Supporting information

Synthesis of Fused Tetrazole Derivatives via a Tandem Cycloaddition and N-allylation Reaction and Parallel Synthesis of Fused Tetrazole Amines

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Supporting information file 1(current file)

General experimental paragraph.

Experimental procedure and characterization data for **7b-7f**, **8b-8f** and **11b-11f**.

¹H-NMR and mass spectral data for **26a**, **26c-f**, **27b-f**, **28a-d**, **28f** and **29-31**.

¹H-NMR- and/or ¹³C-NMR spectra for **6f**, **7b**, **7d**, **7f**, **8a-f**.

Supporting information file 2

¹H-NMR-/and mass spectra and HPLC chromatogram for **26a-f**.

Supporting information file 3

¹H-NMR-/and mass spectra and HPLC chromatogram for **27a-f**.

Supporting information file 4

¹H-NMR-/and mass spectra and HPLC chromatogram for **28a-f** and **29-31**.

General. Computer aided structural analyses were made using PC Spartan Pro version 1.1. HPLC analyses were performed on a HiChrom column (Kromasil 100-5C18, 150x4.6 mm); eluent: CH₃CN (HPLC grade) / H₂O; flow rate 1 mL/min. NMR spectra were recorded on a 400 MHz or 300 MHz instrument using CDCl₃, acetone-d₆ or DMSO-d₆ as internal standard. Mass spectra were recorded in the following modes: EI(+), CI(+) and FAB(+) using direct inlet and ESP(+)(25V) using inlet via a HPLC equipped with a HiChrom column (Kromasil 100-5C18, 150x4.6 mm; eluent: CH₃CN (HPLC grade) / H₂O; flow rate 1 mL/min). Preparative chromatographic separations were performed on Matrex Amicon normal phase silica gel 60 (0.035-0.070 mm). Thin-layer chromatography was performed on Merck precoated TLC plates with Silica gel 60 F-254, 0.25 mm. After elution, the TLC plates were first visualized with UV light and then sprayed with a solution of KMnO₄ (10 g), K₂CO₃ (50 g), NaOH (20 mL, 5 %) and H₂O (900 mL) followed by heating. Chemicals were reagent grade and all reagents were used as received if not otherwise noted. 3-Bromo-2-bromomethylpropene,^{1,2} 2-amino-4-trifluoromethylbenzonitrile³ and 2-amino-4-nitrobenzonitrile⁴ were synthesized according to literature procedures.

5-Bromo-2-(2-bromomethyl-2-propenyl)benzonitrile (7b). The reaction was performed according to the synthesis of **7a** starting from **6b** (0.39 g, 2.0 mmol). The yield of **7b** was determined to be 82% using internal standard. Column chromatography (heptane-EtOAc 95:5) of the residue followed by recrystallization (heptane-diethyl ether 10:1) gave 0.39 g (62%) of **7b** as white crystals; mp 45-46°C; ¹H NMR (CDCl₃, 400 MHz) δ 7.78, (d, 1H, J = 2.1 Hz), 7.68, (dd, 1H, J = 8.3, 2.1 Hz), 7.29, (d, 1H, J = 8.3Hz), 5.34, (br s, 1H), 4.91, (br s, 1H), 3.92, (s, 2H), 3.73, (s, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 142.4, 141.3, 136.3, 135.7, 132.2, 120.9, 118.6, 116.5, 115.2, 38.1, 35.7; HRMS (FAB⁺) Calcd. for C₁₁H₁₀Br₂N (M+H): 313.9181. Found:

313.9174; Anal. Calcd for $C_{11}H_9Br_2N$: C, 41.94; H, 2.88; N, 4.45. Found: C, 42.04; H, 2.90; N, 4.37.

2-(2-Bromomethyl-2-propenyl)-4-nitrobenzonitrile (7c). The reaction was performed according to the synthesis of **7a** starting from **6c** (0.33 g, 2.0 mmol). The yield of **7c** was determined to be 65% using internal standard. Column chromatography (heptane-EtOAc 23:2) of the residue followed by recrystallization (heptane-EtOAc 85:15) gave 0.27 g (48%) of **7c** as pale yellow crystals; mp 71-72 °C. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.27 (d, 1H, $J = 2.2$ Hz), 8.23 (dd, 1H, $J = 8.4, 2.2$ Hz), 7.87 (d, 1H, $J = 8.5$ Hz), 5.43 (s, 1H), 4.93 (s, 1H), 3.97 (s, 2H), 3.90 (s, 2H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 150.2, 144.8, 141.7, 134.4, 125.2, 122.4, 119.3, 119.2, 116.0, 38.5, 35.4; HRMS (EI^+) Calcd for $C_{11}H_8BrN_2O_2$ (M-H): 278.9767. Found: 278.9772.

2-(2-Bromomethyl-2-propenyl)-5-nitrobenzonitrile (7d). The reaction was performed according to the synthesis of **7a** starting from **6d** (0.33 g, 2.0 mmol). The yield of **7d** was determined to be 67% using internal standard. Column chromatography (heptane-EtOAc 23:2) of the residue gave 0.23 g (41%, 90-95% purity) of **7d** as a yellow oil. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.52 (d, 1H, $J = 2.4$ Hz), 8.41 (dd, 1H, $J = 8.5, 2.7$ Hz), 7.65 (d, 1H, $J = 8.6$ Hz), 5.41 (s, 1H), 4.93 (s, 1H), 3.95 (s, 2H), 3.89 (s, 2H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 149.3, 146.8, 141.6, 131.8, 128.3, 127.6, 119.3, 115.7, 114.9, 38.6, 35.5; HRMS (CI^+) Calcd for $C_{11}H_{10}O_2N_2Br$ (M+H): 280.9927. Found: 280.9910.

2-(2-Bromomethyl-2-propenyl)-4-trifluoromethylbenzonitrile (7e). The reaction was performed according to the synthesis of **7a** starting from **6e** (0.37 g, 2.0 mmol). The yield of **7e** was determined to be 72% using internal standard. Column chromatography (heptane-EtOAc 9:1) of the residue gave 400 mg (65%, 80-85% purity) of **7e** as a pale yellow oil; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.79 (d, 1H, $J = 8.0$ Hz), 7.66 (s, 1H), 7.63 (d, 1H, $J = 8.1$ Hz), 5.45 (s, 1H), 4.89 (s, 1H), 3.95 (s, 2H), 3.84 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.5, 142.1, 134.7

(q, $J = 33$ Hz), 133.8, 127.4 (m), 125.1, 124.5 (m), 121.8, 118.9, 117.0, 116.6, 38.5, 35.6; HRMS (Cl^+) Calcd. for $\text{C}_{12}\text{H}_8\text{BrF}_3\text{N}$ ($\text{M}-\text{H}$): 301.9792. Found: 301.9776.

5-Bromo-2-(2-bromomethyl-2-propenyl)-4-chlorobenzonitrile (7f). The reaction was performed according to the synthesis of **7a** starting from **6f** (0.46 g, 2.0 mmol). The yield of **7f** was determined to be 75% using internal standard. Column chromatography (heptane-EtOAc 9:1) followed by crystallization (heptane, dissolved at +20 °C and cooled to -20 °C) of the residue gave 0.38 g (54%) of **7f** as white crystals; mp 66-67 °C; ^1H NMR (CDCl_3 , 400 MHz) δ 7.88 (s, 1H), 7.49 (s, 1H), 5.38 (br s, 1H), 4.93 (br s, 1H), 3.93 (br s, 2H), 3.70 (s, 2H); ^{13}C NMR (CDCl_3 , 100 MHz) δ 142.7, 141.8, 140.2, 137.6, 132.2, 121.4, 119.0, 115.8, 113.2, 37.9, 35.6; HRMS (Cl^+) Calcd. for $\text{C}_{11}\text{H}_9\text{Br}_2\text{ClN}$ ($\text{M}+\text{H}$): 347.8790. Found: 347.8792.

9-Bromo-5-methylene-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (8b). **Procedure A.** The reaction was performed according to the synthesis of **8a** starting from crude **7b**. Column chromatography (heptane-EtOAc 2:1) followed by recrystallization (heptane-acetone) gave 305 mg (67%) of **8b** as white crystals; mp 121-124 °C; ^1H NMR (acetone- d_6 , 400 MHz) δ 8.26 (s, 1H, $J = 2.1$ Hz), 7.62 (dd, 1H, $J = 8.2, 2.1$ Hz), 7.23 (d, 1H, $J = 8.2$ Hz), 5.23 (m, 1H), 5.20 (m, 3H), 3.53 (s, 2H); ^{13}C NMR (acetone- d_6 , 400 MHz) δ 153.5, 139.9, 136.8, 135.1, 132.7, 131.2, 124.9, 121.7, 115.8, 53.4, 40.2; HRMS (FAB^+) Calcd. for $\text{C}_{11}\text{H}_{10}\text{BrN}_4$ ($\text{M}+\text{H}$): 277.009. Found: 277.0100

Procedure B. The reaction was performed according to the synthesis of **8a** but at 0.5 mmol scale and in a sealed tube at 200 °C in a oil bath for 25 min. The reaction mixture was worked up and purified according to the synthesis of **8b** to give 100 mg (63%) of **8b**.

Procedure C. The reaction was performed according to the synthesis of **8a** but at 0.5 mmol scale and using microwave assisted heating (200 °C for 20 min). The reaction mixture was worked up and purified according to the synthesis of **8b** to give 95 mg (60%) of **8b**.

5-Methylene-8-nitro-5,6-dihydro-4*H*-1,2,3,3a tetraaza-benzo[*e*]azulene (8c). The reaction was performed according to the synthesis of **8a** starting from crude **7c**. Column chromatography (heptane-EtOAc 1:1) followed by recrystallization (heptane-acetone) gave 220 mg (63%) of **8c** as pale yellow crystals; mp 211-211 °C (dec); ¹H NMR (CDCl₃, 400 MHz) δ 8.40 (m, 1H), 8.34 (m, 1H), 5.46 (t, 2H, J = 1.5 Hz), 5.39 (dd, 2H, J = 10.4, 0.8 Hz), 4.00 (s, 2H); ¹³C NMR (CDCl₃, 400 MHz) δ 153.8, 150.5, 141.9, 140.6, 131.8, 130.3, 125.2, 123.1, 116.8, 54.6, 40.3; HRMS (EI⁺) Calcd for C₁₁H₉O₂N₅ (M): 243.0756. Found: 243.0744.

5-Methylene-9-nitro-5,6-dihydro-4*H*-1,2,3,3a-tetraaza-benzo[*e*]azulene (8d). The reaction was performed according to the synthesis of **8a** starting from crude **7d**. Column chromatography (heptane-EtOAc 1:1) gave 210 mg (64%) of **8d** as pale yellow crystals; mp 126-128 °C; ¹H NMR (CDCl₃, 400 MHz) δ 8.81 (d, 1H, J = 2.5 Hz), 8.35 (dd, 1H, J = 8.5, 2.5 Hz), 7.79 (d, 1H, J = 8.5 Hz), 5.42 (t, 2H, J = 1.5 Hz), 5.35 (dd, 2H, J = 8.0, 0.5 Hz), 3.91 (s, 2H); ¹³C NMR (CDCl₃, 400 MHz) δ 153.2, 147.6, 146.5, 139.5, 131.6, 126.5, 125.2, 124.6, 116.9, 54.2, 40.1; HRMS (CI⁺) Calcd for C₁₀H₁₀O₂N₅ (M+H): 243.0756 Found: 243.0747.

5-Methylene-8-trifluoromethyl-5,6-dihydro-4*H*-1,2,3,3a-tetraaza-benzo[*e*]azulene (8e). The reaction was performed according to the synthesis of **8a** starting from crude **7e**. Column chromatography (heptane-EtOAc 2:1) followed by recrystallization (heptane-acetone) gave 230 mg (60%) of **8e** as white crystals; mp 121-122 °C; ¹H NMR (acetone-d₆, 400 MHz) δ 8.28 (d, 1H, J = 8.1 Hz), 7.89 (s, 1H), 7.83 (d, 1H, J = 8.1 Hz), 5.43 (br s, 2H), 5.34 (br s, 2H), 3.88 (s, 2H); ¹³C NMR (acetone-d₆, 100 MHz) δ 154.1, 141.2, 141.1, 133.4 (q, J = 32 Hz), 131.2, 128.2, 127.2 (m), 125.0 (m), 116.2, 54.3, 40.3; HRMS (EI⁺) Calcd. for C₁₂H₉BrF₃N (M): 266.0779. Found: 266.0770.

9-Bromo-8-chloro-5-methylene-5,6-dihydro-4*H*-1,2,3,3a-tetraaza-benzo[*e*]azulene (8f). The reaction was performed according to the synthesis of **8a** starting from crude **7f**. Column chromatography (heptane-EtOAc 2:1) followed by recrystallization (heptane-EtOAc) gave 320

mg (68%) of **8f** as white crystals; mp 174-176 °C; ¹H NMR (acetone-d₆, 400 MHz) δ 8.33 (s, 1H), 7.76 (s, 1H), 5.41 (br s, 1H), 5.34 (d, 2H, J = 9.0 Hz), 3.78 (s, 2H); ¹³C NMR (acetone-d₆, 100 MHz) δ 153.2, 141.0, 140.5, 137.7, 134.9, 132.1, 124.8, 121.1, 116.8, 54.5, 39.8; HRMS (EI⁺) Calcd. for C₁₁H₈BrClN₄ (M): 309.9621. Found: 309.9621.

9-Bromo-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene-5-one (11b). The reaction was performed according to the synthesis of **11a** starting from **8b** (300 mg, 1.08 mmol). Column chromatography (heptane-EtOAc 2:1) followed by recrystallization (pentane-acetone 5:1) gave 195 mg (64%) of **11b** as white crystals; mp 176-178 °C (dec); ¹H NMR (acetone-d₆, 400 MHz) δ 8.2 (s, *J* = 2.1 Hz, 1H), 7.7 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.3 (d, *J* = 8.2 Hz, 1H), 5.2 (s, 2H), 3.8 (s, 2H). ¹³C NMR (acetone-d₆, 400 MHz) δ 198.2, 153.5, 136.1, 132.7, 132.2, 129.3, 124.4, 123.2, 56.1, 48.6; Anal. Calcd. for C₁₀H₇BrN₄O: C, 43.03; H, 2.53; N, 20.07; Found: C, 42.99; H, 2.38; N, 20.15.

8-Nitro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene-5-one (11c). The reaction was performed according to the synthesis of **11a** starting from **8c** (200 mg, 0.82 mmol) except that the solvent mixture (1:1 to 9:1 CH₂Cl₂-MeOH) and amount of solvent (10 + 10 mL) were changed. Recrystallization (heptane-acetone) gave 160 mg (79%) of **11c** as a pale yellow solid; mp 243 °C (dec); ¹H NMR (DMSO-d₆, 400 MHz) δ 8.52 (d, 1H, *J* = 2.2 Hz), 8.40 (dd, 1H, 8.5, 2.4 Hz), 8.24 (d, 1H, *J* = 8.5 Hz), 5.46 (s, 2H), 4.22 (s, 2H); ¹³C NMR (DMSO-d₆, 100 MHz) δ 199.9, 153.2, 149.5, 133.8, 130.8, 128.7, 125.4, 123.1, 56.7, 47.7; Anal. Calcd. for C₁₀H₇ClN₅O₃: C, 48.98; H, 2.88; N, 28.56; Found: C, 48.96; H, 2.93; N, 28.66.

9-Nitro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene-5-one (11d). The reaction was performed according to the synthesis of **11a** starting from **8d** (190 mg, 0.78 mmol) except that the solvent composition (1:1 to 9:1 CH₂Cl₂-MeOH) and amount of solvent (10 + 10 mL) were changed. Column chromatography (heptane-EtOAc 1:1) gave 140 mg (73%) of **11d** as a pale

yellow solid; mp 193-195 °C (dec); ^1H NMR (acetone- d_6 , 400 MHz) δ 8.74 (d, 1H, J = 2.5 Hz), 8.49 (dd, 1H, J = 8.5, 2.5 Hz), 7.90 (d, 1H, J = 8.5 Hz), 5.45 (s, 2H), 4.25 (s, 2H); ^{13}C NMR (acetone- d_6 , 400 MHz) δ 199.4, 154.0, 148.6, 139.5, 133.1, 127.4, 125.8, 124.7, 57.2, 49.3; Anal. Calcd. for $\text{C}_{10}\text{H}_7\text{ClN}_5\text{O}_3$: C, 48.98; H, 2.88; N, 28.56; Found: C, 48.84; H, 2.96; N, 28.43.

8-Trifluoromethyl-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene-5-one (11e). The reaction was performed according to the synthesis of **11a** starting from **8e** (220 mg, 0.82 mmol). Column chromatography (heptane-EtOAc 1:1) gave 180 mg (81%) of **11e** as a white solid; mp 130-132 °C; ^1H NMR (acetone- d_6 , 400 MHz) δ 8.22 (d, 1H, J = 7.9 Hz), 7.97 (s, 1H), 7.95 (d, 1H, J = 7.9 Hz), 5.44 (s, 2H), 4.19 (s, 2H); ^{13}C NMR (acetone- d_6 , 100 MHz) δ 200.0, 154.4, 134.0 (q, J = 32 Hz), 134.0, 131.1, 128.3 (m), 128.1, 126.0 (m), 123.3, 57.1, 49.0; Anal. Calcd. for $\text{C}_{11}\text{H}_7\text{F}_3\text{N}_4\text{O}$: C, 49.26; H, 2.63; N, 20.89; Found: C, 49.14; H, 2.68; N, 21.02.

9-Bromo-8-chloro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene-5-one (11f). The reaction was performed according to the synthesis of **11a** starting from **8f** (310 mg, 1.0 mmol) except that the solvent composition (1:1 to 9:1 CH_2Cl_2 -MeOH) and amount of solvent (10 + 10 mL) were changed. Recrystallization (heptane-EtOAc) gave 230 mg (74%) of **11f** as a white solid; mp 253 °C (dec); ^1H NMR (DMSO- d_6 , 400 MHz) δ 8.26 (s, 1H), 7.95 (s, 1H), 5.41 (s, 2H), 4.01 (s, 2H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ 199.8, 152.5, 136.9, 133.4, 133.0, 132.2, 123.4, 121.0, 56.5, 47.3; Anal. Calcd. for $\text{C}_{10}\text{H}_6\text{BrClN}_4\text{O}$: C, 38.31; H, 1.93; N, 17.87; Found: C, 38.42; H, 2.04; N, 17.85.

Benzylamino derivatives.

The reactions were performed according to the synthesis of **26b**.

5-(N-Benzylamino)-9-chloro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (26a). ^1H NMR (CDCl_3 , 300 MHz) δ 8.08 (d, 1H, J = 2.3 Hz), 7.46 (dd, 1H, J = 8.2, 2.3 Hz), 7.40-7.25 (m, 6H), 4.48 (d, 2H, J = 5.3 Hz), 3.92 (d, 1H, J = 13.5 Hz), 3.88 (d, 1H, J = 13.5 Hz), 3.71 (m, 1H), 3.00 (dd, 1H, J = 15.0, 4.8 Hz), 2.79 (dd, 1H, J = 15.0, 7.1 Hz); MS (ESP $^+$) (M+H): 326.4.

5-(N-Benzylamino)-8-nitro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (26c). ^1H NMR (CDCl_3 , 300 MHz) δ 8.33 (d, 1H, $J = 8.4$ Hz), 8.28 (dd, 1H, $J = 8.6, 2.2$ Hz), 8.20 (d, 1H, $J = 2.2$ Hz), 7.40-7.25 (m, 5H), 4.55 (d, 2H, $J = 4.9$ Hz), 3.93 (d, 1H, $J = 13.4$ Hz), 3.88 (d, 1H, $J = 13.3$ Hz), 3.80 (m, 1H), 3.18 (dd, 1H, $J = 15.2, 4.4$ Hz), 2.99 (dd, 1H, $J = 15.2, 7.2$ Hz); MS (ESP^+) (M+H): 337.4.

5-(N-Benzylamino)-9-nitro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (26d). ^1H NMR (CDCl_3 , 300 MHz) δ 9.00 (d, 1H, $J = 2.4$ Hz), 8.31 (dd, 1H, $J = 8.4, 2.4$ Hz), 7.53 (d, 1H, $J = 8.4$ Hz), 7.40-7.25 (m, 5H), 4.56 (d, 2H, $J = 5.2$ Hz), 3.92 (d, 1H, $J = 13.4$ Hz), 3.87 (d, 1H, $J = 13.3$ Hz), 3.78 (m, 1H), 3.17 (dd, 1H, $J = 15.3, 4.4$ Hz), 3.00 (dd, 1H, $J = 15.3, 7.3$ Hz); MS (ESP^+) (M+H): 337.4.

5-(N-Benzylamino)-8-trifluoromethyl-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (26e). ^1H NMR (CDCl_3 , 300 MHz) δ 8.23 (d, 1H, $J = 9.0$ Hz), 7.72 (br d, 1H, $J = 8.3$ Hz), 7.59 (s, 1H), 7.40-7.25 (m, 5H), 4.54 (dd, 1H, $J = 15.6, 5.2$ Hz), 4.48 (dd, 1H, $J = 15.7, 5.2$ Hz), 3.95 (d, 1H, $J = 13.3$ Hz), 3.89 (d, 1H, $J = 13.3$ Hz), 3.76 (m, 1H), 3.10 (dd, 1H, $J = 14.9, 4.7$ Hz), 2.87 (dd, 1H, $J = 14.9, 7.2$ Hz); MS (ESP^+) (M+H): 360.3.

5-(N-Benzylamino)-9-bromo-8-chloro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (26f). ^1H NMR (CDCl_3 , 300 MHz) δ 8.39 (s, 1H), 7.41 (s, 1H), 7.40-7.25 (m, 5H), 4.50 (d, 2H, $J = 5.2$ Hz), 3.92 (d, 1H, $J = 13.3$ Hz), 3.86 (d, 1H, $J = 13.4$ Hz), 3.70 (m, 1H), 3.00 (dd, 1H, $J = 15.2, 4.5$ Hz), 2.81 (dd, 1H, $J = 15.3, 7.1$ Hz); MS (ESP^+) (M+H): 404.3.

Morpholino derivatives.

The reactions were performed according to the synthesis of **27a**.

9-Bromo-5-(morpholino)-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (27b). ^1H NMR (CDCl_3 , 300 MHz) δ 8.18 (d, 1H, $J = 2.1$ Hz), 7.62 (dd, 1H, $J = 8.2, 2.1$ Hz), 7.27 (d, 1H, $J = 8.2$ Hz), 4.86 (dd, 1H, $J = 14.8, 4.8$ Hz), 4.33 (dd, 1H, $J = 14.8, 6.1$ Hz), 3.67 (t, 4H, $J = 4.7$

Hz), 3.50 (m, 1H), 2.95 (dd, 1H, J = 14.8, 5.3 Hz), 2.85 (dd, 1H, J = 14.8, 8.7 Hz), 2.64 (m, 4H); MS (ESP⁺) (M+H): 350.2.

5-(Morpholino)-8-nitro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (27c). ¹H NMR (CDCl₃, 300 MHz) δ 8.30 (m, 3H), 4.96 (dd, 1H, J = 14.8, 4.8 Hz), 4.40 (dd, 1H, J = 14.9, 4.8 Hz), 3.67 (t, 4H, J = 4.6 Hz), 3.55 (m, 1H), 3.17 (dd, 1H, J = 14.8, 4.8 Hz), 3.05 (dd, 1H, J = 14.8, 8.8 Hz), 2.65 (m, 4H); MS (ESP⁺) (M+H): 317.3.

5-(Morpholino)-9-nitro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (27d). ¹H NMR (acetone-d₆, 300 MHz) δ 8.90 (d, 1H, J = 2.5 Hz), 8.36 (dd, 1H, J = 8.5, 2.5 Hz), 7.87 (d, 1H, J = 8.6 Hz), 5.08 (dd, 1H, J = 14.8, 5.1 Hz), 4.63 (dd, 1H, J = 14.8, 4.9 Hz), 3.60 (m, 1H), 3.50 (t, 4H, J = 4.6 Hz), 3.42 (dd, 1H, J = 15.7, 4.7 Hz), 3.34 (dd, 1H, J = 15.5, 7.8 Hz), 2.64 (m, 4H); MS (ESP⁺) (M+H): 317.3.

5-(Morpholino)-8-trifluoromethyl-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (27e). ¹H NMR (CDCl₃, 300 MHz) δ 8.18 (d, 1H, J = 8.1 Hz), 7.72 (br d, 1H, J = 8.1 Hz), 7.67 (s, 1H), 4.94 (dd, 1H, J = 14.8, 4.5 Hz), 4.34 (dd, 1H, J = 14.8, 6.1 Hz), 3.68 (t, 4H, J = 4.6 Hz), 3.55 (m, 1H), 3.08 (dd, 1H, J = 14.6, 5.0 Hz), 2.95 (dd, 1H, J = 14.6, 9.1 Hz), 2.65 (m, 4H); MS (ESP⁺) (M+H): 340.3.

9-Bromo-8-chloro-5-(morpholino)-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (27f). ¹H NMR (CDCl₃, 300 MHz) δ 8.35 (s, 1H), 7.50 (s, 1H), 4.89 (dd, 1H, J = 14.8, 4.9 Hz), 4.35 (dd, 1H, J = 14.8, 5.8 Hz), 3.67 (t, 4H, J = 4.6 Hz), 3.47 (m, 1H), 2.98 (dd, 1H, J = 14.9, 4.9 Hz), 2.89 (dd, 1H, J = 14.9, 8.6 Hz), 2.62 (m, 4H); MS (ESP⁺) (M+H): 326.4.

Benzylethylamino derivatives.

The reactions were performed according to the synthesis of **28e**.

5-(N-Benzylethylamino)-9-chloro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (28a). ¹H NMR (CDCl₃, 300 MHz) δ 7.96 (d, 1H, J = 2.3 Hz), 7.44 (dd, 1H, J = 8.2, 2.2 Hz), 7.35-7.20 (m, 6H), 4.72 (dd, 1H, J = 14.6, 5.9 Hz), 4.37 (dd, 1H, J = 14.6, 6.7 Hz), 3.78 (d, 1H, J

= 13.9 Hz), 3.75 (m, 1H), 3.67 (d, 1H, J = 13.9 Hz), 2.94 (m, 1H), 2.86 (dd, 1H, J = 14.5, 8.4 Hz), 2.63 (m, 2H), 1.10 (t, 1H, 7.0 Hz); MS (ESP⁺) (M+H): 354.3.

5-(N-Benzylethylamino)-9-bromo-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene

(28b). ¹H NMR (CDCl₃, 300 MHz) δ 8.13 (d, 1H, J = 2.1 Hz), 7.59 (dd, 1H, J = 8.2, 2.1 Hz), 7.35-7.20 (m, 6H), 4.71 (dd, 1H, J = 14.6, 6.1 Hz), 4.38 (dd, 1H, J = 14.6, 6.7 Hz), 3.78 (d, 1H, J = 14.3 Hz), 3.74 (m, 1H), 3.67 (d, 1H, J = 14.3 Hz), 2.92 (dd, 1H, J = 14.6, 5.6 Hz), 2.84 (dd, 1H, J = 14.5, 8.2 Hz), 2.62 (m, 2H), 1.09 (t, 1H, 7.0 Hz); MS (ESP⁺) (M+H): 398.3.

5-(N-Benzylethylamino)-8-nitro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (28c).

¹H NMR (CDCl₃, 300 MHz) δ 8.28-8.20 (m, 3H, J = 8.6, 2.2 Hz), 7.35-7.20 (m, 5H), 4.82 (dd, 1H, J = 14.6, 5.9 Hz), 4.42 (dd, 1H, J = 14.6, 6.6 Hz), 3.82 (d, 1H, J = 14.3 Hz), 3.80 (m, 1H), 3.71 (d, 1H, J = 14.4 Hz), 3.12 (dd, 1H, J = 14.8, 4.7 Hz), 3.02 (dd, 1H, J = 14.7, 8.7 Hz), 2.65 (m, 2H), 1.13 (t, 1H, 7.0 Hz); MS (ESP⁺) (M+H): 365.4.

5-(N-Benzylethylamino)-9-nitro-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (28d).

¹H NMR (CDCl₃, 300 MHz) δ 8.86 (d, 1H, J = 2.4 Hz), 8.30 (dd, 1H, J = 8.4, 2.4 Hz), 7.57 (d, 1H, J = 8.4 Hz), 7.35-7.20 (m, 5H), 4.78 (dd, 1H, J = 14.7, 6.4 Hz), 4.45 (dd, 1H, J = 14.7, 6.5 Hz), 3.81 (d, 1H, J = 14.4 Hz), 3.78 (m, 1H), 3.68 (d, 1H, J = 14.3 Hz), 3.11 (dd, 1H, J = 14.7, 5.1 Hz), 3.02 (dd, 1H, J = 14.6, 8.4 Hz), 2.64 (m, 2H), 1.12 (t, 1H, 7.0 Hz); MS (ESP⁺) (M+H): 365.4.

5-(N-Benzylethylamino)-9-bromo-8-chloro-5,6-dihydro-4H-1,2,3,3a-tetraaza-

benzo[e]azulene (28f). ¹H NMR (CDCl₃, 300 MHz) δ 8.26 (s, 1H), 7.45 (s, 1H), 7.40-7.20 (m, 5H), 4.74 (dd, 1H, J = 14.6, 6.2 Hz), 4.40 (dd, 1H, J = 14.6, 6.5 Hz), 3.78 (d, 1H, J = 14.3 Hz), 3.72 (m, 1H), 3.67 (d, 1H, J = 14.3 Hz), 2.94 (dd, 1H, J = 14.6, 5.3 Hz), 2.85 (dd, 1H, J = 14.6, 8.3 Hz), 2.62 (m, 2H), 1.10 (t, 1H, J = 7.1 Hz); MS (ESP⁺) (M+H): 432.3.

5-(4-Benzylpiperazinyl)-9-bromo-5,6-dihydro-4H-1,2,3,3a-tetraaza-benzo[e]azulene (29).

The reaction was performed according to the synthesis of **28e** at 0.05 mmol scale except that

1,1,2-trichloroethene was used as solvent and 4-benzylpiperazine was used instead of benzylamine. ^1H NMR (CDCl_3 , 300 MHz) δ 8.16 (d, 1H, $J = 2.1$ Hz), 7.60 (dd, 1H, $J = 8.2$, 2.1 Hz), 7.35-7.20 (m, 6H), 4.81 (dd, 1H, $J = 14.7$, 5.1 Hz), 4.33 (dd, 1H, $J = 14.7$, 6.3 Hz), 3.55 (m, 1H), 3.49 (s, 2H), 2.92 (dd, 1H, $J = 14.7$, 5.5 Hz), 2.84 (dd, 1H, $J = 14.6$, 8.6 Hz), 2.73 (m, 2H), 2.63 (m, 2H), 2.45 (br s, 4H); MS (ESP^+) ($\text{M}+\text{H}$): 438.4.

Methyl N-(9-bromo-5,6-dihydro-4*H*-1,2,3,3a-tetraaza-benzo[*e*]azulen-5-yl) glycinate (30).

The reaction was performed according to the synthesis of **26b** except that two equivalents of methyl glycinate hydrochloride (0.1 mmol) and triethylamine (0.1 mmol) was used in addition to the ketone and acetic acid. Saturated aqueous NaHCO_3 (1 mL) was used in the work up instead of NaOH (1M). ^1H NMR (CDCl_3 , 300 MHz) δ 8.23 (d, 1H, $J = 2.2$ Hz), 7.62 (dd, 1H, $J = 8.1$, 2.2 Hz), 7.26 (d, 1H, $J = 8.2$ Hz), 4.48 (dd, 1H, $J = 14.4$, 5.0 Hz), 4.42 (dd, 1H, $J = 14.4$, 5.0 Hz), 3.76 (s, 3H), 3.70 (m, 1H), 3.55 (d, 1H, $J = 17.6$ Hz), 3.47 (d, 1H, $J = 17.6$ Hz), 3.01 (dd, 1H, $J = 15.0$, 4.7 Hz), 2.78 (dd, 1H, $J = 14.9$, 7.2 Hz); MS (ESP^+) ($\text{M}+\text{H}$): 352.2.

9-Chloro-5-(N-methylamino)-5,6-dihydro-4*H*-1,2,3,3a-tetraaza-benzo[*e*]azulene (31). The reaction was performed according to the synthesis of **26b** except that anhydrous methylamine (g) was used in excess (bubbled into the reaction solution at 0 °C). The reaction mixture was then stirred for 16 h while slowly increasing the temperature to 20 °C. The remaining methylamine was removed before the purification by passing a gentle stream of argon into the organic phase maintaining the temperature at 25 °C. ^1H NMR (CDCl_3 , 300 MHz) δ 8.08 (d, 1H, $J = 2.2$ Hz), 7.47 (dd, 1H, $J = 8.2$, 2.3 Hz), 7.30 (d, 1H, $J = 8.2$ Hz), 4.50 (dd, 1H, $J = 14.3$, 5.3 Hz), 4.43 (dd, 1H, $J = 14.4$, 5.2 Hz), 3.59 (m, 1H), 3.00 (dd, 1H, $J = 14.9$, 4.8 Hz), 2.75 (dd, 1H, $J = 14.9$, 7.3 Hz), 2.53 (s, 3H); MS (ESP^+) ($\text{M}+\text{H}$): 249.3.

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