Supporting Information:

An Effective Strategy for the Preparation of Indolecarbazole Aglycons and Glycosides: Total Synthesis of Tjipanazoles B, D, E, and I

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Melting points are uncorrected. All solvents and reagents were used as received from commercial sources. Analytical samples were obtained by chromatography on silica gel using an ethyl acetate-hexane mixture as the eluent unless specified otherwise. Elemental analyses were performed by Quantitative Technologies, Inc., Whitehouse, NJ. Water content (KF) was determined by Karl Fisher titration on a Metrohm 737 KF coulometer.

General Procedure for the Preparation of Nitrostyrenes. To a mixture of (6.15 mmol) of the appropriate TMS-nitro compound and (5.13 mmol) of the appropriate substituted-2-indolecarboxaldehyde in 35 mL of THF was added 1.23 mL (1.23 mmol) of a 1 M solution of TBAF in THF. The solution was stirred at rt for 30 min and 1.55 g (7.38 mmol) of TFAA was added in one portion. After stirring at rt for 30 min, 2.81 g (18.5 mmol) of DBU was added and the mixture heated to 60 °C for 15 min and then cooled to rt. The reaction mixture was diluted with 75 mL of brine and 75 mL of isopropylacetate and the layers separated. The organic layer was washed with 50 mL of water and dried over MgSO₄. The solvent was removed under reduced pressure and the

residue purified by either silica gel chromatography or crystallization from MTBE/hexane.

2-[*trans*-2-(5-Chloro-2-nitrophenyl)vinyl]-1-(phenylsulfonyl)-1*H*-indole (10).

According the general procedure, treatment of 1.5 grams (6.15 mmol) of **7**¹ and 1.46 g (5.13 mmol) of 1-phenylsulfonyl-2-indolecarboxaldehyde (**8**) with 1.23 mL of TBAF gave 1.92 g (85%) of **10** as yellow solid: mp 180-181 °C; ¹H NMR (CDCl₃, 400 MHz) δ 6.92 (s, 1H), 7.24-7.50 (m, 8H), 7.77 (m, 4H), 8.00 (d, 1H, *J* = 8.8 Hz), 8.21 (d, 1H, *J* = 8.4 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 111.4, 115.4, 121.3, 124.5, 125.2, 125.7, 126.1, 126.5, 126.7, 128.6, 128.7, 129.2, 130.0, 134.0, 134.4, 137.4, 137.8, 137.9, 138.4, 140.1, 146.1. Anal. Calcd. For C₂₂H₁₅ClN₂O₄S: C, 60.21; H, 3.44; N, 6.38. Found: C, 59.89; H, 3.23; N, 6.26.

2-[*trans*-2-(5-Methoxy-2-nitrophenyl)vinyl]-1-(phenylsulfonyl)-1*H*-indole (12).

According to the general procedure, treatment of 810 mg (4.00 mmol) of 4-nitro-3-trimethylsilylmethylanisole² and 950 mg (3.33 mmol) of **8** with 0.8 mL of TBAF gave 870 mg (60%) of **12** as a yellow solid: mp 173-174 °C; ¹H NMR (CDCl₃, 400 MHz) δ

3.98 (s, 3H), 6.91 (s, 1H), 6.93 (dd, 1H, $J = 9.1$ and 2.8 Hz), 7.25 (m, 2H), 7.36 (m, 3H), 7.47 (m, 2H), 7.60 (d, 1H, $J = 15.9$ Hz), 7.76 (m, 3H), 8.13 (d, 1H, $J = 9.1$ Hz), 8.20 (d, 1H, $J = 8.4$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 56.1, 110.9, 113.5, 114.0, 115.3, 121.2, 123.9, 124.4, 125.4, 126.7, 127.8, 128.7, 129.2, 130.2, 133.9, 135.7, 137.9, 138.9, 163.6. Anal. Calcd. For $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_5\text{S}$: C, 63.58; H, 4.18; N, 6.45. Found: C, 63.39; H, 3.87; N, 6.35.

2-[*trans*-2-(5-{[4-(methanesulfonyl)piperazin-1-yl]methyl}-2-nitrophenyl)vinyl]-1-(phenylsulfonyl)-1H-indole (14). To a stirred solution of 4.50 g (20.8 mmol) of 4-nitrobenzyl bromide in 42 mL of THF was added 2.11 g (20.8 mmol) of NEt_3 followed by 3.76 g (23.0 mmol) of 1-methanesulfonylpiperazine³ in 20 mL of THF. The resulting slurry was stirred at rt for 6 h, diluted with 30 mL of isopropyl acetate, and washed with 20 mL of water. The organic layer was separated and concentrated to a final volume of 20 mL at which point the product began to precipitate. To the slurry of the product was added 50 mL of heptane and the product was collected by filtration to give 5.42 g (87%) of 1-methanesulfonyl-4-(4-nitrobenzyl)-piperazine as a colorless solid: mp 116-117 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 2.58 (m, 4H), 2.80 (s, 3H), 3.27 (m, 4H), 3.65 (s, 2H), 7.51 (d, 2H, $J = 8.8$ Hz), 8.18 (d, 2H, $J = 8.8$ Hz); ^{13}C NMR (CDCl_3 , 100 MHz) δ 34.5, 46.0, 52.6, 61.8, 123.8, 129.6, 145.7, 147.5; Anal. Calcd. For $\text{C}_{12}\text{H}_{17}\text{N}_3\text{O}_4\text{S}$: C, 48.15; H, 5.72; N, 14.04. Found: C, 48.16; H, 5.52; N, 13.91.

To a solution of 7.00 g (23.4 mmol) of the above nitro compound in 130 mL of THF at $-25\text{ }^{\circ}\text{C}$ was added dropwise 30 mL (30.4 mmol, 1M solution in THF) of trimethylsilylmethylmagnesium chloride at such a rate that the internal temperature did not rise above $-15\text{ }^{\circ}\text{C}$. After stirring at $-20\text{ }^{\circ}\text{C}$ for 15 min, 6.4 g (28.2 mmol) of DDQ in 20 mL of THF was added and the reaction mixture allowed to warm to $10\text{ }^{\circ}\text{C}$ over 2 h. The reaction mixture was diluted with 100 mL of isopropyl acetate and washed with 100 mL sat. NaHCO_3 (3X) and concentrated under reduced pressure to afford 7.85 g (95%) of 1-methanesulfonyl-4-(4-nitro-3-trimethylsilylmethyl-benzyl)-piperazine as a dark solid which could be used in the next reaction without any further purification. An analytical sample could be obtained by crystallization from EtOAc/hexane: mp $57\text{--}58\text{ }^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz) δ -0.01 (s, 9H), 2.57 (m, 4H), 2.59 (s, 2H), 2.79 (s, 3H), 3.25 (m, 4H), 3.55 (s, 2H), 7.11 (s, 1H), 7.16 (d, 1H, $J = 8.4\text{ Hz}$), 7.90 (d, 1H, $J = 8.4\text{ Hz}$); ^{13}C NMR (CDCl_3 , 100 MHz) δ -1.40, 25.0, 34.4, 45.9, 52.4, 61.7, 125.3, 125.5, 131.7, 137.8, 143.2, 146.9; Anal. Calcd. For $\text{C}_{16}\text{H}_{27}\text{N}_3\text{O}_4\text{SSi}$: C, 49.84; H, 7.06; N, 10.90. Found: C, 49.62; H, 7.08; N, 10.82.

According to the general procedure, treatment of 920 mg (2.40 mmol) of the above TMS-nitro compound and 570 mg (2.00 mmol) of **8** with 0.48 mL of TBAF gave 720 mg (62%) of **14** as a light yellow solid: mp $179\text{--}180\text{ }^{\circ}\text{C}$; ^1H NMR (CDCl_3 , 400 MHz) δ 2.65 (m, 4H), 2.80 (s, 3H), 3.32 (m, 4H), 3.70 (s, 2H), 6.91 (s, 1H), 7.25-7.54 (m, 8H), 7.74 (d, 2H, $J = 8.3\text{ Hz}$), 7.78 (d, 1H, $J = 16.0\text{ Hz}$), 7.88 (s, 1H), 8.00 (d, 1H, $J = 8.3\text{ Hz}$), 8.18 (d, 1H, $J = 8.4\text{ Hz}$); ^{13}C NMR (CDCl_3 , 100 MHz) δ 34.2, 46.0, 52.4, 61.4, 110.9, 115.3, 121.2, 124.1, 124.5, 125.2, 125.5, 126.7, 127.4, 128.6, 129.2, 130.1, 132.9, 134.0,

137.6, 137.8, 138.9, 144.6, 146.9. Anal. Calcd. For $C_{28}H_{28}N_4O_6S_2 \cdot H_2O$: C, 56.17; H, 5.05; N, 9.36. Found: C, 55.80; H, 5.31; N, 9.09.

2-[*trans*-2-(5-Chloro-2-nitrophenyl)vinyl]-5-chloro-1-(phenylsulfonyl)-1*H*-indole

(17). To a solution of 22 mL of LDA (44.2 mmol, 2M in THF) in 14 mL of THF at -40 °C was added dropwise 9.90 g (34.0 mmol) of 1-benzenesulfonyl-5-chloroindole⁴ in 35 mL of THF. The reaction mixture was warmed to 0 °C and stirred for 3 h. The reaction mixture was cooled to -20 °C and then 5.25 mL of DMF was added in one portion. The reaction mixture was warmed to rt and quenched with 100 mL of 0.25 N HCl and extracted with 250 mL of CH_2Cl_2 . The extracts were washed with 75 mL of water and 75 mL of brine and dried over $MgSO_4$. The solvent was removed under reduced pressure to give 10.00 g (92%) of **16** which was sufficiently pure for use in the next reaction: 1H NMR ($CDCl_3$, 400 MHz) δ 7.37 (s, 1H), 7.43 (m, 3H), 7.58 (m, 2H), 7.76 (d, 2H, $J = 7.7$ Hz), 8.16 (d, 1H, $J = 9.1$ Hz), 10.50 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 116.5, 117.9, 123.0, 122.7, 129.2, 129.3, 129.6, 130.8, 134.7, 136.7, 137.4, 138.7, 182.9.

According to the general procedure, treatment of 2.00 g (8.20 mmol) of **7** and 2.10 g (6.57 mmol) of **16** with 1.60 mL of TBAF afforded 1.68 g (52%) of **17** as a yellow solid: mp 179 - 180 °C; 1H NMR ($CDCl_3$, 400 MHz) δ 6.84 (s, 1H), 7.31 (dd, 1 $J = 8.9$ and 2.1 Hz), 7.42 (d, 1H, $J = 16.0$ Hz), 7.45 (m, 4H), 7.53 (dt, 1H, $J = 7.4$ and 1.2 Hz), 7.75 (m, 3H), 7.76 (d, 1H, $J = 16.0$ Hz), 8.03 (d, 1H, $J = 8.9$ Hz), 8.14 (d, 1H, $J = 9.0$ Hz); ^{13}C

NMR (CDCl₃, 100 MHz) δ 110.3, 116.4, 120.8, 124.6, 125.8, 126.5, 126.7, 127.1, 128.7, 128.8, 129.4, 130.3, 131.2, 134.2, 134.3, 136.0, 137.7, 139.7, 140.2, 146.1. Anal. Calcd. For C₂₂H₁₄Cl₂N₂O₄S: C, 55.82; H, 2.98; N, 5.92. Found: C, 55.43; H, 2.91; N, 5.70.

2-[*trans*-2-(5-Methoxy-2-nitrophenyl)vinyl]-1-methyl-1*H*-indole (20). According to the general procedure, treatment of 1.50 g (7.38 mmol) of 4-nitro-3-trimethylsilylmethylanisole² and 0.98 g (6.15 mmol) of 1-methylindole-2-carboxaldehyde with 1.50 mL of TBAF gave 0.731 g (43%) of **20** as an orange solid: mp 109-110 °C; ¹H NMR (CDCl₃, 400 MHz) δ 3.80 (s, 3H), 3.94 (s, 3H), 6.84 (dd, 1H, *J* = 9.1 and 2.6 Hz), 6.88 (s, 1H), 7.07 (d, 1H, *J* = 15.9 Hz), 7.14 (m, 2H), 7.29 (m, 2H), 7.63 (d, 1H, *J* = 7.7 Hz), 7.97 (d, 1H, *J* = 15.9 Hz), 8.07 (d, 1H, *J* = 9.1 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 30.2, 56.0, 101.5, 109.4, 112.8, 112.9, 120.2, 120.9, 122.3, 122.6, 126.1, 127.8, 127.9, 136.0, 137.4, 138.7, 141.0, 163.3. Anal. Calcd. For C₁₈H₁₆N₂O₃: C, 70.12; H, 5.23; N, 9.03. Found: C, 70.02; H, 5.26; N, 9.09.

2-[*trans*-2-(5-Chloro-2-nitrophenyl)vinyl]-1-benzyl-1*H*-indole (23). According to the general procedure, treatment of 5.00 g (20.5 mmol) of **7** and 3.86 g (16.4 mmol) of 1-

benzylindole-2-carboxaldehyde⁵ with 4.00 mL of TBAF afforded 1.60 g (25%) of **23** as an orange solid: mp 116-117 °C; ¹H NMR (CDCl₃, 400 MHz) δ 5.50 (s, 2H), 7.01 (s, 1H), 7.05 (d, 1H, *J* = 15.9 Hz), 7.11 (m, 2H), 7.17 (m, 1H), 7.23 (m, 1H), 7.32 (m, 5H), 7.50 (d, 1H, *J* = 2.2 Hz), 7.61 (d, 1H, *J* = 15.9 Hz), 7.69 (d, 1H, *J* = 7.7 Hz), 7.92 (d, 1H, *J* = 8.7 Hz); ¹³C NMR (CDCl₃, 100 MHz) δ 47.1, 102.7, 109.8, 120.7, 121.2, 123.2, 123.6, 123.9, 126.1, 126.5, 127.7, 127.9, 128.0, 129.1, 134.8, 136.8, 137.6, 138.7, 139.6, 145.9. Anal. Calcd. For C₂₃H₁₇ClN₂O₂: C, 71.04; H, 4.41; N, 7.20. Found: C, 70.71; H, 4.17; N, 7.09.

3-[*trans*-2-(5-Chloro-2-nitrophenyl)vinyl]-1-(phenylsulfonyl)-1*H*-indole (26).

According to the general procedure, treatment of 554 mg (2.27 mmol) of **7** and 540 mg (1.89 mmol) of 1-phenylsulfonylindole-3-carboxaldehyde⁶ with 0.45 mL of TBAF yielded 500 mg (60%) of **26** as a light brown solid: mp 220 °C (decomp); ¹H NMR (DMSO-*d*₆, 400 MHz) δ 7.38 (m, 2H), 7.56 (m, 5H), 7.63 (m, 1H), 7.98 (m, 5H), 8.07 (s, 1H), 8.21 (s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ 113.9, 120.3, 121.3, 122.9, 124.6, 126.0, 126.2, 127.0, 127.2, 127.3, 127.7, 128.6, 128.7, 130.5, 134.7, 135.3, 135.4, 137.3, 138.8, 146.2. Anal. Calcd. For C₂₂H₁₅ClN₂O₄S: C, 60.21; H, 3.44; N, 6.38. Found: C, 60.08; H, 3.26; N, 6.47.

2-[*trans*-2-[5-Chloro-2-nitrophenyl]vinyl]-1*H*-indole (29). According to the general procedure, treatment of 1.33 g (5.46 mmol) of **7** with 1.00 g (4.07 mmol) of 1-Bocindole-2-carboxaldehyde with 1.10 mL of TBAF gave 0.622 g (51%) of **29** as an orange solid: mp 168-169 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 6.74 (s, 1H), 7.15 (t, 1H, $J = 8.0$ Hz), 7.17 (d, 1H, $J = 16.4$ Hz), 7.26 (m, 1H), 7.37 (m, 2H), 7.42 (d, 1H, $J = 16.4$ Hz), 7.61 (d, 1H, $J = 8.0$ Hz), 7.77 (s, 1H), 7.98 (d, 1H, $J = 8.7$ Hz), 8.34 (br s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 107.1, 111.0, 119.7, 120.6, 121.2, 124.1, 125.4, 126.7, 127.4, 127.8, 128.7, 134.5, 135.0, 137.6, 139.8. Anal. Calcd. For $\text{C}_{16}\text{H}_{11}\text{ClN}_2\text{O}_2$: C, 64.33; H, 3.71; N, 9.38. Found: C, 64.14; H, 3.56; N, 9.21.

2-[*trans*-2-[5-Chloro-2-nitrophenyl]vinyl]-5-chloro-1*H*-indole (32). To a solution of 3.80 g (21.0 mmol) of 5-chloroindole-2-carboxaldehyde⁷ in 30 mL of THF was added 4.85 g (22.2 mmol) of Boc_2O and 10 mg of DMAP. The resulting solution was stirred for 3 h at rt and concentrated under reduced pressure. The residue was purified over a plug of silica gel to afford 5.92 g (100%) of 1-Boc-5-chloroindole-2-carboxaldehyde **31** as a light tan solid which was used without further purification: ^1H NMR (CDCl_3 , 400 MHz)

δ 1.71 (s, 9H), 7.29 (s, 1H), 7.39 (m, 1H), 7.58 (m, 1H), 8.06 (m, 1H), 10.4 (br s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 28.0, 86.2, 115.0, 117.3, 122.4, 128.4, 128.6, 129.5, 136.1, 138.7, 149.4, 183.8.

According to the general procedure, treatment of 1.59 g (6.52 mmol) of **7** with 1.52 g (5.44 mmol) of the above aldehyde with 0.80 mL of TBAF gave 0.574 g (33%) of **32** as an orange solid: mp 198-199 °C; ^1H NMR ($\text{DMSO}-d_6$, 400 MHz) δ 6.65 (s, 1H), 7.10 (dd, 1H, $J = 8.8$ and 1.9 Hz), 7.37 (m, 2H), 7.55 (m, 3H), 7.97 (d, 1H, $J = 8.8$ Hz), 8.07 (d, 1H, $J = 1.9$ Hz), 11.71 (br s, 1H); ^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz) δ 105.8, 113.2, 120.1, 120.4, 123.3, 124.5, 126.2, 127.0, 127.4, 128.6, 129.7, 133.8, 136.7, 137.7, 138.6, 146.9. Anal. Calcd. For $\text{C}_{16}\text{H}_{10}\text{Cl}_2\text{N}_2\text{O}_2$: C, 57.68; H, 3.03; N, 8.41. Found: C, 57.35; H, 2.79; N, 8.19.

General Procedure for Reductive Cyclization of Nitrostyrenes. Method A. A solution of 1.00 mmol of the appropriate nitrostyrene in 5 mL of $\text{P}(\text{OEt})_3$ was heated to 155 °C for 2 h and the solvent removed under reduced pressure. The residue was purified by flash silica gel chromatography to give the product.

Method B. To a solution containing (3.43 mmol) of the appropriate nitrostyrene in 20 mL of MeCN was added 46.2 mg (0.206 mmol) of $\text{Pd}(\text{OAc})_2$ and 216 mg (0.823 mmol) of PPh_3 . The resulting mixture was heated at 70 °C under CO (6 atm) for 12 h. The resulting mixture was filtered over celite and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give the product which was identical to that prepared by Method A.

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1-Benzenesulfonyl-2-(5'-chloroindol-2'-yl)indole (11). colorless solid: mp 206-207 °C; ^1H NMR (DMSO- d_6 , 400 MHz) δ 6.73 (s, 1H), 7.01 (s, 1H), 7.14 (dd, 1H, J = 8.6 and 1.8 Hz), 7.27 (t, 1H, J = 7.5 Hz), 7.41 (m, 6H), 7.45 (m, 2H), 7.65 (s, 1H), 8.14 (d, 1H, J = 8.4 Hz), 11.80 (br s, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ 104.3, 113.4, 116.1, 116.4, 120.0, 121.9, 122.6, 124.4, 125.3, 126.1, 126.8, 128.9, 129.8, 130.5, 130.9, 133.8, 134.9, 135.8, 136.6, 138.0. Anal. Calcd. For $\text{C}_{22}\text{H}_{15}\text{ClN}_2\text{O}_2 \cdot \frac{1}{2}\text{H}_2\text{O}$: C, 63.53; H, 3.88; N, 6.74. Found: C, 63.57; H, 3.53; N, 6.55.

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1-Benzenesulfonyl-2-(5'-methoxyindol-2'-yl)indole (13). Colorless solid: mp 211-212 °C; ^1H NMR (DMSO- d_6 , 400 MHz) δ 3.79 (s, 3H), 6.69 (s, 1H), 6.81 (dd, 1H, J = 8.8 and 2.4 Hz), 6.97 (s, 1H), 7.11 (s, 1H), 7.31 (m, 2H), 7.47 (m, 5H), 7.56 (m, 2H), 8.15 (d, 1H, J = 8.4 Hz), 11.40 (br s, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ 55.8, 102.1, 104.5, 112.6, 113.1, 115.3, 116.4, 121.6, 125.2, 125.7, 126.8, 128.1, 129.5, 129.7, 130.6, 132.6, 134.6, 134.8, 136.6, 137.8, 154.0. Anal. Calcd. For $\text{C}_{23}\text{H}_{18}\text{N}_2\text{O}_3\text{S}$: C, 68.64; H, 4.51; N, 6.96. Found: C, 68.44; H, 4.28; N, 6.87.

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1-Benzenesulfonyl-2-{5'-[4-(methanesulfonyl)-1-piperazin-1-ylmethyl]indol-2'-yl}indole (15).

Colorless foam: ^1H NMR (CDCl_3 , 400 MHz) δ 2.62 (m, 4H), 2.79 (s, 3H), 3.28 (m, 4H), 3.68 (s, 2H), 6.69 (s, 1H), 6.81 (s, 1H), 7.27 (m, 4H), 7.45 (m, 6H), 7.56 (s, 1H), 8.34 (d, 1H, $J = 8.4$ Hz), 9.01 (br s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 34.2, 46.0, 52.3, 63.2, 105.2, 111.4, 115.2, 116.4, 121.0, 121.3, 124.7, 125.5, 126.9, 127.7, 128.8, 129.2, 130.2, 133.4, 134.0, 136.6, 137.0, 138.3. Anal. Calcd. For $\text{C}_{28}\text{H}_{28}\text{N}_4\text{O}_4\text{S}_2 \cdot \text{H}_2\text{O}$: C, 59.34; H, 5.34; N, 9.89. Found: C, 59.38; H, 4.98; N, 9.57.

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5-Chloro-1-benzenesulfonyl-2-(5'-chloroindol-2'-yl)indole (18). colorless solid: mp 221-222 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 6.62 (dd, 1H, $J = 2.0$ and 0.8 Hz), 6.76 (s, 1H), 7.25 (m, 3H), 7.38 (m, 4H), 7.47 (m, 2H), 7.61 (d, 1H, $J = 2.0$ Hz), 8.28 (d, 1H, $J = 8.9$ Hz), 9.00 (br s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 105.3, 112.5, 114.3, 117.4, 120.2, 120.6, 123.8, 125.8, 126.1, 126.8, 128.6, 129.0, 129.4, 130.6, 131.3, 134.1, 134.3, 135.5, 136.7, 136.8. Anal. Calcd. For $\text{C}_{22}\text{H}_{14}\text{Cl}_2\text{N}_2\text{O}_2\text{S}$: C, 59.87; H, 3.20; N, 6.35. Found: C, 59.66; H, 3.05; N, 6.13.

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1-Methyl-2-(5'-methoxyindol-2'-yl)indole (21). Colorless solid: mp 193-194 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 3.86 (s, 3H), 3.96 (s, 3H), 6.68 (s, 1H), 6.71 (s, 1H), 6.92 (dd, 1H, $J = 8.7$ and 2.4 Hz), 7.15 (m, 2H), 7.31 (m, 2H), 7.40 (d, 1H, $J = 8.3$ Hz), 7.65 (d, 1H, $J = 7.8$ Hz), 8.19 (br s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 31.4, 55.9, 100.9, 102.4, 102.5, 109.6, 111.6, 113.2, 120.2, 120.7, 122.3, 127.8, 129.5, 130.4, 131.6, 133.3, 138.6, 154.7. Anal. Calcd. For $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O} \cdot \frac{1}{3}\text{H}_2\text{O}$: C, 76.57; H, 5.95; N, 9.92. Found: C, 76.86; H, 5.70; N, 9.95.

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1-Benzyl-2-(5'-chloroindol-2'-yl)indole (24). Colorless solid: mp 92-93 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 5.54 (s, 2H), 6.48 (d, 1H, $J = 1.9$ Hz), 6.82 (s, 1H), 7.12 (m, 2H), 7.21 (s, 2H), 7.32 (m, 6H), 7.56 (s, 1H), 7.78 (m, 1H), 8.13 (br s, 1H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 47.9, 102.0, 102.4, 110.4, 111.9, 120.2, 120.8, 121.0, 123.0, 123.1, 126.0, 126.1, 127.7, 128.1, 129.2, 130.0, 130.8, 132.7, 134.8, 138.0, 138.7. Anal. Calcd. For $\text{C}_{23}\text{H}_{17}\text{ClN}_2$: C, 77.41; H, 4.80; N, 7.85. Found: C, 77.09; H, 4.63; N, 7.77.

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1-Benzenesulfonyl-3-(5'-chloroindol-2'-yl)indole (27). Colorless solid: mp 192-193 °C; ^1H NMR ($\text{DMSO-}d_6$, 400 MHz) δ 6.97 (s, 1H), 7.10 (d, 1H, $J = 8.7$ Hz), 7.39 (m, 3H), 7.56 (m, 3H), 7.65 (m, 1H), 7.99 (m, 4H), 8.39 (s, 1H), 11.73 (br s, 1H); ^{13}C NMR ($\text{DMSO-}d_6$, 100 MHz) δ 100.5, 112.9, 114.0, 115.6, 119.6, 121.5, 122.3, 124.1, 124.4, 124.9, 126.0, 128.1, 130.3, 130.4, 132.4, 135.2, 137.2, 141.5, 164.9. Anal. Calcd. For $\text{C}_{22}\text{H}_{15}\text{ClN}_2\text{O}_2\text{S}$: C, 64.94; H, 3.72; N, 6.88. Found: C, 64.62; H, 3.54; N, 6.68.

30

2-(5'-Chloroindol-2'-yl)indole (30). Colorless solid: mp 275 °C (decomp); ^1H NMR ($\text{DMSO-}d_6$, 400 MHz) δ 6.88 (m, 2H), 6.91 (m, 1H), 7.08 (m, 2H), 7.38 (m, 2H), 7.60 (m, 2H), 11.60 (br s, 1H), 11.70 (br s, 1H); ^{13}C NMR ($\text{DMSO-}d_6$, 100 MHz) δ 98.6, 99.5, 111.6, 112.9, 119.6, 119.9, 120.7, 122.0, 122.4, 124.4, 128.8, 130.1, 131.3, 133.6, 135.9, 137.5. Anal. Calcd. For $\text{C}_{16}\text{H}_{11}\text{ClN}_2$: C, 72.05; H, 4.16; N, 10.50. Found: C, 72.37; H, 4.07; N, 10.17.

33

5,5'-Dichloro-2,2'-biindole (33). Tan solid: mp 300 °C (decomp); ^1H NMR ($\text{DMSO-}d_6$, 400 MHz) δ 6.91 (s, 2H), 7.10 (d, 2H, $J = 8.4$ Hz), 7.37 (d, 2H, $J = 8.4$ Hz), 7.61 (s, 2H), 11.76 (br s, 2H); ^{13}C NMR ($\text{DMSO-}d_6$, 100 MHz) δ 99.1, 113.1, 119.8, 122.3, 124.5,

130.0, 133.0, 135.9. Anal. Calcd. For C₁₆H₁₀Cl₂N₂: C, 63.81; H, 3.35; N, 9.30. Found: C, 63.79; H, 3.27; N, 9.28.

General Procedure for the Preparation of Tjipanazole Aglycons. To a refluxing solution of 250 mg (0.937 mmol) of biindole **30** in 10 mL of AcOH was added in 0.10 mL portions 1.51 g (9.37 mmol) of (dimethylamino)acetaldehyde diethyl acetal over a period of 1 h. The resulting mixture was refluxed for 45 min, cooled to rt, and concentrated under reduced pressure. The residue was purified by silica gel chromatography to give 215 mg (79%) of tjipanazole I.

1

Tjipanazole I (1). Light Brown solid: mp 320 °C (decomp); ¹H NMR (acetone-*d*₆, 400 MHz) δ 7.23 (t, 1H, *J* = 7.5 Hz), 7.35 (dd, 1H, *J* = 8.5 and 2.0 Hz), 7.36 (dd, 1H, *J* = 8.5 and 2.0 Hz), 7.39 (m, 1H), 7.61 (dd, 1H, *J* = 8.6 and 2.3 Hz), 7.98 (s, 2H), 8.17 (d, 1H, *J* = 7.2 Hz), 8.18 (s, 1H), 10.50 (br s, 1H), 10.60 (br s, 1H); ¹³C NMR (acetone-*d*₆, 100 MHz) δ 112.2, 112.3, 112.5, 113.6, 119.5, 119.7, 119.8, 120.3, 121.1, 123.8, 124.2, 124.7, 125.2, 125.6, 126.0, 127.0, 137.9, 139.5. Anal. Calcd. For C₁₈H₁₁ClN₂: C, 74.36; H, 3.81; N, 9.63. Found: C, 74.01; H, 3.67; N, 9.44.

2

Tjipanazole D (2). tan solid: mp 310 °C (decomp); ¹H NMR (DMSO-*d*₆, 400 MHz) δ 7.39 (m, 2H), 7.72 (dd, 2H, *J* = 8.6 and 2.9 Hz), 7.95 (d, 2H, *J* = 2.9 Hz), 8.25 (d, 2H, *J* =

1.9 Hz), 11.3 (br s, 2H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ 112.3, 113.2, 119.3, 119.8, 123.4, 124.4, 125.0, 126.3, 137.4. Anal. Calcd. For $\text{C}_{18}\text{H}_{10}\text{Cl}_2\text{N}_2$: C, 66.48; H, 3.10; N, 8.61. Found: C, 66.23; H, 2.88; N, 8.30.

34

Compound 34 light brown solid: mp 297 °C; ^1H NMR (acetone- d_6 , 400 MHz) δ 3.90 (s, 3H), 4.33 (s, 3H), 7.01 (dd, 1H, J = 8.8 and 2.4 Hz), 7.20 (dt, 1H, J = 7.8 and 0.8 Hz), 7.41 (dt, 1H, J = 7.1 and 1.2 Hz), 7.51 (d, 1H, J = 8.8 Hz), 7.55 (d, 1H, J = 8.3 Hz), 7.69 (d, 1H, J = 2.4 Hz), 7.89 (s, 2H), 8.13 (d, 1H, J = 7.8 Hz), 10.49 (br s, 1H); ^{13}C NMR (acetone- d_6 , 100 MHz) δ 31.0, 55.3, 102.1, 108.8, 111.6, 111.8, 112.1, 112.2, 114.3, 118.9, 119.5, 120.5, 122.1, 124.0, 124.6, 126.7, 127.8, 134.9, 140.6, 154.3. Anal. Calcd. For $\text{C}_{20}\text{H}_{16}\text{N}_2\text{O}$: C, 79.98; H, 5.37; N, 9.33. Found: C, 79.86; H, 5.15; N, 9.25.

3

Preparation of Tjipanazole B (3). To a slurry of 740 mg (2.28 mmol) of tjipanazole D (2) and 1.30 g (2.96 mmol) of α -D-xylopyranosyl chloride (35)⁸ in 15 mL of MTBE was added 12 mL of 45% aqueous KOH followed by 1.29 g (3.19 mmol) of Aliquot 336. The resulting biphasic mixture was stirred at rt for 12 h. The aqueous layer was removed and the MTBE layer washed with 25 mL of 2 N HCl, 25 mL of water, and 25 mL of brine.

The organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was purified over silica gel to give 1.24 g (79%) of protected tjipanazole B which was used directly in the deprotection step.

To a solution of 1.05 g (1.44 mmol) of the above protected tjipanazole was added 250 mg of 20% $\text{Pd}(\text{OH})_2$ and the mixture was stirred under balloon pressure of hydrogen for 2 h. The reaction mixture was filtered over a pad of Celite and concentrated under reduced pressure. The residue was purified by silica gel chromatography to give 548 mg (83%) of tjianazole B (**3**) as a colorless solid. An analytical sample was obtained by recrystallization from DMSO/ H_2O : $[\alpha]_{\text{D}} = +9.48$ (*c* 0.01, 1:1 $\text{CHCl}_3/\text{MeOH}$); mp 226-227 °C; ^1H NMR ($\text{DMSO}-d_6$, 400 MHz, 100 °C) δ 3.66 (t, 1H, $J = 8.7$ Hz), 3.78 (t, 1H, $J = 5.4$ Hz), 3.91 (m, 2H), 4.25 (m, 1H), 4.69 (br s, 2H), 4.84 (br s, 1H), 6.01 (d, 1H, $J = 8.9$ Hz), 7.39 (dt, 2H, $J = 8.5$ and 2.0 Hz), 7.73 (d, 1H, $J = 8.5$ Hz), 7.80 (d, 1H, $J = 8.5$ Hz), 7.96 (d, 1H, $J = 8.3$ Hz), 8.00 (d, 1H, $J = 8.3$ Hz), 8.19 (m, 2H), 10.60 (br s, 1H); ^{13}C NMR ($\text{DMSO}-d_6$, 100 MHz, 100 °C) δ 68.4, 69.2, 71.9, 77.2, 86.6, 111.8, 112.6, 112.9, 113.6, 118.5, 118.54, 120.6, 121.2, 123.5, 123.9, 124.0, 124.2, 124.5, 125.3, 125.8, 126.2, 137.4, 137.5; Anal. Calcd. For $\text{C}_{23}\text{H}_{18}\text{Cl}_2\text{N}_2\text{O}_4 \cdot 2\text{H}_2\text{O}$: C, 56.00; H, 4.49; N, 5.68. Found: C, 56.21; H, 4.10; N, 5.44.

Preparation of Tjipanazole E (4). To a slurry of 1.00 g (3.08 mmol) of tjipanazole D (2) and 2.30 g (4.25 mmol) of α -D-glycopyranosyl chloride (36)⁹ in 24 mL of MTBE was added 15 ml of 45% aqueous KOH followed by 1.74 g (4.31 mmol) of Aliquot 336. The resulting biphasic mixture was stirred at rt for 12 h. The aqueous layer was removed and the MTBE layer washed with 35 mL of 2 N HCl, 35 mL of water, and 35 mL of brine. The organic layer was dried over MgSO₄ and concentrated under reduced pressure. The residue was purified over silica gel to give 2.32 g (89%) of protected tjipanazole E which was used directly in the deprotection step.

To a solution of 2.32 g (2.74 mmol) of the above protected tjipanazole was added 400 mg of 20% Pd(OH)₂ and the mixture was stirred under balloon pressure of hydrogen for 2 h. The reaction mixture was filtered over a pad of Celite and concentrated under reduced pressure. The residue was purified by silica gel chromatography to give 1.16 g (87%) of tjipanazole E (4) as a colorless amorphous solid: $[\alpha]_D = +60.00$ (*c* 0.001, 1:1 CHCl₃/MeOH); mp 206-207 °C; ¹H NMR (DMSO-*d*₆, 400 MHz) δ 3.52 (m, 2H), 3.77 (m, 1H), 3.84 (d, 1H, *J* = 10.4 Hz), 3.93 (m, 1H), 4.03 (dd, 1H, *J* = 11.2 and 4.0 Hz), 4.85 (br s, 1H), 5.06 (br s, 1H), 5.28 (br s, 1H), 5.94 (br s, 1H), 6.08 (d, 1H, *J* = 8.8 Hz), 7.39 (dt, 2H, *J* = 8.4 and 2.4 Hz), 7.51 (d, 1H, *J* = 8.4 Hz), 7.80 (d, 1H, *J* = 8.4 Hz), 8.01 (d, 1H, *J* = 8.4 Hz), 8.07 (d, 1H, *J* = 8.4 Hz), 8.25 (dd, 2H, *J* = 8.4 and 2.4 Hz), 11.20 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ 58.4, 67.5, 73.4, 76.7, 78.4, 84.4, 112.2, 112.9, 113.0, 113.6, 119.0, 119.3, 121.0, 121.8, 123.4, 123.9, 124.3, 124.4, 124.6, 125.0, 125.3, 126.9, 137.9, 139.0. Anal. Calcd. For C₂₄H₂₀Cl₂N₂O₅: C, 59.15; H, 4.14; N, 5.75. Found: C, 59.02; H, 4.13; N, 5.71.

37

Preparation of 6-Benzyl-3-chloro-12,13-dihydro-5H-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7(6H)-dione (37). To a solution of 110 mg (0.270 mmol) of **11** and 55 mg (0.293 mmol) of *N*-benzylmaleimide in 6 mL of chlorobenzene was heated in a sealed tube at 150 °C for 12 h. The reaction mixture was cooled to rt and the resulting solid filtered to give 60 mg (50%) of **37** as a yellow solid: mp 360 °C (decomp); ¹H NMR (DMSO-*d*₆, 400 MHz) δ 4.74 (s, 2H), 7.32 (m, 1H), 7.34 (m, 5H), 7.49 (m, 2H), 7.74 (d, 2H, *J* = 8.6 Hz), 8.84 (s, 1H), 8.88 (d, 1H, *J* = 7.8 Hz), 11.70 (br s, 1H), 11.80 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ 41.1, 112.6, 114.1, 115.1, 116.5, 118.9, 119.4, 120.9, 121.8, 123.0, 123.6, 124.7, 124.9, 127.1, 127.5, 127.8, 128.0, 129.1, 130.0, 137.9, 139.2, 140.8, 169.7, 169.9. Anal. Calcd. For C₂₇H₁₆ClN₃O₂: C, 72.08; H, 3.58; N, 9.34. Found: C, 71.89; H, 3.23; N, 9.15.

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