ELECTRONIC SUPPLEMENTARY INFORMATION

Stereoselective synthesis of syn and anti 1,2-hydroxyalkyl moieties by Cu-catalyzed asymmetric allylic alkylation

Martín Fañanás-Mastral, Bjorn ter Horst, Adriaan J. Minnaard and Ben L. Feringa*

Stratingh Institute for Chemistry, University of Groningen, Nijenborgh 4, 9747 AG, Groningen, The Netherlands.
Table of Contents:

General Procedures S3

General procedure for the stereoselective Cu-catalyzed synthesis of 1,2-hydroxyalkyl compounds 5 S3

Characterization of *anti* and *syn* compounds 5 S4

General procedure for the synthesis of compounds 7 and *α,β*-unsaturated δ-lactones 8 S8

Characterization of compounds 7 and 8 S9

NMR spectra S12

Proposed mechanism for the copper-catalyzed AAA of allyl bromide 4 with Grignard reagents S25

GC traces for the temperature-depending experiments for the AAA of allyl bromide 4 with MeMgBr catalyzed by Cu-TaniaPhos S26
General Procedures:

Chromatography: Merck silica gel type 9385 230-400 mesh, TLC: Merck silica gel 60, 0.25 mm. Components were visualized by UV and cerium/molybdenum staining. Progress and conversion of the reaction were determined by GC-MS (GC, HP6890: MS HP5973) with an HP1 or HP5 column (Agilent Technologies, Palo Alto, CA). Mass spectra were recorded on a AEI-MS-902 mass spectrometer (EI+) or a LTQ Orbitrap XL (ESI+). $^1$H- and $^{13}$C-NMR were recorded on a Varian AMX400 (400 and 100.59 MHz, respectively) or a Varian VXR300 (300 and 75 MHz, respectively) using CDCl$_3$ as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CHCl$_3$: $\delta$ 7.26 for $^1$H, $\delta$ 77.0 for $^{13}$C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), and integration. Carbon assignments are based on APT $^{13}$C-NMR experiments. Optical rotations were measured on a Schmidt + Haensch polarimeter (Polartronic MH8) with a 10 cm cell ($c$ given in g/100 mL).

All reactions were carried out under a nitrogen atmosphere using oven dried glassware and using standard Schlenk techniques. CH$_2$Cl$_2$ was dried and distilled over calcium hydride. Substrate 4 was prepared according to literature procedures.$^1$ CuBr$\cdot$SMe$_2$, Grubbs 2$^{\text{nd}}$ generation and Hoveyda-Grubbs 2$^{\text{nd}}$ generation catalysts, ligands L1-4 and commercially available reagents were purchased from Aldrich, and used without further purification. Grignard reagents were purchased from Aldrich (MeMgBr, EtMgBr, n-HexMgBr, c-C$_5$H$_9$MgBr) or prepared from the corresponding alkyl bromides and magnesium turnings in Et$_2$O following standard procedures (PhCH$_2$CH$_2$MgBr). Grignard reagents were titrated using s-BuOH and catalytic amounts of 1,10-phenanthroline.

General procedure for the stereoselective Cu-catalyzed synthesis of 1,2-hydroxyalkyl compounds 5

In a Schlenk tube equipped with septum and stirring bar, CuBr$\cdot$SMe$_2$ (10 μmol, 2.06 mg) and ligand L1 (12 μmol, 8.24 mg) were dissolved in CH$_2$Cl$_2$ (2 mL) and stirred under nitrogen at room temperature for 15 min. The mixture was cooled to -80 °C and the

corresponding Grignard reagent (solution in Et₂O, 0.75 mmol) was added dropwise. Allyl bromide 4 (0.5 mmol, 110 mg) was then added dropwise as a solution in CH₂Cl₂ (0.8 mL) at that temperature over 1 h via a syringe pump. Once the addition was complete the resulting mixture was further stirred at -80 °C for 4 h. The reaction was quenched by addition of MeOH (0.5 mL) and the mixture was allowed to reach rt. Then, saturated aqueous NH₄Cl solution (2 mL) was added to the mixture. The organic phase was separated, and the resulting aqueous layer was extracted with Et₂O (3 x 5 mL). The combined organic layers were dried with anhydrous Na₂SO₄, filtered and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel using a mixture of pentane:Et₂O as eluent to yield the corresponding 1,2-hydroxyalkyl compound 5.

**Note:** GC analysis was carried out on a sample obtained after aqueous extraction with Et₂O, which has been passed through a short plug of silica gel to remove transition metal residues.

\[
\text{(-)-(S)-4-((S)-but-3-en-2-yl)-2,2-dimethyl-1,3-dioxolane (anti-5a):} \quad \text{Purification by column chromatography (SiO₂, pentane/Et₂O 30:1) afforded anti-5a (71 mg, 91%) as a colourless oil.} \quad [\alpha]_D^{20} = -2.8 \text{ (c = 0.5 in CHCl}_3\text{).} \quad \text{[lit.}^2 [\alpha]_D^{20} = -2.5 \text{ (c = 1.21 in CHCl}_3\text{)].}
\]

\[\text{\textsuperscript{1}H NMR (400 MHz, CDCl}_3\text{) } \delta 5.87 - 5.78 \text{ (m, 1H), 5.09 - 5.04 \text{ (m, 2H), 4.00 - 3.94 \text{ (m, 2H), 3.65 - 3.60 \text{ (m, 1H), 2.33 \text{ (sext., } J = 6.5 \text{ Hz, 1H), 1.40 \text{ (s, 3H), 1.35 \text{ (s, 3H), 1.00 \text{ (dd, } J = 6.8, 1.0, 3H).}}\text{\textsuperscript{13}C NMR (101 MHz, CDCl}_3\text{) } \delta 140.2, 115.2, 109.2, 79.5, 67.6, 41.0, 26.8, 25.7, 15.7.}\]

\[\text{HRMS (APCI+, m/z): calculated for C}_9\text{H}_{17}\text{O}_2\text{ [M+H}^+\text{]: 157.1223, found: 157.1219.}\]

---

(+)-(S)-4-((R)-but-3-en-2-yl)-2,2-dimethyl-1,3-dioxolane (syn-5a): Purification by column chromatography (SiO$_2$, pentane/Et$_2$O 30:1) afforded syn-5a (66 mg, 85%) as a colourless oil. $[\alpha]_{D}^{20} = 7.6$ (c = 0.65 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.74 – 5.65 (m, 1H), 5.08 (d, $J$ = 17.4 Hz, 1H), 5.04 (d, $J$ = 10.3 Hz, 1H), 3.97 – 3.87 (m, 2H), 3.64 (t, $J$ = 7.3 Hz, 1H), 2.32 (sext., $J$ = 6.8 Hz, 1H), 1.41 (s, 3H), 1.35 (s, 3H), 1.09 (d, $J$ = 6.7, 4H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 139.7, 115.6, 109.2, 79.6, 67.9, 41.9, 26.9, 25.7, 16.6. HRMS (APCI+, $m/z$): calculated for C$_9$H$_{17}$O$_2$ [M+H$^+$]: 157.1223, found: 157.1220.

(+)-(S)-2,2-dimethyl-4-((S)-pent-1-en-3-yl)-1,3-dioxolane (anti-5b): Purification by column chromatography (SiO$_2$, pentane/Et$_2$O 30:1) afforded anti-5b (76 mg, 89%) as a colourless oil. $[\alpha]_{D}^{20} = 6.0$ (c = 1.0 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.67 – 5.58 (m, 1H), 5.13 (dd, $J$ = 10.3, 0.6 Hz, 1H), 5.05 (dd, $J$ = 17.2, 0.6 Hz, 1H), 4.06 – 3.96 (m, 2H), 3.63 (t, $J$ = 7.4 Hz, 1H), 2.04 – 1.97 (m, 1H), 1.47 – 1.40 (m, 1H), 1.38 (s, 3H), 1.33 (s, 3H), 1.32 – 1.20 (m, 1H), 0.87 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 138.3, 117.3, 108.9, 78.5, 67.7, 49.3, 26.7, 25.7, 23.9, 11.9. HRMS (ESI+, $m/z$): calculated for C$_{10}$H$_{19}$O$_2$ [M+H$^+$]: 171.1370, found: 171.1379.

(+)-(S)-2,2-dimethyl-4-((R)-pent-1-en-3-yl)-1,3-dioxolane (syn-5b): Purification by column chromatography (SiO$_2$, pentane/Et$_2$O 30:1) afforded syn-5b (68 mg, 80%) as a colourless oil. $[\alpha]_{D}^{20} = 3.0$ (c = 1.0 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.54 – 5.42 (m, 1H), 5.12 – 5.00 (m, 2H), 3.95 – 3.90 (m, 2H), 3.61 (t, $J$ = 10.2 Hz, 1H), 2.08 – 1.99 (m, 1H), 1.80 – 1.71 (m, 1H), 1.39 (s, 3H), 1.34 (s, 3H), 1.32 – 1.18 (m, 1H), 0.87 (t, $J$ = 7.4 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 138.0, 117.5, 109.2, 78.5, 68.3, 50.3,
27.0, 25.9, 24.1, 11.5. HRMS (ESI+, m/z): calculated for C_{10}H_{19}O_{2} [M+H^+]: 171.1370, found: 171.1378.

(+)-(S)-2,2-dimethyl-4-((S)-5-phenylpent-1-en-3-yl)-1,3-dioxolane (anti-5c):
Purification by column chromatography (SiO₂, pentane/Et₂O 20:1) afforded anti-5c (103 mg, 84%) as a colourless oil. [α]_{D}^{20} = + 25.4 (c = 1.0 in CHCl₃). \(^1\)H NMR (400 MHz, CDCl₃) δ 7.31 – 7.27 (m, 2H), 7.21 – 7.17 (m, 3H), 5.78 – 5.69 (m, 1H), 5.25 (d, J = 10.2 Hz, 1H), 5.13 (d, J = 17.2 Hz, 1H), 4.08 (dd, J = 12.5, 6.4 Hz, 1H), 4.01 – 3.97 (m, 1H), 3.64 (t, J = 7.6 Hz, 1H), 2.77 – 2.70 (m, 1H), 2.57 – 2.49 (m, 1H), 2.22 – 2.15 (m, 1H), 1.79 – 1.64 (m, 2H), 1.41 (s, 3H), 1.36 (s, 3H). \(^1\)C NMR (101 MHz, CDCl₃) δ 142.5, 138.1, 128.7, 128.6, 126.0, 118.0, 109.1, 78.7, 67.6, 47.0, 33.6, 32.9, 26.7, 25.7. HRMS (APCI+, m/z): calculated for C_{16}H_{23}O_{2} [M+H^+]: 247.1693, found: 247.1690.

(-)-(S)-2,2-dimethyl-4-((R)-5-phenylpent-1-en-3-yl)-1,3-dioxolane (syn-5c):
Purification by column chromatography (SiO₂, pentane/Et₂O 25:1) afforded syn-5c (89 mg, 72%) as a colourless oil. [α]_{D}^{20} = - 1.4 (c = 1.0 in CHCl₃). \(^1\)H NMR (400 MHz, CDCl₃) δ 7.30 – 7.26 (m, 2H), 7.23 – 7.10 (m, 3H), 5.63 – 5.54 (m, 1H), 5.18 – 5.12 (m, 2H), 3.98 – 3.92 (m, 2H), 3.67 – 3.62 (m, 1H), 2.77 – 2.70 (m, 1H), 2.57 – 2.49 (m, 1H), 2.23 – 2.15 (m, 1H), 2.13 – 2.05 (m, 1H), 1.62 – 1.53 (m, 1H), 1.38 (s, 3H), 1.35 (s, 3H). \(^1\)C NMR (101 MHz, CDCl₃) δ 142.5, 138.1, 128.7, 128.5, 125.9, 118.0, 109.3, 78.6, 68.2, 48.2, 33.3, 32.8, 27.0, 25.9. HRMS (APCI+, m/z): calculated for C_{16}H_{23}O_{2} [M+H^+]: 247.1693, found: 247.1691.
(+)-(S)-2,2-dimethyl-4-((S)-non-1-en-3-yl)-1,3-dioxolane (anti-5d): Purification by column chromatography (SiO₂, pentane/Et₂O 40:1) afforded anti-5d (99 mg, 87%) as a colourless oil. [α]D²⁰ = +33.8 (c = 1.0 in CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 5.64 (dt, J = 17.2, 10.2 Hz, 1H), 5.12 (dd, J = 10.2, 1.1 Hz, 1H), 5.04 (dd, J = 17.2, 1.1 Hz, 1H), 4.05 – 3.97 (m, 2H), 3.63 (t, J = 7.2 Hz, 1H), 2.15 – 2.05 (m, 1H), 1.39 (s, 3H), 1.34 (s, 3H), 1.33 – 1.18 (m, 10H), 0.87 (t, J = 6.5 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 138.6, 117.1, 109.0, 78.8, 67.7, 47.6, 32.0, 31.0, 29.5, 27.3, 26.7, 25.7, 22.8, 14.3. HRMS (APCI+, m/z): calculated for C₁₄H₂₇O₂ [M+H⁺]: 227.2006, found: 227.2005.

(+)-(S)-2,2-dimethyl-4-((R)-non-1-en-3-yl)-1,3-dioxolane (syn-5d): Purification by column chromatography (SiO₂, pentane/Et₂O 40:1) afforded syn-5d (88 mg, 79%) as a colourless oil. [α]D²⁰ = +2.0 (c = 1.0 in CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 5.54 – 5.45 (m, 1H), 5.09 – 5.02 (m, 2H), 3.94 – 3.88 (m, 2H), 3.65 – 3.60 (m, 1H), 2.16 – 2.07 (m, 1H), 1.72 – 1.64 (m, 1H), 1.40 (s, 3H), 1.35 (s, 3H), 1.33 – 1.18 (m, 9H), 0.87 (t, J = 6.8, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 138.4, 117.3, 109.2, 78.7, 68.2, 48.7, 32.0, 31.2, 29.5, 27.1, 25.9, 22.9, 14.3. HRMS (APCI+, m/z): calculated for C₁₄H₂₇O₂ [M+H⁺]: 227.2006, found: 227.2005.
(+)-(S)-4-((R)-1-cyclopentylallyl)-2,2-dimethyl-1,3-dioxolane (anti-5e): Purification by column chromatography (SiO$_2$, pentane/Et$_2$O 30:1) afforded anti-5e (84 mg, 80%) as a colourless oil. $[\alpha]_{D}^{20} = +13.8$ (c = 1.0 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.79 – 5.70 (m, 1H), 5.12 (d, $J$ = 10.3 Hz, 1H), 5.00 (d, $J$ = 17.2 Hz, 1H), 4.23 – 4.17 (m, 1H), 3.97 (t, $J$ = 7.0 Hz, 1H), 3.63 (t, $J$ = 7.7 Hz, 1H), 1.93 – 1.79 (m, 3H), 1.66 – 1.48 (m, 4H), 1.37 (s, 3H), 1.34 (s, 3H), 1.23 – 1.07 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 137.2, 117.4, 108.8, 77.4, 67.9, 52.3, 41.5, 30.9, 30.8, 26.6, 25.7, 25.2, 25.1. HRMS (ESI+, $m/z$): calculated for C$_{13}$H$_{23}$O$_2$ [M+H$^+$$]$: 211.1693, found: 211.1690.

General procedure for the synthesis of compounds 7 and $\alpha$,$\beta$-unsaturated $\delta$-lactones 8.

To a solution of 5 (1 mmol) in water (2 mL) at room temperature was added AcOH (5 mL). The solution was stirred at this temperature during 16 h. After some coevaporations with toluene (4 x 10 mL), the residue was dissolved in DMF (2 mL) and imidazole (75 mg, 1.1 mmol), DMAP (1 mg, 0.08 mmol) and tert-butyl(chloro)diphenylsilane (0.29 mL, 1.1 mmol) were added at 0 °C. The mixture was warmed to room temperature and was stirred during 16 h. Then it was poured into water (5 mL) and extracted with CH$_2$Cl$_2$ (3 x 5 mL). The combined organic layers were washed with water and brine and dried.
over Na$_2$SO$_4$. The resulting product S1 was used in the next step without further purification.

To a solution of S1 (1 mmol) and DIPEA (0.34 mL, 2 mmol) in CH$_2$Cl$_2$ (5 mL), acryloyl chloride (0.13 mL, 1.5 mmol) was added at 0 °C. The mixture was stirred at this temperature for 2 h. Then it was quenched with saturated aqueous solution of NaHCO$_3$ (2 mL), extracted with CH$_2$Cl$_2$ (3 x 5 mL) and dried over Na$_2$SO$_4$. The product was purified by flash chromatography on silica gel using a mixture of Pentane:Et$_2$O as eluent to yield the corresponding compound 7.

$$\text{(-)-(2S,3R)-1-((\text{tert-butyldiphenylsilyl})\text{oxy})-3-ethylpent-4-en-2-yl acrylate (7a):}$$

Purification by column chromatography (SiO$_2$, pentane/Et$_2$O 30:1) afforded 7a (337 mg, 80%, over 3 steps) as a colourless oil. $[\alpha]_D^{20} = -25.8$ (c = 1.0 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.67 – 7.64 (m, 4H), 7.45 – 7.34 (m, 6H), 6.43 (dd, $J = 17.3$, 1.5 Hz, 1H), 6.17 (dd, $J = 17.3$, 10.4 Hz, 1H), 5.85 (dd, $J = 10.4$, 1.5 Hz, 1H), 5.55 – 5.46 (m, 1H), 5.10 – 5.00 (m, 3H), 3.80 – 3.72 (m, 2H), 2.40 (ddd, $J = 18.3$, 9.4, 3.5 Hz, 1H), 1.59 – 1.49 (m, 1H), 1.28 – 1.17 (m, 1H), 1.03 (s, 9H), 0.84 (t, $J = 7.4$ Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 165.8, 137.6, 135.6, 135.5, 133.4, 133.4, 130.5, 129.6, 129.6, 128.8, 127.6, 117.5, 76.4, 63.6, 46.6, 26.7, 22.9, 19.2, 11.4. HRMS (ESI+, m/z): calculated for C$_{26}$H$_{34}$O$_3$SiNa [M+Na$^+$]: 445.2169, found: 445.2178.

$$\text{(+-)-(2S,3S)-1-((\text{tert-butyldiphenylsilyl})\text{oxy})-3-vinylnonan-2-yl acrylate (7b):}$$

Purification by column chromatography (SiO$_2$, pentane/Et$_2$O 40:1) afforded 7b (85%, over 3 steps) as a colourless oil. $[\alpha]_D^{20} = +9.0$ (c = 0.98 in CHCl$_3$). $^1$H NMR (400 MHz,
CDCl$_3$ δ 7.67 – 7.64 (m, 4H), 7.45 – 7.34 (m, 6H), 6.38 (dd, $J$ = 17.3, 1.5 Hz, 1H), 6.11 (dd, $J$ = 17.3, 10.4 Hz, 1H), 5.81 (dd, $J$ = 10.4, 1.5 Hz, 1H), 5.58 (dt, $J$ = 17.1, 9.8 Hz, 1H), 5.12 (q, $J$ = 5.1 Hz, 1H), 5.06 – 4.98 (m, 2H), 3.75 (dd, $J$ = 10.8, 6.3 Hz, 1H), 3.68 (dd, $J$ = 10.8, 4.8 Hz, 1H), 2.47 – 2.40 (m, 1H), 1.45 – 1.38 (m, 1H), 1.33 – 1.18 (m, 9H), 1.02 (s, 9H), 0.87 (t, $J$ = 6.7 Hz, 3H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.6, 137.8, 135.6, 135.53, 133.4, 133.4, 130.4, 129.6, 129.6, 128.8, 127.6, 127.6, 117.2, 76.0, 63.5, 44.9, 31.7, 30.7, 29.1, 27.0, 26.7, 22.6, 19.2, 14.1. HRMS (ESI+, m/z): calculated for C$_{30}$H$_{43}$O$_3$Si [M+H$^+$]: 479.2976, found: 479.2969.

General procedure for the RCM

Grubbs 2nd generation catalyst (4.3 mg, 0.005 mmol) was added to a degassed solution of 7 (0.1 mmol) in CH$_2$Cl$_2$ (10 mL), and the mixture was refluxed during 14 h. The solvent was removed and the residue was purified by by flash chromatography on silica gel using a 5:1 mixture of Pentane:Et$_2$O as eluent to yield the corresponding compound 8.

(-)-(5R,6S)-6-(((tert-butyldiphenylsilyl)oxy)methyl)-5-ethyl-5,6-dihydro-2H-pyran-2-one (8a): Purification by column chromatography (SiO$_2$, pentane/Et$_2$O 5:1) afforded 8a (39 mg, 97%) as a colourless oil. [α]$_D^{20}$ = -136.2 (c = 1.0 in CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.68 – 7.63 (m, 4H), 7.47 – 7.37 (m, 6H), 7.04 (dd, $J$ = 9.8, 6.0 Hz, 1H), 6.03 (dd, $J$ = 9.8, 0.9 Hz, 1H), 4.56 (dddd, $J$ = 8.0, 5.9, 3.8 Hz, 1H), 3.92 (dd, $J$ = 10.6, 5.9 Hz, 1H), 3.81 (dd, $J$ = 10.6, 8.0 Hz, 1H), 2.56 – 2.50 (m, 1H), 1.69 – 1.59 (m, 1H), 1.45 (ddq, $J$ = 14.7, 9.8, 7.5 Hz, 1H), 1.07 (s, 9H), 0.94 (t, $J$ = 7.5 Hz, 1H). $^{13}$C NMR (101 MHz, CDCl$_3$) δ 163.8, 150.3, 135.5, 132.9, 132.8, 129.9, 127.8, 120.9, 79.5, 62.1, 36.1, 26.8, 20.5, 19.2, 11.0. HRMS (ESI+, m/z): calculated for C$_{24}$H$_{30}$O$_3$SiNa [M+Na$^+$]: 417.1856, found: 417.1863.
(±)-(5S,6S)-6-(((tert-butylidiphenylsilyl)oxy)methyl)-5-hexyl-5,6-dihydro-2H-pyran-2-one (8b): Purification by column chromatography (SiO₂, pentane/Et₂O 5:1) afforded 8b (38 mg, 84%) as a colourless oil. [α]D²⁰ = + 84.2 (c = 0.92 in CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 7.67 – 7.64 (m, 4H), 7.46 – 7.37 (m, 6H), 6.73 (dd, J = 9.9, 4.0 Hz, 1H), 5.93 (dd, J = 9.9, 1.8 Hz, 1H), 4.32 – 4.28 (m, 1H), 3.86 (dd, J = 11.0, 4.9 Hz, 1H), 3.83 (dd, J = 11.0, 4.2 Hz, 1H), 2.77 – 2.70 (m, 1H), 1.58 – 1.50 (m, 1H), 1.46 – 1.26 (m, 9H), 1.07 (s, 9H), 0.90 (t, J = 6.9 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 163.3, 149.0, 135.6, 135.5, 132.9, 132.7, 129.9, 129.9, 127.8, 127.8, 119.9, 81.4, 63.4, 34.0, 31.6, 31.2, 29.2, 26.8, 26.3, 22.6, 19.2, 14.0. HRMS (ESI+, m/z): calculated for C₂₈H₃₈O₃SiNa [M+Na⁺]: 473.2482, found: 473.2459.
Proposed mechanism for the copper-catalyzed AAA of allyl bromide 4 with Grignard reagents

In analogy with the proposed mechanism by Goering and co-workers, the catalytic cycle depicted above can be proposed for the Cu-taniaphos catalyzed AAA of allyl bromide 4. In this mechanism the precatalyst A and the Grignard reagent form the active catalyst B. Subsequently, the interaction with allyl bromide 4 forms the Cu\textsuperscript{I}π-complex C. Oxidative addition and allylic rearrangement from C gives the Cu\textsuperscript{III}σ-complex D which leads to the S\textsubscript{N}2' product via reductive elimination.

The formation of the competing S\textsubscript{N}2 product can be explained through an isomerization of the Cu\textsuperscript{III}σ-complex D into the Cu\textsuperscript{III}π-complex E. It has been shown that this conversion of the Cu\textsuperscript{III}σ-complex into the Cu\textsuperscript{III}π-complex is faster at higher

---

temperatures. Intermediate E would evolve to the $S_N2$ product via reductive elimination (initially Goering and co-workers proposed the formation of a $F$ type Cu$^{III}$ $\sigma$-complex before the reductive elimination can take place). Recent calculations by Nakamura and co-workers have shown that reductive elimination will proceed directly from the $\pi$-complex.

GC traces for the temperature-depending experiments for the AAA of allyl bromide 4 with MeMgBr catalyzed by Cu-TaniaPhos (Table 1).

Product ratio was determined by GC analysis of the reaction crude, (GC, HP6890: MS HP5973) with an HP5 column, initial temp. 50°C then 10 °C/min to 270 °C (hold for 3 min, final temp).

Retention times (min): 4.2 (syn-5a), 4.4 (anti-5a); and 5.3 (6).

---

- \( L = (R,R)-(+)\text{-taniaphos}, T = -75 \, ^\circ\text{C} \) (Table 1, entry 1):

\[
\begin{array}{|c|c|c|c|c|c|}
\hline
& & & & & \\
\hline
\text{Number} & 0 & 2 & 5 & 10 & 20 \\
\hline
\text{TIC} & 0 & 2 & 5 & 10 & 20 \\
\hline
\text{Time} & 0 & 2 & 5 & 10 & 20 \\
\hline
\end{array}
\]

- \( L = (R,R)-(+)\text{-taniaphos}, T = -80 \, ^\circ\text{C} \) (Table 1, entry 11):

\[
\begin{array}{|c|c|c|c|c|c|}
\hline
& & & & & \\
\hline
\text{Number} & 0 & 2 & 5 & 10 & 20 \\
\hline
\text{TIC} & 0 & 2 & 5 & 10 & 20 \\
\hline
\text{Time} & 0 & 2 & 5 & 10 & 20 \\
\hline
\end{array}
\]

Supplementary Material (ESI) for Chemical Communications
This journal is © The Royal Society of Chemistry 2011

S27
- \( L = (S,S)\)-(\(-\))\-taniaphos, \( T = -75^\circ\text{C} \) (Table 1, entry 2):

- \( L = (S,S)\)-(\(-\))\-taniaphos, \( T = -80^\circ\text{C} \) (Table 1, entry 12):
- \( L = (S,S)\)-\((-\)-taniaphos, \( T = -50 \, ^\circ\text{C}: \)