Supporting Information for:

Palladium Promoted Cascade Reaction of Isonitriles: Synthesis of Polycyclic Quinolines

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Experimental procedure, analytical data and NMR spectra for polycyclic quinolines reported in this paper.

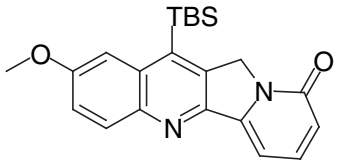
General: Toluene, THF were freshly distilled from Na/benzophenone. Reagents were used as they were received from Aldrich. Isonitriles 4 were prepared according to reported procedure. Iodopyridone **5a**-**5d** were prepared according to reported procedure. Iodopyridone **5e** was prepared by known procedure. Compound **11** was prepared by propargylation of compound **15** whose synthesis will be reported later. ^{1}H and ^{13}C spectra were taken on an IBM model AF-300 (300 Hz) or an IBM Model AM-500 (500 MHz) NMR spectrometer. Chemical shifts are reported in ppm. $CDCl_3$ was used as NMR solvent unless otherwise noted. In reporting spectral data, the following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet doublet. Coupling constants are reported in Hertz (Hz). Infrared spectra were taken on a Mattson genesis Series FTIR using thin film deposition on NaCl plate unless otherwise noted. Peaks were reported in wavenumbers (cm^{-1}). High resolution mass spectra were obtained on a VG 70/70 double focusing machine and were reported in units of m/e.

General procedure for Pd promoted synthesis of polycyclic quinoline:

Iodopyridone **5** (0.027 mmol), Ag_2CO_3 (0.04 mmol, 1.5 eqiv) and $Pd(OAc)_2$ (0.005 mmol, 20%) were suspended in 0.5 mL of toluene. Then to this suspension was slowly added a solution of isonitrile **4** (0.05 mmol, 2 equiv) in toluene (1 mL) in 0.5 h. This reaction mixture was stirred at room temperature for 20 h and then filtered though celite. Solvent was removed, and the residue was mixed with $Pd(OAc)_2$ (0.0025 mmol, 10%)

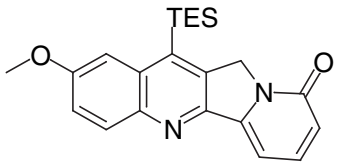
and Ag_2CO_3 (0.02 mmol, 0.7 equiv) in 0.5 mL of toluene. Then a solution of isonitrile **4** (0.025 mmol, 1 equiv) in 0.5 mL of toluene was added. The mixture was stirred at room temperature for another 20 h. TLC showed that **5** disappeared. The reaction mixture was then filtered though celite, the filtrate was concentrated to give a crude product. Purification by chromatography on silica gel gave product **6** as yellow solid in 40-90% yield.

12-(*tert*-Butyl-dimethyl-silanyl)-2-methoxy-11*H*-indolizino[1,2-*b*]quinolin-9-one (6a)



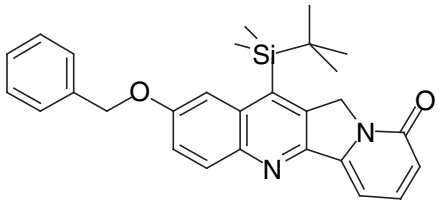
Using the general procedure, the title compound was prepared in 82% yield as yellow solid: IR 2933, 2861, 1671, 1599, 1537, 1507, 1326, 1244, 1208, 1167, 1033, 847, 832, 801; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.72 (s, 6H), 1.02 (s, 9H), 3.98 (s, 3H), 5.29 (s, 2H), 6.70 (d, *J* = 9.2 Hz, 1H), 7.24 (d, *J* = 7.0 Hz, 1H), 7.43 (dd, *J* = 9.2, 2.6 Hz, 1H), 7.54 (d, *J* = 2.6 Hz, 1H), 7.67 (dd, *J* = 9.2, 7.0 Hz, 1H), 8.15 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ –0.7, 19.6, 27.2, 52.3, 55.5, 100.0, 108.1, 119.5, 122.3, 131.7, 134.0, 136.7, 140.5, 143.8, 146.3, 149.0, 157.8, 161.4; HRMS (EI) *m/z* calcd for $C_{22}H_{26}N_2O_2Si$ 378.1764, found 378.1772, LRMS (EI) *m/z* 378 (M^+), 321, 307, 278.

2-Methoxy-12-(triethyl-silanyl)-11*H*-indolizino[1,2-*b*]quinolin-9-one (6b)



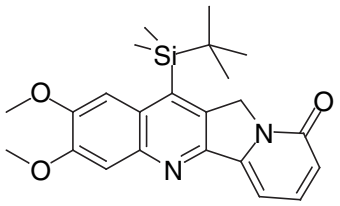
Using the general procedure, the title compound was prepared in 66% yield as yellow solid: IR 2945, 1665, 1598, 1535, 1244, 1213, 1124, 1031, 844, 807, 734; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.01 (t, *J* = 7.6 Hz, 9 H), 1.19 (q, *J* = 7.6 Hz, 6H), 3.99 (s, 3H), 5.29 (s, 2H), 6.70 (d, *J* = 8.7 Hz, 1H), 7.24 (d, *J* = 7.0 Hz, 1H), 7.45 (dd, *J* = 9.2, 1.9 Hz, 1H), 7.54 (s, 1H), 7.67 (t, *J* = 8.0 Hz, 1H), 8.12 (d, *J* = 9.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 4.9, 7.7, 52.1, 55.7, 100.0, 106.6, 119.6, 122.1, 132.2, 133.9, 136.7, 139.8, 140.6, 143.9, 146.6, 149.4, 158.2, 161.6; HRMS (EI) *m/z* calcd for $C_{22}H_{26}N_2O_2Si$ 378.1764, found 378.1762; LRMS (EI) *m/z* 378 (M^+), 351, 321, 293, 275, 231, 215, 149.

2-Benzyloxy-12-(*tert*-Butyl-dimethyl-silanyl)-11*H*-indolizino[1,2-*b*]quinolin-9-one (6c)



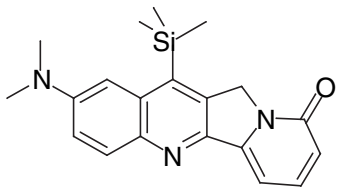
Using the general procedure, the title compound was prepared in 92% yield as yellow solid: IR 2934, 2861, 1667, 1600, 1538, 1504, 1465, 1325, 1241, 1202, 1137, 1028, 837, 809, 736, 703; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.64 (s, 6H), 0.95 (s, 9H), 5.23 (s, 2H), 5.27 (s, 2H), 6.69 (d, *J* = 9.4 Hz, 1H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.3-7.6 (m, 7H), 7.67 (dd, *J* = 9.1, 7.0 Hz, 1H), 8.12 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ –0.79, 19.4, 27.2, 52.4, 70.3, 99.9, 109.3, 119.5, 122.6, 127.2, 128.3, 128.8, 131.9, 134.0, 136.1, 136.7, 140.4, 144.1, 146.4, 149.3, 157.1, 161.4; HRMS (EI) *m/z* calcd for $C_{28}H_{30}N_2O_2Si$ 454.2077, found 454.2088; LRMS (EI) *m/z* 454 (M^+), 397, 363, 307, 277, 91.

12-(*tert*-Butyl-dimethyl-silanyl)-2,3-dimethoxy-11*H*-indolizino[1,2-*b*]quinolin-9-one (6d)



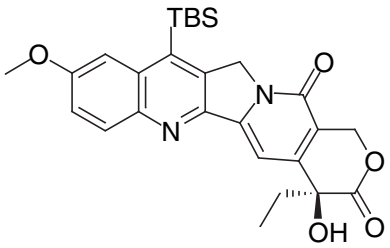
Using the general procedure, the title compound was prepared in 83% yield as yellow solid: IR 2957, 2930, 2860, 1667, 1598, 1507, 1475, 1432, 1330, 1250, 1164, 1014, 907, 849, 730; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.71 (s, 6H), 1.01 (s, 9H), 4.05 (s, 3H), 4.08 (s, 3H), 5.26 (s, 2H), 6.69 (d, *J* = 9.2 Hz, 1H), 7.22 (d, *J* = 6.7 Hz, 1H), 7.51 (s, 2H), 7.66 (dd, *J* = 8.9, 7.1 Hz, 1H), 8.12 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ –0.78, 19.6, 27.15, 27.23. 52.4, 56.0, 56.2, 99.7, 107.8, 108.3, 119.3, 129.0, 134.7, 140.4, 145.3, 146.5, 149.0, 149.7, 152.2, 161.4; HRMS (EI) *m/z* calcd for $C_{23}H_{28}N_2O_3Si$ 408.1869, found 408.1870; LRMS (EI) *m/z* 408 (M^+), 351, 335, 307, 149, 84.

2-Dimethylamino-12-(trimethyl-silanyl)-11*H*-indolizino[1,2-*b*]quinolin-9-one (6e)



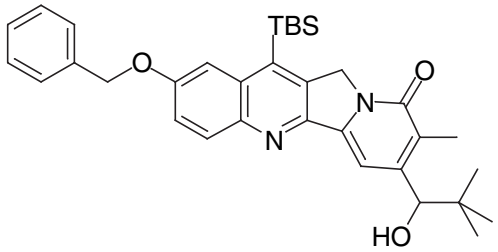
Using the general procedure, the title compound was prepared in 67% yield as yellow solid: IR 1661, 1588, 1540, 1340, 1250, 1171, 821, 797; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.63 (s, 9H), 3.15 (s, 6H), 5.24 (s, 2H), 6.64 (d, *J* = 8.9 Hz, 1H), 7.15 (s, 1H), 7.16 (d, *J* = 6 Hz, 1H), 7.40 (dd, *J* = 9.3, 2.2 Hz, 1H), 7.63 (dd, *J* = 8.6, 7.9 Hz, 1H), 8.03 (d, *J* = 9.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 1.2, 40.6, 51.8, 99.2, 106.1, 118.7, 119.0, 131.3, 133.6, 135.3, 139.2, 140.4, 141.6, 146.9, 147.3, 148.5, 161.6; HRMS (EI) *m/z* calcd for $C_{20}H_{23}N_3OSi$ 349.1610, found 349.1605; LRMS (EI) *m/z* 349 (M^+), 334, 305, 290.

7-tert-Butyldimethylsilyl-10-methoxy-camptothecin (6h)



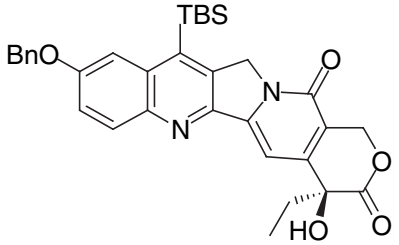
Using the general procedure, the title compound was prepared in 53% yield as yellow solid: IR 3309, 2928, 2862, 1752, 1664, 1603, 1559, 1509, 1465, 1239, 1162, 1051, 845, 836; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.72 (s, 6H), 1.02 (s, 9H), 1.05 (t, J = 7.4 Hz, 3H), 1.90 (m, 2H), 3.98 (s, 3H), 5.29 (s, 2H), 5.31 (d, J = 16.2 Hz, 1H), 5.76 (d, J = 16.2 Hz, 1H), 7.45 (dd, J = 9.3, 2.7 Hz, 1H), 7.53 (d, J = 2.6 Hz, 1H), 7.61 (s, 1H), 8.12 (d, J = 9.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ -0.66, 7.9, 19.7, 27.3, 31.7, 52.5, 55.7, 66.5, 72.9, 97.0, 108.2, 117.6, 122.5, 132.1, 134.3, 136.7, 140.6, 144.3, 146.9, 148.7, 150.3, 157.6, 158.2, 174.2; HRMS (EI) *m/z* calcd for $C_{27}H_{32}N_2O_5Si$ 492.2081, found 492.2073; LRMS (EI) *m/z* 492 (M^+), 448, 435, 391, 323, 261, 211, 165.

2-Benzyloxy-12-(*tert*-butyl-dimethyl-silanyl)-7-(1-hydroxy-2,2-dimethyl-propyl)-8-methyl-11*H*-indolizino[1,2-*b*]quinolin-9-one (6i)



Using the general procedure, the title compound was prepared in 62% yield as yellow solid: IR 3351, 2955, 2865, 1656, 1627, 1582, 1509, 1463, 1294, 1226, 1017, 836, 808, 734; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.70 (s, 3H), 0.75 (s, 3H), 0.87 (s, 9H), 1.00 (s, 9H), 2.13 (s, 3H), 4.23 (br s, 1H), 4.71 (s, 1H), 5.00 (d, J = 18.8 Hz, 1H), 5.08 (s, 2H), 5.29 (d, J = 18.9 Hz, 1H), 7.22-7.44 (m, 8 H), 7.72 (d, J = 8.9 Hz, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ -0.87, -0.25, 14.1, 19.5, 26.4, 27.1, 36.9, 52.4, 70.2, 76.1, 100.6, 108.6, 121.7, 126.0, 127.4, 128.3, 128.8, 131.4, 133.3, 136.2, 136.5, 139.7, 141.1, 143.3, 148.9, 152.7, 156.5, 161.2; HRMS (EI) *m/z* calcd for $C_{34}H_{42}N_2O_5Si$ 554.2965, found 554.2980; LRMS (EI) *m/z* 554 (M^+), 536, 498, 463, 407, 350, 293, 91.

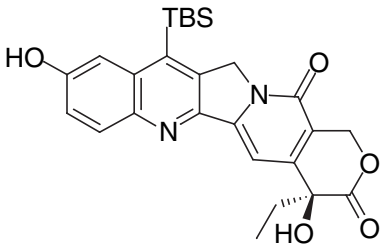
7-*tert*-Butyldimethylsilyl-10-phenylmethoxy-camptothecin (12)



Using the general procedure, the title compound was prepared in 70% yield.

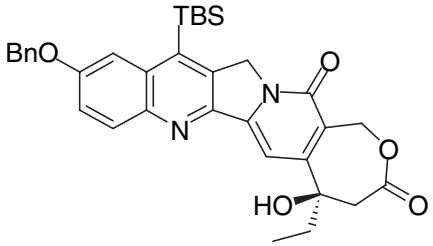
IR 3395, 2931, 2863, 1751, 1662, 1604, 1509, 1461, 1235, 1161, 1050, 834; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.64 (s, 6H), 0.95 (s, 9H), 1.05 (t, J = 7.4 Hz, 3H), 1.90 (m, 2H), 5.24 (s, 2H), 5.28 (s, 2H), 5.31 (d, J = 16.2 Hz, 1H), 5.76 (d, J = 16.2 Hz, 1H), 7.35-7.56 (m, 7H), 7.61 (s, 1H), 8.14 (d, J = 10.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ -0.82, 7.8, 19.5, 27.1, 31.6, 52.5, 66.4, 70.3, 72.8, 97.1, 109.2, 117.6, 123.0, 127.2, 128.3, 128.8, 132.0, 134.2, 136.0, 136.6, 140.8, 144.2, 146.7, 148.6, 150.2, 157.4, 157.5, 174.1; **HRMS (EI) *m/z* calcd for $C_{26}H_{30}N_2O_5Si$, found; LRMS (EI) *m/z* 478 (M^+), 434, 421, 393, 377, 347, 320, 291.**

7-*tert*-Butyldimethylsilyl-10-hydroxy-camptothecin (3, DB-67)



Compound **12** (11 mg, 0.02 mmol) was dissolved in a mixture of TFA (1 mL) and thioanisole (0.1 mL). The reaction was heated at 55 ˚C for 10 h, then was diluted with EtOAc and washed with saturated $NaHCO_3$ and brine. The ester layer was collected and solvent was removed under reduced pressure. The crude product was purified by flash chromatography (10% acetone in dichloromethane) to give the title compound (6.8 mg) as yellow solid in 75% yield: IR 3373, 2931, 2862, 1751, 1656, 1592, 1557, 1508, 1463, 1235, 1155, 1051, 833; ^{1}H NMR (300 MHz, $CDCl_3$ with a small amount of CD_3OD) δ 0.67 (s, 6H), 0.97 (s, 9H), 1.02 (t, J = 7.4 Hz, 3H), 1.88 (m, 2H), 5.25 (s, 2H), 5.28 (d, J = 16.2 Hz, 1H), 5.71 (d, J = 16.2 Hz, 1H), 7.38 (dd, J = 9.1, 2.1 Hz, 1H), 7.55 (d, J = 2.5 Hz, 1H), 7.61 (s, 1H), 8.05 (d, J = 9.1 Hz, 1H); ^{13}C NMR ($CDCl_3$ with a small amount of CD_3OD, 125 MHz) δ -0.83, 7.8, 19.2, 27.1, 31.5, 52.6, 66.2, 72.9, 97.3, 111.4, 117.5, 122.3, 131.7, 134.6, 136.4, 140.5, 143.2, 146.7, 147.8, 150.8, 156.0, 157.7, 174.0; HRMS (EI) *m/z* calcd for $C_{26}H_{30}N_2O_5Si$ 478.1924, found 478.1924; LRMS (EI) *m/z* 478 (M^+), 434, 421, 393, 377, 347, 320, 291.

7-*tert*-Butyldimethylsilyl-10-phenylmethoxy-homocamptothecin (13)

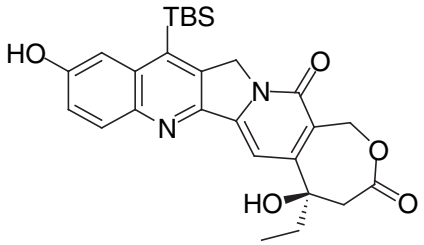


Using the general procedure, the title compound was prepared as yellow solid in 82% yield.

IR 3322, 2931, 2859, 1753, 1655, 1583, 1506, 1270, 1223, 1064, 833; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.71 (s, 6H), 0.95 (m, 12H), 2.02 (m, 2H), 3.34 (d, J = 13.6 Hz, 1H), 3.40 (d, J = 13.6 Hz, 1H), 4.42 (s, 1H), 5.04 (d, J = 19.0 Hz, 1H), 5.18 (s, 2H), 5.37 (d, J = 15.8 Hz, 1H), 5.44 (d, J = 19.0 Hz, 1H), 5.65 (d, J = 15.8 Hz, 1H), 7.24-7.56 (m, 9H); ^{13}C NMR ($CDCl_3$) δ -0.96, -0.51, 8.1, 19.6, 27.1, 35.4, 42.6, 52.9, 62.2, 70.3, 73.6, 99.6,

108.8, 121.9, 122.1, 127.2, 128.3, 128.8, 131.4, 133.8, 136.0, 136.2, 140.4, 143.5, 145.2, 147.7, 156.6, 157.0, 159.8, 171.3; HRMS (EI) *m/z* calcd for $C_{34}H_{38}N_2O_5Si$ 582.2550, found 582.2575; LRMS (EI) *m/z* 582 (M^+), 564, 525, 483, 435, 375.

7-*tert*-Butyldimethylsilyl-10-hydroxy-homocamptothecin (14, DB-91)



Using the procedure similar to compound **3**, the title compound was prepared in 61% yield: IR 3312, 2931, 2859, 1745, 1651, 1585, 1469, 1259, 1226, 1060, 834; ^{1}H NMR (300 MHz, $CDCl_3$ with a small amount of CD_3OD) δ 0.64 (s, 3H), 0.66 (s, 3H), 0.95 (m, 12H), 1.97 (m, 2H), 3.21 (d, J = 13.6 Hz, 1H), 3.38 (d, J = 13.6 Hz, 1H), 5.09 (d, J = 19.0 Hz, 1H), 5.22 (d, J = 19.0 Hz, 1H), 5.36 (d, J = 15.3 Hz, 1H), 5.61 (J = 15.3 Hz, 1H), 7.25 (dd, J = 9.0, 2.3 Hz, 1H), 7.40 9s, 1H0, 7.46 (d, J = 2.0 Hz, 1H), 7.75 (d, J = 9.1 Hz, 1H); ^{13}C NMR ($CDCl_3$ with a small amount of CD_3OD, 125 MHz) δ -0.95, -0.69, 8.2, 19.3, 27.2, 36.1, 42.5, 52.9, 62.3, 73.7, 100.0, 111.4, 121.7, 122.0, 131.1, 134.5, 136.3, 140.7, 142.7, 145.7, 147.4, 155.9, 156.8, 159.9, 172.5; HRMS (EI) *m/z* calcd for $C_{27}H_{32}N_2O_5Si$ 492.2081, found 492.2087; LRMS (EI) *m/z* 492 (M^+), 474, 445, 432, 417, 389, 375, 207, 91.