Supporting Information

Enantioselective Reactions of Scalemic Acyclic α -(Alkoxy)alkyl- and α -(*N*-Carbamoyl)alkylcuprates

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General. NMR spectra were recorded as CDCl₃ solutions on a Bruker AC-300 or JEOL 500 MHz instrument. The ¹H NMR chemical shifts are reported as δ values in parts per million (ppm) relative to tetramethylsilane (TMS) or CHCl₃ (δ = 7.24 ppm) as internal standard. The ¹³C NMR chemical shifts are reported as δ values in parts per million (ppm) downfield from TMS and referenced with respect to the CDCl₃ signal (triplet, centerline δ = 77.0 ppm). Infrared spectra (IR) were recorded on a Nicolet Magna 550 FT-IR spectrometer as neat samples (liquid films on NaCl plates) unless otherwise noted. Gas chromatography/mass spectrometry measurements were performed on a Hewlett-Packard 5890A GC coupled to a 5970B mass selective detector at 70 eV. Analytical thin-layer chromatography (TLC) was performed on Scientific Adsorbents Inc. silica gel plates, 200 μ mesh with F-254 indicator. Visualization was accomplished by UV light (254 nm), 4% ethanol solution of phosphomolybdic acid, or 5% *p*-anisaldehyde. Flash column chromatography was performed with 200-400 μ mesh silica gel. Bulb to bulb distillation was performed on a Büchi micro-distillation oven model GKR. Elemental analyses were determined by Atlantic Microlab, Inc., Norcross Georgia, USA from doubly purified samples involving column chromatography.

General Procedure A (lithium cuprates). Treatment of the organostannane with either *n*-BuLi [THF (–95 °C, 5 min.) or toluene (–78 °C, 1.0 equiv. TMEDA, 4 h)] or with *s*-BuLi [Et₂O, –78 °C, 2 h] generates the corresponding alkyllithium reagent. Addition of a THF solution of CuCN•2LiCl (0.5 or 1.0 equiv., 30 min, temperature specified in the first step) affords the lithium dialkylcuprate (R₂CuLi) or lithium alkyl(cyano) cuprate (RCuCNLi) reagent, respectively. For reactions involving solvents other than THF for the initial transmetallation, the final solvent: THF ratio was 1:1.

General Procedure B (zinc cuprates). Treatment of the organostannane with either *n*-BuLi [THF (–95 °C, 5 minutes) or toluene (4 hours, –78 °C, 1.0 equiv. TMEDA)] or with *s*-BuLi [Et₂O, –78 °C, 2 h]

generates the corresponding alkyllithium reagent. Addition of a THF solution of ZnBr_2 (1.0 equiv., 30 min, temperature specified in the first step) results in formation of the organozinc reagent which is then treated with a THF solution of $\text{CuCN}\cdot 2\text{LiCl}$ (1.0 equiv., 30 min, temperature specified in the first step) to give the zinc alkyl(cyano)cuprate (RCuCNZnBr) reagent. For reactions involving solvents other than THF for the initial transmetallation step, the final solvent: THF ratio was 1:1.

Representative Procedure for Reaction with Electrophiles. Stannane **3** (469 mg, 1 mmol) was dissolved in freshly distilled THF (3.0 mL) and cooled to $-95\text{ }^\circ\text{C}$ [Et_2O , $\text{CO}_2(\text{s})$ slush bath] under an argon atmosphere. The solution was treated with *n*-BuLi (dropwise) and the mixture was allowed to stir for 5 min before a solution of ZnBr_2 (226 mg, 1.0 mmol) in THF (3.0 mL) was added dropwise. The reaction mixture was allowed to stir for 30 min and then a solution containing CuCN (90 mg, 1 mmol) and LiCl (90 mg, 2 mmol) in THF (3 mL) was added dropwise. The resulting solution was allowed to stir for 30 min at $-95\text{ }^\circ\text{C}$ before addition of propargyl bromide (118 mg, 1.0 mmol, neat). The mixture was allowed to slowly warm to room temperature ($22\text{ }^\circ\text{C}$) overnight and then quenched with 5% aqueous HCl (10 mL). The organic phase was extracted with diethyl ether (3 x 10 mL), separated, dried (MgSO_4) and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (10% Et_2O /petroleum ether, 10:90, v/v) afforded allene **19a** as a clear colorless oil in 70% yield (80% ee).

6-Methylene-7-[(methoxy)methoxy]-9-phenylnonane (14a). General procedure A was employed on a 0.5 mmol scale to give **14a** which was purified by flash column chromatography [$R_f = 0.3$, silica gel (Et_2O /petroleum ether, 2:98, v/v)]: IR (neat) 2948 (s), 1658 (w), 1606 (w), 1470 (m), 1153 (m), 1042 (vs) cm^{-1} ; ^1H -NMR (CDCl_3) δ 0.86 (t, $J = 6.7\text{ Hz}$, 3H), 1.20-1.40 (m, 4H), 1.40-1.52 (m, 2H), 1.75-2.10 (m, 4H), 2.50-2.70 (m, 1H), 2.70-2.85 (m, 1H), 3.39 (s, 3H), 4.03 (dt, $J = 5.5\text{ Hz}$, 2.1 Hz, 1H), 4.56 (center AB quartet, $J_{AB} = 6.7\text{ Hz}$, $\Delta\nu_{AB} = 37\text{ Hz}$, $\delta_A = 4.63$, $\delta_B = 4.50$, 2H), 4.90-4.95 (m, 1H), 5.00-5.10 (m, 1H), 7.10-7.30 (m, 5H); ^{13}C -NMR (CDCl_3) δ 14.1, 22.6, 27.4, 30.4, 31.8, 32.3, 36.0, 55.6, 79.6, 93.8, 112.0, 125.8, 128.3 (4 carbons), 141.9, 148.8; mass spectrum, m/z (rel intensity) 276 (0.06, M^+), 244 (4), 214 (5), 172 (26), 158 (10), 143 (38), 129 (20), 91 (100), 65 (24).

Carbamic acid, methyl-1-(2-methylenehexyl)-1-(2-phenylethyl), 1,1-dimethylethyl ester (14b). General procedure A was employed on a 0.5 mmol scale to give **14b** which was purified by flash column chromatography [$R_f = 0.10$, silica gel (Et_2O /petroleum ether, 2:98, v/v)]: IR (neat) 2954 (s), 2936 (s), 2859 (m), 1693 (vs), 1393 (s) cm^{-1} ; ^1H -NMR (CDCl_3) δ 0.79 (t, $J = 8\text{ Hz}$, 3H), 1.20-1.50 (m, 4H), 1.44 (s, 9H), 1.75-2.15 (m, 2H), (2.55) 2.60 (s, 3H), 4.50-4.70 (4.70-4.85) (m, 1H), 4.86 (s, 1H), 4.96 (s, 1H), 7.10-7.35 (m, 5H) (rotamers); ^{13}C -NMR (CDCl_3) δ 13.9, 22.5, 28.4, 30.1, 31.3, 32.7, 34.3, 45.2, 56.6 (79.0), 79.5, 111.3, 125.8 (126.5), 128.3 (4 carbons), 141.9, (142.5), 148.0, 156.3 (rotamers);

mass spectrum, m/z (rel intensity) 331 (0.1, M^+), 275 (84), 258 (12), 232 (7), 200 (9), 184 (40), 170 (69), 143 (19), 126 (45), 91 (59), 57 (100).

(Z)-2-Hexenoic acid, 4-[(methoxy)methoxy]-6-phenyl, ethylester (15a). General procedure A was employed on a 0.5 mmol scale to give **15a** which was purified by flash column chromatography [R_f = 0.3, silica gel (Et₂O/petroleum ether, 10:90, v/v)]: $[\alpha]_D^{22}$ +73.23 (c 1.65, CHCl₃) for 99-100% ee; IR (neat) 2982 (s), 2940 (s), 1957 (m), 1692 (vs), 1401 (s), 1145 (s) cm⁻¹; ¹H-NMR (CDCl₃) δ 1.24 (t, J = 7.1 Hz, 3H), 1.75-1.95 (m, 2H), 2.6-2.9 (m, 2H), 3.38 (s, 3H), 4.14 (q, J = 7.1 Hz, 2H), 4.64 (center AB quartet, J_{AB} = 6.7 Hz, $\Delta\nu_{AB}$ = 20 Hz, δ_A = 4.67, δ_B = 4.61, 2H), 5.2-5.3 (m, 1H), 5.83 (dd, J = 10.6 Hz, 1.2 Hz, 1H), 6.1-6.3 (m, 1H), 7.1-7.35 (m, 5H); ¹³C-NMR (CDCl₃) δ 14.2, 31.7, 36.8, 55.7, 60.3, 73.1, 95.5, 120.7, 125.7, 128.3 (4 carbons), 142.0, 150.1, 165.7; mass spectrum, m/z (rel intensity) 278 (0.1, M^+), 246 (19), 233 (8), 217 (18), 187 (11), 142 (19), 129 (14), 112 (32), 91 (100).

(Z)-2-Hexenoic acid, 4-[N-[(1,1-dimethylethoxy)carbonyl]-N-methyl-amino]-6-phenyl, ethyl ester (15b). General procedure B was employed on a 0.5 mmol scale to give **15b** which was purified by flash column chromatography [R_f = 0.15, silica gel (Et₂O/petroleum ether, 5:95, v/v)]: $[\alpha]_D^{22}$ +28.13 (c 1.9, CHCl₃) for 78% ee; IR (neat) 2976 (m), 2933 (m), 1719 (s), 1694 (vs), 1402 (s), 1161 (s) cm⁻¹; ¹H-NMR (CDCl₃) δ 1.21 (t, J = 6.7 Hz, 3H), 1.43 (s, 9H), 1.75-2.15 (m, 2H), 2.60 (t, J = 8 Hz, 2H), 2.82 (s, 3H), 4.12 (q, J = 7 Hz, 2H), 5.49-5.52 (m, 1H), 5.78 (d, J = 12 Hz, 1H), 6.20-6.40 (m, 1H), 7.10-7.35 (m, 5H); ¹³C-NMR (CDCl₃) δ 14.2, 28.4, 29.2, 32.5, 34.0, 54.2, 60.1, 79.7, 120.2, 125.8, 128.3 (4 carbons), 141.6, 146.0, 155.8, 165.5; mass spectrum, m/z (rel intensity) 347 (0.1, M^+), 291 (7), 247 (30), 218 (28), 202 (10), 156 (8), 142 (71), 110 (21), 96 (36), 91 (49), 57 (100). Anal. Calcd for C₂₀H₂₉O₄N: C, 69.16; H, 8.36; N, 4.03. Found: C, 69.14; H, 8.48; N, 3.99.

4-[(methoxy)methoxy]-6-phenyl-1,2-hexadiene (16a). General procedure B was employed on a 0.5 mmol scale to give **16a** which was purified by flash column chromatography [R_f = 0.5, silica gel (Et₂O/petroleum ether, 10:90, v/v)]: $[\alpha]_D^{22}$ +54.64 (c 2.3, CHCl₃) for 99-100% ee; IR (neat) 2957 (m), 1957 (m), 1470 (m), 1153 (s), 1034 (vs) cm⁻¹; ¹H-NMR (CDCl₃) δ 1.8-2.1 (m, 2H), 2.60-2.80 (m, 2H), 3.39 (s, 3H), 4.14 (dt, J = 7.4 Hz, J = 6.2 Hz, 1H), 4.69 (center AB quartet, J_{AB} = 6.8 Hz, $\Delta\nu_{AB}$ = 68.7 Hz, δ_A = 4.81, δ_B = 4.58, 2H), 4.75-7.85 (m, 2H), 5.07 (dt, J = 7.7 Hz, J = 6.7 Hz, 1H), 7.10-7.35 (m, 5H); ¹³C-NMR (CDCl₃) δ 31.8, 37.6, 55.6, 74.1, 76.0, 91.3, 94.1, 125.8, 128.4 (4 carbons), 141.9, 209.5; mass spectrum, m/z (rel intensity) 218 (0.02, M^+), 188 (9), 173 (4), 156 (41), 147 (19), 113 (25), 91 (100), 65 (36); high-resolution mass spectrum m/z 218.1305 (M^+) (calcd for C₁₄H₁₈O₂ 218.1307).

Carbamic acid, methyl-1-[(2-phenylethyl)-2,3-butadiene], 1,1-dimethylethyl ester (16b). General procedure A was employed on a 0.5 mmol scale to give **16b** which was purified by flash column chromatography [R_f = 0.3, silica gel (Et₂O/petroleum ether, 5:95, v/v)]: IR (neat) 2982 (s), 2940 (s), 1957 (m), 1692 (vs), 1401 (s), 1145 (s) cm⁻¹; ¹H-NMR (CDCl₃) δ (1.42) 1.43 (s, 9H), 1.75-1.95 (m, 2H), 2.45-2.75 (m, 2H), 2.68 (br s, 3H), 4.50-4.75 (4.80-4.90) (m, 1H), 4.80-4.95 (m, 2H), 5.10-5.20 (m, 1H), 7.10-7.35 (m, 5H) (rotamers); ¹³C-NMR (CDCl₃) δ 28.4, 32.6, 33.3, 34.5, 52.9, 77.4, 79.6, 90.8, 125.9, 128.4 (4 carbons), 141.7, 155.9, 208.4; mass spectrum, m/z (rel intensity) 287 (0.01, M⁺), 248 (2), 231 (13), 192 (14), 156 (13), 148 (34), 126 (27), 117 (17), 91 (64), 82 (25), 57 (100).

3-[(3-phenyl)propyl]-4-[(methoxy)methoxy]-6-phenyl-1,2-hexadiene (17a). General procedure B was employed on 0.5 mmol scale to give **17a** which was purified by flash column chromatography [R_f = 0.23, silica gel (Et₂O/petroleum ether, 5:95, v/v)]: IR (neat) 3062, 3026, 2914, 1954, 1603, 1496, 1454, 1147, 1031 cm⁻¹; ¹H-NMR (CDCl₃) δ 1.82-1.92 (m, 2H), 1.95-2.15 (m, 4H), 2.72 (t, J = 8.1 Hz, 2H), 2.77-2.90 (m, 2H), 3.47 (s, 3H), 4.22 (t, J = 6.7 Hz, 1H), 4.73 (center AB quartet, J_{AB} = 6.8 Hz, $\Delta\nu_{AB}$ = 51.84 Hz, δ_A = 4.82, δ_B = 4.65, 2H), 4.92 (dd, J = 3.7 Hz, 7.4 Hz, 2H), 7.27-7.30 (m, 6H), 7.33-7.39 (m, 4H); ¹³C-NMR (CDCl₃) δ 25.9, 29.4, 32.3, 35.7 (2 carbons), 55.8, 77.3 (2 carbons), 94.1, 103.5, 125.8 (2 carbons), 128.4 (8 carbons), 142.5, 143.2, 206.7; mass spectrum, m/z (rel intensity) 336 (0.3, M⁺), 306 (16), 274 (48), 259 (13), 201 (61), 170 (42), 147 (34), 117 (26), 104 (62), 91 (100), 65 (21); high-resolution mass spectrum m/z 336.2095 (M⁺) (calcd for C₂₃H₂₈O₂ 336.2089).

Carbamic acid, methyl-[1-(2-phenylethyl)-2-(3-phenylpropyl)] -2,3-butadiene, 1,1-dimethylethylester (17b). General procedure B was employed on 0.5 mmol scale to give **17b** which was purified by flash column chromatography [R_f = 0.4, silica gel (Et₂O/petroleum ether, 1:9, v/v)]: IR (neat) 3026(m), 2930(s), 2859(w), 1954(s), 1850(w), 1690(vs), 1453(s), 1365(s) cm⁻¹; ¹H-NMR (CDCl₃) δ 1.50 (1.58) (s, 9H), 1.75-2.20 (m, 6H), 2.60-2.93 (m, 4H), (2.69) 2.76 (s, 3H), 4.55-4.65 (4.80-4.95) (m, 1H), 4.85-5.10 (m, 2H), 7.25-7.45 (m, 10H) (rotamers); ¹³C-NMR (CDCl₃) δ 27.6, 28.3, 28.5, 29.2, 32.2, 32.4, 35.6, 53.5, 78.1, 79.9, 104.6, 125.8(2 carbons), 128.5 (8 carbons), 142.1, 142.3, 157.2, 194.5; mass spectrum, m/z (rel intensity) 343 (0.24, M⁺), 243 (8), 148 (12), 138 (100), 110 (10), 91 (29), 65 (6).

5-[(methoxy)methoxy]-7-phenyl-heptan-2-one (18a). General procedure A was employed on a 0.5 mmol scale to give **18a** which was purified by flash column chromatography [R_f = 0.55, silica gel (Et₂O/petroleum ether, 50:50, v/v)]: [α]_D²² - 5.4 (c 3.5, CHCl₃) for 70%ee; IR (neat) 2945 (s), 1727 (vs), 1367 (m), 1033 (vs), cm⁻¹; ¹H-NMR (CDCl₃) δ 1.65-1.95 (m, 4H), 2.12 (s, 3H), 2.51 (t, J = 7.4 Hz), 2.53-2.76 (m, 2H), 3.35 (s, 3H), 3.57 (quint., J = 6.3 Hz, 1H), 4.62 (center AB quartet, J_{AB} = 7 Hz, $\Delta\nu_{AB}$

= 5 Hz, δ_A = 4.63, δ_B = 4.61, 2H), 7.10-7.29 (m, 5H); ^{13}C -NMR (CDCl_3) δ 27.9, 29.9, 31.5, 36.2, 39.1, 55.6, 76.5, 95.7, 125.8, 128.2, 128.3 (4 carbons), 141.9, 208.4; mass spectrum, m/z (rel intensity) 250 (0.03, M^+), 218 (10), 205 (8), 189 (9), 169 (5), 160 (62), 130 (53), 101 (41), 91 (100), 83 (26).

Carbamic acid, methyl-1-(2-phenylethyl)-1-(4-butan-2-one), 1,1-dimethylethyl ester (18b).

General procedure A was employed on a 0.5 mmol scale to give **18b** which was purified by flash column chromatography [R_f = 0.4, silica gel (Et_2O /petroleum ether, 50:50, v/v)]: $[\alpha]_D^{22}$ +0.59 (c 4.4, CHCl_3) for 70% ee; IR (neat) 2979 (m), 2945 (m), 1722 (s), 1689 (vs), 1371 (s), 1168 (s) cm^{-1} ; ^1H -NMR (CDCl_3) δ 1.41, (1.45)(s, 9H), 1.50-1.75 (m, 4H), 2.09 (s, 3H), 2.32 (t, J = 7 Hz, 2H), 2.40-2.55 (m, 2H), (2.58), 2.65 (s, 3H), (3.80-4.10), 4.10-4.25 (m, 1H), 7.10-7.30 (m, 5H) (rotamers); ^{13}C -NMR (CDCl_3) δ 26.1, 27.3, 28.4, 30.0, 32.6 (32.9), 34.7, 39.9 (40.0), 54.0 (54.9), (79.0), 79.4, 125.9, 128.2 (128.3) (4 carbons), 141.5 (141.8), 156.4, 207.8 (rotamers); mass spectrum, m/z (rel intensity) 319 (0.9, M^+), 263 (12), 248 (5), 192 (22), 148 (44), 130 (14), 114 (100), 91 (43), 57 (87).

3-[1-(methoxy)methoxy-3-phenyl]propyl-cyclohex-2-en-1-one (19a). General procedure B was employed on 0.5 mmol scale to give **19a** which was purified by flash column chromatography [R_f = 0.38, silica gel (Et_2O /petroleum ether, 4:6, v/v)]: $[\alpha]_D^{22}$ +11.6 (c 0.75, CHCl_3) for 74% ee; IR (neat) 3025(w), 2943 (vs), 1737 (w), 1672 (vs), 1454 (m), 1376 (w), 1290 (w), 1147 (m), 1025 (w) cm^{-1} ; ^1H -NMR (CDCl_3) δ 1.95-2.20 (m, 4H), 2.35-2.51 (m, 4H), 2.70-2.85 (m, 2H), 3.47 (s, 3H), 4.21 (dd, J = 5.1 Hz, J = 2.5 Hz, 1H), 4.66 (center AB quartet, J_{AB} = 6.8 Hz, $\Delta\nu_{AB}$ = 4.4 Hz, δ_A = 4.67, δ_B = 4.65, 2H), 6.10 (s, 1H), 7.24-7.38 (m, 5H); ^{13}C -NMR (CDCl_3) δ 22.7, 25.4, 31.8, 35.5, 38.0, 56.0, 78.7, 95.1, 126.1 (2 carbons), 128.4 (2 carbons), 128.5 (2 carbons), 141.9, 170.2, 199.9; mass spectrum, m/z (rel intensity) 274 (4, M^+), 221 (57), 207 (57), 147 (61), 73 (100), 54 (10).

3-[1-[*N*-(1,1-dimethylethoxy)carbonyl-*N*-methyl]amino-3-phenyl] propyl-cyclohex-2-en-1-one (19b). General procedure B was employed on 0.5 mmol scale to give **19b** which was purified by flash column chromatography [R_f = 0.38, silica gel (Et_2O /petroleum ether, 4:6, v/v)]: $[\alpha]_D^{22}$ -27.7 (c 4.2, CHCl_3) for 78% ee; IR (neat) 3062(w), 2943 (vs), 2931 (s), 1669 (vs), 1626 (vs), 1454 (w), 1389 (m), 1322 (m), 1166 (vs) cm^{-1} ; ^1H -NMR (CDCl_3) δ 1.55(s, 9H), 2.00-2.07 (m, 4H), 2.30 (s, 2H), 2.44 (t, J = 6.6 Hz, 2H), 2.66-2.69(m, 5H), (4.65) 4.95 (s, 1H), 6.47 (s, 1H), 7.23-7.38 (m, 5H), (rotamers); ^{13}C -NMR (CDCl_3) δ 22.7, 28.2, 28.4, 28.5, 30.4, 32.4, 37.6, 58.1, 81.4, 126.1, 126.2, 128.3 (2 carbons), 128.5 (2 carbons), 141.8, 156.1, 163.8, 199.8; mass spectrum, m/z (rel intensity) 405 (0.3, M^+), 303 (20), 212 (42), 200 (64) 148 (64), 108 (100), 91 (60), 65 (13). Anal. Calcd for $\text{C}_{21}\text{H}_{29}\text{NO}_3$: C, 73.30; H, 8.44; N, 4.07 found C, 72.81; H, 8.25; N, 3.76.

PPM

PPM

PPM

PPM

8.11085

7.36949
7.35331
7.34356
7.33864
7.33002
7.27471

6.10208

5.27318
4.98262
4.97152
4.95975
4.94907
4.93876
4.92898
4.91899
4.90840
4.89572
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4.43849

3.69701

3.22134

2.93127
2.81576
2.75894
2.69337
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2.64491
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2.51772
2.01531
1.98841
1.96958
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1.88682
1.88137
1.85040
1.80112
1.50762
1.42635
1.36397
1.32717
1.31773
1.30463
1.29502
1.23011
0.82889
0.83916
0.82845
0.80472
0.80095
0.85880
0.83838
0.86236

19a

Racemic (RCuCNZnBr) 15b
 99:1 (v: v) Hexane: ⁱPrOH
 0.5mL/ min
 14.7 and 16.5 min
 50: 50 (0% ee)

Scalemic (RCuCNZnBr) 15b
 99:1 (v: v) Hexane: ⁱPrOH
 0.5mL/ min
 14.7 and 16.5 min
 89: 11 (78% ee)

Racemic (R₂CuLi) 18a
 70:30 (v: v) Hexane: ⁱPrOH
 1.0 mL/ min
 4.82 and 5.13 min
 50: 50 (0% ee)

Scalemic (R₂CuLi) 18a
 70:30 (v: v) Hexane: ⁱPrOH
 1.0 mL/ min
 4.82 and 5.13 min
 85: 15 (70% ee)

Racemic (R₂CuLi) 18b
 95:5 (v: v) Hexane: ¹PrOH
 0.5 mL/ min
 15.2 and 16.8 min
 50: 50 (0% ee)

Scalemic (R₂CuLi) 18b
 95:5 (v: v) Hexane: ¹PrOH
 0.5 mL/ min
 15.6 and 17.2 min
 85: 15 (70% ee)