Pergamon

Tetrahedron 54 (1998) 2339–2346

TETRAHEDRON

Metal Ion-Induced Self Assembly of Open-Chain Tetrapyrrole Derivatives: Double Stranded Dinuclear Complexes from 10-Oxo-5,15-biladienes

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Received 13 November 1997; accepted 15 December 1997

Key words: open chain tetrapyrroles; metal coordination; X-ray structure; NMR dynamics

Abstract: Syntheses of double stranded neutral species via the complexation of Zn, Cd, and Hg with 10-oxo-5,15-biladiene LH_2 are described. Formation of the single stranded Cd complex indicates that the self assembly process which affords the double stranded system is not simply a consequence of relief of steric strain. The crystal structure of the cadmium(II) double stranded dimer **8** is described. Long contact distances between carbonyl spacers and Cd ions in the crystal structure of **8** complete the coordination sphere of each Cd, concomitantly forming two distorted trigonal bipyramidal metal centers. Fast coordination/decoordination phenomena involving the carbonyl spacers and the two metallic centers in the zinc(II), cadmium(II) and mercury(II) dimeric complexes **7**, **8** and **9**, respectively, are investigated by using variable temperature ^{1}H NMR. A bending/twisting process is proposed, and its associated energy barrier (40-50 kJ mol^{-1}) is determined for the first time.

INTRODUCTION

Due to the important roles they play in nature, oligopyrroles have been extensively studied.[1] In particular, many open-chain tetrapyrroles serve both as natural products in their own right (bile pigments, biliproteins),[1,2] and as important intermediates in synthetic approaches to naturally occurring porphyrins, chlorins and corrins.[2] As part of these synthetic studies, the X-ray structure of a formylbiliverdin double-stranded molecule was reported as early as 1976 by Fuhrhop and coworkers.[3] Two crystalline forms of this zinc(II) bilatriene complex were obtained. The first form was a monomer with the ligand wrapped around an aquo-zinc(II) center. Dehydration with a strong acid yielded a four-coordinate zinc complex with a tetrahedral configuration stabilized by the formation of a double stranded dimer. Biladienes also formed 2:2 complexes[4] which were characterized by the crystal structure of the zinc(II) decamethyl-a,c-biladiene.[5] Previously published work[6] on 5-oxo-10,15-biladienes (e.g. **1**) and 10-oxo-5,15-biladienes **2** revealed that with the majority of transition metals studied, a 1:1 complex was formed with the metal coordinating to four pyrrole nitrogen atoms; in some instances (e.g. 5-oxo-10,15-biladienes with Ni^{II}) two products were isolated, one being the normal tetra-N coordinated derivative, and the other a complex in which the metal was coordinated with three pyrrole N-atoms and the 5-carbonyl oxygen atom. Coordination of the 10-carbonyl oxygen to the metal in 10-oxo-5,15-biladienes was not observed.

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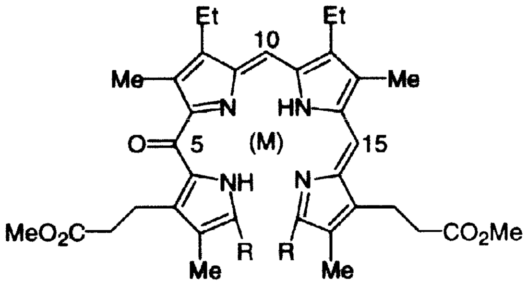
PII: S0040-4020(98)00003-9



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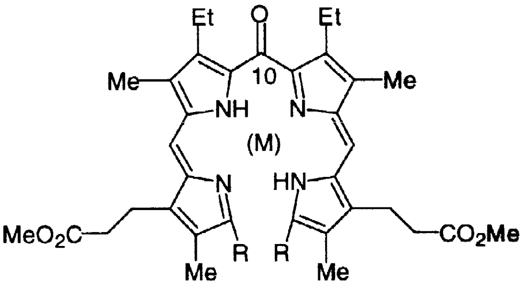


2

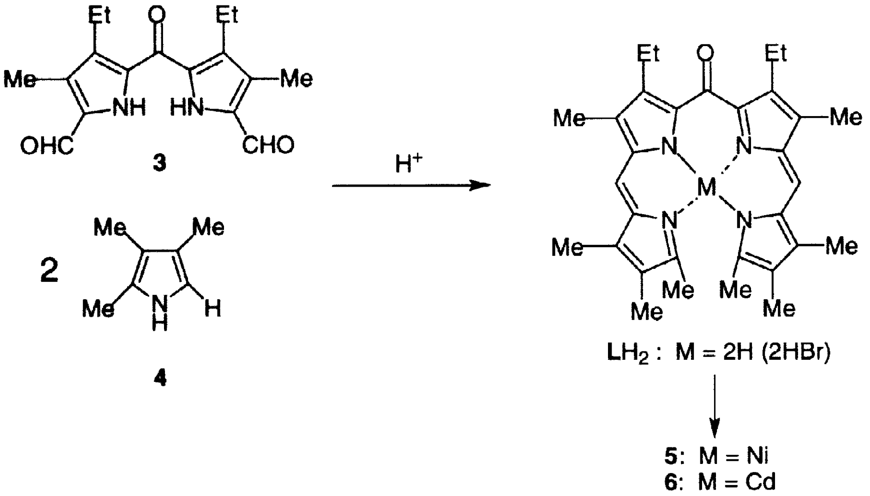
R = CO_2CH_2Ph

Despite these earlier results, no polypyrroles or other pyrrolic ligands have been synthesized to promote or study self assembled molecular arrays, despite the fact that pyrroles are readily functionalized building blocks.[1,2] Indeed, polypyrroles can be functionalized in a double-ended fashion to yield linear cyclic chromophores such as bisporphyrin-biladienes[7] and various spacers can also be introduced between dipyrrin units of tetrapyrroles.[8] Herein, we describe a convenient synthetic approach to symmetrical 10-oxo-5,15-biladienes, LH_2. Introduction of a carbonyl spacer dissects this tetrapyrrole into two chelating dipyrromethene regimes, both of which can act as potential ligands.

RESULTS AND DISCUSSION

Complex Formation and Characterization.

The LH_2 ligand was synthesized by acid catalyzed condensation[9] of two equivalents of the 1,9-diformyl-5-oxodipyrromethane **3** with 2,3,4-trimethylpyrrole **4**.



3

2 **4**

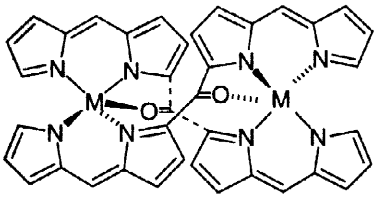
H^+

LH_2 : M = 2H (2HBr)

5: M = Ni
6: M = Cd

Metallations of LH_2 with metal acetates in presence of sodium acetate were achieved in 20 min at room temperature in dry methanol. Complexes Ni(II)L **5** and Cd(II)L **6** precipitated as purple crystals and could be easily isolated by filtration.[6] Complexes $Zn(II)_2L_2$ **7**, $Cd(II)_2L_2$ **8** and $Hg(II)_2L_2$ **9** were purified by chromatography on alumina. While complexes **7** and **8** were stable over a period of one year in solution, mercury complex **9** was found to decompose even in the solid state over a long period of time. Compound Cd(II)L **6** showed a low intensity molecular peak at m/z 593.0 and an intense peak corresponding to the loss of the metal (at m/z 483.3). Dimeric complexes $Zn(II)_2L_2$ **7**, $Cd(II)_2L_2$ **8** and $Hg(II)_2L_2$ **9** did not exhibit any peak assigned to the uncomplexed ligand in their fast atom bombardment mass spectra but an intense peak assigned to double charged $M_2L_2^{2+}$ species and a molecular peak at m/z 1185.4, 1092.5 and 1362.6, respectively. Infrared spectral studies were inconclusive; both C=O and C=C bonds absorb in the 1600 cm^{-1} region and are sensitive to a change in the metal. 2:2 Complexes (**7**-**9**) displayed similar proton NMR spectra but with resonances shifted upfield (notably the methylene CH_2CH_3 protons, $\Delta\delta$ = *ca* 0.5- 0.7 ppm) compared to the 1:1 complexes (**5** and **6**).

In solution and in the solid state, 10-oxo-a,c-biladiene LH_2 may preferentially adopt a cyclic overall geometry, or an open semi-circular conformation, although flexibility of the methene fragments may be influenced by a variety of factors, as is well illustrated for 1,19-bilindiones.[1] This porphyrin-like configuration appears to favor the formation of compressed circular monomer upon complexation with Ni(II), Cu(II) and Pd(II), (as shown by their X-ray structures).[6]



Substituents omitted for clarity

7 : M = Zn
8 : M = Cd
9 : M = Hg

Complexation of Cd(II) at room temperature yielded the monomeric and dimeric species **6** and **8** in a 2:1 ratio, respectively. When cadmium chelation was performed in refluxing methanol, compound **8** was preferentially formed (3:1 ratio with **6**). Mercury complexation at room temperature yielded also a mixture of mono-[6] and double-stranded complexes (in a 1:1 ratio). Performing this reaction in boiling methanol gave only the dimeric species $Hg(II)_2L_2$ **9**. Heating samples of **7** and **8** (100°C, toluene-d_8) did not reveal any rate process on the NMR timescale, precluding the hypothesis of a dynamic interconversion process between 1:1 and 2:2 complexes. However, a NMR sample of pure Cd(II)L **6** ($CDCl_3$, room temperature), when doped with a small amount of the corresponding double stranded complex, was converted quantitatively, over two weeks, into the thermodynamically more stable 2:2 complex **8**. Formation of Cd(II)L **6**, despite existence of a less strained dimeric structure (Cd_2L_2 **8**), suggests a macrocyclic pre-organization of LH_2.

The X-ray structure of **8** is shown in Figure 1; selected bond lengths and bond angles are reported in Table 1. The double stranded complex is chiral, and both enantiomers are present equally. Formation of the double-helical geometry is achieved by a twist of 65° and 115° between the dipyrromethene subunits of each strand, such that both Cd(1) and Cd(2) are each coordinated with a dipyrromethene subunit from each ligand along with one oxygen from one of the ligands. In agreement with the literature,[10] the N-Cd bond lengths range from 2.17-2.31 Å. All N-Cd-N angles are distorted from those expected for a trigonal bipyramidal complex, and range from 88.5(3)-134.7°(3) for Cd(1) and 84.7(2)-136.2°(3) for Cd(2). The coordination sphere is completed by Cd···O bonds[11] of 2.585(6) Å and 2.665(6) for Cd(1) and Cd(2), respectively. We are uncertain whether this carbonyl interaction is a key feature in the self-assembly process, or whether it is a serendipitous consequence of the adoption of the double stranded structure. Compound **8** possesses a pitch height of 7.45 Å and the intramolecular Cd(1)-Cd(2) distance is 5.116(1) Å, which is larger than twice the atomic radius of cadmium and precludes any direct Cd(II)-Cd(II) interactions. Each dipyrromethene moiety is slightly twisted with interplanar angles between adjacent rings in the range of 5.3-8.0°. A stacking interaction is observed between dipyrromethene subunits of two strands with closest interplanar contacts between C(4)-C(26) (3.52 Å) and C(6)-C(29) (3.39 Å) (Figure 1B). This stacking interaction between pyrrole units also help drive the assembly process.

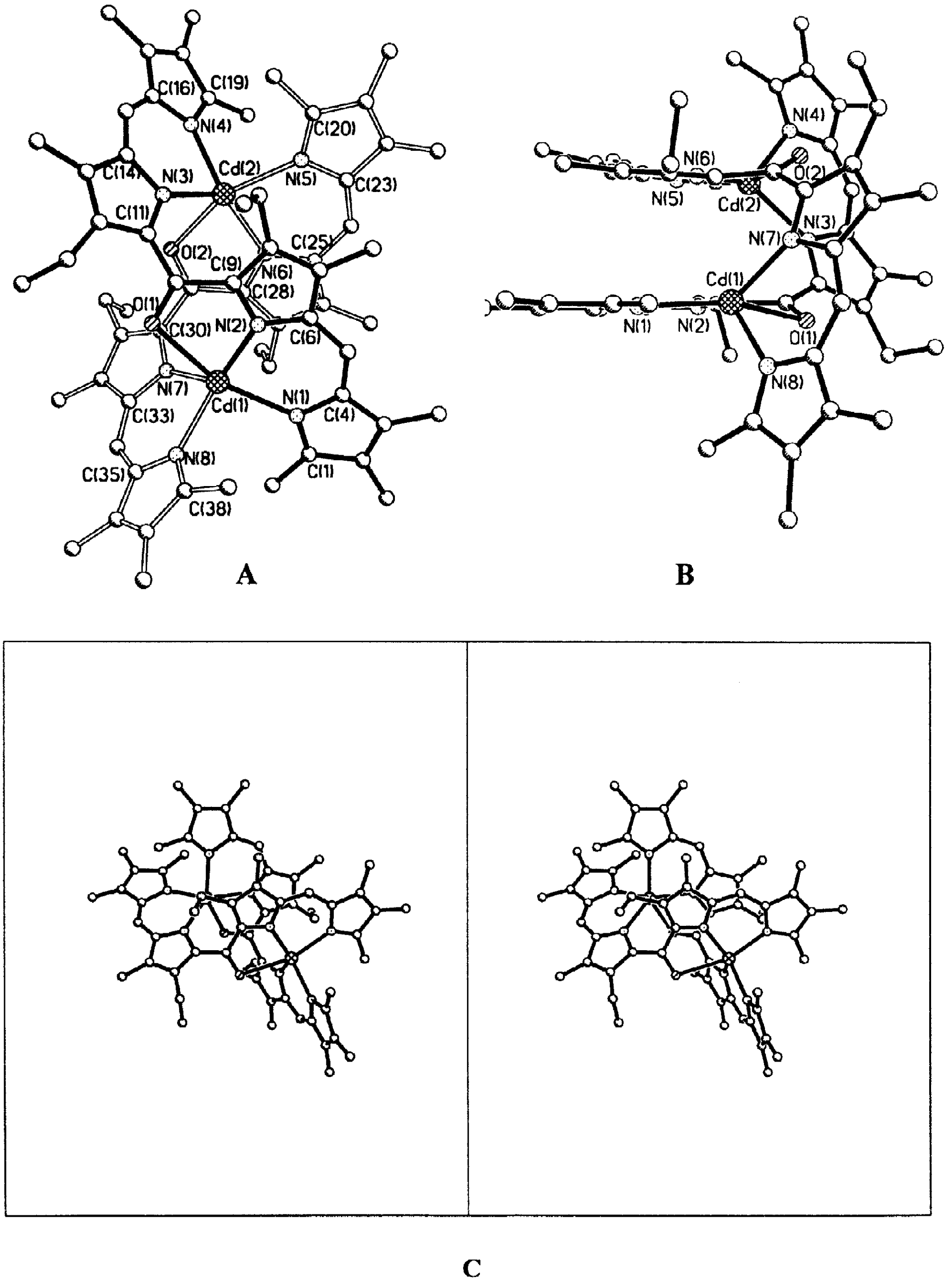


Figure 1. (A) View of the molecular structure of the right-handed double-stranded complex **8**. (B) Illustration of the π-stacking interactions. (C) Stereo-plot of **8**.

Table 1. Selected Structural Data for **8** (estimated standard deviations are given in parentheses).

N-Cd Bond Lengths (Å)			
N(1)-Cd(1)	2.312(7)	N(3)-Cd(2)	2.207(7)
N(2)-Cd(1)	2.175(7)	N(4)-Cd(2)	2.224(7)
N(7)-Cd(1)	2.206(8)	N(5)-Cd(2)	2.300(7)
N(8)-Cd(1)	2.228(7)	N(6)-Cd(2)	2.169(7)

Angles (°) in the Distorted Trigonal Bipyramid of Cd(1)			
N(1)-Cd(1)-N(2)	84.9(3)	O(1)-Cd(1)-N(1)	150.4(2)
N(1)-Cd(1)-N(7)	121.5(3)	O(1)-Cd(1)-N(2)	67.6(2)
N(1)-Cd(1)-N(8)	97.7(2)	O(1)-Cd(1)-N(7)	85.8(2)
N(2)-Cd(1)-N(7)	128.4(3)	O(1)-Cd(1)-N(8)	94.2(2)
N(2)-Cd(1)-N(8)	134.7(3)		
N(7)-Cd(1)-N(8)	88.5(3)		

Angles (°) in the Distorted Trigonal Bipyrimid of Cd(2)			
N(3)-Cd(2)-N(4)	87.8(3)	O(2)-Cd(2)-N(3)	90.2(2)
N(3)-Cd(2)-N(5)	120.3(3)	O(2)-Cd(2)-N(4)	95.4(2)
N(3)-Cd(2)-N(6)	130.0(2)	O(2)-Cd(2)-N(5)	148.3(2)
N(4)-Cd(2)-N(5)	94.3(3)	O(2)-Cd(2)-N(6)	67.6(2)
N(4)-Cd(2)-N(6)	136.2(3)		
N(5)-Cd(2)-N(6)	84.7(2)		

Dynamic NMR Studies.

Variable temperature ^{1}H NMR studies of complexes **5-9** provided an insight into the metal dependence of these complexes, their chiral nature, and their structure in solution. Proton NMR spectra of Ni(II)**L 5** displayed diastereotopic methylene protons (ABX$_3$ multiplet at δ ca, 2.85 ppm) due to the prochirality introduced by the enforced conformations in these molecules. At the highest temperature studied (378 K, toluene-d$_8$), no broadening of this multiplet was observed; this is consistent with the retention of a helical chiral structure in solution and indicates an inversion barrier larger than 80 kJmol^{-1}.[12] Methylene protons of compound Cd(II)**L 6** did not show this diastereotopic behavior and appeared as a well-defined quartet (293 K, CDCl$_3$, J = 7.35 Hz). This apparent C_{2v} symmetry indicates that a dynamic exchange is occurring which makes the methylene protons equivalent on the NMR time scale. Indeed, upon cooling an NMR sample of **6** in CD$_2$Cl$_2$, coalescence of these protons was observed at 225 K, with a broad multiplet emerging at 183 K. Interconversion of the two chiral atropisomers of **6** must proceed via a coplanar conformation of the tetrapyrrolic ligand despite the steric crowding generated by the terminal methyl substituents. This dynamic process is favored in the case of large cations such as Cd^{2+} which increase the size of the macrocyclic core via long nitrogen-metal bonds, and therefore minimize the steric interactions between terminal substituents.

Proton NMR spectra of **7**, **8** and **9** showed resonances corresponding to one quarter of the complex, as underlined by a single resonance for the methine hydrogen, indicating D_2 symmetry on the NMR time scale. Dynamic processes that produced this symmetrization of the ligand environment may involve a fast coordination-decoordination of each keto group oscillating between both cadmium centers by the way of a dynamic bending-twisting process.[12] The methylene protons appeared as two distinct multiplets (ABX$_3$ system) partially hidden under the methyl peaks, and did not broaden at 373 K. The methine protons formed a convenient probe to study the fluxionality of these systems. Upon cooling an NMR sample of Cd(II)$_2$L$_2$ **8** in CD$_2$Cl$_2$, coalescence of the methine protons was observed at 268 K before sharpening to give two singlets (2H each), well resolved at 243 K (300 MHz, Δν = 168 Hz). If these changes result from an exchange of the carbonyl spacer over the two cadmium centers via the bending-twisting process, the energy barrier associated with such a process is estimated to be 52 $kJmol^{-1}$. Variable temperature studies on the zinc and mercury complexes **7** and **9** in CD_2Cl_2 showed a similar coalescence of their methine protons and, upon further cooling, a gradual appearance of two singlets (**7**: Tc = 203 K, Δν = 138 Hz, $\Delta G^{\#}$ = 39 $kJmol^{-1}$; **9**: Tc = 221 K, Δν = 158, $\Delta G^{\#}$ = 43 $kJmol^{-1}$). This further confirms their dimeric nature in solution. A smaller energy barrier observed for the dimeric zinc species **7** may arise from a smaller distance between the two metallic centers facilitating the coordination/decoordination process; this assumption is reasonable, the distance between both zinc ions in Fuhrhop's dimer being 3.37 Å,[4] compared with a 5.12 Å distance between both Cd ions in **8**. The fast coordination/decoordination process of the carbonyl spacers is consistent with the long Cd···O contact distances revealed in the X-ray structure of **8**.

CONCLUSIONS

Complexation of dications by the 10-oxo-a,c-biladiene LH_2, a porphyrin like ligand, generated single or double stranded neutral molecules. Since there is no ligand field stabilization effect in Zn^{2+} and Cd^{2+} ions, the steric preference for the tetrahedral arrangement yielded the dimeric species $Zn(II)_2L_2$ **7** and $Cd_2(II)L_2$ **8**. However, isolation of monomer Cd(II)L **6**, shown to be less sterically strained than Ni(II)L **5**, suggests that steric factors are not the main driving force toward the formation of these double stranded complexes. In solution, slow conversion of **6** into **8** may involve the coordination of a carbonyl spacer from one complex Cd(II)L to the cadmium of another molecule in order to assist the formation of the double stranded complex **8**. Long distance contacts between carbonyl spacers and cadmium ions have been found in the crystal structure of **8**. Fast coordination/decoordination processes of these carbonyl spacers over the two metallic centers of complexes **7**, **8** and **9** proved to be a versatile tool for confirmation of their dimeric nature and for study of their fluxionality in solution. By using the methine proton signals as a probe in dynamic ^1H NMR studies, we have been able to estimate, for the first time, the energy barrier (40-50 $kJmol^{-1}$) associated with the bending-twisting process taking place in these double stranded molecules.

EXPERIMENTAL

M.p.s were measured on a Thomas/Bristoline microscopic hot stage apparatus and were uncorrected. Silica gel 60 (70-230 and 230-400 mesh, Merck) or neutral alumina (Merck; usually Brockmann Grade III, i.e. deactivated with 6% water) were used for column chromatography. Reactions were monitored by TLC and spectrophotometry and were carried out under nitrogen and in the dark (aluminum foil). ^1H-NMR spectra were obtained in deuteriochloroform solution at 300 MHz using a General Electric QE300 spectrometer; chemical shifts are expressed in ppm relative to chloroform (7.258 ppm). Elemental analyses were performed at the Midwest Microlab., Inc., Indianapolis, IN. Unless stated otherwise, electronic absorption spectra were measured in dichloromethane solution using a Hewlett-Packard 8450A spectrophotometer. Mass spectra were obtained at the Mass Spectrometry Facility, University of California, San Francisco, CA. Compounds $LH_2{\cdot}2HBr$ and **6**-**7** were prepared according to literature methods;[6] the molecular structure of dimeric complex **7** was earlier assumed erroneously to be a monomeric species.[6]

Crystal Structure Analysis for Compound 8 [$C_{62}H_{72}Cd_2N_8O_2$•$2(C_6H_{12})$]. Single crystals were grown from dichloromethane/cyclohexane. The crystals were immersed in hydrocarbon oil and a single crystal was selected, mounted on a glass fiber, and placed in low-temperature N_2 stream generated by a LT-1 device. X-ray diffraction data were collected on a Siemens $P2_1$ diffractometer with a fine-focus sealed tube [(λ(Cu Kα) 1.54178 Å] at 130(2)K in $\theta/2\ \theta$ scan mode to $2\theta_{max} = 112°$. The unit cell was monoclinic and of space group P2(1)/c (No. 14) with cell dimensions: a = 17.476(4), b = 21.249, c = 19.787(4) Å, β = 112.02(2)°, V = 6812(2) Å^3 and Z = 4 (FW = 1342.29, ρ_{calc} = 1.309 g.cm^{-3}). Unit-cell parameters were derived from the setting angles of 40 reflections in the range of $55° \leq 2\theta \leq 60°$. Two standard reflections were measured every 198 reflections in a total reflections of 9561 of which 8803 were unique (R_{int} = 0.085); number of parameters = 369. Final R factors were $R1$ = 0.076 (based on observed data), and w$R2$ = 0.226 (based on all data). The intensities were corrected for Lorentz and polarization effects. An absorption correction was applied using XABS2;[13] extinction effects were disregarded. The structure solution of compound **8** was solved using direct methods and refined (based on F^2 using all independent data) by full matrix least squares methods (Siemens SHELXTL V. 5.02). Hydrogen atoms were included at calculated positions by using a riding model. One of the cyclohexane molecules also exhibited high thermal motion and isotropic thermal parameters were subsequently fixed to 0.1 Å^2 and hydrogens were not added. Only Cd(1) and Cd(2) were refined with anisotropic thermal parameters due to absorption problems of Cu radiation by Cd(1) and Cd(2).

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Center (CCDC).

Bis-[(8,12-diethyl-1,2,3,7,13,17,18,19-octamethyl-a,c-biladienato-10-one)cadmium(II)] (8). In 40 mL of dry methanol, 63 mg (2.36 mmol) of $Cd(OAc)_2 \cdot 2H_2O$ and 40 mg of NaOAc were dissolved. After 10 min, 80 mg (1.25 mmol) of 8,12-diethyl-1,2,3,7,13,17,18,19-octamethyl-a,c-biladiene-10-one dihydrobromide, $LH_2 \cdot 2HBr$, was added and the mixture was allowed to stir for an additional 20 min. Purple crystals were filtered off and recrystallized from CH_2Cl_2/MeOH to give compound **6** (39 mg, 53%).[6] The mother liquor was concentrated under vacuum to yield a green residue which was further purified on a neutral alumina (Brockmann Grade III, elution with CH_2Cl_2) and identified as compound **8** (25 mg, 34%): mp 219-221°C; UV-visible (CH_2Cl_2) λ nm 534 (ε 39 800), 558 (38 100); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82 (s, 4H), 2.25 (m, 4H), 2.17 (s, 12H), 1.99 (m, 4H), 1.93 (s, 12H), 1.89 (s, 12H), 1.86 (s, 12H), 0.82 (m, 12H); MS m/z 1185.4 [M^+], 593.1 [M^{2+}]. Anal. Calcd for $C_{62}H_{72}Cd_2N_8O_2 \cdot H_2O$: C, 61.84; H, 6.19; N, 9.31. Found: C, 61.68; H, 5.94; N, 9.12.

Bis-[(8,12-diethyl-1,2,3,7,13,17,18,19-octamethyl-a,c-biladienato-10-one)mercury(II)] (9). To a refluxing solution of MeOH (40 mL) containing $LH_2 \cdot 2HBr$ (80 mg, 1.24 mmol) and 30 mg of NaOAc, was added under argon 2.2 equiv. (86 mg) of $Hg(OAc)_2$. The reaction mixture was refluxed for 20 min. Methanol was then removed under vacuum and the resulting mixture was purified on an alumina column (Brockmann Grade III, elution with CH_2Cl_2). The residue was recrystallized from dichloromethane/cyclohexane to yield 55 mg (65%) of a red powder: mp 223-225°C; UV-visible (CH_2Cl_2) λ nm 486 (ε 12 000), 524 (13 000); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.74 (s, 4H), 2.35 (m, 4H), 2.16 (s, 12H), 2.18 (m, 4H), 1.87 (s, 12H), 1.85 (s, 12H), 0.85 (m, 12H); MS m/z 1362.6 [M^+, 22%], 681.3 [M^{2+}, 100]. Anal. Calcd for $C_{62}H_{72}Hg_2N_8O_2 \cdot H_2O$: C, 53.86; H, 6.71; N, 8.10. Found: C, 54.05; H, 6.49; N, 8.34.

ACKNOWLEDGMENTS

This work was supported by grants from the National Science Foundation (CHE-96-23117) and the National Institutes of Health (HL-22252). Mass spectrometric analyses were performed by the University of California, San Francisco Mass Spectrometry Facility, (A. L. Burlingame, Director) supported by the Biomedical Research Technology Program of the National Center for Research Resources, NIH NCRR BRTP 01614.

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