

# Effects of side chain amino nitrogen donor atoms on metal complexation of aminohydroxamic acids: New diamino-hydroxamates chelating Ni(II) more strongly than Fe(III) †

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Complexes of diamino-hydroxamic acids 2,6-diamino-*N*-hydroxyhexanamide (lysinehydroxamic acid, Lysha), 2,4-diamino-*N*-hydroxybutanamide (2,4-diaminobutyrohydroxamic acid, Dambha) and 2,3-diamino-*N*-hydroxypropanamide (2,3-diaminopropionohydroxamic acid, Dampha) with manganese(II), cobalt(II), iron(II), nickel(II), copper(II), zinc(II), iron(III), aluminium(III) and molybdenum(VI) in aqueous solution were studied by pH-potentiometric, UV-visible spectrophotometric and EPR methods. The two latter diamino-hydroxamic acids were synthesised as new ligands and characterised. The results were compared to those of a simple  $\alpha$ -amino acid derivative,  $\alpha$ -alaninehydroxamic acid ( $\alpha$ -Alaha) and the effects of the side chain amino group on the co-ordination mode and on the stability of the complexes formed were evaluated. As expected, the side chain amino nitrogen atom of Lysha does not co-ordinate to any of the studied metals but remains free for possible further interactions. The amino groups do not co-ordinate to aluminium(III) or iron(III) at all and the closer the side chain amino group is situated to the  $\alpha$ -aminohydroxamic residue the less stable the hydroxamate complex formed in the order of Lysha, Dambha, Dampha, and hydrolytic processes become increasingly dominant. The co-ordination of the side chain amino nitrogen of Dampha and Dambha to nickel(II) and copper(II) was unambiguously observed.

## Introduction

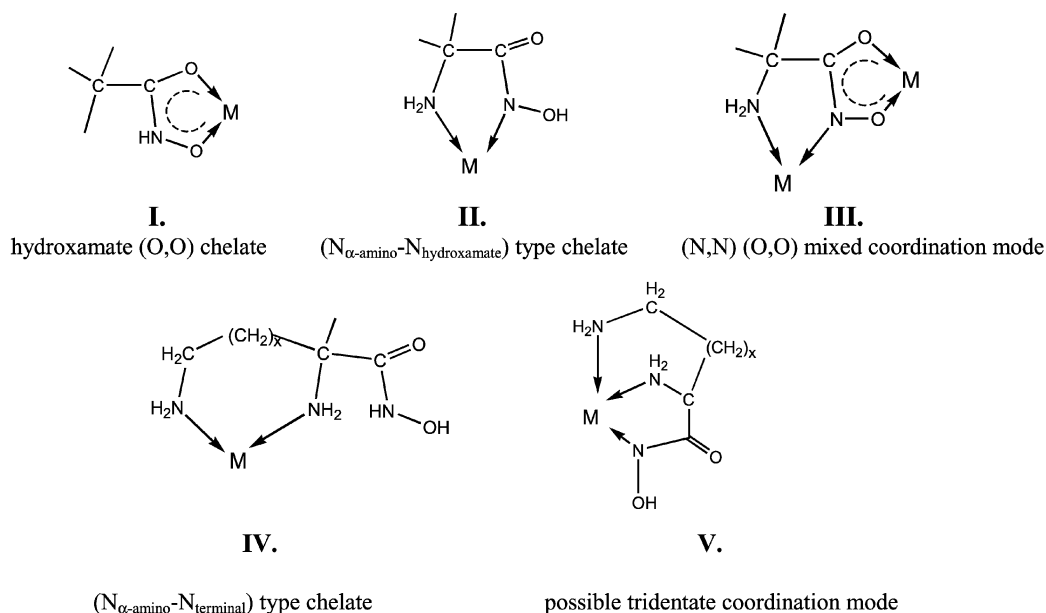
Natural hydroxamate-based compounds, siderophores, play a crucial role in microbial iron(III) storage and transport<sup>1,2</sup> and might be involved in molybdenum uptake in  $N_2$ -fixing bacteria.<sup>3,4</sup> Hydroxamic acids can also chelate aluminium(III), in fact the only drug currently available for the treatment of aluminium intoxication is a siderophore, desferrioxamine B.<sup>5</sup> They are also efficient chelating agents for other environmental metal ions (e.g. zinc(II), nickel(II), copper(II)),<sup>6–9</sup> and are effective inhibitors of metalloenzymes (e.g. nickel(II) containing urease).<sup>10,11</sup> Numerous previous results confirm the (O,O) binding mode of hydroxamic acids (Scheme 1, **I**).<sup>1,2,6,7</sup> With metal ions such as copper(II), iron(III) or molybdenum(VI) deprotonation of the co-ordinated primary hydroxamate leads to the more stable hydroximato ( $-\text{CONO}^{2-}$ ) chelate.<sup>7,12</sup>

Hydroxamic acid derivatives of amino acids have also become a focus of interest,<sup>9,13–15</sup> some of which have been prepared to chelate certain trace elements essential in animal nutrition.<sup>16</sup> Compared to the simple hydroxamic acids, the presence of the amino group increases the number of co-ordination sites. When an amino group is situated in the  $\alpha$ -position of the hydroxamic moiety, two types of five-membered chelates (*via* the nitrogens or the oxygens) can be realised (Scheme 1, **I** and **II**) and a mixed type co-ordination mode is also possible (**III**).<sup>9</sup> Aminohydroxamic acids co-ordinate to the hard metal ions (e.g. aluminium(III) or iron(III))

through their oxygen atoms exclusively (**I**). However, due to the electron-withdrawing effect of the amino group and electronic repulsion between the  $\text{NH}_3^+$  group and the  $\text{M}^{3+}$  ion, the  $\alpha$ -amino group decreases the stability of the hydroxamate chelate.<sup>17</sup> On the other hand, borderline metal ions like nickel(II), prefer the five-membered (N,N)-chelate (**II**) over the (O,O) one (**I**) as first proved for the nickel(II)–glycinehydroxamate square planar bis-complex by X-ray investigations.<sup>18</sup> This co-ordination mode also predominates with copper(II) ion at  $\text{pH} > 6$ . Although, the four nitrogens remain co-ordinated at higher pH, through the deprotonation of one of the hydroxamate groups a hydrogen bond is realised between the two ligands and the complex  $[\text{MA}_2\text{H}_{-1}]^-$  is formed in the copper(II)– or nickel(II)– $\alpha$ -Alaha system.<sup>9</sup> For steric reasons, the mixed co-ordination mode always results in the formation of polynuclear species with copper(II), cobalt(II) or zinc(II) (**III**).<sup>9,13,19</sup>

Additional donor atoms in the side chain of aminohydroxamic acids increase the number of possible co-ordination modes. Amino nitrogen, being an effective donor atom for many metal ions, can significantly change the metal binding behaviour of the ligand. The ligands studied contain the side chain amino moieties in  $\beta$ ,  $\gamma$  and  $\epsilon$  terminal positions. Two of them, 2,4-diamino-*N*-hydroxybutanamide (Dambha) and 2,3-diamino-*N*-hydroxypropanamide (Dampha), were synthesised as new compounds. The possible co-ordination modes of these ligands other than those with  $\alpha$ -aminohydroxamic acids (**I**, **II** and **III**) could be: the ligand binds through the two amino nitrogens (**IV**), or some tridentate mode like **V** is realised. Side chain amino group situated far from the  $\alpha$ -aminohydroxamic moiety (like in Lysha) most probably remains uncoordinated and free for further eventual interactions as was suggested for the copper(II)–Lysha and nickel(II)–Lysha complexes.<sup>20</sup>

† Electronic supplementary information (ESI) available: UV–VIS spectra and concentration distribution curves for the iron(III)–Lysha system, pH-metric titration curves and mass spectra for Dampha and Dambha. See <http://www.rsc.org/suppdata/dt/b1/b111184a/>



Scheme 1

In the present work pH-potentiometric, UV–visible spectrophotometric and EPR measurements for the complexes of Dampha, Dambha and Lysha formed with different metal ions in aqueous solution were carried out. The results were always compared to the corresponding literature data of  $\alpha$ -alaninehydroxamic acid.

## Experimental

### Chemicals

$\alpha$ -Alaninehydroxamic acid ( $\alpha$ -Alaha), 2,6-diamino-*N*-hydroxyhexanamide (Lysha) and solvents were of the highest purity available commercially (Sigma) and used without further purification. 2,4-Diamino-*N*-hydroxybutanamide (Dambha), 2,3-diamino-*N*-hydroxypropanamide (Dampha) were prepared from carboxylic methylesters and hydroxylamine<sup>21</sup> using standard procedures as described below.

### Preparation of Dampha and Dambha

The corresponding amino acids (2,4-diaminobutyric acid dihydrochloride (2 g, 0.011 mol) or 2,3-diaminopropionic acid monohydrochloride (2.5 g, 0.018 mol)) were added to  $\text{SOCl}_2$  (at 5% excess to amino acids) dissolved in methanol (20  $\text{cm}^3$ ) and the resulting mixture was stirred for one day. From the cold solution the corresponding methyl esters precipitated and were filtrated off under a  $\text{N}_2$  atmosphere.  $\text{NH}_2\text{OH}\cdot\text{HCl}$ , dissolved in a small amount of methanol (at 10% excess to methyl esters), was added to an equivalent amount of KOH also dissolved in methanol. KCl precipitation was separated by filtration and the solution was added dropwise to methyl esters suspended in methanol (5  $\text{cm}^3$ ). The mixture was stored for one day at a temperature below zero. The final products were isolated by filtration under a  $\text{N}_2$  atmosphere as white powders.

**Analysis for the methyl ester of 2,3-diaminopropionic acid.**  $\delta_{\text{H}}$  (360 MHz; solvent  $\text{D}_2\text{O}$ ): 3.92 (O- $\text{CH}_3$ ), 4.54 (CH(A)), 3.63 (CH<sub>2</sub>(B)), 3.55 (CH<sub>2</sub>(C)),  $^3J_{\text{AB}} = 8.4$  Hz,  $^3J_{\text{AC}} = 5.2$  Hz,  $^2J_{\text{BC}} = 13.7$  Hz;  $\delta_{\text{C}}$  (90.5 MHz, solvent  $\text{D}_2\text{O}$ , ref.  $\text{CDCl}_3$ ): 53.74 ( $\text{CH}_3$ ), 49.03 (CH), 37.34 ( $\text{CH}_2$ ).

**Analysis for the methyl ester of 2,4-diaminobutyric acid.**  $\delta_{\text{H}}$ , 3.85 (O- $\text{CH}_3$ ), 4.27 (CH(A)), 3.26 (CH<sub>2</sub>(B)), 3.20 (CH<sub>2</sub>(C)), 2.37 (CH<sub>2</sub>(D)), 2.25 (CH<sub>2</sub>(E)),  $^3J_{\text{AD}} = 7.9$  Hz,  $^3J_{\text{AE}} = 5.8$  Hz,  $^3J_{\text{BD}} = 5.6$  Hz,  $^3J_{\text{BE}} = 10.8$  Hz,  $^3J_{\text{CD}} = 10.1$  Hz,  $^3J_{\text{CE}} = 5.0$  Hz,

$^2J_{\text{BC}} = 12.9$  Hz,  $^2J_{\text{DE}} = 13.8$  Hz;  $\delta_{\text{C}}$  (90.5 MHz, solvent  $\text{D}_2\text{O}$ , ref.  $\text{t-BuOH}$ ): 55.86 ( $\text{CH}_3$ ), 52.21 (CH), 29.30 ( $\text{CH}_2$ ), 37.81 ( $\text{CH}_2$ ).

**Analysis for Dampha.**  $\delta_{\text{H}}$ , 3.44 (d,  $^3J_{\text{HH}} = 7.2$  Hz, 2H,  $\text{CH}_2$ ), 3.99 (t,  $^3J_{\text{HH}} = 7.2$  Hz, 1H, CH);  $\delta_{\text{C}}$  (90.5 MHz, solvent  $\text{D}_2\text{O}$ , ref. MeOH): 52.71 (CH), 43.82 ( $\text{CH}_2$ ), IR:  $\nu_{\text{CO}} = 1672$   $\text{cm}^{-1}$ ,  $\nu_{\text{max}}/\text{cm}^{-1} = 2360, 2616, 2860$  ( $\text{NH}_3^+$ ).

**Analysis for Dambha.**  $\delta_{\text{H}}$ , 3.82 (CH(A)), 3.21 (CH<sub>2</sub>(B)), 3.17 (CH<sub>2</sub>(C)), 2.21 (CH<sub>2</sub>(D)), 2.20 (CH<sub>2</sub>(E)),  $^3J_{\text{AD}} = 7.9$  Hz,  $^3J_{\text{AE}} = 5.8$  Hz,  $^3J_{\text{BD}} = 6.5$  Hz,  $^3J_{\text{BE}} = 10.1$  Hz,  $^3J_{\text{CD}} = 8.9$  Hz,  $^3J_{\text{CE}} = 5.6$  Hz,  $^2J_{\text{BC}} = 12.0$  Hz,  $^2J_{\text{DE}} = 13.6$  Hz;  $\delta_{\text{C}}$  (90.5 MHz, solvent  $\text{D}_2\text{O}$ , ref. MeOH): 52.9 (CH), 28.5 ( $\text{CH}_2$ ), 36.9 ( $\text{CH}_2$ ) IR:  $\nu_{\text{CO}} = 1672$   $\text{cm}^{-1}$ , IR:  $\nu_{\text{CO}} = 1698$   $\text{cm}^{-1}$ ,  $\nu_{\text{max}}/\text{cm}^{-1} = 2363, 2535, 2803$  ( $\text{NH}_3^+$ ); MS spectra are available as ESI. †

Results of elemental analyses are not presented because the ligands synthesized always contained some KCl.

The purity of the ligands and the concentrations of the ligand stock solutions were determined by Gran's method.<sup>22</sup> The metal ion stock solutions were prepared from  $\text{MnCl}_2\cdot 4\text{H}_2\text{O}$ ,  $\text{CoCl}_2\cdot 6\text{H}_2\text{O}$ ,  $\text{CuCl}_2\cdot 2\text{H}_2\text{O}$ ,  $\text{NiCl}_2\cdot 5\text{H}_2\text{O}$ ,  $\text{AlCl}_3\cdot 6\text{H}_2\text{O}$ ,  $\text{Na}_2\text{MoO}_4\cdot 2\text{H}_2\text{O}$  (Reanal) dissolved in doubly distilled water.  $\text{ZnO}$ ,  $\text{FeCl}_3$  and iron (Reanal) were dissolved in a known amount of HCl solution. The iron(II) stock solution was prepared under strictly oxygen free argon atmosphere and the  $\text{FeCl}_2$  solution was filtered and stored under anaerobic conditions. KSCN solution was used to check whether there were any iron(III) traces in the stock solution. The concentrations of the metal ion stock solutions, except for iron(II), were determined gravimetrically *via* precipitation of quinolin-8-olates, while the concentration of the iron(II) solution was determined by titrimetry using  $\text{KMnO}_4$  as titrant under acidic conditions. The HCl concentrations of the iron(II), iron(III) and zinc(II) stock solutions were determined by pH potentiometry.

### Potentiometric and spectrophotometric studies

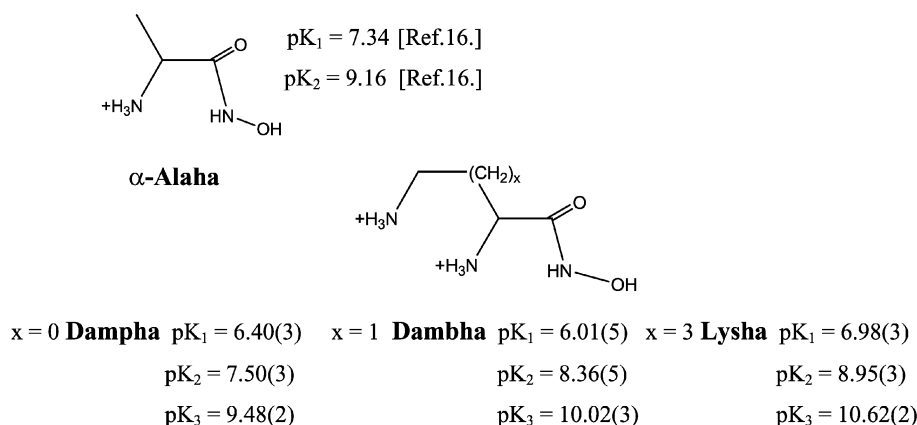
All the measurements were carried out at 0.2  $\text{mol dm}^{-3}$  ionic strength (KCl) and  $298 \pm 0.1$  K. Carbonate-free KOH solutions of known concentrations (*ca.* 0.2  $\text{mol dm}^{-3}$ ) were used as titrant.

Argon overpressure was used when iron(II) solutions were added to the samples which were in all cases completely deoxygenated by bubbling a stream of argon for *ca.* 20 minutes before iron(II) was added.

**Table 1** Stability constants ( $\log\beta_{pqr}$ ) for polymolybdates and hydroxo complexes of iron(III) and aluminium(III) ( $T = 298\text{ K}$ ,  $I = 0.2\text{ mol dm}^{-3}$ )

Complex	$\log\beta^a$	Complex <sup>b</sup>	$\log\beta^c$	Complex <sup>b</sup>	$\log\beta^c$
$[\text{HMoO}_4]^-$	4.03	$[\text{FeH}_{-1}]^{2+}$	-3.21	$[\text{AlH}_{-1}]^{2+}$	-5.52
$[\text{H}_2\text{MoO}_4]$	6.7	$[\text{FeH}_{-2}]^+$	-6.73	$[\text{Al}_2\text{H}_{-2}]^{4+}$	-7.70
$[\text{H}_8(\text{MoO}_4)_7]^{6-}$	53.18	$[\text{Fe}_2\text{H}_{-2}]^{4+}$	-4.09	$[\text{Al}_3\text{H}_{-4}]^{5+}$	-13.57
$[\text{H}_9(\text{MoO}_4)_7]^{5-}$	58.10	$[\text{Fe}_3\text{H}_{-4}]^{5+}$	-7.58	$[\text{AlH}_{-4}]^-$	-23.46
$[\text{H}_{10}(\text{MoO}_4)_7]^{4-}$	62.11			$[\text{Al}_{13}\text{H}_{-32}]^{7+}$	-109.1
$[\text{H}_{11}(\text{MoO}_4)_7]^{3-}$	64.54				

<sup>a</sup> Ref. 25. <sup>b</sup> Ref. 26. <sup>c</sup> Ref. 27. <sup>d</sup> Complexes formed by deprotonation of the coordinated water molecules to hydroxide ions.

**Scheme 2**

The pH-metric titrations were performed throughout the approximate pH range 2.0–10.5 or below precipitation on samples of 4.00 or 10.00 cm<sup>3</sup>. The ligand concentrations were varied in the range  $2 \times 10^{-3}$ – $4 \times 10^{-3}$  mol dm<sup>-3</sup>; the metal to ligand ratios were in general in the range of 1 : 1–1 : 8. Samples at four or five different ratios were measured. Reproducibility of pH values for parallel titrations was within 0.005 units. The pH-metric titrations were made with a Radiometer pHM84 instrument equipped with a Metrohm 62104130 combined electrode. The titrant was added from a Metrohm 715 Dosimat autoburette. The electrode system was calibrated by the method of Irving *et al.*<sup>23</sup> so that the pH-meter readings could be converted into hydrogen ion concentrations.

The pH-metric results were utilised to establish the stoichiometry of species and to calculate the stability constants. The calculations were performed with the computer program PSEQUAD<sup>24</sup> using the literature data for polymolybdates,<sup>25</sup> iron(III)<sup>26</sup> and aluminium(III)<sup>27</sup> hydroxo complexes (see Table 1). Volumes of titrant were fitted and the accepted fittings were always below  $1 \times 10^{-2}$  cm<sup>3</sup>.

UV–Visible measurements on systems containing nickel(II), copper(II), iron(III) and molybdenum(VI) were also performed. The metal ion to ligand ratios were varied from 1 : 2 to 1 : 8 at metal ion concentrations from  $5 \times 10^{-4}$  to  $5 \times 10^{-3}$  mol dm<sup>-3</sup>. A HP 8453 spectrophotometer was used to record the spectra in the region of 250–800 nm.

EPR spectra of copper(II)–Dampha, –Dambha and –Lysha systems were recorded on a Varian E9 spectrometer at the X-band frequency (9.15 GHz) at 120 K. Ethylene glycol was added to aqueous samples to ensure glass formation.

<sup>1</sup>H and <sup>13</sup>C NMR spectra were registered on a Bruker AM 360 spectrometer. Trimethylsilylpropane sulfonate (TSP) and CH<sub>3</sub>CN were used as references in the case of <sup>1</sup>H NMR and <sup>13</sup>C NMR, respectively.

A Perkin-Elmer FT–IR spectrometer (Paragon 1000 PC) was used to record solid state IR spectra (KBr pellets).

Mass spectrometry (ionization mode FAB(+)) was used to confirm the molecular weight for the two new hydroxamic acids (VG-70MS (VG Analytical Ltd., Manchester, England), reagent gas: Xe (8 kV, 1  $\mu$ A); matrix: diethanolamine; resolution: 1000).

## Results and discussion

### Acidity of the ligands

The structural formulae for the protonated ligands are shown together with their dissociation constants in Scheme 2.

All the studied protonated diamino hydroxamic acids ( $\text{H}_3\text{A}^{2+}$ ) have three dissociable protons. The dissociation constants of Lysha were published previously<sup>19</sup> and identical values have been obtained in the present work. Although the dissociation processes overlap and the dissociation microconstants are not known, comparison of the pKs of Lysha (the amino groups are the most separated in this ligand) with the corresponding values of  $\alpha$ -Alaha and lysine<sup>28</sup> was made. It led to the conclusion that the two lower pK values of Lysha belong mainly to the  $\alpha$ -amino and hydroxamic groups and the highest one, pK<sub>3</sub>, mainly to the side chain amino moiety. The  $\alpha$ -NH<sub>3</sub><sup>+</sup> and –CONHOH functions of Lysha probably have similar acidities, as seen in the case of  $\alpha$ -Alaha where the dissociation microconstants<sup>29</sup> showed the former moiety to be slightly more acidic.

The side chain NH<sub>3</sub><sup>+</sup> moiety is progressively less isolated in Dambha and Dampha which results in increasing mutual electronic effects, an increase in the acidities and a decrease in pK values. The only exception is the pK<sub>1</sub> value of Dampha where a hydrogen bond between the two amino groups in the mono-protonated molecule is the most achievable.

### Iron(III), aluminium(III) and molybdenum(VI) complexes

Precipitation occurs in all the studied systems except in those containing Lysha. The shorter distance between the terminal amino group and the  $\alpha$ -aminohydroxamic moiety results in precipitation at lower pH. Consequently, precipitation occurs at slightly above pH *ca.* 7 in the iron(III)– and aluminium(III)–Dambha systems, but occurs below pH 7 for the corresponding Dampha systems. In the molybdenum(VI)–Dampha system, the formation of polynuclear complexes most probably causes precipitation below pH 3.5. Calculations were always made from the experimental results obtained before precipitation, the stoichiometry of the complexes and the formation constants yielding the best fit of the pH-metric experimental data are given in Table 2. The table does not contain data for

**Table 2** Stability constants ( $\log\beta$ ) for the complexes formed between Fe(III), Al(III), Mo(VI) ions and diaminohydroxamic acids and  $\alpha$ -Alaha ( $T = 298\text{ K}$ ,  $I = 0.2\text{ mol dm}^{-3}$ . Standard deviations are shown in parentheses only if the values have been determined in the present work)

Complex	Dampha		Dambha		Lysha		$\alpha$ -Alaha	
	Fe(III)	Al(III)	Fe(III)	Al(III)	Fe(III)	Al(III)	Fe(III)	Al(III)
[MAH <sub>2</sub> ] <sup>4+</sup>	—	—	—	—	—	24.21(4)	—	—
[MAH] <sup>3+</sup>	—	—	22.06(2)	17.3(2)	23.33(4)	—	17.15 <sup>a</sup>	14.35 <sup>a</sup>
[MA] <sup>2+</sup>	16.41(7)	11.7(1)	—	—	—	—	13.92 <sup>a</sup>	—
[MA <sub>2</sub> H <sub>3</sub> ] <sup>4+</sup>	—	—	45.14(5)	—	47.8(1)	—	—	—
[MA <sub>2</sub> H <sub>2</sub> ] <sup>3+</sup>	—	—	38.36(7)	34.0(1)	43.1(1)	36.94(4)	—	—
[MA <sub>2</sub> H] <sup>2+</sup>	—	24.2(3)	—	27.2(1)	—	29.84(3)	28.36 <sup>a</sup>	—
[MA <sub>2</sub> ] <sup>+</sup>	—	17.6(1)	—	19.81(7)	—	21.28(4)	21.99 <sup>a</sup>	16.7 <sup>a</sup>
[MA <sub>2</sub> H <sub>-1</sub> ]	—	—	—	—	—	—	14.54 <sup>a</sup>	9.62 <sup>a</sup>
[MA <sub>2</sub> H <sub>-2</sub> ] <sup>-</sup>	—	—	—	—	—	—	—	-0.16 <sup>a</sup>
[MA <sub>3</sub> H <sub>4</sub> ] <sup>4+</sup>	—	—	—	—	66.1(1)	—	—	—
[MA <sub>3</sub> H <sub>3</sub> ] <sup>3+</sup>	—	—	—	—	59.7(1)	—	—	—
[MA <sub>3</sub> H <sub>2</sub> ] <sup>2+</sup>	—	—	—	—	52.0(1)	—	—	—
[MA <sub>3</sub> H] <sup>+</sup>	—	—	—	—	—	—	33.90 <sup>a</sup>	—
[M <sub>2</sub> A <sub>2</sub> H] <sup>5+</sup>	—	—	—	—	37.3(1)	—	—	—
[M <sub>2</sub> A <sub>2</sub> ] <sup>4+</sup>	—	—	—	—	—	—	—	22.21 <sup>a</sup>
[M <sub>2</sub> A <sub>2</sub> H <sub>-1</sub> ] <sup>3+</sup>	—	—	—	—	—	—	—	17.59 <sup>a</sup>
[M <sub>2</sub> A <sub>2</sub> H <sub>-2</sub> ] <sup>2+</sup>	—	—	—	—	—	—	—	12.63 <sup>a</sup>
[M <sub>2</sub> A <sub>2</sub> H <sub>-3</sub> ] <sup>+</sup>	—	—	—	—	—	—	—	5.85 <sup>a</sup>
[M <sub>2</sub> A <sub>2</sub> H <sub>-4</sub> ]	—	—	—	—	—	—	—	-2.44 <sup>a</sup>
[MoO <sub>2</sub> A <sub>2</sub> H <sub>4</sub> ] <sup>4+</sup>	—	—	63.65(7)	—	66.65(5)	—	45.90 <sup>b</sup>	—
[MoO <sub>3</sub> AH <sub>2</sub> ] <sup>+</sup>	Precipitation	—	32.7(1)	—	34.16(8)	—	—	—
[MoO <sub>3</sub> AH]	—	—	27.8(1)	—	29.15(7)	—	24.00 <sup>b</sup>	—
[MoO <sub>3</sub> A] <sup>-</sup>	—	—	—	—	—	—	18.65 <sup>b</sup>	—

<sup>a</sup> Ref. 19. <sup>b</sup> Ref. 30.

molybdenum(VI)–Dampha complexes, where any calculation was unsuccessful because of the precipitation. For comparison, the values for the corresponding  $\alpha$ -Alaha containing complexes are also presented.

As Table 2 shows, various protonated complexes are formed in these systems. In order to get a better insight into the coordination modes, UV–visible spectrophotometric measurements for the iron(III)- and molybdenum(VI)-containing systems were performed. Fortunately, these complexes have characteristic charge-transfer absorption bands. Iron(III)–monohydroxamate complexes have spectra with  $\lambda_{\max}$  at *ca.* 510 nm ( $\epsilon_{\max} \approx 1000\text{ mol}^{-1}\text{ dm}^3\text{ cm}^{-1}$ ), whereas the bis-hydroxamate complexes display  $\lambda_{\max}$  at *ca.* 470 nm ( $\epsilon_{\max} \approx 1800\text{ mol}^{-1}\text{ dm}^3\text{ cm}^{-1}$ ), while  $\lambda_{\max}$  for the tris-complexes is at *ca.* 425 nm ( $\epsilon_{\max} \approx 2600\text{ mol}^{-1}\text{ dm}^3\text{ cm}^{-1}$ ).<sup>2</sup> The spectra for iron(III)–Lysha (see ESI) support the co-ordination of one hydroxamate chelate (corresponding to [FeAH]<sup>3+</sup>) at pH 2. On increasing the pH, the second and third hydroxamate chelates are coordinated in succession and only tris-hydroxamate complexes exist at pH 6.5–7.0. Hydrolytic processes might cause the change in the spectrum registered at pH 9.

In contrast with results for Lysha, the  $\lambda_{\max}$  does not shift below *ca.* 460 nm if the ligand is Dambha, supporting the suggestion that tris-hydroxamate complexes fail to form in this system. The charge-transfer band is insignificant in the case of Dampha. There is no indication, however, for the co-ordination of the amino nitrogen atoms even with Dampha. In acidic solutions the first complex formation reaction between iron(III) and a diamino-monohydroxamic molecule is expected to proceed *via* eqn. (1) where the two amino groups are still protonated.

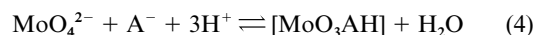
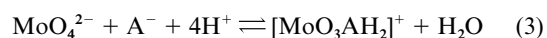
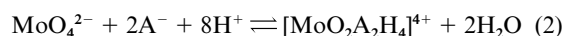


However, the formation of [FeAH<sub>2</sub>]<sup>4+</sup> in measurable concentration was not found in any case. This contradiction can be solved by considering that the hydrolytic processes occurred below pH 2.<sup>26</sup> Most probably, there is one hydroxide ion in the co-ordination sphere of the monochelated species, therefore the stoichiometry of this species is not [FeAH<sub>2</sub>]<sup>4+</sup> but [FeAH<sub>2</sub>(OH)]<sup>3+</sup>, which is formally [FeAH]<sup>3+</sup>. Due to Lysha having

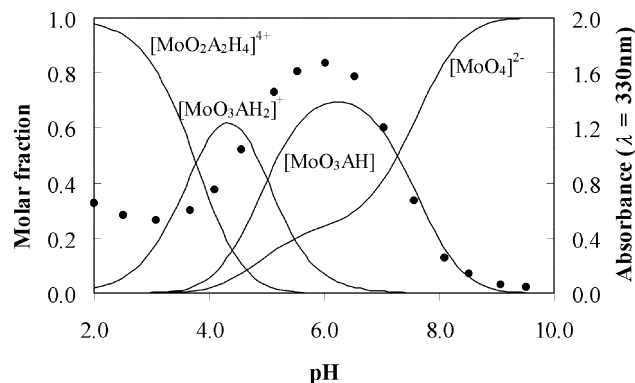
the highest basicity of the co-ordinating donor atoms and the largest distance between the positively charged groups and the coordinating Fe<sup>3+</sup> ion, this ligand forms the most stable iron(III) complexes. Bis- and even tris-hydroxamate complexes are also formed with this ligand. In contrast, the hydrolytic processes are increasingly favoured from Dambha to Dampha, and the latter molecule forms only a single monochelated, most probably mixed, hydroxo complex, [FeA]<sup>2+</sup>.

The hydrolysis of aluminium(III) starts at somewhat higher pH than that of iron(III) (see Table 1). Therefore, the first complex, [AlAH<sub>2</sub>]<sup>4+</sup> is really formed according to equilibrium (1) in the aluminium(III)–Lysha system. With Dambha and Dampha, however, the metal complex formation starts at an even higher pH and overlap with hydrolytic processes becomes increasingly significant, consequently the first species formed are [AlAH]<sup>3+</sup> and [AlA]<sup>2+</sup>, respectively. Most probably it is for steric reasons that dinuclear complexes, being so important with  $\alpha$ -Alaha (see Table 2), are not formed with the ligands studied here.

In the molybdenum(VI)-containing systems the components are MoO<sub>4</sub><sup>2-</sup>, A<sup>-</sup> and H<sup>+</sup>. Therefore, the  $\log\beta$  values in Table 2 relate to the following reactions:



Unfortunately, in the case of  $\alpha$ -amino acid derivatives the characteristic charge-transfer band ( $\lambda_{\max}$  is at *ca.* 290 nm) of bis(hydroxamate)dioxomolybdenum(VI) is almost covered by ligand bands (it appears as a shoulder), however, a new band appears at *ca.* 325–330 nm if co-ordination occurs *via* the  $\alpha$ -amino-N and hydroxamate-N donors.<sup>30</sup> Fig. 1 presents the concentration distribution curves and absorbances measured at 330 nm in the molybdenum(VI)–Lysha system (those for the molybdenum(VI)–Dambha are quite similar). It clearly shows the increase of the absorbance above pH 4, where the species [MoO<sub>3</sub>AH] starts to form, reaching a maximum value close to the maximum concentration of [MoO<sub>3</sub>AH] and decreases with

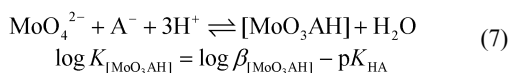
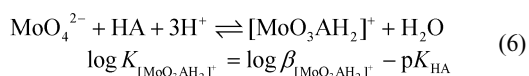
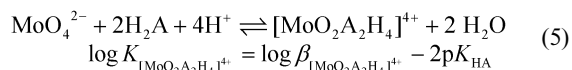


**Fig. 1** Concentration distribution curves for molybdenum(vi)–Lysha complexes plotted together with the absorbance values at  $\lambda = 330$  nm as a function of pH (●) ( $c_{\text{Mo(vi)}} = 1.0 \times 10^{-3}$  mol dm $^{-3}$ , metal to ligand ratio = 1 : 6).

the decreasing concentration of this species. (The absorbances measured at 330 nm below pH 4 originate from the characteristic shoulder of  $[\text{MoO}_2\text{A}_2\text{H}_4]^{4+}$ ).

All the above results support the hypothesis that, following the hydroxamate type co-ordination (Scheme 1, **I**) in the  $[\text{MoO}_2\text{A}_2\text{H}_4]^{4+}$  and  $[\text{MoO}_3\text{AH}_2]^+$  complexes, the  $\alpha$ -amino-N and hydroxamate-N donors are co-ordinated in the  $[\text{MoO}_3\text{AH}]$  mode (**II**), in which the terminal amino-N is still protonated. Hydrolytic processes displace the Lysha completely by pH *ca.* 9 and above this pH only  $\text{MoO}_4^{2-}$  and the uncoordinated Lysha exist.

As the molybdenum(vi)–Lysha complexes contain the terminal amino groups in their protonated form, only the stability constants for eqns. (5)–(7) are comparable with the corresponding data for  $\alpha$ -Alaha.



Assuming that the  $pK_3$  of Lysha belongs mainly to the dissociation of the terminal  $-\text{NH}_3^+$  moiety,  $\log K$  values for eqns. (5)–(7) can be calculated. Those for processes (5), (6) and (7) are 45.90, 24.00 and 18.53, respectively and agree very well with the corresponding constants for  $\alpha$ -Alaha containing complexes (Table 2) which strongly supports the “ $\alpha$ -Alaha-like” co-ordination of Lysha.

As a final conclusion it can be stated that the iron(III), aluminium(III) and molybdenum(vi) binding ability of these ligands decreases in the order Lysha > Dambha > Dampha and the chelating ability of Lysha is similar to that of  $\alpha$ -Alaha.

### Complexation with bivalent metal ions

The complex formation with different 3d metal ions is accompanied by significantly different pH-effects (representative titration curves are available as ESI), which suggest great differences in the stability of the complexes. For example, the complex formation starts at about pH 2.5 with copper(II) but there is no interaction with manganese(II) up to pH 7. The stoichiometry of the complexes and the formation constants ( $\log \beta_{\text{ML}}$ ), giving the best fit of the pH-metric experimental data for manganese(II)–, cobalt(II)–, iron(II)–, nickel(II)–, copper(II)– and zinc(II)–, Lysha–, Dambha and Dampha systems, are shown in

Table 3. This table also includes the results for metal ion– $\alpha$ -Alaha complexes. The stability constants for nickel(II)– and copper(II)–Lysha complexes were determined in our previous work<sup>20</sup> and measurements were performed only for selected metal ion–Dampha systems. Although steric and basicity diversity cause some differences between the equilibrium models for the Dampha-, Dambha- and Lysha-containing systems, first of all mono- and bis-complexes and, in the case of copper(II), some binuclear complexes are also formed in measurable concentrations.

Due to the fact that both O- and N-donor ligands are able to co-ordinate to these dipositive metal ions, different isomers of many complexes shown in Table 3 are possible. To obtain a somewhat deeper insight into the bonding modes, the stability trends of the various chelates were evaluated by using model ligands, acetohydroxamic acid (Aha), 1,2-diaminoethane (en) and 1,3-diaminopropane (pn). Aha was used to model hydroxamate-(O,O) chelation and, assuming that there is no significant difference between the stability of (N,N)-chelates formed *via* two amino N-donors and *via* amino-N and hydroxamate-N donors, en was the model for both the hydroxamate- and amine-type five-membered chelates whereas pn was applied for modelling of the six-membered (N,N)-chelate. Since the donor atoms in our ligands (and also in the models) are protonated up to high pH (see Scheme 2), the metal ions must compete with protons for the binding sites. In such cases, only the pH-dependent conditional constants ( $K'$ ) indicate the metal binding ability of a specific site at a specific pH directly. To compare the stability of the different types of chelates with each other, the conditional constants for the monochelated metal complexes of the model ligands were calculated. The conditional stability constant can be defined as:

$$K' = \beta_{\text{MA}}/a_{\text{H}} \quad (8)$$

where:  $\beta_{\text{MA}}$  = the corresponding overall stability constants taken from refs. 31–36.

$$\alpha_{\text{H}} = [\text{A}](1 + \sum_{i=1}^n \beta_{\text{H}_i\text{A}}[\text{H}^i])$$

[A] = the totally deprotonated form of Aha, en and pn;  $n = 1$  if hydroxamate chelate is formed and 2 in the cases of amine-type chelates;  $\beta_{\text{H}_i\text{A}}$  = the corresponding protonation constant taken from refs. 31 and 32.

Out of the calculated results the logarithmic  $K'$  values for the different chelates and for manganese(II), nickel(II), copper(II) and zinc(II) metals as a function of pH are shown in Fig. 2. Unfortunately, only a few results have been published for complexes formed with pn under our conditions, but it is still completely clear that values for the six-membered (N,N)-chelate always remain below those for the five-membered one.

As Fig. 2 clearly shows, in all cases the hydroxamate chelate is preferred (it has the highest  $\log K'$  value) in the acidic region, where, however, there is no measurable metal complex formation except in copper(II) containing systems (see the numerical values of  $\log K'$  in Fig. 2). There is a change in the order of  $\log K'$  values at *ca.* pH 6, 6.5 and 9 for the nickel(II), copper(II) and zinc(II) complexes respectively, and en binds these metals more strongly than Aha above these pH values. (The change occurs at *ca.* pH 6.5 in the case of cobalt(II)-containing systems.) Manganese(II) and also iron(II), however, prefer the hydroxamate chelate to the amine type in the whole measured pH-range. Based on the stability trends the following conclusion can be drawn: hydroxamate co-ordination is favoured by manganese(II), iron(II) and zinc(II), and it depends on the pH and on the basicity of amino groups as to whether or not the non-co-ordinated groups are protonated. With other metals, however, especially with nickel(II) and copper(II), changes occur

**Table 3** Stability constants ( $\log\beta$ ) for the complexes formed between  $3d^5$ – $3d^{10}$  M(II) ions and diaminohydroxamic acids and  $\alpha$ -Alaha ( $T = 298$  K,  $I = 0.2$  mol dm $^{-3}$ ). Standard deviations are shown in parentheses only if the values have been determined in the present work

Metal ion	M	A	H	Dampha	Dambha	Lysha	$\alpha$ -Alaha
Mn(II)	1	1	1	—	12.88(3)	13.41(4)	10.92 <sup>a</sup>
	1	1	0	—	3.77(3)	—	3.47 <sup>a</sup>
	1	1	-1	—	-4.93(6)	—	-5.99 <sup>a</sup>
	1	2	2	—	25.89(6)	26.3(2)	—
	1	2	1	—	16.47(9)	—	14.30 <sup>a</sup>
Fe(II)	1	2	0	—	—	—	5.97 <sup>a</sup>
	1	1	1	12.28(8)	14.02(3)	14.92(2)	11.99 <sup>a</sup>
	1	1	0	4.34(5)	—	—	4.57 <sup>a</sup>
	1	1	-1	-5.54(7)	—	—	—
Co(II)	1	2	0	—	—	—	9.3 <sup>a</sup>
	1	1	1	—	14.32(3)	15.38(1)	12.12 <sup>a</sup>
	1	1	0	—	7.31(2)	—	4.74 <sup>a</sup>
	1	1	-1	—	-1.38(9)	—	-2.64 <sup>a</sup>
	1	2	2	—	—	29.83(4)	—
	1	2	1	—	20.82(7)	20.41(8)	—
	1	2	0	—	13.03(4)	10.13(8)	9.39 <sup>a</sup>
Ni(II)	1	2	-1	—	—	-2.2(3)	1.59 <sup>a</sup>
	2	3	0	—	—	—	17.69 <sup>a</sup>
	1	1	1	15.92(3)	15.70(8)	16.73 <sup>b</sup>	—
	1	1	0	—	—	—	6.76 <sup>a</sup>
	1	2	2	30.16(5)	31.00(8)	34.56 <sup>b</sup>	—
	1	2	1	23.83(5)	24.18(8)	26.40 <sup>b</sup>	—
	1	2	0	16.22(6)	16.75(7)	16.12 <sup>b</sup>	14.13 <sup>a</sup>
	1	2	-1	6.10(7)	4.96(9)	5.43 <sup>b</sup>	5.47 <sup>a</sup>
Cu(II)	1	1	2	22.25(6)	23.20(7)	—	—
	1	1	1	18.09(5)	19.38(6)	20.72 <sup>b</sup>	18.89 <sup>a</sup>
	1	2	2	33.31(6)	36.73(5)	40.06 <sup>b</sup>	—
	1	2	1	26.60(7)	29.05(8)	30.62 <sup>b</sup>	—
	1	2	0	17.61(9)	19.87(9)	20.22 <sup>b</sup>	19.87 <sup>a</sup>
	1	2	-1	—	8.9(2)	9.30 <sup>b</sup>	9.98 <sup>a</sup>
	2	2	1	—	38.08(5)	40.95 <sup>b</sup>	—
	2	2	0	28.6(1)	—	—	—
	2	2	-1	—	—	—	20.89 <sup>a</sup>
	2	2	—	—	—	—	—
Zn(II)	1	1	1	13.58(3)	14.34(3)	15.49(5)	12.27 <sup>a</sup>
	1	1	0	—	7.13(3)	—	5.29 <sup>a</sup>
	1	1	-1	—	-0.96(4)	—	-2.26 <sup>a</sup>
	1	2	2	26.29(8)	—	30.83(4)	—
	1	2	1	19.64(2)	20.77(6)	22.24(6)	—
	1	2	0	11.20(3)	12.05(9)	12.5(1)	9.32 <sup>a</sup>
	1	2	-1	0.25(8)	1.6(2)	2.4(2)	—
2	3	0	—	—	—	18.77 <sup>a</sup>	

<sup>a</sup> Ref. 31. <sup>b</sup> Ref. 20.

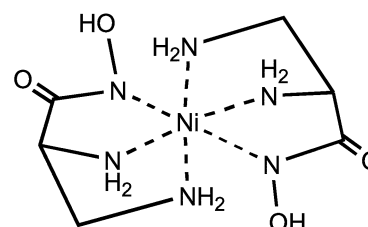
in the co-ordination modes as a function of pH. Fortunately, UV-visible spectrophotometric studies for the nickel(II)- and copper(II)-containing systems and also EPR for the copper(II) complexes can be used to distinguish between the various bonding modes.

[MAH]<sup>2+</sup> is the first species formed in all of our systems. The formation of its different isomers (*e.g.* **I**, **II** or **IV**) is possible. With nickel(II) the maximum amount of the species [NiAH]<sup>2+</sup> increases in the order of Lysha, Dambha, Dampha (it is 10%, 45% and 80%, respectively at 1 : 1.5 metal to ligand ratios for a  $6 \times 10^{-3}$  mol dm $^{-3}$  concentration of the ligand), suggesting increasingly significant amounts of isomer **IV** are present. In this case the hydroxamic function remains in its protonated form.

In the nickel(II)-simple aminohydroxamate bis-complexes a preference for the formation of ( $N_{\alpha\text{-amino}}, N_{\text{hydroxamate}}$ ) chelates in square planar bis-complexes, [NiA<sub>2</sub>] and [NiA<sub>2</sub>H<sub>-1</sub>]<sup>-</sup> is well known.<sup>9,13</sup> This co-ordination mode was exclusively found in previous work with  $\alpha$ -Alaha and Lysha above pH 6. (Due to the side chain NH<sub>3</sub><sup>+</sup> group, the stoichiometry of the complexes of Lysha is different).<sup>19,20</sup> Two characteristic bands, one in the range 425–435 nm and another in the range 490–500 nm, assigned to <sup>1</sup>A<sub>1g</sub> → <sup>1</sup>A<sub>2g</sub> and <sup>1</sup>A<sub>1g</sub> → <sup>1</sup>B<sub>1g</sub> transitions, respectively, can be observed in the electronic absorption spectra of the above nickel(II) complexes. In the case of Dambha, these characteristic bands start to increase above pH 5, reaching a maximum at pH 6.5–7.0 and above this pH, parallel to the

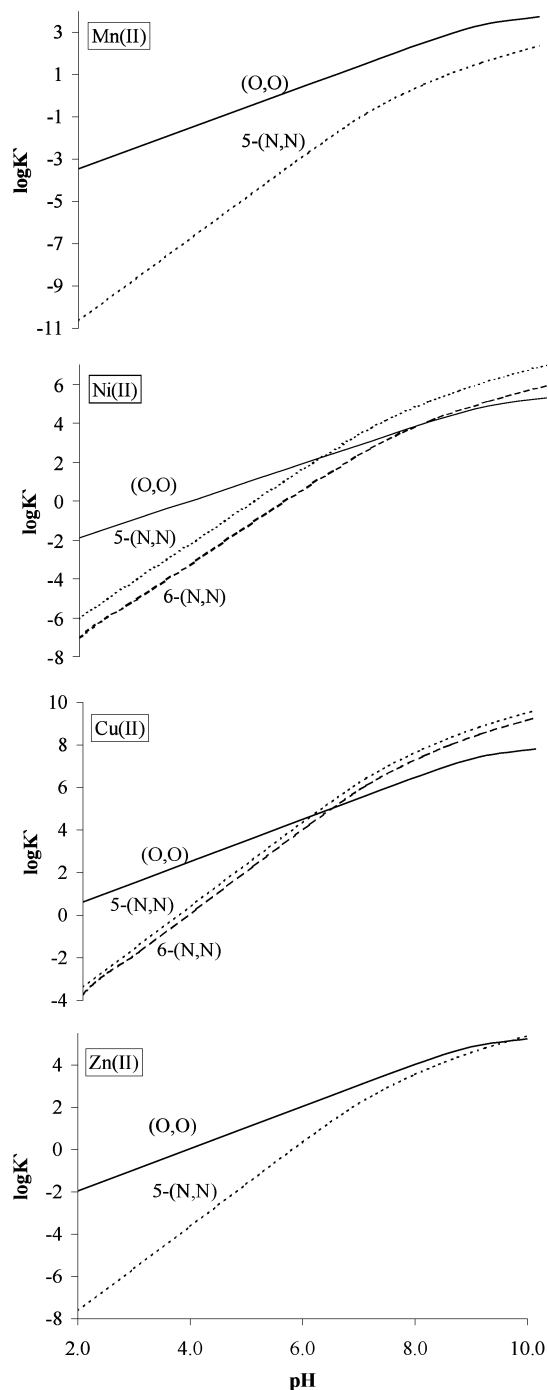
formation of the [NiA<sub>2</sub>] complex, start to decrease (Fig. 3a and b).

Consequently, the spectrophotometric results support both the formation of the well known planar bis-complexes involving ( $N_{\alpha\text{-amino}}, N_{\text{hydroxamate}}$ ) chelates in the pH-range *ca.* 5–8 and the disappearance of this geometry above pH 7. Most probably, this interesting change in the co-ordination geometry is caused by the tridentate co-ordination of two Dambha ligands to the nickel(II) ion following the deprotonation of their terminal amino group. The most probable structure for the octahedral [NiA<sub>2</sub>] complex is shown in Scheme 3.



Scheme 3

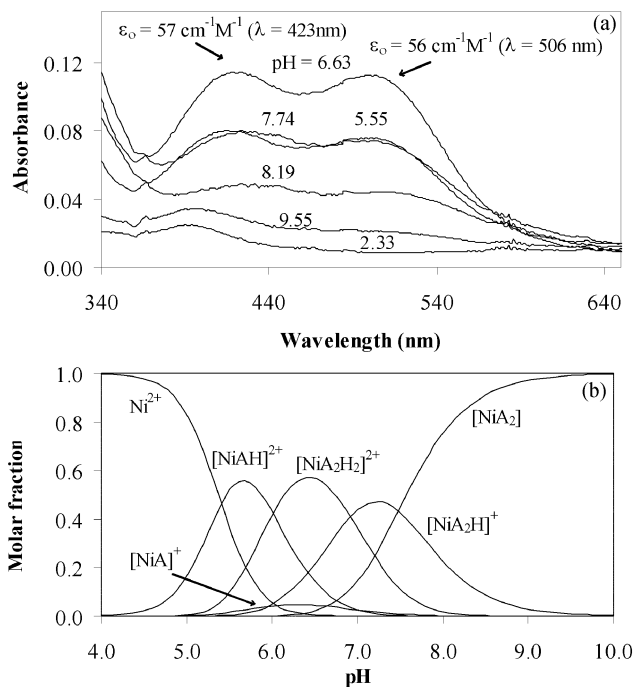
Nickel(II)-Dampha exhibits a further difference from nickel(II)-Dambha, -Lysha and - $\alpha$ -Alaha, since, according to the electronic absorption spectra, no square planar complex can be found with this ligand in the measured pH range (even [NiA<sub>2</sub>H<sub>2</sub>]<sup>2+</sup> is octahedral) and the obtained UV-visible data for



**Fig. 2** The pH dependence of conditional stability constants ( $\log K'$ ) calculated for equimolar (1 : 1) Mn(II), Ni(II), Cu(II) and Zn(II) complexes formed with model ligands, Aha (O,O) (—), en (5-N,N) (···) and pn (6-N,N) (---).

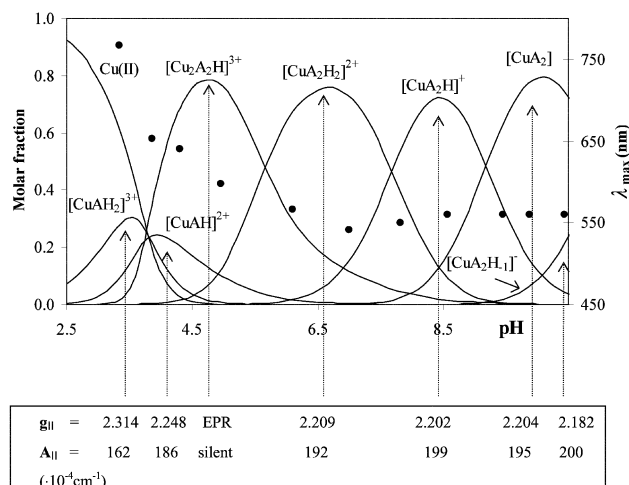
the species  $[\text{NiA}_2]$ ,  $\lambda_{\text{max}} = 529 \text{ nm}$  ( $\epsilon = 9 \text{ mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$ ),  $\lambda_{\text{max}} = 350 \text{ nm}$  ( $\epsilon = 15 \text{ mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$ ), are comparable to those of  $[\text{Ni}(\text{en})_3]^{2+}$ .<sup>37</sup> This result supports the hypothesis that the structure of  $[\text{NiA}_2]$  formed with Dampha is probably similar to that in Scheme 3. In this case there are two joined five-membered chelates per Dampha in the co-ordination sphere.

According to our previous results, in the copper(II)-*a*-Alaha and copper(II)-Lysha systems the co-ordination starts on the hydroxamate oxygens which changes into a mixed type co-ordination mode in polynuclear species, then a bis-complex with ( $\text{N}_{\alpha\text{-amino}}$ ,  $\text{N}_{\text{hydroxamate}}$ )-type chelates emerges and finally at high pH (above 9) the deprotonation of one of the co-ordinated hydroxamates occurs resulting in the formation of stable hydrogen bonds between the co-ordinated ligands.<sup>19,20</sup> Complexation of Dampha and Dambha with copper(II) shows differences



**Fig. 3** UV-VIS spectra recorded for the nickel(II)-Dambha system at different pH values (a) and concentration distribution curves for the same system (b) ( $c_{\text{Ni(II)}} = 2 \times 10^{-3} \text{ mol dm}^{-3}$ , metal to ligand ratio = 1 : 4).

from the above models. Out of the results representative concentration distribution curves for copper(II)-Dambha complexes plotted together with the  $\lambda_{\text{max}}$  values in the dependence of pH, are shown in Fig. 4. EPR parameters for the different species can also be found in this figure.



**Fig. 4** Concentration distribution curves for copper(II)-Dambha complexes (—), the pH dependence of  $\lambda_{\text{max}}$  values (●) ( $c_{\text{Cu(II)}} = 2 \times 10^{-3} \text{ mol dm}^{-3}$ , metal to ligand ratio = 1 : 2) and the corresponding EPR parameters.

As Fig. 4 shows, the complexation starts at pH 2.5 and the stoichiometry of the first complex formed is  $[\text{CuAH}_2]^{3+}$  (see also Table 3). Since only one proton is displaced by metal ion in this complex, the hydroxamate oxygens should be co-ordinated and the amino nitrogens are still protonated (Scheme 1, I). Corresponding  $\lambda_{\text{max}}$  and EPR parameters for both the Dampha and Dambha containing species ( $\lambda_{\text{max}} \approx 750 \text{ nm}$ ,  $g_{\parallel} = 2.314$ ,  $A_{\parallel} = 162 \times 10^{-4} \text{ cm}^{-1}$  and  $\lambda_{\text{max}} \approx 750 \text{ nm}$ ,  $g_{\parallel} = 2.314$ ,  $A_{\parallel} = 163 \times 10^{-4} \text{ cm}^{-1}$ , respectively), are comparable with those for the monochelated copper(II)-Aha complex.<sup>7</sup>

At pH  $\approx 3$  dimeric species appear in the studied systems but, owing to the different basicity of the non-co-ordinated terminal amino group in the different diamino hydroxamic acids, the

**Table 4** EPR and absorption parameters for some bis-complexes formed between copper(II) and en, pn,  $\alpha$ -Alaha, Lysha, Dambha and Dampha ligands

Ligand	Species	Coordinated chelates	$\lambda_{\max}/\text{nm}$	$\epsilon_{\max}/\text{mol}^{-1} \text{ dm}^3 \text{ cm}^{-1}$	$g_{\parallel}$	$A_{\parallel} (\times 10^{-4})/\text{cm}^{-1}$
en	$[\text{CuA}_2]^{2+}$	$2 \times 5\text{-}(\text{N}_{\text{amino}}\text{-N}_{\text{amino}})$	548	75	2.199 <sup>a</sup>	192 <sup>a</sup>
pn	$[\text{CuA}_2]^{2+}$	$2 \times 6\text{-}(\text{N}_{\text{amino}}\text{-N}_{\text{amino}})$	574 <sup>b</sup>	110 <sup>b</sup>	2.212	194
$\alpha$ -Alaha	$[\text{CuA}_2]$	$2 \times 5\text{-}(\text{N}_{\alpha\text{-amino}}\text{-N}_{\text{hydroxamate}})$	536 <sup>c</sup>	86 <sup>c</sup>	2.185 <sup>c</sup>	213 <sup>c</sup>
Lysha	$[\text{CuA}_2\text{H}_2]^{2+}$	$2 \times 5\text{-}(\text{N}_{\alpha\text{-amino}}\text{-N}_{\text{hydroxamate}})$	530	90	2.184	205
Dambha	$[\text{CuA}_2\text{H}_2]^{2+}$		536	82	2.209	192
Dampha	$[\text{CuA}_2\text{H}_2]^{2+}$		ca. 565	ca. 76	2.219	193

<sup>a</sup> Ref. 42. <sup>b</sup> Ref. 43. <sup>c</sup> Ref. 9.

stoichiometry of the dimeric species is also different (see Table 3). These complexes are EPR silent, they are formed in the pH-range 4–6 and their  $\lambda_{\max}$  values (ca. 600 nm) correspond well to the co-ordination of two oxygen and two nitrogen donor atoms per copper(II).<sup>38</sup> Therefore the results are in good agreement with Fig. 2 and support the co-ordination of both oxygen and nitrogen atoms to copper(II) in this pH range. According to the EPR results, the dimeric species formed in the Cu(II)–Dampha and –Dambha systems, however, coexists with the species  $[\text{CuAH}]^{2+}$  for which the calculated  $g_{\parallel} = 2.239$  and  $2.248$  and  $A_{\parallel} = 190 \times 10^{-4}$  and  $186 \times 10^{-4} \text{ cm}^{-1}$ , respectively, are close, e.g., to the values for the Cu(II)–glycylglycine 1 : 1 complex ( $2.248$  and  $185 \times 10^{-4} \text{ cm}^{-1}$ ) with the co-ordination of ( $\text{NH}_2$ ,  $\text{N}^-$ ,  $\text{COO}^-$ ). This means that initial nitrogen co-ordination in  $[\text{CuAH}]^{2+}$  can be proposed.

At 1 : 1 metal to ligand ratio precipitation hindered the pH potentiometric measurements above pH 5, but EPR measurements proved the appearance of a new species at pH ca. 7.5 with  $g_{\parallel} = 2.232$  and  $A_{\parallel} = 191 \times 10^{-4} \text{ cm}^{-1}$  in the Cu(II)–Dambha system. The EPR parameters of this latter complex are very close to those of the mono-chelated-bis(hydroxo) species,  $[\text{Cu}(\text{bipyridine})(\text{OH})_2]^{39}$  supporting the co-ordination of two hydroxide ions in that new species.

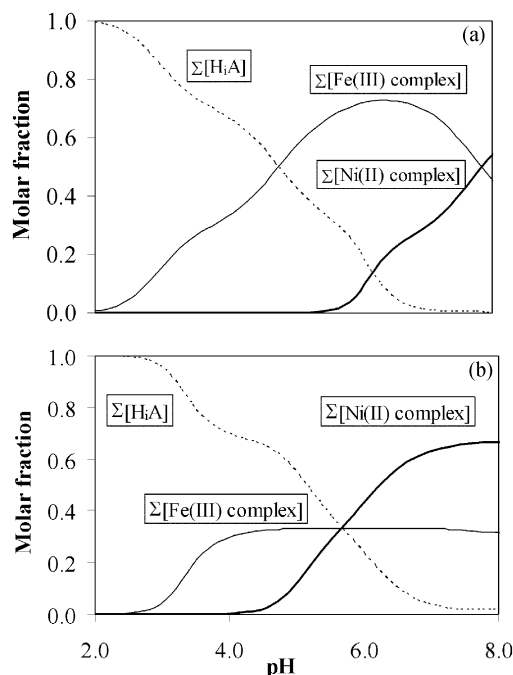
At ligand excess, above pH 6, bis-hydroxamate complexes with various stoichiometries are formed. EPR parameters and  $\lambda_{\max}$  values for some bis-complexes are collected in Table 4.

As shown in Table 4, spectral parameters for the species  $[\text{MA}_2\text{H}_2]^{2+}$  formed in the copper(II)–Dampha and –Dambha system are not completely consistent with the equatorial co-ordination of two ( $\text{N}_{\alpha\text{-amino}}$ ,  $\text{N}_{\text{hydroxamate}}$ ) donor sets. Though the  $\lambda_{\max}$  value measured for copper(II)–Dambha at pH 7 is close to the expected value (536 nm), on increasing the pH, it shifts slightly to ca. 560 nm. On the other hand,  $\lambda_{\max}$  values do not decrease below ca. 565–570 nm with Dampha at all, and  $[\text{MA}_2\text{H}_2]^{2+}$  was formed with this latter ligand only in low concentration. On the basis of the above experimental findings we can conclude that after their deprotonations the terminal amino-N atoms of Dambha and Dampha play a decisive role in the co-ordination. As is well known, the formation of ternary copper(II) complexes involving five- and six-membered chelates or oxygen and nitrogen donors is preferred.<sup>40</sup> Therefore, a rearrangement of the donor atoms in the equatorial positions and a ternary co-ordination mode according to **II** and **IV** (and perhaps also **I**) is probable. As can be seen in Table 4, both the EPR and UV–visible results of Dambha are consistent with this conclusion, since both the  $\lambda_{\max}$  and the  $g_{\parallel}$ ,  $A_{\parallel}$  parameters of its  $[\text{CuA}_2\text{H}]^+$  are between those for the corresponding bis-complexes of Lysha (or  $\alpha$ -Alaha) and pn.

At pH > 8, the  $[\text{CuA}_2]$  complex starts to form both in copper(II)–Dampha and copper(II)–Dambha systems. In parallel, the  $g_{\parallel}$  value increases somewhat and  $A_{\parallel}$  decreases indicating measurable axial co-ordination in these species (**V**). It is well known that axial co-ordination in copper(II) complexes results in a red shift (ca. 60–70 nm) of the  $\lambda_{\max}$  value.<sup>41</sup> With our ligands, however, the red shift is relatively small, only ca. 25–30 nm, which can be accounted for by the existence of isomeric species with or without axial co-ordination.

## Conclusions

The side chain amino site, depending on its distance from the aminohydroxamic moiety and on the character of the metal ion, may have a significant influence both on the co-ordination mode and on the metal ion selectivity of the ligand. Namely, for oxygen preferring metal ions the effect of the side chain amino group is realised mainly in the decrease of the basicity of the hydroxamate function and in the electrostatic repulsion between the positively charged groups and metal ions. There is a parallel decrease in the stability of the complexes formed, but it is able to co-ordinate to nickel(II) and copper(II) ions. As a consequence, while formation of highly stable octahedral nickel(II) complexes with Dambha and Dampha occurs, hydrolytic processes become more and more favoured in the order of Lysha, Dambha and Dampha e.g. with iron(III) or with aluminium(III). This results in the interesting phenomenon which is quite unusual with hydroxamic derivatives, that in a wide pH-range Dambha and especially Dampha bind dipositive ions, like nickel(II), much more strongly than iron(III). This is clearly demonstrated in Fig. 5 where the total amount of



**Fig. 5** Concentration ratio of the total free ligand (···), iron(III) complexes (—) and nickel(II) complexes (—) in hypothetical Ni(II)–Fe(III)–Lysha (a) and Ni(II)–Fe(III)–Dampha (b) systems ( $c_{\text{metal}} = 5 \times 10^{-3} \text{ mol dm}^{-3}$ , Ni(II) : Fe(III) : ligand ratio = 1 : 1 : 2).

iron(III) and nickel(II) chelated by Dampha as a function of pH is shown together with the corresponding results for Lysha.

Due to the changes occurring in metal complexation of these new molecules they might also have significantly different biological effects (such as enzyme inhibition) compared to their parent molecules. Such kinds of studies, however, were beyond the scope of this work.



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