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Metal Chelation Aptitudes of Bis(*o*-azaheteroaryl)methanes As Tuned by Heterocycle Charge Demands[1]

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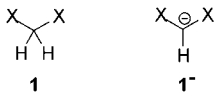
We describe the synthesis of a number of 1,3-azol-2-yl-, 1,3-benzazol-2-yl-, and azinyl-based bis(*o*-azaheteroaryl)methanes (LH, $L^- = Het_2CH^-$) and their coordinating properties toward divalent transition metals (Zn, Cu, Co, Ni, Hg, Pd). This extended investigation includes both symmetrical and unsymmetrical ligands based on several substituted and/or unsubstituted thiazole, benzothiazole, benzoxazole, benzimidazole, pyridine, and quinoline derivatives. Depending on the structure and electron properties of the ligand, a vast set of neutral chelates ML_2 were obtained, where the ligand is present in its carbanionic form L^-. Additionally, we have prepared salt complexes $[M(LH)_n]X_m$, where the ligand is present as a neutral system. Neutral chelates were typically obtained by the reaction of the ligand with metal acetates in alcoholic solution; salt complexes were formed by reaction with other metal salts such as chlorides. By exploring the coordinating properties of several bisheteroarylmethane ligands based on heteroaromatics of variable π-electron structure and substitution pattern, we demonstrate that the formation of neutral chelates is strictly dependent on the electron-withdrawing capacity (charge demand) of the heteroaromatic moiety. The latter primarily dictates the efficiency by which the negative charge of the anionic ligand L^- is stabilized by delocalization in ML_2 and, therefore, the stability of the chelate itself. On the basis of the large number and the variable nature of the nitrogen ligands used, we confirm the general validity of the charge-demand-dependent formation of chelates. This key factor can therefore be used for the efficient design of new π-deficient heteroaromatic nitrogen ligands in chelates of great potential in many synthetic, catalytic, and technological fields.

Introduction

Heteroaromatic nitrogen ligands[2] find extended applications in several important research and technological fields, including C−C bond formation,[3] asymmetric homogeneous and heterogeneous catalysis,[4] DNA binding,[5] use as diagnostic agents and drugs,[6] radioimmunotherapy,[7] tumor targeting,[8] electroluminescent (LED)[9] and nonlinear optical[10] materials, and other applications in electrooptical and photonic devices.[11] Still, the vast majority of heteroaromatic nitrogen ligands covers solely pyridine-based structures, which appears as a serious limitation to the strong potential coordinating properties of other heteroaromatic structures, the bipyridine moiety being by far the most widely used ligand.[12] In contrast, azole- and benzazole-based ligands have so far received scant interest in their use as nitrogen ligands toward transition metals.

Over the last few years, we have undertaken a systematic investigation on bisheteroarylmethanes **1** and their corresponding deprotonated forms at the methylene bridge, **1**$^-$. Our primary interest was to elucidate and



1 **1**$^-$

quantitatively rank the electron-acceptor properties of

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π-deficient heteroaromatics using, as a method of choice, multinuclear NMR investigation of anionic systems in DMSO, and get a deep insight into their experimental charge distribution mapping[13] obtained by largely validated ^{13}C and ^{15}N shift/charge relationships.[14,15] Among other organic systems, we included in our multiyear study the following heterocycles: azines (2- and 4-pyridyl, pyrazinyl, 4-pyrimidyl, 3-pyridazinyl, and 2- and 4-quinolyl),[15a,16] 1,3-azoles (2-oxazolyl, 2-thiazolyl, and 2-imidazolyl and their benzo-fused analogues),[17] triazoles,[18] and purines (8-purinyl).[19]

Ranking of the π-electron-withdrawing (EW) power of heterocycles was conveniently expressed in terms of the charge demand c,[20] defined as the fraction of π-charge transferred from an adjacent negatively charged trigonal carbon atom to the X group.[13,14b,21] Charge demands are directly correlated to the π-electron density residing on the trigonal carbanionic carbon q^{π}_{C}, as obtained from its ^{13}C chemical shift and shift/charge relationships,[14] using eqs 1 and 2.[22]

$$c^{X}_{X} = (2 - q^{\pi}_{C})/2 \quad (1)$$

$$c^{X}_{Ph} = 2 - c_{Ph} - q^{\pi}_{C} \quad (2)$$

Depending on whether the capacity of delocalizing an adjacent negative charge by the group X is measured in symmetrical anions $\mathbf{1}^-$ (c^{X}_{X}) or benzyl carbanions PhCH−X (c^{X}_{Ph}), two sets of c values can be obtained. Table 1 lists the values of charge demands for various heterocyclic groups and, for comparison, primary organic functionalities.[14,21]

TABLE 1. Charge Demands of Heteroaryl and Primary Organic Substituents (X)[a]

X	c^{X}_{Ph}	c^{X}_{X}
Ph[b]	0.29	0.29
$CONMe_2$[b]	0.42	0.275
CO_2Me[b]	0.40	0.268
COMe[b]	0.51	0.325
COPh[b]	0.56	0.341
CN[b]	0.28	0.207
SOPh[b]	0.26	0.233
SO_2Ph[b]	0.28	0.206
$PO(OEt)_2$[b]	0.26	0.122
2-thiazolyl[c]	0.413−0.380	0.318
2-oxazolyl[c]	0.346	
N-methylimidazol-2-yl[c]	0.283	0.254
2-benzothiazolyl[c]	0.457−0.471	0.316
2-benzoxazolyl[c]	0.424−0.436	0.288
N-methylbenzimidazol-2-yl[c]	0.382	0.276[d]
1,2,4-triazol-5-yl[e]	0.411	0.286
2-pyridyl[f,g]	0.411	0.302
4-pyridyl[f,g]	0.408	0.299
2-quinolyl[g]		0.313
3-pyridazinyl[h]	0.417	
2-pyrimidyl[h]	0.430	
4-pyrimidyl[h]	0.501	
pyrazinyl[h]	0.446	
N-methylpurin-8-yl[i]	0.536	0.305

[a] The c^{X}_{X} values are smaller than the c^{X}_{Ph} values because of saturation phenomena; the two sets of values are linearly related (refs 13, 15b, and 21). [b] References 14b and 21. [c] Reference 17a. [d] Reference 19. [e] Reference 18. [f] Reference 13a. [g] Reference 16b. [h] Reference 15a. [i] Reference 19.

The table clearly shows that most of the listed azaheterocycles are as strong electron acceptors as common EW primary organic functionalites. In particular, it can be noted that the EW capacity of the thiazolyl ring is comparable to that of an alkoxycarbonyl group. Benzofusion further increases their charge demand: the benzothiazolyl substituent is as powerful as the acetyl group. The benzoxazolyl ring is located in the middle of these two situations. In general, the following trend was found in the EW power of azole derivatives: (a) thiazole > oxazole > imidazole; (b) benzazole > azole. Analogously, six-membered rings such as azines, diazines, and purine are powerful EW systems. The charge demand of the *N*-methylpurin-8-yl was found to be the highest among the investigated azinyl and azolyl substituents and is comparable to that of the strongest classical EW functionalities.

These findings lead to the general expectation that bisheteroarylmethanes **1** (X = azinyl or azolyl substituent) behave as active methylene compounds, showing a reactivity pattern close to that of β-diketones and malonic esters toward electrophilic reagents. Indeed, we have shown that these systems, for instance, bis(benzothiazol-2-yl)methane (**2**) and bis(benzoxazol-2-yl)methane (**3**), do undergo classical electrophilic reactions under mild conditions, including azo-coupling with benzenediazonium chloride, nitrosation, and crotonic-type condensations.[19,23] The highly reactive nature of the central methylene moiety of **1** was also revealed in an additional number of reactions, such as oxidation to carbinols and ketones, dimerization to ethane or ethene derivatives, and metal-promoted coupling reactions.[24]

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(20) One of the reviewers questioned the suitability of the term "charge demand" for describing the ability of a group or substituent in distributing the electron density of a carbanionic carbon into an extended π-array. While we concede that a better term might be "π-charge demand" or "π-electron- withdrawing power" we emphasize that c is a charge, and more specifically a π-charge because of its NMR source. We stress that c provides a static picture of the charge distribution and has little to do with "reactivity" substituent constants such as σ_R^- as previously defined. Values of c and σ_R^- are somewhat linearly related[13] but have a different implication. We thank the reviewer for stimulating us in providing the general reader with a caveat in avoiding any arbitrary use of the π-charge demand c values.

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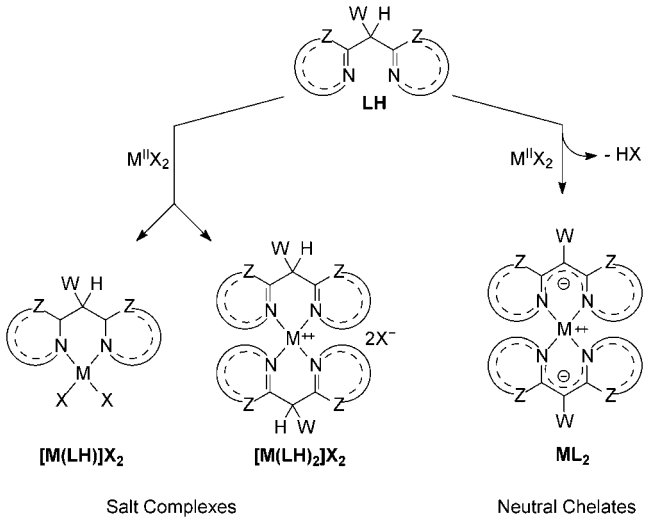
SCHEME 1

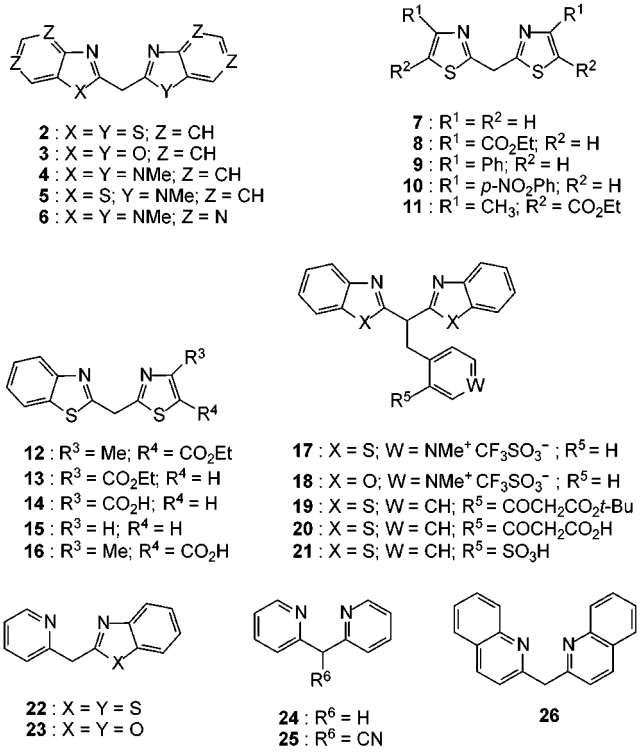


Given the remarkable similar reactivity of bisheteroarylmethanes with β-carbonyl derivatives, it is evident that the $-N{=}C{-}CH_2{-}C{=}N-$ fragment, present in bis-*o*,*o*′-(azaheteroaryl)methanes, becomes particularly interesting since it mimics, in its deprotonated form, the well-known coordinating properties of β-diketonate moieties. These heterocyclic systems can potentially behave as both neutral (LH) and anionic (L^-) nitrogen ligands toward transition-metal ions. In the former case, salt complexes of general formula $[M(LH)_n]^{m+}$ are obtained, whereas the latter should lead to neutral chelates of the type ML_n. The few known examples concerning the coordinating properties of simple bisheteroarylmethanes are basically limited to bis(quinol-2-yl)methane[25] and bis(pyrid-2-yl)methane.[26] However, with very few exceptions,[27] in none of these studies were neutral chelates ML_n reported.

We herein report the first systematic and extensive investigation on the coordinating properties of bisheteroarylmethanes, acting both as neutral ligands LH, to give *salt complexes* $[M(LH)_n]^{m+}$, and as anionic ligands L^-, to afford *neutral chelates* ML_n (Scheme 1).

The latter can be formally obtained by preliminary deprotonation of the ligand LH, followed by metal coordination. To account for the formation of the neutral complexes ML_n, where the ligand is present in its anionic form L^-, the acidity of the $-CHW-$ bridge is expected to play a strategic role, together with the stabilizing energy of the metal−ligand coordination.

We have considered the following bisheteroarylmethane ligands: (A) *symmetrical and asymmetrical bis(benzazolyl)methanes*, bis(benzothiazol-2-yl)methane (**2**), bis(benzoxazol-2-yl)methane (**3**), bis(*N*-methylbenzimidazol-2-yl)methane (**4**), (benzothiazol-2-yl)(*N*-methylbenzimidazol-2-yl)methane (**5**), and bis(7-methylpurin-8-yl)methane (**6**); (B) *unsubstituted and substituted bis(thiazol-2-yl)methanes*, bis(thiazol-2-yl)methane (**7**), bis[4-(ethoxycarbonyl)thiazol-2-yl]methane (**8**), bis(4-phenylthiazol-2-yl)methane (**9**), bis[4-(*p*-nitrophenyl)thiazol-2-yl]methane (**10**), and bis(5-ethoxycarbonyl-4-methylthiazol-2-yl)methane (**11**); (C) *mixed (benzothiazol-2-yl)(thiazol-2-yl)methanes*, (benzothiazol-2-yl)(5-ethoxycarbonyl-4-methylthiazol-2-yl)methane (**12**), (benzothiazol-2-yl)(4-ethoxycarbonylthiazol-2-yl)methane (**13**), (benzothiazol-2-yl)(4-hydroxycarbonylthiazol-2-yl)methane (**14**), (benzothiazol-2-yl)(thiazol-2-yl)methane (**15**), (benzothiazol-2-yl)(5-hydroxycarbonyl-4-methylthiazol-2-yl)methane (**16**); (D) *bis(benzazolyl)methanes functionalized at the methylene bridge*, ligands **17**−**21**; (E) *mixed azine−azole bisheteroarylmethanes*, (pyrid-2-yl)(benzothiazol-2-yl)methane (**22**) and (pyrid-2-yl)(benzoxazol-2-yl)methane (**23**); (F) *azine-based bisheteroarylmethanes*, bis(pyrid-2-yl)methane (**24**), bis(pyrid-2-yl)acetonitrile (**25**), and bis(quinol-2-yl)methane (**26**).



The choice of heteroaromatic ligands was made to elucidate electronic and structural effects in the formation of complexes. Ligands **2**−**6** are expected to lead to stable neutral chelates ML_n, due to the relevant charge demand of the benzazolyl substituents, which should stabilize the anionic structure of the ligand in the complex. In this series, the stabilization of the anionic ligand should reflect the different charge demands of the

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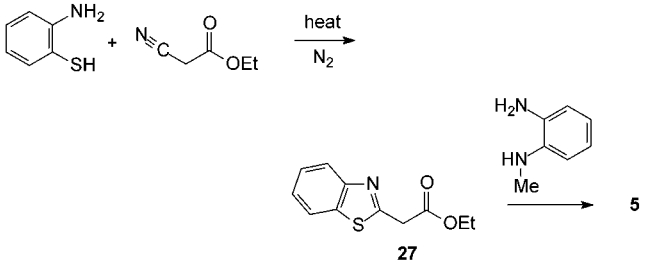
heterocyclic rings, which increases on going from *N*-methylbenzimidazol-2-yl to *N*-methylpurin-8-yl. Similar considerations prompted the design of ligands **7**−**11**, where ring substitution with EW groups should play a stabilizing effect in L^-. Compound $\mathbf{11}^-$ differs from $\mathbf{8}^-$ in the fact that the electron-withdrawing substituent CO_2Et is in a position that is analogous to the benzenoid *para* one with respect to the negative charge on the bridging carbon atom, supplying a more favorable stabilizing delocalization. Following the same reasoning, we have added ligands **12**, **13**, and **15** where the thiazole ring is either unsubstituted or substituted with a strong electron-acceptor group. A number of hydroxycarbonyl-substituted systems, **14** and **16**, and methylene-bridge-functionalized bisbenzazolylmethanes, **17**−**21**, were thus introduced to investigate the formation of chelates with potential additional properties such as improved solubility in protic solvents, a desirable property in view of biodiagnostic applications, and to furnish a convenient linking site for subsequent derivatization in DNA-binding[28] and tumor-targeting[8] applications. Finally, a number of azine-based derivatives, **22**−**26**, were included to compare the azine vs azole coordination properties toward transition metals and the possible steric effect exerted by the six- vs five-membered ring. Again, we have designed different ligands reasoning on electronic effects. The mixed systems **22** and **23** combine the commonly used coordinating properties of the pyrid-2-yl moiety[12] with that of two strong benzazolyl acceptors (see Table 1). Ligands **25** and **26** furnish an additional stabilizing effect in the corresponding conjugate anions with respect to the pyridine derivative **24** due to the presence of a third acceptor group (CN) and a larger charge demand of the azine ring, respectively.

Over the past few years, we have sporadically communicated a number of salt complexes and neutral chelates based on bisheteroarylmethanes. We have preliminarily reported the synthesis and characterization of some complexes afforded by **2**,[29] **3**,[30] **5** and **6**,[19] **25**,[16b] and **26**,[16b] and explored their catalytic activity.[30] X-ray,[29] spectroscopic, and magnetic studies[31] have shown that neutral chelates of **2** and **3** with Ni(II), Cu(II), Co(II), and Zn(II) present a distorted tetrahedral geometry. In the case of the Cu(II) neutral chelate of **2** the data suggested an oligo- or polynuclear structure.[29,31] It is worth noting that most of our previously published chelates have been very recently patented by others in their use as electroluminescent materials.[32]

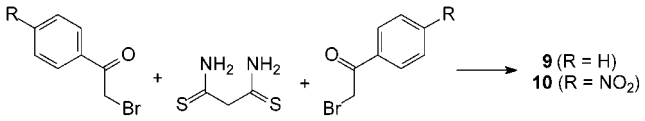
Results

Synthesis of Ligands. We have previously reported the synthesis of bisheteroarylmethanes **4**, **6**−**8**, **11**, and **18**−**21**, and prepared derivatives **2** and **3** according to known methods (see the Experimental Section). All the remaining compounds were previously unknown, with very few exceptions concerning **5**[33] and **19**.[34]

SCHEME 2



SCHEME 3



The mixed benzothiazolyl−benzimidazolyl derivative **5** was obtained according to Scheme 2, where the two heterocycle rings are formed in two subsequent steps. The benzothiazolyl intermediate **27** was prepared by condensation, under neat conditions, of 2-aminothiophenol with ethyl cyanoacetate. The subsequent ring closure to benzimidazole was carried out, with low yields, under conditions similar to those previously used for the synthesis of **4**,[24] with no solvent and distilling off the ethanol formed during the condensation with the aid of a continuous flow of inert gas, to keep the reaction temperature constant at the initial value (160 °C). The crude product was purified by acid−base treatment.

Ring-substituted bis(thiazol-2-yl) derivatives **9** and **10** were conveniently prepared in high yields according to the general Hantzsch[35] thiazole synthesis, by condensing malonodithioamide[23] with the corresponding phenacyl bromides (Scheme 3). We have found that the replacement of DMF, used in the Hantzsch synthesis of **8** (intermediate for **7**),[17a] with the mixture acetone−water (4:1) as a reaction solvent led to higher yields and lower amounts of byproducts. Isolation of the practically pure product is particularly easy for the nitrophenyl derivative, since it readily separates from the reaction mixture thanks to its low solubility in the used solvent. It is worth noting that whereas the parent unsubstituted derivative **7** is liquid at room temperature and rather unstable in air (it must be stored, but only for short periods, under nitrogen and in the cold),[17a] 4-aryl derivatives **9** and **10** are stable, relatively high melting compounds.

Synthesis of the thiazolyl−benzothiazolyl ligand **12** implied conversion of the ester **27** to acetamide **28**, and then to thioacetamide **29**, to apply the Hantzsch route to the formation of the thiazolyl ring, as depicted in Scheme 4. Both intermediates **28**[36] and **29**[37] were re-

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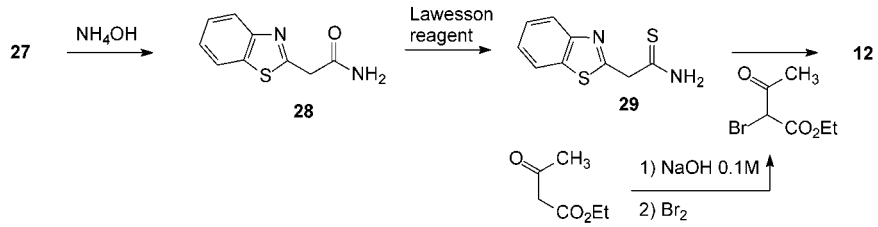
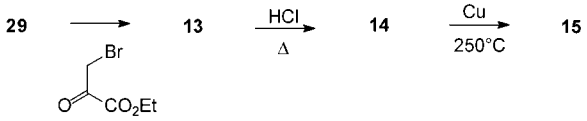
(36) (a) van Dormael, A. E.; de Smet, P. *Chem. Abstr.* **1952**, *46*, 26032. (b) Yakout, E. M. A.; Allam, Y. A.; Nawwar, G. A. M. *Heteroat. Chem.* **1999**, *10*, 177−182.
(37) Elneairy, M. A. A.; Abdel-Rahman, T. M.; Hammad, A. M. *J. Chem. Res., Synop.* **1998**, 684−685.

SCHEME 4



SCHEME 5



ported very few times in the literature. A synthesis of thioamide **29** was only recently communicated, employing the reaction of H_2S with benzothiazol-2-ylacetonitrile.[37] We report here a much more convenient access in good yields to **29** from carboxamide **28** and the simple action of Lawesson's reagent in boiling toluene, avoiding the use of highly toxic hydrogen sulfide. Final ring closure was accomplished by condensation of **29** with ethyl bromoacetoacetate. The use of the commercially available chloroacetoacetate, in different solvents, afforded the product in much less satisfactory yields.

The series of ligands **13**−**15** was prepared by reaction of **29** with ethyl bromopyruvate to give **13** in fair yields. Subsequent acidic hydrolysis of **13** using 10% HCl gave the corresponding carboxylic acid **14** (Scheme 5), which precipitates in the reaction medium and can be easily isolated in good yields. Decarboxylation of **14** upon heating and subsequent distillation under reduced pressure led to the ligand **15** in low yields. In general, thiazole-4-carboxylic acids undergo decarboxylation less easily than the corresponding 2- and 5-isomers,[38] and indeed severe conditions are needed for the decarboxylation of **14**.

All of the attempts to prepare **16** by hydrolysis of **12** failed, as shown in Scheme 6. Therefore, we prepared the system **30**, where the ethoxy group is replaced by the more labile *tert*-butoxy one. In fact, PTSA treatment of **30** in benzene afforded **16** in excellent yields.

Synthetic access to α-heteroarylmethyl-substituted ligands **17** and **18** (Scheme 7) exploited the behavior of bis(benzazol-2-yl)methanes **2** and **3** as active methylene compounds, which makes picolylidene derivatives **31** and **32**, respectively, readily available.[23] Catalytic hydrogenation to picolyl derivatives **33** and **34** and subsequent 100% regioselective alkylation of the pyridine nitrogen with methyl triflate in dry benzene afforded salts **17** and **18**, which can be isolated as crystalline pure analytical samples. When the triflate gegenion is replaced by iodide, isolation of crystalline products is much more tedious and difficult, whereas alkylation with dimethyl sulfate led to mixtures of products, likely due to the simultaneous monoalkylation of the azole nitrogen atoms and polyalkylation side reactions.

The synthetic approach to the mixed pyrid-2-yl−benz-1,3-azol-2-yl derivatives **22** and **23**, shown in Scheme 8, employed the condensation of the commercially available methyl 2-pyridylacetate with *o*-aminothiophenol and *o*-aminophenol, respectively, at ca. 160 °C under neat conditions. Whereas the reaction with *o*-aminothiophenol gave directly the corresponding bisheteroarylmethane **22** in 75% yield, in the case of the oxa analogue condensation led to the isolation of the *o*-hydroxyanilide **35**,[39] which only subsequently could be cyclized to the final product **23** in 50% overall yield using polyphosphoric acid as a condensing agent. The lower yield and higher complexity of the latter procedure are likely due to the instability of the benzoxazole ring under acidic conditions, as described elsewhere.[40] Indeed, the benzoxazole derivative **23** opens back to the anilide **35** in acidic aqueous solution.

Synthesis of Neutral Chelates and Salt Complexes. Tables 2−4 and Tables 5 and 6 collect experimental details and microanalytical data for the preparation and characterization of all of the novel neutral chelates and salt complexes, respectively. Further characterization, including ^{1}H and some ^{13}C NMR spectra of diamagnetic Zn and Pd chelates and UV−vis, MS, and IR data can be found in the Experimental Section.

A key choice concerned the solvent in which to carry out the reaction with metal ions. This factor was found to be critical for the successful obtainment of the neutral and salt complexes and to greatly affect both yields and chelate isolation and purity. Whenever possible, we employed a solvent where the expected chelates are insoluble but the starting inorganic salts and the organic ligands are soluble. Following this approach, microanalytically pure chelates can be readily obtained usually in high yields. Our initial attempts based on a two-phase reaction, where an aqueous solution of the metal acetate was vigorously shaken with a solution of the ligand in either CH_2Cl_2 or $CHCl_3$, afforded, in the organic phase, impure chelates in low yields.

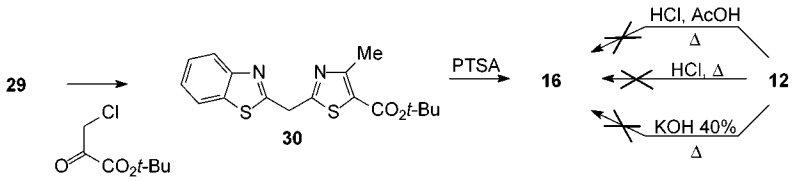
In general, addition of either a methanol or ethanol solution of a metal acetate, $M(OAc)_2 \cdot nH_2O$ (M = Zn, Cu, Ni, Co, Pd), to a solution of ligands **2** (entries 1−5, Table 2), **3** (entries 7−11, Table 2), **11** (entries 5−9, Table 3), and **12** (entries 10−14, Table 3) in the same solvent afforded all of the corresponding neutral chelates. From **2** and $Hg(OAc)_2$ the Hg(II) chelate was also successfully isolated (entry 6, Table 2). The reaction of $M(OAc)_2 \cdot nH_2O$

(38) Katritzky A. R. *Handbook of Heterocyclic Chemistry*; Pergamon Press: Oxford, 1983.

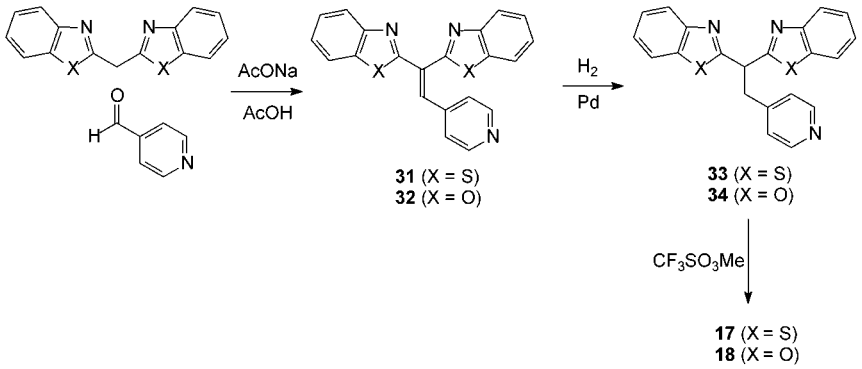
(39) The identification of the condensation product as the isomer *O*-(*o*-aminophenyl)pyrid-2-ylacetate, which would derive from a transesterification reaction, has been excluded on the basis of IR data (1690 cm^{-1}, amidic C=O streching) and solubility in 10% aqueous NaOH.

(40) Sainsbury, M. In *Rodd's Chemistry of Carbon Compounds*; Coffey, S., Ansell, M. F., Eds.; Elsevier: Amsterdam, 1986; Vol. IV, Part C, Chapter 17, p 350.

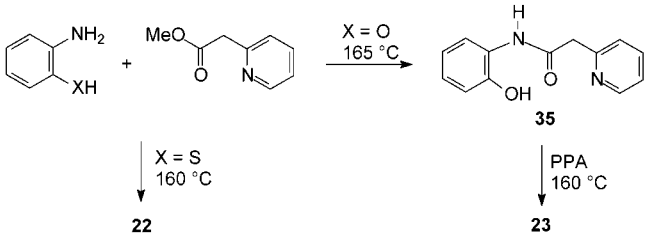
SCHEME 6



SCHEME 7



SCHEME 8



(M = Zn, Cu, Ni, Co) with all of the other ligands in methanol, ethanol, or DMF may or may not lead to the formation of the neutral chelates. We isolated the Zn(II) and Cu(II) chelates of **5** (entries 12 and 13, Table 2) and **13** (entries 1 and 2, Table 4), the Cu(II) and Co(II) chelates of **10** (entries 3 and 4, Table 3), and the Cu(II) chelates of **8** (entry 1, Table 3) and **9** (entry 2, Table 3). Systems **7**, **15**, **22**, and **23** failed to react with any metal acetate, and the unreacted ligand was recovered. The above results confirm that a positive reaction of bisheteroarylmethanes with azaphilic transition-metal acetates gives the corresponding neutral chelates. The only noticeable, but fully explainable, exception is the action of some of the above acetates on ligand **4**, which gives the corresponding salt complexes (entries 1−4, Table 6). In this case we showed[19] that to isolate neutral chelates $M(\mathbf{4}^-)_2$, the presence of a strong base, such as MeONa, is needed.

Reaction of an alcoholic (MeOH or EtOH) solution of a number of metal chlorides, $MCl_2 \cdot nH_2O$ (M = Zn, Cu, Ni, Co, Hg), with a solution of **2** (entries 1−5, Table 5), **3** (entries 7−10, Table 5), **6** (entries 5 and 6, Table 6), **12** (entries 7 and 8, Table 6), **22** (entries 9 and 10, Table 6), and **23** (entry 11, Table 6), generates the corresponding salt complexes. The action of metal sulfates $MSO_4 \cdot nH_2O$ (M = Zn, Cu, Ni, Co) was checked on ligand **2**. They were found to behave somehow between acetates and chlorides. $ZnSO_4$ and $CuSO_4$ afforded the corresponding neutral chelates $Zn(\mathbf{2}^-)_2$ and $Co(\mathbf{2}^-)_2$, whereas $NiSO_4$ gave the salt complex $Ni(\mathbf{2})_2SO_4$ (entry 6, Table 5). Spectroscopic (IR) and microanalytical data suggested that $CuSO_4$ might have afforded a mixture of the two types of complexes.

Attempts to prepare neutral chelates of "hydrophilic" ligands **14**, **16**, and **18**−**21** were performed following the general synthetic protocol depicted above. All of the Zn(II), Cu(II), Ni(II), Co(II), and Pd(II) neutral chelates of **17** (entries 3−7, Table 4) and **18** (entries 8−12, Table 4) were isolated. However, both the ligand and metal acetate should be dissolved in a minimal amount of solvent to allow precipitation of the corresponding chelate, which occurs either immediately or after partial solvent removal. In fact, thanks to the improved ligand solubility in alcohols, their chelates do not readily precipitate and therefore are much more difficult to isolate and purify. Ligand **19** gave both Zn(II) and Pd(II) chelates (entries 13 and 14, Table 4). On the contrary, neutral chelates of hydroxycarbonyl-containing ligands **14**, **16**, and **20** could not be isolated.

Oxidation and Manganese(II)-Promoted Coupling Reactions.[41] We have previously reported[24] that the action of poorly azaphilic transition-metal acetates such as manganese(II), iron(II), and lead(II) on ligands **2**−**4** and **22** promotes their oxidation and/or dimerization reactions instead of leading to the corresponding neutral chelates (Scheme 9). Similarly, the reaction of the highly coordinating ligands **6**, **11**, and **12** with $Mn(OAc)_2 \cdot 4H_2O$ gives rise to variable yields of either pure or mixtures of oxidation/dimerization products **36**−**39**, according to Scheme 10.

Unfortunately, separation and therefore analytical characterization of the oxidation/dimerization products of **6** were not performed due to their poor solubility. ^{1}H NMR spectra of this mixture could not be recorded in

(41) We thank one of the reviewers for pointing out that the formation of the coupling products could be envisioned as occurring via a radical process. See for instance: Newkome, G. R.; Joo, Y. J.; Evans, D. W.; Fronczek, F. R.; Baker, G. R. *J. Org. Chem.* **1990**, *55*, 5714−19. In the original paper we neither investigated the reaction mechanism nor hypothesized any carbanionic intermediate, with the exception of the oxidation to ketones (ref 24).

TABLE 2. Experimental and Analytical Data of Neutral Chelates of Ligands 2−4 with Different Metals

	preparation procedure					product		analytical data				
									EA[a]			notes
entry	LH	mmol	metal salt	mmol	protocol (time)	color	yield (%)	formula	C	H	N	(mp)[b]
1	**2**	5.00	$Zn(OAc)_2{\cdot}2H_2O$	2.50	A (15 min)	yellow	94	$C_{30}H_{18}N_4S_4Zn$	57.08 (57.36)	2.85 (2.89)	8.86 (8.92)	c
2	**2**	1.00	$Cu(OAc)_2{\cdot}H_2O$	0.50	A (15 min)	green	96	$C_{30}H_{18}N_4S_4Cu$	57.26 (57.53)	2.87 (2.90)	8.67 (8.95)	
3	**2**	1.00	$Ni(OAc)_2{\cdot}4H_2O$	0.50	A (30 min)	dark green	78	$C_{30}H_{18}N_4S_4Ni$	57.78 (57.98)	2.97 (2.92)	9.18 (9.02)	d
4	**2**	5.00	$Co(OAc)_2{\cdot}4H_2O$	2.50	A (15 min)	dark purple	68	$C_{30}H_{18}N_4S_4Co$	57.68 (57.95)	2.98 (2.92)	8.79 (9.01)	c
5	**2**	3.00	$Pd(OAc)_2$	1.50	A (30 min)	dark brown	84	$C_{30}H_{18}N_4S_4Pd$	53.25 (53.85)	3.01 (2.71)	8.54 (8.38)	e
6	**2**	2.00	$Hg(OAc)_2$	1.00	A (15 min)	orange	90	$C_{30}H_{18}N_4S_4Hg$	46.72 (47.20)	2.29 (2.38)	7.24 (7.34)	(245)
7	**3**	1.00	$Zn(OAc)_2{\cdot}2H_2O$	0.50	A (15 min)	light brown	85	$C_{30}H_{18}N_4O_4Zn$	64.12 (63.89)	3.31 (3.22)	10.12 (9.93)	
8	**3**	1.00	$Cu(OAc)_2{\cdot}H_2O$	0.50	A (15 min)	blue	89	$C_{30}H_{18}N_4O_4Cu$	63.78 (64.10)	3.30 (3.23)	9.82 (9.97)	
9	**3**	1.00	$Ni(OAc)_2{\cdot}4H_2O$	0.50	A (30 min)	dark green	73	$C_{30}H_{18}N_4O_4Ni$	64.91 (64.66)	3.34 (3.26)	9.93 (10.05)	d
10	**3**	1.00	$Co(OAc)_2{\cdot}4H_2O$	0.50	A (15 min)	red	94	$C_{30}H_{18}N_4O_4Co$	64.68 (64.62)	3.27 (3.26)	9.76 (10.05)	
11	**3**	2.00	$Pd(OAc)_2$	1.00	A (30 min)	red	94	$C_{30}H_{18}N_4O_4Pd$	59.78 (59.56)	3.22 (3.34)	9.25 (9.26)	f
12	**5**	0.20	$Zn(OAc)_2{\cdot}2H_2O$	0.10	A (15 min)	yellow	81	$C_{32}H_{24}N_6S_2Zn$	61.57 (61.78)	3.75 (3.90)	13.37 (13.51)	
13	**5**	0.20	$Cu(OAc)_2{\cdot}H_2O$	0.10	D (1 d)	green	40	$C_{32}H_{24}N_6S_2Cu$	63.56 (61.96)	3.63 (3.91)	13.69 (13.55)	

[a] Calculated values are reported in parentheses. [b] Melting points (°C) are >250 unless indicated in parentheses. [c] These chelates can also be obtained from the corresponding metal sulfates under similar conditions. [d] The reaction was performed at 50 °C. [e] Under nitrogen. [f] This chelate was washed with warm MeOH.

TABLE 3. Experimental and Analytical Data of Neutral Chelates of Ligands 8−12 with Different Metals

	preparation procedure					product		analytical data				
									EA[a]			notes
entry	LH	mmol	metal salt	mmol	protocol (time)	color	yield (%)	formula	C	H	N	(mp)[b]
1	**8**	1.00	$Cu(OAc)_2{\cdot}H_2O$	0.50	B (5 h)	brown	13	$C_{26}H_{26}N_4S_4O_8Cu$	44.02 (43.72)	3.58 (3.67)	7.96 (7.84)	
2	**9**	1.00	$Cu(OAc)_2{\cdot}H_2O$	0.50	D (20 h)	blue	14	$C_{38}H_{26}N_4S_4Cu$	62.38 (62.48)	3.54 (3.59)	7.76 (7.67)	c (160)
3	**10**	1.00	$Cu(OAc)_2{\cdot}H_2O$	0.50	D (2 h)	blue	18	$C_{38}H_{22}N_8O_8S_4Cu$	49.94 (50.12)	2.37 (2.44)	12.12 (12.31)	d
4	**10**	1.00	$Co(OAc)_2{\cdot}H_2O$	0.50	D (2 h)	blue	18	$C_{38}H_{22}N_8O_8S_4Co$	50.61 (50.38)	2.52 (2.52)	12.53 (12.37)	d
5	**11**	2.80	$Zn(OAc)_2{\cdot}2H_2O$	1.40	A (15 min)	orange	79	$C_{30}H_{34}N_4O_8S_4Zn$	46.51 (46.66)	4.13 (4.44)	7.33 (7.29)	c (208)
6	**11**	1.70	$Cu(OAc)_2{\cdot}H_2O$	0.85	A (15 min)	dark green	76	$C_{30}H_{34}N_4O_8S_4Cu$	46.75 (46.77)	4.39 (4.45)	7.00 (7.27)	c (277)
7	**11**	5.00	$Ni(OAc)_2{\cdot}4H_2O$	2.50	A (15 min)	gray	29	$C_{30}H_{34}N_4O_8S_4Ni$	46.83 (47.06)	4.24 (4.47)	7.34 (7.32)	c (202)
8	**11**	1.00	$Co(OAc)_2{\cdot}4H_2O$	0.50	A (15 min)	purple	37	$C_{30}H_{34}N_4O_8S_4Co$	47.20 (47.05)	4.48 (4.48)	7.14 (7.32)	c (208)
9	**11**	1.00	$Pd(OAc)_2$	0.50	A (15 min)	brown	21	$C_{30}H_{34}N_4O_8S_4Pd$	44.71 (44.31)	4.32 (4.21)	7.02 (6.89)	c (247)
10	**12**	1.20	$Zn(OAc)_2{\cdot}2H_2O$	0.60	A (3 h)	red	35	$C_{30}H_{26}N_4O_4S_4Zn$	51.25 (51.45)	3.86 (3.75)	8.22 (8.00)	c (209)
11	**12**	0.80	$Cu(OAc)_2{\cdot}H_2O$	0.40	A (1 h)	brown	86	$C_{30}H_{26}N_4O_4S_4Cu$	51.14 (51.59)	3.80 (3.76)	8.03 (8.02)	c
12	**12**	0.80	$Ni(OAc)_2{\cdot}4H_2O$	0.40	D (24 h)	black	66	$C_{30}H_{26}N_4O_4S_4Ni$	51.66 (51.95)	3.61 (3.78)	8.23 (8.08)	c (210)
13	**12**	0.90	$Co(OAc)_2{\cdot}4H_2O$	0.45	A (3 h)	red	97	$C_{30}H_{26}N_4O_4S_4Co$	51.66 (51.93)	3.67 (3.78)	8.12 (8.08)	c (162)
14	**12**	1.00	$Pd(OAc)_2$	0.50	B (4 d)	brown	27	$C_{30}H_{26}N_4O_4S_4Pd$	48.15 (48.61)	3.24 (3.54)	7.31 (7.56)	c (203)

[a] Calculated values are reported in parentheses. [b] Melting points (°C) are >250 unless indicated in parentheses. [c] In EtOH instead of MeOH. [d] In DMF instead of MeOH.

common deuterated solvents. The IR spectra of the solid arising from the reaction of manganese acetate with **6** shows a typical C=O stretching at 1684 cm^{-1}, suggesting the presence of ketone **36**. However, elemental analysis

TABLE 4. Experimental and Analytical Data of Neutral Chelates of Ligands 13 and 17−19 with Different Metals

	preparation procedure					product		analytical data				
									EA[a]			notes
entry	LH	mmol	metal salt	mmol	protocol (time)	color	yield (%)	formula	C	H	N	(mp)[b]
1	**13**	0.66	$Zn(OAc)_2 \cdot 2H_2O$	0.33	A (30 min)	yellow	28	$C_{28}H_{22}N_4O_4S_4Zn$	50.56 (50.04)	3.57 (3.30)	8.84 (8.34)	c
2	**13**	0.66	$Cu(OAc)_2 \cdot H_2O$	0.33	A (40 min)	green	10	$C_{28}H_{22}N_4O_4S_4Cu$	50.74 (50.17)	3.41 (3.31)	8.68 (8.36)	c
3	**17**	0.40	$Zn(OAc)_2 \cdot 2H_2O$	0.20	C (3 h)	yellow	48	$C_{46}H_{34}F_6N_6O_6S_6Zn$	48.31 (48.52)	3.20 (3.01)	7.23 (7.38)	
4	**17**	0.10	$Cu(OAc)_2 \cdot H_2O$	0.05	D (4 h)	green	59	$C_{46}H_{34}F_6N_6O_6S_6Cu$	48.61 (48.60)	3.31 (3.02)	7.63 (7.40)	c (114)
5	**17**	0.10	$Ni(OAc)_2 \cdot 4H_2O$	0.05	D (5 h)	green	17	$C_{46}H_{34}F_6N_6O_6S_6Ni$	50.12 (48.84)	3.15 (3.03)	7.58 (7.43)	(241)
6	**17**	0.10	$Co(OAc)_2 \cdot 4H_2O$	0.05	D (4 h)	brown-purple	57	$C_{46}H_{34}F_6N_6O_6S_6Co$	48.54 (48.81)	3.28 (3.03)	7.64 (7.43)	c (163)
7	**17**	0.40	$Pd(OAc)_2$	0.20	B (30 min)	light brown	23	$C_{46}H_{34}F_6N_6O_6S_6Pd$	46.67 (46.83)	3.07 (2.91)	7.31 (7.13)	
8	**18**	0.10	$Zn(OAc)_2 \cdot 2H_2O$	0.05	C (15 min)	yellow	45	$C_{46}H_{34}F_6N_6O_{10}S_2Zn$	51.27 (51.42)	3.15 (3.20)	7.70 (7.82)	
9	**18**	0.10	$Cu(OAc)_2 \cdot H_2O$	0.05	C (4 h)	green	57	$C_{46}H_{34}F_6N_6O_{10}S_2Cu$	51.08 (51.51)	2.92 (3.20)	7.75 (7.84)	(210)
10	**18**	0.10	$Ni(OAc)_2 \cdot 4H_2O$	0.05	D (15 min)	green	29	$C_{46}H_{34}F_6N_6O_{10}S_2Ni$	51.94 (51.74)	3.33 (3.22)	7.65 (7.87)	(160)
11	**18**	0.10	$Co(OAc)_2 \cdot 4H_2O$	0.05	D (4 h)	brown	55	$C_{46}H_{34}F_6N_6O_{10}S_2Co$	51.53 (51.73)	3.08 (3.22)	7.64 (7.87)	(162)
12	**18**	0.40	$Pd(OAc)_2$	0.20	A (15 min)	red-brown	78	$C_{46}H_{34}F_6N_6O_{10}S_2Pd$	49.64 (49.53)	3.09 (3.08)	7.72 (7.54)	
13	**19**	0.40	$Zn(OAc)_2 \cdot 2H_2O$	0.20	A (15 min)	yellow	96	$C_{56}H_{50}N_4S_4Zn$	62.73 (62.93)	4.97 (4.73)	5.14 (5.24)	(214)
14	**19**	0.60	$Pd(OAc)_2$	0.30	A (15 min)	light brown	52	$C_{56}H_{50}N_4S_4Pd$	59.97 (60.61)	4.57 (4.55)	4.71 (5.05)	(232)

[a] Calculated values are reported in parentheses. [b] Melting points (°C) are >250 unless indicated in parentheses. [c] In EtOH instead of MeOH.

TABLE 5. Experimental and Analytical Data of Salt Complexes of Ligands 2 and 3 with Different Metals

	preparation procedure					product		analytical data				
									EA[a]			notes
entry	LH	mmol	metal salt	mmol	protocol (time)	composition (color)	yield (%)	formula	C	H	N	(mp)[b]
1	**2**	1.10	$ZnCl_2$	0.55	A (15 min)	$Zn(LH)Cl_2$ (light green)	69	$C_{15}H_{10}Cl_2N_2S_2Zn$	42.93 (43.03)	2.59 (2.41)	7.07 (6.69)	
2	**2**	1.10	$CuCl_2$	0.55	A (15 min)	$Cu(LH)_2Cl_2$ (dark green)	65	$C_{30}H_{20}Cl_2N_4S_4Cu$	51.38 (51.53)	2.99 (2.89)	7.69 (8.01)	
3	**2**	1.10	$NiCl_2$	0.55	B (15 min)	Ni(LH)OHCl (yellow-brown)	96	$C_{15}H_{11}ClN_2OS_2Ni$	45.77 (45.51)	2.82 (2.91)	7.12 (7.33)	
4	**2**	1.10	$CoCl_2 \cdot 6H_2O$	0.55	A (15 min)	$Co(LH)Cl_2$ (blue)	63	$C_{15}H_{10}Cl_2N_2S_2Co$	43.92 (43.70)	2.63 (2.44)	6.73 (6.73)	c
5	**2**	5.00	$HgCl_2$	2.50	A (15 min)	$Hg(LH)Cl_2$ (light green)	13	$C_{15}H_{10}Cl_2N_2S_2Hg$	32.05 (32.52)	2.09 (1.82)	4.78 (5.06)	
6	**2**	2.00	$NiSO_4 \cdot 6H_2O$	1.00	A (15 min)	$Ni(LH)_2SO_4$ (green)	16	$C_{30}H_{20}N_4O_4S_5Ni$	49.67 (50.07)	3.02 (2.81)	7.67 (7.79)	c
7	**3**	1.20	$ZnCl_2$	0.60	A (15 min)	$Zn(LH)Cl_2$ (light yellow)	68	$C_{15}H_{10}Cl_2N_2O_2Zn$	46.27 (46.60)	2.58 (2.56)	7.67 (7.25)	
8	**3**	1.20	$CuCl_2$	0.60	A (15 min)	$Cu(LH)_2Cl_2$ (yellow-brown)	65	$C_{30}H_{20}Cl_2N_4O_4Cu$	56.54 (56.74)	3.00 (3.18)	9.01 (8.83)	
9	**3**	1.20	$NiCl_2$	0.60	C (48 h)	Ni(LH)OHCl (yellow-brown)	92	$C_{15}H_{11}ClN_2O_3Ni$	49.63 (49.84)	2.94 (3.07)	7.50 (7.75)	
10	**3**	1.20	$CoCl_2 \cdot 6H_2O$	0.60	A (15 min)	$Co(LH)_2Cl_2$ (green)	63	$C_{30}H_{20}Cl_2N_4O_4Co$	57.39 (57.15)	3.41 (3.20)	9.32 (8.90)	c

[a] Calculated values are reported in parentheses. [b] Melting points (°C) are >250 unless indicated in parentheses. [c] In EtOH instead of MeOH.

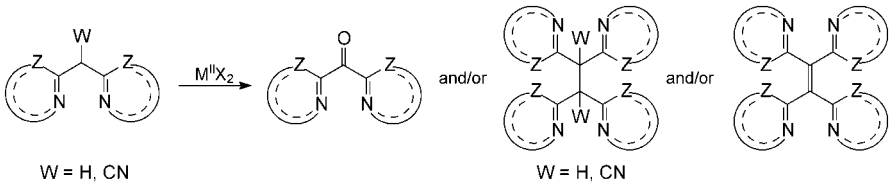
indicates the presence of byproducts, probably arising from coupling and dimerization reactions, which could not be isolated. On the other hand, the reaction of $Mn(OAc)_2$ with the much more soluble systems **11** and **12** gives products which could be investigated in detail. Full analytical, spectroscopic, and mass spectrometric characterization of products **37**−**39** allowed the assignment of the above structures. Compound **11** gives the ethane dimer **37**, whereas from **12** the ketone **38** and dimer **39** can be isolated. Note that, due to the asymmetry of the system **12**, both (*E*)- and (*Z*)-**39** diastereoisomers were clearly detected in solution by ^{1}H NMR, as shown in Figure 1. In contrast to **6** and **12**, the reaction of manganese(II) acetate with **11** does not afford any trace of the corresponding ketone **40**. The latter can be isolated only, leaving **11** to the action of air in a basic

TABLE 6. Experimental and Analytical Data of Salt Complexes of Ligands 4, 6, 12, 22, and 23 with Different Metals

	preparation procedure					product		analytical data				
									EA[a]			notes
entry	LH	mmol	metal salt	mmol	protocol (time)	composition (color)	yield (%)	formula	C	H	N	(mp)[b]
1	**4**	1.00	$Zn(OAc)_2 \cdot 2H_2O$	0.50	A (15 min)	$Zn(LH)(OAc)_2 \cdot 1.5H_2O$ (light green)	35	$C_{21}H_{24}N_4O_5Zn$	52.09 (52.13)	4.71 (5.14)	11.12 (11.58)	
2	**4**	1.00	$Cu(OAc)_2 \cdot H_2O$	0.50	A (15 min)	$Cu(LH)(OAc)_2$ (light blue)	70	$C_{21}H_{22}N_4O_4Cu$	55.31 (55.06)	4.54 (4.85)	12.15 (12.23)	
3	**4**	1.00	$Ni(OAc)_2 \cdot 4H_2O$	0.50	D (12 h)	$Ni(LH)(OAc)_2$ (gray)	39	$C_{21}H_{22}N_4O_4Ni$	55.43 (55.65)	4.62 (4.90)	14.68 (12.36)	
4	**4**	1.00	$Co(OAc)_2 \cdot 4H_2O$	0.50	D (3 h)	$Co(LH)(OAc)_2 \cdot 2H_2O$ (pink)	17	$C_{21}H_{26}N_4O_6Co$	51.64 (51.53)	4.68 (5.36)	12.36 (11.45)	c
5	**6**	0.54	$ZnCl_2$	0.27	E (10 min)	$Zn(LH)_2Cl_2$ (orange)	62	$C_{26}H_{24}Cl_2N_{16}Zn$	44.92 (44.81)	3.48 (3.47)	32.16 (32.16)	
6	**6**	0.54	$CuCl_2$	0.27	E (10 min)	$Cu(LH)_2Cl_2$ (light green)	14	$C_{26}H_{24}Cl_2N_{16}Cu$	44.92 (44.93)	3.49 (3.48)	32.25 (32.24)	
7	**12**	0.56	$ZnCl_2$	0.28	A (15 min)	$Zn(LH)Cl_2$ (yellow)	39	$C_{15}H_{14}Cl_2N_2O_2S_2Zn$	40.15 (39.68)	3.08 (3.10)	6.41 (6.16)	c
8	**12**	1.10	$CuCl_2$	0.55	A (15 min)	$Cu(LH)_2Cl_2$ (green)	24	$C_{30}H_{28}Cl_2N_4O_4S_4Cu$	47.18 (46.71)	3.27 (3.66)	7.55 (7.26)	c
9	**22**	1.00	$ZnCl_2$	0.50	A (15 min)	$Zn(LH)Cl_2$ (white)	65	$C_{13}H_{10}Cl_2N_2SZn$	43.57 (43.06)	3.05 (2.78)	7.63 (7.73)	
10	**22**	1.00	$CuCl_2$	0.50	B (2 h)	$Cu(LH)Cl_2$ (green)	44	$C_{13}H_{10}Cl_2N_2SCu$	43.79 (43.28)	3.15 (2.79)	8.01 (7.77)	
11	**23**	0.80	$ZnCl_2$	0.40	A (15 min)	$Zn(LH)Cl_2$ (light yellow)	86	$C_{13}H_{10}Cl_2N_2OZn$	45.21 (45.06)	3.04 (2.91)	7.83 (8.09)	

[a] Calculated values are reported in parentheses. [b] Melting points (°C) are >250 unless indicated in parentheses. [c] In EtOH instead of MeOH.

SCHEME 9



MeONa/MeOH solution (Scheme 11). A similar result was obtained for ligand **2**.

Discussion

Structure of Neutral Chelates: Multinuclear NMR Investigation. Multinuclear NMR data provide unequivocal evidence of the existence of the ligand as an anionic species, L^-, in the neutral chelates ML_2. Table 7 collects relevant ^1H, ^{13}C, and ^{15}N shifts of ligands **2**−**6**, **11**, **12**, **25**, and **26** and of the corresponding Zn(II) neutral chelates. For comparison, NMR data of solvent-separated ion pair sodium carbanions $\mathbf{2}^-$, $\mathbf{3}^-$, $\mathbf{6}^-$, $\mathbf{25}^-$, and $\mathbf{26}^-$ ($L^-//Na^+$) are also reported. ^1H NMR data clearly show the formation of neutral chelates. The methylene (ligand) → methine (chelate) conversion of the bridge after complexation is evident from both ^1H NMR integration (bridge versus ring protons) and the low-field shift of the −CH− resonance compared to the $-CH_{2-}$ resonance. The close similarity of both the −CH− bridge and ring carbon ^{13}C NMR shifts and $^1J(CH)$ coupling constants of $L^-//Na^+$ and the corresponding ZnL_2 (shown in Figure 2 for L = **3**) is further evidence that all of the ligands are present in the chelates as anions. Note that the π-electronic distribution of the carbon framework of the anionic ligands, as derived from ^{13}C NMR data, is almost identical to that of "free" carbanions in DMSO. This is peculiar in view of the large different properties and reactivity of these two classes of compounds. Finally, ^{13}C NMR spectra of the asymmetric ligand **12** and of the corresponding Zn(II) and Pd(II) chelates (Figure 3) provide insights into the structures of these chelates. The comparison of the two metal complex spectra is clear evidence of the different ligand arrangement around the metal center. We reported that the four-coordinated Zn(II) chelate of **2** is tetrahedral[29] and, accordingly, $Zn(\mathbf{12}^-)_2$ is a mixture of two enantiomers, giving rise to a single set of ^{13}C NMR resonances. Conversely, four-coordinated Pd(II) complexes, such as those of many diketonates, are known to be square planar,[42] and indeed the Pd(II) chelate of **12**, exhibiting two set of resonances with different intensities, provides evidence of the presence of two diastereoisomers in different ratios. Similar conclusions can be drawn by looking at the corresponding proton NMR spectra.

N-Coordination in the neutral chelates is also strongly supported by the ^{15}N NMR chemical shifts, which show a significant difference (30−60 ppm) with respect to the ligand anion. The ^{15}N NMR shifts of the neutral systems compared to the corresponding anions exhibit high-field displacements. These resonances are further high-field-shifted in the neutral chelates. Figure 4 shows the $^1H-^{15}N$ HETCOR NMR spectrum of ligand **5** and of its Zn(II) neutral chelate. Both azine nitrogen atoms (N(1) and N(2)) and the pyrrole-like nitrogen (N(3)) can be clearly

(42) (a) Cotton, F. A.; Wilkinson, G.; Murillo, C. A.; Bochmann, M. *Advanced Inorganic Chemistry*; Wiley: New York, 1999. (b) Thornton, D. A. *Coord. Chem. Rev.* **1990**, *104*, 173−249.

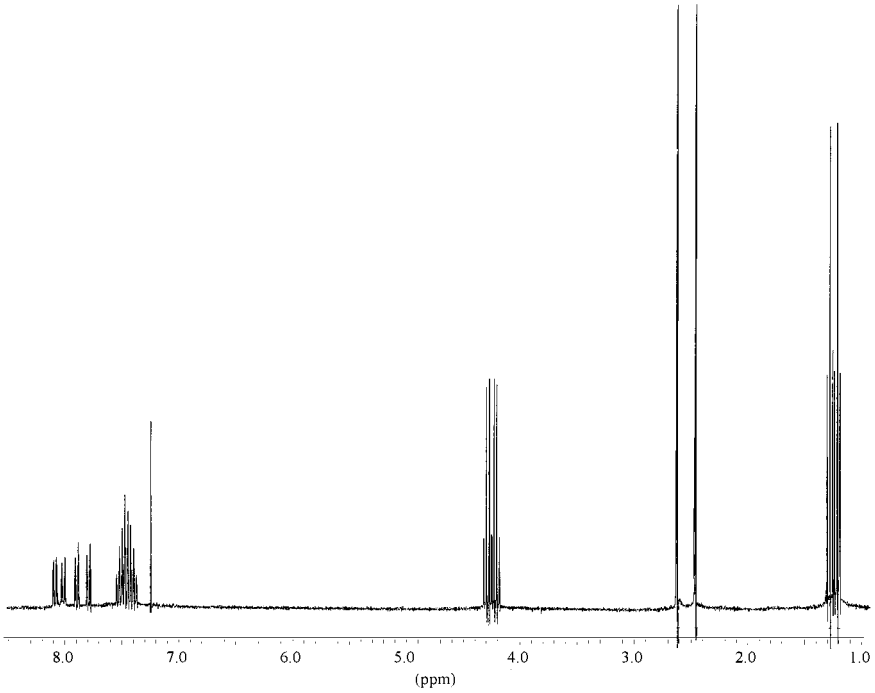
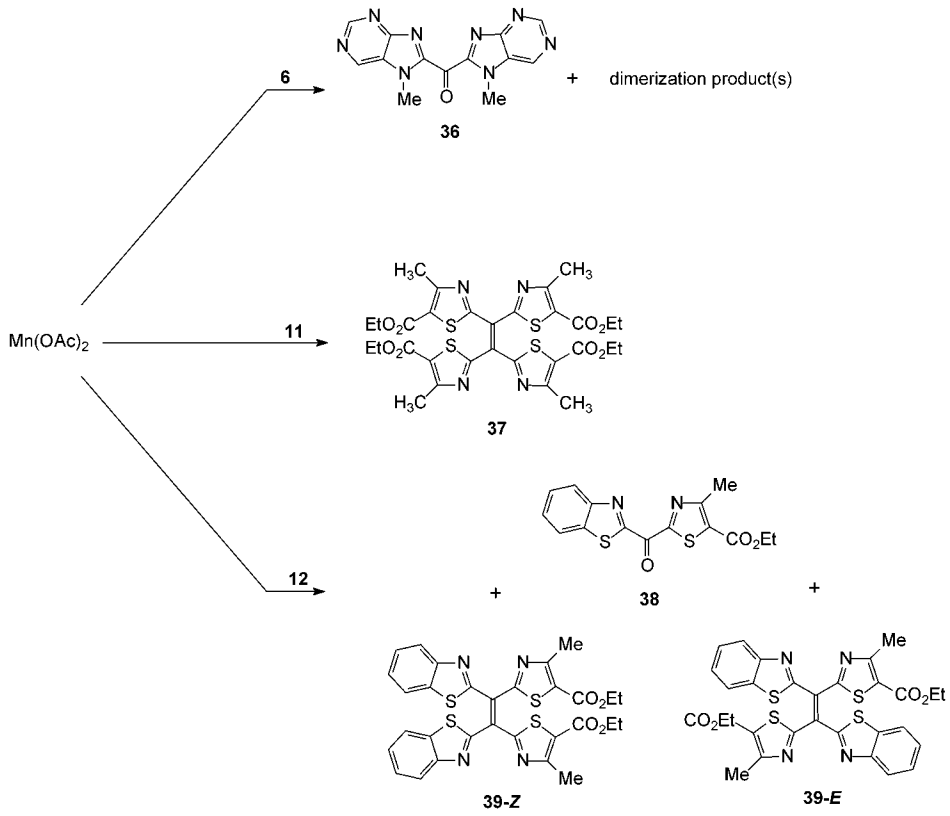


FIGURE 1. ^{1}H NMR spectrum of the (*E*)- and (*Z*)-dimers of **12** in $CDCl_3$.

SCHEME 10



detected. Our results on a series of pyridyl-based carbanions and nitroanions showed that the increase of π-electron density on an sp^2 nitrogen atom conjugatively linked to the anionic site is responsible for its high-field-shifted ^{15}N NMR signal.[43] Conversely, an increased σ-electron density resident on the nitrogen sp^2 orbital coplanar with the ring has an opposite effect. Since the sp^2 electron pair on the nitrogen atom is donated to the metal center in the neutral chelates, the net result is a decreased σ-electron density, which leads to a further high-field displacement of the ^{15}N shifts in the chelates

(43) (a) Barchiesi, E.; Bradamante, S. *J. Phys. Org. Chem.* **1990**, *3*, 139−142. (b) Bradamante, S.; Pagani, G. A. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1055−1061.

SCHEME 11

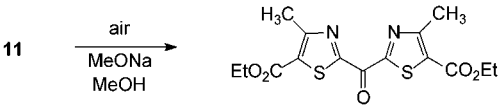


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TABLE 7. Selected ^{1}H, ^{13}C, and ^{15}N NMR Data of Ligands 2−6, 11, 12, 25, and 26, Some of the Corresponding Anions, and Zn(II) and Pd(II) Neutral Chelates

compd	solvent	$\delta(^{13}C)$ (CH_2/CH)	$\delta(^1H)$ (CH_2/CH)	^1J(CH)	$\delta(^{15}N)^a$	notes
2	DMSO-d_6	37.78	4.94	133.8	311.2	b, c
2$^-$	DMSO-d_6	81.42		165.0	241.3	c
Zn(**2**$^-$)$_2$	$CDCl_3$	80.65	5.99	157.8	185.5	d, e
3	DMSO-d_6	28.58	4.68	133.8	245.7	c
3$^-$	DMSO-d_6	55.81		160.0	187.1	c
Zn(**3**$^-$)$_2$	DMSO-d_6	58.90	5.46	169.0	152.9	
Pd(**3**$^-$)$_2$	$CDCl_3$	61.65	5.24	172.1	171.0	
4	DMSO-d_6	26.73	4.68	131.1	242.2	c
Zn(**4**$^-$)$_2$	$CDCl_3$	53.53	4.60	156.7	154.6	
5	$CDCl_3$	33.62	4.82	131.8	309.1, 242.0	
Zn(**5**$^-$)$_2$	$CDCl_3$	68.33	5.41	160.5	178.2, 159.4	
6	DMSO-d_6	26.88	4.93	131.8	246.0	f
6$^-$	DMSO-d_6	60.12		153.4	202.5	f
Zn(**6**$^-$)$_2$	DMSO-d_6	60.02	5.28	153.7		f, g
11	$CDCl_3$	37.49	4.60	133.3	328.6	
Zn(**11**$^-$)$_2$	$CDCl_3$	82.09	5.78	162.7	209.1	
12	$CDCl_3$	38.20	4.80	132.9		
Zn(**12**$^-$)$_2$	$CDCl_3$	81.38	5.87	163.5		
Pd(**12**$^-$)$_2$	$CDCl_3$	87.23, 87.25	5.62	167.1		h
25	DMSO-d_6	66.42			315.0	i
25$^-$	DMSO-d_6	68.03				g, i
Zn(**25**$^-$)$_2$	$CDCl_3$	70.00				g, i
26	DMSO-d_6	47.78	4.75	132.1	307.4	b, i
26$^-$	DMSO-d_6	93.61		149.2	265.6	i, j
Zn(**26**$^-$)$_2$	$CDCl_3$	93.07	5.55	155.1		g, i

^{a} Azine nitrogen(s). ^{b} ^{1}H NMR in $CDCl_3$. ^{c} From ref 17a. ^{d} ^{15}N NMR in THF-d_8. ^{e} From ref 29. ^{f} From ref 19. ^{g} ^{15}N shifts not available due to low solubility. ^{h} Mixture of two isomers. ^{i} From ref 16b. ^{j} Major isomer.

compared to that of the "free" anionic ligands. Therefore, coordination at the nitrogen atom can also be efficiently monitored by ^{15}N NMR spectroscopy.

Formation of Neutral Chelates vs Salt Complexes. The reaction leading to neutral chelates, simply carried out using a neutral ligand and a metal acetate as starting partners, can in principle occur along two routes (Scheme 12). Since the reaction is carried out in a one-pot sequence, we do not know whether the generic ligand **1** is first deprotonated to **1**$^-$ and, only subsequently, metal coordination occurs (route A) or the ionic complexes $[M(LH)_n]^{2+}$ are the intermediates in the formation of the neutral chelates ML_2 (route B). The experimental procedure would discard the hypothesis that the weak acetate base is able to deprotonate bisheteroarylmethanes **1**, which are in no doubt much less acidic than acetic acid. Therefore, it is more likely that deprotonation occurs at some intermediate stage: after that coordination to the metal center has taken place. This metal-coordinated intermediate, which can reasonably be identified as the salt complexes obtained in the reaction with other metal salts such as chlorides, is somewhat more acidic than the ligand itself, and could be deprotonated by the acetate anion.

To confirm this hypothesis, we submitted the salt complex $[Zn(\mathbf{2})]Cl_2$ to the action of the acetate base by using two different stoichiometries, to take into account the different molar ratios in ligand and metal in the salt complex $[Zn(\mathbf{2})]Cl_2$ and in the neutral ligand Zn(**2**$^-$)$_2$ (Scheme 13). In the first stoichiometry (reaction A) 50% of the salt complex is necessarily disrupted to free the second molecule of ligand to be embedded into the neutral chelate Zn(**2**$^-$)$_2$. Alternatively (reaction B) a second molecule of free ligand **2** can be added as reactant. In both cases, the neutral chelate was successfully obtained in very high yields, thus supporting the above considerations. It should be noted, however, that when the acceptor properties of the heteroaromatic substituents are not strong enough to provide efficient delocalization of the negative charge in the anionic ligand L$^-$ (vide infra), even the acetates of the salt complexes cannot be deprotonated to chelates, as found for ligand **4**.

Charge-Demand-Dependent Formation of Neutral Chelates. Although we have investigated the formation of many salt complexes, we were particularly interested in the analogy with the important β-diketonate chelates, where the ligand is anionic and the overall charge of the coordination compound is neutral. In particular, we focused our attention on the search for a relationships between the formation of neutral chelates ML_2 and the π-electron-acceptor properties of the anionic heteroaromatic ligand **1**$^-$, exemplified by their charge demands listed in Table 1. For this reason, our final aim was far from providing a complete and exhaustive compilation of the coordinating properties toward a high number of transition metals, but rather to investigate the coordinating properties with a proper set of ions, depending on the charge demand values and expected formation of neutral chelates containing the ligand in its anionic form.

Our data clearly show that the π-electron delocalization of the anionic ligand in the neutral chelates plays a strategic role in the formation and stability of the latter. These results are summarized in Charts 1−3. Ranking of charge demand values provides evidence that the capacity of the heterocyclic ring to delocalize an adjacent negative charge is the key factor for determining the stability of the anionic ligand in the neutral chelate and, therefore, their formation. We have decided to investigate in more detail the benzothiazolyl and benzoxazolyl derivatives **2** and **3**, respectively, not only for their ease of formation, but also because the charge demand of the corresponding heterocyclic substituents is ranked middle to high and comparable to that of the ester and ketone functionalities. Both ligands are able to form neutral chelates with most of the divalent transition metals we have considered (Chart 1A). Nonetheless, in the reaction with Mn(II), Fe(II), and Pb(II) no chelate was observed but rather the formation of dimerization and/or oxidation products[24] or the recovery of the unreacted ligand. The higher charge demand of the benzothiazolyl ring with respect to the benzoxazolyl ring is experimentally evidenced by the successful formation, in the former, and unsuccessful formation, in the latter, of the Hg(II) neutral chelate. The purinyl substituent, to which the largest charge demand among the heterocycles listed in Table 1 has been associated, was expected to provide ligand **6** with high reactivity toward transition metals, resulting

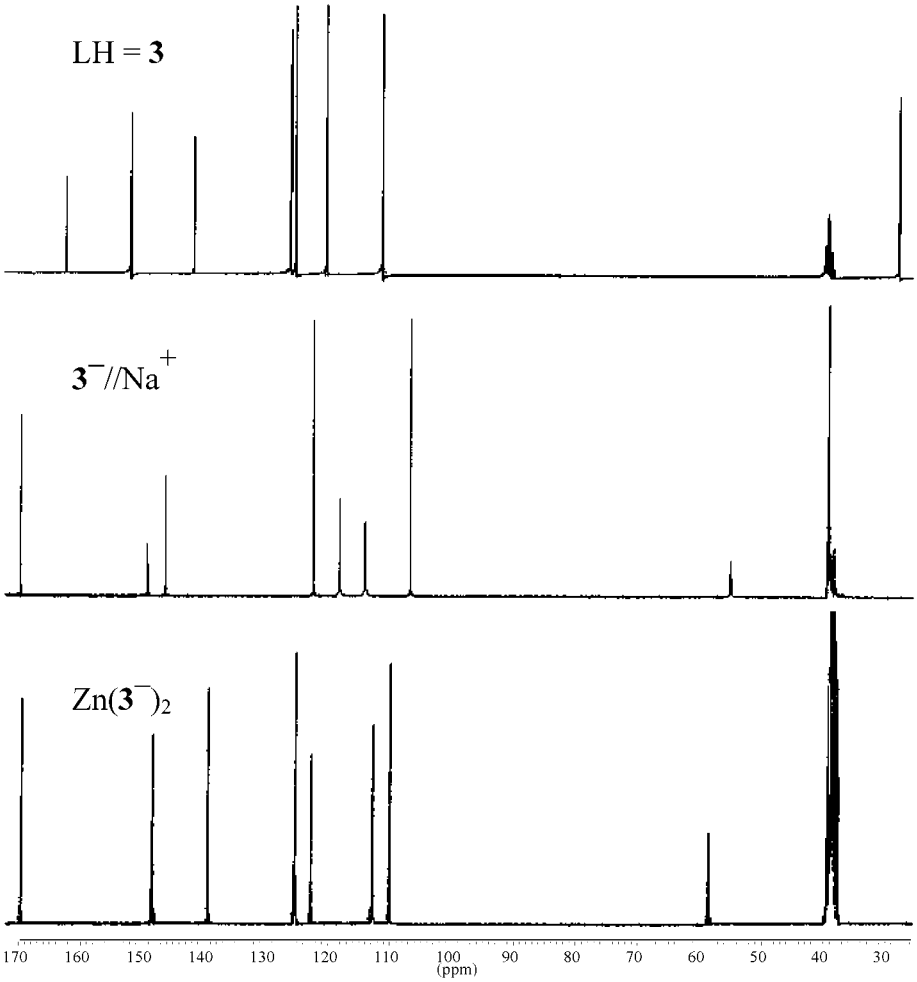


FIGURE 2. ^{13}C NMR spectra of ligand **3** and the corresponding anion $\mathbf{3}^-$ and Zn(II) neutral chelate in DMSO-d_6 at 25 °C.

in the easy formation of the corresponding neutral chelates. Indeed, chelates with a number of metal ions were promptly obtained, and further investigation on this ligand was not considered essential for our purposes. Replacing one and then both benzothiazolyl rings in **2** with the weaker acceptor benzimidazolyl ring, to give ligands **5** and **4**, respectively, correctly decreases the stability of the anionic ligand in ML_2, as probed by the unsuccessful reaction with divalent ions such as Co(II) and Ni(II), under the same conditions where **2**, **3**, and **6** gave ready formation of the corresponding chelates.

The same conclusions are drawn by looking at the data in Chart 1B, where the stability of the anionic ligand L^- in ML_2 is now independent of the charge demand values listed in Table 1 and relies on simple, but unambiguous, considerations based on the position and commonly known EW strength of ring substituents. With this reasoning, we have compiled a qualitative ranking of the EW power of the thiazolyl groups in the series **7**−**11**. Once again, a definitive relationship between the formation of neutral chelates ML_2 and the ability of the heterocyclic substituents to delocalize the central carbanionic negative charge is clearly obtained. The most effective ligand is undoubtedly compound $\mathbf{11}^-$, where the ethoxycarbonyl acceptor group is placed in the *para* position with respect to the carbanionic center and can efficiently delocalize the negative charge. Ligand **11** is somehow comparable to **12** from the electronic point of view. Although the thiazole charge demand is lower than that of benzothiazole, it is quite straightforward to imagine that the presence of the acceptor CO_2Et in position 5 increases the EW capacity to a value comparable to that of the benzo-fused ring. Indeed, we found that the capacity to bind metal ions in neutral chelates ML_2 is almost identical in the compounds **11**, **12**, and **2**. On the opposite end, the parent thiazolyl derivative **7** does not lead to any formation of neutral chelates, in accord with the expected lower charge demand of the heterocycle. The remaining ligands **8**−**10**, **13**, and **15** present an intermediate behavior, as predicted by looking at the acceptor properties of the methylene substituents. Consistently, very few, or no, neutral chelates were obtained. Note how the trend of ion coordination dependence on π-acceptor properties is found for subseries of systems with different structures. For instance, the relative behavior within the pair **8**−**7** can also be found for the benzothiazole-based pair **13**−**15**. The "reproducibility" of these results and the use of more than one azolyl framework provide a check for the accuracy of the obtained data and suggest a general validity of these conclusions.

The reactivity of ligands **22**−**26** with metal ions to form neutral chelates is somewhat more complex (Chart 2). In these systems either one or both five-membered rings

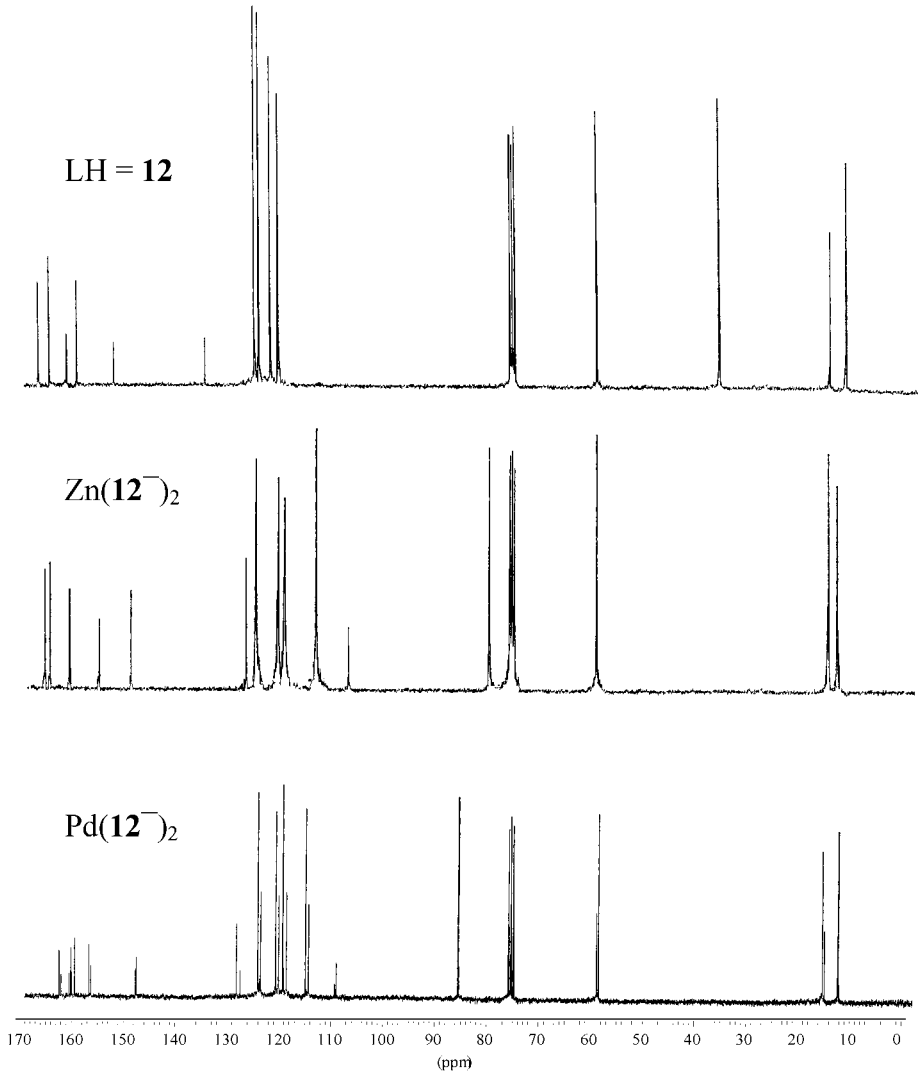


FIGURE 3. ^{13}C NMR spectra of ligand **12** and the corresponding Zn(II) and Pd(II) neutral chelates in $CDCl_3$ at 25 °C.

are sequentially replaced by a six-membered azinyl group. The charge demand of the pyrid-2-yl substituent is lower than that of benzothiazole and benzoxazole but much higher than that of benzimidazole. Therefore, the capacity of the heterocyclic rings in **22** and **23** to efficiently delocalize the negative charge in the corresponding deprotonated ligands L^- should be ranked between those of **2** and **3** and that of **5**. Despite this expectation, ligands **22** and **23** do not form neutral chelates. We believe that this behavior could be ascribed to an additional structural factor associated with the six-membered geometry, which can result in an increased steric hindrance around the metal center in the chelate or a less favorable spatial arrangement of the two nitrogen coordinating sites. The available experimental data for ligands **24**−**26**,[16b] also reported in Chart 2, support this hypothesis. No chelates were obtained for the neutral bis(quinol-2-yl)methane (**26**) in the same conditions where five-membered ligands **2** and **3** easily react with metal acetates. The Zn(II) chelate of **26** was obtained only when NaOH or MeONa was added to the reaction mixture. An even lower reactivity was observed for the pyrid-2-yl ligand **24**, but the presence of the cyano group on the methine bridge of **25** is apparently sufficient to increase the stability of the corresponding anion $\mathbf{25}^-$ in the Zn(II), Cu(II), and Pd(II) neutral chelates. Also it should be noted that anions $\mathbf{24}^-$ and $\mathbf{26}^-$ exist as a mixture of geometric isomers (Scheme 14), as ascertained by multinuclear NMR and computational investigation.[16b] To form coordination compounds, the (*E*,*E*)- and (*E*,*Z*)-isomers must first convert to the geometrically favorable (*Z*,*Z*)-conformer, through an energy barrier of ca. 10 kcal mol^{-1}.[16b]

Synthesis of Water-Soluble Chelates. The obtainment of water-soluble bisheteroarylmethane-based neutral chelates was exploited, keeping in mind the excellent ligand properties exhibited by **2** and **3**. Therefore, these systems were considered the natural candidates of where to introduce moieties containing solubilizing groups such as *N*-methylpyridinium (ligands **17** and **18**), hydroxycarbonyl (ligand **20**), and sulfonyl (ligand **21**). Chart 3 summarizes their coordinating capacities together with those of the hydroxycarbonyl-containing systems **14** and **16**. Indeed, systems **17** and **18** afforded all of the expected neutral chelates. These results mean that both alkyl fuctionalization at the methylene bridge and the pyridinium substituent do not affect the ability of the **2** and **3** cores to coordinate transition-metal ions. A similar

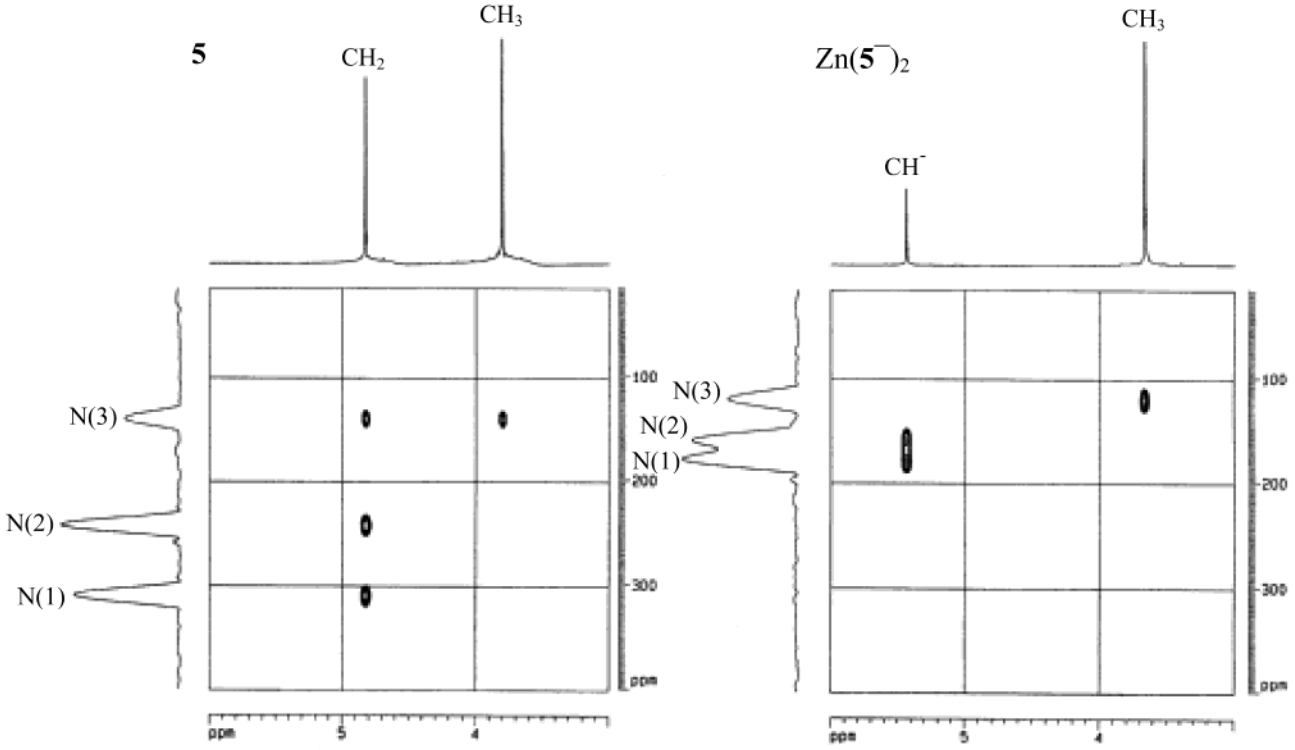
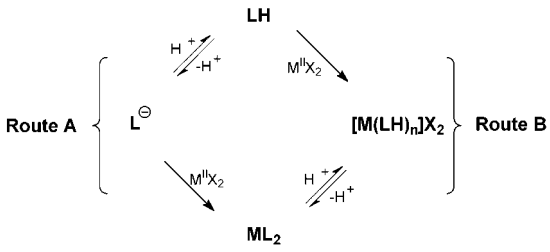


FIGURE 4. $^{1}H-^{15}N$ HETCOR NMR spectra of ligand **5** and its Zn(II) neutral chelate in $CDCl_3$ at 25 °C.

SCHEME 12



SCHEME 13

(A) 2 [Zn(**2**)]Cl_2 + 2 AcONa $\xrightarrow[\text{rt}]{\text{EtOH}}$ Zn($\mathbf{2}^-$)$_2$ + 2 AcOH + 2 NaCl + $ZnCl_2$ (82%)

(B) [Zn(**2**)]Cl_2 + **2** + 2 AcONa $\xrightarrow[\text{rt}]{\text{EtOH}}$ Zn($\mathbf{2}^-$)$_2$ + 2 AcOH + 2 NaCl (91%)

behavior was observed for ligand **19** (precursor of **20**), which further confirms the first of the above results. All of the **17** and **18** neutral chelates are quite soluble in water (up to 0.01 M), and both their formation and pH-dependent stability were investigated by UV−vis spectroscopy.[44] On the opposite side, we have no clear evidence of the behavior of ligands **14**, **16**, **20**, and **21** toward transition-metal ions. The reactions of these systems with metal acetates in either degassed MeOH or water afford quite insoluble precipitates. Microanalytical data of the collected solids disagree with neutral chelate empirical formulas and with those of any reasonable derivatives. When soluble, the ^{1}H NMR spectra of the Zn(II)-containing compounds do not provide any useful information to clarify the molecular structure. We believe that the hydroxycarbonyl group competes with the −N═C−C−C═N− moiety in binding the metal center (Scheme 15).

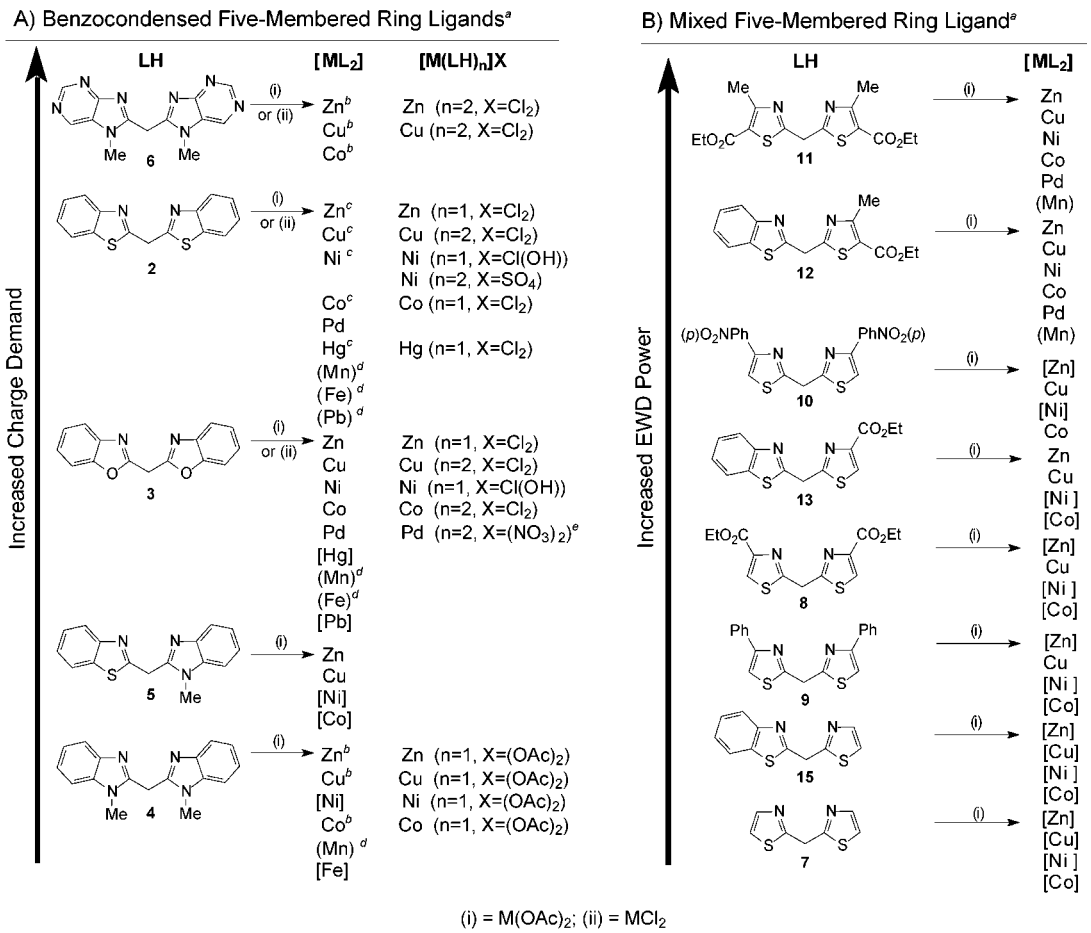
The result is probably the consequence of the formation of polymeric mixed *N*-chelates/carboxylate salts, difficult to characterize. This hypothesis is strongly supported by the evidence that the starting ligands can be recovered by treating these solids with dilute hydrochloric acid.

Conclusion

The present extensive investigation on the coordinating properties of bisheteroarylmethanes toward transition metals expands our long-term study on the synthesis, π-electron distribution, and reactivity of this important class of heteroaromatic systems. We here provide abundant and definitive evidence of the behavior of these compounds as aromatic aza analogues of β-dicarbonyl derivatives, one of the most important building blocks in organic chemistry. We have already documented their behavior as "active methylene compounds" in the reaction toward electrophiles.[23] In this work we show that several bisheteroarylmethanes, based on 1,3-azolyl and azinyl rings, are able to react with a variety of divalent transition metals, affording salt complexes and neutral chelates. The successful formation of neutral chelates, where the ligand is present in its anionic form, is mostly dependent on electronic parameters, associated with the charge demand of the heterocyclic substituents. Therefore, detailed and quantitative knowledge of the EW capacity of heterocyclic systems allows prediction of the formation of neutral chelates, a class of compounds that could have a great potential interest in a number of

(44) Abbotto, A.; Facchetti, A.; Pagani, G. A. University of Milano-Bicocca, Italy, unpublished results.

CHART 1. Ligand Properties of Systems 2−6 (A) and 7−13 and 15 (B)



[a] This work unless otherwise indicated. Metal in parentheses means that dimerization and/or oxidation product(s) were recovered. Metal in brackets means that no reaction was observed and the ligand was recovered. [b]Reference 19. [c]Neutral chelates were communicated in ref 29. [d]Reference 24. [e]Reference 30.

important technological and biodiagnostic fields, in addition to material science. The use of different heterocyclic frameworks and the consistency of experimental results within different sets of systems suggest a general applicability of this approach to the investigation and prediction of the coordinating properties of other aromatic and aliphatic nitrogen ligands based on π-acceptor moieties.

Experimental Section

Extracts were dried over Na_2SO_4. Anhydrous toluene was prepared by distillation over sodium sand, in the presence of benzophenone and under nitrogen, until the blue color of sodium ketyl was permanent. Benzene was dried over Na_2SO_4 or Drierite for a few days. Melting points are uncorrected. In the NMR data, coupling constants J are given in hertz.

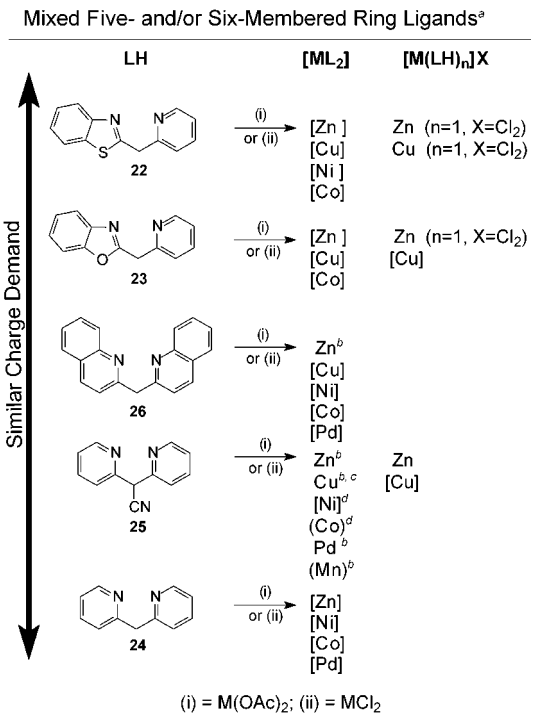
Synthesis of Ligands. Bis(benzothiazol-2-yl)methane (**2**),[45] bis(benzoxazol-2-yl)methane (**3**),[46] bis(*N*-methylbenzimidazol-2-yl)methane (**4**),[24] bis(7-methylpurin-8-yl)methane (**6**),[19] bis(thiazol-2-yl)methane (**7**),[17a] bis[4-(ethoxycarbonyl)thiazol-2-yl]methane (**8**),[17a] bis(5-ethoxy-4-methylthiazol-2-yl)methane (**11**),[23] *O*-{*o*-[β,β-bis(benzothiazol-2-yl)]ethyl}phenylglycolic acid *tert*-butyl ester (**19**),[24] *O*-{*o*-[β,β-bis(benzothiazol-2-yl)]ethyl}-phenylglycolic acid (**20**),[24] and *o*-[β,β-bis(benzothiazol-2-yl)-ethyl]benzenesulfonic acid (**21**)[24] were prepared according to the literature.

Ethyl 2-Benzothiazolylacetate (27). A mixture of ethyl cyanoacetate (6.00 g, 53.0 mmol) and 2-aminothiophenol (6.63 g, 53.0 mmol) was stirred for 2 h at 120 °C under a nitrogen atmosphere. After the mixture was cooled to room temperature, the product was obtained practically pure as a yellow oil (11.07 g, 50.0 mmol, 94%), and used without further purification in the next step. An analytical sample was purified by Kugelrohr distillation: bp 180 °C (0.6 mmHg) (lit.[47] bp 90−95 °C (0.1 mmHg)); ^{1}H NMR ($CDCl_3$) δ 8.02 (d, 1H, J = 8), 7.88 (d, 1H, J = 8), 7.47 (t, 1H, J = 8), 7.39 (t, 1H, J = 8), 4.25 (q, 2H, J = 7.2), 4.16 (s, 2H), 1.30 (t, 3H, J = 7.2). Anal. Calcd for $C_{11}H_{11}NO_2S$: C, 59.70; H, 5.02; N, 6.33. Found: C, 59.54; H, 4.99; N, 6.53.

(Benzothiazol-2-yl)(*N*-methylbenzimidazol-2-yl)-methane (5). A mixture of *N*-methyl-*o*-phenylenediamine[24] (1.86 g, 15.2 mmol) and **27** (3.37 g, 15.2 mmol) was refluxed for 6 h at 160 °C under nitrogen. The EtOH formed in the reaction was continuously distilled off to keep the refluxing temperature at the initial value. The dark brown residue was taken up with diethyl ether, leading to a yellow solid which was separated by filtration and treated with 20% aqueous HCl (300 mL). The acid solution was treated with decolorizing activated charcoal, filtered off, and neutralized with a satu-

(45) Rai, C.; Braunwarth, J. B. *J. Org. Chem.* **1961**, *26*, 3434−3445.
(46) Rai, C.; Braunwarth, J. B. U. S. Patent 3,250,780; *Chem. Abstr.* **1966**, *65*, 7180g.
(47) Klemm, L. H.; Johnstone, S.; Tran, L. K. *J. Heterocycl. Chem.* **1989**, *26*, 1519−1522.

CHART 2. Ligand Properties of Systems 22−26



[a] This work unless otherwise indicated. Metal in parentheses means that dimerization and/or oxidation product(s) were recovered. Metal in brackets means that no reaction was observed and the ligand was recovered. [b]Reference 16b. [c]The dimer was also isolated. [d]Stoppa, F. Laurea Thesis, University of Milano, Italy, 1994.

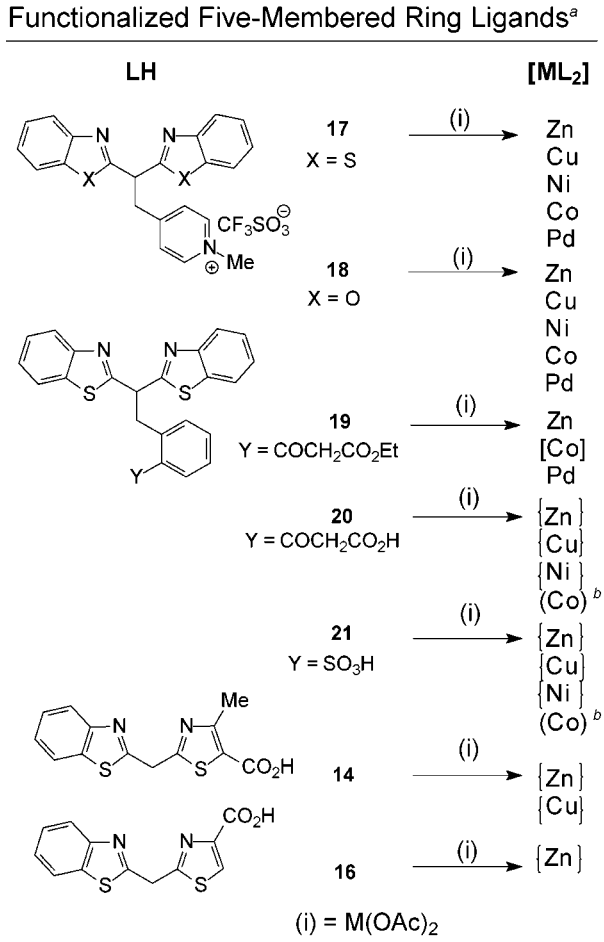
rated $NaHCO_3$ aqueous solution to give a precipitate. The solid was collected by filtration, taken up with water, and extracted with $CHCl_3$. The combined organic layers were dried and evaporated to dryness under reduced pressure to leave the pure product as a light yellow solid (0.266 g, 0.95 mmol, 6%): mp 131−133 °C; ^{1}H NMR ($CDCl_3$) δ 7.98 (d, 1H, J = 8.1), 7.82−7.76 (m, 2H), 7.46 (t, 1H, J = 8.1), 7.36 (t, 1H, J = 8.1), 7.32−7.28 (m, 3H), 4.82 (s, 2H), 3.81 (s, 3H). Anal. Calcd for $C_{16}H_{13}N_3S$: C, 68.79; H, 4.69; N, 15.04. Found: C, 69.01; H, 4.57; N, 15.27.

Bis(4-phenylthiazol-2-yl)methane (9). A solution of phenacyl bromide (1.59 g, 8.00 mmol) in acetone−H_2O (4:1, 5 mL) was added dropwise to a solution of malonodithioamide[23] (0.54 g, 4.00 mmol) in the same solvent (55 mL). After the solution was stirred for 16 h at room temperature, the acetone was distilled off under a reduced pressure. The resulting mixture was neutralized with aqueous $NaHCO_3$, and extracted with $CHCl_3$. The solvent was removed from the dried combined organic layers to leave a brown solid which was submitted to flash chromatography (CH_2Cl_2–AcOEt, 4:1) on silica gel and then crystallized to a white solid (1.04 g, 3.11 mmol, 78%): mp 110−111 °C (toluene) (lit.[48] mp 119−120 °C); ^{1}H NMR ($CDCl_3$) δ 7.91 (d, 4H, J = 8.1), 7.47−7.31 (m, 8H), 4.84 (s, 2H). Anal. Calcd for $C_{19}H_{14}N_2S_2$: C, 68.22; H, 4.22; N, 8.37. Found: C, 68.02; H, 3.79; N, 8.27.

Bis[4-(*p*-nitrophenyl)thiazol-2-yl]methane (10). A solution of *p*-phenacyl bromide (7.32 g, 30.0 mmol) in acetone−H_2O (4:1, 10 mL) was added dropwise to a solution of malonodithioamide[23] (2.01 g, 15.0 mmol) in the same solvent (200 mL). The formation of a red precipitate was observed after 5 min. The reaction mixture was stirred for 4 h at room temperature, and the solid collected by filtration to give the

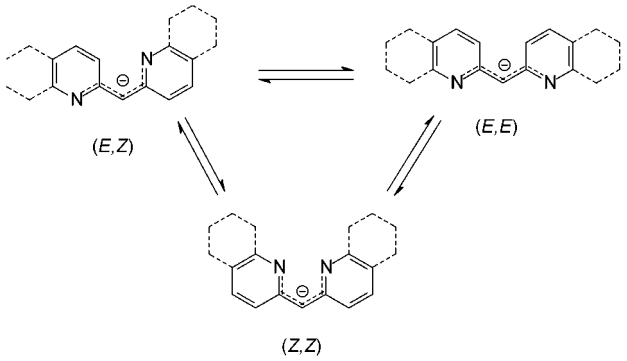
(48) Lehr, H.; Guex, W.; Herlenmeyer, H. *Helv. Chim. Acta* **1944**, *27*, 970−972.

CHART 3. Ligand Properties of Systems 14 and 16−21



[a] This work unless otherwise indicated. Metal in parentheses means that dimerization and/or oxidation product(s) were recovered. Metal in brackets means that no reaction was observed and the ligand was recovered. Metal in braces means that the ligand was recovered after acidification according to Scheme 15. [b]We have evidence that oxidation of the methine bridge afforded the corresponding carbinol: Ferluga, P. Laurea Thesis, University of Milano, Italy, 1993.

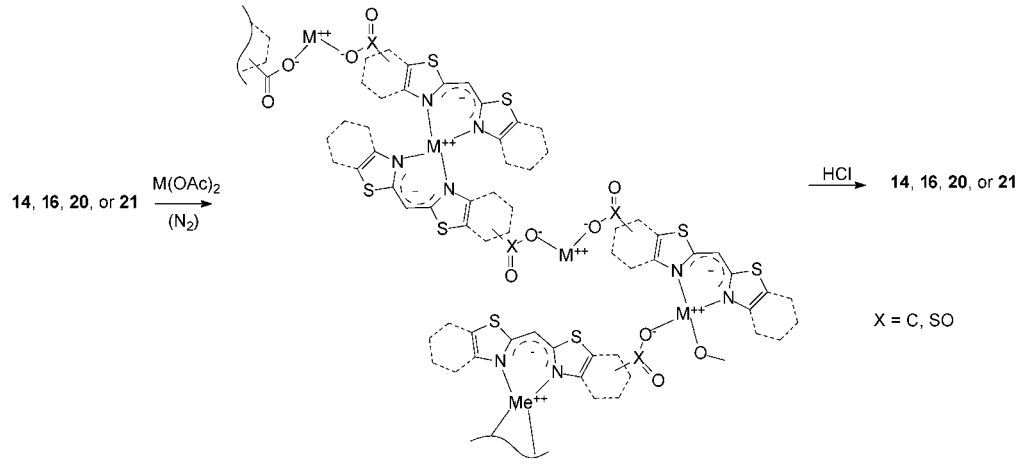
SCHEME 14



light green product (4.70 g, 11.1 mmol, 74%): mp 196−197 °C (DMF); ^{1}H NMR ($CDCl_3$) δ 8.32−8.08 (m, 8H), 7.67 (s, 2H), 4.85 (s, 2H). Anal. Calcd for $C_{19}H_{12}N_4O_4S_2$: C, 53.76; H, 2.86; N, 13.20. Found: C, 53.38; H, 2.95; N, 12.94.

2-Benzothiazolylacetamide (28). A mixture of **27** (11.60 g, 52.4 mmol) in 30% aqueous NH_3 (40 mL) and EtOH (20 mL) was stirred for 18 h at room temperature. The formed

SCHEME 15



precipitate was collected to give the practically pure product as a yellow-green solid (8.01 g, 41.7 mmol, 80%): mp 168 °C (EtOH) (lit.[36a] mp 171−172 °C); ^{1}H NMR ($CDCl_3$) δ 8.10−7.38 (m, 4H), 5.65 (br, 2H), 4.08 (s, 2H).

2-Benzothiazolylthioacetamide (29). A mixture of **28** (7.46 g, 38.8 mmol) and Lawesson's reagent (7.84 g, 19.4 mmol) in anhyd toluene (200 mL) was refluxed for 2 h, resulting in an orange solution. The solvent was removed from the mixture to leave a red residue which was taken up with abs EtOH, leading to the practically pure product as an orange solid (4.04 g, 19.4 mmol, 50%) which was used without further purification in the next step. An analytical sample (light orange solid) was obtained after purification by flash chromatography (CH_2Cl_2–AcOEt, 1:1) on silica gel and crystallization: mp 164−166 °C (AcOEt); ^{1}H NMR ($CDCl_3$) δ 9.18 (br, 2H), 8.06−7.27 (m, 4H), 4.54 (s, 2H). Anal. Calcd for $C_9H_8N_2S_2$: C, 51.89; H, 3.88; N, 13.45. Found: C, 51.63; H, 3.82; N, 13.34.

(Benzothiazol-2-yl)(5-ethoxycarbonyl-4-methylthiazol-2-yl)methane (12). A solution of ethyl bromoacetoacetate[49] (0.627 g, 3.00 mmol) in acetone (1 mL) was added dropwise to a solution of **29** (0.625 g, 3.00 mmol) in acetone−H_2O (11:1, 24 mL). After the solution was stirred for 30 min, the formed precipitate was separated by filtration, taken up with a saturated $NaHCO_3$ aqueous solution, and extracted with CH_2Cl_2. The dried organic layers were evaporated to dryness to leave the crude product as a red-orange oil which was purified by Kugelrohr distillation (0.490 g, 1.54 mmol, 51%): bp 250 °C (0.2 mmHg); ^{1}H NMR ($CDCl_3$) δ 8.06 (d, 1H, J = 7.7), 7.88 (d, 1H, J = 7.7), 7.51 (t, 1H, J = 7.7), 7.41 (t, 1H, J = 7.7), 4.80 (s, 2H), 4.32 (q, 2H, J = 7.3), 2.77 (s, 3H), 1.35 (t, 3H, J = 7.3). Anal. Calcd for $C_{15}H_{14}N_2O_2S_2$: C, 56.57; H, 4.44; N, 8.80. Found: C, 56.48; H, 4.56; N, 8.92.

(Benzothiazol-2-yl)(4-ethoxycarbonylthiazol-2-yl)-methane (13). A solution of ethyl bromopiruvate (1.87 g, 9.60 mmol) in acetone (6 mL) was added dropwise to a solution of **29** (2.00 g, 9.60 mmol) in acetone−H_2O (11:1, 144 mL). After the solution was stirred for 4 h at room temperature, the solvent was evaporated and the residue taken up with a saturated $NaHCO_3$ aqueous solution, and the suspension was extracted with $CHCl_3$. The dried organic layers were evaporated to dryness to leave a red-orange oil which was chromatographed on silica gel (CH_2Cl_2–AcOEt 9:1) to give the pure product as a light yellow solid (1.40 g, 4.60 mmol, 48%): mp 68; ^{1}H NMR ($CDCl_3$) δ 8.15 (s, 1H), 8.03 (dd, 1H, J = 8.1, 1.5), 7.86 (dd, 1H, J = 7.3, 1.5), 7.49 (td, 1H, J = 8.1, 1.5), 7.49 (td, 1H, J = 7.3, 1.5), 4.90 (s, 2H), 4.44 (q, 2H, J = 6.1), 1.42 (t, 3H, J = 6.1). Anal. Calcd for $C_{14}H_{12}N_2O_2S_2$: C, 55.24; H, 3.98; N, 9.20. Found: C, 55.21; H, 4.24; N, 9.84.

(Benzothiazol-2-yl)(4-hydroxycarbonylthiazol-2-yl)-methane (14). A suspension of **13** (0.50 g, 1.64 mmol) in hydrochloric acid (10%, 15 mL) was refluxed for 8 h. After cooling, the formed precipitate was collected, washed with water, and finally dried to give the pure product as a dark yellow solid (0.33 g, 1.19 mmol, 73%): mp 180 °C; ^{1}H NMR ($CDCl_3$) δ 8.41 (s, 1H), 8.09 (d, 1H, J = 7.25), 7.98 (d, 1H, J = 7.3), 7.52 (t, 1H, J = 7.25), 5.00 (s, 2H). Anal. Calcd for $C_{12}H_8N_2O_2S_2 \cdot 5H_2O$: C, 44.86; H, 4.08; N, 8.72. Found: C, 44.59; H, 3.50; N, 9.16.

(Benzothiazol-2-yl)(thiazol-2-yl)methane (15). A mixture of **14** (1.50 g, 5.43 mmol) and electrolytic copper powder (1.60 g) was heated at 240 °C and 0.01 mmHg. The distillation afforded a product which was chromatographed on silica gel (CH_2Cl_2–AcOEt 1:1) to give the pure product as a light yellow solid (0.14 g, 0.60 mmol, 11%): mp 86−90; ^{1}H NMR ($CDCl_3$) δ 8.03 (d, 1H, J = 8.1), 7.85 (d, 1H, J = 7.2), 7.79 (d, 1H, J = 3.4), 7.48 (t, 1H, J = 7.4), 7.38 (t, 1H, J = 7.9), 7.33 (d, 1H, J = 3.4), 4.91 (s, 2H); HRMS m/z calcd for $C_{11}H_8N_2S_2$ 232.0129, found 232,0126.

(Benzothiazol-2-yl)(5-*tert*-butyloxycarbonyl-4-methylthiazol-2-yl)methane (30). A solution of *tert*-butyl chloroacetoacetate (2.56 g, 13.29 mmol) in acetone (5 mL) was added dropwise to a solution of **29** (2.77 g, 13.29 mmol) in acetone−H_2O (11:1, 40 mL). After the solution was stirred for 47 h, the formed precipitate was separated by filtration, taken up with a saturated $NaHCO_3$ aqueous solution, and extracted with CH_2Cl_2. The dried organic layers were evaporated to dryness to leave the crude product as a red-orange oil which was used for the next step without further purification (2.84 g, 8.20 mmol, 62%). An analytical sample was obtained by Kugelrohr distillation: bp 250 °C (0.02 mmHg); ^{1}H NMR ($CDCl_3$) δ 8.05 (dd, 1H, J = 8.5, 1.3), 7.86 (dd, 1H, J = 8.5, 1.3), 7.49 (t, 1H, J = 8.5), 7.39 (t, 1H, J = 8.5), 4.77 (s, 2H), 2.71 (s, 3H), 1.55 (s, 9H); MS (EI) m/z 346 ($M^{\bullet+}$, 41), 290 (100); IR (Nujol) 1713, 1525, 1474, 1315 cm^{-1}. Anal. Calcd for $C_{17}H_{18}N_2O_2S_2$: C, 58.93; H, 5.24; N, 8.09. Found: C, 58.53; H, 5.07; N, 7.88.

(Benzothiazol-2-yl)(5-hydroxycarbonyl-4-methylthiazol-2-yl)methane (16). Under nitrogen, a solution of **30** (0.17 g, 0.49 mmol) and dry PTSA (0.10 g, 0.50 mmol) in benzene (15 mL) was refluxed for 5 h. After cooling, the precipitate was collected and dissolved in a saturated $NaHCO_3$ aqueous solution, and the solution extracted with chloroform. Hydrochloric acid (10%) was added dropwise to the aqueous solution until pH 2−3 was reached. The formed white solid was collected, washed with water, and identified as the pure product (0.10 g, 0.39 mmol, 79%): mp 210 °C (H_2O); ^{1}H NMR (DMSO-d_6) δ 8.10 (d, 1H, J = 8.1), 8.00 (d, 1H, J = 8.1), 7.52 (t, 1H, J = 8.1), 7.44 (t, 1H, J = 8.1), 4.93 (s, 2H), 2.61 (s, 3H). Anal. Calcd for $C_{13}H_{10}N_2O_2S_2$: C, 53.78; H, 3.47; N, 9.65. Found: C, 53.62; H, 3.24; N, 10.01.

4-[β,β-Bis(benzothiazol-2-yl)ethyl]pyridine (33). A solution of the picolylidene derivative **31**[23] (2.10 g, 5.65 mmol) in

(49) Brühl, J. W. *Chem. Ber.* **1903**, *36*, 1722.

AcOEt (120 mL) was subjected to hydrogenation (10% Pd−C) at room temperature and pressure. After 8 h (152 mL of hydrogen volume consumed, 6.22 mmol), the mixture was filtered and evaporated to dryness under reduced pressure to afford the product as a yellow solid (2.11 g, 5.65 mmol, 100%): mp 70−75 °C; ^{1}H NMR ($CDCl_3$) δ 8.45−8.41 (m, 2H) 8.06 (d, 2H, J = 8.1), 7.81 (d, 2H, J = 8.1), 7.49 (t, 2H, J = 8.1), 7.37 (t, 2H, J = 8.1), 7.24−7.20 (m, 2H), 5.33 (t, 1H, J = 7.8), 3.87 (d, 2H, J = 7.8). An analytical sample was purified as styphnate: yellow solid, mp 175−177 °C. Anal. Calcd for $C_{27}H_{18}N_6O_8S_2$: C, 52.41; H, 2.94; N, 13.59. Found: C, 52.73; H, 3.16; N, 13.88.

4-[*β*,*β*-Bis(benzothiazol-2-yl)ethyl]-1-methylpyridinium Triflate (17). A solution of methyl triflate (0.883 g, 5.38 mmol) in dry benzene (34 mL) was added to a solution of **33** (2.01 g, 5.38 mmol) in the same solvent (50 mL). After the solution was stirred for 6 h at room temperature, the formed precipitate was separated by filtration, providing the product as a yellow solid (2.07 g, 3.85 mmol, 72%): mp 182−185 °C; ^{1}H NMR (DMSO-d_6) δ 8.82 (d, 2H, J = 6.6), 8.18 (d, 2H, J = 6.6), 8.08 (d, 2H, J = 7.5), 8.02 (d, 2H, J = 7.5), 7.53 (td, 2H, J = 7.5, 0.5), 7.46 (td, 2H, J = 7.5, 0.5), 6.04 (t, 1H, J = 7.6), 4.20 (s, 3H), 4.15 (d, 2H, J = 7.6). Anal. Calcd for $C_{23}H_{18}F_3N_3O_3S_3$: C, 51.38; H, 3.38; N, 7.82. Found: C, 51.04; H, 3.42; N, 7.65.

4-[*β*,*β*-Bis(benzoxazol-2-yl)ethyl]pyridine (34). A solution of the picolylidene derivative **32**[23] (2.30 g, 6.78 mmol) in AcOEt (170 mL) was subjected to hydrogenation (10% Pd−C) at room temperature and pressure. After 4 h (170 mL of hydrogen volume consumed, 6.96 mmol), the mixtured was filtered and evaporated to dryness under reduced pressure to leave a brown residue which was taken up with diisopropyl ether to afford the product as a brown solid (1.82 g, 5.30 mmol, 79%): mp 125−127 °C (H_2O−EtOH 1:1); ^{1}H NMR ($CDCl_3$) δ 8.45 (d, 2H, J = 5), 7.74−7.68 (m, 2H), 7.52−7.45 (m, 2H), 7.37−7.28 (m, 4H), 7.21 (d, 2H, J = 5), 5.06 (t, 1H, J = 7.8), 3.85 (d, 2H, J = 7.8). Anal. Calcd for $C_{21}H_{15}N_3O_2$: C, 73.92; H, 4.43; N, 12.32. Found: C, 73.70; H, 4.56; N, 12.31.

4-[*β*,*β*-Bis(benzoxazol-2-yl)ethyl]-1-methylpyridinium Triflate (18). A solution of methyl triflate (0.827 g, 5.04 mmol) in dry benzene (35 mL) was added to a solution of **34** (1.72 g, 5.04 mmol) in the same solvent (50 mL). After the solution was stirred for 2 h at room temperature, the precipitate was collected by filtration to provide the product as a light yellow solid (2.45 g, 4.85, 96%): mp 202−203 °C; ^{1}H NMR (DMSO-d_6) δ 8.86 (d, 2H, J = 6.6), 8.19 (d, 2H, J = 6.6), 7.81−7.69 (m, 4H), 7.49−7.34 (m, 4H), 5.79 (t, 1H, J = 7.8), 4.24 (s, 3H), 4.10 (d, 2H, J = 7.8). Anal. Calcd for $C_{23}H_{18}F_3N_3O_5S$: C, 54.64; H, 3.60; N, 8.31. Found: C, 54.95; H, 3.52; N, 8.50.

(Pyrid-2-yl)(benzothiazol-2-yl)methane (22). A mixture of methyl 2-pyridylacetate (3.83 g, 25.3 mmol) and 2-aminothiophenol (3.17 g, 25.3 mmol) was stirred for 5 h at 160 °C under a nitrogen atmosphere. The reaction mixture was cooled to room temperature, leaving an orange oil which was submitted to Kugelrohr distillation, affording the pure product as a yellow oil (4.30 g, 19.0 mmol, 75%): bp 220 °C/0.5 mmHg; ^{1}H NMR ($CDCl_3$) δ 8.60 (d, 1H, J = 4.7), 7.99 (d, 1H, J = 7.7), 7.80 (d, 1H, J = 8.2), 7.64 (t, 1H, J = 7.8), 7.43 (t, 1H, J = 8.2), 7.38−7.28 (m, 2H), 7.18 (dd, 1H, J = 7.7, 4.6), 4.63 (s, 2H). Anal. Calcd for $C_{13}H_{10}N_2S$: C, 68.98; H, 4.46; N, 12.38. Found: C, 68.56; H, 4.36; N, 12.27.

***N*-(*o*-Hydroxyphenyl)pyrid-2-ylacetamide (35).** A mixture of methyl 2-pyridylacetate (3.78 g, 25.0 mmol) and 2-aminophenol (2.73 g, 25.0 mmol) was stirred for 5 h at 165 °C under a nitrogen atmosphere. The reaction mixture was allowed to cool to room temperature, leaving a solid which was taken up with diethyl ether, providing the practically pure product as a brown solid, used without further purification in the subsequent step (4.81 g, 21.1 mmol, 84%). Recrystallization gave an analytical sample (light brown solid): mp 152−154 °C (EtOH); ^{1}H NMR ($CDCl_3$) δ 10.4 (br), 10.0 (br), 8.60 (d, 1H, J = 5.1), 7.78 (t, 1H, J = 7.0), 7.38−7.28 (m, 3H), 7.09 (t, 1H, J = 6.9), 7.00 (d, 1H, J = 7.7), 6.85 (d, 1H, J = 7.0), 3.93 (s, 2H); IR (Nujol) 1690 (C=O). Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.39; H, 5.31; N, 12.27. Found: C, 68.21; H, 5.18; N, 12.06.

(Pyrid-2-yl)(benzoxazol-2-yl)methane (23). 35 (4.49 g, 19.7 mmol) was added to polyphosphoric acid (40 mL) at 70 °C under mechanical stirring. The reaction mixture was stirred for 5 h at 160 °C, then cooled to 40 °C, poured onto ice, and treated with 15% aqueous NH_3 to pH 9−10. The resulting mixture was extracted with $CHCl_3$. The combined organic layers were filtered over Celite, washed with water, dried, and evaporated to dryness to leave a dark oil which was submitted to Kugelrohr distillation, affording the pure product as a yellow oil (2.47 g, 11.7 mmol, 60%): bp 195 °C (0.6 mmHg); ^{1}H NMR ($CDCl_3$) δ 8.58 (d, 1H, J = 4.7), 7.72−7.63 (m, 2H), 7.48 (t, 1H, J = 8.0), 7.37−7.28 (m, 3H), 7.22 (dd, 1H, J = 7.6, 4.7), 4.48 (s, 2H). Anal. Calcd for $C_{13}H_{10}N_2O$: C, 74.26; H, 4.80; N, 13.33. Found: C, 74.04; H, 4.71; N, 13.56.

Synthesis of Salt Complexes and Neutral Chelates. Reaction solvents (MeOH, EtOH, H_2O, and DMF) and metal acetates, sulfates, and chlorides were used as received without further purification. Experimental details (molar amount of ligand and metal salt, type of metal salt, and reaction times) for each preparation and microanalytical data (elemental analysis) of neutral chelates ML_2 and salt complexes $M(LH)_nX_m$ are reported in Tables 2−4 and Tables 5 and 6, respectively. The following are general synthetic protocols for neutral and salt complex preparation.

Method A. A solution of metal salt in methanol was added dropwise to a solution of ligand LH dissolved in the minimal amount of the same solvent. A precipitate was immediately formed. This solid was collected, washed several times with methanol, and finally dried under vacuum at 40−60 °C. Elemental analysis was performed without further purification.

Method B. Under nitrogen, a solution of metal salt in methanol was added dropwise to a solution of ligand LH in the same solvent. After the solution was stirred for the specified time, the precipitate was collected, washed a few times with methanol, and finally dried under vacuum at 40−60 °C. Elemental analysis was performed without further purification.

Method C. Under nitrogen, a solution of metal salt in methanol was added dropwise to a solution of ligand LH in the same solvent. After the solution was stirred for the indicated time, the reaction solvent was evaporated until a precipitate was formed. This solid was collected, washed a few times with cold methanol, and finally dried under vacuum at 40−60 °C. Elemental analysis was performed without further purification.

Method D. Under nitrogen, a solution of metal salt in methanol was added dropwise to a solution of ligand LH in the same solvent. After the solution was stirred for the indicated time, the solvent was removed under reduced pressure. The residue was taken up with water, and the solid was collected, washed with chloroform, THF, or cold methanol, and finally dried under vacuum at 40−60 °C. Elemental analysis was performed either without further purification or after recrystallization (see the notes in Tables 1−5).

Method E. A solution of metal salt in water was added dropwise to a boiling solution of ligand LH in the same solvent. A precipitate immediately formed. The solid was collected, washed with warm water, and dried under vacuum at 80 °C. Elemental analysis was performed without further purification.

Spectroscopic and Spectrometric Characterization of Salt Complexes and Neutral Chelates. LH = 2. ZnL_2: ^{1}H NMR ($CDCl_3$) δ 7.47 (d, 4H, J = 7.6), 7.06−6.97 (m, 8H), 6.94 (td, 4H, J = 6.7, 1.7), 5.99 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 166.32, 150.94, 128.50, 122.10, 120.92, 115.32, 80.65; ^{15}N (THF-d_8) δ 185.5; MS (CI) m/z 631 ($MH^{\bullet+}$, 7), 283 (100). **CuL_2**: MS (CI) m/z 283 ($MH^{\bullet+}$, 18), 256 (100). **NiL_2**: MS (EI) m/z 622 ($M^{\bullet+}$,

25), 282 (100). **CoL$_2$**: MS (EI) *m/z* 621 ($M^{\bullet+}$, 100). **PdL$_2$**: ^{1}H NMR ($CDCl_3$) δ 7.17−7.12 (m, 4H), 6.84−6.78 (m, 4H), 6.66−6.58 (m, 4H), 5.72 (s, 2H). **HgL$_2$**: MS (CI) *m/z* 323 (53), 284 (100).

LH = 3. ZnL$_2$: ^{1}H NMR ($CDCl_3$) δ 7.36−7.24 (m, 4H), 7.05−6.92 (m, 8H), 6.91−6.80 (m, 4H), 5.46 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 168.22, 147.47, 138.65, 124.63, 122.06, 109.57, 58.90; ^{15}N (DMSO-d_6) δ 152.9; MS (EI) *m/z* 566 ($M^{\bullet+}$, 44), 562 (100). **CuL$_2$**: MS (EI) *m/z* 556 (20), 250 (100). **NiL$_2$**: MS (CI) *m/z* 558 ($MH^{\bullet+}$, 15), 119 (100). **CoL$_2$**: MS (EI) *m/z* 557 ($M^{\bullet+}$, 100), 250 (64). **PdL$_2$**: ^{1}H NMR ($CDCl_3$) δ 7.14 (dd, 4H, J = 7.8, 1.2), 6.78 (td, 4H, J = 7.8, 1.2), 6.48 (td, 4H, J = 7.7, 1.2), 6.22 (dd, 4H, J = 7.6, 1.2), 5.24 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 165.90, 148.80, 138.27, 122.88, 121.26, 108.65, 61.65.

LH = 5. ZnL$_2$: ^{1}H NMR ($CDCl_3$) δ 7.36 (d, 2H, J = 7.6), 7.05 (d, 2H, J = 7.8), 6.96 (td, 2H, J = 6.7, 1.7), 6.93−6.78 (m, 10H), 5.41 (s, 2H), 3.62 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 166.24, 154.65, 151.87, 140.35, 134.10, 128.06, 125.99, 121.64, 120.49, 120.31, 114.50, 113.36, 107.20, 68.33, 29.25; IR (Nujol) 1922, 1472, 1344, 1302 cm^{-1}. **CuL$_2$**: IR (Nujol) 1626, 1592, 1401, 1317 cm^{-1}.

LH = 8. CuL$_2$: MS (FAB) *m/z* 713 ($M^{\bullet+}$, 5), 136 (100); IR (Nujol) 1698, 1530, 1288, 1224 cm^{-1}.

LH = 9. CuL$_2$: MS (FAB) *m/z* 729 ($M^{\bullet+}$, 8), 154 (100).

LH = 10. CuL$_2$: MS (FAB) *m/z* 424 (22), 246 (100). **CoL$_2$**: MS (FAB) *m/z* 460 (3), 307 (100).

LH = 11. ZnL$_2$: ^{1}H NMR ($CDCl_3$) δ 5.80 (s, 2H), 4.25 (q, 8H, J = 7.1), 2.25 (s, 12H), 1.37 (t, 12H, J = 7.1); MS (FAB) *m/z* 774 ($M^{\bullet+}$, 67), 770 (100); UV−vis (CH_2Cl_2) λ_{max} = 464 nm, ϵ = 140500 M^{-1} cm^{-1}; IR (Nujol) 1704, 1554, 1499, 1316 cm^{-1}. **CuL$_2$**: MS (FAB) *m/z* 771 ($M^{\bullet+}$, 65), 154 (100); UV−vis (CH_2Cl_2) λ_{max} = 445 nm, ϵ = 135000 M^{-1} cm^{-1}; IR (Nujol) 1704, 1620, 1446, 1428 cm^{-1}. **NiL$_2$**: MS (FAB) *m/z* 766 ($M^{\bullet+}$, 24), 133 (100); UV−vis (CH_2Cl_2) λ_{max} = 448 nm, ϵ = 130500 M^{-1} cm^{-1}; IR (Nujol) 1705, 1555, 1499, 1366 cm^{-1}. **CoL$_2$**: MS (FAB) *m/z* 765 ($M^{\bullet+}$, 100); UV−vis (CH_2Cl_2) λ_{max} = 438 nm, ϵ = 169000 M^{-1} cm^{-1}; IR (Nujol) 1704, 1555, 1495, 1306 cm^{-1}. **PdL$_2$**: ^{1}H NMR ($CDCl_3$) δ 5.58 (s, 2H), 4.20 (q, 8H, J = 7.1), 2.21 (s, 12H), 1.34 (t, 12H, J = 7.1).

LH = 12. ZnL$_2$: ^{1}H NMR ($CDCl_3$) δ 7.48 (d, 2H, J = 8.0), 7.08 (t, 2H, J = 7.8), 6.99 (t, 2H, J = 7.9), 6.91 (d, 2H, J = 7.6), 5.87 (s, 2H), 4.22 (q, 4H, J = 7.4), 2.26 (s, 6H), 1.27 (t, 6H, J = 7.1); ^{13}C NMR ($CDCl_3$) δ 166.83, 165.87, 162.22, 156.59, 150.59, 128.50, 126.63, 122.29, 121.09, 115.02, 108.74, 81.38, 60.75, 16.05, 14.35. **CuL$_2$**: MS (FAB) *m/z* 697 ($M^{\bullet+}$, 2), 154 (100). **NiL$_2$**: MS (FAB) *m/z* 287 (88), 132 (100). **CoL$_2$**: MS (FAB) *m/z* 693 ($M^{\bullet+}$, 100). **PdL$_2$**: Two isomers (**A**, 66%; **B**, 33%) were detected in solution. Isomer **A**: ^{1}H NMR ($CDCl_3$) δ 7.36 (d, 2H, J = 7.5), 7.02 (td, 2H, J = 7.5, 1.5), 6.93 (td, 2H, J = 7.6, 1.5), 6.87 (d, 2H, J = 7.6), 5.62 (s, 2H), 4.07 (q, 4H, J = 7.6), 1.73 (s, 6H), 1.21 (t, 6H, J = 7.6); ^{13}C NMR ($CDCl_3$) δ 163.33, 161.18, 160.49, 157.69, 148.75, 129.75, 125.71, 122.28, 120.93, 116.63, 110.66, 87.25, 60.34, 17.36, 14.38. Isomer **B**: ^{1}H NMR ($CDCl_3$) δ 7.13−7.09 (m, 2H), 6.68−6.56 (m, 6H), 5.62 (s, 2H), 4.24 (q, 4H, J = 7.5), 2.26 (s, 6H), 1.32 (t, 6H, J = 7.5); ^{13}C NMR ($CDCl_3$) δ 162.93, 161.51, 161.00, 157.36, 148.87, 129.02, 125.17, 121.75, 120.23, 116.07, 111.00, 87.23, 60.66, 17.00, 14.32.

LH = 13. ZnL$_2$: ^{1}H NMR (DMSO-d_6) δ (d, 2H, J = 7.2), 7.31 (s, 2H), 7.01 (td, 2H, J = 7.2, 1.4), 6.92−6.85 (m, 4H), 5.87 (s, 2H), 4.10 (q, 4H, J = 7.3), 1.05 (t, 6H, J = 7.3); IR (Nujol) 1698, 1530, 1288, 1224 cm^{-1}. **CuL$_2$**: IR (Nujol) 1712, 1561, 1239, 1107 cm^{-1}.

LH = 17. ZnL$_2$: ^{1}H NMR (DMSO-d_6) δ 8.90 (d, 4H, J = 6.6), 8.20 (d, 4H, J = 6.6), 7.81 (d, 2H, J = 7.5), 7.19 (t, 4H, J = 7.4), 7.08 (t, 4H, J = 7.6), 7.00 (d, 4H, J = 8.0), 4.50 (s, 4H), 4.33 (s, 6H); IR (Nujol) 1642, 1578, 1316, 1270 cm^{-1}. **CuL$_2$**: IR (Nujol) 1646, 1568, 1523, 1265 cm^{-1}. **NiL$_2$**: IR (Nujol) 1649, 1537, 1558, 1260 cm^{-1}. **CoL$_2$**: IR (Nujol) 1651, 1527, 1521, 1224 cm^{-1}. **PdL$_2$**: ^{1}H NMR (DMSO-d_6) δ 8.93 (d, 4H, J = 6.3), 8.25 (d, 4H, J = 6.2), 7.42 (d, 4H, J = 7.5), 6.82 (d, 4H, J = 7.7), 6.60−6.75 (m, 8H), 4.45 (s, 4H), 4.35 (s, 6H); IR (Nujol) 1642, 1525, 1510, 1219 cm^{-1}.

LH = 18. ZnL$_2$: ^{1}H NMR (DMSO-d_6) δ 8.88 (d, 4H, J = 6.6), 8.26 (d, 4H, J = 6.6), 7.45−7.53 (m, 4H), 7.00−7.14 (m, 8H), 6.90−6.67 (m, 4H), 4.50 (s, 4H), 4.20 (s, 6H); IR (Nujol) 1620, 1504, 1350, 1260 cm^{-1}. **CuL$_2$**: IR (Nujol) 1651, 1582, 1522, 1256 cm^{-1}. **NiL$_2$**: IR (Nujol) 1651, 1605, 1582, 1261 cm^{-1}. **CoL$_2$**: IR (Nujol) 1655, 1573, 1348, 1261 cm^{-1}. **PdL$_2$**: ^{1}H NMR (DMSO-d_6) δ 8.87 (d, 4H, J = 6.4), 8.24 (d, 4H, J = 6.4), 7.32 (d, 4H, J = 8.0), 6.84 (t, 4H, J = 7.8), 6.49 (t, 4H, J = 7.9), 6.27 (d, 4H, J = 7.8), 4.45 (s, 4H), 4.30 (s, 6H); IR (Nujol) 1628, 1582, 1325, 1155 cm^{-1}.

LH = 19. ZnL$_2$: ^{1}H NMR ($CDCl_3$) δ 7.44 (d, 4H, J = 7.5), 7.40 (dd, 2H, J = 7.5), 7.24 (td, 2H, J = 7.3), 7.12 (d, 4H,), 7.04 (td, 4H, J = 7.0), 6.95 (t, 4H, J = 6.5), 6.92 (t, 2H, J = 7.2), 6.86 (d, 2H, J = 8.1), 4.75 (s, 4H), 4.28 (s, 4H), 1.58 (s, 18H). **PdL$_2$**: ^{1}H NMR ($CDCl_3$) δ 7.61 (d, 2H, J = 6.4), 7.26 (td, 2H, J = 5.5), 7.06−7.12 (m, 4H), 6.89 (t, 2H, J = 7.4), 6.82−6.89 (m, 6H), 6.53−6.60 (m, 8H), 4.75 (s, 4H), 4.15 (s, 4H), 1.55 (s, 18H).

LH = 22. Zn(LH)Cl$_2$: ^{1}H NMR ($CDCl_3$) δ 8.95 (d, 1H, J = 4.6), 8.07−7.97 (m, 2H), 7.64−7.56 (m, 3H), 7.53−7.46 (m, 2H), 4.79 (s, 2H).

LH = 23. Zn(LH)Cl$_2$: ^{1}H NMR ($CDCl_3$) δ 8.93 (d, 1H, J = 4.7), 8.07−7.96 (m, 2H), 7.65−7.56 (m, 3H), 7.53−7.45 (m, 2H), 4.78 (s, 2H).

Oxidation and/or Dimerization Reactions. Reaction of 11 with Mn(OAc)$_2$·4H$_2$O. A solution of Mn(OAc)$_2$·4H$_2$O (0.10 g, 0.42 mmol) in EtOH (5 mL) was added to a solution of bis(5-ethoxy-4-methylthiazol-2-yl)methane (**11**) (0.30 g, 0.85 mmol) in the same solvent (17 mL). After the solution was stirred at room temperature for 6 h, a precipitate formed. This solid was collected, washed with EtOH, and dried under vacuum to give 1,1,2,2-tetra(5-ethoxy-4-methylthiazol-2-yl)-ethene (**37**) as a yellow solid (0.12 g, 0.17 mmol, 40.5%): mp 157 °C; ^{1}H NMR ($CDCl_3$) δ 4.32 (q, 8H, J = 7.1), 2.64 (s, 12H), 1.34 (t, 12H, J = 7.1); ^{13}C NMR ($CDCl_3$) δ 164.96, 161.76, 160.36, 132.35, 125.66, 61.52, 17.36, 14.20; MS (EI) *m/z* 704 ($M^{\bullet+}$, 40), 587 (100). Anal. Calcd for $C_{30}H_{32}N_4S_4O_8$: C, 51.11; H, 4.58; N, 7.95. Found: C, 51.02; H, 4.53; N, 7.83.

Reaction of 12 with Mn(OAc)$_2$·4H$_2$O. A solution of Mn(OAc)$_2$·4H$_2$O (0.16 g, 0.64 mmol) in EtOH (4 mL) was added to a solution of (benzothiazol-2-yl)(5-ethoxy-4-methylthiazol-2-yl)methane (**12**) (0.41 g, 1.29 mmol) in the same solvent (7 mL). After the solution was stirred at room temperature for 12 h, a precipitate formed. This solid was collected and chromatographied on silica gel (CH_2Cl_2:AcOEt = 9:1). Two fractions were isolated. (A) Benzothiazol-2-yl 5-ethoxy-4-methylthiazol-2-yl ketone (**38**), yellow solid (0.14 g, 0.421 mmol, 32.7%): mp 179 °C (EtOH); ^{1}H NMR ($CDCl_3$) δ 8.39 (dd, 1H, J = 8.0, 2.4), 8.07 (dd, 1H, J = 6.7, 2.5), 7.68−7.60 (m, 2H), 4.45 (q, 2H, J = 7.9) 2.93 (s, 3H), 1.46 (t, 3H, J = 7.9); MS (EI) *m/z* 332 ($M^{\bullet+}$, 100); IR (Nujol) 1713, 1656, 1266, 1094 cm^{-1}. Anal. Calcd for $C_{15}H_{12}N_2S_2O_3$: C, 54.20; H, 3.64; N, 8.43. Found: C, 53.66; H, 3.86; N, 8.66. (B) 1,2-Bis(benzothiazol-2-yl)-1,2-bis(5-ethoxy-4-methylthiazol-2-yl)-ethene (**39**), mixture of (*E*)- and (*Z*)-isomers, red solid (0.03 mg, 0.05 mmol, 3.7%): mp 220 (dioxane); MS (EI) *m/z* 632 ($M^{\bullet+}$, 15), 515 (100); IR (Nujol) 1715, 1599, 1518, 1169 cm^{-1}. Anal. Calcd for $C_{30}H_{24}N_4S_4O_4$: C, 56.94; H, 3.82; N, 8.86. Found: C, 57.11; H, 4.03; N, 8.82. (*Z*)-**39**: ^{1}H NMR ($CDCl_3$) δ 8.09 (d, 1H, J = 8.6), 7.90 (d, 1H, J = 8.6), 7.56−7.48 (m, 2H), 4.42 (q, 2H, J = 8.2) 2.68 (s, 3H), 1.34 (t, 3H, J = 8.2). (*E*)-**39**: ^{1}H NMR ($CDCl_3$) δ 8.02 (d, 1H, J = 8.6), 7.80 (d, 1H, J = 8.6), 7.48−7.38 (m, 2H), 4.25 (q, 2H, J = 8.2) 2.52 (s, 3H), 1.27 (t, 3H, J = 8.2).

Reaction of 11 with Air. A solution of EtONa in EtOH (1 M, 0.3 mL) was added to a warm solution (40 °C) of **11** (0.50 g, 1.41 mmol) in EtOH (10 mL). After the solution was stirred for 1 h at room temperature, a brown solid precipitated. This solid was collected, washed with EtOH, dried under vacuum at 50 °C, and identified as bis(5-ethoxy-4-methylthiazol-2-yl)

ketone (**40**) (0.25 g, 0.60 mmol, 48%): mp 127; ^{1}H NMR ($CDCl_3$) δ 4.40 (q, 8H, J = 8.5), 2.90 (s, 6H), 1.40 (t, 6H, J = 8.5); ^{13}C NMR ($CDCl_3$) δ 173.39, 161.66, 161.59, 161.23, 130.06, 62.02, 17.58, 14.24; MS (EI) m/z 368 ($M^{\bullet+}$, 100); IR (Nujol) 1667 cm^{-1}. Anal. Calcd for $C_{15}H_{16}N_2S_2O_5$: C, 48.90; H, 4.38; N, 7.60. Found: C, 48.78; H, 4.32; N, 7.46.

Conversion of Zn(2)Cl$_2$ to Zn(2$^-$)$_2$. Reaction A. AcONa (15.1 mg, 0.184 mmol) was added to a suspension of Zn(**2**)Cl_2 (70 mg, 0.167 mmol) in MeOH (7 mL). After the suspension was stirred overnight at room temperature, the solid was collected, washed with MeOH, and finally dried under vacuum at 80 °C for 2 h to give Zn(**2**$^-$)$_2$ as a yellow solid (43.1 mg, 0.068 mmol, 82.1%). The ^{1}H NMR spectrum was identical to that of an authentic sample.

Reaction B. AcONa (21.4 mg, 0.262 mmol) was added to a suspension of Zn(**2**)Cl_2 (50 mg, 0.119 mmol) and **2** (33.6 mg, 0.119 mmol) in MeOH (5 mL). After the suspension was stirred overnight at room temperature, the solid was collected, washed with MeOH, and finally dried under vacuum at 80 °C for 2 h to give Zn(**2**$^-$)$_2$ as a yellow solid (68.3 mg, 0.108 mmol, 91.4%). The ^{1}H NMR spectrum was identical to that of an authentic sample.

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