

Three in One: TSA, TSA', and SA Units in One Crystal Structure of a Yttrium(III) Complex with a Monophosphinated H₄dota Analogue

Jan Kotek, Jakub Rudovský, Petr Hermann, and Ivan Lukeš*

Department of Inorganic Chemistry, Universita Karlova (Charles University), Hlavova 2030, 128 40 Prague 2, Czech Republic

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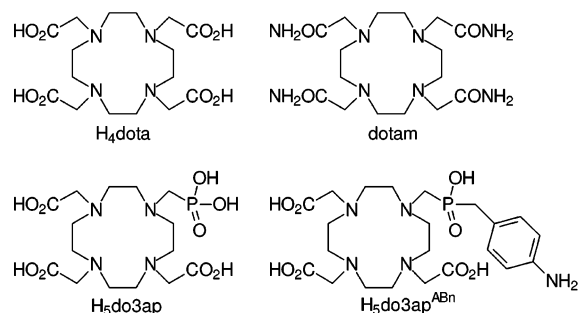
Compound $[Y(Hdo3aP^{ABn})(H_2O)][Y(Hdo3aP^{ABn}) \cdot 6H_2O \cdot iPrOH]$, where H_4do3aP^{ABn} is 1,4,7,10-tetraazacyclododecane-1,4,7-triacetic-10-methyl(4-aminobenzylphosphinic) acid, a monophosphinate analogue of H₄dota, was prepared in the solid state and studied using X-ray crystallography. In contrast to all single-crystal structures of complexes of H₄dota-like ligands published before, three distinct units were found in one cell: two species adopting a twisted-square-antiprismatic configuration with (TSA) and without (TSA') a coordinated water molecule and one isomer with a square-antiprismatic configuration (SA). In addition, this is the first complex with the H₄dota-like ligand for which the structures of three possible species were determined in the solid state.

Introduction

Lanthanide(III) complexes with polyazamacrocycles bearing coordinating pendant arms exhibit thermodynamic as well as kinetic stabilities, which are essential for in vivo applications.¹ Suitable properties of these complexes have been explored in several areas and, especially, as contrast agents in magnetic resonance imaging (MRI).² The most widely studied ligand, H₄dota (H₄dota = 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid; Chart 1), is the prototype for this application and, therefore, a number of H₄dota derivatives and analogues have been synthesized and studied up to now.^{1–3}

All MRI contrast agents used nowadays are predominantly complexes of gadolinium(III). The prototype (dota)^{4–} anion is coordinated to the Gd(III) ion by four ring N atoms and four O atoms coming from the carboxylate groups. The N atoms as well as the O atoms form N₄ and O₄ planes that are parallel. In addition, the O₄ plane is capped with a water

Chart 1. Structures of Ligands Discussed in the Paper



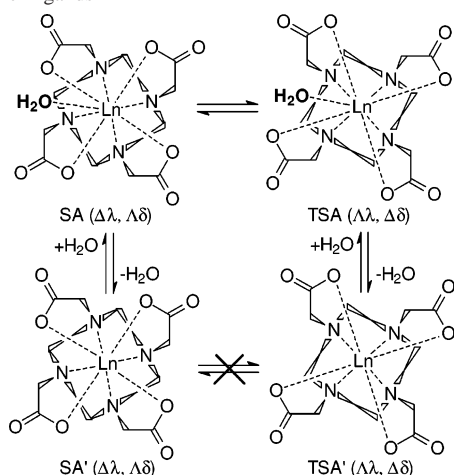
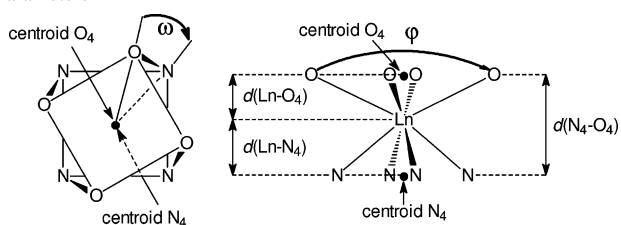
molecule, which increases the coordination number of the central ion to nine. The water coordination is essential for a contrast-enhancement effect because through its exchange with the bulk the magnetic information is distributed.

The efficiency of the contrast agents is commonly expressed as *relaxivity* (r_1), which is an enhancement of the water proton magnetic relaxation rate in a 1 mM solution of a Gd(III) complex. Relaxivity is governed by several parameters such as the exchange rate of the coordinated water molecule, time of tumbling of the complex molecule, or electronic relaxation time of the central Gd³⁺ ion.^{2a,b,d,4} These parameters are associated with the structure of the complex (bond distances and angles, size of the complex, etc.), symmetry of the coordination polyhedron, and distribution of the electron density around the central ion.

* To whom correspondence should be addressed. E-mail: lukes@natur.cuni.cz. Fax: +420-22195-1253.

- (1) (a) Lindoy, L. F. *Adv. Inorg. Chem.* **1998**, *45*, 75. (b) Wainwright, K. P. *Coord. Chem. Rev.* **1997**, *166*, 35. (c) Lincoln, S. F. *Coord. Chem. Rev.* **1997**, *166*, 255.
 (2) (a) *Topics in Current Chemistry*; Springer: Frankfurt am Main, Germany, 2002; Vol. 221. (b) *The Chemistry of Contrast Agents in Medical Magnetic Resonance Imaging*; Merbach, A. E., Tóth, É., Eds.; Wiley: Chichester, U.K., 2001. (c) Botta, M. *Eur. J. Inorg. Chem.* **2000**, 399. (d) Aime, S.; Botta, M.; Fasano, M.; Terreno, E. *Chem. Soc. Rev.* **1998**, *27*, 19.
 (3) (a) Parker, D. *Chem. Soc. Rev.* **2004**, *33*, 156. (b) Liu, S. *Chem. Soc. Rev.* **2004**, *33*, 445. (c) Parker, D.; Dickins, R. S.; Puschmann, H.; Crossland, C.; Howard, J. A. K. *Chem. Rev.* **2002**, *102*, 1977.

- (4) (a) Aime, S.; Botta, M.; Terreno, E. *Adv. Inorg. Chem.* **2005**, *57*, 173. (b) Caravan, P.; Ellison, J. J.; McMurry, T. J.; Laufer, R. B. *Chem. Rev.* **1999**, *99*, 2293.

Scheme 1. Possible Species/Isomers of Ln(III) Complexes with H₄dota-Like Ligands**Scheme 2.** Sketch of the Complexes with the Depicted Structural Parameters

The geometry of the coordination polyhedron in Ln(III) complexes of H₄dota is governed by the torsion of the macrocyclic chelate rings and by the position of the pendants. The ethylene chains of the macrocycle adopt a gauche conformation, forming a five-membered chelate ring with either δ or λ configurations. This results in two possible macrocycle square (3,3,3,3)-B conformations: $\delta\delta\delta\delta$ and $\lambda\lambda\lambda\lambda$.⁵ In addition, the pendant acetate arms may occupy two orientations: Δ or Λ . The ring interconversion $\delta \leftrightarrow \lambda$ and pendant arm rotation $\Delta \leftrightarrow \Lambda$ lead to four stereoisomers (racemic mixture of two diastereoisomers $\Delta\delta\delta\delta/\Lambda\lambda\lambda\lambda$ and $\Delta\lambda\lambda\lambda/\Lambda\delta\delta\delta$, respectively; Scheme 1). In addition, both diastereoisomers differ in absolute value and sign; the angle ω formed by the mutual rotation of the O₄ and N₄ planes (Scheme 2). In the isomers $\Delta\lambda\lambda\lambda/\Lambda\delta\delta\delta$, the rotation about 40° leads to the square-antiprismatic isomer SA (an ideal angle for the square antiprism is 45°). In the pair of enantiomers $\Lambda\lambda\lambda\lambda/\Delta\delta\delta\delta$, the rotation about -25° corresponds to the twisted-square-antiprismatic isomer TSA (an ideal angle of -22.5°).

In solution, an equilibrium between the TSA and SA isomers was proved.⁶ The population of the species is determined mainly by the size of the central ion: for larger ions (lighter Ln³⁺ ions), the TSA arrangement is highly preferred, and by going along the Ln series toward lutetium, the SA isomer is coming forth. In the case of the [Gd(dota)(H₂O)]⁻ complex used in clinical practice, it was found that the SA diastereoisomer has a much higher

abundance (~85%) than the TSA one (~15%).⁷ Therefore, the SA isomer is also usually called *major* (**M**), and the TSA isomer is termed the *minor* (**m**) isomer.

Because the TSA isomer shows a much faster exchange rate of the coordinated water molecule than the SA one^{2a,b,4,8,9} and this effect plays a key role in MRI applications, the H₄-dota-like ligands exhibiting as high TSA abundances in Gd(III) complexes as possible are desired.

Furthermore, both isomers can also lose the coordinated water molecule in the capping O₄ plane and, so, the central metal ions become only octacoordinated. To distinguish such “anhydrous” species from the noncoordinated ones, the notations TSA' and SA' (or **m'** and **M'**, respectively) are usually used for the octacoordinated species (Scheme 1).^{7a} From the comparison of many crystal structures, the opening angle φ between “trans” oxygen atoms and the central Ln(III) ion (Scheme 2) was found to be a crucial parameter governing the water coordination, and it should be larger than 135° to ensure the water binding.¹⁰

In the solid state, Ln(III) complexes of H₄dota¹¹ as well as its amides¹² form mostly SA isomers. The TSA isomers were observed only in the structures with large ions such as lanthanum(III)^{11c} or cerium(III),^{11a} and the TSA' arrangement

(5) Meyer, M.; Dahaoui-Ginderey, V.; Lecomte, C.; Guillard, R. *Coord. Chem. Rev.* **1998**, *178–180*, 1313.

(6) (a) Hoefl, S.; Roth, K. *Chem. Ber.* **1993**, *126*, 869. (b) Aime, S.; Barbero, L.; Botta, M.; Ermondi, G. *Inorg. Chem.* **1992**, *31*, 4291.

(7) Aime, S.; Botta, M.; Fasano, M.; M. P. M. Marques, M. P. M.; Geraldes, C. F. G. C.; Pubanz, D.; Merbach, A. E. *Inorg. Chem.* **1997**, *36*, 2059.

(8) (a) Woods, M.; Botta, M.; Avedano, S.; Wang, J.; Sherry, A. D. *Dalton Trans.* **2005**, 3829. (b) Woods, M.; Kovacs, Z.; Zhang, S.; Sherry, A. D. *Angew. Chem., Int. Ed.* **2003**, *42*, 5889. (c) Zhang, S.; Kovacs, Z.; Burgess, S.; Aime, S.; Terreno, E.; Sherry, A. D. *Chem.—Eur. J.* **2001**, *7*, 288. (d) Woods, M.; Aime, S.; Botta, M.; Howard, J. A. K.; Moloney, J. M.; Navet, M.; Parker, D.; Port, M.; Rousseaux, O. *J. Am. Chem. Soc.* **2000**, *122*, 9781.

(9) (a) Dunand, F. A.; Dickins, R. S.; Parker, D.; Merbach, A. E. *Chem.—Eur. J.* **2001**, *7*, 5160. (b) Dunand, F. A.; Aime, S.; Merbach, A. E. *J. Am. Chem. Soc.* **2000**, *122*, 1506. (c) Aime, S.; Barge, A.; Botta, M.; De Sousa, A. S.; Parker, D. *Angew. Chem., Int. Ed.* **1998**, *37*, 2673.

(10) Lukeš, I.; Kotek, J.; Vojtišek, P.; Hermann, P. *Coord. Chem. Rev.* **2001**, *216–217*, 287.

(11) (a) Benetollo, F.; Bombieri, G.; Calabi, L.; Aime, S.; Botta, M. *Inorg. Chem.* **2003**, *42*, 148. (b) Benetollo, F.; Bombieri, G.; Aime, S.; Botta, M. *Acta Crystallogr. C* **1999**, *55*, 353. (c) Aime, S.; Barge, A.; Benetollo, F.; Bombieri, G.; Botta, M.; Uggeri, F. *Inorg. Chem.* **1997**, *36*, 4287. (d) Aime, S.; Barge, A.; Botta, M.; Fasano, M.; Ayala, J. D.; Bombieri, G. *Inorg. Chim. Acta* **1996**, *246*, 423. (e) Parker, D.; Pulukkody, K.; Smith, F. C.; Batsanov, A.; Howard, J. A. K. *J. Chem. Soc., Dalton Trans.* **1994**, 689. (f) Chang, C. A.; Francesconi, L. C.; Malley, M. F.; Kumar, K.; Gougoutas, J. Z.; Tweedle, M. F.; Lee, D. W.; Wilson, L. J. *Inorg. Chem.* **1993**, *32*, 3501. (g) Dubost, J.-P.; Leger, J.-M.; Langlois, M.-H.; Meyer, D.; Schaefer, M. C. R. *Acad. Sci. Paris, Ser. II* **1991**, *312*, 349. (h) Spirlet, M.-R.; Rebizant, J.; Desreux, J. F.; Loucin, M.-F. *Inorg. Chem.* **1984**, *23*, 359.

(12) (a) Parker, D.; Puschmann, H.; Batsanov, A. S.; Senanayake, K. *Inorg. Chem.* **2003**, *42*, 8646. (b) Aime, S.; Barge, A.; Batsanov, A. S.; Botta, M.; Castelli, D. D.; Fedeli, F.; Mortillaro, A.; Parker, D.; Puschmann, H. *Chem. Commun.* **2002**, 1120. (c) Dickins, R. S.; Howard, J. A. K.; Maupin, C. L.; Moloney, J. M.; Parker, D.; Riehl, J. P.; Siligardi, G.; Williams, J. A. G. *Chem.—Eur. J.* **1999**, *5*, 1095. (d) Aime, S.; Barge, A.; Bruce, J. I.; Botta, M.; Howard, J. A. K.; Moloney, J. M.; Parker, D.; de Sousa, A. S.; Woods, M. *J. Am. Chem. Soc.* **1999**, *121*, 5762. (e) Batsanov, A. S.; Beeby, A.; Bruce, J. J.; Howard, J. A. K.; Kenwright, A. M.; Parker, D. *Chem. Commun.* **1999**, 1011. (f) Alderighi, L.; Branchi, A.; Valabi, L.; Dapporto, P.; Losi, P.; Giorgi, C.; Paleari, L.; Pavli, P.; Rossi, P.; Valtancoli, B.; Virtuani, M. *Eur. J. Inorg. Chem.* **1998**, 1581. (g) Amin, S.; Voss, D. A., Jr.; Horrocks, W. DeW., Jr.; Lake, C. H.; Churchill, M. R.; Morrow, J. R. *Inorg. Chem.* **1995**, *34*, 4, 3294.

was found in the case of the small thulium(III) ion, where there is not space enough for binding of a water molecule.^{11a}

In contrast, complexes of the tetrakis(methylenephosphonic/phosphinic) acid analogues of H₄dota form in the solution exclusively TSA (lighter Ln ions) or TSA' (heavier ions) species. In the solid state, also only TSA [La(III) and Ce(III)] and TSA' species [other Ln(III) ions] were isolated.^{13–15} Thus, combining the conveniences of H₄dota (one coordinated water molecule in its complexes) with properties of tetraphosphonic/phosphinic acid analogues of H₄dota (exclusive formation of the complexes with TSA stereochemistry), we decided to synthesize the ligands with three acetic pendant arms and one phosphonate/phosphinate pendant group. The NMR and relaxometric study confirmed the preferential formation of the TSA and TSA' species and the optimally fast water-exchange rate of their Gd(III) complexes^{16,17} and, in addition, a very good thermodynamic and kinetic stability has been established.¹⁸

The comparison of all of the X-ray crystal structures of the Ln(III) complexes with H₄dota-like ligands found in the literature indicated that the TSA/SA ratio is influenced by the size of the Ln(III) ion and by the geometry of the ligand cavity. The geometry and size of the complex cavity formed by H₄dota-like ligands seem to be mostly governed by the rotation of the pendants. As was shown, the different orientations of the pendant arms lead to different distances between the N₄ and O₄ planes.¹⁰ The lighter Ln ions such as La(III) and Ce(III) enforce a larger cavity and, thus, the N₄–O₄ distance is 2.5 Å or longer and a formation of the TSA arrangement is mostly required for their complexes. As the radius of a Ln(III) ion decreases along the Ln series, the ion moves toward the N₄ plane and, consequently, the coordinated oxygen atoms in the O₄ plane move also closer to the N₄ base and the structure switches to the SA isomer with a N₄–O₄ distance of 2.3–2.4 Å. On the other hand, complexes containing bulky phosphorus acid pendant(s) require a long distance between the N₄ and O₄ planes and, thus, form exclusively TSA or TSA' species.¹⁰

Unfortunately, to our best knowledge, no examples of X-ray structures of any Ln(III) complex having more than one species in the solid state have been published. Thus, the

comparison reported above is based on the coordination parameters found for various complexes with H₄dota-like ligands in different isomeric forms through the Ln series. In this paper, we report on the crystal structure of [Y(Hdo3aP^{ABn})(H₂O)][Y(Hdo3aP^{ABn})]·6H₂O·*i*PrOH, in which, for the first time, three different coordination polyhedrons, TSA-[Y(Hdo3aP^{ABn})(H₂O)], TSA'-[Y(Hdo3aP^{ABn})], and SA-[Y(Hdo3aP^{ABn})(H₂O)], of the same complex were identified.

Results and Discussion

The brief inspection of the structural data showed the presence of two independent molecules of the complex: one with and the other one without the coordinated water molecule. In the first case, the water molecule is coordinated to the yttrium(III) ion and the O atom of this water molecule corresponds to the fifth-highest maximum of the electron density after structure solution (maxima 1 and 2 correspond to two Y atoms, and maxima 3 and 4 correspond to two P atoms, respectively). The atoms belonging to the pendant arms have small thermal parameters, and nothing is pointing to the fact that they should be disordered. However, the high peaks of the electron maximum density in the macrocyclic part of the unit with a coordinated water molecule revealed the disorder of the macrocycle N and C atoms in two positions. This disorder was the best refined with the occupancies 43% and 57% for both possibilities. The less abundant position corresponds to the isomer with a TSA configuration, and the other corresponds to the SA isomer. This refinement was found to be meaningful because the bond lengths and angles in both disordered parts are very reasonable (see the Supporting Information). In the latter molecule, no disorder was found, except a small twist in the aminobenzyl moiety. Absence of a coordinated water molecule, orientation of the pendants, and conformations of ethylene chains of the macrocycle clearly assign the TSA' structure. The benzylamino groups are protonated to ensure electroneutrality of the compound. Additionally, one molecule of 2-propanol was found, and some remaining high peaks in the map of the electron density were attributed to disordered water molecules. Unfortunately, a huge disorder in the water O atoms did not allow one to locate water H atoms. Thus, the correct formula is {TSA-[Y(Hdo3aP^{ABn})(H₂O)]}_{0.43}{SA-[Y(Hdo3aP^{ABn})(H₂O)]}_{0.57}{TSA'-[Y(Hdo3aP^{ABn})]}·6H₂O·*i*PrOH. To our best knowledge, the reported compound is the first fully characterized example of the TSA–SA–TSA' isomerization in the solid state.

A similar disorder between the TSA and SA isomers of one complex in the solid state has already been observed for [Eu(dotam)(H₂O)](CF₃SO₃)₃·2EtOH.^{12g} Unfortunately, in this referred case, the authors refined the disorder of the macrocyclic unit by splitting only the C atoms into two different positions and keeping the N atoms in the averaged positions. Therefore, such a refinement led to some nontypical structural parameters, and the datapoints belonging to this complex lie just halfway between those reported for other TSA and SA structures (see, e.g., Figures 6 and 7 in ref 17 and the charts given in the Supporting Information of this paper).

- (13) (a) Aime, S.; Batsanov, A. S.; Botta, M.; Dickins, R. S.; Faulkner, S.; Foster, C. E.; Harrison, A.; Howard, J. A. K.; Moloney, J. M.; Norman, T. J.; Parker, D.; Williams, J. A. G. *J. Chem. Soc., Dalton Trans.* **1997**, 3623. (b) Aime, S.; Batsanov, A. S.; Botta, M.; Howard, J. A. K.; Parker, D.; Senanayake, K.; Williams, J. A. G. *Inorg. Chem.* **1994**, *33*, 4696.
- (14) (a) Rohovec, J.; Vojtíšek, P.; Lukeš, I.; Hermann, P.; Ludvík, J. *J. Chem. Soc., Dalton Trans.* **2000**, 141. (b) Rohovec, J.; Vojtíšek, P.; Hermann, P.; Mosinger, J.; Žák, Z.; Lukeš, I. *J. Chem. Soc., Dalton Trans.* **1999**, 3585.
- (15) Avecilla, F.; Peters, J. A.; Geraldes, C. F. G. C. *Eur. J. Inorg. Chem.* **2003**, 4179.
- (16) (a) Rudovský, J.; Cígler, P.; Kotek, J.; Hermann, P.; Vojtíšek, P.; Lukeš, I.; Peters, J. A.; Elst, L. V.; Müller, R. N. *Chem.—Eur. J.* **2005**, *11*, 2373. (b) Rudovský, J.; Kotek, J.; Hermann, P.; Lukeš, I.; Mainero, V.; Aime, S. *Org. Biomol. Chem.* **2005**, *3*, 112. (c) Rudovský, J.; Hermann, P.; Botta, M.; Aime, S.; Lukeš, I. *Chem. Commun.* **2005**, 2390.
- (17) Vojtíšek, P.; Cígler, P.; Kotek, J.; Rudovský, J.; Hermann, P.; Lukeš, I. *Inorg. Chem.* **2005**, *44*, 5591.
- (18) Táborský, P.; Lubal, P.; Havel, J.; Kotek, J.; Hermann, P.; Lukeš, I. *Collect. Czech., Chem. Commun.* **2005**, *70*, 1909.

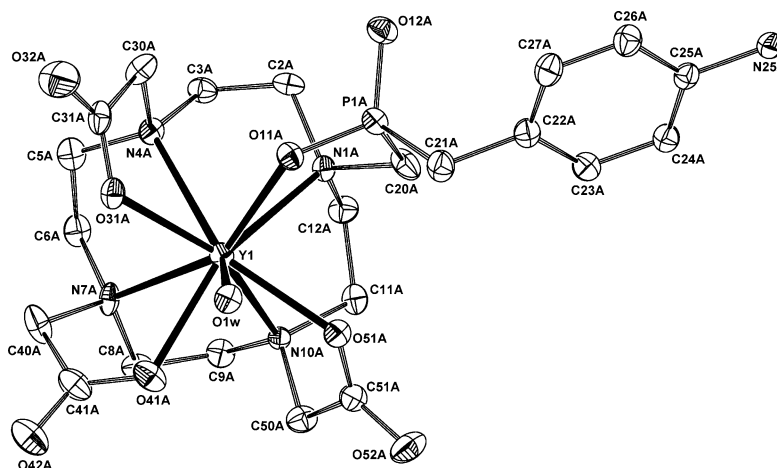


Figure 1. Molecular structure of the TSA-[Y(Hdo3aP^{ABn})(H₂O)] complex with an atom-labeling scheme.

Table 1. Structural Parameters of the TSA, SA, and TSA' Units in the Crystal Structure of [Y(Hdo3aP^{ABn})(H₂O)][Y(Hdo3aP^{ABn})]·6H₂O·iPrOH and Estimated Parameters for the Hypothetical SA' Species

parameter	species			
	TSA	TSA'	SA	SA'
Distances (Å)				
Y–O _w	2.485(3)		2.485(3)	
Y–Q(O ₄) ^a	0.761(2)	1.029(2)	0.761(2)	~1.02
Q(O ₄)–Q(N ₄) ^a	2.501	2.562	2.344	~2.38
Y–Q(N ₄) ^a	1.740(8)	1.532(2)	1.581(6)	~1.38
O1···O41	4.353(4)	3.980(4)	4.353(4)	
O31···O51	4.388(4)	4.170(5)	4.388(4)	
N1···N7	4.12(2)	4.143(6)	4.26(2)	
N4···N10	4.07(2)	4.135(6)	4.14(1)	
Angles (deg)				
opening angle φ^b	140.3(1)	122.4(1)	140.3(1)	<130
	142.7(1)	130.4(1)	142.7(1)	
twist angle ω^b	–24.7(4)	–24.3(2)	40.1(3)	~40
	–26.1(4)	–25.0(1)	41.1(3)	
	–27.4(3)	–27.0(2)	42.2(3)	
	–27.6(4)	–27.7(2)	42.5(3)	

^a Q is the centroid of the N₄ or O₄ planes. ^b For a definition of the angles, see Scheme 2.

The structure of the TSA species of the title complex is shown in Figure 1, and Table 1 lists the selected structural parameters determined for all three species and the parameters estimated for the unknown SA' structure. The additional figures and bond distances and angles are presented in the Supporting Information. As in other H₄dota-like ligands, the (Hdo3aP^{ABn})^{3–} anion is coordinated to the Y(III) ion by the four N atoms and the four O atoms, three coming from the acetates and one from the phosphinate. The N atoms form the N₄ plane. The O atoms of the three acetates and the one phosphinate also form a similar O₄ base that is almost planar. Deviations of the N atoms from planarity are in the range from 0.001(2) Å (TSA') to 0.005(6) Å (SA) and to 0.012(8) Å (TSA). The deviations of the O atoms are higher going from 0.022(2) Å for TSA and SA to 0.065(2) Å for TSA'. The O₄ and N₄ planes are parallel, with the mutual angles about 2.4(4)° (TSA), 1.5(2)° (SA), and 2.2(1)° (TSA'). The deviations from planarity and the mutual angles lie in the range found for the series of TSA-[Ln(Hdo3aP)][–] complexes.¹⁷ In all present polyhedrons, the Y(III) ion lies between these planes, closer to the O₄ (Table 1).

The twist angles ω of the planes around the local 4-fold axis are about –26° for the TSA and TSA' species and about 41° for the SA unit (Scheme 2 and Table 1) and fall to the range expected for these arrangements. The molecule of water capping the O₄ plane completes the coordination sphere of the TSA and SA isomers. The deviation of the Y–O_w bond vector from the local 4-fold axis is 5.0(1)°. The Y–O_w bond length (2.49 Å) is slightly longer than the distance reported for the structures of the [Y(dota)][–] complex (2.42 and 2.44 Å, respectively)^{11e,f} but still within the range observed for the other Ln(III) complexes of H₄dota-like ligands.^{3c,10,17} The presence of the coordinated water molecule in the SA and TSA isomers and its absence in the TSA' species correspond well with the values of the angle φ (Scheme 2), which is larger for the TSA and SA arrangements and lower for the TSA' polyhedron than the limiting value 135°.¹⁰ The bond distances between the Y(III) ion and the donor atoms lie in the range reported for complexes with similar types of ligands.^{11e,f,13,17}

The distances between the O₄ and N₄ planes determined for the TSA and TSA' species as well as for the SA species fall into the plots found for Ln(III) complexes with H₄dota-like ligands¹⁷ (see also the Supporting Information). Comparing the parameters of the [Y(Hdo3aP^{ABn})(H₂O)] isomers, we can find several structural properties that reflect some aspect of the well-known behavior of Gd(III) complexes with H₄dota-like ligands in solution. In the TSA and SA isomers, we observed similarity on their O₄ planes (Table 1). The bond distances Y–O and the opening angles φ are the same as well as the distances of Y(III) from the O₄ plane, the distances of the opposite O atoms, and the Y–O_w bond length. Analogously to the other H₄dota-like complexes, the O₄–N₄ distance is shorter by about 0.2 Å for SA than for TSA arrangements and, thus, in the SA isomer, Y(III) is also closer to the N₄ plane.

A comparison between the TSA and TSA' species indicates that the Y–O₄ distance in the TSA' unit is much longer, distances between the opposite O atoms are shorter, the angles φ are smaller, and, thus, Y is located deeper in the cavity of the TSA' arrangement than in the TSA one (see Table 1). Despite the fact that the distance between the

O₄ and N₄ planes is slightly longer for the TSA' unit, Y is much closer to the N₄ plane in this species.

As was mentioned previously, the distance of the O₄ and N₄ planes in the SA species is noticeably shorter than those in the TSA or TSA' units. If we imagine the changes that would occur when passing from the SA to the hypothetical SA' arrangements, then, in the SA' polyhedron, the Y(III) ion should move closer to the N₄ plane, similarly to that found for the TSA and TSA' species. Structural parameters estimated for the SA' species are listed in Table 1. In literature, the SA' structure was found only for a small scandium(III) ion in the complex with H₄dota.^{11a} Our parameters estimated for the hypothetical SA'-[Y(Hdo3aP^{ABn})] species fit to the parameters of the SA'-[Sc(dota)]⁻ complex very well. As was documented in ref 17, the SA structures are very rigid and tight (much more rigid than TSA ones) and the SA' arrangement would be even more rigid than the SA itself. Considering the facts given previously, we can deduce that the SA' structure is possible only for small ions such is Sc(III) and maybe Y(III) and heavy Ln ions. From this, we can conclude that the SA' arrangement of complexes of H₄dota-like ligands with Gd(III) would be extremely inconvenient and maybe it does not exist at all.

Investigations of the Ln(III) complexes with amide derivatives of H₄dota in solution showed that the TSA and SA isomers interchange each other very slowly, much more slowly than an exchange of a water molecule in the TSA/TSA' pair.^{9a,b,12d} Analogous differences in interchange between the TSA and SA isomers are also assumed for the H₄dota complexes but on a faster time scale.¹⁹ Because the TSA isomers exchange water molecules much faster than the SA ones, it was concluded that the overall water-exchange rate (and, consequently, relaxivity) is determined mostly by the ratio of the TSA and SA isomers in a solution.^{8d,9a} The high value of the water-exchange rate of the TSA species, in contrast to the SA ones, is commonly explained by a steric strain at the O₄ plane. However, our structural parameters found for both TSA and SA species at the O₄ plane are the same. Furthermore, the structural parameters determined for the TSA, TSA', and SA species of the [Y(Hdo3aP^{ABn})] complex and parameters found for the series of Ln(III) complexes published recently¹⁷ indicate that structures of both TSA and TSA' spheres are flexible.

In conclusion, if the water-exchange mechanism is dissociative in its nature, as is commonly accepted in the literature,²⁻⁴ we suggest that a high exchange rate of the coordinated water molecule of the TSA species is caused by the flexibility of this arrangement. The Ln(III) ion can move easily up and down inside the TSA ligand cage, and water release is driven by changes in the pendant arm geometry (associated with changes of φ) forming TSA' species. On the other hand, the SA structure is very rigid and that of SA' should be even more tight; thus, the water exchange (if any) should be extremely slow.

Table 2. Crystallographic Experimental Data

chemical formula	C ₄₇ H ₈₈ N ₁₀ O ₂₄ P ₂ Y ₂
color and shape	colorless prism
cryst size (mm)	0.25 × 0.30 × 0.45
fw	1417.03
cryst syst	monoclinic
space group	P2 ₁ /c (No. 14)
a (Å)	13.3278(2)
b (Å)	35.8714(6)
c (Å)	13.5384(3)
β (deg)	89.9603(7)
V (Å ³)	6472.5(2)
Z	4
T (K)	150(1)
λ (Å)	0.71073
D _{calcd} (g cm ⁻³)	1.454
μ (cm ⁻¹)	1.915
wR (all data), wR' ([I > 2σ(I)] ^a)	0.1614, 0.1504
R (all data), R' ([I > 2σ(I)] ^b)	0.0805, 0.0594

^a $wR = [\sum w(F_o^2 - F_c^2)^2 / \sum w(F_o^2)^2]^{1/2}$, $w = 1/[\sigma^2(F_o^2) + (AP)^2 + BP]$, where $P = (F_o^2 + 2F_c^2)/3$ (SHELXL97²²). ^b $R = \sum |F_o - F_c| / \sum |F_c|$ (SHELXL97²²).

Experimental Section

Preparation of a Single Crystal. The solution of the complex was prepared by the mixing of stoichiometric amounts of H₄-do3aP^{ABn} hydrate^{16b} and YCl₃ hydrate (Strem) in water. The value of the pH was slowly adjusted to ~8 with dilute aqueous NaOH, and the resulting mixture was briefly heated. After standing overnight, the solution was filtered and the pH value was lowered to ~5 with dilute aqueous HCl. The diffraction-quality crystals of the title complex were grown from the aqueous solution by a slow vapor diffusion of *i*PrOH at room temperature over the course of several weeks.

Crystal Structure Solution and Refinement. A selected crystal was quickly transferred into Fluorolub oil, mounted on a glass fiber in a random orientation, and cooled to 150(1) K. The diffraction data were collected at 150(1) K (Cryostream Cooler Oxford Cryosystem) using a Nonius Kappa CCD diffractometer and Mo K α radiation ($\lambda = 0.71073$ Å) and analyzed using the *HKL Denzo* program package.²⁰ The structure was solved by direct methods by the program SIR92²¹ and refined by a full-matrix least-squares technique by the program SHELXL97.²² Scattering factors for neutral atoms used were included in the SHELXL97 program. Table 2 gives pertinent crystallographic data.

Although the value of β is very close to 90° and points to a possible wrong decision of the crystal system (orthorhombic instead of monoclinic), a comparison of R_{int} values (41.1 vs 3.3%, respectively) clearly showed that a solution in a monoclinic space group is preferable. Furthermore, the possibility of twinning of the orthorhombic cell was tested using the TWIN command, but in this case, the refined contribution of the twin was marginal (BAS F ~ 0.003); therefore, the right choice of the monoclinic space group P2₁/c was confirmed.

All non-H atoms were refined anisotropically (except one N atom of the macrocycle in the TSA part of the first molecule, which become nonpositive definite if treated anisotropically and was therefore refined isotropically), and the H atoms were placed in theoretical positions using the riding model.

(20) Otwinowski, Z.; Minor, W. *HKL Denzo and Scalepack Program Package*; Nonius BV: Delft, The Netherlands, 1997. Otwinowski, Z.; Minor, W. *Methods Enzymol.* **1997**, *276*, 307.

(21) Altomare, A.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Crystallogr.* **1994**, *27*, 435.

(22) Sheldrick, G. M. *SHELXL97, A Computer Program for Refinement of Crystal Structures*; University of Göttingen: Göttingen, Germany, 1997.

(19) Jacques, V.; Desreux, J. F. *Inorg. Chem.* **1994**, *33*, 4048.

Crystallographic data reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as CCDC 293689. Copies of the data can be obtained free of charge upon application to CCDC via e-mail deposit@ccdc.cam.ac.uk. The list of selected bond distances and angles, torsion angles, and some other structural parameters is given in the Supporting Information.

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Supporting Information Available: Solution and refinement details for the presented structure (CIF), charts of $d(\text{O}_4-\text{N}_4)$ vs L_n and $d(\text{O}_4-\text{N}_4)$ vs twist angle ω for relevant structures from the literature, and pictures and tables of relevant distances and angles found for TSA, SA, and TSA' species in $[\text{Y}(\text{Hdo3aP}^{\text{ABn}})(\text{H}_2\text{O})]\cdot 6\text{H}_2\text{O}\cdot i\text{PrOH}$.

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