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Synthesis and Characterization of Ga^{III}, In^{III} and Lu^{III} Complexes of a Set of dtpa Bis-Amide Ligands

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The synthesis and characterization of five new diethylenetriaminepentaacetic acid (dtpa) ligands, (dtpa)-*N*,*N*′′-bis(alkoxyphenylamide), and their complexation with Ga^{III}, In^{III} and Lu^{III} are reported. The procedures for the synthesis of all complexes in aqueous media are described as well as a synthetic pathway for the preparation of Ga^{III} complexes in chloroform. All substances were characterized by NMR spectroscopy, mass spectrometry, elemental analysis and HPLC. Single-crystal structure analysis was performed where applicable, which revealed the presence of hepta- and octa-coordinated isomers for In^{III} complexes and a nine-fold coordination of Lu^{III} ions in the solid state. Additional NMR experiments suggested a hepta-coordinated In^{III} species in solution, whereas the Ga^{III} complexes appear to be hexa-coordinated and the Lu^{III} complexes to be octa-coordinated. Both NMR and HPLC studies indicated the presence of a single isomer in every complex.

Introduction

Diethylenetriaminepentaacetic acid (dtpa) is a well-known chelator that has been used since the 1960s as an agent for treating heavy-metal poisoning and radioactive contamination.[1–3] Its metal complexes are useful tools, one major field of interest being medical imaging.

One approved contrast agent for MRI is gadoxetic acid, also known as Eovist® or Primovist®, which was first described in 1991.[4] It is the Gd^{III} complex of EOB-dtpa, a dtpa ligand bearing a *p*-ethoxybenzyl moiety on the diethylenetriamine backbone that improves the lipophilicity of the compound. This property results in a specific uptake of the agent by liver hepatocytes by means of an organic anion transporter.[5] The high liver specificity of gadoxetic acid enables the localization of focal lesions and hepatic tumours by MRI techniques. Although it is a frequently used contrast agent, it does have its drawbacks. As an open-chain-based Gd^{III} complex it cannot be applied to patients in cases of renal impairment or drug intolerance to this often quite toxic agent. Additionally, MRI cannot be used for patients with metallic MRI-incompatible implants (e.g., cardiac pacemakers) or claustrophobia.

dtpa derivatives structurally similar to EOB-dtpa might be promising tracers for liver-specific molecular imaging upon labelling with suitable radionuclides, therefore providing an alternative to MRI. The derivatization of dtpa usually involves either the introduction of structural moieties into the ethylene or methylene groups of the backbone structure[6,7] or the amidation of one or several of the five carboxy groups.[8–11]

Although EOB-dtpa is only accessible through a multistep synthesis in which the lipophilic *p*-ethoxybenzyl moiety is introduced in an early step,[12] dtpa amides can be synthesized much more efficiently by using dtpa bis-anhydride as the starting material. The variety of available anilines used in the amidation step makes a diversity of dtpa bis-amides accessible. Alterations of the amide moiety and the chain length of substituents influence the lipophilicity of complexes thereof and consequently their specificity to hepatocytes and suitability for hepatobiliary imaging. Therefore a set of dtpa-*N*,*N*′′-bis(alkoxyphenylamides) with a different substitution pattern of the phenyl moiety and variable chain lengths were designed and synthesized.

dtpa amides are able to bind a variety of metal ions, ranging from lanthanides[11,13–18] and d elements[19–22] to alkaline-earth metals,[23] pnictogens[24] as well as elements of the boron group.[19,24–32] Among this last group, Ga^{III} is of

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particular interest due to its radioactive isotope ^{68}Ga, which is commonly used in positron emission tomography (PET).

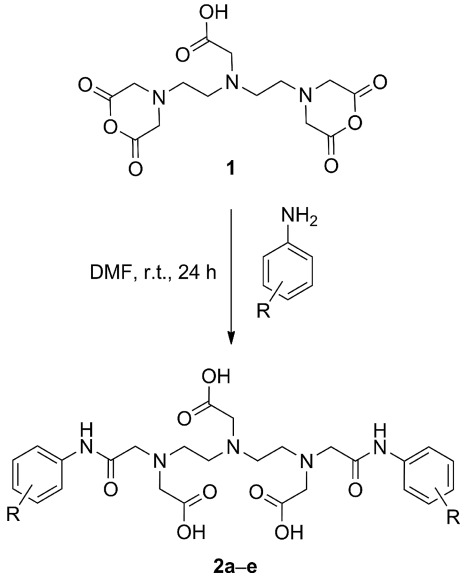
Ga^{III} complexes of dtpa and its derivatives are generally considered not suitable for medical applications due to a lack of kinetic inertness,[33–35] which may result in rapid trans-chelation to transferrin in vivo.[27,36–38] Nevertheless, some promising results in the field can be found. For example, $^{68}Ga^{III}$ complexes of dtpa coupled to proteins through an amide bond have been reported to be stable in vivo over a period of hours.[29,30] A dtpa-conjugated chalcone derivative labelled with $^{68}Ga^{III}$ also showed only slow degradation in human serum.[31]

Although the properties of the $^{68}Ga^{III}$ complexes of dtpa amides have been intensively examined,[27,29–31] investigations of the solution chemistry and the structural behaviour of non-radioactive equivalents are scarcer.[28] To provide new insights into this subject, this study focuses on the synthesis and characterization of Ga^{III} complexes of novel dtpa bis-amide ligands. For means of comparison of their solution chemistry and structural behaviour the respective In^{III} and Lu^{III} complexes have been synthesized as well.

Results and Discussion

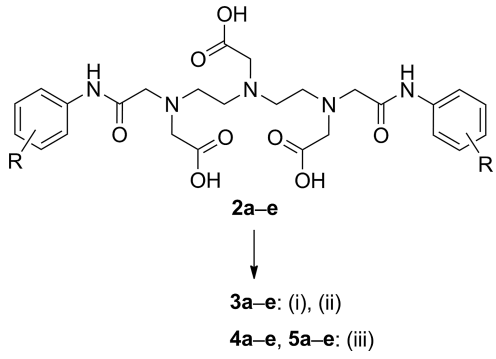
Synthesis

The dtpa-*N*,*N*′′-bis(alkoxyphenylamides) were readily synthesized by the addition of 2 equiv. of the respective aniline bearing the desired substituent to dtpa bis-anhydride **1** in dmf at room temperature (Scheme 1). After stirring for 24 h at room temperature and evaporation of the solvent, recrystallization of the residue from ethanol gave compounds **2a**–**e** in yields of 57–82%.



Scheme 1. Synthesis of ligands **2a**–**e**; R = *m*-OCH_3 (**2a**), *o*-OCH_2CH_3 (**2b**), *m*-OCH_2CH_3 (**2c**), *p*-OCH_2CH_3 (**2d**) and *p*-$O(CH_2)_3CH_3$ (**2e**).

Complexes of compounds **2a**–**e** were prepared by combining equimolar amounts of the respective metal chloride and the ligand either in an aqueous solution or in chloroform. The syntheses in aqueous systems were performed at pH 3.3 for Ga^{III} complexes using an acetate buffer solution and at pH 7.5 for In^{III} and Lu^{III} complexes (Scheme 2). Owing to the poor solubility of the ligands in aqueous media, the yields were improved by dissolving the dtpa bis-amides **2a**–**e** in boiling water and then cooling to room temperature followed by the addition of the respective metal chloride.



Scheme 2. Synthesis of the Ga^{III} (**3a**–**e**), In^{III} (**4a**–**e**) and Lu^{III} complexes (**5a**–**e**). Reagents and conditions: (i) $GaCl_3$ (aq.), acetate buffer, water, pH 3.3, 30 min; (ii) $(nBu)_4N^+OH^-$, $GaCl_3$, chloroform, room temp., 12 h; (iii) $M^{III}Cl_3$ (M = In, Lu), NaOH, water, pH 7.5, room temp., 12 h.

The Ga^{III} complexes **3a**–**e** precipitated from the reaction mixture and the crude products were isolated by filtration. Despite a pH below 3.5, considerable amounts of hydrolysis products formed, as proven by elemental analysis. Recrystallization from boiling methanol afforded analytically pure compounds **3a**–**e** in yields of 15–45%. The absence of free ligands **2a**–**e** was additionally confirmed by reversed-phase HPLC.

Owing to the persistent presence of hydrolysed Ga^{III} in the crude product, other synthetic conditions were investigated. Despite their poor solubility in organic solvents, bis-amides **2a**–**e** could be dissolved in chloroform after treatment with 3 equiv. of a methanolic solution of tetra-*n*-butylammonium hydroxide. Subsequent addition of Ga^{III} chloride in *n*-pentane resulted in the formation of the desired compounds. Although **3e** precipitated directly from the reaction mixture within 12 h, the synthesis of compounds **3a**–**3d** demanded the precipitation by diffusion of diethyl ether into the solution.

The In^{III} and Lu^{III} species in aqueous media were synthesized by using sodium hydroxide solution to adjust the pH to 7.5. Separation of the metal complexes from inorganic impurities represents a problem owing to the poor solubility of the former in organic media and the rather good solubility of both in water. For the In^{III} (**4c**–**e**) and Lu^{III} complexes (**5c**–**e**), the best results were obtained by evaporation of the solvent from the reaction mixture in vacuo and washing of the residue with minimum amounts of water. After drying in vacuo, the complexes were obtained analytically pure in yields of 39–74%. In contrast, compounds **4a**,**b** and **5a**,**b**, which are readily soluble in aqueous media, were purified by column chromatography

on silica using highly polar solvents. However, this procedure provided lower yields of 15–26%.

Crystal Structures

All attempts to isolate suitable crystals of compounds **3a**–**e** for single-crystal structure analysis usually yielded needles lacking adequate thickness. Until now there was no crystallographic evidence for any Ga^{III} complex of dtpa derivatives. Crystals of **4a** suitable for single-crystal structure analysis were obtained upon slow evaporation of a concentrated solution of the complex in a mixture of water/methanol (1:1). Complexes **4c** and **5c** were crystallized by dissolving the compounds in hot water and subsequent slow evaporation of the solvent. Selected crystallographic data are listed in Table 1.

Table 1. Crystal data and refinement details for the X-ray structure determinations of compounds **4a**, **4c** and **5c**.

	4a	**4c**	**5c**
Formula	$C_{28}H_{34}InN_5O_{10}$·0.25(CH_3OH)·5.25(H_2O)	$C_{30}H_{38}InN_5O_{10}$·4.5(H_2O)	$C_{30}H_{40}LuN_5O_{11}$·8(H_2O)
M [g mol^{-1}]	768.47	820.01	965.77
T [°C]	–140(2)	–140(2)	–140(2)
Crystal system	monoclinic	triclinic	triclinic
Space group	$P2_1/n$	$P\bar{1}$	$P\bar{1}$
a [Å]	13.4668(2)	13.3851(3)	7.9065(6)
b [Å]	18.3357(3)	17.0855(5)	10.0450(8)
c [Å]	26.4406(5)	17.7590(5)	25.268(2)
α [°]	90	64.707(1)	89.419(2)
β [°]	90.747(1)	78.872(2)	89.515(3)
γ [°]	90	77.591(2)	81.644(4)
V [Å^3]	6528.24(19)	3562.58(17)	1985.4(3)
Z	8	4	2
P [g cm^{-3}]	1.564	1.529	1.616
μ [cm^{-1}]	7.96	7.38	25.68
Measured data	52352	25868	8929
Data with $I>2\sigma(I)$	13347	13332	8109
Unique data/R_{int}	14832/0.0414	14308/0.0252	8929/0.0553
wR_2 (all data, on F_2)[a]	0.1163	0.1161	0.1254
R_1 [$I>2\sigma(I)$][a]	0.0501	0.0517	0.0505
S[b]	1.136	1.276	1.131
Max./min. resid. dens. [e Å^{-3}]	1.502/–0.690	1.472/–0.584	1.330/–2.388
Abs. method	multi-scan	multi-scan	multi-scan
Abs. corr. T_{min}/T_{max}	0.6912/0.7456	0.6767/0.7456	0.5261/0.7456

[a] Definition of R indices: $R_1 = (\Sigma||F_o| - |F_c||)/\Sigma|F_o|$; $wR_2 = \{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$ with $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$; $P = [2F_c^2 + \max(F_o^2)]/3$. [b] $s = \{\Sigma[w(F_o^2 - F_c^2)^2]/(N_o - N_p)\}^{1/2}$.

[In^{III}(dtpa)] was the first complex found to contain an octa-coordinated In^{III} ion, which came as a surprise because the ion had been considered too small to coordinate so many donors.[33] To the best of our knowledge, the only crystal structure determination of an open-chain dtpa bisamide to have been reported also revealed an octa-coordinated In^{III} complex.[9] In addition, an In^{III} complex of a cyclic derivative crystallizing in a hepta-coordinated structure has also been reported.[10] In accordance with these previous studies, an octa-coordination was also expected for **4a**. Much to our surprise, the single-crystal structure analysis of **4a** revealed the presence of two species; both a hepta- and octa-coordinated isomer were identified, denoted **4a**^{hepta} and **4a**^{octa}, respectively (Figure 1).

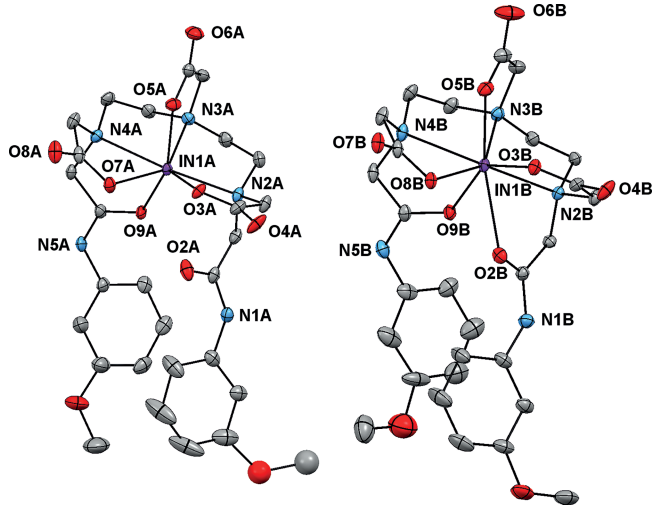


Figure 1. ORTEP drawing of the two crystallized structural isomers **4a**^{hepta} (left) and **4a**^{octa} (right). Ellipsoids are drawn at the 35% probability level. Solvent molecules and hydrogen atoms have been omitted for the purpose of clarity. In **4a**^{hepta}, one of the methoxy moieties shows a structural disorder in two positions, of which only one isotropically refined group is depicted.

In the isomers, the respective donor atoms arrange comparably, forming a distorted mono- (**4a**^{hepta}) or bicapped (**4a**^{octa}) trigonal-prismatic coordination sphere, which in the case of **4a**^{octa} can also be interpreted as a strongly distorted square antiprism. As none of the idealized polyhedra matches satisfactorily and for reasons of comparability, the distorted bicapped trigonal-prismatic structure is preferentially discussed in this paper. In this structure, one triangular plane is formed by the three carboxylato moieties of **2a**$^{3-}$, O3, O5 and O7 (**4a**^{hepta}) or O8 (**4a**^{octa}), respectively. The opposite plane is defined by an [N_2O] donor set, formed by the central (N3) and one terminal (N2) nitrogen atom of the dtpa structure and the oxygen atom (O9) of the distant amide group.

The monocapped structure in **4a**^{hepta} is completed by the coordination of the remaining nitrogen atom (N4) of the dtpa structure and additional coordination of the second amide oxygen atom (O2) completes the formation of the bicapped trigonal prism in **4a**^{octa}. As expected, the distances between the central In^{III} ion and the atoms in the capping positions are elongated compared with the atoms forming the trigonal prism (Table 2).

A comparison of the bond lengths of **4a**^{hepta} and **4a**^{octa} reveals that the additional coordination of the second amide oxygen atom in **4a**^{octa} results in a weakening and elongation of the oppositely arranged In–O5 bond to 2.240(3) Å from 2.170(3) Å in **4a**^{hepta}. The differences in bond lengths between In^{III} and the amide oxygen atoms O2 and O9 in **4a**^{octa}, 2.565(3) Å compared with 2.247(3) Å, can be explained by the capping position of the O2 oxygen atom. In addition to that, the crowding of the central metal ion and steric factors like packing effects might influence

Table 2. Selected bond lengths for the hepta- and octa-coordinated isomers of **4a**.

	Bond length [Å][a]	
	4a^{hepta}	**4a**^{octa}
In1–N2	2.361(3)	2.379(3)
In1–N3	2.398(3)	2.382(3)
In1–N4	2.497(3)	2.516(3)
In1–O3	2.171(3)	2.178(3)
In1–O5	2.170(3)	2.240(3)
In1–O7/O8[b]	2.194(3)	2.194(3)
In1–O9	2.206(3)	2.247(3)
In1–O2	3.083[c]	2.565(3)

[a] Intramolecular bond lengths. [b] In1–O7 in **4a**^{hepta} and In1–O8 in **4a**^{octa}. [c] Non-bonding interatomic distance In···O2.

the structure in the solid state, as has been reported previously for the structure of [In^{III}(dtpa)].[33] However, the differences in bond lengths and therefore in the bond strengths might favour the dissociation of the amide oxygen atom O2 in **4a**^{octa} in solution.

The supramolecular arrangement of the molecules is affected by intermolecular hydrogen bonding between an amide nitrogen atom and a carboxy oxygen atom of a neighbouring molecule of the same isomer, resulting in the formation of chains (Figure 2). The interatomic distances were determined to be 2.756 Å (O4A···N5A) and 2.782 Å (O4B···N5B) in the chains of **4a**^{hepta} and **4a**^{octa}, respectively, which indicates strong hydrogen bonding in the solid state with distances closer than the sum of the van der Waals radii.[39] These chains are further interlinked by weak hydrogen bonding between the second amide nitrogen atom N1A of **4a**^{hepta} and two carboxy oxygen atoms of a molecule of **4a**^{octa} of a neighbouring chain with interatomic distances of 3.035 Å (N1A···O8B) and 3.211 Å (N1A···O7B). These bonds align the molecules in a two-dimensional network.

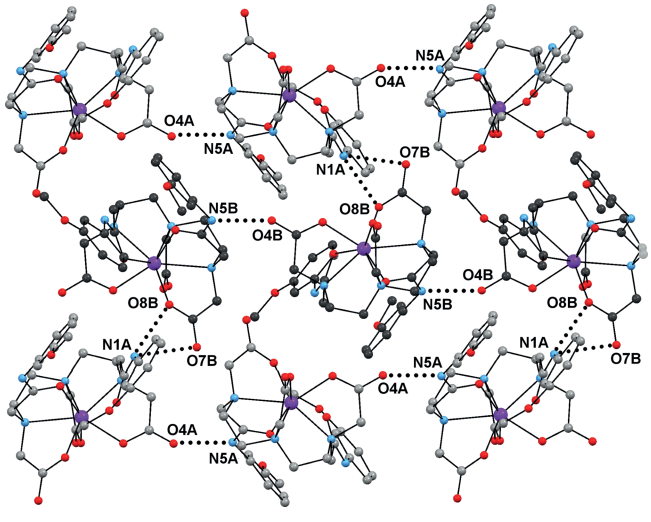


Figure 2. ORTEP drawings of the supramolecular arrangement in the crystal containing **4a**^{hepta} and **4a**^{octa}. Hydrogen bonding is indicated by dotted lines. Owing to structural disorder, only one of the isotropically refined methoxy moieties of **4a**^{hepta} is depicted. To facilitate distinction, carbon atoms of molecules of **4a**^{hepta} are coloured light grey, whereas the carbon atoms of **4a**^{octa} appear in dark grey. Non-coordinating solvent molecules and hydrogen atoms have been omitted for reasons of clarity.

The single-crystal structure analysis of **4c** verifies the presence of two symmetry-independent molecules in the unit cell, both displaying an octa-coordinated complex (Figure 3, left). The bond lengths between the In^{III} ion and the surrounding donor atoms indicate that one In–N and one In–O bond are remarkably longer than the respective metal donor bonds (Table 3). As the coordination sphere can be described as a bicapped trigonal prism, it is evident that the corresponding atoms, N4 and O1, occupy the capping positions therein. The structure of the coordination sphere is comparable to the one discussed for **4a**^{octa}, as is

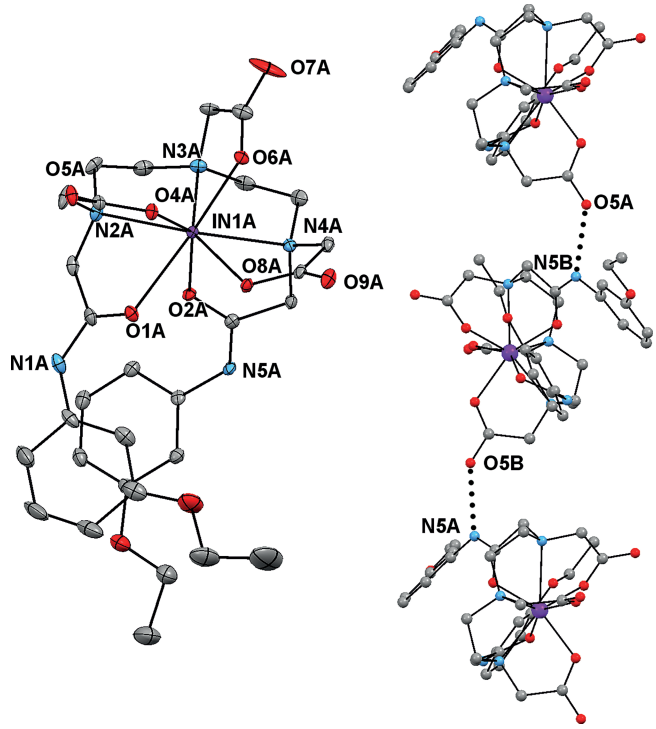


Figure 3. ORTEP drawings of **4c** (left, only one of the symmetry-independent molecules is displayed) and the supramolecular arrangement in the crystal (right). Ellipsoids (left) are drawn at the 35% probability level. Non-coordinating solvent molecules and hydrogen atoms have been omitted for reasons of clarity. Hydrogen bonding (right) is indicated by dotted lines.

Table 3. Selected bond lengths for **4c** and **5c**·H_2O.

	Bond length [Å][a]	
	4c[b]	**5c**·H_2O
M–N2	2.371(4), 2.337(4)	2.745(5)
M–N3	2.383(4), 2.363(4)	2.553(5)
M–N4	2.522(4), 2.517(4)	2.602(5)
M–O4	2.175(3), 2.190(3)	2.228(4)
M–O6	2.224(3), 2.230(3)	2.265(4)
M–O8	2.191(3), 2.159(3)	2.299(4)
M–O1	2.435(3), 2.481(6)	2.406(4)
M–O2	2.266(3), 2.283(3)	2.401(4)
M–O11W	–	2.313(4)

[a] M = In (**4c**), Lu (**5c**·H_2O). [b] Values for two symmetry-independent molecules are given.

the overall alignment of the donors. Although three carboxylato groups (O4, O6, O8) of $\mathbf{2c}^{3-}$ define one triangular face, the other plane is formed by the central (N3) and one terminal amine nitrogen atom (N2) and the distant amide oxygen atom (O2). Intermolecular hydrogen bonding (Figure 3, right) is observed between one terminal carboxylato group and an amide nitrogen atom of an adjacent molecule, resulting in the formation of chains. The interatomic distances were determined to be 2.695 Å for O5A···N5B and 2.739 Å for O5B···N5A and thus are a little shorter than those observed in **4a**. However, in contrast to **4a**, no bonding between adjacent chains is observed.

In the solid state, the Lu^{III} complex $\mathbf{5c}\cdot H_2O$ displays a nona-coordinated central metal ion, binding to all eight donor sites of the ligand moiety and an additional water molecule (Figure 4). The bonds between Lu and the carbonyl oxygen atoms of the amide moieties, O1 and O2, are the longest Lu–O bonds of the coordination sphere (Table 3), which suggests that the coordination of the amide pendant arms to the metal centre is weaker than the carboxy oxygen donors. The three Lu–N bonds are longer than all the Lu–O bonds in the coordination sphere. It has been assumed that the Lu–N bonds have lower bond strengths due to their lower polarity in comparison with the more ionic Lu–O bonds.[15] However, due to the impossibility of all three nitrogen atoms occupying capping positions in the trigonal prism,[9,40] the nitrogen atom N3 occupies a corner and the O11W of the water molecule is capping instead.

The coordination sphere around the central Lu^{III} ion can be described as a distorted tricapped trigonal prism, with O1, O2, O4 and O6, O8, N3 occupying the corners of a triangular plane, respectively. The bond length Lu–N2 and Lu–N4 are the longest in the coordination sphere and therefore N2 and N4 occupy a capping position each. The third capping position is occupied by the oxygen atom of the water molecule, O11W. According to Caravan et al., this is in accordance with the description of the *cis* isomer.[40]

However, the coordination sphere in **5c** might also be described as a distorted monocapped square antiprism in which O2, N4, O8 and O11W define one square plane and O1, O4, N3 and O6 form the other. In this way, the latter is capped by N2, which is in agreement with the respective bond (Lu–N2) being the longest in the coordination sphere. This description is associated with the *syn* isomer, as described by Aime et al.[15]

The supramolecular arrangement is determined by intermolecular hydrogen-bonding interactions between the water ligand and the uncoordinated terminal carboxy oxygen atom O5 of an adjacent molecule (Figure 4). The interatomic distance O11W···O5 measures 2.624 Å. A second, though weaker hydrogen bond measuring 2.846 Å is detected between the oxygen atom O7 of the central carboxylato moiety and the amide nitrogen atom N5 of a neighbouring molecule. These bonds cause a net-like structure in the crystal.

Furthermore, it should be mentioned that the phenyl rings of each molecule are almost coplanar, with the dihedral angle of the averaged ring planes determined to be 175.1°. However, this might solely be explained by packing effects, as neither sandwich nor parallel-displaced π–π stacking interactions could be detected.

It has been agreed that the geometries of Lu^{III} complexes of this nature range between the square-antiprismatic and the trigonal-prismatic description, although the latter is generally favoured.[9,15] A comparison of the dihedral angles in both geometric arrangements assumed for $\mathbf{5c}\cdot H_2O$ with the respective values for idealized polyhedra shows that a distorted tricapped trigonal prism is the best-match-

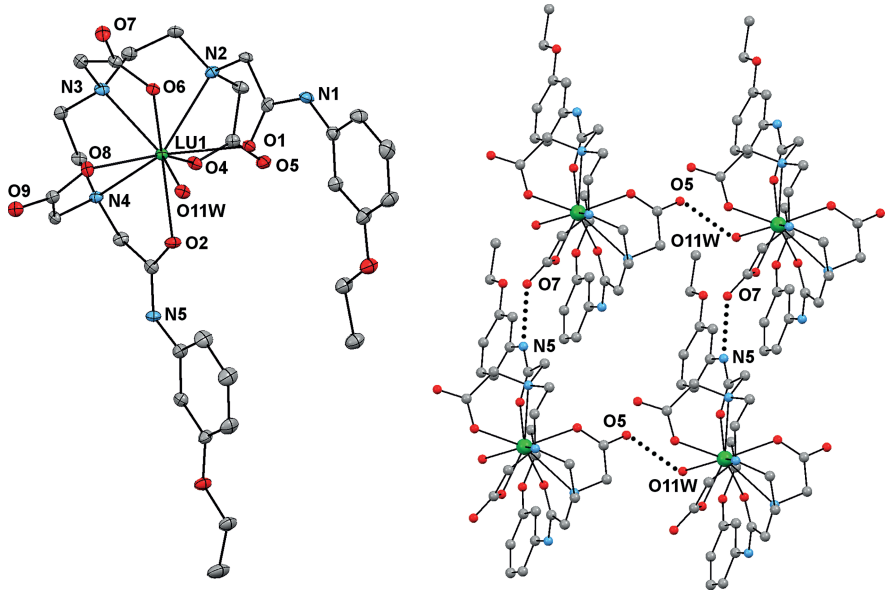


Figure 4. ORTEP drawing of $\mathbf{5c}\cdot H_2O$ (left) and the supramolecular arrangement in the crystal (right). Ellipsoids (left) are drawn at the 35% probability level. Non-coordinating solvent molecules and hydrogen atoms have been omitted for reasons of clarity. Hydrogen bonding (right) is indicated by dotted lines.

ing description (Table 4). For comparison, the dihedral angles determined for **4a**^{octa} and **4c** are also given. In particular, the angles between the neighbouring planes forming the edges that connect the base and top face of the trigonal prism indicate that neither of the idealized polyhedra describes its structure adequately. For the sake of completeness, when assuming a square antiprismatic structure in **4a**^{octa} and **4c**, one square plane is formed by the central and one terminal [NO] donor set, each formed by the amine nitrogen atom and carboxy oxygen atom. The opposite square plane is spanned by the remaining terminal [NO] donor set and both amide oxygen atoms.

Table 4. Dihedral angles between trigonal faces in idealized polyhedra and for the assumed trigonal prismatic structures of **4a**^{octa}, **4c** and **5c**·H_2O.

	Dihedral angle [°]	
	Opposite planes[a]	Neighbouring planes[b]
Trigonal prism[c]	180	26.4
Square antiprism[c]	163.5	0
4a^{octa}	168.7[d]	14.5[e]
4c	168.4, 167.8[f]	14.9,12.2[g]
5c·H_2O	175.0[h]	27.3, 22.3, 16.8[i]

[a] Base and top face of the trigonal prismatic structure. [b] Planes spanned by capping atom and two neighbouring atoms of an edge of the trigonal prism connecting its base and top face. [c] Values for respective idealized polyhedra, see ref.[40] [d] ∠[(N2–N3–O9)‖(O8–O3–O5)]. [e] ∠[(O2–O9–O8)‖(O9–O8–N4)]. [f] ∠[(O4–O6–O8)‖(N2–N3–O2)], values for two symmetry-independent molecules. [g] ∠[(O2–O8–O1)‖(O2–O8–N4)], values for two symmetry-independent molecules. [h] ∠[(O1–O2–O4)‖(O6–O8–N3)]. [i] Dihedral angles for ∠[(N2–O1–O6)‖(O11W–O1–O6)], ∠[(O11W–O2–O8)‖(N4–O2–O8)] and ∠[(N4–O4–N3)‖(N2–O4–N3)], respectively.

NMR Spectroscopy

In ligands **2a**–**e**, the amide pendant arms are chemically equal due to the symmetry of the molecules, exhibiting only one set of signals for each moiety in all spectra. In the ^{1}H NMR spectra, the amide and carboxylic protons appear as singlets, and in the aliphatic region, the anticipated patterns assigned to the dtpa backbone structure and the respective alkoxy moieties could be detected in both the ^{1}H and ^{13}C{^{1}H} NMR spectra.

Room-Temperature NMR Spectroscopy

As expected, the aliphatic protons of the dtpa backbone of all the ^{1}H NMR spectra of complexes **3**–**5** show a complex signal pattern with overlap of multiple couplings, that is, $^2J_{H,H}$ and $^3J_{H,H}$, induced by the chirality of the terminal nitrogen atoms and the non-equivalence of the methylene and ethylene protons upon ligand complexation,. The investigation of this spectral region did not allow reliable conclusions to be drawn on the conformation of the complexes in solution. Thus, the following discussion focuses on the ^{1}H and ^{13}C{^{1}H} NMR signals of the amide pendant arms.

The amide protons serve as an expedient indicator for the prediction of the coordination environment of the central metal ions. The amide protons are inequivalent in all the complexes and are detected as two separated singlets in the ^{1}H NMR spectra recorded in [D_6]dmso. Although the signals show very similar shifts in the spectra of **3a**–**e**, **5c** and **5d**, indicative of a comparable chemical environment, a remarkable difference is observed in the spectra of **4c** and **4d**. This is suggestive of a hepta-coordinated In^{III} ion containing both a coordinating and a non-coordinating amide moiety, as observed in the solid state for **4a**.

As expected, in nearly all the spectra of the complexes recorded in [D_6]dmso, the amide protons are shifted to higher frequencies compared with the respective ligands by about 0.3 ppm in **3a** and **3c**–**e** and 0.8 ppm in the Lu^{III} species **5c** and **5d**. This observation can be explained by non-coordinating amide nitrogen donor atoms in the former and the coordination of the amide moieties in the latter. This is in good accordance with the expectation of hexa-coordinated Ga^{III} complexes and an increased coordination number in the Lu^{III} species. There is a third singlet merging with the signals of the amide protons in **5c**, which can be assigned to the protons of a coordinated water ligand.

A summary of the NMR spectroscopic data assigned to the moieties of the pendant arms (Figure 5) of **2c** and its three metal complexes is presented in Table 5. The following discussion focuses on **3c**–**5c** as representatives of the complexes **3**–**5**.

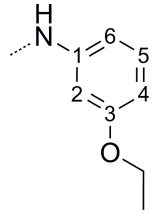


Figure 5. Atomic labelling of the aromatic moieties of **2c**–**5c**.

It is apparent that, in addition to the amide signals, the aromatic structure and the ethoxy moiety of both pendant arms exhibit a double set of signals in both the ^{1}H and ^{13}C{H} NMR spectra upon complexation. Structural moieties positioned farther from the coordination centre may still appear as only one signal set though (e.g., the CH_3 moiety of the ethoxy chain in **3c** and **5c**). A comparison of related signal sets shows that the differences in chemical shifts between respective moieties are usually more pronounced in **4c**. This observation is in accordance with a hepta-coordinated complex, in which the amide pendant arms of **4c** possess a clearly different chemical environment compared with those in **3c** and **5c**, in which the double set of signals is likely caused by a different chemical environment of the pendant arms due to the chirality of the complex.

The Ga^{III}, In^{III} and Lu^{III} complexes of the dtpa bisamides can exist in different diastereomeric forms.[9,15,28,40,41] However, in every diastereomer the amide pendant arms may appear as a double set of signals due to their different chemical environment. If several diastereomers exist in solution and interconversion is slow

Table 5. Selected NMR spectroscopic data of **2c**–**5c** in [D_6]dmso (600 MHz).

	δ [ppm]							
	2c		**3c**		**4c**		**5c**	
	^{1}H	^{13}C{^{1}H}	^{1}H	^{13}C{^{1}H}	^{1}H	^{13}C{^{1}H}	^{1}H	^{13}C{^{1}H}
CH(1)	–	139.9	–	139.6	–	139.7	–	129.6
						138.0		129.5
CH(2)	7.34	105.5	7.31 (s)	105.6	7.53 (s)	106.6	7.32 (s)	107.2
			7.26 (s)	105.7	7.31 (s)	105.6	7.26 (s)	106.7
CH(3)	–	158.8	–	158.7	–	158.9	–	158.8
						158.7		
CH(4)	6.69 (d)	109.3	6.64 (d)	109.8	6.77 (dd)	111.8	6.76 (d)	110.3
				109.5	6.63 (dd)	109.7	6.73 (d)	110.1
CH(5)	7.14 (dd)	129.4	7.21–7.18 (dd)	129.5	7.30–7.28 (dd)	129.8	7.27–7.23	138.7
					7.21–7.18	129.5	7.25–7.22	138.4
CH(6)	7.18 (d)	111.5	7.12–7.11 (m)	111.5	7.13–7.12 (m)	112.3	7.38–7.37 (m)	112.7
			7.09–7.07 (m)	111.4	7.09–7.08 (m)	111.6	7.32–7.30 (m)	112.4
O*CH*$_2$CH$_3$	3.96 (q)	62.9	3.98 (q)	62.9	4.10–4.05 (m)	63.3	4.04–4.00 (m)	63.1
					4.00–3.97 (m)	62.9	4.02–3.98 (m)	63.0
OCH$_2$*CH*$_3$	1.30 (t)	14.7	1.32 (t)	14.6	1.34 (t)	14.6	1.30 (t)	14.6
					1.32 (t)	14.5	1.29 (t)	
N*H*–C=O	10.03	–	10.38 (s)	–	11.44 (s)	–	10.81 (s)	–
			10.26 (s)		10.31 (s)		10.78 (s)	
C=O		173.1	–	170.6	–	171.4	–	175.7
		169.7		170.5		171.2		175.2
		169.4		170.2		170.6		174.9
				166.3		170.5		174.2
				165.9		166.9		173.3

compared with the NMR timescale, more than one set of double signals should be observable for the pendant arms.

As this was not observed in the spectra of **3c**–**5c**, only one detectable isomer for each complex may be present in solution. Furthermore, the ^{13}C{^{1}H} NMR spectral assignment of the aliphatic carbon signals was performed for **3c**–**5c** by using two-dimensional NMR spectroscopy. In no case were more than nine carbon signals of the dtpa backbone detected. Additionally, only five signals for the carboxy and carbonyl carbon atoms were detected in total for **3c**, contrary to a previously reported similar complex.[28]

However, it remains unknown whether the detection of a single isomer is caused by fast interconversion between several conformers at room temperature or is due to the preference of a certain diastereomer in solution. Because coalescence might be reached at higher temperatures and abolished at lower temperatures, additional ^{1}H NMR spectroscopic studies of **3c**–**5c** were performed at 85 and –50 °C.

High-Temperature NMR Spectroscopy

There are three types of isomerism in dtpa amide complexes, induced by "wagging" of the diethylenetriamine backbone, "shuffling" of the two [NO2] donor sets or inversion at the two terminal nitrogen atoms.[8] Even at elevated temperatures, no coalescence of the signals of In^{III} or Lu^{III} complexes was reported and therefore it was concluded that even at high temperatures, inversion of the terminal nitrogen donors occurs slowly compared with the NMR timescale.[9,15] It should be noted that these NMR measurements were performed in D_2O whereas we had to use [D_6]dmso. Therefore the results should be compared with caution.

At 85 °C, only one set of proton signals was detected for the amide pendant arms of **3c**. However, the aliphatic region maintains some of its characteristic signal groups and coupling pattern, proving the integrity of the complex. Apparently, at elevated temperatures the pendant arms of **3c** become chemically equivalent. In the presumed octahedral structure this might be due to a strong fluctuation of the complex as well as interconversion between different conformations, which might occur quickly compared with the NMR timescale. In contrast, a double set of aromatic proton signals is observed in **4c** at elevated temperatures. This double set of signals indicates that the complex maintains its hepta-coordinated structure even at 85 °C. Surprisingly, in the ^{1}H NMR spectra of **5c**, the signals of the aromatic protons 2-H, 5-H and 6-H show exceptionally strong overlap, which prevents definitive assignment. However, the proton 4-H is clearly detectable as a single doublet at these elevated temperatures. Although the amide protons merge into one singlet, the signal assigned to the water ligand is no longer detectable. The remarkable overlapping indicates strong fluxional behaviour.

Low-Temperature NMR Spectroscopy

Fast interconversion between several conformers might result in the observed detection of a single double set of signals suggesting the presence of only one diastereomer. However, more signals might evolve at low temperatures. Therefore the NMR spectra of **3c**–**5c** were recorded at –50 °C in [D_7]dmf as solvent.

For comparison, NMR spectra were also recorded at room temperature in the same solvent, and were comparable to the spectra recorded in [D_6]dmso. Double sets of signals can be seen for the pendant arms of **3c** and **4c**, whereas in **5c** remarkable overlap and broadening of the signals are observed. The differences in the chemical shifts

between respective signal groups of the pendant arms are again most pronounced in **4c**.

No additional signal sets appeared in any of the spectra of **3c**–**5c** at –50 °C. The protons of the pendant arms maintain their pattern of double signal sets, and there are still only nine signals detected for the dtpa backbone structure in the $^{13}C\{^{1}H\}$ NMR spectra. One could assume that even at these low temperatures interconversion might still occur easily enough to result in only one isomer being detectable. But these results rather corroborate our assumption, that only one diastereomer is present in solution, in contrast to previous research of similar metal^{III} complexes in which usually several diastereomers were detected by NMR spectroscopy.[9,15,28]

Additionally, quantum chemical calculations performed on **3c** did not yield precise information on the existence of a preferred structure of the complex because the energy differences between the isomers were all within the error range. Detailed data are given in the Supporting Information.

HPLC Analysis

Although theoretically complexes of the type **3**–**5** may exist as diastereomers, their respective HPLC chromatograms show only a single peak. This is in accordance with previous observations and was associated with fast interconversion between different diastereomers.[9,41] Although this would require the inversion of a terminal nitrogen atom, which was acknowledged to occur slowly even at high temperatures on the basis of NMR studies, the low concentrations of the complexes during HPLC analysis were considered to facilitate the process due to dissociation of the [NO2] donor set.[9] As supported by our previous NMR studies, we assume the exclusive existence of one diastereomer for the described metal complexes.

The In^{III} compounds **4a–d** show lower retention than the corresponding Ga^{III} compounds **3a**–**d**, whereas **4e** shows higher retention than **3e**. However, the differences are only 0.1–0.3 min, and the compounds therefore exhibit a comparable degree of lipophilicity. For comparison, Lu^{III} complexes **5a**–**e** show an additional prolonged retention of approximately 0.5 min and thus are more lipophilic. Owing to the fact that all the complexes are uncharged, the relative lipophilicity is mostly affected by the nature of the coordination sphere of the central metal ion.

It has been noted before that uncoordinated amide moieties possess the ability to form hydrogen bonds with water molecules from the solvent, resulting in increased hydrophilicity.[9,41] This is in agreement with the fact that the Lu^{III} complexes most likely feature strong bonding of the amide moieties and are therefore the most lipophilic species. Apparently, the Ga^{III} and In^{III} complexes have more similar coordination spheres than the respective Lu^{III} complexes. As the Ga^{III} complexes most likely show a hexa-coordinated central metal ion, we suppose that the In^{III} complexes also show at least partial dissociation of the two amide pendant arms in aqueous solution. Furthermore, the dissociation might be followed by association of water ligands, making the In^{III} complexes even slightly more hydrophilic than the respective Ga^{III} species.

Conclusions

We have successfully synthesized and characterized five dtpa bis(alkoxyphenyl)amides and their Ga^{III}, In^{III} and Lu^{III} complexes. Elemental analysis, mass spectrometry and NMR spectroscopy confirmed that one ligand chelates one metal ion. The NMR spectra indicated the existence of hexa-coordinated Ga^{III} species. We found that the In^{III} complex **4a** crystallizes in both a hepta- and octa-coordinated form, whereas the NMR spectra revealed the exclusive existence of the hepta-coordinated species. The Lu^{III} ion coordinates a water molecule in addition to the eight donor atoms of the ligands to form a nona-coordinated complex.

Although the results of quantum-chemical calculations on **3c** indicated that several isomers may exist in solution, the results of our NMR and HPLC analyses strongly indicate the sole existence of a single diastereomer in solution for all complexes.

Experimental Section

General: All reagents were purchased from commercial sources and used without further purification. dmf was distilled from sodium prior to use and stored under nitrogen over molecular sieves (4 Å). Diethyl ether was stored over KOH plates. dtpa bis-anhydride **1** and the dtpa bis-amides **2** were synthesized under nitrogen using standard vacuum-line and Schlenk techniques.

Ga^{III} chloride (1.42 g) was dissolved in 0.3 M acetate buffer (100 mL) to prepare a stock solution with a pH of 1.9. For the syntheses in chloroform, a 0.5 M solution of Ga^{III} chloride in *n*-pentane was used.

For the HPLC analyses a system equipped with a binary pump (HP 1100, G1312A), UV/Vis detector (HP 1100, G1315A) and column (ACE C18-PFP; 150 × 3 mm) was used. Reported values indicate the purity of the compounds as detected by means of their UV absorbance at 220 nm. The following gradient was used: 0–3 min 80% A, 3–6 min 80% A→0% A, 6–10 min 0% A [A: water/trifluoroacetic acid (99.9%/0.1%); B: acetonitrile/trifluoroacetic acid (99.9%/0.1%)].

Unless stated otherwise, ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were recorded at room temperature with either a Bruker AVANCE 400 or 600 spectrometer. The NMR spectra of the ligands were recorded in deuterated dmso, which had been dried prior to use over 4 Å molecular sieves and stored under nitrogen. The NMR spectra of the complexes were recorded in [D_6]dmso or [D_4]MeOH. Additionally, the NMR spectra of complexes **3c**–**5c** were recorded at 85 °C in [D_6]dmso and at room temperature as well as –50 °C in deuteriated anhydrous [D_7]dmf (≥99.5%). In these spectra some of the proton signals of the complexes merge with the signal of residual water in the solvent. The residual peaks of the solvents were used as internal reference.

Mass spectra were recorded with either a Finnigan SSQ 710 (DEI, FAB) or a MAT 95 XL (ESI) spectrometer. Elemental analyses

were performed as single determinations using a Vario EL III CHNS instrument (Elementaranalysensystem GmbH, Hanau, Germany).

Structure Determinations: The intensity data of the compounds were collected with a Nonius–KappaCCD diffractometer using graphite-monochromated Mo-K_α radiation. Data were corrected for Lorentzian and polarization effects and absorption was taken into account on a semi-empirical basis using multiple scans.[42–44]

The structures were solved by direct methods (SHELXS[45]) and refined by full-matrix least-squares techniques against F_o^2 (SHELXL-97[45]). The hydrogen atoms of the amine groups N1A and N1B of compound **4c** were located by difference Fourier synthesis and refined isotropically. All other hydrogen atoms were included at calculated positions with fixed thermal parameters. All non-disordered non-hydrogen atoms were refined anisotropically.[45] The crystallographic data as well as structure solution and refinement details are summarized in Table 1.

CCDC-1048431 (for **4a**), -1048432 (for **4c**) and -1048433 (for **5c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Synthesis of dtpa Bis-anhydride 1: This compound was synthesized according to a literature procedure.[46] Under nitrogen, dtpa (49 g, 125 mmol) was suspended in dry pyridine (62 mL, 770 mmol) and acetic anhydride (53 mL, 560 mmol) and stirred at 65 °C for 24 h. The precipitate was filtered and washed three times with diethyl ether to afford a colourless solid, yield 42 g (117.5 mmol, 94%). ^{1}H NMR (400.1 MHz, [D$_6$]dmso): δ = 3.71 [s, 8 H, N(CH_2CO)$_2$O], 3.31 (s, 2 H, NCH_2COOH), 2.75 (t, $^3J_{H,H}$ = 6.0 Hz, 4 H, NCH_2CH_2N), 2.60 (t, $^3J_{H,H}$ = 6.0 Hz, 4 H, NCH_2CH_2N) ppm. ^{13}C{^{1}H} NMR (150.9 MHz, [D$_6$]dmso): δ = 171.9 (*C*OOH), 165.8 [N(CH$_2$*C*O)$_2$O], 54.6 (*C*H$_2$COOH), 52.6 ppm.

General Procedure for the Preparation of dtpa-*N*,*N*′′-Bis(alkoxyphenylamides) 2a–e:[47,48] Under nitrogen, dtpa bis-anhydride **1** (2 g, 5.6 mmol) was dissolved in dry dmf (50 mL), the respective aniline (11.2 mmol) was added and the solution was stirred for 24 h at room temperature. The solvent was removed in vacuo and the residue was recrystallized from hot ethanol to yield dtpa bis-amides **2a**–**e** as colourless solids.

dtpa-*N*,*N*′′-Bis(*m*-methoxyphenylamide) (2a): Prepared from *m*-methoxyaniline (1.25 mL, 1.38 g, 11.2 mmol), yield 2.67 g (4.4 mmol, 79%). ^{1}H NMR (600.1 MHz, [D$_6$]dmso): δ = 11.92 (br. s, 1.5 H, COO*H*), 10.03 (s, 2 H, N*H*-CO), 7.35 (t, $^4J_{H,H}$ = 1.9 Hz, 2 H, H_{Ar}), 7.19–7.14 (m, 4 H, H_{Ar}), 6.61–6.59 (m, 2 H, H_{Ar}), 3.70 (s, 6 H, OCH_3), 3.53 (s, 2 H, CH_2COO$_{central}$), 3.44 (s, 4 H, CH_2C=O), 3.42 (s, 4 H, CH$_2$C=O), 3.02 (m, 4 H, NCH_2CH_2N), 2.93 (m, 4 H, NCH_2CH_2N) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]dmso): δ = 173.1 (*C*=O), 169.7 (*C*=O), 169.4 (*C*=O), 159.5 (O-C_{Ar}), 139.9 (N-C_{Ar}), 129.4 (C_{Ar}), 111.6 (C_{Ar}), 108.8 (C_{Ar}), 105.1 (C_{Ar}), 58.3 (*C*H$_2$C=O, NCH_2CH_2N), 55.4 (*C*H$_2$C=O, NCH_2CH_2N), 55.3 (*C*H$_2$C=O, NCH_2CH_2N), 55.0 (O*C*H$_3$), 52.3 (*C*H$_2$C=O, NCH_2CH_2N), 51.1 (*C*H$_2$C=O, NCH_2CH_2N) ppm. MS (DEI): calcd. for [M]$^+$ 603; found 604 [M + H]$^+$, 587 [M – OH]$^+$, 164 [H$_3$C–O–C$_6$H$_4$ – NHCO – CH$_2$]$^{+\cdot}$. C$_{28}$H$_{37}$N$_5$O$_{10}$·0.5H$_2$O (612.26): calcd. C 54.89, H 6.25, N 11.43; found C 54.55, H 6.35, N 11.11.

dtpa-*N*,*N*′′-Bis(*o*-ethoxyphenylamide) (2b): Prepared from *o*-ethoxyaniline (1.47 mL, 1.54 g, 11.1 mmol), yield 2.82 g (4.5 mmol, 80%). ^{1}H NMR (600.1 MHz, [D$_6$]dmso): δ = 12.31 (br. s, 2.8 H, COO*H*), 9.75 (s, 2 H, N*H*-CO), 8.20 (d, $^3J_{H,H}$ = 8.0 Hz, 2 H, H_{Ar}), 7.01–6.97 (m, 4 H, H_{Ar}), 6.89–6.86 (m, 2 H, H_{Ar}), 4.01 (q, $^3J_{H,H}$ = 7.0 Hz, 4 H, OCH_2CH$_3$), 3.40 (s, 4 H, CH_2C=O), 3.29 (s, 4 H, CH_2C=O), 3.28 (s, 2 H, CH_2COO$_{central}$), 2.79–2.76 (m, 4 H, NCH_2CH_2N), 2.71–2.69 (m, 4 H, NCH_2CH_2N), 1.33 (t, $^3J_{H,H}$ = 7.0 Hz, 6 H, OCH$_2$CH_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]-dmso): δ = 172.2 (*C*=O), 172.0 (*C*=O), 169.0 (*C*=O), 147.5 (O-C_{Ar}), 127.4 (N-C_{Ar}), 123.6 (C_{Ar}), 120.4 (C_{Ar}), 118.9 (C_{Ar}), 111.8 (C_{Ar}), 63.9 (O*C*H$_2$CH$_3$), 59.4 (*C*H$_2$C=O, NCH_2CH_2N), 55.5 (*C*H$_2$C=O, NCH_2CH_2N), 54.6 (*C*H$_2$C=O, NCH_2CH_2N), 52.8 (*C*H$_2$C=O, NCH_2CH_2N), 52.7 (*C*H$_2$C=O, NCH_2CH_2N), 14.7 (OCH$_2$*C*H$_3$) ppm. MS (DEI): calcd. for [M]$^+$ 631 ; found 632 [M + H]$^+$, 614 [M – H$_2$O]$^+$. C$_{30}$H$_{41}$N$_5$O$_{10}$·H$_2$O (649.30): calcd. C 55.46, H 6.67, N 10.78; found C 55.23, H 6.64, N 10.69.

dtpa-*N*,*N*′′-Bis(*m*-ethoxyphenylamide) (2c): Prepared from *m*-ethoxyaniline (1.49 mL, 1.54 g, 11.2 mmol), yield 2.79 g (4.4 mmol, 79%). ^{1}H NMR (400.1 MHz, [D$_6$]dmso): δ = 11.93 (br. s, 1.7 H, COO*H*), 10.02 (s, 2 H, N*H*-CO), 7.73 (s, 2 H, H_{Ar}), 7.18–7.11 (m, 4 H, H_{Ar}), 7.59–7.57 (m, 2 H, H_{Ar}), 3.95 (q, $^3J_{H,H}$ = 7.0 Hz, 4 H, OCH_2CH$_3$), 3.52 (s, 2 H, CH_2COO$_{central}$), 3.43 (s, 4 H, CH_2C=O), 3.42 (s, 4 H, CH_2C=O), 3.03–3.01 (m, 4 H, NCH_2CH$_2$N), 2.94–2.92 (m, 4 H, NCH$_2$CH_2N), 1.29 (t, $^3J_{H,H}$ = 7.0 Hz, 6 H, OCH$_2$CH_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]dmso): δ = 173.5 (*C*=O), 170.1 (*C*=O), 169.8 (*C*=O), 159.2 (O-C_{Ar}), 140.3 (N-C_{Ar}), 129.8 (C_{Ar}), 111.9 (C_{Ar}), 109.8 (C_{Ar}), 106.0 (C_{Ar}), 63.3 (O*C*H$_2$CH$_3$), 58.8 (*C*H$_2$C=O, NCH_2CH_2N), 55.8 (*C*H$_2$C=O, NCH_2CH_2N), 55.5 (*C*H$_2$C=O, NCH_2CH_2N), 52.7 (*C*H$_2$C=O, NCH_2CH_2N), 51.5 (*C*H$_2$C=O, NCH_2CH_2N), 15.1 (OCH$_2$*C*H$_3$) ppm. MS (DEI): calcd. for [M]$^+$ 631; found 632 [M + H]$^+$. C$_{30}$H$_{41}$N$_5$O$_{10}$·H$_2$O (649.30): calcd. C 55.46, H 6.67, N 10.78; found C 55.25, H 6.62, N 10.71.

dtpa-*N*,*N*′′-Bis(*p*-ethoxyphenylamide) (2d): Prepared from *p*-ethoxyaniline (1.45 mL, 1.54 g, 11.2 mmol), yield 2.89 g (4.6 mmol, 82%). ^{1}H NMR (400.1 MHz, [D$_6$]dmso): δ = 11.86 (br. s, 0.7 H, COO*H*), 9.91 (s, 2 H, N*H*-CO), 7.53 (d, $^3J_{H,H}$ = 9.0 Hz, 4 H, H_{Ar}), 6.80 (d, $^3J_{H,H}$ = 9.0 Hz, 4 H, H_{Ar}), 3.93 (t, $^3J_{H,H}$ = 6.9 Hz, 4 H, OCH_2CH$_3$), 3.50 (s, 2 H, CH_2COO$_{central}$), 3.43 (s, 4 H, CH_2C=O), 3.40 (s, 4 H, CH_2C=O), 3.03–3.01 (m, 4 H, NCH_2CH$_2$N), 2.93–2.90 (m, 4 H, NCH$_2$CH_2N), 1.28 (t, $^3J_{H,H}$ = 6.9 Hz, 6 H, OCH$_2$CH_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]dmso): δ = 173.0 (*C*=O), 169.5 (*C*=O), 168.7 (*C*=O), 154.5 (O-C_{Ar}), 131.8 (N-C_{Ar}), 120.8 (C_{Ar}), 114.2 (C_{Ar}), 63.0 (O*C*H$_2$CH$_3$), 58.2 (*C*H$_2$C=O, NCH_2CH_2N), 55.3 (*C*H$_2$C=O, NCH_2CH_2N), 52.3 (*C*H$_2$C=O, NCH_2CH_2N), 51.0 (*C*H$_2$C=O, NCH_2CH_2N), 14.7 (OCH$_2$*C*H$_3$) ppm. MS (ESI, + mode): calcd. for [M]$^+$ 631; found 654 [M + Na]$^+$, 632 [M + H]$^+$. C$_{30}$H$_{41}$N$_5$O$_{10}$·H$_2$O (649.30): calcd. C 55.46, H 6.67, N 10.78; found C 55.86, H 6.54, N 10.87.

dtpa-*N*,*N*′′-Bis(*p*-butoxyphenylamide) (2e): Prepared from *p*-butoxyaniline (1.85 g, 11.2 mmol), yield 2.20 g (3.2 mmol, 57%). ^{1}H NMR (400.1 MHz, [D$_6$]dmso): δ = 11.50 (br. s, 0.3 H, COO*H*), 9.91 (s, 2 H, N*H*-CO), 7.52 (d, $^3J_{H,H}$ = 9.0 Hz, 4 H, H_{Ar}), 6.80 (d, $^3J_{H,H}$ = 9.0 Hz, 4 H, H_{Ar}), 3.87 (t, $^3J_{H,H}$ = 6.5 Hz, 4 H, OCH_2CH$_2$CH$_2$CH$_3$), 3.53 (s, 2 H, CH_2COO$_{central}$), 3.43 (s, 4 H, CH_2C=O), 3.41 (s, 4 H, CH_2C=O), 3.04 (m, 4 H, NCH_2CH$_2$N), 2.92 (m, 4 H, NCH$_2$CH_2N), 1.65 (m, 4 H, OCH$_2$CH_2CH$_2$CH$_3$), 1.40 (m, $^3J_{H,H}$ = 7.5 Hz, 4 H, OCH$_2$CH$_2$CH_2CH$_3$), 0.91 (t, $^3J_{H,H}$ = 7.5 Hz, 6 H, OCH$_2$CH$_2$CH$_2$CH_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]dmso): δ = 173.0 (*C*=O), 169.5 (*C*=O), 168.8 (*C*=O), 154.7 (O-C_{Ar}), 131.8 (N-C_{Ar}), 120.8 (C_{Ar}), 114.3 (C_{Ar}), 67.2 (O*C*H$_2$CH$_2$CH$_2$CH$_3$), 58.2 (*C*H$_2$C=O, NCH_2CH_2N), 55.3 (*C*H$_2$C=O, NCH_2CH_2N), 55.0 (*C*H$_2$C=O, NCH_2CH_2N), 52.3 (*C*H$_2$C=O, NCH_2CH_2N), 51.0 (*C*H$_2$C=O, NCH_2CH_2N), 30.8 (OCH$_2$*C*H$_2$CH$_2$CH$_3$), 18.8 (OCH$_2$CH$_2$*C*H$_2$CH$_3$), 13.7

($OCH_2CH_2CH_2CH_3$) ppm. MS (ESI, + mode): calcd. for $[M]^+$ 687; found 710 $[M + Na]^+$, 688 $[M + H]^+$. $C_{34}H_{49}N_5O_{10}\cdot 1.5H_2O$ (714.37): calcd. C 57.13, H 7.33, N 9.80; found C 57.28, H 7.30, N 9.77.

General Procedure for the Preparation of Ga^{III} Complexes 3a–e: Two procedures, one in aqueous and one in organic media, have been developed. Either method is suitable for all the described Ga^{III} complexes.

Procedure A: Acetate buffer (100 mL, 0.3 M, pH 4.5) was added to Ga^{III} chloride (1.42 g, 8.2 mmol)to give a stock solution of Ga^{III} (82 mM, pH 1.9). An aliquot of the stock solution was transferred into a flask, followed by the addition of 1 equiv. of ligand, which had been dissolved in hot deionized water. The more lipophilic **2e** did not dissolve completely, resulting in a suspension that could be used for the reaction without remarkably affecting the reaction yield. A stirrer and pH electrode was added to the clear solution or suspension. At room temperature, a solution of 0.3 M acetate buffer (pH 4.5) was added dropwise to raise the pH to 3.2–3.3 upon which a colourless precipitate formed immediately. The solution was stirred at room temperature for 30 min with the pH increasing to 3.5 at most. The precipitate was filtered off and washed thoroughly with deionized water to remove buffer and inorganic salts. The solid was dried in vacuo. Subsequent recrystallization from hot methanol yielded the complexes as colourless solids.

Procedure B: In a flask 1 equiv. of ligand was added to 3 equiv. of a solution of tetra-*n*-butylammonium hydroxide in methanol (1.0 M). Chloroform (20 mL) was added to the mixture to give a clear solution. A stirrer and 1 equiv. of a solution of Ga^{III} chloride in *n*-pentane (0.5 M) was added to the mixture at room temperature. The mixture was stirred at room temperature overnight. Complex **3e** precipitated from the solution as a colourless solid and could be isolated by filtration, followed by washing with chloroform and drying in vacuo. Slow diffusion of diethyl ether into the reaction mixture afforded precipitation of compounds **3a**–**d**.

[Ga^{III}\{dtpa-*N*,*N*′′-bis(*m*-methoxyphenylamide)\}] (3a): Prepared following procedure A from Ga^{III} chloride (3.7 mL, 0.30 mmol) and **2a** (183 mg, 0.30 mmol), yield 90 mg (0.13 mmol, 45%). HPLC: 4.3 min, 96.8%. ^{1}H NMR (600.1 MHz, [D$_6$]dmso): δ = 10.40 (s, 1 H, N*H*-CO), 10.28 (s, 1 H, N*H*-CO), 7.32–7.27 (m, 2 H, H_{Ar}), 7.23–7.20 (m, 2 H, H_{Ar}), 7.14–7.09 (m, 2 H, H_{Ar}), 6.66–6.65 (m, 2 H, H_{Ar}), 4.06–2.81 (m, 18 H, CH_2C=O, NCH_2CH_2N), 3.72 (s, 6 H, OCH_3) ppm. ^{13}C\{^{1}H\} NMR (150.9 MHz, [D$_6$]dmso): δ = 170.7 (*C*=O), 170.5 (*C*=O), 170.2 (*C*=O), 166.3 (*C*=O), 165.9 (*C*=O), 159.5 (O-C_{Ar}), 129.6 (N-C_{Ar}), 111.6 (C_{Ar}), 111.5 (C_{Ar}), 109.2 (C_{Ar}), 108.9 (C_{Ar}), 105.1 (C_{Ar}), 61.3 (*C*H$_2$C=O, NCH_2CH_2N), 60.2 (*C*H$_2$C=O, NCH_2CH_2N), 60.1 (*C*H$_2$C=O, NCH_2CH_2N), 57.1 (*C*H$_2$C=O, NCH_2CH_2N), 56.5 (*C*H$_2$C=O, NCH_2CH_2N), 55.0 (O*C*H$_3$), 54.7 (*C*H$_2$C=O, NCH_2CH_2N), 54.3 (*C*H$_2$C=O, NCH_2CH_2N), 54.0 (*C*H$_2$C=O, NCH_2CH_2N), 51.7 (*C*H$_2$C=O, NCH_2CH_2N) ppm. MS (ESI, + mode): calcd. for $[M(^{71}Ga)]^+$ 671, $[M(^{69}Ga)]^+$ 669; found *m*/*z* (%) = 695 (22) $[M(^{71}Ga) + 1 + Na]^+$, 694 (74) $[M(^{71}Ga) + Na]^+$, 693 (33) $[M(^{69}Ga) + 1 + Na]^+$, 692 (100) $[M(^{69}Ga) + Na]^+$. $C_{28}H_{34}GaN_5O_{10}\cdot H_2O$ (688.33): calcd. C 48.86, H 5.27, N 10.17; found C 48.53, H 5.28, N 10.06.

[Ga^{III}\{dtpa-*N*,*N*′′-bis(*o*-ethoxyphenylamide)\}] (3b): Prepared following procedure A from Ga^{III} chloride (3 mL, 0.25 mmol) and **2b** (150 mg, 0.24 mmol), yield 33 mg (0.05 mmol, 20%). HPLC: 4.6 min, 96.6%. ^{1}H NMR (600.1 MHz, [D$_6$]dmso): δ = 9.66–9.60 (m, 2 H, N*H*-CO), 7.85–7.72 (m, 2 H, H_{Ar}), 7.11–7.09 (m, 2 H, H_{Ar}), 7.04–7.03 (m, 2 H, H_{Ar}), 6.91–6.89 (m, 2 H, H_{Ar}), 4.07 (m, 4 H, OCH_2CH$_3$), 4.14–2.85 (m, 18 H, CH_2C=O, NCH_2CH_2N), 1.41–1.36 (m, 6 H, OCH$_2$CH_3) ppm. ^{13}C\{^{1}H\} NMR (150.9 MHz, [D$_6$]dmso): δ = 170.7 (*C*=O), 170.6 (*C*=O), 170.1 (*C*=O), 166.4 (*C*=O), 166.0 (*C*=O), 150.2 (O-C_{Ar}), 149.5 (O-C_{Ar}), 126.5 (N-C_{Ar}, C_{Ar}), 126.4 (N-C_{Ar}, C_{Ar}), 125.6 (N-C_{Ar}, C_{Ar}), 125.1 (N-C_{Ar}, C_{Ar}), 124.0 (N-C_{Ar}, C_{Ar}), 123.1 (C_{Ar}), 120.0 (C_{Ar}), 112.4 (C_{Ar}), 63.8 (O*C*H$_2$CH$_3$), 61.4 (*C*H$_2$C=O, NCH_2CH_2N), 60.0 (*C*H$_2$C=O, NCH_2CH_2N), 57.2 (*C*H$_2$C=O, NCH_2CH_2N), 56.7 (*C*H$_2$C=O, NCH_2CH_2N), 54.5 (*C*H$_2$C=O, NCH_2CH_2N), 54.3 (*C*H$_2$C=O, NCH_2CH_2N), 53.9 (*C*H$_2$C=O, NCH_2CH_2N), 51.5 (*C*H$_2$C=O, NCH_2CH_2N), 14.6 (OCH$_2$*C*H$_3$) ppm. MS (ESI, + mode): calcd. for $[M(^{71}Ga)]^+$, 699, $[M(^{69}Ga)]^+$ 697; found *m*/*z* (%) = 723 (25) $[M(^{71}Ga) + 1 + Na]^+$, 722 (76) $[M(^{71}Ga) + Na]^+$, 721 (36) $[M(^{69}Ga) + 1 + Na]^+$, 720 (100) $[M(^{69}Ga) + Na]^+$. $C_{30}H_{38}GaN_5O_{10}\cdot 2H_2O$ (734.40): calcd. C 49.06, H 5.76, N 9.54; found C 49.37, H 5.74, N 9.54.

[Ga^{III}\{dtpa-*N*,*N*′′-bis(*m*-ethoxyphenylamide)\}] (3c): Prepared following procedure A from Ga^{III} chloride (2.6 mL, 0.21 mmol) and **2c** (130 mg, 0.21 mmol), yield 22 mg (0.03 mmol, 15%). HPLC: 4.8 min, 94.5%. ^{1}H NMR (600.1 MHz, [D$_6$]dmso, 22 °C): δ = 10.38 (s, 1 H, N*H*-CO), 10.26 (s, 1 H, N*H*-CO), 7.31–7.26 (m, 2 H, H_{Ar}), 7.21–7.18 (m, 2 H, H_{Ar}), 7.12–7.07 (m, 2 H, H_{Ar}), 6.64–6.63 (m, 2 H, H_{Ar}), 4.00–3.96 (m, 4 H, OCH_2CH$_3$), 4.10–2.82 (m, 18 H, CH_2CO, NCH_2CH_2N), 1.32 9 (t, $^3J_{H,H}$ = 7.0 Hz, 6 H, OCH$_2$CH_3) ppm. ^{1}H NMR (600.1 MHz, [D$_6$]dmso, 85 °C): δ = 10.12 (s, 2 H, N*H*-CO), 7.27 (s, 2 H, H_{Ar}), 719 (t, $^3J_{H,H}$ = 8.1 Hz, 2 H, H_{Ar}), 7.11–7.10 (m, 2 H, H_{Ar}), 6.66 (dd, $^3J_{H,H}$ = 8.1, $^4J_{H,H}$ = 2.1 Hz, 2 H, H_{Ar}), 4.03 (q, $^3J_{H,H}$ = 7.0 Hz, 4 H, OCH_2CH$_3$), 3.97–3.23 (m, 18 H, CH_2CO, NCH_2CH_2N), 1.33 (t, $^3J_{H,H}$ = 7.0 Hz, 6 H, OCH$_2$CH_3) ppm. ^{13}C\{^{1}H\} NMR (150.9 MHz, [D$_6$]dmso, room temp.): δ = 170.6 (*C*=O), 170.5 (*C*=O), 170.2 (*C*=O), 166.3 (*C*=O), 165.9 (*C*=O), 158.7 (O-C_{Ar}), 139.6 (N-C_{Ar}), 129.5 (C_{Ar}), 111.5 (C_{Ar}), 111.3 (C_{Ar}), 109.8 (C_{Ar}), 109.8 (C_{Ar}), 105.5 (C_{Ar}), 62.9 (O*C*H$_2$CH$_3$), 61.3 (*C*H$_2$C=O, NCH_2CH_2N), 60.2 (*C*H$_2$C=O, NCH_2CH_2N), 60.1 (*C*H$_2$C=O, NCH_2CH_2N), 57.1 (*C*H$_2$C=O, NCH_2CH_2N), 56.5 (*C*H$_2$C=O, NCH_2CH_2N), 54.7 (*C*H$_2$C=O, NCH_2CH_2N), 54.3 (*C*H$_2$C=O, NCH_2CH_2N), 54.0 (*C*H$_2$C=O, NCH_2CH_2N), 51.7 (*C*H$_2$C=O, NCH_2CH_2N), 14.6 (OCH$_2$*C*H$_3$) ppm. MS (ESI, + mode): calcd. for $[M(^{71}Ga)]^+$ 699, $[M(^{69}Ga)]^+$ 697; found *m*/*z* (%) = 723 (25) $[M(^{71}Ga) + 1 + Na]^+$, 722 (76) $[M(^{71}Ga) + Na]^+$, 721 (36) $[M(^{69}Ga) + 1 + Na]^+$, 720 (100) $[M(^{69}Ga) + Na]^+$. $C_{30}H_{38}GaN_5O_{10}\cdot 2H_2O$ (734.40): calcd. C 49.06, H 5.76, N 9.54; found C 48.98, H 5.51, N 9.63.

[Ga^{III}\{dtpa-*N*,*N*′′-bis(*p*-ethoxyphenylamide)\}] (3d): Prepared following procedure A from Ga^{III} chloride solution (2.6 mL, 0.21 mmol) and **2d** (135 mg, 0.21 mmol), yield 35 mg (0.05 mmol, 23%). HPLC: 4.7 min, 95.6%. ^{1}H NMR (600.1 MHz, [D$_6$]dmso): δ = 10.27 (s, 1 H, N*H*-CO), 10.16 (s, 1 H, N*H*-CO), 7.51–7.47 (m, 4 H, H_{Ar}), 6.97 (d, $^3J_{H,H}$ = 8.7 Hz, 4 H, H_{Ar}), 3.99–3.96 (m, 4 H, OCH_2CH$_3$), 4.04–2.84 (m, 18 H, CH_2CO, NCH_2CH_2N), 1.31–1.29 (m, 6 H, OCH$_2$CH_3) ppm. ^{13}C\{^{1}H\} NMR (100.6 MHz, [D$_6$]dmso): δ = 170.7 (*C*=O), 170.5 (*C*=O), 168.7 (*C*=O), 165.3 (*C*=O), 154.7 (O-C_{Ar}), 154.6 (O-C_{Ar}), 131.6 (N-C_{Ar}), 122.7 (C_{Ar}), 120.8 (C_{Ar}), 114.7 (C_{Ar}), 114.4 (C_{Ar}), 63.3 (O*C*H$_2$CH$_3$), 63.1 (O*C*H$_2$CH$_3$), 60.0 (*C*H$_2$C=O, NCH_2CH_2N), 57.8 (*C*H$_2$C=O, NCH_2CH_2N), 54.7 (*C*H$_2$C=O, NCH_2CH_2N), 54.4 (*C*H$_2$C=O, NCH_2CH_2N), 14.7 (OCH$_2$*C*H$_3$), 14.6 (OCH$_2$*C*H$_3$) ppm. MS (ESI, + mode): calcd. for $[M(^{71}Ga)]^+$ 699, $[M(^{69}Ga)]^+$ 697; found *m*/*z* (%) = 723 (25) $[M(^{71}Ga) + 1 + Na]^+$, 722 (76) $[M(^{71}Ga) + Na]^+$, 721 (36) $[M(^{69}Ga) + 1 + Na]^+$, 720 (100) $[M(^{69}Ga) + Na]^+$. $C_{30}H_{38}GaN_5O_{10}\cdot 2.5H_2O$ (743.41): calcd. C 48.47, H 5.84, N 9.42; found C 48.09, H 5.40, N 9.31.

[Ga^{III}\{dtpa-*N*,*N*′′-bis(*p*-butoxyphenylamide)\}] (3e): Prepared following procedure B from Ga^{III} chloride solution (0.6 mL, 0.32 mmol),

tetra-*n*-butylammonium hydroxide solution (0.87 mL, 0.87 mmol) and **2e** (200 mg, 0.29 mmol), yield 120 mg (0.16 mmol, 55%). HPLC: 5.6 min, 95.0%. ^{1}H NMR (600.1 MHz, [D$_6$]dmso): δ = 10.26 (s, 1 H, N*H*-CO), 10.14 (s, 1 H, N*H*-CO), 7.51–7.46 (m, 4 H, H_{Ar}), 6.86 (m, 4 H, H_{Ar}), 4.02–2.84 (m, 18 H, CH_2CO, NCH_2CH_2N), 3.90 (t, $^3J_{H,H}$ = 6.5 Hz, 4H OCH_2CH$_2$CH$_2$CH$_3$), 1.68–1.62 (m, 4 H, OCH$_2$CH_2CH$_2$CH$_3$), 1.41 (m, 4 H, OCH$_2$CH$_2$CH_2CH$_3$), 0.91 (m, 6 H, OCH$_2$CH$_2$CH$_2$CH_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_6$]dmso): δ = 170.7 (*C*=O), 170.6 (*C*=O), 170.3 (*C*=O), 165.8 (*C*=O), 165.3 (*C*=O), 155.0 (O-C_{Ar}), 154.9 (O-C_{Ar}), 131.5 (N-C_{Ar}), 120.9 (C_{Ar}), 120.8 (C_{Ar}), 114.5 (C_{Ar}), 67.3 (OCH$_2$CH$_2$CH$_2$CH$_3$), 61.3 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 60.2 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 56.7 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 54.7 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 51.7 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 30.8 (OCH$_2$*C*H$_2$CH$_2$CH$_3$), 18.8 (OCH$_2$CH$_2$*C*H$_2$CH$_3$), 13.8 (OCH$_2$CH$_2$CH$_2$*C*H$_3$) ppm. MS (ESI, – mode): calcd. for [M(^{71}Ga)]$^+$ 755, [M(^{69}Ga)]$^+$ 753; found *m*/*z* (%) = 755 (29) [M(^{71}Ga) + 1 – H]$^-$, 754 (76) [M(^{71}Ga) – H]$^-$, 753 (40) [M(^{69}Ga) + 1 – H]$^-$, 752 (100) [M(^{69}Ga) – H]$^-$. $C_{34}H_{46}GaN_5O_{10}$·2H$_2$O (790.50): calcd. C 51.66, H 6.38, N 8.86; found C 51.46, H 6.08, N 8.68.

General Procedure for the Preparation of the In^{III} and Lu^{III} Complexes 4a–e and 5a–e: dtpa-*N*,*N*′′-bis(alkoxyphenyl)amide **2a–d** (1 equiv.) was dissolved or, in the case of **2e**, suspended in hot water, cooled to room temperature and an aqueous solution of In^{III} chloride (1 equiv.) or Lu^{III} chloride hexahydrate (1 equiv.) was added, respectively. The pH of the mixture was raised to 7.5 by the dropwise addition of 2.0 M NaOH solution. The solution was stirred at room temperature overnight and the solvent was evaporated.

Procedure A: The residue was suspended in deionized water and washed thoroughly with water to remove all traces of soluble inorganic salts. The colourless solids were dried in vacuo.

Procedure B: The complexes with a higher solubility in water were redissolved in a small amount of hot methanol and purified by silica column chromatography. The colourless solids were dried in vacuo.

[In^{III}{dtpa-*N*,*N*′′-bis(*m*-methoxyphenylamide)}] (4a): Prepared following procedure B from In^{III} chloride (127 mg, 0.58 mmol) and **2a** (350 mg, 0.58 mmol). Purification by column chromatography (silica, MeOH/H$_2$O, 1:1), yield 100 mg (0.14 mmol, 24%). HPLC: 4.2 min, 99.0%. ^{1}H NMR (400.1 MHz, [D$_4$]MeOH): δ = 7.38–6.58 (m, 8 H, H_{Ar}), 4.12–2.78 (m, 24 H, CH_2C=O, NCH_2CH_2N, OCH_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_4$]MeOH): δ = 177.0 (*C*=O), 176.5 (*C*=O), 176.0 (*C*=O), 175.9 (*C*=O), 175.8 (*C*=O), 175.7 (*C*=O), 175.5 (*C*=O), 175.4 (*C*=O), 170.3 (*C*=O), 168.5 (*C*=O), 161.6 (O-C_{Ar}), 161.5 (O-C_{Ar}), 161.4 (O-C_{Ar}), 140.3 (N-C_{Ar}), 140.2 (N-C_{Ar}), 130.9 (C_{Ar}), 130.8 (C_{Ar}), 130.6 (C_{Ar}), 114.4 (C_{Ar}), 113.7 (C_{Ar}), 113.5 (C_{Ar}), 113.4 (C_{Ar}), 113.1 (C_{Ar}), 111.2 (C_{Ar}), 111.1 (C_{Ar}), 110.9 (C_{Ar}), 107.9 (C_{Ar}), 107.3 (C_{Ar}), 107.2 (C_{Ar}), 106.7 (C_{Ar}), 63.5 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 62.3 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 61.6 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 61.1 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 60.7 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 60.3 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 59.8 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 59.6 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 57.9 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 57.6 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 57.2 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 57.1 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 57.0 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 56.7 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 56.3 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 55.8–55.7 (OCH$_3$) ppm. MS (ESI, + mode): calcd. for [M(^{115}In)]$^+$ 715, [M(^{113}In)]$^+$ 713; found *m*/*z* (%) = 739 (34) [M(^{115}In) + 1 + Na]$^+$, 738 (100) [M(^{115}In) + Na]$^+$, 736 (5) [M(^{113}In) + Na]$^+$. $C_{28}H_{34}InN_5O_{10}$·H$_2$O·0.5CH$_3$OH (749.45): calcd. C 45.67, H 5.11, N 9.34; found C 45.94, H 4.88, N 9.03. The content of methanol was established from its X-ray structure.

[In^{III}{dtpa-*N*,*N*′′-bis(*o*-ethoxyphenylamide)}] (4b): Prepared following procedure B from In^{III} chloride (52 mg, 0.24 mmol) and **2b** (150 mg, 0.24 mmol). Purification by column chromatography (silica, MeOH/H$_2$O, 2:1) followed by flash chromatography (silica, MeOH), yield 36 mg (0.05 mmol, 20%). HPLC: 4.2 min, 95.6%. ^{1}H NMR (400.1 MHz, [D$_4$]MeOH): δ = 8.01–7.80 (m, 2 H, H_{Ar}), 7.42–6.77 (m, 6 H, H_{Ar}), 4.15–2.89 (m, 22 H, CH_2C=O, NCH_2CH_2N, OCH_2CH$_3$), 1.44–1.39 (m, 6 H, OCH$_2$CH_3) ppm. ^{13}C{^{1}H} NMR (100.6 MHz, [D$_4$]MeOH): δ = 175.8 (*C*=O), 175.6 (*C*=O), 172.1 (*C*=O), 169.1 (*C*=O), 152.0 (O-C_{Ar}), 151.5 (O-C_{Ar}), 128.7 (N-C_{Ar}, C_{Ar}), 127.3 (N-C_{Ar}, C_{Ar}), 127.2 (N-C_{Ar}, C_{Ar}), 125.9 (N-C_{Ar}, C_{Ar}), 125.6 (N-C_{Ar}, C_{Ar}), 124.7 (N-C_{Ar}, C_{Ar}), 121.7 (C_{Ar}), 121.4 (C_{Ar}), 113.3 (C_{Ar}), 113.1 (C_{Ar}), 65.5 (OCH$_2$CH$_3$), 65.4 (OCH$_2$CH$_3$), 61.7 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 60.9 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 58.1 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 57.2 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 56.3 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 53.1 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 15.1 (OCH$_2$*C*H$_3$), 15.0 (OCH$_2$*C*H$_3$) ppm. MS (ESI, + mode): calcd. for [M(^{115}In)]$^+$ 743, [M(^{113}In)]$^+$ 741; found *m*/*z* (%) = 767 (34) [M(^{115}In) + 1 + Na]$^+$, 766 (100) [M(^{115}In) + Na]$^+$, 764 (5) [M(^{113}In) + Na]$^+$. $C_{30}H_{38}InN_5O_{10}$·3.5H$_2$O (806.52): calcd. C 44.68, H 5.62, N 8.68; found C 44.30, H 5.16, N 8.41.

[In^{III}{dtpa-*N*,*N*′′-bis(*m*-ethoxyphenylamide)}] (4c): Prepared following procedure A from In^{III} chloride (122 mg, 0.55 mmol) and **2c** (350 mg, 0.55 mmol), yield 230 g (0.31 mmol, 55%). HPLC: 4.5 min, 98.8%. ^{1}H NMR (600.1 MHz, [D$_6$]dmso, 25 °C): δ = 11.44 (s, 1 H, N*H*-CO), 10.31 (s, 1 H, N*H*-CO), 7.54 (s, 1 H, H_{Ar}), 7.31–7.27 (m, 2 H, H_{Ar}), 7.18 (m, 1 H, H_{Ar}), 7.12–7.10 (m, 2 H, H_{Ar}), 6.77 (dd, $^3J_{H,H}$ = 8.2, $^4J_{H,H}$ = 1.7 Hz, 1 H, H_{Ar}), 6.62 (dd, $^3J_{H,H}$ = 8.2, $^4J_{H,H}$ = 1.7 Hz, 1 H, H_{Ar}), 4.10–2.61 (m, 22 H, CH_2C=O, NCH_2CH_2N, OCH_2CH$_3$), 1.35–1.30 (m, 6 H, OCH$_2$CH_3) ppm. ^{1}H NMR (600.1 MHz, [D$_6$]dmso, 85 °C): δ = 10.11 (s, 0.3 H, N*H*-CO), 7.48 (s, 0.5 H, H_{Ar}), 7.33–7.09 (m, 5.5 H, H_{Ar}), 6.77 (s, 1 H, H_{Ar}), 6.65 (s, 1 H, H_{Ar}), 4.13–2.39 (m, 22 H, CH_2C=O, NCH_2CH_2N, OCH_2CH$_3$), 1.38–1.31 (m, 6 H, OCH$_2$CH_3) ppm. ^{13}C{^{1}H} NMR (150.9 MHz, [D$_6$]dmso): δ = 171.4 (*C*=O), 171.2 (*C*=O), 170.5, (*C*=O) 170.4 (*C*=O), 166.9, 158.9 (O-C_{Ar}), 158.7 (O-C_{Ar}), 139.7 (N-C_{Ar}), 138.0 (N-C_{Ar}), 129.7 (C_{Ar}), 129.5 (C_{Ar}), 112.3 (C_{Ar}), 111.8 (C_{Ar}), 111.6 (C_{Ar}), 109.7 (C_{Ar}), 106.6 (C_{Ar}), 105.6 (C_{Ar}), 63.3 (OCH$_2$CH$_3$), 62.9 (OCH$_2$CH$_3$), 60.8 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 60.0 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 59.6 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 56.2 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 55.3 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 55.1 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 54.5 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 52.0 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 50.5 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 14.6 (OCH$_2$*C*H$_3$), 14.5 (OCH$_2$CH$_3$) ppm. MS (ESI, + mode): calcd. for [M(^{115}In)]$^+$ 743, [M(^{113}In)]$^+$ 741; found *m*/*z* (%) = 767 (34) [M(^{115}In) + 1 + Na]$^+$, 766 (100) [M(^{115}In) + Na]$^+$, 764 (5) [M(^{113}In) + Na]$^+$, 744 (115) [M(^{115}In) + H]$^+$. $C_{30}H_{38}InN_5O_{10}$·H$_2$O (761.57): calcd. C 47.32, H 5.29, N 9.20; found C 47.52, H 5.06, N 9.20.

[In^{III}{dtpa-*N*,*N*′′-bis(*p*-ethoxyphenylamide)}] (4d): Prepared following procedure A from In^{III} chloride (127 mg, 0.58 mmol) and **2d** (350 mg, 0.58 mmol), yield 168 mg (0.23 mmol, 39%). HPLC: 4.7 min, 96.7%. ^{1}H NMR (600.1 MHz, [D$_6$]dmso): δ = 11.47 (s, 1 H, N*H*-CO), 10.22 (s, 1 H, N*H*-CO), 7.59 (d, $^3J_{H,H}$ = 7.5 Hz, 2 H, H_{Ar}), 7.50 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, H_{Ar}), 6.96 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, H_{Ar}), 6.86 (d, $^3J_{H,H}$ = 8.9 Hz, 2 H, H_{Ar}), 4.03–2.66 (m, 22 H, CH_2C=O, NCH_2CH_2N, OCH_2CH$_3$), 1.32–1.28 (m, 6 H, OCH$_2$CH_3) ppm. ^{13}C{^{1}H} NMR (150.9 MHz, [D$_6$]dmso): δ = 171.4 (*C*=O), 171.1 (*C*=O), 170.7 (*C*=O), 196.3 (*C*=O), 166.3 (*C*=O), 164.8 (*C*=O), 156.0 (O-C_{Ar}), 154.7 (O-C_{Ar}), 131.6 (N-C_{Ar}), 129.8 (N-C_{Ar}), 122.0 (C_{Ar}), 120.9 (C_{Ar}), 114.6 (C_{Ar}), 114.3 (C_{Ar}), 62.2 (OCH$_2$CH$_3$), 63.1 (OCH$_2$CH$_3$), 60.6 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 59.9 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 59.5 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 56.3 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 55.2 (*C*H$_2$C=O, NCH_2*C*H$_2$N), 55.1

(CH_2C=O, NCH_2CH_2N), 54.5 (CH_2C=O, NCH_2CH_2N), 52.1 (CH_2C=O, NCH_2CH_2N), 50.5 (CH_2C=O, NCH_2CH_2N), 14.7 (OCH_2CH_3), 14.6 (OCH_2CH_3) ppm. MS (ESI, + mode): calcd. for $[M(^{115}In)]^+$ 743, $[M(^{113}In)]^+$ 741; found *m/z* (%) = 767 (34) $[M(^{115}In) + 1 + Na]^+$, 766 (100) $[M(^{115}In) + Na]^+$, 764 (5) $[M(^{113}In) + Na]^+$, 744 (8) $[M(^{115}In) + H]^+$. $C_{30}H_{38}InN_5O_{10}\cdot 3H_2O$ (797.51): calcd. C 45.18, H 5.56, N 8.78; found C 45.02, H 5.30, N 8.64.

[In^{III}\{dtpa-*N,N′′*-bis(*p*-butoxyphenylamide)\}] (4e): Prepared following procedure A from In^{III} chloride (112 mg, 0.51 mmol) and **2e** (350 mg, 0.51 mmol), yield 170 mg (0.21 mmol, 41%). HPLC: 5.8 min, 95.5%. ^1H NMR (600.1 MHz, [D$_4$]MeOH): δ = 7.60–6.69 (m, 8 H, H_{Ar}), 3.94–2.75 (m, 22 H, CH_2C=O, NCH_2CH_2N, $OCH_2CH_2CH_2CH_3$), 1.76–1.61 (m, 4 H, $OCH_2CH_2CH_2CH_3$), 1.52–1.37 (m, 4 H, $OCH_2CH_2CH_2CH_3$), 0.99–0.88 (m, 6 H, $OCH_2CH_2CH_2CH_3$) ppm. $^{13}C\{^1H\}$ NMR (150.9 MHz, [D$_4$]-MeOH): δ = 177.1 (*C*=O), 175.9 (*C*=O), 175.6 (*C*=O), 173.9 (*C*=O), 169.3 (*C*=O), 157.7 (O-C_{Ar}), 157.5 (O-C_{Ar}), 157.0 (O-C_{Ar}), 131.9 (N-C_{Ar}), 129.0 (N-C_{Ar}), 123.2 (C_{Ar}), 122.7 (C_{Ar}), 118.2 (C_{Ar}), 116.6 (C_{Ar}), 115.6 (C_{Ar}), 115.2 (C_{Ar}), 68.9 ($OCH_2CH_2CH_2CH_3$), 68.8 ($OCH_2CH_2CH_2CH_3$), 57.0 (CH_2C=O, NCH_2CH_2N), 56.8 (CH_2C=O, NCH_2CH_2N), 56.7 (CH_2C=O, NCH_2CH_2N), 56.4 (CH_2C=O, NCH_2CH_2N), 55.7 (CH_2C=O, NCH_2CH_2N), 55.3 (CH_2C=O, NCH_2CH_2N), 55.2 (CH_2C=O, NCH_2CH_2N), 53.5 (CH_2C=O, NCH_2CH_2N), 52.8 (CH_2C=O, NCH_2CH_2N), 32.7 ($OCH_2CH_2CH_2CH_3$), 32.5 ($OCH_2CH_2CH_2CH_3$), 20.3 ($OCH_2CH_2CH_2CH_3$), 20.2 ($OCH_2CH_2CH_2CH_3$), 14.2 ($OCH_2CH_2CH_2CH_3$) ppm. MS (ESI, + mode): calcd. for $[M(^{115}In)]^+$ 799, $[M(^{113}In)]^+$ 797; found *m/z* (%) = 822 (14) $[M(^{115}In) + Na]^+$, 801 (34) $[M(^{115}In) + 1 + H]^+$, 800 (100) $[M(^{115}In) + H]^+$. $C_{34}H_{46}InN_5O_{10}\cdot 3H_2O$ (853.70): calcd. C 47.84, H 6.14, N 8.20; found C 47.71, H 5.78, N 8.01.

[Lu^{III}\{dtpa-*N,N′′*-bis(*m*-methoxyphenylamide)\}] (5a): Prepared following procedure B from Lu^{III} chloride hexahydrate (225 mg, 0.58 mmol) and **2a** (350 g, 0.58 mmol), yield 120 mg (0.15 mmol, 26%). HPLC: 4.7 min, 99.0%. ^1H NMR (600.1 MHz, [D$_4$]MeOH): δ = 7.38–7.18 (m, 6 H, H_{Ar}), 6.81–6.74 (m, 2 H, H_{Ar}), 3.84–3.43 (m, 24 H, CH_2CO, NCH_2CH_2N, OCH_3) ppm. $^{13}C\{^1H\}$ NMR (150.9 MHz, [D$_4$]MeOH): δ = 181.3 (*C*=O), 180.6 (*C*=O), 180.4 (*C*=O), 180.1 (*C*=O), 177.0 (*C*=O), 175.4 (*C*=O), 175.3 (*C*=O), 161.8 (O-C_{Ar}), 161.6 (O-C_{Ar}), 139.3 (N-C_{Ar}), 139.1 (N-C_{Ar}), 131.0 (C_{Ar}), 130.9 (C_{Ar}), 130.8 (C_{Ar}), 114.4 (C_{Ar}), 114.3 (C_{Ar}), 112.4 (C_{Ar}), 112.0 (C_{Ar}), 108.2 (C_{Ar}), 108.1 (C_{Ar}), 68.2 (CH_2C=O, NCH_2CH_2N), 68.0 (CH_2C=O, NCH_2CH_2N), 64.0 (CH_2C=O, NCH_2CH_2N), 63.5 (CH_2C=O, NCH_2CH_2N), 63.2 (CH_2C=O, NCH_2CH_2N), 60.0 (CH_2C=O, NCH_2CH_2N), 59.8 (CH_2C=O, NCH_2CH_2N), 57.4 (CH_2C=O, NCH_2CH_2N), 57.2 (CH_2C=O, NCH_2CH_2N), 56.0 (CH_2C=O, NCH_2CH_2N), 55.9 (OCH_3), 55.8 (OCH_3) ppm. MS (ESI, + mode): calcd. for $[M]^+$ 793, $[M - H_2O]^+$ 775; found *m/z* (%) = 798 (100) $[M - H_2O + Na]^+$, 776 (15) $[M - H_2O + H]^+$. $C_{28}H_{34}LuN_5O_{10}\cdot 4H_2O$ (847.62): calcd. C 39.68, H 4.99, N 8.26; found C 39.68, H 4.58, N 8.22.

[Lu^{III}\{dtpa-*N,N′′*-bis(*o*-ethoxyphenylamide)\}] (5b): Prepared following procedure B from Lu^{III} chloride hexahydrate (111 mg, 0.29 mmol) and **2b** (180 mg, 0.29 mmol), yield 35 mg (0.04 mmol, 15%). Purification by column chromatography (silica, MeOH/H_2O, 2:1). HPLC: 5.2 min, 96.5%. ^1H NMR (400.1 MHz, [D$_4$]MeOH): δ = 7.95–7.69 (m, 2 H, H_{Ar}), 7.27–6.82 (m, 6 H, H_{Ar}), 4.16–2.43 (m, 22 H, CH_2CO, NCH_2CH_2N, OCH_2CH_3), 1.45–1.30 (m, 6 H, OCH_2CH_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, [D$_4$]MeOH): δ = 181.2 (*C*=O), 180.6 (*C*=O), 180.4 (*C*=O), 180.3 (*C*=O), 180.1 (*C*=O), 177.3 (*C*=O), 175.8 (*C*=O), 169.9 (*C*=O), 152.8 (O-C_{Ar}), 151.6 (O-C_{Ar}), 128.7 (N-C_{Ar}, C_{Ar}), 128.2 (N-C_{Ar}, C_{Ar}), 128.0 (N-C_{Ar}, C_{Ar}), 126.5 (N-C_{Ar}, C_{Ar}), 126.4 (N-C_{Ar}, C_{Ar}), 126.1 (N-C_{Ar}, C_{Ar}), 126.0 (N-C_{Ar}, C_{Ar}), 125.2 (N-C_{Ar}, C_{Ar}), 121.6 (C_{Ar}), 121.3 (C_{Ar}), 113.4 (C_{Ar}), 113.1 (C_{Ar}), 68.1 (CH_2C=O, NCH_2CH_2N), 65.5 (OCH_2CH_3), 65.4 (OCH_2CH_3), 63.8 (CH_2C=O, NCH_2CH_2N), 63.4 (CH_2C=O, NCH_2CH_2N), 63.0 (CH_2C=O, NCH_2CH_2N), 60.0 (CH_2C=O, NCH_2CH_2N), 59.7 (CH_2C=O, NCH_2CH_2N), 57.4 (CH_2C=O, NCH_2CH_2N), 57.2 (CH_2C=O, NCH_2CH_2N), 15.1 (OCH_2CH_3), 15.0 (OCH_2CH_3) ppm. MS (ESI, + mode): calcd. for $[M]^+$ 821, $[M - H_2O]^+$ 803; found *m/z* (%) = 826 (100) $[M - H_2O, + Na]^+$. $C_{30}H_{38}LuN_5O_{10}\cdot 2.5H_2O$ (848.66): calcd. C 42.46, H 5.11, N 8.25; found C 42.57, H 4.95, N 7.94.

[Lu^{III}\{dtpa-*N,N′′*-bis(*m*-ethoxyphenylamide)\}] (5c): Prepared following procedure A from Lu^{III} chloride hexahydrate (215 g, 0.55 mmol) and **2c** (350 mg, 0.55 mmol), yield 325 mg (0.40 mmol, 74%). HPLC: 5.3 min, 98.6%. ^1H NMR (600.1 MHz, [D$_6$]dmso, 25 °C): δ = 10.82–10.77 (m, 2 H, N*H*-CO, H_2O_{ligand}), 7.38–7.16 (m, 6 H, H_{Ar}), 6.77–6.72 (m, 2 H, H_{Ar}), 4.24–4.21 (m, 0.8 H), 4.25–2.27 (m, 22 H, CH_2CO, NCH_2CH_2N, OCH_2CH_3), 1.31–1.28 (m, 6 H, OCH_2CH_3) ppm. ^1H NMR (600.1 MHz, [D$_6$]dmso, 85 °C): δ = 10.45 (s, 1.2 H, N*H*-CO), 7.29–7.23 (m, 6 H, H_{Ar}), 6.75–6.74 (m, 2 H, H_{Ar}), 4.04 (q, $^3J_{H,H}$ = 7.1 Hz, 4 H, OCH_2CH_3), 4.16–2.38 (m, 18 H, CH_2CO, NCH_2CH_2N), 1.31 (t, $^3J_{H,H}$ = 7.1 Hz, 6 H, OCH_2CH_3) ppm. $^{13}C\{^1H\}$ NMR (150.9 MHz, [D$_6$]dmso): δ = 175.7 (*C*=O), 75.2 (*C*=O), 174.9 (*C*=O), 173.3 (*C*=O), 158.8 (O-C_{Ar}), 138.7 (N-C_{Ar}), 138.4 (N-C_{Ar}), 129.6 (C_{Ar}), 129.5 (C_{Ar}), 112.7 (C_{Ar}), 112.4 (C_{Ar}), 110.4 (C_{Ar}), 110.1 (C_{Ar}), 107.2 (C_{Ar}), 106.7 (C_{Ar}), 66.6 (CH_2C=O, NCH_2CH_2N), 63.1 (OCH_2CH_3), 63.0 (OCH_2CH_3), 62.3 (CH_2C=O, NCH_2CH_2N), 62.2 (CH_2C=O, NCH_2CH_2N), 62.0 (CH_2C=O, NCH_2CH_2N), 58.1 (CH_2C=O, NCH_2CH_2N), 57.9 (CH_2C=O, NCH_2CH_2N), 55.9 (CH_2C=O, NCH_2CH_2N), 55.0 (CH_2C=O, NCH_2CH_2N), 14.6 (OCH_2CH_3) ppm. MS (ESI, + mode): calcd. for $[M]^+$ 821, $[M - H_2O]^+$ 803; found *m/z* (%) = 826 (100) $[M - H_2O + Na]^+$, 804 (26) $[M - H_2O + H]^+$. $C_{30}H_{38}LuN_5O_{10}\cdot 3H_2O$ (875.66): calcd. C 42.01, H 5.17, N 8.17; found C 41.89, H 5.10, N 8.09.

[Lu^{III}\{dtpa-*N,N′′*-bis(*p*-ethoxyphenylamide)\}] (5d): Prepared following procedure A from Lu^{III} chloride hexahydrate (215 mg, 0.55 mmol) and **2d** (350 mg, 0.55 mmol), yield 196 mg (0.24 mmol, 44%). HPLC: 5.1 min, 97.0%. ^1H NMR (600.1 MHz, [D$_6$]dmso): δ = 10.79 (s, 2 H, N*H*-CO), 7.71–7.58 (m, 4 H, H_{Ar}), 6.95–6.86 (m, 4 H, H_{Ar}), 4.22–2.57 (m, 22 H, CH_2C=O, NCH_2CH_2N, OCH_2CH_3), 1.34–1.30 (m, 6 H, OCH_2CH_3) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, [D$_6$]dmso): δ = 175.8 (*C*=O), 175.3 (*C*=O), 175.6 (*C*=O), 175.0 (*C*=O), 173.7 (*C*=O), 173.0 (*C*=O), 172.5 (*C*=O), 155.6 (O-C_{Ar}), 155.3 (O-C_{Ar}), 130.7 (N-C_{Ar}), 130.4 (N-C_{Ar}), 121.9 (C_{Ar}), 121.8 (C_{Ar}), 121.6 (C_{Ar}), 114.5 (C_{Ar}), 114.4 (C_{Ar}), 114.3 (C_{Ar}), 66.7 (CH_2C=O, NCH_2CH_2N), 63.2 (OCH_2CH_3), 63.1 (OCH_2CH_3), 62.6 (CH_2C=O, NCH_2CH_2N), 62.3 (CH_2C=O, NCH_2CH_2N), 61.6 (CH_2C=O, NCH_2CH_2N), 58.1 (CH_2C=O, NCH_2CH_2N), 55.8 (CH_2C=O, NCH_2CH_2N), 55.1 (CH_2C=O, NCH_2CH_2N), 14.6 (OCH_2CH_3) ppm. MS (ESI, + mode): calcd. for $[M]^+$ 821, $[M - H_2O]^+$ 803; found *m/z* (%) = 826 (100) $[M - H_2O + Na]^+$, 804 (5) $[M - H_2O, + H]^+$. $C_{30}H_{38}LuN_5O_{10}\cdot 4H_2O$ (875.68): calcd. C 41.15, H 5.29, N 7.98; found C 41.45, H 5.12, N 8.00.

[Lu^{III}\{dtpa-*N,N′′*-bis(*p*-butoxyphenylamide)\}] (5e): Prepared following procedure A from Lu^{III} chloride hexahydrate (198 g, 0.51 mmol) and **2e** (350 g, 0.51 mmol), yield 225 mg (0.26 mmol, 51%). HPLC: 6.1 min, 95.5%. ^1H NMR (600.1 MHz, [D$_4$]MeOH): δ = 7.58–7.45 (m, 4 H, H_{Ar}), 6.91–6.78 (m, 4 H, H_{Ar}), 4.00–2.46 (m, 22 H, CH_2C=O, NCH_2CH_2N, $OCH_2CH_2CH_2CH_3$), 1.78–1.68 (m, 4 H, $OCH_2CH_2CH_2CH_3$), 1.55–1.44 (m, 4 H,

$OCH_2CH_2CH_2CH_3$), 1.00–0.95 (m, 6 H, $OCH_2CH_2CH_2CH_3$) ppm. $^{13}C\{^1H\}$ NMR (100.6 MHz, [D$_4$]MeOH): δ = 181.2 (*C*=O), 180.7 (*C*=O), 180.2 (*C*=O), 174.7 (*C*=O), 174.5 (*C*=O), 158.4 (O-C_{Ar}), 158.3 (O-C_{Ar}), 131.1 (N-C_{Ar}), 131.0 (N-C_{Ar}), 123.9 (C_{Ar}), 123.1 (C_{Ar}), 122.9 (C_{Ar}), 115.8 (C_{Ar}), 115.6 (C_{Ar}), 115.5 (C_{Ar}), 69.0 ($OCH_2CH_2CH_2CH_3$), 68.9 (CH_2C=O, NCH_2CH_2N), 68.1 (CH_2C=O, NCH_2CH_2N), 63.1 (CH_2C=O, NCH_2CH_2N), 60.0 (CH_2C=O, NCH_2CH_2N), 59.8 (CH_2C=O, NCH_2CH_2N), 57.3 (CH_2C=O, NCH_2CH_2N), 32.6 ($OCH_2CH_2CH_2CH_3$), 32.4 ($OCH_2CH_2CH_2CH_3$), 20.4 ($OCH_2CH_2CH_2CH_3$), 20.3 ($OCH_2CH_2CH_2CH_3$), 14.3 ($OCH_2CH_2CH_2CH_3$) ppm. MS (ESI, + mode): calcd. for $[M]^+$ 877, $[M - H_2O]^+$ 859; found *m*/*z* (%) = 882 (100) $[M - H_2O + Na]^+$. $C_{34}H_{46}LuN_5O_{10}\cdot 4H_2O$ (931.78): calcd. C 43.83, H 5.84, N 7.52; found C 43.65, H 5.51, N 7.52.

Supporting Information (see footnote on the first page of this article): NMR spectra of **3c**–**5c** in [D$_7$]dmf and detail of the quantum chemical calculations.

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