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Structural and Coordination Studies of "Pearl Oysterlike" Porphyrins

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We report the coordination studies of porphyrins with pre-organized but yet flexible straps, each bearing over the center of the porphyrin either a 2,2-malonic acid diethyl ester residue or a 2,2-malonic acid residue. The straps are attached to the porphyrin via two adjacent meso positions, 5,10 and 15,20, respectively, and the 2,2-malonic acid diethyl ester groups are connected to the straps on benzylic carbon atoms. These two structural features allow a significant flexibility of the straps, as confirmed by the comparison of the X-ray structures of the zinc, nickel, and lead complexes of porphyrin **1**. In the latter, the influence of the lone-electron pair of lead is clearly demonstrated. The coordination of bismuth is also reported.

Introduction

The coordination chemistry of lead and bismuth was substantially studied with chelating agents such as (4,7,10-tris-carboxymethyl-1,4,7,10-tetraaza-cyclododec-1-yl) acetic acid (DOTA) or [(2-{[2-(bis-carboxymethylamino)-ethyl]-carboxymethylamino}-ethyl)-carboxymethylamino] acetic acid (DTPA), a polyamine with carboxylic acid arms.[1,2] However, few other chelating agents were studied with respect to the coordination of these two elements.[3] The renewed interest of this coordination chemistry observed during the past decade can be explained by the fact that compounds of bismuth(III) showed their potential applications in medicine, particularly in the therapy of some cancers and gastric ulcers.[4] For these reasons, the search for new effective chelating agents used for the coordination of bismuth has recently drawn increasing attention. Additionally, for radioimmunotherapy, the generation of isotope 212 of bismuth starting from isotope 212 of lead via a β decay has already been studied with DOTA[5] and fully justifies that potential chelates of bismuth(III) should also be evaluated for their aptitude to complex lead(II). Among the new possible chelates, porphyrins have been studied to complex bismuth(III), and several studies and X-ray structures of such complexes have been reported during the two last decades.[6−9] In the field of the coordination chemistry of bismuth(III), we have focused on the synthesis and characterization of functionalized sidearm porphyrins.[10] We have shown that either ester or acid groups located around the coordination site of the macrocycle can increase the kinetics of bismuth insertion and also stabilize the resulting complexes by coordination

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of the ester or acid function on the bismuth cation.[11−13] We have also published the synthesis, conformational, and structural studies of various strapped porphyrins, elaborated in different geometries. For instance, we have previously reported the synthesis of various “U-shaped” strapped porphyrins[14] as well as the structural characterization of three free-base ligands in different geometries.[15] In the $\alpha\alpha\beta\beta$ series,[16] one ethoxycarbonyl group of the ethylmalonyl residues is located just above the center of the free-base porphyrin at a distance of 3.347 Å and proton NMR spectroscopy leads to a faithful image of the structure in solution.[15] We report herein the coordination of $\mathrm{Ni^{II}}$, $\mathrm{Zn^{II}}$, $\mathrm{Pb^{II}}$, and $\mathrm{Bi^{III}}$ by the $\alpha\alpha\beta\beta$ bis-strapped porphyrins bearing either ester or carboxylic acid groups. Since an interaction between the carbonyl of an ester group from a succinyl picket and the bismuth(III) cation was reported in a dimeric structure,[10] it was rational to investigate the coordination properties of a structure such as **1**, in which the ester groups are delivered by a pre-organized strap whose position can change above the center of the porphyrin owing to its links in the 5 and 10 meso positions. Indeed, the strap bearing the malonyl residue can be either vertical or bent over the center of the porphyrin, just like the shell of a pearl oyster in opened or closed position above the pearl.

Experimental Procedures

General Considerations. ^{1}H (500.13 MHz) and ^{13}C (125.30 MHz) NMR spectra were recorded on Bruker Avance spectrometers and referenced to the residual protonated solvent. Mass spectra were performed on a MS/MS ZABSpec TOF spectrometer at the University of Rennes 1 (C.R.M.P.O.). UV−vis spectra were recorded on an Uvikon XL spectrometer. Infrared spectra were recorded on Bruker IFS 66 and 28 spectrometers. All solvents (ACS for analysis) were purchased from Carlo Erba. THF was distilled over potassium metal whereas methanol was distilled over magnesium turnings. CH_2Cl_2 was used as received. Triethylamine was distilled over CaH_2. The starting materials were generally used as received (Acros and Aldrich) without any further purification. All reactions were performed under an argon atmosphere and monitored by thin-layer chromatography (TLC) (silica, CH_2Cl_2/MeOH). Column flash chromatography was performed on silica gel (Merck TLC-Kieselgel 60H, 15 μm). Elemental analyses were obtained on an EA 1108 Fisons Instruments.

Compounds **1**, **1Ni**, and **1Zn** were synthesized according to published procedures.[14]

α-5,10-β-15,20-Bis{2,2′-[3,3′-(2,2-(diethoxycarbonyl)propane-1,3-diyl)dibenzoylamino]diphenyl}lead(II) Porphyrin, 1Pb. In a 50 mL flask, 10 mg (6.9 μmol) of **1** was dissolved in pyridine. The solution was warmed to 50 °C, and 26 mg (0.069 mmol) of $Pb(AcO)_2{\cdot}3H_2O$ was added. After heating overnight, the solvent was evaporated and the residue was dissolved in a minimum of methylene chloride to be purified by column chromatography on silica gel (0.6% MeOH/CH_2Cl_2) to afford a 70% yield (8 mg). ^{1}H NMR (500 MHz, DMSO-d_6, 298 K): δ_H 9.10 (broad s, 2H, NH); 8.94 (s, 2H, β_{pyr}); 8.85 (s, 2H, β_{pyr}); 8.70 (d, 2H, $J = 4.5$ Hz, β_{pyr}); 8.61 (d, 2H, $J = 4.5$ Hz, β_{pyr}); 8.37 (s, 2H, NH); 8.31 (d, 2H, $J_o = 8.5$ Hz); 8.18 (d, 2H, $J_o = 8.5$ Hz); 8.13 (d, 2H, $J_o = 7.0$ Hz); 7.92 (broad d, 2H, $J_o = 7.0$ Hz); 7.87 (t, 2H, $J_o = 7.5$ Hz); 7.84 (t, 2H, $J_o = 7.5$ Hz); 7.65 (t, 2H, $J_o = 7.5$ Hz); 7.59 (t, 2H, $J_o = 7.5$ Hz); 7.36 (d, 2H, $J_o = 7.5$ Hz); 7.32 (d, 2H, $J_o = 7.5$ Hz); 6.96 (t, 2H, $J_o = 7.5$ Hz); 6.90 (t, 2H, $J_o = 7.5$ Hz); 6.55 (t, 4H, $J_o = 7.5$ Hz); 5.03 (s, 2H, H_7); 4.76 (s, 2H, H_7); 3.79 (q, 2H, $J = 5.0$ Hz, $-(CH_2)_oCH_3$); 3.53 (q, 2H, $J = 5.0$ Hz, $-(CH_2)_oCH_3$); 2.84 (q, 2H, $J = 5.0$ Hz, $-(CH_2)_iCH_3$); 2.78 (q, 2H, $J = 5.0$ Hz, $-(CH_2)_iCH_3$); 1.61 (d, 2H, $J = 15.0$ Hz, $(CH_2)_{Bz}$); 1.30 (d, 2H, $J = 15.0$ Hz, $(CH_2)_{Bz}$); 1.21 (d, 2H, $J = 15.0$ Hz, $(CH_2)_{Bz}$); 0.85 (t, 3H, $J = 7.5$ Hz, $-CH_2(CH_3)_o$); 0.74 (d, 2H, $J = 15.0$ Hz, $(CH_2)_{Bz}$); 0.85 (t, 3H, $J = 7.5$ Hz, $-CH_2(CH_3)_o$); −0.08 (t, 3H, $J = 7.5$ Hz, $-CH_2(CH_3)_i$); −0.10 (t, 3H, $J = 7.5$ Hz, $-CH_2(CH_3)_i$). UV−vis (CH_2Cl_2): λ_{max}/nm (10^{-3} ϵ, dm^3 mol^{-1} cm^{-1}) 355 (30.4); 471 (109.7); 606 (12.7); 653 (12.8). ESI-HRMS: calcd $m/z = 1687.4934$ $[M + Na]^+$ for $C_{90}H_{72}N_8O_{12}PbNa$; found, 1687.4942.

α-5,10-β-15,20-Bis{2,2′-[3,3′-(2,2-(diethoxycarbonyl)propane-1,3-diyl)dibenzoylamino]diphenyl}bismuth(III) Nitrato Porphyrin, 1Bi. In a 50 mL flask, 25 mg (0.017 mmol) of **1** was dissolved in pyridine. The solution was warmed to 100 °C, and 85 mg (0.17 mmol) of $Bi(NO_3)_3{\cdot}5H_2O$ was added. After heating for 2 h, the solvent was evaporated and the residue was dissolved in a minimum of methylene chloride to be purified by column chromatography on silica gel. **1Bi** was eluted with a 1% MeOH/CH_2Cl_2 mixture and obtained in 73% yield (21 mg). ^{1}H NMR (500 MHz, DMSO-d_6, 333 K): δ_H 9.06 (broad s, 2H, NHCO); 8.98 (s, 2H, β_{pyr}); 8.95 (s, 2H, β_{pyr}); 8.93 (d, 2H, $J = 4.5$ Hz, β_{pyr}); 8.81 (d, 2H, $J = 4.5$ Hz, β_{pyr}); 8.38 (d, 2H, $J_o = 8.0$ Hz); 8.34 (d, 4H, $J_o = 7.5$ Hz); 8.29 (d, 2H, $J_o = 7.5$ Hz); 7.97 (s, 2H, NHCO); 7.94 (t, 2H, $J_o = 8.0$ Hz); 7.84 (t, 2H, $J_o = 8.0$ Hz); 7.76 (t, 2H, $J_o = 8.0$ Hz); 7.51 (d, 2H, $J_o = 7.5$ Hz); 7.41 (t, 2H, $J_o = 8.0$ Hz); 7.35 (d, 2H, $J_o = 8.0$ Hz); 7.29 (d, 2H, $J_o = 8.0$ Hz); 6.97 (broad s, 2H, H_7); 6.92 (t, 2H, $J_o = 7.5$ Hz); 6.91 (t, 2H, $J_o = 7.5$ Hz); 3.94 (s, 2H, H_7); 3.90 (broad q, 2H, $-(CH_2)_{i-Bi}CH_3$); 3.68 (q, 2H, $J = 5.0$ Hz, $-(CH_2)_oCH_3$); 3.44 (q, 2H, $J = 5.0$ Hz, $-(CH_2)_oCH_3$); 2.79 (q, 2H, $J = 5.0$ Hz, $-(CH_2)_iCH_3$); 0.98 (broad t, 3H, $J = 5.0$ Hz, $-(CH_2)_{i-Bi}CH_3$); 0.83 (t, 3H, $J = 5.0$ Hz, $-CH_2(CH_3)_o$); 0.72 (d, 2H, $J_o = 10.0$ Hz, $(CH_2)_{Bz}$); 0.67 (t, 3H, $J = 5.0$ Hz, $-CH_2(CH_3)_o$); 0.03 (t, 3H, $-CH_2(CH_3)_i$); −0.06 (d, 2H, $J_o = 10.0$ Hz, $(CH_2)_{Bz}$); four benzylic protons from the second strap remain undetectable, whatever the solvent (DMSO or pyridine) or the temperature (from 298 to 403 K). Anal. Calcd for $C_{90}H_{72}BiN_9O_{15}$: C, 62.54; H, 4.20; N, 7.29. Found: C, 61.95; H, 4.34; N, 6.89. UV−vis (CH_2Cl_2): λ_{max}/ nm (10^{-3} ϵ, dm^3 mol^{-1} cm^{-1}) 355 (40.5); 476 (121.3); 600 (14.8); 649 (13.1). ESI-HRMS: calcd $m/z = 1665.5074$ $[M - NO_3]^+$ for $C_{90}H_{72}BiN_8O_{12}$; found, 1665.5041.

α-5,10-β-15,20-Bis{2,2′-[3,3′-(2,2-(dicarboxylic acid)propane-1,3-diyl)dibenzoylamino]diphenyl} Porphyrin, 3. Compound **1** (50 mg, 34.3 μmol) and NaH (250 mg) were added to 30 mL of dry toluene, then stirred under argon at 80 °C for 10 h. A volume

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of 2 mL of MeOH was added dropwise to the reaction mixture. The obtained precipitate was filtered and washed with toluene, then 2 M HCl, H_2O, and finally CH_2Cl_2. The resulting solid was dissolved in MeOH and filtered. After evaporation, the desired compound **3** was obtained in quantitative yield (46 mg). ESI-HRMS: calcd $m/z = 1347.4252$ $[M + H]^+$ for $C_{82}H_{59}N_8O_{12}$; found, 1347.4241. UV−vis (MeOH): λ_{max}/ nm (10^{-3} ϵ, $dm^3\ mol^{-1}\ cm^{-1}$): 421 (221.0), 516 (12.9), 551 (4.1), 591 (4.5), 646 (1.8).

X-ray Crystallographic Studies. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication nos. CCDC 631030 (**1Zn**), 630578 (**1Ni**), and 636998 (**1Pb**). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax, (international) + 44-1223/336-033; e-mail, deposit@ccdc.ca-m.ac.uk). The structures were solved by direct methods using the *SIR97* program,[17] which revealed all the non-hydrogen atoms, and refined with full-matrix least-square methods based on F^2 (*SHELX-97*)[18] with the aid of the *WINGX*[19] program. All non-hydrogen atoms were refined with anisotropic thermal parameters. Hydrogen atoms were finally included in their calculated positions.

1Zn. $C_{98}H_{88}N_8O_{14}Zn \cdot 2(C_2H_3N)$; $M = 1749.29$. A single crystal was obtained from the evaporation of a THF/acetonitrile solution. Intensities were collected on a Bruker-Nonius Kappa-CCD diffractometer, with Mo Kα radiation ($\lambda = 0.71073$ Å), $T = 110$ K: monoclinic, $P2_1/n$, $a = 14.7305(2)$ Å, $b = 20.9723(4)$ Å, $c = 15.4816(3)$ Å, $\beta = 114.939(1)°$, $V = 4336.81(13)$ Å^3, $Z = 2$, $d = 1.340$ g cm^{-3}, and $\mu = 0.357$ mm^{-1}. Hydrogen atoms were included with a riding model with isotropic temperature factors fixed to 1.2 times (1.5 for methyl groups) those of the corresponding parent atoms. A final refinement on F^2 with 9892 unique intensities and 577 parameters converged at $R_w(F^2) = 0.160$ ($R(F) = 0.061$ for 6179 observed reflections with $I > 2\sigma(I)$). The asymmetric unit has been found to contain one-half molecule of $C_{98}H_{88}N_8O_{14}Zn$ (bis-THF zinc porphyrin) and one acetonitrile solvent.

1Ni. $C_{90}H_{72}N_8NiO_{12} \cdot 2(CH_2Cl_2)$; $M = 1682.37$. A single crystal was obtained from the evaporation of a methylene chloride/methanol solution. Intensities were collected on a Bruker-AXS APEXII Kappa-CCD diffractometer, with Mo Kα radiation ($\lambda = 0.71073$ Å), $T = 100$ K: triclinic, $P\bar{1}$, $a = 12.6081(12)$ Å, $b = 14.1098(14)$ Å, $c = 24.181(2)$ Å, $\alpha = 77.743(5)°$, $\beta = 75.776(4)°$, $\gamma = 70.863(5)°$, $V = 3898.5(6)$ Å^3, $Z = 2$, $d = 1.436$ g cm^{-3}, and $\mu = 0.458$ mm^{-1}. A final refinement on F^2 with 17 912 unique intensities and 1054 parameters converged at $R_w(F^2) = 0.125$ ($R(F) = 0.051$ for 12 650 observed reflections with $I > 2\sigma(I)$). The asymmetric unit has been found to contain one molecule of $C_{90}H_{72}N_8O_{12}Ni$ and two methylene chloride solvent molecules.

1Pb. $C_{90}H_{72}N_8O_{12}Pb$; $M = 1664.50$. A single crystal was obtained from the evaporation of a methylene chloride/methanol/water solution. Intensities were collected on a Bruker-AXS APEXII Kappa-CCD diffractometer, with Mo Kα radiation ($\lambda = 0.71073$ Å), $T = 100$ K: triclinic, $P\bar{1}$, $a = 13.1804(11)$ Å, $b = 17.0677(14)$ Å, $c = 20.0012(15)$ Å, $\alpha = 64.844(4)°$, $\beta = 73.031(4)°$, $\gamma = 69.642(4)°$, $V = 3763.0(5)$ Å^3, $Z = 2$, $d = 1.462$ g cm^{-3}, and $\mu = 2.313$ mm^{-1}. A final refinement on F^2 with 17 055 unique intensities and 1010 parameters converged at $R_w(F^2) = 0.123$ ($R(F) = 0.065$ for 10 601 observed reflections with $I > 2\sigma(I)$). The asymmetric unit has been found to contain one molecule of $C_{90}H_{64}N_8O_{12}Pb$. During the structure determination and the structure refinement procedures, a large residual electronic density peak (~11 e$^-$/Å^3) was observed at ~2.61 Å of the Pb_1 crystallographic site, on the other side of the porphyrin plane (at ~1.09 Å of the mean plane). This extra peak was attributed to a partially occupied lead site (Pb_2). The occupation of both lead sites was then finally refined with the constraint that the total occupation was equal to 1 and lead was calculated to have a ~93/7 distribution on Pb_1 and Pb_2, respectively. Indeed, the observed and described crystal structure is then a mean view of the reality of the lead environment and molecular structure, which is here slightly perturbed by the presence of the opposite configuration.

Results

The detailed synthesis of **1** has been described.[14] Briefly, it consists of linking an ethylmalonyl motif to the porphyrin by the means of two benzylic chloride pickets on each side of the porphyrin. When achieved on the $\alpha\alpha\beta\beta$ atropisomer, this synthesis is unambiguous and leads to a single compound. A further ester cleavage step provides a novel interesting ligand **3**, possessing four carboxylic acid functions. To avoid the decarboxylation reaction expected in β-ketoesters such as **1**, we have used a method described by Lamparth and Hirsch to obtain **3** in quantitative yield (Scheme 1).[20]

As test reactions, nickel(II) and zinc(II) were inserted in **1** according to the usual methods.[14,21] Indeed, in a porphyrin, nickel(II) is known to be square-planar four-coordinate and to induce a ruffled distortion of the macrocycle. Accordingly, no interaction between an ester carbonyl from a strap and nickel is expected in **1Ni**. Conversely, in the case of **1Zn**, in which zinc is expected to be square pyramidal five-coordinate with a weakly bound fifth axial ligand, usually a water, THF, or methanol molecule, it would be plausible to observe an intermolecular interaction with a carbonyl ester from a strap. Incidentally, this type of intramolecular interaction has already been reported, both in solution and in the solid state, as a bond stable enough to avoid the exchange between several carbonyl functions at room temperature (bond length of Zn−O = 2.132 Å).[22] The first analysis of the proton NMR spectra of **1**, **1Ni**, and **1Zn** led us to the conclusion that a possible coordination of an ester carbonyl of the strap to the zinc in solution was in existence.[14]

Indeed, this conclusion was supported by both the shielding of H_7, which resonates at 4.8 ppm in **1** and 3.6 ppm in **1Zn**, and the shielding of the methyl and methylene groups in "out" positions (Figure 1). Furthermore, four benzylic protons are also upfield-shifted at −0.5 ppm where they resonate at 0.6 ppm in the free-base porphyrin **1**. However, in such a hypothesis, it would be difficult to rationalize the fact that the "in" groups are not shielded as well. A possible

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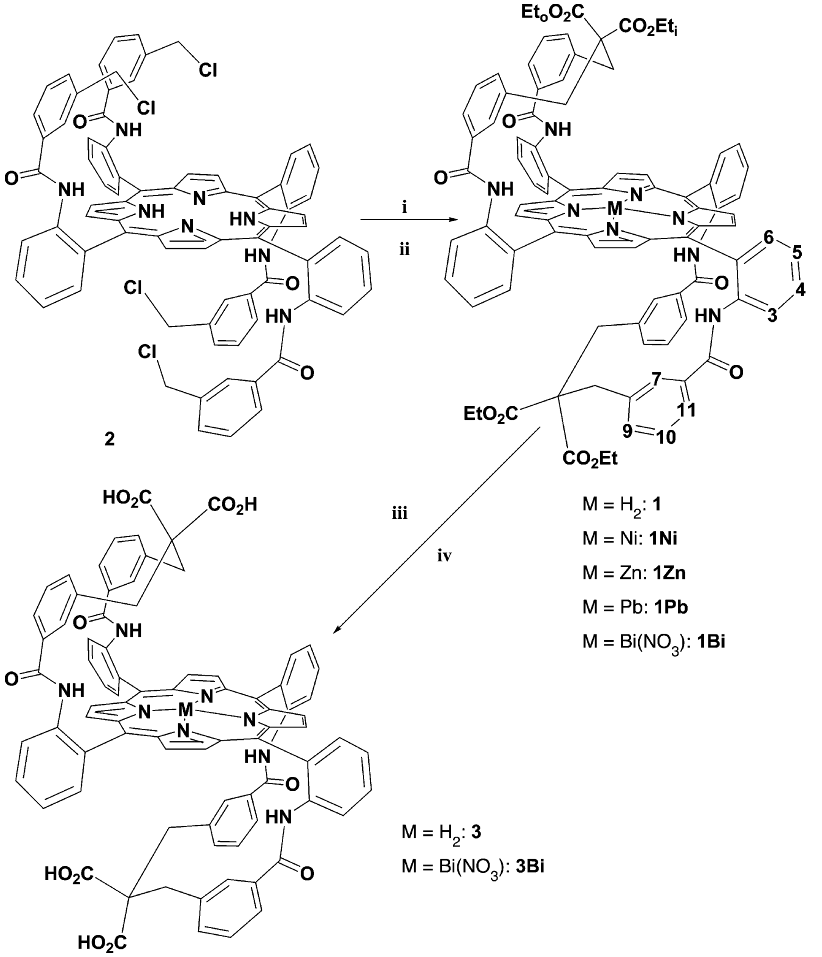
Scheme 1 . Synthesis of “Pearl Oysterlike” Bis-Strapped Porphyrins[a]



[a] Reagents and conditions: (i) $CH_2(CO_2Et)_2$ (20 equiv), THF/EtONa, rt, 2 h (the subscripted letters i and o of the ethyl groups stand for “in” and “out”). (ii) **1Ni**: $Ni(OAc)_2$, pyridine, reflux, 48 h. **1Zn**: $Zn(OAc)_2$, AcONa, $CHCl_3$, reflux, 1 h. **1Pb**: 10 equiv $Pb(OAc)_2 \cdot 3H_2O$, pyridine, 50 °C, overnight. **1Bi**: 10 equiv $Bi(NO_3)_3 \cdot 5H_2O$, pyridine, 100 °C 2 h. (iii) NaH/toluene then MeOH, 80 °C, 10 h. (iv) One to 10 equiv of $Bi(NO_3)_3 \cdot 5H_2O$, pyridine, rt.

explanation comes from Figure 2 in which the straps are depicted in two extreme positions (a and b), resulting from the rotation of the ethymalonyl motif around C1 and C3. Actually, these two extreme positions were observed in an X-ray structure of **1Ni** not suitable for publication because of the disorder of solvent molecules[23] but different from the structure of **1Ni** represented in Figure 3. The distances between the closest carbonyl oxygen atom and the nickel in each conformation are indicated in Figure 2 and show that the out carbonyl oxygen in the “W-shaped” strap (b) is closer to the metal than the in carbonyl oxygen in the expected “V-shaped” strap (a) (3.028 Å versus 3.836 Å). In other words, the W-shaped conformation observed in Figure 2b for **1Ni** in the solid state could also be effective in solution for **1Zn**. On one hand, in the solid state, the shortest distance of around 3 Å is definitely too long to assume a possible bond (ca. 2.2 Å) between a metal located in the plane of the porphyrin as zinc and an carbonyl oxygen from a strap. On the other hand, such a bond should be plausible with a metal such as bismuth coordinated above the plane of the porphyrin with a mean distance of 1.1 Å to the plane, knowing that a bond length of 3 Å between a carbonyl oxygen and bismuth in a porphyrin has been described in a dimer.[10] However, to ascertain whether a bond exists between a carbonyl oxygen from a strap and zinc, a variable temperature study of **1Zn** was performed. Indeed, in the hypothesis of the intramolecular coordination of a carbonyl from the strap(s), their magnetic equivalence at room temperature indicate that **1Zn** is either six-coordinate or five-coordinate with a rapid exchange of the straps on zinc. In this case, at low temperature, such a molecule should lead to an NMR fingerprint with four signals for the four ethyl ester groups. The observation of the NMR spectrum of **1Zn** from 295 down to 225 K shows that it does not (see Supporting Information, Figures S21−S36). This result is rather consistent with a complex in which no intramolecular coordination occurs and also with the downfield-shifted methyl group in the in position of **1Zn**.

Likewise, **1Ni** and **1Zn** were also characterized by X-ray structural analysis. The resulting structures are represented in Figure 3, in both perspective (top) and lateral (bottom) views. The zinc complex is symmetrical, while the nickel complex is not. A simple visual analysis of these structures confirms first the observations made of the base of the proton

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(23) Data of this solid-state structure are supplied as a PDB file in the Supporting Information.

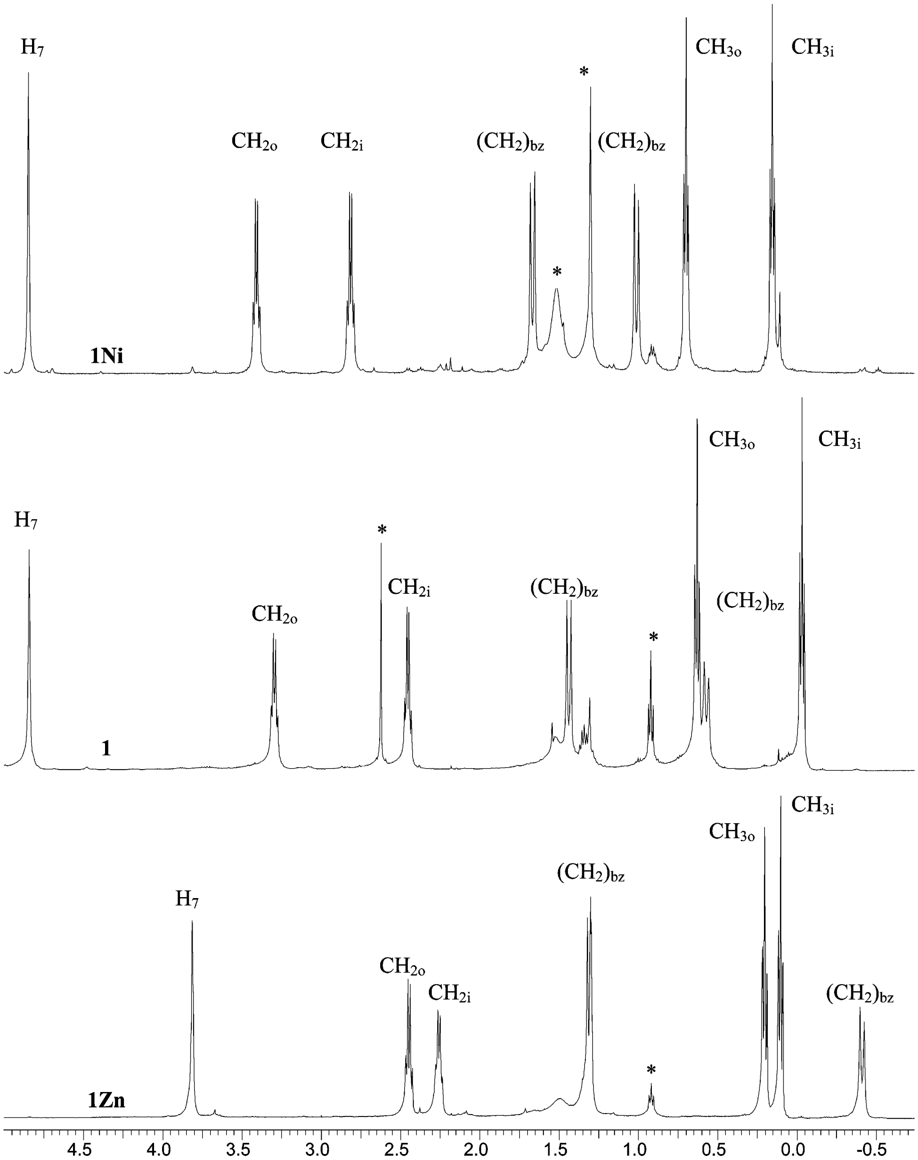

Figure 1. Aliphatic domain of ^{1}H NMR spectra of **1Ni** (top), **1** (middle), and **1Zn** (bottom) ($CDCl_3$, 500 MHz, 323 K, * denote impurities).

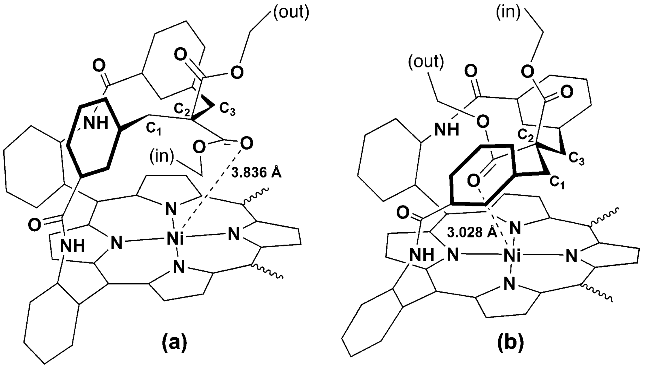

Figure 2. Two possible strap conformations observed in **1Ni** (neither the second strap nor the double bonds are represented for the sake of clarity).

NMR data for both **1Ni** and **1Zn** and, second, the fact that this type of strap is particularly flexible. For instance, it is striking to compare the conformation of the straps in both nickel (left) and zinc (right) porphyrins.

As expected, in the four-coordinate nickel complex, the straps exhibit a relaxed conformation, bent over the metal with an angle of 57° between the mean porphyrin plane and the mean plane of the strap.[24] Conversely, in the case of the zinc complex, which was synthesized to probe if a carbonyl oxygen atom could complex the zinc atom, the straps appear almost in vertical position with an angle to the mean porphyrinic plane of 88°. This conformation is certainly a consequence of the axial coordination of two THF molecules on the metal. A direct consequence of the six-coordination of the zinc[25] is the fact that the ethylmalonyl residue is rejected outside of the pocket of the porphyrin, leading to a conformation in which the out ethyl group is closer to the metal than the in group (Figure 3b). It is worth noting that a proton NMR spectrum recorded with some drops of deuterated THF in the NMR sample does not exhibit the expected deshielding effect on the strap. Hence, the six-

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(24) The mean porphyrin plane was calculated with the 24 atoms of the macrocycle without the metal, and the mean strap plane was calculated considering the two benzylic carbon atoms C1 and C3 and the two aromatic carbon atoms C4 and C5 (Figure 3).

(25) Ehlinger, N.; Scheidt, W. R. *Inorg. Chem.* **1999**, *38*, 1316−1321.

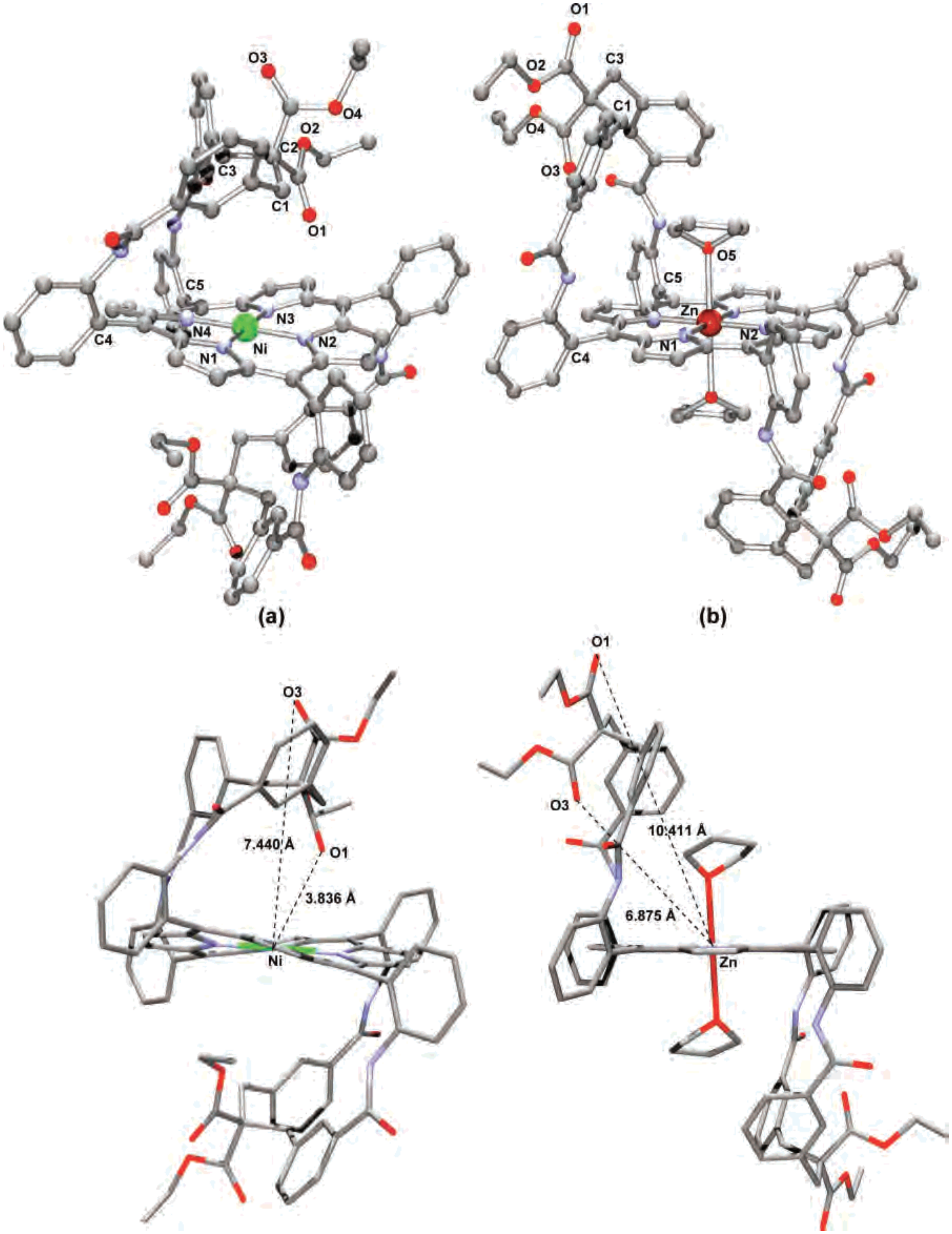

Figure 3. Ball-and-stick and lateral stick views of the solid-state structures of (a) **1Ni** and (b) **1Zn**.

coordinate bis-THF complex seems to exist only in the solid state. In **1Ni**, it should be noted that the porphyrin is significantly ruffled and that the shortest distance between a carbonyl oxygen and the metal is 3.836 Å. Thus, these X-ray data demonstrate that this particular 5,10 strap is indeed flexible at two different levels. First, the strap bearing the malonyl motif can either be vertical or bent over the center of the porphyrin, like the shell of a pearl oyster in opened or closed position. Second, the malonyl unit can be oriented inside or outside the pocket of the porphyrin by a simple rotation around the benzylic carbon atoms C1 and C3 (Figure 2). As these two structural features should allow porphyrin **1** to complex various metals of different sizes and valences as lead(II) and bismuth(III), the coordination of these two elements by **1** was also investigated.

Therefore, the lead insertion was performed by heating overnight at 50 °C the free-base porphyrin **1** in pyridine with 10 equiv of $Pb(OAc)_2 \cdot 3H_2O$. The metal insertion was

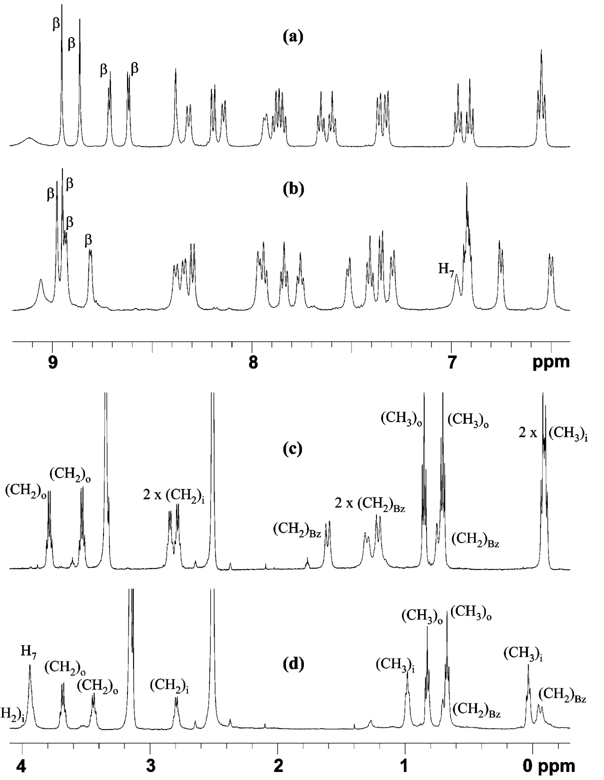

Figure 4. Aromatic domain of ^{1}H NMR spectra of (a) **1Pb** and (b) **1Bi** and aliphatic domain of (c) **1Pb** and (d) **1Bi** (DMSO-d_6, 500 MHz, 298 K for **1Pb** and 333 K for **1Bi**).

monitored by UV−vis spectroscopy and resulted in an “hyper” absorption spectrum[26] with typical split Soret bands at 355 and 471 nm. The compound was purified by silica gel column chromatography without any demetalation. The ^{1}H NMR spectrum was recorded at 298 K and proved to be well-resolved with sharp signals, in which the two sides of the porphyrin are slightly different (Figure 4, parts a and c). These NMR data are in full agreement with an out-of-plane coordination of lead, as reported in three X-ray structures.[27,28] Indeed, in these solid-state structures of lead(II) porphyrins, the metal lies at ca. 1.2 Å above the mean porphyrinic plane without any axial ligand and therefore remains four-coordinate. This type of polyhedron of coordination is fully consistent with the ^{1}H NMR data observed in **1Pb** and in agreement with the lack of coordination of a carbonyl oxygen of a strap with lead. Definitely, if such a coordination occurred, it would be detected on the NMR spectrum by a shift of the ethyl groups, of the proton H_7, and of the benzylic protons of the considered strap. However, none of these protons are significantly different from a strap to the other one in **1Pb**, and all the chemical shifts in **1Pb** are very similar to those of the free-base porphyrin **1**.

Thereafter, we were able to obtain single crystals suitable for X-ray analysis by the slow evaporation of a mixture of **1Pb** in CH_2Cl_2, MeOH, and water. The resulting solid-state structure is represented in Figure 5. Lead is located 1.368 Å out of the plane of the porphyrin with no axial coordination and with an average N−Pb bond length of 2.389 Å. It is particularly striking that lead remains four-coordinate despite the possible close location of the oxygen atom from the ester carbonyl group as seen in the lower strap (Figure 5b). The two straps adopt a W-shaped conformation with the out ethoxy group closest to the metal than the in ethoxy group. In this case, the shortest distance between lead and an ester carbonyl atom is 3.444 Å, whereas the longest distance (with the in group) is 7.034 Å. No comparison can be performed with the other strap as the metal is out-of-plane coordinated.

Conversely to what was observed in solution where the two straps are slightly different because the two sides of the macrocycle are not equivalent, in the solid state, the two straps of the complex are really in two extreme positions. Indeed, the strap on the opposite side to that of lead exhibits the same relaxed “bent-over” conformation as in **1Ni**, with neither any coordination driving force nor any electrostatic repulsion. The angle between the mean porphyrin plane and the mean plane of this strap is 34°, a value even smaller than the angle of 57° found in **1Ni**. This smaller angle is certainly due to the domed distortion of the porphyrin, as the two adjacent meso carbon atoms to which is attached the strap, are displaced (0.20 and 0.08 Å) on the same side of the porphyrin. On the other side of the macrocycle, the strap adopts a vertical conformation, as it does in the solid-state structure of **1Zn**, although no axial ligand exists on lead, with an angle to the mean porphyrin plane equal to 70°. This value compares well with the analogous angle of 84° found in **1Zn**. It clearly appears that in the absence of an axial ligand on lead, this vertical position of the strap is mainly due to the electrostatic repulsion of the strap with the lone-electron pair of lead, which is expected to be in axial position. In fact, in **1Pb**, the position of the strap can be seen as a probe of a “stereochemically active lone pair”.

The same study was performed toward the bismuth insertion in **1** in a mixture of pyridine/MeOH at 100 °C overnight, using 10 equiv of $Bi(NO_3)_3$. Completion of the reaction was also monitored by UV−vis spectroscopy (split Soret band at 355 and 476 nm). **1Bi** was purified via silica gel column chromatography as a mixture of several green bands. However, each band led to the same MALDI-TOF mass spectrum and, therefore, all were collected together. The proton NMR spectrum in DMSO-d_6 appeared at room temperature, not exploitable because of broad signals for most of the peaks. However, at higher temperatures, the spectrum became simpler with well-resolved signals and was typical of a porphyrin in which the two sides are magnetically different, an observation consistent with bismuth insertion on one side of the porphyrin.[6] The resolution of the spectrum was optimal at 333 K, and by comparing the NMR data of **1Pb** at 298 K and those of **1Bi** at 333 K, both in DMSO-d_6, three main differences were observed in **1Bi** (Figure 4). First, the two signals of H_7 are really different, one of them being strongly downfield-shifted to 6.97 ppm. This value compares well with the chemical shift of the same proton of the analogous free-base porphyrin in the αααα geometry, for

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(26) Sayer, P.; Gouterman, M.; Connell, C. R. *Acc. Chem. Res.* **1982**, *15*, 73−79.

(27) Barkigia, K. M.; Fajer, J.; Adler, A.; Williams, G. J. B. *Inorg. Chem.* **1980**, *19*, 2057−2061.

(28) Plater, M. J.; Aiken, S.; Gelbrich, T.; Hursthouse, M. B.; Bourhill, G. *Polyhedron* **2001**, *20*, 3219−3224.

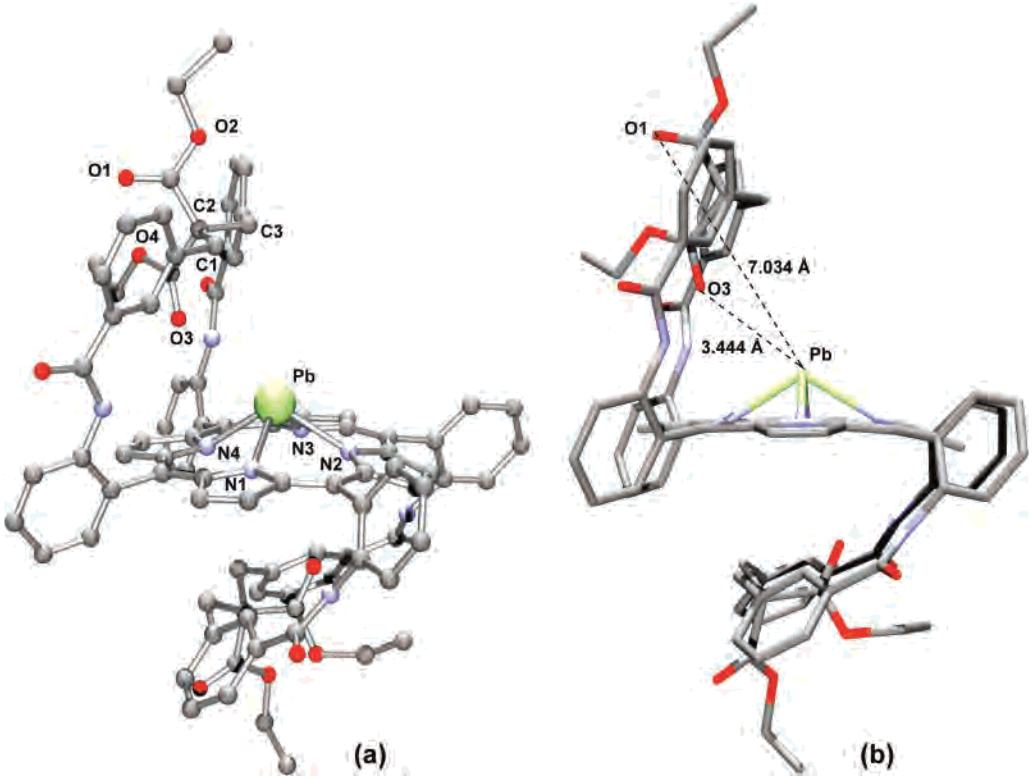

Figure 5. Ball-and-stick (a) and lateral stick (b) views of the solid-state structure of **1Pb**.

which the X-ray structure clearly showed that the straps, located on the same side of the porphyrin and because of a reciprocal steric repulsion, were almost in vertical position.[15] Second, one doublet of the AB system corresponding to the benzylic protons is shielded down to −0.06 ppm, just like in **1Zn** (Figure 1, bottom). Third, one quadruplet (3.90 ppm) and one triplet (0.97 ppm) of an in ester group are downfield-shifted and resonate in the same region that of the out ester groups. These observations are consistent with one strap in vertical position as in the solid-state structure of **1Zn**. As the coordinated Bi^{III} cation needs a counteranion, which is presumably a nitrate residue, the strap of the same side of the bismuth has to “stand up” to accommodate the counteranion. Actually, in terms of the geometry of the straps, the structure in solution of **1Bi** seems to be close to the solid-state structure of **1Zn**. There is no clear spectroscopic evidence in favor of an intramolecular interaction between a carbonyl oxygen atom and the coordinated bismuth in **1Bi**.

In a last step, we reasoned that the situation could be different in porphyrin **3**, resulting from the cleavage of the ester groups of **1**. Indeed, in **3**, the carboxylic acid functions should induce less steric hindrance for bismuth than for the ester groups, and moreover, the metal could have an intramolecular counteranion delivered by the strap. At this step, it is worth mentioning that we were not able to record a ^1H NMR spectrum of **3** suitable for conformational analysis, independent of the recording temperature. Although the HRMS data of **3** were fully consistent with the proposed structure, the ^1H NMR spectrum was representative of a mixture of compounds in exchange. Nevertheless, the bismuth insertion in **3** was performed at room temperature in pyridine. The complexation was rapid, as proved by the appearance of the typical Soret band at ca. 470 nm in the UV−vis spectrum of the reaction mixture, but never went to completion. Additionally, when pyridine was evaporated to purify the resulting mixture of the free base and the metalloporphyrin, demetalation occurred instantaneously. These two last observations concerning both **3** and **3Bi** are consistent with a possible interaction between the carboxylic acid groups and the macrocyclic core. As a result of the coexistence of both the pre-organization and the flexibility of the considered strap, this interaction could result in a partial intramolecular protonation of the internal pyrrolic NH functions. Moreover, this protonation can occur from both sides of the porphyrin with the straps in various conformations as described in Figure 2, hence, the exchange phenomenon observed in the proton NMR spectrum of the free-base porphyrin **3**. In the case of **3Bi**, where one carboxylic acid from one side of the porphyrin can complex bismuth inside the macrocycle, the carboxylic groups from the other side of the porphyrin can protonate the macrocycle. This protonation reaction obviously results in the decomplexation of bismuth and explains why the metalation step cannot be quantitative. This explanation is reinforced by the fact that the porphyrin analogous to **3** in the $\alpha\beta\alpha\beta$ conformation inserts bismuth(III) almost instantaneously, and the resulting complex is definitely stable.[29] Indeed, in the $\alpha\beta\alpha\beta$ conformation in which the straps are attached on the diametrically opposed meso positions, the intramolecular carboxylic acid

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(29) Halime, Z.; Lachkar, M.; Roisnel, T.; Furet, E.; Halet, J.-F.; Boitrel, B. *Angew. Chem., Int. Ed.* **2007**, *46*, 5120−5124.

cannot approach the coordination site of the porphyrin as closely as it can in **3**.

Conclusions

In a first step, we have studied the coordination properties of porphyrins bearing two pre-organized, but still flexible straps, attached on the macrocyclic core by two adjacent meso positions. Each strap can deliver either ethyl ester groups or carboxylic acid functions. The X-ray structures of zinc(II), nickel(II), and lead(II) metalloporphyrins indicate that this type of strap is indeed flexible, as several different positions were found in these complexes. The straps can be "V-shaped" or "W-shaped" and also bent-over the center of the porphyrin or almost in vertical position. In a second step, the coordination study was extended to a trivalent cation, bismuth(III). Whereas the lead complex is easy to synthesize and stable, the bismuth complex is tedious to prepare, but stable in the case of the porphyrin-bearing ester groups. Despite their flexibility, no intramolecular interaction was established with zinc or bismuth. When the porphyrin delivers carboxylic groups around the coordination site, the bismuth complex is rapidly formed but unstable, presumably due to intramolecular protonation reactions. The influence of the malonyl structure is complicated on such a structure, whose flexibility remains interesting for the coordination of various elements. For these reasons, new series of analogous ligands bearing either bulky substituted ethyl acetate residues instead of ethylmalonyl groups or only one strap are under investigation. Both strategies should allow the synthesis of porphyrins delivering only one carboxylic group oriented toward the metal inside the macrocycle.

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Supporting Information Available: CIF, PDB, and PDF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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