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Preparation and Structure of [*iiii*] Tetraphosphonatocavitands Bearing Long Chain Functionality at the Lower Rim: Metal Picrates Extraction Studies

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The stereoselective synthesis of the *iiii* stereoisomer of novel tetraphosphonato-cavitands derived from resorc [4]arene is reported. *o*-Nitrophenyl-*n*-octyl ether and *n*-undecyl-*n*-decanyl thioether functionalities were introduced in the lower rim of 1 and 2, respectively, to develop new molecular devices. The crystal structure of the solvated cavitand 1·6CH_3CN was elucidated by X-ray crystallography. $C_{104}H_{104}O_{24}N_4P_4$·6$CH_3CN$ crystallizes in the monoclinic space group $P2_1/c$, $a = 20.574(4)$, $b = 16.591(4)$, $c = 33.973(7)$ Å, $\beta = 92.09(2)°$, $V = 11589(4)$ Å^3, $Z = 4$, $R = 0.065$. The host molecule has the *iiii* configuration with the four P═O bonds oriented towards the molecular cavity. The affinity of molecules 1 and 2 for metal cations was investigated by the liquid–liquid extraction method: among the investigated metal picrates, Ag^+, Ba^{2+} and Eu^{3+} were the best-extracted cations.

Keywords: Cavitand; Phosphonatocavitand; Crystal structure; Metal picrates extraction

INTRODUCTION

The propensity of phosphoryl (P═O) group to bind cationic species is well known and the molecular design of preorganized structures containing this powerful binding group has been the subject of many recent investigations [1–7]. Phosphorylated cavitands derived from resorc[4]arene are attractive compounds for this purpose [8–11]. In the tetra-bridged phosphocavitands containing four donor P(O)R groups, the P═O bonds can adopt the inward (*i*) or outward (*o*) orientations relative to the molecular cavity, defining six possible stereoisomers [12–18]. For high recognition of cationic species, only the *iiii* isomer with the four P═O groups oriented inwards, can benefit from both cooperativity of P═O binding and π-interactions with the aromatic cavity of the resorc[4]arene framework [19,20]. A series of tetrabridged-phosphorylated cavitands with phosphate bridging units has been prepared as several stereoisomers. The *iiio*, *iioo*, *ioio*, *oooi* and *oooo* isomers were obtained, but the *iiii* isomer was not formed or only in trace amounts [15–17]. Recently, the binding properties of these phosphatocavitands have been investigated in the gas phase by mass spectrometry. The formation of amine guests inclusion complex was strongly dependent on the stereochemistry of the cavitands: the more P═O bonds are oriented toward the inside of the cavity, the stronger is the binding of cationic species [21].

In previous work, we have described the stereoselective synthesis of the *iiii* stereoisomer of cavitands **4** and **5**, which proved to be powerful ligands for alkali metal and primary ammonium cations [19,20]. We report herein the preparation of novel tetraphosphonatocavitands having lower rim functionality. The R groups (Scheme 1) were chosen to increase the lipophilicity of the molecules and for their application in new molecular devices.

Cavitand **1** was designed with four *o*-nitrophenyl-*n*-octyl ether groups to favor its use in supported

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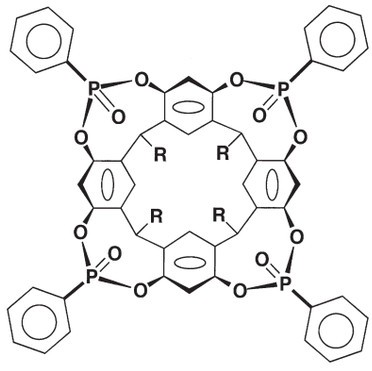


1 : R = -$(CH_2)_7$-O-C_6H_4-*o*NO_2
2 : R = -$(CH_2)_{10}$-S-$(CH_2)_9$-CH_3
3 : R = -$(CH_2)_8$-CH=CH_2
4 : R = -CH_3
5 : R = -$CH_2CH_2C_6H_5$

SCHEME 1

liquid membranes (SLM) for selective transport of cationic guests [22]. The thioether group was introduced in **2** to form stable self-organized monolayers of cavitands (SAM) on a gold surface, which could be used in detector devices for cationic species [23,24]. The complexing properties of new *iiii* tetraphosphonatocavitands **1** and **2** towards metal ions were characterized by extraction experiments from water to chloroform. Additionally, we report the molecular structure of the tetraphosphonatocavitand **1** obtained by single crystal X-ray analysis.

EXPERIMENTAL

^1H, ^{13}C and ^{31}P NMR spectra were recorded on Varian Unity$^{\oplus}$500 and Bruker DPX200 spectrometers. Chemical shifts are in δ values from Me_4Si (^1H and ^{13}C) or H_3PO_4 85% (^{31}P). ^{13}C and ^{31}P NMR spectra are proton decoupled. The aromatic protons were labeled as follows: calix-ArH, P-ArH, respectively, for the protons attached to the resorc [4]arene and the P-phenyl groups. A similar labeling was used for the carbon nuclei. The reported multiplicities of ^{13}C NMR signals represent ^{31}P–^{13}C couplings. Infrared spectra were recorded in KBr with a Perkin–Elmer FTIR 1600 spectrometer, and UV–Visible spectra were measured with a Varian Cary 219 spectrometer. Solvents were purified using standard procedures. *N*-Methylpyrrolidine and dichlorophenylphosphine oxide were distilled prior to use. Silica gel used for column chromatography was Merck Kieselgel 60 (0.040–0.063 mm). Elemental analyses and electrospray mass spectra were undertaken by the Service Central d'Analyses, CNRS. Melting points were measured with a DSC7 Perkin–Elmer calorimeter. Picrate salts were already available or prepared according to well-known procedures [36]. Resorc[4]arene **7** [31], 8-(hydroxyoctyl)-2-nitrophenyl ether **8** [25] and IBX [27] were synthesized according to literature procedures.

8-Octanal-2-nitrophenyl Ether (9)

A solution of 8-(hydroxyoctyl)-2-nitrophenyl ether **8** (6.84 g, 25.6 mmol) in DMSO (20 ml) was added dropwise to a DMSO solution (80 ml) of IBX (7.89 g, 28.2 mmol) at room temperature. The mixture was stirred under argon for 16 h and the white precipitate was filtered off. The organic solution was then poured into water (180 ml) and dichloromethane (180 ml) and stirred for 20 min. After decantation, the organic layer was washed with water (2 × 200 ml) and dried (Na_2SO_4). The solvent was removed *in vacuo* and 8-octanal-2-nitrophenyl ether **9** (5.96 g, 22.5 mmol, 88%) was isolated as a yellowish oil, which was used without further purification: IR (KBr): 2936, 2858 (C–H), 1681 (C=O), 1608, 1526, 1467 (C=C), 1582, 1353 (NO_2), 1256, 1165 (C–O–C), 746 cm^{-1}; ^1H-NMR (499.83 MHz, $CDCl_3$): δ 1.34 (m, 4H, CH_2), 1.43–1.48 (m, 2H, CH_2), 1.61 (q, 2H, CH_2, $J = 7.0$ Hz), 1.79 (q, 2H, CH_2, $J = 7.0$ Hz), 2.40 (t, 2H, CH_2–CHO, $J = 7.5$ Hz), 4.06 (t, 2H, ArO–CH_2, $J = 6.5$ Hz), 6.97 (t, 2H, ArH, $J = 8.0$ Hz), 7.03 (d, 2H, ArH, $J = 8.0$ Hz), 7.47 (t, 2H, ArH, $J = 8.0$ Hz), 7.78 (d, 2H, ArH, $J = 8.0$ Hz), 9.73 (t, 1H, CHO, $J = 1.8$ Hz); ^{13}C-NMR (50.32 MHz, $CDCl_3$): δ 21.83, 25.56, 28.73, 28.84, 43.72 (*C*H_2), 69.39 (*C*H_2–OAr), 114.33 (Ar*C*H), 119.95 (Ar*C*H), 125.37 (Ar*C*H), 133.91 (Ar*C*H), 139.88 (Ar*C*–O), 152.31 (Ar*C*–NO_2), 202.73 (*C*HO); Anal. Calcd for $C_{14}H_{19}O_4N$: C, 63.38; H, 7.22; N, 5.28. Found: C, 62.87; H, 7.18; N, 5.25.

2,8,14,20-Tetrakis[7-(2-nitrophenyloxy)heptyl] pentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26) 21,23-dodecaene-4,6,10,12,16,18,22,24-octol (6)

8-Octanal-2-nitrophenyl ether **9** (6.8 g, 25.66 mmol) was slowly added to a solution of resorcinol (2.18 g, 19.62 mmol) in 95% ethanol (100 ml). The mixture was cooled to 0°C and 36% aqueous hydrochloric acid (2.4 ml, 36.4 mmol) was slowly added under stirring. After being heated to reflux and stirred for 24 h, the reaction mixture was cooled to room temperature and poured into water (250 ml). The precipitate was filtered off, washed with water (5 × 150 ml) until neutrality and dried under vacuum.

Recrystallisation of the orange solid from 95% ethanol yielded resorcinarene **6** (4.92 g, 3.43 mmol, 70%): mp 266.4°C; IR(KBr): 3500–3200 (OH), 2930, 1608, 1523, 1501, 1351, 1279, 1254, 1165, 745 cm^{-1}; ^1H-NMR (499.83 MHz, acetone-d_6): δ 1.32–1.47 (m, 32H, CH_2), 1.77 (m, 8H, CH_2); 2.32 (m, 8H, CH_2), 4.13 (t, 8H, OCH_2, $J = 6.0$ Hz), 4.30 (t, 4H, CH, $J = 7.5$ Hz),

6.23 (s, 4H, calix-ArH_{upper}), 7.06 (t, 4H, ArH, $J = 8.0$ Hz), 7.24 (d, 4H, ArH, $J = 8.0$ Hz), 7.56 (t, 4H, ArH, $J = 8.0$ Hz), 7.59 (s, 4H, calix-ArH_{lower}), 7.78 (d, 4H, ArH, $J = 8.0$ Hz), 8.46 (s, 8H, OH); ^{13}C-NMR (50.32 MHz, acetone-d_6): δ 26.52, 28.83, 29.11, 30.00, 30.17, 34.06 (s, *C*H_2), 34.17 (s, *C*H), 70.09 (*C*−OAr), 103.51 (calix-Ar*C*H_{upper}), 115.45 (Ar*C*H), 120.83 (Ar*C*H), 125.11 (calix-Ar*C*−CH), 125.11 (calix-Ar*C*H_{lower}), 125.50 (Ar*C*H), 134.63 (Ar*C*H), 141.11 (Ar*C*−O), 152.51 (Ar*C*−NO_2), 152.62 (calix-Ar*C*−OH); Anal. Calcd for $C_{80}H_{96}N_4O_{20}$: C, 67.02; H, 6.75; N, 3.91. Found: C, 66.72; H, 6.66; N, 4.01.

1,21,23,25-Tetrakis[7-(2-nitrophenyloxy)heptyl]-5,9,13,17-tetraphenyl-2, 20:3,19-dimetheno-1*H*, 21*H*,23*H*,25*H*-bis[1,3,2]dioxaphosphocino [5,4-*i*:5′,4′-*i*′]benzo[1,2-*d*:5,4-*d*′]bis[1,3,2] benzodioxaphosphocin-5,9,13,17-tetraoxide (1)

The azeotropic distillation of a suspension of **6** (1.12 g, 0.78 mmol) in toluene (100 ml) was performed overnight under dry argon to remove traces of water from the starting material. Afterwards *N*-methylpyrrolidine (0.08 g, 0.94 mmol) and dichlorophenylphosphine oxide (0.64 g, 3.28 mmol) were successively added at room temperature. The resultant mixture was heated to reflux and vigorously stirred for 48 h. The reaction mixture was cooled to room temperature and concentrated *in vacuo*. Silica gel column chromatography (THF/dichloromethane 1:9 and then 1:8 as eluent) of the oily residue afforded the *iiii* stereoisomer of **1** as a yellowish powder (0.73 g, 0.38 mmol, 49%): mp 279°C (dec.); IR(KBr): 3480, 2930, 2855, 1608, 1523, 1486, 1352, 1275 (P═O), 1152, 1134, 1076, 909 cm^{-1}; ^{1}H-NMR (499.83 MHz, $CDCl_3$): δ 1.38–1.47 (m, 32H, CH_2), 1.78 (m, 8H, CH_2), 2.40 (m, 8H, CH_2), 4.05 (t, 8H, OCH_2, $J = 6.0$ Hz); 4.78 (t, 4H, CH, $J = 7.5$ Hz), 6.96 (s, 4H, calix-ArH_{upper}), 6.97 (t, 4H, ArH, $J = 7.5$ Hz), 7.02 (d, 4H, ArH, $J = 8.0$ Hz), 7.44–7.51 (m, 16H, ArH, P-ArH, calix-ArH_{lower}), 7.59 (t, 4H, P-ArH, $J = 7.5$ Hz), 7.78 (d, 4H, ArH, $J = 7.5$ Hz), 8.03 (dd, 8H, P-ArH, $J = 7.5$ Hz, $J_{PH} = 14.0$ Hz). ^{13}C-NMR (50.32 MHz, $CDCl_3$): δ 26.22, 28.09, 28.76, 29.27, 29.46, 30.59 (*C*H_2), 36.46 (*C*H), 69.71 (*C*−OAr), 114.44 (Ar*C*H), 117.59 (calix-ArC_{upper}), 120.01 (Ar*C*H), 122.76 (calix-ArC_{lower}), 125.32 (Ar*C*H), 126.18 (d, P-Ar*C*, $J = 204.2$ Hz), 128.49 (d, P-Ar*C*, $J = 16.4$ Hz), 131.67 (d, P-Ar*C*, $J = 10.4$ Hz), 133.25 (P-Ar*C*), 134.11 (Ar*C*H), 134.97 (calix-Ar*C*−CH) 139.89 (Ar*C*−OCH_2), 146.24 (d, calix-Ar*C*−O, $J = 12.0$ Hz), 152.40 (Ar*C*−NO_2); ^{31}P-NMR (81.02 MHz, $CDCl_3$): δ 7.97; Anal. Calcd for $C_{104}H_{104}N_4O_{24}P_4{\cdot}H_2O$: C, 64.53; H, 5.41; N, 2.89; P, 6.40. Found: C, 64.75; H, 5.70; N, 2.89; P, 6.20. MS (ESI): m/z 1940.3 $(M + Na)^+$.

1,21,23,25-Tetrakis(9-decenyl)-5,9,13,17-tetraphenyl-2,20:3,19-dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3,2]dioxaphosphocino[5,4-i/5′, 4′-i′]benzo [1,2-*d*/5,4-*d*′]bis[1,3,2]benzodioxaphosphocin-5,9,13,17-tetraoxide (3)

The same procedure as for **1** was followed starting from resorc[4]arene **7** (2.5 g, 2.4 mmol), toluene (190 ml), *N*-methylpyrrolidine (0.25 g, 2.88 mmol) and dichlorophenylphosphine oxide (1.96 g, 10.08 mmol). The crude residue was purified by column chromatography (CH_2Cl_2/THF:9/1 then 6/1 as eluent) giving cavitand **3** (1.85 g, 1.22 mmol, 51% yield) as an orange powder: mp 204°C (CH_2Cl_2/hexane; dec); IR(KBr): 3504, 2926, 2853, 1490, 1274 (P═O), 1151, 1134, 1077, 909 cm^{-1}; ^{1}H-NMR (499.83 MHz, $CDCl_3$): δ 1.31–1.47 (m, 48H, CH_2), 2.03 (m, 8H, C*H*$_2$CH═CH_2), 2.34 (m, 8H, C*H*$_2$–$(CH_2)_7$), 4.79 (t, 4H, bridge C*H*, $J = 7.5$ Hz); 4.92 (d, 4H, CH═*CH*$_2$, $J_{cis} = 10.0$ Hz), 4.97 (dd, 4H, CH═*CH*$_2$, $J_{trans} = 17.0$, $J = 1.5$ Hz), 5.75–5.83 (m, 4H, *CH*═CH_2), 6.99 (s, 4H, calix-ArH_{upper}), 7.28 (s, 4H, calix-ArH_{lower}), 7.49 (m, 8H, P-ArH), 7.60 (t, 4H, P-ArH, $J = 7.0$ Hz), 8.03 (dd, 8H, P-ArH, $J = 7.5$ Hz, $J_{PH} = 14.0$ Hz); ^{13}C-NMR (50.32 MHz, $CDCl_3$): δ 27.88, 28.95, 29.11, 29.53, 29.62, (two overlapping signals), 30.74, 33.78 (*C*H_2), 35.97 (*C*H), 114.21 (CH═*C*H_2), 117.51 (calix-ArC_{upper}), 121.75 (calix-ArC_{lower}), 126.96 (d, P-Ar*C*, $J = 205.2$ Hz), 128.4 (d, P-Ar*C*, $J = 16.3$ Hz), 131.72 (d, P-Ar*C*, $J = 10.0$ Hz), 133.03 (P-Ar*C*), 134.66 (calix-Ar*C*−CH), 139.04 (*C*H═CH_2), 146.68 (d, calix-Ar*C*−O, $J = 11.7$ Hz); ^{31}P-NMR (81.02 MHz, $CDCl_3$): δ 7.26; Anal. Calcd for $C_{92}H_{108}O_{12}P_4{\cdot}H_2O$: C, 71.39; H, 7.16; P, 8.00. Found: C, 71.13; H, 7.11; P, 7.67.

1,21,23,25-Tetrakis(11-thiaheneicosyl)-5,9,13,17-tetraphenyl-2,20:3,19-dimetheno-1*H*,21*H*,23*H*,25*H*-bis[1,3,2]dioxaphosphocino[5,4-*i*/5′,4′-*i*′]benzo [1,2-d/5,4-d′]bis[1,3,2]benzodioxaphosphocin-5,9,13,17-tetraoxide (2)

To a solution of cavitand **3** (0.4 g, 0.26 mmol) in THF (18 ml) was successively added 1-decanethiol (0.91 g, 5.23 mmol) and 9-BBN (15.9 mg, 0.13 mmol). The reaction mixture was stirred at room temperature overnight. 9-BBN (15.9 mg, 0.13 mmol) was further added to the mixture, which was maintained at room temperature under stirring for 18 h. Removal of the solvent under reduced pressure gave a beige foam (0.8 g) which was purified by column chromatography (CH_2Cl_2/THF: 9/1 then 6/1 as eluent); to give **2** (0.46 g, 0.21 mmol, 80% yield) as a beige glassy foam which was recrystallized from methanol: mp: 177.4°C; IR(KBr): 2923, 2851, 1488, 1271 (P═O), 1151, 1134, 1073, 909 cm^{-1}; ^{1}H-NMR (499.83 MHz, $CDCl_3$): δ 0.85 (t, 12H, CH_3, $J = 7.0$ Hz), 1.23–1.47 (m, 112H, CH_2), 1.55 (m, 16H, SCH_2CH_2), 2.33 (m, 8H, $CHCH_2$),

TABLE I Crystallographic data, data collection and refinement parameters for **1**

Empirical formula	$C_{104}H_{104}O_{24}N_4P_4{\cdot}6CH_3CN$
Formula weight	2164.12
Temperature	293 K
Wavelength	0.71069 Å
Crystal system	Monoclinic
Space group	$P21/c$
Unit cell dimensions	$a = 20.574(4)$ Å, $\alpha = 90°$ $b = 16.591(4)$ Å, $\beta = 92.09(2)°$ $c = 33.973(7)$ Å, $\gamma = 90°$
Volume, Z	11589(4) Å^3, 4
Density (calculated)	1.240 Mg/m^3
Absorption coefficient	0.139 mm^{-1}
$F(000)$	4560
Crystal size	0.32 × 0.24 × 0.16 mm
θ range for data collection	1.70–20.77°
Index ranges	$0 \le h \le 20$, $0 \le k \le 16$, $-33 \le l \le 33$
Reflections collected	43,700
Independent reflections	11939 [R(int) = 0.069]
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	11933/320/1299
Goodness-of-fit (all data)	1.031 (1.111)
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0648$ [8697 observed], $wR2 = 0.1781$
R indices (all data)	$R1 = 0.0914$, $wR2 = 0.2050$
Extinction coefficient	0.0020(3)
Largest diff. peak and hole	0.59 and −0.28 e Å^{-3}

2.47 (t, 16H, SCH_2, $J = 7.5$ Hz), 4.78 (t, 4H, CH, $J = 7.5$ Hz), 6.97 (s, 4H, calix-ArH_{upper}), 7.28 (s, 4H, calix-ArH_{lower}), 7.50 (m, 8H, P-ArH), 7.60 (t, 4H, P-ArH, $J = 7.5$ Hz), 8.03 (dd, 8H, P-ArH, $J_{PH} = 16.0$ Hz, $J = 7.5$ Hz); ^{13}C-NMR (50.32 MHz, $CDCl_3$): δ 14.48, (CH_3), 23.04, 28.27, 29.35, 29.47, 29.65, 29.68, 29.73, 29.94, 30.00, 30.03, 30.11, 31.17, 32.26, 32.60, 32.62, 34.59 (CH_2), 36.36 (CH), 118.00 (calix-ArC_{upper}), 122.25 (calix-ArC_{lower}), 127.08 (d, P-ArC, $J = 205.2$ Hz), 129.34 (d, P-ArC, $J = 16.0$ Hz), 132.10 (d, P-ArC, $J = 10.3$ Hz), 133.48 (P-ArC), 135.07 (calix-ArC−CH), 146.93 (d, calix-ArC−O, $J = 12.1$ Hz); ^{31}P-NMR (81.02 MHz, $CDCl_3$): δ 8.06. MS (ESI): m/z 2227.4 $(M + H)^+$, 2249.5 $(M + Na)^+$.

X-ray Structural Analysis

Single crystals of **1** suitable for X-ray analysis were grown from dichloromethane/acetonitrile. A crystal with dimensions 0.32 × 0.24 × 0.16 mm was mounted in a Lindemann glass capillary. The data were collected at 293 K on a MAR345 image plate using graphite-monochromated Mo Kα radiation ($\lambda = 0.71069$Å). Ninety images with $\Delta\phi = 2°$ at a crystal to detector distance of 175 mm gave a total of 43,700 measured reflections. The lattice parameters were refined from the data between $2\theta = 8$ and 41.5°. Crystal data are as follows: monoclinic, $P2_1/c$, $a = 20.574(4)$, $b = 16.591(4)$, $c = 33.973(7)$ Å, $\beta = 92.09(2)°$, $V = 11589(4)$ Å^3, $Z = 4$. The crystal did not diffract at a higher resolution than $2\theta = 41.5°$. The completeness to this 2θ value was 98.9%. After merging, there were a total of 11,939 independent reflections of which 8697 were considered as observed [$I > 2\sigma(I)$]. The structure was solved by direct methods and refined by full-matrix least squares on F^2 using SHELXS and SHELXL-97 [37]. The positions of the hydrogen atoms were calculated and included in the refinement with a common isotropic temperature factor ($U = 0.15$ Å^2). Restraints on bond lengths and nonbonded 1–3 distances were applied in the skeleton of the resorc[4]arene, the four lateral chains and in the six co-crystallized acetonitrile molecules. The refinement converged to the final indices: $R_1 = 0.065$ for 8697 observed reflections, $R_1 = 0.091$ for all data. Scattering factors were taken from *The International Tables for X-ray Crystallography* [38].

Table I provides a summary of the crystallographic data, data collection and refinement parameters. Selected bond distances and angles around the phosphorus atoms are compared in Table II. The final atomic coordinates, bond distances, bond angles, anisotropic thermal parameters and hydrogen atoms positions have been deposited with the Cambridge Crystallographic Data Center as CIF files CCDC No 170550 [39].

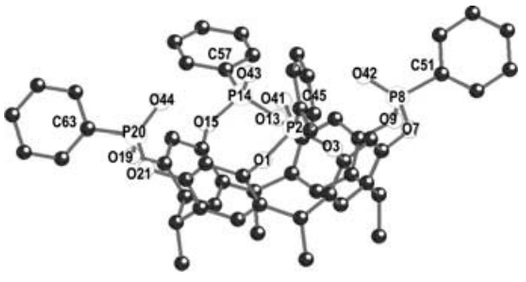


TABLE II Selected bond lengths (Å) and angles (°) in **1** with estimated standard deviation in parentheses

P2–O41:1.461(3)	P8–O42:1.459(3)	P14–O43:1.453(3)	P20–O44:1.453(3)
P2–C45:1.756(3)	P8–C51:1.772(3)	P14–C57:1.784(3)	P20–C63:1.761(3)
P2–O1:1.598(3)	P8–O7:1.597(3)	P14–O13:1.607(3)	P20–O19:1.585(3)
P2–O3:1.601(3)	P8–O9:1.601(3)	P14–O15:1.590(3)	P20–O21:1.601(3)
O41–P2–O1:114.1(2)	O42–P8–O7:114.7(2)	O43–P14–O15:114.5(2)	O44–P20–O19:114.5(2)
O41–P2–O3:114.2(2)	O42–P8–O9:114.5(2)	O43–P14–O13:113.0(2)	O44–P20–O21:115.0(2)
O1–P2–O3:104.6(2)	O7–P8–O9:104.3(2)	O15–P14–O13:105.7(2)	O19–P20–O21:104.9(2)
O41–P2–C45:117.1(2)	O42–P8–C51:116.6(2)	O43–P14–C57:119.2(2)	O44–P20–C63:118.0(2)
O1–P2–C45:102.0(2)	O7–P8–C51:102.3(2)	O15–P14–C57:100.5(2)	O19–P20–C63:102.7(2)
O3–P2–C45:103.2(2)	O9–P8–C51:102.7(2)	O13–P14–C57:102.2(2)	O21–P20–C63:99.6(2)

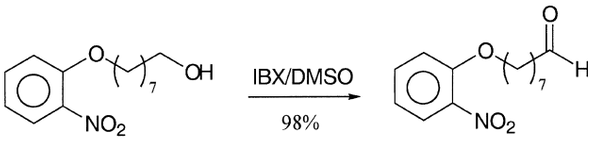
Picrate Salt Extraction by Cavitands 1 and 2

The percent extraction of metal picrate salts from water to chloroform was determined at 20°C following the previous protocol [40,41] by using 0.5 ml of 10^{-3} M initial solutions of host and metal picrate. For each salt, biphasic mixtures were stirred vigorously for 1 min and centrifuged for 10 min. The amount of picrate anion in the aqueous layer was measured by UV–VIS spectroscopy at 380 nm for the extracted phase (A) and the reference phase containing no host (A_0). The percent extracted was given by $100[(A_0 - A)/A_0]$. All experiments were carried out in duplicate and the average results are presented in Table III.

RESULTS AND DISCUSSION

Synthesis of Hosts 1 and 2

Cavitands **1** and **2** were, respectively, synthesized from resorc[4]arenes **6** and **7** as outlined in Scheme 2. Selective and quasi-quantitative oxidation of alcohol **8** [25] into aldehyde **9** was achieved using a stoichiometric amount of *o*-iodoxybenzoic acid (IBX, 1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide) [26], prepared according to the Dess–Martin procedure [27].



8 **9**

Aldehyde **9** was then condensed with resorcinol under acidic conditions to lead to the exclusive formation of the all-*cis* tetrasubstituted resorc[4]arene **6** in 70% yield. Its structure was established from its ^{1}H-NMR spectrum, which showed a single signal for each aromatic proton [28–30]. Resorc[4]arene **7** was prepared from resorcinol and commercially available undecylenic aldehyde using the same procedure [31].

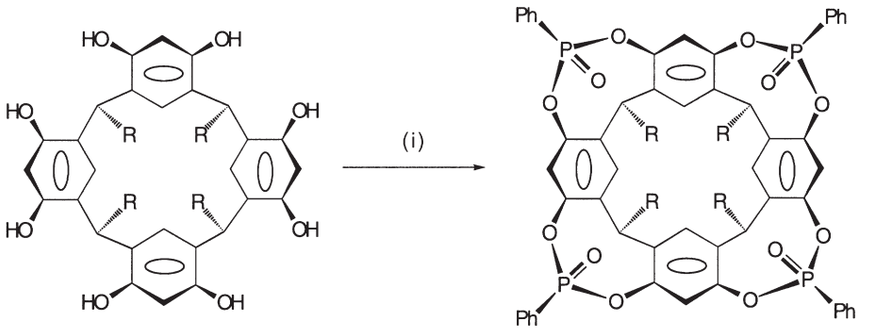
Resorc[4]arenes **6** and **7** were allowed to react with dichlorophenylphosphine oxide in the presence of *N*-methylpyrrolidine to give tetraphosphonatocavitands **1** and **3** in their *iiii* configuration, in 49 and 51% yields, respectively. The addition of 1-decanethiol to **3** in the presence of 9-borabicyclo[3.3.1]nonane (9-BBN) in THF afforded cavitand **2** in 80% yield [32]. The stereochemistry of host molecules **1**–**3** was established from the ^{1}H, ^{13}C and ^{31}P NMR spectra, which revealed a C_{4v} molecular symmetry. In $CDCl_3$, the proton decoupled phosphorus spectra showed a characteristic singlet at 7.97 (**1**), 8.06 (**2**) and 7.26 ppm (**3**). The solid-state structure determination of **1** undoubtedly proved the *iiii* configuration. The *iiio* isomer of **1** and **3** was not isolated, in contrast to compound **5** for which it was formed in low yield [19,20]. This is not surprising since the formation of the other isomers is not easily controlled and mainly depends on solvent and steric effects. The enhanced solubility in toluene of the resorc[4]arenes **6** and **7** as compared to the one used for the preparation of **5** is probably not the only reason for the nonformation of the *iiio* isomer. A better knowledge of the cyclization reaction mechanism is needed to investigate further on this point.

Crystal Structure of Tetraphosphonatocavitand 1

The X-ray crystal structure of cavitand **1** was obtained from a crystal grown from a dichloromethane/acetonitrile mixture. The host has the *iiii* configuration with the four P═O bonds oriented toward the molecular cavity (Fig. 1). The four fused eight-membered rings defining the molecular cavity adopt the boat–chair conformation as defined by the values of the endocyclic torsion angles (average

TABLE III Percentage of extracted metal picrates by tetraphosphonatocavitands **1** and **2**

Host	Li^+	Na^+	K^+	Rb^+	Cs^+	Ag^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}	Eu^{3+}
1	26	34	35	23	34	67	41	54	63	81	67
2	13	21	32	12	25	**91**	31	51	60	76	69



6 : R = -$(CH_2)_7$-O-C_6H_4-*o*NO_2

7 : R = -$(CH_2)_8$-CH=CH_2

1 : R = -$(CH_2)_7$-O-C_6H_4-*o*NO_2 49%

(ii) → **3** : R = -$(CH_2)_8$-CH=CH_2 51%

(ii) → **2** : R = -$(CH_2)_{10}$-S-$(CH_2)_9$-CH_3 80%

(i) NMP (1 eq.), $PhP(O)Cl_2$ (4 eq.), toluene, reflux, 48h ; (ii) 9-BBN, $HS(CH_2)_9CH_3$, THF, 20 °C, 36h

SCHEME 2

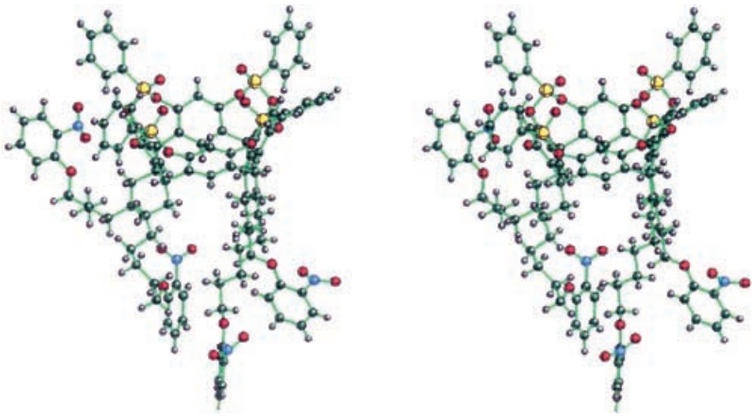


FIGURE 1 Stereoview of the crystal structure of **1**. Solvent molecules are omitted for clarity.

values are −85, 84, −4, −88, 88, 4, −84, and 85°) [33]. The P═O bonds and the phenyl substituents are in the axial and equatorial positions, respectively. The molecular cavity possesses an approximate C_{4v} symmetry since neither horizontal nor vertical distortion was detected. The four aromatic cycles defining the cavity have about the same angle of inclination to the plane perpendicular to the C_4 axis of the molecule (57.6° ± 1.6).

In the crystal, the cavitands are packed tail-to-tail owing to numerous π-interactions between *o*-nitrophenyl groups and/or phenyl substituents with plane-to-plane distances ranging from 3.6 to 5.2 Å (Fig. 2). As a consequence of the packing in the crystal lattice, which favor π−π interactions, three of the P-phenyl groups are coplanar with the adjacent P═O bond, whereas the fourth one is perpendicular to the C−P═O plane. For the same reason, three of

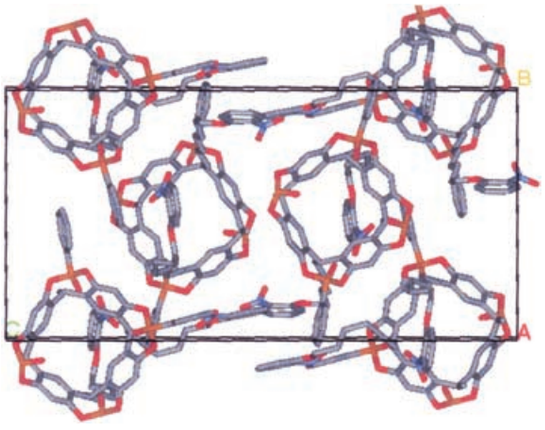


FIGURE 2 Partial view of the unit cell down the A axis showing the crystal packing in **1**; only the main π−π interactions are shown for clarity.

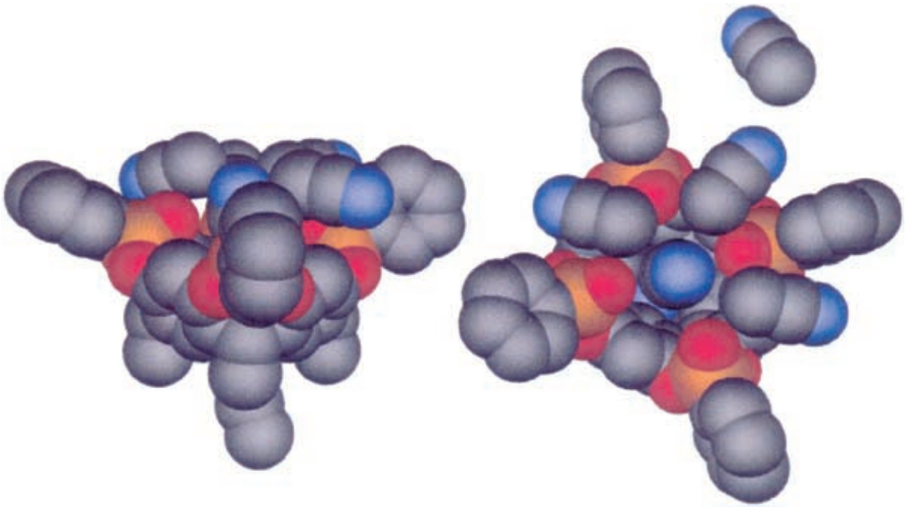


FIGURE 3 Top and side views of **1**·6CH_3CN showing the solvent molecules around the molecular cavity. Long chain substituents and hydrogen atoms are omitted for clarity.

the long chain substituents are elongated and stabilized by π−π stacking between nitrophenoxy and P-phenyl groups of a neighboring molecule as shown in Fig. 2. The fourth one is bent toward the major opening of the cavity in such a way that its aromatic substituent interacts with the corresponding substituent of a neighboring cavitand with average intermolecular carbon−carbon distances of 3.92 Å.

The crystal contains six solvent molecules per host. One acetonitrile was found as a guest in the aromatic cavity. Its methyl group lies 1.08 Å below the plane defined by the oxygen atoms of the PO groups indicating a deep encapsulation of the guest. The methyl carbon is at an average distance of 3.9 Å from the plane of the four aromatic rings of the resorc [4]arene cavity, accounting for attractive CH−π interactions. At the lower rim, a second molecule of acetonitrile occupies a position between the four long chain substituents. Four other acetonitrile molecules are present as solvates and participate in the packing by filling up the interstitial spaces between the host molecules. It is interesting to note that three of them are located near the wide opening of the host and nested between P-phenyl groups with their methyl end pointing inward (Fig. 3).

Metal Picrate Extraction Studies

The affinity of metal ions for hosts **1** and **2** was evaluated by the biphasic extraction method of the metal picrate from aqueous solution into chloroform solution containing the host compound. Following this procedure, the percent of picrate extracted was obtained by measuring the absorbance A of the picrate salt in the extracted aqueous layer at 380 nm. The percent extracted was given by $100[(A_0 - A)/A_0]$, where A_0 is the absorbance of the reference phase containing no host.

The tetraphosphonatocavitands **1** and **2** show a strong affinity for Ag^+ [67% (**1**); 91% (**2**)], Ba^{2+} [81% (**1**); 76% (**2**)] and Eu^{3+} [67% (**1**); 69% (**2**)] (Table III). They have similar affinity for metal picrates except for Ag^+, which is better extracted by **2** (91.4% vs. 67% for **1**). This result is consistent with the fact that Ag^+ can interact not only with the phosphorylated binding sites of the cavitand, but also with the thioether functionality of the lower rim in **2**. For both alkaline and alkaline-earth picrate salts, the extractability of **1** (Fig. 4) and **2** increases with the ionic radius and the charge of the cation. For example, K^+ and Ba^{2+}, which have about the same ionic radius (1.33 and 1.35 Å, respectively), are extracted in

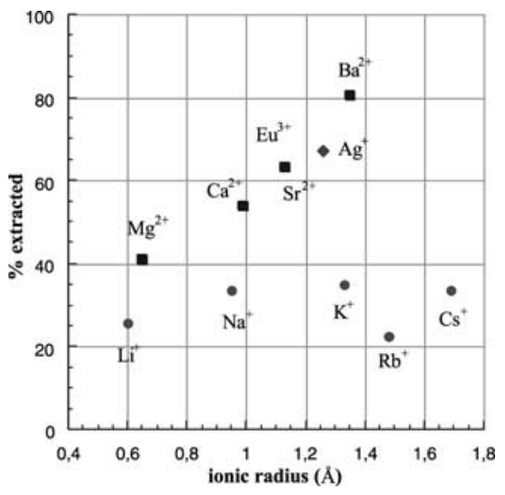


FIGURE 4 Percentage metal picrate salts extraction by cavitand **1**.

35–32% and 81–76% by hosts **1** and **2**, respectively. One can also notice that they are remarkable extractants of alkaline-earth cations, which are much more hydrated than alkaline ones [34]. This strong ability to desolvate can be attributed to both the tetraphosphonate preorganized upper rim and the hydrophobicity of the molecular cavity. The complexation of other metal and organic cations is still under investigation and opens the way to new applications for these phosphorylated cavitands. It is interesting to note that acetylcholine, a biologically relevant cation, was efficiently extracted by tetraphosphonatocavitands **1** (86%) and **2** (64%) [35].

CONCLUSION

New phosphocavitands **1**–**3** derived from resorc [4]renes functionalized at the lower rim, have been synthesized using an improved procedure. **1** was structurally characterized in the solid state. The host molecules have the *iiii* configuration with the four P═O bonds oriented toward the molecular cavity. The formation of the *iiii* stereoisomer is of prime importance to develop efficient hosts for cationic species. Indeed, extraction studies of metal ions by cavitands **1** and **2** revealed that picrate salts of alkaline, alkaline earth metal, and other metal cations like Ag^{+} and Eu^{3+} are efficiently extracted. The results collected with these tetraphosphonatocavitands should prove them to be useful for the design of new molecular devices for the recognition of metal and organic cationic species.

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