MACROCYCLIC DIPHOSPHA-CROWN ETHERS: SYNTHESIS AND ALKALI METAL PICRATE EXTRACTION STUDIES

A. Hannioui[1]*, A. El Malki[1], E.M. Rakib[1], N. Knouzi[2], M. Berrada[2], M.B. El Malouli[3]

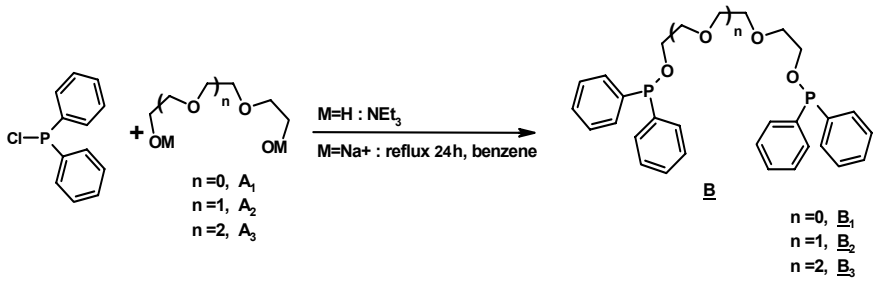
[1]Université Cadi Ayyad, FST Béni-Mellal, B.P.523 Béni-Mellal, Maroc.
[2]Université Hassan II, Faculté Des Sciences Sidi Othmane, BP6023, Casablanca, Maroc.
[3]Université Hassan II Faculté Des Sciences Ain Chock, Maârif, B.P.5366, Casablanca, Maroc.
**E-mail : hannioui@caramail.com*

Abstract : A series of cyclic phospha-crown ethers was synthesised through a cyclisation reaction. These compounds were shown to extract alkali metals, ammonium, strontium and calcium ions from the aqueous phase to the organic one. The selectivity in partitioning varied with the relative fit of the ionic radius of the metal ion with the whole size of the macrocycle. For a typical phospa-crown-metal ion combination, the formation of a 1:1 complex was suggested by UV spectroscopy investigation.
Keywords : extraction; transport; ionophores; alkali picrates; phospha-crown ethers, bathochromic.

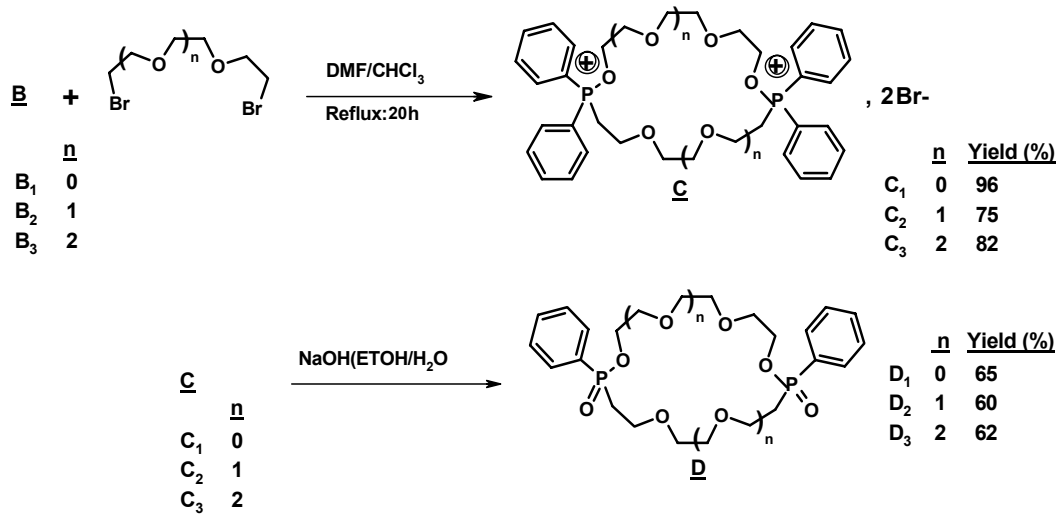
1. INTRODUCTION

Phosphorus containing macrocycles have attracted considerable attention during the last decade [1].There is considerable interest in the complexation of macrocyclic polyethers

or crown ethers to alkali metals and other cations [2]. They have drawn attention in both chemistry and Biology. It is worth noting here that the main characteristic is their selective complexation towards various metal cations [3, 4]. For this purpose, several structural ligands have been synthesized to enhance the ligating properties and to achieve better selectivity [5]. In the light of this, the chemistry of macrocyclic polyphosphines should be of potential interest because of the known versatility of phosphines as ligands for transition metals [6, 7]. Therefore, it is at first glance surprising that only few macrocyclic phospha-containing crown ethers have been prepared to date [8]. Many comments have shown that the failure comes from the difficulty of the chemistry involved [9, 10]. Thus, very little is known about their ionophoric properties and fundamental questions remain to be probed, namely how the ring size, the combinations of donor atoms, the crown distribution as well as the relative stereochemistry within the macrocycles, can modify these properties [11].
We report here the synthesis of macrocycles outlined in schemes 1 and 2 as well as a kinetic investigation leading to the open chain phosphorus compounds Bi (**Scheme 1**), which is allowed of a further cyclisation to give the corresponding diphospha-crown ether Di (**Scheme 2**).



Scheme 1



Scheme 2

We also wish to report results of a further extension including a finding of some more powerful phospha-crown ligands. This will be discussed on the basis of their ionophoric properties.

2. RESULTS AND DISCUSSION

2.1. Synthesis of Macrocycles

The preparation of this macrocycle was made in two stages:
Initially, we synthesized the diphosphapolyéther opened **Bi**. This last is obtained by addition of the sodium dialcoholate of the glycol (prepared beforehand), on the chlorodiphénylphosphine. Its purification was achieved by liquid chromatography on silica gel followed by several extractions to ether. Its structure was confirmed by the traditional analysis (NMR ^{1}H, ^{13}C, I.R...).
The condensation of the open diphospha **Bi** with dibromoTriethylenglycol in a mixture of diméthylformamide: chloroform, led to the macrocycle awaited Di after hydrolysis of the intermediate diphosphonium **C**i in good yields (60-65%). It is the application of the method previously described by Cristau [12].
In a patent, Cristau developed a method of macrocyclic phosphine oxide synthesis, its principle consists in successively introducing the various bridges between the two phosphorus atoms, in order to control the formation of the macrocycle as well in its face in the nature of heteroatoms. This principle corresponds to a recurring method, utilizing several successive substitutions, which breaks up each one into two stages of addition and elimination.
Identities of diphospha-macrocyclic ligands were confirmed by IR, ^{1}H and ^{31}P NMR spectroscopy and by combustion analyses.

2.2. Complexation studies in organic solvent

The ability of these phospha-crown ethers to bind metals was examined by putting into contact a chloroform solution of each macrocycle with metal picrate aqueous solutions; This is the so called: liquid-liquid extraction procedure.
Metal picrates, nearly insoluble in chloroform except for lithium one, are extracted with complex formation, and the decrease in absorbance of the picrate in aqueous phase was taken to be a measure of macrocycles efficiencies as complexing agents for a specific cation [13]. The results are listed in table 1.
In terms of extraction results, a clear tendency to be mentioned is the close relation between the whole size of macrocycles and the ionic diameter of metal cations to be portioned most favorably except for $\mathbf{D_2}$ and $\mathbf{D_3}$. The smallest macrocycle $\mathbf{D_1}$, (fourteen member ring), is structurally much closer to Dibenzo-18-crown-6, which served as a reference. Macrocycle $\mathbf{D_1}$ discriminates between cesium and the rest of alkali metals. Cesium is the lesser extracted. However, it is worth emphasizing that there is a near complete discrimination between sodium and potassium ions in the cases of $\mathbf{D_2}$ and $\mathbf{D_3}$ ″twenty and twenty six member rings respectively″. These cations are extracted with high efficiency compared to dibenzo-18 crown-6.
In the case of $\mathbf{D_2}$, there is a real preference for sodium. However, the result is reversed for potassium in the case of $\mathbf{D_3}$. This is a clear evidence for the whole size of macrocycles and the ionic diameter of metal cations. The evidence comes from compounds $\mathbf{D_2}$ and $\mathbf{D_3}$, both of them contains two phenyl substitutes, their extracting efficiency is therefore higher than that of **DBCE**. This effect is not fully understood, but

might be attributable to steric inhibition by the substitute of the host cycle assuming a favorable geometry to coordination.

Table 1: Extraction of metal picrates from aqueous to organic phase (%) a,b.

Cation	Ionic radius (Å)	% Macrocycle[a]					
		DBCE[c]	B_1	B_2	D_1	D_2	D_3
Li^+	0.60	0	6.6	4.2	4.0	3.6	5.3
Na^+	0.95	1.9	8.5	9.1	41.5	31.5	42.2
K^+	1.33	25.9	7.6	8.5	37.2	38.4	28.0
Rb^+	1.49	9.6	9.6	15.4	6.2	4.3	16.5
Cs^+	1.69	0.0	4.2	4.0	3.1	3.0	2.2
Sr^{2+}	1.20	0.0	10.5	13.3	9.2	11.3	11.4
Ca^{2+}	1.04	0.7	0.5	4.5	6.3	9.2	0.5
NH_4^+	1.48	3.5	3.2	3.4	20.1	22.4	25.6

a) [phosphacrown] = $7.0.10^{-4}$ M in chloroform. [metal picrate]= $7.0.10^{-5}$M; [Metal nitrate]= 0.1 M
b) blank experiments exhibited no observable extraction for all metal picrates. c) DBCE: dibenzo-18-crown-6.

These relationships for alkali metal cations also hold for ammonium ion, which is found most favorably by **D_2** and **D_3** as expected for its ionic diameter.
It is also worth noting that, in general, our extraction data concerning alkaline earth cations are almost of the same magnitude.

2.3. Complexation studies by U.V. spectrophotometry

2.3.1. Spectra of picrate salts and their crown complexes: Results and discussion

It is well known that the maximum of the main optical absorption band of alkalipicrates in THF, chloroform, or other low polarity media, exhibit bathochromic shifts with increasing cation radius [14, 15]. The cause of this shift has been explained [15, 16] as a perturbation of the molecular energy levels by the positive field of the cation. In a simplest manner, in the ground state the cation is located so as to form the smallest dipole. On excitation, the dipole increases, i.e., the negative charge moves away from its original position in the ground state while the position of the cation is not affected (Frank-Condon Principle). Hence, an increase in cation radius destabilizes the ground state more than the excited state, leading to the observed bathochromic shift. Hoijtnik, and al. [16], have pointed out that the perturbation of energy levels should be roughly proportional to the reciprocal of the appropriate interionic separation. In our case, the maxima for picrate salts in the THF are found to be as follows:

Table 2: Maxima for picrates salts in THF.

Picrate salt	λm (nm)	ε
Pic Na	351	16500
Pic K	355	16800
Pic Cs	362	17700

Our aim was to control the shape modification of a specific cation picrate absorption upon addition of a complexing ligand. This has been done in the case of the phospha-crown D_2, which is a higher complexing agent for potassium. The results are shown in figure 1.

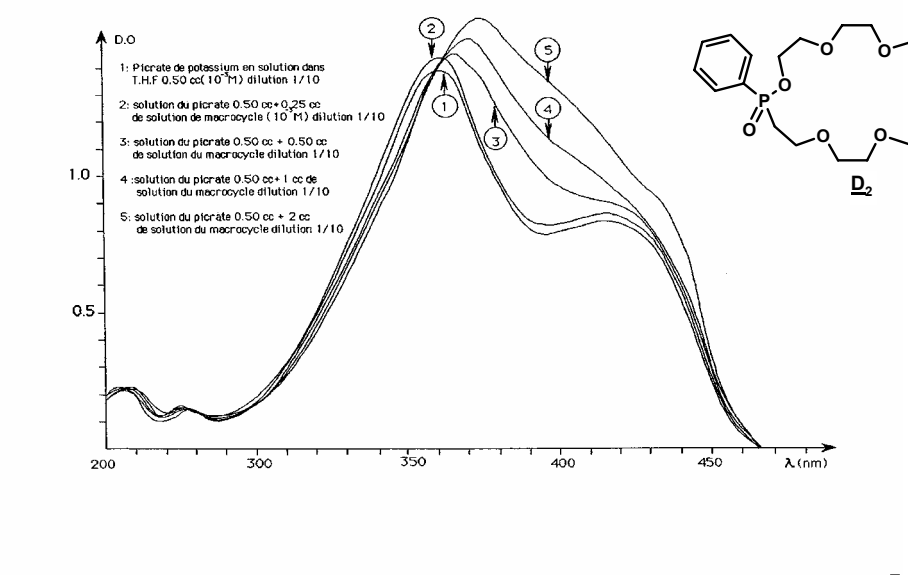


Figure 1: Optical spectra of a 10^{-3} M THF solution of potassium picrate in the presence of varying amounts of the 2.13-dimethyl,2.13-dioxo1,3,6,9,12,14,17,20-octaoxacyclo-docosa diphospholane D_2 at 25°. Molar ratio of phospha-crown to picrate salt : (1) 0; (2) 0.50; (3) 1.00; (4) 2.00; (5) 4.00.

Addition of the open diphospha ethers $\mathbf{B_1}$ and $\mathbf{B_2}$ respectively to a 10^{-3} M THF solution of Pic^-K^+ doesn't change anything of the potassium picrate UV spectrum, hence, excluding any extracting property of such compounds. However, addition of increasing amounts of the phospha-crown compound $\mathbf{D_2}$ to a 10^{-3} M THF solution of Pic^-K^+ leads to the formation of a 1:1 crown coordinated tight ion pair $Pic^-\mathbf{D_2}\ K^+$. The UV spectrum tends to move progressively to higher wavelengths, and the conversion is complete on addition of equal amount of the macrocycle. The spectrum shifts from 355 to 370 nm. From that ratio of concentrations, results the formation of a 1:1 crown separated ion pair complex $Pic^-\mathbf{D_2}K^+$. On the other hand, the observation of a single isosbestic point at 360 nm, meant that the absorption is concerned with a single species. The absorptivities for the separated Pic^-K^+ ion pairs are considerably higher than those of the tight ion pairs.This is partly because of a transition of lower intensity at 415 nm, found in the picrate spectrum in low polarity media (figure 1) apparently, is slightly affected by a change in interionic distance. It, consequently, overlaps more with the main transition of the loose ion pair than with that of the tight ion pair.

3. EXPERIMENTAL SECTION

All manipulations involving air-sensitive species were carried out in Schlenk apparatus dry nitrogen. Ultraviolet spectra were recorded on a KONTRON UVIKON 810 with VARIAN EM-360 Spectrometer. Cmr and Pmr spectra were measured on $CDCl_3$ solution with BRUKER AC 100. Chemical shifts are given in parts per million relative to tetramethylsilane as an internal standard for ^{1}H nmr and ^{13}C nmr and with 85% H_3PO_4 as external standard for ^{31}P nmr Infrared spectra were recorded as a film deposited from CH_2Cl_2 solutions onto NaCl plates. All mass spectra were obtained as FAB^+ in nitrobenzylalcohol. Column chromatography was performed using Merck Kiesegel 60 (230-400 mesh, ASTM).

3.1. Synthesis of methyl-phosphonic acid bis-{2-[2-(2-hydroxy-ethoxy)-ethoxy]-ethyl}ester: B_2

A. Preparation of B_2 from chlorodiphenylphosphine in the presence of triethylamine is representative.
Into a mixture of triethylenglycol (3.40 ml, 25.7 mmol) and triethylamine (7.20 ml, 25.7 mmol) in 60 ml of dry benzene was added drop wise a solution of chlorodipheylphosphine (Aldrich) (9.60 ml, 51.4 mmol) in 40 ml of dry benzene with stirring under cooling in an ice-water bath (5°C). Then the reaction mixture was refluxed on a water bath for 24h, and triethylamine hydrochloride was filtered of. After that benzene was removed from the filtrate. Purification by liquid chromatography over silica gel (eluent: Methanol/Acetone; 4/6, R_f = 0.47) followed by several extractions with ether afforded pure B_2 as a liquid in 86% yield. NMR: ^{1}H δ(ppm) 4.20(m, 4H), 3.68(m, 8H), 7.50(m, 3H), 7.80(m, 2H); ^{13}C δ 61.22,70.36, 71.82, 129.10, 131.36, 134.22; ^{31}P δ 18.9(s, P-Ph). IR : 2885, 1444, 1264, 1110, 1055 cm^{-1}.

3.2. Synthesis of 2,11-diphényl 2,11-dioxo 1,5,8,12,15,18-hexaoxacyclocosa-diphospholane:D_2

B. Preparation of D_2 from B_2 in the presence of triethylamine is representative.
To 1,2 bis (2-bromoethoxy)ethane (1.77g, 5.77 mmol) in 40 ml of a mixture of (diméthylformamide/ chloroform : 3/1), was added at 0°C (3 g, 5.77 mmol) of B_2. Then the reaction mixture was refluxed on a water bath for 20 h and the solvent removed in vacuum to give the product C_2 which was treated immediately with sodium hydroxide (0.46g, 1.15 mmol) in a mixture of (ethanol / water: 5/5). The yellow solution was stirred for 2 h, extracted with benzene. Column chromatography over silica gel (40% acetone-ethylacetate; R_f= 0.48) yielded the macrocycle D_2 in 42% yield.
NMR: ^{1}Hδ(ppm) 4.20(m, 4H), 3.57(m, 16H), 7.58(m, 2H), 7.78(m, 1H), 7.80(m, 2H); ^{13}C δ 61.20,70.42, 71.80[b], 129.15, 130.69, 131.16, 134.10; ^{31}P δ 19.2(s, PPh). IR : 2856, 1442, 1264, 1115, 1055 cm^{-1}. MS 393 $(M+H)^+$. Analytical calculated for $C_{24}H_{34}O_8P_2$: C, 73.00; H, 7.19; P, 14.73. Found C, 40.08; H, 7.18; P, 14.72.
[b] the remaining of carbon-resonances are centred around this value.

3.3. Compound B_1

NMR : ^{1}H δ(ppm) 4.25(m, 2H), 3.56(m, 10H), 3.18(broad s,1H), 7.56(m, 2H, C-H-arom.), 7.88(m, 3H, C-H-arom); ^{13}C δ , 61.23,70,35, 71.91, 129.15, 130.60, 131.21, 134.21;^{31}P δ 18.9. IR : 3390, 2880,1440, 1240, 1112, 1040 cm^{-1}

3.4. Macrocycle D_1

NMR : ^{1}H δ(ppm) 4.15(m, 4H), 3.56(m, 8H), 7.56(m, 2H, C-H-arom.), 7.75(m, 3H, C-H-arom); ^{13}C δ 61.22 70.31, 71.81, 129.14, 130.60, 131.16, 134.08;^{31}P δ 19.2. IR : 2860, 1540, 1440, 1240, 1100, 1060 cm^{-1} MS 545 $(M+H)^{+}$ (G : glycerol). Analytical calculated for $C_{24}H_{34}O_{10}P_2$: C, 52.94; H, 6.29; P, 11.37. Found C, 52.90; H, 6.30; P, 11.30.

3.5. Compound B_3

NMR : ^{1}H δ(ppm) 4.25(m, 2H), 3.56(m, 14H), 3.17(broad S,1H), 7.65(m, 2H, C-H-arom.), 7.88(m, 3H, C-H-arom); ^{13}C δ , 61.23,70,35, 71.91, 129.15, 130.60, 131.21, 134.21;^{31}P δ 18.9. IR : 3390, 2875,1540, 1440 1240, 1120, 1040 cm^{-1}

3.6. Macrocycle D_3

NMR : ^{1}H δ(ppm) 4.22(m, 4H), 3.56(m, 12H), 7.56(m, 2H, C-H-arom.), 7.75(m, 3H, C-H-arom); ^{13}C δ , 61.22 70,32, 71.83, 129.14, 131.16, 134.08;^{31}P δ 19.2. IR : 2860, 1540, 1440, 1240, 1100, 1060 cm^{-1} MS 633 (M+H). Analytical calculated for $C_{28}H_{42}O_{12}P_2$: C, 53.16; H, 6.69; P, 9.79. Found C, 52.98; H, 6.60; P, 9.78.

4. ION TRANSPORT EXPERIMENTS

For all the transport experiments involving alkali metal, ammonium, strontium and calcium picrates, a cell similar to the one described by FURUKAWA and al. [15] was used, which consisted of a glass cylinder (i.d. 4.9 cm, height 8.5 cm) in which was held by three radial glass rod supports an inner glass tube (i.d. 2.3 cm) such that the bottom of the latter was 1.1 cm above the bottom of the outer vessel. A portion (50 ml of a 7.10^{-4} M) solution of the phospha-crown ether in chloroform was placed in the bottom of the cell, and this organic layer isolated the inner compartment was placed an aqueous solution (10 ml) which was 2.10^{-3} $M.l^{-1}$ in alkali metal picrate, 10^{-1} $M.l^{-1}$ in the corresponding alkali metal hydroxide. In the outer annular compartment was placed pure water (12.5 ml). The organic layer was stirred magnetically at a steady rate (60 rot/min) and at known times, a sample was withdrawn from the outer compartment and the concentration of the alkali metal picrate therein was determined by UV spectroscopy using the following constants for lithium, sodium, potassium and cesium: ε_{max} : 16500 at λ_{max} : 355 nm. After each determination the aqueous aliquot was returned to the outer layer. Results are listed in table 1.

In the outer glass cell were placed 5 ml of each of methylene chloride (7.10^{-4} $M.l^{-1}$) and aqueous solution for the uptake of metal picrates, the aqueous solution contained 10^{-2} $M.l^{-1}$ metal picrates and 10^{-1} $M.l^{-1}$ metal nitrate.

REFERENCES

1. For a review on this subject, see:
   a) C.J. Pedersen, H.K. Frensdorff, *Angew. Chem., Int. Engl*., **11** (**1972**) 16.
   b) J.J. Cristensen, J.O. Hill, R.M. Izatt, *Science*, **174** (**1971**) 459.
   c) A.P. Marchand, H-S.Chong, M. Takhi, T.D. Power, *Tetrahedron* **56** (**2000**) 3121.
2. M. Newcomb, D. J. Cram, *J. Am. Chem. Soc*., **97** (**1975**) 1259.
3. D. Graf , J. M. Lehn, *J. Am. Chem. Soc*., **97** (**1975**) 5022.
4. a) D. J. Cram, J. M. Cram, *Science*, **183** (**1974**) 803.
   b) Y. Nakatsuji, H. Kobyashi, M. Okahara, *J. Org. Chem*., **51** (**1986**) 3789.
   c) S. Elshani, E. Kobzar, R. A. Bartsch, *Tetrahedon*, **56** (**2000**) 3291.
5. R.B. King, *Account. Chem. Res*., **5** (**1972**) 177.
6. a) D.J. Brauer, T. Lebbe, O. Stelzer, *Angew. Chem. Int. Ed. Engl*., **27** (**1988**) 438.
   b) J.R. Dilworth, Y. Zheng, J.R. Miller, *J. Chem. Soc.Dalton Trans*., 17557 (**1992**).
   c) T. Lebbe, P. Machnitzi, O. Stelzer, W.S. Sheldrick, *Tetrahedron*, **56** (**2000**) 157.
7. C.B. Allan, L.O. Spreer, *J. Org. Chem.,* **59** (**1994**) 7695.
8. E. Archelas, G. Buono, B. Weagell, *Polyhedron*, **1** (**1982**) 683.
9. D. Houalla, Z. Bounja, S. Skouta, *Tetrahedron Lett*., **33** (**1992**) 2817.
10. a) C.J. Pedersen, *Fed. Am. Soc. Exp. Biol*., **27** (**1968**) 1305.
    b) H.K. Frensdorff, *J. Am. Chem. Soc*., **93** (**1971**) 4684.
    c) C.D. Gutsche, *Calixarenes Revisted*, Monographs Supramolecular Chemistry, J. F. Stoddart, Ed., The Royal Society Of Chemistry : Cambridge (**1998**).
11. K.H. Wong, M. Bourgoin, J. Smid, *J. Chem. Soc., Chem. Commun.,* **715** (**1974**).
12. M.A. Coplan, R.M. Fuoss, *J. Phys. Chem*., **68** (**1964**) 1177.
13. a) K.H.J. Buschow, G.J. Hoijtnik, *J. Chem. Phys*., **40** (**1964**) 2501.
    b) N.H. Velthorst, G.J. Hoijtnik, *J. Am. Chem. Soc*., **87** (**1965**) 4529.
14. T. Mukaiyama, T. Fujisawa, Y.Tamura, Y.Yokota, *Bull. Chem. Soc. Japan*, **37** (**1964**) 2572.
15. Y. Kokube, K. Hahji, K. Horiguchi, M. Asada, Y. Nakayama, J. Furukawa, *J. Am. Chem. Soc.*, **98** (**1976**) 7414.