Supporting Information

A Cycloaddition Protocol for the Assembly of the Hexacyclic Framework Associated with the Kopsifoline Alkaloids

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Experimental Section

3-[3-{2-Benzyloxyethyl}-2-oxo-piperidin-3-yl]-3-oxo-propionic Acid Methyl Ester. To a stirred solution of 8.2 g (48 mmol) of 2-oxopiperidine-3-carboxylic acid ethyl ester in 125 mL of THF at -78 °C was added 20 mL (48 mmol) of a 2.4 M *n*-butyl-lithium solution in hexane. The resulting solution was allowed to warm to 0 °C for 10 min, re-cooled to -78 °C and 12.6 g (48 mmol) of 2-iodoethyl benzyl ether was added. The cooling bath was removed and the solution was heated at reflux for 3 days. The solution was allowed to cool to rt, the solvent was removed under reduced pressure and the residue was subjected to flash silica gel chromatography to give 10.2 g (70%) of 3-(2-benzyloxyethyl)-2-oxo-piperidine-3-carboxylic acid ethyl ester as a colorless oil; IR (neat) 1729, 1669, 1194, 1119 and 1098 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.23 (t, 3H, J = 7.0 Hz), 1.78-1.90 (m, 1H), 1.95 (td, 1H, J = 13.2 and 4.0 Hz), 2.15-2.35 (m, 3H), 3.20-3.35 (m, 2H), 3.64 (td, 1H, J = 6.8 and 2.0 Hz), 4.10-4.23 (m, 2H), 4.46 (s, 2H), 6.03 (brs, 1H) and 7.20-7.73 (m, 5H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.3, 19.8, 30.4, 35.2, 42.5, 53.0, 61.7, 67.3, 73.1, 127.7, 127.8, 128.5, 138.6, 171.0 and 172.8.

To a solution of 23.4 g (77 mmol) of the above ethyl ester in a 1:1 THF/H_2O mixture (300 mL) was added 8.6 g of potassium hydroxide (150 mol) and the mixture was stirred overnight. The solvent was removed under reduced pressure and the residue was taken up in water. The solution was washed with EtOAc and acidified to pH 2. The aqueous layer was extracted with chloroform and the combined organic phase was dried over $MgSO_4$, filtered, and concentrated under reduced pressure to give 19.2 g (91%) of 3-{2-benzyloxyethyl}-2-oxo-piperidine-3-carboxylic acid as a white solid; mp 102-103 °C; IR (neat) 1700, 1653, 1492,1454, 1202 and 1100 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.79-1.92 (m, 2H), 2.03-2.10 (m, 1H), 2.23-2.34 (m, 3H), 3.27-3.36 (m, 2H), 3.59-367 (m, 2H), 4.48 (s, 2H), 6.28 (brs, 1H) and 7.20-7.38 (m, 5H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.2, 27.8, 37.9, 42.9, 50.7, 66.4, 73.4, 127.9, 128.6, 138.2 and 175.5; Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found: C, 64.87; H, 6.74; N, 4.96.

To a solution of 9.0 g (33 mmol) of the above carboxylic acid in 150 mL of CH_2Cl_2 was added 6.3 g (39 mmol) of 1,1'-carbonyldiimidazole. The solution was allowed to stir at rt under N_2 overnight, concentrated under reduced pressure and taken up in 150 mL of THF. A 10.1 g (65 mmol) sample of potassium methyl malonate, 6.2 g (65 mmol) of powdered magnesium chloride and a small amount (0.4 g; 3.2 mmol) of 4-(dimethylamino)pyridine was dissolved in 400 mL of THF and 200 mL of acetonitrile. After stirring for 2 h, the above lactam in THF was added dropwise to the malonate solution together with 9.0 mL (65 mmol) of triethylamine. The solution was allowed to stir at rt overnight and then 200 mL of a 1 *N* HCl solution was added. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 8.9 g (82%) of the titled compound as a colorless solid, mp 57-58 °C; IR (neat) 1749, 1706, 1437, 1319 and 1103 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.53 (pent, 1H, J = 7.2 Hz), 1.66-1.75 (m, 2H), 2.08 (dt, 1H, J = 14.4 and 6.0 Hz), 2.28-2.42 (m, 2H), 3.14-3.21 (m, 2H), 3.37-3.43 (m, 1H), 3.49-3.54 (m, 1H), 3.58 (s, 3H), 3.64 (d, 1H, J = 16.6 Hz), 3.89 (d, 1H, J = 16.6 Hz), 3.35 (s, 2H) and 7.21-7.25 (m, 6H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.3, 27.4, 35.9, 41.9, 45.1, 51.7, 58.0, 65.7, 72.7, 127.2, 127.3, 128.0, 137.7, 167.9, 171.1 and 200.9; Anal. Calcd for $C_{18}H_{23}NO_5$: C, 64.85; H, 6.95; N, 4.20. Found: C, 64.91; H, 7.06; N, 4.31.

Methyl 3-(3-(2-(Benzyloxy)ethyl)-2-oxo-1-(2-(1-tosyl-1*H*-indol-3-yl)acetyl)-piperidin-3-yl)-3-oxopropanoate. To 100 mL of CH_2Cl_2 in a 200 mL round bottomed flask was added 6.0 g (18 mmol) of 2-(1-tosyl-1*H*-indol-3-yl) acetic acid. After stirring for 5 min, 5.3 mL (60 mmol) of $(COCl)_2$ was added dropwise. The solution was stirred for 5 h and then concentrated under reduced pressure. The resulting solid was taken up in 50 mL of CH_2Cl_2 and this solution was added dropwise to a solution of 5.0 g (15 mmol) of the above lactam and 50 g of 4Å mesh molecular sieves in 250 mL of CH_2Cl_2. The reaction mixture was allowed to stir at rt for 12 h, filtered through a pad of Celite, and concentrated

under reduced pressure. The residue was subjected to flash silica gel chromatography to give 8.1 g (84%) of the titled imide as a clear oil; IR (neat) 2954, 2872, 1752, 1683, 1593, 1446, 1360, 1290, 1160, 1115, 1086 and 976 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.61-1.72 (m, 1H), 1.83 (pent, 2H, *J* = 7.2 Hz), 2.21-2.32 (m, 2H), 2.30 (s, 3H), 2.46 (dt, 1H, *J* = 10.4 and 7.2 Hz), 3.42-3.50 (m, 1H), 3.53-3.74 (m, 4H), 3.64 (s, 3H), 3.84 (d, 1H, *J* = 21.2 Hz), 4.20 (s, 2H), 4.38 (s, 2H), 7.16-7.32 (m, 9H), 7.46 (d, 1H, *J* = 8.4 Hz), 7.55 (s, 1H), 7.75 (d, 2H, *J* = 8.4 Hz) and 7.96 (d, 1H, *J* = 8.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 20.0, 21.8, 27.6, 35.6, 36.7, 44.6, 44.9, 52.6, 61.9, 65.9, 73.5, 113.8, 116.0, 120.0, 123.4, 124.9, 125.4, 127.0, 127.8, 127.9, 128.7, 130.1, 131.1, 135.1, 135.5, 137.8, 145.1, 168.0, 173.7, 174.0 and 200.1; HRMS Calcd for $[(C_{35}H_{36}N_2O_8S) + H]^+$: 645.2271. Found: 645.2275.

Methyl 3-(3-(2-(Benzyloxy)ethyl)-2-oxo-1-(2-(1-tosyl-1*H*-indol-3-yl)acetyl)piperidin-3-yl)-2-diazo-3-oxopropanoate (10). To a 2.4 g (3.7 mmol) sample of the above ketoester in 100 mL of CH_3CN was added 0.6 mL (4.5 mmol) of Et_3N. The solution was allowed to stir for 30 min at which time 0.47 g (3.9 mmol) of mesyl azide was added and the reaction mixture was allowed to stir at rt for 5 h. The solution was concentrated under reduced pressure and the residue was subjected to flash chromatography on silica gel to give 2.2 g (88%) of diazoimide **10** as a pale yellow oil; IR (neat) 2982, 2864, 2167, 1707, 1687, 1446, 1368, 1303 and 1168 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.68-1.72 (m, 1H), 1.91-2.02 (m, 2H), 2.21-2.26 (m, 2H), 2.28 (s, 3H), 2.34 (dt, 1H, *J* = 14.4 and 6.0 Hz), 3.51 (dt, 1H, *J* = 10.0 and 6.0 Hz), 3.64-3.77 (m, 2H), 3.75 (s, 3H), 3.92 (d, 1H, *J* = 17.2 Hz), 4.21 (d, 1H, *J* = 17.2 Hz), 4.16-4.23 (m, 1H), 4.39 (s, 2H), 7.14-7.28 (m, 9H), 7.36 (d,1H, *J* = 7.6 Hz), 7.43 (s, 1H), 7.72 (d, 2H, *J* = 8.0 Hz), 7.92 (d, 1H, *J* = 8.0 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.5, 21.7, 30.5, 35.1, 35.2, 43.0, 52.7, 59.4, 67.3, 73.2, 113.7, 116.6, 119.9, 123.3, 124.8, 125.1, 127.0, 127.7, 127.8, 128.5, 130.0, 131.2, 135.1, 135.5, 138.3, 145.0, 161.8, 173.7, 174.4 and 190.6; HRMS Calcd for $[(C_{35}H_{34}N_4O_8S) + H]^+$: 671.2176. Found: 671.2181.

3*a*-{2-Benzyloxyethyl}-5,12*b*-epoxy-6-tosyl-4,12-dioxo-2,3,3*a*,4,5,5*a*,6,11,12,12*b*-decahydro-1*H*-6,12*a*-diaza-indeno[7,1-*cd*]fluorene-5-carboxylic Acid Methyl Ester (11). To a solution of 2.0 g (3 mmol) of the above diazoimide **10** in 100 mL of benzene under N_2 was added 20 mg rhodium(II) acetate, and the mixture was heated at reflux for 1 h. The mixture was allowed to cool to rt and was filtered through a pad of Celite. The solvent was removed under reduced pressure and the residue was subjected to flash silica gel chromatography to give 1.5 g (90%) of the dipolar cycloaddition product **11** as a white solid, mp 169-170 °C; IR (neat) 3076, 3027, 2953, 2859, 1773, 1727, 1478, 1460, 1399, 1361, 1309 and 1171 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.18-0.24 (m, 1H), 1.13 (pent, 1H, J = 7.2 Hz), 1.70-2.06 (m, 5H), 2.35 (d, 1H, J = 17.2 Hz), 2.37 (s, 3H), 2.78 (d, 1H, J = 17.2 Hz), 3.04-3.17 (m, 1H), 3.35-3.42 (m, 1H), 3.43-3.59 (m, 2H), 3.82-3.90 (m, 1H), 3.99 (s, 3H), 4.24 (s, 2H), 4.87 (s, 1H), 6.95 (d, 1H, J = 7.5 Hz), 7.07 (t, 1H, J = 7.5 Hz), 7.17-7.33 (m, 7H), 7.55 (d, 2H, J = 8.1 Hz), and 7.63 (d, 1H, J = 8.1 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 17.7, 21.4, 25.3, 27.1, 39.0, 44.1, 52.2, 53.2, 57.7, 65.7, 72.3, 75.6, 87.9, 104.0, 116.7, 124.4, 125.2, 127.2, 127.3, 128.1, 129.7, 130.1, 130.4, 132.6, 137.9, 142.4, 145.0, 164.6, 175.6 and 203.1; Anal. Calcd for $C_{35}H_{34}N_2O_8S$: C, 65.41; H, 5.33; N, 4.36. Found: C, 65.24; H, 5.50; N, 4.37.

Unusual Reductive Rearrangement of Cycloadduct 11 using Triethylsilylhydride and Boron Trifluoride Etherate. A solution containing 0.06 g (0.1 mmol) of cycloadduct **11** in CH_2Cl_2 (4 mL) was cooled to –78 ºC and 160 μL (1 mmol) of Et_3SiH and 65 μL (0.5 mmol) of BF_3•Et_2O were added. The solution was allowed to warm to rt for 1 h and was then heated at reflux for 24 h. The reaction mixture was cooled to rt and washed with a saturated $NaHCO_3$ solution, brine and H_2O. The solution was extracted with CH_2Cl_2 and dried over $MgSO_4$. Removal of the solvent left a colorless residue which was subjected to flash chromatography on silica gel to afford 0.03 g (60%) of **14** as a colorless solid, mp 250 ºC; IR (neat) 3467, 2956, 2159, 1755, 1692, 1641, 1596, 1460, 1359, 1265, 1169 and 1135 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.36-1.42 (m, 2H), 1.63 (d, 1H, J = 15.2 Hz),

1.66-1.78 (m, 2H), 1.90 (dt, 1H, *J* = 11.2 and 3.2 Hz), 2.10-2.15 (m, 1H), 2.32 (s, 3H), 2.35 (d, 1H, *J* = 11.2 Hz), 3.25-3.30 (m, 1H), 3.56-3.58 (m, 1H), 7.00 (dd, 1H, *J* = 5.2 and 0.4 Hz), 7.12-7.14 (m, 3H), 7.30 (d, 2H, *J* = 5.2 Hz), 7.35 (td, 1H, *J* = 5.2 and 0.8 Hz) and 7.83 (d, 1H, *J* = 5.6 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.8, 21.5, 29.0, 32.6, 38.7, 51.1, 54.6, 55.6, 64.1, 79.2, 79.9, 115.1, 119.1, 124.3, 125.7, 128.0, 129.0, 129.6, 131.7, 134.8, 137.3, 143.4, 145.1, 169.1, 169.8 and 170.6; HRMS Calcd for [($C_{28}H_{28}N_2O_8S$) + H]$^+$: 553.1645. Found: 553.1636.

3*a*-{2-Benzyloxyethyl}-5,12*b*-epoxy-6-tosyl-4-oxo-12-thioxo-2,3,3*a*,4,5,5*a*,6,11,-12,12*b*-decahydro-1*H*-6,12*a*-diaza-indeno[7,1-*cd*]fluorene-5-carboxylic Acid Methyl Ester. To a solution containing 0.72 g (1.1 mmol) of the above cycloadduct **11** in 30 mL benzene under N_2 was added 0.2 g (0.45 mmol) of P_2S_5 and 255 μL (0.76 mmol) of $(TMS)_2O$ at rt. The mixture was heated at reflux for 3 h, cooled to rt and filtered through a pad of Celite. The solvent was removed under reduced pressure and the residue was subjected to flash silica gel chromatography to give 0.67 g (90%) of the corresponding thioamide as a clear oil; IR (neat) 2953, 1776, 1746, 1597, 1477, 1390, 1367, 1320, 1170 and 1088 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.21 (dt, 1H, *J* = 14.8 and 5.6 Hz), 1.12 (pent, 1H, *J* = 8.0 Hz), 1.80-1.92 (m, 3H), 1.98-2.07 (m, 1H), 2.36 (s, 3H), 2.95 (d, 1H, *J* = 17.6 Hz), 3.14-3.22 (m, 1H), 3.23 (d, 1H, *J* = 17.6 Hz), 3.30-3.36 (m, 1H), 3.47-3.54 (m, 1H), 3.97 (s, 3H), 4.23 (s, 2H), 4.32 (dd, 1H, *J* = 13.6 and 4.4 Hz) 4.85 (s, 1H), 6.92 (dd, 1H, *J* = 7.6 and 0.8 Hz), 7.04 (td, 1H, *J* = 7.6 and 0.8 Hz), 7.15-7.34 (m, 8H), 7.53 (d, 2H, *J* = 8.4 Hz) and 7.60 (d, 1H, *J* = 8.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 18.0, 21.5, 24.7, 27.2, 43.5, 52.8, 53.4, 56.1, 60.4, 65.7, 72.4, 74.7, 88.8, 107.4, 116.6, 124.7, 125.3, 127.3, 127.4, 127.5, 128.2, 129.7, 129.8, 130.7, 132.6, 137.9, 142.4, 145.1, 164.4, 202.5 and 207.0; HRMS Calcd for [($C_{35}H_{34}N_2O_7S_2$) + H]$^+$: 659.1886. Found: 659.1875.

3*a*-{2-Benzyloxyethyl}-5,12*b*-epoxy-6-tosyl-4-oxo-2,3,3*a*,4,5,5*a*,6,11,12,12*b*-decahydro-1*H*-6,12*a*-diaza-indeno[7,1-*cd*]fluorene-5-carboxylic Acid Methyl Ester. An excess amount of Raney nickel in 100 mL round bottomed flask under N_2 was washed

three times with H_2O, twice with dry MeOH and finally three times with dry THF. A 0.43 g (0.64 mmol) sample of the above thiolactam in 15 mL of THF was added dropwise to the Raney nickel suspension. The mixture was vigorously stirred for 14 h under 1 atm of hydrogen gas and then filtered through a pad of Celite. The solvent was removed under reduced pressure and the residue was subjected to flash chromatography on silica gel to give 0.38 g (95%) of the titled compound as a clear oil; IR (neat) 2954, 1769, 1741, 1596, 1477, 1392, 1368, 1321 and 1173 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.21 (dt, 1H, J = 14.7 and 5.7 Hz), 1.14 (pent, 1H, J = 7.5 Hz), 1.56-1.99 (m, 5H), 2.08-2.16 (m, 1H), 2.34 (s, 3H), 2.81 (td, 1H, J = 11.1 and 3.6 Hz), 2.96 (dd, 1H, J = 9.6 and 3.6 Hz), 3.11-3.19 (m, 1H), 3.35-3.51 (m, 3H), 3.94 (s, 3H), 4.22 (s, 2H), 4.76 (s, 1H), 7.02-7.08 (m, 2H), 7.16-7.29 (m, 8H) and 7.55-7.61 (m, 3H); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 20.2, 21.9, 25.9, 27.8, 37.6, 46.7, 51.7, 52.0, 53.3, 62.6, 66.7, 72.4, 77.9, 87.6, 116.3, 125.0, 125.6, 127.6, 127.8, 128.4, 129.8, 129.9, 133.3, 133.5, 138.6, 142.5, 144.8, 166.2 and 206.3; HRMS Calcd for $[(C_{35}H_{36}N_2O_7S) + H]^+$: 629.2321. Found: 629.2332.

Methyl 3*a*-(2-(Benzyloxy)ethyl)-5-hydroxy-4-oxo-6-tosyl-2,3,3*a*,3a^1,4,5,5*a*,6, 11,12-decahydro-1*H*-indolizino[8,1-*cd*]carbazole-5-carboxylate. To a 0.38 g sample (0.6 mmol) of the above compound in 10 mL MeOH and 2 mL THF was added 8 mg of PtO_2 and 1 drop of concentrated HCl. The reaction mixture was subjected to hydrogenation at 1 atm of hydrogen gas for 1.5 h. The mixture was filtered through a pad of Celite, diluted with EtOAc, washed with a sat. $NaHCO_3$, solution, brine, and dried over $MgSO_4$. Removal of the solvent left a colorless residue which was subjected to flash chromatography on silica gel to afford 0.26 g (68%) of the titled compound as a clear oil; IR (neat) 3047, 2926, 2859, 1755, 1712, 1596, 1485, 1361, 1264, 1170 and 1090 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.06 (hex, 1H, J = 7.2 Hz), 1.23-1.51 (m, 4H), 1.67 (ddd, 1H, J = 14.4, 10.4 and 4.0 Hz), 1.99-2.05 (m, 1H), 2.31 (s, 3H), 2.28-2.40 (m, 2H), 2.50 (s, 1H), 3.03-3.21 (m, 4H), 3.77 (s, 3H), 4.21 (d, 1H, J = 12.0 Hz), 4.46 (s 1H), 6.99 (d, 1H, J = 7.6 Hz), 7.07 (t, 1H, J = 7.6 Hz), 7.11 (d, 2H, J = 8.4 Hz), 7.16 (d, 2H, J = 7.6 Hz), 7.23-7.31

(m, 4H), 7.48 (d, 2H, *J* = 8.4 Hz), 7.57 (s, 1H) and 7.67 (d, 1H, *J* = 8.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.5, 21.8, 31.0, 33.9, 42.3, 49.1, 51.6, 52.2, 52.5, 52.6, 65.1, 72.5, 74.5, 77.9, 80.1, 117.8, 123.3, 125.5, 127.4, 127.5, 127.9, 128.2, 128.9, 129.3, 132.9, 136.8, 138.1, 141.9, 144.5, 168.3 and 203.7; HRMS Calcd for $[(C_{35}H_{38}N_2O_7S) + H]^+$: 631.2478. Found: 631.2467.

Reductive Ring Opening of Oxabicyclic 11 to Give Hemiketal 15. To a 0.38 g (0.6 mmol) sample of 3*a*-{2-benzyloxyethyl}-5,12*b*-epoxy-6-tosyl-4-oxo-2,3,3*a*,4,5,5*a*,6,11,12,-12*b*-decahydro-1*H*-6,12*a*-diaza-indeno[7,1-*cd*]fluorene-5-carboxylic acid methyl ester in 10 mL of MeOH and 2 mL THF was added 8 mg of PtO_2 and 1 drop of concentrated HCl. The reaction mixture was hydrogenated at 1 atm of hydrogen gas but now for 12 h. The mixture was filtered through a pad of Celite, diluted with EtOAc, washed with a sat. $NaHCO_3$ solution, brine, and dried over $MgSO_4$. Removal of the solvent left a colorless residue which was subjected to flash chromatography on silica gel to give 0.17 g (51%) of the titled compound **15** as a colorless oil; IR (neat) 3047, 2962, 2928, 2850, 1739, 1597, 1358, 1264, 1170 and 1101 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.77-0.82 (m, 1H), 1.29-1.35 (m, 1H), 1.41-1.44 (m, 1H), 1.49 (dt, 1H, *J* = 9.2 and 2.8 Hz), 1.60-1.67 (m, 2H), 1.85-1.88 (m, 1H), 2.10-2.18 (m, 2H), 2.28-2.33 (m, 1H), 2.30 (s, 3H), 2.42-2.46 (m, 1H), 2.50 (s, 1H), 2.99-3.03 (m, 1H), 3.06-3.10 (m, 1H), 3.52 (q, 1H, *J* = 5.6 Hz), 3.92 (s, 3H), 4.24 (s, 1H), 6.97 (d, 1H, *J* = 7.6 Hz), 7.06 (t, 1H, *J* = 7.6 Hz), 7.08 (d, 2H, *J* = 8.4 Hz), 7.22-7.26 (m, 1H), 7.34 (d, 2H, *J* = 8.4 Hz) and 7.71 (d, 1H, *J* = 8.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.7, 22.0, 32.2, 41.0, 42.6, 49.6, 50.3, 51.5, 53.2, 54.4, 63.5, 73.4, 76.3, 81.1, 105.1, 119.4, 122.6, 125.1, 128.1, 128.6, 129.5, 133.9, 136.8, 144.4, 144.5 and 170.2; HRMS Calcd for $[(C_{28}H_{32}N_2O_7S) + H]^+$: 541.2008. Found: 541.1999.

Preparation of Mesylate 16 from Hemiketal 15. To a 0.07 g sample of the above compound **15** (0.13 mmol) in 10 mL of CH_2Cl_2 at 0 ºC was added 2.5 mL of Et_3N followed by 50 μL of MsCl (0.65 mmol). The reaction mixture was stirred at 0 ºC for 1.5 h and then quenched with a saturated NH_4Cl solution and washed with brine, H_2O and dried over

$MgSO_4$. Removal of the solvent left a colorless residue which was subjected to flash chromatography on silica gel to afford 0.07 g (85%) of mesylate **16** as a colorless oil; IR (neat) 3047, 2962, 2921, 2855, 1760, 1711, 1593, 1466, 1352, 1254 and 1176 cm^{-1}; ^{1}H-NMR (600 MHz, $CDCl_3$) δ 1.03-1.07 (m, 1H), 1.24-1.27 (m, 2H), 1.56-1.67 (m, 4H), 2.04-2.08 (m, 1H), 2.16-2.36 (m, 1H), 2.34 (s, 3H), 2.40-2.42 (m, 1H), 2.55 (s, 1H), 2.86 (s, 3H), 3.07-3.09 (m, 1H), 3.14-3.16 (m, 1H), 3.83 (s, 3H), 3.84-3.87 (m, 1H), 3.96-3.99 (m, 1H), 4.47 (s, 1H), 7.04 (d, 1H, *J* = 7.2 Hz), 7.11-7.15 (m, 3H), 7.30 (td, 1H, *J* = 9.0 and 1.2 Hz), 7.50 (d, 2H, *J* = 8.4 Hz) and 7.68 (d, 1H, *J* = 8.4 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$) δ 21.7, 21.7, 31.1, 33.6, 37.2, 42.0, 48.7, 51.3, 52.4, 52.5, 52.9, 65.6, 73.9, 77.8, 80.5, 117.7, 123.1, 125.8, 127.8, 129.2, 129.5, 133.0, 136.2, 141.8, 144.7, 168.3 and 203.8; HRMS Calcd for $[(C_{29}H_{34}N_2O_9S_2) + H]^+$: 619.1784. Found: 619.1774.

Methyl 3-(3-(2-Methoxy-2-oxoethyl)-2-oxopiperidin-3-yl)-3-oxopropanoate. A 8.8 g (28 mmol) sample of methyl 3-(3-(2-*tert*-butoxy-2-oxoethyl)-2-oxopiperidin-3-yl)-3-oxopropanoate[1] in MeOH (40 mL) and $(MeO)_3CH$ (40 mL) was vigorously stirred for 10 min at 100 ºC. To this mixture was added 5.3 g (28 mmol) of *p*-T_SOH.H_2O in one portion and the mixture was allowed to stir for 4 h. The solution was cooled to rt and concentrated under reduced pressure. The colorless residue was subjected to flash chromatography on silica gel to afford 7.5 g (99%) of the titled compound as a colorless oil; IR (neat) 3349, 2953, 1732, 1710, 1655, 1489, 1436, 1354, 1319, 1271, 1223, 1194, 1174 and 1002 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.73-1.89 (m, 3H), 2.33-2.38 (m, 1H), 2.66 (d, 1H, *J* = 16.4 Hz), 3.01 (d, 1H, *J* = 16.4 Hz), 3.27-3.39 (m, 2H), 3.63 (s, 3H), 3.68 (s, 3H), 3.79 (dd, 1H, *J* = 19.6 and 16.8 Hz) and 7.02 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 20.1, 28.9, 40.3, 42.7, 45.9, 52.1, 52.5, 57.8, 167.9, 170.9, 171.1 and 201.0; HRMS Calcd for $[(C_{12}H_{17}NO_6) + H]^+$: 272.1134. Found: 272.1129.

Methyl 3-(3-(2-Methoxy-2-oxoethyl)-2-oxo-1-(2-(1-tosyl-1*H*-indol-3-yl)acetyl)-piperidin-3-yl)-3-oxopropanoate. To 100 mL of CH_2Cl_2 in a 200 mL round bottomed flask was added 6.9 g (21 mmol) of 2-(1-tosyl-1*H*-indol-3-yl) acetic acid. After stirring for 5

min, 7.0 mL (80 mmol) of $(COCl)_2$ was added dropwise together with 2 drops of DMF. The solution was stirred at rt for 4 h and was concentrated under reduced pressure. The resulting solid was taken up in 50 mL of CH_2Cl_2 and added dropwise to a solution of 5.4 g (20.0 mmol) of the above lactam and 90 g of 4Å mesh molecular sieves in 300 mL of CH_2Cl_2. The reaction mixture was allowed to stir at rt for 12 h, filtered through a pad of Celite and concentrated under reduced pressure. The residue was subjected to flash silica gel chromatography to give 10.6 g (91%) of the titled compound as a pale yellow oil: IR (neat) 2953, 1738, 1703, 1689, 1596, 1446, 1396, 1363 and 1171 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.72-1.91 (m, 2H), 1.95-2.02 (m, 1H), 2.29 (s, 3H), 2.38 (dt, 1H, *J* = 14.0 and 4.0 Hz), 2.72 (d, 1H, *J* = 16.8 Hz), 3.19 (d, 1H, *J* = 16.8 Hz), 3.95 (dt, 1H, *J* = 12.4 and 4.4 Hz), 4.30 (dd, 1H, *J* = 25.6 and 17.2 Hz), 7.18 (d, 2H, *J* = 8.0 Hz), 7.22 (dt, 1H, *J* = 8.0 and 0.8 Hz), 7.30 (td, 1H, *J* = 8.0 and 1.2 Hz), 7.52 (d, 1H, *J* = 7.6 Hz), 7.61 (s, 1H), 7.76 (d, 2H, *J* = 8.4 Hz) and 7.97 (d, 1H, *J* = 8.0 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.7, 21.3, 28.8, 35.2, 40.1, 44.6, 52.1, 52.4, 60.8, 113.3, 115.7, 119.6, 123.0, 124.4, 125.0, 126.6, 129.7, 130.7, 134.7, 135.0, 144.7, 166.9, 170.5, 172.8, 173.6 and 199.4; HRMS Calcd for $[(C_{29}H_{30}N_2O_9S) + H]^+$: 583.1750. Found: 583.1748.

Methyl 2-Diazo-3-(3-(2-methoxy-2-oxoethyl)-2-oxo-1-(2-(1-tosyl-1*H*-indol-3-yl)acetyl)-piperidin-3-yl)-3-oxopropanoate. To a 8.7 g (15 mmol) sample of the above keto ester in 140 mL of CH_3CN at 0 ºC was added 2.3 mL (16 mmol) of Et_3N. The solution was allowed to stir for 20 min and then 1.95 g (30 mmol) of mesyl azide was added and the reaction mixture was allowed to stir for 1.5 h. The solution was concentrated under reduced pressure and the residue was subjected to flash chromatography on silica gel to give 8.1 g (89%) of the titled diazoimide as a pale yellow solid; mp 79-80 ºC; IR (neat) 2954, 2143, 1688, 1649, 1437, 1356, 1329, 1294, 1195, 1170, 1127 and 1095 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.80-1.95 (m, 2H), 2.25 (s, 3H), 2.29 (dd, 1H, *J* = 12.0 and 4.4 Hz), 2.48 (dt, 1H, *J* = 13.2 and 3.6 Hz), 2.85 (d, 2H, *J* = 4.0 Hz), 3.65 (s, 3H), 3.68-3.76 (m, 1H), 3.74 (s, 3H), 4.07 (dt, 1H, *J* = 13.2 and 4.0 Hz), 4.20 (dd, 1H, *J* = 19.6 and 17.6

Hz), 7.13 (d, 2H, *J* = 8.0 Hz), 7.17 (t, 1H, *J* = 8.0 Hz), 7.25 (td, 1H, *J* =8.0 and 1.2 Hz), 7.45 (d, 1H, *J* = 7.6 Hz), 7.52 (s, 1H), 7.71 (d, 2H, *J* = 8.4 Hz) and 7.92 (d, 1H, *J* = 8.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.1, 21.3, 27.3, 35.0, 37.2, 44.2, 51.7, 52.3, 60.0, 113.3, 115.9, 119.5, 122.9, 124.4, 124.8, 126.6, 129.6, 130.7, 134.7, 135.1, 144.6, 161.3, 170.7, 172.6, 173.9 and 189.2; Anal. Calcd. for $C_{29}H_{28}N_4O_9S$: C, 57.23; H, 4.64; N, 9.21. Found: C, 57.35; H, 4.75; N, 9.17.

3*a*-(2-Methoxy-2-oxoethyl)-5,12*b*-epoxy-6-tosyl-4,12-dioxo-2,3,3*a*,4,5,5*a*,6,11,12,12*b*-decahydro-1*H*-6,12*a*-diaza-indeno[7,1-*cd*]fluorene-5-carboxylic Acid Methyl Ester (18). To a solution containing 8.4 g (13.8 mmol) of the above diazoimide in 200 mL benzene under N_2 was added 50 mg rhodium(II) acetate and the mixture was heated at reflux for 1 h. The mixture was allowed to cool to rt and was filtered through a pad of Celite. The solvent was removed under reduced pressure and the residue was subjected to flash chromatography on silica gel to give 7.8 g (98%) of cycloadduct **18** as a colorless solid, mp 220-221 ^{o}C; IR (neat) 2952, 1781, 1728, 1731, 1597, 1401, 1364, 1188 and 1171 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.04 (d, 1H, *J* = 15.2 Hz), 1.60 (d, 1H, *J* = 15.2 Hz), 1.64-1.79 (m, 2H), 2.02-2.10 (m, 2H), 2.32 (s, 3H), 2.80 (d, 1H, *J* = 17.6 Hz), 2.76 (d, 1H, *J* = 17.6 Hz), 3.11 (td, 1H, *J* = 12.4 and 4.0 Hz), 3.49 (s, 3H), 3.78-3.82 (m, 1H), 3.92 (s, 3H), 4.85 (s, 1H), 6.93 (dd, 1H, *J* = 7.6 and 0.4 Hz), 7.03 (td, 1H, *J* = 8.0 and 0.8 Hz), 7.18 (d, 2H, *J* = 8.0 Hz), 7.33 (td, 1H, *J* = 7.8 and 1.2 Hz), 7.50 (d, 2H, *J* = 8.0 Hz) and 7.58 (d, 1H, *J* = 8.4 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 17.9, 21.5, 26.3, 32.5, 38.9, 44.1, 51.7, 51.8, 53.3, 57.8, 75.6, 87.8, 103.6, 116.9, 124.4, 125.2, 127.3, 129.5, 129.8, 130.8, 132.6, 142.4, 145.1, 164.3, 169.6, 175.2 and 200.3; Anal. Calcd. for $C_{29}H_{28}N_2O_9S$: C, 59.99; H, 4.86; N, 4.82. Found: C, 60.20; H, 5.01; N, 4.73.

3*a*-(2-Methoxy-2-oxoethyl)-5,12*b*-epoxy-6-tosyl-4-oxo-12-thioxo-2,3,3*a*,4,5,5*a*,6,-11,12,12*b*-decahydro-1*H*-6,12*a*-diaza-indeno[7,1-*cd*]fluorene-5-carboxylic Acid Methyl Ester. To a solution containing 6.3 g (11 mmol) of the above cycloadduct **18** in 200 mL benzene under N_2 was added 1.9 g (4.3 mmol) of P_2S_5 and 2.5 mL (18 mmol) of

$(TMS)_2O$ at rt. The mixture was heated at reflux for 6 h, cooled to rt and filtered through a pad of Celite. The solvent was removed under reduced pressure and the residue was subjected to flash chromatography on silica gel to give 6.4 g (90%) of the titled thiolactam as a white solid, mp 221-222 ºC; IR (neat) 3052, 2953, 2970, 2929, 1785, 1744, 1372, 1270 and 1172 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.30 (d, 1H, *J* = 16.0 Hz), 1.63 (d, 1H, *J* = 16.0 Hz), 1.81-1.97 (m, 2H), 2.06-2.19 (m, 2H), 2.39 (s, 3H), 2.99 (d, 1H, *J* = 18.0 Hz), 3.26 (d, 1H, *J* = 18.0 Hz), 3.34 (td, 1H, *J* = 13.2 and 5.2 Hz), 3.54 (s, 3H), 4.00 (s, 3H), 4.29 (dq, 1H, *J* = 14.0 and 2.8 Hz), 4.89 (s, 1H), 6.95 (dd, 1H, *J* = 7.2 and 0.8 Hz), 7.05 (t, 1H, *J* = 7.2 Hz), 7.22 (d, 2H, *J* = 8.0 Hz), 7.37 (td, 1H, *J* = 8.0 and 1.6 Hz), 7.55 (d, 2H, *J* = 8.0 Hz) and 7.64 (d, 1H, *J* = 8.0 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 18.3, 21.5, 26.1, 33.1, 43.3, 51.8, 52.2, 53.4, 55.9, 60.5, 74.7, 88.4, 107.0, 116.6, 124.7, 125.1127.3, 129.0, 129.8, 130.9, 132.5, 142.4, 145.2, 164.1, 169.5, 199.8 and 206.2; HRMS Calcd for $[(C_{29}H_{28}N_2O_8S_2) + H]^+$: 597.1365. Found: 597.1356.

3*a*-(2-Methoxy-2-oxoethyl)-5,12*b*-epoxy-6-tosyl-4-oxo-2,3,3*a*,4,5,5*a*,6,11,12,12*b*-decahydro-1*H*-6,12*a*-diaza-indeno[7,1-*cd*]fluorene-5-carboxylic Acid Methyl Ester. An excess amount of Raney nickel in a 250 mL round bottomed flask under N_2 was washed three times with H_2O, twice with dry MeOH and finally three times with dry THF. A 6.3 g (10.6 mmol) sample of the above thiolactam in 100 mL THF was added dropwise. The solution was vigorously stirred for 14 h under 1 atm of H_2 gas. The reaction mixture was filtered through a pad of Celite, the solvent was removed under reduced pressure and the residue was subjected to flash chromatography on silica gel to give 5.2 g (87%) of the titled compound as a white solid, mp 200-202 ºC; IR (neat) 2951, 2859, 1774, 1738, 1598, 1477, 1436, 1293, 1267, 1170 and 1036 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.81 (d, 1H, *J* = 14.4 Hz), 1.60-1.69 (m, 2H), 1.73 (d, 1H, *J* = 14.4 Hz), 1.87-2.00 (m, 3H), 2.06-2.13 (m, 1H), 2.32 (s, 3H), 2.80 (td, 1H, *J* = 12.4 and 4.0 Hz), 2.92 (dd, 1H, *J* = 10.4 and 3.2 Hz), 3.08-3.15 (m, 1H), 3.40 (hex, 1H, *J* = 4.0 Hz), 3.49 (s, 3H), 3.90 (s, 3H), 4.73 (s, 1H), 7.01 (d, 2H, *J* = 4.4 Hz), 7.17 (d, 2H, *J* = 7.6 Hz), 7.23-7.28 (m, 1H) and 7.54-7.57

(m, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.6, 21.4, 25.8, 32.1, 37.0, 46.2, 51.1, 51.5, 51.6, 53.0, 62.3, 87.4, 110.8, 116.3, 124.7, 125.0, 127.4, 129.6, 129.8, 132.3, 133.2, 142.3, 144.5, 165.6, 170.7 and 203.1; HRMS Calcd for $[(C_{29}H_{30}N_2O_8S) + H]^+$: 567.1801. Found: 567.1794.

Methyl 5-Hydroxy-3*a*-(2-methoxy-2-oxoethyl)-4-oxo-6-tosyl-2,3,3*a*,3*a*^{1},4,5,5*a*,6, 11,12-decahydro-1*H*-indolizino[8,1-*cd*]carbazole-5-carboxylate (19). To a 0.6 g (1.0 mmol) sample of above compound in 10 mL MeOH and 2 mL THF was added 10 mg of PtO_2 and 1 drop of concentrated HCl. The reaction mixture was hydrogenated at 1 atm of hydrogen gas for 12 h. The mixture was filtered through a pad of Celite, diluted with EtOAc, washed with a sat. $NaHCO_3$ solution, brine and dried over $MgSO_4$. Removal of the solvent left a colorless residue which was subjected to flash chromatography on silica gel to give 0.54 g (95%) of **19** as a white solid, mp 187-188 ºC; IR (neat) 3517, 2950, 2823, 1760, 1739, 1596, 1480, 1435, 1358, 1254, 1169, 1114, 1097 and 1039 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.27-1.35 (m, 1H), 1.51-1.71 (m, 2H), 1.87 (d, 1H, *J* = 17.4 Hz), 2.07 (d, 1H, *J* = 17.4 Hz), 2.09-2.14 (m, 2H), 2.29 (s, 3H), 2.37 (td, 1H, *J* = 10.0 and 6.4 Hz), 3.03 (d, 1H, *J* = 11.2 Hz), 3.14 (td, 1H, *J* = 9.2 and 4.0 Hz), 3.24 (s, 1H), 3.36 (s, 3H), 3.82 (s, 3H), 4.45 (s, 1H), 6.96-7.04 (m, 2H), 7.10 (d, 2H, *J* = 8.4 Hz), 7.22-7.26 (m, 1H), 7.44 (d, 2H, *J* = 8.4 Hz), 7.65 (d, 1H, *J* = 8.0 Hz) and 8.21 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.4, 21.7, 30.2, 37.4, 42.1, 47.5, 51.2, 51.9, 52.1, 52.7, 69.5, 77.6, 79.9, 117.8, 123.7, 125.0, 127.8, 128.9, 129.3, 132.8, 135.6, 141.7, 144.5, 168.0, 169.8 and 202.9; HRMS Calcd for $[(C_{29}H_{32}N_2O_8S) + H]^+$: 569.1958. Found: 569.1951.

Methyl 2-(5-(Methoxycarbonyloxy)-4-oxo-6-tosyl-2,3,3*a*,3*a*^{1},4,5,5*a*,6,11,12-decahydro-1*H*-indolizino[8,1-*cd*]carbazol-3*a*-yl)acetate. To a 0.06 g (0.11 mmol) sample of compound **19** in 5 mL CH_3CN was added 0.21 g (0.6 mmol) of Cs_2CO_3 and the reaction mixture was heated at reflux for 1 h. The mixture was cooled to room temperature and filtered through a pad of Celite. Removal of the solvent left a colorless residue which was subjected to flash chromatography on silica gel to afford 0.41 g (75%)

of the titled carbonate as a colorless solid; mp 97-98 ºC; IR (neat) 2952, 1736, 1597, 1474, 1459, 1439, 1359, 1331, 1267, 1167 and 1097 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.07 (td, 1H, *J* = 13.2 and 4.8 Hz), 1.15-1.29 (m, 2H), 1.40-1.44 (m, 1H), 1.73-1.83 (m, 1H), 1.98-2.10 (m, 1H), 2.14-2.20 (m, 2H), 2.18 (d, 1H, *J* = 14.8 Hz), 2.34 (s, 3H), 2.48 (d, 1H, *J* = 14.8 Hz), 2.88-2.91 (m, 2H), 2.93 (s, 1H), 3.49 (s, 3H), 3.74 (s, 3H), 4.47 (d, 1H, *J* = 8.4 Hz), 5.24 (d, 1H, *J* = 8.4 Hz), 7.10 (t, 1H, *J* = 7.6 Hz), 7.19 (d, 3H, *J* = 8.4 Hz), 7.28 (t, 1H, *J* = 7.6 Hz), 7.63 (d, 1H, *J* = 8.0 Hz) and 7.66 (d, 2H, *J* = 8.0 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 21.2, 21.4, 29.6, 38.0, 42.1, 48.8, 50.5, 51.7, 52.9, 54.3, 55.0, 70.7, 72.8, 78.3, 118.2, 122.7, 125.3, 126.8, 128.9, 129.5, 136.1, 136.6, 140.2, 144.0, 154.5, 169.3 and 200.1; Anal. Calcd for $C_{29}H_{32}N_2O_8S$: C, 61.25; H, 5.67; N, 4.93. Found: C, 61.36; H, 5.77; N, 4.79.

Methyl 2-(4-Oxo-6-tosyl-2,3,3*a*,3*a*^{1},4,5,5*a*,6,11,12-decahydro-1*H*-indolizino[8,1-*cd*]-carbazol-3*a*-yl)acetate. A solution of containing (0.6 g, 1.0 mmol) of the above carbonate in THF (5 mL) together with 0.1 mL of HMPA and was degassed with argon at rt for 15 min. The mixture was allowed to react with a solution of samarium iodide in THF (0.1 M) at 0 ºC until a blue color persisted for 10 sec. The reaction mixture was then quenched with a saturated $NaHCO_3$ solution, extracted with EtOAc and dried over $MgSO_4$. Removal of the solvent left a colorless residue which was subjected to flash chromatography on silica gel to afford 0.37 g (72%) of the titled compound as a clear oil; IR (neat) 2939, 2795, 1738, 1718, 1475, 1459, 1355, 1168 and 1101 cm^{-1}; ^{1}H-NMR (600 MHz, CD_3CN) δ 1.26-1.34 (m, 2H), 1.40-1.56 (m, 2H), 1.62 (td, 1H, *J* = 13.8 and 3.6 Hz), 1.94-2.28 (m, 7H), 2.35 (s, 3H), 2.78 (s, 1H), 2.90-3.02 (m, 2H), 3.05 (dd, 1H, *J* = 16.8 and 6.0 Hz), 3.11-3.14 (m, 1H), 3.35 (s, 3H), 4.26 (s, 1H), 7.10 (t, 1H, *J* = 7.2 Hz), 7.21 (d, 1H, *J* = 7.2 Hz), 7.27 (d, 1H, *J* = 7.8 Hz), 7.30 (d, 2H, *J* = 8.4 Hz), 7.62 (d, 1H, *J* = 7.8 Hz) and 7.79 (dd, 2H, *J* = 6.6 and 1.8 Hz); ^{13}C-NMR (150MHz, CD_3CN) δ 21.9, 23.3, 31.6, 40.8, 41.8, 43.4, 49.7, 52.2, 53.0, 53.8, 71.2, 74.1, 117.1, 125.7,126.3, 128.7, 130.1,

131.2, 135.2, 137.8, 141.8, 146.5, 171.2 and 209.5; Anal. Calcd for $C_{27}H_{30}N_2O_5S$: C, 65.57; H, 6.11; N, 5.66. Found: C, 65.11; H, 6.19; N, 5.46.

2-(4-(*tert*-Butyldimethylsilyloxy)-6-tosyl-2,3,3*a*,3*a*^{1},5*a*,6,11,12-octahydro-1*H*-indolizino[8,1-*cd*]carbazol-3*a*-yl)acetaldehyde (20). To a solution containing 0.12 g (0.2 mmol) of the above keto ester and 120 μL (0.5 mmol) of TBDMSOTf in 10 mL of CH_2Cl_2 was added dropwise 208 μL of (1.5 mmol) Et_3N. After 1 h of stirring at rt, the mixture was hydrolyzed with a saturated $NaHCO_3$ solution. After extraction with CH_2Cl_2, the organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was dissolved in 10 mL of THF and a 1.2 mL of a 1.0 M $LiAlH_4$ solution was added at 0 ºC. After stirring for 4 h, the mixture was quenched with H_2O, 15% NaOH and extracted with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. To the resulting residue was added 5 mL of CH_3CN, 0.15 g of 4 Å molecular sieves, 0.04 g (0.35 mmol) of 4-methylmorpholine *N*-oxide (NMO) and 0.025 g (0.07 mmol) of tetrapropylammonium perruthenate (TPAP) at 0 ºC. The mixture was allowed to warm to rt for 4 h and was filtered through a pad of Celite. After removing the solvent under reduced pressure, the residue was subjected to flash silica gel chromatography to give 0.092 g (68%) of aldehyde **20** as a colorless oil; IR (neat) 2930, 2856, 1718, 1664, 1598, 1475, 1461, 1356, 1261 and 1168 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.20 (s, 3H), 0.26 (s, 3H), 0.87 (s, 9H), 0.91-1.00 (m, 1H), 1.11-1.18 (m, 1H), 1.34-1.41 (m, 1H), 1.45-1.50 (m, 2H), 1.81 (dd, 1H, *J* = 15.2 and 3.6 Hz), 1.96-2.00 (m, 1H), 2.06 (dd, 1H, *J* = 15.2 and 2.0 Hz), 2.14-2.22 (m, 2H), 2.34 (s, 3H), 2.54 (s, 1H), 2.96-3.00 (m, 2H), 4.50 (d, 1H, *J* = 4.4 Hz), 5.03 (d, 1H, *J* = 4.0 Hz), 6.97-7.00 (m, 2H), 7.16-7.25 (m, 3H), 7.57 (d, 2H, *J* = 8.0 Hz), 7.67 (d, 1H, *J* = 8.0 Hz) and 9.43-9.45 (m, 1H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ -4.8, -4.4, 18.0, 21.5, 22.6, 25.6, 30.9, 41.2, 41.9, 51.4, 51.5, 52.4, 54.2, 70.4, 72.0, 101.8, 116.7, 123.5, 124.6, 127.0, 128.6, 129.5, 134.9, 136.7, 140.8, 143.9, 153.6 and 201.4; HRMS Calcd for $[(C_{32}H_{42}N_2O_4SSi) + H]^+$: 579.2713. Found: 579.2707.

Cesium Fluoride Induced Intramolecular Aldol Reaction of Silyl Enol Ether 20. To a solution of 0.05 g (0.086 mmol) of the above aldehyde in 10 mL of CH_3CN was added 0.13 g (0.86 mmol) of Cs_2CO_3 and the reaction mixture was heated at 100 ºC for 1 h. The mixture was then cooled to room temperature and filtered through a pad of Celite. Removal of the solvent left a colorless residue which was subjected to flash chromatography on silica gel to afford 0.03 g (78%) of the aldol product **21** as a colorless solid; mp 249-250 ºC; IR (neat) 3500, 2927, 2787, 1749, 1596, 1553, 1456, 1355, 1168, 1093 and 1043 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.89 (dd, 1H, *J* = 13.2 and 7.6 Hz), 0.94-1.04 (m, 1H), 1.15 (td, 1H, *J* = 13.6 and 4.8 Hz), 1.34 (d, 1H, *J* = 14.4 Hz), 1.48-1.54 (m, 1H), 1.67 (d, 2H, *J* = 26 Hz), 1.88-2.04 (m, 4H), 2.21-2.31 (m, 1H), 2.34 (s, 3H), 2.51 (s, 1H), 2.73 (d, 1H, *J* = 5.6 Hz), 2.82 (t, 1H, *J* = 8.8 Hz), 3.07 (dd, 1H, *J* = 11.2 and 2.8 Hz), 4.00 (d, 1H, *J* = 8.0 Hz), 4.38 (d, 1H, *J* = 5.6 Hz), 7.13-7.16 (m, 2H), 7.18 (d, 2H, *J* = 8.4 Hz), 7.30-7.34 (m, 1H), 7.58 (d, 2H, *J* = 8.0 Hz) and 7.77 (d, 1H, *J* = 8.0 Hz); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.5, 21.6, 28.4, 40.7, 44.2, 47.7, 51.4, 53.2, 54.2, 61.9, 64.3, 75.8, 81.1, 115.9, 122.6, 125.3, 126.9, 128.8, 129.7, 134.9, 138.5, 141.0, 144.4 and 213.1; HRMS Calcd for $[(C_{26}H_{28}N_2O_4S) + H]^+$: 465.1848. Found: 465.1843.

Samarium Iodide Reduction of Hydroxy Ester 19. A solution containing 0.11 g (0.18 mmol) of the above compound **19** in THF (1 mL) together with 0.2 mL of HMPA was degassed with argon at rt for 15 min. A solution of samarium iodide in THF (0.1 M) at 0 ºC was added to this mixture until a blue color persisted for 10 sec. The reaction mixture was quenched with a saturated $NaHCO_3$ solution, extracted with EtOAc and dried over $MgSO_4$. Removal of the solvent under reduced pressure left a colorless residue which was subjected to flash chromatography on silica gel to afford 0.08 g (93%) of compound **22** as a clear oil which consisted of a 4:3:1-mixture of the keto and enol forms; IR (neat) 3068, 2954, 2921, 2855, 1728, 1450, 1258, 1237, 1176 and 1029 cm^{-1}; ^{1}H-NMR (400 MHz, CD_3CN) δ 1.19-1.37 (m, 1H), 1.39-1.67 (m, 3H), 1.67-1.80 (m, 1H), 1.98-2.09 (m, 3H), 2.14 (d, 1H, *J* = 16.8 Hz), 2.20-2.29 (m, 1H), 2.36 (s, 3H), 2.83-2.86 (m, 1H), 2.87 (s,

1H), 2.94 (hex, 1H, *J* = 4.4 Hz), 3.34 (s, 3H), 3.76 (s, 3H), 4.33 (d 1H, *J* = 4.0 Hz), 4.84 (d 1H, *J* = 4.0 Hz), 7.04-7.06 (m, 2H), 7.22 (d, 2H, *J* = 8.0 Hz), 7.25 (t, 1H, *J* = 8.4 Hz), 7.64 (d, 2H, *J* = 8.4 Hz) and 7.72 (d, 1H, *J* = 8.4 Hz); ^{13}C-NMR (100 MHz, CD_3CN) δ 22.3, 21.6, 29.7, 30.9, 38.5, 41.0, 48.4, 51.2, 51.4, 51.8, 52.4, 116.9, 124.1, 124.7, 127.9, 128.9, 129.6, 132.5, 135.4, 141.3, 144.6, 167.2, 170.0 and 205.0; HRMS Calcd for $[(C_{29}H_{32}N_2O_7S) + H]^+$: 553.2008. Found: 553.2000.

Methyl 4-(*tert*-Butyldimethylsilyloxy)-3*a*-(2-methoxy-2-oxoethyl)-6-tosyl-2,3,3*a*,-3*a*^{1},5*a*,6,11,12-octahydro-1*H*-indolizino[8,1-*cd*]carbazole-5-carboxylate. To a solution of 0.06 g (0.11 mmol) keto ester **22** and 100 μL (0.4 mmol) of TBDMSOTf in 5mL of CH_2Cl_2 was added dropwise 121 μL (0.9 mmol) of Et_3N. After stirring overnight at rt, the mixture was hydrolyzed with a saturated $NaHCO_3$ solution. After extraction with CH_2Cl_2, the organic layer was dried over $MgSO_4$ and filtered. Concentration of the solution under reduced pressure followed by flash chromatography on silica gel afforded 0.07 g (96%) of the titled enol ether as a colorless oil; IR (neat) 3402, 2948, 2931, 2857, 2787, 1727, 1596, 1477, 1436, 1358, 1260, 1169 and 1030 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.26 (s, 3H), 0.31 (s, 3H), 0.94 (s, 9H), 1.30-1.38 (m, 1H), 1.43-1.59 (m, 3H), 1.70 (ddd, 1H, *J* = 10.8, 8.8 and 2.0 Hz), 1.96-2.10 (m, 2H), 2.23 (t, 1H, *J* = 4.8 Hz), 2.32 (s, 3H), 2.45 (d, 1H, *J* = 16.4 Hz), 2.84 (s, 1H), 2.92-2.98 (m, 2H), 3.31 (s, 3H), 3.81 (s, 3H), 4.94 (s, 1H), 7.00 (td, 1H, *J* = 7.6 and 1.2 Hz), 7.09 (dd, 1H, *J* = 7.6 and 1.2 Hz), 7.15-7.20 (m, 3H) and 7.63-7.67 (m, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ –3.0, -2.4, 19.2, 21.5, 22.8, 26.2, 30.2, 38.7, 42.0, 43.2, 51.0, 51.6, 51.8, 51.9, 52.6, 70.5, 72.6, 109.2, 116.4, 124.2, 124.4, 127.7, 128.1, 129.4, 134.0, 137.4, 140.8, 143.9, 161.2, 167.1 and 170.7; HRMS Calcd for $[(C_{35}H_{46}N_2O_7SSi) + H]^+$: 667.2873. Found: 667.2866.

Methyl 4-(*tert*-Butyldimethylsilyloxy)-3*a*-(2-hydroxyethyl)-6-tosyl-2,3,3*a*,3*a*^{1},5*a*,6,-11,12-octahydro-1*H*-indolizino[8,1-*cd*]carbazole-5-carboxylate (23). To a solution of 0.069 g (0.1 mmol) of the above compound in 10 mL of THF was added 0.5 mL of a 1.0 M $LiAlH_4$/THF solution at -78 ^{o}C. The solution was allowed to warm to 0 ^{o}C and was stirred

for 5 h. The mixture was quenched with H_2O, 15% NaOH and extracted with EtOAc. The combined organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The solvent was removed under reduced pressure and the residue was subjected to flash silica gel chromatography to give 0.06 g (91%) of the reduced alcohol **23** as a colorless solid, mp 190-192 ºC; IR (neat) 3402, 2948, 2931, 2857, 2787, 1727, 1596, 1477, 1436, 1358, 1260, 1169 and 1030 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.30 (s, 3H), 0.33 (s, 3H), 0.95 (s, 9H), 1.07 (td, 1H, *J* =13.6 and 8.0 Hz), 1.42-1.69 (m, 5H), 1.70-1.90 (m, 3H), 2.17 (s, 1H), 2.12-2.23 (m, 2H), 2.34 (s, 3H), 2.96-3.00 (m, 3H), 3.24 (brs, 1H), 3.81 (s, 3H), 5.01 (s, 1H), 7.03-7.10 (m, 2H), 7.18-7.25 (m, 3H) and 7.65-7.68 (m, 3H); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ –2.7, -2.2, 19.3, 21.5, 22.9, 26.4, 31.0, 39.2, 42.3, 44.3, 51.5, 52.0, 52.4, 53.3, 58.4, 71.0, 76.4, 107.9, 116.1, 123.7, 124.5, 127.7, 128.4, 129.4, 134.0, 138.2, 141.3, 143.9, 164.6 and 167.2; HRMS Calcd for [($C_{34}H_{46}N_2O_6SSi$) + H]$^+$: 639.2924. Found: 639.2919.

Oxidation and Cesium Fluoride Induced Aldol Reaction of Primary Alcohol 23. A solution containing 0.06 g (0.094 mmol) of the above primary alcohol **23** in 5 mL of CH_3CN, containing 200 mg of 4 Å molecular sieves, 17 mg (0.14 mmol) of NMO and 10 mg (0.028 mmol) of TPAP at 0 ºC was allowed to stir at rt for 12 h. The solution was filtered through a pad of Celite, the solvent was removed under reduced pressure and the residue was taken up in 5 mL of CH_3CN. To the resulting mixture was added 0.14 g (0.94 mmol) of Cs_2CO_3 and the reaction mixture was heated at reflux at 80 ºC for 1 h. The mixture was cooled to room temperature and filtered through a pad of Celite. Removal of the solvent left a colorless residue which was subjected to flash chromatography on silica gel to afford 0.017 g (34%) the aldol product **24** as a colorless oil; IR (neat) 3497, 2931, 2850, 2785, 1758, 1714, 1596, 1445, 1362, 1271, 1171 and 1092 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 0.76 (dd, 1H, *J* = 13.6 and 7.6 Hz), 0.96-1.04 (m, 1H), 1.15 (td, 1H, *J* =13.6 and 5.2 Hz), 1.33 (d, 1H, *J* = 14.8 Hz), 1.49-1.53 (m, 1H), 1.79 (dd, 1H, *J* = 14.8 and 8.0 Hz), 1.84-2.04 (m, 3H), 2.33 (s, 3H), 2.25-2.42 (m, 1H), 2.48 (s, 1H), 2.83 (t, 1H, *J* = 8.4

Hz), 3.08 (dd, 1H, *J* = 10.8 and 3.6 Hz), 4.03 (s, 3H), 4.30-4.32 (m, 2H), 4.83 (m, 1H), 7.13 (d, 3H, *J* = 8.0 Hz), 7.20 (d, 1H, *J* = 7.6 Hz), 7.34 (d, 1H, *J* = 8.0 Hz), 7.41 (d, 2H, *J* = 8.0 Hz) and 7.79 (d, 1H, *J* = 8.0 Hz); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 21.5, 21.6, 29.2, 38.5, 43.7, 46.3, 51.7, 53.0, 53.4, 54.5, 65.9, 68.5, 78.5, 81.4, 118.1, 122.6, 126.3, 127.4, 128.9, 129.6, 134.2, 139.8, 141.0, 144.7, 169.4 and 206.2; HRMS Calcd for $[(C_{28}H_{30}N_2O_6S) + H]^+$: 523.1903. Found: 523.1899.

Reference

(1) Mejía-Oneto, J. M.; Padwa, A. *Org. Lett.* **2006**, *8*, 3275.

Ortep Drawing of Intramolecular Aldol Product **21**