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# A $^{13}$C-n.m.r. study of the tungstate and molybdate complexes of perseitol, galactitol, and D-mannitol*

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## ABSTRACT

Perseitol (D-*glycero*-D-*galacto*-heptitol) forms dinuclear complexes with tungstate that have a stability higher than those of galactitol and D-mannitol, and all of the formation constants are three orders of magnitude higher than those for molybdate. The $^{13}$C-n.m.r. data showed that the tungstate and molybdate complexes had similar structures that involved four vicinal hydroxyl groups. The sites of chelation involved the *galacto* group in galactitol and perseitol, and the *arabino* group HO-3,4,5 and HO-6 in D-mannitol. D-Mannitol and perseitol formed pairs of isomeric complexes that involved the same site of chelation but in reversed orientations.

## INTRODUCTION

Alditols are well-known complexing agents for molybdate $MoO_4^{2-}$ and tungstate $WO_4^{2-}$ ions in aqueous acidic solution. Dinuclear anionic complexes are formed as indicated by a series of polarimetric and potentiometric studies[1-8]. The crystal structures of D-mannitol[9,10] and erythritol[11] molybdate complexes showed that the chelation involved four vicinal hydroxyl groups. $^{13}$C-N.m.r. studies demonstrated that the molybdate complexes of most polyols retained this structure in solution, and attempts were made to classify different types of tungstate[8] and molybdate[12,13] complexes. $^{95}$Mo-N.m.r. spectroscopy revealed two non-equivalent Mo atoms[14] in complexes of aldoses of the *lyxo–manno* series, which chelated molybdate as tetradentate donors.

Tungstate complexes have been used for the chromatographic separation of carbohydrates[15], and alditols are useful complexing agents in the acidimetric titration of tungstate[16]. The thermodynamic data showed that the most stable complex was formed with perseitol (D-*glycero*-D-*galacto*-heptitol). We now report on the stabilities and structures of the molybdate and tungstate complexes of perseitol. Since two tetritol

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groups (*galacto* or *manno*) were possible sites for the chelation, galactitol and D-mannitol were also studied as model compounds.

## RESULTS

The formation constants of the complexes were determined potentiometrically by the method described[14,16]. Two equilibria were observed in molybdate–alditol (L)–H$^+$ systems: $2\,MoO_4^{2-} + L + 2\,H^+ \rightleftharpoons (2,1,2)^{2-}$

$2\,MoO_4^{2-} + L + 3\,H^+ \rightleftharpoons (2,1,3)^-$

whereas only the $(2,1,2)^{2-}$ complexes were detected with tungstate.

The corresponding equilibrium constants $K_{212}$ and $K_{213}$ defined the *formation constants* of the complexes[14]. The equilibrium between the molybdate (2,1,2) and (2,1,3) species was characterised by the p$K_a$ value relative to the reaction:

$(2,1,3)^- \rightleftharpoons (2,1,2)^{2-} + H^+$.

The values of the formation constants are presented in Table I. Data obtained using molybdate confirmed the result obtained with tungstate[16], namely, that perseitol formed complexes that were more stable than those of galactitol and D-mannitol.

*N.m.r. spectroscopy.* Identification of the sites of chelation is based on the deshielding of carbons that carry the chelating hydroxyl groups[8,13,14]. The assignments of the $^{13}C$ resonances in the spectra of complexed alditols were achieved through 2D-heterocorrelated $^{13}C$–$^1H$-n.m.r. experiments and supported by the finding that the carbons involved in chelation had increased $^1J_{C,H}$ values[13,14].

Galactitol (Table II) gave a single tungstate complex characterised by six $^{13}C$ resonances. The values of the chemical shifts demonstrated that chelation involved HO-2,3,4,5 and that the symmetry of the ligand was destroyed by complexation. There was a remarkable analogy between $^{13}C$-n.m.r. spectra of the Mo and W species. The variations of chemical shifts due to complexation were similar for both elements, but the coupling constants were slightly higher for the tungstate complex. As for the molybdate complex[13], the asymmetry of the complexed ligand can be attributed to twisting at C-3 or C-4.

The spectra of the tungstate and molybdate complexes of D-mannitol also showed strong analogies (Table III) that indicated similar structures. Each anion formed two

TABLE I

Formation constants[a] of tungstate and molybdate complexes of alditols

| | *Metal* | *Perseitol* | *Galactitol* | D-*Mannitol* |
|---|---|---|---|---|
| log $K_{212}$ | W | 20.35[b] | 20.10[b] | 19.60[b] |
| log $K_{212}$ | Mo | 17.60[c] | 17.30[d] | 16.70[c] |
| p$K_a$ | Mo | 3.60[c] | 3.60[d] | 4.10[c] |
| log $K_{213}$ | Mo | 21.20[c] | 20.90[d] | 20.80[c] |

[a] At 25° in 0.1M KCl. log $K_{xyz}$ is the equilibrium constant for the reaction (M is Mo or W): $x\,MO_4^{2-} + y\,L + z\,H^+ \rightleftharpoons (x,y,z)^{(2x-z)-}$. Accuracy: log $K \pm 0.05$. [b] Ref. 16. [c] This work. [d] Ref. 13.

TABLE II

100.62-MHz $^{13}$C-n.m.r. chemical shifts ($\delta$ in p.p.m.) and $^1J_{C,H}$ values (Hz) for the tungstate and molybdate complexes of galactitol

| | *C-1* | *C-2* | *C-3* | *C-4* | *C-5* | *C-6* |
|---|---|---|---|---|---|---|
| *Galactitol*[a] | | | | | | |
| $\delta$ | 65.5 | 71.5 | 72.1 | 72.1 | 71.5 | 65.5 |
| *Tungstate complex* | | | | | | |
| $\delta$ | 65.3 | 79.0 | 91.4 | 82.9 | 82.4 | 64.5 |
| $^1J_{C,H}$ | 143 | 147 | 150 | 150 | 147 | 142 |
| $\Delta\delta$ | −0.2 | 7.5 | 19.3 | 10.8 | 10.9 | −1.0 |
| *Molybdate complex*[b] | | | | | | |
| $\delta$ | 64.7 | 79.4 | 91.8 | 83.7 | 83.3 | 65.5 |
| $^1J_{C,H}$ | 143 | 144 | 149 | 147 | 146 | 143 |
| $\Delta\delta$ | −0.8 | 7.9 | 19.7 | 11.6 | 11.8 | 0.0 |

[a] $^1J_{C,H}$ 141 Hz for C-1/6; $\delta$ assigned from the literature[17]. Accuracy: $\delta$ ±0.1 p.p.m.; $J$ ±1 Hz. [b] Ref. 13.

TABLE III

100.62-MHz $^{13}$C-n.m.r. chemical shifts ($\delta$ in p.p.m.) and $^1J_{C,H}$ values (Hz) for the tungstate and molybdate complexes of D-mannitol

| | *C-1* | *C-2* | *C-3* | *C-4* | *C-5* | *C-6* |
|---|---|---|---|---|---|---|
| D-*Mannitol*[a] | | | | | | |
| $\delta$ | 65.8 | 74.2 | 71.6 | 71.6 | 74.2 | 65.8 |
| *W complex* $M_1$ | | | | | | |
| $\delta$ | 65.3 | 72.9 | 81.9 | 82.7 | 92.5 | 71.0 |
| $^1J_{C,H}$ | 143 | 143 | 147 | 150 | 150 | 145 |
| $\Delta\delta$ | −0.5 | −1.3 | 10.3 | 11.1 | 18.3 | 5.2 |
| *W complex* $M_2$ | | | | | | |
| $\delta$ | 65.1 | 73.7 | 79.1 | 91.6 | 82.7 | 73.1 |
| $^1J_{C,H}$ | 143 | 143 | 144 | 150 | 150 | 147 |
| $\Delta\delta$ | −0.7 | −0.5 | 7.5 | 20.0 | 8.5 | 7.3 |
| *Mo complex* $M_1$[b] | | | | | | |
| $\delta$ | 65.4 | 73.1 | 83.3 | 83.8 | 93.1 | 71.7 |
| $^1J_{C,H}$ | 142 | 142 | 145 | 149 | 148 | 145 |
| $\Delta\delta$ | −0.4 | −0.9 | 11.7 | 12.2 | 18.9 | 5.9 |
| *Mo complex* $M_2$[b] | | | | | | |
| $\delta$ | 65.9 | 74.1 | 80.3 | 92.3 | 83.8 | 74.1 |
| $^1J_{C,H}$ | 142 | 142 | 143 | 148 | 149 | 145 |
| $\Delta\delta$ | 0.1 | −0.1 | 8.7 | 20.7 | 9.6 | 8.3 |

[a] $^1J_{C,H}$ 141 Hz for C-1/6; $\delta$ assigned from the literature[17]. Accuracy: $\delta$ ±0.1 p.p.m.; $J$ ±1 Hz. [b] Ref. 13.

complexes ($M_1$ and $M_2$) that involved the *arabino* group HO-3,4,5 and HO-6. The deshielding pattern characteristic of the galactitol species (*i.e.*, 7–20–10–10 p.p.m.) was also observed for the D-mannitol complexes. However, for a given pair of complexes, these patterns were reversed, which suggested that the isomerism was due to the asymmetry of the chelating site, in which C-3,6 bore different substituents, in contrast to

C-2,5 in the galactitol analogues. There was no evidence for the existence of a D-mannitol complex that involved the *manno* group.

The $^{13}$C-n.m.r. spectrum of perseitol was assigned readily from data in the literature[17] (Table IV). The addition of tungstate and acid generated 14 new signals, which indicated the formation of two complexes in unequal proportions, $P_1$ (60%) and $P_2$ (40%). Signals for the uncomplexed ligand were absent, which confirmed the high stabilities of the complexes. Three weak signals (93.3, 71.9, and 65.8 p.p.m.) revealed <10% of another minor species that was not considered in this study.

The spectrum of the major species $P_1$ showed that tungstate was bound to the *galacto* group HO-2,3,4,5, and the pattern of variations of chemical shifts was typical of that for a *galacto* chelating-site ($\Delta\delta$ 20.7 p.p.m. for C-3). Since the substituents at C-2,5 were different, the complex $P_2$ was assumed to be the isomer of $P_1$, as in the $M_1$-$M_2$ pair. Assignments for $P_2$ were therefore made on the basis that the pattern of variations of chemical shifts was reversed in $P_1$ and $P_2$ ($\Delta\delta$ 21.3 p.p.m. for C-4).

TABLE IV

100.62-MHz $^{13}$C-n.m.r. chemical shifts ($\delta$ in p.p.m.) and $^1J_{C,H}$ values (Hz) for the tungstate and molybdate complexes of perseitol

| | *C-1* | *C-2* | *C-3* | *C-4* | *C-5* | *C-6* | *C-7* |
|---|---|---|---|---|---|---|---|
| *Perseitol*[a] | | | | | | | |
| $\delta$ | 65.3 | 72.3 | 71.3 | 70.3 | 71.2 | 73.0 | 65.3 |
| *W complex* $P_1$ | | | | | | | |
| $\delta$ | 65.9 | 79.5 | 92.0 | 83.2 | 82.9 | 73.0 | 65.1 |
| $^1J_{C,H}$ | 142 | 146 | 150 | 152 | 148 | 144 | 143 |
| $\Delta\delta$ | 0.6 | 7.2 | 20.7 | 12.9 | 11.7 | 0.0 | −0.2 |
| *W complex* $P_2$ | | | | | | | |
| $\delta$ | 65.2 | 81.8 | 83.3 | 91.6 | 79.1 | 73.8 | 65.0 |
| $^1J_{C,H}$ | 143 | 147 | 152 | 151 | 146 | 144 | 143 |
| $\Delta\delta$ | −0.1 | 9.5 | 12.0 | 21.3 | 7.9 | 0.8 | −0.3 |
| *Mo complex* $P_1$ | | | | | | | |
| $\delta$ | 66.4 | 80.1 | 92.7 | 84.1 | 83.2 | 73.4 | 65.6 |
| $^1J_{C,H}$ | 143 | 145 | 147 | 149 | 145 | 143 | 142 |
| $\Delta\delta$ | 1.1 | 7.8 | 21.4 | 13.8 | 12.0 | 0.4 | 0.3 |
| *Mo complex* $P_2$ | | | | | | | |
| $\delta$ | 66.0 | 84.0 | 84.3 | 92.4 | 80.5 | 74.2 | 65.3 |
| $^1J_{C,H}$ | 142 | 147 | 148 | 149 | 145 | 143 | 143 |
| $\Delta\delta$ | 0.7 | 11.7 | 13.0 | 22.1 | 9.3 | 1.2 | 0.0 |
| *Perseitol*[b] | | | | | | | |
| $\delta$ | 64.6 | 71.5 | 70.5 | 69.5 | 70.4 | 72.2 | 64.6 |
| *Mo complex* $P_1$[b] | | | | | | | |
| $\delta$ | 64.7 | 78.7 | 91.1 | 82.8 | 81.8 | 71.8 | 64.4 |
| $\Delta\delta$ | 0.1 | 7.2 | 20.6 | 13.3 | 11.4 | −0.4 | −0.2 |
| *Mo complex* $P_2$[b] | | | | | | | |
| $\delta$ | 64.7[c] | 72.8 | 79.2 | 91.1 | 83.0 | 82.6 | 63.8[c] |
| $\Delta\delta$ | 0.1 | 1.3 | 8.7 | 21.6 | 13.4 | 10.4 | −0.8 |

[a] $^1J_{C,H}$ 141 Hz for C-1/7; $\delta$ assigned from the literature[17]. Accuracy: $\delta$ ±0.1 p.p.m., $J$ ±1 Hz. [b] Ref. 12. [c] These assignments could be reversed.

For the pair of molybdate complexes (Table IV), although our spectra closely matched those reported[12], the assignments differed. The complexing sites of perseitol had been assigned from $^1$H- and $^{13}$C-n.m.r. data as HO-2,3,4,5 (the *galacto* group) in $P_1$ and HO-3,4,5,6 (the *manno* group) in $P_2$ (see Fig. 1). The second assignment appeared unlikely, since it was shown above that D-mannitol did not complex tungstate or molybdate by its *manno* group, but with the *galacto*-like group HO-3,4,5,6.

Unambiguous assignments for the $P_2$ molybdate complex were made by homonuclear 2D-$^1$H-n.m.r. experiments. The carbon-chain sequence was in agreement with literature data. However, the proposed assignments were reversed in order to verify the above tentative assignment for $P_2$. No evidence was obtained to indicate that the $P_1$–$P_2$ pair of perseitol complexes differed from those formed by alditols that possess related complexing sites such as D-arabinitol, D-mannitol, and D-glucitol[13].

Using an excess of molybdate, the $^{95}$Mo-n.m.r. spectra of perseitol–molybdate–HCl mixtures contained a sharp signal for free molybdate at $\delta$ ~0 and a new broad

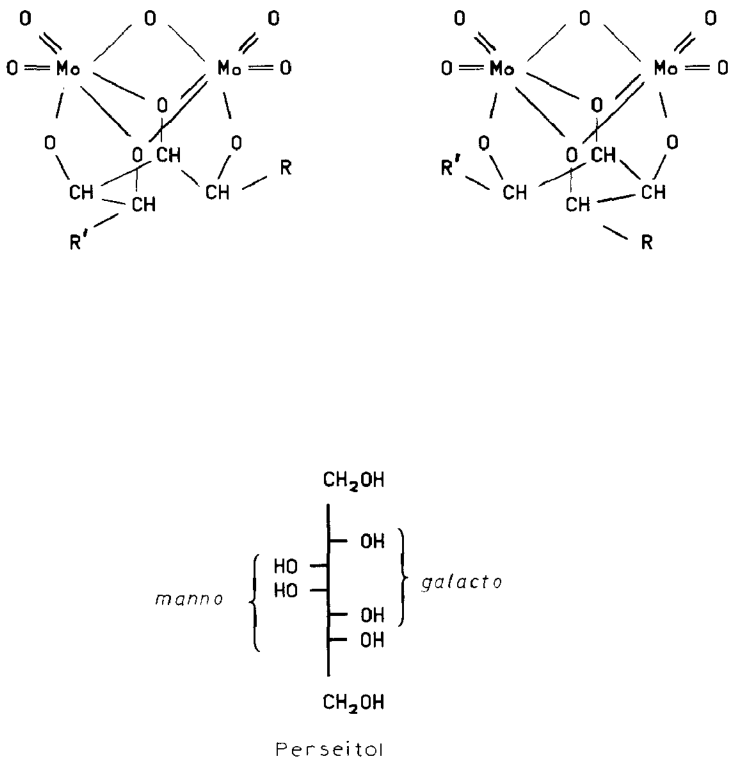

Fig. 1. Schematic representation of the chelation of the dimolybdate anion by four vicinal hydroxyl groups of an alditol molecule; R and R′ are $CH_2OH$ in galactitol, H and $CHOH\text{-}CH_2OH$ in D-mannitol, and $CH_2OH$ and $CHOH\text{-}CH_2OH$ in perseitol. When R ≠ R′, a pair of isomers is formed. The dimolybdate structure is that characterised in the complexes of D-mannitol[9,10] and erythritol[11].

signal ($\delta$ 34 ±0.5, $\Delta\nu$ ~750 Hz) attributed to the complexes. No individual signals could be characterised in these spectra, in contrast to those of complexes of some aldoses which displayed two sharper signals attributed[14] to the Mo atoms in the complex. The chemical shift agreed with Mo being in the +VI oxidation state[18] and it was in the same range as those for the complexes of aldoses of the *lyxo–manno* series[14] ($\delta$ 30 ±4 and 42 ±1) and alditols that complexed molybdate by their central *erythro* groups[13], such as galactitol ($\delta$ 34) and D-mannitol ($\delta$ 31).

## DISCUSSION

It is well established[12,13] that molybdate complexes of alditols, such as those of D-mannitol[9,10] and erythritol[11], possess two Mo atoms bridged by three oxygen atoms, two of which are triply-bonded. Each Mo atom is also bound to one oxygen atom of the ligand. In alditols that possess a central *erythro* group, the four carbons of the complexing site adopt a sickle arrangement that allows the attached hydroxyl groups to point in the same direction and form an array which does not match exactly the acceptor site[13]. Hence, the molecule must twist at one internal carbon, as shown in Fig. 1. This interpretation agrees with the finding that one of the central carbons in the ligands is more strongly deshielded ($\Delta\delta$ ~20 p.p.m.) than the other.

Perseitol and D-mannitol formed pairs of complexes with reversed deshielding patterns, that involved a *galacto* chelating site. Fig. 1 shows how a pair of isomers can be formed when the lateral carbons of the complexing site bear different substituents (R and R′). The proportions of isomers were not equal, the favoured one being that in which the more deshielded carbon was near the shortest side-chain, *i.e.*, the $CH_2OH$ group in perseitol. In contrast, one species only was formed by the symmetrical ligand galactitol (R = R′).

A comparison of the formation constants showed that the perseitol complexes were more stable than those of any other alditol, even galactitol which formed the most stable complexes known hitherto. The lower stabilities of the D-mannitol species probably reflect the loss in entropy due to the bonding of a lateral $CH_2OH$ group[13]. The increase in stability with respect to galactitol was unexpected, because the complexing sites were similar and differed only by the size of the C-5 side-chain. Molybdate complexes were about three orders of magnitude less stable than the tungstate complexes, as found for the complexes of other carbohydrates[14] and alditols[7,13].

The proposed structures allow a rationalisation of the data published on the proportions of products of the periodate oxidation of alditols complexed by tungstate[4] and molybdate[12]. In both complexes, galactitol was protected, as expected if the site of chelation was the *galacto* group. In contrast, D-mannitol gave D-arabinose as the main oxidation product (88% with molybdate), because molybdate was bound to the *arabino* group. Only traces of unreacted D-mannitol were detected, which confirmed that the *manno* group had not been protected. When perseitol was oxidised in the presence of molybdate[12], 60% of D-galactose was obtained, which showed that the *galacto* group had been protected, and only traces of D-mannose were found, whereas the proportion should have been much higher if complex $P_2$ (40% of total) had involved the *manno* group. These results accord with the finding that molybdate is not chelated by the *manno* goups of D-mannitol and perseitol.

Determination of the formation constants of the molybdate complexes provides quantitative support for the interpretation of recent results[19] on the inhibition of the molybdate-catalysed epimerisation of aldoses. It is believed that alditols scavenge the active molybdate species by complexation, thereby reducing the rate of reaction. Published data on the relative yields of the reaction D-glucose → D-mannose (pH 3.5, 3 h, 90°) indicated the order of stability to be perseitol > galactitol > D-mannitol > D-arabinitol > ribitol, in excellent agreement with the results in Table I and earlier results for D-arabinitol and ribitol[13], and confirm that the dinuclear molybdate complexes are the species responsible for the reported decrease in the rate of epimerisation.

## EXPERIMENTAL

All chemicals were of analytical grade and perseitol (Aldrich) was used as supplied. Water was de-ionised in a Millipore apparatus.

Formation constants were determined by potentiometry[14,16], based on the determination of the half-equivalence $pH_{1/2}$ values in acidimetric (HCl) titrations of disodium molybdate or tungstate solutions of known concentration that contained various amounts of alditol. Measurements were made at constant ionic strength (KCl, 0.1M).

All 1D- and 2D-n.m.r. spectra were recorded with a Bruker AM 400 spectrometer equipped with a 5-mm multinuclear probe. Solutions contained alditol (0.5 mmol) and disodium molybdate or tungstate dihydrate (1.5 mmol) in $D_2O$ (0.5 $cm^3$). Conc. HCl (0.75 mmol) was added last, in order to avoid the precipitation of tungsten trioxide.

The $^{95}$Mo-n.m.r. measurements were made as described[13,14]. For the $^{13}$C-n.m.r. experiments, the proton-coupled and -decoupled spectra were obtained with n.O.e. The chemical shifts were determined by the substitution method[20], using the trimethylsilylphosphate reference signal in $D_2O$. 2D-Heteronuclear experiments were performed[21] with polarisation transfer from $^1$H to $^{13}$C, the number of experiments being 64 × 1k. Initial assignments of $^1$H spectra of mixtures of complexes required 2D-homonuclear experiments (COSY-45)[22,23].

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