Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Acid-Base Controlled Multiple Conformation and Aromaticity Switches in Tren-Capped Hexaphyrins

S. Le Gac, E. Caytan, V. Dorcet, B. Boitrel

Experimental part

Experimental part

General

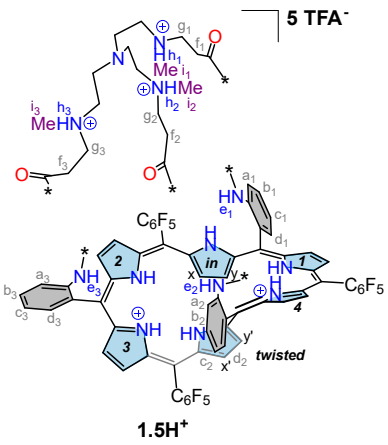
All of the NMR experiments were conducted in 5 mm standard NMR tubes. ^{1}H and ^{19}F NMR spectra were recorded on a Bruker AV III HD 500 MHz NMR spectrometer fitted with a BBFO probehead. ^{1}H NMR spectra were recorded at 500 MHz and ^{19}F spectra at 470 MHz. Chemical shifts are expressed in parts per million, and traces of residual solvents were used as internal standards. When possible, ^{1}H NMR signals were assigned using 2D NMR experiments. ^{1}H NMR assignment abbreviations are the following: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), and multiplet (m). Tren-capped hexaphyrins **1** and **2** were synthesized as previously described.[1] All of the chemicals were commercial products used as received. For **1.5H^{+}**, ^{19}F DOSY was acquired using a stimulated echo sequence (stegp1s) with Δ 50 ms, δ 1.6 ms and a linear ramp of 16 gradients values from 2 to 95 %. ^{19}F 1D-selective-NOESY experiments (selnogp) were acquired using mixing times from 100 to 2000 ms and showed no chemical exchange between TFA signals. Heteronuclear dipolar interactions between ^{19}F and ^{1}H were studied using a modified nOe-difference sequence where ^{19}F signals were selectively saturated and ^{1}H signals were observed. Selective ^{19}F saturation was obtained with a low-power cw irradiation during 10 s before ^{1}H excitation and observation. Difference spectra were obtained subtracting the same "off-resonance ^{19}F saturation" spectrum from each "on-resonance ^{19}F saturation" spectrum.

*Standard protocol for the NMR titration of **1** with TFA :*

In a 5 mm standard NMR tube, 4.0 mg of **1** were dissolved in 500 µL of $CDCl_3$ (previously filtered over basic alumina). The solution was cooled down at 233 K, and ^{1}H and ^{19}F NMR spectra were recorded. Aliquots of 5 µL or 10 µL (0.5 equiv./1 equiv.) of a solution of TFA (275 mM in $CDCl_3$) were successively added, and NMR spectra were recorded after each addition.

*^{1}H and ^{19}F NMR description of **1.5H^{+}***

^{1}H NMR ($CDCl_3$, 500 MHz, 233 K): δ 13.08 (s, 1H, NHπ_{in}), 12.39 (s, 1H, NHh_1), 12.31 (s, 1H, NHCOe_1), 10.01 (s, 1H, NHh_2), 9.58 (s, 1H, NH$\pi_{twisted}$), 9.32 (d, 1H, J = 7.0 Hz, HArd_3), 9.25 (d_b, 1H, J = 4.5 Hz, π_3), 9.20 (d_b, 1H, J = 4.9 Hz, π_3), 9.17 (m_b, 1H, π_2), 9.14 (s_b, 2H, π_1), 8.95 (s_b, 1H, π_2), 8.82 (s_b, 1H, π_4), 8.41 (d, 1H, J = 8.0 Hz, HArd_2), 8.08 (m_b, 2H, π_4+HAra_1), 7.93 (t_b, 1H, J = 7.2 Hz, HArc_3), 7.88 (t_b, 1H, J = 7.2 Hz, HArb_3), 7.77 (d_b, 1H, J = 7.9 Hz, HAra_3), 7.58 (m_b, 1H, HArb_1), 7.37 (s, 1H, NHCOe_3), 7.30 (t_b, 1H, J = 8.0 Hz, HArc_2), 6.98 (m_b 2H, HArc_1b_2), 6.60 (s, 1H, NHtrenh_3), 6.06 (d_b, 1H, J = 6.5 Hz, HAra_2), 5.69 (d_b, 1H, J = 6.5 Hz, HArd_1), 4.62 (s, 1H, $\pi_{twisted\_x'}$), 4.24 (s_b, 1H, CH$_2f_1$), 3.83 (s, 1H, $\pi_{twisted\_y'}$), 3.61 (s, 1H, NHCOe_2), 3.41 (s_b, 2H, CH$_2f_1$+g_1), 3.23 (s_b, 1H, CH$_2g_1$), 2.90 (s_b, 1H, CH$_{2tren}$), 2.63 (s_b, 1H, CH$_2g_3$) 2.54 (s_b, 1H, CH$_2g_3$), 2.34-1.52 (complex region, 11H, CH$_{2tren}$), 2.46 (s, 3H, Mei_1), 2.40 (s_b, 1H, CH$_2g_2$), 1.96 (s, 3H, Mei_2), 1.46 (s_b, 1H, CH$_2g_2$), 1.39 (s_b, 1H, CH$_2f_3$), 0.75 (s, 3H, Mei_3), 0.37 (s_b, 1H, CH$_2f_3$), -0.39 (s, 1H, NHπ_4), -0.60 (s, 1H, π_{in_y}), -0.90 (s,



[1] H. Ruffin, G. Nyame Mendendy Boussambe, T. Roisnel, V. Dorcet, B. Boitrel and S. Le Gac, *J. Am. Chem. Soc.*, 2017, **139**, 13847-13857.

1H, π_{in_x}), -1.34 (s_b, 1H, CH_2f_2), -1.83 (s, 1H, NHπ_3), -2.84 (s_b, 1H, CH_2f_2), -2.94 (s, 1H, NHπ_2), -3.18 (s, 1H, NHπ_1).

^{19}F NMR ($CDCl_3$, 470 MHz, 233 K): δ -75.0 to -76.3 (large signal, TFAtren), -75.66 (s, 3F, TFA1_hexaphyrin), -81.79 (s, 3F, TFA2_hexaphyrin), -135.19 (s_b, 1F, ArF-o), -136.07 (d_b, 1F, *J* = 22.0 Hz, ArF-o), -137.66 (s_b, 1F, ArF-o), -138.78 (d_b, 1F, *J* = 19.3 Hz, ArF-o), -139.67 (d_b, 1F, *J* = 22.0 Hz, ArF-o), -141.58 (s_b, 1F, ArF-o), -148.77 (s_b, 1F, ArF-p), -149.06 (s_b, 1F, ArF-p), -149.21 (s_b, 1F, ArF-p), -159.09 (m_b, 1F, ArF-m), -159.58 (m_b, 2F, ArF-m), -159.90 (t_b, 1F, *J* = 21.3 Hz, ArF-m), -160.06 (t_b, 1F, *J* = 20.4 Hz, ArF-m), -161.54 (m_b, 1F, ArF-m).

Crystal data for ***1.6H$^+$ↄTFA$^-$***

($C_{101}H_{72}Cl_2F_{39}N_{13}O_{19}$); M = 2583.61. D8 VENTURE Bruker AXS diffractometer equipped with a (CMOS) PHOTON 100 detector, Mo-Kα radiation (λ = 0.71073 Å, multilayer monochromator), T = 150(2) K; monoclinic *P* $2_1/n$ (I.T.#14), a = 17.877(3), b = 25.108(5), c = 28.082(5) Å, β = 97.496(6) °, V = 12497(4) Å^3. Z = 4, d = 1.373 g.cm^{-3}, μ = 0.174 mm^{-1}. The structure was solved by dual-space algorithm using the SHELXT program,[2] and then refined with full-matrix least-squares methods based on F^2 (SHELXL).[3] The contribution of the disordered solvents to the calculated structure factors was estimated following the BYPASS algorithm,[4] implemented as the SQUEEZE option in PLATON.[5] A new data set, free of solvent contribution, was then used in the final refinement. All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. H atoms were finally included in their calculated positions and treated as riding on their parent atom with constrained thermal parameters. A final refinement on F^2 with 28621 unique intensities and 1531 parameters converged at ωR(F^2) = 0.4129 (R(F) = 0.1514) for 13767 observed reflections with $I > 2\sigma(I)$. CCDC 1893625.

Comments relative to the alerts level A in the checkcif report: A alerts in the checkcif are the result of highly disordered TFA molecules and to the overall quality of the crystal. However, atomic displacement parameters of the atoms constituting the hexaphyrin were refined freely (except for C91-C96 cycle, F94 and F95), and there's no constrain on the position and the distance between the atoms of the hexaphyrin. As a result, the atomic constitution of the hexaphyrin is considered correct with a high level of confidence.

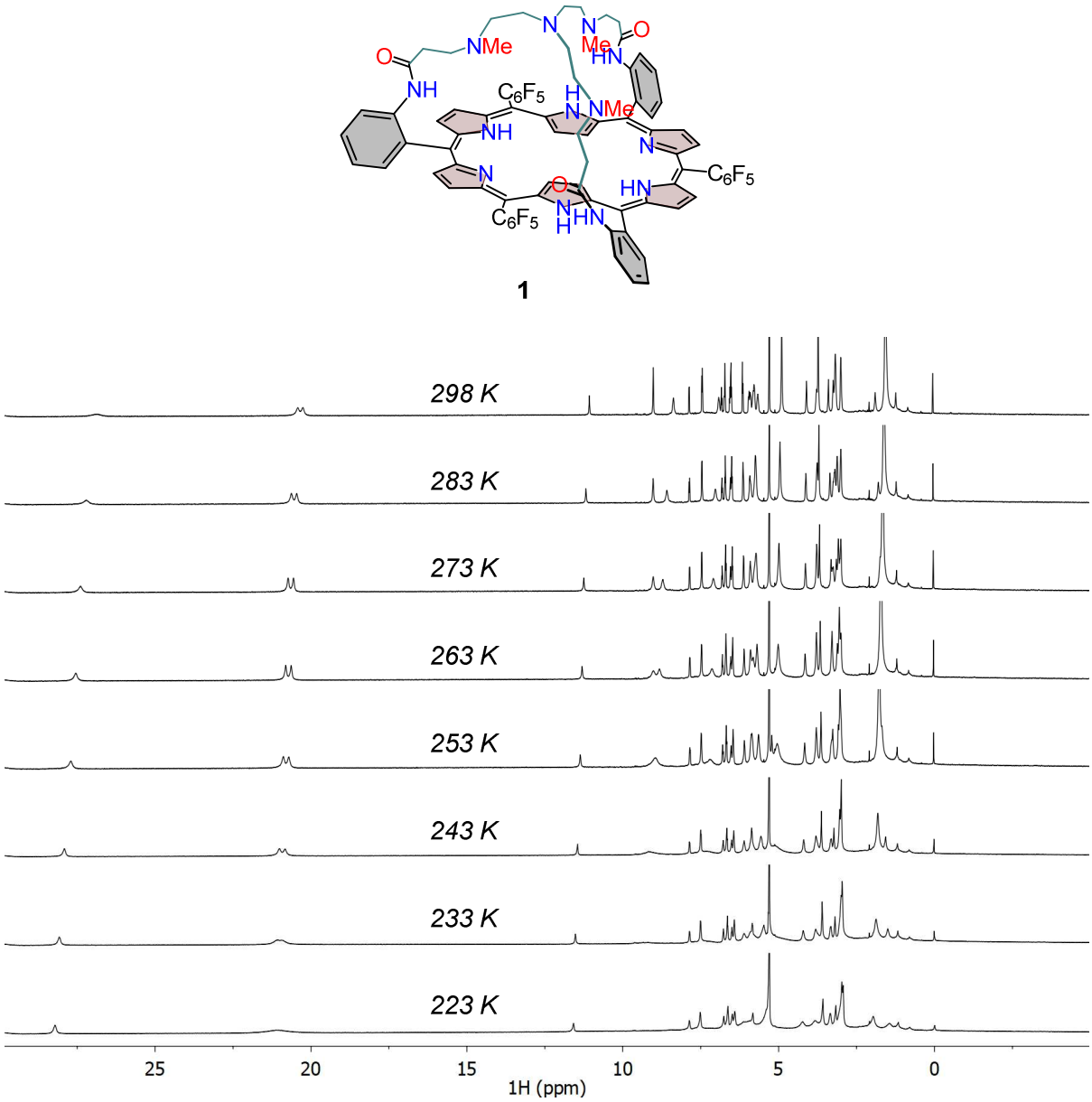


Figure S1. VT ^{1}H NMR spectra of **1** (CD_2Cl_2, 500 MHz).

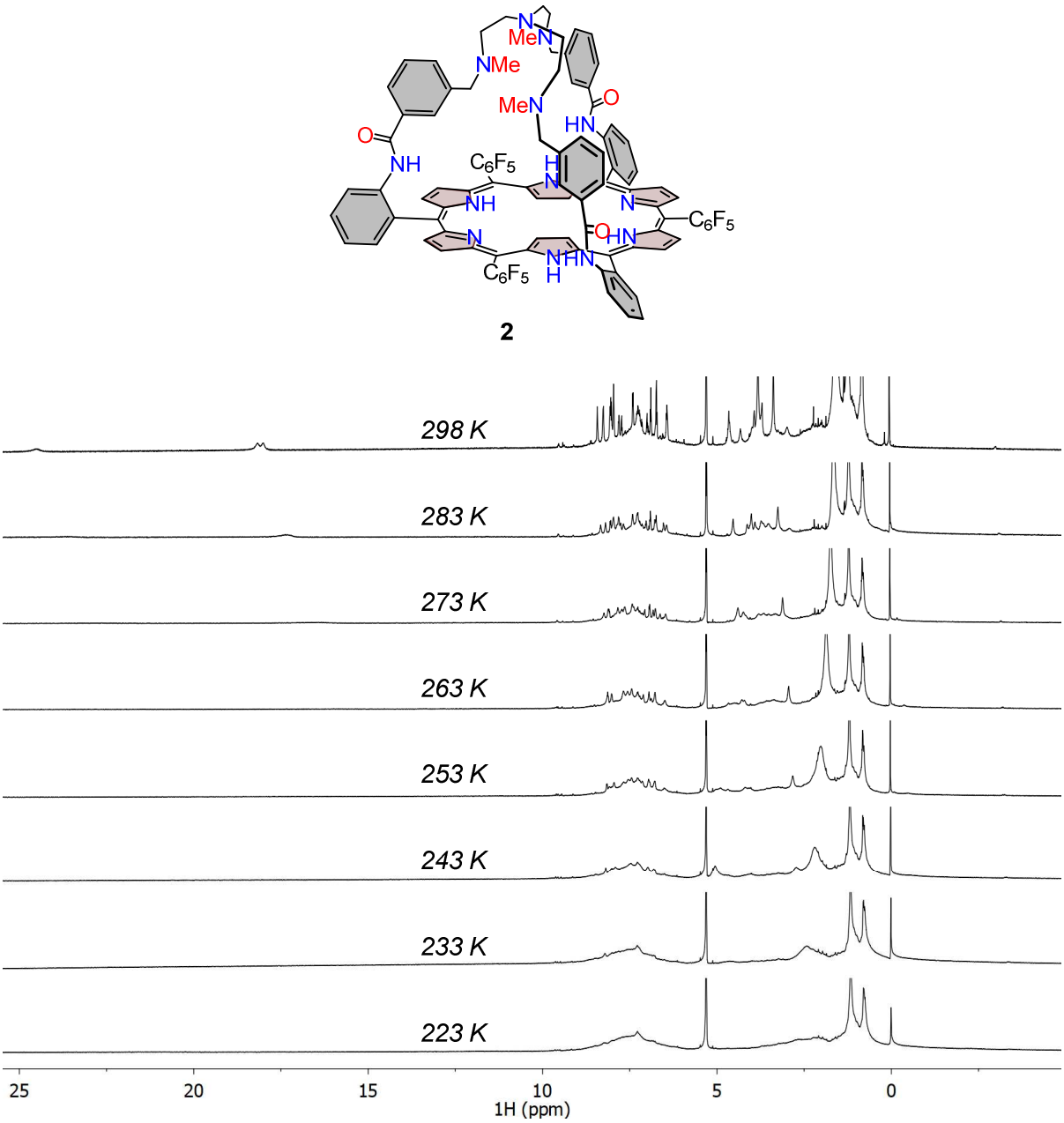


Figure S2. VT ^{1}H NMR spectra of **2** (CD_2Cl_2, 500 MHz).

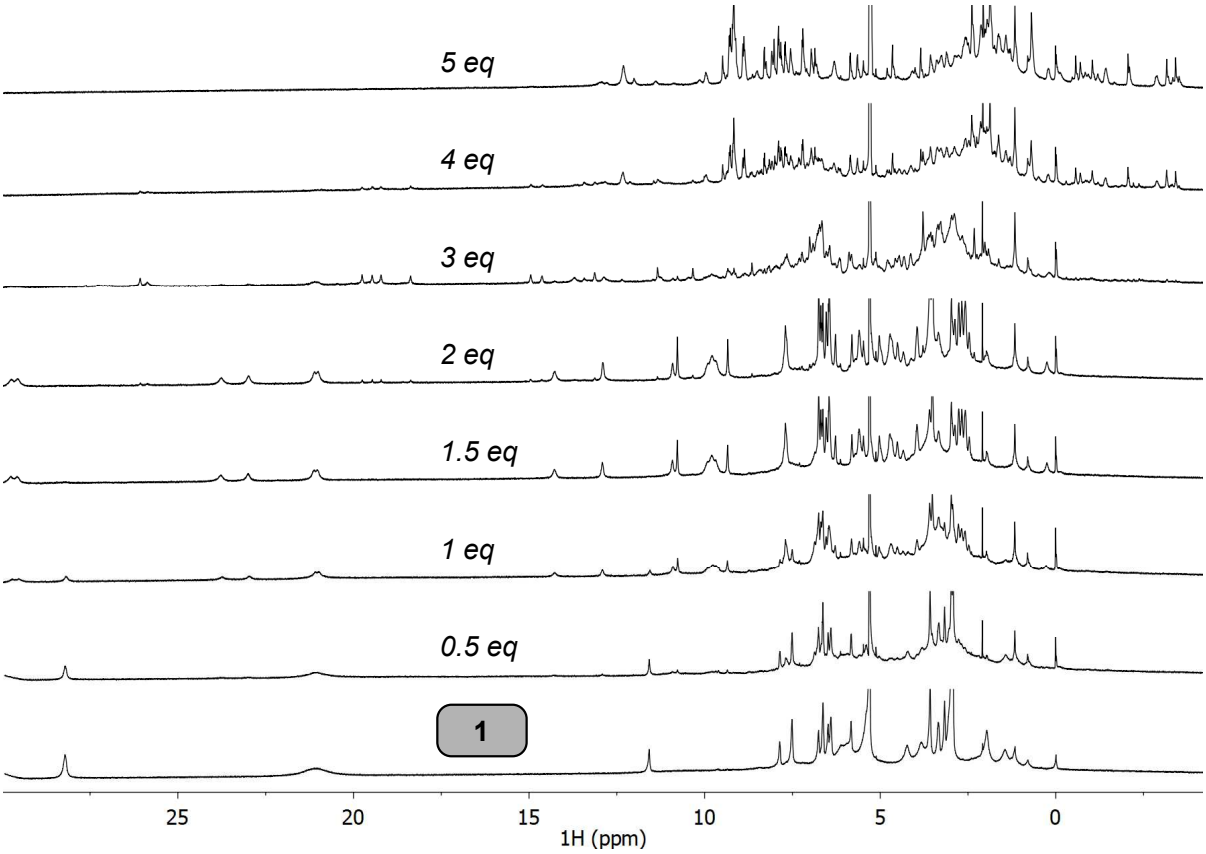


Figure S3. ^{1}H NMR titration experiment of **1** with TFA (CD_2Cl_2, 500 MHz, 223 K).

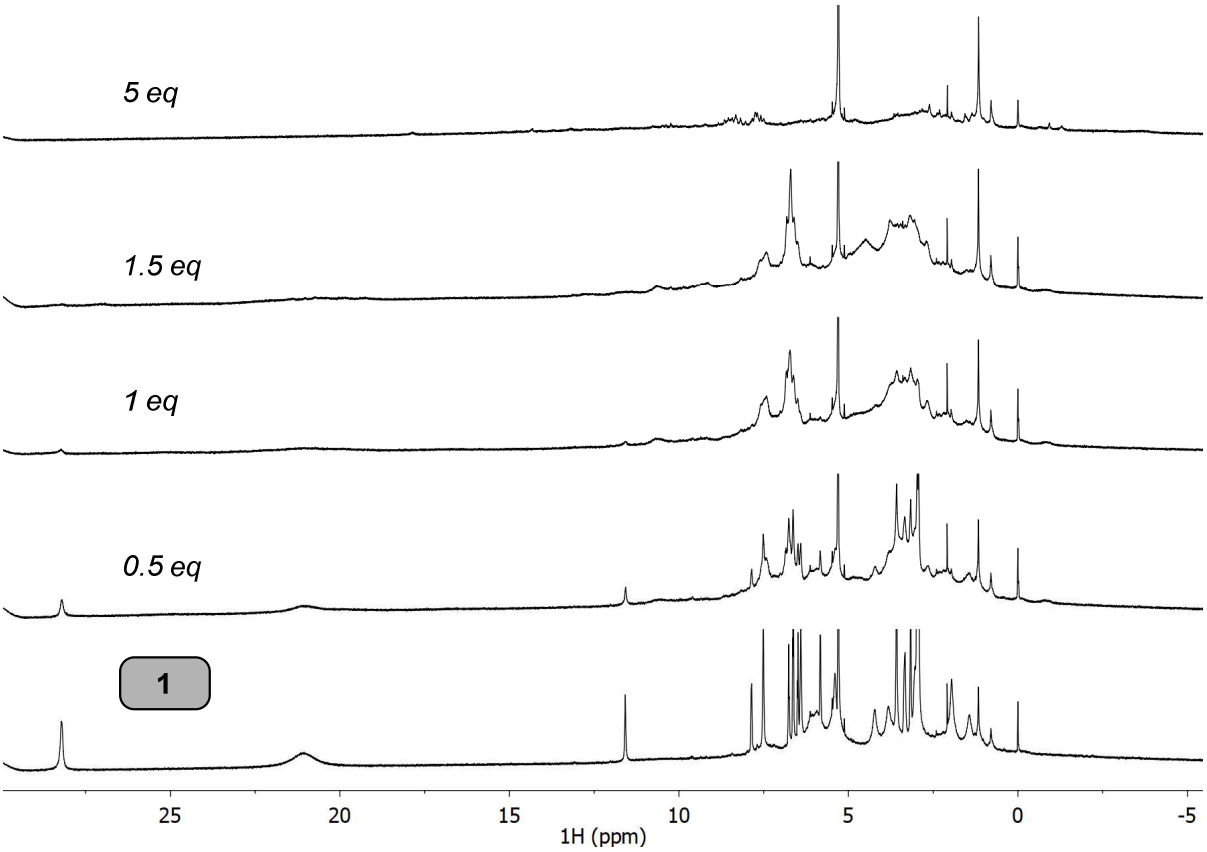


Figure S4. ^{1}H NMR titration experiment of **1** with MSA (CD_2Cl_2, 500 MHz, 223 K).

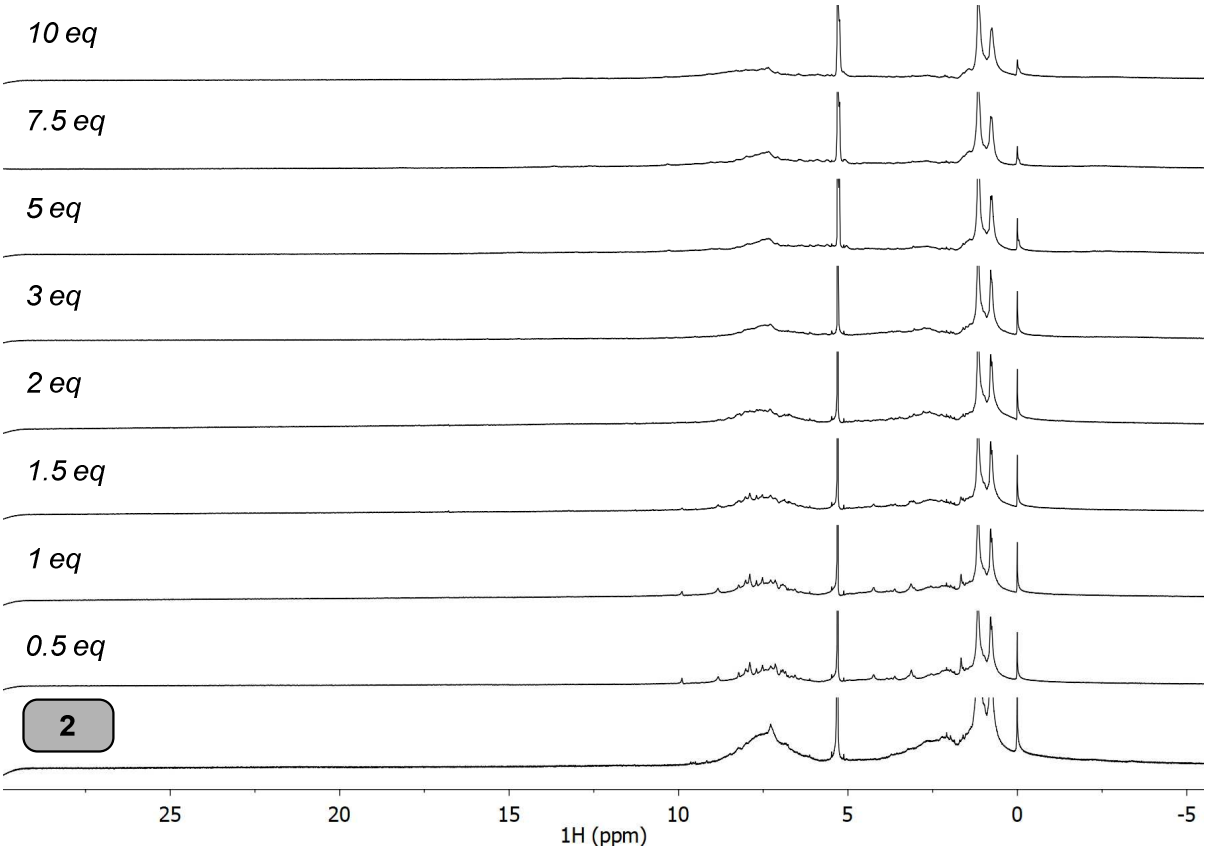


Figure S5. ^{1}H NMR titration experiment of **2** with TFA (CD_2Cl_2, 500 MHz, 223 K).

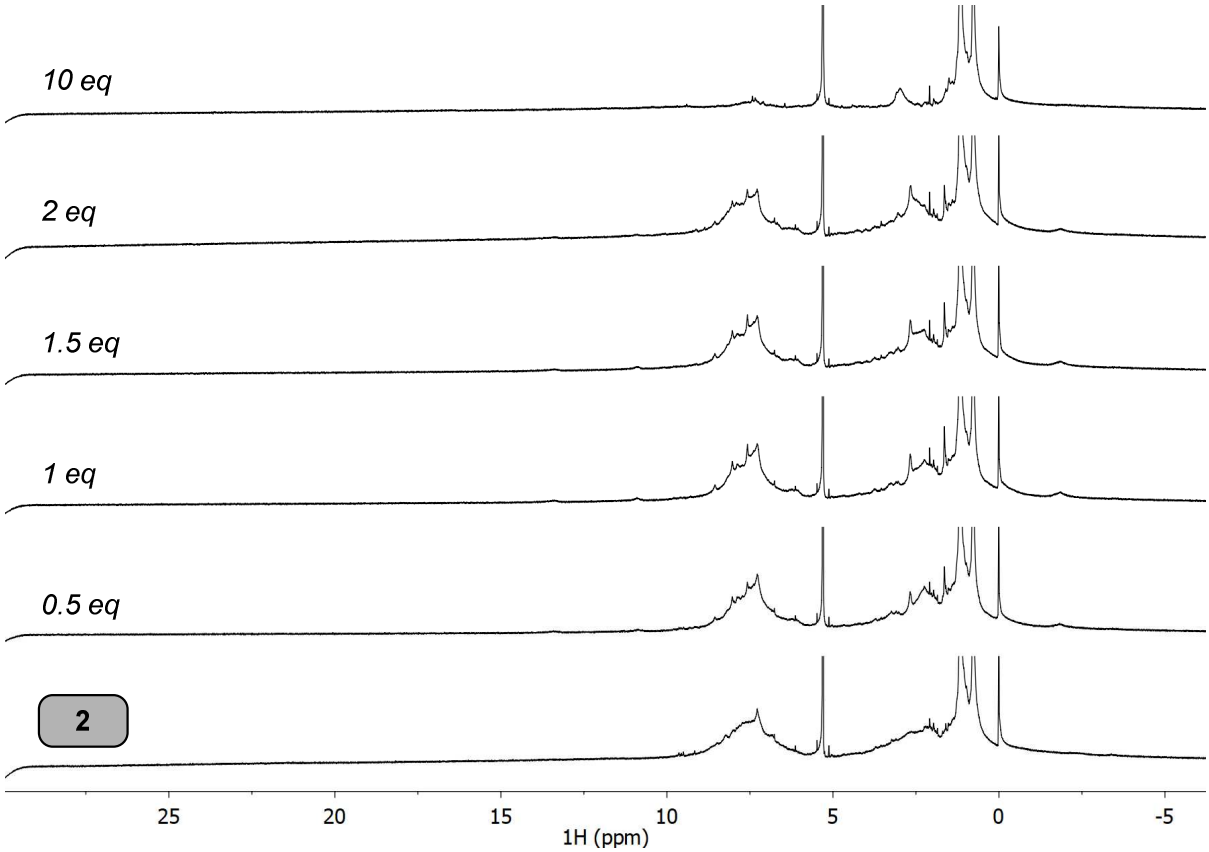


Figure S6. ^{1}H NMR titration experiment of **2** with MSA (CD_2Cl_2, 500 MHz, 223 K).

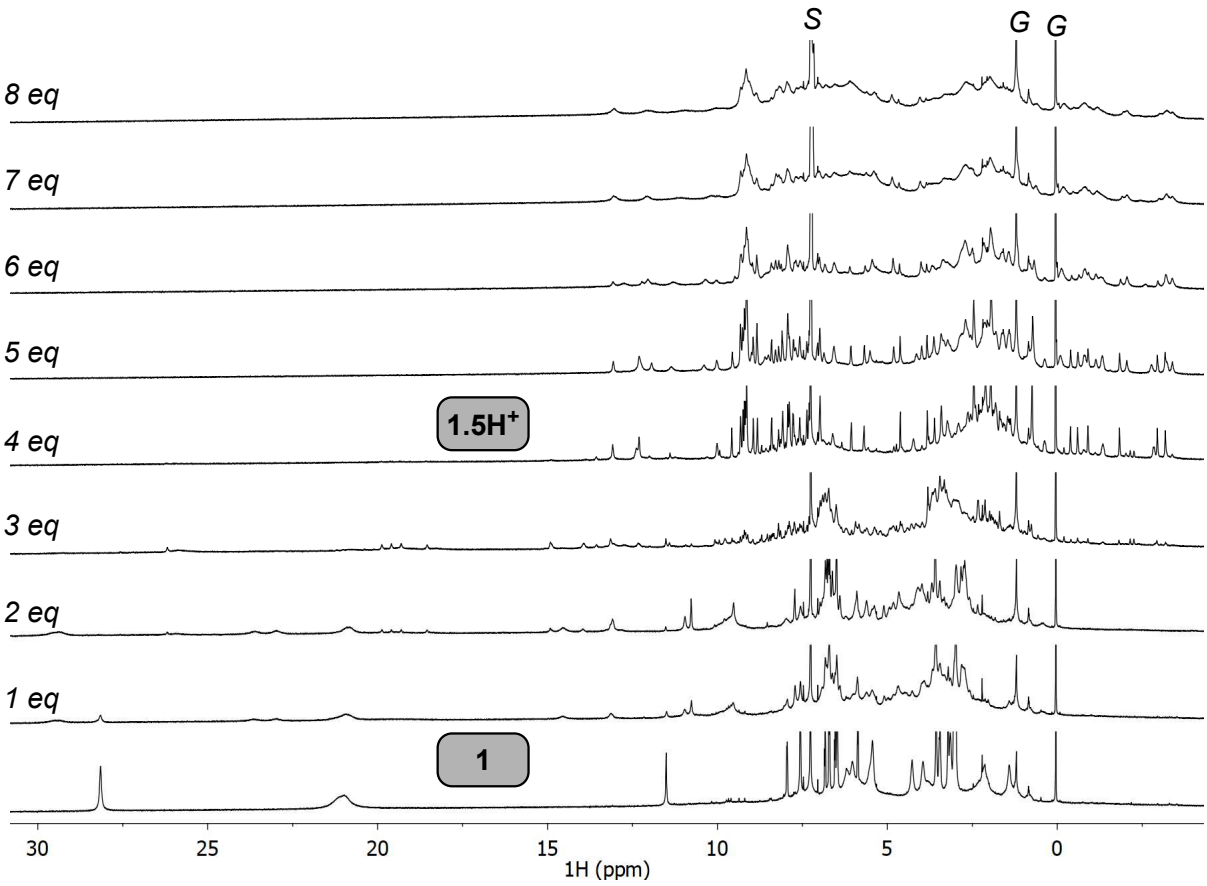


Figure S7. ^{1}H NMR titration experiment of **1** with TFA ($CDCl_3$, 500 MHz, 233 K). S = solvent, G = grease.

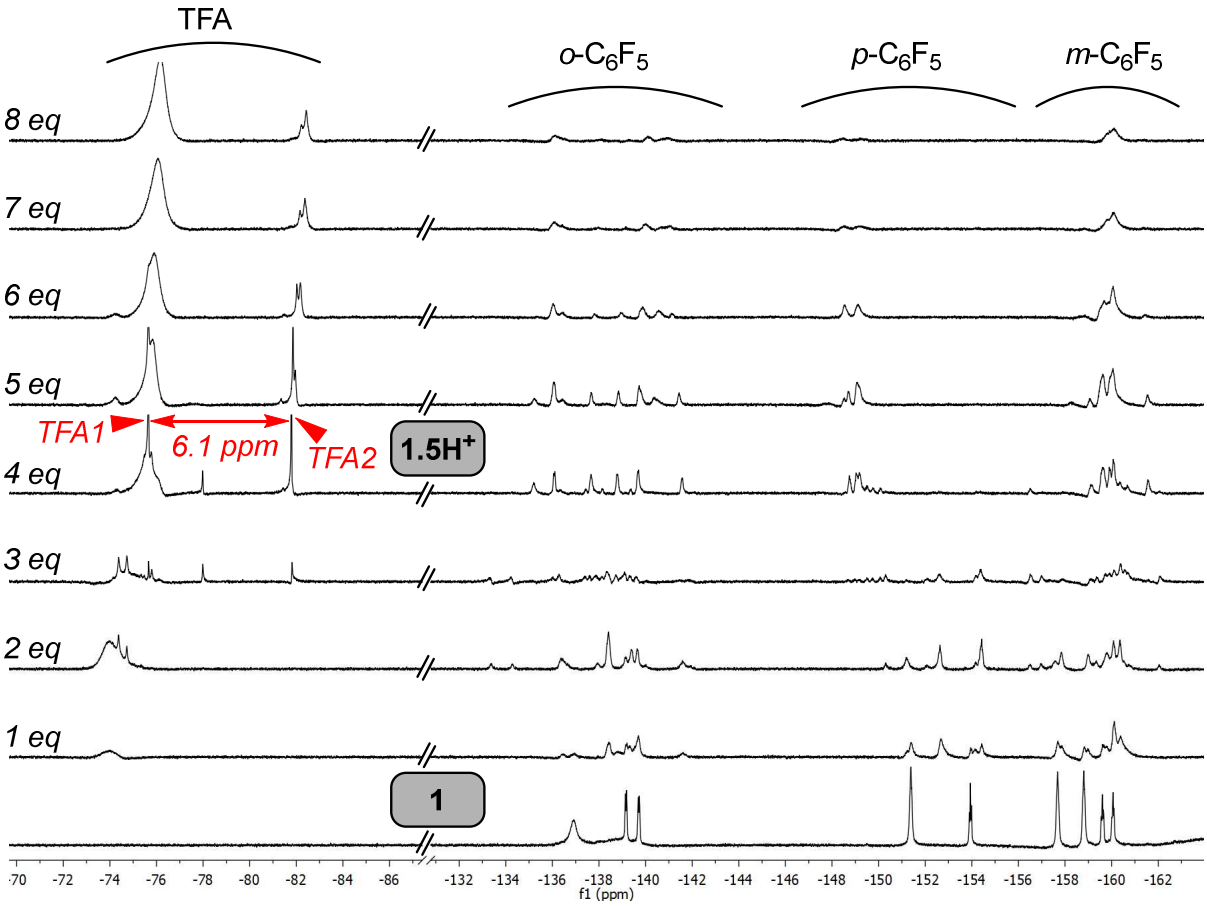


Figure S8. ^{19}F NMR titration experiment of **1** with TFA ($CDCl_3$, 470 MHz, 233 K).

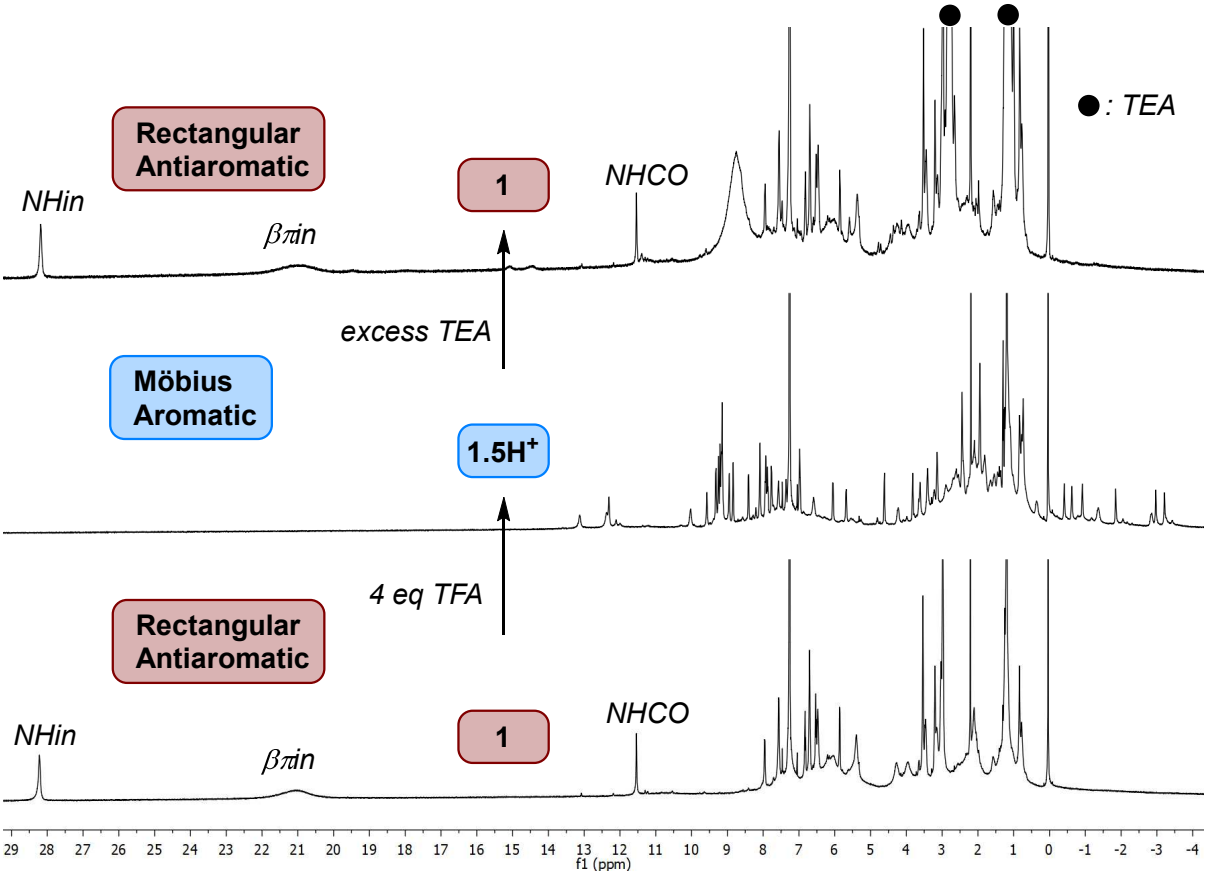


Figure S9. Acid-base conformation and aromaticity switches upon successive addition of TFA and TEA to **1** ($CDCl_3$, 500 MHz, 233 K).

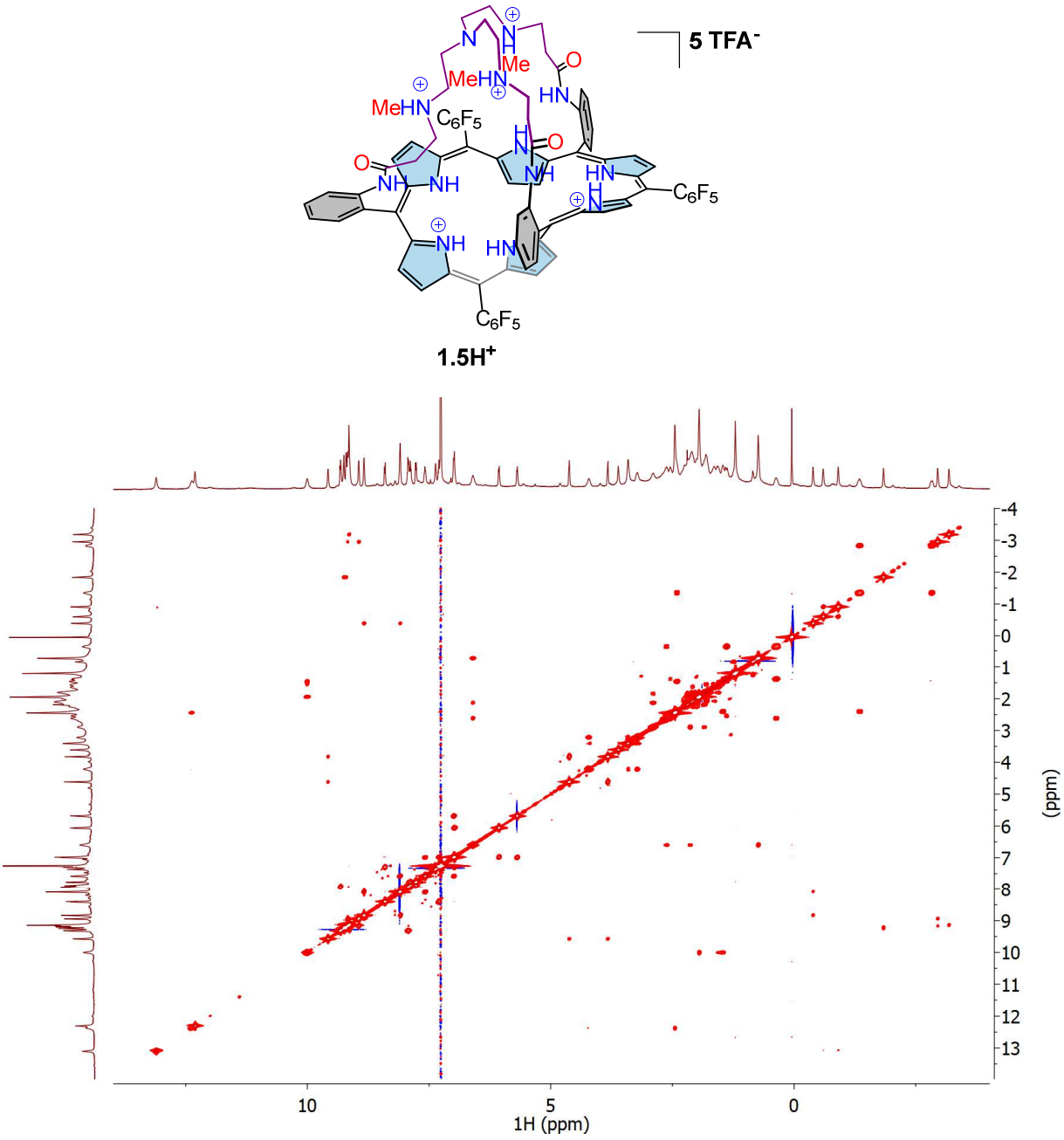


Figure S10. 2D COSY spectrum of **1.5H⁺** ($CDCl_3$, 500 MHz, 233 K).

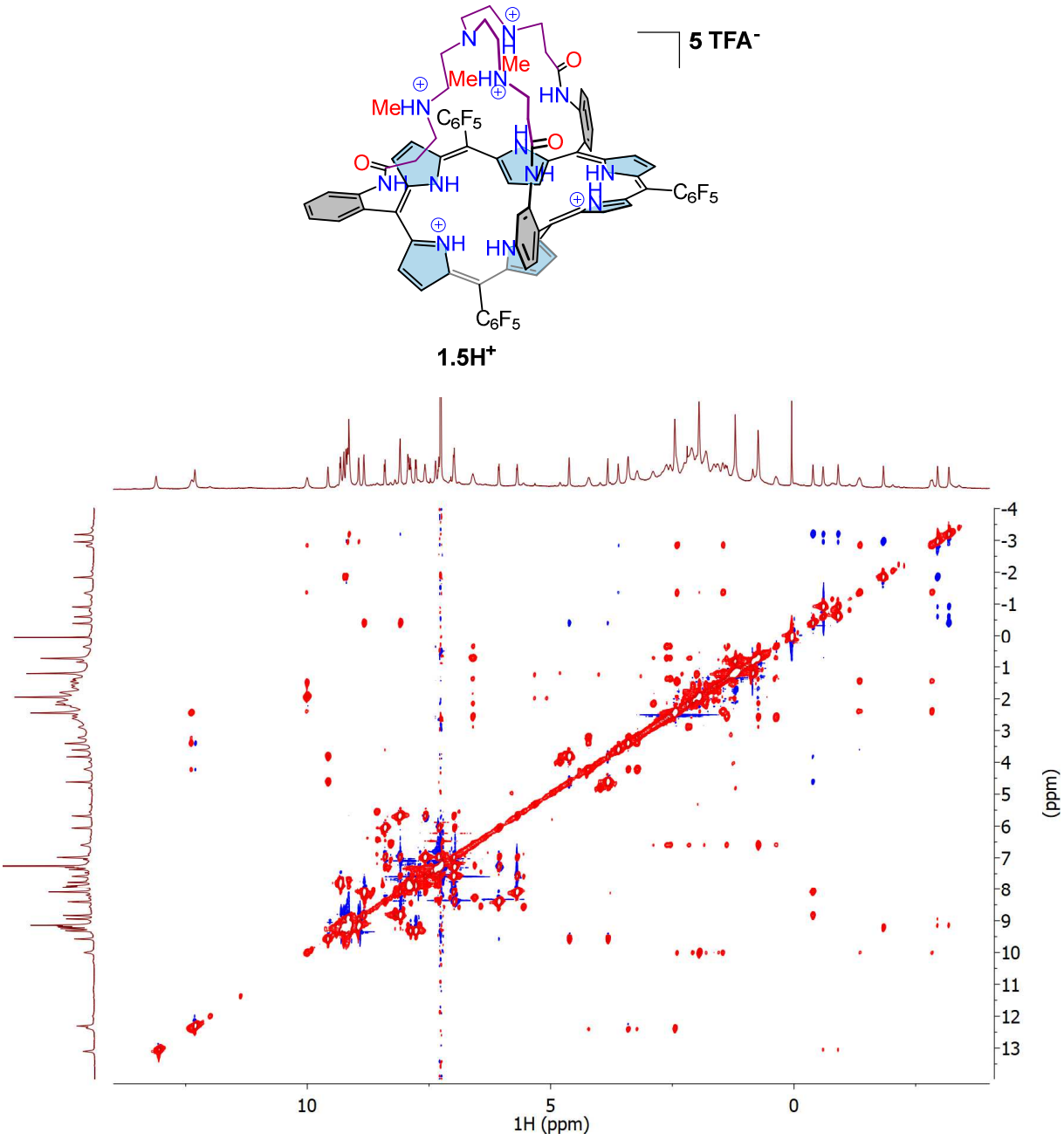


Figure S11. 2D TOCSY spectrum of **1.5H**$^{+}$ ($CDCl_3$, 500 MHz, 233 K).

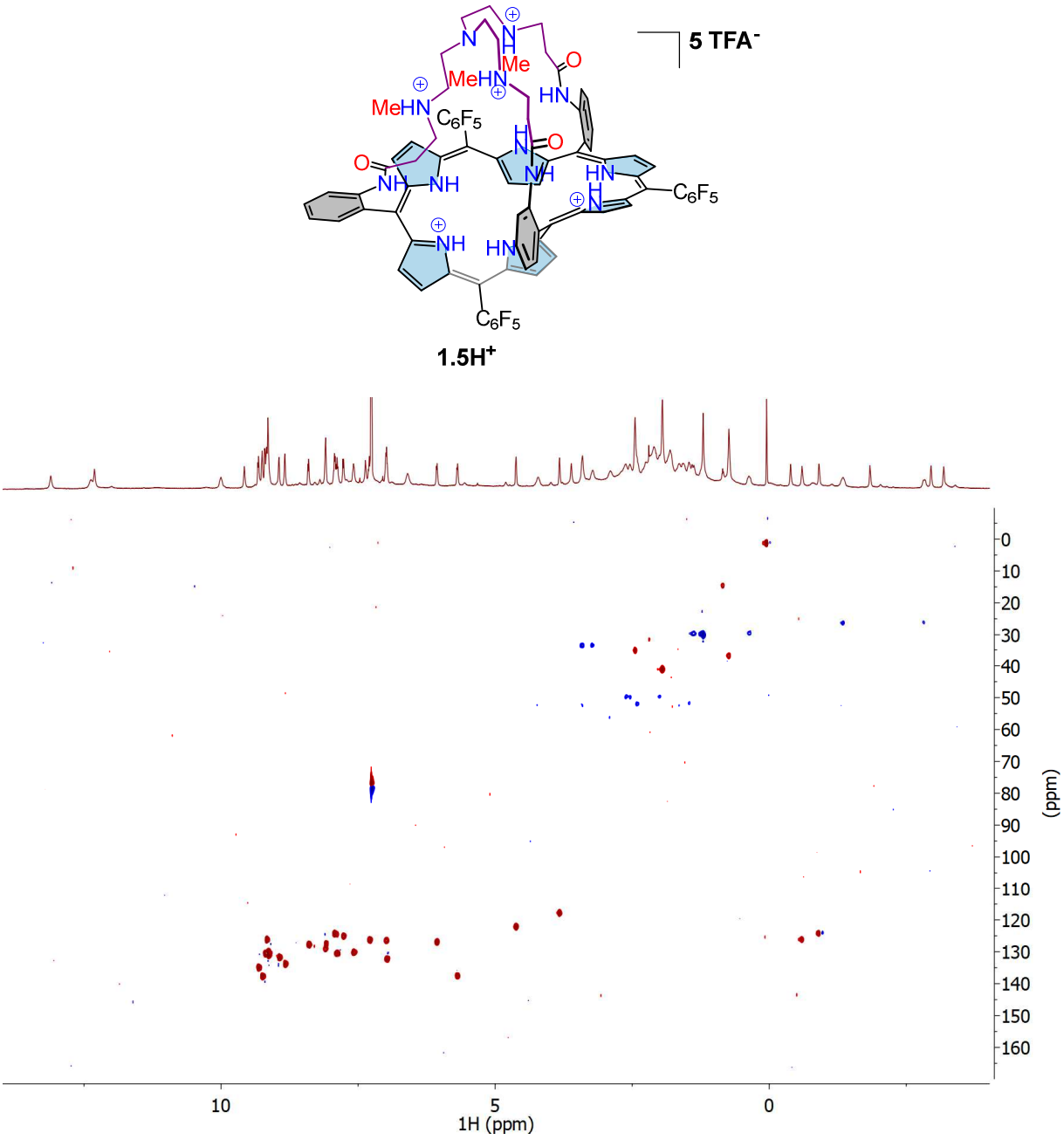


Figure S12. 2D HSQC spectrum of **1.5H⁺** ($CDCl_3$, 500 MHz, 233 K).

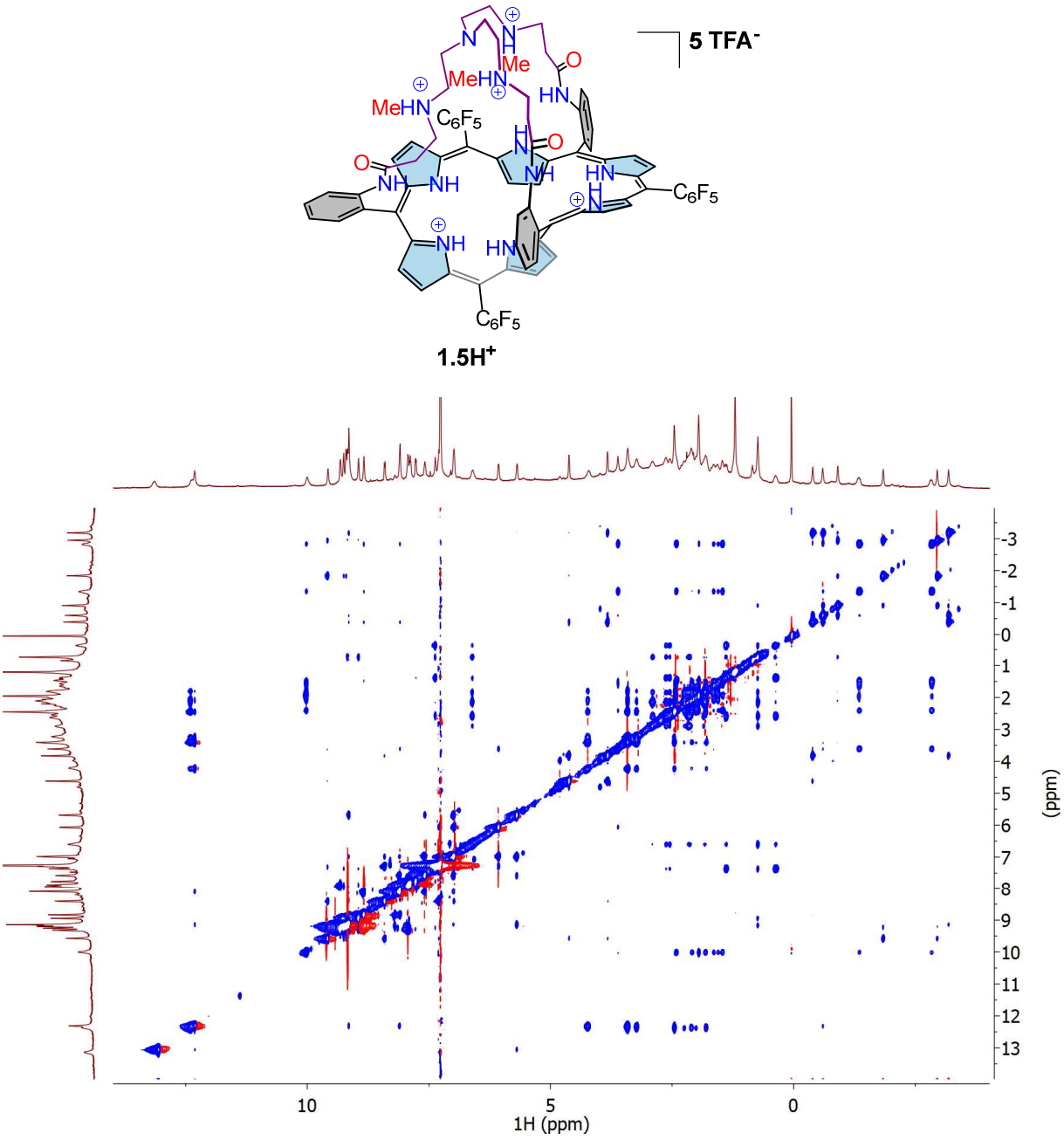


Figure S13. 2D NOESY spectrum of **1.5H**$^{+}$ ($CDCl_3$, 500 MHz, 233 K).

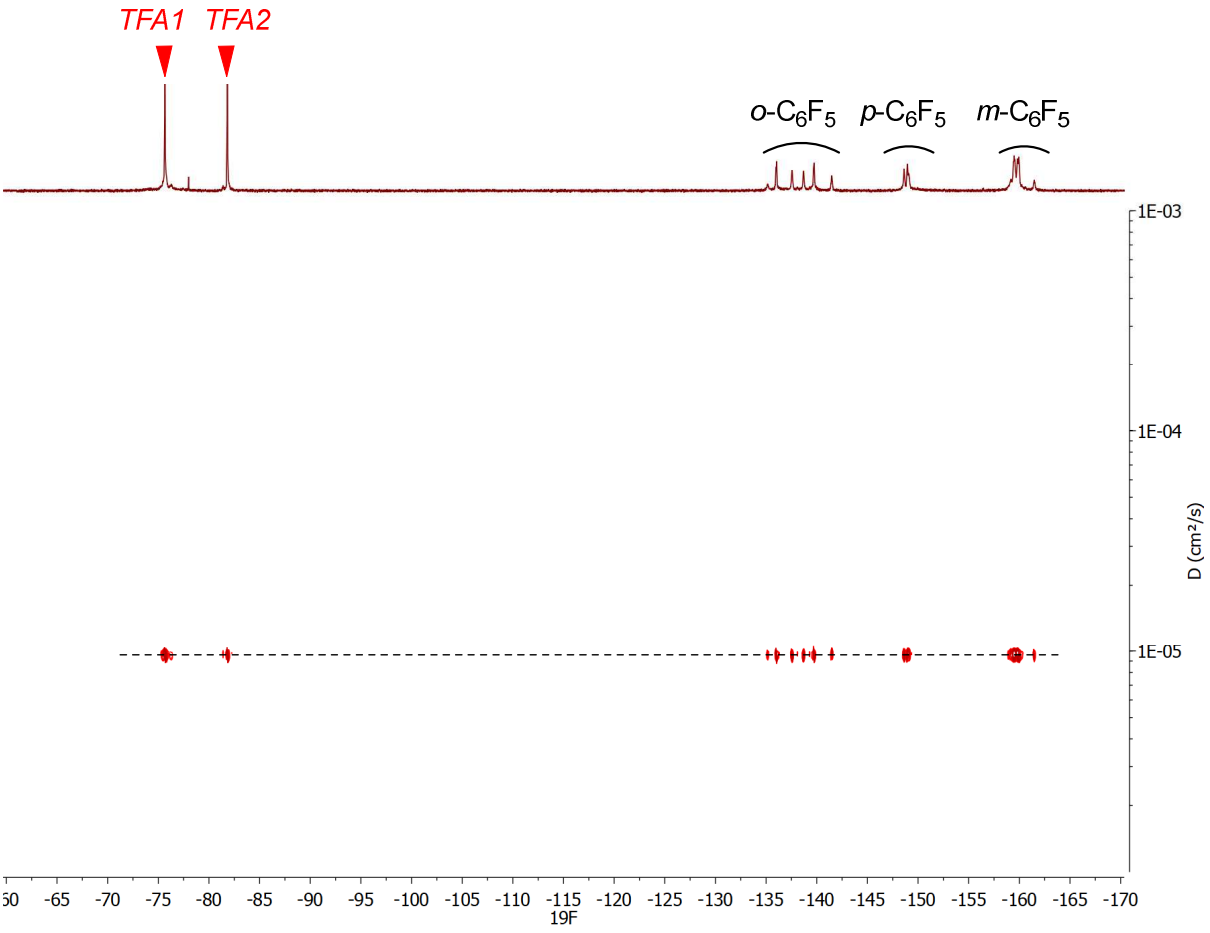


Figure S14. ^{19}F 2D DOSY spectrum of **1.5H$^+$** ($CDCl_3$, 470 MHz, 233 K).

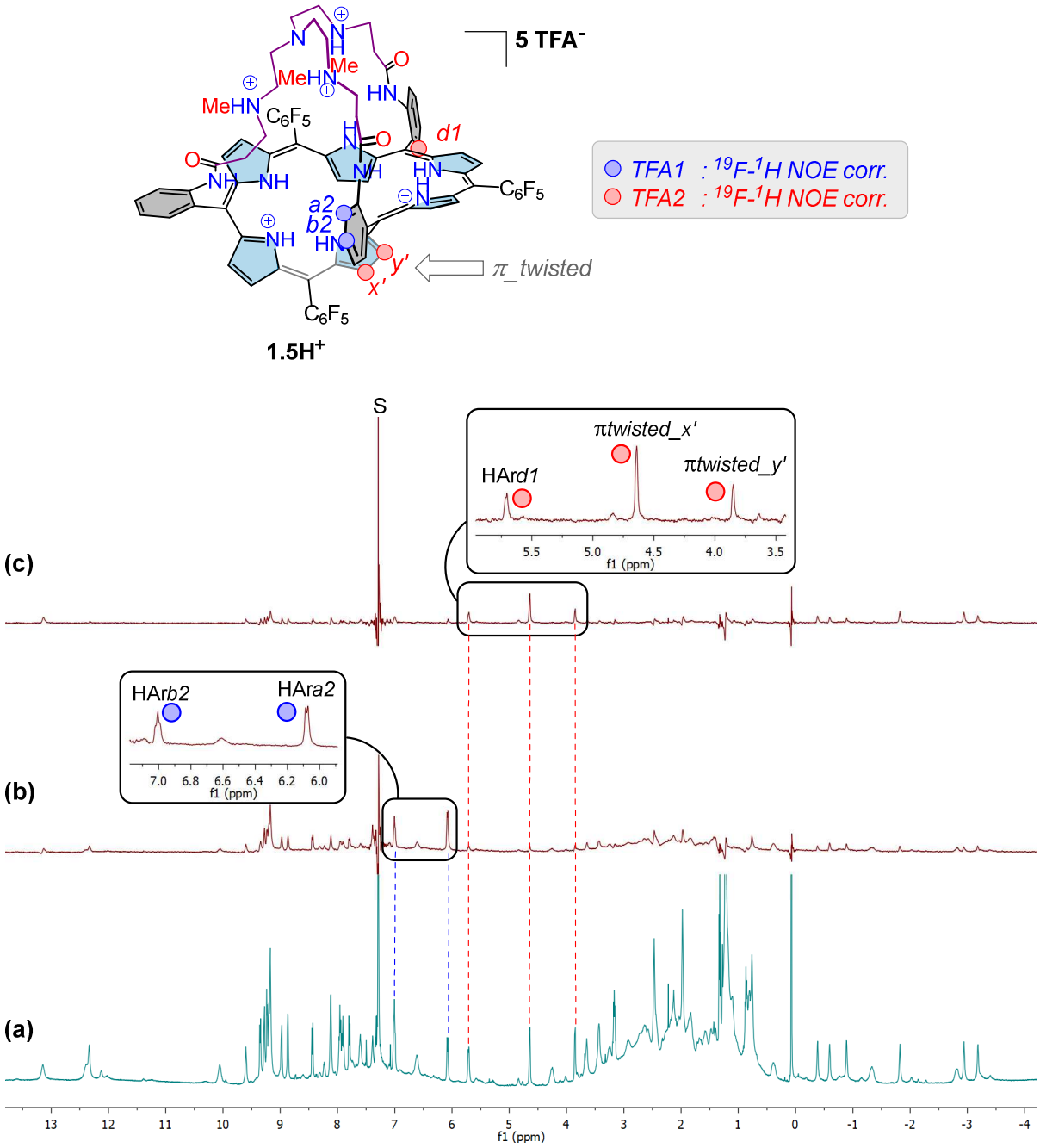


Figure S15. 1D ^{1}H detected ^{1}H-^{19}F nOe-difference spectra of **1.5H^{+}** ($CDCl_3$, 500 MHz, 233 K): (a) reference spectrum without ^{19}F saturation; (b) difference spectrum with selective ^{19}F saturation at -75.6 ppm (TFA1, TFAtren); (c) difference spectrum with selective ^{19}F saturation at -81.8 ppm (TFA2).