Specific recognition of fluoride anion in water by a copper (II) centre embedded in a hydrophobic cavity.

Andrea Brugnara[§], Filip Topić,[≠] Kari Rissanen,[≠] Aurélien de la Lande[†], Benoit Colasson[§] and Olivia Reinaud[§]

[§] Laboratoire de Chimie et de Biochimie Pharmacologiques et Toxicologiques, CNRS UMR 8601, Université Paris Descartes, 45 rue des Saints Pères, 75006 Paris, France.

[≠] Department of Chemistry, Nanoscience Center, University of Jyväskylä, P.O. Box 35, 40014 Jyväskylä, Finland.

[†] Laboratoire de Chimie Physique (CNRS UMR 8000), Université Paris-Sud 11 - Campus Orsay, 15 Rue Georges Clemenceau, 91400 Orsay, France.

General experimental methods

[H**2**]$(NO_3)_4$, [Cu^{II}**2**]$(NO_3)_5$ and [Cu^{II}**3**]$(OTf)_2$ were synthesized as reported in the literature. Chemicals (NaF and NaCl) were obtained commercially and used without further purification. The UV-Visible spectra were recorded with a Jasco V-750 spectrophotometer. EPR spectra were recorded using a Bruker Elexys spectrophotometer (X-band). MS (ESI) analyses were obtained with a ThermoFinnigen LCQ Advantage spectrometer using water as solvent. pH measures were recorded with a Mettler Toledo FiveGo pH equipped with a Mettler Toledo 0402-M3-S7/200 electrode.

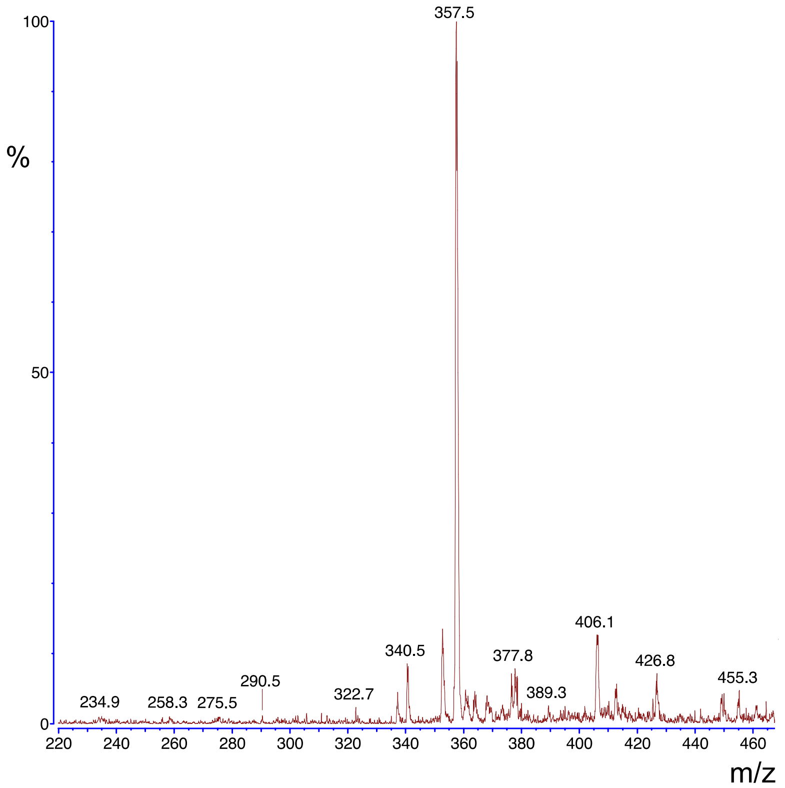

Figure S1: MS (ESI) spectrum for an aqueous solution of [Cu^{II}**2**]$(NO_3)_5$ (20 mM) and NaF (300 mM). Calc. for $C_{87}H_{108}CuFN_7O_6$ [Cu^{II}(F)**2**]$^{4+}$: *m/z* = +357.2; found *m/z* = +357.5.

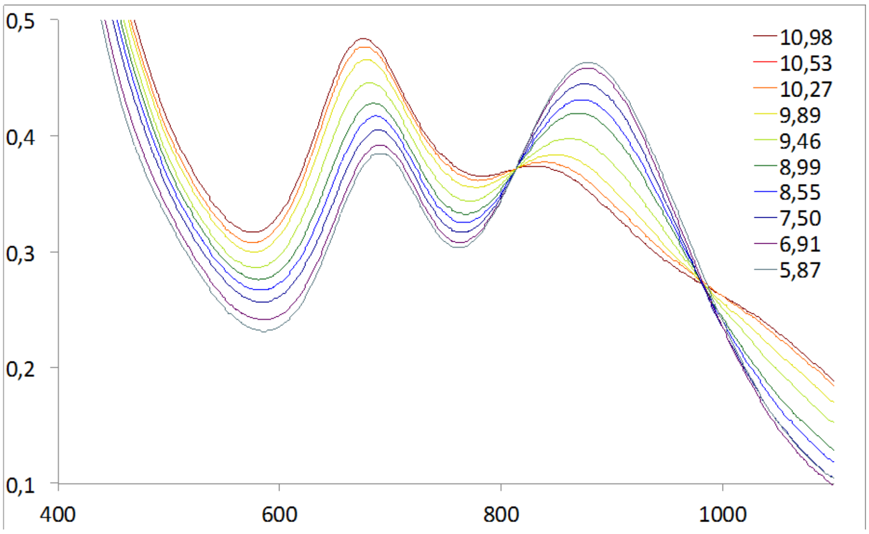

Figure S2: UV-Visible spectra of $[Cu^{II}(F)\mathbf{2}]^{4+}$ ($[Cu^{II}\mathbf{2}](NO_3)_5$ 2.05 mM and NaF 10.3 mM) in water, at different pH values.

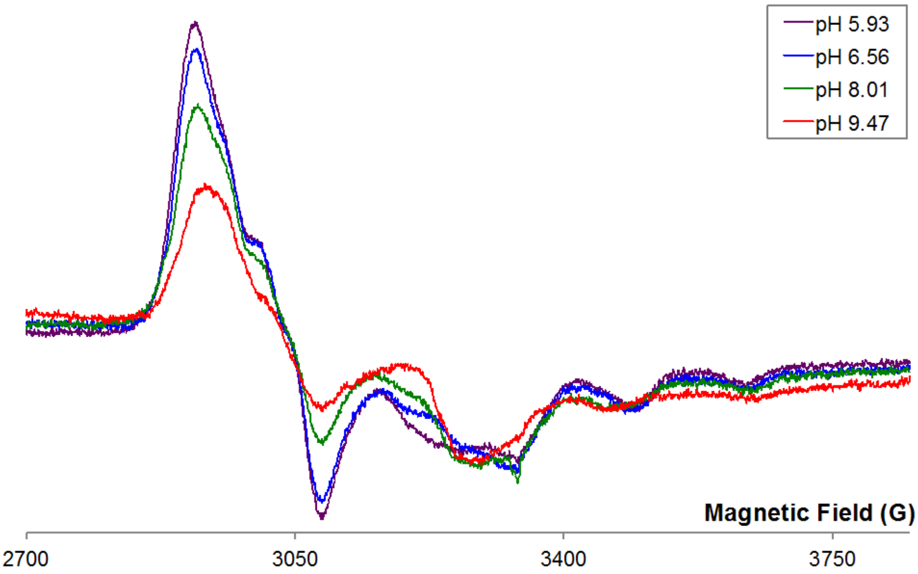

Figure S3: EPR spectra (100K) for $[Cu^{II}(F)\mathbf{2}]^{4+}$ ($[Cu^{II}\mathbf{2}](NO_3)_5$ 2.05 mM and NaF 10.3 mM) in water, at different pH values. ($A_{\|}$=147 for pH 5.9 and 6.6; $A_{\|}$=190 for pH 9.5)

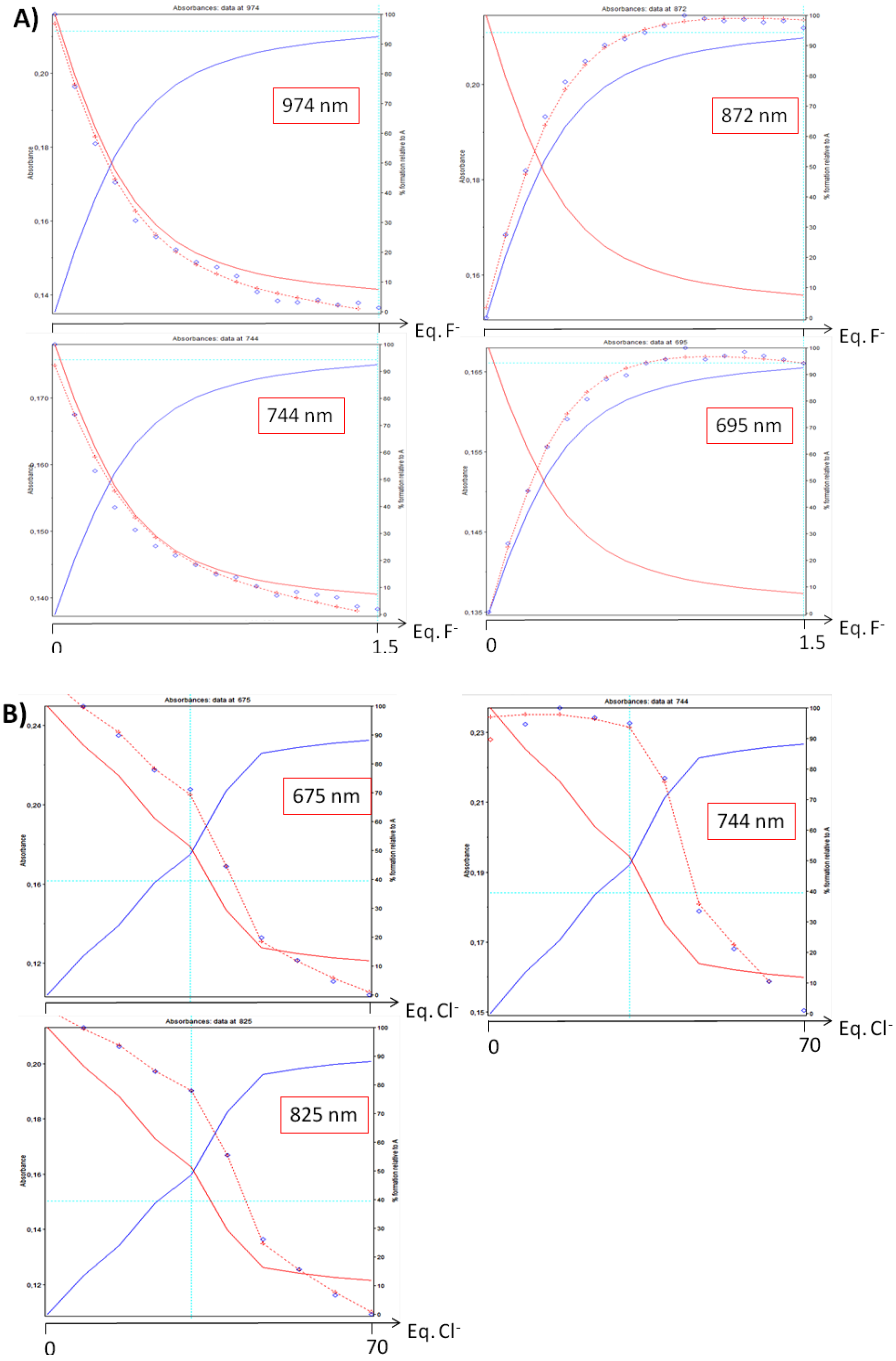

Figure S4: Experimental (blue square) and fitted (dashed red line) variation on the absorbance value (at selected wavelengths) *vs.* number of equivalents of titrant for:

A) $[\mathrm{Cu}^{II}\mathbf{2}](\mathrm{NO}_3)_5$ (1.7 mM) in water (pH 5.9 buffered solution, [MES] = 30 mM) in the presence of NaCl (120 mM), titrated with NaF (from 0 to 1.5 eq.).

B) $[\mathrm{Cu}^{II}\mathbf{2}](\mathrm{NO}_3)_5$ (2.4 mM) in water (pH 5.9 buffered solution, [MES] = 30 mM), titrated with NaCl (from 0 to 70 eq.).

(The blue line correspond to the calculated percentage of the final species and the red line correspond to the percentage of the starting species.)

X-ray crystallography

X-ray crystallographic analysis of [Cu^{II}(F)**1**](ClO$_4$): Single crystals were obtained by slow diffusion of hexane into a chloroform solution of the complex at 4°C. X-ray data were collected on an Agilent SuperNova Dual diffractometer with Atlas detector at $T = 123.0(1)$ K with mirror-monochromatized Cu-$K\alpha$ radiation ($\lambda = 1.54184$ Å). CrysAlisPro[1] software was used for data collection, integration and reduction as well as applying the numerical absorption correction.

The structure was solved by charge flipping with Superflip[2] and refined by full-matrix least-squares using SHELXL-2013[3] within OLEX2[4] package. All non-hydrogen atoms were refined anisotropically. The positions of hydrogen atoms were calculated and refined as riding on the parent carbon or oxygen atoms with $U_H = 1.5\ U_{C/O}$ for methyl and hydroxyl groups or otherwise $U_H = 1.2\ U_C$. The geometrical restraints were applied in such a way that the parameters were allowed to refine freely. All the phenyl and pyridine rings were modelled as rigid bodies. The occupancies of the disordered moieties were also allowed to refine freely. The SQUEEZE[5] routine of PLATON[6] was used to calculate the contributions of the disordered solvent regions to the respective structure factors in the form of FAB files which were then used in respective refinements.

All three perchlorate (ClO_4^-) anions could be located and modelled successfully. Only one of them had to be modeled as disordered over two discrete components with occupancies 0.437(7)/0.563(7). Solvent (chloroform) molecules were observed to be encapsulated in two of the host molecules in the asymmetric unit, of which one was modeled with full occupancy. Due to the disorder of the host, the other encapsulated chloroform was modeled with the occupancy of 0.437(7), since the major disorder component of the host, with the occupancy 0.563(7), has a methoxy group self-included. Of the remaining four chloroform molecules, three were modeled with full occupancy, with one modeled as disordered over two components [occupancies 0.512(10) and 0.488(10)]. The TMAP "cap" in one of the host molecules also had to be modeled as disordered, with the two components' occupancies refining to 0.502(6) and 0.498(6), respectively. Finally, five of the *t*Bu groups were modeled as disordered over two components, with the geometries restrained and the occupancies of the disorder components freely refined [to 0.536(13)/0.464(13), 0.506(13)/0.494(13), 0.621(13)/0.379(13), 0.635(12)/0.365(12) and 0.543(12)/0.457(12)]

Crystal dimensions 0.146×0.051×0.037 mm, $C_{91.81}H_{109.81}Cl_{6.44}CuFN_4O_{10}$, $M = 1740.14$, monoclinic, space group $P\bar{1}$, $a = 17.7109(7)$ Å, $b = 28.5979(15)$ Å, $c = 31.0744(19)$ Å, $\alpha = 67.271(5)°$, $\beta = 79.167(4)°$, $\gamma = 84.672(4)°$, $V = 14254.5(14)$ Å^3, $Z = 6$, $d_c = 1.216$ g cm^{-3}, $\mu = 2.449$ mm^{-1}, $F(000) = 5496$, 52272 reflections ($2\theta_{max} = 100.87°$) measured (29425 unique, $R_{int} = 0.0612$, completeness = 98.6%), Final R indices ($I > 2\sigma(I)$): $R_1 = 0.1384$, $wR_2 = 0.3579$, R indices (all data): $R_1 = 0.2215$, $wR_2 = 0.4234$. $GOF = 1.272$ for 3049 parameters and 6629 restraints, largest diff. peak and hole 1.014/–1.059 eÅ^{-3}. CCDC-997677 contains the

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supplementary data for this structure. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

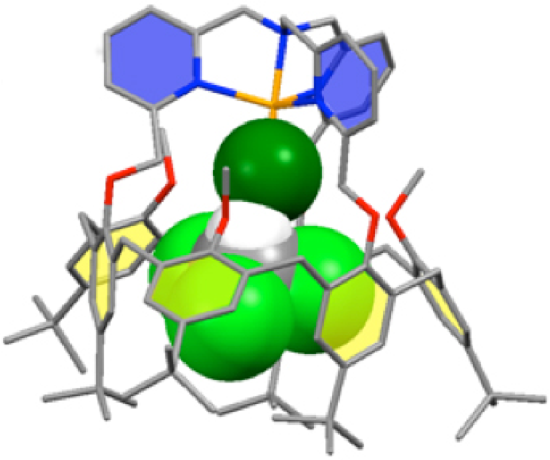


Fig. S5 Structure of B' conformer of the complex [Cu^{II}(F)**1**](ClO$_4$) as observed in the crystal structure. The groups inside the calixarene cavity are depicted in space filling model. The calixarene hydrogen atoms are excluded for clarity. Color code for the atoms: hydrogen in white, carbon in grey, oxygen in red, nitrogen in blue, copper in orange, fluorine in green and chlorine in light green.

Molecular modeling

Geometry optimizations at the DFT level have been performed the program Gaussian09.[1] We have used the CAM-B3LYP functional[2] in combination with the 6-311G** basis set on Cu, C, H, O, N and the 6-311+G** basis set on F and Cl.[3] Dispersion was taken into account thanks with the GD3 model of Grimme et al.[4] Solvation was modeled with the Polarizable Continuum Model of Tomasi and co-workers using the using the integral equation formalism variant.[5] Cavities of the PCM models were defined with the Unified Atom model calibrated based on Kohn-Sham DFT calculations. No symmetry considerations were applied during geometry optimizations. The standard Gibbs free energies associated to the displacement of the ligand H_2O by X ($LCu^{II}(H_2O) + X \longrightarrow LCu^{II}(X) + H_2O$) were calculated according to:

$$\Delta G_{disp} \approx \Delta E_{disp} = E_{sol}\left(LCu^{II}(X)\right) + E_{sol}(H_2O) - E_{sol}\left(LCu^{II}(H_2O)\right) - E_{sol}(X) + C$$

where $E_{sol}(A)$ is the DFT energy of molecule A in solution provided by the PCM method and where the thermal contributions arising from translation, rotation and vibration have been assumed to cancel out. *C* is a constant which equals to $-RT.\ln(55.5)$ with 55.5 M as the molarity of water. The standard Gibbs free energies of binding of ligand X to the cupric complexes ($LCu^{II} + X \longrightarrow LCu^{II}(X)$) are calculated similarly except that no constant *C* is added.

$$\Delta G_{bind} \approx \Delta E_{bind} = E_{sol}\left(LCu^{II}(X)\right) - E_{sol}(LCu^{II}) - E_{sol}(X)$$

Classical Molecular Dynamics (MD) simulations have been realized with the software NAMD.[6] The force field for the calixarene complex is the same as in our previous publications:[7] it is built from the CHARMM c27 force field[8] for the equilibrium bond length, angle bending and torsion angles. The punctual charges for $[Cu^{II}(F)\mathbf{2}]^{4+}$ have been obtained at the DFT level through the iterative Hirshfeld scheme[9] (implemented in our local version of the program deMon2k[10]). The iterative Hirshfeld charges have been shown to correctly reproduce the electrostatic fields created by molecules,[11] and are well adapted for classical force fields. The atomic charges between similar chemical groups have been averaged according to the C_{3v} symmetry of the complex. The list of charges is given in Table S3. The $[Cu^{II}(F)\mathbf{2}]^{4+}$ complex was solvated in a cubical box of water molecules of 50 Å edge. We have used the flexible SPC water model.[12] Four nitrate ions were added to ensure electrical neutrality. Periodic Boundary conditions were applied to calculate the long-range electrostatic interaction using the Ewald summation technique (with a grid spacing of 1 Å). The geometry was optimized at the M level during 40,000 steps. The simulations were conducted in the NPT ensemble using a Langevin thermostat and piston. The integration time-step was set to 1 fs. Then the system was slowly heated from 50 K to 300 K (by steps of 5K) with 20,000 steps at each step. The simulation was equilibrated during 80 ps before a productive phase of 60 ns. Two MDS simulations with different initial velocities were run, thereby producing a total of 120 ns. Pictures in the modeling section have been generated with the VMD software.[13]

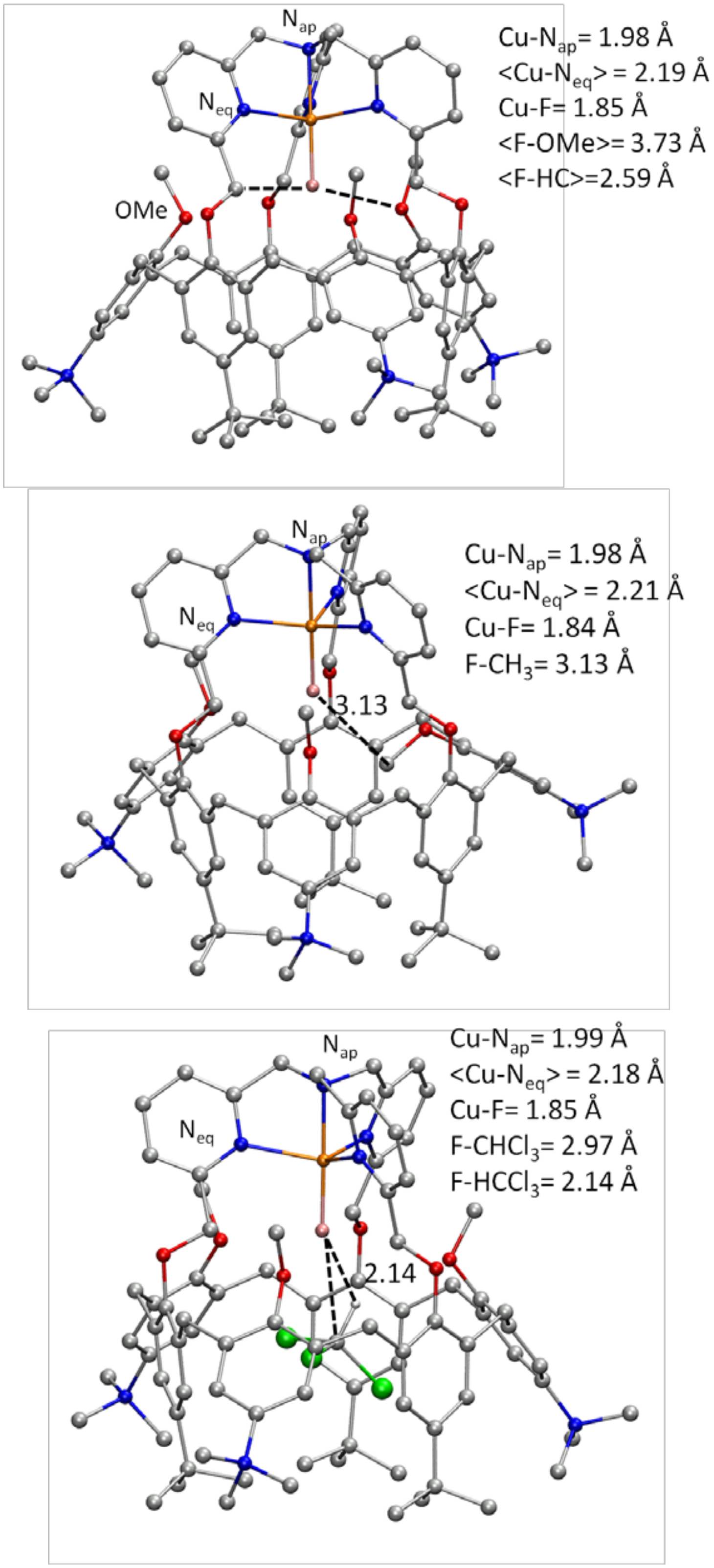


Figure S6: DFT optimized structures of the $[Cu^{II}(F)\mathbf{2}]^{4+}$ complex (top), of the $[Cu^{II}(F)\mathbf{2}]^{4+}$ complex with one OMe group pointing inside the cavity (middle) and of the $[Cu^{II}(F)(CHCl_3)\mathbf{2}]^{4+}$ complex (bottom). Color code: hydrogen in light grey, carbon in grey, oxygen in red, nitrogen in blue, copper in orange, fluorine in pink and chlorine in green. The calixarene hydrogen atoms are not shown for clarity. The distances are given in Å.

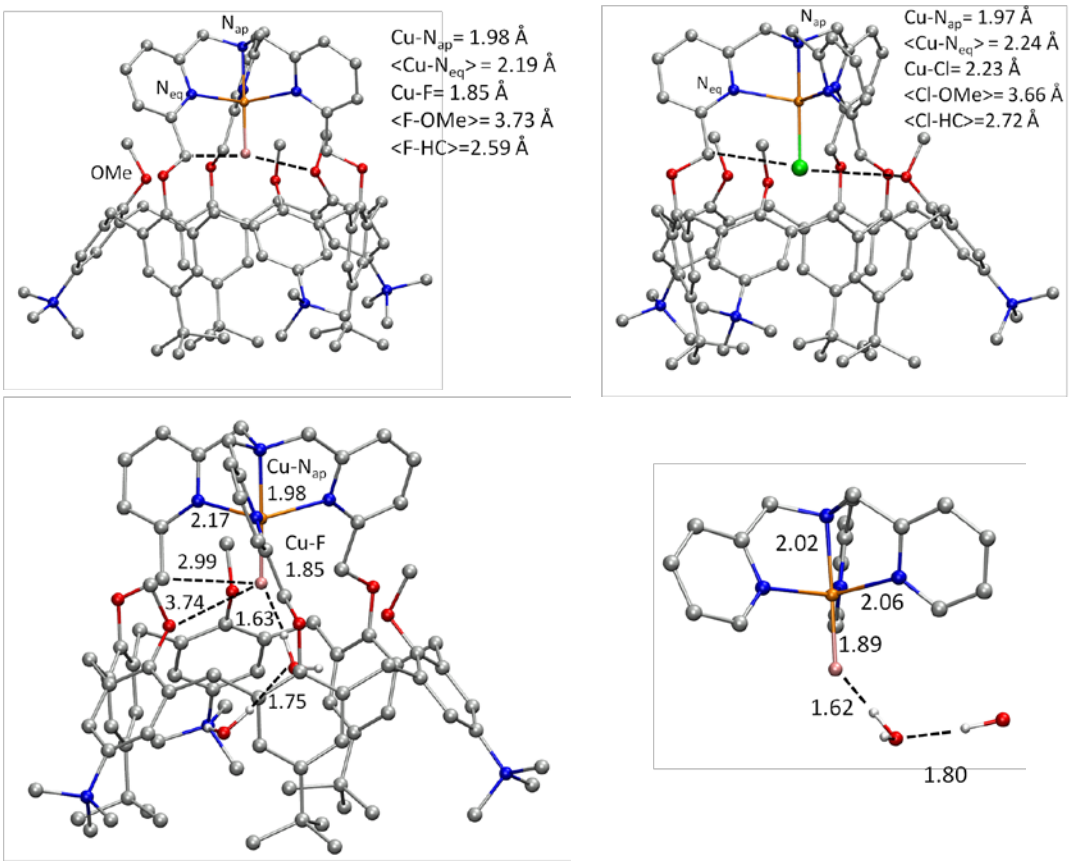


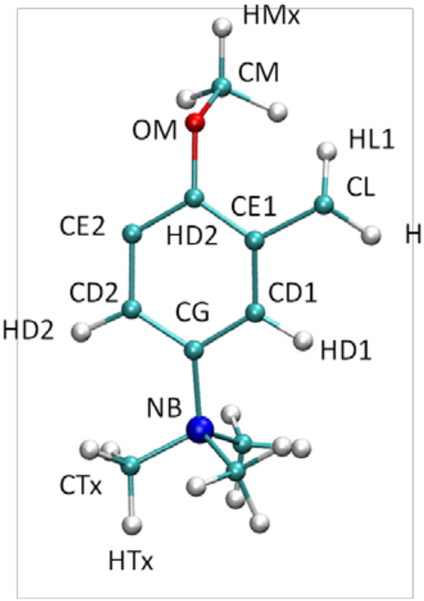
Figure S7: DFT optimized structures of the $[Cu^{II}(F)\mathbf{2}]^{4+}$ (top left), $[Cu^{II}(Cl)\mathbf{2}]^{4+}$ (top right), $[Cu^{II}(F{\cdot}H_2O{\cdot}H_2O)\mathbf{2}]^{4+}$ (bottom left) and $[Cu^{II}(F{\cdot}H_2O{\cdot}H_2O)\mathbf{3}]^{+}$ (bottom right) complexes. The calixarene hydrogen atoms are not shown for clarity. Color code: hydrogen in light grey, carbon in grey, oxygen in red, nitrogen in blue, copper in orange, fluorine in pink and chlorine in green. The distances are given in Å.

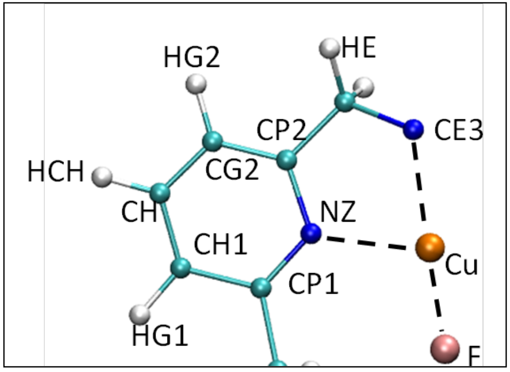
Table S2: Average interaction energies (in kJ mol^{-1}) calculated at the MM level (**AIE^{MM}**) along the MD simulations.

	F^-	CuTMPA	NMe_3^+	Cavity	Total
$(H_2O)_n$	−26.5	6.9	−2.0	−27.4	−48.9

Table S2: Partial charges of the MM force field
The charges have been calculated with the iterative Hirshfeld scheme usind the DFT optimized electronic density (see main text for details).

CG	0.1786	CG	0.1262
NB	0.3930	CB	0.3139
CT1	-0.4744	CT1	-0.5802
HTX	0.1946	HT1	0.1565
CT2	-0.4543	CT2	-0.5517
CT3	-0.4567	CT3	-0.5513
CD1	-0.3123	CD1	-0.2741
HD1	0.1624	HD1	0.1399
CE1	0.1293	CE1	0.8070
CL	-0.4010	CL	-0.3972
HL1	0.1479	HL1	0.1454
HL2	0.1614	HL2	0.1620
CD2	-0.3200	CD2	-0.2500
HD2	0.1693	HD2	0.1324
CE2	0.1254	CE2	0.8150
CZ	0.1990	CZ	0.1782
OM	-0.1619	OM	-0.1762
CM	-0.2400	CM	-0.2027
HMX	0.1205	HM1	0.1112
		HM2	0.1198
Cu	1.4357	NZ	-0.6163
F	-0.5990	CP1	0.4129
		CG1	-0.3103
Nitrates		CH	0.5640
N	1.0250	CP2	-0.3017
O	-0.6750	CG2	0.3950
		HG1	0.1693
		HCH	0.1472
		HG2	0.1778
		CE3	-0.3207
		HE	0.1589





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