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Symetric Triplane Complexes Based on Porphyrins and Phtalocyanines with Earth Rare Metals of Type: [(Po) Ln(Pc) Ln (Po)] for Application in Medical Imaging

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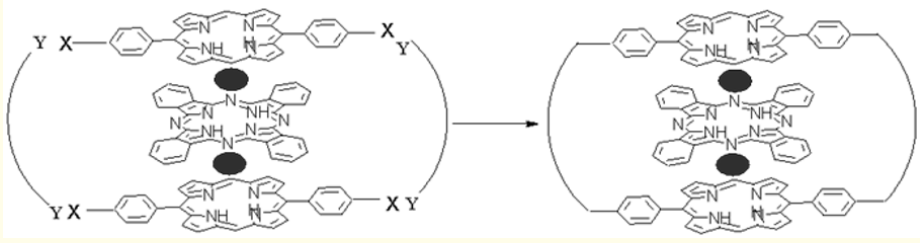
Abstract

Paramagnetic complexes of transition metals and rare earths have attracted a lot of interest in the last year in medical imaging. Indeed, the study by ^{1}H NMR spectroscopy has revealed that these agents increase the contrast between an affected cell and a normal one in biological tissues. This increase in contrast is due to the decrease in the nuclear relaxation time of the ^{1}H proton of water. Due to their high magnetic moment, the dipolar interactions between these agents and water molecules are strong, which mainly reduces the nuclear relaxation time of ^{1}H protons. Bloch was the first to use ferric nitrate as an agent of observation.

Synthetic mixed triplane complexes containing functionalized outer porphyrins and an inner phthalocyanine were prepared and their conditions of obtaining with better yield were studied. These complexes were characterized by UV/Vis. spectroscopy, H NMR mass spectrometry. In the second part we have reported the different strategies of interporphyrin coupling and the appropriate method for obtaining the "cage" complex in which a phthalocyanine ligand is encapsulated by two external porphyrinate ligands. The different parameters that govern this kind of systems are exposed.

Keywords: Meso-tetra.para-propargylphenylperphynate (Tp-PrOP) P; Meso tetra-para-aminophenylprophyrinate (Tp-H2NP) P; Phtalocyanine; octamethyl phtalocyaninate (Pc(Pme); octamethoxyphtalocyaninate (PcMe8); Ln= La; Ce; Gd

Graphical abstract



Introduction

Paramagnetic complexes of transition metals and rare earths have attracted a lot of interest in the last year in medical imaging [1-3]. Indeed, the study by 1 H NMR spectroscopy has revealed that these agents increase the contrast between an affected cell and a normal one in biological tissues. This increase in contrast is due to the decrease in the nuclear relaxation time of the 1H proton of water. Due to their high magnetic moment, the dipolar interactions between these agents and water molecules are strong, which mainly reduces the nuclear relaxation time of 1H protons [4-7]. Bloch was the first to use ferric nitrate as an agent of observation [8]. The work carried out by Bloembergen Solomon [9] and others [10, 11] has allowed the development of the theory that accounts for the structural, dynamic and magnetic phenomena during the interaction between biological macromolecules (DNA...) and tumor marker species. The first human study was developed by Lauterbourg, Young et al [12]. By administering ferric chloride to the patient, the gastrointestinal tract could be better visualized. In parallel, Carr et al [13] used Gadolinium (III) diethyltriaminepentaaacetate [Cd (DPTA(H_2O)] $^{2-}$ to visualize brain tumors. To be used in medical imaging, a contrast agent must meet a number of conditions: 1) Having a dipole moment more or less important in order to act on the nuclear relaxation time of protons and consequently increased the contrast. 2) The dose administered to the patient must not cause toxic effects. 3) Have a specific distribution in vivo i.e. localize preferentially in tumors. 4) Being chemically stable in a biological environment, its decomposition in solution can induce harmful side effects. 5) Should be eliminated by urine a few hours after administration.

Among the contrast agents used, metaloporphyrin has occupied a significant place. Indeed, Cohen et al [14] showed that MnTPPS remains stable in human plasma for about nine days at pH 7.5, whereas Mn(ane$N_4H_2O)_2$ or Mn(cyclam)($H_2O)_2$ decomposes in vivo [14, 15]. On the other hand, Hambright's group [16] and Gilani's group [17] have shown that synthetic paramagnetic metaloperphyrins can be localized in tumors; however, the retention mechanism of this type of complexes (e.g. MnTPPS) is still unexplained. It should be noted, however, that the properties of these complexes are somewhat different from those of the free porphyrin ligands, known as himatoporphyrins (HPDs), which are also localized in tumors when used in phototherapy. All these factors have made porphyrin paramagnetic complexes the most attractive prototype contrast agents. The role played by metallophthalocyanines in this type of use is vital. However, in the literature, the eminent side effects of these compounds, namely the photo-toxicity of some phthalocyanines [16], their pigmentation power [17], have limited their use as tumor markers. Thus, we thought to take advantage of both the known properties of porphyrinic and phthalocyaninic ligands by associating them through rare earths. For the reasons mentioned above, we have chosen the symmetrical triplane in which two porphyrinic ligands are on either side of the phthalocyanine ligand. Moreover, in order to increase the stability of this type of compound in solution, we have considered to cage the central phthalocyanine ligand by means of bridging ligands between the two external porphyrinic ligands. This suggests that it is necessary to work on porphyrins carrying functional groups that can give rise to coupling reactions after formation of the triplanar complex of the type [(Po) Ln(Pc)) Ln(Po)]. In this work we will develop in the first part the synthesis and characterization of this type of complexes and the second part of this work will be devoted to coupling tests.

Synthesis and characterization of symmetric triplanes containing functionalized porphyrin ligands

Choice and position of the functional groups

The synthesis of rare earth triplanes with porphyrins and phthalocyanines began in 1986. In addition to the desired porphyrinic biplane, the porphynic triplane of cerium with tetra(paratolyl)porphynne (H_2TTP) was obtained and its X-ray structure determined by Buchler's team [18]. When applying the same procedure as Hoorcks [19]. (a mixture of tetra(paratalyl)perphyrene H_2TTP and cesium acetylacetcnate (Ce(acac) is heated in 1,2,4 .trichlcrobenzene TCB, for several hours). At the same time, in our laboratory the work on phthalccyanine biplanes of Lutetium, Neodymium, then on mixtures TPP, Pc by applying the method of a synthesis developed by Buchler et al had allowed to obtain a first possible arrangement (Fig.1) with Neodymium [18]. Two years later, the laboratory succeeded in identifying a second arrangement, with cerium. Recently, a third arrangement was also identified with Praseodymium and cerium [20]. The fourth arrangement remains unknown to this day. The fact that this or that lanthanide ion could selectively lead to this or that arrangement with such a yield was random. The mechanism of formation of these different types of complexes had not yet been

elucidated. The studies on the mixed lanthanide biplanes and the attempts to synthesize different triplanes allowed to propose a reaction mechanism summarized in the scheme below.

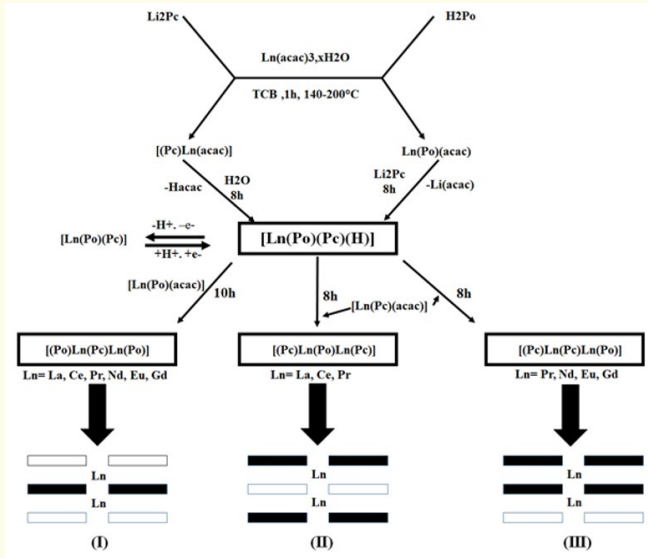


Figure 1: Mechanism of formation of mixed porphyrin-phthalocyanine rare earth triplanes.

Four main factors are involved in the preferred formation of an arrangement over others:

1. The size of a rare earth ion;
2. the ratio Po/ Pc;
3. the basicity of the ligand;
4. steric hindrance induced by the substituents grafted on the complexing ligand.

Thus, for example, the arrangement (I) is all the more favored compared to the arrangements (II), and (III) that the ratio Po/ Pc is higher than 2. The rare earth ion is large and the ligand Pc has large electro-donor substituents (OMe, Me...).

The lanthanides of smaller ionic radius favor the formation of the stable phthalcyanin triplane which reacts on the monoporphyrin complex to lead preferentially to the arrangement. The porphyrin ligand with bulky electro-donor substituents (CH_3, OCH_3,) tends to sit between two phthalcyanine ligands instead, favoring the arrangement (II). All these constraints have direct consequences on the yields of the reactions. In order to optimize the yields in stacking (I), we were forced to choose the least cumbersome position for the substituents to be grafted onto the porphyrin, to use a phthalocyanine bearing large electron-donor groups and to choose the most appropriate lanthanide ion. The X-ray structure of the symmetrical triplane of type (I) shows that the porphyrinic macrocycles are eclipsed [21], and that the ligand Pc is shifted with respect to Po by an angle close to 45° (Fig .2 a) . The ortho position of the phenyl group of TPP does not seem to meet the conditions required for obtaining the arrangement (I) in good yield and would present difficulties for their addition. The free rotation around the C_{phe} -C_{meso} axis would be hindered by the ligand Pc. The meta and para rotations are for them released towards the outside, in steric congestion with the iso indole groups of the ligand Pc are very Weak the author rotation of the axis Cphe and C meso would make it possible to connect these two positions (Fig.2 b).

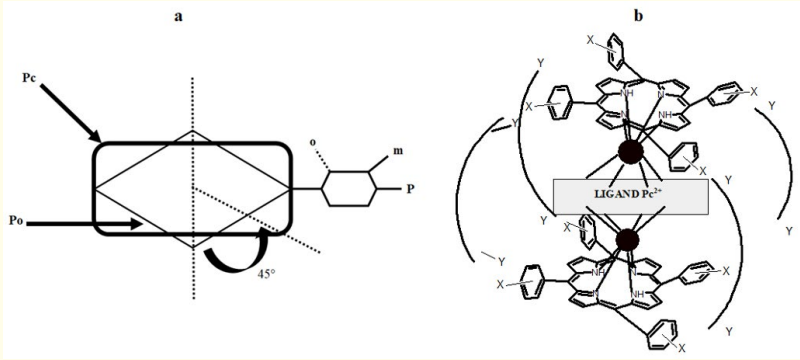


Figure 2: Representation of a symmetric rare earth porphyrin-phthalocyanine mixed triplane of the type [(Po) Ln (Pc) Ln (Po)]; the outer porphyrins take functional groups on "meso" phenyls that can react on a bi-functional group Y- R –Y (a). Projection of the macrocycle Pc2- on the macrocycle TPP 2- according to the axis which connects the centers of these macrocycles while passing by the lanthanide ion (b).

We have made a deliberate choice of the para position which, in all cases, is a unique position (Fig.3). The meta position is on the other hand double (endo and exo position) as shown by the NMR study of the biplanes and triplanes.

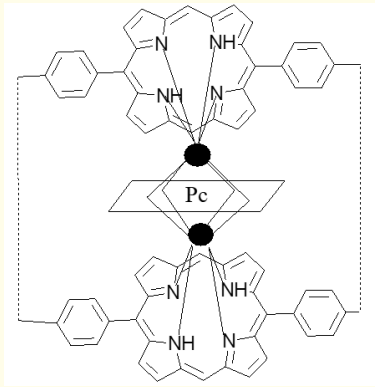


Figure 3: Representation of a symmetric triplane with two external porphyrins linked in para position of the meso phenyls by covalent bridges.

Synthesis strategy

In order to covalently link two porphyrin ligands contained in a triplanar complex two different ways are then possible:

a) The addition, by reduction, of bi-functionalized moieties on a grafted function on the porphyrin ligands (method A: amine + aldehyde Fig .4).
b) An oxidative coupling between two acetylenic groups grafted onto the ends of the precursor triplane (method B, Fig .5).

Method A

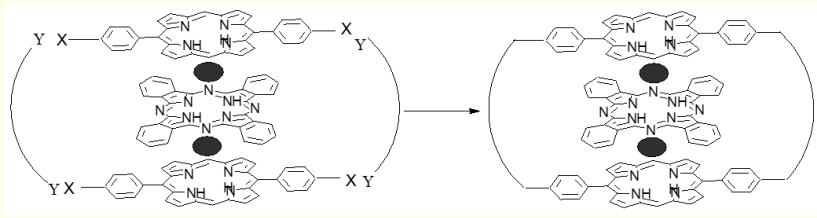


Figure 4: Schema of a coupling reaction between a bifunctional group and a symmetric triple decker complex with external amine functionalized porphyrins.

Method B

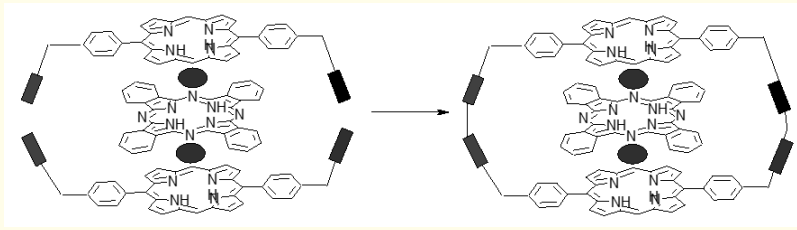


Figure 5: Intramolecular acetylene coupling reaction.

Material and Methods

Synthesis of phthalocyanines

Three types of phthalocyanines have been used in the synthesis of symmetric mixed rare-earth triplanes: Li2Pc, Li2Pc(Me) 8, and Li2Pc(OMe) 8. The method used for the preparation of these salts of di lithium phthalocyaninates is summarized in the Fig .6 below:

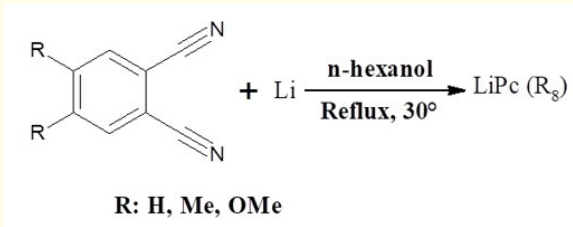


Figure 6: Formation reaction of dilithium phthalocyaninate salt.

It consists in reacting lithium hexanolate with a phthalonitrile derivative for half an hour. The blue compound obtained is then purified by extraction with anhydrous acetone for about 24 hours. The purity of these compounds is verified by UV/Visible spectroscopy, by proton NMR and by elemental analysis.

[(Tp-NH2PP) Ln(Pc) Ln(TpNH2PP)]

The synthesis of porphyrin bearing aniline substituents on the four meso positions is carried out in two steps schematized below and according to the procedure described in the literature [22] The first consists in condensing para-nitrobezaldehyde on the pyrole in propenoic acid in the presence of acetic anhydride. The product obtained is then reduced in acid medium by tin chloride. Tetra-para-aminophenylporphyrin is obtained with an overall yield varying between 15 and 18%. (Fig.7).

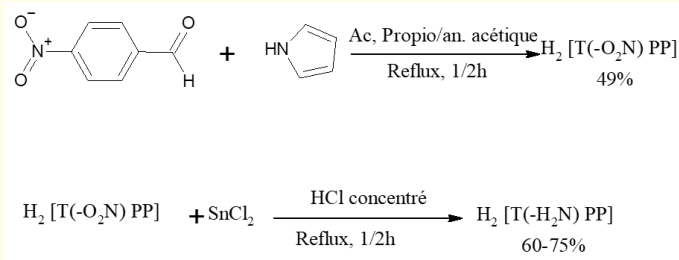


Figure 7: Tetra-para-aminophenylporphyrin formation reactions.

Synthesis of H2[T(p-PrO)PP]

To synthesize this porphyrin, we first go through tetrapara-methoxyphenylporphyrin [23]. The methoxy groups are - then transformed into hydroxyl [23] which react with propargyl bromide in DMF at 55-60°C and in the presence of Caesium carbonate to lead to the desired compound in about 12% overall yield. Fig.8, below, summarizes the synthesis steps of this porphyrin.

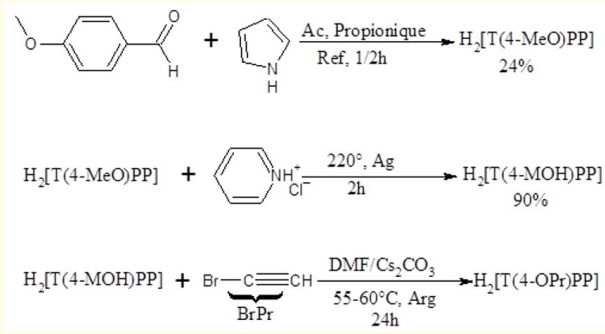


Figure 8: Tetra-para-propargylphenylporphyrin formation reaction.

As previously discussed, the synthesis of mixed triplanes is performed by prolonged heating in trichlorobenzene at reflux. This implies a low reactivity of the factional groups grafted on the porphyrin at this temperature. In order to limit the polymerization phenomenon, the reactions are carried out in the absence of light and the evolution of the latter is done on TLC plates. All the tests carried out showed that only 1/3 of the rational mixture is extracted with chloroform. This one is then chromatographed on a silica column to extract the desired triplane with a yield varying between 12 and 18% with respect to the starting porphyrin.

Synthesis of Tripple decker lanthanide Complexes

The synthesis of mixed triplanes is carried out by prolonged heating in trichlorobenzene at reflux, which explains the low reactivity of the functional groups grafted onto the porphyrin at this temperature in order to limit the polymerization phenomenon. The reactions are carried out in the absence of light and the evolution of these is done on TLC plates, all the tests carried out have shown that the yield of chloroform extracted is very low and it varies from 12 to 18% compared to porphyrin.The Table 1 summarizes the yields of symmetrical mixed triplanes obtained with lanthanum, cerium and gadolinium.

Ln	Po	Pc	Yield
La	TNH_2PP	Pc	8-12%
Ce	TNH_2PP	Pc	8-10%
Gd	TNH_2PP	Pc	12-15%
La	TNH_2PP	$Pc(Me)_8$	15-18%
La	TNH_2PP	$Pc(OMe)_8$	16-20%

Table 1: The experimental yields of the the reaction of synthesis of tripple decker lanthanide complexes.

Results and Discussion

Spectroscopic characterization

UV visible spectroscopy

All mixed triplanes with the same type of arrangement have identical UV/Vis. spectra independent of the rare earth ion. Fig .9 shows the electron spectrum of *[(T-PrOPP)Gd(Pc)Gd(T-PrOPP)]* in dichloromethane. In the absorption spectrum of these triplanes, it will be noticed that the Po/Pc ratio is respected by the measurement of the intensities of the Soret bounds relative to each of the ligands. On the other hand, compared to the reduced mixed diiplane [(Po)LnIII(Pc)]-, the Soret band and the Q bands of phthalocyanine are strongly red-shifted in the symmetric mixed triplane while the Scret band of porphyrin has not undergone any significant shift. The triplanar complex can indeed be considered as two reduced biplanes sharing a phthaloyanin ligand that strongly interacts with the two outer porphyrin macrocycles. This induces a red shift of the bands related to the Pc.

1H-NMR Spectroscopy

Proton NMR spectroscopy of symmetrical triplanes in solution in a suitable deuterated solvent can report the solid state structure of this type of complex [19, 21]. Indeed, the juxtaposition of porohyrinic and phthalocyaninic macrocycles gives rise to a shielding produced by the current effect induced by these macrocycles. The peripheral protons are then shifted towards the strong fields by about 1 ppm compared to the free porphyrins or phthalocyanines precursors [26]. When the rare earth ion that connects the macrocycles is paramagnetic, an additional shielding effect is added to that caused by the aromatic macrocycles. As a result, the protons undergo larger displacements towards the strong fields. While the porphyrin and phthalocyanine protons are located in a range of 5 ppm (6 to 11ppm) for lanthanum (diamagnetic), the dispersion is more important in the case of Cesium (3 to 9 ppm). On the basis of chemical shifts, coupling constants and homonuclear decoupling studies, all signals can be assigned either individually or together with all protons of the same family. The characteristic peaks common to all our triplanes are:

- 16 pyrrolic protons of the two external porphyrins resonating between 7.2 and 7.4ppm.
- 8 ortho (endo) protons of the phenyl group in meso position of the porphyrin resonating between 7.3 and 7.7ppm.
- 8 ortho (exo) protons of the phenyl group in the meso position of the porphyrin resonating between 7.6 and 7, 9 ppm.
- 8 meta (endo) protons of the phenyl group in the meso position of the porphyrin resonating between 6.3 and 6.8 ppm.
- 8 meta (exo) protons of the phenyl group in the meso position of the porphyrin resonating between 6.6 and 7ppm.
- 16 protons Ha et Hb des groupes iso indoles de la phtalocyanine résonant respectivement entre 9,3 et 9,5 ; 8,3 et 8,5.

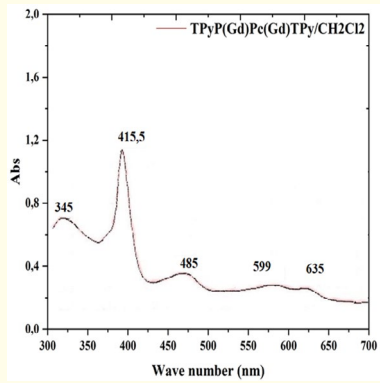


Figure 9: Electronic absorption spectrum of [(T-PrOPP)Gd(Pc)Gd(T-PrOPP)] in dichloromethane.

Some signals are specific to each series in particular those assigned to the protons of the methyl substituents of the phthalocyanine ring, to the amine or propagylate protons (OCH2CCH) in para position of the phenyl group (meso) of the porphynine ring. Fig.10 a,b show the 1 H NMR spectra of symmetric mixed triplanes of Lanthanum in deuterated chlorofam and tables 2 and 3 present the interpretation of the results obtained.

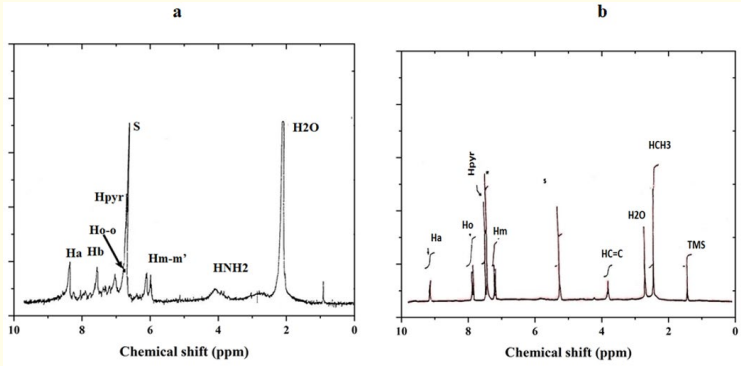


Figure 10: NMR1H spectrum of the triplane complex [(T-NH2PP)2La2(Pc)] in CDCl3 (a). 1HMR spectrum of the triplane complex [(T-PrOPP)2La2(PcMe8)] in CDCl3 (b).

Compound	Solv	Chemical shift								
		Porphyrin						Phtalocyanine		
		Hpyr	Ho	Hm	H_{CH2}	H_{CCH}	H_{SiMe}	Ha		Hb
						H_{Me}				
[(TPrPP)$_2$La$_2$(Pc)]	$CDCl_3$	7,3	7,8		4,6	2,8	….	9,3	....	….
[(TPrPP)$_2$La$_2$(Pc Me8)]	$CDCl_3$	7,3	7,9		4,7	2,9	….	9,4	.....	1,23
[(TMesSiPrPP)$_2$La$_2$(Pc)]	$CDCl_3$	7, 3	7, 9		4, 9	….	0,1	9,4	.....	….

Table 2: Values of the chemical shifts of the different protons of the symmetrical triplane series of Lanthanum (III).

Compound	Solv	Chemical shift						
		Porphyrin				Phtalocyanine		
		Hpyr	Ho	Hm	H_{NH2}	Ha	Hb	H_{Me}
[($T_{p\text{-}NH2}$PP)$_2$La$_2$(Pc)]	$CDCl_3$	7,3	7,6	6,5	4,1	9,3	8,3	….
			7,3	6,3				
[($T_{p\text{-}NH2}$PP)$_2$La$_2$(Pc Me$_8$)]	$CDCl_3$	7,3	7,6	6,6	4,1	9,3	…	1, 3
			7,4	6,4				

Table 3: Values of the chemical shifts of the different protons of the symmetrical triplane series of Lanthanum (III).

At ordinary temperature and at 300 MHz, the rotation, liter around the axis Cméso Cphé is allowed, the ortho protons are then known equivalent, the meta protons also. They come out as doublets compatible with an AB system. The substituents carried by your Pc or Po rings seem to be less and less sensitive to the shielding effect as the distance to each of the macrocycle is large.

All these factors led us to choose a number of ligands based on : Their size, Flexibility or rigidity and Reactivity. Thus, for symmetric triplanes with two tetraaminoporphyrins, four types of aldehydes and two types of acid chlorides were selected Fig.11.

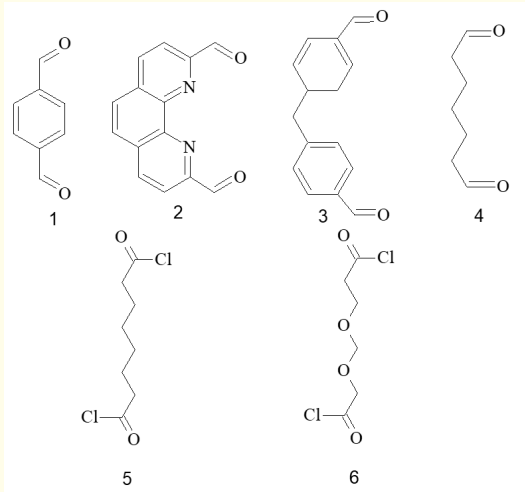


Figure 11: Chemical structure of aldehydes and acid chlorides selected for the tamplet cyclization reaction.

Reactivity of aldehydes towards amine porphyrin triplanes

In order to account for the average distance between the two parallel amine groups, and their orientation; we chose different types of aldehydes 1,2,3 and 4. For aldehydes 1 and 2 [31], 1the O---O distance varies from 6.8 to 7.0 Å [32] respectively, while in aldehyde 3,1the average distance of the free compound is about 7.5 Å. Once bound, this distance can vary from 6.13 to 7.83 Å [41]. Molecules 1, 2 are rigid while molecule 3 is relatively flexible. A distortion of the (Ph-C-Ph) angle can take place to accommodate with the amine groups. In the case of molecule 4, the degree of freedom is even greater and the possibility of joining amine ends becomes numerous. The condensation of aldehydes on amines is very often catalyzed by acids or bases [33]. In some cases, a complexing ion acting as a matrix is also used [34]. The solvent for the reaction is chosen according to the solubility of the reactants. In the literature, several methods have been used. Recently, Vögtle et al [35] successfully coupled two tetraaminophenylporphyrins with a relatively stiff bis-aldehyde using the method of Lindsay et al [36]. To a concentrated solution of diformyl in a mixture of acetonitrile/dimethylacetamide and four equivalents of trifluoroacetic acid, and very slowly added a solution of porphyrin in acetonitrile at ordinary temperature. Because of the preorganization of the molecular blocks, the high dilution reaction is not necessary and the yield of the reaction exceeds 40%. The application of this method to triplanar complexes leads to a partial demetallation of the complex and formation of bridged bis-porphyrins II b as shown in the reaction scheme below (Fig.12) In the case where the reaction is carried out in chloroform or THF at high dilution, type III a compounds are obtained with aldehydes 1 and 2. This shows that the N---N distance in the triplane is greater than that available in the diformyls used.

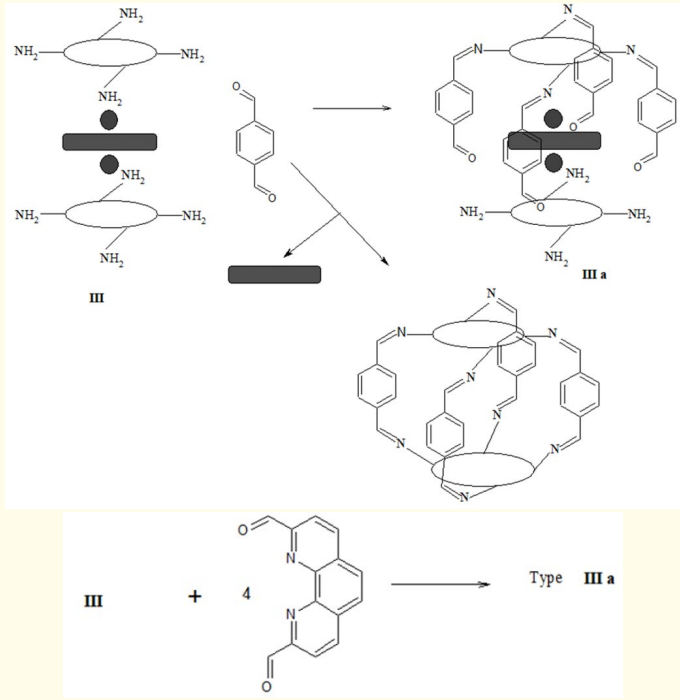


Figure 12: Reactivity of aldehydes towards amine porphyrin triplanes.

With bis-aldehyde 3, only the doubly and triply bridged compounds could be isolated. The tetra-bridged compound could not be obtained in acceptable yield. It is probably retained in very small amounts in the residue containing the polymers or not formed at all. The following figure summarizes the reactions that could be observed (Fig.13).

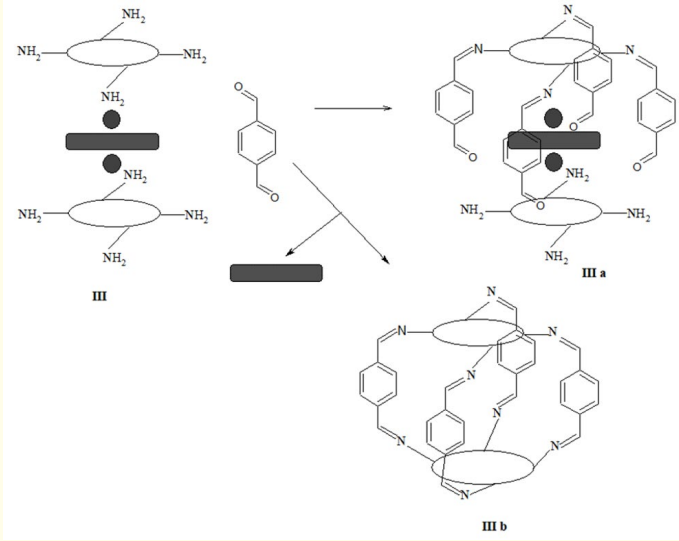


Figure 13: Reaction of the octa-amine triplane with a bis aldehyde.

All attempts to obtain a cage complex from the symmetric triplane containing tetraaminophenylporphyrin have failed. The existence of eight reaction centers and the sensitivity of the precursors to trace acids present real difficulties. The use of another coupling method such as acetylene coupling is necessary.

Diacetylenic coupling

Diacetylenic coupling of bis-propargyl subunits provides efficient access to receptors meeting these criteria. The C1-C6 distance of a 2,4-hexadiyne unit of 6.7 Å defines a cavity of about 4 Å between the walls, consistent with the Wan der Waals thickness [37]. To avoid the chain polymerization reaction, we thought to bring together the propargyl subunits within the same molecule before the coupling, the proximity effect should rather favor intramolecular coupling than intermolecular polymerization. To carry out this intramolecular coupling, Lehn et al, Whitlock et al used the method of Eglinton [38], modified by Matsuoka [39] in the original conditions, the oxidative coupling is carried out in high dilution, at room temperature, by cupric acetate in catalytic amount, this one being regenerated by oxygen. The efficiency of the reaction can be increased by operating at higher temperature (40-60°C) and under inert atmosphere. Breslow et al [40], Dietrich and Sauvage [41], have realized this coupling by operating in high dilution with a CuCl/CuCl2- O2 mixture in pyridine or DMF. On our side, the application of these different methods of oxidative coupling to our triplanar systems causes the breaking of the triplanar edifice. Indeed, the cupric ion present in solution and in large excess presents a great affinity with the porphyrin and phthalocyanine macrocycles. The size of the ion allows its insertion inside the cavity of each of the macrocycles even at ordinary temperature. The larger rare earth ion, being outside the cavities from the start, is then easily substituted by the cupric ions. As a result, we are in the presence of monomeric copper complexes. The result is a statistical mixture that is difficult to separate and identify. Among the compounds formed, we succeeded in isolating and characterizing the porphyrinic dimer of copper (Fig .14).

Recently, Sanders et al [42] used, for the synthesis of porphyrin dimers and trimers, from acetylenic precursors, cuprous chloride (CuCl) in pyridine and in the presence of oxygen at room temperature. This new synthetic route, when applied to our triplanar constructs, provided the cage complex but in very low yield (Fig.15). Although the yield is very low, the desired cage complex obtained, provides us with some useful information about the structure, stability and physicochemical properties of this new complex.

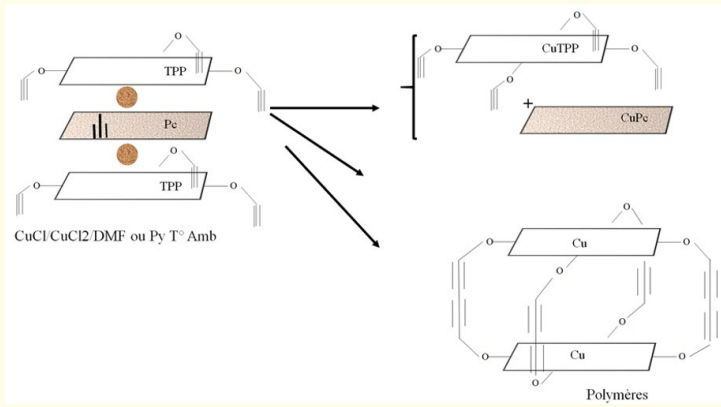


Figure 14: Oxidative coupling reaction of acetylenics by a Cu(I)/Cu(II) mixture in the presence of oxygen.

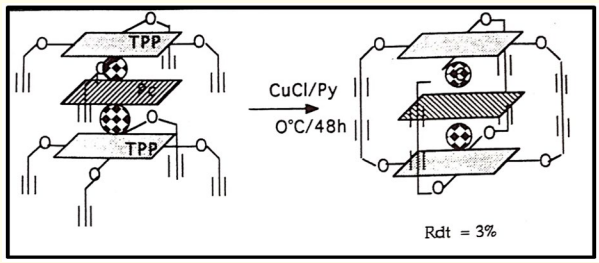


Figure 15: Intramolecular oxidative coupling according to the Sanders method.

Mass spectrometry

Mass spectrometry of the open or closed "caged" triplanes allows to confirm the proposed structures. Indeed, the oxidative coupling of the propargyl groups induces a decrease in the molar mass of the compound by eight units relative to the eight protons carried by acetylenic groups. The calculated and found malar masses for these two types of compounds agree (Fig.16). It should be noted that in the case of the [(Tp- PrPP)2La2(PcMe8)] complex, the coupling took place only on two acetylenes and the molar mass decreased by two units (2560 to 2558). This same triplane, once all the arms are linked, shows a molecular peak of M=2552.7 while the theoretical value is 2552.1. This perfect agreement allows us to conclude that the coupling has indeed affected all the reaction centers.

UV/Visible spectroscopy

The triplanar Lanthanum complex with two tetraponted outer porphyrins shows a typical UV/Visible spectrum of a symmetric triplane with two porphyrins and a phthalocyanine held together by Lanthanum (III) ions. The only noticeable difference is the clear decrease of the Soret band of the phthalocyanine. It is as if the shielding effect exerted by the two external porphyrins is further accentuated. The porphyrin-porphyrin bond is strengthened by the propargyl bridges. The porphyrin related Soret band has not undergone a noticeable shift, but a slight broadening. In the literature, porphyrin biplanes also show this feature [24]. Fig.17 shows the electronic absorption spectrum of the "cage" complex in chloroform.

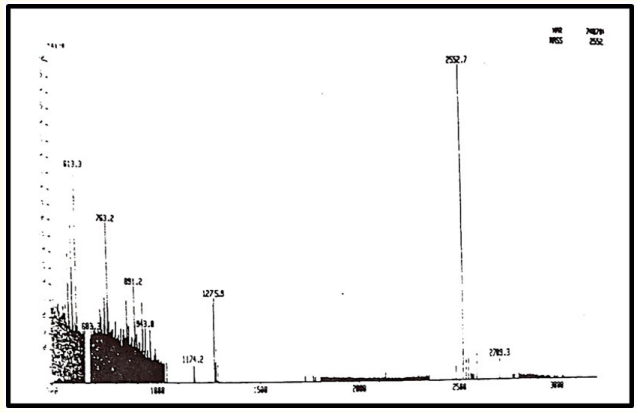


Figure 16: Mass spectrum (FAB+) of the ''cage'' triplane.

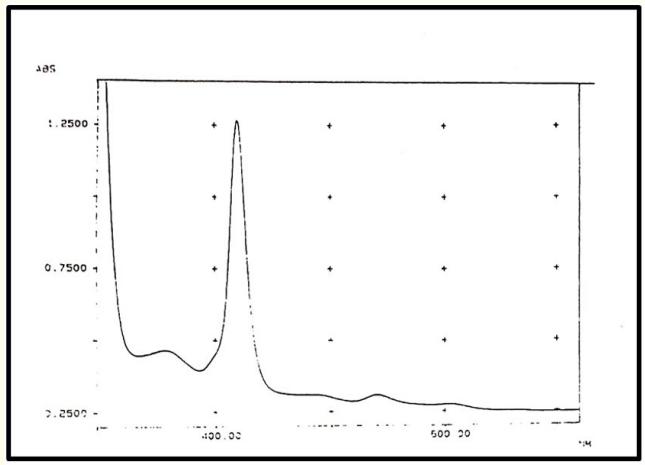


Figure 17: The electronic absorption spectrum of the "cage" complex in chloroform.

Proton NMR spectroscopy

In proton NMR spectroscopy, symmetric triplanar complexes in solution in deuterated chloroform CDCl3 show characteristic spectra. As we can see (Fig.18), the pyrrolic H protons of the two outer porphyrin macrocycles are all equivalent and exit as a singlet at 9.93 ppm. This value is unusually shifted to the low fields compared to its analog in the precursor complexes. This deblooming probably caused by a current effect induced by the intimately bound set of porphyrin macrocycles. The resonance values of the Ho and Hm protons, on the other hand, were not significantly changed. The meso phenyls of both porphyrins are indeed released from the macrocycles. The current effect exerted on this type of protons is relatively small compared to the H and H protons of the pyrrolic groups (Hpyrr). The singlet groups around 4.8 ppm related to the H protons (CH2O) and the total absence of signals related to the acetylenic protons. This shows that the oxidative coupling has affected all reaction centers.

The Ha and Hb protons of the isoindole groups of the phthalocyanine ligand held in a cage between the two porphyrins resonate at usual values little different from those of the parent complexes. When the Hb are substituted with methyl groups, the corresponding protons have chemical shifts almost identical to those of the parent complex.

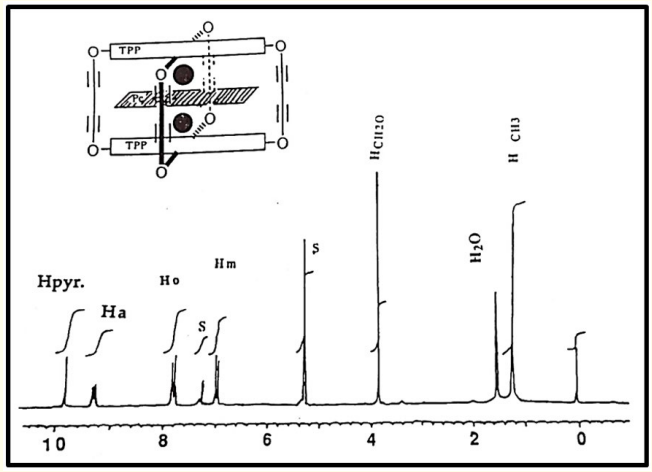


Figure 18: RMN1H spectrum of the ''cage'' triplane.

Conclusion

In sum, the tetraplanar tetraponted complex exhibits similar spectroscopic properties to the precursor complex with slight modifications. By acetylenic couplings, the molecular structure remains invariable and the compound structure becomes more compact. In the intermolecular cavity the phthalocyaninate ligand is inserted. The demetallization of the system by addition of concentrated sulfuric acid leads to a biplanar system with two porphyrins in which a phthalocyanine ligand is encapsulated. This Pc ligand remains inside the interporphyrin cavity and cannot be released (Fig. 18). The different positions that it can adopt make the system go through several thermodynamic states and whose stability depends on the interactions between the π-electron clouds of the macrocycles.

This system is therefore more stable than the open triplane. On the other hand, the exchange of one lanthanide ion by another is possible. It is even possible to replace two lanthanide ions by three transition metals which fit into the cavities of each of the macrocycles. Unfortunately, these tests could not be performed because the amount of triplanar "cage" product obtained is so small that its exploitation in further reactions is excluded. What we can note, however, is that the encapsulation of the phthalocyanine ligand is possible and that the strategies of the work presented a number of difficulties and constraints. The work certainly requires further efforts in determining the average distance that separates the atoms of the phenyl groups of the two eclipsed porphyrins, the orientation of each of the challenged bonds, the judicious choice of bridging ligands, the optimization of the yields of precursor triplanes, the search for more appropriate coupling conditions (dilution, reaction temperature, reagents that avoid the demetallation of the triplane, ...). In short, all the tests that we have performed have allowed us to understand the complexity of the problem and have shed light on all the factors that are involved in the resolution of the problem. By the acetylenic coupling method, although the yield is very low, it allowed to report the real distance that separates the phenyl groups of the two external porphyrins. Indeed, the calculation shows that this distance is about 7.97 Å. In spite of the few attempts to crystallize this product, we did not succeed in obtaining crystals suitable for X-ray diffraction.

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