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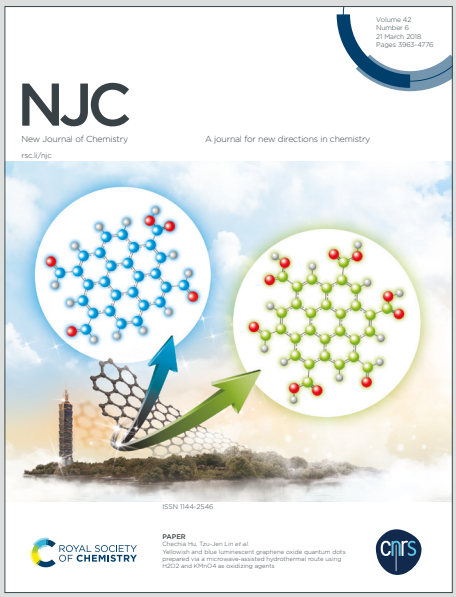

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ARTICLE

Monosubstituted pillar[5]arene functionalized with (amino)phosphonate fragments are "smart" building blocks for constructing nanosized structures with some s- and p-metal cations in the organic phase

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Monosubstituted pillar[5]arenes containing a phosphonate fragment were successfully obtained in good yields. It was found that the introduction of bulky fragments containing tetra-coordinated pentavalent phosphorus atoms prevents self-assembly of monosubstituted pillar[5]arenes and the formation of supramolecular polymers. Pillar[5]arenes with phosphonate and 1-aminophosphonate substituents demonstrated recognition towards Na^+, K^+, Cs^+ and Pb^{2+}. Their ability to form complexes with these cations was evaluated by UV spectroscopy. Dynamic light scattering (DLS) revealed the formation of aggregates with K^+, Cs^+ and Pb^{2+}. It was established that the substituent at the α-carbon atom of the aminophosphonate fragment played a significant role in Pb^{2+} binding. DLS and transmission electron microscopy revealed that Pb^{2+}-induced aggregation formed particles with a monodisperse distribution of 0.02-0.23 and a hydrodynamic diameter of 58-178 nm.

Introduction

Metacyclophanes such as calix[n]arenes[1-3] and thiacalix[n]arenes,[4-7] cucurbit[n]urils[8-10] and cyclodextrins[11-13] are being functionalized to address problems in the separation and extraction of heavy metals. Unlike these metacyclophanes, classical paracyclophanes are rather difficult to functionalize, however, in the last decade, the pillar[n]arene class of paracyclophanes has become widespread.[14] The advent of the pillar[n]arenes has provided an opportunity to fully realize and demonstrate the interesting properties of these paracyclophanes which can be functionalized through their free phenolic groups.[15] Furthermore, pillar[n]arenes are unique compounds with a high symmetry and rigid framework and are relatively easy to synthesize.[16-19] Varying pillar[n]arene substituents allows their physical properties to be changed and opens up the possibility of working in fields previously inaccessible to paracyclophanes.[20-23] In this regard the study of the complexation of metal cations by monosubstituted pillar[n]arenes, as well as the influence of the substituents nature on their binding ability, is of special interest.

Development of the chemistry of phosphorus-containing macrocyclic compounds has been of great interest to scientists with a view to creating new types of supramolecular and coordination systems and studying their molecular recognition behavior.[24-27] Introduction of organophosphorus fragments to highly coordinating macromolecular systems can significantly affect their complexing properties.

A number of examples in the literature describe the binding between pillar[n]arenes and a wide range of guests: from metal cations (for extraction) to anti-cancer drugs (for targeted drug delivery).[28-32] Particular attention has been paid to pillar[5]- and pillar[6]arenes with phosphorus-containing substituents. Phosphonium salts based on pillar[5]arenes have been investigated for antimicrobial activity and used as phase transfer catalysts.[33] Phosphine oxides have been proposed for the extraction and selective separation of heavy metals.[34-36] Supramolecular micelles and vesicles based on salts of phosphonic acids of pillar[5]- and pillar[6]arenes have been used as nanocontainers for targeted drug delivery and for the separation and enrichment of protein cell membranes.[37] Notably, the number of publications devoted to the synthesis of mono- and disubstituted phosphorus-containing pillar[5]arenes is substantially lower compared to their decaphosphorylated analogs[38,39] as are their applications.

One of the most well-known properties of monosubstituted pillar[5]arenes is their tendency for self-association and the further formation of supramolecular polymers.[40-43] Previously, we synthesized monosubstituted pillar[5]arenes containing the 1-aminophosphonate fragment[44] which demonstrated that the introduction both amino and phosphoryl groups blocked self-association. In view of the fact that the monosubstituted pillar[5]arenes containing 1-aminophosphonate fragment are not given to self-association

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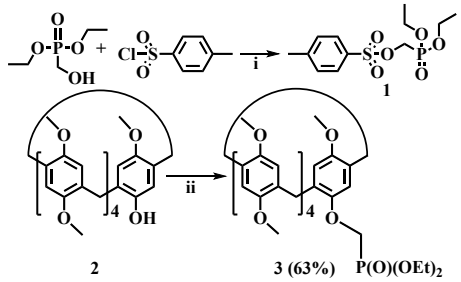
and the consequential formation of supramolecular polymers it was decided to study their complexation with a number metal cations. As the aminophosphonate fragment is known to function as a bidentate ligand it was decided to prepare a structurally similar monodentate ligand based on pillar[5]arene containing a single phosphoryl fragment as a reference substance to evaluation the effect of the amino group on its complexation and aggregation properties.

Results and discussion

Synthesis of the monosubstituted pillar[5]arene containing a phosphonate fragment

The alkylating agent, diethyl[[(p-toluenesulfonyl)oxy[methyl]]phosphonate, was synthesized by the literature method [45]. The reaction between phosphonate **1** and pillar[5]arene **2** using potassium carbonate as the base took 60 hours to complete whereas in the presence of cesium carbonate it took only 30 hours (Scheme 1).



Scheme 1 Reagents and reaction conditions: (i) $NEt_3/(CH_3CH_2)O$, (ii) **1**, Cs_2CO_3/CH_3CN.

There is a single signal at 20.1 ppm in the $^{31}P\{^1H\}$ spectrum of phosphonate **3** and its structure was confirmed by ^1H NMR spectrum (Fig. 1). The proton signals for the methoxy groups and methylene bridges are found between 3.69 and 3.80 ppm. The proton signals of the ethoxy group bound to the phosphorus atom appear as a multiplet and a triplet at 3.93 and 0.94 ppm ($^3J_{HH}$ = 7.0 Hz). The oxymethylene group proton signals are observed as a doublet at 4.26 ppm and $^2J_{PH}$ = 8.8 Hz (Fig. 1). Compounds **4**-**6** (Fig. 2) were obtained using the literature methods.[44]

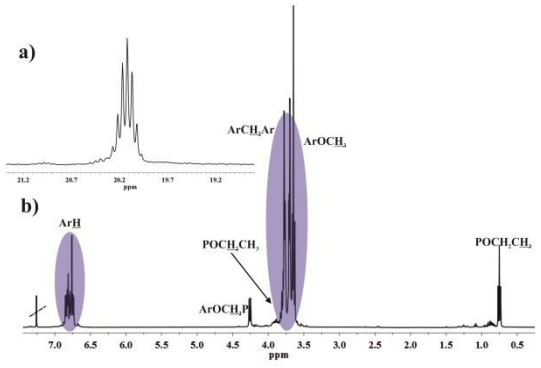


Fig. 1 a) ^{31}P NMR spectrum of compound **3** ($CDCl_3$, 298 K, 162.0 MHz); b) ^1H NMR spectrum of the compound **3** ($CDCl_3$, 298 K, 400.0 MHz).

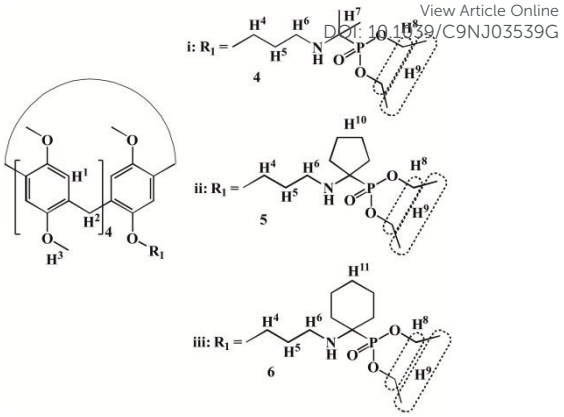


Fig. 2 Monosubstituted pillar[5]arenes containing the 1-aminophosphonate fragment.

Complexation and aggregation of monosubstituted pillar[5]arenes studied by UV-, NMR spectroscopy, dynamic light scattering and transmission electron microscopy

One of the approaches to constructing of polytopic receptors for definite substrates is the combining of binding sites in a single macrocycle. Monofunctionalized pillar[5]arenes **3**-**6**, modified by methoxy, phosphonate and 1-aminophosphonate fragments, contain several potential coordination centers (a phosphoryl group, an amino group, methoxy groups and oxymethylene fragments). Macrocycles **3**-**6** therefore have the potential to form host-guest complexes and/or extended aggregates with metal cations and, consequently, their complexing ability towards Al^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Li^+, Cd^{2+}, Na^+, Pb^{2+}, Ag^+, K^+ and Cs^+[34,46] was studied by electron absorption spectroscopy, NMR spectroscopy, dynamic light scattering (DLS) and transmission electron microscopy (TEM) in a binary system ($CHCl_3$ + 5% CH_3OH). Compound **3** was used as reference to assess the effect of the NH fragment on the complexing properties.

UV spectroscopy

UV spectroscopy is a universal tool for studying host-guest complexes as the deviation of the absorbance of the mixture, $A_{complex}$, from that of the purely additive spectrum, $\sum A_{mixture}$ ($\Delta A = A_{complex} - \sum A_{mixture}$) testifies to the host-guest interaction.

Binding of pillar[5]arenes **3**-**6** on to metal cations of various size and charge (Al^{3+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Li^+, Cd^{2+}, Na^+, Pb^{2+}, Ag^+, K^+, Cs^+) was evaluated by UV-spectroscopy. The counterion in salts was the nitrate anion, since the interaction study of the synthesized pillararenes with tetrabutylammonium nitrate showed that it does not bind. It was determined that all macrocycles bound Pb^{2+} most effectively. Compounds **3**, **4** and **6** also bound Cs^+, pillar[5]arenes **5** and **6** bound K^+ and aminophosphonate **6** bound Na^+.

The association constants of macrocycles **3**-**6** with metal cations Na^+, K^+, Cs^+ and Pb^{2+} were determined by UV titrations at 280 nm.

Further information on the metal ions' binding stoichiometries was obtained from Job's plots. Figure 3 shows the spectrophotometric titration curves of a solution of pillar[5]arene **6** by a lead nitrate solution at 280 nm.

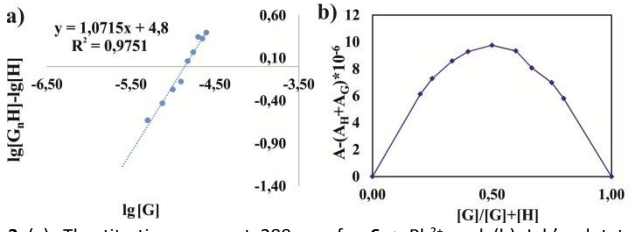


Fig. 3 (a) The titration curve at 280 nm for **6** + Pb^{2+} and (b) Job's plot to determine the stoichiometry in the complex.

The maximum point of the mole fractions on the titration curve was found to be 0.5, suggesting a host-guest ratio of 1:1 in the resulting complex. Using this method it was shown that all the systems studied (compounds **3**-**6** and cations Na^+, K^+, Cs^+ and Pb^{2+}) formed 1:1 complexes.

A decrease in the binding constant correlates with an increase in the volume of the substituent in the aminophosphonate fragment in compounds **4**-**6**. Thus, for Na^+, the binding constant decreases when passing from the compound **4** with methyl substituents to the compound **5** with a cyclopentyl fragment. The similar pattern is also seen for the cesium cation where pillar[5]arene **4** binds Cs^+ with a lgKa of 2.4, while for macrocycle **6** lgKa decreases to 2.0 (Table 1). An interesting parallel is observed when comparing binding constants for Cs^+ with compounds **3** and **4** which are 3.8 and 2.4, respectively. It is likely that the increase in binding constant is due to the absence of a secondary amino group in the macrocycle 3, which led to a better binding of cation by the P=O group. A different picture is observed for Pb^{2+} which is a "soft" base in the HSAB theory. The binding constants of Pb^{2+} with pillar[5]arenes **3** and **4** are both 3.2 (Table 1).

Table 1 The logarithms of the association constants (lgK_a) of complexes formed from pillar[5]arenes **3-6** with metal cations in chloroform-methanol solution at 298 K.

Compound	lgK_a			
	Na^+	K^+	Cs^+	Pb^{2+}
3	-[a]	-[a]	3.8±0.2	3.2±0.2
4	3.0±0.1	-[a]	2.4±0.2	3.2±0.1
5	2.2±0.1	-[a]	-[a]	4.3±0.1
6	-[a]	3.4±0.1	2.0±0.1	4.8±0.3

a) no change in the UV spectra

The binding constants of Pb^{2+} with pillar[5]arenes **3** and **4** are both 3.2 (Table 1). An increase is then observed for compounds **4**-**6**, from 3.2 to 4.8 (Table 1). It should be noted that K^+ is bound only by macrocycle **6**. Both sodium and potassium are the "hard" acids in the HSAB theory, but the potassium cation is milder than the Na^+. Thus, binding of potassium cation by the compound **6** becomes possible due to the two factors: 1) the presence of the lone-electron pair at the nitrogen atom of amino group in addition to the phosphoryl group leads to an increase in the «softness» of the substituent (greater involvement of the lone-electron pair of the nitrogen atom leads to an increase in the softness of the chelate); 2) substituents at the α-carbon atom also affect the binding of cations. An introduction of a six-membered substituent leads to an increase in the "softness" of the macrocycle compared with the cyclopentylidene substituent.

Thus, the presence of the amino group in the substituent led to decreasing binding constants with Cs^+, from 2.0 to 2.4, while the presence of the phosphonate fragment in pillar[5]arene **3** led to binding of Cs^+ with lgKa = 3.8. The milder acid Pb^{2+} is bound by macrocycles **3** and **4** with the same efficiency (lgK_a = 3.2).

NMR study of the complexation of metal cations by pillar[5]arenes containing 1-aminophosphonate and phosphoryl fragments

One-dimensional NMR spectroscopy is a convenient way to study complexation and in this case, could be assessed not only by ^1H NMR spectroscopy but also by assessing changes in chemical shifts on the nuclei of other atoms such as ^{31}P. Solutions of compounds **3**-**6** were prepared at 5 × 10^{-3} M concentration in $CDCl_3$. Complexation with Pb^{2+} (5 × 10^{-3} M in CD_3OD) was investigated at a 1:1 host-guest ratio in which the proportion of CD_3OD was 5%. Analysis of the $^{31}P\{^1H\}$ NMR spectrum of the mixture of the compound **3** and lead nitrate showed no visible changes in the phosphorus chemical shift, and no visible changes were observed in the ^1H NMR spectrum either (Fig. S27-S28). By contrast there was significant broadening of the phosphorus signal in the $^{31}P\{^1H\}$ spectrum of the 6 + Pb^{2+} mixture (Fig. S29-S30) indicating an interaction between phosphorylated pillar[5]arene **6** and Pb^{2+}.

Based on the data obtained by the UV- and NMR spectroscopy we proposed that in these systems it is possible to form ensembles in which the phosphoryl groups act as binding sites for metal cations in polydentate colloidal systems, as a result of which the entropy factor becomes decisive in stabilizing the resulting supramolecular systems.[47] Therefore, we investigated the behavior of pillar[5]arenes **3**-**6** with Na^+, K^+, Cs^+ and Pb^{2+} cations by dynamic light scattering.

Computer simulations

Investigation of macrocycles **3** - **6** using a semiempirical model (PM6) indicated that each broadly adopts one of two conformations (Fig. S47). In one ($P=O_{endo}$) the phosphate-bound oxygen resides within the compound's annulus; in the other ($P=O_{exo}$) it is outside the cavity and the void is filled by a hydrophobic group from the substituent. For **3** it is a phosphonate ethoxy group whereas for **4** - **6** it is the dimethyl, cyclopentyl or cyclohexyl group, respectively. The energy differences between these conformations are predicted to be between 0.1 and 25.5 kJ mol^{-1} (Table 2) but the preferred conformation, $P=O_{exo}$ or $P=O_{endo}$, varies.

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Table 2 Relative energies for the conformers of compounds **3** – **6**.

Compound	lgK_a	
	$P=O_{endo}$	$P=O_{e[o}{}^{+}$
3	0.0	-10.7
4	0.0	-25.5
5	0.0	-0.1
6	-4.2	0.0

Pb^{2+} is bound by all the pillar[5]arene derivatives and its binding is accompanied by a broadening of the phosphorus signal in the $^{31}P\{^1H\}$ spectrum. The semiempirical model for **6**·Pb^{2+} suggests that the cation resides inside the macrocycle in the $P=O_{endo}$ conformation. Such a model supports both the strong binding of the 'soft acid' within a relatively 'soft base' aromatic environment and the observed perturbation of the ^{31}P signal though its inclusion within the pillar[5]arene. The attraction of the cation to the macrocyclic cavity is sufficient to form complexes with compounds **3** - **5**. Conversely, the model of **6**·Na^+ suggests that the macrocyclic annulus has minimal involvement in complex formation (Fig. 4).

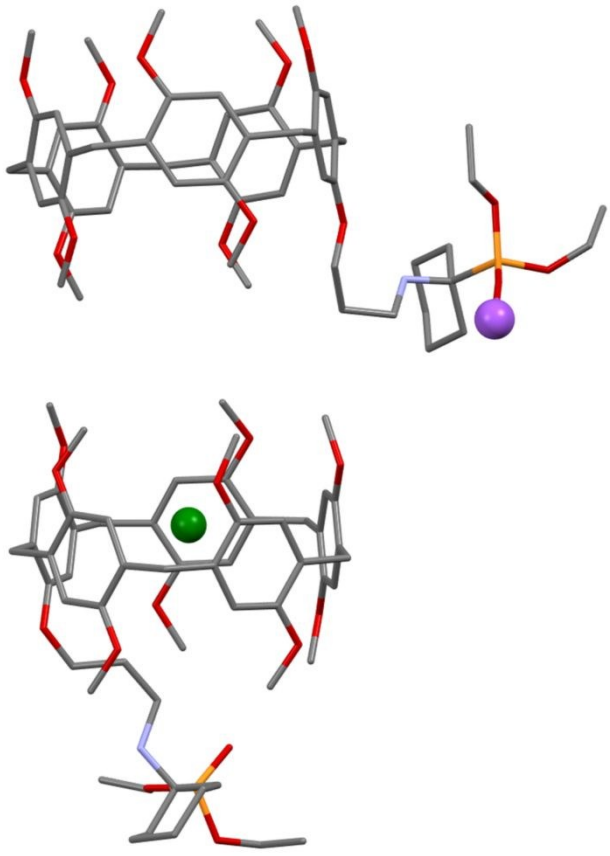

Fig. 4 Simulations of **6**·Na^+ (top) and **6**·Pb^{2+} (bottom), hydrogen atoms removed for clarity.

In previous work, models, supported by electrochemical data, have shown that Na^+ and K^+ can bind within the cavity of decamethoxypillar[5]arene but that Cs^+ cannot.[48] Although the size of Cs^+ would preclude it from entering macrocycles **3** - **6**, its lower charge density makes it 'softer' than either Na^+ or K^+ and it may be this property which allows it to bind to **3**, **4** and **6**. The influence of solvent on macrocycle conformation and cation binding is probably the final factor in the selective binding observed.

Aggregation study of the monosubstituted pillar[5]arenes containing 1–aminophosphonate and phosphoryl fragment with metal cations by DLS and TEM

Aggregation of the compounds **3**-**6** in the binary system ($CHCl_3$ + 5% CH_3OH) was studied by dynamic light scattering to investigate our hypothesis about the nature of the interaction of compounds **3**-**6** with metal cations and whether discrete host-guest complexes or aggregates are formed. It was shown that compounds **3**-**6** did not form an aggregates (PDI ≈ 1) in the concentration range studied ($1 \times 10^{-3} – 1 \times 10^{-5}$ M).

The aggregation of the "macrocycle-cation" system was studied with Na^+, K^+, Cs^+ and Pb^{2+}. It was established that the pillar[5]arenes **3**-**6** did not form any aggregates with Na^+ as the polydispersity index was <0.25 in each case (Table 3).

The average diameters of the particles formed by K^+ and compounds **3** and **4** are very similar at 149 nm and 159 nm, respectively, while the average diameter of aggregates formed by Cs^+ and macrocycles **4**-**6** increases from 212 nm to 362 nm.

The sizes of aggregates for Pb^{2+} with compounds **3** and **4** are similar, at 175 and 178 nm, respectively, but this is followed by a sharp decrease from 178 to 58 nm when passing from aminophosphonate **4**, with methyl substituents, to aminophosphonate **5** with a cyclopentylidene substituent. An increase in size to 144 nm is then observed for aggregates with compound **6** (Fig. 5). Introduction of the phosphoryl group into the pillar[5]arene substituent blocked self-assembly and increased the ability to form inclusion complexes with the target guests.

An interaction of compounds **3**-**6** with the "hard acid" Na^+ leads to formation of host-guest complexes, while increasing cation "softness" promotes aggregation between macrocycle and metal cations by the P=O bond. It is worth noting that the nature of the cation plays an important role in the binding studied cations.

Table 3 Diameters of aggregates formed from compounds **3**-**6** with Na^+, K^+, Cs^+ or Pb^{2+} cations and their corresponding polydispersity indices (PDI).

Compound	d, nm (Z-average) / PDI			
	Na^+	K^+	Cs^+	Pb^{2+}
3	-[a]	159±2 / 0.11	176±2 / 0.23	175±1 / 0.03
4	-[a]	149±1 / 0.24	212±2 / 0.17	178±1 / 0.05
5	-[a]	233±14 / 0.23	246±3 / 0.07	58±21 / 0.23
6	-[a]	277±2 / 0.10	362±4 / 0.08	144±1 / 0.02

[a] no aggregation occurs

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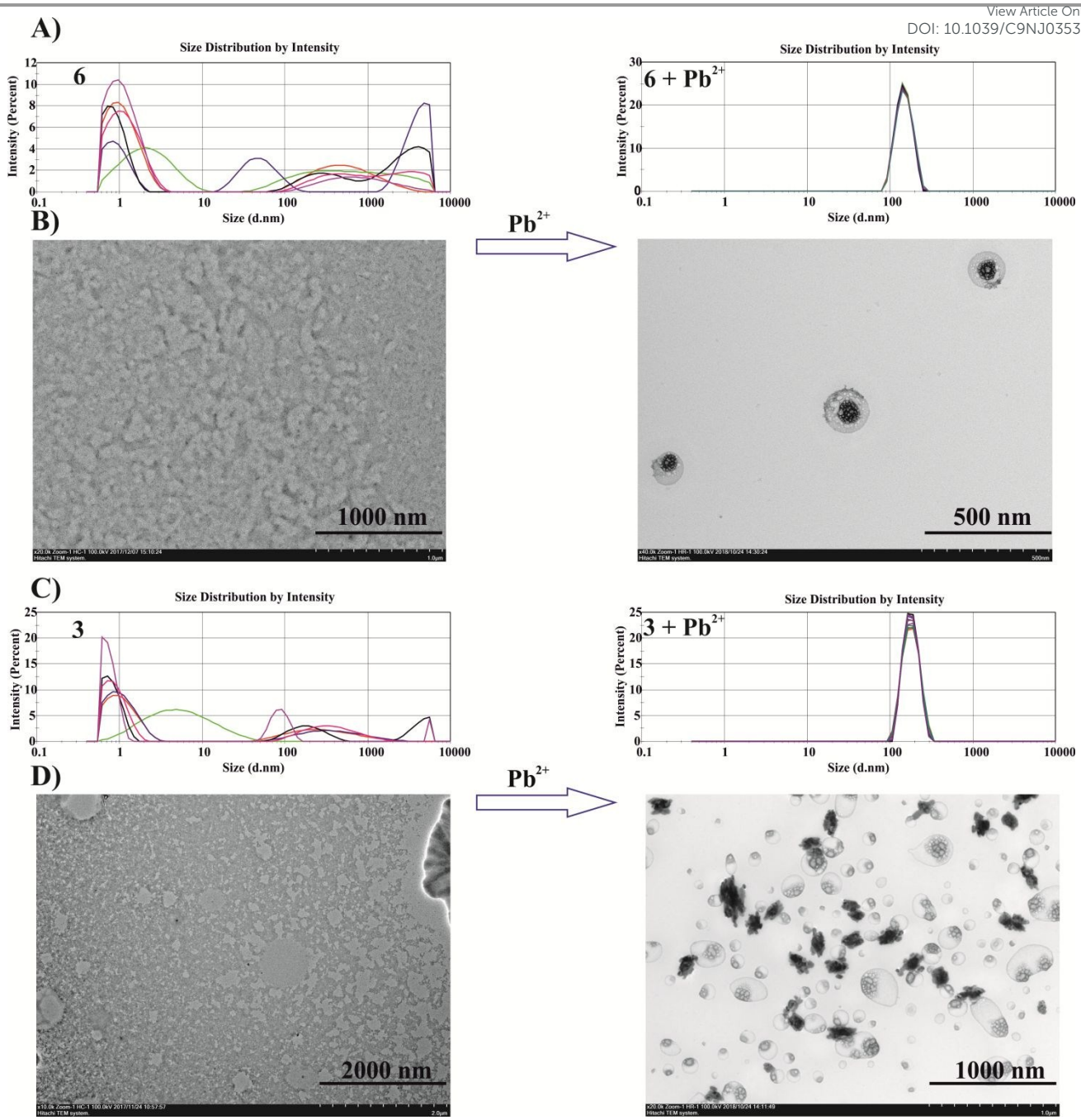

Fig. 5 A) left: size distribution of the particles by intensity from a solution of macrocycle **6** (1×10^{-4} M), right: size distribution of the particles by intensity from a solution of macrocycle **6** (1×10^{-4} M) and $Pb(NO_3)_2$ (1×10^{-4} M) at a molar ratio of 1:1 in chloroform. B) left: TEM images of macrocycle **6**, right: TEM images of the aggregates formed by macrocycle **6** and $Pb(NO_3)_2$. C), left: size distribution of the particles by intensity from a solution of macrocycle **3** (1×10^{-4} M), right: size distribution of the particles by intensity from a solution of the macrocycle **3** (1×10^{-4} M) and $Pb(NO_3)_2$ (1×10^{-4} M) at a molar ratio of 1:1 in chloroform. D) left: TEM images of macrocycle **3**, right: TEM images of the aggregates formed by macrocycle **3** and $Pb(NO_3)_2$.

Lead belongs to the p-block and its complexes are characterized by metal-coordination interactions, whereas complexes of cesium, in the s-block, are characterized by ion-dipole interactions. Thus, the formation of different types of aggregates is due to the different nature of the cations studied. There is the following pattern: the largest average diameter of aggregates is typical for the compounds **3** and **4** in the case of Pb^{2+} cation. The average diameter of particles formed by lead (II) cation and aminophosphonates **5** and **6** differ by twice (58 and 144 nm respectively); this is probably due to steric factors: the compound with bulkier cyclohexylidene fragment forms larger aggregates.

Electron microscopy allows the size and shape of the aggregates to be determined. Confirmation of the formation of supramolecular aggregates from pillar[5]arenes **3**-**6** and Pb^{2+} was given by TEM. From the TEM images (Fig. 5), all the pillar[5]arenes form spherical nanosized particles with Pb^{2+} cations presumably through the high affinity of the phosphoryl group for Pb^{2+} cations.[24]

To characterize the spherically shaped supramolecular aggregates formed by the pillar[5]arenes **3**-**6**, we used the bright field imaging mode of TEM operation. In this mode, the contrast formation, when considered classically, is formed directly by occlusion and absorption of the electrons in the sample. Therefore, regions of the sample with a higher atomic number appear dark, while regions with no sample or with regions of lower atomic number in the beam path appear bright.

Thus, the results obtained and the analysis of structures of the compounds **3** and **6** by TEM (Fig. 6) show that the phosphoryl group in pillar[5]arene **3** and **6** played a key role in the formation of the spherical nanosized aggregates with Pb^{2+}. In the case of compounds **3** and **6** with lead (II) nitrate a dark skeleton clearly appears, from lead with a high atomic number, and pillar[5]arene molecules in the lighter regions spaced equidistantly along this inorganic backbone.

Elemental maps of the spherical nanosized aggregates formed by pillar[5]arenes **3**-**6** and Pb^{2+} were recorded on a Formvar™/carbon coated 3 mm copper grid and shown in Figure 6.

TEM images (Fig. 6) show the area from which the element map was obtained. The element maps for P and Pb (Fig. 6 B-D) unambiguously determine their locations in the supramolecular aggregates. A correlation is shown between the locations of these two elements; the darker areas in Figure 6A are responsible for higher concentration of lead cations, as evidenced by the Pb^{2+} distribution image (Fig. 6D). It should be noted that there is a high density of phosphorus in the same areas (Fig. 6C). These data also confirmed that the TEM images show structures obtained from association of the pillar[5]arenes with lead (II) cations.

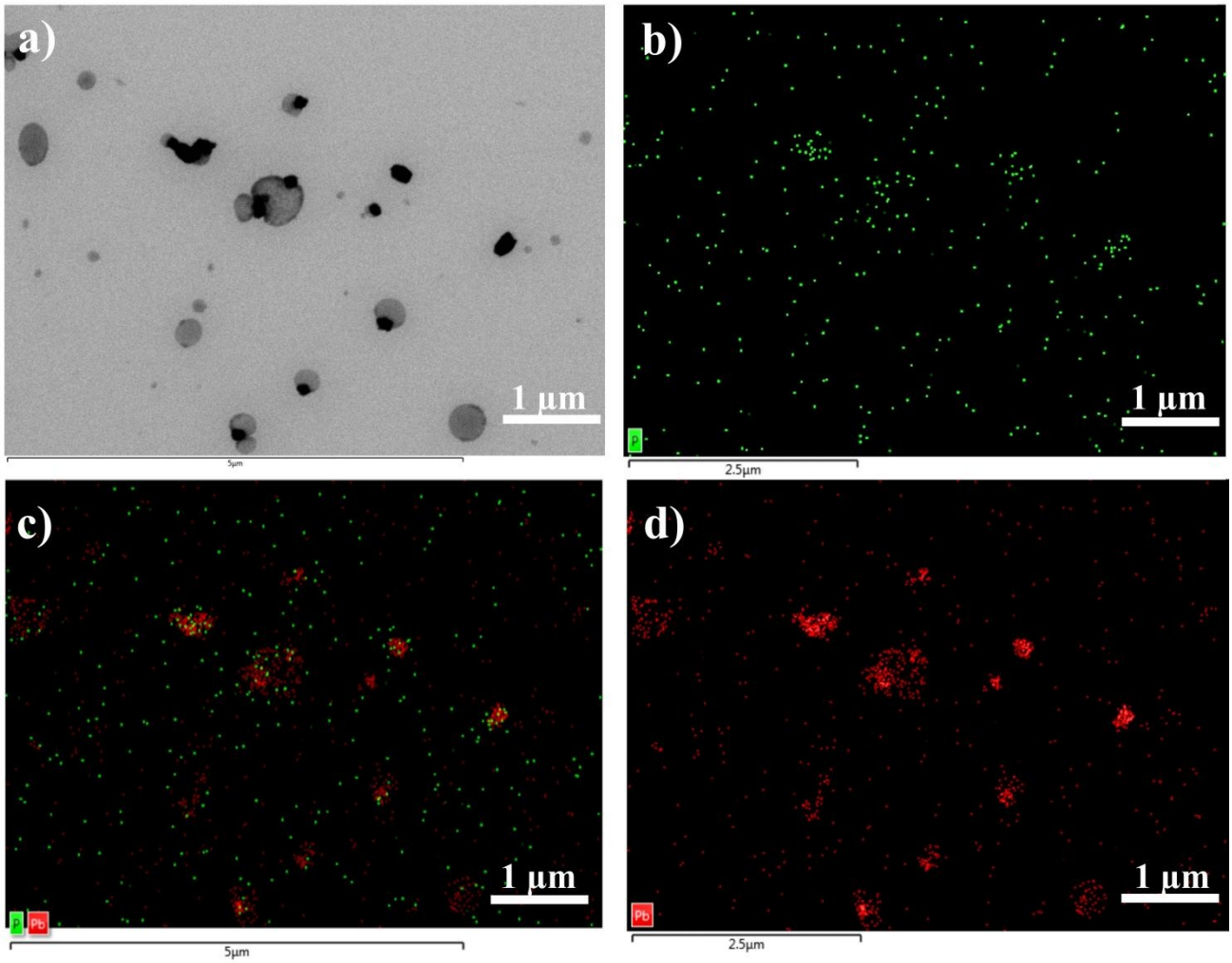

Fig. 6. Energy-dispersion spectra of fractal structures formed by pillar[5]arene **6** and Pb^{2+} on a copper support. A) supramolecular nanometer-sized aggregates formed by compound **6** and Pb^{2+}; B) superposition of elemental maps of P and Pb in the spherical aggregates formed by pillar[5]arene **6** and Pb^{2+}; C) mapping of P; D) mapping of Pb^{2+}.

Conclusions

In conclusion, it has been established that phosphonate- and 1-aminophosphonate-containing monosubstituted pillar[5]arenes form complexes with Na^+, K^+, Cs^+ and Pb^{2+} with a 1:1 stoichiometry and lgK_a values between 2.0 and 4.8, and

that Pb^{2+} is the most effectively bound cation. The introduction of the one substituent containing an (amino)phosphonate fragment to decamethoxypillar[5]arene changed the affinity of the macrocycle towards alkali metal cations and lead(II). All the pillar[5]arenes bound Pb^{2+} but the only alkali metal cation to bind in the presence of the phosphonate fragment was Cs+. For the aminophosphonate pillar[5]arene derivatives, the presence of the methyl substituents at α-carbon atom led to preferential binding for Na^+ over K^+ and Cs^+. The aminophosphonate derivative incorporating a cyclopentylidene substituent was selective for Na^+ with no evidence of K^+ or Cs^+ binding. Expanding the five-membered fragment to a six-membered ring led to more efficient binding of K^+. There was a significant effect of substituents at the α-carbon atom of the aminophosphonate fragment on Pb^{2+}: the macrocycle containing a phosphonate fragment and the compound with an aminophosphonate fragment and methyl groups at the α-carbon atom bound the cation with equal efficiency (lgK_a = 3.2). These data suggest that the secondary amino group does not participate in the binding of the metal cation. However, the picture changes with the introduction of cyclic fragments to the α-carbon atom of the aminophosphonate fragment as the efficiency of Pb^{2+} binding increases by an order (lgK_a = 4.3-4.8). It was shown by DLS and TEM that the complexes formed aggregates with Pb^{2+} with a monodisperse distribution (PDI from 0.02 to 0.23) and hydrodynamic diameters between 58 nm and 178 nm. Moreover, using a semiempirical model (PM6) it was shown that in the case of Pb^{2+}, cation resides inside the macrocycle in the $P{=}O_{endo}$ conformation. The size of Cs^+ would preclude it from entering synthesized macrocycles, its lower charge density makes it 'softer' than either Na^+ or K^+ and it may be this property which allows it to bind to obtained (amino)phosphonate derivatives based on pillar[5]arene. The influence of solvent on macrocycle conformation and cation binding is probably the final factor in the selective binding observed. The results obtained open great future for creating some new materials and application as catalysts based on phosphorylated pillar[5]arene.

Experimental

General

The ^1H, ^{13}C, ^{31}P NMR spectra of 3-5% solutions in CD_3OD, DMSO-d_6 and $CDCl_3$ were recorded on a Bruker Avance-400 spectrometer (400.17 MHz for ^1H-atoms). The residual solvent peaks were used as internal standards. IR spectra were recorded using a Spectrum 400 (Perkin Elmer) IR spectrometer. Elemental analysis was performed with a Perkin Elmer 2400 Series II instrument. Mass spectra were obtained on a Bruker Ultraflex III MALDI-TOF instrument with *p*-nitroaniline as the matrix. Melting points were determined using the Boetius Block apparatus. Chemicals were purchased from Acros (boron tribromide, 1,4-dimethoxybenzene, *N*-(3-bromopropyl)phthalimide) or Lancaster Synthesis (cyclopentanone, cyclohexanone) and used as received without additional purification. Organic solvents were purified by standard procedures. Diethyl phosphite[49] and diethyl[[(p-toluenesulfonyl)oxy[methyl]]phosphonate[45] were prepared by literature methods.

General procedures for the synthesis of compound 2

Pillar[5]arene **2** was obtained from 1,4-dimethoxypillar[5]arene by literature methodology.[38]

*4-Hydroxy-8,14,18,23,26,28,31,32,35-nonamethoxypillar[5]arene (**2**)*. Yield: 3.30 g (70 %), mp: 203 °C (203 °C [38]); ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ 6.90, 6.83, 6.76, 6.74, 6.72, 6.68, 6.65, 6.62, 6.60 (s, 10H, ArH), 3.81, 3.78, 3.77, 3.75, 3.74, 3.71, 3.65, 3.63, 3.62, 3.59, 3.54 (s, 37H, $-CH_2-$ and $-OCH_3$); MALDI-TOF MS $C_{44}H_{48}O_{10}$: calculated $[M^+]$ m/z = 737.3, found $[M^+]$ m/z = 737.4.

General procedure for the synthesis of compounds 4-6

Pillar[5]arenes were prepared by a literature method [44].

4,8,14,18,23,26,28,31,32-Nonamethoxy-35-{N-[1-(O,O-diethylphosphoryl)-1-methylethyl]-(3'-aminopropoxy}pillar[5]arene *(4)*. Yield: 0.16 g (64%), mp: 57 °C (56-57 °C [44]); $^{31}P\{^1H\}$ NMR ($CDCl_3$, 162 MHz, 298 K) δ_P, ppm: 31.2, ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ 1.30 (t, 6H, $^3J_{HH}$ = 7.0 Hz, $C\underline{H}_3CH_2OP$), 1.32 (d, 6H, $^3J_{PH}$ = 15.6 Hz, $(C\underline{H}_3)_2CP$), 1.95 (m, 2H, $-OCH_2C\underline{H}_2CH_2-$), 2.99 (t, 2H, $^3J_{HH}$ = 6.6 Hz, $-CH_2CH_2C\underline{H}_2NH$), 3.68-3.78 (m, 37H, $-C\underline{H}_2-$ and $-OC\underline{H}_3$), 3.95 (t, 2H, $^3J_{HH}$ = 6.0 Hz, $-OC\underline{H}_2CH_2CH_2-$), 4.13 (m, 4H, $CH_3C\underline{H}_2OP$), 6.80-6.83 (m, 10H, Ar<u>H</u>); MS (ESI) $C_{54}H_{70}NO_{13}P$: calculated $[M^+]$ m/z = 971.5, found $[M + H]^+$ m/z = 972.5, $[M + Na]^+$ m/z = 994.5.

4,8,14,18,23,26,28,31,32-Nonamethoxy-35-{N-[1-(O,O-diethylphosphoryl)-1-cyclopentyl]-(3'-aminopropoxy}-pillar[5]arene (5). Yield: 0.14 g (56%); mp: 61 °C (60-61 °C [44]); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 298 K): δ 31.6, ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ 1.29 (t, 6H, $^3J_{HH}$ = 7.0 Hz $C\underline{H}_3CH_2OP$), 1.68-1.78 and 1.95-2.00 (m, 10H, $-(CH_2)_4-$), 1.92 (m, 2H, $-OCH_2C\underline{H}_2CH_2-$), 2.98 (t, 2H, $^3J_{HH}$ = 6.6 Hz, $-CH_2CH_2C\underline{H}_2NH$), 3.64-3.78 (m, 37H, $-C\underline{H}_2-$ and $-OC\underline{H}_3$), 3.94 (t, 2H, $^3J_{HH}$ = 6.0 Hz, $-OC\underline{H}_2CH_2CH_2-$), 4.13 (m, 4H, $CH_3C\underline{H}_2OP$), 6.79-6.83 (m, 10H, Ar<u>H</u>); MS (ESI): calculated $[M^+]$ m/z = 997.6, found $[M + H]^+$ m/z = 998.5.

4,8,14,18,23,26,28,31,32-Nonamethoxy-35-{N-[1-(O,O-diethylphosphoryl)-1-cyclohexyl]-(3'-aminopropoxy}-pillar[5]arene (6). Yield: 0.15 g (60%); mp: 59 °C (59-60 °C [44]); $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 298 K): δ 30.7; ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ 1.29 (t, 6H, $^3J_{HH}$ = 7.0 Hz, $C\underline{H}_3CH_2OP$), 1.46-1.80 (m, 10H, $-(CH_2)_5-$), 1.95 (m, 2H, $-OCH_2C\underline{H}_2CH_2-$), 2.98 (t, 2H, $^3J_{HH}$ = 6.6 Hz, $-CH_2CH_2C\underline{H}_2NH$), 3.63-3.77 (m, 37H, $-C\underline{H}_2-$ and $-OC\underline{H}_3$), 3.96 (t, 2H, $^3J_{HH}$ = 6.2 Hz, $-OC\underline{H}_2CH_2CH_2-$), 4.10 (m, 4H, $CH_3C\underline{H}_2OP$), 6.75-6.79 (m, 10H, Ar<u>H</u>); MS (ESI): calculated $[M^+]$ m/z = 1011.5, found $[M + H]^+$ m/z = 1012.6, $[M + Na]^+$ m/z = 1035.5.

General procedure of the synthesis of the compound 3

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In a round-bottom flask equipped with magnetic stirrer, compound **2** (1.00 g, 1.4 mmol) was mixed with cesium carbonate (2.65 g, 8.1 mmol) and refluxed in acetonitrile (50 ml) for 20 minutes. Then diethyl[[(p-toluenesulfonyl)oxy[methyl]]phosphonate (0.48 g, 1.15 mmol) was added and the reaction mixture was stirred for 24 hours. Solvent from the organic layer was removed under reduced pressure. The resulting precipitate was dissolved in 20 ml of chloroform and 15 ml of dilute hydrochloric acid was added to reach pH 4. The organic phase was separated and the chloroform was evaporated under reduced pressure. The precipitate was washed with hot methanol and dried under reduced pressure over P_2O_5.

4-[(O,O-Diethyl)-phosphoryl-1-oxymethylene]-8,14,18,23,26,28,31,32,35-nonamethoxypillar[5]arene ***(3)*****.** Yield: 0.76 g (63%); mp: 92 °C; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$, 298 K): δ 20.1. ^1H NMR (400 MHz, $CDCl_3$, 298 K): δ 0.94 (t, 6H, $^3J_{HH}$ = 6.8, $POCH_2\underline{CH_3}$), 3.69-3.80 (m, 37H, $-CH_2-$ and $-OC\underline{H_3}$), 3.93 (m, 4H, $POC\underline{H_2}CH_3$), 4.26 (d, 2H, $ArOC\underline{H_2}P$, $^2J_{PH}$ = 8.8), 6.81-6.89 (m, 10H, Ar<u>H</u>), ^{13}C NMR (100 MHz, $CDCl_3$, 298 K): δ 16.4, 32.8, 43.8, 44.5, 56.8, 62.4, 62.5, 113.2, 113.6, 115.7, 131.5, 131.9, 132.8, 149.4, 151.3, 151.4; IR ν cm^{-1}: 1042 (P-O-C), 1206 (P=O); MS (MALDI-TOF): calculated $[M^+]$ m/z = 886.37, found $[M+H_2O]^+$ m/z = 904.7; El. Anal. Calcd for $C_{49}H_{59}O_{13}P$: C, 66.35; H, 6.71; P, 3.49. Found: C, 66.32; H, 6.75; P, 3.74.

UV-spectroscopy

Absorption spectra were recorded on a UV-3600 UV-spectrometer (Shimadzu). Quartz cuvettes with an optical path length of 10 mm were used. Chloroform and methanol were used for preparation of the solutions. Absorption spectra of mixtures were recorded after 1 hour incubation at 20 °C. Solutions of metal nitrates ($Al(NO_3)_3$, $Co(NO_3)_2$, $Ni(NO_3)_2$, $Cu(NO_3)_2$, $LiNO_3$, $Cd(NO_3)_2$, $NaNO_3$, $Pb(NO_3)_2$, $AgNO_3$, KNO_3, $CsNO_3$) in methanol were added to solutions of the compounds **3**-**6** (5×10^{-5} M) in chloroform in a 10:1 ratio to investigate the complex formation of pillar[5]arenes with metal nitrates.

Determination of the stability constant and stoichiometry of the complex by the spectrophotometric titration

Aliquots (15, 30, 45, 60, 75, 90, 105, 120, 135 and 150 µl) of 1×10^{-2} M $NaNO_3$, KNO_3, $CsNO_3$ and $Pb(NO_3)_2$ solutions in methanol were added to 0.3 ml of solutions of receptors **3**-**6** (5×10^{-4} M) in $CHCl_3$ and diluted to final volume of 3 ml with $CHCl_3$. The UV spectra of the solutions were recorded. The stability constants and stoichiometries of complexes were calculated as described elsewhere [44]. Three independent experiments were carried out for each series and the Student's *t*-test was used in statistical data processing.

Job plots

The stoichiometries of the complexes were determined by the isomolar series method. Spectra of the solutions of the pillar[5]arene and metal nitrates were recorded in the chloroform/methanol mixture. The volume of the host and guest solutions varied from 1:4 to 4:1, respectively, with the total concentration of the host (pillar[5]arene **3**-**6**) and guest ($NaNO_3$, KNO_3, $CsNO_3$, $Pb(NO_3)_2$) being constant and equal to 5×10^{-5} M. The solutions were used without further stirring. The optical density, A_i, of each complex was measured at 280 nm. The stoichiometry of each complex was determined from a plot of the increase in absorbance against the mole fraction of the guest. Three independent experiments were carried out for each system.

Computational methods

Calculations were undertaken using the Spartan '18 Parallel Suite [50] running on a Mac Pro with 3.5 GHz 6-Core Intel Xenon E5 processors and two threads per core. The pillar[5]arene hosts were constructed using the Build option. Conformational analysis was used to determine the host conformers with the lowest steric energy which were used as the semiempirical inputs for gas phase geometry optimization (PM6).

Dynamic light scattering (DLS)

Particle sizes were determined by a Zetasizer Nano ZS (Malvern) instrument at 20 °C in quartz cuvettes. The instrument contains a 4 mW He-Ne laser operating at a wavelength of 633 nm and incorporates noninvasive backscatter optics (NIBS). Measurements were performed at a detection angle of 173° and the software automatically determined the measurement position within the quartz cuvette. Processing of the results was performed by the DTS program (Dispersion Technology Software 4.20). Chloroform and methanol were used to prepare the solutions. To study the aggregation of pillar[5]arenes with metal nitrates, methanol solutions of $NaNO_3$, KNO_3, $CsNO_3$ or $Pb(NO_3)_2$ were added to solution of compounds **3**-**6** ($1 \times 10^{-3} - 1 \times 10^{-5}$ M) in chloroform in a 1:1 ratio. The particle sizes were measured 1 hour after mixing. The measurements were carried out after a further 24 and 168 hours under similar conditions to assess the kinetic stability of the systems. The experiments were carried out for each solution in triplicate.

Transmission electron microscopy (TEM)

TEM measurements were made at the Interdisciplinary Center for Analytical Microscopy of the Kazan Federal University. Analysis of samples was carried out using a Hitachi HT7700 Exalens transmission electron microscope with an Oxford Instruments X-Maxn 80T EDS detector working in STEM mode. Samples of compounds **3**-**6** (1×10^{-4} M) were prepared similarly to those studied by the DLS method. 10 µl of the suspension was placed on a carbon-coated 3 mm copper grid and dried at room temperature using special holder for microanalysis. After drying, the grid was placed in the transmission electron microscope and analyzed at an accelerating voltage of 80 kV.

Conflicts of interest

There are no conflicts to declare.

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Monosubstituted pillar[5]arene functionalized with (amino)phosphonate fragments are "smart" building blocks for constructing nanosized structures with some s- and p-metal cations in the organic phase

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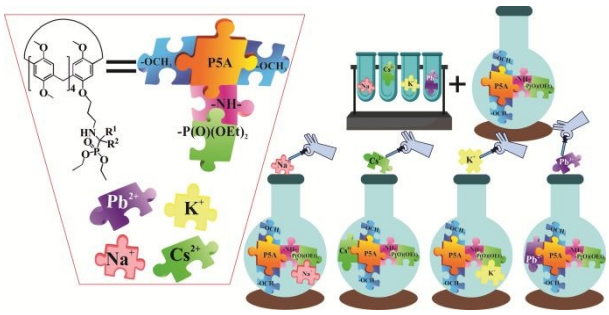

Pillar[5]arenes with phosphonate- and 1-aminophosphonate- substituents form complexes with Na^+, K^+, Cs^+ and Pb^{2+} with a 1:1 stoichiometry and lgK_a values between 2.0 and 4.8, and that Pb^{2+} is the most effectively bound cation.