

Controlled Ligand Deprotonation in Lanthanide Chelates with Asymmetric Semicarbazone/Benzoylhydrazone or Semicarbazone/Thiosemicarbazone Coordination Spheres

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Asymmetric, potentially pentadentate ligands (H_2L^3) are formed by subsequent condensation of a semicarbazide and benzoylhydrazine on 2,6-diacetylpyridine. Two equivalents of H_2L^3 reacts with $CeCl_3 \cdot 7H_2O$, $Ce(SO_4)_2 \cdot 4H_2O$, or $EuCl_3 \cdot 6H_2O$ under formation of $[Ln^{III}(HL^3)_2]^+$ cations ($Ln = Ce, Eu$) with exclusive deprotonation of the benzoylhydrazone ligand arms. The Ce^{4+} ion of the sulfate salt is reduced during the reaction and forms 10-coordinate singly charged complex cations, the structure of which is identical to the product of the reaction of cerium(III) chloride. The exact position of deprotonation in the ligands is resolved by infrared spectroscopy, bond lengths considerations, and the hydrogen bonding in the solid-state structures of the products. A similar approach allows the synthesis of mixed semicarbazone/thiosemicarbazone ligands (H_2L^4). The reaction of H_2L^4 with $Sm(NO_3)_3 \cdot 6H_2O$ leads to the first structurally characterized lanthanide complex with thiosemicarbazone coordination. The solid-state structure of the 10-coordinate complex $[Sm(HL^4)_2]NO_3 \cdot H_2O$ shows exclusive deprotonation of the thiosemicarbazone arms of the ligands. All isolated complexes are air stable and do not undergo ligand exchange reactions or hydrolysis in the presence of water.

Introduction

The increasing interest in the coordination chemistry of lanthanides is focused on potential applications in catalysis, advanced materials, and diagnostic medicine.¹ Additionally, certain group III and lanthanide elements possess radioactive nuclides with a remarkable potential in nuclear medicine.² This includes positron emitters such as ^{86}Y and ^{152}Tb , β^- -emitters such as ^{99}Y , ^{142}Nd , ^{153}Sm , or ^{177}Lu , but also the α -emitting isotope ^{149}Tb , which allows therapeutic applications (radioimmunotherapy or palliative treatment of cancer) under a strict control.

A key requirement for these applications, however, is a detailed knowledge of the coordination behavior of the metal ions and ligands.³ This is not the case with most of the hitherto applied complexes with citrate, phosphonate, or butyrate ligands, which frequently undergo an in vivo ligand exchange, for example, with plasma components.⁴ A promising approach to avoid undesired secondary reactions is the use of bioconjugates with polydentate ligands, which form kinetically inert complexes with a predictable reactivity. This has successfully been demonstrated with tetraaza macrocycles.⁵

With this background, we were interested in the coordination chemistry of lanthanides with polydentate hydrazones, semicarbazones, and thiosemicarbazones. Previous studies indicated that semicarbazones derived from acetylpyridine

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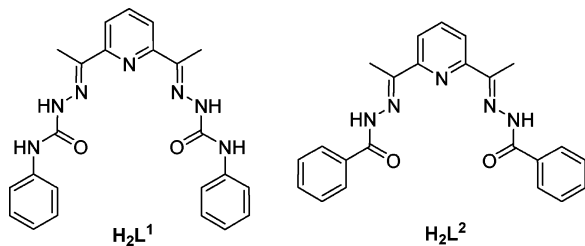
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or 2,6-diacetylpyridine (H_2L^1) act as neutral ligands.⁶ Corresponding benzoylhydrazones (H_2L^2) partially deprotonate, but the number of positions of deprotonations could not be predicted and their position in the complex molecule could not be resolved by crystallography.⁷ Despite many attempts to prepare stable thiosemicarbazone complexes of lanthanides,⁸ to our knowledge there exists no crystallographically characterized compound.



In the present work, we report the synthesis and structural characterization of lanthanide complexes with pentadentate asymmetric ligand systems derived from 2,6-diacetylpyridine or 2,6-diformylpyridine with mixed semicarbazone/benzoylhydrazone and semicarbazone/thiosemicarbazone coordination sites.

Experimental Section

General Considerations. Infrared spectra were measured as KBr pellets on a Shimadzu FTIR-spectrometer. FAB⁺ mass spectra were recorded with a TSQ (Finnigan) instrument using a nitrobenzyl alcohol matrix. Elemental analysis was determined using a Heraeus vario EL elemental analyzer. NMR spectra were taken with a JEOL 400 MHz multinuclear spectrometer.

H_2L^{3a} . 2,6-Diacetylpyridine (1.63 g, 10.0 mmol) was dissolved in about 50 mL of a hot EtOH/ H_2O mixture (v/v 1/1), and 4-phenylsemicarbazide (1.51 g, 10.0 mmol) in about 75 mL of H_2O was slowly added. After being heated on reflux for 1 h, the colorless precipitate was filtered off and washed with EtOH. Yield: 2.75 g, 93%. When necessary, disubstituted byproduct can be removed by recrystallization from $CHCl_3$. Anal. Calcd for $C_{16}H_{16}N_4O_2$ (296.3): C, 64.9; H, 5.4; N, 18.9. Found: C, 64.6; H, 5.5; N, 19.1.

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IR (KBr) (ν_{max}/cm^{-1}): 3375, 3194 (s, N-H), 1697 (s, acetyl C=O), 1680 (s, C=O). ¹H NMR (400 MHz, DMSO- d_6): δ [ppm] = 2.67 (s, 3H, [H₃C-C=O]), 2.42 (s, 3H, [H₃C-C=O]), 7.03–8.65 (8H, [arom. H]), 9.01 (s, 1H, [Ph-N-H]), 10.03 (s, 1H, [N-H]). FAB⁺-MS: m/z = 297 ([M - H]⁺), 204 ([M - NH - Ph]⁺).

H_2L^3 . HL^{3a} (0.34 g, 1.2 mmol) and benzoylhydrazine (0.16 g, 1.2 mmol) were suspended in about 30 mL of i-PrOH and heated on reflux for 36 h. The pure product was filtered off from the hot reaction mixture. Yield: 0.33 g, 66%. Anal. Calcd for $C_{23}H_{22}N_6O_2$ (414.5): C, 66.7; H, 5.4; N, 20.3. Found: C, 66.5; H, 5.6; N, 19.9. IR (KBr) (ν_{max}/cm^{-1}): 3389, 3201 (s, N-H), 1689 (s, semicarbazone C=O), 1653 (s, benzoylhydrazone C=O). ¹H NMR (400 MHz, DMSO- d_6): δ [ppm] = 2.42 (s, 3H, [H₃C-C, semicarbazone]), 2.53 (s, 3H, [H₃C-C, benzoylhydrazone]), 7.04–8.43 (aromat. CH, 13H), 8.99 (s, 1H, [PhNH]), 9.96 (s, 1H, [semicarbazone NH]), 10.89 (s, 1H, [benzoylhydrazone NH]). FAB⁺-MS: m/z = 415 ([M - H]⁺), 105 ([Ph - C=O]⁺).

H_2L^{4a} . 2,6-Diformylpyridine (1.00 g, 7.4 mmol) was dissolved in about 125 mL of hot H_2O . 4-Phenylsemicarbazide (1.12 g, 7.4 mmol) was dissolved in 75 mL of H_2O and slowly added at a temperature of about 50 °C. After being stirred at this temperature for 30 min, the formed precipitate was filtered off and redissolved in 200 mL of hot $CHCl_3$. An almost insoluble colorless solid (disubstituted semicarbazone) was removed by filtration, and the remaining solution was evaporated to dryness to give 970 mg (3.6 mmol, 49%) of H_2L^{4a} which was used in the next step without further purification. Anal. Calcd for $C_{14}H_{12}N_4O_2$ (268.27): C, 62.7; H, 4.5; N, 20.9. Found: C, 62.3; H, 4.3; N, 20.5. IR (KBr) (ν_{max}/cm^{-1}): 3382, 3201 (s, N-H), 1701 (s, formyl C=O), 1689 (s, semicarbazone C=O). ¹H NMR (400 MHz, DMSO- d_6): δ [ppm] = 7.06–8.67 (8H, [arom. H]), 8.10 (s, 1H, [H-C-C=N]), 9.11 (s, 1H, [PhNH]), 10.00 (s, 1H, [H-C=O]), 11.19 (s, 1H, [NH]). FAB⁺-MS: m/z = 268 ([M]⁺), 148 ([M - C₇H₆NO]⁺), 119 ([C₇H₅NO]⁺), 93 ([C₆H₇N]⁺).

H_2L^4 . H_2L^{4a} (0.30 g, 1.1 mmol) and 4-phenylthiosemicarbazide (0.20 g, 1.2 mmol) were suspended in 30 mL of EtOH and heated on reflux for 4 h. The bright yellow precipitate was filtered off and washed with water. Yield: 0.45 g, 98%. Anal. Calcd for $C_{21}H_{19}N_7OS$ (417.47): C, 60.4; H, 4.5; N, 23.4. Found: C, 60.4; H, 4.4; N, 23.5. IR (KBr) (ν_{max}/cm^{-1}): 3382, 3313 (s, N-H), 1686 (s, semicarbazone C=O), 1596, 1542 (s, C=N). ¹H NMR (400 MHz, DMSO- d_6): δ [ppm] = 7.04–8.43 (m, 15H [arom. H + CH=N]), 9.06 (s, 1H, [O=C-NH-Ph]), 10.31 (s, 1H, [S=C-NH-Ph]), 11.13 (s, 1H, [semicarbazone NH]), 12.11 (s, 1H, [thiosemicarbazone NH]). FAB⁺-MS: m/z = 417 ([M]⁺), 324 ([M - C₆H₇N]⁺), 265 ([M - C₇H₆N₂S]⁺), 135 ([C₇H₅NS]⁺), 119 ([C₇H₅NO]⁺), 93 ([C₆N₇N]⁺).

[Eu(HL^3)₂]Cl. $EuCl_3 \cdot 6H_2O$ (44 mg, 0.12 mmol) was dissolved in about 10 mL of EtOH, and H_2L^3 (100 mg, 0.24 mmol) was added. A clear light-orange solution was obtained after adding 10 μ L of Et₃N to the hot reaction mixture. After the mixture was heated on reflux for 3 h, the volume of the solution was halved. A yellow solid precipitated upon cooling. It was filtered off and washed with 2 mL of ethanol. Yield: 84 mg, 68%. Anal. Calcd for $C_{46}H_{42}EuClN_{12}O_4$ (1014.29): C, 54.5; H, 4.1; N, 16.6. Found: C, 53.9; H, 4.4; N, 16.1. IR (KBr) (ν_{max}/cm^{-1}): 1658 (s, semicarbazone C=O), 1600 (s, benzoyl-hydrazone C=O). FAB⁺-MS: m/z = 979 ([Eu(HL^3)₂]⁺ - H), 566 ([Eu(HL^3)⁺ - 2H).

[Ce(HL^3)₂]Cl. $CeCl_3 \cdot 7H_2O$ (44 mg, 0.12 mmol) was dissolved in about 10 mL of ethanol, and H_2L^3 (100 mg, 0.24 mmol) was added. A clear orange-red solution was obtained after adding 10 μ L of Et₃N and 100 μ L of H_2O to the hot reaction mixture. After the mixture was heated on reflux for 3 h, the volume was halved.

Table 1. X-ray Structure Data Collection and Refinement Parameters

	[Eu(HL ³) ₂]Cl·1.5iso-PrOH·H ₂ O	[Ce(HL ³) ₂]Cl	[Ce(HL ³) ₂] ₂ (SO ₄)·7EtOH	[Sm(HL ⁴) ₂](NO ₃)·H ₂ O
formula	C _{50.5} H ₅₆ ClN ₁₂ O _{6.5} Eu	C ₄₆ H ₄₂ ClN ₁₂ O ₄ Ce	C ₁₁₀ H ₁₃₈ N ₂₄ O ₂₁ SCe ₂	C ₄₂ H ₃₆ N ₁₅ O ₆ S ₂ Sm
<i>M_w</i>	1122.48	1002.49	2444.74	1061.33
crystal system	monoclinic	orthorhombic	monoclinic	trigonal
<i>a</i> /Å	11.446(3)	12.891(1)	23.169(5)	49.76(5)
<i>b</i> /Å	31.751(7)	21.859(2)	20.064(5)	49.76(5)
<i>c</i> /Å	15.632(4)	35.026(4)	25.288(5)	13.85(3)
<i>α</i> /deg	90	90	90	90
<i>β</i> /deg	102.78(1)	90	93.07(1)	90
<i>γ</i> /deg	90	90	90	120
<i>V</i> /Å ³	5541(2)	9869(2)	11 739(5)	29 706(80)
space group	<i>P</i> ₂ / <i>n</i>	Pbca	<i>P</i> ₂ / <i>n</i>	<i>R</i> ³
<i>Z</i>	4	8	4	18
<i>D_{calc}</i> /g cm ⁻³	1.344	1.349	1.383	1.068
<i>μ</i> /mm ⁻¹	1.237	1.029	0.860	0.997
no. of reflns	48 520	46 252	94 435	11 364
no. independent	10 795	11 563	20 010	11 364
no. parameters	650	577	1475	586
R1/wR2 ^a	0.0592/0.1115	0.0653/0.1146	0.0287/0.0674	0.0669/0.1558
GOF	1.019	0.865	0.979	0.975
temp/K	173	293	173	173

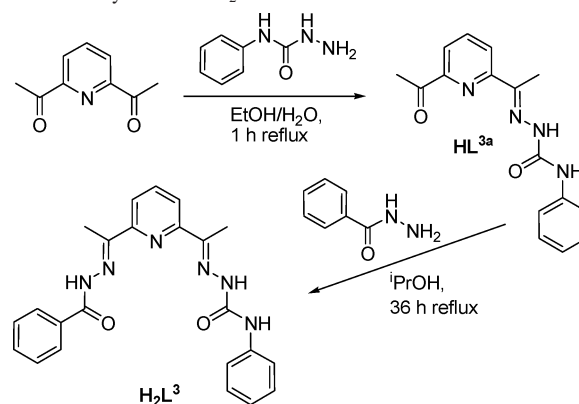
$$^a R1 = \sum(|F_o - F_c|)/\sum|F_o|; wR2 = [\sum w(F_o^2 - F_c^2)^2/\sum wF_o^2]^{-1/2}.$$

An orange-red solid precipitated upon cooling. It was filtered off and washed with 2 mL of EtOH. Yield: 40 mg, 33%. Anal. Calcd for C₄₆H₄₂CeClN₁₂O₄ (1002.5): C, 55.1; H, 4.2; N, 16.7. Found: C, 55.3; H, 4.1; N, 16.3. IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1664 (s, semicarbazone C=O), 1600 (s, benzoylhydrazone C=O). FAB⁺-MS: *m/z* = 966 ([Ce(HL³)₂]⁺ - H), 552 ([Ce(HL³)₂]⁺ - 2H).

[Ce(HL³)₂]₂(SO₄). Ce(SO₄)₂·4H₂O (49 mg, 0.12 mmol) was dissolved in about 20 mL of EtOH, and H₂L³ (100 mg, 0.24 mmol) was added. A pale yellow suspension was obtained after adding 30 μ L of Et₃N to the hot reaction mixture. After being heated on reflux for 8 h, a colorless precipitate was filtered off. The product precipitated in the form of orange-red crystals upon slow evaporation of the mother liquor. Yield: 25 mg, 21%. More product could be obtained by further concentration of the mother liquor, but this material was contaminated impurities (e.g., (Et₄NH)SO₄) and gave insufficient analytical results. Anal. Calcd for C₉₂H₈₄Ce₂N₂₄O₁₂S₁ (2030.1): C, 54.4; H, 4.2; N, 16.7. Found: C, 53.9; H, 3.9; N, 16.4. IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 1666 (s, semicarbazone C=O), 1604 (s, benzoylhydrazone C=O), 1555 (s, C=N). FAB⁺-MS: *m/z* = 1064 ([Ce(HL³)₂]₂(SO₄)⁺ - H), 966 ([Ce(HL³)₂]⁺ - H), 552 ([Ce(HL³)₂]⁺ - 2H).

[Sm(HL⁴)₂]₂(NO₃). Sm(NO₃)₃·5H₂O (35 mg, 0.1 mmol) was dissolved in about 25 mL of hot EtOH, and H₂L⁴ (80 mg, 0.2 mmol) was added. An orange-red suspension was obtained after adding 20 μ L of Et₃N to the hot reaction mixture. After the mixture was heated on reflux for 3 h, the volume of the solution was halved. The orange-red precipitate was filtered off and washed with EtOH. Yield: 54 mg, 53%. Single crystals of the composition [Sm(HL⁴)₂](NO₃)·H₂O were obtained from a two-phase system of the mother liquor and *n*-hexane. Anal. Calcd for C₄₂H₃₆N₁₅O₅S₂Sm (1044.32): C, 48.3; H, 3.4; N, 20.1. Found: C, 47.8; H, 3.2; N, 19.9. IR (KBr) ($\nu_{\max}/\text{cm}^{-1}$): 3282, 3047 (s, N-H), 1658 (s, semicarbazone C=O), 1600, 1554 (s, C=N). FAB⁺-MS: *m/z* = 986 ([M - H]⁺).

X-ray Crystallography. The intensities for the X-ray determinations were collected on a SMART CCD (Bruker) with Mo K α radiation ($\lambda = 0.71073$ Å). Standard procedures were applied for data reduction and absorption correction. Structure solution and refinement were performed with SHELXS97 and SHELXL97.⁹ Hydrogen atom positions were calculated for idealized positions and treated with the "riding model" option of SHELXL, except of those H-atoms, which are bonded to nitrogen atoms and/or are

Scheme 1. Synthesis of H₂L³

involved in hydrogen bonds. Their positions were derived from the final Fourier maps and refined. More details on data collections and structure calculations are contained in Table 1.

Additional information on the structure determinations has been deposited with the Cambridge Crystallographic Data Centre.

Results and Discussion

2,6-Diacetylpyridine benzoylhydrazone-4-phenylsemicarbazone, H₂L³, is obtained in a two-step reaction. The sequence of substitution (Scheme 1) is mandatory. The low reactivity of the monosubstituted semicarbazone (HL^{3a}) requires a long reaction time in the second step. A synthesis via a monosubstituted benzoylhydrazone is not recommended, because it requires additional purification steps due to the formation of disubstituted byproduct.

The reaction of 2 equiv of H₂L³ and cerium trichloride in ethanol yields an orange-red complex of the composition [Ce(HL³)₂]Cl. The infrared spectrum of the compound shows two $\nu(\text{C}=\text{O})$ vibrations at 1664 cm⁻¹ (semicarbazone) and 1600 cm⁻¹ (benzoylhydrazone). This corresponds to bathochromic shifts of 25 and 53 cm⁻¹ with respect to the values

(9) Sheldrick, G. M. SHELXS97 and SHELXL97 – programs for the solution and refinement of crystal structures, University of Göttingen, Germany.

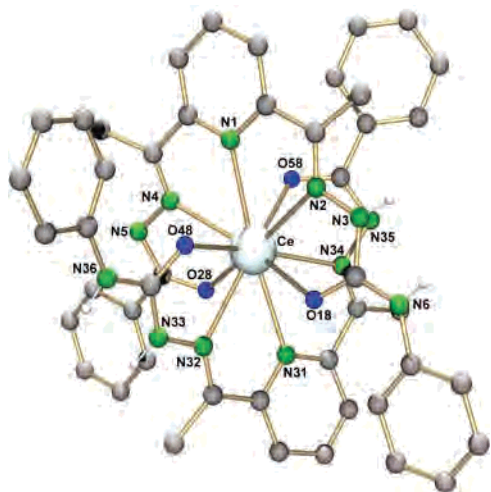


Figure 1. The structure of the complex cation of $[\text{Ce}(\text{HL}^3)_2]\text{Cl}$.

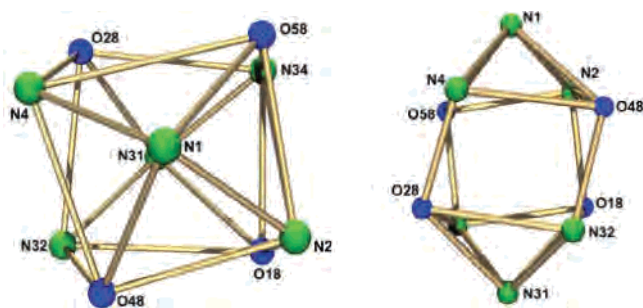


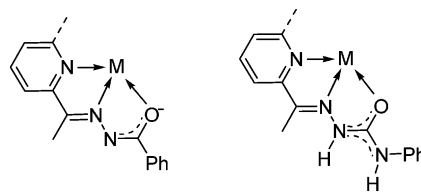
Figure 2. Coordination polyhedron of cerium in $[\text{Ce}(\text{HL}^3)_2]\text{Cl}$.

in noncoordinated H_2L^3 and suggests coordination of both functional groups to the metal. A peak at $m/z = 966$ in the FAB^+ mass spectrum indicates coordination of two ligands.

Orange-red crystals of $[\text{Ce}(\text{HL}^3)_2]\text{Cl}$ were obtained from a two-phase system of ethanol and *n*-hexane. The crystal structure (Figure 1) confirms the composition of the complex as a singly charged cation. The cerium atom is 10-coordinate by two of the singly deprotonated, pentadentate ligands. Its coordination environment can best be described to be intermediate between a bicapped cube and a bicapped square antiprism, where the caps are formed by the pyridine nitrogen atoms (Figure 2).

The bond lengths of the $\text{Ce}-\text{N}(\text{pyridine})$ bonds are in the same magnitude as the $\text{Ce}-\text{N}(\text{azomethine})$ bonds in the semicarbazone arms of the ligands. The shorter $\text{Ce}-\text{N}(\text{azomethine})$ bonds in the benzoylhydrazone bonding sites and the shorter $\text{Ce}-\text{O}$ bonds in these arms strongly suggest

Scheme 2. Bonding Situations in the Side Arms of the Singly Deprotonated Ligand $\{\text{HL}^3\}^-$



different bonding modes for the two parts of the pentadentate ligands. This is supported by the bond lengths inside the chelating functionalities (Table 2), which indicate delocalization of π -electron density in the semicarbazone unit over all $\text{C}-\text{N}$ bonds, whereas solely the chelate ring bonds are included in the benzoylhydrazone arms. This results in an exclusive deprotonation of the benzoylhydrazone functionality in H_2L^3 , whereas the semicarbazone remains protonated (see also Scheme 2). This bonding mode is supported by the detection of hydrogen bonds between the semicarbazone nitrogen atoms and the counterion Cl^- in the solid-state structure of $[\text{Ce}(\text{HL}^3)_2]\text{Cl}$. Details about these hydrogen bonds are summarized in Figure S1 and Table S1 of the Supporting Information.

Similar reaction conditions yield a yellow complex of the composition $[\text{Eu}(\text{HL}^3)_2]\text{Cl}$ when europium trichloride is used as a metal source. Yellow crystals are obtained from a 2-propanol solution by slow evaporation of the solvent. The complex cation is isostructural to $[\text{Ce}(\text{HL}^3)_2]^+$ with identical deprotonation positions in the coordinated ligand molecules (Figure 3). All $\text{Eu}-\text{N}$ and $\text{Eu}-\text{O}$ distances are shorter than the corresponding distances in the cerium complex, readily explained by the smaller ionic radius of Eu^{3+} . Nevertheless, all previously discussed tendencies in bond lengths are identical (Table 2). The coordination polyhedron of europium can also be described to be intermediate between a bicapped cube and a bicapped square antiprism with the pyridine nitrogen atoms as caps.

The infrared spectrum of the complex shows almost similar bathochromic shifts for the $\nu(\text{C}=\text{O})$ vibrations in the semicarbazone (31 cm^{-1}) and benzoylhydrazone arms (53 cm^{-1}). Figure 3 depicts a part of the hydrogen bond situation in the solid-state structure. The formed network includes the counterion Cl^- and the solvent water and confirms the sole deprotonation of the benzoylhydrazone site of the molecule. N5 (benzoylhydrazone) acts as hydrogen acceptor, whereas N36 (semicarbazone) is a hydrogen donor. Additional

Table 2. Selected Bond Lengths (\AA) and Angles (deg) in the $[\text{Eu}(\text{HL}^3)_2]^+$ and $[\text{Ce}(\text{HL}^3)_2]^+$ Cations

	Ce	Eu	Ce	Eu
$\text{O}(18)-\text{Ln}$	2.592(8)	2.446(4)	$\text{O}(28)-\text{Ln}$	2.361(4)
$\text{O}(48)-\text{Ln}$	2.592(8)	2.519(4)	$\text{O}(58)-\text{Ln}$	2.375(4)
$\text{N}(1)-\text{Ln}$	2.775(9)	2.663(5)	$\text{N}(2)-\text{Ln}$	2.617(5)
$\text{N}(4)-\text{Ln}$	2.64(1)	2.564(5)	$\text{N}(31)-\text{Ln}$	2.698(5)
$\text{N}(32)-\text{Ln}$	2.764(9)	2.611(5)	$\text{N}(34)-\text{Ln}$	2.559(5)
$\text{O}(18)-\text{C}(17)$	1.24(1)	1.244(7)	$\text{O}(28)-\text{C}(27)$	1.285(7)
$\text{O}(48)-\text{C}(47)$	1.21(1)	1.244(7)	$\text{O}(58)-\text{C}(57)$	1.277(7)
$\text{N}(2)-\text{N}(3)$	1.34(1)	1.367(7)	$\text{N}(3)-\text{C}(17)$	1.338(9)
$\text{N}(5)-\text{N}(4)$	1.40(1)	1.400(6)	$\text{N}(5)-\text{C}(27)$	1.306(8)
$\text{O}(18)-\text{Ln}-\text{N}(2)$	58.9(3)	61.2(2)	$\text{O}(28)-\text{Ln}-\text{N}(4)$	60.9(2)
$\text{O}(48)-\text{Ln}-\text{N}(32)$	58.3(3)	60.2(3)	$\text{O}(58)-\text{Ln}-\text{N}(34)$	61.5(3)
$\text{N}(31)-\text{Ln}-\text{N}(1)$	173.0(3)	174.6(2)		

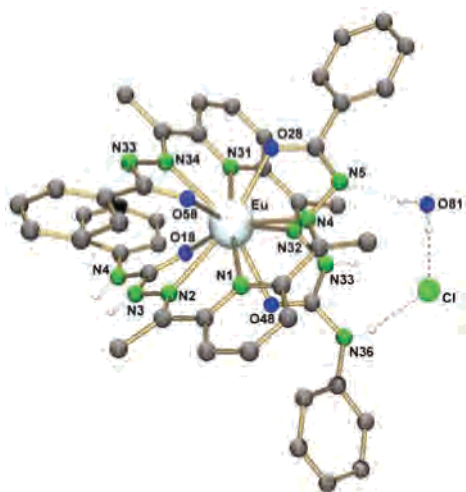


Figure 3. The structure of the complex cation of $[\text{Eu}(\text{HL}^3)_2]\text{Cl}\cdot\text{H}_2\text{O}\cdot 1.5$ iso-PropOH with hydrogen bonds to the Cl^- counterion and solvent water.

Table 3. Selected Hydrogen Bonds in $[\text{Eu}(\text{HL}^3)_2]\text{Cl}$ [Å and deg]^a

D—H···A	<i>d</i> (D—H)	<i>d</i> (H···A)	<i>d</i> (D···A)	∠(DHA)
N(33)—H(33)···Cl	0.86	2.41	3.199(5)	153.0
N(36)—H(36)···Cl	0.86	2	3.224(5)	155.9
N(6)—H(6)···O(81)#1	0.86	2.14	2.909(8)	149.3
N(3)—H(3N)···O(81)#1	0.86(7)	2.00(7)	2.773(7)	149.0(7)
O(81)—H(81A)···N(5)	0.90(6)	1.91(6)	2.793(7)	165.0(7)
O(81)—H(81b)···Cl	0.729(5)	2.499(2)	3.194(5)	159.9(4)

^a Symmetry transformations used to generate equivalent atoms: #1 $x + 1, y, z$.

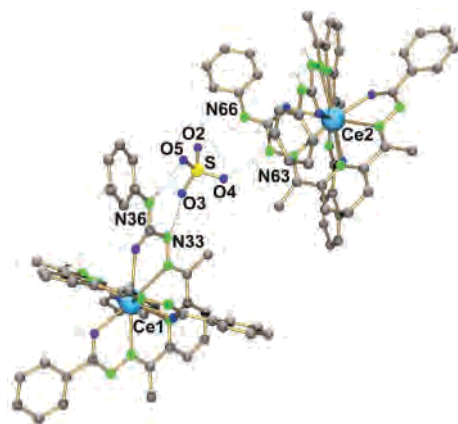


Figure 4. The structure of $[\text{Ce}(\text{HL}^3)_2]_2(\text{SO}_4)$.

hydrogen bonds are formed between the water molecule and the nitrogen atoms N3 and N6 of a neighboring complex cation (Table 3).

The controlled deprotonation of H_2L^3 at the benzoylhydrazone arm was proven by a third example. Cerium(IV) sulfate reacts with the mixed-functional ligand in ethanol under reduction of the metal center and the formation of $[\text{Ce}^{\text{III}}(\text{HL}^3)_2]_2(\text{SO}_4)$. The spectroscopic data of the complex indicate a bonding situation close to that in the chloride.

Single crystals of the composition $[\text{Ce}(\text{HL}^3)_2]_2(\text{SO}_4)\cdot 7\text{EtOH}$ were obtained by slow evaporation of a solution of the complex in ethanol. Figure 4 illustrates that two of the complex cations are connected by a hydrogen-bonded sulfate anion. The hydrogen bonds are established by semicarbazone NH-hydrogen atoms exclusively and confirm the defined

Table 4. Selected Bond Lengths (Å) and Angles (deg) in the Complex Anion of $[\text{Ce}(\text{HL}^3)_2]_2(\text{SO}_4)\cdot 7\text{EtOH}$

Ce(1)—O(18)	2.525(2)	Ce(2)—O(88)	2.396(2)
Ce(1)—O(28)	2.413(2)	Ce(2)—O(118)	2.414(2)
Ce(1)—O(48)	2.541(2)	Ce(2)—O(78)	2.497(2)
Ce(1)—O(58)	2.413(2)	Ce(2)—O(108)	2.541(2)
Ce(1)—N(34)	2.682(3)	Ce(2)—N(94)	2.663(3)
Ce(1)—N(1)	2.790(2)	Ce(2)—N(64)	2.673(3)
Ce(1)—N(2)	2.768(2)	Ce(2)—N(61)	2.759(3)
Ce(1)—N(4)	2.706(3)	Ce(2)—N(62)	2.758(2)
Ce(1)—N(31)	2.804(3)	Ce(2)—N(92)	2.809(3)
Ce(1)—N(32)	2.794(3)	Ce(2)—N(91)	2.840(3)
O(18)—C(17)	1.229(4)	O(78)—C(77)	1.236(4)
O(28)—C(27)	1.271(4)	O(88)—C(87)	1.275(4)
O(48)—C(47)	1.229(4)	O(108)—C(107)	1.221(4)
O(58)—C(57)	1.269(4)	O(118)—C(117)	1.278(4)
N(1)—Ce(1)—N(31)	179.2(1)	N(61)—Ce(2)—N(91)	176.3(1)
O(18)—Ce(1)—N(2)	58.8(1)	O(78)—Ce(2)—N(62)	58.7(1)
O(28)—Ce(1)—N(4)	59.3(1)	O(88)—Ce(2)—N(64)	59.6(1)
O(48)—Ce(1)—N(32)	57.9(1)	O(108)—Ce(2)—N(92)	58.3(1)
O(58)—Ce(1)—N(34)	59.6(1)	O(118)—Ce(2)—N(94)	59.90(1)

deprotonation of the ligands at the benzoylhydrazone arms. They organize the complex molecule into a three-dimensional network. Details are shown and listed in Figure S2 and Table S2 of the Supporting Information. Selected bond lengths and angles are contained in Table 4. The labeling of one of the complex cations (Ce1) is identical to that in Figure 1, whereas the same scheme has been applied for the cation with Ce2, beginning with N61 for the first and N91 for the second ligand. Additional hydrogen bonds are established with the solvent ethanol molecules.

The concept of ligands containing asymmetric arms can be extended to other functional groups such as Schiff bases or thiosemicarbazones. Thiosemicarbazones are under discussion as promising ligand systems for biomedical applications.¹⁰ Many complexes with main group and transition metals were prepared and studied by X-ray crystallography.¹¹ Structural data of corresponding lanthanide complexes to the best of our knowledge are not available. This may be understood by the low affinity of the “hard” lanthanide ions to the “soft” sulfur atoms in thiosemicarbazones and has also been observed for actinide elements, where the first crystalline thiosemicarbazonato complexes have been reported recently.¹¹ All of our attempts to isolate stable lanthanide complexes with a potentially pentadentate ligand derived from 2,6-diformylpyridine and 2 equivalents of 4-phenylthiosemicarbazide failed up to now. Obviously, the presence of two arms containing “soft” thiosemicarbazone sulfur atoms does not allow the formation of stable complexes with “hard” metal ions such as La^{3+} , Sm^{3+} , or Eu^{3+} .

More successful were reactions with the asymmetric ligand H_2L^4 , which contains the “hard” oxygen donor atoms of one semicarbazone arm. The ligand was synthesized by subsequent condensation of 4-phenylsemicarbazide and 4-phenylthiosemicarbazide on 2,6-bisformylpyridine (Scheme 3).

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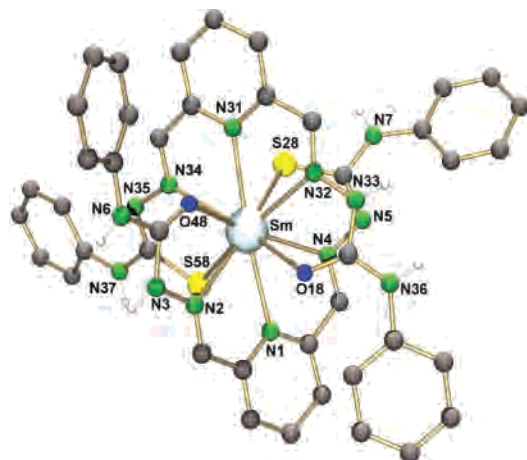
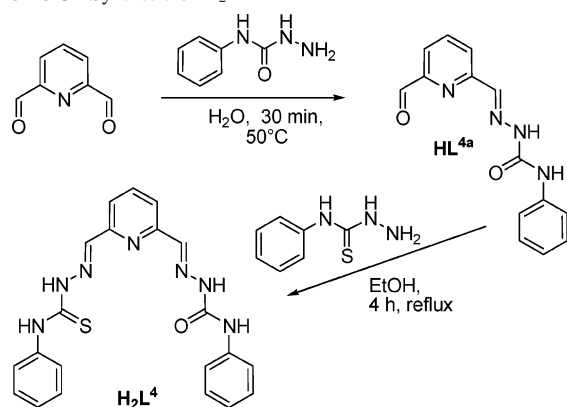


Figure 5. The structure of the complex cation of $[\text{Sm}(\text{HL}^4)_2](\text{NO}_3)_2 \cdot \text{H}_2\text{O}$.

Scheme 3. Synthesis of H_2L^4



The formyl derivative HL^{4a} is prepared in water, which is necessary for an immediate precipitation of the monosubstituted product. The higher reactivity of the formyl group (as compared to that of the corresponding acetyl compound) leads to high yields and allows short reaction times in the

Table 5. Selected Bond Lengths (Å) and Angles (deg) in $[\text{Sm}(\text{HL}^4)_2](\text{NO}_3)_2 \cdot \text{H}_2\text{O}$

Sm–O(18)	2.519(6)	Sm–S(28)	2.913(6)
Sm–O(48)	2.528(8)	Sm–S(58)	2.956(4)
Sm–N(1)	2.682(7)	Sm–N(31)	2.720(8)
Sm–N(2)	2.677(8)	Sm–N(32)	2.681(8)
Sm–N(4)	2.711(7)	Sm–N(34)	2.669(7)
O(18)–C(17)	1.263(9)	S(28)–C(27)	1.758(8)
O(48)–C(47)	1.150(15)	S(58)–C(57)	1.705(9)
O(18)–Sm–N(2)	58.7(2)	O(48)–Sm–N(32)	60.1(3)
N(1)–Sm–N(31)	173.9(2)	N(34)–Sm–S(58)	60.7(2)
N(4)–Sm–S(28)	63.1(2)		

second step, but always causes the formation of disubstituted byproduct in the first step. Due to its insolubility in chloroform, the byproduct diformylpyridine bis-4-phenylsemicarbazone can be readily removed by recrystallization from hot chloroform.

Samarium nitrate reacts with H_2L^4 in ethanol under formation of an orange-red complex. Elemental analysis, IR, and a peak at $m/z = 985$ in the FAB^+ spectrum indicate coordination of two asymmetric, singly deprotonated ligands. A bathochromic shift of the $\nu(\text{C}=\text{O})$ vibrations by 28 cm^{-1} is observed. An X-ray structure analysis confirms the composition of $[\text{Sm}(\text{HL}^4)_2](\text{NO}_3)_2$ and deprotonation of the thiosemicarbazone unit. Figure 5 depicts the structure of the complex cation.

As for the complexes with $\{\text{HL}^3\}^-$, the lanthanide ion in $[\text{Sm}(\text{HL}^4)_2]^+$ is 10-coordinate. The coordination polyhedron does not fit with one of the expected regular polyhedra (bicapped square cube, bicapped square antiprism). The positions of the donor atoms can best be described to be intermediate between these ideal arrangements. The capping positions are occupied by the nitrogen atoms of the pyridine rings. Details are depicted in Figure S3 of the Supporting Information.

Selected bond lengths and angles are summarized in Table 5. The two Sm–S bonds of 2.913(6) and 2.956(6) Å are in

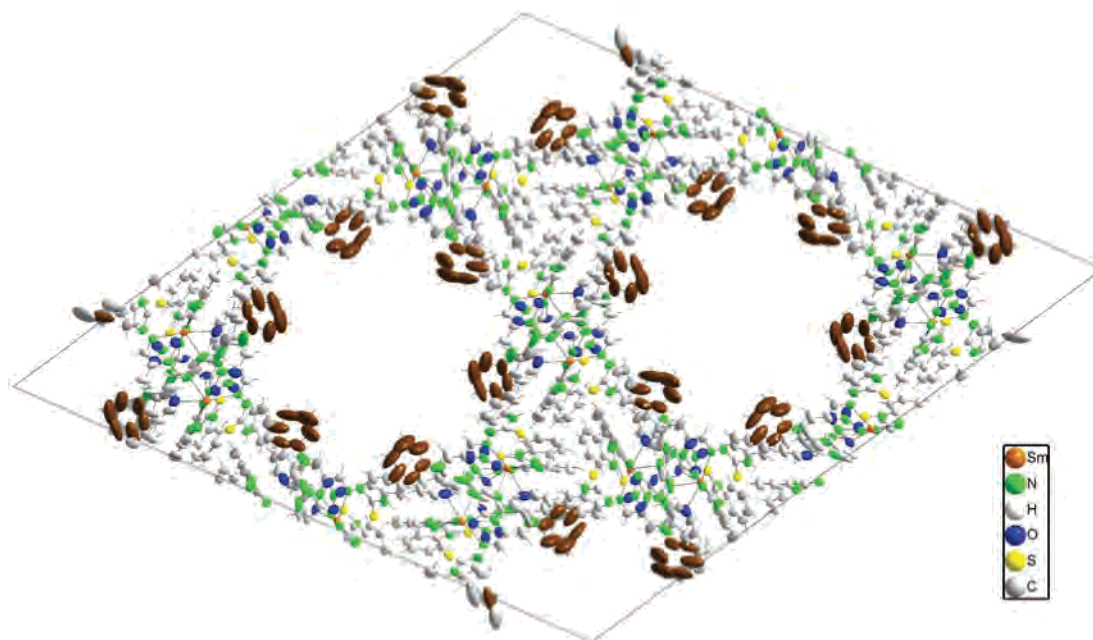


Figure 6. Packing diagram of $[\text{Sm}(\text{HL}^4)_2](\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ with large channels along the z axis.

the range of the corresponding values in dithiophosphato or (partially) dithiocarbamate complexes of early and middle lanthanides,¹² where the Ln–S bonds are lengthened by the restricting bite of the formed four-membered chelate rings or sterical limitations, but are longer than Ln–thiolato bonds to monodentate thiols or such with larger chelate rings.^{13,14}

Hydrogen bonds between the H atoms of the semicarbazone arms and nitrate anions clearly indicate the sole deprotonation of the thiosemicarbazone bonding sites (Table S3 of the Supporting Information). These hydrogen bonds arrange the complex molecules into a three-dimensional network, in which channels are established along the *z* axis (Figure 6). The channels have an approximate diameter of 16.2 Å and are not occupied by solvent molecules in the studied single crystals. The solvent water molecule is hydrogen bonded to one of the semicarbazone arms. The solid-state structure of [Sm(HL⁴)₂](NO₃)·H₂O with an extended channel system results in an unusual low density ($D_c = 1.068 \text{ g/cm}^3$) of the compound. The phenyl ring with the carbon atoms C11–C16 (highlighted in brown) shows exceptionally high thermal displacement parameters, which cannot satisfactorily be explained by a low-quality X-ray crystal structure or crystal artifacts. It results from the distinct position of this phenyl ring, which points into the channels of the structure (Figure 6). This allows the observed high degree of thermal motion even at a low temperature such as 173 K.

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All isolated complexes do not undergo hydrolysis or ligand exchange reactions. They are indefinitely stable in ethanol/water mixtures. In pure water, however, macroscopic amounts of the complexes are insoluble, and tracer studies with radioactively labeled compounds that will allow one to study lower concentrations are planned for the future.

Conclusions

The examples of this paper demonstrate that a combination of appropriate bonding sites in asymmetric ligands allows one to control the deprotonation of such ligands and gives access to hitherto unknown classes of lanthanide complexes. [Sm(HL⁴)₂](NO₃) represents the first lanthanide complex with a thiosemicarbazone coordination. The bonding to this weakly coordinating functionality is directed by the strong bonds to the semicarbazone site of the molecule. All isolated complexes are air stable and do not undergo ligand exchange reaction or hydrolysis in the presence of water. More detailed studies concerning their behavior in biological media are required to allow an evaluation of their potential in medical procedures.

Studies with tripodal ligands of similar types, which will allow one to encapsulate metal ions, are in progress in our laboratory.

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Supporting Information Available: Additional figures and tables describing the hydrogen bonding and the coordination polyhedra of the complexes. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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