Supplementary Material (ESI) for Chemical Communications

CHEMICAL COMMUNICATIONS

Dynamic Nanoscale Borromean Rings

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SUPPORTING INFORMATION

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Preparation of the Homo-Cl_6-, Homo-Br_6-, and Hetero-$Cl_{6-x}Br_x$-Borromean Ring Derivatives

The *t*-Boc-protected bipyridyl ligand **1** was prepared[1] according to a previously reported procedure (Scheme S1). The bisammonium bipyridyl trifluoroacetic acid salt **DAB**-H_n•nTFA was obtained in near quantitative yield by dissolving *t*-Boc-protected bipyridyl ligand **1** in 2 mL of CF_3CO_2H as a result of stirring at RT for 10 min, after which, excess of CF_3CO_2H was removed under reduced pressure. The residue was carried forward to the next step without further purification. The **homo-Br_6** and **homo-Cl_6** Borromean ring derivatives were prepared by reacting equimolar amounts of 4-chloro-2,6-pyridinedicarboxaldehyde[2] or with 4-bromo-2,6-pyridinedicarboxaldehyde[3] $Zn(OAc)_2$, and freshly prepared **DAB**-H_n•nTFA in hot *i*-PrOH. The **hetero-$Cl_{6-x}Br_x$** Borromean ring mixture was prepared by reacting 0.5 molar equivalents of 4-chloro-2,6-pyridine dicarboxaldehyde and 0.5 molar equivalents 4-bromo-2,6-pyridinedicarboxaldehyde with 1.0 molar equivalents of both $Zn(OAc)_2$, and freshly prepared **DAB**-H_n•nTFA in hot *i*PrOH. In all three cases, the desired BR derivatives precipitated from the reaction mixture as 'pure' products and were isolated as off-white solids by filtering the solutions and then washed with *I*-PrOH, and Et_2O, before being dried under vacuum.

Materials and Methods

All solvents (EM Science) were dried prior to use according to literature procedures. 95% EtOH (Pharmco) and deuterated solvents (Cambridge Isotope Laboratories) for NMR spectroscopic analyses were used as received. All reagents and starting materials, were purchased from Aldrich and used without further purification. 4-Chloro-2,6-pyridinedicarboxaldehyde[2] and 4-bromo-2,6-pyridinedicarboxaldehyde[3] were synthesized according to known literature procedures starting from chelidamic acid (TCI Int.). Thin-layer chromatography (TLC) was performed either on aluminum sheets, coated with silica-gel 60F (Merck 5554) or on aluminum sheets, coated with aluminum oxide 60F (Merck 5550/7, neutral). The plates were inspected by UV light. Column chromatography was carried out, either by using silica-gel 60 (Merck 9358, 230–400 mesh) or by using aluminum oxide (Aldrich, 150 mesh, neutral, activity II). All ^1H and ^{13}C NMR spectra were recorded on either a Bruker Avance600 (600 MHz and 150 MHz, respectively), Bruker Avance500 (500 MHz and 125 MHz, respectively), or Bruker ARX500 (500 MHz and 125 MHz, respectively). All chemical shifts are quoted in ppm,

relative to tetramethylsilane, using the residual solvent peak as a reference standard. Mass spectra were measured on an IonSpec 7.0T Ultima FTMS with MALDI and ESI ion sources. Matrix-Assisted Laser Desorption Ionization (MALDI) mass spectra were obtained using dihydroxybenzoic acid as the supporting matrix. Electrospray ionization (ESI) mass spectra were obtained with either MeOH or MeCN as the liquid carrier.

Homo-Cl_6•12TFA: The *t*-Boc-protected bisammonium bipyridyl ligand **1** (241 mg, 0.402 mmol) was dissolved in 2 mL of CF_3CO_2H and stirred at RT for 10 min. Thereafter, excess of CF_3CO_2H was removed under reduced pressure and this product was carried forward to the next step without further purification. In the following order: 4-chloro-2,6-pyridinediacarboxaldehyde (68.2 mg, 0.402 mmol) and $Zn(OAc)_2$ (73.8 mg, 0.402 mmol) were added to a stirred *i*-PrOH solution (5 mL) containing freshly prepared **DAB**-H_n•nTFA (0.402 mmol) and the reaction mixture was heated at 60 °C for 12 h, producing a precipitate in a pale yellow colored solution. The precipitate was removed by filtration and washed with *i*-PrOH (3×5 mL), Et_2O (3×5 mL), dried in air, and finally under vacuum. Yield of **Homo-Cl_6**•12TFA: 325 mg, 95%; ^{1}H NMR (600 MHz, CD_3OD, 25 °C): δ = 4.83 (s, 24H), 6.50 (bs, 12H), 6.68 (d, J = 8.4 Hz, 24H), 6.73 (d, J = 8.4 Hz, 12H), 7.99 (d, J = 2.4 Hz, 12H), 8.41 (s, 12H), 8.83 (s, 12H); ^{13}C NMR (150 MHz, CD_3OD, 25 °C) 16 of 16 signals: δ = 63.2, 112.6, 114.0, 118.1 (q, J = 296 Hz, TFA), 122.3, 130.9, 131.2, 134.9, 149.4, 150.7, 151.7, 153.0, 153.4, 161.3, 162.5 (q, J = 34.6 Hz, TFA) 169.8; HRMS (ESI): *m/z* (%) 1533.8822 (50) $[M - 3CF_3CO_2]^{3+}$, 1122.1286 (100) $[M - 4CF_3CO_2]^{4+}$, 875.0941 (30) $[M - 5CF_3CO_2]^{5+}$.

Homo-Br_6•12TFA: The *t*-Boc-protected bisammonium bipyridyl ligand **1** (219 mg, 0.365 mmol) was dissolved in 2 mL of CF_3CO_2H and stirred at RT for 10 min. Thereafter, excess of CF_3CO_2H was removed under reduced pressure and this product was carried forward to the next step without further purification. In the following order: 4-bromo-2,6-pyridinediacarboxaldehyde (78.1 mg, 0.365 mmol) and $Zn(OAc)_2$ (67.0 mg, 0.365 mmol) were added to a stirred *i*-PrOH solution (5 mL) containing freshly prepared **DAB**-H_n•nTFA (0.365 mmol) and the reaction mixture was heated at 60 °C for 12 h, producing a precipitate in a pale yellow colored solution. The precipitate was removed by filtration and washed with *i*PrOH (3×5 mL), Et_2O (3×5 mL), dried in air, and finally under vacuum. Yield of **Homo-Br_6**•12TFA: 302 mg, 95%; ^{1}H NMR (600 MHz, CD_3OD, 25 °C): δ = 4.83 (s, 24H), 6.50 (bs, 12H), 6.68 (d, J = 8.4 Hz, 24H), 6.73 (d, J = 8.4 Hz, 12H), 7.99 (d, J = 2.4 Hz, 12H), 8.51 (s, 12H), 8.82 (s, 12H); ^{13}C NMR (150 MHz,

CD_3OD, 25 °C) 16 of 16 signals: δ = 63.2, 112.6, 114.0, 118.1 (q, J = 296 Hz, TFA), 122.3, 131.2, 134.0, 134.9, 141.7, 149.0, 150.7, 151.7, 153.4, 161.2, 162.5 (q, J = 34.6 Hz, TFA) 169.8; HRMS (ESI): *m/z* (%) 1622.4430 (50) [M – $3CF_3CO_2$]$^{3+}$ 1188.5620 (100) [M – $4CF_3CO_2$]$^{4+}$, 928.2401 (20) [M – $5CF_3CO_2$]$^{5+}$.

Hetero-$Br_{6-x}Cl_x$•12TFA: The *t*-Boc-protected bisammonium bipyridyl ligand **1** (228 mg, 0.381 mmol) was dissolved in 2 mL of CF_3CO_2H and stirred at RT for 10 min. Thereafter, excess of CF_3CO_2H was removed under reduced pressure and this product was carried forward to the next step without further purification. In the following order: 4-chloro-2,6-pyridinediacarboxaldehyde (32.3 mg, 0.191 mmol), 4-bromo-2,6-pyridinediacarboxaldehyde (40.8 mg, 0.191 mmol), and $Zn(OAc)_2$ (70.0 mg, 0.381 mmol) were added to a stirred *i*-PrOH solution (5 mL) containing freshly prepared **DAB**-H_n•nTFA (0.381 mmol) and the reaction mixture was heated at 60 °C for 12 h producing a precipitate in a pale yellow colored solution. The precipitate was removed by filtration and washed with *i*-PrOH (3×5 mL), Et_2O (3×5 mL), dried in air, and finally under vacuum. Yield of **Hetero-$Br_{6-x}Cl_x$**•12TFA: 317 mg, 95%; ^{1}H NMR (600 MHz, CD_3OD, 25 °C): δ = 4.83 (s, 24H), 6.50 (bs, 12H), 6.68 (d, J = 8.4 Hz, 24H), 6.73 (d, J = 8.4 Hz, 12H), 7.98 (d, J = 2.4 Hz, 12H), 8.42 (s, 6H), 8.57 (s, 6H), 8.82 (s, 6H), 8.83 (s, 6H); ^{13}C NMR (150 MHz, CD_3OD, 25 °C) 20 signals: δ = 63.2, 112.6, 114.0, 118.1 (q, J = 296 Hz, TFA), 122.3, 130.9, 131.2, 134.0, 134.9, 141.7, 149.0, 149.3, 150.7, 151.7, 153.0, 153.3, 161.2, 161.3, 162.5 (q, J = 34.6 Hz, TFA) 169.8; HRMS (ESI): *m/z* (%) 1607.4545 (5) [M(**$ClBr_5$**) – $3CF_3CO_2$]$^{3+}$, 1592.8171 (30) [M(**Cl_2Br_4**) – $3CF_3CO_2$]$^{3+}$, 1578.1598 (40) [M(**Cl_3Br_3**) – $3CF_3CO_2$]$^{3+}$, 1563.1880 (25) [M(**Cl_4Br_2**) – $3CF_3CO_2$]$^{3+}$, 1548.2027 (5) [M(**Cl_5Br**) – $3CF_3CO_2$]$^{3+}$, 1188.5581 (2) [M(**Br_6**) – $4CF_3CO_2$]$^{4+}$, 1177.8123 (30) [M(**$ClBr_5$**) – $4CF_3CO_2$]$^{4+}$, 1166.3271 (70) [M(**Cl_2Br_4**) – $4CF_3CO_2$]$^{4+}$, 1155.0922 (100) [M(**Cl_3Br_3**) – $4CF_3CO_2$]$^{4+}$, 1144.1105 (70) [M(**Cl_4Br_2**) – $4CF_3CO_2$]$^{4+}$, 1132.6204 (20) [M(**Cl_5Br**) – $4CF_3CO_2$]$^{4+}$, 1121.8761 (1) [M(**Cl_6**) – $4CF_3CO_2$]$^{4+}$, 919.6567 (10) [M(**$ClBr_5$**) – $5CF_3CO_2$]$^{5+}$, 910.8648 (22) [M(**Cl_2Br_4**) – $5CF_3CO_2$]$^{5+}$, 901.4720 (25) [M(**Cl_3Br_3**) – $5CF_3CO_2$]$^{5+}$, 893.0800 (15) [M(**Cl_4Br_2**) – $5CF_3CO_2$]$^{5+}$.

Exchanging the Two Homo-BR Derivatives:

The conditions that resulted in the complete scrambling of an equimolar mixture of the two **homo**-BR derivatives (**homo-Cl_6** and **homo-Br_6**) were achieved by investigating and comparing the results of four different experiments (MSExpt1, MSExpt2, MSExpt2a, MSExpt3). In the first set of experiments (MSExpt1 and MSExpt2), two 2 mM

methanolic solutions (5 mL), both containing an equimolar mixture of **homo-Cl$_6$** (49.3 mg, 0.0100 mmol, 2.0 mM) and **homo-Br$_6$** (51.9 mg, 0.0100 mmol, 2.0 mM), without the addition of CF_3CO_2H, one of the reaction mixtures was stirred at room temperature and the other was heated at 60 °C. Both reactions were sampled by removing 250 μL aliquots, followed by dilution with MeOH to 0.5 mL and then injected into the ESI-MS instrument. After 48 and 72 h, the reaction that had been heated at 60 °C (MSExpt1) changed its color from being initially light-yellow to an orange-colored solution and was subsequently sampled for ESI-MS. The major peaks observed in these mass spectra were assigned to the **homo-Cl$_6$** BR derivative at m/z 1122 and the **homo-Br$_6$** BR derivative at m/z 1188 in the tetracationic region. Since no significant change in the distribution and intensity of the peaks in these mass spectra was observed, the color change suggested, that, under these conditions, some decomposition might have occurred. After 5 days, the now dark-orange solution was sampled (MSExpt1) and the mass spectrum acquired from this solution contained very broad signals for the 3^+, 4^+, and 5^+ cations with no indication that exchange had occurred, but, instead suggested that an even more significant amount of decomposition had occurred since the intensities of the parent peaks for the **homo-Cl$_6$** BR derivative and the **homo-Br$_6$** BR derivative were significantly weaker. This observation suggested that the BR compounds could be kinetically nonlabile and so thermodynamically stable under neutral conditions at elevated temperatures apart from slow decompostion. In the reaction (MSExpt2) that was stirred at room temperature, no exchange occurred after 5 days or indeed after 2 weeks: all mass spectra acquired displayed only the peaks that corresponded to the **homo-Cl$_6$** BR derivative at m/z 1122 and the **homo-Br$_6$** BR derivative at m/z 1188 in the tetracationic region. This observation also suggested at the time that the BR compounds are kinetically nonlabile and thermodynamically stable under neutral conditions at room temperature and do not decompose. Five drops of CF_3CO_2H were added to this room temperature reaction (MSExpt2a) and stirring was continued. After two weeks of stirring, the reaction was sampled. The mass spectrum revealed no significant changes in the intensities and distributions for the parent peaks for the **homo-Cl$_6$** BR and the **homo-Br$_6$** BR derivatives. However, sampling the solution (MSExpt2a) after stirring for an additional 5 weeks the two **homo**-BR derivatives were completely scrambled. From this result, the last experiment (MSExpt3) was conducted using a methanolic solution (5 mL) containing an equimolar mixture of **homo-Cl$_6$** (49.3 mg, 0.0100 mmol, 2.0 mM) and **homo-Br$_6$** (51.9 mg, 0.0100 mmol, 2.0 mM), with the addition of 250 μL of CF_3CO_2H. This solution was heated at 60 °C. After 5 days of sampling, this mixture of BR derivatives was completely scrambled as evidenced by

ESI-MS and the fact that it changed from an initially light-yellow to a light-orange colored solution.

References and Notes

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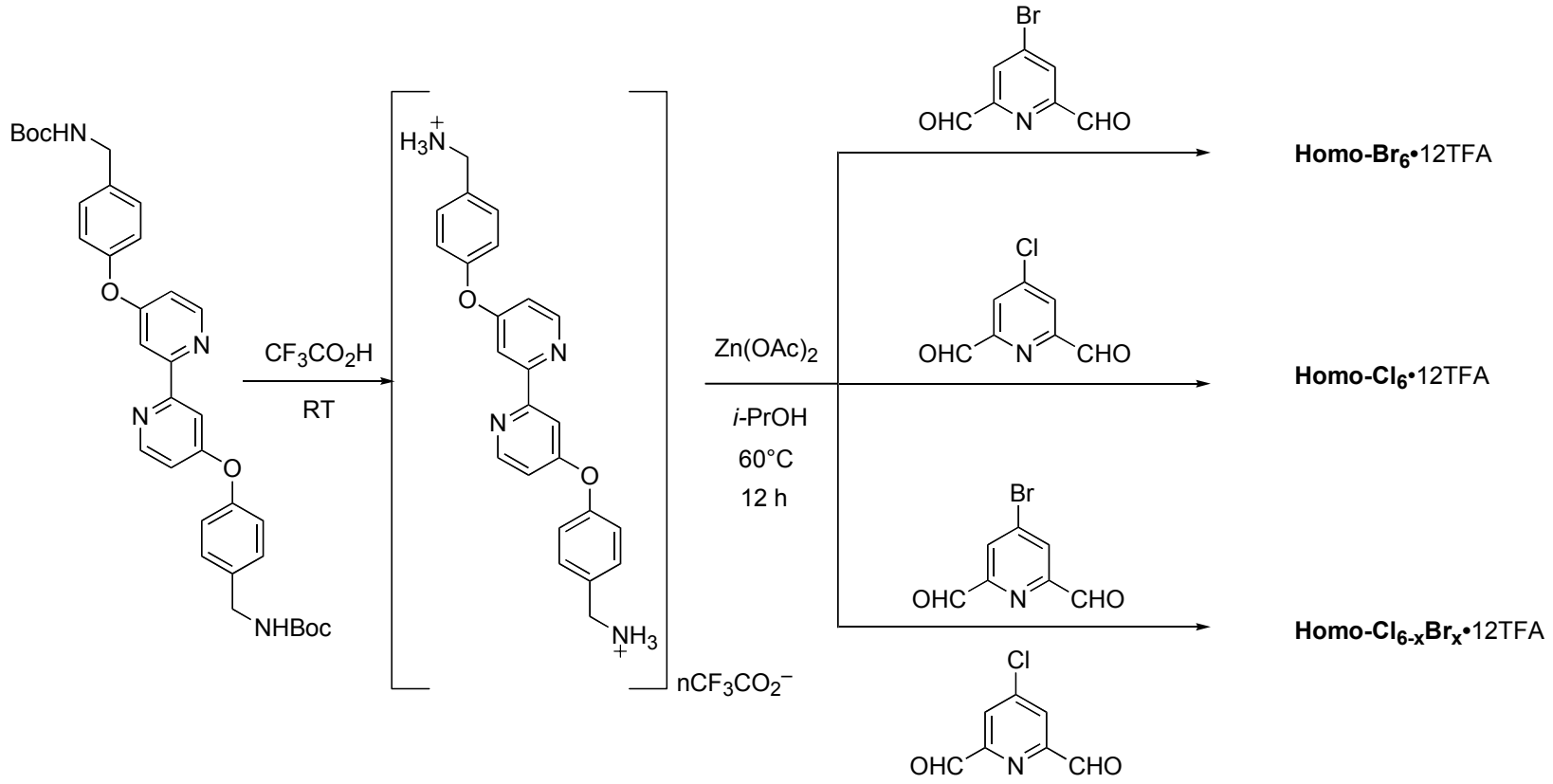

Scheme S1. Synthesis of the BR derivatives **homo-Br_6•12TFA**, **homo-Cl_6•**12TFA, and **hetero**-**$Cl_{6-x}Br_x$•**12TFA.