Dalton
www.rsc.org/dalton

Synthesis and structure of cyclen hydroxylamine ligands and their zinc(II) complexes

Roland Reichenbach-Klinke, Manfred Zabel and Burkhard König *
Institut für Organische Chemie, Universität Regensburg, D-93040 Regensburg, Germany.
E-mail: burkhard.koenig@chemie.uni-regensburg.de

Received 2nd August 2002, Accepted 1st November 2002
First published as an Advance Article on the web 29th November 2002

The synthesis of two new zinc(II) complexes with 1,4,7,10-tetraazacyclododecan-1-ol and 1,4,7,10-tetraazacyclododecan-1,7-diol as ligands is described. One of these complexes is characterized by X-ray structure analysis. By coordination to the metal cation the acidity of the hydroxylamine groups of the ligands is significantly increased as confirmed by potentiometric pH titrations.

Introduction

Metal complexes with substituted 1,4,7,10-tetraazacyclododecane (cyclen) derivatives as ligands are widely used in molecular recognition and catalysis.[1] Kimura *et al.*[2,3] and others have investigated the coordination of imides and phosphates to Zn(II)-cyclen complexes in great detail. Hereby a deprotonated imide moiety or phosphate anion binds reversibly to the Lewis-acidic metal center in Zn(II)-cyclen. This binding motif, like other reversible metal–ligand interactions, offers some advantages over weaker non-covalent interactions such as hydrogen bonds, salt bridges or hydrophobic interactions. It provides sufficient binding strength to allow formation of reversible aggregates in water under physiological conditions and at high dilution. Moreover, the interaction is kinetically labile which is important for applications in catalysis.

Hydroxylamine complexes of transition metals[4] show some interesting aspects regarding the acidity of the ligand. By coordination of the hydroxylamine nitrogen atom to a metal cation the pK_a value of the hydroxy group is changed markedly. While hydroxylamine itself is almost not acidic (pK_a = 13.7 [5]), the acidity increases significantly by coordination to transition metals as outlined in Scheme 1.

The intention of our work presented here is to combine the known excellent binding properties of Lewis-acidic Zn(II)-cyclen with the interesting features of hydroxylamine ligands.

Results and discussion

Design and synthesis

In their synthesis of macrobicyclic Co(III) hydroxylamine complexes Sargeson coworkers[6] reacted the Co(III) azamacrobicyclic complex with H_2O_2 to obtain a mixture of complexes with one to three hydroxylamine ligands. These complexes were difficult to separate and purify. Therefore we chose a different synthetic strategy starting with the selective preparation of the free ligand followed by complexation with the metal.

The synthesis starts with the selective protection of cyclen as 1,4,7-tris-*tert*-butoxycarbonyl-1,4,7,10-tetraazacyclododecane **1** [7] and 1,7-bis(benzyloxycarbonyl)-1,4,7,10-tetraazacyclododecane **4** (Scheme 2).[8] These protected azamacrocycles were then reacted with dimethyldioxirane[9,10] to obtain the corresponding hydroxylamines. The carbamates were cleaved with hydrobromic acid and after elution over a basic anion exchange column the zinc(II) complexes were synthesized by reaction with $Zn(ClO_4)_2 \cdot 6H_2O$.

Table 1 Selected bond distances (Å) and angles (°) for complex **3**

Br(1)–Zn(1)	2.3501(5)	Br(1)–Zn(1)–N(1)	108.73(7)
Zn(1)–N(1)	2.192(2)	Br(1)–Zn(1)–N(2)	115.50(8)
Zn(1)–N(2)	2.148(3)	Br(1)–Zn(1)–N(3)	115.76(7)
Zn(1)–N(3)	2.122(3)	Br(1)–Zn(1)–N(4)	110.12(8)
Zn(1)–N(4)	2.127(3)	Zn(1)–N(1)–O(1)	115.50(17)
O(1)–N(1)	1.447(4)	O(1)–N(1)–C(1)	107.2(2)
		O(1)–N(1)–C(8)	106.8(2)

X-Ray structure of 3

Colourless crystals of complex **3** suitable for X-ray diffraction were obtained by slow evaporation of a methanolic solution of **3**. The structure of **3** in the crystal is shown in Fig. 1 and selected bond distances and angles are listed in Table 1.

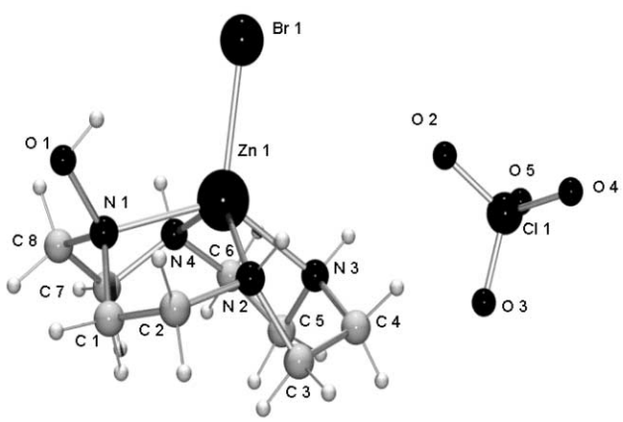
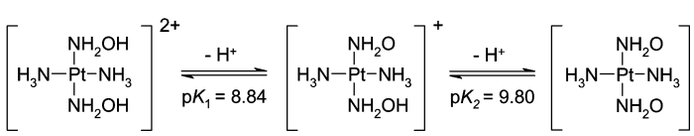


Fig. 1 Structure of complex **3** and the perchlorate counter ion in the crystal.

In complex **3** the water molecule which is usually coordinated to the axial position in aqueous solution is replaced by a bromide anion. The unit cell contains a perchlorate anion as the counter anion. The geometry of the complex is more distorted if compared to Zn(II)-cyclen[2] which is illustrated by the somewhat longer bond length of Zn(1)–N(1).



Scheme 1 pK_a values of the hydroxylamine ligands in *trans*-$[Pt(NH_3)_2(NH_2OH)_2]^{2+}$.

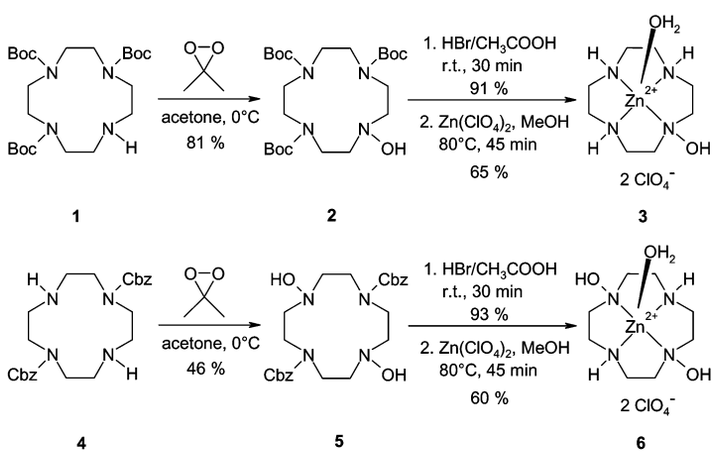
DOI: 10.1039/b207571g

Table 2 Stability constants of ligands $L7H_4$, $L8H_4$ and cyclen

The following equilibria were considered for $L7H_4$:	The following equilibria were considered for $L8H_4$:	The following equilibria for cyclen are given for comparison:
β_2^1: $L7H_3 + H^+ = L7H_4$	β_2^6: $L8H_3 + H^+ = L8H_4$	β_2^{10}: cyclen-H_3 + H^+ = cyclen-H_4
β_2^2: $L7H_2 + H^+ = L7H_3$	β_2^7: $L8H_2 + H^+ = L8H_3$	β_2^{11}: cyclen-H_2 + H^+ = cyclen-H_3
β_2^3: $L7H + H^+ = L7H_2$	K_2^2: $Zn(ClO_4)_2 + L8H_2 = L8H_2$-$Zn(OH_2)(ClO_4)_2$	β_2^{12}: cyclen-H + H^+ = cyclen-H_2
K_2^1: $Zn(ClO_4)_2 + L7H = L7H$-$Zn(OH_2)(ClO_4)_2$	β_2^8: $L8H$-$Zn(OH_2)(ClO_4^-)_2 + H^+ = L8H_2$-$Zn(OH_2)(ClO_4^-)_2$	β_2^{13}: cyclen + H^+ = cyclen-H
β_2^4: $L7H$-$Zn(OH)(ClO_4^-)_2 + H^+ = L7H$-$Zn(OH_2)(ClO_4^-)_2$	β_2^9: $L8$-$Zn(OH_2)ClO_4^- + H^+ = L8H$-$Zn(OH_2)ClO_4^-$	K_2^3: $Zn(ClO_4)_2$ + cyclen = cyclen-$Zn(OH_2)(ClO_4)_2$
β_2^5: $L7$-$Zn(OH)ClO_4^- + H^+ = L7H$-$Zn(OH)ClO_4^-$		β_2^{14}: cyclen-$Zn(OH)(ClO_4)_2 + H^+$ = cyclen-$Zn(OH_2)(ClO_4)_2$

$L7H_4$ [a]	$L8H_4$ [a]	Cyclen [b]
—	—	$\log\beta_2^{10} < 2$
$\log\beta_2^1 = 8.5$ (±0.05) [c]	$\log\beta_2^6 = 2.4$ (±0.04)	$\log\beta_2^{11} < 2$
$\log\beta_2^2 = 10.2$ (±0.03)	$\log\beta_2^7 = 8.9$ (±0.02)	$\log\beta_2^{12} = 9.9$ [a] [15]
$\log\beta_2^3 = 11.6$ (±0.02)	—	$\log\beta_2^{13} = 11.0$ [a] [15]
$\log K_2^1 = 14.4$ (±0.02)	$\log K_2^2 = 6.0$ (±0.1)	$\log K_2^3 = 15.3$ [a] [15]
$\log\beta_2^4 = 8.0$ (±0.04)	$\log\beta_2^8 = 7.8$ (±0.04)	$\log\beta_2^{14} = 7.9$ [16]
$\log\beta_2^5 = 8.4$ (±0.01)	$\log\beta_2^9 = 11.4$ (±0.04)	—

[a] All data were measured at $I = 0.1$ mol L^{-1} (tetraethylammonium perchlorate) and 25 ± 0.5 °C. [b] Data were measured at $I = 0.1$ mol L^{-1} ($NaClO_4$) and 25 °C. [c] Standard deviation.



Scheme 2 Synthesis of the complexes **3** and **6**.

Potentiometric studies

The properties of complexes **3** and **6** and of the free ligands were studied by potentiometric pH titration in aqueous solution. All considered equilibria and the derived stability constants are summarised in Table 2. The data for the parent compound cyclen are added for comparison.

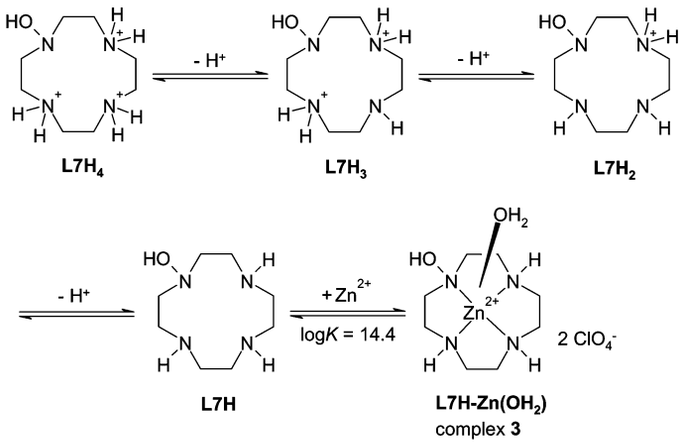
Three equilibrium constants ($\log\beta_2^1$, $\log\beta_2^2$, $\log\beta_2^3$) were derived from the pH profile for ligand $L7H_4$ (see Table 2 and Scheme 3). The values at 10.2 and 11.6 most likely correspond to the protonation of secondary amines of the azamacrocycle. Deprotection of **2** with hydrobromic acid to give $L7H_4$ should protonate the nitrogen of hydroxylamine, too, if its basicity remains similar to reported values of *N*,*N*-diethylhydroxylamine ($pK_a = 5.6$ in H_2O at 30 °C and $I \approx 0.02$ mol L^{-1})[11] or *N*,*N*-dimethylhydroxylamine ($pK_a = 5.3$ in H_2O at 25 °C and $I = 0.06$ mol L^{-1}).[12] However, we could not determine a constant corresponding to this value. Incorporation of the hydroxylamine into the azamacrocycle therefore changes its nitrogen basicity significantly.[13] Deprotonation of the hydroxylamine OH-group can be excluded because the elemental analysis of $L7H_4$ requires the trihydrobromide salt and only three equilibrium constants were observed in the titration. Moreover, comparison with literature data of *N*,*N*-diethylhydroxylamine ($pK_a = 12.88$ in H_2O at 25 °C)[14] also does not support a deprotonation of the hydroxy group.

With a $\log K_2^1$ of 14.4 the zinc(II) cation is nearly as strongly bound in the azamacrocycle as in Zn(II)-cyclen ($\log K_2^3 = 15.3$ in H_2O at 25 °C and $I = 0.1$ mol L^{-1}).[15]

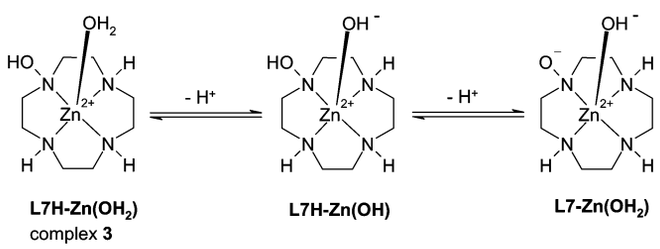
In the titration of complex **3** [L7H-$Zn(OH_2)$] two equilibria were observed (see Table 2 and Scheme 4). These values differ only slightly making an exact discrimination impossible. So the assignment in Scheme 4 is arbitrary. The Lewis acidity of the metal center is preserved and it is in the range of the value measured for Zn(II)-cyclen ($\log\beta_2^{14} = 7.9$ in H_2O at 25 °C and $I = 0.1$ mol L^{-1}).[16] In addition, the acidity of the hydroxylamine is, as expected, significantly enhanced by the coordination to the zinc(II) cation. The species distribution plot calculated from the potentiometric pH titration is shown in Fig. 2.

The two equilibrium constants ($\log\beta_2^6$, $\log\beta_2^7$) observed in the titration of ligand $L8H_4$ were assigned to the protonation of the secondary amines (see Table 2 and Scheme 5). The zinc(II) cation is bound in a significantly weaker fashion by ligand $L8H_2$ ($\log K_2^2 = 6.0$) if compared with L7H.

The titration of complex **6** [$L8H_2$-$Zn(OH_2)$] reveals two acidic protons (Table 2). We assign the two equilibria to the subsequent deprotonation of the hydroxylamine hydroxy groups (see Table 2 and Scheme 6).[17] The first $\log\beta_2^8$ of 7.8 is in



Scheme 3 Protonation and zinc coordination of ligand $L7H_4$.



Scheme 4 Protonation equilibria of complex L7H-Zn(OH_2) (complex **3**).

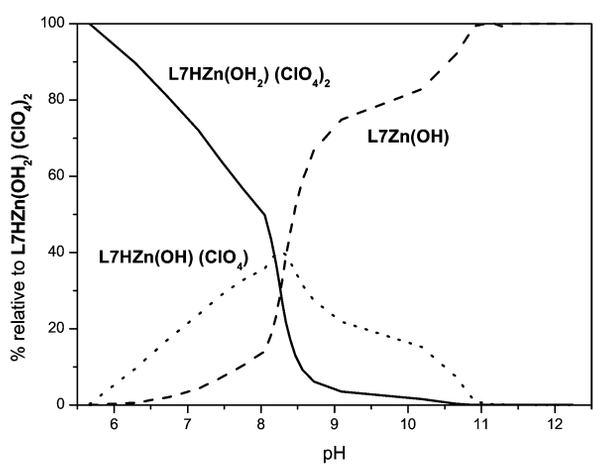
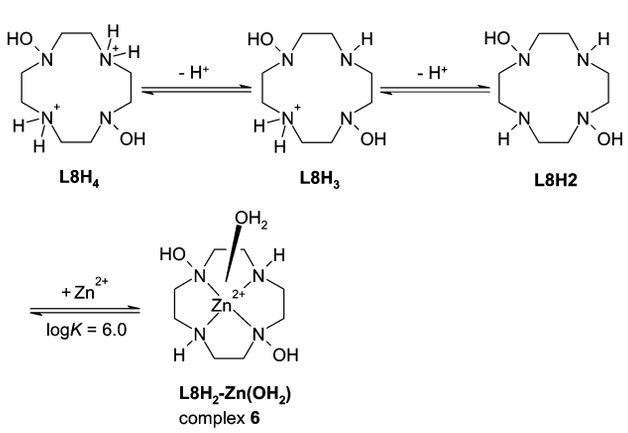
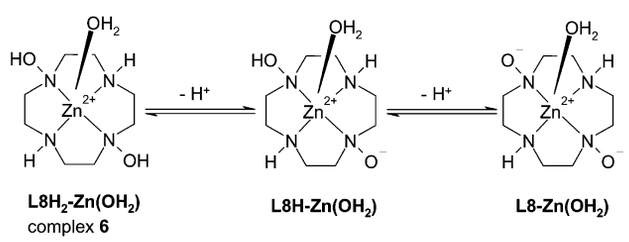


Fig. 2 Species distribution plot of complex **3**. Stoichiometry of equilibria: L7-Zn(OH)$(ClO_4)_2$ + $2H^+$ = L7H-Zn(OH)$(ClO_4)_2$ + H^+ = L7H-Zn(OH_2)$(ClO_4)_2$.



Scheme 5 Protonation and zinc(II) ion coordination of ligand $L8H_4$.



Scheme 6 Protonation equilibria of complex $L8H_2$-Zn(OH_2) (complex **6**).

the range of the value measured for the hydroxylamine in complex **3**, while the second hydroxylamine is significantly less acidic (for comparison see Scheme 1).

Conclusion

We have prepared two new cyclen ligands bearing hydroxylamino moieties. The ligands are able to bind zinc(II) ions tightly. Moreover, by coordination of the metal cation the acidity of the hydroxylamines is increased markedly. Hence these complexes may find use as interesting binding sites for molecular recognition.

Experimental

General

Compounds **1** [7] and **4** [8] as well as dimethyldioxirane [18] were prepared by known methods. Melting points were taken on a hot-plate microscope apparatus and are not corrected. UV/VIS spectra: Varian Cary 50 Bio. IR spectra: Bio-Rad FTS 3000 FT-IR. ^{1}H- and ^{13}C-NMR spectra: Bruker AM 400 or Bruker AC 250; chemical shifts relative to $SiMe_4$; s = singlet, bs = broad singlet, m = multiplet; the multiplicity of the ^{13}C signals was determined using the DEPT technique and quoted as (+) for CH_3 or CH, (−) for CH_2, and (C_{quart}) for quaternary carbons.

10-Hydroxy-1,4,7,10-tetraazacyclododecane-1,4,7-tricarboxylic acid tri-*tert*-butyl ester (2)

1,4,7-Tris-*tert*-butoxycarbonyl-1,4,7,10-tetraazacyclododecane **1** (0.50 g, 1.06 mmol) was dissolved in 5 mL of degassed acetone. Under cooling in an ice-bath 16 mL of dimethyldioxirane in acetone (*ca.* 0.1 M) were added slowly. The reaction mixture was then stirred for 4 h at room temperature. The solvent was evaporated and the crude product was purified by column chromatography on silica (eluent: ethyl acetate, R_f = 0.6). The hydroxylamine **2** (0.42 g, 0.86 mmol, 81%) was obtained as a white solid. M.p. 84 °C. IR (KBr, cm^{-1}): $\bar{\nu}$ = 775, 1174, 1249, 1366, 1420, 1466, 1694, 2933, 2977, 3428. ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.45 (s, 18 H, CH_3), 1.47 (s, 9 H, CH_3), 2.91 (bs, 4 H, CH_2), 3.31–3.95 (m, 12 H, CH_2), 5.85 (bs, 1 H, OH). ^{13}C NMR (62 MHz, $CDCl_3$): δ 28.47 (+), 28.69 (+), 45.27 (−), 46.14 (−), 47.81 (−), 48.15 (−), 49.57 (−), 50.14 (−), 59.07 (−), 59.69 (−), 79.41 (C_{quart}), 79.81 (C_{quart}), 79.94 (C_{quart}), 155.36 (C_{quart}), 156.07 (C_{quart}), 156.41 (C_{quart}). MS (ESI, MeOH/CH_2Cl_2+ 1% AcOH): *m*/*z* (%) = 489 (100) [MH^+]. Anal. calc. for $C_{23}H_{44}N_4O_7$: C, 56.54; H, 9.08; N, 11.47. Found: C, 56.40; H, 9.33; N, 11.12%.

1,4,7,10-Tetraazacyclododecan-1-ol tri-hydrobromide

Compound **2** (0.30 g, 0.62 mmol) was mixed with 2.0 mL of HBr in glacial acetic acid (33%, 4.1 M) and stirred for 30 min at room temperature. Then 5 mL of diethyl ether were added to the suspension. The precipitate was collected by suction filtration and washed with diethyl ether. The hydrobromide (0.24 g, 0.56 mmol, 91%) was obtained as a colourless powder. Decomp. at 210 °C. IR (KBr, cm^{-1}): $\bar{\nu}$ = 1635, 2760, 2926, 3422. ^{1}H NMR (250 MHz, D_2O): δ 2.84–3.52 (m, CH_2). ^{13}C NMR (100 MHz, D_2O): δ 42.61 (−), 43.39 (−), 44.04 (−), 54.39 (−). MS (ESI, H_2O): *m*/*z* (%) = 189 (100) [MH^+]. Anal. calc. for $C_8H_{23}Br_3N_4O{\cdot}0.5CH_3COOH$: C, 23.45; H, 5.47; N, 12.15. Found: C, 23.03; H, 5.46; N, 12.53%.

1,4,7,10-Tetraazacyclododecan-1-ol-zinc(II) di-perchlorate (3)

The above hydrobromide (0.22 g, 0.51 mmol) was dissolved in 2 mL of H_2O and eluted over a basic anion exchange column. The solution was evaporated to dryness and the solid residue was dissolved in 2 mL of methanol. Then a solution of $Zn(ClO_4)_2{\cdot}6H_2O$ (0.28 g, 0.75 mmol) in 2 mL of methanol was added and the mixture was heated at 80 °C for 45 min. After removal of most of the solvent, the reaction mixture was cooled in an ice-bath and the precipitate was collected by suction filtration. Complex **3** (0.15 g, 0.33 mmol, 65%) was isolated as a white solid. Decomp. at 235 °C. IR (KBr, cm^{-1}): $\bar{\nu}$ = 628, 1089, 1459, 2933, 3163, 3254, 3410. ^{1}H NMR (250 MHz, CD_3CN): δ 2.60–2.79 (m, 4 H, CH_2), 2.84–3.20 (m, 12 H, CH_2), 3.36 (bs, 3 H, NH), 6.73 (bs, 1 H, OH). ^{13}C NMR (62 MHz, CD_3CN): δ 43.77 (−), 44.97 (−), 45.15 (−), 56.23 (−). MS (ESI, H_2O + 1% AcOH): *m*/*z* (%) = 311 (100) [($\mathbf{3}^{2+}$ + CH_3COO^-)$^+$], 351 (35) [($\mathbf{3}^{2+}$ + ClO_4^-)$^+$]. Anal. calc. for $C_8H_{20}Cl_2N_4O_9Zn{\cdot}0.5CD_3CN$: C, 22.78; H, 4.88; N, 13.28. Found: C, 22.92; H, 4.98; N, 13.18%.

4,10-Dihydroxy-1,4,7,10-tetraazacyclododecane-1,7-dicarboxylic acid dibenzyl ester (5)

1,7-Bis(benzyloxycarbonyl)-1,4,7,10-tetraazacyclododecane **4** (0.70 g, 1.60 mmol) was dissolved in 10 mL of degassed acetone. Under cooling in an ice-bath 41 mL of dimethyldioxirane in acetone (*ca.* 0.1 M) were added. The reaction mixture was then stirred for 30 min in the ice-bath and for a further 40 min at room temperature. The solvent was evaporated and the crude product was purified by column chromatography on silica (eluent: CH_2Cl_2–MeOH = 10:1, R_f = 0.8). The hydroxylamine **5** (0.34 g, 0.73 mmol, 46%) was isolated as a white solid. M.p. 54 °C. IR (KBr, cm^{-1}): $\bar{\nu}$ = 772, 1020, 1167, 1260, 1361, 1412, 1479, 1699, 2948, 3494, 3540. UV/VIS (CH_3CN): λ_{max} (log ε) = 206 nm (4.297). ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.86–4.14 (m, 16 H, CH_2), 5.22 (m, 2 H, CH_2), 5.27 (m, 2 H, CH_2), 7.35 (m, 10 H, CH). ^{13}C NMR (100 MHz, $CDCl_3$): δ 47.93 (−), 48.70 (−), 48.92 (−), 49.76 (−), 60.48 (−), 61.24 (−), 61.39 (−), 67.67 (−), 67.74 (−), 127.78 (+), 127.90 (+), 127.94 (+), 128.14 (+), 128.34 (+), 128.40 (+), 128.65 (+), 128.69 (+), 128.71 (+), 128.76 (+), 156.37 (C_{quart}), 156.47 (C_{quart}), 175.26 (2 C, C_{quart}). MS (ESI, MeOH/CH_2Cl_2 + 1% AcOH): *m*/*z* (%) = 473 (100) [MH^+], 495 (2) [MNa^+]; HRMS ($C_{24}H_{33}N_4O_6^+$): calc. 473.2400, found. 473.2391 ± 0.0006. Anal. calc. for $C_{24}H_{32}N_4O_6{\cdot}2H_2O$: C, 56.68; H, 7.13; N, 11.02. Found: C, 56.83; H, 7.13; N, 11.02%.

1,4,7,10-Tetraazacyclododecane-1,7-diol di-hydrobromide

Compound **5** (0.28 g, 0.60 mmol) was mixed with 3.0 mL of HBr in glacial acetic acid (33%, 4.1 M) and stirred for 30 min at room temperature. Then 5 mL of diethyl ether were added to the suspension. The precipitate was collected by suction filtration and washed with diethyl ether. The hydrobromide (0.20 g, 0.55 mmol, 93%) was obtained as a colourless powder. M.p. 151 °C. IR (KBr, cm^{-1}): $\bar{\nu}$ = 1457, 1705, 2762, 2960, 3046, 3259, 3427. ^{1}H NMR (250 MHz, D_2O): δ 3.04–3.48 (m, CH_2). ^{13}C NMR (62 MHz, D_2O): δ 42.91 (−), 45.02 (−), 53.08 (−). MS (ESI, H_2O): *m*/*z* (%) = 205 (100) [MH^+]. Anal. calc. for $C_8H_{22}Br_2N_4O_2{\cdot}0.5CH_3CH_2OCH_2CH_3$: C, 29.79; H, 6.75; N, 13.90. Found: C, 30.23; H, 6.22; N, 14.18%.

1,4,7,10-Tetraazacyclododecane-1,7-diol-zinc(II) di-perchlorate (6)

Compound **6** was synthesized from the above hydrobromide (0.20 g, 0.55 mmol) by a method similar to that of **3**. The complex **6** (0.15 g, 0.33 mmol, 60%) was obtained as a white solid. M.p. 138–140 °C. IR (KBr, cm^{-1}): $\bar{\nu}$ = 628, 1090, 1389, 1450, 2941, 3167, 3224, 3422. ^{1}H NMR (250 MHz, CD_3CN): δ 2.65–2.75 (m, 4 H, CH_2), 3.02–3.27 (m, 12 H, CH_2), 3.71 (bs, 2 H, NH), 7.12 (bs, 1 H, OH), 7.39 (bs, 1 H, OH). ^{13}C NMR (62 MHz, CD_3CN): δ 44.05 (−), 56.65 (−). MS (ESI, MeOH + 10 mmol NH_4Ac): *m*/*z* (%) = 327 (100) [($\mathbf{6}^{2+}$ + CH_3COO^-)$^+$].

Potentiometric titrations

Potentiometric pH titrations were performed with a computer-controlled pH-meter (pH 3000, WTW; glass pH electrode Metrohm) and automatic titration apparatus (dosimat 665, Metrohm). For all titrations 0.1 M perchloric acid (Merck, p.a.) and 0.1 M tetraethylammonium hydroxide (TEAOH) (Merck, p.a.) in water containing tetraethylammonium perchlorate to maintain an ionic strength of I = 0.1 mol L^{-1} were used. The water used is of ultrapure HPLC grade deionized with the Milli-Q185 apparatus form Millipore. Tetraethylammonium perchlorate (Fluka, purum) was recrystallized twice from acetonitrile. TEAOH solutions were calibrated with mono sodium phthalate (Merck, p.a.). A titration of perchloric acid with TEAOH solution was used for calibration and to determine log K_w and A_I by the method of Gran.[19] Titrations were measured over a pH range from 2.7 to 12.6 with a minimum of 80 data points recorded. Titrations were performed in duplicate or triplicate. The stability constants given and their standard deviations are average values. All measurements were performed at 25 ± 0.5 °C. Data and error analysis was done with the computer program Hyperquad 2000.[20]

Crystal structure determination

Suitable crystals for X-ray experiments of complex **3** were obtained by slow evaporation of a methanolic solution.

Formula: $C_8H_{20}BrN_4OZn{\cdot}ClO_4$, M = 433.02, crystal system: orthorhombic, space group $P2_12_12_1$, a = 8.9049(5), b = 12.2325(8), c = 14.0969(11) Å, $\alpha = \beta = \gamma$ = 90°, V = 1535.56(18) Å^3, Z = 4, D_c = 1.873 g cm^{-3}, F(000) = 872, μ = 4.398 mm^{-1},

crystal size: 0.525 × 0.454 × 0.375 mm, colourless, rod-like crystals.

Data collection was carried out at 173 K on a STOE-IPDS diffractometer with graphite-monochromated Mo-Kα radiation (λ = 0.71073 Å); 11 144 reflections (2904 unique reflections, R_{int} = 0.0396) were measured from 2.71 to 25.77°.

The structure was solved by direct methods (SIR97)[21] and refined by full-matrix least squares on F^2 for all non-H-atoms.[22] H-atoms were included in calculated positions. $\omega R(F^2)$ (all data) = 0.0843; $R(F)$ = 0.0308, S = 1.073, max. $\Delta\rho$ = 1.248 e Å^{-3}.

CCDC reference number 187581.

See http://www.rsc.org/suppdata/dt/b2/b207571g/ for crystallographic data in CIF or other electronic format.

Acknowledgements

We thank the Volkswagen foundation (priority research area electron transfer) and the DFG (Graduate College Sensory Photoreceptors) for support of this work. We thank the Schering AG, Berlin, and DSM, Regensburg, for their generous gifts of cyclen. We thank Mrs H. Leffler-Schuster for her help with potentiometric titrations.

References and notes

1 R. Reichenbach-Klinke and B. König, *J. Chem. Soc., Dalton Trans.*, 2002, 121.
2 M. Shionoya, E. Kimura and M. Shiro, *J. Am. Chem. Soc.*, 1993, **115**, 6730.
3 E. Kimura, T. Ikeda and M. Shionoya, *Pure Appl. Chem.*, 1997, **69**, 2187.
4 K. Wieghardt, *Adv. Inorg. Bioinorg. Mech.*, 1984, **3**, 213.
5 A. F. Hollemann, E. Wiberg, N. Wiberg, *Lehrbuch der Anorganischen Chemie*, de Gruyter, Berlin, 1985, p. 591.
6 D. J. Bull, I. I. Creaser, A. M. Sargeson, B. W. Skelton and A. H. White, *Inorg. Chem.*, 1987, **26**, 3040.
7 S. Brandes, C. Gros, F. Denat, P. Pullumbi and R. Guilard, *Bull. Soc. Chim. Fr.*, 1996, **133**, 65.
8 Z. Kovacs and A. D. Sherry, *Synthesis*, 1997, 759.
9 R. W. Murray and R. Jeyaraman, *J. Org. Chem.*, 1985, **50**, 2847.
10 R. W. Murray and M. Singh, *US Pat.*, 5001233, 1991.
11 S. Ball and T. C. Bruice, *J. Am. Chem. Soc.*, 1980, **102**, 6498.
12 T. C. Bissot, R. W. Parry and D. H. Campbell, *J. Am. Chem. Soc.*, 1957, **79**, 796.
13 On the basis of the titration data no final assignment of the pK_a values to the protonation of a specific nitrogen atom is possible.
14 M. J. Colthurst, A. J. S. S. Kanagasooriam, M. S. O. Wong, C. Contini and A. Williams, *Can. J. Chem.*, 1998, **76**, 678.
15 T. Koike, S. Kajitani, I. Nakamura, E. Kimura and M. Shiro, *J. Am. Chem. Soc.*, 1995, **117**, 1210.
16 E. Kimura, T. Shiota, T. Koike, M. Shiro and M. Kodama, *J. Am. Chem. Soc.*, 1990, **112**, 5805.
17 Additional evidence for this interpretation comes from proton NMR investigations: the proton NMR of compound L8H_2-Zn(OH_2) in DMSO-d_6 shows two hydroxy signals, at δ 4.82 [bs, 2H, Zn(OH_2)] and δ 8.58 (bs, 2H, N–OH). Upon addition of potassium carbonate as base the signal at δ 8.58 disappears, which supports preferred deprotonation of coordinated hydroxylamine moieties.
18 W. Adam, Y. Chan, D. Cremer, J. Gauss, D. Scheutzow and M. Schindler, *J. Org. Chem.*, 1987, **52**, 2800.
19 G. Gran, *Analyst*, 1952, **77**, 661.
20 P. Gans, A. Sabatini and A. Vacca, *Talanta*, 1996, **43**, 1739.
21 A. Altomare, G. Cascarano, C. Giacovazzo and A. Guagliardi, *J. Appl. Crystallogr.*, 1993, **26**, 343.
22 G. M. Sheldrick, SHELXL97, Program for Refinement of Crystal Structures, University of Göttingen, Germany, 1997.