Metal ion sequestering by borate–(amino)polyhydroxy oxime systems in aqueous solution; a ^{11}B, ^{13}C and ^{113}Cd NMR study

Jacco van Haveren, Joop A. Peters*, Jan G. Batelaan** and Herman van Bekkum
Laboratory of Organic Chemistry, Delft University of Technology, Julianalaan 136, 2628 BL Delft (Netherlands)

(Received July 30, 1991; revised October 28, 1991)

Abstract

Cu(II) and Cd(II) coordination to mixtures of (amino)polyhydroxy oximes and borate has been studied using ^{11}B, ^{13}C and ^{113}Cd NMR and titration procedures. The (amino)polyhydroxy oximes have strong Cu(II) coordinating properties, also in the absence of borate. The polyhydroxy oximes, on the contrary, have only low Cd(II) sequestering abilities. The metal ion complexing abilities of D-glucosamine oxime can be enhanced by the addition of borate. D-Glucosamine oxime forms borate diesters in which the borate is bound to the *threo*-3,4 diol functions. This species coordinates Cd(II) via the *E* isomers of both ligands by two oxime (or oximato) and two amino groups, while probably also two borate oxygens assist in the Cd(II) complexation. Factors determining metal ion coordination by borate diesters are discussed.

Introduction

Oximes and amino oximes are known to possess good complexing abilities for transition metal ions and have found some important applications. Hydroxy oximes are for instance applied in solvent extraction processes [1–3] for extracting metal ions from an aqueous solution into an organic solvent phase, while secondary α-amino oximes [4] have also been suggested as solvent extractants. Although carbohydrate oximes can easily be prepared by oximation of the corresponding monosaccharides, their metal ion coordinating abilities have hardly been investigated and, to our knowledge, only a single study on Pd(II), Pt(II), Co(II), Cu(II) and Ni(II) complexes of the carbohydrate oximes D-glucose oxime and D-glucosamine oxime has been published [5].

The metal ion sequestering properties of polyhydroxycarboxylates are known to increase upon addition of borate [6–10]. This synergic metal ion sequestration finds its origin in the good metal ion coordinating sites that are formed upon linking two polyhydroxycarboxylate ligands by borate. Also for (amino)polyhydroxy oximes addition of borate is expected to enhance metal ion sequestering abilities. Recently we have studied the borate ester formation in (amino)polyhydroxy oximes using ^{11}B and ^{13}C NMR [11]. Scheme 1 shows as a characteristic example the equilibria observed in a solution containing borate (B^-) and DL-glyceraldehyde oxime (L).

At pH > 5 borate mono- (B^-L) and diesters (B^-L_2) are formed, involving adjacent or alternate hydroxy groups. Between pH 5 and 12, borate esters involving the oxime hydroxyl are also formed, leading to six-membered ring borate mono- or diesters [B^-L_n (oxime)] ($n = 1$ or 2) of the *Z* forms of the oximes. As a result of the deprotonation of the oxime hydroxyl ($pK_a \approx 10.5$–11.5 [11, 12]), these esters dissociate above pH 11. For D-glucosamine oxime only B^-L_n esters are formed.

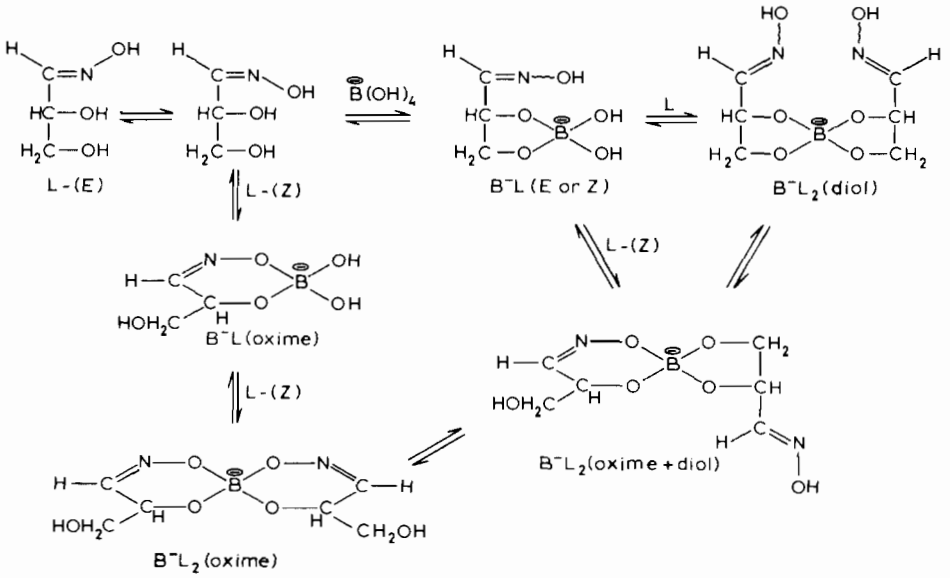
In this paper we present a multinuclear NMR study of the Cu(II) and Cd(II) sequestering abilities of mixtures of borate and the (amino)polyhydroxy oximes depicted in Fig. 1. Cu(II) was selected because of its known high affinity for oximes whereas Cd(II) was chosen as it is an interesting metal ion from an environmental point of view [13]. For D-glucosamine oxime (**7**) the coordinating abilities towards other metal ions were also investigated.

Experimental

DL-Glyceraldehyde oxime (**1**), D-arabinose oxime (**2**), D-mannose oxime (**3**), D-galactose oxime (**4**), D-glucose oxime (**5**), potassium-D-*xylo*-5-hexulosonate-5-oxime (**6**) and D-glucosamine oxime hydrochloride (**7**) were prepared and purified as described previously [11].

*Author to whom correspondence should be addressed.
**AKZO Corporate Research Department, Velperweg 76, 6824 BM Arnhem, Netherlands.

0020-1693/92/$5.00



Scheme 1. Borate ester formation of D-glyceraldehyde oxime.

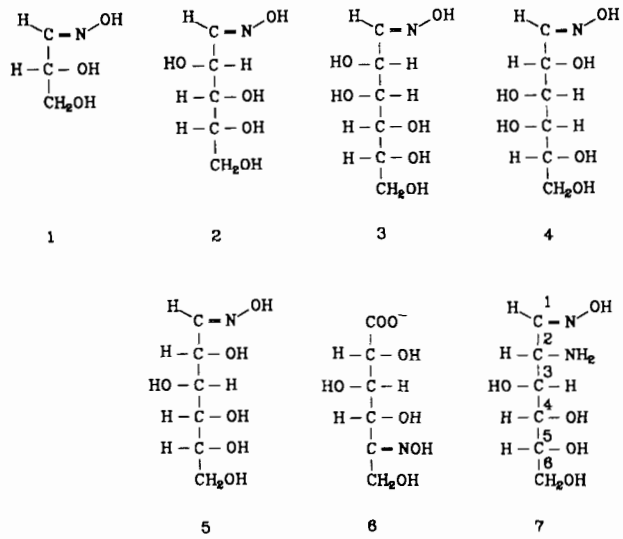


Fig. 1. Structures of the major *E* isomers of the (amino)polyhydroxy oximes (D_2O, 25 °C). For **1** the D-enantiomer is depicted, the major isomer of **6** has not been determined.

^{11}B NMR spectra were recorded at 25 °C on a Varian VXR-400 S spectrometer at 128.3 MHz or on a Nicolet NT-200 WB spectrometer at 64.2 MHz, with 0.1 M boric acid in D_2O as external reference ($\delta = 0.0$ ppm). Baseline correction was applied to remove the broad signal of the boron incorporated in the glass sample tube and the insert. A deconvolution program was used to obtain all the signal characteristics. ^{13}C NMR spectra were recorded at 25 °C on the same spectrometers at 100.6 and 50.3 MHz, respectively, using tert-butanol as internal standard ($\delta(CH_3) = 31.2$ ppm). For the ^{11}B and ^{13}C NMR measurements, the total boron concentration was 0.1–0.2 M, whereas the concentration of the (amino)polyhydroxy oximes varied between 0.1 and 0.4 M. Samples were prepared by dissolution of the appropriate amounts of boric acid and ligand in D_2O. The pH was adjusted with NaOH or HCl and measured with a calibrated MI 412 micro-combination probe from Microelectrodes, Inc. The pH values given are direct meter readings. Metal ions were added to the borate–(amino)polyhydroxy oxime systems as their chloride salts, except for Hg(II) where the nitrate was used and Mg(II) where the sulfate was used. Metal ion(II) sequestering capacities were determined according to Mehltretter *et al.* [14] or to a procedure used by Akzo Chemicals Research Center Deventer [15]. The metal ion sequestering capacities (at ambient temperature) were determined by adding a solution of Cd(II) or Cu(II) chloride to a solution containing 50–100 mg of ligand. Cd(II) sequestering capacities (CdSC), at pH 6.9, were determined using oxalate as the indicator. On using oxalate as the indicator solutions turned turbid only slowly. As endpoint of a titration procedure the first turbidity that appeared within 2 min after the last addition of Cd(II) was taken. CdSC, at pH 11.5, and CuSC were determined with the use of $NaOH/Na_2CO_3$ as indicator. As end point of a titration the first turbidity that had not disappeared within 30 s was taken.

^{113}Cd NMR experiments were performed at 88.70 MHz on a Varian VXR-400 S spectrometer. Samples were prepared by dissolution of the appropriate amounts of boric acid, ligand and $Cd(ClO_4)_2 \cdot 6H_2O$ in D_2O. The adjustment of pH was accomplished with either NaOH or $HClO_4$. Spectra were recorded at 50 °C. The pH values of the samples were measured at 25 °C and are direct meter readings. The ^{113}Cd chemical shift values

are referenced to external 0.1 M $Cd(ClO_4)_2$ ($\delta = 0.0$ ppm).

Results and discussion

Cu(II) and Cd(II) sequestering by the (amino)polyhydroxy oxime systems as studied by ^{11}B NMR and titration procedures

A practical way to determine the Cu(II) and Cd(II) sequestering abilities of the (amino)polyhydroxy oximes (Fig. 1) and their mixtures with borate, at various pH values, is a titration procedure with sodium oxalate or sodium carbonate as the indicator [14, 15]. The results compiled in Table 1 are a good indication of the sequestering abilities as our values obtained for ligands such as D-gluconate and D-glucarate were in good correspondence with literature values [14].

^{11}B NMR is suited for the determination of the species involved in the metal ion sequestration of borate esters. The exchange of borate between the borate anion and the borate mono- or diesters is slow on the ^{11}B NMR time-scale, leading to separate signals for the various boron-containing species (see Fig. 2(a)). Upon addition of metal ions the exchange of borate remains slow on the ^{11}B NMR time-scale and usually no new ^{11}B NMR signals appear. ^{11}B NMR measurements on solutions containing 0.1 M borate and 0.1 M ligand, with a coaxial inner tube containing 1 M borate, show that upon addition of Cd(II) the ratio of the intensity of the ^{11}B NMR signal of the inner tube versus the total intensity of the borate ester signals of the ligand solution remains constant. The linewidths of the borate esters increase proportional with the amount of metal ion added, indicating rapid exchange between the borate esters and their corresponding metal ion complexes. The different metal ion coordinating abilities of the boron-containing species are reflected in the change of the ratio in which the various species are present, in solution, upon metal ion addition (Fig. 2, Tables 2 and 3).

The results of Tables 1 and 2 clearly show that the Cu(II) sequestering abilities of the (amino)polyhydroxy oximes are not enhanced by addition of borate. At pH 11.5 compounds **2–7** exhibit strong Cu(II) sequestering capacities comparable to the sequestering capacities of industrially applied sequestrants like sodium-D-gluconate and potassium sodium-D-glucarate [14]. At pH 11.5 between one and two moles of copper are sequestered by one mole of ligand. Compounds **6** and **7** already have strong Cu(II) complexing abilities at pH 6.9, probably by virtue of the presence of a carboxylate or amino group, respectively, in the ligands (*vide infra*).

The ^{11}B NMR results (Table 2) indicate for all ligands a decrease of the percentage borate diesters present in solution upon Cu(II) addition, except for D-glucosamine oxime (**7**). The percentages of borate monoesters (B^-L and B^-L(oxime)) remain constant or decrease. This implies that in the polyhydroxy oxime–borate systems, upon Cu(II) addition, the amount of free ligand increases and that the amount of borate monoesters relative to the amount of borate diesters increases. Therefore, it can be concluded that in these systems Cu(II) is preferentially coordinated to the free ligand and to borate monoesters. The dissociation of the borate (di)esters upon Cu(II) addition can be explained by ionization of the α-hydroxy functions of **1** to **6** upon binding to Cu(II), which lowers the stabilities of the borate esters due to the proximity of two negative charges [16], or by competition between Cu(II) and borate for the binding sites. This dissociation of the borate (di)esters is similar to that recorded for D-glucarate [16] or polyhydroxyamino acids [17] at pH > 10. For D-glucosamine oxime upon addition of Cu(II) at pH 11.5, the NMR data suggest an increase of the amount of borate diesters. The accuracy, however, is

TABLE 1. Cadmium and copper sequestering capacities (CdSC and CuSC, respectively) of (amino)polyhydroxy oximes in the absence and presence of 0.5 molar equivalent borate[a]

(Amino)polyhydroxy oxime	CdSC in mg Cd(II)/g ligand				CuSC in mg Cu(II)/g ligand			
	without borate		with borate		without borate		with borate	
	pH 6.9	pH 11.5	pH 6.9	pH 11.5	pH 6.9	pH 11.5	pH 6.9	pH 11.5
1 DL-Glyceraldehyde oxime	10	5	10	5	30	80	30	60
2 D-Arabinose oxime	15	20	20	5	40	540	30	540
3 D-Mannose oxime	20	5	20	5	10	540	30	440
4 D-Galactose oxime	10	20	25	60	10	480	20	460
5 D-Glucose oxime	20	10	20	10	10	420	20	450
6 Potassium-D-*xylo*-5-hexulosonate-5-oxime	25	35	60	15	510	680	430	680
7 D-Glucosamine oxime	30	220	260	240	380	315	280	220

[a]Cadmium and copper sequestering values refer to duplicate measurements with an estimated error of 20%.

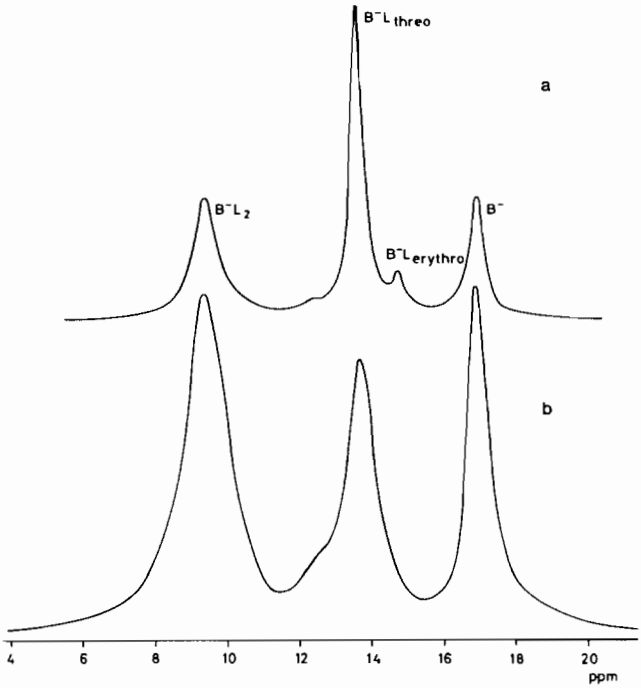


Fig. 2. ^{11}B NMR spectra of solutions containing 0.1 M D-glucosamine oxime and 0.1 M borate, in D_2O, pH 10.6: (a) without Cd(II), (b) with 0.05 M Cd(II). Assignments of the ^{11}B NMR signals of the borate esters were made by comparison with literature values of chemical shifts of related compounds (refs. 11, 16 and 17). The signal at −12 ppm in (a) is tentatively assigned to a $B_3O_3(OH)_5^{2-}$ species or a triborate ester derived thereof [36].

very low in this case, due to the severe line broadening of the ^{11}B NMR signals upon Cu(II) addition. The sequestering capacity (Table 1) points to sequestration of two moles of Cu(II) per mole of ligand and no enhancing effect of borate.

Addition of Cd(II) to the carbohydrate oxime–borate systems resulted in rather complex ^{11}B NMR spectra. The most simple case was that of D-glucosamine oxime (**7**) where addition of Cd(II), at pH > 5.9, led to the increase of the amount of borate diester (Table 3, Fig. 2). The exchange of the borate diesters and their corresponding Cd(II) complexes was fast on the ^{11}B NMR time-scale. However, for the polyhydroxy oxime–borate mixtures of **1–4**, upon addition of 0.04 M Cd(II) at pH 7–12, the metal ion exchange appeared to be slow. Addition of Cd(II) not only resulted in a change in the intensities of the various borate ester signals but also in the appearance of new borate ester signals for **1**, **2** and **4** at −16.9 to −17.2 ppm, which disappeared at pH > 10. On the basis of the chemical shifts and the pH behavior these signals are assigned to Cd(II) complexes of the B^-L(oxime) esters. Though for ligands **2–4** and **6**, at pH 7–8, upon addition of Cd(II) the amount of B^-L(oxime) esters (**2**, **3** and **6**) or B^-L esters (**3** and **4**) increased, these borate esters have only moderate Cd(II) coordinating abilities (Table 1). For none of the polyhydroxy oximes **1** to **6**, did addition of borate result in a significant increase of the Cd(II) sequestering abilities. From the data in Table 1 it can be calculated that less than 0.1 mol of Cd(II) is sequestered per mole of ligand, both in the absence and presence of 0.5 molar equivalent borate. The system borate–D-glucosamine oxime (**7**), on the contrary, showed both good Cd(II) and Cu(II) sequestering abilities and, at pH 6.9, a large increase in Cd(II) sequestering abilities upon adding borate. As this system evidently is the most interesting with regard to Cd(II) sequestration it was studied in more detail.

Metal ion sequestering of the D-*glucosamine oxime–borate system studied by* ^{11}B *NMR*

The effects of metal ion addition to the D-glucosamine oxime–borate system were studied for a series of other metal ions, at various pH values (see Fig. 3(a) and (b)). For Cu(II), Zn(II), Cd(II), Co(II) and Ni(II) other than the borate diester signal at −9.3 ppm and *threo*- and *erythro*-borate monoester signals (at −13.4 and −14.5 ppm, respectively), new borate ester signals at −11.9 to −12.3 ppm appeared upon introducing these metal ions to the borate–ligand solutions. These signals were assigned to $M(II)B^-L$ esters in slow exchange with the corresponding B^-L esters. The integrals showed that these metal ion complexes contained less than 14 mol.% of the total amount of boron. This indicates that, although the borate monoesters have some metal ion coordinating abilities, they are low compared to that of the borate diesters or the free ligands; *vide infra*. The exchange between the borate diesters and their M(II) complexes appeared to be fast on the ^{11}B NMR time-scale except for Ni(II) where, at [Ni(II)] < 0.02 M, two new signals appeared which might be attributed to $Ni(II)B^-L_2$ esters.

Figure 3(a) and 3(b) shows that at both pH 6 and pH 10.5, the coordinating strength of K(I), Ca(II), Mg(II), La(III) or Al(III) to the borate (di)esters of D-glucosamine oxime is comparable with that of the free ligand or the borate monoester(s). Above pH 6 addition of Cd(II), Zn(II), Ni(II) and Hg(II) led to an increase of the amount of ligand bound in borate diester species, demonstrating that these are stronger complexing species than the free ligand. Below pH 5.9 addition of Cd(II) had no influence on the amount of borate diesters. This was also observed for the system borate–2-amino-2-deoxy-D-gluconate [17], where no Cd(II) coordination by the borate diesters took place below pH 6, which reflects the inability of Cd(II) to deprotonate the ammonium group of amino acids at pH < 6 [18].

At pH 5.9 the amount of borate diesters decreased upon addition of Co(II) and Cu(II), indicating that for

TABLE 2. Effect of the addition of copper chloride on the composition of samples with borate and an (amino)polyhydroxy oxime as determined by ^{11}B NMR spectroscopy[a]

(Amino)polyhydroxy oxime	pH	C_b	C_l	$B^- + B^0$ (%)		B^-L_2 (%)		B^-L(oxime) (%)		B^-L (%)	
				$C_{Cu,\ 0.0}$	$C_{Cu,\ 0.04}$	$C_{Cu,\ 0.0}$	$C_{Cu,\ 0.04}$	$C_{Cu,\ 0.0}$	$C_{Cu,\ 0.04}$	$C_{Cu,\ 0.0}$	$C_{Cu,\ 0.04}$
1 DL-Glyceraldehyde oxime	6.9	0.10	0.91	68	55	6	6	19	25	7	14
	10.4			4	8	16	12	47	47	33	33
2 D-Arabinose oxime	7.1	0.10	0.10	61	70	18	7	15	15	6	7
	10.1			8	42	20	4	35	19	37	35
3 D-Mannose oxime	8.0	0.10	0.13	21	29	44	34	18	14	21	19
	10.2			1	14	22	18	40	19	38	48
4 D-Galactose oxime	7.1	0.11	0.10	50	64	27	15	12	9	10	12
	10.2			10	31	30	17	20	9	40	43
5 D-Glucose oxime	7.2	0.10	0.10	62	70	15	8	5	6	18	16
	10.3			14	35	18	4	18	12	50	49
6 Potassium-D-*xylo*-5-hexulosonate-5-oxime	6.8	0.12	0.19	27	30	26	23	12	12	35	35
	11.0			4	10	18	14	37	33	41	42
7 D-Glucosamine oxime	5.9	0.12	0.11	72	83	20	9	–	–	8	8
	11.0			28	31	24	42	–	–	49	27

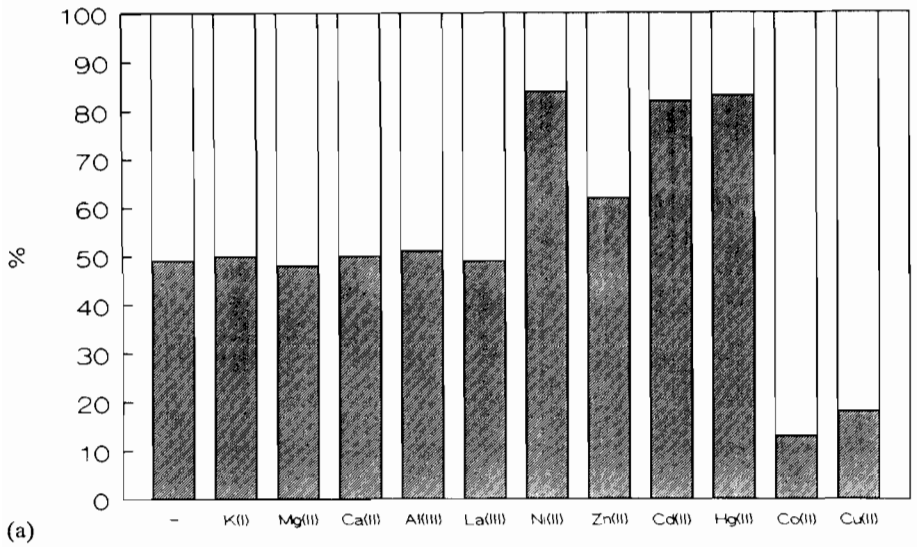
[a]Percentages (%) borate esters are given as the sums of the borate esters, including their corresponding Cu(II) complexes. Total concentrations of boron-containing species (C_b) and oxime (C_l) are in M. Estimated relative errors in the percentrages borate esters are less than 5% in the absence of metal ions and less than 10% in the presence of metal ions.

TABLE 3. Effect of the addition of cadmium chloride on the composition of samples with borate and an (amino)polyhydroxy oxime as determined by ^{11}B NMR spectroscopy[a]

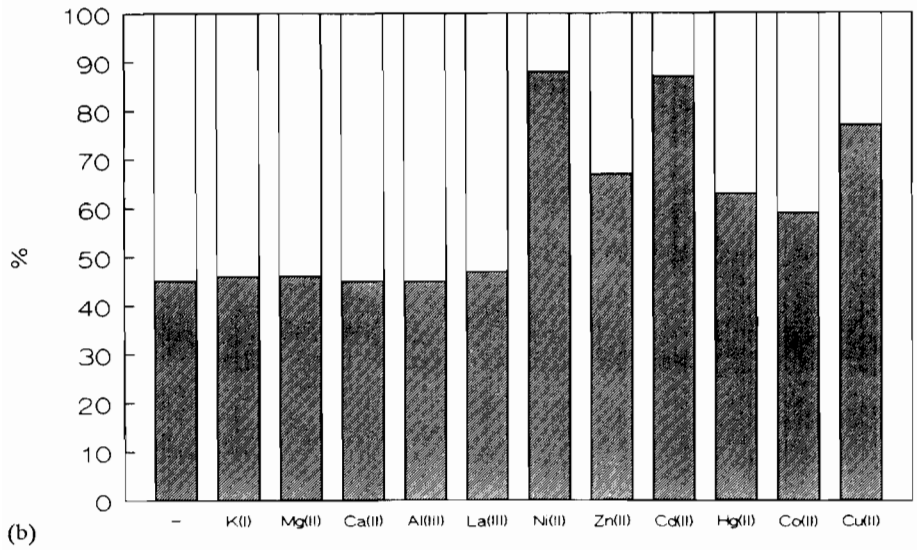
(Amino)polyhydroxy oxime	pH	C_b	C_l	$B^- + B^0$ (%)		B^-L_2 (%)		B^-L(oxime) (%)		B^-L (%)	
				$C_{Cd,\ 0.0}$	$C_{Cd,\ 0.04}$	$C_{Cd,\ 0.0}$	$C_{Cd,\ 0.04}$	$C_{Cd,\ 0.0}$	$C_{Cd,\ 0.04}$	$C_{Cd,\ 0.0}$	$C_{Cd,\ 0.04}$
1 DL-Glyceraldehyde oxime	7.0	0.10	0.89	68	44	7	11	18	29	6	16
	10.4			4	4	18	22	40	39	38	35
2 D-Arabinose oxime	7.6	0.10	0.11	46	16	24	23	17	43	13	19
	11.1			12	16	7	6	49	47	32	31
3 D-Mannose oxime	8.1	0.10	0.10	25	15	32	27	19	29	23	29
	11.2			13	16	16	15	32	32	39	27
4 D-Galactose oxime	7.1	0.10	0.10	48	22	28	23	13	12	11	42
	11.7			7	10	25	37	18	9	49	43
5 D-Glucose oxime	7.2	0.10	0.10	54	59	22	14	5	7	18	18
	11.7			21	33	9	5	14	13	55	52
6 Potassium-D-*xylo*-5-hexulosonate-5-oxime	7.2	0.11	0.12	46	32	13	12	9	38	32	17
	10.8			6	16	11	4	38	41	44	32
7 D-Glucosamine oxime	7.1	0.11	0.12	48	49	29	38	–	–	27	13
	10.5			28	25	24	49	–	–	46	20

[a]Percentages (%) borate esters are given as the sums of the borate esters, including their corresponding Cd(II) complexes. Total concentrations of boron-containing species (C_b) and oxime (C_l) are in M. Estimated relative errors in the percentages borate esters are less than 5% in the absence of metal ions and less than 10% in the presence of metal ions.

these metal ions the free ligands are stronger complexing species than the borate diesters. With the use of ^{13}C longitudinal relaxation rate measurements it has been shown that at pH 6.9 Cu(II) is coordinating to D-glucosamine oxime via the amino and oxime nitrogens [19]. This gives, in a 1:2 complex, a Cu(II) metal ion complexed via two amino and two oxime nitrogens in probably an approximately square plane. In similar complexes the formation of an oxime–oximato hydrogen bond (=N−O−H...$^-$O−N=) lying in the Cu(II) coordinating square plane, significantly attributes to the complex stability [20, 21]. Oxime–oximato hydrogen bonds can, for Cu(II) complexes, be formed at pH values as low as 3, while deprotonation of the second



(a)



(b)

Fig. 3. Percentage ligand bound in the borate diesters (■) of D-glucosamine oxime. (a) pH 6.0–6.2, D_2O, 25 °C, C_B and $C_L = 0.1$ M, C_M: K(I), Ca(II), Mg(II), Cd(II), Co(II), Zn(II), Ni(II), Hg(II); 0.05 M, C_M: La(III); 0.04 M, Al(III); 0.02 M. (b) pH 10.5–10.6, D_2O, 25 °C, C_B and $C_L = 0.1$ M, C_M: K(I), Ca(II), Mg(II), Cd(II), Co(II), Zn(II), Ni(II), Hg(II); 0.05 M, C_M La(III); 0.02 M, Al(III); 0.04 M.

oxime hydroxyl was not observed below pH 10 [21]. In the *threo-3,4*-borate diesters of D-glucosamine oxime, as a result of the linking of the ligands by the tetrahedral boron atom, coordination of Cu(II) or Co(II) via two amino and two oxime nitrogens with the concomitant existence of an intramolecular oxime–oximato hydrogen bond is sterically impossible. Consequently, at pH 5.9, the stability of the Cu(II)– or Co(II)–borate diester complex is considerably lower than that of a 1:2 complex with the free ligand, explaining the decrease of the amount of borate diester upon introducing Cu(II) and Co(II). At pH 10.5, in a 1:2 complex of Cu(II) or Co(II) with **7**, an intramolecular oxime–oximato hydrogen bond no longer contributes to the complex stability for at that pH both oxime hydroxyls are deprotonated. Oxime and oximato groups have about similar coordinating strengths [22] and therefore most probably Cu(II)– and Co(II)–**7** 1:2 complexes are less stable at pH 10.5 than at pH 6.9. Apparently, at pH 10.5, 1:2 complexes of Cu(II) or Co(II) with the free ligand are less stable than the Cu(II)– or Co(II)–borate diester complexes as is reflected by the increase of the amount of borate diesters upon adding Cu(II) or Co(II).

Structures of the borate esters of D-*glucosamine oxime studied by* ^{13}C *NMR*

Chemical shifts of D-glucosamine oxime and its borate esters were recorded as a function of pH (Fig. 4) in

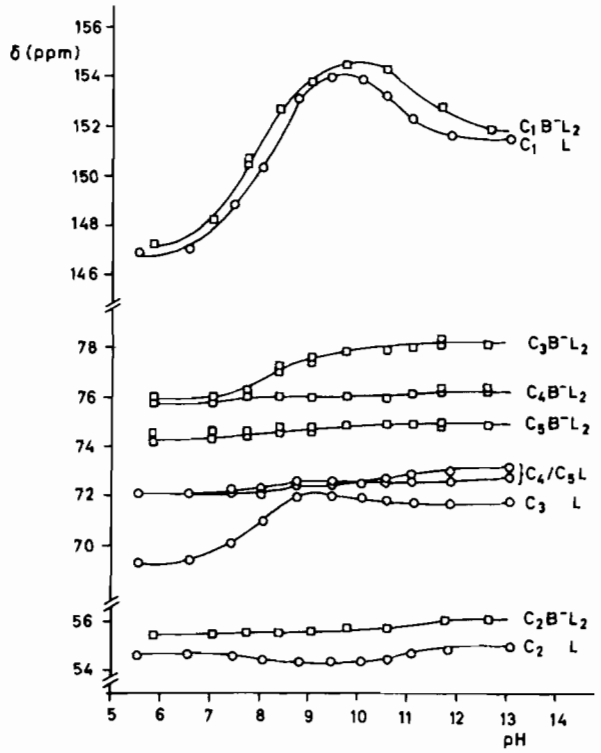


Fig. 4. ^{13}C NMR chemical shifts of *E*-D-glucosamine oxime (7) and its borate diesters as a function of pH (0.2 M borate and 0.4 M 7).

order to further establish the borate binding site proposed on the basis of the ^{11}B NMR data. The ^{13}C NMR signals of the imine carbons of both *E* and *Z* isomers (molar ratio 4:1) of D-glucosamine oxime, underwent a downfield change of chemical shift upon increasing the pH from 6.6 to 9.4. This can be attributed to the deprotonation of the ammonium group [17, 23, 24]. The upfield change of the chemical shifts observed between pH 9.5 and 13.0 results from the deprotonation of the oxime hydroxy groups.

The pH effects on the ^{13}C chemical shifts of amino acids are known to be relatively small for C_α (i.e. the carbon atom bearing the ammonium group), largest for C_β (C3 of **7**) and decrease in the order $C_\beta > C_\gamma > C_\delta$ [17, 23]. Assuming that the magnitudes of the pH effects on the chemical shifts for **7** and its borate esters are similar, the signals (see Fig. 4) were assigned. The substituent effect of 6.3 ppm (pH 11–13) for C3 of **7** upon borate ester formation shows that the C3 carbon is in the borate ester ring, as a similar substituent effect was observed in *threo*-3,4-borate esters of polyhydroxyamino carboxylates [17]. Since the ligands and the boron center in the borate diesters both are chiral two diastereoisomers are possible. For **7** doubling of the signals for C3, C4 and C5 of the borate diesters was observed showing the presence of the two diastereoisomers in about equal amounts. The ratio of both diastereoisomers was almost independent of the pH. Borate esters of both *E* and *Z* isomers of **7** are formed as demonstrated by a signal at 50.6–50.8 ppm, attributed to the C2 carbon of a borate ester having a *Z* configuration (the signal for the C2 carbon of the borate diester with a *E* configuration is at 55.4–55.9 ppm, see Fig. 4). For the other signals no separate borate ester signals of *E* and *Z* isomers could be detected, probably due to the small chemical shift difference.

From the ^{13}C NMR chemical shift versus pH curves (Fig. 4) it was derived that the pK_a value for the ammonium groups of both the *E* and *Z* isomers of D-glucosamine oxime is 7.9 ± 0.2 (D_2O, 25 °C) and that of the oxime group is 10.8 ± 0.2. Taking into account that pK_a (H_2O) = pK_1 (D_2O) − 0.49 [25], the pK_a value of the ammonium group agrees very well with that reported for D-glucosamine [26]. For the borate esters a pK_a value for the ammonium group of 8.1 ± 0.2 was determined, whereas that of the oxime group is 11.3 ± 0.2.

The D-glucosamine oxime–borate–cadmium(II) system as studied by ^{13}C and ^{113}Cd NMR

Stepwise addition of Cd(II) to solutions containing 0.22 M D-glucosamine oxime and 0.1 M borate at pH 8.8, up to $C_{Cd} = 0.09$ M, led to an upfield shift for all the borate diester ^{13}C signals, showing that the exchange of Cd(II) between the various coordinating species is fast on the ^{13}C NMR time-scale. Upon adding Cd(II) resonances broadened and signals for the diastereoisomeric forms were no longer resolved. The addition of Cd(II) resulted in an increase of the intensity of the signals of the borate diesters whereas those of the free ligand decreased. The intensity of the signal at 50.7 ppm, attributed to C2 of a borate-*Z*-(di)ester, also diminished demonstrating that Cd(II) is preferentially coordinated by borate-*E*-diesters. The ^{13}C resonances for the Cd(II)B^-L_2 ester of **7** appeared to be pH dependent. The pH effect on the imine carbon signal was analogous to that observed for the corresponding nuclei of both the free ligand and the borate diesters and can be related to the ionization of the oxime hydroxyls of the Cd(II)B^-L_2 ester of **7**. From the ^{13}C NMR chemical shift versus pH curves a pK_a value for the oxime hydroxy groups for the Cd(II)B^-L_2 ester of 9.6 ± 0.2 was derived, which indicates that Cd(II) lowers the pK_a of the oxime hydroxy group by about 1.7 pH units.

No downfield shift, characteristic for deprotonation of the ammonium groups, for the imine carbon signal of the Cd(II)B^-L_2 ester was recorded implying that in this borate ester the ammonium groups are deprotonated over the pH range 6 to 13. The ^{13}C NMR data suggest preferential binding of Cd(II) by an *E*-glucosamine oxime borate diester via two amino and

two oxime groups at pH 6 to 9 and via two amino and two oximato groups above pH 10. The stoichiometry of this species is in agreement with the data of Table 1 which indicate that one mole of Cd(II) is sequestered by two moles of **7** in the presence of 0.5 molar equivalent borate compared to ligand.

^{113}Cd NMR is suited for revealing coordination sites of complexing species as the ^{113}Cd chemical shift is very sensitive to the coordination mode of the metal ion, including donor atoms, coordination number, geometry and solvent [27, 28]. Cd(II) complexes of small ligands tend to be rather labile, especially in aqueous solution and the exchange of Cd(II) often is fast on the ^{113}Cd NMR time-scale [28], resulting in an average signal for different Cd(II) complexes present in solution. ^{113}Cd NMR on solutions containing Cd(II) and **7** in the presence and absence of borate was performed at 50 °C as at 25 °C linewidths, at 9.4 T, were usually very large ($\Delta\nu_{1/2} > 1000$ Hz) due to exchange phenomena. At pH 10.2 and 50 °C, the chemical shift gradually increased as a function of the ligand to Cd(II) ratio, reaching a limiting value of 209 ppm at a ratio >4. Addition of ligand to a solution containing 0.08 M H_3BO_3 and 0.08 M Cd(II) at pH 6.5 led to the appearance of two signals, the chemical shifts of both being dependent on the amount of ligand added. The intensity of the signal with the highest chemical shift increased at the expense of the other and, after adding 0.16 M ligand only that signal (at 167 ppm) was present. As we know from the ^{11}B and ^{13}C NMR data that under these conditions almost all Cd(II) is sequestered by one of the borate diesters we attribute this ^{113}Cd signal to the Cd(II) complex of the borate diester of **7**.

In a solution containing borate, Cd(II) and **7** in a ratio B^-Cd(II):L = 1:1.7:4.1, at pH 5.4 and 50 °C, one signal was observed with a chemical shift of 96 ppm. Between pH 5.8 and pH 9 two signals were observed which merged into one at pH > 9 (see Fig. 5). The intensity of the signal with the highest chemical shift, assigned to the Cd(II)B^-L_2 complex, increased between pH 5.4 and pH 6.7 (see Fig. 6). Above this pH approximately 55–60% of the total amount of Cd(II) was bound in this Cd(II)B^-L_2 species, very close to the theoretical amount of 1/1.7×100% which has to be expected for such a species given the B^-:Cd(II):L ratio. This therefore affirms the assignment of the signal. The signal at 96 ppm (pH 5.4) is assigned to Cd(II)Cl_n complexes (Cl, $n = 1$ to 4 [27]). The increase of the chemical shift of the signal with the lowest chemical shift between pH 5.4 and pH 9 reflects the formation of Cd(II)L_n complexes (probably $n = 1$ to 3 for **7***). At pH 5.9 the borate diester of **7** appears to be a much stronger coordinating species than the free ligand which gives a large chemical shift difference between the corresponding ^{113}Cd NMR signals and results in slow

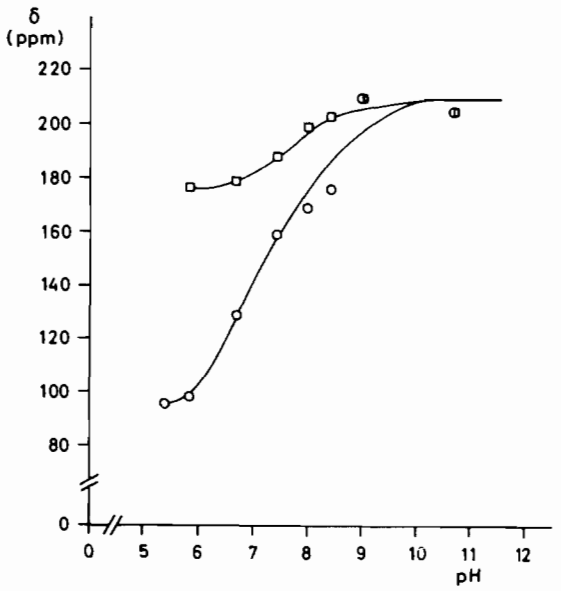


Fig. 5. ^{113}Cd NMR chemical shifts, observed as a function of pH, from a solution containing borate, cadmium(II) and D-glucosamine oxime in a ratio B^-:Cd(II):L = 1:1.7:4.1, in D_2O at 50 °C (0.16 M Cd(II)); □, Cd(II)B^-L_2; ○, Cd(II)Cl_n or Cd(II)L_n.

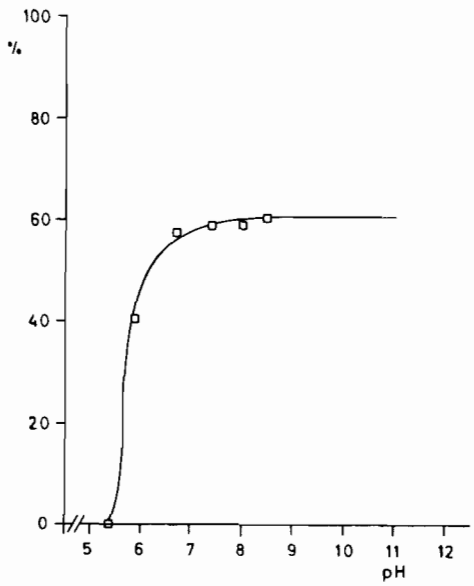


Fig. 6. Percentage Cd(II) bound in the borate diester of **7**, as a function of pH, in a solution containing borate, cadmium(II) and **7** in a ratio B^-: Cd(II):L = 1:1.7:4.1, in D_2O at 50 °C (0.16 M Cd(II)).

*The ^{113}Cd NMR chemical shift for **7** of 209 ppm at a Cd(II): ligand ratio of 7.7 and pH 10.2 is nearly equal to that observed for mixtures of Cd(II) and 2-amino-2-deoxy-D-gluconate [17] at the same ratio and pH ($\delta = 208$ ppm). For 2-amino-2-deoxy-D-gluconate, on the basis of ^{113}Cd NMR results of glycine complexes, it was concluded that this indicated that the highest order complex formed was Cd(ligand)$_3$.

exchange. Increase of the pH reduces the difference in coordinating capacity between the B^-L_2 ester and the free ligand (as is also shown by the Cd(II) sequestering tests; Table 1). The formation of more of the $Cd(II)L_n$ complexes leads to a smaller chemical shift difference between the species and eventually to coalescence (pH > 9).

Complexation of Cd(II) to oxygen donor atoms is known to result in a shielding of the ^{113}Cd NMR signal, whereas complexation to N, S and halogen donor atoms generally leads to deshielding of the ^{113}Cd signals [27, 28]. Recently we have observed a ^{113}Cd NMR chemical shift of 119 ppm for the Cd(II) borate diester of 2-amino-2-deoxy-D-gluconate, at pH 7.0 and 50 °C [17]. In this borate diester the Cd(II) is complexed via two amino and two carboxylate groups. The ^{13}C NMR results for **7** show coordination of the Cd(II) metal ion in the borate diester via two amino and two oxime (or oximato) groups. The somewhat more deshielded ^{113}Cd NMR chemical shift for the $Cd(II)B^-L_2$ species of **7** ($\delta = 167$ ppm) therefore indicates coordination via the oxime nitrogen*. Consequently Cd(II) is complexed by the borate diester of **7** as depicted in Fig. 7.

^{113}Cd NMR spectra of a solution containing Cd(II) and **7** (Cd(II):7 = 1:4.3) as a function of pH showed a pH dependent chemical shift below pH 9. Above pH 9 the chemical shift remained constant and no effect of the ionization of the oxime hydroxyl on the ^{113}Cd NMR chemical shift was noted. This suggests that the coordination mode of the Cd(II) ion is hardly affected by the ionization of the oxime hydroxyl at high pH.

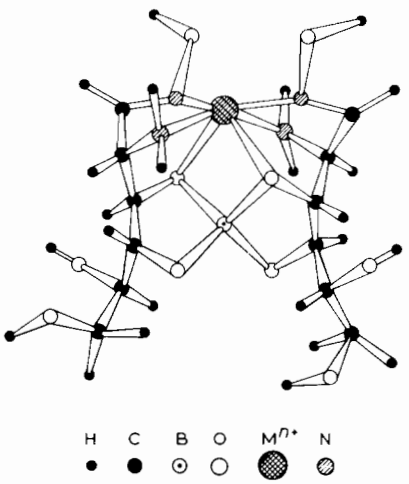


Fig. 7. Structure for the Cd(II) complex of the borate diester of the *E* isomer of D-glucosamine oxime (the oxime hydroxyls are deprotonated above pH ≈ 10).

*It was observed, by addition of excess NaCl, that the presence of Cl had hardly any effect on the chemical shift of the $Cd(II)B^-L_2$ species of **7** (**7** is isolated as the hydrochloride).

Conclusions

Previous studies have shown that synergic metal ion sequestering by borate diesters is related to the metal ion, the stability of the borate diesters, the number and nature of the metal ion binding sites and the pH [8, 10, 16, 17]. In mixtures of polyhydroxy(amino) carboxylates and borate, metal ion complexation was found to be best for borate diesters in which the borate is bound at a *threo*-3,4-diol position and in which the hydroxy or amino group at C2 has a 'gluco configuration'. A gluco configuration at C2 enables the donor group to participate in metal ion sequestering by the borate diesters, whereas a donor group with a manno configuration at C2 is not able to participate in metal ion coordination.

Addition of borate enhances metal ion sequestering abilities most for those metal ions which form complexes of moderate stability with ligands in the absence of borate. A typical representative of such a metal ion is Cd(II), which forms complexes with, for example, a series of aminopolycarboxylates [12] and polyhydroxycarboxylates [29] that are stronger than those of alkaline earth metal ions but, according to the Irving–Williams order, weaker than that of, for example, Cu(II). In the present study synergic Cd(II) complexation is found for the Cd(II)–D-glucosamine oxime–borate system at pH > 6. The amount of Cd(II) sequestered is comparable to that found for the systems borate–D-gluconate and borate–2-amino-2-deoxy-D-gluconate [17]. In both these systems the borate is bound at the *threo*-3,4-diol position and four functional groups (two carboxylate and two hydroxy or two carboxylate and two amino groups, respectively) and probably two borate oxygens are able to cooperate in Cd(II) binding. For none of the borate–polyhydroxy oximes **1**–**6** was a strong Cd(II) coordination recorded. This can partly be explained by the fact that at pH < 11 borate esters involving the oxime hydroxyl are formed thereby blocking the oxime hydroxyl as a coordinating group. Furthermore for the polyhydroxy oximes **1** and **2** no *threo*-3,4 borate diesters are formed whilst in the case of **2** and **3** the ligands do not possess a gluco configuration at C2. Though the polyhydroxy oximes **4** and **5** satisfy the condition of a gluco configuration at C2 and for **5** *threo*-3,4 borate diesters will be formed, no strong Cd(II) complexation has been found for these ligands.

Stabilities of metal ion complexes with ligands are known to be related to the basicity of the donor groups and the estimation of log K_1 values based on donor group additivity can be very successful [30, 31]. Considering the free ligands which in combination with borate have shown strong Cd(II) coordinating abilities, 2-amino-2-deoxy-D-gluconate will form the strongest complexes as the sum of the pK_as of its donor groups

is largest: 2-amino-2-deoxy-D-gluconate; pK_a $NH_3^+ = 9.08$, pK_a COOH = 2.20; 25 °C, $I = 0.05$, H_2O [29], D-glucosamine oxime; pK_a $NH_3^+ = 7.9$ (D_2O, 25 °C) $pK_a = NH^+OH \approx -1$ [32], D-gluconate; pK_a COOH = 3.56; [12] (25 °C, $I = 0.1$, H_2O) and pK_a α-$OH_2^+ \approx pK_a$ $H_3O^+ = -1.74$ [33]. Although the stability constants for the Cd(II) complexes of D-glucose oxime and the other polyhydroxy oximes have not been determined the basicity–stability constant relations indicate that such complexes will be weak, explaining the low Cd(II) sequestering abilities of the polyhydroxy oximes. Cu(II), on the other hand, is known to ionize α-hydroxy functions of polyhydrocarboxylates above pH 4 [34], whereas in the absence of Cu(II) or metal ions α-hydroxy functions of polyhydroxycarboxylates have $pK_a(OH) \approx 14$–15 [34, 35]. This ionization of α-hydroxy functions explains the large Cu(II) sequestering capacities for the polyhydroxycarboxylate **6** at both pH 6.9 and 11.5. For the polyhydroxy oximes **1–5** at pH 11.5 strong Cu(II) sequestering abilities were determined whilst they were low at pH 6.9. This suggests that Cu(II) is able to deprotonate α-hydroxy functions of polyhydroxy oximes at pH 11.5 whereas it is not able to do so at pH 6.9. This is in line with the basicity–stability constant relations that predict that for polyhydroxy oximes the ionization of the α-hydroxy function will occur at higher pH than for polyhydroxycarboxylates.

Acknowledgements

This investigation was carried out with support of the Dutch National Innovation Oriented Program Carbohydrates (IOP-k). We than Akzo Corporate Research for financial support. Mr A. Sinnema is thanked for recording part of the NMR spectra.

References

1 M. Harada, Y. Miyake and Y. Kayahara, *J. Chem. Eng. Jpn., 22* (1989) 168.
2 M. Cox and D. Flett, *Chem. Ind.,* (1987) 188.
3 A. W. Ashbrook, *Coord. Chem. Rev., 16* (1975) 285.
4 E. Uhlig, J. Becher, K. Gloe, P. Mühl and J. Beger, *Z. Anorg. Allg. Chem., 518* (1984) 187.
5 Y. Nagel and W. Beck, *Z. Naturforsch., Teil B, 41* (1986) 1447.
6 H. Peters, *Neth. Patent Applic. 99 202 1961; C. A., 56* (1962) 12682.
7 M. van Duin, J. A. Peters, A. P. G. Kieboom and H. van Bekkum, *Tetrahedron, 41* (1985) 3411.
8 M. van Duin, J. A. Peters, A. P. G. Kieboom and H. van Bekkum, *J. Chem. Soc., Perkin Trans. 2,* (1987) 473.
9 M. van Duin, J. A. Peters, A. P. G. Kieboom and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas, 105* (1986) 488.
10 M. van Duin, J. A. Peters, A. P. G. Kieboom and H. van Bekkum, *Carbohydr. Res., 162* (1987) 65.
11 J. van Haveren, M. H. B. van den Burg, J. A. Peters, J. G. Batelaan, A. P. G. Kieboom and H. van Bekkum, *J. Chem. Soc., Perkin Trans. 2,* (1991) 321.
12 A. E. Martell and R. M. Smith, *Critical Stability Constants,* Vol. 3, Plenum, New York, 1977.
13 R. Lauwerys, in M. Webb (ed.), *The Chemistry, Biochemistry and Biology of Cadmium,* Elsevier/North-Holland Biomedical Press, Amsterdam, 1979, p. 433.
14 C. L. Mehltretter, B. H. Alexander and C. E. Rist, *Ind. Eng. Chem., 45* (1953) 2782.
15 G. Bekendam, Akzo Chemicals Research Center Deventer, personal communication.
16 M. van Duin, J. A. Peters, A. P. G. Kieboom and H. van Bekkum, *J. Chem. Soc., Dalton Trans.,* (1987) 2051.
17 J. van Haveren, J. A. Peters, J. G. Batelaan, A. P. G. Kieboom and H. van Bekkum, *J. Chem. Soc., Dalton Trans.,* (1991) 2649.
18 S. M. Wang and R. K. Gilpin, *Anal. Chem., 55* (1983) 493.
19 J. van Haveren, H. van Bekkum and J. A. Peters, to be published.
20 R. K. Murmann, *J. Am. Chem. Soc., 80* (1958) 4174.
21 J. W. Fraser, G. R. Hedwig, H. K. J. Powell and W. T. Robinson, *Aust. J. Chem., 25* (1972) 747.
22 G. R. Hedwig and H. K. J. Powell, *J. Chem. Soc., Dalton Trans.,* (1974) 47.
23 A. R. Quirt, J. R. Lyerla, I. R. Peat, J. S. Cohen, W. F. Reynold and M. H. Freedman, *J. Am. Chem. Soc., 96* (1974) 570.
24 E. Breitmaier and W. Voelter, *^{13}C NMR Spectroscopy,* Verlag Chemie, Weinheim, FRG, 1974.
25 P. N. Turowski, S. J. Rodgers, R. C. Scarrow and K. N. Raymond, *Inorg. Chem., 27* (1988) 474.
26 A. M. Martell and R. M. Smith, *Critical Stability Constants,* Vol. 5, Plenum, New York, 1982.
27 P. D. Ellis, *Science, 221* (1983) 1141.
28 M. Munakata, S. Kitagawa and F. Yagi, *Inorg. Chem., 25* (1986) 964, and refs. therein.
29 A. E. Martell and R. M. Smith, *Critical Stability Constants,* Vol. 1, Plenum, New York, 1974.
30 R. D. Hancock and A. E. Martell, *Chem. Rev., 89* (1989) 1875.
31 R. D. Hancock and F. Marsicano, *J. Chem. Soc., Dalton Trans.,* (1976) 1096.
32 H. Kipton, J. Powell and J. M. Russell, *Aust. J. Chem., 31* (1978) 2409.
33 F. Coccioli and M. Vicedomini, *J. Inorg. Nucl. Chem., 40* (1978) 2106.
34 M. van Duin, J. A. Peters, A. P. G. Kieboom and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas, 108* (1989) 57.
35 D. C. Neckers and M. P. Doyle, in *Organic Chemistry,* Wiley, New York, 1977, p. 305.
36 J. M. Coddington and M. J. Taylor, *J. Coord. Chem., 20* (1989) 27.