ELECTRONIC SUPPLEMENTARY INFORMATION

Synthesis of new aza-analogs of staurosporine, K-252a and rebeccamycin by nucleophilic opening of C_2 symmetric bis-aziridines

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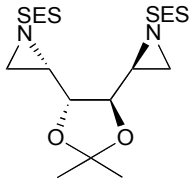
The 1,2-*O*-isopropylidene and 1,2-*O*-dibenzyloxy-*N*H bis-aziridines, precursors of all the *N*-protected bis-aziridines, were obtained according to our previous procedure.[1] Bis-indolylmaleimide **5d** and indolocarbazole **6b** were synthesized according to classical procedures.[2]

General procedure for the synthesis of 9a-d and 10a-c.

To a solution of crude *N*H bis-aziridine (1.0 eq) in DMF (0.4 M) cooled at –15 °C, were slowly added Et_3N (15.0 eq) and a solution of either TsCl, SES-Cl, Mts-Cl, (2.5 eq) or Boc_2O (1.0 eq) in DMF (1 M). After stirring for 4 h at this temperature, the mixture was poured in H_2O and extracted with Et_2O. The organic layers were then dried over $MgSO_4$, filtered and concentrated. The residue was purified by column chromatography (cyclohexane/EtOAc/NH_4OH: 85/15/1).

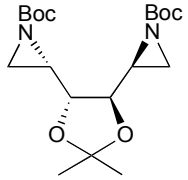
(*2S*,*2'S*)-[(*1R*,*2R*)-1,2-*O*-Isopropylidene-ethan-diyl]-*N*,*N*'-[2-(trimethylsilyl)ethylsulfonyl]-bis-aziridine (9b).



O-Isopropylidene *N*H bis-aziridine, obtained from 3,4-*O*-isopropylidene-1,6-dideoxy-1,6-diazido-D-mannitol (460 mg, 1.69 mmol), and SES-Cl (850 mg, 4.25 mmol) yielded **9b** (550 mg, 64%) as a white solid; R_f 0.30 (cyclohexane/EtOAc, 7/3); mp 87–88 °C; $[\alpha]_D^{20}$ –37 (*c* 1.0 in CH_2Cl_2); IR (ATR) 2954,

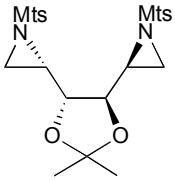
1460, 1423, 1371, 1326, 1253, 1165, 1141, 1111, 1072, 1033; ^{1}H NMR ($CDCl_3$) δ: 0.05 (s, 18 H, 2 x $Si(CH_3)_3$), 1.15 (m, 4 H, 2 x CH_2Si), 1.36 (s, 6 H, $C(CH_3)_2$), 2.45 (d, J = 4.4 Hz, 2 H, 2 x H-1), 2.63 (d, J = 7.1 Hz, 2 H, 2 x H-1'), 2.81 (m, 2 H, 2 x H-2), 3.09 (m, 2 H, 2 x CH_2SO_2), 3.89 (m, 2 H, 2 x H-3); ^{13}C NMR ($CDCl_3$) δ: –2.1 ($Si(CH_3)_3$), 9.7 (CH_2Si), 26.7 ($C(CH_3)_2$), 30.1 (C-1), 37.2 (C-2), 48.9 (CH_2SO_2), 77.2 (C-3), 110.5 ($C(CH_3)_2$); MS (CI): *m/z* 513 ($[M + H]^+$, 100%), 497 (M – CH_3, 50%); HRMS (CI): *m/z* calcd for $C_{19}H_{41}N_2O_6S_2Si_2$ $[M + H]^+$ 513.1944, found 513.1942.

(*2S,2'S*)-[(*1R,2R*)-1,2-*O*-Isopropylidene-ethan-diyl]-*N,N'*-{*tert*-butyloxycarbonyl}-bis-aziridine (9c).



O-Isopropylidene *N*H bis-aziridine, obtained from 3,4-isopropylidene-1,6-dideoxy-1,6-diazido-D-mannitol (1.36 g, 5 mmol), and Boc_2O (1.09 g, 5 mmol) yielded **9c** (1.15 g, 60%) as a white solid; R_f 0.22 (cyclohexane/EtOAc, 85/15); mp 71 °C; $[\alpha]_D^{20}$ –80 (*c* 1.03 in CH_2Cl_2); IR (ATR) 3421, 2986, 2935, 2877, 1720, 1700, 1479, 1413, 1372, 1323, 1245, 1225, 1148, 1113; ^{1}H NMR ($CDCl_3$) δ: 1.36 (s, 6 H, $C(CH_3)_2$), 1.44 (s, 18 H, 2 x *t*-Bu), 2.27 (d, J = 3.9 Hz, 2 H, 2 x H-1), 2.30 (d, J = 6.7 Hz, 2 H, 2 x H-1'), 2.55 (m, 2 H, 2 x H-2), 3.94 (m, 2 H, 2 x H-3); ^{13}C NMR ($CDCl_3$) δ: 26.9 ($C(CH_3)_2$), 27.9 ($C(CH_3)_3$), 28.6 (C-1), 36.9 (C-2), 77.5 (C-3), 81.5 ($C(CH_3)_3$), 110.1 ($C(CH_3)_2$), 162.0 (CO); MS (CI): *m/z* 385 ($[M + H]^+$, 13%), 285 ($[M + H]^+ - C_4H_8 - CO_2$, 92%), 185 ($[M + H]^+ - 2[C_4H_8 - CO_2]$, 60%); HRMS (CI): *m/z* calcd for $C_{19}H_{33}N_2O_6$ $[M + H]^+$ 385.2339, found 385.2347.

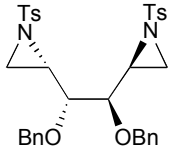
(*2S,2'S*)-[(*1R,2R*)-1,2-*O*-Isopropylidene-ethan-diyl]-*N,N'*-[2,4,6-trimethylphenylsulfonyl]-bis-aziridine (9d).



O-Isopropylidene *N*H bis-aziridine, obtained from 3,4-isopropylidene-1,6-dideoxy-1,6-diazido-D-mannitol (150 mg, 0.55 mmol) and Mts-Cl (300 mg, 1.37 mmol) yielded **9d** (184 mg, 61%) as a white solid; R_f 0.30 (cyclohexane/EtOAc, 7/3); mp 150 °C; $[\alpha]_D^{20}$ –20.5 (*c* 1.15 in CH_2Cl_2); IR (ATR) 3378, 2920, 2851, 1740, 1605, 1457, 1376, 1315, 1263, 1225, 1156, 1076; ^{1}H NMR ($CDCl_3$) δ: 1.19 (s, 6 H, $C(CH_3)_2$), 2.27 (s, 6 H, 2 x CH_3), 2.31 (d, J = 4.0 Hz, 2 H, 2 x H-1), 2.50–2.70 (m, 4 H, 2 x H-1', 2 x H-2), 2.66 (s, 12 H, 4 x CH_3), 3.76 (m, 2 H, 2 x H-3), 6.94 (s, 4 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: 20.8

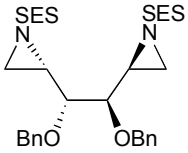
(CH_3), 22.9 (CH_3), 26.6 ((CH_3)$_2$), 30.3 (C-1), 36.4 (C-2), 75.7 (C-3), 109.9 (C(CH_3)$_2$), 131.8 (CH-Ar), 132.0, 140.1, 143.3 (Cq-Ar); MS (CI): *m/z* 566 ([M + NH_4]$^+$, 20%), 549 ([M + H]$^+$, 100%), 367 ([M + H]$^+$ – $C_9H_{10}SO_2$, 100%); HRMS (CI): *m/z* calcd for $C_{27}H_{37}N_2O_6S_2$ [M + H]$^+$ 549.2093, found 549.2098.

(*2S,2'S*)-[(*1R,2R*)-1,2-Dibenzyloxy-ethan-diyl]-*N,N'*-(*para*-toluenesulfonyl)-bis-aziridine (10a).



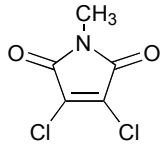
O-Dibenzyl *N*H bis-aziridine, obtained from 3,4-dibenzyl-1,6-dideoxy-1,6-diazido-D-mannitol (1.03 g, 2.5 mmol), and TsCl (1.19 g, 6.2 mmol) yielded **10a** (791 mg, 50%) as a white solid; R_f 0.20 (cyclohexane/EtOAc, 8/2); mp 135–136 °C; $[\alpha]_D^{20}$ –78 (*c* 1.04 in CH_2Cl_2); IR (ATR) 3365, 3032, 2926, 2858, 1716, 1596, 1495, 1456, 1384, 1316, 1226, 1159, 1089, 1069; ^{1}H NMR ($CDCl_3$) δ: 1.91 (d, *J* = 3.8 Hz, 2 H, 2 x H-1), 2.32 (d, *J* = 6.4 Hz, 2 H, 2 x H-1'), 2.39 (s, 6 H, 2 x CH_3), 3.00–3.10 (m, 4 H, 2 x H-2, 2 x H-3), 4.22, 4.39 (AB, *J* = 12.0 Hz, 4 H, 2 x OCH_2Ph), 7.10–7.35 (m, 10 H, H-Ar), 7.84 (d, *J* = 8.3 Hz, 4 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: 21.5 (CH_3), 29.0 (C-1), 40.2 (C-2), 71.7 (OCH$_2$Ph), 78.3 (C-3), 127.8, 128.1, 128.2, 128.3, 129.7 (CH-Ar), 134.2, 137.2, 144.8 (Cq-Ar); MS (CI): *m/z* 650 ([M + NH_4]$^+$, 100%), 633 ([M + H]$^+$, 50%); HRMS (CI): *m/z* calcd for $C_{34}H_{37}N_2O_6S_2$ [M + H]$^+$ 632.2093, found 632.2098.

(*2S,2'S*)-[(*1R,2R*)-1,2-Dibenzyloxy-ethan-diyl]-*N,N'*-[2-(trimethylsilyl)ethylsulfonyl]-bis-aziridine (10b).



O-Dibenzyl *N*H bis-aziridine, obtained from the 3,4-dibenzyl-1,6-dideoxy-1,6-diazido-D-mannitol (2.12 g, 5.14 mmol), and SES-Cl (2.57 g, 12.85 mmol) yielded **10b** (1.16 g, 35%) as a white solid; R_f 0.50 (cyclohexane/EtOAc, 7/3); mp 81–83 °C; $[\alpha]_D^{20}$ –81 (*c* 1.0 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ: 0.02 (s, 18 H, 2 x Si(CH_3)$_3$), 1.11 (m, 4 H, 2 x CH_2Si), 2.16 (d, *J* = 4.4 Hz, 2 H, 2 x H-1), 2.49 (d, *J* = 7.2 Hz, 2 H, 2 x H-1'), 3.07 (m, 6 H, 2 x CH_2SO_2, 2 x H-2), 3.27 (d, *J* = 5.8 Hz, 2 H, 2 x H-3), 4.61, 4.79 (AB, *J* = 11.8 Hz, 2 H, OCH_2Ph), 7.29 (m, 10 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: –2.4 (Si(CH_3)$_3$), 8.9 (CH_2Si), 29.7 (C-1), 37.5 (C-2), 48.3 (CH_2SO_2), 72.2 (OCH$_2$Ph), 78.5 (C-3), 127.5, 127.7, 128.0 (CH-Ar), 137.1 (Cq-Ar); MS (CI): *m/z* 670 ([M + NH_4]$^+$, 100%); HRMS (CI): *m/z* calcd for $C_{30}H_{52}N_3O_6S_2Si_2$ [M + NH_4]$^+$ 670.2836, found 670.2841.

3,4-Dichloro-1-methyl-1*H*-pyrrole-2,5-dione 14.

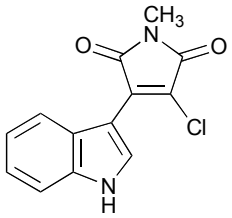


3,4-Dichloromaleic anhydride (20 g, 120 mmol, 1.0 eq) and methylamine hydrochloride (8.5 g, 132 mmol, 1.1 eq) were dried *under vacuo* for 2 h, and added in glacial acetic acid (75 mL). Sodium methylate (7.1 g, 132 mmol, 1.1 eq) was then slowly added to the mixture. After stirring at rt overnight and at reflux for 3 h, the mixture was concentrated and poured in CH_2Cl_2 (500 mL). The organic layer was then washed with water (2 x 250 mL), a solution of saturated $NaHCO_3$ (2 x 250 mL) and water (2 x 250 mL). After drying over $MgSO_4$ and concentrating the organic layer, the residue was purified by column chromatography (cyclohexane/EtOAc: 9/1) to yield **14** as a white solid (16.2 g, 75%); R_f 0.35 (cyclohexane/EtOAc, 9/1); mp 84 °C (lit.,[3] 82–83 °C); ^{1}H NMR ($CDCl_3$) δ: 3.07 (s, 3 H, NCH_3); ^{13}C NMR ($CDCl_3$) δ: 25.0 (NCH_3), 133.2 (CCl), 162.9 (CO).

General procedure for the synthesis of 15a-b.

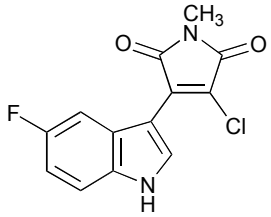
To a solution of EtMgBr 3 M in ether (2.2 eq) was added at 40 °C a solution of indole **13a** or **13b** (2.0 eq) in THF (2 M). After stirring the mixture for 15 min and cooling, a solution of 3,4-dichloro-1-methyl-pyrrole-2,5-dione **14** (1.0 eq) in THF (2 M) was added. After further stirring at rt for 2.5 h, the mixture was poured, at 0 °C, in a solution of HCl (0.5 M) then extracted with EtOAc. The organic layers were then washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was then purified by column chromatography (cyclohexane/EtOAc: 7/3) to yield the desired mono-indolylmaleimide **15a** or **15b** and the excess of indole **13a** or **13b**.

3-Chloro-4-(1*H*-indol-3-yl)-1-methyl-1*H*-pyrrole-2,5-dione (15a).



13a (2.34 g, 20 mmol) and **14** (1.8 g, 10 mmol) yielded **15a** (2.47 g, 95%) as an orange solid; R_f 0.55 (cyclohexane /EtOAc, 7/3); mp 207 °C; ^{1}H NMR ($CDCl_3$) δ: 3.14 (s, 3 H, NCH_3), 7.20–7.40 (m, 2 H, H-Ar), 7.43 (d, J = 7.3 Hz, 1 H, H-Ar), 8.01 (d, J = 2.8 Hz, 1 H, H-Ar), 8.05 (d, J = 8.2 Hz, 1 H, H-Ar), 8.76 (br s, 1 H, NH).

3-Chloro-4-(5-fluoro-1*H*-indol-3-yl)-1-methyl-1*H*-pyrrole-2,5-dione (15b).

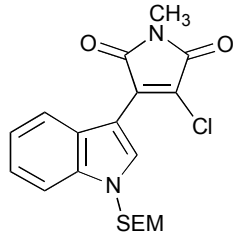


13b (525 mg, 3.88 mmol) and **14** (350 mg, 1.94 mmol) yielded **15b** (480 mg, 89%) as an orange solid; R_f 0.30 (cyclohexane/EtOAc, 7/3); mp 236–237 °C; IR (ATR) 3356, 3157, 3092, 2948, 1766, 1699, 1625, 1598, 1623, 1472, 1444, 1417, 1388, 1330, 1295, 1277, 1218, 1193, 1164, 1121, 1092, 1034; ^{1}H NMR ($CDCl_3$) δ: 3.14 (s, 3 H, NCH_3), 7.05 (td, J = 8.5, 2.0 Hz, 1 H, H-Ar), 7.35 (dd, J = 8.6, 4.4 Hz, 1 H, H-Ar), 7.76 (dd, J = 9.9, 2.0 Hz, 1 H, H-Ar), 8.06 (d, J = 2.6 Hz, 1 H, H-Ar), 8.70 (br s, 1 H, NH).

General procedure for the synthesis of 16a-b.

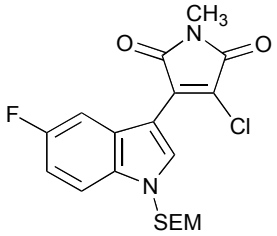
To a solution of NaH 60% suspension in mineral oil (1.5 eq) 1 M in THF were slowly added at 0 °C a solution of mono-indolylmaleimide **15a** or **15b** (1.0 eq) in THF (2 M) then a solution of SEM-Cl (1.3 eq) in THF (1 M). After stirring for 15 min at 0 °C and at rt for 2 h, the mixture was cooled and poured in a solution of saturated NH_4Cl then extracted with EtOAc. The organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was then purified by column chromatography (cyclohexane/EtOAc: 9/1).

3-Chloro-4-[1-{2-(trimethylsilyl)ethoxymethyl}indol-3-yl]-1-methyl-1*H*-pyrrole-2,5-dione (16a).



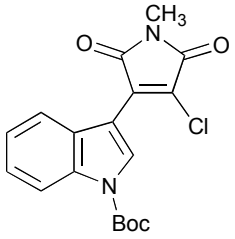
15a (2.4 g, 9.2 mmol) and SEM-Cl (2.45 g, 12.0 mmol) yielded **16a** (2.8 g, 77%) as a yellow-orange solid; R_f 0.50 (cyclohexane/EtOAc, 7/3); mp 91 °C; IR (ATR) 3457, 2950, 2893, 1769, 1706, 1627, 1510, 1437, 1385, 1248, 1207, 1156, 1126, 1080; ^{1}H NMR ($CDCl_3$) δ: –0.06 (s, 9 H, $Si(CH_3)_3$), 0.89 (t, J = 8.2 Hz, 2 H, CH_2Si), 3.11 (s, 3 H, NCH_3), 3.52 (t, J = 8.0 Hz, 2 H, CH_2O), 5.51 (s, 2 H, NCH_2O), 7.20–7.30 (m, 2 H, H-Ar), 7.53 (d, J = 7.5 Hz, 1 H, H-Ar), 7.97 (s, 1 H, H-Ar), 8.04 (d, J = 7.3 Hz, 1 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: –1.5 ($Si(CH_3)_3$), 17.6 (CH_2Si), 24.4 (NCH_3), 66.3 (CH_2O), 76.2 (NCH_2O), 104.4 (Cq-Ar), 110.7, 121.7, 122.9, 123.4 (CH-Ar), 123.6, 126.0, 132.8 (Cq-Ar), 133.1 (CH-Ar), 136.6 (Cq-Ar), 166.2, 168.9 (CO).

3-Chloro-4-[5-fluoro-1-{2-(trimethylsilyl)ethoxymethyl}indol-3-yl]-1-methyl-1*H*-pyrrole-2,5-dione (16b).



15b (480 mg, 1.72 mmol) and SEM-Cl (463 mg, 2.27 mmol) yielded **16b** (520 mg, 74%) as a yellow-orange solid; R_f 0.40 (cyclohexane/EtOAc, 8/2); mp 81–82 °C; IR (ATR) 3462, 3124, 2953, 2884, 1768, 1707, 1624, 1587, 1573, 1512, 1479, 1439, 1382, 1361, 1250, 1218, 1190, 1074; ^{1}H NMR ($CDCl_3$) δ: –0.07 (s, 9 H, $Si(CH_3)_3$), 0.89 (t, J = 8.1 Hz, 2 H, CH_2Si), 3.14 (s, 3 H, NCH_3), 3.50 (t, J = 8.1 Hz, 2 H, CH_2O), 5.51 (s, 2 H, NCH_2O), 7.07 (td, J = 8.8, 2.1 Hz, 1 H, H-Ar), 7.47 (dd, J = 8.9, 4.3 Hz, 1 H, H-Ar), 7.76 (dd, J = 10.1, 2.0 Hz, 1 H, H-Ar), 8.06 (s, 1 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: –1.5 ($Si(CH_3)_3$), 17.6 (CH_2Si), 24.6 (NCH_3), 66.5 (CH_2O), 76.6 (NCH_2O), 104.5 (d, J = 3.7 Hz, Cq-Ar), 108.5 (d, J = 25.6 Hz, CH-Ar), 111.6 (d, J = 10.3 Hz, CH-Ar), 111.9 (d, J = 27.2 Hz, CH-Ar), 124.0 (Cq-Ar), 126.8 (d, J = 10.6 Hz, Cq-Ar), 132.5, 133.1 (Cq-Ar), 134.3 (CH-Ar), 158.7 (d, J = 238 Hz, CF), 166.1, 168.9 (CO).

3-Chloro-4-[1-{*tert*-butyloxycarbonyl}indol-3-yl]-1-methyl-1*H*-pyrrole-2,5-dione (16c).

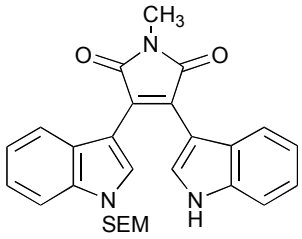


To a solution of **15a** (2.44 g, 9.4 mmol, 1.0 eq) in THF (6 mL) was slowly added, at 0 °C, a catalytical amount of DMAP (225 mg, 1.8 mmol, 0.2 eq) and Boc_2O (2.45 g, 11.2 mmol, 1.2 eq). After stirring for 15 min at this temperature and for 30 min at rt, the mixture was concentrated. The residue was then purified by column chromatography (cyclohexane/EtOAc: 9/1 then 8/2) to yield **16c** (2.58 g, 76%) as a yellow-orange solid; R_f 0.55 (cyclohexane/EtOAc, 7/3); mp 165 °C; IR (ATR) 3176, 2980, 1757, 1706, 1604, 1508, 1475, 1454, 1383, 1370, 1338, 1315, 1266, 1244, 1191, 1152, 1107, 1061; ^{1}H NMR ($CDCl_3$) δ: 1.68 (s, 9 H, $C(CH_3)_3$), 3.15 (s, 3 H, NCH_3), 7.25–7.45 (m, 2 H, H-Ar), 7.82 (d, J = 7.7 Hz, 1 H, H-Ar), 8.12 (s, 1 H, H-Ar), 8.21 (d, J = 8.2 Hz, 1 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: 24.7 (NCH_3), 28.0 ($C(CH_3)_3$), 85.1 ($C(CH_3)_3$), 108.0 (Cq-Ar), 115.4, 122.3, 123.3, 125.3 (CH-Ar), 127.1 (Cq-Ar), 128.8 (CH-Ar), 129.9, 132.1, 135.4 (Cq-Ar), 148.9 (CO-Boc), 168.2 (2 CO).

General procedure for the synthesis of 11a-c.

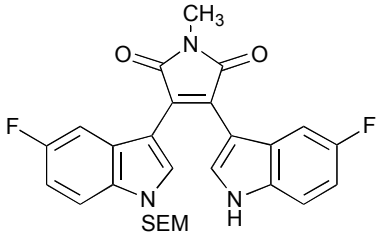
To a solution of EtMgBr 3 M in ether (2.0 eq) was added a solution of indole **13a** or **13b** (2.0 eq) in toluene or THF (1 M). After stirring for 15 min at rt then for 1 h at 60 °C the mixture was cooled and a solution of *N*-protected mono-indolylmaleimide **16a**, **16b** or **16c** (1.0 eq) in toluene or THF (1 M) was added. After 2.5 h at 60 °C, the mixture was cooled at 0 °C, poured in a solution of HCl (0.5 M) then extracted with EtOAc. The organic layers were then washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was then purified by column chromatography (cyclohexane /EtOAc: 9/1).

3-(1*H*-Indol-3-yl)-4-[1-{2-(trimethylsilyl)ethoxymethyl}indol-3-yl]-1-methyl-1*H*-pyrrole-2,5-dione (11a).



13a (600 mg, 5.12 mmol) and *N*-SEM-indolylmaleimide **16a** (1.0 g, 2.56 mmol) in toluene, yielded **11a** (870 mg, 72%) as a red solid; R_f 0.50 (cyclohexane/ EtOAc, 7/3); mp 75 °C; ^{1}H NMR ($CDCl_3$) δ: –0.05 (s, 9 H, $Si(CH_3)_3$), 0.89 (t, J = 8.0 Hz, 2 H, CH_2Si), 3.18 (s, 3 H, NCH_3), 3.50 (t, J = 8.0 Hz, 2 H, CH_2O), 5.48 (s, 2 H, NCH_2O), 6.65–6.75 (m, 2 H, H-Ar), 6.87 (d, J = 8.0 Hz, 1 H, H-Ar), 6.97 (d, J = 8.6 Hz, 1 H, H-Ar), 7.00–7.15 (m, 2 H, H-Ar), 7.25 (d, J = 8.1 Hz, 1 H, H-Ar), 7.42 (d, J = 8.2 Hz, 1 H, H-Ar), 7.69 (d, J = 2.7 Hz, 1 H, H-Ar), 7.76 (s, 1 H, H-Ar), 8.58 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ: –1.4 ($Si(CH_3)_3$), 17.7 (CH_2Si), 24.2 (NCH_3), 66.1 (CH_2O), 76.1 (NCH_2O), 106.9, 107.3 (Cq-Ar), 110.2, 111.1, 120.3, 120.7, 121.8, 122.1, 122.6, 125.6 (CH-Ar), 126.7 (Cq-Ar), 128.1, 131.7 (CH-Ar), 135.8, 136.3 (Cq-Ar), 172.4 (2 CO) ; MS (CI): *m/z* 489 ($[M + NH_4]^+$, 100%), 472 ($[M + H]^+$, 10%), 354 ($[M + H]^+ – (CH_3)_3SiCH_2CH_2O$, 15%).

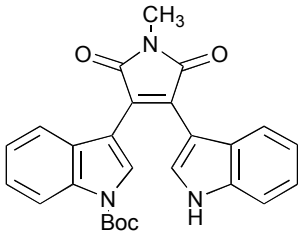
3-(5-Fluoro-1*H*-indol-3-yl)-4-[5-fluoro-1-{2-(trimethylsilyl)ethoxymethyl}indol-3-yl]-1-methyl-1*H*-pyrrole-2,5-dione (11b).



13b (340 mg, 2.52 mmol) and **16b** (515 mg, 1.26 mmol) in toluene yielded **11b** (295 mg, 45%) as a red solid; R_f 0.30 (cyclohexane/EtOAc, 7/3); mp 80 °C; IR (ATR) 3346, 2949, 2892, 1759, 1690, 1625,

1583, 1533, 1482, 1443, 1384, 1330, 1294, 1247, 1210, 1186, 1149, 1093; ^{1}H NMR ($CDCl_3$) δ: –0.05 (s, 9 H, $Si(CH_3)_3$), 0.91 (t, *J* = 8.1 Hz, 2 H, CH_2Si), 3.17 (s, 3 H, NCH_3), 3.52 (t, *J* = 7.9 Hz, 2 H, CH_2O), 5.51 (s, 2 H, NCH_2O), 6.44 (m, 2 H, H-Ar), 6.80 (m, 2 H, H-Ar), 7.16 (m, 2 H, H-Ar), 7.35 (m, 2 H, H-Ar), 7.87 (m, 2 H, H-Ar), 8.54 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ: –1.5 ($Si(CH_3)_3$), 17.5 (CH_2Si), 24.1 (NCH_3), 66.0 (CH_2O), 76.2 (NCH_2O), 106.0 (d, *J* = 4.8 Hz, Cq-Ar), 106.6 (d, *J* = 18.8 Hz, CH-Ar), 106.6 (d, *J* = 23.1 Hz, CH-Ar), 106.8 (d, *J* = 4.3 Hz, Cq-Ar), 110.6 (d, *J* = 10.5 Hz, CH-Ar), 110.9 (d, *J* = 25.0 Hz, CH-Ar), 111.0 (d, *J* = 25.3 Hz, CH-Ar), 112.1 (d, *J* = 9.6 Hz, CH-Ar), 123.0 (Cq-Ar), 126.1 (d, *J* = 11.0 Hz, Cq-Ar), 126.6 (Cq-Ar), 127.4 (d, *J* = 8.0 Hz, Cq-Ar), 129.8, 132.2 (CH-Ar), 132.6, 132.7 (Cq-Ar), 157.7 (d, *J* = 236 Hz, CF), 157.9 (d, *J* = 235 Hz, CF), 172.1, 172.2 (CO).

3-(1*H*-Indol-3-yl)-4-[1-{*tert*-butyloxycarbonyl}indol-3-yl]-1-methyl-1*H*-pyrrole-2,5-dione (11c).

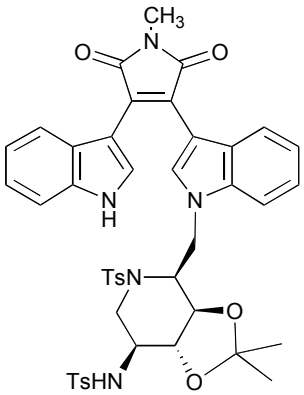


13a (117 mg, 1.0 mmol) and **16c** (180 mg, 0.5 mmol) in THF yielded **11c** (172 mg, 78%) as a red solid; R_f 0.40 (cyclohexane/EtOAc, 7/3); mp 203 °C (lit.,[2a] 200 °C); IR (ATR) 3362, 1739, 1691, 1644, 1556, 1454, 1420, 1359, 1236, 1154, 1110, 1065; ^{1}H NMR ($CDCl_3$) *δ*: 1.66 (s, 9 H, $OC(CH_3)_3$), 3.18 (s, 3 H, NCH_3), 6.70–7.30 (m, 7 H, H-Ar), 7.63 (d, *J* = 8.3 Hz, 1 H, H-Ar), 9.16 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$) *δ*: 24.1 (NCH_3), 27.9 ($OC(CH_3)_3$), 84.2 ($OC(CH_3)_3$), 106.6, 110.9 (Cq-Ar), 111.3, 114.9, 120.5, 121.5, 122.4, 122.6, 124.5, 125.3 (CH-Ar), 128.0 (Cq-Ar), 128.3, 129.3 (CH-Ar), 131.4, 135.0, 135.9 (Cq-Ar), 149.2 (CO-Boc), 171.7, 171.9 (CO).

General procedure for the synthesis of 20a-c, 23b, 25b, 29b, 31b and 38b.

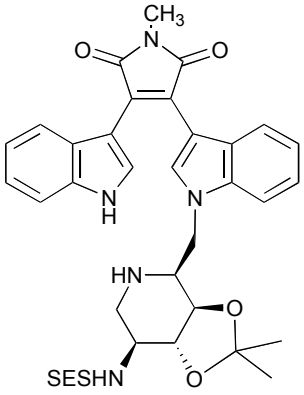
A solution of the reagent (1.0 eq) and TBAF 1 M in THF (2.5–10.0 eq) in THF (0.02 M) was maintained either at gentle reflux or at reflux for 1–6 h. After cooling at 0 °C, the mixture was poured in a solution of saturated NH_4Cl and extracted with EtOAc. The organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was then purified by column chromatography (cyclohexane/EtOAc: 5/5 to cyclohexane/EtOAc/MeOH: 5/5/0.5).

3-{1-[(*2S,3R,4R,5S*)-5-(*para*-Toluenesulfonyl)amino-1-(*para*-toluenesulfonyl)-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (20a).



17a (220 mg, 0.23 mmol) and TBAF 1 M in THF (1.15 mL, 1.15 mmol, 5.0 eq) for 3 h yielded **20a** (165 mg, 87%) as an orange solid; R_f 0.40 (cyclohexane /EtOAc, 5/5); mp 182–185 °C; UV/Vis (EtOH): λ_{max} (ε) = 207 (77490), 224 (71635), 275 (16420), 373 (6450), 473 (9520); IR (ATR) 3388, 3255, 2987, 1758, 1694, 1634, 1614, 1529, 1439, 1387, 1342, 1305, 1225, 1156, 1087, 1044; ^{1}H NMR ($CDCl_3$) δ: 1.27, 1.36 (2 s, 6 H, $C(CH_3)_2$), 2.27, 2.44 (2 s, 6 H, 2 x CH_3), 2.77 (m, 1 H, H-6ax), 3.19 (m, 4 H, H-5, NCH_3), 3.43 (m, 2 H, H-3, H-4), 4.09 (m, 1 H, H-1), 4.34 (m, 2 H, H-1', H-6eq), 4.85 (m, 2 H, NH, H-2), 6.60–7.40 (m, 14 H, H-Ar), 7.51 (s, 1 H, H-Ar), 7.64 (d, J = 2.6 Hz, 1 H, H-Ar), 7.78 (d, J = 8.2 Hz, 2 H, H-Ar), 8.50 (br s, 1 H, NH); MS (CI): *m/z* 851 ($[M + NH_4]^+$, 100%), 833 (M, 40%).

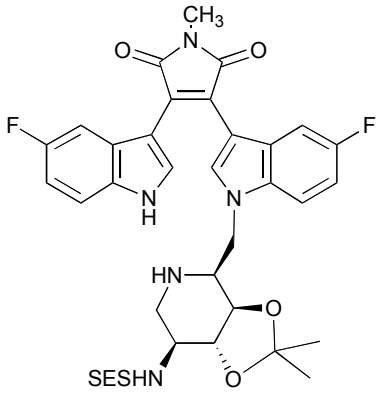
3-{1-[(*2S,3R,4R,5S*)-5-(2-[Trimethylsilyl]ethylsulfonyl)amino-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (20b).



17b (315 mg, 0.32 mmol) and TBAF 1 M in THF (1 mL, 1.00 mmol, 3.1 eq) for 3 h yielded **20b** (182 mg, 82%) as an orange solid; R_f 0.40 (cyclohexane/EtOAc, 5/5); mp 142–145 °C; $[\alpha]_D^{20}$ –78 (*c* 0.51 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ: 0.05 (s, 9 H, $Si(CH_3)_3$), 1.07 (m, 2 H, CH_2Si), 1.42 (s, 6 H, $C(CH_3)_2$), 1.67 (br s, 1 H, NH), 2.27 (dd, J = 13.1, 9.3 Hz, 1 H, H-6ax), 2.82 (dd, J = 13.1, 4.3 Hz, 1 H, H-6eq), 3.05 (m, 2 H, CH_2SO_2), 3.15 (s, 3 H, NCH_3), 3.25–3.60 (m, 4 H, H-2, H-3, H-4, H-5), 3.78 (dd, J = 14.5, 10.5 Hz, 1 H, H-1), 4.10 (d, J = 14.5 Hz, 1 H, H-1'), 4.66 (d, J = 6.3 Hz, 1 H, NH), 6.65–6.95 (m, 3 H, H-Ar), 7.06 (t, J = 7.5 Hz, 1 H, H-Ar), 7.14 (t, J = 7.6 Hz, 1 H, H-Ar), 7.20–7.35 (m, 4 H, H-Ar), 7.69 (d, J = 2.6 Hz, 1 H, H-Ar), 8.63 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ: –1.9 ($Si(CH_3)_3$), 10.4 (CH_2Si), 24.2

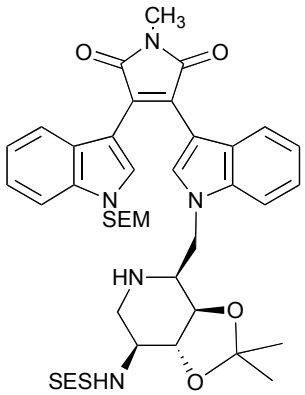
(NCH_3), 26.7, 26.9 ($C(CH_3)_2$), 41.1 (C-1), 45.1 (C-6), 49.7 (CH_2SO_2), 53.8 (C-5), 55.5 (C-2), 77.2 (C-3, C-4), 105.7, 106.5 (Cq-Ar), 109.5 ($C(CH_3)_2$), 109.6, 111.7, 120.0, 120.6, 121.9, 122.3, 122.6 (CH-Ar), 124.6, 126.0, 127.4, 127.9 (Cq-Ar), 128.7, 132.7 (CH-Ar), 136.0, 136.2 (Cq-Ar), 172.3, 172.7 (CO); MS (CI): *m/z* 690 ($[M + H]^+$, 100%).

3-{5-Fluoro-1-[(*2S,3R,4R,5S*)-5-(2-[trimethylsilyl]ethylsulfonyl)amino-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{5-fluoro-1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (20c).



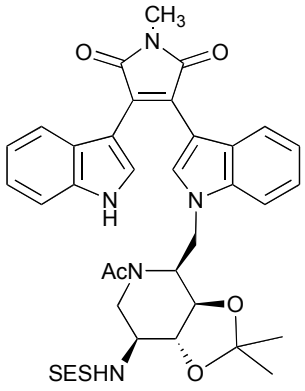
17c (240 mg, 0.235 mmol) and TBAF 1 M in THF (0.7 mL, 0.7 mmol, 3.0 eq) for 3 h yielded **20c** (130 mg, 76%) as an orange solid; R_f 0.40 (cyclohexane/EtOAc, 5/5); mp 127–129 °C; $[\alpha]_D^{20}$ –24 (*c* 1.0 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ: 0.05 (s, 9 H, $Si(CH_3)_3$), 1.09 (m, 2 H, CH_2Si), 1.43 (s, 6 H, $C(CH_3)_2$), 1.66 (br s, 1 H, NH), 2.50 (dd, *J* = 14.0, 9.8 Hz, 1 H, H-6ax), 2.90–3.20 (m, 3 H, H-6eq, CH_2SO_2), 3.08 (s, 3 H, NCH_3), 3.35–3.60 (m, 4 H, H-2, H-3, H-4, H-5), 3.94 (dd, *J* = 14.5, 10.2 Hz, 1 H, H-1), 4.17 (d, *J* = 14.8 Hz, 1 H, H-1'), 5.10 (d, *J* = 5.2 Hz, 1 H, NH), 6.30 (d, *J* = 9.8 Hz, 1 H, H-Ar), 6.59 (d, *J* = 9.9 Hz, 1 H, H-Ar), 6.70 (t, *J* = 10.0 Hz, 1 H, H-Ar), 6.78 (t, *J* = 9.8 Hz, 1 H, H-Ar), 7.14 (m, 2 H, H-Ar), 7.55 (s, 1 H, H-Ar), 7.76 (d, *J* = 1.5 Hz, 1 H, H-Ar), 8.95 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ: –1.9 ($Si(CH_3)_3$), 10.4 (CH_2Si), 24.1 (NCH_3), 26.5, 26.9 ($C(CH_3)_2$), 41.8 (C-1), 45.6 (C-6), 49.9 (CH_2SO_2), 54.0 (C-5), 56.0 (C-2), 77.3 (C-3, C-4), 105.5 (d, *J* = 3.5 Hz, Cq-Ar), 106.6 (d, *J* = 24.2 Hz, CH-Ar), 106.6 (d, *J* = 3.4 Hz, Cq-Ar), 106.8 (d, *J* = 25.0 Hz, CH-Ar), 109.6 ($C(CH_3)_2$), 110.4 (d, *J* = 11.9 Hz, CH-Ar), 111.7 (d, *J* = 27.6 Hz, 2 CH-Ar), 112.2 (d, *J* = 9.1 Hz, CH-Ar), 125.7 (d, *J* = 10.5 Hz, Cq-Ar), 127.0 (d, *J* = 10.3 Hz, Cq-Ar), 127.1 (2 Cq-Ar), 130.0 (CH-Ar), 132.3 (2 Cq-Ar), 133.9 (CH-Ar), 157.5 (d, *J* = 235 Hz, CF), 157.8 (d, *J* = 237 Hz, CF), 172.2, 172.5 (CO); MS (CI): *m/z* 726 ($[M + H]^+$, 100%).

3-{1-[(*2S,3R,4R,5S*)-5-(2-[Trimethylsilyl]ethylsulfonyl)amino-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1-(2-[trimethylsilyl]ethoxymethyl)-1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (23b).



17b (200 mg, 0.2 mmol) and TBAF 1 M in THF (0.5 mL, 0.5 mmol) at gentle reflux yielded **23b** (105 mg, 63%) as an orange solid; R_f 0.55 (cyclohexane/EtOAc, 5/5); mp 124–128 °C; $[\alpha]_D^{20}$ –61 (*c* 0.5 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ: –0.05, 0.07 (2 s, 18 H, 2 x $Si(CH_3)_3$), 0.90 (t, *J* = 8.0 Hz, 2 H, CH_2Si), 1.10 (m, 2 H, CH_2Si), 1.40 (m, 7 H, $C(CH_3)_2$, NH), 2.39 (dd, *J* = 13.0, 9.0 Hz, 1 H, H-6ax), 2.92 (d, *J* = 12.8z, 1 H, H-6eq), 3.08 (m, 2 H, CH_2SO_2), 3.12 (s, 3 H, NCH_3), 3.29 (m, 1 H, H-2), 3.30–3.55 (m, 3 H, H-3, H-4, H-5), 3.50 (t, *J* = 8.0 Hz, 2 H, CH_2O), 3.67 (dd, *J* = 14.3, 10.2 Hz, 1 H, H-1), 3.93 (d, *J* = 13.8 Hz, 1 H, H-1'), 5.27 (d, *J* = 7.1 Hz, 1 H, NH), 5.45, 5.49 (AB, *J* = 11.1 Hz, 2 H, NCH_2O), 6.67 (m, 2 H, H-Ar), 6.79 (t, *J* = 7.5 Hz, 1 H, H-Ar), 7.06 (m, 2 H, H-Ar), 7.19 (t, *J* = 9.2 Hz, 2 H, H-Ar), 7.38 (s, 1 H, H-Ar), 7.41 (d, *J* = 10.1 Hz, 1 H, H-Ar), 7.75 (s, 1 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: –1.9, –1.4 ($Si(CH_3)_3$), 10.4, 17.6 (CH_2Si), 24.1 (NCH_3), 26.6, 26.9 ($C(CH_3)_2$), 41.2 (C-1), 45.4 (C-6), 49.7 (CH_2SO_2), 54.2 (C-5), 55.8 (C-2), 66.1 (CH_2O), 76.0 (NCH_2O), 76.6, 77.3 (C-3, C-4), 105.8, 106.5 (Cq-Ar), 109.5 ($C(CH_3)_2$), 110.3, 120.3, 120.4, 122.1, 122.2, 122.6, 126.2, 126.9, 127.8, 131.8, 132.4, 135.9, 136.4 (CH-Ar, Cq-Ar), 172.1, 172.6 (CO); MS (CI): *m/z* 820 ($[M + H]^+$, 100%).

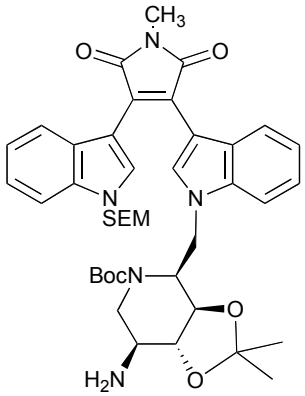
3-{1-[(*2S,3R,4R,5S*)-5-(2-[Trimethylsilyl]ethylsulfonyl)amino-1-acetyl-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (25b).



24b (165 mg, 0.19 mmol) and TBAF 1 M in THF (1 mL, 1.00 mmol, 5 eq) at reflux for 6 h yielded **25b** (93 mg, 66%) as an orange solid; R_f 0.30 (cyclohexane/EtOAc, 5/5); mp 162–164 °C; $[\alpha]_D^{20}$ –76 (*c* 0.26 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, mixture of rotamers in ~ 2:1 ratio) δ: 0.06 (s, 9 H, $Si(CH_3)_3$), 0.80–1.25

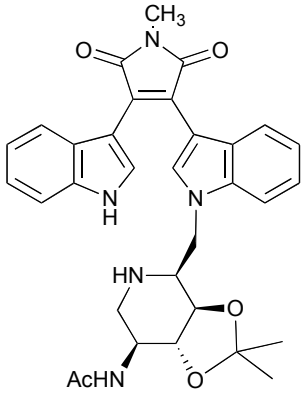
(m, 2 H, CH_2Si), 1.39, 1.45 (2 s, 6 H, $C(CH_3)_2$), 1.92, 2.02 (2 s, 3 H, CH_3CO), 2.55-2.80 (m, 1 H, H-6ax), 3.00–3.20 (m, 2 H, CH_2SO_2), 3.10, 3.13 (2 s, 3 H, NCH_3), 3.40–3.75 (m, 3 H, H-3, H-4, H-5), 3.75–4.00, 4.98 (m, 2 H, H-6eq, H-1), 4.10–4.30 (m, 1 H, H-1'), 4.42, 5.45 (2 m, 1 H, H-2), 5.67 (m, 1 H, NH), 6.50–7.30 (m, 8 H, H-Ar), 7.35–7.55 (m, 2 H, H-Ar), 9.02, 9.35 (2 s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ: –2.0 ($Si(CH_3)_3$), 10.4 (CH_2Si), 20.9, 22.0 (CH_3CO), 24.2 (NCH_3), 26.5, 26.8 ($C(CH_3)_2$), 41.3 (C-1maj, C-6maj), 43.3 (C-1min), 47.0 (C-6min), 49.8 (CH_2SO_2, C-2maj), 52.8, 53.7 (C-5), 56.3 (C-2min), 75.7, 75.8, 75.9 (C-3, C-4), 106.0, 106.5, 106.6, 106.7 (Cq-Ar), 108.8, 109.3 (CH-Ar), 111.1 ($C(CH_3)_2$), 111.5, 112.3, 120.2, 120.4, 120.7, 121.2, 121.8, 122.0, 122.4, 122.9, 125.6, 125.7, 126.2, 127.0, 127.5, 128.1, 128.5, 128.7, 131.5, 131.9, 135.4, 135.7, 135.8, 136.2 ($C(CH_3)_2$, CH-Ar, Cq-Ar), 170.2, 170.7 (CO-Ac), 172.4, 172.6, 172.8 (CO); FAB–MS: *m/z* 732 ($[M + H]^+$, 100%).

3-{1-[(*2S,3R,4R,5S*)-5-(2-Amino-1-(*tert*-butyloxycarbonyl)-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1-(2-[trimethylsilyl]ethoxymethyl)-1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (29b).



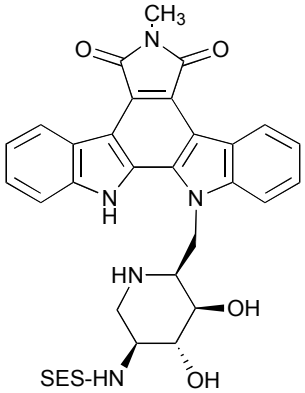
28b (98 mg, 0.10 mmol, 1 eq) and TBAF 1 M in THF (0.25 mL, 0.25 mmol, 2.5 eq) at reflux for 1 h yielded **29b** (70 mg, 83%) as an orange solid; R_f 0.45 (cyclohexane/EtOAc, 5/5); mp 122–124 °C; $[\alpha]_D^{20}$ –56 (*c* 0.2 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ: –0.05 (s, 9 H, $Si(CH_3)_3$), 0.89 (t, *J* = 7.5 Hz, 2 H, CH_2Si), 1.43 (br s, 15 H, $C(CH_3)_2$, $C(CH_3)_3$), 1.71 (br s, 2 H, NH_2), 2.35 (dd, *J* = 12.6, 10.0 Hz, 1 H, H-6ax), 3.16 (m, 4 H, NCH_3, H-6eq), 3.30–3.75 (m, 5 H, CH_2O, H-3, H-4, H-5), 3.95 (dd, *J* = 14.3, 9.9 Hz, 1 H, H-1), 4.21 (d, *J* = 14.3 Hz, 1 H, H-1'), 4.88 (m, 1 H, H-2), 5.47 (s, 2 H, NCH_2O), 6.60–6.90 (m, 3 H, H-Ar), 7.08 (m, 3 H, H-Ar), 7.27 (m, 1 H, H-Ar), 7.42 (d, *J* = 7.8 Hz, 1 H, H-Ar), 7.54 (s, 1 H, H-Ar), 7.75 (s, 1 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: –1.4 ($Si(CH_3)_3$), 17.6 (CH_2Si), 24.1 (NCH_3), 26.6, 26.8 ($C(CH_3)_2$), 28.3 ($C(CH_3)_3$), 41.8 (C-1), 44.7 (C-6), 53.7 (C-5), 54.5 (C-2), 66.1 (CH_2O), 75.7, 77.4 (C-3, C-4), 76.0 (NCH_2O), 79.8 ($C(CH_3)_3$), 106.1, 106.7 (Cq-Ar), 109.4, 109.8 ($C(CH_3)_2$), 110.2, 120.3, 120.3, 122.1, 122.2, 122.6 (CH-Ar), 126.3, 126.4, 126.6, 127.9 (Cq-Ar), 131.6, 132.4 (CH-Ar), 136.1, 136.3 (Cq-Ar), 155.2 (CO-Boc), 172.3, 172.4 (CO); FAB–MS: *m/z* 756 ($[M + H]^+$, 100%).

3-{1-[(*2S,3R,4R,5S*)-5-(2-Acetamido-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (31b).



30b (117 mg, 0.147 mmol) and TBAF 1 M in THF (1.5 mL, 1.5 mmol, 10 eq) yielded **31b** (50 mg, 60%) as an orange solid; R_f 0.35 (CH_2Cl_2/MeOH, 9/1); ^{1}H NMR ($CDCl_3$) δ: 1.49, 1.50 (2 s, 6 H, C(CH_3)$_2$), 2.00, 2.03 (2 s, 3 H, CH_3CO), 2.58 (t, J = 13.1 Hz, 1 H, H-6ax), 3.00 (m, 1 H, H-5), 3.14 (s, 3 H, NCH_3), 3.40–3.70 (m, 3 H, H-2, H-3, H-4), 4.10–4.40 (m, 2 H, 2 x H-1), 4.50 (m, 1 H, NH), 4.89 (dd, J = 13.6, 3.6 Hz, 1 H, H-6eq), 6.50–7.70 (m, 10 H, H-Ar), 9.18 (s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ: 20.7 (CH$_3$CO), 24.1 (NCH_3), 26.4, 26.8 (C(CH$_3$)$_2$), 41.8 (C-1), 46.0 (C-6), 50.9 (C-5), 56.9 (C-2), 75.7, 78.8 (C-3, C-4), 106.7, 106.8 (Cq-Ar), 108.7, 111.1, 111.5, 111.6, 120.0, 120.6, 121.3, 122.3, 122.8, 125.7 (C(CH$_3$)$_2$, CH-Ar), 126.3, 126.9, 127.1, 127.7 (Cq-Ar), 128.4, 131.5, 131.9 (CH-Ar), 135.5, 135.8 (x 2), 136.3 (Cq-Ar), 170.4 (CO-Ac), 172.2, 172.5 (CO); FAB–MS: *m/z* 568 ([M + H]$^+$, 100%).

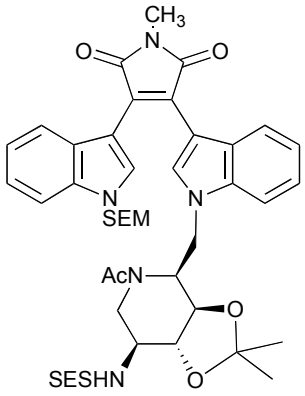
6-Methyl-12-[(*2S,3R,4R,5S*)-5-(2-[trimethylsilyl]ethylsulfonyl)amino-3,4-dihydroxy-piperidin-2-yl-methyl]-6,7,12,13-tetrahydro-5*H*-indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (38b).



37b (110 mg, 0.13 mmol, 1 eq and TBAF 1 M in THF (0.65 mL, 0.65 mmol, 5 eq) yielded **38b** as a yellow solid (84 mg, 75%) after purification by column chromatography (EtOAc/NH_4OH: 100/0.5); R_f 0.35 (EtOAc/NH_4OH: 100/0.5); mp 198–201 °C; ^{1}H NMR (DMF–d_7) δ: 0.09 (s, 9 H, Si(CH_3)$_3$), 1.06 (m, 1 H, CH_2Si), 1.20 (m, 1 H, CH_2Si), 3.09 (m, 1 H, CH_2SO$_2$), 3.19 (s, 3 H, NCH_3), 3.13–3.37 (m, 4 H, CH_2SO$_2$, H-5, 2 x H-6), 3.72 (m, 1 H, H-2), 3.86 (t, J = 7.6 Hz, 1 H, H-4), 3.90 (m, 1 H, H-3), 4.79 (dd,

J = 15.5, 6.5 Hz, 1 H, H-1), 5.02 (d, *J* = 15.5 Hz, 1 H, H-1'), 5.49 (br s, 1 H, OH), 6.85 (d, *J* = 7 Hz 1 H, NH), 7.39 (m, 2 H, H-Ar), 7.58, 7.63 (2 t, *J* = 7.1 Hz, 2 x 1 H, H-Ar), 7.79, 7.86 (2 d, *J* = 7.8 Hz, 2 x 1 H, H-Ar), 9.18 (t, *J* = 8.1 Hz, 2 H, H-Ar), 13.24 (br s, 1 H, NH); ^{13}C NMR (DMF–d_7) δ: –0.7 ($Si(CH_3)_3$), 11.9 (CH_2Si), 24.6 (NCH_3), 44.8 (C-1), 47.9 (C-6), 50.5 (CH_2SO_2), 57.8 (C-5), 60.2 (C-2), 74.1, 74.7 (C-3, C-4), 112.3, 113.8 (CH-Ar), 118.3, 119.1 (Cq-Ar), 122.3 (2 CH-Ar), 123.4, 123.5 (2 Cq-Ar), 126.8, 128.8 (2 CH-Ar), 143.7 (x 2), 144.4 144.5 (Cq-Ar), 172.2 (2 CO); MS (CI): *m/z* 648 ($[M + H]^+$, 100%), HRMS (CI): *m/z* calcd for $C_{32}H_{38}N_5O_6SiS$ $(M + H)^+$, 648.8245, found 648.8248.

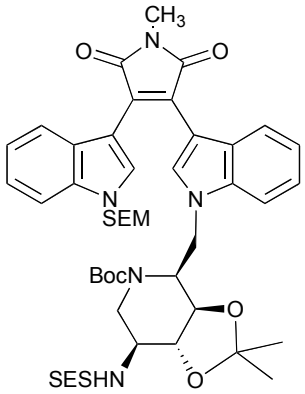
3-{1-[(*2S,3R,4R,5S*)-5-(2-[Trimethylsilyl]ethylsulfonyl)amino-1-acetyl-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1-(2-[trimethylsilyl]ethoxymethyl)-1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (24b).



To a solution of compound **23b** (168 mg, 0.20 mmol, 1.0 eq) in CH_2Cl_2 (8 mL) were added Et_3N (60 µL, 0.43 mmol, 2.1 eq) and Ac_2O (50 µL, 0.53 mmol, 2.6 eq). After stirring at rt for 4 h, the mixture was poured at 0 °C in a solution of saturated NH_4Cl and extracted with EtOAc. The organic layers were then washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was then purified by column chromatography (cyclohexane/EtOAc, 6/4 then 5/5) to yield **24b** as an orange solid (168 mg, 95%); R_f 0.45 (cyclohexane/EtOAc, 5/5); mp 119–122 °C; $[\alpha]_D^{20}$ –75 (*c* 0.25 in CH_2Cl_2); IR (ATR) 3310, 2922, 2851, 1740, 1695, 1537, 1445, 1375, 1263, 1231,1217, 1092; ^{1}H NMR ($CDCl_3$, mixture of rotamers in ~ 2:1 ratio) δ: –0.07, 0.06 (2 s, 18 H, 2 x $Si(CH_3)_3$), 0.85 (m, 2 H, CH_2Si), 1.11 (m, 2 H, CH_2Si), 1.40, 1.44, 1.48 (3 s, 6 H, $C(CH_3)_2$), 1.96, 2.01 (2 s, 3 H, CH_3CO), 2.87 (m, 1 H, H-6ax), 3.05–3.20 (m, 2 H, CH_2SO_2), 3.11, 3.15 (2 s, 3 H, NCH_3), 3.40 (m, 2 H, CH_2O), 3.40–3.85 (m, 3 H, H-3, H-4, H-5), 3.96, 5.09 (2 m, 1 H, H-6eq), 4.07 (m, 1 H, H-1), 4.15–4.50 (m, 1 H, H-1'), 4.53, 5.49 (2 m, 1 H, H-2), 5.36, 5.41 (2 s, 2 H, NCH_2O), 5.75 (m, 1 H, NH), 6.50–7.30 (m, 7 H, H-Ar), 7.37 (d, *J* = 8.1 Hz, 1 H, H-Ar), 7.60–7.75 (m, 2 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: –2.0, –1.5 ($Si(CH_3)_3$), 10.3, 17.5 (CH_2Si), 20.7, 22.0 (CH_3CO), 24.1 (NCH_3), 26.50, 26.7 ($C(CH_3)_2$), 41.4 (C-1, C-6maj), 47.0 (C-6min), 49.5 (C-2maj), 49.8 (CH_2SO_2), 52.8, 53.8 (C-5), 56.3 (C-2 min), 65.8 (CH_2O), 75.6, 75.9 (C-3, C-4), 76.0 (NCH_2O), 106.0, 106.7 (Cq-Ar), 108.7, 109.3, 110.0 (CH-Ar), 110.9 ($C(CH_3)_2$), 111.5, 120.0,

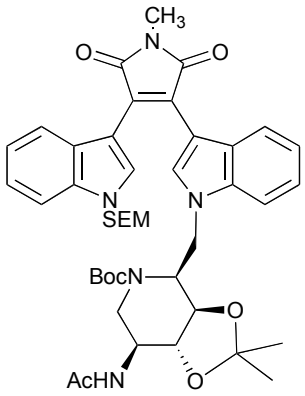
120.4, 120.8, 121.5, 121.7, 122.1, 122.6, 125.8, 126.2, 126.6, 127.0, 131.3, 131.8 (x 2), 135.4, 136.0, 136.1 ($C(CH_3)_2$, CH-Ar, Cq-Ar), 169.9, 170.3 (CO-Ac), 172.2, 172.7 (CO); FAB–MS: *m/z* 861 (M, 100%).

3-{1-[(*2S,3R,4R,5S*)-5-(2-[Trimethylsilyl]ethylsulfonyl)amino-1-(*tert*-butyloxycarbonyl)-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1-(2-[trimethylsilyl]ethoxymethyl)-1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (28b).



To a solution of **23b** (105 mg, 0.13 mmol, 1.0 eq) and DMAP (20 mg, 0.16 mmol, 1.3 eq) in CH_2Cl_2 (2.5 mL) was added at 0 °C a solution of Boc_2O (36 mg, 0.17 mmol, 1.3 eq) of anhydrous CH_2Cl_2 (2.5 mL). After stirring for 15 min at 0 °C and 2 h at rt, the mixture was poured at 0 °C in a solution of saturated NH_4Cl, and extracted with EtOAc. The organic layers were then washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was then purified by column chromatography (cyclohexane/EtOAc: 7/3) to yield **28b** as an orange solid (106 mg, 90%); R_f 0.45 (cyclohexane/EtOAc, 7/3); mp 71–72 °C; $[\alpha]_D^{20}$ –77 (*c* 0.2 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ: –0.05, 0.06 (2 s, 18 H, 2 x $Si(CH_3)_3$), 0.89 (t, *J* = 8.1 Hz, 2 H, CH_2Si), 0.95–1.25 (m, 2 H, CH_2Si), 1.44, 1.45 (2 s, 6 H, $C(CH_3)_2$), 1.55 (s, 9 H, $C(CH_3)_3$), 2.94 (dd, *J* = 13.4, 4.7 Hz, 1 H, H-6ax), 3.16 (s, 3 H, NCH_3), 3.20–3.60 (m, 8 H, CH_2SO_2, CH_2O, H-3, H-4, H-5, H-6eq), 4.10–4.25 (m, 2 H, H-1, H-2), 4.36 (m, 2 H, NH, H-1'), 5.46 (s, 2 H, NCH_2O), 6.69 (t, *J* = 7.5 Hz, 1 H, H-Ar), 6.74 (t, *J* = 7.9 Hz, 1 H, H-Ar), 6.84 (d, *J* = 7.5 Hz, 1 H, H-Ar), 7.06 (d, *J* = 7.7 Hz, 1 H, H-Ar), 7.07 (d, *J* = 8.1 Hz, 2 H, H-Ar), 7.32 (d, *J* = 8.2 Hz, 1 H, H-Ar), 7.42 (d, *J* = 8.2 Hz, 1 H, H-Ar), 7.66 (s, 1 H, H-Ar), 7.75 (s, 1 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: –2.2, –1.5 ($Si(CH_3)_3$), 10.0, 17.6 (CH_2Si), 24.0 (NCH_3), 26.5, 26.8, 27.8 ($C(CH_3)_3$, $C(CH_3)_2$), 42.1 (C-1), 43.1 (C-6), 51.0 (CH_2SO_2), 54.8 (C-5), 60.2 (C-2), 65.9 (CH_2O), 75.9 (NCH_2O), 79.0 (C-3, C-4), 84.7 ($C(CH_3)_3$), 106.0, 106.7 (Cq-Ar), 109.4 ($C(CH_3)_2$), 110.1, 120.2, 122.1, 122.4 (CH-Ar), 126.2, 126.5, 127.9 (Cq-Ar), 131.5, 132.4 (CH-Ar), 136.1, 136.2 (Cq-Ar), 151.1 (CO-Boc), 172.2 (2 CO); FAB–MS: *m/z* 920 ($[M + H]^+$, 100%), 485 ($[M + H]^+$ – piperidine, 55%).

3-{1-[(*2S,3R,4R,5S*)-5-(2-Acetamido-1-(*tert*-butyloxycarbonyl)-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1-(2-[trimethylsilyl]ethoxymethyl)-1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (30b).

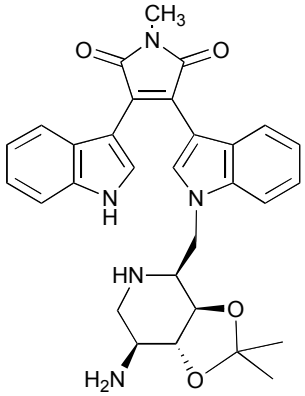


To a solution of **29b** (168 mg, 0.22 mmol, 1.0 eq) in CH_2Cl_2 (10 mL) were added, at 0 °C, Et_3N (60 µL, 0.43 mmol, 1.9 eq) and Ac_2O (50 µL, 0.43 mmol, 1.9 eq). After stirring for 15 min at 0 °C and 2 h at rt, the mixture was poured at 0 °C in a solution of saturated NH_4Cl, and then extracted with EtOAc. The organic layers were then washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was then purified by column chromatography (cyclohexane/EtOAc, 5/5) to yield **30b** as an orange solid (172 mg, 97%); R_f 0.45 (cyclohexane/EtOAc, 5/5); mp 128–130 °C; $[\alpha]_D^{20}$ –78 (*c* 0.26 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ: –0.05 (s, 9 H, $Si(CH_3)_3$), 0.86 (t, J = 7.8 Hz, 2 H, CH_2Si), 1.45 (br s, 15 H, $C(CH_3)_2$, $C(CH_3)_3$), 2.05 (s, 3 H, CH_3CO), 2.65 (dd, J = 12.5, 8.2 Hz, 1 H, H-6ax), 3.16 (s, 3 H, NCH_3), 3.35–3.70 (m, 5 H, CH_2O, H-2, H-3, H-4), 3.90–4.60 (m, 4 H, 2 x H-1, H-5, H-6eq), 5.10 (m, 1 H, NH), 5.41, 5.45 (2 s, 2 H, NCH_2O), 6.50–6.85 (m, 3 H, H-Ar), 6.90–7.15 (m, 3 H, H-Ar), 7.15–7.30 (m, 1 H, H-Ar), 7.39 (d, J = 7.9 Hz, 1 H, H-Ar), 7.64 (s, 1 H, H-Ar), 7.68 (s, 1 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: –1.4 ($Si(CH_3)_3$), 14.0 (CH_2Si), 22.1 (CH_3CO), 24.1 (NCH_3), 26.6, 26.8 ($C(CH_3)_2$), 28.3 ($C(CH_3)_3$), 41.3 (C-1), 45.8 (C-6), 51.7 (C-5), 56.6 (C-2), 65.9 (CH_2O), 75.1, 75.5 (C-3, C-4), 76.0 (NCH_2O), 80.2 ($C(CH_3)_3$), 106.3, 106.8 (Cq-Ar), 108.7, 109.2 (CH-Ar), 110.0 ($C(CH_3)_2$), 111.2, 111.6, 120.0, 120.5, 120.8, 121.6, 121.9, 122.1, 122.3 (CH-Ar), 126.0, 126.9, 127.0, 127.1 (Cq-Ar), 131.6, 131.7 (CH-Ar), 136.0, 136.2 (Cq-Ar), 155.2 (CO-Boc), 169.9 (CO-Ac), 172.2, 172.5 (CO); FAB–MS: *m/z* 820 ([M + Na]$^+$, 100%), 797 (M, 10%).

General procedure for the synthesis of 22b-c, 26b and 5.

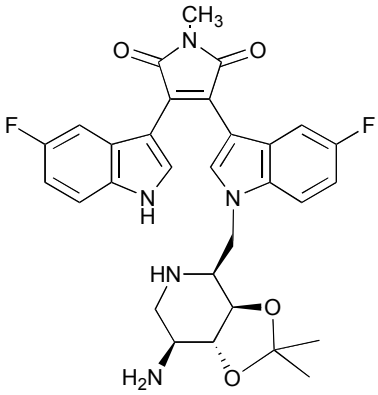
A solution of the reagent (1.0 eq) and CsF (5.0–10.0 eq) in DMF (0.04 M) was heated at 100 °C for 2–15 h. After cooling at 0 °C, the mixture was poured in a 10% aqueous solution of K_2CO_3 then extracted with EtOAc. The organic layers were then washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was then purified by column chromatography (CH_2Cl_2/MeOH: 90/10 to CH_2Cl_2/MeOH/ NH_4OH: 80/20/5) to yield the desired compound and the unreacted starting material.

3-{1-[(*2S,3R,4R,5S*)-5-(2-Amino-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (22b).



20b (180 mg, 0.26 mmol) and CsF (200 mg, 1.32 mmol) for 5 h yielded **22b** (86 mg, 63%) as an orange solid; R_f 0.30 (CH_2Cl_2/MeOH, 9/1); mp 151–155 °C; ^{1}H NMR ($CDCl_3$) δ: 1.45 (s, 6 H, $C(CH_3)_2$), 1.76 (br s, 3 H, NH, NH_2), 2.38 (dd, J = 12.9, J = 10.0 Hz, 1 H, H-6ax), 2.74 (dd, J = 13.0, 4.6 Hz, 1 H, H-6eq), 2.97 (m, 1 H, H-5), 3.16 (s, 3 H, NCH_3), 3.36 (t, J = 9.3 Hz, 1 H, H-4), 3.60 (m, 2 H, H-2, H-3), 4.07 (dd, J = 14.3, 10.0 Hz, 1 H, H-1), 4.33 (d, J = 14.2 Hz, 1 H, H-1'), 6.73 (t, J = 7.5 Hz, 1 H, H-Ar), 6.85 (m, 2 H, H-Ar), 7.00–7.15 (m, 2 H, H-Ar), 7.21 (d, J = 8.2 Hz, 1 H, H-Ar), 7.32 (d, J = 8.6 Hz, 2 H, H-Ar), 7.50 (s, 1 H, H-Ar), 7.71 (d, J = 2.2 Hz, 1 H, H-Ar), 8.69 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ: 24.2 (NCH_3), 26.6, 26.9 ($C(CH_3)_2$), 42.1 (C-1), 46.4 (C-6), 53.6 (C-5), 54.6 (C-2), 79.6, 80.6 (C-3, C-4), 106.2, 107.1 (Cq-Ar), 109.5 (CH-Ar), 109.8 ($C(CH_3)_2$), 111.3, 120.1, 120.4, 121.9, 122.4, 122.5, 122.6 (CH-Ar), 125.1, 126.3, 127.1, 128.1 (Cq-Ar), 128.3, 132.4 (CH-Ar), 136.0, 136.2 (Cq-Ar), 172.4 (2 CO); MS (CI): *m/z* 526 ($[M + H]^+$, 100%).

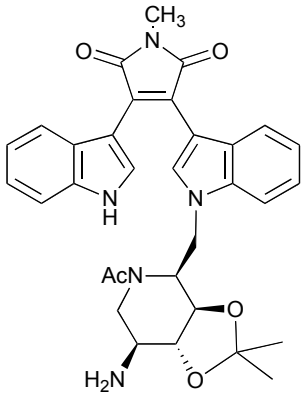
3-{5-Fluoro-1-[(*2S,3R,4R,5S*)-5-(2-amino-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{5-fluoro-1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (22c).



20c (120 mg, 0.16 mmol) and CsF (250 mg, 1.6 mmol) for 15 h yielded **12c** (40 mg, 43%) as an orange solid; R_f 0.20 (CH_2Cl_2/MeOH, 9/1); mp 163–165 °C; $[\alpha]_D^{20}$ –18 (c 0.2 in MeOH); ^{1}H NMR ($CDCl_3$) δ: 1.45 (s, 6 H, $C(CH_3)_2$), 2.10 (br s, 3 H, NH_2, NH), 2.51 (dd, J = 13.2, 10.5 Hz, 1 H, H-6ax), 2.90–3.15

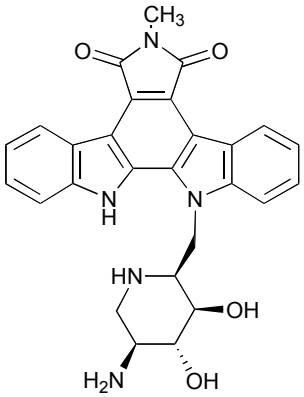
(m, 2 H, H-6eq, H-5), 3.14 (s, 3 H, NCH_3), 3.35–3.65 (m, 3 H, H-2, H-3, H-4), 4.12 (dd, *J* = 14.7, 10.0 Hz, 1 H, H-1), 4.34 (d, *J* = 14.4 Hz, 1 H, H-1'), 6.37 (dd, *J* = 10.3, 2.2 Hz, 1 H, H-Ar), 6.52 (dd, *J* = 10.1, 2.2 Hz, 1 H, H-Ar), 6.70 (td, *J* = 8.7, 2.3 Hz, 1 H, H-Ar), 6.77 (td, *J* = 8.7, 2.3 Hz, 1 H, H-Ar), 7.05–7.25 (m, 2 H, H-Ar), 7.67 (s, 1 H, H-Ar), 7.78 (s, 1 H, H-Ar), 9.16 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$) *δ*: 24.2 (NCH_3), 26.6, 26.9 ($C(CH_3)_2$), 42.6 (C-1), 46.7 (C-6), 54.1 (C-5), 54.7 (C-2), 77.2, 79.6 (C-3, C-4), 105.8 (d, *J* = 4.0 Hz, Cq-Ar), 106.5 (d, *J* = 24.8 Hz, CH-Ar), 106.8 (d, *J* = 25.0 Hz, CH-Ar), 107.1 (d, *J* = 3.6 Hz, Cq-Ar), 109.8 ($C(CH_3)_2$), 110.4 (d, *J* = 10.3 Hz, CH-Ar), 110.7 (d, *J* = 27.1 Hz, CH-Ar), 111.0 (d, *J* = 26.4 Hz, CH-Ar), 112.0 (d, *J* = 9.6 Hz, CH-Ar), 126.0 (d, *J* = 10.8 Hz, Cq-Ar), 126.7 (Cq-Ar), 127.1 (d, *J* = 10.6 Hz, Cq-Ar), 127.4 (Cq-Ar), 129.6 (CH-Ar), 132.4, 132.5 (Cq-Ar), 133.7 (CH-Ar), 157.6 (d, *J* = 235 Hz, CF), 157.8 (d, *J* = 236 Hz, CF), 172.2 (2 CO); FAB–MS: *m/z* 562 ($[M + H]^+$, 100%).

3-{1-[(*2S,3R,4R,5S*)-5-Amino-1-acetyl-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (26b).



25b (75 mg, 0.1 mmol) and CsF (106 mg; 0.7 mmol) for 2 h yielded **26b** (42 mg, 73%) as an orange solid; R_f 0.30 (CH_2Cl_2/MeOH, 9/1); mp 182–186 °C; $[\alpha]_D^{20}$ –58 (*c* 0.2 in CH_2Cl_2); ^{1}H NMR ($CDCl_3$, mixture of rotamers in ~ 2:1 ratio) *δ*: 1.27, 1.51 (2 s, 6 H, $C(CH_3)_2$), 1.30, 2.02 (2 s, 3 H, CH_3CO), 1.61 (s, 2 H, NH_2), 2.55, 2.90 (2 m, 1 H, H-6ax), 3.08 (m, 1 H, H-5), 3.15 (s, 3 H, NCH_3), 3.40–3.65 (m, 2 H, H-3, H-4), 3.75, 4.91 (2 m, 1 H, H-6eq), 4.28 (dd, *J* = 15.2, 9.9 Hz, 1 H, H-1), 4.53, 5.62 (2 m, 2 H, H-1', H-2), 6.55–6.90 (m, 3 H, H-Ar), 6.90–7.20 (m, 3 H, H-Ar), 7.20–7.40 (m, 2 H, H-Ar), 7.55–7.70 (m, 2 H, H-Ar), 8.68, 8.80 (2 s, 1 H, NH); ^{13}C NMR ($CDCl_3$) *δ*: 20.7, 22.2 (CH_3CO), 24.2 (NCH_3), 26.4, 26.6, 26.7, 26.9 ($C(CH_3)_2$), 41.9 (C-1maj, C-6maj), 42.6 (C-1min), 48.4 (C-6min), 50.1 (C-2 maj), 51.0, 52.0 (C-5), 57.0 (C-2min), 75.2, 75.7, 79.3 (C-3, C-4), 106.3, 106.9, 107.0 (Cq-Ar), 108.7, 109.2 (CH-Ar), 111.0 ($C(CH_3)_2$), 111.3, 111.6 (CH-Ar), 120.1, 120.3, 120.6, 121.4 (Cq-Ar), 122.0, 122.4, 122.8, 125.7, 125.9, 126.05, 126.4, 127.0, 127.1, 127.7, 128.2, 128.4, 131.5, 131.9 (CH-Ar), 135.6, 135.7, 135.8, 136.3 (Cq-Ar), 170.3 (CO-Ac), 172.2, 172.3, 172.5, 172.6 (CO); FAB–MS: *m/z* 568 ($[M + H]^+$, 100%).

6-Methyl-12-[(*2S,3R,4R,5S*)-5-(2-amino-3,4-dihydroxy-piperidin-2-yl-methyl]-6,7,12,13-tetrahydro-5*H*-indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (5).

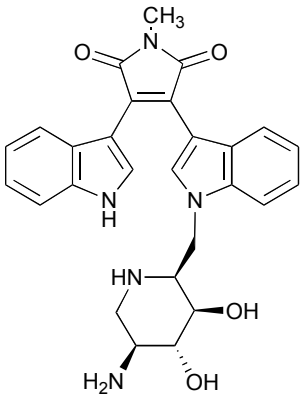


38b (65 mg, 0.1 mmol) and CsF (151.9 mg, 1.0 mmol) for 10 h yielded **5** (48 mg, 71%) as a yellow solid after purification by column chromatography (CH_2Cl_2/MeOH/NH_4OH: 80/20/5); R_f 0.65 (CH_2Cl_2/MeOH/NH_4OH: 70/30/5); mp > 210°C; ^{1}H NMR (DMF–d_7) δ: 3.19 (m, 1 H, H-5), 3.22–3.36 (m, 2 H, 2 x H-6), 3.26 (s, 3 H, NCH_3), 3.76 (m, 1 H, H-2), 3.84 (m, 1 H, H-3), 4.10 (m, 1 H, H-4), 4.99 (m, 1 H, H-1), 5.09 (m, 1 H, H-1'), 7.39 (m, 2 H, H-Ar), 7.56 (m, 1 H, H-Ar), 7.61 (m, 1 H, H-Ar), 7.90 (m, 2 H, H-Ar), 9.18 (d, J = 7.8 Hz, 1 H, H-Ar), 9.20 (d, J = 7.8 Hz, 1 H, H-Ar) ; ^{13}C NMR (DMF–d_7) δ: 24.9 (NCH_3), 45.9 (C-1), 46.3 (C-6), 53.9 (C-5), 58.6 (C-2), 71.3 (C-4), 72.6 (C-3), 112.2, 114.2 (CH-Ar), 118.5, 119.1 (Cq-Ar), 122.2, 122.3, (CH-Ar), 123.4, 123.5, 123.6 (x 2) (Cq-Ar), 126.4, 126.7, 128.7, 128.7, (CH-Ar), 143.5 (x 2), 144.2, 144.4 (Cq-Ar), 172.0 (2 CO); MS (CI): *m/z* 484 ($[M + H]^+$, 100%), HRMS (CI): *m/z* calcd for $C_{27}H_{26}N_5O_4$ $(M + H)^+$, 484.1985, found 484.1982.

General procedure for for the synthesis of 7a-b, 27b, 32b and 37b.

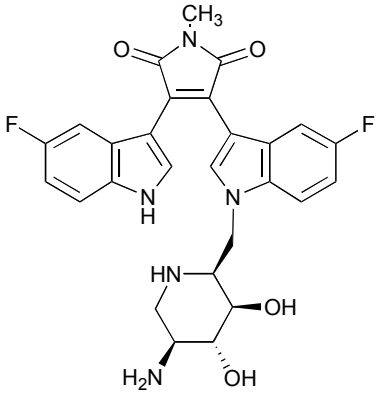
A solution 1 M of the reagent (1.0 eq) in (1 M) HCl–THF or HCl (1 M)–THF–EtOH (1/1/1) or TFA–H_2O (9/1) was stirred at rt for 1 h and concentrated. The residue was poured at 0 °C in a 10% aqueous solution K_2CO_3 then extracted with EtOAc. The organic layers were then washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was then purified by column chromatography (CH_2Cl_2/MeOH/NH_4OH: 80/20/1).

3-{1-[(*2S,3R,4R,5S*)-5-(2-Amino-3,4-dihydroxy-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (7a).



22b (81 mg, 0.154 mmol) yielded **7a** (63 mg, 84%) as a red solid; R_f 0.15 (CH_2Cl_2/MeOH/NH_4OH, 8/2/0.1); mp 185–188 °C; ^{1}H NMR (CD_3OD) δ: 2.74 (d, J = 12.1 Hz, 1 H, H-6ax), 2.85 (m, 2 H, H-5, H-6eq), 2.96 (s, 3 H, NCH_3), 3.33 (m, 1 H, H-2), 3.44 (m, 1 H, H-3), 3.73 (m, 1 H, H-4), 4.08 (dd, J = 13.9, 7.5 Hz, 1 H, H-1), 4.22 (dd, J = 14.2, 6.3 Hz, 1 H, H-1'), 6.45–6.70 (m, 3 H, H-Ar), 6.80–7.05 (m, 3 H, H-Ar), 7.25 (d, J = 8.1 Hz, 1 H, H-Ar), 7.33 (d, J = 8.2 Hz, 1 H, H-Ar), 7.45 (s, 1 H, H-Ar), 7.65 (s, 1 H, H-Ar); ^{13}C NMR (CD_3OD) δ: 24.2 (NCH_3), 45.2 (C-6), 45.8 (C-1), 51.9 (C-5), 55.5 (C-2), 69.9 (C-3, C-4), 107.4, 107.5 (Cq-Ar), 110.7, 112.6, 120.7, 121.1, 122.5, 122.8 (x 2), 123.3 (CH-Ar), 126.5, 127.8, 127.9, 129.4 (Cq-Ar), 130.3, 133.1 (CH-Ar), 137.7, 137.8 (Cq-Ar), 173.9, 174.0 (CO); MS (CI): m/z 486 ($[M + H]^+$, 100%); HRMS (CI): m/z calcd for $C_{27}H_{28}N_5O_4$ $(M + H)^+$ 486.2141, found 486.2137.

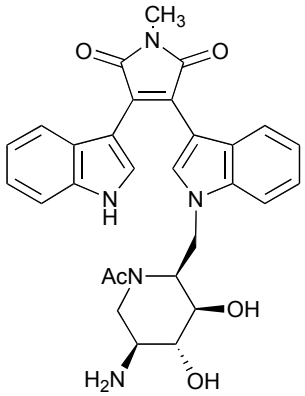
3-{5-Fluoro-1-[(*2S,3R,4R,5S*)-5-(2-amino-3,4-dihydroxy-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{5-fluoro-1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (7b).



22c (50 mg, 0.09 mmol) yielded **7b** (35 mg, 74%) as a red solid; R_f 0.15 (CH_2Cl_2/MeOH/NH_4OH, 8/2/0.1); mp 176–180 °C; $[\alpha]_D^{20}$ +11 (c 0.25 in MeOH); ^{1}H NMR (CD_3OD) δ: 2.65–2.80 (m, 2 H, H-6ax, H-5), 2.98 (dd, J = 14.6, 5.0 Hz, 1 H, H-6eq), 3.03 (s, 3 H, NCH_3), 3.30–3.50 (m, 2 H, H-2, H-3), 3.61 (t, J = 4.8 Hz, 1 H, H-4), 4.21 (dd, J = 14.3, 7.9 Hz, 1 H, H-1), 4.35 (dd, J = 14.3, 6.2 Hz, 1 H, H-1'), 6.33 (dd, J = 10.5, 2.1 Hz, 1 H, H-Ar), 6.39 (dd, J = 10.3, 2.1 Hz, 1 H, H-Ar), 6.60–6.85 (m, 2 H, H-Ar), 7.25 (dd, J = 8.8, 4.5 Hz, 1 H, H-Ar), 7.37 (dd, J = 8.9, 4.3 Hz, 1 H, H-Ar), 7.69 (s, 1 H, H-Ar), 7.75 (s, 1 H, H-Ar); ^{13}C NMR (CD_3OD) δ: 24.2 (NCH_3), 46.8 (C-1, C-6), 52.9 (C-5), 56.5 (C-2), 71.1

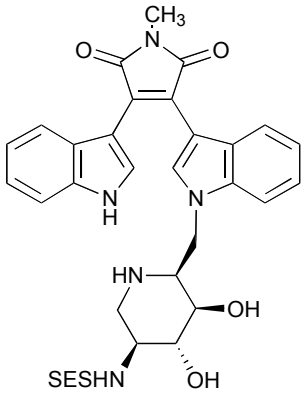
(C-3), 72.4 (C-4), 107.0 (d, J = 25.0 Hz, CH-Ar), 107.1 (d, J = 4.5 Hz, Cq-Ar), 107.5 (d, J = 4.3 Hz, Cq-Ar), 107.6 (d, J = 25.2 Hz, CH-Ar), 111.3 (d, J = 26.5 Hz, CH-Ar), 111.4 (d, J = 26.6 Hz, CH-Ar), 112.0 (d, J = 9.8 Hz, CH-Ar), 113.4 (d, J = 9.8 Hz, CH-Ar), 127.4 (d, J = 10.6 Hz, Cq-Ar), 127.6 (Cq-Ar), 128.32 (d, J = 10.7 Hz, Cq-Ar), 128.6 (Cq-Ar), 131.8, (CH-Ar), 134.2 (2 Cq-Ar), 134.9 (CH-Ar), 158.8 (d, J = 234 Hz, CF), 159.1 (d, J = 235 Hz, CF), 173.6, 173.7 (CO); MS (CI): *m/z* 522 ($[M + H]^+$, 100%), 391 ($[M + H]^+$ – piperidine, 30%); HRMS (CI): *m/z* calcd for $C_{27}H_{26}F_2N_5O_4$ $(M + H)^+$ 522.1953, found 522.1951.

3-{1-[(*2S,3R,4R,5S*)-5-Amino-1-acetyl-3,4-dihydroxy-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (27b).



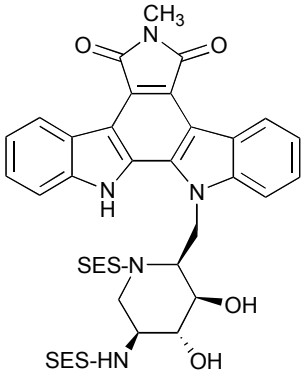
26b (42 mg, 0.075 mmol) yielded **27b** (12.5 mg, 32%) as a red solid; R_f 0.30 (CH_2Cl_2/MeOH, 8/2); mp 194–196 °C; $[\alpha]_D^{20}$ –85 (*c* 0.1 in CH_2Cl_2); ^{1}H NMR (CD_3OD, mixture of rotamers in ~ 2:1 ratio) δ: 1.99, 2.14 (2 s, 3 H, CH_3CO), 2.98, 3.95 (2 m, 1 H, H-6ax), 3.04, 3.34 (2 m, 1 H, H-5), 3.09 (s, 3 H, NCH_3), 3.50–3.80 (m, 2 H, H-3, H-4), 4.30–4.90 (m, 3 H, H-6eq, H-1, H-2min), 5.24 (m, 1 H, H-2maj), 6.45–7.10 (m, 6 H, H-Ar), 7.25–7.45 (m, 2 H, H-Ar), 7.65–7.80 (m, 2 H, H-Ar); ^{13}C NMR ($CDCl_3$) δ: 20.6, 20.7 (CH_3CO), 24.2 (NCH_3), 42.1, 42.5 (C-1, C-6), 54.5 (C-5), 60.7, 60.8 (C-2), 72.2, 72.9 (C-3, C-4), 107.4, 107.6, 107.7, 107.9, 110.3, 110.4, 112.3, 112.5, 120.8, 121.3, 122.2, 122.6, 123.0, 123.1, 123.4, 123.6, 127.3, 127.4, 127.7, 127.8, 127.9, 129.0, 130.0, 133.1, 137.2, 137.6, 137.7, 137.8 (CH-Ar, Cq-Ar), 172.4, 172.5, 173.8, 174.0 (CO); FAB–MS: *m/z* 528 ($[M + H]^+$, 100%); HRMS (FAB): *m/z* calcd for $C_{29}H_{30}N_5O_5$ $(M + H)^+$ 528.2247, found 528.2235.

3-{1-[(*2S,3R,4R,5S*)-5-(2-[Trimethylsilyl]ethylsulfonyl)amino-3,4-dihydroxy-piperidin-2-yl-methyl]-1*H*-indol-3-yl}-4-{1*H*-indol-3-yl}-1-methyl-1*H*-pyrrole-2,5-dione (32b).



20b (69 mg, 0.10 mmol) yielded **32b** (70 mg, 100%) as an orange solid; R_f 0.28 (CH_2Cl_2/MeOH, 95/5); mp 240–243 °C; UV/Vis (MeOH): λ_{max} (ε) = 210 (22105), 277 (6261), 375 (2657), 469 (3780); ^{1}H NMR (CD_3OD) δ: 0.06 (s, 9 H, $Si(CH_3)_3$), 1.06 (m, 2 H, CH_2Si), 2.80 (dd, J = 13.1, 4.5 Hz, 1 H, H-6ax), 2.90–3.10 (m, 3 H, CH_2SO_2, H-6eq), 3.09 (s, 3 H, NCH_3), 3.27 (m, 1 H, H-5), 3.42 (m, 1 H, H-2), 3.49 (m, 1 H, H-3), 3.72 (t, J = 4.8 Hz, 1 H, H-4), 4.19 (dd, J = 14.2, 7.6 Hz, 1 H, H-1), 4.36 (dd, J = 14.2, 6.5 Hz, 1 H, H-1'), 6.61 (t, J = 7.4 Hz, 1 H, H-Ar), 6.65–6.80 (m, 2 H, H-Ar), 6.90–7.10 (m, 3 H, H-Ar), 7.32 (d, J = 8.2 Hz, 1 H, H-Ar), 7.41 (d, J = 8.1 Hz, 1 H, H-Ar), 7.57 (s, 1 H, H-Ar), 7.76 (s, 1 H, H-Ar); ^{13}C NMR (CD_3OD) δ: –2.0 ($Si(CH_3)_3$), 11.5 (CH_2Si), 24.2 (NCH_3), 46.4, 47.2 (C-1, C-6), 50.3 (CH_2SO_2), 54.8, 55.8 (C-5, C-2), 70.4, 71.3 (C-3, C-4), 107.4, 107.5 (Cq-Ar), 110.8, 112.6 (CH-Ar), 120.7, 121.1, 122.5, 123.0, 123.1, 123.3 (CH-Ar), 126.6, 127.9, 127.9, 129.5 (Cq-Ar), 130.3, 133.2 (CH-Ar), 137.7, 137.8 (Cq-Ar), 173.9, 174.1 (CO); MS (CI): *m/z* 650 ($[M + H]^+$, 100%), HRMS (CI): *m/z* calcd for $C_{32}H_{40}N_5O_6SiS$ $(M + H)^+$, 650.2469, found 650.2471.

6-Methyl-12-[(*2S,3R,4R,5S*)-5-(2-[trimethylsilyl]ethylsulfonyl)amino-1-(2-[trimethylsilyl]ethylsulfonyl)-3,4-dihydroxy-piperidin-2-yl-methyl]-6,7,12,13-tetrahydro-5*H*-indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (37b).



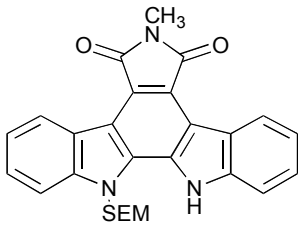
36b (100 mg, 0.12 mmol, 1 eq) in 1 M HCl/THF 1/1 yielded **37b** as a yellow solid (86 mg, 91%); R_f 0.35 (CH_2Cl_2/MeOH, 9/1); mp 188–190 °C; IR (ATR) 3422, 3252, 2924, 1693, 1630, 1574, 1462, 1412, 1379, 1327, 1251, 1136, 1085; ^{1}H NMR (DMF–d_7) δ: –0.30, 0.14 (2 s, 18 H, 2 x $Si(CH_3)_3$), 0.34 (m, 2

H, CH_2Si), 1.09, 1.30 (2 m, 2 H, CH_2Si), 1.31 (s, 2 H, 2 x OH), 2.07, 2.35 (m, 2 H, CH_2SO_2), 3.25 (s, 3 H, NCH_3), 3.32 (m, 2 H, CH_2SO_2), 3.70–4.30 (m, 5 H, H-3, H-4, H-5, 2 x H-6), 4.75 (m, 1 H, H-2), 5.13 (m, 1 H, H-1), 5.29 (m, 1 H, H-1'), 5.91 (br s, 1 H, NH), 7.11 (s, 1 H, H-Ar), 7.46 (m, 2 H, H-Ar), 7.55–7.95 (m, 4 H, H-Ar), 9.24 (s, 2 H, H-Ar, NH) ; ^{13}C NMR (DMF–d_7) δ: –2.0, –1.5 ($Si(CH_3)_3$), 10.4, 11.4 (CH_2Si), 24.2 (NCH_3), 40.7 (C-1), 46.1 (C-6), 49.8, 50.0 (CH_2SO_2), 57.4, 60.6 (C-5, C-2), 73.6, 74.0 (C-3, C-4), 110.5, 112.7, 117.6, 118.2, 120.7, 121.5, 121.7, 122.3, 125.7, 126.2, 128.1, 128.3, 129.5, 142.3, 143.0 (CH-Ar, Cq-Ar), 170.9 (2 CO); FAB–MS: *m/z* 811 (M, 60%), 352 (M – piperidine, 100%).

General procedure for the synthesis of 12a, 21a and 36b.

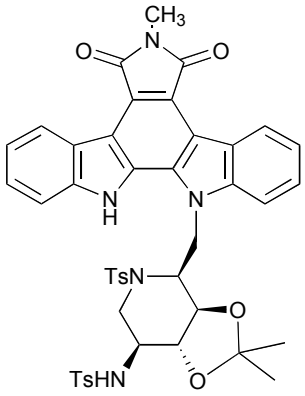
A solution of bis-indolylmaleimide (1.0 eq) and $Pd(CF_3COO)_2$ (2.5 eq) was stirred at 90 °C for 20–30 min according to TLC analysis. After cooling, the mixture was poured in a solution of saturated NH_4Cl and extracted with EtOAc. The organic layers were then washed with brine, dried over $MgSO_4$, filtered and concentrated. The residue was then purified by column chromatography (cyclohexane/EtOAc, 8/2 to 7/3).

6-Methyl-12-[1-{2-(trimethylsilyl)ethoxymethyl}]-6,7,12,13-tetrahydro-5*H*-indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (12a).



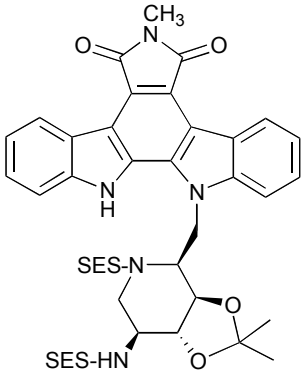
11a (500 mg, 1.06 mmol) and $Pd(CF_3COO)_2$ (881 mg, 2.65 mmol) yielded **12a** (378 mg, 76%) as a yellow solid; R_f 0.6 (cyclohexane/EtOAc, 7/3); mp 214 °C; IR (ATR) 3378, 3054, 2950, 2891, 1749, 1698, 1612, 1576, 1498, 1475, 1458, 1412, 1375, 1329, 1283, 1271, 1243, 1210, 1153, 1117, 1071; ^{1}H NMR ($CDCl_3$) δ: –0.04 (s, 9 H, $Si(CH_3)_3$), 0.95 (t, J = 8.2 Hz, 2 H, CH_2Si), 3.01 (s, 3 H, NCH_3), 3.70 (t, J = 8.2 Hz, 2 H, CH_2O), 5.74 (s, 2 H, NCH_2O), 7.25–7.60 (m, 6 H, H-Ar), 9.12 (t, J = 8.2 Hz, 2 H, H-Ar), 9.76 (s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ: –1.5 ($Si(CH_3)_3$), 17.7 (CH_2Si), 22.6 (NCH_3), 66.1 (CH_2O), 73.4 (NCH_2O), 107.9, 110.8 (CH-Ar), 116.7, 116.9, 118.4, 119.5 (Cq-Ar), 120.5, 120.8 (CH-Ar), 121.6 (2 Cq-Ar), 125.0, 125.3 (CH-Ar), 126.8 (x 2), 128.8, 140.2, 140.8 (Cq-Ar), 168.9 (2 CO).

6-Methyl-12-[(*2S,3R,4R,5S*)-5-(*para*-toluenesulfonyl)amino-1-(*para*-toluenesulfonyl)-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-6,7,12,13-tetrahydro-5*H*-indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (21a).



20a (84 mg, 0.1 mmol) and $Pd(CF_3COO)_2$ (83 mg, 0.25 mmol) for 20–30 min yielded **21a** (48 mg, 57%) as a yellow solid; R_f 0.45 (cyclohexane/EtOAc, 5/5); mp >200 °C; $[\alpha]_D^{20}$ +120 (*c* 0.25 in THF); IR (ATR) 3395, 3287, 2922, 2847, 1748, 1695, 1597, 1576, 1456, 1412, 1375, 1325, 1290, 1229, 1153, 1084, 1045; ^{1}H NMR (CD_3COCD_3) δ: 1.52, 1.75 (2 s, 6 H, $C(CH_3)_2$), 2.17, 2.33 (2 s, 6 H, 2 x CH_3), 2.86 (s, 3 H, NCH_3), 3.34 (m, 2 H, H-5, H-6ax), 3.49 (m, 1 H, H-3), 3.91 (m, 1 H, H-4), 4.05–4.50 (m, 3 H, 2 x H-1, H-6eq), 4.68 (m, 1 H, H-2), 6.70 (d, *J* = 7.8 Hz, 2 H, H-Ar), 6.88 (d, *J* = 7.8 Hz, 2 H, H-Ar), 7.22 (m, 2 H, N*H*Ts, H-Ar), 7.25–7.65 (m, 7 H, H-Ar), 7.83 (d, *J* = 7.7 Hz, 2 H, H-Ar), 9.03 (m, 2 H, H-Ar), 9.97 (br s, 1 H, NH); ^{13}C NMR (CD_3COCD_3) δ: 21.3, 21.4 (CH_3), 23.5 (NCH_3), 27.0, 27.3 ($C(CH_3)_2$), 40.4 (C-1), 45.4 (C-6), 54.6 (C-5), 57.5 (C-2), 76.4, 76.5 (C-3, C-4), 109.8, 111.9, 112.9, 120.0, 121.3, 121.4, 122.2, 122.3, 125.9, 127.0, 127.7, 127.9, 128.4, 130.0, 130.5, 136.6, 139.5, 141.6, 144.2, 144.4 ($C(CH_3)_2$, CH-Ar, Cq-Ar), 170.1 (2 CO); MS (CI): *m/z* 849 ($[M + NH_4]^+$, 60%), 832 ($[M + H]^+$, 100%); HRMS (CI): *m/z* calcd for $C_{44}H_{42}N_5O_8S_2$ $(M + H)^+$ 832.248, found 832.247.

6-Methyl-12-[(*2S,3R,4R,5S*)-5-(2-[trimethylsilyl]ethylsulfonyl)amino-1-(2-[trimethylsilyl]ethylsulfonyl)-3,4-*O*-isopropylidene-piperidin-2-yl-methyl]-6,7,12,13-tetrahydro-5*H*-indolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (36b).



35b (260 mg, 0.30 mmol) and $Pd(CF_3COO)_2$ (250 mg, 0.75 mmol) yielded **36b** (155 mg, 60%) as a yellow solid; R_f 0.60 (cyclohexane/EtOAc, 5/5); mp 176–180 °C; $[\alpha]_D^{20}$ +44 (*c* 0.26 in CH_2Cl_2); IR (ATR) 3565, 3377, 2923, 2854, 1751, 1698, 1577, 1458, 1411, 1376, 1332, 1250, 1140, 1089; ^{1}H NMR

($CDCl_3$) δ: –0.58, 0.06 (2 s, 18 H, 2 x $Si(CH_3)_3$), 0.20 (t, J = 12.1 Hz, 1 H, CH_2Si), 0.43 (t, J = 13.1 Hz, 1 H, CH_2Si), 1.18 (m, 2 H, CH_2Si), 1.45, 1.79 (m, 2 H, CH_2SO_2), 1.66, 1.91 (2 s, 6 H, $C(CH_3)_2$), 3.00 (s, 3 H, NCH_3), 3.20 (m, 2 H, CH_2SO_2), 3.28 (m, 1 H, H-6ax), 3.45–4.05 (m, 5 H, 2 x H-1, H-3, H-4, H-5), 4.10 (m, 1 H, H-2), 4.54 (d, J = 11.4 Hz, 1 H, H-6eq), 5.75 (br s, 1 H, NH), 7.25 (m, 1 H, H-Ar), 7.45 (m, 3 H, H-Ar), 7.61 (m, 2 H, H-Ar), 8.64 (d, J = 7.7 Hz, 1 H, H-Ar), 9.18 (d, J = 7.8 Hz, 1 H, H-Ar), 9.25 (br s, 1 H, NH); ^{13}C NMR ($CDCl_3$) δ: –2.8, –2.0 ($Si(CH_3)_3$), 9.3, 10.5 (CH_2Si), 23.4 (NCH_3), 27.2, 27.4 ($C(CH_3)_2$), 38.3 (C-1), 45.6 (C-6), 49.5, 49.8 (CH_2SO_2), 54.6 (C-5), 57.8 (C-2), 75.3, 75.6 (C-3, C-4), 108.0, 110.3 (CH-Ar), 112.0 ($C(CH_3)_2$), 115.4, 118.1, 119.1, 119.7 (Cq-Ar), 120.7, 121.2, 121.3, 125.6, 126.2 (CH-Ar), 127.0, 127.2 (Cq-Ar), 127.6 (CH-Ar), 140.3, 140.5 (Cq-Ar), 168.3, 169.1 (CO); FAB–MS: *m/z* 874 ($[M + Na]^+$, 50%), 851 (M, 20%), 352 (M – piperidine, 100%).

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