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ORIGINAL ARTICLE

Synthesis and cation complexation of *p-tert*-butyl-calix[4]arene bearing two 8-hydroxyquinoline units

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Abstract

A new *p-tert*-butyl-calix[4]arene receptor containing two 8-hydroxyquinoline unit was prepared and its complexing properties toward lanthanides ions were investigated in acetonitrile by means of UV/vis spectrophotometry and conductivity methods. The stoichiometry of the formed complexes and their stability constants were also determined.

Keywords Calixarene · Complexation · Stability constant · UVvis spectrophotometry

Introduction

Calixarenes have been of great interest in the field of supramolecular chemistry for over 20 years [1, 2]. They can be readily functionalized by numerous selective procedures on the phenolic or phenyl units and are available not only in the calix[4]arene series [3, 4], but also calix[6]arenes [5, 6], calix[5]arenes [7, 8] and calix[8]arenes [9, 10]. Calixarenes can take a variety of conformational forms. For example, calixarene can be locked into one of four kinds of conformers [11–13], which are cone, partial-cone, 1,2-alternate, and 1,3-alternate conformations. 8-Hydroxyquinoline as a coordinating substituent has been previously introduced onto a calix[4]arene via ether linkages to give a bis(8-hydroxyquinoline)calix[4]arene derivative, exhibiting luminescence and energy transfer properties [14]. In this study, we report the synthesis of *p-tert*-calix[4]arene bearing 8-hydroxyquinoline, **3**, and its complexation with lanthanide ions.

Results and discussion

As shown in Scheme 1, ligand **3** was synthesized in three steps from *p-tert*-butylcalix[4]arene. Treatment of the calizarene with $Cl(CH_2)_3CN$ in the presence of K_2CO_3 [15] gave the dicyanopropoxy-*p-tert*-butylcalix[4]arene (**1**) as a white powder in 94% yield. The reduction of the obtained dicyanopropoxy derivative using borane gave calixarene (**2**) bearing 4-aminobutoxy substituents in 90% yield. Coupling calixarene (**2**) with 7-carboxy-8-hydroxyquinoline using DMAP and HBTU in CH_2Cl_2 provided **3** in a yield of 67%. The calix[4]arene unit having the cone conformation was deducted from its ^1H NMR spectrum in $CDCl_3$, as shown by the presence of characteristic AB systems at 3.30 and 4.24 ppm ($J = 13$ Hz) for the $ArCH_2Ar$ protons of the macrocycle. The formation of the amido function was deduced from the presence of a triplet corresponding to the CONH protons. Two singlets (0.94 and 1.30 ppm, 6.78 and 7.07 ppm) in an integration ratio 18:4 were attributed to the $–C(CH_3)_3$ and ArH and triplets at 3.98 ppm to the $ArOCH_2$ groups of the calix[4]arene unit.

The stability constants (β_{xy}) for lanthanoids (La^{3+}, Nd^{3+}, Eu^{3+}, Gd^{3+}, and Yb^{3+}) with calixarene (**3**) being the concentration ratio $[M_xL_y^{xn+}]/[M^{n+}]^x[L]^y$ (where M^{n+} = metal ion and L = ligand **3**) were determined in acetonitrile by UV/vis absorption spectrophotometry at 25 °C.

The spectra of the different concentrations of lanthanum perchlorate with the ligand **3** (at 2.5×10^{-5} mol L^{-1}) in acetonitrile were recorded between 220 and 320 nm, with the ionic strength maintained by Et_4NClO_4 (0.01 mol L^{-1}) (Fig. 1).The formed species in solution and the logarithms

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Dedicated to Prof. Karsten Gloe on the occasion of his 70th birthday.

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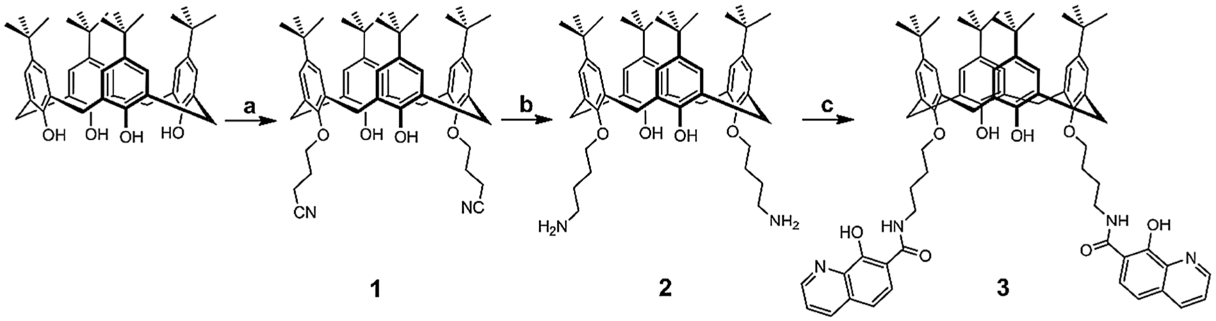

Scheme 1 Synthesis of **3**: **a** K_2CO_3, $Cl(CH_2)_3CN$, acetonitrile, **b** BH_3, THF, **c** DMAP, HBTU, 7-carboxy-8-hydroxyquinoline

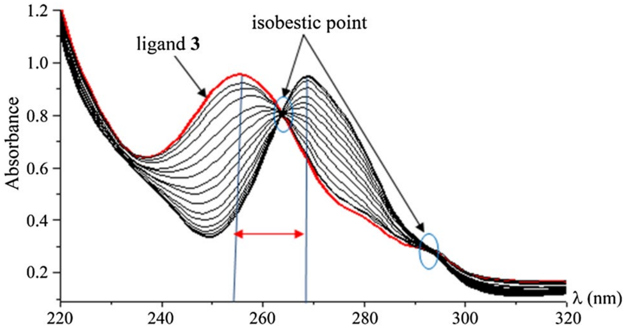

Fig. 1 UV/vis absorption spectra on complexation of La $(ClO_4)_3$ with ligand **3** in acetonitrile ($0 \leq R_{M/L} \leq 1.6$) at 25 °C ($C_L = 2.5 \times 10^{-5}$ mol L^{-1})

Table 1 The stability constants ($Log\beta_{ML}$) for lanthanoids cation complexes with ligand **3** in acetonitrile at 25 °C, $I = 10^{-2}$ M

Cations	M:L	$\log\beta_{xy}$
La^{3+}	1:1	5.66 ± 0.07
	1:2	10.22 ± 0.06
Nd^{3+}	1:1	4.71 ± 0.02
	1:2	8.79 ± 0.13
Eu^{3+}	1:1	6.60 ± 0.18
	1:2	12.46 ± 0.25
Gd^{3+}	1:1	6.35 ± 0.09
	1:2	12.74 ± 0.03
Yb^{3+}	1:1	6.28 ± 0.05
	1:2	12.31 ± 0.03

Table 2 Logarithms of stepwise stability constants formed by the ligand **3** and the lanthanoid cations in acetonitrile

Cations	$\log K_{ML}$	
	$\log K_{11}$	$\log K_{12}$
La^{3+}	5.66	4.56
Nd^{3+}	4.71	4.08
Eu^{3+}	6.60	5.86
Gd^{3+}	6.35	6.39
Yb^{3+}	6.28	6.03

of stability constants were determined and calculated by using the calculation program Letagrop [18]. The best values for the formation constants (β_{xy}) of the various complex species and their molar absorption coefficients in various wavelengths were deduced from the fit between the experimental and calculated spectra. The UV/vis spectra of ligand **3** between 220 and 320 nm corresponded with the $\pi \rightarrow \pi^*$ transitions of the aromatic moieties. Upon the addition of lanthanoid perchlorates (La^{3+}, Nd^{3+}, Eu^{3+}, Gd^{3+}, and Yb^{3+}), the spectra in most cases showed distinct changes. The maximum absorption of the ligand **3** was observed at 256 nm and its complexation with lanthanoids were manifested by a hypochromic displacement.

Table 1 lists the stability constant ($\log\beta_{xy}$) data for the lanthanoid complexation with ligand **3**. The data are in accord with the formation of two mononuclear species and biligand stoichiometry with ligand **3**. Since the lanthanoids have high electropositive and hard acid character, they interact with hard bases such as oxygen, and the amido derivative of calix[4]arene, **3**, is a good candidate for complexation with them [19–23]. Mononuclear lanthanoid species formed by the ligand gave the logarithmic values of the stability constants between 4.71 and 6.60, which significantly increased for Eu^{3+}, where the selectivity $S^{3+3+}_{Eu/Nd}$ is close to 77. It seems that the particular stability of Eu^{3+} complex is due to the coherence between the ion size and the cavity size of the calixarenes amide. The biligand complexes (ML_2) formed by the ligand **3** with the cations Eu^{3+}, Gd^{3+} and Yb^{3+} have similar stability level (from 12.31 to 12.74 logarithmic units). These stability changes indicate the significant complexation selectivity ($S_{Gd^{3+}/Nd^{3+}} = 9 \times 10^3$) in favor of the gadolinium complex compared with the neodymium complex, and suggests that two units of the ligand are organized more effectively around the Gd^{3+} ion through favorable bond distances. Taking into account the logarithm of stepwise constants calculated from $\log\beta$, $\log K_{12}$ is smaller than $\log K_{11}$ except for Gd^{3+} (Table 2).

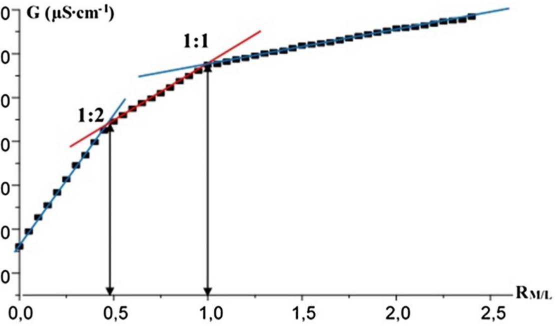

Fig. 2 Conductometric titration of **3** with La^{3+}

Table 3 Extraction percentages (%E) of lanthanoid picrates from water into dichloromethane by ligand **3**, at 25 °C ($C_L = C_M = 2.5 \times 10^{-4}$ mol L^{-1})

Cations	%E
La^{3+}	10
Gd^{3+}	12
Yb^{3+}	14

The stoichiometry of M:L and M:L_2 for the La^{3+} complex with ligand **3** were confirmed by conductometric titration (Fig. 2).

A preliminary evaluation of the binding efficiency ligand **3** base derivatives has been carried out by solvent extraction of metal picrates into dichloromethane at 25 °C under neutral conditions. The extraction percentages (%E) of some lanthanoid metal picrates by ligand **3** from water into dichloromethane are given in Table 3.

The extraction efficiency of each lanthanoid cation with ligand **3** was low at 12–14%, but Yb^{3+} was the most pronounced (14%). These data do not correspond to the stability of complexation with ligand **3** (see Table 1) and show that the complexation with the ligand is not the major driving force for the extraction of these cations.

Experimental

General

UV/vis spectra were obtained by a Perkin Elmer Lambda 25 spectrophotometer. All chemicals were analytical pure and purchased from Aldrich. They were used without further purification. The supporting electrolyte, Et_4NClO_4, for the stability constant determination was purchased from ACROS Organics.^{1}H NMR spectra were recorded at 300 K using a 300 MHz Bruker SY200 spectrometer. Melting points were determined using an Electrothermal apparatus. The extraction experiments of metal picrates from water into dichloromethane were performed according to the literature procedure [16, 17]. Equal volumes (5 mL) of neutral aqueous solutions of metal picrate (2.5×10^{-4} mol L^{-1}) and dichloromethane solution of calixarene derivatives (2.5×10^{-4} mol L^{-1}) were mixed under magnetic agitation for 24 h, then left standing for 1 h in order to obtain the complete separation of two phases. The concentration of metal picrate remaining in the aqueous phase was determined at 355 nm by UV/vis spectrometer. The percentage extraction (%E) was derived from the following expression, where A_0 is the absorbance of the blank solution without calixarene:

$$\%E = 100(A_0 - A)/A_0.$$

Preparation of 1

p-tert-Butylcalix[4]arene (5 g, 7.70 mmol), K_2CO_3 (21 g, 154 mmol) and 4-chlorobutyronitrile (14 mL, 154 mmol) were heated at reflux in acetonitrile (50 mL) for 5 days. The solvent was evaporated and the residue was taken up in dichloromethane (100 mL), washed with 1 M HCl (100 mL), H_2O (50 mL) and brine (50 mL), then dried with $MgSO_4$. Dichloromethane was evaporated and the residue was recrystallized from chloroform and methanol to give as white solid (94%) yield. Mp > 300 °C. IR (KBr, ν/cm^{-1}) = 2250 (CN), 3416 (OH). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.41 (s, 2H, ArOH), 7.05 (s, 4H, ArH), 6.86 (s, 4H, ArH), 4.14 (d, 4H, J = 13.0 Hz, system AB, ArCH$_2$Ar), 4.09 (t, 4H, J = 5.0 Hz, ArOCH$_2$), 3.35 (d, 4H, J = 13.0 Hz, AB system, ArCH$_2$Ar), 3.04 (t, 4H,, J = 5.0 Hz, CH$_2$CN), 2.64 (q, 4H, J = 5.0 Hz, CH_2CH$_2$CN), 1.27 (s, 18H, *tert*-butyl), 0.99 (s,18H, *tert*-butyl). ^{13}C NMR ($CDCl_3$): δ (ppm) = 150.3, 148.8, 147.6, 142.1, 132.5, 127.5, 125.8 and 125.3 (Ar), 119.4 (–CN), 73.3 (–OCH$_2$), 34.0, 33.9, 31.8, 31.7, 31.0, 26.6 and 14.2 (ArCH$_2$Ar, –CH$_2$CH$_2$– and —C(CH$_3$)$_3$). MW = 783.09 calcd for $C_{52}H_{66}O_4N_2$. MALDI-TOF: m/z = 783.2. Anal. calcd for $C_{52}H_{66}O_4N_2$ = C 79.76, H 8.50, N 3.58. Found: C 79.29, H 8.77, N 3.60%.

Preparation of 2

A solution of BH_3•THF (1 M, 10 mL) was added to the stirred suspension of **1** (1.5 g, 1.91 mmol) in THF (40 mL). The mixture was stirred for 1 h at RT and refluxed for 5 h. BH_3•THF (10 mL) was added after cooling the mixture and refluxed for an additional 15 h, then allowed to RT. HCl (6 M, 40 mL) was added and refluxed for 1 h. THF was removed under reduced pressure to give a colorless suspension. The mixture was left for 12 h at 0 °C and filtered, then washed with water and dried under vacuum at room temperature for 24 h to give as white powder (90%) yield. Mp = 168-169 °C. IR (KBr, ν/cm^{-1}) = 3444 (NH), 3385 (OH). ^{1}H NMR ($CDCl_3$): δ (ppm) = 7.65 (s, 2H, ArOH), 7.04 (s, 4H, ArH), 6.82 (s, 4H, ArH), 4.25 (d, 4H, J = 13.0 Hz, AB system, ArCH$_2$Ar), 3.98 (t, 4H, ArOCH$_2$), 3.28 (d, 4H, J = 13.0 Hz, AB system, ArCH$_2$Ar), 2.96 (m, 4H, J = 5.0 Hz, CH$_2$N), 2.87 (t, 4H, NH_2), 2.61 (m, 4H, J = 5.0 Hz, CH_2CH$_2$N), 2.43 (m, 4H, J = 5.0 Hz, CH_2CH$_2$CH$_2$N), 1.27 (s, 18H, *tert*-butyl), 0.98 (s, 18H, *tert*-butyl). ^{13}C NMR ($CDCl_3$): δ (ppm) = 150.6, 149.9, 146.8, 141.5, 132.6, 127.8, 125.5 and 125.1(Ar), 76.2 (–OCH_2–), 41.9 (–CH_2N–), 33.9, 33.8, 31.7, 31.5, 31.0, 30.2 and 27.4 ($ArCH_2Ar$, –CH_2CH_2– and –$C(CH_3)_3$). MW = 791.15 calcd for $C_{52}H_{74}O_4N_2$. MALDI-TOF: m/z = 791.59. Anal. calcd for $C_{52}H_{74}O_4N_2$ = C 78.94, H 9.43, N 3.54. Found: C 76.68, H 8.86, N 3.70%.

Preparation of 3

HBTU (hexafluorophosphate benzotriazole tetramethyl uronium, 1.27 mg, 3.36 mmol) was added to the mixture of **2** (1.12 g, 1.41 mmol), 7-carboxy-8-hydroxylquinoline (0.63 mg, 3.36 mmol) and DMAP (4-dimethylaminopyridine, 0.41 mg, 3.36 mmol) in dichloromethane (120 mL). After stirring for 3 days at RT, the solvent was evaporated under reduced pressure and the residue washed with methanol (3 × 15 mL), then dried under vacuum to give as a white powder (67%) yield. Mp = 158–160 °C. IR (KBr, ν/cm^{-1}) = 3300 (NH), 3400 (OH), 1700 (CO). ^{1}H NMR ($CDCl_3$): δ (ppm) = 8.85 (dd, 2H, J = 1.3 Hz, Ha), 8.21 (t, 4H, J = 6.0 Hz, NH), 8.06 (dd, 2H, J = 1.3 Hz, Hc), 8.05 (d, 2H, J = 8.8 Hz, He), 7.45 (dd, 2H, J = 1.3 Hz, Hb), 7.44 (s, 2H, ArOH), 7.17 (d, 2H, J = 8.8 Hz, Hd), 7.07 (s, 4H, ArH), 6.78 (s, 4H, ArH), 4.24 (d, 4H, J = 13.0 Hz, AB system, $ArCH_2Ar$), 3.98 (t, 4H, $ArOCH_2$), 3.30 (d, 4H, J = 13.0 Hz, AB system, $ArCH_2Ar$), 3.04 (m, 4H, J = 5.0 Hz, CH_2N), 2.65 (m, 4H, J = 5.0 Hz, CH_2CH$_2$N), 2.49 (m, 4H, J = 5.0 Hz, CH_2CH$_2$CH$_2$N), 1.30 (s, 18H, *tert*-butyl), 0.94 (s, 18H, *tert*-butyl). ^{13}C NMR ($CDCl_3$): δ (ppm) = 168.13(C=O), 155.31(C), 150.41(CH), 139.27(CH), 135.90 (C) 123.23(CH), 125.58(CH), 117.33 (C), 112.74(CH) 39.71, 33.93, 33.90, 31.74, 30.99, 27.22 and 27.38 ($ArCH_2Ar$, –CH_2CH_2– and –$C(CH_3)_3$). MW = 1133.46 calcd for $C_{72}H_{84}O_8N_4$. MALDI-TOF: m/z = 1133.62. Anal. calcd for C 76.29, H 7.47, N 4.94. Found: C 75.91, H 7.39, N 4.83%.

Conclusion

The binding properties of lanthanoid cations with **3** have been assessed by the determination of stability constants in acetonitrile using UV/vis spectrophotometry. The quantification of the complexation equilibria was used to estimate the stoichiometry of the formed complexes. The results showed the formation of two mononuclear and biligand species with the ligand **3**. The interrelationships between the stability constants of lanthanide cations with the ligand **3** and their extraction efficiency were inconsistent.

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References

1. Gutsche, C.D., Muthukrishnan, R.: Calixarenes. 1, Analysis of the product mixtures produced by the base-catalyzed condensation of formaldehyde with para-substituted phenols. J. Org. Chem. **43**, 4905–4906 (1978)
2. Vicens, J., Harrowfield, J., Baklouti, L.: Calixarenes in the Nanoworld. Springer, Dordrecht (2007)
3. van Loon, J.-D., Verboom, W., Reinhoudt, D.N.: Selective functionalization and conformational properties of calix[4]arenes, a review. Org. Prep. Proc. Int. **24**, 437–462 (1992)
4. Xu, Z., Lu, Z.S., Chen, L.: Enhanced etherification of calix[4]arenes by microwave irradiation. J. Incl. Phenom. Macrocycl. Chem. **88**, 77–83 (2017)
5. van Duynhoven, J.P.M., Janssen, R.G., Verboom, W., Franken, S.M., Casnati, A., Pochini, A., Ungaro, R., de Mendoza, J., Nieto, P.M., Prados, P., Reinhoudt, D.N.: Control of calix[6]arene conformations by self-inclusion of 1,3,5-tri-*O*-alkyl substitutents: synthesis and NMR studies. J. Am. Chem. Soc. **116**, 5814–5822 (1994)
6. Aloui, L., Elhabiri, M., Platas-Iglesias, C., Esteban-Gómez, D., Abidi, R., Chetcuti, M.J.: Synthesis and characterization of positively charged tris-imidazolium calix[6]arene hosts for anion recognition. ChemistrySelect **4**, 321–328 (2019)
7. Stewart, D.R., Krawiec, M., Kashyap, R.P., Watson, W.H., Gutsche, C.D.: Conformational characteristics of ethers and esters of *p-tert*-butylcalix[5]arene. J. Am. Chem. Soc. **117**, 586–601 (1995)
8. Ingenfeld, B., Straub, S., Frömbgen, C., Lützen, A.: Synthesis of monofunctionalized calix[5]arenes. Synthesis **50**, 676–684 (2018)
9. Neri, P., Geraci, C., Piattelli, M.: "Alternate alkylation" of *p-tert*-butylcalix[8]arene in the presence of weak bases. J. Org. Chem. **60**, 4126–4135 (1995)
10. Hervé, G., Hahn, D.U., Hervé, A.-C., Goodworth, K.J., Hill, A.M., Hailes, H.C.: The selective functionalisation and difunctionalisation of p-substituted calix[6]arene and calix[8]arenes using hydrophilic moieties. Org. Biomol. Chem. **1**, 427–435 (2003)
11. Gutsche, C.D.: Calixarenes Revisited (Monographs in Supramolecular Chemistry)). RSC, Cambridge (1998)
12. Gutsche, C.D., Bauer, L.J.: Calixarenes. 13. The conformational properties of calix[4]arenes, calix[6]arenes, calix[8]arenes, and oxacalixarenes. J. Am. Chem. Soc. **107**, 6052–6059 (1985)
13. Böhmer, V.: Calixarenes, macrocycles with (almost) unlimited possibilities. Angew. Chem. Int. Ed. Engl. **34**, 713–745 (1995)
14. Bagatin, I.Z., Toma, H.E.: A calix[4]arene receptor modified with 8-hydroxyquinoline for supramolecular energy transfer. New J. Chem. **24**, 841–844 (2000)
15. Scheerder, J., Fochi, M., Engbersen, J.F.J., Reinhoudt, D.N.: Urea-derivatized *p-tert*-butylcalix[4]arene: neutral ligands for selective anion complexation. J. Org. Chem. **59**, 7815–7820 (1994)
16. Pedersen, C.J.: New macrocyclic polyethers. J. Am. Chem. Soc. **92**, 391–394 (1970)
17. Frensdorff, H.K.: Salt complexes of cyclic polyethers. Distribution equilibria. J. Am. Chem. Soc. **92**, 4684–4688 (1971)
18. Sillén, L.G., Warnqvist, B.: Equilibrium constants and model testing from spectrophotometric data, using LETAGROP. Acta Chem. Scand. **22**, 3032–3034 (1968)
19. Ohto, K., Yamaga, H., Murakami, E., Inoue, K.: Specific extraction behavior of amide derivative of calix[4]arene for silver(I)

and gold(III) ions from highly acidic chloride media. Talanta **44**, 1123–1130 (1997)

20. Ferreira, J., Bagatin, I.A.: A Cr(VI) selective probe based on a quinoline-amide calix[4]arene. Spectrochim. Acta Part A **189**, 44–50 (2018)
21. Nealon, G.L., Mocerino, M., Ogden, M.I., Skelton, B.W.: The impact of the lanthanide contraction on the structure of complexes of a calix[4]arene trisamide. J. Incl. Phenom. Macrocycl. Chem. **65**, 25–30 (2009)
22. McIldowie, M.J., Skelton, B.W., Mocerino, M., Ogden, M.I.: A lanthanum picrate complex of a 1,2-bisamide substituted calix[4]arene. J. Incl. Phenom. Macrocycl. Chem. **82**, 43–46 (2015)
23. Nealon, G.L., McIldowie, M.J., Skelton, B.W., Mocerino, M., Massi, M., Ogden, M.I.: Structural Variations in the Complete Series of Lanthanoid Complexes of a Calix[4]arene Trisamide. Aust. J. Chem. (2017). https://doi.org/10.1071/ch17484