Interaction of a Symmetrical α,α',δ,δ'-Tetramethyl-cucurbit[6]uril with Ln^{3+}: Potential Applications for Isolation of Lanthanides

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The interaction of a symmetrical α,α',δ,δ'-tetramethyl-cucurbit[6]uril (TMeQ[6]) with a series of lanthanide cations (Ln^{3+}) was investigated in neutral water and in acidic solution. Analysis by single crystal X-ray diffraction revealed that different isomorphous families formed under different synthetic conditions. Such differences in the interaction between TMeQ[6] and Ln^{3+} could potentially be used for isolating heavier Ln^{3+} from their lighter counterparts in neutral solution, and lighter lanthanide cations from their heavier counterparts in acidic solution.

Introduction

The unique optical and magnetic properties of lanthanide cations (Ln^{3+}) have led to their wide application in electronics, lasers and powerful magnets.[1] Due to the chemical similarities of the lanthanides, their elements typically coexist in nature. The cost-effective separation of lanthanide elements is critical for the application of lanthanides in modern technology. Solvent extraction and ion chromatography are currently the preferred methods for the separation of Ln^{3+}. These methods are based on the difference in formation constant (K_f) of Ln^{3+} molecular complexes. However, the development of more environmentally-friendly and efficient separation methods remains an industry goal.[2]

Recent advances in solid-state coordination chemistry,[3] especially in the field of metal-organic frameworks (MOFs),[4] have made possible a unified MOF-based separation strategy capable of the efficient separation of Ln^{3+}. This new strategy is based on the difference in solubility of products (K_{sp}) during fractional crystallization and the difference in the formation constant (K_f) of metal complexes in solvent extraction or chromatography. MOFs can be viewed as 3D polymers of metal complexes, and therefore it is hypothesized that the effect of a small difference in K_f for a molecular Ln^{3+} complex might be amplified during MOF crystallization. This approach has the potential to outperform traditional fractional crystallization.

Cucurbit[*n*]urils (Q[*n*]s)[5] have been utilized to construct Q[*n*]-based MOFs and other supramolecular architectures.[6,7] We previously reported the synthesis and characterization of symmetrical α,α',δ,δ'-tetramethyl-cucurbit[6]uril (TMeQ[6], Figure 1).[8] TMeQ[6] exhibited a greater solubility in water compared to unsubstituted Q[6]. The increased molecular polarity associated with the lower molecular symmetry of TMeQ[6] results in easier interactions with guest molecules in aqueous media. However, Q[*n*]s have a high affinity for Ln^{3+}, forming various Q[*n*]-based complexes, especially adducts, in the presence of structure directing agents, and can form novel coordination polymers and supramolecular assemblies.[7e,7f] For example, Fedin and coworkers[9] systematically investigated the coordination of Q[6] with Ln^{3+} in aqueous solution in the absence of additives and in the presence of structure directing agents. They later introduced 4-cyanopyridine into Q[6]-Ln^{3+} systems, and obtained novel tetranuclear lanthanide aqua hydroxo complexes.[10] More recently, Thuéry[11] also focused on Q[*n*]s-Ln^{3+} coordination chemistry, and introduced a series of chiral amino-acids into Q[6]-Ln^{3+} systems, resulting in the formation of a series of Ln^{3+} complexes and supramolecular assemblies. Our group investigated the coordination of a series of cucurbit[*n*]urils (Q[*n*]s) with a series of Ln^{3+} and their corresponding supramolecular assemblies, and found that cucurbit[*n*]urils not only recognized the Ln^{3+}, but could also be used to isolate them.[12] For example, under the same synthetic conditions, Q[5]-Ln^{3+} systems led to three distinct configurations for the coordination and supramolecular assemblies formed on increasing atomic number of the Ln^{3+}. Specifically, coordination of light Ln^{3+} cations with Q[5] formed one-dimensional coordination polymers, while intermediate Ln^{3+} cations such as Eu(III) or Gd(III) formed Q[5] pairs in which two Q[5] molecules are connected by cations. Coordination of heavy Ln^{3+} cations with Q[5] forms homochiral, one-dimensional helical coordination polymers.[6p,7a] This study also found that Q[6] on coordination with a series of Ln^{3+} cations formed linear coordination polymers in the presence of $[CdCl_4]^{2-}$ and $[ZnCl_4]^{2-}$ anions in acidic aqueous solutions containing HCl. The exceptions were La^{3+}, Ce^{3+}, Pr^{3+}, Nd^{3+} that immediately precipitated, and this could therefore offer a strategy for isolating lighter Ln^{3+} cations from their heavier counterparts.[7c] Similar phenomena can be observed in Q[7]/Ln^{3+} coordination and supramolecular assemblies in the presence of $[M_{\text{d-block}}]^{2-}$ anions in HCl aqueous solutions. In particular, Ln^{3+}/Q[7]-based coordination polymers adopt a “zig-zag” conformation in aqueous solutions containing < 3 M HCl.[12f] Moreover, in the presence of $Cd(NO_3)_3$, *o*-TMeQ[6] can coordinate with most lanthanide cations to form solid crystals, but complexes with the lightest Ln^{3+} (La, Ce, Pr) remain in solution. The *o*-TMeQ[6]-Ln^{3+}-$Cd(NO_3)_3$ systems can separate heavier Ln^{3+} cations from lighter Ln^{3+} cations by forming solid crystals,[12e] as described in our recent review article.[13]

In the present work, a symmetrical TMeQ[6] [8] was selected as a ligand, and coordination of TMeQ[6] with a series of Ln^{3+} under different conditions was investigated using single X-ray diffraction and isothermal titration calorimetry (ITC). Interaction of TMeQ[6] with Ln^{3+} under neutral conditions and using two different interaction ratios gave rise to three isomorphous groups, in contrast to the use of acidic (HCl) conditions which yielded only two isomorphous groups. In neutral water using a 1:10 molar ratio of TMeQ[6] to Ln^{3+} cations, TMeQ[6] coordinated with La^{3+} and Ce^{3+} cations to form a simple 1:1 complex over an extended period (~40 days), whereas TMeQ[6] interacted with the remaining Ln^{3+} to form adducts of TMeQ[6] with aqua complexes of Ln^{3+} cations within 1 day; the exception was products containing either Pr^{3+} and Nd^{3+} which required 2 weeks. In neutral water with a 1:2 molar ratio of TMeQ[6] to Ln^{3+} cations, TMeQ[6] coordinated with La^{3+}, Ce^{3+}, Pr^{3+} and Nd^{3+}, and formed TMeQ[6]-Ln^{3+} triple-decker sandwiches within 1 day, whereas products with the remaining Ln^{3+} ions were characteristic of TMeQ[6] adducts with aqua complexes of Ln^{3+} cations and formed within 6 h. In acidic solution (6 M HCl) at a 1:4 molar ratio of TMeQ[6] to Ln^{3+} cations, TMeQ[6] coordinated with Pr^{3+}, Nd^{3+}, Sm^{3+} and Eu^{3+}, and formed TMeQ[6]-Ln^{3+} molecular capsules within 1 day, whereas products with the remaining heavier Ln^{3+} such as Gd^{3+}, Tb^{3+}, Dy^{3+}, Ho^{3+}, Er^{3+}, Tm3^{+}, Yb^{3+}, and Lu^{3+} were characteristic of TMeQ[6] adducts with aqua complexes of Ln^{3+} and formed over a longer period of time. It should be noted that the interaction of TMeQ[6] with La^{3+}and Ce^{3+} immediately gave rise to precipitation. Such differences in the interaction between TMeQ[6] and Ln^{3+} cations could be used for the isolation of heavier Ln^{3+} from their lighter counterparts in neutral solution, and lighter Ln^{3+} from their heavier counterparts in acidic solution, thereby providing a possible method for separating heavy and light Ln^{3+} cations. The three TMeQ[6]-Ln^{3+} interaction systems described above are summarized in Table 1.

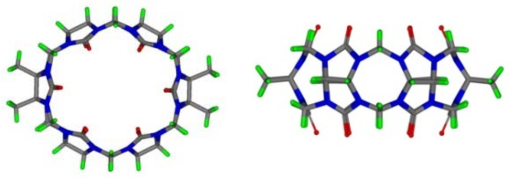


Figure 1. Structure of symmetrical TMeQ[6].

Table 1. The three TMeQ[6]-Ln^{3+} systems characterized in this study.

TMeQ[6]:Ln^{3+} ratio and conditions	Ln^{3+} La·····Lu series and formation time		
1:10 in H_2O	1:1 complexes. La, Ce. 40 day	1:1 adducts. Pr, Nd, Sm. 7 day	Precipitation. Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu. 1 day
1:2 in H_2O	3:2 triple-deckers. La, Ce, Pr, Nd. 1 day	1:1 adducts. Sm, Eu. 1 day	Precipitation Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu. 4 hours
1:4 in HCl (6 M)	Precipitation. La, Ce. 4 hour	1:2 complexes. Pr, Nd, Sm, Eu. 1 day	1:1 adducts. Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu. 15 day

Results and discussion

Description of crystal structures

Cucurbit[*n*]uril (Q[*n*]) and alkyl-substituted cucurbit[*n*]urils (SQ[*n*]s) can interact with Ln^{3+} to form different adducts, simple coordination complexes, and coordination poly-dimensional polymers with supramolecular assemblies.[6g–6p] The interaction or coordination of Q[*n*] molecules with Ln^{3+} is strongly affected by synthetic conditions. TMeQ[6] is much more water-soluble than unsubstituted Q[6], and this allowed for the investigation of its coordination and supramolecular assemblies with Ln^{3+} in neutral aqueous solution. We also evaluated the coordination and supramolecular assemblies of TMeQ[6] with Ln^{3+} in 6 M HCl.

With a molar ratio of TMeQ[6] to Ln^{3+} of 1:10 in a neutral aqueous solution, a simple complex was formed through direct coordination of lighter Ln^{3+} ions with portal carbonyl oxygens of TMeQ[6]. Compound **1** (Figure 2) is a representative example of this isomorphous group. The crystal structure shows a TMeQ[6] molecule coordinated by a single La^{3+} cation at one of the two opening portals. The La^{3+} cation itself is coordinated with nine oxygens (two carbonyl oxygens [O1, O6], five water molecules [O1W, O2W, O3W, O4W, O5W], and two oxygens [O19, O20] from a nitrate anion). The bond distances between La^{3+} cations and the carbonyl oxygen atoms are in the range 2.49–2.54 Å, the distance between La^{3+} and the coordinated water oxygen atoms are 2.49–2.57 Å, and the bond distances between La^{3+} and oxygen atoms from the coordinated nitrate anion are 2.60–2.67 Å. Closer inspection revealed that the portal carbonyl oxygens coordinating the La^{3+} belonged to a dimethyl-substituted glycouril moiety and an unsubstituted glycouril moiety in the TMeQ[6] molecule. The rest of the features of compound **2** in this isomorphous group had a similar structure.

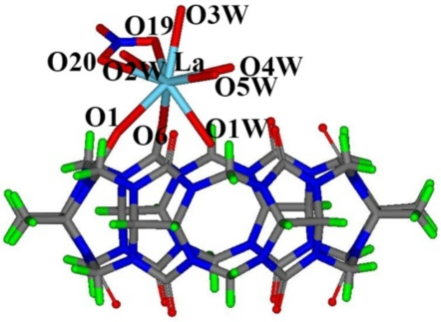


Figure 2. Crystal structure of compound **1** showing the coordination between TMeQ[6] molecules and La^{3+} cations. Solvate water molecules and nitrate anions are omitted for clarity.

TMeQ[6] interacted with the remaining Ln^{3+} cations to form powders containing TMeQ[6] and Ln^{3+} within 1 day, except for Pr^{3+}, Nd^{3+} and Sm^{3+} which required 2 weeks. Compound **3** is an adduct formed through hydrogen bonding between portal carbonyl oxygens and coordinated water molecules of the $[Pr(H_2O)_8]^{3+}$ aqua complex and is a representative example of this isomorphous group. The crystal structure of the adduct revealed the formation of an alternative TMeQ[6] and $[Pr(H_2O)_8]^{3+}$ supramolecular chain (Figure 3a) in which each $[Pr(H_2O)_8]^{3+}$ complex interacts with two TMeQ[6] molecules, and in turn, each TMeQ[6] molecule is sandwiched between two $[Pr(H_2O)_8]^{3+}$ complexes through hydrogen bonding of the coordinated water molecules and six portal carbonyl oxygens (O1W^{a}, O3W^{a}, O5W^{a}, O7W^{a} with O1^{a}, O2^{a}, O3^{a}, O4^{a}, O5^{a}, O6^{a}; O1W^{b}, O3W^{b}, O5W^{b}, O7W^{b} with O1^{b}; O2^{b}, O3^{b}, O4^{b}, O5^{b} and O6^{b}; Figure 3b, c). The distances between the Pr^{3+} cation and coordinated water oxygen atoms are in the range 2.50–2.62 Å, and the bond distances between the coordinated water oxygens with portal carbonyl oxygens of TMeQ[6] are in the range 2.40–2.76 Å. The remainder of the structural features of **4** and **6** were shared by the other structures in this isomorphous family. TMeQ[6] interacted with the heavier Ln^{3+} cations such as Gd^{3+}, Tb^{3+}, Dy^{3+}, Ho^{3+}, Er^{3+}, Tm3+, Yb^{3+} and Lu^{3+}, and formed powders within a short period of time that were not suitable for single crystal X-ray crystallography (Figure S1, see ESI†).

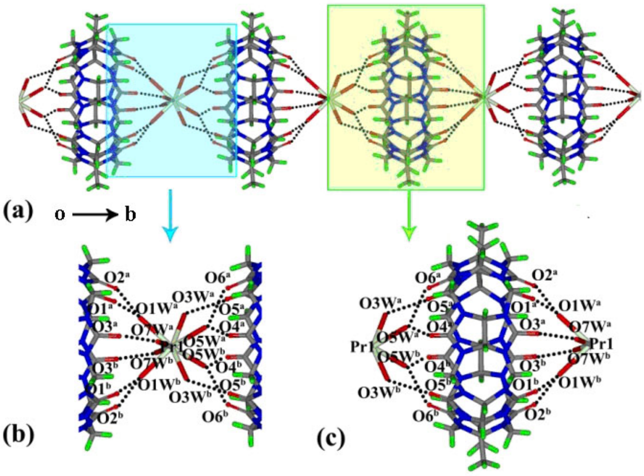


Figure 3. Crystal structure of compound **3**: (a) supramolecular chain of alternating $[Pr(H_2O)_8]^{3+}$ complexes and TMeQ[6] molecules; (b) adduct of TMeQ[6] molecules with a $[Pr(H_2O)_8]^{3+}$ complex; (c) interaction of TMeQ[6] complexes and Pr^{3+} cations. Solvate water molecules and chloride anions are omitted for clarity.

When the molar ratio of TMeQ[6] to Ln^{3+} in neutral aqueous solution was 1:2, four triple-decker sandwich complexes of TMeQ[6] were formed with the four lightest Ln^{3+} cations (La^{3+}, Ce^{3+}, Pr^{3+}, and Nd^{3+}). Compound **1'** containing a La^{3+} cation is a representative example of this isomorphous group (Figure 4). The crystal structure shows three TMeQ[6] molecules linked by two La^{3+} cations, and each La^{3+} cation is itself coordinated by nine oxygens (five carbonyl oxygens O1, O2, O6, O13 and O14 from neighboring TMeQ[6] molecules, and four coordinated water molecules O1W, O2W, O3W and O4W). The bond distances between La^{3+} cations and carbonyl oxygen atoms are in the range 2.46–2.55 Å, and the distances between the La^{3+} cation and coordinated water oxygen atoms are 2.45–2.77 Å. Similarly, the La^{3+} cation preferred to coordinate with the portal carbonyl oxygen belonging to the dimethyl substituted glycouril moiety. The other three isomorphous compounds in this group (**2'**, **3'** and **4'**) possessed similar structural features. Moreover, compound **7'**, an adduct of TMeQ[6] with the aqua complex of Ln^{3+}, exhibited similar structural features to those in the first isomorphous group.

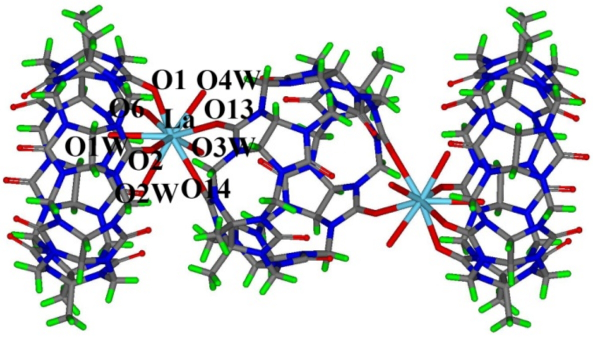


Figure 4. X-ray crystal structure of compound **1'**: (a) coordination between TMeQ[6] molecules and La^{3+} cations. Solvate water molecules and nitrate anions are omitted for clarity.

When the molar ratio of TMeQ[6] to Ln^{3+} was 1:4 in 6 M HCl the interaction of TMeQ[6] with Ln^{3+} resulted in the formation of molecular capsules when Ln^{3+} was Pr^{3+}, Nd^{3+} or Sm^{3+}. A complex of TMeQ[6] with a Pr^{3+}cation (compound **3''**; Figure 5a) is a representative example of this isomorphous group, and the crystal structure shows both portals of the TMeQ[6] molecule coordinated with one Pr^{3+} cation. The Pr^{3+} cation is coordinated by eight atoms (three carbonyl oxygens $O2^a$, $O2^b$ and O3, four water molecules O1W, $O2W^a$, $O2W^b$ and O3W, and an included chlorine anion Cl1. The bond distances between the Pr^{3+} cation and the carbonyl oxygen atoms are in the range 2.45–2.47 Å, the distances between the Pr^{3+} cation and the coordinated water oxygen atoms are in the range 2.44–2.84 Å, and the bond distance between the Pr^{3+} cation and chlorine is 2.83 Å. TMeQ[6]/Pr^{3+} molecular capsules interacted with each other through hydrogen bonding between the coordinated water molecules ($O2W^a$ and $O2W^b$) and the portal carbonyl oxygens ($O1^a$, $O1^b$, O4; Figure 5b and c). It is known that the Pr^{3+} cation coordinates with the portal carbonyl oxygen of the two dimethyl substituted glycouril moieties, due to the electron donating effect of the alkyl-substituted group, such as dimethyl.[27] The other three isomorphous compounds **4''** and **6''** exhibited similar conformations. TMeQ[6] interacted with the heavier Ln^{3+} and formed a series of adducts (**8''**–**15''**), which were isomorphous and shared similar structural features with the aforementioned compounds. It should be noted that TMeQ[6] interacted with La^{3+} and Ce^{3+} cations and rapidly formed solid powders that were not suitable for single crystal X-ray analysis.

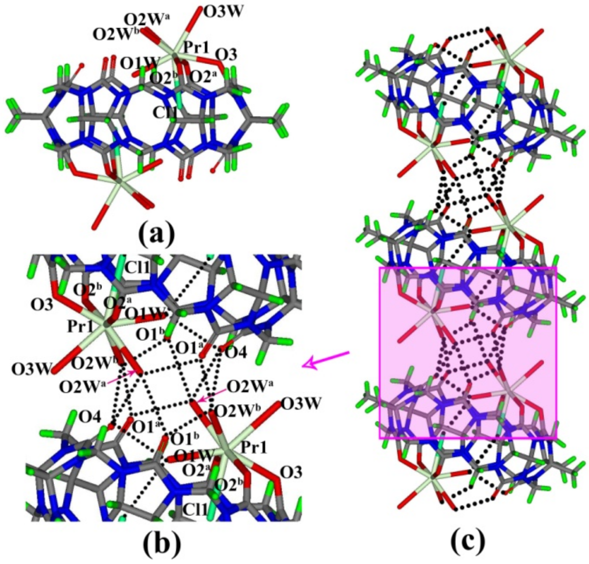


Figure 5. Crystal structure of compound **3''**: (a) coordination between a TMeQ[6] molecule and Pr^{3+} cations; (b and c) interactions between TMeQ[6] molecular capsules through hydrogen bonding. Solvate water molecules and chloride anions are omitted for clarity.

Isothermal Titration Calorimetry (ITC)

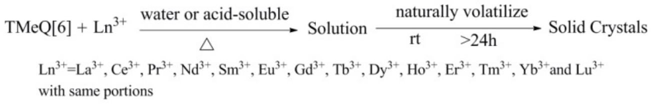
Single crystal X-ray diffraction can be performed to investigate the interactions occurring between TMeQ[6] molecules and Ln^{3+} ions in the solid state. Spectroscopy and spectral analysis are generally not suitable for examining the interactions of Q[*n*]s with metal ions or their complexes in solution. ITC is a quantitative technique for determining dynamic parameters such as association constants (K), enthalpy changes (ΔH), and binding stoichiometry (n) of interactions between two or more molecules in solution. In the present work, the results of ITC showed that the K values for the interactions between TMeQ[6] with Ln^{3+} gradually decreased with increasing atomic number, suggesting that lighter Ln^{3+} cations have a higher affinity for the portal carbonyl oxygens of TMeQ[6] than the heavier Ln^{3+} cations. In particular, the binding stoichiometry (n) for the first three light Ln^{3+} cations (La, Ce, and Pr) was close to 1, whereas that of the remaining Ln^{3+} cations was close to 0.5, suggesting that TMeQ[6] and Ln^{3+} have different 'interaction models' in neutral water. Although we do not know the detailed reasons, the 4f orbitals exhibit poor shielding of the nuclear charge leading to a small monotonic contraction of the ionic radii of the Ln^{3+} ions with increasing atomic number. The radii decrease from 1.03 Å for La^{3+} to 0.86 Å for Lu^{3+}. The differences in the interaction of the individual Ln^{3+} ions with a selected Q[*n*], such as TMeQ[6] in this case could reflect the size differences between these ions. From the initial ITC measurements, changes in the Gibbs free energy (ΔG) and entropy (ΔS) may be determined using the following equation: $\Delta G_{standard} = -RT\ln K = \Delta H_{standard} - T\Delta S_{standard}$, where R is the gas constant and T is the absolute temperature. Generally, $T\Delta S$ values are larger than ΔH, suggesting that $T\Delta S$ is the main driving force of the reaction between TMeQ[6] and Ln^{3+} that results in the formation of complexes or adducts (Table 2, Figure S2, see ESI†).

Table 2. Association constants of related Ln^{3+}– TMeQ[6] interaction products at 277.15 K.

Experiment	K (1/M)	ΔH (kJ/mol)	n	TΔS(kJ/mol)
La	$(4.55 \pm 0.6)\times10^4$	-10.96 ± 0.2	0.858 ± 0.01	13.75
Ce	$(4.07 \pm 0.8)\times10^4$	-8.616 ± 0.3	0.876 ± 0.02	15.84
Pr	$(3.95 \pm 0.6)\times10^4$	-6.720 ± 0.2	0.894 ± 0.02	17.67
Nd	$(2.84 \pm 0.7)\times10^4$	-5.187 ± 0.5	0.511 ± 0.04	18.44
Sm	$(2.74 \pm 0.6)\times10^4$	-8.341 ± 0.6	0.526 ± 0.03	15.21
Eu	$(2.64 \pm 0.4)\times10^4$	-9.730 ± 0.6	0.475 ± 0.02	13.73
Gd	$(2.50 \pm 0.6)\times10^4$	-9.576 ± 0.9	0.457 ± 0.03	13.76
Tb	$(2.43 \pm 0.5)\times10^4$	-8.874 ± 0.8	0.462 ± 0.03	14.40
Dy	$(2.33 \pm 0.4)\times10^4$	-8.242 ± 0.8	0.430 ± 0.03	14.93
Ho	$(2.28 \pm 0.4)\times10^4$	-5.987 ± 0.6	0.404 ± 0.03	17.14
Er	$(2.10 \pm 0.6)\times10^4$	-6.707 ± 0.9	0.421 ± 0.04	16.23
Tm	$(1.68 \pm 0.5)\times10^4$	-4.235 ± 0.6	0.537 ± 0.05	18.18
Yb	$(1.59 \pm 0.4)\times10^4$	-2.864 ± 0.3	0.517 ± 0.04	19.43
Lu	$(1.42 \pm 0.4)\times10^4$	-5.548 ± 0.7	0.528 ± 0.05	16.48

Energy Dispersive spectroscopy (EDS)

As previously mentioned, different Q[*n*]s can selectively interact with a series of Ln^{3+} cations and form different products that are strongly dependent on the synthetic conditions employed. Using such differences, varying strategies for the isolation of Ln^{3+} in solution can be established. For example, a previous study revealed that in the presence of $[CdCl_4]^{2-}$ or $[ZnCl_4]^{2-}$, unsubstituted Q[6] could be used to isolate the first four light Ln^{3+} ions (La, Ce, Pr, Nd) from their heavier counterparts. A recent study demonstrated that in the presence of $Cd(NO_3)_3$, *o*-TMeQ[6] can coordinate with most lanthanide cations to form solid crystals, but not with the lightest Ln^{3+} ions (La, Ce, Pr), which remain in solution. Similarly, *o*-TMeQ[6]-Ln^{3+}-$Cd(NO_3)_3$ systems can separate heavier Ln^{3+} cations from lighter Ln^{3+} cations by forming solid crystals. The alkyl-substituted TMeQ[6] is both water- and acid-soluble, and interactions with lanthanide cations can be investigated in neutral or acidic (e.g., 6 M HCl) conditions (See Scheme 1). Co-precipitation experiments in which all Ln^{3+} cations exist in the same proportions in water and in 6 M HCl revealed that TMeQ[6]-Ln^{3+}-H_2O systems can separate heavier Ln^{3+} cations from lighter lanthanides by forming solid crystals regardless of whether the molar ratio of TMeQ[6] to Ln^{3+} was 1:10 or 1:2 (see Figure 6a). Similarly, TMeQ[6]-Ln^{3+}-HCl systems can separate lighter Ln^{3+} cations from heavier lanthanides by forming solid crystals (see Figure 6b).



Scheme 1. TMeQ[6]-Ln^{3+}-H_2O systems with the same proportion of $Ln^{3+}$and TMeQ[6]-Ln^{3+}-HCl(6 M) systems with the same proportion of Ln^{3+}.

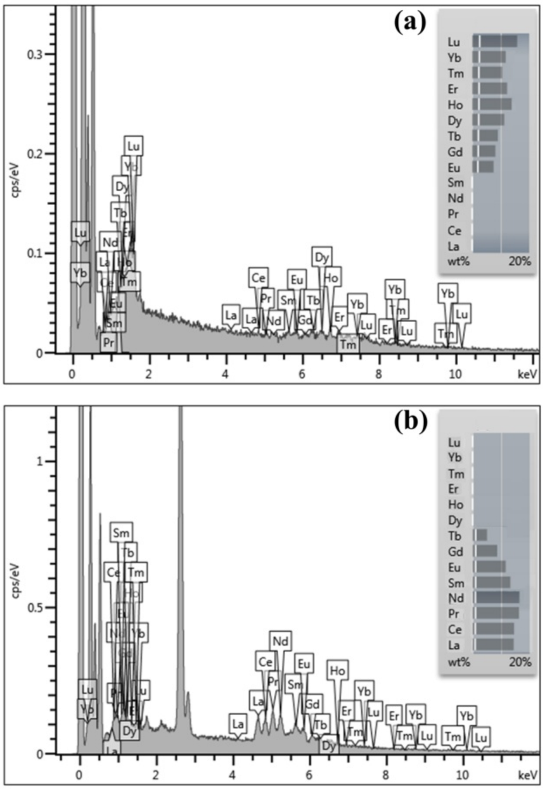


Figure 6. EDS of co-precipitation from (a) a TMeQ[6]-Ln^{3+}-H_2O systems with the same proportion of Ln^{3+}; (b) a TMeQ[6]-Ln^{3+}-HCl(6 M) systems with the same proportion of Ln^{3+}.

$$\text{TMeQ[6]} + Ln^{3+}_{light}\text{-}Ln^{3+}_{heavy} \xrightarrow[\triangle]{\text{water}} \text{Solution} \xrightarrow[\text{rt} \quad >24\text{h}]{\text{naturally volatilize}} \text{Solid Crystals}$$

Ln^{3+}_{light}-Ln^{3+}_{heavy} = La^{3+}-Gd^{3+}, La^{3+}-Dy^{3+}, La^{3+}-Er^{3+}, La^{3+}-Lu^{3+}, Nd^{3+}-Gd^{3+}, Nd^{3+}-Dy^{3+}, Nd^{3+}-Er^{3+}, Nd^{3+}-Lu^{3+}, all in 1:1 Ln^{3+}_{light}:Ln^{3+}_{heavy} ratios

Scheme 2. TMeQ[6] to Ln^{3+} was 1:10 in neutral aqueous solution.

Detailed experiments further confirmed our hypothesis. For example, when the molar ratio of TMeQ[6] to Ln^{3+} was 1:10 in neutral aqueous solution (See Scheme 2), eight typical Ln^{3+}_{light}–Ln^{3+}_{heavy}–TMeQ[6] systems were selected as representatives (Ln^{3+}_{light}–Ln^{3+}_{heavy} = La^{3+}–Gd^{3+}, La^{3+}–Dy^{3+}, La^{3+}–Er^{3+}, La^{3+}–Lu^{3+}, Nd^{3+}–Gd^{3+}, Nd^{3+}–Dy^{3+}, Nd^{3+}–Er^{3+}, Nd^{3+}–Lu^{3+}), all in a 1:1 Ln^{3+}_{light} : Ln^{3+}_{heavy} ratio. EDS results revealed that the crystals from systems with 1:1 Ln^{3+}_{light} : Ln^{3+}_{heavy} ratios contained 80%–100% heavy Ln^{3+} cations (Figure S3, see ESI†), whereas most lighter lanthanides remained in the mother liquor. We also tested a molar ratio of TMeQ[6] to Ln^{3+} of 1:2 in neutral aqueous solution using six typical Ln^{3+}_{light}–Ln^{3+}_{heavy}–TMeQ[6] systems as representative examples (Ln^{3+}_{light}–Ln^{3+}_{heavy} = La^{3+}–Gd^{3+}, La^{3+}–Er^{3+}, La^{3+}–Lu^{3+}, Nd^{3+}–Gd^{3+}, Nd^{3+}–Er^{3+}, Nd^{3+}–Lu^{3+}), all at a 1:1 ratio. EDS showed that these crystals contained 80%–90% heavy lanthanides (Figure S4, see ESI†), whereas the majority of the lighter lanthanides remained in solution. In addition, six typical Ln^{3+}_{heavy}–Ln^{3+}_{light}–TMeQ[6]-HCl systems were selected as representative examples (Ln^{3+}_{heavy}–Ln^{3+}_{light} = Tb^{3+}–Ce^{3+}, Tb^{3+}–Sm^{3+}, Er^{3+}–Ce^{3+}, Er^{3+}–Sm^{3+}, Lu^{3+}–Ce^{3+}, Lu^{3+}–Sm^{3+}), all at a 1:1 ratio. EDS showed that these crystals contained 90%–100% light Ln^{3+} cations (Figure S5, see ESI†), while heavy Ln^{3+} cations remained in the mother liquor. These results suggest that these systems could be effectively used to separate heavy and light Ln^{3+} cations in neutral aqueous solution, and to isolate lighter Ln^{3+} cations from their heavier counterparts under acidic conditions.

Other characteristics of the adducts determined using PXRD, thermal analysis and Fourier transform infrared spectroscopy (FT-IR) are shown in the Electronic supplementary information. PXRD measurements of representative crystals from the four isomorphous groups were compared with simulations, which confirmed that the samples were essentially of a pure crystalline phase (Figure S6–S8, see ESI†). Thermal analysis was performed to generate DSC and TG curves of representative crystals of two isomorphous groups, and this revealed no marked differences between crystals, although they were different from TMeQ[6] complexes (Figure S9–S11, see ESI†). Furthermore, FT-IR spectra showed that the absorption bands of the portal carbonyl of the four isomorphous groups at high-wavelength numbers were different (Figure S12–S14, see ESI†).

Conclusions

In summary, we have investigated the coordination and interaction of TMeQ[6] molecules with a series of Ln^{3+} cations under neutral and acidic solutions with different proportions of TMeQ[6] and Ln^{3+} cations. X-ray diffraction analysis revealed that the structures and properties (e.g., solubility) of the TMeQ[6]/Ln^{3+} complexes and adducts were strongly dependent on the structural features of the lanthanides and on the experimental conditions (e.g., ion dimension, pH, proportion of components in systems) employed. Generally, lighter lanthanides formed complexes with TMeQ[6], presumably due to the larger ionic diameters. In contrast, heavier lanthanides tended to form aqua complexes which formed adducts with TMeQ[6], and this was likely due to the shorter ionic diameters. Generally, the poor shielding of 4f orbitals results in the increase of the nuclear charge and the Ln^{3+} ions have an increased hydrolysis tendency and the hydrolyzed products have a decreased solubility with increasing atomic number. Moreover, the acidic medium prohibited hydrolysis of the lanthanides and subsequent formation of aqua complexes in aqueous solutions, therefore most lanthanide cations formed complexes with TMeQ[6]. Generally, the more acidic the medium, the faster the formation of crystals of complexes or adducts. Importantly, these differences could be used to separate heavier Ln^{3+} cations from their lighter counterparts in neutral solution, and to isolate lighter Ln^{3+} cations from heavier lanthanides in acidic conditions. Further studies aimed towards developing such separation techniques are ongoing in our laboratory.

Experimental

Synthesis: Chemicals including lanthanide nitrates were of reagent grade and were used without further purification. TMeQ[6] was prepared as previously reported.[37] Elemental analyses were carried out using a EURO EA-3000 elemental analyzer. A similar process was used to prepare crystals of related compounds as follows:

(1) $Ln(NO_3)_3\cdot xH_2O$ (0.081 mmol) was dissolved in 2.5 mL neutral water (solution A); TMeQ[6] (10 mg, 0.008 mmol) was dissolved in 2.5 mL neutral water (solution B), added to solution A and stirred. X-ray diffraction-quality crystals were obtained from the solution over a period of hours to months depending on the lanthanide cation present. Crystal colour was also dependent on the lanthanide. To summarize the preparations, $[(C_{40}H_{44}N_{24}O_{12})La(H_2O)_5(NO_3)]\cdot 2(NO_3)\cdot 7(H_2O)$ (**1**) was obtained from $La(NO_3)_3\cdot 6H_2O$ (0.035 g); $[(C_{40}H_{44}N_{24}O_{12})Ce(H_2O)_5(NO_3)]\cdot 2(NO_3)\cdot 7(H_2O)$ (**2**) was obtained from $Ce(NO_3)_3\cdot 6H_2O$ (0.035 g); $[(C_{40}H_{44}N_{24}O_{12})Pr(H_2O)_8]\cdot 4Cl\cdot 13(H_2O)$ (**3**) was obtained from $Pr(NO_3)_3\cdot 6H_2O$ (0.035 g); $[(C_{40}H_{44}N_{24}O_{12})Nd(H_2O)_8]\cdot 4Cl\cdot 19(H_2O)$ (**4**) was obtained from $Nd(NO_3)_3\cdot 5H_2O$ (0.036 g); $[(C_{40}H_{44}N_{24}O_{12})Sm(H_2O)_8]\cdot 4Cl\cdot 12(H_2O)$ (**6**) was obtained from $Sm(NO_3)_3\cdot 6H_2O$ (0.036 g).

(2) $Ln(NO_3)_3\cdot xH_2O$ (0.040 mmol) was dissolved in 1.25 mL neutral water (solution A), TMeQ[6] (25 mg, 0.020 mmol) was dissolved in 1.25 mL neutral water (solution B), and these were mixed and stirred. Crystal colour was again dependent on the lanthanide. To summarize the preparations, $[(C_{120}H_{132}N_{72}O_{36})La_2(H_2O)_8]\cdot 4(NO_3)\cdot 20(H_2O)$ (**1’**) was obtained from $La(NO_3)_3\cdot 6H_2O$ (0.018 g); $[(C_{120}H_{132}N_{72}O_{36})Ce_2(H_2O)_8]\cdot 2(NO_3)\cdot 10Cl\cdot 19(H_2O)$ (**2’**) was obtained from $Ce(NO_3)_3\cdot 6H_2O$ (0.018 g); $[(C_{120}H_{132}N_{72}O_{36})Pr_2(H_2O)_8]\cdot 6Cl\cdot 18(H_2O)$ (**3’**) was obtained from $Pr(NO_3)_3\cdot 6H_2O$ (0.018 g); $[(C_{120}H_{132}N_{72}O_{36})Nd_2(H_2O)_8]\cdot 2(NO_3)\cdot 10Cl\cdot 14(H_2O)$ (**4’**) was obtained from $Nd(NO_3)_3\cdot 5H_2O$ (0.018 g); $[(C_{40}H_{44}N_{24}O_{12})Eu(H_2O)_8]\cdot 4Cl\cdot 15(H_2O)$ (**7’**) was obtained from $Eu(NO_3)_3\cdot 6H_2O$ (0.018 g).

(3) $Ln(NO_3)_3\cdot xH_2O$ (0.080 mmol) was dissolved in 1.25 mL 6 M HCl (solution A), TMeQ[6] (25 mg, 0.020 mmol) was dissolved in 1.25 mL 6 M HCl (solution B), and these were mixed and stirred. Crystal colour was again dependent on the lanthanide. To summarize the preparations, $[(C_{40}H_{44}N_{24}O_{12})Pr_2(H_2O)_8Cl_2]\cdot 6Cl\cdot 7(H_2O)$ (**3’’**) was obtained from $Pr(NO_3)_3\cdot 6H_2O$ (0.035 g); $[(C_{40}H_{44}N_{24}O_{12})Nd_2(H_2O)_4Cl_2]\cdot 6Cl\cdot 3(H_2O)$ (**4’’**) was obtained from $Nd(NO_3)_3\cdot 5H_2O$ (0.036 g); $[(C_{40}H_{44}N_{24}O_{12})Sm_2(H_2O)_4Cl_6]\cdot 8(H_2O)$ (**6’’**) was obtained from $Sm(NO_3)_3\cdot 6H_2O$ (0.036 g); $[(C_{40}H_{44}N_{24}O_{12})Gd(H_2O)_8]\cdot 6Cl\cdot 6(H_2O)$ (**8’’**) was obtained from $Gd(NO_3)_3\cdot 6H_2O$ (0.037g); $[(C_{40}H_{44}N_{24}O_{12})Tb(H_2O)_8]\cdot 3Cl\cdot 10(H_2O)$ (**9’’**) was obtained from $Tb(NO_3)_3\cdot 6H_2O$ (0.037 g); $[(C_{40}H_{44}N_{24}O_{12})Dy(H_2O)_8]\cdot 4Cl\cdot 10(H_2O)$ (**10’’**) was obtained from $Dy(NO_3)_3\cdot 6H_2O$ (0.037 g); $[(C_{40}H_{44}N_{24}O_{12})Ho(H_2O)_6Cl_2]\cdot 2Cl\cdot 2(H_2O)$ (**11’’**) was obtained from $Ho(NO_3)_3\cdot 5H_2O$ (0.036 g); $[(C_{40}H_{44}N_{24}O_{12})Er(H_2O)_6Cl_2]\cdot 2Cl\cdot 3(H_2O)$ (**12’’**) was obtained from $Er(NO_3)_3\cdot 5H_2O$ (0.037 g); $[(C_{40}H_{44}N_{24}O_{12})Tm(H_2O)_6Cl_2]\cdot 2Cl\cdot 2(H_2O)$ (**13’’**) was obtained from $Tm(NO_3)_3\cdot 5H_2O$ (0.036 g); $[(C_{40}H_{44}N_{24}O_{12})Yb(H_2O)_6Cl_2]\cdot 2Cl$ (**14’’**) was obtained from $Yb(NO_3)_3\cdot 5H_2O$ (0.036 g); $[(C_{40}H_{44}N_{24}O_{12})Lu(H_2O)_6Cl_2]\cdot 2Cl\cdot 2(H_2O)$ (**15’’**) was obtained from $Lu(NO_3)_3\cdot 6H_2O$ (0.038 g).

In order to investigate the whole system, the number of compounds increased with increasing atomic number of the Ln^{3+} series. Thus, compounds **1**–**4** and **6**–**15** corresponded to La–Nd and Sm–Lu, respectively.

X-ray crystallography: A suitable single crystal (~0.2 × 0.2 × 0.1 mm^3) was taken up in paraffin oil and mounted on a Bruker SMART Apex II CCD diffractometer equipped with a graphite monochromator Mo-K_α (λ = 0.71073 Å, μ = 0.828 mm^{-1}) radiation source operating in the ω-scan mode with a nitrogen cold stream at –50°C. Data were corrected for Lorentz and polarization effects using SAINT, and semi-empirical absorption corrections based on equivalent reflections were also applied using SADABS. The structures were elucidated by direct methods, and were refined using the full-matrix least-squares method using F^2 and SHELXS-97. All non-hydrogen atoms were refined anisotropically. Carbon-bound hydrogen atoms were introduced at calculated positions, and were treated as riding atoms with an isotropic displacement parameter equal to 1.2 times that of the parent atom. Most of the water molecules in the compounds were omitted using the SQUEEZE option of the PLATON program. Analytical expressions for neutral-atom scattering factors were employed, and anomalous dispersion corrections were incorporated. Details of the crystal parameters, data collection conditions, and refinement parameters for the 21 compounds are summarized in Table S1, see ESI†. In addition, the crystallographic data for the reported structures were deposited at the Cambridge Crystallographic Data Centre with the following supplementary publication numbers: CCDC-1038158 (**1**), 1038166 (**2**), 1038169 (**3**), 1038172 (**4**), 1038174 (**6**); CCDC-1038157 (**1’**), 1038165 (**2’**), 1038168 (**3’**), 1038171 (**4’**); 1038175 (**7’**); CCDC-1038167 (**3’’**), 1038170 (**4’’**), 1038173 (**6’’**), 1038176 (**8’’**), 1038177 (**9’’**), 1038159 (**10’’**), 1038160 (**11’’**), 1038161 (**12’’**), 1038162 (**13’’**), 1038163 (**14’’**), 1038164 (**15’’**). Data can be obtained free of charge at http://www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre (12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033).

Isothermal titration calorimetry: Microcalorimetric experiments were performed using a Nano ITC 2G isothermal titration calorimeter (TA, USA). Each experiment consisted of 25 consecutive injections (10 μL) of 1 mM $Ln(NO_3)_3\cdot 6H_2O$ or $Ln(NO_3)_3\cdot 5H_2O$ into a microcalorimetric reaction cell containing 1.3 mL of 0.1 mM TMeQ[6] at 277.15 K. The heat of reaction was corrected for the heat of dilution of the cell solution which was determined in separate experiments. All solutions were degassed by sonication prior to the titration experiment. Computer simulations (curve fitting) were performed using the Nano ITC Analyze Software.

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Notes and references

‡ Electronic supplementary information (ESI) available: crystallographic data, PXRD, thermal analysis and Fourier transform infrared spectroscopy (FT-IR). For the ESI and crystallographic data in CIF See DOI: 10.1039/x0xx00000x

1. a) S. Aime, M. Botta, M. Fasano and E. Terreno, *Chem. Soc. Rev.,* 1998, **27**, 19-29; b) V. Comblin, D. Gilsoul, M. Hermann, V. Humblet, V. Jacques, M. Mesbahi, C. Sauvage and J. F. Desreux, *Coord. Chem. Rev.,* 1999, **185–186**, 451-470; c) M. Elhabiri, R. Scopelliti, J. C. G. Bunzli and C. Piguet, *J. Am. Chem. Soc.,* 1999, **121**, 10747-10762; d) J. C. G. Bunzli and C. Piguet, *Chem. Soc. Rev.,* 2005, **34**, 1048-1077; e) P. Caravan, J. J. Ellison, T. J. McMurry and R. B. Lauffer, *Chem. Rev.,* 1999, **99**, 2293-2352; f) R. E. Mewis and S. J. Archibald, *Coord. Chem. Rev.,* 2010, **254**, 1686-1712; g) M. D. Ward, *Coord. Chem. Rev.,* 2007, **251**, 1663-1677; h) T. Gunnlaugsson, M. Glynn, G. M. Tocci, P. E. Kruger and F. M. Pfeffer, *Coord. Chem. Rev.,* 2006, **250**, 3094-3117; i) S. V. Eliseeva and J. C. G. Bunzli, *Chem. Soc. Rev.,* 2010, **39**, 189-227; j) J. D. Xu, T. M. Corneillie, E. G. Moore, G. L. Law, N. G. Butlin and K. N. Raymond, *Chem. Soc. Rev.,* 2011, **133**, 19900-19910; k) C. M. G. dos Santos, A. J. Harte, S. J. Quinn and T. Gunnlaugsson, *Coord. Chem. Rev.,* 2008, **252**, 2512-2527; l) S. Liu, *Chem. Soc. Rev.,* 2004, **33**, 445-461; m) H. L. C. Feltham and S. Brooker, *Coord. Chem. Rev.,* 2014, **276**, 1-33. n) J. W. Sharples and D. Collison, *Coord. Chem. Rev.,* 2014, **260**, 1-20.
2. a) Q. Sun, H. M. Luo and S. Dai, *Chem. Rev*., 2012, 112, 2100-2128; b) Zhao, M. Wong, C. Mao, T. X. Trieu, J. Zhang, P. Y. Feng and X. Bu, *J. Am. Chem. Soc*., 2014, 136, 12572-12575.
3. a) Y. Lin, C. Y. Chin, H. L. Huang, W. Y. Huang, M. J. Sie, L. H. Huang, Y. H. Lee, C. H. Lin, K. H. Lii, X. Bu and S. L. Wang, *Science*., 2013, **339**, 811-883; b) He, G. J. Cao, S. T. Zheng and G. Y. Yang, *J. Am. Chem. Soc*., 2009, **131**, 15588-15589.
4. a) H. Furukawa, K. E. Cordova, M. O'Keeffe and O. M. Yaghi, *Science*., 2013, **341**, 1230444-1230412; b) H. C. Zhou, J. R. Long and O. M. Yaghi, *Chem. Rev*., 2012, **112**, 673-674; c) J. J. Perry IV, J. A. Perman and M. J. Zaworotko, *Chem. Soc. Rev*., 2009, **38**, 1400-1417; d) E. R. Parnham and R. E. Morris, *Acc. Chem. Res*., 2007, **40**, 1005-1013; e) S. M. Cohen, *Chem. Rev*., 2012, **112**, 970-1000.
5. a) W. A. Freeman, W. L. Mock and N. Y. Shih, *J. Am. Chem. Soc*., 1981, **103**, 7367-7368; b) J. Kim, I. S. Jung, S. Y. Kim, E. Lee, J. K. Kang, S. Sakamoto, K. Yamaguchi and K. Kim, *J. Am. Chem. Soc*., 2000, **122**, 540-541; c) A. I. Day and A. P. Arnold, *Method for synthesis cucurbiturils*. WO 0068232 2000, 8; d) A. I. Day, R. J. Blanch, A. P. Arnold, S. Lorenzo, G. R. Lewis and I. Dance, *Angew. Chem., Int. Ed.,* 2002, **41**, 275-277; e) X. J. Cheng, L. L. Liang, K. Chen, N. N. Ji, X.; Xiao, J. X. Zhang, Y. Q. Zhang, S. F. Xue, Q. J. Zhu, X. L. Ni and Z. Tao, *Angew. Chem., Int. Ed*. 2013, **52**, 7252-7255.
6. a) K. Kim, *Chem. Soc. Rev*., 2002, **31**, 96-107; b) J. W. Lee, S. Samal, N. Selvapalam, H. J. Kim and K. Kim, *Acc. Chem. Res*., 2003, **36**, 621-630; c) J. Lagona, P. Mukhopadhyay, S. Chakrabarti and L. Isaacs, *Angew. Chem*., *Int. Ed*., 2005, **44**, 4844-4870; d) K. Kim, N. Selvapalam, Y. H. Ko, K. M. Park, D. Kim and J. Kim, *Chem. Soc. Rev.,* 2007, **36**, 267-279; e) L. Isaacs, *Chem. Commun*., 2009, 619-629; f) R. N. Dsouza, U. Pischel and W. M. Nau, *Chem. Rev.,* 2011, **111**, 7941-7980; g) B. C. Pemberton, R. Raghunathan, S. Volla and J. Sivaguru, *Chem. -Eur. J.,* 2012, **18**, 12178-12190; h) E. Masson, X. X. Ling, R. Joseph, L. Kyeremeh-Mensah and X. Y. Lu, *RSC Adv*. 2012, **2**, 1213-1247; i) Y. L. Liu, H. Yang, Z. Q. Wang and X. Zhang, *Chem. Asian J*., 2013, **8**, 1626-1632; j) V. Sindelar, S. Silvi, S. E. Parker, D. Sobransingh and A. E. Kaifer, *Adv. Funct. Mater*., 2007, **17**, 694-701; k) W. Wang, A and E. Kaifer, *Adv. Polym. Sci*., 2009, **222**, 205-235; l) S. Gadde and A. E. Kaifer, *Cur. Org. Chem*., 2011, **15**, 27-38; m) V. Montes-Garcia, J. Perez-Juste, I. Pastoriza-Santos and L. M. Liz-Marzan, *Chem. -Eur. J.* 2014 , **20**, 10874-10883; n) L. Isaacs, *Acc. Chem. Res.* 2014 , **47**, 2052-2062; o) C. Bohne, *Chem. Soc. Rev*. 2014 , **43**, 4037-4050; p) J. Vazquez, P. Remon, R. N. Dsouza, A. I. Lazar, J. F. Arteaga, W. M. Nau, U. Pischel, *Chem. -Eur. J*., 2014, **20**, 9897-9901.
7. a) M. N. Sokolov, D. N. Dybtsev and V. P. Fedin, *Russ. Chem. Bull. Int. Ed*., 2003, **52**, 1041-1060; b) O. A. Gerasko, M. N. Sokolov and V. P. Fedin, *Pure Appl. Chem*., 2004, **76**, 1633-1646; c) V. P. Fedin, *Russ. J. Coordin. Chem*., 2004, **30**, 151-158; d) J. Lü, J. X. Lin, M. N. Cao and R. Cao, *Coord. Chem. Rev*., 2013, **257**, 1334-1356; e) X. L. Ni, X. Xiao, H. Cong, L. L. Liang, K. Chen, X. J. Cheng, N. N. Ji, Q. J. Zhu, S. F. Xue and Z. Tao, *Chem. Soc. Rev*., 2013, **42**, 9480-9508; f) X. L. Ni, X. Xiao, H. Cong, Q. J. Zhu, S. F. Xue and Z. Tao, *Acc. Chem. Res*., 2014, **47**, 1386-1395.
8. Y. J. Zhao, S. F. Xue, Q. J. Zhu, Z. Tao, J. X. Zhang, Z. B. Wei, L. S. Long, M. L. Hu, H. P. Xiao and A. I. Day, *Chin. Sci. Bull.,* 2004, **49**, 1111-1116.
9. D. G. Samsonenko, J. Lipkowski, O. A. Gerasko, A. V. Virovets, M. N. Sokolov, V. P. Fedin, J. G. Platas, R. Hernandez-Molina and A. Mederos, *Eur. J. Inorg. Chem*., 2002, 2380-2388.
10. a) O. A. Gerasko, E. A. Mainicheva, M. I. Naumova, O. P. Yurjeva, A. Alberola, C. Vicent, R. Llusar and V. P. Fedin, *Eur. J. Inorg. Chem.,* 2008, 416-424; b) O. A. Gerasko, E. A. Mainicheva, M. I. Naumova, M. Neumaier, M. M. Kappes, S. Lebedkin, D. R. Fenske and V. P. Fedin, *Inorg. Chem*., 2008, **47**, 8869-8880.
11. a) P. Thuery, *Inorg. Chem.,* 2010, *49*, 9078-9085; b) P. Thuery, *Cryst. Growth Des*., 2012, **12**, 1632-1640; c) P. Thuery, *Inorg. Chem*., 2009, **48**, 825-827.
12. a) K. Chen, Y. F. Hu, X. Xiao, S. F. Xue, Z. Tao, Y. Q. Zhang, Q. J. Zhu and J. X. Liu, *RSC Advances*., 2012, **2**, 3217-3220; b) K. Chen, L. L. Liang, H. J. Liu, Y. Q. Zhang, S. F. Xue, Z. Tao, X. Xiao, Q. J. Zhu, L. F. Lindoy and G. Wei, *CrystEngComm.,* 2012, **14**, 7994-7999; c) B. X. Han, C. Z. Wang, K. Chen, X. Xiao, Z. Tao, S. F. Xue, Y. Q. Zhang and Q. J. Zhu, *CrystEngComm*., 2014, **16**, 1615-1619; d) Y. Zhao, L. L. Liang, K. Chen, T. Zhang, X. Xiao, Y. Q. Zhang, Z. Tao, S. F. Xue and Q. J. Zhu, *CrystEngComm*., 2013, **15**, 7987-7998; e) J. J. Zhou, X. Yu, Y. C. Zhao, X. Xiao, Y. Q. Zhang, S. F. Xue, Z. Tao, J. X. Liu and Q. J. Zhu, *CrystEngComm*., 2014, **16**, 10674-10680; f) L. L. Liang, X. L. Ni, Y. Zhao, K. Chen, X. Xiao, Y. Q. Zhang, C. Redshaw, Q. J. Zhu, S. F. Xue and Z. Tao, *Inorg. Chem*., 2013, **52**, 1909-1915.
13. X. L. Ni, S. F. Xue, Z. Tao, Q. J. Zhu, L, F. Lindoy and G. Wei, *Coord. Chem. Rev*., 2015, **287**, 89-113.