Communication

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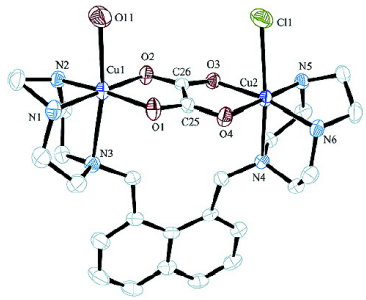

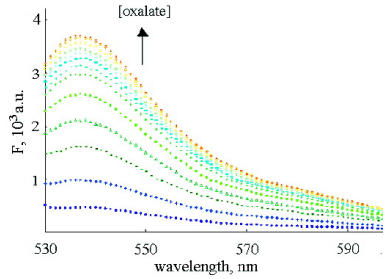

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Tight Binding and Fluorescent Sensing of Oxalate in Water

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Considerable efforts have been devoted to the selective sensing of anions because of the important roles that they play in various chemical and biological processes.[1] Fluorescent sensing of anions has become particularly attractive because of its simplicity and low detection limit.[1,2] Sensing of oxalate is useful in food chemistry and in clinical analysis. The level of oxalate in urine is an indicator of calcium oxalate kidney stones.[3] Current methods for oxalate detection such as colorimetry, liquid and gas chromatography, and capillary electrophoresis often require sample pretreatment and expensive equipment.[4] During the past decade, many artificial sensors for dicarboxylates have been developed.[5] However, very few examples of effective fluorescent sensors for oxalate have been reported to date.[6] In general, it is challenging to develop receptors that bind tightly, reversibly, and selectively to small molecules in water for sensing purposes.[7] In the case of oxalate, there are four oxygen atoms that can coordinate to metal ions. We reasoned that a couple of well-positioned metal complexes could cooperatively bind to all four oxygens of oxalate tightly, reversibly, and selectively over other dicarboxylates such as malonate, succinate, and glutarate. Here we report a dinuclear metal complex ($[Cu_2(1)Cl_4]$) that can be used for fluorescent detection of oxalate in water at physicological pH by a chemosensing ensemble approach.[8]

The ligand (**1**) and dinuclear Cu(II) complex $[Cu_2(\mathbf{1})]^{4+}$ were prepared according to the method previously described.[9] Figure 1 shows the crystal structure of oxalate bound to the dinuclear complex.[10] The two coppers in the structure are octahedral with oxalate bridging the two metal ions. One of the two chlorides has been replaced with a solvent water molecule. It is evident from the structure that oxalate fits nicely to the receptor forming a 1:1 complex.

To measure the equilibrium constant for the binding of oxalate to the dinuclear metal complex, a chemosensing ensemble approach with eosine Y was used. Upon the addition of $[Cu_2(\mathbf{1})]$ to a solution of eosine Y (1.0 μM) buffered at pH = 7.0 (50 mM HEPES), the fluorescence intensity of eosine Y (E-Y) sharply decreased and resulted in complete quenching of the emission above 150 equiv of $[Cu_2(\mathbf{1})]^{4+}$. Nonlinear least-squares fitting of the titration profiles indicated formation of a 1:1 complex with binding constant $K_s = (5.6 \pm 0.2) \times 10^4\ M^{-1}$ (Figure 1).[11]

The receptor−eosine pair was titrated by the indicator displacement method with some representative dicarboxylate anions: oxalate, malonate, succinate, and glutarate. In a typical experiment, increasing amounts of oxalate was added to a chemosensing ensemble solution containing E-Y (1.0×10^{-6} M) and $[Cu_2(\mathbf{1})]^{4+}$ (1.0×10^{-4} M) in a buffered solution at pH 7.0 (50 mM HEPES). A revival of the indicator fluorescence was observed upon addition

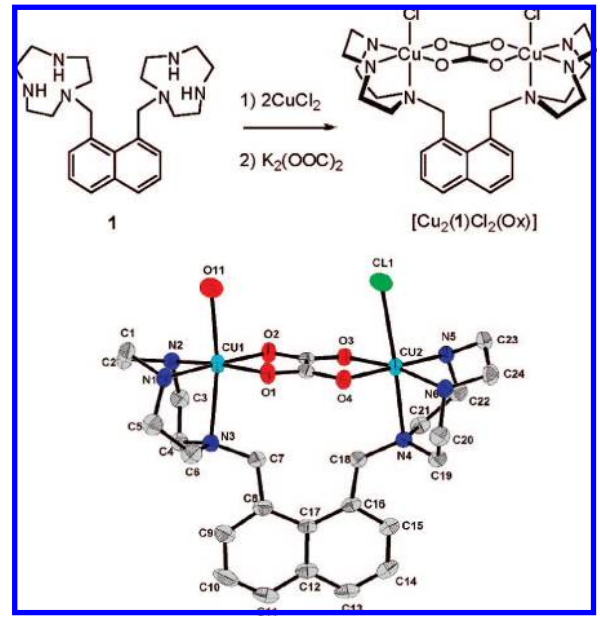

Figure 1. ORTEP plot of the crystal structure of $[Cu_2(\mathbf{1})Cl(Ox)(H_2O)]^+$. All hydrogen atoms are omitted. Selected bond lengths (Å): Cu(1)−O(1), 1.998(2); Cu(1)−O(2), 1.985(2); Cu(1)−O(11), 2.368(3); Cu(2)−O(3), 2.025(2); Cu(2)−O(4), 2.004(2); Cu(2)−N(5), 1.995(2); Cu(2)−N(6), 2.019(2); Cu(2)−N(4), 2.450(2); Cu(2)-C(l1), 2.702(1).

of oxalate. Figure 3 shows the increase in fluorescence of this chemosensing ensemble solution with increase in oxalate concentration. This result indicates the successful competitive binding of the oxalate ion and displacement of the indicator from the receptor. The binding constant for oxalate anion was measured to be $K_s = (1.3 \pm 0.1) \times 10^5\ M^{-1}$ by fitting the data with a competitive binding equilibria model (Figure 3).[11] The above method gave binding constants $K_s = (3.1 \pm 0.2) \times 10^4$, $(2.1 \pm 0.3) \times 10^3$, and $(6.9 \pm 1.2) \times 10^2\ M^{-1}$ for malonate, succinate, and glutarate, respectively. The receptor binds oxalate about 4-, 50-, and 200-fold more tightly than malonate, succinate, and glutarate, respectively. The equilibrium constant for binding of acetate to the receptor is too small to be measured accurately by the above method ($K_s < 10^2\ M^{-1}$). If the value of the binding constant of a dicarboxylate like oxalate is greater than the square of the binding of acetate, it could be reasoned that there is cooperativity for dicarboxylate binding.

The dinuclear copper complex represents a relatively simple receptor that binds tightly and selectively to oxalate over other dicarboxylates (malonate, succinate, glutarate). The two metal complexes in the crystal structure (Figure 1) appear to be ideally positioned for binding oxalate with an intermetal distance of about 5.2 Å. The parallel orientation of the two metal complexes is

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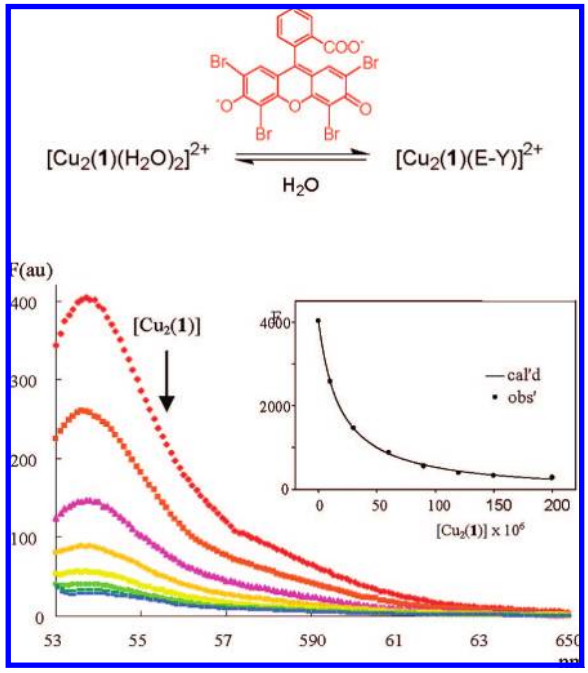

Figure 2. Fluorescence intensity of the indicator by titration with $[Cu_2(\mathbf{1})]^{4+}$. The concentration of E-Y is 1.0×10^{-6} M, all the aqueous solutions are buffered by HEPES (50 mM, pH = 7.0), exited at 524 nm; (inset) plot of F_{537nm} vs equiv of $[Cu_2(\mathbf{1})]^{4+}$.

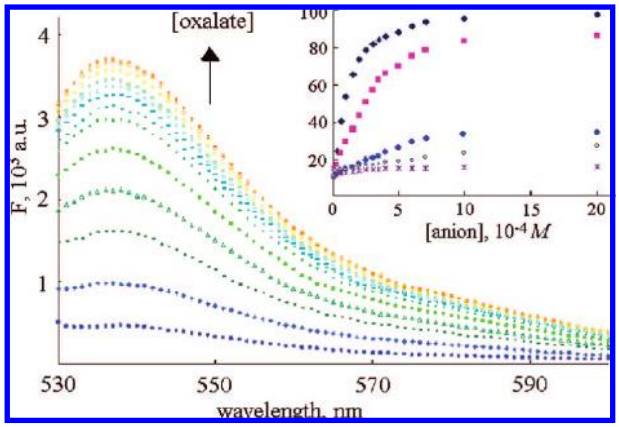

Figure 3. Competitive titration of an aqueous solution of E-Y (1.0×10^{-6} M) and $[Cu_2(\mathbf{1})]^{4+}$ (1.0×10^{-4} M) (pH 7.0, HEPES 0.05 M) with standard solution of oxalate. The inset is a plot of relative F_{537nm} vs concentrations for five anions: (◆) oxalate, (■) malonate, (•) succinate, (○) glutarate, (x) acetate.

suitable for coordinating the four oxygen atoms of oxalate. On the basis of inspection of the crystal structure, it is likely that less steric and ring strain are introduced upon binding of oxalate to the receptor than when other dicarboxylates are bound to the receptor. Indeed, molecular mechanics and DFT computations[12] show that the computed trend for binding of the four dicarboxylates to the receptor is in agreement with the experimental trend obtained by the fluorescence ensemble approach (oxalate > malonate > succinate > glutarate).

In summary, a dinuclear copper complex that binds tightly and selectively to oxalate over other dicarboxylates (malonate, succinate, glutarate) is reported. We developed a highly sensitive and selective fluorescence assay for sensing oxalate in water at neutral pH based on the receptor. Crystal structure of oxalate bound to the receptor together with molecular mechanics and DFT computations provide insights into the tight and selective binding of the anion by the receptor.

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Supporting Information Available: Experimental details for fluorescence assay, data for crystal structure in cif and computed structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Crystal data: monoclinic, $P2_1/c$ (No. 14), $Z = 4$, $a = 15.733(2)$ Å, $b = 14.372(2)$ Å, and $c = 13.662(2)$ Å, $\beta = 102.852(2)°$, $V = 3011.7(7)$ Å^3, $\mu = 1.640$ mm^{-1}, $d_{calcd} = 1.607$ g/cm^3, R1 = 3.57, wR2 = 9.61% for 5914 unique reflections and 395 variables with four restraints. All the X-ray data were collected on a Bruker SMART APEX CCD diffractometer using Mo Kα radiation ($\lambda = 0.71073$ Å). The structure was solved and refined using the SHELXTL program set (*SHELXTL*, version 5.10; Bruker AXS Inc.: Madison, WI, 1998).

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