Supporting Information for

Deuterium Exchange of Pyrrolic NH Protons Accelerated by Fluoride and Bicarbonate Binding in $CDCl_3$, CD_3CN and DMSO-d_6

Nam Jung Heo,[a] Ju Hyun Oh,[a] Jonathan L. Sessler,[*b] and Sung Kuk Kim[*a]

[a] *Department of Chemistry and Research Institute of Natural Science, Gyeongsang National University, Jinju, 660-701, Korea and* [b] *Department of Chemistry, The University of Texas at Austin, 105 E. 24th Street-Stop A5300, Austin, Texas 78712-1224, USA*

1. General experimental and synthetic details

Solvents and reagents used for the synthetic work were purchased from Aldrich, TCI, or Alfa Aesar and used without further purification. NMR spectra were recorded on a Bruker Advance-300 MHz instrument. The NMR spectra were referenced to residual solvent peaks and the spectroscopic solvents were purchased from either Cambridge Isotope Laboratories or Aldrich. Chemical ionization (CI) and fast atom bombardment (FAB) mass spectra were recorded on a VG ZAB-2E instrument and a VG AutoSpec apparatus, respectively. TLC analyses were carried out using Sorbent Technologies silica gel (200 mm) sheets. Column chromatography was performed on Sorbent silica gel 60 (40–63 mm).

2. Determination of association constants using ^{1}H NMR spectral titrations for a slow host-guest association/dissociation equilibrium on the NMR time scale

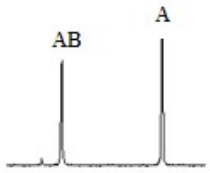
Equilibrium: $A + B \underset{}{\overset{K_a}{\rightleftharpoons}} AB$

Equilibrium constant: $K_a = \dfrac{[AB]}{[A][B]} = \dfrac{[AB]}{(c(A) - [AB])(c(B) - [AB])}$ (1)

c(A) and c(B) are the initial concentrations of A and B, and [A], [B] and [AB] are the equilibrium concentrations of the three species.

A and B is in slow exchange with the complex AB on the ^{1}H NMR time scale.

Two signals for one specific proton on A can be seen in the spectrum, corresponding to complexed and uncomplexed forms of A:



Single-point Methods

K_a is determined from the integrals of complexed and uncomplexed A. If I(A) denotes the integral of a signal for one specific proton of A and I(AB) the integral for the same proton in the complex, the concentration of AB at equilibrium is shown by eq 2. The equilibrium expression is obtrained after substituting into eq. (1):

$$[AB] = \frac{I(AB)}{I(A) + I(AB)} c(A) \quad (2)$$

$$K_a = \frac{\dfrac{I(AB)}{I(A) + I(AB)} c(A)}{I(A)\left(c(B) - \dfrac{I(AB)}{I(A) + I(AB)} c(A)\right)} \quad (3)$$

3. Binding studies of receptors 1 and 2 using ^{1}H NMR spectroscopy

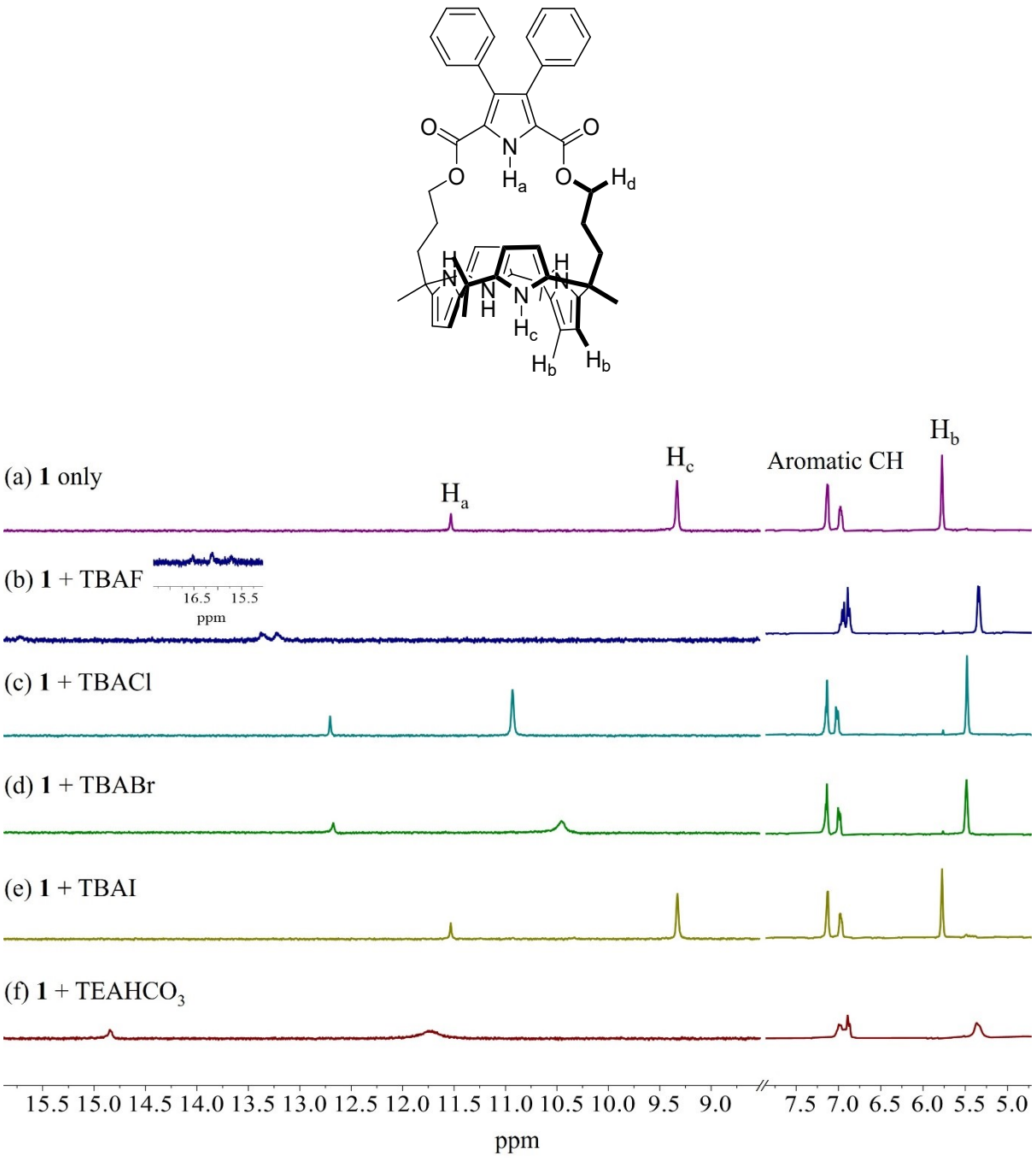


Figure S1. Partial ^{1}H NMR spectra of (a) **1** (3 mM) only, (b) **1** + 10 equiv of TBAF, (c) **1** + 10 equiv of TBACl, (d) **1** + 10 equiv of TBABr, (e) **1** + 10 equiv of TBAI, (f) **1** + 10 equiv of $TEAHCO_3$ in DMSO-d_6.

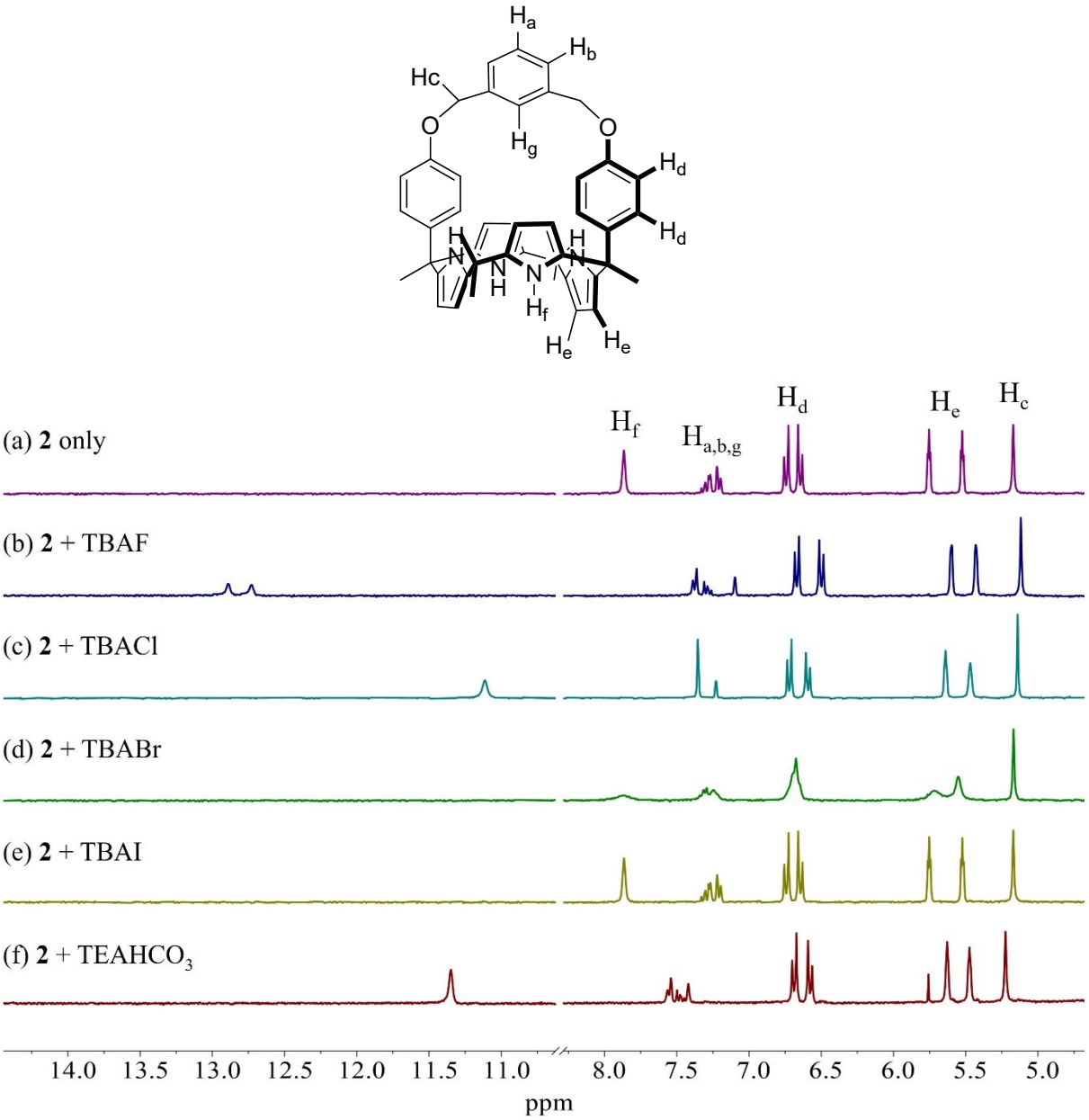


Figure S2. Partial ^{1}H NMR spectra of (a) **2** (3 mM) only, (b) **2** + 10 equiv of TBAF, (c) **2** + 10 equiv of TBACl, (d) **2** + 10 equiv of TBABr, (e) **2** + 10 equiv of TBAI, (f) **2** + 10 equiv of $TEAHCO_3$ in DMSO-d_6.

4. ^{1}H,^{19}F NMR spectra and FAB mass spectra

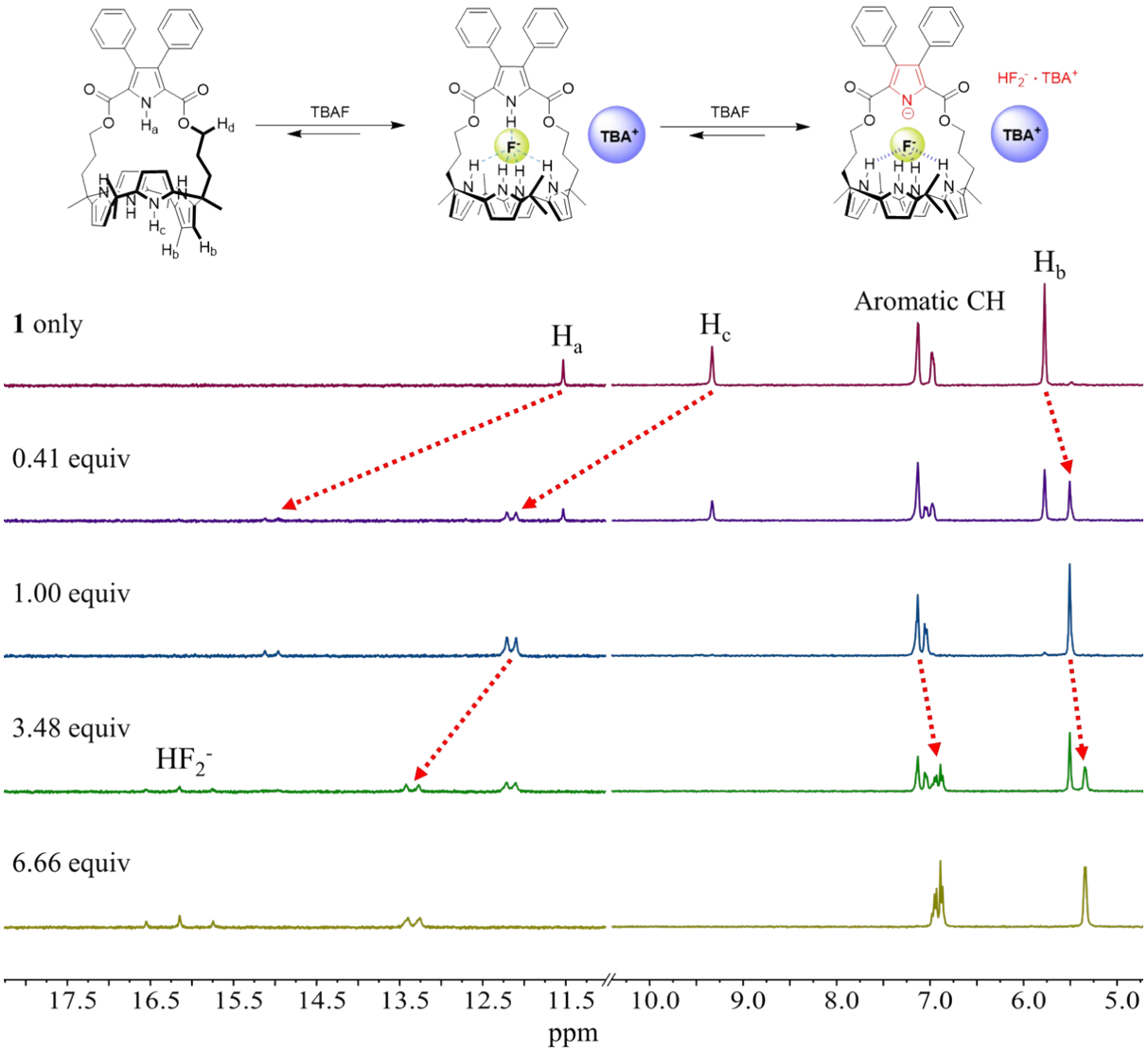


Figure S3. ^{1}H NMR spectra recorded during the titration of **1** (3 mM) with tetrabutylammonium fluoride (TBAF) in DMSO-d_6.

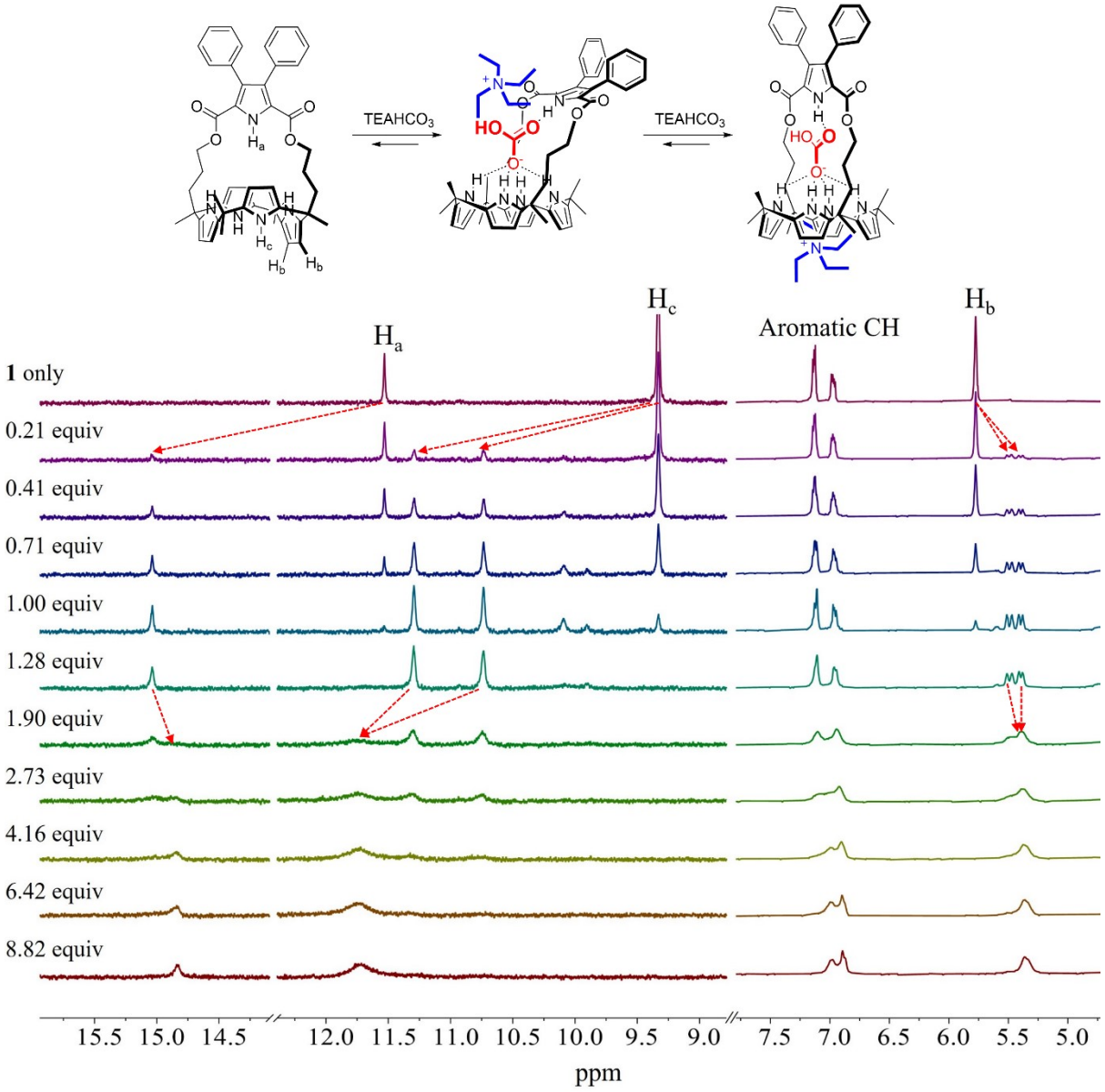


Figure S4. ^{1}H NMR spectra recorded during the titration of **1** (3 mM) with tetraethylammonium bicarbonate ($TEAHCO_3$) in DMSO-d_6.

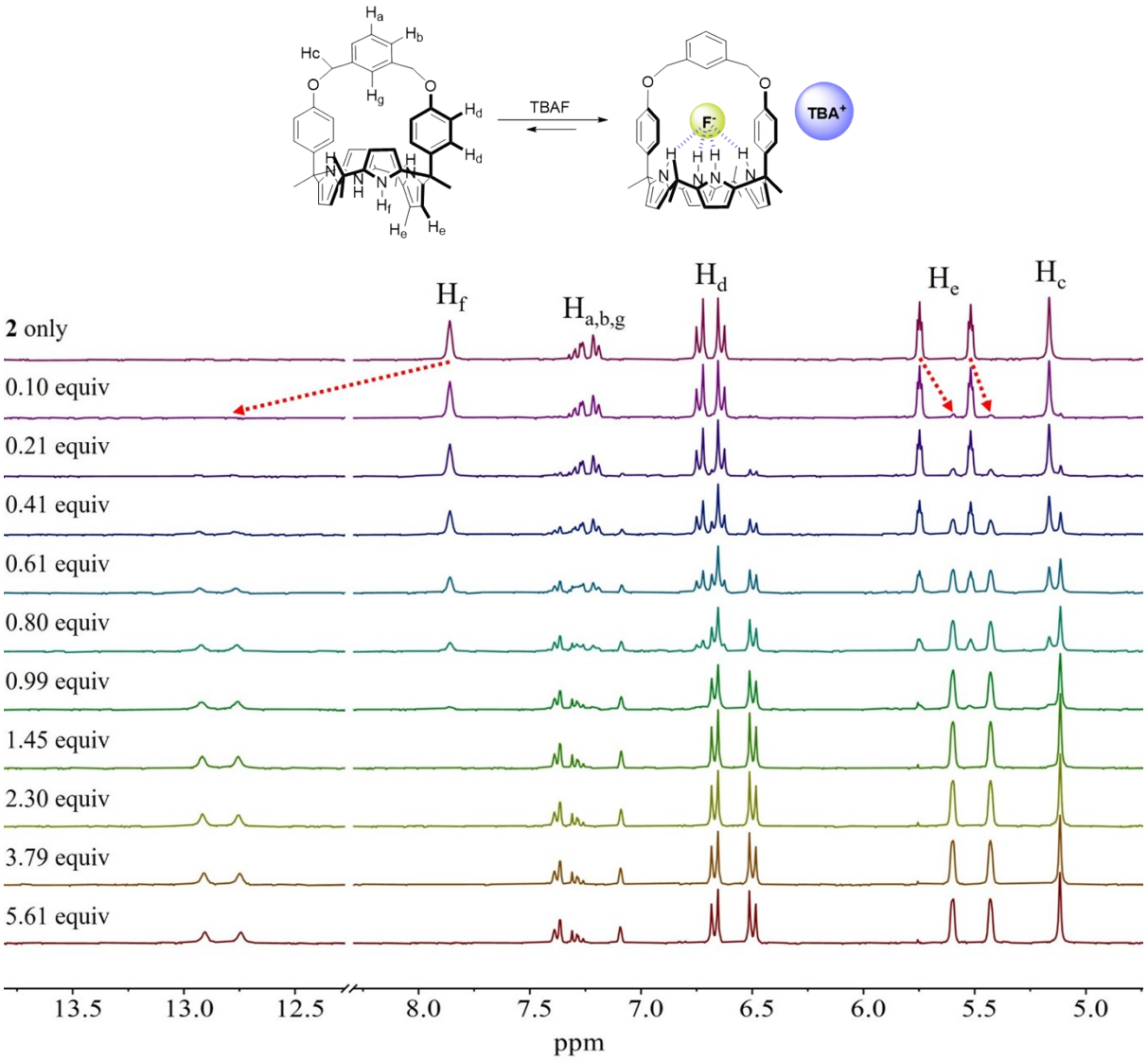


Figure S5. ^{1}H NMR spectra recorded during the titration of **2** (3 mM) with tetrabutylammonium fluoride (TBAF) in DMSO-d_6

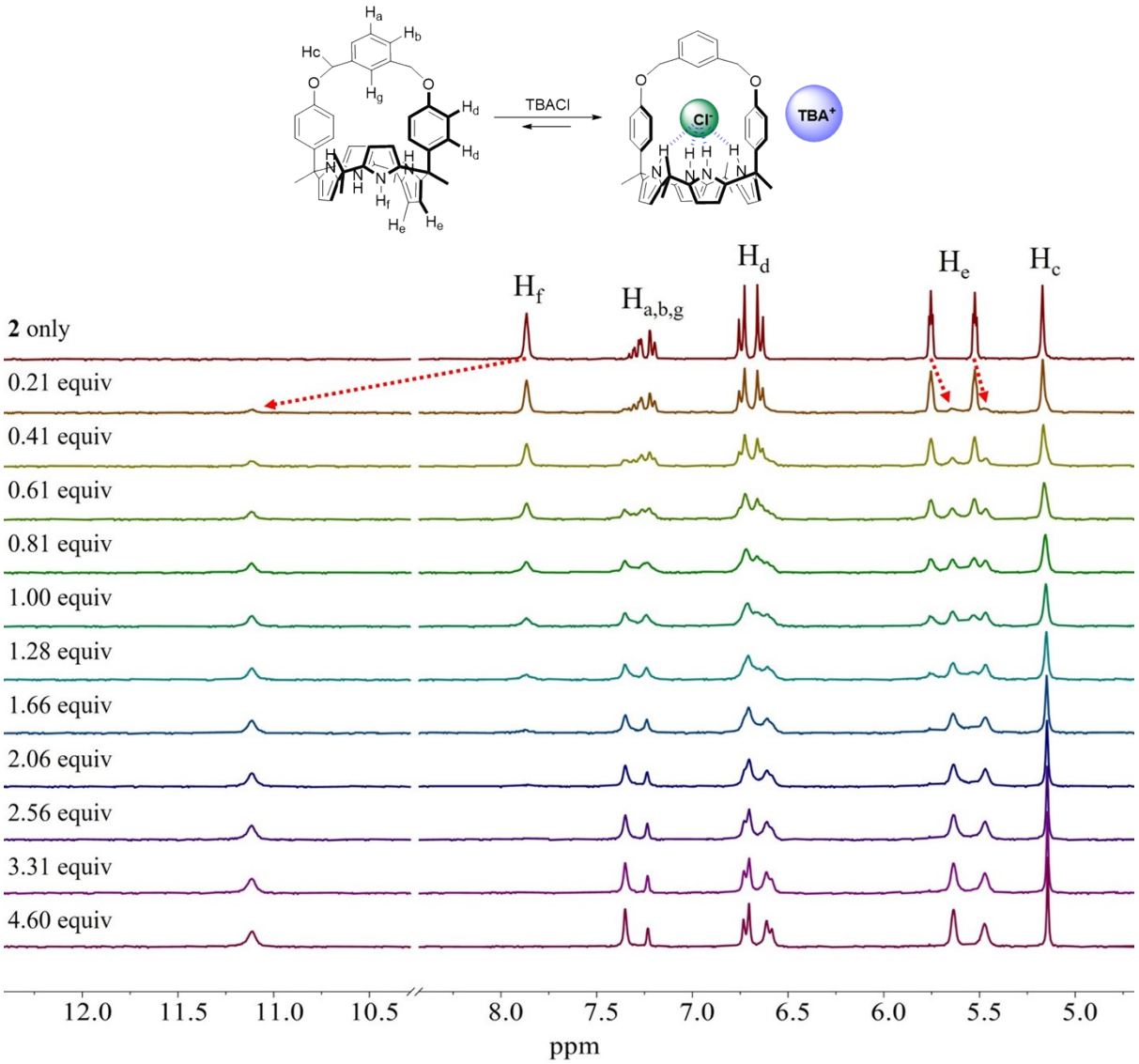


Figure S6. ^{1}H NMR spectra recorded during the titration of **2** (3 mM) with tetrabutylammonium chloride (TBACl) in DMSO-d_6.

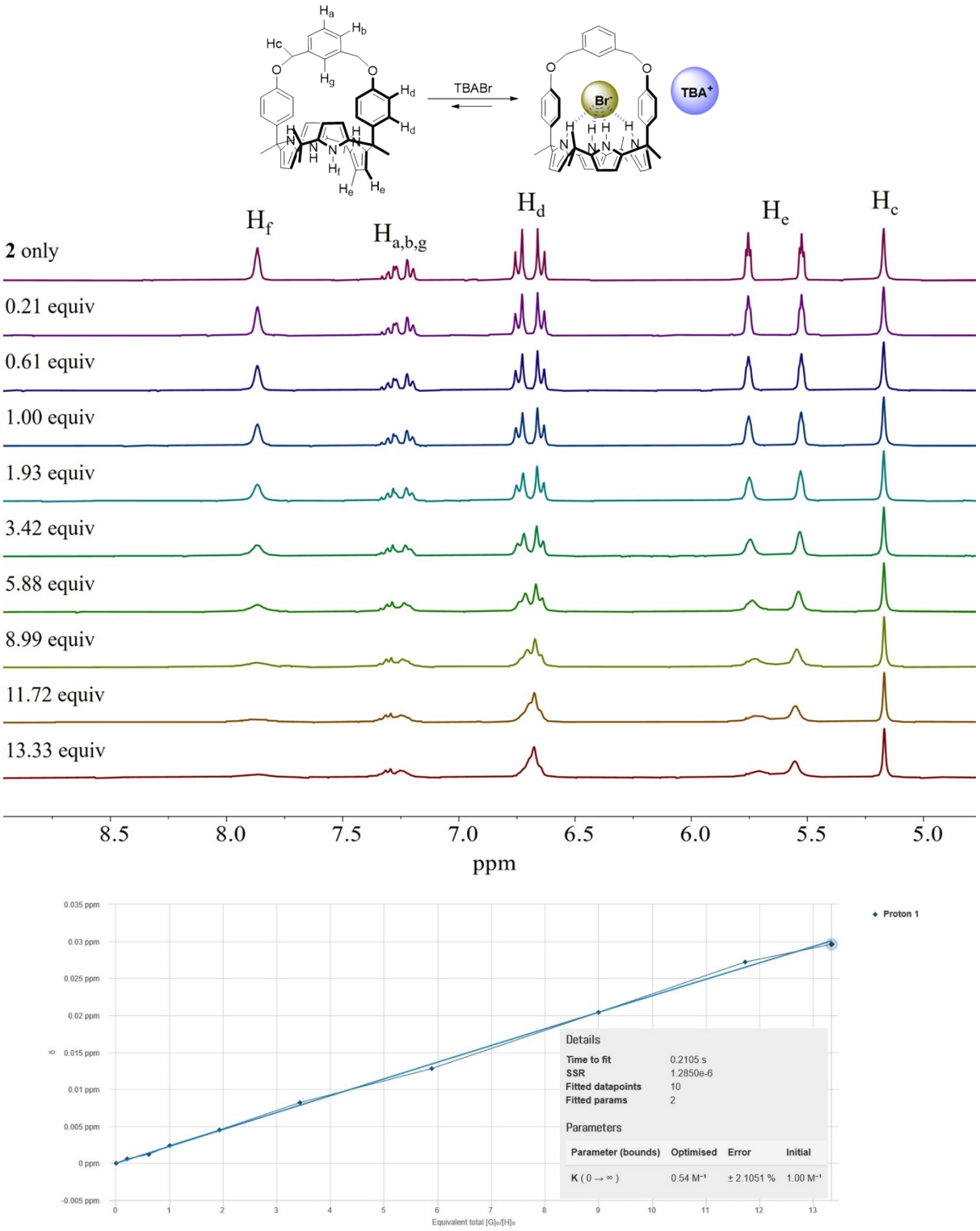


Figure S7. ^{1}H NMR spectra recorded during the titration of **2** (3 mM) with tetrabutylammonium bromide (TBABr) in DMSO-d_6.

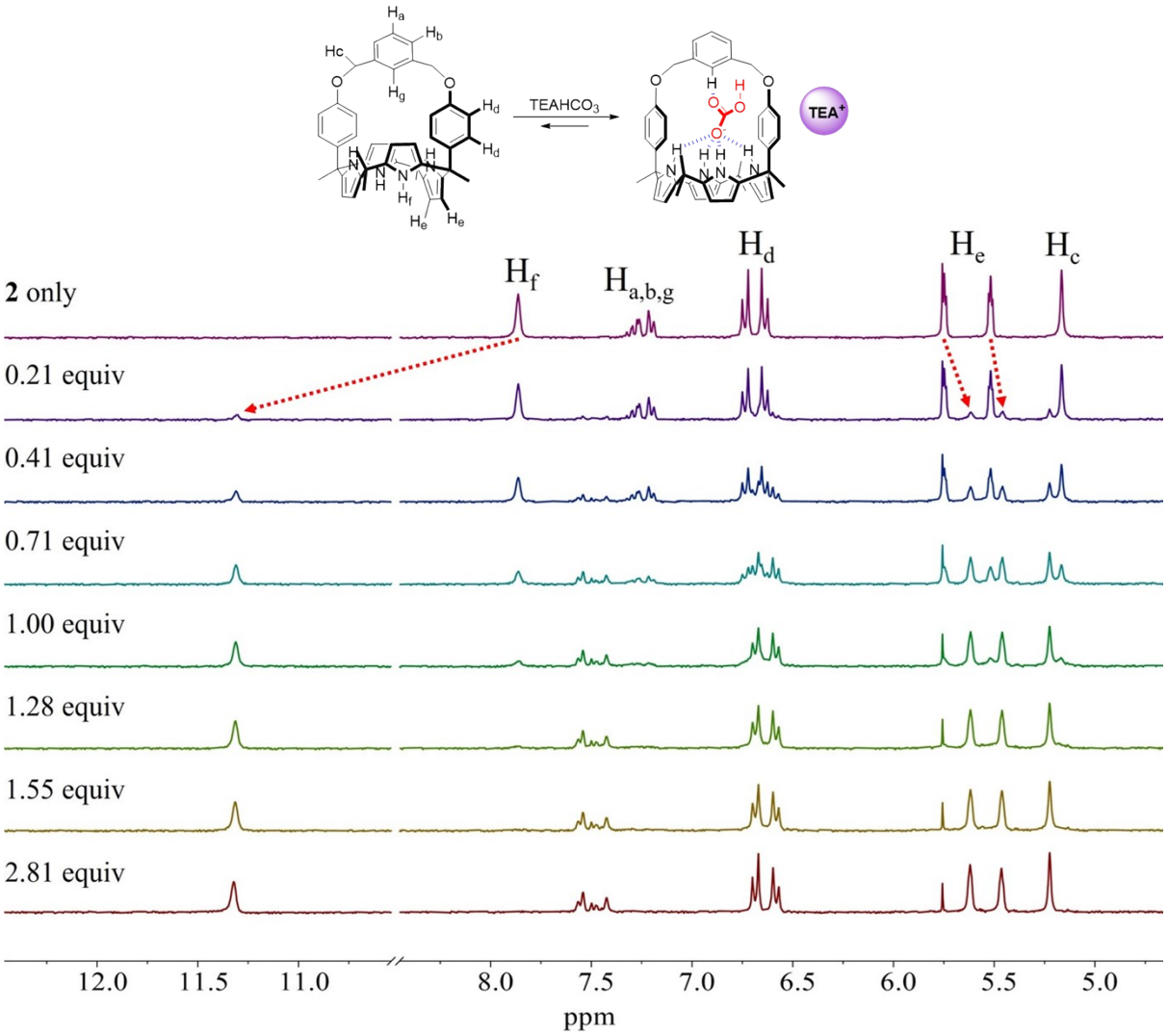


Figure S8. ^{1}H NMR spectra recorded during the titration of **2** (3 mM) tetraethylammonium bicarbonate ($TEAHCO_3$) in DMSO-d_6.

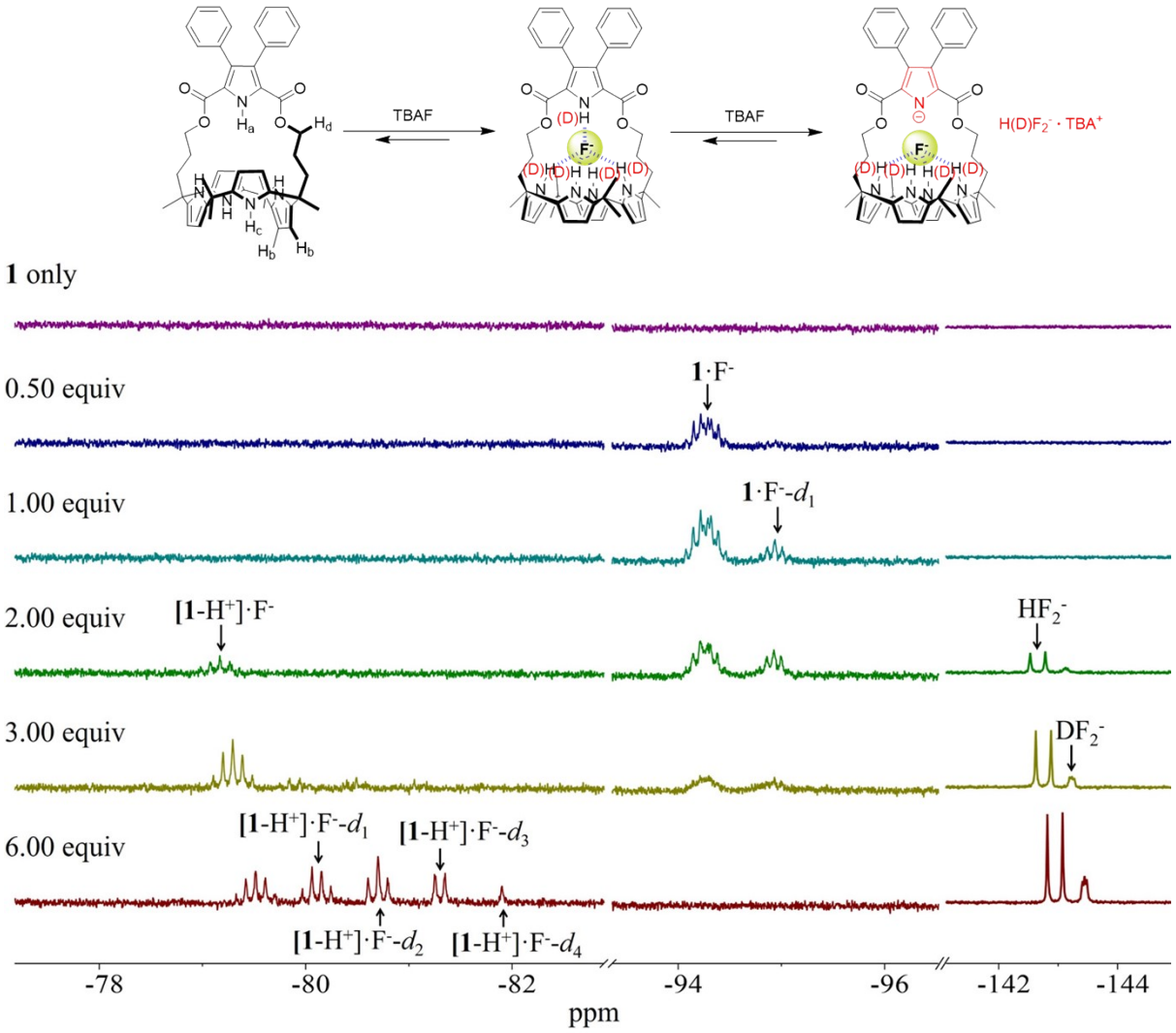


Figure S9. ^{19}F NMR spectra recorded during the titration of **1** (10 mM) with tetrabutylammonium fluoride (TBAF) in DMSO-d_6. Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

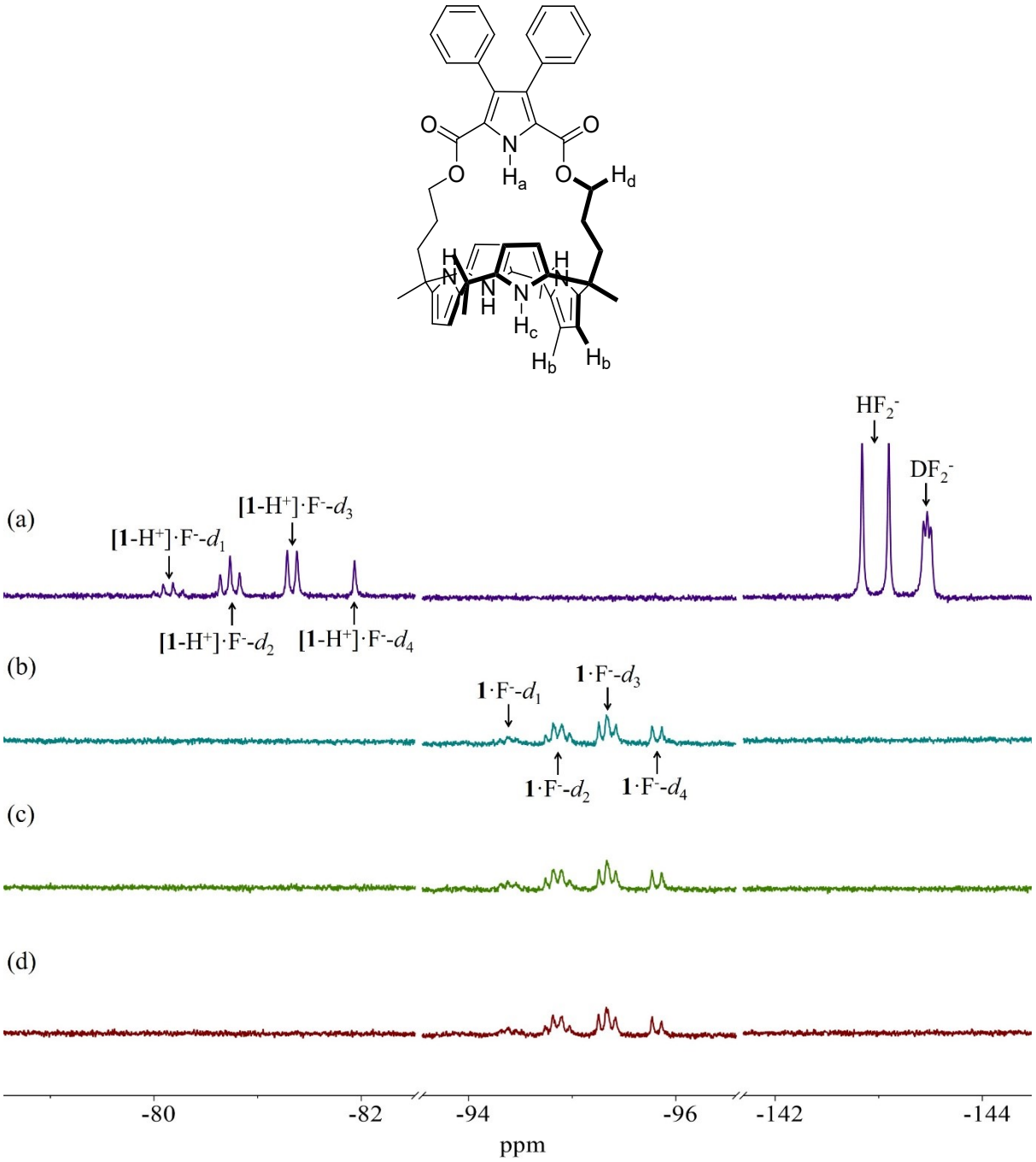


Figure S10. ^{19}F NMR spectra of a solution of **1** (10 mM) + 6.0 equiv of TBAF in DMSO-d_6 (a) after allowing the solution to stand overnight**,** (b) right after adding 10% water to (a), (c) after allowing (b) to stand for 10 minutes, and (d) after allowing (b) to stand for 30 minutes. Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

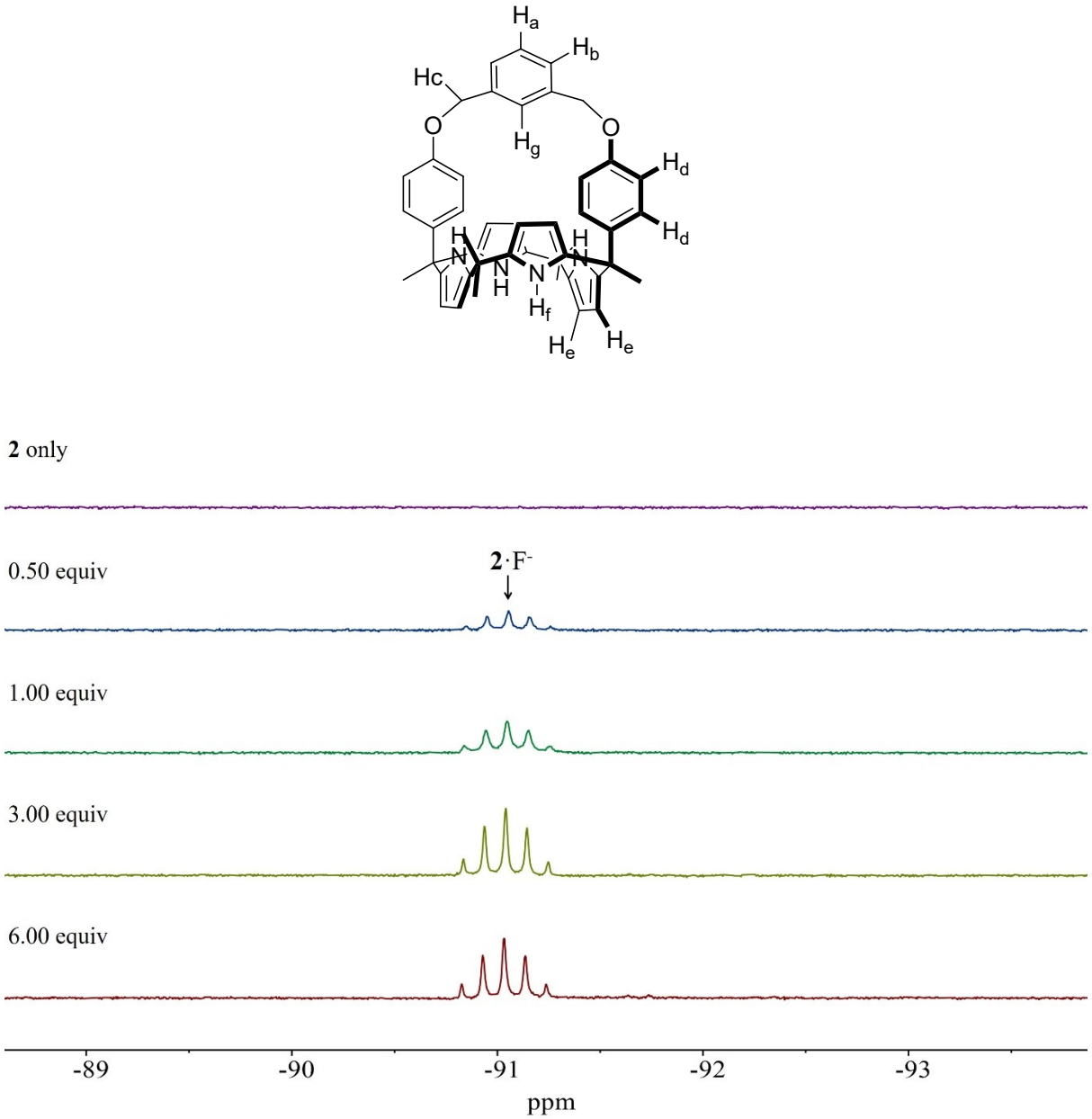


Figure S11. ^{19}F NMR spectra recorded during the titration of **2** (10 mM) with tetrabutylammonium fluoride (TBAF) in DMSO-d_6. Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

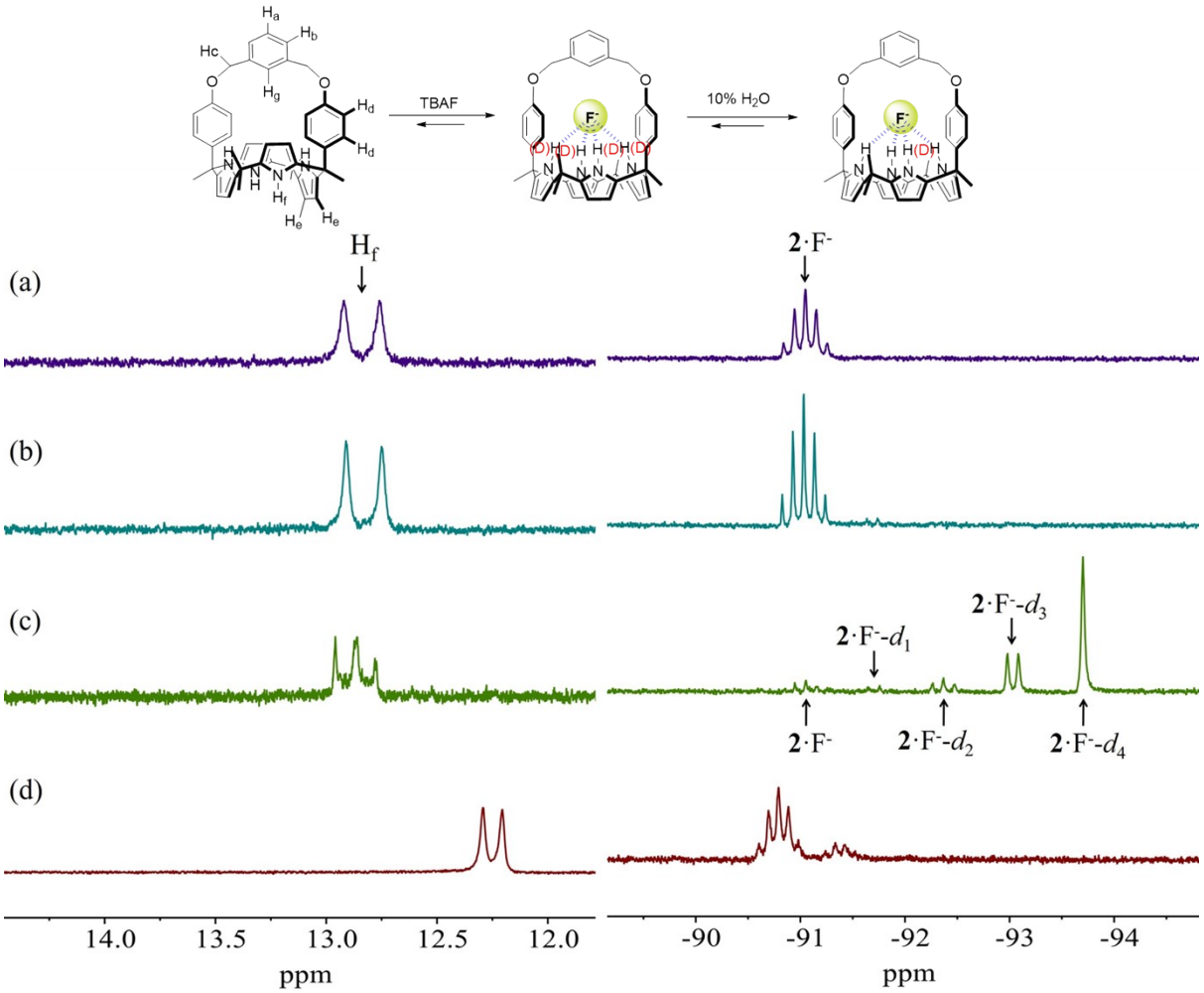


Figure S12. Partial ^{1}H (left) and ^{19}F (right) NMR spectra of **2** (10 mM) recorded (a) with 1.0 equiv of TBAF in DMSO-d_6, (b) with 6.0 equiv of TBAF in DMSO-d_6, (c) after allowing the (b) solution to stand overnight, and (d) after adding 10% water to (c). Fluorobenzene was used as an internal reference.

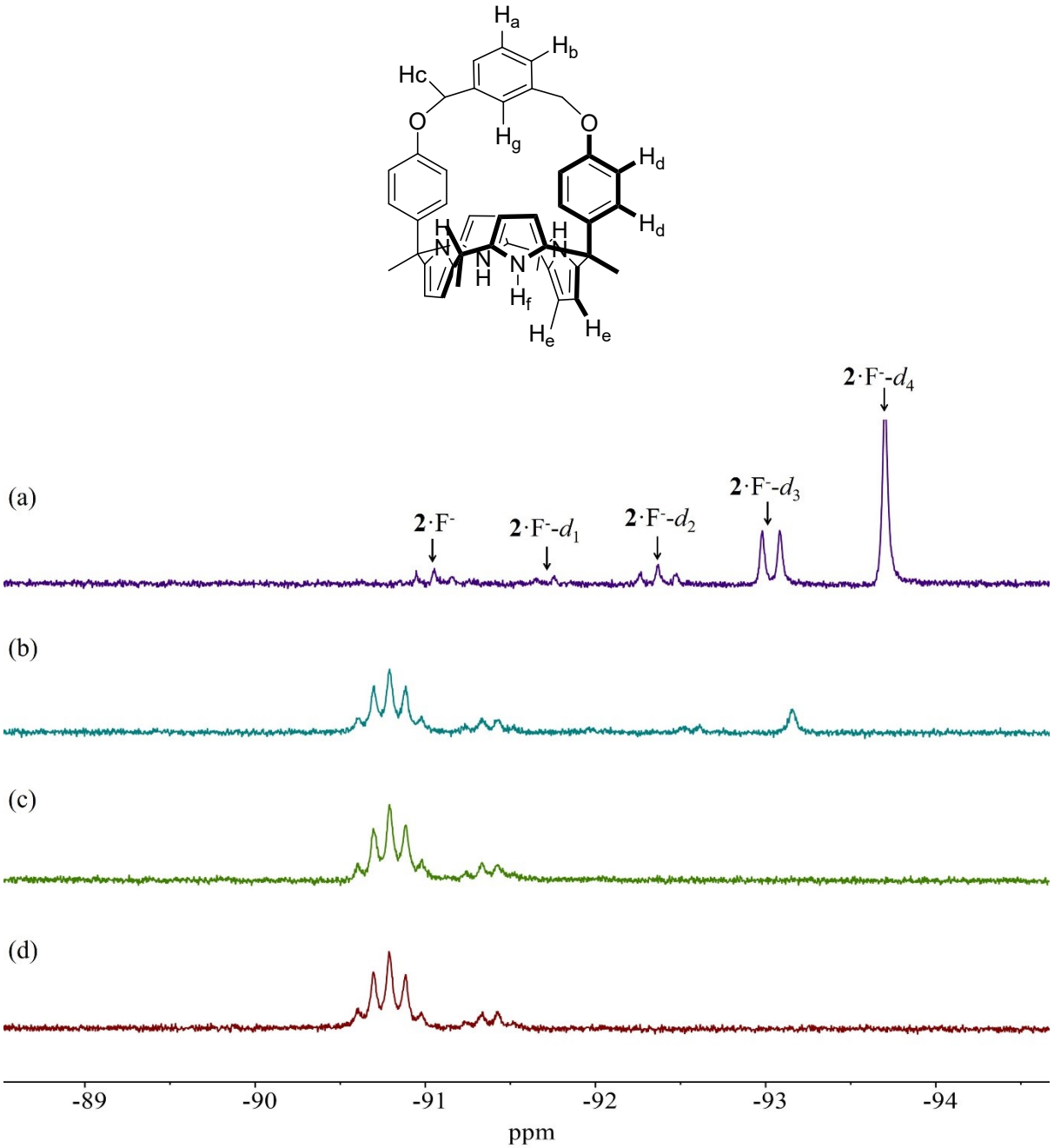


Figure S13. ^{19}F NMR spectra of a DMSO-d_6 solution of **2** (10 mM) (a) after being allowed to stand overnight in the presence of 6.0 equiv of TBAF**,** (b) right after, (c) 10 minutes after, (d) 30 minutes after adding 10% water to the (a) solution. Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

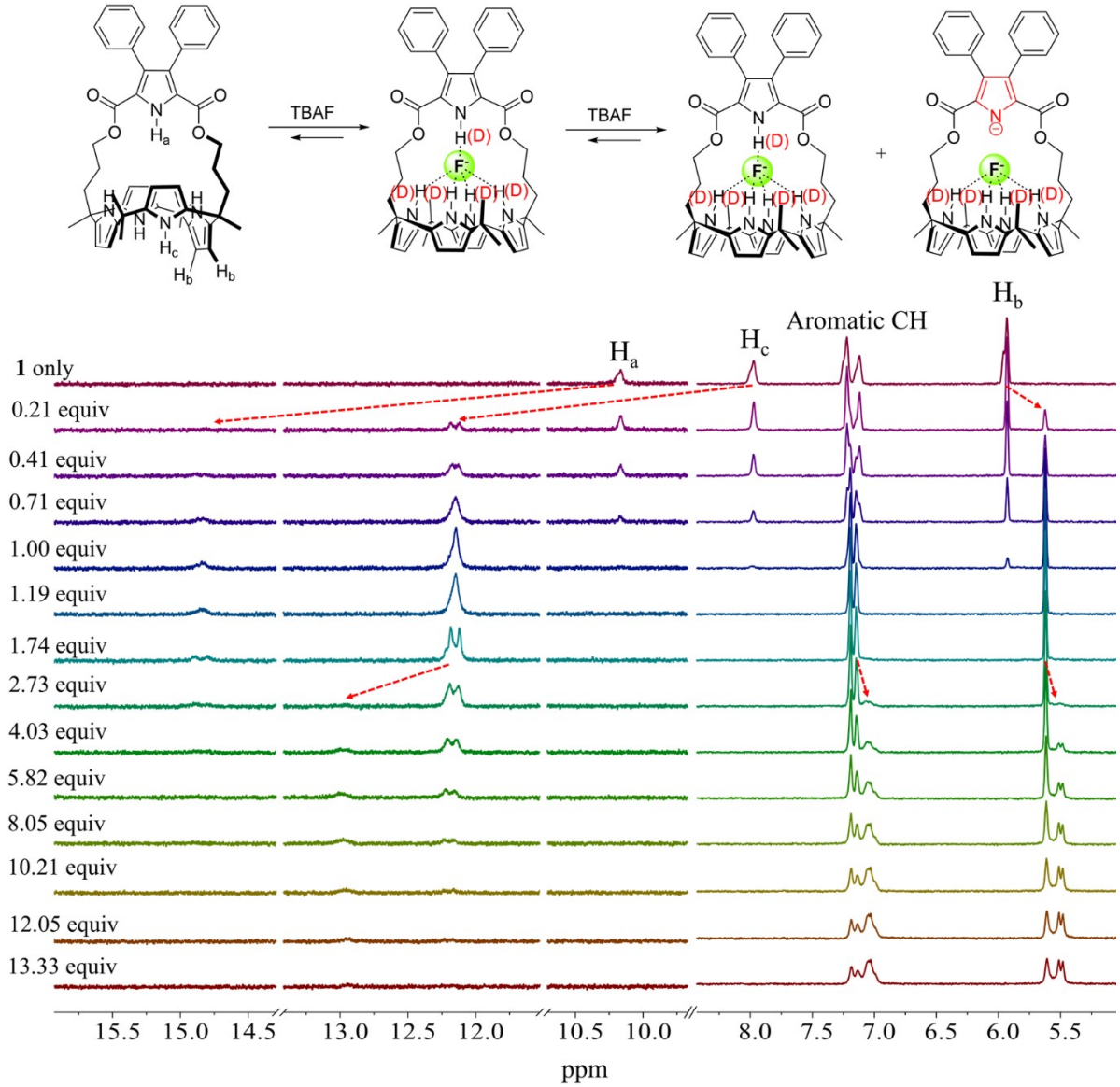


Figure S14. ^{1}H NMR spectra recorded during the titration of **1** (3 mM) with TBAF in CD_3CN.

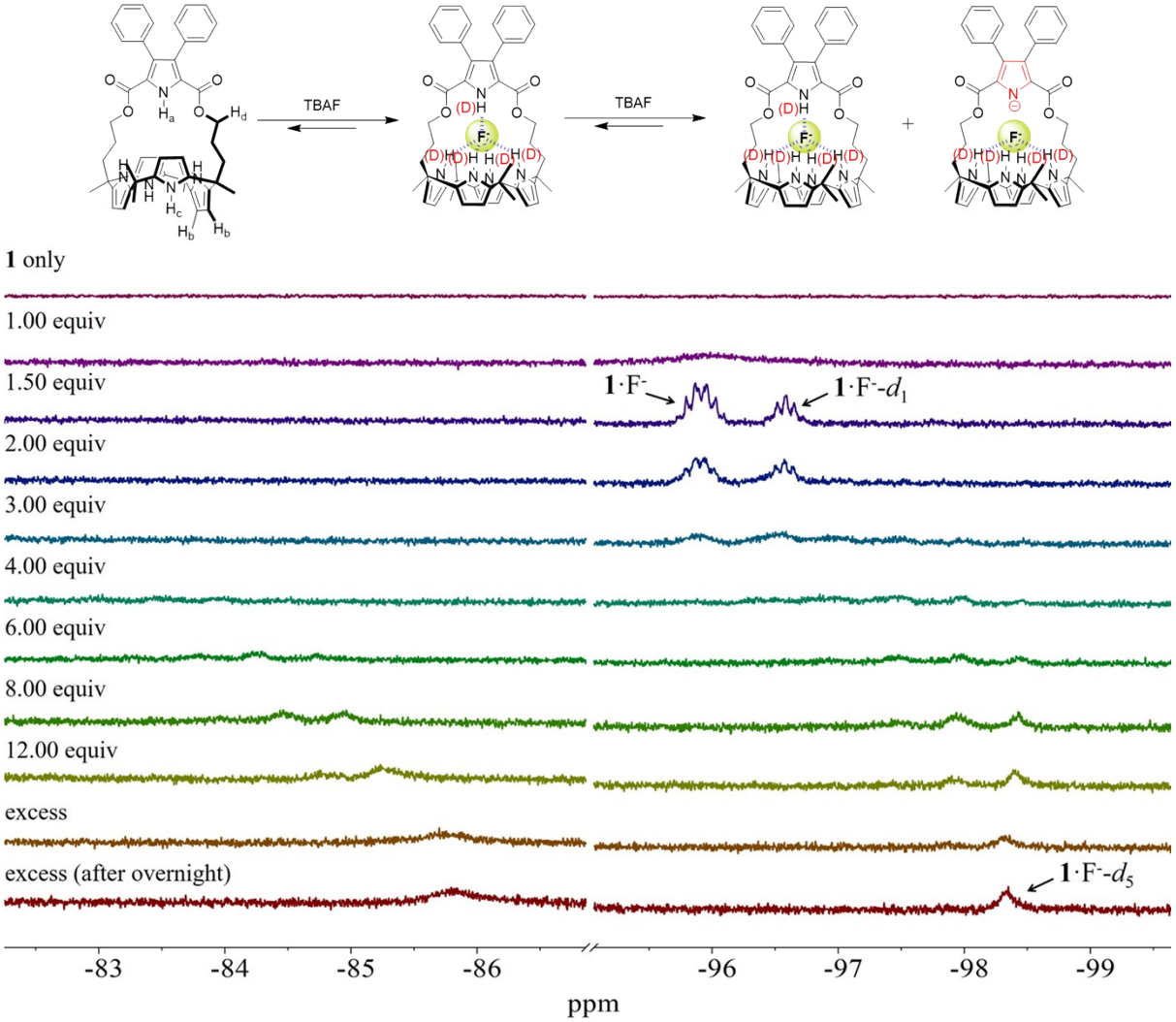


Figure S15. ^{19}F NMR spectra recorded during the titration of **1** (5 mM) with TBAF in CD_3CN. Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

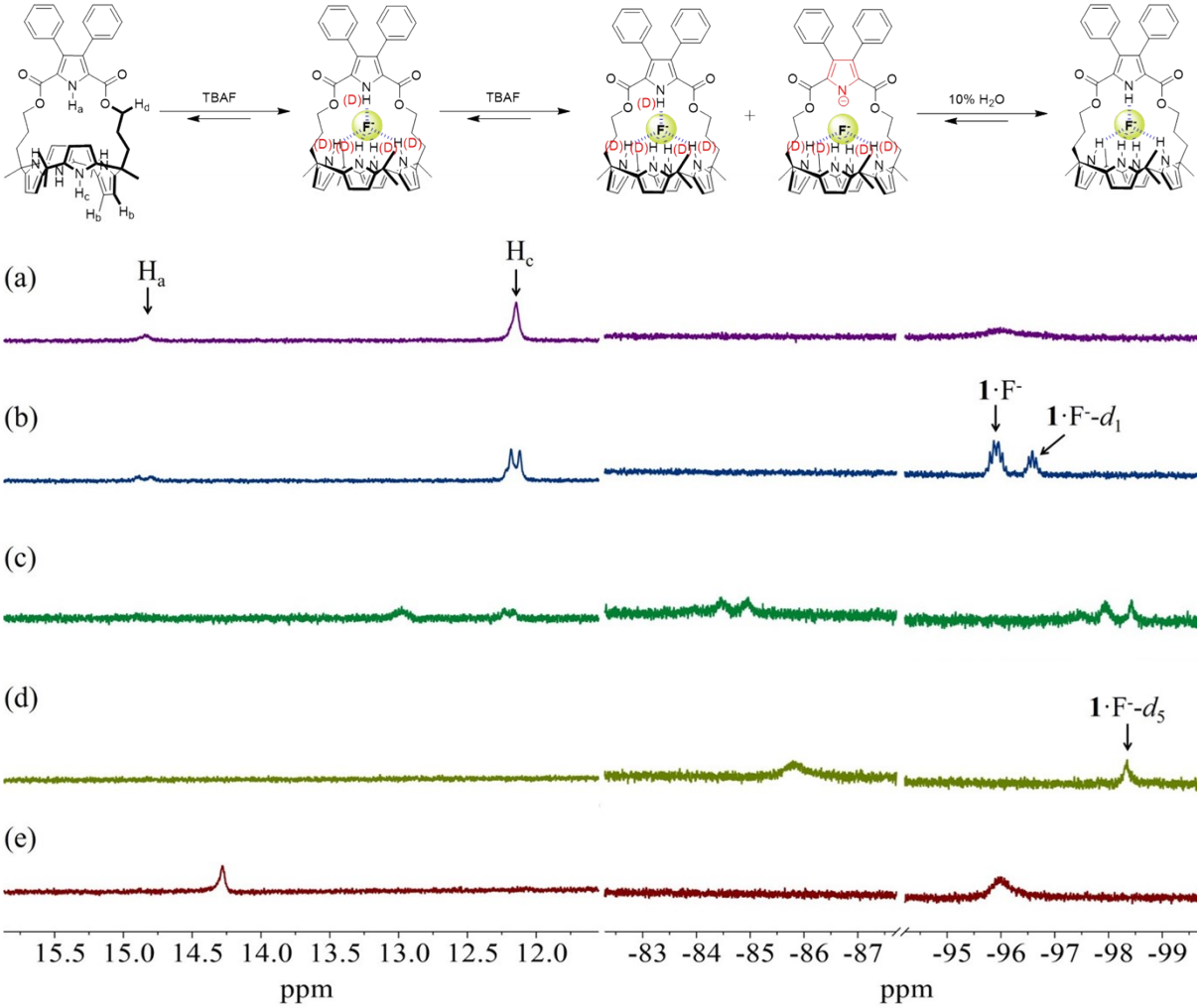


Figure S16. Partial ^{1}H (left) and ^{19}F (right) NMR spectra of CD_3CN solutions of **1** (5 mM) recorded (a) with 1.0 equiv of TBAF, (b) with 1.5 equiv of TBAF, (c) with 8.0 equiv of TBAF, (d) after being allowed to stand overnight with excess TBAF, and (e) after adding 10% water to (d). Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

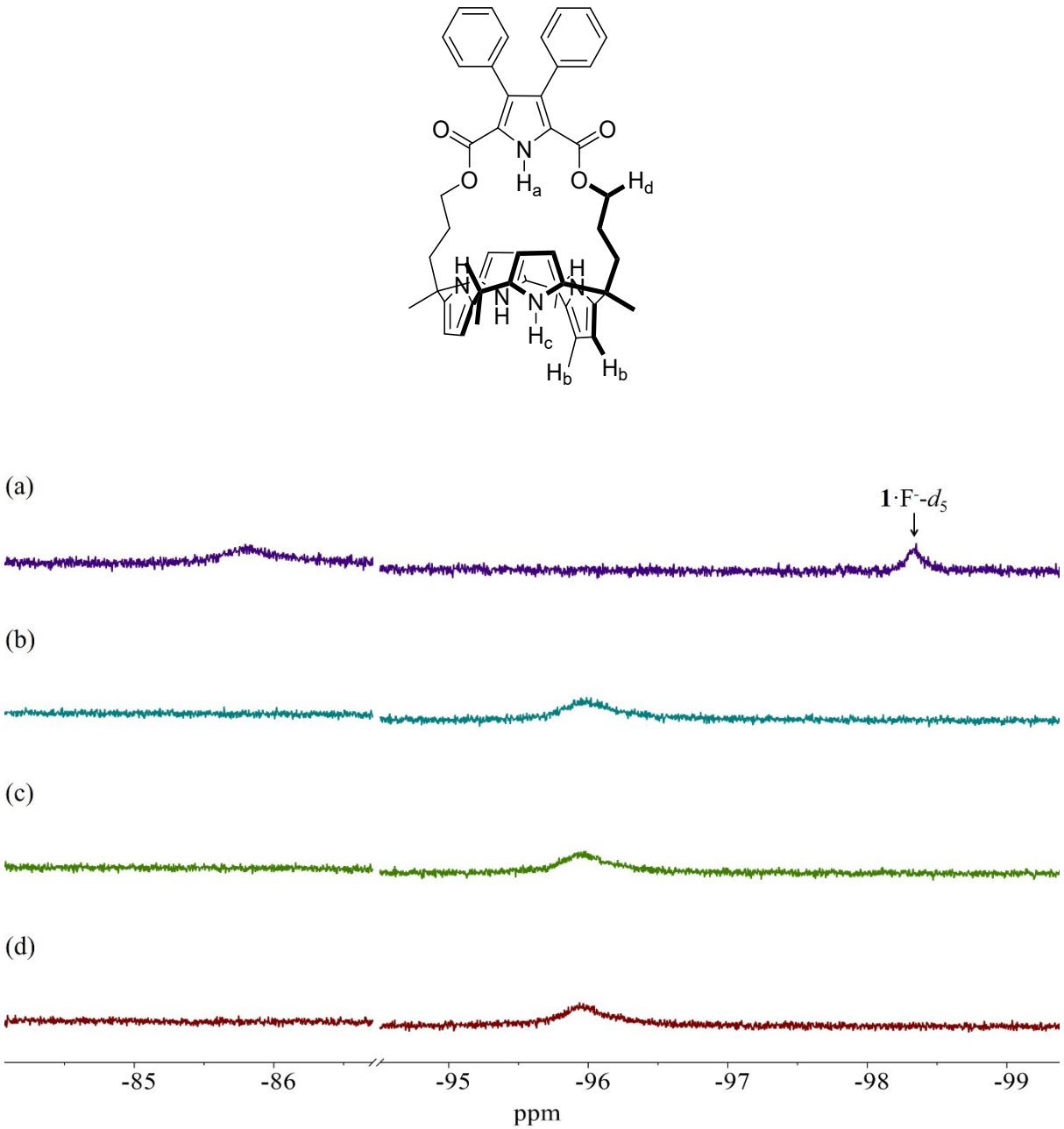


Figure S17. ^{19}F NMR spectra of CD_3CN solutions of **1** with excess TBAF (5 mM) (a) after being allowed to stand overnight**,** (b) right after, (c) 10 minutes after, and (d) 30 minutes after 10% water was added to (a). Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

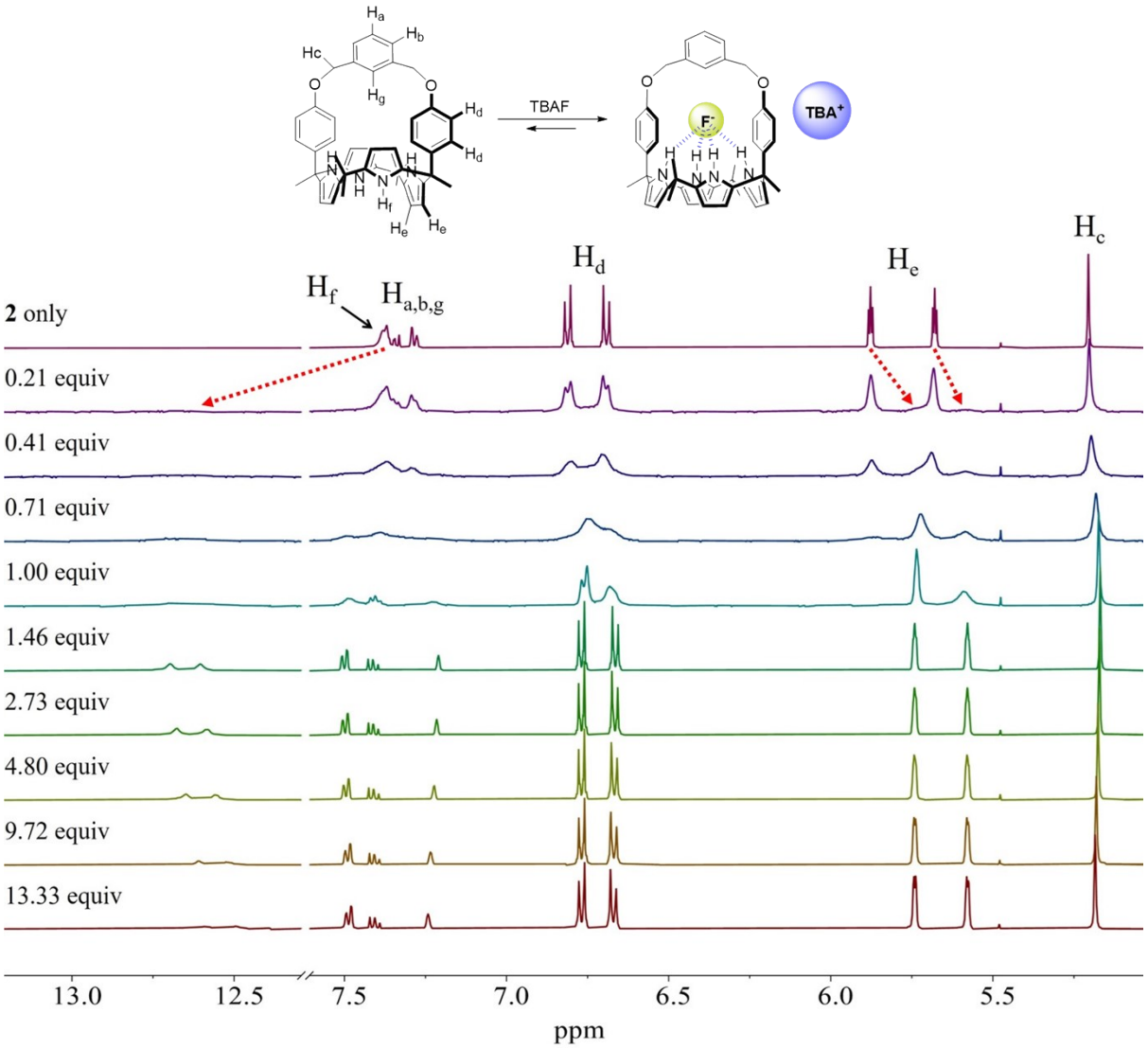


Figure S18. ^{1}H NMR spectra recorded during the titration of **2** (3 mM) with TBAF in CD_3CN.

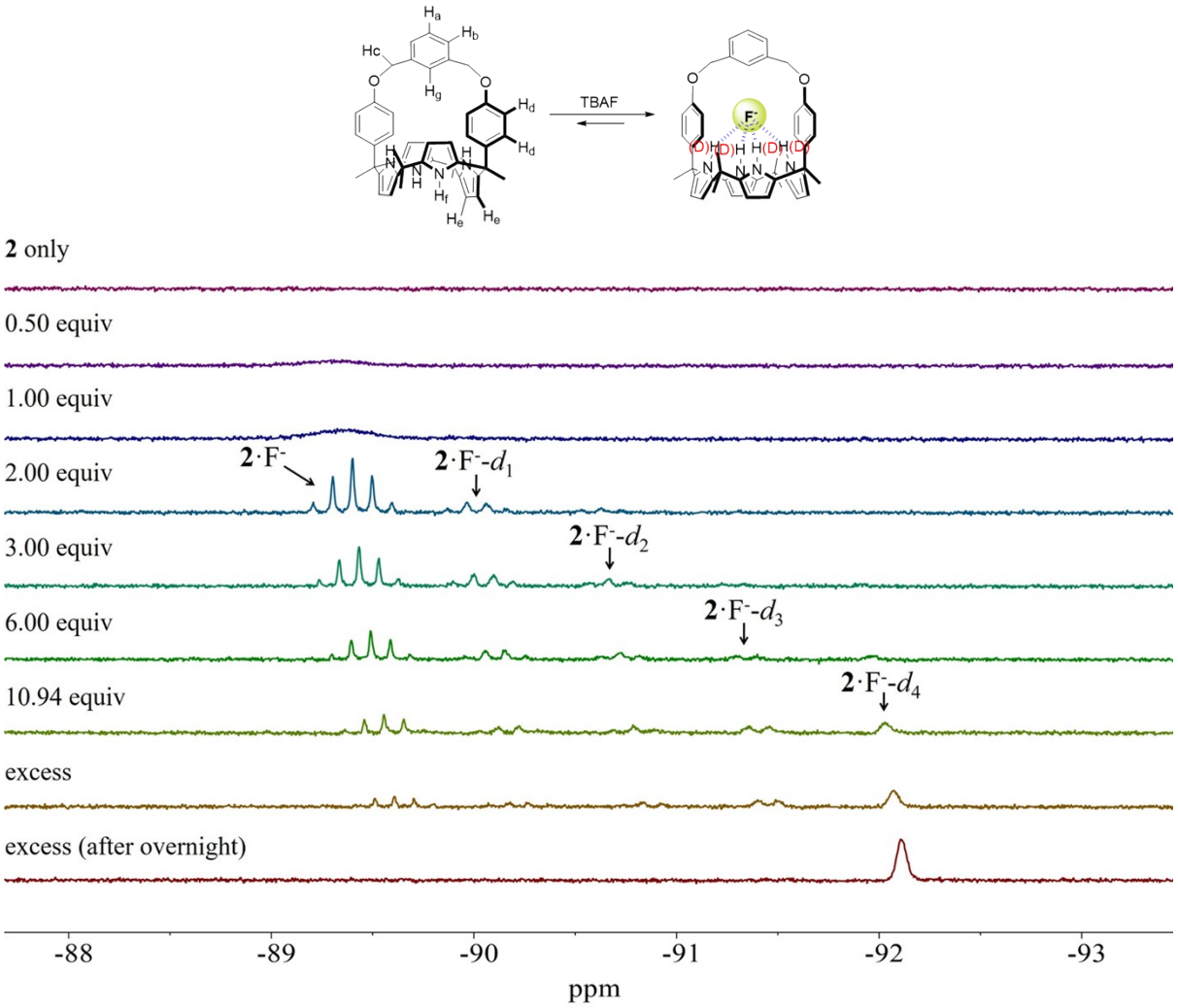


Figure S19. ^{19}F NMR spectra recorded during the titration of **2** (5 mM) with TBAF in CD_3CN. Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

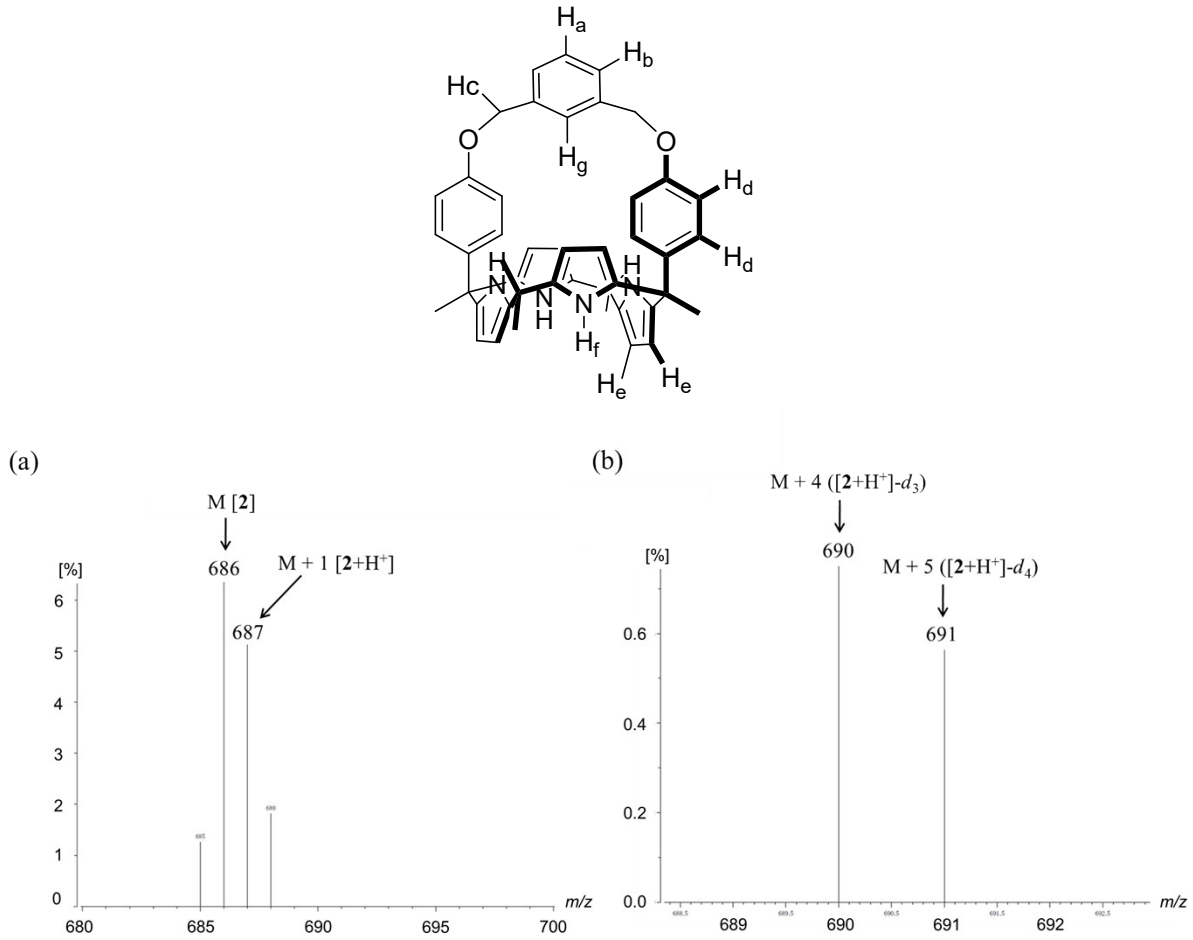


Figure S20. FAB mass spectra of receptor **2** recorded in the absence (a) and presence (b) of TBAF in CD_3CN.

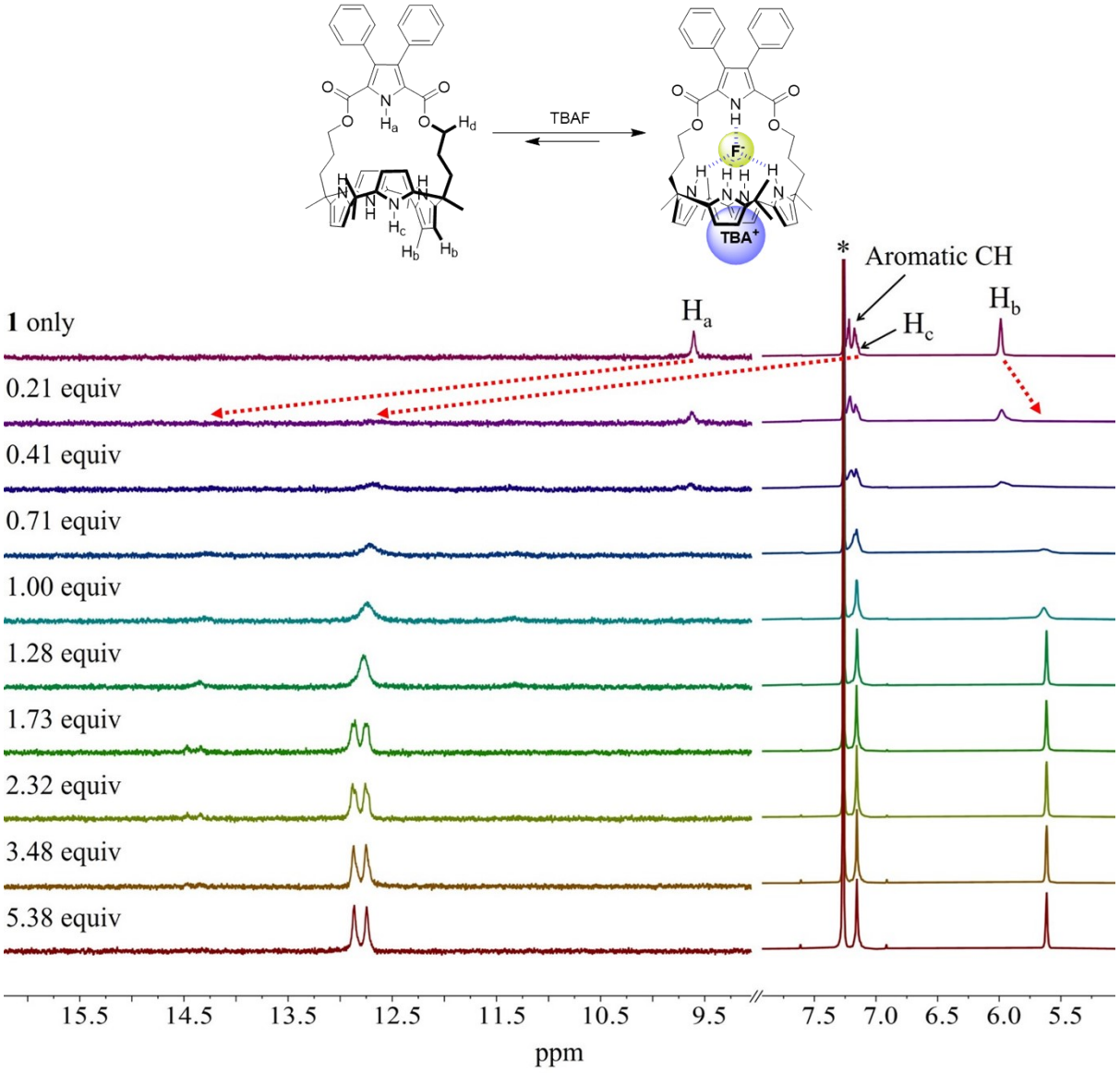


Figure S21. ^{1}H NMR spectra recorded during the titration of **1** (3 mM) with TBAF in $CDCl_3$. * denotes the peak of $CHCl_3$ from the NMR solvent.

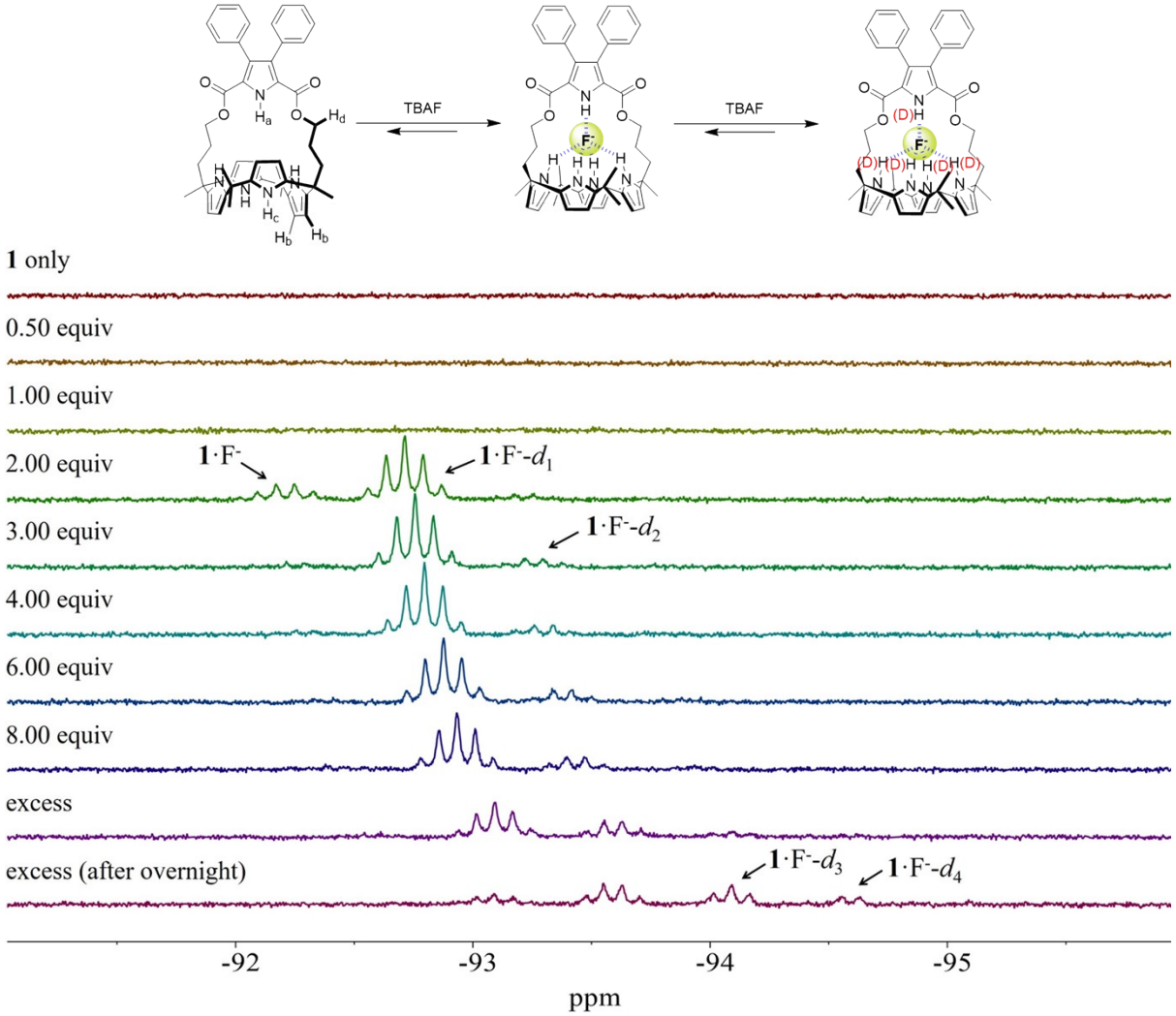


Figure S22. ^{19}F NMR spectra recorded during the titration of **1** (10 mM) with TBAF in $CDCl_3$. Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

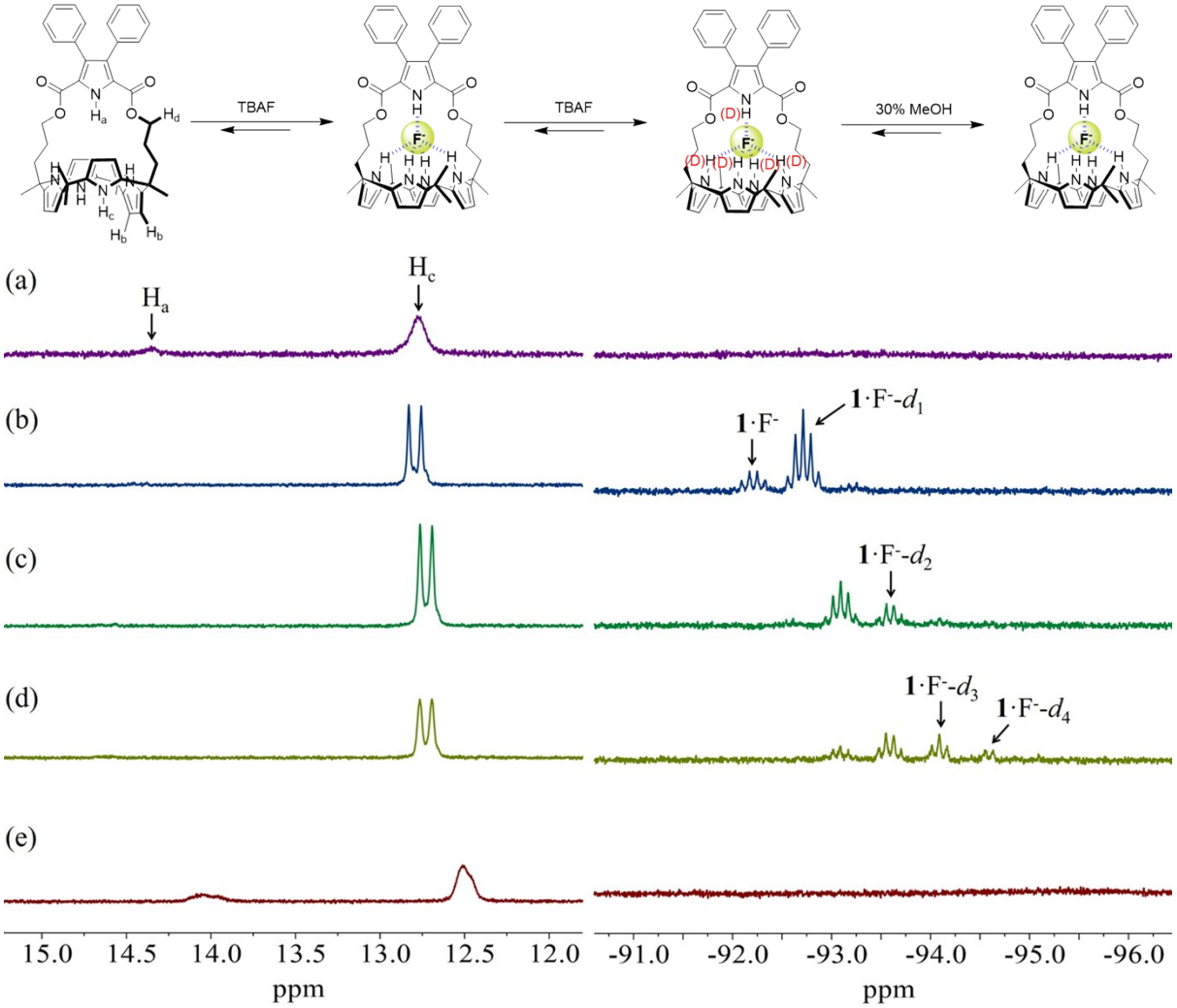


Figure S23. Partial ^{1}H (left) and ^{19}F (right) NMR spectra of **1** (10 mM) recorded (a) with 1.0 equiv of TBAF in $CDCl_3$, (b) with 2.0 equiv of TBAF in $CDCl_3$, (c) with excess equiv of TBAF in $CDCl_3$, (d) after allowing (c) to stand overnight, and (e) after adding 30% methanol to (d). Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

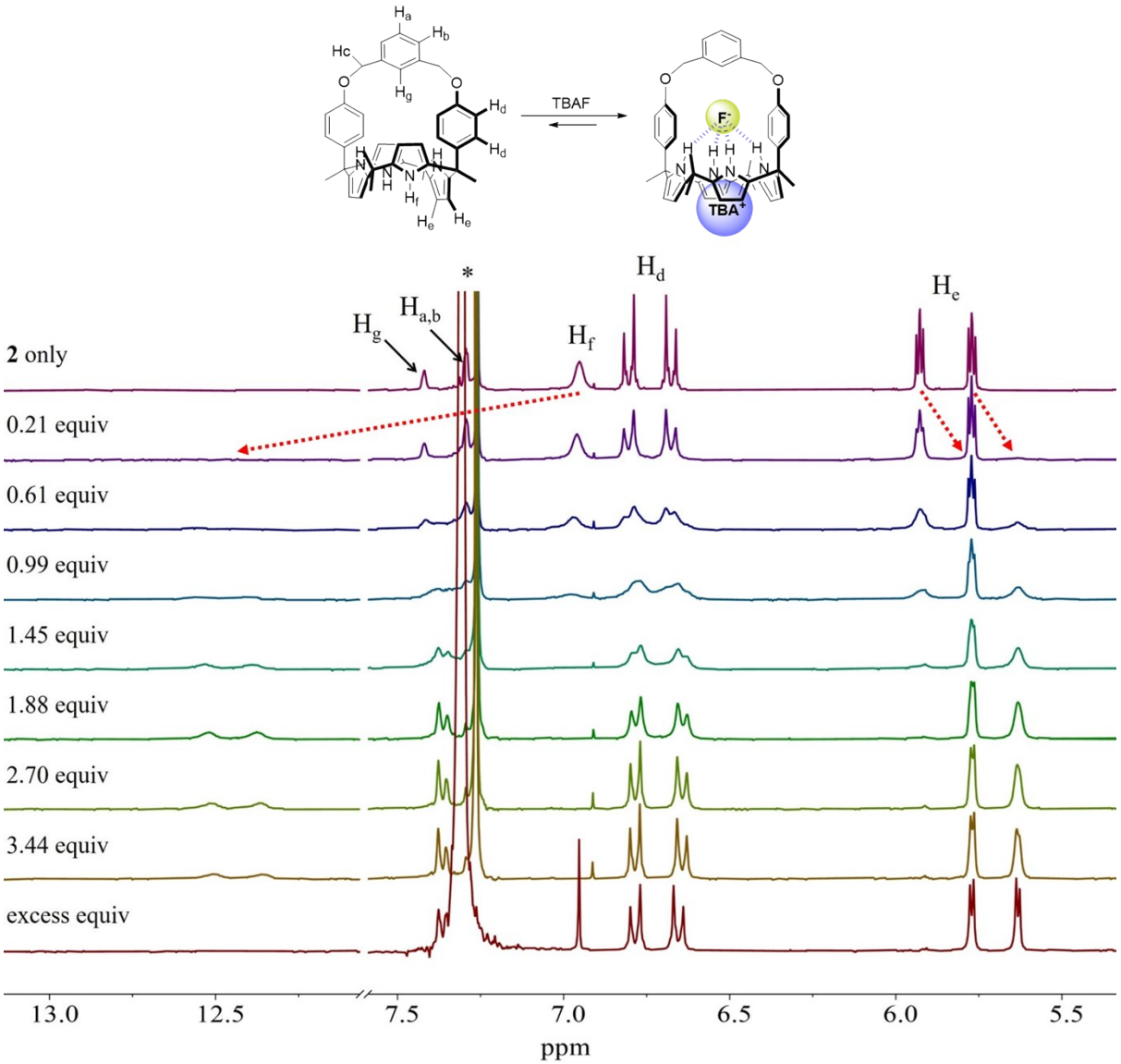


Figure S24. ^{1}H NMR spectra recorded during the titration of **2** (3 mM) with TBAF in $CDCl_3$. * denotes the peak of $CHCl_3$ from the NMR solvent.

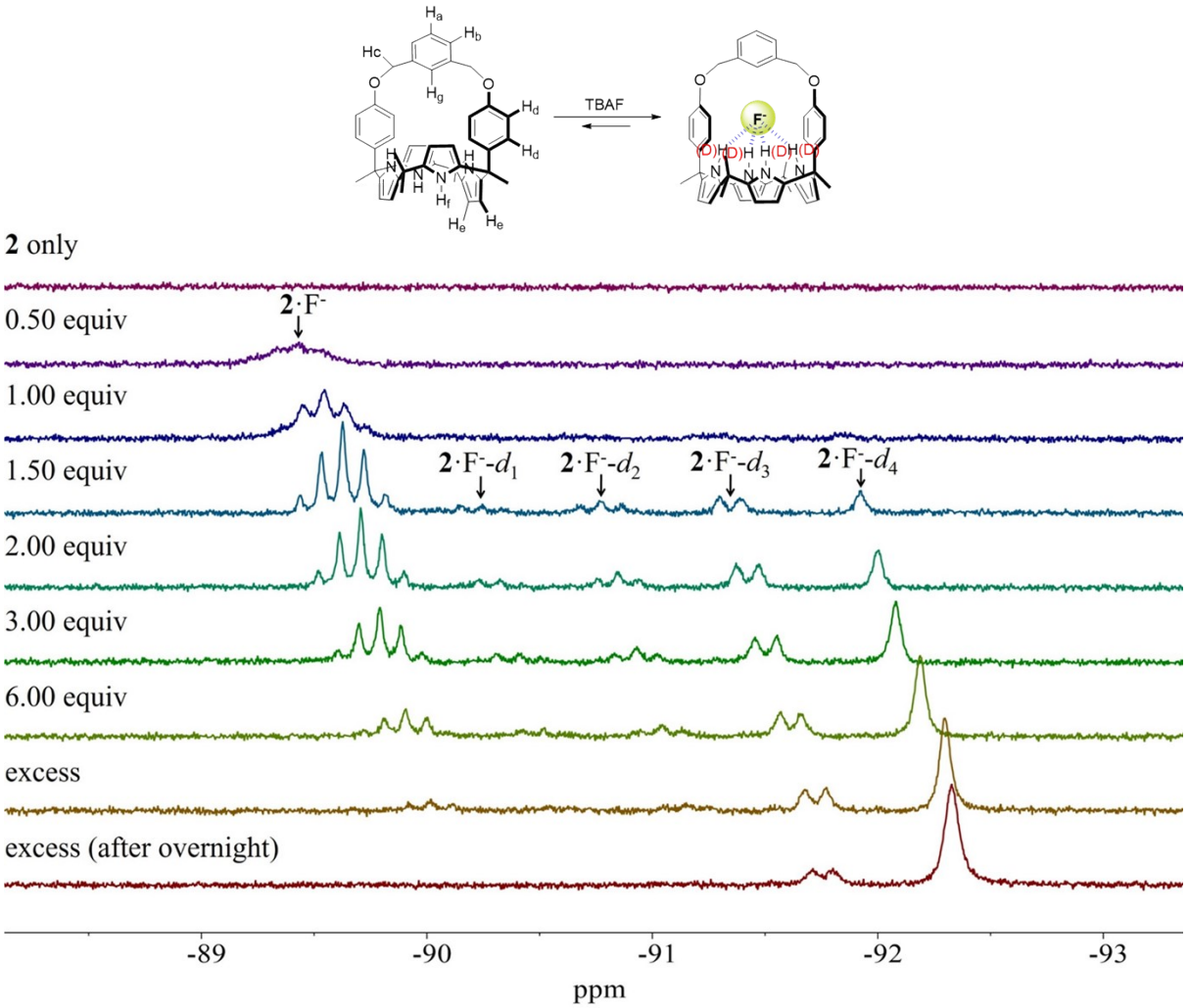


Figure S25. ^{19}F NMR spectra recorded during the titration of **2** (10 mM) with TBAF in $CDCl_3$. Fluorobenzene (C_6H_5F, 16.2 mM) was used as an internal reference.

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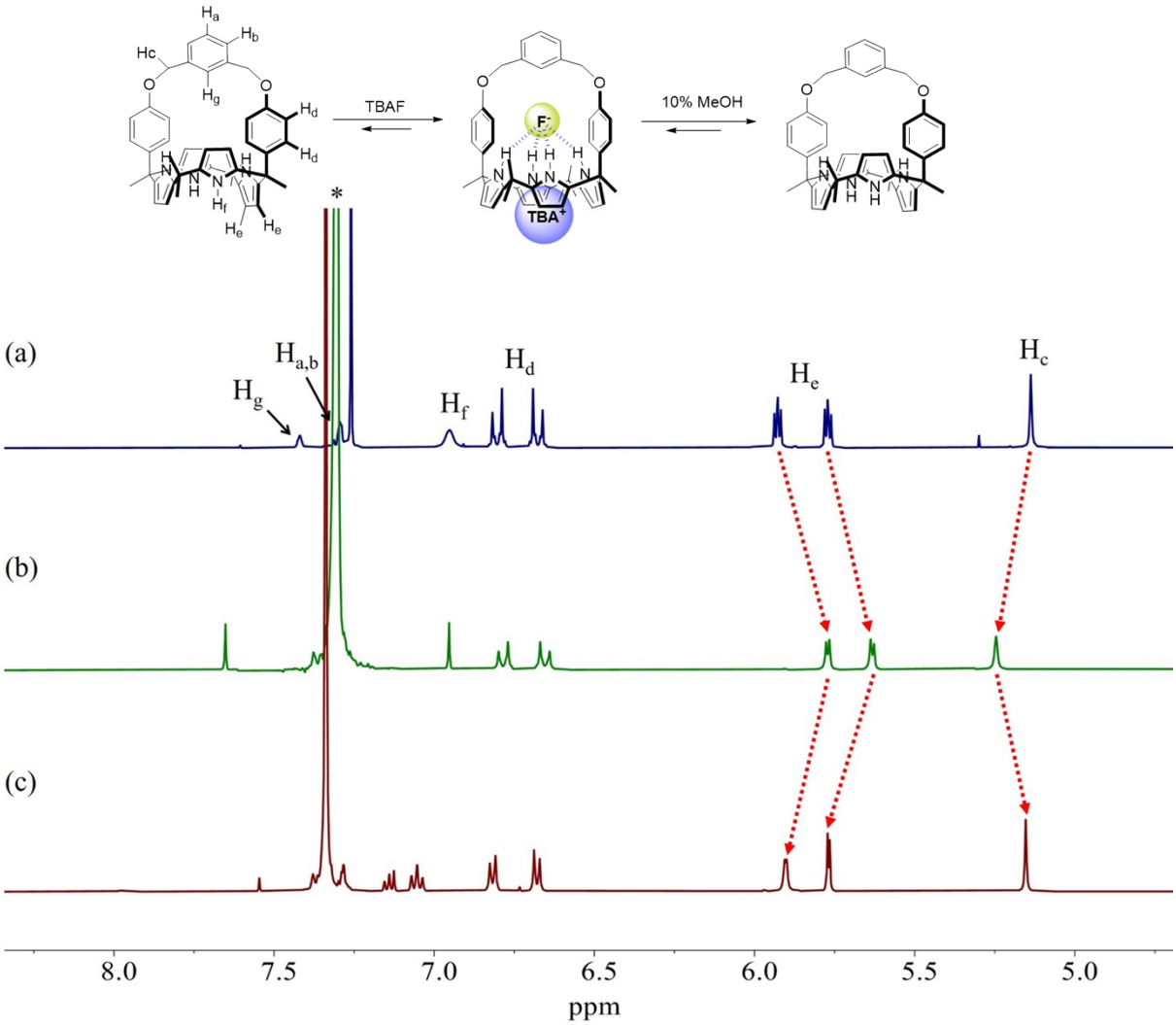

Figure S26. Partial ^{1}H NMR spectra of (a) **2** (3 mM) only, (b) **2** + TBAF (excess equiv), and (c) after adding 10% methanol to (b) in $CDCl_3$. * denotes the $CHCl_3$ peak arising from the NMR solvent.

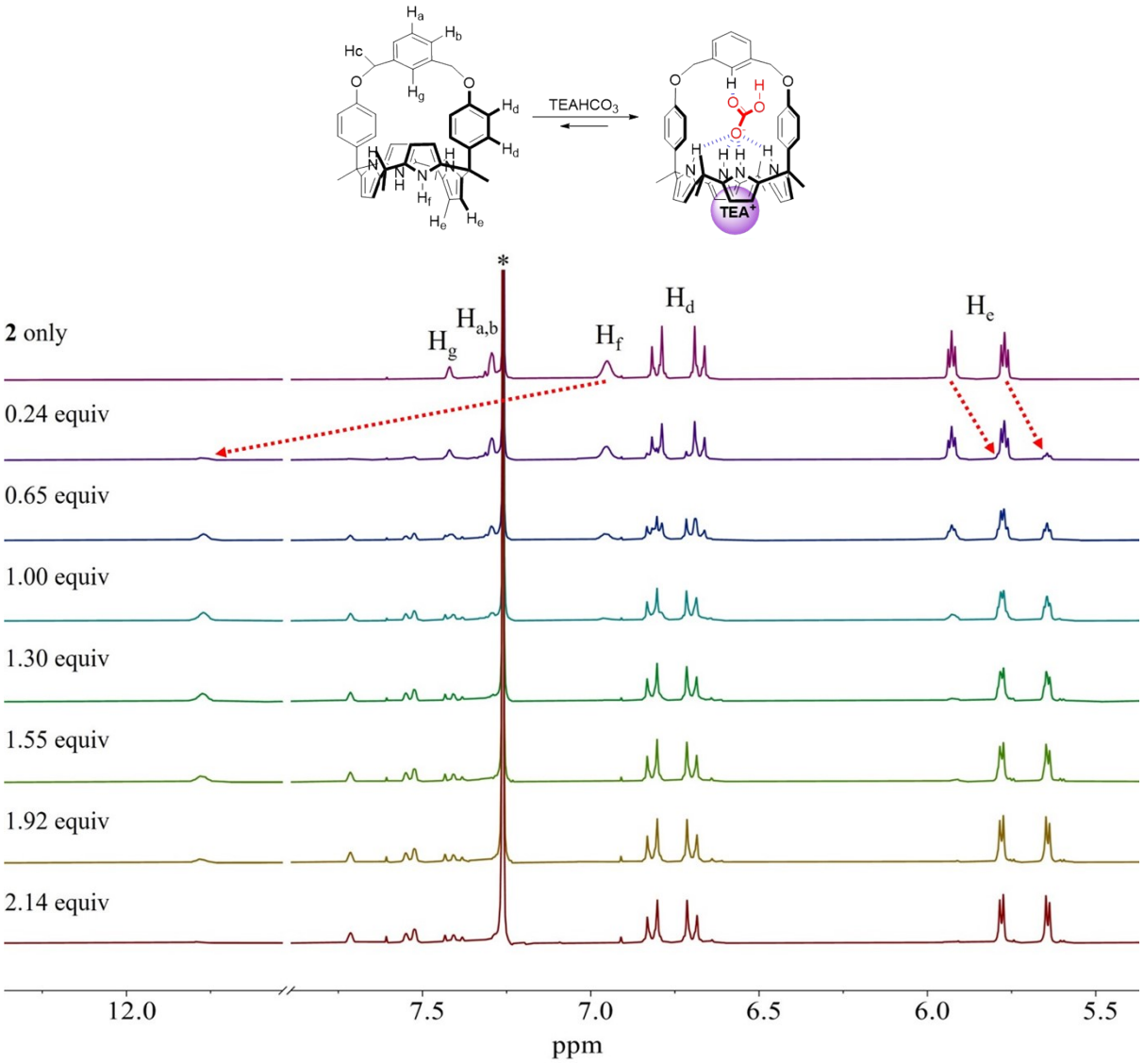

Figure S27. ^{1}H NMR spectra recorded during the titration of **2** (3 mM) with $TEAHCO_3$ in $CDCl_3$.

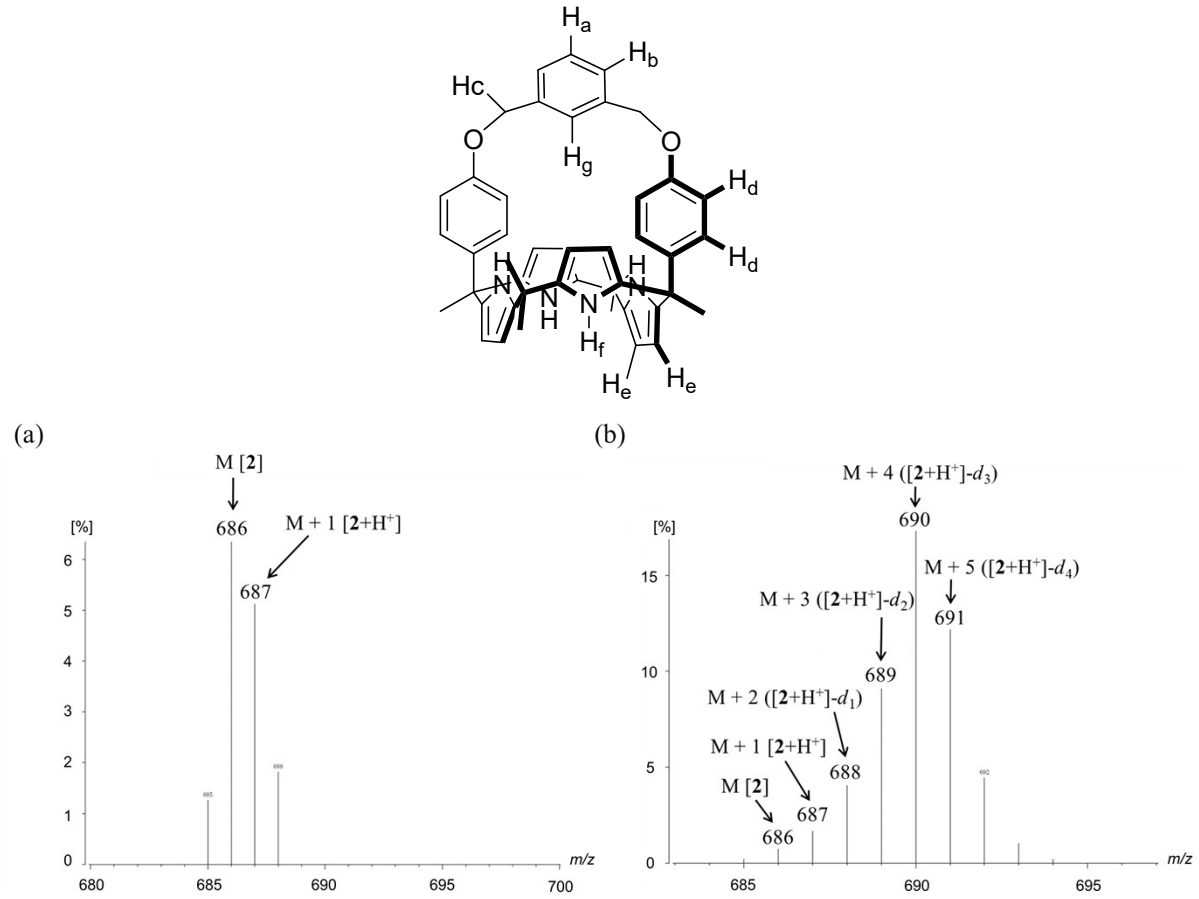

Figure S28. FAB mass spectra of receptor **2** recorded in the absence (a) and presence (b) of 2.5 equiv. of $TEAHCO_3$ in $CDCl_3$.

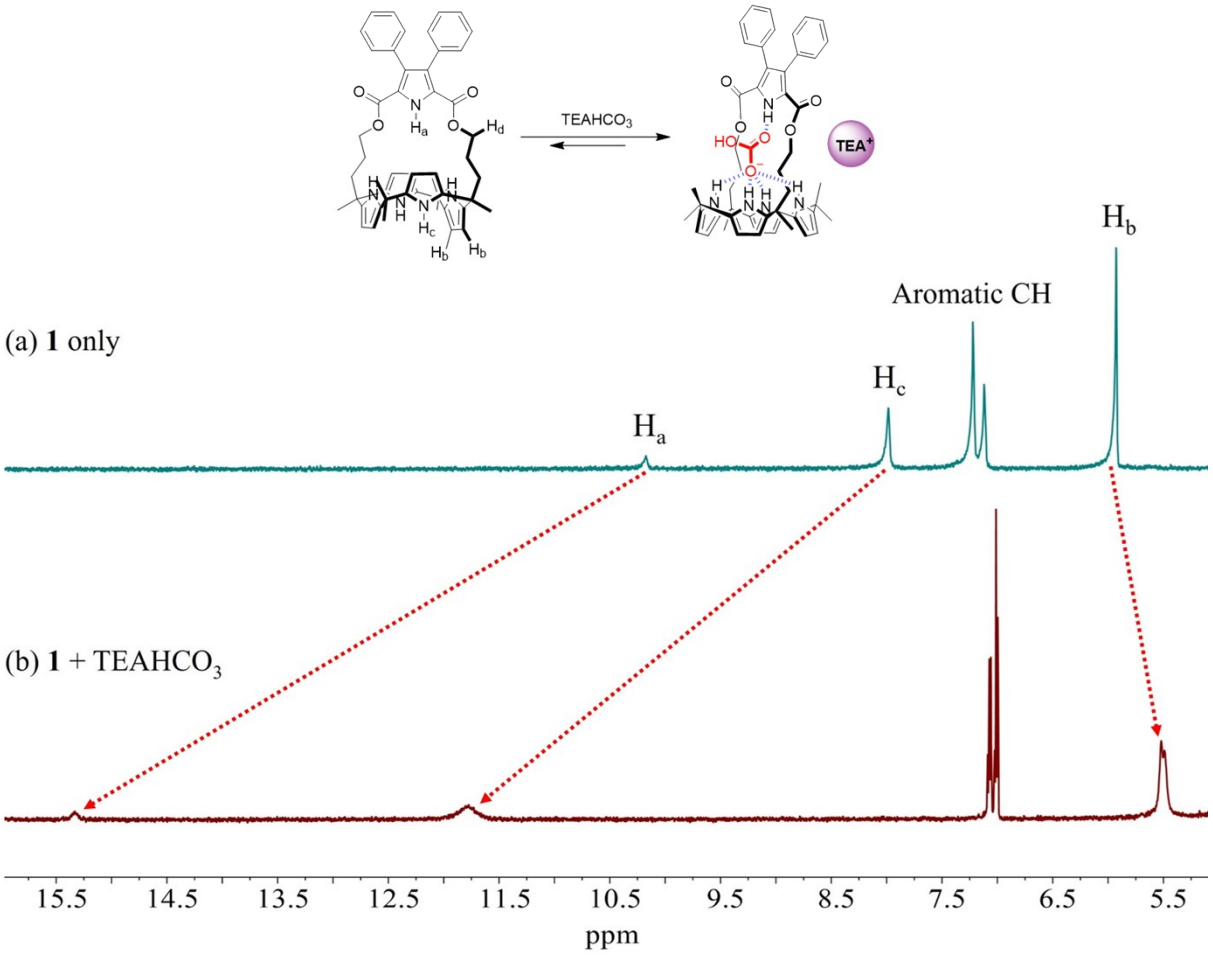

Figure S29. Partial ^{1}H NMR spectra of (a) **1** (3 mM) only, (b) **1** + excess $TEAHCO_3$ (tetraethylammonium bicarbonate) in CD_3CN.

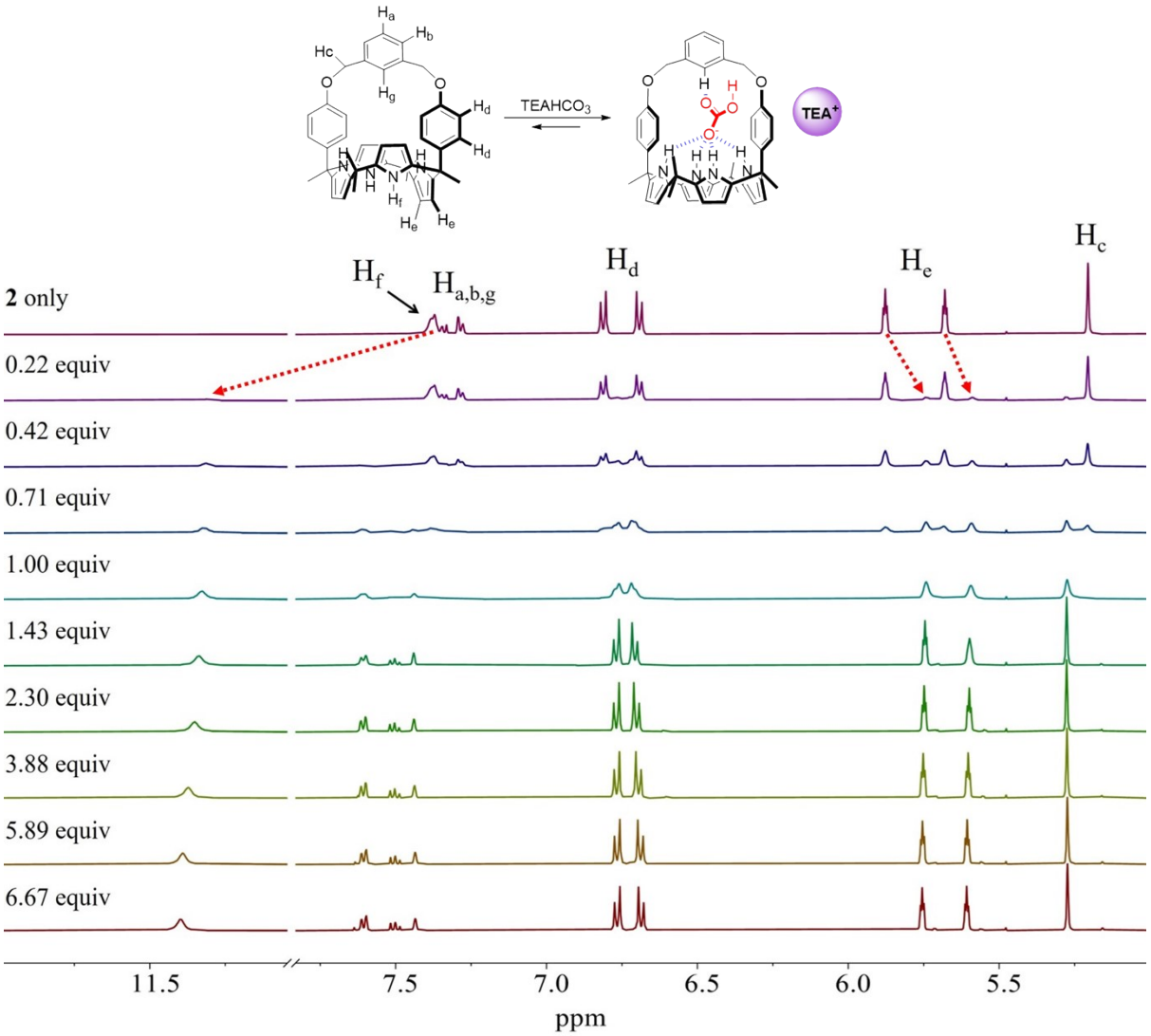

Figure S30. Partial ^{1}H NMR spectra recorded during the titration of **2** (3 mM) with $TEAHCO_3$ in CD_3CN.

5. X-ray experimental for receptors 1 and 2

X-ray experimental for the receptor 1•ethyl carbonate

Table S1. Crystal data and structure refinement for **1**•ethyl carbonate.

Empirical formula	C61 H78 N6 O7	
Formula weight	1007.29	
Temperature	296.15	
Wavelength	0.71073	
Crystal system	monoclinic	
Space group	C 1 2/c 1	
Unit cell dimensions	a = 31.9700(7) Å	α = 90 °.
	b = 22.2512(5) Å	β = 120.4190(10) °.
	c = 21.3925(4) Å	γ = 90 °.
Volume	13123.2(5) $Å^3$	
Z	8	
Density (calculated)	1.020 Mg/m^3	
Absorption coefficient	0.067 mm^{-1}	
F(000)	4336	
Crystal size	0.503 x 0.298 x 0.089 mm^3	
Theta range for data collection	2.21 to 26.19°.	
Index ranges	-42<=h<=42, -29<=k<=29, -28<=l<=28	
Reflections collected	16327	
Independent reflections	11960 [R(int) = 0.0374]	
Completeness to theta = 25.25°	100%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.7457 and 0.7197	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	16327 / 4 / 687	
Goodness-of-fit on F^2	1.038	
Final R indices [I>2sigma(I)]	R1 = 0.0524, wR2 = 0.1394	
R indices (all data)	R1 = 0.0717, wR2 = 0.1525	
Extinction coefficient	-	
Largest diff. peak and hole	0.587 and -0.700 $e.Å^{-3}$	
CCDC	2248755	

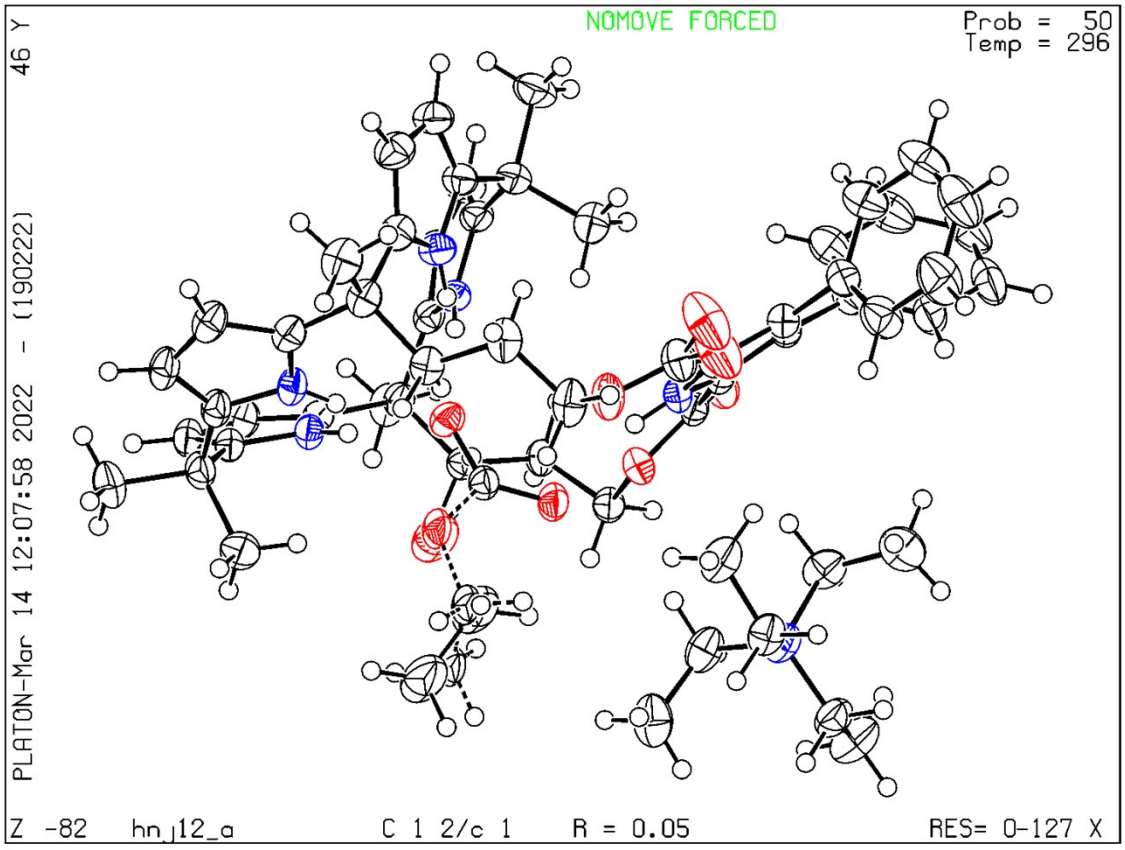

Figure S31. View of the ethyl carbonate complex in **1** showing a partial atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. Most hydrogen atoms have been removed for clarity. Dashed lines are indicative of H-bonding interactions.

X-ray experimental for the receptor 2

X-ray Experimental for complex $C_{46}H_{46}N_4O_2$: Crystals grew as colorless prisms by slow cooling. The data crystal was cut from a larger crystal and had approximate dimensions; 0.30 x 0.25 x 0.15 mm. The data were collected on a Rigaku Oxford Diffraction SuperNova Dual Source diffractometer using a μ-focus Cu Kα radiation source (λ = 1.5418Å) with collimating mirror monochromators. A total of 956 frames of data were collected using ω-scans with a scan range of 1° and a counting time of 4 seconds per frame with a detector offset of -41.7° and 11 seconds per frame with a detector offset of 107.1°. The data were collected at 100 K using an Oxford Cryostream low temperature device. Data collection, unit cell refinement and data reduction were performed using Agilent Technologies CrysAlisPro V 1.171.41.70a.[1] The structure was solved by direct methods using SHELXT[2] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-2016/6.[3] Structure analysis was aided by use of the programs PLATON[4] and OLEX2.[5] The hydrogen atoms on carbon were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms). The hydrogen atoms on the pyrrole group nitrogen atoms were located in a ΔF map and refined with isotropic displacement parameters.

The function, $\Sigma w(|F_o|^2 - |F_c|^2)^2$, was minimized, where $w = 1/[(\sigma(F_o))^2 + (0.0524*P)^2 + (1.2722*P)]$ and $P = (|F_o|^2 + 2|F_c|^2)/3$. $R_W(F^2)$ refined to 0.103, with R(F) equal to 0.0382 and a goodness of fit, S, = 1.03. Definitions used for calculating R(F), $R_W(F^2)$ and the goodness of fit, S, are given below.[6] The data were corrected for secondary extinction effects. The correction takes the form: $F_{corr} = kF_c/[1 + (1.8(4)x10^{-7})* F_c^2 \lambda^3/(\sin 2\theta)]^{0.25}$ where k is the overall scale factor. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).[7] All figures were generated using SHELXTL/PC.[8] Tables of positional and thermal parameters, bond lengths and angles, torsion angles and figures are found elsewhere.

Table S2. Crystal data and structure refinement for **2**.

Empirical formula	C46 H46 N4 O2	
Formula weight	686.87	
Temperature	99.98(10) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 13.20282(17) Å	α = 90°.
	b = 15.89028(16) Å	β = 104.5129(11)°.
	c = 18.32713(20) Å	γ = 90°.
Volume	3722.28(7) $Å^3$	
Z	4	
Density (calculated)	1.226 Mg/m^3	
Absorption coefficient	0.587 mm^{-1}	
F(000)	1464	
Crystal size	0.304 x 0.248 x 0.153 mm^3	
Theta range for data collection	3.721 to 73.274°.	
Index ranges	-16<=h<=15, -13<=k<=19, -21<=l<=22	
Reflections collected	20997	
Independent reflections	7296 [R(int) = 0.0194]	
Completeness to theta = 67.684°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.88935	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7296 / 0 / 491	
Goodness-of-fit on F^2	1.033	
Final R indices [I>2sigma(I)]	R1 = 0.0382, wR2 = 0.0988	
R indices (all data)	R1 = 0.0426, wR2 = 0.1028	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.375 and -0.237 $e.Å^{-3}$	
CCDC	2376015	

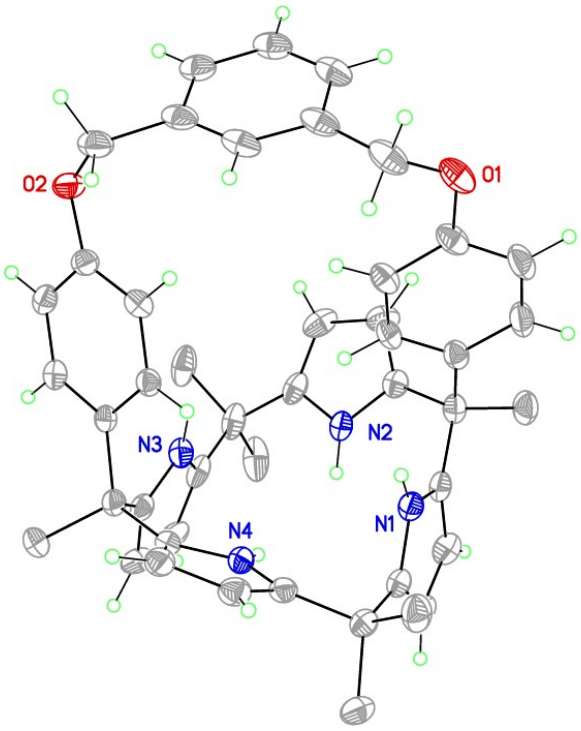

Figure S32. View of **2** showing the heteroatom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. The methyl group hydrogen atoms have been omitted for clarity.

6. References

1) CrysAlisPro V1.171.41.70a. Rigaku Oxford Diffraction, The Woodlands, TX, USA .

2) SHELXT. G. M. Sheldrick, *Acta. Cryst.,* 2015, **A71**, 3-8.

3) G. M. Sheldrick, SHELXL-2018/3. Program for the Refinement of Crystal Structures. University of Gottingen, Germany. *Acta. Cryst.,* 2015, **C71**, 3-8.

4) A. L. Spek, PLATON, A Multipurpose Crystallographic Tool. Utrecht University, The Netherlands. *Acta Cryst.,* 2009, **D65**, 148-155.

5) OLEX2. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, A Complete Structure Solution, Refinement and Analysis Program. *J. Appl. Cryst.,* 2009, **42**, 339-341.

6) $R_W(F^2) = \{\Sigma w(|F_O|^2 - |F_C|^2)^2/\Sigma w(|F_O|)^4\}^{1/2}$ where w is the weight given each reflection. $R(F) = \Sigma (|F_O| - |F_C|)/\Sigma|F_O|\}$ for reflections with $F_O > 4(\sigma (F_O))$. $S = [\Sigma w(|F_O|^2 - |F_C|^2)^2/(n - p)]^{1/2}$, where n is the number of reflections and p is the number of refined parameters.

7) International Tables for X-ray Crystallography. Vol. C, Tables 4.2.6.8 and 6.1.1.4, A. J. C. Wilson, editor, Boston: Kluwer Academic Press.

8) G. M. Sheldrick, 1994, SHELXTL/PC (Version 5.03). Siemens Analytical X-ray Instruments, Inc., Madison, Wisconsin, USA.