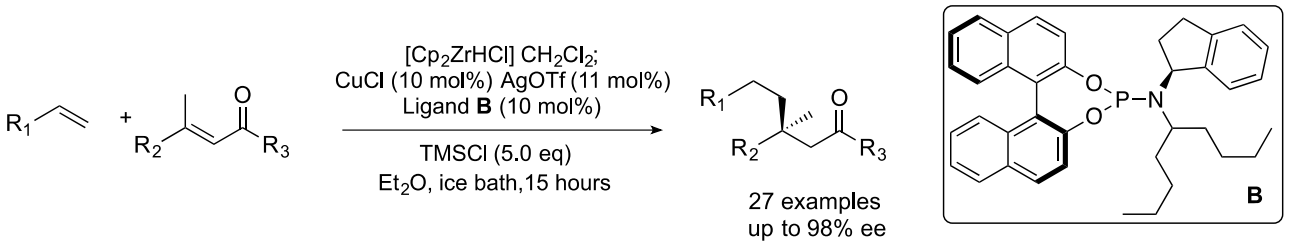
Supporting information

Acyclic Quaternary Centers from Asymmetric Conjugate Addition of Alkylzirconium Reagents to Linear Trisubstituted Enones

Zhenbo Gao and Stephen P. Fletcher*[a]



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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; ^{1}H 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 (δ) 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;

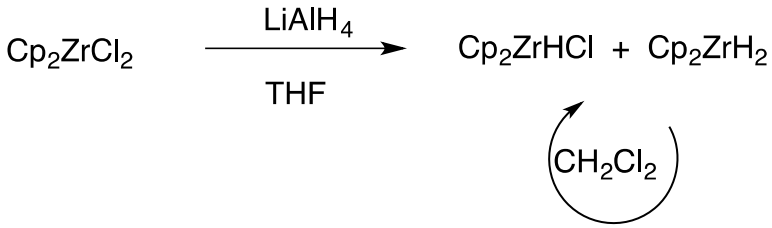
In those cases where silver salts were used the resulting solutions were filtered using syringe filters PTFE (0.2 μm, 13 mm diameter) from Camlab.

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.

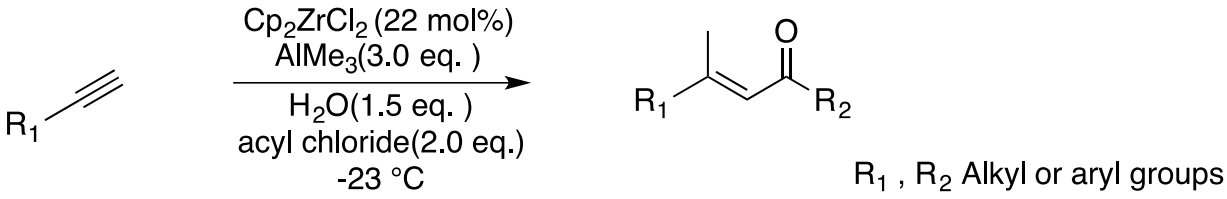
General Methods

A. Preparation of Schwartz reagent[1]

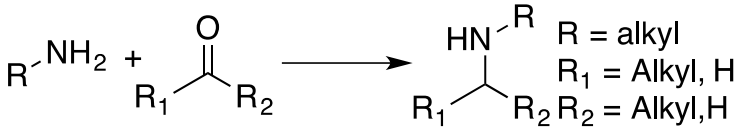


Zirconocene dichloride (30.0 g, 0.103 mol) was added to a flame-dry 250 mL Schlenk flask wrapped with aluminium foil under argon. Dry THF (120 mL) was added and the suspension was stirred at 35 °C for 30 minutes. $LiAlH_4$ in Et_2O (1 M, 28.2 mmol) was added dropwise to the mixture over about 30 minutes. 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.

B. Preparation of trisubstituted enones **1** [2]



C. Preparation of amines



General procedure a

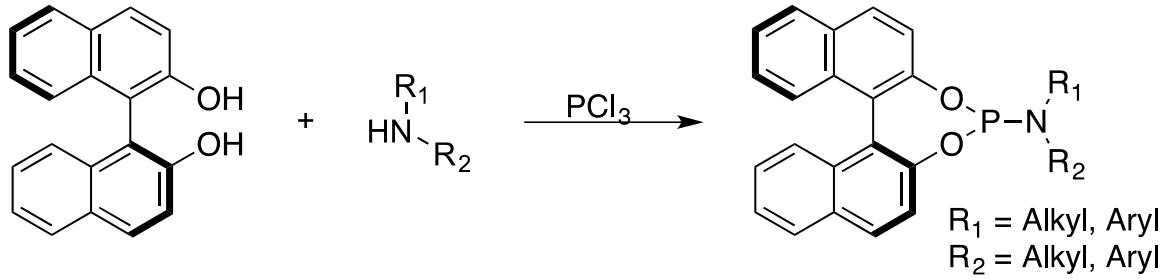
According to a modified procedure from Davies and co-workers[3], Ketone (2.0 eq.) was added to a stirring solution of amine in THF at room temperature. After 5 minutes, $Na(OAc)_3H$ (2.0 eq.) was tipped into the mixture. The reaction was kept under room temperature for 48 hours, and the resulting suspension 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 CH_2Cl_2 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. CH_2Cl_2 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.

General procedure b[4]

$TiCl_4$ (1.1 eq, 1 M solution in CH_2Cl_2) was added slowly to an ice-cooled solution of ketone (1.0 eq) in CH_2Cl_2. The solution was stirred for 10 minutes at room temperature and then a 2 M solution of amine (2.2 eq.) in THF was added dropwise to the reaction mixture. The reaction mixture was stirred for 3 hours before a 1 M solution of $NaB(CN)H_3$ (1.2 eq.) in THF, and then MeOH were added slowly to the reaction mixture and stirring at room temperature was

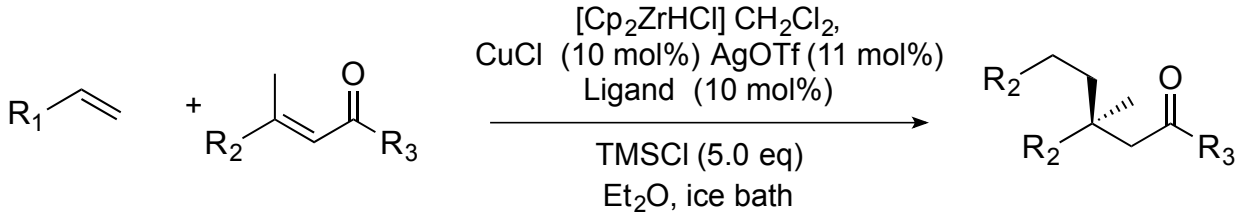
continued for 48 hours. NaOH (2M aq. solution) was added slowly and the mixture was stirred for 30 min before filteration over celite and washing with EtOAc. The mixture was partitioned between the aqueous and organic layers and the aqueous phase extracted with EtOAc (3 times). The combined organic phase was dried ($MgSO_4$), filtered and concentrated in vacuo to afford a yellow oil. Flash column chromatography of the residue (SiO_2) gave the desired amine.

D. Preparation of phosphoramidite ligands[5]



Triethylamine (5.0 eq.) was added dropwise to a stirred, ice-cooled solution of PCl_3 (1.0 eq.) in CH_2Cl_2. The ice bath was removed and the solution left to warm to room temperature before (*S*)-N-cyclohexyl-2, 3-dihydro-1H-inden-1-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 CH_2Cl_2 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.

E. Copper catalysed conjugate addition of alkylzirconium nucleophiles



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 CH_2Cl_2, 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 enone and TMSCl 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.

1b. Asymmetric product

CuCl (0.1 eq.), and the 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, Cp_2ZrHCl (2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (xx mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (1.0 eq.) and then TMSCl (5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of NH_4Cl and then Et_2O. The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O. The combined organic materials were dried with 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.

2b. Asymmetric product

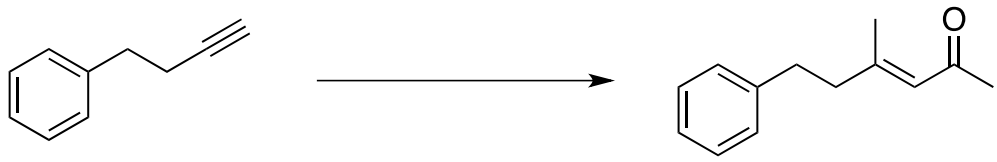
CuCl (0.1 eq.), and the phosphoramidite ligand (0.1 eq.) were added to a flame dried round bottom flask containing 1 mL Et_2O under argon and the resulting mixture was stirred at room temperature. After 1 hour, AgOTf (0.11 eq.) was added and the mixture was stirred for an additional 15 min.

To a second, flame dried, round bottom flask, containing a stirred solution of alkene (2.5 eq.) in CH_2Cl_2, 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 enone and TMSCl 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

(E)-4-methyl-6-phenylhex-3-en-2-one (2a)



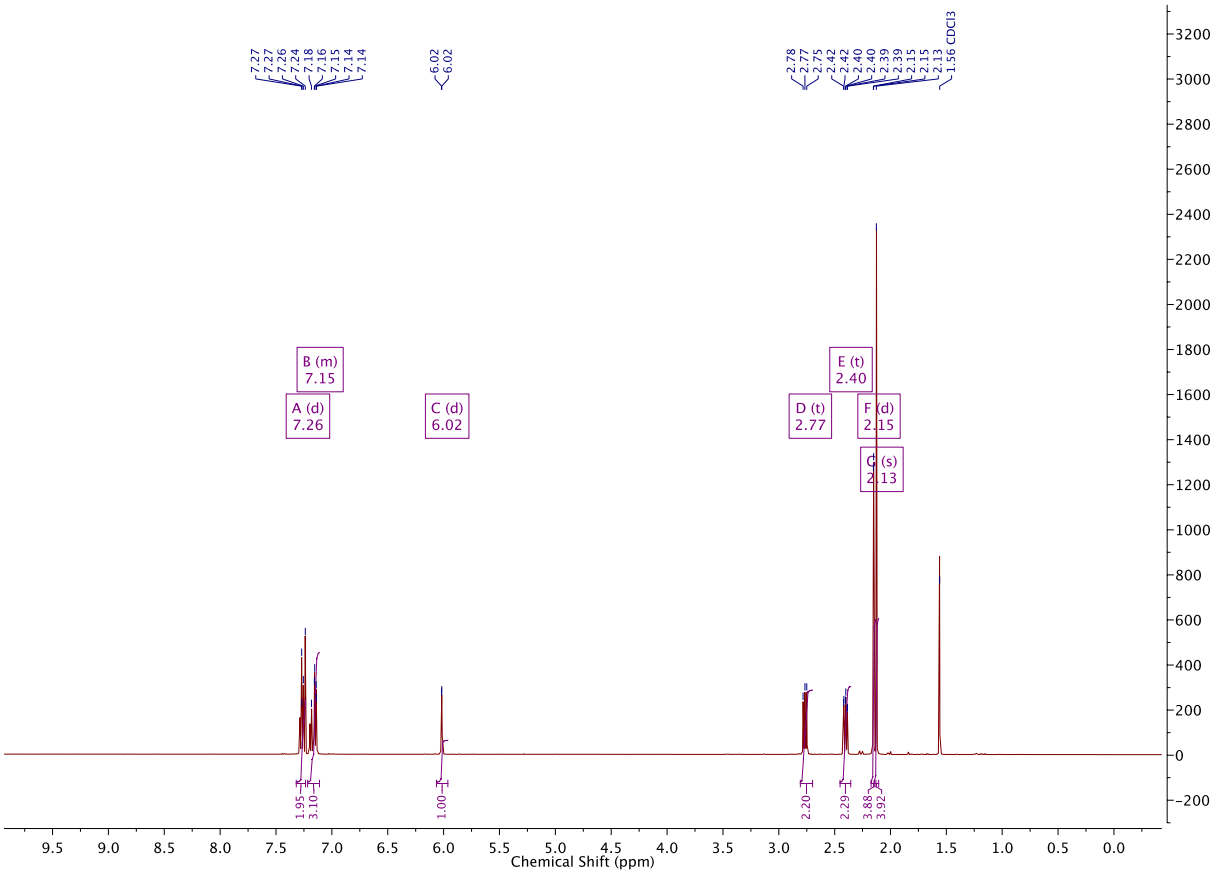
Cp_2ZrCl_2 (643 mg, 2.2 mmol, 0.22 eq.) and dry CH_2Cl_2 (50 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (15 mL, 30 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –23 °C and then distilled H_2O (0.27 mL, 15 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 4-Phenyl-1-pentyne (1.41 mL, 10 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, acetyl chloride (1.42 mL, 20 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 30 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (1.31 g 70% yield)

^{1}H NMR (500 MHz, $CDCl_3$) δ_H/ppm 7.29 (d, *J* = 7.6 Hz, 2H, Ar-*H*), 7.24 – 7.13 (m, 3H, Ar-*H*), 6.04 (d, *J* = 1.3 Hz, 1H, Ar-*H*), 2.79 (t, 2H, PhCH_2), 2.42 (t, 2H,CH_2), 2.17 (d, *J* = 1.3 Hz, 3H,CH_3), 2.15 (s, 3H, COCH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C/ppm 198.9, 157.3, 141.1, 128.5(2C), 128.4(2C), 126.2, 124.1, 43.1, 34.1, 31.9, 19.5.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3027, 2928, 1687, 1616, 1496

HRMS (ESI) m/z calc. for $C_{13}H_{17}O$ $[M+H]^+$: 189.1274, found: 189.1275.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7.27
7.26
7.24
7.18
7.16
7.15
7.14
7.14
6.02
6.02
2.78
2.77
2.75
2.42
2.42
2.40
2.40
2.39
2.39
2.15
2.15
2.13
1.56 CDCl3
B (m)
7.15
A (d)
7.26
C (d)
6.02
E (t)
2.40
D (t)
2.77
F (d)
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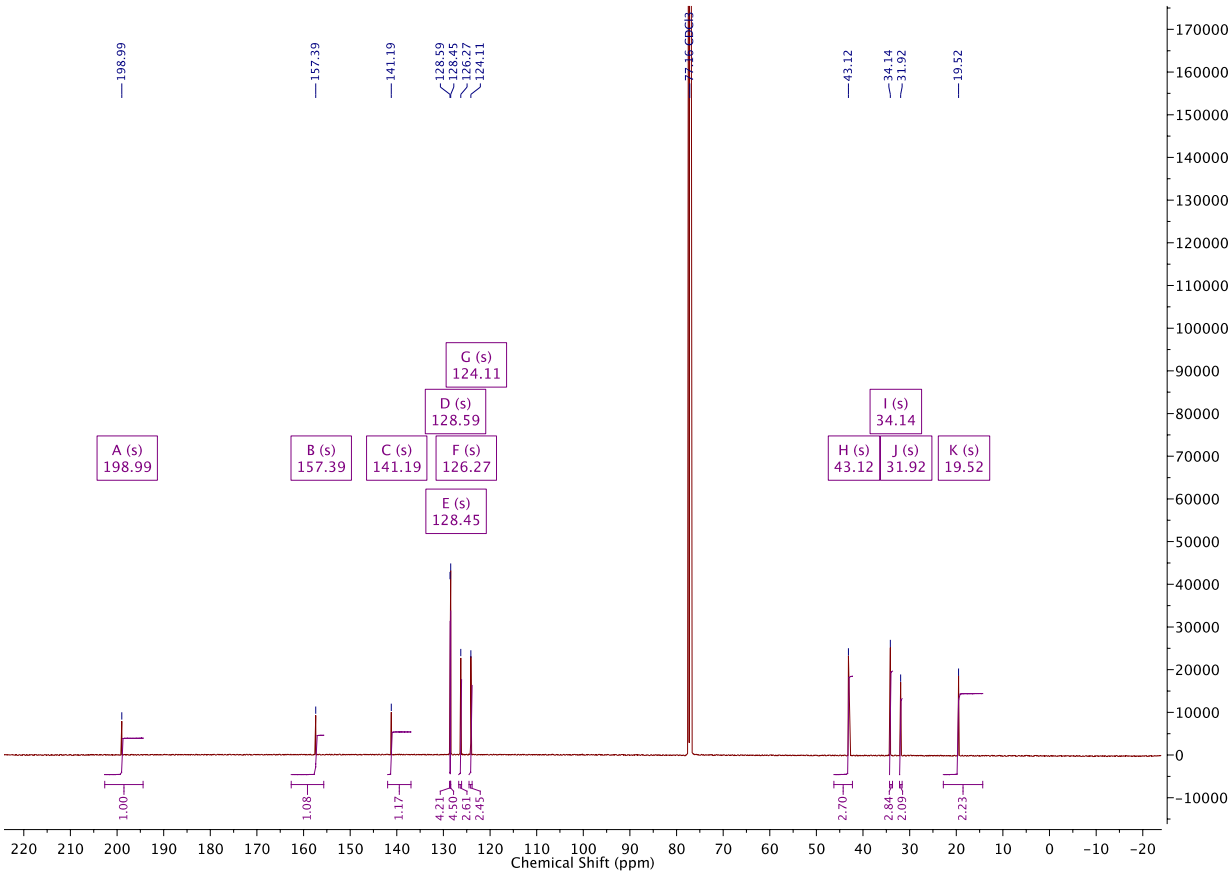
3.92
Chemical Shift (ppm)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141.19
128.59
128.45
126.27
124.11
77.16 CDCl3
43.12
34.14
31.92
19.52
G (s)
124.11
D (s)
128.59
I (s)
34.14
A (s)
198.99
B (s)
157.39
C (s)
141.19
F (s)
126.27
H (s)
43.12
J (s)
31.92
K (s)
19.52
E (s)
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1.00
1.08
1.17
4.21
4.50
2.61
2.45
2.70
2.84
2.09
2.23
Chemical Shift (ppm)

(*E*)-4-Phenylpent-3-en-2-one (2b)

Cp_2ZrCl_2 (643 mg, 2.2 mmol, 0.22 eq.) and dry CH_2Cl_2 (50 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (15 mL, 30 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –23 °C and then distilled H_2O (0.27 mL, 15 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the phenylacetylene (1.1 mL, 10 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, acetyl chloride (1.42 mL, 20 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 30 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 80/20; silica), the enone product was obtained as yellow solid (1.02 g, 64%).

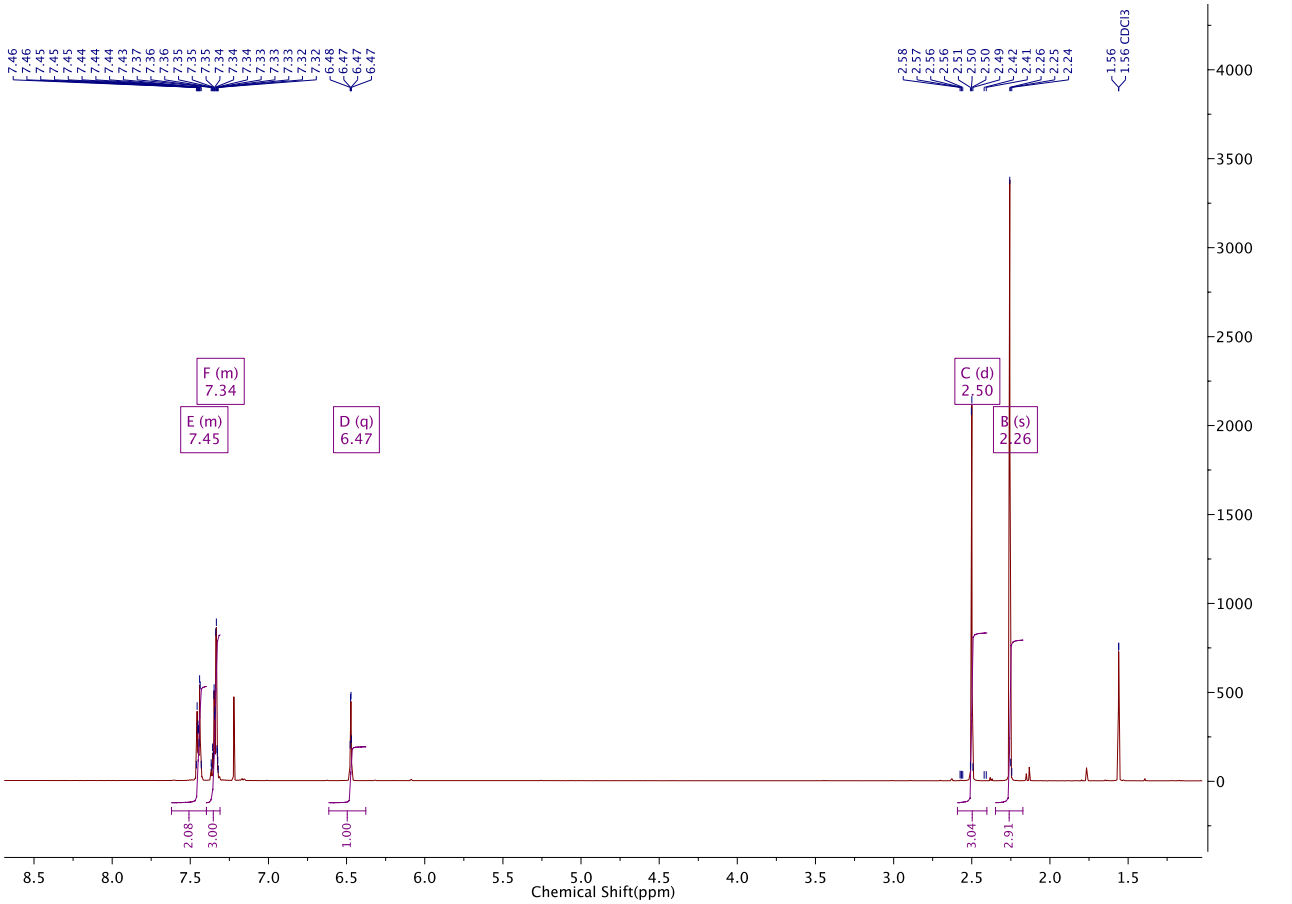
^{1}H NMR (500 MHz, Chloroform-*d*) δ_H/ppm 7.62 – 7.40 (m, 2H, Ar-*H*), 7.40 – 7.31 (m, 3H, Ar-*H*), 6.47 (q, *J* = 1.3 Hz, 1H, C*H*COMe), 2.50 (d, *J* = 1.3 Hz, 3H, CH_3), 2.26 (s, 3H, COCH_3).

^{13}C NMR (126 MHz, Chloroform-*d*) δ_C/ppm 199.0, 153.9, 142.5, 129.1, 128.5(2C), 126.5(2C), 124.5, 32.3, 18.4.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3058, 2360, 1679, 1598, 1574

MS (ESI) m/z $[M+H]^+$: 161.1 (100)

This data was concordant with literature values[6].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E (m)
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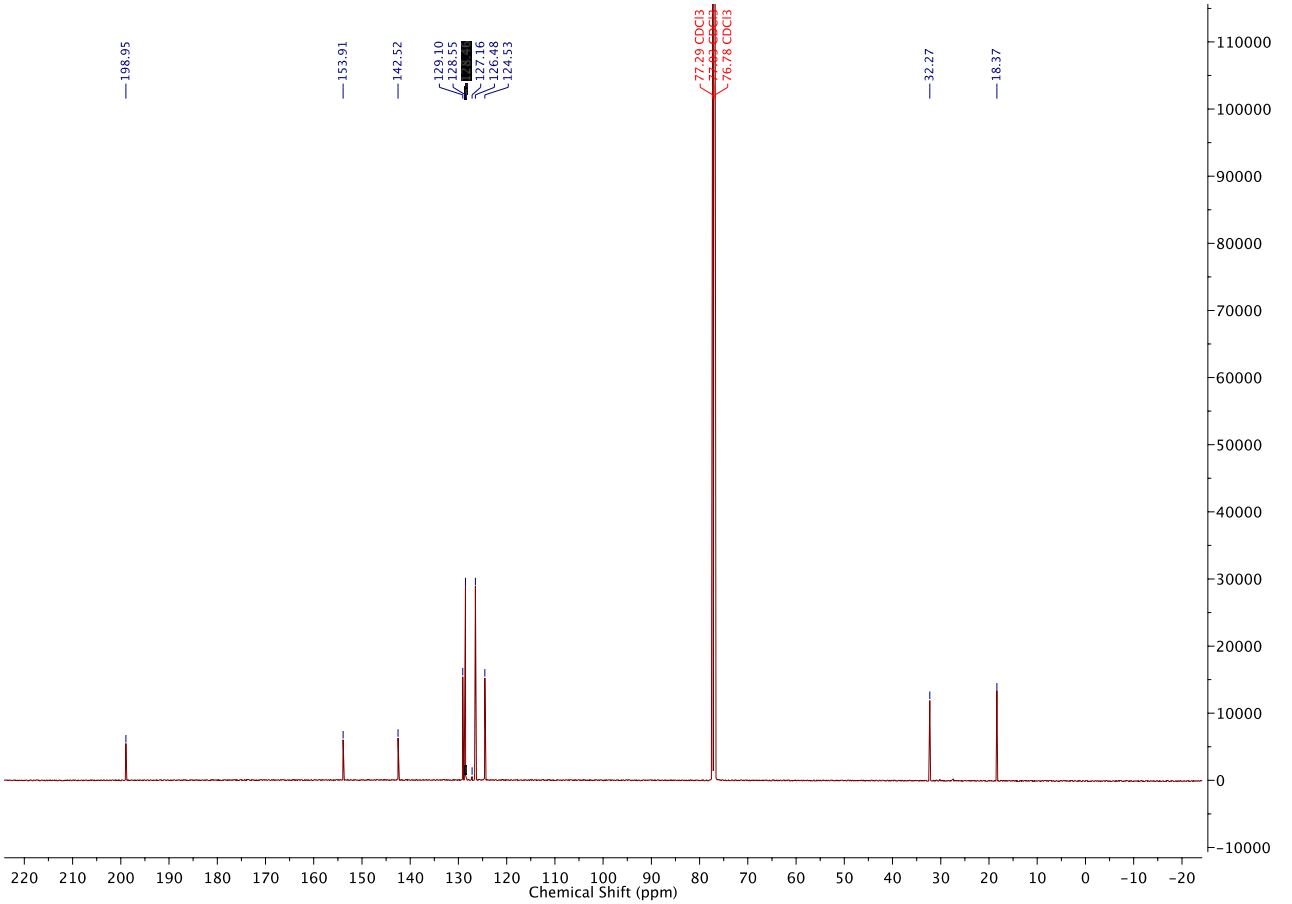
D (q)
6.47
C (d)
2,50
B (s)
2.26
Chemical Shift(ppm)


198.95
153.91
142.52
129.10
128.55
127.16
126.48
124.53
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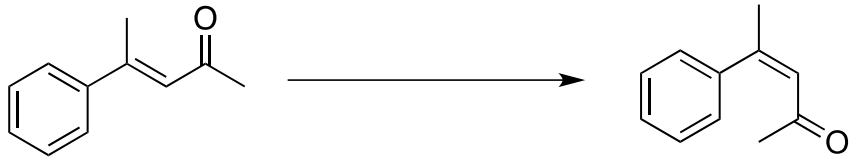
18.37
Chemical Shift (ppm)

(*Z*)-4-phenylpent-3-en-2-one(cis-2b)



Cis-2b was prepared through photocatalysis reactions from literature.[7] (*Z*)-4-phenylpent-3-en-2-one (0.32 g, 2.0mmol, 1.0 eq.), anthracene(20mg, 0.1 mmol, 0.05 eq.) and 30 ml dry MeCN was added in a flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. After 24 h of UV-light (405 nm) irradiation and stirring, the stir bar was removed and the solution was evaporated to dryness by rotavap. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (0.26 g, 81% yield)

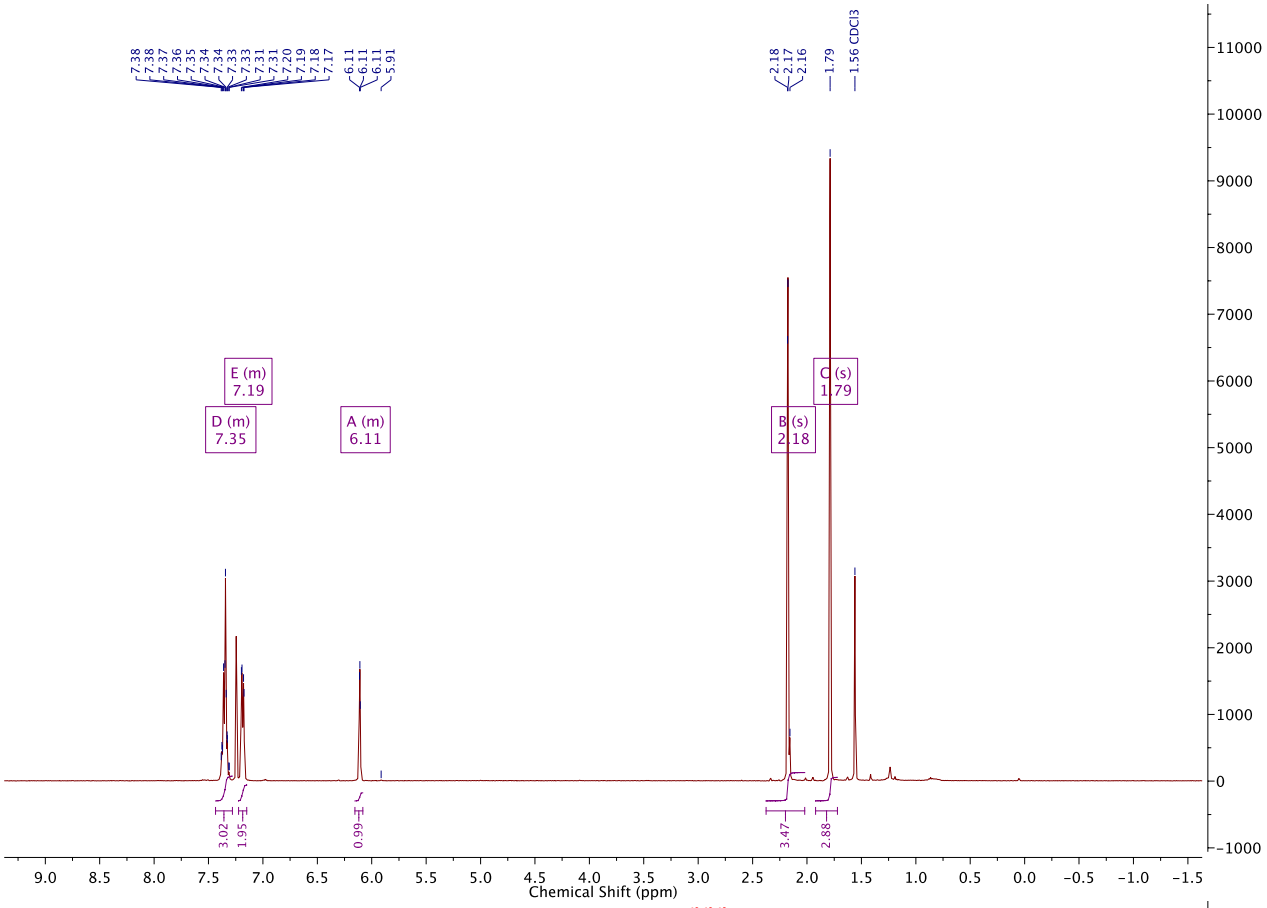
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.44 – 7.28 (m, 3H, Ar-*H*), 7.22 – 7.15 (m, 2H, Ar-*H*), 6.15-6.08(m, 1H, C*H*COMe), 2.18 (d, *J* = 1.3 Hz, 3H, CH_3), 1.79 (s, 3H, COCH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 200.3, 153.0, 140.9, 128.5, 128.4(2C), 128.3, 127.2(2C), 30.2, 27.4.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 2976, 1665, 1619, 1433,1354

MS (ESI) m/z $[M+H]^+$: 161.1 (100)

This data was concordant with literature values[8].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7.34
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7.31
7.31
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7.19
7.18
7.17
6.11
6.11
6.11
5.91
2.18
2.17
2.16
1.79
1.56 CDCl3
E (m)
7.19
D (m)
7.35
A (m)
6.11
B (s)
2.18
C (s)
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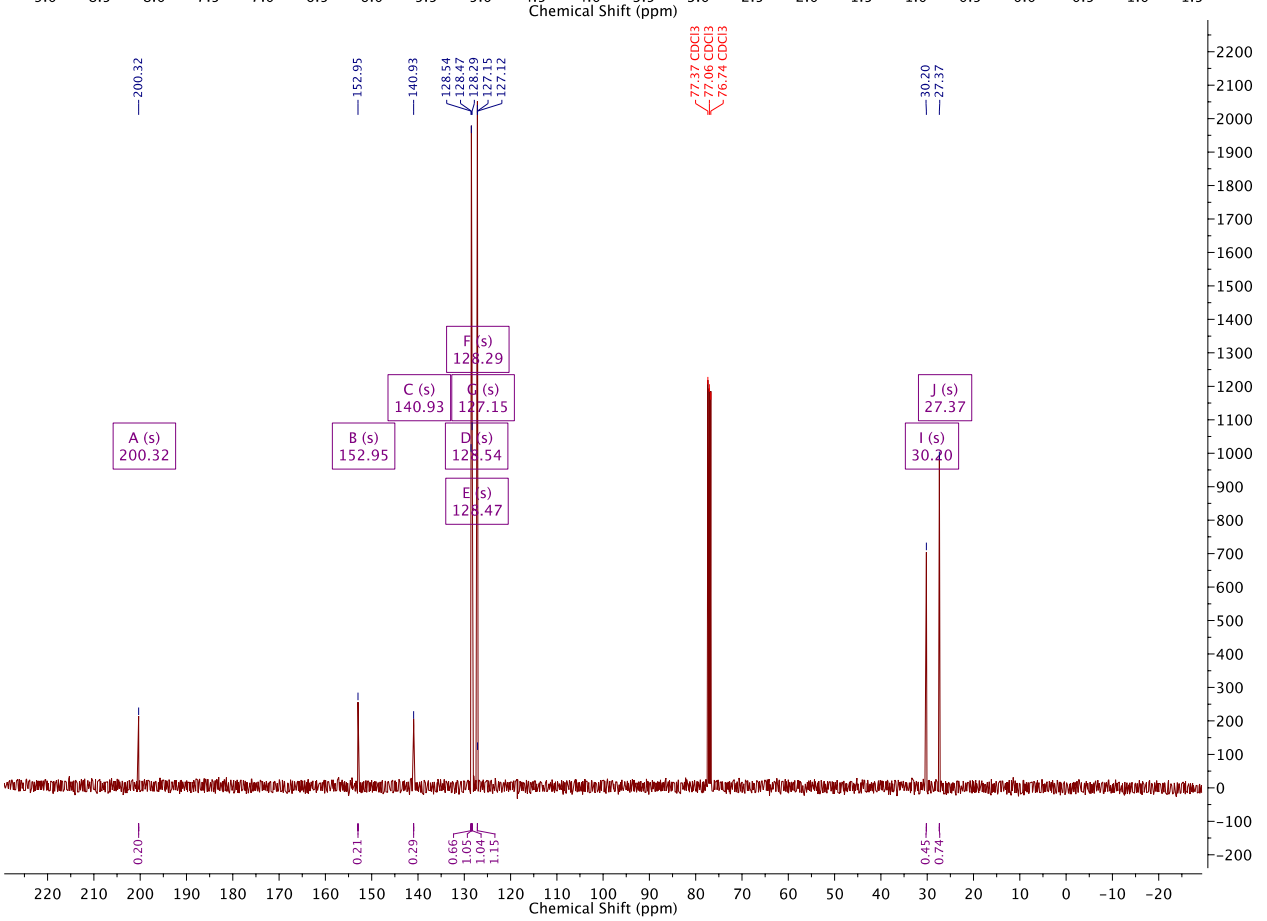
3.02
1.95
0.99
3.47
2.88
Chemical Shift (ppm)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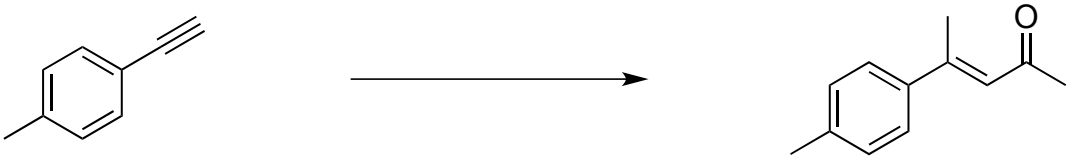
140.93
128.54
128.47
128.29
127.15
127.12
77.37 CDCl3
77.06 CDCl3
76.74 CDCl3
30.20
27.37
A (s)
200.32
B (s)
152.95
C (s)
140.93
D (s)
128.54
E (s)
128.47
F (s)
128.29
G (s)
127.15
I (s)
30.20
J (s)
27.37
0.20
0.21
0.29
0.66
1.05
1.04
1.15
0.45
0.74
Chemical Shift (ppm)

(*E*)-4-(*p*-tolyl) pent-3-en-2-one (2c)



Cp_2ZrCl_2 (428 mg, 1.46 mmol, 0.22 eq.) and dry CH_2Cl_2 (30 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (10 mL, 20 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –15 °C and then distilled H_2O (0.18 mL, 10 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 4-ethynyl toluene (0.842 ml, 6.67 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, Acetyl chloride (0.94 mL, 13.2 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 20 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (0.90 g, 78% yield)

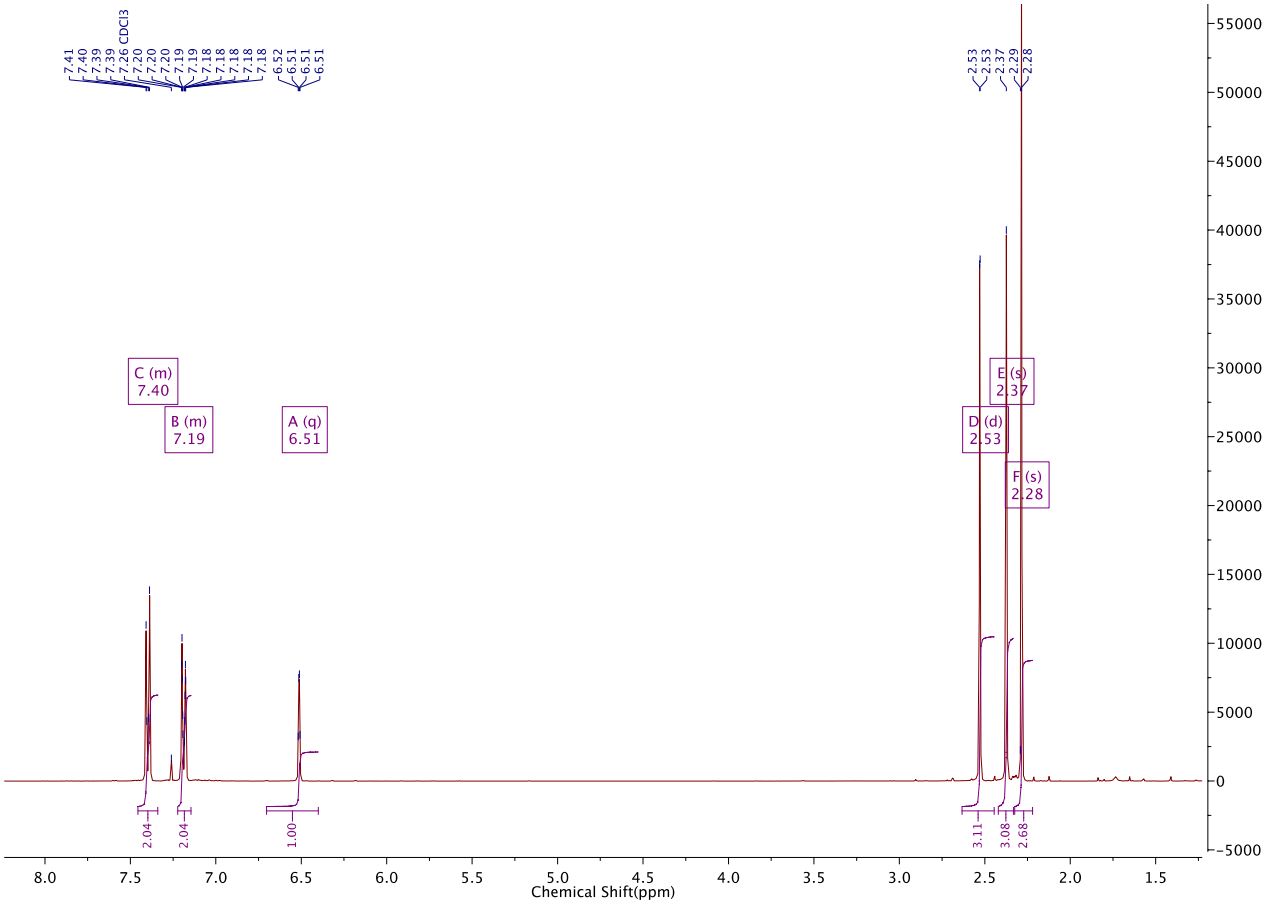
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.46 – 7.34 (m, 2H, Ar-*H*), 7.22 – 7.15 (m, 2H, Ar-*H*), 6.51 (q, *J* = 1.3 Hz, 1H, C*H*), 2.53 (d, *J* = 1.3 Hz, 3H, CH_3C=CH), 2.37 (s, 3H, CH_3), 2.28 (s, 3H, COCH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 198.9, 153.8, 139.5, 139.3, 129.3, 126.4, 123.7, 32.3, 32.2, 21.2, 18.2, 18.2.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 2920, 1679,1594, 1355,1178, 961,809, 611

MS (ESI) m/z $[M+H]^+$: 175.1(100)

This data was concordant with literature values[9].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7.39
7.39
7.26 CDCl3
7.20
7.20
7.19
7.19
7.18
7.18
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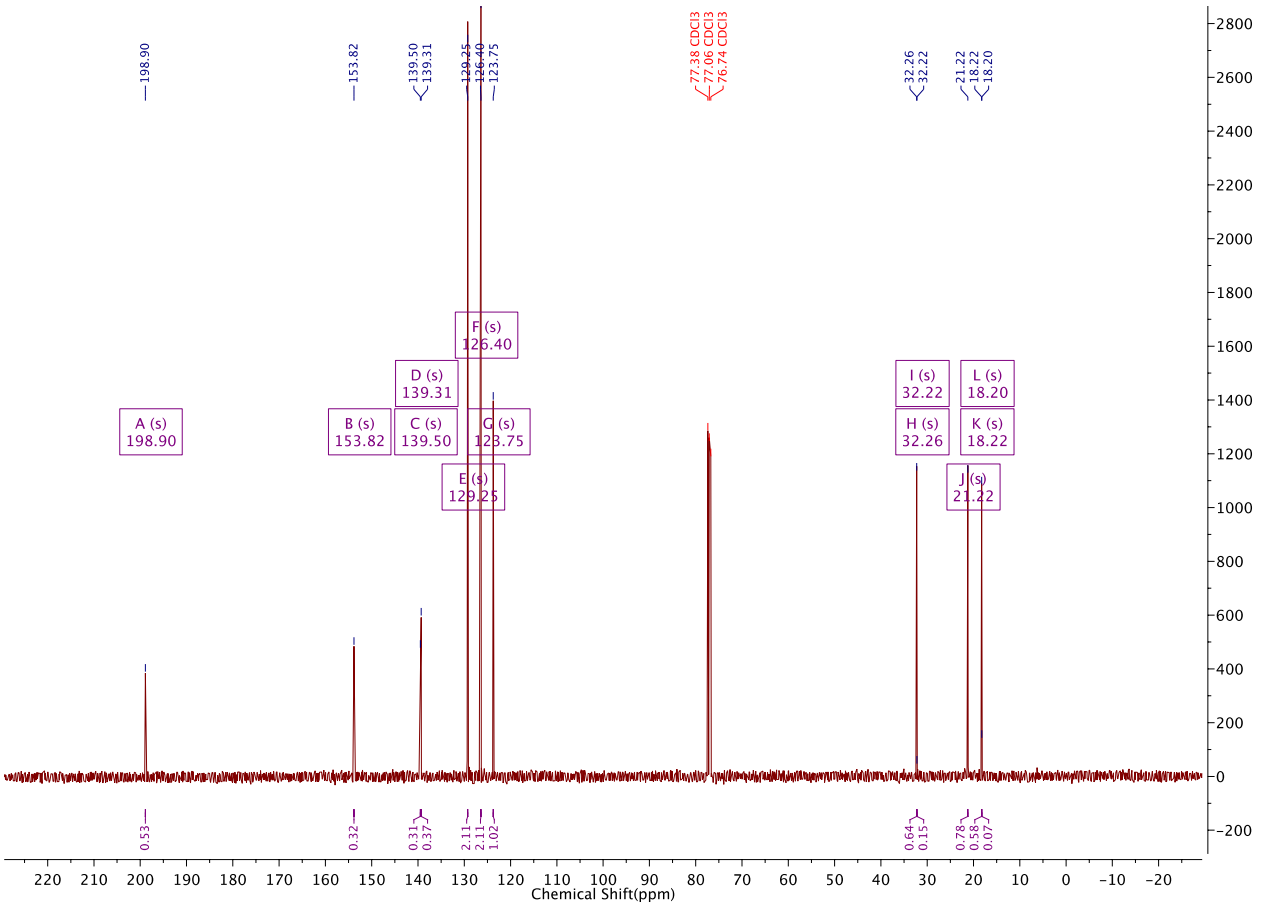
7.18
6.52
6.51
6.51
6.51
2.53
2.53
2.37
2.29
2.28
C (m)
7.40
B (m)
7.19
A (q)
6.51
E (s)
2.37
D (d)
2.53
F (s)
2.28
2.04
2.04
1.00
3.11
3.08
2.68
Chemical Shift(ppm)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139.50
139.31
129.25
126.40
123.75
77.38 CDCl3
77.06 CDCl3
76.74 CDCl3
32.26
32.22
21.22
18.22
18.20
F (s)
126.40
D (s)
139.31
I (s)
32.22
L (s)
18.20
A (s)
198.90
B (s)
153.82
C (s)
139.50
G (s)
123.75
H (s)
32.26
K (s)
18.22
E (s)
129.25
J (s)
21.22
0.53
0.32
0.31
0.37
2.11
2.11
1.02
0.64
0.15
0.78
0.58
0.07
Chemical Shift(ppm)

(*E*)-4-(4-fluorophenyl)pent-3-en-2-one (2d)

Cp_2ZrCl_2 (428 mg, 1.46 mmol, 0.22 eq.) and dry CH_2Cl_2 (30 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (10 mL, 20 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –15 °C and then distilled H_2O (0.18 mL, 10 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 1-Ethynyl-4 fluorobenzene (0.80 g, 6.67 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, Acetyl chloride (0.94 mL, 13.2 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 20 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (0.61 g, 52% yield)

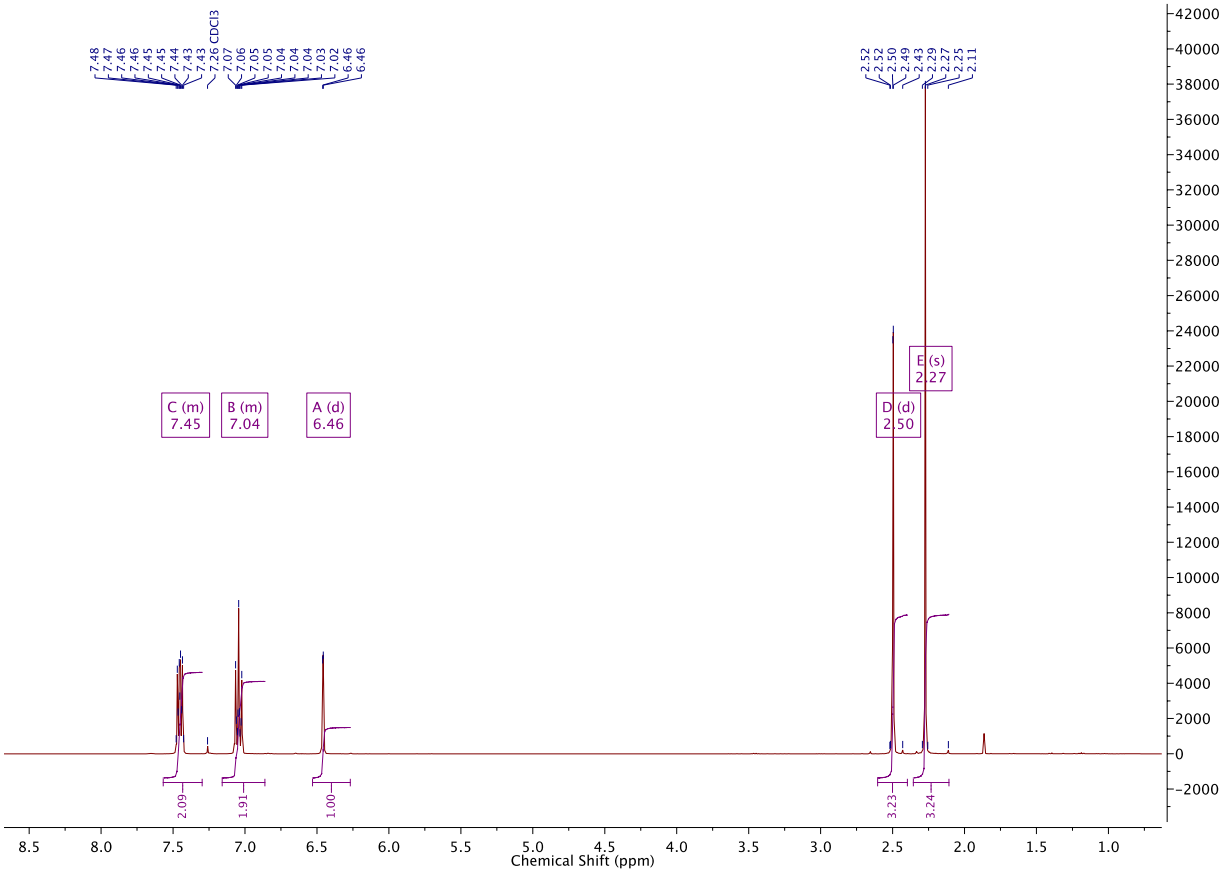
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.57 – 7.30 (m, 2H, Ar-*H*), 7.16 – 6.86 (m, 2H, Ar-*H*), 6.46 (d, *J* = 1.6 Hz, 1H, C*H*COMe), 2.50 (d, *J* = 1.2 Hz, 3H, CH_3C=CH), 2.27 (s, 3H, COCH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 198.7, 163.3, 152.6, 138.4, 128.3 (2C), 124.3, 115.5 (2C), 32.2, 18.3.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 2980, 1681,1599,1507, 1376,1179, 825

MS (ESI) m/z $[M+H]^+$: 179.1(100)

This data was concordant with literature values[6].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7.45
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7.43
7.43
7.26 CDCl3
7.07
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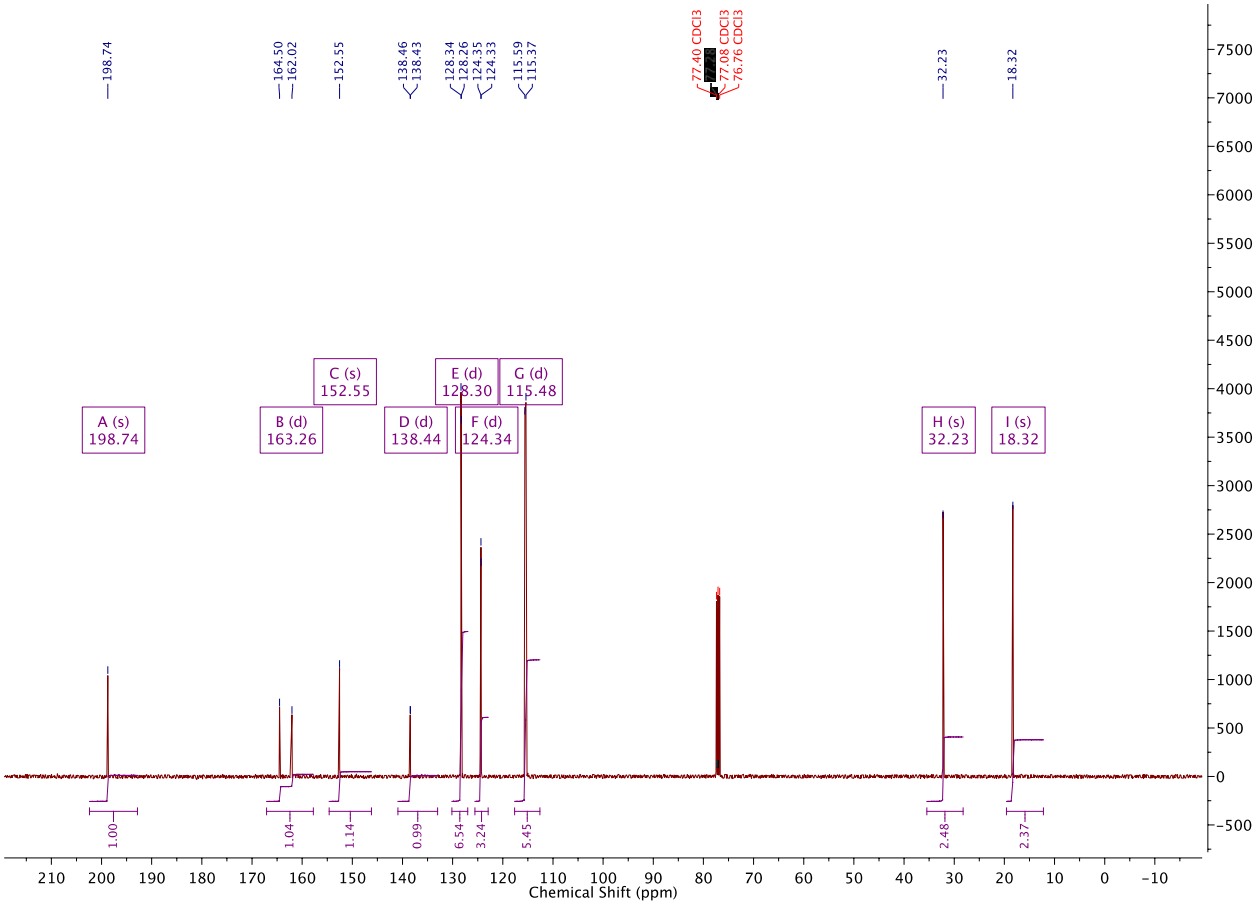
7.05
7.05
7.04
7.04
7.04
7.03
7.02
6.46
6.46
2.52
2.52
2.50
2.49
2.43
2.29
2.27
2.25
2.11
C (m)
7.45
B (m)
7.04
A (d)
6.46
D (d)
2.50
E (s)
2.27
2.09
1.91
1.00
3.23
3.24
Chemical Shift (ppm)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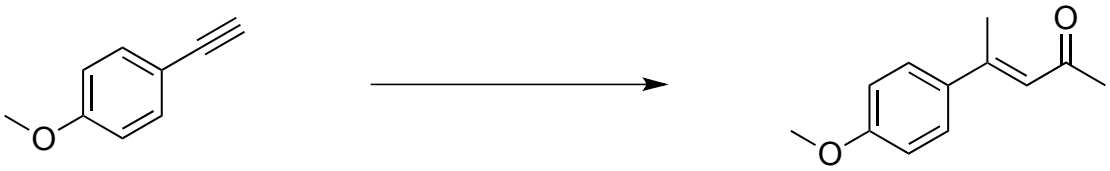
164.50
162.02
152.55
138.46
138.43
128.34
128.26
124.35
124.33
115.59
115.37
77.40 CDCl3
77.08 CDCl3
76.76 CDCl3
32.23
18.32
A (s)
198.74
B (d)
163.26
C (s)
152.55
D (d)
138.44
E (d)
128.30
F (d)
124.34
G (d)
115.48
H (s)
32.23
I (s)
18.32
1.00
1.04
1.14
0.99
6.54
3.24
5.45
2.48
2.37
Chemical Shift (ppm)

(*E*)-4-(4-methoxyphenyl) pent-3-en-2-one (2e)



Cp_2ZrCl_2 (428 mg, 1.46 mmol, 0.22 eq.) and dry CH_2Cl_2 (30 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (10 mL, 20 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –15 °C and then distilled H_2O (0.18 mL, 10 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 4-Ethynylanisole (0.878g, 6.67 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, Acetyl chloride (0.94 mL, 13.2 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 20 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (0.67 g, 53% yield)

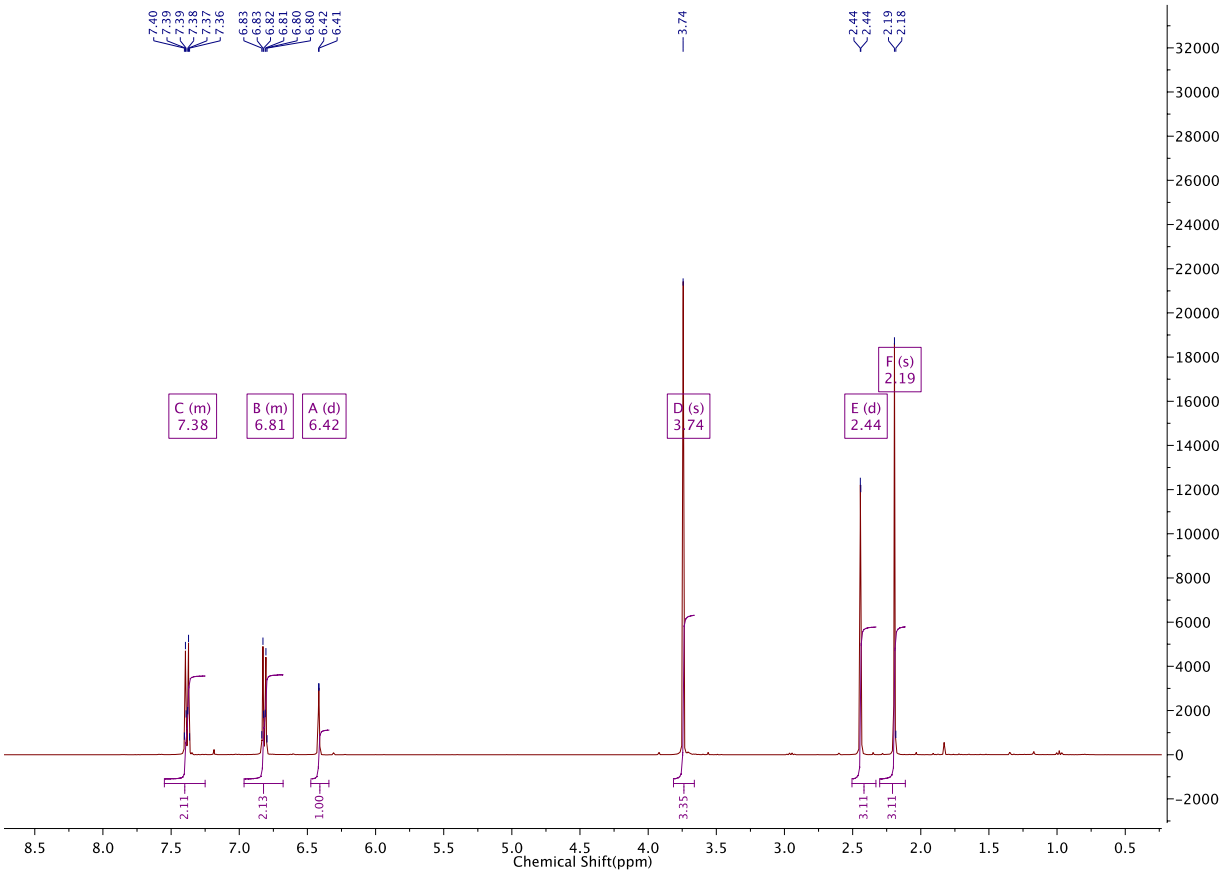
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.55 – 7.25 (m, 2H, Ar-*H*), 6.96 – 6.68 (m, 2H, Ar-*H*), 6.42 (d, *J* = 1.4 Hz, C*H*COMe 1H), 3.74 (s, 3H, OCH_3), 2.44 (d, *J* = 1.2 Hz, 3H, CH_3C=CH), 2.19 (s, 3H, COCH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 198.8, 160.6, 153.3, 134.5, 127.9(2C), 122.8, 113.9(2C), 55.4, 32.3, 18.0.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3017, 2838, 1675, 1588, 1250, 1176, 1030, 825

MS (ESI) m/z $[M+Na]^+$: 213.1(100)

This data was concordant with literature values[6].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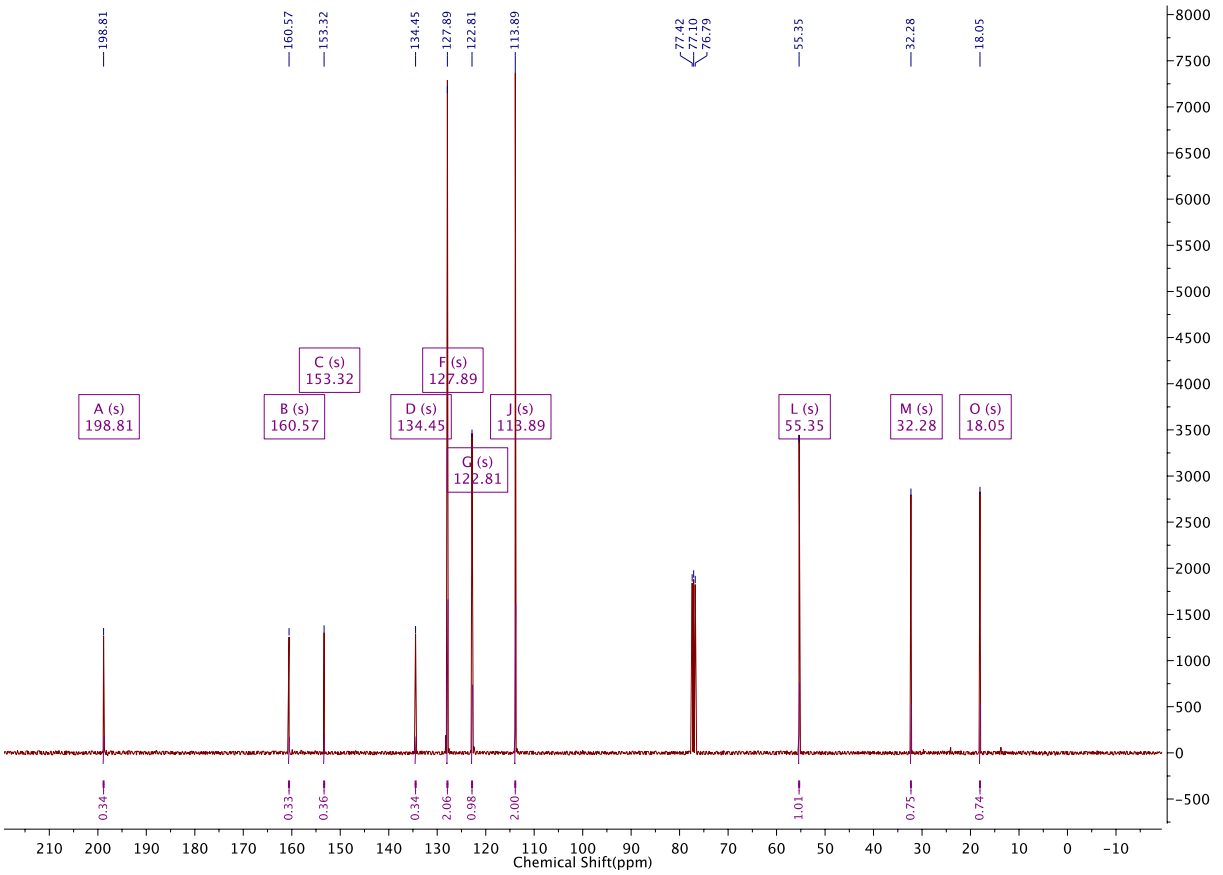
7.39
7.39
7.38
7.37
7.36
6.83
6.83
6.82
6.81
6.80
6.80
6.42
6.41
3.74
2.44
2.44
2.19
2.18
C (m)
7.38
B (m)
6.81
A (d)
6.42
D (s)
3.74
E (d)
2.44
F (s)
2.19
2.11
2.13
1.00
3.35
3.11
3.11
Chemical Shift(ppm)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134.45
127.89
122.81
113.89
77.42
77.10
76.79
55.35
32.28
18.05
A (s)
198.81
B (s)
160.57
C (s)
153.32
D (s)
134.45
F (s)
127.89
G (s)
122.81
J (s)
113.89
L (s)
55.35
M (s)
32.28
O (s)
18.05
0.34
0.33
0.36
0.34
2.06
0.98
2.00
1.01
0.75
0.74
Chemical Shift(ppm)

(E)-4-(thiophen-3-yl) pent-3-en-2-one (2f)

Cp_2ZrCl_2 (428 mg, 1.46 mmol, 0.22 eq.) and dry CH_2Cl_2 (30 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (10 mL, 20 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –15 °C and then distilled H_2O (0.18 mL, 10 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 3-ethynylthiophene (0.718 g, 6.67 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, Acetyl chloride (0.94 mL, 13.2 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 20 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (0.58 g, 53% yield)

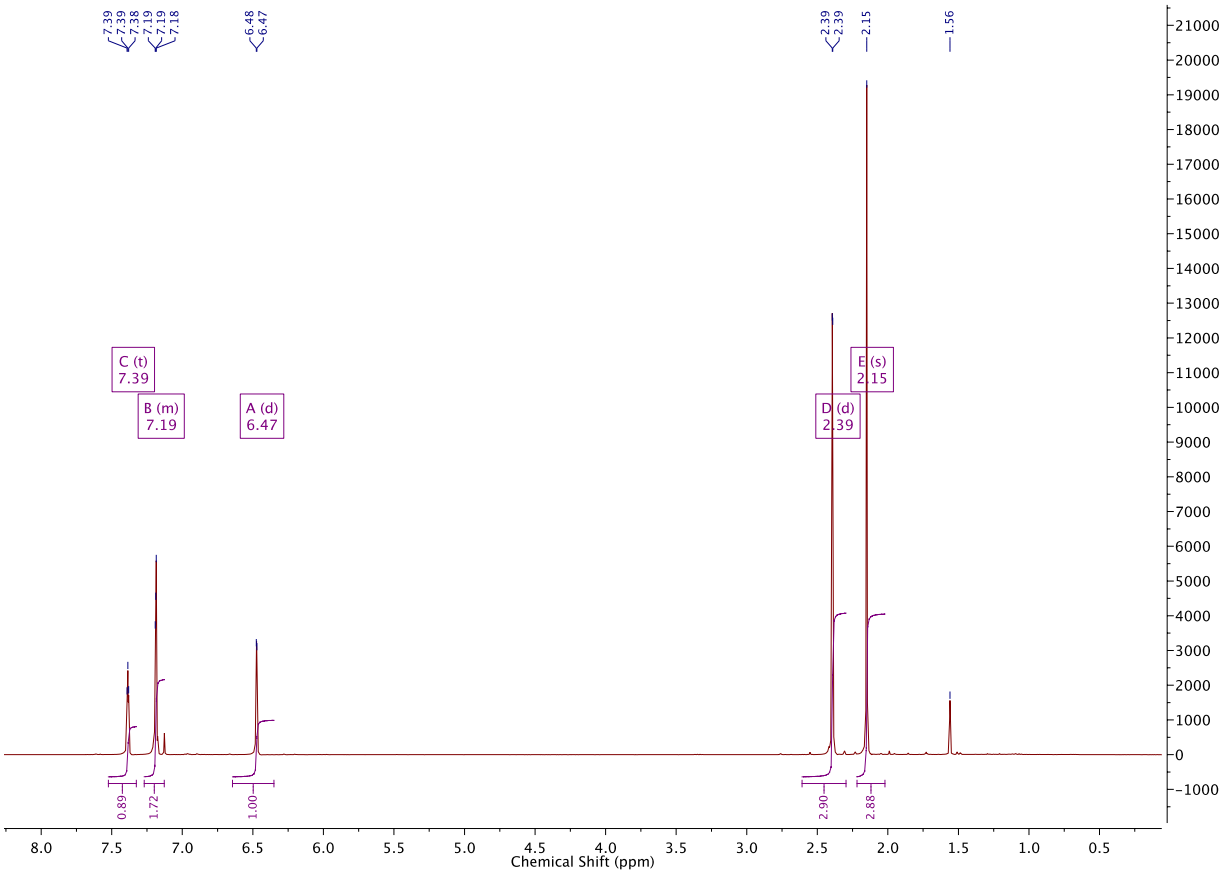
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.39 (t, *J* = 2.2Hz, 1H, Ar-*H*), 7.27 – 7.13 (m, 2H, Ar-*H*), 6.47 (d, *J* = 1.4 Hz, 1H, C*H*COH$_3$), 2.39 (d, *J* = 1.1Hz, 3H, C*H*$_3$C=CH), 2.15 (s, 3HCOC*H*$_3$).

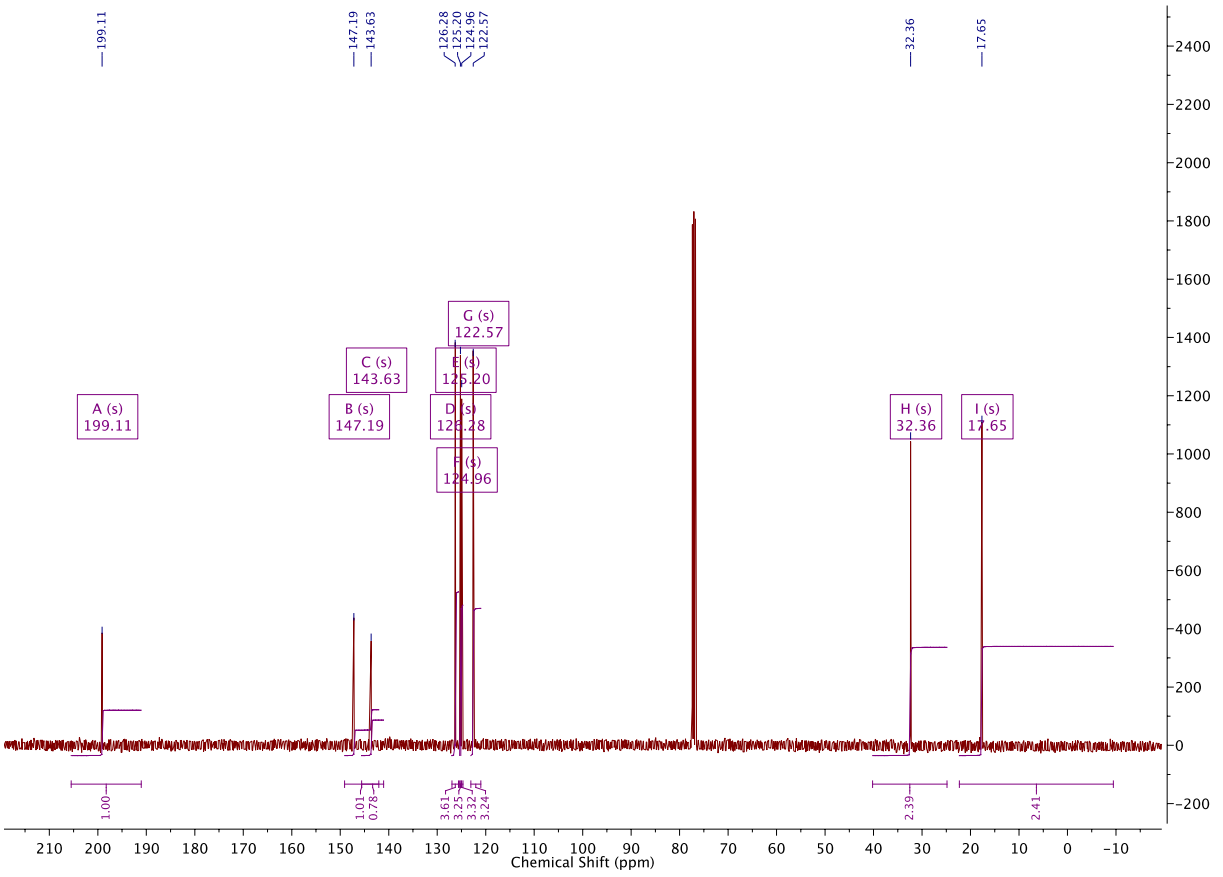
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 199.1, 147.2, 143.6, 126.3, 125.2, 125.0, 122.6, 32.4, 17.7.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3105, 2980, 1677,1589,1507, 1174, 745

MS (ESI) m/z $[M+H]^+$: 167.1(100)

This data was concordant with literature values[6].


7.39
7.39
7.38
7.19
7.19
7.18
6.48
6.47
2.39
2.39
2.15
1.56
C (t)
7.39
B (m)
7.19
A (d)
6.47
D (d)
2.39
E (s)
2.15
0.89
1.72
1.00
2.90
2.88
Chemical Shift (ppm)


199.11
147.19
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126.28
125.20
124.96
122.57
32.36
17.65
A (s)
199.11
B (s)
147.19
C (s)
143.63
D (s)
126.28
E (s)
125.20
F (s)
124.96
G (s)
122.57
H (s)
32.36
I (s)
17.65
1.00
1.01
0.78
3.61
3.25
3.32
3.24
2.39
2.41
Chemical Shift (ppm)

(*E*)-4,5-dimethylhex-3-en-2-one (2g)

Cp_2ZrCl_2 (428 mg, 1.46 mmol, 0.22 eq.) and dry CH_2Cl_2 (30 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (10 mL, 20 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –15 °C and then distilled H_2O (0.18 mL, 10 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 3-methyl butyne (0.68 ml, 6.67 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, Acetyl chloride (0.94 mL, 13.2 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 20 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (0.64 g, 97% yield)

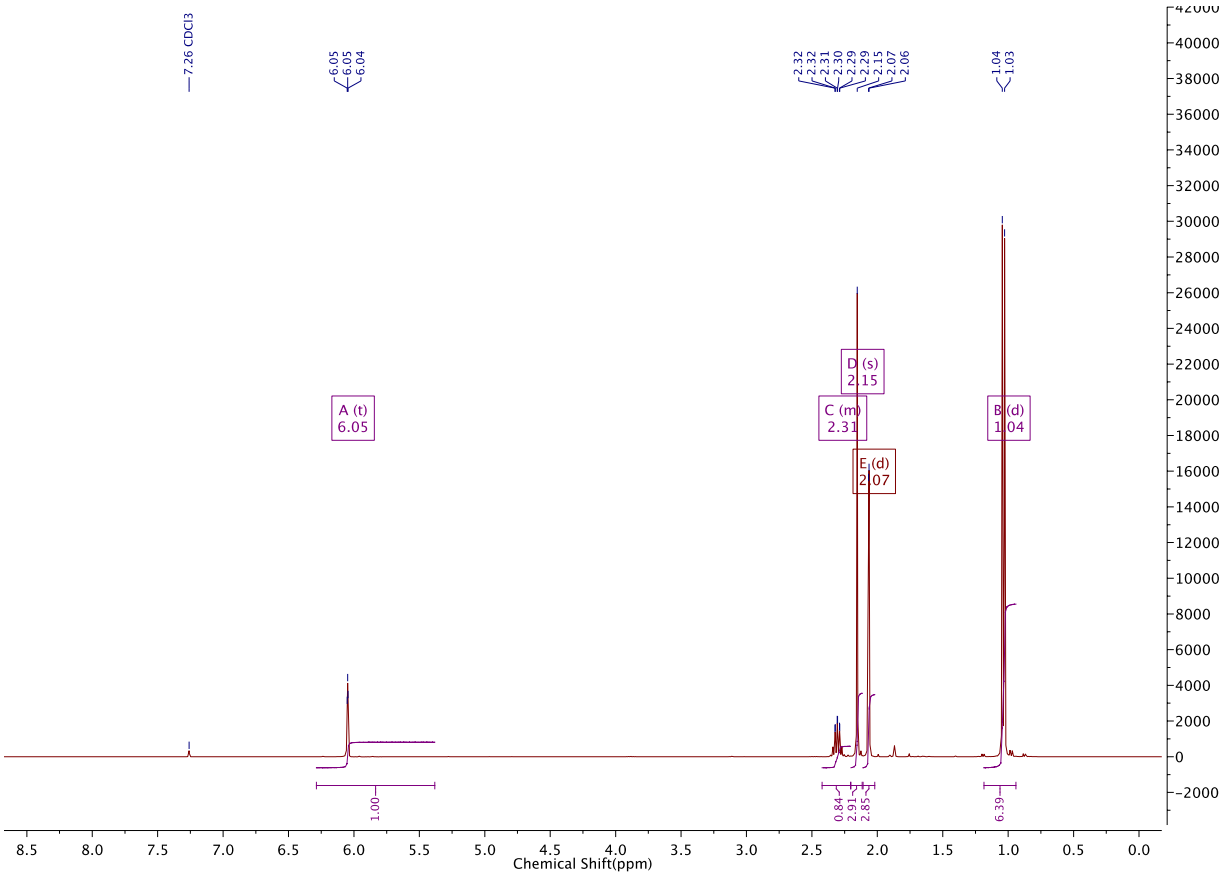
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 6.05 (t, *J* = 1.3 Hz, 1H, C*H*COH_3), 2.43 – 2.23 (m, 1H, C*H*), 2.15(s, 3H, COC*H*$_3$), 2.07 (d, *J* = 1.2 Hz, 3H, C*H*$_3$C=CH), 1.04 (d, *J* = 6.8 Hz, 6H, C*H*$_3$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 199.3, 164.0, 121.4, 38.2, 31.9, 20.9, 16.8 (2C).

IR (ν_{max}/cm^{-1}, $CHCl_3$) 2966, 2875, 1687,1615,1317, 963, 744

MS (ESI) m/z $[M+H]^+$: 127.1(100)

This data was concordant with literature values[10].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6.05
6.04
2.32
2.32
2.31
2.31
2.30
2.29
2.29
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2.07
2.06
1.04
1.03
A (t)
6.05
C (m)
2.31
D (s)
2.15
E (d)
2.07
B (d)
1.04
1.00
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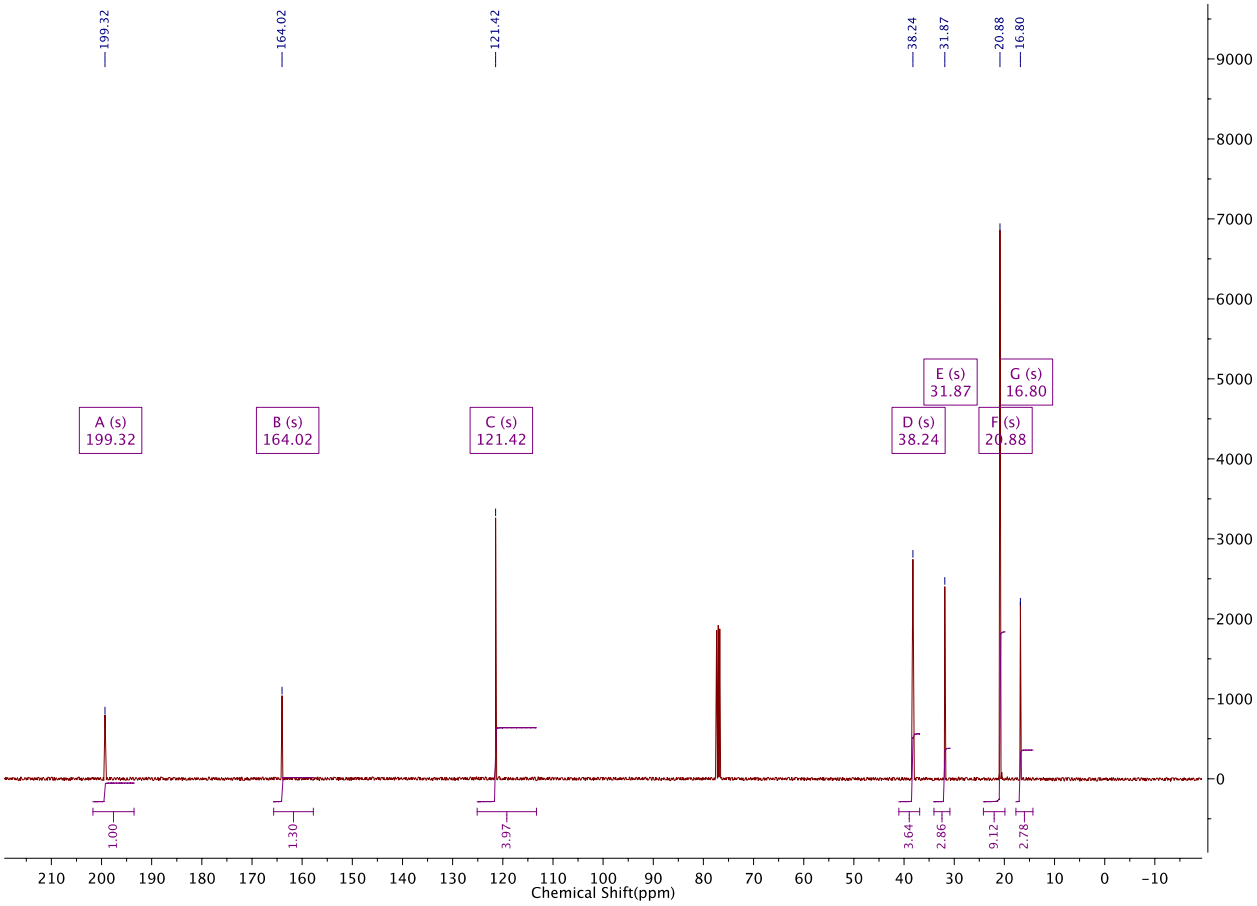
2.91
2.85
6.39
Chemical Shift(ppm)


199.32
164.02
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20.88
16.80
A (s)
199.32
B (s)
164.02
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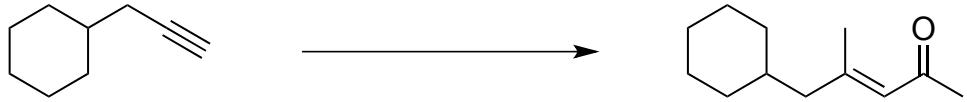
121.42
D (s)
38.24
E (s)
31.87
F (s)
20.88
G (s)
16.80
1.00
1.30
3.97
3.64
2.86
9.12
2.78
Chemical Shift(ppm)

(E)-5-cyclohexyl-4-methylpent-3-en-2-one (2h)



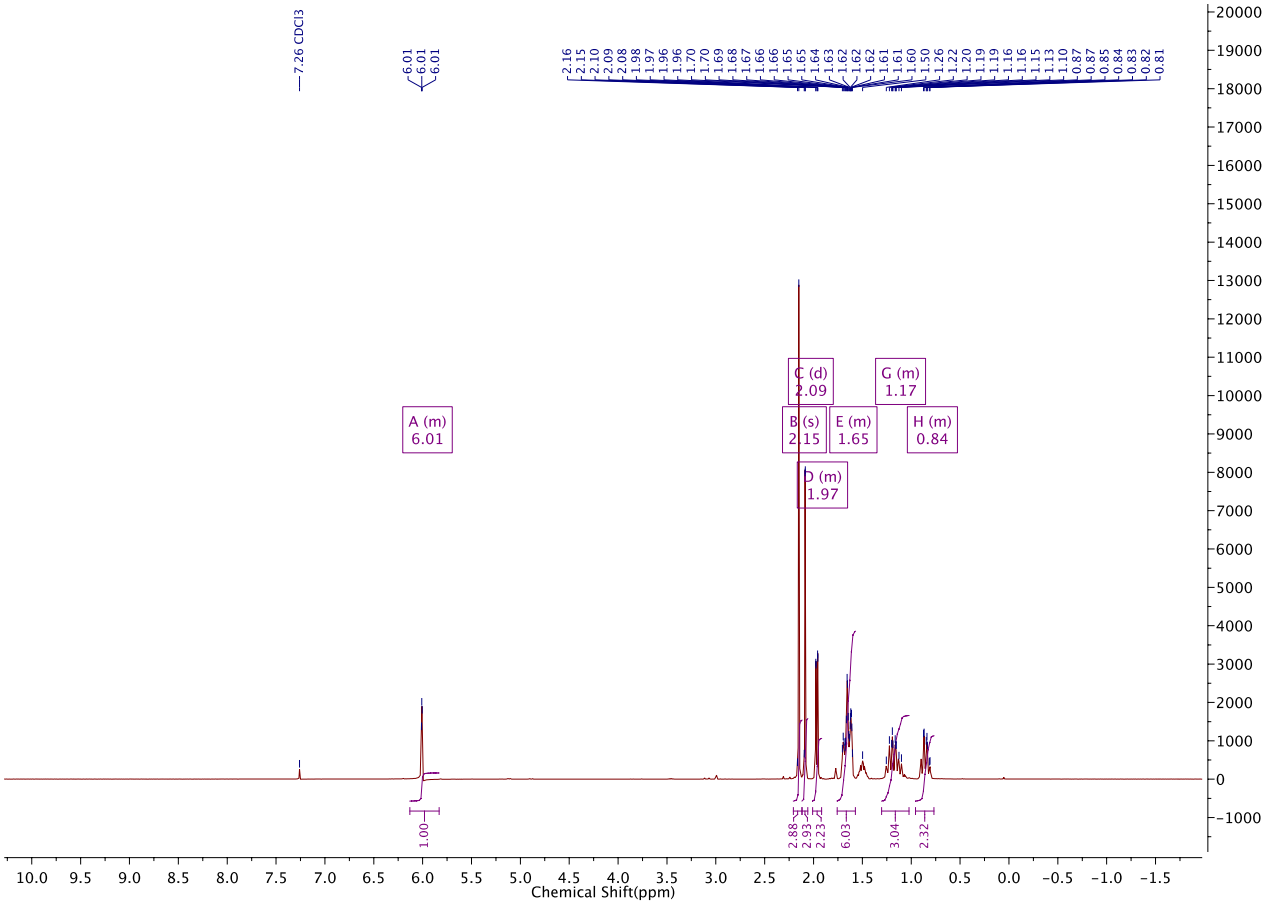
Cp_2ZrCl_2 (214 mg, 0.73 mmol, 0.22 eq.) and dry CH_2Cl_2 (15 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (5 mL, 10 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –23 °C and then distilled H_2O (0.09 mL, 5 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 3-cyclohexyl-1-propyne (0.47 mL, 3.3 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, acetyl chloride (0.47 mL, 6.64 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 10 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (0.35 g, 59% yield)

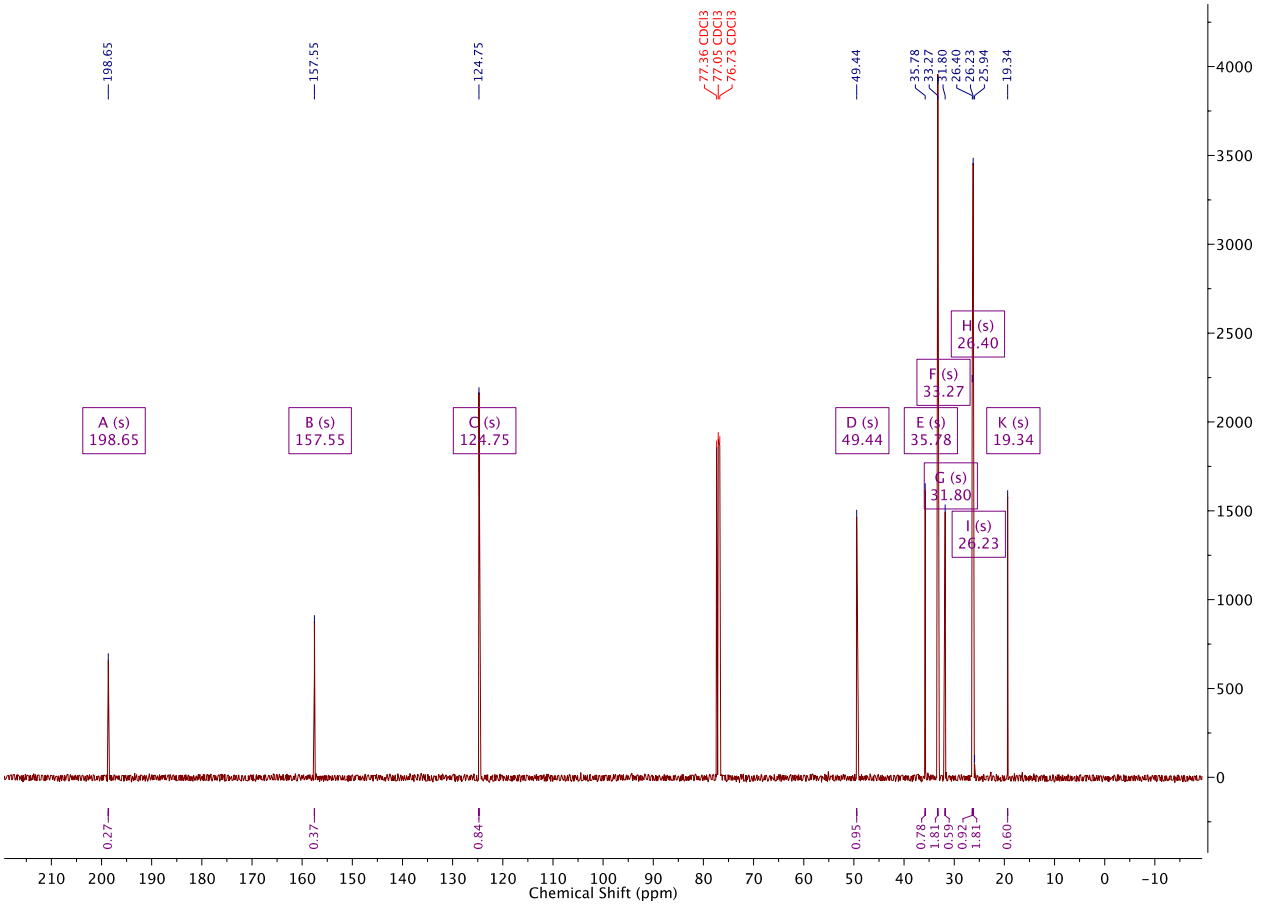
^{1}H NMR (400 MHz, Chloroform-d) δ_H/ppm 6.13 – 5.83 (m, 1H, C*H*COCH$_3$), 2.15 (s, 3H, C*H*$_3$), 2.09 (d, J = 1.2 Hz, 3H, C*H*$_3$C=CH), 2.01 – 1.92 (m, 2H, C*H*$_2$C=CH), 1.76 – 1.57 (m, 6H,C*H*, C*H*$_2$), 1.30 – 1.02 (m, 3H, C*H*$_2$), 0.96 – 0.77 (m, 2H, C*H*$_2$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 198.6, 157.6, 124.8, 49.4, 35.8, 33.3, 31.8(2C), 26.4(3C), 26.2, 19.3.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 2922, 2850, 1688, 1613, 1448, 1215,960

HRMS (ESI) m/z calc. for $C_{12}H_{21}O$ $[M+H]^+$: 181.1587, found: 181.1588.


7.26 CDCl3
A (m)
6.01
B (s)
2.15
C (d)
2.09
D (m)
1.97
E (m)
1.65
G (m)
1.17
H (m)
0.84
Chemical Shift(ppm)


A (s)
198.65
B (s)
157.55
C (s)
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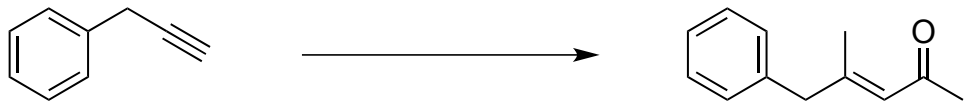
D (s)
49.44
E (s)
35.78
F (s)
33.27
G (s)
31.80
H (s)
26.40
I (s)
26.23
K (s)
19.34
77.36 CDCl3
77.05 CDCl3
76.73 CDCl3
Chemical Shift (ppm)

(E)-4-methyl-5-phenylpent-3-en-2-one (2i)



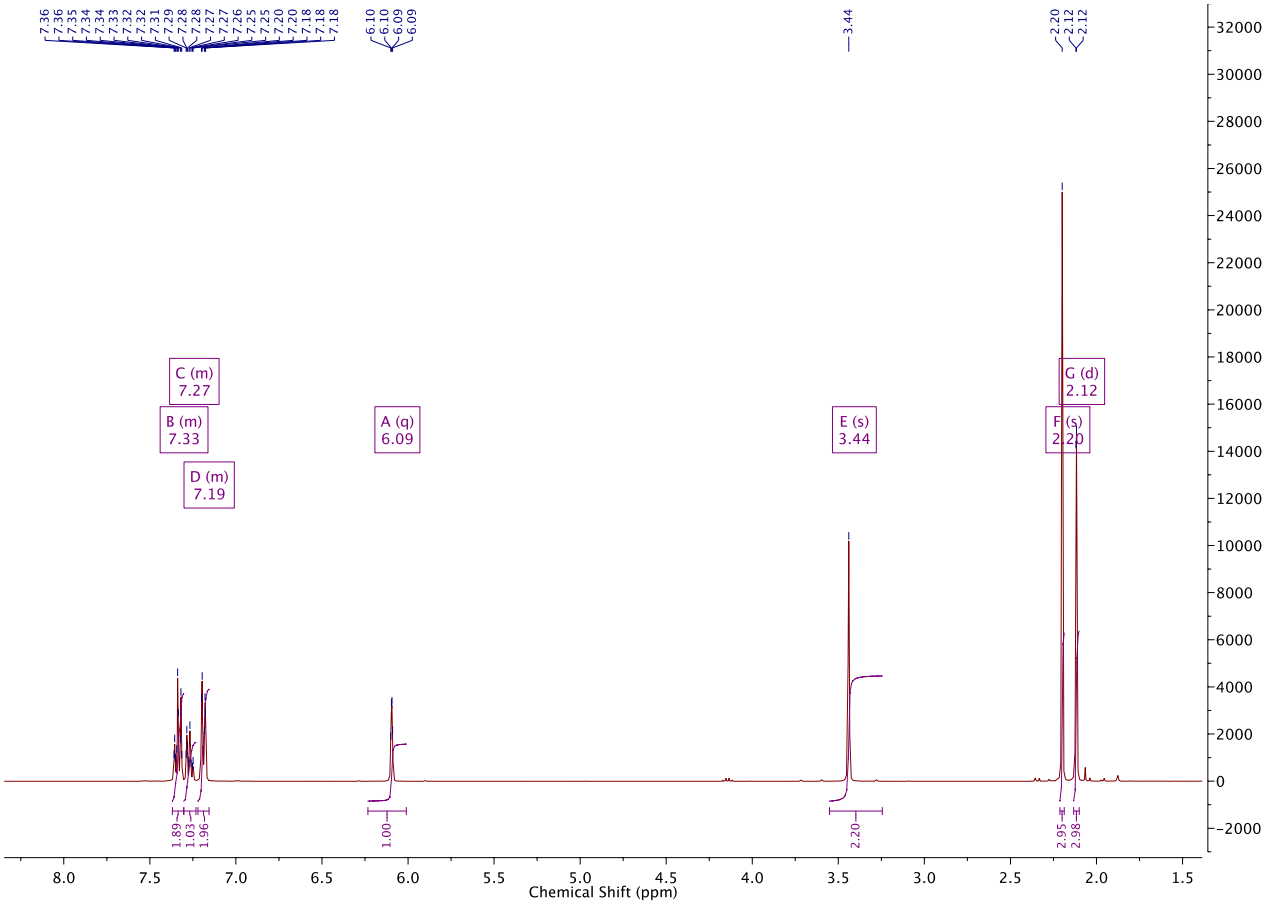
Cp_2ZrCl_2 (214 mg, 0.73 mmol, 0.22 eq.) and dry CH_2Cl_2 (15 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (5 mL, 10 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –23 °C and then distilled H_2O (0.09 mL, 5 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 3-Phenyl-1-propyne (0.41 mL, 3.3 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, acetyl chloride (0.47 mL, 6.64 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 10 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (0.37 g, 63% yield)

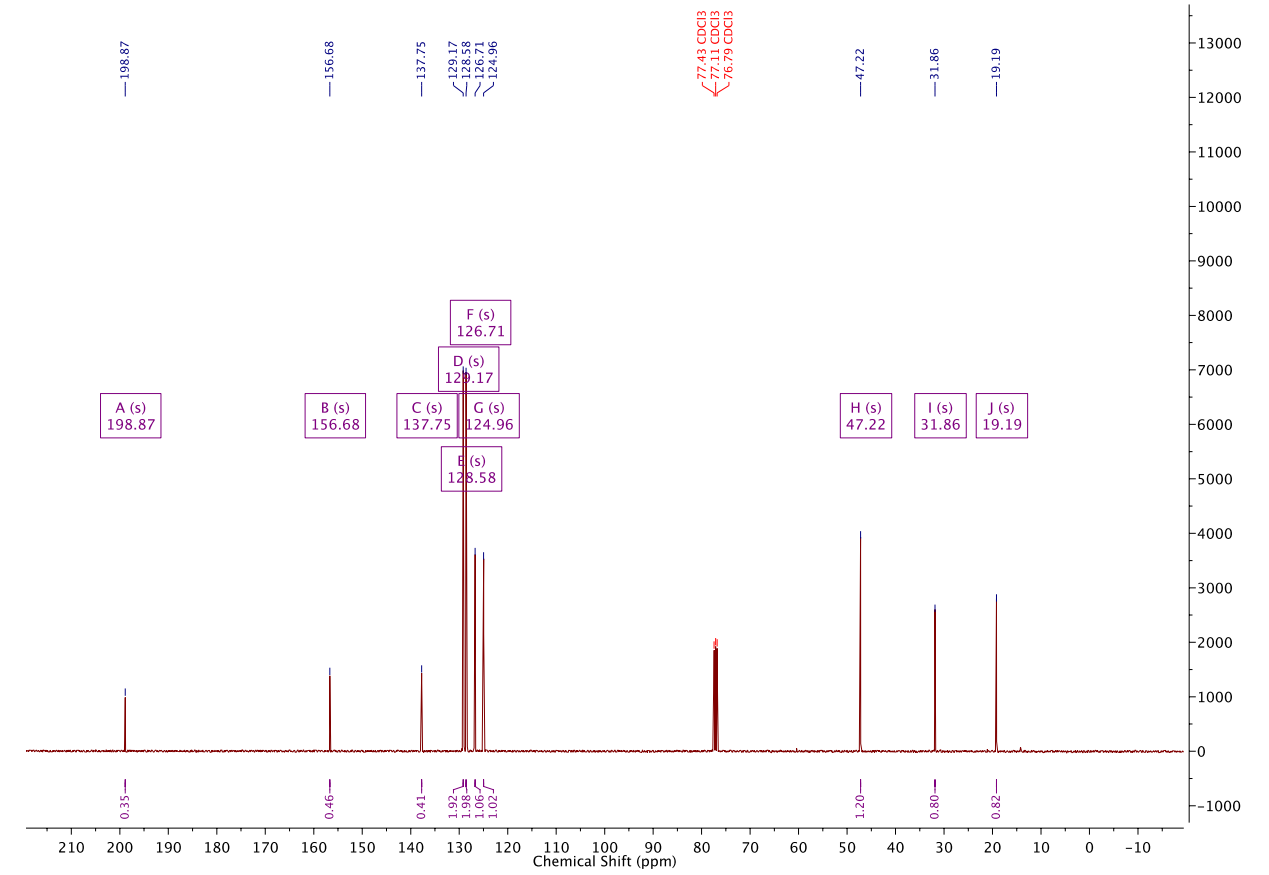
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.37 – 7.30 (m, 2H, Ar-*H*), 7.30 – 7.23 (m, 1H, Ar-*H*), 7.22 – 7.16 (m, 2H, Ar-*H*), 6.09 (q, *J* = 1.3 Hz, 1H, C*H*$COCH_3$), 3.44 (s, 2H, CH_2C=CH), 2.20 (s, 3H, CH_3), 2.12 (d, *J* = 1.2 Hz, 3H, CH_2C=CH).

^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 198.9, 156.7, 137.8, 129.2, 128.6, 126.7, 125.0, 47.2, 31.9, 19.2.

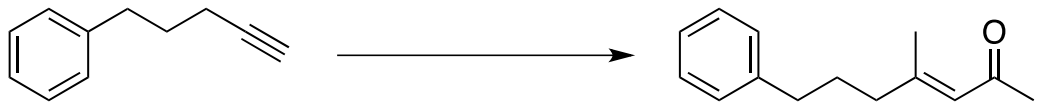
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3028, 1687, 1687, 1616, 1216, 773,770

HRMS (ESI) m/z calc. for $C_{12}H_{15}O$ $[M+H]^+$: 175.1117, found: 175.1118.


C (m)
7.27
B (m)
7.33
D (m)
7.19
A (q)
6.09
E (s)
3.44
G (d)
2.12
F (s)
2.20
Chemical Shift (ppm)


A (s)
198.87
B (s)
156.68
C (s)
137.75
D (s)
129.17
E (s)
128.58
F (s)
126.71
G (s)
124.96
H (s)
47.22
I (s)
31.86
J (s)
19.19
Chemical Shift (ppm)

(*E*)-4-Methyl-7-phenylhept-3-en-2-one (2j)



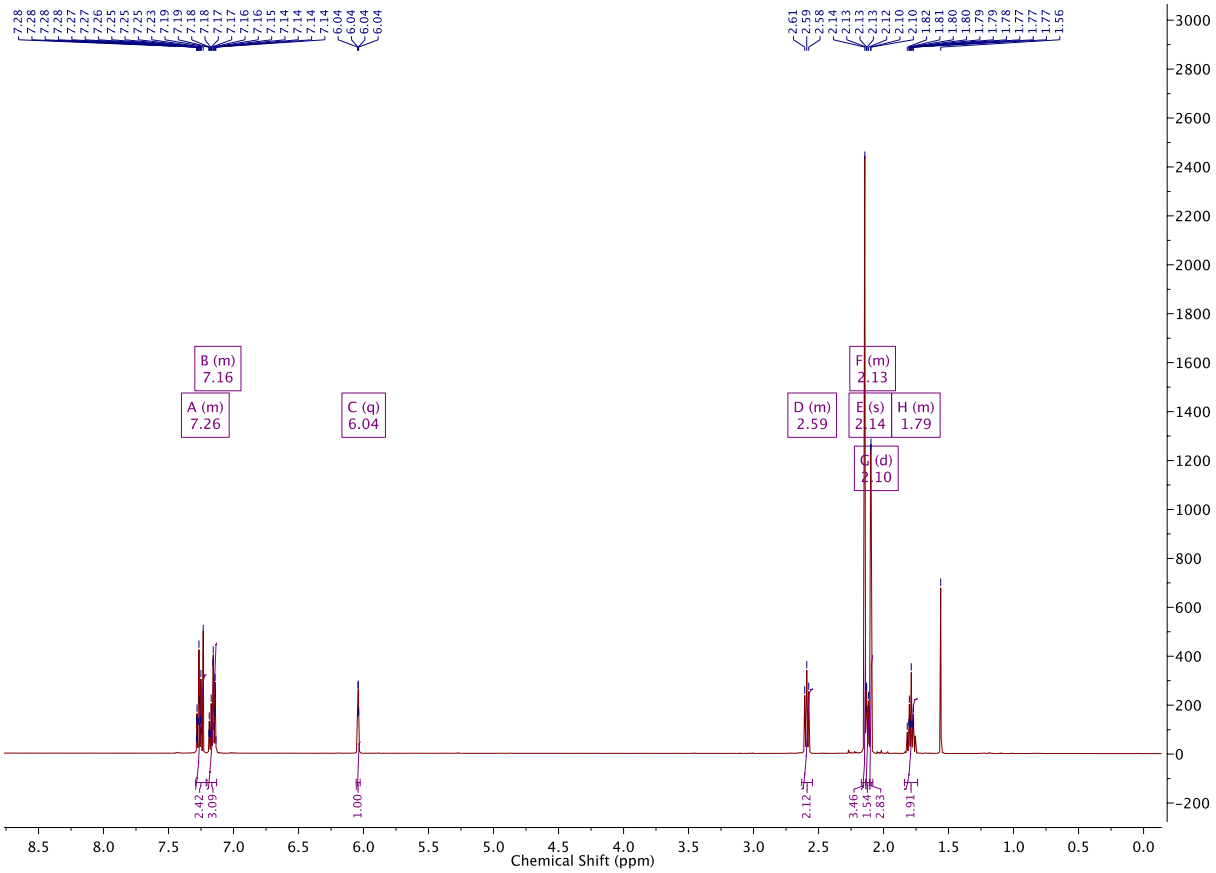
Cp_2ZrCl_2 (643 mg, 2.2 mmol, 0.22 eq.) and dry CH_2Cl_2 (50 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (15 mL, 30 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –23 °C and then distilled H_2O (0.27 mL, 15 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the Phenyl-1-pentyne (1.52 ml, 10 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, acetyl chloride (1.42 mL, 20 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 30 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (1.41 g, 69 %)

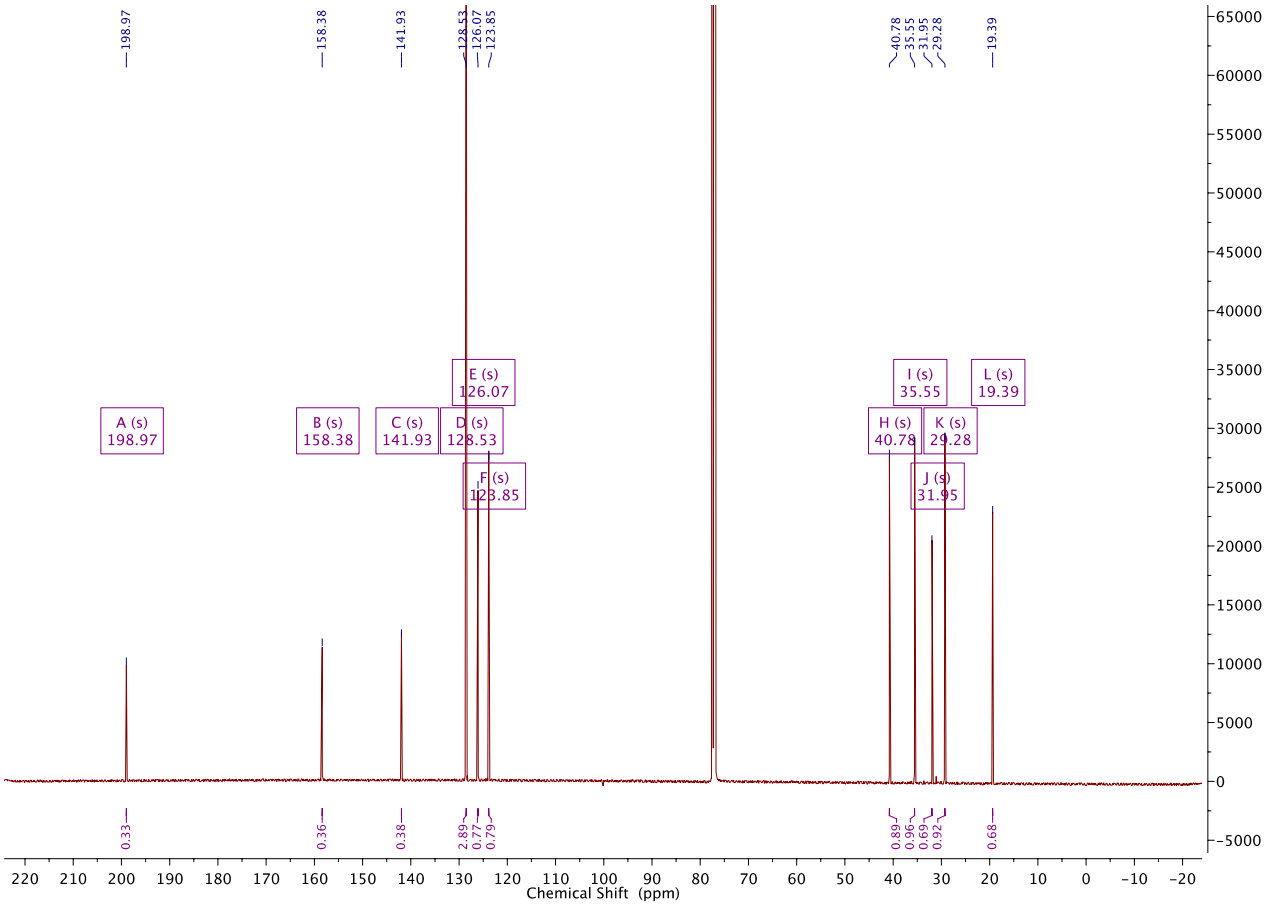
^{1}H NMR (500 MHz, $CDCl_3$) δ_H/ppm 7.29 – 7.21 (m, 2H, Ar-*H*), 7.20 – 7.13 (m, 3H, Ar-*H*), 6.04 (q, *J* = 1.3 Hz, 1H, C*H*COMe), 2.63 – 2.55 (m, 2H, PhCH_2), 2.14 (s, 3H, COCH_3), 2.14 – 2.11 (m, 2H, $PhCH_2CH_2CH_2$), 2.10 (d, *J* = 1.3 Hz, 3H,$CH_3CCHCOCH_3$), 1.84 – 1.74 (m, 2H, $PhCH_2CH_2$).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C/ppm 198.9, 158.4, 141.9, 128.5(4C), 126.1, 123.8, 40.7, 35.55, 31.9, 29.3, 19.4.

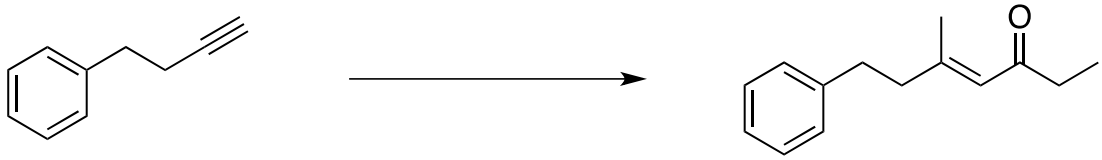
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3062, 2363, 1687, 1616, 1496, 1453

HRMS (ESI) m/z calc. for $C_{14}H_{19}O$ $[M+H]^+$: 203.1430, found: 203.1431.


B (m)
7.16
A (m)
7.26
C (q)
6.04
D (m)
2.59
F (m)
2.13
E (s)
2.14
H (m)
1.79
G (d)
2.10
Chemical Shift (ppm)


A (s)
198.97
B (s)
158.38
C (s)
141.93
E (s)
126.07
D (s)
128.53
F (s)
123.85
I (s)
35.55
H (s)
40.78
K (s)
29.28
J (s)
31.95
L (s)
19.39
Chemical Shift (ppm)

(*E*)-5-methyl-7-phenylhept-4-en-3-one (2k)



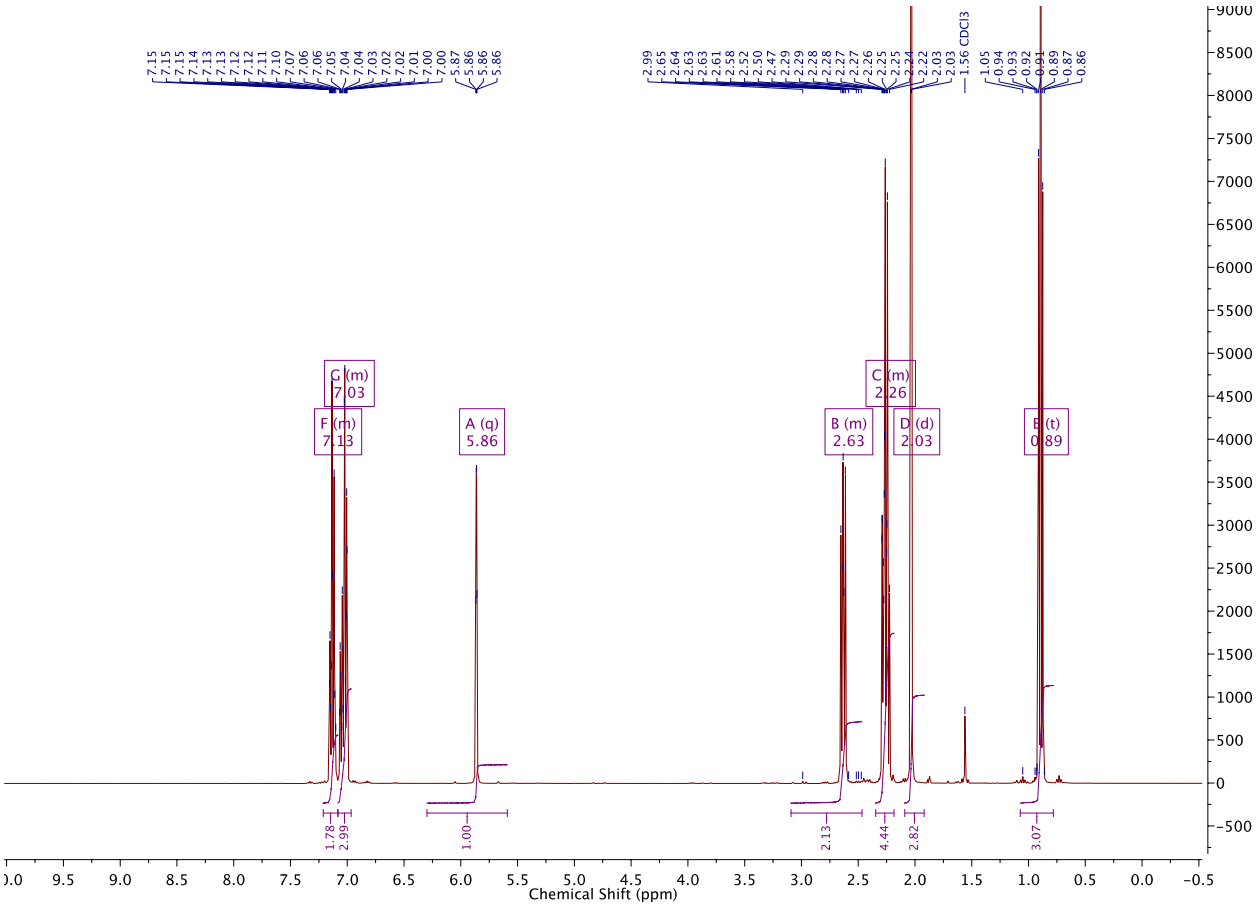
Cp_2ZrCl_2 (428 mg, 1.46 mmol, 0.22 eq.) and dry CH_2Cl_2 (30 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (10 mL, 20 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –15 °C and then distilled H_2O (0.18 mL, 10 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 4-Phenyl-1-pentyne (0.94 mL, 6.67 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, Proponyl chloride (1.16 mL, 13.2 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 20 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 90/10; silica), the enone product was obtained as yellow oil. (0.83 g, 61% yield)

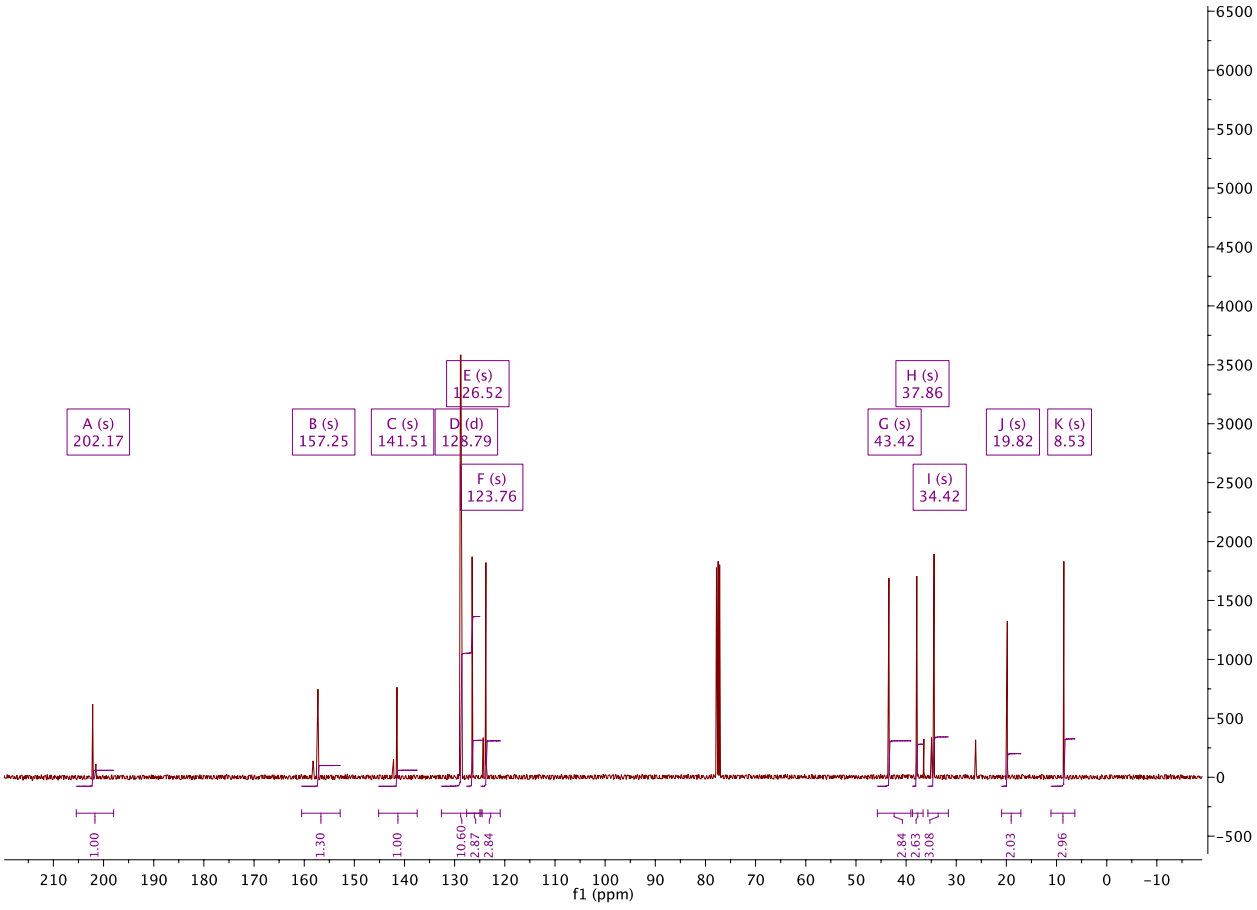
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.21 – 7.08 (m, 2H, Ar-*H*), 7.08 – 6.97 (m, 3H, Ar-*H*), 5.86 (q, *J* = 1.2 Hz, 1H, C*H*COEt), 3.09 – 2.47 (m, 2H, PhCH_2), 2.35 – 2.18 (m, 4H, COCH_2, CH_2C=CH), 2.03 (d, *J* = 1.2 Hz, 3H, CH_3C=CH), 0.89 (t, *J* = 7.3 Hz, 3H, CH_3CH$_2$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 202.2, 157.2, 141.5, 128.8 (4C), 126.5, 123.8, 43.4, 37.9, 34.4, 19.8, 8.5.

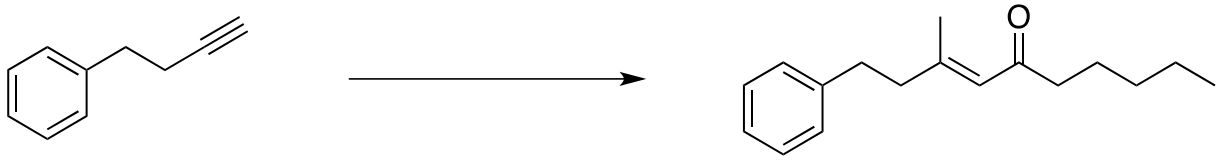
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2980, 2889, 1685, 1619, 1379,1153,699

HRMS (ESI) m/z calc. for $C_{14}H_{18}O$ $[M+H]^+$: 203.1436, found: 203.1432


G (m)
7.03
F (m)
7.13
A (q)
5.86
C (m)
2.26
B (m)
2.63
D (d)
2.03
E (t)
0.89
1.78
2.99
1.00
2.13
4.44
2.82
3.07
Chemical Shift (ppm)


A (s)
202.17
B (s)
157.25
C (s)
141.51
E (s)
126.52
D (d)
128.79
F (s)
123.76
H (s)
37.86
G (s)
43.42
I (s)
34.42
J (s)
19.82
K (s)
8.53
1.00
1.30
1.00
10.60
2.87
2.84
2.84
2.63
3.08
2.03
2.96
f1 (ppm)

(*E*)-3-methyl-1-phenyldec-3-en-5-one (2l)



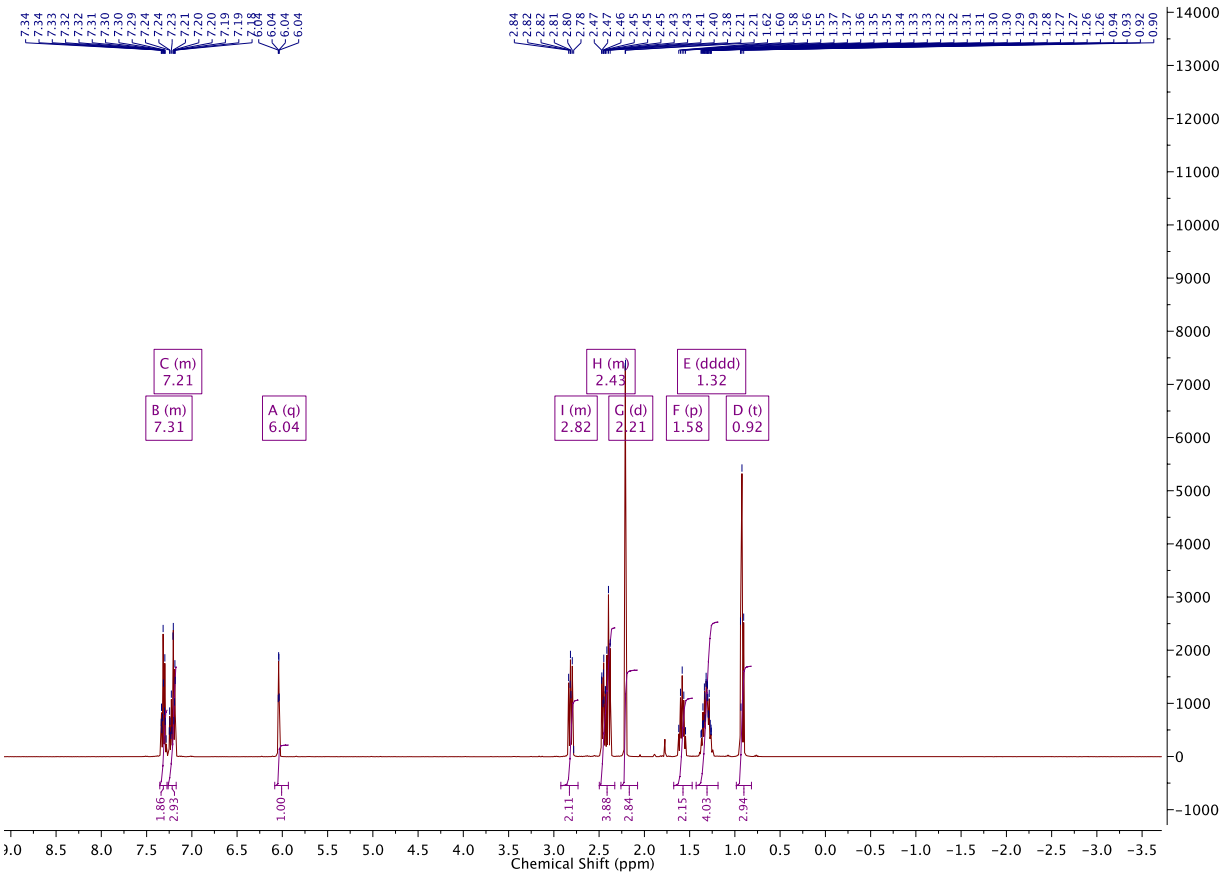
Cp_2ZrCl_2 (428 mg, 1.46 mmol, 0.22 eq.) and dry CH_2Cl_2 (30 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (10 mL, 20 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –15 °C and then distilled H_2O (0.18 mL, 10 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 4-Phenyl-1-pentyne (0.94 mL, 6.67 mmol, 1.0 eq.) was added in one portion via syringe. Then, after 15 additional min, Hexanoyl chloride (1.86 mL, 13.2 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 20 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 95/5; silica), the enone product was obtained as yellow oil. (0.93 g, 57% yield)

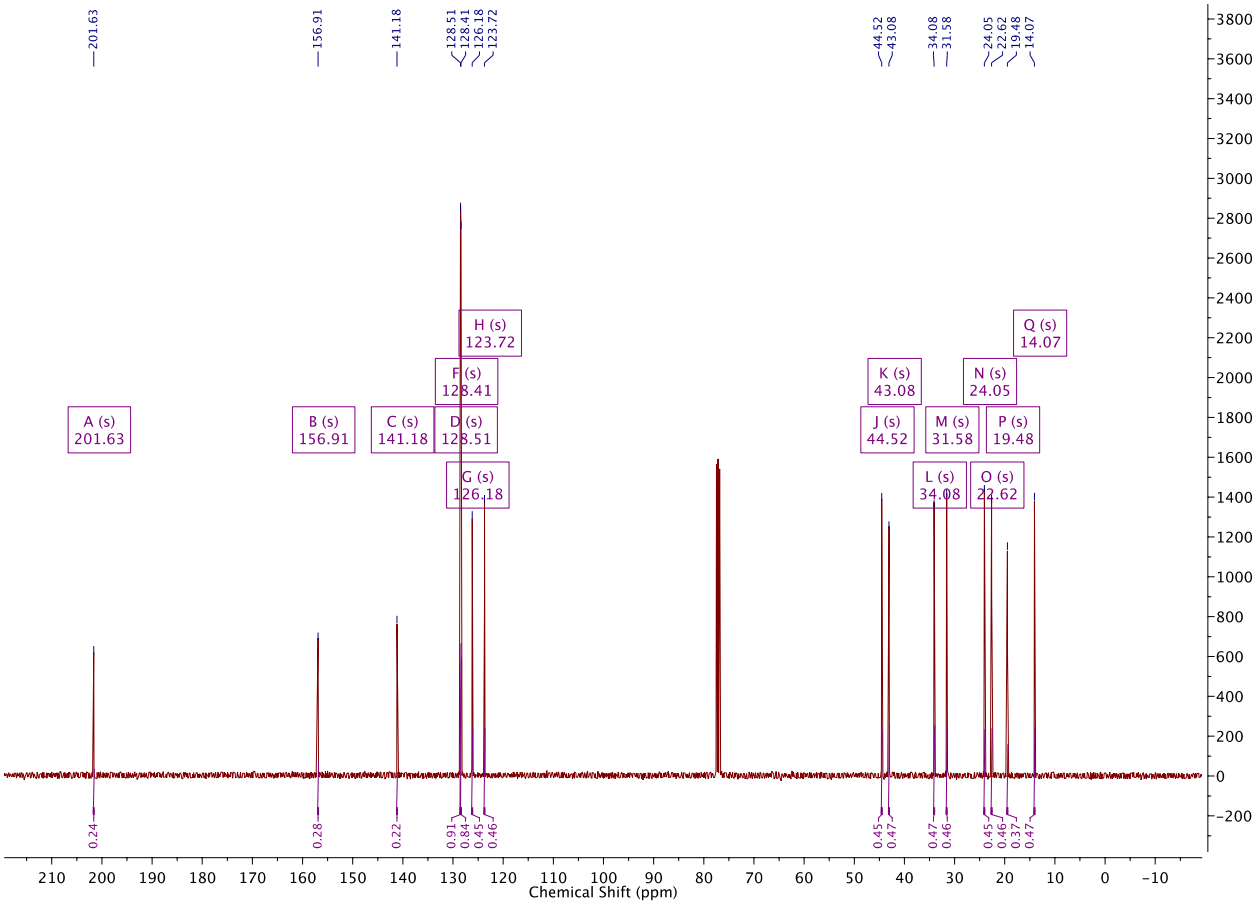
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.35 – 7.27 (m, 2H, Ar-*H*), 7.26 – 7.17 (m, 3H, Ar-*H*), 6.04 (q, *J* = 1.3 Hz, 1H, C*H*CO), 2.92 – 2.73 (m, 2H, PhCH_2), 2.50 – 2.33 (m, 4H, COCH_2, CH_2C=CH), 2.21 (d, *J* = 1.2 Hz, 3H, CH_3CCH), 1.58 (p, *J* = 7.5 Hz, 2H, CH_2), 1.32 (dddd, *J* = 16.5Hz, 15.0 Hz, 8.8 Hz, 3.4 Hz, 4H, CH_2), 0.92 (t, *J* = 7.0 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 201.6, 156.9, 141.2, 128.5(2C), 128.4(2C), 126.2, 123.7, 44.5, 43.1, 34.1, 31.6, 24.1, 22.6, 19.5, 14.1.

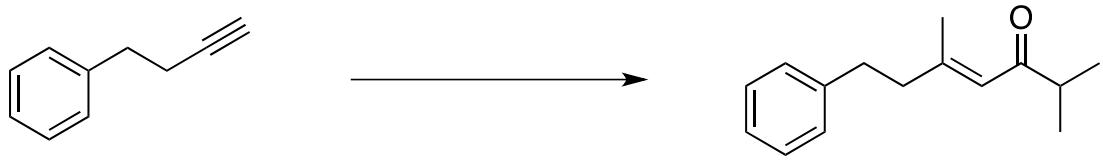
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2980, 2930, 1686, 1618, 1381,1131,698

HRMS (ESI) m/z calc. for $C_{17}H_{24}O$ $[M+H]^+$: 245.1905, found: 245.1901


C (m)
7.21
B (m)
7.31
A (q)
6.04
H (m)
2.43
I (m)
2.82
G (d)
2.21
E (dddd)
1.32
F (p)
1.58
D (t)
0.92
Chemical Shift (ppm)


A (s)
201.63
B (s)
156.91
C (s)
141.18
D (s)
128.51
F (s)
128.41
G (s)
126.18
H (s)
123.72
J (s)
44.52
K (s)
43.08
L (s)
34.08
M (s)
31.58
N (s)
24.05
O (s)
22.62
P (s)
19.48
Q (s)
14.07
Chemical Shift (ppm)

(*E*)-2,5-Dimethyl-7-phenylhept-4-en-3-one (2m)



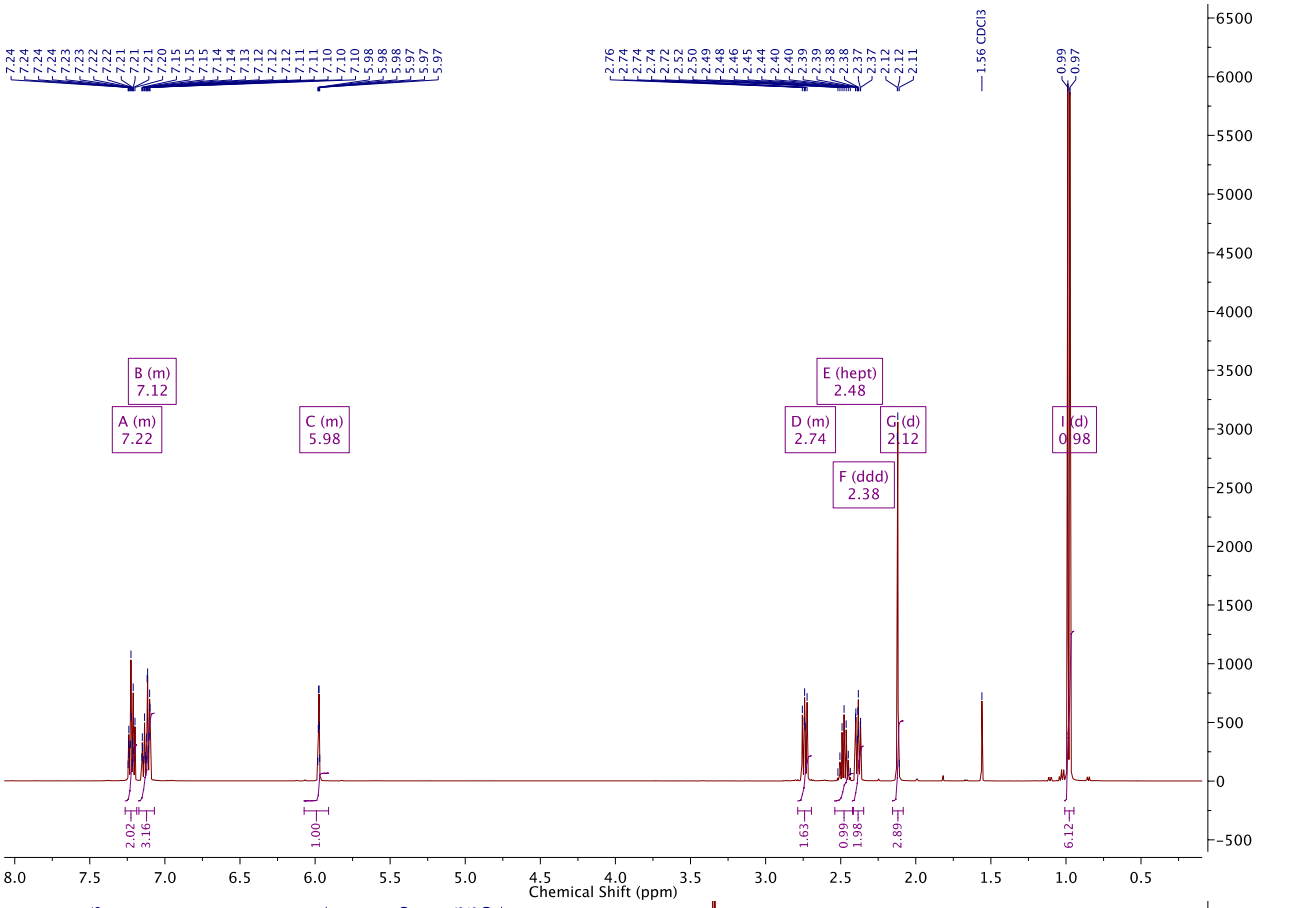
Cp_2ZrCl_2 (643 mg, 2.2 mmol, 0.22 eq.) and dry CH_2Cl_2 (50 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (15 mL, 30 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –15 °C and then distilled H_2O (0.27 mL, 15 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 4-Phenyl-1-pentyne (1.41 mL, 10 mmol, 1.0 eq.), was added in one portion via syringe. Then, after 15 additional min, isobutyl chloride (2.10 mL, 20 mmol, 2.0 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 20 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 95/5; silica), the enone product was obtained as yellow oil. (1.40 g, 65 %)

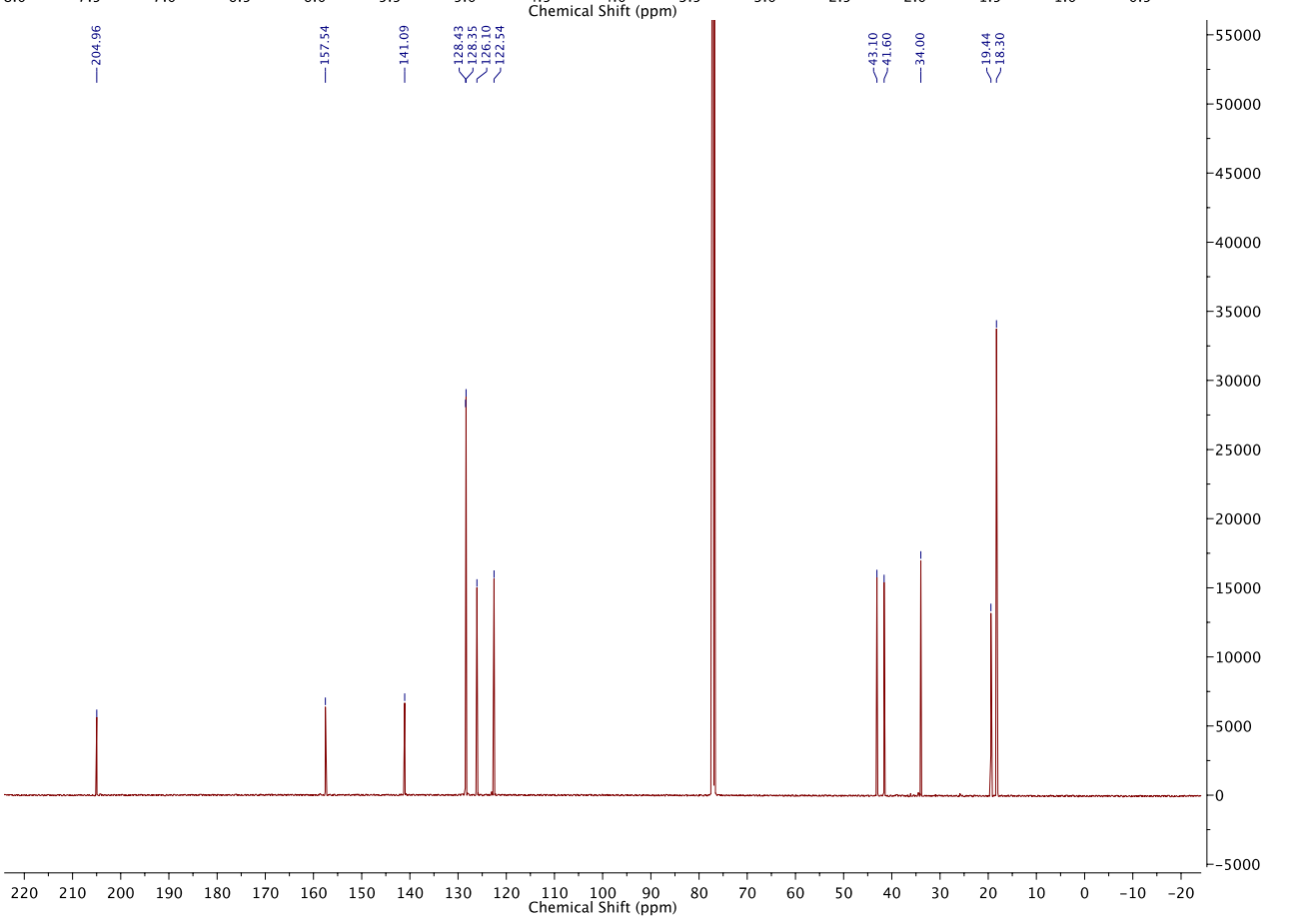
^{1}H NMR (500 MHz, $CDCl_3$) δ_H/ppm 7.33 – 7.25 (m, 2H, Ar-*H*), 7.23 – 7.13 (m, 3H, Ar-*H*), 6.13 – 5.97 (m, 1H, C=C*H*), 2.85 – 2.76 (m, 2H,PhH_2), 2.54 (hept, *J* = 6.9 Hz, 1H, C*H*$(CH_3)_2$), 2.45 (ddd, *J* = 9.0 Hz, 6.2 Hz, 1.1 Hz, 2H, CH_2), 2.18 (d, *J* = 1.4 Hz, 3H, CH_3C=CH), 1.04 (d, *J* = 6.9 Hz, 6H, 2 × CH_3).

^{13}C NMR (126 MHz, $CDCl_3$) δ_C/ppm 204.9, 157.5, 141.0, 128.4(2C), 128.3(2C), 126.1, 122.5, 43.1, 41.6, 34.0, 19.4, 18.3(2C).

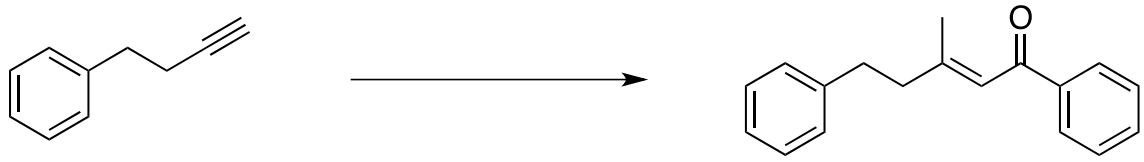
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3648, 2932, 1714, 1603, 1497

MS (ESI) m/z calc. for $C_{15}H_{21}O$ $[M+H]^+$: 217.1587, found: 217.1588.


B (m)
7.12
A (m)
7.22
C (m)
5.98
E (hept)
2.48
D (m)
2.74
G (d)
2.12
F (ddd)
2.38
I (d)
0.98
1.56 CDCl3
Chemical Shift (ppm)


204.96
157.54
141.09
128.43
128.35
126.10
122.54
43.10
41.60
34.00
19.44
18.30
Chemical Shift (ppm)

(E)-3-Methyl-1, 5-diphenylpent-2-en-1-one (2n)



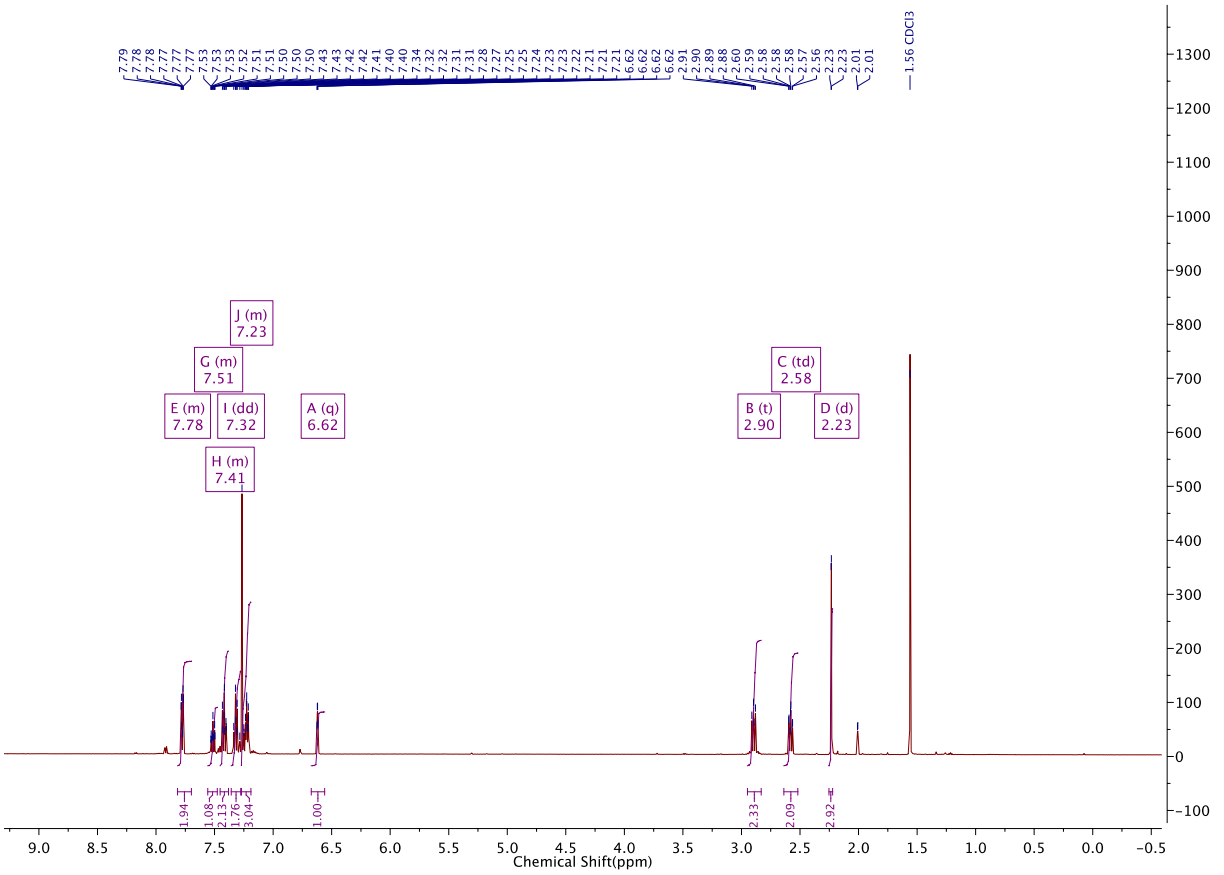
Cp_2ZrCl_2 (643 mg, 2.2 mmol, 0.22 eq.) and dry CH_2Cl_2 (50 mL) were added to flame-dried round bottom flask fitted with a magnetic stir bar under an argon atmosphere. Me_3Al (15 mL, 30 mmol, 3.0 eq.), was added dropwise by syringe over about 5 minutes. The resulting mixture was cooled to –15 °C and then distilled H_2O (0.27 mL, 15 mmol, 1.5 eq.), was added dropwise (over about 5 min) to the flask via syringe, after stirring for 15 min, the 4-Phenyl-1-pentyne (1.41 mL, 10 mmol, 1.0 eq.), was added in one portion via syringe. Then, after 15 additional min, benzoyl chloride (1.85 mL, 16 mmol, 1.6 eq.) was introduced in one portion. The reaction mixture was allowed to continue stirring at –23 °C for 15 min, and then allowed to warm to room temperature while stirring was continued for an additional 15 min. The reaction was quenched by slowly adding sat. aq. K_2CO_3 using a vent needle until gas evolution stopped (~ 20 mL). The water and organic layers were partitioned, and the aqueous phase was extracted with Et_2O. The combined organic phase was dried ($MgSO_4$), filtered and concentrated under reduced pressure. After flash column chromatography (petroleum ether/ Et_2O; 95/5; silica), the enone product was obtained as yellow oil. (0.93 g, 36 % yield)

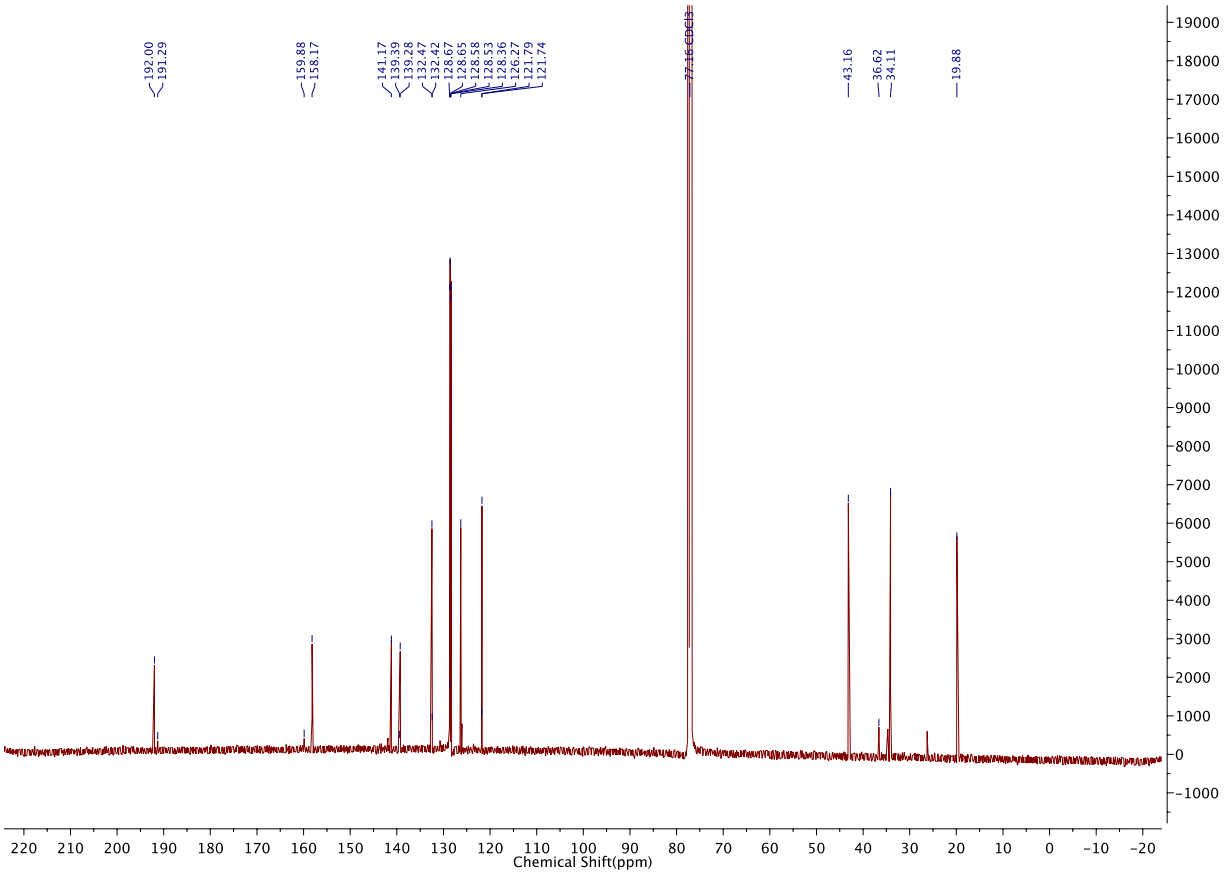
^{1}H NMR (500 MHz, $CDCl_3$) δ_H/ppm 7.81 – 7.69 (m, 2H, Ar-*H*), 7.55 – 7.47 (m, 1H, Ar-*H*), 7.45 – 7.38 (m, 2H, Ar-*H*), 7.32 (dd, *J* = 8.0 Hz, 6.7 Hz, 2H, Ar-*H*), 7.27 – 7.18 (m, 3H, Ar-*H*), 6.62 (q, *J* = 1.2 Hz, 1H, C*H*), 2.89 (t, *J* = 8.8 Hz, 6.8 Hz, 2H, PhCH_2), 2.57 (td, *J* = 7.6 Hz, 1.1 Hz, 2H, CH_2C=CH), 2.23 (d, *J* = 1.3 Hz, 3H, CH_3)

^{13}C NMR (126 MHz, $CDCl_3$) δ_C/ppm 192.0, 158.1, 141.1, 139.2, 132.4, 128.6(2C), 128.5(2C), 128.5(2C), 128.3(2C), 126.2, 121.7, 43.1, 34.1, 19.8.

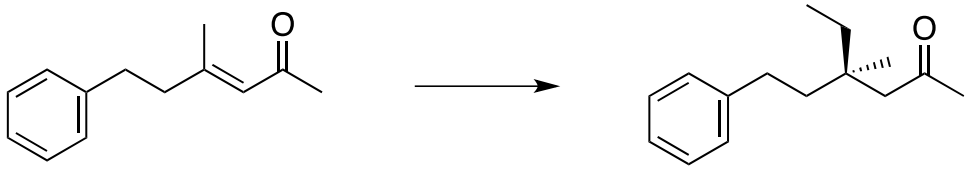
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3061, 2858, 1661, 1579, 1495, 1448

MS (ESI) m/z calc. for $C_{18}H_{19}O$ $[M+H]^+$: 251.1430, found: 251.1432.


J (m)
7.23
G (m)
7.51
E (m)
7.78
I (dd)
7.32
A (q)
6.62
H (m)
7.41
C (td)
2.58
B (t)
2.90
D (d)
2.23
1.56 CDCl3
Chemical Shift(ppm)


192.00
191.29
159.88
158.17
141.17
139.39
139.28
132.47
132.42
128.67
128.65
128.58
128.53
128.36
126.27
121.79
121.74
77.16 CDCl3
43.16
36.62
34.11
19.88
Chemical Shift(ppm)

(+)-(*R*)-4-ethyl-4-methyl-6-phenylhexan-2-one (3a)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (38.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml, 1.0 mmol, 5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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, 80 % yield, 91% *ee*)
HPLC analysis indicated an enantiomeric excess of 91 % [two Chiralpak® ID in series; flow: 0.8 mL/min; hexane/i-PrOH: 99:1; λ = 210 nm; major enantiomer tR = 14.58 min; minor enantiomer, tR = 15.65 min].

^{1}H NMR (400 MHz, $CDCl_3$) δ_H/ppm 7.23 – 7.16 (m, 2H, Ar-*H*), 7.14 – 7.06 (m, 3H, Ar-*H*), 2.51 – 2.39 (m, 2H, PhCH_2), 2.32 (s, 2H, CH_2COCH$_3$), 2.07 (s, 3H, COCH_3), 1.62 – 1.50 (m, 2H, PhCH$_2$CH_2), 1.38 (q, 2H,CH_2CH$_3$), 0.96 (s, 3H, CH_3), 0.79 (t, *J* = 7.5 Hz, 3H,CH$_2$CH_3).

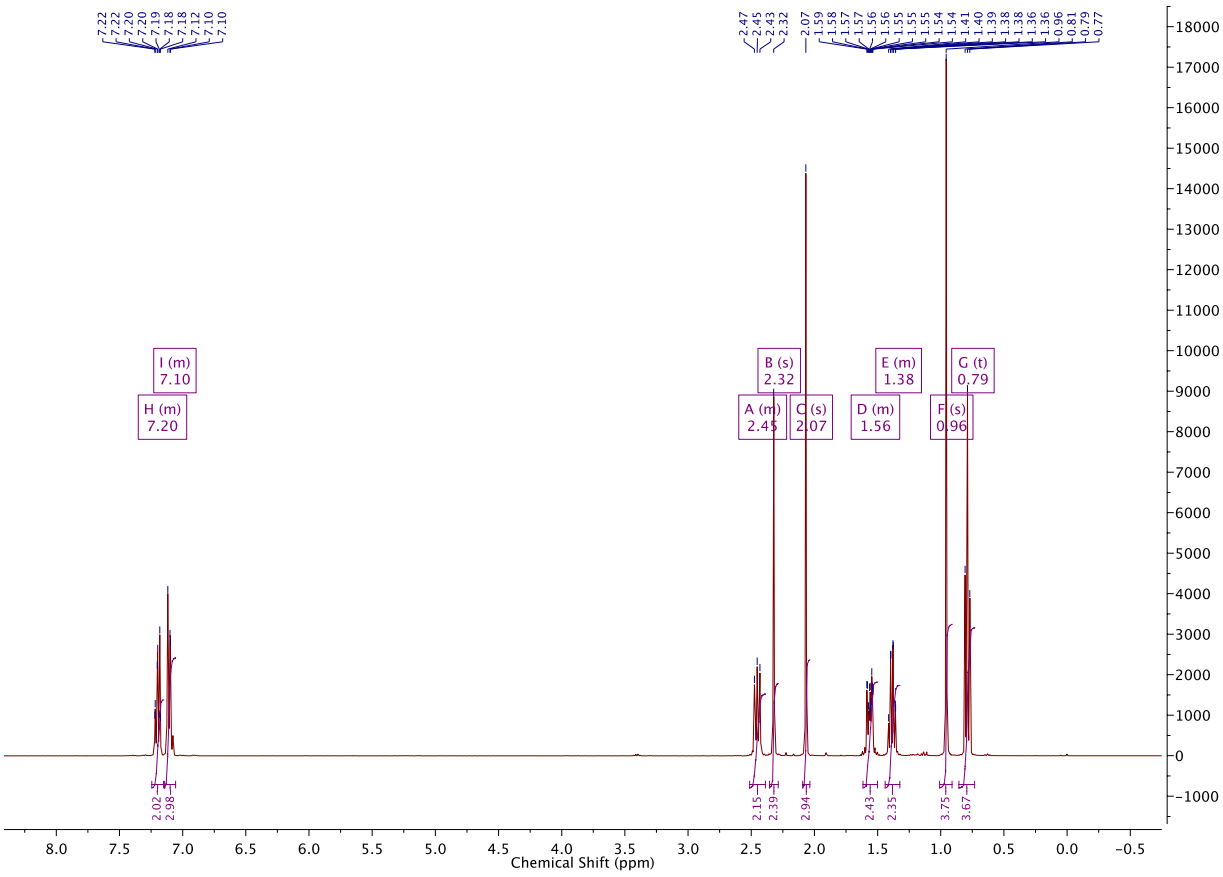
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 208.9, 143.0, 128.4 (4C), 125.7, 51.2, 41.1, 36.3, 32.7, 31.7, 30.4, 24.6, 8.1.

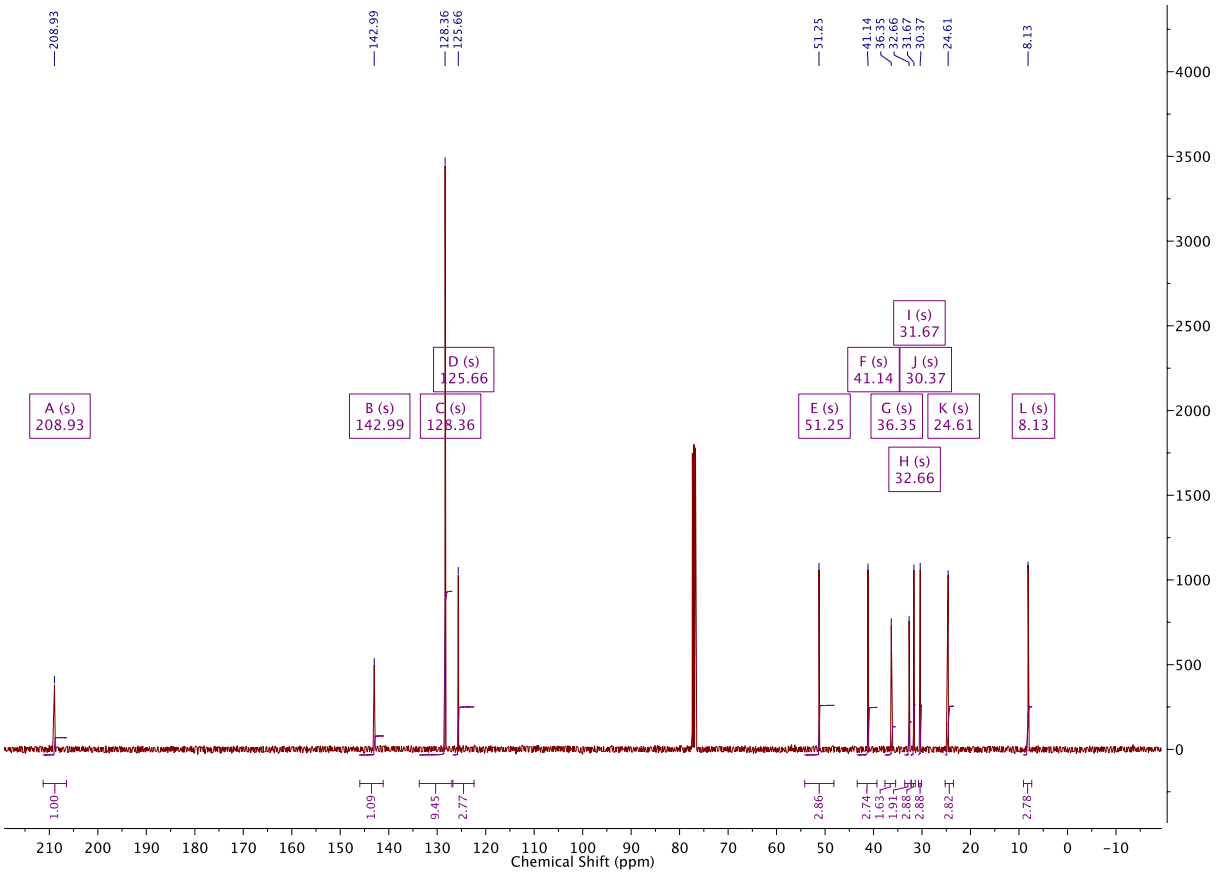
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3063, 2879, 1714,1603, 1496,1153, 699

MS (ESI) m/z calc. for $C_{15}H_{22}O^{23}Na$ $[M+Na]^+$: 241.1563, found: 241.1563

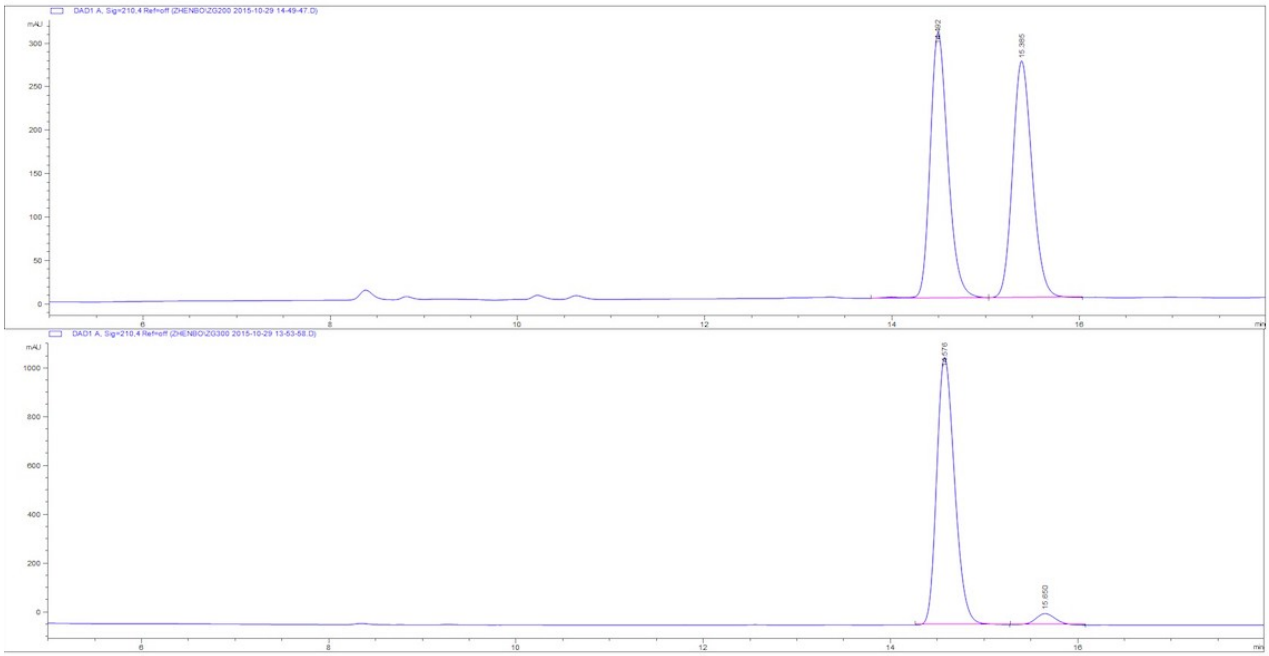
$[\alpha]^{20}_{589}$ = +4.1 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.

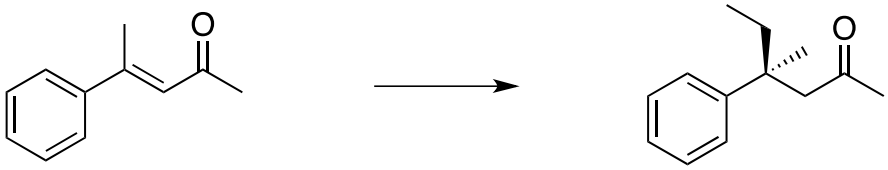



208.93
142.99
128.36
125.66
51.25
41.14
36.35
32.66
31.67
30.37
24.61
8.13
A (s) 208.93
B (s) 142.99
C (s) 128.36
D (s) 125.66
E (s) 51.25
F (s) 41.14
G (s) 36.35
H (s) 32.66
I (s) 31.67
J (s) 30.37
K (s) 24.61
L (s) 8.13
Chemical Shift (ppm)

HPRC Trace



(+)-(*S*)-4-methyl-4-phenylhexan-2-one (3b)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (32.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml, 1.0 mmol, 5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (19 mg, 50 % yield, 90% *ee*)

HPLC analysis indicated an enantiomeric excess of 91 % [Chiralpak® IB; flow: 0.8 mL/min; hexane/i-PrOH: 99:1; λ = 210 nm; major enantiomer tR = 7.33 min; minor enantiomer, tR = 7.68 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.50 – 7.21 (m, 4H, Ar-*H*), 7.23 – 7.02 (m, 1H, Ar-*H*), 2.83 (d, *J* = 14.1 Hz, 1H, CH_2CO), 2.54 (d, *J* = 14.2 Hz, 1H, CH_2CO), 1.80 (dt, *J* = 14.8 Hz, 7.3 Hz, 1H, CH_2CH$_3$), 1.71 (s, 3H,COCH_3), 1.69 – 1.55 (m, 1H, CH_2CH$_3$), 1.36 (s, 3H, CH_3), 0.63 (t, *J* = 7.4 Hz, 3H, CH$_2$CH_3).

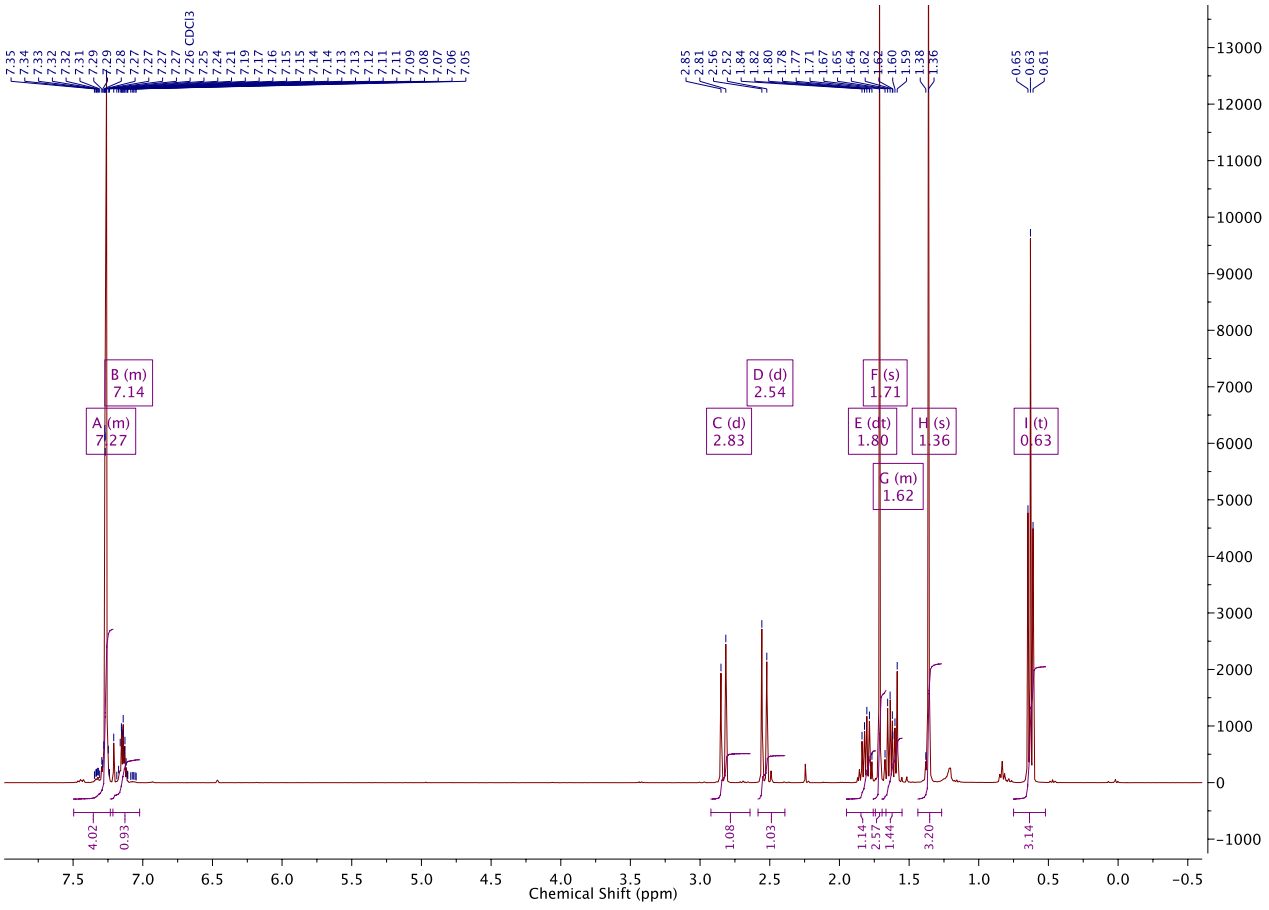
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 208.3, 146.3, 128.5, 128.2 (2C), 126.2 (2C), 125.9, 56.1, 40.7, 35.5, 32.0, 23.2, 8.5.

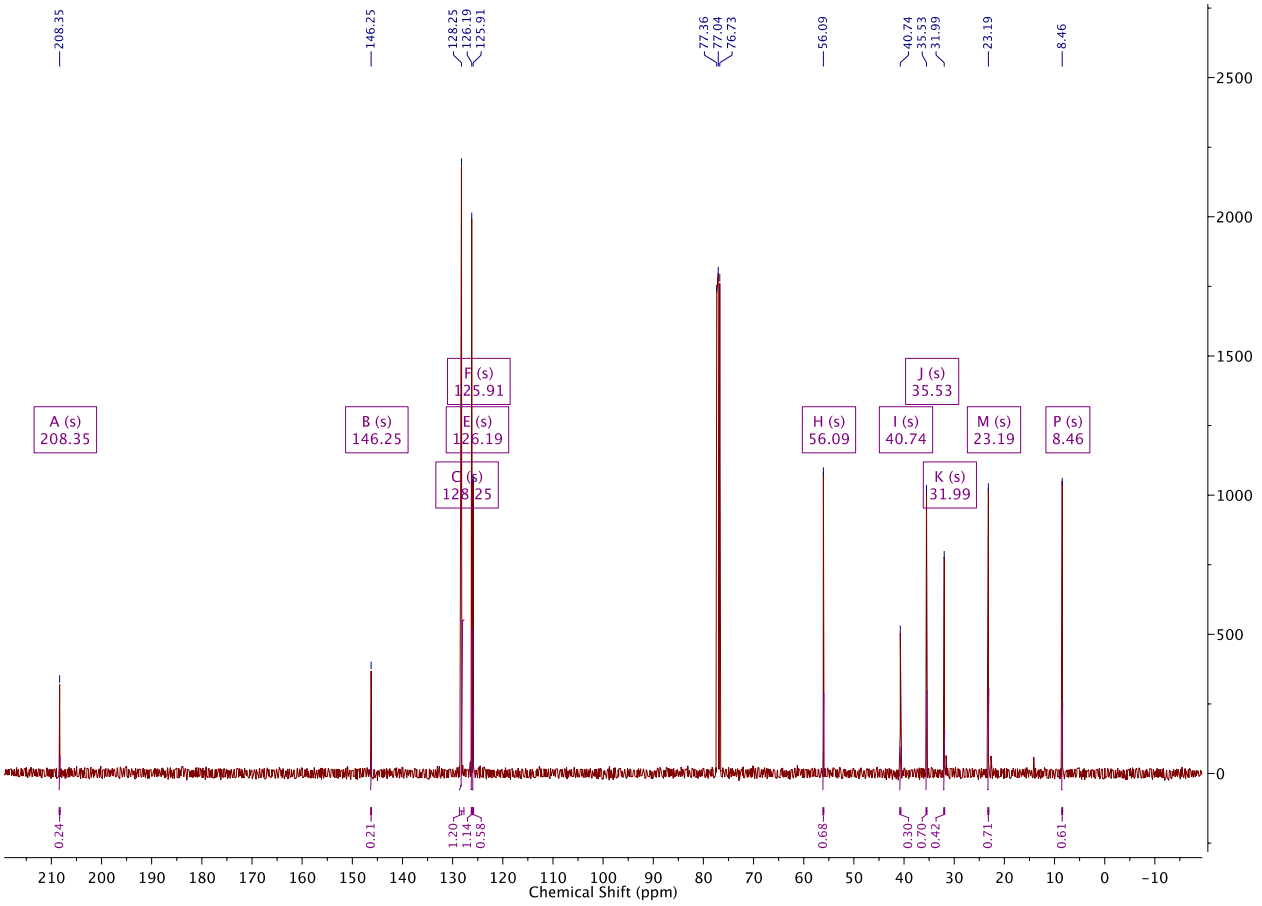
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3025, 2855,1703,1357,760,662

MS (ESI) m/z = $[M+Na]^+$: 213.2(100)

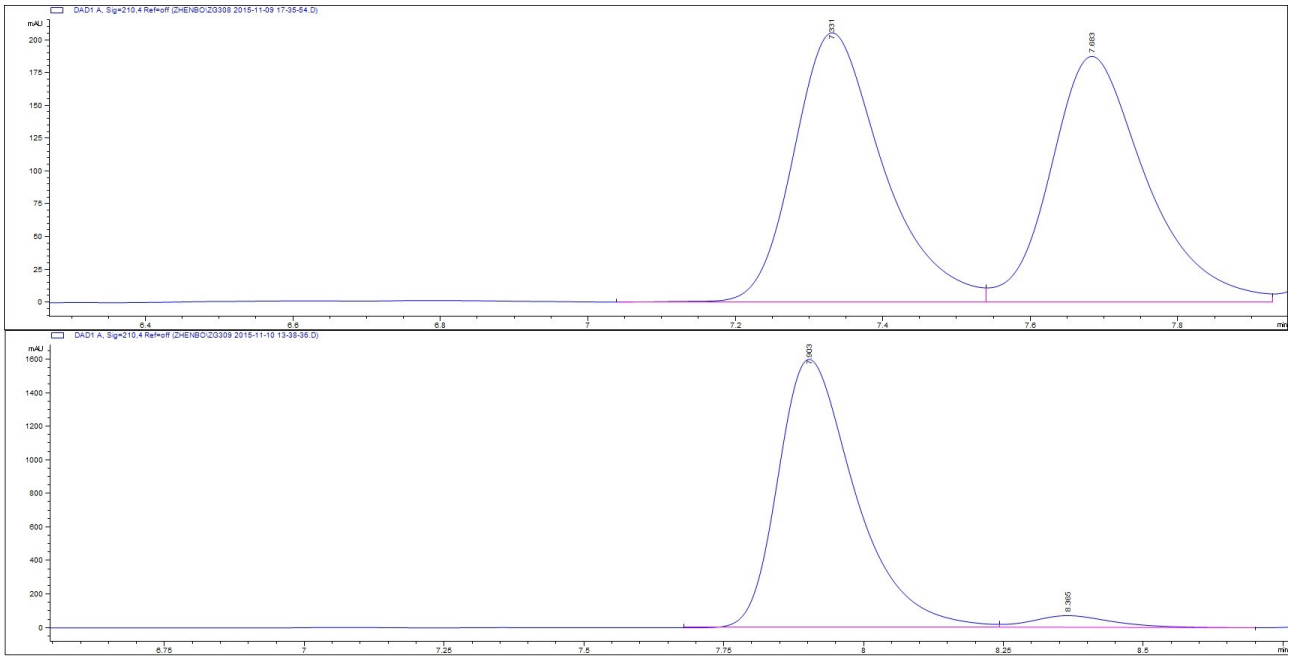
$[\alpha]^{20}_{589}$ = +44.7 ° (c 0.8, $CHCl_3$)

Absolute configuration was assigned by comparison to literature[6] optical rotation values.





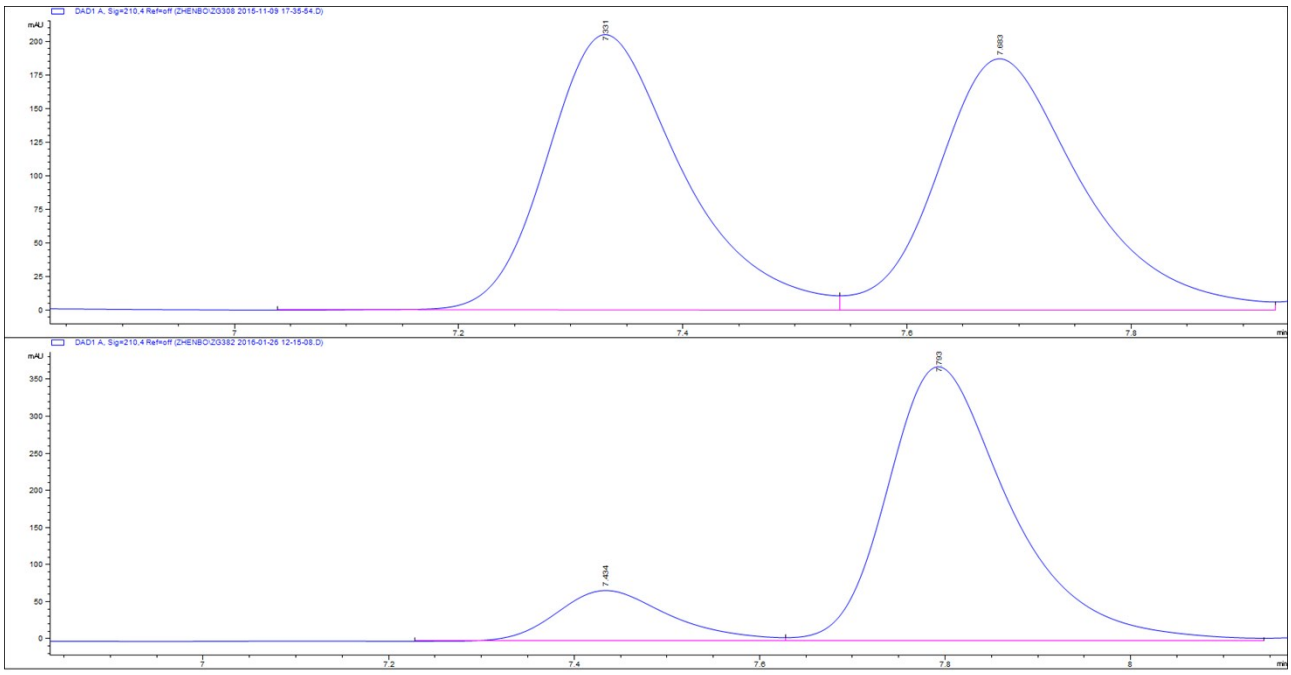
HPLC trace



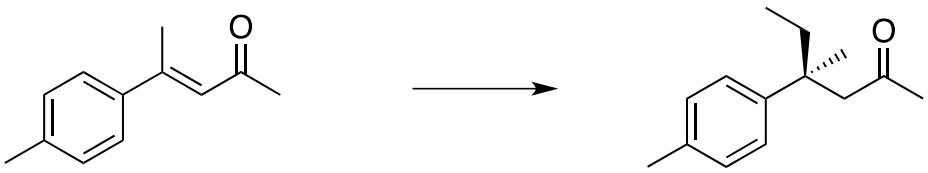
HPLC trace for cis-2b

HPLC analysis indicated an enantiomeric excess of 71 % [Chiralpak® IB; flow: 0.8 mL/min;

hexane/i-PrOH: 99:1; λ = 210 nm; minor enantiomer tR = 7.33 min; major enantiomer, tR = 7.68 min].



(+)-(S)-4-methyl-4-(p-tolyl)hexan-2-one (3c)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (35.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml,1.0 mmol, 5.0

eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (20 mg, 34 % yield, 89% *ee*)

HPLC analysis indicated an enantiomeric excess of 89 % [Chiralpak® IC; flow: 1.0 mL/min; hexane/i-PrOH: 99:1; λ = 210 nm; major enantiomer tR = 9.76 min; minor enantiomer, tR = 10.28 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.23 – 7.17 (m, 2H, Ar-*H*), 7.16 – 7.09 (m, 2H, Ar-*H*), 2.86 (d, *J* = 14.1 Hz, 1H, C*H*$_2$CO), 2.63 – 2.5 (m, 1H, C*H*$_2$CO), 2.32 (s, 3H, Ar-C*H*$_3$), 1.85 (dt, *J* = 13.7 Hz, 7.4 Hz, 1H, C*H*$_2$CH$_3$), 1.77 (s, 3H, COC*H*$_3$), 1.72 – 1.53 (m, 1H, C*H*$_2$CH$_3$), 1.39 (s, 3H, C*H*$_3$), 0.68 (t, *J* = 7.4 Hz, 3H, CH$_2$C*H*$_3$).

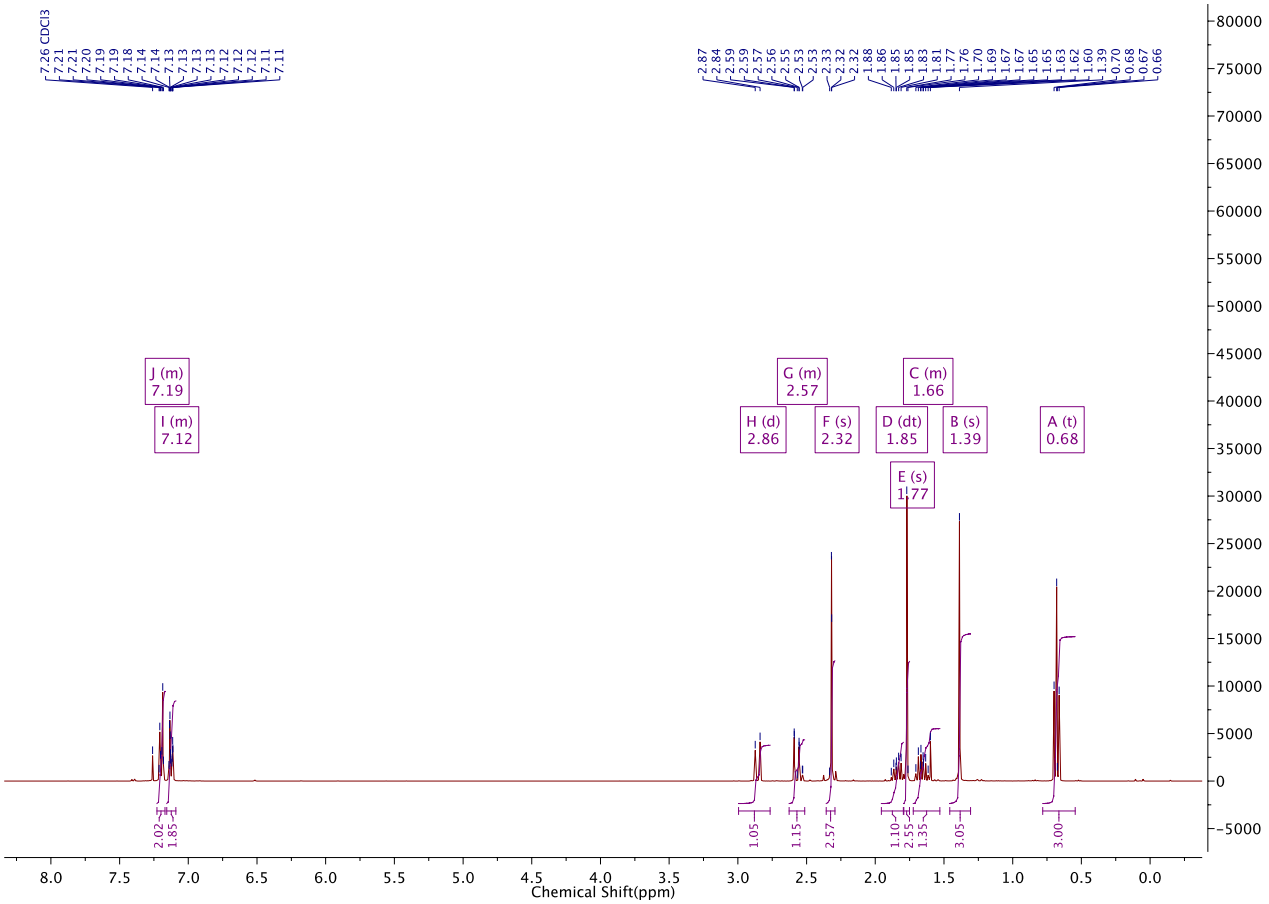
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 208.5, 143.2, 135.3, 129.0(2C), 126.1(2C), 56.1, 40.4, 35.5, 32.1, 23.3, 20.9, 8.5.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2980,2886,1704,1381,1153,955,815

MS (ESI) m/z calc. for $C_{14}H_{20}O^{23}Na$ $[M+Na]^+$: 227.1406, found: 227.1406

$[\alpha]^{20}_{589}$ = +41.0 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.


7.26 CDCl3
7.21
7.21
7.20
7.19
7.19
7.18
7.14
7.14
7.13
7.13
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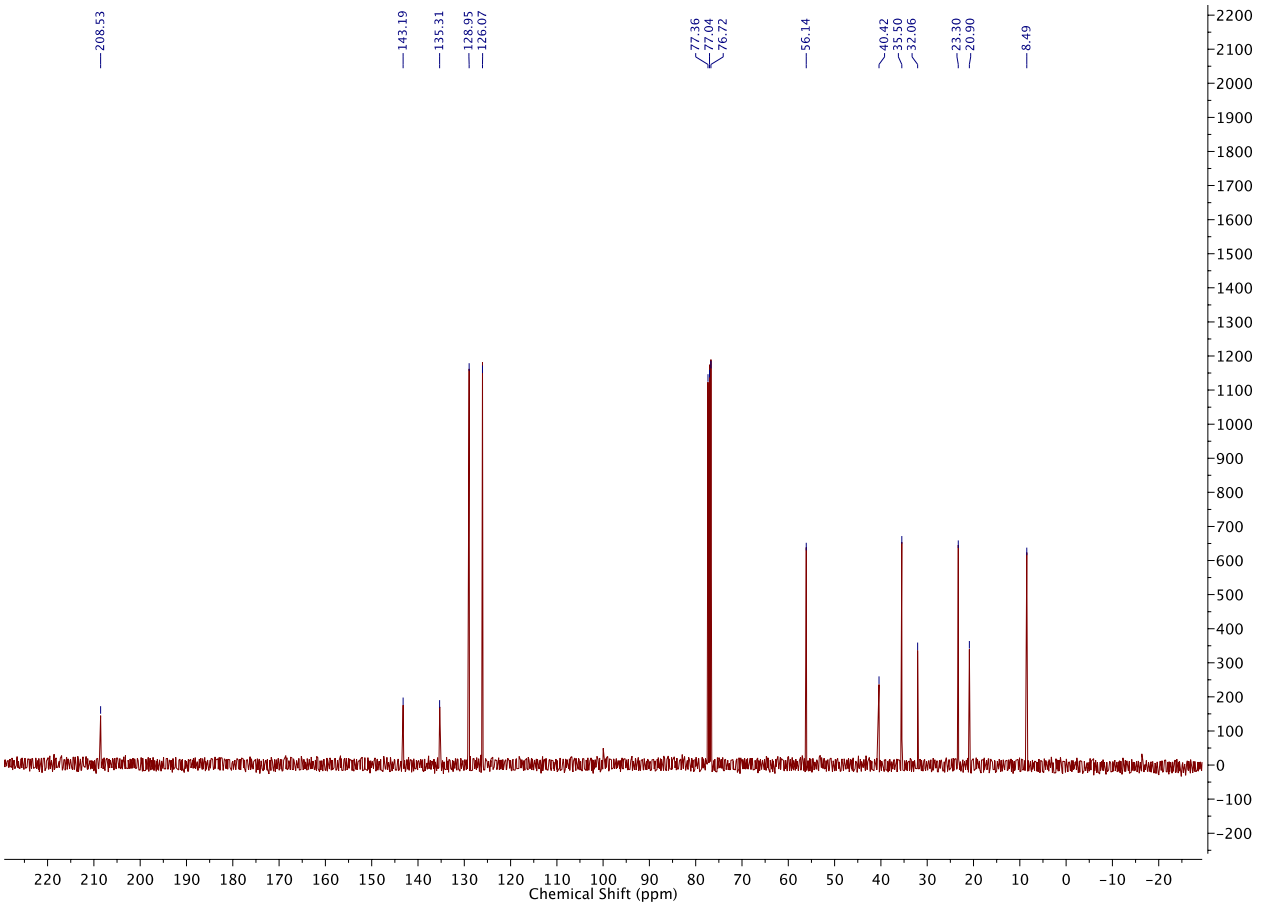
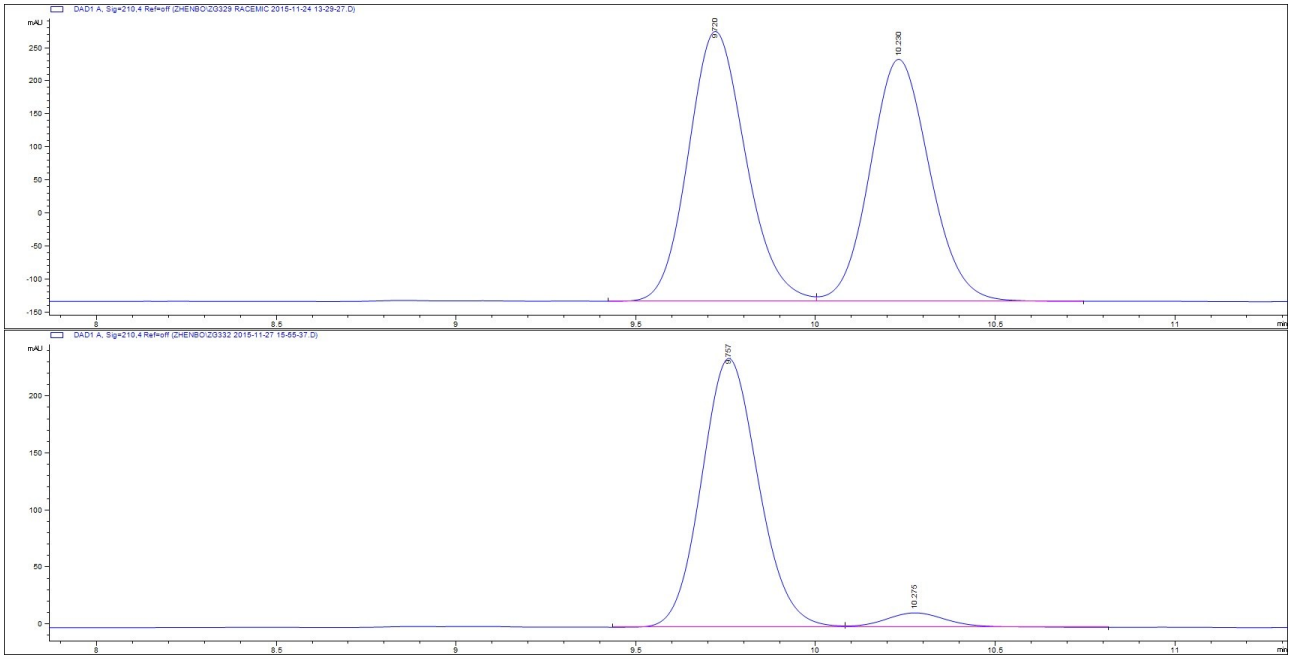
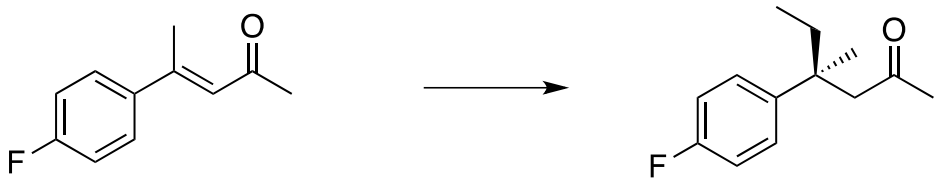
7.13
7.12
7.12
7.12
7.11
7.11
2.87
2.84
2.59
2.59
2.57
2.56
2.55
2.53
2.53
2.33
2.32
2.32
1.88
1.86
1.85
1.85
1.83
1.81
1.77
1.76
1.70
1.69
1.67
1.67
1.65
1.65
1.63
1.62
1.60
1.39
0.70
0.68
0.67
0.66
J (m)
7.19
I (m)
7.12
G (m)
2.57
H (d)
2.86
F (s)
2.32
C (m)
1.66
D (dt)
1.85
B (s)
1.39
E (s)
1.77
A (t)
0.68
2.02
1.85
1.05
1.15
2.57
1.10
2.55
1.35
3.05
3.00
Chemical Shift(ppm)


208.53
143.19
135.31
128.95
126.07
77.36
77.04
76.72
56.14
40.42
35.50
32.06
23.30
20.90
8.49
Chemical Shift (ppm)

HPLC trace



(+)-(*S*)-4-(4-fluorophenyl)-4-methylhexan-2-one (3d)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (36.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml, 1.0 mmol, 5.0

eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (23 mg, 46 % yield, 91% *ee*)

HPLC analysis indicated an enantiomeric excess of 91 % [two Chiralpak® IC in series; flow: 1.0 mL/min; hexane/i-PrOH: 99:1; λ = 210 nm; major enantiomer tR = 17.95 min; minor enantiomer, tR = 18.48 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.31 – 7.16 (m, 2H, Ar-*H*), 7.04 – 6.91 (m, 2H, Ar-*H*), 2.83 (d, *J* = 14.6 Hz, 1H, C*H*$_2$CO), 2.64 – 2.51 (m, 1H, C*H*$_2$CO), 1.85 – 1.71 (m, 4H, COC*H*$_3$, C*H*$_2$CH$_3$), 1.63 (dq, *J* = 13.7 Hz, 7.4 Hz, 1H, C*H*$_2$CH$_3$), 1.37 (s, 3H, C*H*$_3$), 0.64 (t, *J* = 7.4 Hz, 3H, CH$_2$C*H*$_3$),

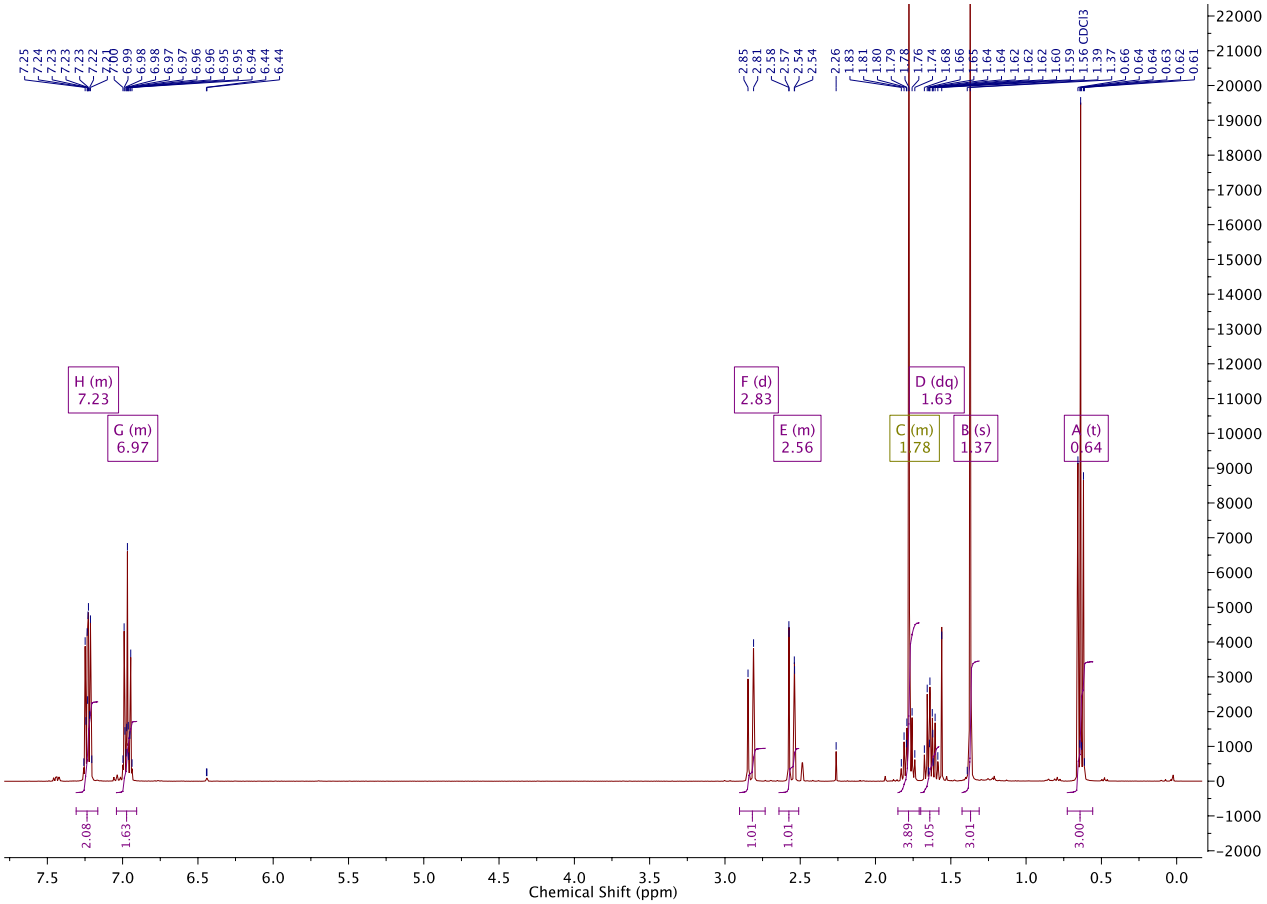
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 207.9, 161.0, 142.0, 127.7 (2C), 114.9 (2C), 56.0, 40.3, 35.7, 32.0, 23.4, 8.4.

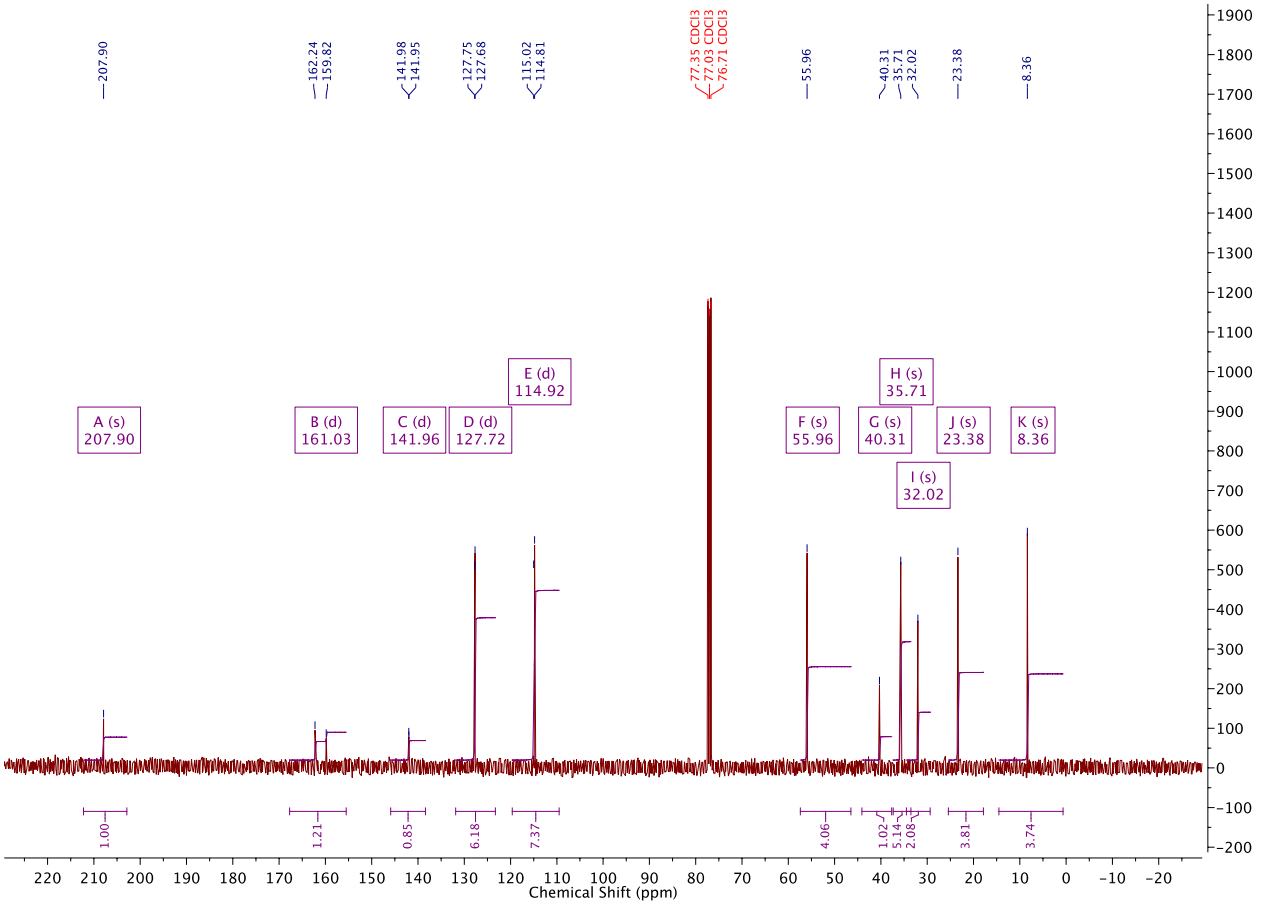
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2981,2885,1510,1381,1165,956,741

MS (ESI) m/z $[M+Na]^+$: 231.1

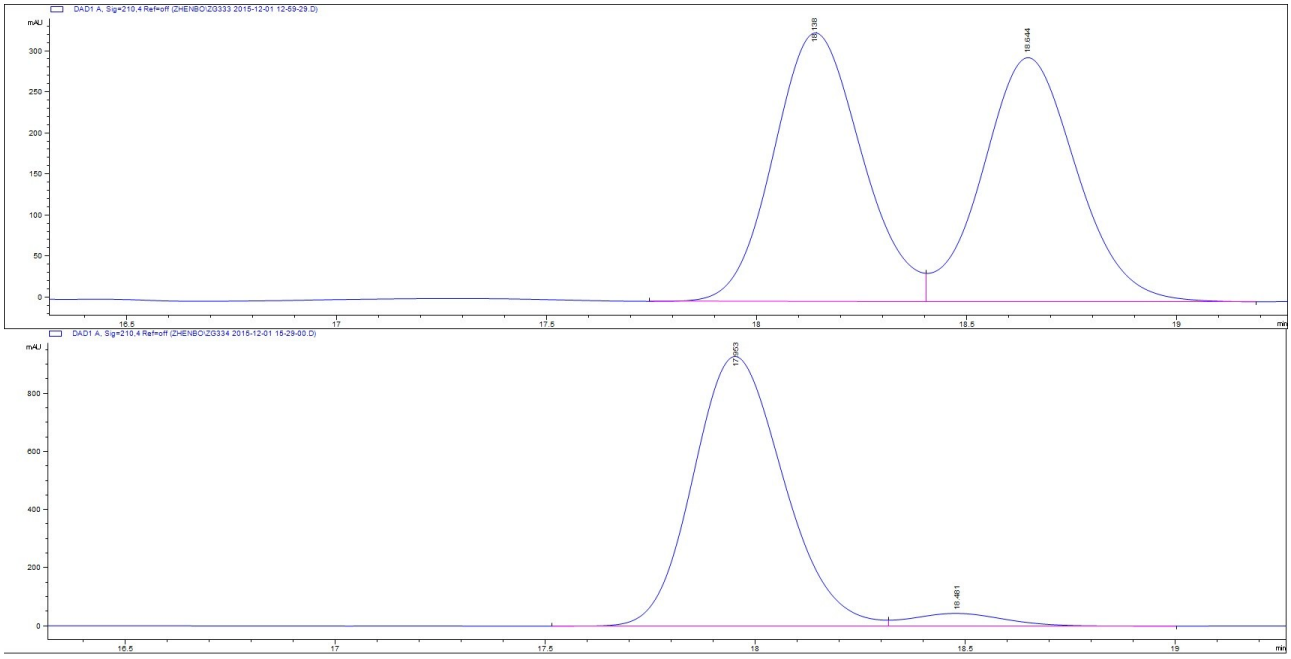
$[\alpha]^{20}_{589}$ = +30.0 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by comparison with literature[6].

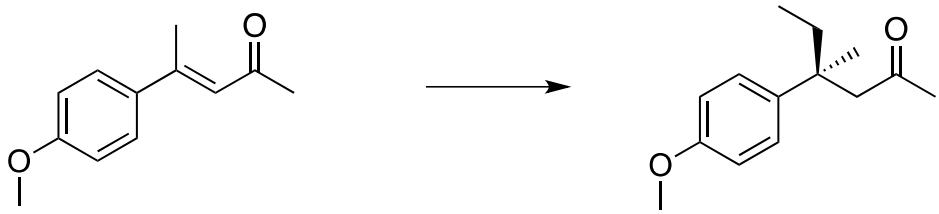

H (m)
7.23
G (m)
6.97
F (d)
2.83
E (m)
2.56
D (dq)
1.63
C (m)
1.78
B (s)
1.37
A (t)
0.64
Chemical Shift (ppm)


A (s)
207.90
B (d)
161.03
C (d)
141.96
D (d)
127.72
E (d)
114.92
F (s)
55.96
G (s)
40.31
H (s)
35.71
I (s)
32.02
J (s)
23.38
K (s)
8.36
Chemical Shift (ppm)

HPLC trace



(+)-(S)-4-(4-methoxyphenyl)-4-methylhexan-2-one (3e)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (38.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml,1.0 mmol, 5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction

was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (15 mg, 39 % yield, 73% *ee*)

HPLC analysis indicated an enantiomeric excess of 73 % [Chiralpak® ID; flow: 1.0 mL/min; hexane/i-PrOH: 95:5; λ = 225 nm; major enantiomer tR = 7.91 min; minor enantiomer, tR = 8.84 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.30 – 7.02 (m, 2H, Ar-*H*), 6.91 – 6.60 (m, 2H, Ar-*H*), 3.73 (s, 3H, OC*H*$_3$), 2.77 (d, *J* = 14.0 Hz, 1H, C*H*$_2$CO), 2.49 (d, *J* = 14.0 Hz, 1H, C*H*$_2$CO), 1.76 (dq, *J* = 14.7 Hz, 7.5 Hz, 1H, C*H*$_2$CH$_3$), 1.69 (s, 3H, COC*H*$_3$), 1.64 – 1.47 (m, 1H, C*H*$_2$CH$_3$), 1.31 (s, 3H, C*H*$_3$), 0.61 (t, *J* = 7.4 Hz, 3H, CH$_2$C*H*$_3$).

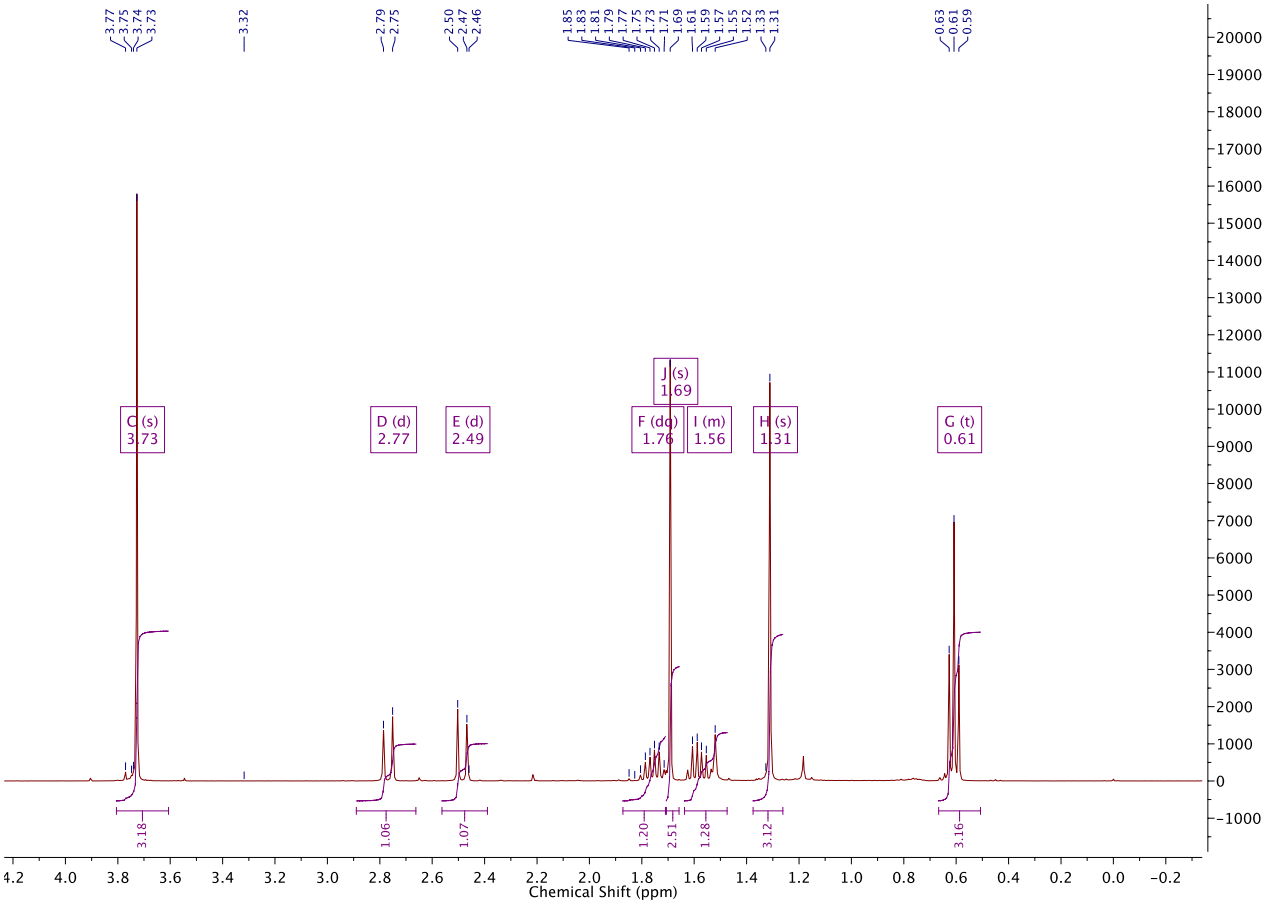
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 208.6, 157.6, 138.2, 127.2(2C), 113.5(2C), 56.3, 55.2, 40.2 35.6, 32.1, 23.3, 8.4.

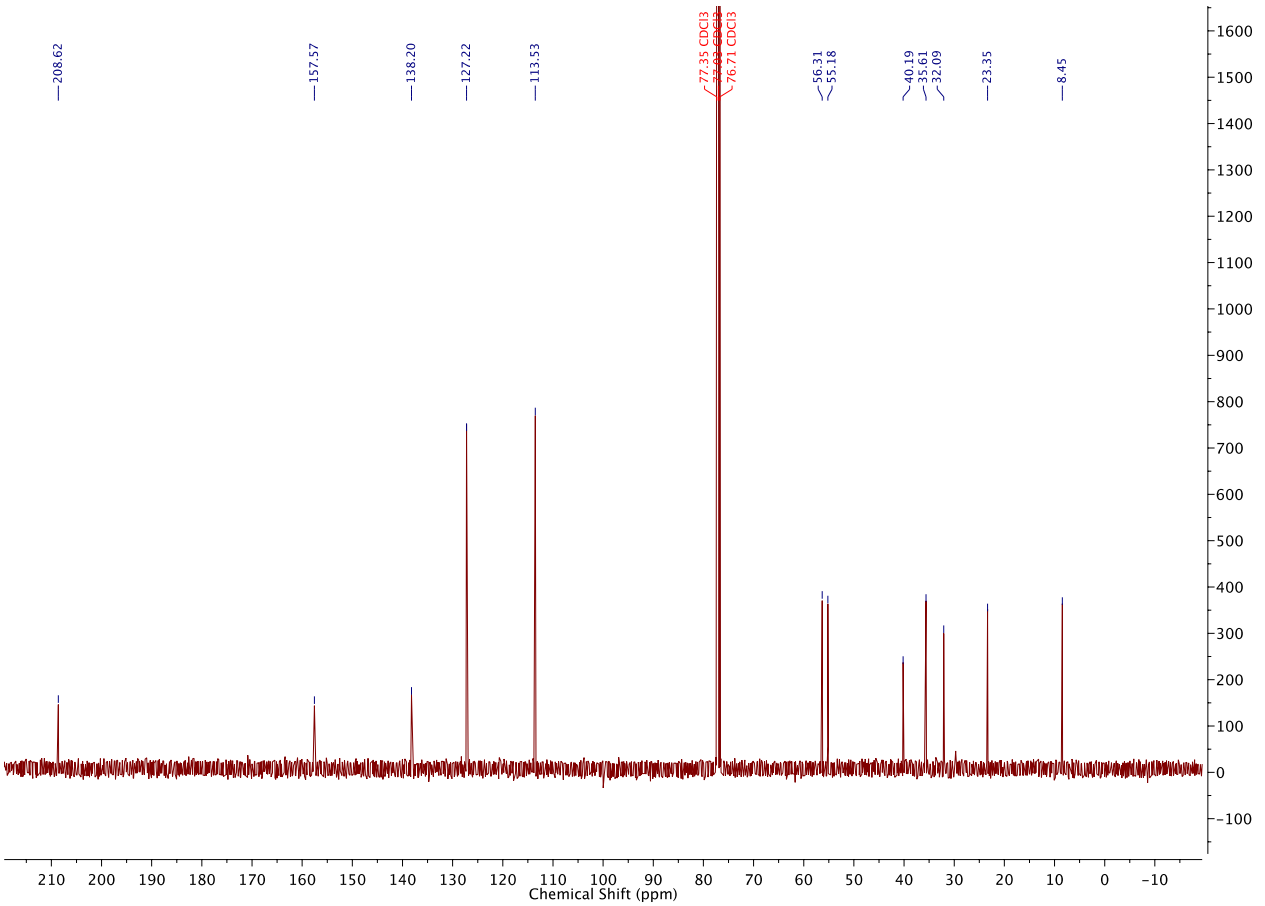
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2981,2888,1514,1382,1153,955,829

MS (ESI) m/z $[M+Na]^+$: 243.1(100)

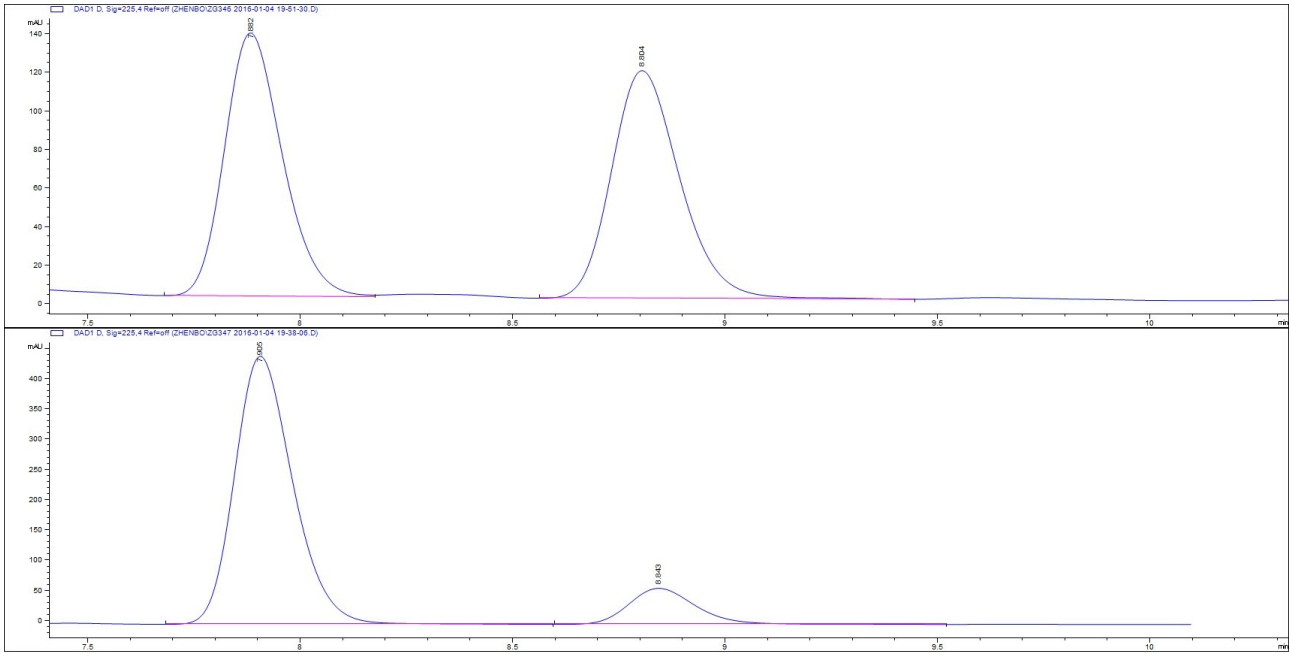
$[\alpha]^{20}_{589}$ = +35.5 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by comparison with literature[6].

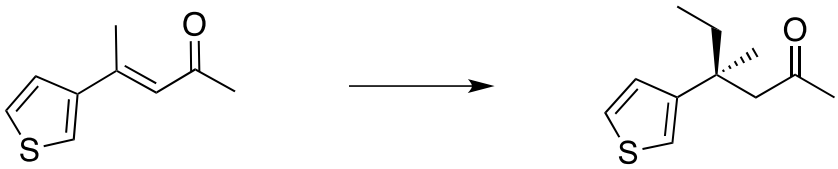

C (s)
3.73
D (d)
2.77
E (d)
2.49
J (s)
1.69
F (dq)
1.76
I (m)
1.56
H (s)
1.31
G (t)
0.61
Chemical Shift (ppm)


208.62
157.57
138.20
127.22
113.53
77.35 CDCl3
76.71 CDCl3
56.31
55.18
40.19
35.61
32.09
23.35
8.45
Chemical Shift (ppm)

HPLC trace



(+)-(*S*)-4-methyl-4-(thiophen-3-yl)hexan-2-one (3f)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (34.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml, 1.0 mmol, 5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was

partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (16 mg, 41 % yield, 85% *ee*)

HPLC analysis indicated an enantiomeric excess of 85 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99:1; λ = 210 nm; major enantiomer tR = 6.65 min; minor enantiomer, tR = 7.15 min].

^{1}H NMR (Chloroform-*d*, 400 MHz) δ_H/ppm 7.26 – 7.08 (1H, m, Ar-*H*), 6.92 (1H, dd, *J* = 5.0 Hz, 1.4 Hz, Ar-*H*), 6.83 (1H, dd, *J* = 2.9 Hz, 1.4 Hz, Ar-*H*), 2.66 (1H, d, *J* = 13.6 Hz, C*H*$_2$CO), 2.45 (1H, d, *J* = 13.7 Hz , C*H*$_2$CO), 1.67 (3H, s, CO C*H*$_3$), 1.65 – 1.39 (2H, m, C*H*$_2$), 1.26 (3H, s, C*H*$_3$), 0.60 (3H, t, *J* = 7.4 Hz, CH_2 C*H*$_3$)

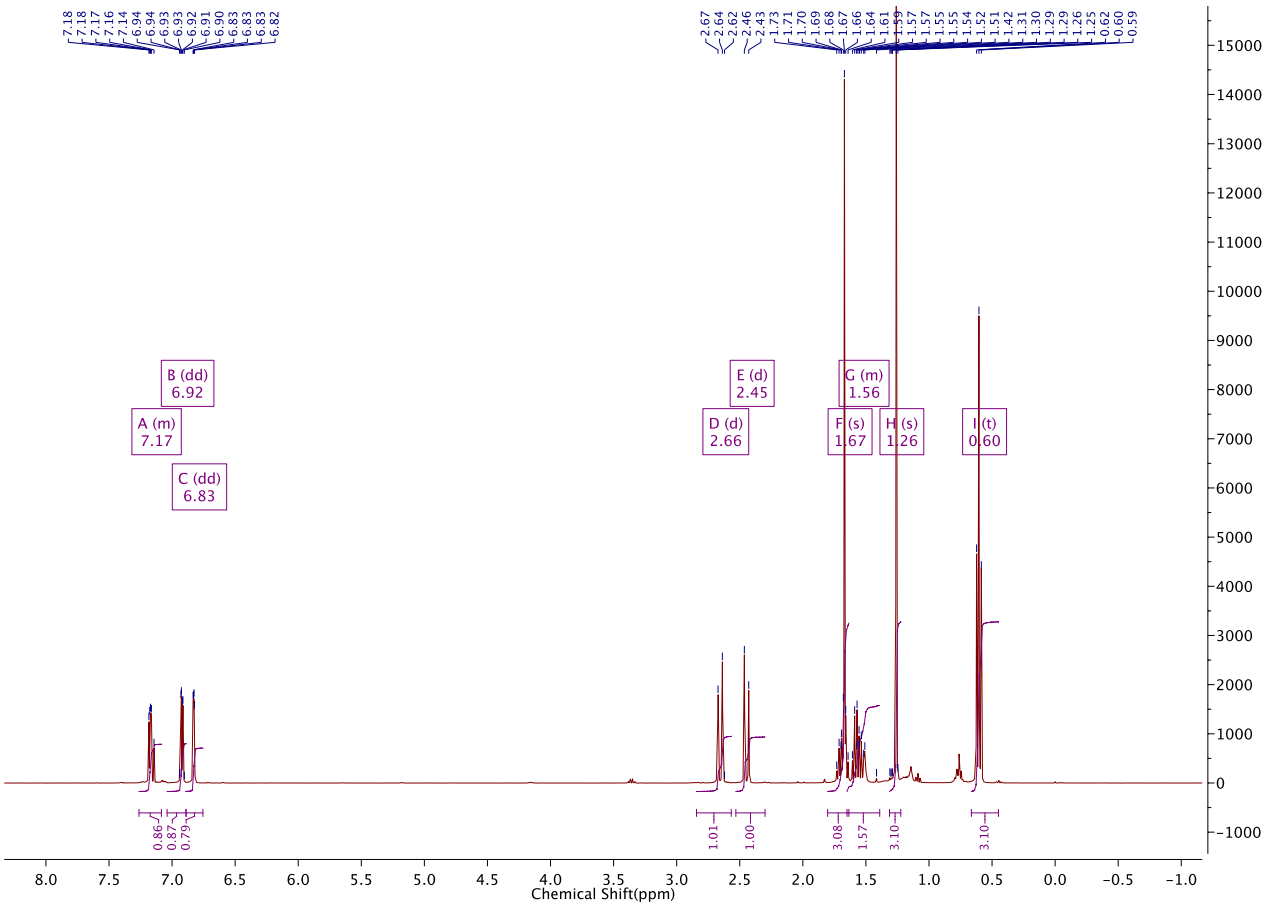
^{13}C NMR (Chloroform-*d*, 101 MHz) δ_C/ppm 208.2, 148.3, 126.0, 125.4, 119.7, 55.3, 39.4, 35.0, 31.7, 23.8, 8.4

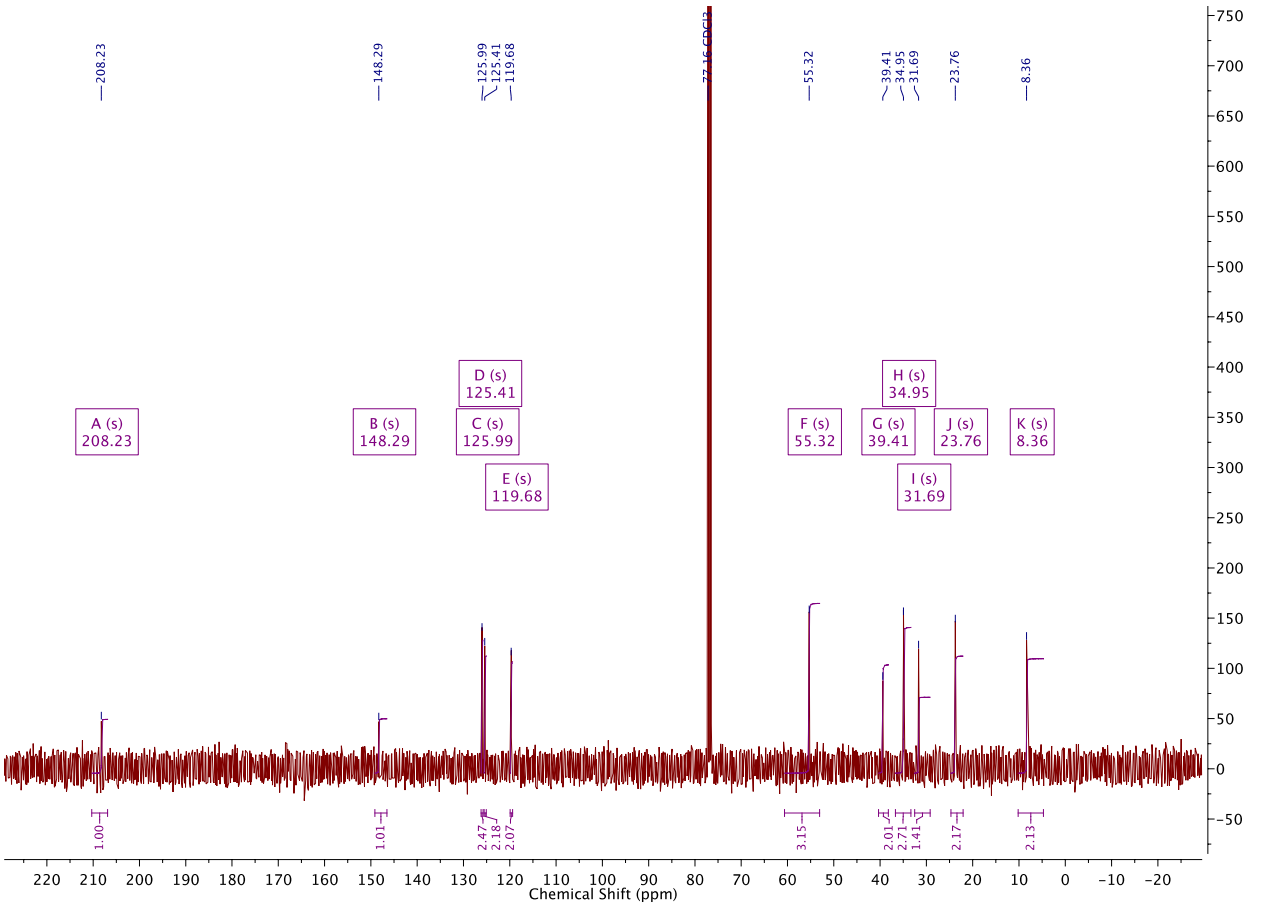
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2981,2888,1703, 1461,1153,955,

MS (ESI) m/z $[M+Na]^+$: 219.1(100)

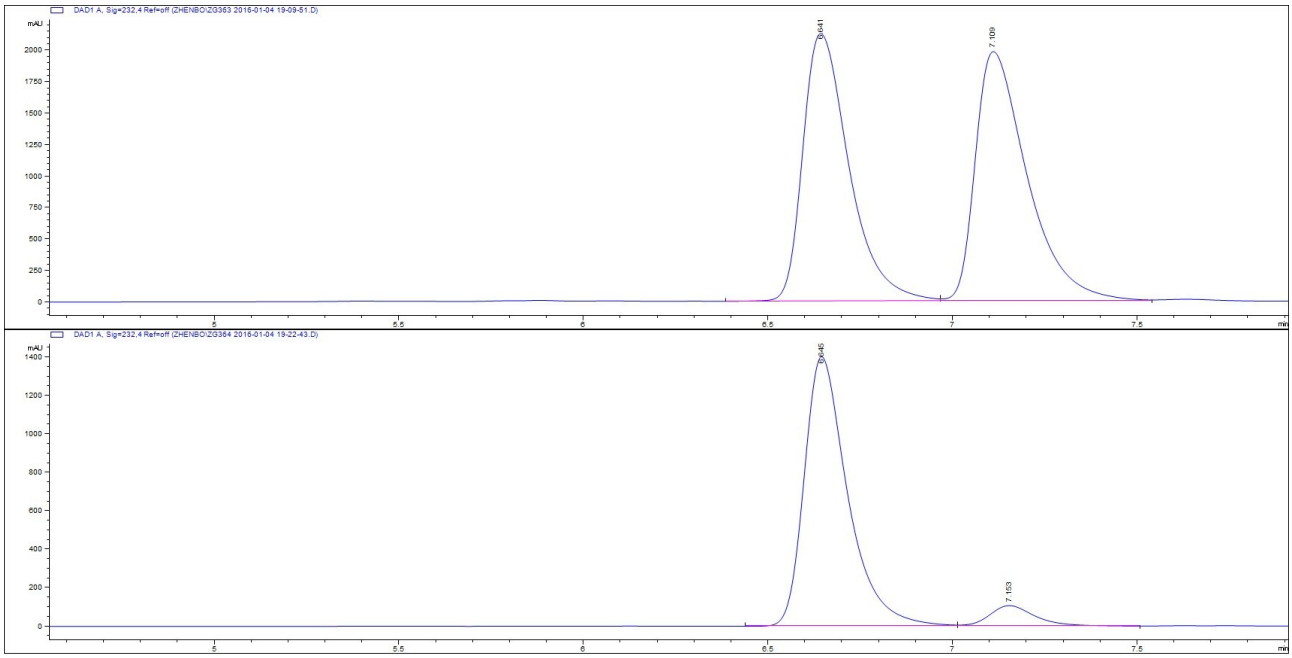
$[\alpha]^{20}_{589}$ = +45.8 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.

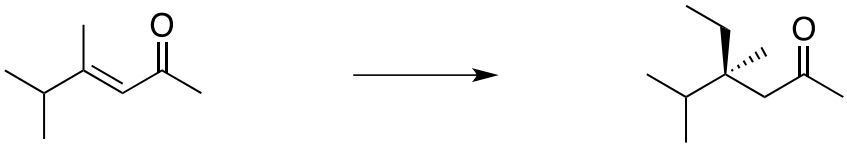

B (dd)
6.92
A (m)
7.17
C (dd)
6.83
E (d)
2.45
D (d)
2.66
G (m)
1.56
F (s)
1.67
H (s)
1.26
I (t)
0.60
Chemical Shift(ppm)


A (s)
208.23
B (s)
148.29
D (s)
125.41
C (s)
125.99
E (s)
119.68
F (s)
55.32
H (s)
34.95
G (s)
39.41
I (s)
31.69
J (s)
23.76
K (s)
8.36
Chemical Shift (ppm)

HPLC trace



(-)-(*S*)-4-ethyl-4,5-dimethylhexan-2-one (3g)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (26.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml, 1.0 mmol, 5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted

with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (15 mg, 48 % yield, 95% *ee*)

GC analysis indicated an enantiomeric excess of 92 % Macherey-Nagel Chiral GC Columns ® HYDRODEX β-3P; flow, major enantiomer tR = 43.14 min; minor enantiomer, tR = 44.00 min.

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 2.30 (d, *J* = 1.5 Hz, 2H, CH_2 $COCH_3$), 2.09 (s, 3H, $COCH_3$), 1.71 (p, *J* = 6.9 Hz, 1H, C*H*), 1.39 (qd, *J* = 7.5 Hz, 1.2 Hz, 2H, CH_2), 0.85 (s, 3H, CH_3), 0.82 – 0.69 (m, 9H, $CHCH_3$, CH_2CH_3).

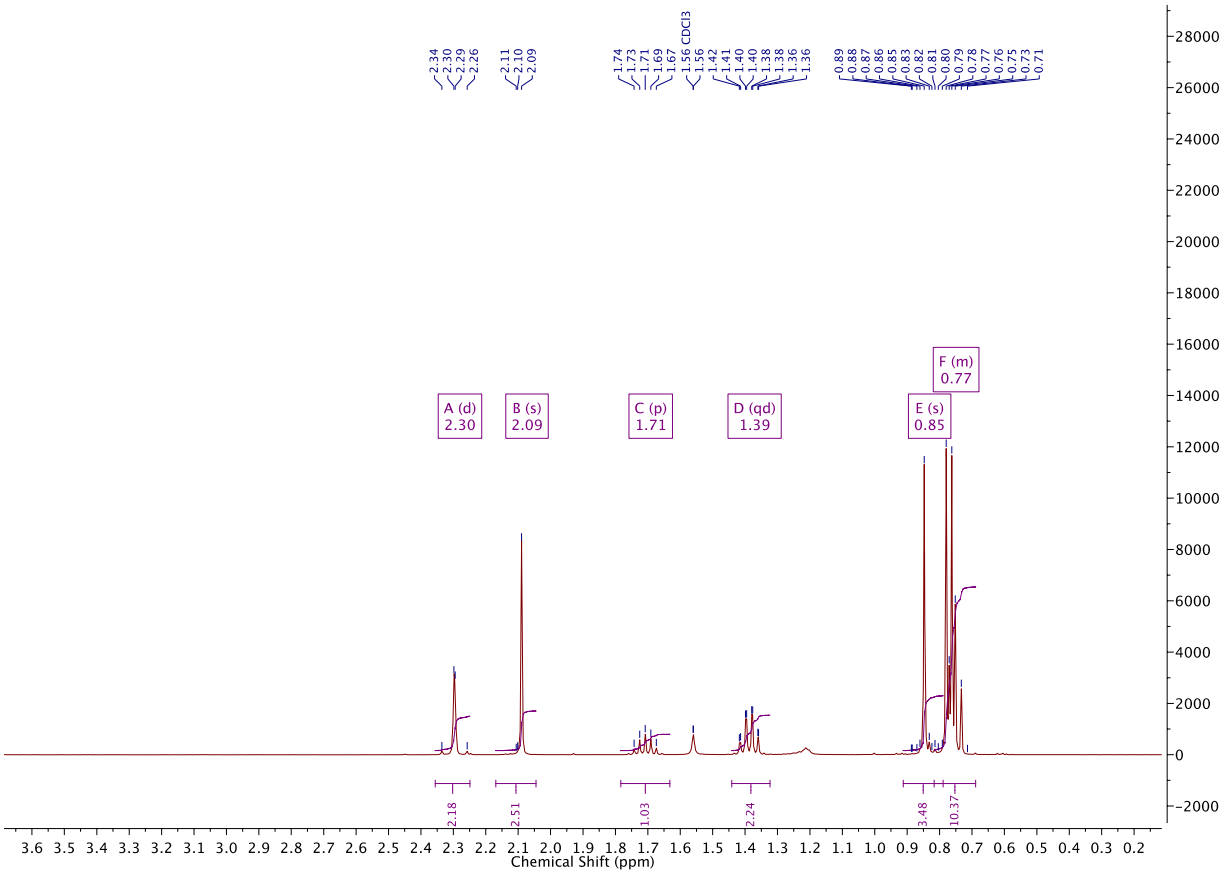
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 209.8, 48.7, 38.6, 33.3, 32.7, 29.1, 21.0, 17.3, 17.0, 8.1.

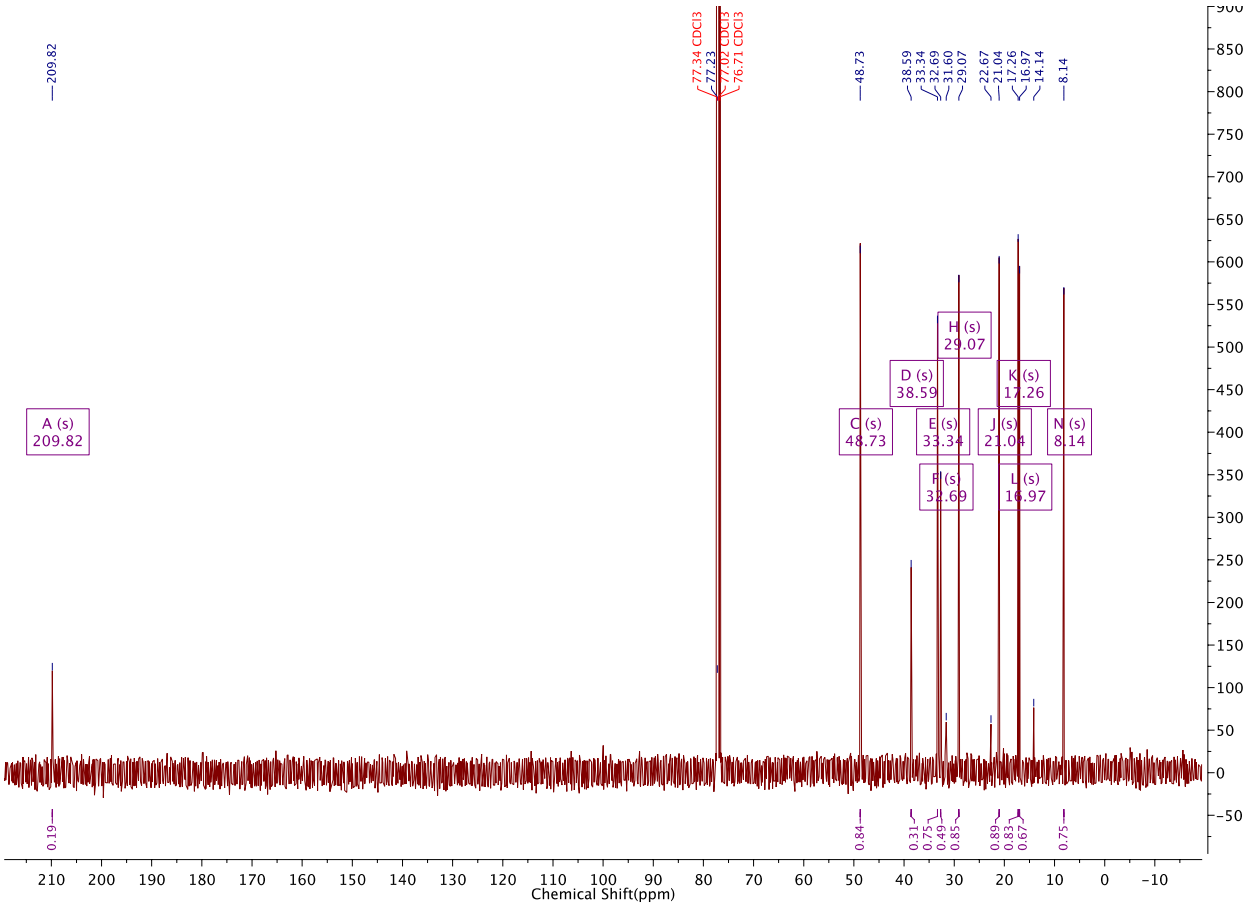
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2981,2889,1510,1382,1251,1152, 1073,954, 816

MS (ESI) m/z $[M+Na]^+$:, found: 179.1 (100)

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

Absolute configuration assigned by analogy to compound 3b.


A (d)
2.30
B (s)
2.09
C (p)
1.71
D (qd)
1.39
E (s)
0.85
F (m)
0.77
Chemical Shift (ppm)


A (s)
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C (s)
38.59
D (s)
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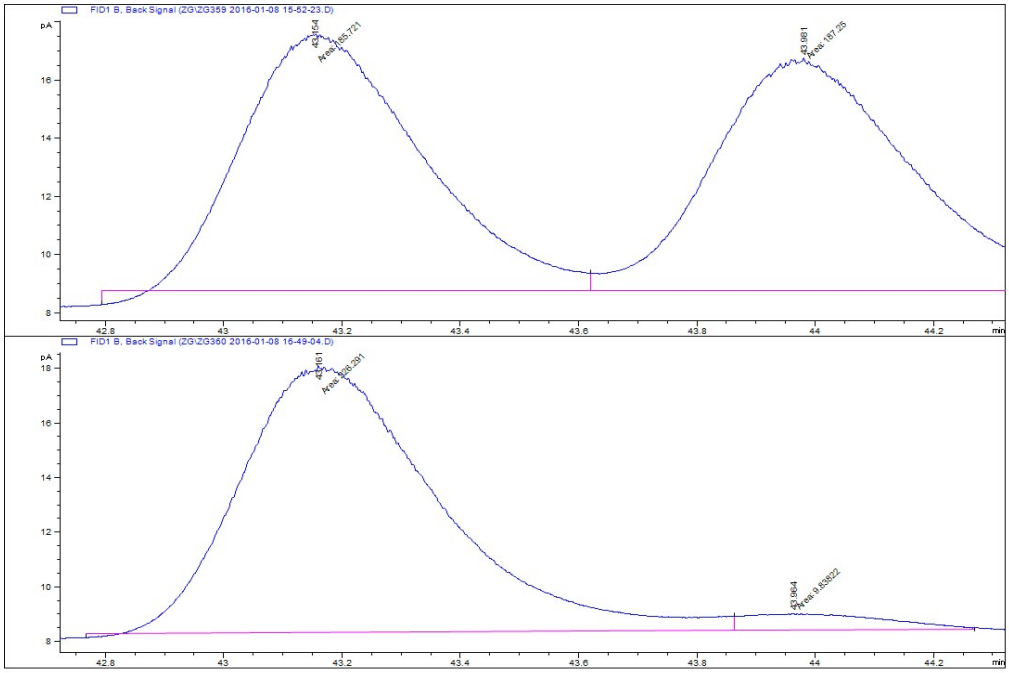
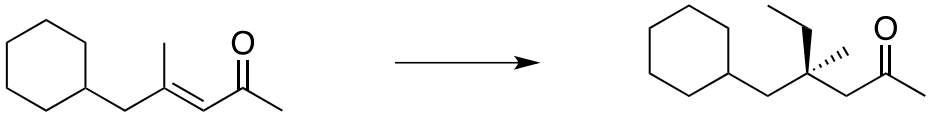
E (s)
32.69
F (s)
31.60
G (s)
29.07
H (s)
22.67
I (s)
21.04
J (s)
17.26
K (s)
16.97
L (s)
14.14
M (s)
8.14
Chemical Shift(ppm)

GC trace



(+)-(R)-4-(cyclohexylmethyl)-4-methylhexan-2-one (3h)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (36.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml,1.0 mmol, 5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction

was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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, 71 % yield, 98% *ee*)

HPLC analysis indicated an enantiomeric excess of 98 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99:1; λ = 222 nm; major enantiomer tR = 5.49 min; minor enantiomer, tR = 6.42 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 2.32 (s, 2H, COCH_2), 2.11 (s, 3H, COCH_3), 1.74 – 1.5- (m, 5H, CH_2, CH), 1.49 – 1.29 (m, 2H, CH_2), 1.32 – 1.01 (m, 6H, CH_2 C), 0.94 (m, 5H, CH_2 ,CH_3), 0.79 (t, *J* = 7.5 Hz, 3H, CH_2CH_3).

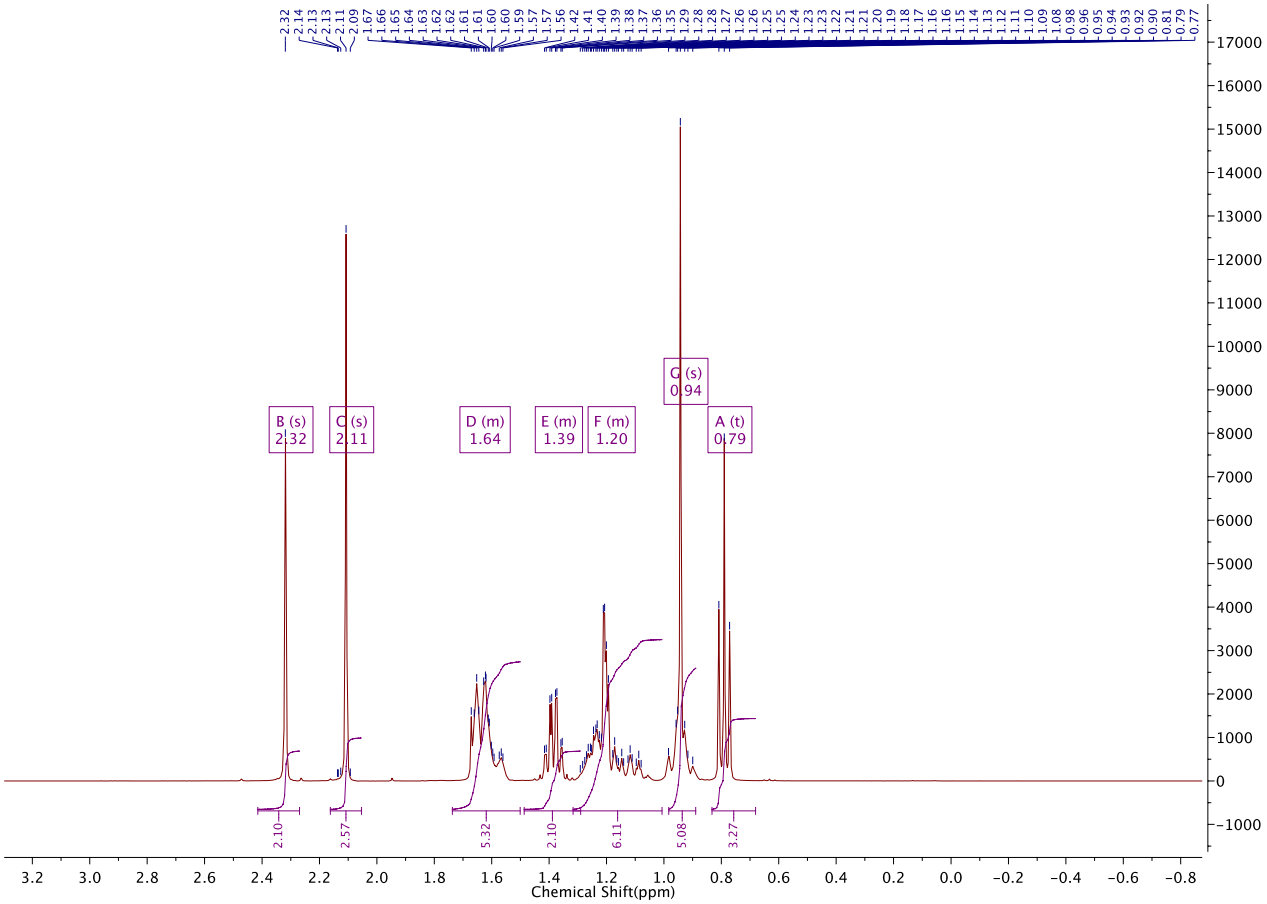
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 209.2, 51.8, 46.6, 36.9, 35.9(2C), 33.4, 32.6, 32.0, 26.7(2c), 26.3, 24.9, 8.4.

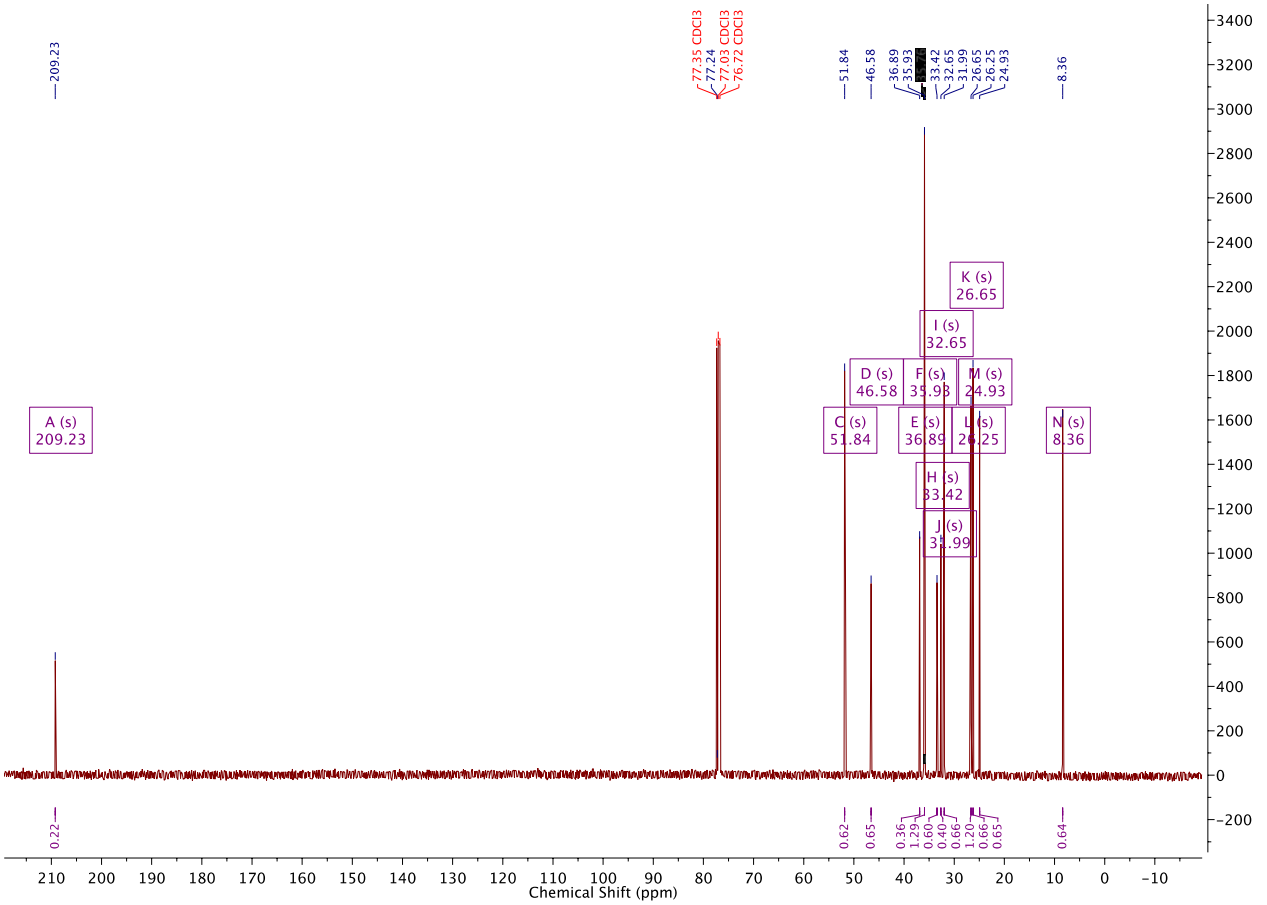
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2981,2889,1715,,1381,1152,1072,954

MS (ESI) m/z calc. for $C_{14}H_{27}O$ $[M+H]^+$: 211.2056, found: 211.2059

$[\alpha]^{20}_{589}$ = +2.2 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.


B (s)
2.32
C (s)
2.11
D (m)
1.64
E (m)
1.39
F (m)
1.20
G (s)
0.94
A (t)
0.79
Chemical Shift(ppm)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C (s)
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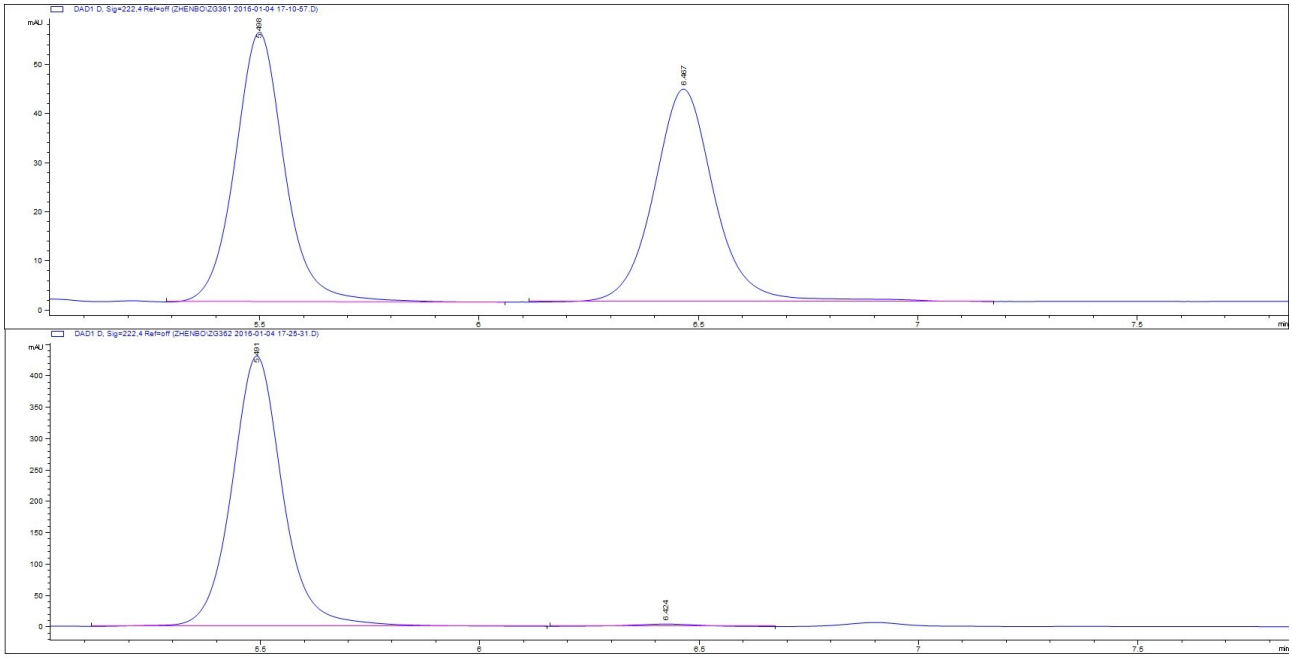
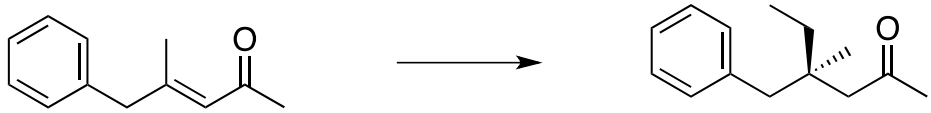
E (s)
36.89
F (s)
35.93
H (s)
33.42
I (s)
32.65
J (s)
31.99
K (s)
26.65
L (s)
26.25
M (s)
24.93
N (s)
8.36
77.35 CDCl3
77.24
77.03 CDCl3
76.72 CDCl3
Chemical Shift (ppm)

HPLC trace



(-)-(*R*)-4-benzyl-4-methylhexan-2-one (3i)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (35.0 mg,0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml,1.0 mmol, 5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3

x10 mL). The combined organic materials were dried with 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.(25mg , 61% yield, 93%*ee*)

HPLC analysis indicated an enantiomeric excess of 93 % [Chiralpak® ID; flow: 0.8 mL/min; hexane/i-PrOH: 99:1; λ = 210 nm; major enantiomer tR = 7.60 min; minor enantiomer, tR = 8.25 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.28 – 7.14 (m, 3H, Ar-*H*), 7.12 – 7.04 (m, 2H, Ar-*H*), 2.74 (d, *J* = 13.1 Hz, 1H, PhC*H*$_2$), 2.63 (d, *J* = 13.1 Hz, 1H, PhC*H*$_2$), 2.23 (d, *J* = 1.9 Hz, 2H, C*H*$_2$CO), 2.08 (s, 3H COC*H*$_3$), 1.52 – 1.27 (m, 2H, C*H*$_2$CH$_3$), 0.92 (s, 3H, C*H*$_3$), 0.86 (t, *J* = 7.5 Hz, 3H, CH$_2$C*H*$_3$).

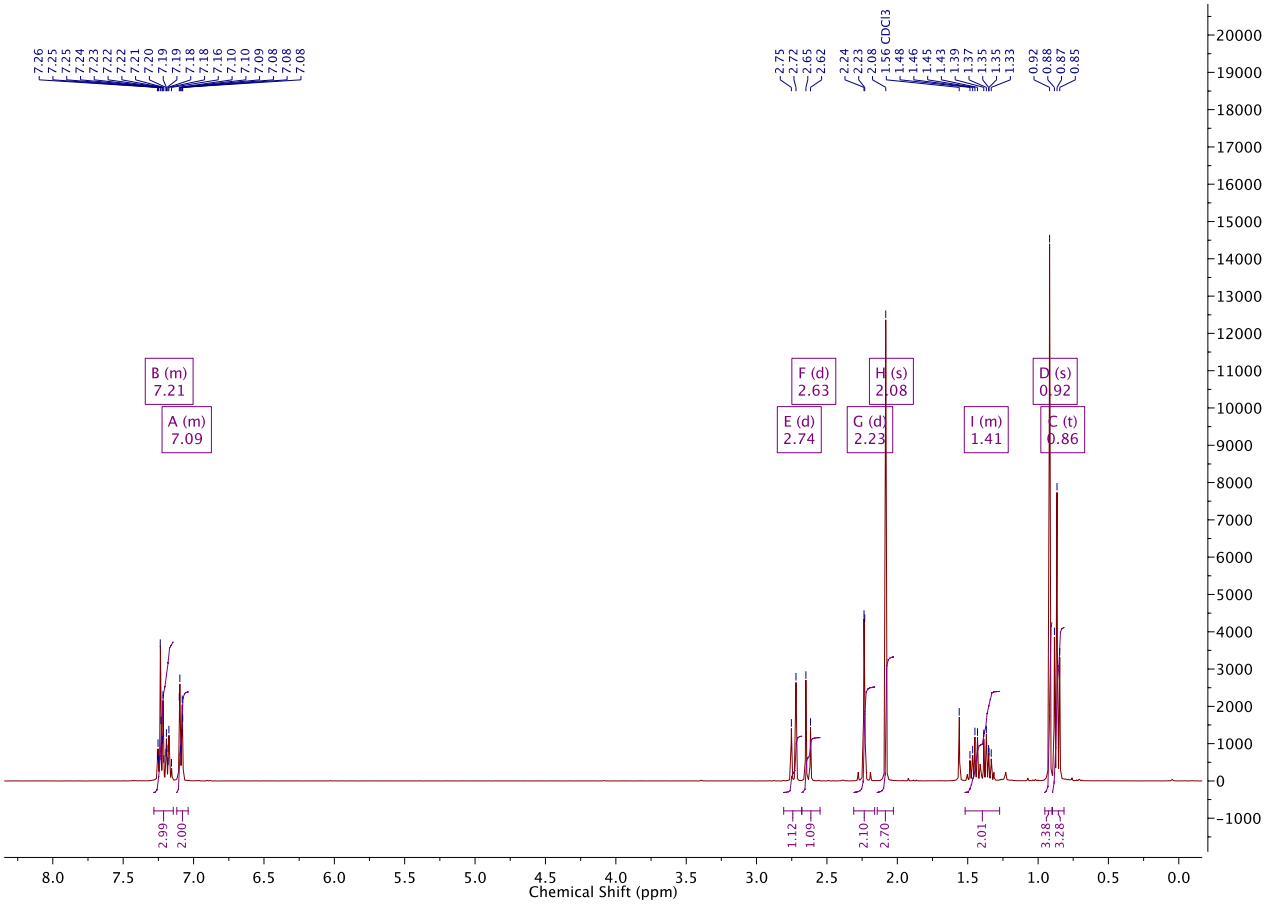
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 209.0, 138.8, 130.6, 127.8(2C), 126.0(2C), 50.1, 44.7, 37.2, 32.4, 31.5, 24.3, 8.4.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3661, 2970,1714,1360,1153,703

MS (ESI) m/z calc. for $C_{14}H_{20}O^{23}Na$ $[M+H]^+$: 227.1406, found: 227.1407

$[\alpha]^{20}_{589}$ = -7.3 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by comparison with literature[6].


B (m)
7.21
A (m)
7.09
F (d)
2.63
E (d)
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H (s)
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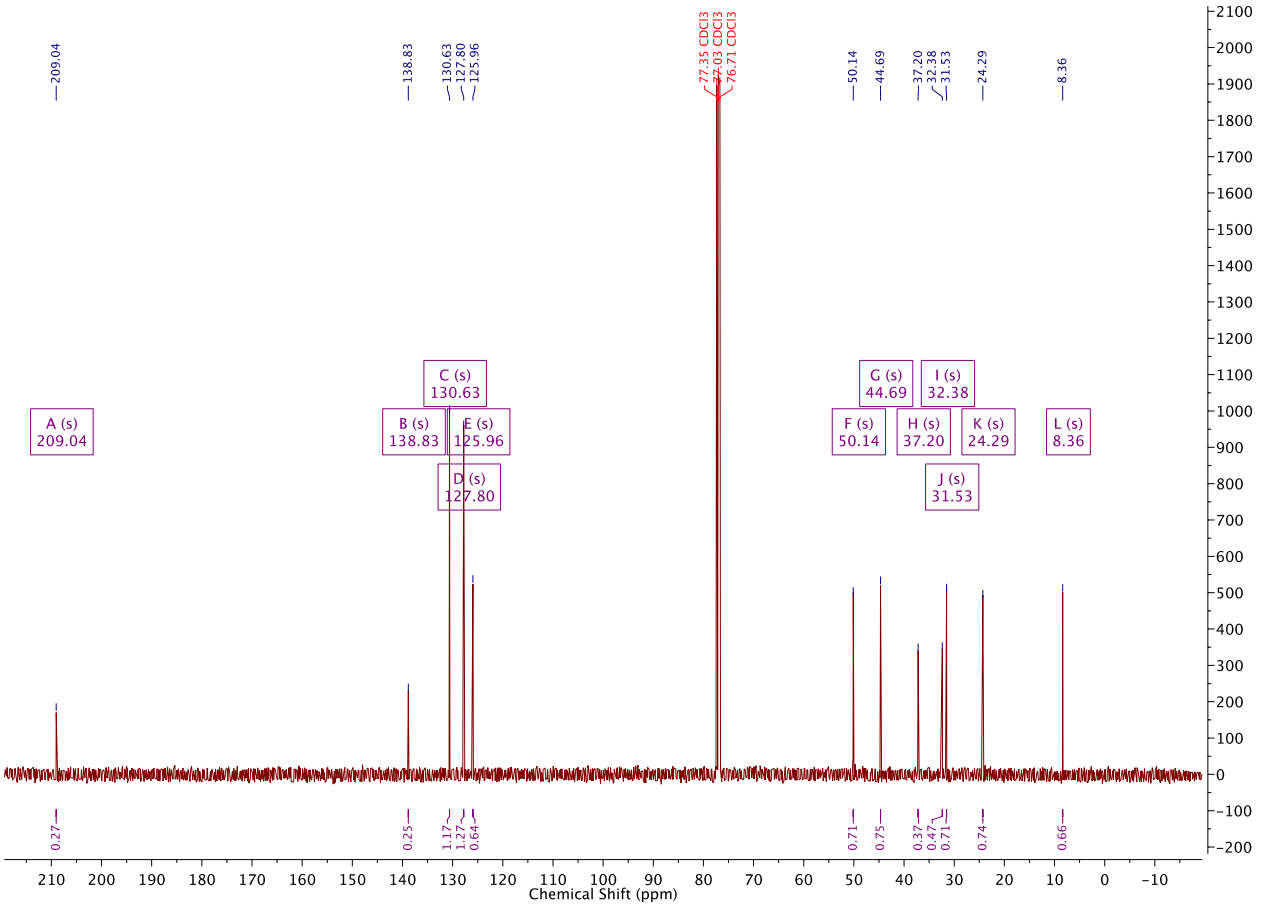
G (d)
2.23
I (m)
1.41
D (s)
0.92
C (t)
0.86
Chemical Shift (ppm)


A (s)
209.04
C (s)
130.63
B (s)
138.83
E (s)
125.96
D (s)
127.80
G (s)
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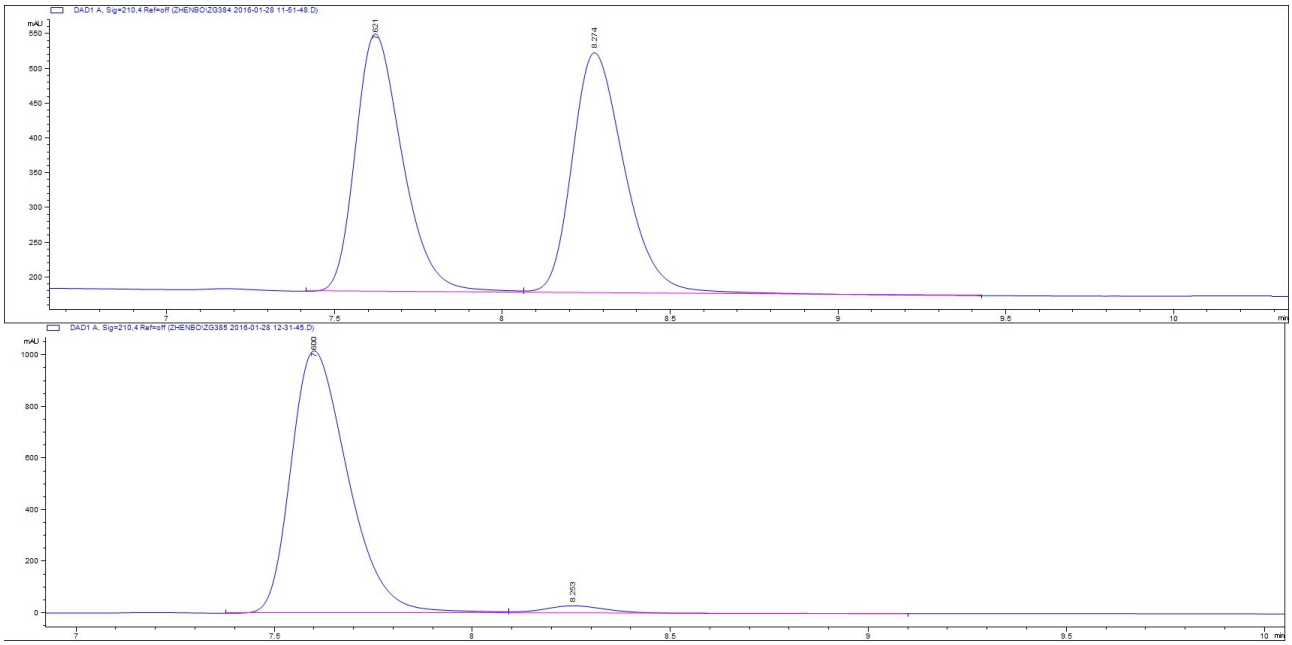
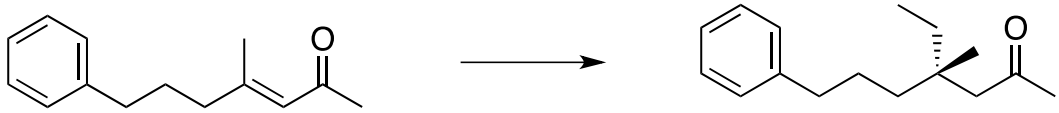
I (s)
32.38
F (s)
50.14
H (s)
37.20
K (s)
24.29
J (s)
31.53
L (s)
8.36
Chemical Shift (ppm)

HPLC trace



(-)-(*S*)-4-ethyl-4-methyl-7-phenylheptan-2-one (3j)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the R-phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (40.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml,1.0 mmol, 5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted

with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (33 mg, 71 % yield, 93% *ee*)

HPLC analysis indicated an enantiomeric excess of 93 % [two Chiralpak® ID in series; flow: 0.8 mL/min; hexane/i-PrOH: 99:1; λ = 210 nm; minor enantiomer tR = 14.17 min; major enantiomer, tR = 14.74 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.30 – 7.15 (m, 2H, Ar-*H*), 7.15 – 7.06 (m, 3H, Ar-*H*), 2.56 – 2.45 (m, 2H, PhCH_2), 2.23 (s, 2H, CH_2COCH$_3$), 2.03 (s, 3H, COCH_3), 1.52 – 1.37 (m, 2H, CH_2), 1.36 – 1.21 (m, 4H, CH_2), 0.86 (s, 3H, CH_3), 0.70 (t, *J* = 7.5 Hz, 3H, CH$_2$CH_3).

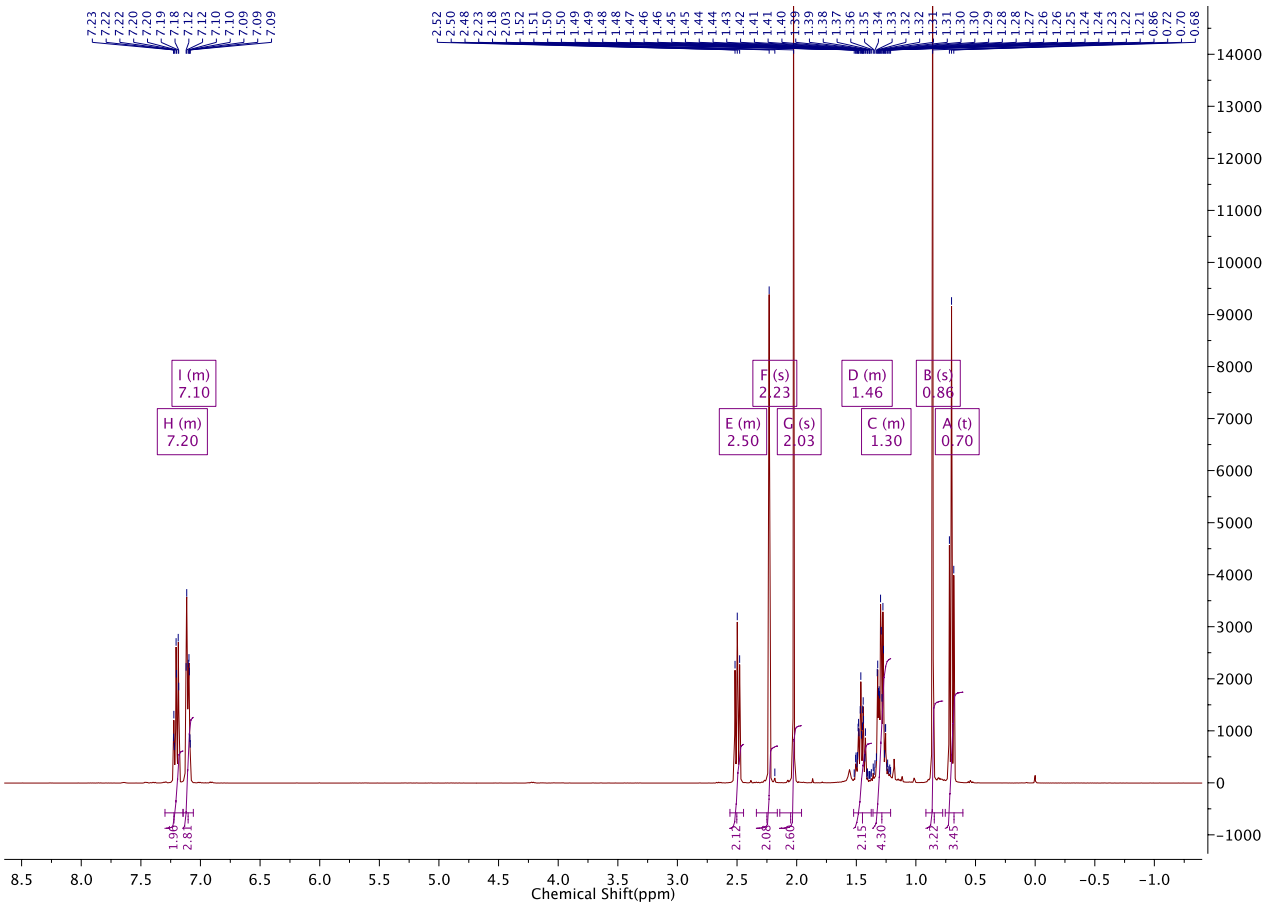
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 209.2, 142.7, 128.4(2C), 128.3(2C), 125.7, 51.4, 38.6, 36.7, 36.1, 32.6, 31.7, 25.9, 24.6, 8.1.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2980,2889,1714,1381,1152,955,699

MS (ESI) m/z calc. for $C_{16}H_{24}O^{23}Na$ $[M+H]^+$ 255.1719, found: 255.1719

$[\alpha]^{20}_{589}$ = -3.1° (c 1.3, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.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H (m)
7.20
F (s)
2.23
E (m)
2.50
G (s)
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D (m)
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C (m)
1.30
B (s)
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A (t)
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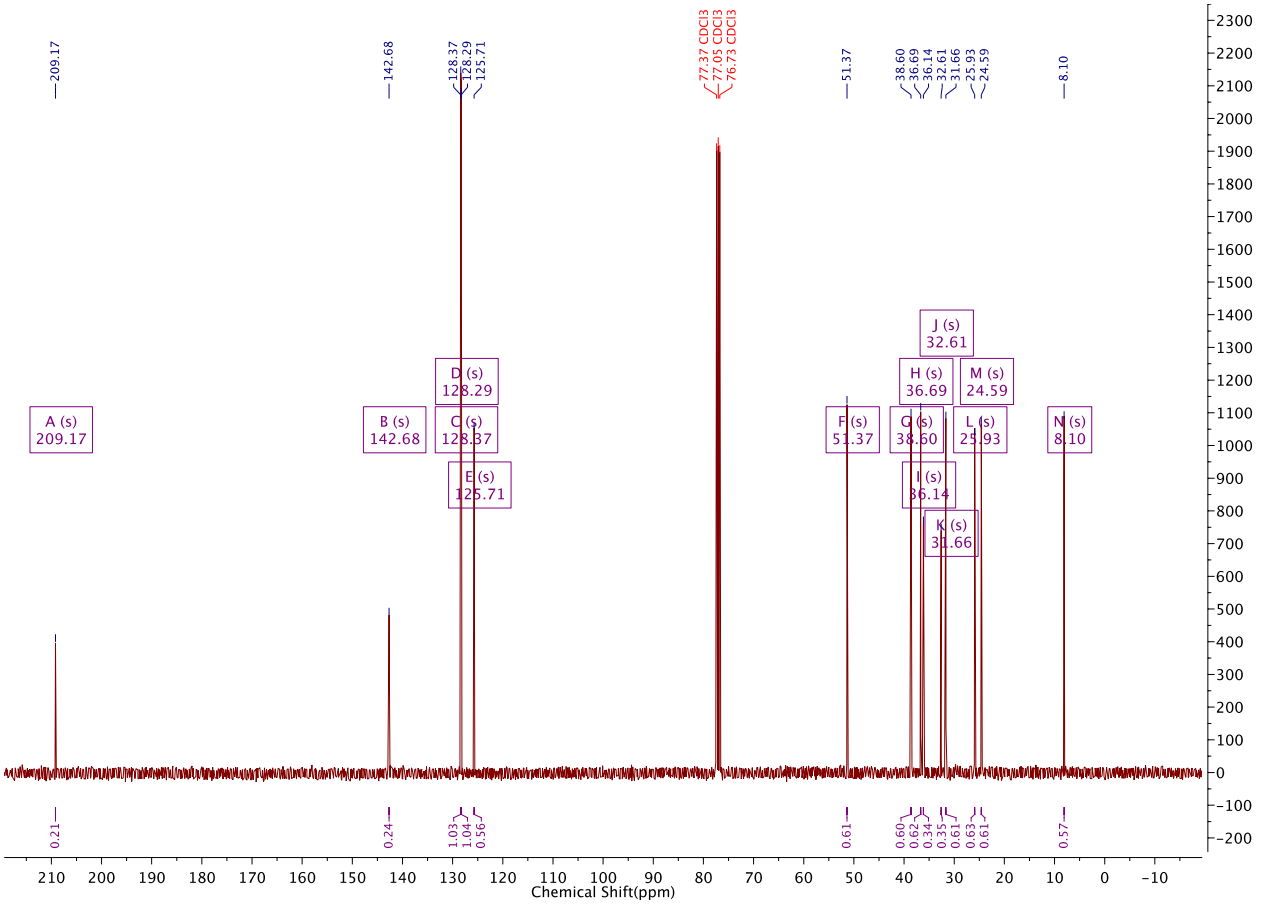
Chemical Shift(ppm)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B (s)
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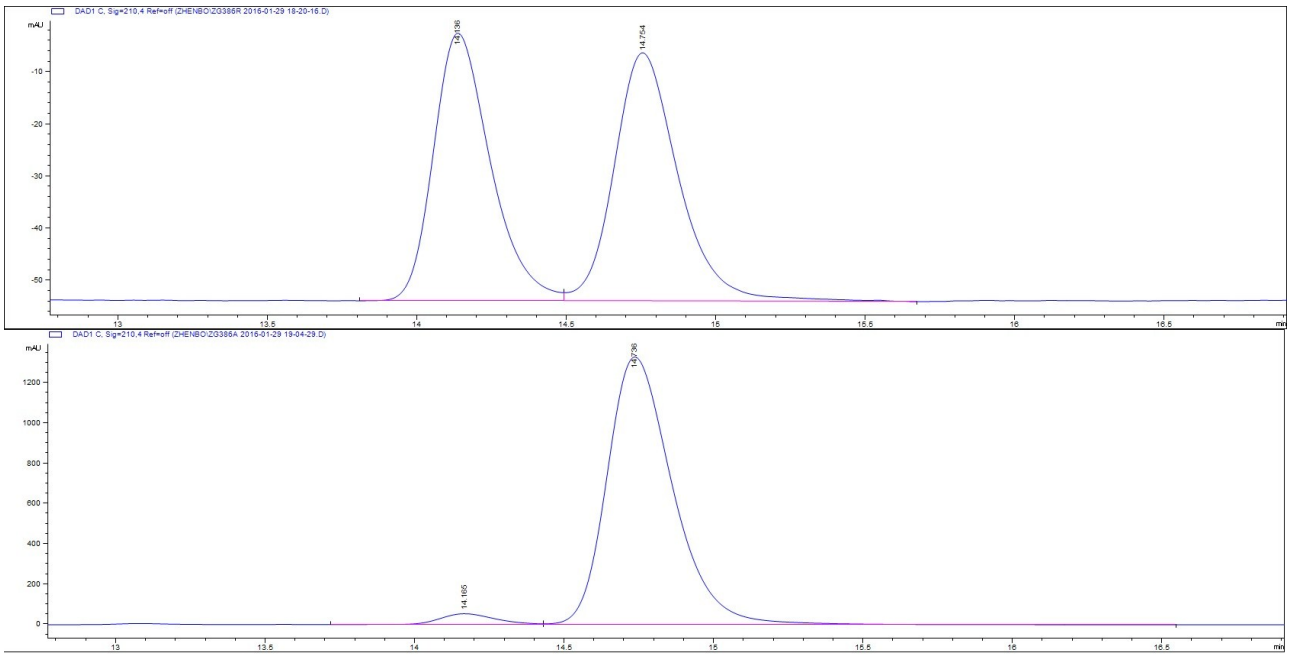
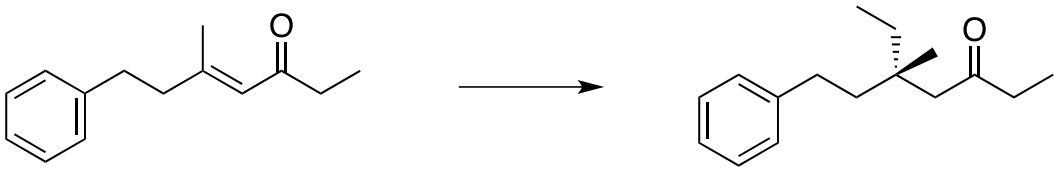
D (s)
128.29
C (s)
128.37
E (s)
125.71
F (s)
51.37
J (s)
32.61
H (s)
36.69
M (s)
24.59
G (s)
38.60
L (s)
25.93
I (s)
36.14
K (s)
31.66
N (s)
8.10
Chemical Shift(ppm)

HPLC trace



(-)-(*S*)-5-ethyl-5-methyl-7-phenylheptan-3-one (3k)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the R-phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (41.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml,1.0 mmol, 5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was

partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (37 mg, 80 % yield, 96% *ee*)

HPLC analysis indicated an enantiomeric excess of 96 % [Chiralpak® AYH; flow: 0.4 mL/min; hexane/i-PrOH: 99.2:0.8; λ = 210 nm; minor enantiomer tR = 15.66 min; major enantiomer, tR = 16.39 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.20 (dd, *J* = 7.9 Hz, 6.8 Hz, 2H, Ar-*H*), 7.16 – 7.06 (m, 3H, Ar-*H*), 2.61 – 2.39 (m, 2H, PhCH_2), 2.34 (q, *J* = 7.3 Hz, 2H, COCH_2CH$_3$), 2.29 (s, 2H, COCH_2), 1.65 – 1.50 (m, 2H, PhCH$_2$ CH_2), 1.44 – 1.30 (m, 2H, CH_2CH$_3$), 1.02 – 0.86 (m, 6H,CH_3), 0.78 (t, *J* = 7.5 Hz, 3H, CH$_2$CH_3).

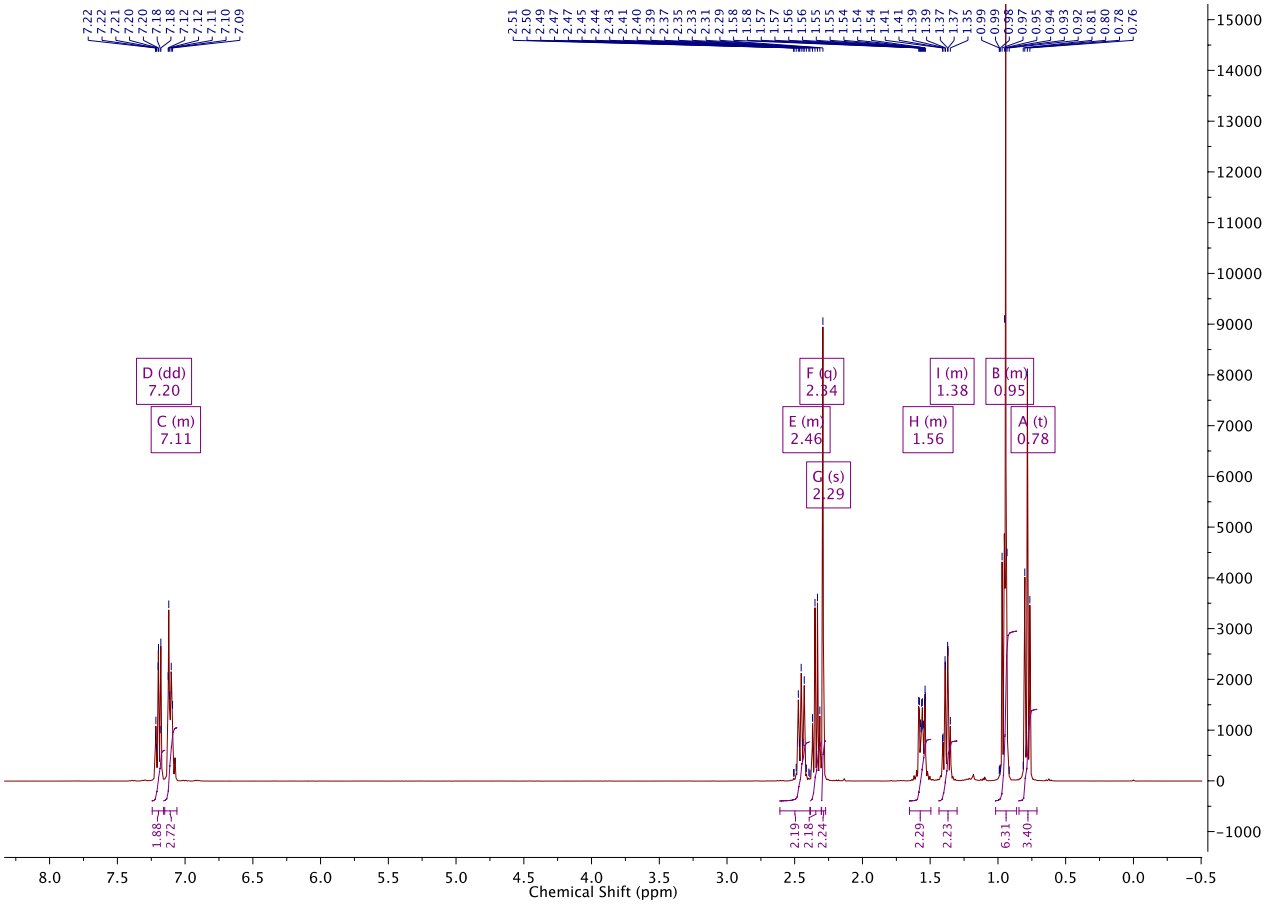
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 211.4, 143.1, 128.4(2C), 128.4(2C), 125.6, 50.0, 41.2, 38.4, 36.4, 31.7, 30.4, 24.7, 8.2, 7.8.

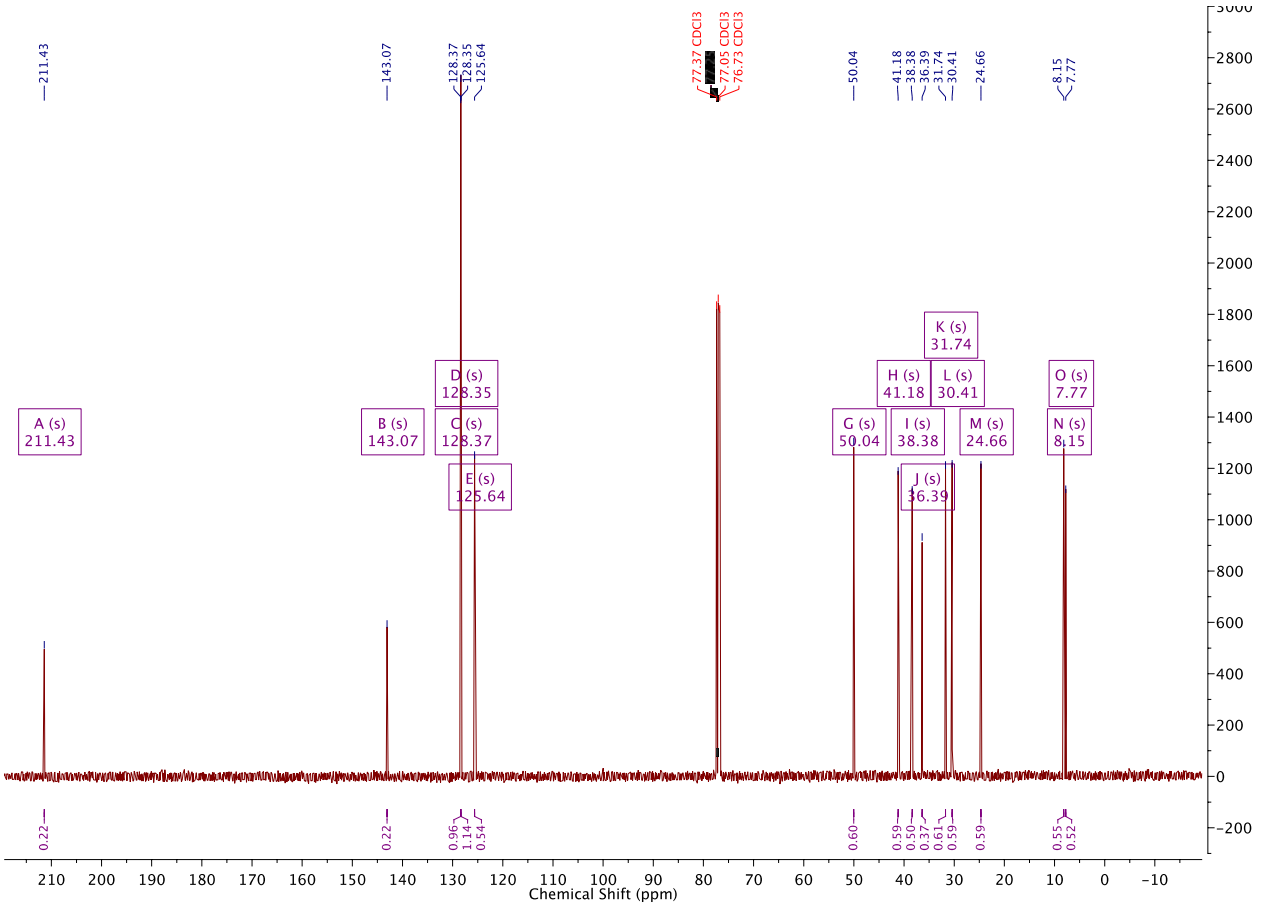
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3026, 2937,1711,1455,1107,1030,698

MS (ESI) m/z calc. for $C_{16}H_{24}O^{23}Na$ $[M+H]^+$: 255.1719, found: 255.1719

$[\alpha]^{20}_{589}$ = -7.9 ° (c 1.4, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.


D (dd)
7.20
C (m)
7.11
F (q)
2.34
E (m)
2.46
G (s)
2.29
I (m)
1.38
H (m)
1.56
B (m)
0.95
A (t)
0.78
Chemical Shift (ppm)


A (s)
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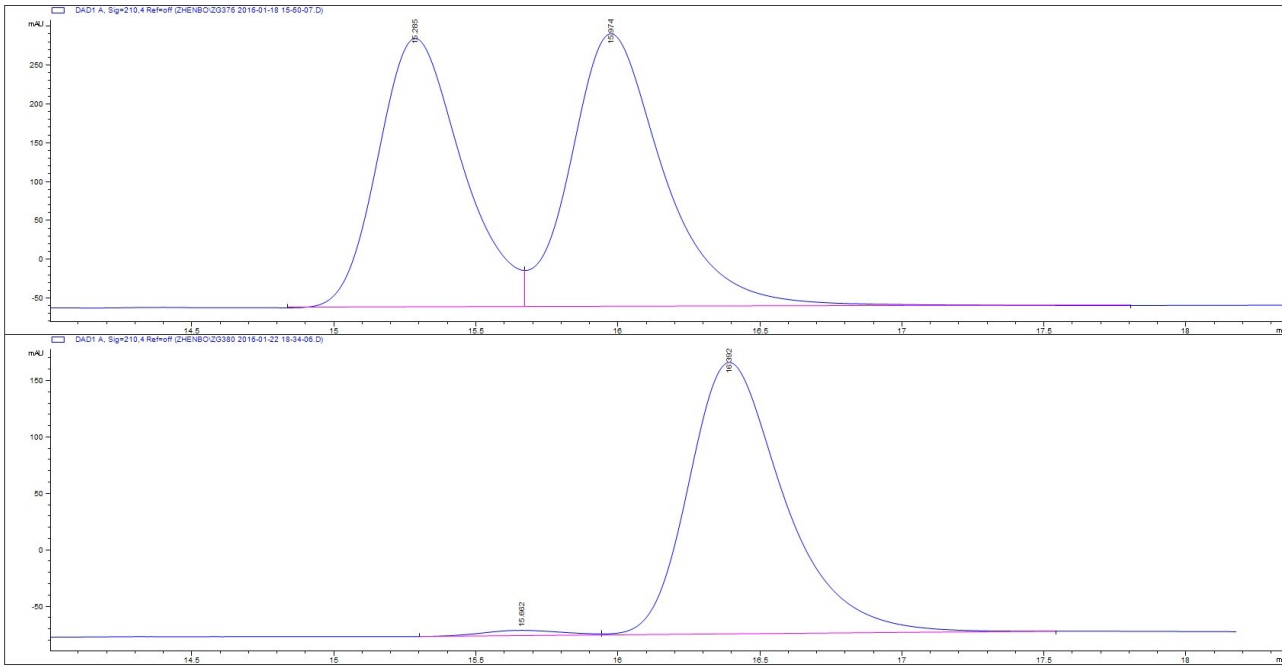
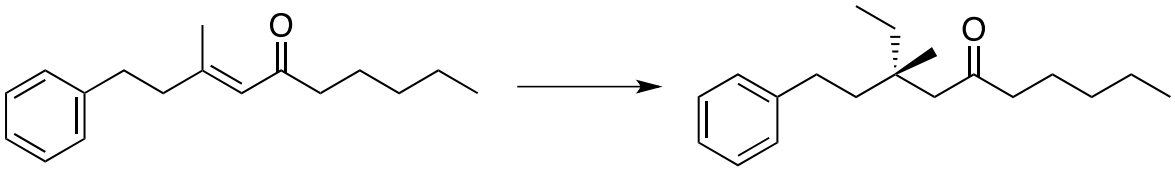
B (s)
143.07
D (s)
128.35
C (s)
128.37
E (s)
125.64
K (s)
31.74
H (s)
41.18
L (s)
30.41
G (s)
50.04
I (s)
38.38
J (s)
36.39
M (s)
24.66
O (s)
7.77
N (s)
8.15
Chemical Shift (ppm)

HPLC trace



(-)-(*S*)-3-ethyl-3-methyl-1-phenyldecan-5-one (3l)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the R-phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 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 (5.6 mg, 0.022 mmol, 0.11 eq.) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) was added. A balloon filled with ethylene was used to purge the flask with ethylene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under an ethylene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (50.0 mg, 0.2 mmol, 1.0 eq.) and then TMSCl (0.127 ml,1.0 mmol, 5.0 eq.) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was

partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (30 mg, 54 % yield, 96% *ee*)

HPLC analysis indicated an enantiomeric excess of 91 % [two Chiralpak® IA in series; flow: 0.8 mL/min; hexane/i-PrOH: 99.4:0.6; λ = 210 nm; minor enantiomer, tR = 12.72 min, major enantiomer tR = 13.33 min;].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.20 (td, *J* = 7.3 Hz, 1.7, 2H, Ar-*H*), 7.11 (dt, *J* = 8.1 Hz, 1.9, 3H, Ar-*H*), 2.51 – 2.39 (m, 2H,), 2.32 (d, *J*=7.3, 2H, PhCH_2), 2.29 (s, 2H, CH_2CO), 1.61 – 1.53 (m, 2H, PhCH_2CH_2), 1.49 (dd, *J* = 12.9 Hz, 5.5 Hz, 2H, CH_2), 1.44 – 1.33 (m, 2H, CH_2), 1.21 (dddd, *J* = 15.8 Hz, 14.1 Hz, 7.3 Hz, 4.2 Hz, 4H, CH_2), 0.94 (s, 3H, CH_3), 0.80 (dt, *J*=13.2, 7.2, 6H, CH_2CH_3, $CH_2CH_2CH_3$).

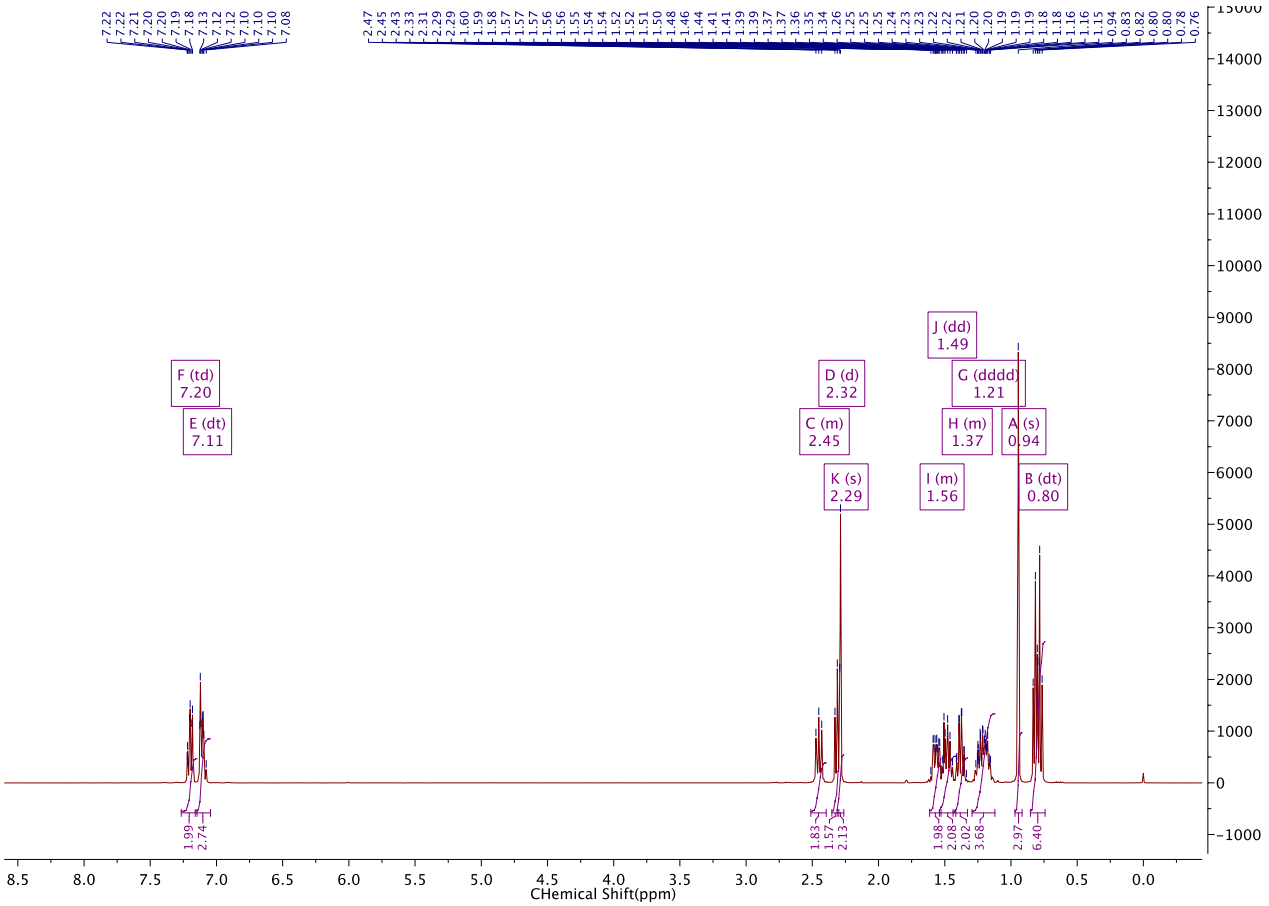
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 211.2, 143.1, 128.4(2C), 128.3(2C), 125.6, 50.3, 45.3, 41.2, 36.4, 31.7, 31.4, 30.4, 24.7, 23.5, 22.5, 14.0, 8.1.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3063, 2931, 1711,1456, 1031, 699

MS (ESI) m/z calc. for $C_{19}H_{30}O^{23}Na$ $[M+Na]^+$: 297.2189, found: 297.2188

$[\alpha]^{20}_{589}$ = -5.9 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.


F (td)
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E (dt)
7.11
D (d)
2.32
C (m)
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K (s)
2.29
J (dd)
1.49
G (dddd)
1.21
H (m)
1.37
A (s)
0.94
I (m)
1.56
B (dt)
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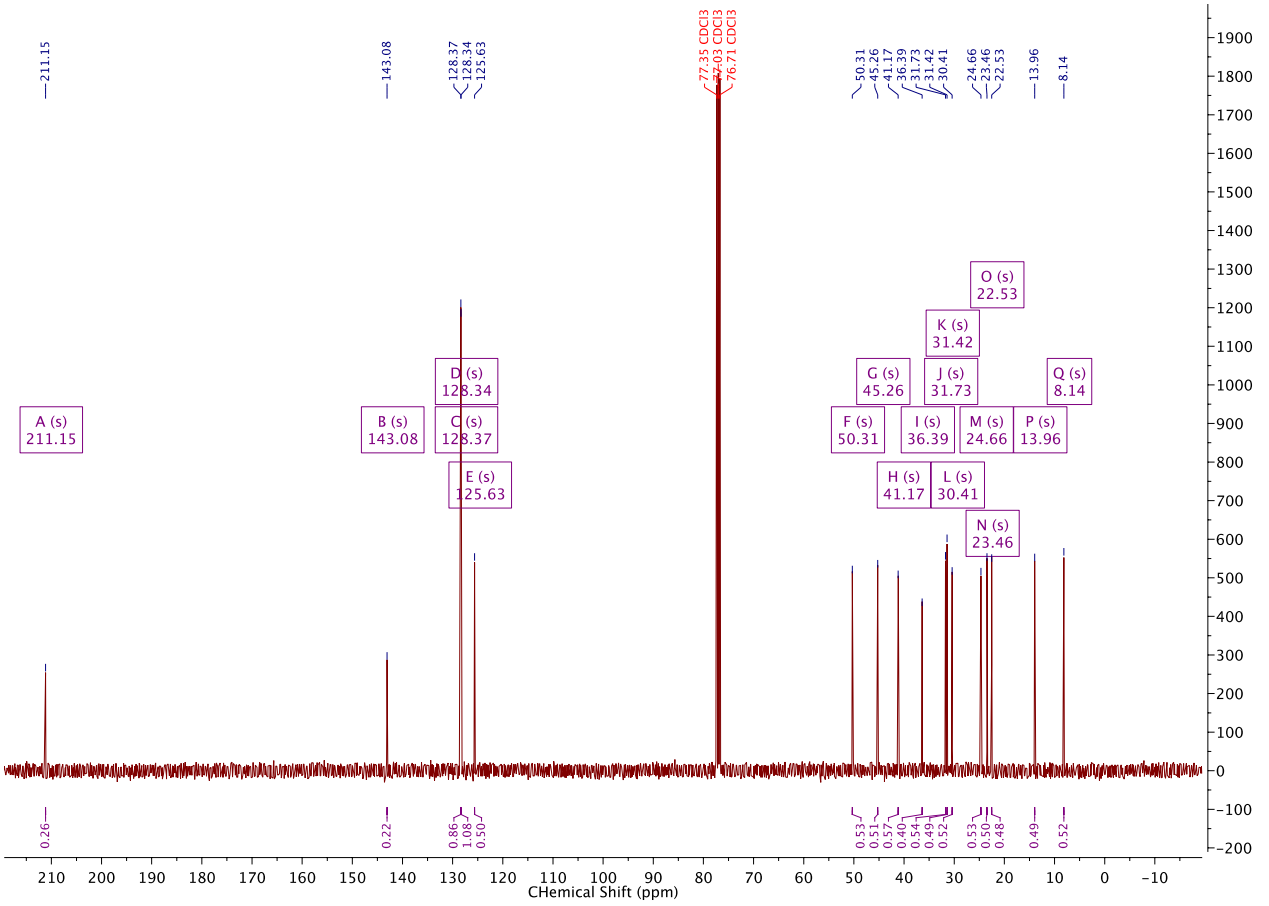
CHemical Shift(ppm)


A (s)
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B (s)
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D (s)
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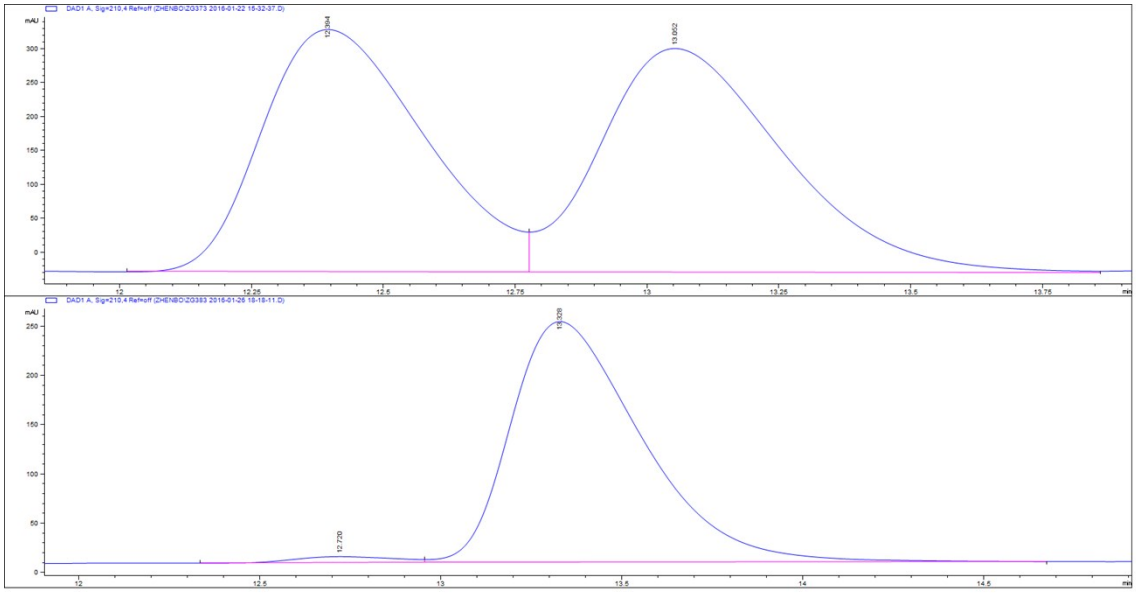
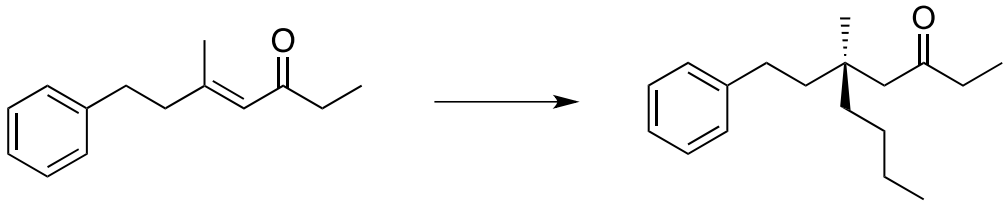
C (s)
128.37
E (s)
125.63
O (s)
22.53
K (s)
31.42
G (s)
45.26
J (s)
31.73
Q (s)
8.14
F (s)
50.31
I (s)
36.39
M (s)
24.66
P (s)
13.96
H (s)
41.17
L (s)
30.41
N (s)
23.46
CHemical Shift (ppm)

HPLC trace



(+)-(*R*)-5-methyl-5-phenethylnonan-3-one (3m)



CuCl (1.9 mg, 0.02mmol, 0.10eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol, 0.10eq) 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 (5.6 mg, 0.022 mmol,0.11 eq) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq) was added. A balloon filled with 1-butene was used to purge the flask 1-butene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under a 1-butene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (40.0 mg, 0.2mmol, 1.0 eq) and then TMSCl (0.127 ml, 1.0 mmol, 5.0 eq) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O. The mixture was partitioned

between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (25 mg, 53 % yield, 93% *ee*)

HPLC analysis indicated an enantiomeric excess of 91 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99.7:0.3; λ = 210 nm; major enantiomer tR = 5.56 min; minor enantiomer, tR = 5.79 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.31 – 7.22 (m, 2H, Ar-*H*), 7.16 (dt, *J* = 8.1 Hz, 1.9 Hz, 3H, Ar-*H*), 2.56 – 2.47 (m, 2H, PhCH_2), 2.39 (q, *J* = 7.3 Hz, 2H, COCH_2CH$_3$), 2.36 (s, 2H, COCH_2), 1.69 – 1.58 (m, 2H, PhCH$_2$CH_2), 1.44 – 1.34 (m, 2H, CH_2), 1.34 – 1.12 (m, 4H, CH_2), 1.08 – 0.95 (m, 6H, CH_3), 0.90 (t, *J* = 7.1 Hz, 3H, CH$_2$CH_3).

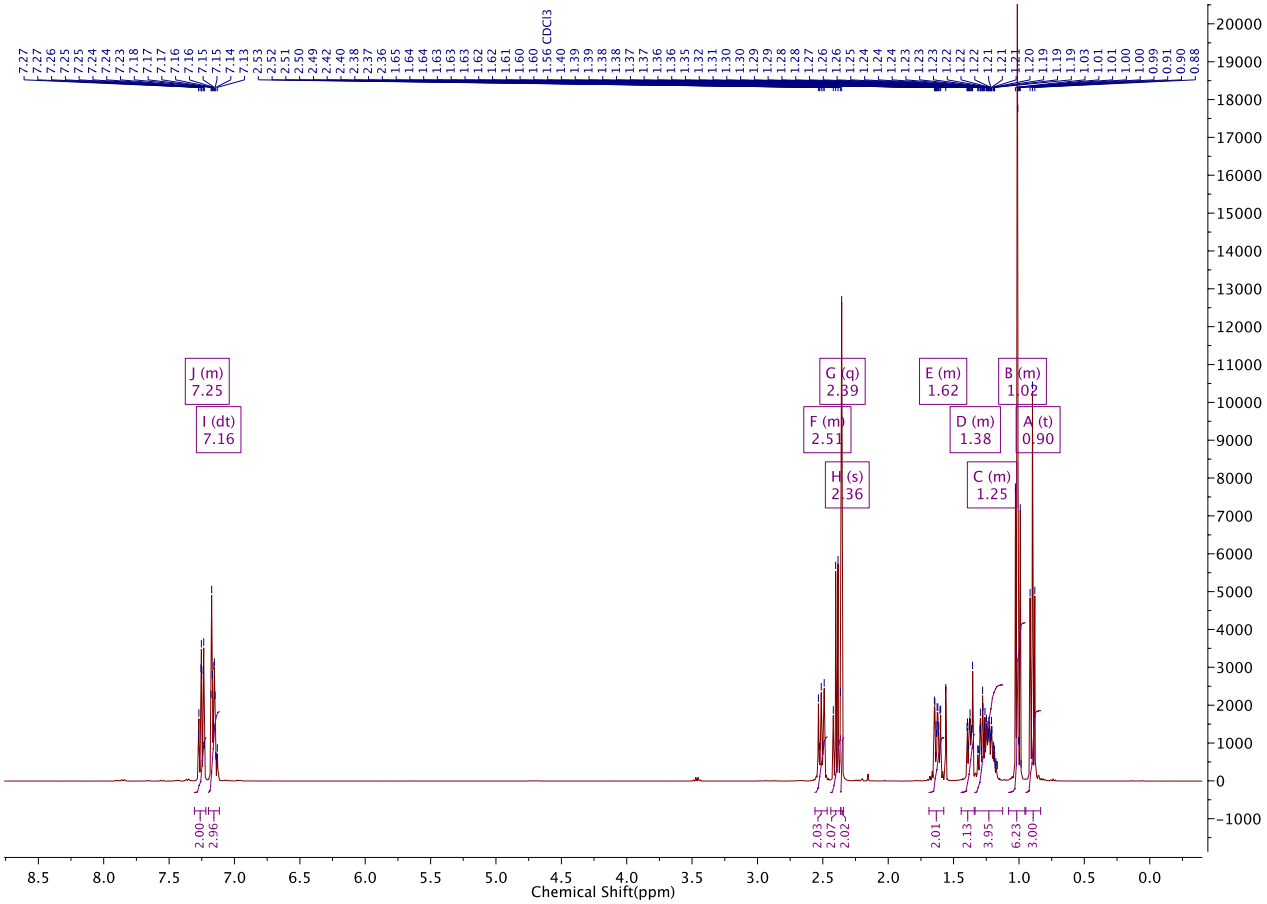
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 211.4, 143.1, 128.4(2C), 128.3(2C), 125.6, 50.5, 41.7, 39.3, 38.4, 36.3, 30.4, 26.0, 25.2, 23.5, 14.2, 7.8.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2980,2888,1382,1252, 1152, 1073,954

MS (ESI) m/z calc. for $C_{18}H_{29}O$ $[M+H]^+$: 261.2213, found: 261.2215

$[\alpha]^{20}_{589}$ = +3.8 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.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G (q)
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F (m)
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H (s)
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D (m)
1.38
B (m)
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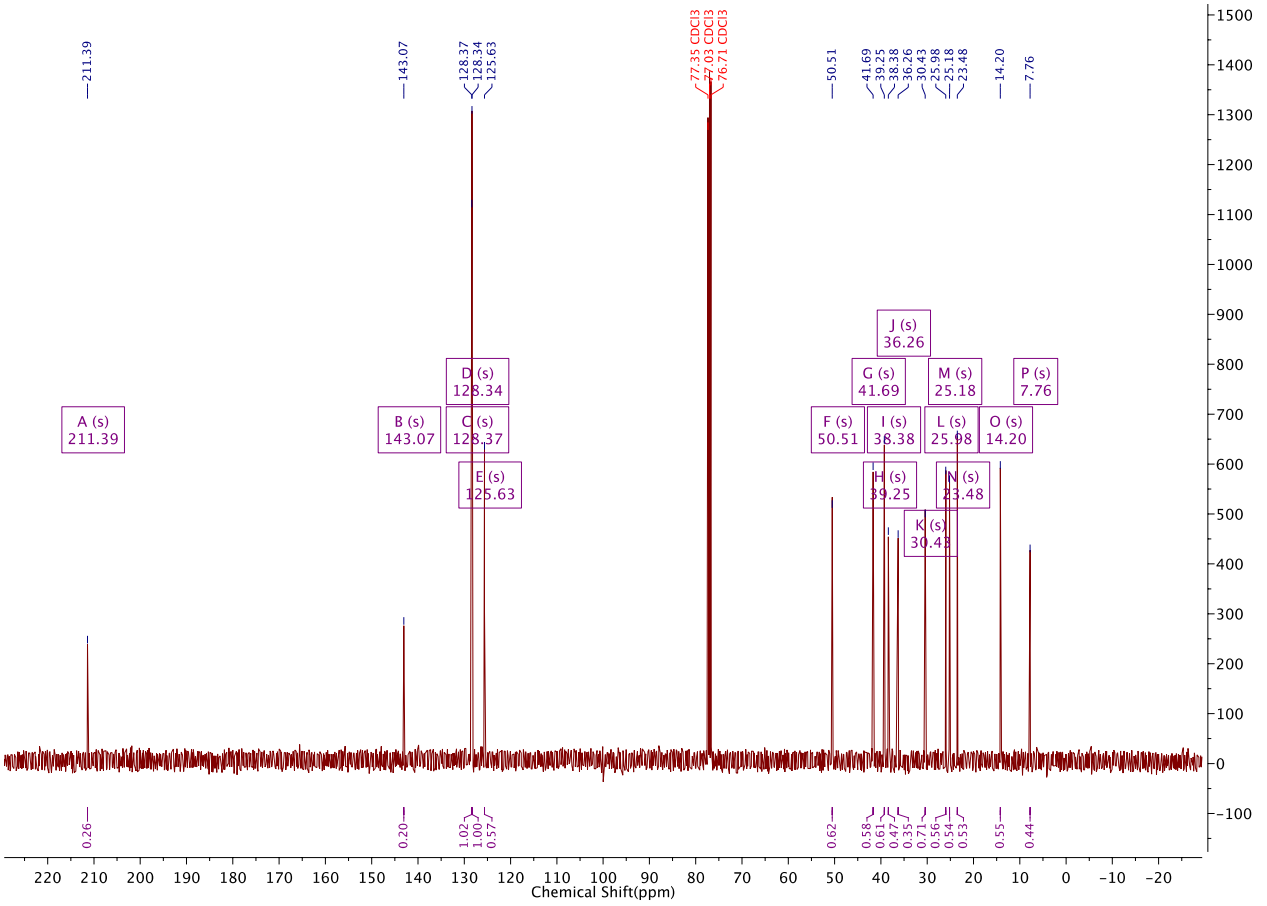
A (t)
0.90
C (m)
1.25
Chemical Shift(ppm)


A (s)
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B (s)
143.07
D (s)
128.34
C (s)
128.37
E (s)
125.63
J (s)
36.26
G (s)
41.69
M (s)
25.18
P (s)
7.76
F (s)
50.51
I (s)
38.38
L (s)
25.98
O (s)
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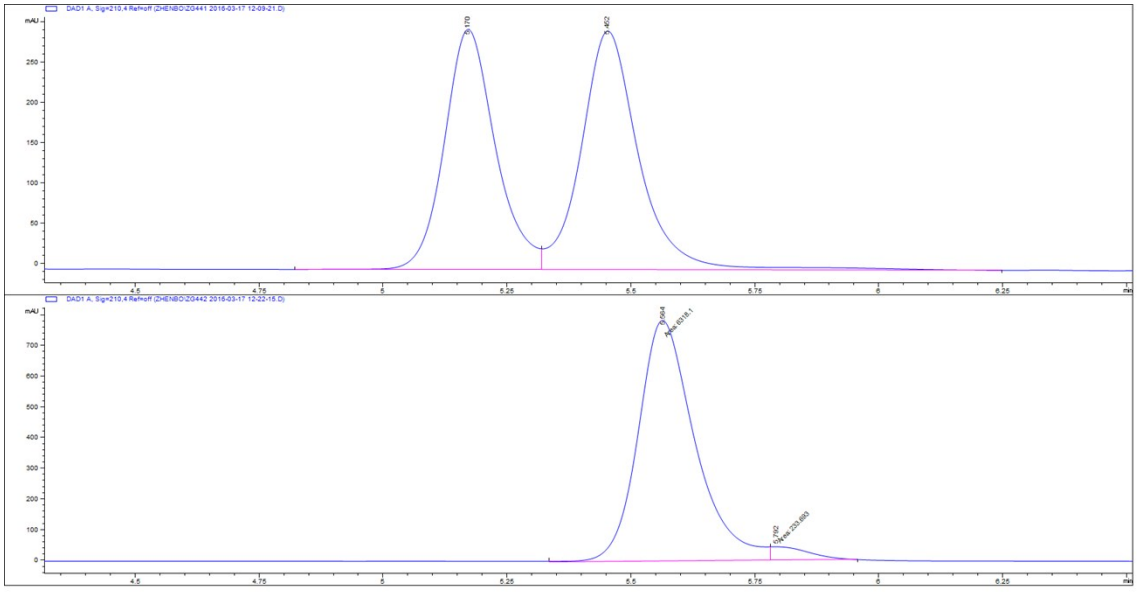
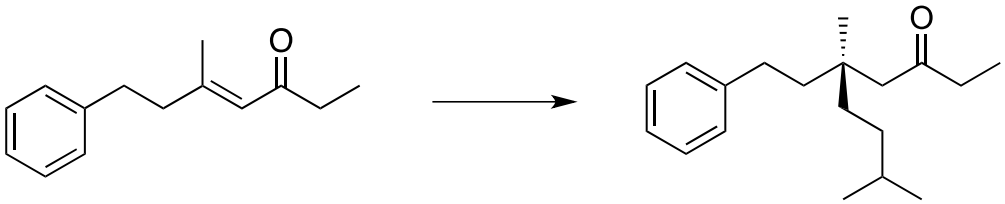
H (s)
39.25
N (s)
23.48
K (s)
30.43
Chemical Shift(ppm)

HPLC trace



(+)-(*R*)-5,8-dimethyl-5-phenethylnonan-3-one (3n)



CuCl (1.9 mg, 0.02mmol, 0.10eq.), and the phosphoramidite ligand **B** (11.5 mg, 0.02 mmol,0.10eq) 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 (5.6 mg, 0.022 mmol,0.11 eq) was added and the mixture was stirred for an additional 15 min. To a second, flame dried, round bottom flask, Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq) was added. A balloon filled with 3 methyl-1 butene was used to purge the flask with 3 methyl-1 butene for 5 min, and then CH_2Cl_2 (0.2 mL) was added. After stirring for 15 min under a 3 methyl-1 butene atmosphere (balloon), a clear yellow solution was obtained. After stirring for 15 min, 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 the enone (40.0 mg, 0.2mmol, 1.0 eq) and then TMSCl (0.127 ml, 1.0 mmol, 5.0 eq) were each added dropwise. Stirring was continued for 15 h at 0 °C, before the reaction was quenched by the addition of 1.5 mL NH_4Cl and then 3.0 mL Et_2O.

The mixture was partitioned between the aqueous and organic phases, and the aqueous layer was extracted with Et_2O (3 x10 mL). The combined organic materials were dried with 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. (40 mg, 70 % yield, 90% *ee*)

HPLC analysis indicated an enantiomeric excess of 91 % [Chiralpak® AYH; flow: 1.0 mL/min; hexane/i-PrOH: 99.5:0.5; λ = 210 nm; major enantiomer tR = 4.26 min; minor enantiomer, tR = 4.45 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.20 (dd, *J* = 8.1 Hz, 6.9 Hz, 2H, Ar-*H*), 7.11 (dt, *J* = 8.0 Hz, 1.8 Hz, 3H, Ar-*H*), 2.51 – 2.39 (m, 2H, PhCH_2), 2.33 (q, *J* = 7.3 Hz, 2H, COCH_2CH$_3$), 2.29 (s, 2H, COCH_2), 1.64 – 1.49 (m, 2H, PhCH$_2$CH_2), 1.47 – 1.35 (m, 1H,C*H*), 1.35 – 1.28 (m, 2H, CH_2), 1.15 – 1.01 (m, 2H, CH_2), 1.01 – 0.89 (m, 6H), 0.82 (d, *J* = 6.6 Hz, 6H, CH_3).

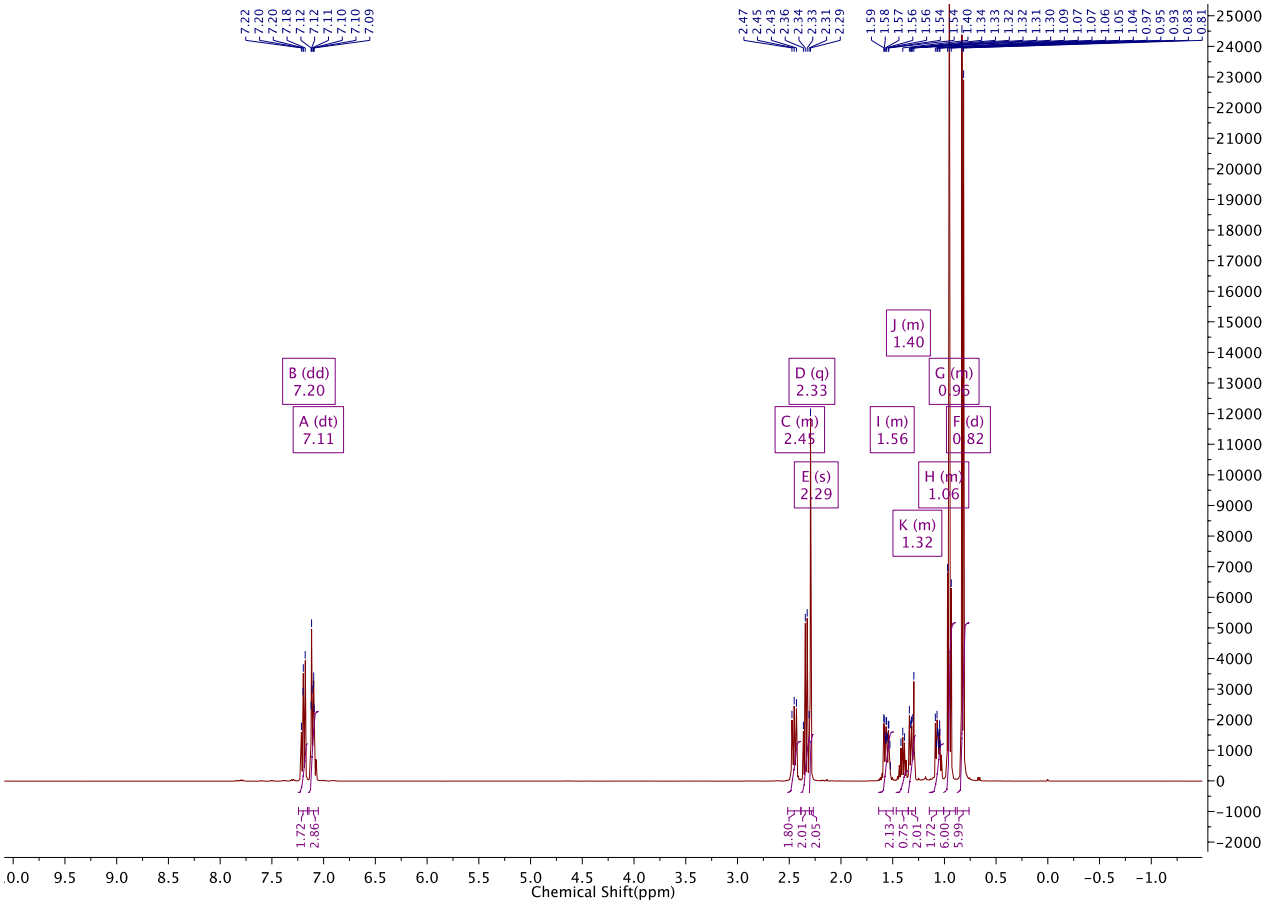
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 211.3, 143.1, 128.4(2C), 128.3(2C), 125.6, 50.5, 41.6, 38.4, 37.1, 36.2, 32.8, 30.4, 28.7, 25.2, 22.8(2C), 7.8.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2981,2885,1510,1381,1165,956,741

MS (ESI) m/z calc. for $C_{19}H_{31}O$ [M+H]$^+$: 275.2369, found: 275.2372

$[\alpha]^{20}_{589}$ = +4.3 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.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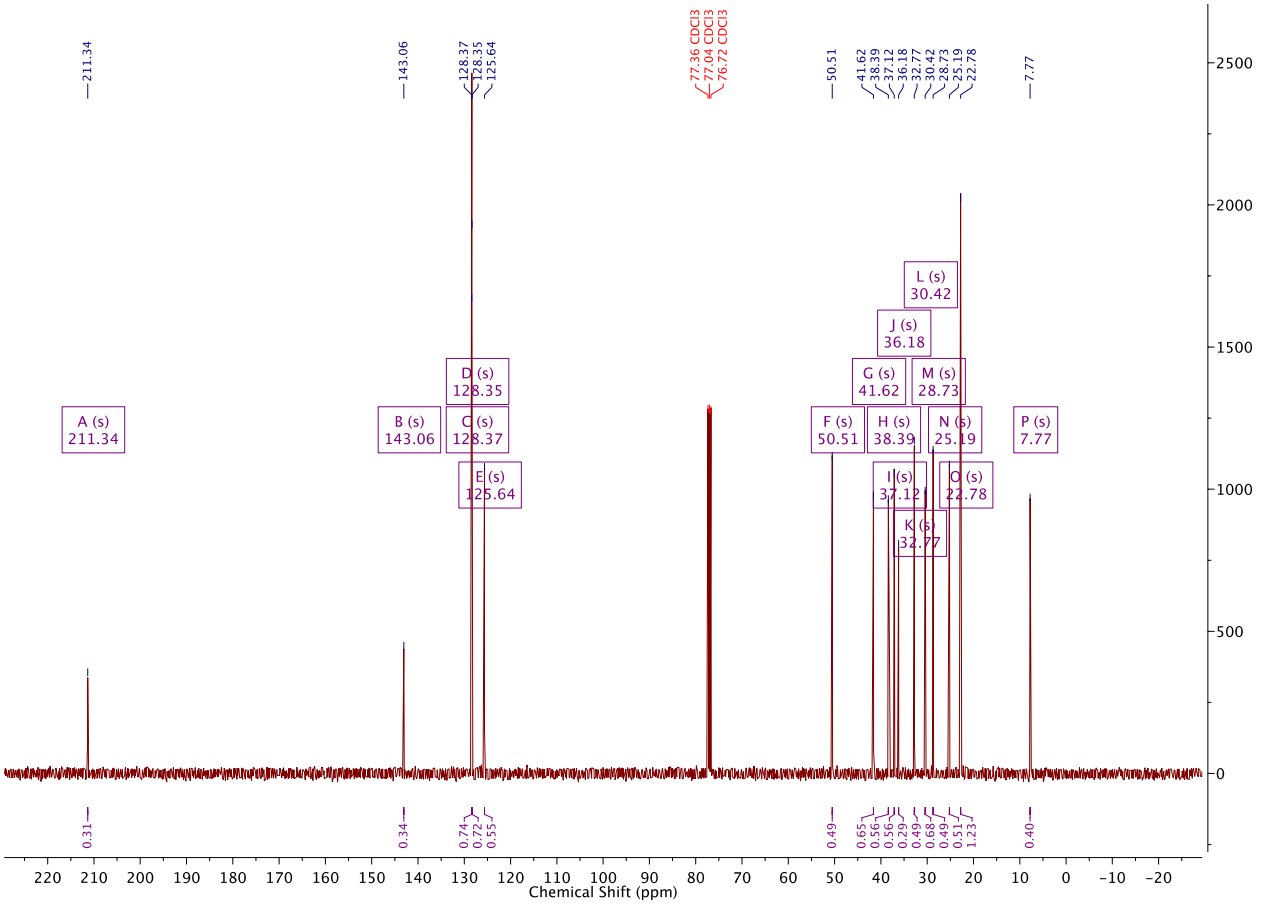
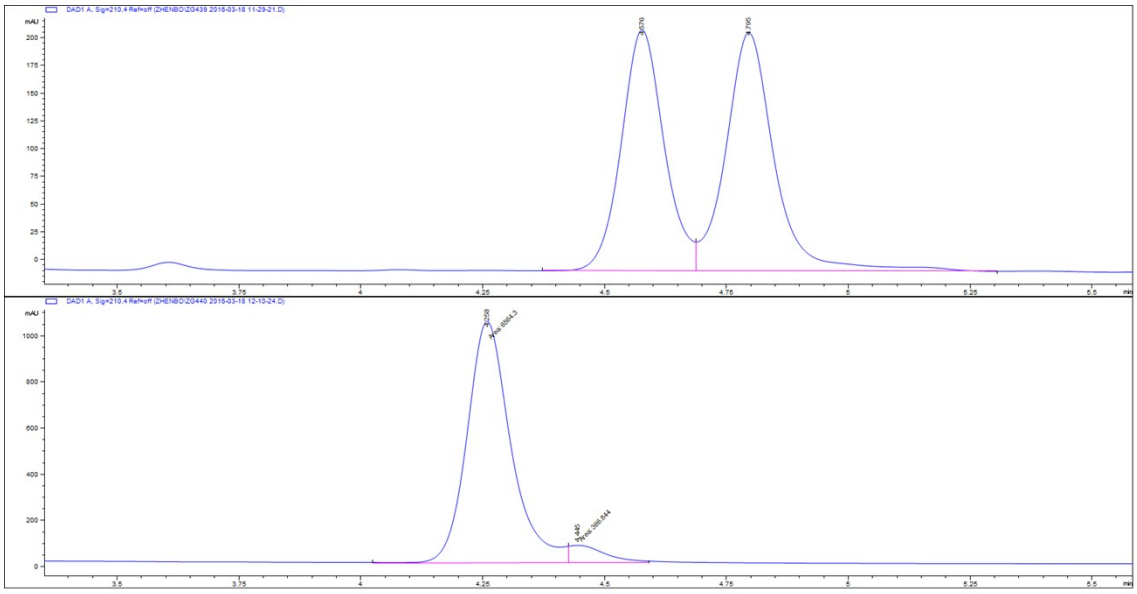
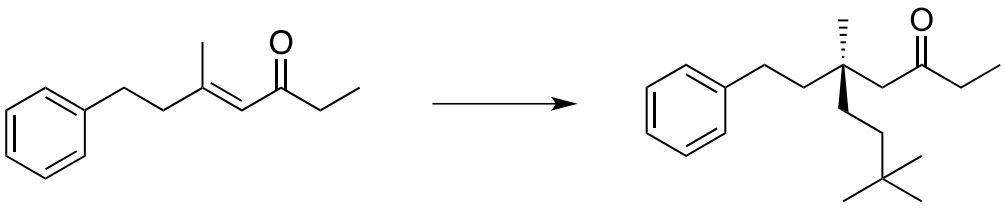
7.20
A (dt)
7.11
D (q)
2.33
C (m)
2.45
E (s)
2.29
J (m)
1.40
I (m)
1.56
G (m)
0.96
F (d)
0.82
H (m)
1.06
K (m)
1.32
Chemical Shift(ppm)


A (s)
211.34
B (s)
143.06
D (s)
128.35
C (s)
128.37
E (s)
125.64
L (s)
30.42
J (s)
36.18
G (s)
41.62
M (s)
28.73
F (s)
50.51
H (s)
38.39
N (s)
25.19
P (s)
7.77
I (s)
37.12
O (s)
22.78
K (s)
32.77
Chemical Shift (ppm)

HPLC trace



(+)-(*S*)-5,8,8-trimethyl-5-phenethylnonan-3-one (3o)



CuCl (1.9 mg, 0.02mmol, 0.10 eq), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol, 0.10 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 (5.6 mg, 0.022 mmol, 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 3,3-dimethyl-1-butene (0.15ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.4 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq), and was heated at 40°C for 1 h before being cooled to room temperature once the hydrozirconation was complete. 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 enone (40 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127 ml,

1.0 mmol, 5.0eq) 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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. (39mg, 69% yield, 85% *ee*)

HPLC analysis indicated an enantiomeric excess of 91 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99.5:0.5; λ = 210 nm; major enantiomer tR = 4.34 min; minor enantiomer, tR = 4.54 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.37 – 7.26 (m, 2H, Ar-*H*), 7.26 – 7.16 (m, 3H, Ar-*H*), 2.61 – 2.51 (m, 2H, PhCH_2), 2.45 (q, *J* = 7.3 hz, 2H, COCH_2CH$_3$), 2.40 (s, 2H, COCH_2), 1.67 (ddt, *J* = 10.9 Hz, 7.4 Hz, 1.7 Hz, 2H, PhCH$_2$C*H*), 1.46 – 1.30 (m, 2H, CH_2), 1.23 – 1.11 (m, 2H, CH_2), 1.11 – 1.01 (m, 6H, CH$_2$CH_3), 0.92 (s, 9H, C (CH_3)$_3$).

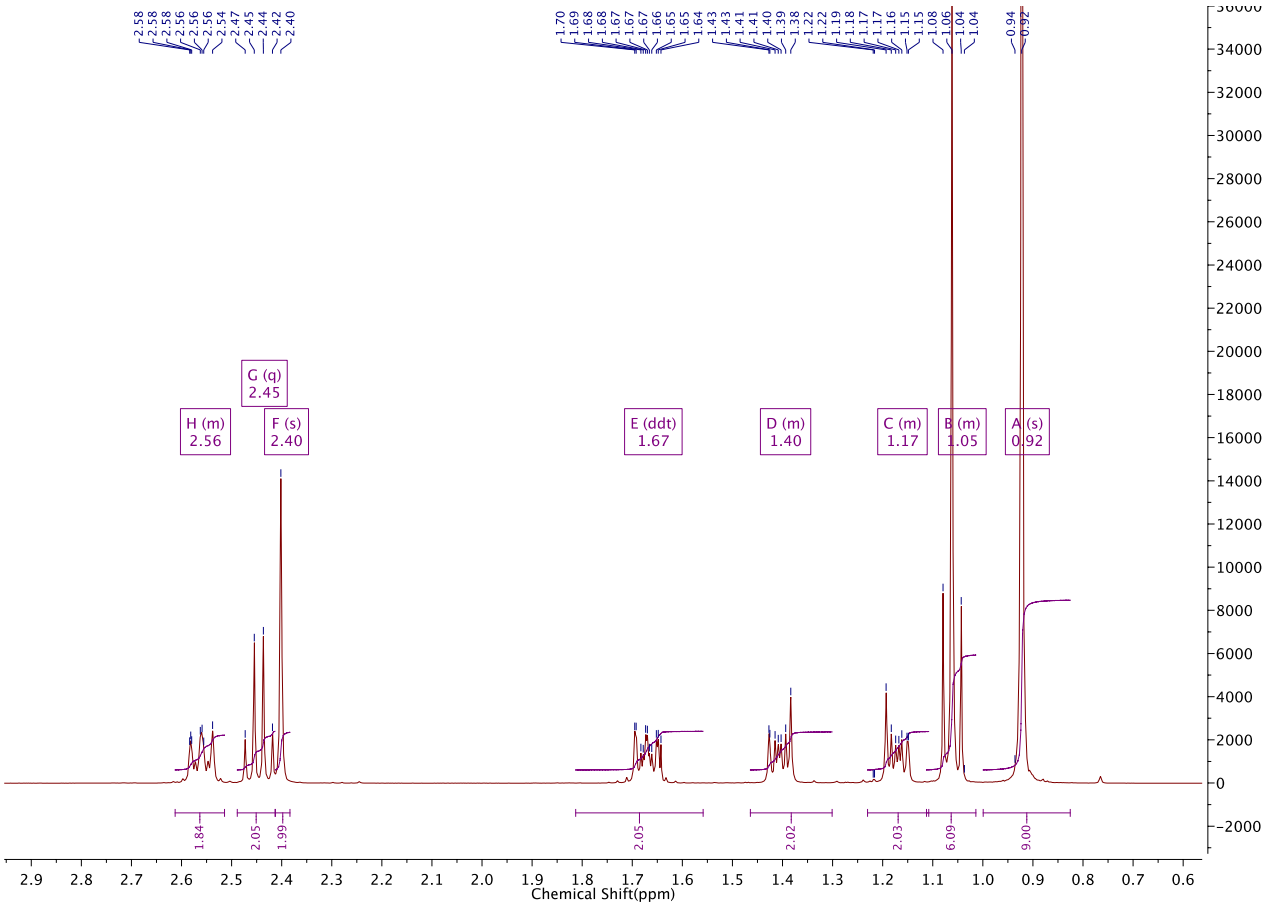
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 211.3, 143.1, 128.4(4C), 125.6, 50.5, 41.5, 38.4, 37.4, 36.0, 33.7, 30.4, 30.2, 29.4 (3C), 25.2, 7.8.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2980,2888,1382,1251,1152,955

MS (ESI) m/z calc. for $C_{20}H_{33}O$ $[M+H]^+$: 289.2526, found: 289.2528

$[\alpha]^{20}_{589}$ = +2.1 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.


G (q)
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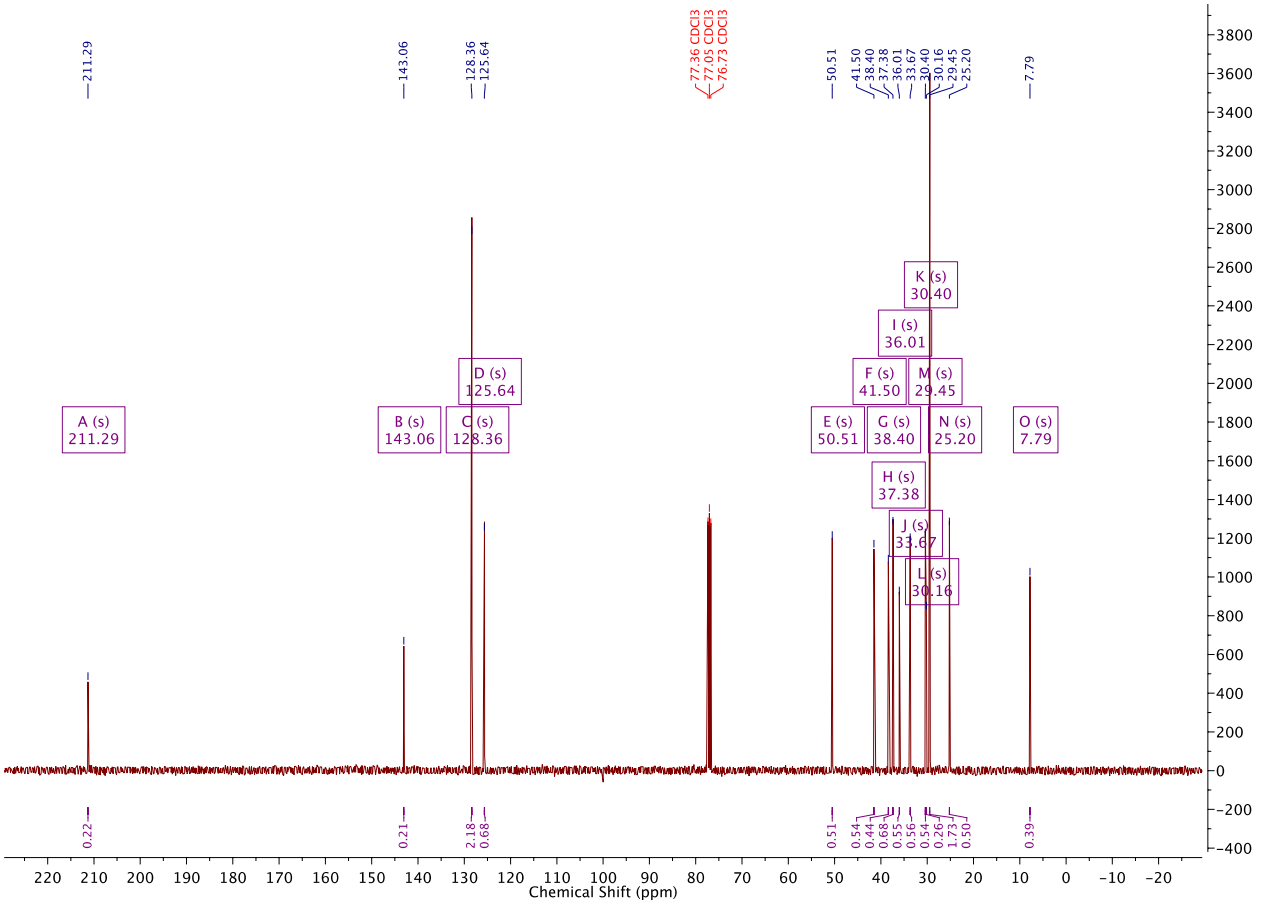
H (m)
2.56
F (s)
2.40
E (ddt)
1.67
D (m)
1.40
C (m)
1.17
B (m)
1.05
A (s)
0.92
Chemical Shift(ppm)


A (s)
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B (s)
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C (s)
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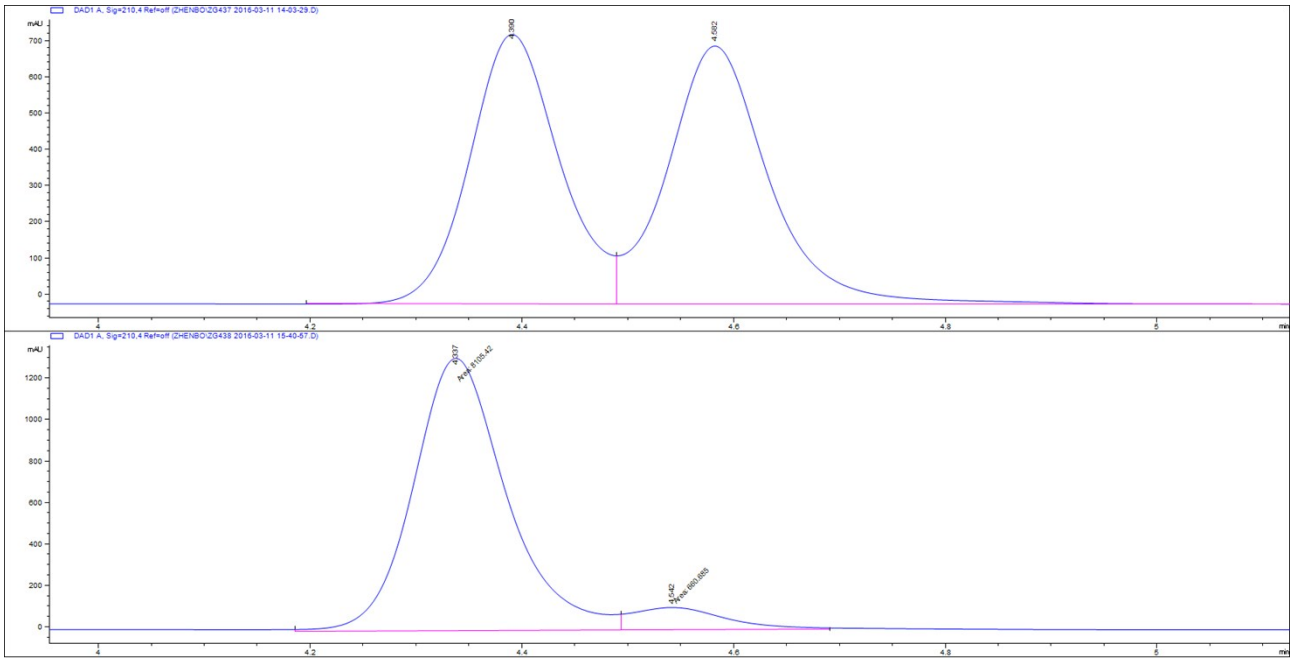
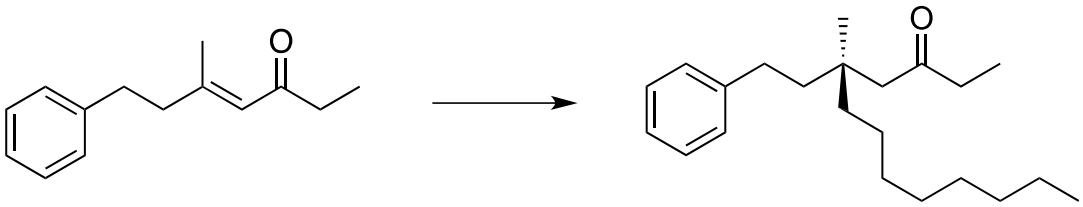
D (s)
125.64
E (s)
50.51
F (s)
41.50
G (s)
38.40
H (s)
37.38
I (s)
36.01
J (s)
33.67
K (s)
30.40
L (s)
30.16
M (s)
29.45
N (s)
25.20
O (s)
7.79
Chemical Shift (ppm)

HPLC trace



(+)-(*R*)-5-methyl-5-phenethyltridecan-3-one (3p)



CuCl (1.9 mg, 0.02mmol, 0.10 eq), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol, 0.10 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 (5.6 mg, 0.022 mmol, 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 Octene (0.1ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (40 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127 ml, 1.0 mmol,5.0eq) 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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. (35mg, 56% yield, 92% *ee*)

HPLC analysis indicated an enantiomeric excess of 92 % [Chiralpak® IA; flow: 0.8 mL/min; hexane/i-PrOH: 99.8:0.2; λ = 210 nm; major enantiomer tR = 8.01 min; minor enantiomer, tR = 8.62 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.38 – 7.25 (m, 2H, Ar-*H*), 7.21 (dt, *J* = 8.0 Hz, 1.9 Hz, 3H, Ar-*H*), 2.61 – 2.51 (m, 2H, PhCH_2), 2.49 – 2.41 (m, 2H, COCH_2CH$_3$), 2.40 (s, 2H, CH_2CO), 1.79 – 1.56 (m, 2H, CH_2), 1.41 (t, *J* = 7.4 Hz, 2H, CH_2), 1.38-1.18 (m, 12H, CH_2 , CH_3), 1.13 – 1.01 (m, 6H, CH_2), 0.92 (t, *J* = 6.8 Hz, 3H, CH_3).

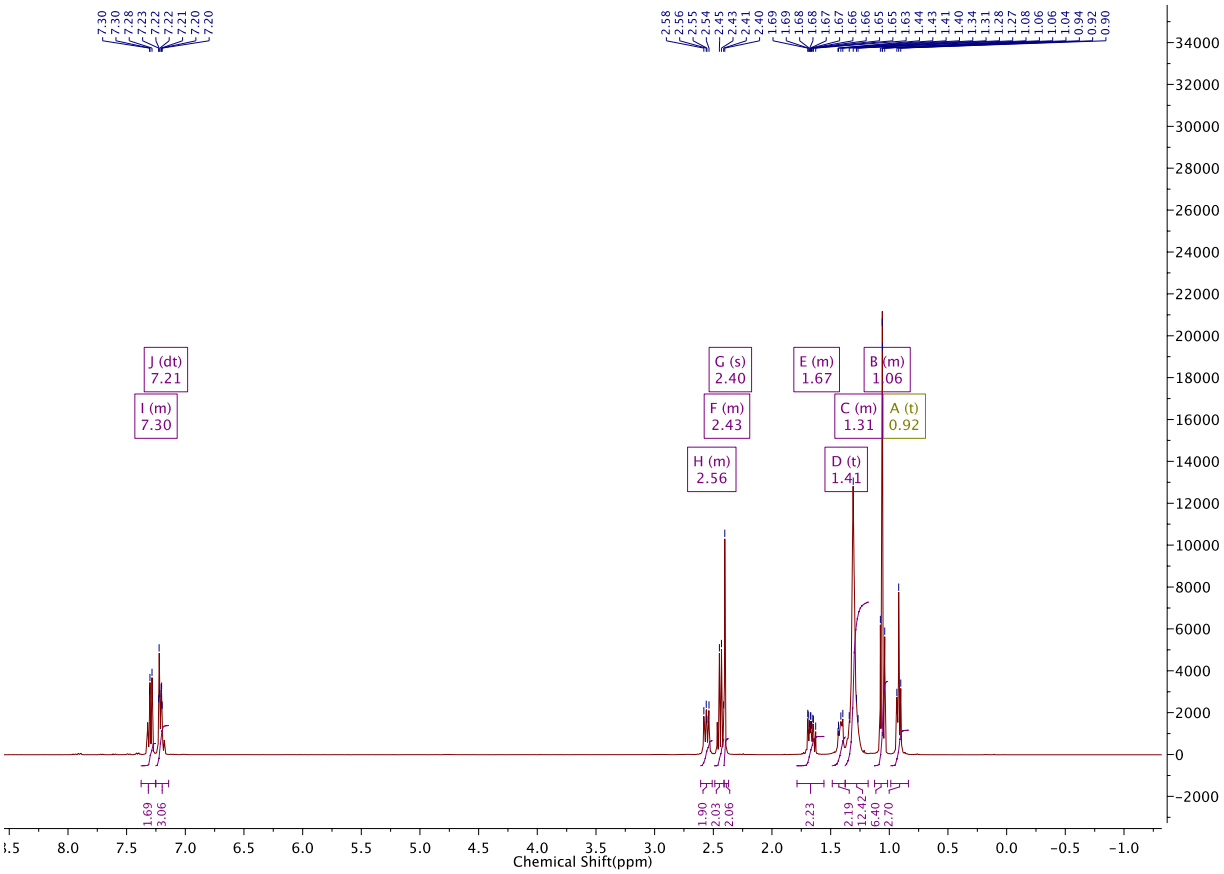
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 211.4, 143.1, 128.4(2C), 128.3(2C), 125.6, 50.5, 41.7, 39.6, 38.4, 36.3, 31.9, 30.5(2C), 29.7, 29.4, 25.2, 23.7, 22.7, 14.1, 7.8.

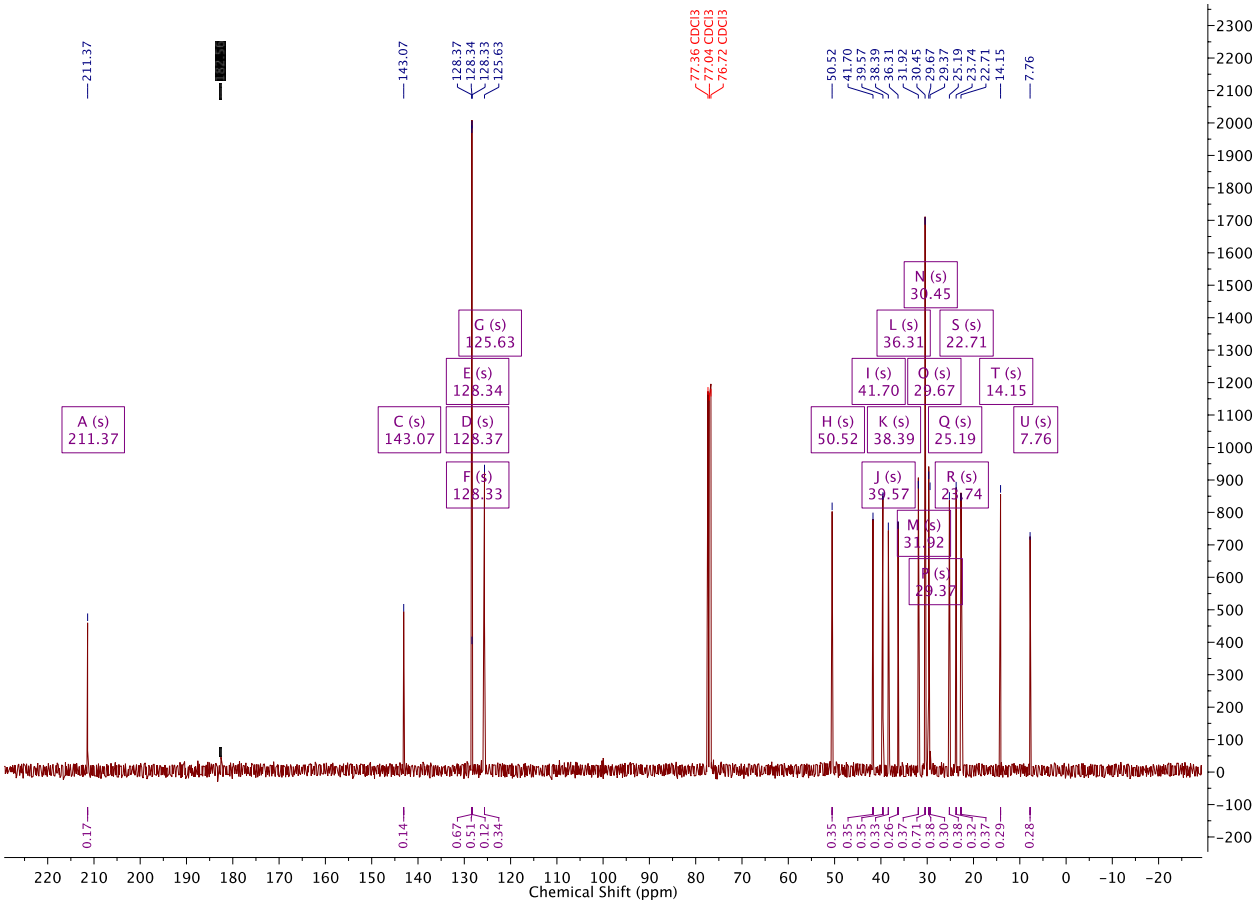
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2980,2889,1382, 1252,1153,1073,954

MS (ESI) m/z calc. for $C_{22}H_{37}O$ $[M+H]^+$: 317.2839, found: 317.2841

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

Absolute configuration assigned by analogy to compound 3b.


J (dt)
7.21
I (m)
7.30
G (s)
2.40
F (m)
2.43
H (m)
2.56
E (m)
1.67
C (m)
1.31
D (t)
1.41
B (m)
1.06
A (t)
0.92
Chemical Shift(ppm)


A (s)
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C (s)
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G (s)
125.63
E (s)
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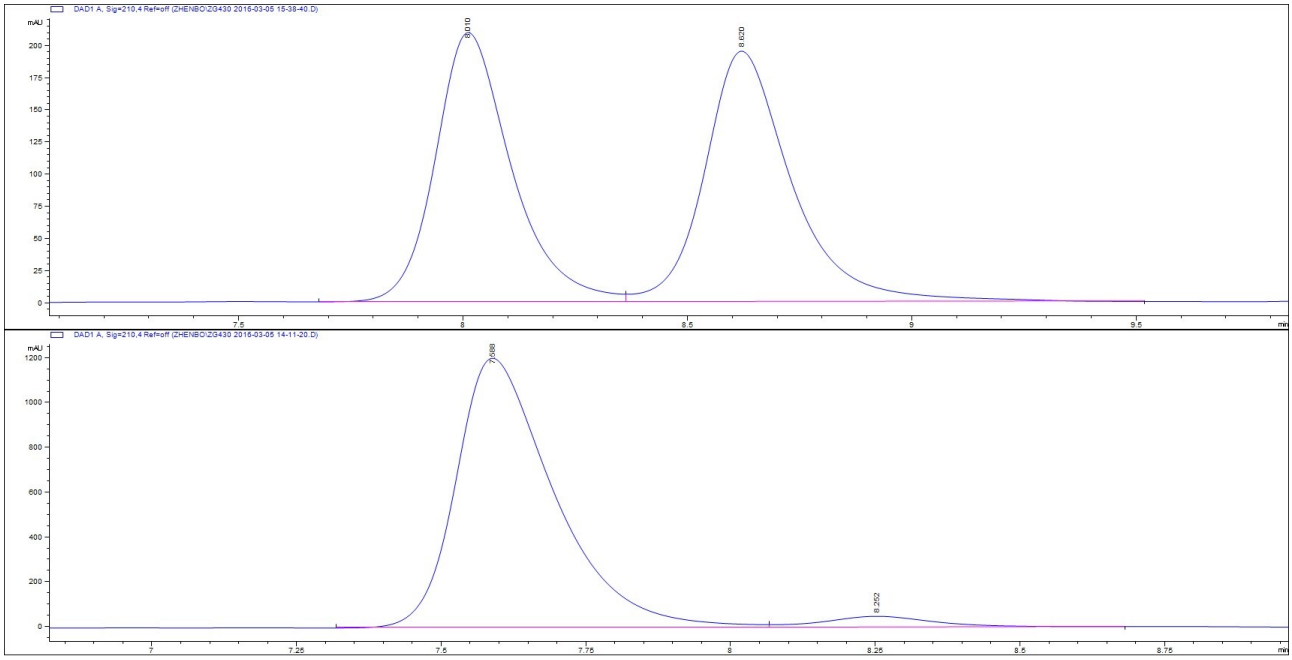
D (s)
128.37
F (s)
128.33
N (s)
30.45
L (s)
36.31
S (s)
22.71
I (s)
41.70
O (s)
29.67
T (s)
14.15
H (s)
50.52
K (s)
38.39
Q (s)
25.19
U (s)
7.76
J (s)
39.57
R (s)
23.74
M (s)
31.92
P (s)
29.37
Chemical Shift (ppm)

HPLC trace



Large Scale

CuCl (25 mg, 0.25mmol, 0.05 eq.), and the phosphoramidite ligand **B** (145 mg, 0.25 mmol, 0.05 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 (70 mg, 0.275, 0.055eq, mmol) was added and the mixture was stirred for an additional 15 min.

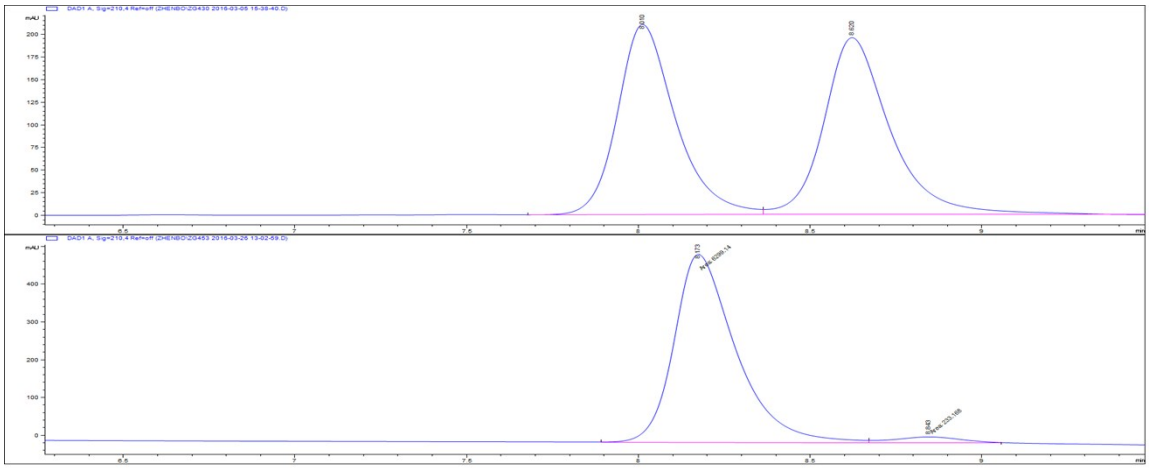
To a second, flame dried, round bottom flask, containing a stirred solution of Octene (2.0ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (5.0 mL), under an argon atmosphere was added Cp_2ZrHCl (1.93 g, 0.4 mmol, 1.5 eq.), and after stirring for 15 min, a clear yellow solution was obtained.

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 enone (1.0 g, 5 mmol, 1.0 eq) and TMSCl (3.2 ml, 25 mmol, 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 20 mL NH_4Cl (sat. aq.) and then 20 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x30 mL). The combined organic materials were dried (Na_2SO_4), filtered, concentrated, and the resulting

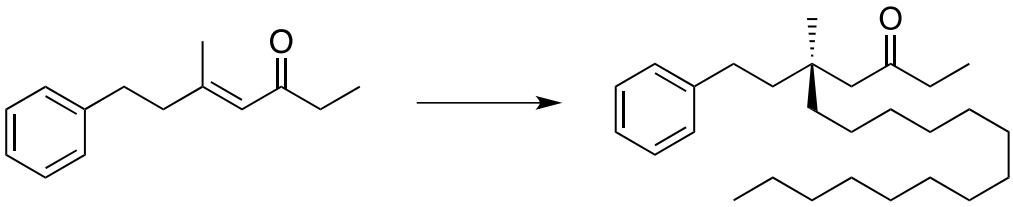
yellow residual purified by flash column chromatography (Petrol: Et_2O; 95:5; SiO_2) to give the desired product. (0.793g, 50% yield, 93% *ee*)

HPLC analysis indicated an enantiomeric excess of 93 % [Chiralpak® IA; flow: 0.8 mL/min; hexane/i-PrOH: 99.8:0.2; λ = 210 nm; major enantiomer tR = 8.01 min; minor enantiomer, tR = 8.62 min].

HPLC trace



(+)-(*R*)-5-methyl-5-phenethylnonadecan-3-one (3q)



CuCl (1.9 mg, 0.02mmol, 0.10 eq), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol, 0.10 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 (5.6 mg, 0.022 mmol, 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 1-tetradecene (0.15ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (40 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127 ml, 1.0 mmol,5.0eq) 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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. (45mg, 59% yield, 90% *ee*)

HPLC analysis indicated an enantiomeric excess of 91 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99.8:0.2; λ = 210 nm; major enantiomer tR = 6.28 min; minor enantiomer, tR = 6.89 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.35 – 7.25 (m, 2H, Ar-*H*), 7.21 (dt, *J* = 8.0 Hz, 1.8 Hz, 3H, Ar-*H*), 2.62 – 2.50 (m, 2H, PhCH_2), 2.44 (q, *J* = 7.3, 2H, COCH_2CH$_3$), 2.40 (s, 2H, COCH_2), 1.75 – 1.58 (m, 2H, PhCH$_2$CH_2), 1.49 – 1.36 (m, 2H, CH_2), 1.29 (s, 24H, CH_2), 1.15 – 0.98 (m, 6H, CH_3,COCH$_2$CH_3), 0.99 – 0.80 (m, 3H, CH$_2$CH_3).

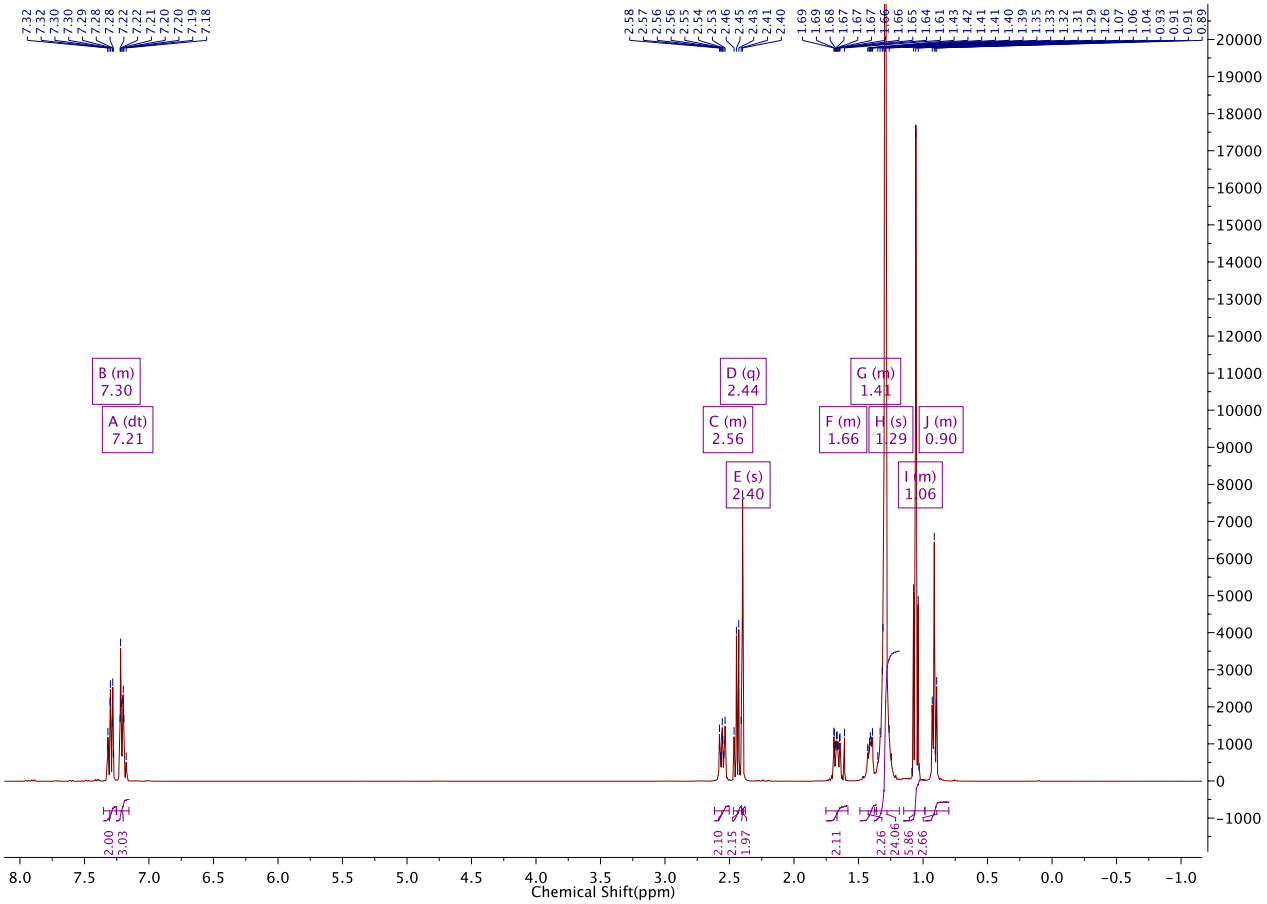
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 211.4, 143.1, 128.4 (2C), 128.3(2C), 125.6, 50.5, 41.7, 39.6, 38.4, 36.3, 31.9, 30.5, 29.7 (8C), 29.4, 25.2, 23.7, 22.7, 14.1, 7.8.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2980,2880,1473,1382,1252,1152,1072,954

MS (ESI) m/z calc. for $C_{28}H_{48}O^{23}Na$ $[M+Na]^+$: 423.3597, found: 423.3596

$[\alpha]^{20}_{589}$ = +2.9 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.


B (m)
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A (dt)
7.21
D (q)
2.44
C (m)
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E (s)
2.40
G (m)
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F (m)
1.66
H (s)
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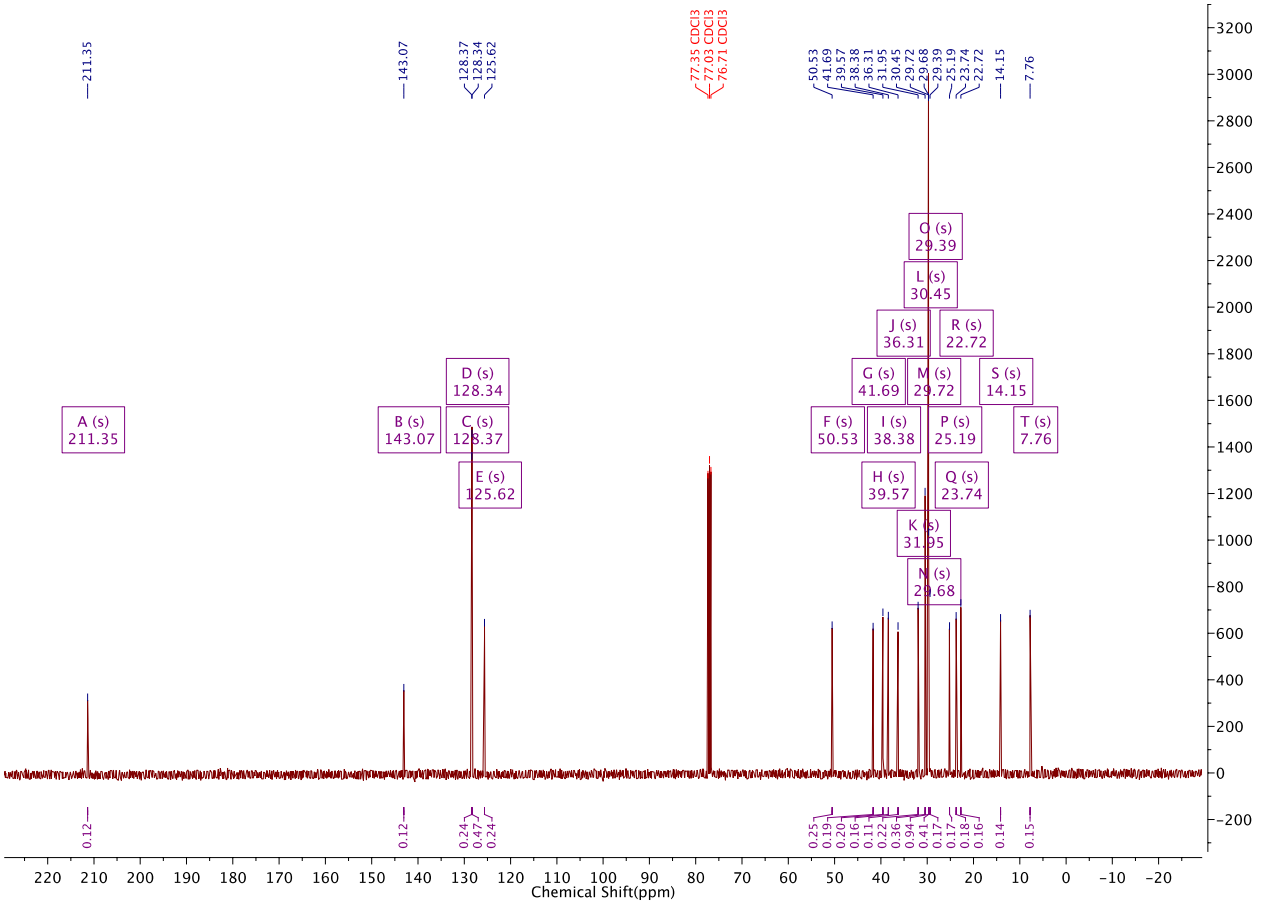
J (m)
0.90
I (m)
1.06
Chemical Shift(ppm)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C (s)
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E (s)
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Q (s)
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L (s)
30.45
J (s)
36.31
R (s)
22.72
G (s)
41.69
M (s)
29.72
S (s)
14.15
F (s)
50.53
I (s)
38.38
P (s)
25.19
T (s)
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K (s)
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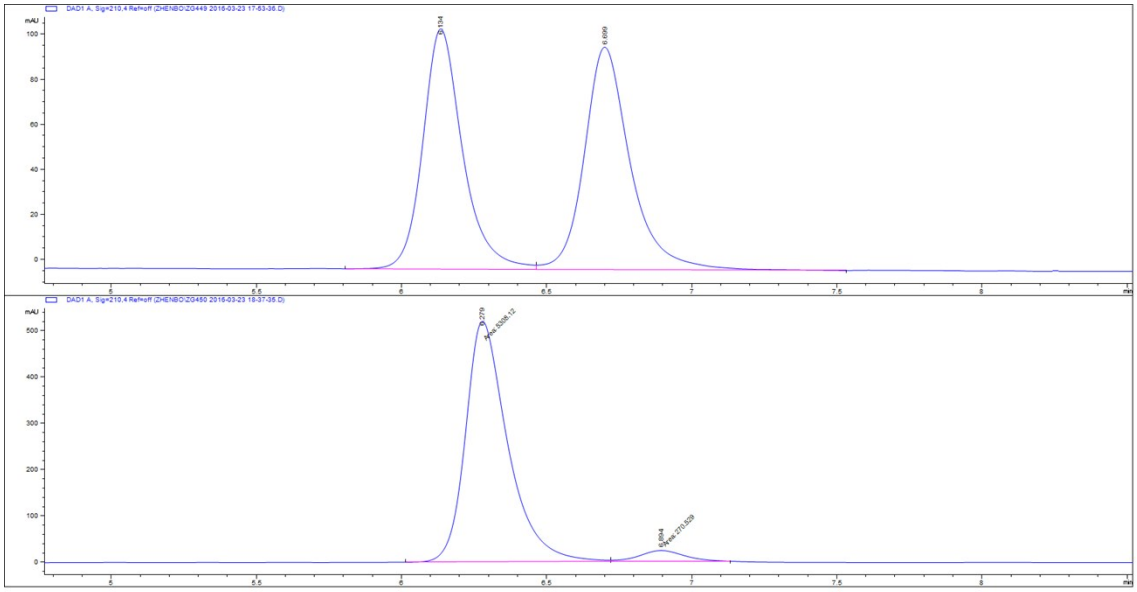
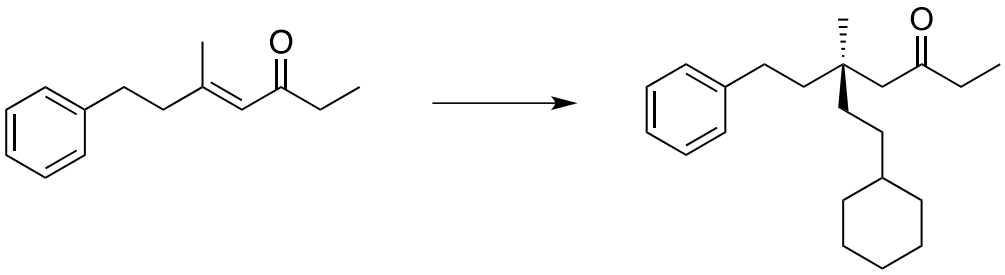
N (s)
29.68
Chemical Shift(ppm)

HPLC trace



(+)-(*R*)-7-cyclohexyl-5-methyl-5-phenethylheptan-3-one (3r)



CuCl (1.9 mg, 0.02mmol, 0.10 eq), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol, 0.10 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 (5.6 mg, 0.022 mmol, 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 vinylcyclohexane (0.08 ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (40 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127 ml, 1.0 mmol, 5.0eq) 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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. (40mg, 64% yield, 90% *ee*)

HPLC analysis indicated an enantiomeric excess of 90 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99.5:0.5; λ = 210 nm; major enantiomer tR = 5.02 min; minor enantiomer, tR = 5.22 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.30 – 7.19 (m, 2H, Ar-*H*), 7.19 – 7.08 (m, 3H, Ar-*H*), 2.54 – 2.45 (m, 2H, PhCH_2), 2.38 (q, *J* = 7.3 Hz, 2H COCH_2CH$_3$), 2.33 (s, 2H, COCH_2), 1.74 – 1.53 (m, 6H, PhCH$_2$CH_2, C*H*, CH$_2$), 1.44 – 1.31 (m, 2H, CH_2), 1.27 – 1.03 (m, 6H, CH_2), 1.03 – 0.97(m, 6H, CH_2), 0.85 (ddd, *J* = 23.7 Hz, 12.0 Hz, 6.2, 3H, CH$_2$CH_3).

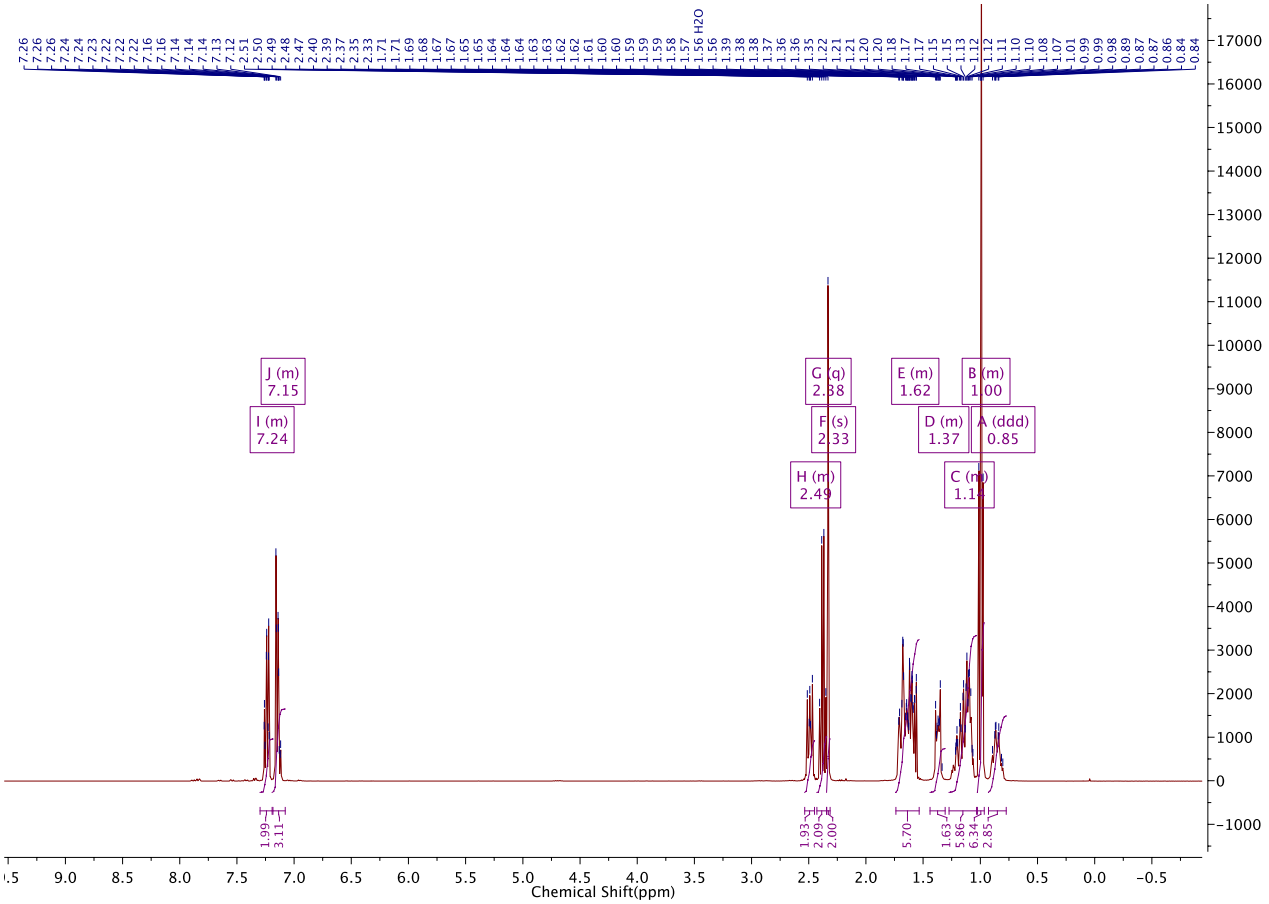
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 211.4, 143.1, 128.4(2C), 128.3(2C), 125.6, 50.5, 41.6, 38.4 (2C), 36.6, 36.2, 33.6(2C), 31.3, 30.4, 26.7, 26.5(2C), 25.2, 7.8.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2980,2889,1382,1252,1152,1073,955

MS (ESI) m/z calc. for $C_{22}H_{35}O$ $[M+H]^+$: 315.2682, found: 315.2685

$[\alpha]^{20}_{589}$ = +3.5 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.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G (q)
2.38
F (s)
2.33
H (m)
2.49
E (m)
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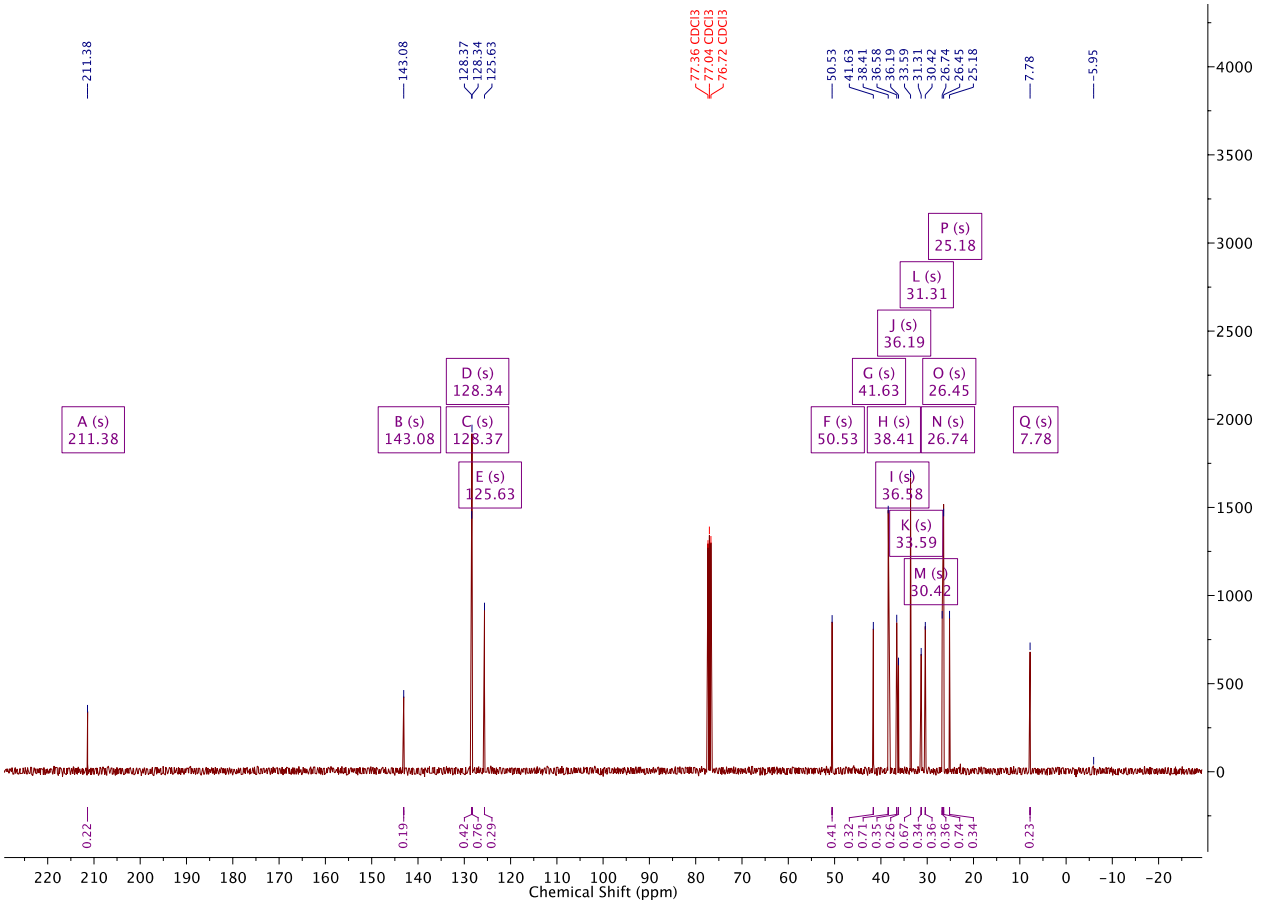
1.37
B (m)
1.00
A (ddd)
0.85
C (m)
1.14
Chemical Shift(ppm)


A (s)
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D (s)
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E (s)
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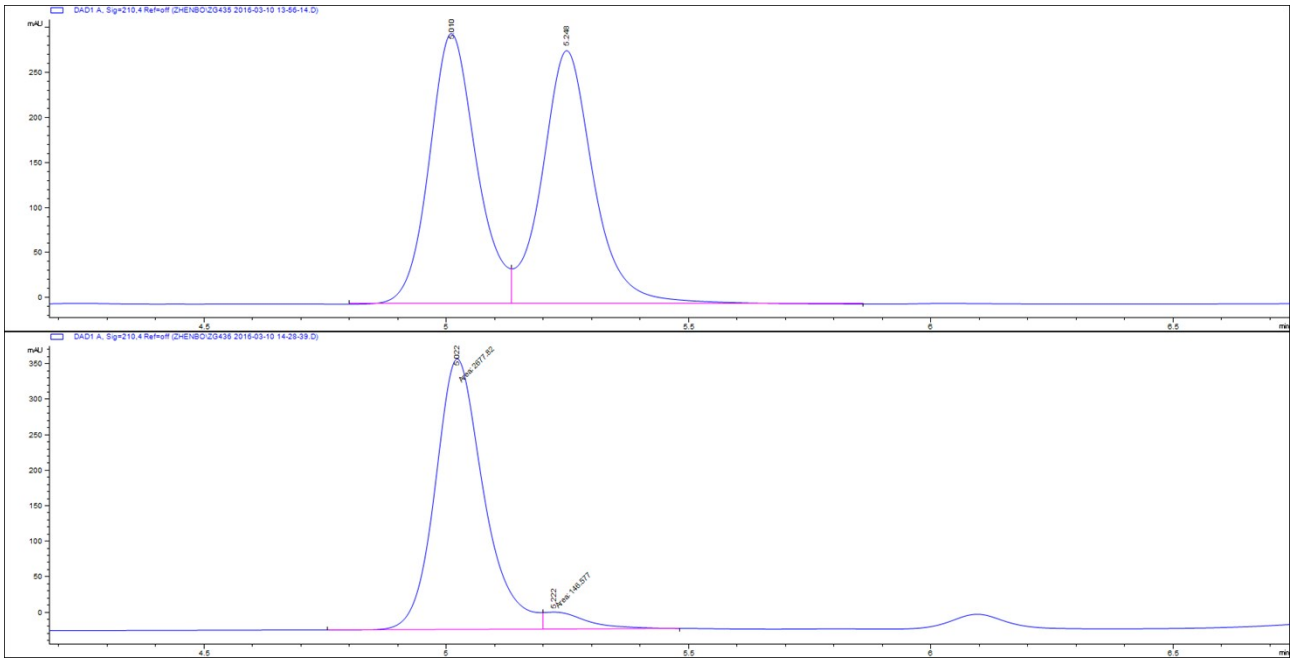
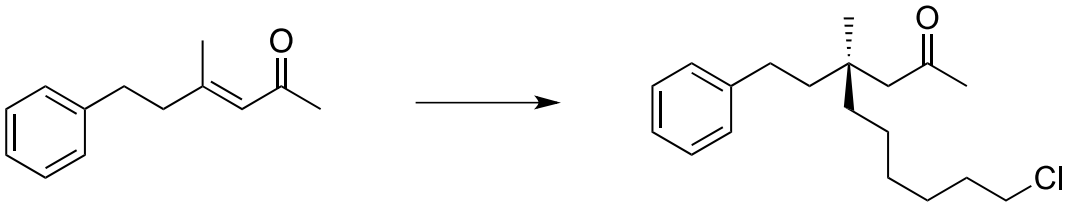
G (s)
41.63
H (s)
38.41
I (s)
36.58
J (s)
36.19
K (s)
33.59
L (s)
31.31
M (s)
30.42
N (s)
26.74
O (s)
26.45
P (s)
25.18
Q (s)
7.78
Chemical Shift (ppm)

HPLC trace



(+)-(*R*)-10-chloro-4-methyl-4-phenethyldecan-2-one (3s)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol) 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 (5.6 mg, 0.022 mmol, 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 6-chlorohex-1-ene (0.08ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (38 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127 ml,1.0 mmol, 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). The combined organic materials were dried (Na_2SO_4), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: Et_2O; 80:20; SiO_2) to give the desired product. (31 mg, 51% yield, 84% *ee*)

HPLC analysis indicated an enantiomeric excess of 91 % [Chiralpak® IA; flow: 0.8 mL/min; hexane/i-PrOH: 98.5:1.5; λ = 210 nm; major enantiomer tR = 6.70 min; minor enantiomer, tR = 7.27 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.23 – 7.12 (m, 2H, Ar-*H*), 7.11 – 7.02 (m, 3H, Ar-*H*), 3.43 (t, *J* = 6.7 Hz, 2H, CH2Cl), 2.42 (t, *J* = 8.7Hz, 2H, PhCH_2), 2.30 (s, 2H, CH_2COCH_3), 2.03 (s, 3H, COCH_3), 1.78 – 1.57 (m, 3H, CH_2), 1.57 – 1.45 (m, 2H, CH_2), 1.41 – 1.23 (m, 3H, CH_2), 1.28 – 1.07 (m, 4H, CH_2), 0.94 (s, 3H, CH_3).

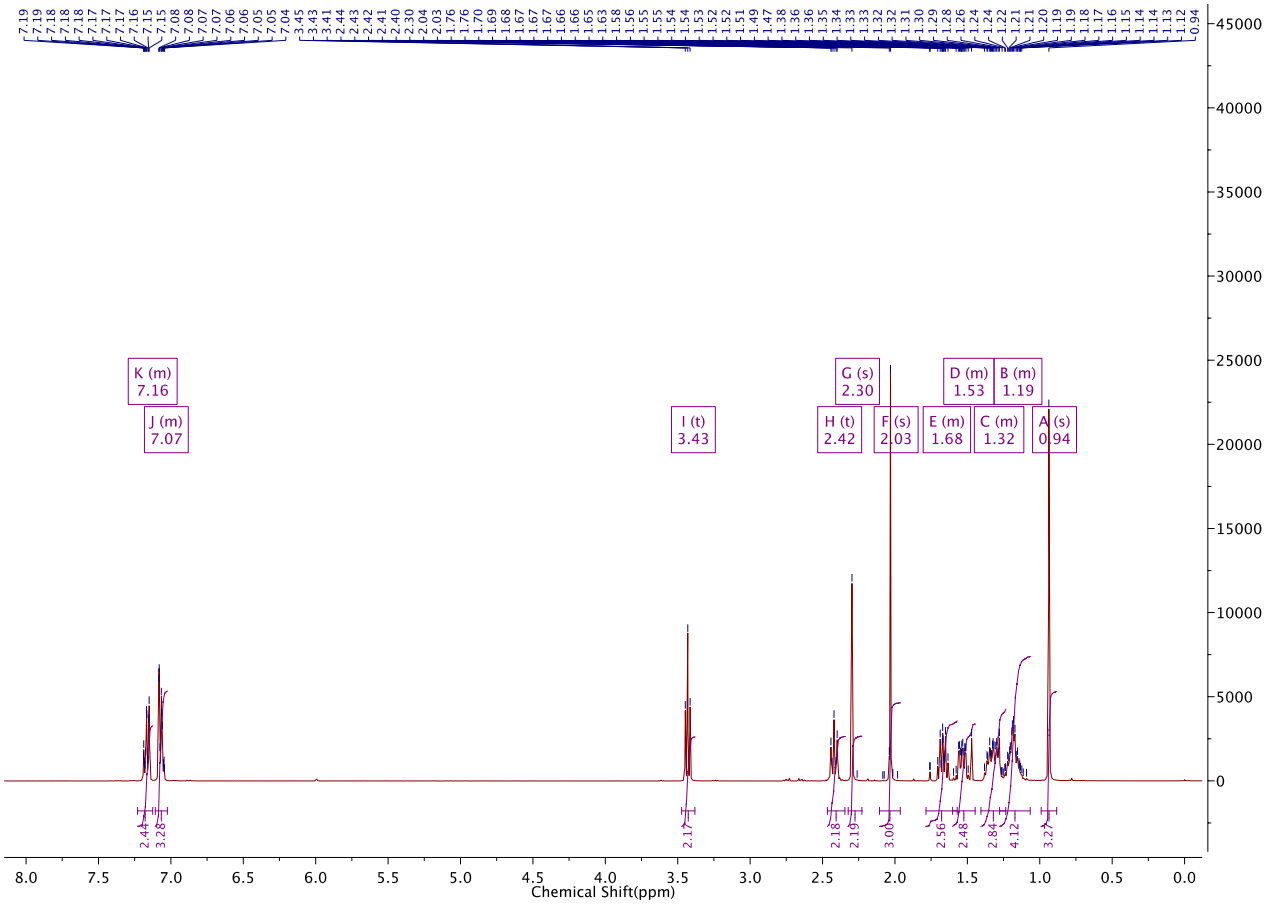
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 208.7, 142.9, 128.4(2C), 128.3(2C), 125.7, 51.6, 45.1, 41.6, 39.3, 36.2, 32.6(2C), 30.4, 29.7, 26.9, 25.1, 23.6.

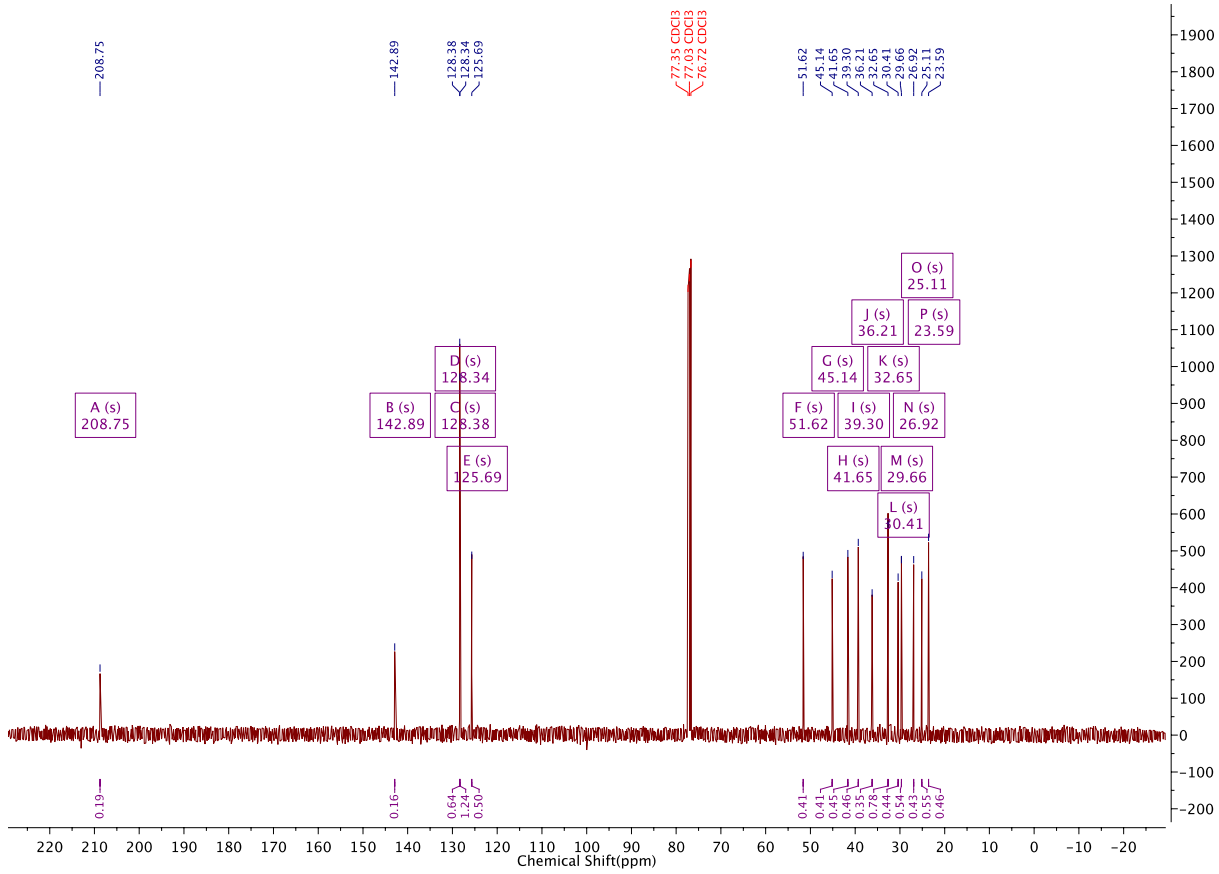
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658,2981,2889, 1382,1252,1153,955

MS (ESI) m/z calc. for $C_{19}H_{30}O^{35}Cl$ $[M+H]^+$: 309.1979, found: 309.1981

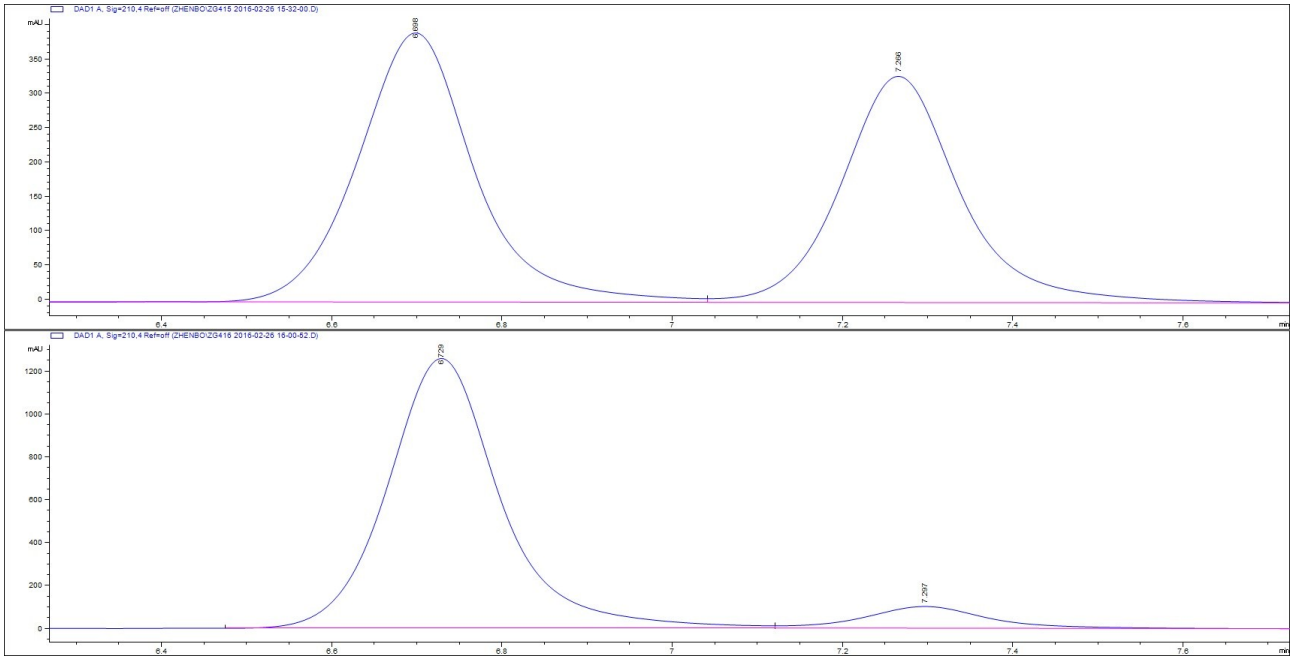
$[\alpha]^{20}_{589}$ = +1.0 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.

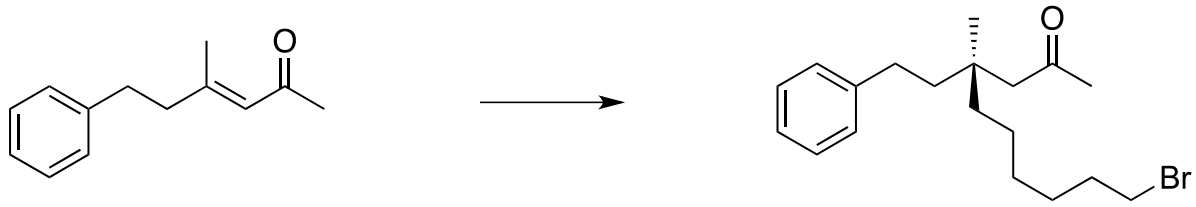

K (m)
7.16
J (m)
7.07
I (t)
3.43
G (s)
2.30
H (t)
2.42
F (s)
2.03
D (m)
1.53
B (m)
1.19
E (m)
1.68
C (m)
1.32
A (s)
0.94
Chemical Shift(ppm)


208.75
142.89
128.38
128.34
125.69
77.35 CDCl3
77.03 CDCl3
76.72 CDCl3
51.62
45.14
41.65
39.30
36.21
32.65
30.41
29.66
26.92
25.11
23.59
A (s)
208.75
B (s)
142.89
C (s)
128.38
D (s)
128.34
E (s)
125.69
F (s)
51.62
G (s)
45.14
H (s)
41.65
I (s)
39.30
J (s)
36.21
K (s)
32.65
L (s)
30.41
M (s)
29.66
N (s)
26.92
O (s)
25.11
P (s)
23.59
Chemical Shift(ppm)

HPLC trace



(-)-(*R*)-9-bromo-4-methyl-4-phenethylnonan-2-one (3t)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol) 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 (5.6 mg, 0.022 mmol, 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 5-bromo-1 pentene (0.06ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (38 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127

ml,1.0 mmol, 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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. (37 mg, 55% yield, 87% *ee*)

HPLC analysis indicated an enantiomeric excess of 87 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99:1; λ = 210 nm; major enantiomer tR = 6.22 min; minor enantiomer, tR = 6.73 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.25 – 7.16 (m, 2H, Ar-*H*), 7.15 – 7.06 (m, 3H, Ar-*H*), 3.34 (t, *J* = 6.8 Hz, 2H, C*H*$_2$Br), 2.62 – 2.40 (m, 2H, PhC*H*$_2$), 2.33 (s, 2H, C*H*$_2$COCH$_3$), 2.07 (s, 3H, COC*H*$_3$), 1.80 (dq, *J* = 8.9 Hz, 6.9 Hz, 2H, C*H*$_2$), 1.57 (ddd, *J* =11.9 Hz, 5.9 Hz, 3.2 Hz, 2H, C*H*$_2$), 1.48 – 1.29 (m, 4H, C*H*$_2$), 1.29 – 1.10 (m, 2H, C*H*$_2$), 0.97 (s, 3H, C*H*$_3$).

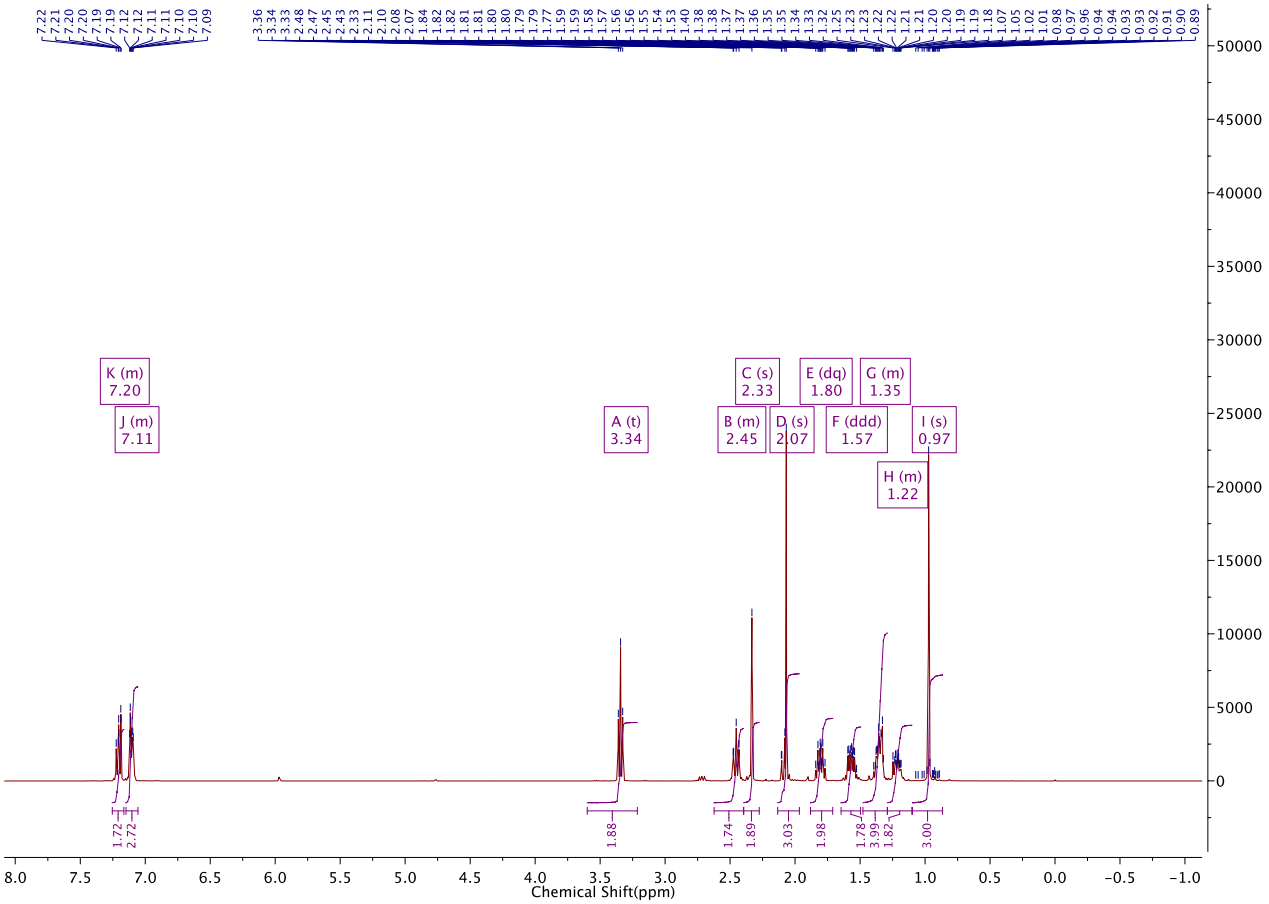
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 208.7, 142.8, 128.4(2C), 128.3(2C), 125.7, 51.6, 41.6, 39.2, 36.2, 33.9, 32.7, 32.7, 30.4, 28.9, 25.1, 22.9.

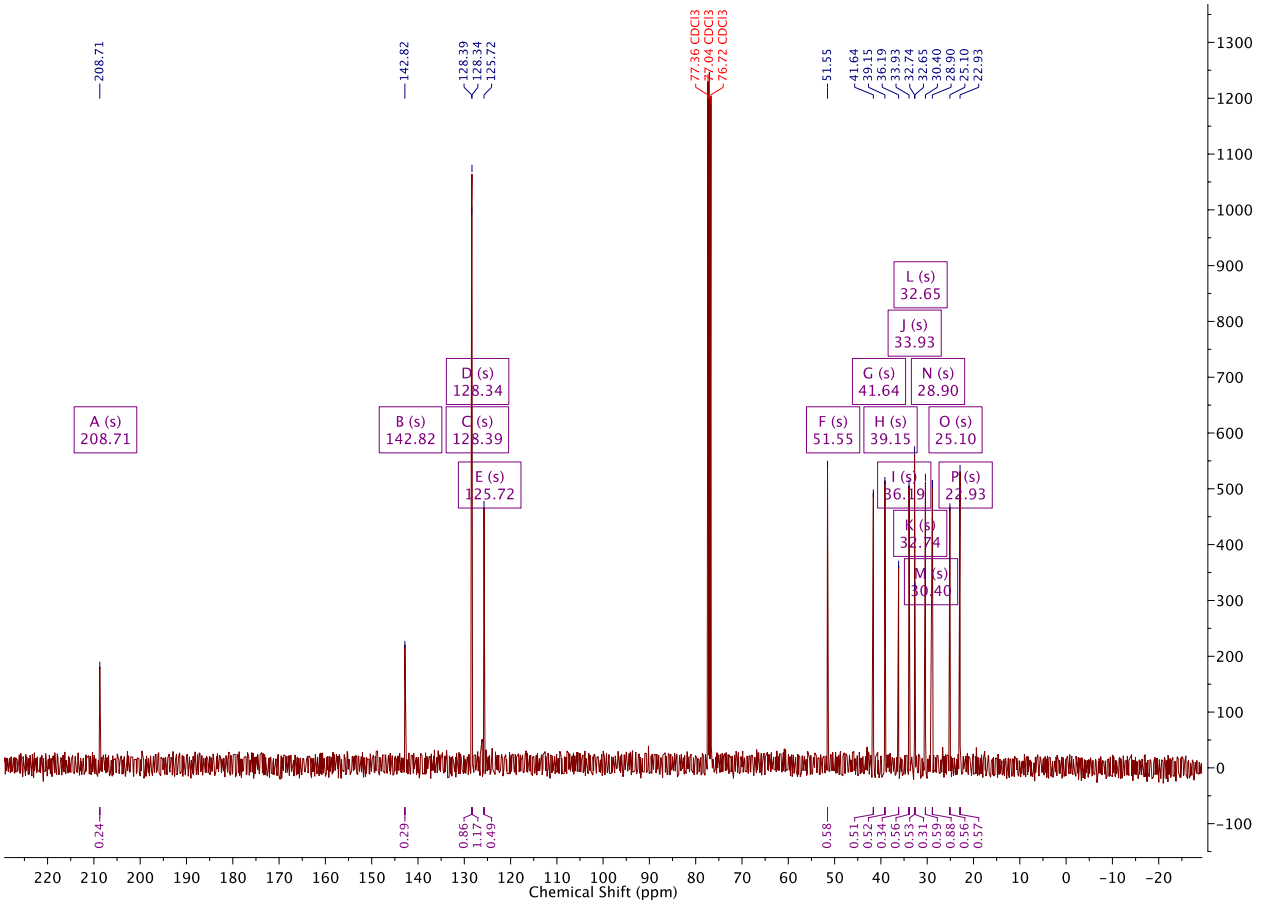
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2981,2885,1510,1381,1165,956,741

MS (ESI) m/z calc. for $C_{19}H_{30}O^{79}Br$ [M+Na]$^+$: 353.1475, found: 353.1473

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

Absolute configuration assigned by analogy to compound 3b.


K (m)
7.20
J (m)
7.11
A (t)
3.34
C (s)
2.33
B (m)
2.45
D (s)
2.07
E (dq)
1.80
F (ddd)
1.57
G (m)
1.35
I (s)
0.97
H (m)
1.22
Chemical Shift(ppm)


A (s)
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B (s)
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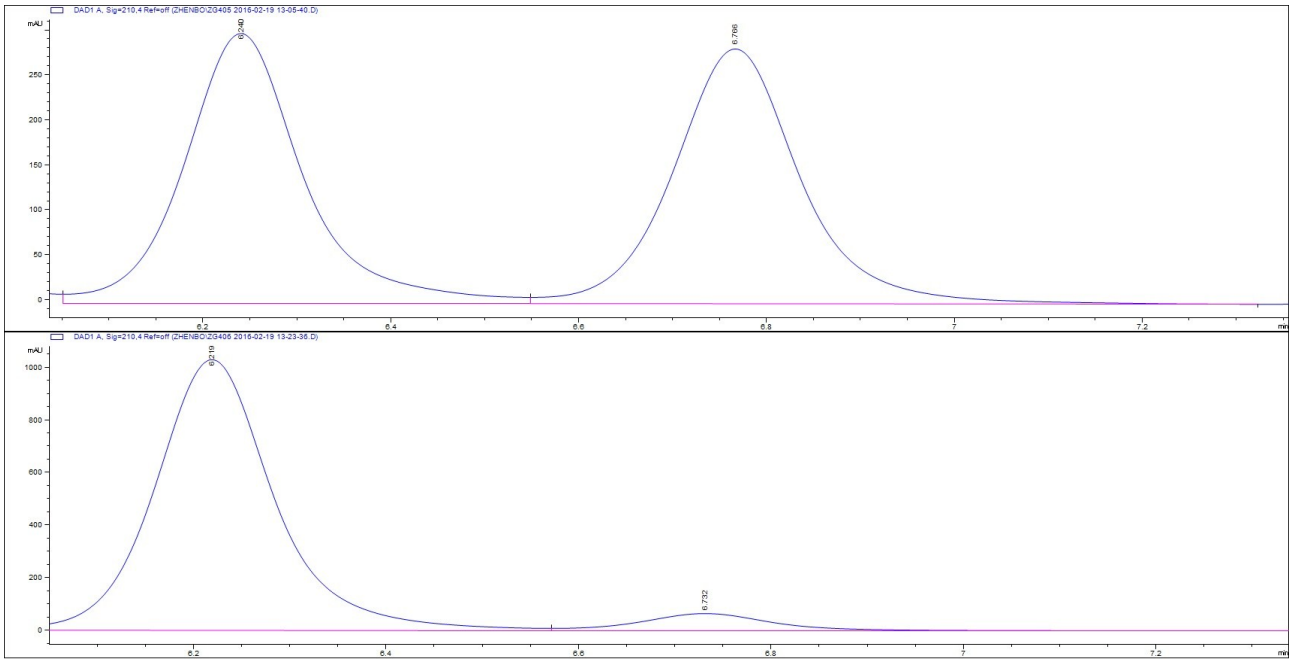
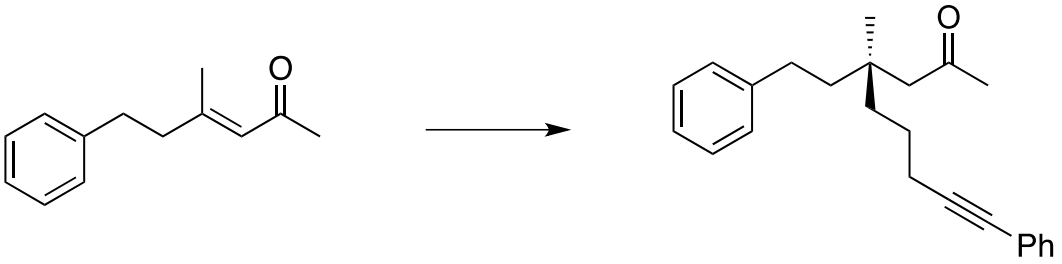
C (s)
128.39
D (s)
128.34
E (s)
125.72
F (s)
51.55
G (s)
41.64
H (s)
39.15
I (s)
36.19
J (s)
33.93
K (s)
32.74
L (s)
32.65
M (s)
30.40
N (s)
28.90
O (s)
25.10
P (s)
22.93
Chemical Shift (ppm)

HPLC trace



(-)-(*R*)-4-methyl-4-phenethyl-8-phenyloct-7-yn-2-one (3u)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol) 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 (5.6 mg, 0.022 mmol, 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 pent-4-en-1-yn-1- ylbenzene (0.08ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (38 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127

ml,1.0 mmol, 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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. (34mg, 52% yield, 78%*ee*)

HPLC analysis indicated an enantiomeric excess of 78 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 98:2; λ = 210 nm; major enantiomer tR = 19.18 min; minor enantiomer, tR = 20.44 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.51 – 7.36 (m, 2H, Ar-*H*), 7.35 – 7.26 (m, 5H, Ar-*H*), 7.22 (dt, *J* = 7.8 Hz, 1.9 Hz, 3H, Ar-*H*), 2.70 – 2.52 (m, 2H, PhCH_2), 2.52 – 2.39 (m, 4H, CH_2), 2.18 (s, 3H, COCH_3), 1.75 – 1.67 (m, 2H, CH_2), 1.67 – 1.56 (m, 4H, CH_2), 1.12 (s, 3H, CH_3).

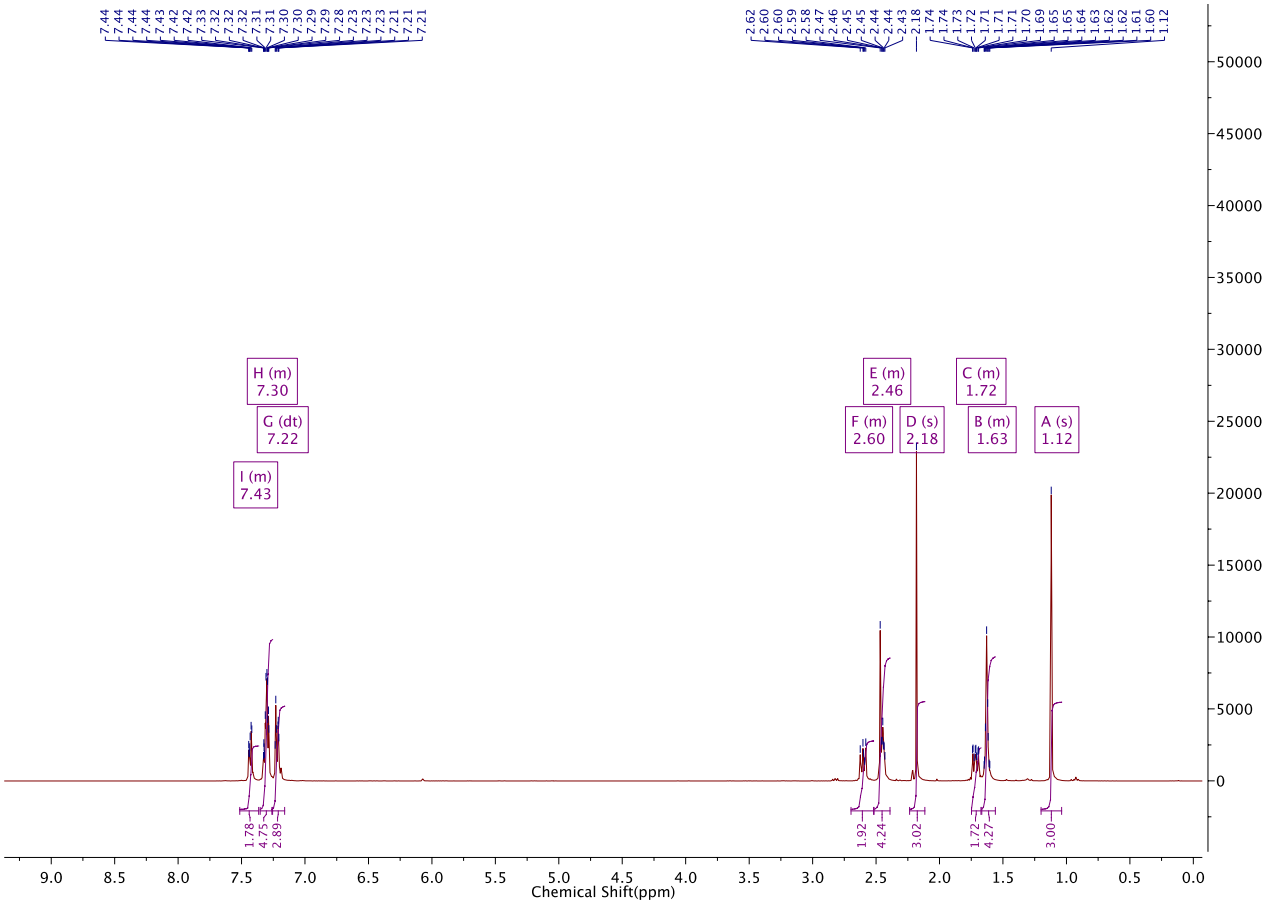
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 208.5, 142.8, 131.6, 128.5(2C), 128.4(2C), 128.2(2C), 127.6(2C), 125.7, 123.9, 90.1, 80.9, 51.6, 41.6, 38.6, 36.1, 32.6, 30.4, 25.1, 23.4, 20.1.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2981,2388,1712,1380,1154,755,667

MS (ESI) m/z calc. for $C_{24}H_{29}O$ $[M+H]^+$ 333.2213:, found: 333.2216

$[\alpha]^{20}_{589}$ = -1.1° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.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G (dt)
7.22
I (m)
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E (m)
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F (m)
2.60
D (s)
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C (m)
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B (m)
1.63
A (s)
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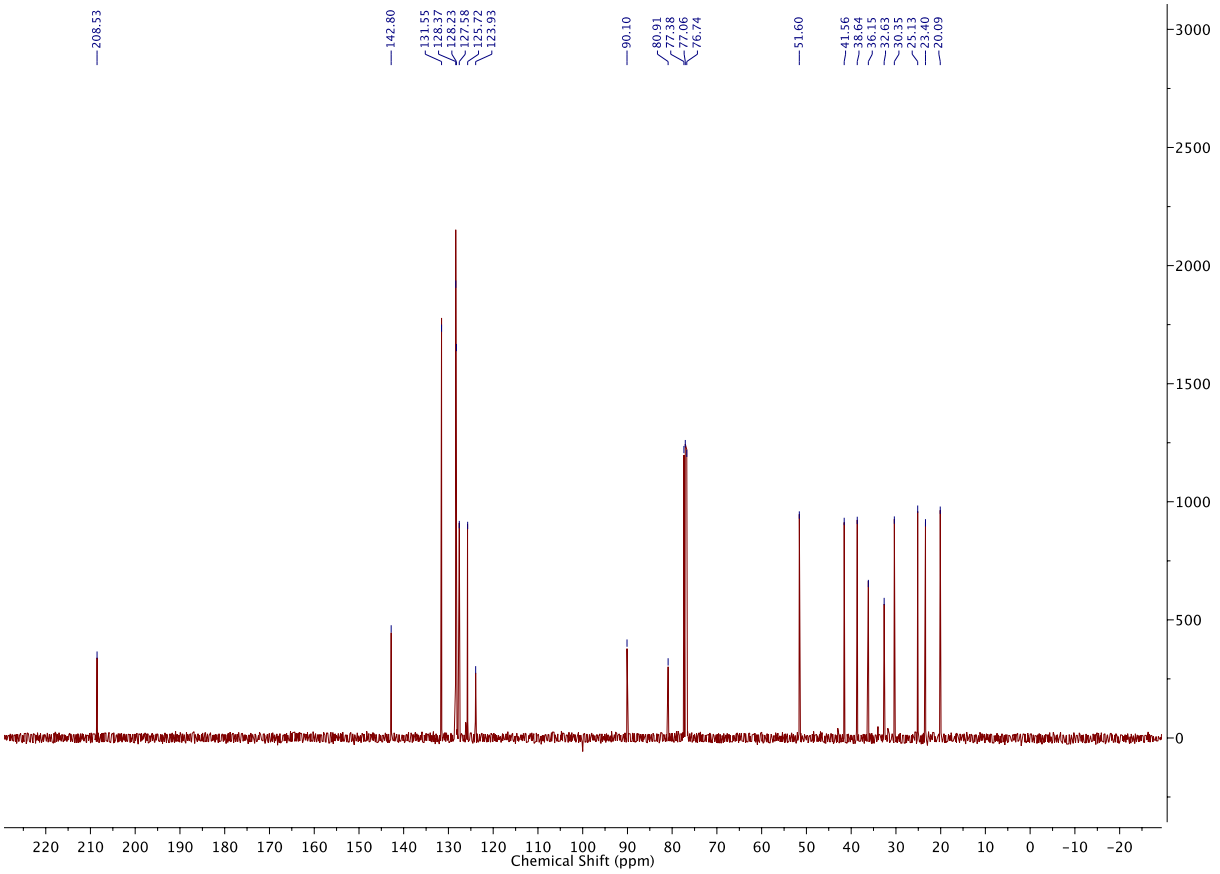
2.89
1.92
4.24
3.02
1.72
4.27
3.00
Chemical Shift(ppm)


208.53
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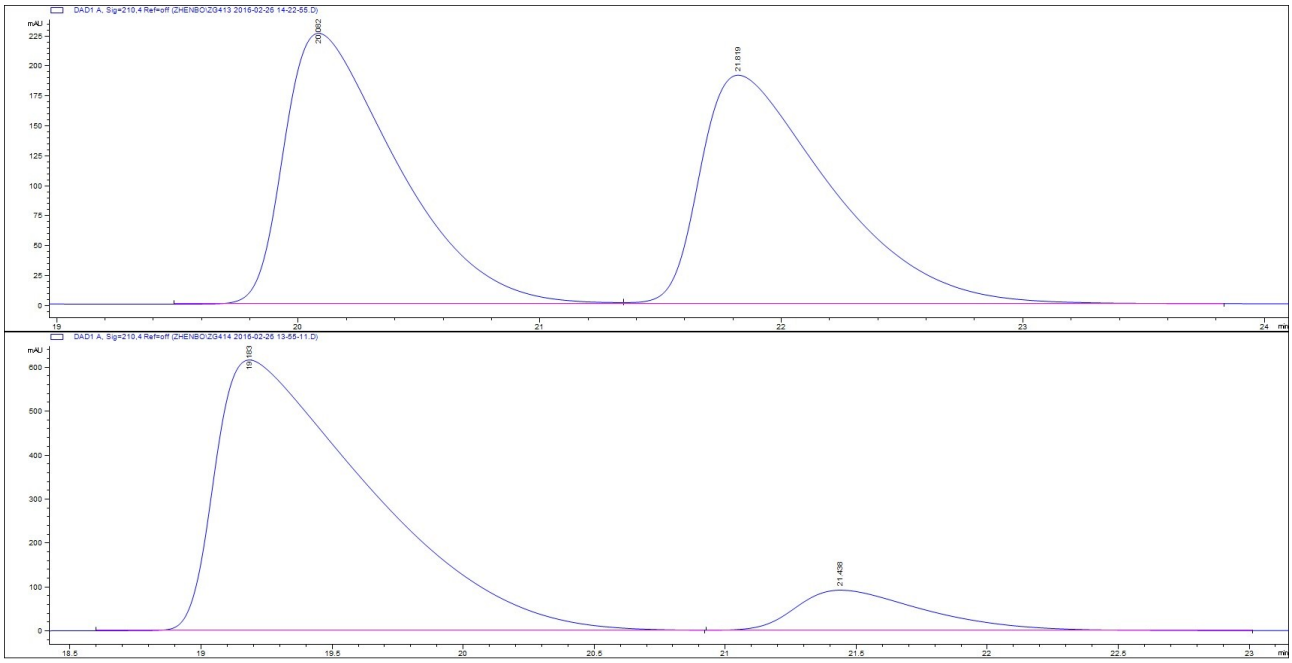
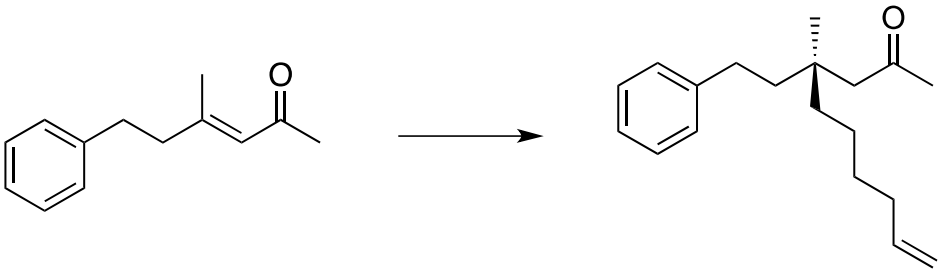
131.55
128.37
128.23
127.58
125.72
123.93
90.10
80.91
77.38
77.06
76.74
51.60
41.56
38.64
36.15
32.63
30.35
25.13
23.40
20.09
Chemical Shift (ppm)

HPLC trace



(+)-(*R*)-4-methyl-4-phenethyldec-9-en-2-one (3v)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol) 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 (5.6 mg, 0.022 mmol, 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 1,5-hexadiene (0.25ml, 2.0mmol, 10 eq.) in CH_2Cl_2 (0.4 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (38 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127

ml,1.0 mmol, 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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.(30 mg, 55% yield, 74% *ee*).

HPLC analysis indicated an enantiomeric excess of 91 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99:1; λ = 210 nm; major enantiomer tR = 4.62 min; minor enantiomer, tR = 4.82 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δH/ppm 7.23 – 7.16 (m, 2H, Ar-*H*), 7.14 – 7.06 (m, 3H, Ar-*H*), 5.74 (ddt, *J* = 16.9 Hz, 10.2 Hz, 6.7 Hz, 1H,C*H*=CH_2), 5.13 – 4.54 (m, 2H, CH=CH_2), 2.56 – 2.38 (m, 2H, PhCH_2), 2.33 (s, 2H, CH_2COCH_3), 2.06 (s, 3H, COCH_3), 2.05 – 1.95 (m, 2H, PhCH_2CH_2), 1.61 – 1.52 (m, 2H, CH_2), 1.38 – 1.25 (m, 4H, CH_2), 1.21 (tdd, *J* = 10.3 Hz, 6.2 Hz, 2.8 Hz, 2H, CH_2), 0.97 (s, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δC/ppm 208.8, 142.9, 139.0, 128.4(4C), 125.7, 114.4, 51.7, 41.6, 39.2, 36.3, 33.7, 32.6, 30.4, 29.6, 25.1, 23.1.

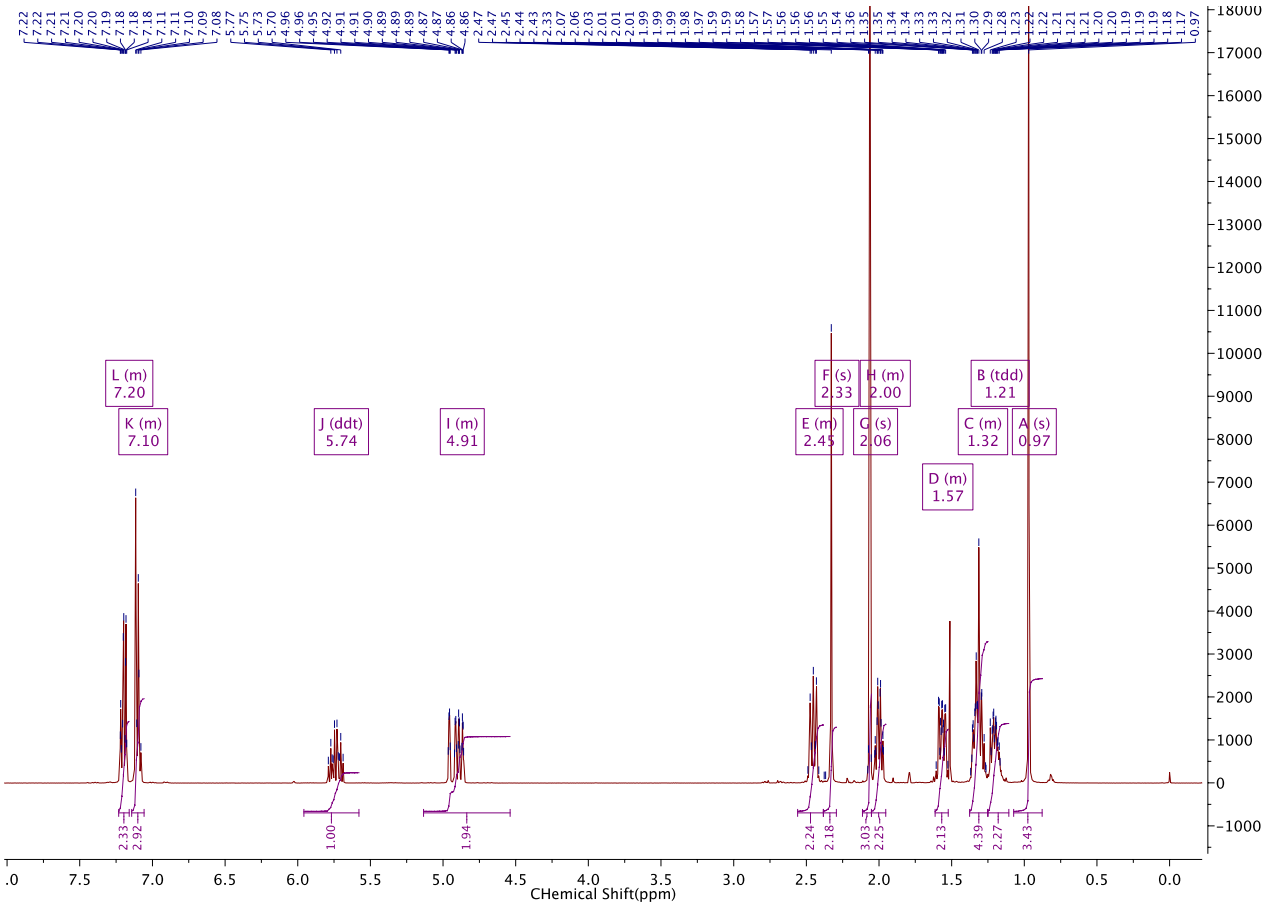
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2980,2888,1382,1252,1152,955

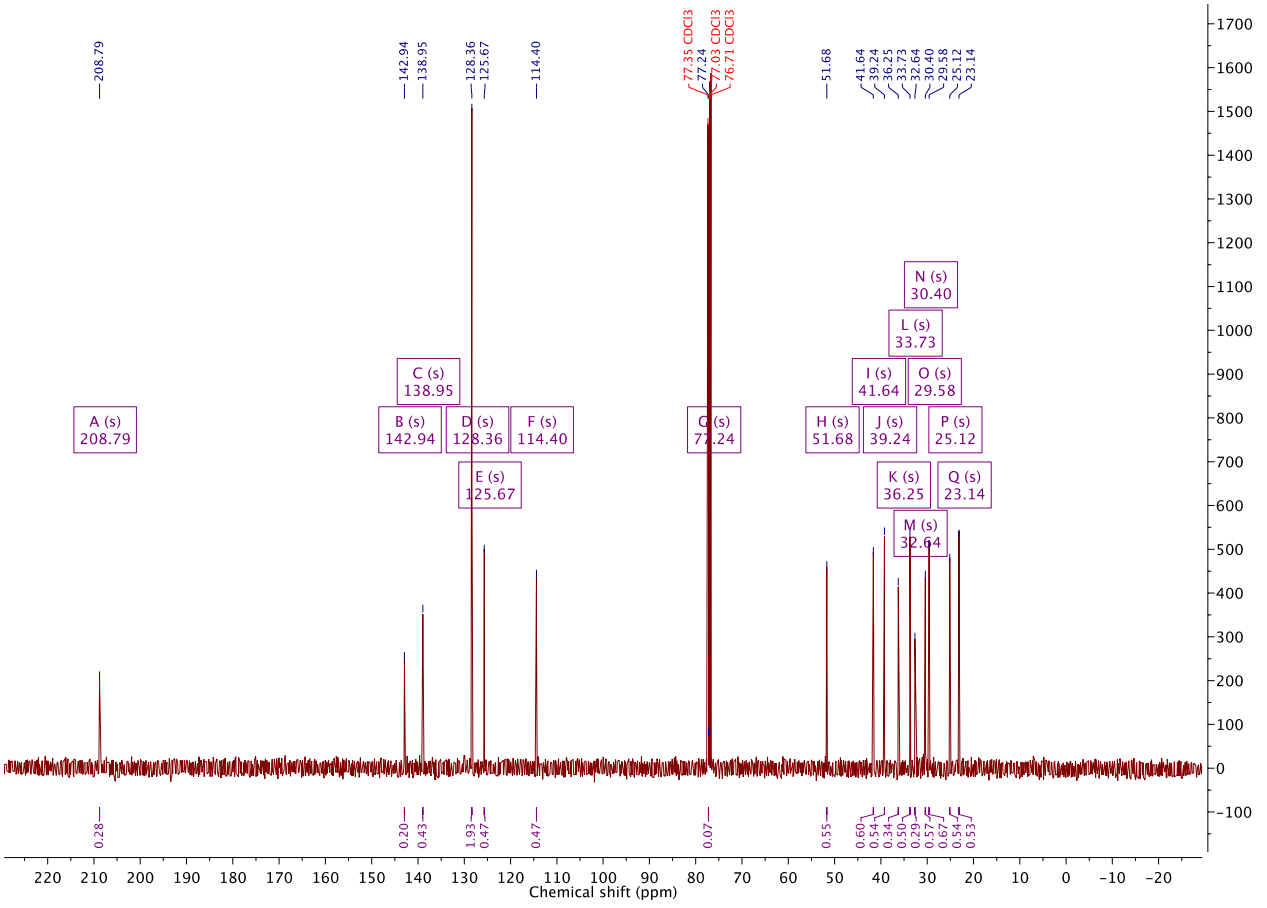
MS (ESI) m/z calc. for $C_{19}H_{29}O$ $[M+H]^+$: 273.2213, found: 273.2215

$[\alpha]^{20}_{589}$ = +0.7 ° (c 1.0, $CHCl_3$)

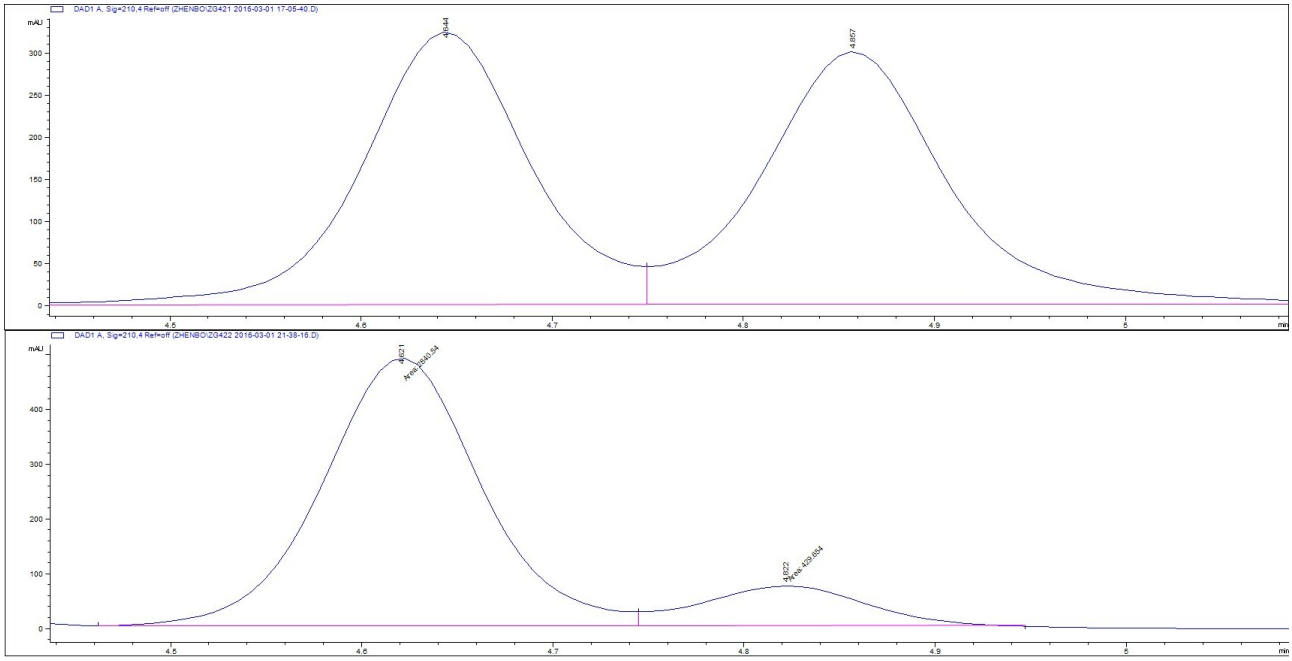
Absolute configuration assigned by analogy to compound 3b

.

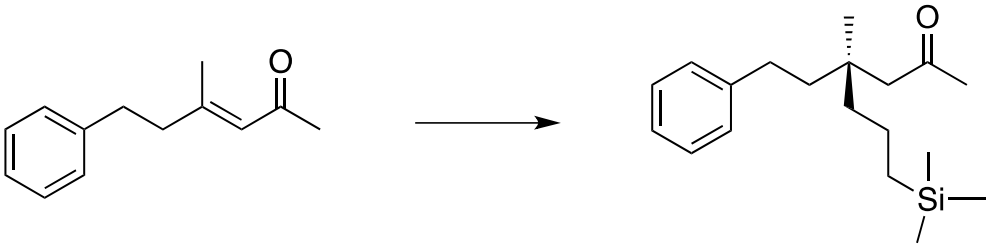

L (m)
7.20
K (m)
7.10
J (ddt)
5.74
I (m)
4.91
F (s)
2.33
H (m)
2.00
E (m)
2.45
G (s)
2.06
B (tdd)
1.21
C (m)
1.32
A (s)
0.97
D (m)
1.57
CHemical Shift(ppm)


A (s)
208.79
C (s)
138.95
B (s)
142.94
D (s)
128.36
F (s)
114.40
E (s)
125.67
G (s)
77.24
H (s)
51.68
I (s)
41.64
J (s)
39.24
K (s)
36.25
L (s)
33.73
M (s)
32.64
N (s)
30.40
O (s)
29.58
P (s)
25.12
Q (s)
23.14
Chemical shift (ppm)

HPLC trace



(+)-(*S*)-4-methyl-4-phenethyl-7-(trimethylsilyl)heptan-2-one (3w)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol) 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 (5.6 mg, 0.022 mmol, 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 allyltrimethylsilane (0.07ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (38 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127 ml,1.0 mmol, 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). The combined organic materials were dried (Na_2SO_4), filtered, concentrated, and the resulting yellow residual purified by flash column chromatography (Petrol: Et_2O; 95:15; SiO_2) to give the desired product. (25 mg, 42% yield, 88% *ee*)

HPLC analysis indicated an enantiomeric excess of 91 % [Chiralpak® AYH; flow: 1.0 mL/min; hexane/i-PrOH: 99.5:0.5; λ = 210 nm; major enantiomer tR = 5.73 min; minor enantiomer, tR = 6.39 min].

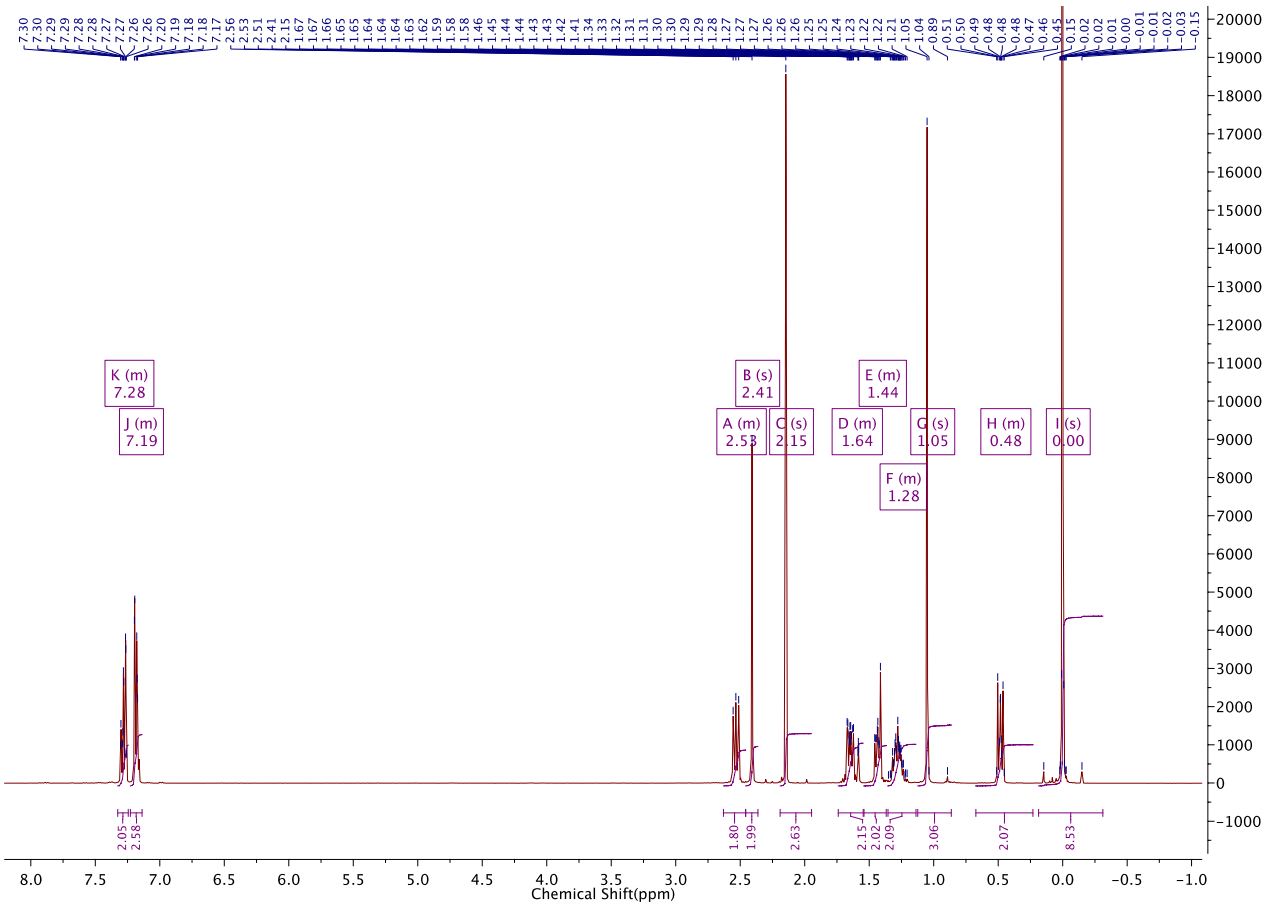
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.33 – 7.24 (m, 2H, Ar-*H*), 7.23 – 7.14 (m, 3H, Ar-*H*), 2.63 – 2.46 (m, 2H, PhC*H*$_2$), 2.41 (s, 2H, C*H*$_2$COCH$_3$), 2.15 (s, 3H, COC*H*$_3$), 1.74 – 1.55 (m, 2H, PhCH$_2$C*H*$_2$), 1.54 – 1.37 (m, 2H, C*H*$_2$), 1.35 – 1.14 (m, 2H, C*H*$_2$), 1.05 (s, 3H, C*H*$_3$), 0.67 – 0.23 (m, 2H, C*H*$_2$ Si), 0.0 (s, 9H,SiC*H*$_3$).
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 210.4, 144.5, 129.9(2C), 129.9(2C), 127.2, 53.3, 45.4, 43.2, 38.0, 34.2, 32.0, 26.6, 19.5, 19.0, 0.0(3C)

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2980,2886,1382,1153, 1073,956

MS (ESI) m/z calc. for $C_{19}H_{33}O^{28}Si$ $[M+H]^+$: 305.2295, found: 305.2296

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

Absolute configuration assigned by analogy to compound 3b.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J (m)
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E (m)
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H (m)
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I (s)
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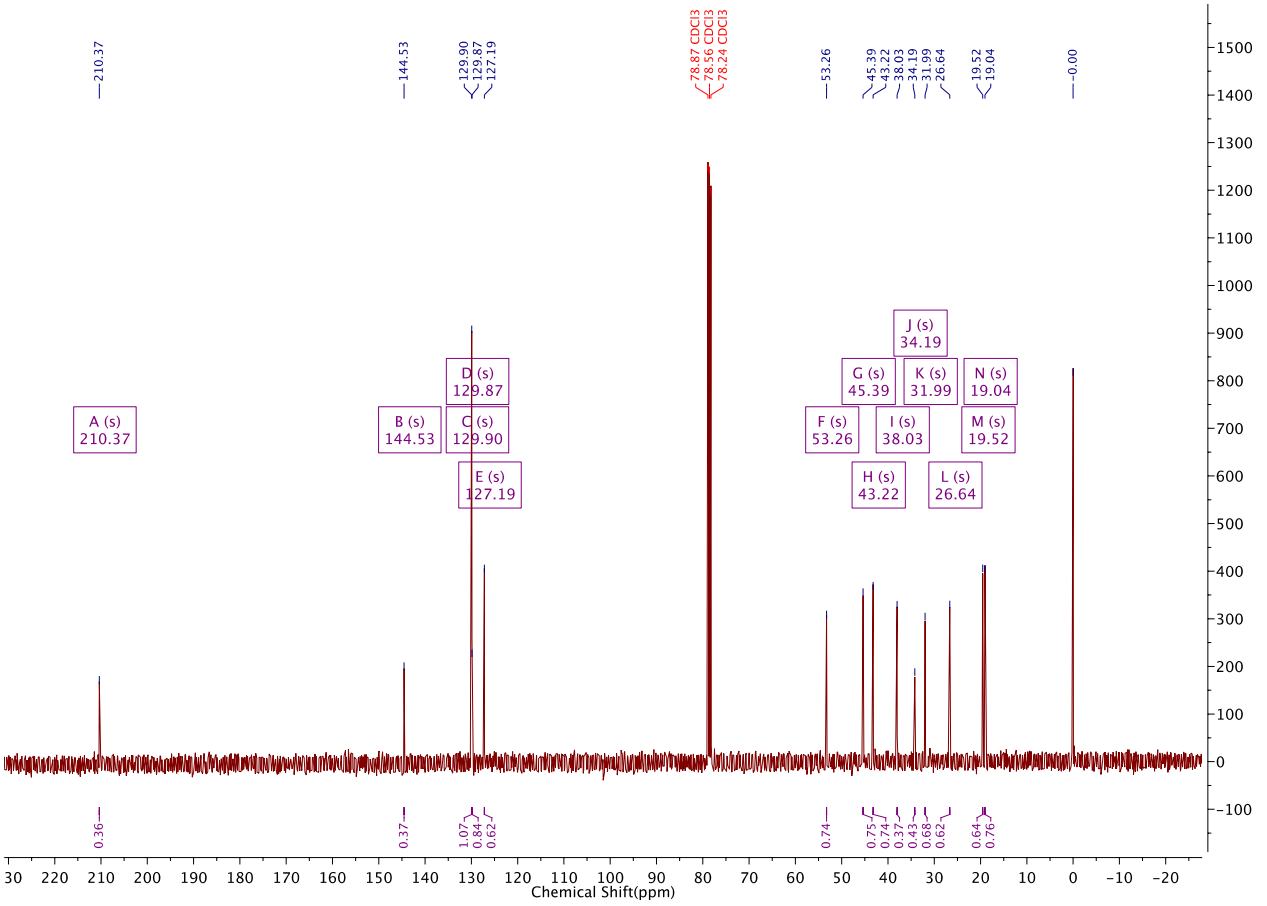
Chemical Shift(ppm)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B (s)
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C (s)
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E (s)
127.19
J (s)
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G (s)
45.39
K (s)
31.99
N (s)
19.04
F (s)
53.26
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M (s)
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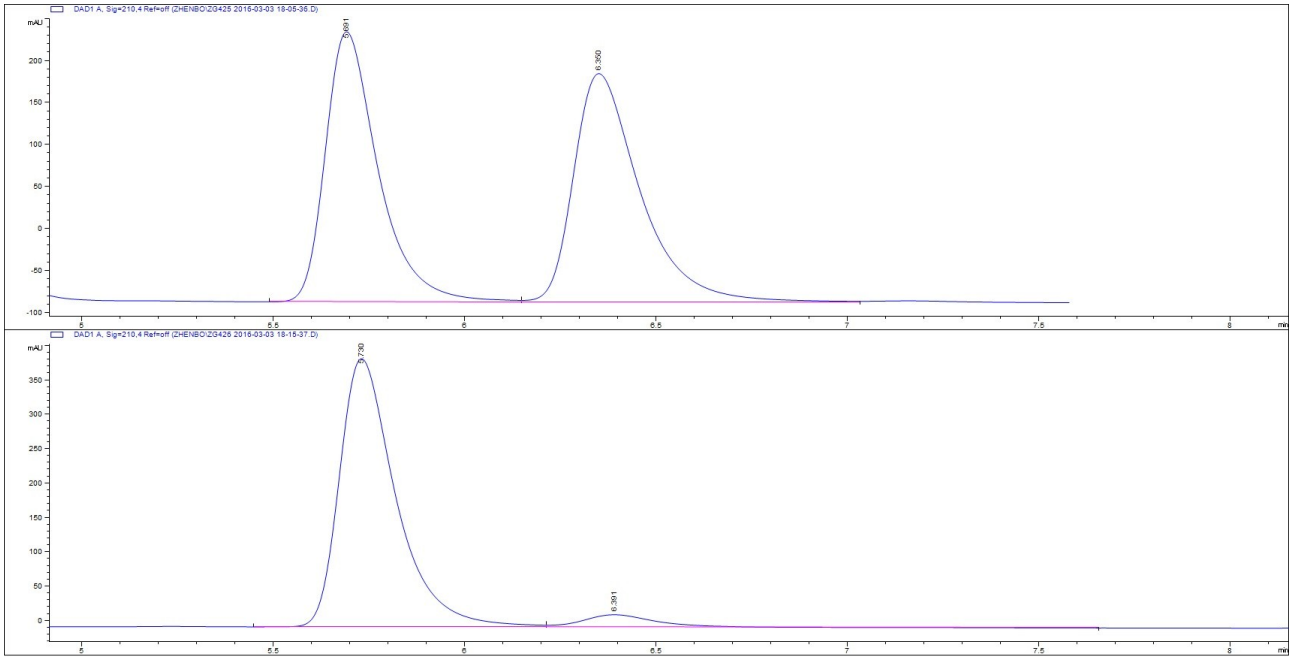
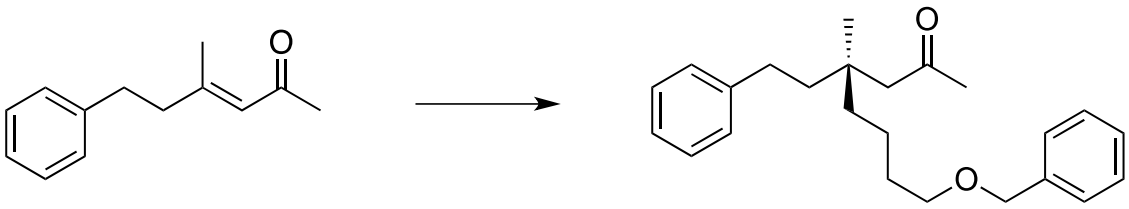
H (s)
43.22
L (s)
26.64
Chemical Shift(ppm)

HPLC trace



(+)-(*R*)-8-(benzyloxy)-4-methyl-4-phenethyloctan-2-one (3x)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol) 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 (5.6 mg, 0.022 mmol, 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 4-benzyloxy-1-butene (0.08ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (38 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127

ml,1.0 mmol, 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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. (38mg, 54% yield, 82% *ee*)

HPLC analysis indicated an enantiomeric excess of 82% % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99:1; λ = 210 nm; major enantiomer tR = 7.57 min; minor enantiomer, tR = 8.36 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.31 – 7.23 (m, 4H, Ar-*H*), 7.23 – 7.15 (m, 3H, Ar-*H*), 7.09 (ddt, *J* = 7.0 Hz, 3.6 Hz, 1.4, 3H, Ar-*H*), 4.43 (s, 2H, OCH_2Ph), 3.41 (t, *J* = 6.5 Hz, 2H, OCH_2), 2.59 – 2.38 (m, 2H, PhCH_2), 2.33 (s, 2H CH_2COCH$_3$), 2.05 (s, 3H, CH$_2$COCH_3), 1.67 – 1.43 (m, 4H, CH_2), 1.45 – 1.15 (m, 4H, CH_2), 0.97(s, 3H, CH_3).

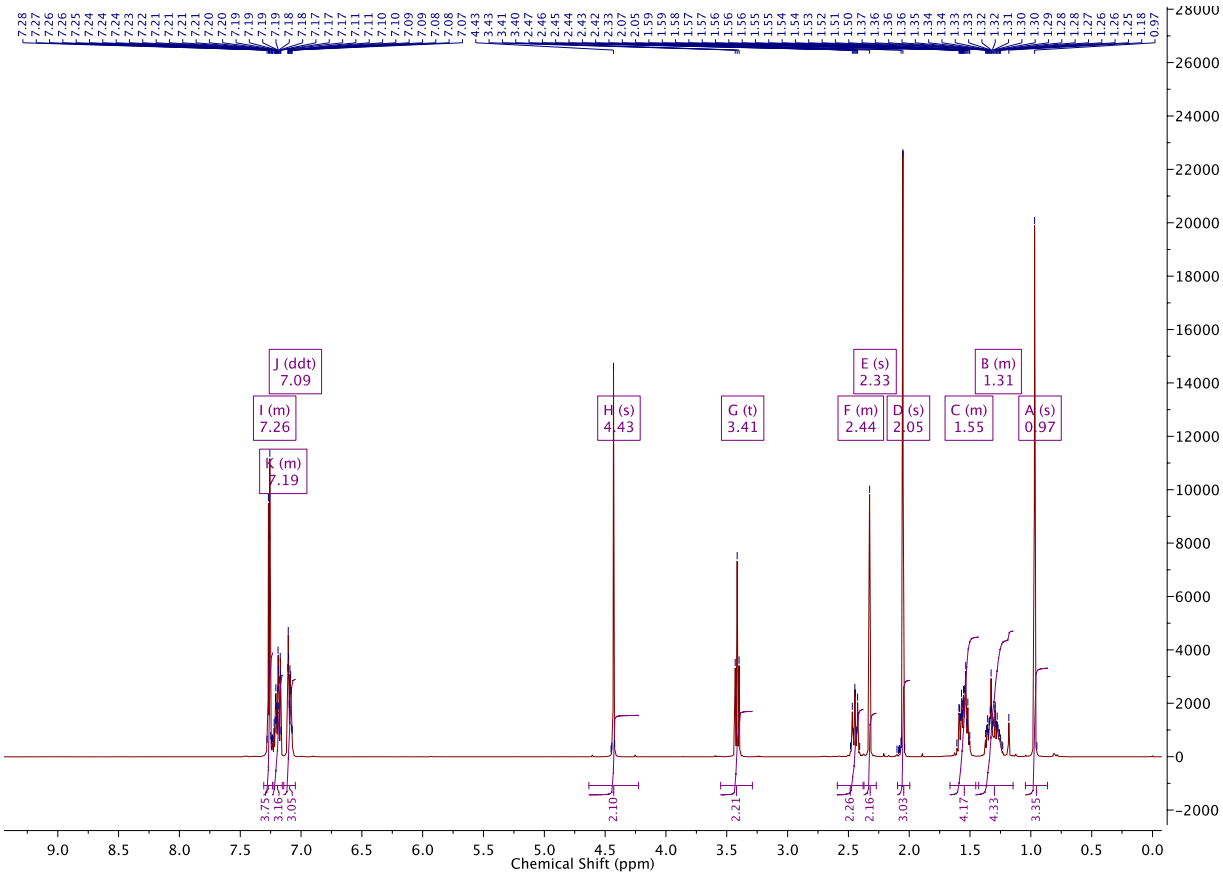
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 208.8, 142.9, 138.6, 128.4(4C), 127.7(3C), 127.5(2C), 125.7, 72.9, 70.2, 51.6, 41.6, 39.2, 36.2, 32.6, 30.4 (2C), 25.1, 20.4.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3659, 2981,2885,1510,1381,1165,956,741

MS (ESI) m/z calc. for $C_{24}H_{33}O_2$ $[M+H]^+$: 353.2475, found: 353.2476

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

Absolute configuration assigned by analogy to compound 3b.


J (ddt)
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I (m)
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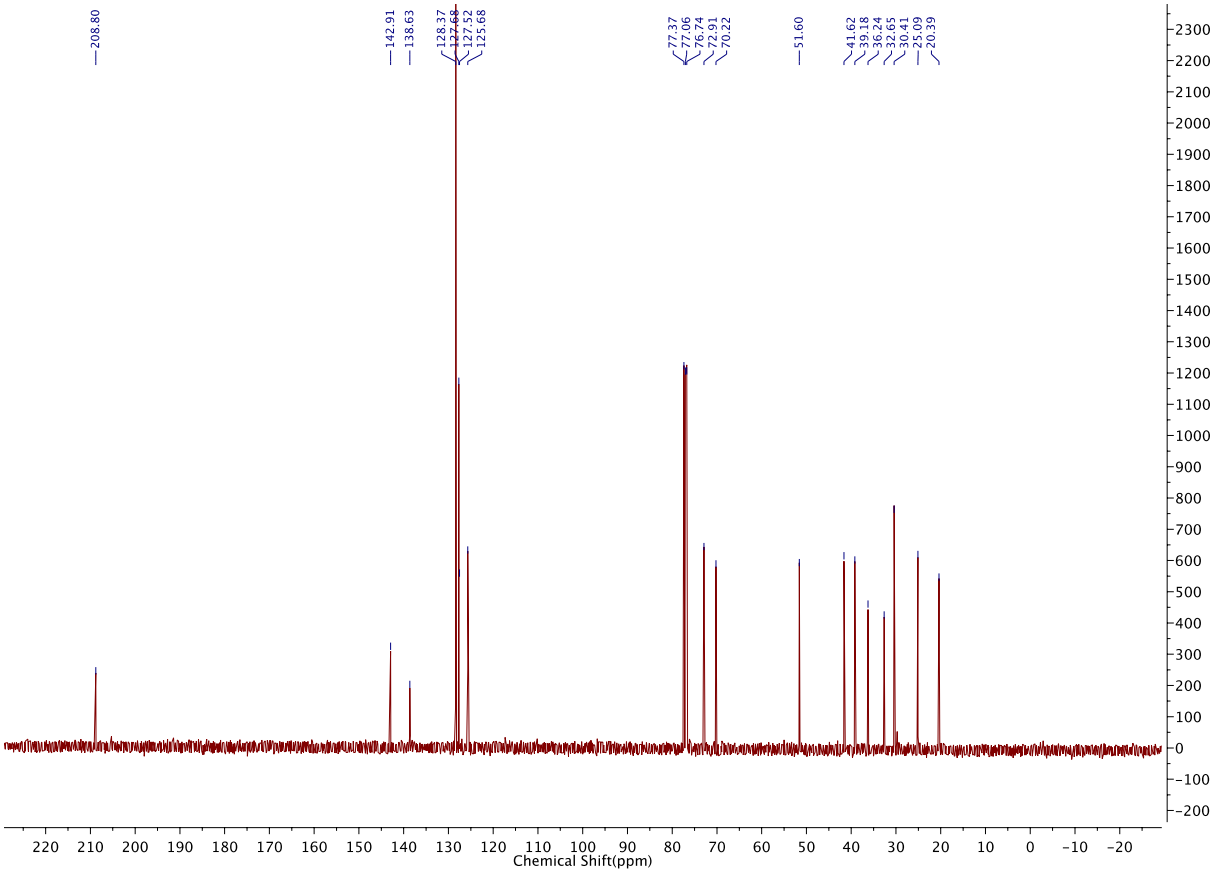
K (m)
7.19
H (s)
4.43
G (t)
3.41
E (s)
2.33
F (m)
2.44
D (s)
2.05
B (m)
1.31
C (m)
1.55
A (s)
0.97
Chemical Shift (ppm)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138.63
128.37
127.68
127.52
125.68
77.37
77.06
76.74
72.91
70.22
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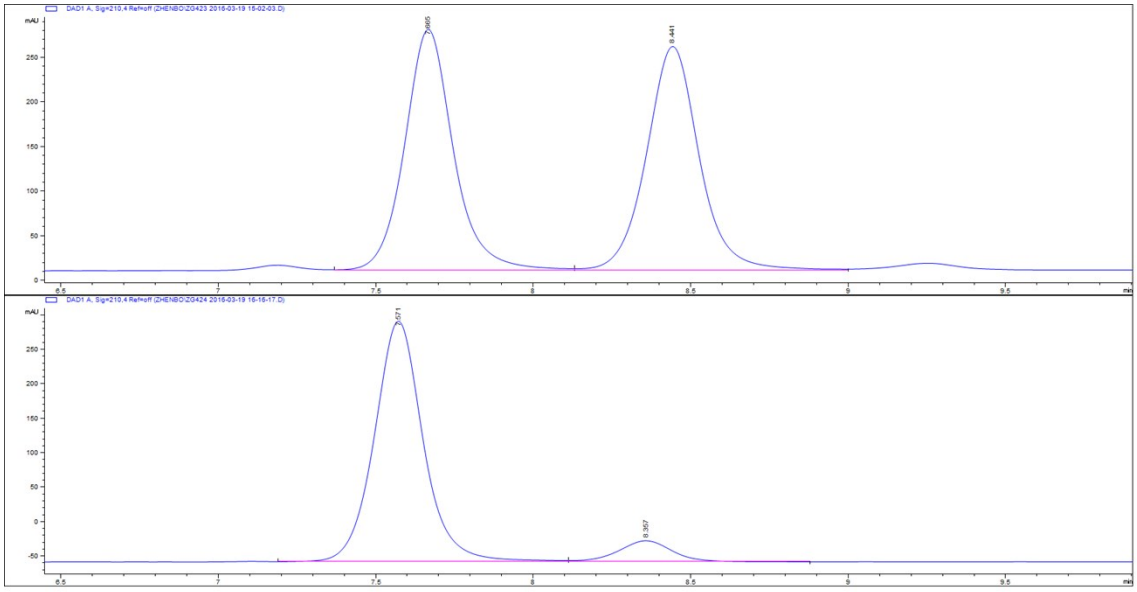
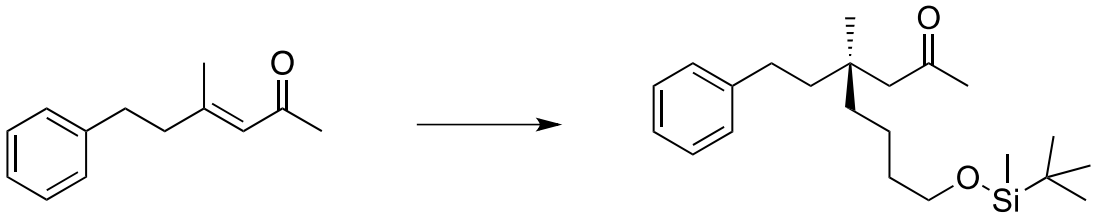
41.62
39.18
36.24
32.65
30.41
25.09
20.39
Chemical Shift(ppm)

HPLC trace



(+)-(*R*)-8-((*tert*-butyldimethylsilyl)oxy)-4-methyl-4-phenethyloctan-2-one (3y)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol) 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 (5.6 mg, 0.022 mmol, 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 4-[(tert-butyldimethylsilyl)oxy]-1-butene (0.11ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (38 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127 ml,1.0 mmol, 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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. (50 mg, 71% yield, 91% *ee*)

HPLC analysis indicated an enantiomeric excess of 91 % [Chiralpak® IB; flow: 1.0 mL/min; hexane/i-PrOH: 99.95:0.05; λ = 210 nm; minor enantiomer tR = 16.30 min; major enantiomer, tR = 16.65 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.26 – 7.16 (m, 2H, Ar-*H*), 7.16 – 7.07 (m, 3H, Ar-*H*), 3.57 (t, *J* = 6.4 Hz, 2H, C*H*$_2$O), 2.54 – 2.40 (m, 2H, PhC*H*$_2$), 2.35 (s, 2H, C*H*$_2$COCH$_3$), 2.08 (s, 3H, COC*H*$_3$), 1.68 – 1.52 (m, 2H, PhCH$_2$C*H*$_2$), 1.50 – 1.41 (m, 2H, C*H*$_2$), 1.41 – 1.32 (m, 2H, C*H*$_2$), 1.31 – 1.19 (m, 2H, C*H*$_2$), 0.99 (s, 3H, C*H*$_3$), 0.84 (s, 9H, C (C*H*$_3$)$_3$), -0.0 (s, 6H, SiC*H*$_3$).

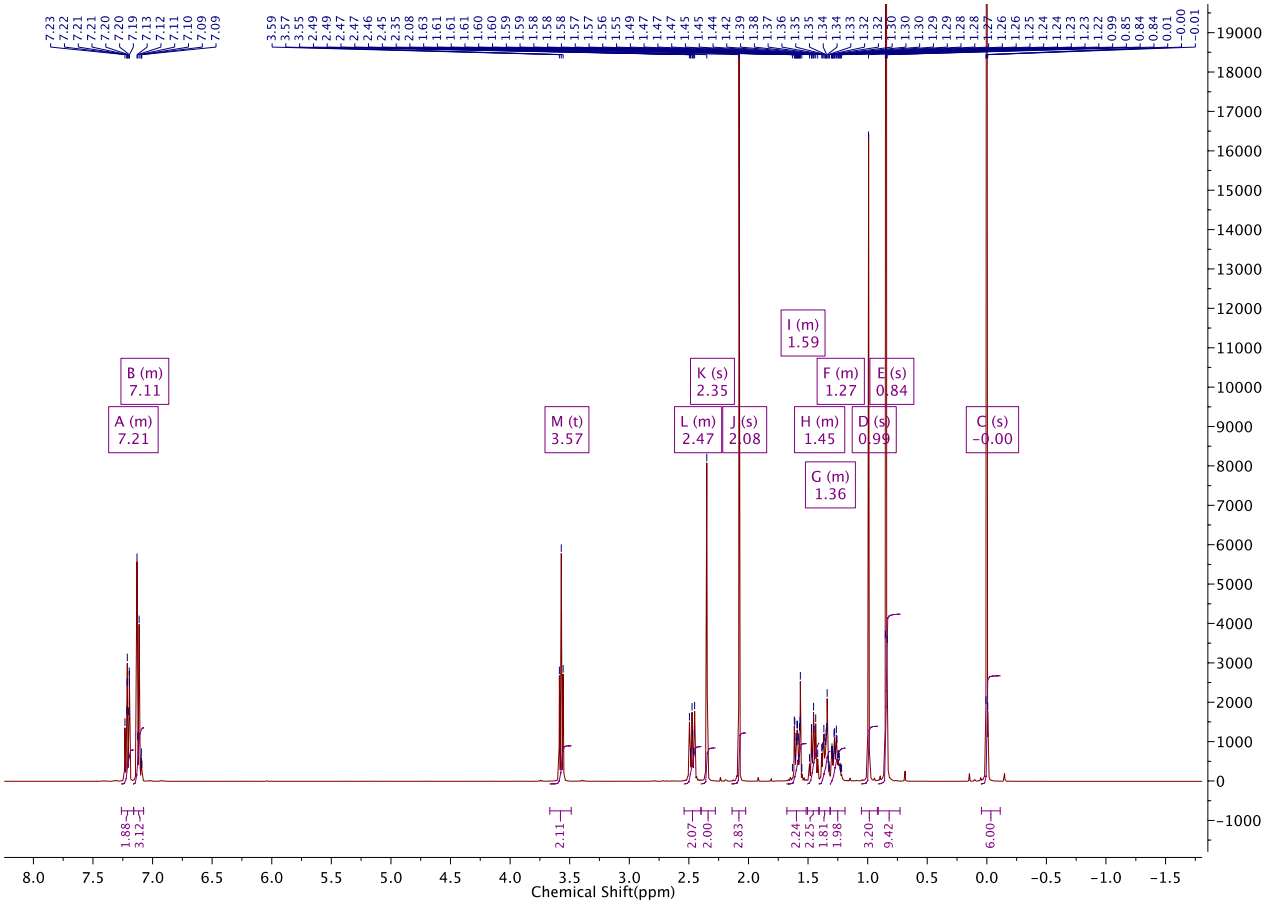
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 208.7, 142.9, 128.4(4C), 125.7, 63.1, 51.6, 41.6, 39.2, 36.3, 33.6, 32.6, 30.4, 26.0, 25.1, 20.0, 18.4, -5.2(3C).

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2980,2888,1383,1252,1073,955

MS (ESI) m/z calc. for $C_{23}H_{41}O_2{}^{28}Si$ $[M+H]^+$: 377.2870, found: 377.2877

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

Absolute configuration assigned by analogy to compound 3b.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L (m)
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J (s)
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I (m)
1.59
F (m)
1.27
E (s)
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D (s)
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G (m)
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C (s)
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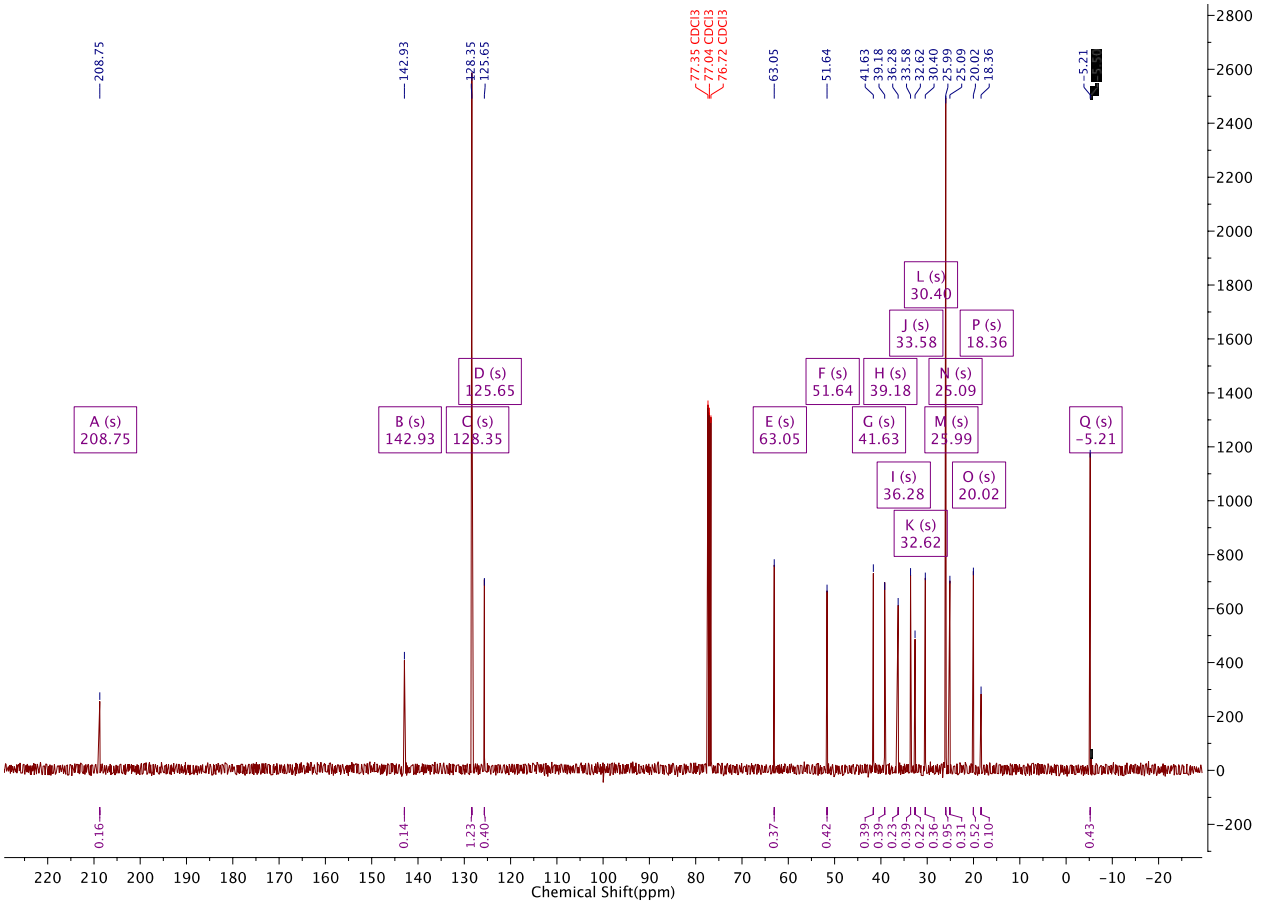
Chemical Shift(ppm)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D (s)
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E (s)
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F (s)
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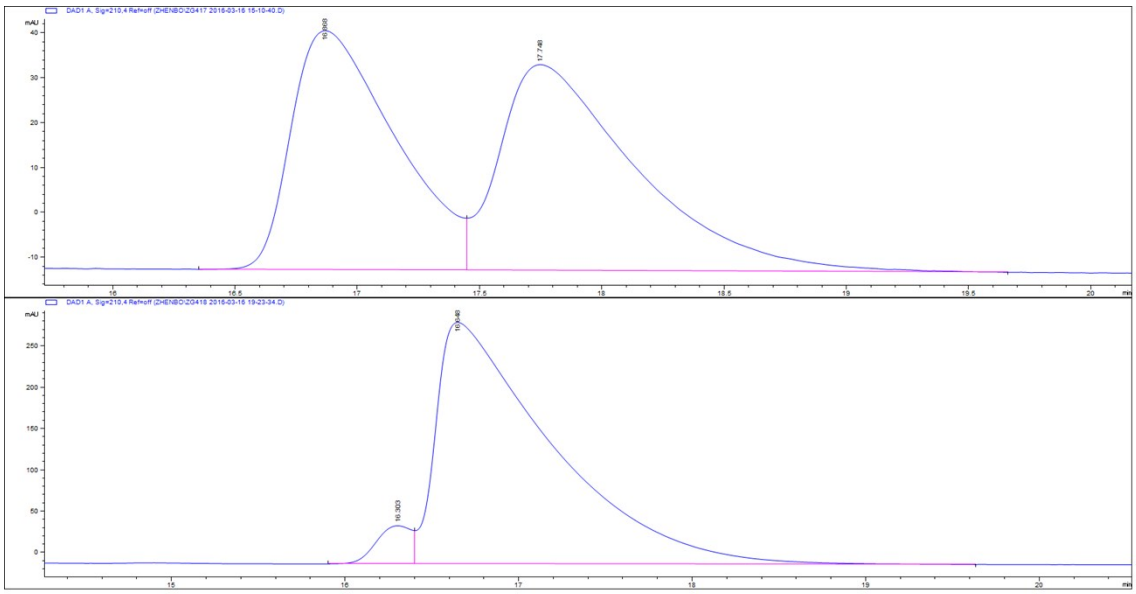
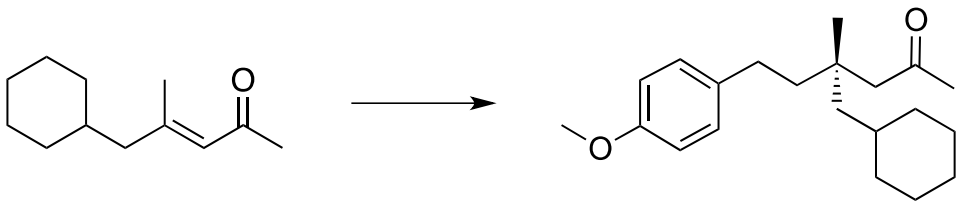
G (s)
41.63
H (s)
39.18
I (s)
36.28
J (s)
33.58
K (s)
32.62
L (s)
30.40
M (s)
29.99
N (s)
25.09
O (s)
20.02
P (s)
18.36
Q (s)
-5.21
Chemical Shift(ppm)

HPLC trace



(-)-(*R*)-4-(cyclohexylmethyl)-6-(4-methoxyphenyl)-4-methylhexan-2-one (3z)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol) 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 (5.6 mg, 0.022 mmol, 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 1-methoxy-4-vinylbenzene (0.07ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 2.0 eq.) , and after stirring for 15 min, a clear 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 enone (36 mg, 0.2 mol, 1.0 eq.) and TMSCl (0.127 ml,1.0 mmol, 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

1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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. (15 mg, 24% yield, 88% *ee*).

HPLC analysis indicated an enantiomeric excess of 88 % [Chiralpak® IA; flow: 1.0 mL/min; hexane/i-PrOH: 99.5:0.5; λ = 210 nm; minor enantiomer tR = 11.27 min; major enantiomer, tR = 11.73 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.18 – 7.04 (m, 2H, Ar-*H*), 6.90 – 6.69 (m, 2H, Ar-*H*), 3.78 (s, 3H, OC*H*$_3$), 2.48 (td, *J* = 9.2 Hz, 2.3Hz, 2H, PhC*H*$_2$), 2.42 (s, 2H, C*H*$_2$COCH$_3$), 2.13 (s, 3H, COC*H*$_3$), 1.80 – 1.51 (m, 6H,C*H*,C*H*$_2$), 1.37 – 1.27 (m, 3H, C*H*$_2$), 1.27 – 1.09 (m, 3H, C*H*$_2$), 1.09-0.91 (m, 6H, C*H*$_2$, C*H*$_3$).

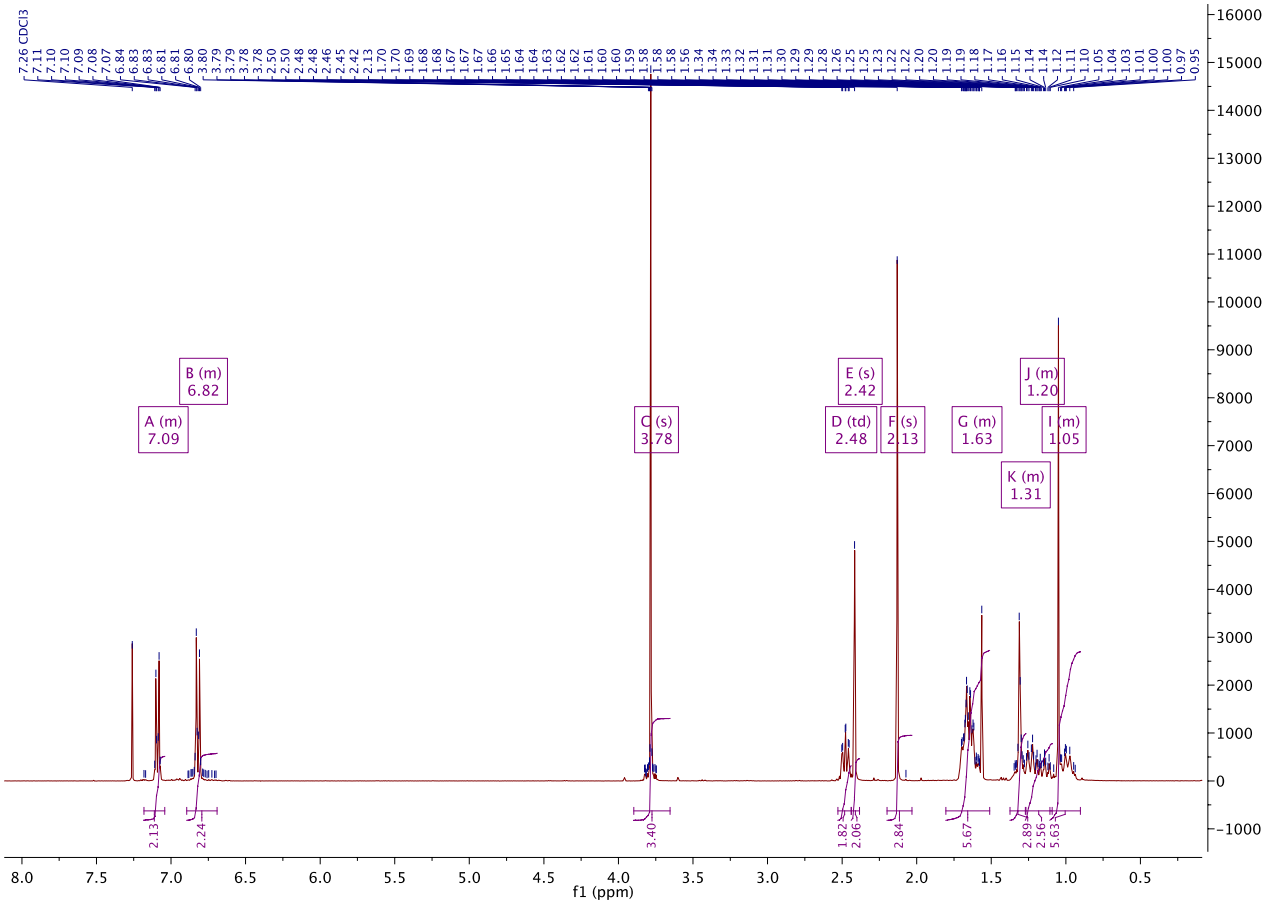
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 208.8, 157.7, 135.0, 129.2(2C), 113.8(2C), 55.3, 52.1, 47.1, 42.2, 36.9, 36.0(2C), 33.5, 32.7, 29.6, 26.6 (2C), 26.2, 25.5.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2980,2889,1383,1251,1152,1073,955,819

MS (ESI) m/z calc. for $C_{21}H_{33}O_2$ $[M+H]^+$: 317.2475, found: 317.2477

$[\alpha]^{20}_{589}$ = -1.7 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.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E (s)
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D (td)
2.48
F (s)
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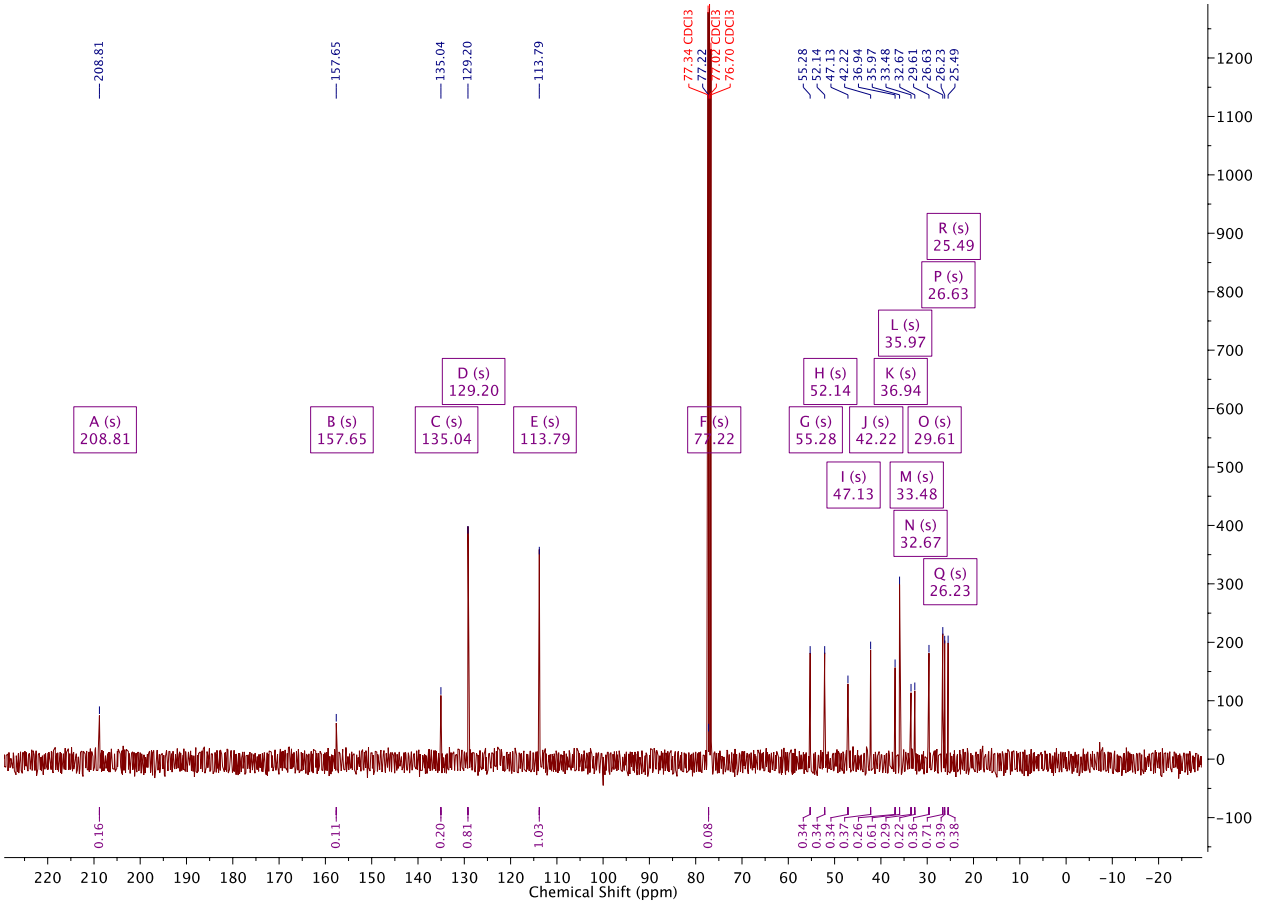
G (m)
1.63
J (m)
1.20
I (m)
1.05
K (m)
1.31
f1 (ppm)


A (s)
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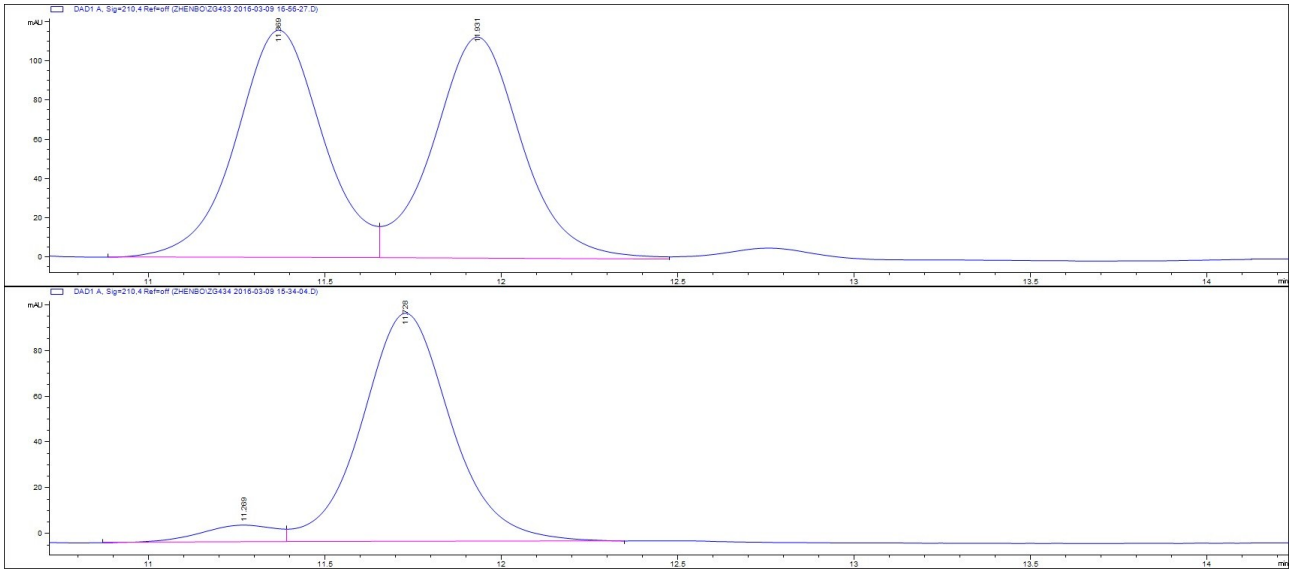
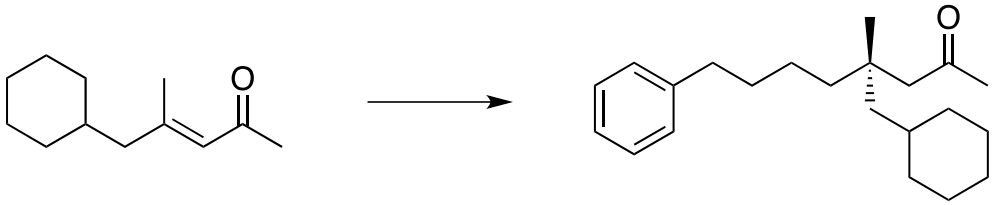
C (s)
135.04
D (s)
129.20
E (s)
113.79
F (s)
77.22
G (s)
55.28
H (s)
52.14
I (s)
47.13
J (s)
42.22
K (s)
36.94
L (s)
35.97
M (s)
33.48
N (s)
32.67
O (s)
29.61
P (s)
26.63
Q (s)
26.23
R (s)
25.49
Chemical Shift (ppm)

HPLC trace



(+)-(*R*)-4-(cyclohexylmethyl)-4-methyl-8-phenyloctan-2-one (3aa)



CuCl (1.9 mg, 0.02mmol, 0.1 eq.), and the phosphoramidite ligand **B** (11.6 mg, 0.02 mmol) 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 (5.6 mg, 0.022 mmol, 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 4-phenyl-1 butene (0.08ml, 0.5mmol, 2.5 eq.) in CH_2Cl_2 (0.2 mL), under an argon atmosphere was added Cp_2ZrHCl (103 mg, 0.4 mmol, 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 enone (36 mg, 0.2 mmol, 1.0 eq.) and TMSCl (0.127 ml,1.0 mmol, 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 1.5 mL NH_4Cl (sat. aq.) and then 3.0 mL Et_2O. The reaction mixture was partitioned between the aqueous and organic phases, and the aqueous layer extracted by Et_2O (3 x10 mL). 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. (23mg, 35% yield, 92% *ee*)

HPLC analysis indicated an enantiomeric excess of 92 % [Chiralpak® IE; flow: 0.8 mL/min; hexane/i-PrOH: 99.5:0.5; λ = 210 nm; major enantiomer tR = 9.96 min; minor enantiomer, tR = 10.97 min].

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.26 – 7.14 (m, 2H, Ar-*H*), 7.14 – 7.05 (m, 3H, Ar-*H*), 2.67 – 2.45 (m, 2H, PhCH_2), 2.25 (s, 2H, CH_2COCH_3), 2.02 (s, 3H,COCH_3), 1.73 – 1.44 (m, 8H, C$H_,$ CH_2), 1.37 – 1.26 (m, 2H, CH_2), 1.25 – 1.00 (m, 7H, CH_2), 0.89 (s, 3H, CH_3), 0.88 – 0.80 (m, 2H, CH_2).

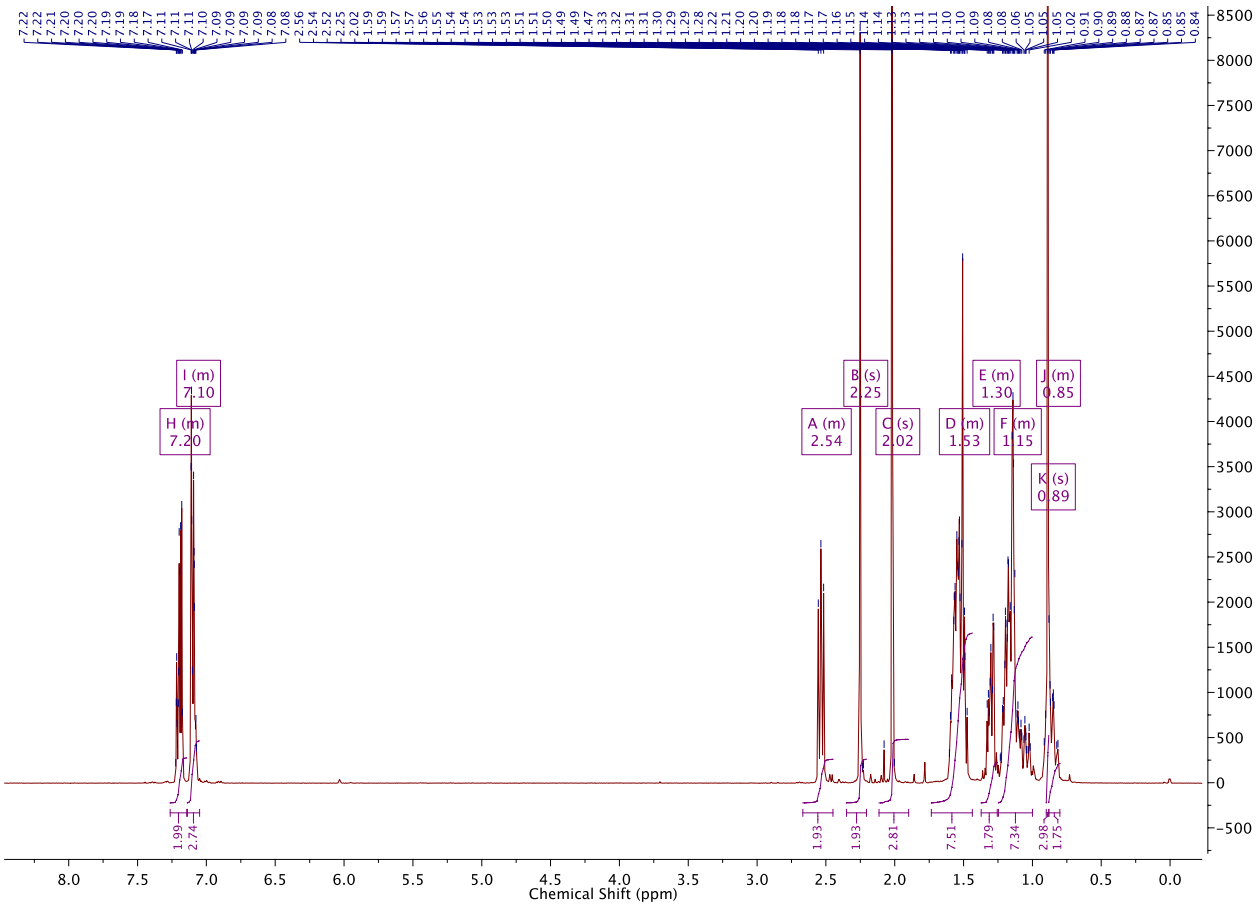
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 209.1, 142.7, 128.4(2C), 128.2(2C), 125.6, 52.2, 47.1, 39.6, 36.8, 35.9, 35.9, 33.4(2C), 32.6, 32.2, 26.6, 26.3, 25.5(2C), 23.6.

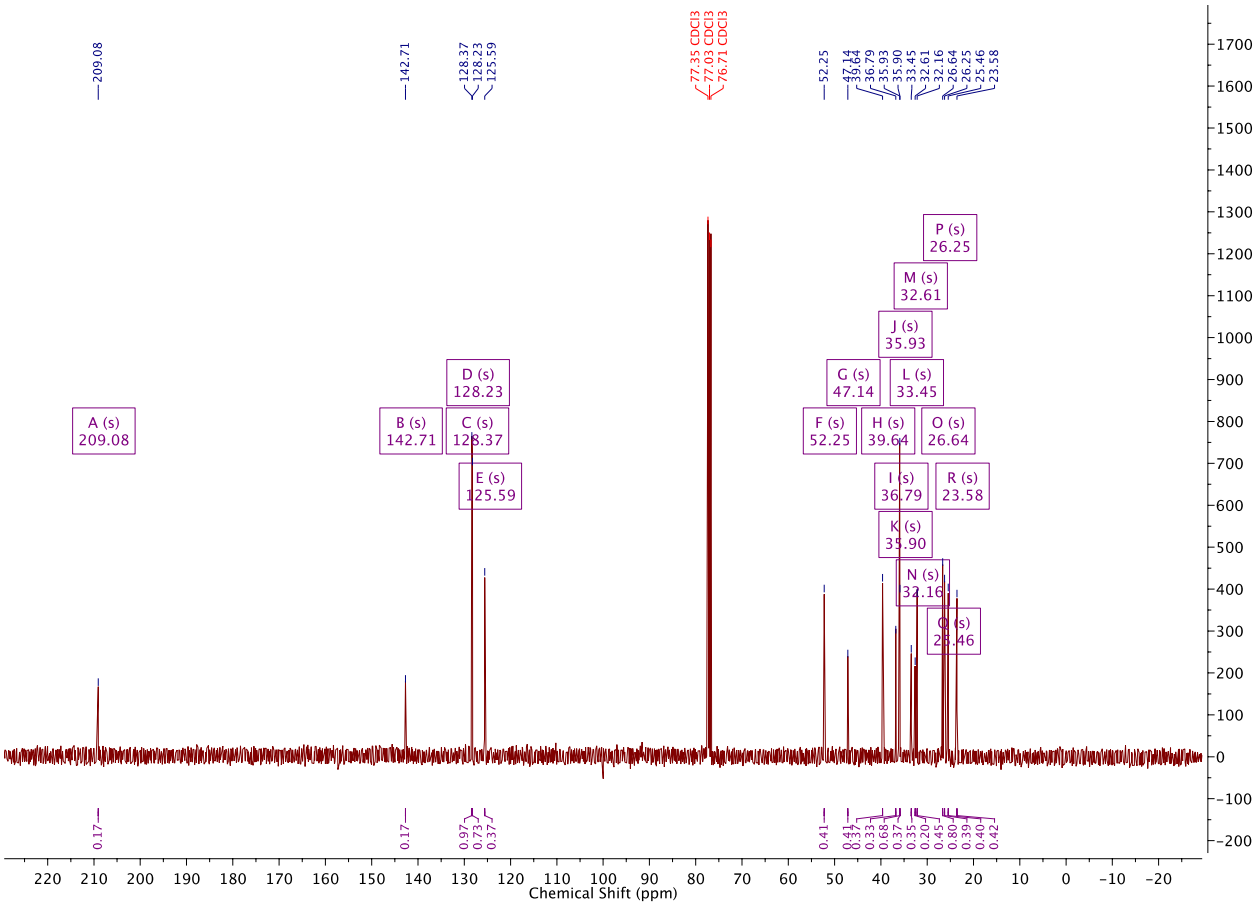
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3658, 2981,1715,1451,1381,1152,954,698

MS (ESI) m/z calc. for $C_{22}H_{34}O^{23}Na$ $[M+Na]^+$: 337.2502 found: 337.2502

$[\alpha]^{20}_{589}$ = +0.6 ° (c 1.0, $CHCl_3$)

Absolute configuration assigned by analogy to compound 3b.


I (m)
7.10
H (m)
7.20
B (s)
2.25
A (m)
2.54
C (s)
2.02
E (m)
1.30
D (m)
1.53
F (m)
1.15
J (m)
0.85
K (s)
0.89
Chemical Shift (ppm)


A (s)
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B (s)
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D (s)
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C (s)
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E (s)
125.59
P (s)
26.25
M (s)
32.61
J (s)
35.93
G (s)
47.14
L (s)
33.45
F (s)
52.25
H (s)
39.64
O (s)
26.64
I (s)
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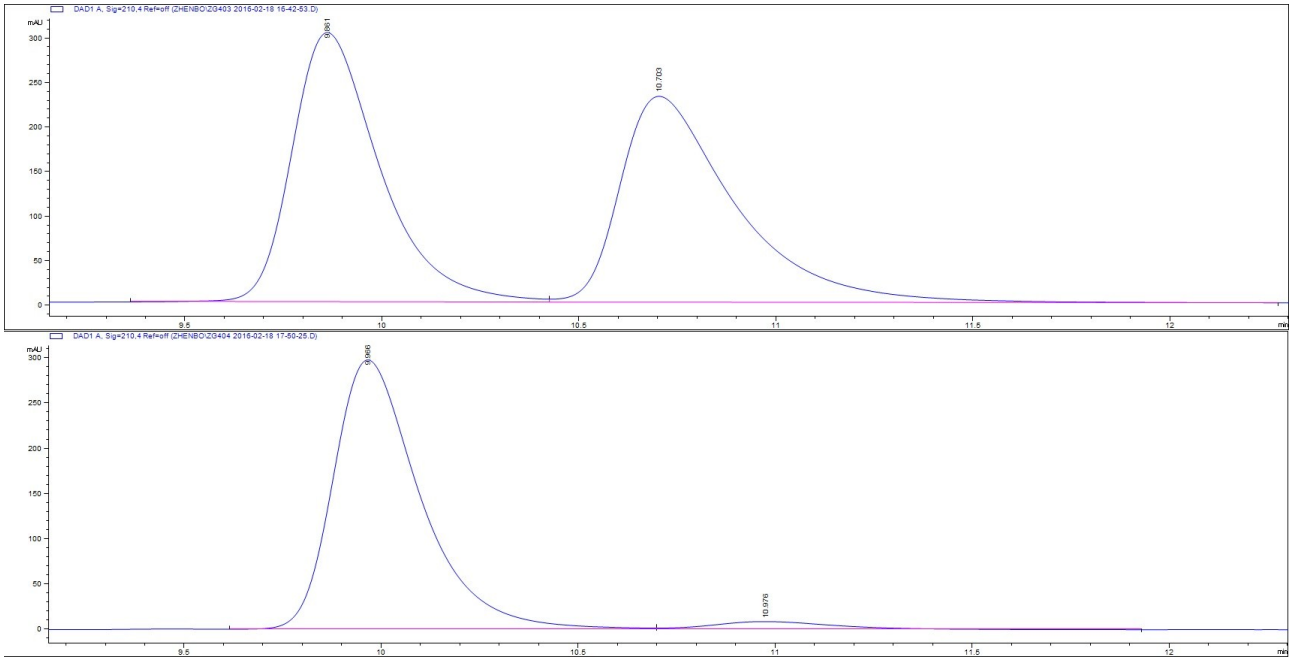
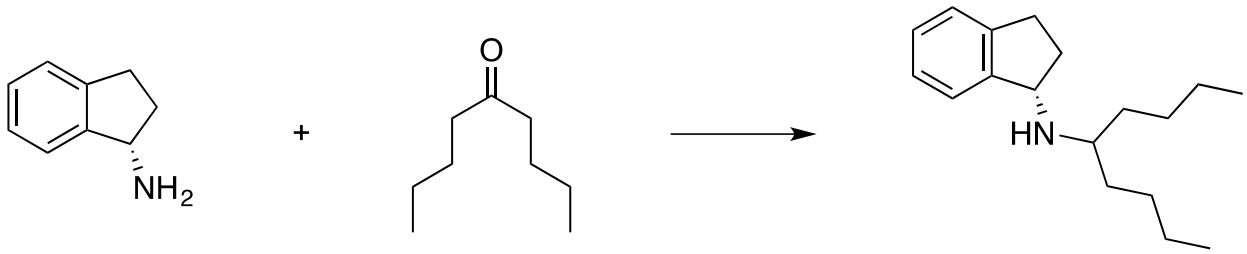
R (s)
23.58
K (s)
35.90
N (s)
32.16
Chemical Shift (ppm)

HPLC trace



(+)-(*S*)-*N*-(nonan-5-yl)-2,3-dihydro-1*H*-inden-1-amine



$TiCl_4$ (3.9 mL (1 M solution in CH_2Cl_2), 1.1 eq, 3.9 mmol),was added slowly to an ice-cooled solution of 2-nonan-5-one (1.33 mL, 1.0 eq, 7.7mmol)in CH_2Cl_2. The solution was stirred for 10 minutes at room temperature and then a 2 M solution of (*S*)-(+)-1-Aminoindane (0.45 mL, 2.2 eq, 3.5 mmol), in THF was added dropwise to the reaction mixture. The reaction mixture was stirred for 3 hours before a 1 M solution of $NaB(CN)H_3$ (1.2 eq.) in THF, and then MeOH (10 mL) were added slowly to the reaction mixture and stirring at room temperature was continued for 48 hours. NaOH (2M aq. solution) was added slowly and the mixture was stirred for 30 min before filteration over celite and washing with EtOAc (30 mL). The mixture was partitioned between the aqueous and organic layers and the aqueous phase extracted with EtOAc (3 times). The combined organic phase was dried ($MgSO_4$), filtered and concentrated in vacuo to afford a yellow oil. Flash column chromatography of the residue (96: 4 $CHCl_3$: MeOH, SiO_2) gave the desired amine, (0.90 g, 98%)

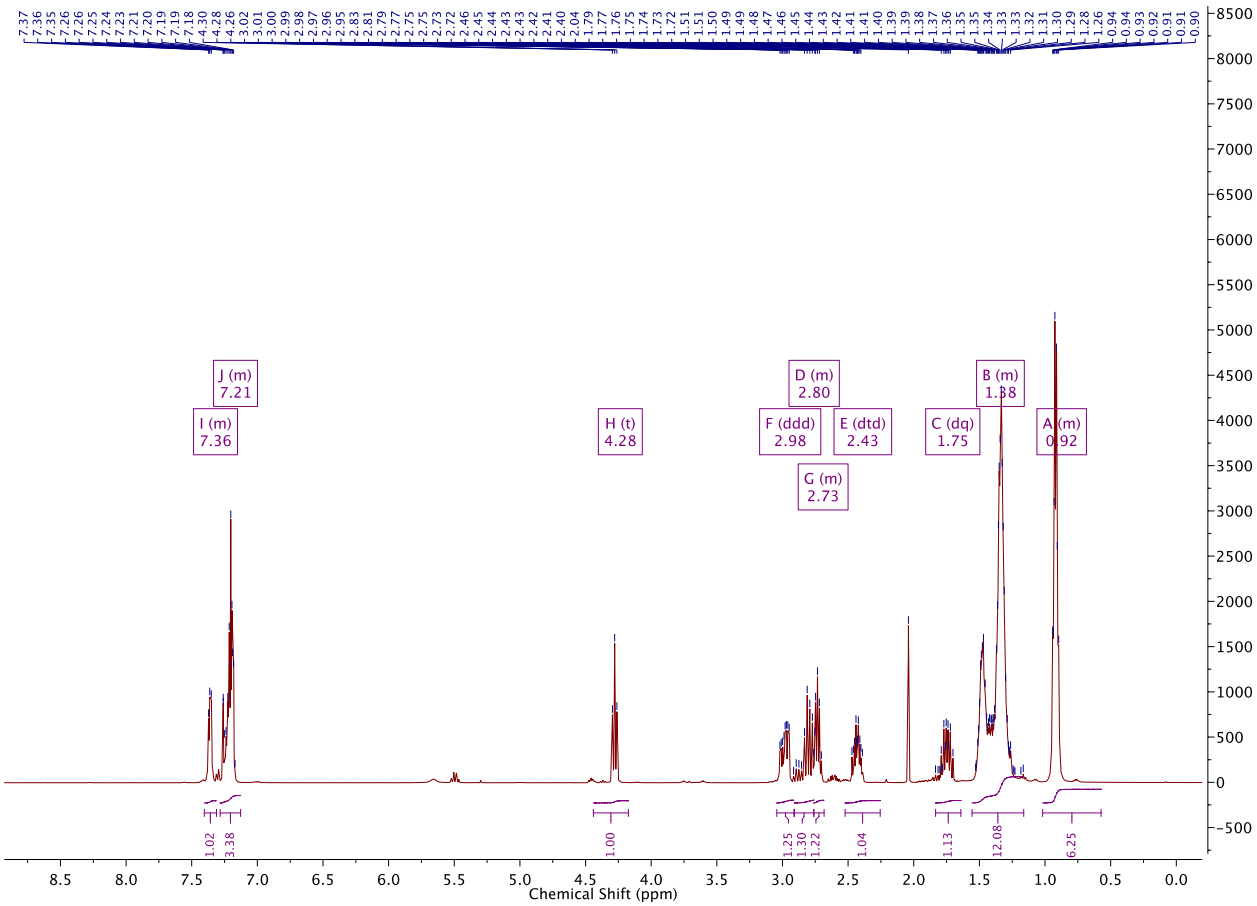
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.40-7.31 (m, 1H, Ar-*H*), 7.28 – 7.13 (m, 3H, Ar-*H*), 4.28 (t, *J* = 6.8 Hz, 1H, PhC*H*NH), 2.98 (ddd, *J* = 15.8 Hz, 8.5 Hz, 4.1 Hz, 1H, PhCH_2), 2.91 – 2.76 (m, 1H, PhCH_2), 2.76 – 2.68 (m, 1H, NHC*H*), 2.43 (dtd, *J* = 12.1 Hz, 7.5 Hz, 4.2 Hz, 1H, NHC*H*), 1.75 (dq, *J* = 12.4 Hz, 7.9 Hz, 1H, NHCHCH_2), 1.56 – 1.16 (m, 12H, 6 x CH_2), 0.8 (m, 6H, 2 x CH_3).

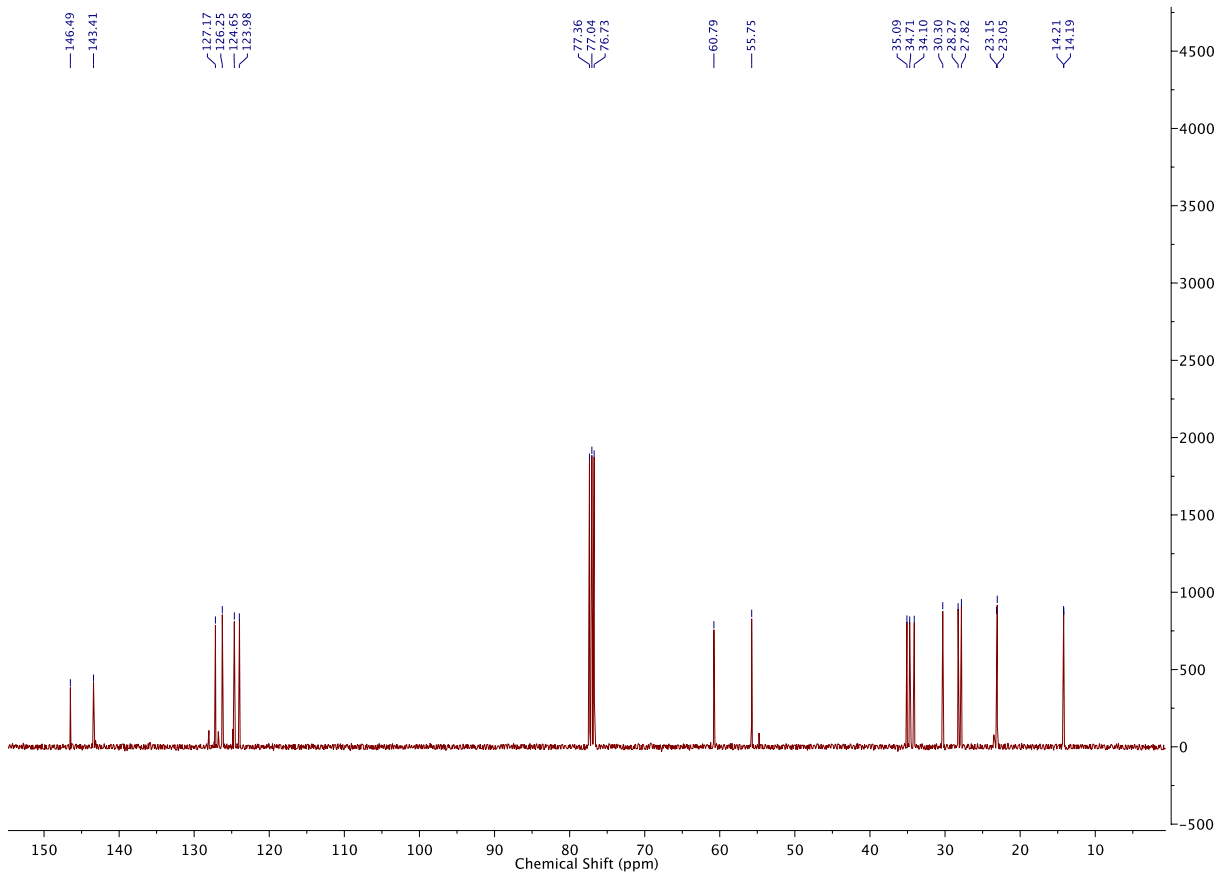
^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 146.5, 143.4, 127.2, 126.3, 124.7, 124.0, 60.8, 55.8, 35.1,34.7,34.1, 30.3, 28.3, 27.8, 23.2, 23.0, 14.2, 14.2,

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3022, 2955, 2858, 2389, 2285

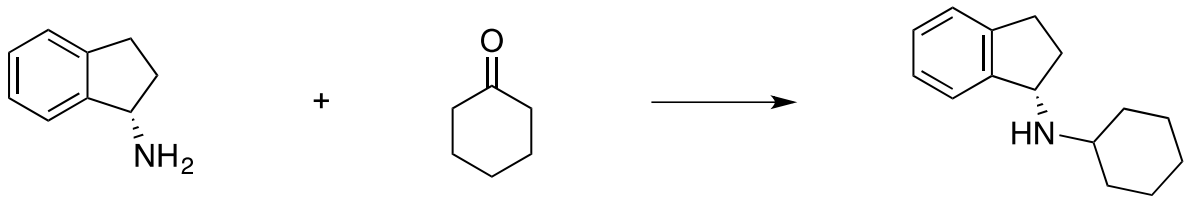
MS (ESI) m/z calc. for $C_{18}H_{30}N$ $[M+H]^+$: 260.2373, found: 260.2371.

$[\alpha]^{20}_{589}$ = +28.0 ° (c 1.0, $CHCl_3$)





(+)-(*S*)-*N*-cyclohexyl-2,3-dihydro-1*H*-inden-1-amine



According to a modified procedure from Davies and co-workers,[25] cyclohexanone (3.0 ml, 1.5 eq. 29.1 mmol) was added to a stirring solution of (*S*)-(+)-1-Aminoindane (2.50 mL, 1.0 eq. 19.4 mmol.) in 100 ml THF at room temperature. After 5 minutes, $Na(OAc)_3H$ (6.20 g, 1.5 eq., 29.1 mmol)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 (50 ml. 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 CH_2Cl_2 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. CH_2Cl_2 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, (4.14 g, 99%) as dark oil

^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.32 – 7.21 (m, 1H, Ar-*H*), 7.18 – 7.05 (m, 3H, Ar-*H*), 4.27 (t, *J* = 6.7 Hz, 1H, PhC*H*NH), 2.90 (ddd, *J* =15.9 Hz, 8.5 Hz, 4.5 Hz, 1H, PhCH_2), 2.71 (dt, *J* = 15.8 Hz, 7.8 Hz, 1H, PhCH_2), 2.61 (tt, *J* = 10.4 Hz, 3.8 Hz, 1H, NHC*H*), 2.34 (dddd, *J* = 12.6 Hz, 8.2Hz, 6.9 Hz, 4.5 Hz, 1H, PhCH$_2$CH_2), 2.03 – 1.78 (m, 2H, PhCH$_2$CH_2 , CH_2), 1.75 – 1.63 (m, 3H, CH_2), 1.56 (ddp, *J* =10.7 Hz, 5.5 Hz, 1.8 Hz, 1H, CH_2), 1.33 – 0.98 (m, 5H, CH_2).

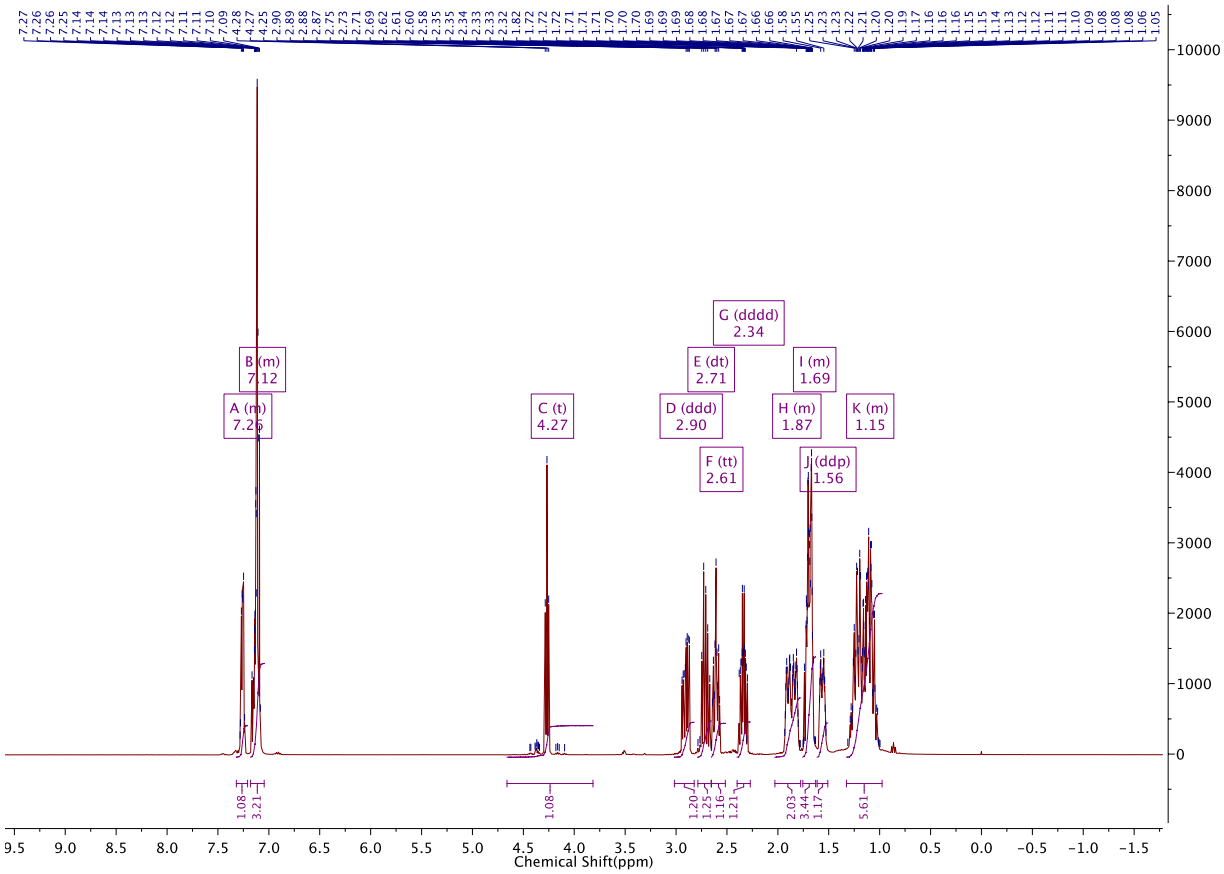
^{13}C NMR (101 MHz, Chloroform-*d*) δC/ppm 146.3, 143.5, 127.2, 126.3, 124.7, 124.0, 60.1, 54.9, 34.9, 34.6, 33.7, 30.3, 26.3, 25.2, 25.1.

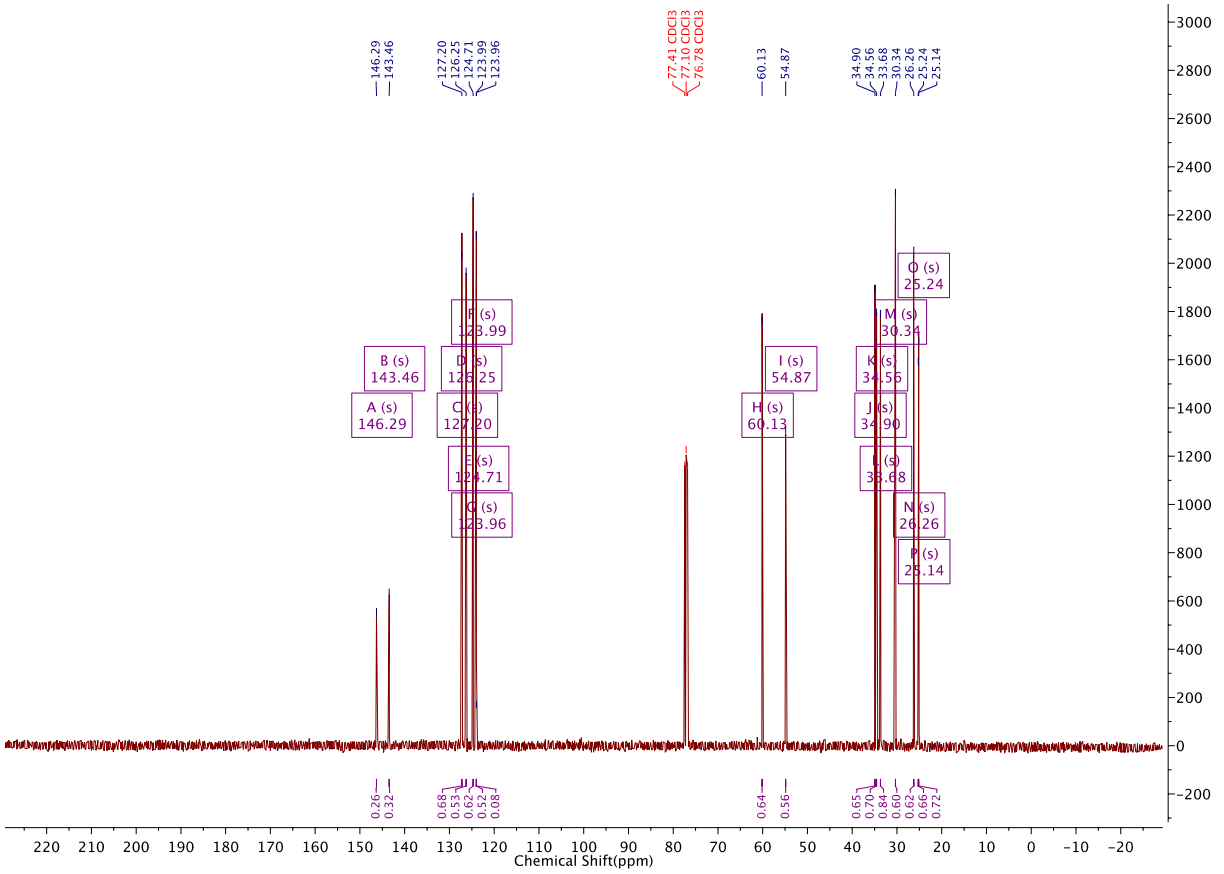
IR (ν_{max}/cm^{-1}, $CHCl_3$) 3022, 2925, 2851, 1447, 1021, 747

MS (ESI) m/z $[M+H]^+$: 216.2(100)

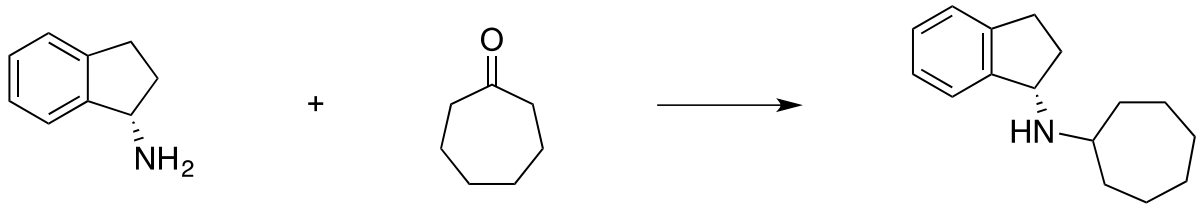
$[\alpha]^{20}_{589}$ = +27.2 ° (c 1.0, $CHCl_3$)

This data was concordant with literature values[11].


A (m) 7.29
B (m) 7.12
C (t) 4.27
D (ddd) 2.90
E (dt) 2.71
F (tt) 2.61
G (dddd) 2.34
H (m) 1.87
I (m) 1.69
J (ddp) 1.56
K (m) 1.15
Chemical Shift(ppm)


A (s) 146.29
B (s) 143.46
C (s) 127.20
D (s) 126.25
E (s) 124.71
F (s) 123.99
G (s) 123.96
H (s) 60.13
I (s) 54.87
J (s) 34.90
K (s) 34.56
L (s) 33.68
M (s) 30.34
N (s) 26.26
O (s) 25.24
P (s) 25.14
Chemical Shift(ppm)

(+)-(*S*)-*N*-cycloheptyl-2, 3-dihydro-1*H*-inden-1-amine



According to a modified procedure from Davies and co-workers,[25] cycloheptanone (0.59 g, 2.0 eq. 5.25 mmol) was added to a stirring solution of (*S*)-(+)-1-Aminoindane (0.45 mL, 1.0 eq. 3.5 mmol.) in THF at room temperature. After 5 minutes, $Na(OAc)_3H$ (1.50 g, 2.0 eq., 7.0 mmol)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 (10 ml. 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 CH_2Cl_2 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. CH_2Cl_2 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, (0.787 g, 98%) as dark oil

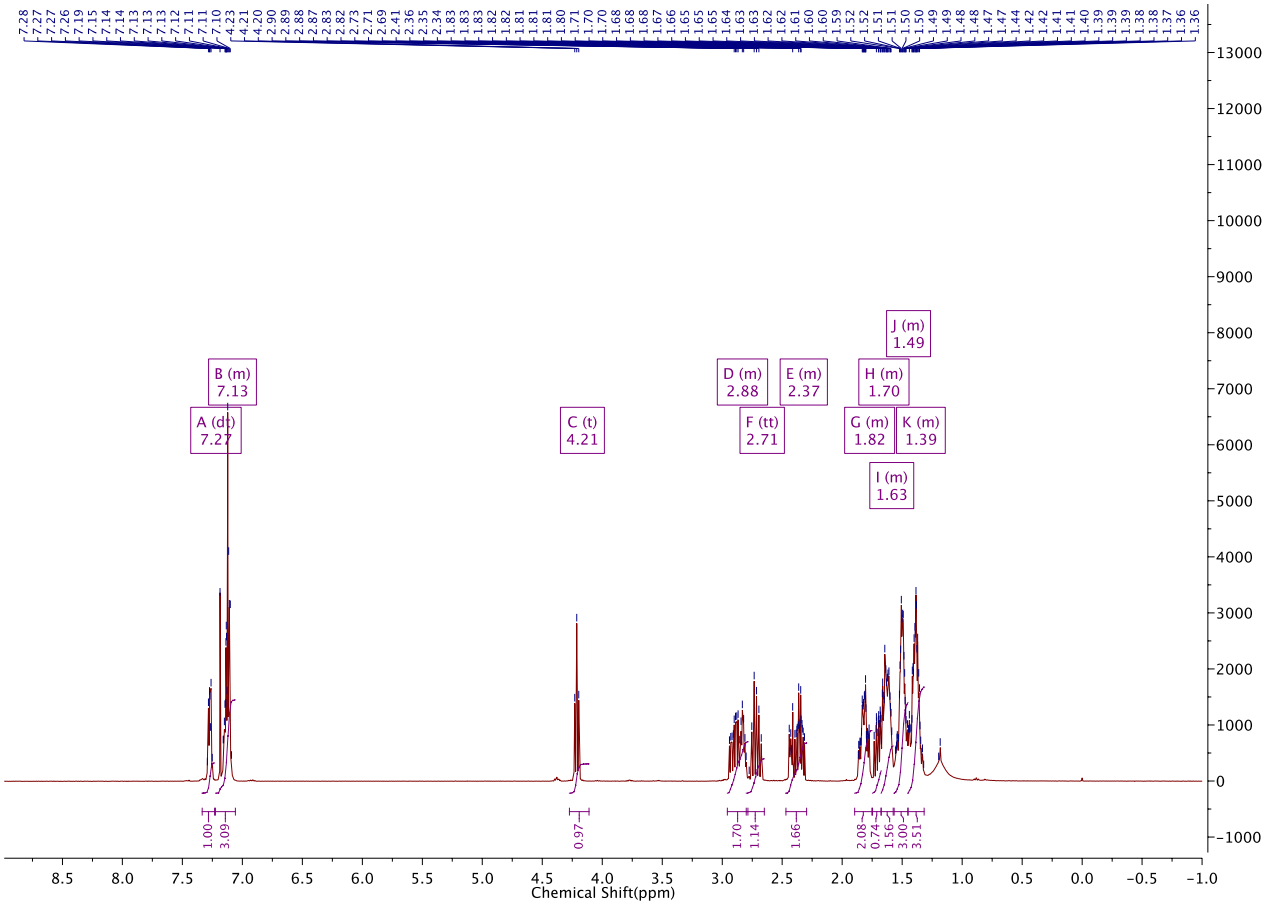
^{1}H NMR (400 MHz, $CDCl_3$) δ_H/ppm 7.27 (dt, *J* = 5.7, 3.6 Hz, 1H, Ar-*H*), 7.22 – 7.06 (m, 3H, Ar-*H*), 4.21 (t, *J* = 6.8 Hz, 1H, PhC*H*NH), 2.96 – 2.79 (m, 2H, PhCH_2), 2.71 (tt, *J* = 15.8 Hz, 7.9 Hz, 1H, NHC*H* $(CH_2)_2$), 2.47 – 2.30 (m, 2H, $PhCH_2CH_2$), 1.90 – 1.75 (m, 2H, CH_2), 1.75 – 1.68 (m, 1H, CH_2), 1.68 – 1.57 (m, 2H, CH_2), 1.57 – 1.45 (m, 3H, CH_2), 1.45 – 1.32 (m, 4H, CH_2).

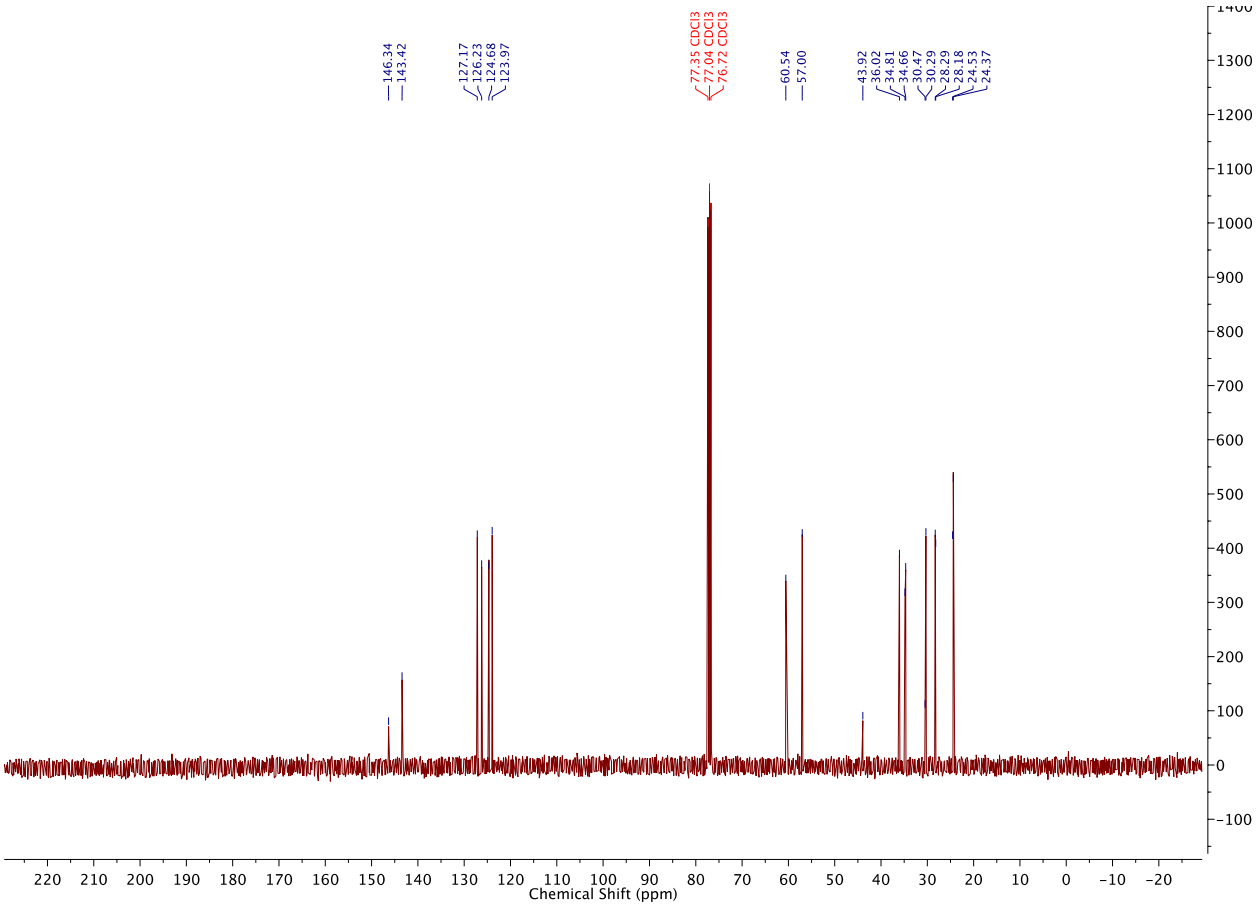
^{13}C NMR (101 MHz, $CDCl_3$) δ_C/ppm 146.3, 143.4, 127.1, 126.2, 124.6, 123.9, 60.5, 57.0, 43.9, 36.0, 34.8, 34.7, 30.5, 30.3, 28.3, 28.1.

IR (ν_{max}/cm^{-1}, $CHCl_3$) 3022, 2922, 2851, 1459

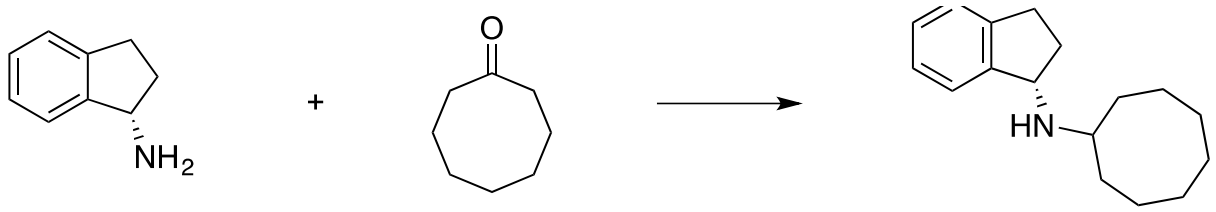
MS (ESI) m/z calc. for $C_{16}H_{24}N$ $[M+H]^+$: 230.1903, found: 230.1903.

$[\alpha]^{20}_{589}$ = +20.8 ° (c 1.0, $CHCl_3$)





(+)-(S)-N-cyclooctyl-2,3-dihydro-1H-inden-1-amine



According to a modified procedure from Davies and co-workers,[25] cyclooctanone (1.47 g, 1.5 eq. 11.6 mmol) was added to a stirring solution of (*S*)-(+)-1-Aminoindane (1.00 mL, 1.0 eq. 7.76 mmol.) in THF at room temperature. After 5 minutes, $Na(OAc)_3H$ (2.50 g, 1.5 eq., 11.6 mmol)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 (25 ml. 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 CH_2Cl_2 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. CH_2Cl_2 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, (1.692 g, 90%) as dark oil

H NMR (200 MHz, CDCl3) δ_H/ppm 7.39 – 7.29 (m, 1H, Ar-*H*), 7.25 – 7.10 (m, 3H, Ar-*H*), 4.28 (t, *J* = 6.8 Hz, 1H, PhC*H*NH), 2.98 (m, *J* = 15.8 Hz, 8.5 Hz, 4.5 Hz, 2H, PhCH_2), 2.80 (q, *J* = 7.9 Hz, 1H, NHC*H*), 2.42 (dddd, *J* = 12.5 Hz, 7.9 Hz, 6.9 Hz, 4.5 Hz, 1H, PhCH$_2$CH_2), 1.81 – 1.71 (m, 1H, PhCH$_2$CH_2), 1.71 – 1.26 (m, 14H, CH_2).

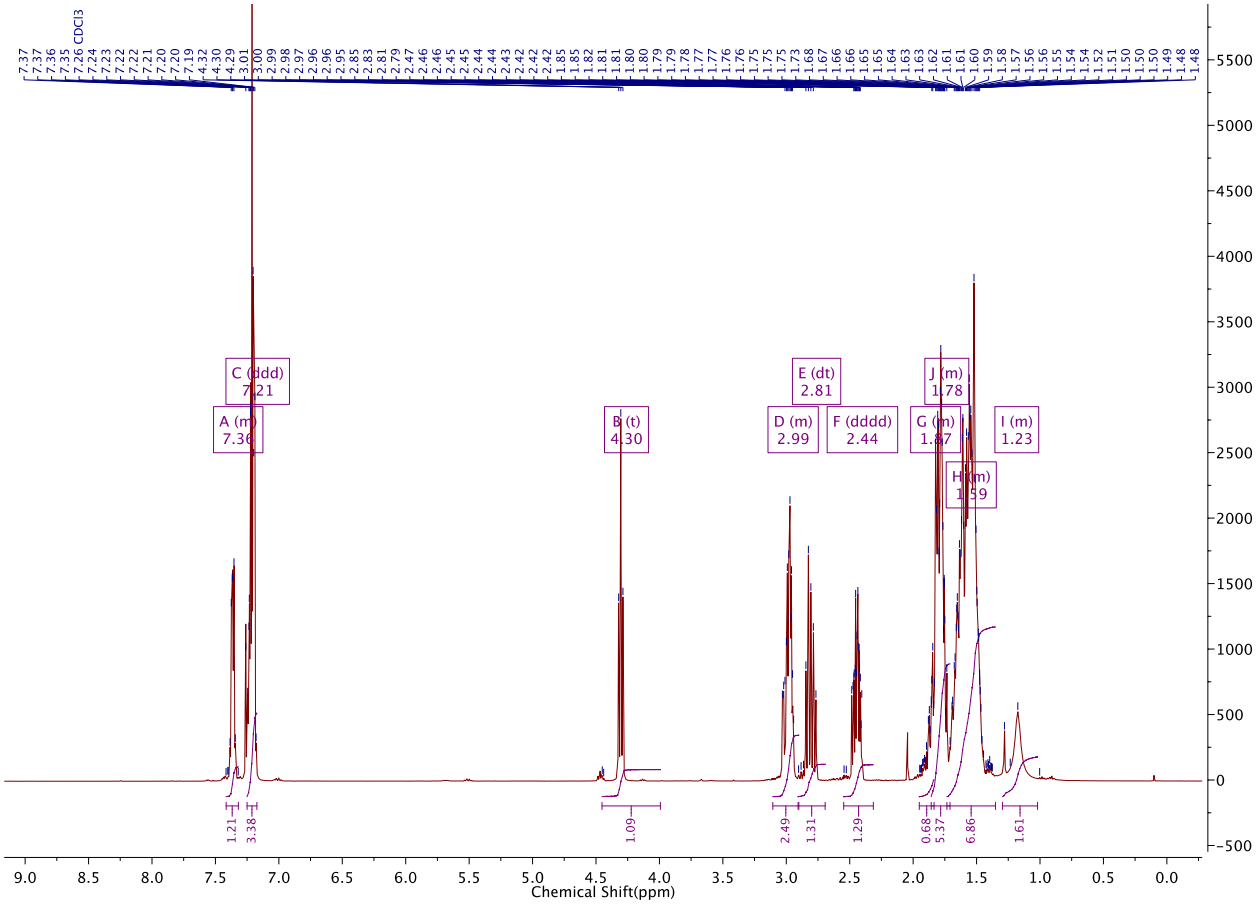
^{1}H NMR (400 MHz, Chloroform-*d*) δ_H/ppm 7.4 – 7.3 (m, 1H, Ar-*H*), 7.2 (m, 3H, Ar-*H*), 4.3 (t, *J* = 6.8 Hz, 1H, PhC*H*NH), 3.1 – 2.9 (m, 2H, PhCH_2), 2.8 (dt, *J* = 15.8 Hz, 7.9 Hz, 1H, NHC*H*), 2.4 (dddd, *J* = 12.5 Hz, 8.1 Hz, 6.9 Hz, 4.3 Hz, 1H, PhCH$_2$CH_2), 2.0 – 1.8 (m, 1H, PhCH$_2$CH_2), 1.8 – 1.7 (m, 5H, CH_2), 1.7 – 1.4 (m, 7H, CH_2), 1..3-1.0 (m, 2H, CH_2).

^{13}C NMR (101 MHz, Chloroform-*d*) δ_C/ppm 146.4, 143.4, 127.2, 126.3, 124.7, 123.9, 60.5, 55.7, 34.8, 33.9, 32.2, 30.3, 27.5, 27.4, 25.8, 24.2, 24.1.

IR (ν_{max}/cm$_{-1}$, $CHCl_3$) 3021, 2919, 2849, 1474, 1258

MS (ESI) m/z calc. for $C_{17}H_{26}N$ $[M+H]^+$: 244.2060, found: 244.2058.

$[\alpha]^{20}_{589}$ = +37.6 ° (c 2.0, $CHCl_3$)


C (ddd)
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A (m)
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B (t)
4.30
E (dt)
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D (m)
2.99
F (dddd)
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J (m)
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G (m)
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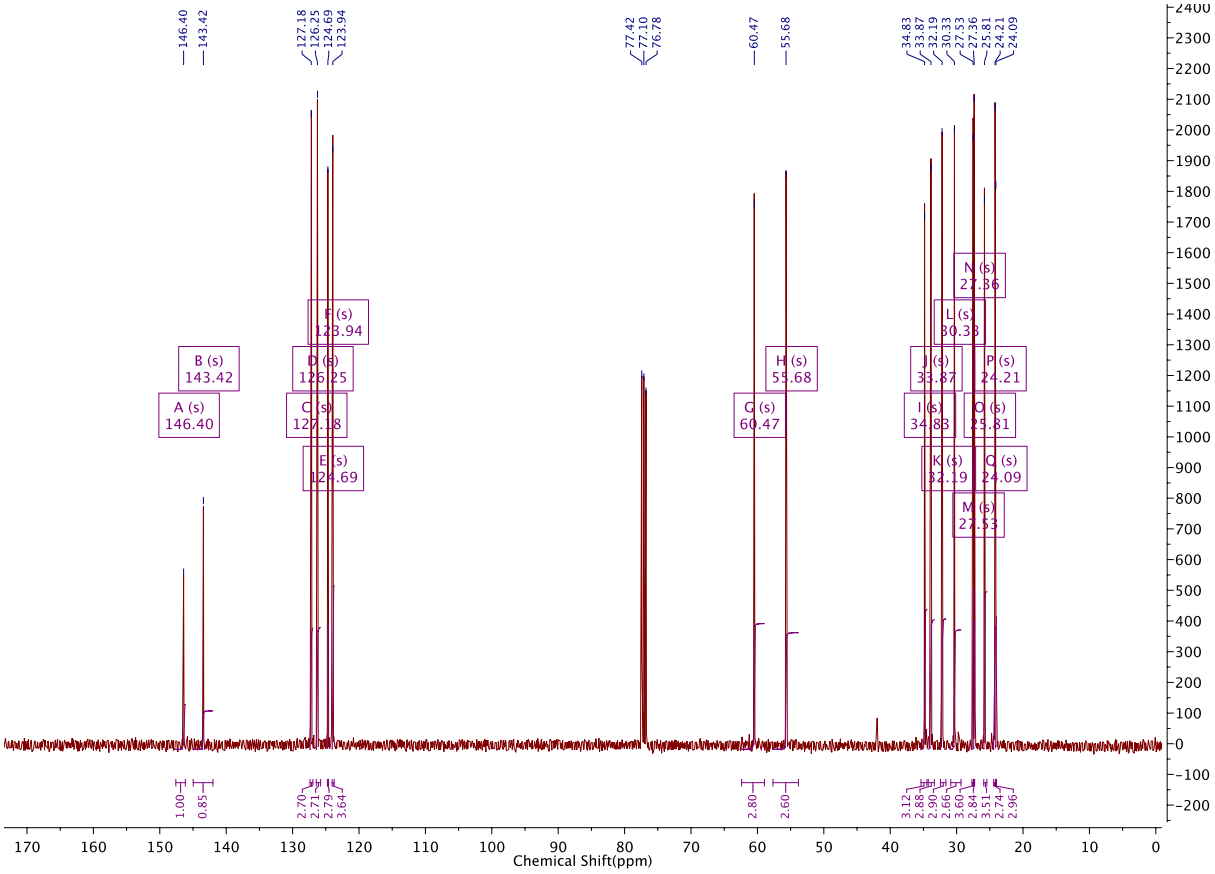
I (m)
1.23
H (m)
1.59
Chemical Shift(ppm)


A (s)
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B (s)
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C (s)
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D (s)
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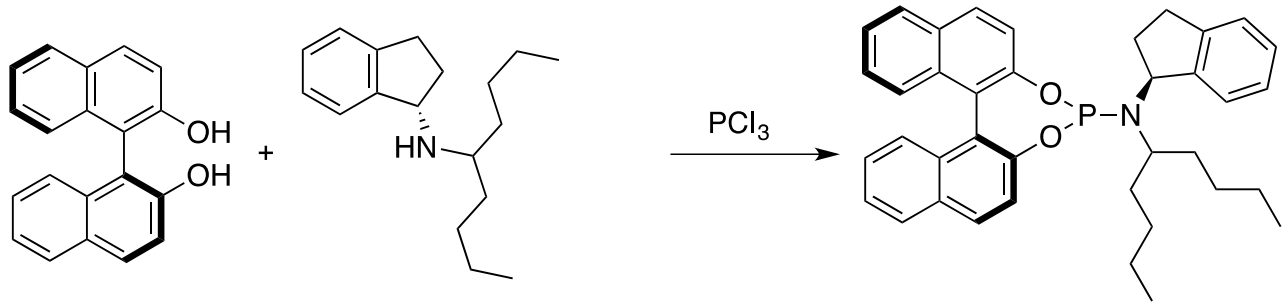
55.68
I (s)
34.83
J (s)
33.87
K (s)
32.19
L (s)
30.33
M (s)
27.53
N (s)
27.36
O (s)
25.81
P (s)
24.21
Q (s)
24.09
Chemical Shift(ppm)

(+)-(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 B)



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, $CDCl_3$) δ_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, PhCH_2), 2.75 (dt, J = 16.1 Hz, 8.3 Hz, 1H, NHC*H*), 2.44 (d, J = 11.3 Hz, 1H, PhCH$_2$CH_2), 2.26 – 2.00 (m, 1H, PhCH$_2$CH_2), 1.78 (tt, J = 12.3 Hz, 4.4 Hz, 1H, CH_2), 1.72 – 1.61 (m, 1H, CH_2), 1.55 – 1.38 (m, 5H, CH_2), 1.39 – 0.97 (m, 5H, CH_2), 0.92 (t, J = 7.3 Hz, 3H, CH_3), 0.87 (t, J = 7.2 Hz, 3H, CH_3).

^{13}C NMR (126 MHz, Chloroform-d) δ_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

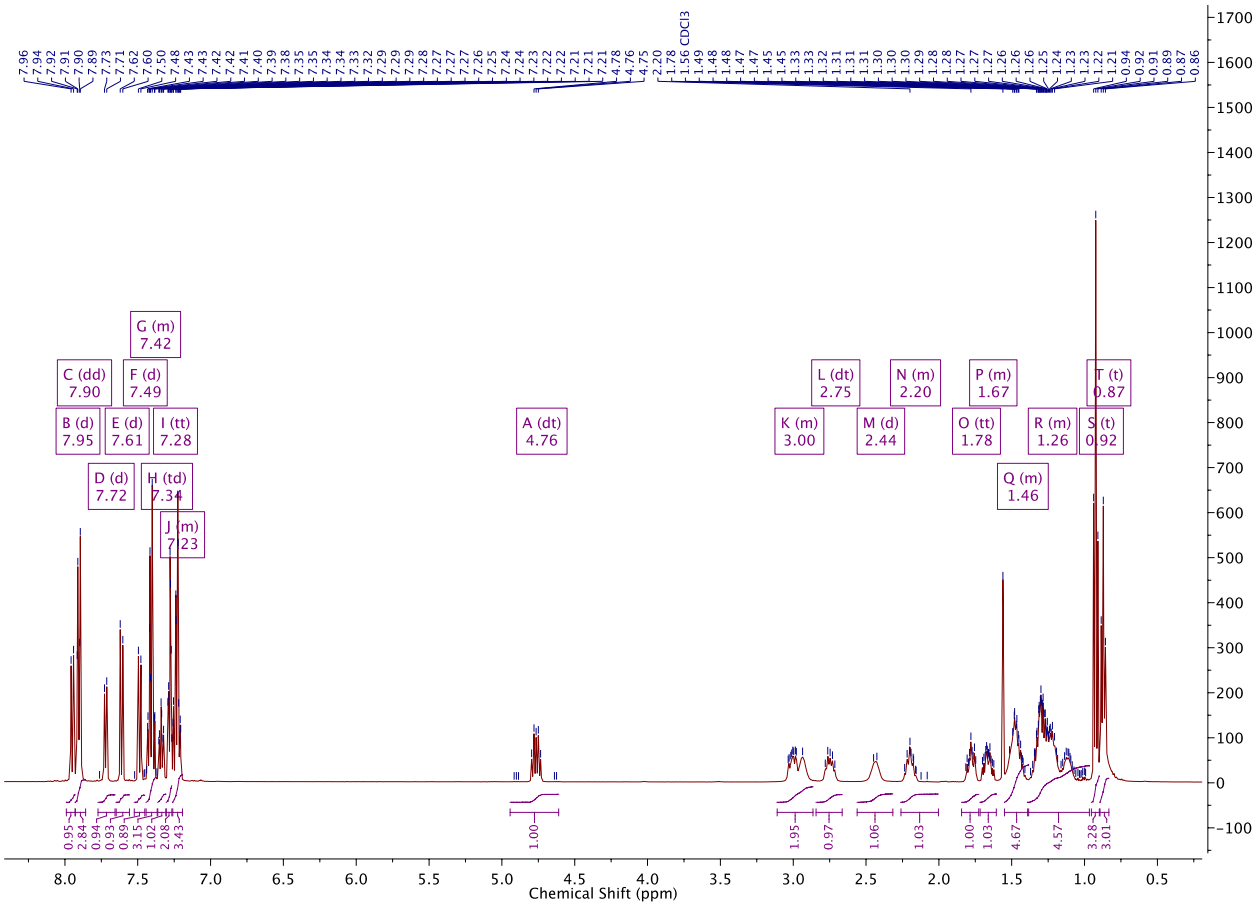
(d, J = 21.3 Hz), 55.15 (d, J = 4.3 Hz), 36.90 (d, J = 5.4 Hz), 34.70, 31.62, 30.4, 29.3, 28.7, 23.1, 22.8, 14.23, 14.1.

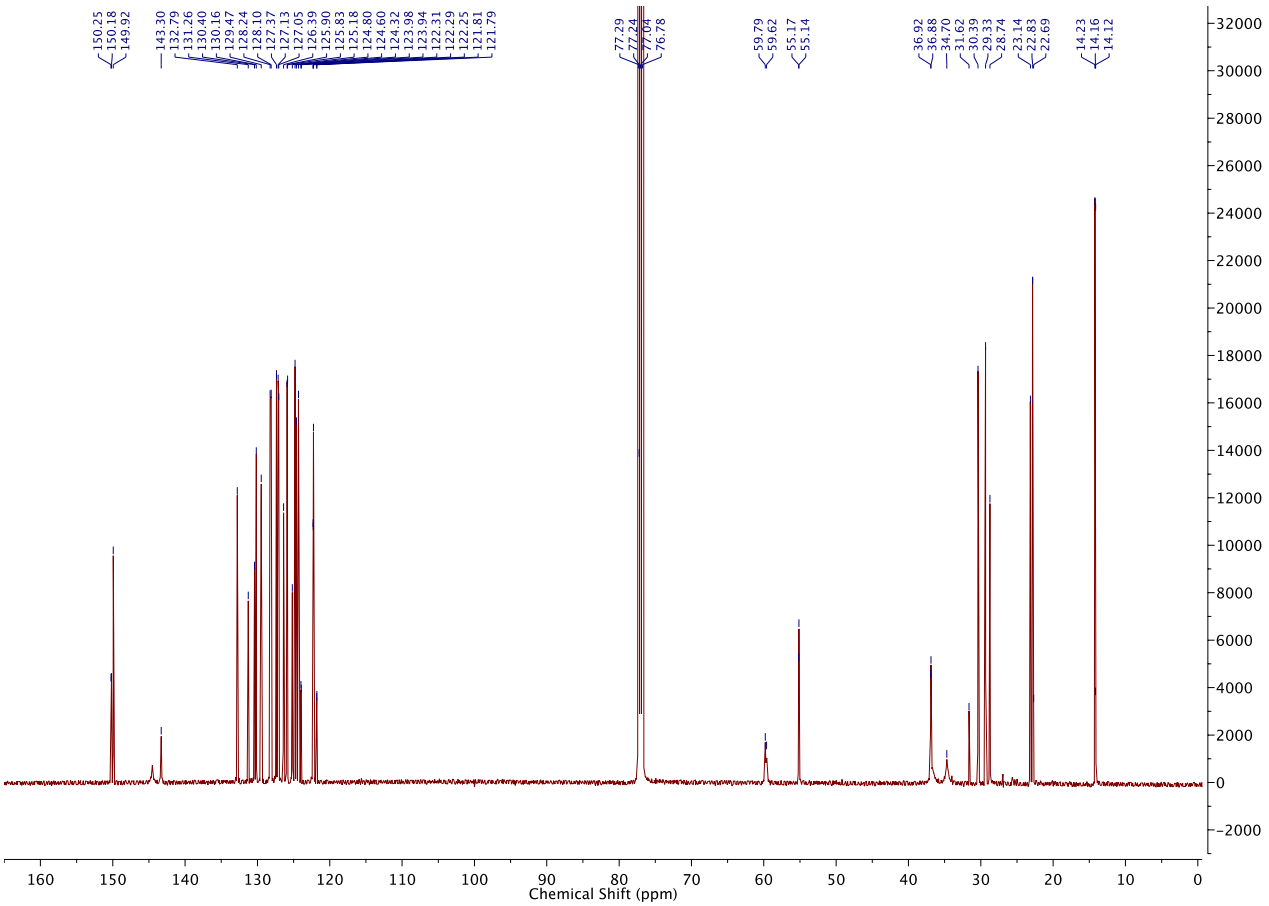
^{31}P NMR (162 MHz, Chloroform-d) δ_p/ppm 149.9.

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

MS (GCMS Ammonica Cl 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, $CHCl_3$)




150.25
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123.94
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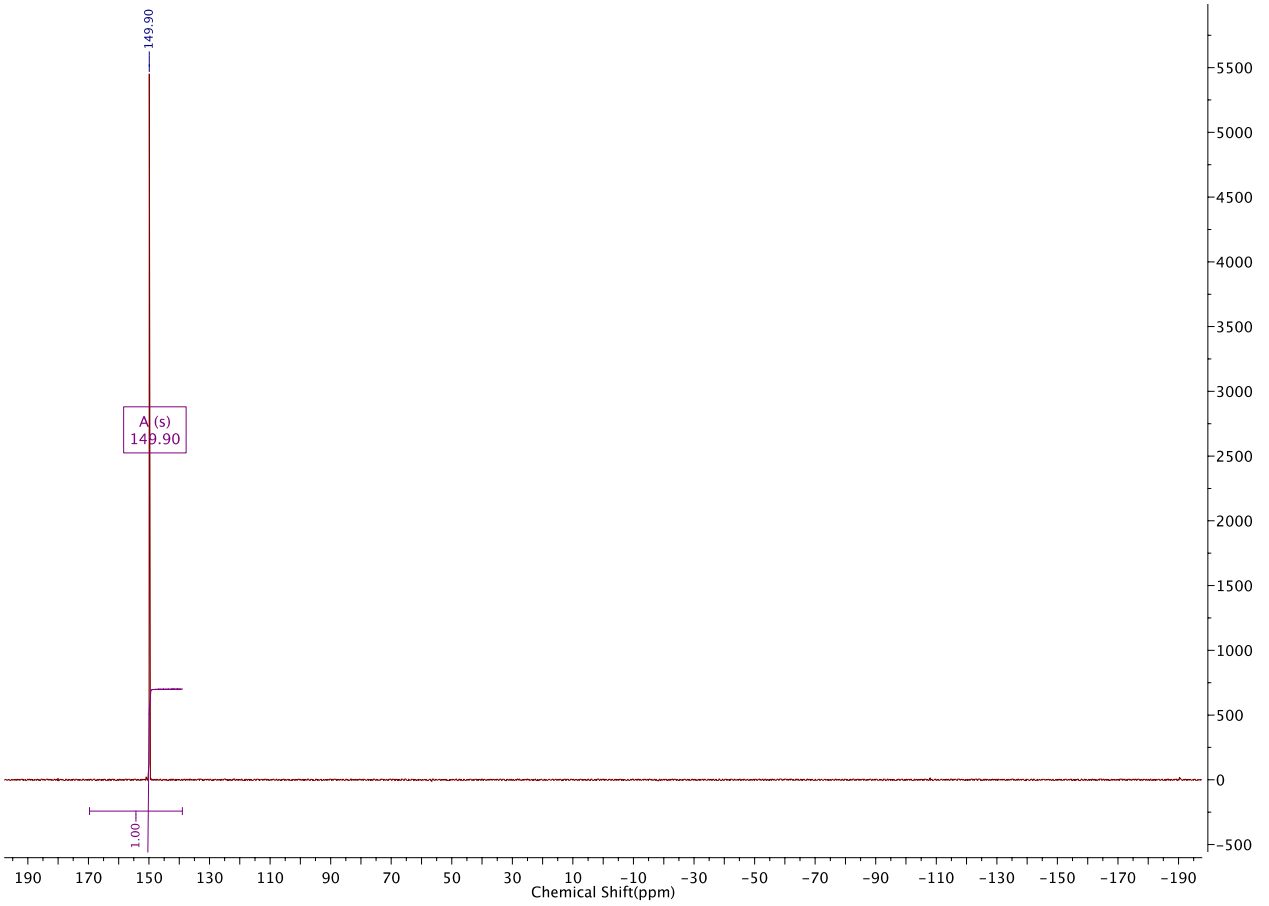
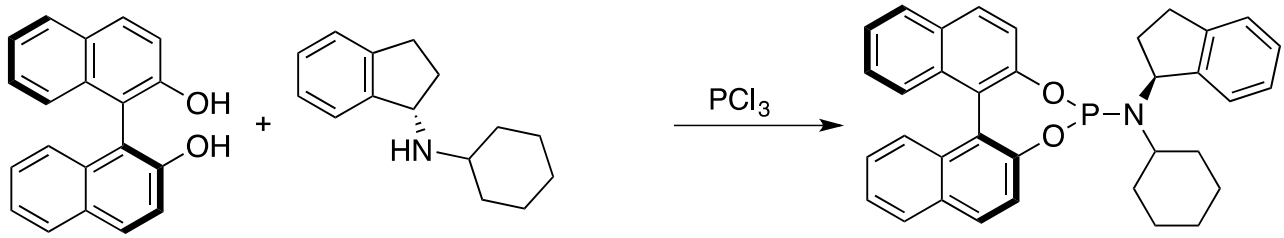
122.29
122.25
121.81
121.79
77.29
77.24
77.04
76.78
59.79
59.62
55.17
55.14
36.92
36.88
34.70
31.62
30.39
29.33
28.74
23.14
22.83
22.69
14.23
14.16
14.12
Chemical Shift (ppm)


149.90
A (s)
149.90
1.00
Chemical Shift(ppm)

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



Triethylamine (8.1 mL, 5 eq. 58.1 mmol), was added dropwise to a stirred, ice-cooled solution of PCl_3 (1.02 ml, 1.0 eq., 11.6 mmol) in CH_2Cl_2. The ice bath was removed and the solution left to warm to room temperature before (*S*)-N-cyclohexyl-2, 3-dihydro-1H-inden-1-amine (2.5 g, 1.0 eq. 11.6 mmol) was added to the stirred solution in one portion. After 5 hours,, (*S*)-binaphthol (3.34 g, 1.0 eq. 11.6 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(2.45 g, 40%).

^{1}H NMR (500 MHz, $CDCl_3$) δ_H/ppm 7.96 (d, *J* = 8.8 Hz, 1H, Ar-*H*), 7.93 – 7.89 (m, 1H, Ar-*H*), 7.87 (dd, *J* = 7.8 Hz, 1.7 Hz 1H, Ar-*H*), 7.83 (d, *J* = 8.8 Hz, 1H, Ar-*H*), 7.64-7.59 (m, 1H, Ar-*H*), 7.55 (dd, *J* = 8.7 Hz, 0.7 Hz, 1H, Ar-*H*), 7.51 (dd, *J* = 8.8 Hz, 0.9 Hz, 1H, Ar-*H*), 7.45-7.36 (m, 3H, Ar-*H*), 7.32 (ddd, *J* = 8.5 Hz, 5.2 Hz, 1.3 Hz, 2H, Ar-*H*), 7.30 – 7.16 (m, 4H, Ar-*H*), 4.76 (dt, *J* = 12.7 Hz, 8.2 Hz, 1H, PhC*H*NH), 2.92 (ddd, *J* = 15.8 Hz, 9.0 Hz, 2.3 Hz, 1H, PhCH_2CH$_2$), 2.79-2.69 (m, 1H, PhCH_2CH$_2$), 2.66 (dd, *J* = 16.5 Hz, 8.9 Hz, 1H, PhCH$_2$CH_2), 2.40 (dtd, J = 10.2 Hz, 7.6 Hz, 2.4 Hz, 1H, NHC*H*), 2.16 – 1.98 (m, 1H, PhCH$_2$CH_2), 1.92 (d, *J* = 12.3 Hz, 1H, CH_2), 1.81 – 1.6 6(m, 1H, CH_2), 1.68 – 1.55 (m, 1H, CH_2), 1.49 – 1.40 (m, 1H, CH_2), 1.39 – 1.21 (m, 1H, CH_2), 1.20 – 0.96 (m, 1H, CH_2), 0.97 – 0.76 (m, 4H, CH_2).

^{13}C NMR (126 MHz, Chloroform-d) δ_C/ppm 150.3 (d, J = 8.1 Hz), 150.0, 144.4, 143.2, 132.8 (d, J = 1.7 Hz), 132.7, 131.3, 130.5, 130.2, 129.5, 128.3, 128.2, 127.2, 127.1, 126.4, 125.9, 125.8, 124.8, 124.6, 124.5, 124.3, 124.1 (d, J = 5.3 Hz), 122.4 (d, J = 2.3 Hz), 122.2 (2C), 121.6 (d, J =

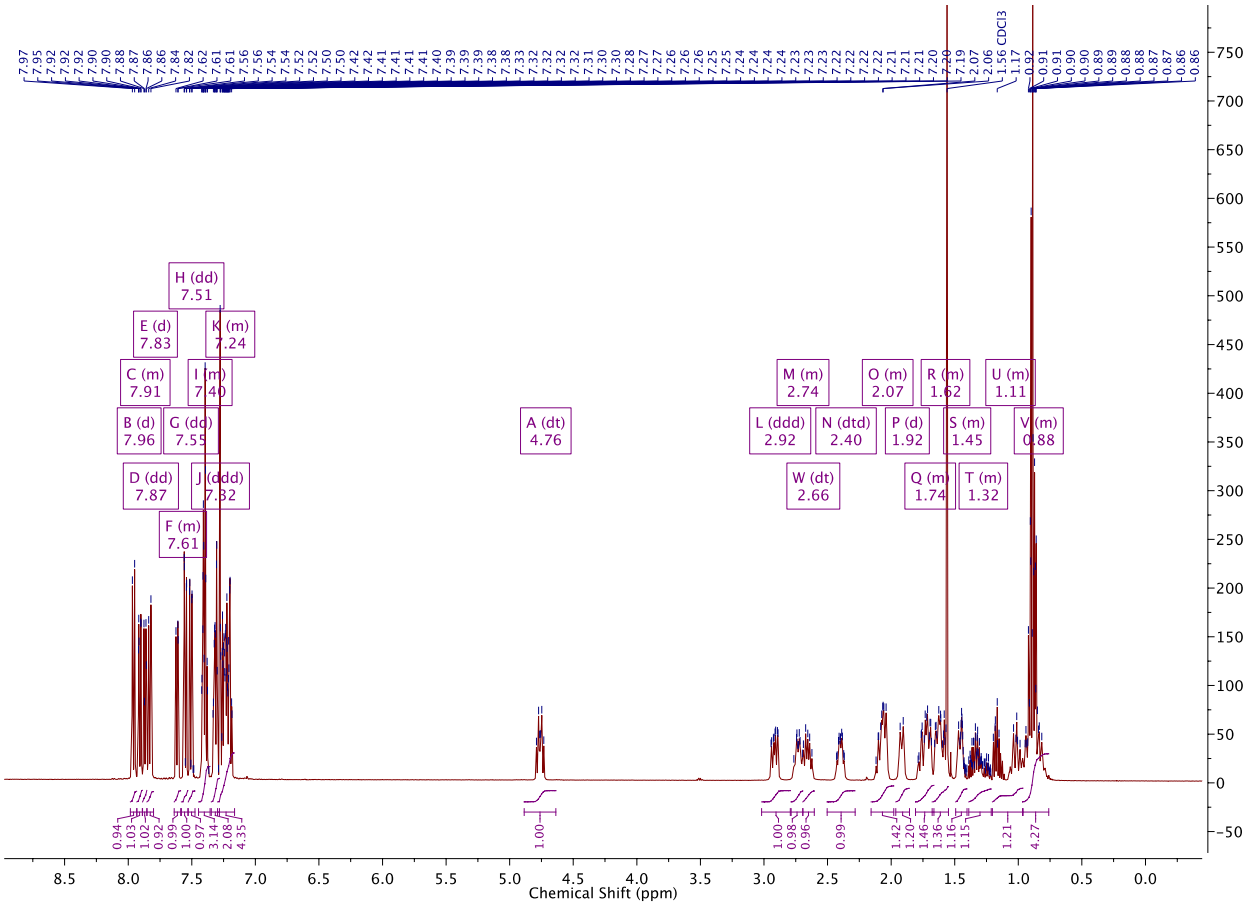
2.5 Hz), 60.4 (d, J = 15.5 Hz), 54.6 (d, J = 9.6 Hz), 30.0, 26.3 (d, J = 6.4 Hz), 25.4, 22.7, 19.5, 14.4, 11.5.

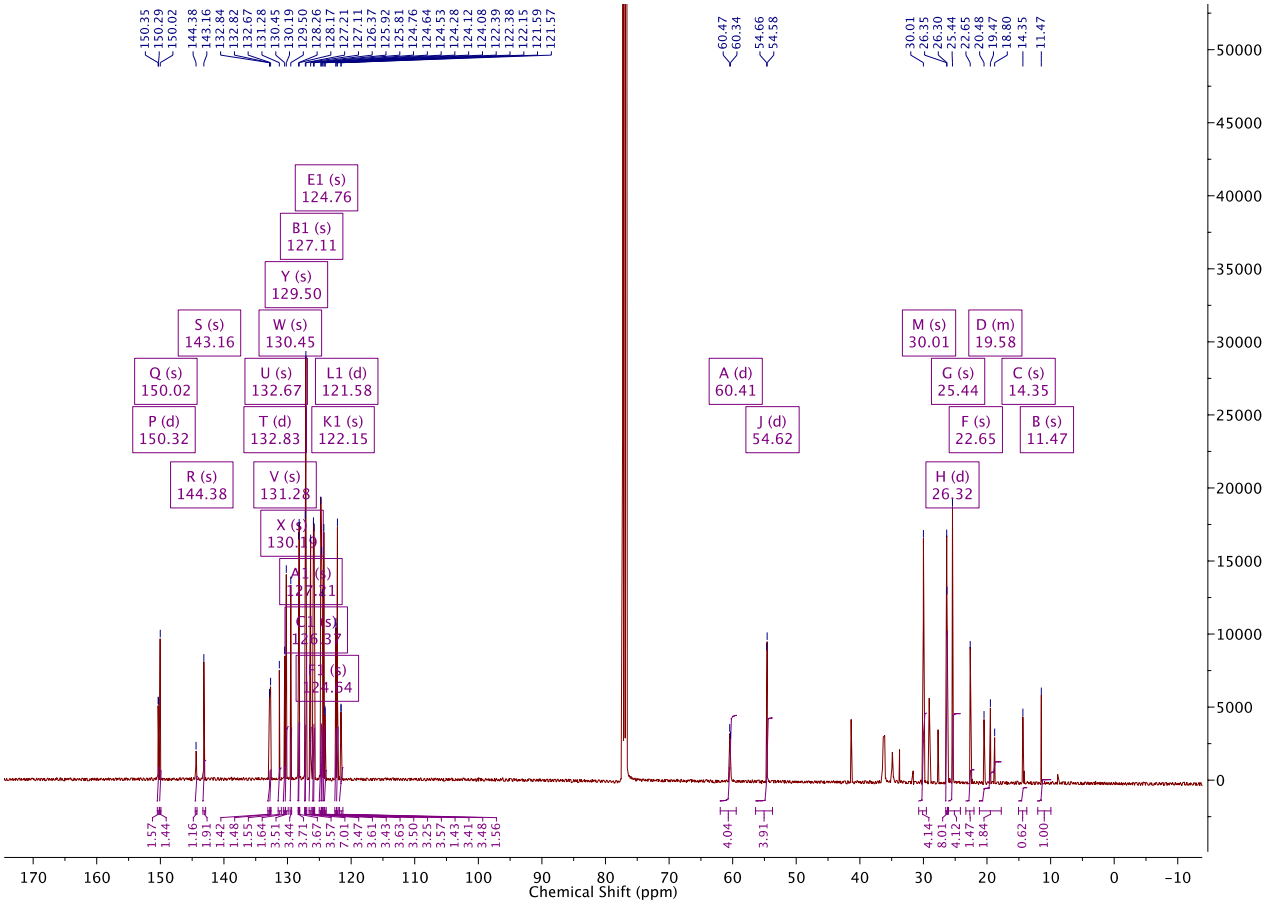
^{31}P NMR (162 MHz, $CDCl_3$) δ_P/ppm 151.5.

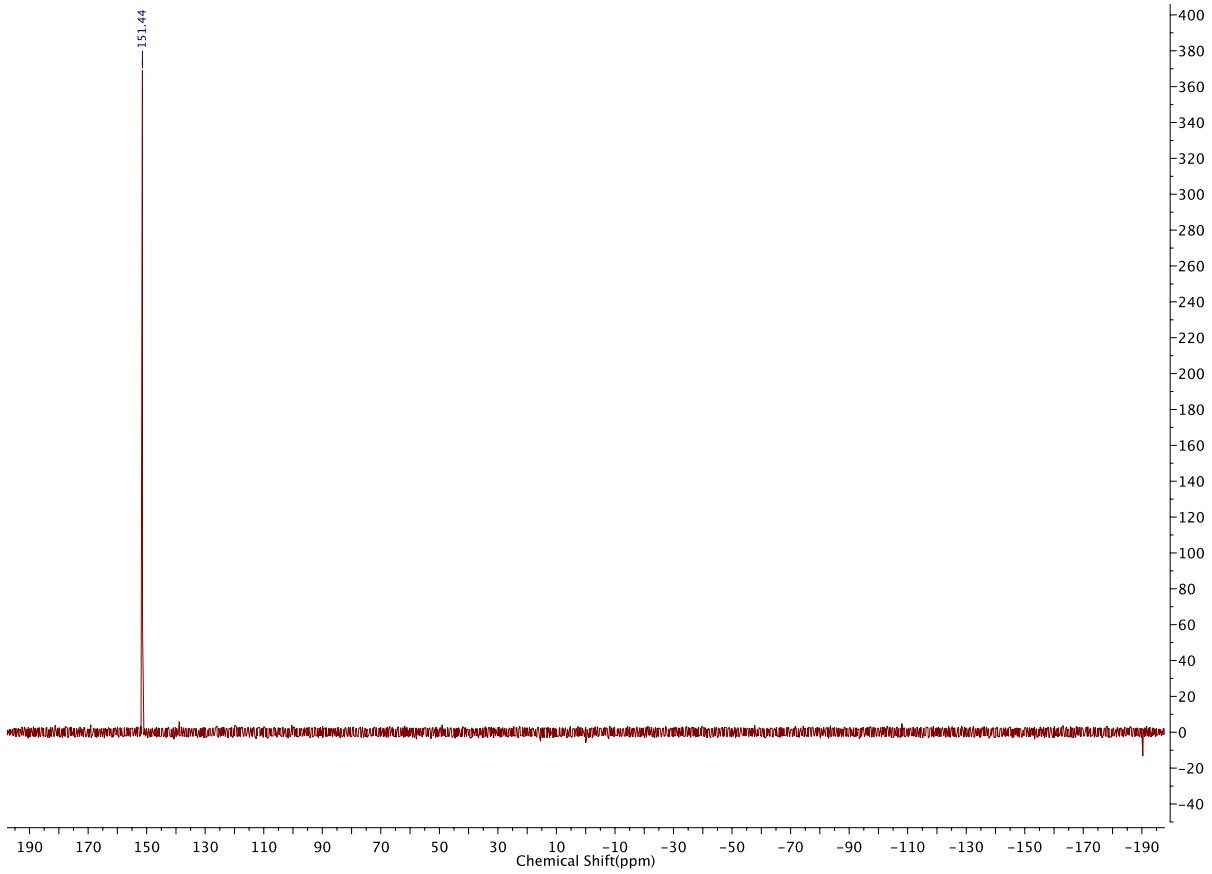
IR (ν_{max}/cm^{-1}): 2931, 1590, 1463, 1328, 1230, 1063, 947, 821, 733

HRMS (EI) m/z calc. for $C_{35}H_{32}NO_2P$ $[M+H]^+$: 529.2171, found: 529.2175.

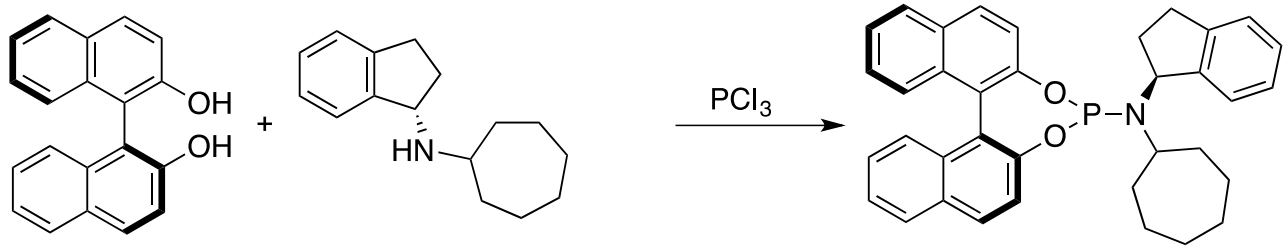
$[\alpha]^{20}_{589}$ = +260.0 ° (c =2.0, $CHCl_3$)




E1 (s)
124.76
B1 (s)
127.11
Y (s)
129.50
S (s)
143.16
W (s)
130.45
Q (s)
150.02
U (s)
132.67
L1 (d)
121.58
P (d)
150.32
T (d)
132.83
K1 (s)
122.15
R (s)
144.38
V (s)
131.28
A (d)
60.41
J (d)
54.62
M (s)
30.01
D (m)
19.58
G (s)
25.44
C (s)
14.35
F (s)
22.65
B (s)
11.47
H (d)
26.32
Chemical Shift (ppm)


151.44
Chemical Shift(ppm)

(+)-(11bS)-N-cycloheptyl-N-((S)-2,3-dihydro-1H-inden-1-yl)dinaphtho[2,1-d:1',2' f][1,3,2]dioxaphosphepin-4-amine (Ligand D)



Triethylamine (0.8 mL, 5.0 eq., 6.0 mmol), was added dropwise to a stirred, ice-cooled solution of PCl_3 (0.11 mL, 1.0 eq., 1.2 mmol) in CH_2Cl_2. The ice bath was removed and the solution left to warm to room temperature before (*S*)-N-cyclohexyl-2, 3-dihydro-1H-inden-1-amine (0.28g, 1.0 eq. 1.2mmol) was added to the stirred solution in one portion. After 5 hours,, (*S*)-binaphthol (0.33 g, 1.0 eq. 1.2 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 (~30 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 (0.37 g, 57%).

^{1}H NMR (500 MHz, Chloroform-d) δ = 7.96 (d, J = 8.8 Hz, 1H, Ar-*H*), 7.91 (dd, J = 8.2 Hz, 1.2 Hz, 1H, Ar-*H*), 7.87 (d, J = 8.2 Hz, 1H, Ar-*H*), 7.85 (d, J = 8.8 Hz, 1H, Ar-*H*), 7.64 (d, J = 7.5 Hz, 1H, Ar-*H*), 7.56 (d, J = 8.7Hz, 1H, Ar-*H*), 7.51 (d, J = 8.8, 1H, Ar-*H*), 7.45 – 7.36 (m, 3H, Ar-*H*), 7.35 – 7.30 (m, 2H, Ar-*H*), 7.30 – 7.17 (m, 4H, Ar-*H*), 4.76 (dt, J = 13.3 Hz, 8.2 Hz, 1H, PhC*H*NH), 3.11 – 2.85 (m, 2H, PhCH_2), 2.68 (dt, J = 15.8, 8.5, 1H, NHC*H*), 2.43 (d, J = 9.9 Hz, 1H, PhCH$_2$CH_2), 2.23 – 2.05 (m, 2H, PhCH$_2$CH_2, CH_2), 2.06 – 1.88 (m, 2H, CH_2), 1.87 – 1.68 (m, 1H, CH_2), 1.68 – 1.52 (m, 2H, CH_2), 1.47 – 1.20 (m, 3H, CH_2), 1.18 – 0.80 (m, 3H, CH_2).

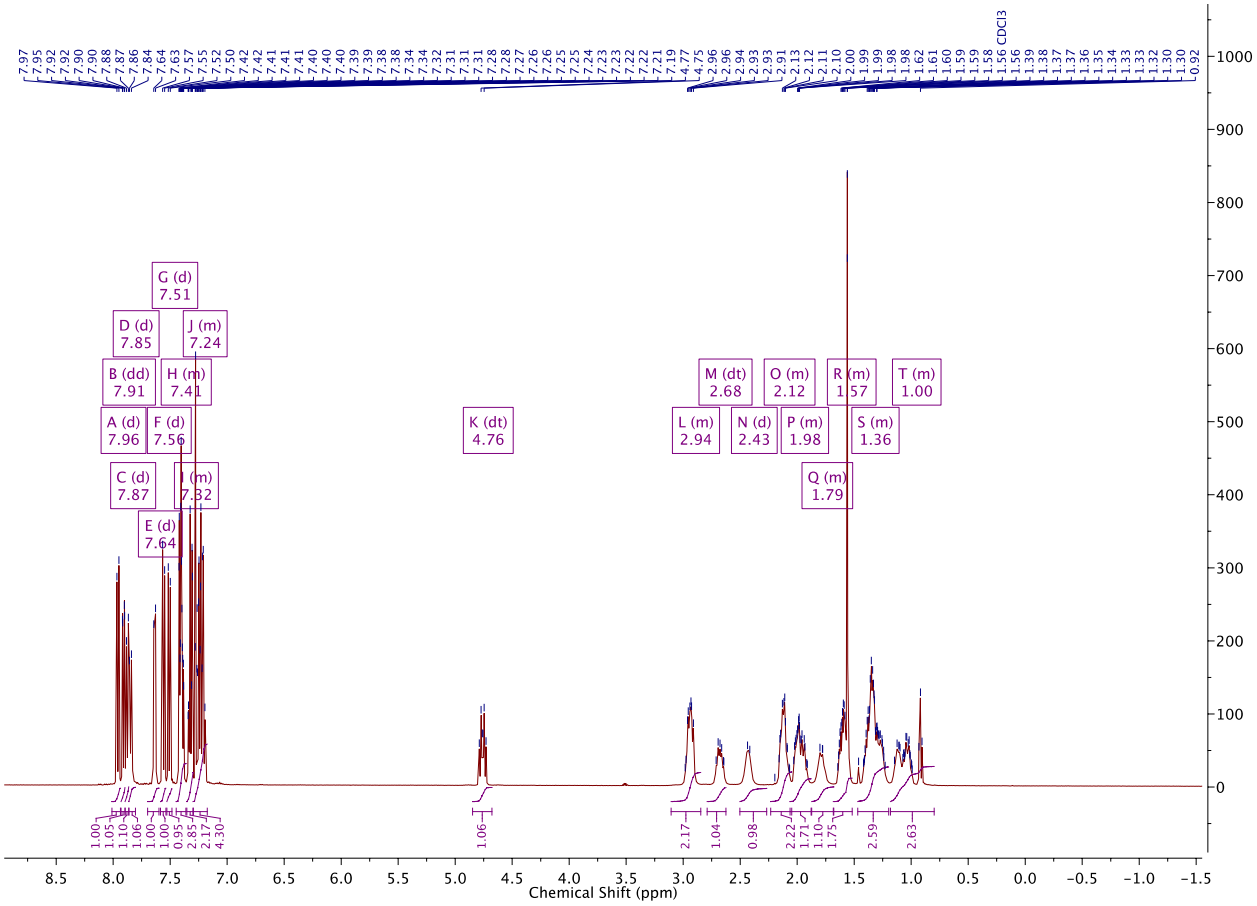
^{13}C NMR (126 MHz, Chloroform-d) δ_C/ppm 150.3 (d, J = 8.1 Hz), 150.1, 144.5, 143.1, 132.8 (d, J = 1.7 Hz), 132.7, 131.3, 130.5, 130.2, 129.6, 128.3, 128.2, 127.2, 127.1, 126.4, 125.9, 125.8, 124.8, 124.6, 124.6, 124.3, 124.1 (d, J = 5.3 Hz), 122.4, 122.4, 122.2, 121.7 (d, J = 2.4 Hz), 60.7 (d, J = 17.0 Hz), 56.6 (d, J = 8.1 Hz), 38.4, 30.1, 27.3, 27.2, 25.2, 25.1, 22.7, 14.2.

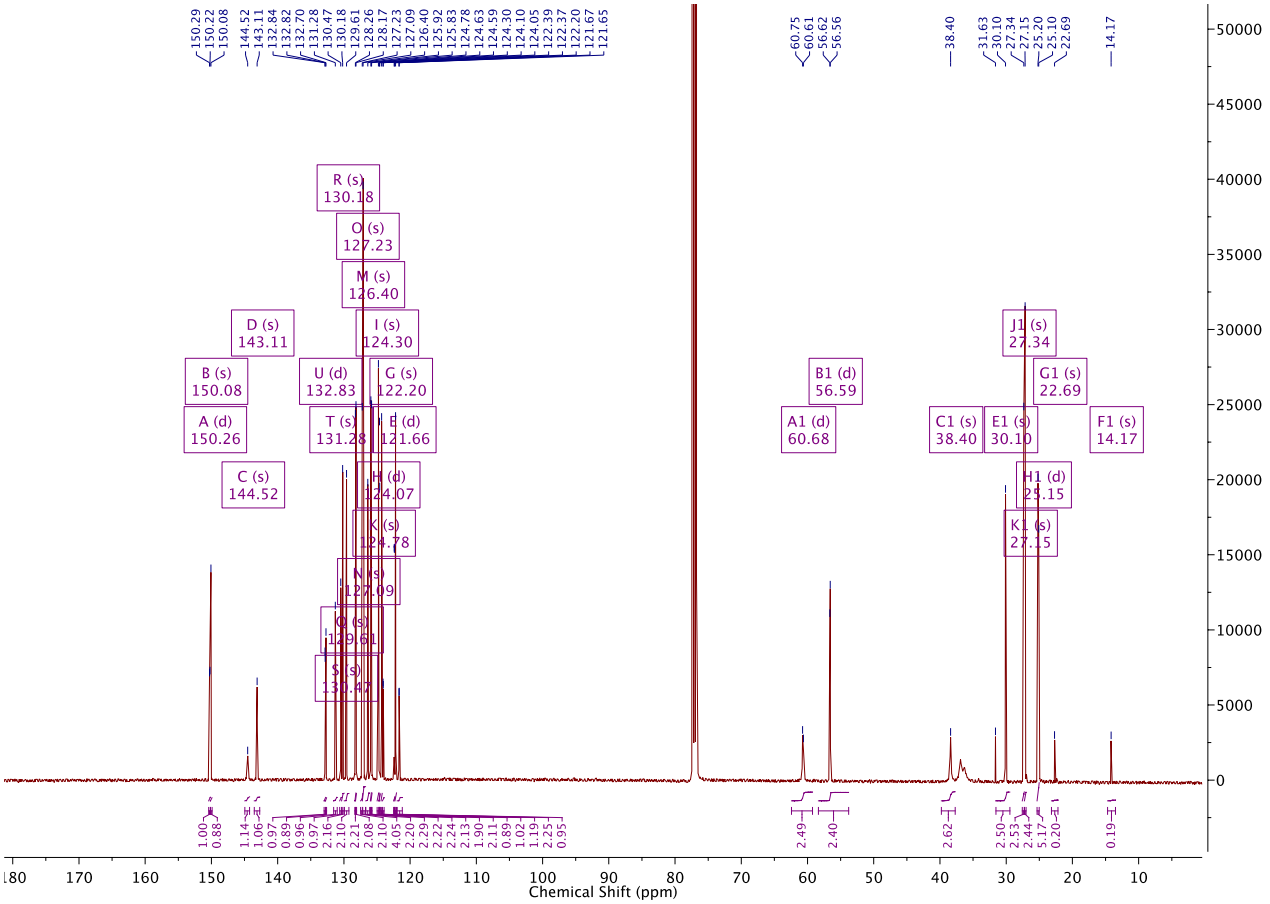
^{31}P NMR (162 MHz, $CDCl_3$) δ_P/ppm 151.2

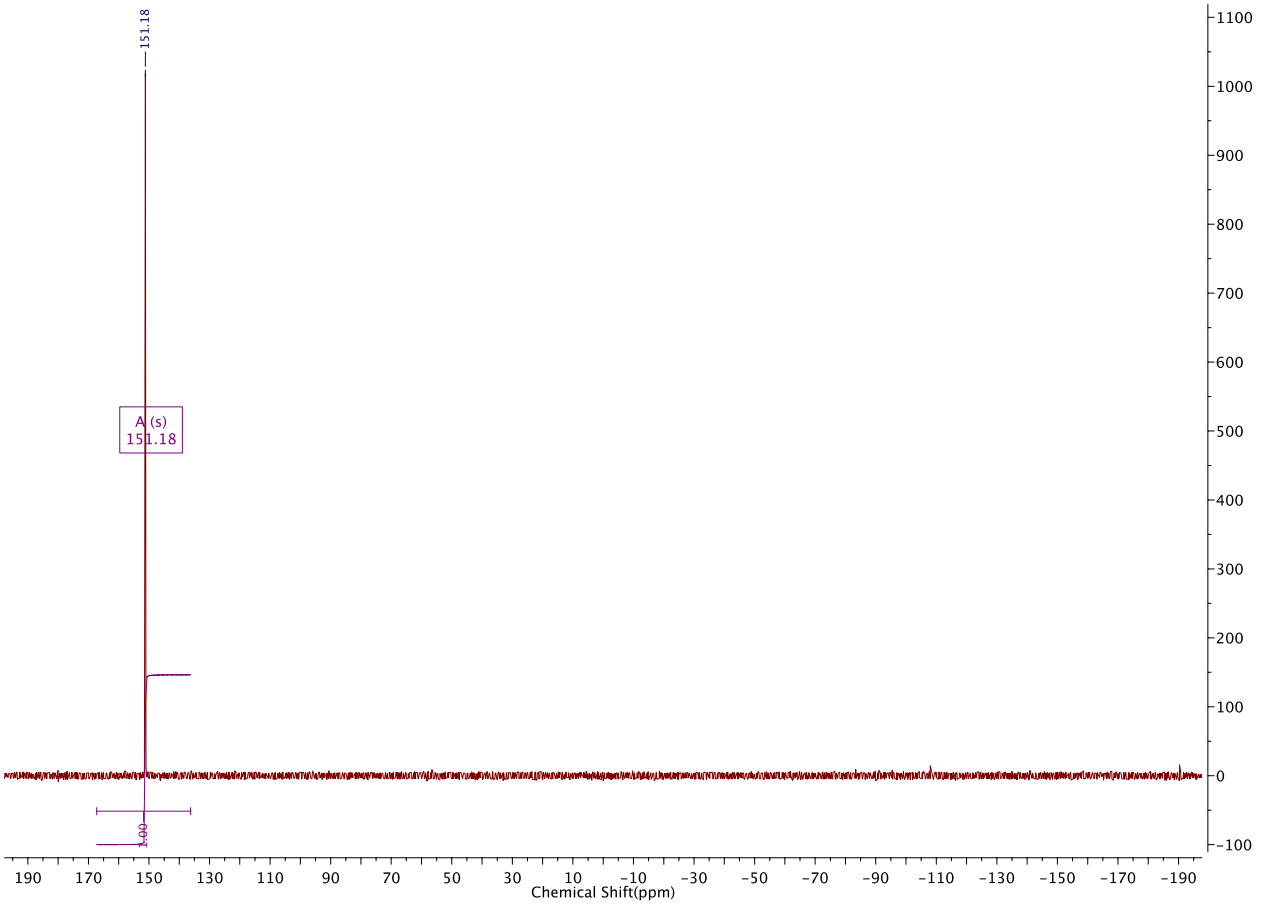
IR (ν_{max}/cm^{-1}, $CHCl_3$) 2929, 2854, 2361, 1590, 1462,1232,1067,947,911, 798, 748

MS (ESI) m/z calc. for $C_{36}H_{35}O_2NP$ [M+H]+: 544.2399, found: 544.2394.

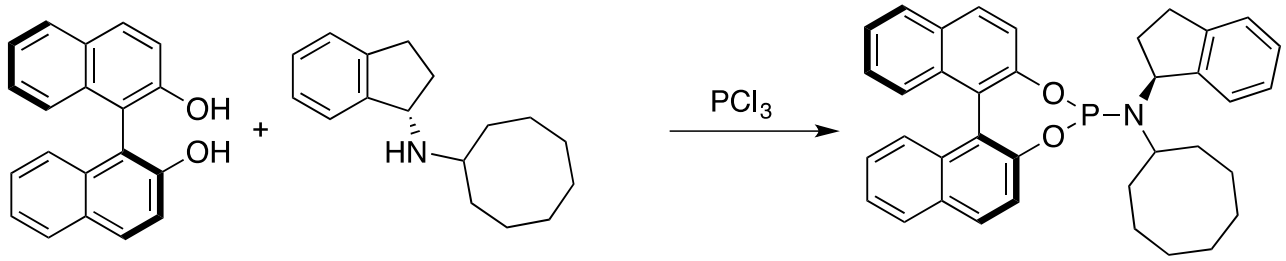
$[\alpha]^{20}_{589}$ = +122.2 ° (c=1.0, $CHCl_3$)




R (s)
130.18
O (s)
127.23
M (s)
126.40
D (s)
143.11
I (s)
124.30
J1 (s)
27.34
B (s)
150.08
U (d)
132.83
G (s)
122.20
B1 (d)
56.59
G1 (s)
22.69
A (d)
150.26
T (s)
131.28
E (d)
121.66
A1 (d)
60.68
C1 (s)
38.40
E1 (s)
30.10
F1 (s)
14.17
C (s)
144.52
H (d)
124.07
H1 (d)
25.15
K (s)
124.78
K1 (s)
27.15
N (s)
127.09
Q (s)
129.91
S (s)
130.47
Chemical Shift (ppm)


151.18
A (s)
151.18
Chemical Shift(ppm)

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



Triethylamine (2.92 mL, 5.0 eq., 20.5 mmol), was added dropwise to a stirred, ice-cooled solution of PCl_3 (0.38 mL, 1.0 eq., 4.1mmol) in CH_2Cl_2. The ice bath was removed and the solution left to warm to room temperature before (*S*)-N-cyclohexyl-2, 3-dihydro-1H-inden-1-amine (0.94 ml, 1.0 eq. 4.1mmol) was added to the stirred solution in one portion. After 5 hours,, (*S*)-binaphthol (1.12 g, 1.0 eq. 4.1 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 (~100 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(1.17 g, 51%).

^{1}H NMR (500 MHz, Chloroform-d) δ_H/ppm 7.97 (d, J = 8.8 Hz, 1H, Ar-*H*), 7.92 (dd, J = 8.3 Hz, 1.2 Hz, 1H, Ar-*H*), 7.90 – 7.83 (m, 2H, Ar-*H*), 7.64 (d, J =7.6 Hz, 1H, Ar-*H*), 7.61 (s, 1H, Ar-*H*), 7.52 (d, J = 8.7 Hz, 1H, Ar-*H*), 7.44 – 7.37 (m, 3H, Ar-*H*), 7.37 – 7.29 (m, 2H, Ar-*H*), 7.30 – 7.18 (m, 4H, Ar-*H*), 4.76 (dt, J = 13.4 Hz, 8.1 Hz, 1H, PhC*H*NH), 3.11 (d, J = 10.6 Hz, 1H, PhCH_2CH$_2$), 3.02 – 2.90 (m, 1H, PhCH_2CH$_2$), 2.70 (p, J = 8.3 Hz, 1H, NHC*H*), 2.44 (d, J = 11.4 Hz, 1H, PhCH$_2$CH_2), 2.16 (p, J = 9.9 Hz, 1H, PhCH$_2$CH_2), 2.09 – 1.79 (m, 3H, CH_2), 1.72 – 1.57 (m, 2H, CH_2), 1.43 – 1.05 (m, 8H, CH_2), 0.99 – 0.75 (m, 1H, CH_2).

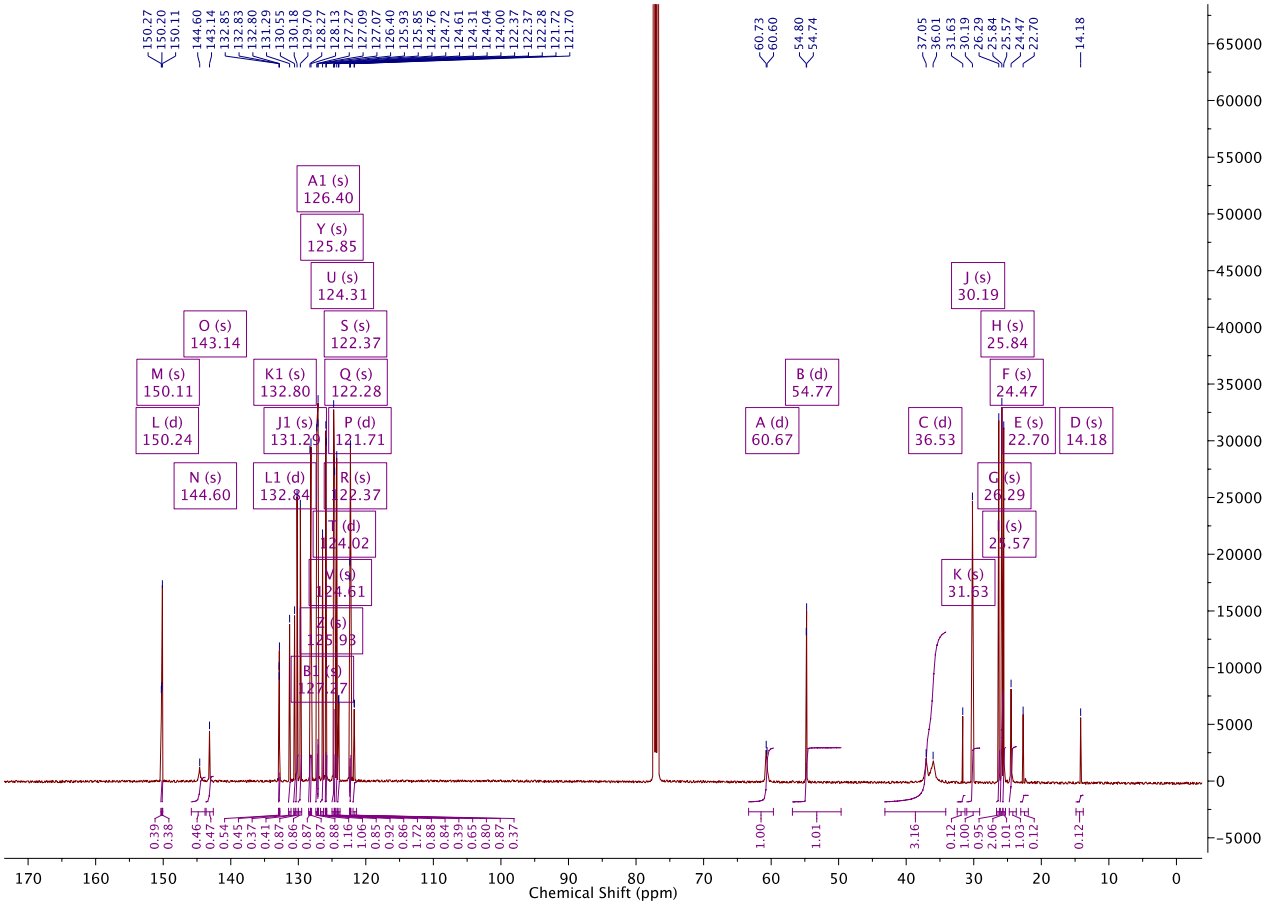
^{13}C NMR (126 MHz, Chloroform-d) δ_C/ppm 150.2 (d, J = 8.0 Hz), 150.1, 144.6, 143.14, 132.8 (d, J = 2.2 Hz), 132.8, 131.3, 130.6, 130.2, 129.7, 128.3, 128.1, 127.3, 127.1, 127.1, 126.4, 125.9, 125.9, 124.7 (d, J = 5.1 Hz), 124.6, 124.3, 124.0 (d, J = 5.3 Hz), 122.4, 122.4, 122.3, 121.7 (d, J = 2.4 Hz), 60.7 (d, J = 16.3 Hz), 54.8 (d, J = 7.7 Hz), 36.5 (d, J=131.2), 31.6, 30.2, 26.3, 25.8, 25.6, 24.5, 22.7, 14.2.

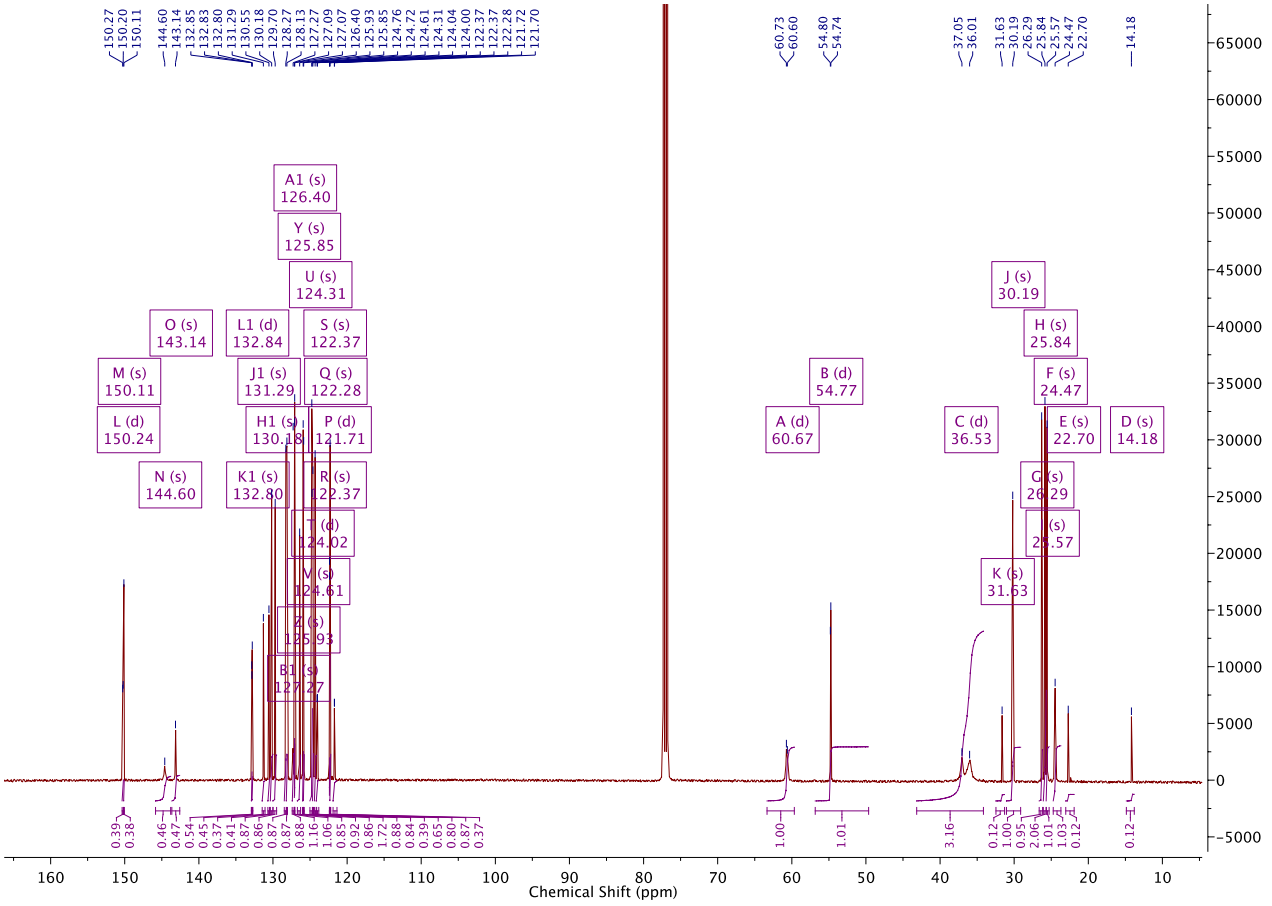
^{31}P NMR (162 MHz, $CDCl_3$) δ_P/ppm 151.7.

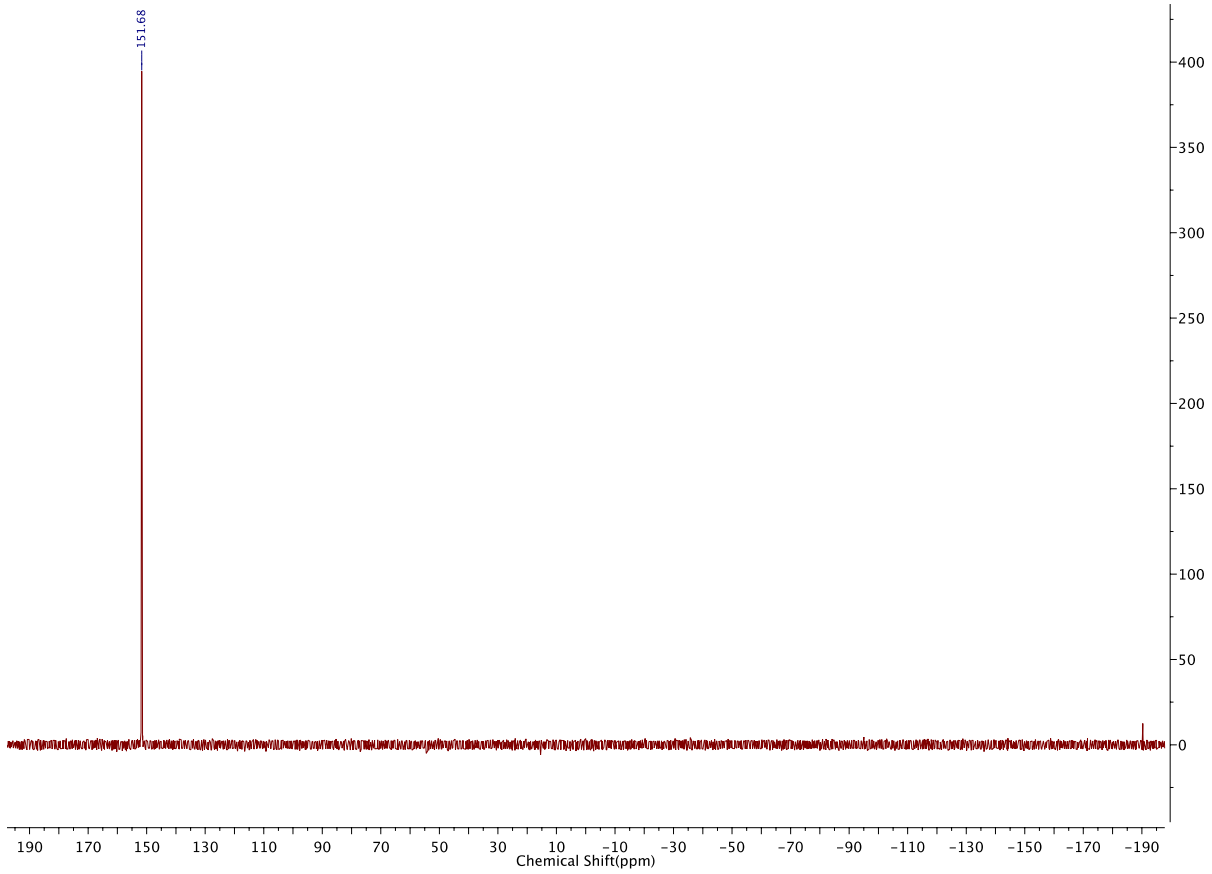
IR (ν_{max}/cm^{-1}, $CHCl_3$) 2929, 2854, 2361, 1590, 1462

MS (GCMS Ammonica Cl Spectrum) m/z calc. for $C_{37}H_{36}O_2NP$ $[M+H]^+$: 557.2484, found: 558.2558

$[\alpha]^{20}_{589}$ = +117.1 ° (c 1.0, $CHCl_3$)




A1 (s) 126.40
Y (s) 125.85
U (s) 124.31
O (s) 143.14
L1 (d) 132.84
S (s) 122.37
M (s) 150.11
J1 (s) 131.29
Q (s) 122.28
L (d) 150.24
H1 (s) 130.18
P (d) 121.71
N (s) 144.60
K1 (s) 132.80
R (s) 122.37
T (d) 124.02
V (s) 124.61
Z (s) 125.93
B1 (s) 127.27
J (s) 30.19
H (s) 25.84
B (d) 54.77
F (s) 24.47
A (d) 60.67
C (d) 36.53
E (s) 22.70
D (s) 14.18
G (s) 26.29
K (s) 31.63
Chemical Shift (ppm)


151.68
Chemical Shift(ppm)

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