Co-ordination of Copper(II) with Monoamino-triols and -tetrols. Effect of Stereochemistry on Complex Formation

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A series of 4-aminobutanetriols and 5-aminopentanetetrols was synthesised and their co-ordination abilities towards copper(II) studied by potentiometry and spectroscopic techniques (UV/VIS, ESR and CD). The basic binding mode involves the amino nitrogen and the adjacent deprotonated hydroxyl group. The latter donor acts as a bridge between two metal ions giving stable dimeric species. No monomeric complexes were detected in the systems studied. The formation of the alkoxo-bridged complexes seems to be the most characteristic feature of the investigated ligands. Other hydroxyl donors are also involved in the metal-ion binding. The stability constants calculated from the pH-metric data showed that the chirality of the carbons in an aminoalcohol molecule may have a considerable effect on its co-ordination ability.

There is much chemical and biochemical interest in metal complexes with a variety of aminopolyalcohols. Aminoalcohols exhibit a great diversity of co-ordination modes with different metal ions exhibiting different N,O environments.[1–10] The structures of the complexes formed are usually monomeric but sometimes oligomeric with interesting physicochemical properties. Biologically, aminosugars, naturally occurring analogues of aminoalcohols, may act as powerful ligands for metal ions such as Cu$^{\mathrm{II}}$, the amino group usually providing an efficient anchor for a metal ion.[1,5,9,10]

Many studies have been performed to elucidate the structures of the complexes formed as well as the physicochemical characteristics of oligomeric structures. Not much is known, however, about the impact of chirality of particular carbons or the influence of the length of the carbon chain bearing various numbers of alcoholic groups on the structure and stability of the metal–aminoalcohol species. In this work we have studied the co-ordination of copper(II) ions to a series of diastereoisomers of monoamino-triols and -tetraols. The spectroscopic and potentiometric results are discussed in this paper.

Experimental

Chemical Synthesis of Aminoalcohols.—(2*S*,3*S*)-4-Aminobutane-1,2,3-triol (*SS*-abto), was prepared by the borane–tetrahydrofuran reduction of the appropriate 2,3,4-trihydroxy-*O*-trimethylsilyl-L-butanamide according to Kiely *et al.*[11] employing as starting material calcium (*R**,*S**)-L-2,3,4-trihydroxybutanoate (Aldrich). M.p. (as toluene-*p*-sulfonate) 95–97 °C [Found: C, 35.65; H, 4.65; N, 16.40. Calc. for $C_{10}H_{14}N_3O_9$ (picrate salt): C, 35.95; H, 4.20; N, 16.75%]. Prepared in the same way were: (2*R*,3*S*)-4-aminobutane-1,2,3-triol (*RS*-abto), starting from calcium (*R**,*R**)-2,3,4-trihydroxybutanoate prepared from starch,[12] m.p. (as toluene-*p*-sulfonate) 109–111 °C [Found: C, 34.60; H, 4.35; N, 16.00. Calc. for $C_{10}H_{14}N_3O_9{\cdot}xH_2O$ (picrate hydrate): C, 34.10; H, 4.60; N, 15.90%], (2*R*,3*S*,4*S*)-5-aminopentane-1,2,3,4-tetrol, (*RSS*-aptteo), starting from calcium D-ribonate prepared from D-ribose, m.p. (as hydrochloride): 129–134 °C, lit., 128–133,[11] 133 °C,[13] (2*R*,3*S*,4*R*)-5-aminopentane-1,2,3,4-tetrol (*RSR*-aptteo), starting from calcium D-arabinoate prepared from D-arabinose, m.p. (as hydrochloride) 134–138 °C, lit., 135–135.5,[14] 136.5–137.5 °C,[15] and (2*R*,3*R*,4*R*)-5-aminopentane-1,2,3,4-tetrol (*RRR*-aptteo), starting from calcium D-lyxonate prepared from D-lyxose, m.p. (as hydrochloride) 255–260 °C, chromatographically pure, analysis as expected of a monohydrate.[14]

Carbon-13 NMR spectra were recorded with a JEOL FX90Q spectrometer and data for the compounds obtained are collected in Table 1. Exact concentrations of solutions of the alcohols were determined by the Gran method.[16]

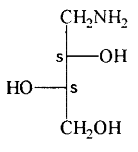
Potentiometric Studies.—The stability constants of the H$^+$ and copper(II) complexes were calculated from the pH titration data obtained at 25 °C with a MOLSPIN automatic titration system. Changes in pH were followed by using a glass–calomel electrode (Russell CMAWL) calibrated for hydrogen-ion activity. The relationship between activity and concentration was calculated daily by titration with HNO_3.[17] All solutions were prepared in 0.1 mol dm^{-3} KNO_3, providing a copper(II) concentration of 10^{-3} mol dm^{-3} and metal to alcohol molar ratios of 1:2, 1:3 and 1:4. Three titrations were performed for each system over the range pH 3–10 using volumes of 2.0 cm^3. Stability constants $\beta_{pqr} = [M_pL_qH_r]/[M]^p[L]^q[H]^r$ were calculated with the aid of the SUPERQUAD computer program.[18] The standard deviations reported were calculated by assuming the random errors.

Spectroscopic Measurements.—Absorption spectra were recorded on a Beckman DU 650 spectrophotometer, ESR spectra on Radiopan SE/X and Varian E102 spectrometers at 120 K in the X-band (9.3 GHz), using ethane-1,2-diol–water (1:2) as solvent and CD spectra on JASCO 600 and JOBIN-YVON CD-6 spectropolarimeters. A metal to alcohol ratio of 1:4 and metal ion concentration of 3×10^{-3} mol dm^{-3} were used.

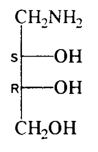
Results and Discussion

All monoaminoalcohols studied in this work behave as HL type ligands, possessing one amino group able to dissociate one proton in basic solution with p*K* 9.3–9.4. No clear effect of stereochemistry or number of hydroxyl groups on the proton dissociation constants of the amino function could be detected (Table 2). However, the amino groups are considerably more basic than those of amino sugars like glucosamine (2-amino-2-deoxyglucopyranose) or mannosamine (2-amino-2-deoxymannopyranose)[9] (p*K* 7.6–7.7) or diaminobutanediols[1] (p*K* 8.5–8.6).

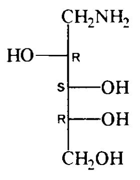
Copper(II) *Complexes with* 4-*Aminotriols*.—According to the ESR spectra all complexes formed in the copper(II)–4-(2*S*,3*S*)-triol (*SS*-abto) and –(2*R*,3*S*)-triol (*RS*-abto) systems above pH 6 are ESR-silent. Calculations based on the potentiometric data fit well a set of dimeric complexes including $Cu_2L_2H_{-2}$, $Cu_2L_2H_{-3}$ and $Cu_2L_2H_{-4}$ species. All these complexes are ESR-silent due to the strong antiferromagnetic coupling of two copper(II) ions bridged by the deprotonated oxygens of the hydroxyl group.[3,19,20] Bridging by deprotonated alkoxo-groups is often found in linear aminoalcohol complexes and the structure of $Cu_2L_2H_{-2}$ could be close to that found by X-ray diffraction analysis for $[Cu_2(Me_2NCH_2CHOHCH_2NMe_2)_2Cl_4]$.[3] The amino and the adjacent deprotonated alkoxo group form a chelate with Cu^{II} and two such subunits are bridged by alkoxo oxygens to form a stable dimeric complex. This co-ordination mode is strongly supported by the CD spectra. The formation of the $Cu_2L_2H_{-2}$ complex in the Cu^{II}–*RS*-abto system is accompanied by clear split d–d bands at 559 and 597 nm and three charge-transfer transitions at 265, 312 and 370 nm (Table 3). Transitions in the 300–400 nm region are usually used as good evidence for the formation of alkoxo-bridged complexes.[21–23] The strong Cotton effect at 265 nm is typical for a $NH_2 \rightarrow Cu^{II}$ charge-transfer transition, indicating the involvement of the amino nitrogen in the co-ordination to Cu^{II}.[24–27] Thus, the formation of this dimeric complex seems to be well documented.



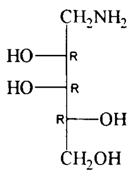
SS-abto



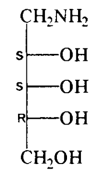
RS-abto



RSR-aptteo



RRR-aptteo



RSS-aptteo

Table 1 Carbon-13 NMR data (D_2O, δ in ppm, internal standard dioxane) for aminodeoxy alditols[a]

Compound	C^1	C^2	C^3	C^4	C^5
SS-abto	42.9	68.1	73.0	63.0	—
RS-abto	41.8	67.7	73.1	62.6	—
RSS-aptteo	41.9	68.6	73.7[b]	72.6[b]	63.4
RSR-aptteo	43.4	67.1	72.0[b]	71.4[b]	63.6
RRR-aptteo	43.6	68.8	73.7	68.8	63.7

[a] As appropriate salts. [b] Assignment may be reversed.

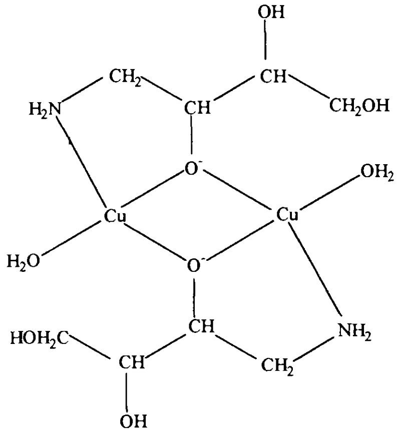
According to potentiometric calculations, increase of pH above 7 leads to deprotonation of consecutive alcohol groups and their co-ordination to Cu^{II}. This is supported by a shift of the d–d band towards higher energy from 656 nm at pH 6 to 630 nm at pH above 9 (Table 3).[24–26,28] The most revealing information about the distinct change in co-ordination mode is obtained from the CD spectra. Transformation of the $Cu_2L_2H_{-2}$ species into $Cu_2L_2H_{-4}$ results in a change of the Cotton effect signs in the d–d as well as in the charge-transfer region (Table 3, Fig. 1). The concentration of the intermediate $Cu_2L_2H_{-3}$ species is low (Fig. 2) and this complex cannot be distinguished clearly in the CD or absorption spectra. The formation of the $Cu_2L_2H_{-4}$ dimeric species, which contains two kind of alkoxo-groups bound to the metal ion, bridging and terminal, is accompanied by three charge-transfer transitions: one characteristic for a bridging alkoxo-group at 333 nm and two at 246 and 278 nm characteristic for the terminal alkoxo→Cu^{II}[29] and $NH_2 \rightarrow Cu^{II}$[24–27] charge-transfer transitions. Thus, the spectroscopic data seem to provide reasonable evidence for the co-ordination model proposed according to the potentiometry. Spectroscopic data for the Cu^{II}–*SS*-abto system are less clear although indicative of co-ordination equilibria analogous to those discussed for the Cu^{II}–*RS*-abto system.

Comparison of the stability constants for the dimeric species with those of the *SS*- and *RS*-abto diastereoisomers indicates distinct differences between the binding abilities of the alcohols. Complex formation is favoured for the (2*S*,3*S*) diastereoisomer by 0.87, 1.18, 1.38 log units for $Cu_2L_2H_{-2}$, $Cu_2L_2H_{-3}$ and $Cu_2L_2H_{-4}$, respectively (Table 2). These differences derive from the difference in stereochemistry of the (2*S*)-OH group. In 4-aminobutanetriols, according to stability constants, such a group interacts more effectively with the metal ion than does a (2*R*)-OH group. The stabilising effect derived from the interactions with the hydroxyl groups (in this case 2-OH in $Cu_2L_2H_{-2}$ species) has also been observed for other amino polyalcohols.[9,10,28] As mentioned above, the formation of $Cu_2L_2H_{-3}$ and $Cu_2L_2H_{-4}$ dimeric species is a consequence of deprotonation of the 2- or 1-OH group due to metal-ion co-ordination. Assuming that the same type of alkoxo-bridge is present in all the dimeric complexes, the 2- or 1-OH groups of the ligand bound *via* a $\{NH_2, 3\text{-}O^-\}$ donor set may co-ordinate to the adjacent bridged copper(II) ion. Consideration of molecular models indicates that the involvement of a 1-O$^-$ group is sterically more likely as it results in less hindrance than binding of 2-O$^-$ (see below).

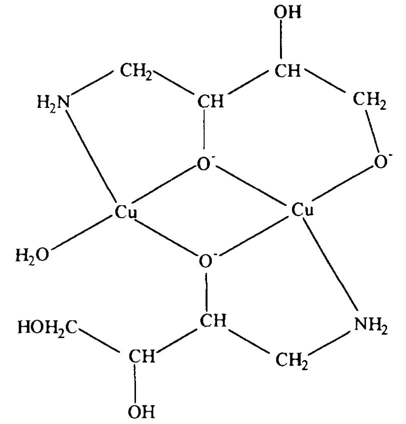
Copper(II) *Complexes with* 5-*Aminotetrols*.—(2*R*,3*S*,4*S*)-(*RSS*-aptteo), (2*R*,3*S*,4*R*)- (*RSR*-aptteo) and (2*R*,3*R*,4*R*)-5-

Table 2 Proton dissociation constants (p*K*) and copper(II) complex-formation constants (log β) of monoaminoalcohols at 25 °C and *I* = 0.1 mol dm^{-3} (KNO_3)

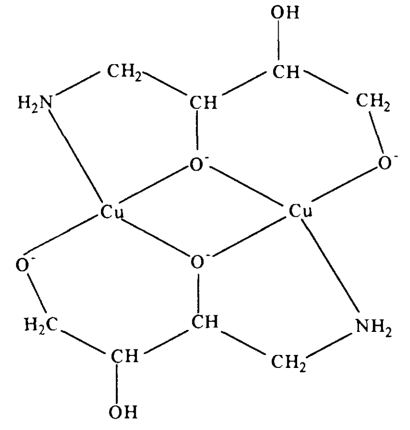
Species $M_pL_qH_r$	*SS*-abto	*RS*-abto	*RSR*-aptteo	*RRR*-aptteo	*RSS*-aptteo
0 1 1	9.318(1)	9.336(1)	9.329(2)	9.379(1)	9.400(1)
2 2 −2	1.41(1)	0.54(1)	1.32(2)	1.68(14)	1.02(1)
2 2 −3	−6.46(1)	−7.84(2)	−5.53(1)	−4.55(3)	−5.69(1)
2 2 −4	−15.30(2)	−16.68(3)	−13.79(2)	−13.37(5)	−14.14(1)
2 2 −5	—	—	−23.13(3)	−23.48(9)	−23.08(1)



2,2,-2



2,2,-3



2,2,-4

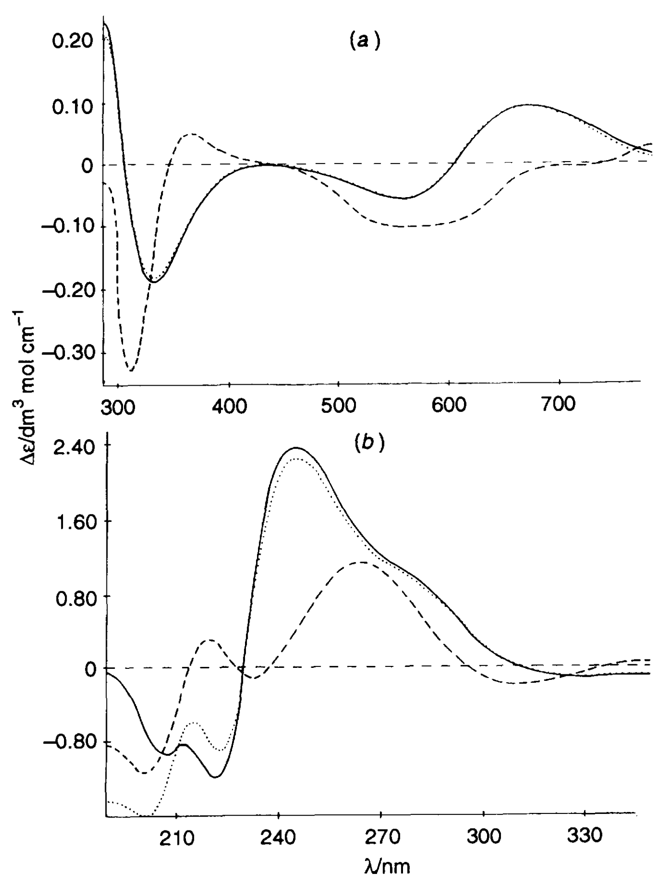


Fig. 1 The CD spectra for Cu^{II}–*RS*-abto solutions, c_{Cu} = 0.003 mol dm^{-3}, $c_L : c_{Cu}$ = 4 : 1 at pH 7.62 (– – – –), 9.30 (———) and 10.76 (· · · ·); (*a*) d–d bands; (*b*) UV region

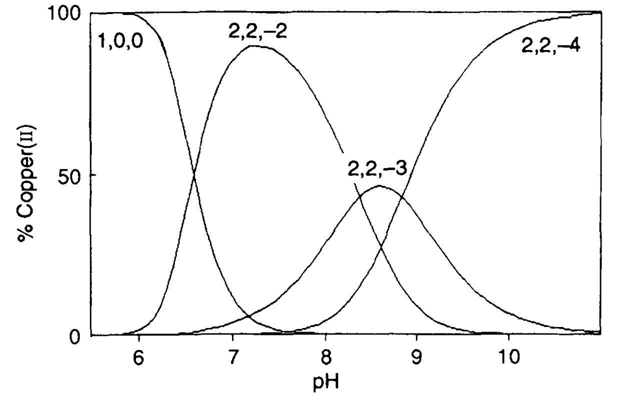


Fig. 2 Species distribution curves for Cu^{II}–*RS*-abto complexes: c_{Cu} = 0.003 mol dm^{-3}, $c_L : c_{Cu}$ = 4 : 1; (1,0,0) corresponds to free metal ion

aminopentane-1,2,3,4-tetrol (*RRR*-aptteo) behave as ligands very similarly to the triols discussed above (Tables 2 and 3). Two ESR-silent dimeric species, $Cu_2L_2H_{-2}$ and $Cu_2L_2H_{-3}$, are formed in the range pH 5.5–9.5 (Fig. 3). The structure of the $Cu_2L_2H_{-2}$ species is the same as that of the butanetriol derivative discussed above, *i.e.* with a {NH$_2$, 4-O$^-$} donor set involved in the copper(II) co-ordination and with 4-O$^-$ acting as a bridging group. The formation of the $Cu_2L_2H_{-3}$ and $Cu_2L_2H_{-4}$ complexes indicates deprotonation and involvement of the 3- or 2-OH group in metal-ion binding (see above). The effect of the carbon chirality on the stability constants is slightly less pronounced than for the triol complexes (Table 2). The most stable species are formed with *RRR*-aptteo, *i.e.* the ligand with the carbons bearing the hydroxyl groups having the same chiralities. The same was observed above for the triol complexes. It is interesting that *RSS*-aptteo forms the weakest species among the ligands studied. Thus, the chirality of 4- and 3-OH is not the critical factor for complex stability. This suggests that 2- rather than 3-OH is involved in metal-ion binding, as mentioned above for the triol derivatives.

For the 5-aminopentanetetrols a $Cu_2L_2H_{-5}$ species is clearly observed above pH 9 (Fig. 3). The stability of this complex is almost independent of the ligand chirality (Table 2), and the

Table 3 Spectral parameters (UV/VIS, CD) for copper(II) complexes of monoaminoalcohols (λ/nm; ε,Δε/dm^3 mol^{-1} cm^{-1})

Species	*SS*-abto				*RS*-abto			
	UV/VIS		CD		UV/VIS		CD	
$M_pL_qH_r$	λ	ε	λ	Δε	λ	ε	λ	Δε
2 2 −2	658	50	589	−0.16	656	50	597	−0.10
			375	+0.01			559	−0.11
			348	−0.01			370	+0.04
			301	+0.20			312	−0.33
			264	+0.82			265	+1.12
			227	−0.65				
2 2 −3	636	50	578	−0.18	634	44		
			337	−0.11				
			302	+0.16				
			253	+1.31				
			227	−1.24				
2 2 −4	626	50	724	+0.08	614	40	674	+0.09
			578	−0.24			567	−0.06
			324	−0.24			333	−0.18
			247	+2.96			278	+0.93
			227	−2.93			246	+2.22

Species	*RSR*-aptteo				*RRR*-aptteo				*RSS*-aptteo			
	UV/VIS		CD		UV/VIS		CD		UV/VIS		CD	
$M_pL_qH_r$	λ	ε	λ	Δε	λ	ε	λ	Δε	λ	ε	λ	Δε
2 2 −2	—	—	—	—	—	—	—	—	—	—	—	—
2 2 −3	662	56	789	−0.19	655	57	771	−0.15	660	62	782	+0.15
			584	+0.12			623	+0.37			581	−0.09
			339	+0.03			374	−0.03			339	−0.11
			262	−0.62			328	+0.14			271	+0.50
			227	+0.44			260	−1.00			239	−0.12
							224	+1.26				
2 2 −4	634	49	725	−0.07	634	57	772	−0.16	—	—	—	—
			574	−0.07			604	+0.36				
			333	+0.20			378	−0.01				
			249	−1.20			328	+0.18				
			227	+1.13			259	−1.14				
							224	+1.39				
2 2 −5	630	51	721	−0.10	662	52	764	−0.16	612	48	741	+0.08
			573	+0.22			589	+0.40			584	−0.13
			324	+0.29			332	+0.08			363	+0.01
			248	−2.46			254	−1.93			253	+1.51
			227	+2.77			220	+0.88			227	−1.07

spectra show only minor effects of its formation (Table 3). It is likely that the formation of this species involves proton dissociation from the axially bound water molecule. The absence of a similar process in the case of the butanetriol derivatives could suggest stabilisation of the axial hydroxyl bonding by the 5-OH group.

The absorption and CD spectra strongly support the proposed binding modes (Table 3). The most distinct CD spectra were observed for the Cu^{II}–*RRR*-appteo system. The intensity and energy of the positive band in the d–d region increase with increasing pH and formation of consecutive species. Two well shaped bands are observed in the UV region at around 230 and 250 nm, corresponding to alkoxo $O^- \rightarrow Cu^{II}$ and $NH_2 \rightarrow Cu^{II}$ charge-transfer transitions, respectively. The transitions characteristic for the bridging alkoxo-group are centred around 330–370 nm (Table 3). In the case of the aminopentanetetrols the concentrations of the $Cu_2L_2H_{-2}$ species are rather low (Fig. 3) and spectroscopic data could be obtained only for the three other species (Table 3).

Monoaminopolyalcohols are effective ligands forming very stable dimeric complexes with Cu^{II}. Although the amino group usually acts as an anchoring donor for a metal ion, the adjacent hydroxyl group deprotonates easily and forms an alkoxo-bridge between two copper(II) ions. It should be mentioned that the cyclic aminosugars do not form any dimeric species using this kind of alkoxo-bridge.[9,10,24–29] The presence of additional alcoholic groups on the vicinal C(3), C(2) and C(1) carbons leads to the involvement of the second and possibly third hydroxyl group in metal-ion binding. Thus, the metal ion anchored to the nitrogen of the amino group may form several bonds with the alcoholic moieties of the aminopolyalcohol. The chirality of the carbons bearing the hydroxyl groups may have a distinct effect on the structure and stability of the complexes formed.

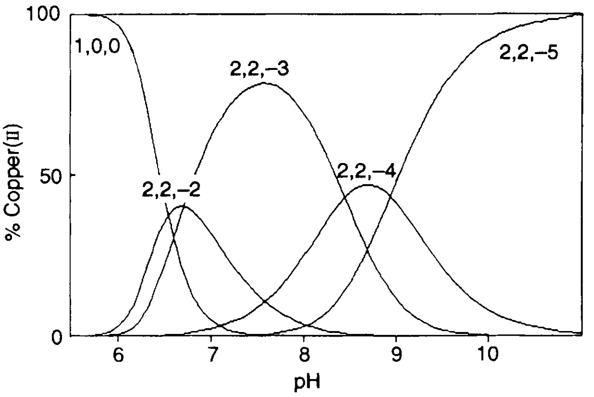


Fig. 3 Species distribution curves for Cu^{II}–*RRR*-aptteo complexes: c_{Cu} = 0.003 mol dm^{-3}, $c_L : c_{Cu}$ = 4:1; (1,0,0) corresponds to free metal ion

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