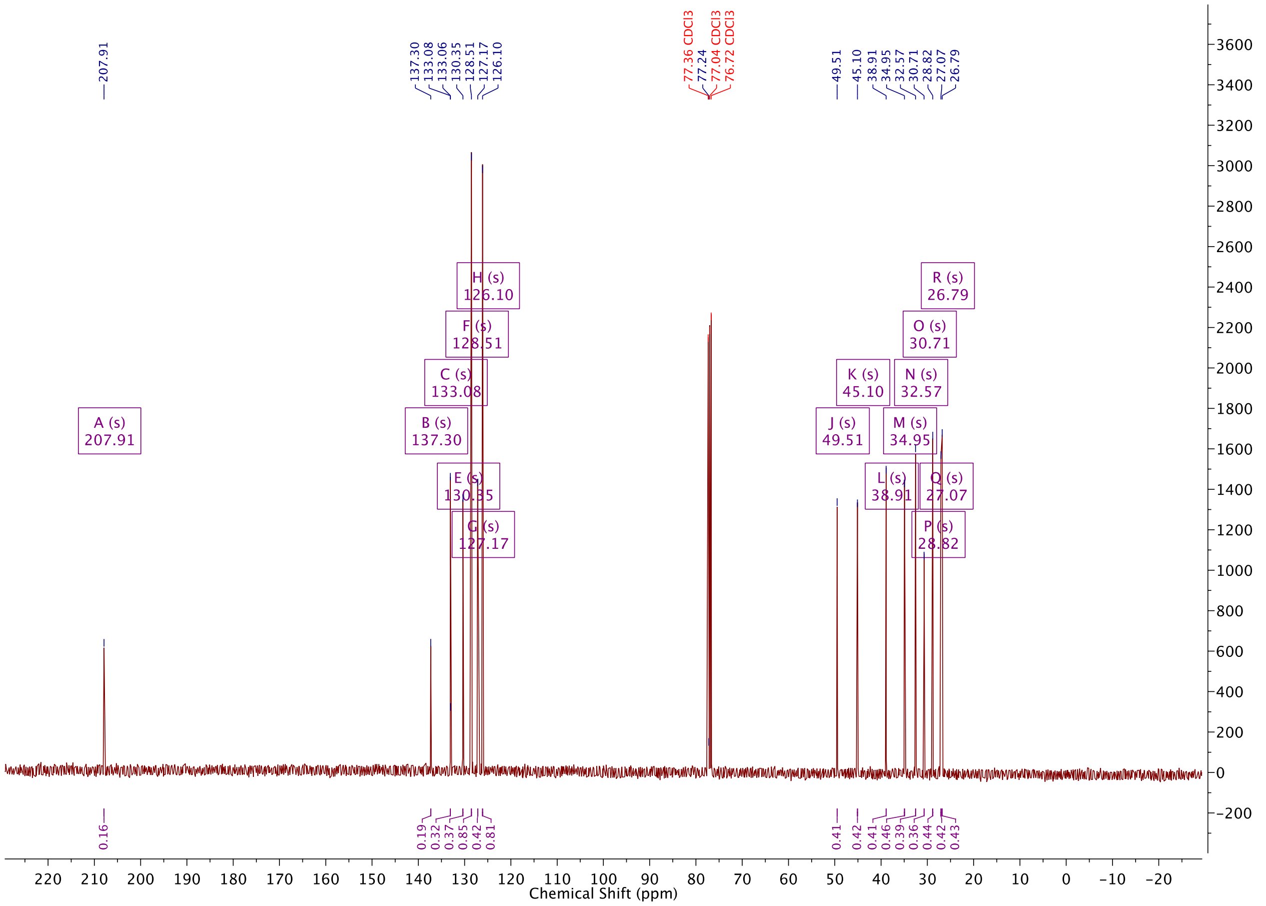
IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1715, 1382,1158, 967

HRMS (ESI) m/z calc. for $C_{18}H_{26}O^{35}Cl$ $[M+H]^+$: 293.1667, 295.1637, found: 293.1669, 295.1639

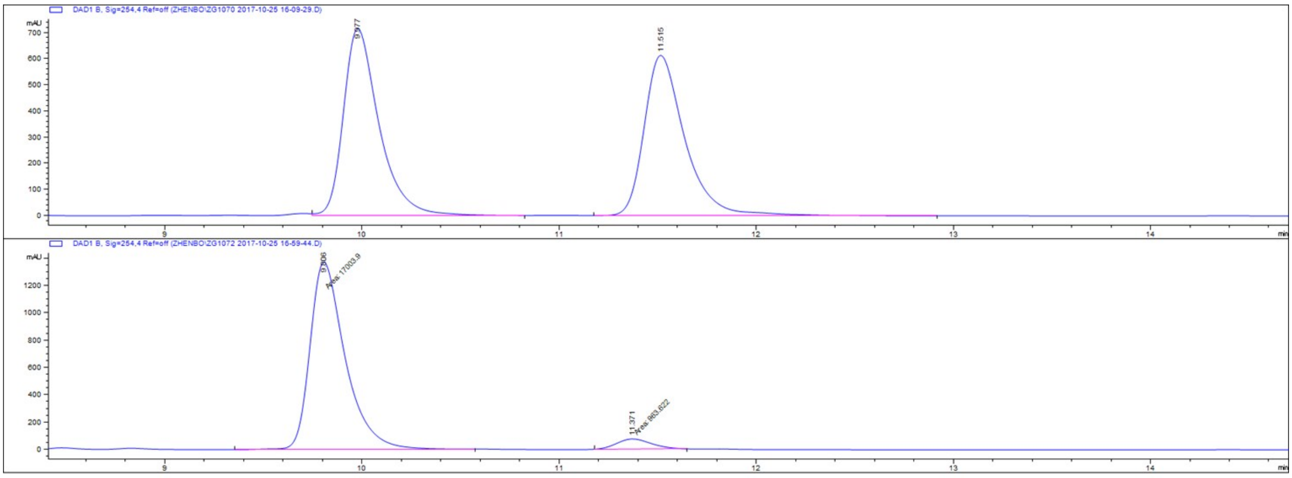
$[\alpha]^{20}_{589}$ = +9.8 ° (c 1.0, $CHCl_3$)

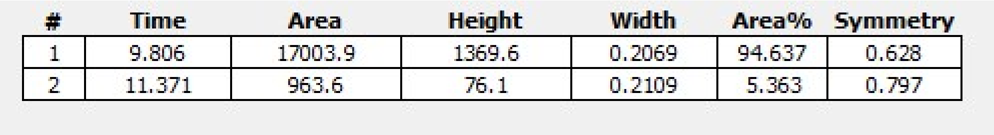
Absolute configuration assigned by analogy to **3p**.


7.31 7.30 7.30 7.29 7.29 7.28 7.28 7.27 7.26 7.25 7.25 7.25 7.25 7.23 7.23 7.22 7.18 7.18 7.18 7.17 7.16 7.16 7.14 6.36 6.32 5.98 5.96 5.94 5.92 3.49 3.47 3.46 2.69 2.69 2.69 2.68 2.67 2.67 2.49 2.47 2.09 1.74 1.73 1.72 1.71 1.71 1.69 1.69 1.67 1.56 1.43 1.42 1.41 1.41 1.41 1.39 1.39 1.38 1.38 1.37 1.37 1.35 1.35 1.34 1.34 1.34 1.32 1.32 1.31 1.31 1.30 1.29 1.28 1.28 1.27 1.27 1.26 1.25 1.25 1.24 1.24 1.24
D (m) 7.27
C (m) 7.17
B (d) 6.34
A (dd) 5.95
E (t) 3.47
F (m) 2.67
G (d) 2.48
H (s) 2.09
I (dq) 1.71
J (m) 1.32
4.18 0.93 0.93 1.00 2.06 1.05 1.97 2.83 2.05 2.76
18000 17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 −1000
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5
Chemical Shift (ppm)


207.91
137.30 133.08 133.06 130.35 128.51 127.17 126.10
77.36 CDCl3 77.24 77.04 CDCl3 76.72 CDCl3
49.51 45.10 38.91 34.95 32.57 30.71 28.82 27.07 26.79
A (s) 207.91
B (s) 137.30
C (s) 133.08
E (s) 130.35
F (s) 128.51
G (s) 127.17
H (s) 126.10
J (s) 49.51
K (s) 45.10
L (s) 38.91
M (s) 34.95
N (s) 32.57
O (s) 30.71
P (s) 28.82
Q (s) 27.07
R (s) 26.79
0.16 0.19 0.32 0.37 0.85 0.42 0.81 0.41 0.42 0.41 0.46 0.39 0.36 0.44 0.42 0.43
3600 3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 −200
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
Chemical Shift (ppm)

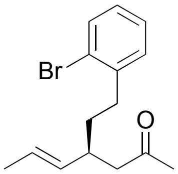
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 9.806 | 17003.9 | 1369.6 | 0.2069 | 94.637 | 0.628 |
| 2 | 11.371 | 963.6 | 76.1 | 0.2109 | 5.363 | 0.797 |

## (+)-(*S*, E)-4-(2-bromophenethyl) hept-5-en-2-one (3h)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 1-bromo-2-vinylbenzene (91 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before ((3E, 5E)-hepta-3, 5-dien-2-one (22 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (35 mg, 12 mmol, 60%).

HPLC analysis indicated an enantiomeric excess of 90 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1.0; λ = 210 nm; major enantiomer tR = 7.43 min; minor enantiomer, tR = 6.93 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.50 (dd, *J* = 7.8 Hz, 1.1, 1H, Ar-*H*), 7.30 – 7.10 (m, 2H, Ar-*H*), 7.03 (m, 1H, Ar-*H*), 5.62 – 5.44 (m, 1H, C*H*), 5.28 (m, 1H, C*H*), 2.75 (m, 1H, C*H*$CH_2COCH_3$), 2.61 (m, 2H, C*H*$_2$Ar), 2.50 – 2.37 (m, 2H, C*H*$_2$$COCH_3$), 2.10 (s, 3H, COC*H*$_3$), 1.68 (dd, *J* = 6.5 Hz, 1.6 Hz, 3H, C*H*$_3$), 1.66 – 1.61 (m, 1H, C*H*$_2$), 1.52 (m, 1H, C*H*$_2$).

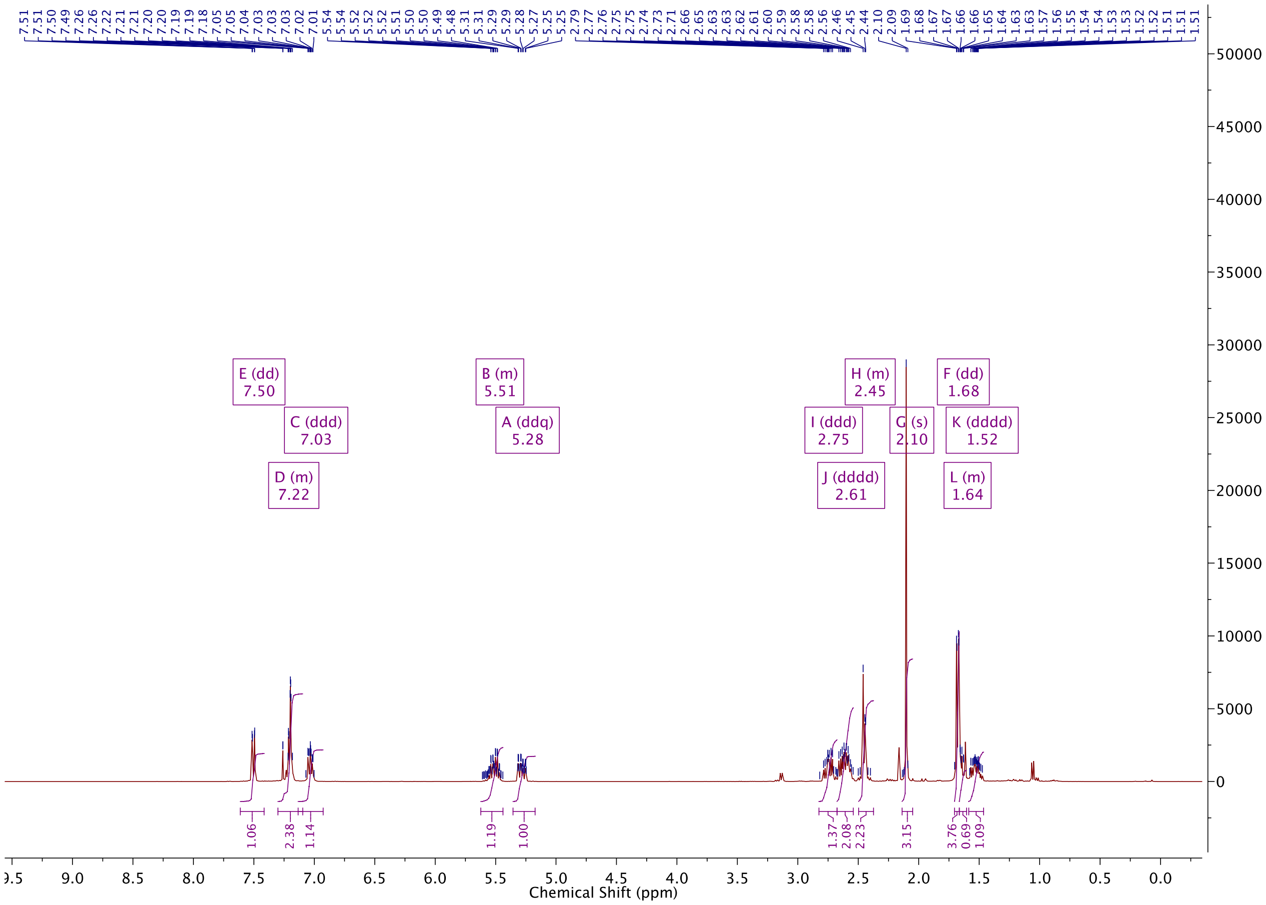
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 208.2, 141.7, 133.4, 132.8, 130.3, 127.5, 127.4, 126.3, 124.3, 49.6, 38.6, 35.3, 34.0, 30.6, 18.0

IR ($\nu_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1716, 1382,1153, 966

HRMS (ESI) m/z calc. for $C_{15}H_{20}O^{79}Br$ [M+H]$^+$: 295.0692, 297.0672, found: 295.0695, 297.0674

$[\alpha]^{20}_{589}$ = +2.4 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.


7.51 7.51 7.50 7.49 7.26 7.22 7.21 7.21 7.20 7.20 7.19 7.19 7.18 7.05 7.05 7.04 7.03 7.03 7.03 7.02 7.01
5.54 5.54 5.52 5.52 5.51 5.50 5.50 5.49 5.48 5.31 5.31 5.29 5.29 5.28 5.27 5.25
2.79 2.77 2.76 2.75 2.75 2.74 2.73 2.71 2.66 2.65 2.63 2.63 2.62 2.61 2.60 2.59 2.58 2.58 2.56 2.46 2.45 2.44 2.10 2.09
1.69 1.68 1.67 1.66 1.66 1.65 1.64 1.63 1.63 1.57 1.56 1.55 1.54 1.54 1.53 1.53 1.53 1.52 1.52 1.51 1.51 1.51
E (dd) 7.50
C (ddd) 7.03
D (m) 7.22
B (m) 5.51
A (ddq) 5.28
H (m) 2.45
I (ddd) 2.75
J (dddd) 2.61
G (s) 2.10
F (dd) 1.68
K (dddd) 1.52
L (m) 1.64
1.06
2.38
1.14
1.19
1.00
1.37
2.08
2.23
3.15
3.76
0.69
1.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical Shift (ppm)
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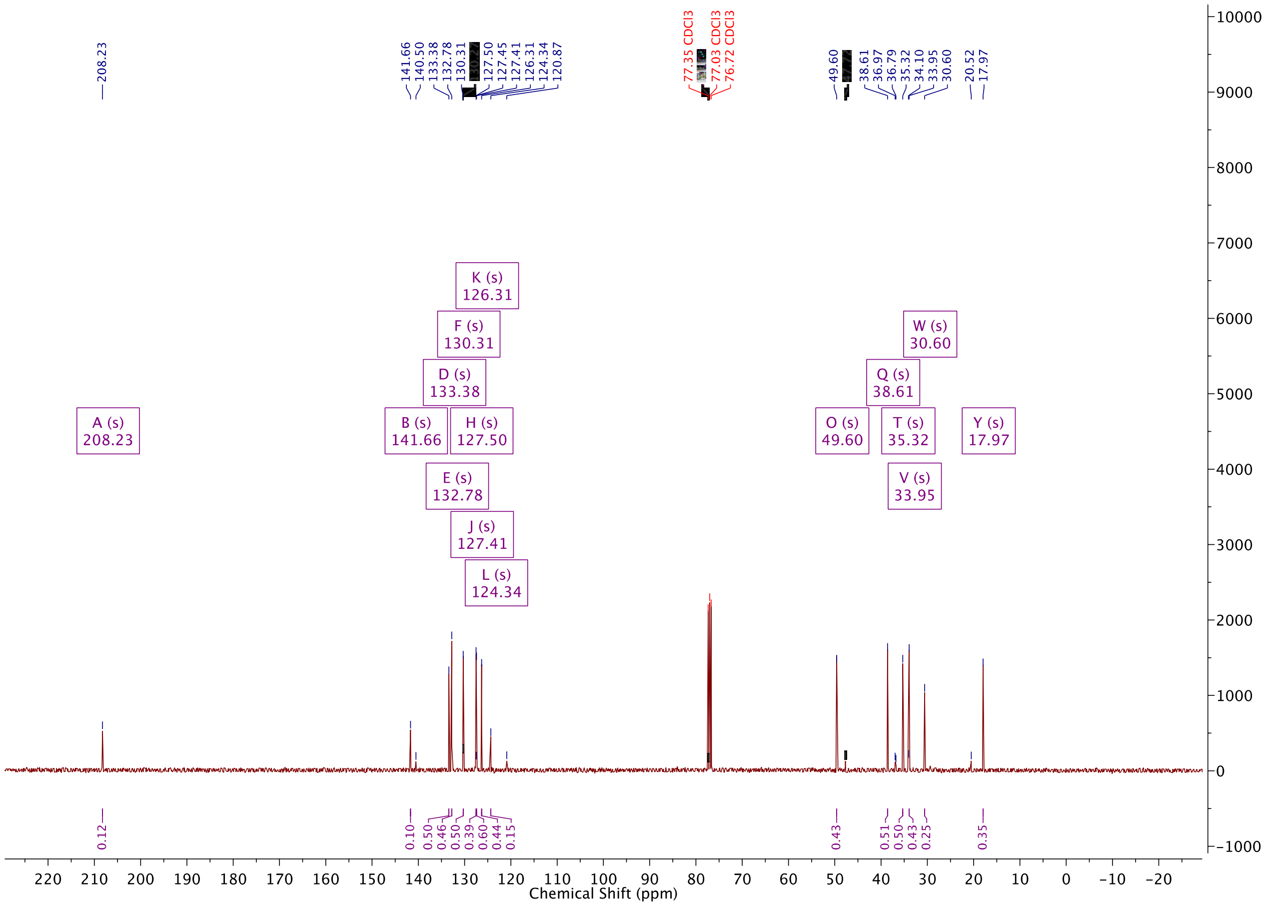
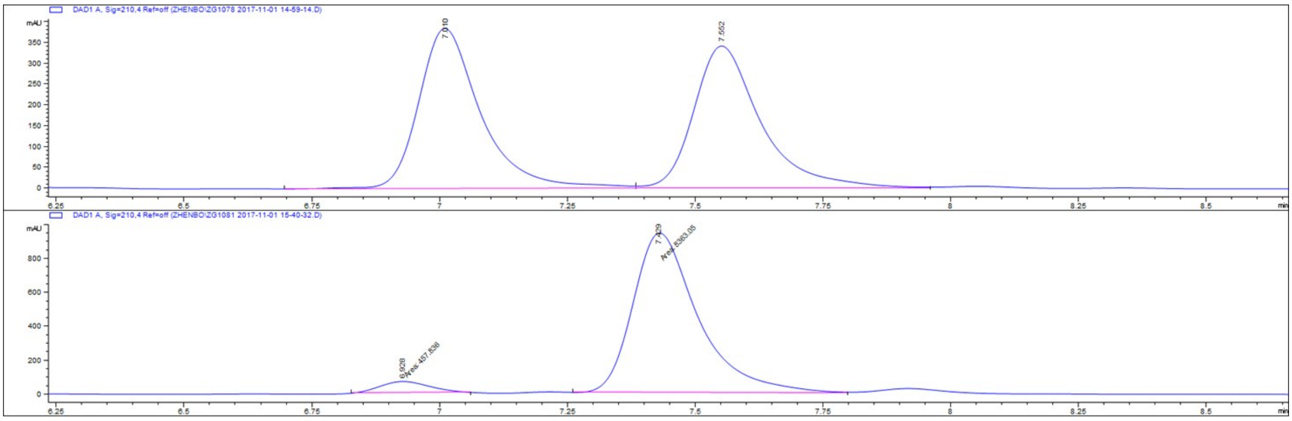
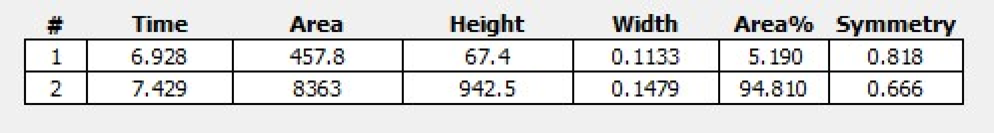

208.23
141.66 140.50 133.38 132.78 130.31 127.50 127.45 127.41 126.31 124.34 120.87
77.35 CDCl3
77.03 CDCl3
76.72 CDCl3
49.60 38.61 36.97 36.79 35.32 34.10 33.95 30.60 20.52 17.97
K (s) 126.31
F (s) 130.31
D (s) 133.38
A (s) 208.23
B (s) 141.66
H (s) 127.50
E (s) 132.78
J (s) 127.41
L (s) 124.34
W (s) 30.60
Q (s) 38.61
O (s) 49.60
T (s) 35.32
V (s) 33.95
Y (s) 17.97
0.12
0.10 0.50 0.46 0.50 0.39 0.60 0.44 0.15
0.43
0.51 0.50 0.43 0.25
0.35
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
Chemical Shift (ppm)
10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 −1000

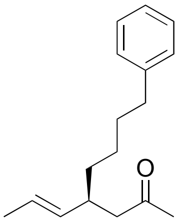
HPCL trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.928 | 457.8 | 67.4 | 0.1133 | 5.190 | 0.818 |
| 2 | 7.429 | 8363 | 942.5 | 0.1479 | 94.810 | 0.666 |

## (+)-(*S*, E)-8-phenyl-4-(prop-1-en-1-yl) octan-2-one (3i)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of but-3-en-1-ylbenzene (0.08 ml, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-hepta-3,5-dien-2-one (22 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (30 mg, 12 mmol, 61%).

The enantiomeric excess of 97% was determined by SFC [Chiralpak® IG; 1500 psi, 30°C; 1% to 30% MeOH in 5 mins; flow: 1.5 ml/min; λ= 243 nm; minor enantiomer tR = 2.36 mins, major enantiomer tR = 2.23 mins]

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.12 – 7.01 (m, 2H, Ar-*H*), 7.01 – 6.86 (m, 3H, Ar-*H*), 5.32 – 5.11 (m, 1H, C*H*), 5.08 – 4.87 (m, 1H, C*H*), 2.37 (td, *J* = 7.8 Hz, 3.2 Hz, 2H, C*H*$_2$Ph), 2.26 (td, *J* = 8.2 Hz, 4.8 Hz, 1H, C*H*$CH_2COCH_3$), 2.23 – 2.06 (m, 2H, C*H*$_2$CO), 1.88 (s, 3H, COC*H*$_3$), 1.41 (dd, *J* = 6.4 Hz, 1.6 Hz, 3H, C*H*$_3$), 1.42 – 1.25 (m, 3H, C*H*$_2$), 1.24 – 0.93 (m, 3H, C*H*$_2$).

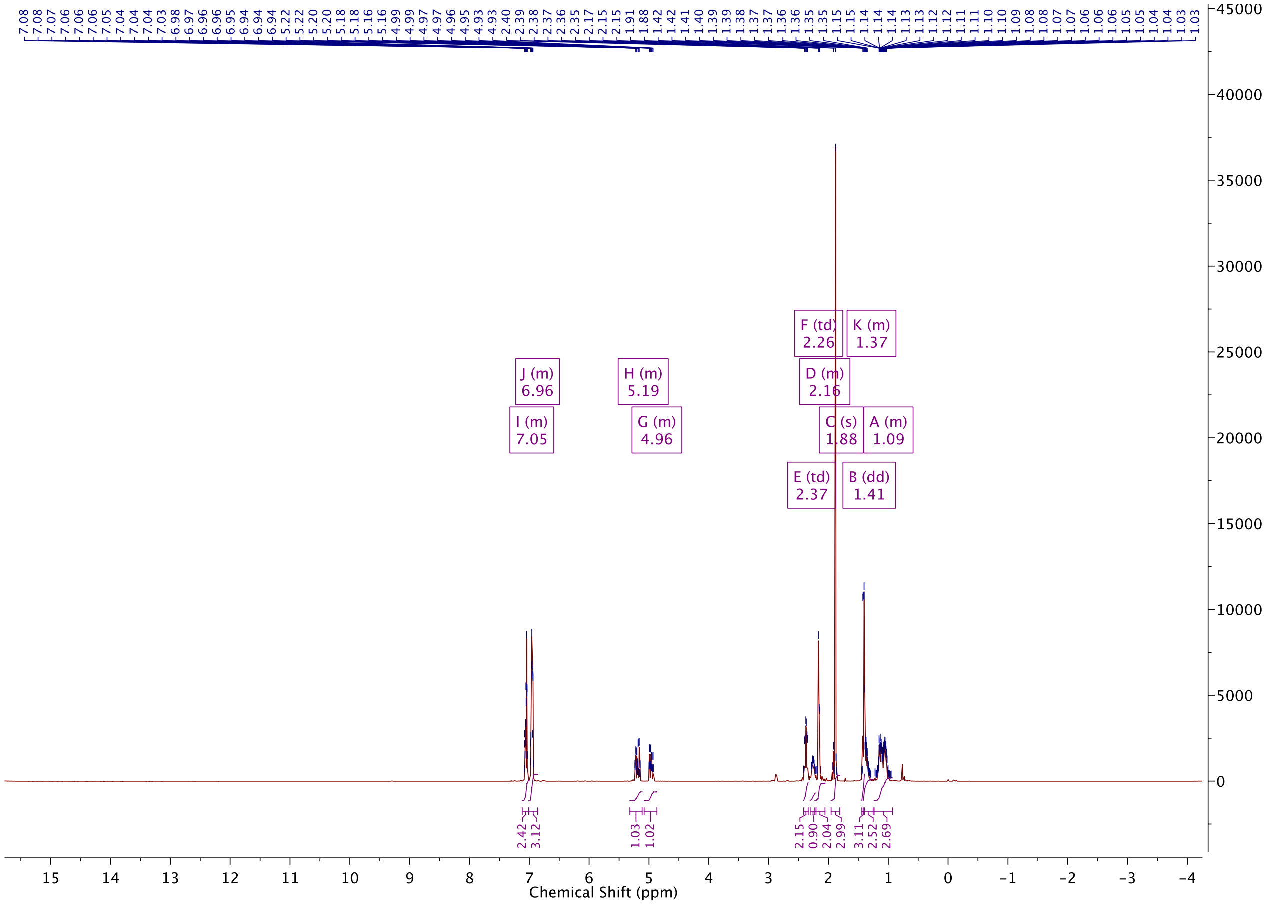
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 208.7, 142.7, 133.9, 128.4 (2C), 128.2 (2C), 125.6, 125.5, 49.8, 38.7, 35.9, 35.0, 31.4, 30.6, 26.8, 17.9.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1716, 1382,1153, 997

HRMS (ESI) m/z calc. for $C_{17}H_{25}O$ $[M+H]^+$: 245.1900, found: 245.1901

$[\alpha]^{20}_{589}$ = +1.3 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.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7.08
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1.03
1.03
F (td) 2.26
K (m) 1.37
J (m) 6.96
H (m) 5.19
D (m) 2.16
I (m) 7.05
G (m) 4.96
C (s) 1.88
A (m) 1.09
E (td) 2.37
B (dd) 1.41
2.42
3.12
1.03
1.02
2.15
0.90
2.04
2.99
3.11
2.52
2.69
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
15
14
13
12
11
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6
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4
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1
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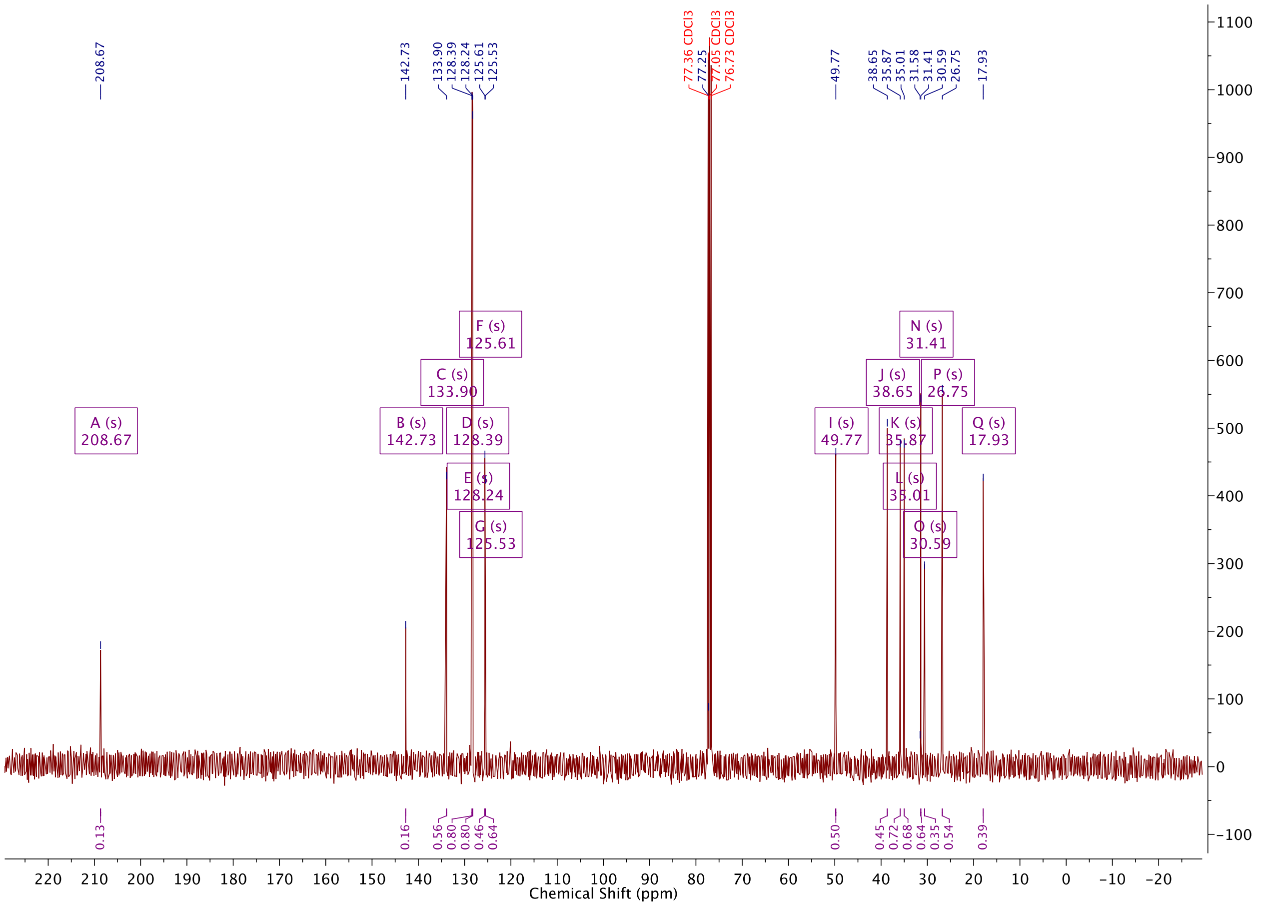
-1
-2
-3
-4
Chemical Shift (ppm)


208.67
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128.39
128.24
125.61
125.53
77.36 CDCl3
77.25
77.05 CDCl3
76.73 CDCl3
49.77
38.65
35.87
35.01
31.58
31.41
30.59
26.75
17.93
F (s) 125.61
C (s) 133.90
A (s) 208.67
B (s) 142.73
D (s) 128.39
E (s) 128.24
G (s) 125.53
N (s) 31.41
J (s) 38.65
P (s) 26.75
I (s) 49.77
K (s) 35.87
Q (s) 17.93
L (s) 35.01
O (s) 30.59
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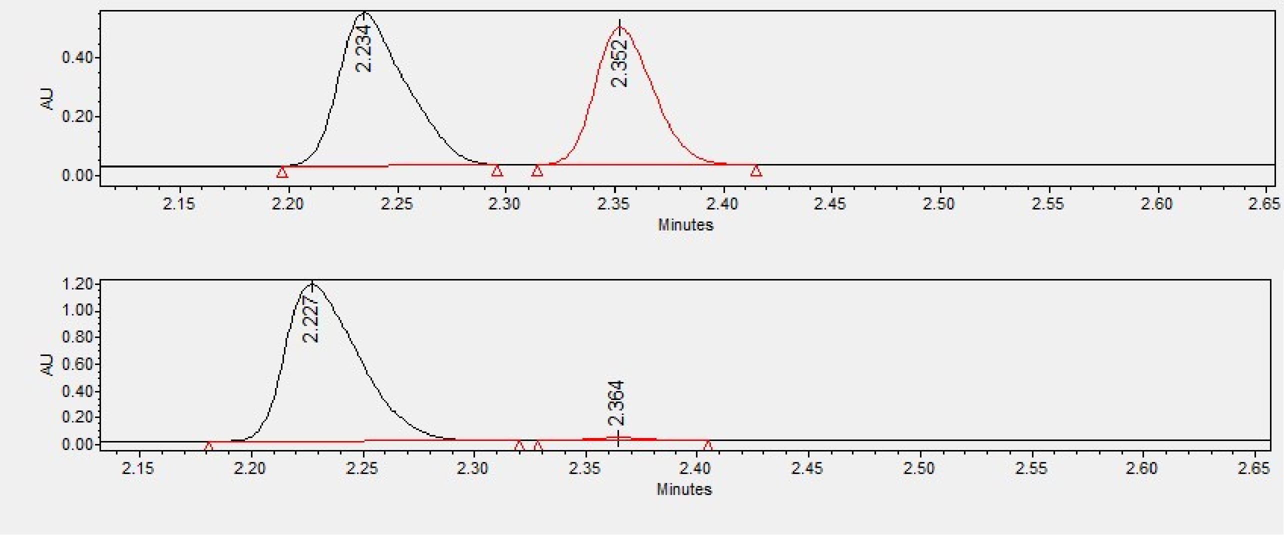
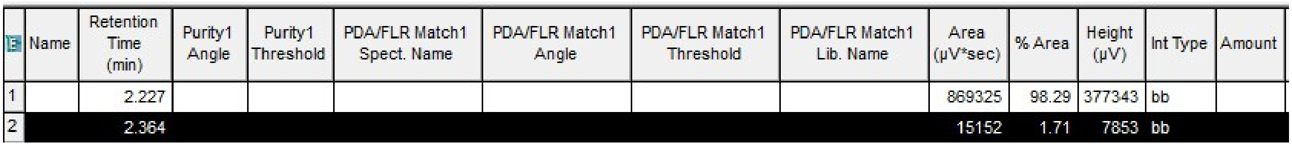
0.16
0.56
0.80
0.80
0.46
0.64
0.50
0.45
0.72
0.68
0.64
0.35
0.54
0.39
1100
1000
900
800
700
600
500
400
300
200
100
0
-100
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
Chemical Shift (ppm)

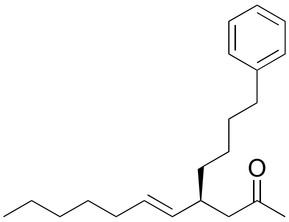
SFC trace





| | Name | Retention Time (min) | Purity1 Angle | Purity1 Threshold | PDA/FLR Match1 Spect. Name | PDA/FLR Match1 Angle | PDA/FLR Match1 Threshold | PDA/FLR Match1 Lib. Name | Area (µV*sec) | % Area | Height (µV) | Int Type | Amount |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | | 2.227 | | | | | | | 869325 | 98.29 | 377343 | bb | |
| 2 | | 2.364 | | | | | | | 15152 | 1.71 | 7853 | bb | |

## (+)-(*S*, E)-4-(4-phenylbutyl) undec-5-en-2-one (3j)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of but-3-en-1-ylbenzene (0.08 ml, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-undeca-3, 5-dien-2-one (33 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (39 mg, 13 mmol, 65%).

The enantiomeric excess of 97% was determined by SFC [Chiralpak® IG; 1500 psi, 30°C; 1% to 30% MeOH in 5 mins; flow: 1.5 ml/min; λ= 210 nm; minor enantiomer tR = 2.99 mins, major enantiomer tR = 2.58 mins]

$^1$H NMR (400 MHz, Chloroform-d) $\delta_H$/ppm 7.27 – 7.19 (m, 2H, Ar-*H*), 7.13 (td, m, 3H, Ar-*H*), 5.47 – 5.25 (m, 1H, C*H*), 5.10 (m, 1H, C*H*), 2.54 (tt, J = 8.9 Hz, 6.7 Hz, 2H, $CH_2Ph$), 2.48 – 2.39 (m, 1H, $CHCH_2COCH_3$), 2.37 – 2.26 (m, 2H, $CH_2CO$), 2.05 (s, 3H, $COCH_3$), 1.98 – 1.83 (m, 2H, $CH_2CH{=}CH$), 1.63 – 1.43 (m, 2H, $CH_2$), 1.39 – 1.08 (m, 10H, 5 x $CH_2$), 0.84 (t, J = 7.0 Hz, 3H, $CH_3$).

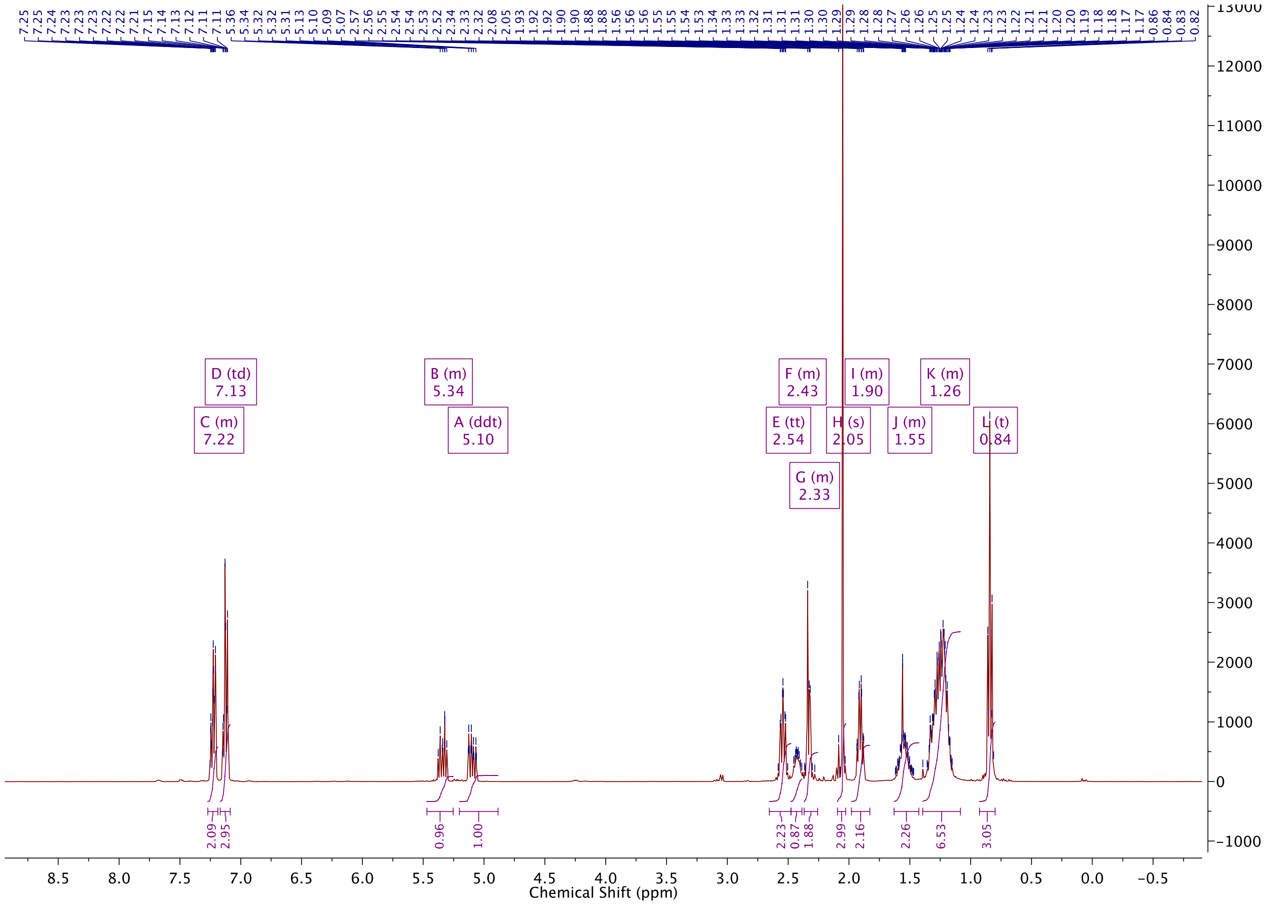
$^{13}$C NMR (101 MHz, Chloroform-d) $\delta_C$/ppm 208.7, 142.7, 132.6, 131.4, 128.4 (2C), 128.2 (2C), 125.6, 49.9, 38.8, 35.9, 35.0, 32.5, 31.4, 31.4, 30.6, 29.2, 26.8, 22.5, 14.1

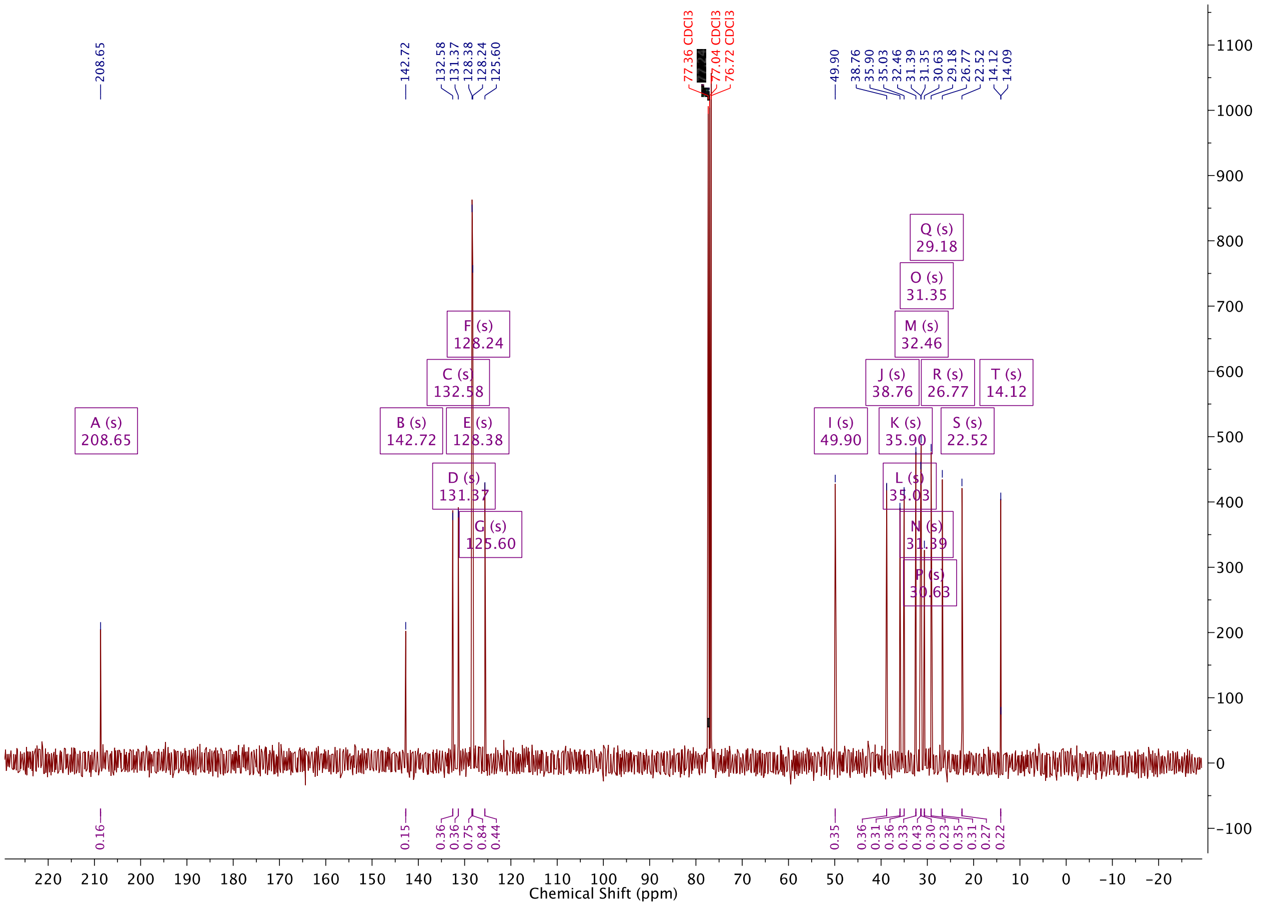
IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1715, 1382,1153, 954

HRMS (ESI) m/z calc. for $C_{21}H_{33}O$ $[M+H]^+$: 301.2526, found: 301.2524

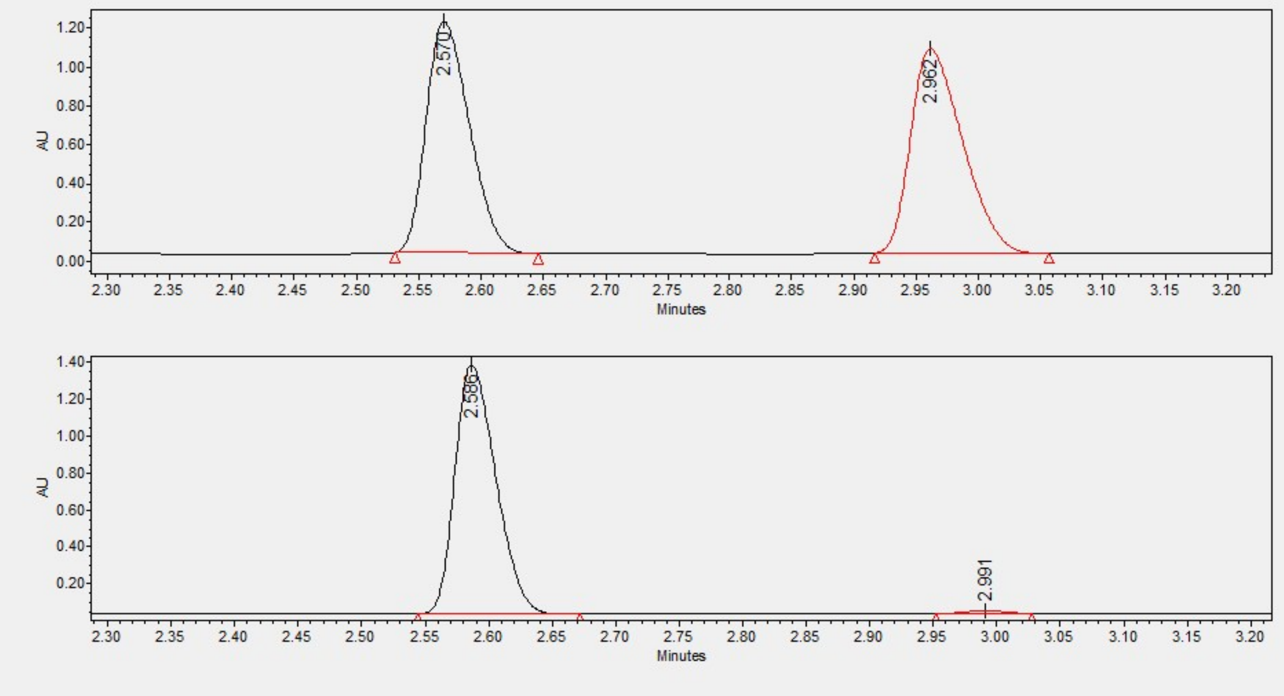
$[\alpha]^{20}_{589}$ = +1.8 ° (c 1.0, $CHCl_3$)

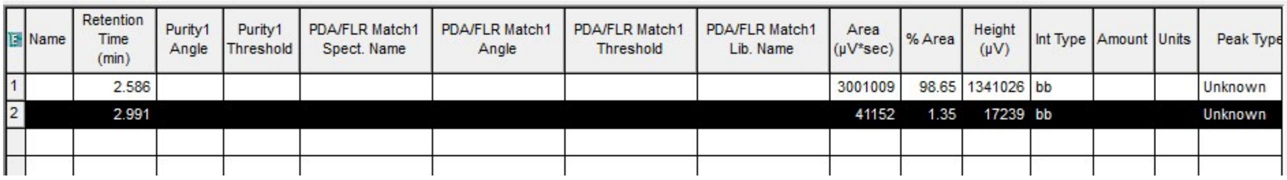
Absolute configuration assigned by analogy to **3p**.


D (td) 7.13
C (m) 7.22
B (m) 5.34
A (ddt) 5.10
F (m) 2.43
E (tt) 2.54
G (m) 2.33
H (s) 2.05
I (m) 1.90
J (m) 1.55
K (m) 1.26
L (t) 0.84
2.09
2.95
0.96
1.00
2.23
0.87
1.88
2.99
2.16
2.26
6.53
3.05
Chemical Shift (ppm)


208.65
142.72
132.58
131.37
128.38
128.24
125.60
77.36 CDCl3
77.04 CDCl3
76.72 CDCl3
49.90
38.76
35.90
35.03
32.46
31.39
31.35
30.63
29.18
26.77
22.52
14.12
14.09
A (s) 208.65
B (s) 142.72
C (s) 132.58
D (s) 131.37
E (s) 128.38
F (s) 128.24
G (s) 125.60
I (s) 49.90
J (s) 38.76
K (s) 35.90
L (s) 35.03
M (s) 32.46
N (s) 31.39
O (s) 31.35
P (s) 30.63
Q (s) 29.18
R (s) 26.77
S (s) 22.52
T (s) 14.12
Chemical Shift (ppm)

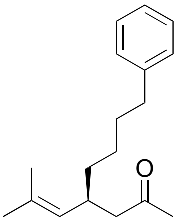
SFC trace





| E | Name | Retention Time (min) | Purity1 Angle | Purity1 Threshold | PDA/FLR Match1 Spect. Name | PDA/FLR Match1 Angle | PDA/FLR Match1 Threshold | PDA/FLR Match1 Lib. Name | Area (µV*sec) | % Area | Height (µV) | Int Type | Amount | Units | Peak Type |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 |  | 2.586 |  |  |  |  |  |  | 3001009 | 98.65 | 1341026 | bb |  |  | Unknown |
| 2 |  | 2.991 |  |  |  |  |  |  | 41152 | 1.35 | 17239 | bb |  |  | Unknown |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |

### (+)-(*S*)-4-(2-methylprop-1-en-1-yl)-8-phenyloctan-2-one (3k)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of but-3-en-1-ylbenzene (0.08 ml, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before ((E)-6-methylhepta-3, 5-dien-2-one (25 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (45 mg, 17 mmol, 87%).

HPLC analysis indicated an enantiomeric excess of 92 % [Chiralpak® AYH; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1.0; λ = 210 nm; major enantiomer tR = 7.24 min; minor enantiomer, tR = 6.97 min].

$^1$H NMR (400 MHz, Chloroform-d) $\delta_H$/ppm 7.16 – 6.99 (m, 2H, Ar-*H*), 7.00 – 6.87 (m, 3H, Ar-*H*), 4.59 (dp, J = 9.8 Hz, 1.4 Hz, 1H, C*H*), 2.63 – 2.43 (m, 1H, C*H*$CH_2COCH_3$), 2.43 – 2.28 (m, 2H, C$H_2$Ph), 2.11 (qd, J = 15.1 Hz, 7.0 Hz, 2H, C$H_2$CO), 1.86 (s, 3H, COC$H_3$), 1.42 (m, 7H, 2 x C$H_3$, $CH_2$), 1.40 – 1.26 (m, 1H, $CH_2$), 1.25 – 0.91 (m, 4H, $CH_2$).

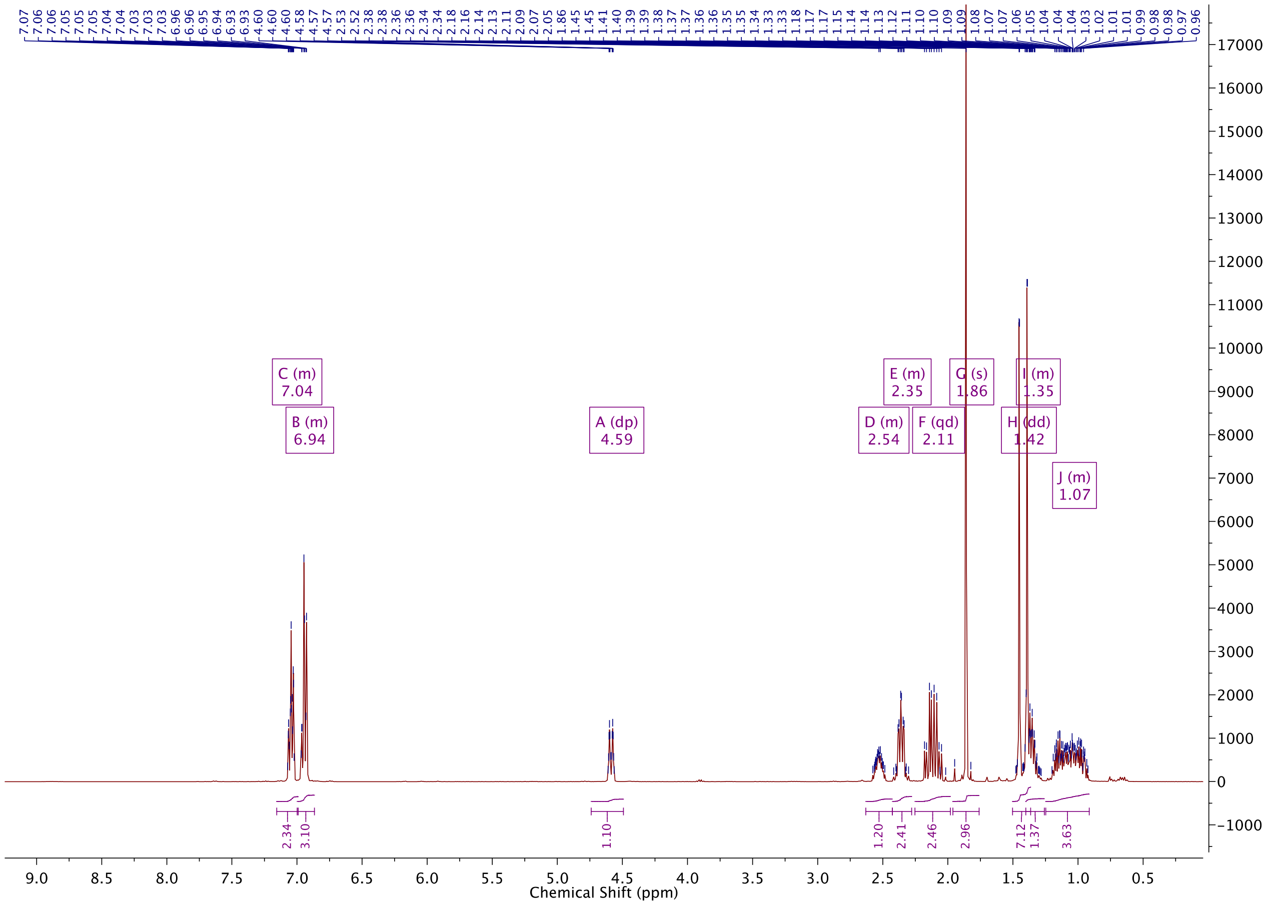
$^{13}$C NMR (101 MHz, Chloroform-d) $\delta_C$/ppm 208.8, 142.8, 132.2, 128.4 (2C), 128.2 (2C), 128.1, 125.6, 50.1, 35.9, 35.7, 34.4, 31.6, 30.6, 26.9, 25.8, 18.2.

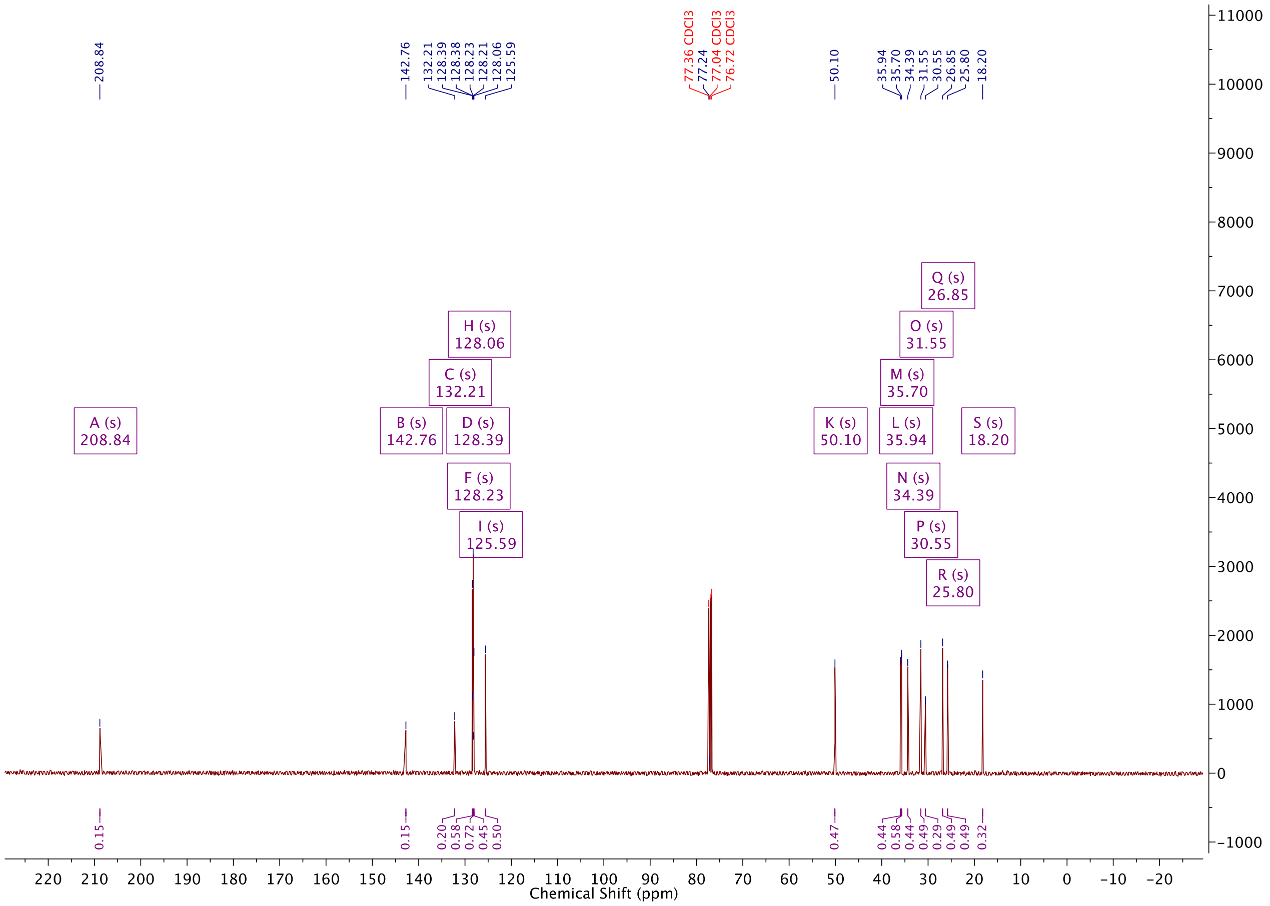
IR ($\nu_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1716, 1382,1153, 966

HRMS (ESI) m/z calc. for $C_{18}H_{27}O$ $[M+H]^+$: 259.2056, found: 259.2058

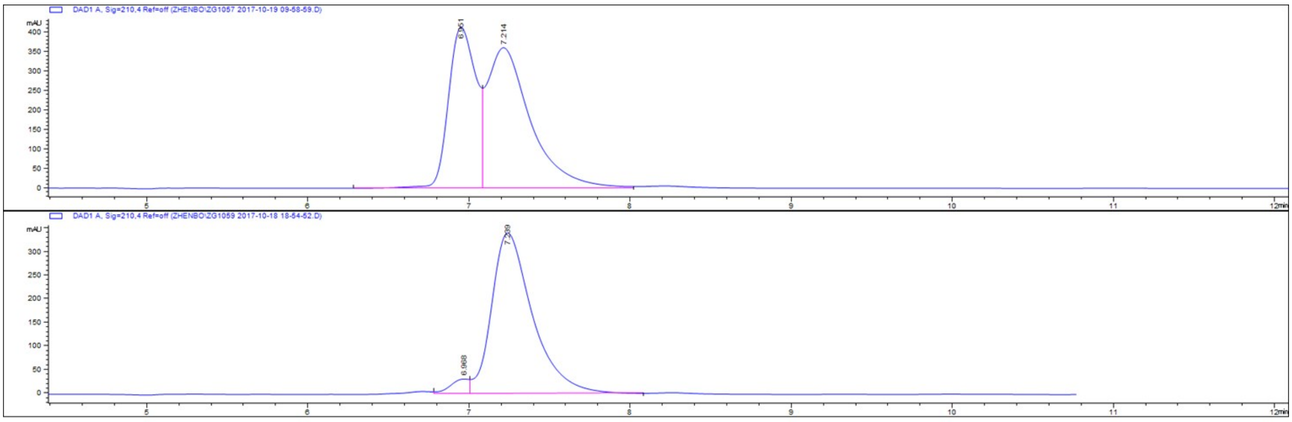
$[\alpha]^{20}_{589}$ = +9.9 ° (c 1.0, $CHCl_3$)

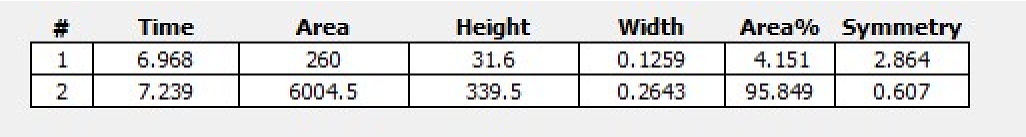
Absolute configuration assigned by analogy to **3p**.


7.07 7.06 7.06 7.05 7.05 7.04 7.04 7.03 7.03 7.03 6.96 6.96 6.95 6.94 6.93 6.93 4.60 4.60 4.58 4.57 4.57 2.53 2.52 2.38 2.38 2.36 2.36 2.34 2.34 2.18 2.16 2.14 2.13 2.11 2.09 2.07 2.05 1.86 1.45 1.45 1.41 1.40 1.39 1.39 1.38 1.37 1.37 1.36 1.36 1.35 1.35 1.34 1.33 1.33 1.18 1.17 1.17 1.15 1.14 1.14 1.13 1.12 1.11 1.10 1.10 1.09 1.09 1.08 1.07 1.06 1.05 1.04 1.04 1.04 1.03 1.02 1.01 1.01 0.99 0.98 0.98 0.97 0.96
C (m) 7.04
B (m) 6.94
A (dp) 4.59
E (m) 2.35
D (m) 2.54
G (s) 1.86
F (qd) 2.11
I (m) 1.35
H (dd) 1.42
J (m) 1.07
2.34
3.10
1.10
1.20
2.41
2.46
2.96
7.12
1.37
3.63
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)
17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 −1000


208.84
142.76
132.21 128.39 128.38 128.23 128.21 128.06 125.59
77.36 CDCl3 77.24 77.04 CDCl3 76.72 CDCl3
50.10
35.94 35.70 34.39 31.55 30.55 26.85 25.80
18.20
A (s) 208.84
B (s) 142.76
C (s) 132.21
H (s) 128.06
D (s) 128.39
F (s) 128.23
I (s) 125.59
K (s) 50.10
L (s) 35.94
M (s) 35.70
N (s) 34.39
O (s) 31.55
P (s) 30.55
Q (s) 26.85
R (s) 25.80
S (s) 18.20
0.15
0.15
0.20 0.58 0.72 0.45 0.45 0.50
0.47
0.44 0.58 0.44 0.49 0.29 0.49 0.49 0.32
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
Chemical Shift (ppm)
11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 −1000

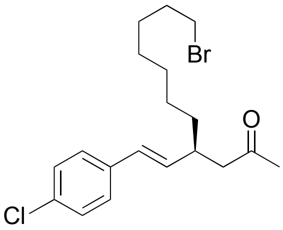
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.968 | 260 | 31.6 | 0.1259 | 4.151 | 2.864 |
| 2 | 7.239 | 6004.5 | 339.5 | 0.2643 | 95.849 | 0.607 |

### (+)-(*S*, E)-11-bromo-4- (4-chlorostyryl) undecan-2-one (3m)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 7-bromohept-1-ene (89 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-6-(4-chlorophenyl)hexa-3,5-dien-2-one (41 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 70:30; $SiO_2$) to give the desired product (41 mg, 11 mmol, 53%).

HPLC analysis indicated an enantiomeric excess of 47 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 95: 5.0; λ = 210 nm; major enantiomer tR = 7.68 min; minor enantiomer, tR = 8.08 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.23 (s, 4H, Ar-*H*), 6.31 (dd, *J* = 15.8 Hz, 0.9 Hz, 1H, C*H*), 5.95 (dd, *J* = 15.8 Hz, 8.7 Hz, 1H, C*H*), 3.37 (t, *J* = 6.8 Hz, 2H, $CH_2Br$), 2.81 – 2.58 (m, 1H, C*H* $CH_2COCH_3$), 2.58 – 2.42 (m, 2H, $CH_2COCH_3$), 2.11 (s, 3H, $COCH_3$), 2.00 – 1.71 (m, 2H, $CH_2$), 1.51 – 1.05 (m, 10H, 5 x $CH_2$).

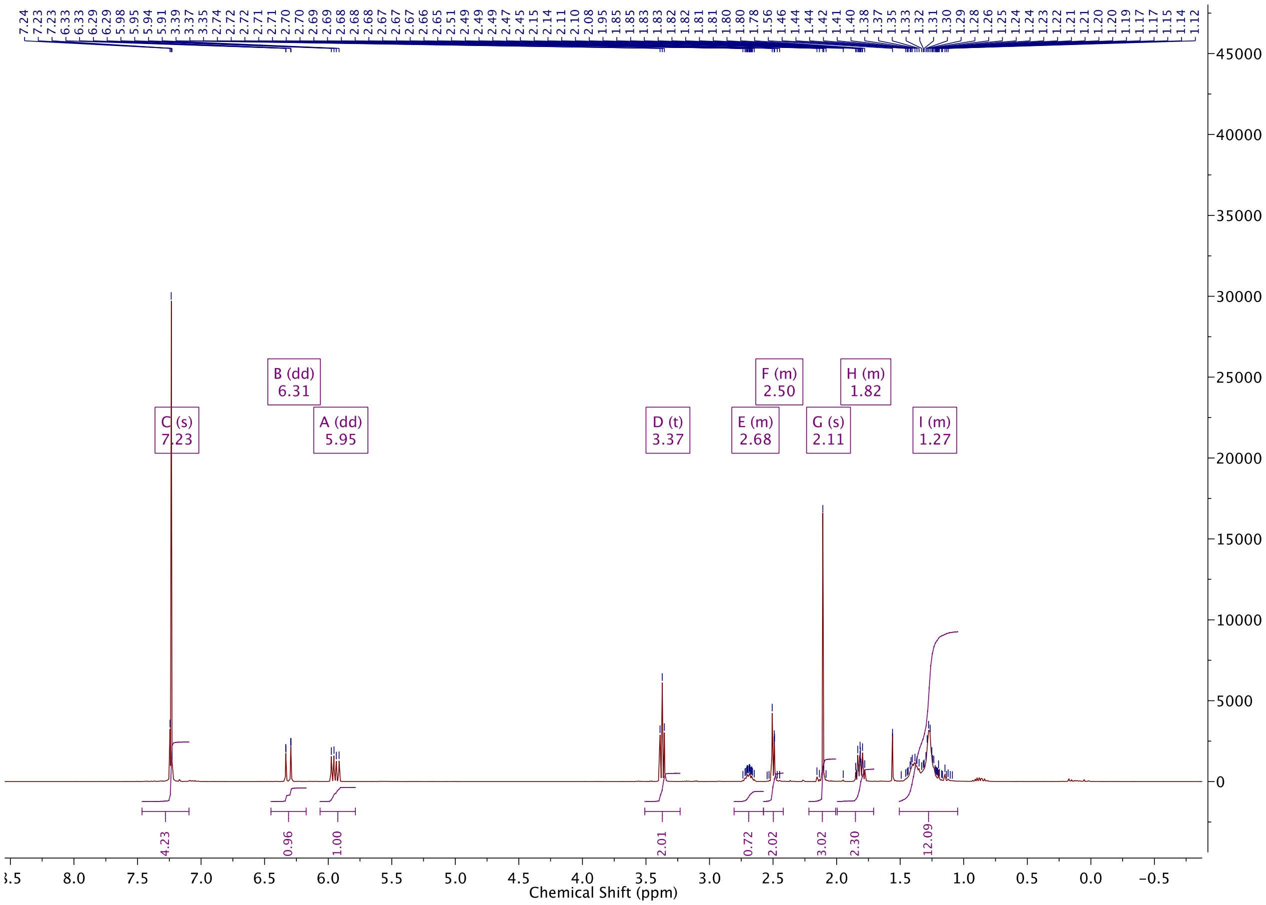
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 207.9, 135.8, 133.9, 132.7, 129.1, 128.6 (2C), 127.3 (2C), 49.4, 38.8, 34.9, 34.0, 32.8, 30.7, 29.4, 28.7, 28.1, 27.1.

IR ($v_{max}$/$cm^{-1}$, $CHCl_3$) 2981, 2929, 1716, 1490, 1091, 967

HRMS (ESI) m/z calc. for $C_{19}H_{27}O^{79}Br^{35}Cl$ $[M+H]^+$: 385.0928, 387.0908, 389.0878, 390.0912 found: 385.0928, 387.0905, 389.0879, 390.0911

$[\alpha]^{20}_{589}$ = +3.2 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.


7.24
7.23
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6.29
6.29
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5.94
5.91
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3.35
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1.29
1.28
1.26
1.25
1.24
1.24
1.23
1.22
1.21
1.21
1.20
1.20
1.19
1.17
1.17
1.15
1.14
1.12
B (dd) 6.31
C (s) 7.23
A (dd) 5.95
D (t) 3.37
F (m) 2.50
E (m) 2.68
G (s) 2.11
H (m) 1.82
I (m) 1.27
4.23
0.96
1.00
2.01
0.72
2.02
3.02
2.30
12.09
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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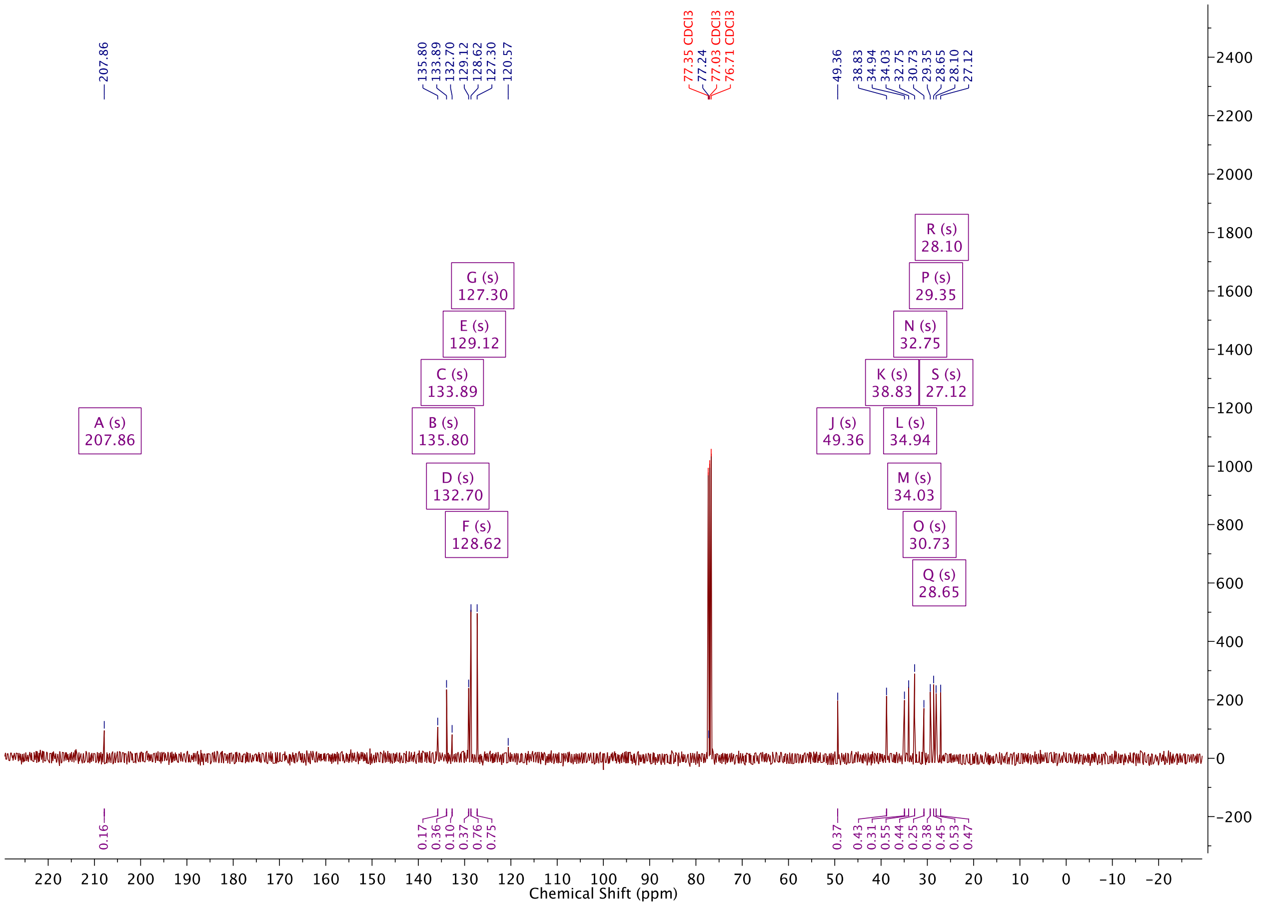
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
Chemical Shift (ppm)


207.86
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132.70
129.12
128.62
127.30
120.57
77.35 CDCl3
77.24
77.03 CDCl3
76.71 CDCl3
49.36
38.83
34.94
34.03
32.75
30.73
29.35
28.65
28.10
27.12
A (s) 207.86
B (s) 135.80
C (s) 133.89
D (s) 132.70
E (s) 129.12
F (s) 128.62
G (s) 127.30
J (s) 49.36
K (s) 38.83
L (s) 34.94
M (s) 34.03
N (s) 32.75
O (s) 30.73
P (s) 29.35
Q (s) 28.65
R (s) 28.10
S (s) 27.12
0.16
0.17
0.36
0.10
0.37
0.76
0.75
0.37
0.43
0.31
0.55
0.44
0.25
0.38
0.45
0.53
0.47
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
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200
190
180
170
160
150
140
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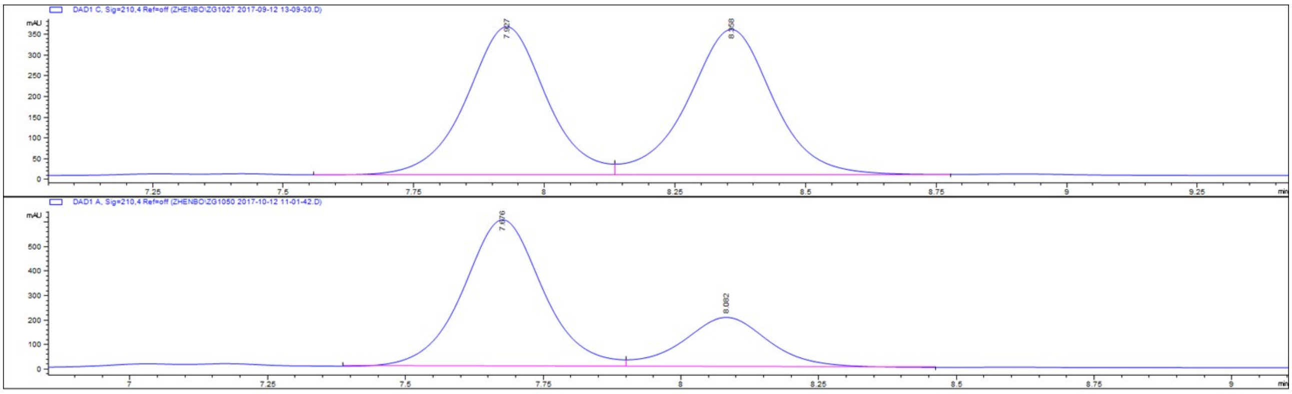
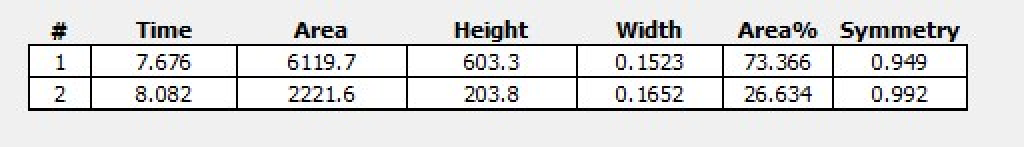
20
10
0
-10
-20
Chemical Shift (ppm)

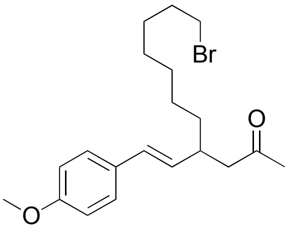
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.676 | 6119.7 | 603.3 | 0.1523 | 73.366 | 0.949 |
| 2 | 8.082 | 2221.6 | 203.8 | 0.1652 | 26.634 | 0.992 |

### (+)-(E)-11-bromo-4- (4-methoxystyryl)undecan-2-one (3n)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 7-bromohept-1-ene (89 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-6-(4-methoxyphenyl) hexa-3, 5-dien-2-one (40 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 70:30; $SiO_2$) to give the desired product (40 mg, 14 mmol, 70%).

HPLC analysis indicated an enantiomeric excess of 43 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 95: 5.0; λ = 254 nm; major enantiomer tR = 8.94 min; minor enantiomer, tR = 9.75 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.28 – 6.97 (m, 2H, Ar-*H*), 6.80 – 6.50 (m, 2H, Ar-*H*), 6.16 (d, *J* = 15.8 Hz, 1H, C*H*), 5.68 (dd, *J* = 15.8 Hz, 8.7 Hz, 1H, C*H*), 3.63 (s, 3H,O C*H*$_3$ ), 3.23 (t, *J* = 6.9 Hz, 2H, C*H$_2$*Br), 2.52 (t, *J* = 7.7 Hz, 1H, C*H*), 2.35 (d, *J* = 6.9 Hz, 2H, C*H$_2$*$COCH_3$), 1.97 (s, 3H, COC*H*$_3$), 1.78 – 1.53 (m, 2H, C*H$_2$*), 1.44 – 0.87 (m, 10H, 5 x C*H$_2$*).

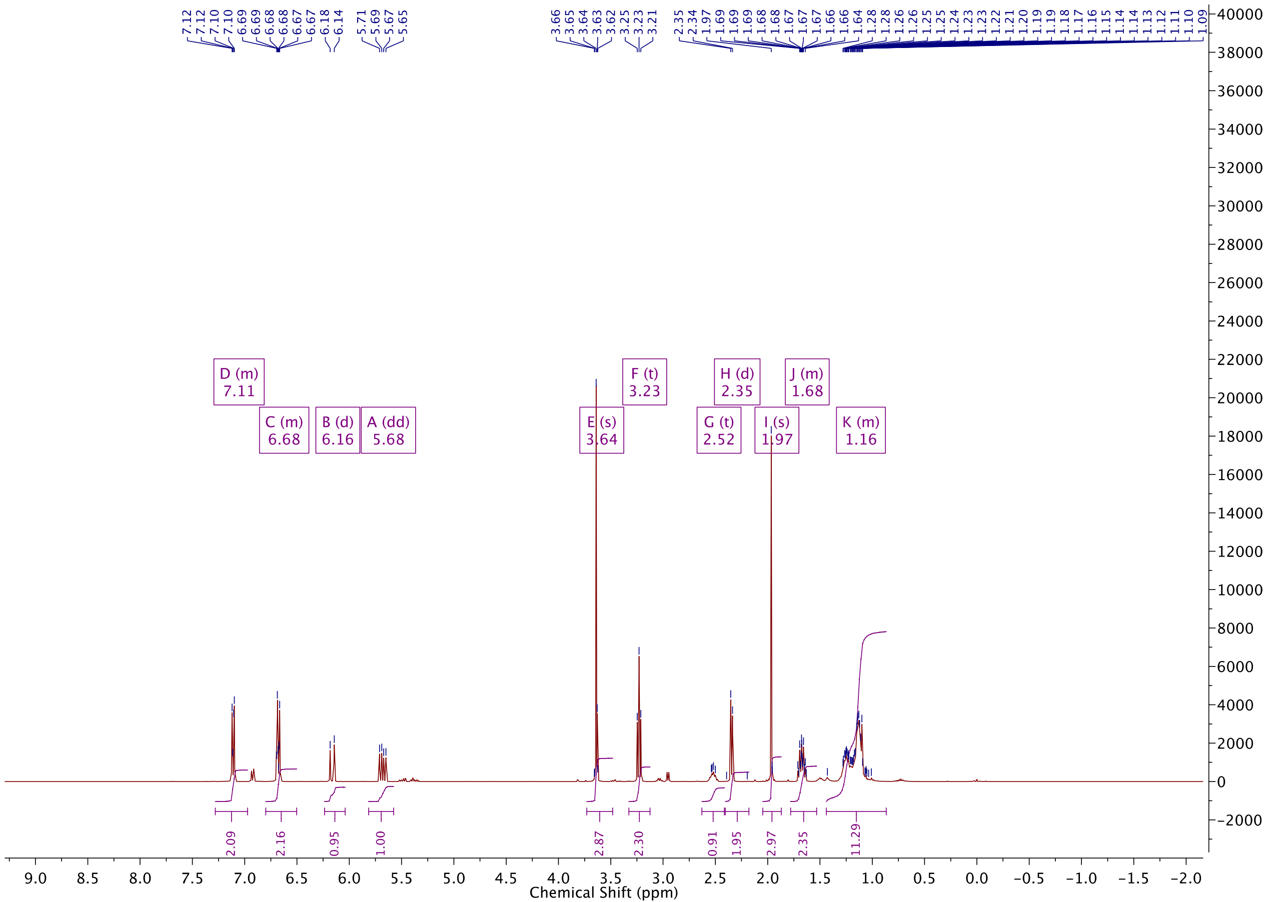
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 208.2, 158.9, 131.0, 130.2, 129.6, 127.2 (2C), 113.9 (2C), 55.3, 49.7, 39.0, 35.1, 34.0, 32.8, 30.7, 29.4, 28.7, 28.1, 27.1.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2927, 2853, 1713, 1510, 1247, 968

HRMS (ESI) m/z calc. for $C_{20}H_{30}O_2{}^{79}Br$ $[M+H]^+$: 381.1424, 383.1403 found: 381.1427, 383.1406

$[\alpha]^{20}_{589}$ = +6.5 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.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7.10
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3.66
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3.64
3.63
3.62
3.25
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1.64
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1.25
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1.23
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1.22
1.21
1.20
1.19
1.19
1.18
1.17
1.16
1.15
1.14
1.14
1.13
1.12
1.11
1.10
1.09
D (m) 7.11
C (m) 6.68
B (d) 6.16
A (dd) 5.68
E (s) 3.64
F (t) 3.23
G (t) 2.52
H (d) 2.35
I (s) 1.97
J (m) 1.68
K (m) 1.16
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2.16
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1.00
2.87
2.30
0.91
1.95
2.97
2.35
11.29
9.0
8.5
8.0
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7.0
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6.0
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4.0
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3.0
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2.0
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−1.0
−1.5
−2.0
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36000
34000
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6000
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2000
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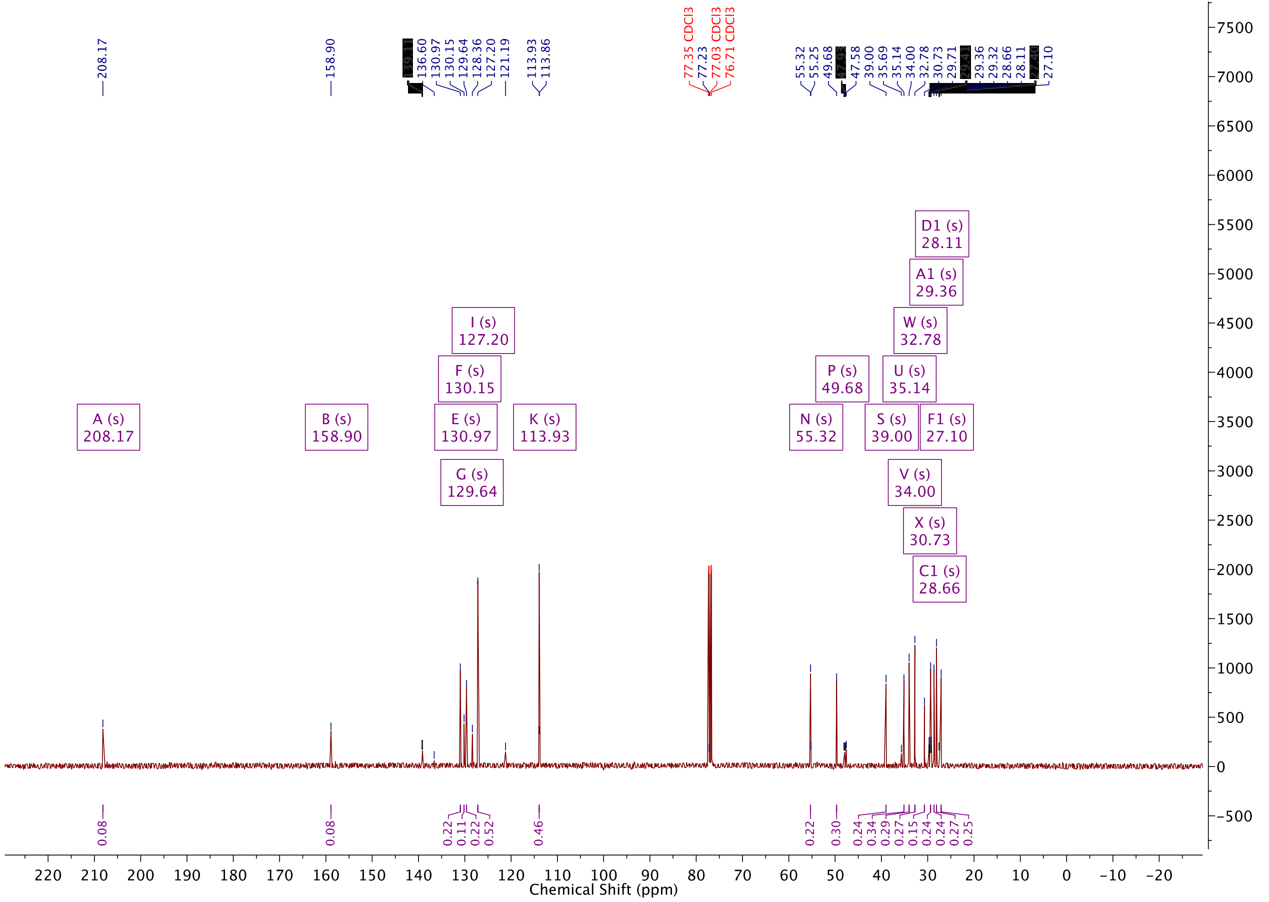
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136.60
130.97
130.15
129.64
128.36
127.20
121.19
113.93
113.86
77.35 CDCl3
77.23
77.03 CDCl3
76.71 CDCl3
55.32
55.25
49.68
47.58
39.00
35.69
35.14
34.00
32.78
30.73
29.71
29.36
29.32
28.66
28.11
27.10
A (s) 208.17
B (s) 158.90
E (s) 130.97
F (s) 130.15
G (s) 129.64
I (s) 127.20
K (s) 113.93
N (s) 55.32
P (s) 49.68
S (s) 39.00
U (s) 35.14
V (s) 34.00
W (s) 32.78
X (s) 30.73
A1 (s) 29.36
C1 (s) 28.66
D1 (s) 28.11
F1 (s) 27.10
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0.08
0.22
0.11
0.22
0.52
0.46
0.22
0.30
0.24
0.34
0.29
0.27
0.15
0.24
0.24
0.27
0.25
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200
190
180
170
160
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130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
Chemical Shift (ppm)
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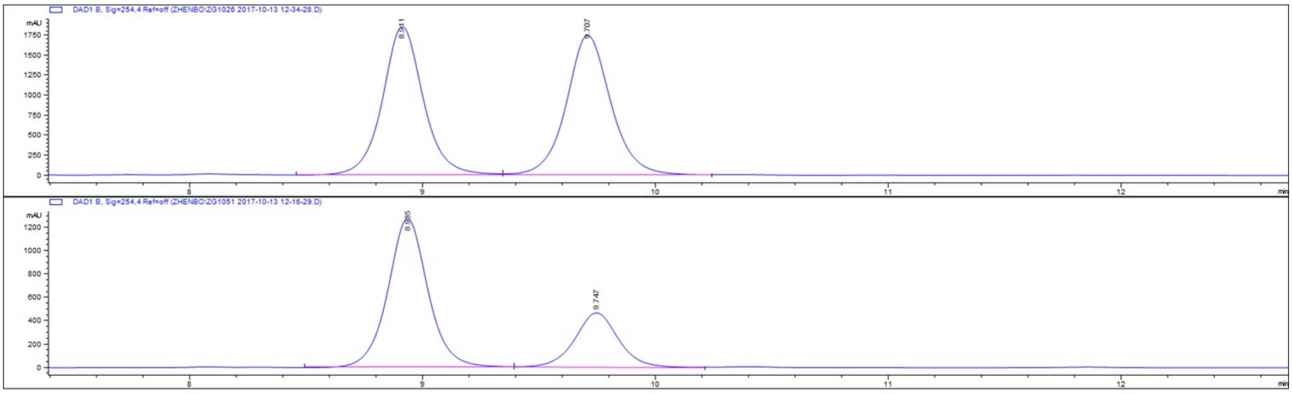
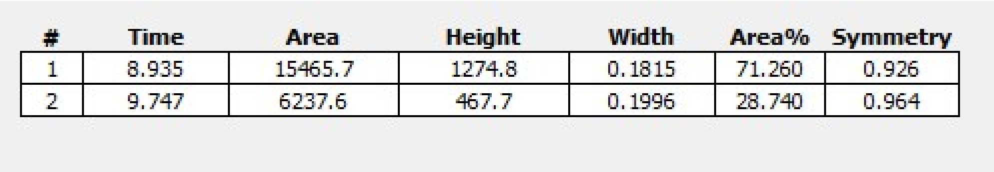
3500
3000
2500
2000
1500
1000
500
0
−500

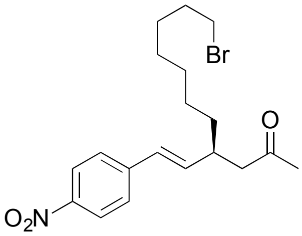
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 8.935 | 15465.7 | 1274.8 | 0.1815 | 71.260 | 0.926 |
| 2 | 9.747 | 6237.6 | 467.7 | 0.1996 | 28.740 | 0.964 |

### (+)-(*S*, E)-11-bromo-4- (4-nitrostyryl) undecan-2-one (3o)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 7-bromohept-1-ene (89 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (3E, 5E)-6-(4-nitrophenyl) hexa-3, 5-dien-2-one (43 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$.

The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 70:30; $SiO_2$) to give the desired product (49 mg, 12 mmol, 62%).

HPLC analysis indicated an enantiomeric excess of 86 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 96: 4.0; λ = 210 nm; major enantiomer tR = 19.55 min; minor enantiomer, tR = 21.13 min].

$^1H$ NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 8.32 – 7.98 (m, 2H, Ar-*H*), 7.56 – 7.38 (m, 2H, Ar-*H*), 6.45 (d, *J* = 15.9 Hz, 1H, C*H*), 6.20 (dd, *J* = 15.9 Hz, 8.7 Hz, 1H, C*H*), 3.39 (t, *J* = 6.8, 2H, C*H₂*Br), 2.97 – 2.69 (m, 1H, C*H*), 2.67 – 2.38 (m, 2H, $CH_2COCH_3$), 2.14 (s, 3H, $COCH_3$), 1.95 – 1.70 (m, 2H, $CH_2$), 1.64 – 0.96 (m, 10H, 5 x $CH_2$).

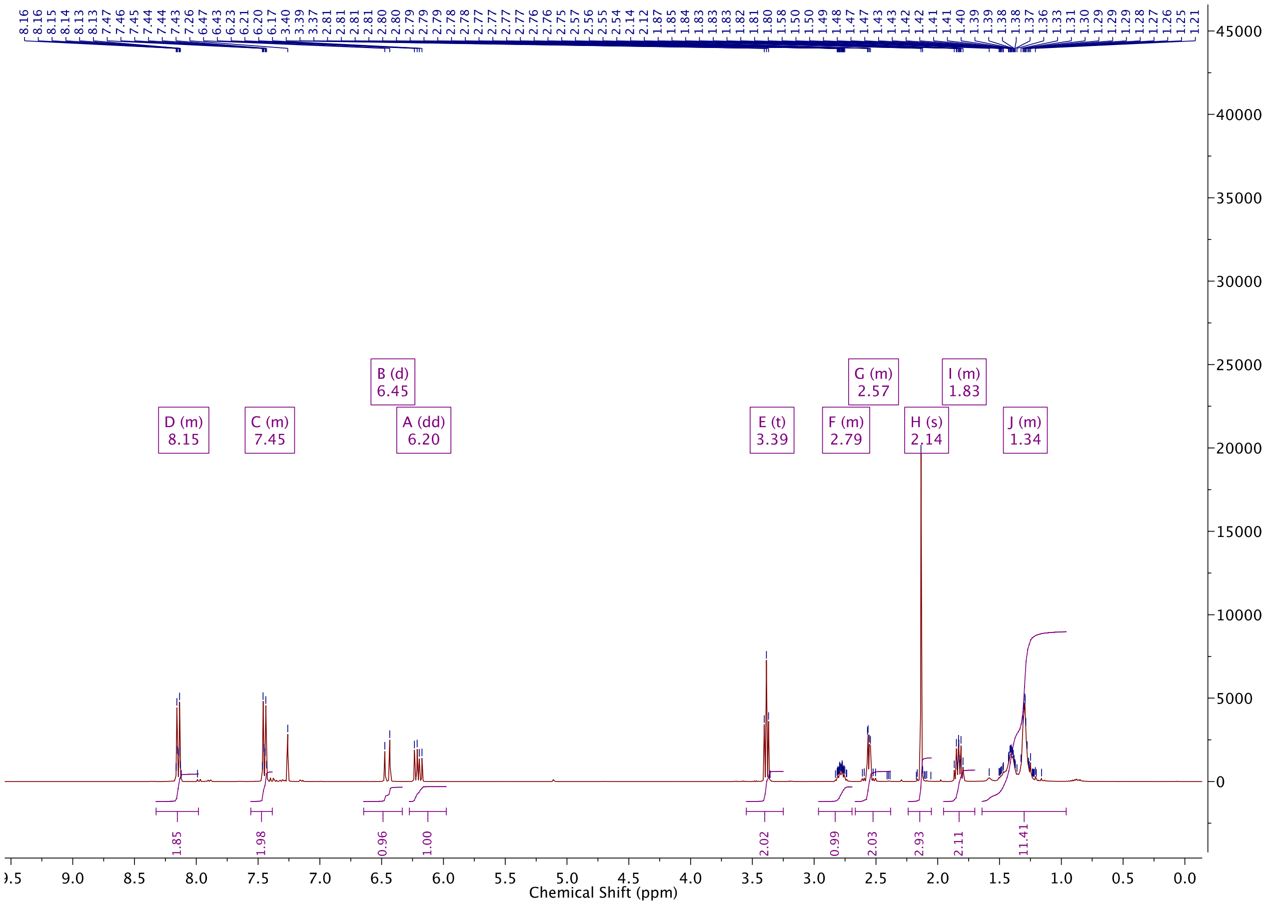
$^{13}C$ NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 207.3, 146.7, 143.8, 138.5, 128.6, 126.6 (2C), 124.0 (2C), 48.9, 38.8, 34.7, 34.0, 32.7, 30.7, 29.3, 28.6, 28.1, 27.1.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 2930, 1716, 1515, 1341,968

HRMS (ESI) m/z calc. for $C_{19}H_{26}O_3{}^{79}Br^{23}Na$ $[M+Na]^+$: 418.0988,420.0968 found: 418.0985, 420.0964

$[\alpha]^{20}_{589}$ = +1.2 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.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D (m) 8.15
C (m) 7.45
B (d) 6.45
A (dd) 6.20
E (t) 3.39
F (m) 2.79
G (m) 2.57
H (s) 2.14
I (m) 1.83
J (m) 1.34
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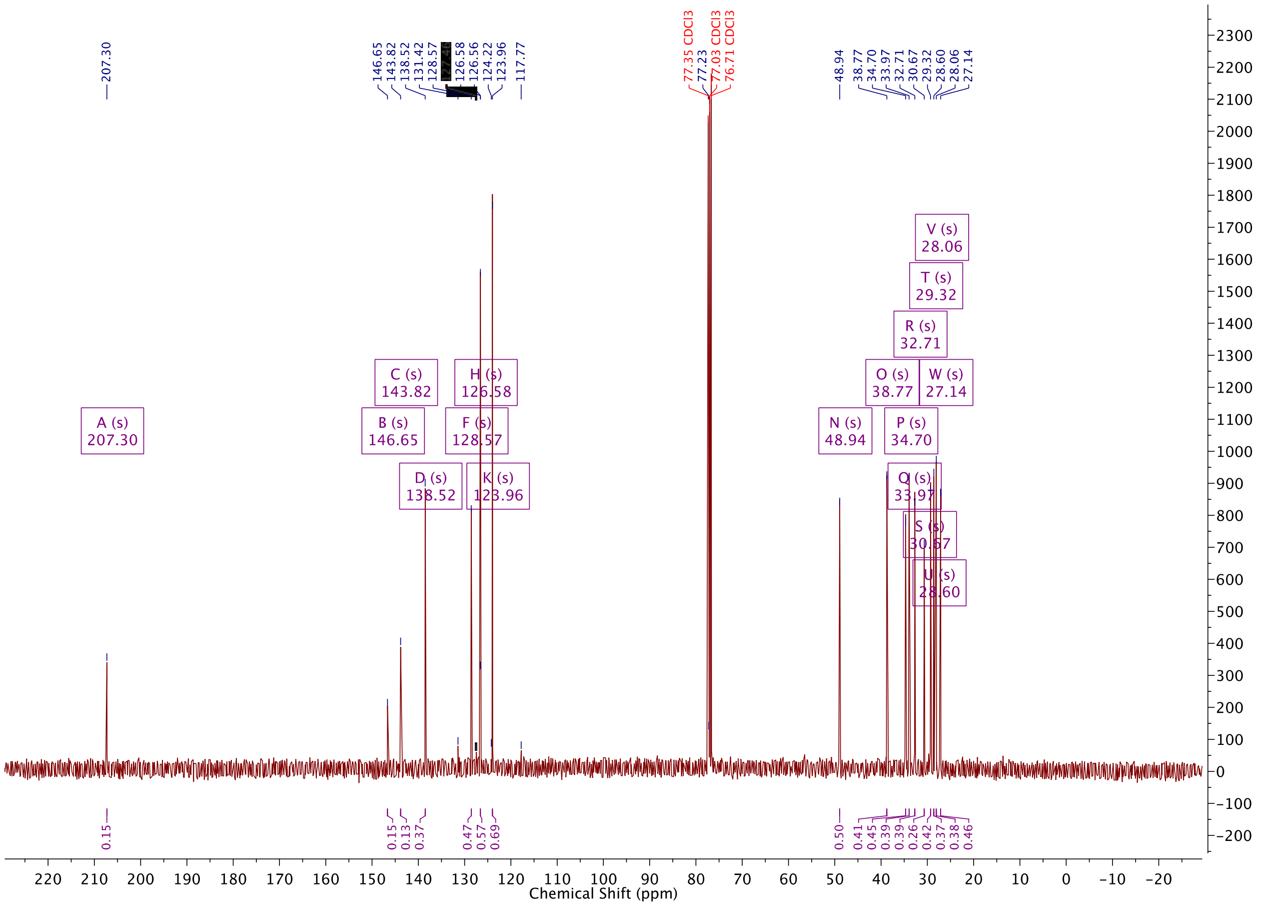
1.98
0.96
1.00
2.02
0.99
2.03
2.93
2.11
11.41
Chemical Shift (ppm)
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
45000 40000 35000 30000 25000 20000 15000 10000 5000 0


207.30
146.65 143.82 138.52 131.42 128.57 126.58 126.56 124.22 123.96 117.77
77.35 CDCl3
77.23
77.03 CDCl3
76.71 CDCl3
48.94 38.77 34.70 33.97 32.71 30.67 29.32 28.60 28.06 27.14
A (s) 207.30
B (s) 146.65
C (s) 143.82
D (s) 138.52
F (s) 128.57
H (s) 126.58
K (s) 123.96
N (s) 48.94
O (s) 38.77
P (s) 34.70
Q (s) 33.97
R (s) 32.71
S (s) 30.67
T (s) 29.32
U (s) 28.60
V (s) 28.06
W (s) 27.14
0.15 0.15 0.13 0.37 0.47 0.57 0.69 0.50 0.41 0.45 0.39 0.39 0.26 0.42 0.37 0.38 0.46
Chemical Shift (ppm)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
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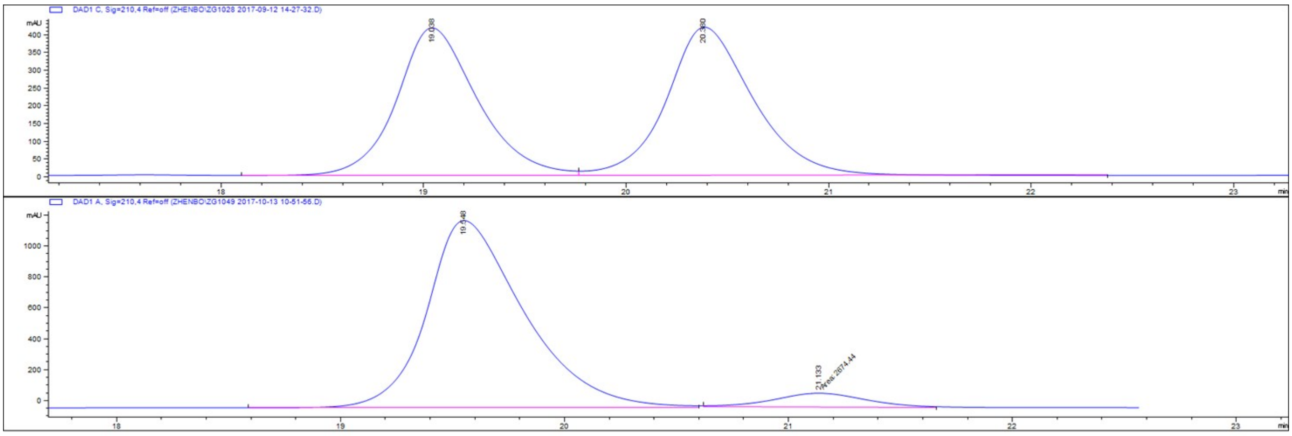
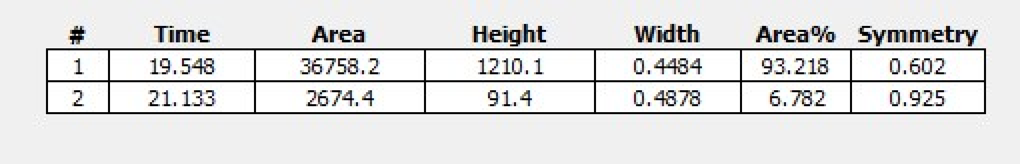
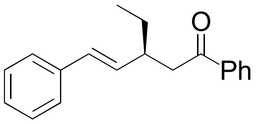
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 19.548 | 36758.2 | 1210.1 | 0.4484 | 93.218 | 0.602 |
| 2 | 21.133 | 2674.4 | 91.4 | 0.4878 | 6.782 | 0.925 |

## (+)-(*S*,*E*)-3-ethyl-1,5-diphenylpent-4-en-1-one (3p)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, $Cp_2ZrHCl$ (103mg, 2.0 eq., 0.4 mmol) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then DCM (0.2 ml) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before (2E,4E)-1,5-diphenylpenta-2,4-dien-1-one (47 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 95:5; $SiO_2$) to give the desired product (27 mg, 0.10 mmol, 51%).

The enantiomeric excess of 54% was determined by SFC [Chiralpak® IF; 1500 psi, 30°C; 1% to 30% MeOH in 5 mins; flow: 1.5 ml/min; λ= 243 nm; minor enantiomer tR = 3.12 mins, major enantiomer tR = 2.96 mins]

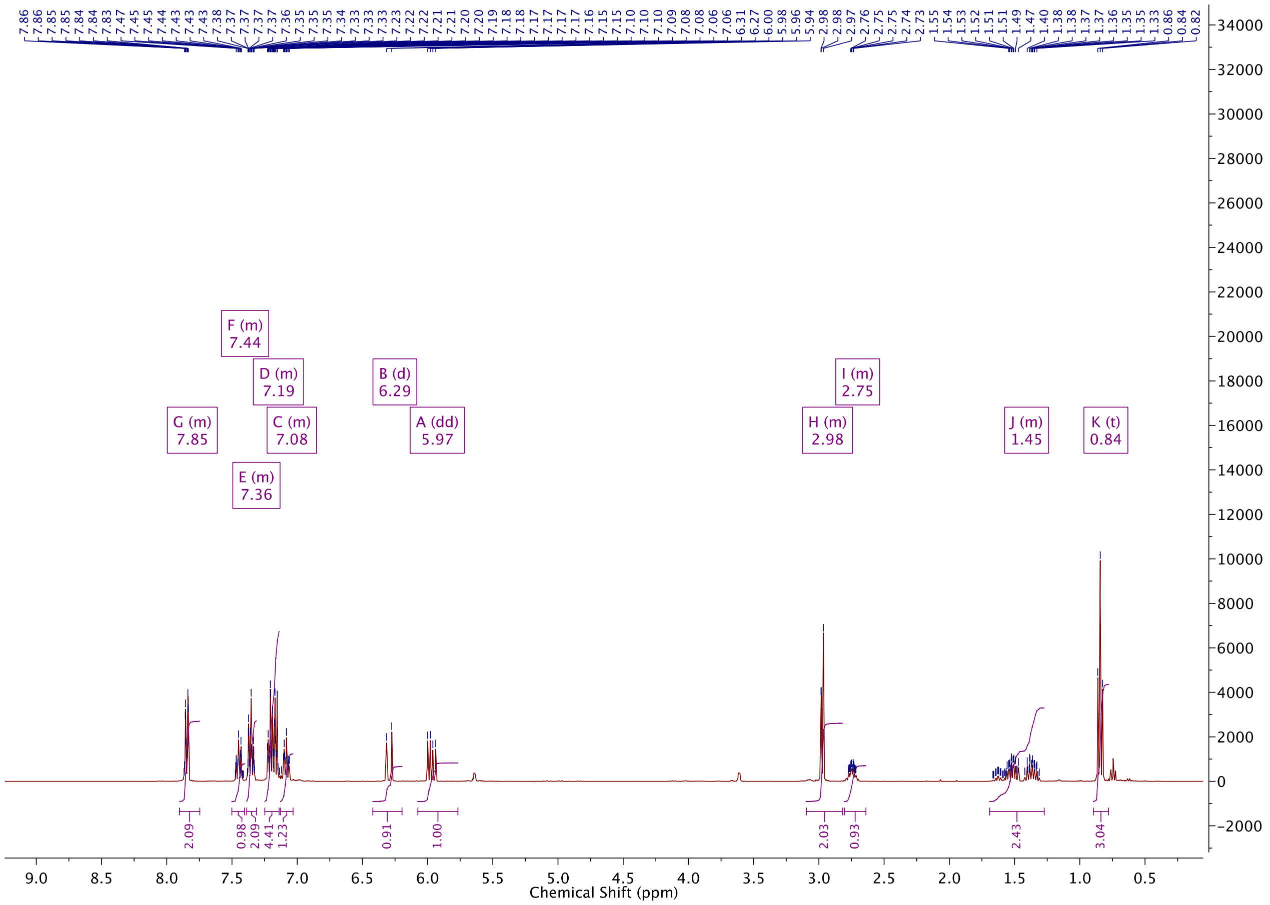
$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.90 – 7.75 (m, 2H, Ar-*H*), 7.50 – 7.40 (m, 1H, Ar-*H*), 7.39 – 7.31 (m, 2H, Ar-*H*), 7.25 – 7.14 (m, 4H, Ar-*H*), 7.13 – 7.03 (m, 1H, Ar-*H*), 6.29 (d, J = 15.8 Hz, 1H, C*H*), 5.97 (dd, J = 15.8 Hz, 8.6 Hz, 1H, C*H*), 3.10 – 2.82 (m, 2H, $CH_2CO$), 2.80 – 2.64 (m, 1H, $CHCH_2CH_3$), 1.69 – 1.27 (m, 2H, $CH_2CH_3$), 0.84 (t, J = 7.4 Hz, 3H, $CH_3$).

$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 199.4, 137.5, 137.4, 133.3, 132.9, 130.4, 128.6 (2C), 128.5(2C), 128.1(2C), 127.0, 126.1(2C), 44.0, 40.8, 27.9, 11.8.
IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2961, 2360, 1685, 1448, 748

HRMS (ESI) m/z calc. for $C_{19}H_{21}O$ $[M+H]^+$: 265.1587 found: 265.1586

$[\alpha]^{20}_{589} = +11.7$ ° (c 0.6, $CHCl_3$)

Absolute configuration assigned by comparing optical rotations to literature.[9]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G (m) 7.85
C (m) 7.08
A (dd) 5.97
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J (m) 1.45
K (t) 0.84
E (m) 7.36
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16000
14000
12000
10000
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6000
4000
2000
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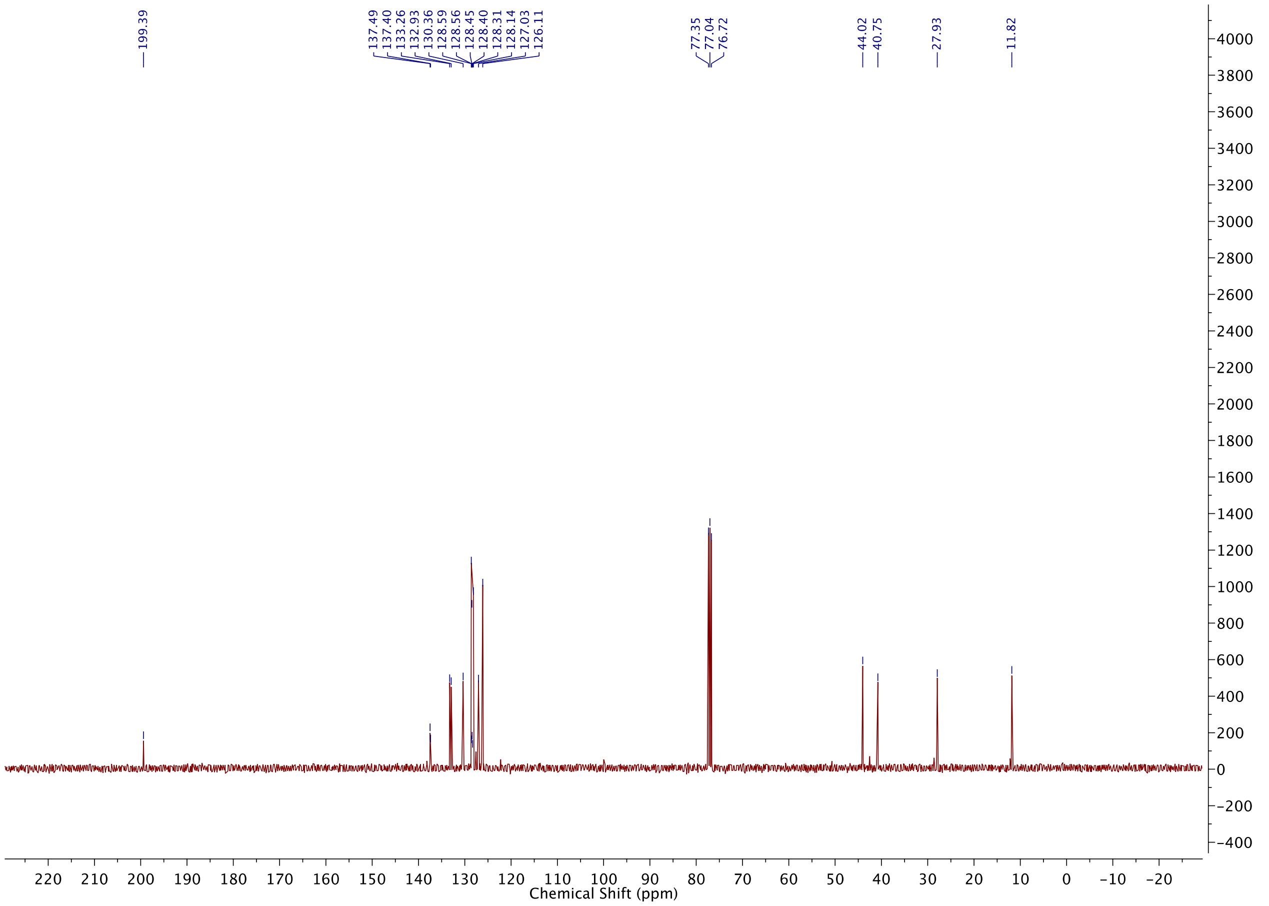
Chemical Shift (ppm)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3600
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3200
3000
2800
2600
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2200
2000
1800
1600
1400
1200
1000
800
600
400
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150
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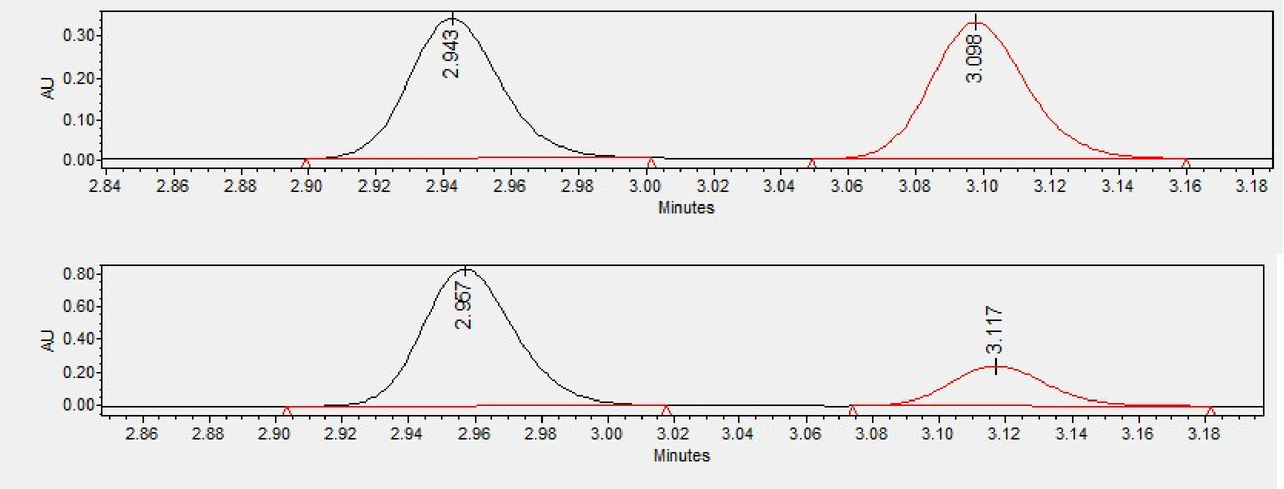
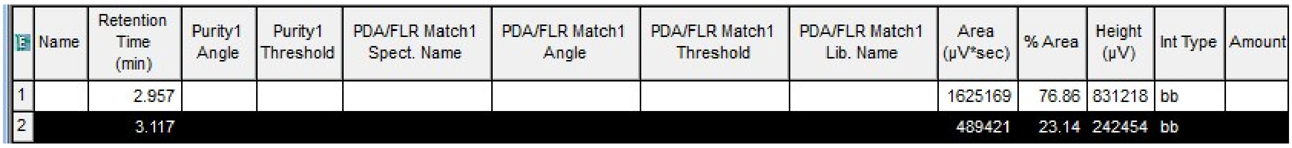
Chemical Shift (ppm)

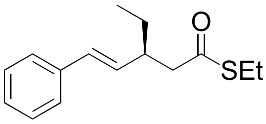
SFC trace





|  | Name | Retention Time (min) | Purity1 Angle | Purity1 Threshold | PDA/FLR Match1 Spect. Name | PDA/FLR Match1 Angle | PDA/FLR Match1 Threshold | PDA/FLR Match1 Lib. Name | Area (µV*sec) | % Area | Height (µV) | Int Type | Amount |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 |  | 2.957 |  |  |  |  |  |  | 1625169 | 76.86 | 831218 | bb |  |
| 2 |  | 3.117 |  |  |  |  |  |  | 489421 | 23.14 | 242454 | bb |  |

## (+)-S-ethyl (S,E)-3-ethyl-5-phenylpent-4-enethioate (3q)



CuCl (3.8 mg, 0.2 eq., 0.04 mmol), and the phosphoramidite ligand (22.8 mg, 0.2 eq., 0.04 mmol) were added to a flame dried round bottom flask containing 1ml 1ml $Et_2O$/DCM (1/1) under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (11.2 mg, 0.22 eq., 0.044 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then DCM (0.2 ml) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before S-ethyl (2E,4E)-5-phenylpenta-2,4-dienethioate (43 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 97:3; $SiO_2$) to give the desired product (38 mg, 0.15 mmol, 77%).

The enantiomeric excess of 95% was determined by SFC [Chiralpak® IG; 1500 psi, 30°C; 1% to 30% MeOH in 5 mins; flow: 1.5 ml/min; λ= 243 nm; minor enantiomer tR = 2.25 mins, major enantiomer tR = 2.35 mins]

$^1$H NMR (400 MHz, Chloroform-d) $\delta_H$/ppm 7.38 – 7.25 (m, 4H, Ar-*H*), 7.23 – 7.15 (m, 1H, Ar-*H*), 6.40 (d, J = 15.8 Hz, 1H, C*H*), 6.16 – 5.81 (m, 1H, C*H*), 2.85 (q, J = 7.4 Hz, 2H, $SC\mathit{H}_2CH_3$), 2.74 – 2.54 (m, 3H, $C\mathit{H}_2CO$, C*H*), 1.66 – 1.50 (m, 1H, $C\mathit{H}_2CH_3$), 1.46 – 1.33 (m, 1H, $C\mathit{H}_2CH_3$), 1.20 (t, J = 7.4 Hz, 3H, $SCH_2C\mathit{H}_3$), 0.91 (t, J = 7.4 Hz, 3H, $C\mathit{H}_3$).

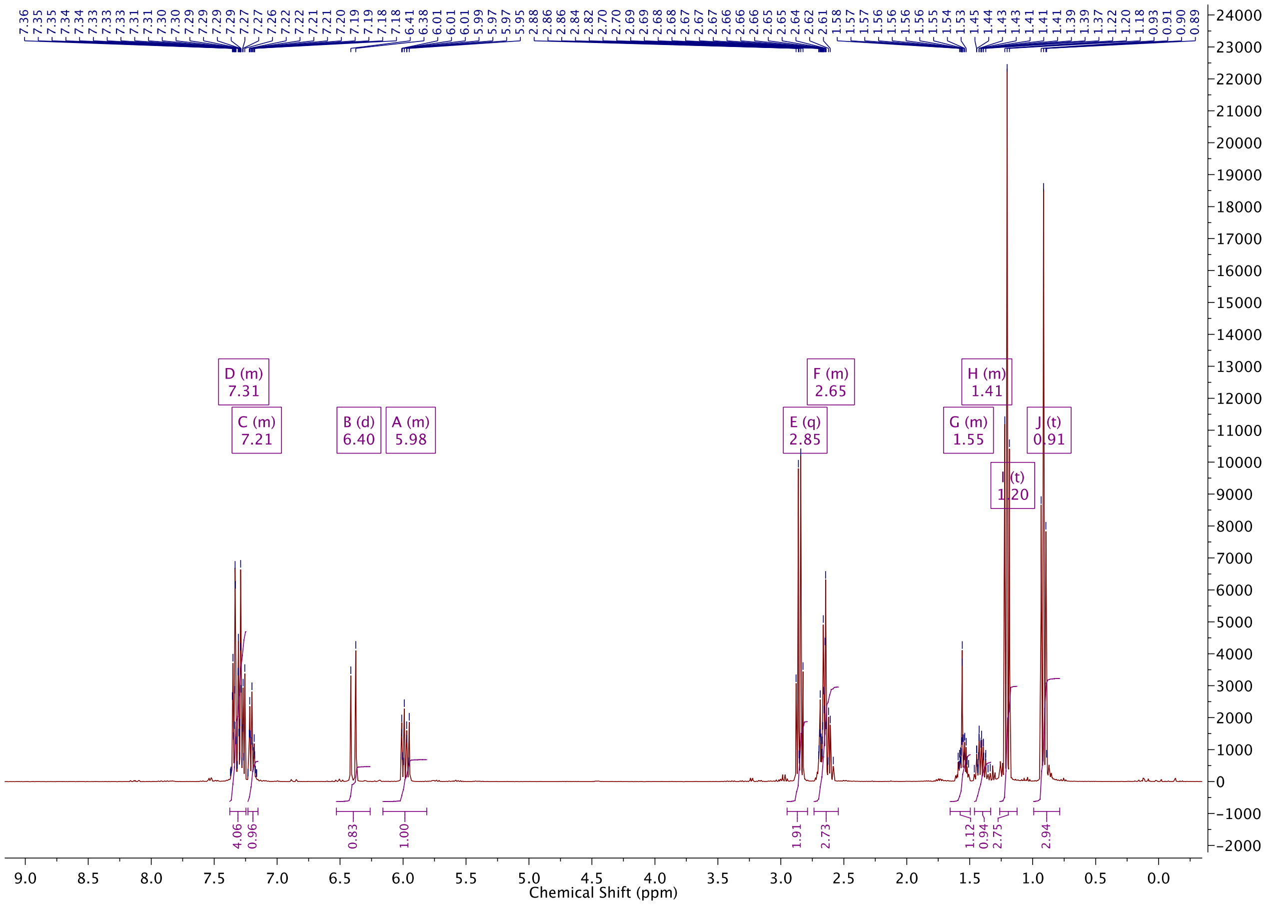
$^{13}$C NMR (101 MHz, Chloroform-d) $\delta_C$/ppm 198.4, 137.4, 132.3, 130.8, 128.5 (2C), 127.1, 126.2 (2C), 49.4, 42.1, 27.6, 23.4, 14.8, 11.6.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2969, 2341, 1685, 1449, 1022, 748

HRMS (ESI) m/z calc. for $C_{15}H_{21}O^{32}S$ [M+H]$^+$: 249.1308 found: 249.1308

$[\alpha]^{20}_{589}$ = +72.6 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.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7.19
7.19
7.18
6.41
6.38
6.01
6.01
5.99
5.97
5.97
5.95
2.88
2.86
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1.41
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1.22
1.20
1.18
0.93
0.91
0.90
0.89
D (m) 7.31
C (m) 7.21
B (d) 6.40
A (m) 5.98
E (q) 2.85
F (m) 2.65
G (m) 1.55
H (m) 1.41
I (t) 1.20
J (t) 0.91
4.06
0.96
0.83
1.00
1.91
2.73
1.12
0.94
2.75
2.94
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
Chemical Shift (ppm)
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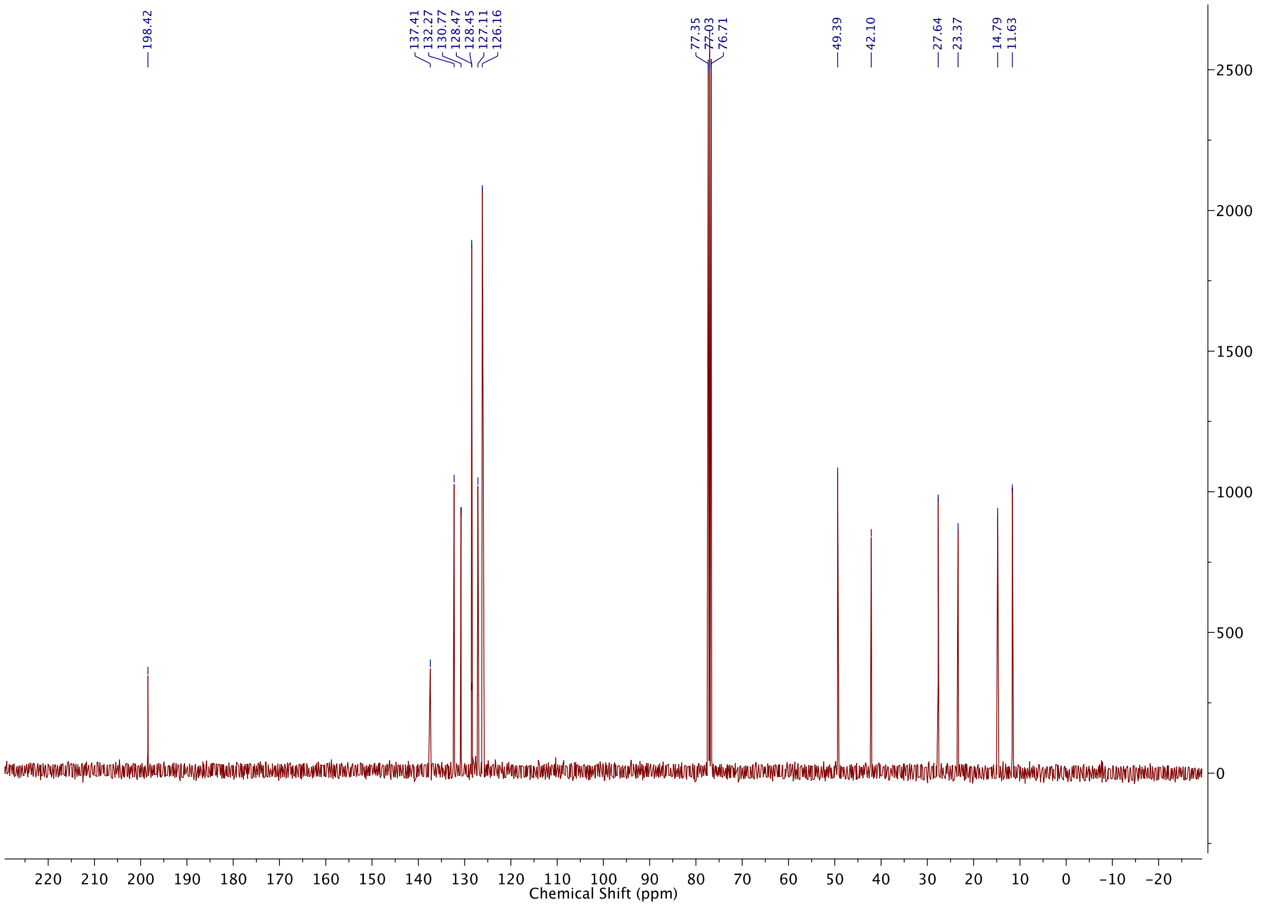
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130.77
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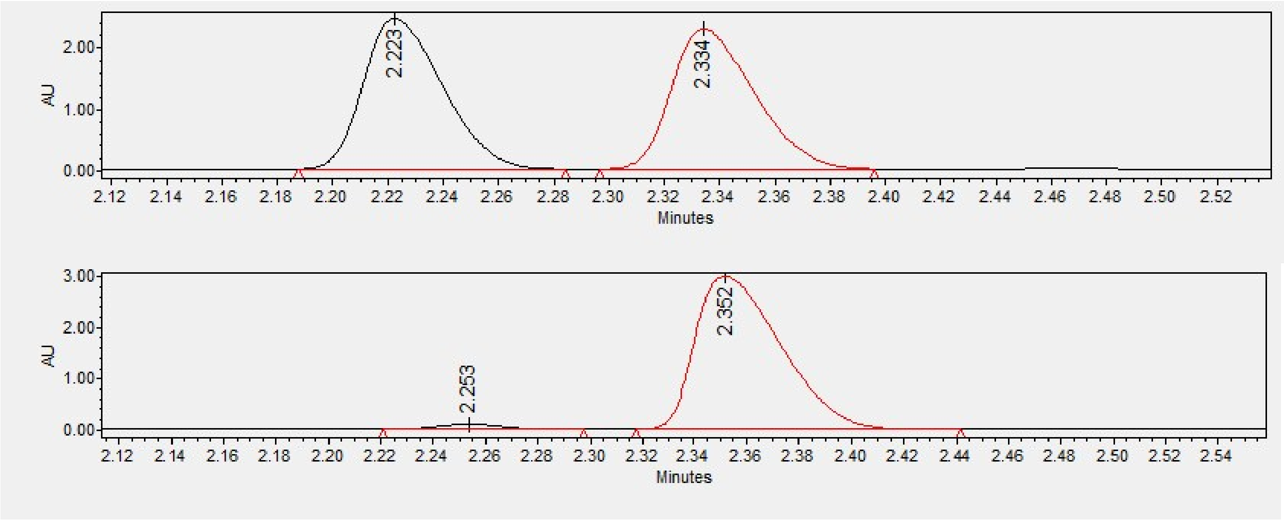
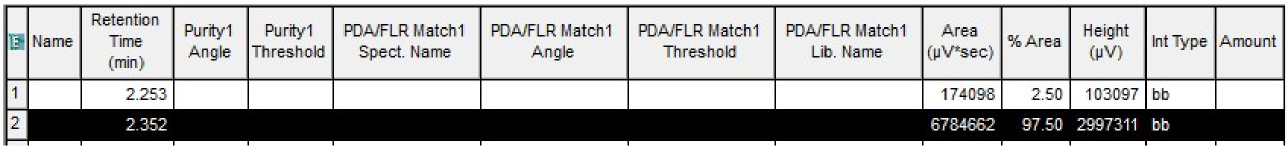
128.45
127.11
126.16
77.35
77.03
76.71
49.39
42.10
27.64
23.37
14.79
11.63
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
Chemical Shift (ppm)
2500 2000 1500 1000 500 0

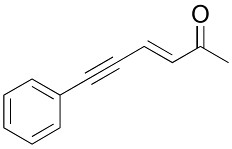
SFC trace





| | Name | Retention Time (min) | Purity1 Angle | Purity1 Threshold | PDA/FLR Match1 Spect. Name | PDA/FLR Match1 Angle | PDA/FLR Match1 Threshold | PDA/FLR Match1 Lib. Name | Area (µV*sec) | % Area | Height (µV) | Int Type | Amount |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | | 2.253 | | | | | | | 174098 | 2.50 | 103097 | bb | |
| 2 | | 2.352 | | | | | | | 6784662 | 97.50 | 2997311 | bb | |

## (E)-6-phenylhex-3-en-5-yn-2-one (4a)



*n*-BuLi (4.8 ml, 1.0 eq in hexane, 7.5 mmol) was added to a stirring solution of Diethyl (2-oxopropyl)phosphonate (1.45 ml, 1.0 eq, 7.5 mmol) in 20 ml THF at 0°C under argon. The mixture was stirred for another 20 min. A solution of 3-phenylpropiolaldehyde (0.98 g, 1.0 eq., 7.5 mmol) in THF was added dropwise. The mixture was slowly warmed to room temperature and was continued overnight. The mixture was quenched with aqueous $NH_4Cl$ (sat.). The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$ three times. The combined organic materials were dried ($MgSO_4$), filtered, concentrated, and further purified by flash column chromatography (pentane: $Et_2O$; 90:10; $SiO_2$) to afford the desired product (1.03 g, 6.0 mmol, 81%).

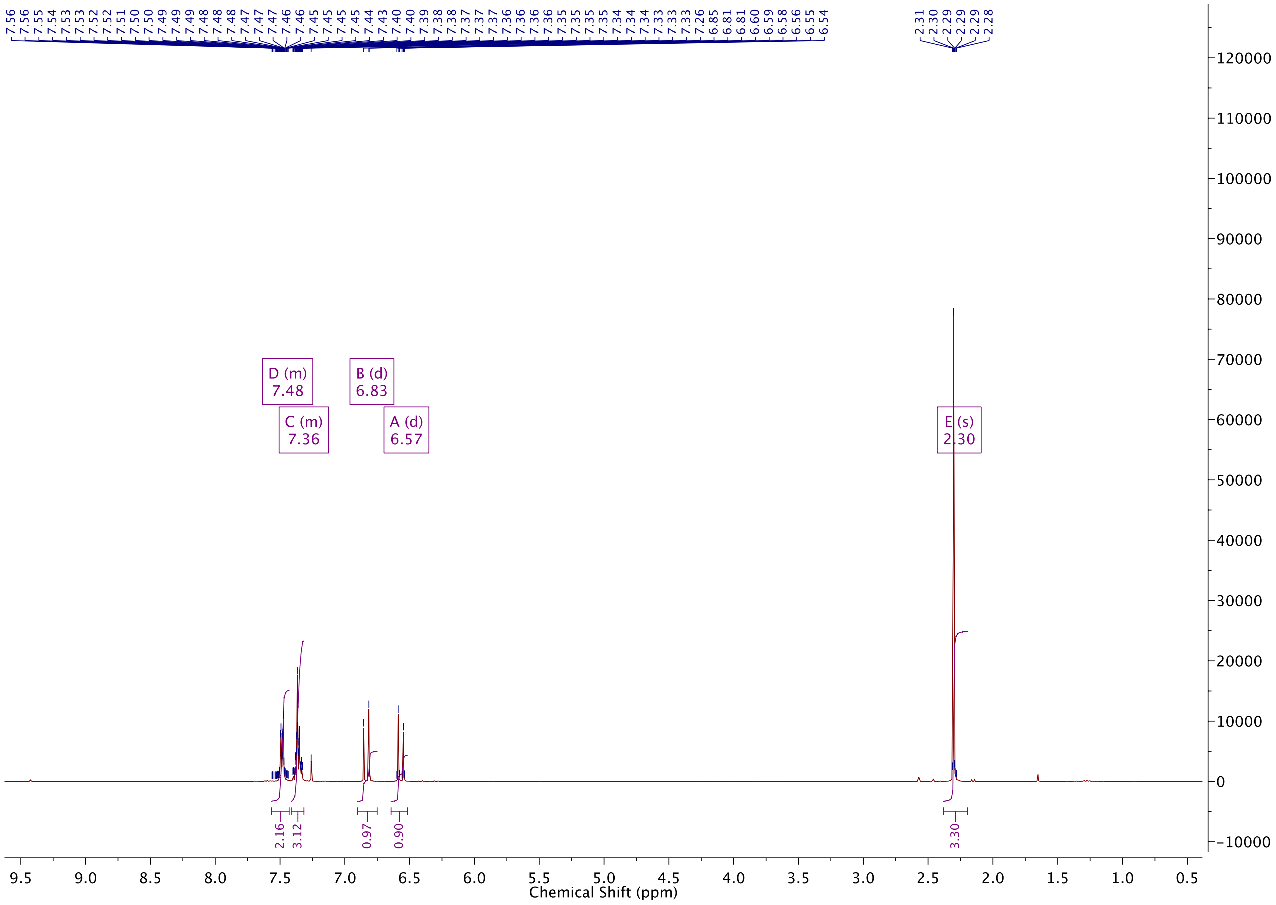
$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.57 – 7.43 (m, 2H, Ar-*H*), 7.41 – 7.32 (m, 3H, Ar-*H*), 6.83 (d, *J* = 16.0 Hz, 1H, C*H*), 6.57 (d, *J* = 16.0 Hz, 1H, C*H*), 2.30 (s, 3H, C$H_3$).

$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 197.0, 137.8, 132.0 (2C), 129.4, 128.5 (2C), 123.8, 122.2, 99.7, 86.7, 27.7.

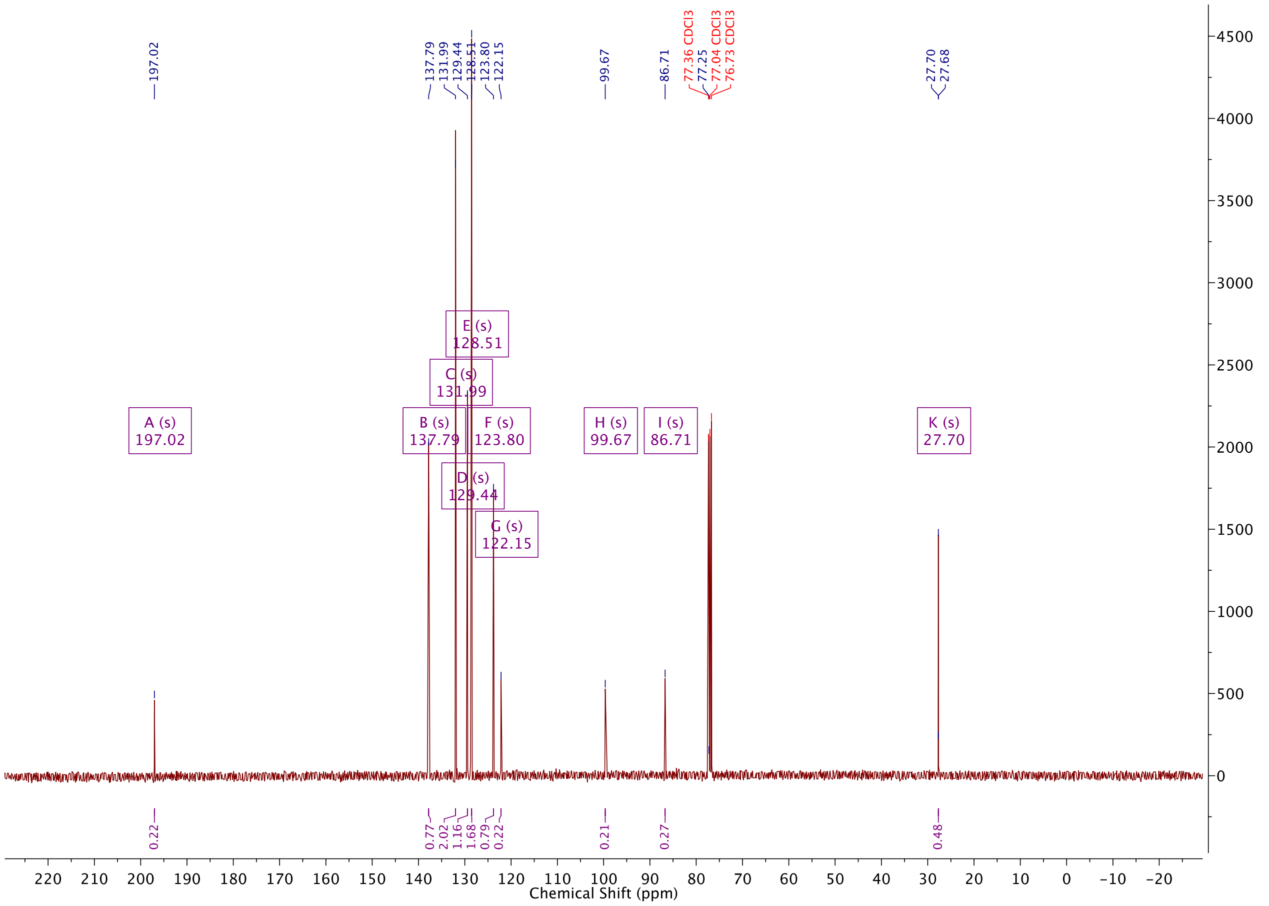
IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2980, 2196, 1671, 1586, 1361, 1248, 957

HRMS (ESI) m/z calc. for $C_{12}H_{11}O$ $[M+H]^+$: 171.0804, found: 171.0805

This data was concordant with literature values.[10]

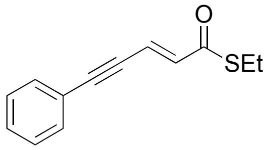


7.56 7.56 7.55 7.54 7.53 7.53 7.52 7.52 7.51 7.50 7.50 7.49 7.49 7.49 7.48 7.48 7.47 7.47 7.47 7.46 7.46 7.45 7.45 7.45 7.45 7.44 7.43 7.40 7.39 7.38 7.38 7.37 7.37 7.37 7.36 7.36 7.36 7.35 7.35 7.35 7.35 7.34 7.34 7.33 7.33 7.33 7.26 6.85 6.81 6.81 6.60 6.59 6.58 6.56 6.55 6.54
2.31 2.30 2.29 2.29 2.29 2.28
D (m) 7.48
C (m) 7.36
B (d) 6.83
A (d) 6.57
E (s) 2.30
2.16
3.12
0.97
0.90
3.30
Chemical Shift (ppm)



197.02
137.79 131.99 129.44 128.51 123.80 122.15
99.67
86.71
77.36 CDCl3
77.25
77.04 CDCl3
76.73 CDCl3
27.70 27.68
A (s) 197.02
B (s) 137.79
C (s) 131.99
D (s) 129.44
E (s) 128.51
F (s) 123.80
G (s) 122.15
H (s) 99.67
I (s) 86.71
K (s) 27.70
0.22
0.77
2.02
1.16
1.68
0.79
0.22
0.21
0.27
0.48
Chemical Shift (ppm)

### S-ethyl (E)-5-phenylpent-2-en-4-ynethioate (4b)



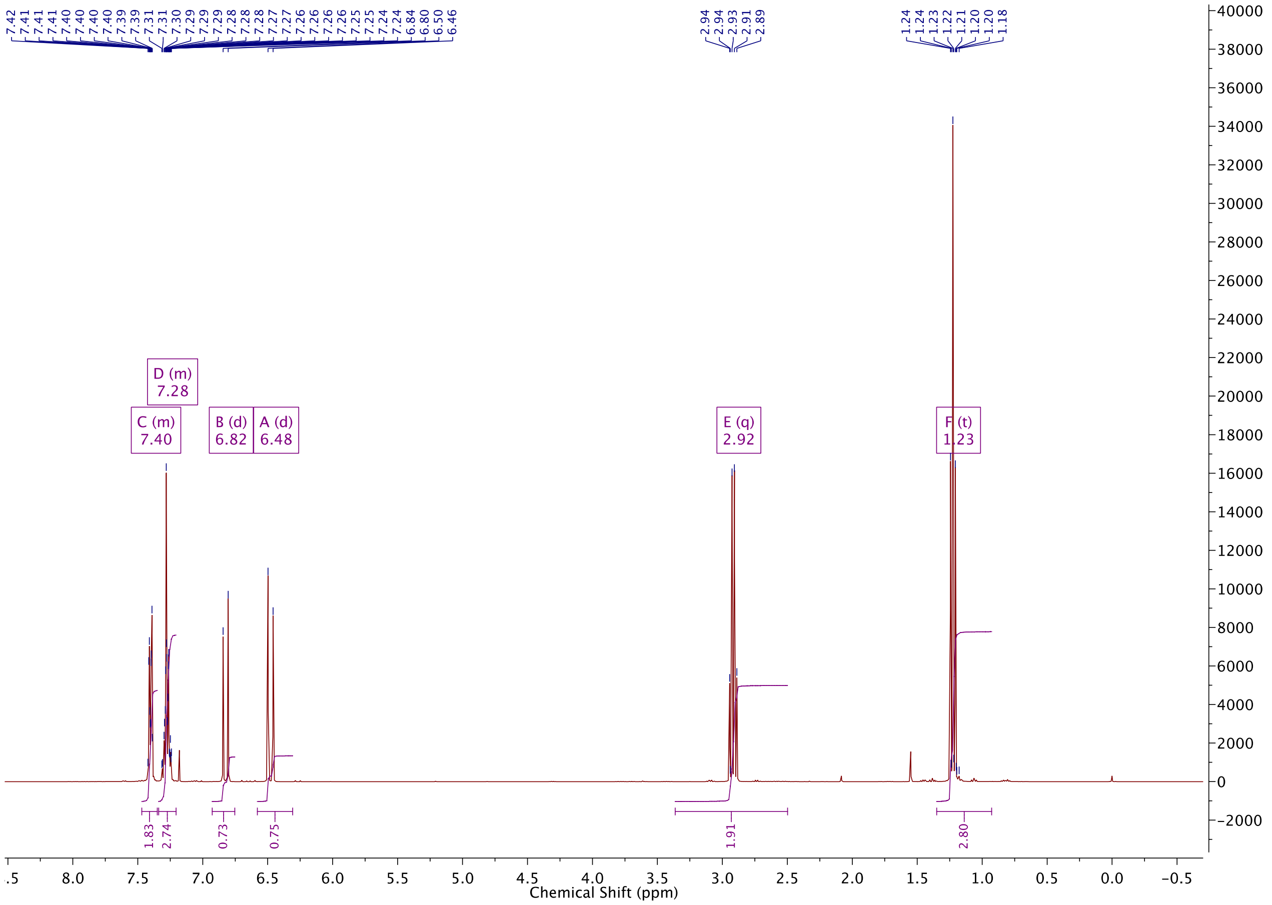
*n*-BuLi (4.8 ml, 1.0 eq in hexane, 7.5 mmol) was added to a stirring solution of S-ethyl 2-(diethoxyphosphoryl)ethanethioate (1.8 ml, 1.0 eq, 7.5 mmol) in 20 ml THF at 0°C under argon. The mixture was stirred for another 20 min. A solution of 3-phenylpropiolaldehyde (0.98 g, 1.0 eq., 7.5 mmol) in THF was added dropwise. The mixture was slowly warmed to room temperature and was continued overnight. The mixture was quenched with aqueous $NH_4Cl$ (sat.). The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$ three times. The combined organic materials were dried ($MgSO_4$), filtered, concentrated, and further purified by flash column chromatography (pentane: $Et_2O$; 97:3; $SiO_2$) to afford the desired product (1.23 g, 5.7 mmol, 75%).

$^1$H NMR (400 MHz, Chloroform-d) $\delta_H$/ppm 7.47 – 7.35 (m, 2H, Ar-*H*), 7.34 – 7.21 (m, 3H, Ar-*H*), 6.82 (d, J = 15.6 Hz, 1H, C*H*), 6.48 (d, J = 15.5 Hz, 1H, C*H*), 2.92 (q, J = 7.4 Hz, 2H, S$CH_2$), 1.23 (t, J = 7.4 Hz, 3H, $CH_3$).

$^{13}$C NMR (101 MHz, Chloroform-d) $\delta_C$/ppm 188.9, 136.1, 132.0 (2C), 129.4, 128.5 (2C), 122.2, 120.7, 98.7, 86.8, 23.5, 14.7.

IR ($\nu_{max}$/cm$^{-1}$, $CHCl_3$) 2975, 2190, 1658, 1589, 1054, 976,756

HRMS (ESI) m/z calc. for $C_{13}H_{13}O^{32}S$ [M+H]$^+$: 217.0682, found: 217.0682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6.46
2.94
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2.91
2.89
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1.23
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1.21
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1.18
D (m) 7.28
C (m) 7.40
B (d) 6.82
A (d) 6.48
E (q) 2.92
F (t) 1.23
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0.75
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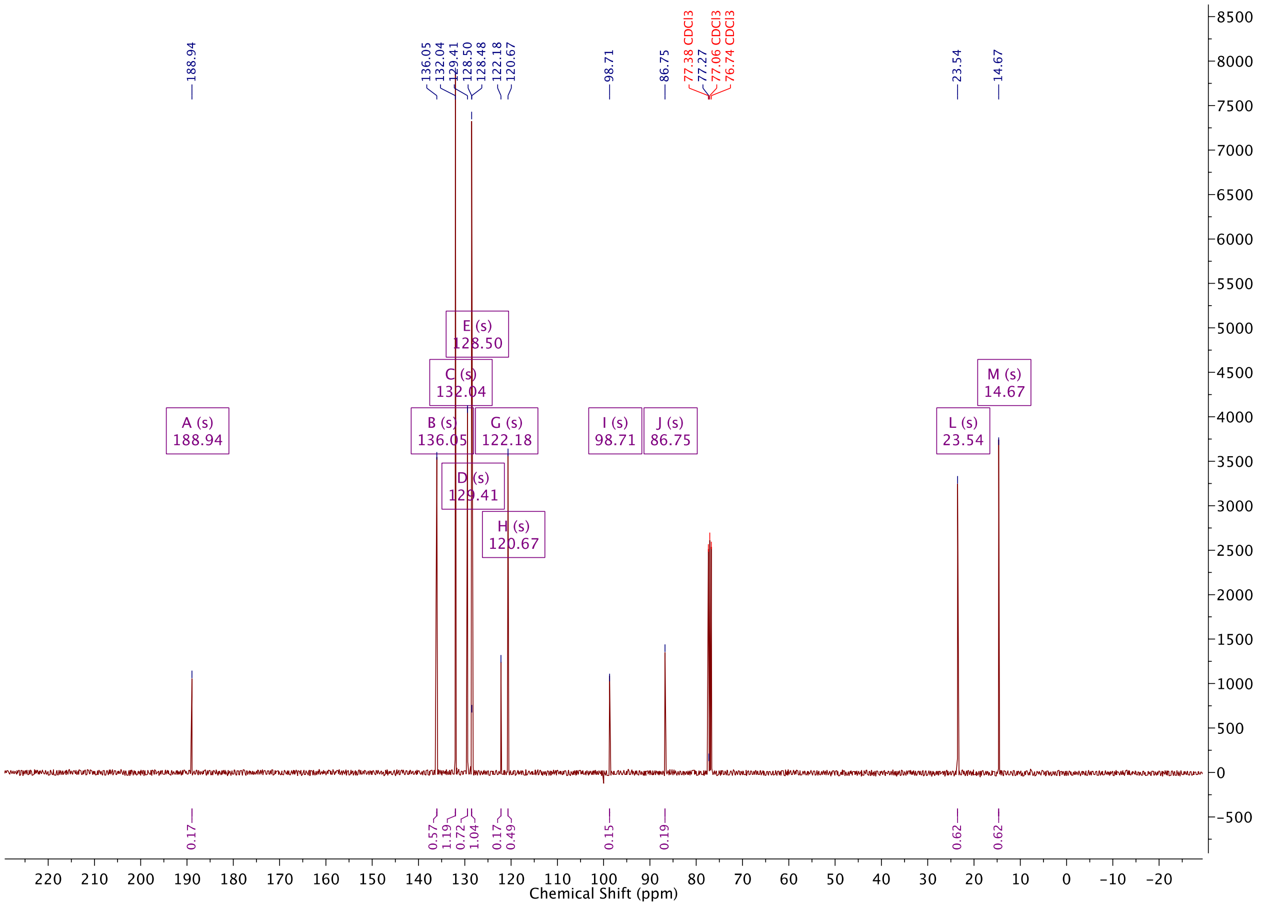
2.80
Chemical Shift (ppm)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128.48
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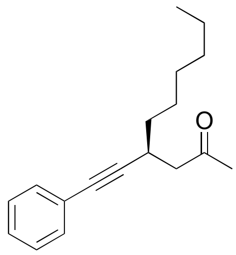
120.67
98.71
86.75
77.38 CDCl3
77.27
77.06 CDCl3
76.74 CDCl3
23.54
14.67
E (s) 128.50
C (s) 132.04
A (s) 188.94
B (s) 136.05
G (s) 122.18
D (s) 129.41
H (s) 120.67
I (s) 98.71
J (s) 86.75
L (s) 23.54
M (s) 14.67
0.17
0.57
1.19
0.72
1.04
0.17
0.49
0.15
0.19
0.62
0.62
Chemical Shift (ppm)

## (–)-(*S*)-4-(phenylethynyl) decan-2-one (5a)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.
To a second, flame dried, round bottom flask, containing a stirred solution of hex-1-ene (42 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.
The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before 6-phenylhex-5-yn-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (36 mg, 14 mmol, 70%).

HPLC analysis indicated an enantiomeric excess of 94 % [Chiralpak® IB; flow: 0.8 mL/min; hexane/i-PrOH: 99: 1; λ = 210 nm; major enantiomer tR = 7.39 min; minor enantiomer, tR = 7.83 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.25 – 7.16 (m, 2H, Ar-*H*), 7.15 – 7.04 (m, 3H, Ar-*H*), 3.12 – 2.72 (m, 1H, C*H*), 2.58 (dd, *J* = 16.2 Hz, 7.6 Hz, 1H, C$H_2$COC$H_3$), 2.42 (dd, *J* = 16.2 Hz, 6.4 Hz, 1H, C$H_2$COC$H_3$), 2.04 (s, 3H, COC$H_3$), 1.47 – 1.05 (m, 10H, 5 x C$H_2$), 0.82 – 0.66 (m, 3H, C$H_3$).

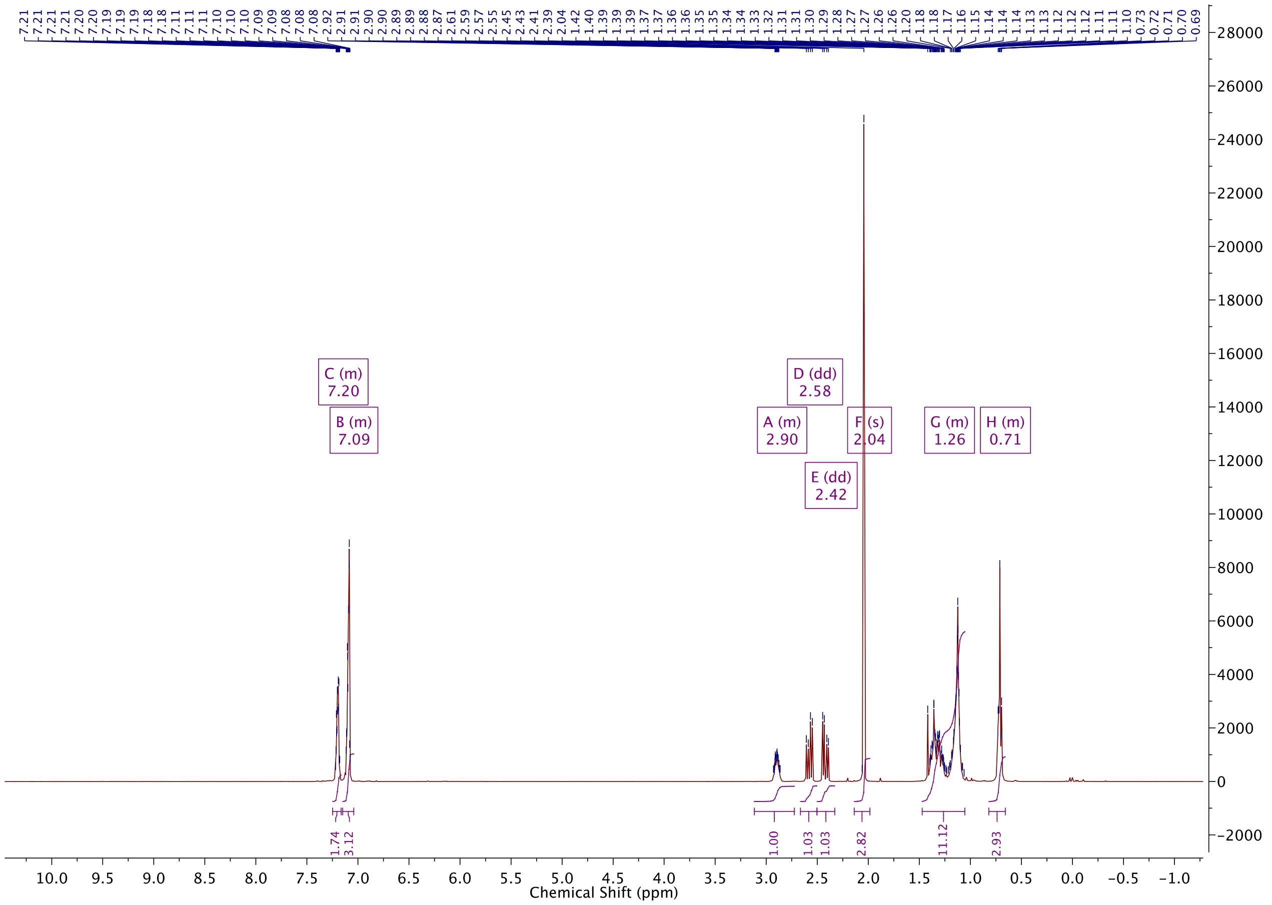
$^{13}C$ NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 207.0, 131.6 (2C), 128.2 (2C), 127.7, 123.6, 92.1, 81.9, 49.0, 34.9, 31.8, 30.6, 29.0, 27.8, 27.3, 22.7, 14.1.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2980, 2929, 1717, 1362, 1159, 757

HRMS (ESI) m/z calc. for $C_{18}H_{25}O$ $[M+H]^+$: 257.1900 found: 257.1899

$[\alpha]^{20}_{589} = -7.9°$ (c 1.0, $CHCl_3$)

Absolute configuration was assigned by analogy to **3p** or by comparing optical rotations to literature.[11]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1.11
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1.10
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0.70
0.69
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D (dd) 2.58
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F (s) 2.04
E (dd) 2.42
G (m) 1.26
H (m) 0.71
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1.03
1.03
2.82
11.12
2.93
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24000
22000
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18000
16000
14000
12000
10000
8000
6000
4000
2000
0
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10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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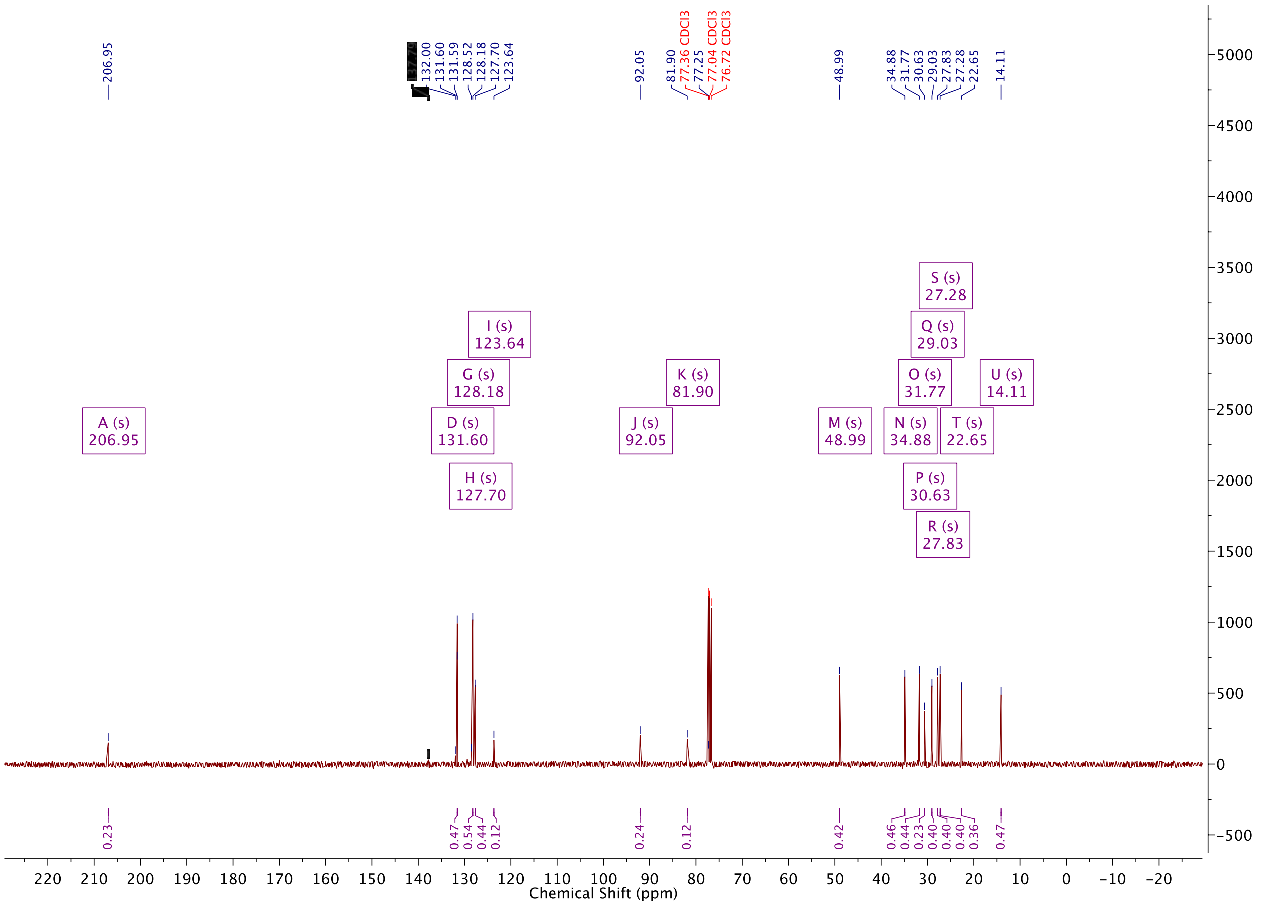
Chemical Shift (ppm)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81.90
77.36 CDCl3
77.25
77.04 CDCl3
76.72 CDCl3
48.99
34.88
31.77
30.63
29.03
27.83
27.28
22.65
14.11
A (s) 206.95
D (s) 131.60
G (s) 128.18
H (s) 127.70
I (s) 123.64
J (s) 92.05
K (s) 81.90
M (s) 48.99
N (s) 34.88
O (s) 31.77
P (s) 30.63
Q (s) 29.03
R (s) 27.83
S (s) 27.28
T (s) 22.65
U (s) 14.11
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0.47
0.54
0.44
0.12
0.24
0.12
0.42
0.46
0.44
0.23
0.40
0.40
0.36
0.47
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
220
210
200
190
180
170
160
150
140
130
120
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50
40
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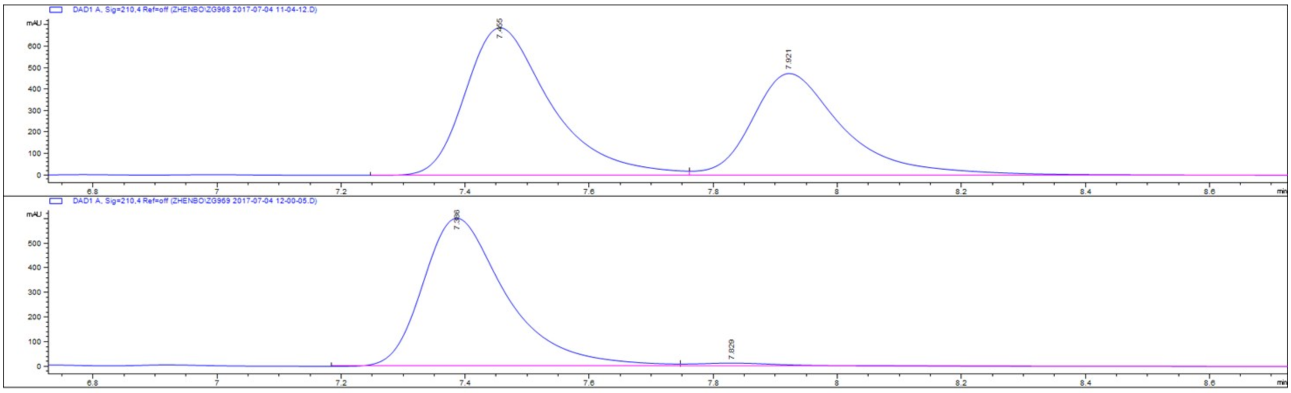
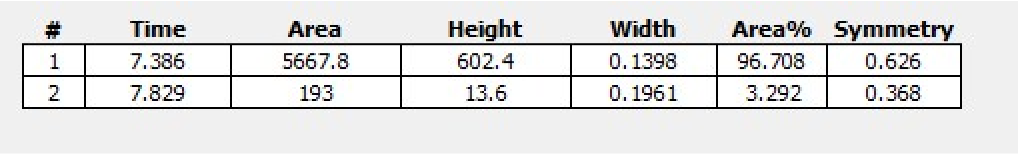
20
10
0
-10
-20
Chemical Shift (ppm)

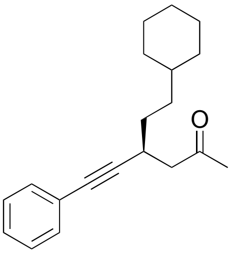
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.386 | 5667.8 | 602.4 | 0.1398 | 96.708 | 0.626 |
| 2 | 7.829 | 193 | 13.6 | 0.1961 | 3.292 | 0.368 |

## (–)-(*S*)-4-(2-cyclohexylethyl)-6-phenylhex-5-yn-2-one (5b)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.
To a second, flame dried, round bottom flask, containing a stirred solution of vinylcyclohexane (44 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.
The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before 6-phenylhex-5-yn-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction

mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (49 mg, 17 mmol, 87 %).

HPLC analysis indicated an enantiomeric excess of 95 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1; λ = 242 nm; major enantiomer tR = 6.00 min; minor enantiomer, tR = 6.39 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.35 – 7.26 (m, 2H, Ar-*H*), 7.24 – 7.15 (m, 3H, Ar-*H*), 2.97 (m, 1H, C*H*), 2.68 (dd, *J* = 16.2 Hz, 7.6 Hz, 1H, $CH_2COCH_3$), 2.52 (dd, *J* = 16.2 Hz, 6.4 Hz, 1H, $CH_2COCH_3$)), 2.15 (s, 3H, $COCH_3$), 1.74 – 1.53 (m, 5H, C*H, 2 x* $CH_2$), 1.52 – 1.02 (m, 7H, 3.5 x $CH_2$), 0.96 – 0.68 (m, 3, 1.5 x $CH_2$).

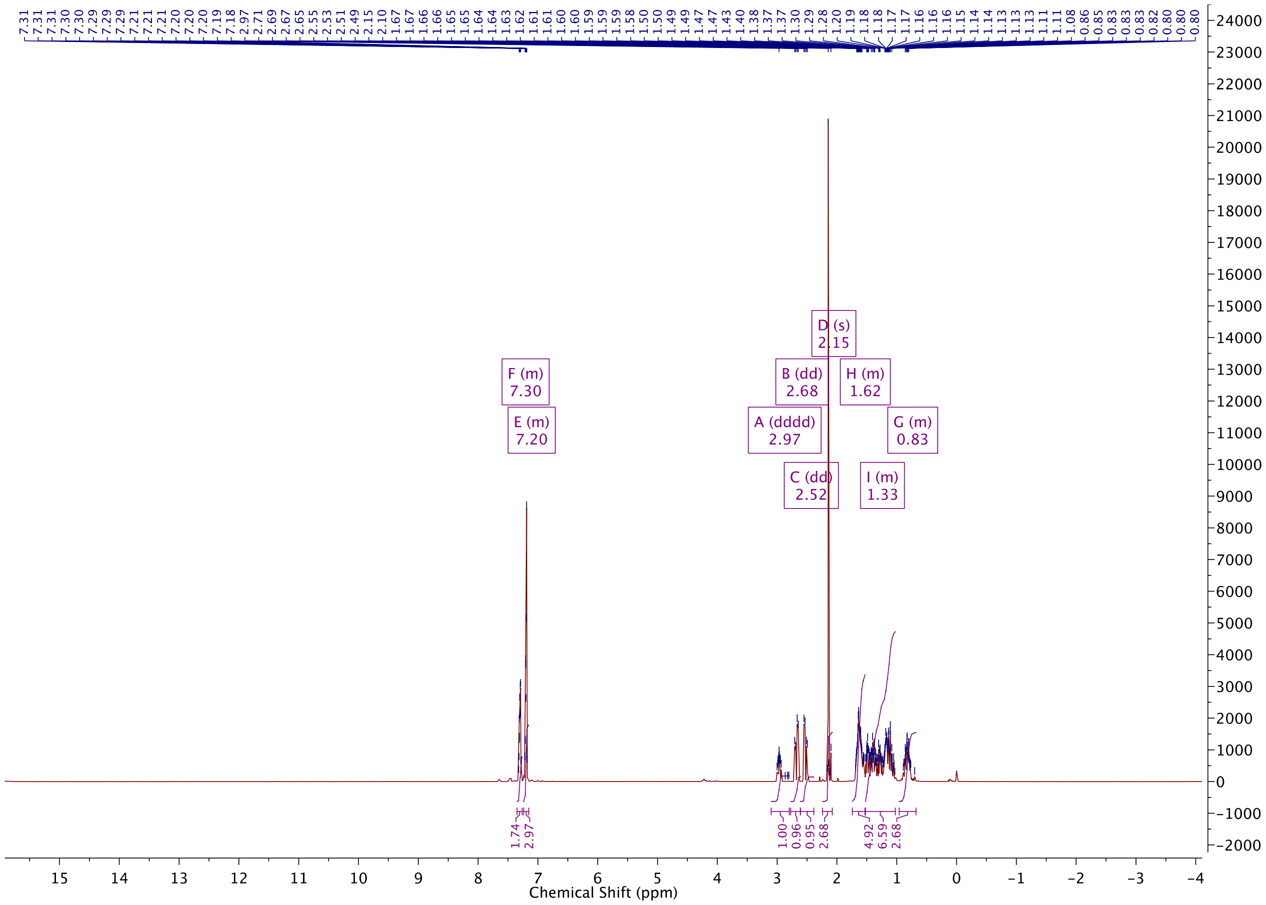
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 206.9, 131.6 (2C), 128.2 (2C), 127.7, 123.7, 92.1, 81.9, 49.0, 37.5, 35.0, 33.6, 33.2, 32.3, 30.6, 28.1, 26.7, 26.4(2C).

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1462, 1383, 1153, 954

HRMS (ESI) m/z calc. for $C_{20}H_{27}O$ $[M+H]^+$: 283.2056 found: 283.2057

$[\alpha]^{20}_{589}$ = –5.8 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.


7.31 7.31 7.30 7.30 7.29 7.29 7.29 7.21 7.21 7.21 7.20 7.20 7.19 7.18 2.97 2.71 2.69 2.67 2.65 2.55 2.53 2.51 2.49 2.15 2.10 1.67 1.67 1.66 1.65 1.65 1.64 1.64 1.63 1.62 1.61 1.61 1.60 1.60 1.59 1.59 1.59 1.58 1.50 1.50 1.49 1.49 1.47 1.47 1.43 1.40 1.38 1.37 1.37 1.30 1.29 1.28 1.20 1.19 1.18 1.18 1.17 1.17 1.16 1.16 1.15 1.14 1.14 1.13 1.13 1.13 1.11 1.11 1.08 0.86 0.85 0.83 0.83 0.83 0.82 0.80 0.80 0.80
D (s) 2.15
F (m) 7.30
B (dd) 2.68
H (m) 1.62
E (m) 7.20
A (dddd) 2.97
G (m) 0.83
C (dd) 2.52
I (m) 1.33
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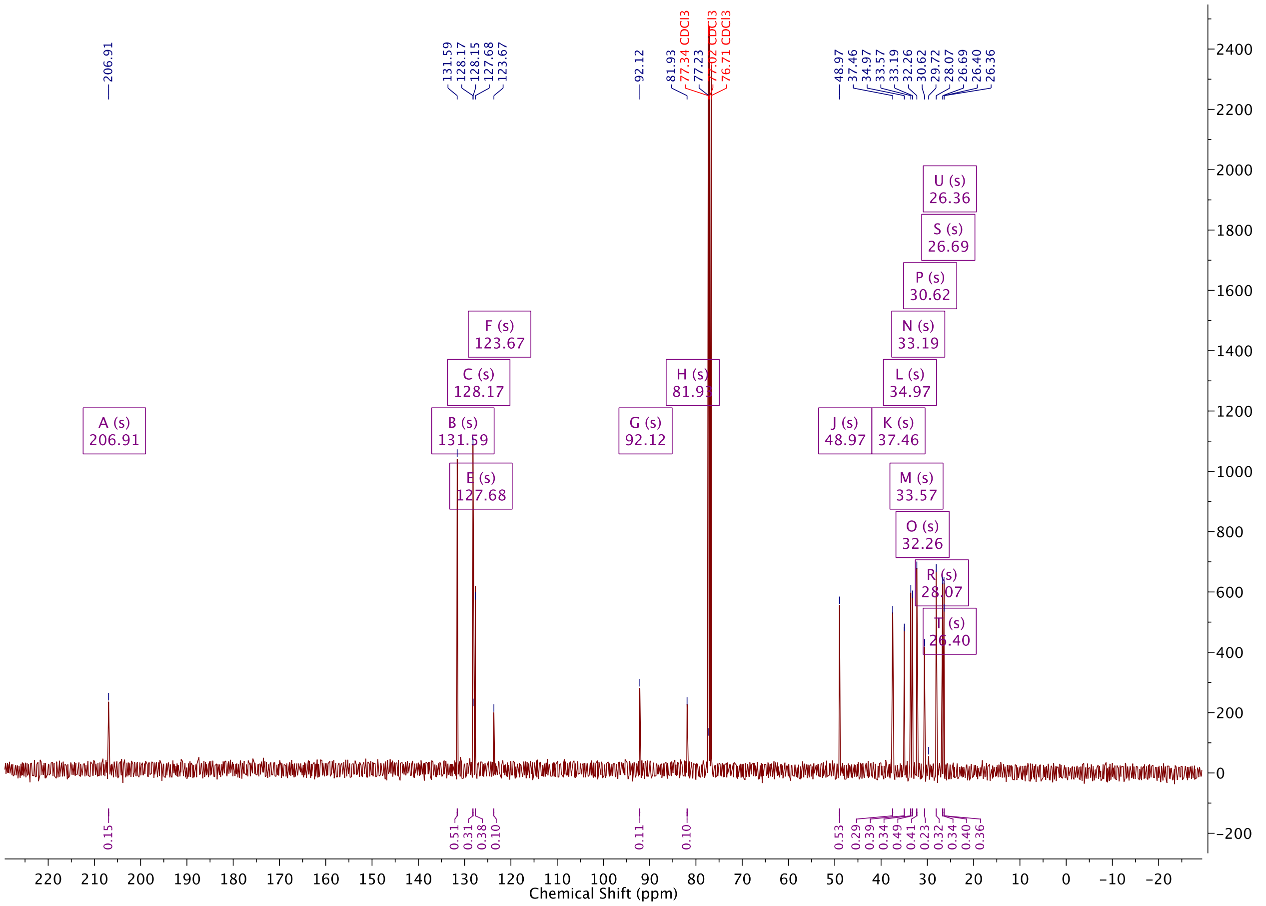
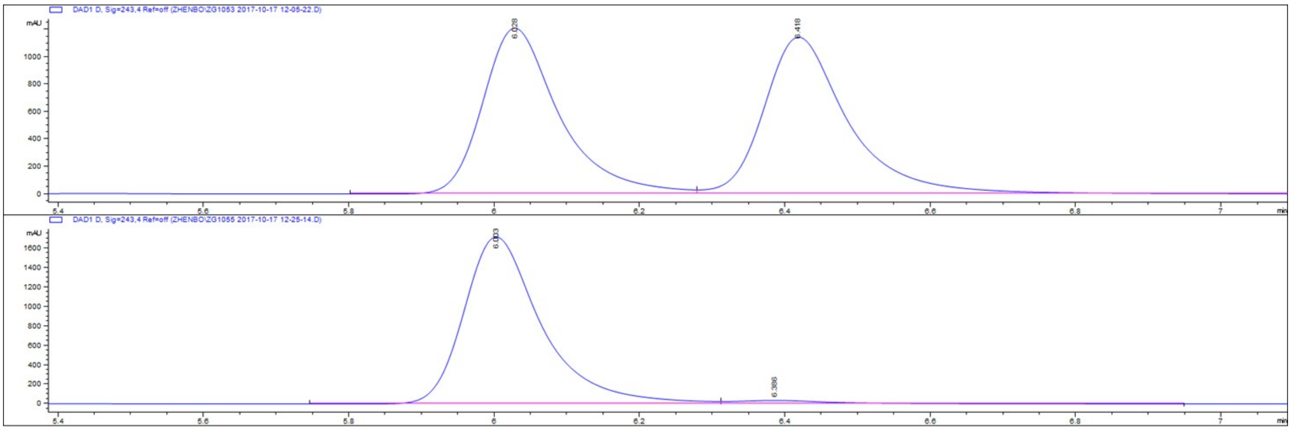
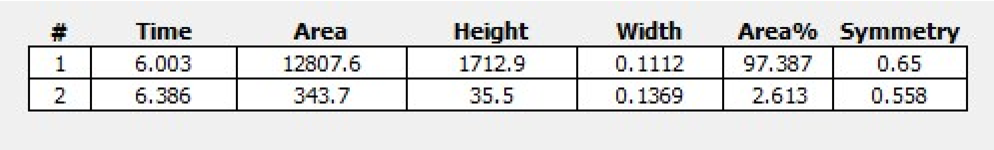
2.97
1.00
0.96
0.95
2.68
4.92
6.59
2.68
Chemical Shift (ppm)


206.91
131.59 128.17 128.15 127.68 123.67
92.12
81.93 77.34 CDCl3 77.23 77.02 CDCl3 76.71 CDCl3
48.97 37.46 34.97 33.57 33.19 32.26 30.62 29.72 28.07 26.69 26.40 26.36
U (s) 26.36
S (s) 26.69
P (s) 30.62
F (s) 123.67
N (s) 33.19
C (s) 128.17
H (s) 81.93
L (s) 34.97
A (s) 206.91
B (s) 131.59
G (s) 92.12
J (s) 48.97
K (s) 37.46
E (s) 127.68
M (s) 33.57
O (s) 32.26
R (s) 28.07
T (s) 26.40
0.15 0.51 0.31 0.38 0.10 0.11 0.10 0.53 0.29 0.39 0.34 0.49 0.41 0.23 0.32 0.34 0.40 0.36
Chemical Shift (ppm)

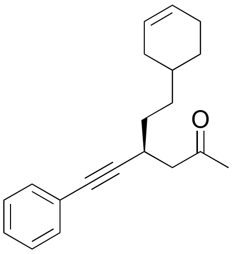
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.003 | 12807.6 | 1712.9 | 0.1112 | 97.387 | 0.65 |
| 2 | 6.386 | 343.7 | 35.5 | 0.1369 | 2.613 | 0.558 |

### (–)-(4*S*)-4-(2-(cyclohex-3-en-1-yl) ethyl)-6-phenylhex-5-yn-2-one (5c)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 4-vinylcyclohex-1-ene (43 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before 6-phenylhex-5-yn-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction

mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (47 mg, 17 mmol, 84 %).

HPLC analysis indicated an enantiomeric excess of 96 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1; λ = 242 nm; major enantiomer tR = 6.49 min; minor enantiomer, tR = 7.01min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.23 – 7.15 (m, 2H, Ar-*H*), 7.11 – 7.01 (m, 3H, Ar-*H*), 5.63 – 5.32 (m, 2H, C*H*=C*H*), 3.04 – 2.79 (m, 1H C*H* $CH_2COCH_3$), 2.57 (dd, *J* = 16.3 Hz, 7.5 Hz, 1H, C$H_2$COC$H_3$), 2.41 (dd, *J* = 16.3 Hz, 6.5 Hz, 1H, C$H_2$COC$H_3$), 2.02 (s, 3H, COC$H_3$), 1.96 – 1.79 (m, 3H,CH=CHC$H_2$), 1.66 – 1.17 (m, 5H, CH=CHC$H_2$, 2 x C$H_2$), 1.13 – 0.95 (m, H, C*H*).

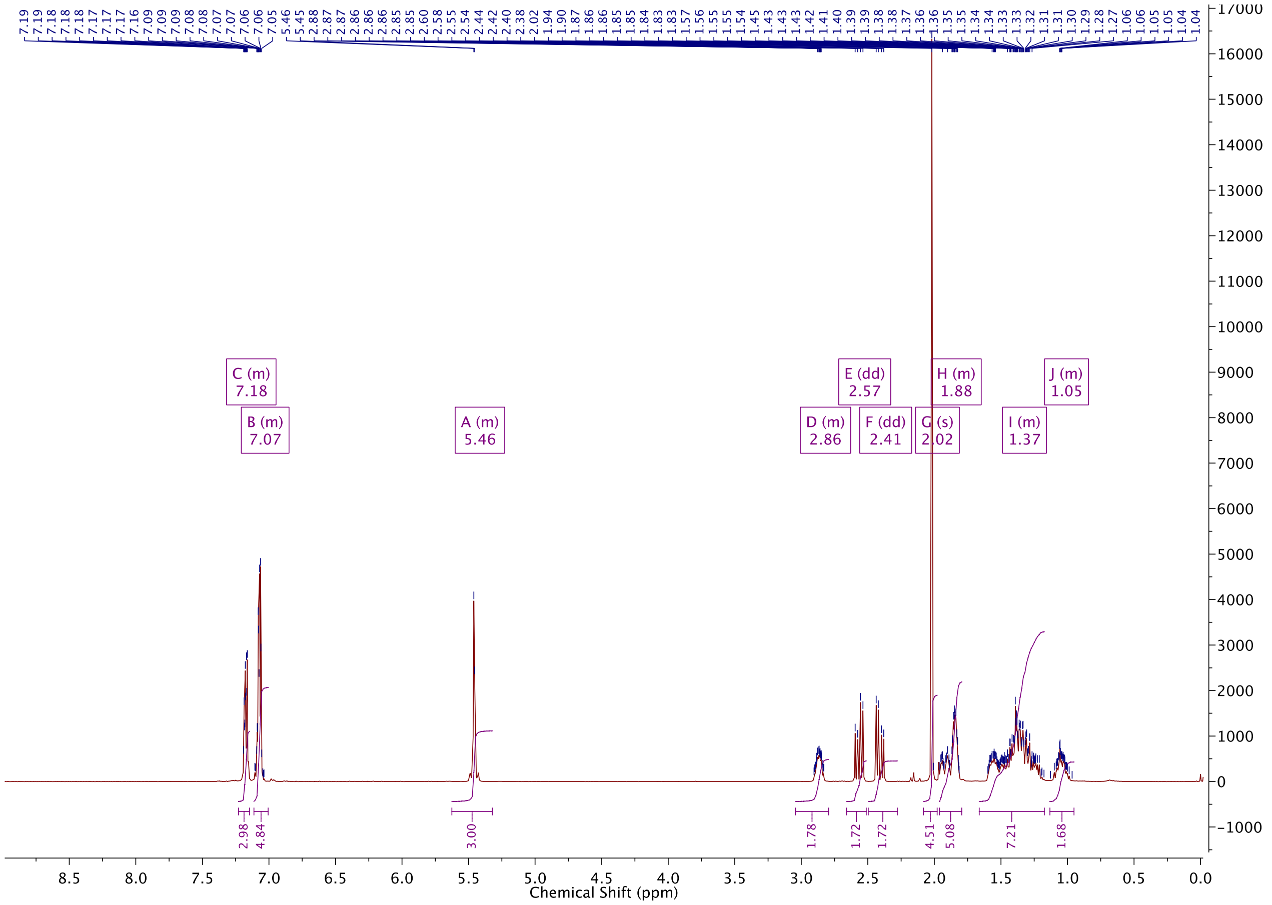
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 206.8, 131.6 (2C), 128.2 (2C), 127.7, 127.1, 126.5, 123.6, 92.0, 82.0, 49.0, 34.2, 33.3, 32.3, 32.1, 30.6, 29.1, 28.0, 25.3.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1716, 1461, 1382, 1154, 955

HRMS (ESI) m/z calc. for $C_{20}H_{25}O$ $[M+H]^+$: 281.1900 found: 281.1901

$[\alpha]^{20}_{589}$ = –11.1 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.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1.27
1.06
1.06
1.05
1.05
1.04
1.04
C (m) 7.18
B (m) 7.07
A (m) 5.46
E (dd) 2.57
D (m) 2.86
F (dd) 2.41
G (s) 2.02
H (m) 1.88
I (m) 1.37
J (m) 1.05
2.98
4.84
3.00
1.78
1.72
1.72
4.51
5.08
7.21
1.68
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Chemical Shift (ppm)
17000
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15000
14000
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12000
11000
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9000
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7000
6000
5000
4000
3000
2000
1000
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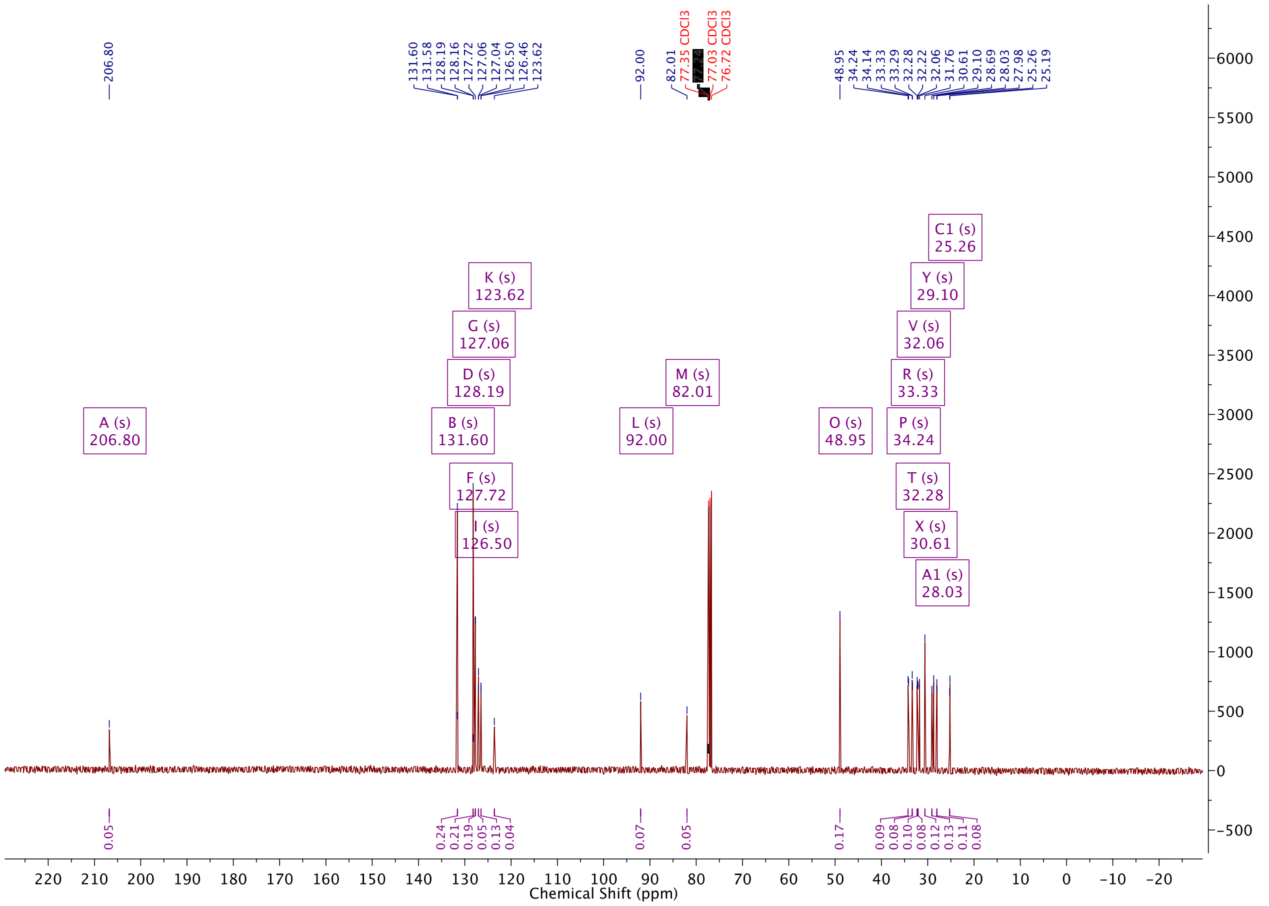
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128.19
128.16
127.72
127.06
127.04
126.50
126.46
123.62
92.00
82.01
77.35 CDCl3
77.03 CDCl3
76.72 CDCl3
48.95
34.24
34.14
33.33
33.29
32.28
32.22
32.06
31.76
30.61
29.10
28.69
28.03
27.98
25.26
25.19
C1 (s) 25.26
K (s) 123.62
Y (s) 29.10
G (s) 127.06
V (s) 32.06
D (s) 128.19
M (s) 82.01
R (s) 33.33
A (s) 206.80
B (s) 131.60
L (s) 92.00
O (s) 48.95
P (s) 34.24
F (s) 127.72
T (s) 32.28
I (s) 126.50
X (s) 30.61
A1 (s) 28.03
0.05
0.24
0.21
0.19
0.05
0.05
0.13
0.04
0.07
0.05
0.17
0.09
0.08
0.10
0.08
0.12
0.13
0.11
0.08
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
Chemical Shift (ppm)
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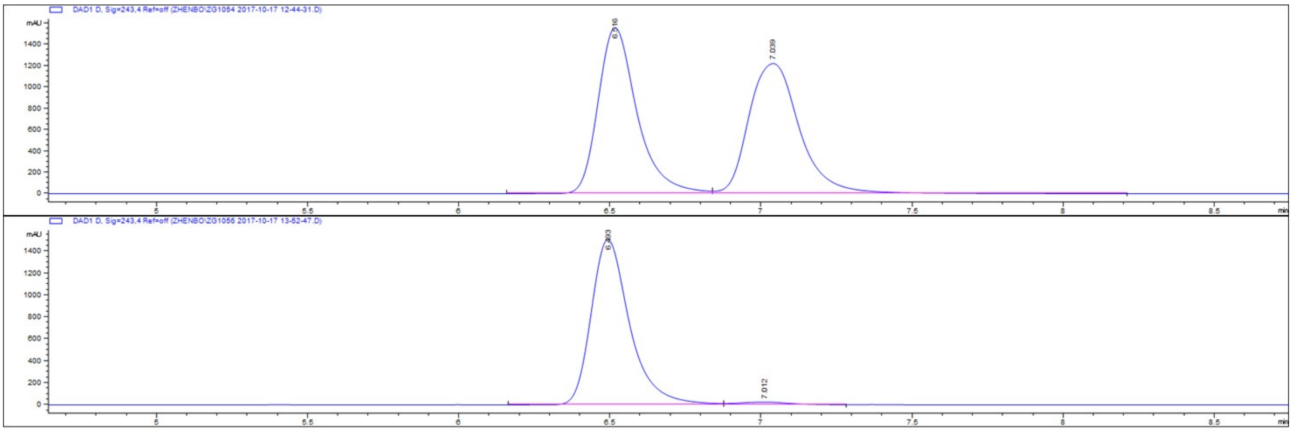
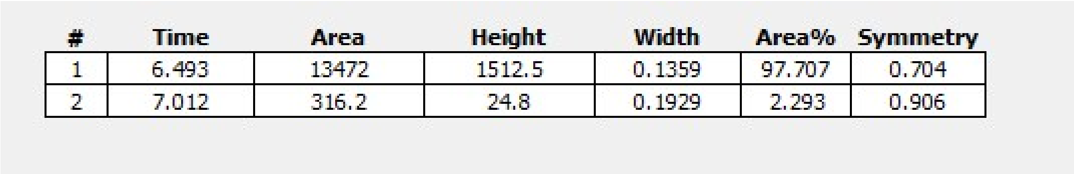
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
−500

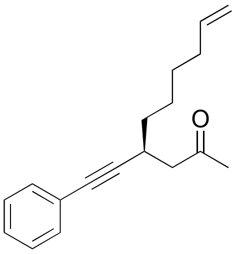
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.493 | 13472 | 1512.5 | 0.1359 | 97.707 | 0.704 |
| 2 | 7.012 | 316.2 | 24.8 | 0.1929 | 2.293 | 0.906 |

### (–)-(*S*)-4-(phenylethynyl) dec-9-en-2-one (5d)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of hexa-1,5-diene (41 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before 6-phenylhex-5-yn-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction

mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (40 mg, 16 mmol, 79 %).

HPLC analysis indicated an enantiomeric excess of 92 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1; λ = 210 nm; major enantiomer tR = 6.28 min; minor enantiomer, tR = 6.73 min].

$^1H$ NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.30 – 7.13 (m, 2H, Ar-*H*), 7.12 – 7.00 (m, 3H, Ar-*H*), 5.62 (m, 1H, C*H*=$CH_2$), 4.95 – 4.60 (m, 2H, CH=C$H_2$), 2.88 (m, 1H, C*H*), 2.56 (dd, *J* = 16.3 Hz, 7.5 Hz, 1H, C$H_2$COC$H_3$), 2.40 (dd, *J* = 16.3 Hz, 6.5 Hz, 1H, C$H_2$COC$H_3$), 2.02 (s, 3H, COC$H_3$), 1.88 (dtt, *J* = 8.0 Hz, 6.6 Hz, 1.3 Hz, 2H, C$H_2$CH=C$H_2$), 1.58 – 1.05 (m, 6H, 3 x C$H_2$).

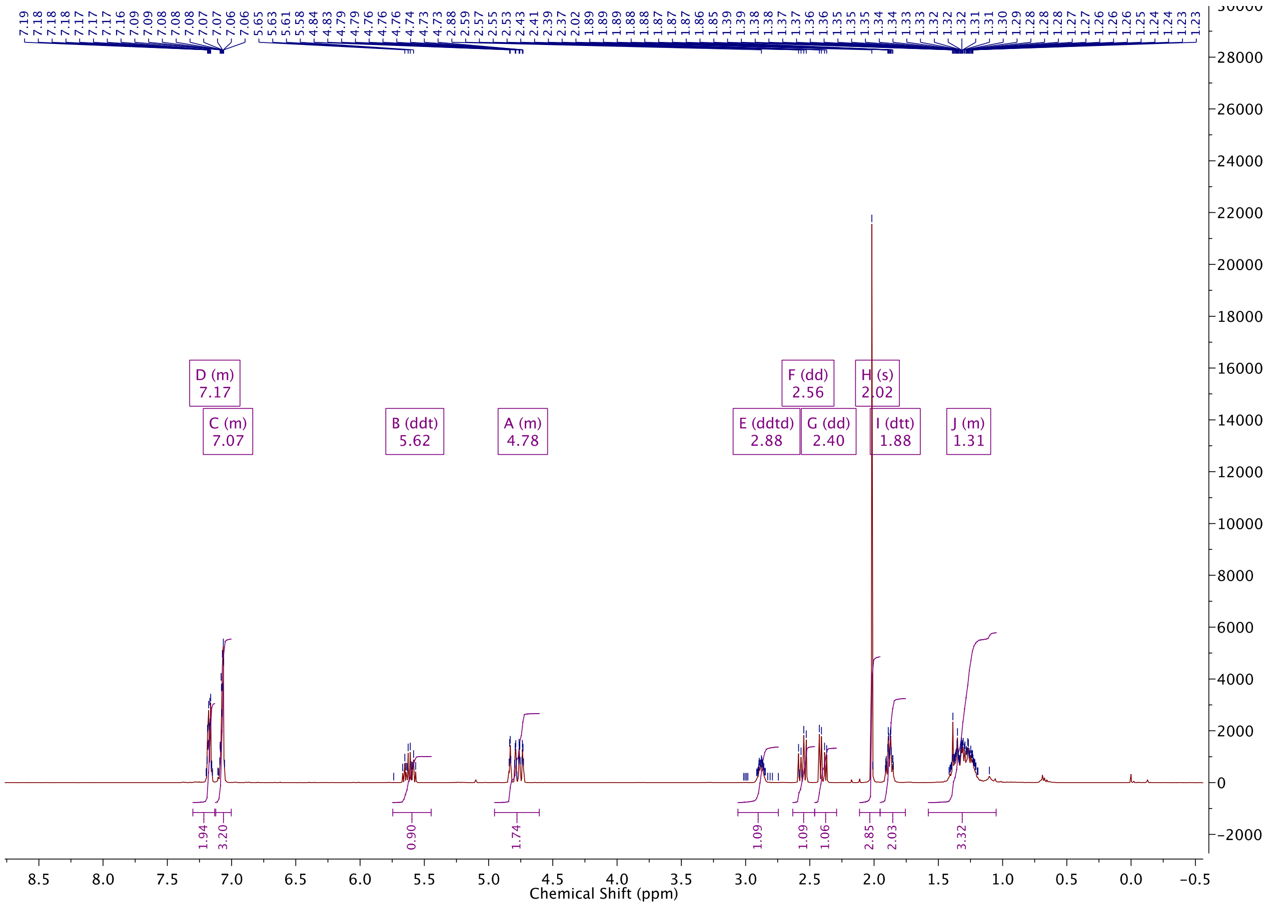
$^{13}C$ NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 206.8, 138.9, 131.6 (2C), 128.2 (2C), 127.7, 123.6, 114.4, 91.9, 82.0, 49.0, 34.7, 33.7, 30.6, 28.6, 27.8, 26.8.

IR ($\nu_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1717, 1462, 1383, 1154, 954

HRMS (ESI) m/z calc. for $C_{18}H_{23}O$ $[M+H]^+$: 255.1743 found: 255.1744

$[\alpha]^{20}_{589}$ = –6.0 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.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B (ddt)
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G (dd)
2.40
H (s)
2.02
I (dtt)
1.88
J (m)
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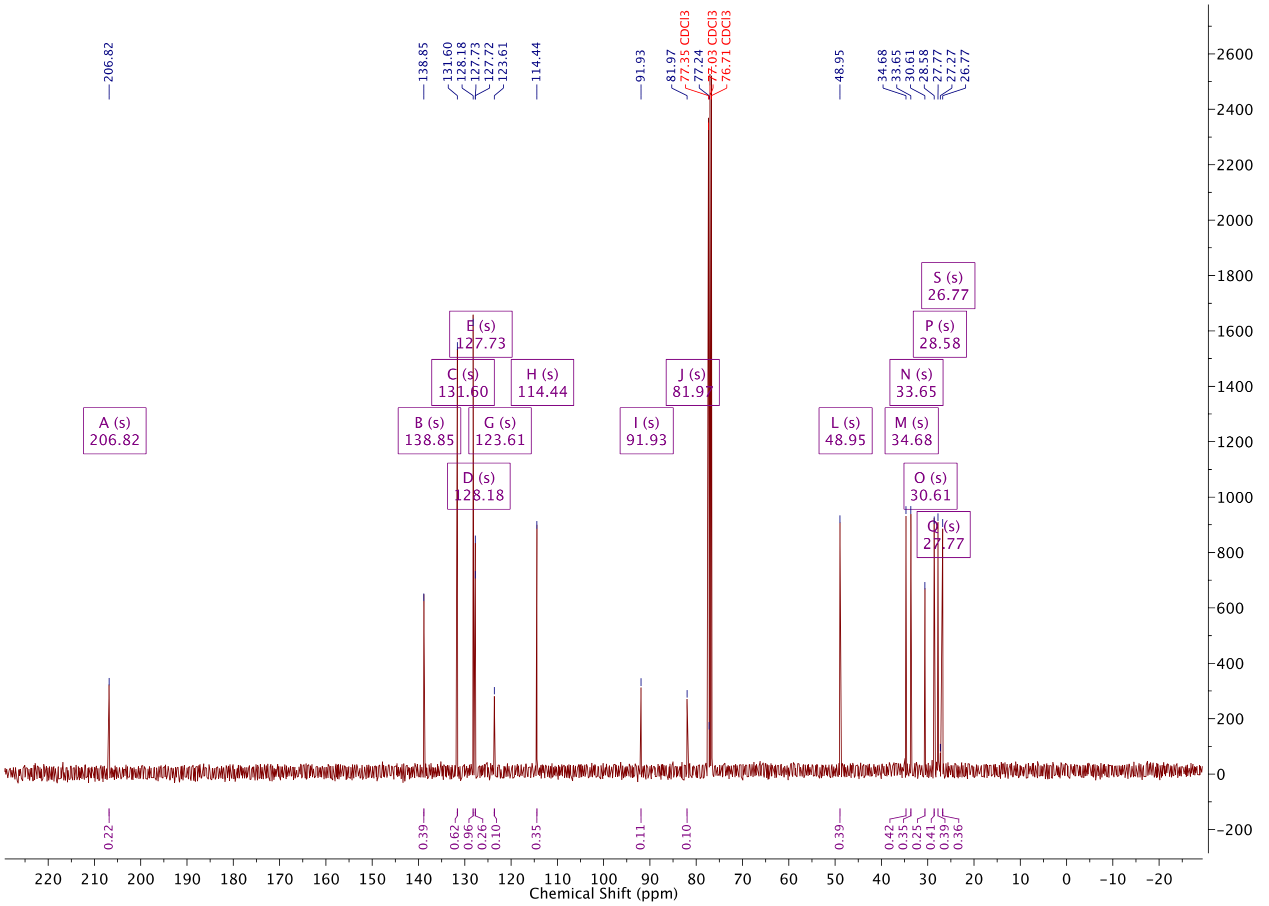
2.85
2.03
3.32
Chemical Shift (ppm)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127.72
123.61
114.44
91.93
81.97
77.35 CDCl3
77.24
77.03 CDCl3
76.71 CDCl3
48.95
34.68
33.65
30.61
28.58
27.77
27.27
26.77
A (s)
206.82
B (s)
138.85
C (s)
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D (s)
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E (s)
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G (s)
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H (s)
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J (s)
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L (s)
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M (s)
34.68
N (s)
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P (s)
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Q (s)
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S (s)
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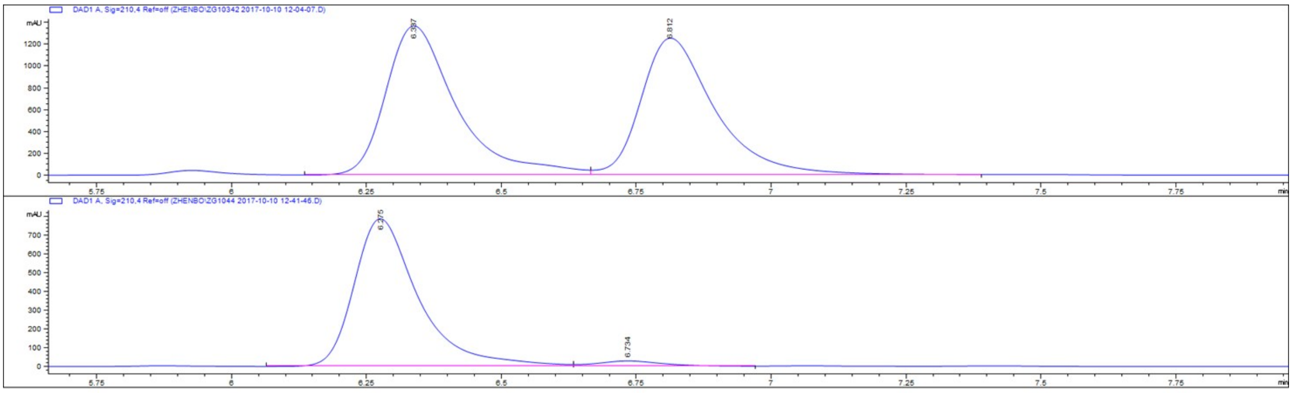
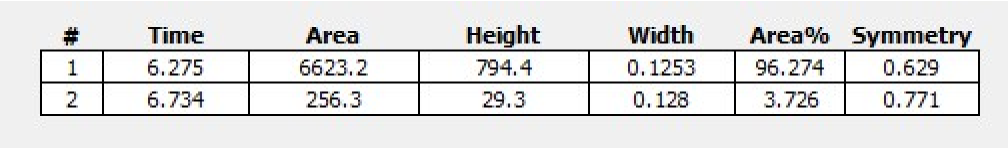
Chemical Shift (ppm)

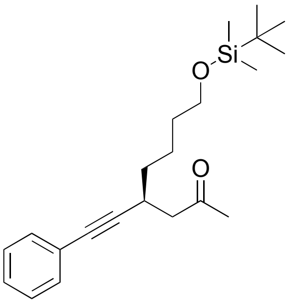
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 6.275 | 6623.2 | 794.4 | 0.1253 | 96.274 | 0.629 |
| 2 | 6.734 | 256.3 | 29.3 | 0.128 | 3.726 | 0.771 |

## (–)-(*S*)-8-((tert-butyldimethylsilyl) oxy)-4-(phenylethynyl)octan-2-one (5e)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of tert-butyldimethyl(pent-4-en-1-yloxy)silane (80 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before 6-phenylhex-5-yn-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (47 mg, 13 mmol, 66%).

HPLC analysis indicated an enantiomeric excess of 94 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1; λ = 210 nm; major enantiomer tR = 5.64 min; minor enantiomer, tR = 6.04 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.39 – 7.32 (m, 2H, Ar-*H*), 7.30 – 7.20 (m, 3H, Ar-*H*), 3.61 (t, *J* = 5.9 Hz, 2H, C*H₂*OSi), 3.18 – 2.96 (m, 1H, C*H*), 2.89 – 2.67 (m, 1H, $CH_2COCH_3$), 2.58 (m, 1H, $CH_2COCH_3$), 2.20 (s, 3H, $COCH_3$), 1.71-1.26 (m, 6H, 3 x $CH_2$), 0.87 (s, 9H, $SiC(CH_3)_3$), 0.03 (s, 6H,$Si(CH_3)_2$).

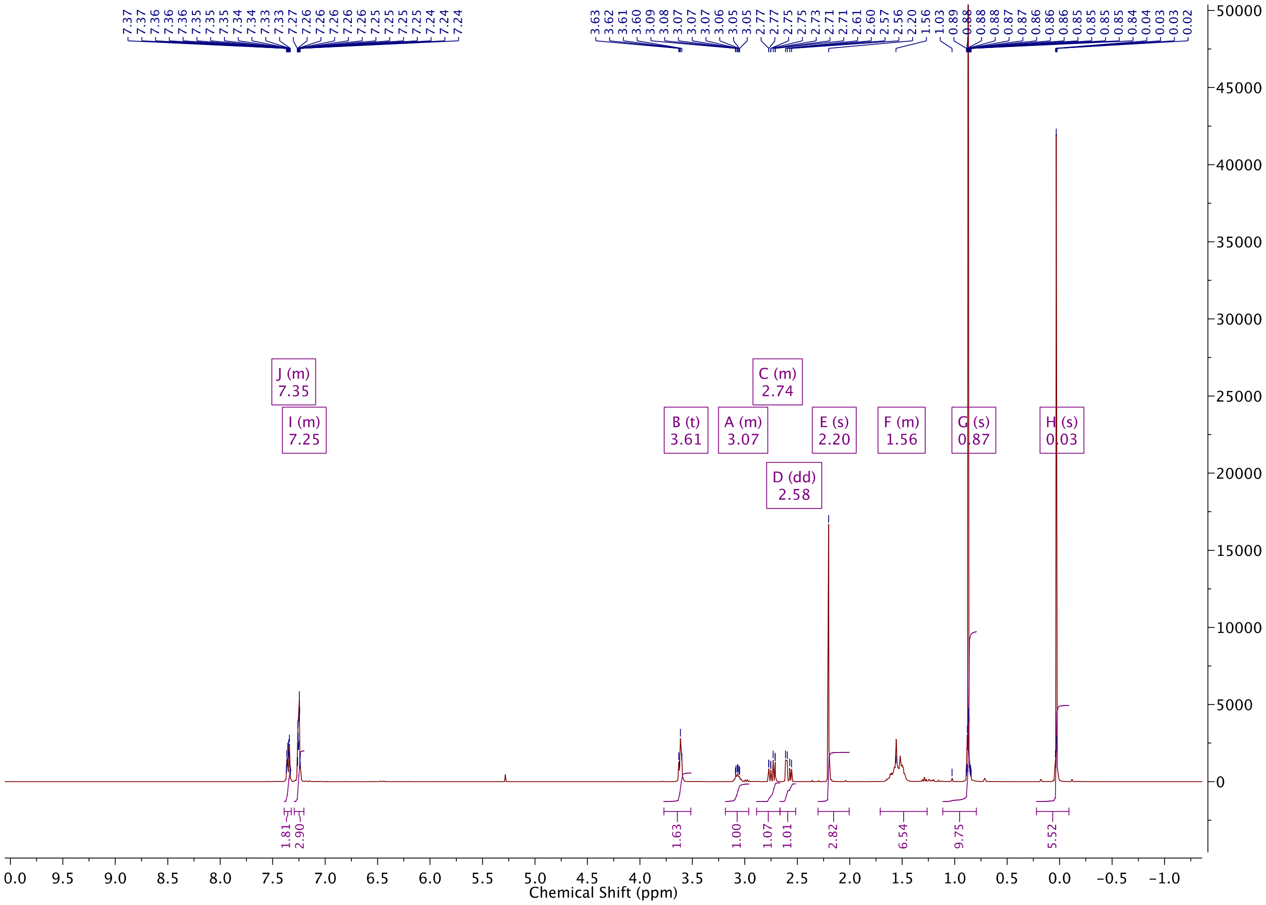
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 206.8, 131.6 (2C), 128.2 (2C), 127.7, 123.6, 91.8, 82.0, 63.0, 49.0, 34.7, 32.6, 30.6, 27.8, 26.0(3C), 23.7, 18.4, -5.3 (2C)

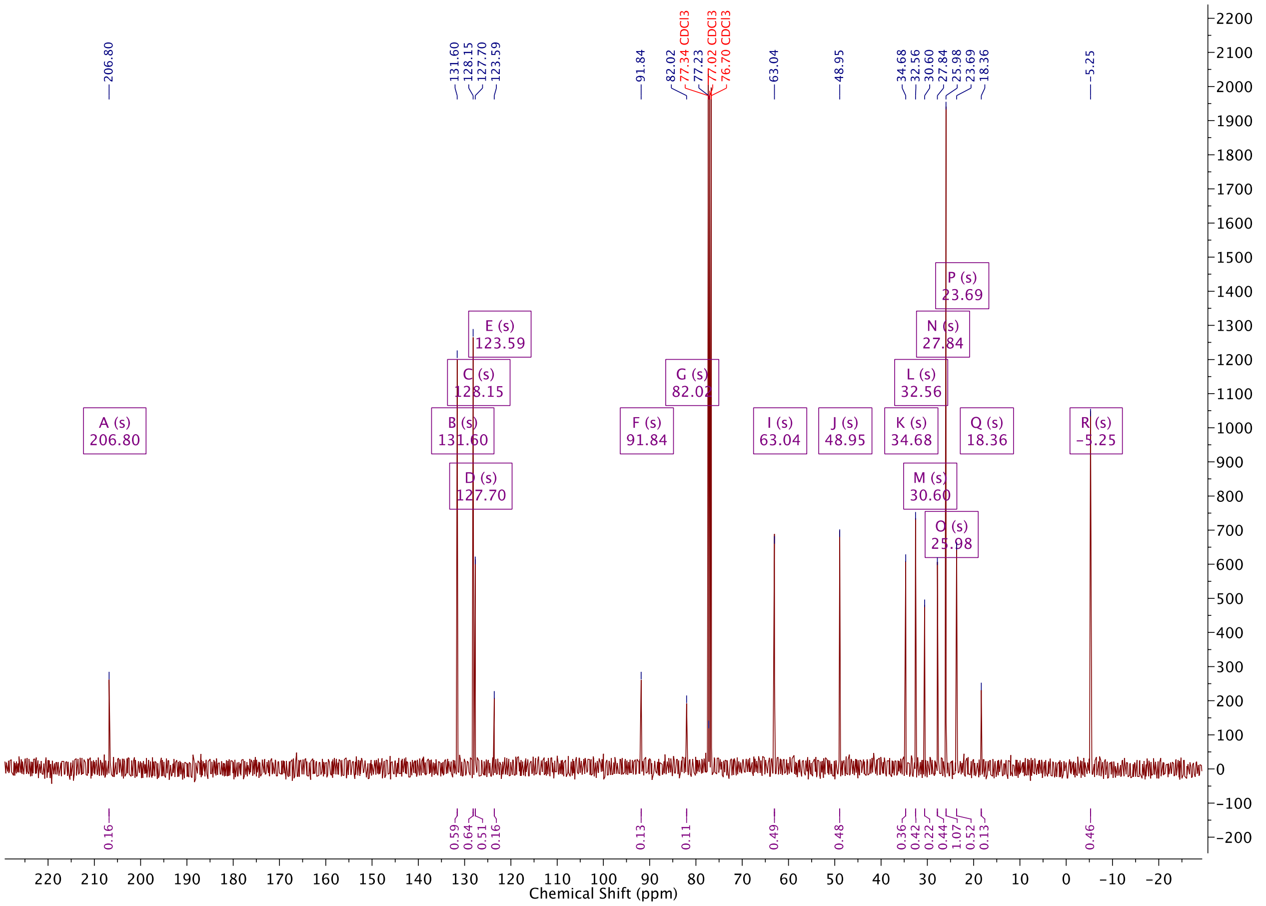
IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1462, 1383, 1153, 955

HRMS (ESI) m/z calc. for $C_{22}H_{35}O_2{}^{28}Si$ $[M+H]^+$: 359.2401, 360.2434 found: 359.2405, 360.2437

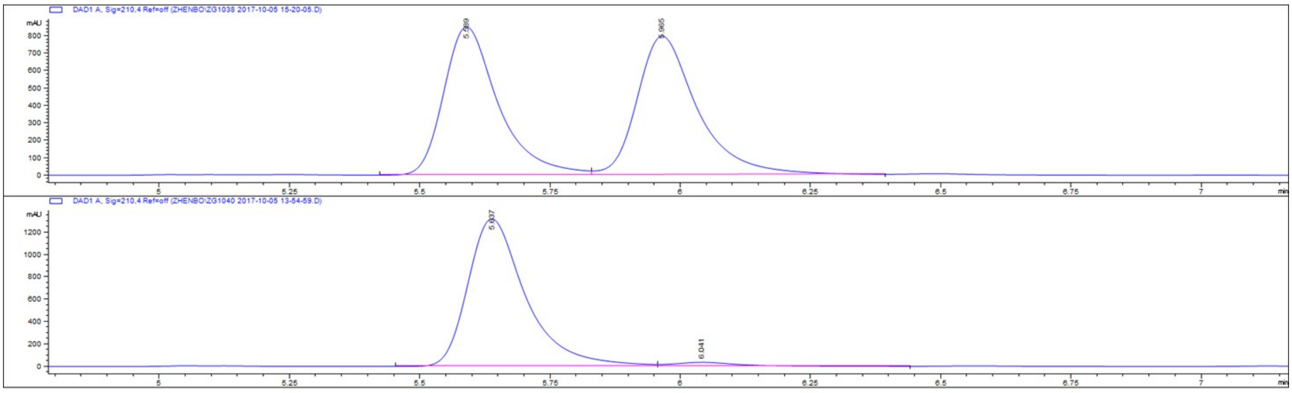
$[\alpha]^{20}_{589}$ = –6.9 ° (c 1.0, $CHCl_3$)

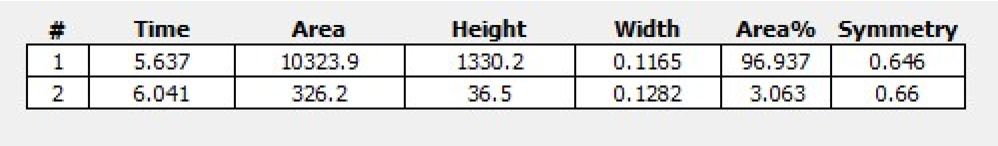
Absolute configuration assigned by analogy to **3p**.


7.37 7.37 7.36 7.36 7.35 7.35 7.35 7.34 7.34 7.33 7.33 7.27 7.26 7.26 7.26 7.26 7.26 7.25 7.25 7.25 7.25 7.24 7.24 7.24
3.63 3.62 3.61 3.60 3.09 3.08 3.07 3.07 3.07 3.06 3.05 3.05 2.77 2.77 2.75 2.75 2.73 2.71 2.61 2.60 2.57 2.56 2.20 1.56 1.03 0.89 0.88 0.88 0.88 0.87 0.87 0.86 0.86 0.86 0.85 0.85 0.85 0.85 0.84 0.04 0.03 0.03 0.02
J (m) 7.35
I (m) 7.25
B (t) 3.61
A (m) 3.07
C (m) 2.74
D (dd) 2.58
E (s) 2.20
F (m) 1.56
G (s) 0.87
H (s) 0.03
1.81
2.90
1.63
1.00
1.07
1.01
2.82
6.54
9.75
5.52
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.0
Chemical Shift (ppm)


206.80
131.60 128.15 127.70 123.59
91.84
82.02
77.34 CDCl3
77.23
77.02 CDCl3
76.70 CDCl3
63.04
48.95
34.68 32.56 30.60 27.84 25.98 23.69 18.36
−5.25
A (s) 206.80
B (s) 131.60
C (s) 128.15
D (s) 127.70
E (s) 123.59
F (s) 91.84
G (s) 82.02
I (s) 63.04
J (s) 48.95
K (s) 34.68
L (s) 32.56
M (s) 30.60
N (s) 27.84
O (s) 25.98
P (s) 23.69
Q (s) 18.36
R (s) −5.25
0.16
0.59 0.64 0.51 0.16
0.13
0.11
0.49
0.48
0.36 0.42 0.22 0.44 1.07 0.52 0.13
0.46
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
−100
−200
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
Chemical Shift (ppm)

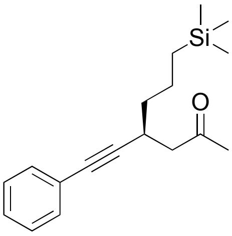
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.637 | 10323.9 | 1330.2 | 0.1165 | 96.937 | 0.646 |
| 2 | 6.041 | 326.2 | 36.5 | 0.1282 | 3.063 | 0.66 |

### (–)-(*S*)-4-(phenylethynyl)-7-(trimethylsilyl) heptan-2-one (5f)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.
To a second, flame dried, round bottom flask, containing a stirred solution of allyltrimethylsilane (57 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.
The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before 6-phenylhex-5-yn-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer

extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (42 mg, 15 mmol, 75 %).

HPLC analysis indicated an enantiomeric excess of 94 % [Chiralpak® IB; flow: 0.7 mL/min; hexane/i-PrOH: 99: 1; λ = 242 nm; major enantiomer tR = 7.57 min; minor enantiomer, tR = 7.96 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.42 – 7.33 (m, 2H, Ar-*H*), 7.31 – 7.24 (m, 3H, Ar-*H*), 3.10 (m, 1H, $C\mathit{H}CH_2COCH_3$), 2.75 (dd, *J* = 16.2 Hz, 7.7 Hz, 1H, $C\mathit{H}_2COCH_3$), 2.59 (dd, *J* = 16.2 Hz, 6.4 Hz, 1H, $C\mathit{H}_2COCH_3$), 2.22 (s, 3H, $COC\mathit{H}_3$), 1.70 – 1.23 (m, 4H, 2 x $C\mathit{H}_2$), 0.79 – 0.32 (m, 2H, $C\mathit{H}_2Si$), -0.00 (s, 9H, 3 x $C\mathit{H}_3$).

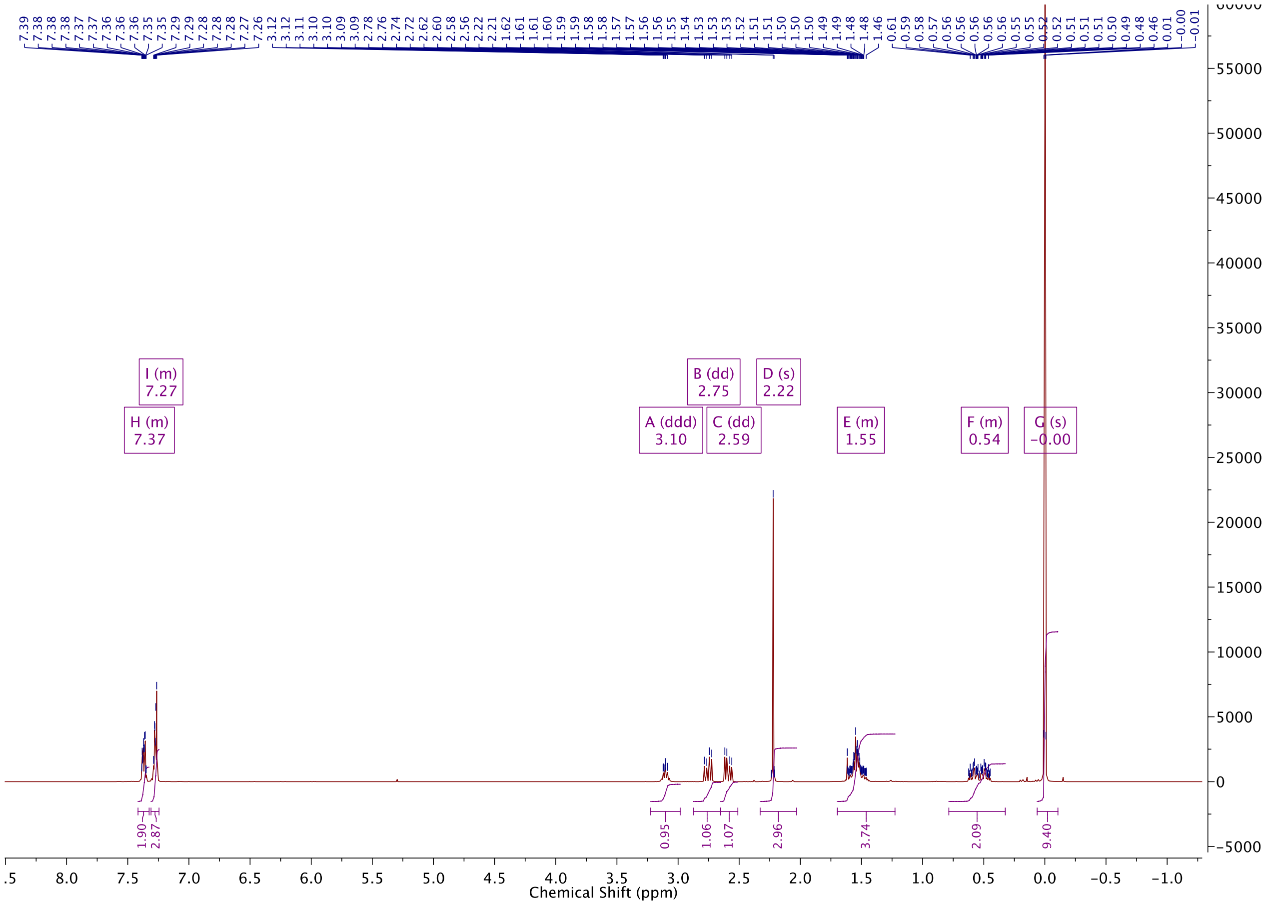
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 208.5, 133.2 (2C), 129.8 (2C), 129.3, 125.3, 93.6, 83.6, 50.6, 40.2, 32.2, 29.2, 23.3, 17.9, 0.0 (3C)

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1461, 1383, 1251, 1153, 954

HRMS (ESI) m/z calc. for $C_{18}H_{27}O^{28}Si$ $[M+H]^+$: 287.1826, 288.1859 found: 287.1825, 288.1861

$[\alpha]^{20}_{589}$ = –23.5 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.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H (m)
7.37
B (dd)
2.75
D (s)
2.22
A (ddd)
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C (dd)
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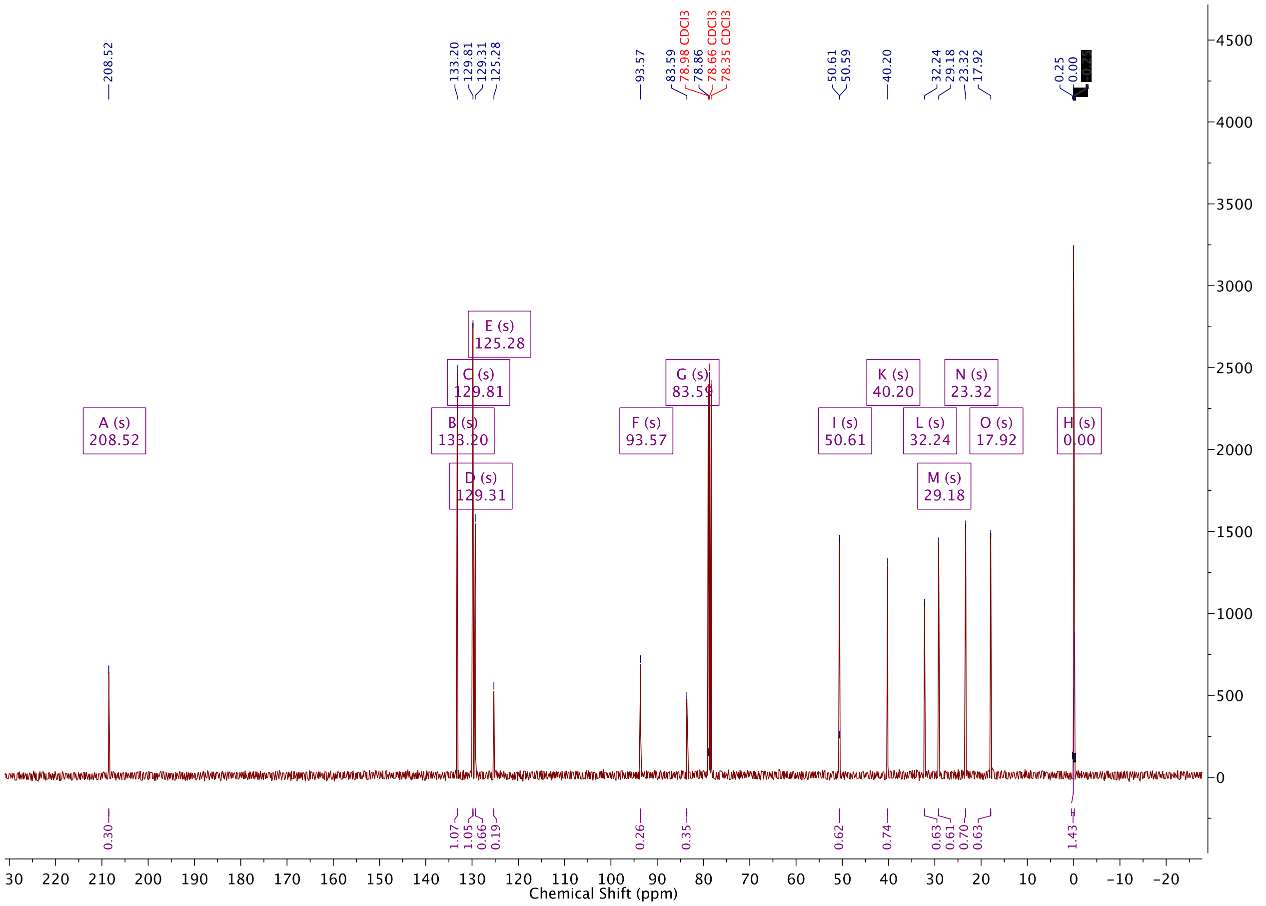
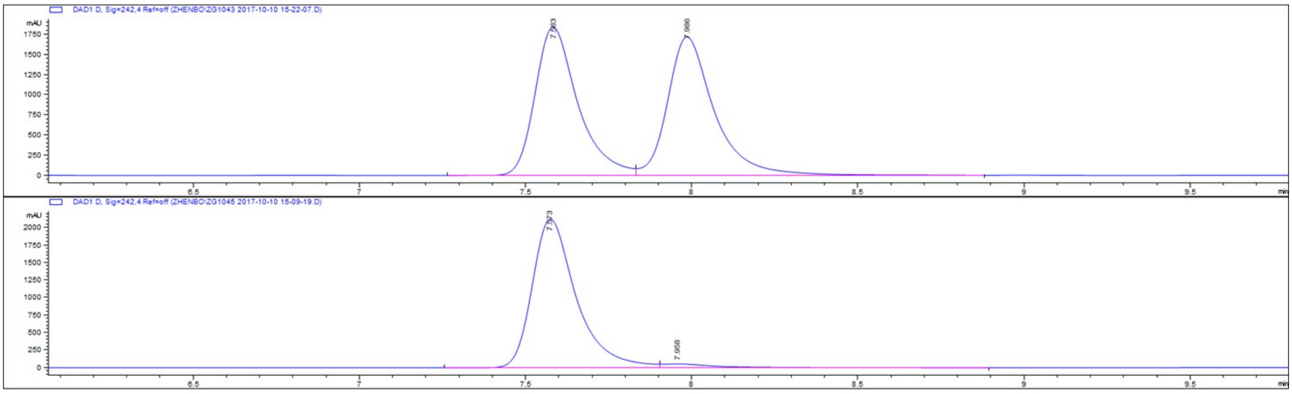
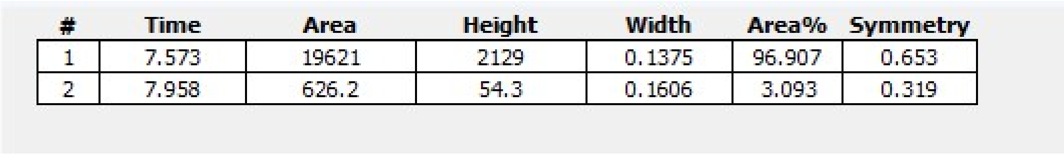
E (m)
1.55
F (m)
0.54
G (s)
-0.00
Chemical Shift (ppm)


208.52
133.20
129.81
129.31
125.28
93.57
83.59
78.98 CDCl3
78.86
78.66 CDCl3
78.35 CDCl3
50.61
50.59
40.20
32.24
29.18
23.32
17.92
0.25
0.00
A (s)
208.52
B (s)
133.20
C (s)
129.81
D (s)
129.31
E (s)
125.28
F (s)
93.57
G (s)
83.59
H (s)
0.00
I (s)
50.61
K (s)
40.20
L (s)
32.24
M (s)
29.18
N (s)
23.32
O (s)
17.92
Chemical Shift (ppm)

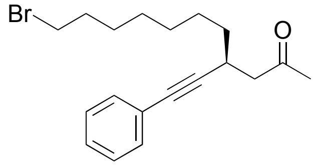
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.573 | 19621 | 2129 | 0.1375 | 96.907 | 0.653 |
| 2 | 7.958 | 626.2 | 54.3 | 0.1606 | 3.093 | 0.319 |

## (–)-(*S*)-11-bromo-4-(phenylethynyl) undecan-2-one (5g)



CuCl (1.9 mg, 0.1 eq., 0.02 mmol), and the phosphoramidite ligand (11.4 mg, 0.1 eq., 0.02 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$ under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (5.6 mg, 0.11 eq., 0.022 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 7-bromohept-1-ene (89 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before 6-phenylhex-5-yn-2-one (34 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered,

concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (53 mg, 15mmol, 76%).
HPLC analysis indicated an enantiomeric excess of 96 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1; λ = 210 nm; major enantiomer tR = 7.96 min; minor enantiomer, tR = 9.12 min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.22 – 7.14 (m, 2H, Ar-*H*), 7.11 – 7.03 (m, 3H, Ar-*H*), 3.20 (t, *J* = 6.9 Hz, 2H, C$H_2$Br), 3.01 – 2.75 (m, 1H, C*H*), 2.56 (dd, *J* = 16.3 Hz, 7.5 Hz, 1H, C$H_2$COC$H_3$), 2.40 (dd, *J* = 16.3 Hz, 6.5 Hz, 1H, C$H_2$COC$H_3$), 2.02 (s, 3H, COC$H_3$), 1.75 – 1.54 (m, 2H, C$H_2$), 1.46 – 0.97 (m, 10H, 5 x C$H_2$).

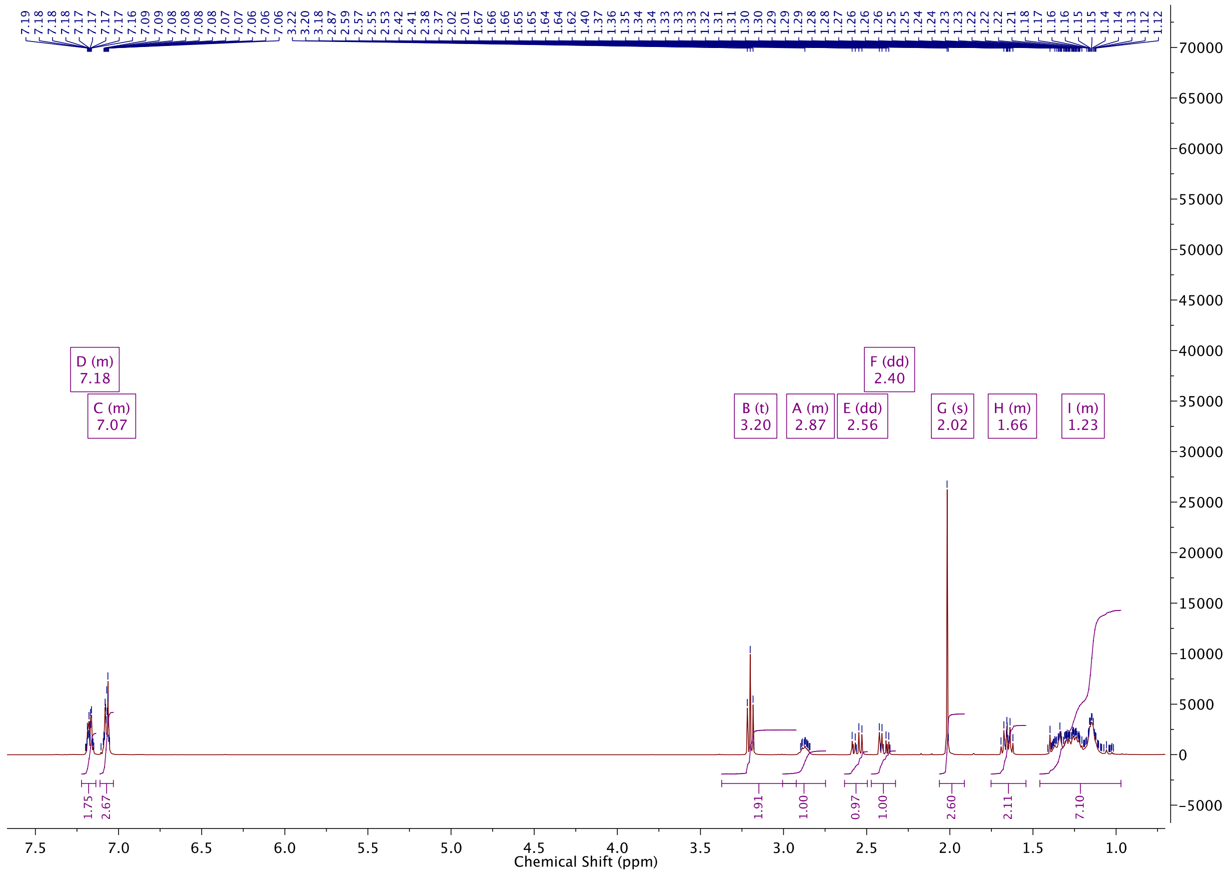
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 206.8, 131.6 (2C), 128.2 (2C), 127.7, 123.6, 91.9, 82.0, 49.0, 34.8, 34.0, 32.8, 30.6, 29.1, 28.6, 28.1, 27.8, 27.2.

IR ($v_{max}$/cm$^{-1}$, $CHCl_3$) 2981, 1717,1462, 1154, 954

HRMS (ESI) m/z calc. for $C_{19}H_{26}O^{79}Br$ $[M+H]^+$: 349.1162, 351.1141 found: 349.1162, 351.1141

$[\alpha]^{20}_{589}$ = –10.1 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.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C (m)
7.07
B (t)
3.20
A (m)
2.87
E (dd)
2.56
F (dd)
2.40
G (s)
2.02
H (m)
1.66
I (m)
1.23
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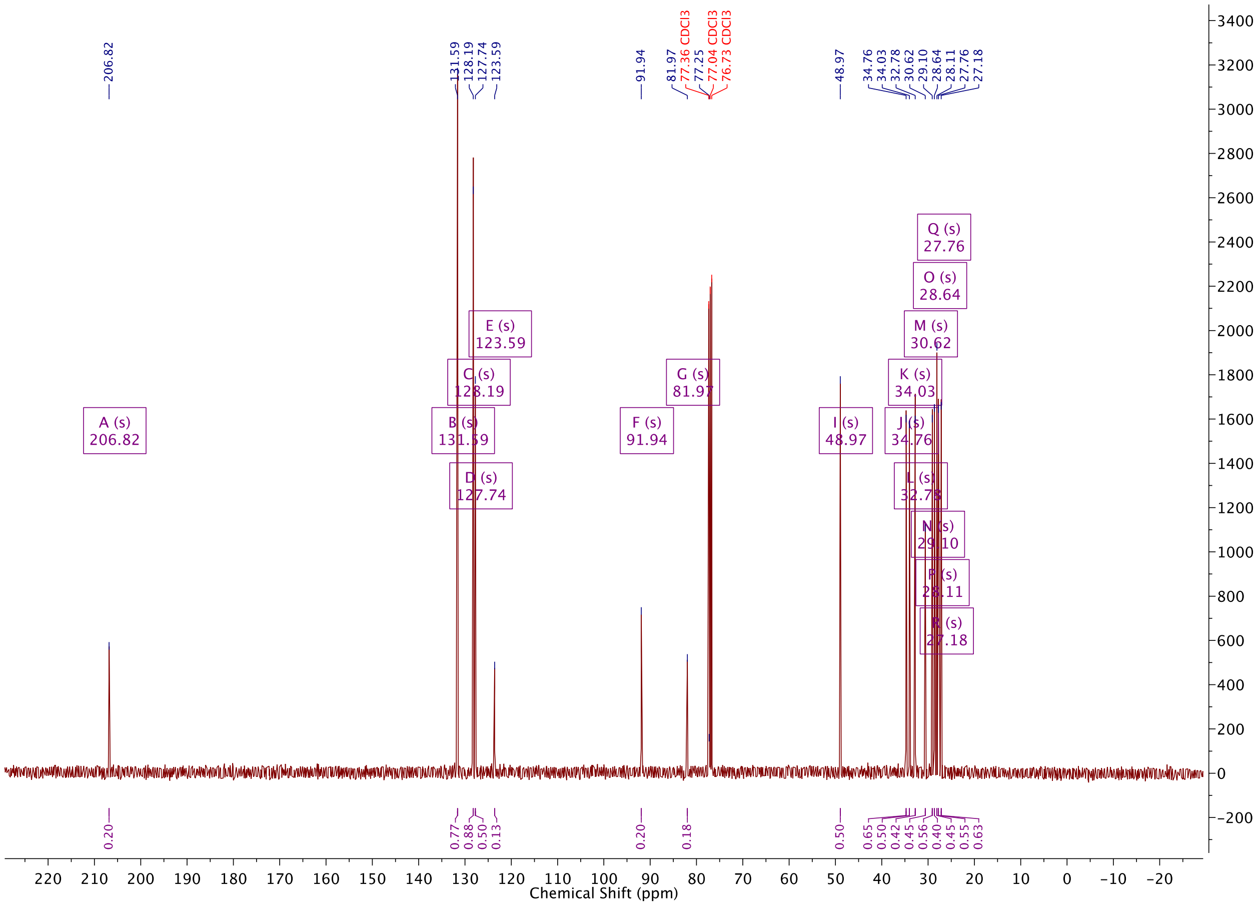
2.67
1.91
1.00
0.97
1.00
2.60
2.11
7.10
Chemical Shift (ppm)


206.82
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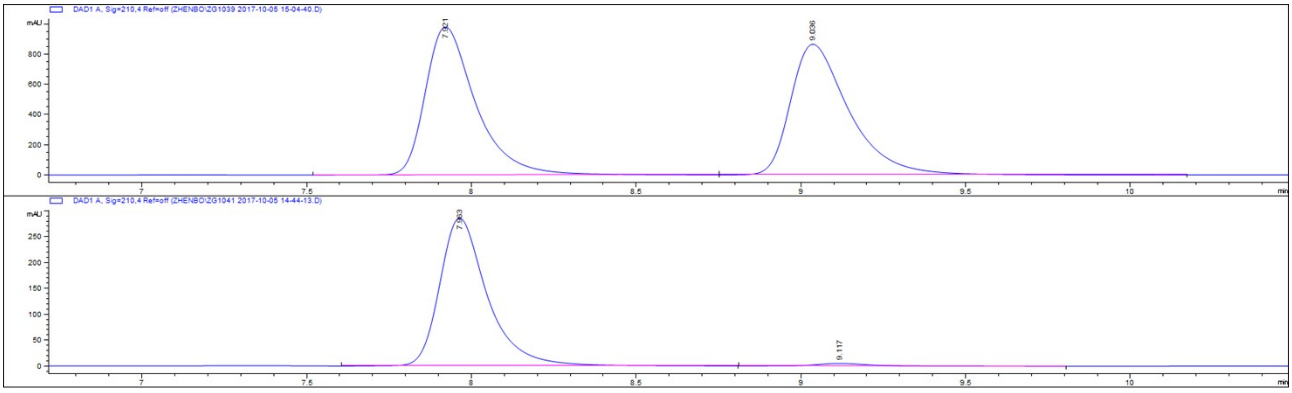
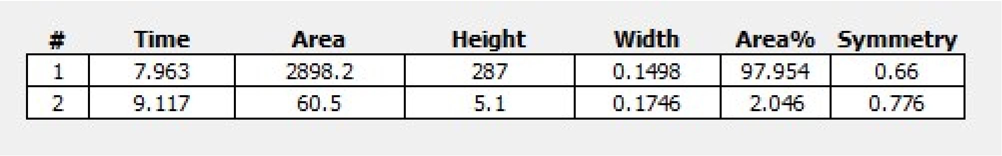
123.59
91.94
81.97
77.36 CDCl3
77.25
77.04 CDCl3
76.73 CDCl3
48.97
34.76
34.03
32.78
30.62
29.10
28.64
28.11
27.76
27.18
A (s)
206.82
B (s)
131.59
C (s)
128.19
D (s)
127.74
E (s)
123.59
F (s)
91.94
G (s)
81.97
I (s)
48.97
J (s)
34.76
K (s)
34.03
L (s)
32.78
M (s)
30.62
N (s)
29.10
O (s)
28.64
P (s)
28.11
Q (s)
27.76
R (s)
27.18
Chemical Shift (ppm)

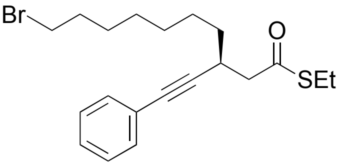
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 7.963 | 2898.2 | 287 | 0.1498 | 97.954 | 0.66 |
| 2 | 9.117 | 60.5 | 5.1 | 0.1746 | 2.046 | 0.776 |

## (+)-S-ethyl (*S*)-10-bromo-3- (phenylethynyl)decanethioate (5h)



CuCl (3.8 mg, 0.2 eq., 0.04 mmol), and the phosphoramidite ligand (22.8 mg, 0.2 eq., 0.04 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$/DCM (1/1) under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (11.2 mg, 0.22 eq., 0.044 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 7-bromohept-1-ene (89 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before S-ethyl (E)-5-phenylpent-2-en-4-ynethioate (43 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (52 mg, 15 mmol, 66%).

HPLC analysis indicated an enantiomeric excess of 97 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1; λ = 243 nm; major enantiomer tR = 5.44 min; minor enantiomer, tR = 6.44min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.18 (m, 2H, Ar-*H*), 7.06 (m, 3H, Ar-*H*), 3.20 (t, *J* = 6.8 Hz, 2H, C*H*$_2$Br), 2.91 (td, *J* = 7.5 Hz, 3.9 Hz, 1H, C*H*), 2.71 (q, *J* = 7.4 Hz, 2H, SC*H*$_2$CH$_3$), 2.63 (dd, *J* = 14.8 Hz, 7.4 Hz, 1H, C*H$_2$*COCH$_3$), 2.52 (dd, *J* = 14.8 Hz, 7.1 Hz, 1H, C*H$_2$*COCH$_3$), 1.65 (p, *J* = 7.0 Hz, 2H, C*H$_2$*), 1.45 – 1.10 (m, 10H, 5 x C*H$_2$*), 1.06 (t, *J* = 7.4 Hz, 3H, C*H$_3$*).

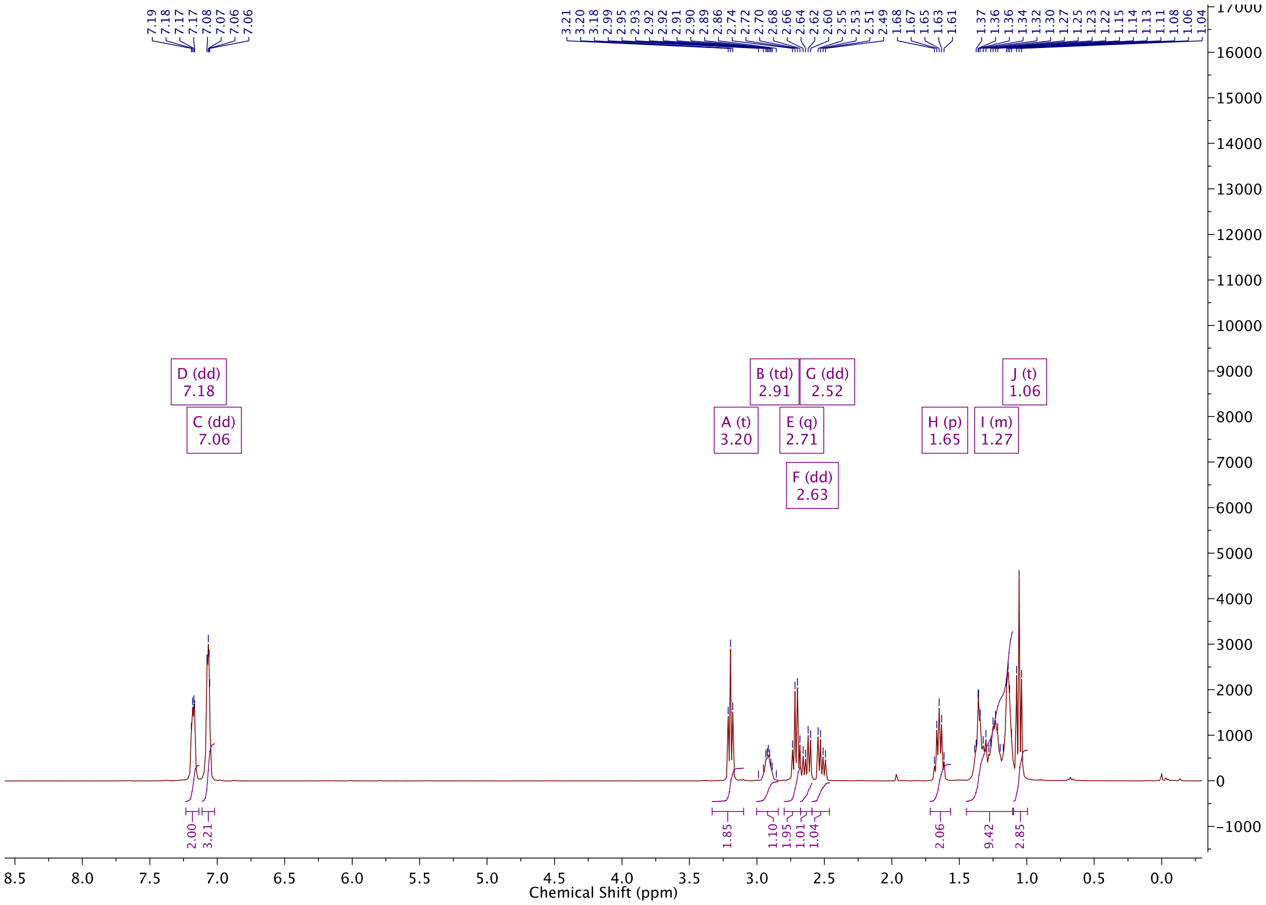
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 197.6, 131.6 (2C), 128.2 (2C), 127.8, 123.6, 91.1, 82.5, 49.1, 34.4, 34.0, 32.8, 29.3, 29.1, 28.6, 28.1, 27.1, 23.5, 14.8.

IR ($\nu_{max}$/cm$^{-1}$, $CHCl_3$) 3026, 2842, 1687, 1429, 1305, 1016, 911

HRMS (ESI) m/z calc. for $C_{20}H_{28}O^{79}Br^{32}S$ [M+H]$^+$: 395.1039, 397.1018, 398.1052, 399.0976 found: 395.1037, 397.1015, 398.1047, 399.0976

$[\alpha]^{20}_{589}$ = +5.2 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to **3p**.


7.19
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7.17
7.08
7.07
7.06
7.06
3.21
3.20
3.18
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2.95
2.93
2.92
2.92
2.91
2.90
2.89
2.86
2.74
2.72
2.70
2.68
2.66
2.64
2.62
2.60
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2.53
2.51
2.49
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1.23
1.22
1.15
1.14
1.13
1.11
1.08
1.06
1.04
D (dd) 7.18
C (dd) 7.06
A (t) 3.20
B (td) 2.91
G (dd) 2.52
E (q) 2.71
F (dd) 2.63
H (p) 1.65
I (m) 1.27
J (t) 1.06
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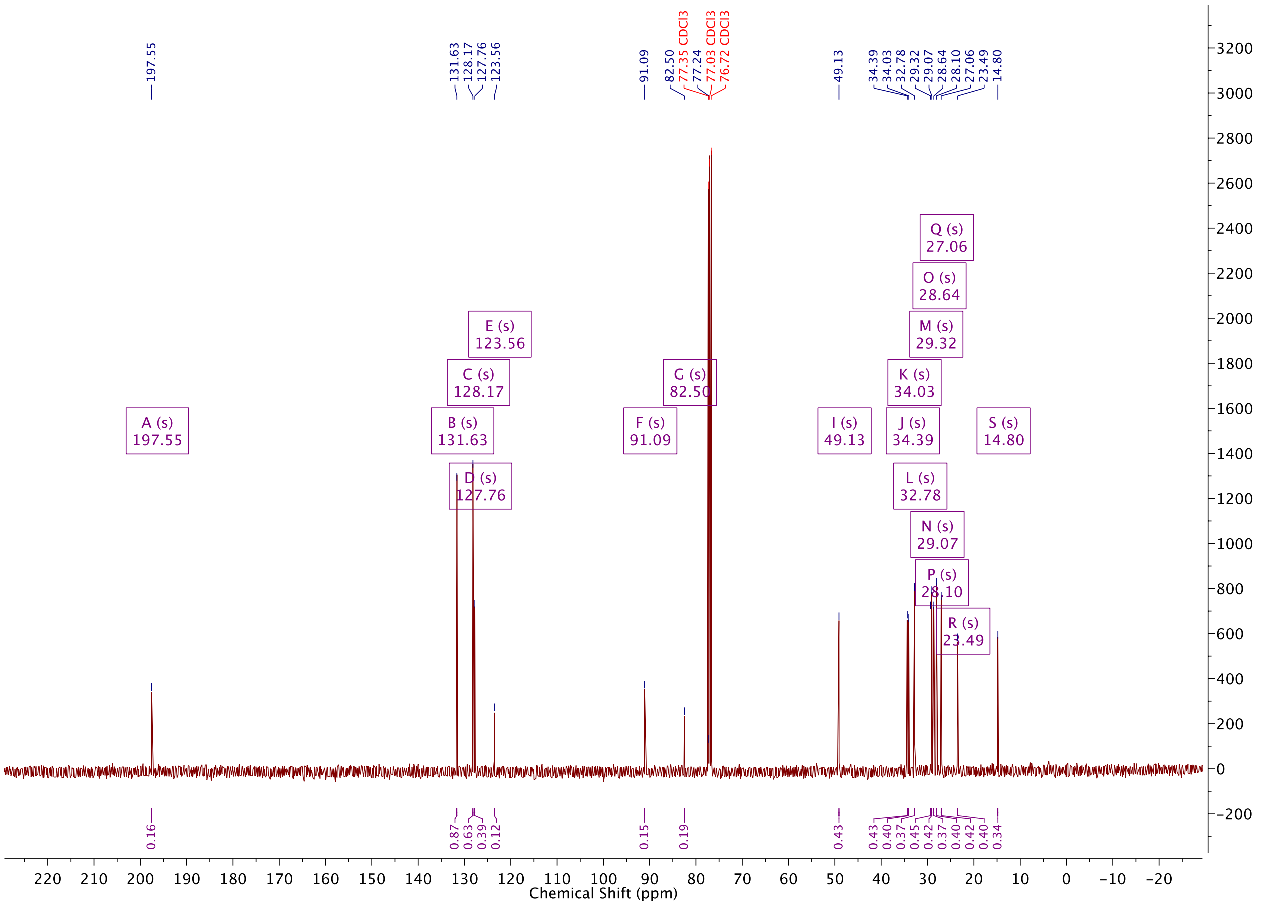
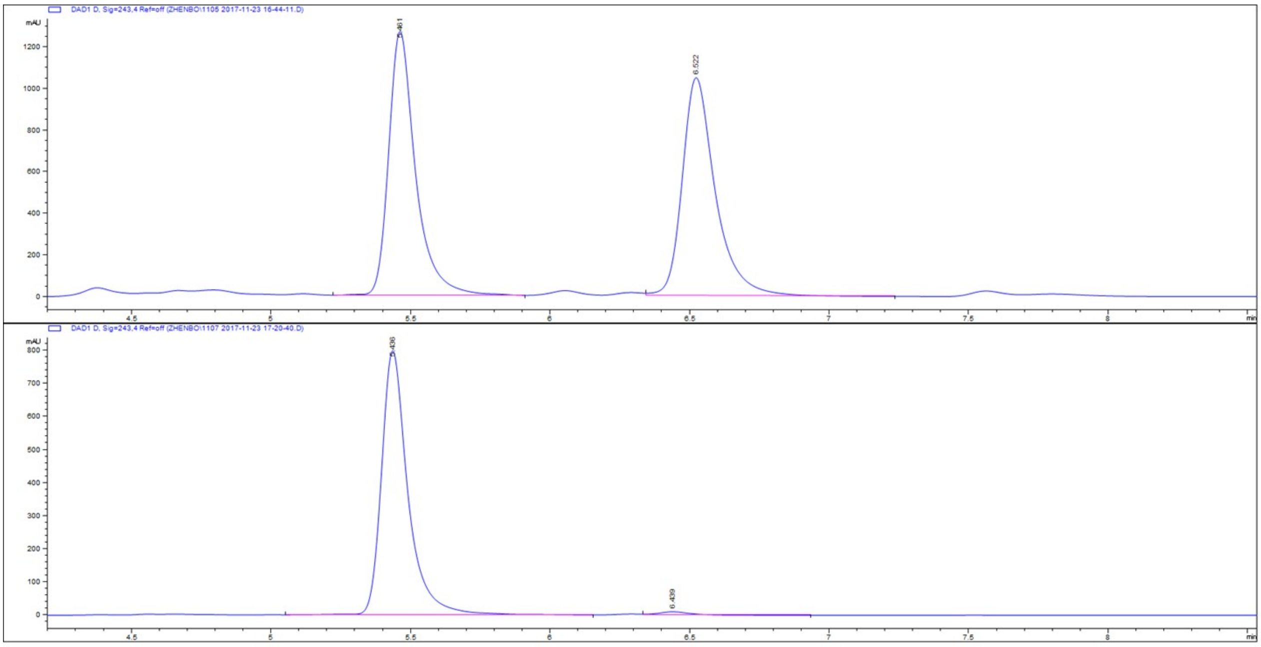
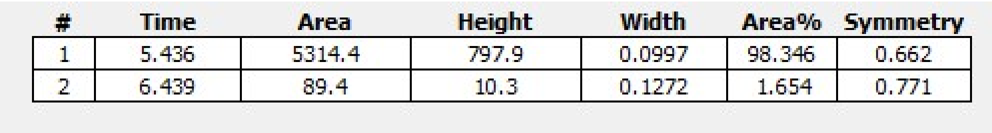
3.21
1.85
1.10
1.95
1.01
1.04
2.06
9.42
2.85
Chemical Shift (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
−1000


197.55
131.63
128.17
127.76
123.56
91.09
82.50
77.35 CDCl3
77.24
77.03 CDCl3
76.72 CDCl3
49.13
34.39
34.03
32.78
29.32
29.07
28.64
28.10
27.06
23.49
14.80
A (s) 197.55
B (s) 131.63
C (s) 128.17
D (s) 127.76
E (s) 123.56
F (s) 91.09
G (s) 82.50
I (s) 49.13
J (s) 34.39
K (s) 34.03
L (s) 32.78
M (s) 29.32
N (s) 29.07
O (s) 28.64
P (s) 28.10
Q (s) 27.06
R (s) 23.49
S (s) 14.80
0.16
0.87
0.63
0.39
0.12
0.15
0.19
0.43
0.43
0.40
0.37
0.45
0.42
0.37
0.40
0.42
0.40
0.34
Chemical Shift (ppm)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
−200

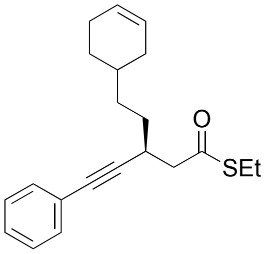
HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 5.436 | 5314.4 | 797.9 | 0.0997 | 98.346 | 0.662 |
| 2 | 6.439 | 89.4 | 10.3 | 0.1272 | 1.654 | 0.771 |

### (+)-S-ethyl (3*S*)-3-(2-(cyclohex-3-en-1-yl) ethyl)-5-phenylpent-4-ynethioate (5i)



CuCl (3.8 mg, 0.2 eq., 0.04 mmol), and the phosphoramidite ligand (22.8 mg, 0.2 eq., 0.04 mmol) were added to a flame dried round bottom flask containing 1ml $Et_2O$/DCM (1/1) under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (11.2 mg, 0.22 eq., 0.044 mmol) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of 4-vinylcyclohex-1-ene (54 mg, 2.5 eq., 0.5 mmol) in 0.2 ml DCM, under an argon atmosphere was added $Cp_2ZrHCl$ (103 mg, 2.0 eq., 0.4 mmol), and after stirring for 15 min, a clear yellow solution was obtained.

The stirred solution containing the copper and ligand was transferred, and filtered – using a syringe filter, to the solution containing the zirconocene species. The resulting black mixture was stirred for another 10 min before S-ethyl (E)-5-phenylpent-2-en-4-ynethioate (43 mg, 1.0 eq., 0.2 mmol) and TMSCl (0.127 ml, 5.0 eq., 1.0 mmol) were sequentially added dropwise over about 1 min for each. Stirring at 0 °C was continued for 15 additional hours, before the reaction was quenched by the addition of $NH_4Cl$ (sat. aq.) and then $Et_2O$. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by $Et_2O$. The combined organic materials were dried ($Na_2SO_4$), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: $Et_2O$; 90:10; $SiO_2$) to give the desired product (49 mg, 15 mmol, 75%).

HPLC analysis indicated an enantiomeric excess of 96 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99: 1; λ = 243 nm; major enantiomer tR = 4.76 min; minor enantiomer, tR = 5.16min].

$^1$H NMR (400 MHz, Chloroform-*d*) $\delta_H$/ppm 7.23 – 7.13 (m, 2H, Ar-*H*), 7.13 – 6.97 (m, 3H, Ar-*H*), 5.45 (d, *J* = 2.3 Hz, 2H, 2 x C*H*), 3.07 – 2.80 (m, 1H, C*H*), 2.76 – 2.67 (m, 2H,SC*H*$_2$), 2.64 (dd, *J* = 14.7 Hz, 7.4 Hz, 1H, C*H*$_2$COCH$_3$), 2.53 (dd, *J* = 14.8 Hz, 7.1 Hz, 1H, C*H*$_2$COCH$_3$), 1.99 – 1.88 (m, 2H, C*H*$_2$CH=CH), 1.86 – 1.79 (m, 2H, C*H*$_2$CH=CH), 1.65 – 1.19 (m, 7H, C*H,* 3 x C*H*$_2$), 1.06 (t, *J* = 7.4 Hz, 3H, C*H*$_3$).

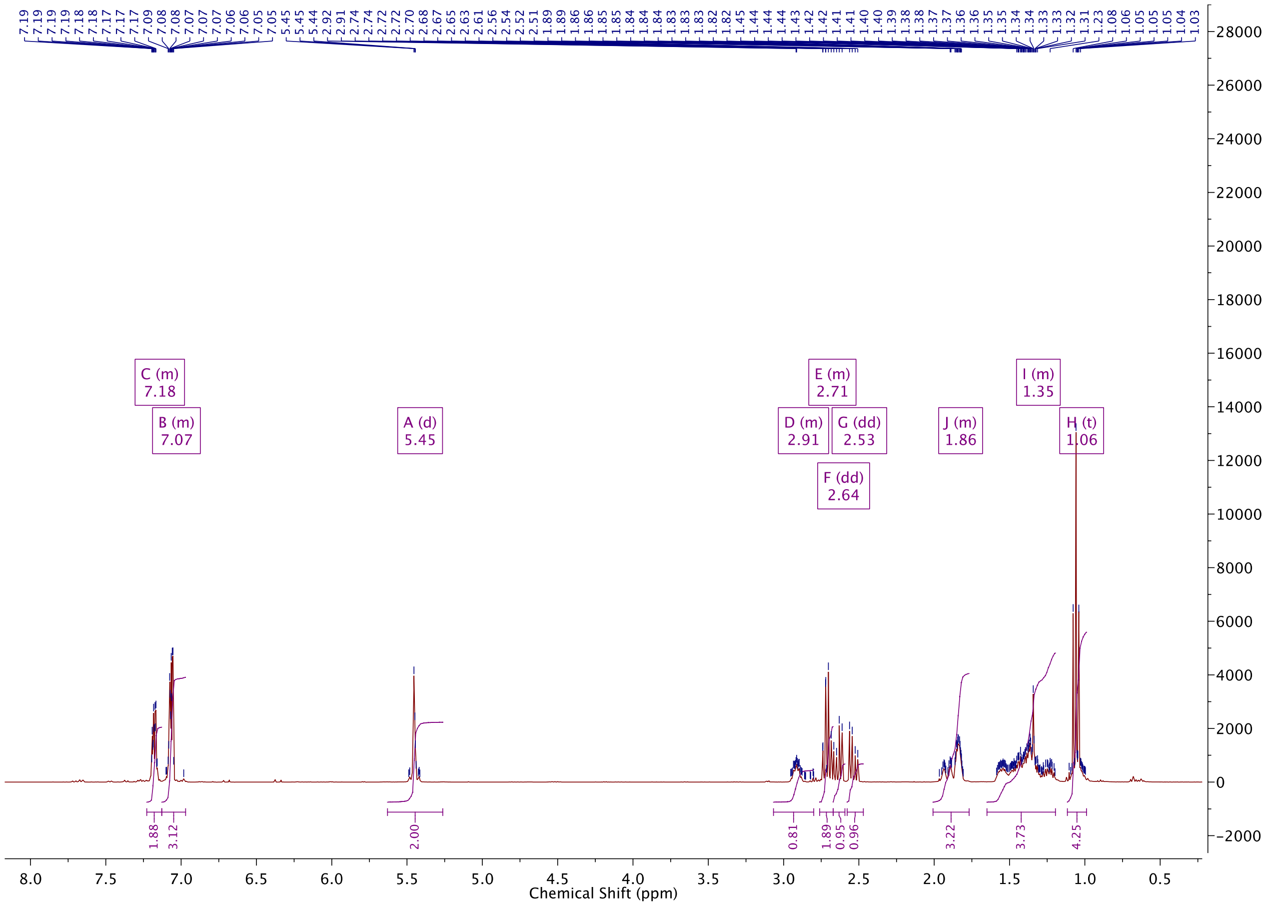
$^{13}$C NMR (101 MHz, Chloroform-*d*) $\delta_C$/ppm 197.5, 131.6 (2C), 128.16 (2C), 127.7, 127.1, 126.5, 123.6 91.2, 82.5, 49.1, 34.1, 33.3, 31.9, 31.7, 29.6, 29.1, 25.3, 23.5, 14.8.

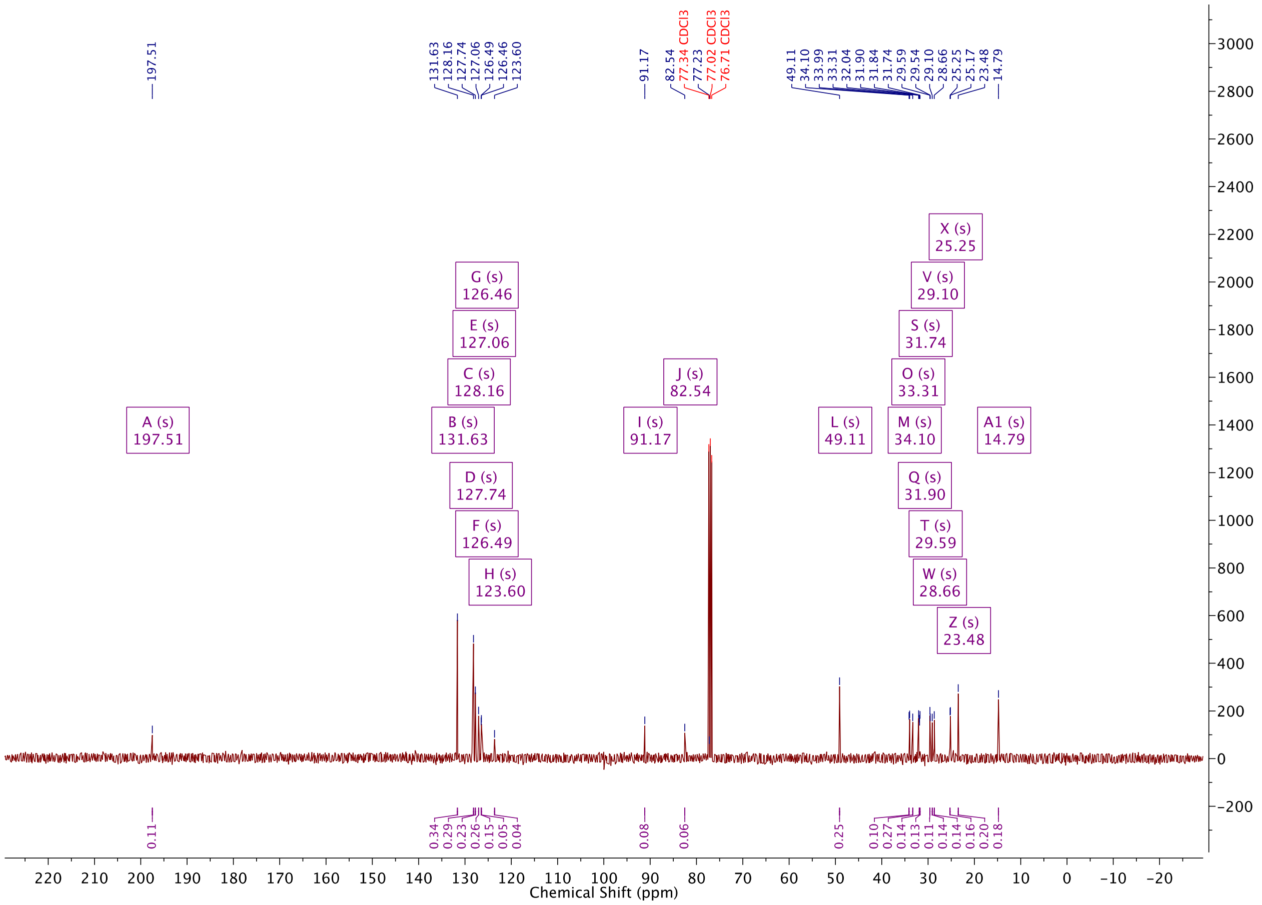
IR ($\nu_{max}$/cm$^{-1}$, CHCl$_3$) 3024, 2839, 1687, 1432, 1305, 1025, 912

HRMS (ESI) m/z calc. for $C_{21}H_{27}O^{32}S$ [M+H]$^+$: 327.1777, 328.1811 found: 327.1776, 328.1811

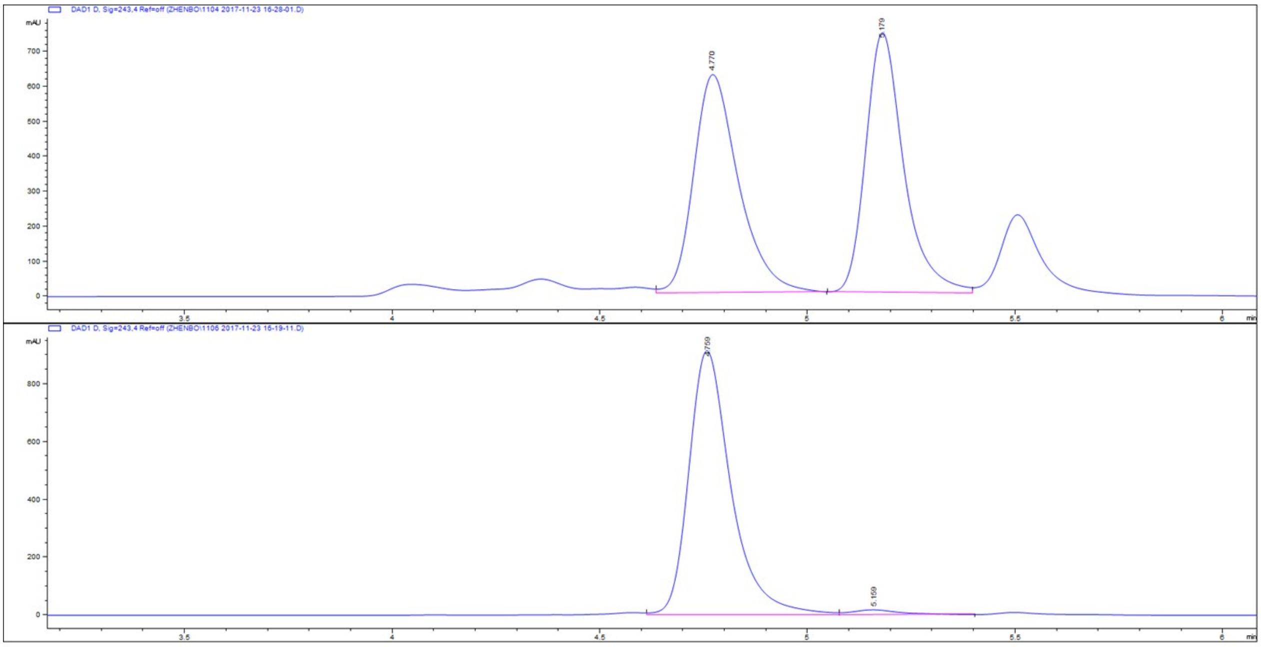
$[\alpha]^{20}_{589}$ = +18.4 ° (c 1.0, CHCl$_3$)

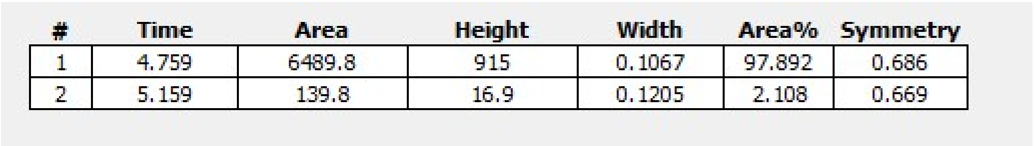
Absolute configuration assigned by analogy to **3p**.


7.19 7.19 7.19 7.19 7.18 7.18 7.17 7.17 7.17 7.09 7.08 7.08 7.07 7.07 7.07 7.06 7.05 7.05 5.45 5.45 5.44 2.92 2.91 2.74 2.74 2.72 2.72 2.70 2.68 2.67 2.65 2.63 2.61 2.56 2.54 2.52 2.51 1.89 1.89 1.86 1.86 1.85 1.85 1.84 1.84 1.84 1.83 1.83 1.83 1.82 1.82 1.45 1.44 1.44 1.44 1.43 1.42 1.42 1.41 1.41 1.40 1.40 1.39 1.38 1.38 1.37 1.37 1.36 1.36 1.35 1.35 1.34 1.34 1.33 1.33 1.32 1.31 1.23 1.08 1.06 1.05 1.05 1.04 1.03
C (m) 7.18
B (m) 7.07
A (d) 5.45
D (m) 2.91
E (m) 2.71
G (dd) 2.53
F (dd) 2.64
J (m) 1.86
I (m) 1.35
H (t) 1.06
1.88
3.12
2.00
0.81
1.89
0.95
0.96
3.22
3.73
4.25
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
Chemical Shift (ppm)



## HPLC trace





| # | Time | Area | Height | Width | Area% | Symmetry |
|---|---|---|---|---|---|---|
| 1 | 4.759 | 6489.8 | 915 | 0.1067 | 97.892 | 0.686 |
| 2 | 5.159 | 139.8 | 16.9 | 0.1205 | 2.108 | 0.669 |

## References:

1 S. L. Buchwald, S. J. LaMaire, R. B. Nielsen, B. T. Watson and S. M. King, *Org. Synth.*, 1993, **71**, 77.

2 B. t. Horst, J. v. Wermeskerken, B. L. Feringa and A. J. Minnaard, *Eur. J. Org. Chem.*, 2010, DOI: 10.1002/ejoc.200901120, 38–41.

3 A. F. Abdel-Magid and S. J. Mehrman, *Org. Process Res. Dev.* , 2006, **10**, 971–1031.

4 B. M. Trost, S. M. Silverman and J. P. Stambuli, *J. Am. Chem. Soc.*, 2011, **133**, 19483-19497.

5 (a) Gary E. Keck, Eugene P. Boden and S. A. Mabury, *J. Org. Chem.*, 1985, **50**, 709-710; (b) Z. Gao and S. P. Fletcher, *Chem. Commun.*, 2017, **53**, 10216-10219.

6 Z. Gao and S. P. Fletcher, *Chem. Sci.*, 2017, **8**, 641-646.

7 K. Huang, H. Wang, L. Liu, W. Chang and J. Li, *Chem. Eur. J.*, 2016, **22**, 6458-6465.

8 T. Hayashi, S. Yamamoto and N. Tokunaga, *Angew. Chem. Int. Ed.* , 2005, **44**, 4224-4227.

9 Z. Ma, F. Xie, H. Yu, Y. Zhang, X. Wu and W. Zhang, *Chem. Commun.*, 2013, **49**, 5292-5294.

10 C. Xu, S. Wittmann, M. Gemander, V. Ruohonen and J. S. Clark, *Org. Lett.*, 2017, **19**, 3556-3559.

11 B. M. Trost, J. T. Masters, B. R. Taft and J. P. Lumb, *Chem. Sci.*, 2016, **7**, 6217-6231.