**Neighboring Group Effect In Pd-catalyzed Carbonylation Terminated By Lactonization: A Need For a Protective Group and/or DMF**

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## Supporting information

**General remarks.** THF was distilled from benzophenone ketyl; DMF was sequentially dried (3x) over freshly activated 4 Å molecular sieves. Chemicals and silica gel (230-400 mesh) for column chromatography were purchased from commercial sources and used as received. All anhydrous reactions were performed in flame-dried Schlenk tubes under argon. Analytical thin-layer chromatography was conducted on TLC plates (silica gel 60 $F_{254}$, aluminum back). Melting points were determined on a Kofler block and are uncorrected. $^{1}H$ and $^{13}C$ NMR spectra were recorded for $CDCl_3$ solutions at ambient temperature on a 300 MHz spectrometer. Chemical shifts were recorded as δ values in parts per million (ppm), and were indirectly referenced to tetramethylsilane (TMS) *via* the solvent signal (7.26 for $^{1}H$, 77.0 for $^{13}C$ in $CDCl_3$). All assignments were made on the basis of NOESY, gCOSY, gHSQC and gHMBC experiments. Where mixtures of inseparable diastereomers were obtained, NMR spectra of both isomers are described separately as **A** and **B**. Infrared spectra were recorded in $CDCl_3$. Apart from usual spectral analysis, the identity of all intermediates has been unequivocally confirmed by X-ray analysis of compound **5**.

**(*Z*)-3-iodo-4-(tetrahydropyran-2-yloxy)but-2-en-1-ol (7).** A solution of 4-(tetrahydropyran-2-yloxy)but-2-yn-1-ol[1] (1.0 g, 5.90 mmol) in dry THF (6 ml) was added dropwise to a solution of Red-Al® (3.1 ml of 65% solution in $PhCH_3$, 10.30 mmol) in dry THF (6 ml) precooled to 0 °C in a Schlenk tube under Ar, and the reaction mixture was stirred at this temperature for 1h. EtOAc (2 ml) was then added and the resultant mixture stirred at 0 °C for 10 min. The mixture was cooled to –78 °C, and a solution of $I_2$ (1.9 g, 7.34 mmol) in dry THF (8 ml) was added dropwise. The reaction mixture was allowed to gradually warm to room temperature and then poured into $Et_2O$. The resultant mixture was washed with a mixture of a 5% aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ (1:1), the organic phase dried over anhydrous $Na_2SO_4$ and the solvent removed. The crude product was purified by column chromatography on silica gel (PE/$Et_2O$ 8:2) to afford the product as a yellowish oil in 86% yield; **$^{1}H$ NMR** (300 MHz, $CDCl_3$) δ 6.29-6.23 (1H, m, H2), 4.69 (1H, t, *J*=3.3 Hz, THP CHO), 4.38-4.16 (4H, m, H1+H4), 3.93-3.83 (1H, m, THP $CH_2O$). 3.58-3.49 (1H, m, THP $CH_2O$), 1.95-1.48 (6H, m, THP $CH_2$); **$^{13}C$ NMR** (75 MHz, $CDCl_3$) δ 135.5, 104.2, 97.2, 74.2, 66.6, 62.1, 30.3, 25.3, 19.0; **IR** ($CHCl_3$) $\nu_{max}$ 3612 (m), 3010 (m), 2947 (s), 2742 (w),

1651 (w), 1155 (m), 1345 (m), 1261 (m) $cm^{-1}$; **LRMS** 213 ($M^+$-THP, 2), 196 (3), 183 (2), 171 (2), 153 (2), 136 (2), 125 (1), 101 (8), 85 (100), 67 (5), 55 (4).

**(*Z*)-1-bromo-3-iodo-4-(tetrahydropyran-2-yloxy)but-2-en (8).** *N*-bromosuccinimide (5.6 g, 31.54 mmol) was added to a solution of alcohol **7** (4.7 g, 15.77 mmol) in dry $CH_2Cl_2$ (15 ml) precooled to –20 °C under Ar. $Me_2S$ (2.3 ml, 31.54 mmol) was added dropwise to the solution and the reaction mixture was maintained at –20 °C for 2 hrs. The mixture was diluted with $Et_2O$ and washed with 5% aqueous solution of $Na_2CO_3$. The organic phase was dried over anhydrous $Na_2SO_4$ and the solvent removed. The crude product was purified by column chromatography on silica gel (PE/$Et_2O$ 95:5) to afford the title compound as a colorless oil in 84% yield; **$^1$H NMR** (300 MHz, $CDCl_3$) δ 6.30-6.22 (1H, m, H2), 4.67 (1H, t, *J*=3.4 Hz, THP CHO), 4.41-4.21 (2H, m, H4), 4.05 (2H, d, *J*=8.0 Hz, H1), 3.91-3.81 (1H, m, THP $CH_2O$), 3.58-3.49 (1H, m, THP $CH_2O$), 1.93-1.45 (6H, m, THP $CH_2$); **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 131.5, 109.9, 97.3, 74.1, 62.1, 34.1, 30.2, 25.3, 19.0; **IR** ($CDCl_3$) $\nu_{max}$ 2947 (s), 2854 (m), 2359 (m), 2341 (m), 2246 (m), 1452 (w) $cm^{-1}$; **LRMS** 281 ($M^+$-HBr, 5), 276 (8), 261 (3), 221 (2), 207 (4), 197 (20), 169 (35), 147 (3), 127 (22), 121 (2), 105 (3), 93 (3), 79 (6), 70 (100), 50 (12).

**Dimethyl-(3-phenylprop-2-yn-1-yl)malonate.** CuI (0.014 g, 0.075 mmol), $(PPh_3)_2PdCl_2$ (0.05 g, 0.075 mmol) and iodobenzene (0.35 ml, 3.00 mmol) were added to a solution of dimethyl-propargylmalonate[2] (0.51 g, 3.00 mmol) in $CH_2Cl_2$ (6 ml) and $Et_3N$ (1.6 ml) and the reaction mixture was stirred at room temperature for 12 hrs. The mixture was then diluted with EtOAc and washed with saturated aqueous $NaHCO_3$. The organic phase was dried over anhydrous $Na_2SO_4$ and the solvent removed. The crude product was purified by column chromatography on silica gel (PE/EtOAc 92.5:7.5) to afford the title compound as a yellowish oil in 89% yield; **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.39-7.34 (2H, m, Ar), 7.30-7.25 (3H, m, Ar), 3.79 (6H, s, $COOCH_3$), 3.70 (1H, t, *J*=7.8 Hz, H2), 3.01 (2H, d, *J*=8.0 Hz, $CH_2$); **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 168.4, 131.6, 128.2, 128.0, 123.1, 85.1, 82.5, 52.8, 51.2, 19.5; **IR** ($CHCl_3$) $\nu_{max}$ 3028 (m), 2955 (m), 2846 (w), 1752 (s), 1491 (m), 1437 (s), 1344 (m) $cm^{-1}$; **LRMS** 247 ($M^+$+H, 10), 241 (2), 229 (8), 215 (3), 205 (1), 187 (100), 171 (12), 155 (11), 144 (8), 128 (9), 115 (19), 102 (5), 89 (2), 77 (2), 59 (3), 51 (2).

**(*Z*)-Dimethyl-2-[3-iodo-4-(tetrahydropyran-2-yloxy)but-2-enyl]-2-(3-fenylprop-2-yn-1-yl) malonate (12).** NaH (60% dispersion in mineral oil, 0.054 g, 2.23 mmol) was placed in a dry Schlenk tube under Ar and washed with petroleum ether (3 x 4 ml). Dry THF (20 ml) was then added, the resultant suspension cooled to 0 °C and dimethyl-(3-phenylprop-2-yn-1-yl)malonate (0.5 g, 2.0 mmol) added. After a complete dissolution of NaH (ca 1 h), bromide **8** (0.8 g, 2.23 mmol) in dry THF (5 ml) was added to the solution, the reaction mixture allowed to warm to laboratory temperature and stirred for 2 hrs. The mixture was diluted with $Et_2O$ and washed with saturated aqueous NaCl. The organic phase was dried over anhydrous $Na_2SO_4$ and the solvent removed. The crude product was purified by column chromatography on silica gel (PE/EtOAc 95:5) to afford malonate **12** as a yellowish oil in 78% yield; **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.41-7.34 (2H, m, Ar), 7.30-7.26 (3H, m, Ar), 5.92-5.85 (1H, m, CH), 4.64 (1H, t, *J*=3.3 Hz, THP CHO), 4.37-4.01 (2H, m, $CH_2O$), 3.91-3.75 (1H, m, THP $CH_2O$), 3.77 (6H, s, $COOCH_3$), 3.57-3.47 (1H, m, THP $CH_2O$), 3.08-2.99 (4H, m, $CH_2$), 1.93-1.46 (6H, m, THP $CH_2$); **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 170.1, 131.7, 131.0, 128.2, 128.0, 107.9, 96.8, 84.0, 83.9, 74.6, 62.1, 56.8, 53.0, 52.8, 38.9, 30.3, 25.3, 24.4, 19.1; **IR** ($CHCl_3$) $\nu_{max}$ 2954 (m), 2248 (w), 1735 (s), 1491 (m), 1438 (m), 1295 (m) $cm^{-1}$; **LRMS** 527 ($M^+$, 40), 509 (22), 495 (18), 481 (8), 477 (48), 463 (10), 449 (18), 435 (22), 431 (26), 417 (100), 399 (16), 381 (14), 373 (10), 350 (14), 349 (14), 323 (5), 322 (28), 290 (86), 271 (30), 262 (32), 245 (58), 243 (58), 219 (38), 217 (15), 199 (45), 191 (15), 181 (10), 157 (4).

**(*Z*)-Dimethyl-2-(3-jod-4-hydroxybut-2-en-1-yl)-2-(3-fenylprop-2-yn-1-yl) malonate (14).** Dowex 50 (0.25 g) was added to a solution of derivative **12** (0.50 g, 0.91 mmol) in MeOH (10 ml) and the suspension was vigorously stirred for 1h. The resin was filtered off and the solvent removed to furnish the pure deprotected alcohol **14** in 92% yield; **$^1$H NMR:** (300 MHz, $CDCl_3$) δ 7.40-7.36 (2H, m, Ar), 7.31-7.25 (3H, m, Ar), 5.94-5.87 (1H, m, CH), 4.26-4.24 (2H, m, $CH_2O$), 3.78 (6H, s, $COOCH_3$), 3.07-3.02 (4H, m, $CH_2$); **$^{13}$C NMR:** (75 MHz, $CDCl_3$) δ 170.1, 131.7 129.5, 128.2, 128.1, 123.0, 112.9, 84.1, 83.9, 71.7, 56.8, 53.0, 38.9, 24.4.

**(*Z*)-Methyl-2-hydroxymethyl-5,5-bis-(methoxycarbonyl)-8-phenyloct-2-en-7-ynoate (15)**. The compound was obtained as the major product from the carbonylation of **14**, carried out in MeOH for 24 hrs as an inseparable oily mixture with lactone **5** in 4:1 ratio. Total yield 40% based on $^1$H NMR, recovery of the starting material 50%. **$^1$H NMR:** (300 MHz, $CDCl_3$) δ

7.46-7.33 (3H, m, Ar), 7.29-7.25 (2H, m, Ar), 6.29-6.17 (1H, m, H3), 4.25 (2H, d, *J*=0.9 Hz, $OCH_2$), 3.77 (6H, s, $COOCH_3$), 3.72 (3H, s, $COOCH_3$), 3.36 (2H, d, *J*=7.4 Hz, H4), 3.04 (2H, s, H6); **$^{13}$C NMR:** (75 MHz, $CDCl_3$) δ 170.1, 167.0, 137.7, 134.0, 131.6, 129.9, 128.2, 128.1, 83.91, 83.85, 64.9, 57.1, 53.0, 51.7, 32.4, 24.6; **IR** ($CHCl_3$) $\nu_{max}$ 3027 (m), 2955 (m), 1735 (s), 1491 (m), 1437 (m), 1295 (m) $cm^{-1}$; **MS**: 375 ($M^+$+H, 5), 357 (100), 342 (3), 325 (8), 313 (6), 297 (20), 293 (4), 281 (3), 265 (7), 253 (2), 223 (3), 159 (4), 147 (10).

**(*Z*)-5-iodo-2-methyl-6-(tetrahydropyran-2-yloxy)hex-4-en-3-ol (20)**. Prepared from 2-methyl-6-(tetrahydropyran-2-yloxy)hex-4-yn-3-ol[3], see the preparation of **7** for details; **$^1$H NMR** (300 MHz, $CDCl_3$) δ **A:** 6.01 (1H, t, *J*=1.4 Hz, H4), 4.69 (1H, t, *J*=3.6 Hz, THP CHO), 4.38-4.29 (1H, m, H6), 4.25-4.16 (1H, m, H6), 4.12 (1H, dd, *J*=8.0 Hz, *J*=6.5 Hz, H3), 3.94-3.80 (1H, m, THP $CH_2O$), 3.58-3.47 (1H, m, THP $CH_2O$), 1.97-1.45 (7H, m, H2+THP $CH_2$), 0.99 (3H, d, *J*=6.5 Hz, $CH_3$), 0.94 (3H, d, *J*=6.5 Hz, H1) **B:** 5.98 (1H, t, *J*=1.4 Hz, H4), 4.66 (1H, t, *J*=3.6 Hz, THP CHO), 4.33 (1H, ddd, *J*=13.7 Hz, *J*=3.9 Hz, *J*=1.4 Hz, H6), 4.21 (1H, ddd, *J*=13.7 Hz, *J*=8.2 Hz, *J*=1.4 Hz, H6), 4.12 (1H, dd, *J*=8.0 Hz, *J*=6.5 Hz, H3), 3.94-3.80 (1H, m, THP $CH_2O$), 3.58-3.47 (1H, m, THP $CH_2O$), 1.97-1.45 (7H, m, H2+THP $CH_2$), 0.99 (3H, d, *J*=6.5 Hz, $CH_3$), 0.94 (3H, d, *J*=6.5 Hz, H1); **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ **A:** 137.4, 105.7, 97.2, 80.2, 74.4, 62.2, 33.6, 30.3, 25.3, 19.1, 18.3, 17.9 **B:** 137.2, 105.5, 97.1, 80.2, 74.4, 62.1, 33.6, 30.3, 25.3, 19.0, 18.3, 17.8; **IR** ($CHCl_3$) $\nu_{max}$ 3605 (m), 2960 (s) $cm^{-1}$; **LRMS** 323 ($M^+$-OH, 1), 305 (1), 255 (1), 237 (1), 221 (6), 195 (3), 167 (1), 141 (1), 127 (1), 111 (4), 101 (11), 94 (3), 85 (100), 67 (9), 55 (6).

**(*Z*)-2-iodo-5-methylhex-2-en-1,4-diol (21)**. Dowex 50 (0.20 g) was added to a solution of (*Z*)-5-iodo-2-methyl-6-(tetrahydropyran-2-yloxy)hex-4-en-3-ol **20** (0.40 g, 1.56 mmol) in MeOH (15 ml). The reaction mixture was stirred at room temperature for 1 h, the resin filtered off and the solvent removed. The crude product was purified by column chromatography on silica gel (PE/$Et_2O$ 6:4) to afford the product as a white crystalline substance in quantitative yield. **$^1$H NMR** (300 MHz, $CDCl_3$) δ 5.99 (1H, dt, *J*=8.1 Hz, *J*=1.4 Hz, H3), 4.26 (2H, bs, H1), 4.11 (1H, dd, *J*=8.1 Hz, *J*=6.6 Hz, H4), 2.70 (1H, bs, OH), 2.21 (1H, bs, OH), 1.92-1.76 (1H, m, H5), 0.99 (3H, d, J=6.6 Hz, $CH_3$), 0.94 (3H, *J*=6.6 Hz, H6).

**(*Z*)- 4-acetoxy-2-iodo-5-methyl-1-(tetrahydropyran-2-yloxy)hex-2-en (26)**. Acetanhydride (0.48 ml, 5.08 mmol), $Et_3N$ (0.7 ml, 5.02 mmol) and a catalytic amount of DMAP were added to a solution of (*Z*)-5-iodo-2-methyl-6-(tetrahydropyran-2-yloxy)hex-4-en-3-ol **20** (0.57g,

1.68 mmol) in $CH_2Cl_2$ (15 ml), and the reaction mixture was maintained at room temperature for 6 hrs. The mixture was then diluted with $Et_2O$ and washed with 5% HCl and 5% $NaHCO_3$ (2x). The organic phase was dried over anhydrous $Na_2SO_4$ and the solvent removed. The crude product was purified by column chromatography on silica gel (PE/$Et_2O$ 9:1) to afford the product as a colorless oil in 90% yield; **$^1$H NMR** (300 MHz, $CDCl_3$) δ **A:** 6.00-5.93 (1H, m, H3), 5.29 (1H, dd, J=6.4 Hz, *J*=2.8 Hz, H4), 4.65 (1H, t overlaped, *J*=3.7 Hz, THP CHO), 4.32 (1H, m, H1), 4.20 (1H, m, H1), 3.92-3.79 (1H, m, THP $CH_2O$), 3.57-3.45 (1H, m, THP $CH_2O$), 2.05 (3H, s, $COCH_3$), 2.14-1.43 (7H, m, H5+THP $CH_2$), 0.95 (6H, d, *J*=6.4 Hz, H6+$CH_3$) **B:** 6.00-5.93 (1H, m, H3), 5.27 (1H, dd, J=6.4 Hz, *J*=2.7 Hz, H4), 4.64 (1H, t overlaped, *J*=3.7 Hz, THP CHO), 4.32 (1H, dt, *J*=13.7 Hz, *J*=1.5 Hz, H1), 4.20 (1H, ddd, *J*=13.7 Hz, *J*=4.4 Hz, *J*=1.5 Hz, H1), 3.92-3.79 (1H, m, THP $CH_2O$), 3.57-3.45 (1H, m, THP $CH_2O$), 2.05 (3H, s, $COCH_3$), 2.14-1.43 (7H, m, H5+THP $CH_2$), 0.95 (6H, d, *J*=6.4 Hz, H6+$CH_3$).

**Carbonylation of vinyl iodides 20, 21 and 26**. The procedure was the same as for the preparation of **5** except that all reactions were terminated after 24 hrs.

**3-Hydroxymethyl-5-*i*-propyl-2,5-dihydrofuran-2-one** (**22**). **$^1$H NMR** (300 MHz, $CDCl_3$) δ 7.29 (1H, q, *J*=1.7 Hz, H4), 4.81-4.75 (1H, m, H5), 4.44 (2H, t, *J*=1.7 Hz, $CH_2O$), 2.08-1.91 (1H, m, *i*-Pr), 1.01 (3H, d, *J*= 6.9 Hz, *i*-Pr), 0.98 (3H, d, *J*= 6.9 Hz, *i*-Pr); **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ 172.7, 147.8, 134.1, 86.7, 57.2, 31.8, 17.9, 17.7; **IR** ($CHCl_3$) $\nu_{max}$ 3615 (w), 2928 (m), 1750 (s) $cm^{-1}$; **LRMS** 157 ($M^+$+H, 4), 149 (1), 139 (3), 131 (1), 125 (1), 114 (6), 109 (2), 96 (100), 85 (3), 81 (4), 68 (36), 55 (8).

**5-*i*-Propyl-3-(tetrahydropyran-2-yloxymethyl)- 2,5-dihydrofuran-2-one** (**23**). **$^1$H NMR** (300 MHz, $CDCl_3$) δ **A:** 7.30 (1H, q, *J*=1.9 Hz, H4), 4.78-4.73 (1H, m, H5), 4.69-4.64 (1H, m, CHO THP), 4.55-4.52 (1H, m, $CH_2O$), 4.27-4.23 (1H, m, $CH_2O$), 3.91-3.80 (1H, m, $CH_2O$ THP), 3.57-3.47 (1H, m, $CH_2O$ THP), 2.07-1.90 (1H, m, *i*-Pr), 1.90-1.46 (6H, $CH_2$ THP), 1.00 (3H, d, *J*=6.9 Hz, *i*-Pr), 0.98 (3H, d, *J*=6.9 Hz, *i*-Pr) **B:** 7.30 (1H, q, *J*=1.9 Hz, H4), 4.78-4.73 (1H, m, H5), 4.69-4.64 (1H, m, CHO THP), 4.50-4.47 (1H, m, $CH_2O$), 4.22-4.18 (1H, m, $CH_2O$), 3.91-3.80 (1H, m, $CH_2O$ THP), 3.57-3.47 (1H, m, $CH_2O$ THP), 2.07-1.90 (1H, m, *i*-Pr), 1.90-1.46 (6H, $CH_2$ THP), 1.00 (3H, d, *J*=6.9 Hz, *i*-Pr), 0.98 (3H, d, *J*=6.9 Hz, *i*-Pr).

**(*Z*)-methyl-4-acetoxy-5-methyl-2-(tetrahydropyran-2-yloxymethyl)hex-2-enoate (27)**. **$^{1}$H NMR** (300 MHz, $CDCl_3$) δ **A:** 6.07-6.04 (1H, m, H3), 5.91-5.82 (1H, m, H4), 4.66-4.58 (1H, m, THP CHO), 4.49-4.30 (1H, m, $CH_2O$), 4.24-4.07 (1H, m, $CH_2O$), 3.87-3.71 (1H, m, THP $CH_2O$), 3.75 (3H, s, $CH_3O$), 3.54-3.42 (1H, m, THP $CH_2O$), 2.02 (3H, s, $COCH_3$), 2.05-1.95 (1H, m, H5), 1.87-1.42 (6H, m, THP $CH_2$), 0.93 (6H, d, *J*=6.9 Hz, H6+$CH_3$) **B:** 6.04-6.01 (1H, m, H3), 5.91-5.82 (1H, m, H4), 4.66-4.58 (1H, m, THP CHO), 4.49-4.30 (1H, m, $CH_2O$), 4.24-4.07 (1H, m, $CH_2O$), 3.87-3.71 (1H, m, THP $CH_2O$), 3.75 (3H, s, $CH_3O$), 3.54-3.42 (1H, m, THP $CH_2O$), 2.02 (3H, s, $COCH_3$), 2.05-1.95 (1H, m, H5), 1.87-1.42 (6H, m, THP $CH_2$), 0.93 (6H, d, *J*=6.9 Hz, H6+$CH_3$); **$^{13}$C NMR** (75 MHz, $CDCl_3$) δ **A:** 170.4, 166.1, 139.6, 131.2, 98.3, 75.3, 67.0, 62.1, 51.7, 32.4, 30.4, 25.3, 21.1, 19.3, 18.5, 17.5 **B:** 174.4, 166.1, 139.6, 131.1, 97.5, 75.2, 66.6, 62.0, 51.7, 32.3, 30.3, 25.3 21.1, 19.2 18.5, 17.5; **IR** ($CHCl_3$) $\nu_{max}$ 2965 (s), 1724 (s) $cm^{-1}$.

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