Stereoselective Functionalization of β -Iodo- α,β -Unsaturated Ketone *via* an Iodine-Copper Exchange Reaction

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Supporting Information

General considerations

Unless otherwise indicated, all reactions were carried out with a magnetic stirring in flame-dried glassware under argon. Syringes used to transfer reagents and solvent were purged with argon prior to use. Reactions were monitored by gas chromatography (GC and GC-MS) or thin layer chromatography (TLC).

The β -iodo- α,β -unsaturated ketones were prepared according to literature procedures.¹ Organolithium solutions were titrated using the method of Paquette.²

Preparation of neophyl lithium:³

A dry and argon flushed 500 mL round-bottom flask was charged with lithium dust (3.0 g, 432 mmol) and 2,2-dimethyl-2-phenylethyl chloride (14.0 mL, 86.9 mmol) in *n*-hexane (75 mL). The reaction mixture was refluxed overnight. After cooling to rt the *n*-hexane was removed *in vacuo* and then dry diethyl ether was added. The resulting mixture was cannulated into a flame dried Schlenk tube and centrifuged (2000 rpm, 30 min). The clear solution of neophyllithium thus obtained was titrated before use with menthol using *o*-phenanthroline as indicator and could be stored at -30 °C for several days.

¹ (a) Taniguchi, M.; Kobayashi, S.; Nakagawa, M.; Hino, T. *Tetrahedron Lett.* **1986**, 27, 4763; (b) Verkruijsse, H. D.; Heus-Kloos, Y. A.; Brandsma, L. *J. Organomet. Chem.* **1988**, 338, 289.

² Lin, H.-S.; Paquette, L. A. *Synth. Commun.* **1994**, 24, 2503.

³ (a) Cano, A.; Cuenca, T.; Galakov, M.; Rodríguez, G. M.; Royo, P.; Cardin, C. J.; Convery, M. A. *J. Organomet. Chem.* **1995**, 493, 17. (b) Negishi, E.; Swanson, D. R.; Rousset, C. J. *J. Org. Chem.* **1990**, 55, 5406.

Synthesis of (1*E*)-1-phenyl-1-octen-3-one

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum was charged with CuCN (108 mg, 1.2 mmol) and dry THF (5 mL). A solution of neophyllithium (1.3 M/Et₂O, 1.9 mL, 2.4 mmol) was added at -78 °C. The resulting solution was stirred at rt for 10 min and then the Et₂O was removed carefully under vacuum. The remaining solution was cooled to -100 °C and cannulated into a solution of (1*Z*)-1-iodo-1-phenyl-1-octen-3-one (**1a**) (328 mg, 1.0 mmol) in dry THF (4 mL) at -100 °C. After 5 min, water (0.5 mL) was added and the mixture stirred at rt for 30 min. The reaction was quenched with sat. aq. NH₄Cl solution (5 mL) and poured into water (10 mL). The aq. phase was extracted with Et₂O (3 × 10 mL) and the combined organic fractions were washed with brine (10 mL), dried over Na₂SO₄ and concentrated in vacuo. Purification by flash chromatography yielded (1*E*)-1-phenyl-1-octen-3-one (203 mg, 93%) as a yellow oil. ¹H-NMR (CDCl₃, 300 MHz): δ = 7.59-7.50 (m, 3H), 7.40-7.33 (m, 3H), 6.77-6.73 (d, *J* = 16.2 Hz, 1H), 2.66-2.64 (t, *J* = 7.46 Hz, 2H), 1.74-1.62 (m, 2H), 1.41-1.30 (m, 4H), 0.91-0.89 (t, *J* = 6.86 Hz, 3H). ¹³C-NMR (CDCl₃, 75 MHz): δ = 200.4, 142.1, 134.5, 130.2, 128.8, 128.1, 126.2, 40.8, 31.4, 24.0, 22.4, 13.8. MS (EI, 70 eV), *m/z* (%): 202 (8) [M⁺], 173 (3), 146 (54), 131 (100), 103 (34), 77 (18).

Synthesis of (2*Z*)-1,2-diphenyl-2-nonene-1,4-dione (**4a**)

Typical procedure A. A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum was charged with CuCN (86 mg, 0.96 mmol) and dry THF (5 mL). A solution of neophyllithium (1.3 M, 1.5 mL, 1.92 mmol) was added at -78 °C. The resulting solution was stirred at rt for 10 min and then the Et₂O was removed carefully under vacuum. The

remaining solution was cooled to -100 °C and cannulated into a solution of (1Z)-1-iodo-1-phenyl-1-octen-3-one (**1a**) (262 mg, 0.8 mmol) in dry THF (2 mL). After 5 min, benzoyl chloride (280 mg, 2.0 mmol) was added and the mixture stirred at rt for 30 min. The reaction was quenched with sat. aq. NH₄Cl solution (5 mL) and poured into water (10 mL). The aq. phase was extracted with Et₂O (3 x 10 mL) and the combined organic fractions were washed with brine (10 mL), dried over Na₂SO₄ and concentrated in vacuo. Purification by flash chromatography yielded **4a** (203 mg, 83 %) as a yellow solid, mp. 67 °C. ¹H-NMR (CDCl₃, 300 MHz): δ = 7.85-7.82 (m, 2H), 7.47-7.41 (m, 3H), 7.36-7.28 (m, 5H), 6.77 (s, 1H), 2.51-2.46 (t, *J* = 7.30 Hz, 2H), 1.54-1.45 (m, 2H), 1.22-1.13 (m, 4H), 0.80-0.76 (t, *J* = 6.86 Hz, 3H). ¹³C-NMR (CDCl₃, 75 MHz): δ = 199.1, 197.9, 154.3, 136.4, 134.8, 133.6, 130.9, 129.5, 129.1, 127.5, 124.3, 43.8, 31.7, 23.9, 22.8, 14.3. IR (KBr, cm⁻¹): $\tilde{\nu}$ = 3447 (w), 2933 (m), 1683 (vs), 1671 (vs), 1585 (s), 1573 (s), 1495 (m), 1450 (s), 1347 (m), 1215 (s), 1128 (s), 1079 (s), 947 (m), 689 (m). MS (EI, 70 ev), *m/z* (%): 306 (18) [M⁺], 277 (3), 250 (4), 235 (45), 201 (4), 105 (100), 77 (28). HRMS (EI): calcd. for C₂₁H₂₂O₂ [M⁺]: 306.1620, found 306.1598.

Synthesis of (2Z)-1-(2-furyl)-2-phenyl-2-nonene-1,4-dione (**4b**)

Prepared according to typical procedure A from (1Z)-1-iodo-1-phenyl-1-octen-3-one (**1a**) (328 mg, 1.0 mmol), lithium dineophylcuprate **2** (1.2 mmol) and 2-furoyl chloride (393 mg, 3.0 mmol). Reaction time: 15 min at -100 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **4b** as a brown solid (231 mg, 78%), mp. 85-85 °C. ¹H-NMR (CDCl₃, 300 MHz): δ = 7.46-7.42 (m, 3H), 7.33-7.29 (m, 3H), 7.02-7.01 (dt, *J* = 3.65 Hz, *J* = 0.77 Hz, 1H), 6.70 (s, 1H), 6.42-6.40 (ddd, *J* = 3.54 Hz, *J* = 1.66 Hz, *J* = 0.89 Hz, 1H), 2.53-2.48 (t, *J* = 7.30 Hz, 2H), 1.58-1.48 (m, 2H), 1.26-1.13 (m, 4H), 0.82-0.77 (t, *J* = 7.07 Hz, 3H). ¹³C-NMR (CDCl₃, 75 MHz): δ = 199.2, 185.5, 152.7, 152.3, 147.1, 134.6, 130.9, 129.4, 127.5, 125.2, 118.4, 112.7, 43.9, 31.7, 23.9, 22.8, 14.3. IR (KBr, cm⁻¹): $\tilde{\nu}$ = 3436 (w), 2929 (w), 1681 (vs), 1654 (vs), 1597 (s), 1574 (w), 1468 (s), 1401 (s), 1371 (m),

1290 (w), 1130 (w), 1081 (s), 1059 (m), 789 (m). MS (EI, 70 ev), m/z (%): 296 (36) [M^+], 267 (100), 239 (4), 225 (14), 211 (4), 197 (5), 141 (4), 115 (4), 95 (93), 77 (2). HRMS (EI): calcd. for $C_{19}H_{20}O_3$ [M^+]: 296.1412, found 296.1393.

Synthesis of (2Z)-1-(6-chloro-3-pyridinyl)-2-phenyl-2-nonene-1,4-dione (**4c**)

Prepared according to typical procedure A from (1Z)-1-iodo-1-phenyl-1-octen-3-one (**1a**) (328 mg, 1.0 mmol), lithium dineophtylcuprate **2** (1.2 mmol) and 6-chloronicotinoyl chloride (528 mg, 3.0 mmol). Reaction time: 15 min at $-100\text{ }^{\circ}\text{C}$. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **4c** as a light yellow solid (277 mg, 81%), mp.: $67\text{ }^{\circ}\text{C}$. $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 8.66-8.65 (dd, J = 2.43 Hz, J = 0.66 Hz, 1H), 8.17-8.13 (dd, J = 8.30 Hz, J = 2.43 Hz, 1H), 7.43-7.28 (m, 6 H), 6.79 (s, 1H), 2.54-2.49 (t, J = 7.40 Hz, 2H), 1.56-1.45 (m, 2H), 1.27-1.13 (m, 4H), 0.82-0.77 (t, J = 6.80 Hz, 3H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 199.4, 195.4, 155.9, 153.0, 150.8, 138.5, 133.6, 131.5, 130.9, 129.8, 127.5, 125.1, 124.8, 43.8, 31.6, 23.8, 22.8, 14.2. IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3436 (w), 1686 (vs), 1673 (vs), 1585 (vs), 1572 (vs), 1463 (m), 1371 (s), 1299 (m), 1132 (m), 1074 (m), 942 (w), 768 (w), 603 (m). MS (EI, 70 ev), m/z (%): 341 (12) [M^+], 323 (10), 285 (100), 244 (8), 201 (7), 140 (35), 112 (13), 102 (17), 91 (4), 77 (5). HRMS (EI): calcd. for $C_{20}H_{20}\text{ClNO}_2$ [M^+]: 341.1183, found 341.1161.

Synthesis of 3-[(1E)-3-oxo-1-phenyl-1-octenyl]-2-cyclohexen-1-one (**4d**)

Prepared according to typical procedure A from (1*Z*)-1-iodo-1-phenyl-1-octen-3-one (**1a**) (328 mg, 1.0 mmol), lithium dineophylcuprate **2** (1.2 mmol) and 3-iodo-2-cyclohexen-1-one (666 mg, 3.0 mmol). Reaction time: 15 min at $-100\text{ }^{\circ}\text{C}$. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **4d** as a light yellow oil (210 mg, 71%). $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 7.40-7.25 (m, 5H), 6.45 (s, 1H), 5.77-5.76 (t, J = 1.54 Hz, 1H), 2.50-2.36 (m, 6H), 2.16-2.07 (m, 2H), 1.65-1.51 (m, 2H), 1.30-1.19 (m, 5H), 0.85-0.80 (t, J = 7.07 Hz, 3H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 198.8, 198.0, 162.0, 151.9, 135.6, 129.2, 128.0, 126.3, 126.0, 122.1, 43.3, 36.4, 30.4, 28.8, 22.8, 22.0, 21.4, 12.9. IR (film, cm^{-1}): $\tilde{\nu}$ = 3355 (w), 2954 (s), 2930 (s), 1678 (vs), 1622 (m), 1570 (s), 1447 (m), 1371 (w), 1238 (m), 1132 (m), 1072 (s), 966 (m), 764 (s), 696 (m). MS (EI, 70 ev), m/z (%): 296 (5) [M^+], 268 (21), 240 (100), 225 (14), 211 (7), 197 (65), 141 (15), 115 (11), 91 (5), 77 (2). HRMS (EI): calcd. for $\text{C}_{20}\text{H}_{24}\text{O}_2$ [M^+]: 296.1776, found 296.1766.

Synthesis of (2*Z*)-2-butyl-1-(2-thienyl)-2-decene-1,4-dione (**4e**)

Prepared according to typical procedure A from (5*Z*)-5-iodo-5-tetradecen-7-one (**1b**) (336 mg, 1.0 mmol), lithium dineophylcuprate **2** (1.2 mmol) and 2-furoyl chloride (438 mg, 3.0 mmol). Reaction time: 15 min at $-100\text{ }^{\circ}\text{C}$. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **4e** as a colorless oil (250 mg, 78%). $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 7.65-7.63 (d, J = 4.87 Hz, 1H), 7.51-7.50 (d, J = 4.42 Hz, 1H), 7.10-7.08 (dd, J = 4.78 Hz, J = 4.42 Hz, 1H), 6.30-6.29 (t, J = 1.33 Hz, 1H), 2.49-2.44 (t, J = 7.52 Hz, 2H), 2.45-2.40 (dt, J = 7.52 Hz, J = 1.33 Hz, 2H), 1.59-1.22 (m, 14H), 0.94-0.90 (t, J = 7.52 Hz, 3H), 0.90-0.85 (t, J = 7.08 Hz, 3H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 198.9, 191.8, 156.9, 143.1, 134.1, 132.8, 128.4, 125.7, 43.5, 35.5, 32.0, 29.6, 29.4, 29.4, 24.1, 22.9, 22.7, 14.4, 14.1. IR (film, cm^{-1}): $\tilde{\nu}$ = 3103 (w), 2957 (vs), 2929 (vs), 2858 (s), 1692 (s), 1650 (vs), 1614 (vs), 1516 (m), 1413 (s), 1378 (w), 1247 (s), 1051 (m), 721 (m). MS (EI, 70 ev), m/z (%): 320 (6) [M^+], 277 (8), 235 (9), 221 (100), 209 (5), 193 (7), 179 (6), 111 (98), 97 (4), 57 (4). HRMS (EI): calcd. for $\text{C}_{19}\text{H}_{28}\text{O}_2\text{S}$ [M^+]: 320.1810, found 320.1803.

Synthesis of (2Z)-2-butyl-1-(4-fluorophenyl)-2-undecene-1,4-dione (**4f**)

Prepared according to typical procedure A from (5Z)-5-iodo-5-tetradecen-7-one (**1b**) (336 mg, 1.0 mmol), lithium dineophylcuprate **2** (1.2 mmol) and 4-fluoro-benzoyl chloride (477 mg, 3.0 mmol). Reaction time: 15 min at $-100\text{ }^{\circ}\text{C}$. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **4f** as a colorless oil (249 mg, 75%). $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 7.91-7.86 (dd, J = 8.74 Hz, J = 5.42 Hz, 2H), 7.15-7.09 (t, J = 8.56 Hz, 2H), 6.34-6.33 (t, J = 1.44 Hz, 1H), 2.49-2.44 (t, J = 7.36 Hz, 2H), 2.41-2.35 (dt, J = 7.74 Hz, J = 1.32 Hz, 2H), 1.62-1.24 (m, 14H), 0.94-0.90 (t, J = 7.30 Hz, 3H), 0.90-0.85 (t, J = 6.81 Hz, 3H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 199.1, 198.1, 166.2 (d, J = 254.7 Hz), 157.9, 132.0 (d, J = 3.0 Hz), 131.3 (d, J = 9.4 Hz), 125.4, 116.2 (d, J = 22.0 Hz), 43.4, 35.2, 32.0, 29.5, 29.4, 29.4, 24.0, 22.9, 22.7, 14.4, 14.1. IR (film, cm^{-1}): $\tilde{\nu}$ = 3074 (w), 2957 (vs), 2928 (vs), 2858 (s), 1690 (vs), 1673 (vs), 1598 (vs), 1504 (m), 1466 (w), 1378 (m), 1235 (s), 1150 (m), 956 (w), 849 (m), 772 (w). MS (EI, 70 eV), m/z (%): 332 (6) [M^+], 289 (8), 247 (7), 233 (45), 205 (8), 163 (7), 123 (100), 109 (6), 95 (25), 57 (10). HRMS (EI): calcd. for $\text{C}_{21}\text{H}_{29}\text{FO}_2$ [M^+]: 332.2152, found 332.2165.

Synthesis of ethyl (2E,4Z)-4-butyl-6-oxo-2,4-tridecadienoate (**4g**)

Prepared according to typical procedure A from (5*Z*)-5-iodo-5-tetradecen-7-one (**1b**) (336 mg, 1.0 mmol), lithium dineophylcuprate **2** (1.2 mmol) and ethyl propiolate (294 mg, 3.0 mmol). Reaction time: 15 min at $-100\text{ }^{\circ}\text{C}$. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **4g** as a colorless oil (246 mg, 80%). $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 8.38-8.32 (dd, J = 16.25 Hz, J = 0.77 Hz, 1H), 6.23 (s, 1H), 6.22-6.16 (d, J = 16.70 Hz, 1H), 4.29-4.22 (q, J = 7.08 Hz, 2H), 2.53-2.48 (t, J = 7.62 Hz, 2H), 2.37-2.32 (dt, J = 7.30 Hz, J = 0.66 Hz, 2H), 1.65-1.25 (m, 17H), 0.97-0.92 (t, J = 7.19 Hz, 3H), 0.92-0.87 (t, J = 6.97 Hz, 3H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 201.5, 167.0, 149.7, 140.9, 129.7, 124.6, 61.1, 45.0, 34.2, 32.0, 31.4, 29.5, 29.5, 24.6, 23.0, 22.9, 14.6, 14.4, 14.2. IR (film, cm^{-1}): $\tilde{\nu}$ = 3431 (w), 2957 (vs), 2930 (vs), 2858 (s), 1721 (vs), 1686 (s), 1581 (s), 1465 (m), 1274 (s), 1173 (s), 1040 (m), 993 (w), 877 (w). MS (EI, 70 eV), m/z (%): 308 (11) [M^+], 279 (20), 235 (100), 181 (12), 136 (14), 107 (15), 55 (15). HRMS (EI): calcd. for $\text{C}_{19}\text{H}_{32}\text{O}_3$ [M^+]: 308.2351, found 308.2322.

Synthesis of ethyl (4*Z*)-4-butyl-2-methylene-6-oxo-4-tridecenoate (**4h**)

Prepared according to typical procedure A from (5*Z*)-5-iodo-5-tetradecen-7-one (**1b**) (336 mg, 1.0 mmol), lithium dineophylcuprate **2** (1.2 mmol) and ethyl bromomethylacrylate (376 mg, 3.0 mmol). Reaction time: 15 min at $-100\text{ }^{\circ}\text{C}$. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **4h** as a colorless oil (290 mg, 90%). $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 6.31-6.19 (d, J = 34.7 Hz, 1H), 6.19 (s, 1H), 5.58-5.47 (d, J = 34.7 Hz, 1H), 4.25-4.18 (q, J = 7.08 Hz, 2H), 3.64-3.14 (d, J = 149.27 Hz, 2H), 2.57-2.07 (m, 4H), 1.65-1.25 (m, 17H), 0.93-0.86 (m, 6H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 201.2, 167.5, 158.1, 137.9, 127.8, 125.3, 124.5, 61.2, 44.8, 40.7, 38.2, 33.9, 32.1, 31.0, 30.3, 29.5, 24.5, 23.0, 14.5, 14.4. IR (film, cm^{-1}): $\tilde{\nu}$ = 3433 (w), 2957 (vs), 2929 (vs), 2858 (s), 1719 (vs), 1689 (s), 1618 (s), 1465 (m), 1300 (w), 1138 (s), 1028 (m), 948 (w), 817 (w). MS (EI, 70 eV), m/z (%): 322 (7) [M^+], 293 (20), 235 (11), 249 (100), 195 (10), 177 (8), 150 (9), 121 (6), 57 (9). HRMS (EI): calcd. for $\text{C}_{22}\text{H}_{34}\text{O}_3$ [M^+]: 322.2508, found 322.2505.

Synthesis of (2*E*)-1-phenyl-2-(trimethylsilyl)-2-hexene-1,4-dione (**4i**)

Prepared according to typical procedure A from (1*Z*)-1-iodo-1-(trimethylsilyl)-1-penten-3-one (**1c**) (282 mg, 1.0 mmol), lithium dineophtylcuprate **2** (1.2 mmol) and benzoyl chloride (420 mg, 3.0 mmol).. Reaction time: 15 min at $-100\text{ }^{\circ}\text{C}$. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **4i** as a colorless oil (218 mg, 84%). $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 7.67-7.64 (m, 2H), 7.38-7.32 (m, 1H), 7.28-7.23 (m, 2H), 6.43 (s, 1H), 2.40-2.33 (q, J = 7.19 Hz, 2H), 0.85-0.80 (t, J = 7.19 Hz, 3H), 0.00 (s, 9H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 202.7, 199.8, 165.4, 137.8, 136.2, 134.6, 130.3, 130.0, 37.8, 9.3, 0.0. IR (film, cm^{-1}): $\tilde{\nu}$ = 2962 (w), 1695 (vs), 1658 (vs), 1581 (m), 1449 (m), 1354 (w), 1250 (m), 1227 (vs), 1122 (s), 10523 (w), 846 (vs), 756 (w), 691 (w). MS (EI, 70 ev), m/z (%): 260 (18) [M^+], 245 (9), 231 (33), 217 (17), 203 (45), 105 (100), 73 (45). HRMS (EI): calcd. for $\text{C}_{15}\text{H}_{20}\text{O}_2\text{Si}$ [M^+]: 260.1233, found 260.1217.

Synthesis of (2*E*)-1-(2-thienyl)-2-(trimethylsilyl)-2-hexene-1,4-dione (**4j**)

Prepared according to typical procedure A from (1*Z*)-1-iodo-1-(trimethylsilyl)-1-penten-3-one (**1c**) (282 mg, 1.0 mmol), lithium dineophtylcuprate **2** (1.2 mmol) and 2-thiophenecarbonyl chloride (438 mg, 3.0 mmol).. Reaction time: 15 min at $-100\text{ }^{\circ}\text{C}$. Purification by flash chromatography (*n*-pentane/diethyl ether = 5/1) yielded **4j** as a colorless oil (202 mg, 76%). $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 7.41-7.39 (dd, J = 4.98 Hz, J = 1.11 Hz, 1H), 7.24-7.23 (dd, J = 3.76 Hz, J = 1.22 Hz, 1H), 6.88-6.86 (dd, J = 4.98 Hz, J = 3.76 Hz, 1H), 6.34 (s, 1H),

2.37-2.30 (q, $J = 7.29$ Hz, 2H), 0.83-0.79 (d, $J = 7.19$ Hz, 3H), 0.00 (s, 9H). ^{13}C -NMR (CDCl_3 , 75 MHz): $\delta = 199.9, 194.7, 163.6, 145.4, 136.6, 135.1, 133.9, 129.8, 38.0, 9.4, 0.0$. IR (film, cm^{-1}): $\tilde{\nu} = 2961$ (w), 1696 (vs), 1634 (vs), 1585 (w), 1412 (vs), 1357 (m), 1236 (vs), 1122 (m), 846 (vs), 723 (m), 632 (w). MS (EI, 70 eV), m/z (%): 266 (25) [M^+], 251 (19), 237 (55), 223 (25), 209 (50), 165 (12), 111 (100), 83 (11), 73 (50). HRMS (EI): calcd. for $\text{C}_{13}\text{H}_{18}\text{O}_2\text{SSi}$ [M^+]: 266.0797, found 266.0788.

Synthesis of 1-hydroxy-5-methyl-4-oxo-2-trimethylsilyl-cyclopent-2-enecarboxylic acid ethyl ester (**4k**)

Prepared according to typical procedure A from (1Z)-1-iodo-1-(trimethylsilyl)-1-penten-3-one (**1c**) (282 mg, 1.0 mmol), lithium dineophylcuprate **2** (1.2 mmol) and ethyl oxalyl chloride (411 mg, 3.0 mmol). Reaction time: 15 min at -100 °C. Purification by flash chromatography (n -pentane/diethyl ether = 3/1) yielded **4k** as a colorless oil (184 mg, 72%). ^1H -NMR (CDCl_3 , 300 MHz): $\delta = 6.30$ (s, 1H), 4.05-3.98 (q, $J = 7.19$ Hz, 2H), 2.46-2.39 (q, $J = 7.19$ Hz, 2H), 1.07-1.01 (t, $J = 7.19$ Hz, 3H), 0.87-0.85 (d, $J = 7.29$ Hz, 3H), 0.00 (s, 9H). ^{13}C -NMR (CDCl_3 , 75 MHz): $\delta = 207.1, 178.5, 175.0, 144.6, 88.5, 64.4, 56.4, 15.6, 9.7, 0.0$. IR (film, cm^{-1}): $\tilde{\nu} = 3490$ (w), 2977 (w), 1719 (vs), 1449 (m), 1216 (m), 1119 (m), 1032 (w), 884 (m), 843 (vs), 760 (m), 60 (w). MS (EI, 70 eV), m/z (%): 256 (5) [M^+], 241 (19), 210 (10), 183 (15), 167 (100), 139 (45), 123 (10), 75 (30), 65 (4). HRMS (EI): calcd. for $\text{C}_{12}\text{H}_{20}\text{O}_4\text{Si}$ [M^+]: 256.1131, found 256.1128.

Synthesis of ethyl (4E)-2-methylene-6-oxo-4-(trimethylsilyl)-4-octenoate (**4l**)

Prepared according to typical procedure A from (1Z)-1-iodo-1-(trimethylsilyl)-1-penten-3-one (**1c**) (282 mg, 1.0 mmol), lithium dineophylcuprate **2** (1.2 mmol) and ethyl bromomethylacrylate (376 mg, 3.0 mmol). Reaction time: 15 min at $-100\text{ }^{\circ}\text{C}$. Purification by flash chromatography (*n*-pentane/diethyl ether = 10/1) yielded **4l** as a colorless oil (239 mg, 89%). $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 6.49 (s, 1H), 6.16-6.06 (d, J = 32.4 Hz, 1H), 5.31-5.21 (d, J = 32.4 Hz, 1H), 4.14-4.07 (q, J = 7.07 Hz, 2H), 3.54-3.17 (d, J = 113.7 Hz, 1H), 2.43-2.36 (q, J = 7.18 Hz, 2H), 1.22-1.17 (t, J = 7.19 Hz, 3H), 0.98-0.93 (t, J = 7.19 Hz, 3H), 0.04 (s, 3H), 0.00 (s, 6H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 202.5, 168.7, 159.8, 140.5, 137.8, 126.4, 62.4, 38.8, 33.9, 15.8, 9.5, 0.0. IR (film, cm^{-1}): $\tilde{\nu}$ = 2979 (m), 1718 (vs), 1692 (s), 1579 (m), 1460 (w), 1302 (w), 1249 (m), 1136 (s), 1028 (m), 840 (vs), 757 (w), 698 (w). MS (EI, 70 eV), m/z (%): 268 (2) [M^+], 239 (12), 211 (10), 195 (100), 183 (14), 121 (12), 93 (11), 73 (35). HRMS (EI): calcd. for $\text{C}_{14}\text{H}_{24}\text{O}_3\text{Si}$ [M^+]: 268.1495, found 268.1466.

Synthesis of 3-(2-furyl)-6-pentyl-4-phenylpyridazine (**5a**)

Typical Procedure B: A 10 mL flask, equipped with a magnetic stirrer, a refluxing condenser and a septum, was charged with a solution of **4b** (90 mg, 0.3 mmol) in ethanol (5 mL). The solution was refluxed and a solution of hydrazine hydrate in ethanol (0.5 M/ethanol, 0.7 mL; 0.35 mmol) was added. The resulting mixture was refluxed for 15 min to complete the cyclization (checked by GC-MS analysis of reaction aliquots). The solution was concentrated *in vacuo*. Purification by flash chromatography (SiO_2 , *n*-pentane/diethyl ether = 1:1) yielded **5a** as a yellow oil (85 mg, 96%). $^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 7.38-7.33 (m, 3H), 7.30-7.29 (dd, J = 1.66 Hz, J = 0.66 Hz, 1H), 7.22-7.19 (m, 2H), 7.13 (s, 1H), 6.47-6.45 (dd, J = 3.43 Hz, J = 0.66 Hz, 1H), 6.31-6.30 (dd, J = 3.43 Hz, J = 1.66 Hz, 1H), 2.98-2.92 (t, J = 7.74 Hz, 2H), 1.81-1.71 (m, 2H), 1.38-1.27 (m, 4H), 0.86-0.81 (d, J = 7.19 Hz, 3H). $^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 162.4, 150.9, 149.1, 144.1, 138.1, 137.6, 129.1, 129.0, 128.7, 127.6, 113.0, 111.8, 36.2, 31.8, 29.7, 22.8, 14.4. IR (film, cm^{-1}): $\tilde{\nu}$ = 3058 (w), 2955 (vs), 2928 (vs), 2858 (vs), 1573 (m), 1494 (m), 1444 (m), 1403 (s), 1005 (m), 743 (s), 700 (vs), 595 (w). MS

(EI, 70 ev), m/z (%): 292 (8) [M^+], 263 (8), 249 (15), 236 (100), 219 (5), 139 (9). HRMS (EI): calcd. for $C_{19}H_{20}N_2$ [M^+]: 292.1576, found 292.1563.

Synthesis of 4-butyl-6-heptyl-3-(2-thienyl)pyridazine (5b)

Prepared according to typical procedure B from **4f** (160 mg, 0.50 mmol) and hydrazine hydrate (0.55 mmol). Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **5b** as a yellow oil (145 mg, 92%). 1H -NMR ($CDCl_3$, 300 MHz): δ = 7.42-7.42 (dd, J = 3.78 Hz, J = 1.11 Hz, 1H), 7.40-7.38 (dd, J = 5.08 Hz, J = 1.11 Hz, 1H), 7.09-7.06 (dd, J = 5.08 Hz, J = 3.78 Hz, 1H), 7.07 (s, 1H), 2.90-2.85 (t, J = 7.62 Hz, 2H), 2.80-2.75 (t, J = 7.62 Hz, 2H), 1.77-1.67 (m, 2H), 1.63-1.53 (m, 2H), 1.42-1.12 (m, 10H), 0.91-0.87 (t, J = 7.30 Hz, 3H), 0.83-0.78 (t, J = 6.97 Hz, 3H). ^{13}C -NMR ($CDCl_3$, 75 MHz): δ = 162.1, 154.0, 141.0, 139.3, 128.5, 128.1, 127.8, 127.1, 36.1, 32.8, 32.1, 31.4, 29.9, 29.6, 29.5, 23.0, 22.9, 14.4, 14.2. IR (film, cm^{-1}): $\tilde{\nu}$ = 3074 (w), 2956 (vs), 2927 (vs), 2856 (vs), 1583 (w), 1435 (w), 1258 (w), 851 (w), 700 (s), 702 (m). MS (EI, 70 ev), m/z (%): 316 (8) [M^+], 287 (7), 273 (6), 259 (6), 245 (20), 232 (100). HRMS (EI): calcd. for $C_{19}H_{28}N_2S$ [M^+]: 316.1973, found 316.1964.

Synthesis of 6-ethyl-3-phenyl-4-(trimethylsilyl)pyridazine (5c)

Prepared according to typical procedure B from **4i** (80 mg, 0.30 mmol) and hydrazine hydrate (0.33 mmol). Reaction time: 15 min at 78 °C. Purification by flash chromatography (*n*-pentane/diethyl ether = 1/1) yielded **5c** as a yellow oil (72 mg, 92%). 1H -NMR ($CDCl_3$, 300 MHz): δ = 7.40-7.38 (m, 6H), 3.01-2.94 (q, J = 7.63 Hz, 2H), 1.38-1.33 (t, J = 7.63 Hz, 3H),

0.00 (s, 9H). ^{13}C -NMR (CDCl_3 , 75 MHz): δ = 164.8, 162.2, 141.0, 138.8, 132.8, 129.8, 129.1, 128.5, 29.7, 14.3, 0.0. IR (film, cm^{-1}): $\tilde{\nu}$ = 2969 (m), 2935 (w), 2987 (w), 1460 (w), 1395 (vs), 1251 (s), 1121 (w), 1013 (w), 879 (m), 838 (vs), 762 (s), 701 (s), 626 (w). MS (EI, 70 eV), m/z (%): 256 (60) [M^+], 241 (13), 174 (33), 159 (100), 73 (18). HRMS (EI): calcd. for $\text{C}_{19}\text{H}_{28}\text{N}_2\text{S}$ [M^+]: 256.1396, found 256.1374.

4a

4a

4b

4b

4d

4d

4i

4i

4l

4l

5a

5a

5b

5b

5c

5c