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Supporting Information

Pd-Cu Bimetallic Catalyzed Domino Cyclization of a -Allenols–Coupling Reactions. New Sequence Leading to Functionalized Spirolactams

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Indium promoted reaction between 1-bromo-2-butyne and *N*-methylisatin 1a. Synthesis of a-Allenic Alcohol 2a. 1-Bromo-2-butyne (199 mg, 1.5 mmol) was added to a well stirred suspension of the 2,3-indolinedione **1a** (81 mg, 0.50 mmol) and indium powder (344 mg, 3.0 mmol) in THF/H_2O (1:1, 5 mL) at 5 °C. After 1 h, saturated aqueous sodium hydrogen carbonate (2.5 mL) was added at 0 °C, and the mixture was allowed to warm to room temperature, before being extracted with ethyl acetate (3 x 3 mL). The organic extract was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue eluting with ethyl acetate/dichloromethane (1:40) gave 97 mg (90%) of compound **2a**. **3-Hydroxy-1-methyl-3-(1-methyl-propa-1,2-dienyl)-1,3-dihydro-indol-2-one, 2a.** Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 7.37 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.35 and 7.10 (td, *J* = 7.5, 1.0 Hz, each 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 5.04 (q, *J* = 3.1 Hz, 2H), 3.21 (s, 3H), 1.55 (t, *J* = 3.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 204.8, 176.7, 143.8, 129.9, 129.1, 124.5, 123.2, 108.4, 100.7, 80.3, 26.3, 13.7; IR ($CHCl_3$): ν = 3298, 1954, 1715 cm^{-1}; MS (EI): *m/z* (%): 216 (9) $[M + H]^+$, 215 (100) $[M]^+$; elemental analysis calcd (%) for $C_{13}H_{13}NO_2$ (215.3): C 72.54, H 6.09, N 6.51; found C 72.66, H 6.05, N 6.45.

Indium promoted reaction between 3-substituted prop-2-ynyl bromides and azetidine-2,3-diones (–)-1b and (+)-1c; general procedure for the synthesis of a-allenic alcohols 2b–d. 1-Bromo-2-butyne or 1-bromo-3-phenyl-2-propyne (3.0 mmol) was added to a well stirred suspension of the corresponding azetidine-2,3-dione **1** (1.0 mmol) and indium powder (6.0 mmol) in THF/NH_4Cl (aq. sat.) (1:5, 5 mL) at 0 °C. After disappearance of the starting

material (TLC) the mixture was extracted with ethyl acetate (3 x 5 mL). The organic extract was washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue using ethyl acetate/hexanes or dichloromethane/ethyl acetate mixtures gave analytically pure compounds **2**. Spectroscopic and analytical data for some representative pure forms of **2** follow.

(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-hydroxy-1-benzyl-3-(1-methyl-propa-1,2-dienyl)-azetidin-2-one, (–)-2b. From 210 mg (0.766 mmol) of azetidine-2,3-dione (–)-**1b**, 236 mg (94%) of compound (–)-**2b** was obtained as a colorless oil; $[\alpha]_D$ = –16.9 (*c* = 0.7 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 ^{o}C): δ = 7.30 (m, 5H), 4.87 (d, *J* = 14.6 Hz, 1H), 4.79 (m, 2H), 4.64 (br s, 1H), 4.41 (m, 1H), 4.18 (d, *J* = 14.4 Hz, 1H), 4.16 (m, 1H), 3.71 (dd, *J* = 9.0, 5.4 Hz, 1H), 3.52 (d, *J* = 8.0 Hz, 1H), 1.73 (t, *J* = 3.2 Hz, 3H), 1.36 and 1.35 (s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 ^{o}C): δ = 205.1, 169.5, 135.4, 128.8, 128.5, 127.8, 109.8, 98.0, 84.3, 76.4, 64.7, 64.6, 45.6, 26.6, 25.1, 14.0; IR ($CHCl_3$): ν = 3342, 2990, 1941, 1744 cm^{-1}; MS (ES): *m/z* (%): 330 (100) $[M + H]^+$, 329 (9) $[M]^+$; elemental analysis calcd (%) for $C_{19}H_{23}NO_4$ (329.4): C 69.28, H 7.04, N 4.25; found C 69.40, H 7.00, N 4.23.

(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-hydroxy-1-benzyl-3-(1-phenyl-propa-1,2-dienyl)-azetidin-2-one, (–)-2c. From 200 mg (0.727 mmol) of azetidine-2,3-dione (–)-**1b**, 280 mg (98%) of compound (–)-**2c** was obtained as a colorless oil; $[\alpha]_D$ = –28.5 (*c* = 0.8 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 ^{o}C): δ = 7.58 (dd, *J* = 7.7, 1.8 Hz, 2H), 7.31 (m, 6H), 7.14 (m, 2H), 5.18 (d, *J* = 12.4 Hz, 1H), 5.09 (d, *J* = 12.4 Hz, 1H), 4.92 (d, *J* =

14.9 Hz, 1H), 4.48 (dd, 1H, *J* = 6.6, 5.4 Hz), 4.16 (d, 1H, *J* = 14.9 Hz), 4.14 (dd, *J* = 8.9, 6.9 Hz, 1H), 3.89 (br s, 1H), 3.68 (d, *J* = 6.3 Hz, 1H), 3.64 (dd, *J* = 8.9, 5.3 Hz, 1H), 1.38 and 1.35 (s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 ^{o}C): δ = 207.2, 168.6, 135.2, 132.6, 128.7, 128.6, 128.5, 128.4, 127.7, 127.6, 110.0, 85.0, 80.5, 75.7, 66.6, 64.2, 44.9, 26.4, 25.0; IR ($CHCl_3$): ν = 3344, 2992, 1940, 1743 cm^{-1}; MS (ES): *m/z* (%): 392 (100) $[M + H]^+$, 391 (16) $[M]^+$; elemental analysis calcd (%) for $C_{24}H_{25}NO_4$ (391.5): C 73.64, H 6.44, N 3.58; found C 73.51, H 6.48, N 3.60.

(3*R*,4*S*)-4-[(*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-hydroxy-1-(4-methoxyphenyl)-3-(1-methyl-propa-1,2-dienyl)-azetidin-2-one, (+)-2d. From 50.5 mg (0.173 mmol) of azetidine-2,3-dione (+)-**1c**, 44 mg (74%) of compound (+)-**2d** was obtained as a colorless oil; $[\alpha]_D$ = +75.4 (*c* = 0.7 in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 25 ^{o}C): δ = 7.63 and 6.86 (dd, *J* = 7.0, 2.5 Hz, each 2H), 4.98 (dd, *J* = 6.4, 3.0 Hz, 2H), 4.49 (q, *J* = 7.0 Hz, 1H), 4.32 (dd, *J* = 8.8, 6.8 Hz, 1H), 4.24 (d, *J* = 7.7 Hz, 1H), 4.14 (brs, 1H), 3.80 (dd, *J* = 8.8, 6.4 Hz, 1H), 3.79 (s, 3H), 1.85 (t, *J* = 3.0 Hz, 3H), 1.51 and 1.36 (s, each 3H),; ^{13}C NMR (75 MHz, $CDCl_3$, 25 ^{o}C): δ = 205.2, 166.6, 156.7, 130.7, 120.0, 114.0, 109.7, 98.6, 83.5, 79.4, 76.8, 66.8, 66.5, 55.4, 26.6, 25.0, 13.9; IR ($CHCl_3$): ν = 3340, 2991, 1940, 1742 cm^{-1}; MS (ES): *m/z* (%): 346 (100) $[M + H]^+$, 345 (20) $[M]^+$; elemental analysis calcd (%) for $C_{19}H_{23}NO_5$ (345.4): C 66.07, H 6.71, N 4.06; found C 66.13, H 6.65, N 4.00.

Procedure for the metal-catalyzed oxybromination of the α-allenol 2a; preparation of spiranic bromodihydrofuran 8. Palladium(II) acetate (0.012 mmol), lithium bromide (0.656 mmol), potassium carbonate (0.16 mmol) and copper(II) acetate

(0.28 mmol) were sequentially added to a stirred solution of the α-allenol **2a** (29 mg, 0.134 mmol) in acetonitrile (7 mL). The resulting suspension was stirred at room temperature under an oxygen atmosphere for 20 h at room temperature. The organic phase was diluted with brine (2 mL), extracted with ethyl acetate (3 x 5 mL), washed with brine (2 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with dichloromethane/ethyl acetate (10:1) gave 20 mg (52%) of analytically pure compound **8**. Colorless solid; m. p. 230–231 ^oC; ^1H NMR (300 MHz, $CDCl_3$, 25 ^oC): δ = 7.54 (d, *J* = 15.9 Hz, 1H), 7.36 (td, *J* = 7.7, 1.5 Hz, 1H), 7.24 (ddd, *J* = 7.3, 1.5, 0.5 Hz, 1H), 7.10 (td, *J* = 7.4, 1.0 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 5.15 and 5.05 (dq, *J* =11.5, 2.0 Hz, each 1H), 3.22 (s, 3H), 1.41 (t, *J* = 2.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 ^oC): δ = 175.3, 144.1, 133.3, 130.4, 129.3, 128.1, 124.5, 123.3, 108.4, 93.7, 77.2, 26.3, 10.8; IR ($CHCl_3$): ν = 1722 cm^{-1}; MS (ES): *m/z* (%): 296 (98) $[M + 2 + H]^+$, 294 (100) $[M + H]^+$; elemental analysis calcd (%) for $C_{13}H_{12}BrNO_2$ (294.1): C 53.08, H 4.11, N 4.76; found C 53.21, H 4.07, N 4.80.

Procedure for the metal-catalyzed domino cyclization of α-allenols–cross coupling reactions in the absence of LiBr. Palladium(II) acetate (0.009 mmol), triphenylphosphine (0.02 mmol), potassium carbonate (0.70 mmol), copper(II) acetate (0.21 mmol), and methyl acrylate (0.12 mmol) were sequentially added to a stirred solution of the corresponding α-allenic alcohol **2** (0.10 mmol) in acetonitrile (5 mL). The resulting suspension was stirred at room temperature under an oxygen atmosphere until disappearance (TLC) of the starting material. The organic phase was diluted with brine(2 mL), extracted with ethyl acetate (5 x

5 mL), washed with brine (2 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure spirolactams **3**.

Procedure for the metal-catalyzed domino cyclization of a-allenols–cross coupling reactions on replacing LiBr for LiI. Palladium(II) acetate (0.009 mmol), triphenylphosphine (0.02 mmol), lithium iodide (0.49 mmol), potassium carbonate (0.70 mmol), copper(II) acetate (0.21 mmol), and methyl acrylate (0.12 mmol) were sequentially added to a stirred solution of the corresponding α-allenic alcohol **2** (0.10 mmol) in acetonitrile (5 mL). The resulting suspension was stirred at room temperature under an oxygen atmosphere until disappearance (TLC) of the starting material. The organic phase was diluted with brine (2 mL), extracted with ethyl acetate (5 x 5 mL), washed with brine (2 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure spirolactams **3**.

Procedure for the metal-catalyzed domino cyclization of a-allenols–cross coupling reactions on replacing LiBr for LiF. Palladium(II) acetate (0.009 mmol), triphenylphosphine (0.02 mmol), lithium fluoride (0.49 mmol), potassium carbonate (0.70 mmol), copper(II) acetate (0.21 mmol), and methyl acrylate (0.12 mmol) were sequentially added to a stirred solution of the corresponding α-allenic alcohol **2** (0.10 mmol) in acetonitrile (5 mL). The resulting suspension was stirred at room temperature under an oxygen atmosphere until disappearance (TLC) of the starting material. The organic phase was diluted with brine (2 mL), extracted with ethyl acetate (5 x 5 mL), washed with brine

(2 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure spirolactams **3**.

Procedure for the metal-catalyzed domino cyclization of α-allenols–cross coupling reactions on replacing $Pd(OAc)_2$ for $PdCl_2$. Palladium(II) chloride (0.009 mmol), triphenylphosphine (0.02 mmol), lithium bromide (0.49 mmol), potassium carbonate (0.70 mmol), copper(II) acetate (0.21 mmol), and methyl acrylate (0.12 mmol) were sequentially added to a stirred solution of the corresponding α-allenic alcohol **2** (0.10 mmol) in acetonitrile (5 mL). The resulting suspension was stirred at room temperature under an oxygen atmosphere until disappearance (TLC) of the starting material. The organic phase was diluted with brine (2 mL), extracted with ethyl acetate (5 x 5 mL), washed with brine (2 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure spirolactams **3**.

Procedure for the metal-catalyzed domino cyclization of α-allenols–cross coupling reactions in the absence of $Cu(OAc)_2$ and O_2. Palladium(II) acetate (0.009 mmol), triphenylphosphine (0.02 mmol), lithium bromide (0.49 mmol), potassium carbonate (0.70 mmol), and methyl acrylate (0.12 mmol) were sequentially added to a stirred solution of the corresponding α-allenic alcohol **2** (0.10 mmol) in acetonitrile (5 mL). The resulting suspension was stirred at room temperature under an argon atmosphere until disappearance (TLC) of the starting material. The organic phase was diluted with brine (2 mL), extracted with ethyl acetate (5 x 5 mL), washed with brine (2 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography

of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure spirolactams **3** together with dihydrofuran **9**.

Procedure for the metal-catalyzed domino cyclization of α-allenols–cross coupling reactions in the absence of LiBr, $Cu(OAc)_2$ and O_2. Palladium(II) acetate (0.009 mmol), triphenylphosphine (0.02 mmol), potassium carbonate (0.70 mmol), and methyl acrylate (0.12 mmol) were sequentially added to a stirred solution of the corresponding α-allenic alcohol **2** (0.10 mmol) in acetonitrile (5 mL). The resulting suspension was stirred at room temperature under an argon atmosphere until disappearance (TLC) of the starting material. The organic phase was diluted with brine (2 mL), extracted with ethyl acetate (5 x 5 mL), washed with brine (2 mL), dried ($MgSO_4$) and concentrated under reduced pressure. Chromatography of the residue eluting with hexanes/ethyl acetate mixtures gave analytically pure spirolactams **3** together with dihydrofuran **9**.

Spirodihydrofuran 9. Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$, 25 ^{o}C): δ = 7.32 (td, *J* = 7.6, 1.5 Hz, 1H), 7.20 (ddd, *J* = 7.3, 1.5, 0.5 Hz, 1H), 7.07 (td, *J* = 7.4, 1.0 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 1H), 5.96 (m, *J* = 1.6 Hz, 1H), 5.02 and 4.90 (dq, *J* =12.5, 2.0 Hz, each 1H), 3.20 (s, 3H), 1.43 (t, *J* = 2.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 ^{o}C): δ = 176.1, 144.4, 136.2, 130.5, 128.7, 125.3, 124.9, 123.6, 108.7, 92.9, 76.8, 26.7, 11.6; IR ($CHCl_3$): ν = 1724 cm^{-1}; MS (ES): *m/z* (%): 230 (100) $[M + 1]^+$, 229 (14) $[M]^+$; elemental analysis calcd (%) for $C_{14}H_{15}NO_2$ (229.3): C 73.34, H 6.59, N 6.11; found C 73.47, H 6.56, N 6.09.