Self-Assembling, Chromogenic Receptors for the Recognition of Dicarboxylic Acids

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Abstract: The synthesis of ligands (2,9-disubstituted phenanthrolines) bearing one or two acylaminopyridine binding sites, compounds **1** and **2** respectively, is described. Each ligand can assemble on a Cu(I) template, forming two different receptors for dicarboxylic acids, $Cu(\mathbf{1})_2^+BF_4^-$ and $Cu(\mathbf{2})_2^+BF_4^-$. These orange Cu(I) complexes are shown to bind ($K_a > 10^4\ M^{-1}$) to a variety of dicarboxylic acids in chloroform, with a slight preference for the C_5-dicarboxylic acids, glutaric and *N*-CBz-glutamic acids, over shorter and longer substrates. Complexation is analyzed both by NMR chemical shift changes and UV−visible absorption changes. The data indicate formation of 1:1 complexes for $Cu(\mathbf{1})_2^+BF_4^-$ and 2:1 complexes for $Cu(\mathbf{2})_2^+BF_4^-$, with the dicarboxylic acid substrate hydrogen bonding simultaneously to an acylaminopyridine binding site on each ligand. For $Cu(\mathbf{2})_2^+BF_4^-$, the complexation event results in large shifts in the visible absorption bands and a color change from orange to red. The change in the visible absorbance, and therefore the chromogenicity, was found to be substrate dependent. The chromogenic effect is explained by a conformational change in the receptors resulting from hydrogen bond formation with the substrate.

Introduction

The development of synthetic receptors for neutral molecules has been an area of active research in recent years.[1−9] These systems include complexes stabilized by hydrophobic interactions (e.g., cyclophanes[1]), $\pi-\pi$ stacking (e.g., "molecular tweezers" [4]), and hydrogen bonding.[2,3,5−9] The study of these complexes has contributed to an understanding of the relative strengths of the various forces involved in binding and a growing knowledge of the subtle design changes that can be used to effect substrate selectivity, including stereoselectivity.[10]

The success of these systems largely depends on the skills of the synthetic chemist, who must properly orient the binding groups of the receptor to complement those of the intended substrate. While there have been many notable successes using this approach, an alternative method can be envisioned in which a receptor self-assembles from smaller constituents. This strategy is commonly seen in biological receptors. For example, the dimerization of HIV protease is a prerequisite for its biological activity.[11] Self-assembly is defined here as two or more *separate* molecules coming together through noncovalent interactions to form the active receptor. Self-assembled receptors offer several advantages over traditional receptors. Smaller subunits are easier to synthesize than fully elaborated receptors. In addition, careful control over the self-assembly process can potentially lead to a large number of different receptors from the combination of just a few subunits. Moreover, self-assembly has the potential to provide access to large and complex receptors for the recognition of large structures (e.g., protein surfaces and DNA). To date there have been only a few reports involving the self-assembly of synthetic receptors.[12−14]

Ligand coordination to metals has been used extensively to assemble elaborate structures, including helices,[15−18] multicomponent photochemical devices,[19] and catenanes.[20] In addition,

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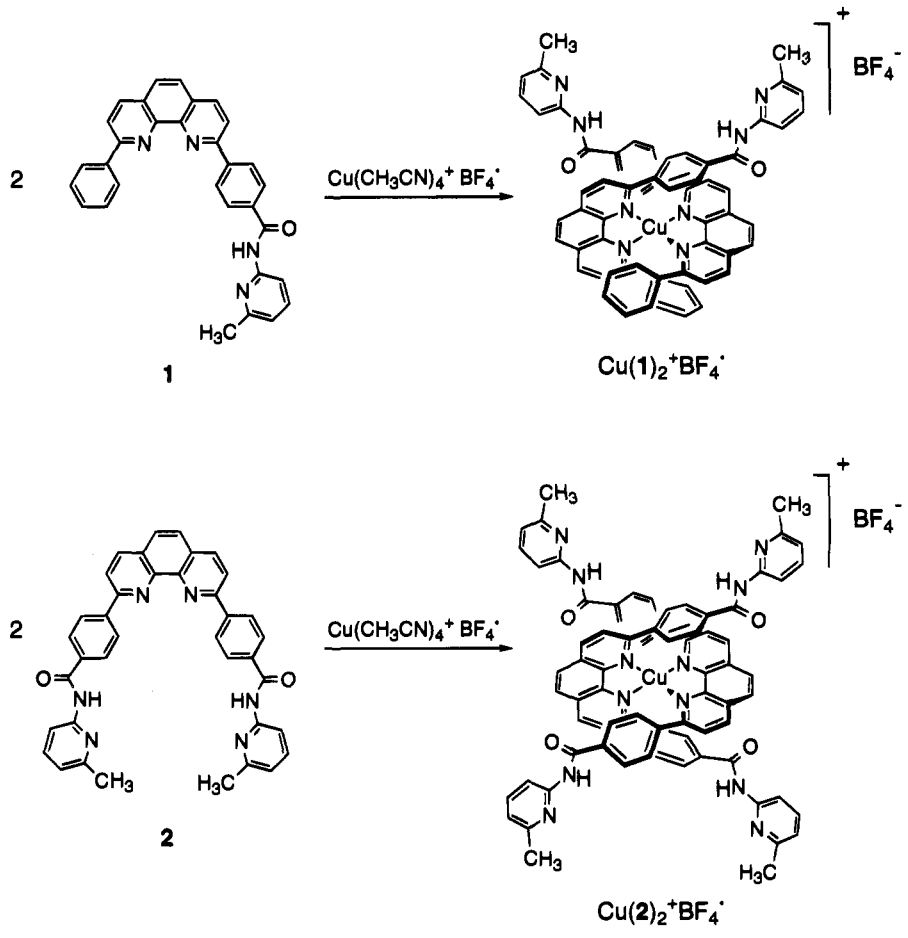
Scheme 1



receptors have been constructed in which metal binding to a coordination site on the receptor produces an allosteric effect on binding at another site.[21-23] The use of transition metals as templates for the assembly of artificial receptors has received little attention.[13,14,24] The idea at its simplest involves covalently linking a hydrogen bond recognition site to a potentially strong binding ligand for metal ions. Addition of an appropriate metal ion will then lead to chelation by two or more ligands and the resultant accumulation of several binding sites to create a functioning receptor. This concept has potential in the creation of biomimetic catalysts. For example, a metal-chelate receptor might be designed with open coordination sites for the purpose of metal ion catalyzed reactions on the bound substrate.[25] Metal ions also offer some other advantages. First, the coordination sphere around a metal can be chiral, so the potential for enantioselective binding (and reactions) exists. Also, the metal complex can be studied by a variety of techniques, such as ESR, NMR, UV-vis spectroscopy, and luminescence spectroscopy. The metal ion provides a sensitive probe for changes close to its coordination sphere.

In this paper,[26] we describe a self-assembling receptor for dicarboxylic acids (Scheme 1). The subunits consist of a 2-aminopyridine attached to a 2,9-disubstituted 1,10-phenanthroline (**1**). Addition of Cu(I) creates a complex with two acylaminopyridine moieties properly oriented for dicarboxylic acid binding. In addition, the receptor is chiral, which allowed us to investigate its enantioselective binding behavior. Extension of this concept to a bis(dicarboxylic acid) receptor (**2**) provided us with the first chromogenic receptor for dicarboxylic acids.

Results

Synthesis of 1 and $Cu(1)_2^+BF_4^-$. The receptor subunit **1** was synthesized as shown in Scheme 2. 1,10-Phenanthroline was converted into 2-phenyl-1,10-phenanthroline (**3**) by reaction with 1 equiv of phenyllithium followed by oxidation with activated MnO_2.[27] The product was then subjected to analogous conditions using *p*-tolyllithium followed by MnO_2 oxidation. This afforded 2-phenyl-9-tolyl-1,10-phenanthroline (**4**) in excel-

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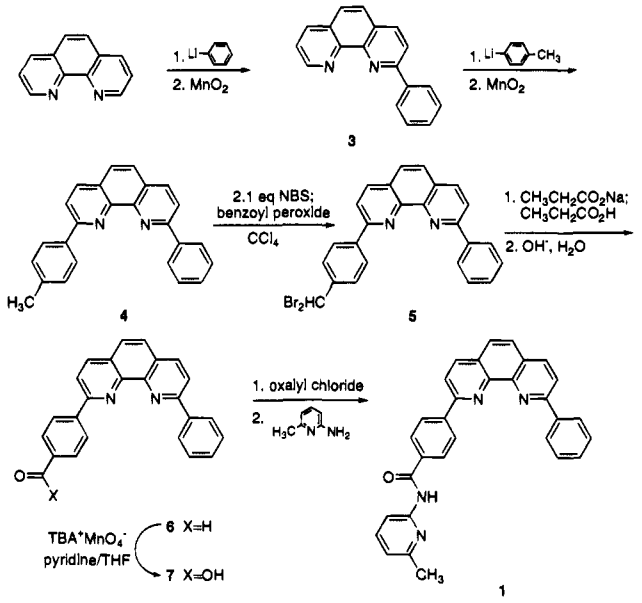
Scheme 2



lent overall yield. The initial synthetic strategy called for oxidation of the methyl group of **4** directly to the carboxylic acid (**7**) with tetrabutylammonium permanganate ($TBA^+MnO_4^-$). Several attempts were made, and in each case insoluble materials that were not the desired product were produced, presumably due to oxidation of the 5,6-double bond of the phenanthroline. This approach was abandoned for the stepwise method shown. Analogous to a previously reported synthesis,[28] aldehyde **6** was obtained by bromination of **4** (2.1 equiv NBS, CCl_4) to dibromo compound **5** followed by esterification with sodium propionate in refluxing propionic acid and then hydrolysis in basic solution. Aldehyde **6** was easily oxidized to **7** with a stoichiometric amount of $TBA^+MnO_4^-$ in pyridine/THF. The carboxylic acid was converted into the acid chloride with oxalyl chloride and then allowed to react with 2-amino-6-picoline to give compound **1**.

Compound **1** was converted by treatment with 0.5 equiv of $Cu(CH_3CN)_4^+BF_4^-$ in CH_3CN/CH_2Cl_2 to the dark red, air stable Cu(I) complex, which was easily purified by flash chromatography.

Complexation of 1 with Carboxylic Acids. The ability of compound **1** to form complexes with dicarboxylic acids in $CDCl_3$ was tested by standard NMR titrations.[29] Glutaric acid and **1** were found to form a 1:1 complex but with an association constant ($K_a = 2.7 \times 10^3\ M^{-1}$) somewhat higher than expected for one carboxylic acid–aminopyridine interaction, even when the statistical effect of having two identical carboxylic acid groups in the substrate is considered. The association constant for this type of interaction in $CDCl_3$ is normally about $2.0 \times 10^2\ M^{-1}$.[30] As a control experiment, a second titration was performed with propionic acid as the substrate. Propionic acid and **1** were shown to form a 1:1 complex with an association constant of $1.9 \times 10^2\ M^{-1}$, as expected. These results suggest that receptor **1** is capable of forming a bidentate interaction with glutaric acid as proposed in Figure 1. The receptor provides a strong binding site (2-acylaminopyridine) and a weaker binding site (1,10-phenanthroline) for carboxylic acids.

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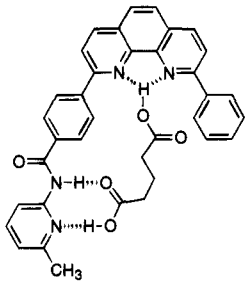


Figure 1. Proposed binding mode of **1** with glutaric acid.

Table 1. NMR-Derived Binding Constants for $Cu(\mathbf{1})_2^+BF_4^-$ with Dicarboxylic Acids

dicarboxylic acid	$K_a\ (M^{-1})$
glutaric acid	4.3×10^4
pimelic acid	1.6×10^4
diethylmalonic acid	4.8×10^3
1,3-phenylenediacetic acid	2.4×10^4
N-Cbz-glutamic acid	3.9×10^4

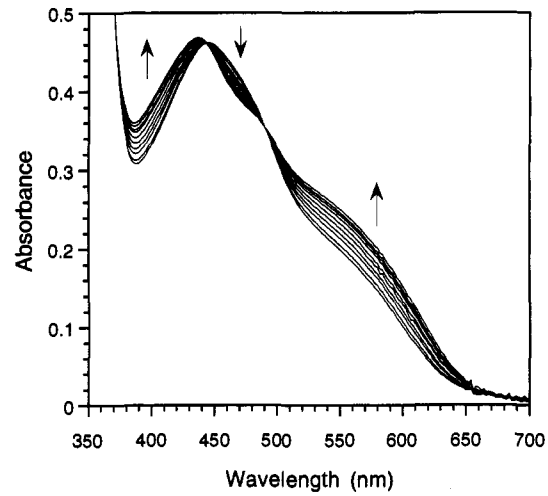


Figure 2. Change in the visible absorption spectrum of $Cu(\mathbf{1})_2^+BF_4^-$ upon addition of glutaric acid in $CHCl_3$. $[Cu(\mathbf{1})_2^+BF_4^-] = 0.125$ mM, [glutaric acid] = 0–0.40 mM.

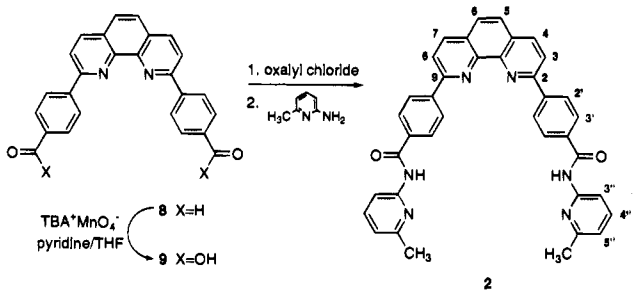
Complexation of $Cu(\mathbf{1})_2^+BF_4^-$ with Dicarboxylic Acids. The titration with glutaric acid is typical. Addition of small aliquots of glutaric acid to a 1.00 mM $CDCl_3$ solution of $Cu(\mathbf{1})_2^+BF_4^-$ resulted in chemical shift changes in all the protons of the receptor. The most pronounced changes occurred in the NH proton of the receptor which shifted downfield by 2.4 ppm, indicating strong hydrogen bond formation. Nonlinear regression analysis of the titration curve gave an association constant of approximately $4.3 \times 10^4\ M^{-1}$. This value is too high to be measured accurately by the NMR method but does show that the complexation is much stronger than for receptor **1** alone. Results for other dicarboxylic acids are tabulated in Table 1. The association constants are consistent with results from other dicarboxylic acid receptors in which two acylaminopyridines function as the binding groups. A modest preference for C_5-diacids was shown with shorter and longer substrates binding more weakly. In addition, the 1:1 stoichiometry for glutaric acid was confirmed by the method of Job.

A slight color change (red-orange → orange-red) had been noted in $Cu(\mathbf{1})_2^+BF_4^-$ solutions upon addition of dicarboxylic acids. Figure 2 shows the effect of glutaric acid on the UV–visible spectrum of $Cu(\mathbf{1})_2^+BF_4^-$. A slight blue shift occurs in the maximum, while an increase in the shoulder near the red edge is also seen. This change in the UV–visible spectrum could be used to conveniently study binding, since the lower

Table 2. UV−vis Binding Constants for $Cu(\mathbf{1})_2^+BF_4^-$ with Dicarboxylic Acids

dicarboxylic acid	K_a (M^{-1})	λ_{max} (nm) complex	% increase (λ = 550 nm)
glutaric acid	4.9×10^4	436	30
pimelic acid	1.5×10^4	440	15
1,3-phenylenediacetic acid	3.4×10^4	434	31
N-Cbz-glutamic acid	7.0×10^4	436	31

Scheme 3



concentrations used lead to a more accurate determination of the value of the association constant for a variety of dicarboxylic acids. The results are tabulated in Table 2, and are in good agreement with the NMR data reported in Table 1.

Also reported in Table 2 are the λ_{max} and the relative change in the absorptivity at 550 nm for each substrate/receptor combination. The changes in the absorption spectra are clearly substrate dependent. For example, complexation of pimelic acid results in a less pronounced increase in the shoulder near the red edge and a smaller blue shift in λ_{max} (for $Cu(\mathbf{1})^+BF_4^-$, λ_{max} = 445 nm) than complexation of the 5-carbon acids, glutaric and *N*-Cbz-glutamic. Remarkably, a lengthening of the dicarboxylic acid by only two carbon atoms results in half the change in absorptivity upon complexation. The isosbestic points for pimelic acid complexation are also significantly different from those of glutaric acid. This is a reflection of a difference in λ_{max} in the two complexes. The sensitivity of the absorption spectrum of the receptor on the substrate is unexpected and could be used in the design of chemoselective sensors.

Complexation of $Cu(\mathbf{1})_2^+BF_4^-$ with Chiral Dicarboxylic Acids. The Cu(I) templated receptor is a chiral molecule, reminiscent of chiral spirobifluorene, helicene, and binaphthyl receptors with C_2-symmetry investigated by ourselves[7] and others.[31] Addition of an optically pure dicarboxylic acid to a racemic mixture of $Cu(\mathbf{1})_2^+BF_4^-$ should result in the formation of two diastereomeric complexes. This was indeed found to be the case. Addition of *N*-Cbz-glutamic acid to a $CDCl_3$ solution of $Cu(\mathbf{1})_2^+BF_4^-$ resulted in the splitting of the receptor NMR peaks into two distinct sets of signals. It is not possible to assign the peaks to a specific stereoisomer of the receptor. It was possible, however, to perform an NMR titration and follow the formation of both complexes independently. The two sets of data that resulted were analyzed by curve fitting. The conclusion was that there is no significant stereoselectivity.

Synthesis of 2 and $Cu(\mathbf{2})_2^+BF_4^-$. The receptor **2** was synthesized analogously to receptor **1** (*vide supra*), as shown in Scheme 3. Dialdehyde **8** was prepared from 1,10-phenanthroline as previously described.[28] Compound **8** was carefully oxidized with $TBA^+MnO_4^-$ to the diacid **9**,[32] which was converted to the corresponding acid chloride with oxalyl chloride. Treatment of the acid chloride with 2 equiv of 2-amino-6-picoline afforded the desired bis(acylaminopyridine) receptor **2**.

Compound **2** was converted by treatment with 0.5 equiv of $Cu(CH_3CN)_4^+BF_4^-$ in CH_3CN/CH_2Cl_2 to the dark red, air stable Cu(I) complex, which was easily purified by chromatography.

Table 3. UV−vis and NMR Binding Constants for $Cu(\mathbf{2})_2^+BF_4^-$ with Dicarboxylic Acids

dicarboxylic acid	K_a (M^{-1}) UV−vis	K_a (M^{-1}) NMR
glutaric acid	7.8×10^4	7.1×10^4
pimelic acid	1.7×10^4	4.0×10^4
1,3-phenylenediacetic acid	3.5×10^4	
N-Cbz-glutamic acid	$\approx 4.0 \times 10^4$	

Complexation of Receptor 2 with Dicarboxylic Acids. Receptor **2** is a bis(acylaminopyridine) derivative and as such was expected to form strong bidentate interactions with dicarboxylic acids in chloroform. This was indeed the case, as **2** was found by NMR to bind glutaric acid with an association constant of 3.6×10^4 M^{-1}. Large changes in proton chemical shifts of **2** indicate that the dicarboxylic acid is hydrogen bonded simultaneously to both acylaminopyridines groups. Relatively large downfield shifts were observed in the H3″ of the aminopyridine ring ($\Delta\delta \sim 0.13$ ppm), the amide protons ($\Delta\delta \sim 2.4$ ppm), and H3′ of the phenyl rings ($\Delta\delta \sim 0.14$ ppm). The contribution of the phenanthroline to binding is uncertain, but it appears to play only a minor role; no protons on the phenanthroline ring shifted more than 0.01 ppm during the course of the titration.

Complexation of $Cu(\mathbf{2})_2^+BF_4^-$ with Dicarboxylic Acids. The Cu(I) complex of **2** was found to form strong complexes with various dicarboxylic acids in $CHCl_3$. The results are presented in Table 3. The stoichiometry of the complexes was 2:1 as determined by the concentration of dicarboxylic acid at which saturation of the receptor was found and independently determined by a Job's plot. Binding was most conveniently followed by UV−vis spectroscopy (ΔA_{550}) and was checked against NMR results for pimelic acid and glutaric acid. The binding data were analyzed by assuming that two independent and equal bidentate binding sites are interacting with the substrate. In this way a single association constant is obtained that represents the strength of binding of one of the receptor binding sites with one substrate.[33] This method resulted in very good fits to the data in most cases. An exception was *N*-Cbz-glutamic acid, which is understandable because there are several diastereomeric complexes present (*vide infra*), each with a different value of K_a.

In each of these cases, binding is accompanied by a distinct color change from orange to red. The change in the visible absorption spectrum of $Cu(\mathbf{2})_2^+BF_4^-$ in a typical titration with glutaric acid is shown in Figure 3. From comparison of Figure 2 with Figure 3, it is clear that the bisdicarboxylic acid receptor, $Cu(\mathbf{2})_2^+BF_4^-$, is more chromogenic than the monodicarboxylic acid receptor, $Cu(\mathbf{1})_2^+BF_4^-$. The relative change in A_{550} is 3−4 times greater for $Cu(\mathbf{2})_2^+BF_4^-$ than for $Cu(\mathbf{1})_2^+BF_4^-$. A summary of the spectral changes that occur upon complex

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(33) The association constants determined in this manner are the microscopic association constants (K_a). The macroscopic binding constants (K_1 and K_2) determined in terms of $Cu(\mathbf{2})_2^+BF_4^-$ concentration are subject to a statistical factor leading to $K_1 = 2K_a$, $K_2 = K_a/2$, and $K_1 = 4K_2$. The assumption that the two binding sites are independent is supported by the nonsigmoidal binding curves. The assumption is also made that each binding event results in the same incremental change in the observed parameter (δ_{NH} for NMR or A_{550} for UV−visible).

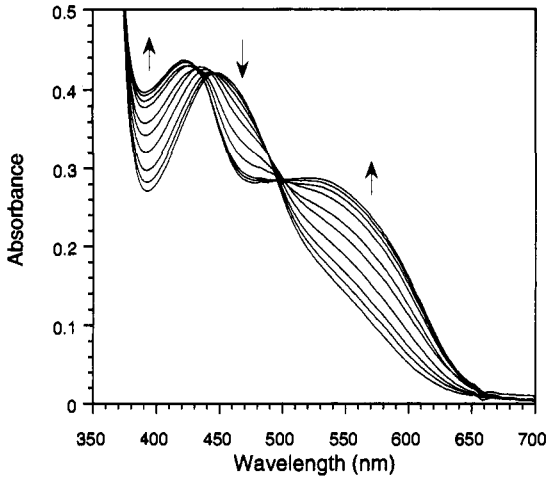

Figure 3. Change in the visible absorption spectrum of $Cu(\mathbf{2})_2^+BF_4^-$ upon addition of glutaric acid in $CHCl_3$. $[Cu(\mathbf{2})_2^+BF_4^-] = 0.106$ mM, [glutaric acid] = 0–0.50 mM.

Table 4. UV–vis Spectral Changes of $Cu(\mathbf{2})_2^+BF_4^-$ with Dicarboxylic Acids

dicarboxylic acid	λ_{max} (nm) 2:1 complex	% increase (λ = 550 nm)
glutaric acid	420, 518	101
pimelic acid	434	62
1,3-phenylenediacetic acid	422, 534	111
N-Cbz-glutamic acid	420, 526	105

formation is presented in Table 4. As with $Cu(\mathbf{1})_2^+BF_4^-$, there is some variation in the spectrum of the complex depending on which substrate is bound. Pimelic acid induced the smallest change in the spectrum and 1,3-phenylenediacetic acid caused the largest change.

Discussion

The results presented here show that the complexation of dicarboxylic acids can be achieved by organizing two "half receptors" around a metal atom. The mono(acylaminopyridine) **1** is a moderate receptor for dicarboxylic acids, due in part to a second, weaker interaction between one carboxylic acid moiety and the free phenanthroline nitrogens. Coordination of the phenanthroline subunit to Cu(I) affords the fully assembled receptor, which has been shown to bind strongly to different dicarboxylic acids. A similar effect is observed with the analogous receptor **2**, except that uncoordinated **2** is a good receptor for dicarboxylic acids due to the presence of two appropriately spaced acylaminopyridines.

The binding mode for these Cu(I) complexes to dicarboxylic acids was investigated by molecular modeling.[34] The uncoordinated receptor **2** was minimized using the Amber force field within the MacroModel program and manually coordinated to a Cu(I) atom, utilizing bond angles and lengths from the X-ray crystal structure of the similar bis(2,9-diphenyl-1,10-phenanthroline) Cu(I) complex.[35–37] The resulting model proved to be a useful representation of the structure of the metal complex. The model of the receptor/substrate complex between

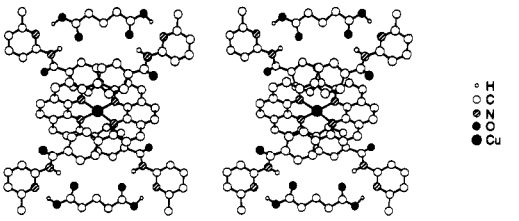

Figure 4. A stereoview of the molecular model of the 2:1 complex formed between glutaric acid and $Cu(\mathbf{2})_2^+$. Non-hydrogen bonded H atoms have been omitted for clarity.

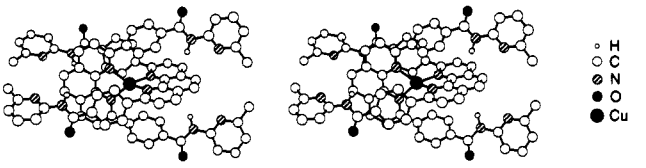

Figure 5. Computer generated structure of $Cu(\mathbf{2})_2^+$ in which the acylaminopyridines of the same ligand are oriented toward each other.

$Cu(\mathbf{2})_2^+BF_4^-$ and two glutaric acids is shown in Figure 4. The Cu(I) template allows the assembly of a recognition unit whose formation would otherwise be disfavored. The acylaminopyridine binding sites in this structure are well-oriented for forming strong hydrogen bonds to dicarboxylic acids. Hypothetical removal of the metal ion from this would lead to a large macrocyclic 2:2 complex.[38] A similar structure for the 1:1 complex between $Cu(\mathbf{1})_2^+BF_4^-$ and dicarboxylic acids is proposed.

An alternative binding mode for dicarboxylic acids with $Cu(\mathbf{2})_2^+BF_4^-$ needs to be considered. A hydrogen bonded catenate[20] structure can be envisioned in which a single dicarboxylic acid binds to two acylaminopyridines on the same ligand. This would result in a interlocking loop (catenate) structure for the 2:1 complex. Inspection of molecular models suggests that this type of complex is unlikely (Figure 5). When the acylaminopyridines are turned to face each other, the phenanthroline ring of the second ligand is positioned directly between the two binding groups, completely occupying the potential binding site. This strongly disfavors the binding of a dicarboxylic acid to two acylaminopyridines of the same ligand. Furthermore, an important comparison can be made to the dicarboxylic acid complex of $Cu(\mathbf{1})_2^+BF_4^-$, which can only form an interphenanthroline complex of the type shown in Figure 4. If an additional binding mode were operating in the $Cu(\mathbf{2})_2^+BF_4^-$ receptor and not in the $Cu(\mathbf{1})_2^+BF_4^-$ receptor, a significant difference in the respective binding strengths of the Cu(I) templated receptors with dicarboxylic acids would be expected. This was not observed, thus this binding mode was discounted based on modeling and experimental data.

In the binding mode proposed in Figure 4, the structure of the 2:1 complex of glutaric acid with $Cu(\mathbf{2})_2^+BF_4^-$ is chiral. It is important to note that the uncomplexed receptor is achiral and becomes chiral only upon complexation of the first dicarboxylic acid. For an achiral substrate this results in a racemic mixture of complexes. For an optically pure dicarboxylic acid such as *N*-Cbz-glutamic acid, the first substrate has a choice of enantiotopic binding sites, and the initially formed 1:1 complex therefore consists of two diastereomeric complexes. In addition, the initial binding event leaves an available binding site on the opposite face of the receptor that is no longer C_2-symmetric. Thus the second substrate can bind in two different orientations, so that there are four different

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(36) Burke, P. J.; Herrick, K.; McMillin, D. R. *Inorg. Chem.* **1982**, *21*, 1881.

(37) Klemens, F. K.; Palmer, C. E. A.; Rolland, S. M.; Fanwick, P. E.; McMillin, D. R.; Sauvage, J.-P. *New J. Chem.* **1990**, *14*, 129–133.

(38) For another hydrogen bonded macrocyclic 2:2 complex, see: Yang, J.; Fan, E.; Geib, S. J.; Hamilton, A. D. *J. Am. Chem. Soc.* **1993**, *115*, 5314–5315.

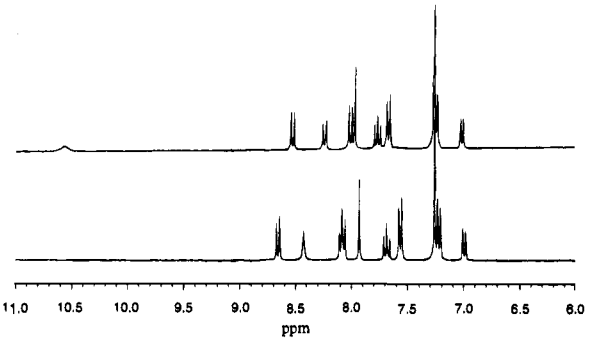

Figure 6. The ^{1}H NMR spectrum of Cu(**2**)$_2^+BF_4^-$ (1.00 mM) in $CDCl_3$ in the absence (bottom trace) and presence (top trace) of 2.00 mM glutaric acid.

diastereomeric 2:1 complexes formed. This greatly complicates the analysis of binding because six, possibly different, binding constants need to be evaluated. For this study, the assumption was made that all six association constants were equal. This resulted in adequate (but not perfect) fits to the titration data.

The NMR spectra of the complexes support the proposed binding model. An illustrative example of the changes that occur upon complexation is shown in Figure 6. The chemical shifts of Cu(**2**)$_2^+BF_4^-$ receptor/glutaric acid complex are substantially different from those of the unbound receptor. The most important change occurs in the chemical shift of the NH proton of the receptor, which shifts downfield from 8.4 to 10.6 ppm. This shift is strongly indicative of hydrogen bond formation between the NH proton of the acylaminopyridine group of the receptor and the carbonyl oxygen of the dicarboxylic acids. The aromatic protons of the pyridine rings and the adjacent H3′ protons of the phenyl groups all display downfield shifts ($\Delta\delta$ = 0.02−0.19 ppm). Another notable feature of this system is the upfield shifts in H3 (δ = 8.07 ppm, $\Delta\delta$ = −0.10 ppm) and H4 (δ = 8.66 ppm, $\Delta\delta$ = −0.17 ppm) of the phenanthroline groups and the downfield shift of H2′ (δ = 7.56 ppm, $\Delta\delta$ = 0.20 ppm) of the phenyl groups of the receptor. Because these protons are remote from the aminopyridine binding site, the shifts are not likely to be the result of a decrease in the electron density of the ligand induced by dicarboxylic acid binding but rather reflect a change in the overall structure of the receptor upon complexation.[35] In support of this, the uncoordinated ligand **2** shows similar changes in the aminopyridine portion of the molecule upon complexation but displays almost no changes in the chemical shifts of the phenanthroline protons.

Complexes of dicarboxylic acids with Cu(I) templated receptors have significantly different UV−vis spectra than the uncomplexed receptors. The origin of the chromogenic effect is still unclear, but it is a direct result of the bidentate binding of dicarboxylic acids to the receptors and does not involve proton transfer or ill-defined solvation effects. Addition of large excesses of monocarboxylic acids (acetic or trifluoroacetic) to a $CHCl_3$ solution of either Cu(**1**)$_2^+BF_4^-$ or Cu(**2**)$_2^+BF_4^-$ leads to only minor changes in the absorption spectrum. Furthermore, the addition of small amounts of ethanol (which would be expected to disrupt the hydrogen bonded complex) to the 2:1 glutaric acid/Cu(**2**)$_2^+BF_4^-$ complex in $CHCl_3$ resulted in a complete reversion to the uncomplexed spectrum.

The visible absorption spectra displayed in Figure 7 show the chromogenic effect in more detail. The absorption spectrum of these complexes are typical for Cu(I) complexes of 2,9-diaryl phenanthrolines.[39-41] They exhibit broad MLCT bands in the

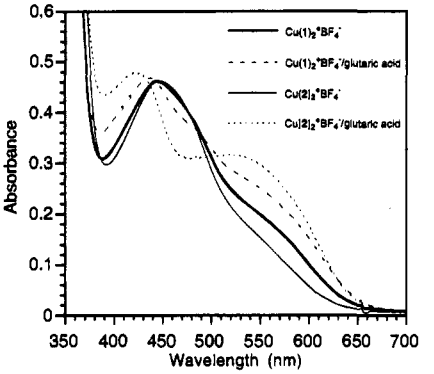

Figure 7. Comparison of the visible spectrum (in $CHCl_3$) of both Cu(I)-based receptors before and after complexation with glutaric acid.

visible region, with a maximum near 440 nm and shoulder near 530 nm. It is clear that the long wavelength shoulder of the Cu(I) templated receptors becomes more pronounced as substrate is added. The shoulder for Cu(**2**)$_2^+BF_4^-$ is weaker before and more intense after complex formation than the shoulder for Cu(**1**)$_2^+BF_4^-$. This corresponds to an overall absorbance change in that region that is approximately three times greater for the Cu(**2**)$_2^+BF_4^-$ complex. This translates into a markedly more intense color change for the Cu(**2**)$_2^+BF_4^-$ receptor than for the Cu(**1**)$_2^+BF_4^-$ receptor upon substrate binding. Complexation of 1 equiv of glutaric acid with Cu(**1**)$_2^+BF_4^-$ in $CHCl_3$ results in a barely discernible color change from red-orange to orange-red. A similar experiment with 2 equiv of glutaric acid and Cu(**2**)$_2^+BF_4^-$ results in an obvious color change from bright orange to bright red.

The color change upon complexation is unlikely to be caused by simple electronic effects related to the hydrogen bonding interaction. If this were the case, the addition of both monocarboxylic acids and dicarboxylic acids would result in similar color changes in the absorbance spectra of the receptors. A change in the geometry of the receptors is a more probable cause of the observed color changes. Two general types of geometrical changes can occur upon complexation to accommodate the substrate; one in which the sidearms of the phenanthrolines pinch together decreasing the dihedral angle between the planes of the phenanthrolines and another in which bonds in the sidearms rotate relative to the phenanthroline.

Distortion of the pseudotetrahedral coordination sphere around Cu(I) to a lower symmetry structure is a possible explanation for the chromogenic effect. Complexes of Cu(I) with 2,9-diarylphenanthrolines exhibit significant distortions from D_{2d} symmetry in the solid state and in solution.[37,40] This results in the splitting of the MLCT bands and the appearance of the long wavelength shoulder. A further distortion of the coordination geometry induced by substrate binding would be expected to induce further splitting of the MLCT band. Indeed, a blue shift in the 440 nm band does occur, but the 530 nm shoulder does not shift but instead increases in intensity. In addition, this explanation for the chromogenicity can be partially discounted as it would not adequately explain the greater color change for the 2:1 dicarboxylic acid/Cu(**2**)$_2^+BF_4^-$ complex compared to the 1:1 dicarboxylic acid/Cu(**1**)$_2^+BF_4^-$ complex. It would predict that the main distortion should occur during the initial binding event, with the second dicarboxylic acid producing only minor additional distortion of the coordination sphere.

Bond rotations in the receptor to properly orient the dicarboxylic acid binding sites are the most likely explanation for

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(41) Phifer, C. C.; McMillin, D. R. *Inorg. Chem.* **1986**, *25*, 1329−1333.

the observed chromogenic effect. Among the freely rotating bonds in the sidearms of the receptors, the bond between the phenyl ring and the phenanthroline would have a large influence on the electron density in the phenanthroline rings. Such a rotation would reduce the conjugation of the benzoylaminopyridine group with the phenanthroline, in turn increasing its electron density. This also explains the substrate dependence of the chromogenic effect. A longer, more flexible substrate such as pimelic acid is able to hydrogen bond to the acylaminopyridines without causing a large conformational change in the receptor. This would lead to a relatively smaller change in the visible absorption spectrum.

Support for this model is provided by a detailed analysis of the ^{1}H NMR shifts that occur on diacid binding. Conversion of compound **2** into Cu(**2**)$_2^+BF_4^-$ results in an upfield shift of 1.05 ppm for H2′ and 0.96 ppm for H3′ of the phenyl rings. This is consistent with a phenyl−phenanthroline torsional angle (ϕ) of 50° when compared to calculated ring-current induced shifts.[35] In this model of the uncomplexed receptor, the largest upfield shifts would occur when $\phi = 0°$ and H2′ and H3′ are forced into the face of the π-system of the second phenanthroline.[42] Titration of Cu(**2**)$_2^+BF_4^-$ with glutaric acid results in a downfield shift of H2′ by 0.20 ppm. This suggests that glutaric acid binding causes the phenyl−phenanthroline angle to become more perpendicular ($\phi > 50°$). In contrast the downfield shift of the phenyl−H2′ is smaller (0.11 ppm) on binding pimelic acid, consistent with a smaller distortion of the conformation.[43] A distortion of the Cu(I) tetrahedral symmetry caused by a decrease in the relative angle of the two phenanthroline rings on substrate binding is unlikely. This type of conformational change would bring the phenyl groups closer to phenanthroline π-systems and would be expected to lead to an upfield shift of H2′ on diacid binding.

Previous studies[39] have shown that cooling the Cu(I) complex of 2,9-diphenylphenanthroline to 90 K results in an increase in the intensity of the longer wavelength shoulder relative to the shorter wavelength peak in the MLCT band. This effect was attributed to fixing the complex in a low energy geometry, causing a narrowing of the angular distribution of the phenyl groups at lower temperatures. This result suggests that a partial freezing of the bond rotation between the phenyl ring and the phenanthroline ring induced by substrate binding might be responsible for the observed increase in the intensity of the long wavelength charge transfer band in the present study. Longer, more flexible substrates would tend to allow more rotation about the phenyl−phenanthroline bond, leading to smaller absorbance changes.

Conclusion

The Cu(I) complexes of **1** and **2** bind dicarboxylic acids with high binding constants ($K_a = 0.5 - 8 \times 10^4$ M^{-1}) in $CHCl_3$. The binding was followed by NMR and, more conveniently, by UV−vis spectroscopy. The variations in the absorption spectrum are particularly interesting in that they are large enough to be easily seen as a color changes, especially for the complexes of Cu(**2**)$_2^+BF_4^-$. This chromogenic effect was also substrate dependent, with pimelic acid consistently producing the smallest effects. This system could serve as a basis for a chemoselective sensor for biologically important dicarboxylic acids (e.g., glutamic acid).

The system described in this paper is also an example of how self-assembly can be used to generate a fully active receptor from lesser components. Extensions of these concepts to other transition metals, coordinating units, and substrate binding sites are in progress.

Experimental Section

General Methods. Dichloromethane was obtained from Fisher and distilled from calcium hydride. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were obtained from Fisher and distilled from sodium benzophenone ketyl. Toluene was distilled from Na. Pyridine was distilled from KOH pellets. $TBA^+MnO_4^-$ [44] and $Cu(CH_3CN)_4^+BF_4^-$ [45] were prepared according to the literature. 2-Amino-6-picoline (Aldrich) was recrystallized from ethyl acetate. Chloroform used in titrations was passed through a column of activated neutral alumina before use. All other reagents, unless otherwise noted, were obtained from the Aldrich Chemical Company and used without further purification.

^{1}H NMR and ^{13}C NMR spectra were recorded on either a Bruker AM-300 or AM-500. NMR chemical shifts are reported in ppm downfield from internal TMS. Mass spectra were determined at the Department of Chemistry, University of Pittsburgh. EI and FAB mass spectra (MS) were obtained using a Varian MAT CH-5 or VG 7070 mass spectrometer. Melting points (mp) were determined using an electrothermal capillary melting point apparatus and are uncorrected. Ultraviolet/visible (UV−vis) spectra were recorded using a Hewlett Packard 8452A photodiode array spectrophotometer. Elemental analysis was carried out by Atlantic Microlab, Inc., Norcross, GA.

Analytical thin layer chromatography (TLC) was conducted using PolyGram 0.25 mm silica gel precoated plates with fluorescent indicator UV_{245}. Silica gel 60 silica (particle size 0.063−0.200 mm, 70−230 mesh ASTM) (EM Science) was used for flash chromatography.

2-Phenyl-1,10-phenanthroline (3). A 1.55 M solution of phenyllithium (21.8 mL, 33.8 mmol) in cyclohexane/ether (70:30) was added at 0 °C to a stirred solution of 1,10-phenanthroline (5.00 g, 27.7 mmol) in ether (300 mL) under argon. The reaction was allowed to proceed for 2 h then was carefully quenched with ice water (80 mL). The organic layer was separated, and the remaining aqueous layer was extracted with CH_2Cl_2 (2 × 150 mL). The combined organic layers were dried (Na_2SO_4) and evaporated to a volume of 300 mL under reduced pressure. The solution of crude product was oxidized by stirring with activated MnO_2 (25 g). An additional portion of MnO_2 (25 g) was added to the reaction after 1 h to ensure complete oxidation. After a total of 2 h, anhydrous $MgSO_4$ (40 g) was added, and the mixture was filtered. The $MnO_2/MgSO_4$ was washed with CH_2Cl_2 (300 mL), and the solvent was concentrated to a yellow, oily solid. Toluene (10 mL) was added, and the solution was cooled in the freezer. The light yellow crystals of product were filtered and dried: yield 5.71 g (80%); mp 141−144 °C; ^{1}H NMR ($CDCl_3$) δ 9.23 (dd, J = 4.4, 1.7 Hz, 1H), 8.33 (d, J = 7.8 Hz, 2H), 8.28 (d, J = 8.3 Hz, 1H), 8.24 (dd, J = 8.0, 1.7 Hz, 1H), 8.08 (d, J = 8.3 Hz, 1H), 7.77 (AB, J = 8.8 Hz, 2H), 7.62 (dd, J = 8.2, 4.4 Hz, 1H), 7.54 (t, J = 7.4 Hz, 2H), 7.46 (t, J = 7.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) 150.4, 136.8, 136.1, 129.3, 128.7, 127.9, 126.4, 126.2, 122.8, 120.6; EIMS *m/z* (rel intensity) 256 (100, M$^+$); HRMS *m/e* for $C_{18}H_{12}N_2$ calcd 256.1000, obsd 256.1000. Anal. Calcd for $C_{18}H_{12}N_2$: C, 84.35; H, 4.72; N, 10.93. Found: C, 84.27; H, 4.73; N, 10.91.

2-Phenyl-9-*p*-tolyl-1,10-phenanthroline (4). *p*-Iodotoluene (6.12 g, 28.1 mmol) was dissolved in ether (50 mL) and cooled to −78 °C under argon. A 1.7 M solution of *tert*-butyllithium (33.0 mL, 56.0 mmol) was added dropwise over 15 min with stirring. The solution of *p*-tolyllithium was allowed to warm to 0 °C for 40 min and then to room temperature for 20 min. The solution of *p*-tolyllithium was added via cannula to a stirred suspension of **3** (5.71 g, 22.3 mmol) in toluene (50 mL) at 0 °C. The dark red reaction mixture was held at 0 °C for 2 h and then carefully quenched with water (80 mL). The organic layer was separated, and the remaining aqueous layer was extracted with CH_2Cl_2 (2 × 150 mL). The combined organic layers were dried (Na_2SO_4) and evaporated to a volume of 200 mL under reduced

(42) This discussion is based on the calculated ring current effects on proton chemical shifts as a function of distance and angle from the center of an aromatic ring as described previously. Abraham, R. J.; Bedford, G. R.; McNeillie, D.; Wright, B. *Org. Magn. Reson.* **1980**, *14*, 418.

(43) Similar, although smaller, effects are seen with the phenyl−H3′ protons.

(44) Sala, T.; Sargent, M. V. *J. Chem. Soc., Chem. Commun.* **1978**, 253−254.

(45) Kubas, G. J. *Inorg. Synth.* **1979**, *19*, 90−92.

pressure. The solution of crude product was oxidized by stirring with activated MnO_2 (20 g). An additional portion of MnO_2 (10 g) was added to the reaction after 1.5 h to ensure complete oxidation. After a total of 2.5 h, anhydrous $MgSO_4$ (30 g) was added, and the mixture was filtered. The $MnO_2/MgSO_4$ was washed with CH_2Cl_2 (250 mL), and the solvent was concentrated to a volume of 15 mL. The product was precipitated with ether/hexanes (1:1, 25 mL), cooled in the freezer, and filtered. The light yellow product was washed with a small amount of cold ether/hexanes (1:2) and dried: yield 6.67 g (86%); mp 133–135 °C; ^{1}H NMR ($CDCl_3$) δ 8.47 (d, J = 7.4 Hz, 2H), 8.38 (d, J = 8.2 Hz, 2H), 8.31 (d, J = 8.4 Hz, 1H), 8.29 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 8.4 Hz, 1H), 7.78 (s, 2H), 7.59 (t, J = 7.4 Hz, 2H), 7.49 (t, J = 7.3 Hz, 1H), 7.40 (d, J = 8.0 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$) 156.7, 156.6, 146.0, 139.4, 136.8, 136.7, 136.6, 129.5, 129.3, 128.8, 127.8, 127.7, 127.6, 127.5, 126.0, 125.7, 119.8, 119.7, 21.4; EIMS *m/z* (rel intensity) 346 (100, M^+); HRMS *m/e* for $C_{25}H_{18}N_2$ calcd 346.1470, obsd 346.1475. Anal. Calcd for $C_{18}H_{12}N_2$: C, 86.68; H, 5.24; N, 8.09. Found: C, 86.63; H, 5.29; N, 8.09.

2-(4-Dibromomethylphenyl)-9-phenyl-1,10-phenanthroline (5). A mixture of **3** (3.00 g, 8.66 mmol), NBS (3.30 g, 18.5 mmol), and benzoyl peroxide (0.20 g, 0.83 mmol) in CCl_4 (250 mL) was heated at reflux for 8 h. The mixture was cooled and washed with water (2 × 100 mL). The solution was dried (Na_2SO_4) and evaporated to give a yellow foam. The crude material was ~90% pure by NMR and could be further purified by trituration with hot toluene (50 mL) followed by precipitation with acetone (50 mL): yield 2.00 g (46%); mp 170–185 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.45 (d, J = 7.6 Hz, 4H), 8.33 (d, J = 8.4 Hz, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.16 (d, J = 8.4 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.81 (s, 2H), 7.79 (d, J = 8.0 Hz, 2H), 7.60 (t, J = 7.5 Hz, 2H), 7.49 (t, J = 7.2 Hz, 1H), 6.76 (s, 1H); ^{13}C NMR (10% $CD_3OD/CDCl_3$) 155.9, 155.1, 144.0, 142.9, 139.4, 138.9, 137.7, 133.8, 131.8, 129.5, 128.8, 128.4, 128.2, 128.1, 127.7, 127.3, 126.1, 123.3, 123.2, 39.8; EIMS *m/z* (rel intensity) 506 (10, M^+), 504 (20, M^+), 502 (10, M^+), 425 (25), 423 (25), 360 (100); HRMS *m/e* for $C_{25}H_{16}N_2{}^{81}Br$ (M^+ − Br) calcd 425.0476, obsd 425.0419; *m/e* for $C_{25}H_{16}N_2{}^{79}Br$ (M^+ − Br) calcd 423.0497, obsd 423.0489.

4-(9-Phenyl-1,10-phenanthrolin-2-yl)benzaldehyde (6). Compound **5** (1.96 g, 3.89 mmol) and powdered NaOH (0.47 g, 11.7 mmol) were heated at reflux in propionic acid (25 mL) for 6 h under argon. Propionic acid was evaporated under reduced pressure and replaced with THF (25 mL) and 2 M NaOH (5 mL). The solution was stirred for 1 h, and then the THF was evaporated. Water (20 mL) was added, and the pH was adjusted to ~8 with HCl. The solution was extracted with CH_2Cl_2 (3 × 100 mL). The combined extracts were dried (Na_2SO_4) and evaporated to give a yellow foam. The crude material was ~90% pure by NMR and could be further purified by trituration with toluene (2 × 25 mL) to give **6** as a foamy, amorphous solid: yield 1.05 g (75%); mp 75–85 °C; ^{1}H NMR ($CDCl_3$) δ 10.14 (s, 1H), 8.64 (d, J = 8.1 Hz, 2H), 8.46 (d, J = 8.4 Hz, 2H), 8.38 (d, J = 8.4 Hz, 1H), 8.35 (d, J = 8.7 Hz, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.18 (d, J = 8.1 Hz, 1H), 8.11 (d, J = 8.1 Hz, 2H), 7.84 (AB, J = 8.7 Hz, 2H), 7.62 (t, J = 7.5 Hz, 2H), 7.51 (t, J = 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) 192.1, 157.0, 155.0, 146.2, 146.0, 144.9, 139.2, 137.1, 137.0, 136.6, 130.2, 129.6, 128.8, 128.4, 128.1, 127.9, 127.6, 126.8, 125.8, 120.2; EIMS *m/z* (rel intensity) 360 (80, M^+), 331 (40); HRMS *m/e* for $C_{25}H_{16}N_2O$ calcd 360.1263, obsd 360.1245.

4-(9-Phenyl-1,10-phenanthrolin-2-yl)benzoic Acid (7). A solution of $TBA^+MnO_4^-$ (340 mg, 0.941 mmol) in pyridine (8 mL) was added dropwise over 30 min to aldehyde **6** (0.50 g, 1.4 mmol) dissolved in pyridine (4 mL). The reaction was stirred for an additional hour. The solution was concentrated to ~4 mL under reduced pressure and then poured into a solution of Na_2SO_3 (400 mg) in 2 N HCl (50 mL). The mixture was stirred 2 h, the precipitate was filtered, and the solid product was rinsed with water (20 mL). The material was dried *in vacuo* and used in the next step without further purification: yield 320 mg (62%); ^{1}H NMR (DMSO-d_6) δ 8.65 (d, J = 8.0 Hz, 1H), 8.63 (d, J = 8.3 Hz, 3H), 8.51 (d, J = 7.5 Hz, 2H), 8.49 (d, J = 8.2 Hz, 1H), 8.44 (d, J = 8.5 Hz, 1H), 8.18 (d, J = 8.2 Hz, 2H), 8.05 (s, 2H), 7.64 (t, J = 7.4 Hz, 2H), 7.55 (t, J = 7.1 Hz, 1H); ^{13}C NMR (DMSO-d_6) 167.1, 155.4, 154.3, 144.9, 144.8, 142.6, 138.4, 137.9, 137.8, 131.5, 130.0, 129.8, 129.0, 128.3, 127.9, 127.4, 126.7, 126.3, 120.6, 120.4.

***N*-(6-Methylpyridin-2-yl)-4-(9-phenyl-1,10-phenanthrolin-2-yl)-benzamide (1).** A suspension of **7** (300 mg, 0.80 mmol) in CH_2Cl_2 (10 mL) was treated with oxalyl chloride (200 μL, 2.3 mmol) and heated at reflux under argon. After 2 h, more oxalyl chloride (200 μL) was added, and refluxing was continued for an additional 2 h. The greenish suspension was cooled, and the volatiles were removed under reduced pressure. The crude acid chloride was dried overnight under vacuum. A solution of 2-amino-6-picoline (90 mg, 0.83 mmol) in CH_2Cl_2 (20 mL) was added to the acid chloride. The resulting homogeneous reaction mixture was stirred for 24 h under a drying tube. The reaction was quenched with saturated $NaHCO_3$ (25 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL), and the combined organic layers were dried (Na_2SO_4) and evaporated to a yellow foam. The material was purified by flash chromatography (silica gel, 1–3% MeOH/CH_2Cl_2): yield 200 mg (54%) of light yellow solid; mp 219–221 °C; ^{1}H NMR ($CDCl_3$) δ 8.70 (br, 1H), 8.60 (d, J = 8.5 Hz, 2H), 8.46 (d, J = 8.5 Hz, 2H), 8.36 (d, J = 8.4 Hz, 1H), 8.33 (d, J = 8.7 Hz, 1H), 8.25 (d, J = 8.3 Hz, 1H), 8.20 (d, J = 8.3 Hz, 1H), 8.17 (d, J = 8.3 Hz, 1H), 8.16 (d J = 8.4 Hz, 2H), 7.82 (AB, J = 8.8 Hz, 2H), 7.68 (t, J = 7.9 Hz, 1H), 7.61 (t, J = 7.3 Hz, 2H), 7.52 (t, J = 7.2 Hz, 1H), 6.96 (d, J = 7.4 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR ($CDCl_3$) 165.2, 157.0, 156.9, 155.2, 150.8, 146.2, 146.0, 143.0, 139.3, 138.8, 137.1, 137.0, 134.7, 129.6, 128.9, 128.3, 128.0, 127.8, 127.6, 126.6, 125.9, 123.8, 120.2, 120.1, 119.5, 111.0, 24.1; EIMS *m/z* (rel intensity) 466 (80, M^+), 359 (100), 331 (95); HRMS *m/e* for $C_{31}H_{22}N_4O$ calcd 466.1794, obsd 466.1782.

Receptor $Cu(1)_2^+BF_4^-$. Compound **1** (100 mg, 0.21 mmol) was dissolved in CH_2Cl_2 (10 mL) under argon. A solution of $Cu(CH_3CN)_4BF_4^-$ (34 mg, 0.11 mmol) in CH_3CN (4 mL) was added slowly via syringe. The resulting dark red solution was stirred for 30 min and evaporated. The crude Cu(I) complex was purified by flash chromatography (silica gel, 5% MeOH/CH_2Cl_2): yield 92 mg (79%) of dark purple solid; mp 158–168 °C dec; ^{1}H NMR ($CDCl_3$) δ 8.60 (d, J = 8.4 Hz, 1H), 8.58 (d, J = 8.4 Hz, 1H), 8.41 (br, 1H), 8.07 (d, J = 8.2 Hz, 1H), 7.99 (d, J = 8.3 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.96 (s, 2H), 7.68 (t, J = 7.9 Hz, 1H), 7.49 (d, J = 7.4 Hz, 2H), 7.45 (d, J = 8.3 Hz, 2H), 7.11 (d, J = 8.2 Hz, 2H), 6.99 (d, J = 7.4 Hz, 1H), 6.89 (t, J = 7.5 Hz, 1H), 6.64 (t, J = 7.8 Hz, 2H), 2.66 (s, 3H); ^{13}C NMR ($CDCl_3$) 163.9, 157.1, 156.9, 155.5, 150.3, 143.5, 143.3, 142.3, 138.9, 138.6, 138.1, 137.8, 133.9, 129.1, 128.6, 128.3, 127.9, 127.5, 127.0, 126.6, 126.1, 125.2, 125.0, 119.8, 111.0, 24.0; UV–vis ($CHCl_3$) [λ, nm (ϵ, mol L^{-1} cm^{-1})] 256 (85 400), 310 (85 600), 445 (3690), 550 (1590); FABMS for $C_{62}H_{44}N_8O_2Cu$ calcd 995, obsd 995.

2,9-Bis(4-carboxyphenyl)-1,10-phenanthroline (9). A solution of $TBA^+MnO_4^-$ (520 mg, 1.44 mmol) in pyridine (10 mL) was added dropwise over 1.5 h to dialdehyde **8** (400 mg, 1.03 mmol) and dissolved in pyridine (6 mL) and THF (2 mL). The reaction was stirred for an additional 1.5 h. The solution was concentrated to ~4 mL under reduced pressure and then poured into a solution of Na_2SO_3 (600 mg) in 2 N HCl (50 mL). The mixture was stirred 2 h, the precipitate was filtered, and the solid product was rinsed with water (40 mL). The material was dried *in vacuo* and used in the next step without further purification: yield 325 mg (75%); ^{1}H NMR (DMSO-d_6) δ 8.66 (d, J = 8.4 Hz, 4H), 8.64 (d, J = 8.4 Hz, 2H), 8.51 (d, J = 8.4 Hz, 2H), 8.20 (d, J = 8.4 Hz, 4H), 8.06 (s, 2H); ^{13}C NMR (DMSO-d_6) 167.2, 154.2, 145.4, 142.6, 137.6, 131.4, 130.0, 128.2, 127.4, 126.7, 120.5.

2,9-Bis[4-(6-methylpyridin-2-ylcarbamoyl)phenyl]-1,10-phenanthroline (2). A suspension of diacid **9** (89 mg, 0.21 mmol) in CH_2Cl_2 (6 mL) was treated with oxalyl chloride (110 μL, 1.26 mmol) and a trace of DMF. The mixture was heated at reflux under argon until all the solid had dissolved (~6 h) The volatiles were removed under reduced pressure, and the crude acid chloride was dried overnight under vacuum. The acid chloride was suspended in CH_2Cl_2 (5 mL) and added to a solution of 2-amino-6-picoline (50 mg, 0.46 mmol) in CH_2Cl_2 (2 mL). The resulting homogeneous reaction mixture was stirred for 12 h under a drying tube. The reaction was quenched with saturated $NaHCO_3$ (20 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 100 mL), and the combined organic layers were dried (Na_2SO_4) and evaporated to a yellow foam. The material was purified by flash chromatography (silica gel, 1–5% MeOH/CH_2Cl_2), followed by trituration with ethanol (3 × 20 mL): yield 70 mg (55%) of light yellow powder; ^{1}H NMR ($CDCl_3$) δ 8.75

(br s, 2H), 8.61 (d, J = 8.3 Hz, 4H), 8.39 (d, J = 8.4 Hz, 2H), 8.26 (d, J = 7.8 Hz, 2H), 8.23 (d, J = 8.4 Hz, 2H), 8.20 (d, J = 8.4 Hz, 4H), 7.86 (s, 2H), 7.69 (t, J = 7.8 Hz, 2H), 6.96 (d, J = 7.4 Hz, 2H), 2.51 (s, 6H); ^{13}C NMR ($CDCl_3$) 165.2, 156.7, 155.5, 150.8, 146.2, 142.9, 139.1, 137.2, 134.8, 128.4, 127.9, 127.8, 126.6, 120.4, 119.5, 111.1, 23.9; EIMS *m/z* (rel intensity) 600 (1, M^+), 99 (100); FABMS for $C_{38}H_{29}N_6O_2$, calcd 601, obsd 601.

Receptor Cu(2)$_2^+$BF$_4^-$. Compound **2** (70 mg, 0.12 mmol) was dissolved in CH_2Cl_2 (10 mL) and CH_3OH (4 drops) under argon. A solution of $Cu(CH_3CN)_4^+$ BF_4^- (19 mg, 0.060 mmol) in CH_3CN (5 mL) was added and stirred for 1 h. The solvents were evaporated, and the resulting red compound was purified by chromatography (silica gel, 5% CH_3OH/CH_2Cl_2): yield 75 mg (92%); ^{1}H NMR ($CDCl_3$) δ 8.67 (d, J = 8.3 Hz, 2H), 8.45 (br s, 2H), 8.10 (d, J = 8.2 Hz, 2H), 8.07 (d, J = 8.4 Hz, 2H), 7.93 (s, 2H), 7.68 (t, J = 7.9 Hz, 2H), 7.55 (d, J = 8.1 Hz, 4H), 7.22 (d, J = 8.1 Hz, 4H), 6.99 (d, J = 7.4 Hz, 2H), 2.55 (s, 6H); ^{13}C NMR ($CDCl_3$) 163.7, 157.1, 155.8, 150.4, 143.4, 142.2, 138.9, 138.5, 134.2, 128.6, 127.8, 127.0, 126.4, 125.5, 119.8, 111.0, 24.0; UV−vis ($CHCl_3$) [λ, nm (ϵ, mol L^{-1} cm^{-1})] 258 (71 200), 306 (78 000), 446 (3970), 550 (1320); FABMS for $C_{76}H_{56}N_{12}O_4Cu$ calcd 1263, obsd 1263.

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