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Chloroform-Soluble Schiff-Base Zn(II) or Cd(II) Complexes from a Dynamic Combinatorial Library

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A dynamic combinatorial library of metal ion Schiff-base complexes have been studied for the extraction of Zn(II) or Cd(II) from aqueous solution into chloroform. Library components consist of different aminophenols and 2-pyridinecarboxaldehyde. Extraction of both Zn(II) and Cd(II) into chloroform was observed from aqueous solutions containing 0.0500 mM $M(NO_3)_2$, 0.100 M aminophenol, 0.100 M 2-pyridinecarboxaldehyde, 0.100 M NaCl, and 5.00 mM buffer at pH 8.5. Extraction was dependent on pH but not on counterions including Cl^-, Br^-, or NO_3^-. Studies showed that equilibrium was attained between the Schiff-base complexes across the two-phase chloroform−water system after 24 h of stirring. Analysis of the extracted species by use of ^1H NMR spectroscopy and mass spectrometry as well as solubility studies on characterized complexes suggested that the major extracted species is the neutral bis-Schiff-base metal ion complex. In libraries containing mixtures of two different aminophenols and 2-pyridinecarboxaldehyde, an enhanced extent of extraction of Zn(II) into chloroform is observed. Studies suggest that a Zn(II) complex, which is likely the mixed Schiff-base complex, has superior extraction properties compared to simple libraries with a single aminophenol component. The structures of two bis-Schiff-base complexes of Zn(II) and one of Cd(II) have been determined by X-ray crystallography. The geometries of the two Zn(II) complexes, which differ only by a methyl substituent on the Schiff-base ligand, are markedly different, supporting the use of combinatorial methods in coordination chemistry. $Zn(SB14)_2$ crystallized as the sesquihydrate ($C_{24}H_{18}N_4O_2Zn{\cdot}1.5\ H_2O$) in the space group $C2/c$, with cell dimensions $a = 23.219(15)$ Å, $b = 11.299(7)$ Å, $c = 16.822(11)$ Å, $\beta = 102.91(5)°$, $V = 4302(5)$ Å^3, and $Z = 8$. $Zn(SB15)_2$ crystallized as a 1:1 methanol solvate ($C_{26}H_{22}N_4O_2Zn{\cdot}CH_3OH$) in the space group $P2_1/c$ with cell dimensions $a = 13.981(5)$ Å, $b = 7.978(3)$ Å, $c = 22.568(8)$ Å, $\beta = 104.53(3)°$, $V = 2436.8(15)$ Å^3, and $Z = 4$. $Cd(SB14)_2$ crystallized as a 1:1 ethanol solvate ($C_{24}H_{18}N_4O_2Cd{\cdot}CH_3CH_2OH$) in the space group $R\bar{3}$ with unit cell dimensions of $a = 36.423(2)$ Å, $c = 9.2930(10)$ Å, $V = 10678(2)$ Å^3, and $Z = 18$.

Introduction

Dynamic combinatorial libraries consist of families of compounds that interact with one another and/or with a target compound through covalent or noncovalent interactions.[1−4] Studies are conducted under conditions where the compounds formed by these interacting library members are at equilibrium with one another. Upon addition of a target, the equilibrium is shifted toward the component combinations that interact more strongly with the target. The applications of dynamic combinatorial chemistry have been recently reviewed.[1−4]

Metal complexes are useful in the formation of dynamic combinatorial libraries given that metal ligand bonds are often labile enough to produce equilibrating mixtures under mild conditions. Metal ions with multiple coordination sites assemble ligands to form unique molecular shapes under dynamic equilibrium conditions.[5−10] Alternatively, metal complexes may be used as scaffolds for molecular recognition processes.[11,12] Here we demonstrate that dynamic combinatorial chemistry is useful in the design of ligands for metal ion extraction. The selection of chloroform-soluble Schiff-base Zn(II) and Cd(II) complexes from a dynamic library is accomplished. In this study, the library is generated through the reversible formation of both metal−ligand and imine bonds. Substantial improvement in extraction is accomplished in relatively small libraries. The structure of the putative extracted species is shown to be readily distorted by minor ligand changes that may very well lead to differences in extraction.

Ligands that facilitate metal ion extraction have been extensively studied.[13−15] In particular, chelating and macrocyclic ligands have been useful in the design of ligands for specific

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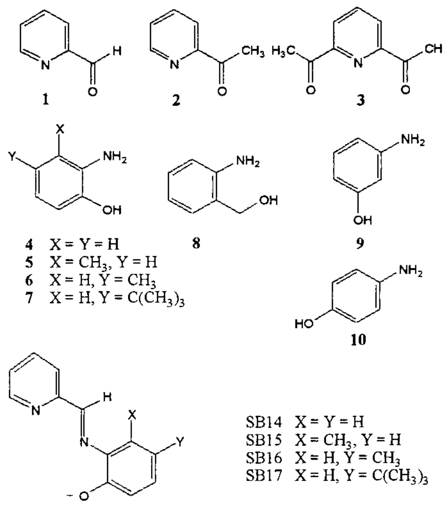
10.1021/ic000938t CCC: $20.00

Chart 1



metal ion binding and extraction.[15] Such metal ion separations have important applications in the removal of toxic metal ions from the environment and in the remediation of radioactive wastes containing metal ions.[15,16] Yet, it remains a challenge to design ligands that are specific for the extraction of a particular metal ion. Important factors such as metal ion complex solubility and synergistic ligand−ligand interactions[17−20] are not easily predicted and incorporated into ligand design. Thus, combinatorial methods that allow ready variation of ligands and their substituents may be a useful in improving metal ion extraction processes.

Results and Discussion

Aqueous−organic phase liquid extractions are used for metal ion recovery and purification.[13] In these liquid−liquid extractions, a metal cation that is soluble in the aqueous phase is extracted into an organic phase upon binding to specific ligands. The extent of extraction is dependent on several factors including the stability of the metal ion complex and its partitioning between the organic and aqueous phases.[13] In building a dynamic library of complexes for extraction, Schiff-base complexes were chosen in order to capitalize on the reversible nature of imine bond formation. Schiff bases are not very stable in aqueous solution, although metal ions may have a stabilizing effect.[21] However, Schiff-base complex stability is typically higher in organic solvents such as chloroform. Schiff-base ligands have been successfully used for extraction of metal ions from aqueous to organic solutions.[22,23]

Library components were chosen to optimize stability and chloroform solubility of metal complexes. Aldehydes or ketones containing a metal ion binding site were used (Chart 1). A series of aminophenols were studied for Schiff-base formation. Deprotonation of the phenol group of the Schiff base gives an anionic ligand that should facilitate the extraction of cationic metal ions. There are numerous examples of chelating Schiff-base ligands similar to those used here;[24] our choice was based on the good availability of a variety of aminophenols, aminobenzyl alcohols, and anilines as well as aldehydes and ketones of aromatic heterocycles. Tridentate Schiff-base ligands were studied with the goal of forming bis-Schiff-base complexes to allow us to examine synergistic ligand effects. For metal ions, Cd(II) and Zn(II) were chosen given that these d^{10} metal ions have relatively flexible coordination geometries. The geometry of such complexes may be influenced by subtle intraligand interactions. Ligand exchange kinetics are typically quite rapid for Zn(II) and Cd(II), facilitating the rapid equilibration of metal ion complex libraries.

Table 1. Extraction of Zn(II) or Cd(II) (0.0500 mM) from Aqueous Solutions Containing 0.100 mM **1**, 0.100 mM Aminophenol, 5.0 mM Buffer, 0.10 M NaCl into 1.00 mL of $CHCl_3$

aminophenol	%Zn[a]	%Zn[b]	%Cd[a]
4	29 ± 2	1.5 ± 0.7	9.3 ± 2
5	4.6 ± 0.4	0	1.4 ± 0.7
6	47 ± 0.9	7.6 ± 0.3	23 ± 3
7	39 ± 3	16 ± 1	37 ± 2

[a] pH = 8.5, CHES buffer. [b] pH = 6.5, cacodylate buffer.

Extraction studies were carried out with solutions containing 0.0500 mM $Zn(NO_3)_2$ or $Cd(NO_3)_2$ and 0.100 mM **1**, **2**, or **3**, 0.100 mM aminophenol (**4**−**9**) or 2-aminobenzyl alcohol (**10**), 0.10 M NaCl, and 5.00 mM buffer. To these solutions, 1 mL of chloroform was added, and the solution was stirred vigorously under an atmosphere of nitrogen. The extent of extraction of Zn(II) or Cd(II) into chloroform was determined by use of a dithizone colorimetric test. In order for this system to function as a dynamic library, it was necessary to test whether the two-phase system was at equilibrium. We anticipated that transport of compounds between the two phases would be relatively slow. Another potentially slow step is the dissociation of the Schiff-base complexes dissolved in chloroform. Consistent with these predictions, extraction of Zn(II) or Cd(II) was time-dependent for the first few hours but stabilized by 24 h. To further demonstrate that our extraction process was at equilibrium, we compared the extent of Zn(II) or Cd(II) extraction with reagents initially dissolved in either the chloroform or water layer. For experiments starting with components in the chloroform layer, a bis-Schiff-base metal complex ($Zn(SB14)_2$ or $Cd(SB14)_2$) was prepared, dissolved in chloroform, and added to a stirred buffered aqueous solution. Zn(II) and Cd(II) concentrations distributed into chloroform after 24 or 48 h were identical within experimental error for both methods, suggesting that equilibrium was established between the two layers. Mixtures for all further experiments were stirred for a 24 h equilibration time.

Several different aminophenols and carbonyl compounds were examined to construct a suitable library. Little extraction of metal ion (1% or less) was observed under the conditions given in Table 1 (pH 8.5) with either **2** or **3** in the presence of **4**, whereas **1** and **4** were quite effective in promoting extraction of Cd(II) or Zn(II). In the presence of **1**, no extraction was observed with aminophenols **8** or **9** or aminobenzyl alcohol **10**. ^{1}H NMR studies suggested that Zn(II) Schiff-base complexes of **1** and **9** and **1** and **10** were formed to a small extent in D_2O, athough it is not clear whether these are mono- or bis-Schiff-

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base complexes. However, these complexes did not extract into chloroform likely because of the fact that the phenol groups cannot readily chelate to Zn(II) to facilitate deprotonation and formation of a neutral bis-Schiff-base complex. For **1** and **8** no new imine ^{1}H NMR resonances were observed in buffered solutions containing D_2O or in $D_2O/CDCl_3$ mixtures under conditions similar to those in Table 1, suggesting that no Schiff-base complex was formed. Similarly, acetylpyridine (**2**) does not form Schiff-base complexes with **4** as demonstrated by ^{1}H NMR studies in D_2O and $CDCl_3$ mixtures under conditions similar to those in Table 1. However, free Schiff-base (SB24) does form and extract into chloroform. The only combinations we examined that gave extraction had **1** and either **4**, **5**, **6**, or **7**. Schiff-base formation was necessary for extraction because little Cd(II) or Zn(II) (<2%) was extracted in solutions containing **1** alone or any of the aminophenols (**4**−**7**) alone in buffered solutions at pH 6.5 or 8.5. An exception was **7**, which gave 19% extraction of Zn(II) at pH 8.5 in the absence of **1**. In contrast, solutions containing both **1** and a 2-aminophenol led to the extraction of as much as 47% of the Zn(II) or 37% of the Cd(II) (Table 1).

Attempts were made to characterize the species that were extracted. Even in these simple two-component systems there are at least four possible neutral Schiff-base complexes that may be extracted including the bis-Schiff-base complex as well as mono-Schiff-base complexes containing a 2-aminophenoxide ($\mathbf{4}^-$, $\mathbf{5}^-$, $\mathbf{6}^-$, $\mathbf{7}^-$) nitrate or hydroxide as counterions. However, no variation in extent of extraction within experimental error was observed in the presence of sodium salts with different counterions including 0.100 M NaBr, NaCl, or $NaNO_3$, suggesting that simple counterions did not participate in the extraction. Extraction was pH-dependent with less Zn(II) and no Cd(II) being extracted at pH 6.5 than at pH 8.5 (Table 1). This pH dependence is consistent with extraction being enhanced by deprotonation of the phenol group of the Schiff base to form a neutral bis-Schiff-base complex. Interestingly, extraction was selective for Zn(II) over Cd(II) at both pH values. This trend is consistent with the higher formation constant of Zn(II) with 2-aminophenol-type ligands.[25] FAB-MS studies on the chloroform extracts of the **1**−**4** Zn(II) or Cd(II) extraction system supported bis-Schiff-base complexes as the major extracted species. Peaks were observed by FAB-MS for $[M(SB14)_2 + H^+]$ for both the prepared Schiff-base complexes (experimental) and for the chloroform extracts. In addition, complexes of Zn(II) and Cd(II) containing two Schiff-base ligands prepared in ethanol including $Zn(SB14)_2$ and $Cd(SB14)_2$ showed the expected solubility properties. The ^{1}H NMR spectrum of the major species (>90%) extracted from D_2O solutions of Zn(II) **1** and **4** into $CDCl_3$ matched that of the prepared bis-Schiff-base complex. While these studies strongly support neutral bis-Schiff-base complexes as the primary complexes extracted into chloroform, other neutral complexes may be present in the extraction mixture including M(SB)(AP) (SB = anionic schiff-base, AP = aminophenoxide $\mathbf{4}^-$, $\mathbf{5}^-$, $\mathbf{6}^-$, $\mathbf{7}^-$), or for **7**, $Zn(\mathbf{7}^-)_2$. Even in a solution containing a single aminophenol and a single aldehyde, there are several possible different metal complex species that may form, and this increases the complexity of the dynamic library. Unfortunately, background extraction of both free aminophenols and **1** into chloroform in the absence of metal ion prevented us from correlating the concentration of extracted library components in chloroform to the metal complex speciation in chloroform.

Table 2. Extraction of Zn(II) (0.0500 mM) from Aqueous Solutions Containing **1** (0.100 mM) and Two Different Aminophenols (0.100 mM Each), pH 8.5, 5.0 mM CHES Buffer, 0.10 M NaCl into 1.00 mL of $CHCl_3$

aminophenols	%Zn extracted	%Zn calculated
4 + **5**	39 ± 0.8	30
4 + **6**	63 ± 10	53
4 + **7**	67 ± 9	47
5 + **6**	48 ± 1	47
5 + **7**	60 ± 2	39
6 + **7**	75 ± 6	57

If a dynamic library of Schiff bases is to be useful for improved extraction of metal ions, it should produce compounds with superior extraction properties. Most interesting would be cases in which an unexpected combination of library components formed new metal complexes with mixed ligands. Several mixtures were examined that contained two different aminophenols and **1** (Table 2). To calculate a cooperative effect between two aminophenols, we assumed that the bis-Schiff-base complex was the only complex extracted into chloroform, then calculated the percent Zn(II) or Cd(II) that should have been extracted (without cooperativity) based on the measured extraction coefficients and the concentration of library components (Experimental Section). For Cd(II), the calculated and observed percent extraction does not differ within experimental error (data not shown). For Zn(II), however, several combinations were promising with the **1**−**5**−**7** system showing the highest degree of cooperativity (Table 2). An additional 21% extraction was observed above the calculated percent extraction. Our assumption that the only extracting species is a bis-Schiff-base complex may not be entirely valid because in these three-component systems, there are 10 possible neutral metal ion complexes including neutral bis-Schiff-base and mixed Schiff-base aminophenoxide and bis-aminophenoxide complexes. There must be, nonetheless, cooperative extraction given that the percent extraction in the mixture (60%) is higher than the sum of the percentages of the two two-component systems (39% + 4.6%).

This cooperativity may be due to the superior extraction properties of a neutral Schiff-base complex such as a mixed bis-Schiff-base complex (Zn(SB15)(SB17)). Analysis of the chloroform extracts by use of mass spectrometry (FAB-MS) supported the presence of a mixed bis-Schiff-base complex (Zn(SB15)(SB17) as a major species. In addition, ^{1}H NMR spectra of these mixtures of extracted complexes containing **1, 5**, and **7** in $CDCl_3$ have new imine ^{1}H resonances attributed to new mixed Schiff-base complexes. However, the ^{1}H NMR spectrum of the mixture is complex and we cannot rule out extraction of mono-Schiff-base complexes Zn(SB15)($\mathbf{7}^-$) or Zn(SB17)($\mathbf{5}^-$) as important species. A mixed aminophenoxide complex (Zn($\mathbf{7}^-$)($\mathbf{5}^-$)) is excluded from consideration because no extraction was observed in mixtures that did not contain **1**.

There are other reports of synergistic effects of two different ligands in metal ion extraction processes.[17−20] In one of these reports, it is shown that the two ligands form a host−guest assembly that enhances metal ion binding and extraction.[18] Whether the synergistic effects observed here are due to such ligand assembly effects or, alternatively, are due to enhanced binding of two different ligands or to favorable solubility properties of a mixed Schiff-base ligand complex is unknown. However, as we show below, subtle changes in ligand substituent modify the Zn(II) complex geometry and it is conceivable that two different ligands may complement each other to form a more stable complex or a more soluble complex.

An interesting observation is that extraction of Cd(II) does not show any synergistic effects. If steric interactions involving

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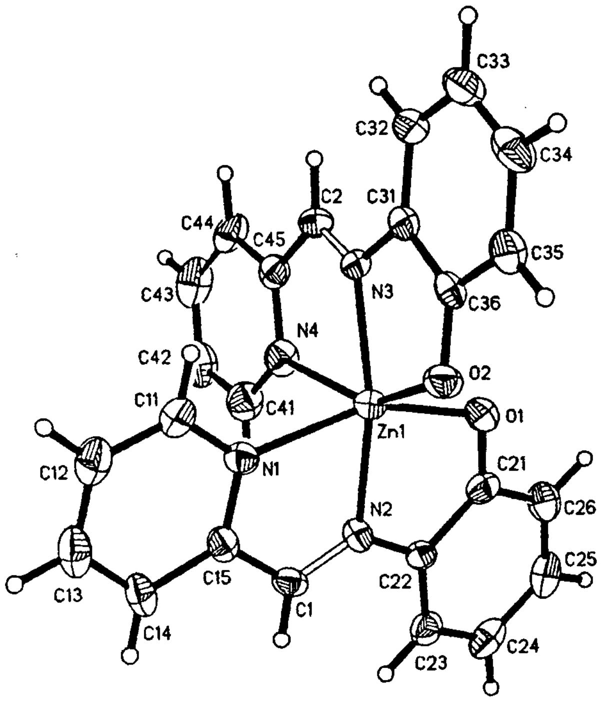


Figure 1. Structure of the [Zn(SB14)$_2$] complex with the following selected distances and angles: Zn1−O1 = 2.073(5) Å and Zn1−O2 = 2.101(5) Å, Zn1−N2 = 2.101(5) and Zn1−N3 = 2.084(6) Å, Zn1−N1 = 2.222(6) Å and Zn1−N4 = 2.341(5) Å, N2−Zn1−N1 = 75.2(2)°, O1−Zn1−N2 = 78.5(2)°.

ligand substituents are important in changing the geometry and properties of the metal ion complex (as shown below), then one would predict that steric effects would be less pronounced for the larger Cd(II) ion than for the Zn(II) ion. Studies are underway to test this hypothesis on larger libraries with more bulky substituents.

To characterize the bis-Schiff-base complexes and to study their geometries with different substituents, X-ray crystal structures of three bis-Schiff-base complexes were determined. All three complexes [Cd(SB14)$_2$]·CH_3CH_2OH, [Zn(SB14)$_2$]·1.5H_2O, and [Zn(SB15)$_2$]·CH_3OH have two meridional Schiff-base ligands with pseudo-octahedral coordination geometry (Figures 1−3). The coordination geometry about Zn(II) or Cd(II) in the complexes with SB14 is rather irregular. Trans angles (within the meridional ligands) for the Zn(II) complex are O1−Zn−N1 = 153.6(2)° and O2−Zn−N4 = 151.8(2)° with an interligand trans angle of only 162.3(2)° for ∠N2−Zn1−N3. For the Cd(II) complex, the trans-meridional angles are O−Cd−N = 141.9(1)° and 142.0(1)° and the interligand trans angle is N(imido)−Cd−N(imido) = 161.5(1)°. Zn(SB15)$_2$ has a more regular coordination geometry. The trans angles within the meridional ligands remain distorted (O11−Zn1−N21 = 153.4(1)° and O31−Zn1−N41 = 153.0(1)°), but the interligand trans angle is now close to the ideal value, with N12−Zn1−N32 = 175.6(1)°. Zn(II)−ligand distances are similarly more regular than in the unsubstituted complexes (see Figures 1−3). The dihedral angle between the planes formed by the pyridine nitrogen, imine nitrogen, and phenoxide oxygen is also more regular for the latter complex with 83.2°, 89.4°, and 90.5° for Cd(SB14)$_2$, Zn(SB14)$_2$, and Zn(SB15)$_2$, respectively.

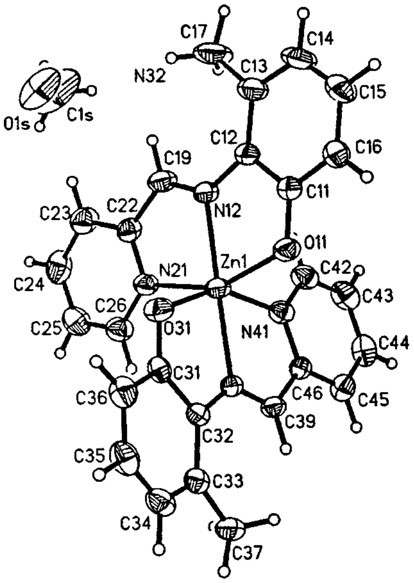


Figure 2. Structure of the [Zn(SB15)$_2$] complex including a methanol of crystallization, with the following selected distances and angles: Zn1−O11 = 2.029(3) Å and Zn1−O31 = 2.035(3) Å, Zn1−N12 = 2.155(3) Å and Zn1−N32 = 2.149(3) Å, Zn1−N21 = 2.183(3) Å and Zn1−N41 = 2.224(3) Å, N12−Zn−N21 = 75.6(1)°, O11−Zn−N12 = 78.0(1)°.

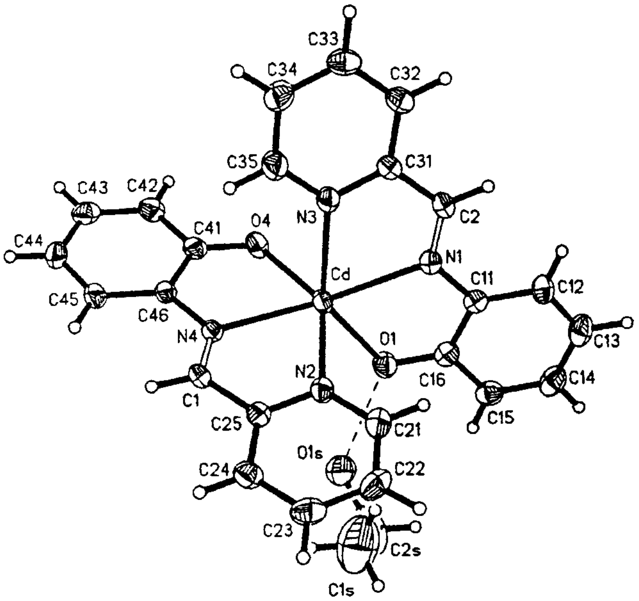


Figure 3. Structure of the [Cd(SB14)$_2$] complex including an ethanol of crystallization, with the following selected distances and angles: Cd−O1 = 2.259(3) Å and Cd−O4 = 2.253(4) Å, Cd−N1 = 2.304(3) Å and Cd−N4 = 2.334(3) Å, Cd−N3 = 2.436(3) Å and Cd−N2 = 2.404(4) Å, O1−Cd−N1 = 72.7(1)°, N1−Cd−N3 = 69.3(1)°.

The variation in these three structures demonstrates that the geometry of these d^{10} Zn(II) and Cd(II) complexes is easily modified by subtle ligand changes. What is particularly surprising is the differences observed between the two Zn(II) complexes. On the basis of studies with molecular models, it was anticipated that the methyl group of the SB15 ligand might cause the ligand geometry to depart from planarity because the methyl group may interact with hydrogens of the pyridine ring. However, the SB15 ligand is relatively planar. The greatest deviations from each side of the O11−N12−N21 plane are −0.211 Å for C17 (the methyl group) and +0.111 Å for C23. For the O31−N32−N41 plane, maximum deviations are +0.130 Å for C37 (the methyl group) and −0.303 Å for C43. Neither is the influence of ligand substituents on the metal geometry easy to rationalize. From inspection of molecular models, it is not evident why the more highly substituted Zn(II) Schiff-base complex exhibits the more regular coordination geometry.

Extraction efficiency depends on several factors including the metal complex stability as well as its solubility in organic solvent.[13] Superior extraction with SB17, which contains a *tert*-butyl group, would be anticipated on the basis of the good chloroform solubility of the ligand and its higher molar volume. Large differences in extraction efficiency for SB16 and SB15 are more difficult to rationalize. Methyl substituents would not be expected to greatly change stability constants of the Schiff-base complexes. The pK_a values of methylphenols do not change substantially with position of the methyl group.[25,26] Thus, the ligand basicity of the cresols and their binding constants to metal ions should be similar. However, it is clear that the position of the methyl group may change the overall geometry of the complex. For SB15, the methyl group affects the overall geometry of the complex quite markedly. Changes in the geometry at the metal center may reasonably influence both stability and solubility of the complexes.

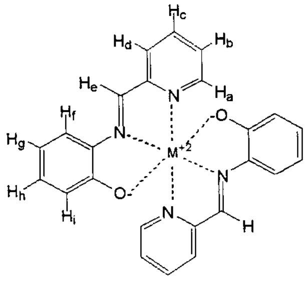
In summary, we have developed the first example of a dynamic combinatorial library of Schiff-base complexes for the aqueous chloroform extraction of Zn(II) or Cd(II) ions. In these studies, the metal ion complex that best forms and solubilizes in the chloroform layer is selected from multiple possible metal complexes in solution. Even simple mixtures show promise for improving extraction by virtue of the different ligand combinations accessible in the library. While it is difficult to correlate extraction results involving both formation constants and solubility properties with the metal ion complex structure, it is evident here that subtle changes such as a methyl group substituent markedly influence the geometry of these bis-Schiff-base complexes. Given that the effect of subtle geometric changes on solubility properties and formation constants is not readily predicted, combinatorial methods will likely be useful in metal ion separations.

Experimental Section

Materials and Instrumentation. 2-Aminophenol, 2-amino-*m*-cresol, 2-amino-*p*-cresol, 6-amino-*m*-cresol, 2-amino-4-*tert*-butylphenol, 2-aminothiophenol, 2-pyridinecarboxaldehyde, and 2-acetylpyridine were purchased from Aldrich and used without further purification. Buffers CHES, MES, and cacodylic acid were purchased from Sigma. Millipore MILLI-Q purified water was used in all experiments. An Orion Research ionalyzer/501 with an Orion model 9165 silver/chloride SURE-FLOW pH electrode was used to adjust the pH of all solutions used. ^{1}H NMR spectra were recorded on a Varian Unity INOVA-500 spectrometer. A VG 70-SE high-mass, high-resolution mass spectrometer with an OPUS data system with fast atom bombardment ionization was utilized. A Hewlett-Packard diode array 8452A spectrophotometer was used for all UV−vis spectra and kinetic measurements. X-ray crystallographical data were acquired with a Siemens R3m/V diffractometer.

Extractions. To a 20 mL vial with aluminum-lined Teflon crimp-cap was added a 10 mL solution containing 0.100 M NaCl, 0.0500 mM metal, 5.00 mM buffer, and 0.100 mM PCA in water. To prevent oxidation of the aminophenols,[27] the solution was degassed with nitrogen before adding 2 μL of 0.500 M aminophenol solution (in DMSO) to give a final concentration of 0.100 mM aminophenol. The vials were sealed, and the solution was degassed again for a few minutes. A total of 1 mL of degassed $CHCl_3$ was added by syringe. This sample was then vigorously stirred for 24 h. The color of the $CHCl_3$ solution changed over a period of time to dark hues of purple, red, or green. Aliquots were taken directly from the $CHCl_3$ layer, and the samples were analyzed for metal ion concentration by the dithizone assay.

Chart 2



Dithizone is a widely used extraction photometric reagent.[28] In chloroform, dithizone has two absorbance bands at 440 nm ($\epsilon = 15\,900$ M^{-1} cm^{-1}) and 606 nm ($\epsilon = 41\,400$ M^{-1} cm^{-1}). Dithizone forms a bis complex with Cd(II) and Zn(II) ions with absorbance bands (in $CHCl_3$) at 520 nm ($\epsilon = 85\,600$ M^{-1} cm^{-1}) and 530 nm ($\epsilon = 88\,000$ M^{-1} cm^{-1}), respectively. The number of moles of metal ion was calculated from the change in absorbance of free dithizone at 606 nm, recognizing that each Cd(II) or Zn(II) binds 2 mol of dithizone. As controls, solutions containing a known amount of bis-Schiff-base Zn(II) or Cd(II) complex (as prepared below) were added to the dithizone solution. The expected decrease in the free dithizone absorbances was observed, confirming that there was no interference from the Schiff base for this assay. Extraction measurements were repeated a minimum of three times.

To calculate the expected amount of $CHCl_3$ extraction of Zn(II) or Cd(II) by mixtures, we assumed that all metal ion was extracted as the bis-Schiff-base complex ($M(SB)_2$). The concentration of Schiff-base complex was calculated from the amount of Zn(II) or Cd(II) extracted into chloroform. K_{ex} values were calculated for each two-component system containing an aminophenol (**4**−**7**) and **1**. Then K_{ex} values were used to calculate the expected total extent extraction (Table S1 of Supporting Information). Equations 2−5 were fit using Mathcad where $[AP]_{tot,}$ $[PCA]_{tot}$, and $[M^{2+}]$ denote the total concentration of aminophenol, pyridine-2-carboxaldehyde and metal ion, respectively, [PCA], [AP], and $[M^{2+}]$ denote the equilibrium concentrations of pyridine-2-carboxaldehyde, aminophenol, and metal ion, respectively, and $[M(SB)_2]$ is the Schiff-base complex concentration.

$$2PCA + 2AP + M^{2+} \rightarrow M(SB)_2 \tag{1}$$

$$K_{ex} = \frac{[M(SB)_2]}{[PCA]^2[AP]^2\,[M^{2+}]} \tag{2}$$

$$[AP]_{tot} = 2[M(SB)_2] + [AP] \tag{3}$$

$$[PCA]_{tot} = 2[M(SB)_2] + [PCA] \tag{4}$$

$$[M^{2+}]_{tot} = [M(SB)_2] + [M^{2+}] \tag{5}$$

Syntheses. 1. Zn(SB14)$_2$. $Zn(NO_3)_2$ (0.7826 g, 2.63 mmol) was dissolved in 100 mL of absolute ethanol. To this solution, 2-pyridinecarboxaldehyde (**1**) (0.501 mL, 5.27 mmol) was added, and the solution was stirred. 2-Aminophenol (0.5747 g, 5.26 mmol) was added followed by addition of triethylamine (0.740 mL, 5.31 mmol), and the solution was brought to a gentle boil and stirred for 15 min. The precipitate was filtered and recrystallized from ethanol. ^{1}H NMR (δ = ppm, $CDCl_3$; see labeling in Chart 2): 8.62 (1H, s, H_e), 7.95 (2H, d, $J = 4.5$ Hz, H_a), 7.72 (2H, t, $J = 7.75$ Hz, H_c), 7.49 (4H, m, H_d and H_b), 7.13 (4H, m, H_i and H_g), 6.82 (2H, d, $J = 8.0$ Hz, H_f), 6.46 (2H, t, $J = 7.5$ Hz, H_h). FAB MS *m/e*: $[Zn(SB14)_2 + H^+]$, 459, 460, 461, 462, 463, 464, 465.

2. Zn(SB15)$_2$. $Zn(SB15)_2$ was prepared by a similar synthesis and recrystallized from methanol. ^{1}H NMR (δ = ppm, $CDCl_3$; see labeling in Chart 2): 9.01 (1H, s, H_e), 7.94 (2H, d, $J = 4.5$ Hz, H_a),

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7.89 (2H, t, $J = 7.75$ Hz, H_c), 7.76 (2H, d, H_d), 7.25 (2H, t, H_b), 6.92 (2H, t, $J = 8.0$ Hz, H_h), 6.34 (2H, d, $J = 7.0$ Hz, H_i), 6.19 (2H, d, $J = 7.0$ Hz, H_g). FAB MS *m*/*e*: [$Zn(SB15)_2 + H^+$], 487, 488, 489, 490, 491, 492, 493.

3. $Cd(SB14)_2$. $Cd(NO_3)_2{\cdot}4H_2O$ (0.540 g, 50.0 mmol) was dissolved in 100 mL of absolute ethanol. The solution was stirred until all solid was dissolved. To this 0.950 mL of 2-pyridinecarboxaldehyde (100 mmol) and 2-aminophenol (1.09 g, 100 mmol) were added. The solution was stirred and boiled for 15 min. Triethylamine (1.40 mL, 100 mmol) was added, and the solution was brought to a gentle boil. The solution was cooled to room temperature before filtering. The precipitate was recrystallized from ethanol. Dark-red crystals of $Cd(PCA\text{-}2AP)_2{\cdot}CH_3CH_2OH$ were obtained. ^1H NMR (δ = ppm, $CDCl_3$; see Chart 2 for numbering): 8.61 (2H, Cd satellites, H_e, $^3J(^1H-^{111,113}Cd) = 42.5$ Hz), 8.06 (2H, d, $J = 3.5$ Hz, H_a), 7.77 (2H, t, $J = 7.5$ Hz, H_c), 7.50−7.45 (4H, m, H_d & H_b), 7.17−7.15 (4H, m, H_i & H_g), 6.84 (2H,d, $J = 8.5$, H_f), and 6.44 (2H, t, $J = 7.5$, H_h). FAB-MS *m*/*e* {$Cd(SB14)_2 + H^+$}, 505, 506, 507, 508, 509, 510, 511.

X-ray Crystallography. $Zn(SB14)_2$ was crystallized from aqueous solution as the sesquihydrate. A red crystal (0.21 mm × 0.26 mm × 0.34 mm) was mounted on the diffractometer. The crystal belongs to space group $C2/c$, with cell dimensions $a = 23.219(15)$ Å, $b = 11.299(7)$ Å, $c = 16.822(11)$ Å, $\beta = 102.91(5)°$, $V = 4302(5)$ Å^3, and $Z = 8$. A total of 8917 reflections were collected and reduced to a unique set of 2817 reflections of which 1876 with $I > 2\sigma(I)$ and 2θ(Mo Kα) = 5−45° were treated as observed. Data were corrected for Lp factors and absorption. The crystal structure was solved under the SHELXTL PLUS, release 4.11 (VMS),[29] and refined to $R = 5.26\%$. Hydrogen atoms of the Zn complex were included in calculated positions.[30] Those of the water molecules were not located.

$Zn(SB15)_2$ was crystallized out of methanol as the 1:1 solvate. A red crystal (0.17 mm × 0.26 mm × 0.64 mm) was selected. The crystal belongs to space group $P2_1/c$ with cell dimensions $a = 13.981(5)$ Å, $b = 7.978(3)$ Å, $c = 22.568(8)$ Å, $\beta = 104.53(3)°$, $V = 2436.8(15)$ Å^3, and $Z = 4$. A total of 6732 reflections were collected and reduced to a unique set of 3208 reflections of which 3197 were treated as observed. Data were corrected for Lp factors and for absorption and were refined to $R = 3.58\%$ for data with 2θ(Mo Kα) = 5−45°. Hydrogen atoms were included in calculated positions.

$Cd(SB14)_2$ was crystallized from ethanol as the 1:1 solvate. A deep-red parallelepiped crystal of size (0.34 mm × 0.38 mm × 0.60 mm) was mounted on the diffractometer. The crystal belonged to space group $R\bar{3}$ with unit cell dimensions of $a = 36.423(2)$ Å, $c = 9.2930(10)$ Å, $V = 10678(2)$ Å^3, and $Z = 18$. A total of 11 397 reflections were collected and reduced to a unique set of 3122 reflections of which 2471 with 2θ(Mo Kα) = 5−45° were treated as "observed". Data were corrected for Lp factors and absorption. The crystal structure was solved under the SHELXTL PLUS, release 4.11(VMS),[29] and refined to $R = 2.91\%$. Hydrogen atoms were included in calculated positions.[30]

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Supporting Information Available: Tables of X-ray crystal stucture refinement data, positional and thermal parameters for all structures, and sample calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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