Supporting Information

Effect of Additives on the Stereochemical Integrity and Reactivity of α -Alkoxy carbonyl Alkenylcopper Intermediates. Optimal Conditions for the Synthesis of Isomerically Pure Tetrasubstituted Alkenes

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1. General experimental details

Iodomethylboronpinacolate¹, iodomethyltributyltin², methyl-5-(tert-butyl-diphenylsilyloxy)-2-pentynoate³ were prepared by literature procedures. Tetrahydrofuran was distilled from sodium-benzophenone. HMPA was distilled over CaH₂ and other additives were redistilled by Kugelrohr work before use. Methyl lithium was titrated according to the Gilman double titration method⁴ prior to use. All other chemicals were purchased from commercial sources and used as received. Glassware for the reactions was flame-dried under vacuum and then allowed to cool under N₂. NH₄Cl_(aq) refers to saturated aqueous solutions. Thin layer chromatography was performed on Silica Gel 60 F254 plates and were visualized with UV light and either 5% phosphomolybdic acid in ethanol (PMA) or 1% KMnO_{4(aq)}. NMR spectra were recorded on 300, 400 or 500 MHz instruments. The residual solvent protons (¹H) or the solvent carbons (¹³C) were used as internal standards. ¹H NMR data are presented as follows: chemical shift in ppm downfield from tetramethylsilane (multiplicity, coupling constant, integration). The following abbreviations are used in reporting NMR data: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. High resolution mass spectra were recorded using either electron impact (EI) or electrospray (ES) ionization techniques.

¹ Phillion, D. P.; Neubaure, R.; Andrew, S. S. *J. Org. Chem.*, **1986**, *51*, 1610.

² Jens Ahman; Peter Somfai. *Synthetic Communications*, **1994**, *24*(8), 1117.

³ Nagaoka, H.; Kishi, Y. *Tetrahedron*, **1981**, *37*, 3873.

⁴ *Organocopper Reagents: A Practical Approach* Taylor, R. J. K., ed.; Oxford University Press: New York, **1994**, p.53.

2. Model procedures

Model procedure for the additive studies:

A slurry of CuBr.Me₂S (0.052 g, 0.25 mmol) in THF (4mL) at 0°C under N₂ was treated with MeLi (1.4 M in Et₂O, 0.36 mL, 0.50 mmol). When the clear, colorless solution had formed, the flask was placed in an acetone/CO₂ bath and ethyl 2-pentynoate (33 uL, 0.25 mmol) was added dropwise. The resulting light yellow mixture was stirred at –78°C for 1h and then treated sequentially with additives (0.50 mmol), the mixture was allowed to warm up at 0°C for 2hrs. Reaction was quenched with NH₄Cl_(aq) (1 mL) and the layers were separated and the aqueous layer was extracted with ether (4 x 5 mL). The combined organic layers were washed with water (5 x 5 mL) and brine (5 mL), dried (anhydrous Na₂SO₄), and concentrated to give the product as a liquid. The ratio of *cis*- and *trans*-addition isomers **6a** and **7a** was measured on crude product. Chemical shift of vinyl proton of **7a** is a little bit lower field than that of **6a**.

Model procedure for the allylboronate **8a**:

A slurry of CuBr.Me₂S (0.208 g, 1.01 mmol) in THF (12 mL) at 0°C under N₂ was treated with MeLi (1.4 M in Et₂O, 1.4 mL, 2.0 mmol). When the clear, colorless solution had formed, the flask was placed in an acetone/CO₂ bath and ethyl 2-pentynoate (140 uL, 1.0 mmol) was added dropwise. The resulting light yellow mixture was stirred at –78°C for 1h and then treated sequentially with 12-crown-4, HMPA (Table 2) and iodomethylboronpincolate (0.6 mL, 3.0 mmol). The mixture was allowed to warm up at 0°C for 2hrs. Reaction was quenched with NH₄Cl_(aq) (5 mL) and the layers were separated and the aqueous layer was extracted with ether (3 x 10 mL). The combined organic layers were washed with water (5 x 10 mL) and brine (10 mL), dried (anhydrous Na₂SO₄), and concentrated to give the product as an oil. The product was purified by chromatography (Et₂O : Hexanes = 1 : 10) to give a colorless oil. The ratio of *cis*- and *trans*-addition isomers **8a** and **9a** was measured according to the allyl-proton height and integration.

Model procedure for other electrophiles (Products **8a-8b**):

A slurry of CuBr.Me₂S (0.208 g, 1.01 mmol) in THF (12 mL) at 0°C under N₂ was treated with MeLi (1.4 M in Et₂O, 1.4 mL, 2.0 mmol). When the clear, colorless solution had formed, the flask was placed in an acetone/CO₂ bath and ethyl 2-pentynoate (140 uL, 1.0 mmol) was added dropwise. The resulting light yellow mixture was stirred at –78°C for 1h and then treated sequentially with 12-crown-4 (161 uL, 1.0 mmol), HMPA (346 uL, 2.0 mmol) and electrophile (3 or 4 mmol, see Table 3). The mixture was stirred at 0°C for 2 or 3 hrs and then quenched with NH₄Cl_(aq) (5 mL). The layers were separated and the aqueous layer was extracted with ether (3 x 10 mL). The combined organic layers were washed with water (5 x 10 mL) and brine (10 mL), dried (anhydrous Na₂SO₄), and concentrated to give the product as an oil. The product was purified by chromatography (Et₂O : Hexanes = 1 : 20).

3. Characterization data for compounds 8b-8i

Ethyl (2Z)-2-(tri-butyltin-methyl)-3-methylpent-2-enoate 8b:

Colorless oil, yield 80%. ^1H NMR (500 MHz, CDCl_3): δ 4.15 (q, $J = 7.8$ Hz, 2H), 2.36 (q, $J = 7.8$ Hz, 2H), 1.82 (t, $J = 26.9$ Hz, 2H), 1.68 (t, $J = 7.8$ Hz, 3H), 1.46(m, 6H), 1.28 (m, 9H), 1.02 (t, $J = 7.8$ Hz, 3H), 0.85 (m, 15H); ^{13}C NMR (125 MHz, CDCl_3): δ 169.9, 139.5, 127.3, 59.9, 29.4, 29.0 (t), 27.4 (t), 19.5, 14.3, 13.6, 13.3, 13.2, 10.0; IR (CH_2Cl_2 cast, cm^{-1}): 2956, 1715, 1621, 1122; HRMS(ES, m/z) Calcd for $\text{C}_{21}\text{H}_{42}\text{SnO}_2$, ($M + \text{Na}$) 469.2102 Found: 469.2105

Ethyl (2Z)-2-(trimethylsilane-methyl)-3-methylpent-2-enoate 8c:

Colorless oil, yield 30%. ^1H NMR (300 MHz, CDCl_3): δ 4.14 (q, $J = 7.7$ Hz, 2H), 2.25 (q, $J = 7.7$ Hz, 2H), 1.76 (s, 2H), 1.69 (s, 3H), 1.28 (t, $J = 7.7$ Hz, 3H), 1.02 (t, $J = 7.7$ Hz, 3H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 170.1, 142.3, 124.9, 60.0, 29.5, 20.3, 19.7, 14.2, 13.2, -1.1; IR (CH_2Cl_2 cast, cm^{-1}): 2956, 1713, 1624, 1204; HRMS(EI, m/z) Calcd for $\text{C}_{12}\text{H}_{24}\text{SiO}_2$: 228.1546, Found: 228.1546

Ethyl (2Z)-2-benzyl-3-methylpent-2-enoate 8d:

Colorless oil, yield 40%. ^1H NMR (500 MHz, CDCl_3): δ 7.10-7.30 (m, 5H), 4.18 (q, $J = 6.1$ Hz, 2H), 3.62 (s, 2H), 2.40 (q, $J = 6.1$ Hz, 2H), 1.82 (s, 3H), 1.15 (t, $J = 6.1$ Hz, 3H), 1.09 (t, $J = 6.1$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 169.1, 149.2, 139.9, 128.23, 128.21, 128.1, 126.2, 125.8, 60.0, 35.5, 29.7, 19.7, 14.1, 13.0; IR (CH_2Cl_2 cast, cm^{-1}): 3027, 2935, 1712, 1630, 1200; HRMS(EI, m/z) Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_2$: 232.1463, Found: 232.1464

Ethyl (2Z)-2-allyl-3-methylpent-2-enoate 8e:

Colorless oil, yield 76%. ^1H NMR (300 MHz, CDCl_3): δ 5.76 (m, 1H), 5.04-4.92 (m, 2H), 4.18 (q, $J = 7.8$ Hz, 2H), 3.02 (d, $J = 7.8$ Hz, 2H), 2.32 (q, $J = 7.8$ Hz, 2H), 1.78 (s, 3H), 1.28 (t, $J = 7.8$ Hz, 3H), 1.04 (t, $J = 7.8$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 169.2, 148.8, 135.3, 124.9, 114.9, 60.0, 34.1, 29.6, 19.1, 14.2, 12.9; IR (CH_2Cl_2 cast, cm^{-1}): 3079, 2978, 1713, 1198; HRMS(EI, m/z) Calcd for $\text{C}_{11}\text{H}_{18}\text{O}_2$: 182.1307, Found: 182.1304

Ethyl (2Z)-2-(2-bromo-allyl)-3-methylpent-2-enoate 8f:

Colorless oil, yield 57%. ^1H NMR (500 MHz, CDCl_3): δ 5.53 (s, 1H), 5.40 (s, 1H), 4.16 (q, $J = 6.5$ Hz, 2H), 3.45 (s, 2H), 2.40 (q, $J = 6.5$ Hz, 2H), 1.80 (s, 3H), 1.26 (t, $J = 6.5$ Hz, 3H), 1.08 (t, $J = 6.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 168.0, 152.7, 131.0, 123.6, 116.4, 60.2, 41.7, 29.7, 19.9, 14.2, 12.8; IR (CH_2Cl_2 cast, cm^{-1}): 2977, 1714, 1631, 1278, 1199; HRMS(EI, m/z) Calcd for $\text{C}_{11}\text{H}_{17}\text{O}_2\text{Br}$: 262.0392, 260.0412, Found: 262.0390, 260.0408

Ethyl (2Z)-2-(3,3-dimethyl-allyl)-3-methylpent-2-enoate 8g:

Colorless oil, yield 78%. ¹H NMR (300 MHz, CDCl₃): δ 5.00 (m, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.95 (d, *J* = 8.0 Hz, 2H), 2.26 (q, *J* = 7.1 Hz, 2H), 1.76 (s, 3H), 1.56 (s, 3H), 1.54 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 169.7, 146.1, 132.1, 126.9, 121.6, 60.0, 29.5, 29.0, 25.7, 18.8, 17.7, 14.2, 12.9; IR (CH₂Cl₂ cast, cm⁻¹): 2976, 1713, 1633, 1203; HRMS(EI, *m/z*) Calcd for C₁₃H₂₂O₂: 210.1620, Found: 210.1619

Ethyl-(2E)-(2-propenyl)- 3-ethyl-4-methyl-hexenoate 8h:

The dibutyl cuprate was formed by adding s-BuLi (1.16M in cyclohexane, 2 mmol, 1.72 mL) to a slurry of CuBr.SMe₂ in THF at -40°C, after a black mixture formed, the preparation was carried out as above with 12-crown-4, HMPA and allyl bromide. The product was purified by flash to give colorless oil, yield 72%. ¹H NMR (500 MHz, CDCl₃): δ 5.80 (m, 1H), 5.00 (m, 2H), 4.18 (q, *J* = 7.41 Hz, 2H), 3.02 (m, 2H), 2.60 (m, 1H), 2.30 (m, 1H), 2.22 (m, 1H), 1.40 (m, 2H), 1.28 (t, *J* = 6.68 Hz, 3H), 1.04 (t, *J* = 6.67 Hz, 3H), 1.00 (d, *J* = 6.67 Hz, 3H), 0.20 (t, *J* = 6.67 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 169.8, 155.4, 136.2, 125.8, 115.0, 60.0, 38.6, 33.6, 27.8, 22.1, 18.5, 15.4, 14.2, 12.5; IR (CH₂Cl₂ cast, cm⁻¹): 3079, 2966, 1715, 1638, 1275, 1194; HRMS(EI, *m/z*) Calcd for C₁₄H₂₄O₂: 224.1776, Found: 224.1776

Methyl-(2Z)-(2-propenyl)-3-methyl-(4-tert-butylphenylsilyloxy)-butynoate 8i:

Colorless oil, yield 85%. ¹H NMR (300 MHz, CDCl₃): δ 7.65 (m, 4H), 7.38 (m, 6H), 5.55 (m, 1H), 5.00 (m, 2H), 4.50 (s, 2H), 3.52 (s, 3H), 3.08 (d, *J* = 7.18 Hz, 2H), 1.88 (s, 3H), 1.08 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 168.6, 147.7, 135.5, 134.8, 133.6, 129.6, 127.6, 125.2, 115.2, 65.2, 51.2, 33.9, 26.8, 19.2, 16.2; IR (CH₂Cl₂ cast, cm⁻¹): 3071, 3050, 1714, 1638, 1589, 1208, 1112; HRMS(EI, *m/z*) Calcd for C₂₅H₃₂O₃Si: 408.2121, Found: 408.2116

4. Copies of ¹H and ¹³C NMR spectra for compounds 8b-8i

Note: spectrometer frequency for ¹³C NMR spectra is 125 MHz (not 500 MHz).

8b, in CDCl₃, 500 MHz ¹H NMR and 500 MHz ¹³C NMR

8c, in CDCl₃, 300 MHz ¹H NMR and 500 MHz ¹³C NMR

8d, in CDCl₃, 500 MHz ¹H
NMR and 500 MHz ¹³C NMR

8e, in CDCl₃, 300 MHz ¹H NMR and 500 MHz ¹³C NMR

8f, in CDCl₃, 500 MHz ¹H NMR
and 500 MHz ¹³C NMR

8g, in CDCl₃, 300 MHz ¹H NMR
and 500 MHz ¹³C NMR

8h, in CDCl₃, 500 MHz ¹H NMR
and 500 MHz ¹³C NMR

8i, in CDCl₃, 300 MHz ¹H NMR
and 500 MHz ¹³C NMR