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Preparation of a New Ligand Containing Disulfide and Imidazole Donor Groups. Structure of Dibromo[5-(1,2,5-dithiazepan-5-ylmethylene)-4-methyl-2-ethylimidazole]cadmium(II). ^{113}Cd and ^{13}C NMR Studies of Complex Formation

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The title ligand (MAMI) was prepared by reaction of 2-ethyl-4-methylimidazole and diethanolamine under basic (pH 11) Mannich conditions and treatment of the resultant alcohol with thionyl chloride. The nitrogen mustard formed was derivatized with thiourea to afford a bis(isothiuronium) salt. Hydrolysis of this material to a dimercaptide could only be accomplished efficiently in the presence of transition-metal salts. Treatment of the isothiuronium salt with $NiCl_2$ under basic conditions afforded an incompletely characterized derivative in which, by IR spectroscopy and C:N ratio, the ligand had been completely hydrolyzed to a dimercaptide. Oxidation of this material by I_2 and extraction into $HCCl_3$ afforded the title ligand. Changes in the ^{13}C NMR spectrum of MAMI in Me_2SO-d_6 as a function of added $Cd(NO_3)_2$ revealed the formation of a 1:1 complex with $K_f \sim 60\ M^{-1}$. The coordinated and free ligand are in fast exchange on the ^{13}C NMR scale, and the assessement of the groups involved in complex formation was unclear. However, ^{113}Cd NMR is consistent with coordination by the two N donors in MAMI. The 1:1 complex is in slow exchange on the ^{113}Cd NMR time scale. Crystalline complexes of MAMI with $CdCl_2$ and $CdBr_2$ were isolated. The $CdBr_2$ complex was investigated by X-ray methods. Crystal data: $P2_1/n$, a = 12.988 (4) Å, b = 10.899 (3) Å, c = 13.148 (3) Å, β = 108.74 (2)°, Z = 4, R = 0.0235 for 1474 independent reflections. The complex is a highly distorted trigonal bipyramid with 2 Br, 2 N (from imidazole and the tertiary amine functions), and a disulfide S in the coordination sphere. The Cd-S bond is very long (2.938 Å).

Introduction

During the course of developing heavy-metal containing ligands for the enhancement of heavy-metal Os labels of nucleic acids,[2-4] we prepared and characterized some N,S ligands. We report here our studies on a disulfide ligand system that is readily reduced to a tetradentate 2N, 2S donor ligand that contains one imidazole N donor and two mercaptide donors. This ligand system and the general synthetic strategy employed in its synthesis may prove useful in model studies related to Cu and Mo enzymes and also to metallothionein.[5-10]

The ligand prepared is 5-(1,2,5-dithiazepan-5-ylmethylene)-4-methyl-2-ethylimidazole, (V, MAMI, vide infra). We have characterized Cd(II) complexes formed by this ligand in solution by ^{113}Cd and ^{13}C NMR spectroscopy and in the solid state by a three-dimensional X-ray structure of the $CdBr_2$ derivative.

Experimental Section

Reagents. Reagents were from Aldrich unless otherwise noted and were used without further purification. HCl gas was from Linde. $NiCl_2 \cdot 2H_2O$ and $CdCl_2 \cdot 2^1/_2H_2O$ were from Fisher, and $Cd(NO_3)_2 \cdot 4H_2O$ was from Alfa.

Instrumentation. NMR spectral data were obtained on Varian EM390 (90 MHz, ^1H), Varian CFT20 (20 MHz, ^{13}C), and IBM WP200-SY (44.39 MHz, ^{113}Cd; 50.33 MHz, ^{13}C) spectrometers. For ^{13}C and ^1H NMR data, signals in Me_2SO-d_6 and D_2O were referenced to internal Me_4Si and TSP, respectively, except for ^{13}C signals in D_2O that were referenced to internal *p*-dioxane (δ 67.39). ^{113}Cd NMR chemical shifts were referenced to external $Cd(NO_3)_2$ (1.0 M, Me_2SO-d_6) in keeping with our previous convention.[11] IR data were obtained with a Perkin-Elmer 727B or 467 spectrometer. UV spectra were obtained on a Cary 14 spectrophotometer. GC-MS data were obtained on a Finnigan 4000 instrument. Elemental analyses were performed by Atlantic Microlabs and Galbraith Laboratories.

Preparations. 5-[(Bis(2-hydroxyethyl)amino)methyl]-2-ethyl-4-methylimidazole (I). A solution of 2-ethyl-4(5)-methylimidazole (20 g, 182 mmol) in water (75 mL) was added over a period of 1 h to a solution of diethanolamine (17.5 mL, 182 mmol), formaldehyde (21.9 mL 37% aqueous), and water (75 mL). The solution was left at room temperature for 48 h. The solution was adjusted to pH 11 with 20% KOH. The product, a viscous yellow oil, was salted out with potassium carbonate. The oil was separated from the aqueous layer and dissolved in absolute EtOH. Dry HCl gas was bubbled through the ethanolic solution until it was acidic, and it was then placed in a freezer. White crystals formed and were collected; yield 38 g (70%). It was crystallized from MeOH; mp 193-4 °C. Anal. Calcd for $C_{11}H_{21}N_3O_2 \cdot 2HCl$: C, 44.00; H, 7.72; N, 14.00. Found: C, 43.91; H, 7.78; N, 13.98. ^1H NMR (Me_2SO-d_6): δ 1.35 (t), 2.4 (s), 3.0 (q), 3.35 (t), 3.9 (t), 4.65 (s). ^{13}C NMR (D_2O): δ 9.49, 10.98, 19.97, 47.75, 55.31, 56.11, 116.68, 133.07, 150.97. ^1H NMR (D_2O, pD 9): δ 1.15 (t), 2.1 (s), 2.7 (q), 2.8 (t), 3.75 (t), 4.8 (s).

5-[(Bis(2-chloroethyl)amino)methyl]-2-ethyl-4-methylimidazole (II). I (10 g, 30 mmol) was suspended in $CHCl_3$ (35 mL). A solution of thionyl chloride (9.0 mL) in $CHCl_3$ (10 mL) was added over a period of 90 min. The resulting solution was kept at reflux for 3 h during which time a white precipitate formed. The mixture was cooled and filtered. Quantitative yields of white product were obtained: yield 10 g; mp 188-9 °C dec. Anal. Calcd for $C_{11}H_{19}Cl_2N_3 \cdot 2HCl$: C, 39.20; H, 6.28; N, 12.46, Found: C, 39.36; H, 6.35; N, 12.40. ^1H NMR (Me_2SO-d_6): δ 1.3 (t), 2.35 (s), 2.95 (q), 3.4 (t), 4.05 (t), 4.45 (s). ^{13}C NMR (D_2O): δ 9.55, 11.02, 19.94, 37.97, 48.13, 55.27, 116.10, 133.76, 151.38.

5-[(Bis(2-thioureido)amino)methyl]-2-ethyl-4-methylimidazole (III). Thiourea (6.85 g, 90 mmol) and II (15 g, 45 mmol) were dissolved in 95% ethanol (90 mL). The solution was kept at reflux (gently) overnight. After it had cooled, dry HCl gas was bubbled through the solution and the solvent removed. The resulting residue crystallized with difficulty; yield 17.4 g (79%). Often it was not purified before use in the next step; mp 165-80 °C. Anal. Calcd for $C_{13}H_{27}Cl_2N_7S_2 \cdot 2^1/_2H_2O \cdot 2HCl$: C, 29.22; H, 6.41; N, 18.35. Found: C, 29.17; H, 6.41; N, 18.29. ^1H NMR Me_2SO-d_6): δ 1.35 (t), 2.4

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(s), 3.0 (q), 3.3 (t), 3.77 (t), 4.4 (s), 9.7 (s). ^{13}C NMR (DCl): δ −0.11, 11.24, 18.06, 26.80, 48.07, 52.62, 117.17, 133.06, 151.04. IR (KBr): 2500–3400, 2200, 2025, 1775, 1705, 1603, 1400 (b), 1290, 1240, 1190, 1070, 1030, 990, 940, 895, 825 cm^{-1}. UV (MeOH): 230 ($\epsilon = 8.08 \times 10^3$).

Hydrolysis of III with $NiCl_2$. $NiCl_2 \cdot 2H_2O$ (1.49 g, 2 mmol) was dissolved in water (30 mL) and concentrated NH_4OH added to make the solution 0.5 M in NH_4OH. A solution of III (1.0 g, 2 mmol) in water (5 mL) was added dropwise. The stirred blue solution turned dark brown. After 2 h, a brown precipitate (IV) was collected, washed well with 0.5 M NH_4OH and water, and air-dried. IV is soluble in EtOH, MeOH, Me_2SO, acid, and pyridine; it is insoluble in acetone, ether, and base; it is slightly soluble in CH_2Cl_2, ethyl acetate, and water. IR (KBr): loss of peak at 2160 cm^{-1}. ^1H NMR (DCl, all peaks are broad): δ 1.1, 2.15, 2.65, 3.35, 4.35. UV (MeOH): 230 ($A = 0.730$, $c = 1.3$ mg/25 mL, 270–320 (sh) nm. Anal. Found: C, 36.9; H, 5.4; N, 11.7; Cl, 4.3; Ni (grav), 18.75.

5-(1,2,5-Dithiazepan-5-ylmethylene)-4-methyl-2-ethylimidazole (V, MAMI). The Ni complex IV (9.6 g) was dissolved in 0.2 N HCl (200 mL), which resulted in a deep brown-purple solution. An I_2/MeOH solution was added dropwise until the solution turned pale green. A little excess I_2 was then added, as indicated by a yellow color. The solution was left stirring at room temperature for 4 h. It was neutralized with dilute NH_4OH and the volume reduced to 20 mL on a rotary evaporator. The excess I_2 appeared as a red film on the flask. The aqueous solution was extracted six times with $CHCl_3$, and each time the pH was adjusted with dilute NH_4OH until the final pH was 9–11. The organic layers were combined, washed with dilute NH_4OH (to remove any remaining Ni), and concentrated. A white solid (3.6 g) formed and was collected; mp 129–30 °C. ^1H NMR: in ($CDCl_3$) δ 1.2 (t), 2.1 (s), 2.6 (q), 2.8 (t), 3.1 (t), 3.7 (s), 9.5; (in Me_2SO-d_6) δ 1.1 (t), 2.0 (s), 2.5 (q under Me_2SO), 2.85 (m), 3.1 (m), 3.65 (s); (in D_2O/TFA) δ 1.4 (t), 2.4 (s), 3.0 (q), 3.25 (m), 3.9 (m), 4.7 (s). ^{13}C NMR (Me_2SO-d_6): δ 10.64, 12.67, 21.08, 39.43, 47.66, 54.18, 126.92, 127.03, 146.76. Anal. Calcd for $C_{11}H_{19}N_3S_2 \cdot {}^1/_2H_2O$: C, 49.59; H, 7.57; N, 15.77. Found: C, 49.59; H, 7.61; N, 15.75. The mass spectrum contains a peak at the expected molecular weight of 257, and there is only one peak in the gas chromatogram. IR (KBr): 2800–2900, 1620, 1540, 1440 (s), 1390, 1030, 990, 900 cm^{-1}.

Dihalo[5-(1,2,5-dithiazepan-5-ylmethylene)-4-methyl-2-ethylimidazole]cadmium(II). To a solution of V (0.75 g, 3 mmol) in MeOH (75 mL) was added a solution of $CdCl_2$ (0.68 g, 3 mmol) in water (10 mL). The resulting solution was allowed to stir overnight. The white precipitate that formed was collected; yield (0.64 g (50%). Recrystallization from MeOH or EtOH resulted in tiny crystals. ^1H NMR: (in D_2O/TFA) 1.45 (t, 3 H), 2.5 (s, 3 H), 3.13 (q, 2 H), 3.4 (t, 4 H), 4.0 (t, 4 H), 4.8 (s, 2 H); (in Me_2SO-d_6) 1.18 (t), 2.1 (s), 2.83 (q), 2.9 (t), 3.3 (t), 3.75 (s). ^{13}C NMR (Me_2SO-d_6): 8.94, 13.23, 20.51, 36.59, 44.74, 52.95, 123.78, 128.16, 150.06. Anal. Calcd for $C_{11}H_{19}CdCl_2N_3S_2$: C, 29.98; H, 4.35; N, 9.53. Found: C, 29.99; H, 4.38; N, 9.48.

The same procedure was followed with $CdBr_2$. Recrystallization from EtOH resulted in pale yellow crystals. Anal. Calcd for $C_{11}H_{19}Br_2CdN_3S_2$: C, 24.95; H, 3.62; N, 7.93. Found: C, 25.10; H, 3.69; N, 7.88.

Summary of Methods of Data Collection, Solution, and Refinement. A well-formed, colorless, and translucent crystal of needle habit was wedged into a 0.5-mm diameter capillary. Table I lists unit cell and data collection parameters; complete details of data collection and reduction and subsequent structure analysis may be found in ref 12.

The details of the solution and refinement are summarized in Table I. No correction for the effects of secondary extinction was required. The final difference Fourier map showed no excursions of electron density greater than 0.1 e/Å^3 on a scale where a carbon atom showed a density of 4.5 e/Å^3. Final positional and isotropic thermal parameters for non-hydrogen atoms are given in Table II. Anisotropic temperature factors and calculated hydrogen positional parameters and isotropic temperature factors are listed in Tables V and VI (supplementary material).

Results and Discussion

Organic Synthesis. The initial synthetic step is the alkylation of imidazole via a Mannich reaction. Bachman and Heisey had reported that imidazole derivatives did not react under Mannich reaction conditions whereas benzimidazole did.[13] More recently Stocker et al. showed that imidazoles did react under Mannich reaction conditions and that the products formed are pH dependent.[14] Under acidic conditions N-al-

Table I. Summary of Crystal Data and Experimental Details for the Structural Study of $[Cd(C_{11}H_{19}N_3S_2)Br_2]$

(A) Crystal Parameters[a] at 23 °C

$a = 12.988$ (4) Å	$V = 1762.5$ (9) Å^3
$b = 10.899$ (3) Å	space group: $P2_1/n$
$c = 13.148$ (3) Å	$Z = 4$
$\beta = 108.74$ (2)°	$D_{calcd} = 1.996$ g/cm^3

(B) Measurement of Intensity Data

cryst dimens: 0.30 × 0.35 × 0.47 mm
instrument: Nicolet R3m
radiation: Mo Kα (λ = 0.710 69 Å)
scan mode: coupled θ(cryst) − 2θ(counter)
scan rate: 6–30°/min
scan length: from [2θ(Kα$_1$) − 1.0]° to [2θ(Kα$_2$) + 1.0]°
bkgd measurement: 10 s at each end of 2θ scan range
stds: 3 collcd every 197 reflcns; no signif dev obsd
no. of reflcns collcd: 1642
no. of indep reflcns used in soln: 1474 with $(F_o) \geq 6\theta$

(C) Reduction of Intensity Data and Summary of Structure Solution and Refinement[b]

data corrcd for bkgd, attenuators, Lorentz and polarizn effects in the usual fashion
abs coeff: 59.54 cm^{-1}
abs cor: scans on 4 reflcns with χ near 90°; $T_{max}/T_{min} = 1.09$
structure soln: position of Cd obtained from a three-dimen dimensional Patterson synthesis; all remaining non-hydrogen atoms from successive difference Fourier syntheses
atomic scattering factors:[c] for neutral atoms
anomalous dispersion:[d] both real and imaginary components included for all atoms
final discrepancy factor:[e] $R = 0.0235$; $R_w = 0.0240$
goodness of fit:[f] 1.385

[a] From a least-squares fitting of the setting angle of 25 reflections. [b] All calculations were performed on a Data General Nova 3 computer with 32K of 16-bit words using local versions of the Nicolet SHELXTL interactive crystallographic software package as described in: Sheldrick, G. M. "Nicolet SHELXTL Operations Manual"; Nicolet XRD Corp.: Cupertino, CA, 1979. [c] Cromer, D. T.; Mann, J. B. *Acta Crystallog., Sect. A* 1968, *A24*, 321. [d] "Interactional Tables for X-Ray Crystallography"; Kynoch Press: Birmingham, England, 1962; Vol. III. [e] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2]^{1/2}$ ($w = 1/\sigma^2(F_o) + g^*(F_o)^2$). [f] GOF = $[\Sigma w(|F_o| - |F_c|)/(NO - NV)]^{1/2}$ where NO is the number of observations and NV is the number of variables.

Table II. Atom Coordinates (×10^4) for $[Cd(C_{11}H_{19}N_3S_2)Br_2]$

atom	x	y	z
Cd	2088 (1)	2517 (1)	9381 (1)
Br(1)	3992 (1)	2792 (1)	9270 (1)
Br(2)	1914 (1)	2103 (1)	11252 (1)
S(1)	573 (2)	−701 (2)	8537 (2)
S(2)	2128 (2)	−89 (2)	8826 (1)
N(1)	1166 (4)	4302 (4)	8868 (4)
N(2)	200 (4)	5956 (4)	8595 (4)
N(3)	754 (4)	2082 (4)	7626 (4)
C(1)	987 (5)	5328 (5)	9326 (5)
C(2)	−159 (5)	5319 (5)	7641 (5)
C(3)	468 (5)	4294 (5)	7837 (4)
C(4)	550 (5)	3294 (5)	7090 (4)
C(5)	−1018 (6)	5763 (6)	6684 (5)
C(6)	1587 (6)	5753 (6)	10429 (5)
C(7)	2695 (8)	6130 (10)	10586 (7)
C(11)	−277 (5)	1649 (5)	7790 (5)
C(12)	−131 (5)	687 (5)	8659 (5)
C(21)	1118 (5)	1191 (6)	6952 (5)
C(22)	2101 (5)	483 (6)	7521 (5)

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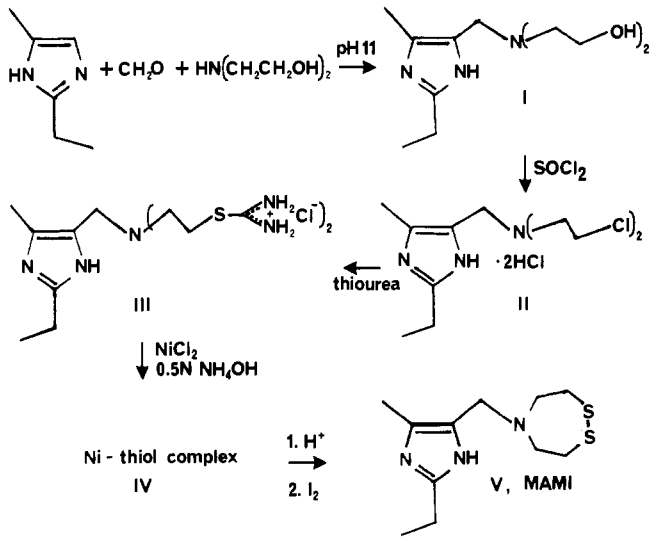
Scheme I



kylation occurs, whereas under basic conditions a mixture of N-and C-alkylation occurs. The N-alkylated product readily decomposes in the presence of base; therefore, only the C-alkylated product is isolated. Indeed, we found that *N*-[(bis(2-chloroethyl)amino)methyl]imidazole could be prepared by the Mannich reaction of bis(2-chloroethyl)amine with imidazole under acidic conditions, as evidenced by NMR (at pD 3, the methylene bridge resonances were at 5.5 ppm (H) and 72 ppm (C)). It was very unstable, and recrystallization or sublimation resulted in its decomposition. Subsequent nucleophilic reaction conditions also resulted in its decomposition.

Because under basic Mannich conditions imidazole can be alkylated at positions 1, 2, 4, and 5 with the formation of mixtures of mono-, di-, tri-, and tetrasubstituted compounds,[14] a highly substituted imidazole, 2-ethyl-4(5)-methylimidazole, was employed here. Only one product (I) was formed (Scheme I). It is a yellow oil that was isolated as its HCl salt. The NMR chemical shifts for the methylene bridge of I are greatly different from those of *N*-[(bis(2-chloroethyl)amino)-methyl]imidazole; for I at pD 3 the shift values are 4.7 ppm (H) and 55 ppm (C). These values are indicative of C-substituted imidazoles. A similar compound, 4(5)-[(bis(hydroxyethyl)amino)methyl]imidazole, was prepared by the alkylation of diethanolamine with 4(5)-(chloromethyl)imidazole.[15]

Compound I·2HCl is readily converted to II by using thionyl chloride. If I·2HCl is deprotonated and then treated with thionyl chloride, no product is obtained. A similar observation has been reported for ethanolamine.[16]

Compound II is a substituted nitrogen mustard and should undergo nucleophilic reactions.[16] Nucleophilic displacements are usually done under basic conditions. Under these conditions deprotonation of the amine and cyclization of the nitrogen mustard occur.[17] Once cyclization has occurred, a second mode of attack by the nucleophile appears. Attack at C(3) appears to be the preferred site of attack. Spectral data suggested that 2-ethyl-4-((methylthio)methyl)-5-methylimidazole was formed when II was treated with CH_3S^-. Nucleophilic displacements carried out under acidic conditions eliminated this problem. Addition of thiourea resulted in the formation of III.

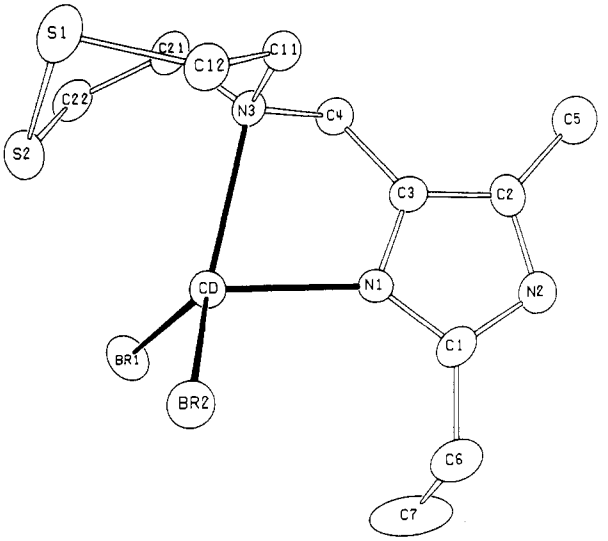


Figure 1. Perspective view of $Cd(MAMI)Br_2$.

Table III. Bond Lengths (Å) for $[Cd(C_{11}H_{19}N_3S_2)Br_2]$

Cd-Br(1)	2.542 (1)	Cd-Br(2)	2.581 (1)
Cd-S(2)	2.938 (2)	Cd-N(1)	2.270 (4)
Cd-N(3)	2.446 (4)	S(1)-S(2)	2.042 (3)
S(1)-C(12)	1.801 (6)	S(2)-C(22)	1.815 (7)
N(1)-C(1)	1.326 (8)	N(1)-C(3)	1.366 (6)
N(2)-C(1)	1.343 (7)	N(2)-C(2)	1.376 (8)
N(3)-C(4)	1.480 (7)	N(3)-C(11)	1.499 (8)
N(3)-C(21)	1.491 (9)	C(1)-C(6)	1.483 (8)
C(2)-C(3)	1.358 (8)	C(2)-C(5)	1.470 (8)
C(3)-C(4)	1.494 (8)	C(6)-C(7)	1.446 (13)
C(11)-C(12)	1.517 (9)	C(21)-C(22)	1.473 (9)

Although isothiuronium compounds are readily hydrolyzed by base to the corresponding thiol,[18] attempts to hydrolyze III with base did not result in a useful product. A rearrangement involving the imidazole nitrogens could be responsible since compounds containing primary or secondary amines β to thiourea rearrange to the corresponding (mercaptoethyl)-guanidine compound.[19-21]

Hydrolysis of isothiuronium salts by metal salts has been reported.[22-25] Pt(II)[23,24] and Pd(II)[25] convert benzylisothiuronium hydrochloride and methylisothiuronium to the corresponding (alkylmercapto)metal complexes. Reaction of ethylene diisothiuronium bromide with Ni(II), Cu(II), and Zn(II) in dilute ammonia results in a mixture including the desired product metal ethanedithiolate.[22] Reaction of compound III with Ni(II), Cu(II), and Pt(II) resulted in a mixture of metal complexes. The amount of hydrolysis was conveniently monitored by the disappearance of the characteristic C-N stretch at 2160 cm^{-1}. Treatment of III with $NiCl_2$ gave IV, with complete hydrolysis of the thiourea. Only partial hydrolysis was observed with Pt(II) or Cu(II) salts.

Complex IV is insoluble in many common solvents, and it may be a polymeric species. ^1H NMR spectra of an acidic

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Table IV. Bond Angles (deg) for $Cd[Cd(C_{11}H_{19}N_3S_2)Br_2]$

Br(1)-Cd-Br(2)	117.42 (1)	Br(1)-Cd-S(2)	90.33 (3)
Br(2)-Cd-S(2)	94.74 (2)	Br(1)-Cd-N(1)	108.2 (1)
Br(2)-Cd-N(1)	103.5 (1)	S(2)-Cd-N(1)	143.5 (1)
Br(1)-Cd-N(3)	112.1 (1)	Br(2)-Cd-N(3)	127.8 (1)
S(2)-Cd-N(3)	69.0 (1)	N(1)-Cd-N(3)	74.9 (1)
S(2)-S(1)-C(12)	102.1 (2)	Cd-S(2)-S(1)	105.5 (1)
Cd-S(2)-C(22)	84.6 (2)	S(1)-S(2)-C(22)	102.7 (2)
Cd-N(1)-C(1)	137.8 (4)	Cd-N(1)-C(3)	114.1 (3)
C(1)-N(1)-C(3)	107.3 (4)	C(1)-N(2)-C(2)	110.6 (5)
Cd-N(3)-C(4)	103.9 (3)	Cd-N(3)-C(11)	108.7 (3)
C(4)-N(3)-C(11)	108.6 (4)	Cd-N(3)-C(21)	115.0 (3)
C(4)-N(3)-C(21)	109.9 (5)	C(11)-N(3)-C(21)	110.4 (4)
N(1)-C(1)-N(2)	108.0 (5)	N(1)-C(1)-C(6)	126.4 (5)
N(2)-C(1)-C(6)	125.5 (6)	N(2)-C(2)-C(3)	103.6 (5)
N(2)-C(2)-C(5)	123.8 (5)	C(3)-C(2)-C(5)	132.6 (6)
N(1)-C(3)-C(2)	110.4 (5)	N(1)-C(3)-C(4)	119.5 (5)
C(2)-C(3)-C(4)	129.8 (5)	N(3)-C(4)-C(3)	112.1 (5)
C(1)-C(6)-C(7)	114.5 (7)	N(3)-C(11)-C(12)	115.1 (4)
S(1)-C(12)-C(11)	117.2 (5)	N(3)-C(21)-C(22)	115.3 (5)
S(2)-C(22)-C(21)	114.2 (5)		

solution are consistent with release of a dithiol ligand. The analysis gives a C:N ratio of 3.7, which confirms the total hydrolysis of the thiourea.

Nevertheless, V (MAMI) was readily isolated from IV by the oxidation of the ligand with iodine and extraction into chloroform. The ligand thus isolated was assumed to be a cyclic disulfide. The chemical shift for the carbon α to a thiol is ~40 ppm. The chemical shift found for compound V is 39.05 ppm. Similar disulfides have been reported by Herbrandson and Wood[26] and Boyland and Nery.[27]

Attempts to isolate the dithiol compound after treatment of V with reducing agents were unsuccessful. Interactions between the basic imidazole nitrogen and the thiol may account for this problem.

Cadmium Complexes. Description of the Structure of Cd(MAMI)Br_2. The crystal consists of discrete molecules of $[Cd(C_{11}H_{19}N_3S_2)Br_2]$ that are separated by normal van der Waals distances. A perspective view of the molecule, giving the atom-labeling scheme, is shown in Figure 1. Interatomic distances and their estimated standard deviations (esd's) are listed in Table III while interatomic angles and their esd's are given in Table IV.

The molecule consists of a central Cd(II) atom coordinated to a pair of bromide groups, an imidazole nitrogen, and the amine nitrogen of MAMI and weakly bonded to a sulfur of the disulfide linkage of the MAMI ligand. The geometry about the Cd atom may be described as highly distorted trigonal bipyramidal, with the bromide ligands and the amine nitrogen N(3) defining the equatorial plane and the imidazole nitrogen N(1) and disulfide sulfur S(2) occupying the axial sites. The CdBr(1)Br(2)N(1)N(3) grouping is distinctly pyramidal, with the Cd displaced 0.4 Å from the Br(1)Br(2)N(3) plane toward the apical N(1) donor. Although unexceptional, the Cd–Br distances are inequivalent, a consequence of the absence of mirror symmetry through the CdN(1)N(3)S(2) plane. The Cd–imidazole nitrogen N(1) distance is significantly shorter (0.18 Å) than the Cd–amine nitrogen N(3) distance, presumably as a result of sp^2 vs. sp^3 hybridization at the respective nitrogen donors.

The Cd–S(2) distance, 2.938 Å, is considerably longer than the calculated single-bond distance of 2.40 Å[28] but significantly shorter than the sum of the van der Waals radii, 3.40 Å.[29] This observation, together with the folding of the dithiazepane ring so as to direct the lone pairs of the sulfur and nitrogen donors toward the Cd center, provides strong evidence for Cd–S(2) covalent bonding. The unusually long distance is in part a consequence of the steric requirements of the tridentate MAMI ligand, which must generate two five-membered chelate rings and a six-membered chelate ring with the Cd atom. The consequent displacement of the Cd atom toward the imidazole group and the concomitant steric interplay of the bulky bromide donors with the disulfide linkage prevent close approach of the S(2) donor to the central Cd. A similar effect has been observed for [Cu(pyridylbis((ethylthio)-ethyl)amine)NO_3]$^+$ where an unusually long Cu–S bond results from steric congestion.[30]

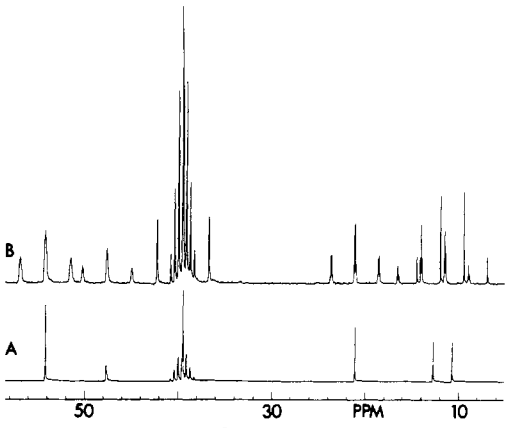

Figure 2. Decoupled (A) and coupled (B) ^{13}C NMR spectra of MAMI in Me_2SO-d_6.

The MAMI ligand generates three chelate rings with the Cd: the five-membered rings CdN(1)C(3)C(4)N(3) and CdS(2)C(22)C(21)N(3) assume asymmetric envelope conformations;[31] the six-membered ring CdS(2)S(1)C(12)C(11)N(3) displays an asymmetric boat conformation.

Solution NMR Studies. The upfield region of the ^{13}C NMR spectra for ^1H coupled and decoupled MAMI in Me_2SO-d_6 is shown in Figure 2. The downfield region is shown in the supplementary material.

The upfield signals at 10.64, 12.67, and 21.08 ppm are assigned to C(5), C(7), and C(6), respectively, on the basis of $^1J_{CH}$ and $^2J_{CH}$ couplings (see Figure 2). The signal at 47.66 ppm is assigned to C(4) on the basis of results of selective ^1H decoupling of the C(4) protons.

Both C(11), C(21) and C(12), C(22) give triplets in the coupled ^{13}C NMR spectra, and the respective ^1H NMR signals are difficult to assign. However, one of signals in the ^1H-coupled ^{13}C NMR spectrum (Figure 2) is significantly broader than the other signal and probably results from quadrupolar relaxation effects of ^{14}N. Thus, this signal at 54.18 ppm is assigned to C(11), C(21) and the signal at 39.43 ppm assigned to C(12), C(22). This is consistent with the general shift ranges for RCH_2N and RCH_2S of ~45–55 and ~22–42 ppm, respectively.[32] It should be noted that the resonance for C(4), which is also bonded to N, is as broad as the C(11), C(21) resonance.

In the downfield region, the signal at 146.76 ppm is assigned to C(2) on the basis of two-bond CH coupling to the C(5) methyl protons. Selective ^1H irradiation of the protons at C(4) during ^{13}C data acquisition results in a sharpening of the signal at 126.92 ppm, possibly due to the elimination of long-range

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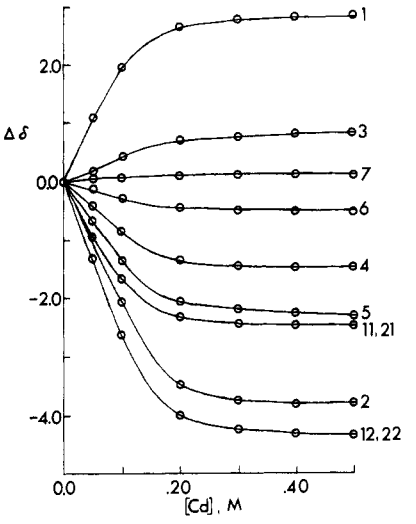

Figure 3. Change in chemical shift of MAMI ^{13}C NMR signals (0.2 M in Me_2SO-d_6) as a function of added $Cd(NO_3)_2$. Negative values are for upfield shifts.

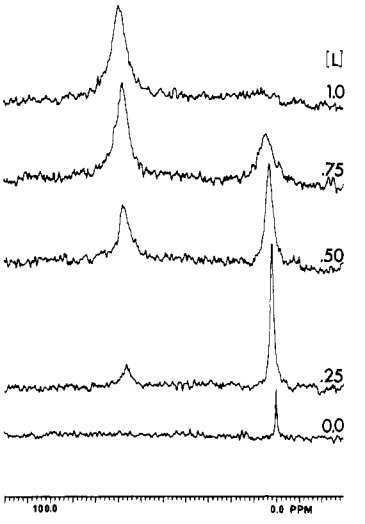

Figure 4. Change in the ^{113}Cd NMR spectrum of $Cd(NO_3)_2$ (1.0 M in Me_2SO-d_6) as MAMI is added to the concentrations indicated (M) in the individual traces.

$^2J_{CH}$ coupling. Thus, these signals at 126.92 and 127.03 ppm are tentatively assigned to C(3) and C(1), respectively.

^{13}C NMR spectral data for solutions of MAMI (0.20 M, Me_2SO-d_6) and the effects of $Cd(NO_3)_2 \cdot 4\,H_2O$ (0.05–0.5 M) are given in Table VII (supplementary material) and are shown in Figure 3. The ^{13}C resonances are shifted significantly up to 0.20 M added $Cd(NO_3)_2$. This indicates that a 1:1 complex is the principal species in solution and treatment of the shift data in the usual way[33] leads to a formation constant of $\sim 60\ M^{-1}$.

The ^{13}C resonances are in fast exchange between free and complexed MAMI. The resonances assigned to C(12), C(22) shift most significantly whereas one imidazole resonance and the C(11), C(21) resonance also shift appreciably. However, simple disulfides such as CH_3SSCH_3 do not appear to interact with Cd(II) under these conditions, and we cannot determine whether the magnitude of the ^{13}C shift for C(12), C(22) is consistent with a Cd–S interaction or is caused by a ring conformational change.

^{113}Cd NMR spectral data were obtained for solutions containing $Cd(NO_3)_2$ (1.0 M, Me_2SO-d_6) and the ligand MAMI (Figure 4). From these data it is clear that complex formation is nearly quantitative since, at 1:1 Cd:MAMI, the signal due to free Cd (σ = 0 ppm) has almost entirely disappeared and a new signal due to Cd(MAMI) (σ = 69 ppm) is obtained. This finding is consistent with the ^{13}C NMR data.

We have previously reported ^{113}Cd NMR chemical shifts for an extensive series of Cd–amine complexes that give rise to slow-exchange signals,[11] including complexes containing the related ligands 1,10-phenanthroline (σ = 61 ppm) and *N,N,N'N'*-tetramethylethylenediamine (σ = 66 ppm). In addition, we obtained shifts for Cd–amine complexes with the following amines: 2-((diethylamino)methyl)pyridine[34] (δ 64), 2-((dimethylamino)methyl)-3-hydroxypyridine (δ 66). All these values compare favorably with the calculated value of 62 ppm[11] for 1:1 Cd:L complexes containing L = bidentate, secondary N-donor, especially considering that the range of chemical shifts for Cd–amine complexes is $\sim$340 ppm.[11] The effect of S binding on Cd shifts is usually appreciable.[35] Thus, there is no strong evidence for Cd–S binding in Me_2SO-d_6 solution for Cd–MAMI complexes.

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Registry No. I, 90823-14-6; II, 90823-15-7; III, 90823-16-8; V, 90823-17-9; $Cd(MAMI)Cl_2$, 90823-12-4; $Cd(MAMI)Br_2$, 90823-13-5; 2-ethyl-4(5)-methylimidazole, 931-36-2; diethanolamine, 111-42-2; formaldehyde, 50-00-0; thiourea, 62-56-6.

Supplementary Material Available: Anisotropic thermal parameters (Table V), hydrogen atom coordinates (Table VI), ^{13}C NMR data for MAMI as a function of added $Cd(NO_3)_2 \cdot 4H_2O$ (Table VII), figure of the downfield region of the ^{13}C NMR spectrum of MAMI (Figure 5), and observed and calculated structure factors (Table VIII) (13 pages). Ordering information is given on any current masthead page.

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