Formation of borate esters from, and sequestration of metal ions by, bis(polyhydroxyalkyl)amines and their *N*-carboxymethyl derivatives studied by ¹¹B and ¹³C NMR spectroscopy

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ABSTRACT

Catalytic hydrogenation of aldose oximes affords bis(polyhydroxyalkyl)amines. These compounds and their N-carboxymethyl derivatives react with borate ions to give macrocyclic diborate diesters. The presence of an N-carboxymethyl group raises the capacities for the sequestration of Ca^{2+} , Cu^{2+} , and Cd^{2+} . The N-carboxymethyl derivatives possess strong affinity for Ca^{2+} (pH > 11) and Cd^{2+} both in the absence and presence of borate.

INTRODUCTION

Aldonic acids and oxidised polysaccharides have promising metal-ion chelating properties¹⁻³. Such systems are possible substitutes for sodium triphosphate in detergent formulations since they have strong metal-ion sequestering capacities with good biodegradabilities. Substituted polyhydroxyamines also possess strong metal-ion chelating properties and are used in detergents and cosmetics⁴, and bis(polyhydroxyalkyl)amines have potential as metal-ion chelating agents for use in plant therapeutics⁵.

For aldonic acids, the metal-ion sequestering capacities at pH > 9 increase upon addition of borate⁶⁻⁸. In these systems, the borate anion links two aldonic acid molecules and strong metal-ion coordinating sites are formed. Borate esters formed from polyhydroxy compounds that contain functional groups other than carboxylate and hydroxyl exhibit good metal-ion sequestering capacities. Thus,

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mixtures of borate and aminoaldonic acids or (amino)aldose oximes coordinate transition metal ions more selectively than aldonic acids^{9,10}.

Hodge et al.⁵ reported that the capacity of bis(D-gluco-2,3,4,5,6-pentahydroxyhexyl)amine (2d) to sequester Cu²⁺, Ca²⁺, Sr²⁺, and Fe³⁺ is substantially higher than that of the equally basic N-methyl-D-gluco-2,3,4,5,6-pentahydroxyhexylamine. These authors concluded that two freely rotating polyhydroxyalkyl chains in one molecule result in better metal-ion sequestering than a single such chain and predicted that attachment of a third such chain would further increase the metal-ion chelating properties. However, attempts to react bis(D-gluco-2,3,4,5,6pentahydroxyhexyl)amine with D-glucose or tetra-O-acetyl- α -D-glucopyranosyl bromide failed. We now report that the metal-ion complexing abilities of these compounds can be enhanced by the formation of (a) N-carboxymethyl (NCH₂COOH) derivatives and (b) borate esters.

Bis(polyhydroxyalkyl)amines have been prepared by hydrogenation of dialdosylamines¹¹ and by hydrogenolysis of *N*-benzyl(polyhydroxyalkyl)amines¹². We have synthesised bis(polyhydroxyalkyl)amines by catalytic hydrogenation of aldose oximes. Although alkyl or aryl oximes can be transformed easily into primary and secondary amines by catalytic hydrogenation¹³, there has been no report of the application of this reaction to prepare bis(polyhydroxyalkyl)amines.

RESULTS AND DISCUSSION

Synthesis of bis(polyhydroxyalkyl)amines and their N-carboxymethyl derivatives. —Hydrogenation (Pt–C) of D-arabinose oxime (**1a**), D-mannose oxime (**1b**), and D-galactose oxime (**1c**) gave the corresponding bis(polyhydroxyalkyl)amines **2a**–c in yields of 26–80%. These compounds were characterised by ¹³C NMR spectroscopy and FABMS.

Heard et al.¹⁴ reported the formation of **2a** as a byproduct [D-*arabino*-2,3,4,5-te-trahydroxypentylamine (**3a**) was the main product] during the hydrogenation of D-arabinose oxime at ambient temperature and 1 atm. ¹³C NMR spectroscopy of the crude reaction mixtures showed clearly that, at 50°C and 100 atm, **2a** was the major product.

D-Glucose oxime (1d) was reduced much more slowly than the oximes 1a-c. After 24 h at 50°C and 100 atm, reduction was incomplete and bis(D-gluco-2,3,4,5,6-pentahydroxyhexyl)amine (2d) could not be crystallised from the reaction mixture. Also, on electrochemical reduction, the conversion of D-glucose oxime into D-gluco-2,3,4,5,6-pentahydroxyhexylamine (3d) was much slower¹⁵ than that of the oximes 1a-c. This may be ascribed to the considerable proportion of cyclic forms present in the solution of glucose oxime in contrast to the other oximes¹⁶. Catalytic hydrogenation of a mixture of D-glucose and D-gluco-2,3,4,5,6-pentahydroxyhexylamine (3d), however, afforded almost exclusively 2d, which could be purified by crystallisation.



The N-carboxymethyl derivatives 4b-d were synthesised by reacting the bis(polyhydroxyalkyl)amines with bromoacetate.

Formation of borate esters.—The formation of borate esters from D-gluco-2,3,4,5,6-pentahydroxyhexylamine (3d), the bis(polyhydroxyalkyl)amines 2a-d, and the N-carboxymethyl derivatives 4b-d was investigated using ¹¹B and ¹³C NMR spectroscopy. Studies with ¹¹B NMR spectroscopy^{17,18} and other techniques¹⁹ have shown that alditols, aldonic acids, aldaric acids, and aldose oximes react with boric acid/borate to give monoesters (B⁻L) and diesters (B⁻L₂) that are formed from 1,2- and 1,3-diols (see Scheme 1). The exchange between B⁻, B⁻L, and B⁻L₂ is slow on the ¹¹B NMR time scale so that the chemical shifts, line widths, and association constants of the various boron-containing species can be determined. Thus, in studying the reactions of 2a-d and 4b-d with borate as a function of pH and at a ligand-to-borate ratio of 0.5 or 1.0, the ¹¹B signals could be assigned easily to B⁻L or B⁻L₂ on the basis of literature values (Table I)^{17,18}. For most of the ligands, however, there was an unusually high proportion of borate diester species.

¹¹B NMR measurements for *D-gluco-2,3,4,5,6-pentahydroxyhexylamine* (3d), as a function of the ligand-to-borate ratio (ρ), revealed mainly *threo* borate mo-



Scheme 1. Equilibria between borate (B⁻) and a diol function of a polyhydroxyalkyl compound (X = CHOH, CH₂OH, COO⁻, C=NOH).

Ligand	Ester type	δ (p.p.m.)		$\Delta \nu_{1/2}$ (Hz)	
		$\overline{B^-L}$	$B^{-}L_{2}^{a}$	B-L	B ⁻ L ₂ ^{-//}
Bis(D-arabino-2,3,4,5-tetra- hydroxypentyl)amine (2a)	threo-2,3	- 13.7	- 9.1	71	137
	syn / anti ^b	- 18.1		19	
Bis(D-manno-2,3,4,5,6-penta- hydroxyhexyl)amine (2b)	threo-3,4	- 13.6	- 9.1	49	167
	ervthro	-14.3		23	
	syn / anti	- 18.3		11	
Bis(D-galacto-2,3,4,5,6-penta- hydroxyhexyl)amine (2c)	threo	- 13.7	- 9.7	94	153
Bis(D-gluco-2,3,4,5,6-penta- hydroxyhexyl)amine (2d)	threo	-13.5	- 9.2	65	208
	erythro	-14.2		44	
	syn / anti	-18.1			
D-gluco-2,3,4,5,6-Penta- hydroxyhexylamine (3d)	threo	- 13.5	- 9.4	52	109
	erythro	- 14.4		58	
	syn / anti	-18.3		31	
N-Carboxymethyl 2b (4b)	threo-3,4	-13.3	- 9.0	89	109 209
	erythro	- 14.4		27	
	syn / anti	- 18.1			
N-Carboxymethyl 2c (4c)	threo	-13.5	- 9.0	91	166
	erythro	- 14.4		25	
	syn / anti	- 18.2		16	
N-Carboxymethyl 2d (4d)	threo	-13.5	- 9.3	76	187
	erythro	- 14.4		45	
	svn / anti	- 18.2		17	

TABLE I

¹¹B NMR data (chemical shifts and line widths) for the borate esters (D_2O , 25°C)

^a Structures 5, 7, 10, or 11. ^b syn and anti refer to 1,3-diol-type esters.

noesters at $\rho = 1$ and mainly borate diesters at $\rho = 2$ (see Fig. 1). This pattern of borate ester formation resembles those of D-glucitol, D-mannitol, and D-arabinitol^{20,21}. Fig. 1 shows that, at pH 12 for the secondary amines **2a-d** and a ligand-to-borate ratio of ~ 1, practically all of the borate anion is incorporated in a borate diester species ($\delta \sim -9$) with an apparent relatively high stability. However, a borate anion complexed to such an extent via two diol functions of different ligands (i.e., B^-L_2 in Scheme 1) is impossible at a ligand : borate ratio (ρ) of ~ 1. Therefore, borate diester species other than those mentioned in the literature may be present. The presence of 8–10 hydroxyl groups in the various bis(polyhydroxyalkyl)amines creates several possibilities (**5–11**) for the formation of borate diesters at $\rho = 1-2$.

For the bis(polyhydroxyalkyl)amines 2a-d, the chemical shifts of the ¹¹B resonances of the main 1,2-diol-type borate monoesters are characteristic of *threo*



Fig. 1. Percentage of the total boron involved in a borate diester species (structure 5, 7, 10, or 11) as a function of the borate-to-ligand ratio with 0.05–0.20 M borate and 0–0.31 M ligand, pH 12.2–12.7, D_2O , 25°C: \bigcirc , 2a; \bullet , 2c; \blacktriangle , 2d; \blacksquare , 3d.

structures in agreement with the finding^{20,22} that such monoesters are more stable than the *erythro* isomers. Therefore, it is likely that, in the borate diester species also, the borate is bound at the *threo* positions. This inference was confirmed for



(for 2a - 2dR = H, for $4b - 4dR = CH_2COOH$)

	Species	2a	2b	2c	2d	3d	4d
C-1,1'	L B ⁻ L ₂	52.7 54.6 ^b 55.2 °	52.7 51.5	52.9 55.2, 53.1 [#] 54.6, 53.3 ^c	51.8 54.3 ^b 52.6 ^c	44.3 45.0 ^b 44.9 ^c	60.6 or 59.9
C-5,5′	L B ~ L ₂	64.5 64.7					
C-6,6′	L B ⁻ L ₂		64.7 64.9	64.8 65.3 66.0	64.4 64.7	64.4 64.7	64.4 64.7

¹³C NMR data ^{*a*} (δ in ppm) for 2a-2d, 3d, and 4d and their borate diester species in D₂O, pH 12.2-12.7, 25°C

^{*a*} The CHOH signals of the ligand and the borate diester species could not be assigned unambiguously. ^{*b*} Predominant signal at $\rho = 1$. ^{*c*} Predominant signal at $\rho = 2$.

2a, **2b**, and **2d** by ¹³C NMR substituent effects, at $\rho = 1$ and 2, on the formation of borate esters (see Table II). The downfield shifts of only 0.2–0.3 ppm for the signals of C-6,6'(C-5,5' of **2a**) on the formation of borate esters indicate that C-5,5'(C-4,4' of **2a**) and C-6,6' are not involved in the borate ester ring²³. Furthermore, since the substituent effect (-1.2 ppm) for C-1,1' of **2b** indicates a *threo*-3,4-borate ester²³, it can be concluded that for **2a**, **2b**, and **2d** the borate moiety in the borate diester species is bound at the *threo* positions. Therefore, borate esters of structures **6**, **8**, and **9** are not present. For **2c**, the ¹³C NMR results indicate that the borate can be bound at both *threo* positions (2,3 or 4,5). Borate esters of structures **6**, **8**, and **9** are unlikely to be formed with **2c** since the separation of the oxygens of the two borate units is only 1 Å.

For the bis(polyhydroxyalkyl)amines 2a-d, the ¹³C NMR spectra at $\rho = 1$ (pH > 12) showed nearly all of the ligand to be complexed, indicating the existence of borate diesters of structures 5 or 7. At $\rho = 1$, for 2a and 2b, the ¹³C NMR spectra contained only five and six signals, respectively, suggesting that only one type of borate diester was present with structure 5 or 7. For 2c and 2d at $\rho = 1$, more than six signals were present, which reflects the presence of two different *threo*-diol functions. At $\rho = 2$, 2a-d appeared to be present as 50-70% of free ligand, which shows that the borate diesters of structure 5 or 7 have a relatively high stability. In addition, relatively weak ¹³C signals, attributed to borate esters other than those at $\rho = 1$, were discerned (Fig. 2) possibly of structure 10 or 11.

For the N-carboxymethyl derivatives **4b**-**d**, the formation of borate esters at pH 12.2-12.7 was also studied as a function of ρ (see Fig. 3 for **2d** and **4d**). As is clear from Fig. 3, at $\rho = 1$, less of the boron is included in a borate diester species than for the bis(polyhydroxyalkyl)amines. On the other hand, for the N-carboxymethyl derivative **4d**, much more ligand is present in a borate diester species at $\rho = 1$ than for D-gluco-2,3,4,5,6-pentahydroxyhexylamine (**3d**). The fact that, at $\rho = 1$ for the N-carboxymethyl derivatives, 55-65% of the total borate is present as a borate

TABLE II



Fig. 2. ¹³C NMR spectra of bis(*p*-arabino-2,3,4,5-tetrahydroxypentyl)amine (2a) and borate at $\rho = 0, 1$, and 2, D₂O, pH 12.2-12.7, 25°C.

diester and 30-40% as a borate monoester (not shown in Fig. 1) points to the occurrence of boron-containing species having structures 5 or 7, which, apparently, are less stable than the corresponding borate esters of the unsubstituted bis(poly-



Fig. 3. Percentage of the total borate involved in a borate diester species (structures 5, 7, 10, or 11) as a function of the borate-to-ligand ratio at pH 12.2-12.7, 0.05 M borate and 0-0.31 M ligand, D_2O , 25°C: **A**, 2d; Δ , 4d.

hydroxyalkyl)amines. This difference may reflect steric hindrance by the carboxymethyl groups or repulsive interactions of the negatively charged borate and carboxyl groups.

Although the borate diester species of 2a-d and 4b-d showed only one ¹¹B resonance, this does not exclude diborate diesters of structure 5 since, in these species, the borate moieties have similar environments. A further indication of the presence of borate esters of structure 5 or 7 can be obtained from the line widths of the ¹¹B signals which are dominated by quadrupolar relaxation²⁴ as approximated by the equation²⁵

$$1/T_2 = \frac{3}{10}\pi^2 \frac{(2l+3)}{l^2(2l-1)} \left(e^2 q Q/h\right)^2 \left(1 + \frac{\eta^2}{3}\right) \frac{4\pi r^3 \eta_s}{3kT}$$
(1)

where e^2qQ/h is the quadrupolar coupling constant in Hz, η is the electric-fieldgradient asymmetry, η_s is the viscosity of the solution, and r is the radius of the molecule which is considered as a rigid sphere. Line widths of B⁻L₂ signals increase on going from such small diols as ethylene glycol or 1,2-propanediol to C₅ or C₆ alditols or aldonic acids. For *D-gluco*-2,3,4,5,6-pentahydroxyhexylamine, a line width for the borate diester signal of 109 Hz was found, close to that found for borate diesters of other ligands containing 5 or 6 carbon atoms^{22,26}. For the bis(polyhydroxyalkyl)amines **2a-d** and the *N*-carboxymethyl derivatives **4b-d**, line widths of the borate diester species (~ -9 ppm) were substantially larger (Table I). The electric-field asymmetry (η) will be nearly the same for all borate diester species and therefore, assuming equal viscosities of the solutions, the larger line widths indicate that the molecular radii for the borate diester species of the bis(polyhydroxyalkyl)amines are larger than those for alditols and aldonic acids. The line widths at $\rho \approx 1$ were in agreement with those estimated for **5**, using eq. *1* and molecular radii from molecular models.

It is concluded that, in solutions of borate and bis(polyhydroxyalkyl)amines, diborate diesters of structure **5** are formed. The existence of such diborate diesters is of interest with regard to cation sequestration because, in these structures, crown-ether-like coordinating cavities are formed.

Sequestration of Cd^{2+} and Ca^{2+} by borate N-carboxymethylbis(polyhydroxyalkyl)amine systems.—The sequestration of Cd^{2+} and Ca^{2+} by **4b**-**d** was studied in the presence and absence of borate since their complexation can be enhanced by addition of borate⁶⁻¹⁰. The sequestration of Cu^{2+} by **2a**-**2d** and **4d** was studied also. The capacities (CdSC and CaSC, respectively) for the sequestration of Cd^{2+} and Ca^{2+} by **4b**-**d** were determined at pH 6.7-7.0 and 11.5-12.3, in the absence and presence of 1 mol equiv of borate, using a titration procedure¹. The results in Table III show that the *N*-carboxymethyl derivatives are poor Ca^{2+} sequestrants at pH 7, probably as a result of the inability of Ca^{2+} to deprotonate the ammonium functions at that pH, but strong Ca^{2+} chelators at pH > 11, at which pH ca. 1 mmol of Ca^{2+} is sequestered per mmol of ligand. Compounds **4b-d** possess good CdSC at both pH 7 and 11.5-12.3, amounting to 0.7 and ~1 mmol of Cd^{2+}

Ligand	рН	CdSC		CaSC		
		without borate	with borate	without borate	with borate	
4b (D-manno)	7.0	220	220	<1	< 1	
	11.5	340	360	140	200	
4c (D-galacto)	6.7	160	160	<1	< 1	
	12.3	240	330	120	150	
4d (D-gluco)	7.0	170	200	<1	<1	
	11.5	150	280	130	150	

TABLE III

 Ca^{2+} and Cd^{2+} sequestering capacities ^a (mg/g of ligand) of the N-carboxymethyl derivatives in the absence and presence of 1 mol equiv of borate

^a Determined by adding a solution of Ca^{2+} or Cd^{2+} chloride to a solution containing ~ 100 mg of ligand and indicator (oxalate at pH 6.7 and NaOH-Na₂CO₃ at pH 11.5-12.3). The estimated errors are $\pm 20\%$.

sequestered per mmol of ligand, respectively. For 2a-c, only 20-30 mg of Cd²⁺ per g of ligand was sequestered at pH 11.5, which shows that the *N*-carboxymethyl group increases their Cd²⁺-sequestering abilities significantly. The Cu²⁺-sequestering abilities of 2a-2d as well as of their *N*-carboxymethyl derivatives were high at both pH 7 and 11-12. For 2a-2d at neutral pH, ~ 1 mmol of Cu²⁺ is sequestered per mmol of ligand, which rises to 1.5-2 mmol at pH 11-12. The *N*-carboxymethyl derivatives sequester 2-3 mmol of Cu²⁺ per mmol of ligand at neutral pH and as much as 4 mmol at high pH. Addition of borate to solutions of 2a-2d or 4d did not increase the sequestering abilities. The higher abilities of 2a-2d to sequester Cu²⁺ than Ca²⁺ and Cd²⁺ can be explained by the higher effective charge of the Cu²⁺ ion, thereby causing a stronger interaction of the bis(polyhydroxyalkyl)amine and the metal ion. The strong CdSC and CaSC of the free *N*-carboxymethyl derivatives may be rationalised by assuming coordination of the metal ions via the nitrogen atom and the carboxylate group, the alditol chains assisting in complexation by encapsulating the metal ions.

¹¹B NMR spectroscopy on mixtures of the *N*-carboxymethyl derivatives **4b**-**d** and borate, at $\rho = 0.9$ (Table IV), showed that the addition of Ca²⁺ did not alter the ratios of B⁻, B⁻L, and B⁻L₂. Also, the addition of Ba²⁺ to mixtures of borate and **4b** had no influence on these ratios. Thus, Ca²⁺ and Ba²⁺ are not coordinated preferentially by one of the borate esters. Addition of Cd²⁺ resulted in an increase in the proportion of B⁻L₂ species for **4b** and **4d**, and the CdSC increased upon adding borate (Table III).

Although the results in Tables III and IV indicate that addition of borate to solutions of the *N*-carboxymethyl derivatives has only a small synergistic effect on the sequestration of Cd^{2+} and Ca^{2+} , the borate diester species form complexes with Cd^{2+} and Ca^{2+} of strength equal or higher than those in the absence of borate. In the diborate diesters, with the borate bound at the *threo*-2,3-position (4c and 4d), 16-membered rings are formed, wherein 2 carboxylate groups, 2 nitrogen

Ligand	рН	B ⁻ L ₂ ^{b,c}		$B^{-}L_{2}^{b,c}$	
		C _{Ca,0.0}	C _{Ca,0.16}	C _{Cd.0.0}	C _{Cd.0.05}
4b (D-manno)	6.3	56	75	55	71
	12.3	74	73	53	72
4c (D-galacto)	7.2	66	80	69	63
	12.7	78	75	68	65
4d (D-gluco)	6.8	67	69	72	78
	12.7	53	48	55	82

TABLE IV

Effect of the addition " of CaCl₂ (0.16 M) or CdCl₂ (0.05 M) on the percentage of borate diester species present in solutions of borate and the *N*-carboxymethyl derivatives, at pH 12, as determined by ¹¹B NMR spectroscopy

^{*a*} For Ca²⁺, C_B = 0.1 M and C_{4b-4d} = 0.1 M; for Cd²⁺, C_B = 0.05 M and C_{4b-4d} = 0.05 M. ^{*b*} The percentage borate included in a borate diester species is given in the absence (C_{Ca,0} or C_{Cd,0}) and presence (C_{Ca,0.16} and C_{Cd,0.05}) of Ca²⁺ and Cd²⁺, respectively. The sum of the borate diesters, including their metal ion complexes is given. ^{*c*} B⁻L₂ represents a borate ester of structure 5 or 7.

atoms, and 4 oxygen atoms can assist in metal-ion coordination. In diborate diesters of structure 5, with the borate bound at the *threo*-3,4-position (**4b** and **4d**), complexing cavities are formed that are somewhat larger than that of the 18-crown-6-ether ligand (see 12). Strong metal-ion coordination by diborate diesters of the *N*-carboxymethyl derivatives might be hampered by their high flexibility or the dynamics of the borate ester formation. For synergistic metal-ion sequestration, the latter effect may be an advantage, because the metal ions can be removed easily from their diborate diesters.

EXPERIMENTAL

NMR measurements.—¹¹B NMR spectra (external 0.1 M boric acid in D₂O) were recorded at 25°C with a Varian VXR-400 S (128.3 MHz) or Nicolet NT-200 WB (64.2 MHz) spectrometer. Baseline correction was applied in order to remove the broad signal of the boron incorporated in the glass sample tube and in the insert. Usually, a deconvolution program was used to obtain all the signal characteristics. ¹³C NMR spectra (internal *tert*-butyl alcohol, δ 31.2) were recorded with the above spectrometers at 100.6 and 50.3 MHz, respectively.

Samples were prepared by dissolution of the appropriate amounts of boric acid and ligand in D_2O . The total boron concentration was 0.05-0.20 M, whereas the concentrations of the bis(polyhydroxyalkyl)amines and their *N*-carboxymethyl derivatives were 0.00-0.31 M. The pH was adjusted with NaOH or HCl and was measured with a calibrated MI 412 micro-combination probe (Microelectrodes, Inc.) or with a calibrated Z11,344-1 combination pH electrode (Aldrich). The pH values are direct meter readings.



 Ca^{2+} , Cu^{2+} , Cd^{2+} , and Ba^{2+} ions were added to the borate-ligand systems as their chloride salts. Metal-ion sequestering capacities were determined according to Mehltretter et al.¹. Cd^{2+} and Ca^{2+} sequestering capacities (CdSC and CaSC, respectively) were determined at ambient temperature by adding a solution of Cd^{2+} or Ca^{2+} chloride to a solution containing 50-100 mg of ligand. CdSC and CaSC were determined at pH 6.9 by using oxalate as the indicator. Solutions of ligand and Cd^{2+} slowly turned turbid. As the end point of a titration, the first turbidity that appeared within 2 min after the last addition of Cd^{2+} was taken. At pH 11.5, CdSC and CaSC were determined with the use of NaOH-Na₂CO₃ as indicator. As the end point of a titration, the first turbidity that had not disappeared within 30 s was taken.

FAB-mass spectra.—A VG 70-250 SE mass spectrometer was used with glycerol as the matrix.

Bis(D-arabino-2,3,4,5-tetrahydroxypentyl)amine (2a).—To a solution of Darabinose oxime (17.94 g, 109 mmol) in water (150 mL) was added 5% Pt-C (1.4 g). The mixture was hydrogenated during 24 h at 50°C and 100 atm H₂, then filtered, and concentrated, and the residue was crystallised from 3:2 MeOH-H₂O to give 2a (4.06 g, 26.1%); mp 175–176°C (dec); $[\alpha]_{578}^{25}$ + 14.1° (*c* 0.9, H₂O). ¹³C NMR data (pD 10.6, D₂O): δ 52.7 (C-1,1'), 69.9, 72.6, 73.5 (C-2,2',3,3',4,4'), and 64.5 (C-6,6'). FAB-mass spectrum: m/z 286 [100% (M + H)⁺]. Anal. Calcd for C₁₀H₂₃NO₈: C, 42.08; H, 8.13; N, 4.91. Found: C, 42.01; H, 8.19; N, 4.92.

Bis(D-manno-2,3,4,5,6-pentahydroxyhexyl)amine (2b).—Prepared from D-mannose oxime (15.03 g), according to the procedure described above, 2b (6.54 g, 49.2%) had mp 185–186°C (dec); $[\alpha]_{578}^{25}$ + 2.44° (*c* 0.9, H₂O). ¹³C NMR data (pD 11.0, D₂O): δ 52.8 (C-1,1'), 70.6, 70.9, 72.4, 72.9 (C-2,2',3,3',4,4',5,5'), and 64.8 (C-6,6'). FAB-mass spectrum: m/z 346 [100%, (M + H)⁺]. Anal. Calcd for C₁₂H₂₇NO₁₀: C, 41.72; H, 7.88; N, 4.06. Found: C, 41.50; H, 7.54; N, 3.97.

Bis(D-galacto-2,3,4,5,6-pentahydroxyhexyl)amine (2c).—Prepared from D-galactose oxime (5.0 g), according to the procedure described above, 2c (3.51 g, 79.5%) had mp 195–196°C (dec.); $[\alpha]_{578}^{25} - 11.7$ ° (*c* 0.9, H₂O). ¹³C NMR data (pD 10.8, D₂O): δ 52.9 (C-1,1'), 69.9, 71.1, 71.8, 72.6 (C-2,2',3,3',4,4',5,5'), and 64.8 (C-6,6'). FAB-mass spectrum: m/z 346 [100%, (M + H)⁺]. Anal. Calcd for C₁₂H₂₇NO₁₀; C, 41.72: H, 7.88; N, 4.06. Found: C, 41.52; H, 7.89; N, 4.02.

Bis(D-gluco-2,3,4,5,6-pentahydroxyhexyl)amine (2d).—To a solution of D-glucose (20.6 g, 111 mmol) and D-gluco-2,3,4,5,6-pentahydroxyhexylamine (23.6 g, 130 mmol) in H₂O (100 mL, pH 11.4) was added 5% Pt–C (1.5 g). The mixture was hydrogenated during 24 h at 50°C and 100 atm H₂, then filtered, and concentrated, and the residue was crystallised from 1:1 MeOH–H₂O to give 2d (12.1 g, 31.6%); mp 180–181°C (dec.); $[\alpha]_{578}^{25}$ – 19.2° (*c* 0.9, H₂O). ¹³C NMR data (pD 9.8, D₂O): δ 51.8 (C-1,1'), 72.2, 72.3, 72.6 (C-2,2',3,3',4,4',5,5'), and 64.4 (C-6,6'). FAB-mass spectrum *m*/*z* 346 [78%, (M + H)⁺]. Anal. Calcd for C₁₂H₂₇NO₁₀: C, 41.72; H, 7.88; N, 4.06. Found: C, 41.45; H, 7.62; N, 4.07.

N-Carboxymethylbis (D-manno-2,3,4,5,6-pentahydroxyhexyl)amine (4b).—The pH of a solution of 2b (4 g, 11.6 mmol) and bromoacetic acid (3.2 g, 23.2 mmol) in water (40 mL) was raised to 10–11 with LiOH. The mixture was heated for 5 h at 90°C when no 2b remained, then concentrated in vacuo, and the residue was eluted from a column (50 × 3 cm) of Dowex 50W (H⁺) resin with a gradient of $0 \rightarrow 0.7$ M NH₄OH. The fractions were concentrated and analysed by ¹³C NMR spectroscopy. Pure 4b (1.5 g, 32.1%) was isolated. ¹³C NMR data (pD 1.3, D₂O): δ 57.6 (C-1,1'), 66.3 (C-2,2'), 70.4, 72.2, 72.8 (C-3,3',4,4',5,5'), 64.6 (C-6,6'), 59.9 (b. C-7), and 170.6 (C-8). FAB-mass spectrum: m/z 404 [42%, (M + H)⁺], 346 [14%, (M⁺ – CH₂COO)].

N-Carboxymethylbis(D-galacto-2,3,4,5,6-pentahydroxyhexyl)amine (4c).—Treatment of 2c (2 g, 5.8 mmol) with bromoacetic acid (1.6 g, 11.6 mmol), as described for 2b, gave 4c (0.9 g, 39%). ¹³C NMR data (pD 0.6, D₂O): δ 56.8 (C-1,1'), 65.8 (C-2,2'), 70.8, 71.4, 71.8 (C-3,3',4,4',5,5'), 64.6 (C-6,6'), 60.1 (b, C-7), and 170.1 (C-8). FAB-mass spectrum: m/z 404 [33%, (M + H)⁺].

N-*Carboxymethylbis*(D-gluco-2, 3, 4, 5, 6-pentahydroxyhexyl)amine (4d).—Treatment of 2d (7.0 g, 20.3 mmol) with bromoacetic acid (5.5 g, 39.6 mmol), as described for 2b, gave 4d (2.4 g 29.3%). ¹³C NMR data (pD 6.7, D₂O): δ 58.6 (C-1,1'), 68.2 (C-2,2'), 72.2, 72.3, 72.5 (C-3,3',4,4',5,5'), 64.3 (C-6,6'), 58.3 (b, C-7), and 172.08 (C-8). FAB-mass spectrum: m/z 404 [10%, (M + H)⁺].

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REFERENCES

- 1 C.L. Mehltretter, B.H. Alexander, and C.E. Rist, Ind. Eng. Chem., 45 (1953) 2782-2784.
- 2 M. Floor, L.P.M. Hofsteede, W.P.T. Groenland, L.A.Th. Verhaar, A.P.G. Kieboom, and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas*, 108 (1989) 384–392.
- 3 M. Floor, J.H. Koek, F.L.M. Smeets, R.E. Niemantsverdriet, J.A. Peters, H. van Bekkum, and A.P.G. Kieboom, *Carbohydr. Res.*, 203 (1990) 19-32.
- 4 H. Kelkenberg, Tenside, Surfactants, Deterg., 25 (1988) 8-13.
- 5 J.E. Hodge, E.C. Nelson, and B.F. Moy, Agric. Food Chem., 11 (1963) 126-129.
- 6 M. van Duin, J.A. Peters, A.P.G. Kieboom, and H. van Bekkum, J. Chem. Soc., Perkin Trans. 2, (1987) 473-478.
- 7 M. van Duin, J.A. Peters, A.P.G. Kieboom, and H. van Bekkum, Carbohydr. Res., 162 (1987) 65-78.
- 8 M. van Duin, J.A. Peters, A.P.G. Kieboom, and H. van Bekkum, J. Chem. Soc., Dalton Trans., (1987) 2051-2057.
- 9 J. van Haveren, J.A. Peters, J.G. Batelaan, A.P.G. Kieboom, and H. van Bekkum, J. Chem. Soc., Dalton Trans., (1991) 2649-2656.
- 10 J. van Haveren, J.A. Peters, J.G. Batelaan, A.P.G. Kieboom, and H. van Bekkum, Inorg. Chim. Acta, 192 (1992) 261-270.
- 11 J.E. Hodge and B.F. Moy, J. Org. Chem., 28 (1963) 2784-2789.
- 12 F. Kagan, M.A. Rebenstorf, and R.V. Heinzelmann, J. Am. Chem. Soc., 79 (1957) 3541-3544.
- 13 R. Paul, Bull. Soc. Chim. Fr., 4 (1937) 1121-1125.
- 14 D.D. Heard, B.G. Hudson, and R. Barker, J. Org. Chem., 35 (1970) 464-467.
- 15 G. Ryan and J.H.P. Utley, Tetrahedron Lett., 29 (1988) 3699-3702.
- 16 P. Finch and Z. Merchant, J. Chem. Soc., Perkin Trans. 1, (1975) 1682-1686.
- 17 W.G. Henderson, M.J. How, G.R. Kennedy, and E.F. Mooney, Carbohydr. Res., 28 (1973) 1-12.
- 18 M. van Duin, J.A. Peters, A.P.G. Kieboom, and H. van Bekkum, Tetrahedron, 40 (1984) 2901-2911.
- 19 J. Böeseken, Adv. Carbohydr. Chem., 4 (1949) 189-210.
- 20 C.F. Bell, R.D. Beauchamp, and E.L. Short, Carbohydr. Res., 185 (1989) 39-50.
- 21 M. Makkee, A.P.G. Kieboom, and H. van Bekkum, Carbohydr. Res., 138 (1985) 225-236.
- 22 M. van Duin, J.A. Peters, A.P.G. Kieboom, and H. van Bekkum, Tetrahedron, 41 (1985) 3411-3421.
- 23 M. van Duin, J.A. Peters, A.P.G. Kieboom, and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas*, 105 (1986) 488-493.
- 24 H. Nöth and B. Wrackmeyer, in P. Diehl (Ed.), NMR Basic Principles and Progress, Vol. 14, 1978, p. 6.
- 25 A. Abragam, The Principles of Nuclear Magnetism, Clarendon Press, Oxford, 1961.
- 26 S. Chapelle and J.F. Verchere, Tetrahedron, 44 (1988) 4469-4482.