Metalloporphyrins

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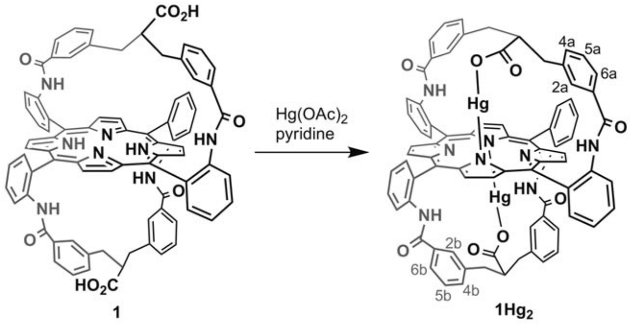
Formation of a Dinuclear Mercury(II) Complex with a Regular Bis-Strapped Porphyrin Following a Tunable Cooperative Process**

*Nicolas Motreff, Stéphane Le Gac, Michel Luhmer, Eric Furet, Jean-François Halet, Thierry Roisnel, and Bernard Boitrel**

The richness of metalloporphyrin chemistry is an important source of innovative features which justifies active investigation of their coordination properties towards post-transition elements.[1] Mercury(II) complexation by porphyrins was first motivated by the observation of its catalytic effect on the complexation of other elements (Cu, Zn),[2] and regained attention in view of the sensing of toxicological organomercury(II) compounds.[3] Although first studies appeared in the 1970s,[4] the coordination of mercury by porphyrins is still largely misunderstood. Solution studies, mostly performed with "naked" porphyrins, revealed various Hg^{II}–porphyrin stoichiometries, such as 1:1, 2:1, 2:2, and 3:2, on the basis of spectroscopic investigations.[4c,5] Equilibria between the different species are often solvent-, concentration-, and pH-dependent, and there are no definite elements in the literature for a possible correlation between an XRD-based coordination mode and the corresponding species observed in solution. Such analysis is crucial for a better understanding of the complexation processes and could also provide elements for the rational design of mercury-based porphyrinoid objects.[6] To the best of our knowledge, XRD structures of mercury–porphyrin complexes are very scarce. Five of the six reported examples involve an N-modified macrocycle,[3,7] a single report being related to a regular porphyrin.[7b] In this mononuclear complex, the mercury atom is four-coordinate to the four nitrogen atoms of the porphyrin, and is sitting 0.60 Å above the 24-atom mean plane with an average covalent mercury to nitrogen bond length of 2.20 Å.

In this context, the design of new porphyrin ligands with purposely introduced coordinating groups deserves particular attention. We recently reported a centrosymmetrical homodinuclear complex of lead(II) with the L^{4-} ditopic ligand **1** (Scheme 1).[8] We reasoned that, in the case of mercury(II), such a bis-strapped chelate with hanging COOH groups could provide a means to obtain discrete species, rather than sandwich assemblies, and better control of the nuclearity. Herein, we describe the first solid-state structure of a dinuclear mercury(II) complex with a regular porphyrin, and report on the evidence for a tunable cooperative process for its formation.



Scheme 1. Complexation of mercury(II) with ditopic bis-strapped porphyrin **1**.

Mercury insertion was performed at room temperature in pyridine with a 3 equivalent excess of mercury acetate (Scheme 1). The reaction was monitored by UV/Vis spectroscopy and a final pattern showing three absorption bands at $\lambda = 448$, 550, and 576 nm was obtained after 15 min. After solvent evaporation, the green solid was taken up in neutralized CH_2Cl_2, and excess mercury salt was removed by filtration on celite. The mercury complex was isolated upon precipitation with pentane (82 % yield). Elemental analysis indicated a 1:2 **1**/Hg stoichiometry, which is in agreement with the formation of dinuclear bis(mercury) complex **1·Hg$_2$**.[9]

Crystals suitable for X-ray diffraction were obtained by slow evaporation of a solution of **1·Hg$_2$** in a mixture of DMSO/MeOH/H_2O (Figure 1 a–c and the Supporting Information). The structure reveals a dinuclear complex with a mercury ion located on each side of the macrocycle. In contrast to the dinuclear lead complex of **1**,[8] **1·Hg$_2$** lacks the C_2 symmetry, and the two metal ions sit in two different environments. The two sides of the porphyrin mainly differ by 1) the conformation of the two straps, the strap {Hg1} being more twisted than the strap {Hg2} (Figure 1 b,c), and 2) the out-of-plane positions of Hg1 and Hg2, which are located 1.733 and 1.408 Å from the 24-atom mean plane, respectively. At first glance, the metal ions appear to be in a trigonal-antiprismatic coordination polyhedron, Hg1 being six-coor-

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[*] N. Motreff, Dr. S. Le Gac, Dr. E. Furet, Dr. J.-F. Halet, Dr. T. Roisnel, Dr. B. Boitrel
Université de Rennes1—Ecole Nationale Supérieure de Chimie de Rennes
Sciences Chimiques de Rennes, UMR CNRS 6226
263 avenue du Général Leclerc, CS 74205
35042 Rennes Cedex (France)
Fax: (+33) 2-2323-5637
E-mail: bernard.boitrel@univ-rennes1.fr
Prof. M. Luhmer
Laboratoire de RMN Haute Résolution
Université Libre de Bruxelles (Belgium)

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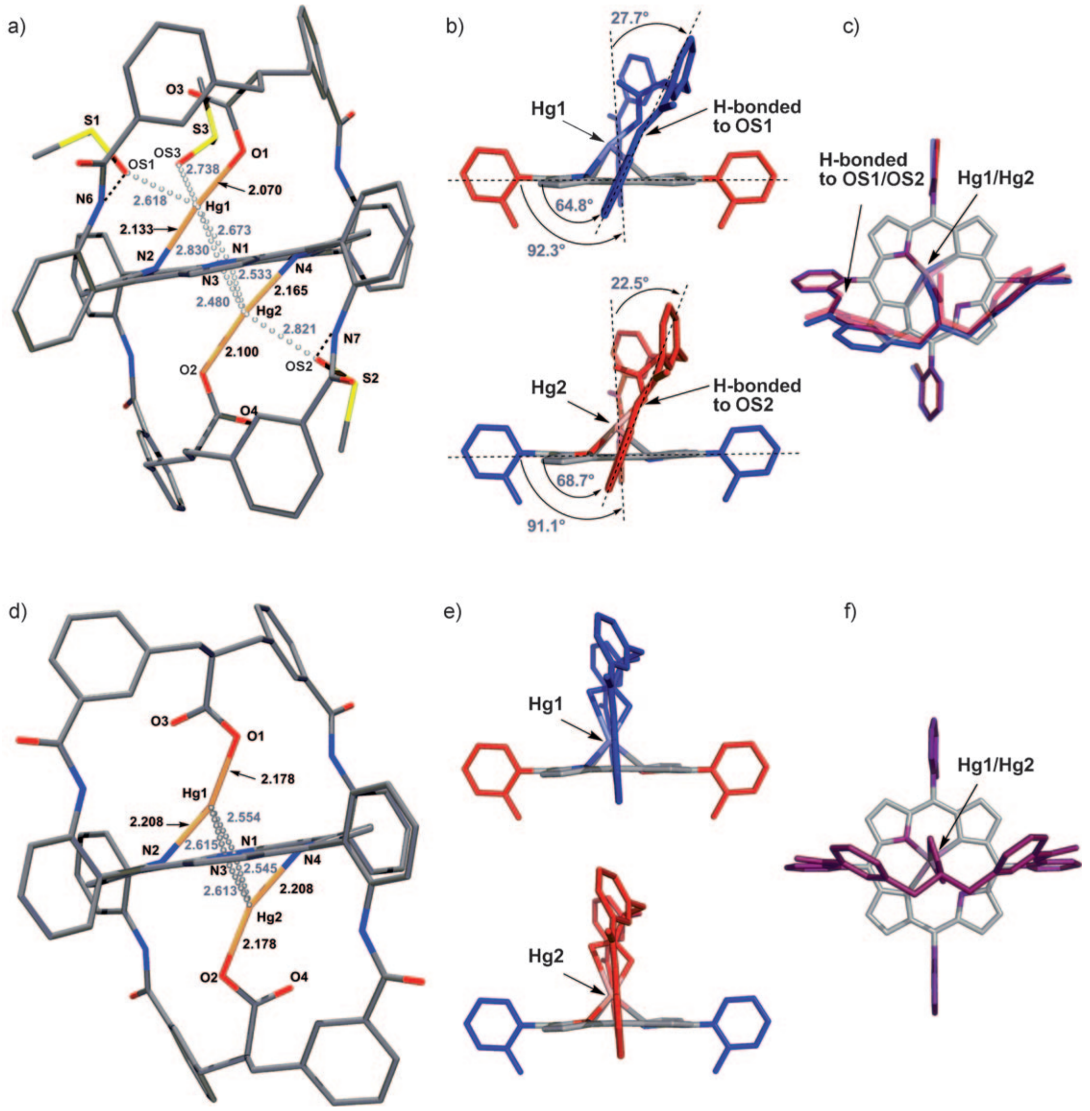

Figure 1. a) Crystal structure of **1·Hg$_2$**; hydrogen atoms and noninteracting solvent molecules removed for clarity (distances [Å] and angles [°]: Hg1–Hg2 3.258; Hg1(/Hg2) to 24-atom mean plane 1.733(/1.408); N2-Hg1-O1 166.2; N4-Hg2-O2 161.3). b) Side and c) top views of strap {Hg1} (blue) and {Hg2} (red), upon 180° rotation of the latter around the pseudotwofold axis, revealing their different conformation; bound DMSO molecules removed. d) DFT-optimized structure of **1·Hg$_2$** upon removal of the coordinated DMSO molecules (computed distances [Å] and angles [°]: Hg1–Hg2 3.095; Hg1(/Hg2) to 24-atom mean plane 1.506(/1.505); N2-Hg1-O1 157.2; N4-Hg2-O2 157.2). e) Side and f) top views of strap {Hg1} and {Hg2} as in (b) and (c).

dinate but Hg2 being five-coordinate. For Hg1, the polyhedron is composed of three nitrogen atoms from the porphyrin (N1, N2, N3), one monohapto carboxylate group (O1), and two DMSO molecules from the solvent of crystallization (OS1 and OS3). In the case of Hg2, this polyhedron is lacking one DMSO molecule but again is described by three nitrogen atoms from the macrocycle (N1, N3, N4), one monohapto carboxylate group (O2), and one DMSO molecule (OS2) (Figure 1 a). Each mercury atom exhibits two short bond lengths, one with a nitrogen atom of the porphyrin and the other with an oxygen atom of the hanging carboxylate function (Hg1−N2 2.133, Hg1−O1 2.070, Hg2−N4 2.165, and Hg2−O2 2.100 Å). All the other contacts are much longer and should be considered mainly as electrostatic interactions with both the nitrogen atoms of the porphyrin and the oxygen atom of the DMSO molecules (see depicted values in Figure 1 a). Moreover, the angles O1-Hg1-N2 and O2-Hg2-N4 are close to 180° (166.2° and 161.3°, respectively). Therefore, a linear coordination (14-electron ML$_2$-type complex) is a better description for both mercury atoms in the complex **1·Hg$_2$**.

The origin of such dissymmetry, and notably the higher degree of coordination of Hg1 versus Hg2, was particularly intriguing. One part of the explanation should lie in the fact that the two straps interact owing to their connection to the macrocycle, the metal ions forming two allosterically connected binding sites with homotropic communication. In addition, a closer look at the X-ray structure of **1·Hg$_2$** revealed that one DMSO molecule on each side of the porphyrin interacts via a hydrogen bond with one CONH group of the straps (OS1–N6 2.840 and OS2–N7 2.934 Å), thus defining a second sphere of coordination that may play a role in the overall desymmetrization process. Indeed, the larger angle to the macrocycle of the meso-Ar units close to the hydrogen-bonded DMSO molecules (Figure 1 b,c) may contribute to the optimization of these two hydrogen-bonding interactions. In contrast, the third DMSO molecule does not interact in such a way, but might also influence this second sphere of coordination since OS1–N6 is shorter than OS2–N7, and OS1–Hg1 is shorter than OS2–Hg2 (2.618 vs. 2.821 Å).

To investigate the influence of the DMSO molecules on the dissymmetry of **1·Hg$_2$**, density functional calculations (DFT) were carried out at the B88P86/SDD level of theory using Gaussian 09 package (see the Supporting Information).[10] A full in vacuo geometry optimization of **1·Hg$_2$(DMSO)$_3$** was first performed starting from the X-ray experimental structure. The computed geometry does not show significant modifications of the complex, indicating that packing forces are not responsible of its unsymmetrical structure. In a second step, the DMSO molecule interacting with Hg1 through OS3 (i.e., the one not hydrogen bonded to a CONH group) was removed, and the geometry was fully reoptimized, leading to **1·Hg$_2$(DMSO)$_2$**. In a third step, the two last DMSO molecules were discarded, and the structure was relaxed, yielding **1·Hg$_2$(DMSO)$_0$** (Figure 1 d).

Interestingly, the two sides of the complex become symmetric with the successive removal of the DMSO molecules, the DMSO free complex displaying a C_2 symmetry (see new computed distances in Figure 1 d). Both straps in **1·Hg$_2$(DMSO)$_0$** stand in a rather straight conformation and are superimposable upon 180° rotation around the twofold axis (Figure 1 e,f). The ML$_2$-type coordination mode is hardly affected by the successive removals of the DMSO molecules, the two corresponding N-Hg-O angles being equal to 157.2° (ca. 160° for **1·Hg$_2$(DMSO)$_3$**). It can therefore be concluded that the DMSO molecules that crystallize in the vicinity of **1·Hg$_2$**, although weakly coordinated, play a fundamental role in the observed unsymmetrical structure. Although the binding of one DMSO molecule per mercury atom induces a slight dissymmetry of the ligand with a minor twist of the straps (see the Supporting Information), these calculations provide evidence that the binding of the third DMSO molecule drastically amplifies the twisting of the straps and the overall dissymmetry of the complex, which reflects a homotropic allosteric binding process. The complex **1·Hg$_2$(DMSO)$_3$** is stabilized by 13 kcal mol^{-1} relative to **1·Hg$_2$(DMSO)$_2$**, which, in turn, is 33 kcal mol^{-1} more stable than the DMSO-free complex. In contrast, the a priori possible binding of a fourth DMSO molecule to Hg2 is probably hampered by steric interactions with the strap, which cannot adapt its conformation as a result of the interdependence of the two connected binding sites.

The complex **1·Hg$_2$** was further investigated in solution. The ^{1}H NMR spectra in CDCl$_3$ (298 K) of both the free base and the isolated **1·Hg$_2$** complex display a C_2-symmetrical pattern, the β-pyrrolic protons being the most affected by the metalation (see the Supporting Information). The latter appear as two doublets and two singlets, and the four protons labeled H$_{2a}$ and H$_{2b}$ (Scheme 1) resonate as two singlets, showing that in both cases the two straps are equivalent.[11] This NMR signature is consistent with a symmetrical dinuclear complex, which is in agreement with the DFT calculations in the absence of exogenous ligands.

Insights into the formation of **1·Hg$_2$** were obtained from titration experiments. Titration of **1** by Hg(OAc)$_2$ was first performed in a noncoordinating medium (CDCl$_3$/CD$_3$OD 9:1) in the presence of a base (diisopropylethylamine; DIPEA). A two-step process leading to the final NMR pattern of **1·Hg$_2$** was observed, with the formation of an intermediate species of apparent C_2 symmetry that likely corresponds to the mononuclear complex **1·Hg** (Figure 2 a).[12] Slow exchange between **1**, **1·Hg**, and **1·Hg$_2$** is observed in these spectra. Complex **1·Hg$_2$** was obtained quantitatively upon addition of approximately 2 equivalents of Hg$^{\text{II}}$, indicating strong binding. Upon addition of 1 equivalent of Hg$^{\text{II}}$, the **1/1·Hg/1·Hg$_2$** ratio is about 1:3:1, suggesting a noncooperative process ($K_{a_1} \approx K_{a_2}$, inset in Figure 2 a). When the titration was performed in the same medium but without a base, a single-step process leading to **1·Hg$_2$** was observed, and the intermediate mononuclear complex was not detected (Figure 2 b). This result indicates a highly cooperative insertion of the two metal ions, that is, $K_{a_2} \gg K_{a_1}$, with an overall strong binding. We explain this positive cooperativity by a low stability of the mononuclear complex in the absence of a base. Indeed, the mercury ion is expected to be four-coordinate to the N$_4$ core of the macrocycle in **1·Hg** (inset in Figure 2 a,b).[7b] The two dangling COOH groups of the straps are "free" and thus can protonate the macrocycle, which makes the complex relatively unstable. In contrast, both carboxylate groups are involved in the mercury coordination of the dinuclear complex, the intramolecular protonation being therefore no longer possible.

We probed the affinity of exogenous ligands for **1·Hg$_2$** and their effects on the overall complexation process. The ^{1}H NMR pattern of **1·Hg$_2$** in CDCl$_3$ was barely affected by the addition of 20 equivalents of DMSO or pyridine, which showed a relatively weak affinity of these ligands (see the Supporting Information).[13] Conversely, 4-(dimethylamino)-pyridine (DMAP) showed stronger affinity for **1·Hg$_2$**, as quantitative binding was achieved upon addition of approximately 4 equivalents of this ligand.[14] Significant shifts in the NMR pattern were observed upon DMAP binding (e.g., protons H$_{2a}$ and H$_{2b}$ were shifted downfield by ca. 0.5 ppm), which are consistent with an important conformational rearrangement of the straps (see the Supporting Information).

The titration experiment described in Figure 2 a (noncooperative metalation process) was repeated in the presence of 4 equivalents of DMAP. Under these conditions, a significant change in the cooperativity of the metalation process was observed, since the formation of **1·Hg$_2$**, relative to **1·Hg**, was favored. Indeed, at 1 equivalent of Hg$^{\text{II}}$, the **1·Hg/1·Hg$_2$** ratio changed from around 3:1 to 1:1 without and with DMAP, respectively (see the Supporting Information). In contrast to **1·Hg$_2$**, the NMR spectrum of **1·Hg** was barely affected by DMAP, which indicates weak DMAP/mercury interactions. This result probably arises from a steric hindrance with the straps, since the mercury ion is expected to be

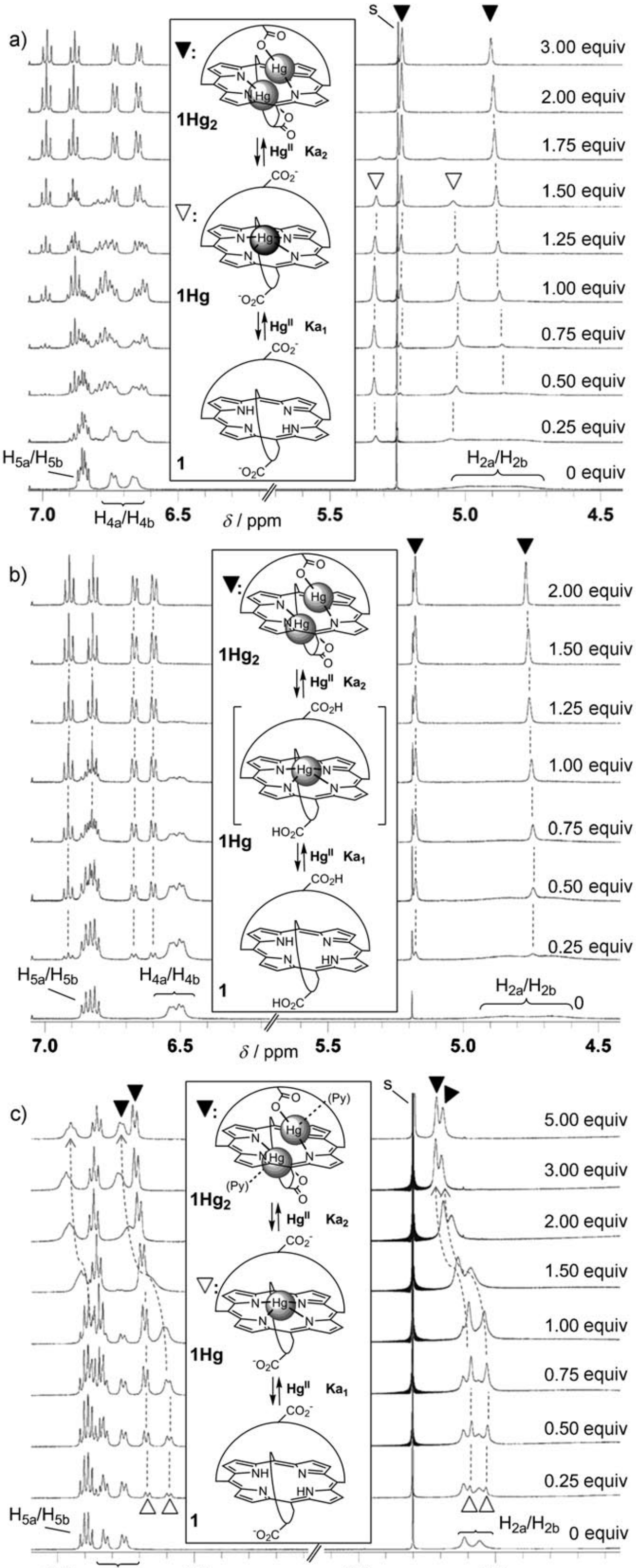

Figure 2. ^{1}H NMR spectra (selected area) of the titration of **1** with Hg(OAc)$_2$ (500 MHz, 298 K): a) in CDCl$_3$/CD$_3$OD 9:1, with 15 equiv of DIPEA; b) in CDCl$_3$/CD$_3$OD 9:1; c) in [D$_5$]pyridine/[D$_6$]DMSO 9:1. S = solvent.

coordinated in a more confined environment in the mononuclear complex, thus preventing the formation of a five-coordinate complex with DMAP. Thus, the positive cooperativity likely lies in the stabilization of **1·Hg$_2$** upon DMAP binding.

Major differences in the metal insertion process were noticed when titration of **1** by Hg(OAc)$_2$ was performed in strongly coordinating media such as [D$_5$]pyridine/CD$_3$OD (see the Supporting Information) or [D$_5$]pyridine/[D$_6$]DMSO mixtures (Figure 2c). A two-step binding process with different association constants was observed, the first event being significantly favored (i.e., $K_{a_1} > K_{a_2}$). Below one equivalent of Hg(OAc)$_2$, a distinct second set of signals appeared, and this new C_2 symmetrical species was present as the major one (ca. 80 %) at 1 equivalent of Hg^{II}. Above one equivalent of Hg(OAc)$_2$, a continuous shift of the signals of this new pattern was observed, revealing a second binding event with a fast exchange process on the NMR timescale. The final NMR spectrum obtained after addition of 3 equivalents of Hg(OAc)$_2$ is identical to that of the isolated **1·Hg$_2$** complex. Association constant values of $K_{a_1} > 10^5\,\mathrm{M}^{-1}$ and $K_{a_2} \approx 5 \times 10^3\,\mathrm{M}^{-1}$ were estimated for the two equilibria. These data are in agreement with the successive formation of the mono- and dimercury complexes with a negative cooperativity, accordingly to a $0.25\,K_{a_1}/K_{a_2}$ ratio > 1.[15]

In conclusion, the first example of a dinuclear mercury(II) complex with a regular bis-strapped porphyrin has been structurally characterized. The delivery of a carboxylic acid group on each side of the porphyrin plane allows the mercury ions to adopt a linear coordination mode. Calculations have shown that the conformation of the straps and the symmetry of the dinuclear complex depend on the interaction with an exogenous ligand acting as an allosteric effector. Concomitantly, the straps prevent the formation of sandwich type complexes and help to control the binding of an exogenous ligand. The overall metalation process reveals an unprecedented tunable cooperative process, that can switch from positive to negative, depending on 1) the presence of base and 2) the interaction of the Hg^{II} ions with an exogenous ligand. This work provides the basis towards stable heterodinuclear mercury-based metalloporphyrins, and experiments along these lines are in progress in our laboratories.

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[9] In order to simplify the notations, the loss of protons upon complexation is not indicated. The free ligand denoted **1** corresponds formally to **1·H$_4$** and the ligand in the neutral dinuclear complex **1·Hg$_2$** to **1**$^{4-}$ with two carboxylate groups.

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[11] The fact that **1** and **1·Hg$_2$** display two sets of signals for a strap (for example, protons labeled H_{2a} and H_{2b}) is due to the intrinsic chirality of the molecule.

[12] The C_2 symmetry of the NMR pattern of **1·Hg** is rather surprising as one would have expected differentiation of the two straps as in the case of **1·Bi** (see Ref. [8]). As the large size of Hg^{II} does not allow in-plane complexation (see Ref. [7b]), this result suggests a fast exchange process on the NMR timescale of the Hg^{II} ion between the two sides of the ligand.

[13] The C_2 symmetry of the NMR spectra was retained at low temperature (223 K). While a dissymmetric structure could be expected with the DMSO ligand on the basis of the X-ray structure, an averaged NMR pattern cannot be excluded.

[14] The values $\log K_a = 1.45$ and $\log K_a = 4.04$ were reported in the case of 1:1 five-coordinate complexes of Hg–TPP with pyridine and DMAP, respectively (TPP = tetraphenylporphyrin): K. M. Kadish, L. R. Shiue, *Inorg. Chem.* **1982**, *21*, 3623 – 3630.

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