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Complex formation between polyols and rare earth cations. The crystal structure of galactitol · $2PrCl_3 \cdot 14\ H_2O$ *

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ABSTRACT

Alditols form stronger complexes with Nd^{3+}, Sm^{3+}, and Eu^{3+} than with La^{3+} cations, but weaker ones with the higher lanthanides. There is a clear relationship between ionic radii and stability constants. Chromatographic ion-exchange columns can be smaller when prepared with Nd^{3+} rather than the usual Ca^{2+} columns. Galactitol, alone amongst the hexitols, can form 1:2 complexes with lanthanide ions. The crystal structure of galactitol·$2PrCl_3 \cdot 14H_2O$ has been determined.

INTRODUCTION

Many polyols are readily separated from each other by chromatography on a cation-exchange column in the calcium form[2,3]. Petruš et al.[4] have shown that alditols, but not reducing sugars, complex more strongly with La^{3+} than with Ca^{2+} cations; a better separation is achieved on a La^{3+} column, particularly of those alditols which have a *threo–threo* sequence of hydroxyl groups[5]. Reuben[6] found stability constants for complexing of xylitol with Pr^{3+}, Nd^{3+}, and Eu^{3+} (2.0, 4.0, and 3.8 M^{-1}, respectively) much higher than the value (1.2 M^{-1}) reported[7] for Ca^{2+}. A recent paper on HPLC separation of polyols[8] indicates that complex formation of alditols is much stronger with Pr^{3+} than with La^{3+} cations. This appears surprising since all the rare earth metals have similar chemical properties and electronic configurations, and would be expected to show similar behaviour on complex formation. Hence, it appeared of interest to have a closer look at the complexing properties of the lanthanide cations with alditols.

RESULTS AND DISCUSSION

Complexing of pentitols and hexitols with all of the rare earth cations (except prometheum, which is not readily available, and lutetium, which is very expensive)

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* Complexes of Carbohydrates with Metal Cations, Part XVII. For Part XVI, see ref. 1.

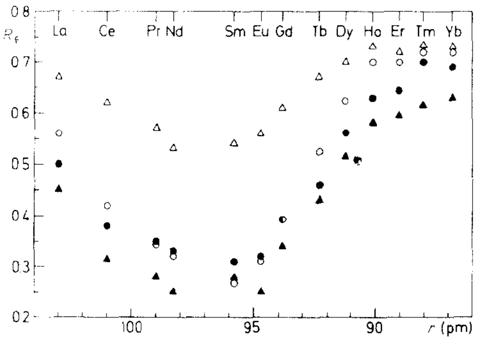

Fig. 1. R_f values on TLC plates versus ionic radii: △, mannitol; ○, galactitol; ●, glucitol; ▲, iditol.

was tested by TLC on plates coated with a cation-exchange resin[9]. The stronger the complex formation, the lower is the R_f value. The results for mannitol, galactitol, glucitol, and iditol are shown in Fig. 1. For each alditol the R_f values lie on a smooth curve, and each curve has a pronounced minimum at Nd^{3+}–Eu^{3+}. The higher lanthanides complex weakly and there is little change beyond Ho^{3+}; Lu^{3+} would, undoubtedly, have given values similar to those found for Yb^{3+}. Xylitol behaves similarly. The R_f values of other alditols and polyols also show a minimum in the same position, but it is less pronounced; these values are shown in Table I. Those of mannitol, galactitol, glucitol, and iditol are not included in Table I; they can be readily obtained from Fig. 1.

Such a maximum in the complexing ability of lanthanides is unusual. There is one reported example of 4-*tert*-butylbenzo-15-crown-5, the maximum being at Ce^{3+}–Sm^{3+}, but here we are dealing with a ligand that has a cavity of defined dimensions[10]. For highly flexible alditols, such behaviour is unexpected. The chemical properties of the lanthanides being so similar, the reason for this behaviour must be a physical property which varies regularly in the series from one cation to the other. The ionic radius is such a property; hence, in Fig. 1, the R_f values were plotted versus the hexa-coordinated ionic radii[11]. It has been stated before[3] that the best ionic radius for complex formation with polyols is ~ 1.0–1.1 Å. The lanthanides now give a much closer definition: the best ionic radius is found to be 0.95–0.98 Å. Ions smaller than 0.9 Å complex weakly.

The importance of the ionic radius for complex formation is further illustrated by the behaviour of Y^{3+}. Yttrium is not a lanthanide but is above lanthanum in the periodic table; its ionic radius (0.90 Å) is the same as that of Ho^{3+} and its R_f values are similar: 0.77 for mannitol, 0.70 for galactitol, 0.63 for glucitol, and 0.61 for iditol. Similar R_f values for Y^{3+} were also recorded by Hämäläinen and Lönnberg[12].

The behaviour of galactitol is somewhat divergent. Its complexing ability is increased more in the Nd–Eu region than that of the other hexitols. With Ca^{2+}, La^{3+}, and the higher lanthanides, it shows higher R_f values than does glucitol but, in the region of the minimum R_f values, it complexes as well, and even better,

TABLE I

R_f values of some polyols on a TLC plate prepared with a lanthanide nitrate

Polyol	La	Ce	Pr	Nd	Sm	Eu	Dy	Tm	Yb
Xylitol	0.48	0.46		0.39	0.33	0.30	0.55	0.62	0.65
–, 1-deoxy		0.43							
Ribitol	0.75			0.70					
Arabinitol	0.65	0.60		0.54					
–, 1-deoxy		0.59		0.54					
Allitol	0.78			0.69					
Altritol	0.66	0.58		0.50					
Galactitol, 1-deoxy	0.58	0.55		0.46					
Glucitol, 6-deoxy		0.37		0.29					
meso-glycero-gulo- Heptitol		0.42		0.28					
D-*glycero-*L-*gulo-* Heptitol		0.41		0.29					
Glucose	0.87			0.87			0.85		
Fructose	0.71	0.73	0.74	0.74					
epi-Inositol	0.39	0.34		0.28	0.15	0.23	0.51		0.57
1,6-Anhydro-β-D-allopyranose	0.27	0.27		0.30	0.09	0.14	0.30		0.36

than does glucitol. The best site for complex formation in alditols is a *threo–threo* sequence of three hydroxyl groups[5]; galactitol lacks such an arrangement. Earlier studies[5] with Eu^{3+} have shown that galactitol, in contrast to arabinitol and altritol, complexes predominantly at O-1,O-2,O-3; in the alternative complexing at O-2,O-3,O-4, there would be two *gauche* arrangements in the carbon chain (which do not occur in arabinitol or altritol). For galactitol, the greatest lanthanide-induced shift in the NMR spectrum is found at H-2; for glucitol, at H-3. In most alditols, the primary hydroxyl group does not take part in complex formation with cations: 1-deoxyxylitol, 1-deoxyarabinitol, and 6-deoxyglucitol have the same R_f values on Nd^{3+} plates as their parent alditols (see Table I), just as on Ca^{2+} plates[14]. However, 1-deoxygalactitol behaves differently: even with Ca^{2+}, it has a slightly higher R_f value (0.67) than galactitol (0.64); the difference is substantial on Ce^{3+} (0.55 versus 0.42) and Nd^{3+} plates (0.46 versus 0.32). Clearly, in the case of galactitol, the primary hydroxyl groups are involved in complex formation; even the loss of one hydroxyl group substantially affects complex formation. Galactitol being symmetrical, complexing can equally occur on 0-4,0-5,0-6; it is suggested that, with cations which form strong complexes, a considerable proportion of the 1:2 complex is formed, having cations attached to O-1,O-2,O-3 and O-4,O-5,O-6. In contrast to the other hexitols, this double complexing occurs in the (most stable) planar zigzag conformation. It requires a *threo* configuration of O-2,O-3 and O-4,O-5; galactitol has this configuration; hence, of all the pentitols and hexitols, galactitol alone will form a substantial proportion of the 1:2 complex.

Our many attempts to form crystalline adducts from glucitol and iditol and various salts have been uniformly unsuccessful. However, when we mixed aqueous solutions of galactitol with ethanolic solutions containing two equivalents of

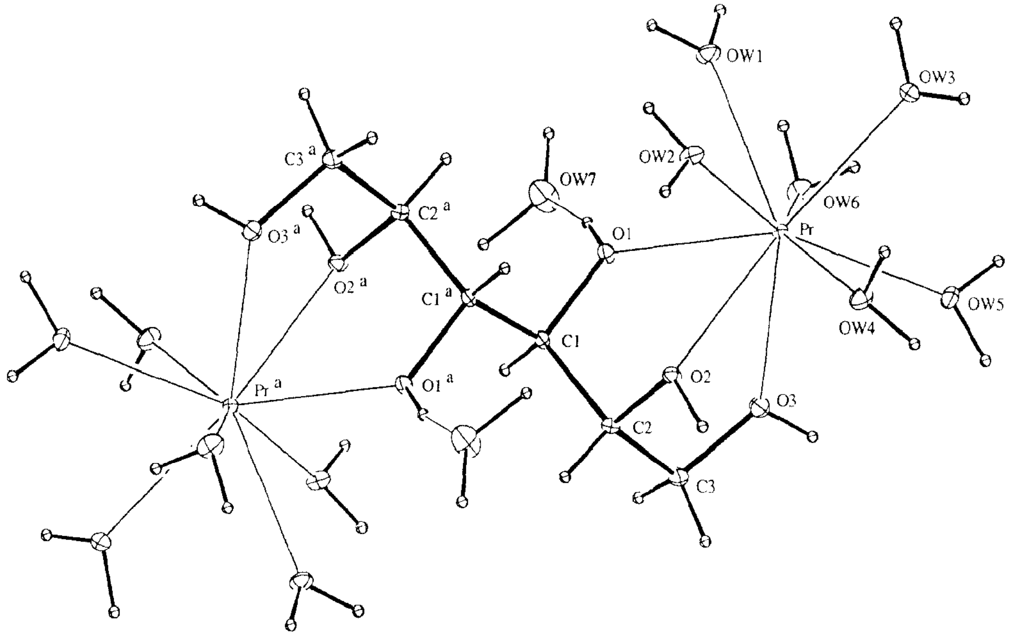

Fig. 2. ORTEP drawing of galactitol·$2PrCl_3$·$14H_2O$.

various metal chlorides, crystalline compounds separated. With $CaCl_2$, $LaCl_3$, and $EuCl_3$, very small crystals were obtained; however, with $PrCl_3$, large crystals formed which were suitable for X-ray crystal analysis. This analysis, fully reported in the next section, showed that the hexitol is, indeed, in the planar zigzag form, with two cations attached to O-1,O-2,O-3 and O-4,O-5,O-6 ($O3^a$, $O2^a$, and $O1^a$ in Fig. 2), respectively. This analysis, therefore, proves that in alditols three consecutive hydroxyl groups in a *threo–threo* configuration are involved in complex formation, a conclusion previously derived only from NMR data[5,7]. The adduct with $LaCl_3$ also contained two La^{3+} cations, but the one formed with $CaCl_2$ had a ratio of 1 : 1. When only one equivalent of $CaCl_2$ was used, galactitol crystallized out.

The behaviour of xylitol is also anomalous. On Ca^{2+} and La^{3+} plates, it is retained more strongly than glucitol[15], probably because complexes can be formed, by 120° rotation, from two equivalent enantiomorphous conformations; or simply because xylitol is smaller than glucitol. In the Nd–Eu minimum, however, xylitol has higher R_f values than glucitol, for reasons not understood.

There is little difference between the complexing ability of Nd^{3+}, Sm^{3+}, and Pr^{3+}; we choose neodymium for column separations because it is the least expensive. However, galactitol and glucitol are not separated from each other; if both are present, Ce^{3+} is recommended (which is even less expensive) for columns, though complexing is somewhat weaker. Caruel et al.[8] showed good separation of galactitol and glucitol in HPLC on a column of Pr^{3+}; the difference between their results and ours may be due to the higher temperature (50°C) used for HPLC, or to the different ion-exchange resin used. The two heptitols (D-*glycero*-L-*gulo*- and *meso*-*glycero*-*gulo*-) that we were unable to separate on Ca^{2+} or La^{3+} columns[16] were not separated on any of the lanthanide columns either.

It is obvious that the higher capacity factors of Nd^{3+}, Sm^{3+}, or Pr^{3+} columns allow the use of smaller chromatographic columns, compared to Ca^{2+}. We have published[2] conditions suitable for the industrially significant separation of glucitol and mannitol on a calcium column. Now we have reduced the size of the column to one-half, converted it into the Nd^{3+} form, and eluted 2.5 times the amount of the hexitol mixture; a similar separation was achieved. Hence, we recommend Nd^{3+} columns for this system. The cost of the metal is about the same as the cost of the ion-exchange resin, but the reduction in the size of the column makes it cheaper. The money is spent on the metal which can be fully recovered, rather than on the resin which deteriorates in use. Moreover, lanthanides can be obtained with purity of 99.0% or less at prices much lower than those of the pure elements. Such a grade is quite suitable for chromatographic separations, as the impurities are other lanthanides which do not interfere with complex formation.

The other industrially interesting separation, that of glucose and fructose, is not substantially improved by the use of rare earth metals.

For comparison, the R_f values of *epi*-inositol and 1,6-anhydro-β-D-allopyranose on rare-earth metal TLC plates were also determined. These compounds are typical representatives of six-membered rings bearing three vicinal hydroxyl groups in an *ax,eq,ax* arrangement but lacking the flexibility of the alditols. The minimum in the R_f values (Table I) is sharper at Sm^{3+}–Eu^{3+} than that of the alditols; the optimum ionic radius is 0.95–0.96 Å. However, samarium or europium are not recommended for preparative separations because of their high cost.

CRYSTAL STRUCTURE DETERMINATION

Crystal data. — $C_6H_{14}O_6 \cdot 2PrCl_3 \cdot 14H_2O$, M 928.9, space group $P\bar{1}$; $a = 8.046(2)$, $b = 9.765(3)$, $c = 10.425(3)$ Å; $\alpha = 88.42(2)$, $\beta = 71.76(2)$, $\gamma = 87.23(2)°$; $V = 776.8(4)$ Å^3, $D_c = 1.99$ g·cm^{-3}, $Z = 1$, $\mu_{Mo} = 36.77$ cm^{-1}, $2\theta_{max} = 50°$. The sample used was a roughly equidimensional fragment ~0.2 mm in size, broken from a large single triclinic crystal. The number of reflexions was 2640 considered observed out of 2742 unique data. Final residuals R and R_w were 0.024 and 0.038.

Structure determination. — Reflection data were measured with an Enraf–Nonius CAD-4 diffractometer in $\theta/2\theta$ scan mode, using graphite-monochromatized molybdenum radiation (λ 0.7107 Å). Absorption corrections were not applied. Reflections with $I > 3\sigma(I)$ were considered observed. The structure was determined by Patterson and Fourier methods. Hydrogen atoms were located in a difference Fourier, and were assigned thermal parameters equal to those of the atom to which they were bonded. Positional and anisotropic thermal parameters

TABLE II

Atomic parameters (other than hydrogen) for galactitol·$2PrCl_3 \cdot 14H_2O$

Atom	x/a	y/b	z/c	B_{eq} [a]
Pr	0.14305(2)	0.24766(1)	0.20994(1)	1.44(1)
Cl-1	0.3587(1)	0.4627(1)	−0.2378(1)	2.82(2)
Cl-2	−0.3731(1)	−0.0243(1)	0.2819(1)	1.22(3)
Cl-3	−0.2197(1)	0.2386(1)	−0.0930(1)	3.36(3)
O-1	−0.0288(3)	0.3325(2)	0.4364(2)	1.95(6)
O-2	0.2724(3)	0.4390(2)	0.3046(2)	1.95(6)
O-3	0.2948(4)	0.1826(3)	0.3878(3)	3.24(8)
C-1	0.0389(4)	0.4283(3)	0.5085(3)	1.73(8)
C-2	0.2370(4)	0.4199(3)	0.4482(3)	1.91(8)
C-3	0.3236(5)	0.2844(4)	0.4741(4)	2.64(10)
OW-1	−0.1747(3)	0.2492(3)	0.2333(3)	2.95(8)
OW-2	0.0491(3)	0.4721(2)	0.1313(3)	2.61(7)
OW-3	0.1066(4)	0.1578(3)	0.0002(3)	3.46(8)
OW-4	0.3936(3)	0.3441(3)	0.0330(2)	2.87(7)
OW-5	0.3565(3)	0.0520(3)	0.1269(3)	2.77(7)
OW-6	0.0035(4)	0.0325(3)	0.3320(3)	3.44(8)
OW-7	−0.2632(5)	0.1942(4)	0.6220(3)	5.05(11)

[a] B_{eq}(Å^2) is the isotropic equivalent of the anisotropic temperature factor.

for the non-hydrogen atoms were refined using full-matrix least squares. Reflection weights used were $1/\sigma^2(F_o)$, with $\sigma(F_o)$ being derived from $\sigma(I_o) = [\sigma^2(I_o) + (0.04I_o)^2]^{1/2}$. The weighted residual is defined as $R_w = (\Sigma w\Delta^2/\Sigma wF_o^2)^{\frac{1}{2}}$. Atomic scattering factors were from International Tables for X-ray Crystallography[17]. Structure solutions used parts of the MULTAN-80 package[18], and refinement used BLOCKLS, a local version of ORFLS[19]. ORTEP-II (ref. 20), running on a Macintosh IIcx, was used for the structural diagram, and an IBM 300 computer was used for the calculations.

The structure and atom numbering scheme is shown in Fig. 2. The numbering is not by carbohydrate conventions, but crystallographic: the unit being centrosymmetrical, the same numbers were allocated to corresponding atoms in the two asymmetric half-units. Atomic parameters are given in Table II and selected bond length, angles, and torsional angles are shown in Table III*.

There is a crystallographic centre of symmetry in the C-1–C-1^a bond of the alditol, so the asymmetric unit consists of $C_3H_7O_3 \cdot PrCl_3 \cdot 7H_2O$. Each praseodymium atom is co-ordinated to nine oxygen atoms, three from the alditol and six from water molecules, with Pr–O distances from 2.473 to 2.571 Å. The seventh water molecule is hydrogen-bonded by the hydroxyl hydrogen on O-1. As would be expected, there is an extensive network of hydrogen bonds involving

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* Tables of positional and anisotropic thermal parameters, and bond distances, angles and torsional angles, as well as observed and calculated structure factors, are deposited with, and may be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, Netherlands. Reference should be made to No. BBA/DD/526/*Carbohydr. Res.*, 241 (1993) 1–8.

TABLE III

Bond lengths (Å), bond angles (degrees), and selected torsion angles (degrees) (esd in parentheses)

Bond	Bond length	Bond	Bond length
Pr–O-1	2.475(2)	Pr–OW-6	2.545(3)
Pr–O-2	2.545(2)	C-1–C-2	1.518(4)
Pr–O-3	2.571(3)	C-2–C-3	1.522(5)
Pr–OW-1	2.491(2)	C-1–C-1^a	1.535(6)
Pr–OW-2	2.485(2)	C-1–O-1	1.443(4)
Pr–OW-3	2.484(2)	C-2–O-2	1.442(4)
Pr–OW-4	2.473(2)	C-3–O-3	1.432(4)
Pr–OW-5	2.489(2)		
Bonds	Bond angles	Bonds	Bond angles
O-1–C-1–C-2	106.9(2)	C-2–C-3–O-3	108.8(3)
C-1–C-2–O-2	105.7(2)	O-1–C-1–C-1^a	108.2(3)
O-2–C-2–C-3	108.9(3)	C-2–C-1–C-1^a	112.2(3)
C-1–C-2–C-3	114.7(3)		
Bonds	Torsion angles	Bonds	Torsion angles
C-2^a–C-1^a–C-1–O-1	62.2(4)	O-1–C-1–C-2–O-2	52.6(3)
C-1^a–C-1–C-2–C-3	174.2(3)	C-1–C-2–C-3–O-3	75.3(4)
C-1^a–C-1–C-2–O-2	−65.9(4)	O-2–C-2–C-3–O-3	−42.8(4)
O-1–C-1–C-2–C-3	−67.3(3)		

[a] Indicates the symmetry transformation $-x, 1-y, 1-z$.

hydroxyl groups, water molecules, and chloride ions. The carbon chain of galactitol is in a near-ideal planar zigzag form, but the two terminal carbon atoms are not fully staggered with their neighbours: the C-1–O-1 and the C-3–O-3 bonds are not strictly parallel.

EXPERIMENTAL

General methods. — Polygram Ionex-25 SA sheets (Macherey-Nagel) were immersed in deionized water, then in aq 5% lanthanide nitrate for 1 h, and then washed with deionized water several times. Nitrates were used, rather than chlorides, because it was found that, on plates treated with europium, and even more with praseodymium, chloride solution, the R_f values were much higher than on plates dipped into the nitrates. The chlorides are not fully dissociated in aqueous solution. For this reason, the stability constants reported by Reuben[6], which were determined in solutions of lanthanide chlorides, are probably too low.

Separation of D*-mannitol from* D*-glucitol.* — A mixture (1.0 g) of equal amounts of mannitol and glucitol was chromatographed on a column (2.3 × 10 cm) of Dowex 50W-X4 resin in the Nd^{3+} form with water as eluant at a rate of 40–50 mL/h; 10-mL fractions were collected. Fractions 3–5 contained mannitol, fraction 6 contained mannitol contaminated with a trace of glucitol, and fractions 6–10 contained glucitol. The separation is even better when 30% MeOH is used as eluant[2].

Preparation of galactitol complexes — To concentrated aqueous solutions of galactitol were added concentrated ethanolic solutions containing 2 equiv of metal chlorides. The mixtures were kept in a desiccator over concd H_2SO_4, with occasional additions of EtOH, until they crystallized. Anal. Calcd for $C_6H_{14}O_6 \cdot 2PrCl_3 \cdot 14H_2O$: C, 7.76; H, 4.57. Found: C, 7.69; H, 4.65. Calcd for $C_6H_{14}O_6 \cdot 2LaCl_3 \cdot 14H_2O$: C, 7.76; H, 4.58. Found: C, 7.76; H, 4.13. Calcd for $C_6H_{14}O_6 \cdot EuCl_3 \cdot 3H_2O$: C, 15.19; H, 4.24. Found: C, 15.39; H, 4.14. Calcd for $C_6H_{14}O_6 \cdot CaCl_2 \cdot 6H_2O$: C, 17.96; H, 6.49. Found: C, 18.00; H, 6.05.

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