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Synthesis and Inclusion Properties of Macrocyclic Polyethers Containing Phosphonic Groups

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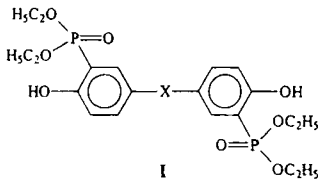
Three novel polyether macrocycles II–IV bearing phosphonic groups have been synthesised in satisfactory yields. Macrocycle II was found to form a 1:1 inclusion compound with cyclohexane and thus was easily isolated from the reaction mixture as a clathrate. The crystal and molecular structure of the cyclohexane solvate has been determined by single crystal X-ray analyses and refined to an R of 0.028 for 3199 reflection. The compound is monoclinic, space group $P2_1/n$ with $a = 15.886(6)$ Å, $b = 11.657(5)$ Å, $c = 18.621(6)$ Å, $\beta = 90.12(3)°$, $Z = 2$. The whole molecule exhibits a great deal of disorder and the different conformations were modelled as consisting of two different primary conformers with population approximately 60:40.

Keywords: Polyethers, phosphonic, derivatives, para-cyclophane, inclusion formation, synthetic routes

INTRODUCTION

It is well known [1] that dialkyl aryl phosphates can be rearranged by treatment with lithium diiso- propylamide (LDA) or butyllithium to dialkyl aryl phosphonates, which, in turn, can be easily hydrolyzed to *o*-hydroxy aryl phosphonic acids.

Considering the great interest in the production of phosphonates, both for medical as well as for analytical applications [2], we decided to use the 1,3-phosphorotropic rearrangement described by Dhawan and Redmore [1] for preparing bis-hydroxy aryl diphosphonates [3] of general formula **I** in order to use such molecules as monomers for polycondensates having oxygen bridges between aromatic nuclei and possessing pendant phosphonic groups in the chain.



I

X	
$C(CH_3)_2$	**Ia**
S	**Ib**
SO_2	**Ic**

Besides the interest in obtaining flame retardant and thermally stable polymers, compounds of general formula **I** can be also used for preparing novel macrocyclic polyethers possessing ancillary groups (the phosphonic ones) which improve their water solubility or their complexing

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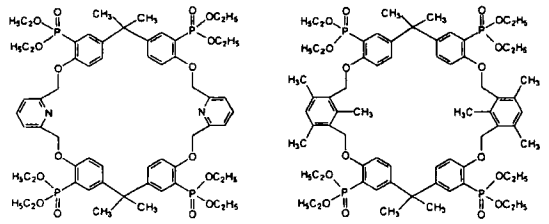
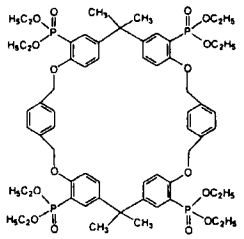
properties towards particular cations [4], such as the lanthanides, extensively used in diagnostic medicine [5, 6].

In this paper we shall report the synthesis and full characterization of three novel polyether macrocycles, **II – IV**, obtained by condensing the phosphorilated bis-phenol **Ia** with 2,6-bis (bromomethyl) pyridine, 2, 4-bis(chloromethyl)-1,3,5-trimethylbenzene and α,α'-dibromo-*p*-xylene, respectively.



II

III



IV

The three novel macrocycles, **II – IV**, are of interest in supramolecular chemistry due to the presence of the phosphonate groups which can generate, after hydrolysis to phosphonic acids or mono-esters, novel architectures by hydrogen bond formation; these molecules are also able to incorporate neutral molecules into the cavity, as shown by X-ray diffraction techniques, in the case of cycle **II**.

RESULTS AND DISCUSSION

The three macrocycles, 17,17,40,40-tetramethyl-1,10,24,33-teraoxa[2](2,6)pyridino[2.1] paracyclo [2] (2,6)-pyridino [2.1] paracyclophane-12,20, 35,43-tetraphosphonic acid diethylester (**II**), 4, 6,8,17,17,27,29,31,40,40-decamethyl-1,10,24,-33-teraoxa[2](2,6) benzeno[2.1]paracyclo[2](2,6)-benzeno[2.1]paracyclophane-12,20,35,43 tetraphosphonic acid diethylester (**III**) and 17,17, 40, 40-tetramethyl-1, 10, 24, 33-teraoxa[2](1, 4) benzeno[2.1] paracyclo[2] (1,4)-benzeno[2.1] paracyclophane-12,20,35,43-tetraphosphonic acid diethylester (**IV**), were synthesized by reacting, under reflux conditions for 24 hours, dilute solutions of the appropriate bis(bromomethyl)-derivatives with **Ia** in acetonitrile in the presence of solid K_2CO_3 as a base. ^{1}H-, ^{13}C-, ^{31}P-NMR, FAB-MS and X-ray analysis data support the formulation of the synthesized compounds.

The 500 MHz ^{1}H-NMR spectrum of macrocycle **II** at room temperature in $CDCl_3$ solution shows a triplet ($\delta = 1.34$) and a multiplet ($\delta = 4.20$) for the ethoxy groups linked to the phosphorus atoms, a sharp singlet ($\delta = 1.64$) for the methyl group attached to the bridgehead quaternary carbons, a single sharp peak ($\delta = 5.27$) for the benzylic protons linked to the pyridine nuclei and the expected multiplicity for the aromatic hydrogens. This pattern, coupled with the ^{13}C- and ^{31}P-NMR spectra, clearly indicates a great mobility of macrocycle **II**, which interconverts itself in solution among various possible conformations.

Interesting enough, crystals of **II**, obtained from a cyclohexane/ethylacetate solution show, in the NMR spectrum, the presence of the saturated hydrocarbon included in a molar ratio 1:1; the same observation was also found by thermogravimetric analysis which shows total loss of one mol of cycloexane in two steps at 170.3 and 179.0°C. The geometry of the inclusion compound formed will be discussed later on in the X-ray section.

Also for macrocycles **III** and **IV** ^{1}H-, ^{13}C- and ^{31}P-NMR spectra can be interpreted in terms of high conformational mobility occuring in solution at room temperature (single sharp signal for the benzylic protons, only one phosphorus peak, *etc.*, as detailed in the experimental section). Contrary to **II**, macrocycles **III** and **IV**, which lack

the polarity of the pyridine nitrogens, is not able to form inclusion complexes, at least with the large number of the organic solvents tried so far (benzene, toluene, ethylacetate, cyclohexane, *etc.*).

Comparing the proton and carbon chemical shifts of the parent monomers with those of the cognate macrocycles **II**–**IV**, no significant change in the spectra is observed. This fact confirms, once again, the great mobility of such cycles and that their averaged geometry in solution is the summation of several different conformers.

However, a significant change in chemical shift values between the starting phosphonate and the corresponding macrocycle is observed in the $^{31}P\{H\}$-NMR spectra. In fact, in monomers **Ia**, the phosphorus signal is present as a singlet at $\delta = 21.24$ ppm, whereas in macrocycles **II**–**IV** the ^{31}P signals still appear as singlets but resonating at $\delta = 16.36$ ppm, $\delta = 17.65$ ppm and $\delta = 16.28$ ppm, respectively.

No doubt this difference is due to the presence of a strong intramolecular hydrogen bonds present in monomers of type **I** involving the phenolic OH and the adjacent P=O group, which breaks down and disappears after the formation of the macrocycles.

Further evidence of the presence of intramolecular chelation in **I** comes from the inspection of the ^1H-NMR phenolic OH signal which resonates at *ca.* 10.4 ppm (figure diagnostic for the presence of hydrogen bonding [7]) and whose value does not depend on the solution concentration in $CDCl_3$.

In addition, the ^{31}P chemical shifts of type **Ia** compounds where the phenolic OH has been transformed into a methoxy group are observed at $\delta = 16.40$ ppm, a value very close to that found for our macrocycles.

To confirm that our synthesis leads to oligomeric paracyclophanes we used the FAB-MS technique. In Figure 1 is shown the FAB-MS spectrum of the crude product isolated from the reaction of **Ia** with 2,6-bis(bromomethyl)-pyridine in order to obtain compound **II**.

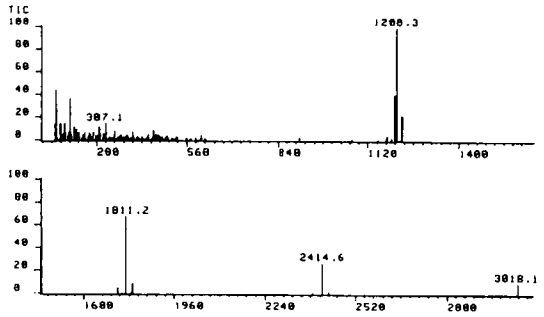
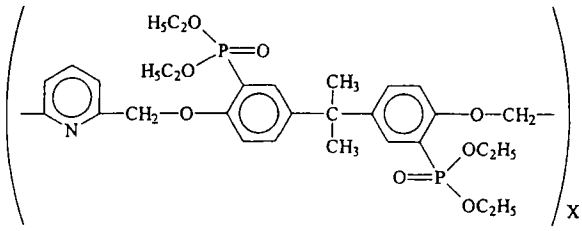


FIGURE 1 FAB-MS spectrum of the crude product isolated from the macrocyclization reaction which yields **II**.

Inspection of Figure 1 reveals the presence of peaks at m/z 1208.3 (100%), 1811.2 (75%), 2414.6 (38%) and 3018.1 (11%) in the crude mixture. These peaks all correspond to cyclic oligomers whose molecular skeleton is formed by the repeating unit ***X*** below indicated; starting from the lowest mass peak above reported, ***X*** is equal to 2, 3, 4 and 5, respectively.



A linear correlation is observed for the ln-ln plot of the experimental concentration (C_x) of the cyclic compounds as a function of the repeating units (x) present in the molecule (Fig. 2).

Considering that our experimental values fall in the line with slope $\alpha = -2.5$ we can conclude [8] that our cyclization reaction follows the thermodynamically-controlled regime according to the theory of macrocyclization equilibria formulated by Jacobson and Stockmayer [9] which predicts that: (i) if the chains in solution obey Gaussian statistics, (ii) if all rings are equally probable on steric grounds and (iii) if the reactivity of all functionalities along the growing chain remains the same, the equilibrium concentration of each cyclic unit should

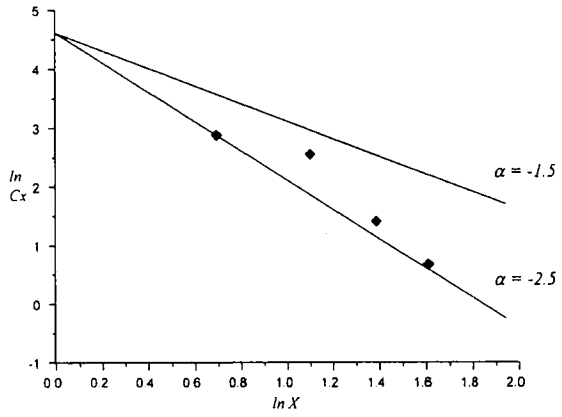


FIGURE 2 Plot of the experimental concentration C_x (◆) of cyclic compounds *vs.* the 'ring size' in the macrocyclization reaction which yields **II**. The two lines are calculated according to the law $C_x = AX^{-1.5}$ and $C_x = AX^{-2.5}$, respectively.

decrease according to the law:

$$C_x = AX^{-2.5}$$

where C_x is the concentration of the given cycle with X repeating units and A is a constant. Deviation from the thermoldynamically-controlled regime can arise if kinetic enhancement (or depression) of cyclic molecules takes place at an early stage of the reaction [8], and the slope of the line should change to $\alpha = -1.5$.

By column chromatography of the crude mixture on silica gel using chloroform/methanol as eluent we isolated, in satisfactory yield, macrocycles **II**–**IV** whose spectral characteristics are fully reported in the experimental section. Selective cyclohexane inclusion was observed when compound **II** was crystallized from a cyclohexane/ethyl acetate mixture. By taking advantages of such property, the [2+2] macrocycle could be separated selectively from the reaction mixture by formation of inclusion complex with cyclohexane in ethyl acetate solution. Under these conditions, the crystallization of macrocycle **II** was near quatitative. In other words, a "supramolecular" purification method can be used for compound **II**; on the contrary, the isolation of macrocycles **III** and **IV** must be performed by cromatography, because they are not able to include any solvents so far used. This different behaviour can be ascribed to the para-substituted spacer molecules that are not pre-organised and thus give more flexibility to the macrocyclic molecules.

The structure of **II** included with one molecule of cyclohexane was unequivocally established by a single-crystal X-ray diffraction study. Atomic coordinates are given in Table I whereas selected

TABLE I Atomic coordinates [$\times 10^4$] and equivalent isotropic displacement parameters [$Å^2 \times 10^3$] for cycle **II**. U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor

	x	y	z	U(eq)
P(1)	15329(2)	3952(2)	8041(1)	73(1)
P(2)	9809(1)	877(2)	8144(1)	68(1)
O(1)	18884(3)	935(5)	11615(3)	68(2)
O(2)	15740(3)	3608(4)	9614(3)	61(1)
O(3)	14869(4)	3947(6)	7359(3)	99(2)
O(4)	16061(3)	3068(5)	8092(3)	81(2)
O(5)	15784(3)	5093(5)	8254(3)	79(2)
O(6)	9341(3)	1952(5)	8170(3)	82(2)
N(1)	17226(4)	2675(5)	10913(4)	56(2)
C(1)	18313(5)	1870(6)	11659(4)	67(2)
C(2)	18035(6)	2313(6)	10937(5)	59(2)
C(3)	18540(6)	2285(7)	10363(6)	75(3)
C(4)	18236(6)	2671(7)	9698(5)	75(3)
C(5)	17400(5)	3047(7)	9664(5)	64(2)
C(6)	16932(5)	3042(6)	10289(5)	53(2)
C(7)	16027(4)	3399(6)	10313(4)	52(2)
C(8)	14901(5)	3644(6)	9491(5)	57(2)
C(9)	14632(5)	3752(6)	8783(4)	53(2)
C(10)	13780(5)	3731(6)	8631(4)	56(2)
C(11)	13163(5)	3649(6)	9156(4)	49(2)
C(12)	13468(5)	3616(6)	9850(4)	57(2)
C(13)	14310(5)	3605(6)	10026(4)	55(2)
C(14)	12235(5)	3602(6)	8973(4)	59(2)
C(15)	11970(5)	2346(6)	8833(4)	51(2)
C(16)	11144(5)	2114(7)	8618(4)	57(2)
C(17)	10861(5)	1022(7)	8467(4)	57(2)
C(18)	11421(5)	112(7)	8543(4)	54(2)
C(19)	12223(5)	316(7)	8772(4)	59(2)
C(20)	12495(5)	1434(7)	8904(4)	55(2)
C(21)	11697(5)	4060(7)	9601(5)	77(3)
C(22)	12046(5)	4339(7)	8306(5)	75(3)
C(23A)	15861(13)	1873(15)	7935(15)	80
C(24A)	16794(13)	1243(17)	8055(15)	100
C(23B)	16110(21)	2019(25)	7674(19)	80
C(24B)	16599(22)	1313(26)	7758(21)	100
C(25)	16175(19)	5899(29)	7720(14)	70
C(26A)	17040(23)	6152(34)	8047(16)	100
C(25)	16436(11)	5465(15)	7791(8)	70
C(26B)	16655(13)	6696(16)	8022(9)	100
O(7A)	9846(8)	540(10)	7337(7)	70
C(27A)	10223(11)	991(17)	6851(10)	80
C(28)	10893(13)	−31(16)	6579(12)	100

TABLE I (Continued)

	x	y	z	U(eq)
O(8A)	9402(7)	−248(10)	8412(6)	70
C(29A)	8655(11)	−398(15)	8694(10)	80
C(30)	8668(13)	−1333(16)	9248(10)	100
O(7B)	9840(8)	51(11)	7492(7)	70
C(27B)	10336(14)	275(19)	6921(11)	80
C(28)	10517(14)	404(19)	6202(12)	100
O(8B)	9440(8)	19(11)	8755(8)	70
C(29B)	9068(13)	−283(18)	9133(12)	80
C(30)	8205(14)	−994(20)	9103(13)	100
C(1S)	15416(3)	−493(5)	9402(4)	105(3)
C(2S)	15426(3)	209(5)	106363(4)	115(4)
C(3S)	16026(3)	276(5)	9908(4)	116(4)

TABLE II Selected bond lengths [Å] and angles [°] for cycle **II**. Averaged values for chemically equivalent atoms are listed as*. Symmetry transformations used to generate equivalent atoms: #1 −x+3, −y, −z+2

P(1)-O(3)	1.464(3)	P(1)-O(4/5)	1.560(6)*
P(1)-C(9)	1.788(8)	P(2)-O(6)	1.459(6)
P(2)-O(7A/8A)	1.55(1)*	P(2)-O(7B/8B)	1.59(1)*
P(2)-C(17)	1.783(8)	O(1)-C(18)#1	1.347(8)
O(1)-C(1)	1.420(8)	O(2)-C(8)	1.352(8)
O(2)-C(7)	1.401(8)	O(4)-C(23A/23B)	1.46(2)*
O(5)-C(25A/25B)	1.46(2)*		
O(3)-P(1)-O(4)	114.9(4)	O(3)-P(1)-O(5)	116.9(4)
O(4)-P(1)-O(5)	101.7(3)	O(3)-P(1)-C(9)	111.1(4)
O(4)-P(1)-C(9)	109.3(3)	O(5)-P(1)-C(9)	101.6(3)

bond lengths and angles are reported in Table II. The molecule of paracyclophane **II** with the cyclohexane guest and its numbering scheme is represented in Figure 3. It crystallizes in the monoclinic space group $P2_1/n$ with two molecules in the unit cell. The unit cell dimension together with crystal data and the structure refinement data are reported in the experimental section.

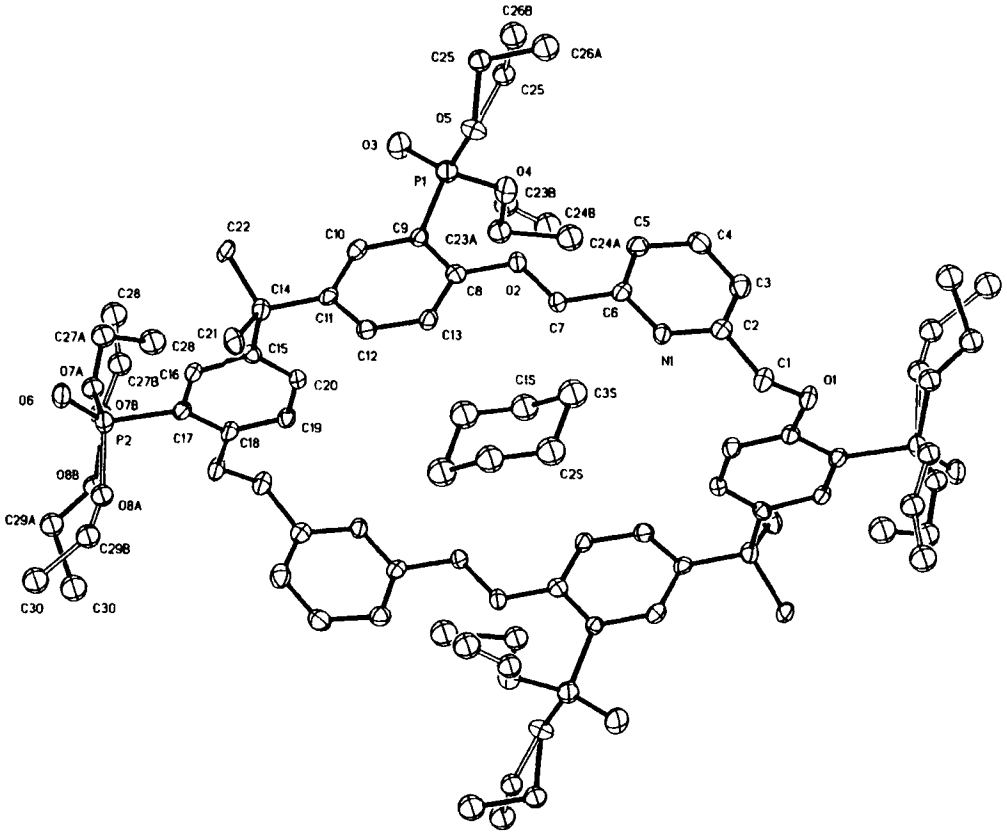


FIGURE 3 Molecular conformation of two different conformers and atomic numbering scheme of **II** • Cyclohexane.

For the most part, bond distances and angles are normal and have values consistent with other comparable structures. However, the ADP's on O(7), C(27), C(28), O(8), C(29), C(30), C(23), C(24) and C(25), C(26) were unreasonably large after anisotropic refinement and suggested disorder of those atoms. Final refinements confirmed that there is considerable static disorder in molecules of **II** in that the pendant ethoxy groups of the phosphite moieties have different conformations. They were modelled to consist of two primary conformers with populations of approximately 60% and 40%, respectively as shown in Figure 3. Other conformer contributions are very small.

The guest cyclohexane molecule fits nicely into the hydrophobic cavity of the cycle **II** host molecule with intermolecular distances which are all less than the van der Waals distances expected, *i.e.*, there are no strong intermolecular interactions, rather only weak non-polar-non-polar interactions.

EXPERIMENTAL

Materials

Unless otherwise stated, commerical chemicals were used as supplied: diethyl phosphite, 2, 6-bis (bromomethyl)-pyridine, 2, 4-bis-(chloromethyl)-1, 3, 5-trimethylbenzene, α,α'-dibromo-*p*-xylene, 2, 2-bis-(4-hydroxyphenyl)-propane, triethylamine, *n*-butyllithium in hexane (1.6 M) and anhydrous diisopropylamine were obtained from Aldrich.

All reactions were performed under an inert atmosphere of nitrogen, and the solvents were refluxed and freshly distilled before use. Melting points are uncorrected. All other reagents were reagent grade from Carlo Erba.

Physical Measurements

^{1}H-, ^{13}C-, ^{31}P-NMR spectra were recorded on a Varian-Inova 500 MHz operating at 500 MHz, 125 MHz and 200 MHz respectively, using $SiMe_4$ as internal reference and 85% H_3PO_4 as external reference.

Mass spectra were obtained using a double-focusing Kratos MS 50S instrument equipped with a standard FAB source and DS 90 data system using 3-nitro-benzylalcohol as matrix.

Preparations

2,2-Bis(3-diethylphosphono-4-hydroxyphenyl)-propane Ia

Triethylamine (0.11 mol) was added dropwise to a stirred mixture of 2,2-bis(4-hydroxyphenyl)-propane (0.05 mol) and diethyl phosphite (0.11 mol), in carbon tetrachloride (100 mL), which had been cooled to 0°C; the temperature of the mixture was maintained below 10°C by external cooling throughout this addition. The mixture was then stirred overnight at room temperature and the salt that formed filtered off. The organic solution was washed with 2N sodium hydroxide, water and dried over anhydrous Na_2SO_4. Removal of solvent under vacuum left the bisphosphate precursors as a colorless oil. part of this oil (0.02 mol) was placed in a dry THF solution (50 mL) and added from a dropping funnel to a lithium diisopropylamide (LDA) (0.08 mol) solution in 100 mL of dry THF at −78°C. After the addition was completed, the reaction mixture was stirred at −78°C for two additional hours, then the temperature of the reaction mixture was raised to −20°C and quenched with 200 mL of saturated aqueous ammonium chloride. The organic mass was extracted with ether and chloroform and dried over anhydrous Na_2SO_4. Evaporation of the solvents at reduced pressure gave a white solid, which was purified by column chromatography on silica gel using as eluent a gradient of ethylacetate in cycloexane to give pure **Ia**. White needles, yield 75%, m.p. 103–104°C; ^{1}H-NMR ($CDCl_3$) δ:10.07 (s, 2H, ArOH), 7.24 (m, 4H, ArH), 6.86 (m, 2H, ArH), 4.05 (m, 8H, OCH_2), 1.62 (s, 6H,

CH_3), 1.28(t, 12H, $^2J_{HH}$ = 7 Hz); $^{13}C\{^1H\}$-NMR δ: 160.10 (d, $^2J_{CP}$ = 7.4 Hz), 141.35 (d, $^3J_{CP}$ = 12.8 Hz), 134.04, 128.71 (d, $^2J_{CP}$ = 2.7 Hz), 117.30 (d, $^3J_{CP}$ = 8.3 Hz), 107.95 (d, $^1J_{CP}$ = 178.7 Hz), 62.54 (d, $^2J_{CP}$ = 4.4 Hz), 41.61, 30.64, 16.08 (d, $^3J_{CP}$ = 6.4 Hz); $^{31}P\{^1H\}$-NMR δ: 21.97; FAB-MS: m/z 501 $[M + H]^+$ base peak.

17,17,40,40-Tetramethyl-1,10,24,33-teraoxa[2](2,6)pyridino[2.1] paracyclo[2](2,6)-pyridino[2.1]paracyclophane-12,20,35,43-tetraphosphonic acid diethylester (II)

A solution of **Ia** (1.0 g, 2 mmol) and 2,6-bis (bromomethyl)-pyridine (0.53 g, 2 mmol) in CH_3 CN (100 mL in total) were added dropwise, at equal rates over a period of 4 h from two different dropping funnels, to a stirred suspension of anhydrous K_2CO_3 (1.38 g, 10 mmol) in anhydrous CH_3CN (250 mL) at refluxing temperature. After the addition was completed, the reaction mixture was refluxed overnight with stirring, filtered, and the solvent was evaporated to give a yellowish powder, which was collected by filtration and washed several times with water. The product was purified by slow crystallization from hexane-ethylacetate to give 0.36 g of **II** (30%) as white prisms, m.p. 218–220°C. ^{1}H-NMR ($CDCl_3$) δ: 7.85 (dd, 4H, $^3J_{HP}$ = 16 Hz, $^4J_{HH}$ = 2.3, ArH), 7.73 (m, 2H, PyH), 7.66 (m, 4H, PyH), 6.88 (dd, 4H, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 2.3 Hz, ArH), 5.27 (s, 8H, $PyCH_2$), 4.2 (m, 16H, OCH_2), 1.64 (s, 12H, CH_3), 1.42 (s, 12H, cyclohexane), 1.34 (t, 24H, $^3J_{HH}$ = 7 Hz); $^{13}C\{^1H\}$-NMR δ: 157.89 (d, $^2J_{CP}$ = 2.3 Hz), 156.31, 142.48 (d, $^3J_{CP}$ = 13.6 Hz), 137.95, 133.65 (d, $^4J_{CP}$ = 1.8 Hz), 132.04 (d, $^2J_{CP}$ = 7.9 Hz), 120.62, 115.82 (d, $^1J_{CP}$ = 187.3 Hz), 112.26 (d, $^3J_{CP}$ = 9.7 Hz), 70.68, 62.14 (d, $^2J_{CP}$ = 5.7 Hz), 41.92, 30.75, 26.91 (cyclohexane) 16.41 (d, $^3J_{CP}$ = 6.4 Hz); $^{31}P\{^1H\}$-NMR δ:16.36; FAB-MS: m/z 1208.3 $[M + H]^+$ base peak; elemental analysis: found C 59.47%, H 6.76%, N 2.09%, calculated for $C_{60}H_{78}N_2O_{16}P_{14}$: C 59.70%, H 6.51%, N 2.32%.

4, 6, 8, 17, 17, 27, 29, 31, 40, 40-Decamethyl-1, 10, 24, 33-teraoxa[2] (2, 6) benzeno[2.1] paracyclo[2] (2, 6)-benzeno[2.1] paracyclophane-12, 20, 35, 43-tetrophosphonic acid diethylester (III)

Compound **III** was prepared following the same procedure described for compound **II**, using 2, 4-bis-(chloromethyl)-1, 3, 5-trimethylbenzene as spacer. The product was purified by column chromatography (SiO_2; $CHCl_3$:CH_3OH 9:1) followed by recrystallization from cyclohexane/ethylacetate mixture to give (25%) as white prisms, m.p. 252–254°C. ^{1}H-NMR ($CDCl_3$) δ: 7.72 (d, 4H, $^3J_{HP}$ = 15.5 Hz, ArH), 7.16 (d, 4H, $^3J_{HH}$ = 8.50 Hz), 6.92 (s, 2H, ArH), 6.87 (t, 4H, $^3J_{HH}$ = 8.50 Hz, $^4J_{HP}$ = 7.50 Hz, ArH), 5.17 (s, 8H, $ArCH_2$), 3.90 (m, 16H, OCH_2), 2.44 (s, 12H, Ar-CH_3), 2.19 (s, 6H, Ar-CH_3), 1.67 (s, 12H, CH_3), 1.11 (t, 24H, $^2J_{HH}$ = 7 Hz); $^{13}C\{^1H\}$-NMR δ:158.78, 142.64 (d, $^3J_{CP}$ = 14.38 Hz), 138.73, 138.31, 132.65, 132.36 (d, $^2J_{CP}$ = 8.38 Hz), 131.19, 130.09, 117.18 (d, $^1J_{CP}$ = 187.4 Hz), 113.62 (d, $^3J_{CP}$ = 10.63 Hz), 66.37, 61.90 (d, $^2J_{CP}$ = 5.4 Hz), 41.59, 30.07, 19.86, 16.20 (d, $^3J_{CP}$ = 6.2 Hz), 15.81; $^{31}P\{^1H\}$-NMR δ:17.65; FAB-MS: m/z 1290.5 $[M + H]^+$ base peak.

17,17,40,40-Tetramethyl-1,10,24,33-teraoxa[2](1, 4)benzeno[2.1] paracyclo[2](1, 4)-benzeno[2.1]paracyclophane-12,20,35,43-tetraphosphonic acid diethylester (IV)

Compound **IV** was prepared following the same procedure described for compound **II**, the only difference being the different starting bis(bromomethyl) derivative. The product was purified by column chromatography (SiO_2; $CHCl_3$: CH_3 OH 9:1) followed by recrystallization from chloroform hexane yielded pure **IV** (35%), as white needles, m.p. 238–240°C; ^{1}H-NMR ($CDCl_3$) δ: 7.72 (dd, 4H, $^3J_{HP}$ = 15.7 HZ, $^4J_{HH}$ = 2.0, ArH), 7.36 (s, 8H, ArH), 6.95 (dd, 4H, $^2J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 1.5, ArH), 6.60 (m, 4H, ArH), 5.18 (s, 8H, $ArCH_2$), 4.11 (m, 16H, OCH_2), 1.63 (s, 12H, CH_3), 1.25 (t, 24H, $^2J_{HH}$ = 7 Hz); $^{13}C\{^1H\}$-NMR δ:157.93 (d, $^2J_{CP}$ = 2.3 Hz); 142.55 (d, $^3J_{CP}$ = 13.6 Hz), 136.28,

133.31, (d, $^4J_{CP}$ = 1.8 Hz), 131.71 (d, $^2J_{CP}$ = 8.07 Hz), 126.57, 115.88 (d, $^1J_{CP}$ = 187.5 Hz), 112.73 (d, $^3J_{CP}$ = 10.1 Hz), 69.72, 62.07 (d, $^2J_{CP}$ = 5.8 Hz), 41.61, 30.18, 16.33 (d, $^3J_{CP}$ = 6.5 Hz); $^{31}P\{^1H\}$-NMR δ:16.28; FAB-MS: m/z 1206.7 $[M+H]^+$ base peak.

Crystal Structure Determination of II • Cyclohexane. Crystal Data. A suitable single crystal of II (crystallized from ethylacetate/cyclohexane) was mounted on a glass fiber, placed in a goniometer head on the Enraf-Nonius CAD4 diffractometer and centered optically. Unit cell parameters and an orientation matrix for data collection were obtained by using the centering programs in the CAD4 system. Details of the crystal data are given Table I. For each crystal, the actual scan range was calculated by scan width = scan range + 0.35 tanθ. A total of 7117 reflections were measured using the ω-2θ mode and averaged to give 3199 unique reflections (Rmerge = 0.028) used in the final refinements. Two representative reflections were monitored every 2 hrs as a check on instrument stability and an additional two reflections were monitored periodically for crystal orientation control. Lorentz, polarization, and decay corrections were applied to the data and the weighting scheme used during refinement was $1/\sigma^2$, based on counting statistics.

The structure was solved by the Direct methods using SHELXS-86 [10], which revealed the positions of most of the atoms. Any other non-hydrogen atoms were found by successive difference Fourier syntheses. Hydrogen atoms were placed at their expected chemical positions using the HFIX comand in SHELXL-93 [11] and were included in the final cycles of least squares with isotropic U_{ij}'s related to the atom's ridden upon. All other non-hydrogen atoms were refined anisotropically.

Scattering factors and anomalous dispersion corrections were taken from the International Tables for X-ray Crystallography [12]. All data processing was carried out on a DEC 3000 AXP computer using the Open MolEN system of programs [13]. Structure solution, refinement and preparation of figures and table for publication were carried out on PC's using SHELXS-86 [10], SHELXL-93 [11] and XP/PC [14].

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