Copper-Catalyzed Cross-Coupling of Alkyl Grignard Reagents and Propargylic Ammonium Salts: Stereospecific Synthesis of Allenes

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1 GENERAL EXPERIMENTAL DETAILS

Tetrahydrofuran and dichloromethane were purified by passing through a Pure Solv™ column drying system from Innovative Technology, Inc. Additionally, Tetrahydrofuran and dichloromethane were degassed passing Ar through them for 15 min. Diethyl ether was dried using activated 4Å molecular sieves and stored under argon. Unless indicated otherwise, all reactions were conducted under an argon atmosphere using flame-dried glassware with standard vacuum-line techniques. NMR spectra were acquired on a Bruker 300 spectrometer, running at 300, and 75 MHz for ^1^H and ^13^C respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals (CDCl₃, 7.26 ppm for ^1^H NMR and 77.2 ppm for ^13^C NMR respectively). ^13^C NMR spectra were acquired on a broad band decoupled mode. The following abbreviations are used to describe peak patterns when appropriate: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sex (sextet), sept (septuplet), m (multiplet), br (broad). Analytical thin layer chromatography (TLC) was performed using pre-coated aluminium-backed plates (Merck Kieselgel 60 F254) and visualized by ultraviolet irradiation or phosphomolybdic acid dip or potassium permanganate dip. Purification of reaction mixtures was carried out by flash chromatography (FC) using silica gel Merck-60. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The enantiomeric ratio (er) of the products was determined by stationary phase SFC, HPLC or GC using chiral columns. Mass Spectrometry (MS) and High-Resolution Mass Spectrometry (HRMS) were registered in a spectrometer GCT Agilent Technologies 6890N using Electronic Impact (E.I.) techniques at 70 eV, Fast Atom Bombardment and electrospray (ESI⁺ or ESI⁻).

All ligands and [Cu(CH₃CN)₄]PF₆ were acquired from commercial sources and were used without further purification. Grignard reagents were acquired from commercial sources and were tritritated prior to use. Propargylic ammonium salts were prepared following reported procedures and the enantiomeric ratios are specified in scheme 1.

![Scheme 1: Enantiomeric ratios of ammonium salts.](image-url)
2 OPTIMIZATION DETAILS

General procedure for the copper-catalyzed reaction of propargylic ammonium salts and Grignard reagents

An oven-dried vial was charged with Cu(I), the ligand and the corresponding ammonium salt (0.2 mmol) and sealed with a septum. The vial was connected to an argon-vacuum line, evacuated and backfilled with argon (x3). CH$_2$Cl$_2$ (2 mL) was added and the mixture was stirred for 5 min at room temperature. The reaction mixture was cooled to −40 ºC and a (1,3-Dioxan-2-ylethyl)magnesium bromide solution in THF (0.3 M, 0.22 mmol) was added dropwise. The mixture was stirred at −40 ºC for 5 minutes. Water (0.1 mL) was added and the solution was filtered through a short pad of MgSO$_4$ and rinsed with CH$_2$Cl$_2$. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography using n-hexane as eluent. The enantiomeric ratio was determined by SFC using Chiralpak-ID column [CO$_2$/MeOH (98:2)], 1.0 mL/min, $\tau_{\text{major}}$ = 10.9 min, $\tau_{\text{minor}}$ = 12.4 min.

Table S1: Influence of the copper and temperature.

<table>
<thead>
<tr>
<th>Entry</th>
<th>[Cu] (mol%)</th>
<th>L (mol%)</th>
<th>T (ºC)</th>
<th>Yield$^b$ (%)</th>
<th>er$^c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Cu(CH$_3$CN)$_2$PF$_6$ (5)</td>
<td>Sphos (6)</td>
<td>-40</td>
<td>90</td>
<td>98.2</td>
</tr>
<tr>
<td>2</td>
<td>Cu(CH$_3$CN)$_2$PF$_6$ (5)</td>
<td>Sphos (6)</td>
<td>0</td>
<td>76</td>
<td>95.5</td>
</tr>
<tr>
<td>2</td>
<td>Cu(CH$_3$CN)$_2$PF$_6$ (5)</td>
<td>Sphos (6)</td>
<td>rt</td>
<td>77</td>
<td>95.5</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>-</td>
<td>rt</td>
<td>24</td>
<td>78.22</td>
</tr>
</tbody>
</table>

$^a$Reaction conditions: following general procedure. $^b$Isolated yield after column chromatography. $^c$Determined by chiral SFC.
Table S2: Influence of the nature of the counterion.\textsuperscript{a}

![Chemical structure](image)

\[
\begin{array}{cccc}
\text{Entry} & X & \text{Yield (%)}^b & \alpha/\gamma^c & \text{er}^d \\
1 & \text{OTf} & 90 & \geq 98:2 & 98:2 \\
2 & \text{OMs} & 57 & \geq 98:2 & 71:29 \\
3 & \text{BF}_4^- & 63 & \geq 98:2 & 66:34 \\
4 & \text{I} & 51 & \geq 98:2 & 88:12 \\
5 & \text{OTs} & 51 & \geq 98:2 & 65:35 \\
\end{array}
\]

\textsuperscript{a}Reaction conditions: following general procedure. \textsuperscript{b}Isolated yield after column chromatography. \textsuperscript{c}Determined by \textsuperscript{1}H-NMR. \textsuperscript{d}Determined by chiral SFC.

Table S3: Influence of the nature of the leaving group.\textsuperscript{a}

![Chemical structure](image)

\[
\begin{array}{cccc}
\text{Entry} & X & \text{Yield (%)}^b & \alpha/\gamma^c & \text{er}^d \\
1 & \text{NMe}_3\text{OTf} & 90 & \geq 98:2 & 98:2 \\
2 & \text{OMs} & 55 & \geq 98:2 & 87:13 \\
\end{array}
\]

\textsuperscript{a}Reaction conditions: following general procedure. \textsuperscript{b}Yield was determined by isolation. \textsuperscript{c}Determined by \textsuperscript{1}H-NMR. \textsuperscript{d}Determined by chiral SFC.
3 SYNTHESIS OF STARTING MATERIALS

3.1 Synthesis of \((-\)-(S)-6-phenylhex-3-yn-2-ol, \(\text{(S)}\)-SI-1z

To an oven-dried round bottom flask was added \((\pm)-6\)-phenylhex-3-yn-2-ol (1.90 g, 10.9 mmol), molecular sieves (0.95 g) and Amano Lipase from Pseudomonas fluorescens (0.95 g). The flask was connected to an argon-vacuum line, evacuated and backfilled with argon (x3). \(n\)-Hexane (100 mL) and Vinyl acetate (2.7 mL, 33 mmol) were added and the reaction mixture was stirred at room temperature for 2 h. After completion (checked by chiral HPLC) the reaction was filtered and the solvent was removed under reduced pressure. Longer reaction times, results in complete acetylation of the alcohol. Compound \((\text{S})\)-SI-1z (853 mg, 4.9 mmol) was obtained in 45% yield as a yellowish oil after flash column chromatography (Cy/\(\text{EtOAc}\), 90/10).

Compound \((\text{S})\)-SI-1s was obtained in 99:1 enantiomeric ratio determined by HPLC using Chiralpak-IBN column [\(\text{CO}_2/\text{MeOH}\) (95:5)], 1.0 mL/min, \(t_{\text{major}}=11.2\) min, \(t_{\text{minor}}=6.4\) min. \(\text{H}\) NMR, \(\text{C}\) NMR and MS data were consistent with literature values. \(^3\) \([\alpha]^{20}_D=\ -33.1\) (\(c=1.0, \text{CHCl}_3\)).

3.2 Synthesis of \((+)-N,N\)-Dimethyl-6-phenylhex-3-yn-2-amine, \(\text{SI-2z}\).

To a solution of \((\text{S})\)-SI-1z (800 mg, 4.6 mmol) and triethylamine (3.2 mL, 23 mmol) in THF (12 mL) was added methanesulfonyl chloride (708 \(\mu\)L, 9.2 mmol) at 0 °C. The reaction was stirred for 1 h at room temperature and then, a solution of dimethylamine (12 mL, 2 M in THF, 23 mmol) was added to the mixture. The temperature was raised to 50 °C and the reaction mixture was stirred for 16 h. The reaction mixture was filtered through a short pad of Celite® and rinsed with \(\text{Et}_2\text{O}\). The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (From Cy/\(\text{EtOAc}\) 2:1 to \(\text{EtOAc}\) gradient). Compound \((\text{R})\)-SI-2z (845 mg, 4.2 mmol) was obtained in 91% yield as a yellowish oil.

\(^1\)H NMR, \(^{13}\)C NMR and MS data were consistent with literature values. \(^2\) \([\alpha]^{20}_D=\ +18.4\) (\(c=1.0, \text{CHCl}_3\)).
3.3 Synthesis of (+)-(R)-N,N,N-trimethyl-6-phenylhex-3-yn-2-aminium trifluoromethanesulphonate, (R)-1z.

To a solution of (R)-SI-2z (800 mg, 4 mmol) in Et₂O (8 mL) was added methyl trifluoromethanesulphonate (540 µL, 4.77 mmol) at 0 °C. The reaction was stirred for 1 h at 0 °C and a white solid precipitated. The mixture was filtered through a fritted funnel and was washed with cold Et₂O. The white solid was dried under vacuum for 16 h. Compound (R)-SI-2z (1.35 g, 3.75 mmol) was obtained in 93% yield as a white solid.

¹H NMR, ¹³C NMR and MS data were consistent with literature values.² [α]²⁰_D = +7.5 (c = 1.0, CHCl₃).

4 PREPARATION OF (4-PHENYLBUTYL)MAGNESIUM BROMIDE SOLUTION

An oven-dried flask was charged with magnesium (72 mg, 3 mmol, 1 equiv) and a couple of crystals of iodine under Ar atmosphere. Dry THF (6 mL) was added and the mixture was stirred for 2 min. (4-bromobutyl)benzene was added dropwise to the mixture observing a gentle reflux. The mixture was stirred for 2 h and then, it was allowed to rest for 24 h. The supernatant was filtered and the solution was tritrated to determine its concentration (0.43M).¹

5 COPPER-CATALYZED REACTION OF PROPARGYLIC AMMONIUM TRIFLATES WITH ALKYL GRIGNARD REAGENTS.

General procedure for the reactions of (±) propargylic ammonium (1) salts with alkylmagnesium halides.

An oven-dried vial was charged with [Cu(CH₃CN)₄]PF₆ (3.8 mg, 0.01 mmol) and the correspondent ammonium salt (0.2 mmol) and sealed with a septum. The vial was connected to an argon-vacuum line, evacuated and backfilled with argon (x3). DCM (2 mL) was added and the mixture was stirred for 5 min at room temperature. The reaction
mixture was cooled to -40 °C and the alkyl magnesium bromide solution in THF (0.22 mmol) was added dropwise and the mixture was stirred at -40 °C for 5 minutes. After total conversion observed by TLC (5 minutes), water (0.1 mL) was added and the solution was filtered through a short pad of MgSO₄ and rinsed with DCM. Solvent was removed under reduced pressure and the crude product was purified by flash column chromatography.

**General procedure for the reactions of enantiopure propargylic ammonium (1) salts with alkylmagnesium halides.**

An oven-dried vial was charged with [Cu(CH₃CN)₄]PF₆ (3.8 mg, 0.01 mmol), Sphos (4.9 mg, 0.012 mmol) and the correspondent ammonium salt (0.2 mmol) and sealed with a septum. The vial was connected to an argon-vacuum line, evacuated and backfilled with argon (x3). DCM (2 mL) was added and the mixture was stirred for 5 min at room temperature. The reaction mixture was cooled to -40 °C and the alkyl magnesium bromide solution in THF (0.22 mmol) was added dropwise and the mixture was stirred at -40 °C for 5 minutes. After total conversion observed by TLC (5 minutes), water (0.1 mL) was added and the solution was filtered through a short pad of MgSO₄ and rinsed with DCM. Solvent was removed under reduced pressure and the crude product was purified by flash column chromatography.

$$\text{(-)-}(R)-2-(3\text{-phenylhexa-3,4-dien-1-yl})\text{-}1,3\text{-dioxane (2a).}$$

From (R)-1a (67 mg, 0.2 mmol) and (1,3-Dioxan-2-ylethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound (R)-2a (44 mg, 0.18 mmol) was obtained in 90% yield as a pale yellow oil, after purification by flash column chromatography (cyclohexane/EtOAc 95:5). From (±)-1a, following the same procedure without Sphos, compound (±)-2a (42 mg, 0.17 mmol) was obtained in 86% yield.

$^1$H NMR, $^{13}$C NMR and MS data for (±)-2a were consistent with literature values. Compounds (R)-2a was obtained in 98:2 enantiomeric ratio determined by SFC using Chiralpak-ID column [CO₂/MeOH (98:2)], 1.0 mL/min, $\tau_{\text{major}}$= 12.9 min, $\tau_{\text{minor}}$= 14.4 min. [α]$_D^{25}$ = -64.1 (c = 1.0, CHCl₃).

The reaction was also carried out in gram scale, from (R)-1a (1.0 g, 2.96 mmol) and (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (3.3 mmol) affording compound (R)-2a (614 mg, 2.47 mmol) in 85% yield as a yellow oil and enantiomeric ratio of 98:2.
(−)-(R)-2-(3-(3-methoxyphenyl)hexa-3,4-dien-1-yl)-1,3-dioxane (2b).

From (R)-1b (74 mg, 0.2 mmol) and (1,3-dioxan-2-yethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound (R)-2b (51 mg, 0.19 mmol) was obtained in 93% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et₂O 97:3). From (±)-1b, following the same procedure without SPhos, compound (±)-2b (51 mg, 0.19 mmol) was obtained in 93% yield.

1H NMR, 13C NMR and MS data for (±)-2b were consistent with literature values.⁴

Compound (R)-2a was obtained in 98:2 enantiomeric ratio determined by SFC using Chiralpak-IA column [CO₂/MeOH (99:1)], 1.0 mL/min, t_major= 25.5 min, t_minor= 27.3 min. [α]²⁵_D = -66.7 (c = 1.0, CHCl₃).

(±)-2-(3-(4-Methoxyphenyl)hexa-3,4-dien-1-yl)-1,3-dioxane (2c).

From 1c (74 mg, 0.2 mmol) and (1,3-dioxan-2-yethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound 2c (33 mg, 0.12 mmol) was obtained in 60% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et₂O 97:3).

1H NMR (300 MHz, CDCl₃) δ 7.35 – 7.29 (m, 2H), 6.88 – 6.82 (m, 2H), 5.53 – 5.41 (m, 1H), 4.62 (t, J = 5.2 Hz, 1H), 4.19 – 4.06 (m, 2H), 3.81 – 3.71 (m, 2H), 3.80 (s, 3H), 2.51 – 2.42 (m, 2H), 2.16 – 2.03 (m, 1H), 1.89 – 1.80 (m, 2H), 1.74 (d, J = 7.0 Hz, 3H), 1.38 – 1.31 (m, 1H). 13C NMR (75 MHz, CDCl₃) δ 204.0, 158.5, 129.8, 127.2, 113.9, 104.3, 102.1, 89.7, 67.1, 55.4, 33.8, 26.0, 24.4, 14.7. HRMS (EI) calculated for C₁₇H₂₁O₃ [M]+: 274.1491; Found 274.1495.

(±)-2-(3-(4-chlorophenyl)hexa-3,4-dien-1-yl)-1,3-dioxane (2d).

From 1d (74 mg, 0.2 mmol) and (1,3-dioxan-2-yethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound 2d (50 mg, 0.18 mmol) was obtained in 90% yield as a pale yellow oil, after purification by flash column chromatography (cyclohexane/Et₂O 95:5). 1H NMR, 13C NMR and MS data were consistent with literature values.⁴
(−)-(R)-2-(3-(4-fluorophenyl)hexa-3,4-dien-1-yl)-1,3-dioxane (2e).

From (R)-1e (71 mg, 0.2 mmol) and (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound (R)-2e (50 mg, 0.19 mmol) was obtained in 95% yield as a pale yellow oil, after purification by flash column chromatography (pentane/EtO 97:3).

From (±)-1e, following the same procedure without SPhos, compound (±)-2e (44 mg, 0.17 mmol) was obtained in 84% yield.

Compound (R)-2e was obtained in 97:3 enantiomeric ratio determined by SFC using Chiralpak-ID column [CO2/MeOH (99:1)], 1.0 mL/min, t_major = 18.7 min, t_minor = 20.8 min. 

$^1$H NMR (300 MHz, CDCl₃) δ 7.40 – 7.30 (m, 2H), 7.03 – 6.92 (m, 2H), 5.49 (qt, J = 6.9, 3.2 Hz, 1H), 4.62 (t, J = 5.1 Hz, 1H), 4.20 – 4.04 (m, 2H), 3.86 – 3.69 (m, 2H), 2.56 – 2.35 (m, 2H), 2.19 – 2.00 (m, 1H), 1.88 – 1.80 (m, 2H), 1.75 (d, J = 7.0 Hz, 3H), 1.40 – 1.30 (m, 1H). 

$^{13}$C NMR (75 MHz, CDCl₃) δ 204.3 (d, J_C-F = 2.0 Hz), 161.8 (d, J_C-F = 245.4 Hz), 133.4 (d, J_C-F = 3.2 Hz), 127.6 (d, J_C-F = 7.9 Hz), 115.2 (d, J_C-F = 21.4 Hz), 140.0, 101.9, 90.1, 67.1, 33.7, 26.0, 24.4, 14.5. 

HRMS (EI) calculated for C_{16}H_{18}FO_{2} [M-H]^+: 261.1291; Found: 261.0887. [α]$_{D}^{25}$ = -68.1 (c = 1.0, CHCl₃).

(±)-2-(3-(3-Bromophenyl)hexa-3,4-dien-1-yl)-1,3-dioxane (2f).

From 1f (83 mg, 0.2 mmol) and (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound 2f (58 mg, 0.18 mmol) was obtained in 90% yield as a pale yellow oil, after purification by flash column chromatography (pentane/EtO 95:5).

$^1$H NMR (300 MHz, CDCl₃) δ 7.52 (t, J = 1.9 Hz, 1H), 7.30 (ddt, J = 8.0, 5.1, 1.3 Hz, 2H), 7.15 (t, J = 7.9 Hz, 1H), 5.53 (qt, J = 7.0, 3.3 Hz, 1H), 4.61 (t, J = 5.2 Hz, 1H), 4.19 – 4.07 (m, 2H), 3.84 – 3.71 (m, 2H), 2.55 – 2.36 (m, 2H), 2.19 – 2.02 (m, 1H), 1.88 – 1.79 (m, 2H), 1.76 (d, J = 7.0 Hz, 3H), 1.40 – 1.30 (m, 1H). 

$^{13}$C NMR (75 MHz, CDCl₃) δ 204.7, 140.0, 129.8, 129.4, 129.1, 124.6, 122.7, 104.0, 102.0, 90.5, 67.1, 33.7, 26.0, 24.4, 14.5. 

HRMS (EI) calculated for C_{16}H_{19}BrO_{2} [M]^+: 322.0568; Found: 322.0552.
(±)-Methyl 4-(1-(1,3-dioxan-2-yl)hexa-3,4-dien-3-yl)benzoate (2g).

From 1g (79 mg, 0.2 mmol) and (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound 2g (54 mg, 0.17 mmol) was obtained in 89% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et₂O 90:10). ¹H NMR, ¹³C NMR and MS data were consistent with literature values.⁴

(±)-Methyl 2-(1-(1,3-dioxan-2-yl)hexa-3,4-dien-3-yl)benzoate (2h).

From 1h (79 mg, 0.2 mmol) and (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound 2h (30 mg, 0.10 mmol) was obtained in 50% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et₂O 90:10).

¹H NMR (300 MHz, CDCl₃) δ 7.67 (dd, J = 7.7, 1.5 Hz, 1H), 7.45 – 7.37 (m, 1H), 7.33 – 7.26 (m, 2H), 5.25 (qt, J = 6.8, 3.2 Hz, 1H), 4.61 (t, J = 5.2 Hz, 1H), 4.14 – 4.05 (m, 2H), 3.86 (s, 3H), 3.81 – 3.69 (m, 2H), 2.46 – 2.35 (m, 2H), 2.14 – 2.00 (m, 1H), 1.85 – 1.77 (m, 2H), 1.66 (d, J = 7.0 Hz, 3H), 1.37 – 1.28 (m, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 203.2, 168.8, 139.5, 131.1, 130.8, 129.7, 129.28, 126.6, 104.5, 101.8, 87.8, 66.9, 52.0, 33.6, 27.7, 25.9, 14.3. HRMS (EI) calculated for C₁₈H₂₂O₄ [M⁺]: 302.1518; Found: 302.1509.

(±)-4-(1-(1,3-Dioxan-2-yl)hexa-3,4-dien-3-yl)benzonitrile (2i).

From 1i (72 mg, 0.2 mmol) and (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound 2i (45 mg, 0.17 mmol) was obtained in 84% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et₂O 90:10). ¹H NMR, ¹³C NMR and MS data were consistent with literature values.⁴
(--)-(R)-3-(1,3-dioxan-2-yl)hexa-3,4-dien-3-yl)benzonitrile (2j).

From (R)-1j (72 mg, 0.2 mmol) and (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound (R)-2j (50 mg, 0.19 mmol) was obtained in 93% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et₂O 90:10). From (±)-1j, following the same procedure, compound (±)-2j (49 mg, 0.18 mmol) was obtained in 91% yield.

Compound (R)-2j was obtained in 95:5 enantiomeric ratio determined by SFC using Chiralpak-IB column [CO₂/MeOH (99:1)], 1.0 mL/min, \( t_{\text{major}} = 28.3 \text{ min}, t_{\text{minor}} = 26.6 \) min. \(^1\)H NMR (300 MHz, CDCl₃) \( \delta 7.65 (t, J = 1.8 \text{ Hz}, 1\text{H}), 7.59 (dt, J = 7.7, 1.7 \text{ Hz}, 1\text{H}), 7.46 – 7.33 (m, 2\text{H}), 5.57 (qt, J = 7.0, 3.3 \text{ Hz}, 1\text{H}), 4.61 (t, J = 5.1 \text{ Hz}, 1\text{H}), 4.16 – 4.06 (m, 2\text{H}), 3.83 – 3.69 (m, 2\text{H}), 2.51 – 2.38 (m, 2\text{H}), 2.17 – 1.99 (m, 1\text{H}), 1.87 – 1.77 (m, 2\text{H}), 1.76 (d, J = 7.1 \text{ Hz}, 3\text{H}), 1.39 – 1.30 (m, 1\text{H}). \(^{13}\)C NMR (75 MHz, CDCl₃) \( \delta 204.8, 139.0, 130.1, 129.8, 129.6, 129.1, 119.2, 112.4, 103.5, 101.6, 91.1, 67.0, 33.5, 25.9, 23.8, 14.2. \) HRMS (ESI) calculated for C₁₇H₁₉NNaO₂ [M+Na]⁺: 292.1313; Found: 292.1318. \([\alpha]^{25}_D = -89.3 \) (c = 1.0, CHCl₃).

(±)-1-(4-(1,3-Dioxan-2-yl)hexa-3,4-dien-3-yl)phenyl)ethanone (2k).

From 1k (76 mg, 0.2 mmol) and (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above (catalytic charge was changed to 0.02 mmol), compound 2k (23 mg, 0.08 mmol) was obtained in 40% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et₂O 80:20). \(^1\)H NMR, \(^{13}\)C NMR and MS data were consistent with literature values.

(±)-2-(3-(4-(Trifluoromethyl)phenyl)hexa-3,4-dien-1-yl)-1,3-dioxane (2l).

From 1l (81 mg, 0.2 mmol) and (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound 2l (58 mg, 0.19 mmol) was obtained in 93% yield as a pale yellow oil, after purification by flash column chromatography (hexane/ACOEt 95:5). \(^1\)H NMR, \(^{13}\)C NMR and MS data were consistent with literature values.
(±)-2-(3-(Thiophen-2-yl)hexa-3,4-dien-1-yl)-1,3-dioxane (2m).

From 1m (69 mg, 0.2 mmol) and (1,3-dioxan-2-yethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound 2m (40 mg, 0.16 mmol) was obtained in 80% yield as a pale yellow oil, after purification by flash column chromatography (cyclohexane/EtOAc 95:5).

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.13 (dd, $J = 5.0, 1.4$ Hz, 1H), 7.00 – 6.90 (m, 2H), 5.51 (qt, $J = 6.9, 3.2$ Hz, 1H), 4.62 (t, $J = 5.2$ Hz, 1H), 4.18 – 4.09 (m, 2H), 3.83 – 3.73 (m, 2H), 2.54 – 2.44 (m, 2H), 2.16 – 2.03 (m, 1H), 1.91 – 1.82 (m, 2H), 1.72 (d, $J = 3.3$ Hz, 3H), 1.40 – 1.31 (m, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 203.4, 143.0, 127.4, 124.1, 122.7, 101.9, 100.8, 90.6, 67.1, 33.6, 26.0, 25.5, 14.6.

HRMS (EI) calculated for C$_{14}$H$_{17}$O$_2$S [M-H]$^+$: 249.0949; Found: 249.0553.

(±)-2-(3-Phenethylhexa-3,4-dien-1-yl)-1,3-dioxane (2n).

From 1n (73 mg, 0.2 mmol) and (1,3-dioxan-2-yethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above (temperature was changed to rt), compound 2n (33 mg, 0.12 mmol) was obtained in 61% yield as a pale yellow oil, after purification by flash column chromatography (cyclohexane/EtOAc 95:5).

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.29 – 7.24 (m, 2H), 7.22 – 7.13 (m, 3H), 5.08 (qt, $J = 7.8, 3.4$ Hz, 1H), 4.54 (t, $J = 5.2$ Hz, 1H), 4.16 – 4.05 (m, 2H), 3.82 – 3.68 (m, 2H), 2.77 – 2.66 (m, 2H), 2.29 – 2.18 (m, 2H), 2.15 – 1.99 (m, 3H), 1.79 – 1.68 (m, 2H), 1.55 (d, $J = 7.1$ Hz, 3H), 1.39 – 1.29 (m, 1H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 201.7, 142.5, 128.5, 128.31, 125.8, 102.8, 102.1, 87.9, 67.1, 34.7, 34.2, 33.4, 27.0, 26.0, 15.0. HRMS (ESI) calculated for C$_{18}$H$_{24}$NaO$_2$ [M+Na]$^+$: 295.1674; Found: 295.1665.

(--)(R)-2-(3-Phenylundeca-3,4-dien-1-yl)-1,3-dioxane (2o).

From (R)-1o (82 mg, 0.2 mmol) and (1,3-dioxan-2-yethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound (R)-2o (48 mg, 0.15 mmol) was obtained in 76% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et$_2$O 95:5).

From (±)-1o, following the same procedure without SPhos, compound (±)-2o (51 mg, 0.16 mmol) was obtained in 81% yield.

Compound (R)-2o was obtained in 98:2 enantiomeric ratio determined by SFC using Chiralpak-IB column [CO$_2$/MeOH (99:1)], 1.0 mL/min, $t_{\text{major}}$ = 28.3 min, $t_{\text{minor}}$ = 27.7
min. **H NMR** (300 MHz, CDCl$_3$) δ 7.45 – 7.38 (m, 2H), 7.33 – 7.27 (m, 2H), 7.21 – 7.13 (m, 1H), 5.53 (tt, J = 6.6, 3.3 Hz, 1H), 4.63 (t, J = 5.2 Hz, 1H), 4.20 – 4.05 (m, 2H), 3.83 – 3.68 (m, 2H), 2.57 – 2.45 (m, 2H), 2.16 – 2.06 (m, 3H), 1.92 – 1.81 (m, 2H), 1.56 – 1.21 (m, 10H), 0.96 – 0.82 (m, 3H). **13C NMR** (76 MHz, CDCl$_3$) δ 203.6, 137.6, 128.4, 126.5, 126.0, 105.2, 102.1, 95.5, 67.1, 33.8, 31.8, 29.4, 29.3, 29.1, 26.0, 24.2, 22.8, 14.2. **HRMS** (EI) calculated for C$_{21}$H$_{30}$O$_2$ [M]$^+$: 314.2246; Found: 314.2223. [α]$^D_{25} = -78.2$ (c = 1.0, CHCl$_3$).

(±)-2-(7-(Methylthio)-3-phenethylhepta-3,4-dien-1-yl)-1,3-dioxane (2p).

From 1p (85 mg, 0.2 mmol) and (1,3-dioxan-2-ylethyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above (temperature was changed to rt), compound 2p (48 mg, 0.14 mmol) was obtained in 72% yield as a pale yellow oil, after purification by flash column chromatography (cyclohexane/EtOAc 90:10).

**H NMR** (300 MHz, CDCl$_3$) δ 7.31 – 7.22 (m, 2H), 7.22 – 7.13 (m, 3H), 5.18 (qt, J = 6.2, 3.1 Hz, 1H), 4.54 (t, J = 5.1 Hz, 1H), 4.15 – 4.05 (m, 2H), 3.83 – 3.67 (m, 2H), 2.74 (t, J = 7.9 Hz, 2H), 2.51 – 2.41 (m, 2H), 2.32 – 2.01 (m, 10H), 1.79 – 1.68 (m, 2H), 1.38 – 1.29 (m, 1H). **13C NMR** (75 MHz, CDCl$_3$) δ 201.0, 142.2, 128.5, 128.3, 125.8, 104.4, 102.0, 91.8, 67.0, 34.6, 34.1, 33.8, 33.4, 29.3, 26.9, 26.0, 15.69. **HRMS** (EI) calculated for C$_{20}$H$_{28}$O$_2$S [M]$^+$: 332.1810; Found: 332.1797.

(±)-1-Bromo-3-(octa-2,3-dien-4-yl)benzene (2q).

From 1f (83 mg, 0.2 mmol) and n-butylmagnesium chloride solution in THF (0.22 mmol) following the general procedure described above, compound 2q (30 mg, 0.11 mmol) was obtained in 57% yield as a pale yellow oil, after purification by flash column chromatography (hexane/Et$_2$O 98:2).

**H NMR** (300 MHz, CDCl$_3$) δ 7.51 (t, J = 1.8 Hz, 1H), 7.34 – 7.27 (m, 2H), 7.16 (dd, J = 8.3, 7.4 Hz, 1H), 5.49 (qt, J = 6.9, 3.1 Hz, 1H), 2.41 – 2.31 (m, 2H), 1.76 (d, J = 0.7 Hz, 3H), 1.58 – 1.34 (m, 4H), 0.93 (t, J = 7.1 Hz, 3H). **13C NMR** (75 MHz, CDCl$_3$) δ 205.0, 140.3, 129.8, 129.3, 129.2, 124.6, 122.7, 104.3, 89.5, 30.1, 29.6, 22.5, 14.4, 14.1. **HRMS** (EI) calculated for C$_{14}$H$_{17}$Br [M]$^+$: 264.0514; Found: 264.0478.
(±)-1-(Octa-2,3-dien-4-yl)-4-(trifluoromethyl)benzene (2r).

From 1l (81 mg, 0.2 mmol) and n-butylmagnesium bromide chloride solution in THF (0.22 mmol) following the general procedure described above, compound 2r (42 mg, 0.17 mmol) was obtained in 83% yield as a pale yellow oil, after purification by flash column chromatography (pentane/EtO 98:2).

$^1$H NMR (300 MHz, CDCl3) δ 7.54 (d, $J = 8.4$ Hz, 2H), 7.48 (d, $J = 8.4$ Hz, 2H), 5.52 (qt, $J = 6.8, 3.1$ Hz, 1H), 2.45 – 2.35 (m, 2H), 1.78 (d, $J = 7.0$ Hz, 3H), 1.58 – 1.35 (m, 5H), 0.94 (t, $J = 7.2$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl3) δ 205.6, 141.7, 128.4 (q, $J_{C-F} = 32.4$ Hz), 126.3, 125.3 (q, $J_{C-F} = 3.9$ Hz), 124.5 (q, $J_{C-F} = 270.3$ Hz), 104.5, 89.6, 30.2, 29.6, 22.5, 14.3, 14.1. HRMS (EI) calculated for C$_{15}$H$_{17}$F$_3$ [M]$^+$: 254.1282; Found: 254.1279.

(±)-1-Bromo-3-(1-phenylhexa-3,4-dien-3-yl)benzene (2s).

From (±)-1f (83 mg, 0.2 mmol) and phenethylmagnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound (±)-2s (55 mg, 0.18 mmol) was obtained in 88% yield as a pale yellow oil, after purification by flash column chromatography (hexane/EtO 98:2).

$^1$H NMR (300 MHz, CDCl3) δ 7.52 (t, $J = 1.9$ Hz, 1H), 7.34 – 7.27 (m, 4H), 7.24 – 7.14 (m, 4H), 5.51 (qt, $J = 6.9, 3.1$ Hz, 1H), 2.88 – 2.79 (m, 2H), 2.74 – 2.59 (m, 2H), 1.69 (d, $J = 7.0$ Hz, 3H).

$^{13}$C NMR (76 MHz, CDCl3) δ 205.1, 142.0, 139.9, 129.9, 129.5, 128.6, 128.5, 126.0, 124.6, 122.8, 103.8, 90.3, 34.2, 31.7, 14.3. HRMS (EI) calculated for C$_{18}$H$_{17}$Br [M]$^+$: 312.0514; Found: 312.0485.

(−)-(R)-1-Methoxy-3-(2-methylhexa-3,4-dien-3-yl)benzene (2t).

From (R)-1b (75 mg, 0.2 mmol) and phenethylmagnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound (R)-2t (50 mg, 0.19 mmol) was obtained in 95% yield as a pale yellow oil, after purification by flash column chromatography (pentane/EtO 95:5). From (±)-1b, following the same procedure without SPhos, compound (±)-2t (52 mg, 0.20 mmol) was obtained in 97% yield.

Compound (R)-2t was obtained in 96:4 enantiomeric ratio determined by SFC using Chiralpak-IB column [CO$_2$/MeOH (99:1)], 1 mL/min, $t_{\text{major}} = 25.4$ min, $t_{\text{minor}} = 30.8$ min. $^1$H NMR (300 MHz, CDCl3) δ 7.26 – 7.08 (m, 7H), 6.96 – 6.87 (m, 2H), 6.68 (ddd, $J = 8.2, 2.5, 1.1$ Hz, 1H), 5.39 (qt, $J = 6.9, 3.0$ Hz, 1H), 3.73 (d, $J = 1.1$ Hz, 3H), 2.77 (dd, $J = 8.2, 5.8$ Hz, 2H), 2.69 – 2.57 (m, 2H), 1.61 (dd, $J = 7.1, 1.1$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl3) δ 205.0, 159.9, 142.3, 139.1, 129.4, 128.7, 128.4, 125.9, 118.7, 112.1, 111.9, 104.5, 84.4, 30.8.
104.7, 89.7, 55.4, 34.4, 31.9, 14.4. **HRMS** (EI) calculated for C_{18}H_{20}O [M]^+: 264.1514; Found: 264.1481. [α]^{25b}_{D} = -52.0 (c = 1.0, CHCl_{3}).

(−)-(R)-Octa-5,6-diene-1,5-diyl dibenzene (2u).

From (R)-1a (75 mg, 0.2 mmol) and (4-phenylbutyl)magnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound (R)-2u (47 mg, 0.18 mmol) was obtained in 90% yield as a pale-yellow oil, after purification by flash column chromatography (hexanes). From (±)-1a, following the same procedure, compound (±)-2u (46 mg, 0.18 mmol) was obtained in 88% yield.

Compound (R)-2u was obtained in 98:2 enantiomeric ratio determined by SFC using Chiralpak-ID column [CO_{2}/MeOH (99:1)], 1 mL/min, \(t_{\text{major}} = 11.3\) min, \(t_{\text{minor}} = 12.9\) min. \(^1\)H NMR, \(^{13}\)C NMR and MS data were consistent with literature values. \(^5\) [α]^{25b}_{D} = -54.0 (c = 1.0, CHCl_{3}).

(±)-1-Methoxy-4-(2-methylhexa-3,4-dien-3-yl)benzene (2v).

From 1c (75 mg, 0.2 mmol) and isopropylmagnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound 2v (40 mg, 0.20 mmol) was obtained in 98% yield as a pale-yellow oil, after purification by flash column chromatography (cyclohexane/\text{EtOAc} 95:5).

\(^1\)H NMR (300 MHz, CDCl_{3}) \(\delta 7.38 – 7.28\) (m, 2H), \(6.91 – 6.83\) (m, 2H), 5.47 (qd, \(J = 6.9, 2.4\) Hz, 1H), 3.81 (s, 3H), 2.87 – 2.66 (m, 1H), 1.76 (dd, \(J = 6.9, 0.7\) Hz, 3H), 1.13 (d, \(J = 5.8\) Hz, 3H), 1.10 (d, \(J = 5.6\) Hz, 3H). \(^{13}\)C NMR (75 MHz, CDCl_{3}) \(\delta 203.4, 158.4, 129.9, 127.7, 113.9, 112.1, 89.8, 55.4, 28.2, 22.7, 22.3, 14.8.** HRMS (EI) calculated for C_{14}H_{16}O [M]^+: 202.1358; Found: 202.1354.

(−)-(R)-1-Methoxy-3-(1-phenylhexa-3,4-dien-3-yl)benzene (2w).

From (R)-1b (75 mg, 0.2 mmol) and isopropylmagnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound (R)-2w (33 mg, 0.16 mmol) was obtained in 82% yield as a pale yellow oil, after purification by flash column chromatography (pentane/\text{Et}O 95:5). From (±)-1b, following the same procedure, compound (±)-2w (29 mg, 0.14 mmol) was obtained in 71% yield.

Compound (R)-2w was obtained in 97:3 enantiomeric ratio determined by SFC using Chiralpak-IB column [CO_{2}/MeOH (99.5:0.5)], 0.5 mL/min, \(t_{\text{major}} = 26.3\) min, \(t_{\text{minor}} = 24.5\) min. \(^1\)H NMR (300 MHz, CDCl_{3}) \(\delta 7.23\) (t, \(J = 7.8\) Hz, 1H), 7.02 – 6.97 (m, 1H), 6.97 – 

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6.94 (m, 1H), 6.78 – 6.72 (m, 1H), 5.49 (qd, J = 6.9, 2.3 Hz, 1H), 3.81 (s, 3H), 2.79 (pd, J = 6.7, 2.3 Hz, 1H), 1.76 (d, J = 6.9 Hz, 3H), 1.13 (d, J = 5.3 Hz, 3H), 1.11 (d, J = 5.2 Hz, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ 203.9, 159.8, 139.3, 129.3, 119.2, 112.7, 112.6, 111.6, 90.0, 55.3, 28.1, 22.7, 22.4, 14.6. HRMS (EI) calculated for C$_{14}$H$_{15}$O [M+H]$^+$: 204.1436; Found: 204.1427. $[a]^{25}_{D}$ = -47.6 (c = 1.0, CHCl$_3$)

(--)-(R)-Methyl 4-(2-methylhexa-3,4-dien-3-yl)benzoate (2x).

From (R)-1g (79 mg, 0.2 mmol) and isopropylmagnesium bromide solution in THF (0.22 mmol) following the general procedure described above, compound (R)-2x (39 mg, 0.17 mmol) was obtained in 85% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et$_2$O 97:3). From (±)-1g, following the same procedure without SPhos, compound (±)-2x (44 mg, 0.19 mmol) was obtained in 95% yield.

Compound (R)-2x was obtained in 97:3 enantiomeric ratio determined by SFC using Chiralpak-ID column [CO$_2$/MeOH (99:1)], 1 mL/min, $\tau_{major}$ = 14.4 min, $\tau_{minor}$ = 14.0 min.

Using isopropylmagnesium chloride solution in THF (0.22 mmol) compound (R)-2x (41 mg, 0.18 mmol) was obtained in 89% yield and 97:3 enantiomeric ratio as a pale yellow oil, after purification by flash column chromatography (pentane/Et$_2$O 97:3).

Using isopropylmagnesium chloride solution in Et$_2$O (0.22 mmol) compound (R)-2x (12 mg, 0.05 mmol) was obtained in 26% yield and 90:10 enantiomeric ratio as a pale yellow oil, after purification by flash column chromatography (pentane/Et$_2$O 97:3). The low yield could be due to a lower solubility of the starting material in the final CH$_2$Cl$_2$/Et$_2$O solution.

$^1$H NMR (300 MHz, CDCl$_3$) δ 8.02 – 7.89 (m, 2H), 7.49 – 7.38 (m, 2H), 5.55 (qd, J = 7.0, 2.4 Hz, 1H), 3.90 (s, 3H), 2.82 (septd, J = 6.7, 2.4 Hz, 1H), 1.78 (d, J = 7.0 Hz, 3H), 1.13 (d, J = 6.7 Hz, 3H), 1.11 (d, J = 6.7 Hz, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ 204.8, 167.2, 142.6, 129.7, 127.9, 126.4, 112.3, 90.6, 52.1, 27.8, 22.6, 22.3, 14.4. HRMS (ESI) calculated for C$_{15}$H$_{16}$NaO$_2$ [M+Na]$^+$: 253.1204; Found: 253.1198. $[a]^{25}_{D}$ = -83.7 (c = 1.0, CHCl$_3$).

(--)-(R)-1-Bromo-3-(2,2-dimethylhexa-3,4-dien-3-yl)benzene (2y).

From (R)-1f (83 mg, 0.2 mmol) and tert-butylmagnesium chloride solution in THF (0.22 mmol) following the general procedure described above, compound (R)-2y (43 mg, 0.16 mmol) was obtained in 81% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et$_2$O 97:3). From (±)-1f, following the same procedure, compound (±)-2y (38 mg, 0.14 mmol) was obtained in 72% yield.

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Compound (R)-2y was obtained in 98:2 enantiomeric ratio determined by GC on a Chirasil Dex-CB column (60 °C, hold 3 min, 60→120 °C @ 10 °C/min, hold 2 min, then →160 °C @ 0.5 °C/min, then →180 °C @ 10 °C/min; flow rate 1.0 mL/min.). \( t_{\text{major}} = 27.6 \text{ min}, \ t_{\text{minor}} = 27.9 \text{ min}. \) \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.52 – 7.30 (m, 2H), 7.22 – 7.07 (m, 2H), 5.20 (q, \( J = 6.9 \) Hz, 1H), 1.69 (d, \( J = 6.9 \) Hz, 3H), 1.12 (s, 9H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 202.6, 140.6, 132.4, 129.5, 129.3, 128.1, 121.8, 114.1, 86.8, 34.3, 30.0, 14.8.

HRMS (EI) calculated for C\(_{14}\)H\(_{17}\)Br [M\(^+\)]: 264.0514; Found: 264.0506. \([\alpha]^{25}_{D} = -22.3 \ (c = 1.0, \text{CHCl}_3). \]

\((S)-(3\text{-isopropylhexa-3,4-dien-1-yl})\text{benzene (2z). }\)

From (R)-1z (73 mg, 0.2 mmol) and isopropylmagnesium chloride solution in THF (0.22 mmol) following the general procedure described above, compound (S)-2z (35 mg, 0.18 mmol) was obtained in 88% yield as a pale yellow oil, after purification by flash column chromatography (pentane/Et\(_2\)O 97:3). From (±)-1z, following the same procedure, compound (±)-2z (33 mg, 0.17 mmol) was obtained in 83% yield.

Compound (R)-2z was obtained in 98:2 enantiomeric ratio determined by GC on a Chirasil Dex-CB column (60 °C, hold 3 min, then 60→80 °C @ 10 °C/min, hold 2 min, then \( t_{\text{major}} = 68.5 \text{ min}, \ t_{\text{minor}} = 70.1 \text{ min}. \) \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.24 – 7.04 (m, 5H), 5.14 – 4.98 (m, 1H), 2.70 – 2.58 (m, 2H), 2.23 – 2.12 (m, 2H), 2.10 – 1.92 (m, 1H), 1.52 (d, \( J = 6.8 \) Hz, 3H), 0.93 (dd, \( J = 6.8, 1.5 \) Hz, 6H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \( \delta \) 200.9, 142.8, 128.6, 128.3, 125.8, 110.0, 88.3, 34.5, 32.7, 31.4, 22.0, 21.9, 15.2. HRMS (EI) calculated for C\(_{15}\)H\(_{20}\) [M\(^+\)]: 200.1565; Found: 200.1573. \([\alpha]^{25}_{D} = -8.4 \ (c = 1.0, \text{CHCl}_3). \]
ASSIGNMENT OF ABSOLUTE CONFIGURATION

The absolute configuration was established for compound (R)-2u, by comparison of the sign of the optical rotation with that reported in the literature.\textsuperscript{4} The absolute configuration of (R)-2u reveals an \textit{anti} \textit{S}_{N}2' attack of the \textit{in situ} formed cuprate to the ammonium salt. We assumed the same stereochemical outcome for all the enantiomerically enriched compounds prepared.

\textit{Previously reported}

\[ \text{Ph} + 99\% \text{ ee} \xrightarrow{\text{OPO(OEt)}_{2}, \text{ICyCuCl (10 mol\%), tBuOLi, pentane}} 35 \text{ }^\circ\text{C, 6h}} \xrightarrow{} \text{Me} \]

\[ \text{(S)-3} \]

\[ 93\% \]

\[ \text{er} \text{ 98:2} \]

\[ [\alpha]_{D}^{20} = +90.6 \text{(c 1.4, CH}_{2}\text{Cl}_{2}). \]

\textit{Org. Lett. 2012, 14, 362.}

\textit{This work}

\[ \text{(R)-1a} \xrightarrow{\text{Cu(CH}_{3}\text{CN})_{4}\text{PF}_{6} (5 mol\%), Sphos (6 mol\%), Ph(CH}_{3}\text{)_{4}MgBr (1.1 equiv)}} \xrightarrow{\text{DCM (0.1M), } -40 \text{ }^\circ\text{C, 5 min}} \text{Me} \]

\[ \text{(R)-2u} \]

\[ 90\% \]

\[ \text{er} \text{ 98:2} \]

\[ [\alpha]_{D}^{20} = -54.0 \text{ (c = 1.0, CHCl}_{3}). \]
NMR SPECTRA
(R)-2w
SFC CROMATOGRAMS

(S)-SI-1z

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9 REFERENCES